Check for updates

Volume 77 • Number S9 • October 2025

Arthritis & Rheumatology

AN OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF RHEUMATOLOGY

ABSTRACT SUPPLEMENT

ACR Convergence 2025

October 24–29, 2025

Chicago, IL

WILEY | American College of Rheumatology
Empowering Rheumatology Professionals

Table of Contents

ACR Convergence 2025 Abstract Sessions

Sunday, October 26

10:30 AM – 12:30 PM
Poster Session A
(#0001–0771)

9:30 – 11:00 AM
Plenary Session I
(#0772–0776)

1:00 – 2:30 PM
Oral Abstract Sessions
(#0777–0782) Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases
(#0783–0788) Abstracts: Orthopedics, Low Back Pain, & Rehabilitation
(#0789–0794) Abstracts: Patient Outcomes, Preferences, & Attitudes
(#0795–0800) Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis
(#0801–0806) Abstracts: Systemic Lupus Erythematosus – Treatment I
(#0807–0812) Abstracts: Systemic Sclerosis & Related Disorders-Basic Science

3:00 – 4:30 PM
Oral Abstract Sessions
(#0813–0818) Abstracts: Pain in Rheumatic Disease Including Fibromyalgia
(#0819–0824) Abstracts: Pediatric Rheumatology – Basic Science
(#0825–0830) Abstracts: Professional Education
(#0831–0836) Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction)
(#0837–0842) Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis
(#0843–0848) Abstracts: Systemic Sclerosis & Related Disorders – Clinical I

Monday, October 27

10:30 AM – 12:30 PM
Poster Session B
(#0897–1649)

8:00 – 9:30 AM
Plenary Session II
(#0849–0854)

10:00 – 11:30 AM
Oral Abstract Sessions
(#0855–0860) Abstracts: Antiphospholipid Syndrome
(#0861–0866) Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research
(#0867–0872) Abstracts: Rheumatoid Arthritis – Animal Models
(#0873–0878) Abstracts: Spondylarthritis Including Psoriatic Arthritis – Treatment I: Therapies
(#0879–0884) Abstracts: Systemic Sclerosis & Related Disorders – Clinical II
(#0885–0890) Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
(#0891–0896) Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside

1:00 – 2:30 PM
Oral Abstract Sessions
(#1650–1655) Abstracts: Cytokines & Cell Trafficking
(#1656–1661) Abstracts: Health Services Research
(#1662–1667) Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms
(#1668–1673) Abstracts: Pediatric Rheumatology – Clinical I
(#1674–1679) Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments
(#1680–1685) Abstracts: Sjögren's Disease – Basic & Clinical Science

3:00 – 4:30 PM
Oral Abstract Sessions
((#1686–1691) Abstracts: ARP I: Multidimensional Influences on Health in SLE
(#1692–1697) Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
(#1698–1703) Abstracts: Genetics, Genomics & Proteomics
(#1704–1709) Abstracts: Healthcare Disparities in Rheumatology
(#1710–1715) Abstracts: Spondylarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease
(#1716–1721) Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality

Tuesday, October 28

10:30 AM – 12:30 PM
Poster Session C
(#1770-2566)

8:00 – 9:30 AM
Plenary Session III
(#1722-1727)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

10:00 – 11:30 PM
Oral Abstract Sessions
(#1728–1733) Abstracts: Immunological Complications of Medical Therapy
(#1734–1739) Abstracts: Osteoarthritis & Joint Biology – Basic Science
(#1740–1745) Abstracts: Pediatric Rheumatology – Clinical II
(#1746–1751) Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary)
(#1752–1757) Abstracts: Spondylarthritis Including Psoriatic Arthritis – Basic Science
(#1758–1763) Abstracts: Systemic Lupus Erythematosus – Animal Models
(#1764–1769) Abstracts: Vasculitis – ANCA-Associated

1:00 – 2:30 PM
Oral Abstract Sessions
(#2567–2572) Abstracts: Epidemiology & Public Health II
(#2573–2578) Abstracts: Infection-related Rheumatic Disease
(#2579–2584) Abstracts: Innate Immunity
(#2585–2590) Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science
(#2591–2596) Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science
(#2597–2602) Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis

3:00 – 4:30 PM
Oral Abstract Sessions
(#2603–2608) Abstracts: ARP II: Perception, Prediction, and Prevention
(#2609–2614) Abstracts: Imaging of Rheumatic Diseases
(#2615–2620) Abstracts: Measures & Measurement of Healthcare Quality
(#2621–2626) Abstracts: Osteoarthritis – Clinical
(#2627–2632) Abstracts: Reproductive Issues in Rheumatic Disorders
(#2633–2638) Abstracts: Spondylarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondylarthritis

Wednesday, October 29

9:30 AM – 11:00 AM
Oral Abstract Sessions
(#2639–2644) Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization
(#2645–2650) Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III
(#2651–2656) Abstracts: Systemic Sclerosis & Related Disorders – Clinical III

11:30 AM – 1:00 PM
Oral Abstract Sessions
(#2657–2662) Abstracts: Epidemiology & Public Health I
(#2663–2668) Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye
(#2669–2674) Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics
(2675–2680) Abstracts: Pediatric Rheumatology – Clinical III
(2681–2686) Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes)
(#2687–2692) Abstracts: Spondylarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions
(2693–2698) Abstracts: Systemic Lupus Erythematosus – Treatment II
(2699–2704) Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II

Late-Breaking Abstracts

Friday, October 24

10:30 AM – 12:30 PM
Poster Session C
(#L01–L18) Late-Breaking Abstract Poster

Wednesday, October 29

Oral Session
8:00 – 9:30 AM
(#L19–L24) Late-Breaking Abstracts

Patient Perspectives

Sunday, October 26

10:30 AM – 12:30 PM
Poster Session A
(#PP01–PP08) Patient Perspectives Poster

Patient Perspectives

Tuesday, October 28

Oral Session
8:15 – 9:30 AM
(#PP09–PP13) Patient Perspectives

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Embargo Policy

All abstracts accepted to ACR Convergence are under media embargo once the ACR has notified presenters of their abstract's acceptance. They may be presented at other meetings or published as manuscripts after this time but should not be discussed in non-scholarly venues or outlets. The following embargo policies are strictly enforced by the ACR.

Accepted abstracts are made available to the public online in advance of the meeting and are published in a special online supplement of our scientific journal, *Arthritis & Rheumatology*. Information contained in those abstracts may not be released until the abstracts appear online. In an exception to the media embargo, academic institutions, private organizations, and companies with products whose value may be influenced by information contained in an abstract may issue a press release to coincide with the availability of an ACR abstract on the ACR website. However, the ACR continues to require that information that goes beyond that contained in the abstract (e.g., discussion of the abstract done as part of editorial news coverage) is under media embargo until **10:00 AM CT on October 25**. Journalists with access to embargoed information cannot release articles or editorial news coverage before this time. Editorial news coverage is considered original articles/videos developed by employed journalists to report facts, commentary, and subject matter expert quotes in a narrative form using a variety of sources (e.g., research, announcements, press releases, events, etc.).

Violation of this policy may result in the abstract being withdrawn from the meeting and other measures deemed appropriate. Authors are responsible for notifying colleagues, institutions, communications firms, and all other stakeholders related to the development or promotion of the abstract about this policy. If you have questions about the ACR abstract embargo policy, please contact ACR abstracts staff at abstracts@rheumatology.org.

Abstract Reprint (Reproduction) Policy

Copyright law covers all annual meeting abstracts published by the American College of Rheumatology. All rights reserved. No abstracts may be reproduced in any form or by any means without the prior permission of the publisher, except as permitted under section 107 and 108 of the 1976 United States Copyright Act.

For the purposes of this statement, the term "**ACR Abstracts"** refers to all annual meeting abstracts as published in *Arthritis & Rheumatology* and posted online, including the abstracts accepted for presentation during ARP sessions and the late-breaking category.

For the purposes of this statement, the term "**ACR Posters"** refers to the accepted abstract **POSTER PRESENTATIONS** as presented in the poster hall during the annual meeting. **This does not include abstract text published in the online supplement of *Arthritis & Rheumatology*.** All **ACR Posters** are the property of the ACR or the presenting author and cannot be reproduced or distributed without written permission from the ACR and the presenting author.

For the purposes of this statement, the term "reproduce" includes all forms of reproduction, including, but not limited to, print, electronic and photographed formats.

For the purposes of this statement, the term "presenting author" refers to the author who is designated as the individual who will present the work during the ACR's annual meeting, as identified through the abstract submission process.

Approval Process for ACR Abstracts

- Excerpts or the entirety of **ACR Abstracts** may not be reproduced without the prior written permission of the publisher.
- Permission requests for abstract content and other permission inquiries should be addressed to:

  Permissions Department

  c/o John Wiley & Sons, Inc.
  111 River Street
  Hoboken, NJ 07030
  Fax: 201-748-6008
  wiley.com/go/permissions
- Commercial entities seeking permission to reprint must obtain all materials from the author and/or publisher John Wiley & Sons, Inc. The ACR cannot provide any materials.

Approval Process for ACR Posters

- Reprint requests for the actual poster abstract text published in the *Arthritis & Rheumatology* supplement are considered **ACR Abstracts** and must submitted to Wiley (see approval process above).
- Requests to reproduce individual ACR posters, figures from ACR posters, or booklets of poster presentations (e.g., two or more) must be submitted via e-mail to abstractreprints@rheumatology.org.
- Poster reproduction requests must include the following:
  – Abstract ID Number
  – Abstract Title
  – Presenting Author's Name
  – A copy of Presenting Author's written approval (Please Note: An e-mail approval from Presenting Author is acceptable)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Reproducing ACR Abstracts and Posters for Dissemination Prior to ACR Convergence

- Requests to reproduce abstracts for dissemination prior to ACR Convergence *will not be approved*.
- Per the ACR Embargo Policy (see above), academic institutions, private organizations, and companies with products whose value may be influenced by information contained in an abstract may issue a press release to coincide with the availability of an abstract online.
- Permission to issue a press release does not require ACR approval. However, it must comply with the **ACR Embargo Policy;** violation of this policy may result in the abstract being withdrawn from the meeting or other measures deemed appropriate.
- For more information regarding press releases, please contact the ACR public relations department at pr@rheumatology.org.

Reproducing ACR Abstracts and Posters for Dissemination During ACR Convergence

Following approval (see approval process above), an exhibiting organization may:

- Disseminate copies of individual ACR Abstracts from its exhibit space. Booklets of abstracts (e.g., two or more) may not be produced.
- Disseminate information summaries (title/date/time/poster number) of ACR Abstracts from its exhibit space. Summaries may not reference company or product names. Requests for approval must be submitted in writing to abstractreprints@rheumatology.org.
- Presenting authors may disseminate individual copies of their ACR Poster during their assigned poster presentation time.
- Dissemination must be limited to the area directly in front of their assigned poster space and may not interfere with other poster presentations.
- An electronic copy of the poster may be provided via a QR code generated by the presenter and included on the poster

Reproducing ACR Abstracts and ACR Posters for Dissemination After ACR Convergence

ACR Abstracts

Following approval from Wiley (see approval process above), the ACR permits **ACR Abstracts** (i.e., all abstract content published in the online supplement) to be reprinted and disseminated following ACR Convergence.

- Abstracts and booklets of abstracts (e.g., two or more) must include the following statement on the front of the abstract/booklet:
  Abstract(s) reprinted from ACR Convergence held [insert meeting dates]. The American College of Rheumatology does not guarantee, warrant, or endorse any commercial products or services. Reprinted by [insert name of supporting company].
- Booklets cannot contain corporate or product logos or any advertisements. No exceptions.

ACR Posters

Following approval from the presenting author and the ACR (see approval process above), copies of actual ACR poster presentations (i.e., the actual graphic file of the poster) may be reproduced.

1. Reprint requests for the actual poster abstract text published in the *Arthritis & Rheumatology* supplement are considered **ACR Abstracts** and must be submitted to Wiley (see approval process above).

- **IMPORTANT: The ACR does not retain and cannot provide poster presentation images.**
- The following statement must be listed under each Poster reprint:
  Reprinted from ACR Convergence held [insert meeting dates]. The American College of Rheumatology does not guarantee, warrant, or endorse any commercial products or services. Reprinted by [insert name of supporting company].

Use of the ACR Name

The names, insignias, logos and acronyms of the ACR, the ARP, and the Rheumatology Research Foundation are proprietary marks. Use of the names in any fashion, by any entity, for any purpose, is prohibited without the express written permission of the American College of Rheumatology.

Use of the ACR Scientific Program Content

- ACR educational activities are not public events. Information presented at these activities is for the education of attendees and/or purchasers as authorized by the ACR. Any materials or information displayed during these activities are the property of the ACR and the presenter and should not be photographed, copied, photocopied, transferred to electronic formats, reproduced or distributed without written permission of the ACR and the presenter.
- Any use of ACR educational content for commercial purposes, which includes but is not limited to oral presentations, audiovisual materials used by speakers and/or program handouts without written consent from the ACR is prohibited. This policy applies before, during and after each activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The ACR will enforce its intellectual property rights and penalize those who infringe upon it.

- The names, insignias, logos and acronyms of the ACR, the ARP and the Foundation are proprietary marks. Use of these in any fashion, by any entity, for any purpose, is prohibited without the express written permission of the ACR

Use of the ACR Disclosure Key

It is suggested when referencing disclosures in the reprints, that the ACR's disclosure key be added to provide adequate context for abstracts:

None: Has no relevant financial relationship to disclose.

1. Advisor or Review Panel member
2. Consultant
3. Employee
4. Officer or Board Member
5. Grant/Research Support
6. Speaker/honoraria includes speakers bureau, symposia, and expert witness
7. Independent contractor
8. Executive role and/or ownership interest
9. Royalties and/or patient beneficiary
10. Intellectual Property / Patents
11. Stock options or bond holdings in a for-profit corporation or self-directed pension plan
12. Private investigator
13. Expert witness
14. Equity interest
15. Other: *specify details*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Arthritis & Rheumatology
Vol. 77, No. S9, October 2025, pp 7–5439
DOI 10.1002/art.43418
© 2025 American College of Rheumatology

American College of Rheumatology
Empowering Rheumatology Professionals

Abstract Number: 0001

ATG-201, a Novel Steric Hindrance-based Masking CD19xCD3 T-cell Engager (TCE) for the Treatment of B Cell-related Autoimmune Diseases

Gang Bian[1], Tengteng Li[1], Huiling Liu[2], Zaoshun Hu[2], Peng Chen[1], Jay Mei[3] and **Bing Hou**[3], [1]Shanghai Antengene Corporation Limited, Shanghai, China (People's Republic), [2]Antengene (Hangzhou) Biologics, Hangzhou, Zhejiang, China (People's Republic), [3]Antengene Corporation, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: CD19-targeted therapies, such as chimeric antigen receptor (CAR)-T or T-cell engagers (TCE), have been approved for the treatment of B cell malignancies. By depleting autoreactive B cells, CD19-targeted therapies have shown early yet promising efficacy in treating patients with B cell-driven autoimmune diseases. However, the clinical application of TCE continues to be greatly hindered by the unfavorable pharmacokinetics, incomplete B cell depletion and toxicity associated with cytokine release syndrome (CRS). Here we developed a "2+1" CD19 x CD3 TCE, ATG-201, for the treatment of B cell driven autoimmune diseases, which utilizes a steric hindrance-based masking technology and a novel fast-on-fast-off CD3 binder, and effectively depletes B cells with minimal risk of CRS.

Methods: ATG-201 was constructed by introducing a novel fast-on-fast-off, conformational epitope-targeted anti-CD3 single chain fragment variable (scFv) to the hinge region of one of the heavy chains of a CD19 monoclonal antibody. It was evaluated in a series of *in vitro* and *in vivo* studies for binding affinity, B cell depletion, cytokine release, anti-disease efficacy and drug developability. The safety and pharmacokinetic (PK) parameters of ATG-201 were evaluated in hCD19/hCD3 knock-in mice, and non-human primates (NHP) using a monkey surrogate TCE antibody.

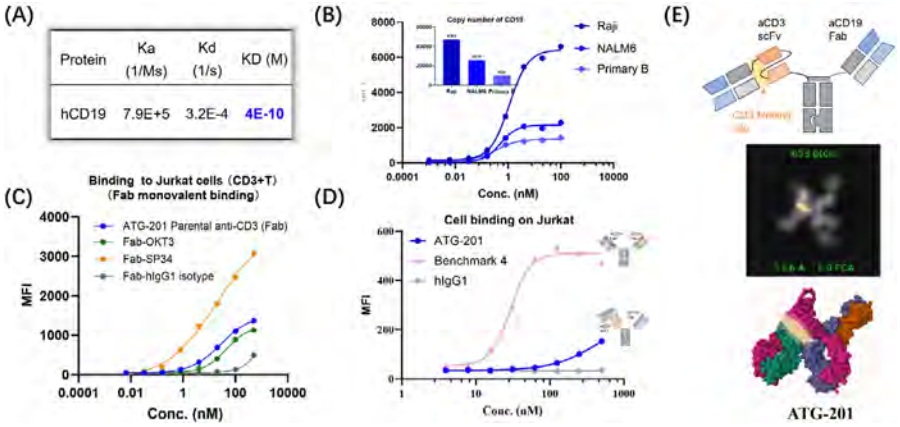


Figure 1. ATG-201 showed limited CD3+ T cell binding before CD19-crosslinking. (A) CD19 protein binding KD of ATG-201 detected by SPR. (B) Binding of ATG-201 to Raji, NALM6 and primary B cells. (C) Monovalent binding of ATG-201's parental anti-CD3 Fab binder to CD3+T cell. (D) Binding of ATG-201 and BMK4 to T cells before CD19 crosslinking. (E) The CD3 binding site is masked by the constant region of the CD19-targeting Fab arm in the absence of CD19 crosslinking by cryo-EM analysis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

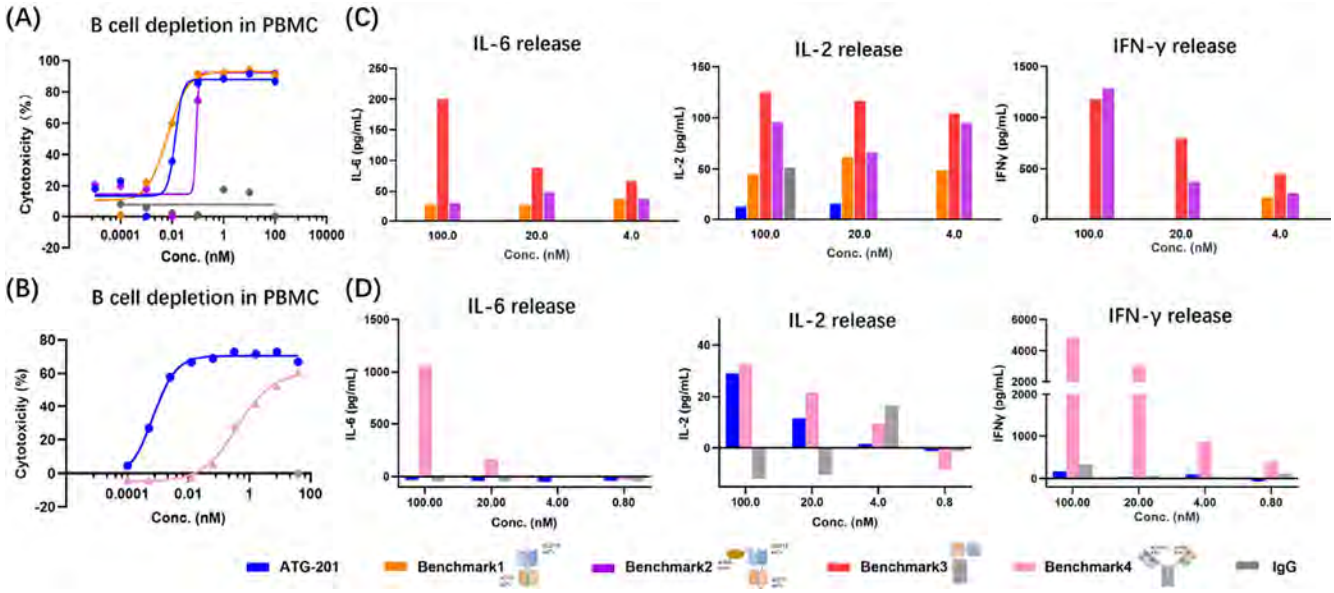


Figure 2. ATG-201 induced enhanced naïve B cell depletion and reduced cytokine release compared to clinical benchmarks. B cell depletion (A, B) and concentration of the indicated cytokines in the supernatant (C, D) of isolated human PBMC incubated with ATG-201 or Benchmarks for 48 hours.

Results: According to cryo-EM data, the CD3 binding site is masked by the constant region of the CD19-targeting Fab arm in the absence of CD19 cross-linking. ATG-201 showed limited CD3+ T cell binding before CD19-crosslinking (Figure 1). It activated T cells and only in the presence of CD19+ cells. ATG-201 demonstrated stronger B cell depletion activity in PBCMs derived from SLE patient and healthy donors with much lower cytokine release compared to benchmark TCEs *in vitro* (Figure 2). Single dose of ATG-201 completely and deeply depleted B cells in blood, bone marrow and spleen of CD34+ cells humanized NDG mice (Figure 3). The mouse surrogate CD19xCD3 TCE demonstrated potent efficacy in MOG-EAE model and MRL-lpr mouse SLE model, with deeper B cell depletion observed compared to CD20-targeted TCE. ATG-201 and its monkey surrogate CD19xCD3 TCE exhibited a favorable pharmacokinetic profile in hCD19/hCD3 knock-in mice and NHP respectively. ATG-201 was stable at high concentration (125mg/ml) and under stress conditions. ATG-201 and its monkey surrogate CD19xCD3 TCE were well tolerated in hCD19/hCD3 knock-in mice and NHP.

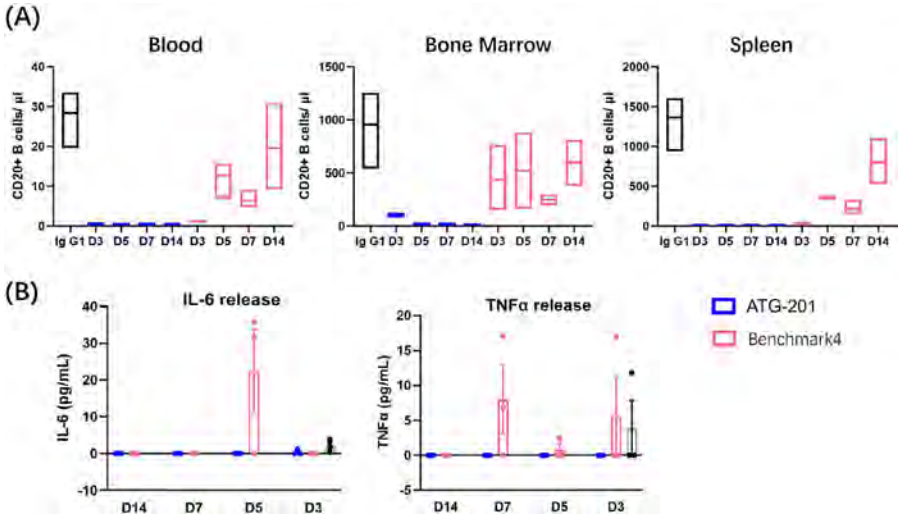


Figure 3. ATG-201 induces complete B cell depletion in CD34+ hematopoietic stem cells humanized mice with reduced cytokine release. CD34+-cell humanized NDG mice were treated with a single dose of 1.5 mg/kg ATG-201 or Bechmark4 (Molar equivalent dose of 1.5 mpk ATG-201). (A) Blood, bone marrow and spleen were collected and analyzed for B cells counts by FACS 3 days (D3), 5 days (D5), 7days (D7), or 14 days (D14) post treatment. (B) Plasma cytokine concentration post treatment.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: ATG-201 demonstrates CD19-dependent CD3 binding and activation, inducing effective B cell depletion and anti-disease activity *in vitro* and *in vivo* with good PK and safety profile, which warrants further clinical evaluation in the treatment of B cell related autoimmune diseases.

Disclosure: G. Bian: Shanghai Antengene Corporation Limited, 3; **T. Li**: Shanghai Antengene Corporation Limited, 3; **H. Liu**: Antengene (Hangzhou) Biologics, 3; **Z. Hu**: Antengene (Hangzhou) Biologics, 3; **P. Chen**: Shanghai Antengene Corporation Limited, 3; **J. Mei**: Antengene Corporation, 12, 3; **B. Hou**: Antengene Corporation, 12, 3.

Abstract Number: 0002

KITE-363: An Autologous Anti-CD19/CD20 CAR-T Product for the Treatment of Autoimmune Rheumatic Diseases

Brian Kim, Christine Lowe, Francisco Flores, Jeremy Margaitis, Alessandro Calo, Stacey Valny, Anna Konecny, Eva Jaghatspanyan, Sean Yoder, Kenneth Ertel, Simone Filosto, Jodi Murakami and David Barrett, Kite, a Gilead Company, Santa Monica, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: B-cell dysregulation is a key factor in the development and progression of autoimmune diseases, and B-cell inhibition has been a cornerstone of treatment for decades. Recent studies on B-cell depletion using chimeric antigen receptor (CAR) T-cell therapies in autoimmune diseases highlight the potential for reestablishing immune tolerance and achieving rapid, sustained remission without chronic use of systemic immunosuppressants (Taubmann J, et al. Arthritis Rheumatol. 2024). Both CD19 and CD20 are transmembrane proteins expressed on B-cells with variable expression throughout B cell development and thus, targeting both CD19 and CD20 may provide more comprehensive B-cell depletion than what could be achieved by targeting either antigen alone. KITE-363 is a dual-targeting anti-CD19/CD20 CAR T-cell therapy with 2 costimulatory domains, CD28 and 41BB, and is being evaluated in a Phase 1 clinical study of relapsed/refractory B-cell lymphoma (KT-US-499-0150).

Methods: CD19 and CD20 expression on B cell subsets from healthy donors and patients with systemic lupus erythematosus (SLE) with and without lupus nephritis (LN), systemic sclerosis (SSc), and idiopathic inflammatory myopathy (IIM) were analyzed by flow cytometry. Using a bicistronic lentiviral vector and T cells from patients, we generated anti-CD19/CD20 CAR-T cells (KITE-363). The bicistronic lentiviral vector encodes for an anti-CD19 CAR, containing the FMC63 binder and CD28 costimulatory domain, and anti-CD20 CAR, containing a novel CD20 binder and 41BB costimulatory domain. The final products were characterized via immunophenotyping and functionally assessed in vitro.

Results: Most B cells in the peripheral blood co-expressed CD19 and CD20 ($CD19^+CD20^+$), albeit at variable expression levels. Subsets of both $CD19^+CD20^-$ and $CD19^-CD20^+$ B cells were observed in all autoimmune conditions. Plasmablasts were abundantly $CD19^+CD20^-$, while double negative (IgD^-CD27^-) B cells were enriched for $CD19^-CD20^+$ compared to other B cell subsets. Patient-derived KITE-363 T cell products exhibited high expression of both the anti-CD19 and anti-CD20 CARs and demonstrated CAR- and antigen-specific T-cell functionality including cytokine production, proliferation, and cytotoxicity against autologous B cells and cell lines expressing either CD19 and/or CD20 antigens.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Highly variable expression of CD19 and/or CD20 in B cell subsets, jointly with antigen-specific and B-cell depleting activity of KITE-363, support clinical development of KITE-363 in B cell-mediated auto-immune conditions. With dual-antigen targeting and optimized co-stimulation, KITE-363 has the potential to induce a more comprehensive B-cell depletion and achieve durable, drug-free remission in these diseases. A Phase 1 open-label, multicenter study is underway to evaluate the safety and efficacy of KITE-363 in participants with refractory autoimmune rheumatic diseases.

Disclosure: B. Kim: Kite, a Gilead Company, 3, 11; **C. Lowe**: Kite, a Gilead Company, 3, 11; **F. Flores**: Kite, a Gilead Company, 3, 11; **J. Margaitis**: Kite, a Gilead Company, 3, 11; **A. Calo**: Kite, a Gilead Company, 3, 11; **S. Valny**: Kite, a Gilead Company, 3, 11; **A. Konecny**: Kite, a Gilead Company, 3, 11; **E. Jaghatspanyan**: Kite, a Gilead Company, 3, 11; **S. Yoder**: Kite, a Gilead Company, 3, 11; **K. Ertel**: Kite, a Gilead Company, 3, 11; **S. Filosto**: Kite, a Gilead Company, 3, 11; **J. Murakami**: Kite, a Gilead Company, 3, 11; **D. Barrett**: Kite, a Gilead Company, 3, 11.

Abstract Number: 0003

In Vivo Generation of anti-CD19 CAR T Cells Utilizing Circular RNA Encapsulated in Targeted Lipid Nanoparticles

Xiaoyu Pan[1], Xiaoning Wang[1], Zhihao Chen[1], Xiaowen Zou[1], Siqi Li[1], Jian Ye[1], Fei Lin[1], Yang He[1], **Edo Kon**[2], Peng Zhu[1], Mengyun Chen[1] and Weiyi Zhang[1], [1]RiboX Therapeutics, Shanghai, China (People's Republic), [2]RiboX Therapeutics, Cambridge, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chimeric Antigen Receptor (CAR) T-cell therapy has revolutionized cancer treatment and shown promise in addressing autoimmune diseases. However, current *ex vivo* CAR T-cell therapies encounter challenges such as complex manufacturing processes, scalability issues, reliance on viral vectors, and the necessity for lymphodepleting chemotherapy, which limit broader clinical applications. To address these limitations, there is a critical need for an off-the-shelf *in vivo* CAR technology that can simplify delivery and expand therapeutic potential. We have developed tLNP-circCAR, a novel in vivo anti-CD19-CAR circular RNA product delivered via targeted lipid nanoparticles (tLNPs). Preclinical studies in animal models demonstrate its efficacy in B cell depletion, marking a significant advancement towards overcoming existing barriers in CAR T-cell therapy and expanding its applicability to a broader range of diseases.

Methods: tLNP-circCAR encapsulates a circular RNA encoding an anti-CD19-CAR within a tLNP containing a novel ionizable lipid and a T cell targeting domain, enabling efficient transfection of primary human T cells. The functional activity of tLNP-circCAR-mediated CAR T cells was evaluated using multiple *in vitro* and *in vivo* systems.

Results: In activated primary human T cells, circCAR mediated CAR expression lasted up to 9 days. Notably, tLNP-circCAR efficiently engineered non-activated primary human T cells into functional CAR T cells. *In vitro*, these engineered CAR T cells exhibited robust cytotoxicity against autologous B cells and the $CD19^+$ Raji cell line. *In vivo*, utilizing a humanized NOG-PBMC mouse model, a single intravenous dose of tLNP-circCAR resulted in efficient CAR engineering of T cells, leading to complete B cell depletion in the spleen. In humanized NOG-PBMC mice bearing CD19+ NALM-6-Luc lymphoma xenografts, tLNP-circCAR treatment induced complete tumor remission at the dose of sub-microgram per mouse. In

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cynomolgus monkeys, single dose of tLNP-circCAR treatment achieved remarkable B cell reduction in circulating whole blood, lymph node, bone marrow and spleen.

Conclusion: tLNP-circCAR represents a novel *in vivo* CAR therapy that delivers therapeutic anti-CD19 CAR circular RNA efficiently to human T cells, generating highly functional CAR T cells both *in vitro* and *in vivo*. These results support the further development of tLNP-circCAR for treating B cell disorders, including B cell lymphoma and autoimmune diseases. This innovative approach promises to enhance the accessibility and efficacy of CAR T-cell therapy.

Disclosure: X. Pan: RiboX Therapeutics, 3; **X. Wang**: RiboX Therapeutics, 3; **Z. Chen**: RiboX Therapeutics, 3; **X. Zou**: RiboX Therapeutics, 3; **S. Li**: RiboX Therapeutics, 3; **J. Ye**: RiboX Therapeutics, 3; **F. Lin**: RiboX Therapeutics, 3; **Y. He**: RiboX Therapeutics, 3; **E. Kon**: RiboX Therapeutics, 3; **P. Zhu**: RiboX Therapeutics, 3; **M. Chen**: RiboX Therapeutics, 3; **W. Zhang**: RiboX Therapeutics, 3.

Abstract Number: 0005

LBL-047, A First-In-Class Anti-BDCA2/TACI Fusion Protein, Inhibits the Function of Both pDCs and B cells

Fengxia Li[1], Jianming Sun[1], Hailin Wang[1], Yan Zhu[1], Xiaoxiao Liu[1], Jing Li[1], Yurong Qin[1], Guojin Wu[1], Jing Guan[1], Min Chen[1], Jordan Zhu[2], Xiaoqiang Kang[1], Xiao Huang[1] and **Hong Ling**[1], [1]Nanjing Leads Biolabs Co., Ltd., Nan Jing, China (People's Republic), [2]Nanjing Leads Biolabs Co., Ltd., Nan Jing

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Blood dendritic cell antigen 2 (BDCA2) is specifically expressed on pDCs whose uncontrolled production of type I IFN play a crucial role in the pathogenesis of autoimmune disorders. Litifilimab, an anti-BDCA2 antibody, has demonstrated promising preliminary efficacy and excellent safety profile in patients with cutaneous lupus erythematosus. Meanwhile B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) bind to the transmembrane activator and CAML interactor (TACI) on B cells, facilitating B cell proliferation and differentiation. Targeting this pathway, two TACI based recombinant fusion proteins, such as Povetacicept and Telitacicept, have shown clinical benefits and favorable safety profile in autoimmune disease trials. Therefore, we have developed LBL-047, which simultaneously targets BDCA2 on pDCs and block TACI-mediated signaling on B cells. This dual-targeting approach may hold promise for the treatment of autoimmune diseases.

Methods: LBL-047 was obtained by fusing CRD2 domain of TACI to the N-terminal of the humanized, afucosylated anti-BDCA2 antibody, and the YTE mutation was introduced to extend its half-life. The potency of LBL-047-induced pDCs depletion and pro-inflammatory cytokines inhibition were evaluated in human peripheral blood mononuclear cells (PBMCs). The internalization assay was performed using the BDCA2 overexpressed cell line and measured by flow cytometry. The inhibition of human primary B cells' proliferation and differentiation induced by LBL-047 was evaluated by flow cytometry. The keyhole limpet hemocyanin (KLH)-immunized human $CD34^+$ hematopoietic stem cells- engrafted immunodeficient NCG mouse model (huHSC-NCG model) was used to test the efficacy of LBL-047 in inhibiting the function of pDCs and B cells. The pharmacokinetics (PK), pharmacodynamics (PD) and toxicity of LBL-047 were evaluated in cynomolgus monkeys.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: LBL-047 robustly depleted pDCs and activated BDCA2 downstream signaling pathways, thereby suppressing pDCs produced IFN-α, TNF-α and IL-6. Additionally, LBL-047 mediated potent inhibition of B cells' proliferation and differentiation. When co-bound to BAFF and cell-surface-expressed BDCA2, both LBL-047 and BAFF protein were rapidly internalized into the cells. In KLH immunized huHSC-NCG mouse model, LBL-047 effectively inhibited the function of both pDCs and B cells. LBL-047 also exhibited a linear PK characteristic following single S.C administration in cyno monkeys across 0.3-10 mg/kg, and serum IgM, IgA, and IgG levels were significantly decreased up to 6 weeks in a dose-dependent manner. In a 4-week GLP toxicology study, LBL-047 was shown a favorable safety profile with a NOAEL of 100 mg/kg.

Conclusion: LBL-047 has shown dual immunosuppressive effects, inhibiting simultaneously the function of pDCs and B cells both in vitro and in vivo. In addition, it has demonstrated excellent PK and PD profile, coupled with good safety profile and tolerability in cynomolgus monkeys. Taken together, these findings support the clinical development of LBL-047 and highlight its promise as a therapeutic candidate for autoimmune diseases.

Disclosure: F. Li: None; **J. Sun**: None; **H. Wang**: None; **Y. Zhu**: None; **X. Liu**: None; **J. Li**: None; **Y. Qin**: None; **G. Wu**: None; **J. Guan**: None; **M. Chen**: None; **J. Zhu**: None; **X. Kang**: None; **X. Huang**: None; **H. Ling**: None.

Abstract Number: 0006

QEL-005: CD19 CAR-Regulatory T cell therapy, a novel approach for the treatment of complex immune mediated inflammatory diseases including Rheumatoid Arthritis and Systemic Sclerosis

Jenny McGovern, Georgios Eleftheriadis, Thomas Grothier, Eva Bugallo Blanco, Anna Koi, Mahsa Nemani, Cameron Allum, Emily Hurley, Daniela Penston, Marc Martinez-Llordella, Luke Devey and Nathalie Belmonte, Quell Therapeutics, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid Arthritis (RA) and Systemic Sclerosis (SSc) are immune mediated inflammatory diseases (IMID) where a complex interplay of tissue and immune cell activation drives a chronic loop of inflammation resulting in significant tissue damage. B cell depletion approaches highlight the contribution of B cells in IMIDs, but they are limited to targeting a single immune cell type and carry safety and tolerability risks in certain patient populations. Regulatory T cells (Tregs) are key mediators of immune and tissue homeostasis with an essential role in restraining autoimmunity. Tregs employ a wide array of mechanisms to mediate this effect and therefore can exert control over multiple immune pathways across a broad range of tissues and cell types. In IMIDs driven by complex immune responses and aberrant tissue processes such as RA and SSc, a Treg cell therapy has the unique potential to modulate multiple disease mechanisms with a single drug. In this study we describe the pre-clinical data supporting the development of QEL-005, a novel CD19 CAR-Treg product containing a FOXP3 phenotype lock. Upon infusion these CAR-Treg cells will be activated by B cells in lymph nodes and tissue resulting in a dampening of autoreactive B cell responses including autoantibody production, antigen presentation and B cell cytokine production. Moreover, through bystander suppression, activation of these CAR-Tregs will elicit modulation of other

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

immune cells in the inflamed niche, such as autoreactive T cells and disease-associated monocytes and macrophages. This broader mechanism of action modulating multiple cell compartments differentiates CAR-Tregs from CAR-T and other conventional B-cell depletion assets.

Methods: We generated a construct containing a CAR with an FMC63 aCD19 ScFv binder and a FOXP3 phenotype lock. CD45RA+ Tregs were transduced and expanded for 14 days before cryopreservation. Thawed cells were characterised by flow cytometry to ensure CAR function and Treg stability. The mechanism of action was investigated using co-culture assays with primary human cells.

Results: QEL-005 CD19 CAR Tregs maintain a Treg phenotype, as determined by (i) a panel of Treg markers (ii) maintenance of a demethylated TSDR region, (iii) low levels of cytokine production and (iv) suppression of T cell responses. QEL-005 CAR-Tregs can be activated by CD19, driving antigen-specific proliferation and suppression but with no evidence of cytotoxicity. Culture of QEL-005 Tregs with primary B cells showed a reduction in antigen presentation potential through the depletion of CD80/86 co-stimulatory molecules, a reduction in antibody production and a reduction in B cell cytokine production. In addition, we show that co-culture of CD19 CAR Tregs with T cells and monocytes/macrophages leads to a reduction in their pro-inflammatory potential, demonstrating bystander suppression.

Conclusion: In diseases such as RA and SSc with complex interactions of immune effector and tissue cell types, QEL-005 CD19 CAR-Tregs have the potential to durably restore homeostasis in chronically inflamed tissues with limited risk of drug associated toxicity.

Disclosure: J. McGovern: None; **G. Eleftheriadis**: None; **T. Grothier**: None; **E. Bugallo Blanco**: None; **A. Koi**: None; **M. Nemani**: None; **C. Allum**: None; **E. Hurley**: None; **D. Penston**: None; **M. Martinez-Llordella**: None; **L. Devey**: None; **N. Belmonte**: None.

Abstract Number: 0008

Characterization of S-1117, a novel pan-IgG protease engineered for reduced immunogenicity using the IMPACT platform

Julia Manasson[1], Liliana Sanmarco[2], Alex Pellerin[2], Maria Cecilia Ramello[2], Agustin Plasencia[2], Jordan Anderson[2], Tobias Green[2], Andita Newton[2], Ryan Peckner[2], Yi Xing[2], Heather Vital[3], Nathan Higginson-Scott[2], John Sundy[4], Kevin L. Otipoby[2] and Ivan Mascanfroni[2], [1]Seismic Therapeutic, New York, NY, [2]Seismic Therapeutic, Watertown, MA, [3]Seismic Therapeutic, Lexington, MA, [4]Seismic Therapeutic, Durham, NC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Pathogenic autoantibodies are key effectors of inflammation, promoting tissue damage in autoantibody-mediated diseases such as inflammatory myopathies, lupus nephritis, Sjogren's syndrome, antiphospholipid syndrome, and ANCA-associated vasculitis. Antibody degradation using an IgG protease represents a new therapeutic opportunity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We present S-1117, a novel pan-IgG protease fused to an effectorless human IgG1 Fc domain and engineered for chronic subcutaneous administration using a proprietary machine learning enabled platform to reduce immunogenicity and augment manufacturability while maintaining potency. S-1117 cleaves and reduces soluble IgG, disrupts IgG effector function, degrades IgG immune complexes (IC), and cleaves the IgG+ B cell receptor (BCR) on surface of memory B cells, reducing IgG+ BCR mediated activation. These features allow S-1117 to simultaneously address multiple mechanisms of autoimmunity.

Methods: Immunogenicity of S-1117 was assessed *in vitro* by major histocompatibility complex (MHC)-associated peptide proteomics (MAPPs) and validated by CD4 T cell proliferation assays. *In vivo*, IgG antidrug antibody (ADA) was quantified in C57BL/6 mice in response to S-1117 protease domain administration vs the parental protease. The polypharmacology of S-1117 was determined through *in vitro* plasma IgG, IgG+ BCR, and IC cleavage, as well as antibody mediated effector function assays. S-1117 function was tested pre-clinically *in vivo* in rabbits and mice.

Results: *In vitro*, S-1117 demonstrates reduced epitope display compared to the wildtype protease by MAPPs. Furthermore, the wildtype protease elicits CD4 T cell proliferation responses from 65% of healthy donors with a response index of 2.60 (magnitude of response over background signal). In comparison, S-1117 demonstrates a reduction in the number of responders to 20% and a 10-fold lower response index.

In vivo, a single dose of S-1117 induces rapid (< 24 hours), deep (>90%), and sustained (over 10 days) reduction of endogenous IgG in rabbits. In mice, repeat dosing of parental protease induced immediate hypersensitivity reactions, causing mortality in 60% of mice and high ADA response. In contrast, all mice treated with the protease domain of S-1117 survived multiple doses without anaphylactic reactions or induction of ADA.

Functionally, S-1117 cleaves all IgG subclasses in human plasma. It directly eliminates IgG effector function and IC-mediated immune cell activation. Moreover, it cleaves the IgG+ BCR on memory B cells in humans *in vitro*, reducing IgG+ BCR driven B cell activation.

Conclusion: S-1117 is a novel pan-IgG protease engineered with our machine learning enabled platform to reduce immunogenicity. It demonstrates rapid, deep, and sustained reduction of IgG levels, IgG effector function, and cleavage of the IgG+ BCR on memory B cells, reducing BCR mediated B cell activation. Advantages of enzymatic degradation, sustained PK, and titratable PD are expected to enable a convenient patient-tailored treatment regimen. Since S-1117 addresses multiple pathogenic mechanisms as a single drug, it has the potential to provide superior clinical outcomes in autoantibody-mediated diseases with complex pathology.

Disclosure: J. Manasson: Seismic Therapeutic, 3, 11; **L. Sanmarco**: Seismic Therapeutic, 3, 11; **A. Pellerin**: Biogen, 12, Immediate family member has stock., Seismic Therapeutic, 3, 11; **M. Ramello**: Seismic Therapeutic, 3, 11; **A. Plasencia**: Seismic Therapeutic, 3, 10; **J. Anderson**: Seismic Therapeutic, 3, 11; **T. Green**: Seismic Therapeutic, 3, 11; **A. Newton**: Seismic Therapeutic, 3, 11; **R. Peckner**: Seismic Therapeutic, 3, 11; **Y. Xing**: Seismic Therapeutic, 3, 11; **H. Vital**: Relay Therapeutics, 11, Seismic Therapeutic, 3, 11; **N. Higginson-Scott**: ComboLink Therapeutics, 1, 11, Seismic Therapeutic, 3, 11; **J. Sundy**: Neutrolis, Inc, 4, 11, Rome Therapeutics, 2, 11, Sanofi S.A., 4, 11, Seismic Therapeutic, 3, 11, Upstream Bio, 2, 11; **K. Otipoby**: Eurofins Scientific, 12, Member of the Scientific Advisory Board, LogicBio Therapeutics, 2, Lucy Therapeutics, 2, Seismic Therapeutic, 3, 11; **I. Mascanfroni**: Seismic Therapeutic, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0009

MRT-6160, a VAV1-Directed Molecular Glue Degrader, Attenuates T and B Cell Effector Functions and Inhibits Disease Progression in a Spontaneous MRL-Fas^{lpr} Mouse Model

Adam Cartwright[1], Lucas Gyger[1], Foram Desai[2], Shailee Vora[2], Anna Kostikova[1], Xudong Wang[2], Peter Trenh[2], Katie May[2], Sophia Nguyen[2], Chris King[2], Daniel Lam[2], Xavi Lucas[1], Mary Zlotosch[2], Elisa Liardo[1], Daric Wible[2], Ilaria Lamberto[2], Bradley Demarco[2], Debora Bonenfant[1], Sharon Townson[2], Eswar Krishnan[2], Filip Janku[2], John Castle[1], Laura McAllister[1], Alison Paterson[2] and **Marisa Peluso**[2], [1]Monte Rosa Therapeutics, Basel, Switzerland, [2]Monte Rosa Therapeutics, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: VAV1, an immune cell restricted guanine nucleotide exchange factor (GEF) and scaffolding protein, plays a critical role in mediating T- and B-cell receptor activity. Genetic loss of *hVAV1* in CRISPR-based screens confers reduced T-cell effector function and murine (m)VAV1 knockout mice are resistant to T- and T/B-cell mediated autoimmune disease models. MRT-6160 is a highly selective, first-in-class oral VAV1-targeting molecular glue degrader currently being evaluated in healthy subjects [NCT06597799]. Given the role of VAV1 in T- and B-cells, MRT-6160-mediated degradation of VAV1 could have broad therapeutic implications in lymphocyte-driven autoimmune and rheumatic disorders, including primary Sjögren's Syndrome (pSS) and systemic lupus erythematosus (SLE).

Methods: PBMCs from pSS and SLE patients were pre-treated with MRT-6160 prior to TCR or T cell-dependent-like BCR stimulation and assessed for VAV1 levels, IL-2 secretion, and IgG production. Primary human T follicular helper cells and B cells were enriched from allogenic healthy patient PBMCs, treated with or without MRT-6160, co-cultured for 6 days, then assessed for IgG secretion and plasmablast differentiation. MRL-Fas^{lpr} mice were treated with vehicle, prednisone (10 mg/kg, PO QD), anti-CD40L (5 mg/kg, IP Q3D), or MRT-6160 (1 mg/kg, PO QD) from 11 to 18 weeks of age following onset of disease at around 9 weeks of age. Mice were assessed in-life from 9 weeks of age for body weight, lymphadenopathy, skin lesions, proteinurea and autoantibody levels. At the end of the study, organomegaly and kidney histopathological assessments were performed.

Results: MRT-6160 degraded VAV1 in healthy and pSS patient PBMCs, concomitant with an attenuation of TCR stimulation-induced IL-2 and T cell-dependent-like BCR stimulation-induced IgG secretion. Treatment of Tfh and B cell co-cultures with MRT-6160 reduced plasmablast differentiation ($CD38^+CD27^+CD20^-$ cells) of both naïve and memory B cells and concurrently reduced in IgM and IgG respectively. In MRL-Fas^{lpr} mice, whilst blockade of the CD40/CD40L axis had no effect, MRT-6160 inhibited lymphadenopathy and skin lesion formation comparable to prednisone and levels of proteinuria and anti-dsDNA levels were inhibited to a greater extent than prednisone. At study termination, MRT-6160 reduced organomegaly of lymph nodes, spleen and kidneys. In histopathological assessment of the kidneys, MRT-6160 significantly reduced glomerulonephritis and vascular nephritis comparable to prednisone.

Conclusion: MRT-6160-mediated degradation of VAV1 attenuates TCR- and BCR-mediated activation *in vitro* diminishing activation and effector functions of pSS/SLE patient PBMCs and Tfh-mediated differentiation and immunoglobulin production. *In vivo*, MRT-6160 inhibited disease progression and kidney histopathological organ damage in an MRL-Fas^{lpr} mouse model of rheumatic disease. These data demonstrate the therapeutic potential of MRT-6160 in various lymphocyte-driven autoimmune and rheumatic diseases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Cartwright: Monte Rosa Therapeutics, 3, 11; **L. Gyger**: Monte Rosa Therapeutics, 3, 11, Novartis, 11, Roche, 11; **F. Desai**: Monte Rosa Therapeutics, 3, 11; **S. Vora**: Monte Rosa Therapeutics, 3; **A. Kostikova**: Monte Rosa Therapeutics, 3, Novartis, 11; **X. Wang**: Monte Rosa Therapeutics, 3; **P. Trenh**: Monte Rosa Therapuetics, 3, 11; **K. May**: Monte Rosa Therapeutics, 3, 11; **S. Nguyen**: Monte Rosa Therapeutics, 3, 11; **C. King**: Monte Rosa Therapeutics, 3, 11; **D. Lam**: Monte Rosa Therapeutics, 3, 11; **X. Lucas**: Monte Rosa Therapeutics AG, 3, 10; **M. Zlotosch**: Monte Rosa Therapeutics, 3, 11; **E. Liardo**: Monte Rosa Therapeutics, 3, 10; **D. Wible**: Monte Rosa Therapeutics, 3, 11; **I. Lamberto**: Monte Rosa Therapeutics, 3, 11; **B. Demarco**: Monte Rosa Therapeutics, 3, 11; **D. Bonenfant**: Monte Rosa Therapeutics, 3, 11; **S. Townson**: Monte Rosa Therapeutics, 3, 11; **E. Krishnan**: Monte Rosa Therapeutics, 3, 11; **F. Janku**: Monte Rosa Therapeutics, 3, 11; **J. Castle**: Monte Rosa Therapeutics, 3, 4, 8, 11; **L. McAllister**: Monte Rosa Therapeutics, 3, 11; **A. Paterson**: Monte Rosa Therapeutics, 3, 11; **M. Peluso**: Monte Rosa Therapeutics, 3, 11.

Abstract Number: 0010

XmAb657, a CD19 x CD3 T-Cell Engaging Bispecific Antibody for Autoimmune Disease

Matthew Bernett[1], Gregory Moore[2], Katrina Bykova[2], Viralkumar Davra[2], Seung Chu[2], Michael Sheard[2], Ruschelle Love[2], Norman Barlow[2], Engie Salama[2], Jitendra Kanodia[2], Panida Lertkiatmongkol[2], Dipankar Chaudhuri[2], Kendra Avery[2], Hanh Nguyen[2], Rumana Rashid[2], Ke Liu[2], Jing Qi[2], Araz Eivazi[2], Thuy Truong[2], Sher Karki[2], James Ernst[2], Rena Bahjat[2] and John Desjarlais[2], [1]Xencor, Inc., Pasadena, CA, [2]Xencor, Inc., Pasadena

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: B cell depletion is a validated therapeutic strategy in autoimmune disease, but current approaches targeting CD20 may only partially eliminate disease-driving subsets such as early lineage B cells and plasma cells. T-cell engagers (TCEs) that redirect cytotoxic T cells to B-lineage targets offer a promising path to achieve deeper and more durable depletion. XmAb657 is a CD19 x CD3 bispecific antibody specifically engineered for autoimmune indications. CD19 is broadly expressed across the B cell lineage, including on subsets not addressed by CD20-targeted therapies. XmAb657 incorporates a bivalent CD19-binding arm to enhance avidity and improve engagement of CD19+ B cells, while the TCE format facilitates potent T cell–mediated cytotoxicity, including in tissue compartments where conventional therapies may have limited activity. XmAb657 was designed using a clinically validated 2+1 bispecific format and an Fc domain engineered for extended half-life.

Methods: XmAb657 was tested in a human PBMC-based redirected T cell cytotoxicity (RTCC) assay to assess B cell killing, cytokine production (IFNγ), and T cell activation (CD69, CD25). In vivo pharmacokinetics, pharmacodynamics, and tissue depletion were evaluated in cynomolgus monkeys following a single intravenous (IV) or subcutaneous (SC) dose. Peripheral blood, bone marrow, and lymph node B cells and plasma cells were measured for up to 42 days. Extent of lymph node B cell depletion was also assessed by IHC using a non-competing anti-CD19 antibody.

Results: In vitro, XmAb657 induced potent B cell cytotoxicity and T cell activation at low nanomolar concentrations. In cynomolgus monkeys, a single IV or SC dose of XmAb657 led to rapid and sustained depletion of peripheral B cells, and B cell counts were suppressed to levels below reliable quantitation (< 5 B cells/μL blood) for at least 42 days. Tissue analysis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

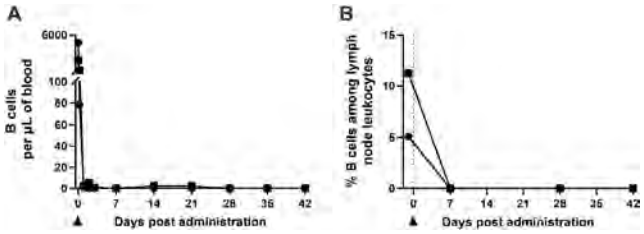


Figure 1. B cell depletion in cynomolgus monkeys (n = 2) following a single intravenous dose of XmAb657. (A) Peripheral blood B cell counts, expressed as absolute cells/µL. (B) Lymph node B cells, expressed as percentage of total leukocytes. B cells were quantified by flow cytometry.

confirmed marked reductions in CD19+ B cells as well as CD19+ plasma cells in both lymph nodes and bone marrow. Serum half-life was approximately 15 days. XmAb657 was well tolerated in cynomolgus monkeys, with no clinical signs consistent with cytokine release.

Conclusion: XmAb657, a CD19 x CD3 bispecific antibody engineered for treatment of autoimmune disease, demonstrated potent in vitro activity and deep, durable depletion of circulating and tissue-resident B cells in cynomolgus monkeys after a single dose. Targeting CD19 may complement other B-lineage–directed approaches by extending depletion to a broader range of B cell subsets. These findings support the ongoing advancement of XmAb657 into first-in-human clinical studies.

Disclosure: M. Bernett: Xencor, Inc., 3, 10, 11; **G. Moore**: Xencor, Inc., 3, 10, 11; **K. Bykova**: Xencor, Inc., 3, 11; **V. Davra**: Xencor, Inc., 3, 11; **S. Chu**: Xencor, Inc., 3, 10, 11; **M. Sheard**: Xencor, Inc., 3, 11; **R. Love**: Xencor, Inc., 3, 11; **N. Barlow**: Xencor, Inc., 3, 11; **E. Salama**: Xencor, Inc., 3, 11; **J. Kanodia**: Xencor, Inc., 3, 11; **P. Lertkiatmongkol**: Xencor, Inc., 3, 11; **D. Chaudhuri**: Xencor, Inc., 3, 11; **K. Avery**: Xencor, Inc., 3, 11; **H. Nguyen**: Xencor, Inc., 3, 11; **R. Rashid**: Xencor, Inc., 3, 11; **K. Liu**: Xencor, Inc., 3, 11; **J. Qi**: Xencor, Inc., 3, 11; **A. Eivazi**: Xencor, Inc., 3, 11; **T. Truong**: Xencor, Inc., 3, 11; **S. Karki**: Xencor, Inc., 3, 11; **J. Ernst**: Xencor, Inc., 3, 11; **R. Bahjat**: Xencor, Inc., 3, 11; **J. Desjarlais**: Xencor, Inc., 3, 10, 11.

Abstract Number: 0011

KT502, a novel CD19-directed TCE (T-cell engager), leads to rapid and deep B-cell depletion with low cytokine release

Min Bao, John Wang, Jay Zhao and Weihao Xu, Kali Therapeutics, San Mateo, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chimeric antigen receptor T-cell (CAR-T) therapies targeting CD19 have shown unprecedented effects in treatment-resistant autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and others. However, the limitations in patient selection for CAR-T arise from significant safety concerns, complex logistical hurdles, cost and unsuccessful retreatment if flare occurs. Recently, bispecific antibodies (e.g. Blinatumomab), which may offer an alternative approach to CART with similarly effective B cell depletion but off-the-shelf convenience, have been approved in B cell malignancies and showed impressive efficacy in patients with autoimmune indications in case reports. However, the safety profile and treatment options are not optimized. Therefore, the aim is to develop a novel

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

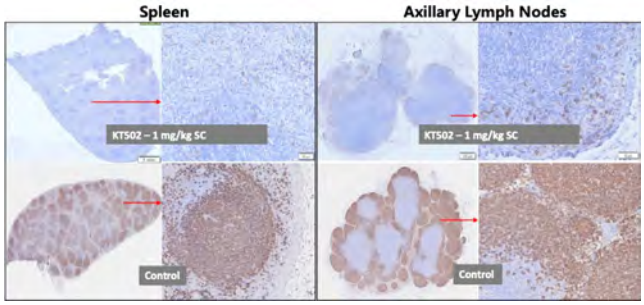


Figure 1: B cell Depletion in Spleen and Lymph Nodes in NHP (CD20 Immunohistochemistry Staining at Day 22)

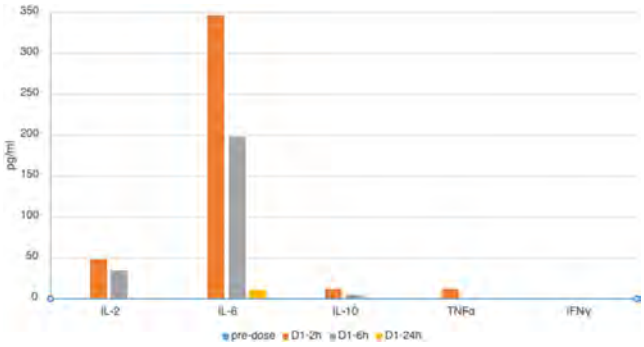


Figure 2: Cytokine Release Following 1 mg/kg SC in NHP (Predose to 24hrs on Day 1)

bispecific antibody targeting CD19/CD3 that can achieve a rapid and deep B cell depletion with an optimized safety profile through subcutaneous injection for the beneficial of patients with autoimmune disorders across multiple therapeutic areas.

Methods: KT502 was selected on an innovative molecular design that maximizes B cell cytotoxicity while minimizes cytokine release through a unique CD3 masking technology. KT502 also has cross-activity with non-human primate (NHP), facilitating preclinical safety and efficacy evaluation. Peripheral blood mononuclear cells (PBMC) from healthy donors were cultured in the presence of KT502 or blinatumomab for 48 hours. Cynomolgus monkeys were treated with KT502 intravenously (IV) or subcutaneously (SC) in the prove-of-concept toxicology study.

Results: In vitro, KT502 exhibits superior potency in B cell killing but lower cytokine release compared with Blinatumomab. In the preclinical study using cynomolgus monkeys, KT502 induced rapid and profound B cell depletion while cytokine release remained low and transient, highlighting KT502's a favorable and differentiated safety from CAR-T therapies and other TCEs with similar target. Following three weekly SC injection of 1mg/kg, robust B cell depletion in spleen and lymph nodes were achieved by day 22 (Figure 1) with no fever or other clinical signs/symptoms observed. The cytokine release syndrome relevant biomarkers were generally low after the initial dose; importantly, all were back to the levels similar to pre-dose within 24 hrs (Figure 2). Furthermore, reductions from baseline for serum IgM, IgA and IgG levels were 65%, 54% and 34%, respectively by day 21.

Conclusion: KT502, a novel CD19/CD3 TCE developed through a unique CD3 masking technology, demonstrated a rapid and deep B depletion in vitro and in NHP study with a favorable and differentiated safety profile. These early findings strongly support the clinical development of KT502 as a potential effective treatment with an optimized safety profile that may also provide patient-friendly treatment option for a broad range of autoimmune diseases. A Phase I first-in-human clinical trial is anticipated to begin in Q1 2026.

Disclosure: M. Bao: Kali Therapeutics, 3; **J. Wang**: Kali Therapeutics, 3; **J. Zhao**: Kali Therapeutics, 3; **W. Xu**: Kali Therapeutics, 3, 8.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0012

KT501, a CD19/BCMA/CD3 trispecific antibody, leads to rapid and deep B-cell depletion with well-tolerated safety

Min Bao, John Wang, Jay Zhao and Weihao Xu, Kali Therapeutics, San Mateo, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chimeric antigen receptor T-cell (CAR-T) therapies targeting CD19 or B-cell maturation antigen (BCMA) have shown unprecedented effects in treatment-resistant autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and others. However, the limitations in patient populations for CAR-T arise from significant safety concerns, complex logistical hurdles and unsuccessful retreatment. Recently, bispecific antibodies (e.g. Blinatumomab and Teclistamab), which may offer an alternative approach to CART with similarly effective B cell depletion but off-the-shelf convenience, have been approved in B cell malignancies and showed impressive efficacy in patients with autoimmune indications in case reports. Furthermore, in some patients, disease may be anchored in the long-lived plasma cells that express BCMA but not CD19. Therefore, the aim is to develop a first-in-class tri-specific antibody targeting CD19/BCMA/CD3 to achieve a rapid and deep B cell depletion with a differentiated safety profile, potentially beneficial for the treatment of autoimmune disorders across multiple therapeutic areas.

Methods: KT501 is a novel IgG-like trispecific T cell engager, designed to bind CD3, CD19, BCMA with high affinity, thereby targeting a broad range of B cell populations. Utilizing an innovative molecular design aimed at maximizing potency while minimizing cytokine release by a unique CD3 masking platform, KT501 has demonstrated robust B cell cytotoxicity and reduced cytokine production in vitro and in non-human primate (NHP) due to its cross activity in NHP.

Results: In vitro, KT501 is more potent in B cell killing and results in lower cytokine release compared with Blinatumomab. In preclinical studies using cynomolgus monkeys, KT501 induced rapid and profound B cell depletion following a single 1 mg/kg intravenous (IV) dose in peripheral blood, bone marrow, spleen and lymph nodes (Figure 1), with minimal cytokine release. Furthermore, a single subcutaneous (SC) administration of 1mg/kg led to reduction from baseline for serum IgA, IgG and IgM levels by 67%%, 44% and 39%, respectively at day 26. In the ongoing repeated dose cyno toxicology study with a wide range of doses (0.01 to 10 mg/kg) by SC injection, KT501 was well tolerated with no fever and other clinical signs/symptoms observed at all dose levels. As presented in Figure 2, after the initial SC administration, peripheral CD20+ B cells were depleted within 24 hrs at the lowest dose of 0.01 mg/kg. Cytokine release syndrome relevant cytokines were transiently increased but all back to the levels similar to pre-dose level within 24 hrs, with no increased cytokines at the subsequent doses.

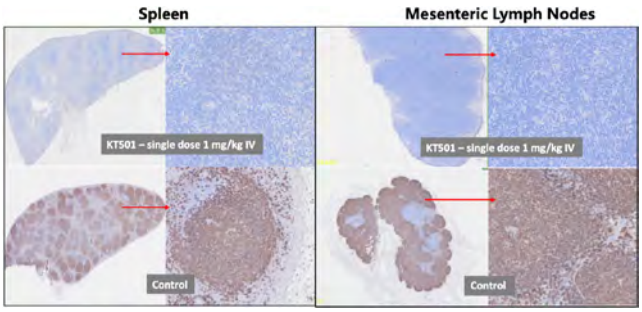


Figure 1: B cell Depletion in Spleen and Lymph Nodes in NHP (CD20 Immunohistochemistry Staining)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

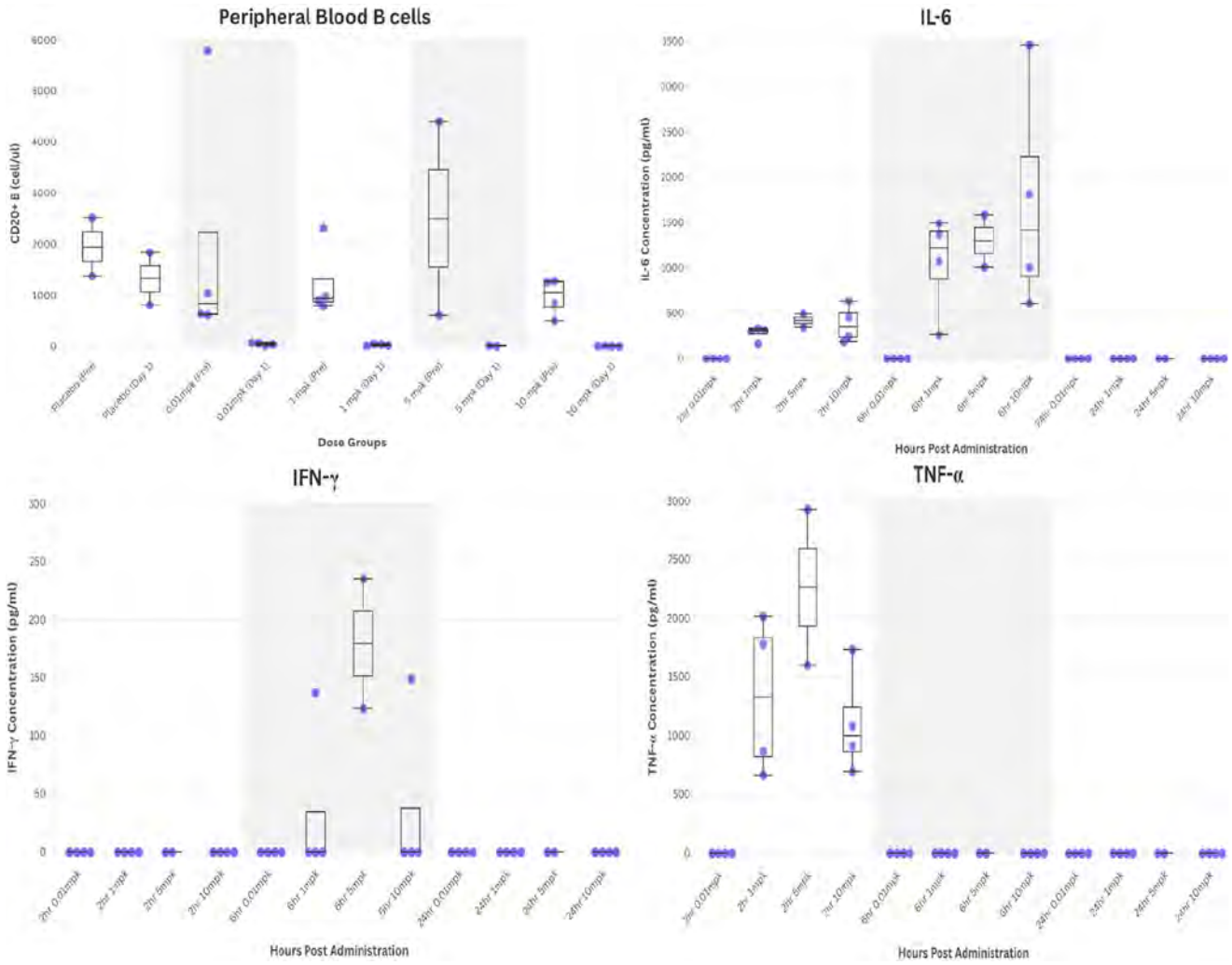


Figure 2: Peripheral Blood B cell Depletion and Cytokines After Initial SC Dose in NHP (0.01, 1, 5 and 10 mg/kg)

Conclusion: These findings in preclinical studies strongly support the clinical development of KT501 as a first-in-class trispecific TCE that is potentially effective and convenient therapy with a differentiated safety profile for many autoimmune diseases. A Phase I first-in-human clinical trial is anticipated to begin in Q1 2026.

Disclosure: M. Bao: Kali Therapeutics, 3; **J. Wang**: Kali Therapeutics, 3; **J. Zhao**: Kali Therapeutics, 3; **W. Xu**: Kali Therapeutics, 3, 8.

Abstract Number: 0013

Discovery and Characterization of SIM0710, a Novel B and T Lymphocyte Attenuator (BTLA) Agonistic Antibody for Autoimmune/Inflammatory Diseases

Xiaofeng Zhao[1], Xiaoqing Liu[1], Yuxi Yan[2], Tiezheng Liu[3], Yong Fu[3], Yulan Hu[2], Kangmin Zhou[2], **Minyun Zhou**[4], Yingying Hu[2] and Shunwei Zhu[2], [1]State Key Laboratory of Neurology and oncolog Drug Development, Simcere Pharmaceutical Group, Nanjing, China (People's Republic), [2]State Key Laboratory of Neurology and Oncology Drug Development, Simcere Pharmaceutical Group, Shanghai, China (People's Republic), [3]State Key Laboratory of Neurology and Oncology Drug Development, Simcere Pharmaceutical Group, Nanjing, China (People's Republic), [4]State Key Laboratory of Neurology and Oncology Drug Development, Simcere Pharmaceutical group, Nanjing

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: B and T lymphocyte attenuator (BTLA) is an immune checkpoint molecule that contributes to the regulation of T cell, B cell and dendritic cell function through its interaction with its ligand herpesvirus entry mediator (HVEM) on cells *in trans* and on the same cell *in cis*. Here we discovered and characterized SIM0710, which is a novel BTLA agonistic monoclonal antibody without interrupting native HVEM-BTLA interaction.

Methods: The binding activities to human BTLA protein were determined by ELISA and BLI while the blockade of BTLA-HVEM interaction were evaluated by ELISA. Agonistic functionality of SIM0710 was evaluated using a BTLA/SHP2 reporter assay. Antibody-mediated inhibition of HVEM cis-signaling was assessed using a light-driven HVEM-dependent NF-κB assay, while trans-signaling blockade was evaluated in a HVEM-dependent NF-κB assay on CHO-K1-BTLA cells. Diverse *in vitro* functional cellular assays were performed including TLR7/9-mediated IFN-α release in pDCs and modulation of co-stimulatory molecules in LPS-activated mDCs (ELISA or FACS), anti-IgM-stimulated B cell proliferation (FACS) and IL-6 secretion (ELISA), as well as anti-CD3/CD28-activated PBMC proliferation (FACS) and Th1/Th2/Th17/Th22 cytokine profiling (ELISA). *In vivo* efficacy was further assessed in humanized GvHD and TLR7 agonist-induced humanized SLE mouse models.

Results: SIM0710 demonstrates the potential to directly induce co-inhibitory agonistic signaling through BTLA, which can be further enhanced by Fc receptor engagement. Additionally, SIM0710 preserves the formation of anti-inflammatory BTLA/HVEM *cis* complex while simultaneously blocking the pro-inflammatory co-stimulatory signal mediated by HVEM through *trans* BTLA interaction. *In vitro*, SIM0710 effectively inhibited the proliferation of human primary B and T cells with concurrent reduction of IL-6 and multiple Th cytokines. Furthermore, SIM0710 modulated the functions of human primary DCs, including inhibition of the TLR7/9-induced IFN-α secretion from pDC and downregulation of co-stimulatory molecules on mDCs. *In vivo*, SIM0710 improved overall survival in a humanized GvHD mouse model. Notably, SIM0710 also significantly reduced the anti-dsDNA IgG level in the serum of an TLR7-agonist induced SLE model in hu-CD34 HSC NOG-EXL mice.

Conclusion: Taken together, SIM0710 shows broad functional inhibition in diverse pathogenic immune cells and may offer potential therapeutic benefit for treating multiple autoimmune diseases.

Disclosure: X. Zhao: Simcere Pharmaceutical Group, 3; **X. Liu**: Simcere Pharmaceutical Group, 3; **Y. Yan**: Simcere Pharmaceutical Group, 3; **T. Liu**: Simcere Pharmaceutical Group, 3; **Y. Fu**: Simcere Pharmaceutical Group, 3; **Y. Hu**: Simcere Pharmaceutical Group, 3; **K. Zhou**: Simcere Pharmaceutical Group, 3; **M. Zhou**: Simcere Pharmaceutical Group, 3; **Y. Hu**: Simcere Pharmaceutical Group, 3; **S. Zhu**: Simcere Pharmaceutical Group, 3.

Abstract Number: 0014

NKX019, an allogeneic off-the-shelf CD19 targeting CAR-NK cell therapy, induces deep CD19+ B cell depletion in hematological malignancy and models of autoimmune disease

Mira Tohmé, Meriam Vejiga, Wendy Yu, Emily Kang, Katharine Yu, Jessica Sood, Ivan Chan, Kyle Hansen, David Shook and Phung Gip, Nkarta, South San Francisco, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Autologous CAR T-cell therapies have remarkable clinical activity in autoimmune disease (AD) via B-cell targeting, with many patients achieving durable, drug-free remission. However, safety concerns persist, including toxicities such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Long manufacturing times and complex logistics that limit patient access also limit broader adoption. Allogeneic natural killer (NK) cell therapy may help address these challenges. NKX019 is an allogeneic, CD19-targeted CAR NK-cell therapy derived from healthy donor peripheral blood mononuclear cells (PMBCs) and cryopreserved for off-the-shelf use. NKX019 expresses a humanized anti-CD19 scFv CAR fused to co-stimulatory (OX40) and signaling (CD3ζ) domains to enhance killing, along with membrane-bound interleukin-15 to support persistence. In a Phase 1 clinical trial for relapsed or refractory B-cell malignancies [NCT05020678], NKX019 demonstrated a favorable safety profile, including no ICANS or life-threatening CRS, as well as encouraging anti-tumor activity. In this study, we evaluate the therapeutic potential of NKX019 in AD.

Methods: NHL patient samples and PBMCs obtained from patients with various B-cell mediated AD (SLE, SSc, IIM, MG, RA, MS) were evaluated to assess depletion of CD19+ B cells, B-cell reconstitution and immune repertoire using flow cytometry and genomic analyses (10X Genomics 5' Single Cell Gene Expression profiling paired with B-Cell Receptor (BCR) sequencing). In vivo studies were performed in NGS mice inoculated with human CD19+ B-cell lymphoma cell lines treated with NKX019 to evaluate activity and biodistribution of NKX019 in tissue samples by bioluminescence imaging (IVIS spectrum) and qPCR, respectively.

Results: NKX019 targets and kills CD19+ cells from patients with NHL and AD. In non-clinical studies, NKX019 potently and selectively depletes B cells from patients with SLE, SSc, IIM, MG, RA, and MS in a dose-dependent manner. In a B-cell lymphoma *in vivo* efficacy model, NKX019 eliminated $CD19^{+}$ lymphoma cells and trafficked to several organs including secondary lymphoid tissue, kidneys and lungs. Translational data from patient samples from the NHL trial demonstrated that NKX019 induces potent and sustained depletion of CD19+ cells from circulation. Following treatment, detailed analyses of the BCR repertoire diversity and phenotypic characterization revealed a shift of the B-cell immune repertoire toward a naïve-dominant profile.

Conclusion: In summary, non-clinical in vitro and in vivo data demonstrated that NKX019 effectively depletes CD19+ cells derived from AD patients and in CD19+ lymphoma models, respectively. In NHL patients, NKX019 induced robust B cell depletion followed by reconstitution of the B cell compartment. These data provide compelling support for NKX019 as a novel therapeutic approach for treatment of B-cell driven AD. NKX019 is currently being evaluated in Phase 1 trials for SLE LN (NCT06557265, Ntrust-1); and SSc, IIM, and ANCA-AAV (NCT06733935, Ntrust-2) and investor-sponsored trials for SLE (NCT06518668) and MG.

Disclosure: M. Tohmé: Nkarta Therapeutics, 3; **M. Vejiga**: Nkarta Therapeutics, 3; **W. Yu**: Nkarta Therapeutics, 3; **E. Kang**: Nkarta Therapeutics, 3; **K. Yu**: Nkarta Therapeutics, 3; **J. Sood**: Nkarta Therapeutics, 3; **I. Chan**: Nkarta Therapeutics, 3; **K. Hansen**: Nkarta Therapeutics, 3; **D. Shook**: Nkarta Therapeutics, 3; **P. Gip**: Nkarta Therapeutics, 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0015

CDR111 is a novel CD19 and BCMA dual-targeting T cell engager (TCE) for the treatment of severe and refractory autoimmune diseases

Philipp Richle, Stephanie Jungmichel, Alessio Vantellini, André Fonseca, Anna Howald, Fabian Scheifele, Loredana iuliano, Ariadna Vilarrasa, Romina Doerig, Hannes Merten, Philip Knobel, Daniel Lenherr-Frey, Christian Leisner and Leonardo Borras, CDR-Life, Horgen, Zurich, Switzerland

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: B cells and plasma cells are central to the pathogenesis of many autoimmune diseases. While B cell depletion therapies (BCDTs), such as anti-CD20 monoclonal antibodies, have improved outcomes in diseases like systemic lupus erythematosus (SLE), their efficacy is limited by the persistence of plasma cells, leading to disease relapses or refractory cases. Immunotherapies targeting CD19 have revolutionized the treatment of various hematological malignancies. Recently, such therapies have been used in refractory autoimmune diseases with encouraging results. CD19 is a B cell marker expressed from early B cell development through plasma cells, making it an attractive target for broad B cell depletion. However, CD19 targeting BCDT does not address accumulated long-lived plasma cells, leading to persistent autoantibody production despite B cell depletion. B cell maturation antigen (BCMA) is highly expressed on plasma cells, including long-lived plasma cells in lymphoid reservoirs (bone marrow, spleen, lymph nodes). We present a novel TCE designed to target both CD19-positive B cells and BCMA-positive plasma cells. This TCE enables cytotoxic T cells to recognize and eliminate the entire spectrum of B cell lineages, from naïve and memory B cells to plasma blasts and long-lived plasma cells. This dual-targeting approach is designed to overcome a key limitation of current BCDTs by eradicating both the precursors and the ultimate producers of pathogenic autoantibodies.

Methods: Cancer cell lines representing early B cell lineages (CD19+/BCMA-), plasma cells (CD19+/BCMA+), and fully differentiated long-lived plasma cells (CD19-/BCMA+) were co-cultured with isolated T cells and CDR111 for 48h. Peripheral blood mononuclear cells (PBMC) from autoimmune patients and bone marrow (BM) samples from healthy donors were incubated with CDR111. NCG-M mice engrafted with CD34+ human hematopoietic stem cells and treated with toll-like receptor 7 (TLR7) agonist to induce SLE-like symptoms were administered with CDR111.

Results: CDR111 showed potent in vitro killing of all tested cancer cell lines representing the entire B cell compartment. In contrast, CD19-directed control TCE showed no killing of CD19-negative cancer cells, mimicking long-lived plasma cells. Full depletion of B cells and plasma cells was achieved in patient-derived PMBCs. Potent cell killing was observed on plasma cells from BM where BCMA expression is high. CDR111 led to eradication of B cells and plasma cells in peripheral blood, spleen, and bone marrow in the NCG-M mouse model.

Conclusion: CDR111 demonstrates a differentiated approach to treating autoimmune patients. While showing peripheral B cell depletion with controlled cytokine release, it achieves potent plasma cell eradication in lymphoid organs (bone marrow and spleen). CDR111 holds the potential for a true B cell reset, resulting in durable treatment-free disease remission in patients with severe or refractory autoimmune diseases like SLE and rheumatoid arthritis.

Disclosure: P. Richle: None; **S. Jungmichel**: None; **A. Vantellini**: None; **A. Fonseca**: None; **A. Howald**: None; **F. Scheifele**: None; **L. iuliano**: None; **A. Vilarrasa**: None; **R. Doerig**: None; **H. Merten**: None; **P. Knobel**: None; **D. Lenherr-Frey**: None; **C. Leisner**: None; **L. Borras**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0016

Pharmacology Analyses of Sail's In Vivo hCD19 CAR-T Product Reveal Mechanistic Insights Underlying its Optimal Dose Efficiency Profile in Both Healthy Donors and SLE Patient Samples

Siobhan Rice, Sanket Bhagat, Jeremy Burns, Kerry Benenato, Volker Boehnert, Stacie Clark, Manali Deepak Kadam, Deborah Dodge, Paul Durfee, Sarah Gardner, Emilie Giaime, Amber Hoggatt, Khristina Holscher, Kelsey Joyce, Jane Liu, Dinesh Manvar, Paola Quintanilla, Viorel Simion, Akshi Thakkar, Michael Tsui, Jason Wade, Marc Wolfgang, Yi Yao, Vincent Hennemand, Trevor Hallam and Michael Mingueneau, Sail Biomedicines, Cambridge, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Ex vivo chimeric antigen receptor (CAR) T cell therapy has demonstrated encouraging clinical efficacy in small trials enrolling patients with B cell driven autoimmune diseases (AID), such as Systemic Lupus Erythematosus (SLE). However, existing autologous CAR-T therapies suffer from challenges in manufacturing complexity, scalability and safety. Sail Biomedicines is developing a targeted lipid nanoparticle (tLNP) encapsulating Endless RNA (eRNA^{TM})-encoded hCD19 CAR for in vivo transient reprogramming of pan-T cells.

Methods: Sail's tLNP-eRNA platform was assessed in peripheral blood mononuclear cells (PBMCs) from a cohort of healthy donors and SLE patients in an *in vitro* assay. The mechanistic contribution of various CAR expression variables as well as CD4 and CD8 CAR-T cells to autologous B cell killing was assessed in PBMCs from multiple healthy donors that were depleted of either CD4 or CD8 T cells prior to treatment with tLNP-eRNA. Using humanized mice, *in vivo* engineered T cells were characterized to further understand possible mechanisms underlying the deep B cell depletion observed in blood and lymphoid tissues.

Results: By assessing a large cohort of healthy donors in our in vitro PBMC assay, we determined the CAR expression levels required to achieve maximal B cell killing in terms of frequency of CAR$^+$ T cells, CAR$^+$ T:B ratio and number of CAR molecules per cell. We observed no correlation between the CD4:CD8 ratio of CAR$^+$ T cells and potency of B cell depletion. To investigate the contribution of each T cell subset, we transfected PBMCs depleted of either CD4 or CD8 T cells and found similar dose efficiency relationships in absence of CD4 or CD8 T cells. Healthy donors and SLE patients demonstrated comparable dose-expression and dose-functional potency relationships following treatment with our tLNP-eRNA in vitro. We optimized our dosing regimen in a B cell repopulating humanized mouse model and were able to observe deep B cell depletion in blood and lymphoid tissues, including B cell progenitors in the bone marrow. Detailed immunophenotyping and characterization of in vivo engineering kinetics revealed mechanisms underlying deep depletion of B cells in lymphoid tissues.

Conclusion: Here we explored the mechanisms underlying the optimal dose efficiency profile demonstrated by Sail's pan-T cell tLNP-eRNA. Efficient engineering of both CD4 and CD8 T cells, including T cell memory subsets with tissue migrating potential, likely explains the profound level of B cell depletion in primary and secondary lymphoid tissues and effective immune reset observed *in vivo*. Importantly, *in vitro* tLNP-eRNA engineered CD4 CAR T cells exhibited a comparable capacity to eliminate autologous B cells as CD8 CAR T cells, further supporting our pan-T targeting approach. Moreover, comparable *in vitro* pharmacology relationships in PBMCs from healthy donors and SLE patients suggest a similar dose efficiency profile will be observed in patients. Sail's tLNP-eRNA off-the-shelf IV injectable CAR-T product is poised to transform the care of patients with AID by increasing access, reducing safety risk and negating the need for lymphoablative conditioning while bearing the potential of lentiviral CAR-T efficacy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Rice: None; **S. Bhagat**: None; **J. Burns**: None; **K. Benenato**: Moderna, 12, 7; **V. Boehnert**: None; **S. Clark**: None; **M. Deepak Kadam**: None; **D. Dodge**: None; **P. Durfee**: None; **S. Gardner**: None; **E. Giaime**: None; **A. Hoggatt**: moderna, 11; **K. Holscher**: None; **K. Joyce**: None; **J. Liu**: None; **D. Manvar**: None; **P. Quintanilla**: None; **V. Simion**: None; **A. Thakkar**: None; **M. Tsui**: None; **J. Wade**: Pfizer, 11; **M. Wolfgang**: BioNtech US, 3; **Y. Yao**: None; **V. Hennemand**: None; **T. Hallam**: None; **M. Mingueneau**: Biogen, 12.

Abstract Number: 0018

Development of a noval '1+1+1' CD19- and BCMA-dual targeted T cell engager for autoimmune diseases

Lin Huan, Hao Ran, Shiyi Wang, Xiaoping Zhang, Bing Yang, Yang He, Dandan Liu, Chenpeng Su, Chuan Chen, Xiaoqian Chen, Kezhen Ye, Liang Tian, Jian Peng and **Zhenping Zhu**, Helixon Therapeutics, New York

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0001–0018) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: B cells and autoantibodies play a central role in the pathogenesis of various autoimmune diseases. Although CD19-targeted B cell depletion shows promising therapeutic potential, its clinical application is limited by the pharmacokinetic (PK) limitations of BLINCYTO and the high costs associated with CAR-T therapies. Moreover, targeting B cells or plasma cells alone is insufficient to eliminate both pathogenic B cells and autoantibody production. To overcome these challenges, we engineered HXN-1031, an innovative trispecific T cell engager (TCE) capable of dual targeting CD19 and BCMA. This approach seeks to establish a transformative treatment strategy for autoimmune conditions.

Methods: The 1+1+1 format trispecific antibody targeting CD19, BCMA, and CD3 was designed and optimized to meet both activity and druggability criteria. The binding affinity of each arm to its respective target was measured using FACS, while its cytotoxic activity was evaluated in pan-T cell cultures containing $CD19^+$, $BCMA^+$, or mixed cell populations. *In vivo* stability was examined in SD rats, and *in vivo* efficacy was assessed in PBMC-reconstituted mice bearing Raji ($CD19^+$) or H929 ($BCMA^+$) tumor cells.

Results: HXN-1031 exhibits sub-micromolar affinity for CD3 while maintaining nanomolar binding affinity for CD19 and BCMA. The trispecific TCE showed a maximum CD19-positive tumor cell-killing efficacy that is comparable to Blinatumomab and other clinical stage benchmarks, while inducing lower T cell activation and cytokine release. On the other end, HXN-1031 showed high potency in *in vitro* cytotoxicity assays across tumor cells with varying BCMA expression, exhibiting efficacy comparable to the benchmarks. Moreover, it effectively kills both CD19-positive and BCMA-positive cells simultaneously within a mixed cell population while maintaining moderate T cell activation and cytokine release. In contrast, CD19 TCE and BCMA TCE selectively target only B cells or H929 ($CD19^-BCMA^+$) cells, respectively. In animal models, HXN-1031 demonstrates good *in vivo* stability and, as a result, exhibits superior efficacy to Blinatumomab in a CD19-positive tumor model when administered twice per week. HXN-1031 significantly suppresses BCMA-positive tumor growth, showing comparable efficacy to Teclistamab analogue. Additionally, HXN-1031 showed potent efficacy in depleting B cells and plasma cells in cynomolgus monkeys.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: HXN-1031 is an innovative T cell engager with finely tuned activity against both CD19 and BCMA, designed to reset the immune system by simultaneously depleting pathogenic B cells and plasma cells. It holds great potential to significantly enhance the clinical efficacy, with the possibility of even curing certain autoimmune diseases.

Disclosure: L. Huan: None; **H. Ran**: None; **S. Wang**: None; **X. Zhang**: None; **B. Yang**: None; **Y. He**: None; **D. Liu**: None; **C. Su**: None; **C. Chen**: None; **X. Chen**: None; **K. Ye**: None; **L. Tian**: None; **J. Peng**: None; **Z. Zhu**: None.

Abstract Number: 0019

Single cell characterization of the circulating immune system in Sjögren's Syndrome

Alejandro Gómez Gómez[1], Héctor Corominas[2], Rosario Garcia Vicuña[3], Mercedes Freire Gonzlez[4], Sheila Melchor-Díaz[5], Paloma Vela Casasempere[6], Paula Estrada-Alarcón[7], Jose Luis Tandaipan[8], Monica Fernandez Castro[9], Sara Maria Rojas Herrera[10], Marina Rodríguez López[11], Beatriz Paredes-Romero[12], Santiago Muñoz[13], Marta Lpez[14], Ignacio Braña[15], Gema Bonilla[16], Raúl Menor Almagro[17], Sara Manrique-Arija[18], Mª Angeles Blazquez Cañamero[19], Lilian López-Núñez[20], Carles Galisteo Veiga[21], Juan José Alegre-Sancho[22], Jose Rosas Gómez de Salazar[23], Jose Javier Pérez Venegas[24], Judit Font-Urgelles[25], José Andrés Román Ivorra[26], José Miguel Sequí-Sabater[27], Rafaela Ortega-Castro[28], Clara Moriano[29], Guadalupe Manzano-Canabal[30], Cilia Peralta-Ginés[31], Javier Narváez[32], Rafael Cáliz-Cáliz[33], Javier Martínez-Ferrin[34], Lara Sánchez Bilbao[35], Belén Serrano-Benavente[36], Natalia Boix- Martí[37], Ares Selles-Rius[38], Maribel Pérez[39], Juan Cañete[40], Núria Palau Balaña[38], Damiana Alvarez Errico[39], Yolanda Guillén[41], Juan Ángel Patiño Galindo[41], Antonio Julià[1], Sara Marsal Barril[42], Jose Luis Andreu[43] and IMID Consortium, [1]Vall d'Hebron Hospital Research Institute, Rheumatology Research Group, Barcelona, Spain, [2]Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Barcelona, Spain, [3]Hospital Universitario de la Princesa, Madrid, Spain, [4]4 Hospital Universitario A Coruña, Rheumatology, A Coruña, La coruna, Spain, [5]Hospital Universitario 12 de Octubre, Rheumatology, Madrid, Madrid, [6]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [7]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [8]Rheumatology. Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Spain, [9]PUERTA DE HIERRO HOSPITAL, Madrid, Spain, [10]Hospital de Mérida, Rheumatology, Badajoz, Badajoz, Spain, [11]Complejo Hospitalario Universitario de Santiago, Rheumatology, Santiago de Compostela., Santiago de Compostela, Spain, [12]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, San Sebastian de los Reyes, Spain, [13]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Spain, [14]Complex Hospitalari Universitari Moiss Broggi, Barcelona, Spain, [15]Hospital Universitario Central de Asturias, Oviedo, Spain, [16]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [17]Department of Rheumatology, Hospital de Jerez, Spain, Puerto De Santa Mara, Spain, [18]Hospital Regional Universitario Mlaga, Malaga, Spain, [19]Hospital Ramon y Cajal, Madrid, Spain, [20]Hospital Son Llatzer, Rheumatology, Palma de Mallorca, Palma de Mallorca, Spain, [21]Hospital Parc Taulí, Rheumatology, Sabadell, Sabadell, Spain, [22]Hospital Universitario Doctor Peset, Valencia, Spain, [23]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [24]Virgen Macarena University Hospital, Sevilla, Spain, Sevilla, Spain, [25]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [26]Hospital Universitari i Politècnic La Fe, Valencia, Spain, [27]Hospital Universitario La Fe (Valencia), Valencia, Spain, [28]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [29]Hospital Len, LEON, Castilla y Leon, Spain, [30]Hospital Virgen de la Concha (Zamora), Zamora, Spain, [31]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [32]Hospital Universitario de Bellvitge, Barcelona, Spain, [33]Hospital Universitario Virgen de las Nieves, Rheumatology, Granada, Granada, Spain, [34]Hospital Universitario Virgen de la Arrixaca, Rheumatology, Murcia, Murcia, Spain, [35]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [36]Hospital Gregorio Marañon, Madrid, Spain, [37]Hospital Univetsitari Vall d'Hebron, Rheumatology Department, Barcelona, Spain, [38]Rheumatology Research Group, Vall d'Hebron University Hospital, Barcelona, Spain, [39]IMIDomics, Barcelona, Barcelona, Spain, [40]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [41]IMIDomics, Barcelona, Spain, [42]Vall Hebron Hospital Research Institute, Barcelona, Spain, [43]Hospital Universitario Puerta de Hierro, Majadahonda, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sjögren's syndrome (SS) is a chronic autoimmune disease characterized by the infiltration of circulating immune cells into the salivary and lacrimal glands. The properties of the peripheral immune cells associated to SS are only partially understood. In this work we aimed to comprehensively characterize the compositional cell changes and the gene expression changes of the circulating immune system associated to Sjögren's Syndrome.

Methods: Peripheral Blood Mononuclear Cells were collected from 32 SS patients and 10 sex and age matched healthy controls. Single cell transcriptome analysis was performed using droplet-based 3' scRNA-Seq technology. After clustering and annotation of the main circulating innate and adaptive immune cell types, compositional differences were tested using the cell frequencies using linear modelling. Alternatively, we used Covariant Neighborhood Analyses to identify compositional changes associated to diseases and not captured by the standard cell clusters. For each cell type, differential gene expression was performed using MAST.

Results: A total of 198,078 peripheral blood cells passed the quality control and were clustered and annotated into 27 immune cell types. SS was associated with an increased abundance of cells from the T compartment, including CD4+-TH2, CD8+TEM and proliferative T. Conversely, SS had significantly less circulating CD4 and CD8+ naive T cells, MAIT, pDC, DC3 and memory B cells compared to healthy controls. CNA analysis identified an independent subpopulation of CD8+ T cells significantly expanded in SS. Differential gene expression analyses revealed transcriptomic changes in all cell compartments, with more significant regulation occurring in specific cell types including NKCD16+, Tregs, TFH, B memory, and CD14+CCL2Hi monocytes. Pathway analysis identified a strong interferon-response signature across many cell types as well as cell-specific aberrant regulatory changes. The CD8+ T cell subpopulation associated to SS through CNA showed a significant enrichment of genes associated to SS risk.

Conclusion: This study provides the largest single cell transcriptomic analysis of circulating immune cells in SS performed to date. The changes both at the compositional and gene expression levels provide a comprehensive characterization of the immunological processes that are altered in the disease.

Disclosure: A. Gómez Gómez: None; **H. Corominas**: None; **R. Garcia Vicuña**: None; **M. Freire González**: None; **S. Melchor-Díaz**: None; **P. Vela Casasempere**: None; **P. Estrada-Alarcón**: None; **J. Tandaipan**: None; **M. Fernandez Castro**: None; **S. Rojas Herrera**: None; **M. Rodríguez López**: None; **B. Paredes-Romero**: None; **S. Muñoz**: Janssen, 1, 2, 5, 6, 7; **M. López**: None; **I. Braña**: None; **G. Bonilla**: None; **R. Menor Almagro**: None; **S. Manrique-Arija**: None; **M. Blazquez Cañamero**: Astrazeneca, 12, conference registrations, Gsk, 6, Novartis, 12, conference registrations, Rubio, 12, conference registrations; **L. López-Núñez**: None; **C. Galisteo Veiga**: None; **J. Alegre-Sancho**: None; **J. Rosas Gómez de Salazar**: None; **J. Pérez Venegas**: AstraZeneca, 6, Janssen, 4, 6, UCB, 6; **J. Font-Urgelles**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6; **J. Sequí-Sabater**: None; **R. Ortega-Castro**: None; **C. Moriano**: None; **G. Manzano-Canabal**: None; **C. Peralta-Ginés**: None; **J. Narváez**: None; **R. Cáliz-Cáliz**: None; **J. Martínez-Ferrin**: None; **L. Sánchez Bilbao**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **B. Serrano-Benavente**: None; **N. Boix- Martí**: None; **A. Selles-Rius**: None; **M. Pérez**: None; **J. Cañete**: None; **N. Palau Balaña**: None; **D. Alvarez Errico**: None; **Y. Guillén**: None; **J. Patiño Galindo**: None; **A. Julià**: None; **S. Marsal Barril**: None; **J. Andreu**: None.

Abstract Number: 0020

Bulk RNA-sequencing of Leukocytoclastic Vasculitis Skin Biopsies Show Upregulation of Leukocyte Migration Genes

Anne Carlton, Lam Tsoi, Joseph Kirma, Jennifer Fox, Paul Harms and Johann Gudjonsson, University of Michigan, Ann Arbor, MI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Vasculitis encompasses multiple conditions united by end-organ damage due to an immune-mediated reaction against the vasculature. Leukocytoclastic vasculitis (LCV) is a subtype of cutaneous vasculitis with considerable heterogeneity in etiology, duration, prognosis, and treatment. The pathophysiology underlying LCV remains poorly characterized and targeted treatments are limited.

Methods: 43 skin biopsies with confirmed LCV on histopathology and 5 skin biopsies from healthy controls underwent bulk RNA sequencing. Medical records were reviewed to determine an underlying etiology of LCV, when possible. Differential gene expression analysis and unsupervised hierarchical clustering were performed using DESeq2. Differentially expressed genes were identified with FDR < 0.5, padj ≤ 0.05, and log2FoldChange ≥ 0.5 (upregulated) or ≤ -0.5 (downregulated). Gene ontology enrichment analysis was performed using clusterProfiler. Etiologies with three or more samples were included in comparative analysis. This study was completed under University of Michigan Medical School IRB HUM00261031.

Results: Age at the time of biopsy ranged from 5-85 years old. Etiologies of LCV were unknown (33%), infection (26%), rheumatologic (21%), medications (14%), paraneoplastic (4.7%), and inflammatory bowel disease (IBD) (2.3%). Principal

Table 1. Patient characteristics

	N = 43[1]
Age at biopsy	45 (5, 85)
Sex	
F	22 (51%)
M	21 (49%)
Etiology	
Unknown	14 (33%)
Infection	11 (26%)
Rheumatologic	9 (21%)
Medication	6 (14%)
Paraneoplastic	2 (4.7%)
IBD	1 (2.3%)

[1]Mean (Min, Max); n (%)

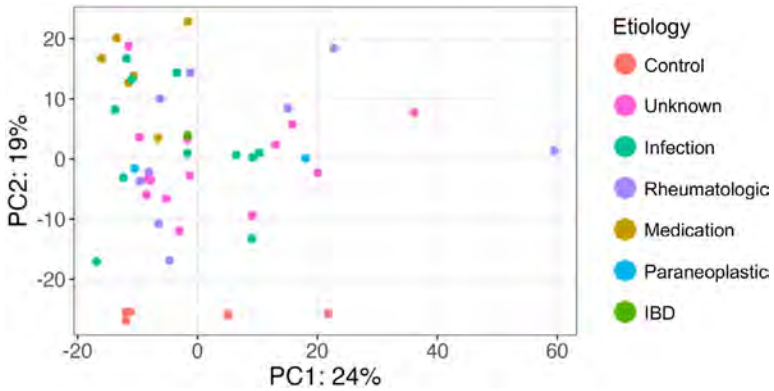


Figure 1. PCA plot of bulk RNA-sequencing data stratified by LCV etiology

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

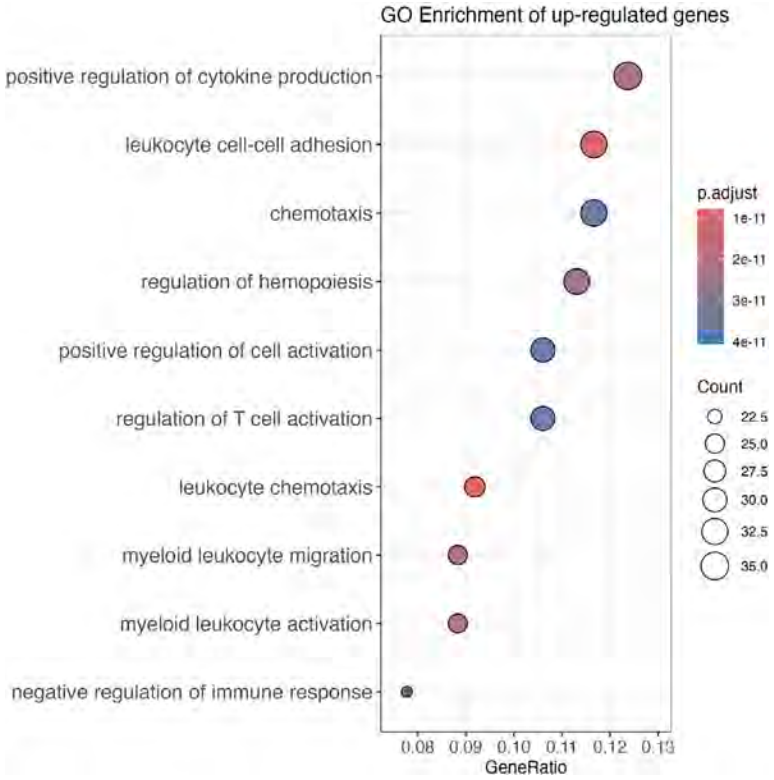


Figure 2. GO biologic process enrichment of 301 common upregulated genes

component analysis showed considerable heterogeneity between LCV samples. 2,246 genes are differentially expressed between all LCV samples and controls (915 upregulated, 1,331 downregulated). Genes upregulated in LCV were enriched for GO biological processes, including leukocyte migration, chemotaxis, and leukocyte cell-cell adhesion. 301 upregulated genes were shared in all LCV etiologies (unknown, infection, rheumatologic, medications) and were enriched for GO biological process of chemotaxis, leukocyte migration, and leukocyte cell-cell adhesion.

Conclusion: Analysis of LCV samples revealed shared upregulation of GO biologic processes related to leukocyte adhesion. Pharmacologic targeting of this pathway may serve as a potential therapeutic treatment for this subtype of vasculitis. Limitations of this study include small sample size and variable availability of associated clinical information. Future work with a larger sample size may validate these findings.

Disclosure: A. Carlton: None; **L. Tsoi**: Galderma, 5, Janssen, 5; **J. Kirma**: None; **J. Fox**: None; **P. Harms**: None; **J. Gudjonsson**: None.

Abstract Number: 0021

Doctis: A Single Cell Rna-seq Atlas of Drug Response to Targeted Therapies

Antonio Julià[1], Yolanda Guillén[2], Paloma Vela Casasempere[3], Antonio Fernández Nebro[4], Carlos Marras[5], Santos Castañeda[6], Jaime Calvo Alén[7], Jesús Tornero Molina[8], Juan Cañete[9], Eugeni Domènech[10], Javier Gisbert[11], Jose M. Carrascosa[12], Eduardo Fonseca[13], Luis Bujanda Fernández De pierola[14], Valle García Sánchez[15], Britta Siegmund[16], Giampiero Girolomoni[17], Holger Heyn[18], Laura Jiménez Gracia[18], Pere Santamaria[19], Edgar Angelats[20], Richard Myers[21], Sergio H. Martínez Mateu[2], Juan Ángel Patiño Galindo[2], Ernest Choy[22], Sara Marsal[1] and IMID Consortium, [1]Vall d'Hebron Hospital Research Institute, Rheumatology Research Group, Barcelona, Spain, [2]IMIDomics, Barcelona, Spain, [3]Hospital General Universitario de Alicante, Rheumatology, Alicante, Spain, [4]Hospital Regional Universitario Carlos Haya, Rheumatology, Málaga, Spain, [5]Hospital Universitario Virgen de la Arrixaca, Rheumatology, Murcia, Spain,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[6]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [7]Hospital Universitario de Araba, Rheumatology, Vitoria, Spain, [8]Hospital Universitario de Guadalajara, Rheumatology, Guadalajara, Spain, [9]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [10]Hospital Universitari Germans Trias i Pujol, Gastroenterology, Badalona, Spain, [11]Hospital Universitario La Princesa, Rheumatology, Madrid, Spain, [12]Hospital Universitari Germans Trias i Pujol, Dermatology, Badalona, Spain, [13]Complejo Hospitalario Universitario de A Coruña, Dermatology, A Coruña, Spain, [14]Hospital Universitario de Donostia, Gastroenterology, San Sebastián, Spain, [15]Hospital Universitario Reina Sofía, Gastroenterology, Córdoba, Spain, [16]Charité-Universitätsmedizin Berlin, Gastroenterology, Berlin, Germany, [17]University of Verona, Dermatology, Verona, Spain, [18]Centre for Genomic Regulation (CNAG-CRG), Barcelona, Spain, [19]Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelonoa, Spain, [20]Hospital Clínic-IDIBAPS, Barcelona, Spain, [21]HudsonAlpha Institute for Biotechnology, Huntsville, AL, [22]Division of Infection and Immunity, CREATE Centre, Cardiff University, Cardiff, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Targeted therapies have revolutionized the management of immune-mediated inflammatory diseases (IMIDs), however, there is a substantial number of patients who respond poorly to a given drug. There is a big need to understand the factors that are associated with this heterogeneity. The DoCTIS project aims to characterize molecular variation both at the disease and drug-response levels across six different IMIDs.

Methods: We applied single cell RNA sequencing to 360 samples from 176 patients from six prevalent IMIDs -psoriasis, psoriatic arthritis, Crohn's Disease, ulcerative colitis, rheumatoid arthritis, systemic lupus erythematosus- treated with five different drugs targeting TNF, IL12p40, IL6R, BLySS, IL17 and JAK pathways. All patients were analyzed at two time points including baseline and at the week of clinical response creating an immune landscape of more than two million peripheral immune cells.

Results: We found large inter-disease differences both at the compositional and genetic regulatory programs. ScRNA-Seq analysis revealed large differences at the systemic level between the six IMIDs. We found expected findings, like the predominant interferon response signature affecting multiple cell types in SLE, but also novel findings like strong regulatory differences between diseases with a shared genetic risk like Psoriatic Arthritis and Psoriasis. The impact of each drug was found to be largely disease-specific. Furthermore, we found multiple regulatory features associated with the effect of each drug as well the association to response.

Conclusion: The scRNA-Seq atlas developed in DoCTIS provides a unique resource for the understanding of drug response and disease heterogeneity across immune-mediated inflammatory diseases.

Disclosure: A. Julià: None; **Y. Guillén**: None; **P. Vela Casasempere**: AbbVie/Abbott, 5, 6, AstraZeneca, 5, GlaxoSmithKlein(GSK), 2, 5, 6, Lilly, 5, 6, Novartis, 5, Pfizer, 5, Roche, 5; **A. Fernández Nebro**: None; **C. Marras**: None; **S. Castañeda**: None; **J. Calvo Alén**: None; **J. Tornero Molina**: None; **J. Cañete**: None; **E. Domènech**: AbbVie/Abbott, 1, 5, 6, Adacyte Therapeutics, 1, 5, 6, Biogen, 1, 5, 6, Celltrion, 1, 5, 6, Ferring, 1, 5, 6, Galapagos, 1, 5, 6, Gilead, 1, 5, 6, GoodGut, 1, 5, 6, Janssen, 1, 5, 6, Kern Pharma, 1, 5, 6, Lilly, 1, 5, 6, Merck/MSD, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Samsung, 1, 5, 6, Takeda, 1, 5, 6, Tillots, 1, 5, 6; **J. Gisbert**: None; **J. Carrascosa**: AbbVie/Abbott, 1, 2, 6, almirall, 2, 6, Amgen, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, 6, galderma, 1, 6, imidomics, 1, johsson and johnsson, 1, 6, leo pharma, 1, Novartis, 1, 2, 6, Pfizer, 1, 6, sanofi, 1, 6, UCB, 1; **E. Fonseca**: None; **L. Bujanda Fernández De pierola**: None; **V. García Sánchez**: None; **B. Siegmund**: AbbVie/Abbott, 2, 6, Abivax, 2, AlfaSigma, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 6, CED Service GmbH,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Dr. Falk Pharma, 2, 6, Eli Lilly, 2, Endpoint Health, 2, Falk, 2, Ferring, 6, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Landos, 2, Lilly, 2, Materia Prima, 2, MSD, 6, Pfizer, 2, 5, 6, PredictImmune, 2, Takeda, 2, 6; **G. Girolomoni**: None; **H. Heyn**: Genentech, 6, Moderna, 2, Nanostring, 1, Omniscope, 4, 8, Singularity, 2; **L. Jiménez Gracia**: None; **P. Santamaria**: Parvus Therapeutics, 4, 8, Sanofi, 2; **E. Angelats**: None; **R. Myers**: None; **S. Martínez Mateu**: None; **J. Patiño Galindo**: None; **E. Choy**: AbbVie, 2, 6, Alfasigma, 6, Bio-Cancer, 2, 5, Biocon, 2, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 6, Fresenius Kabi, 2, 6, Gedeon Richter, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 6, Viatris, 2, 6; **S. Marsal**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 1, 5, IMIDomics, 4, 8, Janssen, 5, Merck/MSD, 5, Novartis, 5, Roche, 5, UCB, 5.

Abstract Number: 0022

Genome-wide association study identifies novel genetic risk factors for rheumatoid arthritis-associated interstitial lung disease

Austin Wheeler[1], Thomas Riley[2], Riku Takei[3], Joshua Baker[2], Yangyuna Yang[1], Punyasha Roul[4], Katherine Wysham[5], Grant Cannon[6], Gary Kunkel[7], Gail Kerr[8], Dana Ascherman[9], Paul Monach[10], Andreas Reimold[11], Jill Poole[1], Ted Mikuls[1], Tony Merriman[12] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Alabama at Birmingham, Birmingham, AL, [4]UNMC, Omaha, NE, [5]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [6]University of Utah and Salt Lake City VA, Salt Lake City, UT, [7]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [8]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [9]University of Pittsburgh, Pittsburgh, PA, [10]VA Boston Healthcare System, Boston, MA, [11]Dallas VA Medical Center, Dallas, TX, [12]University of Alabama at Birmingham, Homewood, AL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is clinically present in ~10% of individuals with RA. There is recognized overlap between RA-ILD and idiopathic pulmonary fibrosis (IPF) with shared genetic risk, namely the *MUC5B* rs35705950 promoter variant. Genome-wide association studies (GWAS) in IPF have identified other single nucleotide polymorphism (SNP) risk alleles, but GWAS in RA-ILD have been limited. We aimed to identify novel genetic risk alleles for RA-ILD in a large, multicenter RA cohort.

Methods: We utilized the Veterans Affairs Rheumatoid Arthritis (VARA) registry, a multicenter, prospective cohort of US Veterans with RA. ILD was systematically identified and validated via medical record review. All participants underwent genotyping on banked DNA via the Illumina Global Screening Array. Imputation was performed using the Trans-omics for Precision Medicine (TOPMed) imputation panel on the NHLBI TOPMed imputation server, and filtered for minor allele frequency, missingness, and Hardy-Weinberg equilibrium. Population stratification was accounted by ancestral principal components. GWAS was performed using SAIGE v1.3.0 (R 3.6.3) for MAF >1%. After accounting for linkage disequilibrium (r^2 >0.8), variants reaching a suggestive genome-wide level of significance ($p < 1x10^{-6}$) were investigated using the National Center for Biotechnology Information dbSNP database and National Human Genome Research Institute GWAS Catalog. Plots were generated using LocusZoom. A genetic risk score (GRS) for ILD was calculated using additive counts of the six significant variants weighted by the natural log of the OR compared to an additive model of the *MUC5B* variant alone using logistic regression.

Results: We studied 3295 participants (87% male, mean age 73 years), of whom 345 had RA-ILD. A total of 28,233,561 SNPs were included. ILD signals appeared on chromosomes (chr) 6, 7, 11, 16, 20, and 22 (**Figure 1**). Six SNPs reached the threshold for significant associations with ILD (**Table 1**). As expected, *MUC5B* rs35705950 was the strongest risk variant for RA-ILD (**Figure 2**). In addition to *MUC5B*, we identified 5 novel SNPs. The strongest of these (rs191761566) was an

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

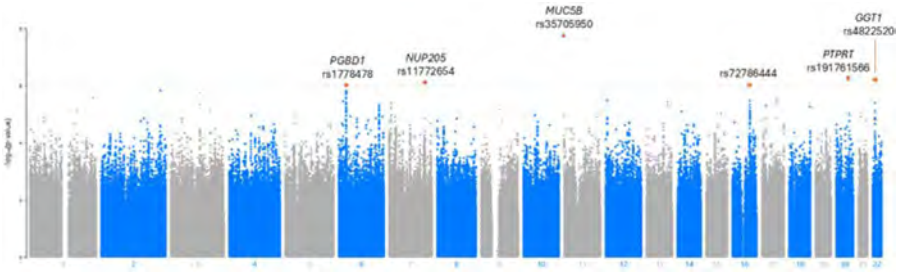


Figure 1. Manhattan plot.

Table 1. Rheumatoid arthritis-associated interstitial lung disease risk loci detected in genome-wide association study. Abbreviations: chromosome (chr), reference single nucleotide polymorphism (rs), minor allele frequency (MAF), odds ratio (OR) GRCh38 position given.

			Allele		MAF (effect allele)		Effect allele	
Chr:Position	rs ID	Gene	Other	Effect	Case	Control	OR	p-value
11:1219991	rs35705950	MUC5B	G	T	0.164	0.093	1.95	1.68E-08
20:43134854	rs191761566	PTPRT	G	A	0.033	0.009	3.98	5.41E-07
22:24615302	rs4822520	GGT1	T	C	0.312	0.222	1.57	6.18E-07
7:135592878	rs11772654	NUP205	C	G	0.157	0.094	1.79	7.31E-07
16:66359939	rs72786444	-	G	T	0.123	0.069	1.92	9.10E-07
6:28279861	rs1778478	PGBD1	A	T	0.245	0.175	1.66	9.21E-07

uncommon variant on chr20 in the *PTPRT* gene, a gene implicated in the STAT3 pathway and that predicts lung cancer response to immune checkpoint inhibitors. *GGT1* (chr22) is associated with IPF, *NUP205* (chr7) contributes to ciliary dysfunction, *PGBD1* (chr6) has been associated with RA and implicated in lung cancer, and rs72786444 (chr16) lies in a predicted enhancer region for *CDH5*, which is expressed in lung endothelial cells. A GRS containing the 6 variants (AUC 0.67 [0.64-0.70) significantly outperformed the *MUC5B* variant alone (AUC 0.57, 0.54-0.59) in discrimination of ILD in patients with RA (p< 0.001).

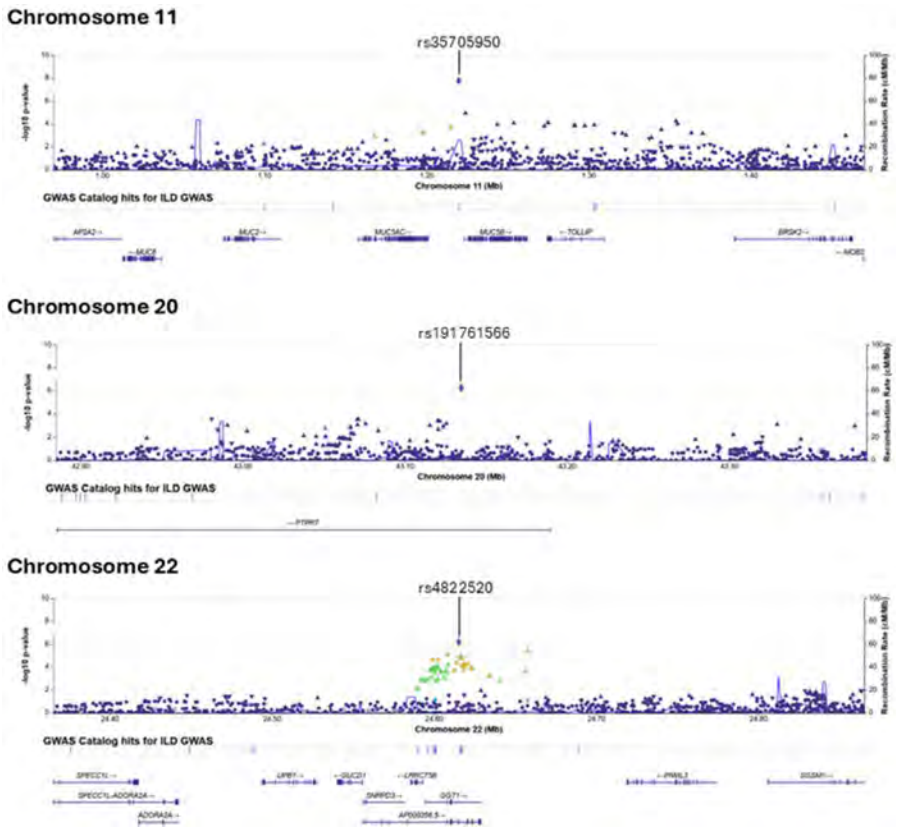


Figure 2. LocusZoom plots for top three risk loci detected by p-value.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In addition to the well-established *MUC5B* promoter variant, this GWAS of ILD in a large RA cohort with validated ILD cases identified several other novel SNPs within genes and regions that have potential pathophysiologic connections to ILD. A GRS containing these SNPs provided significant improvement in ILD discrimination beyond *MUC5B* alone.

Disclosure: A. Wheeler: None; **T. Riley**: None; **R. Takei**: None; **J. Baker**: Amgen, 5; **Y. Yang**: None; **P. Roul**: None; **K. Wysham**: None; **G. Cannon**: None; **G. Kunkel**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **D. Ascherman**: None; **P. Monach**: Boehringer-Ingelheim, 2; **A. Reimold**: None; **J. Poole**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **T. Merriman**: None; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 0023

Longitudinal Proteomic Effects of Hydroxychloroquine in Individuals at Risk of Lupus: Differential Signatures in Progressors and Non-Progressors

Benjamin Jones[1], Miles Smith[2], Rufei Lu[2], Carla Guthridge[2], Susan Macwana[2], Wade DeJager[3], Nancy Olsen[4], Catriona Wagner[5], Judith James[2], David Karp[6] and Joel Guthridge[2], [1]Oklahoma State University, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma city, OK, [3]Oklahoma Medical Research Foundation, Oklahoma City, [4]Penn State University/Milton S Hershey, Hershey, PA, [5]Oklahoma Medical Research Foundation, Santa Cruz, CA, [6]UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is routinely prescribed for treatment of systemic lupus erythematosus (SLE) due to its efficacy at decreasing disease activity/SLE flares and strong benefit:risk ratio. However, the heterogeneity in the molecular mechanism of HCQ responses is not fully appreciated. The Study of Anti-Malarials in Incomplete Lupus Erythematosus (SMILE; NCT03030118), a double-blind, randomized, placebo-controlled trial to evaluate whether HCQ could delay or halt progression to SLE, provides longitudinal samples to characterize molecular differences in individuals who remained stable incomplete lupus erythematosus patients compared to those who gained additional criteria at some point during the 2-year study.

Methods: Baseline, 3 month, and 6 month serum samples from 105 Non-Progressors (did not gain SLICC criteria; 54 HCQ, 51 Placebo) and 54 Progressors (gained 1 or more SLICC criteria, 27 HCQ, 27 Placebo) from the SMILE trial were analyzed using the Olink Explore HT proteomics platform (>5,000 proteins). After stringent quality control, analytes were retained only if the intra-individual coefficient of variation (CV) across multiple visits exceeded the technical CV in $\geq$90% of samples, resulting in 1,490 proteins for downstream analysis. Linear mixed effects models assessed protein changes over time by group. Proteins with nominal $p < 0.2$ were further analyzed by Gene Set Enrichment Analysis (GSEA) using Kyoto Encyclopedia of Genes and Genomes and Gene Ontology pathways.

Results: Proteomic analysis revealed both treatment- and progression-specific signatures. Analysis with GSEA found that both Non-Progressors and Progressors on HCQ showed downregulation of Toll-like receptor, TNF, IL-17 signaling pathways in addition to viral protein interaction pathways (Figure 1A), suggesting that these pathways represent HCQ effects independent of disease trajectory. Additionally, Non-Progressors on HCQ exhibited downregulation of JAK-STAT and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

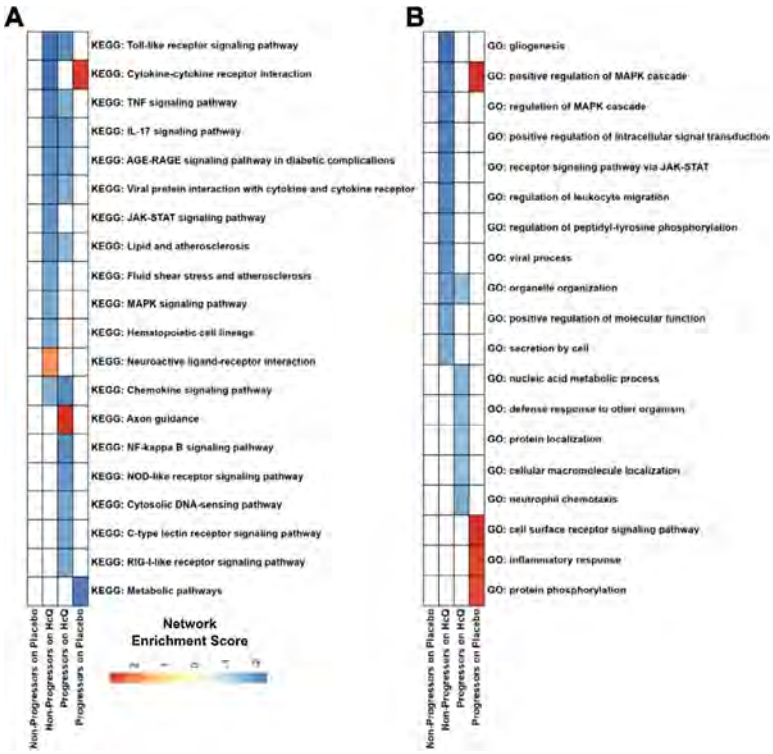
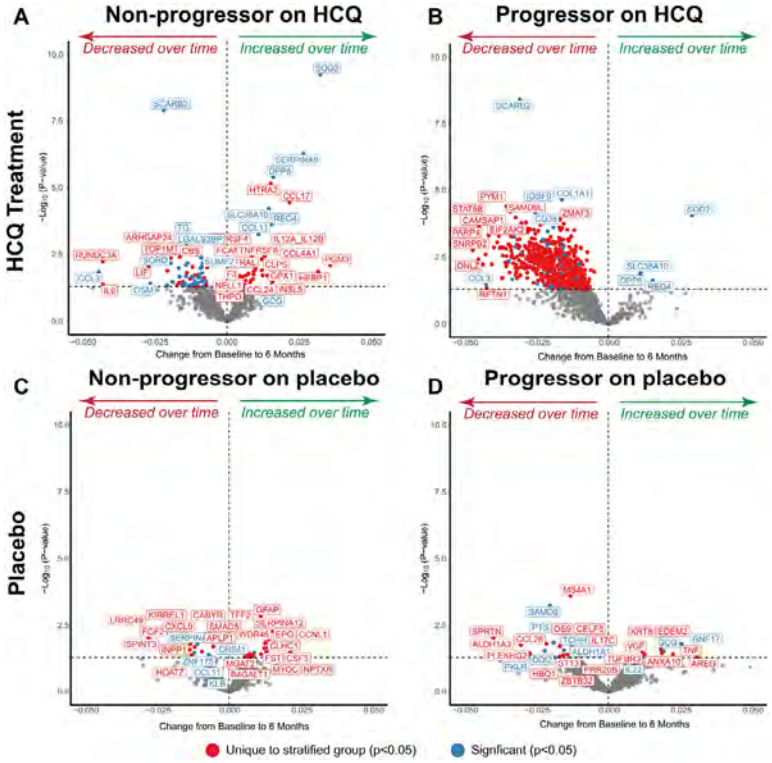


Figure 1. Pathway enrichment shows treatment and disease-specific signatures. Normalized enrichment scores (NES) for significantly enriched pathways (Q < 0.05), as identified by GSEA using Kyoto Encyclopedia of Genes and Genomes terms (A) and Gene Ontology Biological Process (B), comparing the first 6 months within each group.



Volcano plots showing changes in protein abundance between baseline and 6 months, as determined by linear mixed effects models in (A)Non-Progressors on HCQ, (B) Progressors on HCQ, (C) Non-Progressors on Placebo, and (D) Progressors on Placebo. X-axis indicates the fixed effect coefficient representing the change over time per stratified group, while legends indicate whether the protein was found to be significantly changed at P<0.05 uniquely in the stratified group (red) or in multiple groups (blue).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

MAPK signaling pathways while Progressors on Placebo show an increase in MAPK cascade over the first 6 months (Figure 1B). Progressors on Placebo also had increased inflammatory response pathways, while there was no pathway enrichment observed in Non-Progressors on placebo. IL-6 was uniquely decreased in Non-Progressors on HCQ (Figure 2A), while CCL3 was decreased and SOD2 was increased in Non-Progressors and Progressors on HCQ (Figure 2B). Non-Progressors on Placebo exhibited a decrease in CCL11, contrary to the increase seen in Non-Progressors on HCQ (Figure 2C). Progressors showed an increase in TNF over time (Figure 2D).

Conclusion: Within the first six months of treatment, HCQ exerts both disease-dependent and independent molecular effects, with distinct proteomic and pathway changes in individuals at risk for SLE progression. These findings illustrate the pleiotropic effect of HCQ and offer insight into pathways up-regulated in pre-clinical lupus.

Disclosure: B. Jones: None; **M. Smith**: None; **R. Lu**: None; **C. Guthridge**: None; **S. Macwana**: None; **W. DeJager**: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5; **C. Wagner**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **D. Karp**: Ampel Biosciences, 2, Biogen, 5, Bristol-Myers Squibb(BMS), 5, Caribou, 1, Eli Lilly, 5, Novartis, 5, Sanofi, 1, UCB, 5, Zura, 1; **J. Guthridge**: None.

Abstract Number: 0024

Biobank-scale genetic mapping identifies the shared genetic landscape of rheumatic and cardiovascular disease

Daniel Panyard[1], Daniel Li[2], Pik Fang Kho[2], Rodrigo Guarischi-Sousa[3], Jiayan Zhou[2], Austin Hilliard[4], Christie Bartels[5], Philip Tsao[2] and Themistocles Assimes[2], [1]Stanford University, Sunnyvale, CA, [2]Stanford University, Palo Alto, CA, [3]Palo Alto Veterans Institute for Research, Palo Alto, CA, [4]VA Palo Alto Health Care, Palo Alto, CA, [5]University of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatic conditions are at increased risk for cardiovascular (CV) problems, striking on average a decade before peers and conferring substantial morbidity and mortality. Understanding the mechanisms underlying this elevated CV risk could lead to improved care for rheumatology patients and novel treatments for CV conditions. While genetic studies have illuminated several mutual risk loci between certain pairs of conditions, these studies have been limited in size, scope, and replication. Our goal was to conduct a comprehensive joint genetic analysis across 8 rheumatic conditions and 8 CV conditions based on two nation-wide data repositories, characterizing the shared genetic risk, loci, and putative causal SNPs.

Methods: We used the Million Veteran Program (MVP; n = 453,878) and UK Biobank (UKB; n = 406,492) EUR cohorts and genome-wide association study (GWAS) statistics based on PheCode definitions of 8 rheumatic (rheumatoid arthritis [RA], lupus [SLE], ankylosing spondylitis [AS], psoriatic arthropathy [PA], regional enteritis, sicca syndrome, ulcerative colitis [UC], and chronic UC) and 8 CV traits (coronary artery disease [CAD], arterial embolism, aortic aneurysm [AA], venous embolism, myocardial infarction [MI], congestive heart failure [CHF], peripheral vascular disease [PVD], and cerebrovascular disease [CVD]) (MVP: Verma et al. 2024, UKB: Zhou et al. 2018) (Figure 1). Genetic heritability (LDSC), global genetic correlation (LDSC), local genetic correlation (HESS), systematic colocalization (coloc, with adaptive locus identification), fine-mapping (SuSiE), and functional enrichment (STRING) were performed for each rheumatic-CV trait pair in a bidirectional replication framework.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

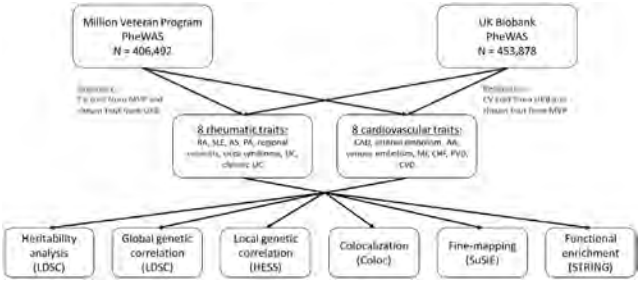


Figure 1. Study design. Genome-wide association study (GWAS) summary statistics from PheWAS performed in both MVP (Verma et al. 2024) and UKB (Zhou et al. 2018) for 16 total rheumatic and CV traits were used. The rheumatic traits included rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), psoriatic arthropathy (PA), regional enteritis, sicca syndrome, ulcerative colitis (UC), and chronic UC. The CV traits included coronary artery disease (CAD), arterial embolism and thrombosis, aortic aneurysm, other venous embolism and thrombosis, myocardial infarction MI), congestive heart failure (nonhypertensive) (CHF), peripheral vascular disease (PVD), and cerebrovascular disease (CVD). For the discovery analysis, the CV trait was taken from MVP and the rheumatic trait taken from UKB; the replication analysis reversed this order.

Results: Heritabilities were generally higher in MVP than UKB, particularly for CV traits. A total of 31 significant genetic correlations (false discovery rate [FDR] < 0.05) were identified, all positive. Four rheumatic-CV trait pair genetic correlations replicated in the reverse cohort setup (all involving RA; range: 0.08 – 0.30). A total of 76 regions showed nominal local genetic correlation (P < 0.05), with 23 of those regions at the 6p21.32/6p21.33 locus. All genome-wide-significant SNPs (P < 5e-8) were tested for colocalization (posterior probability for H3 or H4 > 0.8) and fine-mapped (4,773 loci), yielding 25 loci estimated to share the same causal variant (H3) and 26 loci estimated to have different causal variants (H4). These 51 loci were functionally enriched for genes related to antigen processing and peptide presentation (Gene Ontology BP; FDR < 0.05).

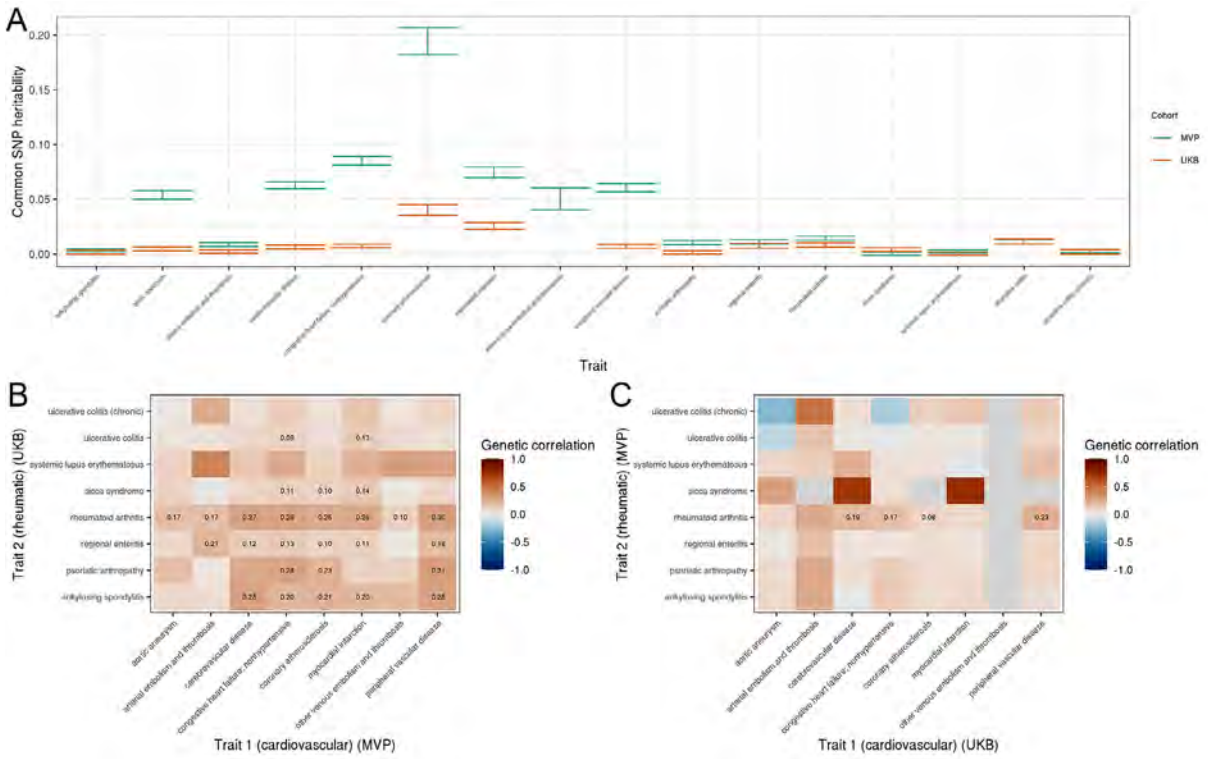


Figure 2. Heritability and global genetic correlation between rheumatic and cardiovascular traits. (A) The heritabilities estimated by LD score regression (LDSC) in a EUR population for each trait (defined by PheCode) are shown by cohort. The pairwise global genetic correlations between each rheumatic and CV trait are shown for both the discovery (B) (CV trait from MVP and rheumatic trait from UKB) and replication (C) (CV trait from UKB and rheumatic trait from MVP) analyses. Statistically significant correlations (FDR < 0.05) are indicated by text showing the estimated correlation in the heatmap. Gray indicates failed estimations (likely due to low heritability in one or both traits).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

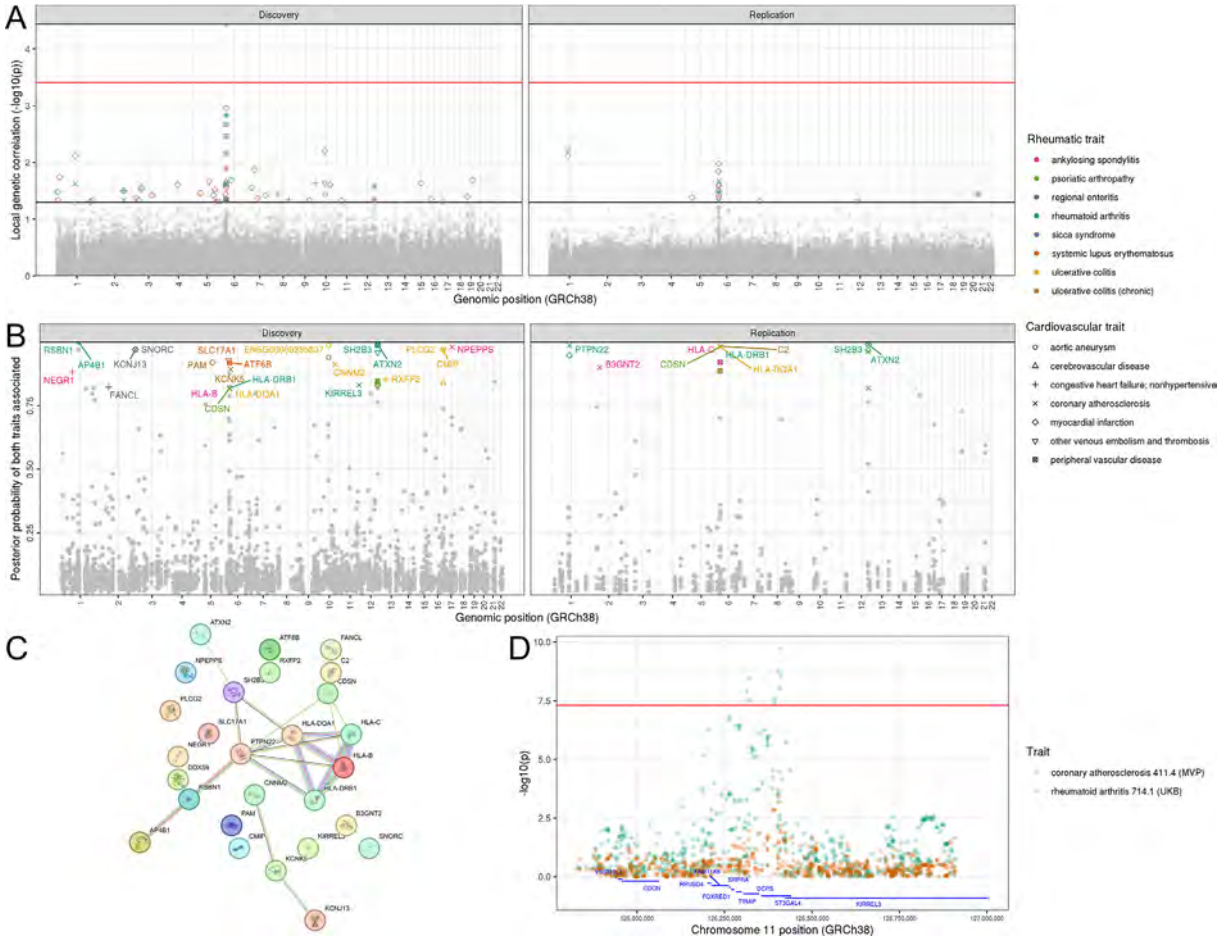


Figure 3. Colocalization and fine-mapping of genetic loci underlying rheumatic and cardiovascular traits. (A) The local genetic correlation for each tested region and for all 128 trait pairs is shown. The color indicates the rheumatic trait, and the shape indicates the CV trait. Significant enrichment of correlated loci with bidirectional replication was found in the 6p21.32/6p21.33 region. (B) The posterior probabilities of both traits being associated (y axis; sum of H3 and H4 coloc hypotheses) for each of the 4,773 tested loci are shown. For significantly colocalized loci (posterior probability > 0.8), the label shows the nearest gene. Insignificant loci are shown as gray points. (C) A functional gene network (STRING) of the genes implicated by the colocalization analysis is shown, including genes from loci either with shared or different casual variants (H3 or H4 > 0.8). (D) The GWAS assocations for the 11p34.1 locus underlying both RA and CAD are shown (results show discovery analysis). The red line indicates the genome-wide significance threshold (5e-8). The blue lines and labels indicate protein-coding genes near the locus (GENCODE).

Implicated loci for RA included *ATXN2* (with CAD, MI, CVD, venous embolism), *SH2B3* (with MI, PVD), *RSBN1* (with CHF), and the 11p34.1 locus near *ST3GAL4* and *KIRREL3* (with CAD).

Conclusion: Our findings support the presence of shared genetic risk between numerous rheumatic and CV conditions, both on the level of mutually implicated genes and of potentially causal variants. Genes related to antigen processing and peptide presentation were enriched among the colocalized loci of rheumatic and CV traits. The strongest shared genetic signal was seen for RA, implicating *ATXN2*, *SH2B3*, *RSBN1*, and the 11p34.1 locus.

Disclosure: D. Panyard: None; **D. Li**: None; **P. Kho**: None; **R. Guarischi-Sousa**: None; **J. Zhou**: None; **A. Hilliard**: None; **C. Bartels**: None; **P. Tsao**: None; **T. Assimes**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0025

Expansion and Transcriptional Reprogramming of CD14$^+$ and CD16$^+$ Monocytes in Behçet's Disease

Elio Carmona[1], Rabia Deniz[2], Cemal Bes[3], Haner Direskeneli[4], Ahmet Gul[5] and Amr Sawalha[6], [1]Division of Pediatric Rheumatology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA, Pittsburgh, [2]University of Health Sciences Basaksehir Çam and Sakura City Hospital, Istanbul, Turkey, [3]University of Health Sciences, Basaksehir Çam and Sakura City Hospital, Istanbul, Turkey, [4]Marmara University, ISTANBUL, Turkey, [5]Istanbul University, Istanbul, Turkey, [6]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's disease (BD) is a chronic, relapsing inflammatory disease characterized by complex immunopathogenesis and limited treatment options. Monocytes are known to play a significant role in BD, with studies indicating alterations in monocyte subsets and functions. However, the detailed transcriptional programs and subset-specific contributions of monocytes to BD pathogenesis remain to be fully characterized. In this study, we leveraged single-cell transcriptomics to uncover monocyte subset-specific immune alterations in BD.

Methods: We performed single-cell RNA sequencing using GEM-X technology (10X Genomics) on PBMCs from 50 individuals (38 BD patients, 12 matched healthy controls). Sample multiplexing was enabled by antibody-based cell hashing. Data preprocessing, normalization, and clustering were performed using Seurat v5. Differential expression, cell composition analyses, and pathway enrichment (GO and GSEA) were conducted to identify disease-associated profiles.

Results: After quality control filtering, we analyzed a total of 251,924 PBMCs, successfully characterizing all major immune cell populations. Focusing on monocyte subsets, we observed significant transcriptional alterations in BD patients. CD14$^+$ monocytes exhibited a significant expansion compared to healthy controls as well as an upregulation of inflammatory and interferon-stimulated genes including *IFI27, IFITM1/2, IFI6*, and *S100A9*. Gene Ontology analysis showed enrichment of cytokine signaling and innate immune activation pathways. Gene Set Enrichment Analysis (GSEA) further highlighted hallmark pathway enrichment for inflammatory response and IL6/JAK/STAT3 signaling, consistent with known BD immunopathology. Similarly, CD16$^+$ monocytes were expanded in BD but exhibited a distinct transcriptional program. Upregulated genes included cytotoxicity-associated effectors (*PRF1, GIMAP4–8*), chemotactic receptors (*CCR5, CX3CR1, CMKLR1*), inflammasome components (*CASP1, PYCARD*), and stress-response genes (*HSPA1A, HSPA6*). Increased expression of immune checkpoints (*CD200R1, SLAMF6, BTLA*) and ISGs (*RSAD2, IFI44L, OAS1*) suggested a pro-inflammatory, non-classical activation state in CD16$^+$ monocytes. Functional enrichment pointed to immune effector functions, cell death, and migration pathways.

Conclusion: Our study provides a comprehensive single-cell map of PBMCs in Behçet's disease, revealing profound transcriptional remodeling of monocyte subsets. While CD14$^+$ monocytes display canonical inflammatory features, we identify an expansion of CD16$^+$ monocytes with a distinct cytotoxic, chemotactic, and interferon-responsive profile. These findings highlight monocyte heterogeneity in BD and uncover candidate pathways that may guide future therapeutic strategies targeting innate immune dysregulation.

Disclosure: E. Carmona: None; **R. Deniz**: None; **C. Bes**: None; **H. Direskeneli**: None; **A. Gul**: None; **A. Sawalha**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0026

Spatial Proteomic-based Phenotyping of Muscle Stem Cells and their Niches in Myositis

Bilgesu Safak Tümerdem[1], Yi-Nan Li[2], Tim Filla[3], Rolf Schröder[4], Anna Brunn[5], Alexandru Micu[6], Ayla Nadja Stuetz[1], Laura-Marie Lahu[6], Aleix Rius Rigau[7], Christina Bergmann[8], Alexandru-Emil Matei[9], Jörg Distler[10] and **Andrea-Hermina Györfi**[11], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Nordrhein-Westfalen, Germany, [2]University Hospital of Dösseldorf, Dösseldorf, Germany, [3]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [4]Institute of Neuropathology, Friedrich-Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [5]Institute of Neuropathology, Heinrich-Heine University, University Hospital of Düsseldorf, Düsseldorf, Germany, [6]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Germany, [7]Department of Internal Medicine 3, Rheumatology and Clinical Immunology, Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen. Deutsches Zentrum Immuntherapie (DZI), Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [8]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [9]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany, [10]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [11]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Immune-mediated inflammatory myopathies (IIMs) are a heterogeneous group of diseases characterized by chronic inflammation, damage and impaired regeneration of the skeletal muscle leading to progressive muscle weakness. Muscle stem cells (MuSCs) play a key role in muscle regeneration, together with other myogenic and non-myogenic stromal cells. However, the exact mechanisms of impaired skeletal muscle regeneration in IIMs are incompletely understood.

Methods: We applied imaging mass cytometry (IMC) to explore the heterogeneity of MuSCs at the single-cell level and characterize cellular alterations of MuSC niches *in situ* in muscle biopsies of IIM patients. Muscle biopsies of patients with dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), and control individuals (CO) were analyzed.

Results: We analyzed a total of 69288 cells, including 57623 stromal cells, of which 14595 MuSCs, and identified 17 stromal cell subpopulations, including four subpopulations of MuSCs. We observed IIM-subtype-specific changes in the frequencies of MuSC subpopulations. $CD56^{hi}$;$CD90^{hi}$;$PAX7^{low}$ MuSCs were particularly upregulated in PM and DM, while $CD82^{hi}$;$PAX7^{low}$ MuSCs were mostly upregulated in IBM muscle biopsies. $GLI1^{hi}$;$PAX7^{hi}$ MuSCs were upregulated only in PM patients and $CD82^{neg}$;$PAX7^{low}$ MuSCs were not changed in frequency compared with CO. Each MuSC subpopulation was characterized by a unique spatial niche. Two MuSC niches were enriched for distinct stromal cells ($CD82^{hi}$;$PAX7^{low}$ and $CD82^{neg}$;$PAX7^{low}$ MuSC niches) and the other two ($CD56^{hi}$;$CD90^{hi}$;$PAX7^{low}$ and $GLI1^{hi}$;$PAX7^{hi}$ MuSC niches) for distinct subsets of immune cells. The $CD82^{hi}$;$PAX7^{low}$ MuSC niche was composed of LECs, while the $CD82^{neg}$;$PAX7^{low}$ MuSC niche was composed of ECs and muscle fibers. The $CD56^{hi}$;$CD90^{hi}$;$PAX7^{low}$ MuSC cellular neighborhood (CN) was enriched in NK cells,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

HLA-DR$^-$ M2 macrophages, and regenerating muscle fibers, while the GLI1^{hi};PAX7^{hi} MuSC CN was enriched in HLA-DR$^+$ M2 macrophages, HLA-DR$^+$ CD20$^+$ B cells, HLA-DR$^+$ CD28$^-$ T cells, and helper T cells. Furthermore, we identified IIM-subtype-specific perturbations in the cellular interaction network of MuSC populations. The frequencies of MuSC subpopulations correlated with standard histopathological measures of muscle regeneration.

Conclusion: Using spatial proteomics, we unraveled the heterogeneity of MuSCs in DM, PM and IBM patients and identified IIM-subtype-specific changes in the frequencies of the distinct MuSC subpopulations together with unique perturbations in their local niches and cellular interactions. These data might offer potential for therapeutic modulation of individual MuSC subpopulations in IIM, aiming to improve skeletal muscle regeneration and thus combat disabling muscle weakness.

Disclosure: B. Tümerdem: None; **Y. Li**: None; **T. Filla**: None; **R. Schröder**: None; **A. Brunn**: None; **A. Micu**: None; **A. Stuetz**: None; **L. Lahu**: None; **A. Rius Rigau**: None; **C. Bergmann**: Kyverna Therapeutics, Inc., 5; **A. Matei**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6.

Abstract Number: 0027

Consistent Method to Generate Hyaline Cartilage from Human Induced Pluripotent Stem Cell-Derived Multi-Tissue Organoids

Huzefa Husain[1], Manci Li[2], Juan Abrahante[3], Natalia Mancipe[3], Amanda Vegoe[4], Yi Wen Chai[5], Beth Lindborg[6], Marc Tompkins[7], Brenda Ogle[8], Peter Larsen[9], Timothy O'Brien[10] and Ferenc Tóth[11], [1]Department of Biomedical Engineering, University of Minnesota, Minneapolis, [2]Department of Electrical and Computer Engineering, Minnesota Center for Prion Research and Outreach, University of Minnesota, Minneapolis, [3]Minnesota Supercomputing Institute, University of Minnesota, Minneapolis, [4]Department of Veterinary Population Medicine and Stem Cell Institute, University of Minnesota, Sarcio, Inc, St. Paul, [5]Stem Cell Institute, University of Minnesota, Minneapolis, [6]Sarcio, Inc., St. Paul, [7]Department of Orthopedic Surgery, University of Minnesota, Sarcio, Inc., Minneapolis, [8]Department of Biomedical Engineering, Stem Cell Institute, University of Minnesota, Minneapolis, [9]Department of Veterinary and Biomedical Sciences, Minnesota Center for Prion Research and Outreach, University of Minnesota, St. Paul, [10]Department of Veterinary Population Medicine and Stem Cell Institute, University of Minnesota, Sarcio, Inc, Minneapolis, [11]Department of Veterinary Clinical Sciences, University of Minnesota, St. Paul

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Existing methods to produce hyaline cartilage from human induced pluripotent stem cells (hiPSCs) face significant limitations, such as complex culture conditions, instability of the cartilage phenotype, and variability across batches. Our objective was to develop a robust, consistent, and animal component-free (xeno-free) method to generate hyaline cartilage through self-organized multi-tissue organoids (MTOs).

Methods: We developed a xeno-free culture method for differentiating hiPSCs to MTOs in which hyaline cartilage differentiation emerged by 8 weeks in culture. MTOs were cultured under defined conditions for up to 15 weeks, with evaluations conducted at multiple time points. Differentiation into cartilage was characterized by histological analysis for cartilage-specific matrix components. Independent bulk RNA sequencing (bulk-seq) at weeks 8, 11, and 15 was performed to profile

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

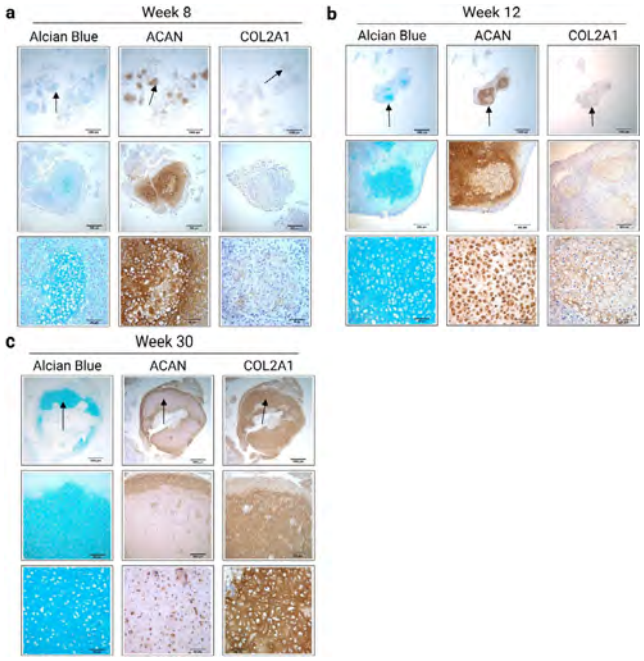


Figure 1. Histology of multi-tissue organoids (MTOs) at 8, 12, and 30 weeks. a. MTOs at 8 weeks show a developing cartilage nodule with diffuse Alcian blue staining (blue) of the early cartilaginous matrix, diffuse labeling for aggrecan (ACAN, brown) in cells and matrix, and type II collagen labeling (COL2A1, brown) in the cartilaginous matrix. Size bars = 1000 μm, 200 μm, 50 μm. Arrows indicate areas magnified in the second and third rows. b. MTOs at 12 weeks show maturing cartilage with increased Alcian blue positive cartilaginous matrix separating chondrocytes, moderate diffuse staining for type II collagen, and diffuse aggrecan labeling. Arrows indicate areas magnified in the second and third rows. Size bars = 1000 μm, 200 μm, 50 μm. c. MTOs after 30 weeks in culture show further maturation to hyaline cartilage morphology with chondrocytes surrounded by an abundant matrix with diffuse Alcian blue and type II collagen staining, and aggrecan staining apparent in the periphery. Arrows indicate areas magnified in the second and third rows. Size bars = 1000 μm, 200 μm, 50 μm.

gene expression changes over time, while single-cell RNA sequencing (scRNA-seq) was independently employed to elucidate cellular heterogeneity and specific differentiation trajectories within the organoids. Both sequencing approaches were essential for thoroughly characterizing hiPSC-derived cartilage.

Results: Histological analysis confirmed robust cartilage formation at 15 weeks, evidenced by intense immunohistochemical staining for collagen type II and aggrecan, indicative of characteristic cartilage extracellular matrix deposition (Fig 1). Bulk-seq analyses comparing weeks 8, 11, and 15 showed significant maturation of cartilage phenotype, with notable upregulation of cartilage-specific genes, including COL2A1 and ACAN ($p< 0.01$), and downregulation of pluripotency markers ($p< 0.001$) by week 15. Further bulk-seq analysis revealed that the gene expression profile of week-15 hiPSC-derived cartilage closely resembled that of developing human cartilage (Fig 2), and was distinct from adult cartilage, suggesting a developmental progression in vitro. Single-cell RNA sequencing identified minimal off-target differentiation, with chondrocytes constituting the majority (>85%) of cells and minimal residual pluripotent cell population (> 3%) (Fig 3). Additional staining exhibited limited pluripotent marker expression across batches, with 6.94 ± 1.65% Oct4+ cells and 17.54 ± 4.68% SSEA4+ cells (Fig 3).

Conclusion: We present a reproducible, xeno-free method for generating high-quality hyaline cartilage from hiPSC-derived MTOs. The integrated use of bulk-seq and scRNA-seq validated the chondrogenic differentiation process, demonstrating stable cartilage phenotype, minimal off-target differentiation, and developmental progression, thus making this approach highly promising for cartilage tissue engineering and the basis for potential clinical applications.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

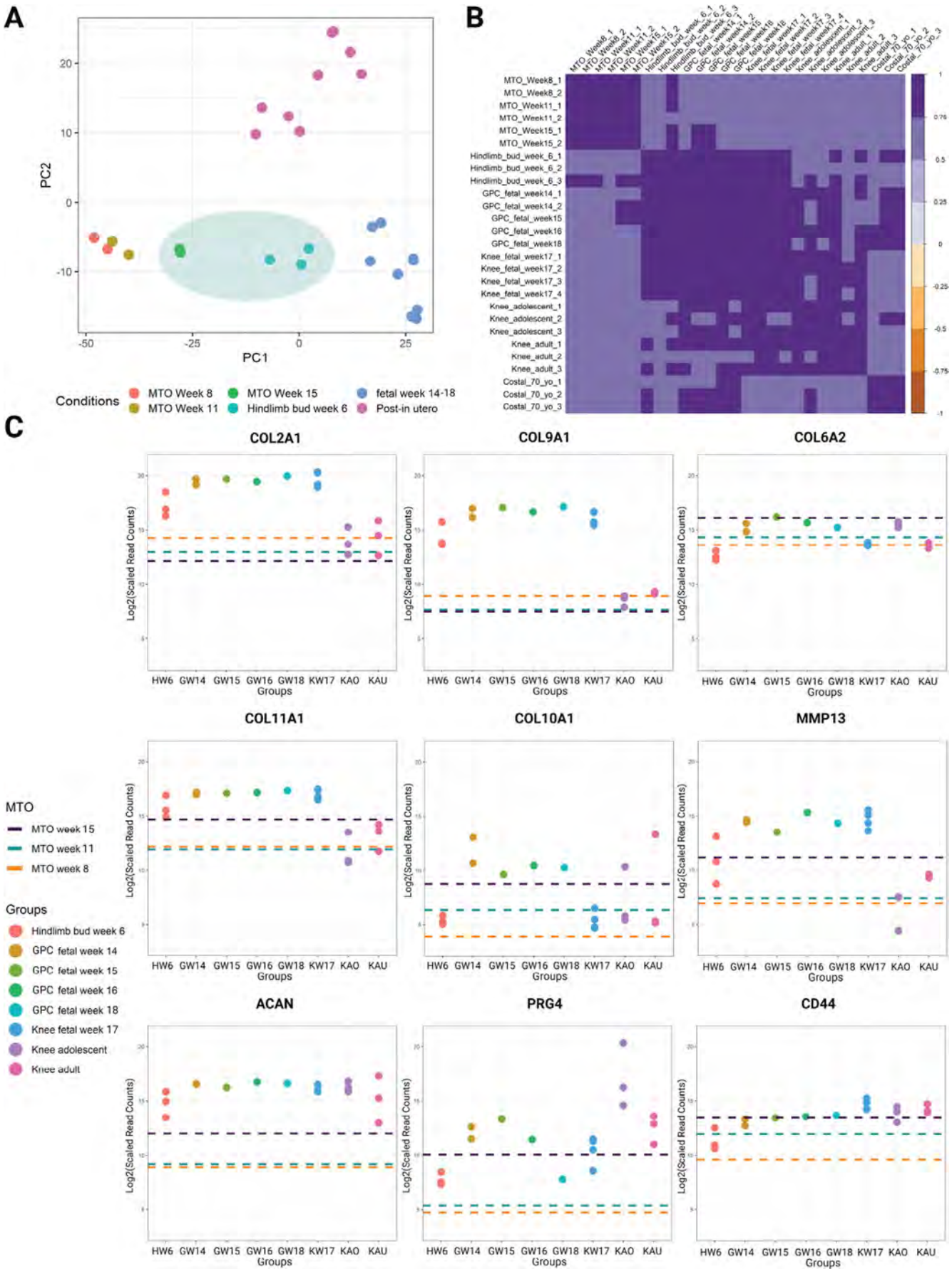


Figure 2. Transcription signatures in MTOs compared to human lower limb bud cartilage at 6 weeks of development (hindlimb bud week-6), fetal weeks 14-17, adolescent knee cartilage (kao), and adult knee and costal cartilage (kau). a. Principal component analysis (PCA) on 325 chondrocyte-specific genes shows closest matching for wk15 MTOs and human lower limb bud cartilage (green ellipse). b. Pearson correlation plot of 325 chondrocyte-specific genes showing closest match for wk15 MTOs and human lower limb bud cartilage, but with overall close matching with all stages of human cartilage. c. Representative comparisons of marker transcripts (COL2A1, COL9A1, COL6A2, COL11A1, COL10A1, MMP13, ACAN, CD44, PRG4) in MTOs and human cartilage at each growth stage. Wk15 MTOs showed closest matches to all stages of human cartilage. MTOs – multi-tissue organoids; GPC – growth plate chondrocytes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

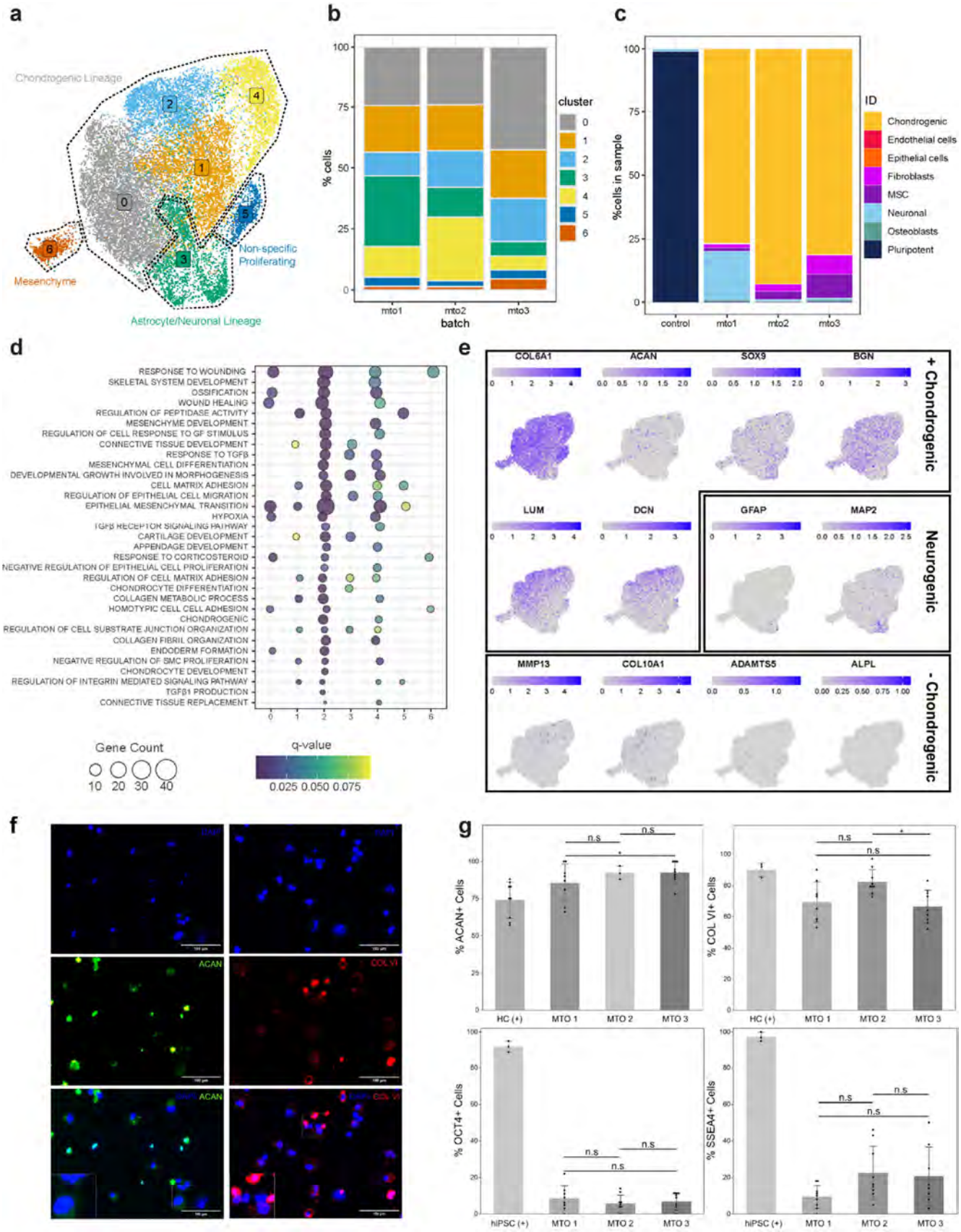


Figure 3. Single-cell RNA-sequencing data showing uniformity of cell populations within and across MTOs. a. Uniform Manifold Approximation Projection (UMAP) and b. Split-bar graph generated using scRNA-seq data of cells derived from 3 batches of MTOs. Results show homogeneity at the cluster levels across the MTO batches, with clusters 0, 1, 2, and 4 representing cells within the chondrogenic lineage, cluster 3 corresponding to neurogenic lineage cells, cluster 5 indicative of non-specific proliferating cells, and cluster 6 containing cells consistent with a mesenchyme phenotype. c. SingleR algorithmic labeling of the unique cell populations found across MTOs at the single cell level in comparison to undifferentiated hiPSC control based on the Human Primary Cell Atlas (HPCA) reference. d. Dot plot depicting enriched biological process terms related to chondrogenesis in the top 300 upregulated marker genes across chondrogenic-lineage clusters. e. Feature plots of positive and negative chondrogenic markers, as well as positive neurogenic markers. f. Immunocytochemistry images of singularized cells of MTOs verifying the expression of chondrogenic markers, type VI collagen (Col VI) and Aggrecan (ACAN) at the protein level, co-stained with DAPI. Scale bar = 100 μm g. Quantification of ICC images of COL VI, ACAN, and pluripotent markers OCT4 and SSEA4. Data represent mean ± SD from each MTO biological replicate (n=8) in comparison to respective positive control (n=3). Statistical significance was assessed by Tukey's HSD test. (* = $p < 0.05$).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Husain: None; **M. Li**: None; **J. Abrahante**: None; **N. Mancipe**: None; **A. Vegoe**: Sarcio, Inc., 12, 4, 8, 10, 11; **Y. Chai**: Sarcio, Inc., 11; **B. Lindborg**: Sarcio, Inc., 12, 4, 8, 10, 11; **M. Tompkins**: Sarcio, Inc., 12, 4, 11; **B. Ogle**: None; **P. Larsen**: None; **T. O'Brien**: Sarcio, Inc., 12, 4, 8, 10, 11; **F. Tóth**: Sarcio, Inc., 1, 11.

Abstract Number: 0028

Computational and Laboratory Identification of Risk-Driving Alleles on Juvenile Idiopathic Arthritis (JIA)-Associated Haplotypes

Adam He[1], Hannah Ainsworth[2], Kaiyu Jiang[3], Ekaterina Khtovatkova[2], Yanmin Chen[3], Carl Langefeld[4], Charles G Danko[1] and **James N. Jarvis**[5], [1]Cornell University Baker School of Veterinary Medicine, Ithaca, NY, [2]Wake Forest University, Winston-Salem, NC, [3]University of Washington School of Medicine, Seattle, WA, [4]Wake Forest University School of Medicine, Winston Salem, NC, [5]University of Washington Center for Indigenous Health, Seattle, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Multiple genomic regions are known to confer risk for JIA. However, identifying the SNPs that exert the biological effects that confer risk, and therefore the target genes, is confounded by linkage disequilibrium (LD). LD makes the true risk-driving SNPs statistically indistinguishable from those (the majority) with which they are co-inherited. We used novel analytics and wet lab procedures to identify three SNPs within JIA risk regions whose biological properties make them likely disease-driving variants.

Methods: Our groups have developed independent methods for assessing the likelihood that a SNP on a disease haplotype exerts risk-driving biological effects. The first is an AI-based approach that captures the effect of JIA SNPs on each of the distinct stages of enhancer assembly (as we have previously shown that JIA risk variants are likely to be situated in active or poised enhancers). We trained sequence-to-activity models to predict three different types of genomic data, ATAC-seq, PRO-cap, and PRO-seq, that capture different stages of enhancer assembly. The second method predicts allelic effects on DNA shape/topology, a critical feature of DNA function (e.g., transcription factor binding). To verify the utility of these approaches, we undertook wet lab confirmation of computational predictions using enhancer reporter and DNA pulldown assays.

Results: Using the AI-based method for assessing enhancer (and transcriptional) effects, we identified a SNP within the JIA-associated *IRF1* locus, rs2548998 G to A, as likely to influence transcription. This SNP lies within a large enhancer cluster

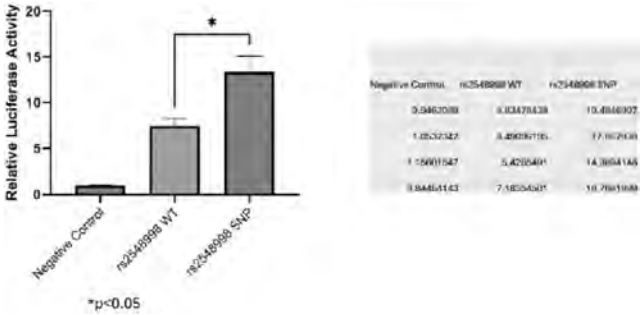


Figure 1 – Results of an enhancer reporter assay performed in CD3/CD28/IL2-activated primary humanCD4+ T cells. We compared the common allele ("rs2548998 WT") with the G to A variant ("rs2548998 SNP"). The SNP showed 2-fold enhancer activity compared with the common allele. Raw data from each of 4 experiments (relative luciferase expression) is shown in the table on the right. The negative control consisted of the green fluorescence protein vector without reporter vector without the enhancer construct inserted.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

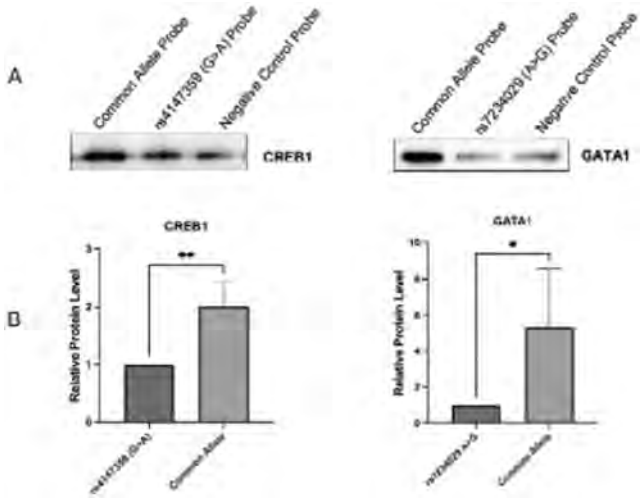


Figure 2 - Identification of proteins with different binding affinity to common allele or allele of single nucleotide polymorphismsidentified via DNA topology analyses as likely to have significant effects on transcription factor binding. (A) Western blot verification of DNA pull-down assay. Nuclear protein extracts from Jurkat cells were incubated with Streptavidin MicroBeads and biotin-labeled probes representing the common allele or allele of rs4147359 (GA, TF CREB1). Nuclear protein extracts from K562 cells were incubated with Streptavidin MicroBeads and biotin-labeled probes representing the common allele or allele of rs7234029 (AG, TF GATA1). (B) The protein levels were quantified using the iBright Analysis System (Thermo Fisher Scientific). Significant differences were marked with an asterisk (*$p < 0.05$; **$p < 0.01$; n=4).

upstream of the *IRF1* transcription start site, marked by both H3K27ac ChIPseq and PROseq-dREG peaks. Using a luciferase enhancer reporter assay, we demonstrated that the rs2548998 G®A allele showed 2x more activity than the common allele in activated primary human CD4+ T cells (**Figure 1)**. We used a DNA pulldown assay to corroborate predictions from DNA topology analyses regarding effects of SNPs' effects on transcription factor binding. We tested 2 SNPs, rs4147359 G to A, within an a CREB1 binding site upstream of *IL2RA* (using nuclei extracted from Jurkat T cells), and rs7234029 A®G, situated in a GATA1 binding site within the first intron of *PTPN2* (using myeloid K562 cells; GATA1 is not expressed in lymphoid cells). **Figure 2** summarizes the results of these experiments. The SNP, rs4147359 G®A reduced CREB1 by approximately 2-fold compared to the common allele ($p< 0.01$), while rs7234029 A®G reduced GATA1 binding by more than 4-fold compared to the common allele ($p< 0.05$).

Conclusion: We demonstrate that, by using a combination of computational techniques that predict different features of DNA/chromatin, and corroborating computational predictions with wet lab techniques, we can identify true risk-driving alleles on JIA risk haplotypes.

Disclosure: A. He: None; **H. Ainsworth**: None; **K. Jiang**: None; **E. Khtovatkova**: None; **Y. Chen**: None; **C. Langefeld**: None; **C. Danko**: None; **J. Jarvis**: None.

Abstract Number: 0029

A Novel B Cell Subpopulation Characteristic of Iga Vasculitis Identified by Single-cell RNA Sequencing

Joao Carlos Batista-Liz[1], María Sebastián Mora-Gil[2], Evan Troendle[3], Oisin Cappa[3], Maite Leonardo[4], Ana Peñalba[4], Luis mARTIN pENAGOS[5], Ligia Gabrie-Rodriguez[6], Rafael Gálvez Sánchez[6], Jose Luis Callejas[7], Belen Sevilla[8], Diego de Argila[9], Esther Vicente-Rabaneda[9], Santos Castañeda[10], David Simpson[3], Ricardo Blanco[11], Verónica Pulito Cueto[1] and Raquel Lopez Mejias[1], [1]IDIVAL, Santander, Spain, [2]Immunopathology Group, IDIVAL, Santander, Spain, [3]Queens University, Wellcome-Wolfson Institute for Experimental Medicine, Belfast, United Kingdom, [4]Division of Pediatrics, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [5]Immunopathology Group, IDIVAL and Division of Nephrology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [6]Division of Rheumatology, Hospital Universitario

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [7]Department of Internal Medicine, Hospital San Cecilio, Granada, Spain, [8]Division of Pediatrics, Hospital Universitario San Cecilio, Granada, Spain, [9]Hospital Universitario de la Princesa, Madrid, Spain, [10]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [11]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IgA vasculitis (IgAV) is a systemic small-vessel vasculitis characterized by immune complex deposition containing aberrantly glycosylated IgA1. While its clinical manifestations are well defined [1], the molecular mechanisms driving disease onset and progression remain poorly understood. Diagnosis still relies on invasive tissue biopsies, underscoring the need for molecular biomarkers to support non-invasive alternatives. Although B cells are central to IgA biology, their role in IgAV pathogenesis remains unclear [2], particularly regarding the regulation of IgA glycosylation [3]. Here, we present the first single-cell RNA sequencing (scRNA-seq) analysis of peripheral B cells in IgAV, with the aim to identify cell subpopulations presenting transcriptional alterations associated with the disease's ethiopathogenesis.

Methods: For this study we recruited 12 Caucasian IgAV patients in the acute phase of the disease and 12 healthy individuals matched by sex, age, and ethnicity to the patients. From the extracted peripheral blood, mononuclear cells were isolated using a density gradient with Ficol and purified the CD19+ B Cells using a magnetic separation kit using MACS® Technology. Single-cell separation and library preparation was carried out using the Chromium platform (10X technologies)

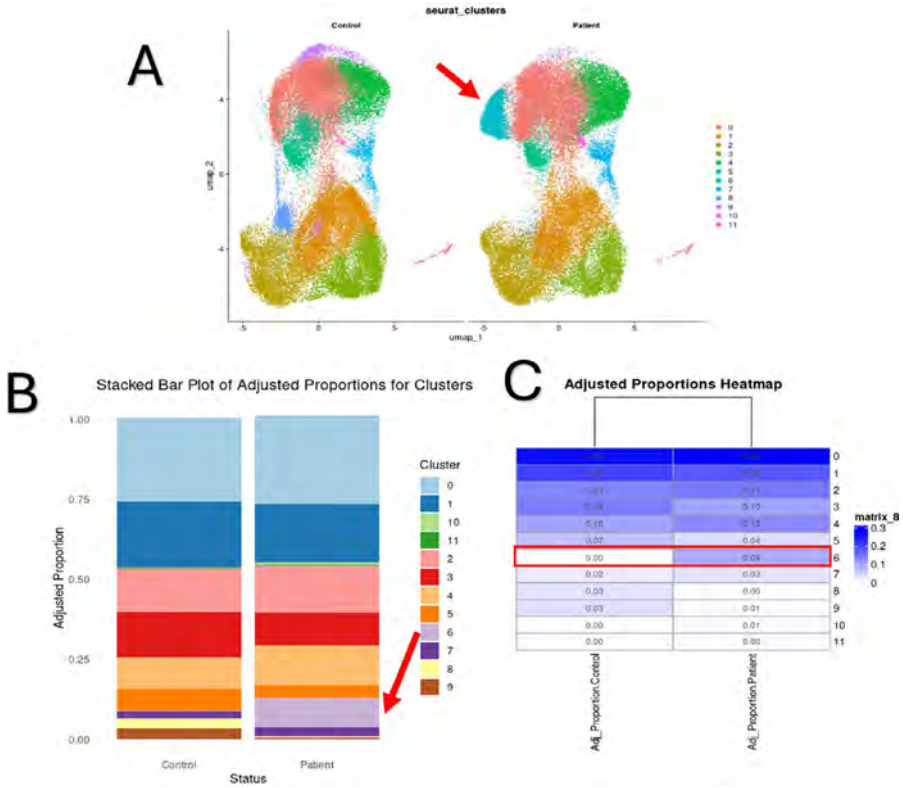


Figure 1. A) UMAP visualization of B cell subpopulations identified by Leiden clustering in IgAV patients and healthy controls. The red arrow indicates the cluster of interest (Leiden cluster 6), which is enriched in IgAV samples. B) Stacked bar plot showing the relative proportions of B cell clusters in each group. Leiden cluster 6, highlighted with a red arrow and box, is overrepresented in IgAV patients. C) Heatmap summarizing B cell cluster proportions across individual samples, further illustrating the expansion of Leiden cluster 6 in IgAV.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

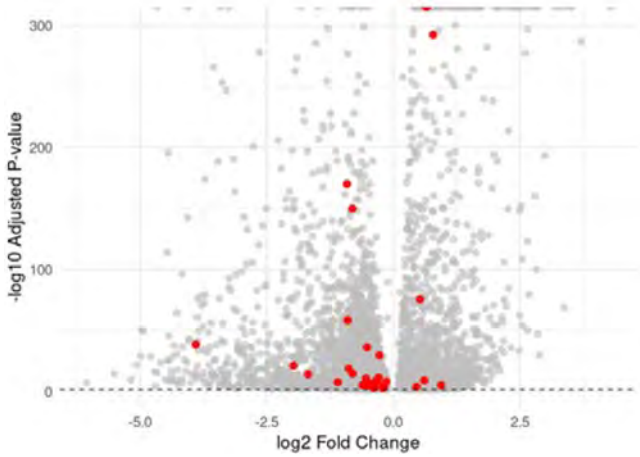


Figure 2. Volcano plot of differential gene expression from the B cell subpopulation identified in Leiden cluster 6. Genes highlighted in red are associated with glycosylation pathways implicated in the production of aberrantly glycosylated IgA. Dotted line represents a 0.05 p-value threshold.

and Illumina library preparation kits. Transcriptomic sequencing was carried out on a Novaseq X plus instrument. Raw sequencing data was preprocessed with cellranger and its outputs were analysed with Scanpy and Seurat.

Results: Interestingly, our results reveal for the first time a B cell subpopulation significantly enriched in IgAV patients compared to healthy controls (Fig. 1A). This subset, corresponding to Leiden cluster 6, showed a marked overrepresentation in the IgAV group, as illustrated by both the cluster-wise proportion comparison (Fig. 1B) and the heatmap of cluster proportions (Fig. 1C). Of note, differential gene expression analysis of this population revealed dysregulation of key genes involved in O-glycosylation pathways (Fig. 2), including known regulators of IgA glycosylation. These findings suggest that this B cell subset may contribute to IgAV pathogenesis through the production of aberrantly glycosylated IgA, highlighting its potential relevance as both a mechanistic driver and a biomarker of disease.

Conclusion: Our results reveal, for the first time, a B cell subpopulation with dysregulated glycosylation genes characteristic of IgAV, highlighting its potential as a disease-specific biomarker and a contributor to pathogenic IgA production.

References:[1] Arthritis Rheum. 2013 Jan;65(1):1-11. [2] Front Immunol. 2022 Oct 3:13:921864. [3] Semin Nephrol. 2024 Sep;44(5):151571.

Funding: European Union FEDER funds and "Fondo de Investigaciones Sanitarias" from "Instituto de Salud Carlos III" (ISCIII, Health Ministry, Spain), (PI21/00042 and PI24/00382). JCBL: PFIS program fellowship from the ISCIII, co-funded by the European Social Fund (`Investing in your future'), (FI22/00020), M-AES mobility grant (MV24/00004). RL-M: Miguel Servet type II program fellowship from the ISCIII, co-funded by ESF ("Investing in your future" (CPII21/00004).

Disclosure: J. Batista-Liz: None; **M. Sebastián Mora-Gil**: None; **E. Troendle**: None; **O. Cappa**: None; **M. Leonardo**: None; **A. Peñalba**: None; **L. mARTIN pENAGOS**: None; **L. Gabrie-Rodriguez**: None; **R. Gálvez Sánchez**: None; **J. Callejas**: None; **B. Sevilla**: None; **D. de Argila**: None; **E. Vicente-Rabaneda**: None; **S. Castañeda**: None; **D. Simpson**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6; **V. Pulito Cueto**: None; **R. Lopez Mejias**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0030

Immune-related Diagnoses Associated with *NOD2* Variants in Human Subjects: A Phenome-wide Association Study

John Davis[1], Elizabeth Atkinson[1], Vanessa Kronzer[1], Cynthia Crowson[2], Afsaneh Alavi[3], John Damianos[1], Loftus Edward[1], Joseph Murray[1], Ann Moyer[1] and Filippo Pinto e Vairo[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Stewartvillle, MN, [3]Department of Dermatology, Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The nucleotide-binding oligomerization domain-containing protein 2 (*NOD2*) gene is associated with risk for several inflammatory diseases, including Crohn disease, Blau syndrome, and Yao syndrome (YAOS). Growing awareness of the heterogeneity of *NOD2*-associated conditions has exposed a knowledge gap about the spectrum of *NOD2*-related phenotypes. Our aim was to perform a phenome-wide association study (PheWAS) of *NOD2* variants.

Methods: This study leveraged resources of a population-scale research program with available genomic sequencing data for nearly 100,000 participants recruited in the Midwest, Southeast, and Southwest United States. Participants were 18 to 50 years old, registered as patients at our institution, and had email and web access. Patients were excluded if they had a comorbidity that interfered with study participation, allogeneic bone marrow transplant, active hematological cancer, or non-U.S. residents. Twenty-seven *NOD2* variants were pre-specified based on literature review. A sample of subjects carrying at least one pre-specified *NOD2* variant was identified and matched to *NOD2* variant-unexposed subjects by age, sex, residence, and length of medical records (i.e., >5 years). Subjects' ICD-10 codes were pulled electronically for the prior 5 years and mapped to general PheWAS codes. For this analysis, one code appearance in five years was sufficient to count. PheWAS categories that appeared in fewer than 5 subjects were excluded. Chi-square tests were used to evaluate differences in the frequencies of PheWAS categories between NOD2 variant-exposed and unexposed subjects.

Results: The study included 500 subjects with *NOD2* variants and 500 matched subjects without any *NOD2* variants. The top four were c.2717+158C >T (IVS8+158), c.2782G >A (p.Val928Ile), c.2023C >T (p.Arg675Trp), and c.2938dup (p.Leu980ProfsTer2), with gnomAD allele frequencies 0.109 to 0.015 in descending order. *NOD2* variant-exposed subjects had significantly higher frequencies than *NOD2*-unexposed subjects of twelve PheWAS categories ($p < 0.05$), including 'rheumatoid arthritis and other inflammatory polyarthropathies', 'inflammatory bowel disease (IBD) and other gastroenteritis

Table 1. Phenome-wide association study of *NOD2* variant-exposed subjects and matched *NOD2* variant-unexposed subjects. Shown are selected categories with p<0.10.

PheWAS Category	NOD2 variant-exposed	Unexposed	p-value
Rheumatoid arthritis and other inflammatory polyarthropathies	3.2%	0.6%	0.003
Inflammatory bowel disease and other gastroenteritis and colitis	3.6%	1.2%	0.013
Encounter for long-term (current) use of antibiotics	1.2%	0%	0.014
Other signs and symptoms involving emotional state	1.6%	0.2%	0.019
Acute and chronic tonsillitis	4.0%	2.0%	0.021
Thoracic or lumbosacral neuritis or radiculitis, unspecified	7.0%	4.0%	0.037
Neuralgia, neuritis, and radiculitis NOS	4.2%	2.0%	0.045
Muscular dystrophies and other myopathies	1.2%	0.2%	0.058
Other perinatal conditions of fetus or newborn	3.4%	1.6%	0.062
Disorders of the pituitary gland and its hypothalamic control	2.8%	1.2%	0.071
Psoriasis and related disorders	2.8%	1.2%	0.071
Poisoning by other anti-infectives	6.0%	3.6%	0.076
Benign neoplasm of other endocrine glands and related structures	1.8%	0.6%	0.081
Other disorders of intestine	6.2%	3.8%	0.082
Abnormal movement	8.4%	5.6%	0.083
Other endocrine disorders	1.4%	0.4%	0.094
Venous/cerebrovascular complications in pregnancy and the puerperium	1.4%	0.4%	0.094

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Most important variants driving the associations between *NOD2* variants and 'rheumatoid arthritis or other inflammatory arthritis' (phe714).

NOD2 SNP	HGVS (MANE Select)	No (N = 981)	RA-related (N = 19)	p-value
rs2066844	c.2023C>T (p.Arg675Trp)	11.8	36.8	0.001
rs5743289	c.2717+158C>T (IVS8+158)	34.3	57.9	0.032
rs2066847	c.2938dup (p.Leu980ProfsTer2)	8.3	0.0	0.192
rs5743291	c.2782G>A (p.Val928Ile)	15.7	26.3	0.210
rs5743271	c.785A>G (p.Asn262Ser)	1.6	0.0	0.575
rs5743277	c.2026C>T (p.Arg676Cys)	1.4	0.0	0.600
rs61755182	c.485C>T (p.Thr162Met)	1.2	0.0	0.628
rs104895444	c.2296G>A (p.Val766Met)	1.0	0.0	0.655
rs104895431	c.1211C>T (p.Ser404Leu)	0.8	0.0	0.693
rs104895427	c.850C>T (p.Arg284Trp)	0.4	0.0	0.780
rs2066845	c.2651G>C (p.Gly881Arg)	4.1	5.3	0.796
rs104895464	c.2291G>A (p.Arg764Aln)	0.3	0.0	0.809
rs104895467	c.2474A>G (p.Asn825Ser)	0.3	0.0	0.809
rs201586544	c.59C>T (p.Ser20Leu)	0.2	0.0	0.844
rs146054564	c.379G>A (p.Asp127Asn)	0.1	0.0	0.889
rs540122692	c.1459T>C (p.Tyr487His)	0.1	0.0	0.889
rs5743276	c.1969C>T (p.Arg657Trp)	0.1	0.0	0.889
rs5743278	c.2093C>G (p.Ala698Gly)	0.1	0.0	0.889

Table 3. Most important variants driving the associations between *NOD2* variants and 'inflammatory bowel disease or other gastroenteritis or colitis' (phe555).

NOD2 SNP	HGVS (MANE Select)	No (N = 976)	IBD-related (N = 24)	p-value
rs2066844	c.2023C>T (p.Arg675Trp)	11.9	29.2	0.011
rs5743289	c.2717+158C>T (IVS8+158)	33.9	66.7	0.001
rs2066847	c.2938dup (p.Leu980ProfsTer2)	7.6	29.2	<0.001
rs5743291	c.2782G>A (p.Val928Ile)	16	12.5	0.645
rs5743271	c.785A>G (p.Asn262Ser)	1.6	0.0	0.527
rs5743277	c.2026C>T (p.Arg676Cys)	1.4	0.0	0.555
rs61755182	c.485C>T (p.Thr162Met)	1.2	0.0	0.585
rs104895444	c.2296G>A (p.Val766Met)	0.9	4.2	0.115
rs104895431	c.1211C>T (p.Ser404Leu)	0.7	4.2	0.061
rs104895427	c.850C>T (p.Arg284Trp)	0.4	0.0	0.783
rs2066845	c.2651G>C (p.Gly881Arg)	4.2	0	0.306
rs104895464	c.2291G>A (p.Arg764Aln)	0.3	0.0	0.786
rs104895467	c.2474A>G (p.Asn825Ser)	0.3	0.0	0.786
rs201586544	c.59C>T (p.Ser20Leu)	0.2	0.0	0.824
rs146054564	c.379G>A (p.Asp127Asn)	0.1	0.0	0.875
rs540122692	c.1459T>C (p.Tyr487His)	0.1	0.0	0.875
rs5743276	c.1969C>T (p.Arg657Trp)	0.1	0.0	0.875
rs5743278	c.2093C>G (p.Ala698Gly)	0.1	0.0	0.875

and colitis', 'treatment with long-term antibiotics', 'other signs and symptoms involving emotional state', and 'acute and chronic tonsilitis' (Table 1). The most important variants driving the associations for arthritis-related diagnoses were c.2023C >T (p.Arg675Trp) and c.2717+158C >T (IVS8+158) while the most important variants for IBD-related diagnoses were c.2023C >T (p.Arg675Trp), c.2717+158C >T (IVS8+158), and c.2938dup (p.Leu980ProfsTer2) (Tables 2 and 3).

Conclusion: Our findings confirm and expand on previous reports that common *NOD2* variants are associated with an increased risk of immune-related conditions. These include not only IBD and other forms of gastroenteritis and colitis, but also inflammatory arthritis, illnesses requiring long-term treatment with antibiotics, acute and chronic tonsilitis, and other related diagnoses. Further research is underway to illuminate autoinflammatory phenotypes causally related to *NOD2* variants.

Disclosure: J. Davis: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **E. Atkinson**: None; **V. Kronzer**: None; **C. Crowson**: None; **A. Alavi**: AbbVie, 1, 2, Almirall, 1, 2, 12, Serves on data monitoring board, Avalo Therapeutics, 1, 2, Boehringer Ingelheim, 1, 2, Cantargia, 1, 2, Hidradenitis Suppurativa Foundation, 4, 5, Incyte, 1, 2, InflaRx, 12, Serves on data monitoring board, La Roche-Posay, 5, LEO Pharma, 1, 2, National Institutes of Health, 5, Navigator Medicines, 1, 2, Novartis, 1, 2, Sanofi, 1, 2, UCB, 1, 2, Zura Bio, 12, Serves on data monitoring board; **J. Damianos**: ExeGi Pharma, 2, i-Health, 6; **L. Edward**: None; **J. Murray**: None; **A. Moyer**: None; **F. Pinto e Vairo**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0031

Meta-Analysis of Trans-Disease Microbial Biomarkers of Protection and Pathogenesis in Autoimmune Conditions: Results from the AMP AIM Consortium

Kevin Bu[1], Rebecca Blank[2], Alba Boix-Amoros[3], Adam Cantor[4], Jose Scher[5], Jose Clemente[1] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM), [1]Icahn School of Medicine at Mount Sinai, New York, NY, [2]NYU Langone Health, New York, NY, [3]Icahn School of Medicine, New York, NY, [4]Icahn School of Medicine, New York, [5]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune and immune-mediated diseases (AIMDs) affect over 20 million Americans. The sharp increase in prevalence of these disorders over recent decades suggests that factors other than genetics may be involved in pathogenesis. While the microbiome has been previously investigated as a risk factor, most studies have considered AIMDs in isolation. Here, we hypothesize that analysis across patients with different AIMDs will identify protective and deleterious microbial factors that are unique or shared across diseases.

Methods: As a part of the Accelerating Medicines Partnership-Autoimmune and Immune Mediated Diseases (AMP AIM) consortium, we characterized the microbiome of 126 subjects across six AIMDs: rheumatoid arthritis (RA; n=43), psoriasis (PsO=28), psoriatic arthritis (PsA=28), Sjögren's disease (SjD=10), non-Sjögren's sicca (NSS=12), and systemic lupus erythematosus (SLE=5), as well as 6 healthy controls. Four previously published studies in which data was publicly available were used as validation cohorts (**Table 1**). All studies consisted of 16S rRNA sequencing and were analyzed using QIIME2, the GreenGenes2 taxonomy, and LEfSe. Statistical tests (Wilcoxon Rank-Sum, Kruskal-Wallis) were performed in R 4.4.2 using the base stats library, and comparisons of features across groups was visualized using UpSetR.

Results: Within the AMP AIM cohort, AIMD patients exhibited significantly lower alpha diversity ($p < 0.05$) and significant differences in beta diversity compared to healthy controls for all diseases (except for SLE where p=0.08) (**Figure 1**). LEfSe identified taxa that were differential in disease conditions; *Lawsonibacter* was enriched in SjD patients, while *Anaerotignaceae* and *Othenecus* were depleted in PsO, RA, and SLE patients. Across all six AIMDs, *Phascolarctobacterium* was significantly depleted relative to healthy controls.

In four validation datasets, when comparing disease groups to healthy controls, we observed significantly reduced alpha diversities in one study (Valid2 SjD) and significantly different beta diversities in all four. *Lawsonibacter* was enriched in the affected patients within the Valid1 SLE, Valid2 SjD, and Valid3 RA studies. Conversely, *Anaerotignaceae* and *Othenecus*, were depleted in the Valid1 SLE and Valid2 SjD studies. Additionally, *Phascolarctobacterium* exhibited lower mean abundances in the disease subgroups relative to healthy controls in Valid1 SLE and Valid3 RA studies (although not significantly).

Table 1. Cohort sizes and breakdown of diagnoses in meta-analysis datasets.

Cohort	Author	Journal (Year)	Disease(s)	N (AIMD)	N (healthy)
AMPAIM	N/A	N/A	RA, PsO, PsA, SLE, SjD, NSS	126	6
Valid1 SLE	Su et al.	Gut Microbes (2020)	SLE	37	20
Valid2 SjD	Wang et al.	Cell Reports (2022)	SjD	133	40
Valid3 RA	Yu et al	Front Cell Infect Microbiol (2022)	RA	26	26
Valid4 PsO	Luca	Mendeley Data (2024)	PsO	36	23
	Total			232	109

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

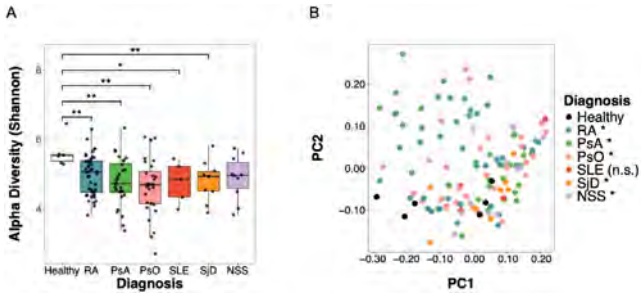


Figure 1. Patients with AIMDs exhibit distinct microbiome compositions from healthy controls. (A) Alpha diversity (Shannon index) within the AMP-AIM cohort. (B) PCoA of beta diversity (Unweighted UniFrac) of AMP AIM cohort samples, *p<0.05, **p<0.01.

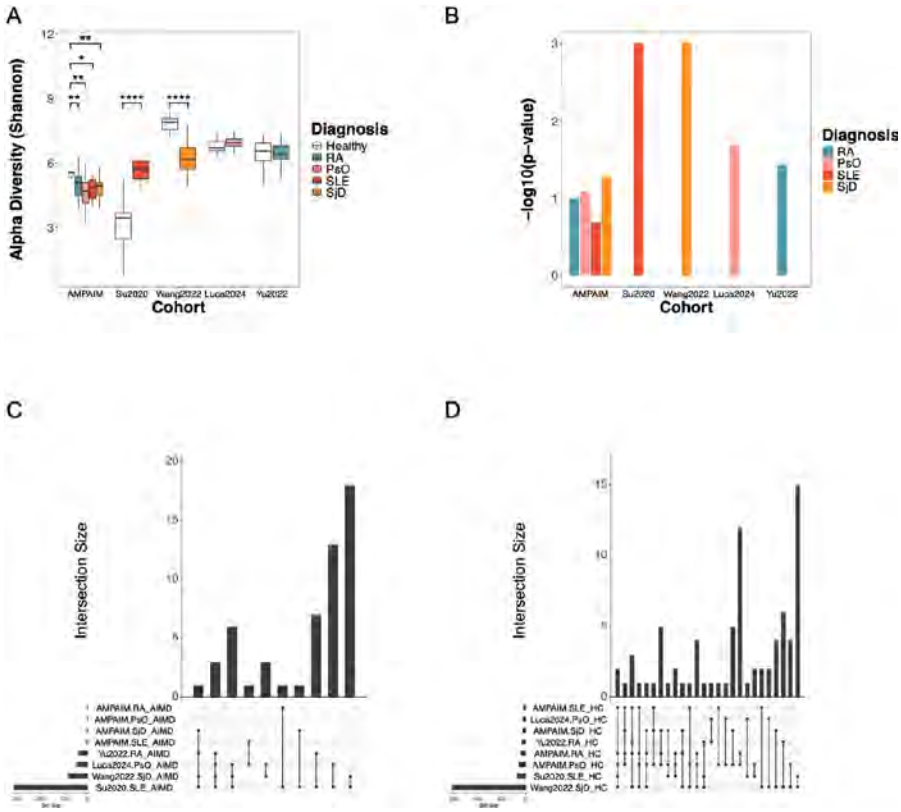


Figure 2. Healthy controls and patients with AIMDs exhibit distinct microbiome compositions across validation studies with overlap in differential taxonomic features. (A) Alpha diversity (Shannon index) of AMP AIM cohort along with 4 validation datasets, broken down by diagnoses. (B) PERMANOVA p-values (negative log-transformed) testing the difference in composition between AIMD and healthy control subgroups within each study for each diagnosis. (C-D) UpSetR plots showing the sizes of intersections of taxa identified as enriched (C) or depleted (D) in disease state relative to healthy controls across AMP AIM and validation cohorts.

Conclusion: In our AMP AIM cohort and across validation studies, comparison of healthy controls and patients with AIMDs revealed differences in alpha diversity, beta diversity, or both. We identified several taxa commonly enriched (*Lawsonibacter*) and depleted (*Phasolarctobacterium, Anaerotignaceae, and Othenecus*) across multiple AIMDs in both AMP AIM and validation studies. Across studies, there was a greater overlap among taxa that were depleted across disease states than among taxa enriched across AIMDs. Our meta-analysis suggests that microbes associated with pathogenesis are likely unique to each disease, potential mechanisms of protection (or lack thereof) tend to be shared.

Disclosure: K. Bu: None; **R. Blank**: None; **A. Boix-Amoros**: None; **A. Cantor**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **J. Clemente**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0033

Development and Internal Validation of Two Human Leukocyte Antigen Genetic Risk Scores for Predicting Rheumatoid Arthritis Progression and Anti-Citrullinated Protein Antibody-Positivity

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Human leukocyte antigen (HLA) class II genes play a central role in antigen presentation and immune modulation. The shared epitope (SE) region within HLA-DRB1 is a well-established genetic risk factor for rheumatoid arthritis (RA) and is associated with anti-citrullinated protein antibody (ACPA) positivity. RA is a heterogeneous disease, with some individuals developing ACPA positivity years before clinical symptoms, while others seroconvert only after disease onset or remain seronegative. Although prior studies have linked individual HLA alleles with disease risk, there are no composite genetic scores exist that capture HLA-driven risk for key disease features, such as RA stage progression or the emergence of ACPA positivity.

Methods: Using the Accelerating Medicines Partnership (AMP) cross-sectional dataset (n=349, Inamo et. al, *JCI* 2025), we developed two HLA-based genetic risk scores targeting distinct outcomes: (1) natural RA progression across clinical stages (control, at-risk, RA), and (2) ACPA positivity, defined as CCP3.0 and/or CCP3.1 >20 units. At-risk was defined as being either ACPA+ and/or having a first degree relative (FDR) with RA. Genotyping was performed using the Illumina Multi-Ethnic Genotyping Array, and classical HLA alleles were imputed using the TOPMed reference panel. We restricted analyses to participants of European ancestry (n=153, Table 1). Each score was derived using a three-step pipeline: (1) individual regression models performed for each imputed HLA allele, modeling both additive (0/1/2 copies) and heterozygous genotype effects, while adjusting for sex, age, and the first five genetic principal components. For the RA progression score, we used ordinal logistic regression with RA stage (control, ACAP positive at-risk, early seropositive RA) as the outcome, while the ACPA positivity score used a traditional logistic model with ACPA positivity (yes/no) regardless of RA status as the outcome and additionally adjusted for RA status in the model (Figure 1). (2) Markers with FDR-adjusted p-values < 0.05 from likelihood ratio

Table 1. Demographic characteristics of European ancestry participants in AMP. Demographic characteristics are shown for the 153 participants of European ancestry in the AMP study, stratified by original clinical group (control, at-risk, or early RA). Data are presented as mean (standard deviation) for continuous variables and N (%) for categorical variables.

	Control (N=16)	At-Risk (N=53)	RA (N=84)
Age (years)	59.0 (10.7)	59.3 (12.3)	56.9 (15.6)
Female	6 (37.5%)	35 (66.0%)	59 (70.2%)
First Degree Relative with RA	NA	38 (71.7%)	NA
ACPA Positivity*	NA	24 (45.3%)	56 (66.7%)
Rheumatoid Factor Positivity**	NA	6 (11.3%)	NA
Any Smoking History	NA	NA	47 (56.0%)
Body Mass Index (BMI)	NA	NA	27.4 (6.82)

*Positivity defined as ≥ 20 units for CCP3.0 or CCP3.1
**Positivity defined as ≥ 20 units for IgA, IgG or IgM RF

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

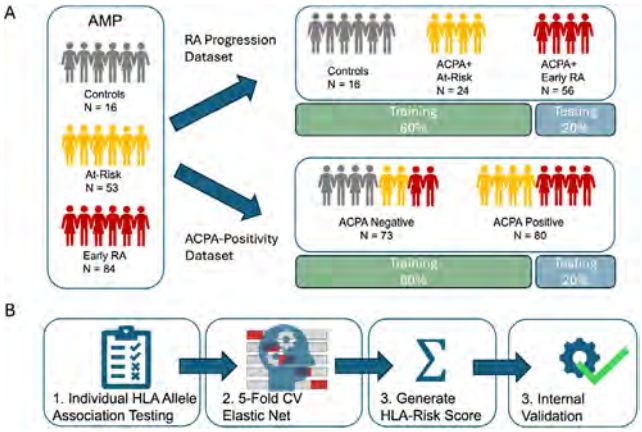


Figure 1. Study design and HLA risk score development pipeline. A. Participants with European ancestry from the AMP cohort were used to train and internally validate (test) a genetic risk score for RA progression and ACPA positivity based on HLA allele markers. The AMP dataset includes controls, at-risk (ACPA-positive and/or first degree relative with RA) individuals, and early RA cases (both seropositive and seronegative). ACPA negative individuals were removed from the at-risk and RA groups in the disease progression risk-score development, while all individuals were used in the ACPA positivity risk-score, but groups defined based on ACPA-positivity status and not the original group. B. Each HLA risk score was constructed using a three-step pipeline: (1) FDR-filtered regression (either ordinal logistic or logistic for the RA progression and ACPA positivity risk scores respectively), adjusting for age, sex, and the first five genetic PCs (RA status was an additional covariate in the ACPA positivity model); to identify outcome-associated HLA allele markers; (2) 5-fold cross-validated elastic net modeling to select and weight markers; and (3) weighted summation of coefficients to compute the HLA risk score. The scores were internally validated with the 20% testing dataset.

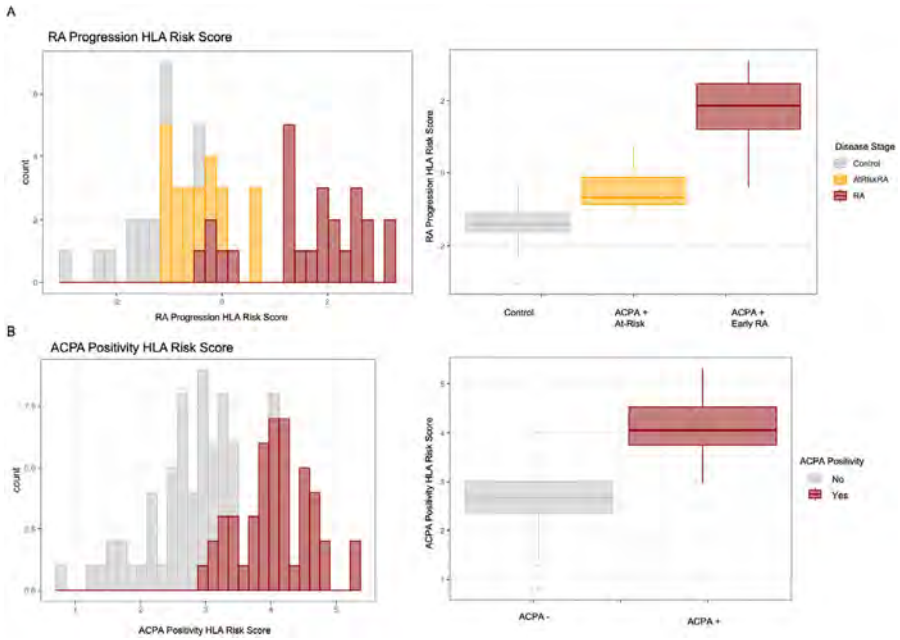


Figure 2. Distribution of Two HLA Risk Scores. A. Histogram and boxplot representations of the RA progression HLA risk score, stratified by disease stage (control, ACPA-positive at-risk, and ACPA-positive early RA), which was the outcome used to train the score. B. Histogram and boxplot representations of the ACPA positivity HLA risk score, stratified by ACPA positivity status (no vs yes), which was the binary outcome used to train the score.

tests were entered into a 5-fold cross-validated elastic net model. (3) Resulting coefficients were used to calculate a weighted genetic risk score. Each score was trained on 80% of the data and tested in the remaining 20%.

Results: Figure 2 depicts the distributions of the two HLA risk scores. The RA progression score showed strong performance with AUCs of 0.900 (early RA vs control), 0.708 (at-risk vs control), and 0.791 (early RA vs at-risk) in the testing set. The ACPA positivity score also demonstrated moderate discriminative ability, with an AUC of 0.671 (ACPA+ vs ACPA–).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Each score included multiple markers beyond traditional SE alleles and incorporated both additive and heterozygous effects, allowing for more nuanced modeling of HLA-driven risk.

Conclusion: We developed and internally validated two HLA-based genetic risk scores that distinguish between stages of RA progression and predict ACPA positivity within a single cross-sectional cohort. These tools provide a foundation for improved HLA-based stratification and may help clarify the genetic mechanisms underlying distinct features of RA development.

Disclosure: L. Vanderlinden: None; **J. Inamo**: None; **J. Seifert**: None; **V. Holers**: None; **J. Guthridge**: None; **K. Deane**: Inova Diagnostics, 1; **F. Zhang**: None.

Abstract Number: 0034

Meta-Analysis of GWAS data from 10,003 Sjögren's Disease Cases Identifies Thirteen Sjögren's Risk Loci.

Marcin Radziszewski[1], Bhuwan Khatri[1], Philip Stuart[2], Astrid Rasmussen[1], Kandice Tessneer[1], Cherilyn Pritchett-Frazee[1], Matthew Pattrick[2], Elena Pontarini[3], michele Bombardieri[4], Maureen Rischmueller[5], Marika Kvarnström[6], Torsten Witte[7], Hendrika Bootsma[8], Gwenny Verstappen[9], Frans Kroese[9], Arjan Vissink[10], Sarah Pringle[9], Athanasios Tzioufas[11], Clio Mavragani[12], Alan Baer[13], Marta Alarcon-Riquelme[14], Javier Martin[15], Xavier Mariette[16], Gaetane Nocturne[17], Jacques-Olivier Pers[18], Jacques-eric GOTTENBERG[19], Wan-Fai Ng[20], Caroline Shiboski[21], Kimberly Taylor[22], Lindsey Criswell[23], Blake M. Warner[24], A. Darise Farris[1], Judith James[1], R Hal Scofield[1], Joel Guthridge[1], Daniel Wallace[25], Swamy Venuturupalli[26], Mike Brennan[27], Juliana Imgenberg-Kreuz[28], Lars Rönnblom[28], Eva Baecklund[29], Maija-Leena Eloranta[28], Svein Joar Auglend Johnsen[30], Roald Omdal[31], Lara Aqrawi[32], Øyvind Palm[33], Johan Brun[34], Daniel Hammenfors[34], Malin Jonsson[34], Silke Appel[34], Sara Bucher[35], Helena Forsblad[36], Thomas Mandl[37], Per Eriksson[38], Marie Wahren-Herlenius[6], Erik Abner[39], Tõnu Esko[39], Benjamin A. Fisher[40], Rachel Gordon[41], Gabriela Hernandez-Molina[42], Adrian Lee[43], Johann Gudjonsson[44], Lam Tsoi[44], Gunnel Nordmark[29] and Christopher Lessard[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Michigan Medical School, Ann Arbor, MI, [3]Queen Mary University of London, London, United Kingdom, [4]Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, UK, London, United Kingdom, [5]RheumatologySA, Adelaide, Australia, [6]Karolinska Institutet, Stockholm, Sweden, [7]Dept of Rheumatology and Immunology, Hannover, Niedersachsen, Germany, [8]UMCG, Groningen, Netherlands, [9]University Medical Center Groningen, Groningen, Netherlands, [10]University of Groningen, Leek, Netherlands, [11]LAIKO HOSPITAL, Athens, Greece, [12]National and Kapodistrian University of Athens, Athens, Greece, [13]Johns Hopkins University School of Medicine, Baltimore, MD, [14]Fundación Progreso y Salud, Andalusian Government, Granada, Spain, [15]Department of Cell Biology and Immunology, Institute of Parasitology and Biomedicine López-Neyra, CSIC, Granada, Spain, [16]Université Paris-Saclay, Le Kremlin Bicetre, France, [17]University Paris Saclay, Le Kremlin Bicetre, Ile-de-France, France, [18]CHU de Brest, Brest, France, [19]Hautepierre Hospital, STRASBOURG, Alsace, France, [20]Newcastle University, Gateshead, United Kingdom, [21]University of California San Francisco, San Francisco, CA, [22]UC San Francisco, San Francisco, CA, [23]NIH/NHGRI, Bethesda, MD, [24]National Institutes of Health, Bethesda, MD, [25]Cedars Sinai Medical Center, Studio City, CA, [26]Attune Health, Beverly Hills, CA, [27]Atrium Health, Charlotte, NC, [28]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [29]Uppsala University, Uppsala, Sweden, [30]Stavanger University Hospital, Stavanger, Norway, [31]Stavanger University Hospital, Stavanger, Nepal, [32]Kristiania University College, Oslo, Norway, [33]Oslo University Hospital, Oslo, Norway, [34]University of Bergen, Bergen, Norway, [35]Örebro University, Örebro, Sweden, [36]University of Gothenburg, Gothenburg, Sweden, [37]Lund University, Malmö, Sweden, [38]Linköping University, Linköping University, [39]University of Tartu, Tartu, Estonia, [40]King's College London, London, UK; Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK, [41]University of Pittsburgh School of Medicine, Pittsburgh, PA, [42]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico, [43]University of Sydney, Sydney, Australia, [44]University of Michigan, Ann Arbor, MI.

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

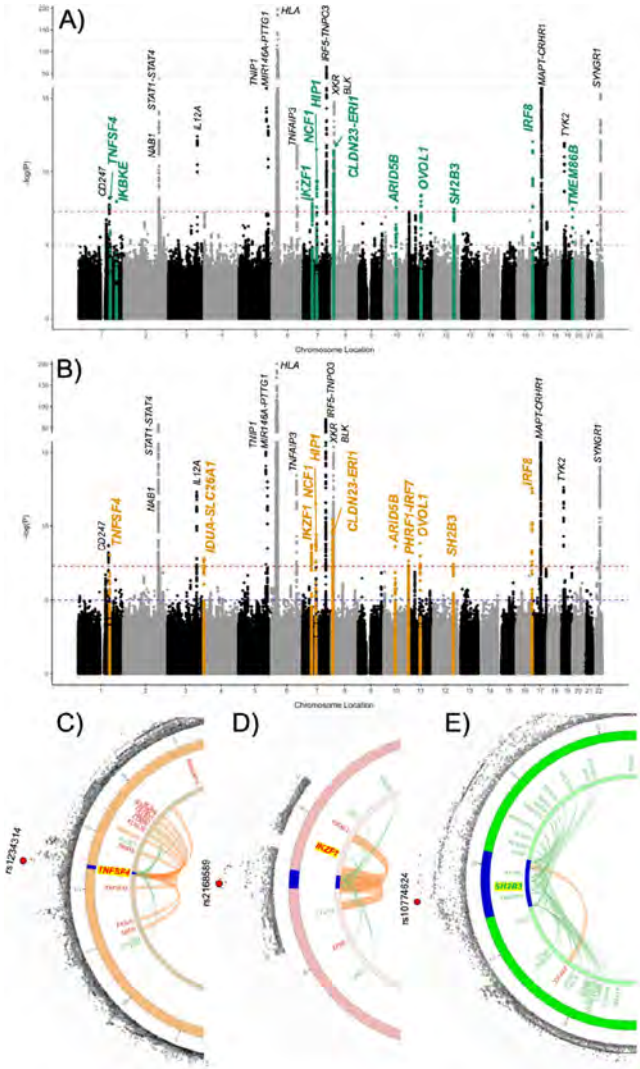


Fig 1. (A-B) The summary statistics of meta-analysis (A) 9,139 EUR cases (green indicates GWS SjD risk loci) or (B) 10,003 EUR+EAS cases (orange indicates GWS SjD risk loci). The -log10(P) for each variant is plotted against genomic locations. Red line indicates GWS (5x10-8) threshold, blue line suggestive threshold (1x10-5). (C-E) Regional maps of the genetic risk locus showing variants associations from the EUR+EAS GWAS shown in B (outer ring; index SNP labeled) and mapped chromatin interactions (orange), eQTLs (green), or both (red) (inner ring) spanning the (C) TNFSF4 (chromosome 1), (D) IKZF1 (chromosome 7), and (E) SH2B3 (chromosome 12) GWS risk loci (indicated as blue in the middle ring).

Background/Purpose: Sjögren's disease (SjD) is a systemic autoimmune condition with a complex genetic architecture. To date, 22 genome-wide significant (GWS) SjD risk loci have been identified, while >100 risk loci have been described in other related autoimmune diseases (Khatri et al. 2022). The objective of this study is to perform large-scale genome-wide association study (GWAS) to identify new GWS SjD risk loci ($p < 5x10^{-8}$; suggestive: $p< 5x10^{-5}$).

Methods: Institutional IRB/EC approval was obtained. GWAS were performed separately using PLINK2 for individuals of European (EUR) (4,855 cases, 25,408 controls) or East Asian (EAS) (561 cases, 1,760 controls) ancestry classified with SjD. After standard quality control, datasets were phased and imputed using the TOPMed reference panel. Data were meta-analyzed using inverse variance-weighted fixed-effect models in METAL with publicly available biobank GWAS summary statistics for cases [Phecode 709.2 (ICD-10 M35.0, ICD-9 710.2)]: Japanese Biobank (303 EAS cases, 175,599 controls [exclusion criteria Phecodes 690-697.99, 708-709]), UK Biobank (511 EUR cases, 397,694 controls [exclusion criteria Phecodes 690-697.99, 708-709]), Estonian Biobank (464 EUR cases, 204,701 controls [exclusion criteria not-cases]), FinnGen (3,309 EUR cases, 484,260 controls [exclusion criteria ICD-10 M30, M31, M32, M33, M34, M35, M36, and ICD-9 136.1, 446, 447.5, 447.6, 710, 725]).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Thirteen novel GWS risk loci were identified: *TNFSF4, IKBKE, IDUA-SLC26A1, IKZF1, NCF1, HIP1, CLDN23-ERI1, ARID5B, PHRF1-IRF7, OVOL1, SH2B3, IRF8*, and *TMEM86B* (Figure 1A and B), with most having been previously implicated in other autoimmune diseases. To investigate the regulatory potential of GWS variants, we analyzed three loci - *TNFSF4, IKZF1*, and *SH2B3* - using FUMA, which integrates chromatin interaction and expression quantitative trait locus (eQTL) data from publicly available immune cell datasets. At the *TNFSF4* locus, GWS variants showed both chromatin interactions and eQTLs with *RABGAP1L, RC3H1, SERPINC1, ZBTB37, DARS2, CENPL, KLHL20, PRDX6, TNFSF4, TNFSF18, FASLG* and *SUCO* (Figure 1C). At the *IKZF1* locus, GWS variants showed both chromatin interactions and eQTLs with *FIGNL1, IKZF1* and *ZPBP* (Figure 1D). At the *SH2B3* locus, GWS variants showed both chromatin interactions and an eQTL with *PPP1CC* (Figure 1E).

Conclusion: By conducting a GWAS using a larger sample size and performing meta-analysis, this study advances the genetic understanding of SjD. Further, SjD risk loci previously established in related autoimmune diseases may be indicative of shared mechanisms of disease. While loci are annotated by the gene closest to the lead variant, this does not necessarily indicate functional relevance. Three loci were evaluated for risk variant impact on chromatin interactions and gene expression changes in immune cells (Figure 1C-D). As both chromatin interactions and eQTLs are often cell-type specific, further analyses across all novel loci and in disease-relevant cell types and tissues are needed. Additional datasets from other SjD clinical partners and biobanks to further increase power are needed to discover novel loci.

Acknowledgements

Estonian Biobank Research Team

Disclosure: M. Radziszewski: None; **B. Khatri**: None; **P. Stuart**: None; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **K. Tessneer**: None; **C. Pritchett-Frazee**: None; **M. Pattrick**: None; **E. Pontarini**: None; **m. Bombardieri**: Amgen, 5, 12, Personal fees, GlaxoSmithKlein(GSK), 5, 12, Personal fees, Janssen, 5, 12, Personal fees, Ono Pharmaceuticals Co. Ltd, 1, 2, UCB, 12, Personal fees; **M. Rischmueller**: Johnson and Johnson, 12, Servier, Advisory Board, Novartis, 6, 12, Clinical trials; **M. Kvarnström**: None; **T. Witte**: None; **H. Bootsma**: Bristol-Myers Squibb(BMS), 2, 5, Medimmune, 2, Novartis, 2, Roche, 2, 5, Union Chimique Belge, 2; **G. Verstappen**: argenx, 2; **F. Kroese**: argenx, 2; **A. Vissink**: None; **S. Pringle**: None; **A. Tzioufas**: None; **C. Mavragani**: None; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **M. Alarcon-Riquelme**: None; **J. Martin**: None; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **G. Nocturne**: None; **J. Pers**: None; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **W. Ng**: Abbvie, 2, Argenx, 2, BMS, 2, IQVIA, 2, Janssen, 2, Novartis, 2, Resolve Therapeutics, 2, Sanofi, 2; **C. Shiboski**: None; **K. Taylor**: None; **L. Criswell**: None; **B. Warner**: Mitobridge, subsidiary of Astellas Bio, 5, Pfizer, Inc., 5; **A. Farris**: Johnson & Johnson Innovative Medicine, 5; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **R. Scofield**: IQVIA, 1, Jannsen Pharmaceuticals, 1; **J. Guthridge**: None; **D. Wallace**: PPD, 2; **S. Venuturupalli**: None; **M. Brennan**: Lipella, 2, MeiraGTx, 2, SUN pharmaceuticals, 2; **J. Imgenberg-Kreuz**: None; **L. Rönnblom**: AstraZeneca, 6, Biogen, 2; **E. Baecklund**: None; **M. Eloranta**: None; **S. Johnsen**: None; **R. Omdal**: None; **L. Aqrawi**: None; **Ø. Palm**: None; **J. Brun**: None; **D. Hammenfors**: None; **M. Jonsson**: None; **S. Appel**: None; **S. Bucher**: None; **H. Forsblad**: None; **T. Mandl**: UCB, 3, **P. Eriksson**: None; **M. Wahren-Herlenius**: None; **E. Abner**: None; **T. Esko**: None; **B. Fisher**: Bristol-Myers Squibb (BMS), 2, Galapagos, 5, Janssen, 2, 5, Novartis, 2, Servier, 2, 5; **R. Gordon**: None; **G. Hernandez-Molina**: None; **A. Lee**: Novartis, 6; **J. Gudjonsson**: None; **L. Tsoi**: Galderma, 5, Janssen, 5; **G. Nordmark**: None; **C. Lessard**: Janssen Global Services, 2, Johnson & Johnson, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0035

Clinical and Transcriptomic Heterogeneity in Patients With RA: A Multi-Centric International Study of Anti-TNF Response

Maryna Borshchivska[1], Thibault Helleputte[1], Laurent Meric de Bellefon[2], Silvana di Romana[3], Elsa Vieira-Sousa[4], Vasco Romão[4], João Eurico Fonseca[5], Alla Ishchenko[6], Patrick Verschueren[6], Ruth Wittoek[7], Peggy jacques[7], Dirk Elewaut[8], Bernard Lauwerys[9] and Patrick Durez[10], [1]DNAlytics, Louvain-la-Neuve, Belgium, [2]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatologie, Brussels, Belgium, [3]Department of Rheumatology, Saint Pierre University Hospital, Brussels, Belgium, [4]Faculdade Medicina, Universidade de Lisboa, ULS Santa Maria, Centro Académico Medicina de Lisboa, Lisboa, Portugal, [5]Faculdade Medicina, Universidade de Lisboa, ULS Santa Maria, Centro Académico Medicina de Lisboa, Lisboa, Lisboa, Portugal, [6]Rheumatology, University Hospital Leuven and Skeletal Biology and Engineering Research Centre, KU Leuven, Leuven, Belgium, [7]VIB Center for Inflammation Research, Ghent University and Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [8]VIB Center for Inflammation Research, and Ghent University Hospital, Department of Rheumatology, Ghent, Belgium, [9]Systemic and Inflammatory Rheumatic Diseases Section, Institute of Experimental and Clinical Research (IREC), UCLouvain, Brussels, Belgium, [10]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatologie, Brussels, Brussels Hoofdstedelijk Gewest, Belgium

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease that can lead to joint damage and disability. Although methotrexate is the standard first-line treatment, about 40% of patients fail to reach remission/low disease activity and require escalation to bDMARDs. Anti-TNF agents are frequently used, but responses vary and predicting individual treatment responses remains difficult.

Methods: This international multi-centrer prospective observational study, recruited RA patients who were non-responders to synthetic DMARDs and eligible for anti-TNF therapy. Patients were followed from Visit 1 to 5 (∼20 weeks). Due to selective criteria and missing data, 42 of the 55 enrolled patients were analysed. Demographic and clinical characteristics were

Table 1. Baseline age and BMI by EULAR response

Variable	Group	N	Mean	Median	SD	Min	Max
Age (years)	Non-responder	14	44.4	44	9.39	27	57
	Responder	29	51.5	50	18.5	21	84
	NA	12	52.1	55	15.2	28	68
BMI	Non-responder	14	27.3	27.9	4.76	17.3	35.1
	Responder	29	24.4	22.8	4.82	17.0	35.1
	NA	11	26.5	26.7	4.53	19.1	35.1

Table 2. Smoker and gender status by EULAR response

Variable	Category	Non-responder	Responder	NA
Gender	Female (f)	13	22	10
	Male (m)	1	7	2
Smoker	True	5	15	6
	False	9	14	6

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

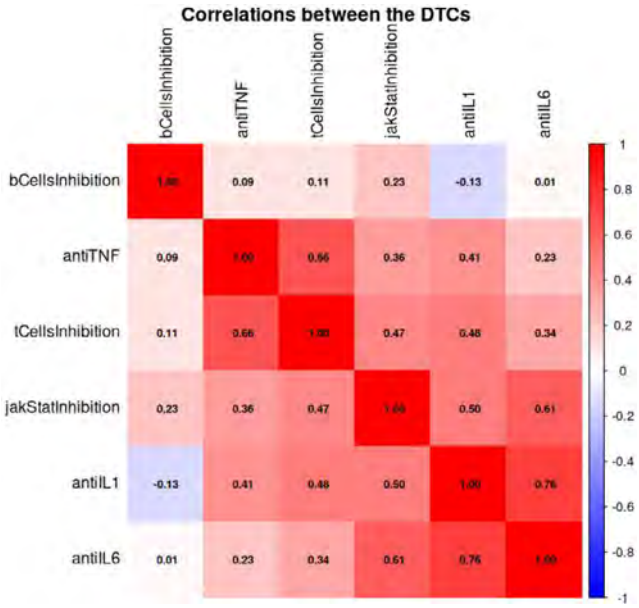


Figure 1. Correlations between the main DMARDs families

recorded at each visit and analysed to assess anti-TNF response in RA. In parallel, pre-treatment transcriptomic profiling (RNASeq by Quantseq method with sequencing depth of ∼20M single-end reads / sample) of synovial biopsies (Visit 2) was performed to provide transcriptomic data, and anti-TNF therapy was initiated thereafter.

Prediction of anti-TNF response via transcriptomic scoring will be presented separately. At baseline, the level of expression of mRNA corresponding to proteins directly involved in the mechanism of actions (Drug Target Complex or DTC (Paul et al., 2019)) of main DMARDs families (BCellInhibitors, AntiIL1, AntiIL6, JakStatInhibitors, AntiTNF, TCellInhibition) have been studied. Treatment response was assessed using the EULAR criteria based on DAS28-CRP, patients were classified as responders (good or moderate), or non-responders. Statistical analysis used Pearson's chi-squared and Wilcoxon rank-sum tests to assess links between baseline traits and treatment response.

Results: Based on the EULAR DAS28-CRP criteria at Visit 5, 32.6% of patients were classified as non-responders and 67.4% as responders (good or moderate). No significant associations were found between treatment response and sex ($p = 0.356$), smoking status ($p = 0.653$), or age ($p = 0.243$). However, BMI was significantly linked to treatment response ($p = 0.049$), suggesting higher BMI may reduce clinical response. Transcriptomic data of DTCs revealed two main observations: (1) transcriptomic profiles of patients are highly heterogeneous, each set of mRNA related to the different DTCs appearing as predominant in similar proportions of patients. (2) two clusters emerged: patients with high B-cell DTC expression tended to show low expression of other DTCs, and vice versa. In contrast, expression levels of non–B-cell DTCs are mutually correlated.

Conclusion: The clinical characteristics and early treatment outcomes align with expectations for this population. Initial analyses suggest that BMI may be associated with therapeutic response, while sex, age, and smoking are not. Early transcriptomic profiling may reveal mechanistic subtypes of RA, with opposing expression patterns between B-cell–related and other DMARDs-related mechanisms. Future analyses will assess the predictive ability of a synovial transcriptomic signature to improve patient stratification and personalize RA treatment.

Disclosure: M. Borshchivska: None; **T. Helleputte**: None; **L. Meric de Bellefon**: None; **S. di Romana**: None; **E. Vieira-Sousa**: None; **V. Romão**: None; **J. Fonseca**: None; **A. Ishchenko**: None; **P. Verschueren**: AbbVie, 6, 12, Support for attending meeting, Alfasigma S.p.A., 2, 5, Boehringer Ingelheim, 2, Citryll, 2, Eli Lilly & Co., 2, 6, Fresenius

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kabi, 12, Support for attending meeting, Galapagos, 2, 5, 6; **R. Wittoek**: None; **P. jacques**: None; **D. Elewaut**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6, UCB, 2, 6; **B. Lauwerys**: UCB, 3, 12, Shareholder; **P. Durez**: None.

Abstract Number: 0036

Integrated Analysis of Polygenic and Environmental Risk Scores for Late-Onset Systemic Lupus Erythematosus

Mehmet Hocaoglu[1] and Amr Sawalha[2], [1]University of Pittsburgh Medical Center, Piitsburgh, PA, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

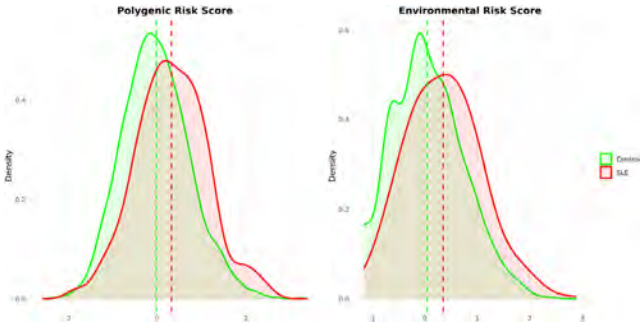
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Polygenic risk scores (PRS) have been constructed to summarize genetic risk but there is limited research on environment-wide analysis of risk factors for systemic lupus erythematosus (SLE). In this study, we performed an environment-wide association study to construct an environment risk score (ERS) for SLE and compare the risk conferred by ERS and PRS.

Methods: A total of 335 incident SLE cases were identified in the UK Biobank and matched 1:10 with age, sex, and ethnic background 3350 healthy controls. We examined the association between 37 environmental factors and SLE, using a univariate followed by a multivariate analysis. We summed the natural logarithm of the odds ratios (OR) of statistically significant environmental variables in the multivariable model to derive an ERS for SLE. Model discrimination was compared by DeLong`s test. PRS was calculated using the ORs of previously reported SLE genetic risk loci.

Results: The multivariate analysis revealed the association between daily sunlight exposure, depression, sleeplessness, sex hormone binding globulin levels, and air pollution with increased risk of SLE, while moderate physical activity was a protective factor. Increasing quartiles of the newly developed ERS were associated with similar degree of risk for SLE as the PRS. Integrating PRS with environmental factors significantly improved model performance.

Conclusion: We devised an ERS for SLE that summarizes the environmental component of the disease risk. We show that ERS confers a comparable degree of SLE risk as the PRS. Combining genetic and environmental factors could improve risk prediction models in SLE.



Comparison of standardized polygenic and environmental risk scores between SLE cases and matched controls. P values for the mean difference between cases and matched controls for polygenic and environmental risk score are 2.41x10-13 and 1.76x10-13, respectively.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Hocaoglu: None; **A. Sawalha**: None.

Abstract Number: 0037

A Proteomic Signature Containing TNF Receptor Superfamily Member 10A (TNFRSF10A) and Growth/differentiation Factor 15 (GDF-15) Improves Prediction of All-cause Mortality Among Individuals with Gout, Beyond Atherosclerotic Cardiovascular and Other Clinical Risk Factors

Natalie McCormick[1], Sharan Rai[2], Chio Yokose[3], Tony Merriman[4], Robert Terkeltaub[5] and Hyon K. Choi[6], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [3]Massachusetts General Hospital, Waltham, MA, [4]University of Alabama at Birmingham, Homewood, AL, [5]Retired, San Diego, CA, [6]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Gout affects >12 million US adults and is associated with premature all-cause and cardiovascular (CV) mortality which has failed to improve over recent decades, unlike in the general population.[1,2] Comorbidities and treatment inequity contribute, but underlying gout disease-specific mechanisms may also play a role, since the elevated mortality persists with adjustment for cardiometabolic comorbidities, kidney function, BMI, alcohol, all atherosclerotic cardiovascular (ASCVD) risk factors, and serum urate (SU) levels.[1] Since detailed characterisation of the plasma proteome can illuminate mechanisms and risk stratification of premature mortality in gout, we leveraged large-scale proteomics data for a nationwide prospective cohort.

Methods: We studied 2,013 UK Biobank participants with diagnosis of gout and proteomic profiling available (mean age 60 years, 83% males). Proteomic measures (n=2923, via Olink Explore 3072) were quantified from baseline blood samples via Proximity Extension Assay technology. After division into training (80%) and testing (20%) sets, least absolute shrinkage and selection operator (LASSO) regression with 10-fold cross validation was used to identify most robust prognostic proteins and construct a proteomic risk score (signature) for mortality in the training set.

Table 1. Associations of a proteomic risk score with all-cause mortality among individuals with gout, training set

	Quintiles of Proteomic Risk Score						
	1=Lowest	2	3	4	5=Highest	Per SD	P-Value of Continuous Score
N Deaths	7	22	50	94	213	386	-
N	323	322	322	322	323	1,612	
Person-Years (PY)	4,479	4,365	4,282	4,076	3,366	20,569	
Rate Ratio, per 1000 PY	1.56	5.04	11.7	23.1	63.3	18.8	-
Multivariable HR, 95% CI*	1.0 (ref)	1.53 (0.65 to 3.60)	2.81 (1.26 to 6.26)	4.40 (2.01 to 9.62)	12.8 (5.82 to 28.0)	2.53 (2.25 to 2.84)	<0.001
Multivariable HR, 95% CI*, + serum urate levels	1.0 (ref)	1.53 (0.65 to 3.60)	2.83 (1.27 to 6.30)	4.42 (2.02 to 9.67)	12.7 (5.79 to 27.8)	2.52 (2.24 to 2.83)	<0.001

HR, hazard ratio; 95% CI, 95% confidence interval.
*Adjusted for age, sex, race, body mass index, diuretic medication use, coronary heart disease, kidney function (eGFR), alcohol consumption, and all other atherosclerotic cardiovascular [ASCVD] risk factors (aspirin use, statin use, anti-hypertensive medication use, systolic blood pressure, diastolic blood pressure, type 2 diabetes, smoking status, total cholesterol levels, and high density lipoprotein cholesterol levels).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Proteomic biomarkers associated with all-cause mortality among individuals with gout, five highest-weighted associations in the proteomic risk score

Protein Name	Hazard Ratio per SD (95% CI)	P_{FDR}
N-terminal prohormone of brain natriuretic peptide (NT-proBNP)	1.38 (1.25 to 1.52)	4.1×10^{-8}
Growth/differentiation factor 15 (GDF-15)	1.61 (1.45 to 1.79)	2.4×10^{-2}
TNF receptor superfamily member 10A (TNFRSF10A)	1.59 (1.43 to 1.77)	4.83×10^{-15}
Proto-oncogene tyrosine-protein kinase receptor Ret (RET)	0.83 (0.75 to 0.91)	1.04×10^{-3}
Glutathione hydrolase 5 proenzyme (GGT5)	1.46 (1.33 to 1.60)	3.3×10^{-13}

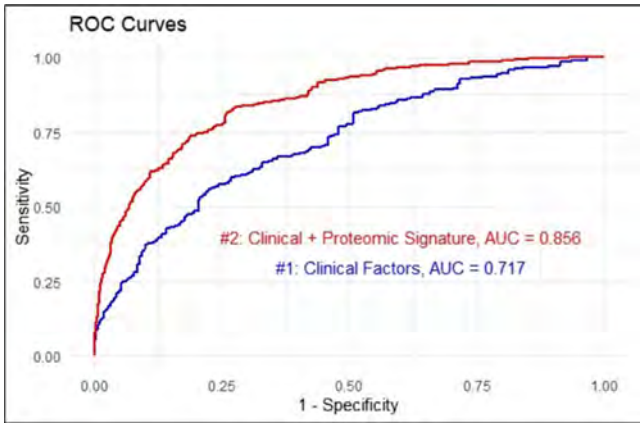


Figure: Receiver operating characteristic curves for discrimination of all-cause mortality with clinical factors and a proteomic signature. AUC= area under the receiver operating characteristic curve. Clinical factors include age, sex, race, body mass index, alcohol consumption, diuretic medication use, coronary heart disease, kidney function (eGFR), atherosclerotic cardiovascular (ASCVD) risk factors (aspirin use, statin use, antihypertensive medication use, systolic blood pressure, diastolic blood pressure, type 2 diabetes, smoking status, total cholesterol levels, high density lipoprotein cholesterol levels), and serum urate levels.

Multivariable Cox models were compared between clinical factors (age, sex, race, alcohol, other ASCVD risk factors, BMI, cardiometabolic comorbidities, kidney function, diuretic medications, and SU levels), with and without the proteomic signature, using area under the receiver operating characteristic curve (AUC). Two-sided DeLong test was used to compare AUCs of each model in training and testing sets.

Results: We documented 469 deaths over 25,751 person-years (PY) of follow-up (18.2 per 1000 PY) in the gout cohort. In the training set (386 deaths), clinical factors alone discriminated mortality with an AUC of 0.717 (95% CI: 0.698, 0.737).

From 790 individually-associated proteins ($P_{FDR} < 0.05$), LASSO regression generated a 76-protein signature of mortality risk; each unit increase in risk score was associated with 2.5-fold greater mortality risk (**Table 1**). Highest-weighted markers in the signature included NT-proBNP, growth-differentiation factor 15 (biomarker of major organ injury, cardiac and cancer risk, and predictive factor for CV disease and mortality), and TNF-R superfamily member 10A (TNFRSF10A) (**Table 2**). Excess TNFRSF10A transduces apoptosis and marked release of multiple inflammatory cytokines (e.g., IL-8, TNF, and CCL20).

Addition of the proteomic signature to the clinical model significantly improved discrimination over the clinical model alone ($P < 0.001$), with AUC of 0.856 (0.844, 0.868) **(Figure)**. Proteomic signature also performed well in the testing set (83 deaths), with AUC 0.672 (0.639, 0.705) for the clinical model alone and 0.812 (0.785, 0.840) for the combined.

Conclusion: Addition of a proteomic signature improves ability to predict risk of all-cause mortality among individuals with gout. The component proteomic biomarkers may allow for risk prediction and stratification, and identification of potential novel therapeutic targets.

[1]PMID 38191784; [2]PMID 28122760

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. McCormick: None; **S. Rai**: None; **C. Yokose**: None; **T. Merriman**: None; **R. Terkeltaub**: Atom Bioscience, 2, BPG Bio, 2, Crystalys, 2, Novartis, 2, Shanton, 2; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2.

Abstract Number: 0038

DNA Methylation Signatures of Smoking in Labial Salivary Gland Tissue in a Sjögren's Disease Cohort

Priya Bhatt[1], Mary Horton[2], Caroline Shiboski[3], Lisa Barcellos[4], Lindsey Criswell[2], and the Sjögren's International Collaborative Clinical Alliance (SICCA), [1]Mayo Clinic Alix School of Medicine, Toledo, [2]NIH/NHGRI, Bethesda, MD, [3]University of California San Francisco, San Francisco, CA, [4]UC Berkeley, Berkeley

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cigarette smoking has been linked to the development of several autoimmune diseases, including Sjögren's Disease (SjD). Since DNA methylation (DNAm) is altered by cigarette smoking and plays a significant role in autoimmune disease pathophysiology, it may provide some insight into the influence of smoking on SjD progression. Although previous studies have identified genome-wide DNAm changes in whole blood associated with smoking, similar analyses have not yet been conducted in the exocrine glands, which are the primary target tissues in SjD. Salivary glands, in particular, are directly exposed to cigarette smoke and may exhibit distinct epigenetic changes. Here, we aim to compare DNAm in labial salivary gland (LSG) tissue among individuals with different self-reported smoking behaviors.

Methods: We obtained LSG DNAm data from the Sjögren's International Collaborative Clinical Alliance (SICCA) cohort (n = 1,453) that was profiled using the Illumina EPIC v1.0 array (~850,000 CpG sites). We used linear models (limma) to identify sites with differential methylation by smoking status (current v. never smoker, former v. never smoker), adjusting for age, sex, batch effects, SjD status as determined by 2016 ACR-EULAR classification criteria, estimated cell type proportions, and genetic principal components. GO, KEGG, and Reactome pathway enrichment analyses were conducted.

Results: We identified 106,285 differentially methylated sites in current smokers and 13 sites in former smokers at a false discovery rate (q) < 0.05. Of these, 3,891 CpG sites in current smokers and only one in former smokers had at least a 3% average DNAm difference compared to never smokers. These were enriched in pathways related to cellular migration, morphogenesis, and neuronal development. The site cg22103736 (-7.1%, FDR q = 2.3e-29) showed the strongest combination of effect size and significance in both current and former smokers. Cg22103736 is located in *AHRR*, which encodes aryl

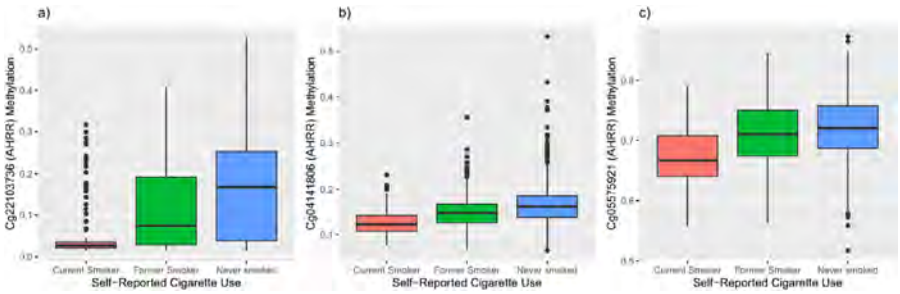


Figure 1. Stepwise relationship between self-reported cigarette use and methylation beta values in AHRR CpGs including a) cg22103736, one of the strongest and most significant differentially methylated positions (DMPs), b) cg04141806, another significant DMP, and c) cg05575921, a DMP that has been widely associated with smoking in whole blood DNAm studies.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hydrocarbon receptor repressor and is a gene widely linked to smoking-related changes in whole blood DNAm. The median methylation value of cg22103736 among current smokers was very low (0.026) and demonstrated a stepwise increase for former and never smokers (Figure 1a). This trend was replicated in another *AHRR* CpG, cg04141806 (Figure 1b). Interestingly, a well-known CpG within *AHRR* that differentiates smoking behavior in whole blood, cg05575921, did not have as large differences in DNAm between smoking status groups in the gland tissue (Figure 1c).

Conclusion: Our findings suggest that cigarette smoking may significantly perturb normal cellular processes in salivary glands. These changes occur in many more CpGs with stronger and more significant associations in current compared to former smokers. Pathway analysis implicated processes important for fibrosis, such as epithelial-mesenchymal transition and extracellular matrix remodeling, indicating that smoking may exacerbate and accelerate gland atrophy in SjD patients or individuals with xerostomia. The limited number of significant results in former smokers indicates that quitting smoking may allow individuals to acquire DNAm profiles comparable to that of individuals who have never smoked.

Disclosure: P. Bhatt: None; **M. Horton**: None; **C. Shiboski**: None; **L. Barcellos**: None; **L. Criswell**: None.

Abstract Number: 0039

Hemophagocytic Lymphohistiocytosis Gene Variants in Severe COVID-19 Cytokine Storm Syndrome

randy Cron[1], Abhishek Kamath[1], Mingce Zhang[1], Devin Abhser[2], Lesley Jackson[1] and Walter Winn Chatham[3], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Kaiser Permanente Research Bank, Oakland, CA, [3]University of Nevada, Las Vegas, Las Vegas, NV

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Severe COVID-19 infection resulting in hospitalization shares features with frequently fatal cytokine storm syndromes (CSS), such as hemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS). Repeatedly, 30-40% of patients in published secondary (beyond infancy) HLH cohorts possess rare heterozygous mutations in established familial HLH (fHLH) genes. These mutations are thought to contribute to CSS via hypomorphic or dominant-negative effects on lymphocyte cytolytic activity. Diminished lymphocyte cytolytic activity results in prolonged lymphocyte with antigen presenting cell engagement yielding increased pro-inflammatory cytokine production contributing to multi-organ system failure.

Table 1: Performance of cytokine scoring systems in total patient cohort

	Total Patients (n = 32)
2016 sJIA/MAS Score: Yes	6/32 (19%)
MS Score, Median (IQR)	-2.5 (-3.0 to -1.4)
Ferritin:ESR > 11.3	27/32 (84%)
Ferritin:ESR > 21.5	13/32 (41%)
Ferritin:ESR, Median (IQR)	18.6 (12.8 to 36.6)
CSS Score: Pos	26/32 (81%)
cHIS Score, Median (IQR)	3 (3 to 4)
Caricchio Score	1/32 (3.1%)

Performance of cytokine scoring systems in total patient cohort. Abbreviations: sJIA - systemic juvenile idiopathic arthritis; MAS - macrophage activation syndrome; MS - MAS/sJIA; IQR - interquartile range; CSS - cytokine storm syndrome score; cHIS - COVID-19-associated hyperinflammatory syndrome

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

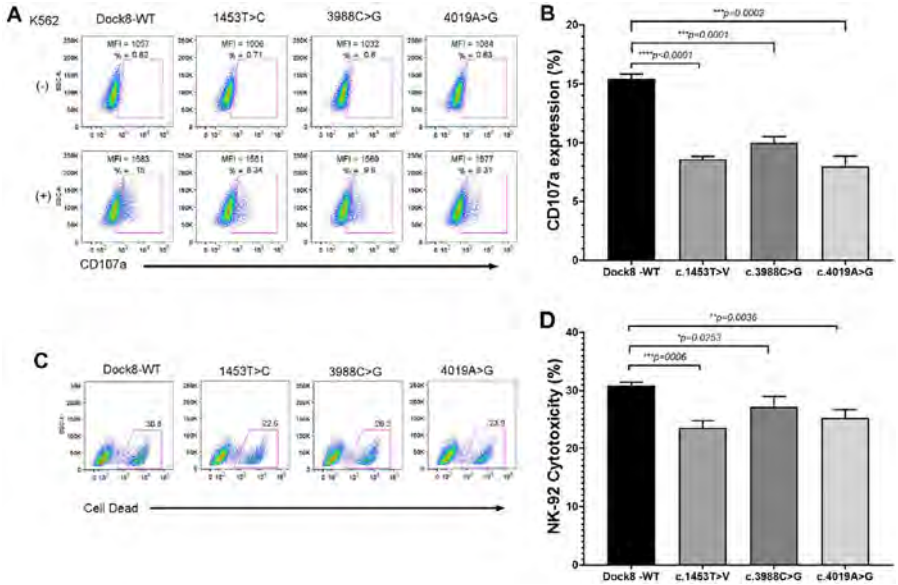
#	Gene	Gene description	Mutation	Frequency (gnomAD)
3	IFNGR1	IFN-gamma receptor 1	c.58G>A (p.Val20Ile)	0.27%
	LYST	Chediak-Higashi (fHLH)	c.8683A>G (p.Asn2228Ser)	0.17%
	NLRC4	Enterocolitis autoinflammatory	c.787+102T>C (intron)	0.38%
	NLRP12	Cold autoinflammatory 2	c.1063 (p.Glu355Lys)	0.16%
4	LRBA	Hyper-IgE syndrome (NK function)	c.3784C>G (p.Leu1262Val)	0.09%
	LACC1	Oxidoreductase (systemic IIA)	c.-239+12_-239+13ins (5' UTR)	Novel
	NLRP4	Pathogenic E. coli infections	c.2119_2122dcltCTC (p.Ser707Valfs)	Novel
	RAG1	SCID (immunodeficiency)	c.295G>A (p.Gly99Ser)	0.09%
6	C7	Complement 7	c.1561C>A (p.Arg521Ser)	0.25%
	CARMIL2	Combined immunodeficiency	c.2489G>A (p.Arg830Gln)	0.56%
	TNFAIP3	Behcet-like autoinflammatory	c.755A>G (p.Tyr252Cys)	0.0007%
10	IKBKB	Hyper-IgE syndrome (NK function)	c.53+199C>G (intron)	0.21%
	MRTFA	Immunodeficiency 66 (TF)	c.1693dupG (p.Ala565GlyfsTer67)	Novel
11				
12	DOCK8	Hyper-IgE syndrome (NK function)	c.1249T>C (p.Phe417Leu)	0.001%
	IL17RA	Immunodeficiency 51 (IL-17 rec. A)	c.1361 (p.Pro454Arg)	0.001%
	ITK	IL-2 induc. T cell kinase (agamma.)	c.1510A>T (p.Thr504Ser)	0.09%
	LRBA	Common variable immunodef. 8	c.7708+387C>T (intron)	0.12%
	XIAP	X-linked lymphoproliferative 2	c.1408A>T (p.Thr470Ser)	0.06%
13	LYST	Chediak-Higashi (fHLH)	c.891T>G (p.ASn2971Lys)	0.27%
	STAT2	Immunodeficiency 44	c.2378A>T (p.His793Leu)	Novel
	STXBP2	UNC18-2 (fHLH)	n.1610G>C (non-coding exon)	0.14%
14	IFNGR1	IFN-gamma receptor 1	c.1325A>G (p.Glu442Gly)	Novel
15	LYST	Chediak-Higashi (fHLH)	c.1889C>T (p.Pro630Leu)	Novel
	LYST	Chediak-Higashi (fHLH)	c.3359G>T (p.Ser1120Ile)	0.29%
	NLRC4	Enterocolitis autoinflammatory	c.262+118G>A (intron)	0.14%
	RAB27A	Griscelli 2 syndrome (fHLH)	c.408-3C>T (3' splice site)	0.23%
	STAT3	Hyper-IgE syndrome (TF)	c.550+250C>A (intron)	1.7%
16	IKBKB	Hyper-IgE syndrome (NK function)	c.3815A>G (p.Tyr1272Cys)	0.27%
17				
18	STXBP2	UNC18-2 (fHLH)	c.1529+10C>T (intron)	0.21%
20	WAS	Wiskott-Aldrich syndrome	c995T>C (p.Val332Ala)	0.49%
21				
22	LRBA	Common variable immunodef. 8	c.5791+8DNA>G (interior intron)	0.019%
	PIK3CD	PI kinase catalytic	c.*120C>T	0.081%
23				
24				
25	CASP10	ALPS lymphoproliferative syndrome	c.*1043C>T (3' coding exon)	0.35%
	STAT4	SLE 11 (IL-23 signaling)	c.719G>A (p.Arg240Gln)	0.14%
	UNC13D	MUNC13-4 (fHLH)	c.2542A>C (p.Ile848Leu)	0.10%
	UNC13D	MUNC13-4 (fHLH)	c.2583G>C (p.Ala995Pro)	0.10%
26	MRTFA	Immunodeficiency 66 (TF)	c.1603G>A (p.Glu535Lys)	0.025%
27				

BRID gene; DOCK8-like; autoinflammatory; immunodeficiency

80% 75% 15% 60%

Immunologic rare gene variants identified by whole genome sequencing of COVID-19 clinical trial participants. Abbreviations: fHLH - familial hemophagocytic lymphohistiocytosis; NK - natural killer

Methods: Various published criteria were studied to define CSS among patients (n=32) enrolled in a randomized, double-blinded, placebo-controlled COVID-19 clinical trial exploring interleukin-1 blockade treatment for severe COVID-19. Whole genome sequencing (WGS) was undertaken to explore immunologic gene mutation associations among the first 20 patients



NK cell lytic function of DOCK8 missense variants. A. Flow cytometry plots of CD107a expression on NK-92 cells transfected with WT cDNA or patient-derived DOCK8 variants after co-incubation with K562 target cells. B. Summary plots of CD107a expression from 4 experiments. C. Flow cytometry plots of K562 target cell lysis (death) after incubation with WT DOCK8 or patient-derived variant-expressing NK-92 cells. D. Summary plots NK-92 cell cytotoxicity from 4 experiments.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

enrolled in the trial for whom samples for WGS were available. Foamy viral transduction of human NK-92 natural killer (NK) cells with wild-type (control) *DOCK8* cDNA or patient-derived *DOCK8* missense mutations was used to explore NK cell degranulation (CD107a expression) and cytolytic activity against K562 target cells by flow cytometry.

Results: None of the patients met HLH-04 or HScore criteria, but the ferritin to erythrocyte sedimentation rate (ferritin:ESR) ratio and the COVID-19 cytokine storm syndrome score (CSS score) identified 84% and 81% of patients, respectively (Table 1). Rare mutations in fHLH genes were identified by WGS in 6 patients (30%), and 4 patients (20%) possessed rare mutations in *DOCK8* (a novel CSS gene) (Table 2). The 3 patient-derived *DOCK8* missense mutations introduced into NK-92 cells each diminished NK cell cytolytic function and degranulation (Figure). In addition, variants in autoinflammatory and primary immunodeficiency genes were identified in 15% and 60% of patients, respectively (Table 2).

Conclusion: This severe COVID-19 cohort, like others, shares CSS features but is best identified by ferritin:ESR ratio. Rare heterozygous CSS gene (fHLH genes and *DOCK8*) mutations were frequently (45%) identified in this severe COVID-19 cohort, and the *DOCK8* missense mutations may have contributed to CSS in severe COVID-19 patients via diminished lymphocyte cytolytic activity.

Disclosure: r. Cron: AbbVie/Abbott, 1, American Board of Pediatrics, 12, Board Question Writer, AS2 Biotherapeutics, 2, CareerPhysician, 1, Neurogene, 2, Pfizer, 1, Sobia, 1, Springer, 9, VIDA Ventures, 2; **A. Kamath**: None; **M. Zhang**: None; **D. Abhser**: None; **L. Jackson**: None; **W. Chatham**: Sobi, 2.

Abstract Number: 0040

Identification Of A Novel, Expressed, Alternatively Spliced FCER1G Protein That Inhibits Receptor Function

Andrew Gibson[1], Jianming Wu[2], Chaoling Dong[1], R. Curtis Hendrickson[1], Travis Ptacek[1], Jeffrey Edberg[1] and **Robert Kimberly**[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Minnesota, Saint Paul, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The Tyrosine Activation Motif (ITAM)-containing FcRg chain, encoded by FCER1G, non-covalently couples with the immunoglobulin binding receptors, -- FcγRI (CD64), FcγRIIIa (CD16), and FcaRI (CD89), -- to initiate intracellular signals and mediate phagocytosis, cytokine production and other functions. While functionally impactful variants have been identified in the ligand-binding alpha-chains of receptors associated with FcRg, variants in the signal-generating FcRg have not been explored. Signal modulation through structural variants at the level of FcRγ would have implications for all FcRγ-associated receptors and their role in the pathogenesis of immune-mediated diseases.

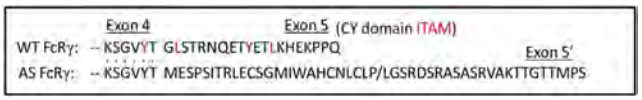


Figure 1. Sequence of FcRγ isoforms. The partial amino acid sequences of WT-FcRγ and AS-FcRγ are shown. Exon 5' in AS-FcRγ replaces exon 5 and encodes a novel cytoplasmic domain with no traditional signaling motifs. The ITAM signaling motif [YxxL(x7)YxxL] present in the WT-FcRγ is highlighted.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

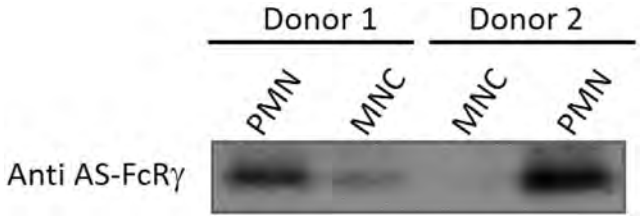


Figure 2. Western blot analysis of FcαR1 immunoprecipitates showing that AS-FcRγ protein pairs with and co-precipitates with FcαR1 in monocytes (MNC) and neutrophils (PMN).

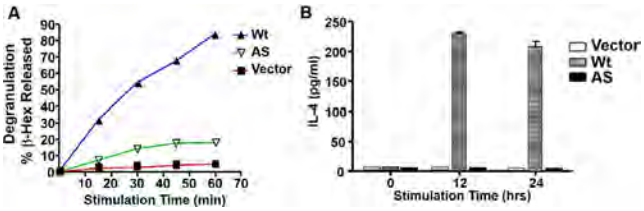


Figure 3. Stimulation of AS-FcRγ chimeric construct. A) Degranulation of β-Hexosaminidase activity. RBL-2H3 cells stably expressing vector alone or a chimeric receptor consisting of the extracellular domain of FcαRI fused to the cytoplasmic domain of WT-FcRγ or AS-FcRγ were stimulated with anti-FcαRI antibody A59 F(ab')2 for the times indicated. Cell degranulation was measured as a percent of total β-Hexosaminidase released by triton X-100 treated cells. B) IL-4 cytokine production. RBL-2H3 cells stably expressing the chimeric receptors were stimulated as outlined above for the indicated times. Cell culture media was then assayed by ELISA for the presence of IL-4 cytokine.

Methods: We carried out *in silico* analyses of whole genome DNA sequence databases based on short read sequencing (eg, gnomAD with ~79,000 genomes) and long-read sequencing (eg, >600 genomes from All of Us, the Arab and Chinese Pangenomes, and local long-read sequenced cohorts). We also assessed whole exome sequences (eg, gnomAD, UK Biobank and Regeneron totally >1M participants) as well as RNA transcript databases. We used Sanger sequencing of cDNAs derived from FcRg mRNAs isolated from local participants to confirm ESTs (eg, BG548748) in circulating immune cells. We used hg38 reference genome to identify genomic DNA and cDNA structural variants at the single nucleotide and larger variant levels.

Results: In the human genome, insertions, deletions and rearrangements of FCER1G are absent, and with the exception of very rare single nucleotide variants (allele frequency < 0.01), the FcRγ protein is monomorphic. Surprisingly, we confirmed that in addition to the canonical FcRγ transcript encoding the classically recognized FcRγ protein, an alternatively spliced (AS) form of FcRg message encodes a translated protein (AS-FcRg) which is expressed in human myeloid cells. AS-FcRγ is able to pair with ligand binding α-chains. The incorporation of the alternate exon 5' in AS-FcRγ creates a novel cytoplasmic domain with a disrupted ITAM signaling motif (Figure 1). The AS-FcRg mRNA is expressed in cell lines (U937, THP-1, HL-60) and in circulating neutrophils, monocytes and platelets, but not in lymphocytes, from normal donors. Co-immunoprecipitation experiments show that AS-FcRg associates with FcaRI in circulating neutrophils and mononuclear cells (Figure 2). An engineered chimeric molecule consisting of the extracellular domain of FcaRI fused to the cytoplasmic domain of AS-FcRg fails to stimulate cellular degranulation and cytokine production (Figure 3)

Conclusion: The AS-FcRg variant is not signaling competent and may represent a novel inhibitory mechanism limiting the ability of Fc receptors to stimulate cellular signaling in myeloid cells with important implications for host defense and antibody-mediated autoimmune diseases, including SLE and RA.

Disclosure: A. Gibson: None; **J. Wu**: None; **C. Dong**: None; **R. Hendrickson**: None; **T. Ptacek**: None; **J. Edberg**: None; **R. Kimberly**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0041

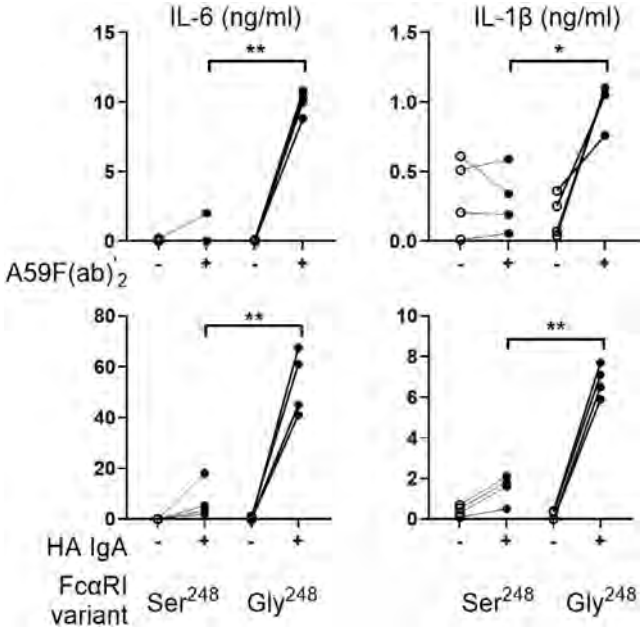
A Genetically Determined, Serine-based and Phosphorylation-dependent Molecular Switch Regulates the Inflammatory Potential of Human Iga

Andrew Gibson[1], Jianming Wu[2], R. Curtis Hendrickson[1], Travis Ptacek[1], Jeffrey Edberg[1] and **Robert Kimberly**[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Minnesota, Saint Paul, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

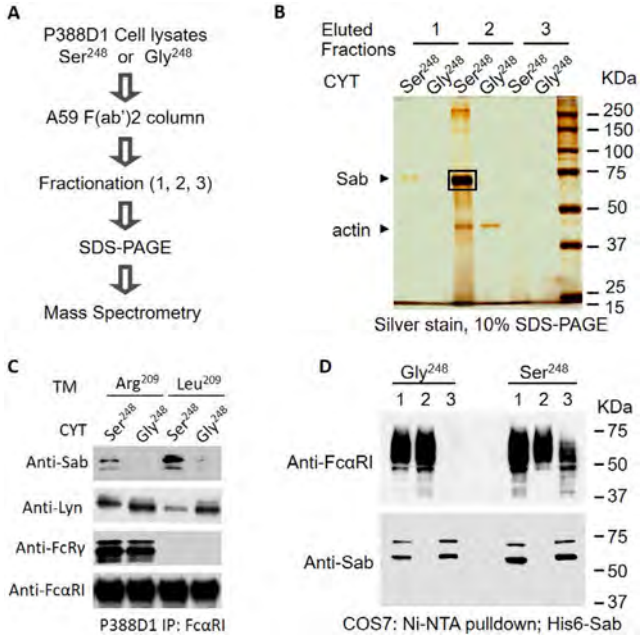
Background/Purpose: Human serum IgA can paradoxically inhibit immune cell activation. Inhibition of such activation, mediated by the inhibitory configuration of the immunoreceptor tyrosine-based activation motif (ITAM) in the Fc receptor common γ-chain (FcRγ), suggests a potential dual role for FcαRI (CD89)-FcRγ signaling pairs. However, in monocytes and neutrophils FcαRI is often expressed in the absence of FcRγ (Launay *et al*,1999). We previously reported a common FcaRI Ser^{248}Gly variant in the cytoplasmic domain of CD89 that affects receptor function in neutrophils. In the absence of FcRg, the Ser^{248} allele does not initiate signaling while the Gly^{248} allele maintains robust signaling. To elucidate the basis for this α-chain functon, we sought allele-specific FcαRI-associated molecules

Methods: To isolate and identify cellular proteins binding to the FcaRI Ser^{248} allele we used an anti-FcαRI affinity column followed by mass spectrometry. We used pull down assays with His6-tagged proteins to confirm direct protein-protein interactions. To test the differential function of the FcaRI Ser^{248}Gly alleles in mononuclear cells, we used freshly isolated human monocytes from donors homozygous for each allele. To investigate the molecular mechanisms underlying differential allele effects, we used the P388D1 murine monocytic cell line stably expressing FcaRI Ser^{248} or Gly^{248} with or without the engineered R^{209}L point mutation in the transmembrane, which abrogates FcRg chain pairing. We also used the U937 human

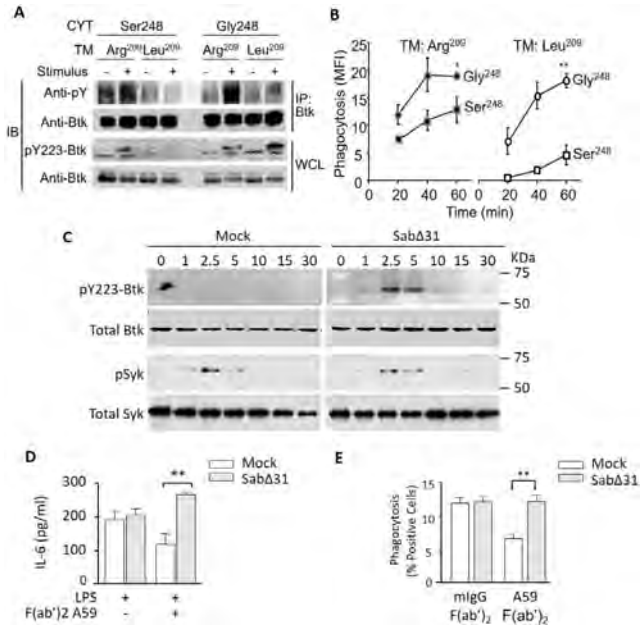


Sequence variation of FcαRI (S248G) alters IL-6 and IL-1β production in human monocytes . Peripheral blood monocytes (MNC) (n = 4) homozygous for FcαRI Ser248 or Gly248 variants were stimulated with mAb A59 F(ab')2 or heat aggregated IgA (HA IgA). IL-6 and IL-1β release were determined by ELISA at 24 hours following stimulation. * $p < 0.05$; ** $p < 0.01$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Identification of Sab as an FcαRI-binding protein. (A) A workflow diagram showing steps for isolating and identifying FcαRI variant-specific binding proteins. (B) FcαRI was immuno-isolated from P388D1 transfectants stably expressing human FcαRI-Ser248 or Gly248 using anti-FcαRI A59 F(ab')2-conjugated Sepharose column. The prominent 65KDa co-eluting protein band was subjected to MALDI-Mass Spectrometry analysis for identification. (C) Sab co-precipitates with FcαRI Ser248 independent of FcRγ pairing. (D) His6-Sab specifically pulls down FcαRI-Ser248. Input (1), the unbound flow through (2) and the bound (3) fractions are shown.



The FcαRI Ser248 variant attenuates Btk activation-dependent FcαRI-mediated functions. (A) P388D1 cells expressing FcαRI Ser248 or Gly248 variants with or without the Arg209Leu transmembrane change were stimulated for 3 minutes. Btk immunoprecipitates and whole cell lysates were blotted with anti-phosphotyrosine mAb, 4G10, and anti-pY223 Btk mAb, respectively. (B) The P388D1 transfectants were incubated with A59-opsonized FITC-conjugated Ox RBCs and phagocytosis of the RBCs measured by FITC fluorescence. C,D,E) Dominant negative Sab reverses FcαRI Ser248 failure to signal. C) The U937-SabΔ31 transfectants were opsonized with A59 F(ab')2 and stimulated with GAM F(ab')2 cross-linking for the indicated times. Whole cell lysates of the cells were immunoblotted for phospho-Btk, total Btk and total Syk. For phospho-Syk, phosphorylated proteins were immunoprecipitated using PY20 and immunoblotted for phospho-Syk. D) SabΔ31-expressing U937 cells were stimulated with LPS and A59 F(ab')2 for 24 hours, and secreted IL-6 was measured by ELISA. E) SabΔ31-expressing U937 cells were opsonized for 30 minutes with A59 F(ab')2 and incubated with human IgG-opsonized FITC-conjugated Ox RBC for 1 hour. Internalized RBCs were measured as intracellular FITC fluorescence. * $p < 0.05$; ** $p < 0.01$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

monocyte cell line, which endogenously expresses FcaRI Ser^{248} to test the effects of the dominant negative truncation of SH3BP5 (SabD31) which is incapable of inhibiting Btk.

Results: FcaRI Ser^{248} does not stimulate production of cytokines by human monocytes while FcaRI Gly^{248} consistently activates cytokine production (Figure 1). FcαRI Ser^{248} specifically recruited Sab (SH3-domain binding protein that preferentially associates with Bruton's tyrosine kinase, Btk), a trans-inhibitor of Btk, in a phosphorylation-dependent fashion, whereas the Gly^{248} variant reciprocally recruited the protein tyrosine kinase Lyn (Figure 2B,C,D). Compared to FcαRI Gly^{248}, FcαRI Ser^{248} recruitment of Sab results in inhibition of Btk phosphorylation/activation (Figure 3A) and suppression of effector functions (Figure 3B) independent of FcRγ-pairing. A dominant negative Sab incapable of binding to Btk fails to inhibit Btk phosphorylation/activation (Figure 3C) and releases FcαRI-mediated inhibition by the Ser^{248}-allele (Figure 3D,E). Ser^{248}-phosphorylation amplifies Sab association and disrupts Lyn binding through an overlapping region containing an unconventional SH3-domain binding motif.

Conclusion: These findings reveal a novel and reversible serine-based phosphorylation-dependent Sab/Lyn switch for regulation of receptor-mediated inhibition/activation that couples FcαRI α-chain to divergent inflammatory properties of human IgA. This genetically determined switch has important implications for the role of IgA in antibody-mediated autoimmune disease and host defense as well as implications for the use of IgA as the backbone for therapeutic antibodies.

Disclosure: A. Gibson: None; **J. Wu**: None; **R. Hendrickson**: None; **T. Ptacek**: None; **J. Edberg**: None; **R. Kimberly**: None.

Abstract Number: 0042

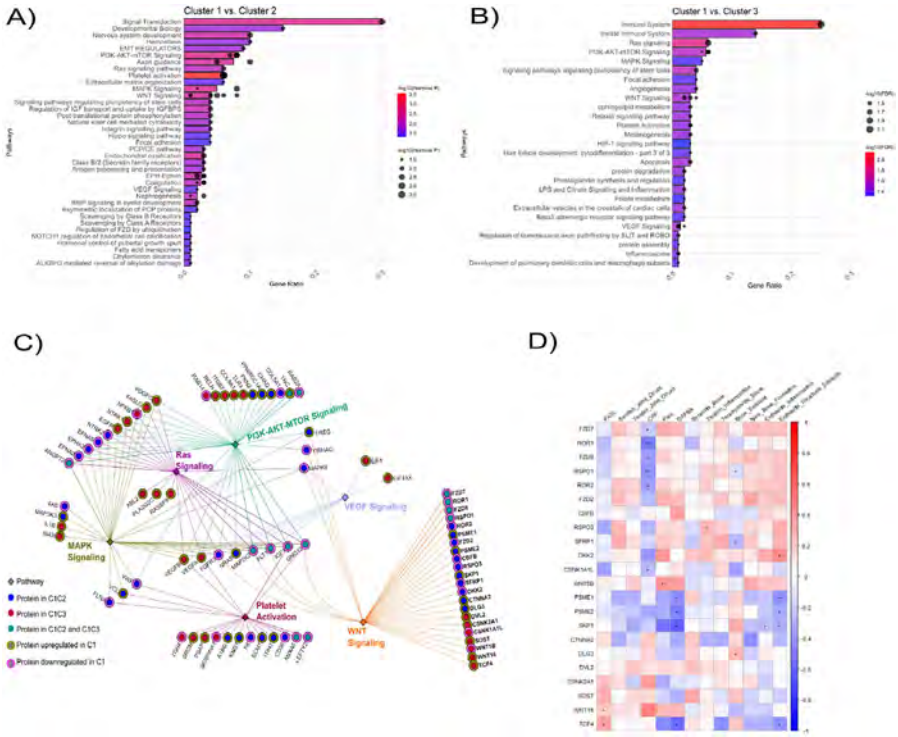
Serum Proteomic Analysis of Cellular Immune Clusters in Psoriatic Arthritis

Steven Dang[1], Xianwei Li[2], Sydney Thib[3], Darshini Ganatra[4], liqun Diao[5], Igor Jurisica[6], Vinod Chandran[7] and Lihi Eder[8], [1]Institute of Medical Science, University of Toronto, Toronto, Canada, [2]Department of Statistics and Actuarial Science, University of Waterloo, Waterloo, Canada, [3]Women's College Research Institute, Toronto, Canada, [4]Gladman Krembil Psoriatic Arthritis Research Program; Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Canada, [5]Department of Statistics and Actuarial Science, University of Waterloo, Toronto, Canada, [6]University Health Network, Toronto, Canada, [7]Division of Rheumatology, Departments of Medicine and Laboratory Medicine and Pathobiology, University of Toronto, and Gladman Krembil Psoriatic Arthritis Research Program, Krembil Research Institute, University Health Network, Toronto, Canada, [8]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Our recent study characterized immune endotypes in psoriatic arthritis (PsA) patients using mass cytometry of peripheral blood[1]. We identified an endotype characterized by high levels of CD4+ central and effector memory T cells (cluster 1), which was associated with higher levels of sonographic musculoskeletal inflammation and lower response to biologic therapy compared with the other two endotypes (cluster 2: innate immune cells (ILC) and cluster 3: terminal effector/Th1 cells). Further characterization of these clusters may enhance our understanding of PsA phenotypes. We aim to characterize the proteomic profile of the CD4+ memory T cell endotype in comparison with the other two immune endotypes and identify key proteins and biological pathways associated with disease severity and treatment outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Pathway enrichment and network visualization of differentially expressed proteins across clusters. (A) Pathways enriched in cluster 1 vs. cluster 2 and (B) pathways enriched in cluster 1 vs. cluster 3 ranked in descending order based on gene ratio; (C) Protein-pathway network plot of the shared enriched pathways characterizing cluster 1 vs. cluster 2 and 3. Coloured diamond nodes = shared pathways, blue circular node = DEPs in C1C2, red = DEP in C1C3 and green = DEP in both comparisons. An olive circular highlight = downregulated protein in C1, pink circular highlight = upregulated protein in C1; (D). Correlation matrix of the relationship between DEPs belonging to the WNT signalling pathway and PsA disease features.

Methods: A total of 30 patients initiating advanced therapies for active PsA were analyzed (9 patients in cluster 1, 11 in cluster 2, and 10 in cluster 3). For each patient, we measured 6402 different serum proteins using an aptamer-based platform. Differential expression analysis was performed between cluster 1 vs. cluster 2 and cluster 1 vs. cluster 3, with significance as $p < 0.05$. Pathway enrichment was performed reusing pathDIP v5, using literature-curated pathways from all 12 database sources. Protein-pathway networks of the shared pathways between cluster 1 vs. cluster 2 and cluster 1 vs. cluster 3 were created using NAViGaTOR v3.

Results: Differential analysis identified 285 proteins in cluster 1 vs. cluster 2 (176 upregulated and 109 downregulated in cluster 2) and 349 in cluster 1 vs. cluster 3 (160 upregulated and 189 downregulated in cluster 1). Pathways shared between these two comparisons (differentially expressed in cluster 1) included WNT signalling, platelet activation, VEGF, PI3K-AKT-MTOR, and MAPK signalling (Figure 1A-C). Additionally, WNT signalling appeared most distinct to the CD4+ memory cell endotype, containing the highest number of DEPs unique to this pathway, whereas other pathways shared multiple proteins. Among the deregulated proteins in the WNT pathway, DKK2, WNT5b, ROR2, FZD7, FZD8, and FZD2, were all proteins upregulated in the CD4+ memory cell endotype and correlated with disease activity measures (Figure 1D).

Conclusion: Given that WNT signalling is known to play a role in PsA pathogenesis, its activity in the CD4+ memory cell endotype may underlie the poorer response to advanced therapy observed in these patients. Overall, these results provide new insights into the biological mechanisms driving PsA and help to define distinct patient subgroups with shared clinical and biological features.

1 Eder L, Li X, Thib S, Ganatra D, Diao L, Chandran V. Deep Cellular Immune Profiling in Psoriatic Arthritis Correlates with Imaging Phenotypes and Response to Targeted Advanced Therapy [abstract]. *Arthritis Rheumatol*. 2023; 75 (suppl 9).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

https://acrabstracts.org/abstract/deep-cellular-immune-profiling-in-psoriatic-arthritis-correlates-with-imaging-phenotypes-and-response-to-targeted-advanced-therapy/. Accessed May 12, 2025.

Disclosure: S. Dang: None; **X. Li**: None; **S. Thib**: None; **D. Ganatra**: None; **I. Diao**: None; **I. Jurisica**: None; **V. Chandran**: AbbVie, 1, 2, AstraZeneca, 12, Spousal employment, Bristol Myers Squibb, 1, 2, Eli Lilly, 1, 2, 5, Fresenius Kabi, 1, 2, Johnson & Johnson, 1, 2, 5, Novartis, 1, 2, UCB, 1, 2; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5.

Abstract Number: 0043

Single-cell and Spatial Transcriptomic Profiling of Muscle Reveals Inflammatory Mechanisms in Anti-glycyl tRNA Synthetase Syndrome

Takuya Harada[1], Hiroyuki Yamashita[1], Ami Isoda[1], Ken Kawaue[1], Mayuko Hayashi[1], Yutaro Misawa[1], Aruto Yamamoto[1], Miyu Wakatsuki[1], Yuya Akiyama[1], Setsuko Oyama[1], Kyoko Motomura[1], Hiroyuki Takahashi[1], Akiko Mitsuo[2], Yuichi Goto[3], Eisei Noiri[3] and Hiroshi Kaneko[1], [1]Division of Rheumatic Diseases, National Center for Global Health and Medicine, Japan Institute for Health Security, Tokyo, Japan, [2]Division of Clinical Laboratory Medicine, National Center for Global Health and Medicine, Japan Institute for Health Security, Tokyo, Japan, [3]National Center Biobank Network, Tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: We characterized the spatial distribution of immune cells and identified hub genes within activated molecular networks in key immune cell populations, based on the muscle transcriptome profile of a patient with anti-glycyl tRNA synthetase syndrome.

Methods: Single-cell and spatial transcriptome analyses were performed on muscle biopsy specimens from a male patient in his 40s diagnosed with anti-glycyl tRNA synthetase syndrome. Spatial transcriptomic profiling identified gene expression clusters corresponding to regions of intense inflammation, characterized by immune cell infiltration. Differential gene expression analysis of these immune cell populations was performed using single-cell transcriptomic data. Subsequent molecular network and topological analyses were used to identify hub genes within activated signaling pathways. Validation of hub gene expression was conducted using the publicly available dataset GSE48280, comprising transcriptomic data from patients with idiopathic inflammatory myopathies.

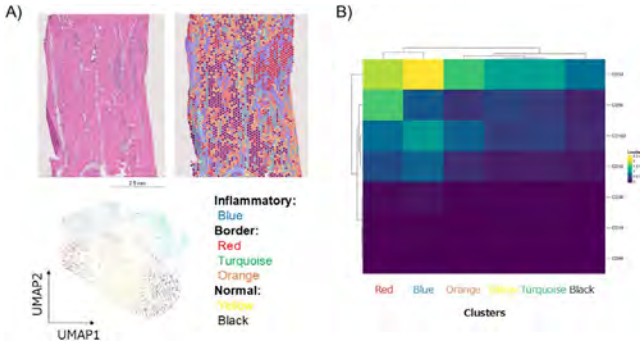


Figure 1. Spatial transcriptomic profiling. A) Six spatial clusters were identified. Blue cluster localized to a region of pronounced inflammation. B) Blue cluster was predominantly composed of $CD14^{+}CD163^{+}$ M2 macrophages.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

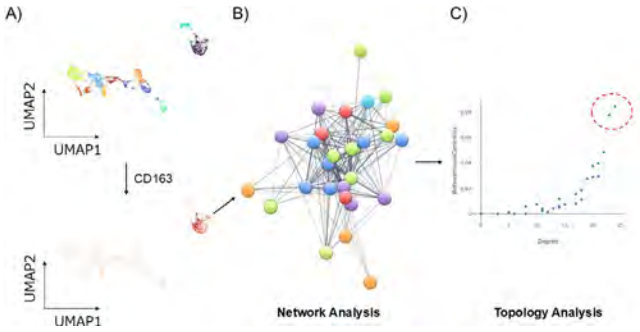


Figure 2. Single-cell transcriptomic profiling. A) Ten distinct cell clusters were delineated. Black cluster corresponded to CD163-positive M2 macrophages. B, C) Molecular network construction and topological analysis of the top 30 differentially expressed genes in the CD163-positive M2 macrophage cluster identified two hub genes.

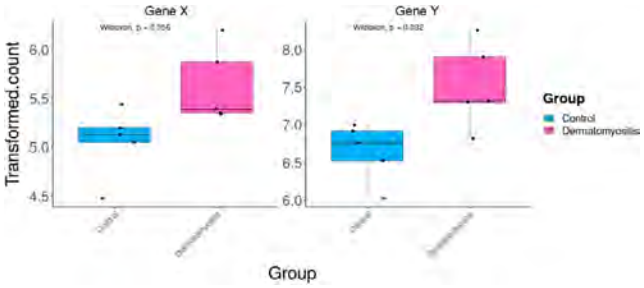


Figure 3. Comparison of the expression of two identified hub genes in muscle biopsy specimens from five healthy subjects and five patients with dermatomyositis. All identified hub genes exhibited a trend toward elevated expression in dermatomyositis patients.

Results: Gene expression profiling of muscle biopsy specimens identified six spatial clusters, one of which localized to a region of pronounced inflammation. This inflammatory cluster was predominantly composed of $CD14^{+}CD163^{+}$ M2 macrophages (Figure 1). Single-cell transcriptomic analysis further delineated 10 distinct cell clusters, including one corresponding to CD163-positive M2 macrophages. Molecular network construction and topological analysis of the top 30 differentially expressed genes in the CD163-positive M2 macrophage cluster identified two hub genes (Figure 2). Validation using the GSE48280 dataset, which includes RNA microarray data from muscle biopsies of five healthy controls and five patients with dermatomyositis, demonstrated that all identified hub genes exhibited a trend toward elevated expression in dermatomyositis patients (Figure 3).

Conclusion: In myositis associated with anti-glycyl tRNA synthetase syndrome, CD163-positive M2 macrophages, characterized by a limited set of hub genes, play a pivotal role in orchestrating the local inflammatory response within affected muscle tissue.

Disclosure: T. Harada: None; **H. Yamashita**: None; **A. Isoda**: None; **K. Kawaue**: None; **M. Hayashi**: None; **Y. Misawa**: None; **A. Yamamoto**: None; **M. Wakatsuki**: None; **Y. Akiyama**: None; **S. Oyama**: None; **K. Motomura**: None; **H. Takahashi**: None; **A. Mitsuo**: None; **Y. Goto**: None; **E. Noiri**: None; **H. Kaneko**: None.

Abstract Number: 0044

DNA Methylation Signatures in Systemic Lupus Erythematosus and Rheumatoid Arthritis Highlight Divergent Immune Pathways

Rufei Lu[1], **Tayte Stephens**[2], Carla Guthridge[1], Miles Smith[1], Joseph Kheir[1], Cristina Arriens[1], Joan Merrill[3], Marci Beel[4], Susan Macwana[1], Wade DeJager[5], Nicholas Domingez[1], Teresa Aberle[1], Joel Guthridge[1] and Judith James[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Oklahoma Health Science Center, Oklahoma City, OK,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

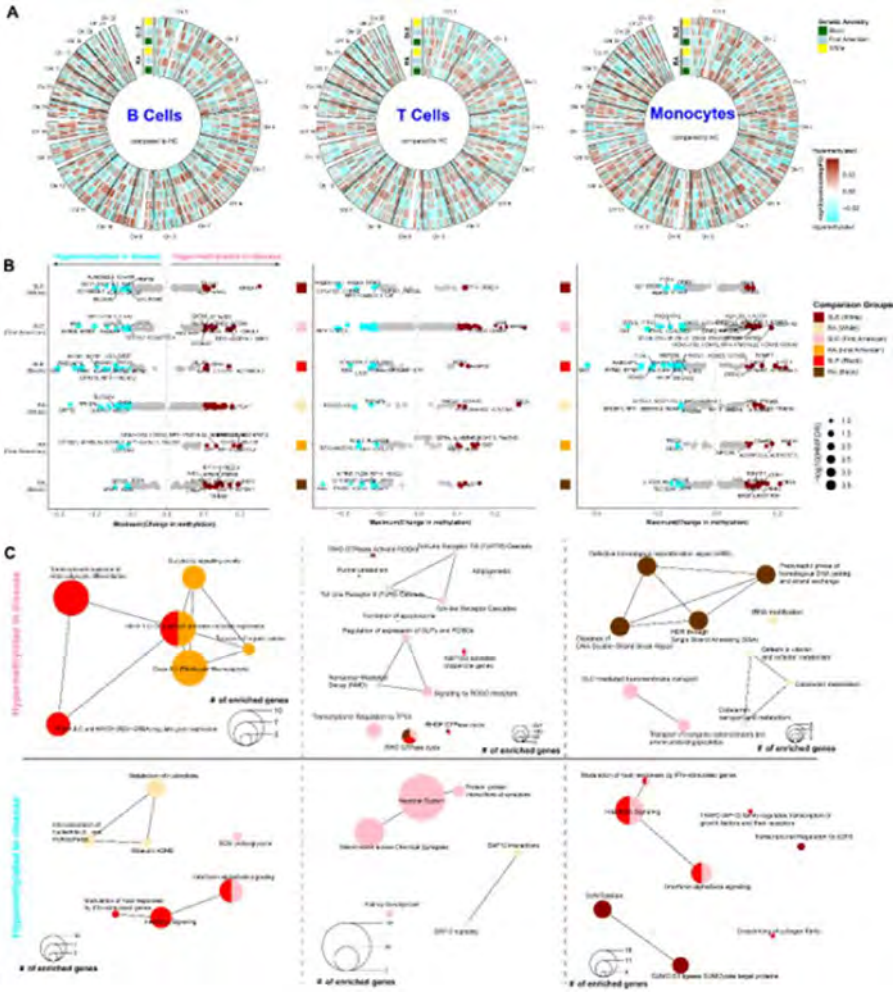
[3]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [4]Oklahoma Medical Research Foun, Oklahoma City, OK, [5]Oklahoma Medical Research Foundation, Oklahoma City

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are autoimmune diseases with distinct clinical and immunopathological features. Epigenetic modifications, particularly DNA methylation, contribute to immune dysregulation in these diseases. While SLE is characterized primarily by type I interferon (IFN) pathway activation, RA involves complex inflammatory pathways. Both are complex human diseases which share synovitis as a feature. Understanding ancestry-specific methylation patterns in immune cell subsets may elucidate disease mechanisms and explain differences in disease severity and response.

Methods: We performed genome-wide DNA methylation profiling using Infinium MethylationEPIC v1.0 on sorted B cells, monocytes, and T cells from Black (24 SLE and 21 RA), First American (22 SLE and 27 RA), and White (25 SLE and



A, Circular Manhattan plot showing distinct methylation profiles among different genetic ancestries between SLE and RA patients when compared to HC for B, T, and monocytes. B. Differential methylated region analyses for each sorted immune cell population. C. Gene set enrichment analyses of hyper- and hypomethylated genetic regions revealed different cellular pathways unique to disease and genetic ancestry within all three sorted immune cells.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

24 RA) female patients with SLE or RA and with age-matched healthy controls (n=30/ancestry). Probes above the limit of detections based on negative controls and samples with < 1% poor-quality probes were retained for subsequent analyses. Additionally, probes associated with known single nucleotide polymorphisms were also excluded. Differentially methylated regions were identified and analyzed with respect to immune pathways and ancestry.

Results: Overall, the differences observed in SLE and RA highlight methylation signatures that are unique to both diseases (**Fig 1**). In SLE, B cells and monocytes from Black and First American patients exhibited significant hypomethylation in type I Interferon (IFN) response genes (*MX1, IFITM2, IFITM1, IFI44L*), consistent with IFN hypersensitivity, a signature absent in White patients (**Fig 1 B&C**). First American T cells demonstrated hypermethylation of Toll-like receptor (TLR) response genes (*MYD88* and *TLR9*)., whereas White and Black T cells showed no significant changes in these pathways. In contrast, RA patients showed distinct methylation patterns: White monocytes displayed uniquely hypermethylated regions related to vitamin B12 metabolism (*LMBRD1* and *MMADHC*), and T cells exhibited hypermethylation in TLR-related genes (*MYD88*, *TLR9*, *JUN*, and *IRF7*). AI and Black RA patients displayed minimal methylation alterations in these immune cell types. These findings underscore divergent epigenetic regulation between SLE and RA, with SLE marked by IFN pathway dysregulation predominantly in Black and First American ancestries, and RA characterized by metabolic and TLR pathway methylation changes primarily in WHITE patients (**Fig 1**).

Conclusion: Ancestry-specific DNA methylation signatures in SLE and RA distinct immune pathway involvement. The pronounced type I IFN hypomethylation in Black and First American SLE patients contrasts with the unique methylation of vitamin B12 and TLR-related genes in White RA patients. These results highlight the necessity of incorporating ancestry and disease context in epigenetic studies to better understand autoimmune pathogenesis and guide personalized therapeutic strategies.

Disclosure: R. Lu: None; **T. Stephens**: None; **C. Guthridge**: None; **M. Smith**: None; **J. Kheir**: None; **C. Arriens**: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **M. Beel**: None; **S. Macwana**: None; **W. DeJager**: None; **N. Domingez**: None; **T. Aberle**: None; **J. Guthridge**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5.

Abstract Number: 0045

Genetic regulators of corticosteroid response in hepatic and adipose tissue and risk of adverse metabolic outcomes in patients with rheumatoid arthritis initiating glucocorticoids.

Thomas Riley[1], Bryant England[2], Austin Wheeler[2], Punyasha Roul[3], Grant Cannon[4], Brian Sauer[5], Gary Kunkel[6], Katherine Wysham[7], Beth Wallace[8], Andreas Reimold[9], Gail Kerr[10], Isaac Smith[11], John Richards[12], Iris Lee[13], Mitchell Lazar[1], Wenxiang Hu[14], Michael Levin[15], Scott Damrauer[15], Rui Xiao[16], Tate Johnson[2], Ted Mikuls[2], Joshua Baker[1] and Michael George[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]UNMC, Omaha, NE, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]Salt Lake City VA/University of Utah, Salt Lake City, UT, [6]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [7]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [8]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [9]Dallas VA Medical Center, Dallas, TX, [10]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [11]Duke University Hospital, Durham, NC, [12]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [13]Washington University in St Louis, Saint Louis, MO, [14]Guangzhou National Laboratory, Guangzhou, China (People's Republic), [15]University of Pennsylvania / Corporal Michael J. Crescenz VAMC, Philadelphia, PA, [16]Children's Hospital of Philadelphia, Philadelphia, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Previous studies identified single nucleotide polymorphisms (SNPs) that affect hepatocyte and adipocyte response to glucocorticoids (GCs). We aimed to determine if these candidate SNPs impact the risk of metabolic adverse events (AEs) in patients with RA treated with GCs.

Methods: We genotyped participants from the Veterans Affairs RA (VARA) registry, a prospective cohort of RA, using the Illumina GSA v2. Imputation was performed using TopMED Imputation Server. We evaluated 22 candidate SNPs known to impact hepatocyte or adipocyte response to GCs. Among participants initiating a GC course (identified through prescription fill data), Cox proportional hazard models assessed associations between each SNP and composite metabolic AEs (incident diabetes, acute cardiovascular event, or sustained weight gain ≥3kg), censoring 90 days after GC discontinuation, end of follow-up, or death. Models were adjusted for sex, age, and principal components of genetic background and clustered by participant to account for multiple observations per patient. As a negative control, we repeated analyses among participants initiating a DMARD with no GC exposure in the preceding 180 days. Using the Benjamini-Hochberg false discovery rate (FDR), a p-value < 0.0021 was considered significant. SNPs with the strongest associations were screened in the Genotype-Tissue Expression Portal (GTEx) for expression quantitative trait loci (eQTL) in hepatic or adipose tissue to understand the effect of genetically regulated gene expression on the composite outcome. Two sample mendelian randomization (MR) was performed for the effect of rs6495481 on metabolic AEs.

Results: In 2597 VARA participants (88% male, mean age 68 years), there were 1559 prednisone initiations among 994 participants, and 3482 DMARD initiations among 1330 participants unexposed to GCs. Incidence of all metabolic AEs were higher in the prednisone initiation cohort (**Table 1**). In time to event analysis, no SNP reached experiment-wide significance for the primary or secondary outcomes (**Fig. 1)**. The SNP rs6495481 C >T demonstrated the strongest negative association with composite AEs, driven by less sustained weight gain, but did not reach significance (composite OR 0.76, 95% CI 0.63, 0.93, p = 0.007, **Fig. 1, Fig. 2**). rs6495481 was not associated with composite AEs in the cohort unexposed to GCs. In GTEx, rs6495481 is an eQTL for fumarylacetoacetate hydrolase (*FAH)* in several tissues, including the liver. MR demonstrated a strong protective effect of downregulated hepatic gene expression of *FAH* on the risk of composite AEs following GC exposure (Wald ratio 3.74, SE 0.65, p = 9.0 x10^{-9}).

Table 1. Incidence of metabolic adverse events in patients with RA initiating prednisone compared to those unexposed to glucocorticoids initiating a disease-modifying anti-rheumatic drug.

	Group 1 Prednisone Initiation		Group 2 DMARD Initiation (glucocorticoid unexposed)		
	Number of Events	Event Incidence (per 1000 person-years)	Number of Events	Event Incidence (per 1000 person-years)	p-value
Composite Metabolic Adverse Event*	449	353.6	783	76.7	< 0.0001
New-Onset Diabetes	13	9.8	20	2.1	< 0.0001
Acute Cardiovascular Event	152	98.7	344	28.3	< 0.0001
Coronary Artery Disease	44	26.7	116	9.4	< 0.0001
Acute Stroke	16	9.6	51	4.0	0.0036
Heart Failure Hospitalization	112	70.9	180	14.2	< 0.0001
Cardiovascular Death	29	17.2	130	9.9	0.0088
Sustained Weight Gain	357	288.1	579	56.8	< 0.0001

*Composite metabolic adverse events outcome: new-onset diabetes, acute cardiovascular event**, or sustained weight gain

**Acute cardiovascular events: incident coronary artery disease, acute stroke, hospitalization for congestive heart failure, and cardiovascular death, validated in VA and national death index data.

Event incidence rate was calculated using at-risk person-time following each exposure; statistical comparisons were performed using log-rank testing.

Abbreviations: DMARD - disease-modifying anti-rheumatic drug

Single Nucleotide Polymorphism	Effect Allele	Allele Frequency	Composite Metabolic Adverse Event	New-Onset Diabetes	Cardiovascular Event	Sustained Weight Gain
			449	13	152	357
rs2456828	A	0.17	1.01	1.45	0.86	1.06
rs6433354	A	0.19	1.06	1.02	0.95	0.97
rs56384862	G	0.35	0.90	1.11	1.02	0.88
rs6555439	G	0.40	0.97	0.48	0.82	1.02
rs75053571	C	0.33	1.04	1.08	0.92	1.02
rs4282515	G	0.10	0.90	0.72	0.55	1.11
rs16890473	A	0.10	1.00	0.96	1.20	0.92
rs6651233	T	0.19	1.16	0.84	0.97	1.17
rs10980797	G	0.44	0.90	0.78	0.93	0.90
rs509482	A	0.29	1.04	1.05	1.11	0.99
rs10881935	G	0.32	1.13	1.77	1.00	1.10
rs7099556	T	0.31	0.96	0.77	0.90	0.91
rs4635039	T	0.11	1.03	1.39	1.14	1.01
rs67446678	T	0.16	1.01	0.98	1.18	0.98
rs2060982	A	0.47	1.01	0.53	0.79	1.06
rs73600715	C	0.34	1.00	0.95	1.18	0.94
rs114801506	T	0.24	1.04	1.87	1.20	0.96
rs6495481	T	0.27	**0.78**	1.03	1.00	**0.76**
rs28788799	G	0.30	0.91	**0.39**	0.82	0.94
rs116546108	C	0.08	1.18	1.83	0.95	1.23
rs226694	T	0.32	1.01	0.75	1.14	0.95
rs6026774	G	0.11	0.89	0.52	1.21	0.85

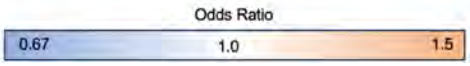


Figure 1. Association of SNPs related to glucocorticoid metabolism with adverse metabolic outcomes in VARA. Bold text indicate p-value < 0.05. No tests reached the experiment-wide significance threshold of 0.0021. Values are hazard ratios from Cox regression model adjusting for age, sex, and population structure. Composite events include new-onset diabetes, acute cardiovascular event, and sustained weight gain. Cardiovascular events include coronary artery disease, acute stroke, congestive heart failure, cardiovascular death.

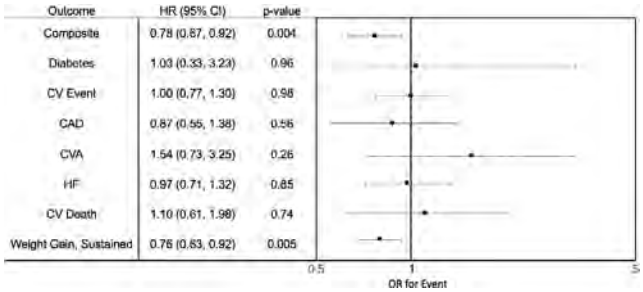


Figure 2. Association of rs6495481 with adverse metabolic outcomes in VARA participants initiating glucocorticoids. Patients with one T allele at rs6495481 (chr15, 80500456, C>T) had lower risk of the composite metabolic adverse event, driven by lower risk for sustained weight gain, but results were not statistically significant at a threshold of p < 0.0021. Confidence intervals are not corrected for the FDR.

Conclusion: Individual genetic variants impacting hepatocyte and adipocyte response to GCs did not meet the experiment-wide threshold for associations with the risk of metabolic AEs in patients with RA initiating prednisone. These analyses may have been underpowered to identify more modest associations. MR results suggest a potential biologic effect of these pathways on GC toxicity. Future studies should assess whether a combination of genetic factors can be combined with clinical factors to identify patients at high risk of metabolic AEs to guide clinical decision making.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Riley: None; **B. England**: Boehringer-Ingelheim, 2, 5; **A. Wheeler**: None; **P. Roul**: None; **G. Cannon**: None; **B. Sauer**: None; **G. Kunkel**: None; **K. Wysham**: None; **B. Wallace**: None; **A. Reimold**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **I. Smith**: None; **J. Richards**: None; **I. Lee**: None; **M. Lazar**: Flare Therapeutics, 1, 8, Pfizer, 1; **W. Hu**: None; **M. Levin**: None; **S. Damrauer**: Amgen, 12, Non-financial research support, Novo Nordisk, 12, Non-financial research support, US Department of Veterans Affairs, 10; **R. Xiao**: None; **T. Johnson**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **J. Baker**: Amgen, 5; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5.

Abstract Number: 0046

Association of Genetic Variation in *xist* and *Ftx* with Susceptibility to Female-biased Systemic Autoimmune Disease

Thomas Riley[1], Dana DiRenzo[1], Ellen Romich[2], Michael Levin[3], Scott Damrauer[3], Michael George[1], Montserrat Anguera[1], Joshua Baker[1] and Nikhil Jiwrajka[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Media, PA, [3]University of Pennsylvania / Corporal Michael J. Crescenz VAMC, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The mechanisms underlying female sex bias in autoimmune diseases remain unclear. Recent work has suggested that impaired maintenance of X-chromosome inactivation (XCI) in female murine immune cells can result in systemic lupus erythematosus (SLE)-like phenotypes. *XIST* (X-linked) encodes a long non-coding (lnc) RNA that helps maintain XCI in XX individuals. The Genome-Tissue Expression (GTEx) study has identified genetic variants that are expression quantitative trait loci (eQTL) for *XIST* or its X-linked positive regulator lncRNA *FTX*. This study hypothesized that eQTLs which lead to decreased expression of *XIST* or *FTX* in immune tissue would be positively associated with risk of female-biased autoimmunity.

Table 1. Demographic and Disease Statistics within Penn Medicine Biobank

		Total N=43,590	Male N=21,900	Female N=21,690
Age (yr), median (IQR)		64 (50-74)	68 (57-76)	60 (43-72)
Most Similar Reference Population	AFR	11,268 (25.8%)	4,201 (19.2%)	7,067 (32.6%)
	AMR	698 (1.6%)	303 (1.4%)	395 (1.8%)
	EAS	471 (1.1%)	257 (1.2%)	214 (1.0%)
	EUR	30,284 (69.5%)	16,724 (76.4%)	13,560 (62.5%)
	SAS	570 (1.3%)	295 (1.3%)	275 (1.3%)
	UNKNOWN	299 (0.6%)	120 (0.5%)	179 (0.8%)
Rheumatoid Arthritis		546 (1.3%)	167 (0.8%)	379 (1.9%)
Systemic Lupus Erythematosus		306 (0.7%)	51 (0.2%)	255 (1.3%)
Systemic Sclerosis		147 (0.4%)	32 (0.2%)	115 (0.6%)
Immune Mediated Myopathy (IMM)		89 (0.2%)	25 (0.1%)	64 (0.3%)
Sjögren's Disease		319 (0.8%)	39 (0.2%)	280 (1.4%)

Phenotype definitions:
Rheumatoid Arthritis (RA): 2 outpatient ICD-9 or ICD-10 codes plus a disease modifying anti-rheumatic drug used for RA
Systemic Lupus Erythematosus (SLE): 3 outpatient ICD-9 or ICD-10 codes plus a disease modifying anti-rheumatic drug used for SLE
Systemic Sclerosis (SSc): 2 outpatient ICD-9 or ICD-10 codes
Immune Mediated Myopathy (IMM): 1 inpatient or 2 outpatient ICD-9 or ICD-10 codes
Sjogren's Disease (SjoD): 2 outpatient ICD-9 or ICD-10 codes
Diagnosis assignment (if met multiple algorithms), assigned SSc, then IMM, then SLE, then RA, then SjoD
Abbreviations: IQR – interquartile range. AFR – African; AMR – admixed American; EAS – East Asian; EUR – European; SAS – South East Asian; ICD – International Classification of Disease

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

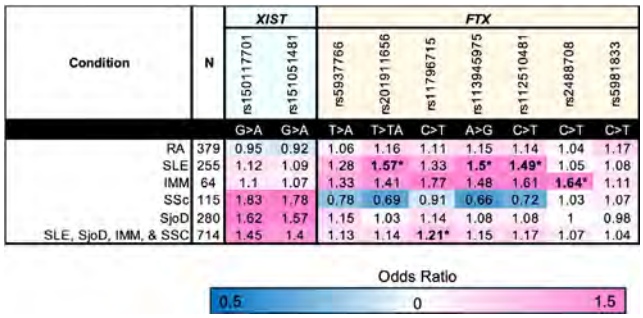


Figure 1. Heat Map of eQTL and sex-biased autoimmune conditions within the Penn Medicine Biobank. eQTLs for FTX were associated with statistically significantly higher odds of systemic lupus, immune mediated myopathy, and pooled sex-biased autoimmune disease. Analysis was performed using logistic regression, adjusted for the first 10 principal components of population structure and restricted to female sex. *Bold font indicates associations with p < 0.05; no associations met the experiment-wide significance threshold < 0.0056. Abbreviations: RA – Rheumatoid Arthritis; SLE – Systemic Lupus Erythematosus; SjoD – Sjogren's Disease: ICD – International Classification of Disease; IMM – Immune Mediated Myopathy; SSc – Systemic Sclerosis; ACR – American College of Rheumatology.

Methods: Participants in this study come from the Penn Medicine Biobank (PMBB), a health system-based biorepository. Participants underwent genotype sequencing using the Illumina Global Sequencing Array v2 by the Regeneron Genetics Center (Tarrytown, NY). Imputation was performed using the TOPMED Imputation Server. eQTLs associated with decreased expression of *XIST* and *FTX* in human splenic tissue were identified using the GTEx portal. Cases were identified using ICD-code and medication algorithms for SLE, systemic sclerosis (SSc), dermatomyositis or polymyositis (immune mediated myopathy, IMM), and Sjögren's Disease (SjoD). RA, a more modestly sex-biased disease not previously associated with X chromosome dosage, was selected as a negative control outcome. Logistic regression was performed to test the association of eQTLs with female-biased autoimmune disease, adjusted for the first 10 principal components of population structure and stratified by female sex. Using the Benjamini-Hochberg false discovery rate, a p-value < 0.0056 was considered significant.

Results: Among 43,590 individuals in PMMB, 21,690 (49.8%) were female (Table 1). By autoimmune condition, 546 (1.3%) had RA, 319 (0.8%) had SjoD, 306 (0.7%) had SLE, 147 (0.4%) had SSc, and 89 (0.2%) had IMM, with a higher prevalence in females compared to males. eQTLs associated with decreased *FTX* in the spleen were associated with increased risk for SLE in females; the strongest associations were for rs201911656 (T >TA) with OR 1.57, but did not meet experiment-wide significance thresholds (p = 0.009, Fig. 1, Table 2). eQTLs associated with decreased *XIST* expression were not statistically significant for individual conditions, including RA (Fig. 1). Examining the risk in diseases previously associated with X chromosome dosage (SLE, IMM, SjoD, and SSc), both *XIST* and *FTX* eQTLs were associated with higher odds of pooled autoimmune disease amongst females, but this result was not statistically significant (*FTX* rs11796715 (C >T) OR 1.21, 95% CI 1.02-1.45, p = 0.03).

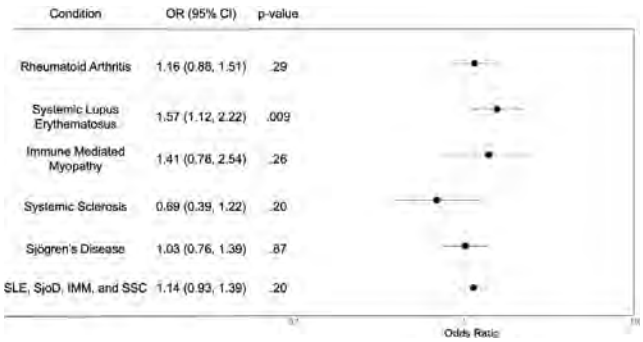


Figure 2. Association with autoimmune disease and FTX eQTL rs201911656. Logistic regression was performed to test the association of eQTL in an additive model with the female-biased autoimmune disease, adjusted for the first 10 principal components of population structure and restricted to female sex. Abbreviations: RA – Rheumatoid Arthritis; SLE – Systemic Lupus Erythematosus; SjoD – Sjogren's Disease: ICD – International Classification of Disease; IMM – Immune Mediated Myopathy; SSc – Systemic Sclerosis; ACR – American College of Rheumatology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Genetic variation associated with altered expression of regulators of XCI maintenance in immune cells was associated with increased risk for specific female-biased autoimmune disease, but did not reach experiment wide-significance thresholds. These results further suggest that impaired regulation of X chromosome dosage via decreased XIST expression may contribute to the female bias of SLE and other systemic autoimmune diseases.

Disclosure: T. Riley: None; **D. DiRenzo**: Amgen, 2, Novartis, 2, Sjogren's Foundation, 5; **E. Romich**: Lungpacer Medical, Inc., 11, Teva Pharmaceuticals, 12, Spouse employment; **M. Levin**: None; **S. Damrauer**: Amgen, 12, Non-financial research support, Novo Nordisk, 12, Non-financial research support, US Department of Veterans Affairs, 10; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **M. Anguera**: None; **J. Baker**: Amgen, 5; **N. Jiwrajka**: None.

Abstract Number: 0047

Monocyte Transcriptomic Signatures Uncover Potential Pathogenic Mechanisms of the APOL1 High Risk Genotype (HRG)

Vishnuprabu Pandian[1], Adebola Agboola[1], Sivasubramanian ramani[2], Christele Felix[3], Andrra Nimoni[3], Jasmin Divers[4], Timothy Niewold[5] and Ashira Blazer[2], [1]University of Maryland, Baltimore, Baltimore, Maryland, [2]University of Maryland Baltimore, Baltimore, Maryland, [3]Hospital for Special Surgery, New York, NY, [4]NYU Grossman Long Island School of Medicine, New York, New York, [5]Hospital for Special Surgery, New York, New York

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Compared to the low-risk genotype (LRG) the APOL1 high-risk genotype (HRG) confers an increased risk of end stage kidney disease among individuals with systemic lupus erythematosus (SLE). Despite this association, the cellular and molecular mechanisms driving APOL1-mediated cytotoxicity in SLE remain unclear. Monocytes both express APOL1 and are exposed to the SLE inflammatory milieu. This study aimed to define differential pathways of monocyte cytotoxicity in SLE patients stratified by APOL1 genotype.

Methods: THP-1 monocytes were stimulated with IFN-γ, and APOL1 expression was quantified via qRT-PCR and Western blot. Monocytes from SLE patients were isolated using Ficoll density gradient and magnetic bead separation. Blood DNA was extracted from patients and genotyped for APOL1 risk variants. Type-I interferon activity in plasma was assessed using the WISH cell bioassay. RNA-seq was performed on patient's monocytes, and differential gene expression analysis compared high-risk (2 APOL1 variants) and zero-risk groups, followed by gene ontology and pathway enrichment analyses.

Results: Demographic and clinical data from 23 SLE patients were stratified by APOL1 risk allele count (0, 1, or 2). Those with 2 risk variants (n=5) had lower mean eGFR (64 ± 28.5 mL/min/1.73 m^2) and SLEDAI scores (4 ± 2) than patients with 0 (97 ± 15.6; 7.7 ± 5.7) or 1 variant (105.4 ± 18.2; 8.4 ± 6.3). Type I interferon activity, assessed via WISH cell assay, declined with increasing APOL1 variants (mean: 0RV 9.28, 1RV 4.25, 2RV 1.34; p=0.07). IFN-γ treatment of THP-1 monocytes confirmed APOL1 expression, showing 31.1-fold (qRT-PCR) and 2.5-fold (western blot) increases. Transcriptomic profiling revealed that monocytes from high-risk genotype (HRG) patients upregulated genes in TNF-α signaling, coagulation, inflammation, and cholesterol homeostasis. Key upregulated genes included CD5L, TRAP1, HLA-DQA, TNFRSF19, KIR3DL2, and platelet receptor, P2RY12. Conversely, HLA-DRB5, IFNGR2, and TNFSF13B (BAFF) were downregulated in HRG vs low-risk genotype (LRG) monocytes.

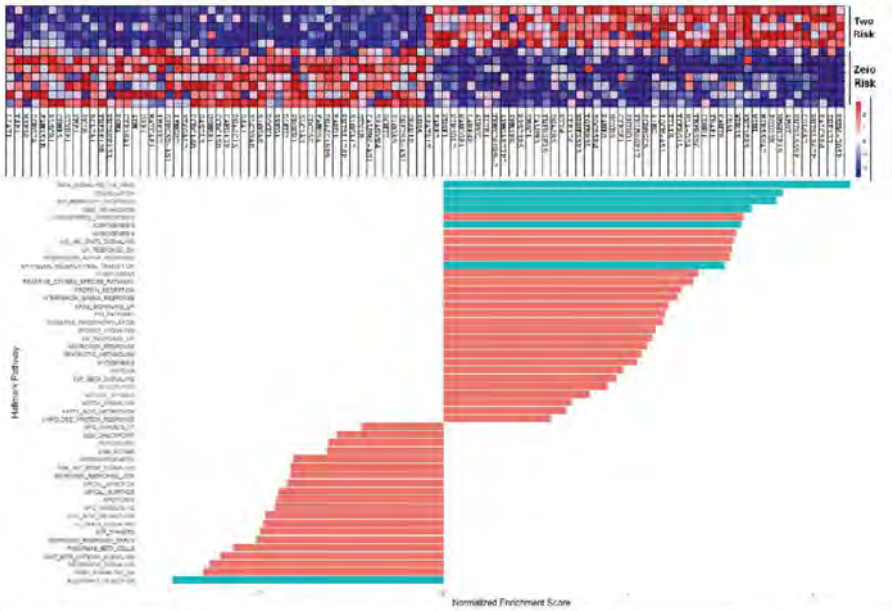
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table-1 Clinical and Demographic Characteristics of SLE Patients Stratified by APOL1 Risk Alleles

	Number of APOL1 Risk Alleles			Full Cohort
Number of Samples (n)	**0 (7)**	**1 (11)**	**2 (5)**	**23**
Demographics				
Age (SD)	45.6 (13.2)	42 (13)	49 (15)	44.7 (13.4)
Female (%)	6 (85.7)	8 (72.7)	4 (80)	18 (78.3)
Male (%)	1 (14.3)	3 (27.3)	1 (20)	5 (21.7)
SLEDAI score (SD)	7.7 (5.7)	8.4 (6.3)	4 (2)	7.2 (5.7)
Proteinuria (%)	43%	55%	40%	49%
eGFR (SD)	97 (15.6)	105.4 (18.2)	64 (28.5)	93.8 (25.8)
Immunology				
ANA Titer (SD)	2(1.3)	1.2 (1)	1.1 (1)	1.4 (1.1)
C3 (SD)	98.6 (30.2)	89.1 (28.8)	108.1 (15.0)	96.1 (28)
C4 (SD)	19 (8.6)	34.6 (38.6)	25.7 (8.8)	27.8 (28.2)
Medications				
Hydroxychloroquine (%)	4 (57.1)	9 (81.8)	5 (100)	18 (78.3)
Prednisone (%)	1 (14.3)	2 (18.2)	4 (80)	7 (30.4)
Mycophenolate (%)	3 (42.9)	4 (36.4)	3 (60)	10 (43.5)
Azathioprine (%)	1 (14.3)	1 (9.1)	1 (20)	3 (13)
Methotrexate (%)	1 (14.3)	0 (0)	1 (20)	2 (8.7)
Benlysta (%)	3 (42.9)	1 (9.1)	1 (20)	5 (21.7)

Demographic, clinical, immunological, and treatment-related characteristics of systemic lupus erythematosus (SLE) patients grouped by the number of APOL1 risk alleles (0, 1, or 2). The full cohort includes 23 patients. Continuous variables are presented as mean (standard deviation), and categorical variables are shown as counts (percentage). Proteinuria is reported as the percentage of patients with documented proteinuria. Medication use reflects the proportion of patients on each treatment at the time of sample collection.

Figure-1 Heatmap and Gene Set Enrichment Analysis of Monocyte transcriptome from Patients with Zero and Two APOL1 Risk Alleles



The top panel displays a heatmap of gene expression profiles from monocytes of patients carrying either zero or two APOL1 risk alleles. Each row represents an individual patient, and each column corresponds to a gene.

The bottom panel shows the normalized enrichment scores (NES) for statistically significant differentially expressed gene sets, with positive NES indicating pathways upregulated and negative NES indicating downregulated in the two-risk group than zero risk. This analysis highlights distinct molecular pathways associated with APOL1 two risk variants.

Conclusion: Our findings indicate that circulating monocytes from HRG SLE patients exhibit a transcriptomic profile characterized by proinflammatory and procoagulant signatures, alongside diminished antigen presentation capacity. These results provide novel insights into how APOL1 risk variants may contribute to cytotoxicity in SLE beyond classical interferon-driven mechanisms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Pandian: None; **A. Agboola**: None; **S. ramani**: None; **C. Felix**: ACR, 6, Lupus Research Alliance, 1, 6, 7; **A. Nimoni**: None; **J. Divers**: None; **T. Niewold**: AstraZeneca, 2, Pioneering Medicines, 2, Progentec, 2, 4, Zenas, 5; **A. Blazer**: AstraZeneca, 2, GlaxoSmithKlein(GSK), 5, 12, Medical educators network.

Abstract Number: 0048

Integrative Spatial Proteomics and Single-Cell RNA Sequencing Unveil Molecular Complexity in Rheumatoid Arthritis for Novel Therapeutic Targeting

Xue Wang[1], Fei Wang[2], Sílvia Sisó[2], Archana Iyer[2], Heather Knight[2], Lori Duggan[2], Yingli Yang[2], Liang Jin[2], Baoling Cui[2], **Yupeng He**[3], Jan Schejbal[2], Lucy Phillips[2], Bohdan Harvey[4] and Yu Tian[2], [1]AbbVie, South San Francisco, CA, [2]AbbVie, Worcester, MA, [3]AbbVie, North Chicago, IL, [4]AbbVie, Cambridge, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0019–0048) Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent inflammation, fibroblast proliferation and progressive joint damage. Understanding the heterogeneity of RA and identifying therapeutic targets remain challenging using traditional bulk transcriptomics alone, as it lacks the spatial and protein-level resolution needed to fully capture disease and tissue complexities. While scRNA-seq provides a high-resolution of dynamics of gene expression at the single-cell level, it lacks the topographical or spatial context.

Methods: In this study, we applied Laser Capture Microdissection (LCM) coupled with mass spectrometry-based proteomics to analyze histopathological niches of the RA synovium, enabling the identification of protein expression profiles of the diseased synovial lining and sublining microenvironments compared to their healthy counterparts. To enhance our understanding of cellular dynamics within the dissected regions, we further integrated the proteomic dataset with single-cell RNA sequencing (scRNA-seq) and deduced cell type enrichment including T cells, fibroblasts, NK cells, myeloid cells, B cells and synovial endothelial cells.

Results: Using the in-house spatial proteomics workflow, we generated a protein expression abundance dataset containing 3,818 quantified proteins. protein expression changes were more pronounced between disease conditions than between different histopathological compartments. Key pathogenetic RA proteins like membrane proteins (TYROBP, AOC3, SLC16A3, TCIRG1 and NCEH1), and extracellular matrix (ECM) proteins (PLOD2, OGN and LUM) showed different expression patterns in diseased synovium compartments. Integration of scRNAseq and spatial proteomics provide cellular and molecular landscapes of cell type/cluster enrichments in distinct histopathological regions, highlighting fibroblasts enrichment in RA fibrous sublining regions and immune cells enrichment in RA immune sublining regions.

Conclusion: By combining high-resolution spatial proteomics and transcriptomic analyses, we provide novel insights into the molecular mechanisms driving RA and highlight potential protein targets for therapeutic intervention. This integrative approach offers a more comprehensive view of RA synovial pathology and mitigates the limitations of traditional bulk transcriptomics in target discovery.

Disclosure: X. Wang: None; **F. Wang**: None; **S. Sisó**: None; **A. Iyer**: AbbVie/Abbott, 3; **H. Knight**: AbbVie/Abbott, 3; **L. Duggan**: AbbVie/Abbott, 3; **Y. Yang**: None; **L. Jin**: None; **B. Cui**: None; **Y. He**: AbbVie/Abbott, 3; **J. Schejbal**: AbbVie/Abbott, 3; **L. Phillips**: AbbVie/Abbott, 3; **B. Harvey**: AbbVie/Abbott, 3, 11; **Y. Tian**: Abbvie, 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0049

Enhanced Src Homology Region 2 Domain-containing Phosphatase 1 Activity Ameliorates Murine Inflammatory Arthritis Through the Innate Immune System

Jun Li, Katalin Mikecz and **Adrienn Markovics**, Rush University Medical Center, Chicago

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Src homology region 2 domain-containing phosphatase 1 (SHP-1) is a cytoplasmic protein tyrosine phosphatase expressed in hematopoietic cells (PMID9069265). SHP-1 is a key negative regulator of adaptive and innate immune cell signaling; its function is critical in preventing and eliminating excessive immune cell activation (PMID12490957). Suboptimal SHP-1 function has been linked to autoimmune and inflammatory diseases (PMID27216862). We reported that genetically and pharmacologically enhanced SHP-1 activity reduced disease severity in a T cell-driven murine model of inflammatory arthritis (PMID32586377). Our objective was to determine if the protective role of enhanced SHP-1 activity is mediated by T cells and the adaptive immunity.

Methods: Proteoglycan-induced arthritis (PGIA) was induced in 12-weeks old female wildtype (WT) and Shp1- overexpressing transgenic (Shp1-Tg) mice. For adoptive cell transfer, unseparated spleen cells, regulatory T cells or conventional T cells were isolated from WT or Shp1-Tg mice and transferred to 12-weeks old female mice with Severe Combined Immunodeficiency (SCID). Collagen antibody-induced arthritis (CAIA) was induced in 12-weeks old female WT and Shp1-Tg mice by an antibody cocktail to collagen II. SHP-1 activity was enhanced by regorafenib (REG) treatment of WT mice with CAIA (20 mg/kg/day). Arthritis incidence and severity were determined by Visual Arthritis Score (VAS). Spleens were harvested to determine inflammatory cytokine gene expression by qPCR. Ankle joint histopathology was quantified. Animal experiments were approved by IACUC #23-059 at Rush University Medical Center. Data analysis software: GraphPad Prism v10.1.2. Statistical significance was set at $p< 0.05$.

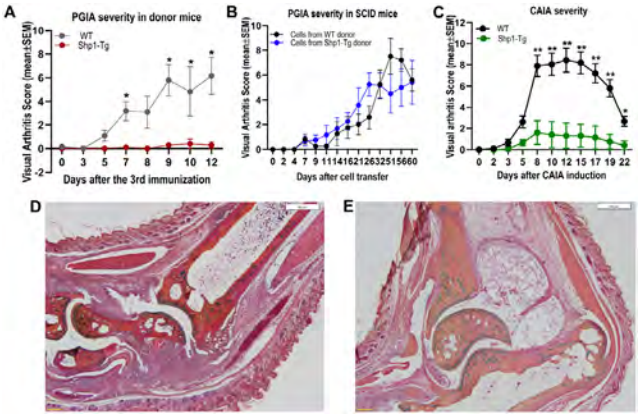


Figure 1. The anti-arthritic effect of SHP-1 overexpression is mediated by the innate immune system. A: Significantly reduced PGIA severity in spleen cell donor Shp1-Tg mice (12-weeks old female, n=10-12/group). B: No significant difference in PGIA severity in spleen cell recipient SCID mice (12-weeks old female, n=6-7/group). C: Shp1-Tg mice show significantly reduced CAIA severity compared to WT mice (n=10/group). D-E: Representative images of the tibiotarsal joint of WT mice with CAIA and treated with vehicle (D) or SHP-1 activator regorafenib (E). Alcian blue/hematoxylin/orange G staining. ($p^*<0.05$, $p^{**}<0.01$;two-way ANOVA followed by Sidak`s multiple comparison).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In the PGIA adoptive transfer model, SCID mice developed PGIA in each transfer group. PGIA severity in SCID mice was not statistically different following spleen cell transfer or T cell transfer from Shp1-Tg mice, indicating that the protective effect of genetically enhanced SHP-1 activity cannot be transferred by T (or B) cells (Fig 1A-B). In the CAIA model, Shp1-Tg mice showed significantly lower CAIA incidence and severity (Fig 1C) than WT mice. REG treatment of arthritic WT mice significantly reduced CAIA severity. REG treatment also significantly reduced expression of interleukin-1β, IL-6, IL-17 and interferon gamma transcripts. Ankle joint histopathology (synovial thickness, cartilage/bone damage, pannus, inflammatory cell infiltration) was significantly improved after REG treatment (Fig 1D-E).

Conclusion: Enhanced SHP-1 activity was protective/therapeutic in two different murine models of inflammatory arthritis. Since this protective effect was not transferred by spleen cells or T cells from Shp1-Tg mice, it is conceivable that innate immune cells (macrophages, neutrophils) are responsible for the anti-inflammatory effect of enhanced SHP-1 activity. Given the significant role of macrophages and neutrophils in RA, future studies will explore if enhanced SHP-1 activity in these cells can be utilized as a cell-based therapeutic approach in RA.

Disclosure: J. Li: None; **K. Mikecz**: None; **A. Markovics**: None.

Abstract Number: 0050

TL1A expression is upregulated in rheumatic diseases and anti-TL1A antibody reduces disease symptoms and pathological changes in rat collagen-induced arthritis

Preeyam Patel[1], Matthew Siegel[2], Emily Lewis[3], David Giles[3], Justin LaFountaine[3], Joshua Friedman[3] and **Andy Spencer**[3], [1]Spyre Therapeutics, Waltham, [2]Spyre Therapeutics, Menlo Park, CA, [3]Spyre Therapeutics, Waltham, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The development of disease-modifying anti-rheumatic drugs (DMARDs) has reduced disease activity in patients living with rheumatic diseases. Despite this, there is continued unmet need for safe and effective agents with improved convenience. TNF-like protein 1A (TL1A) is a pro-inflammatory and pro-fibrotic cytokine. TL1A inhibition has shown proof-of-concept in inflammatory bowel disease (IBD) and is under investigation in additional autoimmune conditions. Spyre Therapeutics is developing half-life extended antibodies targeting TL1A for the treatment of patients with IBD and rheumatic diseases. Animal model and translational data are needed to support the development of TL1A inhibitors in rheumatic diseases.

Methods: Gene expression data from published rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), and psoriatic arthritis (PsA) studies deposited in NCBI GEO were merged and queried to assess TL1A expression in controls and those with rheumatic diseases. To further characterize the role of TL1A in arthritis, the rat collagen-induced arthritis (CIA) model was used to assess the impact of TL1A inhibition on arthritic endpoints. Female Wistar rats were injected with a bovine type II collagen emulsion on days 0 and 7. Antibody treatments were injected (IV) once weekly. Etanercept was injected (IP) every 3 days. Body weight, hind paw volume and arthritis scores were measured twice per week. At study conclusion, X-ray images of the hind paws were taken and scored. Decalcified hind paw sections were scored by a blinded pathologist for cell infiltration, pannus severity, cartilage lesion severity, and bone resorption. RNA sequencing was performed on knee synovium.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: TL1A gene expression is upregulated in the blood of RA and axSpA patients and in skin lesions of PsA patients compared to healthy controls. In the rat CIA model, initiating treatment prior to symptom onset resulted in significantly improved disease activity score and hind paw volume with anti-TL1A antibodies compared to etanercept. Treatment with either anti-TL1A or etanercept improved hind paw X-ray scores relative to control groups with the magnitude of improvement being greater for animals treated with anti-TL1A than with etanercept. Anti-TL1A treatment, but not etanercept treatment, resulted in improvement across all histopathology scores compared to the vehicle control group. When initiated after the development of symptoms, treatment with anti-TL1A and etanercept showed comparable improvements in disease activity score, hind paw volume, and hind paw X-ray score relative to vehicle controls.

Conclusion: TL1A gene expression is increased in the blood of RA and axSpA patients and in skin lesions of PsA patients compared to healthy controls. Anti-TL1A antibody treatment reduced disease symptoms and pathology scores in the rat model of CIA. In this model, anti-TL1A treatment resulted in superior efficacy relative to etanercept when initiated prior to symptom onset and had comparable efficacy to etanercept when initiated at the start of symptom onset. These data support the clinical development of anti-TL1A therapy in rheumatic diseases.

Disclosure: P. Patel: Spyre Therapeutics, 3; **M. Siegel**: Spyre Therapeutics, 3; **E. Lewis**: Spyre Therapeutics, 3; **D. Giles**: Spyre Therapeutics, 3; **J. LaFountaine**: Spyre Therapeutics, 3; **J. Friedman**: Spyre Therapeutics, 3; **A. Spencer**: Spyre Therapeutics, 3.

Abstract Number: 0051

Spp1+ Macrophages Are Specifically Enriched in Arthritic Joints and Associated with Abnormal Bone Metabolism in Collagen-Induced Arthritis Mice

Chenjia He, Xuyang Xia, Heng Xu, Geng Yin and Qibing Xie, West China Hospital, Sichuan University, Chengdu, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Synovial fluid (SF) of RA patients contains unique *SPP1*$^{+}$ macrophages that drive pathogenesis by activating fibroblast-like synoviocytes (FLS). Single-cell RNA sequencing (scRNA-seq) data from SF, synovial tissue (ST), and peripheral blood of same RA patient shows *SPP1*$^{+}$ macrophages are enriched in SF and ST but absent in peripheral blood. This limits research on these cells. Previous studies focused on RA patients and lack research on the distribution and functional characteristics of *Spp1*$^{+}$ macrophages in animal models. This study explores the distribution and function of *Spp1*$^{+}$ macrophages in collagen-induced arthritis (CIA) mice, addressing clinical sample limitations and providing insights into RA pathogenesis and therapeutic strategies.

Methods: CIA mouse model was established, and scRNA-seq was performed on joints from CIA and control mice. Sequencing data was annotated and clustered to identify cell populations. Flow cytometry analyzed *Spp1*$^{+}$ macrophage proportions in peripheral blood, spleen, and joints based on established gating strategies. Micro-computed tomography (Micro-CT) was used to assess bone metabolism parameters and their correlation with *Spp1*$^{+}$ macrophage proportions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

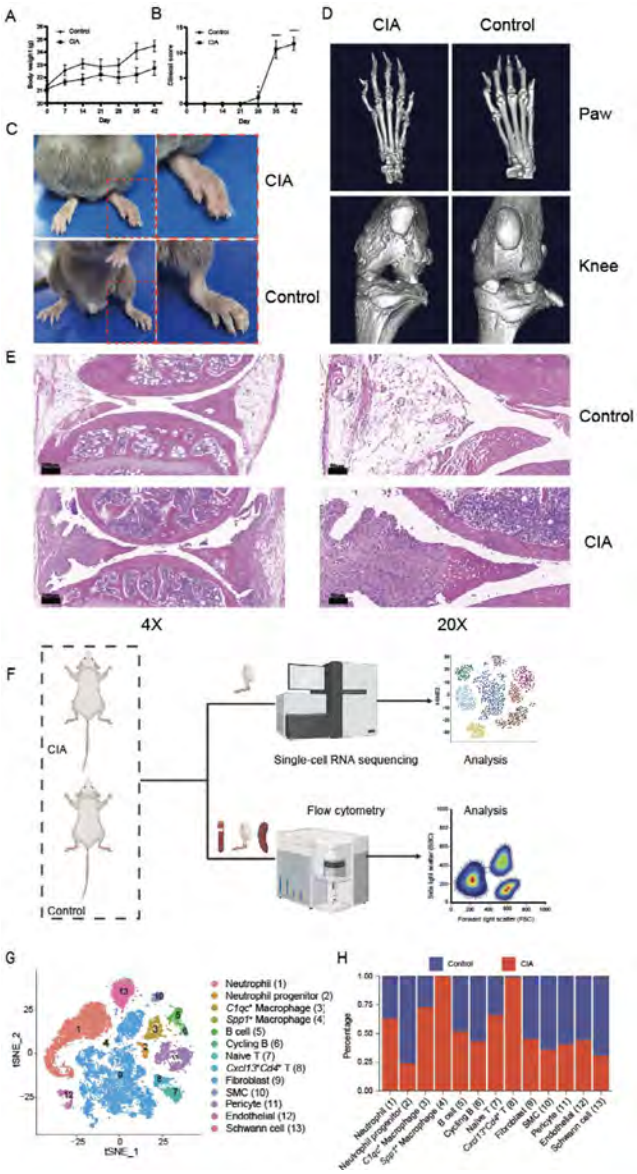


Fig. 1 Establishment of the CIA mouse model and single-cell sequencing analysis. A Body weight of CIA and control mice. B Clinical arthritis scores of CIA and control mice. C Hind paws of mice 42 days after primary immunization. D Representative micro-CT images of hind paws and knee joints. E Hematoxylin and Eosin staining of knee joint pathological sections. F Schematic diagram of the study workflow. G t-distributed stochastic neighbor embedding (t-SNE) plot showing single-cell transcriptional profiles of paws from CIA and control mice. H Proportion analysis of cell clusters in CIA versus control mice. *$p < 0.05$, ****$p < 0.0001$.

Results: On day 42 post-immunization, CIA mice showed significant weight loss, higher clinical scores, severe synovial inflammation, and joint destruction compared to controls, confirming successful model induction (Fig. 1A-E). scRNA-seq of paws from one CIA and one control mouse revealed *Spp1*$^{+}$ macrophages specifically in CIA joints, absent in controls (Fig. 1F-H). Flow cytometry showed higher *Spp1*$^{+}$ macrophage proportions in CIA joints than in peripheral blood and spleen (Fig. 2B-C). Proportion of *Spp1*$^{+}$ macrophages in the joints of CIA mice were significantly elevated compared to controls, with no differences in peripheral blood and spleen (Fig. 2E-F). Three-dimensional reconstruction of knee joints showed severe joint surface damage and bone erosion in CIA mice. Bone volume (BV)/tissue volume (TV), bone surface (BS)/TV, trabecular number (Tb.N), and trabecular sepamtion (Tb.Sp) analysis in the proximal tibia showed significant decreases in BV/TV, BS/TV, and Tb.N in CIA mice (Fig. 3A-C), while Tb.Sp was higher (Fig. 3D), indicating bone loss and osteoporosis. Spearman correlation analysis showed *Spp1*$^{+}$ macrophage proportions in joints were negatively correlated with BV/TV, BS/TV, and Tb.N but positively correlated with Tb.Sp (Fig. 3E-H), suggesting a link between elevated *Spp1*$^{+}$ macrophages and bone abnormalities in CIA mice.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

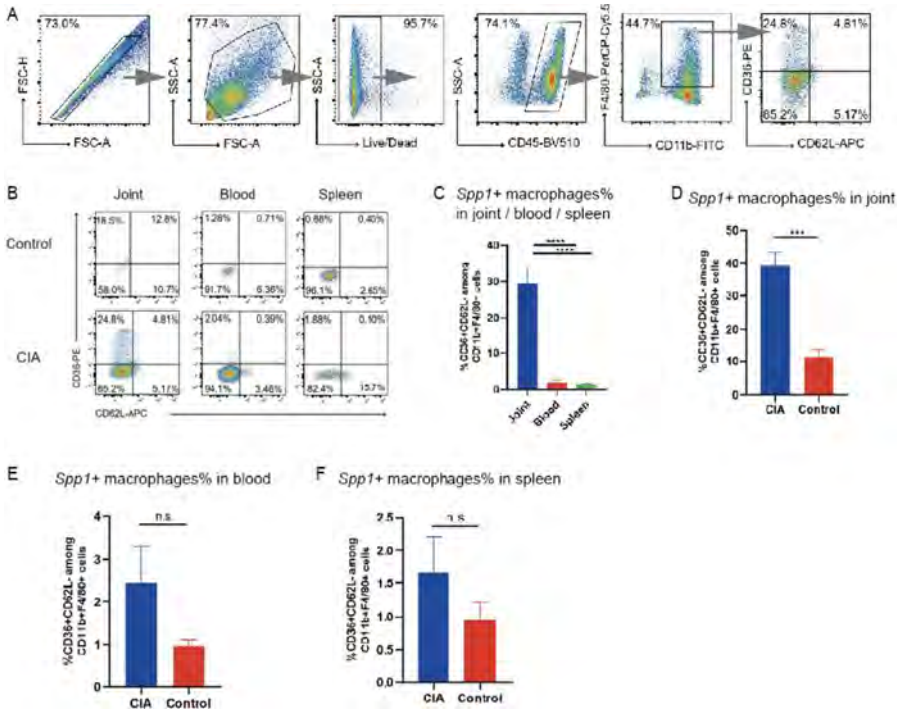


Fig. 2 Flow cytometry analysis of peripheral blood, joints, and spleen in mice. A Gating strategy for identifying Spp1+ macrophages by flow cytometry. B Representative flow cytometry plots of Spp1+ macrophages in joints, peripheral blood, and spleen from collagen-induced arthritis (CIA) (n=9) and control (n=5) mice. C Quantitative analysis of the proportion of Spp1+ macrophages across different tissues. D Quantitative comparison of spp1+ macrophage proportions in joints between CIA and control mice. E Quantitative comparison of Spp1+ macrophage proportions in peripheral blood between CIA and control mice. F Quantitative comparison of Spp1+ macrophage proportions in spleen between CIA and control mice. n.s., not significant ($p > 0.05$); ***$p < 0.001$; ****$p < 0.0001$.

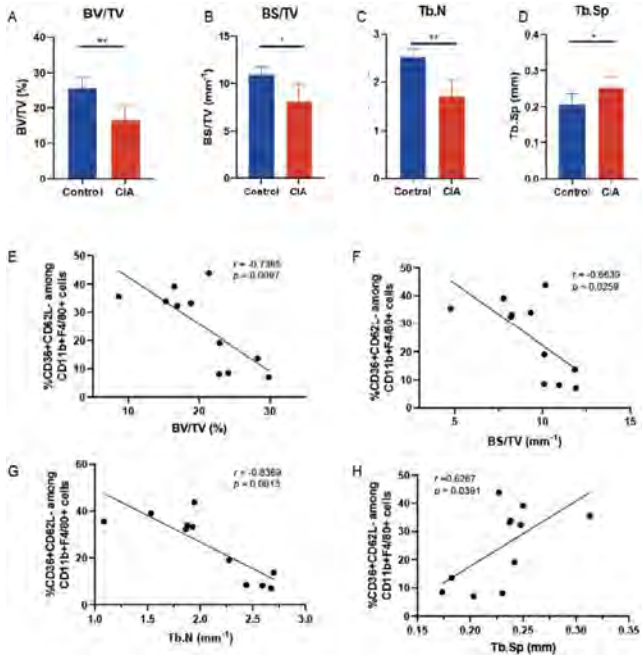


Fig. 3 Correlation analysis between bone metabolic parameters and Spp1+ macrophages. (A) Bone volume to tissue volume ratio (BV/TV), (B) bone surface to tissue volume ratio (BS/TV), (C) trabecular number (Tb.N), and (D) trabecular separation (Tb.Sp) in the proximal tibia of CIA (n=6) and control (n=5) mice. (E-H) Correlation analysis between the proportion of Spp1+ macrophages in joints and (E) BV/TV, (F) BS/TV, (G) Tb.N, and (H) Tb.Sp. *$p < 0.05$, **$p < 0.01$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study reveals that *Spp1*$^{+}$ macrophages are specific enrichment in CIA mouse joints and their association with abnormal bone metabolism. These findings offer new insights into RA pathogenesis, address clinical sample limitations, and provide experimental evidence for developing therapeutic strategies.

Disclosure: C. He: None; **X. Xia**: None; **H. Xu**: None; **G. Yin**: None; **Q. Xie**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GSK, 5, 6, Novartis, 6.

Abstract Number: 0052

Profiling of MT-3534, a Humanized Monoclonal Antibody Targeting Peptidylarginine Deiminase 4, as a Candidate Drug for the Treatment of RA

Hisae Niki[1], Akitoshi Nishizawa[2], Yuuichi Ono[1], Makoto Yamazaki[1], Satoshi Takanashi[3], Keiko Yoshimoto[4], Mitsuhiro Akiyama[3], Tsutomu Takeuchi[5] and Yuko Kaneko[4], [1]Mitsubishi Tanabe Pharma Corporation, Yokohama, Kanagawa, Japan, [2]Mitsubishi Tanabe Pharma Corporation, Fujisawa, Kanagawa, Japan, [3]Keio University School of Medicine, Tokyo, Japan, [4]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan, [5]Saitama Medical University and Keio University, Tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Although the management of rheumatoid arthritis (RA) has been remarkably improved, there are still patients who have not responded to existing targeted drugs that mainly suppresses inflammatory cytokines. We hypothesize that the pathophysiology mediated by activated neutrophils is responsible for non-response to existing drugs, and inhibiting peptidyl arginine deiminase type 4 (PAD4), which are released by activated neutrophils and plays a key role in the development and progression of RA, could be a new therapy for difficult-to-treat RA. Based on this concept, we have developed MT-3534, a humanized monoclonal antibody that binds to human, mouse, and cynomolgus monkey PAD4, but not to other human PAD family proteins. Non-clinical safety studies in animals have shown no notable adverse events, and a Phase 1 clinical trial is currently ongoing. The objectives of this study were to provide evidence that PAD4-related pathophysiology is the cause of non-response to existing bDMARDs and to profile the anti-arthritic effects of MT-3534 in mouse arthritis models.

Methods: Human plasma PAD4 levels were measured in samples obtained from 29 RA patients treated with TNF inhibitors, IL-6 receptor inhibitors, or abatacept, and 25 healthy controls. Patients were categorized as responders (R) or inadequate responders (IR) to bDMARDs based on their treatment history and disease activity, and plasma PAD4 levels were compared between them. Next, MT-3534 was administered to collagen antibody-induced arthritis (CAIA) and collagen-induced arthritis (CIA) models in mice. Arthritis progression was monitored by scoring the swelling of digits and paws. Various biomarkers in mouse sera and joint homogenates were measured using ELISA. PAD4 in mouse joints was detected using standard immunostaining techniques.

Results: Pre-treatment plasma PAD4 levels in bDMARD-IR patients were higher than that in healthy controls and bDMARD-R patients. After bDMARD treatment, the decrease in plasma PAD4 levels were less in bDMARD-IR patients compared with bDMARD-R patients. In CAIA models, while prophylactic etanercept administration prevented arthritis development but therapeutic etanercept administration did not improve arthritis after arthritis development, MT-3534 suppressed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

arthritis development and improved developed arthritis equally with prophylactic and therapeutic usage, respectively. Time-course immunostaining of PAD4 in the joints of CIA model mice revealed that MT-3534 worked after neutrophil infiltrated and PAD4 expression increased with arthritis onset. MT-3534 significantly suppressed related biomarkers in the CIA model. Furthermore, it was confirmed that the administration of MT-3534 to mice in which arthritis progressed despite etanercept treatment inhibited the progression of arthritis compared to mice that continued etanercept treatment alone.

Conclusion: MT-3534 inhibited arthritis in mice through a mechanism distinct. The unique mechanism of action of MT-3534 has the potential to fill an unmet medical need in the treatment of RA.

Acknowledgements

MT-3534 was produced in collaboration with Pharma Foods International Co., Ltd.

Disclosure: H. Niki: Mitsubishi Tanabe Pharma, 3; **A. Nishizawa**: Mitsubishi Tanabe Pharma, 3; **Y. Ono**: Mitsubishi Tanabe Pharma, 3; **M. Yamazaki**: Mitsubishi Tanabe Pharma, 3; **S. Takanashi**: AbbVie, 6, Asahi Kasei, 6, Astellas Pharma, 6, Ayumi Pharmaceutical, 6, Bristol-Myers Squibb, 6, Eisai, 6, Eli Lilly, 6, Janssen, 6, Mitsubishi Tanabe Pharma, 6, Pfizer, 6, Sanofi, 6, Taisho Pharmaceutical, 6, UCB, 6; **K. Yoshimoto**: None; **M. Akiyama**: AbbVie, 6, Asahi Kas, 6, Astellas Pharma, 6, Boehringer-Ingelheim, 6, Chugai Pharmaceutical, 6, Eisai, 6, Eli Lilly, 6, Gilead Sciences, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Taisho Pharmaceutical, 6, UCB, 6; **T. Takeuchi**: AbbVie, 2, 6, Astellas Pharma, 6, AstraZeneca, 6, Chugai Pharmaceutical, 6, Eisai, 6, Eli Lilly, 2, 6, Gilead Sciences, 2, 6, Janssen, 6, Mitsubishi Tanabe Pharma, 2, 6, Pfizer, 6, Taisho Pharmaceutical, 2, 6; **Y. Kaneko**: AbbVie, 2, 5, 6, Asahi Kasei, 2, 5, 6, Astellas Pharma, 6, AstraZeneca, 6, Ayumi, 5, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 2, 6, Chugai Pharmaceutical, 5, 6, Daiichi Sankyo, 6, Eisai, 5, 6, Eli Lilly, 2, 6, Gilead Sciences, 2, 5, 6, Glaxo SmithKline, 6, Janssen, 6, Mitsubishi Tanabe Pharma, 5, 6, Novartis, 6, Pfizer, 2, 6, Sanofi, 6, Taisho Pharmaceutical, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0053

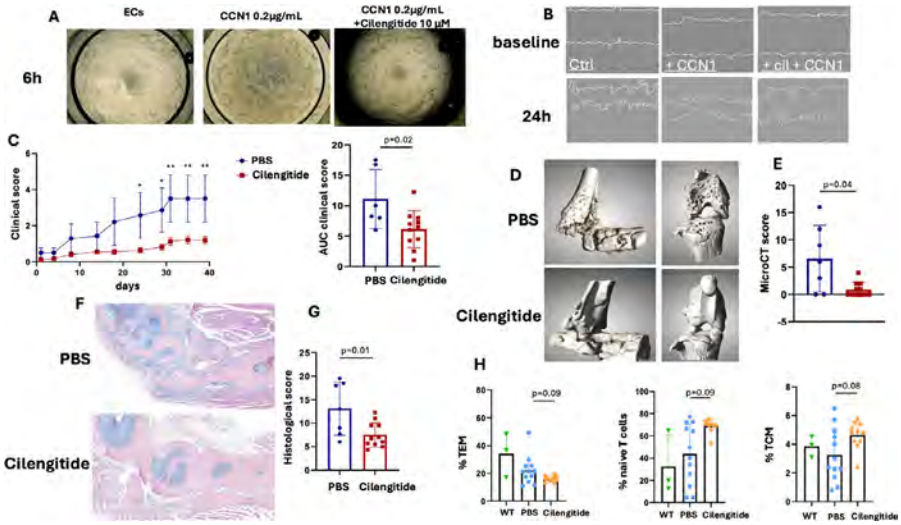
The Integrin Inhibitor Cilengitide Targets CCN1-Mediated Angiogenesis and Reduces Disease Severity in a Preclinical Rheumatoid Arthritis Model

Jérôme Avouac[1], manon lesturgie[2], Virginie Gonzalez[3], Sujeeba Arulananthan[2], Anne Cauvet[3], Francoise Tilotta[4] and Yannick Allanore[5], [1]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France, [2]INSERM U1016, Paris, France, [3]INSERMU1016, Paris, France, [4]Université Paris Cité, Montrouge, France, [5]Université Paris Cité, Paris, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: CCN1, a matricellular protein with angiogenic and immunomodulatory properties, is overexpressed in endothelial and synovial tissues of rheumatoid arthritis (RA) patients. Previous findings demonstrated that CCN1 inhibition reduces synovial angiogenesis and structural damages in preclinical arthritis models. However, it remains unclear whether these therapeutic effects of CCN1 inhibition are mediated through a reduction in angiogenesis. This study investigates the ability of Cilengitide, a cyclic pentapeptide integrin inhibitor, to block CCN1-mediated effects on endothelial cells (ECs) and evaluates its potential therapeutic impact in the TNF-dependent Tg197 arthritis model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A, Representative images of tube formation at 6 hours in RA endothelial cells (ECs) alone, or following treatment with recombinant CCN1 (0.2 g/mL) with or without Cilengitide (10 M) (4x magnification). B, Representative images of EC migration at baseline and 24 hours in RA ECs alone, or following treatment with recombinant CCN1 (0.2 g/mL) with or without Cilengitide (10 M). C, Experimental arthritis in Tg197 mice receiving IP injections of Cilengitide (10 mg/kg) or PBS (100 L) 3 times weekly. Y-axis shows clinical score and the area under the curve (AUC) of the clinical score (PBS: n=7 mice, Cilengitide, n=11 mice). D, Representative 3D reconstructions of ankles, tarsus and knees of Tg197 mice treated with Cilengitide or PBS. E, Y-axis shows the mean erosion score (from 0 to 16). F, Sections of ankle and tarsus joints from Tg197 mice receiving Cilengitide or PBS stained with hematoxylin (scale bar = 200m). G, Histomorphometric analysis of the area of synovitis and bone destruction. H, Flow cytometry analysis of T cell subsets (effector memory T cells, TEM, naive T cells and central memory T cells, TCM) from the spleen of wild type (WT) mice (n=3) and Tg197 mice treated with Cilengitide or PBS. All data are shown as the means ± SD. Statistical tests: Student's t test for 2-group comparisons, ANOVA with Dunnett's multiple comparisons test for 3-group comparisons. Data are representative of a single experiment.

Methods: The effects of CCN1 inhibition on angiogenesis through Cilengitide were assessed *in vitro* using ECs derived from circulating progenitors. Cells were cultured with CCN1 (0.2 µg/ml), either alone or with Cilengitide (10 µM). We analyzed capillary-like tube formation on Matrigel and EC migration using scratch assay.

For in vivo studies, TNF-transgenic mice (Tg197) received intraperitoneal injections of either Cilengitide (10 mg/kg) or PBS three times weekly. Clinical arthritis scores were monitored bi-weekly, and after six weeks, paws were analyzed using micro-CT and histology. Immune profiling from the spleen of TG197 mice was performed via flow cytometry.

Results: *In vitro*, CCN1 induced capillary-like tube formation and EC migration / invasion, which were significantly inhibited by Cilengitide at a dose of 10µM. (**Figure 1A-B**), strongly supporting that CCN1 effects on ECs are mediated through integrins αvβ3 and αvβ5, which are critical for angiogenesis.

In vivo, Cilengitide significantly improved clinical arthritis scores (**Figure 1C**). The AUC of the clinical score of Cilengitide-injected mice decreased significantly by 55±6% (p=0.020). Micro-CT analysis demonstrated better-preserved joint integrity in Cilengitide-treated mice, with markedly fewer bone erosions compared to controls (**Figure 1D-E**). Histological analysis of hind paw sections confirmed previous results, with significantly less inflammation and structural damage in Cilengitide-treated mice (**Figure 1F-G**).

Flow cytometry showed decreased activation of CD4+ T cells in treated mice, with reduced PD-1 expression, indicating lower exhaustion levels following Cilengitide treatment. CD4+ T cells exhibited a shift in memory subsets, with fewer effector memory T cells and an increase in central memory and naïve T cells (**Figure 1H**).

Conclusion: Cilengitide effectively inhibits CCN1-induced angiogenesis *in vitro*, confirming that CCN1 exerts its effects on endothelial cells through integrins αvβ3 and αvβ5. *In vivo*, Cilengitide significantly reduces clinical, structural, and histological damage in the Tg197 arthritis model while modulating immune profiles. These findings suggest that CCN1's effects in RA,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

including structural and inflammatory damage, are mediated by its role in promoting pathological angiogenesis. Targeting CCN1 and associated pathways offers a promising therapeutic strategy for RA, complementing current treatments.

Disclosure: J. Avouac: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6; **m. Iesturgie**: None; **V. Gonzalez**: None; **S. Arulananthan**: None; **A. Cauvet**: None; **F. Tilotta**: None; **Y. Allanore**: None.

Abstract Number: 0054

Microbial Cues Promote Arthritis and Alter T Cell Selection in SKG Mice

Astha Patel[1], Steven yu[1], Yuka Nakao[1], Mohana Mukherjee[1], Diego Orellana[2], Jose Scher[3], Peter Turnbaugh[1], Renuka Nayak[4] and **Judith Ashouri**[1], [1]University of California, San Francisco, San Francisco, CA, [2]University of California San Francisco, San Francisco, CA, [3]New York University School of Medicine, New York, NY, [4]University of California, San Francisco (UCSF), San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Dysbiosis of the gut microbiota has been linked to rheumatoid arthritis (RA), but it remains unclear whether these microbial alterations are causal or secondary to inflammation, as most patients present after disease onset. The SKG mouse, which develops $CD4^+$ T cell–driven autoimmune arthritis resembling RA including erosive joint disease, rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs), and pneumonitis, providing a tractable model to dissect these relationships. Under germ-free (GF) conditions, SKG mice fail to develop arthritis, underscoring the requirement for microbial cues in disease initiation. This model enables dissection of microbiota-dependent versus genetically encoded immune mechanisms, including the largely unexplored gut–thymus axis. We investigated how commensal microbes influence thymic selection, peripheral T cell activation, and tolerance to endogenous antigens.

Methods: GF SKG mice (n=8) and conventionalized GF SKG mice (n=9) received intraperitoneal zymosan injections, and arthritis scores were monitored over time. Clinical scores were assessed blindly, and cumulative disease burden was calculated as area under the curve (AUC); group differences were analyzed using the Wilcoxon test. Immune cell populations in thymocytes, peripheral lymphoid organs and Peyer's patches were analyzed by flow cytometry using FlowJo software,

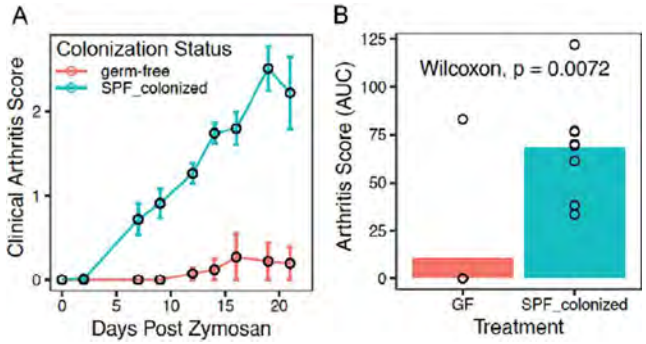


Figure 1. Microbiota are required for arthritis development in SKG mice. Germ-free (GF) SKG mice (n=8) and conventionalized GF SKG mice (n=9) were injected intraperitoneally with zymosan and monitored over time for clinical arthritis scores in a blinded fashion. (A) Blinded longitudinal arthritis scores are shown for each group. (B) Cumulative disease burden, measured by area under the curve (AUC) of arthritis scores, was significantly higher in conventionalized mice (Wilcoxon test, p = 0.0072).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and group comparisons were made using Student's *t* test. Thymocyte subsets and T cell signaling in thymocytes and peripheral $CD4^+$ T cells were assessed using calcium flux and phospho-flow cytometry.

Results: Only 1 GF SKG mouse developed arthritis, compared to all 9 conventionalized GF SKG mice, which showed significantly higher disease activity (Fig. 1). Conventionalized mice exhibited a significant expansion of T follicular helper (Tfh) cells and a significant reduction in regulatory T cells in Peyer's patches (both $p < 0.001$). In zymosan-free conditions, GF SKG mice showed reduced frequencies of mature $CD4^+$ single-positive (SP4) thymocytes despite normal levels of $CD4^+CD8^+$ double-positive cells, indicating intact positive selection but enhanced negative selection. Thymocytes from GF SKG mice expressed higher CD5, consistent with increased tonic TCR signaling. Accordingly, SKG SP4 thymocytes and peripheral $CD4^+$ T cells from GF mice exhibited more robust signaling responses upon stimulation than their SPF counterparts.

Conclusion: Microbial cues are essential for permissive arthritis in SKG mice and shape both thymic selection and peripheral T cell activation. The enhanced signaling responses in GF-derived T cells, despite reduced basal signaling markers, suggest an unrecognized role for the gut–thymus axis in setting thresholds for T cell reactivity. This model offers a unique opportunity to define how commensals calibrate T cell selection and autoimmune potential.

Disclosure: A. Patel: None; **S. yu**: None; **Y. Nakao**: None; **M. Mukherjee**: None; **D. Orellana**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **P. Turnbaugh**: None; **R. Nayak**: None; **J. Ashouri**: None.

Abstract Number: 0055

TCR Signaling Thresholds Govern Anergy and Tolerance in ZAP70 Hypomorphic Models of Autoimmune Arthritis

Yuka Nakao, Astha Patel, Letitia Yang, Steven yu, Arthur Weiss and **Judith Ashouri**, University of California, San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: T cell receptor (TCR) signaling strength is a key determinant of immune tolerance and autoimmunity, yet the threshold needed to prevent pathogenic self-reactivity remains poorly defined. ZAP70 is a critical kinase in the TCR signaling cascade, and the SKG and YYAA mice carry distinct hypomorphic ZAP70 mutations—resulting in different degrees of impaired TCR signaling, more severe in SKG. Both strains generate rheumatoid factor (RF) autoantibodies, but only SKG mice develop $CD4^+$ T cell mediated erosive arthritis. This divergence allows us to define how TCR signaling thresholds shape $CD4^+$ T cell fate and identify the minimum signaling needed to maintain tolerance and prevent arthritis.

Methods: SKG and YYAA mice were crossed to Nur77-eGFP reporter mice to quantify TCR signal strength during thymic development and in the periphery. We analyzed expression of Nur77-eGFP, inhibitory receptors, and TCR Vβ repertoire by flow cytometry in thymocyte subsets and peripheral $CD4^+$ T cells. Frequencies of anergic $CD4^+$ T cells ($CD73^+FR4^+$) were compared across genotypes. Functional signaling was assessed via calcium flux and phospho-flow (pERK, pS6) after stimulation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

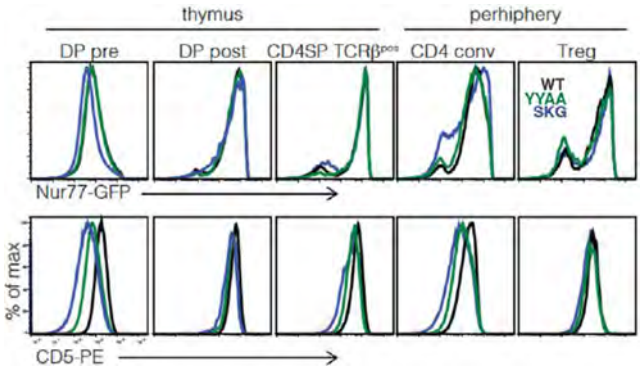


Figure 4. Nur77-eGFP and CD5 expression reveal genotype-dependent differences in TCR signaling across thymic and peripheral CD4$^+$ T cell subsets. Nur77-eGFP serves as a cumulative readout of integrated TCR signaling, while CD5 reflects proximal TCR signal strength. Histograms show expression of Nur77-eGFP (top) and CD5 (bottom) in pre-selection (DP pre; CD69loTCRβlo) and post-selection (DP post; CD69hiTCRβhi) double-positive thymocytes, CD4 single-positive thymocytes (CD4+TCRβpos), peripheral conventional CD4$^+$CD25$^-$ T cells (CD4 conv), and CD4$^+$CD25$^+$ regulatory T cells (Treg) from WTNur (black), YYAANur (green), and SKGNur (blue) mice. Data are representative of ≥ 2 independent experiments with 3 mice per genotype.

Results: Nur77-eGFP expression track with TCR signal strength and reveal genotype-dependent differences in self-reactivity (Fig. 1). In GFPlo thymocytes and peripheral naïve CD4$^+$ T cells, mean fluorescence intensity (MFI) scaled with ZAP70 function: WT > YYAA > SKG. In contrast, GFPhi CD4$^+$ T cells were more abundant in SKG, likely reflecting a more self-reactive repertoire (Fig. 2). Consistent with prior self-antigen encounter, GFPhi CD4 single-positive thymocytes and peripheral CD4$^+$ T cells in SKG and YYAA mice showed dampened signaling upon restimulation, including reduced calcium flux and pERK/S6. Repertoire analysis further supported increased self-reactivity in SKG: TCR Vβ chains recognizing endogenous retroviral superantigens—typically deleted in WT mice—escape deletion in SKG and, to a lesser extent, YYAA. This suggests impaired TCR signaling compromises central tolerance and permits expansion of autoreactive clones. YYAA retain similar or higher frequencies of CD73$^+$FR4$^+$ anergic CD4$^+$ T cells than SKG. Although GFPhi CD4$^+$ T cells from all genotypes upregulate inhibitory receptors (CD5, PD-1, LAG3, TIM-3, FR4), SKG show reduced expression of CD5, PD-1, and FR4 following peripheral self-antigen encounter. In contrast, YYAA more effectively induced these pathways.

Conclusion: TCR signaling strength controls the balance between deletion, anergy, and activation in developing and peripheral CD4$^+$ T cells. Hypomorphic ZAP70 mutations impair thymic selection—altering the TCR repertoire—and

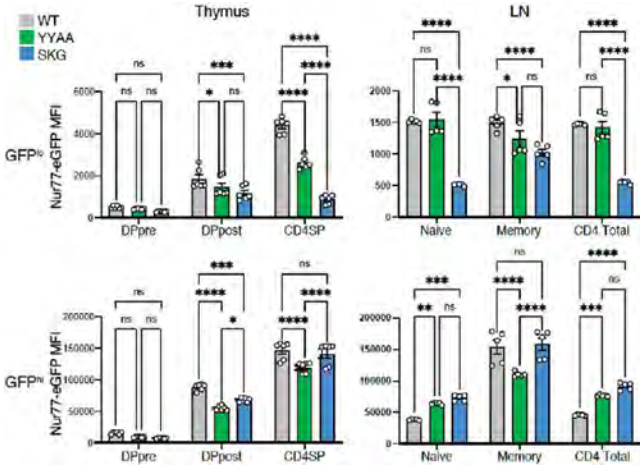


Figure 2. Nur77-eGFP expression in SKG peripheral T cells reflects their increased self-reactivity. Mean fluorescence intensity (MFI) of Nur77-eGFP was quantified in GFPlo (top panels) and GFPhi (bottom panels) thymocyte subsets (left panels; n = 6/genotype) and peripheral CD4$^+$CD25$^-$ T cells from lymph nodes (right panels; n = 5/genotype) in WTNur (gray), YYAANur (green), and SKGNur (blue) mice. GFPlo cells reflect basal/tonic TCR signaling, while GFPhi cells represent cells with higher self-reactivity. In the thymus, GFPlo MFI scales with ZAP70 function (WT > YYAA > SKG), whereas in the periphery, SKG mice exhibit increased GFPhi cells. Statistical significance determined by two-way ANOVA with multiple comparisons. ns: P > 0.05; *P < 0.05; **P < 0.01; ***P < 0.001; ****P < 0.0001. Data pooled from two independent experiments.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

peripheral tolerance. Our findings suggest anergy may serve as an additional central tolerance mechanism when deletion is inefficient. In SKG, defective peripheral tolerance permits self-reactive $CD4^+$ T cell activation and arthritis. In contrast, less impaired anergy and tolerance pathways in YYAA may restrain autoreactive T cells and prevent disease despite RF autoantibody production. These findings highlight a TCR signaling threshold that governs tolerance enforcement and autoimmune risk.

Disclosure: Y. Nakao: None; **A. Patel**: None; **L. Yang**: None; **S. yu**: None; **A. Weiss**: Nurix Therapeutics, 12, 1, 12, Co-founder; **J. Ashouri**: None.

Abstract Number: 0056

Repository Corticotropin Injection Reduces Inflammation and Bone Turnover Markers in the Murine CIA Model

Maripat Corr[1], Grace Hsueh[2], Aaron place[2], David Lucas[2] and NANCY LANE[3], [1]ucsd, San Diego, CA, [2]ANI Pharmaceuticals, Inc., Baudette, MN, [3]University of California at Davis, School of Medicine, Sacramento, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Melanocortin receptor agonists, such as adrenocorticotropic hormone (ACTH), are anti-inflammatory with pleotropic functions. We aimed to evaluate the effects of a repository corticotropin injection (RCI; ANI Pharmaceuticals, Inc.), a complex mixture of ACTH, ACTH related peptides and other porcine pituitary derived peptides, on the inflammatory response and bone damage in the mouse CIA model.

Methods: CIA was induced in six-week-old male DBA/1J mice by subcutaneous injection with CFA emulsified with chicken type II collagen, and IFA and collagen on day 21. Mice (n = 15-16 per group) received subcutaneous RCI (ANI Pharmaceuticals, Inc.; 40, or 400 U/kg twice daily), or vehicle days 21-35 (Figure 1A). Changes in hind paw thickness was measured with a caliper, and joints scored (28-point scale). Hind limbs (day 35) were imaged with a micro-computed tomography (CT) scanner, at 9 μm voxel size by standardized methods. Cortical bone analyses were performed on the femoral and tibial diaphysis. Each femur was analyzed at a region of interest 4500 μm proximal to the distal femur growth plate and extended 900 μm proximally. Each tibia was analyzed at a region of interest 4500 μm distal to the proximal tibial growth plate and extended 900 μm distally. CXCL-1 (KC), IL-6, P1NP, CTX-1, and anti-mouse CII antibody levels in sera were determined by ELISA. Statistical analyses were performed by ANOVA followed by post hoc tests.

Results: RCI administration resulted in dose-dependent decreases in ankle swelling in the 40 and 400 U/kg treatment groups compared to vehicle treated [AUC 2.90±39, 1.00±0.19, and 50±0.7, respectively; $F(13, 616)=24$, $P< 0.001$; Figure 1B] and similarly for clinical scores [AUC 47±5.3, 9.4±3.2 and 75±5.9; $F(13,616)=48.59$; $P< 0.0001$; Figure 1C]. There were no differences in the levels of anti-mouse type II collagen antibody generation between the vehicle, 40, or 400 U/kg treatment groups (67680±6637, 68670±8862, 59360±6768 arbitrary units, respectively; P=0.61; Figure 1D). There were lower levels of serum CXCL-1 in the 400 U/kg treatment compared to the vehicle treated group (P=0.016; Figure 1E) and lower levels of IL-6 (P=0.03; Figure 1F). Both serum levels of CTX-1 and PINP were significantly lower in the 400 U/kg treatment compared to the vehicle treated group (P=0.04; Figure 1G and P=0.02; Figure 1H, respectively). MicroCT measures of BV/TV, Tb.Th., and Tb.Sp. were similar between the groups; however, TMD was higher in both the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

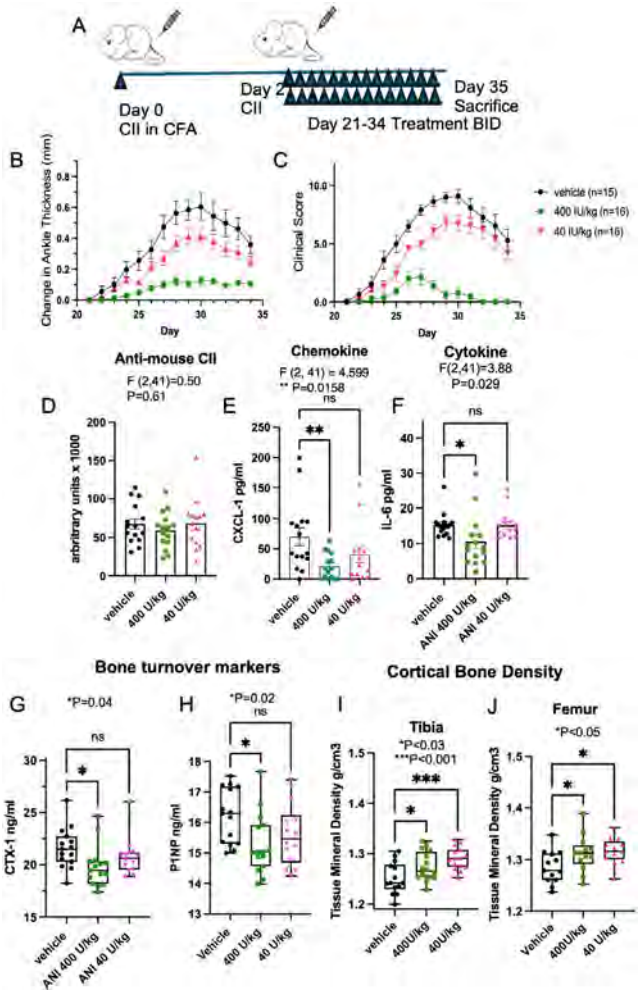


Figure 1. Effects of RCI on CIA. Schematic of experimental protocol (A). DBA/J mice were injected with type II chicken collagen in CFA on day 0 and in IFA on day 21. Starting day 21 mice received RCI or vehicle s.c. injections BID. The ankle widths of the mice were serially measured (B) and the joint inflammation scored (C) demonstrating a reduction in the RCI treated mice compared to vehicle treated. After 14 days of treatment the mice were sacrificed and serum obtained. There were no differences in anti-type II collagen antibody levels (D), but there were reduced serum levels of CXCL-1 (E), IL-6 (F), CTX-1 (G) and P1NP (H) in the 400 U/kg treatment group compared to the vehicle treated mice. Cortical bone density in the tibia (I) and femur (J) of RCI treated mice were greater than the vehicle treated mice.

tibia and femurs in the 40 U/kg and 400 U/kg treatment groups compared to the vehicle treated group ($P < 0.05$; Figure 1I and J).

Conclusion: As monotherapy, RCI significantly reduced CIA-induced joint swelling in male mice. In addition, RCI treatment resulted in a reduction in inflammatory cytokine responses, but no disruption of IgG formation and less bone loss. These findings demonstrate significant reductions in systemic inflammation in the CIA arthritis model with RCI treatment.

Disclosure: M. Corr: ANI Pharmaceuticals, 5; **G. Hsueh**: ANI Pharmaceuticals, 3; **A. place**: ANI, 3; **D. Lucas**: ANI Pharmaceuticals, 3, 11; **N. LANE**: ANI, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0057

TNF Inhibition with Small-molecule Agents Results in Amelioration of Inflammation Similar to that of Anti-TNF Biologics While Preserving TNFR2 Signaling and Maintaining a Suppressive Regulatory T cell Phenotype

Rajesh Singh[1], Bindi Patel[2], Rameshwari Rayaji[2], Archana Sidalaghatta Nagaraja[2], Saranya Chandrasekar[2], Yihong Guan[2], Ritu Kushwaha[2], Yue Tong Lee[2], Cesar Meleza[2], Matthew Epplin[2], Brandon Rosen[2], Manmohan R Leleti[2], Matthew J Walters[2] and Daniel DiRenzo[2], [1]Arcus Biosciences, inc., Santa Clara, CA, [2]Arcus Biosciences, inc., Hayward, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-TNF biologics are effective in the treatment of inflammatory diseases such as rheumatoid arthritis and psoriasis. However, they can lead to *de novo* inflammation occurrences, termed paradoxical adverse events, driven by inappropriate Th1/Th2/Th17 skewing and suboptimal function of regulatory T cells (Treg). Studies have reported that TNF blocking biologics downregulate both pro-inflammatory TNFR1 and anti-inflammatory TNFR2-mediated signaling. A TNF small molecule inhibitor that blocks pro-inflammatory TNFR1 signaling but spares beneficial TNFR2 signaling has been reported previously and may circumvent these shortcomings of biologic drugs. Herein, we describe the effects of TNF small molecule inhibitors on TNF-mediated inflammatory signaling, inhibition of TNFR1 vs TNFR2 signaling, Treg cell activity and control of murine arthritis.

Methods: NF-κB reporter-expressing HEK293 cells were used to measure cellular potency of TNF small molecule inhibitors. Soluble TNF trimer inhibition and IL-8 secretion were assessed in human umbilical vein endothelial (HUVEC) cells using ELISA and MSD assays. HeLa cells expressing a mutant non-cleavable TNF that allows expression of membrane TNF to activate TNFR2 signaling were generated. For measurement of TNFR1 and TNFR2-specific signaling, NF-κB reporter-expressing K562 cells were stimulated with soluble TNF and membrane TNF-expressing cells. Treg stability and function were evaluated using cytokine and phenotypic marker levels by flow cytometry. The collagen antibody-induced arthritis mouse model was used to demonstrate the activity of TNF signaling blockade.

Results: TNF small molecule inhibitors displayed a concentration-dependent reduction in soluble TNF/TNFR1-stimulated NF-κB activation in HEK293 cells and IL-8 production in HUVEC cells, equivalent to blockade using anti-TNF biologics. Using K562 cells pre-incubated with TNFR1-blocking antibody and co-cultured with membrane TNF-expressing cells, TNFR2-dependent NF-κB activation was retained with small molecule inhibitors but abolished using anti-TNF biologics. TNFR2 signaling has been established to promote Treg functionality *in vitro*. The proliferation of stable FoxP3^{high}Helios^{+} Tregs, and expression of suppressive cytokines IL-10 and TGF-β was retained using TNF small molecule inhibitors but impaired using an anti-TNF biologic. In a murine collagen antibody-induced arthritis model, TNF small-molecule inhibition showed equivalent disease suppression to an anti-TNF biologic but, interestingly, anti-TNF treatment led to enhanced circulating IL-17 levels in the biologic-treated group but not with small-molecule inhibition.

Conclusion: Taken together, these data demonstrate that TNF small-molecule inhibition is effective at inhibiting pro-inflammatory signaling and providing control of murine arthritis like anti-TNF biologics. We also show that TNF small-molecule inhibition has the potential to promote Treg stability and potentially circumvent paradoxical adverse events observed following anti-TNF biologic therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Singh: Arcus Biosciences, inc., 3; **B. Patel**: Arcus Biosciences, inc., 3; **R. Rayaji**: Arcus Biosciences, inc., 3; **A. Sidalaghatta Nagaraja**: Arcus Biosciences, inc., 3; **S. Chandrasekar**: Arcus Biosciences, inc., 3; **Y. Guan**: Arcus Biosciences, inc., 3; **R. Kushwaha**: Arcus Biosciences, inc., 3; **Y. Tong Lee**: Arcus Biosciences, inc., 3; **C. Meleza**: Arcus Biosciences, inc., 3; **M. Epplin**: Arcus Biosciences, inc., 3; **B. Rosen**: Arcus Biosciences, inc., 3; **M. Leleti**: Arcus Biosciences, inc., 3; **M. Walters**: Arcus Biosciences, inc., 3; **D. DiRenzo**: Arcus Biosciences, inc., 3.

Abstract Number: 0058

Training for increased inflammatory arthritis in mice is not modulated by type 1 interferon

Richard Bell[1], Mary Huang[1], Claire Weigert[2], Ruoxi Yuan[2], Toolika Singh[2], Seda Seren[2] and Lionel Ivashkiv[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, New York

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Disease flares, or episodic escalating inflammation, is a hallmark of autoimmune diseases, like Rheumatoid Arthritis (RA). They are particularly hard to predict and treat and often signify an overall worsening of disease. The biologic mechanism underpinning disease flares is not well understood, potentially due to limitations of mouse models. Type 1 interferon (IFN) is thought to be a pathogenic cytokine in autoimmune diseases by pre-conditioning cells for hyper-reactive responses during episodic inflammatory challenges. However, type 1 IFN has not been investigated in an in vivo episodic inflammatory arthritis model. Therefore, we tested the hypothesis that loss of type 1 IFN will reduce the flaring inflammation in an episodic zymosan induced arthritis (ZIA) challenge.

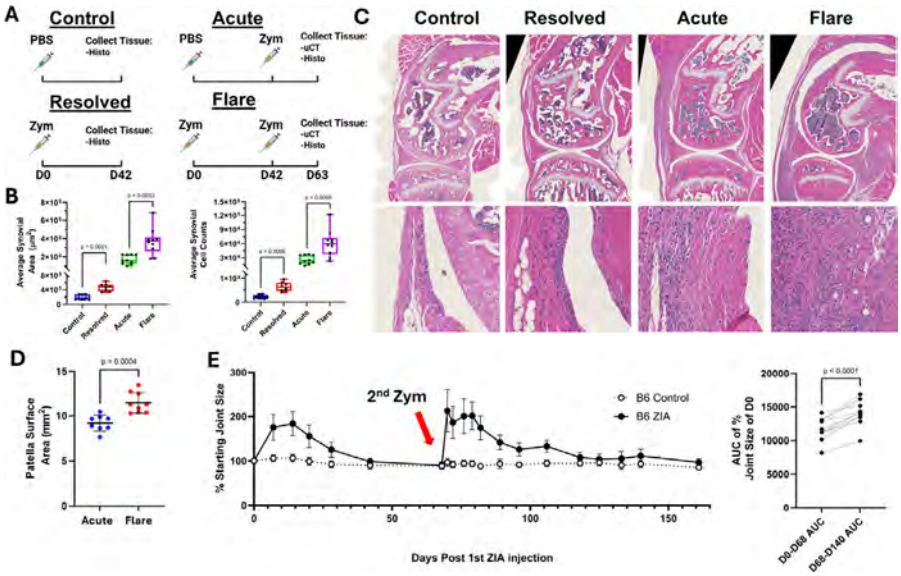


Figure 1. Episodic zymosan induces a joint flare. A) The study design. B) Average synovial area and cell counts via automated histomorphometry, each point is one knee average across 3 anatomic levels in the medial compartment, One-Way ANOVA with Tukey's Post-hoc. C) Representative images of Control, Resolved, Acute and Flare knees. D) uCT analysis of patella bone surface area, t-test. E) Joint widths percent of starting size over time with the 2nd Zym injection at D68 and AUC calculated from D0-D68 vs D68-D140 (right panel, paired t-test). Un-injected contralateral joints used as controls.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

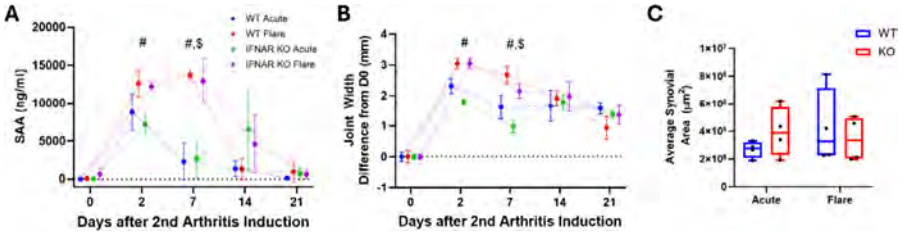


Figure 2. IFNAR1 KO does not modify the flare. A) Serum amyloid A concentration after 2nd ZIA induction at D42. B) Joint widths difference compared to D0 after 2nd ZIA induction at D42. # indicates p<0.05 IFNAR KO Acute vs IFNAR KO Flare; $ indicates p<0.05 WT KO Acute vs WT KO Flare in A and B, repeated one-way ANOVA with Tukey's post-hoc. C) Average synovial area in acute and flaring inflammation between WT and Ifnar1-/-. each point is one knee average across 3 anatomic levels in the medial compartment.

Methods: We performed intra-articular knee injections of 180 μg of zymosan (Zym) or PBS into female C57BL6 and IFN receptor 1 knock out (*Ifnar1-/-*) mice (n=4-10 per group). The same knees were then injected either 42 days or 68 days later with 180 μg of Zym (Fig1 A). Serial cheek bleeds for serum amyloid A (SAA) ELISA and joint widths were collected. After 21 days the mice were euthanized for joint μCT and histology. Patella surface was quantified and automated histomorphometry was performed to measure synovial area and cell counts within the synovium. ANOVA with Tukey's post-hoc, t-test or paired t-test were used to assess differences

Results: In clinically resolved joints, residual elements of synovial pathology were still modestly increased compared to PBS injected controls with some infiltrates and thickening of the synovial lining (Fig. 1B). Strikingly, flaring joints demonstrated a large increase (~2x) in synovial area and cell counts compared to acute inflammation controls demonstrating escalating inflammation after episodic zymosan challenges (Fig 1B-C). Patella surface area is also increased in flared joints suggesting increased bone metabolism (Fig 1D). When Zym was instead re-injected at D68, the trained phenotype persisted as demonstrated by the increased AUC of joint widths (Fig1 E). However, when *Ifnar1* null mice are re-injected at D42 there was no difference in SAA, joint widths or D21 synovial area compared to WT controls (Fig 2A-C).

Conclusion: Our results establish ZIA as a useful model for investigation of training and arthritis disease flare, and demonstrate that type 1 IFN does not play a role in changing joint inflammatory response to episodic zymosan challenges. This is in contrast with the known role of type 1 IFN in controlling many aspects of inflammation in acute and distinct episodic contexts. Further work to dissect mechanisms of training and the temporal and cell specific IFN responses to episodic inflammation is on-going.

Disclosure: R. Bell: None; **M. Huang**: None; **C. Weigert**: None; **R. Yuan**: None; **T. Singh**: None; **S. Seren**: None; **L. Ivashkiv**: None.

Abstract Number: 0059

Formyl Peptide Receptor 1 (FPR1) Influences Arthritis Severity in a Sex- and Compartment-Specific Manner

Ryan D. Stultz[1], Payton Hermanson[2], Noelle Mullin[3], Simeon Ramsey[3] and Christian Lood[2], [1]University of Washington, Division of Rheumatology, Seattle, WA, [2]University of Washington, Seattle, WA, [3]Pfizer Inc., Cambridge, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disease that disproportionately affects females over males (3:1). Although sex-based immune differences have been documented, particularly in neutrophil effector functions, the molecular drivers of sex bias in RA remain unclear. Our lab previously implicated N-formylated peptides, danger-associated molecular patterns from bacteria and mitochondria, in RA pathogenesis via activation of formyl peptide receptor 1 (FPR1) on neutrophils. While the related receptor FPR2 regulates sex differences in steatohepatitis, whether FPR1 mediates sex-specific immune responses in arthritis is unknown.

Methods: Male and female C57/BL6 *fpr1*+/+ (WT) and *fpr1*-/- mice were intraperitoneally injected with K/BxN sera at days 0 and 2 for induction of inflammatory arthritis. Joint scores tracking arthritis were recorded by a blinded observer over 7 days. Joints and spleens were harvested for flow cytometry and cytokine expression, respectively. To assess the contribution of hematopoietic versus non-hematopoietic FPR1, bone marrow chimeras were generated by transplanting *fpr1*-/- marrow into irradiated WT male and female recipients, followed by arthritis induction and scoring over 8 days.

Results: FPR1 knockout and wild-type arthritic mice both showed elevated levels of N-formyl methionine in circulation (Figure 1A). Overall arthritis severity was similar between genotypes (Figure 1B). However, when stratified by sex, male *fpr1*-/- mice had worse arthritis than wild-type, while female *fpr1*-/- mice had improved disease (Figure 1C, 1D). There were no significant differences between male and female wild-type mice (Figure 1E). Flow cytometric analysis revealed increased immune cell infiltration in joints of male *fpr1*-/- mice, whereas no major differences were observed in females (Figure 2A-E) and qPCR showed increased TNFa in male KO mice (Figure 2F). To determine whether FPR1 in hematopoietic cells mediated these effects, we performed bone marrow chimera experiments. Female WT mice receiving *fpr1*-/- marrow showed no change in arthritis severity compared to controls (Figure 3A). In contrast, male WT mice receiving *fpr1*-/- marrow developed less severe arthritis than non-chimeric WT males (Figure 3B), suggesting that somatic (non-hematopoietic) FPR1 expression may drive joint inflammation in males.

Conclusion: FPR1 contributes to inflammatory arthritis in a sex- and compartment-specific manner. In females, FPR1 appears to promote inflammation, as its deletion is protective. In males, however, FPR1 deficiency paradoxically worsens arthritis—yet transfer of fpr1-/- bone marrow into WT male hosts reduces disease. These findings suggest that in males, FPR1 expression in non-hematopoietic tissues (e.g., joint stromal or endothelial cells) may exacerbate arthritis, whereas hematopoietic FPR1 may exert a protective effect. Together, our data support a model in which FPR1 plays dual, sex-dependent roles in arthritis pathogenesis, highlighting its potential relevance to understanding sex bias in RA and identifying tissue-specific therapeutic targets.

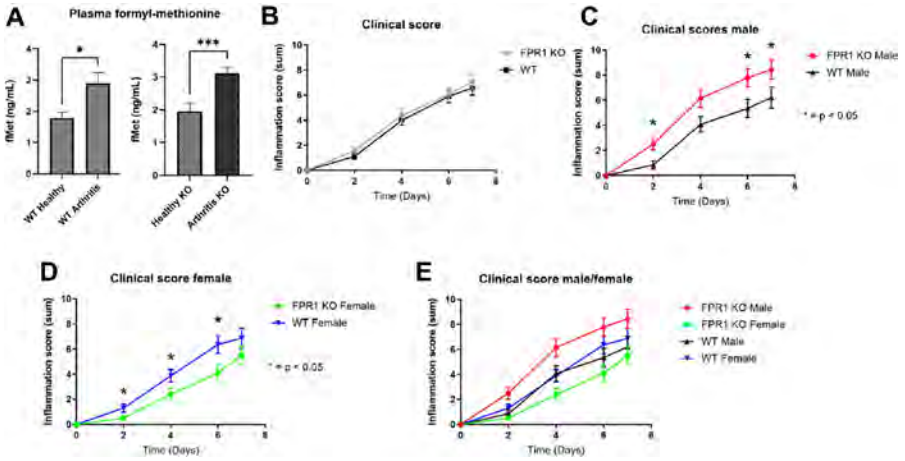


Figure 1. FPR1 worsens arthritis in males while improving arthritis in female mice. Eight to twelve-week-old mice were injected with serum from K/BxN mice on days 0 and 2. Plasma from C57BL/6 wild-type and fpr1-/- (KO) mice at day 0 (WT healthy, Healthy KO) and arthritic wild-type and KO mice at day 7 (WT arthritis, arthritis KO) was analyzed for formylated methionine (fMet) levels by ELISA (A). Mice were followed for 7 days and calculation of paw score (calculated by sum of all 4 paws on scale of arthritis 0-3) was recorded each day by blinded observer. Paw scores were evaluated by segregation by FPR1 genotype (B), genotype and male sex (C), genotype and female sex (D), and all sexes and genotypes (E). n = 10 - 15 mice for each group. * = $p < 0.05$ based on Mann-Whitney t-test.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

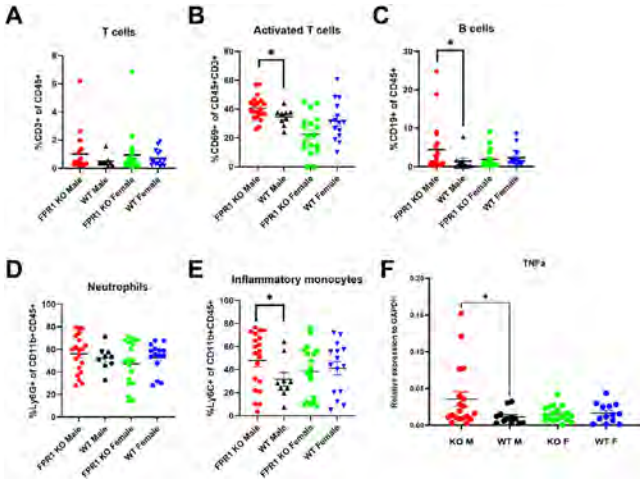


Figure 2. Immune cell infiltration and systemic inflammation are increased in a sex-specific manner mediated by FPR1. On day 7 after induction of serum transfer arthritis in male (M) and female (F) fpr1-/- (KO) and C57BL/6 (WT) mice, mice were sacrificed and one ankle joint was harvested and digested into single cell suspension for flow cytometry. Cells were first selected for CD45 positivity and then stained for markers of T cells (A), activated T cells (B), B cells (C), neutrophils (D), and inflammatory monocytes (E). After sacrifice on day 7, spleens were harvested from all mice for RNA extraction. Quantitative, reverse transcription real-time PCR for TNF-alpha was compared between KO and WT male and female animals (F). * = $p < 0.05$ based on Mann-Whitney t-test.

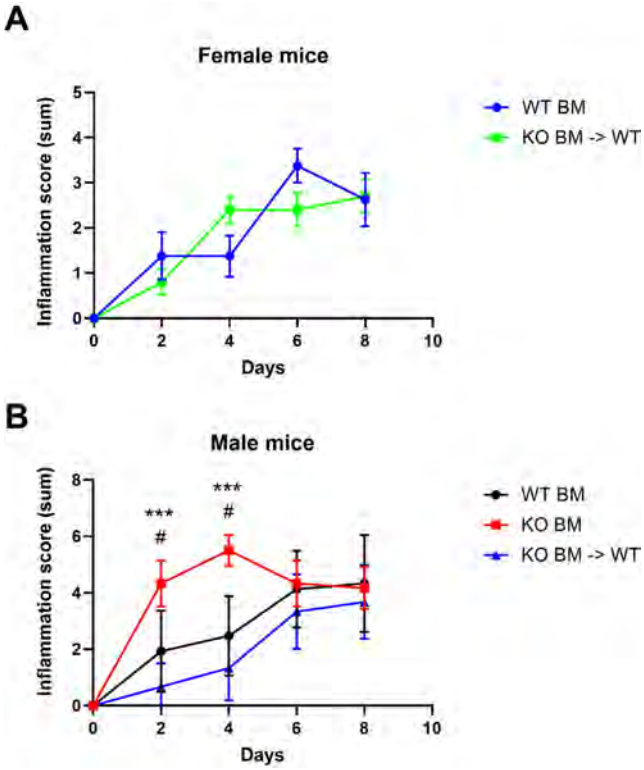


Figure 3. FPR1-deficient bone marrow protects against arthritis in male but not female mice. Arthritis was induced with K/BxN sera in female (A) and male (B) mice as in Figure 1. (A) Female WT mice (blue) were monitored for arthritis severity over 8 days. Bone marrow chimeras were generated by transplant of fpr1-/- bone marrow from female mice into lethally irradiated fpr1+/+ mice. Following engraftment, arthritis was induced with K/BxN serum (KO BM -> WT, green). (B) Similarly to (A), male WT and KO mice were monitored for arthritis severity over 8 days (black and red, respectively) and compared to arthritis development in bone marrow chimera (KO BM -> WT, blue) after successful engraftment and K/BxN sera injection.

Disclosure: R. Stultz: None; **P. Hermanson**: None; **N. Mullin**: Pfizer Inc., 3; **S. Ramsey**: Pfizer Inc., 3; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0060

Dietary Management of Rheumatoid Arthritis: A Functional Investigation of the Synbiotic Medical Food, SBD121

Ryan Green[1], Daniela Diaz-Infante Morales[1], Alicia Ballok[1], Kristine Kuhn[2], Christopher Ritchlin[3], Mark Charbonneau[1], Eric Schott[1] and Gerardo Toledo[1], [1]Solarea Bio Inc, Waltham, MA, [2]2022 - 2023 / Adult/ University of Colorado, Aurora, CO, [3]University of Rochester Medical Center, Canandaigua, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA), affecting approximately 1% of the global population RA is a leading cause of disability worldwide. Despite available treatments, including methotrexate (MTX) and biologics, many patients fail to achieve lasting remission.

RA is associated with intestinal dysbiosis and increased intestinal permeability, two features that associate with local and systemic inflammation in RA. Certain probiotic strains have been shown to benefit patients with RA by reducing disease activity scores, indirect measures of increased intestinal permeability, and some pro-inflammatory measures. These observations highlight the potential of probiotics as a complementary approach for managing inflammation in RA.

To support RA management, we developed SBD121, a synbiotic medical food composed of plant-derived probiotics and prebiotic fibers. This study aimed to evaluate the preclinical efficacy of SBD121 in reducing RA severity, alone and in combination with MTX, as well as to explore its mechanisms of action *in vitro*.

Methods: We examined SBD121 in a collagen-induced arthritis (CIA) mouse model. Mice received SBD121 ($1x10^{10}$ colony forming units) or a water control via oral gavage twice daily for 42 days. Arthritis was induced 28 days after SBD121 initiation, followed by injection with MTX (5 mg/kg) or a vehicle control 3 times weekly. Joint swelling and clinical scores were assessed on days 18, 24, 28, 31, and 35.

To dissect SBD121's cellular effects *in vitro*, human intestinal epithelial cells and immune cells were exposed to SBD121. Barrier integrity (transepithelial electrical resistance), cytokine production (ELISA), and transcriptional responses (RT-qPCR) were measured.

Results: SBD121, co-administered with MTX, significantly reduced RA clinical scores relative to MTX + vehicle in a CIA mouse model. SBD121 alone did not affect clinical score relative to the CIA control.

In vitro, SBD121 improved intestinal barrier integrity without inducing inflammatory cytokine secretion; an effect associated with reduced systemic inflammation. SBD121 also reduced Th17-associated immune cell responses (IL-23, IL-6, IL-8, and CXCL1 secretion).

Conclusion: Here, we have demonstrated that SBD121 potentiates the effects of MTX in a CIA model of RA. Our *in vitro* results suggest that this synergy may be due to attenuated Th17 responses and/or improved intestinal barrier function. Ongoing studies aim to elucidate SBD121's specific effects on articular cells and determine the role of MTX in SBD121-influenced responses. The efficacy of SBD121 in combination with MTX in newly diagnosed RA patients is being evaluated in an ongoing double-blind placebo-controlled clinical trial (NCT06005220).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Green: Solarea Bio Inc, 3; **D. Diaz-Infante Morales**: Solarea Bio Inc, 3; **A. Ballok**: Solarea Bio, 3; **K. Kuhn**: Solarea, 2; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, Moon-Lake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **M. Charbonneau**: Solarea Bio, Inc, 12, 3, 10; **E. Schott**: Solarea Bio Inc, 3; **G. Toledo**: Solarea Bio, 3.

Abstract Number: 0061

IL-22 Contributes to Autoantibody-induced Arthritis Via Modulation of Inflammatory Cytokine and Chemokine Expression in the Inflamed Synovium of a Murine Model

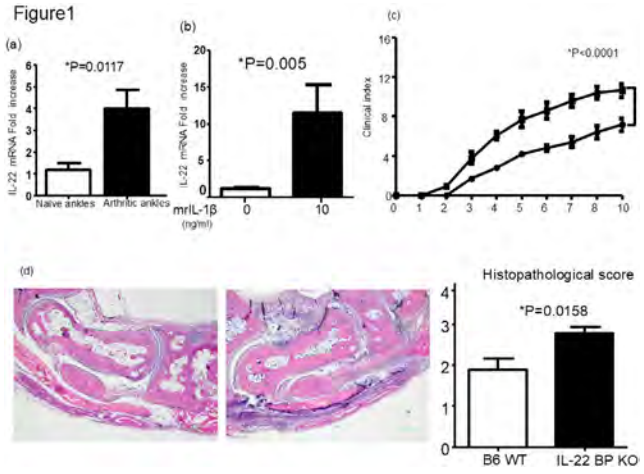
Shinjiro Kaieda[1], Suzuna Sugi[1], Takuma Koga[2], Takashi Kinoshita[1] and Tomoaki Hoshino[1], [1]Kurume university School of Medicine, Kurume, Japan, [2]Kurume Universty School of Medicine, Kurume, Japan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

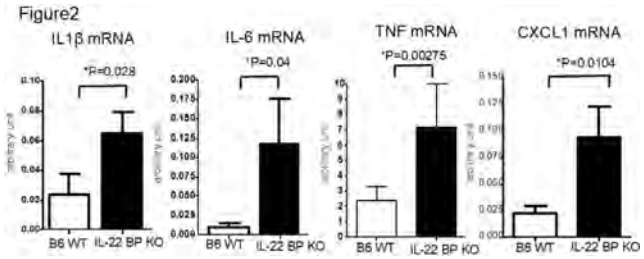
Background/Purpose: IL-22 is a key cytokine involved in modulating tissue responses during inflammation and is markedly upregulated in inflammatory diseases, such as psoriasis, inflammatory bowel diseases, and rheumatoid arthritis. IL-22 binding protein (IL-22BP) inhibits IL-22 signaling by binding to it, and treatment with IL-22BP reduces the severity of cutaneous inflammation in psoriatic mice (Front Immunol. 2018;9:1418). Several studies have shown that IL-22 is critical in the pathophysiology of collagen-induced arthritis (CIA), a condition mediated by cellular and humoral immune responses (Arthritis Rheum. 2009;60:390. Arthritis Rheum. 2014;66:1492). IL-22 deficient mice develop less severe arthritis, although the effectiveness of IL-22 neutralizing antibodies in the same models varies depending on the timing of administration. While IL-22 signaling is involved in animal models of CIA, its role in autoantibody-induced arthritis remains unclear. The K/BxN serum transfer model of autoantibody-induced arthritis reflects the effector phase of arthritis and is crucial for innate immunity but not for acquired immunity. This study aimed to assess the role of IL-22 pathway in autoantibody-induced arthritis using IL-22BP-deficient mice.

Methods: C57BL/6 IL-22BP gene-deficient (-/-) mice were subjected to K/BxN serum transfer to induce arthritis, and joint inflammation was assessed histologically in a blinded manner. Murine fibroblast-like synoviocytes (mFLS) were stimulated with recombinant mouse IL-1β or IL-22. mRNA expression levels of IL-22, CXCL1 and IL-1β were analyzed in cultured cells

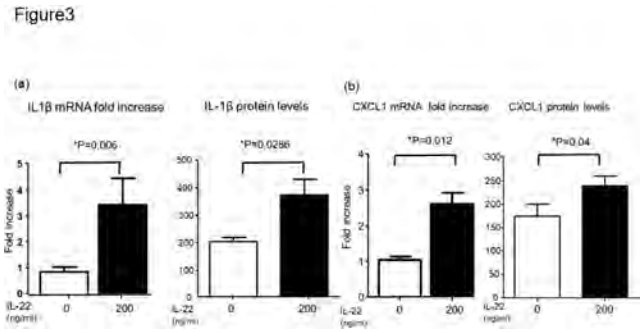


IL-22BP deficiency exacerbates K/BxN serum transfer arthritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Inflammatory cytokines and chemokine expression in inflamed synovial tissue during K/BxN serum transfer arthritis.



IL-22 induces mFLS to produce inflamatory cytokine and chemokine.

using RT-PCR, while protein levels of IL-1β and CXCL1 were examined using ELISA. Additionally, synovial tissue expression of IL-6, IL-1β, TNFα, and CXCL1 mRNA was evaluated using RT-PCR.

Results: IL-22 mRNA expression was significantly elevated in inflamed synovial tissues of mice after K/BxN serum transfer arthritis induction (Fig. 1a). Consistent with *in vivo* data, mFLS can produce IL-22 mRNA after stimulation with recombinant IL-1β (Fig 1b). Disease severity was more pronounced in IL-22BP-/- mice than in wide-type (WT) controls (Fig. 1c). Histomorphometric analysis confirmed these observations, showing significantly higher histopathological scores in IL-22BP-/- mice (Fig. 1d). Consistent with these findings, the expression of pro-inflammatory genes, IL-1β, TNFα, IL-6, and CXCL1, was significantly upregulated in the inflamed synovium of IL-22BP-/- mice compared to WT controls (Fig. 2). Stimulation of mFLS with recombinant IL-22 led to increased expression of IL-1β and CXCL1 at both the mRNA and protein levels (Fig. 3a and b).

Conclusion: The IL-22/IL-22BP axis contributes to autoantibody-induced arthritis by modulating the expression of pro-inflammatory cytokines and chemokines. IL-22 directly induces mFLS to produce IL-1β and CXCL1, thereby exacerbating joint inflammation. Targeting IL-22 signaling may represent a promising therapeutic strategy for rheumatoid arthritis.

Disclosure: S. Kaieda: None; **S. Sugi**: None; **T. Koga**: None; **T. Kinoshita**: None; **T. Hoshino**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0062

Neddylation as a Therapeutic Target in Autoimmune Arthritis: Evidence from SKG Mice

Sho Sendo[1], Alfonso Del Peral Fanjul[2], Kazuma Nishisaka[2], Hirotaka Yamada[1], Takaichi Okano[1], Keisuke Nishimura[1], Yo Ueda[1] and Jun Saegusa[2], [1]Kobe University Hospital, Kobe, Japan, [2]Kobe University, Kobe, Japan

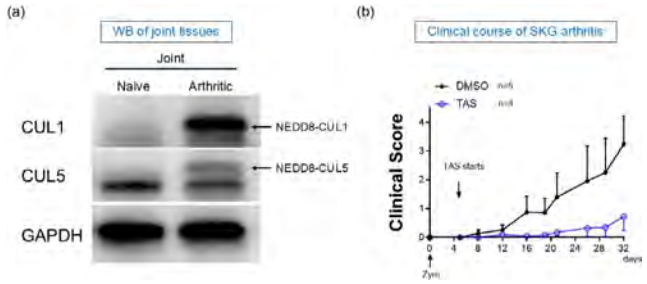
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Neddylation, NEDD8 conjugating process, is a post-translational modification that plays a crucial role in regulating ubiquitination by targeting cullin (CUL)-ring E3 ubiquitin ligases. Our previous research indicated that neddylation is dysregulated in RA FLS, and that its inhibition can reduce arthritis severity in the K/BxN serum transfer model. However, the dysregulation of neddylation in SKG mice remains largely unexplored. This study aims to investigate whether neddylation is dysregulated in arthritic SKG mice and to evaluate its potential as a therapeutic target for arthritis.

Methods: Arthritis was induced in SKG mice through intraperitoneal injection of zymosan. The neddylation status of CUL1 and CUL5, and the relative gene expression of *Nub1* and *Csn1* in joint tissue were compared between arthritic and naïve SKG mice using Western blotting, and RT-qPCR, respectively. In vitro, we assessed the effects of the selective neddylation inhibitor TAS4464 on the induction and maturation of bone marrow-derived dendritic cells (BMDCs), on T cell proliferation, as well as on co-culture T cells with TAS4464-treated BMDCs.

Results: We first investigated the neddylation status in arthritic SKG mice and discovered that the neddylation of CUL1 and CUL5 was upregulated in the joints of arthritic SKG mice (**Figure a**). Gene expressions of *nub1* and *csn1*, negative regulators of neddylation, were decreased in arthritic SKG mice (*Nub1*: 1.03 ± 0.76 and 0.28 ± 0.12; p=0.019, *Csn1*: 1.06 ± 0.59 and 0.50 ± 0.34; p=0.029 for naïve mice and arthritic mice, respectively), which indicated that neddylation systems were dysregulated in the arthritic joints. Subsequently, we assessed the effects of neddylation inhibition on DC differentiation, maturation, and T cell proliferation. The neddylation inhibitor promoted the differentiation of PD-L1-positive DCs (78.7 ± 8.2 % and 91.1 ± 4.7 % for DMSO and TAS4464, respectively; p=0.021), reduced the maturation of MHC II-positive DCs (60.7 ± 10.3 % and 36.9 ± 10.6 % for DMSO and TAS4464, respectively; p=0.008) without altering PD-L1 expression, and had a trend to suppress T cell proliferation (37.8 ± 10.3 % and 13.6 ± 5.5 % for DMSO and TAS4464, respectively; p=0.058). Finally, we assessed the efficacy of neddylation inhibition on arthritis, and revealed the neddylation inhibitor alleviated arthritis severity in SKG mice (**Figure b**).

Conclusion: Upregulated neddylation in inflamed joints could be a novel therapeutic target in autoimmune arthritis.



(a) Representative images of western blotting of CUL1, CUL5 and GAPDH in the joints of naive and arthiritic SKG mice. (b) Clinical scores of zymosan injected SKG mice treated with TAS4464 or DMSO.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Sendo: None; **A. Fanjul**: None; **K. Nishisaka**: None; **H. Yamada**: None; **T. Okano**: None; **K. Nishimura**: None; **Y. Ueda**: None; **J. Saegusa**: None.

Abstract Number: 0063

Effect of alpha-ketoglutarate on Synovial Fibroblasts-Mediated Inflammation in Arthritis

Surabhi Gautam, Vinay Devulapalli, Akash Sathiyamurthi, Jayla Whittaker and Pallavi Bhattaram, Emory University, Atlanta, GA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) and related autoimmune joint disease patients exhibit cyclic episodes of resolution and exacerbation of joint inflammation, referred to as flares. Fibroblast-like synoviocytes (FLSs) that are epigenetically and metabolically transformed by chronic inflammation are implicated as the orchestrators of these flares. The tricarboxylic acid cycle (TCA) is the primary energy-producing metabolic pathway that occurs in the mitochondria. Biomolecules (enter the TCA cycle as acetyl-CoA to undergo a series of enzymatic reactions leading to the production of ATP. Another lesser investigated, but highly significant role of the TCA cycle is that its intermediate enzymatic byproducts, like alpha-ketoglutarate (AKG), enter the nucleus to function as an epigenetic modifier that has the potential to inhibit the expression of pro-inflammatory genes. We hypothesized that AKG can be developed as a drug to inhibit the deregulated metabolic and epigenetic state of the RA FLSs and effectively treat RA flares.

Methods: We isolated FLSs from the synovial joints of a transgenic mouse model of inducible human Tumor Necrosis Factor alpha expression (iTNF-tg). We further generated disease states equivalent to homeostasis, inflammatory, and resolution phases of arthritis pathology to mimic the characteristics of the flare pathology in RA patients. We studied the effect of AKG treatment on FLSs from various disease phases. Outcome measures included histological, immunohistochemical, ATP generation, gene expression, epigenetic regulation, cell cycle, and oxidative stress measurements.

Results: Our in vitro results in FLSs from the homeostasis, inflammatory, and resolution phase of the iTNF-tg mouse FLSs showed that AKG inhibited the expression of inflammatory genes. We utilized a luminescence-based assay to measure ATP and reactive oxygen species in live FLSs. Our data suggests that treatment with AKG inhibited the amount of ATP produced by FLSs from all stages. However, the anti-inflammatory and metabolic effects of AKG were maximal during the resolution phase. Our cell cycle analysis and found that AKG did not change the proliferation rate of FLSs. These results suggest that treatment with AKG inhibits inflammation and changes ATP production without altering cell proliferation. We will further discuss the results of our ongoing epigenetic and transcriptomic studies evaluating the in vivo effect of two different forms of dietary AKG treatment (cell-permeable and non-cell-permeable dietary forms) on the inflammatory arthritis features of the iTNF-tg mouse model.

Conclusion: AKG may inhibit RA FLSs' inflammation by downregulating pro-inflammatory gene expression. AKG may show its most effective inhibition of the pathological of RA FLSs during the resolution phase of the disease. Mechanistically, these inhibitory effects may act via blocking the NF-kappaB signaling pathway and cellular senescence pathways. AKG supplementation during the resolution phase of RA may serve as an effective co-treatment with current disease-modifying antirheumatic drugs to prevent the epigenetic deregulation of RA FLSs and thereby the onset of subsequent flares.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Gautam: None; **V. Devulapalli**: None; **A. Sathiyamurthi**: None; **J. Whittaker**: None; **P. Bhattaram**: None.

Abstract Number: 0064

Sclerostin from marrow adipogenic precursors is essential for bone and joint homeostasis in mice

Tailin He and Yifang Mei, Shenzhen Third People's Hospital, Shenzhen, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: A novel mesenchymal subpopulation known as 'marrow adipogenic lineage precursors' (MALPs) has been identified, characterized by the expression of various adipocyte markers while lacking lipid droplets. Serving as precursors for lipid-laden adipocytes, MALPs are predominantly found as pericytes and stromal cells, creating a comprehensive three-dimensional network within the marrow cavity. Nevertheless, the precise mechanisms by which MALPs regulate bone and joint homeostasis under both physiological and pathological conditions remain elusive. Sclerostin serves as a significant inhibitor of bone formation, antagonizing Wnt/β-catenin signaling. Prior research has demonstrated that the use of neutralizing monoclonal antibodies against sclerostin has been shown to enhance bone mass and is being explored as a treatment for osteoporosis. However, it might increase the risk of cardiovascular diseases, potentially because sclerostin plays a role in protecting cardiovascular system. Conditional ablation of sclerostin in MALPs might increase bone mass and promote bone and joint homeostasis, while ameliorating the systemic side effects.

Methods: We assessed the bone mass of conditional knockout (cKO) mice and control mice at various ages utilizing micro-computed tomography (μ-CT), followed by histological analyses. Additionally, we evaluated the osteogenic potential of bone marrow stromal cells (BMSCs) derived from both cKO and control mice *in vitro*. Finally, we established two animal disease models to measure the bone and joint parameters across both groups.

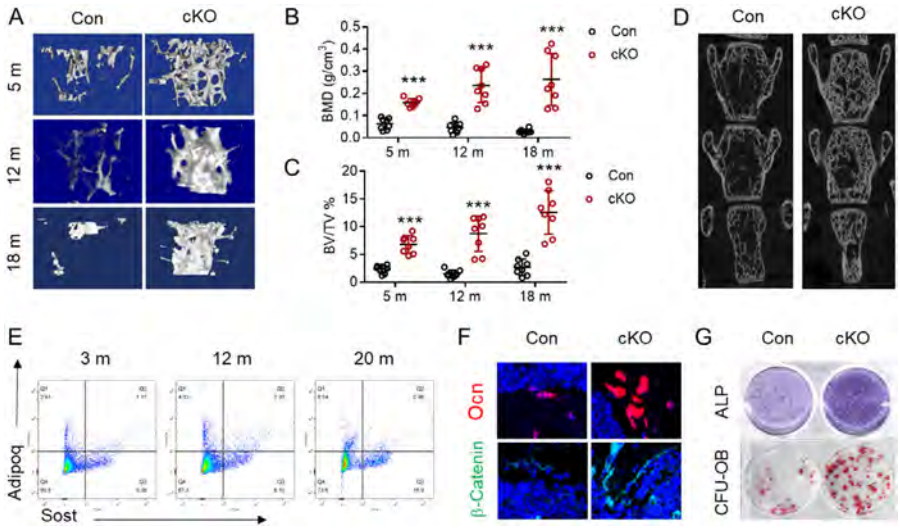


Figure 1. Bone marrow Adipoq+Sost+ cell subpopulation plays an important role in bone formation and BMSC osteogenic differentiation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

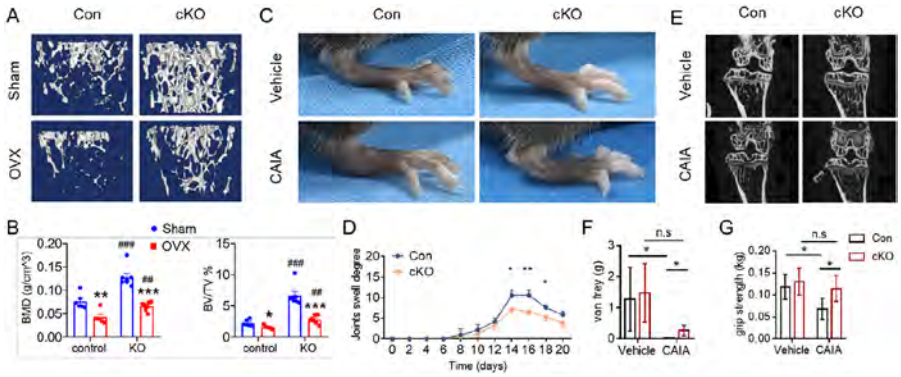


Figure 2. Depletion of Sost in MALPs ameliorates osteoporosis and rheumatoid arthritis in mice.

Results: μCT analysis of the skeletal structure indicated that cKO mice demonstrated an increase in bone mass at 5 months of age, particularly within the female group (Figure 1A-C). This phenotype became increasingly pronounced with advancing age. Notably, the spinal bone mass showed a significant increase at 18 months in cKO mice (Figure 1D). Simultaneously, we observed an increase in the proportion of Adipoq^{+}Sost^{+} cells as the mice aged (Figure 1E). Immunofluorescence staining revealed a higher presence of osteoblasts surrounding the trabecular regions, along with an elevated expression of active-β-catenin protein in the bone of cKO mice compared to controls (Figure 1F). The levels of osteogenic marker proteins were markedly enhanced in primary BMSC cultures derived from cKO mice (Figure 1G).

Subsequently, we assessed the impact of sclerostin deficiency in mice subjected to ovariectomy and a collagen antibody-induced arthritis model. The deletion of Sost in MALPs partially mitigated the osteoporotic characteristics associated with estrogen deficiency (Figure 2A, B). Additionally, Sost deletion alleviated the symptoms of collagen antibody-induced arthritis, including ameliorated joint swell (Figure 2C, D), bone erosion (Figure 2E), mechanical pain threshold (Figure 2F), and grip strength (Figure 2G).

Conclusion: We establish that the Adipoq^{+}Sost^{+} cell subpopulation within the bone marrow plays a vital role in the BMSC osteogenic differentiation. This distinct cell population in the bone marrow could serve as a valuable target for therapeutic interventions in osteoporosis and rheumatoid arthritis.

Disclosure: T. He: None; **Y. Mei**: None.

Abstract Number: 0065

Expression and Co-Localization of Malondialdehyde-Acetaldehyde and Citrullinated Proteins in Myocardial Tissues Precedes the Development of Cardiac Fibrosis in Collagen-Induced Arthritis

Wenxian Zhou[1], Hannah Johnson[2], Michael Duryee[2], Ali Namvaran[3], Julian Garcia[2], Carlos Hunter[2], Tate Johnson[2], Daniel Anderson[4], Kishore Bidasee[2], Geoffrey Thiele[2] and Ted Mikuls[2], [1]University of Nebraska Medical Center, Bellevue, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Nebraska Medical Center, Omaha, [4]0587964, Durham, NC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with rheumatoid arthritis (RA) experience increased morbidity and mortality due to heart failure with preserved ejection fraction (HFpEF), a condition characterized by diastolic dysfunction largely driven by cardiac fibrosis. However, the underlying mechanisms of HFpEF in RA remain poorly understood. Recent studies from our group have identified the synergistic role of post-translational modifications (PTMs)—specifically citrulline (CIT) and malondialdehyde-acetaldehyde (MAA)—in promoting local inflammation and fibrosis in the joints and lungs of RA patients. Furthermore, these PTMs are increasingly expressed and co-localized in heart tissues of mice with early collagen-induced arthritis (CIA), indicating their potential role in promoting cardiac fibrosis and dysfunction. Therefore, the purpose of this study was to evaluate the temporal relationship between the cardiac expression of these PTMs and cardiac fibrosis in CIA mice.

Methods: Arthritis prone male DBA/1J mice were subjected to CIA (n=8) by standard protocols with saline injections used as control (n=6). Three mice per group were sacrificed at 5 weeks (early CIA) with the remainder sacrificed at 10 weeks (chronic CIA). Prior to being euthanized at 10 weeks, transthoracic echocardiography was performed to assess diastolic function (early to late transmitral diastolic flow [E:A] and myocardial relaxation [E':A'] velocity ratios) and systolic function (left ventricular ejection fraction %). Additionally, bovine serum albumin coupled to fluorescein isothiocyanate (BSA-FITC) was injected into the left ventricle immediately before sacrifice to visualize microvascular leakage. Hearts were resected and myocardial tissues were paraffin-embedded, sectioned, and stained with trichrome to quantify collagen deposition. Statistical comparisons of functional and morphologic features in CIA vs. control mice were performed using Student's t-test.

Results: Though CIT and MAA expression were increased and co-localized in heart tissues from mice with early CIA, (Zhou et al. ACR Convergence 2024, Abst 0032), there were no differences in myocardial collagen deposition in early CIA vs. control mice (**Fig. 1A**). In contrast, we observed significantly increased perivascular and interstitial collagen deposition in chronic CIA vs. control mice (**Fig. 1B**). Mice with chronic CIA also had increased microvascular leakage (**Fig. 2**), impaired diastolic function (**Fig. 3**), and diminished systolic function (**Fig. 3**) vs. controls.

Conclusion: This study is the first to demonstrate that an increase in CIT and MAA deposition in heart tissues precedes the onset of cardiac fibrosis, microvascular leakage and myocardial dysfunction in mice with CIA. Coupled with our recent studies revealing that CIT and MAA synergistically promote the activation of fibroblasts and endothelial cells in vitro, our findings

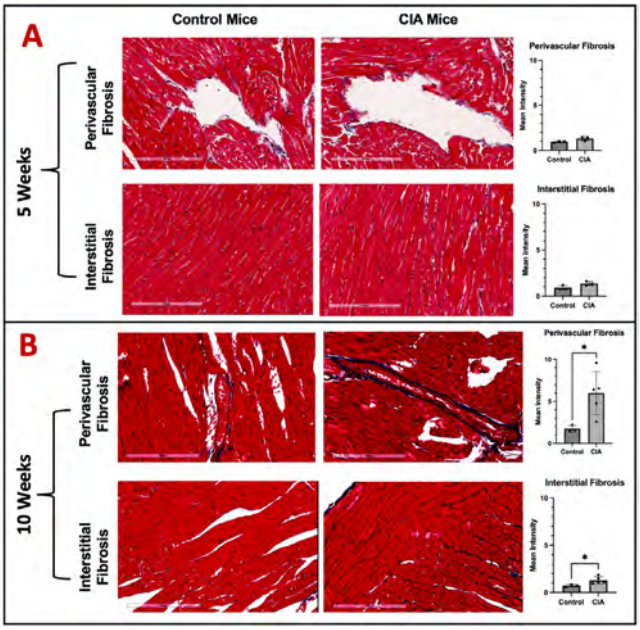


Figure 1. Trichrome Stain Demonstrated Increased Cardiac Fibrosis in CIA Mice at Week 10. Representative image of 20X frame at left ventricle was shown. White scale bar at the bottom indicates 200 μm. Tissue fibrosis (blue) was quantified for control and CIA mice A) 5 weeks and B) 10 weeks post injection. Data shown on graphs are mean ± standard deviation.

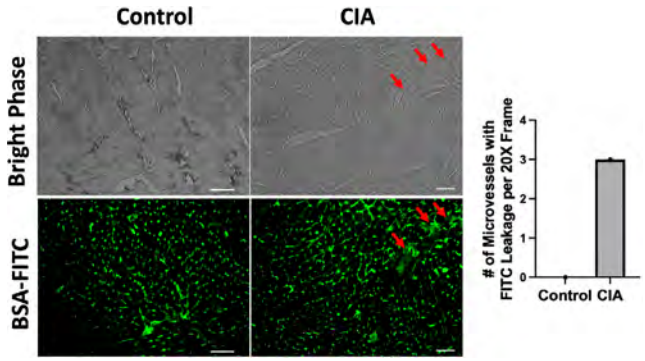


Figure 2. BSA-FITC Revealed Increased Microvascular Leakage in CIA Mice at Week 10. n=1 per group. Representative image of 20X frame at left ventricle was shown. Red arrow points to the sites of micro-vessels with FITC leakage. White scale bar at the bottom indicates 200 μm.

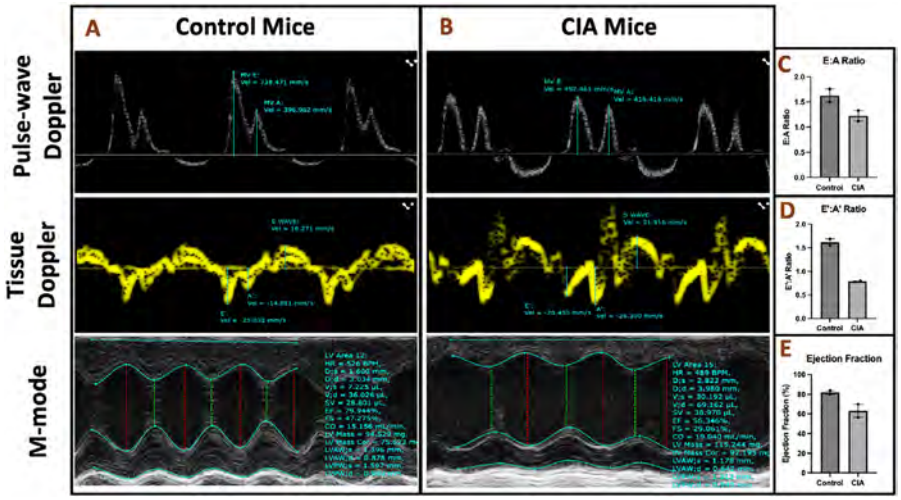


Figure 3. Echocardiography of Collagen Induced Arthritis (CIA) and Control Mice at Week 10. Echocardiography was performed on CIA (n=2) and saline-injected Control Mice (n=2) 10 weeks after the first injection. Raw Echocardiographic data was obtained using Pulse-wave, tissue Doppler, and M-mode, and representative images were shown for: A) Control mice; B) CIA mice. These images were used to measure C) E:A ratio, D) E':A' ratio, and E) Ejection fraction, respectively. Low E:A ratio and E':A' ratio (normal range 1.52 ± 0.40) indicates diastolic dysfunction, and low ejection fraction (normal range 71 ± 11) indicates systolic dysfunction. Data shown on graphs are mean ± standard deviation.

suggest that CIT and MAA together may be significant drivers of cardiac dysfunction in RA. Further research will explore whether inhibitors of CIT, MAA, or their downstream signaling pathways can attenuate cardiac dysfunction in RA.

Disclosure: W. Zhou: None; **H. Johnson**: None; **M. Duryee**: None; **A. Namvaran**: None; **J. Garcia**: None; **C. Hunter**: None; **T. Johnson**: None; **D. Anderson**: None; **K. Bidasee**: None; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0066

RA-required synovial tissue-resident monocyte lineage cells are comprised of three distinct subpopulations.

Yidan Wang[1], Samuel Dowling[2], Jessica Maciuch[2], Vanessa Manada De Lobos[2], Meghan Mayer[2], Kainat Mian[1], Tyler Therron[3], Hadijat Makinde[1], Carla Marie Cuda[1], Deborah Rachelle Winter[4] and Harris R Perlman[1], [1]Northwestern University, Chicago, IL, [2]Northwestern University, Chicago, [3]Northwestern Feinberg School of Medicine, Chicago, IL, [4]Northwestern University, Skokie, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0049–0066) Rheumatoid Arthritis – Animal Models Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Tissue-resident monocyte-lineage cell (TRMC) are an extravascular population distinct from circulating monocytes and synovial macrophages and are critical for the development of inflammatory arthritis. Previous fate-mapping results demonstrated that TRMC are at least partially derived from the fetal liver and are traceable using various myeloid-related fate-mapping models, suggesting potential heterogeneity within this population. However, the precise identities and origins of TRMC subpopulations remain unclear.

Methods: We first measured the long-lived and bone marrow (BM)-derived TRMC in bone marrow chimeras (BMC) and parabiosis mice. Next, we used single-cell RNA-sequencing with surface marker detection (CITE-seq) to investigate the heterogeneity of TRMC during homeostasis and their dynamic changes after the synovial disruption induced by clodronate-laden liposome (Clo. Lip) and throughout the progression of RA-like disease in mice. To investigate the dependence of TRMC subpopulations on *Ccr2*, we utilized BMC and parabiosis mice models between CD45.1 B6 and *Ccr2*$^{-/-}$ mice.

Results: We characterized the ontogeny of TRMC, which comprises both bone-marrow (BM)-derived and long-lived populations. Furthermore, CITE-seq identified three TRMC subpopulations, distinguished by TIM4, CX3CR1, and MHCII surface marker expression, each exhibiting distinct functions. TIM4^{+}CX3CR1^{+} TRMC were enriched for pathways involved in synovial hemostasis, whereas MHCII^{+} TRMC were more enriched for inflammatory response pathways, with TIM4^{+} TRMC exhibiting functional features of both.

Clo. Lip modestly reduced the absolute number of TRMC but did not impact proportions or transcriptional profile of TRMC at 7 days post administration. Under steady state, TIM4^{+}CX3CR1^{+} and TIM4^{+} TRMC represented the long-lived population, whereas MHCII^{+} TRMC were BM-derived and dependent on *Ccr2*. During synovial inflammation, BM-derived TRMC expanded up to threefold at the peak of arthritis compared to baseline and replenished the TIM4^{+}CX3CR1^{+} and TIM4^{+} TRMC compartments. Additionally, TIM4^{+} TRMC underwent transcriptional and functional changes resembling MHCII^{+} TRMC during the peak and plateau stages of RA-like arthritis in mice.

Conclusion: These findings underscore the heterogeneity within TRMC and highlight their distinct responses to synovial disruption and potential roles in rheumatoid arthritis (RA). Future therapeutic target strategies should focus on TRMC by targeting their specific subpopulations.

Disclosure: Y. Wang: None; **S. Dowling**: None; **J. Maciuch**: None; **V. Manada De Lobos**: None; **M. Mayer**: None; **K. Mian**: None; **T. Therron**: None; **H. Makinde**: None; **C. Cuda**: None; **D. Winter**: None; **H. Perlman**: AbbVie/Abbott, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0067

Identification of Neutrophil Extracellular Traps in Explanted Human Lungs with Rheumatoid Arthritis-related Interstitial Lung Disease

Amara Seng[1], Kensuke Suga[2], Diana Tran[3], Anvita Singaraju[4], Tanyalak Parimon[5], Youn Jung Choi[6], Justyna Fert-Bober[7], Jon Giles[8], Peter Chen[5] and Nunzio Bottini[9], [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]Kao Autoimmunity Institute, Cedars-Sinai Medical Center, Beverly Hills, CA, [3]Cedars Sinai Medical Center, La Cñada Flintridge, CA, [4]Kao Autoimmunity Institute, Cedars-Sinai Medical Center, Los Angeles, [5]Women's Guild Lung Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [6]Kao Autoimmunity Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [7]Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [8]Cedars Sinai Medical Center, Los Angeles, CA, [9]Cedars Sinai Medical Center, Beverly Hills, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Symptomatic rheumatoid arthritis-related interstitial lung disease (RA-ILD) is prevalent in about 10% of patients with RA and confers a higher mortality compared with RA patients without ILD. Anti-citrullinated protein antibodies (ACPAs) are strongly linked to RA-ILD, suggesting a pathogenic role for citrullinated proteins. Citrullinated histone H3 (Cit H3), a component of neutrophil extracellular traps (NETs), has been identified as a potential biomarker of RA-ILD. Our aim was to quantify and characterize Cit H3 expression in explanted lungs from patients undergoing lung transplant who have RA-ILD compared to patients with other connective tissue disease (CTD)-ILD or idiopathic pulmonary fibrosis (IPF).

Methods: Formalin fixed paraffin embedded explanted lung tissues were obtained from patients with RA-ILD (n=9), other CTD-ILD (n=4) or IPF (n=6). Deceased donor lungs without known pulmonary disease (HC, n=4) were used as controls.

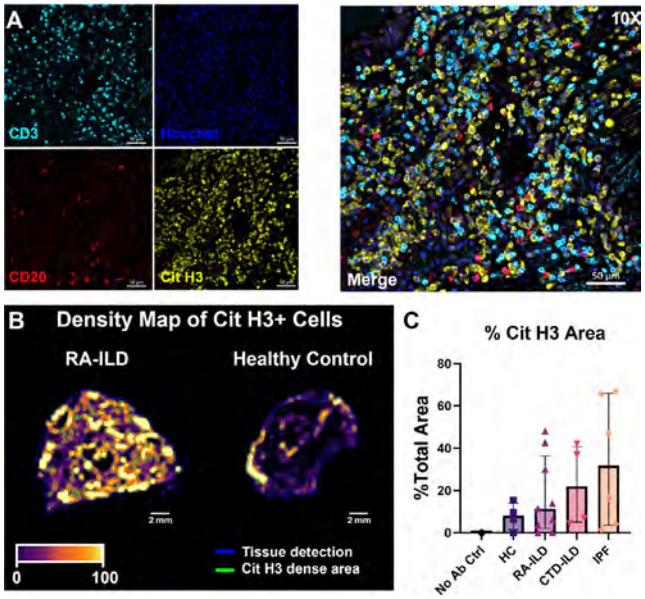
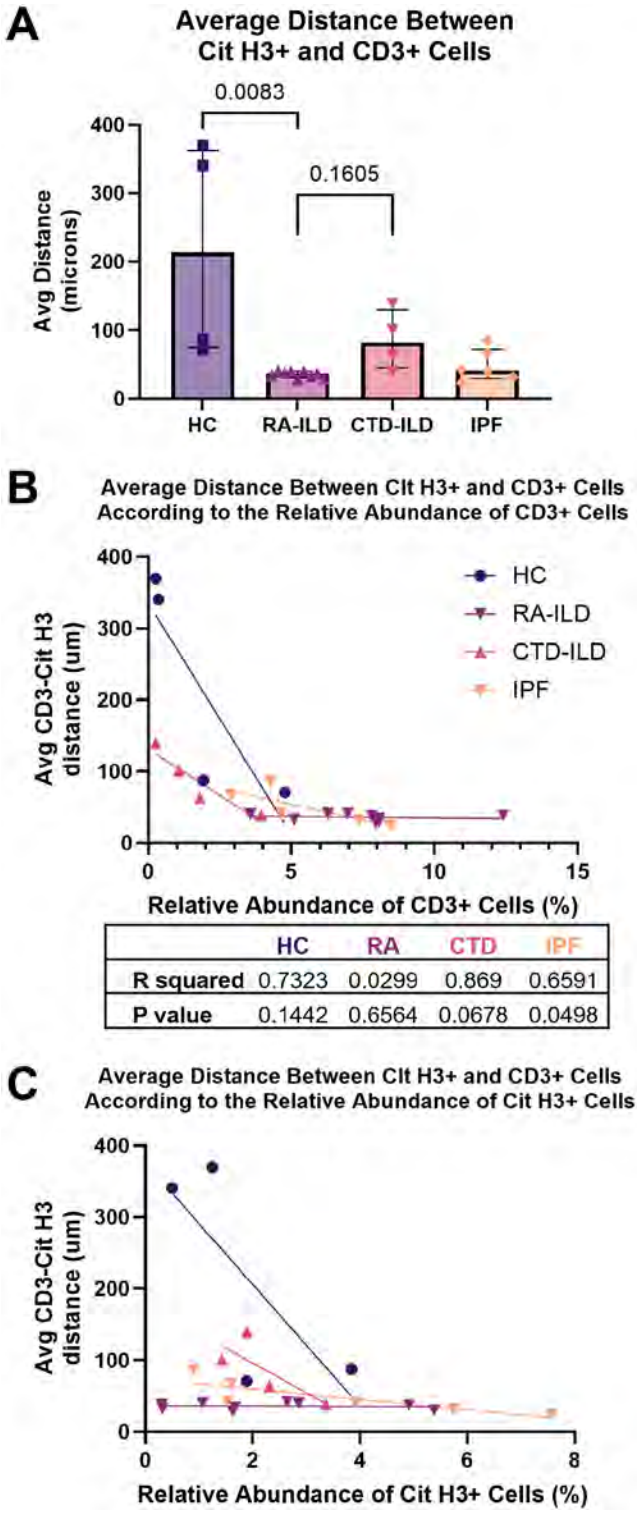


Figure 1: Density of Cit H3+ Cells in RA-ILD, CTD-ILD and, IPF explanted lungs. A) Representative immunofluorescence image of an FFPE section from an RA-ILD explanted lungs to show Cit-H3 (yellow), CD3 (cyan) and CD20 (red). B) Representative density maps of RA-ILD and HC lungs. Maps were generated based on raw cell counts in a 300 μm radius. The blue outline is the tissue based on Hoescht thresholding. The green outline is an area of Cit H3 density with greater than 46 Cit H3+ cells/300 μm radius. C) Percentage of Cit H3 dense areas represented by the Cit H3 dense area (green outline) divided by the total area of the tissue (blue outline). Data are represented as median ±IQR. Kruskal-Wallis test, p values <0.5 noted above columns.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



	HC	RA	CTD	IPF
R squared	0.7323	0.0299	0.869	0.6591
P value	0.1442	0.6564	0.0678	0.0498

Figure 2: Proximity of Cit H3+ and CD3+ cells in RA-ILD, CTD-ILD and, IPF explanted lungs. A) Average distances Cit H3 cells and the nearest CD3+ cell for HC, RA-ILD, CTD-ILD and IPF lungs. Data are represented as median ±IQR. Kruskal-Wallis test, p values <0.5 noted above columns. Correlation of (B) relative abundance of CD3+ or (C) Cit H3+ cells (plotted as percentage of total cells) with average nearest distance between Cit H3+ and CD3+ cells. Simple linear regression, R squared and p values noted in tables below.

Using immunofluorescence, CD3+, CD20+, Cit H3+ and neutrophil elastase+ (NE) cells were quantified. Single cell RNA sequencing was completed on CD45+ immune cells sorted from 5 disaggregated RA-ILD lungs.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

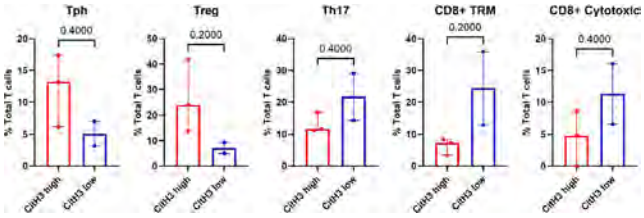


Figure 3: Frequency of T cell subsets based on single cell RNA sequencing of CD45+ immune cells from Cit H3 high and Cit H3 low RA-ILD lung explants. Percentages of T peripheral helper cells (Tph), regulatory T cells (Treg), T helper 17 (Th17) cells, T resident memory (TRM) CD8+cells and, cytotoxic CD8+ T cells in Cit H3 high (n=3) and Cit H3 low (n=2) RA-ILD lung explants. Data are represented as median ±IQR. Mann-Whitney test, p values <0.5 noted above columns.

Results: Cit H3+ cells were identified in explanted lungs with RA-ILD, other CTD-ILD and IPF. A subset of patients in each group had higher Cit H3 density in lung tissue (Fig 1C). In the RA-ILD samples, a portion of the Cit H3+ cells were also NE + indicating the presence of NETs. The average distance of Cit H3+ cells to the nearest CD3+ cells was shorter in RA-ILD (37 μm) vs HC (214 μm) (p=0.008) (Fig 2A). The closer proximity of Cit H3+ cells to CD3+ cells in RA-ILD was independent of the number of CD3+ or Cit H3+ cells present (Fig 2B-C). Single cell RNA sequencing from RA-ILD patients with Cit H3 high (n=3) vs Cit H3 low (n=2) samples revealed non-significant trends in T cell subsets (Fig 3). In the Cit H3 high vs low groups, there were higher percentages of T peripheral helper cells (median 13.2% vs 5.1%, p=0.4) and regulatory T cells (median 23.9% vs 7.3%, p=0.2) and lower percentages of helper 17 cells (median 11.8% vs 21.8%, p=0.4), T resident memory CD8+ T cells (median 7.3% vs 24.5%, p=0.2) and cytotoxic CD8+ T cells (median 4.8% vs 11.3%, p=0.4).

Conclusion: These findings suggest a role for NETs in RA-ILD, highlighting the potential interaction of T cells with NETs. Future direction includes single cell TCR sequencing and spatial transcriptomics to further explore the interplay between T cells and NETs and its impact on the pathogenesis of RA-ILD.

Disclosure: A. Seng: None; **K. Suga**: None; **D. Tran**: None; **A. Singaraju**: None; **T. Parimon**: None; **Y. Choi**: None; **J. Fert-Bober**: None; **J. Giles**: AbbVie/Abbott, 2, Eli Lilly, 2, Genentech, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Sana, 2; **P. Chen**: Gilead, 1; **N. Bottini**: Merck/MSD, 2.

Abstract Number: 0068

Unique Fibroblast-like Synoviocyte Phenotype with Elevated MCSF Expression Induced by TLR5 Activation in Rheumatoid Arthritis

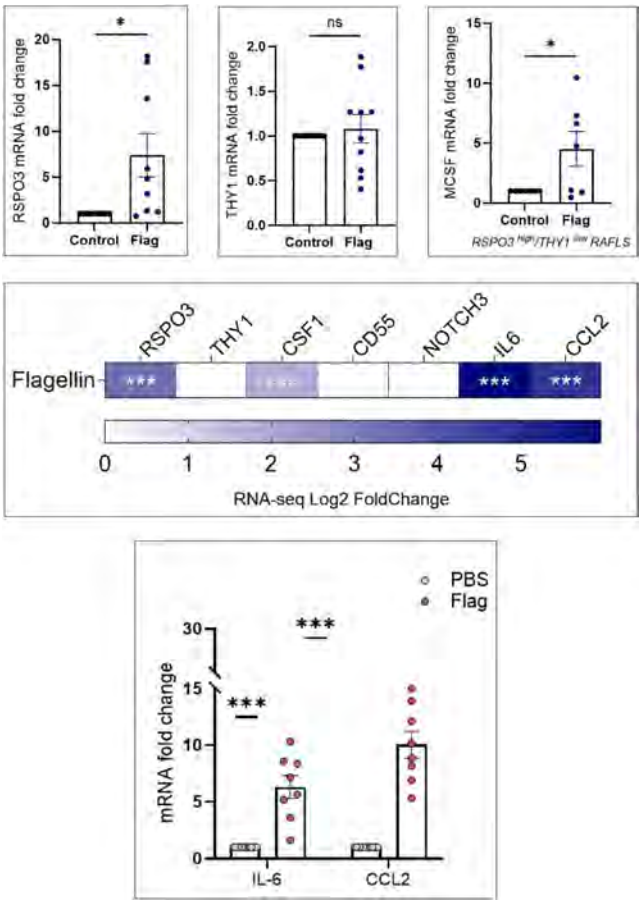
Aryan Patel[1], Osama Al Zoubi[2] and Shiva Shahrara[3], [1]University of Illinois at Chicago, Chicago, [2]University of Illinois at Chicago, Chicago, IL, [3]University of Illinois, Chicago, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting approximately 1% of the global population, causing significant morbidity and disability. Fibroblast-like synoviocytes (FLS) are key effector cells in RA, contributing to inflammation and exhibiting invasive properties that facilitate joint damage. Despite extensive research, the underlying pathophysiology and immunometabolic dysregulation in RA remain incompletely understood.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



qPCR Data and Heat Map for Gene Markers

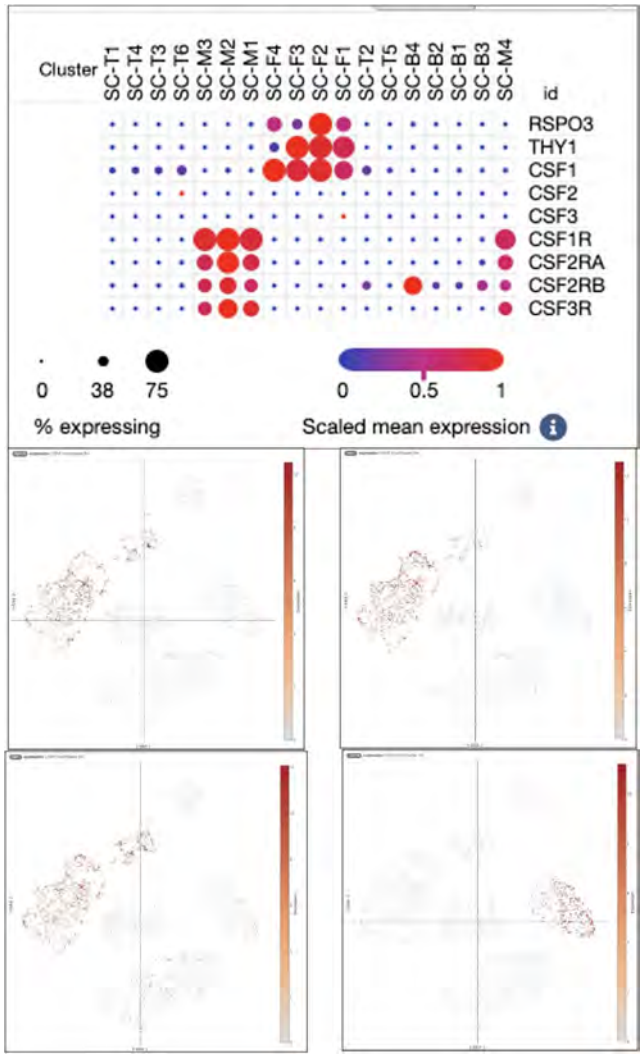
Methods: This project aimed to investigate the immunometabolic reprogramming resulting from Toll-like receptor 5 (TLR5) pathway activation in RA FLS, uncovering cellular markers of reprogrammed FLS and exploring cellular crosstalk mechanisms between RA FLS and peripheral blood mononuclear cells (PBMCs). RA FLS were isolated from fresh synovial tissue and treated with flagellin (TLR5 ligand) or PBS (control) for 6 or 18 hours. Gene expression analysis was performed using quantitative reverse transcription polymerase chain reaction (qRT-PCR) and RNA sequencing to assess the change in key inflammatory and cellular markers.

Results: TLR5-activated RA FLS exhibited a unique RSPO3^high/THY1^low signature, characterized by significantly higher expression of RSPO3 (RNA-seq Log2 FoldChange: 3.34, p< 0.0001; qPCR: Mean Fold Change: 7.370, p=0.016), while CD90 (THY1) expression remained unchanged (RNA-seq Log2 FoldChange: -0.16, p=0.15; qPCR: Mean Fold Change: 1.079, p=0.6276). This RSPO3/THY1 phenotype exhibited a significantly higher expression of IL-6 and CCL2, qPCR: 6.31 and 10.05, respectively, supporting its proinflammatory role in the RA joint environment. Additionally, this phenotype was associated with significantly increased expression of Macrophage colony-stimulating factor (MCSF/CSF1) (RNA-seq Log2 FoldChange: 1.84, p< 0.0001; qPCR: Mean Fold Change: 4.959, p=0.0080).

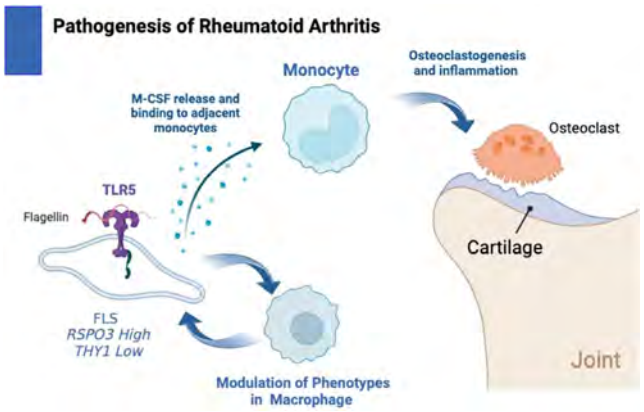
Conclusion: Publicly available single-cell RNA sequencing databases further revealed that CSF1 is almost exclusively expressed by fibroblasts, while CSF1R is nearly exclusively expressed by macrophages, indicating a paracrine axis of fibroblast–macrophage communication that may be central to inflammation and tissue remodeling in RA. This was in contrast to CSF2 and CSF3, which were not significantly expressed in RA FLS.

In conclusion, we have identified a distinct RSPO3^high/THY1^low RA FLS phenotype with elevated CSF1 expression, suggesting a functionally reprogrammed subset of FLS with pro-inflammatory and pro-osteoclastogenic potential. RSPO3, a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Cell Locations and Heat Map Expression for Unique Phenotype and M-CSF



Pathogenisis Diagram

potent enhancer of Wnt signaling, has been previously reported to be upregulated in the synovium of RA patients and experimental arthritis models. Our study provides insights into the role of TLR5 in activating this invasive phenotype, which may play a crucial role in RA pathogenesis through CSF1-mediated interactions with macrophages, potentially influencing osteoclast differentiation. These findings enhance our understanding of RA pathophysiology and direct us to explore potential interventions to target this fibroblast subset.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Patel: None; **O. Al Zoubi**: None; **S. Shahrara**: None.

Abstract Number: 0069

Spatial transcriptomics in rheumatoid arthritis (RA) synovium reveals distinct region-specific fibroblast functions

Camilla R.L. Machado[1], Mina Yao[1], David Boyle[2], Robert J. Benschop[3], James T. Parker[3], Wei Wang[2] and Gary Firestein[1], [1]University of California, San Diego, San Diego, CA, [2]University of California, San Diego, San Diego, [3]Eli Lilly, San Diego

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: RA synovium displays cellular heterogeneity, with gene expression driving disease pathogenesis. Unbiased cell-specific transcriptomes in RA synovium have previously relied primarily on disaggregated tissues to understand these pathogenic processes, however, this approach can cause cell loss and gene induction. Therefore, we interrogated RA and OA synovial tissue using spatial transcriptomics to investigate spatial and cell-type differences, focusing on lining and sublining regions segmented into fibroblasts and macrophages.

Methods: Fresh frozen synovial tissues from 7 RA and 8 OA patients were prepared for the NanoString GeoMX DSP Whole Transcriptome Assay. Lining and sublining regions were segmented to fibroblasts (vimentin+ CD68-) and macrophages

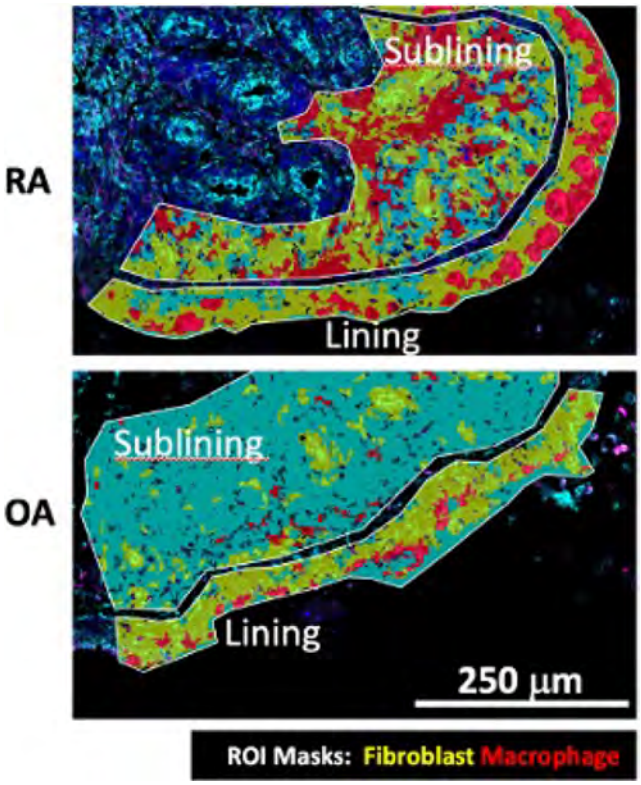


Figure 1. Spatial transcriptomics analysis using NanoString GeoMX DSP Whole Transcriptome Assay. Panel shows examples of RA and OA synovial tissues stained and visualized for fibroblasts (vimentin; yellow-green) and macrophages (CD68; red). The lining and sublining regions were identified as regions of interest (ROI) to quantify gene expression normalized to cell lineage.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

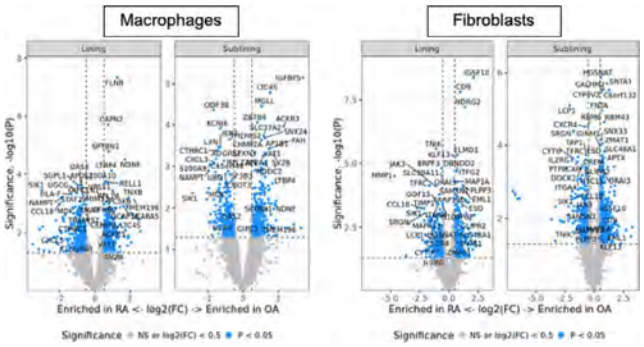


Figure 2. Volcano plots of differentially expressed genes between OA and RA groups for macrophages and fibroblasts in lining and sublining regions. DEGs were identified using linear mixed models (LMM) with a significance threshold of p-value < 0.05 and log2(FC) > 0.5. DEGs in blue are significant genes enriched in RA or OA.

Table 1. Different enriched pathways in lining and sublining fibroblasts from synovial tissue of patients with RA versus OA. Pathways highlighted in bold represent those related to the adaptive immune system. The Reactome pathway analysis was performed using differentially expressed genes in the RA versus OA in lining and sublining fibroblasts (p<0.05). The table displays only pathways that were significantly enriched exclusively in either lining or sublining fibroblasts.

Regions	Representative Enriched Pathways
Lining Fibroblasts (RA vs OA)	• Degradation of ECM • Chemokine receptors bind chemokines • Collagen degradation • IL-10 signaling • Interferon signaling • IL4 and IL13 signaling
Sublining Fibroblasts (RA vs OA)	• **Antigen processing cross-presentation** • **Antigen presentation: folding, assembly and peptide loading of class I MHC** • **Phosphorylation of CD3 and TCR zeta chains** • **Translocation of ZAP-70 to the immunological synapse** • **IL-2 signaling** • **PD-1 signaling** • **Immunoregulatory interactions between lymphoid and non-lymphoid cells** • Platelet activation signaling and aggregation • Elastic fibre formation • RAC1 GTPase cycle

(vimentin– CD68+) (Fig.1). NovaSeq 6000 was used for sequencing. 121 segments passed QC, with 10,363 genes detected and Q3-normalized. A logistic regression (LR) classifier was trained on principal components to find the top 500 genes separating RA from OA. Differentially expressed genes (DEG) were analyzed by linear mixed models (p-value< 0.05 and log2(FC) >0.5), and Reactome pathway analysis (FDR< 0.02).

Results: LR models separation RA from OA found discriminative genes enriched in inflammation and tissue remodeling pathways (e.g., TNF/IL17/IFN signaling, ECM). DEG analysis showed distinct RA vs OA gene signatures across regions and cell types (Fig.2). RA lining fibroblasts had 700 DEG compared with OA lining, with enrichment for 18 pathways that were focused on inflammation and matrix regulation (see Fig.3). RA sublining fibroblasts showed 834 DEG with OA sublining, with enrichment for 29 pathways. Although some inflammatory pathways were identified, sublining fibroblasts also included multiple pathways related to regulation of adaptive immunity (see Fig.3). Spatial comparisons between lining and sublining in RA showed that lining fibroblasts displayed 1176 DEG with 37 enriched pathways, including RAC1 GTPase cycle, collagen biosynthesis/modifying enzymes, and post-translational protein phosphorilation. Therefore, RA lining fibroblasts display a highly activated phenotype compared with sublining cells and help define the aggressive biology of fibroblast-like synoviocytes which are a hallmark in RA. RA lining macrophages showed 628 DEG compared to OA lining, enriched for 60 pathways (e.g., ECM organization, IFN gamma signaling, translation). Surprisingly, even though RA sublining macrophages had 672 DEGs compared to OA, they were only enriched in 2 pathways, suggesting that the differences are random and that sublining macrophages in RA might not drive pathology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Spatial transcriptomic analysis reveals distinct region- and cell-type-specific transcriptional profiles distinguishing RA from OA synovium. Regional analysis identifies niche-specific fibroblast functions related to inflammation in the lining and adaptive immunity in the sublining were identified, which could help identify subsets as therapeutic targets for patient-specific mechanisms of disease.

Disclosure: C. Machado: None; **M. Yao**: None; **D. Boyle**: None; **R. Benschop**: Eli Lilly, 12, 3, 8; **J. Parker**: Eli Lilly, 3; **W. Wang**: None; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 0070

Integrating Synovial Protein Signatures and Serum Profiles to Predict Disease Activity and Treatment Response in Early Rheumatoid Arthritis

Chary López pedrera[1], Sagrario Corrales[2], Julio Osuna[3], Rafaela Ortega-Castro[4], Jerusalén Calvo[5], Lourdes Ladehesa[6], Ismael Sanchez-Pareja[2], Laura muñoz-Barrera[2], Desiree Ruiz-Vilchez[7], Christian Merlo[8], MARIA ANGELES AGUIRRE ZAMORANO[2], Nuria Barbarroja[9], Tomás Cerdó[2], Marta Alarcon-Riquelme[10], Carlos Pérez Sánchez[11], Alejandro Escudero Contreras[5] and Concepción Aranda-Valera[5], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [3]IMIBIC/Reina Sofia Hospital/University of Cordoba, Spain., Córdoba, Republic of Korea, [4]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [5]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [6]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [7]Department of Rheumatology, Reina Sofía University Hospital / Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [8]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain, Cordoba, Spain, [9]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [10]Fundación Progreso y Salud, Andalusian Government, Granada, Spain, [11]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The analysis of synovial tissue has been instrumental in advancing our understanding of Rheumatoid Arthritis (RA) pathogenesis. As an alternative, the identification of serum biomarkers that mirror synovial activity offers a promising and less invasive strategy for diagnosing and monitoring RA. This approach could address existing challenges and significantly enhance the implementation of precision medicine in the management of RA. The objectives of this study were: 1- To characterize synovial tissue-secreted proteins in early RA patients that contribute to serum inflammatory profiles, 2- To identify subsets of early RA patients with distinct serum levels of the protein signature and evaluate their association with disease activity and clinical response to conventional DMARDs (cDMARDs).

Methods: Synovial explants obtained via ultrasound-guided biopsies from 15 early RA patients were cultured *in vitro* for 24 hours to profile secreted proteins using proximity extension assay (PEA) technology (Olink), targeting 92 inflammation-related proteins. Proteomic profiles were also evaluated in serum samples from the same subjects, and correlation studies

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

were performed. Validation of the identified protein signature was performed in an independent cohort of 86 early RA patients, aiming to assess its association with clinical response to cDMARDs.

Results: Eleven synovial-secreted proteins (CXCL6, CXCL9, CXCL11, DNER, FGF-5, IL1α, MCP-1, βNGF, STAMBP, TNF, TNFβ) showed significant correlations with their serum levels in early RA patients. These proteins are involved in biological processes closely linked to RA pathophysiology, such as cell proliferation, cytokine/chemokine signaling, neutrophil chemotaxis and inflammation. Clinically, higher levels of this inflammatory signature were observed in RA patients with active disease, elevated acute-phase reactants and high titres of autoantibodies.

Unsupervised clustering in an independent cohort of 86 early-stage RA patients treated with cDMARDs identified two patient groups with distinctive baseline serum protein profiles. The group with higher levels of the inflammatory signature exhibited higher disease activity and a better clinical response to cDMARDs after 6 and 12 months of treatment. Machine learning algorithms identified clinical and molecular signatures as potential predictors of response to cDMARDs treatment with high accuracy, which was further increased when both features were integrated in a mixed model (AUC: >0.8).

Conclusion: This study identifies a synovial tissue–secreted protein signature that contributes to both the circulating inflammatory profile and clinical characteristics of early RA patients. This signature stratifies early RA patients into subgroups with distinct clinical responses, demonstrating its potential as a robust predictor of therapeutic response to cDMARDs. These findings underscore the value of serum biomarkers reflecting the molecular profile of the synovium to advance personalized medicine in RA.

Funded by Instituto de Salud Carlos III (ISCIII) and co-funded by the European Union. Supported by EU/EFPIA IMI-JU 3TR, ISCIII (PI24/00959, CD21/00187, RICOR-21/0002/0033) and RYC2021-033828-I.

Disclosure: C. López pedrera: None; **S. Corrales**: None; **J. Osuna**: None; **R. Ortega-Castro**: None; **J. Calvo**: None; **L. Ladehesa**: None; **I. Sanchez-Pareja**: None; **L. muñoz-Barrera**: None; **D. Ruiz-Vilchez**: None; **C. Merlo**: None; **M. AGUIRRE ZAMORANO**: None; **N. Barbarroja**: None; **T. Cerdó**: None; **M. Alarcon-Riquelme**: None; **C. Pérez Sánchez**: None; **A. Escudero Contreras**: None; **C. Aranda-Valera**: None.

Abstract Number: 0071

Unravelling Transcriptomic Landscapes in Rheumatoid Arthritis and Systemic Lupus Erythematosus: Shared and Unique Molecular Signatures related to relevant clinical features.

Chary López pedrera[1], Tomás Cerdó[2], Ismael Sanchez-Pareja[2], Daniel Toro[3], MARIA ANGELES AGUIRRE ZAMORANO[2], Elena Moreno-Caño[4], Laura muñoz-Barrera[2], Sagrario Corrales[2], Rafaela Ortega-Castro[5], Concepción Aranda-Valera[6], Lourdes Ladehesa[7], Jerusalén Calvo[6], Pilar Font[8], M Carmen Abalos-Aguilera[9], Desiree Ruiz-Vilchez[10], Christian Merlo-Ruiz[9], Nuria Barbarroja[11], Carlos Pérez Sánchez[12], Marta Alarcon-Riquelme[13] and Alejandro Escudero Contreras[6], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [3]GENYO / Karolinska Institutet, Granada / Stockholm, Spain, [4]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Córdoba, Spain, [5]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [6]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [7]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [8]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, SpainBiomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [9]Rheumatology service/Maimonides Institute for Research in Biomedicine

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [10]Department of Rheumatology, Reina Sofía University Hospital / Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [11]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [12]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [13]Fundación Progreso y Salud, Andalusian Government, Granada, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aimed to identify shared and distinct gene and protein expression profiles associated with clinical features in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and SLE with antiphospholipid syndrome (SLE+APS) patients, using integrated multimodal analyses.

Methods: Advanced computational approaches combined clinical data, transcriptomic profiles from peripheral blood mononuclear cells (RNA sequencing), and serum proteomic profiles (proximity extension assays) in 257 RA and 66 SLE patients (20 with SLE+APS). Transcriptomic data were processed and normalized, followed by gene set variation analysis (GSVA) for pathway-level changes. Unsupervised hierarchical clustering identified patient subgroups and gene modules. Correlation analyses explored associations between gene modules, inflammatory protein profiles, and clinical parameters.

Results: Clustering identified three clusters with unique gene expression patterns across 11 gene modules, reflecting different biological pathways. Clinically, C1 was linked to increased cardiovascular (CV) risk in RA and higher disease activity / renal involvement in SLE. C2 exhibited high disease activity and lung involvement in RA and increased CV risk in SLE. C3 showed an intermediate profile, with autoantibody positivity and significant renal involvement, thrombosis and abortions in SLE+APS.

Molecularly, C2 had heightened activity in myeloid cells and inflammation; C1 and C3 displayed increased T and B cell activity. Integrin-mediated cell adhesion pathways were commonly altered. Proteomic analysis supported these findings, revealing the greatest inflammatory protein changes in C2. Correlation analyses revealed relationships among modules related to myeloid cell activity, cell adhesion, inflammation, and T-cell activation correlating with several cytokines and chemokines. Specifically, the IFN response module linked with high IFN-gamma, CXCL10, and MCP-2 levels, while cell adhesion modules connected to several chemokines. Reduced T and B cell activity correlated negatively with increased levels of inflammatory proteins, suggesting different sources of inflammation and immune dysfunction.

Shared genomic modules correlating with clinical profiles included cell cycle regulation with disease activity in RA and SLE, integrin-mediated cell adhesion with CV risk in RA, and myeloid cell activity with CV risk in SLE. Distinct correlations included inflammatory networks and IFN response with disease activity in RA and CV risk in SLE, T cell activity negatively with activity in RA and B cell activity with lung involvement in RA.

Conclusion: Overall, our integrated analysis reveals distinct transcriptomic clusters and molecular heterogeneity in RA, and SLE, driven by inflammation and immune dysregulation. These findings highlight both shared and disease-specific molecular signatures associated with clinical manifestations, providing insights into disease mechanisms and potential therapeutic targets.

Supported by EU/EFPIA IMI-JU 3TR, ISCIII (PI24/00959, CD21/00187, and RICOR-24/0007/0019), co-financed by the European Union, MINECO (RYC2021-033828-I/PID2022-141500OA-I00).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. López pedrera: None; **T. Cerdó**: None; **I. Sanchez-Pareja**: None; **D. Toro**: None; **M. AGUIRRE ZAMORANO**: None; **E. Moreno-Caño**: None; **L. muñoz-Barrera**: None; **S. Corrales**: None; **R. Ortega-Castro**: None; **C. Aranda-Valera**: None; **L. Ladehesa**: None; **J. Calvo**: None; **P. Font**: None; **M. Abalos-Aguilera**: None; **D. Ruiz-Vilchez**: None; **C. Merlo-Ruiz**: None; **N. Barbarroja**: None; **C. Pérez Sánchez**: None; **M. Alarcon-Riquelme**: None; **A. Escudero Contreras**: None.

Abstract Number: 0072

Impact of Baricitinib on Cardiovascular Health in Biologic-naïve Rheumatoid Arthritis patients: A Comparative Study with TNF Inhibitors and Conventional DMARDs

Chary López pedrera[1], Laura muñoz-Barrera[2], Rafaela Ortega-Castro[3], Sagrario Corrales[2], Jerusalen Calvo Gutierrez[4], Concepción Aranda Valera[5], Lourdes Ladehesa[6], Pilar Font[7], Ismael Sanchez-Pareja[2], Elena Moreno-Caño[5], M Carmen Abalos-Aguilera[8], Christian Merlo-Ruiz[8], MARIA ANGELES AGUIRRE ZAMORANO[2], Pedro Seguí-Azpilcueta[9], Tomás Cerdó[2], Nuria Barbarroja[10], Rocío González Conejero[11], Constantino Martínez[11], Carlos Pérez Sánchez[12] and Alejandro Escudero[13], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [4]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Sevilla, Spain, [5]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Córdoba, Spain, [6]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [7]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, SpainBiomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [8]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [9]Radiology Service, Reina Sofia Hospital/Maimonides Institute for Research in Biomedicine of Cordoba/University of Cordoba, Spain, Córdoba, United Kingdom, [10]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [11]Servicio de Hematología, Hospital Universitario Morales Meseguer, Centro Regional de Hemodonación, Universidad de Murcia, IMIB Pascual Parrilla., Murcia, Spain, [12]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [13]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Andalucia, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Therapeutic advances in RA have introduced effective treatments, including b/tsDMARDs such as Baricitinib. However, its cardiovascular safety profile remains unclear, partly due to the limited scope of existing studies, limiting its optimal positioning within treatment strategies. This study's objective was to conduct clinical-molecular analyses to elucidate the effects of Baricitinib (4mg/day) on the proinflammatory, prothrombotic, and cardiovascular risk profiles of RA patients, in comparison with TNF inhibitors (TNFi) and cDMARDs

Methods: A longitudinal, prospective study was conducted in three RA patient cohorts (n=25 each) who received standard-dose treatment with cDMARDs, TNFi or Baricitinib. All had moderate-severe disease activity (DAS28≥3.2), inadequate response to methotrexate and were naïve to b/tsDMARDs. A control group of 25 age- and sex- matched healthy donors was included.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Clinical-demographic data were collected at baseline and after 6 and 12 months. Carotid ultrasound evaluated atherothrombotic risk.Blood samples were obtained to isolate serum, plasma and monocytes prior to and after treatment. Consequent analyses included: screening for hypercoagulability-associated polymorphisms (Factor V Leiden and prothrombin); quantification of prothrombotic markers (D-dimer, prothrombin F1+2 and TAT complex); transcriptomic monocyte profiling via RNA-seq;and serum proteomic analysis of 276 inflammation- and CV-related proteins using proximity extension assay (Olink/Cobiomic)

Results: At baseline, disease activity was comparable across groups. All treatments led to significant improvements at 6-12 months, although Baricitinib demonstrated superior clinical efficacy, achieving the highest remission rates at both timepoints. Patients exhibited a baseline hypercoagulable state, although all therapies reduced D-dimer levels supporting their capacity to attenuate prothrombotic activity. Genetic hypercoagulability variants were infrequent, while carotid plaque prevalence and traditional CV risk factors were similar among cohorts.

Transcriptomic analysis showed that each therapy induced distinct gene expression changes, with shared effects on inflammation, interferon response and cell metabolism. Proteomic profiling revealed broad molecular shifts, with Baricitinib altering 68 proteins, TNFi 38, and sDMARDs 39. Common changes involved inflammation and vascular remodeling, while Baricitinib uniquely regulated 51 proteins related to cytokine signaling, angiogenesis, and matrix remodeling. Several modulated genes and proteins were linked to known CV risk markers. However, the unique molecular shifts highlight the differential impact of each treatment on CV risk

Conclusion: Baricitinib showed superior clinical efficacy, with higher rates of sustained remission beyond one year. Molecular studies suggest it not only does not increase CV risk but may confer beneficial effects by normalizing gene and protein profiles linked to elevated CV risk.

Funded by Instituto de Salud Carlos III (ISCIII), co-funded by European Union. Supported by Lilly (I4V-NS-0032), ISCIII (PI23/00027, PI24/00959, CD21/00187, RICORS: 24/0007/0019), and RYC2021-033828-I

Disclosure: C. López pedrera: None; **L. muñoz-Barrera**: None; **R. Ortega-Castro**: None; **S. Corrales**: None; **J. Calvo Gutierrez**: None; **C. Aranda Valera**: None; **L. Ladehesa**: None; **P. Font**: None; **I. Sanchez-Pareja**: None; **E. Moreno-Caño**: None; **M. Abalos-Aguilera**: None; **C. Merlo-Ruiz**: None; **M. AGUIRRE ZAMORANO**: None; **P. Seguí-Azpilcueta**: None; **T. Cerdó**: None; **N. Barbarroja**: None; **R. González Conejero**: None; **C. Martínez**: None; **C. Pérez Sánchez**: None; **A. Escudero**: None.

Abstract Number: 0073

HLA-DQA1*01:02 Is Associated With IgG Multi-Reactivity With Citrulline-Containing Type II Collagen Epitopes While HLA-DRB*04:01 Is Associated With More Private Reactivity With Citrulline-Containing IgG Epitopes In Rheumatoid Arthritis

S. Janna Bashar[1], **Courtney Myhr**[1], Adam Titi[1], Zihao Zheng[1] and Miriam Shelef[2], [1]University of Wisconsin-Madison, Madison, [2]University of Wisconsin-Madison, Madison, WI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Anti-citrullinated protein antibodies (ACPAs) in rheumatoid arthritis (RA) can be promiscuous, with cross-reactive binding to many antigens containing short motifs, or more private with little cross-reactivity. Also, ACPA reactivity patterns differ among people with RA, including for motif-containing epitopes in important self-antigens like type II collagen and IgG (the latter of which is bound by RA-associated rheumatoid factors, RFs), with limited understanding of the underlying mechanism. The objective of this study was to determine if HLA alleles associate with ACPA reactivity patterns.

Methods: For 100 ACPA+RF+ RA participants, serum IgG binding was quantified by enzyme-linked immunosorbent assay to five citrulline-containing peptides derived from type II collagen (all with citrulline-glycine motifs) and five citrulline-containing peptides derived from IgG1 (four with citrulline-serine motifs). Also, antibody and serum multi-reactivity were evaluated. HLA loci were genotyped, and HLA alleles present differentially in RA participants with high versus low IgG binding to specific peptides as well as with multi-reactivity versus limited reactivity were identified by Fisher's exact test.

Results: Serum IgG multi-reactivity for citrulline-glycine motif-containing collagen peptides was high, at least partially due to promiscuous antibodies. HLA-DQA1*01:02 was present in more participants with anti-citrullinated collagen antibodies and sera multi-reactive with the collagen peptides. In contrast, serum multi-reactivity was low for IgG1-derived peptides due at least in part to more private antibodies. Shared epitope-containing HLA-DRB*04:01 and HLA-DRB*10:01 were present more frequently in participants with some RA-associated RFs that bind citrulline-containing IgG epitopes, irrespective of a citrulline-serine motif. Several HLA alleles associated with specific IgG reactivities.

Conclusion: These findings suggest that specific HLA alleles may contribute to the different reactivity patterns of promiscuous anti-citrullinated collagen antibodies and more private RA-associated RFs. Moreover, to the best of our knowledge, these findings provide the first evidence for a role for HLA-DQA1*01:02 in RA as well as the first HLA association with autoantibody multi-reactivity.

Disclosure: S. Bashar: None; **C. Myhr**: None; **A. Titi**: None; **Z. Zheng**: None; **M. Shelef**: Revel Pharmaceuticals, 2.

Abstract Number: 0074

Rheumatoid Factors (RFs) in RA Patient Sera Do Not Bind To Fc-Free Certolizumab Pegol, But Do Bind To Fc-Containing Anti-TNF-α Biological DMARDs, Driving Immune Complex Formation and Cellular Clearance

Sophie Hopkin[1], Kathryn Malpas[1], David Kallenberg[1], Jacqueline O'Neill[1], Geofrey Odede[1], Kerry Tyson[1], Sue Cross[1], Tatiana SOKOLOVA[2], Bernard Lauwerys[3], Baran Ufuktepe[4], Patrick Durez[5], Susanna Bidgood[1] and **David Humphreys**[1], [1]UCB Pharma, Slough, England, United Kingdom, [2]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Brussels Hoofdstedelijk Gewest, Belgium, [3]Systemic and Inflammatory Rheumatic Diseases Section, Institute of Experimental and Clinical Research (IREC), UCLouvain, Brussels, Belgium, [4]UCB Pharma Istanbul, Turkey, istanbul, Turkey, [5]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatologie, Brussels, Brussels Hoofdstedelijk Gewest, Belgium

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: RFs are polyclonal autoantibodies which bind the Fc domain of IgGs. Patients with RA and high RF levels experience reduced serum drug concentrations and disease control when treated with Fc-containing biological

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

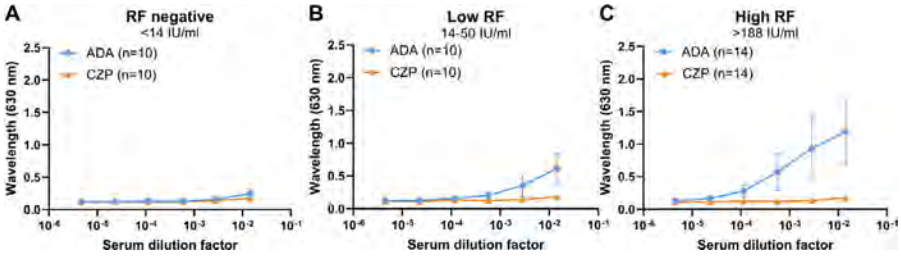
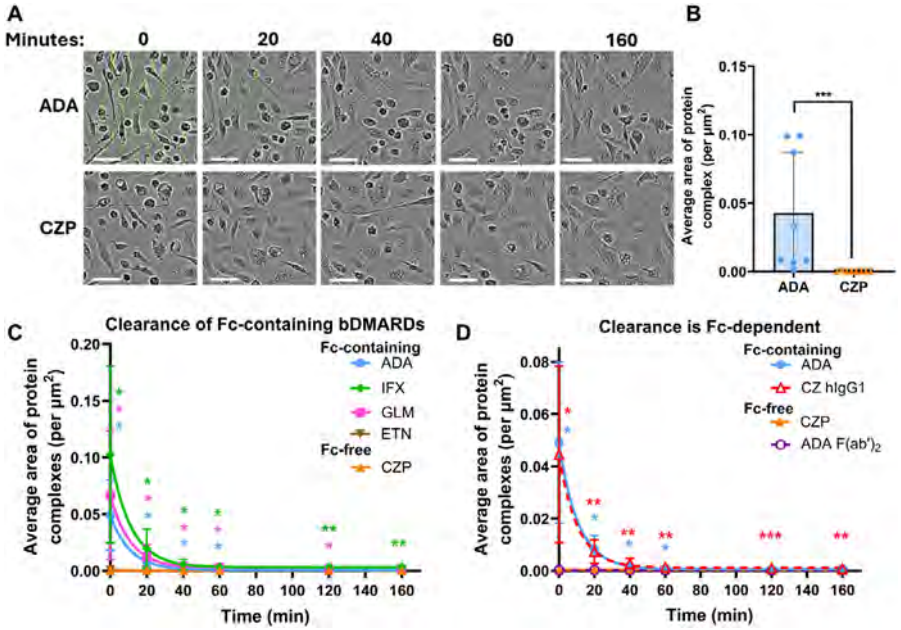


Figure 1. In RA patient sera, RFs bound to Fc-containing ADA but not Fc-free CZP. ELISA assays showed (A) no detectable binding of RF IgM in RF negative (<14 IU/mL) patient sera to ADA (blue) or CZP (orange), (B & C) binding of RF IgM in low RF (14-50 IU/mL) and high RF (>188 IU/mL) patient sera to ADA (blue) but not to CZP (orange). (n=10-14/patient group; n=2 independent experiments; mean±SD)

DMARDs (bDMARD). Fc-free certolizumab pegol (CZP) exhibits stable serum drug concentrations and efficacy independent of patient RF levels[1-4]. Previously, we have shown that monoclonal recombinant RF IgMs bind to Fc-containing bDMARDs *in vitro* and form protein complexes that are cleared by human macrophages. Fc-free CZP is not bound and avoids clearance[5-6]. In this study, serum samples from RA patients were classified according to RF level, and the ability of human sera RFs to bind to and clear Fc-containing anti-TNF-α bDMARDs was investigated.

Methods: RF levels in human patient sera were quantified by RF latex agglutination and the sera was classified as "high RF" (>188 IU/ml), "low RF" (14-50 IU/ml) or "RF negative" (<14 IU/ml). bDMARDs [adalimumab (ADA), infliximab (IFX), golimumab (GLM), etanercept (ETN), CZP] were expressed and purified as previously described[5-6]. The CZP variable region sequence was incorporated into a full length human IgG1 to produce Fc-containing certolizumab hIgG1 (CZ hIgG1). ADA was digested with FabRICATOR (Genovis) to produce Fc-free ADA di-Fab (ADA F(ab')$_2$). RF binding to bDMARDs was assessed by ELISA. Live cell imaging of primary human macrophages was performed with an Incucyte microscope (Sartorius).



Protein complexes formed between patient sera RFs, Fc-containing bDMARDs and TNF-α were cleared by human macrophages in vitro. (A) High RF patient sera, bDMARDs and TNF-α were mixed and incubated with primary human macrophages at 4°C. Cells were washed and remaining protein complexes detected with Fab anti-human IgM Fc5µ FITC. Cells were moved to 37°C and imaged for 160 minutes (scale bar=100 µm). Quantification of the protein complex area in the images presented as area of protein complex per µm2 at (B) timepoint 0 minutes (random sampling; n=8/bDMARD; mean±SD), and (C-D) over time (non-random sampling; n=4/bDMARD; mean±SD), * P<0.05, ** P<0.01, *** P<0.001 by (B) paired t-test and (C-D) two-way ANOVA with Dunnett's multiple comparison test (compared to CZP group) on log-transformed data.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In low and high RF patient sera, RFs bound to Fc-containing ADA by ELISA but not to Fc-free CZP. The magnitude of RF binding to ADA was greater in high RF sera than in the low RF sera. RF negative patient sera had no detectable binding to either bDMARD (**Figure 1**). Human sera RFs formed protein complexes with Fc-containing ADA, IFX, and GLM in the presence of TNF-α, but not with ETN or Fc-free CZP. No complexes formed in RF negative sera. The binding of human sera RFs to bDMARDs was Fc-dependent. Protein complexes formed in high RF sera with Fc-containing ADA and CZ hIgG1, but not with Fc-free CZP or ADA $F(ab')_2$. RF-bDMARD-TNF-α protein complexes were rapidly cleared by primary human macrophages (**Figure 2**).

Conclusion: In RA patient sera, RFs bound to Fc-containing bDMARDs, but not to Fc-free CZP. Serum RF levels corresponded with the magnitude of binding observed. RF binding to Fc-containing bDMARDs drove protein complex formation in the presence of TNF-α, which were cleared by macrophages *in vitro*. These findings provide mechanistic insights into why high RF levels negatively impact Fc-containing bDMARD efficacy, while CZP efficacy is independent of patient RF levels.

References: 1. Martínez-Feito A. Clin Exp Rheumatol. 2024;42(5):999-1005; **2**. Smolen J S. Rheumatol. 2024;63 (11):3015-24 **3**. Smolen J S. Arthritis Rheumatol. 2024;76(suppl 9) **4**. Miyazaki Y. Mod Rheumatol. 2025;35:S56 **5**. Bidgood S. Ann Rheum Dis. 2024; 83(1):727 **6**. Bidgood S. Arthritis Rheumatol. 2024;76(suppl 9)

Disclosure: S. Hopkin: UCB Pharma, 3; **K. Malpas**: UCB Phama, 3; **D. Kallenberg**: UCB Pharma, 3; **J. O'Neill**: UCB Pharma, 3; **G. Odede**: UCB Pharma, 3; **K. Tyson**: UCB Pharma, 3, 11; **S. Cross**: UCB Pharma, 3, 11; **T. SOKOLOVA**: None; **B. Lauwerys**: UCB, 3, 12, Shareholder; **B. Ufuktepe**: UCB Pharma, 3, 11; **P. Durez**: None; **S. Bidgood**: UCB Pharma, 3; **D. Humphreys**: UCB Pharma, 3, 3, 11, 11.

Abstract Number: 0075

Impact of CXCL2 and IL-11 from Rheumatoid Arthritis Synovial Fibroblasts on Angiogenesis and Endothelial Cell Network Formation

Elena Neumann[1], Frederik Loetfering[2], Paula Welbrink[3], Corinna Heck[3], Daria Kuersammer[3], Klaus Frommer[1], Stefan Rehart[4] and Ulf Müller-Ladner[1], [1]Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Justus-Liebig-University, Germany, Bad Nauheim, Hessen, Germany, [2]Justus Liebig University Giessen, Campus Kerckhoff, Bad Nauheim, [3]Justus-Liebig-Universität Gießen, Campus Kerckhoff, Bad Nauheim, Germany, [4]Agaplesion Markus Hospital, Frankfurt, Hessen, Germany

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In rheumatoid arthritis (RA), hypervascularization contributes to synovial inflammation. RA synovial fibroblasts (RASF) contribute to cartilage and bone erosion but also promote angiogenesis. Activated RASF secrete inflammatory, angiogenesis and matrix remodeling factors including CXCL2 and IL-11. While CXCL2 is primarily recognized for recruiting leukocytes to inflamed tissues, it also promotes angiogenesis. IL-11 is involved in bone resorption and fibrosis. Angiopoietin-2 (ANGPT2) is known to be dysregulated in pathological vessel formation. Therefore the role of CXCL2 and IL-11 in RASF-mediated altered angiogenesis was evaluated.

Methods: In the SCID mouse model of RA, healthy cartilage was subcutaneously co-implanted with RASF. RASF-mediated helix-like vessel (HLV) formation was evaluated after 3-45 days. Implants, RA and osteoarthritis (OA) synovium were stained for ANGPT2 and CXCL2. RASF were stimulated with 0.1 or 1ng/ml IL-1β once or repetitively and ELISA, realtime-PCR and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

RNAseq performed and supernatants used for 2D tube formation assays (TFA). TFA were performed by seeding HUVEC on Matrigel®. HUVEC were treated with supernatants or CXCL2 (25/50/100ng/ml) or 50ng/ml CXCL2 was combined with the CXCR2 antagonist SB225002 (0.015/0.03/0.06μM) or 10ng/ml IL-11 with/without the IL-11 inhibitor AF-218 (100/250/500ng/ml). To evaluate the role of VEGF, bevacizumab or ECM without VEGF with/without stimulants were used. After 4h, cell network area of TFA was measured using the Keyence BZ-X800© software.

Results: In SCID mice, RASF-specific HLV formation started at d3 and increased until d30. Compared to OA synovium, ANGPT2 was significantly upregulated in RA vessels and implants. RNAseq showed altered signaling pathways of angiogenesis. Repetitive RASF-stimulation significantly reduced IL-1β-induced IL-6, IL-11 and CXCL2 compared to RASF stimulated once (e.g. IL-6: 1^{st}: 5076±1730 vs 3^{rd}: 1890±758pg/ml, p< 0.0001; IL-11: 1^{st}: 451±205 vs 3^{rd}: 69±51pg/ml, p< 0.0001). Repetitive stimulation of HUVEC+15%RASF resulted in a significant IL-6 increase for subsequent stimulations (1^{st}vs.3^{rd}: p=0.02). RASF significantly reduced tube thickness (22.9μm *SD=6.3* to 16.6μm *SD=2.2*) compared to HUVEC alone (p=0.014) but increased ANGPT2 release (4h: 5%, 48h: 14%). IL-1β-stimulated RASF supernatants (1^{st} vs 3^{rd}) reduced HUVEC network area to 78%, p=0.01 vs 77%, p=0.04 (100%: no supernatant-transfer control). CXCL2 decreased the network area (e.g. 50ng/ml: 71% of 100% control, p=0.02; 25ng/ml: 73%, p=0.04). SB225002 partially reversed the CXCL2 effect (0.015: 93%; 0.03: 87%; 0.06: 92%). IL-11 also disturbed the network area (63%, p=0.08) and AF-218 partially reversed the effect (e.g. 250ng/ml: 72%, 500: 90%). Bevacizumab prevented tube formation which could in part be restored by addition of ANGPT2. Addition of ANGPT2 to ECM had a similar effect.

Conclusion: RASF affect vascularization in vitro and in vivo. CXCL2, IL-11 and RASF-derived supernatants altered the HUVEC network. These findings suggest that CXCL2 as well as IL-11 produced by RASF may significantly contribute to the dysregulated angiogenesis involving ANGPT2 observed in RA.

Disclosure: E. Neumann: None; **F. Loetfering**: None; **P. Welbrink**: None; **C. Heck**: None; **D. Kuersammer**: None; **K. Frommer**: None; **S. Rehart**: None; **U. Müller-Ladner**: None.

Abstract Number: 0076

Antibodies to Malondialdehyde-acetaldehyde Are Associated with Circulating Inflammatory Mediators During the Preclinical Stages of Rheumatoid Arthritis

Emma Weis[1], Harlan Sayles[1], Geoffrey Thiele[1], Samir Rachid Zaim[2], Tony Merriman[3], Bryant England[1], Xiaojun Li[2], LauraKay Moss[4], Jess Edison[5], Marie Feser[4], V. Michael Holers[6], Kevin Deane[7], Ted Mikuls[1] and Austin Wheeler[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]Allen Institute for Immunology, Seattle, WA, [3]University of Alabama at Birmingham, Homewood, AL, [4]University of Colorado Anschutz Medical Campus, Aurora, CO, [5]Uniformed Services University of the Health Sciences / National Capital Consortium- Walter Reed Bethesda, Bethesda, MD, [6]University of Colorado, Denver, CO, [7]University of Colorado Denver Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Circulating concentrations of anti-malondialdehyde-acetaldehyde (MAA) antibodies distinguish patients with RA and are detectable years prior to arthritis onset. Recent data demonstrate that anti-MAA antibodies play a pathogenic role in RA by promoting osteoclastogenesis and 'priming' monocytes for pro-inflammatory responses. While

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical and demographic characteristics of participants. Abbreviations: malondialdehyde-acetaldehyde adduct (MAA), immunoglobulin (Ig) Values shown as mean ± standard deviation unless specified.

	RA cases (n = 122)
Age at Diagnosis, years	37.20 ± 7.73
Female sex, n (%)	63 (51.6)
Race, n (%)	
White	66 (54.1)
Black	38 (31.2)
Other	19 (14.7)
Number of pre-diagnosis samples per individual	1.59 ± 0.68
Range of pre-diagnosis samples, years	4.22 ± 5.81
Anti-MAA antibody concentration, all samples (ng/mL)	
IgA	216.5 ± 340.0
IgG	655.9 ± 685.7
IgM	424.1 ± 331.9
Individuals with ≥1 anti-MAA antibody upper quartile measurement, n (%)	
IgA	36 (29.5)
IgG	35 (28.7)
IgM	38 (31.1)
All	8 (6.6)

these data suggest that anti-MAA antibodies are involved in the transition from pre-RA to clinical disease, their pathogenic role remains unknown. We evaluated whether anti-MAA antibody status is associated with differences in serum protein expression during the preclinical stage of RA development.

Methods: We used pre-diagnosis serum samples from RA cases meeting 1987 ACR criteria from the Department of Defense Serum Repository (Zaim et al., *Arthritis Rheum* 2025). Serum was tested for anti-MAA IgA, IgG, and IgM by ELISA, with high anti-MAA for each subtype defined as the upper quartile of all measurements. Olink Proteomics Immune

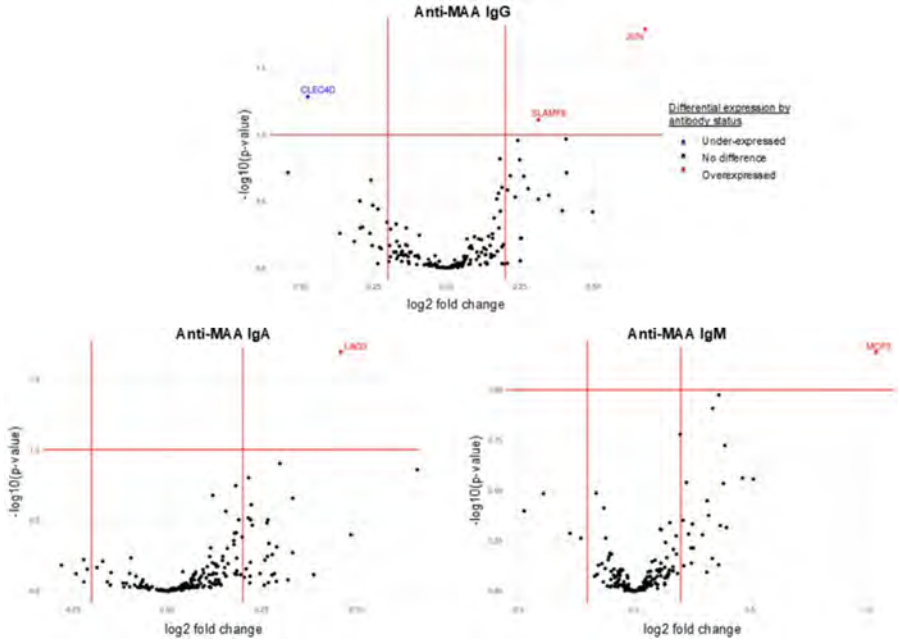


Figure 1. Volcano plots for differential protein expression based on anti-malondialdehyde adduct antibody status. Abbreviations: malondialdehyde-acetaldehyde adduct (MAA), immunoglobulin (Ig)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Proteins differentially expressed based on anti-malondialdehyde antibody status in pre-RA to early RA period. Abbreviations: immunoglobulin (Ig), lymphocyte activation gene-3 (LAG3), transcription factor AP-1 (JUN), signaling lymphocytic activation molecule family member 8 (SLAMF8), C-type lectin domain family 4 (CLEC4D), monocyte-chemotactic protein 3 (MCP3), chemokine C-C motif ligand 7 (CCL7) Negative log2 fold change indicates inverse relationship (CLEC4D).

Protein	Ig Subtype	Log2 FC	Adjusted p-value	General Function & Proposed Relation to RA Pathogenesis
LAG3	IgA	0.381	0.01	T-cell regulation ***RA:*** *Associated with radiographic progression and seropositivity*
JUN	IgG	0.676	0.02	T-cell regulation ***RA:*** *Pro-inflammatory role in macrophage-driven inflammation and bone destruction*
SLAMF8	IgG	0.313	0.08	Immune regulation ***RA:*** *Increased in RA synovial tissue*
CLEC4D	IgG	-0.472	0.05	Cell signaling
MCP3 (CCL7)	IgM	1.039	0.06	Immune regulation ***RA:*** *Increased expression RA serum and synovial fluid; Drives macrophage polarization*

Regulation, Inflammation, and Cell Regulation panels were performed on all samples (n = 197 analytes). The association of each protein (normalized expression value) with anti-MAA antibody status in longitudinally collected samples was tested via linear mixed models accounting for age, race, gender, and time to diagnosis with a subject-level random effect. P-values were adjusted for false discovery rate (FDR) and specific proteins were selected for further evaluation based on FDR-adjusted $p < 0.1$ and absolute log2 fold-change (FC) ≥ 0.2.

Results: A total of 122 participants with RA were included (mean age at diagnosis 37 years, 52% female), all with ≥1 pre-RA sample available (mean 1.59, **Table 1**). For each anti-MAA subtype, ~30% of participants had ≥1 value in the upper quartile at any time (6.6% for all 3 subtypes; **Table 1**). Five proteins were significantly overexpressed in the presence of high anti-MAA isotypes: 1 with IgA, 3 with IgG, and 1 with IgM (**Figure 1, Table 2**); most with established or suspected roles in RA pathogenesis. The largest fold-change was observed with IgM-MAA and macrophage chemotactic protein 3 (MCP3), which is highly expressed in RA synovium and promotes synovitis. The protein associated with IgA-MAA, lymphocyte activation gene-3 (LAG3), inhibits T cell activation, and high serum levels in RA are associated with autoantibody positivity and radiographic progression. IgG-MAA showed the most associations, where the largest was with transcription factor AP-1 (JUN), known to promote synovitis and bone destruction in RA. The only negative association was seen with IgG-MAA and C-type lectin domain family 4D (CLEC4D), a protein thought to have an important role in resolving inflammation.

Conclusion: Anti-MAA antibody status is associated with differences in the serum proteome during the preclinical stages of RA, particularly among mediators of inflammation and immune responses. This differential expression implicates several established pathogenic mechanisms in RA (**Table 2**), suggesting that anti-MAA antibodies may comprise part of a distinct pathophysiologic state leading towards progression of clinical disease during the transition from pre-RA.

Disclosure: E. Weis: None; **H. Sayles**: None; **G. Thiele**: None; **S. Rachid Zaim**: None; **T. Merriman**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **X. Li**: Eli Lilly, 5; **L. Moss**: None; **J. Edison**: None; **M. Feser**: None; **V. Holers**: None; **K. Deane**: Inova Diagnostics, 1; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **A. Wheeler**: None.

Abstract Number: 0077

Transformer-based multi-omics study identifies important role of glycine, serine and threonine metabolism pathway in rheumatoid arthritis complicated by anemia

Fanxin zeng[1], Jianxin Huang[2], Yuanli Wei[3], Dongmei Wang[3], Jianghua Chen[4], Congcong Jian[1], Xiaoting Zhu[5], Shilin Li[5], Jie Zhang[5], Tingting Wang[3], Caizhen Liu[6], Lingli Wei[3], Jing Gao[3], Jing Zhu[7], Qinghua Zou[8] and Jianhong Wu[3], [1]Departmant of Clinical Research Center, Sichuan Clinical Research Center for Medical Imaging, Dazhou Central Hospital; Medical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

School, Sichuan University of Arts and Sciences; School of Basic Medical Science, Chengdu University of Traditional Chinese Medicine, Dazhou, China (People's Republic), [2]Institute of Basic Medicine and Forensic Medicine, North Sichuan Medical College, Nanchong, China (People's Republic), [3]Department of Rheumatology and Immunology, Dazhou Central Hospital, Dazhou, China (People's Republic), [4]Dazhou Vocational College of Chinese Medicine, Dazhou, China (People's Republic), [5]Departmant of Clinical Research Center, Sichuan Clinical Research Center for Medical Imaging, Dazhou Central Hospital, Dazhou, China (People's Republic), [6]Department of Rheumatology and Immunology, Dazhou Central Hospital, Dazhou, [7]Department of Rheumatology and Immunology, Sichuan Provincial People's Hospital, Chengdu, China (People's Republic), [8]Department of Rheumatology and Immunology, First Affiliated Hospital of Army Medical University, Chongqing, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Anemia is a prevalent hematologic complication of rheumatoid arthritis (RA) that exacerbates the disease process and severely impacts clinical performance and treatment strategies. We propose to explore the potential molecular changes in RA complicated by anemia (RA_ane) based on transformer architecture and comprehensive multi-omics analysis.

Methods: This study recruited 257 RA patients, 113 controls, and disease comparison groups including 88 systemic lupus erythematosus (SLE) and 37 gout patients. Their plasma samples were collected for metabolomics sequencing, fecal samples for 16S rRNA sequencing, and peripheral blood mononuclear cells were used for transcriptomics, proteomics and phosphoproteomics studies. The transformer architecture and difference analysis were used to obtain overlapping difference features, and 5 machine learning algorithms (k-nearest neighbor algorithm [KNN], support vector machine [SVM], random forest [RF], recursive feature elimination-RF [RFE-RF], and eXtreme gradient boosting algorithm [XGBoost]) were further used to perform significant feature screening and construct clinical diagnostic models.

Results: By integrating the results of the above characterization screen, L-tryptophan, glyceric acid, L-malic acid, ALAS2, CA1, SELENBP1, and RPIA were identified as key biomarkers of RA_ane. Further functional enrichment analyses revealed the core role of the glycine, serine and threonine metabolism (GSTM) pathway in RA_ane and were validated by functional enrichment analyses in other dimensions of multi-omics, in addition to metabolomics and microbiomics analyses of SLE and gout, which indicated that alterations in the GSTM pathway are RA_ane-specific features. Subsequently, we developed and validated multi-omics diagnostic models for RA_ane patients with AUC values ranging from 0.75 to 0.84, and finally, we constructed a molecular map of GSTM-based multidimensional changes in the RA_ane population.

Conclusion: This study demonstrated that GSTM pathway plays a crucial role in RA_ane, shedding light on potential therapeutic interventions.

Disclosure: F. zeng: None; **J. Huang**: None; **Y. Wei**: None; **D. Wang**: None; **J. Chen**: None; **C. Jian**: None; **X. Zhu**: None; **S. Li**: None; **J. Zhang**: None; **T. Wang**: None; **C. Liu**: None; **L. Wei**: None; **J. Gao**: None; **J. Zhu**: None; **Q. Zou**: None; **J. Wu**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0078

Citrullinated Serum Albumin Is Not an Autoantigen in Rheumatoid Arthritis

Farheen Sultan Shaikh, cecilia mustelin, Xiaoxing Wang and Tomas Mustelin, University of Washington, Seattle, WA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoantibodies against citrullinated proteins (ACPAs) are diagnostic of rheumatoid arthritis (RA), an autoimmune disease primarily affecting synovial joints. Proteomic analyses have identified human serum albumin as a target

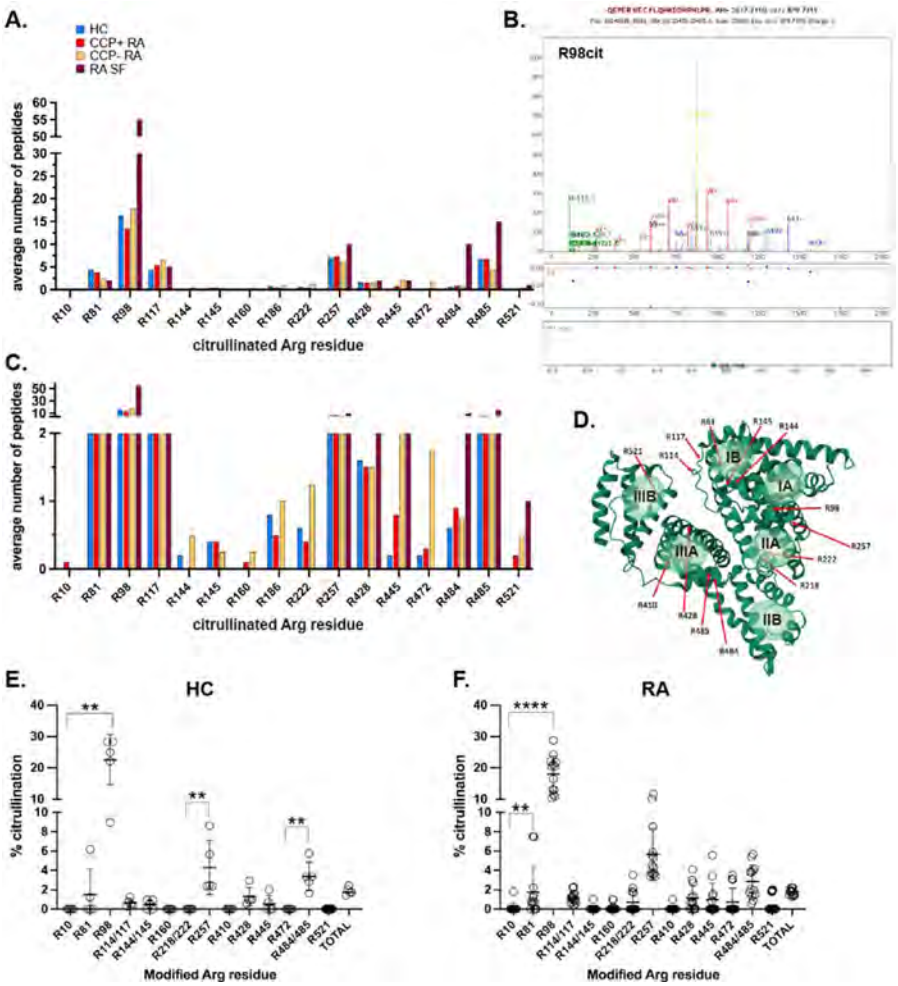


Fig. 1. Summary of mass spectrometry analyses to identify citrullinated Arg residues in albumin. A., Identified sites by the average number of peptides detected in LC-MS/MS experiments in healthy controls (HC, blue bars), CCP-positive RA patients (red bars), CCP-negative RA patients (golden bars), and in synovial fluid from an RA patient (purple bars). B., Mass spectrum for the peptide containing citrullinated R98. C. Same data as in panel A., but with the bottom half of the Y-axis magnified to better visualize the lowest peptide quantities. D., Location of the modified Arg residues in the three-dimensional structure of albumin. The 6 ligand binding pockets are indicated as pale green spheres. E., stoichiometry of Arg citrullination in albumin from healthy donors (HC; n=5) and RA patients (n=13). Statistical significance was assessed using the Mann-Whitney U test. **, p<0.01, ****, p<0.001.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

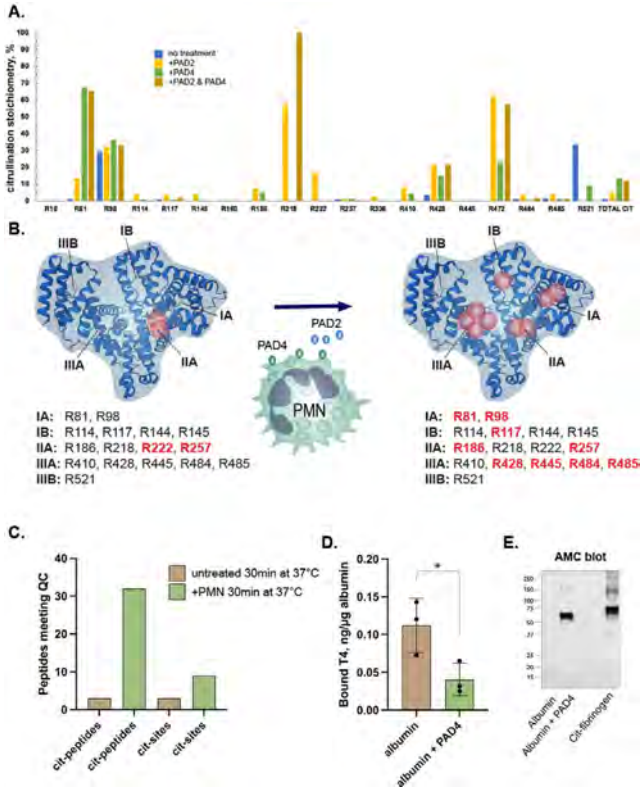


Fig. 2. Citrullination of albumin by PAD2, PAD4, and live neutrophils. A., Stoichiometry of citrullination of albumin at all sites after treatment without (blue) or with PAD2 (golden), PAD4 (green), or both enzymes (tan). B., Arg residues in albumin citrullinated (red) by live neutrophils. C., Numbers of citrullinated sites and peptides in panel B. D., Binding of thyroxin (T4) by albumin treated with (green) or without (brown) PAD4, as indicated. Statistical significance was assessed using the Mann-Whitney U test. E., Anti-modified citrulline (AMC) of albumin treated with PAD4, with citrullinated fibrinogen as a positive control.

of citrullination in RA, and anti-citrullinated albumin antibodies have been reported. This study aimed to characterize the extent and immunological relevance of albumin citrullination in RA.

Methods: Sera from individuals with RA (n = 87), SLE (n = 24), and healthy controls (n = 33) were obtained from the UW Rheumatology Biorepository, and neutrophils were isolated from freshly collected blood samples of RA patients. Anti-CCP status in RA sera was confirmed by ELISA. Neutrophils from RA blood or recombinant PAD2/PAD4 enzymes were used to citrullinate human albumin in vitro. Citrullination was assessed by AMC blotting and LC-MS/MS after in-gel tryptic digestion. Citrullinated and unmodified peptide pairs (14 sites) were tested by ELISA for IgG binding; responses above the 95th percentile of controls were considered positive. Thyroxine binding to native versus citrullinated albumin was measured using competitive ELISA. All protocols were IRB-approved. Mann-Whitney U tests were used for statistical analyses, with $p < 0.05$ considered significant.

Results: This study analyzed serum from 87 RA patients, confirming CCP positivity in 59.5%, and identified 17 citrullinated arginine residues in albumin from both RA patients and healthy donors using LC-MS/MS. Surprisingly, the stoichiometry of citrullination was similar in both groups, suggesting it is a physiological process. Increased citrullination was observed only in RA synovial fluid, albeit at the same sites. The citrullinated residues were surface-exposed and located near ligand-binding pockets, including R81 and R521 near the FcRn binding interface, indicating potential structural or functional consequences. In vitro, PAD2, PAD4, and live RA neutrophils rapidly citrullinated albumin at multiple sites, with PAD4 inducing the most extensive changes. Citrullination significantly reduced thyroxin binding by 64%, suggesting a regulatory role of citrullination in ligand binding. However, ELISA assays showed minimal IgG ACPA reactivity to either physiologically citrullinated albumin or synthetic citrullinated peptides, with only a few RA sera slightly exceeding control thresholds, likely due

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

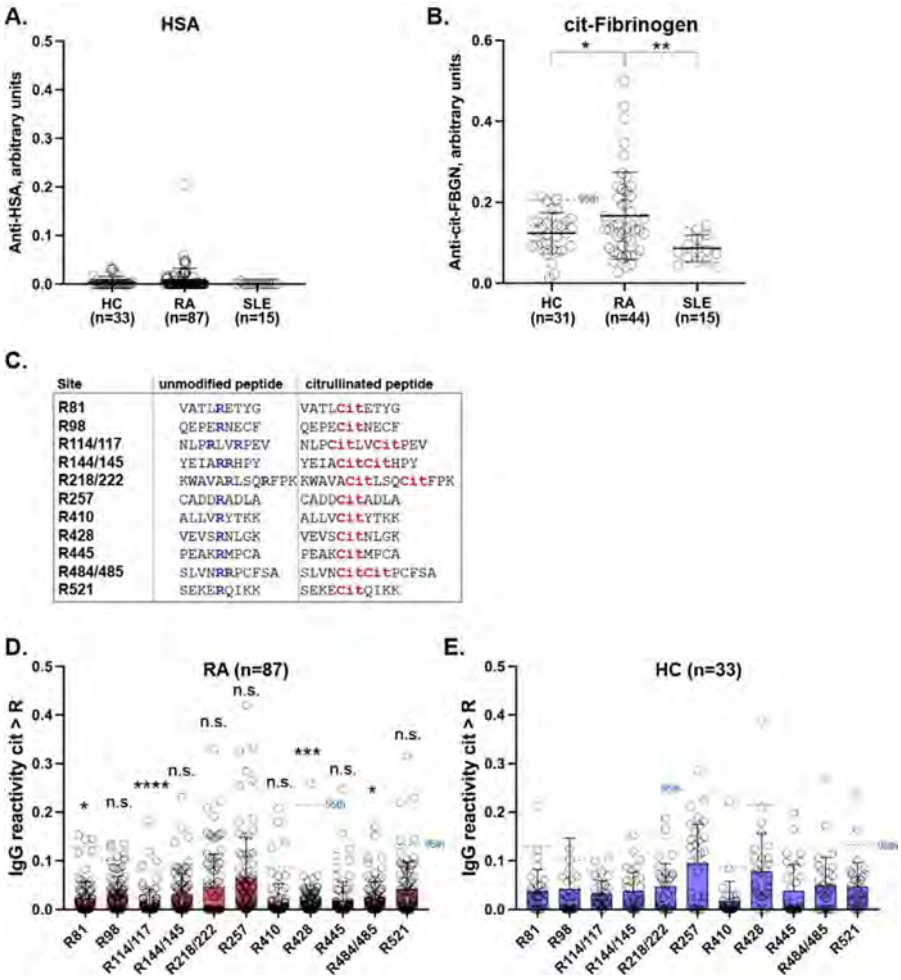


Fig. 3. ELISAs with intact albumin and citrullinated albumin peptides. A., Detection by ELISA of IgG antibodies binding purified albumin. B., Positive control ELISA with the same serum samples detecting IgG binding to citrullinated fibrinogen. Statistical significance was assessed using the Mann-Whitney test. C., Sequence of all peptides used in ELISAs. The unmodified Arg residues are indicated in blue and the citrulline residues in red. D., IgG reactivity in RA sera (n=87) against the indicated citrullinated peptides after subtraction of the reactivity against the unmodified peptide. E., The exact same ELISA using healthy control (HC) sera (n=33). The 95th percentile of the HC distribution for each peptide is indicated as a horizontal dotted line. Statistical significance was assessed using the Mann-Whitney U test between reactivity for each peptide between HC and RA. Note that the statistically significant values all represent lower reactivity in RA than in HC. *, p<0.5; **, p<0.01; ***, p<0.005, ****, p<0.001.

to cross-reactivity of ACPA against other citrullinated proteins. These findings suggest that albumin citrullination is a physiological process and not a major immune target in RA.

Conclusion: Albumin citrullination appears to be a physiological process and is not immunogenic in RA, with similar stoichiometry to healthy controls and minimal ACPA recognition. We conclude that citrullinated albumin is unlikely to contribute significantly to ACPA responses in RA and that immunological tolerance against citrullinated albumin is maintained in RA.

Disclosure: F. Shaikh: None; **c. mustelin**: None; **X. Wang**: None; **T. Mustelin**: Bristol-Myers Squibb(BMS), 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0079

Association of Protein Arginine Deiminase 4 with the myosin-9 Motor Complex

Fatemeh Neela Moadab, Farheen Shaikh, Xiaoxing Wang, cecilia mustelin, Ethan Le, Rayan Najjar, Jie An, Alison Bays and Tomas Mustelin, University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

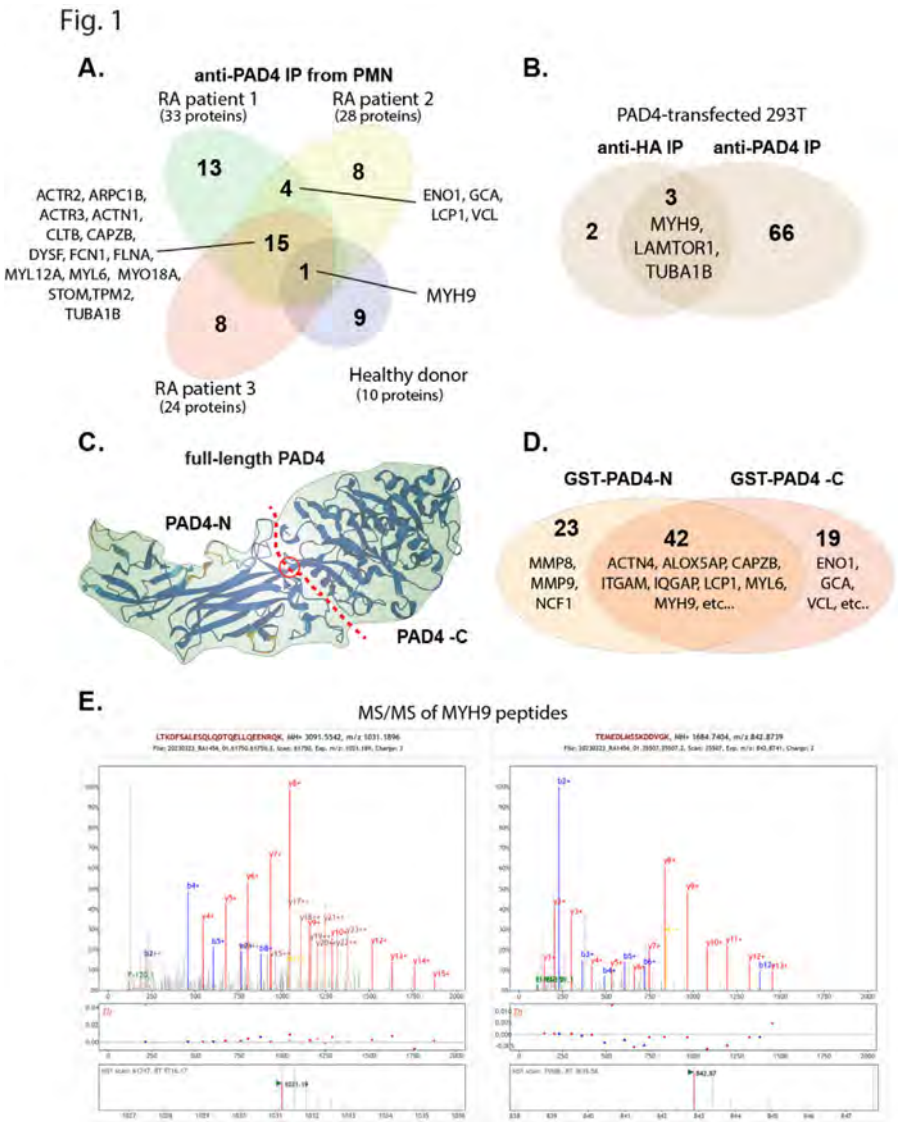


Fig. 1. Summary of mass spectrometry analyses to identify PAD4-associated proteins. A., Venn diagram of proteins present in anti-PAD4 immunoprecipitates, but not in control precipitates, from 3 RA patient and one healthy donor neutrophils. B., Venn diagram of PAD4 immunoprecipitates from transfected 293T cells. C., Illustration of the hinge (red circle) where PAD4 was cut into two halves for the construction of the two GST fusion proteins. D., Venn diagram of proteins precipitated by the N- and C-terminal halves of PAD4 fused to GST. E., Two representative mass spectra of myosin-9 peptides from the immunoprecipitates in panel A.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Genetic association data, immunohistochemistry, and functional experiments implicate protein arginine deiminase 4 (PAD4) in the pathogenesis of rheumatoid arthritis (RA). This disease is characterized by immunity against epitopes with deiminated arginine (=citrulline) originating from a multitude of intra-and extracellular proteins that are modified in this manner only in RA patients, not in healthy individuals. However, it remains uncertain how, where, and why PAD4 citrullinates these proteins in the RA patients.

Methods: To gain insights into the physical interactions of PAD4 with other cellular proteins, we identified candidate PAD4-associated proteins by mass spectrometry. PAD4 in neutrophils from RA patients and healthy controls co-

Fig. 3

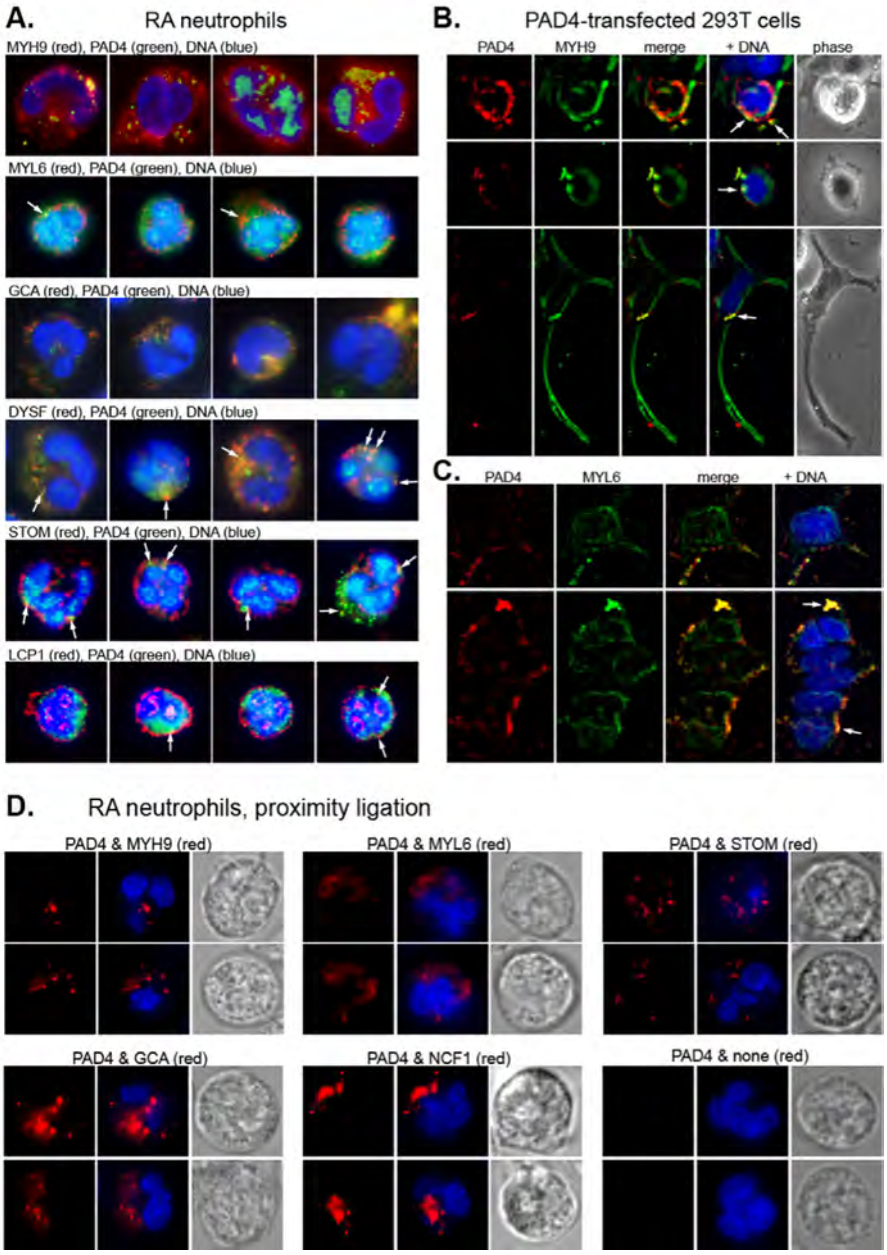


Fig. 2. Immunofluorescence microscopy of PAD4 and putative interactors. A., RA neutrophils stained for PAD4 (green) and the indicated proteins (red): myosin-9 (top row), myosin light chain-6 (second row), grancalcin (third row), dysferlin (fourth row), stomatin (fifth row), and plastin-2 (sixth row). B. PAD4-transfected 293T cells stained for PAD4 (red) and myosin-9 (green)., C., Same cells stained for PAD4 (red) and myosin light chain-6 (green). D., Proximity-ligation assays in RA neutrophils for the pairs of PAD4 plus myosin-9, myosin light chain-6, stomatin, grancalcin, NCF1, or no second antibody, as indicated.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig. 4

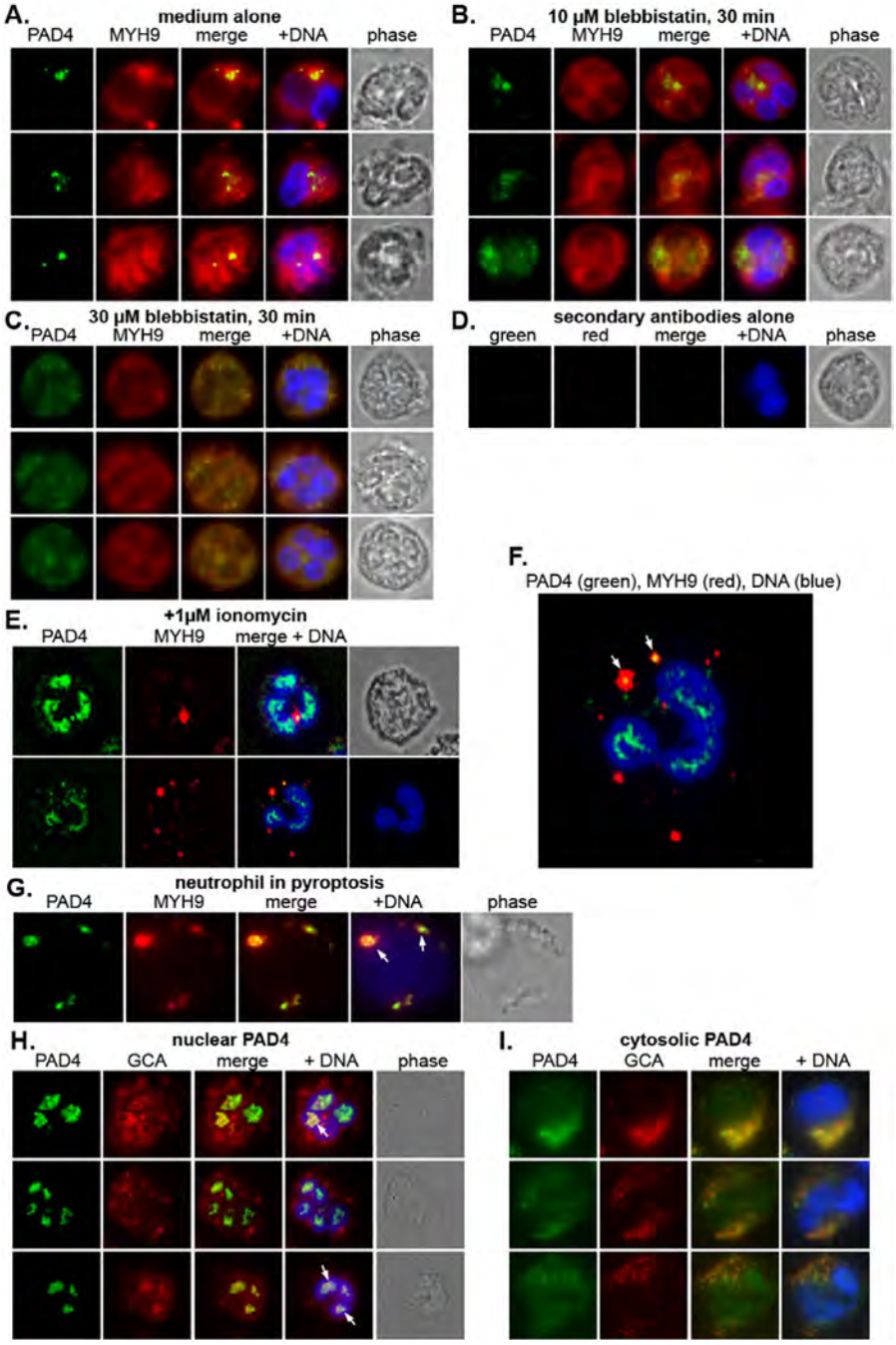


Fig. 3. Effects of myosin-9 inhibition or ionomycin on PAD4 localization. A., RA neutrophils stained for PAD4 (green) and myosin-9 (red) after a 30 min incubation at 37°C. B., Same staining of neutrophils incubated with 10 µM blebbistatin for 30 min at 37°C. C., Same for neutrophils incubated with 30 µM blebbistatin for 30 min at 37°C. D., Negative control staining with secondary antibodies alone. E., PAD4 (green) and myosin-9 (red) in neutrophils treated with 1 µM ionomycin for 30 min at 37°C. F., Magnified view of the third panel, second row, in panel E. G., PAD4 (green) and myosin-9 (red) in a neutrophil undergoing spontaneous cell death by pyroptosis. H., RA neutrophils stained for PAD4 (green) and grancalcin (red) focusing on neutrophils with nuclear PAD4. I. same in neutrophils with cytosolic PAD4. Note that grancalcin is nuclear only when PAD4 is nuclear.

immunoprecipitated with myosin-9, and 20 other proteins, many of which were also present in myosin-9 immunoprecipitates. By immunofluorescence microscopy, myosin-9 co-localized with PAD4 in RA neutrophils, as well as with myosin-9 and myosin light chain 6 in transfected 293T cells. This was confirmed by proximity ligation assays in intact neutrophils.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Inhibition of the motor domain of myosin-9 by blebbistatin resulted in a more diffuse PAD4 location indicating that myosin-9 serves to transport PAD4 within the cells. However, PAD4 translocation to the nucleus involved dissociation from myosin-9. In complex with PAD4, myosin-9 was citrullinated at both N-terminal and C-terminal sites. Citrullinated peptides corresponding to these sites were recognized by IgG autoantibodies in RA patients.

Conclusion: We conclude that at least a portion of intracellular PAD4 in neutrophils interacts physically and catalytically with a myosin-9 containing macromolecular machinery involved in the cell migration and transport of organelles and membrane.

Disclosure: F. Moadab: None; **F. Shaikh**: None; **X. Wang**: None; **c. mustelin**: None; **E. Le**: None; **R. Najjar**: None; **J. An**: None; **A. Bays**: None; **T. Mustelin**: Bristol-Myers Squibb(BMS), 1.

Abstract Number: 0080

The Role of DICAM in Modulating Macrophage Differentiation and Inflammatory Responses via αvβ3 Integrin Signaling in Rheumatoid Arthritis

Hanna Lee[1], Youn-Kwan Jung[2], Sang-il Lee[3], Yun-Hong Cheon[4] and Hyunjin Lim[4], [1]Division of Rheumatology, Department of Internal Medicine, Gyeongsang National University Hospital, Changwon, Changwon-si, Kyongsang-namdo, Republic of Korea, [2]Institute of Medical Science, Gyeongsang National University, Jinju, Jinju, Kyongsang-namdo, Republic of Korea, [3]Department of Internal Medicine and Institute of Medical Science, College of Medicine, Gyeongsang National University and Hospital, Jinju, Republic of Korea, [4]Division of Rheumatology, Department of Internal Medicine, Gyeongsang National University Hospital, Jinju, Jinju, Kyongsang-namdo, Republic of Korea

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by persistent joint inflammation, cartilage destruction, and bone erosion. Among the various immune cells involved in RA pathogenesis, macrophages play a central role by mediating inflammatory responses and tissue damage. Integrins, particularly αvβ3 integrin, are critical regulators of macrophage differentiation and inflammatory signaling via the PI3K/Akt pathway and its downstream effectors, including FOXO3a and IRF7. DICAM (Mxra8), a transmembrane protein, has been identified as a negative regulator of αvβ3 integrin signaling, yet its role in RA remains unclear. This study explores the regulatory function of DICAM in macrophage differentiation and inflammation in the context of RA.

Methods: We utilized the **K/BxN serum transfer mouse model of rheumatoid arthritis** to evaluate whether **DICAM deficiency influences cartilage destruction and macrophage infiltration** in vivo. To investigate the role of DICAM in macrophage signaling in vitro, we employed **THP-1-derived macrophages**. In addition, we performed rescue experiments to confirm whether the regulatory effects of DICAM on macrophage differentiation and inflammatory responses were mediated, at least in part, by suppression of β3 integrin.

Results: Using a K/BxN serum transfer mouse model of RA, we demonstrate that DICAM deficiency exacerbates arthritis severity, cartilage degradation, and macrophage infiltration. In vitro experiments with THP-1-derived macrophages show that DICAM inhibits macrophage differentiation, phagocytic activity, and pro-inflammatory cytokine expression by suppressing αvβ3 integrin expression and downstream PI3K/Akt signaling. Overexpression of DICAM reduced integrin activation,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

FOXO3a phosphorylation, and IRF7 expression, while knockdown enhanced these processes, promoting an inflammatory macrophage phenotype. Rescue experiments further confirmed that the inhibitory effects of DICAM on macrophage differentiation and inflammatory responses are mediated, at least in part, by the suppression of β3 integrin.

Conclusion: These results, indicating DICAM's protective role in mitigating joint pathology, highlight DICAM as a critical modulator of macrophage function in RA and a potential therapeutic target for reducing inflammation and tissue damage. This study advances our understanding of DICAM's role in RA pathogenesis and its potential as a biomarker and therapeutic intervention.

Disclosure: H. Lee: None; **Y. Jung**: None; **S. Lee**: Samsung Bioepis, 5; **Y. Cheon**: None; **H. Lim**: None.

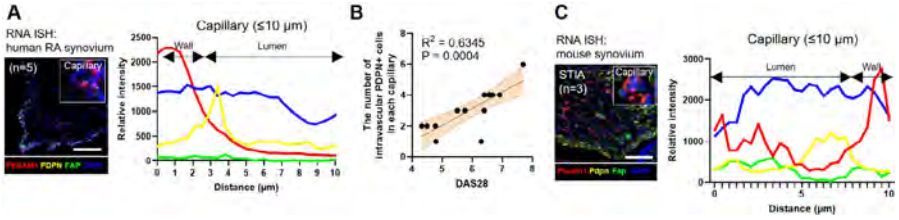
Abstract Number: 0081

Trans-endothelial Trafficking of Fibroblast-like Synoviocytes Amplifies Synovial Inflammation in Rheumatoid Arthritis

Jaeyeon Kim[1], Sanaz Panahandeh[2], Hieu Nguyen[3], Kainat Mian[4], Hadijat Makinde[4], Kyoung Jae Won[5], Arminja Kettenbach[3], Harris R Perlman[4], Costantino Pitzalis[6] and Nunzio Bottini[7], [1]Cedars Sinai Medical Center, Los Angeles, CA, [2]Cedars-Sinai Medical Center, Los Angeles, [3]Geisel School of Medicine at Dartmouth, Lebanon, NH, [4]Northwestern University, Chicago, IL, [5]Cedars-Sinai Medical Center, Los Angeles, CA, [6]QMUL, Bromley Kent, United Kingdom, [7]Cedars Sinai Medical Center, Beverly Hills, CA

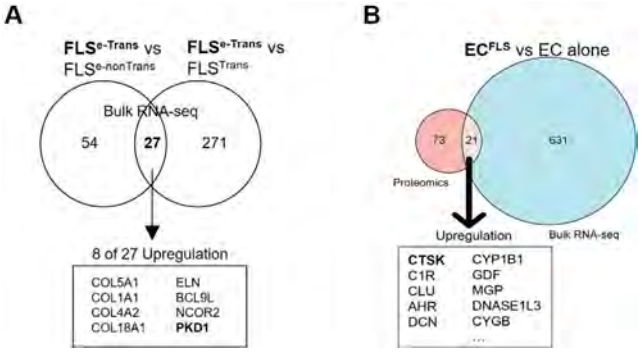
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The discovery of circulating fibroblast-like synoviocyte (FLS), known as PRIME cells, in RA patients suggests that synovial FLS may enter the circulation through blood vessels and contribute to systemic inflammation. This study aimed to detect trans-endothelial migration of FLS and dissect the molecular crosstalk between FLS and endothelial cells (EC) during this process and its relevance in rheumatoid inflammation.



(A) Left: trans-EC migration of RA FLS. Representative microscopy of RA (n=5) synovium subjected to RNA in situ hybridization (ISH) for Podoplanin (PDPN, yellow), Fibroblast Activating Protein (FAP, green), Platelet/Endothelial Cell Adhesion Molecule 1 (PECAM1, red), and Hoechst (blue). Scale bar: 100 μm. Right: Representative quantification of ISH intensities through a capillary (≤ 10 micron) wall and lumen in RA synovium. Data were analyzed using Zen (black edition). (B) Correlation between the number of intravascular PDPN+ cells in RA biopsies (n=15) and disease activity score (DAS28). Simple linear regression. P=0.0004. (C) Left: trans-EC migration of mouse FLS. Representative microscopy of serum transfer induced arthritis (STIA) synovium subjected to RNA ISH for Pdpn (yellow), Fap (green), and Pecam1 (red), and Hoechst (blue). Scale bar: 100 μm. Right: Representative quantification of ISH intensities through a capillary (≤ 10 micron) wall and lumen in STIA synovium. Data were analyzed using Zen (black edition).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

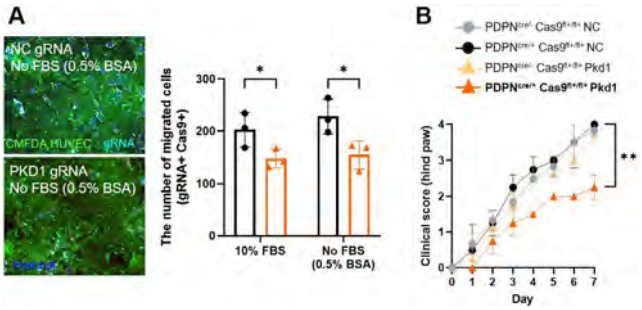


(A) Venn diagram from bulk RNA-seq of trans-EC migrated RA FLS (FLSe-Trans) compared to non-migrated FLS (FLSe-nonTrans) or FLS trans-migrated without EC (FLSTrans), highlighting a shared set of upregulated genes, including polycystin 1 (PKD1). (B) Venn diagram from integrated proteomic and transcriptomic analysis of EC co-cultured with RA FLS (ECFLS) compared to EC alone, highlighting upregulated genes, including Cathepsin K (CTSK).

Methods: Human and mouse arthritic synovium were analyzed using immunofluorescence and RNA in situ hybridization (ISH) to identify trans-endothelial migrating FLS. An in vitro trans-endothelial migration model was established using RA FLS and human umbilical vein ECs (HUVEC), followed by transcriptomics and proteomic analysis. Spatial transcriptomics was performed on RA synovial biopsies. Functional experiments were conducted through gene knockdown in vitro and in vivo.

Results: We identified FLS transmigration through EC layers of capillaries in RA synovium, but not in osteoarthritis (OA), which correlated with RA disease activity. ISH confirmed the presence of intravascular FLS in human and mouse arthritic synovium (**Fig. 1A, B, C**, R^2=0.6, P=0.0004). In vitro trans-endothelial migration assay demonstrated that RA FLS actively transmigrate across EC layers. Bulk RNA-seq of trans-endothelial migrated FLS identified increased expression of polycystin-1 (PKD1) (**Fig. 2A**). Integration of transcriptomics and proteomic data identified cathepsin K (CTSK) as upregulated in EC after transmigration of FLS (**Fig 2B**), Spatial transcriptomics studies showed that PKD1$^+$ FLS are located in close proximity to CTSK$^+$ ECs in RA synovium, supporting a spatially organized induction of CTSK by FLS in EC. In vitro assays confirmed that PKD1 knockdown significantly impaired FLS transmigration across EC layers while PKD1 knockdown in FLS reduced the severity of arthritis in vivo (**Fig. 3A, B**). CTSK knockdown in ECs exposed to FLS impaired angiogenesis while systemic administration of the CTSK inhibitor Odanacatib attenuated joint inflammation and vascular leakage in arthritic mice.

Conclusion: Our findings demonstrate that FLS undergo trans-endothelial migration in RA synovium and identify a mechanism driven by such migration and involving PKD1 and CTSK, which amplifies EC-driven inflammation and RA severity. These results might also provide mechanistic insight into the generation of PRIME cells and highlight FLS–EC spatial interactions as a potential therapeutic target in RA.



(A) Left: representative fluorescence microscopy images from an in vitro trans-EC migration assay of RA FLS transfected with PKD1 gRNA-AF647 (cyan) compared to negative control (NC). HUVEC were loaded with 5-chloromethylfluorescein diacetate dye (CMFDA). gRNA-AF647 is cyan, CMFDA is green, and Hoechst is blue. Right: quantification of trans-EC migrated PKD1 gRNA transfected RA FLS compared to NC gRNA under serum-containing (10% FBS) and serum-free (0.5% BSA) conditions. Each point in A (right) represents an experiment. Two-way ANOVA, Bonferroni's multiple comparison test. *P < 0.05. (B) In vivo electroporation using tweezer electrodes and intra-articular injection of Pkd1 gRNA into joints of PDPNcre/+ Cas9 knock-in (KI) fl+/fl+ mice. Clinical arthritis scores (0 – 4) over time in PDPNcre/+ Cas9 KIfl+/fl+ and control mice following intra-articular injection of PKD1 or NC gRNA. Two-way ANOVA, Bonferroni's multiple comparison test. **P < 0.01.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Kim: None; **S. Panahandeh**: None; **H. Nguyen**: None; **K. Mian**: None; **H. Makinde**: None; **K. Won**: None; **A. Kettenbach**: None; **H. Perlman**: AbbVie/Abbott, 2; **C. Pitzalis**: None; **N. Bottini**: Merck/MSD, 2.

Abstract Number: 0082

IBI3011, a Humanized anti-IL1RAP Monoclonal Antibody, Inhibits IL1, IL33, IL36-driven Inflammation Pathway, and Attenuates Inflammation in Preclinical Inflammatory Disease Model

Hongling Tian, Lidan Liang, Chenjuan Zhu, Bin Li, Lei Cao, Meng Ni, Fan Chen, Zhimin Zhang, Min Wu, Tong Liu, **Jinyang Li**, Yao Xiong, Li Li, Shuaixiang Zhou, Enhong Zhong and Huizhong Xiong, Innovent Biologics (Suzhou) Co., Ltd., Suzhou, Jiangsu, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin 1 receptor accessory protein (IL1RAP) serves as a co-receptor that forms receptor complexes with IL1R1, ST2, and IL36R and mediates signaling pathways triggered by IL1α/β, IL33, and IL36α/β/γ, which implicated in several autoimmune or inflammatory diseases, such as gout, psoriasis, and systemic sclerosis. IBI3011 is a fully humanized IgG1-LALA antibody targeting the extracellular segment of IL1RAP, blocks IL1α/β, IL33, and IL36α/β/γ signaling pathways and without ADCC. IBI3011 has shown potent anti-inflammatory properties in several preclinical models and is currently under development for treatment of gout and auto-inflammatory diseases.

Methods: We evaluated the binding affinity of IBI3011 with human, cynomolgus monkey and mouse IL1RAP in protein level by **Biosensor Layer Interferometry (BLI), and in** cellular level by flow cytometry. The blocking activity of IBI3011 was evaluated via ELISA to quantify target cell activation *in vitro*. Human peripheral blood mononuclear cells (PBMCs) were stimulated with IL1α/β, IL33, or IL36α, respectively, and the secreted inflammatory cytokines were detected. The *in vivo* efficacy of IBI3011 was evaluated in humanized IL1RAP knock-in mice with MSU induced gout and collagen antibody-induced arthritis (CAIA) models. In both studies, mice were treated with IBI3011 or control reagent in a therapeutic fashion, and the blockade efficacy were analyzed by footpad thickness and/or inflammatory cytokines level in footpad tissue.

Results: IBI3011 showed high binding affinity with human and cynomolgus monkey IL1RAP at protein and cellular levels, but not with mouse IL1RAP. For *in vitro* function assay, IBI3011 blocked the inflammatory cytokines TNFα, IFNγ secretion from PBMC when stimulated with IL1α/β, IL33, and IL36α/β/γ. In the acute gout model, IBI3011 demonstrated a dose-dependent inhibition of the gout development in hIL1RAP mice compared to controls, as 10 mg/kg and 20 mg/kg of IBI3011 significantly reduced the thickness and inflammation of the footpad tissues. In the rheumatoid arthritis model, IBI3011 dose-dependently reduced the ankle joint thickness and inhibited the inflammation in joint. The 3 mg/kg and 10 mg/kg dosage groups exhibited significant inhibitory effect on the arthritic joint redness and inflammatory response in mice, while the lower dose of 1 mg/kg showed no significant inhibition, suggesting that IBI3011 can dose-dependently inhibit the initiation of rheumatoid arthritis in the preclinical model.

Conclusion: The *in vitro* study has shown that IBI3011 inhibits the activation of IL1, IL33, and IL36 signaling pathway effectively through blocking the co-receptor IL1RAP. The preclinical mouse models have demonstrated that IBI3011 exerts a dose-dependent anti-inflammatory effect. These preclinical results underscore the potential of IBI3011 as a therapeutic candidate for autoimmune and inflammatory diseases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Tian: Innovent Biologics (Suzhou) Co., Ltd, 3; **L. Liang**: Innovent Biologics (Suzhou) Co., Ltd, 3; **C. Zhu**: Innovent Biologics (Suzhou) Co., Ltd., 3; **B. Li**: Innovent Biologics (Suzhou) Co., Ltd., 3; **L. Cao**: Innovent Biologics (Suzhou) Co., Ltd, 3; **M. Ni**: Innovent Biologics (Suzhou) Co., Ltd., 3; **F. Chen**: Innovent Biologics (Suzhou) Co., Ltd, 3; **Z. Zhang**: Innovent Biologics (Suzhou) Co., Ltd., 3; **M. Wu**: Innovent Biologics (Suzhou) Co., Ltd, 3; **T. Liu**: Innovent Biologics (Suzhou) Co., Ltd, 3; **J. Li**: Innovent Biologics (Suzhou) Co., Ltd., 3; **Y. Xiong**: Innovent Biologics (Suzhou) Co., Ltd., 3; **L. Li**: Innovent Biologics (Suzhou) Co., Ltd, 3; **S. Zhou**: Innovent Biologics (Suzhou) Co., Ltd., 3; **E. Zhong**: Innovent Biologics (Suzhou) Co., Ltd, 3; **H. Xiong**: Innovent Biologics (Suzhou) Co., Ltd., 3.

Abstract Number: 0083

Confirmatory Factor Analysis of the Plutchik Suicide Risk Scale in Patients with Rheumatoid Arthritis

Pedro Quevedo[1], Javier mora[2], william garcia[2], alejandra Solano[2], **juliana Muñoz**[2] and Daniela Lopez[2], [1]San Rafael Cinic University Hospital, Bogota, Distrito Capital de Bogota, Colombia, [2]san rafael clinic universtity hospital, Bogota, Distrito Capital de Bogota, Colombia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Prevalence of depression in RA patients ranging from 10% to 25%, making it the most common psychiatric disorder in this population. The Plutchik Suicide Risk Scale is a tool validated in Colombia for assessing suicide risk. It consists of 15 items and evaluates aspects such as suicidal ideation, history of previous attempts, and emotional severity, with a cutoff score of 6 or higher indicating risk. Our Objectives were: To perform an exploratory factor analysis of the Plutchik Suicide Risk Scale in patients with rheumatoid arthritis, and to evaluate the correlation between this score and disease activity and quality of life scales. Additionally, to estimate the prevalence of suicide risk in our population with rheumatoid arthritis.

Methods: A cross-sectional study with ambispective data collection was conducted. Patients over 18 years of age with a diagnosis of rheumatoid arthritis, based on the 2010 ACR/EULAR criteria, and treated at the Rheumatology Department of the Hospital Universitario Clínica San Rafael in Bogotá were included. Patients with major depressive disorder, anxiety disorders, or neurocognitive disorders were excluded. To assess the correlation between the Plutchik scale and the DAS28, HAQ, and CDAI indices, Spearman's correlation coefficient. For the confirmatory factor analysis (CFA), the weighted least squares means and variance adjusted (WLSMV) estimator was applied, as it is suitable for dichotomous items. A theoretical three-factor model was established, and factor loadings, standard errors, and p-values were calculated. Goodness-of-fit

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

measures were then estimated: chi^2, TLI (Tucker-Lewis Index), CFI (Comparative Fit Index), SRMR (Standardized Root Mean Square Residual), and RMSEA (Root Mean Square Error of Approximation). The analysis was performed using MPLUS version 8.11 and RStudio version 4.3.2

Results: A total of 91 patients were included in the study, of whom 78% were women. The mean age was 54 years (±14), and the median disease duration was 60 months (120). The median DAS28 score was 3.5 (2.7), and CDAI score was 12 (14). Quality of life, assessed using the HAQ, showed a median score of 1.1 (IQR: 1.55). The Plutchik Suicide Risk Scale yielded a median score of 3 (4.5). When evaluating suicide risk using the Plutchik scale, 26.3% of our population was found to be at risk. Analysis of the correlation between this scale and disease activity scores showed no statistically significant associations with DAS28 or CDAI However, a significant correlation was observed between suicide risk and quality of life, as assessed by the HAQ (rho = 0.60; $p < 0.001$). The exploratory factor analysis supported a three-factor model, with statistically significant factor loadings for all items except for item P10: "Are you separated, divorced, or widowed?" which had an estimate of 0.19 and a p-value of 0.18. The goodness-of-fit indices indicated acceptable model fit: RMSEA = 0.07, CFI = 0.92, and TLI = 0.91.

Conclusion: The prevalence of suicide risk, according to the Plutchik scale, in our population was 26.3%. A statistically significant correlation was found between this scale and quality of life, demonstrating an acceptable performance of the Plutchik scale in patients with rheumatoid arthritis.

Disclosure: P. Quevedo: None; **J. mora**: None; **w. garcia**: None; **a. Solano**: None; **j. Muñoz**: None; **D. Lopez**: None.

Abstract Number: 0084

Regulation of the same chemokine gene transcription by different histone lysine methyltransferases, MLL1 and MLL3, in rheumatoid arthritis synovial fibroblasts

Keita Okamoto[1], Yasuto Araki[2], Yoshimi Aizaki[2], Hiroshi Kajiyama[3], Kazuhiro Yokota[2], Yu Funakubo[2], Yuho Kadono[4], Yuji Akiyama[5] and Toshihide Mimura[6], [1]Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Moroyama-chou, Iruma-gun, Saitama, Japan, [2]Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Saitama, Japan, [3]Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Iruma-gun, Saitama, Japan, [4]Department of Orthopaedic Surgery, Saitama Medical University, Moroyama-machi, Iruma-gun, Saitama, Japan, [5]Department of Rheumatology and Applied Immunology, Faculty of Medicine, Saitama Medical University, Moroyama-machi, Iruma-gun, Saitama, Japan, [6]Saitama Seikeikai Hospital, Higashimatsuyama, Saitama, Japan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis synovial fibroblasts (RASFs) produce various matrix metalloproteinases (MMPs), cytokines, and chemokines. Histone lysine methylation has been shown to play an important role in the activation of RASFs. We reported that histone lysine methyltransferases (HKMTs), including myeloid/lymphoid or mixed-lineage leukemia 1 (MLL1) and MLL3, are aberrantly expressed in RASFs (PMID: 29465369). MLL1 and MLL3 catalyze histone H3 lysine 4 (H3K4) methylation and are each part of complex proteins associated with Set1 (COMPASS)-like complexes that include

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

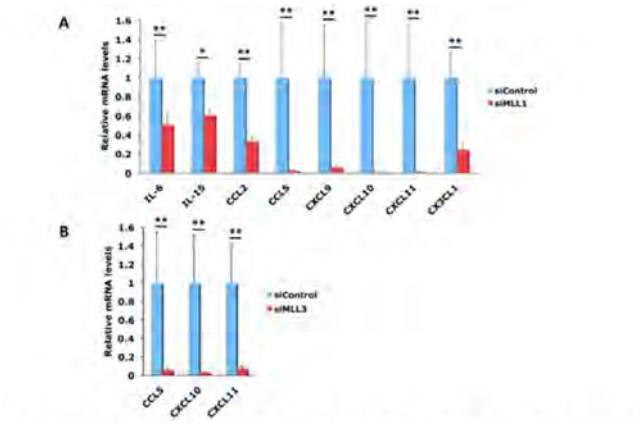


Figure 1. Reduction in mRNA levels of RA-associated genes in RASFs upon siRNA-mediated inhibition of MLL1 (A) or MLL3 (B). Bars shown the mean ± SEM (n=12). Values are expressed as the fold-increase versus the value for control siRNA-treated RASFs. *=P<0.05; **=P<0.01 by Wilcoxon signed-rank test.

WD repeat domain 5 (WDR5) (PMID: 22663077). WDR5 is essential for methylation of H3K4 by MLL1 and MLL3. We investigated the role of MLL1 and MLL3 in RASFs in terms of epigenetic mechanisms of RA pathogenesis.

Methods: Human SFs were isolated from synovial tissues obtained from RA or osteoarthritis (OA) patients undergoing total knee arthroplasty. MLL1 and MLL3 mRNA levels of the above SFs were determined after tumor necrosis factor alpha (TNFα) stimulation. Trimethylation of H3K4 (H3K4me3) is present at the promoters of actively transcribed genes. We investigated changes in mRNA levels of RA-associated genes (matrix-degrading enzymes, cytokines, and chemokines) and H3K4me3 levels in the promoters of these genes upon small interfering RNA-mediated depletion of MLL1 and MLL3 in RASFs. We then determined the levels of H3K4me3 and mRNAs after treatment with MM-102, a WDR5 inhibitor. H3K4me3 levels in the gene promoters were also compared between RASFs and OASFs. Differences between unpaired or paired groups were evaluated using the Mann–Whitney U test or the Wilcoxon signed-rank test, respectively.

Results: MLL1 and MLL3 mRNA levels were significantly higher in RASFs than in OASFs after TNFα stimulation. MLL1 depletion significantly decreased the mRNA levels of several genes of cytokines (IL-6 and IL-15) and chemokines (CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1) in RASFs (Figure 1A). Correspondingly, MLL1 depletion significantly reduced H3K4me3 levels in the promoters of the cytokine and chemokine genes in RASFs (Figure 2). These results indicate that MLL1 activates the cytokine and chemokine genes by increasing promoter H3K4me3 levels in RASFs. Interestingly, MLL3 depletion also suppressed the mRNA levels of CCL5, CXCL10, and CXCL11 genes in RASFs (Figure 1B). However, H3K4me3 levels in the promoters of the chemokine genes were not altered by MLL3 depletion in RASFs (Figure 2). Since it has been reported that MLL3 is involved in the generation of H3K4 monomethylation (H3K4me1) in the enhancers of actively transcribed genes (PMID: 24081332), our results suggest that MLL3 may activate CCL5, CXCL10, and CXCL11

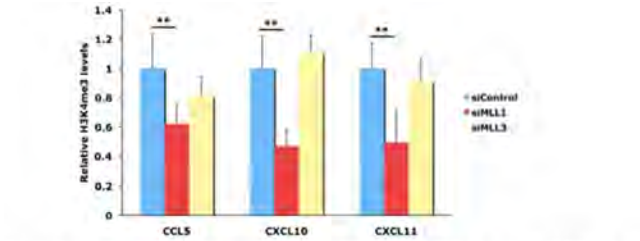


Figure 2. Changes in H3K4me3 levels of CCL5, CXCL10, and CXCL11 genes in RASFs upon siRNA-mediated inhibition of MLL1 or MLL3. Bars shown the mean ± SEM (N=8). Values are expressed as the fold-increase versus the value for control siRNA-treated RASFs. **=P<0.01 by Wilcoxon signed-rank test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

genes by increasing enhancer H3K4me1 levels. MM-102 significantly decreased promoter H3K4me3 and mRNA levels of CCL5, CXCL9, CXCL10, and CXCL11 genes in RASFs. H3K4me3 levels in the promoters of IL-6, IL-15, CCL2, CCL5, CXCL9, CXCL10, CXCL11, and CX3CL1 genes were significantly higher in RASFs than in OASFs.

Conclusion: This study elucidated the epigenetic mechanism by which MLL1 and MLL3 cooperate to activate chemokine genes in RASFs. These findings may lead to new treatments such as targeting histone methyltransferases for RA.

Disclosure: K. Okamoto: None; **Y. Araki**: None; **Y. Aizaki**: None; **H. Kajiyama**: None; **K. Yokota**: None; **Y. Funakubo**: None; **Y. Kadono**: None; **Y. Akiyama**: None; **T. Mimura**: None.

Abstract Number: 0085

Single Cell RNA-seq Revealed Immune/epithelial Cell Abnormalities Underlying the Pathogenesis of Rheumatoid Arthritis-related Interstitial Lung Disease

Kensuke Suga[1], Amara Seng[2], Changfu Yao[3], Tanyalak Parimon[3], Youn Jung Choi[2], Justyna Fert-Bober[4], Barry Stripp[3], Jon Giles[5], Peter Chen[3] and Nunzio Bottini[6], [1]Kao Autoimmunity Institute, Cedars-Sinai Medical Center, Beverly Hills, CA, [2]Kao Autoimmunity Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [3]Women's Guild Lung Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [4]Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [5]Cedars Sinai Medical Center, Los Angeles, CA, [6]Cedars Sinai Medical Center, Beverly Hills, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is one of the extra-articular manifestations of rheumatoid arthritis (RA) characterized by inflammation and/or fibrosis. Clinically relevant RA-ILD occurs in approximately 10% of RA patients and is associated with poor prognosis. Recent single-cell RNA-sequencing (scRNA-seq) analysis have revealed the effects of the cellular makeup and molecular pathways on pathological changes in several lung diseases, but little is known about RA-ILD. This study aimed to characterize immune/epithelial cells in RA-ILD through scRNA-seq analysis.

Methods: We processed explant tissues from 5 RA-ILD patients, 3 non-RA connective tissue disease (CTD)-ILD (2 with dermatomyositis (DM) and 1 mixed connective tissue disease (MCTD)), and 4 control patients. CD45+CD31-EpCAM- immune cells and CD45-CD31-EpCAM+ epithelial cells were FACS sorted and subjected to scRNA-seq. Ingenuity pathway analysis was used to perform upstream regulator analysis.

Results: We analyzed 184,814 cells after quality-control filtering and identified 18 distinct cell clusters (Figure 1). By differential abundance analysis, we found that AT2 cells were 65% lower in abundance in RA-ILD lung tissue compared with control lung tissue, and 10% lower in RA-ILD compared with non-RA CTD-ILD. We identified a reciprocal higher abundance of other epithelial cell types (basal cells, club cells, and ciliated cells). We also found fewer FCN1+ CD14+ macrophages and more SPP1+ macrophages in RA-ILD lungs. We calculated the number of differentially expressed genes (DEGs) in each cell cluster between the disease groups (RA vs control and RA vs CTD) and found that AT2 cells, club cells, FCN1+ CD14+ macrophages, FABP4+ macrophages, and SPP1+ macrophage had a higher number of DEGs (Figure 2). Upstream regulator analysis revealed that TNFa was potentially activated as an upstream molecule which drived differential changes in RA-ILD AT2 cells. T cell sub-clustering analysis revealed that peripheral T cells (Tph) are exclusively found in RA-ILD lungs (Figure 3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

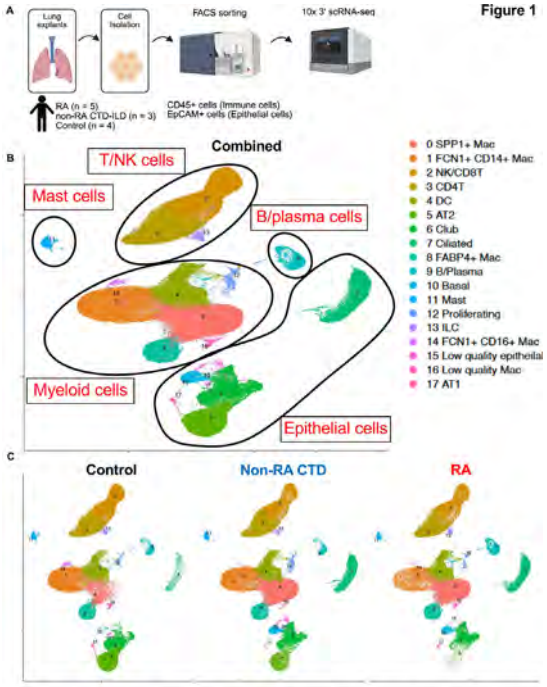


Figure 1. Single-cell RNA-sequencing (scRNA-seq) analysis of 5 RA-ILD, 3 non-RA CTD-ILD, and 4 control lung explants.
(**A**) Scheme of scRNA-seq workflow on human explanted lungs.
(**B**) Visualization of clustering by UMAP plot of all 12 combined RA-ILD, non-RA CTD-ILD, and control lungs.
(**C**) UMAP plot of cells colored according to disease status.

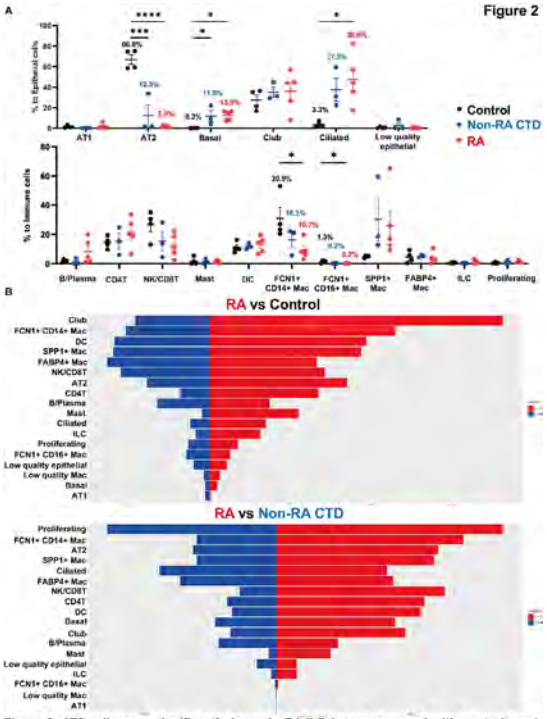


Figure 2. AT2 cells were significantly lower in RA-ILD lungs compared with controls and non-RA CTD-ILD.
(**A**) Differential abundance analysis for each cell clusters among disease groups.
(**B**) Differentially expressed genes (DEGs) between disease groups. False discovery rate (FDR) threshold = 0.05, and log fold change (FC) threshold = 1.5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

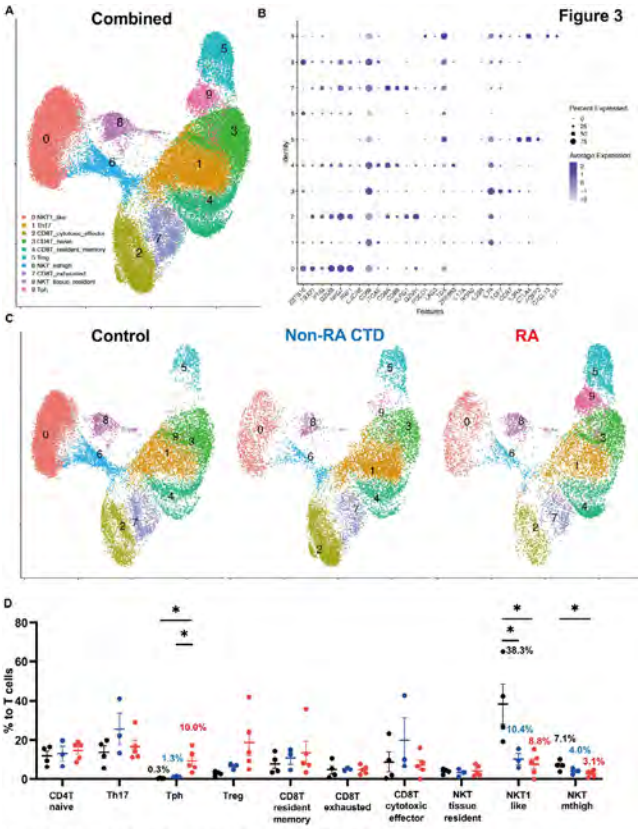


Figure 3. Tph cells were exclusively observed in RA-ILD lungs.
(**A**) UMAP plot of T cell subclusters from 12 combined RA-ILD, non-RA CTD-ILD, and control lungs.
(**B**) Dot plots showing signature gene expression in each clusters.
(**C**) UMAP plot of T cell subclusters colored according to disease status.
(**D**) Differential abundance analysis for each cell clusters among disease groups.

Conclusion: There was heterogeneity in several key cell types, such as AT2 cells, club cells, FCN1+ CD14+ macrophages, FABP4+ macrophages, SPP1+ macrophages, and Tph cells between RA-ILD, non-RA CTD-ILD, and control lungs. An upstream regulator analysis suggested that TNF signaling might be involved in the phenotypic change of AT2 cells in RA-ILD. Our study suggests that immune/epithelial cell abnormalities underlie the pathogenesis of RA-ILD.

Disclosure: K. Suga: None; **A. Seng**: None; **C. Yao**: None; **T. Parimon**: None; **Y. Choi**: None; **J. Fert-Bober**: None; **B. Stripp**: None; **J. Giles**: AbbVie/Abbott, 2, Eli Lilly, 2, Genentech, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Sana, 2; **P. Chen**: Gilead, 1; **N. Bottini**: Merck/MSD, 2.

Abstract Number: 0086

Androgen Upregulates Interferon Signaling in Osteoclast Differentiation During Inflammatory State

Kiana Chen[1], Chia-Lung Wu[2], Gulzada Kulzhanova[2] and Homaira Rahimi[3], [1]University of Rochester School of Medicine and Dentistry, Bronx, NY, [2]University of Rochester Medical Center, Rochester, [3]University of Rochester, Rochester, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

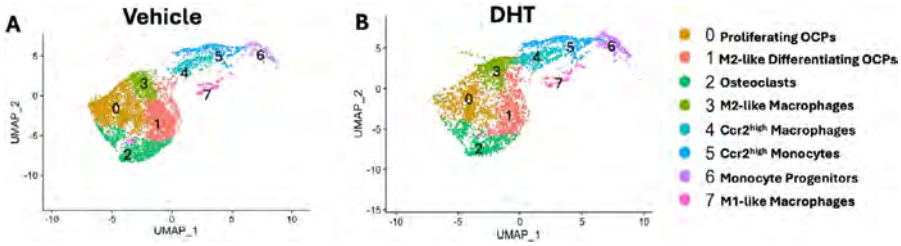


Figure 1. Myeloid Lineage Cells in an Inflammatory Osteoclast Culture. Bone marrow derived cells from a male C57BL/6J mouse were plated and treated with either DHT or vehicle control in osteoclast culture media and collected for single-cell RNA-sequencing. Myeloid lineage populations were subset out from the dataset and defined as 8 unique cluster as illustrated in the uniform manifold approximation and projections (UMAPs) for vehicle-treated (A) and DHT-treated samples (B).

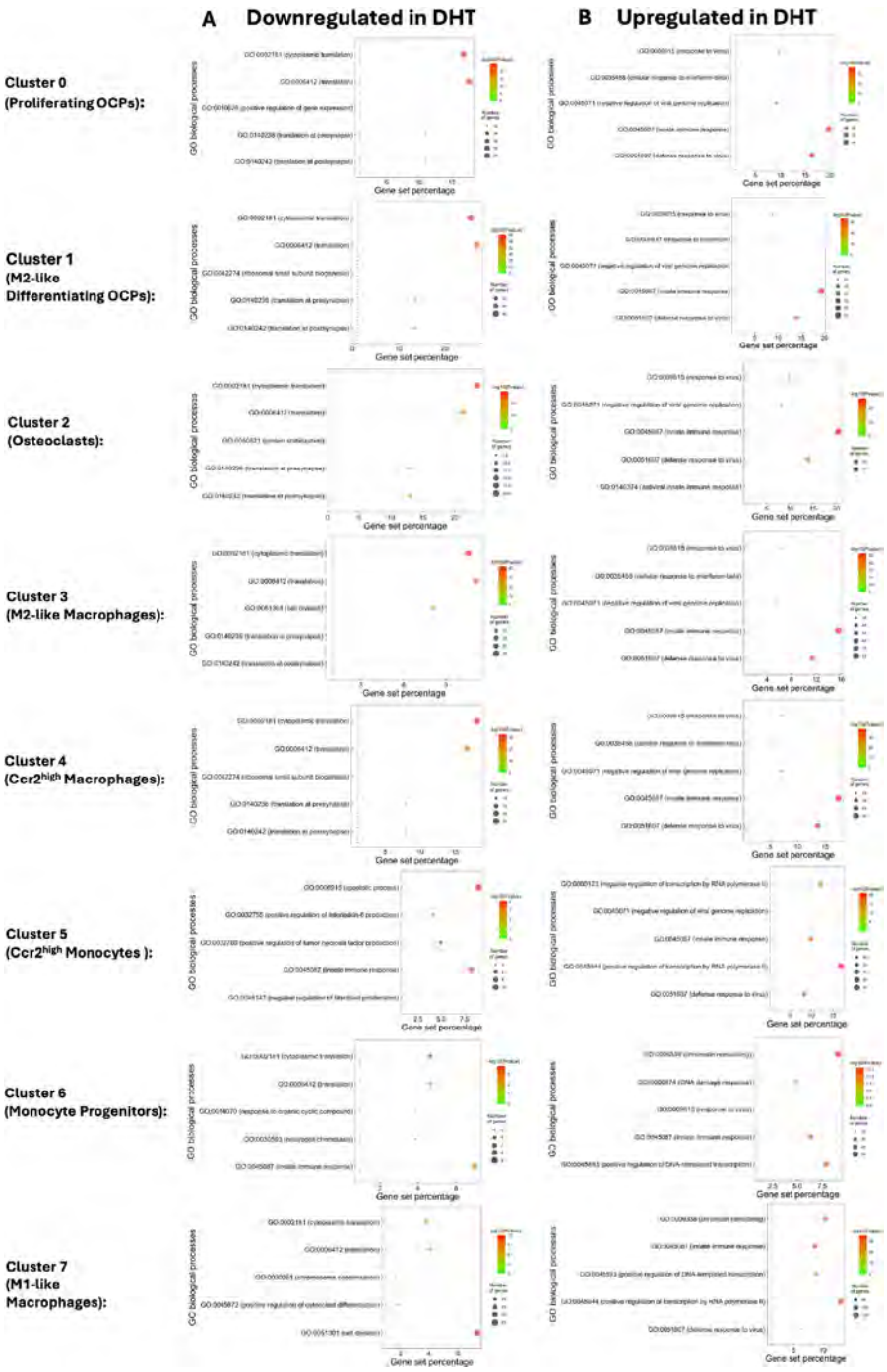


Figure 2. Androgen Treatment Alters the Biological Processes in Myeloid Lineage Cells. Differentially expressed genes (DEGs) between the vehicle and DHT-treated samples in each cluster were used to determine the gene ontology (GO) terms downregulated (A) and upregulated with DHT treatment (B). GO terms that are downregulated with DHT treatment include translation-related terms throughout majority of the clusters and terms that are upregulated with DHT treatment include immune defense response and interferon-related terms throughout majority of the cluster.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

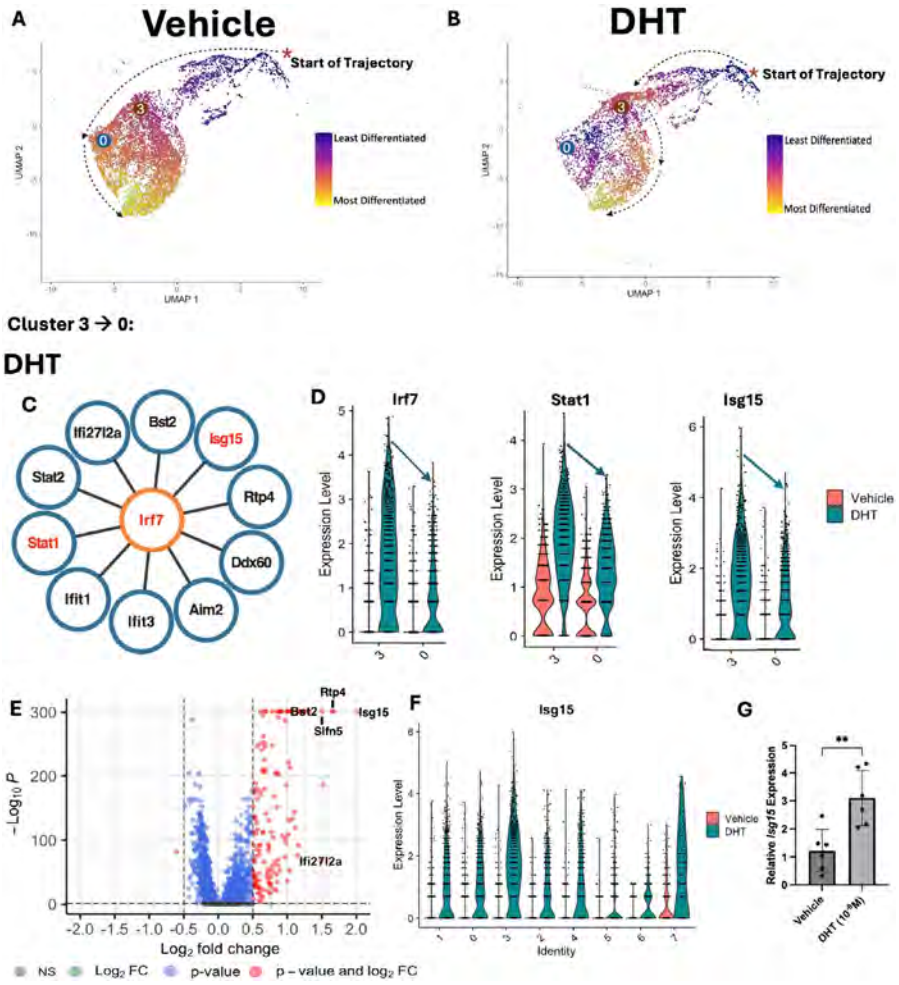


Figure 3. Interferon-Related Gene Expression is Increased with Androgen Treatment. Pseudotime trajectory analysis was performed on vehicle-treated (A) and DHT-treated (B) myeloid lineage cells. Cluster 6 (monocyte progenitors) was the root trajectory. Trajectory analysis of the vehicle-treated sample displays the progression of differentiation through monocyte and macrophage populations into differentiating OCPs and osteoclasts. In comparison, the DHT-treated subset illustrates differentiation from monocytes to M2-like differentiating OCPs and osteoclasts, with proliferating OCP clusters determined to be less differentiated. Transcription factor gene expression was analyzed between cluster 3 (M2-like macrophages) to 0 (proliferating OCPs) in the DHT-treated sample (C), and the transcription factor Irf7 was found to be decreased in cluster 0, along with Stat1 and Isg15 (D). In comparison, vehicle-treated cells did not express Irf7 or Isg15 and had lower expression of Stat1 overall. Differentially expressed genes (DEGs) of the DHT-treated sample were exhibited in a volcano plot (E), with Isg15 as the most upregulated DEG. A violin plot illustrates that Isg15 is differentially expressed with DHT treatment in all clusters (F). RT-qPCR of DHT and vehicle-treated cell culture confirmed increased relative expression of Isg15 in DHT-treated cells (G). Plots and analysis were performed with the Cytoscape software and Monocle3, Seurat and EnhancedVolcano R packages. Bars show mean ± standard deviation. Comparisons in RT-qPCR analysis were made with an unpaired t-test. ** = $p<0.01$.

Background/Purpose: Rheumatoid arthritis (RA) is characterized by chronic inflammatory erosions and female predominant disease. Androgen, the dominant sex hormone in males, is protective against bone loss. We have previously shown that androgen limits erosions in a TNF-mediated model of RA and potentially targets osteoclast precursor (OCP). Here, we investigated androgen's effect on osteoclast differentiation and hypothesized that androgen negatively regulates osteoclastogenesis in precursor cells.

Methods: Bone marrow derived cells were harvested from a 3-month-old male C57BL/6J mouse and plated in media containing either 10^{-9}M of 5α-dihydrotestosterone (DHT) or vehicle control and M-CSF. After 48 hours, RANK-L, and human TNFα (hTNFα) were added to media and cells were incubated for 24 hours. Adherent cells were captured with the 10X Genomics Chromium system to undergo single-cell RNA-sequencing (scRNA-seq). Cell typing was determined by the mouse cell atlas and "FindAllMarkers" command in Seurat. Gene ontology (GO) analysis was performed by determining the differentially

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

expressed genes (DEGs) between vehicle and DHT-treated samples in each cluster and submitting them to the DAVID Bioinformatics database. Pseudotime trajectory analysis was performed with the Monocle3 R package. Transcription factor (TF) analysis was performed by generating gene modules between clusters using Monocle3 and the pseudotime dataset. DEGs from this analysis were inputted into the iRegulon package in Cytoscape to determine TFs. DEGs between samples were illustrated in a volcano plot. Using the same cell culture protocol, RT-qPCR was performed on DHT and vehicle-treated samples to compare gene expression.

Results: In the scRNA-seq dataset, 8 clusters were defined as myeloid-lineage cells (Fig. 1A-B). The GO terms that were downregulated with DHT treatment and conserved throughout the clusters included terms associated with translation (Fig. 2A). In comparison, terms upregulated with DHT treatment included innate immune response and response to interferon (Fig. 2B). Pseudotime trajectory analysis of the vehicle and DHT-treated samples showed a difference in differentiation trajectory, where differentiation is decreased in proliferating OCPs with DHT treatment (Fig. 3A-B). TF analysis between our clusters of interest exhibit greater expression of the TF *Irf7* and other interferon-related genes with DHT (Fig 3C-D). The top DEG in the DHT-treated sample for most clusters was *Isg15* (Fig. 3E-F). Relative *Isg15* expression was also significantly increased in DHT-treated OCPs (Fig. 3G).

Conclusion: Androgen treatment in an inflammatory in vitro system of osteoclastogenesis caused a change in the expression of interferon genes and the trajectory of osteoclast differentiation. DHT treatment upregulated interferon signaling, particularly *Isg15* expression, which has been found to negatively regulate osteoclastogenesis (1). This increase in expression may potentially limit differentiation and therefore erosive disease. Further studies will involve examining how androgen targets interferon-related genes and their role in osteoclastogenesis.

1) MacLauchlan et al. *Proc Natl Acad Sci U S A* 120(15) 2023.

Disclosure: K. Chen: None; **C. Wu**: None; **G. Kulzhanova**: None; **H. Rahimi**: None.

Abstract Number: 0087

Integrative Metabolomic and Inflammatory Profiling in Rheumatoid Arthritis: Disease activity, therapeutic modulation, and underlying hepatic mechanisms

Laura muñoz-Barrera[1], Carlos Pérez Sánchez[2], Rafaela Ortega-Castro[3], Sagrario Corrales[1], Tomás Cerdó[1], Ismael Sanchez-Pareja[1], Pilar Font[4], Jerusalen Calvo Gutierrez[5], M Carmen Abalos-Aguilera[6], Desiree Ruiz-Vilchez[7], Pedro Seguí-Azpilcueta[8], Christian Merlo-Ruiz[6], Jose Javier Pérez Venegas[9], DOLORES RUIZ MONTESINOS[10], Carmen Maria Romero Barco[11], Antonio Fernández-Nebro[12], Natalia Mena Vázquez[13], FRANCISCO JAVIER GODOY NAVARRETE[14], ALBA MARIA CABEZAS LUCENA[15], MARIA ANGELES AGUIRRE ZAMORANO[1], Nuria Barbarroja[16], Alejandro Escudero[17] and Chary López pedrera[18], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [4]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, SpainBiomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [5]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Sevilla, Spain, [6]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [7]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, [8]Radiology Service, Reina Sofia Hospital/Maimonides Institute for Research in Biomedicine of Cordoba/University of Cordoba, Spain, Córdoba,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

United Kingdom, [9]Virgen Macarena University Hospital, Sevilla, Spain, Sevilla, Spain, [10]Virgen Macarena University Hospital, Sevilla, Spain, Cordoba, [11]Virgen de la Victoria Hospital Malaga, Spain, Malaga, Spain, [12]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [13]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [14]Jaen University Hospital, Spain, Jaen, Spain, [15]Jaen University Hospital, Spain, Jaen, [16]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [17]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Andalucia, Spain, [18]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Lipid metabolism plays a key role in immune cell plasticity, influencing activation, differentiation and function. Inflammation alters this metabolism, contributing to disease progression. Extensive analyses of these profiles in Rheumatoid Arthritis (RA) using high throughput metabolomics may improve disease characterization.

This study objectives were to analyze circulating lipid and inflammatory profiles of RA patients, explore their association with disease activity and their modulation by b/tsDMARDs and identify mechanisms underlying altered lipid metabolism.

Methods: Clinical data and blood samples were collected from 362 RA patients and age- and sex-matched healthy donors (HDs). Serum lipid profiles were analyzed using Nightingale's NMR spectroscopy (>200 lipid markers). Inflammatory proteins were measured by proximity extension assay (Olink/Cobiomic). A 6-month follow-up was performed in active RA patients treated with TNFi (n=80), IL6Ri (n=27), or JAK inhibitors (n=46). *In vitro* studies in HepG2 liver cells treated with serum from active RA patients included Bodipy staining for lipid accumulation and PCR assays for lipid metabolism gene expression.

Results: Patients were classified as high (n=97) and moderate-low (n=265) disease activity (DAS28). Around 100 lipid markers differed significantly between groups. High activity was associated with reduced levels of most lipids, including apolipoproteins, fatty acids, phospholipids, and total lipid, cholesterol, and triglyceride content. Notably, LDL and VLDL-related proatherogenic markers were reduced. Many lipids negatively correlated with CRP, ESR, ACPAs, RF, cardiovascular risk, and liver enzymes (AST, ALT, GGT).

Some proinflammatory proteins-cytokines, chemokines, and growth factors-were increased in high activity. These also correlated with clinical parameters and the altered lipids identified, indicating a shared dysregulation in high disease activity. At 6-month follow-up, treatment significantly reversed the altered lipid markers and inflammatory proteins, paralleling clinical improvements, including common and specific molecules modulated by each drug.

In vitro HepG2 cells treated with active RA serum showed altered lipid accumulation and dysregulated gene expression compared to HDs. Genes related to lipolysis, β-oxidation, lipid transport and scavenger receptors were over expressed in active RA, whereas genes related to lipogenesis and cholesterol homeostasis were under expressed. These changes were partially reversed by TNFi, IL6Ri or JAKi mirroring *in vivo* effects.

Conclusion: Active RA is characterized by reduced circulating lipids and proinflammatory dysregulation. These changes are partially reversed by biologics and JAKi in parallel with clinical improvement. *In vitro* findings suggest an adaptive hepatic response to inflammation favoring energy mobilization over lipid synthesis, potentially contributing to metabolic dysfunction and CV risk, which may be mitigated by targeted therapies. Ongoing studies aim to further clarify these mechanisms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Supported by ISCIII (PI21/0591, PI24/00959, CD21/00187 and RICOR-24/0007/0019), and RYC2021-033828-I; co-financed by European Union.

Disclosure: L. muñoz-Barrera: None; **C. Pérez Sánchez**: None; **R. Ortega-Castro**: None; **S. Corrales**: None; **T. Cerdó**: None; **I. Sanchez-Pareja**: None; **P. Font**: None; **J. Calvo Gutierrez**: None; **M. Abalos-Aguilera**: None; **D. Ruiz-Vilchez**: None; **P. Seguí-Azpilcueta**: None; **C. Merlo-Ruiz**: None; **J. Pérez Venegas**: AstraZeneca, 6, Janssen, 4, 6, UCB, 6; **D. RUIZ MONTESINOS**: None; **C. Romero Barco**: None; **A. Fernández-Nebro**: Argenx, 5, AstraZeneca, 2, 5, 6, Chemo, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Gebro Pharma, 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 5, Merck Serono, 5, MSD, 5, Novartis, 2, 5, 6, Takeda, 5, UCB, 5; **N. Mena Vázquez**: None; **F. GODOY NAVARRETE**: None; **A. CABEZAS LUCENA**: None; **M. AGUIRRE ZAMORANO**: None; **N. Barbarroja**: None; **A. Escudero**: None; **C. López pedrera**: None.

Abstract Number: 0088

Imbalance of Inflammation-Regulating Microorganisms and Predicted Metabolomic Pathways Associates With Disease Evolution in Individuals At-Risk for Rheumatoid Arthritis

Lyndsey Cole[1], Brendan Allen[2], Sucai Liu[2], Marie Feser[3], Le Yi Phyo[2], LauraKay Moss[2], Daniel Frank[2], J. Kirk Harris[2], Kristen Demoruelle[4], Kevin Deane[5], V. Michael Holers[6] and Kristine Kuhn[7], [1]University of Colorado School of Medicine, Centennial, CO, [2]University of Colorado School of Medicine, Aurora, CO, [3]University of Colorado Anschutz Medical Campus, Aurora, CO, [4]University of Colorado Anschutz Medical Campus, Golden, CO, [5]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [6]University of Colorado Anschutz Medical Campus, Aurora, [7]2022 - 2023 / Adult/ University of Colorado, Aurora, CO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1: Participant Characteristics and Laboratory Values

Table 1: Participant Characteristics and Laboratory Values

Variable[a]	Non-Converters	Converters	P-value
N total	31	14	
Age (years)	67 (50, 73)	57 (43.8, 68.8)	0.31
Female sex	22 (71%)	11 (78.6%)	0.73
Shared epitope[b]	12 (38.7%)	5 (35.7%)	>0.99
Ever smoker	11 (35.5%)	4 (26.7%)	0.74
Current smoker	1 (3.2%)	0 (0%)	>0.99
Body Mass Index			
Underweight	1 (3.2%)	0 (0%)	>0.99
Healthy	10 (32.3%)	4 (28.6%)	
Overweight	11 (35.5%)	6 (42.9%)	
Obese	9 (29%)	4 (28.6%)	
First degree relative with RA	5 (16.1%)	5 (35.7%)	0.24
Non-Hispanic/White race/ethinicity	27 (71.1%)	11 (78.6%)	0.66
Medication use			
Daily NSAIDs, baseline	1 (3.2%)	3 (21.4%)	0.08
Acid blocker, baseline	4 (12.9%)	1 (7.1%)	>0.99
Probiotics, baseline	9 (27.6%)	4 (28.6%)	>0.99
Daily NSAIDs, follow up	3 (9.7%)	3 (21.4%)	0.36
Acid blocker, follow up	3 (9.7%)	1 (7.1%)	>0.99
Probiotics, follow up	5 (20%)	3 (23.1%)	>0.99
Baseline laboratory values[c]			
RF positive	8 (25.8%)	7 (50%)	0.17
CCP3	51.5 (38.0, 120.4)	83.3 (41.2, 427.3)	0.23
CCP3.1	66.2 (37.7, 132.3)	59.2 (37.1, 362.0)	0.77
Follow up variables			
Days between baseline & follow up sample	500 (398, 524)	542.5 (743.4, 1566)	0.59
Days between follow up sample & diagnosis	NA	0 (-47.3, 0)	NA
RF positive	11 (35.5%)	8 (57.1%)	0.21
CCP3	49.4 (20.9, 84.5)	64.3 (14.7, 474.9)	0.54
Change in CCP3	0.30 (-26.6, 22.3)	-16.6 (-48.5, 9.9)	0.22
CCP3.1	80.8 (22.5, 132.2)	54.0 (14.8, 559.2)	0.85
Change in CCP3.1	-5.4 (-33.9, 26.5)	-0.1 (-21.0, 91.0)	0.46

[a] Categorical variables presented as number (%). Continuous variables presented as median (interquartile range). Variables represent baseline values except where specified. Variables described as "follow up" were obtained at the timepoint closest to identification of IA in Converters and the timepoint in Non-Converters that was closest to the median number of days after baseline that Converter follow ups were obtained.
[b] Defined as the presence of 1 or more HLA-DR4 alleles.
[c] CCP3/3.1 ELISA (Werfen) results are in units; a positive result cutoff of ≥20 units was used.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The mucosal origins hypothesis of RA proposes that immune responses to microorganisms at mucosal sites (e.g. intestine) lead to systemic inflammation and autoimmunity. Little is known about how the fecal microbiome composition and functional capacity may evolve in the pre-clinical period to contribute to development of clinical inflammatory arthritis (IA). The study objective was to compare the fecal microbiome over time among individuals at-risk for RA (ARI) who converted to IA (Converters) versus those who did not (Non-Converters).

Methods: Fecal samples for shotgun metagenomic sequencing of fecal DNA by Illumina NovaSeqX were prospectively collected intermittently over 3 years from ARI, defined as adults with serum cyclic citrullinated peptide antibodies (CCP3 ^{3}20) with no IA at baseline. ARI were grouped into Converters, who developed RA-like synovitis of ^{3}1 joint during follow-up, and Non-Converters. Taxonomic and functional microbiome profiling was performed by MetaPhlAn4 and HUMAnN3. Differential abundance was assessed by MaAsLin3 by mixed linear models. A single baseline and follow up sample from each participant were analyzed. Follow up samples selected were those obtained at the timepoint closest to identification of IA in Converters and the timepoint in Non-Converters that was closest to the median number of days after baseline that Converter follow ups were obtained.

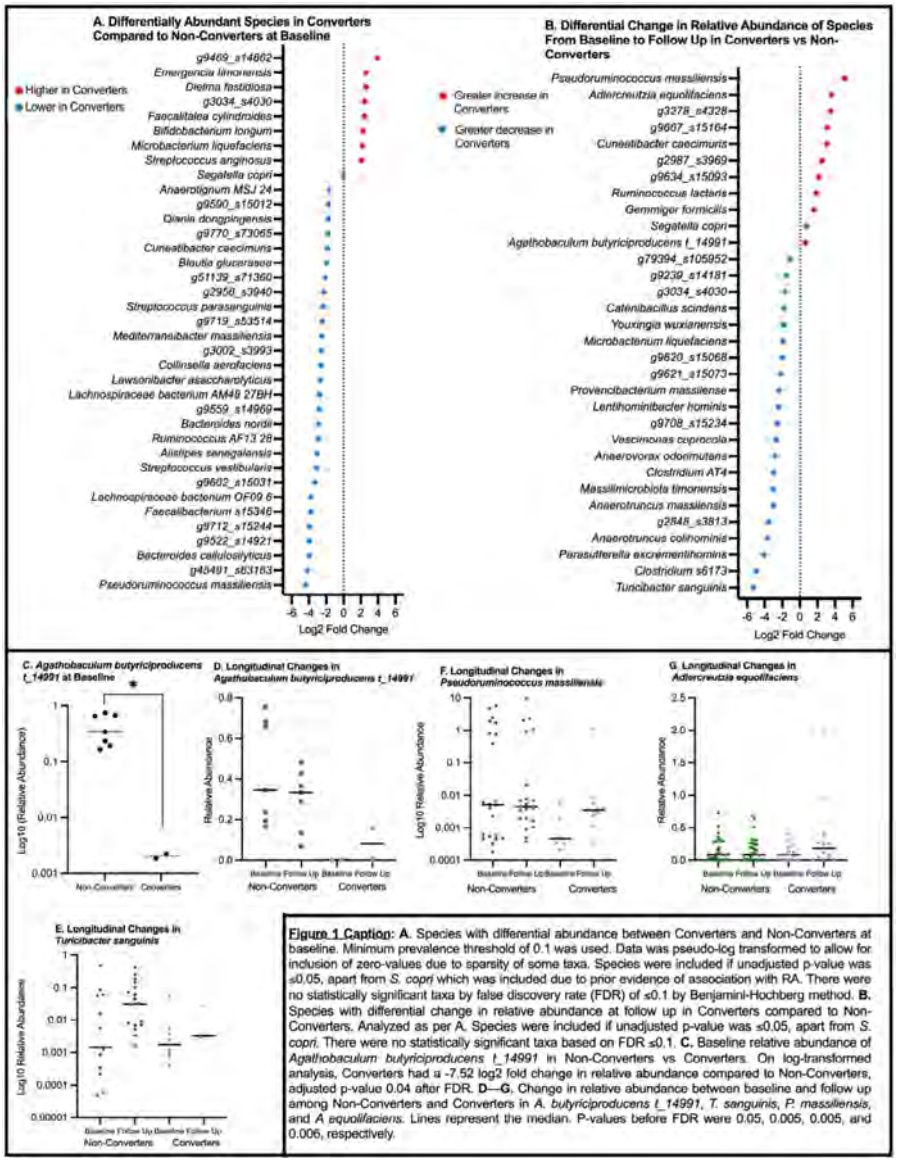


Figure 1: Taxonomic Differences Between Converters and Non-Converters at Baseline and Follow Up

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

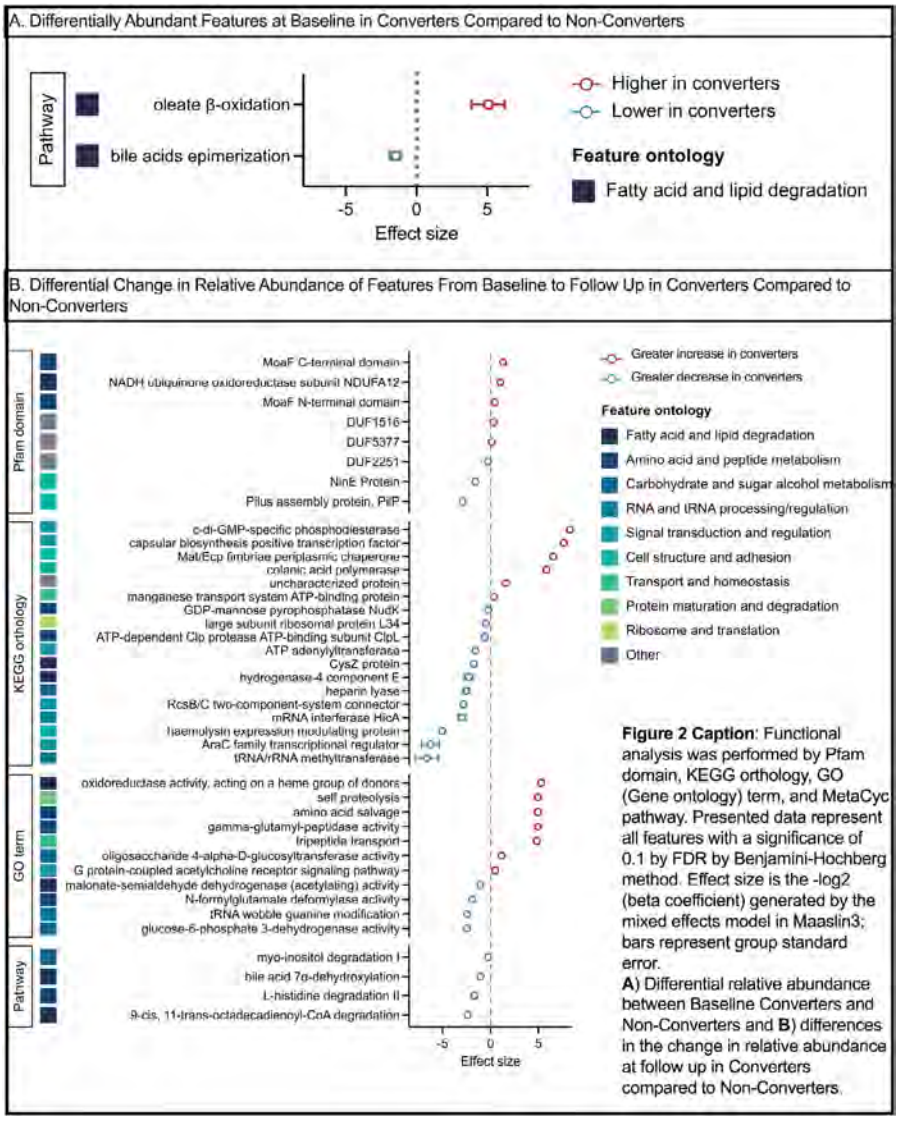


Figure 2: Predicted Functional Gene Features and Pathway Differences Between Converters and Non-Converters at Baseline and Follow Up

Results: There were no significant differences between Converters (n=14) and Non-Converters (n=31) in baseline demographics and labs (**Table 1**). Taxonomic analysis demonstrated -7.5 log2fold lower *Agathobaculum butyriciproducens t_14991* in Converters compared to Non-Converters at baseline; multiple other taxa were differentially abundant but not statistically significant after false discovery rate (FDR) (**Figure 1**). Between baseline and follow up, Converters had a greater increase in *A. butyriciproducens t_14991*, *Pseudoruminococcus massiliensis*, and *Adlercreutzia equolifaciens*; and a greater decrease in *Turicibacter sanguinis*; not significant after FDR. Functional analysis showed significant alterations in fatty acid degradation pathways at baseline among Converters (**Figure 2**). Longitudinally, fatty acid degradation gene features and pathways in Converters changed more significantly over time.

Conclusion: Among a longitudinal cohort of ARI, Converters showed baseline depletion of immunoregulatory bacteria *A. butyriciproducens t_14991*, a short-chain fatty acid (SCFA) producer. Moreover, the trend of changes in several SCFA-producing and starch-metabolizing bacteria in Converters at baseline and over time suggest that Converters harbor gut microbiomes with altered inflammation-regulating capacity compared to Non-Converters. Many of the predicted functional changes at baseline and over time in Converters involve metabolism of immunomodulatory metabolites, including fatty acid degradation pathways. Together, these data indicate complex feedback interactions between the gut microbiome and the

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

host during IA development. Further exploration into longitudinal gut microbiome changes in ARI is needed to better understand potential diagnostic, preventative, and therapeutic applications.

Disclosure: L. Cole: None; **B. Allen**: None; **S. Liu**: None; **M. Feser**: None; **L. Phyo**: None; **L. Moss**: None; **D. Frank**: None; **J. Harris**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5; **K. Deane**: Inova Diagnostics, 1; **V. Holers**: Q32 Bio, 12, 2; **K. Kuhn**: Solarea, 2.

Abstract Number: 0089

Expansion of PD-1^{hi} Tfh and Tph cells in the peripheral blood of seropositive clinically suspect arthralgia patients: association with progression to rheumatoid arthritis

Maria-Eugenia Miranda-Carus[1], Mariana Gutierrez-Riart[2], Beatriz Nieto-Carvalhal[3], Laura Nuño[2], Alejandro Villalba[1], Diana Peiteado[1], Irene Monjo Henry[1], Marta Novella-Navarro[1] and Eugenio de Miguel[1], [1]Hospital Universitario La Paz, Madrid, Spain, [2]Hospital Universitario La Paz, Madrid, [3]Hospital Universitario La Paz, Mdrid

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Subjects with clinically suspect arthralgia (CSA) are at risk for developing rheumatoid arthritis (RA) and therapeutic interventions may prevent or delay progression. Still, a better identification of potential progressors would minimize exposure to unnecessary treatment. CD4+CXCR5+PD-1^{hi} follicular helper (Tfh) and CD4+ CXCR5-PD-1^{hi}

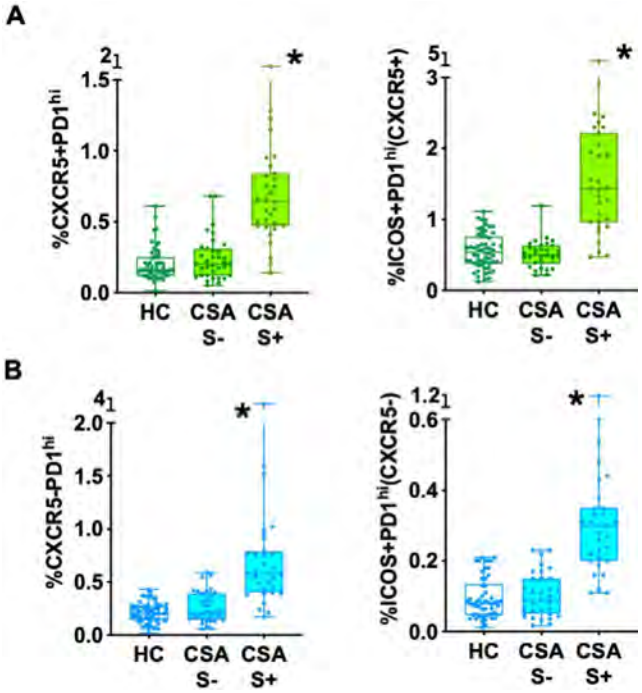


Fig. 1. Frequency of circulating Tfh and Tph cells in HC, seronegative CSA (CSA S-) and seropositive CSA (CSA S+) subjects. A. Frequencies of cTfh (left) and cICOS+Tfh cells(right). B. Frequencies of cTph (left) and cICOS+cTph cells (right)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

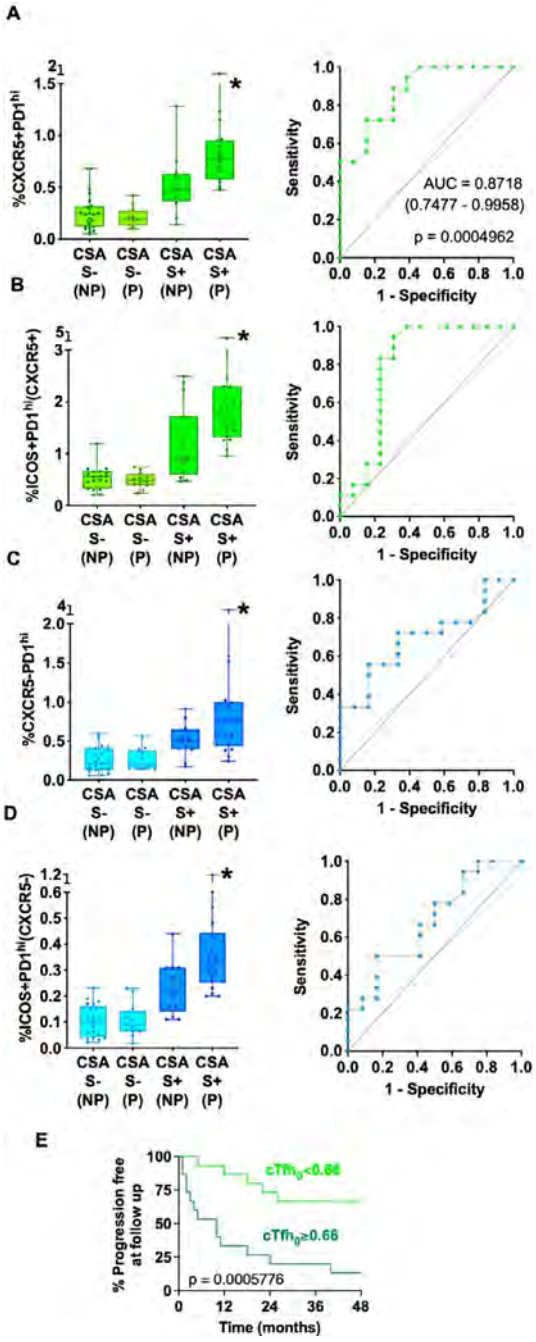


Figure 2. Relation of the baseline cTfh and cTph cell frequencies with the occurrence of progression to inflammatory arthritis in CSA patients. A-D. Baseline cTfh (A), ICOS+cTfh (B), cTph (C), and ICOS+cTph (D) cell frequencies, in CSA patients who did not progress (non-progressors, NP), vs CSA patients who progressed (progressors, P) to develop inflammatory arthritis. Bars in the left panels represent the median and interquartile range; whiskers represent the maximum and minimum values. *p<0.05, Mann-Whitney test. The right panels show the ROC curves representing the relation of the baseline cTfh (A), ICOS+ cTfh (B), cTph (C) and ICOs+ cTph (D) cell frequencies with the occurrence of progression during the observation period (48 months) (ROC AUC and p values calculated with logistic regression analysis). E. Kaplan-Meier survival curves displaying the probability of progression-free follow-up, stratified using the optimal cTfh cut-off value for progression prediction obtained from the ROC curve.

peripheral helper (Tph) T cells are implicated in RA pathogenesis; characterizing their profile in CSA can enhance our understanding of the RA preclinical stage. Therefore, our objective was to examine the frequencies of circulating Tfh (cTfh) and Tph (cTph) cells in CSA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Prospective, non-interventional study in patients with CSA (EULAR definition). Immediately upon initial evaluation, peripheral blood was drawn from each patient and an age/gender-matched healthy control (HC). Ficoll-Hypaque isolated PBMCs were examined by cytometry. Patients were subsequently followed until RA onset or alternatively for up to 48 months.

Results: As compared with HC, patients with seropositive (RF and/or ACPA+) (n=32) but not seronegative (n=37) CSA demonstrated expanded baseline frequencies of cTfh and cTph cells. These frequencies were significantly higher in seropositive CSA patients who progressed to develop classified RA vs those who did not. A cTfh cell frequency > 0.66 predicted progression with a sensitivity of 72% and a specificity of 85%. At the time of RA onset, seropositive progressors (n=18) demonstrated a significant further increase of the cTph but not of the cTfh cell frequency.

Conclusion: Seropositive CSA patients demonstrate increased baseline cTfh and cTph cell frequencies. Higher baseline proportions of cTfh cells associate with progression. This may help identify patients who would benefit from therapeutic interventions directed at delaying or preventing RA onset.

Disclosure: M. Miranda-Carus: None; **M. Gutierrez-Riart**: None; **B. Nieto-Carvalhal**: None; **L. Nuño**: None; **A. Villalba**: None; **D. Peiteado**: None; **I. Monjo Henry**: None; **M. Novella-Navarro**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6.

Abstract Number: 0090

Interleukin-36β modulates the progression of rheumatoid arthritis by altering the behavior of rheumatoid arthritis synovial fibroblasts

Marie Svenja Kümmel[1], Mona Arnold-Gräf[2], Selina Ohl[2], Klaus Frommer[3], Nils Schulz[4], Stefan Rehart[5], Ulf Müller-Ladner[3] and Elena Neumann[3], [1]Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Justus-Liebig-University, Germany, Gießen, Germany, [2]Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Justus-Liebig-University, Germany, Bad Nauheim, Germany, [3]Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Bad Nauheim, Justus-Liebig-University, Germany, Bad Nauheim, Hessen, Germany, [4]Kerkchoff Klinik, Dep. of rheumatology, Bad Nauheim, Germany, [5]Agaplesion Markus Hospital, Frankfurt, Hessen, Germany

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis synovial fibroblasts (RASF) play a central role in driving inflammation and promoting cartilage degradation in Rheumatoid arthritis (RA). In our study, we observed that RASF from patients in clinical remission exhibit reduced expression levels of Interleukin-36β (IL-36β). As IL-36β is a pro-inflammatory cytokine involved in immune regulation, we investigated its role in modulating RASF behavior.

Methods: Patients with RA were stratified into remission or active disease groups based on clinical assessments and laboratory markers. RNA sequencing was conducted on RASF isolated from both groups, with and without stimulation using 0.05ng/ml IL-1β. Subsequent analyses included pathway enrichment and identification of the top 50 dysregulated genes. To assess cell adhesion, RASF pre-treated with 1ng/ml IL-1β and/or IL-36β were subjected to a 6-hour assay, followed by quantification of adherent cells after 2 hours. Cell migration was evaluated using transwell assays with 8μm pores and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

an FBS gradient, comparing pre-stimulated RASF populations based on the stained surface area after crystal violet labeling. Proliferation was determined via BrdU assay 19–24 hours after stimulation with IL-1β, IL-36β, or both. Immunofluorescence staining was employed to analyze IL-36 receptor (IL-36R) expression in synovial tissues from RA patients (active/remission) and individuals with osteoarthritis, with quantification of signal intensity per visual field.

Results: RNA sequencing revealed a marked reduction in IL-36β (-7,14 fold) and its antagonist IL-36Ra (-11,49 fold) in RASF derived from patients in remission compared to those with active rheumatoid arthritis (n=4). Consistent with these findings, elevated IL-36β expression was detected in synovial tissue samples from patients with active disease. Immunofluorescence analysis demonstrated that IL-36 receptor (IL-36R) was predominantly localized to the synovial lining layer across all RA samples, with a more pronounced signal intensity observed in tissues from patients with active RA. Functional assays showed that IL-36β stimulation significantly reduced the adhesive capacity of RASF compared to both unstimulated and IL-1β-stimulated cells ($p < 0.0075, n = 14$). In contrast, IL-36β stimulation led to a significant increase in RASF migration relative to unstimulated controls ($p< 0.002, n=14$), an effect also observed specifically in remission-derived RASF ($p< 0.026, n = 7$). IL-36β treatment increased RASF proliferation compared to IL-1β stimulated cells ($p< 0.009, n=5$), with no significant difference between cells derived from patients with active disease versus remission.

Conclusion: The modulation of adhesion and enhanced migratory capacity of IL-36β-stimulated RASF indicates a potential mechanism by which these cells may more effectively localize to sites of tissue damage in RA. Moreover, the IL-36β-induced increase in RASF proliferation, combined with the diminished IL-36R signal in synovial tissues from patients with active disease, highlights the pathogenic relevance of elevated IL-36β levels in the context of RA progression.

Disclosure: M. Kümmel: None; **M. Arnold-Gräf**: None; **S. Ohl**: None; **K. Frommer**: None; **N. Schulz**: None; **S. Rehart**: None; **U. Müller-Ladner**: None; **E. Neumann**: None.

Abstract Number: 0091

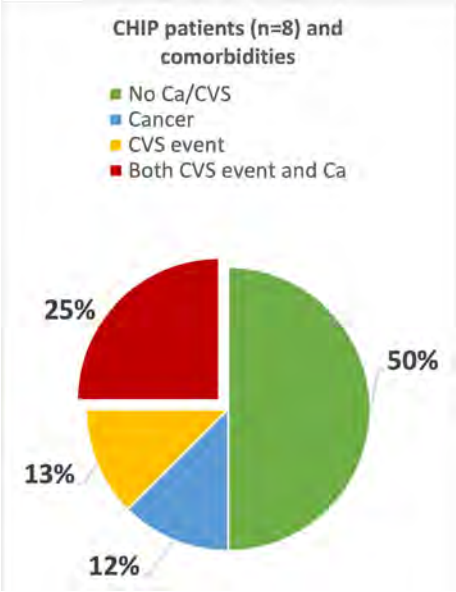
Clonal Hematopoiesis of Indeterminate Potential (CHIP) in Rheumatoid Arthritis: associations with treatment response and comorbidities

Athena Chin[1], susan branford[2], Annabelle Small[3], malcolm Smith[1], monika Kutyna[4], Robert King[5], Susanna Proudman[6], Devendra Hiwase[7] and **Mihir Wechalekar**[8], [1]Flinders Medical Centre, KURRALTA PARK, South Australia, Australia, [2]SA Pathology, Adelaide, [3]Flinders University, Bedford Park, South Australia, Australia, [4]South Australian Health and Medical Research Institute, Adelaide, [5]Flinders Medical Centre, Adelaide, South Australia, Australia, [6]Royal Adelaide Hospital and University of Adelaide, Medindie, South Australia, Australia, [7]Royal Adelaide Hospital, Adelaide, [8]Flinders Medical Centre and Flinders University, Bedford Park, South Australia, Australia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Clonal hematopoiesis (CH) of indeterminate potential (CHIP) is defined as the detection of recurrent somatic mutations, at a variant allele frequency (VAF) < ![if !msEquation] >< ![if !vml] >< ![endif] >< ![endif] >2%, in genes that are known to drive hematological malignancies (such as *DNMT3A, TET2, ASXL1)* in individuals without hematological abnormalities. CHIP is associated with increased risk of cardiovascular morbidity and all-cause mortality, likely by driving inflammation[1]. We hypothesised that the chronic inflammatory microenvironment in an autoimmune condition such as rheumatoid arthritis (RA) provides selective advantage to CH, thereby promoting an inflammatory state in a self-perpetuating feedback

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



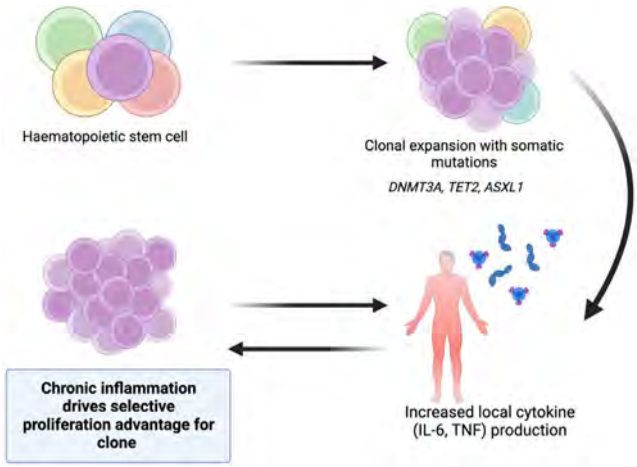
CHIP patients and comorbidities

loop. We therefore evaluated the prevalence and pattern of CHIP in RA and its impact on disease activity (DA) and comorbidities.

1. Rossi M, Meggendorfer M, Zampini M, et al. Clinical relevance of clonal hematopoiesis in the oldest-old population. *Blood*. 2021;14doi:https://doi.org/10.1182/blood.2021011320

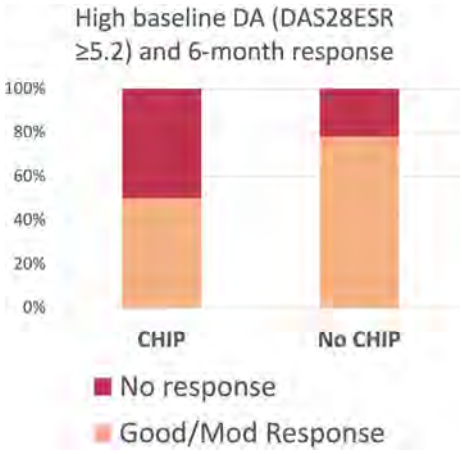
Methods: DNA was extracted from the peripheral blood of 112 patients with early RA and was analysed for CH using a custom-designed myeloid gene panel. Correlation between CH and disease parameters was performed.

Results: Somatic mutations at VAF levels < ![if !msEquation] >< ![if !vml] >< ![endif] >< ![endif] >0.5% and < ![if !msEquation] >< ![if !vml] >< ![endif] >< ![endif] >2% were detected in 27.7% (31/112) and 9.8% (11/112) RA patients, respectively. RA patients >60years old (53.9%) were more likely to have CHIP (20.5% *vs*. 4.1%; *P*=0.015). This is significantly higher than the reported frequency in an unselected population of 5.6%[2]. The majority of the 48 identified pathogenic variants involved *DNMT3A* (47.9%), *TET2* (16.7%) and *ASXL1* (12.5%). 9/31 (29%) harboured ≥2 variants. Though there was a higher prevalence of CHIP in seronegative patients (11.1%) compared to seropositive (8.2%); this was not statistically significant (p=0.75). Patients with high baseline DA (DAS28-ESR >5.1) and CHIP or ≥2 distinct CH mutations were less likely to



Clonal Haematopoiesis and Chronic Inflammation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



RA Patients with High Disease Activity and Treatment Response at 6 months

respond to therapy at 6-months (23.5% *vs*. 7.8%; *P*=0.1; 23.5% *vs*. 3.9%; *P*=0.031, respectively). Strikingly, patients with CHIP had higher rates of incident malignancy (38% *vs*. 8%; *P*=0.04), and those with any CH were more likely to have cardiovascular event after RA diagnosis (57% *vs*. 25%; *P*=0.05).

2. Jaiswal S, Fontanillas P, Flannick J, et al. Age-related clonal hematopoiesis associated with adverse outcomes. *N Engl J Med*. Dec 25 2014;371(26):2488-98. doi:10.1056/NEJMoa1408617

Conclusion: Patients with RA have increased prevalence of CH, with associated implications for DA, response to therapy and risk of comorbidity. Further prospective studies are required to characterise this subset of RA patients.

Disclosure: A. Chin: None; **s. branford**: None; **A. Small**: None; **m. Smith**: None; **m. Kutyna**: None; **R. King**: None; **S. Proudman**: Boehringer-Ingelheim, 5, 6, Janssen, 5, 6, Merck/MSD, 1; **D. Hiwase**: None; **M. Wechalekar**: GlaxoSmithKlein(GSK), 5, Janssen, 5.

Abstract Number: 0092

SynovAI: A Revolutionary AI Framework for Enhanced Detection and Differentiation of Rheumatoid Arthritis, Osteoarthritis, and Spondyloarthritis via Advanced Ultrasound Imaging

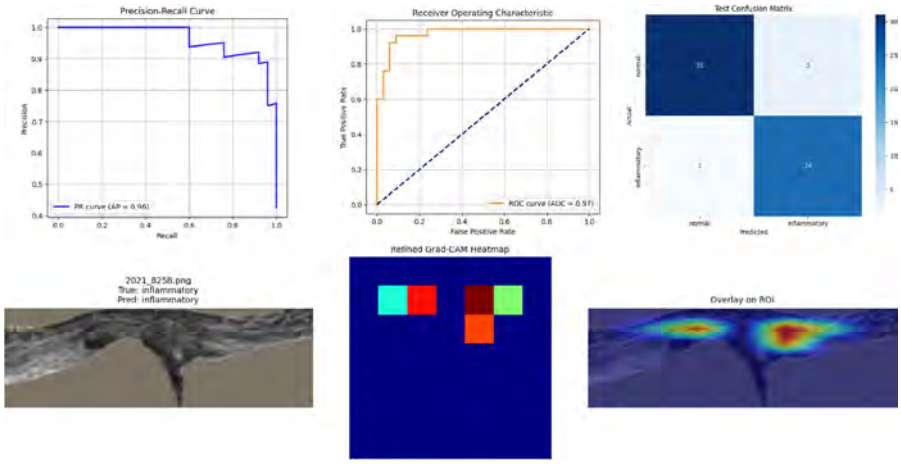
Mojtaba S. Fazli[1], Mariani Diaz Deluna[2], Suzanne Tamang[2] and Robert Fairchild[2], [1]Stanford University, San Francisco, CA, [2]Stanford University, Stanford, CA

SESSION INFORMATION

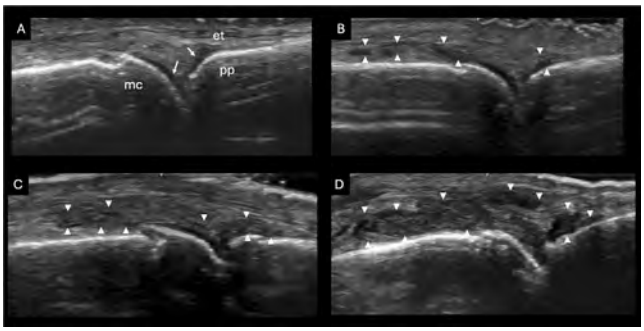
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology musculoskeletal ultrasound (MSKUS) is a powerful technique to identify and differentiate arthritidies joint pathology, yet MSKUS is highly dependent on user experience. Techniques improve ultrasound training, imaging explainability, and aid clinical interpretation can increase the utility of MSKUS. We have begun work on SynovAI, an innovative, next-generation artificial intelligence (AI) framework designed to augment MSKUS interpretation and diagnostic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Performance of synovial AI on the test set of metacarpophalangeal joints with varying degrees of synovial hypertrophy (top). Image segmentation, grad-CAM heat map, and visualization of the region of interest identified by SynovAI (bottom)



views of the dorsal MCP with normal synovium (A, arrows) and abnormal synovial hypertrophy (B-D, arrowheads). mc= metacarpal head; et = extensor tendon; pp = proximal phalanx.

accuracy. The goal SynovAI is to develop a framework which can identify, quantify, and highlight relevant pathologic features on MSKUS and provide likely rheumatic diagnoses based on the imaging alone, or in combination with clinical data inputs.

Methods: SynovAI framework integrates a suite of pioneering deep learning (DL) strategies designed for maximal diagnostic efficiency and interpretability. The framework begins with (1) an attention-enhanced U-Net architecture that adeptly segments synovial regions of interest (ROI), significantly reducing diagnostic noise. Subsequently, (2) an innovative dual-branch neural network merges global semantic insights derived from a Convolutional Block Attention Module (CBAM)-enhanced ResNet architecture with subtle textural details extracted by a unique diffusion-inspired model, enabling precise discrimination between B-mode ultrasound features. Then, (3) an advanced, attention-based adaptive feature fusion mechanism synthesizes these complementary features into highly robust representations.

Pilot evaluation was conducted on a retrospective clinical dataset of 588 B-mode ultrasound images from dorsal longitudinal metacarpophalangeal (MCP) views, all of which were interpreted by an expert ultrasonographer for the presence or absence of synovial hypertrophy. The dataset was split into 424 training images, 105 validation images, and 59 held-out test images, and reflected real-world clinical variability, including imaging artifacts and inconsistent probe angulation. Training included mixup augmentation, focal loss, gradient clipping, and cosine annealing with warm restarts. Model predictions were further refined via ensemble learning, adaptive thresholding, and test-time augmentation (TTA). Interpretability was enhanced with Grad-CAM visualizations.

Results: On the test set, SynovAI achieved 93.2% accuracy and a macro-averaged F1-score of 0.93, with F1-scores of 0.94 for normal and 0.92 for inflammatory joints. These results highlight SynovAI's strong and consistent performance in detecting early synovial abnormalities in routine ultrasound imaging.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this early proof of concept work, SynovAI could identify synovial changes with high accuracy by combining state-of-the-art deep learning methodologies with unparalleled interpretability. We plan to explore identification of associated bony, tendinous, and soft tissue features to synthesize in a predictive model to identify likely diseases, with the addition capability of handling secondary clinical inputs and providing explainable imaging outputs.

Disclosure: M. S. Fazli: None; **M. Diaz Deluna**: None; **S. Tamang**: None; **R. Fairchild**: None.

Abstract Number: 0093

Soluble CD13 engages protease-activated receptor 4 to promote synovial inflammation and angiogenesis in rheumatoid arthritis

Chenyang Lu[1], Megan N Mattichak[2], Simin Xu[1], William D Brodie[3], Neha Khanna[2], Hafsa Amin[2], Qi Wu[2], Phillip Campbell[2], David Fox[4] and **Pei-Suen Tsou**[5], [1]Division of Rheumatology, Department of Internal Medicine, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, Guangzhou, China (People's Republic), [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, Ann Arbor, [4]University of Michigan, Dexter, MI, [5]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Soluble CD13 (sCD13), the soluble form of aminopeptidase N/CD13, exhibits potent chemoattractant, angiogenic, and arthritogenic properties. While we previously identified certain G protein-coupled receptors (GPCR) including bradykinin receptor B1 as receptors for sCD13 in rheumatoid arthritis (RA), its complete receptor repertoire remains unclear. In this study, we aimed to investigate protease-activated receptor 4 (PAR4) as a novel receptor for sCD13.

Methods: Single-cell RNA sequencing datasets were reanalyzed to determine the expression of PAR4 on synovial cells in RA, which was then validated by immunofluorescence, Wester blotting, and flow cytometry. Induction of PAR4 in human umbilical vein endothelial cells (HUVECs) by TNF-a or IL-1b was assessed by qPCR and Western blotting. PAR4 was overexpressed in RA fibroblast-like synoviocytes (FLS), and cytokine production in sCD13-treated FLS was determined by qPCR and ELISA. The effect of CD13 blocking antibodies (WM15) on proliferation of FLS was dynamically analyzed using the IncuCyte. Effects of PAR4 knockdown or blocker (BMS986120) on the migration and angiogenesis abilities of HUVECs were evaluated by Transwell chambers and tube formation assay, respectively. The binding model of CD13-PAR4 was predicted and constructed using AlphaFold-multimer. Enzymatic inhibitor for CD13, bestatin, was also utilized to assess the enzymatic mechanism of sCD13 activating PAR4. Western blot was performed to identify signaling pathways stimulated by sCD13 in the presence of BMS986120 or WM15. BMS986120 was administered orally to collagen-induced arthritis (CIA) mice and joint inflammation was evaluated.

Results: PAR4 was abundantly expressed in RA synovium, especially in endothelial cells and FLS. While the expression of PAR4 in RA synovium was significantly higher compared to normal and osteoarthritis synovium, it was not induced by TNF-a or IL-1b. In RA FLS, PAR4 overexpression augmented sCD13-mediated proliferation, cytokine production, and ERK1/2 signaling. Both blocking and knocking down PAR4 could suppress sCD13-induced HUVEC migration and angiogenesis *in vitro*. BMS986120 also suppressed sCD13-mediated ERK1/2 phosphorylation in HUVECs. In addition, The CD13-PAR4 interaction involves the center domain of CD13 and the PAR4's pro-peptide region, which needs to be cleaved

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

off for receptor activation. Inhibiting enzymatic activities of sCD13 with bestatin partially reduced sCD13 stimulated migration and angiogenesis of HUVECs. *In vivo*, BMS986120 attenuated joint synovitis and bone erosion in CIA mice.

Conclusion: We identified PAR4 as a second functional sCD13 receptor that mediates proinflammatory signaling in RA FLS and angiogenic responses in endothelial cells, which positions PAR4 as a therapeutic target in RA.

Disclosure: C. Lu: None; **M. Mattichak**: None; **S. Xu**: None; **W. Brodie**: None; **N. Khanna**: None; **H. Amin**: None; **Q. Wu**: None; **P. Campbell**: None; **D. Fox**: None; **P. Tsou**: None.

Abstract Number: 0094

Distinct immune-molecular signatures modulated ex vivo by JAK and TNF predict Rheumatoid Arthritis therapy outcomes in patients naïve to biologic and targeted synthetic DMARDs

Sagrario Corrales[1], Laura muñoz-Barrera[1], Rafaela Ortega-Castro[2], Elena Moreno-Caño[3], Jerusalén Calvo[4], Concepción Aranda-Valera[4], Lourdes Ladehesa[5], Pilar Font[6], Ismael Sanchez-Pareja[1], M Carmen Abalos-Aguilera[7], Desiree Ruiz-Vilchez[8], Christian Merlo[9], MARIA ANGELES AGUIRRE ZAMORANO[1], Tomás Cerdó[1], Nuria Barbarroja[10], Marta Alarcon-Riquelme[11], Alejandro Escudero Contreras[4], Carlos Pérez Sánchez[12] and Chary López pedrera[13], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [3]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Córdoba, Spain, [4]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [5]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [6]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, SpainBiomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [7]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [8]Department of Rheumatology, Reina Sofía University Hospital / Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [9]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain, Cordoba, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [11]Fundación Progreso y Salud, Andalusian Government, Granada, Spain, [12]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [13]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite advances in rheumatoid arthritis (RA) treatment, 20–40% of patients do not respond to biologic or targeted synthetic DMARDs (b/tsDMARDs). Understanding each drug's molecular effects may help identify subgroups of patients likely to respond to specific therapies.

Objectives:

1-Characterize the *ex vivo* molecular and cellular effects of JAK (JAKi) and TNF (TNFi) inhibitors on RA immune cells.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2-Identify, in vivo, RA patient subgroups with distinct baseline levels of drug-specific proteomic signatures and assess their association with clinical response.

Methods: Peripheral blood mononuclear cells (PBMC) and neutrophils from 48 RA patients naïve to b/tsDMARDs were cultured with autologous serum and Baricitinib (JAKi) or Etanercept (TNFi) (10μM) for 24 and 12 hours, respectively. Proliferation, adhesion and NETosis were quantified using specialized kits. Protein changes were assessed via proximity extension assay, analysing a 92-protein inflammation panel in the supernatant. To identify subgroups of patients likely to respond to therapies guided by the identified proteomic signatures, a total of 193 RA patients were included (36 treatment-naïve and 32 previously treated patients initiating JAKi, and 125 treatment-naïve patients starting TNFi) where those proteomic signatures were analysed.

Results: Baricitinib and Etanercept reduced proliferation, adhesion and NETosis in PBMC and neutrophils from naïve RA patients. Each drug modulated distinct inflammatory protein signatures: Baricitinib primarily affected Th17/adaptive immunity while Etanercept targeted acute inflammation.

Unsupervised clustering analysis of JAKi–naïve patients, based on the ex vivo–derived JAKi proteomic signature, revealed two distinct subgroups. Patients with high expression of this signature showed a significantly greater reduction in disease activity (ΔDAS28-CRP) at 3, 6, and 12 months. In contrast, applying the same stratification to non-naïve patients did not predict treatment response. In TNFi-treated naïve patients, the JAKi-associated proteomic signature also stratified into distinct subgroups; however, high baseline levels were not associated with clinical response, supporting the specificity of this signature to JAK inhibitor therapy.

The ex vivo–derived Etanercept proteomic signature effectively stratified TNFi-treated patients, with high baseline levels correlating with improved clinical response at 6 and 12 months. This signature was specific to TNFi and showed no association with treatment response in JAKi-treated patients.

Conclusion: 1. JAKi and TNFi have specific functional and proteomic effects on RA immune cells. 2. Both ex vivo-derived JAKi and TNFi signatures effectively stratified RA patients into subgroups, with each being specific to its respective treatment and not applicable for predicting the clinical response to the other. This highlights the value of drug-specific molecular signatures to personalize and optimize RA treatment strategies.

Funded by Instituto de Salud Carlos III (ISCIII) and co-funded by European Union. Supported by EU/EFPIA IMI-JU 3TR, ISCIII (PI24/00959, CD21/00187, RICOR-21/0002/0033) and RYC2021-033828-I.

Disclosure: S. Corrales: None; **L. muñoz-Barrera**: None; **R. Ortega-Castro**: None; **E. Moreno-Caño**: None; **J. Calvo**: None; **C. Aranda-Valera**: None; **L. Ladehesa**: None; **P. Font**: None; **I. Sanchez-Pareja**: None; **M. Abalos-Aguilera**: None; **D. Ruiz-Vilchez**: None; **C. Merlo**: None; **M. AGUIRRE ZAMORANO**: None; **T. Cerdó**: None; **N. Barbarroja**: None; **M. Alarcon-Riquelme**: None; **A. Escudero Contreras**: None; **C. Pérez Sánchez**: None; **C. López pedrera**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0095

Effect of JAK Inhibitors on Osteoblast Differentiation

Toshihiro Tanioka[1] and Takeo Isozaki[2], [1]Graduate School of Pharmacy, Showa Medical University, Shinagawa-ku,Tokyo, Tokyo, Japan, [2]Graduate School of Pharmacy, Showa Medical University, Tokyo, Tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation and joint destruction. Among the therapeutic strategies available, Janus kinase (JAK) inhibitors have emerged as an important class of targeted treatments. Currently, five JAK inhibitors are approved for RA treatment in Japan. While their immunomodulatory effects are well-established, their influence on bone metabolism, particularly osteoblast differentiation, remains unclear. This study investigates the effects of different JAK inhibitors on osteoblast differentiation using an in vitro model.

Methods: To assess the impact of JAK inhibitors on osteoblast differentiation, mouse MC3T3-E1 pre-osteoblast cells were cultured in the presence of various JAK inhibitors, specifically Baricitinib (Bari), Peficitinib (Pefi), and Filgotinib (Filgo). The degree of osteoblast maturation was evaluated using Alizarin Red S staining, which detects calcium deposits indicative of mineralized bone matrix, and alkaline phosphatase staining, a marker of osteogenic differentiation. Additionally, the expression of key osteoblast differentiation markers was analyzed to determine molecular correlations with differentiation patterns.

Results: The study revealed distinct effects of different JAK inhibitors on osteoblast differentiation. Bari and Pefi: Both exhibited inhibitory effects on osteoblast maturation, with Bari demonstrating a particularly strong suppression of differentiation. Cells treated with these inhibitors showed reduced mineralization in Alizarin Red S staining and lower alkaline phosphatase activity. Filgo: Unlike Bari and Pefi, Filgo did not inhibit osteoblast differentiation. Even at high concentrations, osteoblasts successfully matured, displaying significant mineralization. Expression of Osterix, a critical transcription factor for osteoblast differentiation, was notably observed in Filgo-treated cells, further supporting its lack of inhibitory effects. FOXM1 Expression: In Filgo-treated cells and control groups, FOXM1 expression increased, suggesting its potential role in osteoblast differentiation. Conversely, FOXM1 levels remained unchanged in cells exposed to Bari and Pefi, reinforcing the hypothesis that JAK signaling influences osteoblast maturation through FOXM1-mediated pathways.

Conclusion: These findings indicate that JAK inhibitors exert differential effects on osteoblast differentiation. Bari and Pefi demonstrated inhibitory activity, whereas Filgo did not affect osteoblast maturation. Furthermore, the regulation of FOXM1 expression by JAK signaling suggests a possible mechanistic link to osteoblast differentiation, warranting further investigation into its role in bone remodeling and therapeutic implications for RA treatment.

Disclosure: T. Tanioka: None; **T. Isozaki**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0096

GLUT1-Dependent Targeting and Enhanced Selectivity of a Glucose-Methotrexate Conjugate in Rheumatoid Arthritis Fibroblast-Like Synoviocytes

Sebastian Makuch[1], Jacek Polański[1] and **Wojciech Tański**[2], [1]Wrocław Medical University, Wrocław, Poland, [2]Wrocław University of Science and Technology, Wrocław, Poland

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease where fibroblast-like synoviocytes (FLS) play a central role in joint inflammation and destruction. Methotrexate (MTX), a standard treatment, has limitations due to systemic toxicity and variable efficacy. RA-FLS exhibit altered glucose metabolism, notably increased glycolysis and upregulation of glucose transporter 1 (GLUT1), presenting a potential therapeutic target. We developed a glucose-methotrexate conjugate (Glc-MTX) designed to selectively target RA-FLS via GLUT transporters, potentially increasing efficacy and reducing toxicity. This study aimed to evaluate for the first time the in vitro effects of the Glc-MTX conjugate compared to free MTX on proliferation, inflammatory mediator production, and GLUT1-dependent uptake in human RA-FLS.

Methods: Cell proliferation of commercially available primary human FLSs, isolated from the synovial tissues of patients with RA and OA, was assessed using the MTT assay after treatment with Glc-MTX or MTX (doses ranging from 0.01 μM to 10 μM) for 24-48h. For inflammatory response, RA-FLS were stimulated with TNF-α (10 ng/ml) for 48h and treated with Glc-MTX or MTX (0.01 μM to 10 μM) for 24-48h. Levels of key inflammatory mediators (IL-6, IL-8) and matrix-degrading enzymes (MMP-1, MMP-3) in RA-FLS supernatants were quantified by ELISA. To assess GLUT1 dependence, RA-FLS were pre-treated with the selective GLUT1 inhibitor BAY-876 (1 mM) for 60 min before treatment.

Results: MTT assays showed that Glc-MTX inhibited RA-FLS proliferation with an IC_{50} of 2.87 μM, comparable to free MTX (IC_{50}: 2.55 μM). Glc-MTX exhibited greater selectivity for RA-FLS over OA-FLS (IC_{50}: 7.34 μM; Selectivity Index: 2.56) compared to free MTX, which showed higher potency against OA-FLS (IC_{50}: 0.25 μM; Selectivity Index: 0.098). Furthermore, Glc-MTX displayed lower cytotoxic activity against RA-FLS not stimulated with TNF-α compared to those that were stimulated (p=0.013). In TNF-α-stimulated RA-FLS, ELISA results demonstrated that both MTX and Glc-MTX inhibited the secretion of IL-6, IL-8, MMP-1, and MMP-3 compared to stimulated controls, with MTX generally showing stronger inhibition than Glc-MTX at the tested concentrations. Pre-treatment with the GLUT1 inhibitor BAY-876 significantly attenuated the antiproliferative effect of Glc-MTX on RA-FLS, increasing its IC_{50} from 2.87 μM to 12.4 μM ($p< 0.01$), while having minimal impact on the IC_{50} of free MTX (IC_{50}: 2.55 μM without BAY-876 vs. 2.24 μM with BAY-876, $p>0.05$).

Conclusion: The Glc-MTX conjugate inhibits RA-FLS proliferation in vitro with potency similar to MTX but demonstrates significantly improved selectivity over OA-FLS. Both Glc-MTX and MTX inhibited inflammatory and matrix-degrading mediator production. The significant reduction in Glc-MTX efficacy following GLUT1 blockade with BAY-876 confirms its reliance on GLUT1-mediated uptake. These findings show the promising potential of Glc-MTX as a novel, targeted therapeutic strategy for RA. Further in vivo studies are required to fully understand the therapeutic potential of Glc-MTX.

Disclosure: S. Makuch: None; **J. Polański**: None; **W. Tański**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0097

Aberrant Histone Marks Increase the Inflammatory Phenotype of Rheumatoid Arthritis Fibroblast-like Synoviocytes (RA FLS) by Suppressing NUB1 Induction

Yosuke Ono[1], Camilla R.L. Machado[2], Eunice Choi[1], Wei Wang[1], David Boyle[1] and Gary Firestein[2], [1]University of California, San Diego, San Diego, [2]University of California, San Diego, San Diego, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0067–0097) Rheumatoid Arthritis – Etiology and Pathogenesis Poster

Session Type: Poster Session A

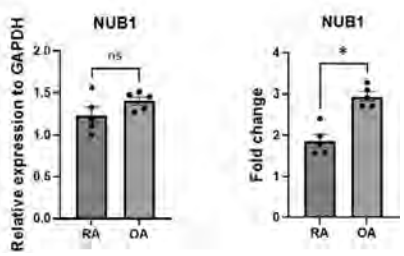
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibroblast-like synoviocytes (FLS) play a central role in cartilage destruction and cytokine production in rheumatoid arthritis (RA). Neddylation, a post-translational modification involving NEDD8 conjugation, is a key regulator of inflammatory signaling. NUB1, a negative regulator of neddylation, is dysregulated in FLS with defective induction after cytokine stimulation that can lead to increased NF-kB activation. Previous studies have shown that this defect is associated with differential histone modification at the NUB1 promoter between RA and osteoarthritis (OA). However, the molecular mechanism of insufficient NUB1 induction in RA remains unclear.

Methods: FLS were isolated from RA and OA synovial tissues and used from passages 4–8. To evaluate mRNA half-life, cells were stimulated with IL-1β (2 ng/mL) for 6 hours, followed by treatment with actinomycin D (10 μg/mL) to interrupt transcription. SNHG12, a long non-coding RNA that binds to NUB1 was depleted with SNHG12 siRNA (knockdown >85). Gene expression was quantified by RT-qPCR after IL-1 stimulation in the presence of EPZ6438 (a histone methylation inhibitor) or MS-275 (an HDAC1/HDAC3 inhibitor).

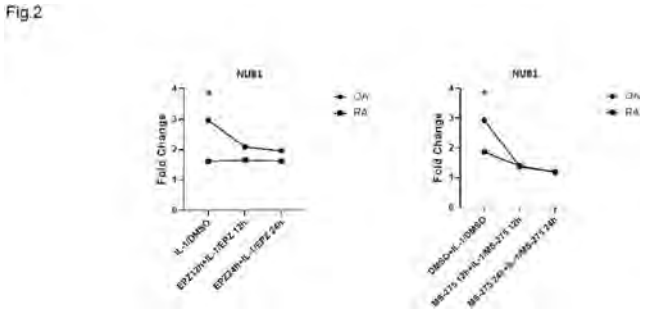
Results: We initially confirmed that NUB1 induction was deficient in RA compared with OA FLS after IL-1 stimulation (Fig. 1). Actinomycin D treatment revealed no significant difference in NUB1 mRNA half-life between RA and OA FLS that might account for this difference, with the half-life for RA=11.3h and for OA=10.7h. In addition, SNHG12 deficiency did not affect NUB1 gene expression or induction in either RA and OA FLS. These findings suggest that the differential expression of NUB1 between RA and OA is likely due to transcriptional differences rather than post-transcriptional regulation. Because NUB1 regulatory regions have distinct epigenetic marks in RA compared to OA, we evaluated this possibility by treated the cells with epigenetic modulators and then stimulated FLS with IL-1 (Fig. 2). IL-1 stimulation resulted in significantly higher

Fig.1



(Fig.1) Reduced induction of NUB1 by IL-1 in RA FLS compared to OA FLS. Basal and IL-1-induced expression of NUB1 in RA and OA FLS is shown. Left: Basal NUB1 mRNA expression in RA and OA FLS, normalized to GAPDH. Right: Fold change in NUB1 expression following IL-1 stimulation (2ng/mL, 6 h), relative to unstimulated (DMSO-treated) cells (RA and OA, n=5 each). Bars represent mean values; individual dots represent biological replicates. Error bars indicate SEM. *; $p < 0.05$, ns; not significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(Fig.2) Reversal of NUB1 differential induction between RA and OA FLS by epigenetic modifiers EPZ6438 (histone methylation inhibitor) and MS-275 (HDAC1/HDAC3 inhibitor). RA and OA FLS were stimulated with IL-1β (2 ng/mL) after pretreatment with epigenetic inhibitors. Fold change was calculated as the ratio of NUB1 expression in IL-1–stimulated cells to that in the corresponding unstimulated control. For the IL-1/DMSO condition, fold change reflects expression relative to DMSO alone. For inhibitor-treated conditions, fold change was calculated relative to cells treated with the same inhibitor without IL-1 stimulation. Circles and squares represent mean fold change for OA and RA FLS, respectively (n = 5 each). *; $p < 0.05$

induction of NUB1 mRNA in OA FLS compared to RA FLS (RA: 1.6-fold, OA: 3.0-fold; $p = 0.01$). EPZ treatment partially reversed this difference (see Fig. 2). MS-275 completely reversed differential induction of NUB1 in OA compared with RA. In addition, 2 week treatment with a DNA methylation inhibitor 5-azacytidine did not alter differential induction of NUB1 in RA compared with OA.

Conclusion: The mechanism of reduced induction of NUB1 in RA FLS is related to differential histone marks in the promoter, most notably histone methylation and acetylation. Because low levels of NUB1 are associated with increased NF-kB activation and cytokine production, this could contribute to increased neddylation and cytokine production in RA FLS. Therapeutic approaches that modify the epigenetic landscape in RA could potentially suppress the inflammatory milieu.

Disclosure: Y. Ono: None; **C. Machado**: None; **E. Choi**: None; **W. Wang**: None; **D. Boyle**: None; **G. Firestein**: Eli Lilly, 5.

Abstract Number: 0098

The Deubiquitinase TRABID is a Regulator of Osteogenesis and Inflammation in Spondyloarthritis:

Archita Srinath[1], Sungsin Jo[2], Daniele Mauro[3], Mariia Korshko[4], Mansi Aparnathi[5], Shaghayegh Foroozan Boroojeni[6], Tae-Hwan Kim[7], Francesco Ciccia[8] and Nigil Haroon[9], [1]University of Toronto, Toronto, ON, Canada, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [3]University of Campania, Italy, Naples, Italy, [4]UHN, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [6]University Health Network/University of Toronto, Toronto, ON, Canada, [7]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [8]University of Campania, Naples, Italy, [9]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial Spondyloarthritis (AxSpA) is characterized by both inflammation and new bone formation. Current therapeutic targets aim to control inflammation, however over 40% of patients do not respond to them. The novel deubiquitinase molecule TRABID has been shown to epigenetically control the expression of IL12/23 in the experimental

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

autoimmune encephalomyelitis mouse model. Furthermore, our group has previously shown significantly increased expression of TRABID in inflamed human SpA tissues (bone marrow, synovium and gut). We have also shown that the inhibition of TRABID in monocyte and osteoblast cell culture models significantly supresses cytokine production and bone mineralization respectively. Furthermore, TRABID inhibition in-vivo in curdlan-treated SKG mice significantly suppresses the clinical and histopathological signs of arthritis. Therefore, this study aims to understand the genetic and proteomic mechanisms behind these phenotypes.

Methods: To understand if TRABID can contribute to new bone formation in the spine, facet joint tissues from 5 AxSpA and 5 disease controls were stained using immunohistochemistry to determine TRABID expression patterns. Furthermore, TRABID interactome during osteogenesis was identified by proximity-dependant biotin identification (BioID). Cells were transfected with miniTurbo-tagged TRABID constructs and incubated for 6 days in McCoy's growth or osteogenic media. Biotinylated proteins were enriched using streptavidin beads and identified by mass spectrometry. Biological pathways associated with top significant interactors were identified using PathDip. To assess in-vivo transcriptomic changes induced by TRABID inhibition, 8-week-old SKG mice were injected with curdlan or PBS. For 8 weeks, mice received PBS or high-dose TRABID inhibitor NSC112200 (300mM/kg every 2 days). At 16 weeks, ankle/lymph nodes were collected for RNA extraction and transcriptomic profiling using the murine Nanostring Immunology panel. Pathway analysis for overrepresented gene sets was conducted using Gene Set Enrichment Analysis (GSEA).

Results: We found that TRABID was significantly overexpressed by periosteal cells, osteochondroprogenitor cells that have been shown to promote new bone formation, in the AxSpA facet joints compared to disease controls. Excitingly, we find that TRABID significantly and uniquely interacts with signal transduction, tight junction markers and Rho GTPases during osteogenesis. Moreover, these interactors were predominantly associated with the actin cytoskeleton and membrane bound vesicles. Finally, TRABID inhibition in-vivo significantly altered the expression of genes that belong to antigen processing and presentation pathways in SKG mice. Moreover, these altered genes were found to be associated with the endocytic vesicle membrane and MHC protein complex.

Conclusion: Taken together, our data suggests that TRABID may contribute to new bone formation and inflammation in AxSpA by regulating vesicle transport within the cell. Future work will focus on identifying the exact mechanism by which this process occurs to contribute to AxSpA disease pathology.

Disclosure: A. Srinath: None; **S. Jo**: None; **D. Mauro**: None; **M. Korshko**: None; **M. Aparnathi**: None; **S. Foroozan Boroojeni**: None; **T. Kim**: Samsung Bioepis, 5; **F. Ciccia**: None; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2.

Abstract Number: 0099

Time course and impact of IL17A on hepatic inflammation and fibrosis in adjuvant induced arthritis

Arthur Dollinger[1], Frédéric Meyer[1], Hélène Martin[2], Céline Delougeot[3], Delphine Weil-Verhoeven[1] and Frank Verhoeven[4], [1]CHU Besancon, Besancon, France, [2]Université Marie et Louis Pasteur, Besancon, France, [3]université Marie et Louis Pasteur, Besancon, [4]CHU de Besançon, Besançon, Franche-Comte, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The management of spondyloarthritis. (SpA) includes controlling disease activity as well as comorbidities such as metabolic syndrome. Metabolic syndrome can be associated with metabolic dysfunction-associated fatty liver disease (MAFLD) or even steatohepatitis (MASH).

The IL-23/TH17 axis plays a central role in the pathophysiology of SpA, but it is also implicated in hepatic steatosis and its progression to fibrosis.

This study aims to evaluate, in an adjuvant-induced arthritis (AIA) rat model, the presence of hepatic inflammation and fibrosis at different stage of arthritis and to assess the effect of early treatment with anti-IL-17A.

Methods: Arthritis was induced in 6-weeks-old male Lewis rats by a subcutaneous injection at the base of the tail with 1.2 mg of inactivated Mycobacterium butyricum suspended in Freund's incomplete adjuvant (AIA groups) at Day 0. At different stages of arthritis (Day 4 post-induction: preclinical phase; Day 11: arthritis onset; Day 30: acute phase; Day 90: resolution phase), intrahepatic inflammation was assessed by measuring mRNA expression of pro-inflammatory cytokines (TNFα, IL-6, IL-17A, IL-23p19, IL-33) using RT-qPCR (delta-delta Ct method, relative expression normalized to GAPDH), and by detecting T lymphocytes (CD3+) and helper T lymphocytes (CD4+) using immunohistochemistry. Fibrosis was evaluated by hepatic TGFβ mRNA expression (RT-qPCR), serum AST/ALT ratio, and histology with picrosirius red staining. The same analyses were performed in non-arthritic control rats and AIA rats treated with secukinumab (20 mg/kg intraperitoneally every three days).

abnormalities associated with SpA but encourage further investigation into the roles of other cytokines, particularly TNF and IL-33, in their pathophysiology.

Results: Compared to controls, AIA rats exhibited early and sustained hepatic inflammation. At preclinical stage, overexpression of TNFα and IL-33 was observed, with additional overexpression of IL-17A and IL-23p19 beginning at arthritis onset ($p < 0.015$). During the acute phase, TNFα, IL-33, and IL-17A remained overexpressed, while only TNFα and IL-33 were still overexpressed at the resolution phase. Hepatic fibrosis was histologically present at all stages ($p < 0.05$), supported by overexpression of TGFβ at Day 11 ($p < 0.001$), Day 30 ($p = 0.06$, NS), and Day 90 ($p < 0.001$). However, the AST/ALT ratio was significantly elevated only during arthritis onset (Day 11, $p < 0.0001$).

Preventive treatment with secukinumab did not alter hepatic pro-inflammatory cytokine genes expression in AIA rats. However, secukinumab increased hepatic CD3+ and CD4+ T cell counts on Day 11 ($p < 0.05$) and TGFβ mRNA expression ($p < 0.01$) compared to untreated AIA rats.

Figure 1. RT-qPCR, biochemical, and histological results for AIA groups compared to control groups.

	Preclinical (Day 4)	Arthritis onset (Day 11)	Acute phase (Day 30)	Arthritis resolution (Day 90)
TNFα	↗	↗	↗	↗
IL-33	↗	↗	↗	↗
IL-17A	–	↗	↗	–
IL-23p19	–	↗	–	–
IL-6	–	–	–	–
TGFβ	–	↗	–	↗
AST/ALT	–	↗	–	–
Fibrosis	↗	↗	↗	↗

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. RT-qPCR, biochemical, and histological results for AIA-SK groups compared to AIA-NT groups.

	Preclinical (Day 4)	Arthritis onset (Day 11)
TNFα	=	=
IL-33	=	=
IL-17A	=	=
IL-23p19	=	=
IL-6	=	=
CD3+ T cells	↗	↗
CD4+ T cells	=	↗
TGFβ	=	↗
AST/ALT	=	=
Fibrosis	=	=

Conclusion: Our results demonstrate early hepatic inflammation and fibrosis in a murine model of reactive arthritis. Preventive administration of anti-IL-17 did not reduce these abnormalities but instead partially exacerbated them. These findings do not support a major role for IL-17 in initiating hepatic

Disclosure: A. Dollinger: None; **F. Meyer**: None; **H. Martin**: None; **C. Delougeot**: None; **D. Weil-Verhoeven**: None; **F. Verhoeven**: None.

Abstract Number: 0100

Therapeutic Modulation of NAD$^+$ Metabolism in Inflammatory Rheumatic Disorders by TNFi and NAD$^+$ Precursors

Beatriz Vellón-García[1], Gema Dolores García-Delgado[2], Adrián Llamas Urbano[3], Yas Hanaee[3], Pedro Ortiz Buitrago[4], Christian Merlo[5], Maria del carmen abalos-aguilera[5], julio Manuel Martinez Moreno[6], Iván Arias de la Rosa[7], María Dolores López-Montilla[8], Rafaela Ortega-Castro[9], Jerusalén Calvo[10], Lourdes Ladehesa[11], Clementina López Medina[12], María Ángeles Puche-Larrubia[13], Nuria Barbarroja[14], Eduardo Collantes estévez[15], Alejandro Escudero-contreras[5], Chary López pedrera[16], Jose manuel Villalba[17] and Carlos Pérez Sánchez[18], [1]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain/Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Córdoba, Córdoba, Spain, Cordoba, Spain, [2]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain/Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Cordoba, Cordoba, Spain., Cordoba, Spain, [3]Cobiomic Bioscience SL. EBT University of Cordoba/IMIBIC, Cordoba, Spain., Cordoba, Spain, [4]Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), Cordoba, Andalucia, Spain, [5]Rheumatology Service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain, Cordoba, Spain, [6]Cobiomic Bioscience SL. EBT University of Cordoba/IMIBIC, Cordoba, Spain, Cordoba, Spain, [7]IMIBIC/FIBICO/Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso; Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain; Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd) Toledo, Spain., Córdoba, Spain, [8]Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., CORDOBA, Spain, [9]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [10]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [11]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [12]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [13]Reina Sofia University Hospital, Granada, Spain, [14]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [15]Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [16]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [17]Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Cordoba, Cordoba, Spain, Cordoba, Spain, [18]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: This study aims to:

1. Characterize the NAD^+ metabolome in CIRDs and their association with clinical traits.
2. Evaluate the impact of TNFi therapy on NAD^+ metabolome alterations.
3. Test the potential of a group of NAD^+ boosters to restore NAD^+ alterations and promote anti-inflammatory effects.

Methods: Whole blood samples were collected from 310 subjects: 70 healthy donors (HDs), 80 rheumatoid arthritis (RA) patients, 80 psoriatic arthritis (PsA) patients, and 80 spondyloarthritis (SpA) patients. Key NAD^+ pathway metabolites (NAD^+, NADH, NAM, NMN, NR, NADP and Tryp) were analyzed using two-dimensional Nuclear Magnetic Resonance. A longitudinal analysis in 90 CIRDs patients, 30 from each disease group, assessed NAD^+ metabolome changes after 6 months of TNFi therapy. Peripheral blood mononuclear cells (PBMCs) from 45 patients (15 from each disease group) were treated *ex-vivo* with NAD^+ boosters (NR, NMN, NRT, NRH, and NAR) for 24 hours, followed by intracellular NAD^+/NADH measurement. In parallel, secreted inflammatory mediators were assessed (Olink Inflammation Panel, Cobiomic).

Results: RA, PsA and SpA patients showed reduced NAD^+/NADH ratio and elevated NAM and NMN levels compared to HDs. RA had decreased NAD+ levels, while PsA and SpA displayed increased NADH levels; SpA also had reduced NADP and elevated Trp levels. These disease-specific NAD^+ metabolism alterations correlated with distinct clinical features: in RA, the NAD^+/NADH ratio was negatively associated with DAS28, while NADH and NMN correlated positively with CRP, tender and swollen joint counts (TJC and SJC). Autoantibodies correlated positively with NADH levels. In PsA, the NAD^+/NADH ratio and NAD^+ levels correlated negatively with TJC and SJC, and disease activity (DAPSA) respectively. Uveitis was positively correlated with NAD^+ levels, and psoriasis with NAM levels. In SpA, axial forms had a lower NAD^+/NADH ratio, with positive correlations between ESR and NMN, entesitis and NADH, and dactylitis with Trp. TNFi therapy induced disease-specific changes in NAD^+ metabolites, partially restoring levels toward those seen in HDs. All NAD^+ boosters increased intracellular NAD^+ in patientes PBMCs, with NRH being the most effective. Boosters also reduced inflammatory mediator secretion, showing disease and booster specific effects.

Conclusion: 1-The NAD^+ metabolome was altered in CIRDs, with disease-specific disruption patterns associated with key clinical manifestations.

2-TNFi treatment normalized NAD^+ metabolite levels, indicating a potential role in metabolic rebalancing during therapeutic response.

3- NAD^+ boosters increase intracellular NAD^+ levels and attenuates inflammation, exhibiting both common and disease-specific effects.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Targeting the NAD^+ pathway emerges as a promising therapeutic approach in CIRDs.

Supported by: CPS: MICIU (RYC2021-033828-I; PID2022-141500OA-I00); FAR2023-24; JA (PIP-0149-2024); AEI (DIN2022-012766). CLP: ISCIII (PI21/0591, PI24/00959, CD21/00187 y RICOR-21/0002/0033). JMV: RTI2018-100695-B-I00, PID2021-126280OB-I00,P18-RT-4264. AEC: ISCIII (ICI23/00100). CLM, ECE y NBP: ISCIII(PI22/00539 y PMP21/00119); JA (I-0243-2022); MICIU (PID2023-152503OB). Cofinanciados por la UE.

Disclosure: B. Vellón-García: None; **G. García-Delgado**: None; **A. Llamas Urbano**: None; **Y. Hanaee**: None; **P. Ortiz Buitrago**: None; **C. Merlo**: None; **M. abalos-aguilera**: None; **j. Martinez Moreno**: None; **I. Arias de la Rosa**: None; **M. López-Montilla**: None; **R. Ortega-Castro**: None; **J. Calvo**: None; **L. Ladehesa**: None; **C. López Medina**: None; **M. Puche-Larrubia**: None; **N. Barbarroja**: None; **E. Collantes estévez**: None; **A. Escudero-contreras**: None; **C. López pedrera**: None; **J. Villalba**: None; **C. Pérez Sánchez**: None.

Abstract Number: 0101

Enrichment of putative bacteria-reactive gut-derived IL-17+ tissue resident memory helper T cells in arthritic ankles in the SKG mouse model of spondyloarthritis

Benjamin Cai[1], Megan Soon[2], Zewen Kelvin Tuong[2], Mark Morrison[2], Anne-Sophie Bergot[3] and Ranjeny Thomas[4], [1]Frazer Institute, The University of Queensland, Brisbane, Queensland, Australia, [2]Frazer Institute, The University of Queensland, Brisbane, Australia, [3]Frazer Institute, The University of Queensland, Woolloongabba, Queensland, Australia, [4]Frazer Institute, University of Queensland, Brisbane, Queensland, Australia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In spondyloarthropathy (SpA), arthritis is often associated with gut inflammation. The strong genetic association with HLA-B27 implicates involvement of T cells, but how gut dysbiosis, T cells and SpA are mechanistically linked remain unknown. In the SpA-susceptible ZAP-70W163C SKG mice, Gram-negative dysbiosis is associated with disease severity following curdlan injection. They exhibit defective thymic selection and impaired T cell tolerance, including dysfunctional Tregs, aberrant CD4+CD8+ intraepithelial cytotoxic T lymphocytes, and impaired control of mouse mammary tumour virus (MMTV) superantigen responses. In this study, we investigated the T cell response mediating ileitis and arthritis to gut pathobiont Parabacteroides goldsteinii (*Pg*; a species of Bacteroidaceae enriched in the SKG stool post-curdlan) and its role in mediating ileitis and arthritis in SKG and BALB/c mice.

Methods: Germ-free (GF) SKG and BALB/c mice were orally mono-associated with *Pg* or remained GF for 4 weeks prior to i.p. curdlan injection. CD4+ and CD8+ T cells were FACS-sorted from mesenteric (MLN), popliteal lymph nodes (PLN) at day 6 post curdlan and from ankle joints at day 35 post curdlan. The transcriptome, TCR clonality and usage were analysed by paired scRNA/TCR sequencing combined with CITE-seq using the 10x Genomics pipeline. Bioinformatics analysis was performed using ScanPy, Dandelion, Scirpy pipelines and IEDB database.

Results: At 5 weeks post-curdlan, *Pg*-SKG mice developed ileitis and SpA whilst *Pg*-BALB/c and GF animals were resistant. Naïve T cells, T follicular helper cells (Tfh), early activated T cells, resident-memory T cells (Trm), regulatory Trm cells (Treg-Trm), α4β7 integrin+ T cells were found in the CD4+ compartment, whilst many cell clusters in CD8+ T cells expressed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

exhaustion-related genes, such as *Hspa1a*, *Tox*, *Lag3* and *Ctla4*. Notably, many α4β7 integrin+ effector T cells were found in *Pg*-SKG ankle and PLN suggestive of their gut origins. Also, IL-17-producing Trm and Treg-Trm cells were enriched in the arthritic ankle joints of *Pg*-SKG mice and exhibited the highest clonality within the CD4+ compartment. These IL-17+ subsets preferentially used TRBV31, TRBV20, and TRBV12-2, of which TRBV12-2 is known to recognize MMTV superantigens. A conserved TCR motif consisted of 14 amino acids was observed across the expanded clones. Structural prediction for this TCR using IEDB database implicated microbial and host-derived proteins, including GPER protein, inner membrane protein YeiH, small nuclear ribonucleoprotein Prp3, and type II secretion system protein GspD in *Chlamydia trachomatis*, as potential reactive antigens.

Conclusion: Gut-derived *Pg* drives ileitis and arthritis in SpA-prone SKG mice by promoting an IL-17+ tissue-resident memory T cell response in the joints. These pathogenic helper T cells may arise from conventional or regulatory T cells in the gut responding to bacterial or viral superantigens in the ankle, providing insight into how gut pathobionts can trigger SpA. Targeting specific TCR motifs, IL-17+ Trm, or their microbial/viral triggers may offer new revenues for treating gut-joint axis inflammation in an antigen-specific manner.

Disclosure: B. Cai: None; **M. Soon**: None; **Z. Tuong**: None; **M. Morrison**: None; **A. Bergot**: None; **R. Thomas**: AbbVie/Abbott, 2, CSL, 2.

Abstract Number: 0102

Iron Metabolism Dysregulation and Inflammation in Ankylosing Spondylitis: Role of SLC39A14 in Extracellular Matrix Remodeling

Dachun Zhuo[1], Yulong Tang[2], Xiaobei Ma[2], Chengchun Geng[1], Jiangnan Xie[1], Jiucun Wang[2] and Jing Liu[1], [1]Fudan University, Shanghai, Shanghai, China (People's Republic), [2]Fudan university, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Iron metabolism dysregulation has been increasingly recognized as a key factor in the pathogenesis of inflammatory arthritis, with evidence linking altered iron homeostasis to disease progression. However, the mechanisms through which iron dysregulation contributes to inflammation and tissue remodeling in inflammatory arthritis, particularly in ankylosing spondylitis, remain poorly understood. This study aims to investigate the role of iron metabolism dysregulation, particularly the inflammatory mediator SLC39A14, in driving extracellular matrix (ECM) remodeling and ectopic ossification in inflammatory arthritis, using ankylosing spondylitis as a model.

Methods: Primary fibroblasts were isolated from spinal ligament tissues of AS patients, and THP-1 cells were differentiated into macrophages for in vitro studies. The CAIA and SKG mouse models were used, with ferric ammonium citrate (FAC) injected locally in the SKG model to induce iron overload. SLC39A14 conditional knockout (CKO) mice were generated by crossing SLC39A14-flox mice with SCX-cre mice. Ferritin levels and plasma iron concentrations were measured using a colorimetric assay. Immunohistochemistry and immunofluorescence were performed to assess co-localization of Ferritin in fibroblasts and macrophages. CRISPR-Cas9 was used to knock out SLC39A14 in the TTD6 fibroblast cell line, and gene

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

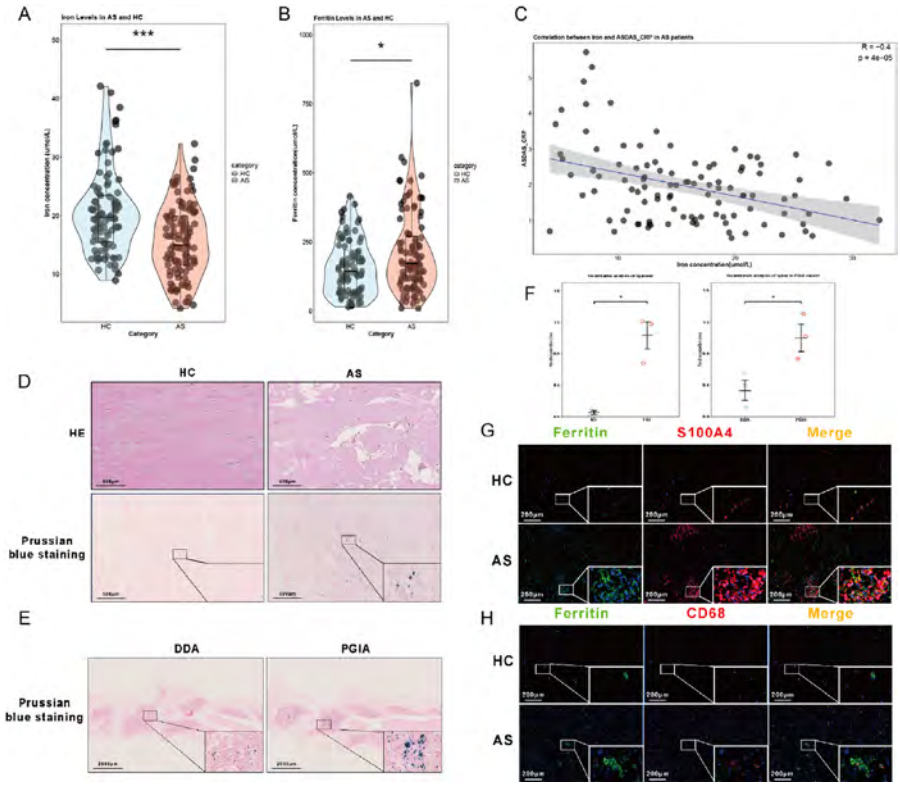


FIGURE 1. Iron Accumulation in Spinal Ligaments of Patients with Ankylosing Spondylitis (AS) (A) Violin plot showing significantly lower serum iron levels in AS patients compared to healthy controls (HC), with statistical significance ($p < 0.05$). (B) Violin plot displaying higher Ferritin concentrations in AS patients relative to HC ($p < 0.05$). (C) Correlation between serum iron levels and ASDAS-CRP scores in AS patients, showing a negative correlation ($r = -0.4$, $p = 4e\text{-}5$). (D) Hematoxylin and eosin (HE) staining and Prussian blue staining of spinal ligament tissues, highlighting iron deposits (blue staining) in AS compared to HC. Scale bars: 50 μm (HE) and 500 μm (Prussian blue). (E) Prussian blue staining of spinal ligaments in the DDA (control group, Dimethyl-dioctadecyl-ammonium) and PGIA (Proteoglycan- induced arthritis) models, showing iron accumulation. Scale bars: 200 μm. (F) Quantification of iron levels and expression of ECM-related genes, demonstrating significant differences ($p < 0.05$). (G) Immunofluorescence staining for Ferritin (green) and S100A4 (red) in spinal ligaments, showing co-localization of Ferritin with activated fibroblasts (S100A4) in AS compared to HC. Scale bars: 200 μm. (H) Immunofluorescence staining for Ferritin (green) and CD68 (red) in spinal ligaments, showing co-localization of Ferritin with macrophages (CD68) in AS compared to HC. Scale bars: 200 μm.

editing efficiency was confirmed by PCR and western blotting. FerroOrange, combined with flow cytometry, assessed iron uptake in treated cells. In vivo, the effects of iron overload were evaluated in the CAIA and SKG models, with western blotting to analyze SLC39A14, Ferritin, and ECM-related proteins.

Results: Our research demonstrated that inflammation-induced iron overload in spinal ligaments led to ECM remodeling and ectopic ossification. Increased Ferritin levels and decreased plasma iron were observed in AS patients, with serum iron negatively correlated with ASDAS-CRP scores, linking iron metabolism to disease severity. TNFα stimulation upregulated SLC39A14 in fibroblasts, promoting excessive ECM deposition. SLC39A14 knockout in fibroblasts inhibited ECM-related gene expression, such as TNC, FN1, and collagen types I and III, highlighting its role in ECM remodeling. Immunohistochemistry showed co-localization of SLC39A14 and Ferritin in activated fibroblasts and macrophages. Single-cell RNA sequencing identified fibroblast subpopulations sensitive to iron accumulation, with elevated ECM gene expression. In vivo, FAC injections in the SKG mouse model induced ectopic ossification in the Achilles tendon, further supporting the role of iron overload in ECM remodeling.

Conclusion: In an inflammatory state, upregulation of SLC39A14 in fibroblasts leads to iron overload, driving ECM remodeling and ectopic ossification in inflammatory arthritis, such as ankylosing spondylitis. Targeting SLC39A14 and modulating iron metabolism may offer potential therapeutic strategies to prevent these pathological changes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

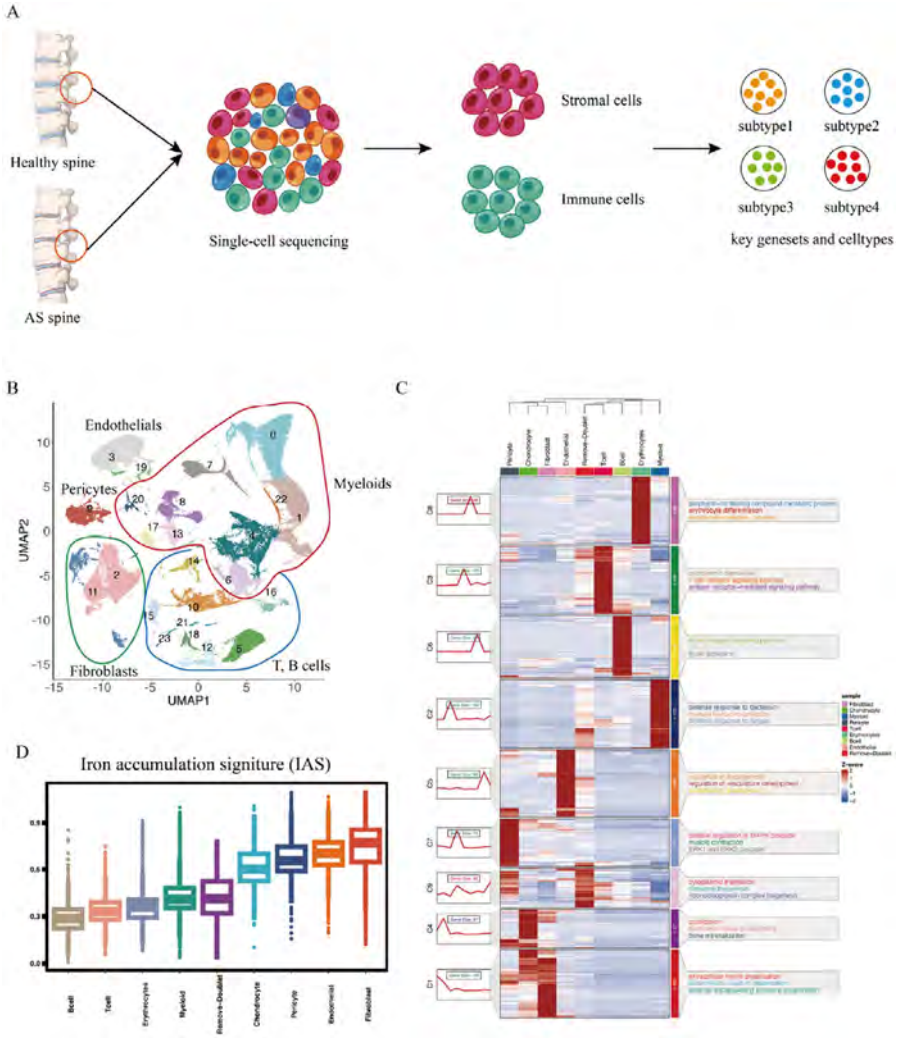


FIGURE 2. Single-Cell Sequencing Reveals Iron Accumulation and Cellular Heterogeneity in Spinal Ligaments of Ankylosing Spondylitis (AS) (A) Schematic representation of single-cell sequencing analysis on spinal ligament tissues from healthy and AS patients. Stromal and immune cell populations were identified and classified into subtypes, with key genes and cell types highlighted. (B) UMAP plot showing the clustering of different cell populations in the spinal ligaments of AS patients, including endothelial cells, pericytes, fibroblasts, myeloid cells, and T/B cells. Each cluster is numbered and color-coded. (C) Heatmap of differentially expressed genes in various cell populations, illustrating key biological processes related to immune response, ECM remodeling, and metabolic pathways. Gene expression patterns in different cell types are shown, with color-coded gene categories. (D) Boxplot showing the iron accumulation signature (IAS) across different cell populations, indicating the extent of iron accumulation in various subtypes of cells within the spinal ligaments.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

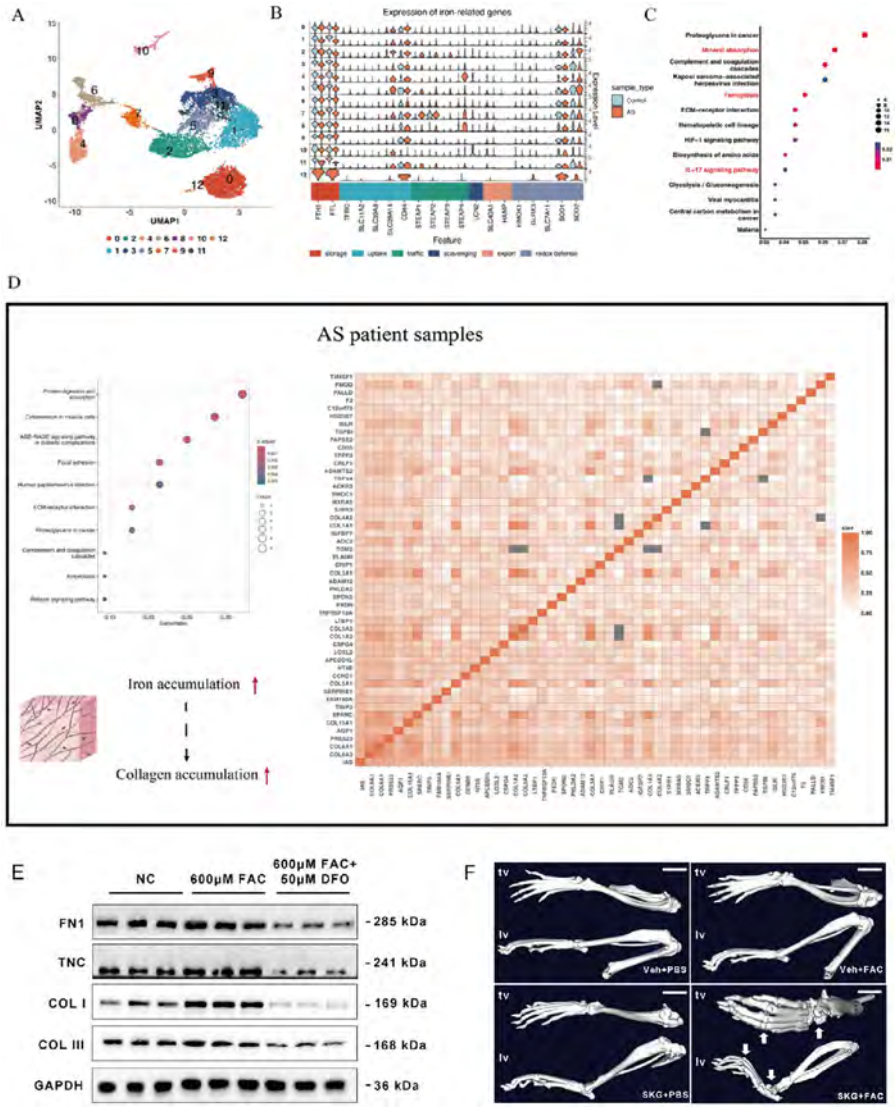


FIGURE 3. Iron Accumulation and ECM Remodeling in Ankylosing Spondylitis (AS) Revealed by Single-Cell Sequencing and In Vivo Imaging (A) UMAP plot showing the clustering of different cell populations in the spinal ligaments of AS patients, including subpopulations associated with iron metabolism. (B) Expression of iron-related genes across different cell types in AS and control samples. Genes involved in iron storage, uptake, traffic, and export are shown with varying expression patterns between AS and control groups. (C) Bubble plot highlighting significantly enriched pathways in AS patients, with a focus on iron metabolism, ECM remodeling, and related inflammatory pathways. (D) Correlation analysis of iron and collagen accumulation in AS patient samples, showing that increased iron accumulation is associated with higher collagen accumulation in spinal ligaments. (E) Western blot analysis of ECM-related proteins (FN1, TNC, COL I, COL III) in fibroblasts treated with ferric ammonium citrate (FAC) and/or deferoxamine (DFO), demonstrating the effect of iron overload on ECM protein expression. (F) Micro-CT images of SKG mice showing ectopic ossification in the Achilles tendon following FAC injection, with the arrows indicating the regions of ossification. tv, top view. lv, lateral view. Scale bars: 5 mm.

Disclosure: D. Zhuo: None; **Y. Tang**: None; **X. Ma**: None; **C. Geng**: None; **J. Xie**: None; **J. Wang**: None; **J. Liu**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0103

Common and Rare Variant Contributions to Familial Aggregation in Spondyloarthritis

Félicie Costantino[1], roula Said-Nahal[2], Hendrick Mambu Mambueni[3], Anne Boland[4], Jean-François Deleuze[4], Matthew Brown[5], Henri-Jean Garchon[3] and Maxime Breban[6], [1]Department of Rheumatology, Ambroise Paré Hospital, AP-HP, Paris, France and Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Montigny-Le-Bretonneux, France, [2]Department of Rheumatology, Ambroise Paré Hospital, AP-HP, Paris, France and Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Boulogne-Billancourt, France, [3]Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Montigny le Bretonneux, France, [4]Centre National de Recherche en Génomique Humaine (CNRGH), Centre National de Recherche en Génomique Humaine (CNRGH), Université Paris-Saclay, CEA, Evry, France, [5]Department of Medical and Molecular Genetics, King's College London, London, United Kingdom, [6]CHU Ambroise-Paré, Boulogne-Billancourt, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Spondyloarthritis (SpA) exhibits strong familial aggregation, with close relatives of patients having a significantly higher risk of developing the disease. This pattern might be driven by an accumulation of common variants that collectively increase disease risk or by rare variants in high linkage disequilibrium (LD) with common risk alleles, amplifying the genetic predisposition in affected families. Our aim was to investigate whether the familial form of SpA is influenced by an excess burden of common risk variants or by rare variants located within SpA-associated loci.

Methods: We examined two independent patient groups: (1) a family-based cohort of 376 SpA patients from 68 French families with at least four affected members, all of whom underwent whole genome sequencing (WGS), and (2) a cohort of 242 French unrelated ankylosing spondylitis (AS) patients with and without a family history of SpA, genotyped on the Illumina CoreExome array. Polygenic risk score (PRS) for AS were calculated using a model developed by Li et al. for Western European population (Li Z et al. doi: 10.1136/annrheumdis-2020-219446). Linear regression was applied to identify PRS-associated factors, and HLA-B27 frequency differences between sporadic and familial cases were analyzed using the chi-square test. We identified 46 coding genes overlapping with SNPs in high LD (r^2 >0.8) with lead SNPs from the 42 known AS-associated loci (Ellinghaus D et al. doi : 10.1038/ng.3528). To examine whether rare variants within these genes contribute to familial SpA, we conducted a rare variant burden test in our family cohort using gnomAD data as controls (Lali R et al. doi: 10.1038/s41467-021-26114-0).

Results: PRS was significantly increased in patients with familial history of SpA (68 probands from multiplex families and 123 patients from the unrelated cohort) compared to 119 sporadic cases (β-estimate (β)± standard error (SE): 0.09 ± 0.03; p-value (p) = 0.004; Figure 1A). However, the HLA-B27 positivity rate was significantly higher in familial cases

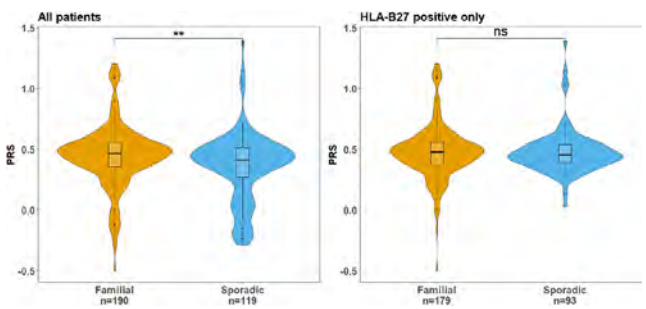


Figure 1 – Distribution of PRS according to family history status in all SpA patients (panel A) or in HLA-B27 positive patients only (panel B)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

compared to sporadic cases (94.2% vs 78.2%; p = 6x10^{-5}) and the PRS difference was no longer significant when comparing only HLA-B27 positive patients (β ± SE: 0.003 ± 0.03; p = 0.9; figure 1B). Within the familial cohort, PRS was inversely associated with the number of affected family-members (β ± SE: -0.08 ± 0.03; p = 0.03). WGS data from the familial cohort revealed at least one non-synonymous SNPs with a minor allele frequency below 1% in non-Finnish European population and a predicted pathogenicity CADD score above 20 in 19 of the 46 AS-associated coding genes. The rare variant-burden test showed nominal association with familial SpA only for the *PDE4A* gene (p=0.05).

Conclusion: Besides the higher prevalence of HLA-B27, we found no significant accumulation of common AS-associated variants in familial cases of SpA. Furthermore, there was no excess of rare variants in genes within AS-associated loci, with the exception of a nominal association for *PDE4A*. Altogether these results suggest the involvement of other genetic factors, such as rare variants in additional genes, or environmental factors contributing to the strong familial aggregation of SpA.

Disclosure: F. Costantino: AbbVie, 2, 6, Amgen, 2, 6, Celltrion, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, UCB, 2, 6; **r. Said-Nahal**: None; **H. Mambu Mambueni**: None; **A. Boland**: None; **J. Deleuze**: None; **M. Brown**: Altis Medicines, 2, Clementia, 2, Grey Wolf, 2, Incyte, 2, Ipsen, 2, UCB, 5; **H. Garchon**: None; **M. Breban**: MSD, 5, Novartis, 2, 5, UCB, 2.

Abstract Number: 0104

Dissecting the Genetic and Functional Association of CARD9 with Axial Spondyloarthritis

Félicie Costantino[1], Eva Frison[2], Andrew Brown[3], Carla Cohen[3], Manon Jacoutot[4], Gabriele Migliorini[3], roula Said-Nahal[5], Giuseppe Scozzafava[3], Paul Bowness[6], Paul Wordsworth[6], Henri-Jean Garchon[2], Simon Glatigny[4], Maxime Breban[7] and Julian Knight[6], [1]Department of Rheumatology, Ambroise Paré Hospital, AP-HP, Paris, France and Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Montigny-Le-Bretonneux, France, [2]Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Montigny le Bretonneux, France, [3]NIHR Oxford Biomedical Research Centre, University of Oxford, Centre for Human Genetics, Oxford, United Kingdom, [4]Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Montigny-Le-Bretonneux, France, [5]Department of Rheumatology, Ambroise Paré Hospital, AP-HP, Paris, France and Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Boulogne-Billancourt, France, [6]NIHR Oxford Biomedical Research Centre, University of Oxford, NDORMS, Oxford, United Kingdom, [7]CHU Ambroise-Paré, Boulogne-Billancourt, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic immune-mediated inflammatory disease with strong genetic predisposition, driven by HLA-B27 and over 100 additional loci identified by genome-wide association studies (GWAS). As most risk variants lie in non-coding regions, pinpointing causal variants and their functional roles remains a major post-GWAS challenge. CARD9 encodes an adaptor protein critical for innate and adaptive immune responses, promoting NF-κB and MAP kinase activation, proinflammatory cytokine production, and Th17 differentiation—key processes in axSpA. Although the CARD9 locus is associated with axSpA, the causal variant(s) and their functional impact are still unknown. The aim of this study was to identify the functional basis for the genetic association of *CARD9* variants with axSpA and its consequences on proinflammatory cytokines production.

Methods: Bayesian fine mapping on the CARD9 locus was conducted using the British subset of the IGAS Immunochip GWAS (*Cortes A et al. doi: 10.1038/ng.2667*). To assess regulatory effects of candidate causal variants, expression quantitative trait *loci* (eQTL) and chromatin accessibility quantitative trait *loci* (caQTL) mappings were performed using RNA-seq

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

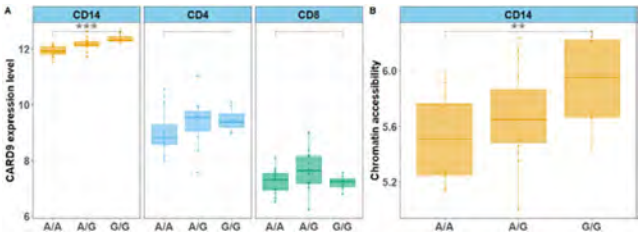


Figure 1. CARD9 mRNA expression levels in CD14+ monocytes, CD4+ and CD8+ T cells (panel A) and chromatin accessibility of CD14+ monocyte-specific regulatory region upstream of CARD9 promoter (panel B) according to genotype of SNVCARD9 (axSpA-susceptibility allele : G); ** : p-value <0.01; *** pvalue <0.001.

and ATAC-seq from CD14+ monocytes, CD4+ and CD8+ T cells of 45 individuals (20 axSpA, 35 healthy controls (HC)) (*Brown AC et al. doi: 10.1016/j.xgen.2023.100306*). Transcription factor binding disruption was evaluated via ATAC-seq footprinting with Tobias (*Bentsen M et al. doi: 10.1038/s41467-020-18035-1*) in public CD14+ ATAC-seq data from 41 controls (*Stevens NE et al. doi: 10.1172/JCI171742*).

Finally, TNFα, IL-6 and IL-23 production was measured by flow cytometry in monocytes from 59 axSpA patients before and after stimulation with lipopolysaccharide (LPS) or *Candida albicans* (C.alb) , and associations with candidate variant genotypes were tested using linear regression adjusting for age, sex, cell mortality, stimulation, and biologics use.

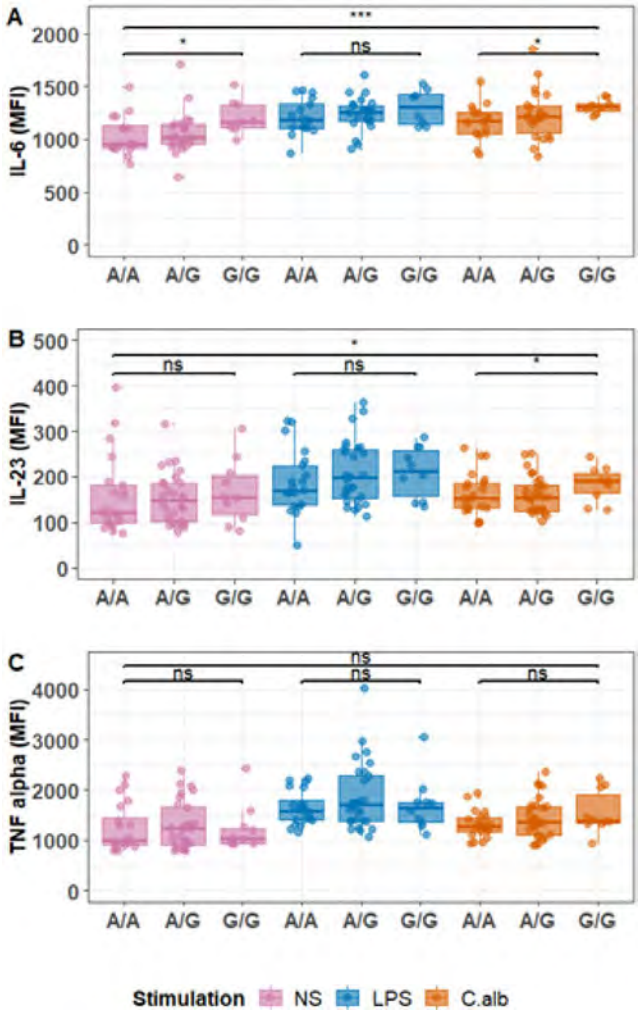


Figure 2. Mean fluorescence intensity (MFI) of IL-6 (panel A), IL-23 (panel B), and TNF alpha (panel C) in monocytes of 59 axSpA patients according to SNVCARD9 genotype in monocytes left unstimulated ("NS") or after stimulation with lipopolysaccharide (LPS) or Candida albicans (C.alb). ns: not significant * : p-value <0.05; *** pvalue <0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Fine mapping in 4,101 axSpA patients and 9,700 HC prioritized one variant -denoted "SNV_{CARD9}"- with >95% posterior probability of causality. This variant lies in a monocyte-specific open chromatin region upstream of the CARD9 promoter. The axSpA-risk G allele was associated with increased CARD9 mRNA expression and with enhanced chromatin accessibility in its surrounding region (figure 1). ATAC-seq footprinting predicted an allele-specific binding of the transcription factor ZBTB24. Functionally, the G allele was associated with a dose-dependent increase in IL-6 (p-value< 0.001) and IL-23 (p-value < 0.05), production but not with TNFα production (Figure 2).

Conclusion: These findings identify "SNV_{CARD9}" as a likely causal variant at the CARD9 *locus* in axSpA, linking increased CARD9 expression and IL-6/IL-23 production to disease risk. This supports the functional role of CARD9 in axSpA pathogenesis and its potential as a therapeutic target in risk allele carriers.

Disclosure: F. Costantino: AbbVie, 2, 6, Amgen, 2, 6, Celltrion, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, UCB, 2, 6; **E. Frison**: None; **A. Brown**: Janssen, 5; **C. Cohen**: None; **M. Jacoutot**: None; **G. Migliorini**: None; **r. Said-Nahal**: None; **G. Scozzafava**: None; **P. Bowness**: Benevolent AI, 5, GlaxoSmithKlein(GSK), 5, Merck/MSD, 5, Novartis, 5, regeneron, 5; **P. Wordsworth**: None; **H. Garchon**: None; **S. Glatigny**: None; **M. Breban**: MSD, 5, Novartis, 2, 5, UCB, 2; **J. Knight**: None.

Abstract Number: 0105

Inflammatory Cytokines, Matrix Metalloproteinases and Bone Markers Expressions Are Modulated in the Joints in the Chronic Murine Model of Imiquimod-Induced Psoriasis

Guillaume LARID[1], Cassandre Dumonteix Moreau[2], Adrien JAMAI[2], Hanitriniaina Rabeony[2], Jean Claude LECRON[2], Elisabeth Gervais[1], Jean François JEGOU[2] and franck MOREL[2], [1]Poitiers University Hospital - Poitiers University - LITEC Laboratory UR 15560, Poitiers, France, [2]Poitiers University - LITEC Laboratory UR 15560, Poitiers, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic disease is a systemic inflammatory condition which encompasses both cutaneous psoriasis (PsO), psoriatic arthritis (PsA) and multiple comorbidities. The chronic Imiquimod (IMQ) induced psoriasiform dermatitis mouse model is a classical model to study psoriasis and has been used in analysing psoriasis associated liver fibrosis. However less is known about joint inflammation and cytokines modification after IMQ psoriasis induction. The objectives of this study were to analyse the expression of cytokines, metalloproteinases and bone markers inside the mice's joints to evaluate the potential of long-term application of IMQ as a new PsA mouse model as well as the involvment of Oncostatin M (OSM).

Methods: Wild type (WT) and OSM-KO male C57BL/6 mice were studied. For the induction of PsO-like inflammation, mice were shaved and depilated on their back before a daily topical application of 62.5 mg of Aldara cream (5% IMQ; Meda) for six consecutive days every other week during 5 (W5) to 9 weeks (W9). Control mice were treated with a similar dose of Vaseline. Mice were euthanized after 5 weeks or 9 weeks of treatment. Knee joints were dissected, collected, rapidly frozen in liquid nitrogen. Total RNA was extracted, reverse transcribed, and transcripts were quantified using the LightCycler-FastStart DNA Master Plus SYBR Green I kit on LightCycler 480 instrument. Samples were normalized to the independent control housekeeping gene, glyceraldehyde 3-phosphate dehydrogenase (GAPDH), and reported according to the ΔΔCT method

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

as RNA fold increase over untreated samples. Comparison were made using Mann Whitney test. p-values < 0.05 were considered significant.

Results: Chronic application of IMQ on the mice skin induced a pro-inflammatory state within the joints as shown by the increased expression of TNF alpha at W5 and W9 in both WT and OSM-KO mice and decreased expression of the anti-inflammatory cytokine PEDF. IL-1 family cytokines seem to be implicated in the initiation of the inflammatory response as suggested by IL1a increase at W5 in the IMQ treated WT mice and the decreased expression at W9 of IL-18. IL10 expression was increased at both W5 and W9 indicating an attempt to regulate joint's inflammation. While at W5 no difference was observed for MMP3, MMP9, and MMP13, a lower expression was found in IMQ treated mice for MMP3 and MMP13 at W9 while no difference were observed for MMP9. Concerning bone turnover, no modification of Sclerostin was found in both groups at W5 and W9 while there was a DKK1 expression decrease only in the WT group at both W5 and W9. M-CSF, an osteoclast differentiation driver, was decreased only at W9 in both groups and at W5 in the WT group only. These results confirm the role of OSM as a modulator of bone biology upon inflammatory conditions. No difference was found at both W5 and W9 for IL1B, VEGFa, MMP9, SOST, TLR7, TRPV1, IL1RA in both groups.

Conclusion: In the long term IMQ induced psoriasis mouse model intra-articular inflammation is observed and modifications of bone cell markers as well as metalloproteinases expression are modulated in a time dependant manner. Those results pave the way to a more detailed analysis of this model which seems a promising new PsA model as well as a PsO to PsA mechanistic model.

Disclosure: G. LARID: AbbVie/Abbott, 6, Amgen, 12, Support for attending meetings, Eli Lilly, 12, Support for attending meetings; **C. Dumonteix Moreau**: None; **A. JAMAI**: None; **H. Rabeony**: None; **J. LECRON**: None; **E. Gervais**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Galapagos, 6, Janssen, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **J. JEGOU**: None; **f. MOREL**: None.

Abstract Number: 0106

Investigation of DNA Methylation Inhibition in a Mouse Model of Ankylosing Spondylitis

Goh Murayama[1], Kurisu Tada[2], Naoto Tamura[3], Eri Hayashi[1], Taiga Kuga[4], Ken Yamaji[5] and **HOSHIKO FURUSAWA**[6], [1]Department of Internal Medicine and Rheumatology, Juntendo University Graduate School of Medicine, Tokyo, Japan, [2]Department of Internal Medicine and Rheumatology, Juntendo University Graduate School of Medicine, Tokyo, [3]Juntendo University School of Medicine, Tokyo, Japan, [4]Juntendo University, Tokyo, Japan, [5]Juntendo University, Department of Internal Medicine and Rheumatology, Tokyo, Japan, [6]juntendo, tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease characterized by enthesitis in axial joints, bone erosion near the entheses, and subsequent irreversible ankylosis due to new bone formation. Although AS has a strong association with HLA-B27, its occurrence in HLA-B27-negative individuals suggests the involvement of epigenetic factors. Decitabine is a DNA methylation inhibitor that induces demethylation and reactivation of silenced genes and is used to treat myelodysplastic syndromes. This study aimed to evaluate the effects of decitabine in a mouse model of spondyloarthritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Spondyloarthritis was induced in SKG mice by intraperitoneal injection of β-glucan under SPF conditions. Mice were treated weekly with either decitabine (1 mg/kg/week) or vehicle. Body weight and arthritis scores were monitored until week 12. At week 12, and histological analysis was performed on the limb joints, spine, and tail. At weeks 4, 8, and 12, splenic T cell subsets and cytokine production were analyzed by flow cytometry. DNA methylation analysis was performed on the achilles tendon to identify genes with suppressed methylation by decitabine. Furthermore, to assess the functional effects of decitabine in vitro, splenocyte supernatants from arthritic mice were co-cultured with decitabine, and production of IL-17 and TGF-β was evaluated.

Results: Mice treated with decitabine showed significantly improved arthritis scores compared to the control (vehicle) group. Histological scores of the limb joints and tail at week 12 were significantly improved as assessed by both H&E and toluidine blue staining. Flow cytometry of splenocytes revealed a significant suppression of IL-17 production in mice at weeks 4 and 8. Although the number of regulatory T cells ($CD4+CD25^{+}FOXP3^{+}$) remained unchanged in mice sacrificed at week 12, PD-1 expression on Tregs was significantly reduced. DNA methylation analysis of the Achilles tendon at week 12 revealed significant demethylation of the *FOXP3* and *IL17rd* genes. In vitro experiments showed that stimulation of splenocyte supernatants with IL-2 and anti-CD3/CD28 antibodies, followed by co-culture with decitabine, resulted in a significant increase in TGF-β production as measured by ELISA. After additional 24-hour stimulation with PMA/ionomycin, IL-17 production tended to be suppressed in the decitabine-treated cultures.

Conclusion: DNA methylation inhibitors may alleviate systemic symptoms and arthritis in a mouse model of spondyloarthritis by suppressing IL-17 production and enhancing Treg function.

Disclosure: G. Murayama: Cell Exosome Therapeutics Co., Ltd., 5; **K. Tada**: None; **N. Tamura**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, AstraZeneca, 6, Ayumi, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, 6, Cell Exosome Therapeutics Co., Ltd., 5, Chugai, 5, 6, Daiichi Sankyo, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 6, Novartis, 6, Taisho, 5, UCB, 6; **E. Hayashi**: None; **T. Kuga**: None; **K. Yamaji**: None; **H. FURUSAWA**: None.

Abstract Number: 0107

Role of Achilles Elastography in Differentiating Patients with Early Psoriatic Arthritis

IRENE MARTIN MARTIN[1], CARMEN SAN JOSE MENDEZ[2], SONIA JIMENEZ BARRIOS[3], ELENA MARTIN FERNANDEZ[4], JULIA MIRANDA MANZANO[5], DIEGO DIOS SANTOS[6], JORGE GONZALEZ MARTIN[7], PABLO ZURITA PRADA[7], MONICA VAZQUEZ DIAZ[8] and CARLOS GUILLEN-ASTETE[9], [1]HOSPITAL VIRGEN DE LAS NIEVES, GRANADA, [2]Complejo Hospitalario Universitario de A Coruña (CHUAC), A Coruña, Spain, [3]Hospital Universitario Ramón y Cajal, Madrid, Spain, [4]HOSPITAL UNIVERSITARIO RAMON Y CAJAL, MADRID, [5]FACULTAD BIOMEDICINA, MADRID, [6]HOSPITAL DE VERÍN, OURENSE, [7]HOSPITAL UNIVERSITARIO HM SANCHINARRO, MADRID, [8]HOSPITAL UNIVERSITARIO HLA MONCLOA, MADRID, [9]H.U Ramón y Cajal, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Elastography (EL) is an imaging technique that evaluates the biomechanical properties of tissues. Pathological tissues have different elastic properties compared to healthy tissues.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In diseases like psoriatic arthritis (PsA), tendon structure and function can be affected, leading to enthesitis, being the Achilles tendon one of the most commonly involved structures. EL allows for the evaluation of tendons´ response to mechanical strain, detecting changes in their elasticity that may indicate inflammation or structural damage. The underlying hypothesis is that Achilles tendon stiffness increases significantly after physical activity in patients with Achilles involvement, while in those without enthesitis, elasticity remains stable.

The purpose of this study is to demonstrate the utility of Achilles elastography (EL-AQ) in the diagnosis of PsA in patients with clinically referred Achilles involvement (PsA-A) or without it, compared to three types of controls.

Methods: Baseline and post-exercise EL-AQ results were compared between PsA and PsA-A patients (diagnosed < 24 months) from four rheumatology centers and three control groups: athletes, non-athletic individuals with normal weight, and overweight/obese subjects, all without known psoriatic disease. Controls were matched to patients by sex and age (±2 years). Baseline and post-exercise comparisons were performed, and correlations between these results, clinical characteristics, and MASEI scores were analyzed. EL-AQ was performed using a General Electric S8 ultrasound machine equipped with a low-frequency linear probe. Tendon stiffness was measured using shear wave elastography, averaging three 1 cm^2 regions of interest within the enthesis of the non-dominant Achilles tendon (controls and PsA patients) or the symptomatic tendon (PsA-A patients). The controlled exercise consisted of 20 minutes on a stationary bicycle at medium resistance with a target of 150% of the resting heart rate.

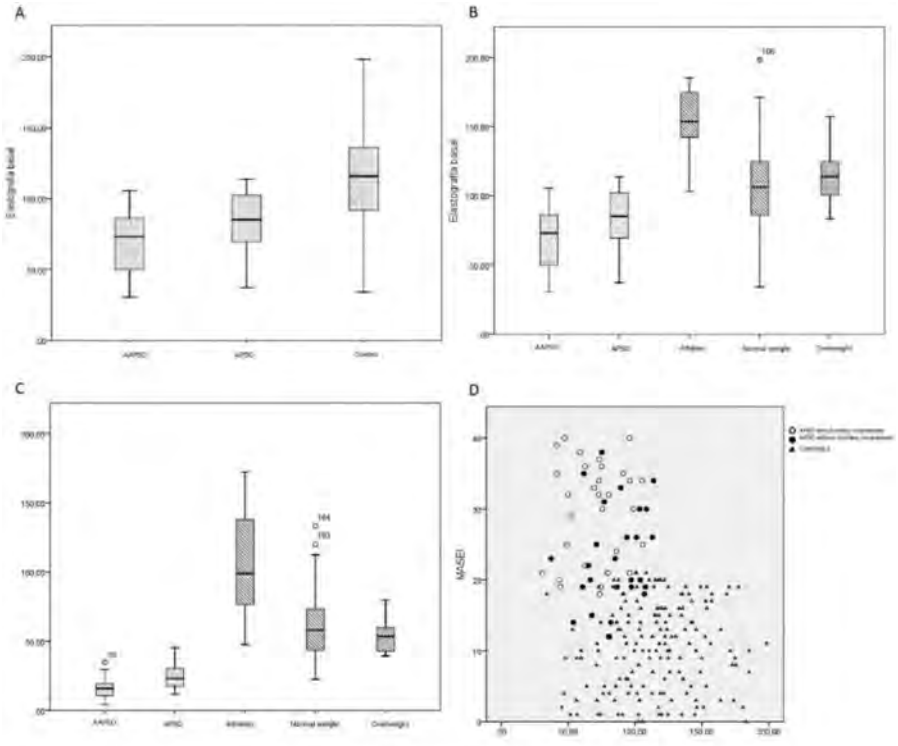


Figure 1A: Comparison of baseline Achilles elastography (EL-AQ) in patients with psoriatic arthritis with Achilles symptoms (PsA-A), PsA without Achilles symptoms (PsA), and all controls.
B: Comparison of baseline EL-AQ in patients and the three control subgroups.
C: Comparison of post-exercise stiffness increase between patients and control subgroups.
D: Correlation between MASEI and baseline EL-AQ in patients and controls.
EL-AQ measurements are expressed in kPa.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 57 patients (27 PsA, 30 PsA-A) and 171 controls were included. Patients' mean age (SD) = 39.9 (6.7) years. Time since diagnosis = 12 (7) months. Baseline EL-AQ results for controls and patients were 114.6 (32.9) and 77.0 (21.6) kPa, respectively ($p < 0.001$). EL-AQ post-exercise gradients in controls and patients were 65.7 (28.7) and 20.0 (9.3) kPa, respectively ($p < 0.001$). An inverse correlation was observed between MASEI and EL-AQ post-exercise change (Pearson's coefficient -0.445; $p < 0.001$). Among patients, baseline EL-AQ was 70.1 (21.0) in the PsA-A group and 84.7 (19.9) kPa in the PsA group ($p < 0.05$); EL-AQ post-exercise gradient was 15.9 (7.2) in the PsA-A group and 24.5 (9.4) kPa in the PsA group ($p < 0.001$).

Conclusion: Baseline EL-AQ demonstrates discriminatory diagnostic capacity between PsA patients with or without clinical Achilles involvement and healthy controls. Adaptive ability to physical exercise, analyzed via post-exercise EL-AQ gradient, also demonstrated strong discriminatory capacity between patients and control subgroups. EL-AQ should be considered a test of interest for evaluating patients suspected of having PsA with or without Achilles involvement.

Disclosure: I. MARTIN MARTIN: None; **C. SAN JOSE MENDEZ**: None; **S. JIMENEZ BARRIOS**: None; **E. MARTIN FERNANDEZ**: None; **J. MIRANDA MANZANO**: None; **D. DIOS SANTOS**: None; **J. GONZALEZ MARTIN**: None; **P. ZURITA PRADA**: None; **M. VAZQUEZ DIAZ**: None; **C. GUILLEN-ASTETE**: None.

Abstract Number: 0108

In Vivo and In Vitro Analysis of IL-23 Modulation Following Anti-TNF Therapy in Psoriatic Arthritis

Jesús Eduardo Martín Salazar[1], Clementina López Medina[2], Carlos Pérez Sánchez[3], María Ángeles Puche-Larrubia[4], Pedro Ortiz Buitrago[5], María Dolores López-Montilla[6], Iván Arias de la Rosa[7], Laura Cuesta López[8], Miriam Ruiz Ponce[8], Antonio Barranco[8], Laura Romero Zurita[8], Elena Moreno-Caño[9], Rafaela Ortega-Castro[10], Jerusalén Calvo[11], M Carmen Abalos-Aguilera[12], Desiree Ruiz-Vilchez[13], Chary López pedrera[14], Alejandro Escudero Contreras[11], Eduardo Collantes estévez[15] and Nuria Barbarroja[16], [1]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Rheumatology service/Department of Medical and Surgical Sciences, Cordoba, Spain, Cordoba, Andalucia, Spain, [2]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [4]Reina Sofia University Hospital, Granada, Spain, [5]Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), Cordoba, Andalucia, Spain, [6]Rheumatology Department, Reina Sofía University Hospital, Cordoba/ IMIBIC/University of Cordoba., CORDOBA, Spain, [7]IMIBIC/FIBICO/Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso; Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Toledo, Spain; Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd) Toledo, Spain., Córdoba, Spain, [8]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Rheumatology service/Department of Medical and Surgical Sciences, Cordoba, Spain, Córdoba, Spain, [9]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Córdoba, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [11]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [12]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [13]Department of Rheumatology, Reina Sofía University Hospital / Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [14]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [15]Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [16]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease for which TNFα inhibitors are the standard first-line biologic therapy. Nonetheless, a significant proportion of patients exhibit an inadequate response, requiring a switch to alternative agents. There are several second-line treatment options, such as IL-17 inhibitors, IL-23 inhibitors, or JAK inhibitors. Among these options, IL-23 inhibitors are increasingly used, yet there is no clear guidance to inform their selection in clinical practice. Exploring how TNFα inhibition influences the IL-23 levels may offer valuable insights into whether anti-IL-23 therapies represent a rational and effective choice after anti-TNF failure. This study aims to investigate the effect of anti-TNFa therapy on IL-23 serum levels in PsA patients and explore the mechanistic regulation of IL-23 and other inflammatory markers by TNFa in vitro.

Methods: Serum IL-23 levels were measured by ELISA in a cohort of 40 PsA patients before and after six months of anti-TNFa therapy. In parallel, primary human dermal fibroblasts were cultured and stimulated with recombinant TNFα in the presence or absence of anti-TNFα agents using varying concentrations and exposure times (6h, 24h and 48h). IL-23 expression and other key inflammatory markers were assessed by RT-qPCR to evaluate the impact of TNFα blockade.

Results: Serum IL-23 levels were significantly reduced after six months of anti-TNFα therapy. In vitro, TNFα stimulation induced a robust upregulation of IL-23 expression in dermal fibroblasts which was effectively reversed by anti-TNFα agents. Additionally, anti-TNFα exposure led to a significant decrease in the expression of inflammatory mediators such as IL-6, while genes like IL-17 remained largely unchanged. These findings suggest that TNFα directly promotes IL-23 production in resident skin cells, and that its inhibition downregulates this axis both systemically and at the tissue level.

Conclusion: Our findings demonstrate that anti-TNFα therapy significantly modulates key inflammatory pathways in PsA. Anti-TNFα treatment leads to a notable reduction in IL-23 levels both in vivo and in vitro, highlighting IL-23 as a downstream target of TNF signaling in PsA. Therefore, quantification of IL-23 could serve as a promising biomarker for personalizing biologic sequencing and guiding second-line therapy selection in PsA patients with suboptimal responses to anti-TNFα agents.

Acknowledgements. Project " PMP21/00119", funded by Instituto de Salud Carlos III (ISCIII) and co-funded by the European Union.

Disclosure: J. Martín Salazar: None; **C. López Medina**: None; **C. Pérez Sánchez**: None; **M. Puche-Larrubia**: None; **P. Ortiz Buitrago**: None; **M. López-Montilla**: None; **I. Arias de la Rosa**: None; **L. Cuesta López**: None; **M. Ruiz Ponce**: None; **A. Barranco**: None; **L. Romero Zurita**: None; **E. Moreno-Caño**: None; **R. Ortega-Castro**: None; **J. Calvo**: None; **M. Abalos-Aguilera**: None; **D. Ruiz-Vilchez**: None; **C. López pedrera**: None; **A. Escudero Contreras**: None; **E. Collantes estévez**: None; **N. Barbarroja**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0109

Application of Psoriatic Arthritis Mouse Models in Preclinical Pharmacodynamic Evaluation

Juan Liang[1] and Yinlian Zhang[2], [1]Gempharmatech, Nanjing, Jiangsu, China, [2]GemPharmatech, Nanjing, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA), a complex inflammatory disorder that affects up to 30% of psoriasis patients. It is marked by clinical heterogeneity and a lack of standardized diagnostic criteria, posing significant challenges in therapeutic development. Despite advancements in targeted therapies, gaps in understanding disease pathogenesis and variable clinical phenotypes highlight the need for robust, translational preclinical models. Here, we established two inducible PsA mouse models to support preclinical drug efficacy testing and accelerate therapeutic discovery.

Methods:

Two distinct PsA models were developed:

1. Mannan-induced PsA model, female BALB/c mice (12-13 weeks) received intraperitoneal mannan injections (every 4 days) combined with a single subcutaneous Complete Freund's Adjuvant (CFA) injection into the hind paw. On day 12, ear and paw tissues were analyzed for histopathology (HE staining, inflammation scoring), qPCR (inflammatory cytokines: *Ifng*, *Il6*, *Il17a*, *Tnf*, *Il23*), and serum cytokines (CBA assay: IL-12, IFN-γ, IL-6).

2. AAV-hIL23-induced PsA model, female NOD ShiLtj mice (8 weeks) were injected intravenously with 1×10^{12} particles/mL AAV-hIL23. Serum hIL-23 levels were monitored weekly (ELISA), and tissues were analyzed at day 35 for histopathology and cytokine expression.

Pharmacodynamic evaluation in the mannan-induced PsA model: Treatment arms included dexamethasone (1 mg/kg, daily oral) and upadacitinib (20 mg/kg, BID oral). In as separate study, PsA was induced with mannan in BALB/c-hIL23AhIL12B mice (GemPharmatech), followed by subcutaneous injection with risankizumab (10 mg/kg, BIW). Disease progression was monitored via psoriasis/arthritis scoring of the ears and hind limbs.

Results: Mannan-induced model, PsA mice exhibited marked ear erythema, paw/ankle swelling, elevated psoriasis/arthritis scores, as well as elevated expression of inflammatory cytokines (*Ifng*, *Il6*, *Il17a*, *Tnf*, *Il23*), and increased serum IL-12, IFN-γ, and IL-6. Histopathology revealed epidermal hyperplasia, inflammatory infiltration, and bone erosion. Both dexamethasone and upadacitinib reduced skin/joint inflammation and disease scores. Risankizumab effectively suppressed skin/joint pathology and disease scores in mannan-induced BALB/c-hIL23AhIL12B mice PsA model. In AAV-hIL23 model, sustained hIL-23 expression (serum, days 14–35) drove progressive skin thickening, elevated psoriasis scores, and arthritis-associated swelling, with upregulated *Il6*, *Il17a*, *Il22*, and *Tnf*.

Conclusion: We validated two inducible PsA models that reproduce key clinical features of human PsA. The mannan-induced model enables the evaluation of small molecules (e.g., JAK inhibitors) and biologics in humanized strains, while

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the AAV-hIL23 model may provide a platform for IL-23 pathway-targeted therapies. Together, these models help address critical gaps in the preclinical PsA drug development process.

Disclosure: J. Liang: None; **Y. Zhang**: None.

Abstract Number: 0110

SKG Mice Develop CD4$^+$ T Cell–Driven Psoriasis and Enable Study of Endogenous Antigen-Specific Responses

Yuka Nakao[1], Astha Patel[1], Bahram Razani[2], Steven yu[1], Steven Lazarevsky[2], Marlys Fassett[2] and **Judith Ashouri**[1], [1]University of California, San Francisco, San Francisco, CA, [2]UCSF Department of Dermatology, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriasis (Pso) and psoriatic arthritis (PsA) are chronic immune-mediated diseases affecting millions, yet early immunologic triggers remain poorly defined. Therapies targeting TNFα, IL-17, and IL-23 help many, but inadequate or transient responses highlight the need to understand upstream mechanisms. CD4$^+$ T cells are central to disease, but early events are hard to study in humans due to genetic variability, late-stage clinical presentation, and limited tissue access. The SKG mouse, with a hypomorphic Zap70 mutation impairing negative selection, develops CD4$^+$ T cell–driven, spontaneous and environmentally induced erosive arthritis with features of RA (RF$^+$, ACPA$^+$, pneumonitis) and spondyloarthritis (skin, eye, gut inflammation, enthesitis). While joint disease is well described, associated skin inflammation is not. Our data reveal psoriatic-like changes reflecting key features of human Pso and PsA. This study aims to define the molecular and cellular mechanisms of Pso skin disease in SKG and characterize the pathogenic TCR repertoire involved.

Methods: Disease was induced by intraperitoneal injection of zymosan into SKG mice or by adoptive transfer of SKG CD4$^+$ T cells into SCID hosts. Psoriasis-like skin disease incidence and clinical arthritis scores were monitored. Skin was evaluated by histology and flow cytometry to assess immune cell infiltration and TCR Vβ repertoire; group differences were analyzed by t-tests and exact permutation tests.

Results: We found that SKG mice develop Pso-like skin inflammation in response to environmental triggers (e.g., zymosan), histologically mirroring human disease with acanthosis, hyperkeratosis, neutrophilic micro abscesses, and lymphohistiocytic

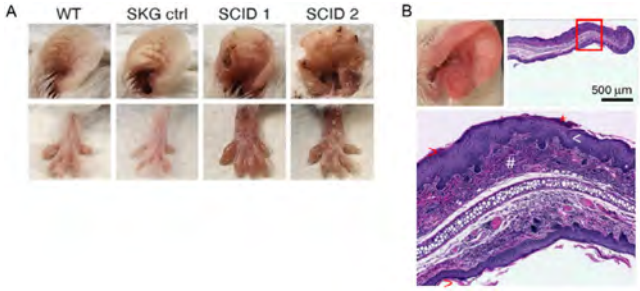


Figure 1. Microbiota are required for arthritis development in SKG mice. Germ-free (GF) SKG mice (n=8) and conventionalized GF SKG mice (n=9) were injected intraperitoneally with zymosan and monitored over time for clinical arthritis scores. (A) Longitudinal arthritis scores are shown for each group. (B) Cumulative disease burden, measured by area under the curve (AUC) of arthritis scores, was significantly higher in conventionalized mice (Wilcoxon test, p = 0.0072).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

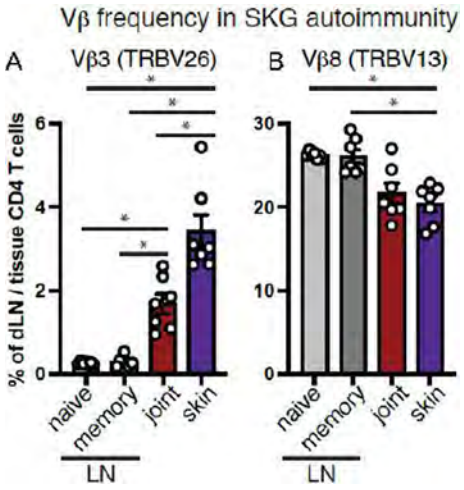


Figure 2. Sag-reactive T cells accumulate in SKG psoriatic skin. Mean frequency (± SEM) of SKG CD4 T cells with Sag-reactive TCR Vβ3 (A) or non-cognate Vβ8 (B) protein usage determined by flow cytometry in LN, joints & skin 5 weeks post zymosan. P value < 0.05 (*) calculated from exact permutation test (A-B).

infiltrates. We demonstrate for the first time that SKG $CD4^+$ T cells alone are sufficient to induce Pso in SCID hosts (Fig. 1), establishing a $CD4^+$ T cell–dependent mechanism of pathogenesis. Flow cytometry shows increased conventional dendritic cells (p=0.02), a trend toward greater neutrophil infiltration and expansion of $V\gamma2^+$ $CD4^+$ T cells—key IL-17 producers implicated in Pso. We identify pathogenic $CD4^+$ T cells enriched for TCR Vβ chains recognizing superantigens (Sags) from an endogenous retrovirus (ERV)—genomic elements that incorporated into the mammalian genome in ancient times and shape innate and adaptive immunity. These Sag-reactive TCRs are significantly enriched in Pso skin relative to peripheral lymphoid organs, while non-cognate Vβs show no enrichment (Fig. 2), supporting an ERV-driven mechanism of tissue-specific autoimmunity.

Conclusion: SKG mice model the chronicity and immune complexity of human Pso, integrating innate (e.g., neutrophil accumulation) and adaptive ($CD4^+$ T cell–driven) pathways without exogenous chemicals. The discovery of Sag-reactive $CD4^+$ T cells recognizing ERV-encoded superantigens in affected skin defines a novel molecular axis of psoriatic autoimmunity. This model provides a robust platform to study disease initiation, antigen-specific responses, and test targeted therapies—advancing translational understanding of Pso and PsA.

Disclosure: Y. Nakao: None; **A. Patel**: None; **B. Razani**: None; **S. yu**: None; **S. Lazarevsky**: None; **M. Fassett**: Boehringer-Ingelheim, 2, Sanofi-Regeneron, 1; **J. Ashouri**: None.

Abstract Number: 0111

Predicting Response To Adalimumab In Patients With Psoriatic Arthritis Using Epigenetic Chromosome Conformation Signatures

Patricia Riedlova[1], Ewan Hunter[2], Christine Huppertz[3], Maarten de Wit[4], Stephen R. Pennington[5], Oliver FitzGerald[6], Jochen M. Schwenk[7], Rik Lories[8], Carl S. Goodyear[1] and Stefan Siebert[1], [1]University of Glasgow, Glasgow, United Kingdom, [2]Oxford BioDynamics Plc, Oxford, United Kingdom, [3]Novartis Pharma AG, Basel, Switzerland, [4]Patient Research Partner, Stichting Tools, Amsterdam, Netherlands, [5]University College Dublin, DUBLIN, Ireland, [6]UCD, Dublin 6, Dublin, Ireland, [7]KTH Royal Institute of Technology, Solna, Sweden, [8]KU Leuven, Leuven, Belgium

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

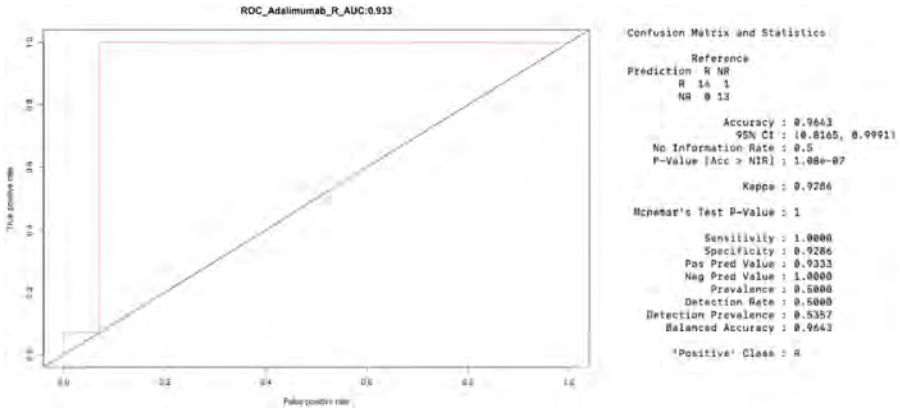


Figure 1: ROC curve displaying the performance of the selected 12-loop signature for PsA responders and non-responders to adalimumab, along with associated statistical matrix.

Background/Purpose: TNF inhibitors (TNFi) have proven efficacy in psoriatic arthritis (PsA) and are commonly prescribed as first line targeted therapy in PsA. However, response to TNFi is unpredictable and many patients fail to respond adequately, with a substantial minority not responding at all. Thus, there is an urgent need for biomarkers that can predict treatment response. Epigenetic chromosome conformation signatures (CCS) using EpiSwitch™ technology have shown predictive potential in various cancers and in predicting a methotrexate response in patients with rheumatoid arthritis [1] but have not been studied in PsA. This work aimed to identify predictive biomarkers of therapeutic response to adalimumab in patients with PsA using baseline peripheral blood CCS.

Methods: Baseline whole blood samples were used from participants in the OPAL Broaden phase III trial (NCT01877668) who received the TNFi adalimumab in the active comparator arm [2]. Response was defined using ACR response at 3 months. Baseline samples and response data were available for 91 participants, with 11 defined as extreme good responders (achieving at least an ACR70 response) and 11 as extreme non-responders (failing to reach at least ACR20 response) selected for the discovery set. Baseline peripheral blood samples underwent genome-wide chromosomal loop screening using the EpiSwitch™ Explorer microarray (Oxford Biodynamics), which consists of $\sim 10^6$ chromatin loops probes. Differential chromatin loops were identified and translated into qPCR assays for further feature reduction and signature refinement using penalised logistic regression.

Results: EpiSwitch™ Explorer microarray analysis of 22 (8 females, 14 males) extreme responders/non-responders, after correcting for biological sex, identified 2,291 chromatin loops (fold change >1.1, p-value < 0.05). Feature reduction narrowed these down to 50 loops, which were further analysed by qPCR in extreme responders/non-responders, as well as in moderate responders (achieving ACR50 but not ACR70 response), and partial responders (achieving ACR20 but not ACR50 response). 30 loops successfully passed the qPCR process. From these, a predictive model for treatment response containing 12 chromatin loop markers was developed, achieving an accuracy of 96.4% and an AUC of 0.93 (Figure 1).

Conclusion: A 12-loop chromosome conformation signature was modelled as a potential biomarker for predicting the therapeutic response to adalimumab in PsA patients in a phase III trial. This model demonstrated 96.4% accuracy and shows promise in correctly identifying not only extreme responders and non-responders, but also moderate/partial responders, highlighting its potential to help select the most effective personalised treatment for every individual. Further validation in an independent cohort is being planned to confirm the accuracy and reliability of these 12 loops as predictive biomarkers for TNFi response in PsA.

References

[1] Carini, C. et al. J Transl Med 2018;16.
[2] Mease, P. et al. NEJM 2017; 377:1537–50.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Riedlova: None; **E. Hunter**: Oxford Biodynamics Plc, 3, 10, 11; **C. Huppertz**: Novartis Pharma AG, 3, 11; **M. de Wit**: Celgene, 2, Eli Lilly, 2, Janssen-Cilag, 2, Pfizer, 2, UCB, 2; **S. Pennington**: None; **O. FitzGerald**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5; **J. Schwenk**: ABC Development AB, 1, Luminex Corp, 5, 6, Olink Proteomics AB, 6; **R. Lories**: AbbVie/Abbott, 2; **C. Goodyear**: AstraZeneca, 5, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 5, UCB, 6; **S. Siebert**: AbbVie, 6, Amgen, 6, AstraZeneca, 6, BMS, 5, Boehringer-Ingelheim, 5, Eli Lilly, 5, GlaxoSmithKlein, 5, Johnson & Johnson, 5, 6, Novartis, 6, Pfizer, 6, Syncona, 6, Teijin Pharma, 6, UCB, 5, 6.

Abstract Number: 0112

Proteome-wide Mendelian Randomization Identifies Therapeutic Targets in Psoriatic Arthritis

Quan Li[1] and **Proton Rahman**[2], [1]University of Toronto, Toronto, Canada, [2]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: While numerous proteins have been linked to psoriatic arthritis (PsA), the causal nature of these associations remains unconfirmed. This study aims to employ a Mendelian randomization (MR) approach to evaluate whether circulating plasma protein levels, derived from extensive international databases, are causally associated with PsA.

Methods: The study analyzed 1,553 PsA patients and 147,221 controls, all of whom had undergone genome-wide association scans, as identified from the FinnGen consortium. Large-scale plasma protein quantitative trait locus (pQTL) data were sourced from the UK Biobank Proteomics Project (UKB-PPP) (2,923 unique proteins), the INTERVAL study (2,995 unique proteins), and the Icelandic study (Ferkingsatad et al. 2021) with (4,719 proteins). Potential protein candidates were identified based on SNP associations with proteins ($p < 5x10^{-8}$), LD clumping to identify independent pQTLs for each protein ($r^2 < 0.001$), and defining SNPs when the leading SNP was located within 500kb of the transcription site of the protein-coding gene. A two-sample MR was then performed, using the Wald ratio for genes with one SNP and inverse variance weighting (IVW) for genes with more than one SNP. Appropriate MR sensitivity and pleiotropy analyses were conducted.

Results: A total of 19 unique proteins were identified as being associated with the risk of PsA. UKB-PPP dataset revealed four proteins linked to an increased risk of PsA (ATP6V1G2, LTA, HLA-E, APOF) and five proteins associated with a decreased risk (IL12A_IL12B, AGER, MICB_MICA, IL12B, HCG22) (Table 1). The INTERVAL dataset identified five proteins correlated with an elevated risk of PsA (HLA-DRB9, TNXB, HLA-DQB1, HLA-DRB1, HLA-DQA2) and three proteins linked to a reduced risk (IL12B, P4HA2, HLA-DQA1) (Table 1). From Ferkingsatad et al. 2021 dataset, MR identified five proteins significantly associated with PsA (C2,TNXB,HSPA1A and APOF increased PsA risk, while AGER decreased the risk, Table 2).A protein-protein interaction network was constructed using the STRING database, with a required interaction score of >0.4, illustrating the connections among these proteins. Notably, many of these proteins were found within the drug repurposing hub, therapeutic target database, and druggable genome compendium.

Conclusion: This proteome-wide MR study identified 19 unique proteins associated with PsA risk, offering novel insights into the disease's pathogenesis. These prioritized proteins also present potential druggable targets, warranting further investigation to explore novel therapeutic opportunities. More in depth studies are needed to assess the role and utility of these proteins.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

UKB-PPP Dataset	OR	lci95	uci95	pvalue
IL12A_IL12B	0.77	0.70	0.84	9.58e-09
ATP6V1G2	5.20	3.75	7.21	4.26e-23
LTA	1.193	1.11	1.27	3.27e-07
AGER	0.34	0.25	0.47	2.46e-11
MICB_MICA	0.74	0.71	0.77	5.28e-50
HLA-E	1.42	1.23	1.63	8.39e-07
IL12B	0.77	0.71	0.84	9.58e-09
HCG22	0.73	0.65	0.82	1.13e-07
APOF	2.09	1.56	2.79	5.57e-07
INTERVAL Dataset	**OR**	**lci95**	**uci95**	**pvalue**
HLA-DRB9	1.59	1.34	1.88	1.05e-07
TNXB	1.63	1.47	1.80	9.90e-21
IL12B	0.63	0.54	0.74	1.12e-08
P4HA2	0.62	0.52	0.75	6.76e-07
HLA-DQB1	4.73	3.32	6.76	9.37e-18
HLA-DQA1	0.63	0.53	0.74	5.06e-08
HLA-DRB1	1.32	1.187	1.47	4.98e-07
HLA-DQA2	1.27	1.158	1.40	5.81e-07

Table 2

Ferkingsatad et al. 2021 Dataset	OR	lci95	uci95	pvalue
AGER	0.127162	0.07	0.21	2.97e-15
C2	11.94246	3.19	44.66	2.28e-4
TNXB	2.91523	1.11	7.64	2.9e-2
HSPA1A	31.75637	17.21	58.59	1.86e-28
APOF	2.304613	1.66	3.19	5.57e-07

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

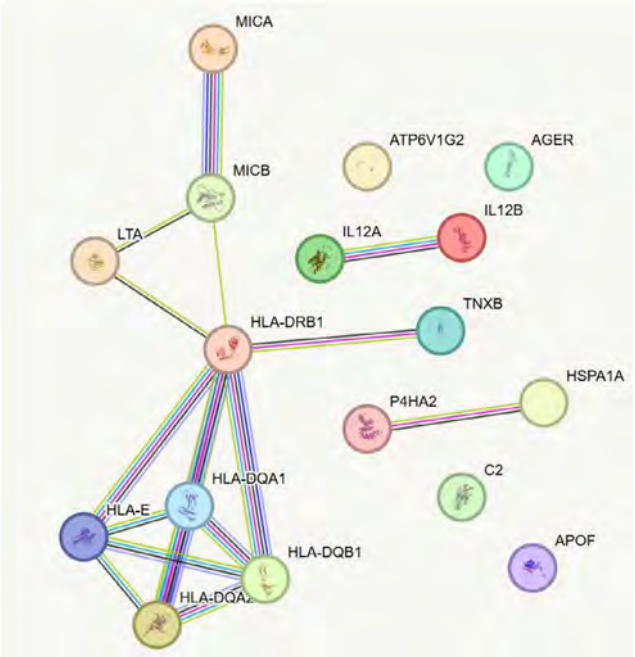


Figure 1

Disclosure: Q. Li: None; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2.

Abstract Number: 0113

ZEB2 and MLCK1 may impair gut barrier integrity in MIF-Deficient SKG Mice

Shaghayegh Foroozan Boroojeni[1], Mansi Aparnathi[2], Akihiro Nakamura[3], Zoya Qaiyum[2] and Nigil Haroon[4], [1]University Health Network/University of Toronto, Toronto, ON, Canada, [2]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [3]Queen's University, Kingston, ON, Canada, [4]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial Spondyloarthritis (AxSpA) is a chronic inflammatory condition that primarily affects the musculoskeletal system and has multifactorial origins. The majority of AxSpA patients experience gut inflammation, with 60% having microscopic changes and 10% having overt Inflammatory Bowel Disease (IBD). Over the years, researchers have linked many pathways and cell populations to the pathogenesis of gut inflammation in AxSpA. One notable player is the macrophage migration inhibitory factor (MIF), which assumes a crucial role in AxSpA development. In a SpA mouse model (SKG mice), MIF overexpression mirrors key clinical features of AxSpA, while inhibiting or depleting MIF attenuates these symptoms. However, the exact role of MIF in SpA-related gut inflammation is unknown. In this study, we aimed to investigate the effects of MIF on intestinal barrier integrity in SKG mice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Eight-week-old SKG mice were used for this four-arm study: SKG control mice (WT), SKG mice treated with curdlan (WT_Curdlan), SKG-MIF Knock Out (KO) mice (MKO), and SKG-MIFKO mice treated with curdlan (MKO_Curdlan). After eight weeks of curdlan/vehicle treatment, 16-week-old mice were euthanized. Formalin-fixed paraffin-embedded (FFPE) blocks of the ileum from these mice (n=2/arm) were used for single-cell RNA sequencing (scRNA-seq) Flex Gene Expression assay to investigate the effects of MIF on the expression of genes related to gut homeostasis. These results were validated by Immunohistochemistry (IHC) or qPCR in WT (n=7) and MKO (n=9) mice. Intestinal permeability was assessed in vivo using the FITC-dextran assay. Mice were administered FITC-dextran orally, and serum fluorescence was measured after 4 hours.

Results: scRNA-seq analysis revealed differential expressions of genes potentially related to gut homeostasis: *Zeb2, Mylk, Muc2, Cdh1, Ocln and Cldn7*, across the four arms. As compared to WT mice (± curdlan), downregulation of mucin *Muc2*, adherens junction protein *Cdh1 and* tight junction proteins *Ocln and Cldn7* was observed in MKO mice (± curdlan), which was further confirmed by qPCR and IHC, respectively. These proteins are critical in maintaining gut barrier integrity. Additionally, overexpression of *Zeb2* (a transcriptional repressor of *Cdh1*) and *Mylk* (responsible for endocytosis of occludin from tight junctions) was observed in MKO mice (± curdlan), further validated by IHC. These findings suggest a potential defect in intestinal epithelial regulation in the absence of MIF. Functional assessment of the intestinal barrier using the FITC-dextran assay demonstrated significantly increased intestinal permeability in MKO mice compared to WT controls ($p < 0.05$), consistent with the molecular findings.

Conclusion: MIF maintains gut barrier integrity by regulating the expression of ZEB2 and MLCK1. In the absence of MIF, upregulation of ZEB2 and MLCK1 disrupts the expression of *Muc2*, and function of epithelial tight junction (Cldn7 and Ocln) and adherens junction (Cdh1) markers, contributing to impaired barrier function and increased intestinal permeability in MKO SKG mice. These results highlight the critical role of MIF in maintaining intestinal homeostasis.

Disclosure: S. Foroozan Boroojeni: None; **M. Aparnathi**: None; **A. Nakamura**: AbbVie/Abbott, 6, Novartis, 6; **Z. Qaiyum**: None; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2.

Abstract Number: 0114

A Rare Variant in the *extl3* Gene Is Associated with Altered Wnt Signaling Pathway in a Novel Mouse Model of Axial Spondyloarthritis

Stéphane HILLIQUIN[1], Karim IBRAHIM[2], Olivier Fogel[3], Marcio DO CRUZEIRO[4], Patricia Albanese[5], Xavier HOUARD[6], Claire BARDET[2] and Corinne MICELI-RICHARD[7], [1]Département de Rhumatologie, Hôpital Cochin, Assistance publique des Hôpitaux de Paris, Université Paris-Cité, Paris, France, PARIS, France, [2]Université Paris Cité, Institut des maladies musculo-squelettiques, Laboratory Orofacial Pathologies, UMR-S 1333 Santé Orale and FHU-DDS-Net, Dental School, and Plateforme d'Imagerie du Vivant (PIV), Montrouge, France, Montrouge, France, [3]AP-HP, Paris, France, [4]Plateformes PDA et MouseT'IC, Institut Cochin, Université Paris Cité, Paris, France, Paris, France, [5]Laboratoire Gly-CREET, Université Paris-Est Créteil Val de Marne (UPEC) Faculté des sciences et technologies, Créteil, France, [6]Centre de Recherche Saint-Antoine, UMR_S938 INSERM /Sorbonne Université, Paris, France, PARIS, France, [7]Rheumatology Department, Hôpital Cochin, APHP, PARIS, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0098–0114) Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The ossification processes observed in ankylosing spondylitis (AS) remain incompletely understood. Substantial evidence from both human and animal studies implicates the Wnt signaling pathway in the excessive

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

endochondral ossification characteristic of AS. Through linkage analysis, we identified a rare variant in the *EXTL3* gene within a family affected by a severe familial form of AS. *EXTL3* is a member of the exostosin gene family and is essential for heparan sulfate biosynthesis.

We generated a mouse model heterozygous for the *Extl3* mutation (*Extl3*$^{mut/+}$) that develops osteoarticular lesions of the sacroiliac joint (SIJ), resembling those found in axial spondyloarthritis (axSpA), along with altered trabecular bone structure in the spine and SIJ. These abnormalities are accompanied by accelerated chondrocyte differentiation, disrupted cartilage architecture in the SIJ, and impaired osteoblast differentiation and mineralization.

Objective

To investigate the role of Wnt signaling and the effects of its modulation in this mouse model of axSpA.

Methods: Immunohistochemical analysis of Tcf1 was performed on SIJs from 6-month-old *Extl3*$^{mut/+}$ mice and wild-type littermates (*Extl3*$^{mut/+}$). In vitro, primary osteoblast and chondrocyte cultures were established at various differentiation stages. RNA sequencing, qPCR, and Western blot (WB) analyses were conducted at different time points.

To confirm the involvement of Wnt signaling, three Wnt pathway inhibitors—Dkk-1, sFRP2, and PKF 118-310—targeting different components of canonical and non-canonical pathways were applied to osteoblast and chondrocyte cultures. The aforementioned analyses were repeated following inhibitor treatment.

Results: Tcf1 immunostaining was markedly increased in chondrocyte columns and subchondral bone of *Extl3*$^{mut/+}$SIJs. RNA-seq revealed downregulation of Wnt pathway inhibitors *Dkk-1* and *Sclerostin* at late stages of both chondrocyte and osteoblast differentiation. qPCR analysis demonstrated overexpression of Wnt pathway components, including

β-catenin

and *Tcf7*. Accelerated chondrocyte differentiation appeared to involve *Wnt3*, *Wnt4*, *Wnt5a*, and *Wnt5b*.

Overexpression of Tcf1 in *Extl3*$^{mut/+}$ osteoblast cultures was confirmed by Western blot at day 21 (terminal differentiation), and by immunohistochemistry in SIJ cartilage and subchondral bone. Notably, Wnt pathway inhibition, particularly with Dkk-1, reversed the observed phenotypes, including delayed osteoblast and accelerated chondrocyte differentiation.

Conclusion: Our findings demonstrate that the *Extl3* mutation disrupts Wnt signaling in both osteoblasts and chondrocytes. These results align with prior studies in mouse models and human data, reinforcing the critical role of Wnt signaling in the pathological ossification associated with AS. This work highlights potential therapeutic targets aimed at modulating ossification mechanisms in AS.

Disclosure: S. HILLIQUIN: None; **K. IBRAHIM**: None; **O. Fogel**: None; **M. DO CRUZEIRO**: None; **P. Albanese**: None; **X. HOUARD**: None; **C. BARDET**: None; **C. MICELI-RICHARD**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0115

Dysfunctional Mitophagy Propels Neutrophil Hyperactivity and Thrombosis in Antiphospholipid Syndrome

Ajay Tambralli[1], Emily Becker[2], Kaitlyn Sabb[3], NaveenKumar Somanathapura[1], Srilakshmi Yalavarthi[1], Cyrus Sarosh[4], Jacqueline Madison[1], Yu (Ray) Zuo[1] and Jason S. Knight[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, [3]University of Michigan - Ann Arbor, Ann Arbor, MI, [4]University of Michigan, Temperance, MI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Neutrophil hyperactivity and neutrophil extracellular trap (**NET**) release (**NETosis**) contribute to antiphospholipid syndrome (**APS**) pathogenesis. We recently discovered that APS patient neutrophils have more glycolytic flux than healthy neutrophils and that inhibiting glycolysis in mice reduces neutrophil hyperactivity and thrombosis. In addition, our transcriptomic analysis of APS neutrophils identified regulation of autophagosome assembly ($p=1.9E^{-5}$) and ubiquitin-protein ligase activity (p=0.0057) as among the top-upregulated pathways. It has previously been shown that dysfunctional mitochondrial autophagy (**mitophagy**) can enhance glycolysis across various disease contexts. Here, we began to characterize the potential influence of dysfunctional neutrophil mitophagy on the pathogenesis of APS by determining its role in augmenting glycolysis, NETosis, and thrombosis.

Methods: For patient profiling, neutrophils were freshly isolated from healthy controls (n=8) or individuals with primary APS (n=11). For *in vitro* studies, control neutrophils were stimulated with IgG pooled from either controls or individuals with APS who had high-titer anti-β_2GPI IgG. Wild-type C57BL/6 (**WT**) mice and mitophagy-deficient *Pink1*$^{-/-}$ mice were used for animal studies. Thioglycolate-elicited mouse neutrophils were isolated from the peritoneum 16 hours after administration of IgG. Neutrophil mitophagy (MtPhagy), mitochondrial polarization (JC-10), and mitochondrial reactive oxygen species (MitoSOX) were assessed by flow cytometry. NETosis was quantified with SYTOX Green, and glycolytic capacity (the maximal cellular utilization of glycolysis) was assessed using a Seahorse metabolic flux analyzer. Thrombosis was modeled via electrolytic activation of the mouse inferior vena cava.

Results: Compared with controls, APS patients had fewer neutrophils undergoing beneficial mitophagy (66% vs 28%, p< 0.05). In addition, APS patients had more neutrophils with dysfunctional, depolarized mitochondria (11% vs 20%, p< 0.01) and produced more harmful mitochondrial reactive oxygen species (1.3-fold, p< 0.05). The mitophagy activator valinomycin reduced human APS IgG-mediated NETosis to levels seen with control IgG (p< 0.05). Further, compared with neutrophils from WT mice, neutrophils from mitophagy-deficient *Pink1*$^{-/-}$ mice (n=3 mice for each genotype) had increased glycolytic capacity (1.3-fold, p< 0.05) and augmented APS IgG-mediated NETosis (1.4-fold, p< 0.01). Finally, when APS-associated thrombosis was modeled in mice (n=9 WT and n=5 *Pink1*$^{-/-}$), *Pink1*$^{-/-}$ mice developed significantly larger thrombi (mean 5.1 mg vs 8.0 mg, p< 0.01).

Conclusion: APS patient neutrophils demonstrated defective mitophagy and dysfunctional mitochondria. Mice with a baseline defect in mitophagy (*Pink1*$^{-/-}$) phenocopied APS patients by demonstrating more glycolytic flux, NETosis, and thrombosis. Notably, activating mitophagy tempered APS IgG-mediated human NETosis. These results identify dysfunctional mitophagy as a driver of neutrophil hyperactivity and thrombosis in APS, and restoring normal mitophagy could be a promising approach for a future therapeutic intervention.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Tambralli: None; **E. Becker**: None; **K. Sabb**: None; **N. Somanathapura**: None; **S. Yalavarthi**: None; **C. Sarosh**: None; **J. Madison**: None; **Y. Zuo**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

Abstract Number: 0116

Cerebral small vessel disease in antiphospholipid syndrome: subtypes and total burden of cSVD on MRI

Chun Li[1], Jianping Guo[2], Yangyi Fan[1], Yu Kang[1] and Xiaodan Hu[1], [1]Peking University People's Hospital, Beijing, China (People's Republic), [2]Peking University People's Hospital, Beijing, Beijing, China

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cerebrovascular diseases are common and severe neurological complications in antiphospholipid syndrome (APS). However, few studies focused on cerebral small vessel disease (cSVD) in APS. We undertook this study to investigate the subtypes, the total burden on MRI and potential risk factors for cSVD in APS.

Methods: We retrospectively analyzed the medical records and brain magnetic resonance imaging (MRI) scans of patients with APS who visited our hospital between January 2015 and July 2022. An age and gender-matched healthy control group were recruited from the Health Care Center affiliated with Peking University People's Hospital. Four major cSVD markers on MRI were assessed, including lacune, enlarged perivascular space (EPVS), microbleed and white matter hyperintensities (WMH). Total cSVD score, ranging from 0 to 4, were rated using validated visual scales. Univariate and multivariate logistic regression model was applied to analyze the association between clinical and laboratory indices and cSVD risks in APS.

Results: Among 132 enrolled patients, 76.5% (101/132) were females with a mean age of 47.0 years. 26.5% (35/132) were primary APS, and 51.5% (68/132) exhibited at least one of the cSVD markers. Lacune was the most frequent cSVD marker [46.2% (61/132)], followed by moderate-to-severe WMH [16.7% (22/132)], EPVS [14.4% (19/132)] and microbleed [12.1% (16/132)]. After adjusting for age, gender and disease duration, the cSVD was significantly associated with hypertension (OR 3. 688, 95%CI 1.17-11.65, P = 0.026), the incidence of thrombosis events (OR 22.145, 95%CI 2.11-232.27, P = 0.010), and the history of stroke (OR 10.709, 95%CI 2.47-46.36, P = 0.002).

Conclusion: In the present study, we observed a high incidence of cSVD in patients with APS. Hypertension, thrombotic events and the history of stroke are risk factors for cSVD in APS.

Disclosure: C. Li: None; **J. Guo**: None; **Y. Fan**: None; **Y. Kang**: None; **X. Hu**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0117

Are Thrombotic or Obstetric Events Associated with Additional Clinical Domains in Triple Antiphospholypid Syndrome?

Cristina Rocamora-Gisbert[1], Francina salabert-Carreras[2], Raquel Ugena-García[3], Cristina Calomarde-Gómez[3], Clara Churtichaga Domenech[2], Judith Vidal-Ripoll[2], Laia Gifre-Sala[2], Agueda Prior-Español[2], Annika Nack[1], Susana Holgado[4], Maria Aparicio[1], Melania Martínez-Morillo[2], LOURDES MATEO SORIA[5], Anne Riveros frutos[1], Ivette Casafont-Solé[3] and Judit Font-Urgelles[3], [1]Hospital Germans Trias i Pujol, Barcelona, Spain, [2]Hospital Germans Trias i Pujol, Barcelona, [3]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [4]Hospital Germans Trias i Pujol, Barcelona, Catalonia, Spain, [5]HOSPITAL GERMANS TRIAS I PUJOL, BADALONA, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: It is known that triple positive antiphospholipid syndrome (APS-TP) is related to an increased presence of thrombotic and obstetric manifestations. Triple positivity is referred by the concurrence of anticardiolipin antibodies, anti-beta2 glycoprotein I antibodies and lupus anticoagulant. Up until the definition of the new American College of Rheumatology (ACR)/ European Alliance of Associations for Rheumatology (EULAR) classification criteria, APS was only classified by a laboratory domain and a clinical domain including thrombotic or obstetric events. The addition of other clinical manifestations -thrombocytopenia, cardiac valve afectation, cutaneous, among others- will allow a greater number of patients to be early and systematically detected.

The objective is to analyze the prevalence of other clinical domains in the presence or absence of thrombotic or obstetric events in patients with APS-TP, and to determine the prevalence of the new manifestations included in the 2023 ACR/EULAR classification.

Methods: Cross-sectional descriptive study was carried out in a tertiary care hospital. APS-TP patients diagnosed between 1990 and 2023 were included. Patients under 18 years of age were excluded. Patients were classified into two groups: APS-TP with the presence of thrombotic and/or obstetric events (APS-TP1) and APS-TP with neither thrombotic nor obstetric events but with the presence of another clinical domain (APS-TP2). Sociodemographic, clinical and analytical variables were collected from both groups.

	APS TP-1 36 (70.58)	APS TP-2 15 (29.41)	p-value
Females, n (%)	19 (52.8)	11 (73.3)	0.174
Age, mean (SD)	45 (14.6)	47.06 (17.85)	0.166
Smoking, ever, n (%)	26 (72.2)	9 (60)	0.103
Arterial hypertension, n (%)	19 (52.8)	4 (26.67)	0.125
Dyslipidemia, n (%)	10 (27.8)	6 (40)	0.391
Diabetes mellitus, n (%)	6 (14.63)	2 (13.33)	1.000
Thrombophilia, other (%)	1 (2.8)	1 (6.7)	0.506
Ischemic cardiomyopathy, n (%)	3 (8.3)	1 (6.7)	1.000
Connective tissue disease, n (%)	13 (36.1)	6 (40)	0.750
- SLE, n (%)	12 (33.3)	6 (40)	0.649
- Sjögren syndrome, n (%)	1 (2.78)	0	1.000

SLE: Systemic lupus erithematosus.

Figure 1. Patients included

	Total 51 (100)	APS-TP1 36 (70.58)	APS-TP2 15 (29.41)	p-value
Hematologic, n (%)	18 (35.3)	14 (38.9)	4 (26.7)	0.527
- **Thrombocytopenia, n (%)**	15 (29.4)	13 (36.1)	2 (13.3)	0.177
- **AIHA, n (%)**	6 (11.8)	4 (11.1)	2 (13.3)	1.000
Valve disease, n (%)	19 (37.3)	12 (33.3)	7 (46.7)	0.669
- **Stenosis, n (%)**	5 (9.8)	2 (5.6)	3 (20)	0.144
- **Regurgitation, n (%)**	13 (25.5)	8 (20.5)	5 (33.3)	0.487
- **Others*, n(%)**	6 (11.8)	4 (11.1)	2 (13.3)	1.000
Pulmonary, n (%)	5 (9.8)	4 (11.1)	1 (6.7)	1.000
- **Pulmonary hemorrhage, n (%)**	3 (5.9)	3 (8.3)	0 (0)	0.546
- **Hypertension (type I), n (%)**	2 (3.9)	1 (2.8)	1 (6.7)	0.506
Cutaneous, n (%)	21 (41.2)	13 (36.1)	8 (53.3)	0.255
- **Raynaud, n (%)**	12 (23.5)	7 (19.4)	5 (33.3)	0.287
- **Others**, n (%)**	3 (5.9)	2 (5.6)	1 (6.7)	1.000
TMA renal, n (%)	5 (9.8)	5 (13.9)	0 (0)	0.304
Neurologic, n (%)	10 (19.6)	8 (22.2)	2 (13.3)	0.703
- **Migraine, n (%)**	3 (5.9)	2 (5.6)	1 (6.7)	1.000
- **Epilepsy, n (%)**	5 (9.8)	3 (8.3)	2 (13)	0.623
- **Others***, n (%)**	3 (5.9)	2 (5.6)	1 (6.7)	1.000
Adrenal hemorrhage, n (%)	2 (3.9)	2 (5.6)	0 (0)	0.351

AIHA: Autoinmune hemolytic anemia. TMA: Thrombotic microangiopathy.

** Multivalvular heart disease, nonbacterial thrombotic endocarditis. ** livedo racemosa, livedoid vasculitis. ***cognitive impairment, white matter lesions.*

Figure 2 Prevalence of non-criteria manifestations

Results: A total of 51 APS-TP patients were identified, 36 (70.6%) APS-TP1 patients and 15 (29.4%) APS-TP2 patients. The majority of patients were female (59.3%) with a mean age of diagnosis of 47.2 years (Figure 1). Only 5 patients (9.8%) were classified as catastrophic APS. In the APS-TP1 group, 34 patients (66.7%) presented thrombosis (venous: 20 [58.8%], arterial 12 [35.2%] and

both 4 [11.8%]) and 7 patients (13.7%) presented obstetric events. The most frequent "new domain" in the APS-TP1 group was thrombocytopenia (36.1%), while in the APS-TP2 group was valvular heart disease (46.1%) followed by Raynaud's phenomenon (33.3%). There were no significant differences in any of the observed variables (Figure 2).

Conclusion: In our cohort, the most common clinical manifestation overall was thrombosis. In patients without either thrombosis or obstetric events, the most prevalent manifestations were valvular heart disease and Raynaud's phenomenon. The importance of studying antiphospholipid syndrome in patients with non-thrombotic manifestations is rising, especially in patients who do not meet criteria for other connective tissue diseases. Although some manifestations were exclusive to the thrombotic or obstetric morbidity group (renal microangiopathy, alveolar hemorrhage, bilateral adrenal hemorrhage), we did not find significant differences. This may be influenced by the small sample size, so it could be considered as a further object of study.

Disclosure: C. Rocamora-Gisbert: None; **F. salabert-Carreras**: None; **R. Ugena-García**: None; **C. Calomarde-Gómez**: None; **C. Churtichaga Domenech**: None; **J. Vidal-Ripoll**: None; **L. Gifre-Sala**: None; **A. Prior-Español**: None; **A. Nack**: None; **S. Holgado**: None; **M. Aparicio**: None; **M. Martínez-Morillo**: None; **L. MATEO SORIA**: None; **A. Riveros frutos**: None; **I. Casafont-Solé**: None; **J. Font-Urgelles**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0118

Single-cell RNA sequencing of skin reveals vascular dysregulation in antiphospholipid syndrome

Ecem Sevim[1], Sumith Panicker[2], Gustaf Wigerblad[3], Stefania Dell'orso[4], Sharon Osgood[2], Leslie Castelo-Soccio[5], Keisuke Nagao[6] and Yogendra Kanthi[7], [1]NIAMS/NIH, Bethesda, MD, [2]NHLBI/NIH, Bethesda, [3]National Institutes of Health, Stockholm, Sweden, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [5]NIAMS/NIH, Bethesda, [6]NIAMS, Bethesda, MD, [7]National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid syndrome (APS) is a systemic autoimmune thromboinflammatory disorder defined by persistent antiphospholipid antibodies (aPL) and characterized clinically by macrovascular thrombosis, microvascular disease, and pregnancy morbidity. While aPL-mediated activation of endothelial cells and immune pathways has been established, the molecular drivers of tissue-level vascular dysfunction remain elusive. We performed single-cell RNA sequencing (scRNA-seq) of skin biopsies from patients with APS to identify local cellular and molecular drivers of disease pathogenesis.

Methods: Non-lesional skin biopsies were obtained from the upper thigh of patients with APS (n=6) and healthy controls (n=5). Single-cell suspensions were prepared via enzymatic and mechanical dissociation (Miltenyi Biotec), followed by SYTOX-Green-based FACS for live cell enrichment. Libraries were generated using Chromium Single Cell 5′ HT chemistry (10x Genomics), targeting ~20,000 cells/sample.

Sequencing data were processed with Cell Ranger v8.0.1 and analyzed using Seurat v5 in R for QC, integration, clustering, and annotation. Endothelial cells (ECs) were identified by canonical markers (VWF, CDH5, PECAM1); non-ECs (keratinocytes, immune cells, fibroblasts, pericytes, SMCs) were excluded. Differential gene expression and pathway enrichment analyses were performed comparing APS vs. control ECs.

Results: Four patients with APS had a triple-positive aPL profile; phenotypes included microvascular disease (n=2), macrovascular thrombosis (n=1), and one exhibited both. One APS patient was lupus anticoagulant-positive and had macrovascular disease with cardiac valve involvement; and one patient was positive for LA and anti-cardiolipin IgG with a history of macrovascular thrombosis. None of the patients had skin lesions at the time of biopsy.

Transcriptomic profiling of skin endothelial cells in APS revealed upregulation of genes involved in glycolysis, response to cytokine stimulus, NF-κB signal transduction, mitochondrial metabolism, cAMP signaling, and VEGF response (*ALDOA, PLCG2, NDUFB1, SDF4, PRKAR1A, METAP2, EIF3J*). Concurrently, genes related to RAS signaling, endosomal trafficking, chromatin organization, cell migration, endothelial cell development, tube formation, and barrier establishment were downregulated (*RASGEF1B, RAPGEF6, RBFOX1, BCOR, ZNF366, RNF7, CTS, THSD7A*). These gene expression changes were observed consistently across all six patients with APS compared to healthy controls.

Conclusion: Our single-cell transcriptomic analysis of non-lesional APS skin reveals a metabolically reprogrammed, pro-inflammatory, and stress-responsive endothelial phenotype.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Endothelial cells in APS skin demonstrated upregulation of genes associated with activation and inflammatory signaling, alongside downregulation of pathways involved in vascular homeostasis, signaling regulation, and barrier integrity. Together, these findings reveal a consistent transcriptional signature of endothelial dysfunction in APS skin and highlight opportunities to identify tissue-based biomarkers and potential therapeutic strategies targeting endothelial dysfunction in APS.

Disclosure: E. Sevim: None; **S. Panicker**: None; **G. Wigerblad**: None; **S. Dell'orso**: None; **S. Osgood**: None; **L. Castelo-Soccio**: None; **K. Nagao**: None; **Y. Kanthi**: None.

Abstract Number: 0119

Thrombin Generation Assays Inform Hypercoagulability Mediated by Antiphospholipid Antibodies in Children with Systemic Lupus Erythematosus

Elizabeth Sloan[1], Blake Baay[2], Lynnette Walters[2], Paola Sparagana[2], Kristina Ciaglia[1], Simrat Morris[1], Julie Fuller[1], Lorien Nassi[1], Tracey Wright[1] and Ayesha Zia[3], [1]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [2]Scottish Rite for Children, Dallas, TX, [3]UT Southwestern and Children's Medical Center, Dallas, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: In pediatric systemic lupus erythematosus (**SLE**), antiphospholipid antibodies (**aPL**) are independent risk factors for thrombosis. However, data are limited on how aPL impact hypercoagulability. No biomarkers or risk-stratification tools exist to predict thrombosis in aPL-positive pediatric SLE. We aimed to investigate the use of thrombin generation (**TG**) potential to assess aPL-induced hypercoagulability in pediatric SLE patients without a history of thrombosis.

Methods: Three groups of patients were prospectively enrolled: children with SLE and persistently positive aPL (n = 12), children with SLE and persistently negative aPL (n = 20), and children with non-systemic juvenile idiopathic arthritis (**JIA**, n = 20) (**Table 1**). aPL status at enrollment was determined based on historical laboratory data. Participants were excluded if they had a history of thrombosis, known hypercoagulable disorder, or were receiving anticoagulation. Testing for inherited and acquired thrombophilia was performed, and aPL profiles were followed for > 12 weeks. TG assays were performed via the calibrated automated thrombogram method using platelet poor plasma with and without the addition of thrombomodulin, an activator of protein C. TG parameters were compared across the three groups.

Table 1. Demographics of patient cohorts

	SLE with aPL (n=12)	SLE without aPL (n=20)	JIA (n=20)
Age in years (mean ± SD)	14.3 ± 3.5	14.9 ± 2.7	14.6 ± 2.3
Women, n (%)	9 (75%)	19 (95%)	14 (70%)
BMI (mean ± SD)	28.2 ± 6.7	26.9 ± 9.2	25.2 ± 5.3
BMI Percentile (mean % ± SD)	88.4 ± 13.3	78.8 ± 21.8	77.1 ± 24.0
Race, n (%)			
Asian	1 (8%)	0 (0%)	0 (0%)
Black or African American	0 (0%)	3 (15%)	1 (5%)
White	11 (92%)	16 (80%)	19 (95%)
Other	0 (0%)	1 (5%)	0 (0%)
Ethnicity, n (%)			
Hispanic	11 (92%)	14 (70%)	11 (55%)
Non-Hispanic	1 (8%)	6 (30%)	9 (45%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

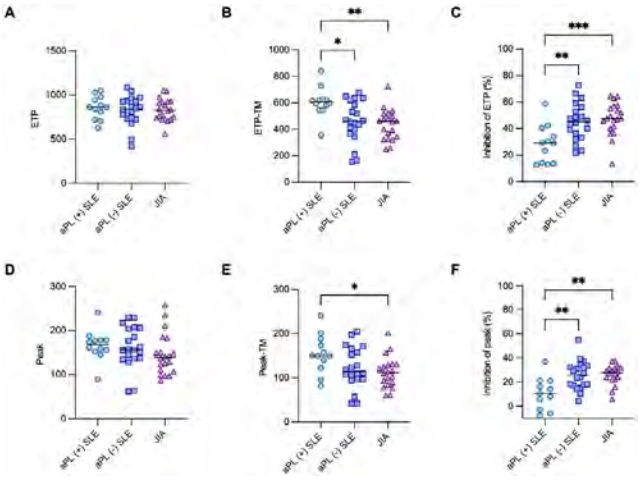


Figure 1. Thrombin generation assays were performed via the calibrated automated thrombogram method in platelet poor plasma from pediatric patients with SLE with positive antiphospholipid antibodies (aPL), SLE with negative aPL, and JIA. A, Endogenous thrombin potentials (ETP) were similar between all three groups. B, When thrombomodulin was added, ETP was higher in the aPL positive group. C, The aPL positive group showed diminished inhibition of ETP in the presence of thrombomodulin compared to the other groups, which is consistent with activated protein C resistance. D, There was no significant difference in peak thrombin height between groups. E, With the addition of thrombomodulin, the aPL positive group had a statistically significant higher thrombin peak than the JIA group. F, The aPL positive group had diminished peak inhibition in the presence of thrombomodulin, again suggesting activated protein C resistance. ETP and peak parameters were compared between groups by the Kruskal-Wallis test adjusted for multiple comparisons by Dunn's method; *p<0.05, **p<0.01, ***p<0.001.

Table 2. Measures of thrombin generation parameters with and without thrombomodulin in children with SLE and positive aPL, SLE without aPL, and JIA

	Parameter	SLE with aPL	SLE without aPL	JIA	*P*
PPP	ETP, *nM x min*	859.7 ± 130.6	822.9 ± 164.7	830.3 ± 125.8	ns
	Lag time, *min*	4.85 ± 3.23	2.59 ± 0.49	2.51 ± 0.39	< 0.001
	Peak height, *nM*	166.3 ± 24.5	162.0 ± 46.9	145.7 ± 47.1	ns
	Time to peak, *min*	7.90 ± 3.56	5.67 ± 0.84	5.91 ± 0.78	0.020
	Velocity Index, *nM/min*	57.8 ± 18.6	56.9 ± 24.3	46.3 ± 24.6	ns
PPP-TM	ETP, *nM x min*	606.5 ± 114.3	459.3 ± 156.3	435.5 ± 115.7	0.002
	Lag time, *min*	4.54 ± 3.20	2.36 ± 0.48	2.34 ± 0.32	0.001
	Peak height, *nM*	154.1 ± 43.7	122.7 ± 46.7	112.0 ± 35.4	0.028
	Time to peak, *min*	7.02 ± 3.52	4.76 ± 0.59	4.78 ± 0.46	0.009
	Velocity Index, *nM/min*	66.0 ± 25.1	53.1 ± 23.8	48.0 ± 38.4	ns

SLE: systemic lupus erythematosus, aPL: antiphospholipid antibodies, JIA: juvenile idiopathic arthritis, PPP: platelet poor plasma, PPP-TM: platelet poor plasma with thrombomodulin, ETP: endogenous thrombin potential, ns: not significant

Results: The median age of the entire cohort was 15 (range 7 to 18) years. All groups were predominantly female, White race, and of Hispanic ethnicity (**Table 1**). Almost all (92%) of the aPL positive SLE group had positive lupus anticoagulant, and three (25%) had triple aPL positivity. Persistent antiphosphatidylserine/prothrombin IgG and IgM antibodies were present in 58% and 67% of the aPL positive group, respectively. Except for aPL positivity, there were no differences between groups in the presence of inherited or acquired hypercoagulable disorders, including Factor V Leiden, prothrombin mutations, antithrombin, and protein C and S activity. There was no difference in the endogenous thrombin potential (**ETP**) between the groups (p = 0.772) (**Figure 1 A, Table 2**). However, in the presence of thrombomodulin, ETP was higher in the aPL positive group compared to the other two groups (607 ± 114 nM x min vs. 459 ± 156 nM x min vs. 436 ± 116 nM x min, p = 0.002) (**Figure 1 B**). In fact, inhibition of ETP by thrombomodulin was significantly blunted in the aPL positive group versus the aPL negative and JIA groups (25.9% vs. 45.1% vs. 47.4%, p < 0.001) (**Figure 1 C**), suggesting resistance to activated protein C. Change in peak height was also less sensitive to the addition of thrombomodulin in the aPL positive group versus the aPL negative and JIA groups (10.7% vs. 25.8% vs. 26.1%, p < 0.001) (**Figure 1 D-F**). Independent of thrombomodulin, the aPL positive group showed increased lag time (p < 0.001) and time to peak (p = 0.020) (**Table 2**). There were no differences in velocity index between the three groups (p = 0.082).

Conclusion: Our study provides the biologic basis that aPL confer hypercoagulability in pediatric SLE. Activated protein C resistance appears to be an important mechanism of hypercoagulability in aPL-positive pediatric SLE patients, even without thrombosis. TG potential is a potential biomarker of aPL-induced hypercoagulability in pediatric SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Sloan: None; **B. Baay**: None; **L. Walters**: None; **P. Sparagana**: None; **K. Ciaglia**: None; **S. Morris**: None; **J. Fuller**: None; **L. Nassi**: None; **T. Wright**: None; **A. Zia**: None.

Abstract Number: 0120

The Prevalence and Clinical Significance of Heritable Thrombophilia in Antiphospholipid Antibody Positive Patients: Descriptive Results from the Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Registry

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Although antiphospholipid antibodies (aPL) are well-established risk factors for thrombosis, heritable thrombophilias (HT) are also associated with venous thromboembolism (VTE). The latter includes deficiencies of the naturally occurring anticoagulants (antithrombin, protein C, and protein S), and factor V Leiden (FVL) and prothrombin (PT) G20210A gene mutations. Methylene tetrahydrofolate reductase (MTHFR) C677T and A1298C polymorphisms are not considered part of the HT screen in clinical practice. The primary objective of this ongoing study was to determine the prevalence of HT in persistently aPL-positive patients. Secondly, we analyzed the association between thrombosis and HT in aPL-positive patients, individually and in combination.

Methods: A web-based data capture system is used to store patient demographics and aPL-related medical history in APS ACTION registry. Inclusion criteria are positive aPL, based on the Revised Sapporo Antiphospholipid Syndrome (APS) classification criteria, tested at least twice within one year prior to enrollment. Patients are followed every 12±3 months with clinical data and blood collection. For this cross-sectional analysis, baseline data were used including demographic, clinical, and HT laboratory (either center-reported [CR] or APS ACTION United Kingdom Core Laboratory [CL] data (following testing in the CL)). When evaluating the results of the HT included (see Table 1), CL were used over CR if both were available; Chi square or Fisher's exact tests were used for comparisons.

Results: Of 1,252 patients recruited as of January 2025, 741 (59%) had at least one CR and/or CL HT result (female: 515 [70%]; mean age at registry entry: 55±13.5; thrombotic APS: 456 [62%]; triple aPL-positive: 273 [37%], lupus anticoagulant with/without aCL or aβ_2GPI: 308 [42%]). The prevalence of each HT and the association with vascular events are shown in Tables 1 and 2, respectively. Homozygosity for the MTHFR C677T and A1286 polymorphisms were reported in 20 (6%) and 4 (1%), respectively, with high homocysteine in 2/20 with MTHFR C677T and none with MTHFR A1298C. In

Table 1. Prevalence of Heritable Thrombophilia and Methylene tetrahydrofolate reductase (MTHFR) C677T and A1298C Polymorphisms Among APS ACTION Registry Patients

N: 741	Abnormal / Tested	Heterozygous	Homozygous
Low Protein C	28/665 (4%)	-	-
Low Protein S	42/653 (6%)	-	-
Low Antithrombin	42/687 (6%)	-	-
Factor V Leiden Mutation	25/627 (4%)	23 (3.6%)	2 (0.4%)
Prothrombin G20210A Mutation	22/565 (4%)	22 (4%)	0
MTHFR C677T Polymorphism	56/325 (17%)	36 (11%)	20 (6%)
- High Homocysteine	6/56 (11%)	4/36 (11%)	2/20 (10%)
MTHFR A1298C Polymorphism	18/280 (6%)	14 (5%)	4 (1%)
- High Homocysteine	0/18	-	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. The Frequency of Arterial/Venous Thrombosis is Patients with Individual Heritable Thrombophilia and Methylene tetrahydrofolate reductase (MTHFR) C677T and A1298C Polymorphisms Among APS ACTION Registry Patients (those with heterozygous MTHFR polymorphisms were not included)

N: 741	Arterial Event*	Venous Event*	No Event
Low Protein C (n: 665)			
- Yes (n: 28)	7 (25%)	18 (64%)	6 (21%)
- No (n: 637)	231 (36%)	272 (43%)	193 (30%)
Low Protein S (n: 653)			
- Yes (n: 42)	12 (29%)	24 (57%)	9 (21%)
- No (n: 611)	219 (36%)	255 (42%)	190 (31%)
Low Antithrombin (n: 687)			
- Yes (n: 42)	18 (43%)	22 (52%)	9 (21%)
- No (n: 645)	231 (36%)	287 (44%)	186 (29%)
Factor V Leiden Mutation (n: 627)			
- Yes (n: 2)	1 (50%)	2 (100%)	0
- No (n: 625)	222 (36%)	276 (44%)	185 (30%)
Prothrombin G20210A Mutation (n: 565)			
- Yes (n: 0)	0	0	0
- No (n: 565)	206 (36%)	244 (43%)	170 (30%)
MTHFR C677T Polymorphism (n: 325)			
- Yes (n: 20)	6 (30%)	8 (40%)	7 (35%)
- No (n: 305)	119 (39%)	128 (42%)	94 (31%)
MTHFR A1298C Polymorphism (n: 280)			
- Yes (n: 4)	1 (25%)	1 (25%)	3 (75%)
- No (n: 276)	108 (39%)	110 (40%)	87 (32%)

*Some patients with both arterial and venous events

Table 3. Comparison of Arterial and Venous Events Between Patients With and Without Heritable Thrombophilia (HT) Among APS ACTION Registry Patients (those with MTHFR polymorphisms were not included)

n= 316	No HT (n= 230)	≥1 HT (n= 86)	*P* value
Arterial Event	86 (37%)	33 (38%)	0.87
Venous Event	88 (38%)	46 (53%)	**0.015**

the subgroup analysis of 316 (43%) patients, we compared those with at least one abnormal HT result (n: 86; excluding heterozygous HT) and those with normal results for all HT assessed (n=230); the former group had significantly more VTE, but not arterial, events (p=0.015) (Table 3).

Conclusion: Based on our large-scale international cohort, up to six percent of persistently aPL-positive patients may have one or more heritable thrombophilia (antithrombin, protein C, or protein S deficiencies, FVL or PT G20210A), which may increase the risk of VTE. Our preliminary results have limitations, including reporting/selection bias, and the lack of information on testing methodology/confirmation and factors that may affect results of naturally occurring anticoagulants, e.g. anticoagulation and pregnancy/puerperium. However, these results and the relatively high frequency of HT in the general population highlight the potential additive risk of HT in aPL-positive patients that may be contributory in the stratification and management of such patients.

Disclosure: E. Sahin: None; **M. Efthymiou**: None; **D. Andrade**: None; **M. Barber**: AstraZeneca, 1, GlaxoSmithKlein(-GSK), 1; **M. Tektonidou**: None; **V. Pengo**: None; **M. Radin**: None; **J. Pardos-Gea**: None; **M. AGUIRRE ZAMORANO**: None; **N. Kello**: None; **D. Paredes-Ruiz**: None; **H. Belmont**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1; **D. WAHL**: None; **W. Branch**: UCB, 5; **M. Gerosa**: None; **G. Ramires de Jesus**: None; **Z. Zhang**: AbbVie/Abbott, 1, 6, Amgen, 6, BMS, 1, Eisai, 5, 6, Eli Lilly, 6, GSK, 6, Novartis, 6, Rongchang Pharmaceutials, 6, Xiansheng Pharmaceutials, 6; **T. Atsumi**: None; **G. Pazzola**: None; **L. Andreoli**: Pfizer, 2, UCB, 2; **A. Duarte-Garcia**: None; **E. Rodriguez-Almaraz**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **R. Cervera**: None; **B. Artim Esen**: None; **G. Pons-Estel**: AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen, 1, 6; **H. Shi**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **R. Willis**: None; **M. Bertolaccini**: None; **H. Cohen**: GlaxoSmithKlein(GSK), 6, Roche, 2, Roivant, 2; **D. Erkan**: Chugai, 5, GlaxoSmithKlein(GSK), 1, 5, 6, Merida Biosciences, 2, NIH, 5, Roche, 1, Roivant Sciences, 2, Star Therapeutics, 1, Up-To-Date, 9.

Abstract Number: 0121

The Prevalence and Clinical Significance of IgA Anticardiolipin and Anti-β2-Glycoprotein-I Antibody Isotypes in Antiphospholipid Antibody Positive Patients: Descriptive Results from the Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking Registry

Emre Sahin[1], Yu (Ray) Zuo[2], Danieli Andrade[3], Maria Tektonidou[4], Vittorio Pengo[5], Massimo Radin[6], Chary López pedrera[7], Diana Paredes-Ruiz[8], H Michael Belmont[9], Paul Fortin[10], Denis WAHL[11], Ware Branch[12], Maria Gerosa[13], Guilherme Ramires de Jesus[14], Tatsuya Atsumi[15], Maria Efthymiou[16], Angela Tincani[17], Esther Rodriguez-Almaraz[18], Michelle Petri[19], Ricard Cervera[20], Rohan Willis[21], Katrien Devreese[22], Maria Laura Bertolaccini[23], Hannah Cohen[24], Jason S. Knight[2] and Doruk Erkan[1], [1]Hospital for Special Surgery, New York, NY, [2]University of Michigan, Ann Arbor, MI, [3]University of Sao Paulo, São Paulo, São Paulo, Brazil, [4]National and Kapodistrian University of Athens, Athens, Greece, [5]Padova University Hospital, Padova, Italy, [6]University of Turin, Turin, Turin, Italy, [7]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [8]Biobizkaia Health Research Institute, Barakaldo, Spain, [9]NYU School of Medicine, New York, NY, [10]Centre ARThrite - CHU de Québec - Université Laval, Quebec, QC, Canada, [11]University of Lorraine, Nancy, France, [12]University of Utah Health Sciences Center, Salt Lake City, UT, [13]University of Milan, Milano, Italy, [14]Universidade do Estado do Rio de Janeiro, Rio De Janeiro, Rio de Janeiro, Brazil, [15]Hokkaido University, Sapporo, Japan, [16]University College London, London, United Kingdom, [17]ASST Spedali Civili-University of Brescia, Gussago, Brescia, Italy, [18]Hospital Universitario 12 de Octubre, Madrid, Spain, [19]Johns Hopkins University School of Medicine, Timonium, MD, [20]Hospital Clinic Barcelona, Barcelona, Spain, [21]University of Texas Medical Branch, Galveston, TX, [22]Ghent University, Gent, Belgium, [23]King's College London, London, United Kingdom, [24]University College London Hospitals NHS Foundation Trust, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The 2023 ACR/EULAR Antiphospholipid Syndrome (APS) Classification Criteria (CC) focus on IgG and IgM anticardiolipin (aCL) and anti-β_2-glycoprotein-I antibodies (aβ_2GPI). IgA isotypes were excluded due to limited evidence linking isolated IgA positivity to thrombosis, uncertain incremental value beyond established criteria, and a lack of assay standardization. However, emerging data from the general population suggest that individuals with IgA aβ_2GPI may face an elevated risk of atherosclerotic cardiovascular disease, potentially due to impaired cholesterol efflux capacity and endothelial injury. Our primary objective was to compare the demographic, clinical, and laboratory characteristics of aCL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of Anticardiolipin (aCL) and Anti-β_2-glycoprotein-I antibodies (aβ_2GPI) IgA-positive and IgA-negative patients Among APS ACTION Registry Patients (Cut-off for positivity ≥20U)

n= 706	IgA-Negative (n= 468)	IgA-Positive (n= 238)	P value
Demographics			
Mean age (Registry Entry)	46.2 ± 13.4	44.6 ± 12.7	0.13
Female	347 (74%)	171 (72%)	0.51
Race			
White	332 (71%)	166 (70%)	0.74
Latin American	57 (12%)	22 (9%)	0.24
Asian	13 (3%)	9 (4%)	0.47
Black	18 (4%)	5 (2%)	0.22
History of Systemic Lupus Erythematosus	139 (30%)	84 (35%)	0.13
History of Any Arterial Event	165 (35%)	78 (33%)	0.51
Stroke	104 (22%)	59 (25%)	0.44
Myocardial Infarction	24 (5%)	12 (5%)	0.96
Other	47 (10%)	18 (8%)	0.28
History of Any Venous Event	190 (41%)	116 (49%)	**0.04**
Deep Vein Thrombosis	143 (31%)	93 (39%)	**0.02**
Pulmonary Embolism	54 (12%)	44 (18%)	**0.01**
Other	35 (7%)	16 (7%)	0.71
History of Microvascular APS	32 (7%)	23 (10%)	0.19
History of Pregnancy Morbidity	96/347 (28%)	56/171 (33%)	0.23
Unexplained Death at or Beyond 10th week	70/347 (20%)	40/171 (23%)	0.4
Premature Birth Before 34th Week Due to Eclampsia, Preeclampsia or Placental Insufficiency	33/347 (10%)	26/171 (15%)	0.06
Three CONSECUTIVE Unexplained Spontaneous Abortions Before 10th Week	22/347 (6%)	4/171 (2%)	0.055
Other aPL Manifestations (Ever)	195 (42%)	105 (45%)	0.53
Thrombocytopenia (<100x10^9/L) *	69 (15%)	61 (26%)	**0.0004**
Hemolytic Anemia **	18 (4%)	13 (5%)	0.32
Heart Valve Disease (Old Criteria)	26/414 (6%)	26/209 (12%)	**0.008**
Cognitive Dysfunction***	12 (3%)	6 (3%)	0.97
White Matter Changes	86/322 (27%)	33/165 (20%)	0.1
Seizure Disorder	41 (9%)	17 (7%)	0.48
Multiple Sclerosis-like Disease	5 (1%)	0	0.17
Chorea	5 (1%)	4 (2%)	0.5
Concomitant SARD			
aPL with other SARD	51 (11%)	23 (10%)	0.61
APS with other SARD	117 (25%)	76 (32%)	0.06
Primary aPL (no APS classification)	60 (13%)	25 (11%)	0.37
Primary APS	240 (51%)	114 (48%)	0.4
aPL/APS Classification			
aPL without APS	110 (24%)	48 (20%)	0.31
Thrombotic APS (TAPS)	268 (57%)	134 (56%)	0.8
Obstetric APS (OAPS)	39 (8%)	16 (7%)	0.45
TAPS + OAPS	51 (11%)	40 (17%)	**0.02**
aCL/aβ_2GPI Profile			
IgG	234 (50%)	235 (99%)	**<0.00001**
IgM	119 (25%)	101 (42%)	**<0.00001**
LA/aCL/aβ_2GPI Profile			
Triple aPL	101 (22%)	127 (53%)	**<0.00001**
Double aPL	124 (26%)	86 (36%)	**0.008**
LA + aCL IgG/M	70 (15%)	38 (16%)	0.72
LA + aβ_2GPI IgG/M	9 (2%)	12 (6%)	**0.02**
aCL IgG/M + aβ_2GPI IgG/M	45 (10%)	36 (15%)	**0.03**
Single aPL			
LA	164 (35%)	15 (6%)	**<0.00001**
aCL IgG/M	59 (13%)	9 (4%)	**0.002**
aβ_2GPI IgG/M	20 (4%)	1 (<1%)	**0.0036**
Cardiovascular Risk Factors	379 (81%)	195 (82%)	0.66
Hypertension	155 (33%)	71 (30%)	0.38
Diabetes	30 (6%)	5 (2%)	**0.013**
Hyperlipidemia	118 (25%)	44 (18%)	**0.039**
Obesity (BMI>30)	140 (30%)	53 (22%)	0.11
Nephrotic Syndrome	3 (1%)	2 (1%)	1
Chronic or End-stage Renal Disease	13 (3%)	9 (4%)	0.47
Active Known Malignancy (less than 12 months)	5 (1%)	2 (1%)	1
Sedentary Lifestyle	225 (48%)	101 (42%)	0.16
Family History of Early Cardiovascular Disease	67 (14%)	31 (13%)	0.64
History of Smoking (Current or Previous)	172 (37%)	92 (39%)	0.62

* Thrombocytopenia is defined as platelet count <100,000 per microliter, tested twice at least 12 weeks apart; ** Autoimmune hemolytic anemia is defined as persistent anemia with hemolysis and a positive direct antiglobulin test; *** Neuropsychiatric test proven.
aCL: anticardiolipin antibodies; **aβ_2GPI**: anti-β_2-glycoprotein-I antibodies; **BMI**: body mass index; and **SARD**: systemic autoimmune rheumatic diseases.

and/or aβ_2GPI IgA-positive *versus* IgA-negative patients. A secondary objective was to identify clinical and serological factors independently associated with IgA positivity.

Methods: The APS ACTION registry uses a web-based system to capture patient demographics, APS-related history, and medications. Inclusion requires aPL positivity per Revised Sapporo APS CC, confirmed within one year prior to enrollment. Patients are followed every 12±3 months with clinical assessments and blood collection. For this cross-sectional analysis of baseline data, we first compared demographic, clinical, and laboratory features between IgA-positive (aCL and/or aβ_2GPI IgA ≥20 U; analysis repeated with ≥40 U cutoff) and IgA-negative (< 20 U) patients using chi-square or Fisher's exact tests, based on APS ACTION Core Lab results (BioFlash, Werfen). We then conducted multivariate logistic regression to identify factors independently associated with IgA positivity.

Results: Of 1,252 patients recruited as of January 2025, 706 (56%) had baseline aCL/aβ_2GPI IgA results. Using the ≥20U threshold recommended by the manufacturer, the IgA-positive group (n: 238 [34%]) had significantly higher rates of venous

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Predictors of Anticardiolipin (aCL) and Anti-β_2-glycoprotein-I antibodies (aβ_2GPI) IgA Positivity Among APS ACTION Registry Patients (Cut-off for positivity ≥20U) (multivariate logistic regression)

Patient characteristics (N = 706)	Adjusted OR (95% CI)	*P* value
Triple aPL-Positivity	**12.34** (7.4740-20.3650)	**<0.0001**
Double aPL-Positivity	**6.56** (3.9800-10.8183)	**<0.0001**
Heart Valve Disease	1.57 (0.8373-2.9354)	0.1600
Thrombocytopenia (<100x109/L)	**1.57** (1.0186-2.4224)	**0.0410**
History of Any Venous Event	1.41 (0.9939-2.0096)	0.0541
History of SLE	**1.54** (1.0521-2.2668)	**0.0265**
History of Any CVD Risk Factor	0.94 (0.6074-1.4602)	0.7886

aPL: antiphospholipid antibodies; **SLE:** systemic lupus erythematosus; **CVD:** cardiovascular disease

events, thrombocytopenia, heart valve disease, and triple/double aPL-positivity. Diabetes, hyperlipidemia, and single aPL-positivity were significantly higher in IgA-negative group (Table 1). In the multivariate analysis, after adjusting for the aPL profile, history of venous events, heart valve disease, thrombocytopenia, systemic lupus erythematosus (SLE), and any traditional cardiovascular disease risk factor, IgA-positivity was significantly associated with triple/double aPL-positivity, SLE, and thrombocytopenia (Table 2). When the IgA positivity cut-off of $\geq$ 40U used: a) there was no change in the univariate results, except that diabetes, and hyperlipidemia no longer differed between the groups; and b) in multivariate analysis, IgA-positivity was significantly associated with triple/double aPL-positivity and history of venous events (data not shown).

Conclusion: In our well-established international cohort of persistently aPL-positive (lupus anticoagulant, aCL IgG/M, and/or aβ_2GPI IgG/M) patients, concomitant aCL/aβ_2GPI IgA-positivity correlates with a more severe clinical and, especially, serological phenotype. Future prospective analysis of the registry will help us further clarify the clinical significance of aCL/aβ_2GPI IgA antibodies in aPL-positive patients.

Disclosure: E. Sahin: None; **Y. Zuo**: None; **D. Andrade**: None; **M. Tektonidou**: None; **V. Pengo**: None; **M. Radin**: None; **C. López pedrera**: None; **D. Paredes-Ruiz**: None; **H. Belmont**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1; **D. WAHL**: None; **W. Branch**: UCB, 5; **M. Gerosa**: None; **G. Ramires de Jesus**: None; **T. Atsumi**: None; **M. Efthymiou**: None; **A. Tincani**: Galapagos, 1, UCB, 1; **E. Rodriguez-Almaraz**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **R. Cervera**: None; **R. Willis**: None; **K. Devreese**: None; **M. Bertolaccini**: None; **H. Cohen**: GlaxoSmithKlein(GSK), 6, Roche, 2, Roivant, 2; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **D. Erkan**: Chugai, 5, GlaxoSmithKlein(GSK), 1, 5, 6, Merida Biosciences, 2, NIH, 5, Roche, 1, Roivant Sciences, 2, Star Therapeutics, 1, Up-To-Date, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0122

The role of low profile antiphospholipid antibodies and adverse pregnancy outcomes.

Eugenia Chock[1], Tong Wang[2], Areeka Memon[3], Zeyan Liew[4] and Pengfei Guo[4], [1]Yale School of Medicine, New Haven, CT, [2]Yale School of Public Health, New Haven, [3]Yale New Haven Health, New Haven, CT, [4]Yale Center for Perinatal, Pediatric and Environmental Epidemiology, New Haven

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Presence of high titer antiphospholipid antibodies (aPLs) confer adverse pregnancy outcomes (APOs). Patients with low titer aPLs often receive conflicting counseling on treatment, many are treated with dual antiplatelet and low molecular weight heparin (LMWH) therapy without clear benefit. We conducted a pilot study to investigate the association of low profile aPLs and APOs.

Methods: We performed a retrospective cohort study using electronic health record (EHR) data of all pregnant women who received aPL testing and hospitalized in a major tertiary care center from 2013 to 2022. Women were categorized into three exposure groups: (1) negative aPLs: anti-cardiolipin ± anti-b2- glycoprotein IgG, IgA, or IgM < 20 GPL/MPL; (2) low profile

Table 1. Characteristics of study population by aPL profile.

Characteristic / Group	Negative aPLs (N=1,938)	Low aPLs (N=96)	High aPLs (N=99)	Overall (N=2,133)
Age at delivery				
Mean (SD)	32.5 (5.21)	33.7 (6.04)	33.7 (5.76)	32.6 (5.28)
Race and Ethnicity (N, %)				
Non-Hispanic Asian	63 (3.3%)	7 (7.3%)	3 (3.0%)	73 (3.4%)
Hispanic or Latino	388 (20.0%)	18 (18.8%)	32 (32.3%)	438 (20.5%)
Non-Hispanic Black or African American	415 (21.4%)	17 (17.7%)	25 (25.3%)	457 (21.4%)
Non-Hispanic White or Caucasian	995 (51.3%)	51 (53.1%)	37 (37.4%)	1083 (50.8%)
Others+	77 (4.0%)	3 (3.1%)	2 (2.0%)	82 (3.8%)
Insurance (N, %)				
Medicare	27 (1.4%)	0 (0%)	0 (0%)	27 (1.3%)
Private insurance	1101 (56.8%)	55 (57.3%)	62 (62.6%)	1218 (57.1%)
Publicly-funded insurance	810 (41.8%)	41 (42.7%)	37 (37.4%)	888 (41.6%)
Parity* (N, %)				
0	5 (0.3%)	0 (0%)	0 (0%)	5 (0.2%)
1-3	1637 (84.4%)	82 (85.4%)	88 (88.9%)	1807 (84.7%)
4+	268 (13.8%)	14 (14.6%)	10 (10.1%)	292 (13.7%)
Co-morbidities (N, %)				
Smoking	150 (7.7%)	5 (5.2%)	4 (4.0%)	159 (7.5%)
Obesity	906 (46.7%)	36 (37.5%)	56 (56.6%)	998 (46.8%)
Diabetes	120 (6.2%)	6 (6.2%)	24 (24.2)	150 (7.0%)
Chronic Kidney Disease	66 (3.4%)	5 (5.2%)	2 (2.0%)	73 (3.4%)
Pre-eclampsia/ eclampsia	360 (18.6%)	17 (17.7%)	23 (23.2%)	400 (18.8%)
Pregnancy-related and gestational hypertension	357 (18.4%)	18 (18.8%)	27 (27.3%)	402 (18.8%)
Rheumatic diseases	392 (20.2%)	10 (10.4%)	41 (41.4%)	443 (20.8%)
History of Recurrent Pregnancy Loss (N, %)	389 (20.1%)	34 (35.4%)	24 (24.2%)	447 (21.0%)
Aspirin use* (N, %)	617 (31.8%)	44 (45.8%)	61 (61.6%)	722 (33.8%)
Low Molecular Weight Heparin use* (N, %)	189 (9.8%)	15 (15.6%)	53 (53.5%)	257 (12.0%)

*contains missing data
+Not reported

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Risks of adverse pregnancy outcomes among women with low aPLs.

	Preeclampsia and eclampsia					Late pregnancy loss and stillbirths				
Group	Frequency	Crude OR (95% CI)	p-value	Adjusted OR (95% CI) *	p-value	Frequency	Crude OR (95% CI)	p-value	Adjusted OR (95% CI) ^	p-value
Negative aPLs	360/1938	Ref	Ref	Ref	Ref	200/1938	Ref	Ref	Ref	Ref
Low profile aPLs	17/96	0.96 (0.55, 1.60)	0.891	0.92 (0.49, 1.66)	0.792	8/96	0.62 (0.25, 1.29)	0.219	0.51 (0.20, 1.11)	0.092

aPLs: antiphospholipid antibodies; OR: Odds Ratio, CI: Confidence Interval;
* adjusted for age at delivery, race and ethnicity, history of recurrent pregnancy loss, parity, diabetes, chronic kidney disease, pregnancy-related and gestational hypertension, obesity, rheumatic diseases, aspirin use, low molecular weight heparin use.
^adjusted for age at delivery, race and ethnicity, history of recurrent pregnancy loss, parity, diabetes, chronic kidney disease, pregnancy-related and gestational hypertension, obesity, rheumatic diseases, pre-eclampsia and eclampsia, aspirin use, low molecular heparin use

aPLs, defined as anti-cardiolipin ± anti-ß2- glycoprotein IgG, IgA, or IgM 20-39 GPL/MPL; (3) high profile aPLs, defined as anti-cardiolipin ± anti-ß2- glycoprotein IgG, IgA, or IgM ≥40 GPL/MPL, and/or presence of lupus anticoagulant. The outcomes of interest were: (1) late pregnancy losses and stillbirths; (2) pre-eclampsia and eclampsia. Next, we performed logistic regression to determine the exposure-outcome associations in the low profile aPLs group. The analyses were adjusted for age, parity, obesity, co-morbidities including rheumatic diseases, hypertensive disorders, diabetes, history of recurrent pregnancy losses, aspirin and LMWH use.

Results: We included 2,133 women who were hospitalized during the latter part of pregnancy and tested for aPLs. < 10% of women had positive aPLs and among those, almost half of these women were considered low profile. The mean age of women with low and high profile aPLs was the same (33.7 years of age), Caucasian women constitute more than half in all groups. Most women had private insurance (N=1218; 57.1%). Several conditions were most prevalent in the high-profile group, including obesity (N=56, 56.6%), hypertensive diseases during pregnancy (N=27, 27.3%), and rheumatic diseases (N=41, 41.4%). Women with low profile aPLs were more likely to have history of recurrent pregnancy losses (N=34, 35.4%); smoking (N=150, 7.7%) during pregnancy was most frequent among negative aPL group (Table 1).

Among women with low profile aPLs, the adjusted Odds Ratio (aOR) of pre-eclampsia and eclampsia compared to negative aPL group was 0.92 (95%CI 0.49, 1.66; *p=0.792*), and the aOR of late pregnancy loss and stillbirths was 0.51(95%CI 0.20, 1.11; *p=0.092*) (Table 2).

Conclusion: In the low profile group, the odds of developing the APOs of interest were lower or similar, compared to those with negative aPLs despite treatment with aspirin or LMWH. Women with negative aPLs may be more ill and therefore required inpatient care in this study sample. The limitations of this pilot study include small sample sizes, potential selection bias, and incomplete ascertainment of specific variables. Our findings may not be representative of the general population, but the associations of this pilot study inform additional EHR data collection to improve the limitations above. Future work would include the use of propensity score weighting to account for confounding and to balance the characteristics among groups.

Disclosure: E. Chock: None; **T. Wang**: None; **A. Memon**: None; **Z. Liew**: None; **P. Guo**: None.

Abstract Number: 0123

Prognosis of Cardiac Involvement in Antiphospholipid Syndrome

Juliette Guiraud Chaumeil[1], david saadoun[2], Laurent Alric[1], Laurent Sailler[1], Sébastien De Almeida Chaves[1], Olivier Lairez[1], Patrice CACOUB[3] and **Grégory Pugnet**[4], [1]CHU Toulouse, Toulouse, France, [2]APHP, neuilly sur seine, France, [3]Sorbonne Université, Paris, France, [4]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Cardiac involvement in antiphospholipid syndrome (APS) includes valvular, coronary, and myocardial manifestations. Valvular involvement is the most frequent, affecting approximately 30% of patients, while myocardial infarction is the second leading cause of death in APS. Although a few studies have examined the progression of valvular disease, data on coronary and myocardial involvement are lacking. Furthermore, the prognostic implications of the different types of APS-related cardiac involvement have not been directly compared. This study aimed to evaluate the long-term prognosis associated with each type of cardiac involvement in APS.

Methods: We conducted a bicentric, retrospective observational cohort study in France, including patients followed at La Pitié-Salpêtrière Hospital (Paris) and Toulouse University Hospital. Patients met the 2023 APS classification criteria and were diagnosed between January 1, 2000, and July 1, 2023. The primary endpoint was the occurrence of a major APS-related complication, defined as death, catastrophic APS (CAPS), admission to intensive care, heart failure, myocardial infarction, or intra-alveolar hemorrhage. Overall survival and incidence of major complications were compared between groups using the log-rank test.

Results: A total of 138 patients were included, of whom 93 were women (67.4%), with a median age of 41 years (IQR 33–52). Cardiac involvement was the initial APS manifestation in 69 patients (50.0%). Compared with those with coronary or myocardial involvement, patients with valvular involvement more frequently had a history of stroke, livedo reticularis, and Sneddon syndrome.

The median follow-up was 6 years (IQR 3–11). During follow-up, 89 patients (64.5%) experienced at least one APS-related complication. The probability of event-free survival was 70% at 1 year and 43% at 5 years. No significant differences in overall or event-free survival were observed across the different types of cardiac involvement. However, patients with myocardial involvement had a significantly higher incidence of arrhythmias ($p = 0.050$), intensive care unit admissions ($p = 0.031$), and hemorrhagic events ($p = 0.046$).

Conclusion: Cardiac involvement in APS is frequent and associated with a substantial risk of adverse outcomes over time. Although overall and event-free survival did not differ significantly across valvular, coronary, and myocardial subtypes, myocardial involvement was independently associated with a higher incidence of severe complications, including arrhythmias, intensive care unit admissions, and hemorrhagic events. These findings underscore the prognostic relevance of the type of cardiac involvement and support the need for stratified risk assessment and targeted management in patients with APS.

Disclosure: J. Guiraud Chaumeil: None; **d. saadoun**: None; **L. Alric**: None; **L. Sailler**: None; **S. De Almeida Chaves**: None; **O. Lairez**: None; **P. CACOUB**: None; **G. Pugnet**: None.

Abstract Number: 0124

Single-cell atlas reveals the central-and-peripheral immune remodeling mechanism and clinical benefits of talitacicept therapy in patients with primary antiphospholipid syndrome

Haoyu Pan[1], Shiyan Gu[1], Xiaohan Wei[2], Yuying Fan[1], Jinyi Qian[1], Shuyi Yu[1] and Hui Shi[3], [1]Department of Rheumatology and Immunology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [2]Shanghai JiaoTong University, Shanghai, China (People's Republic), [3]Shanghai Jiaotong University Affiliated Ruijin Hospital, Shanghai, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: To elucidate the molecular and cellular mechanisms underlying Talitacicept therapy in primary antiphospholipid syndrome (PAPS) patients using integrated single-cell RNA and TCR/BCR profiling of paired bone marrow (BM) and peripheral blood (PB) samples.

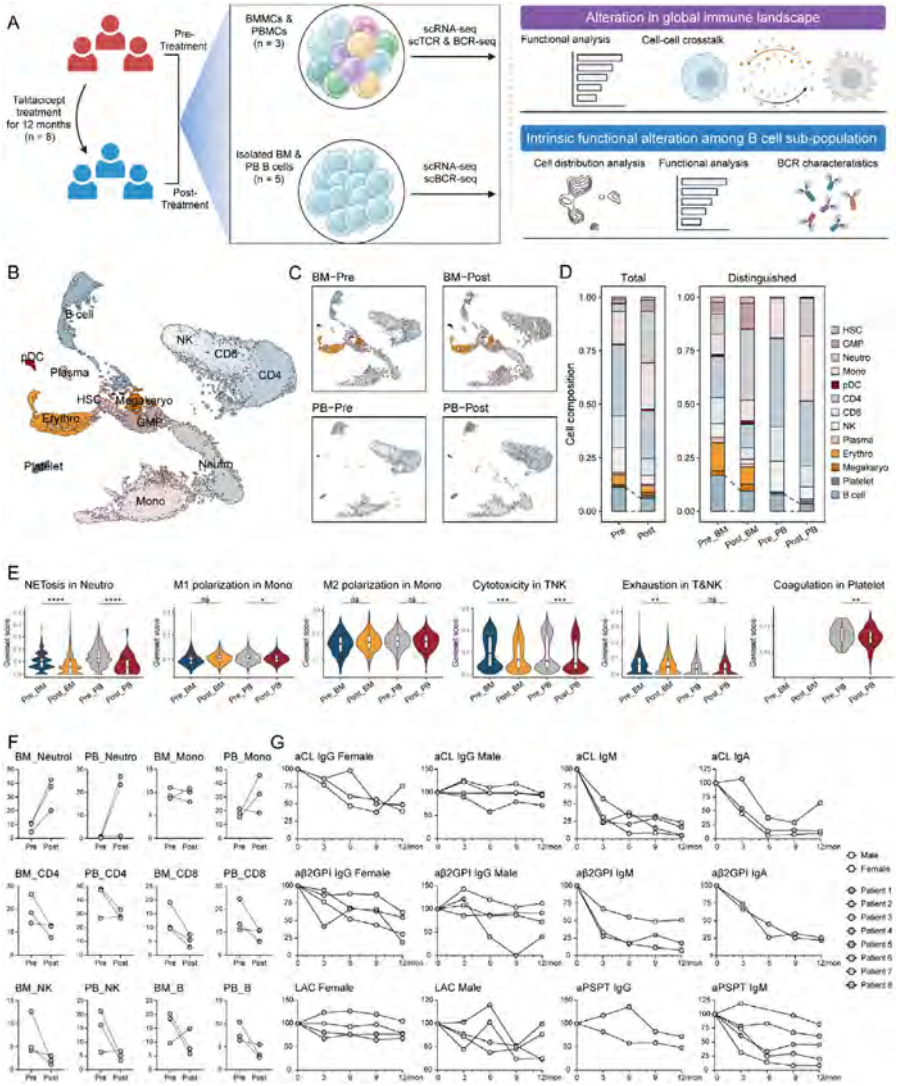


Figure 1: The impact of telitacicept therapy on the overall immune landscape of PAPS patients with therapeutic benefits. A) Schematic diagram of the experimental design for the study. B) Uniform Manifold Approximation and Projection (UMAP) plot depicting 13 immune cell clusters in paired pre- and post- bone marrow (BM) and peripheral blood (PB) samples from PAPS patients who received Talitacicept therapy (n=3). C) Cell-type distribution in UMAP blueprint from distinguished groups, respectively. D) Stacked bar graphs depicting the composition of different cell clusters in Pre- and Post- subjects. Left: celltype from BM and PB samples merged; right: celltype from BM and PB samples distinguished. E) Characteristic cell-type function revealed by geneset score calculated by the UCell Method. Ns: not significant; *: p<0.05; **: p<0.01; ***: p<0.001; ****: p<0.0001. F) Paired pre- and post- celltype composition in each subject reveal change of celltype abundance pre- and post-treatment. G) Longitudinal changes in serum antiphospholipid antibody (aPL) levels in PAPS subjects. Antibody levels were measured at baseline and at 3, 6, 12, and 18 months after initiation of therapy. For each antibody indicator, PAPS subject must have at least one positive test result to be displayed. For aCL IgG, aβ2GPI IgG and LAC, female subjects and male subjects were distinguished in order to be visualized more clearly.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

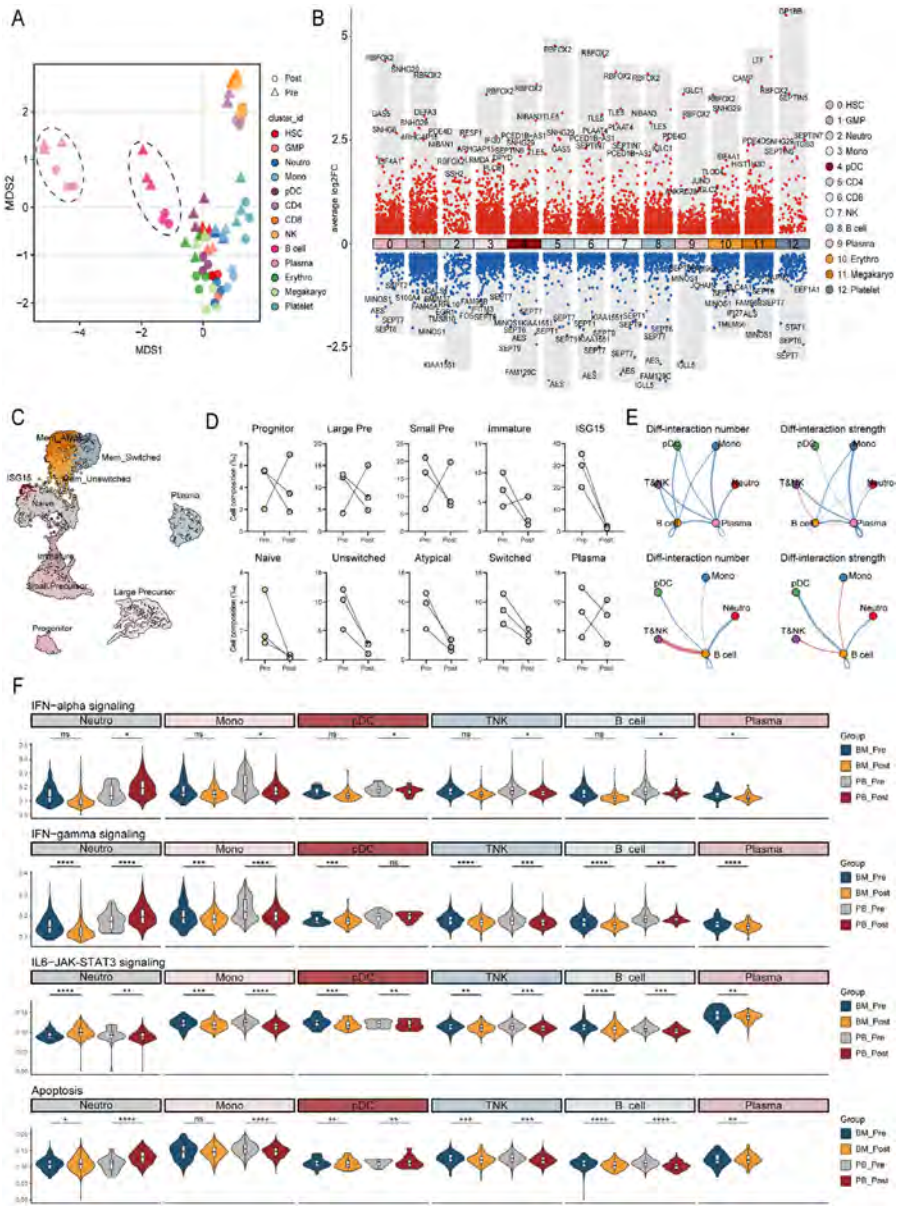


Figure 2: Talitacicept reduces interferon and inflammatory signatures in global immune cell types in PAPS patients. A) Multi-dimensional scaling (MDS) plot showing the differential state between Pre- and Post-groups of each cell type based on aggregated pseudo-bulk form. B) Volcanoplot showing differentially expressed genes (DEGs) in each celltype, DEGs with log2FC > 0.25 and padj < 0.25 were shown. Red refers to genes up-regulated post-talitacicept and blue refers to genes down-regulated post-talitacicept. C) Re-constructed "central-to-periphery" developmental lineage of B cell, including 11 B cell sub-populations. D) Paired Pre- and post- celltype composition in each subject reveal change of B cell sub-population abundance Pre- and post-treatment. E) Circle plot showing differential cell-cell communication network between B/Plasma cells and other immune celltypes to illustrate the changes in the B cells' effects on other immune celltypes after talitacicept therapy. The width of edges represented the relative number of interactions or interaction strength. Red (or blue) colored edges represent increased (or decreased) signaling after talitacicept therapy. F) Characteristic celltype function revealed by geneset score calculated by UCell Method. Ns: not significant; *: p<0.05; **: p<0.01; ***: p<0.001; ****: p<0.0001.

Methods: 8 PAPS patients were recruited to receive standard Talitacicept treatment for 12 months. Clinical data were recorded every 3 months during treatment. Paired BM and PB samples were collected pre-treatment and after the 12-month treatment is completed. In 3 patients scRNA and BCR/TCR sequencing were performed on BMMCs and PBMCs to reveal the global changes in immune landscape; and for the other 5 patients, BM and PB B cells were sequenced to reveal intrinsic change in B cell subpopulations.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

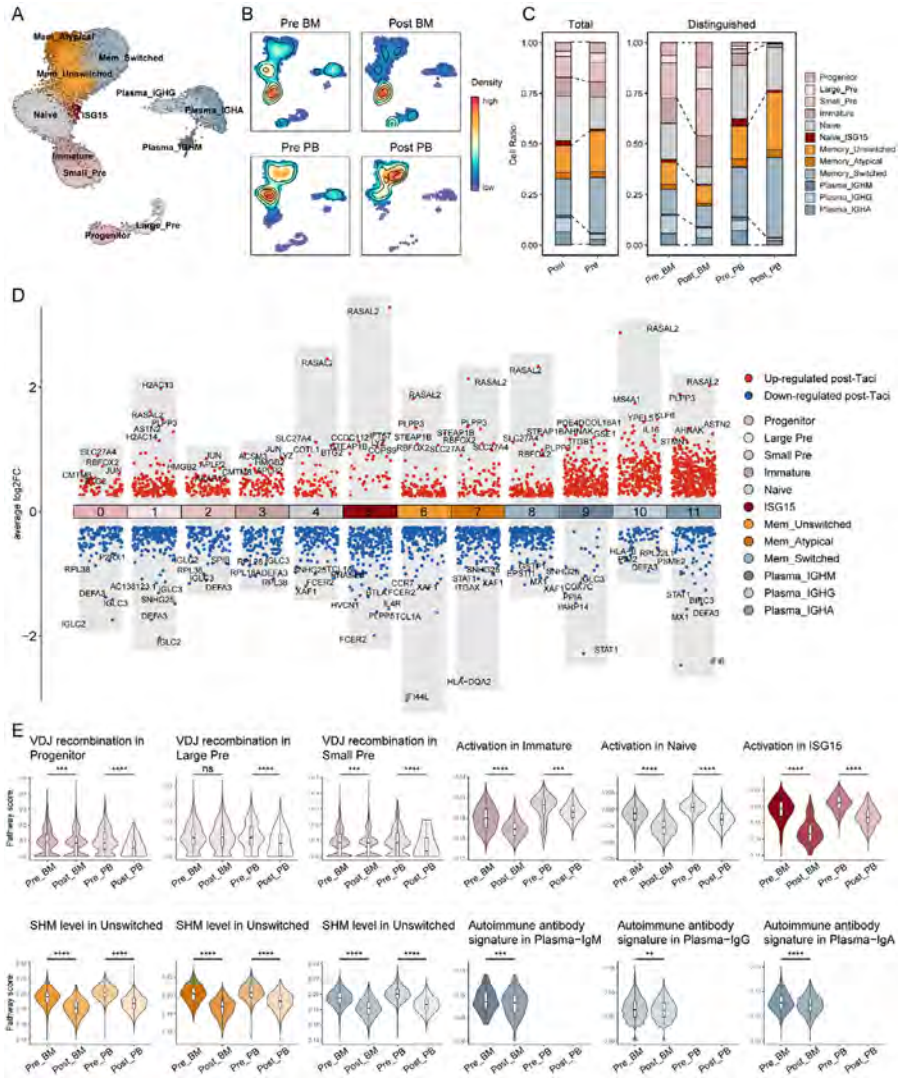


Figure 3: Talitacicept influences the intrinsic distribution and molecular characteristics within B cells and reduces the autoreactivity-associated alongside the developmental lineage. A) Uniform Manifold Approximation and Projection (UMAP) plot depicting 12 B cell sub-populations in paired Pre- and post- bone marrow (BM) and peripheral blood (PB) samples from PAPS patients who received Talitacicept therapy (n=5). B) Distribution density of BM and PB B cell sub-population abundance in respective groups. C) Stacked bar graphs depicting the composition of different cell clusters in Pre- and Post- subjects. Left: celltype from BM and PB samples merged; right: celltype from BM and PB samples distinguished. D) Volcanoplot showing differential expressed genes (DEGs) in each celltype, DEGs with log2FC > 0.25 and padj < 0.25 were shown. Red refers to genes up-regulated post-talitacicept, and blue refers to genes down-regulated post-talitacicept. E) Characteristic function alongside B cell lineage revealed by geneset score calculated by the UCell Method. SHM: somatic hypermutation; Ns: not significant; *: p<0.05; **: p<0.01; ***: p<0.001; ****: p<0.0001.

Results: 12 months of standard talitacicept treatment effectively reduced the number of B cells and plasma cells in both BM and PB. The number of neutrophils increased in all 3 patients after treatment, while CD4 T, CD8 T and NK cell showed a coordinated decrease in both BM and PB. However, a male patient with a poor treatment response (defined as no significant decrease in pan-aPL antibodies after treatment) showed an opposite increase in BM B cells. We also confirmed that most aPLs were effectively reduced, but the decline in aCL IgG and aβ2GPI IgG was relatively insignificant in male patients (**-Figure 1**). The differential states of overall transcriptional characteristics revealed that B cells and plasma cells were the most significantly different cell subpopulations. Additionally, DEG (differential expressed gene) analysis showed each celltype presented significant downregulation of abundant interferon and inflammation-related genes. A B cell blueprint was constructed and confirmed that talitacicept effectively cleared most B cell subpopulations. Cellchat analysis indicated that the interactions from B cells and plasma cells toward other immune cells generally decreased after treatment, and UCell scoring also confirmed that the interferon, JAK-STAT pathway and apoptosis levels among global immune landscape were effectively reduced (**Figure 2**). For intrinsic changes in B cell lineage, naive B cells and plasma cells were the main subpopulations that

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

decreased in BM and PB, while the relative proportions of pro-, pre-, and memory B cells increased. Additionally, B cell subpopulations presented similar downregulation of interferon and inflammation-related genes after treatment. Features potentially related with autoimmunity were evaluated, and the V-D-J rearrangement activity was reduced in pro/pre B cells, the activation level of naive B cells and the SHM level in memory B cell stage was reduced, while the autoantibody-related signature in plasma cells decreased as well (**Figure 3**).

Conclusion: Our study revealed the mechanism of talitacicept in treating PAPS patients, including reducing the level of pathogenic antibodies by eliminating mature B cells and plasma cells, inhibiting the interferon and inflammatory pathways among the global immune landscape, and reprogramming autoreactivity-related functions alongside B cell development trajectory. These findings provide important theoretical basis for optimizing the targeted treatment strategy of PAPS.

Disclosure: H. Pan: None; **S. Gu**: None; **X. Wei**: None; **Y. Fan**: None; **J. Qian**: None; **S. Yu**: None; **H. Shi**: None.

Abstract Number: 0125

The IFN Signature is Less Pronounces in Primary Antiphospholipid Syndrome Compared with other Systemic Autoimmune Diseases

Dionysis Nikolopoulos[1], Konstantinos Charitidis[2], Julius Lindblom[2], Maria O Borghi[3], Guillermo Barturen[4], Marta Alarcon-Riquelme[5], Lorenzo Beretta[6], **Ioannis Parodis**[7] and PRECISESADS consortium, [1]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [2]Karolinska Institutet, Stockholm, Sweden, [3]IRCCS, Istituto Auxologico Italiano, Milan, Italy, [4]Center for Genomics and Oncological Research (GENYO), Andalusia, Spain, [5]Fundacin Progreso y Salud, Andalusian Government, Granada, Spain, [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Milan, Italy, [7]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Primary antiphospholipid syndrome (pAPS) is an autoimmune disease that, unlike many other autoimmune diseases, commonly presents with thrombotic events rather than inflammatory manifestations. A peripheral type I interferon (IFN) signature distinguishes patients with pAPS from healthy individuals, but its broader molecular landscape compared with other autoimmune diseases remains unknown.

Methods: We analysed bulk RNA sequencing data from whole blood obtained from patients with pAPS (n=83), systemic lupus erythematosus (SLE; n=249), Sjögren's disease (SjD; n=253), systemic sclerosis (SSc; n=247), and 497 matched healthy controls (HC) from the PRECISESADS project (NCT02890121). We applied supervised pathway enrichment analysis, unsupervised weighted gene co-expression network analysis (WGCNA), and deconvolution analysis to characterise the molecular profile of pAPS.

Results: A total of 85 upregulated and 10 downregulated differentially expressed genes (DEGs) were found in patients with pAPS compared with HC, including genes indicating an overall upregulation of type I and II IFN signalling, complement cascade, and coagulation in pAPS, coupled with differentially enriched neutrophil degranulation and monocyte chemotaxis pathways. However, only 15 of those genes were uniquely differentially expressed in patients with pAPS compared with those with any other of the investigated autoimmune diseases. The comparison between pAPS and SLE revealed 334 DEGs (71 up- and 263 downregulated). Enrichment analysis revealed downregulation of type I and II IFN signalling and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

complement cascade pathways in pAPS versus SLE. Moreover, type I and II IFN signalling was significantly downregulated in pAPS compared to SjD or even SSc. WGCNA identified 19 modules of co-expressed genes, with pAPS strongly linked only to upregulation of the "IFN" module compared to HC. However, the upregulation of the "IFN" gene module was more pronounced in SLE, SjD and SSc compared with pAPS, supporting a gradient in the upregulation of IFN-related genes across these diseases, as previously shown for APS-SLE[1-2]. Within pAPS, a history of miscarriages was positively associated with the "methylation" module, while thrombocytopenia was negatively associated with the "T cell" and "RNA processing" modules. Deconvolution analysis showed that patients with pAPS exhibited significant alterations in the proportions of neutrophils, NK, naïve T, and memory T, compared to HC. However, these differences were evident in patients with SLE compared to HC.

Conclusion: Patients with pAPS exhibit a distinct molecular profile within the spectrum of systemic autoimmune diseases, marked by a modest activation of interferon signalling.

1. Nikolopoulos D, et al. Disentangling the riddle of systemic lupus erythematosus with antiphospholipid syndrome: blood transcriptome analysis reveals a less-pronounced IFN-signature and distinct molecular profiles in venous versus arterial events. Ann Rheum Dis. 2024 Aug 27;83(9):1132-43.

2. Barturen G, et al. Integrative Analysis Reveals a Molecular Stratification of Systemic Autoimmune Diseases. Arthritis Rheumatol. 2021 Jun;73(6):1073-1085. doi: 10.1002/art.41610.

Disclosure: D. Nikolopoulos: None; **K. Charitidis**: None; **J. Lindblom**: None; **M. Borghi**: None; **G. Barturen**: None; **M. Alarcon-Riquelme**: None; **L. Beretta**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5.

Abstract Number: 0126

Performance of the 2023 and 2006 APS Classification Criteria in Pediatric Patients Diagnosed with APS: A Multisite Cohort Study

Jacqueline Madison[1], Elizabeth Sloan[2], Cristina Saez[3], Olivia Kwan[4], Kevin Lewis[1], Jonathan Marilao[5], Blake Baay[6], Rasha Elrefai[4], Marissa Dale[7], Deborah McCurdy[8], Jheel Bhatt[9], Sasidhar Goteti[10], Ekemini Ogbu[11], Jason S. Knight[1], Yu (Ray) Zuo[1] and the APS workgroup of the CARRA SLE Committee, [1]University of Michigan, Ann Arbor, MI, [2]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [3]Children's Hospital Colorado, Glendale, CO, [4]Baylor College of Medicine, Houston, TX, [5]University of Texas Southwestern, Dallas, TX, [6]Scottish Rite for Children, Dallas, TX, [7]Hospital for Special Surgery/NYP Cornell, New York, NY, [8]UCLA Medical Center, Los Angeles, CA, [9]Advent Health Orlando, Orlando, FL, [10]University of Utah, Salt Lake City, UT, [11]Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid syndrome (APS) is a thrombo-inflammatory disorder that causes significant morbidity and mortality, even in children. The 2023 ACR/EULAR classification criteria, which use weighted clinical and laboratory scores, improve specificity (99% vs. 86%) but reduce sensitivity (84% vs. 99%) compared to the 2006 criteria in adults. However, no pediatric-specific criteria exist, and the 2023 criteria have not been validated in children. This multisite North American study aims to assess the performance of both the 2023 and 2006 criteria in pediatric APS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients with pediatric APS and childhood-onset SLE were initially identified by rheumatologists at 5 academic institutions through electronic medical record searches using diagnosis codes. APS diagnosis was determined by documentation of a confirmed diagnosis at age ≤18 by a pediatric hematologist or rheumatologist. SLE controls had a confirmed diagnosis by age 18 and ≥2 antiphospholipid antibody (aPL) test results available. Analyses were performed using Python (v3.10).

Results: We evaluated the performance of the adult 2023 and 2006 APS classification criteria in a well-characterized, multicenter cohort of pediatric patients diagnosed with APS (n=57) and lupus (n=25) (Table 1). When applied to pediatric patients, the 2023 criteria demonstrated improved but similar **specificity** compared with the 2006 version (100% vs. 96%) and reduced **sensitivity** (68% vs. 75%). The 2023 criteria also showed a slightly higher positive predictive value (**PPV**) for diagnosis, reflecting a modest increase in precision (100% vs. 98%), but lower negative predictive value (**NPV**, 58% vs. 63%). The **F1 score**, reflecting overall diagnostic performance, was also lower with the 2023 criteria (0.81 vs. 0.85). ROC analysis favored the 2006 criteria (**AUC** = 0.86 vs. 0.84) (Table 2). Both criteria demonstrated strong agreement (Cohen's kappa = 0.88). Among the 18 APS patients who failed to meet the 2023 criteria (including all 14 who also failed the 2006 criteria), 4 did not reach the clinical criteria threshold, and 14 lacked sufficient laboratory points—8 of whom had only a single positive lupus anticoagulant test. Of the 4 patients meeting the 2006 but not the 2023 criteria, 2 failed to

Table 1. Demographic features, clinical characteristics, and fulfilment of classification criteria in patients with clinical diagnoses of pediatric APS and childhood-onset SLE without APS

	APS (n=57)	Lupus without APS (n=25)
Sex		
Female	40 (70%)	22 (88%)
Male	17 (30%)	3 (12%)
Ethnicity		
Hispanic, Latino/a, or Spanish origin	18 (32%)	7 (28%)
Not Hispanic, Latino/a, or Spanish origin	39 (68%)	18 (72%)
Race		
White	46 (81%)	13 (52%)
Black or African American	6 (10%)	8 (32%)
Asian	2 (4%)	4 (16%)
Unknown	3 (5%)	1 (4%)
Deceased	2 (4%)	0 (0%)
Lupus	22 (39%)	25 (100%)
Other systemic autoimmune disease	4 (7%)	0 (0%)
Median age at APS diagnosis (range)	15 (6-18)	n/a
Median age at most recent follow-up (range)	17 (9-31)	18 (10-29)
APS clinical features		
Venous thromboembolism	43 (75%)	4 (16%)
Multiple venous thromboembolism	14 (25%)	2 (8%)
Arterial thrombosis	12 (21%)	1 (4%)
Multiple arterial thrombotic events	4 (7%)	1 (4%)
Microvascular feature	18 (32%)	3 (12%)
Livedo (reticularis or racemosa suspected by exam or confirmed on pathology)	15 (26%)	3 (12%)
Nephropathy (aPL nephropathy or thrombotic microangiopathy on renal biopsy)	5 (8%)	2 (8%)
Pulmonary hemorrhage	3 (5%)	0 (0%)
Myocardial disease or adrenal hemorrhage	0 (0%)	0 (0%)
Catastrophic APS (possible, probable, or confirmed)	6 (11%)	1 (4%)
Obstetric event	3 (5%)	0 (0%)
Cardiac valve event	5 (9%)	0 (0%)
Thrombocytopenia (otherwise unexplained)	25 (44%)	3 (12%)
Clinical criteria score >3	53 (93%)	4 (16%)
APS laboratory features		
Positive lupus anticoagulant - once	42 (74%)	5 (20%)
Positive lupus anticoagulant - persistent	31 (54%)	2 (8%)
Persistent moderate or high anti-cardiolipin IgG	32 (56%)	2 (8%)
Persistent moderate or high anti-cardiolipin IgM	12 (21%)	2 (8%)
Persistent moderate or high anti-β2GPI IgG	31 (54%)	2 (8%)
Persistent moderate or high anti-β2GPI IgM	13 (23%)	2 (8%)
Laboratory criteria score >3	43 (75%)	3 (12%)
Fulfills 2023 ACR/EULAR classification criteria	39 (68%)	0 (0%)
Fulfills 2006 classification criteria	43 (75%)	1 (4%)

aPL = antiphospholipid antibody, anti-β2GPI = anti-beta-2 glycoprotein I

Table 2. Performance evaluation of the 2023 and 2006 APS classification criteria in pediatric patients with antiphospholipid syndrome and lupus

Criteria	Sensitivity	Specificity	PPV	NPV	AUC	F1
2023	0.68	1.00	1.00	0.58	0.84	0.81
2006	0.75	0.96	0.98	0.63	0.86	0.85

PPV=positive predictive value , NPV=negative predictive value, AUC=area under the curve

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

meet clinical and 2 failed to meet lab thresholds. To better understand the profile of missed cases, we compared domain scores between false negatives and the overall cohort. False negatives under the 2006 criteria had significantly lower laboratory scores ($p = 0.033$), suggesting under-recognition of patients with weaker serologic profiles. No significant differences were observed in clinical scores.

Conclusion: Both the 2006 and 2023 APS criteria perform reasonably well in children but with lower sensitivity than in adults. The 2006 criteria are more sensitive—especially for cases with milder, lower-scoring aPL profiles—while the 2023 criteria offer greater specificity. Their high concordance supports the reliability of both systems, but also underscores the need to refine adult-based criteria to better capture true pediatric APS. Our ongoing multisite study (target n=300 across 7 sites), using expert-confirmed diagnoses, will help guide optimal classification in this population.

Disclosure: J. Madison: None; **E. Sloan**: None; **C. Saez**: None; **O. Kwan**: None; **K. Lewis**: None; **J. Marilao**: None; **B. Baay**: None; **R. Elrefai**: None; **M. Dale**: None; **D. McCurdy**: None; **J. Bhatt**: None; **S. Goteti**: None; **E. Ogbu**: Cartesian Therapeutics, 2; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **Y. Zuo**: None.

Abstract Number: 0127

Single-cell Profiling of Dermal Endothelial Cells Reveals Potential Cell-Cell Interactions in Patients with APS and a History of Cardiac Valve Disease

Wenying Liang[1], Qinmengge Li[2], Jacqueline Madison[1], Ran Jing[1], Emily Chong[1], Yiran Shen[1], Rachael Bogle[3], Srilakshmi Yalavarthi[1], Cyrus Sarosh[4], Ajay Tambralli[1], Yu (Ray) Zuo[1], Johann Gudjonsson[1], Hui Shi[5], Pei-Suen Tsou[1], Alex Tsoi[3] and **Jason S. Knight**[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ypsilanti, MI, [3]University of Michigan, Holland, OH, [4]University of Michigan, Temperance, MI, [5]Shanghai Jiaotong University Affiliated Ruijin Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Some of the rarer manifestations of antiphospholipid syndrome (**APS**), such as cardiac valve disease, remain poorly understood at the molecular level. A previous study profiling skin biopsies from a few patients with marked livedo racemosa preliminarily identified the endothelial cell (**EC**) Hippo-YAP1-CCN2 axis as a key player in APS vasculopathy. Here, we expanded dermal single-cell profiling to include 30 individuals with primary APS, with the goal of identifying unique tissue signatures associated with some of the more poorly understood features of APS, including cardiac valve disease and nephropathy. In this abstract, we focused on the ligand-receptor pairs predicted to be driving cellular communication in the dermis of patients with a history of cardiac valve disease.

Methods: Single-cell RNA sequencing was used to characterize upper-thigh skin biopsies (epidermis removed) from 30 patients with primary APS (including a subset of eight patients with confirmed valve disease) and 14 healthy controls. Cell-cell interaction analysis was performed using CellPhoneDB to identify enriched (i.e., highly correlated)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

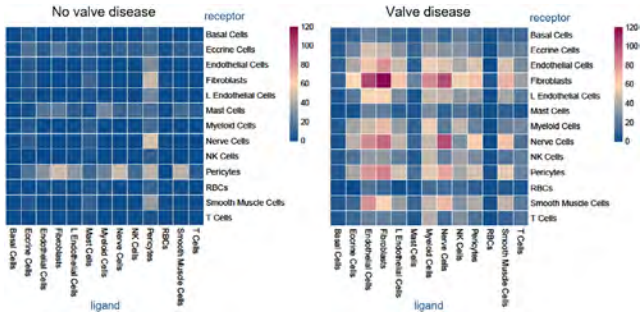


Figure 1: Dermal ligand-receptor analysis of patients with valve disease. Potentially interacting ligands (x-axis) and receptors (y-axis) were compared between APS patients with a history of valve disease (n=8, right panel) and those without (n=22, left panel). The analysis used CellPhoneDB to identify enriched (i.e., highly correlated) ligand-receptor pairs between dermal cell types. Associations with a history of valve disease were tested via logistic regression.

ligand-receptor pairs between ECs and other potentially interacting cell types. Differential expression and pathway enrichment were evaluated using g:Profiler. Associations with a history of valve disease were tested via logistic regression.

Results: Thirteen cell types were detected within the dermis, with endothelial cells representing 18% of the population in primary APS patients, compared with 16% in controls ($p < 0.001$). In patients with valve disease (n=8), versus those without (n=22), endothelial cells showed a markedly increased potential for interactions with myeloid cells, smooth muscle cells, and fibroblasts, amongst others (**Figure 1**). For myeloid cells, highlighted interactions between EC ligands and myeloid cell receptors included CCL23-CCR1, ICAM2-CD209, JAG2-NOTCH1, and DLL1-NOTCH1, with the potential to support inflammatory signaling, leukocyte adhesion, and immune activation. Featured EC interactions with smooth muscle included ANGPT2-TIE2, EDN1-EDNRA, JAG2-NOTCH3, and EFNB1-EPHB6, suggesting increased vascular constriction and remodeling. Notable ligand-receptor interactions between endothelial cells and fibroblasts included PDGFB-PDGFRA, CCL2-CCR2, FN1-ITGA5, and WNT2B-SFRP2, emphasizing fibroblast activation and extracellular matrix (**ECM**) transformation. Finally, pathway analysis underscored the potential for more leukocyte adhesion, angiogenesis, and ECM remodeling in the tissues of APS patients with a history of valve pathology.

Conclusion: Our findings reveal that endothelial cells of patients with a history of valve disease have significant potential—through their production of chemokines, cell adhesion molecules, and ECM-interacting molecules—to engage in proinflammatory and profibrotic interactions with myeloid cells, smooth muscle cells, and fibroblasts. The identified interactions and pathways provide a roadmap for future research into the valvular pathology that causes significant morbidity for some patients living with APS.

Disclosure: W. Liang: None; **Q. Li**: None; **J. Madison**: None; **R. Jing**: None; **E. Chong**: None; **Y. Shen**: None; **R. Bogle**: None; **S. Yalavarthi**: None; **C. Sarosh**: None; **A. Tambralli**: None; **Y. Zuo**: None; **J. Gudjonsson**: None; **H. Shi**: None; **P. Tsou**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0128

Defining a Consensus for Critical Data Fields for International Pediatric Antiphospholipid Syndrome Research

Jheel Bhatt[1], Elizabeth Sloan[2], Selcan Demir[3], Mojca Avramovic[4], Seza zen[5], Doruk Erkan[6], Tadej Avcin[7], Delphi collaborators, CARRA SLE-APS Workgroup, PRES SLE Working Party, [1]Advent Health Orlando, Orlando, FL, [2]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [3]Eskisehir Osmangazi University, Eskişehir, Turkey, [4]University Children's Hospital, Ljubljana, Slovenia, [5]Hacettepe University Medical Faculty, Ankara, Turkey, [6]Hospital for Special Surgery, New York, NY, [7]University Children's Hospital University Medical Center Ljubljana, Ljubljana, Slovenia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Pediatric antiphospholipid syndrome (APS) is a rare, thrombo-inflammatory autoimmune disease characterized by thrombosis and nonthrombotic manifestations in patients with persistent positive antiphospholipid antibodies, with clinical features that differ from adult APS. Current APS classification criteria are derived from adult data, and pediatric APS data collection is fragmented and inconsistent between institutions and regions. This project aims to develop an international consensus that defines critical data fields to facilitate international registry-based pediatric APS research.

Methods: Data fields were compared from existing International Ped-APS Registry and CARRA Registry, which identifies patients with APS within the lupus cohort. The 2023 ACR/EULAR APS classification criteria were reviewed and systematic literature review of pediatric APS between 2003-2024 was conducted to identify potential data elements for future registries (Figure 1). Delphi surveys were completed by physicians with APS experience, which included pediatric rheumatologists, med/peds rheumatologists, adult rheumatologists, and pediatric hematologists representing 12 countries and two caregiver representatives. Items were scored from 1 (not important) to 9 (very critical). Consensus "in" was reached for core items

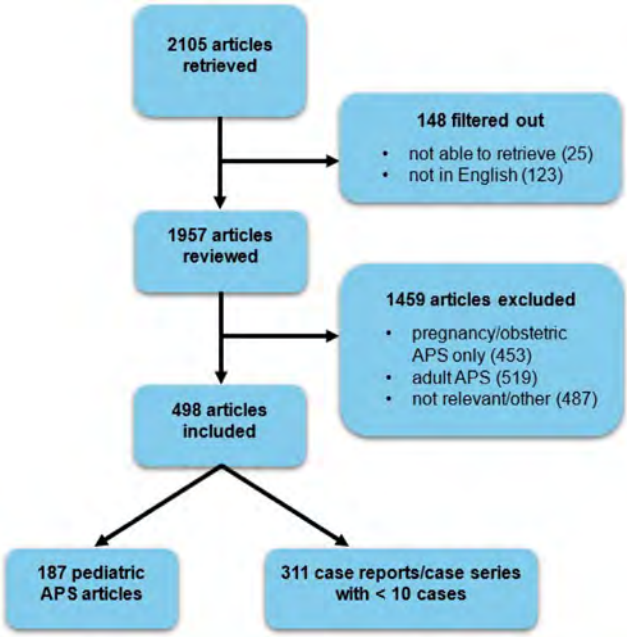


Figure 1. Flow diagram of literature review to identify candidate items

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

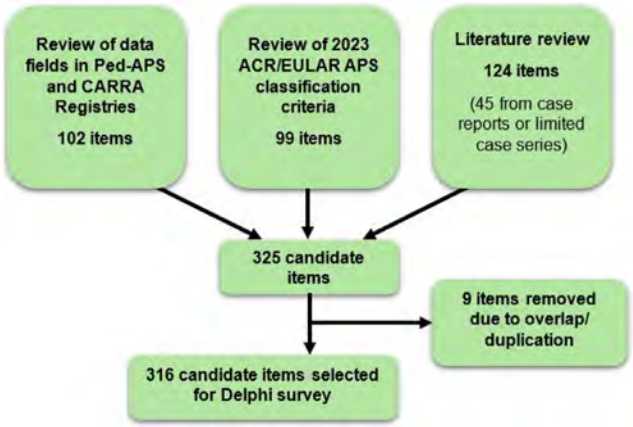


Figure 2. Flow diagram showing selection process of candidate items for Delphi survey to identify critical data fields in pediatric APS registries

scored > 7 by > 70% of experts, as well as all items included in the adult 2023 APS Classification Criteria. Consensus "out" was reached for items with average score < 5. The remaining items were labeled "equivocal" for voting at a hybrid consensus meeting. During the meeting, items with ≥80% agreement were included in the final dataset (either Core or Expanded),

Table 1: List of consolidated core and expanded clinical datasets

SECTOR	CORE Dataset	Expanded Dataset
DEMOGRAPHICS AND MEDICAL HISTORY	Biologic Sex Year of birth Year of 1st detection of aPL Year of 1st aPL-related clinical manifestation Year of APS diagnosis	Year of the last follow-up visit
FAMILY HISTORY		Family history of APS or other autoimmune diseases (specify which) Family history of thrombosis
UNDERLYING DISEASE	SLE Other autoimmune diseases (specify which)	
CONGENITAL PROTHROMBOTIC STATES:	Presence of hereditary or other acquired thrombophilia (e.g., Factor V Leiden, Prothrombin 20210A mutation, AT deficiency, Protein C/S deficiency, or others - specify)	
ACQUIRED RISK FACTORS FOR THROMBOSIS	Acquired risk factors for thrombosis – any Hormone replacement therapy, estrogen-containing oral contraceptives, on-going IVF Arterial thrombosis Venous thromboembolism Small vessel thrombosis Recurrent thrombosis Microvascular thrombosis on pathology Fetal loss/prefetal loss/preeclampsia Location of thrombosis	Hospital admission Major trauma Surgery Acute severe infection (if yes please specify trigger: viral or bacterial) Cardiovascular risk factors (e.g., arterial hypertension, tobacco smoking, hyperlipidemia, diabetes mellitus, please specify).
HEMATOLOGICAL	Thrombocytopenia Hemolytic anemia/autoimmune hemolytic anemia LA associated hypoprothrombinemia syndrome	
NEUROLOGICAL	Ischemic event, if yes specify (e.g., ischemic stroke, acute hemiplegia) Transient ischemic attack Chorea	Cerebral white matter lesions or changes on MRI, including atypical multiple sclerosis Epilepsy/seizures
SKIN	Livedo racemosa Livedoid vasculopathy	Skin ulcer or cutaneous necrosis Digital ischemia Livedo reticularis
CARDIOPULMONARY	Cardiac valve thickening Cardiac valve vegetation Libman Sachs /noninfectious endocarditis Pulmonary hemorrhage, including pulmonary alveolar hemorrhage and pulmonary capillaritis	Pulmonary hypertension
RENAL	aPL nephropathy chronic/acute	
GASTROINTESTINAL		Budd Chiari syndrome
ENDOCRINE	Adrenal hemorrhage	
MUSKULOSKELETAL		Avascular bone necrosis/osteonecrosis
OPHTHALMOLOGIC	Ischemic retinopathy	
TREATMENT	Anticoagulation therapy (drug, dose, duration) Target INR reached Antiaggregation therapy (drug, dose, duration) Treatment of underlying disease (drug, dose, duration) Immunosuppressive treatment of APS - any Immunosuppressive treatment for APS - specify	Adverse effects of anticoagulation (e.g., bleeding) Other therapy (specify)
FOLLOW UP/OUTCOME	New thrombosis Year of new thrombosis Treatment at the time of new thrombosis development Location of the new thrombosis Treatment of the new thrombosis Identified triggers of new thrombosis Death, related to APS Year of death, related to APS	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and items failing to meet consensus were either excluded or revised and re-evaluated when appropriate. Items scoring $\geq$6 were eligible for either Core or Expanded datasets. Items scoring $\geq$ 5 but < 6 were only voted upon for the Expanded dataset.

Results: Thirty-two Delphi surveys were completed in round 1 and twenty-six in round 2. Two caregiver representatives completed a modified Delphi. Of 316 final candidate items (Figure 2), 72 items reached consensus "in", 87 items were consensus "out" and 157 "equivocal" items were discussed at the hybrid consensus meeting (Table 1). Nineteen participants voted upon Core and Expanded Datasets for each "equivocal" item. The final dataset included 60 core data elements and 22 expanded data elements, spanning 18 thematic domains.

Conclusion: Through systematic evaluation of existing registries, literature review, and Delphi process, we have identified several critical variables to inform future pediatric APS registries. By leveraging international expertise and integrating it with patient patient perspectives, we are laying a solid foundation for the development of a harmonized dataset to advance pediatric APS research efforts globally.

Disclosure: J. Bhatt: None; **E. Sloan**: None; **S. Demir**: None; **M. Avramovic**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **D. Erkan**: Chugai, 5, GlaxoSmithKlein(GSK), 1, 5, 6, Merida Biosciences, 2, NIH, 5, Roche, 1, Roivant Sciences, 2, Star Therapeutics, 1, Up-To-Date, 9; **T. Avcin**: None.

Abstract Number: 0129

Analysis of Antiphosphatidylserine/prothrombin Antibodies as a Predictor of Lupus Anticoagulant in the Pediatric Population

Jonathan Marilao[1], Sean Yates[2] and Elizabeth Sloan[3], [1]University of Texas Southwestern, Dallas, TX, [2]University of Texas Southwestern, Dallas, [3]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid Syndrome (**APS**) is a systemic thromboinflammatory autoimmune disease characterized by thrombotic or obstetric events occurring in individuals with persistently positive antiphospholipid antibodies (**aPL**). Recently, research in adult populations has shown that antiphosphatidylserine/prothrombin antibodies (**aPS/PT**) are a reliable predictor of lupus anticoagulant (**LA**). These findings have yet to be reproduced in the pediatric population. We aim to ascertain the sensitivity, specificity, negative predictive value, and positive predictive value of aPS/PT to anticardiolipin (**aCL**), anti-beta-2 glycoprotein I (**aβ2GPI**), and LA in the pediatric population.

Methods: A retrospective chart review was performed of pediatric patients from 2019 to 2024 who had a full aPL panel (aPS/PT, aCL, aβ2GPI, LA) obtained as part of their medical evaluation for suspected or diagnosed conditions potentially related to aPL positivity. A cut-off of 40 units was used for aPL positivity for all antibodies. LA positivity was determined in accordance with international guidelines, and LA values obtained on anticoagulation were excluded. Sensitivities, specificities, negative predictive values, and positive predictive values were calculated with 95% confidence intervals.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics and aPL prevalence of 298 patients under investigation for aPL-associated clinical manifestations

Characteristics	Number (n)	Percent
Sex		
Male	82	27.52%
Female	216	72.48%
Race		
American Indian or Alaska Native	3	1.01%
Asian	23	7.72%
Black or African American	83	27.85%
White	170	57.04%
Mixed Race	7	2.35%
Other	12	4.03%
Ethnicity		
Hispanic	111	37.25%
Non-Hispanic	187	67.25%
Age in years (mean ± SD)	13.5 ± 4.3	
Rheumatologic Diagnosis	134	44.97%
Antiphospholipid Syndrome	12	4.03%
Systemic lupus erythematosus	89	29.87%
Sjogren's Syndrome	6	2.01%
Mixed connective tissue disease	2	0.67%
Undifferentiated connective tissue disease	12	4.03%
aPS/PT Positivity*	65	21.81%
aPS/PT IgG	30	10.01%
aPS/PT IgM	56	18.79%
LA Positivity†	41	13.76%
aCL Positivity*	16	5.37%
aCL IgG	6	2.01%
aCL IgM	12	4.03%
aCL IgA	3	1.01%
aβ2GPI Positivity*	15	5.03%
aβ2GPI IgG	9	3.02%
aβ2GPI IgM	8	2.68%
aβ2GPI IgA	5	1.68%
Triple positivity‡	10	3.36%

aPL: antiphospholipid antibodies. SD: standard deviation. aPS/PT: antiphosphatidylserine/prothrombin; LA: lupus anticoagulant. aCL: anticardiolipin. aβ2GPI: anti-beta-2 glycoprotein I.
**aPS/PT, aCL, and aβ2GPI titers ≥ 40 units*
†LA positivity determined by clinical laboratory data, in accordance with international guidelines
‡Triple positivity: positive LA, aCL, and aβ2GPI.

Results: Our cohort included 298 patients who underwent aPL testing (**Table 1**). The majority of patients were female (72.4%), white (56.7%), and non-Hispanic (62.8%). Mean age at time of laboratory evaluation was 13.5 ± 4.3 years. Almost half (45%) of the cohort were diagnosed with a rheumatologic disease, most commonly systemic lupus erythematosus (n=89). Twelve patients (4%) had confirmed APS. Twenty patients with rheumatologic disease experienced at least one thrombotic event (**Table 2**). In the entire cohort, 30 patients (10.1%) had positive aPS/PT IgG and 56 (18.8%) had positive aPS/PT IgM (**Table 1**). Positive aPS/PT IgG and IgM showed high specificity (IgG 96.9%, 95%CI 94.0-98.4%; IgM 89.5%, 95%CI 85.1-92.7%) and low to moderate sensitivity (IgG 53.7%, 95%CI 38.8-67.9%; IgM 70.7%, 95%CI 54.0-80.9%) for

Table 2. Clinical and non-thrombotic manifestations prevalence of 134 patients diagnosed with rheumatologic disease

	Any aPL Positive (n=53)		No aPL Positive (n=81)	
Clinical Manifestation	Number (n)	Percent	Number (n)	Percent
Obstetric	1	1.9 %	0	0 %
Thrombotic (any)	11	20.8 %	9	11.1 %
Venous thrombosis	9	17.0 %	8	9.9 %
Arterial thrombosis	3	5.7 %	1	1.2 %
Small vessel thrombosis*	1	1.9 %	0	0 %
Catastrophic APS	1	1.9 %	0	0 %
Non-Thrombotic Manifestations				
Thrombocytopenia	17	32.1 %	23	28.4 %
Autoimmune hemolytic anemia	12	22.6 %	11	13.6 %
Livedo reticularis/racemosa	5	9.4 %	3	3.7 %
White matter lesions on MRI	1	1.9 %	3	3.7 %
Seizure	2	3.8 %	2	2.5 %
APS nephropathy	1	1.9 %	0	0 %
Skin ulceration	3	5.7 %	2	2.5 %
Cardiac valve abnormality	0	0 %	0	0 %
Lupus nephritis	23	43.4 %	34	42.0 %

aPL: antiphospholipid antibodies. APS: antiphospholipid syndrome. MRI: magnetic resonance imaging.
**Confirmed by pathology*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Sensitivity, specificity, positive predictive value, and negative predictive value of antiphosphatidylserine/prothrombin antibodies to lupus anticoagulant and other antiphospholipid antibodies

	aPS/PT IgG				aPS/PT IgM			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
LA	53.66%	96.89%	73.33%	92.91%	70.73%	89.49%	51.79%	95.04%
aβ2GPI IgG	55.56%	91.35%	16.67%	98.51%	66.67%	83.04%	10.91%	98.77%
aβ2GPI IgM	75%	91.72%	20%	99.25%	100%	83.79%	14.54%	100%
aβ2GPI IgA	60%	90.78%	10%	99.25%	60%	82.25%	5.45%	99.18%
aCL IgG	100%	91.78%	20%	100%	100%	93.22%	10.91%	100%
aCL IgM	58.33%	91.96%	23.33%	98.13%	83.33%	84.27%	18.18%	99.18%
aCL IgA	66.67%	90.51%	6.67%	99.63%	66.67%	82.03%	3.64%	99.59%
Triple Positive	80%	92.36%	26.67%	99.25%	90%	83.68%	16.07%	99.59%

aPS/PT: antiphosphatidylserine/prothrombin. LA: lupus anticoagulant. aCL: anticardiolipin. aβ2GPI, anti-beta-2 glycoprotein I; PPV: positive predictive value. NPV: negative predictive value.
**Triple Positive: positive LA, aβ2GPI, and aCL*

LA positivity (**Table 3**). The negative predictive value of both aPS/PT IgG and IgM were high (>90%) for LA, aCL, and aβ2GPI. Ten patients were triple positive for LA, aCL, and aβ2GPI, and aPS/PT IgG was highly specific (92.4%, 95%CI 88.7-94.9%) and moderately sensitive (80%, 95%CI 49.0-96.5%). Negative predictive value of aPS/PT IgG and IgM for triple positivity exceeded 99%.

Conclusion: Overall, the high specificity combined with the strong negative predictive values of aPS/PT IgG and IgM highlights the ability to use such antibodies to rule in the presence of LA and other aPL when positive and to confidently exclude them when negative. These findings align with previous adult literature and highlight the usefulness of aPS/PT as a predictor of lupus anticoagulant in the pediatric population. As anticoagulation can affect the interpretation of LA, positive aPS/PT, when associated with a positive LA, offers a useful alternative to monitor LA regardless of patients' anticoagulation status. Additionally, with institutional variation in the conduct of LA, aPS/PT may provide a more comparable measure for multicenter research collaborations.

Disclosure: J. Marilao: None; **S. Yates**: None; **E. Sloan**: None.

Abstract Number: 0130

Plasminogen activator inhibitor 1 increases thrombotic risk in Antiphospholipid syndrome

Koshy Nithin Thomas[1], Pratibha Singh[2], Anu Balakrishnan[3], Amita Aggarwal[4] and Able Lawrence[5], [1]Christian Medical College, Vellore, Tamil Nadu, India, [2]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [3]Sanjay Gandhi Post Graduate Institute, India, Lucknow, Uttar Pradesh, India, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India, [5]SGPGIMS, Lucknow, Lucknow, Uttar Pradesh, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical characteristics of the antibody positive and antibody negative antiphospholipid syndrome groups

Clinical feature	aPL positive (n=38)	aPL negative (n=25)	p-value
Male: Female	5:33	5:20	0.5
Age (years)	34 (±8.1)	38 (±9.8)	0.08
Primary APS	24 (63%)	14 (56%)	0.6
Vascular	29 (76%)	14 (56%)	0.1
Obstetric	19 (50%)	15 (60%)	0.4
Vascular and Obstetric			
Fetal loss <10w	6 (15%)	7 (28%)	0.3
Fetal loss >10w	14 (36%)	12 (48%)	0.4
Preterm with placental insufficiency	6 (15%)	5 (20%)	0.7
Venous	16 (42%)	13 (52%)	0.6
Deep Vein thrombosis	13 (36%)	8 (32%)	1
Venous thrombosis excluding lower limb DVT	**3 (7%)**	**7 (28%)**	**0.02**
Arterial	16 (42%)	4 (16%)	0.05
Stroke	9 (23%)	2 (8%)	0.1
Gangrene	3 (7%)	1 (4%)	1
COVID vaccination	28 (73)	16 (64%)	1
BMI (kg/m2)	24.3 (±4.0)	23.0 (±5.9)	0.3
HCQ	23 (60%)	11 (44%)	0.3
Prednisolone	18 (47%)	11 (44%)	1
PAI-1 level (ng/ml)	16.3 (±6.8)	13.7 (±8.0)	0.1
tPA level (pg/ml)	396.6 (±698.7)	173.6 (±306)	0.1

aPL antiphospholipid antibody; DVT deep vein thrombosis; PAI 1 plasminogen activator inhibitor 1; tPA tissue plasminogen activator

Table 2. PAI-1 as a predictor of vascular and obstetric antiphospholipid syndrome

	Unadjusted OR			Adjusted OR			
PAI-1 (ng/ml)	OR	CI (95%)	p-value	PAI-1 (ng/ml)	OR	CI (95%)	p-value
Thrombosis	**1.11**	**1.01 – 1.22**	**0.02**				
				Age adjusted	1.10	1.00 – 1.21	0.03
				Gender adjusted	1.11	1.01 – 1.21	0.02
				BMI adjusted	1.11	1.01 – 1.22	0.03
				Lupus adjusted	1.11	1.01 – 1.22	0.02
				aPL adjusted	1.10	1.00 – 1.21	0.03
				Prednisolone adjusted	1.10	1.00 – 1.21	0.04
Obstetric	0.90	0.82 – 0.99	0.03				

Background/Purpose: Antiphospholipid antibody syndrome (APS) is a common cause for acquired thrombophilia. The group termed 'seronegative' APS has not made any headway in the revised APS ACR 2023 criteria as no new antibodies were included. Increased levels of Plasminogen activation inhibitor -1 (PAI-1) has been observed in patients with connective tissue disease. It may account for the increased risk of thrombotic events in APS the form of a second hit or function independently as a risk factor for thrombosis. We assessed the role of PAI-1 in antiphospholipid syndrome in relation to the presence of criteria antiphospholipid antibodies (aPL).

Methods: A case control study was done at a tertiary level Rheumatology centre in North India between September 2022 and 2024. The primary objective was to compare PAI-1 levels between those with APS (aPL+ APS), patients with thrombosis or obstetric morbidity but with antibody profile not satisfying criteria as put forward by the modified Sapporo criteria (aPL-APS) and healthy controls. An SLE group without APS or aPL was also included. Adults (age > 18 years) who had clinical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

features of APS as per the Modified Sapporo criteria were enrolled. Plasma levels of PAI-1 was estimated by sandwich ELISA. To obtain a power of 0.99 and a confidence interval of 0.95, a sample size of 24 was required in each group. Plasma tPA levels were also estimated in each group. Comparison between the 4 groups was done by ANOVA. Analysis was done using IBM SPSS statistics for windows [Version 26.0].

Results: Sixty-three cases of APS (females 84%) with mean age 35.2 (±8.9) were included. This included 38 aPL+APS and 25 aPL-APS cases (Table 1). Twenty-five SLE cases and 27 healthy controls were also included. **Plasma PAI-1 levels were higher in aPL+APS compared to healthy controls (16.3 vs 10.6 ng/ml; p-0.03)**. The PAI-1 levels were similar among aPL-APS group, SLE controls and healthy controls. No specific aPL antibody (anticardiolipin, anti-β2GP1 or lupus anticoagulant) showed any association with PAI-1 levels. **PAI 1 level was a positive predictor of thrombosis [OR 1.11 (1.01 – 1.22); p – 0.03]**. This association remained significant after adjusting for age, gender, BMI, presence of SLE, presence of antiphospholipid antibodies and prednisolone intake (Table 2). There was no dichotomy in risk for arterial or venous thrombosis. Those with recurrences did not have higher PAI-1 levels [OR 1.07 (95% CI 0.98 – 1.17), p 0.09]. Higher PAI-1 levels reduced the risk of obstetric APS (n= 20) [OR 0.90 (0.82- 0.99). p =0.03]. Plasma tPA was higher in both antiphospholipid groups and SLE compared to healthy controls. It did not have any effect on thrombosis. There was a poor correlation between tPA and PAI-1 levels (r-0.11).

Conclusion: Plasminogen activation inhibitor 1 is an independent contributor of thrombosis in APS. Targeting PAI-1 directly or by drug repurposing may improve outcomes in APS.

Disclosure: K. Thomas: None; **P. Singh**: None; **A. Balakrishnan**: None; **A. Aggarwal**: None; **A. Lawrence**: None.

Abstract Number: 0131

Libman-Sacks Endocarditis in APS: A Case-Control Study of Clinical and Serologic Features

Kyla Rodgers[1], Cyrus Sarosh[2], Srilakshmi Yalavarthi[3], Emily Becker[4], Yiran Shen[5], Kaitlyn Sabb[4], Peter Hagan[4], Ajay Tambralli[5], Jacqueline Madison[5], Yu (Ray) Zuo[5] and Jason S. Knight[5], [1]University of Michigan, Whitmore Lake, MI, [2]University of Michigan, Temperance, MI, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, [4]University of Michigan, Ann Arbor, [5]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Libman-Sacks endocarditis (LSE) is an inflammatory phenomenon, typically involving the mitral or aortic valve, that affects some patients with systemic lupus erythematosus (SLE) and/or antiphospholipid syndrome (APS). These thrombotic vegetations can cause valve failure or become a nidus for bacterial endocarditis. The pathophysiologic mechanisms underlying LSE, including the role played by specific APS-associated autoantibodies (aPL), are poorly understood. Here, we set out to define any unique clinical characteristics of patients with a history of LSE. We also sought preliminary evidence of inflammatory pathways more likely to be activated in these patients.

Methods: We identified cases of LSE from an academic cohort of approximately 300 patients with durably positive aPL testing; roughly 75% of the cohort met criteria for APS. All available TTE and TEE reports were reviewed to identify APS patients with and without valve disease. Those with TTE/TEE evidence of LSE and/or those who had undergone valvular replacement

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

for LSE were selected as cases (n=10). Patients with positive blood cultures or with valve thickening without vegetation were excluded. Age- and sex-matched controls were randomly selected from the cohort of APS patients with normal TTE/TEE results (n=20). Clinical characteristics, including comorbid conditions and standard laboratory results (e.g., platelet count, complement levels), were noted. Plasma levels of selected aPL were measured by ELISA. We also assessed biomarkers tending to track with activation of endothelial cells (E-selectin), platelets (P-selectin), and neutrophils (calprotectin).

Results: In our patient population, the average age was 47.9 years in the case group and 47.8 years in the control group. In both groups, 80% of patients were female, and 20% had SLE. LSE most frequently involved the mitral valve (90%), followed by the aortic valve (10%). Overall, 60% of patients required valve surgery. Patients with LSE were significantly more likely to have a history of hypertension (80% vs. 25%, p=0.007), catastrophic APS (30% vs. 0%, p=0.039), and white matter hyperintensities (70% vs. 25%, p=0.045) than those without; significant differences were not found in the rates of hyperlipidemia (30% vs. 5%), venous thrombosis (60% vs. 50%), or stroke (70% vs. 40%). Patients with LSE tended to have lower platelet counts (mean 225 K/μl vs. 289, p=0.028), as well as lower complement C4 levels (mean 19.6 mg/dl vs. 25.5, p=0.029). LSE patients were more likely to have positive testing for anti-β_2GPI IgG and anti-PS/PT IgG; however, these differences were not statistically significant. Though E-selectin and calprotectin levels were not statistically different between the groups, P-selection was increased in the LSE patients (mean 32.2 ng/ml vs. 25.0, p=0.035).

Conclusion: Durably aPL-positive patients with a history of LSE were more likely to have a history of hypertension, catastrophic APS, and white matter hyperintensities, as compared to those without. They also tended to have lower platelet counts and complement C4 levels. Candidate biomarker testing suggests that platelet activation likely deserves further study as a contributor in the pathogenesis of aPL-associated LSE.

Disclosure: K. Rodgers: None; **C. Sarosh**: None; **S. Yalavarthi**: None; **E. Becker**: None; **Y. Shen**: None; **K. Sabb**: None; **P. Hagan**: None; **A. Tambralli**: None; **J. Madison**: None; **Y. Zuo**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

Abstract Number: 0132

Increased Expression of Gas6 and Its Tyrosine Kinase Receptor Tyro3 Are Associated with Antiphospholipid Syndrome

Fanshu Li, Ranran Yao, Fanlei Hu, **Liling Xu** and Chun Li, Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Growth arrest specific protein 6 (Gas6) is a member of the vitamin K-dependent protein family. It participates in apoptosis, inflammatory response and immunomodulation by binding to its receptors Tyro3, Axl and Mer (TAM). Previous studies have suggested that Gas6 is able to affect the coagulation system by regulating platelet and vascular cell function through the TAM signaling pathway. However, its role in antiphospholipid syndrome (APS) is unclear. This research focuses on the expression level and clinical significance of Gas6 in APS to further understand the role of Gas6/TAM signaling pathway in the pathogenesis of APS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: 102 patients diagnosed APS with Sydney criteria were recruited from the Department of Rheumatology and Immunology at Peking University People's Hospital. 104 healthy volunteers were enrolled as control. Among them, the serum Gas6 concentrations of 92 APS patients were determined by ELISA, and the relationship between Gas6 and clinical characteristics was analyzed. The expression of TAM receptor on the surface of peripheral blood monocytes in 10 APS patients was further examined. The results were analyzed by Mann-Whitney U test, Kruskal-Wallis test followed by Dunn's posttest for multiple comparisons and Spearman's rank correlation test as appropriate. $p < 0.05$ was considered significant.

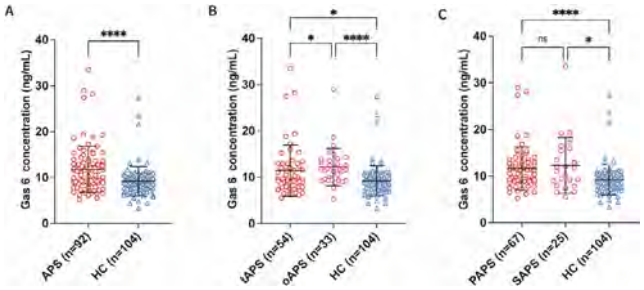


Fig.1. A) Serum Gas6 concentration was significantly higher in antiphospholipid syndrome (APS) patients than in healthy controls (HC) ($p < 0.0001$). B) Serum Gas6 concentration was significantly higher in both thrombotic antiphospholipid syndrome (tAPS) ($p = 0.0203$) and obstetric antiphospholipid syndrome (oAPS) ($p < 0.0001$) patients, and the concentration in the oAPS was significantly higher ($p = 0.0476$). C) Serum Gas6 concentration was significantly higher in both primary antiphospholipid syndrome (PAPS) ($p < 0.0001$) and secondary antiphospholipid syndrome (SAPS) ($p = 0.0008$) patients, and there was no significant difference between them ($p > 0.9999$).

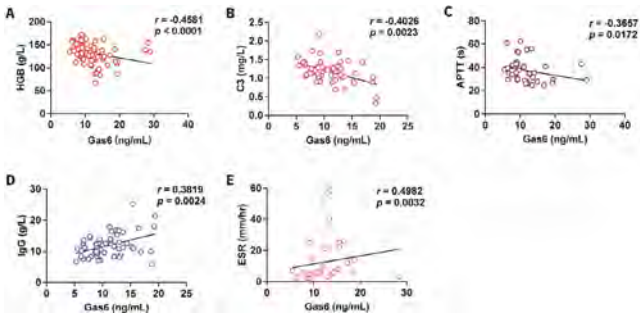


Fig.2. Correlation analysis between serum Gas6 concentration and clinical features in APS patients, which showed negative correlation with HGB (A), C3 (B), APTT (E), and positive correlation with IgG (C) and ESR (D).

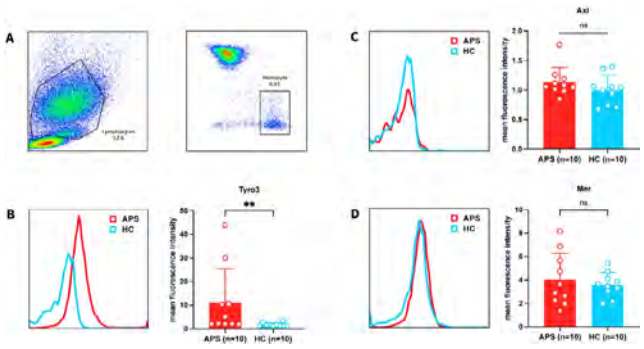


Fig.3. A) Monocytes in the peripheral blood of APS patients were sorted by CD14 and CD16. B) The expression level of Tyro3 on the surface of monocytes in the peripheral blood of APS was significantly higher than HC ($p = 0.0015$). C/D) There was no significant difference in the expression levels of Axl ($p = 0.2176$) and Mer ($p = 0.9705$) between APS and HC.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Compared to HC, APS patients had higher serum expression of Gas6 (11.81±5.02 vs. 9.22±3.22 ng/mL, $p < 0.0001$) (Fig.1A). Furthermore, serum Gas6 concentrations in patients with thrombotic APS (tAPS) and obstetric APS (oAPS) were analyzed. While oAPS was higher than tAPS (12.21 ± 4.057 vs. 11.42 ± 5.537 ng/mL, $p = 0.0476$) (Fig.1B). And serum Gas6 concentrations in tAPS ($p = 0.0203$) and oAPS ($p < 0.0001$) were significantly higher than in HC. In PAPS (11.63 ± 4.655 ng/mL, $p < 0.0001$) and SAPS (12.28 ± 5.973 ng/mL, $p = 0.0008$), serum Gas6 concentrations were higher than in HC, with no significant difference between PAPS and SAPS ($p > 0.9999$) (Fig. 1C). Next, the correlation between patients' serum Gas6 concentrations and clinical features was explored. The results showed that patients' serum Gas6 concentrations showed negative correlation with HGB ($r = –0.4581$ $p < 0.0001$), C3 ($r = –0.4026$ $p = 0.0023$), and APTT ($r = –0.3657$ $p = 0.0172$), and positive correlation with IgG ($r = 0.3819$ $p = 0.0024$) and ESR ($r = 0.4982$ $p = 0.0032$) (Fig.2). Moreover, Gas6 concentration was higher in patients with low C3 ($p = 0.0015$) and low C4 ($p < 0.0001$) than in patients with normal complement, and were also higher in ANA-positive patients than in ANA-negative patients ($p = 0.0101$). The expression level of Tyro3 on the surface of peripheral blood monocytes in APS (MFI: 11.01 ± 14.44) was significantly higher than HC (MFI: 1.744 ± 0.7233, $p = 0.0015$) (Fig. 3B). For Axl (MFI: 1.136 ± 0.2480 vs. 0.9975 ± 0.2477, $p = 0.2176$) and Mer (MFI: 4.022 ± 2.257 vs. 3.576 ± 1.049, $p = 0.9705$), no significant differences were detected between APS and HC (Fig. 3C/D).

Conclusion: Serum Gas6 was significantly overexpressed in APS patients and correlated with parameters of inflammation, immunity and coagulation, suggesting that the Gas6/TAM signaling pathway may play a potential role in APS.

Disclosure: F. Li: None; **R. Yao**: None; **F. Hu**: None; **L. Xu**: None; **C. Li**: None.

Abstract Number: 0133

Differences in cardiovascular risk factor control between primary and systemic lupus erythematosus-related antiphospholipid syndrome in a multiethnic cohort of 1003 patients with antiphospholipid syndrome: the SUrvey of cardiovascular disease Risk Factors (SURF) in SLE and APS project

Eleana Bolla[1], Anne Grete Semb[2], Michelle Petri[3], Petros Sfikakis[4], Bahar Artim Esen[5], Gabriela Hernandez-Molina[6], Eric Hachulla[7], Haner Direskeneli[8], George Karpouzas[9], Marta Mosca[10], Mohit Goyal[11], Nathalie Costedoat-Chalumeau[12], Angela Tincani[13], Ayten Yazici[14], Karoline Lerang[15], Anne Troldborg[16], Sofia Ajeganova[17], Tatiana Popkova[18], Elisabet Svenungsson[19], Nikos Pantazis[20], **Maria Tektonidou**[21] and SURF-SLE and APS collaborators, [1]Rheumatology Unit, First Department of Propaedeutic Internal Medicine, Joint Academic Rheumatology Program, Medical School, National and Kapodistrian University of Athens, Laiko General Hospital, Athens, Greece, [2]Preventive Cardio-Rheuma clinic, Dept Rheum, Diakonhjemmet Hospital, Oslo, Norway, Oslo, Norway, [3]Johns Hopkins University School of Medicine, Timonium, MD, [4]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [5]Istanbul University, Istanbul, Istanbul, Turkey, [6]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Federal District, Mexico, [7]University of Lille, LILLE, France, [8]Marmara University, ISTANBUL, Turkey, [9]Harbor-UCLA Medical Center, Torrance, CA, [10]University of Pisa, Pisa, Pisa, Italy, [11]CARE Pain & Arthritis Centre, Udaipur, Rajasthan, India, [12]Inserm DR Paris 5, Paris, France, [13]ASST Spedali Civili-University of Brescia, Gussago, Brescia, Italy, [14]Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey, [15]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [16]Aarhus University Hospital, Aarhus, Denmark, [17]Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden, [18]V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, [19]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden, [20]Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Athens, Greece, [21]National and Kapodistrian University of Athens, Athens, Greece

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Cardiovascular disease (CVD) in antiphospholipid syndrome (APS) is driven by antiphospholipid antibody-mediated immunothrombotic mechanisms and traditional cardiovascular risk factors (CVRFs). Although the EULAR recommendations for cardiovascular risk management highlighted the importance of CVRF control, CVRF target achievement and the differences between primary APS (PAPS) and systemic lupus erythematosus (SLE)/APS remain uncertain.

In the context of the SUrvey of Cardiovascular Disease Risk Factors-SURF in SLE and APS project (1), this study aimed to assess the prevalence and control of traditional CVRFs in a multi-centre group of SLE/APS and PAPS patients across four continents.

Methods: CVRF data were collected from medical records in 17 centres from 11 countries between 2015 and 2020 (extended to 2022 due to COVID-19 pandemic). We evaluated the prevalence of traditional CVRFs, and individual's cardiovascular risk (low/moderate/high/very-high) using the Systematic Coronary Risk Evaluation (SCORE) algorithm. Target attainment was assessed for the following CVRFs: blood pressure (BP) (< 140/90 mm Hg), lipids, smoking, and body mass index (BMI) according to 2016 European Society of Cardiology guidelines, as well as a composite CVRF (at least two, three, and all four CVRF targets of BP, smoking, low-density lipoprotein [LDL], BMI). An additional BP target of < 130/80 mmHg was assessed according to the 2022 EULAR recommendations for cardiovascular risk management. Multivariable regression models were applied.

Results: 1003 patients meeting the Sydney APS criteria (median age 47.0 years, females: 77.7%, White: 66.2%, median disease duration 11.0 years) were included; 539 with PAPS and 464 with SLE/APS (additionally fulfilling 2012 ACR SLE classification criteria). We found a high CVRF prevalence (hypertension 41.0%, hyperlipidemia 34.3%, obesity 32.1%, current smoking 19.3%) and inadequate individual (BP < 130/80 mm Hg, body mass index [BMI], lipids) and multiple CVRF control in the entire APS cohort.

Higher prevalence of hypertension (50.4% vs 32.8%, p< 0.001) and hyperlipidemia (39.7% vs 29.7%, p=0.001) was observed in SLE/APS versus PAPS, but a lower prevalence of current smoking (15.9% vs 22.3%, p=0.012). Patients with PAPS had worse target attainment than SLE/APS patients for smoking (no current smoking) (77.7% vs 84.1%, p=0.012), BP < 130/80 mmHg (47.9% vs 56.6%, p=0.007) and ≥2 CVRF targets in the entire group, and additionally for BMI, LDL, triglycerides and ≥3 CVRF targets in the high/very high CVD risk subgroup. In multivariable analysis, age, sex and arterial thrombosis history, were the main independent predictors of ≥3 and four target attainment.

Conclusion: In this large real-world survey, high prevalence and suboptimal CVRF control were observed in APS, highlighting the need for increased CVD risk awareness, especially in PAPS, a clinical entity with frequently under-recognised cardiovascular risk compared to SLE.

References:

1. Bolla E et al. Prevalence and target attainment of traditional cardiovascular risk factors in patients with systemic lupus erythematosus: a cross-sectional study including 3401 individuals from 24 countries. Lancet Rheumatol. 2024 :e447–59.

Disclosure: E. Bolla: None; **A. Semb**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **P. Sfikakis**: None; **B. Artim Esen**: None; **G. Hernandez-Molina**: None; **E. Hachulla**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, Pfizer, 5, Roche-Chugai, 5, Sanofi-Genzyme, 2, 5, Sobi, 5; **H. Direskeneli**: None; **G. Karpouzas**: Janssen, 1, Pfizer, 5, Scipher, 2; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **M. Goyal**: None; **N. Costedoat-Chalumeau**: Bristol-Myers Squibb(BMS), 6, Roche, 5, UCB Pharma France, 5; **A. Tincani**: Galapagos, 1, UCB, 1; **A. Yazici**: None; **K. Lerang**: None; **A. Troldborg**: None; **S. Ajeganova**: None; **T. Popkova**: None; **E. Svenungsson**: AstraZeneca, 11, Pfizer, 11; **N. Pantazis**: None; **M. Tektonidou**: None.

Abstract Number: 0134

Neutrophil Gasdermin D Pores as Potential Therapeutic Targets in APS-Associated Thromboinflammation

NaveenKumar Somanathapura[1], Thalia Newman[1], Chao Liu[2], Srilakshmi Yalavarthi[3], Cyrus Sarosh[4], Jacqueline Madison[1], Ajay Tambralli[1], Yu (Ray) Zuo[1] and Jason S. Knight[1], [1]University of Michigan, Ann arbor, MI, [2]University of Michigan, Superior Charter Twp, MI, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, [4]University of Michigan, Temperance, MI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Emerging evidence implicates neutrophil activation and neutrophil extracellular trap (**NET**) formation (i.e., NETosis) in amplifying APS-associated thromboinflammation. Gasdermin D (**GSDMD**), a substrate of inflammatory caspases that is best known for forming membrane pores during macrophage pyroptosis, can also support interleukin-1β (**IL-1β**) release and NETosis by neutrophils. Based on preliminary data demonstrating elevated inflammatory caspase activity in APS neutrophils, we investigated the potential role of neutrophil GSDMD in APS pathophysiology.

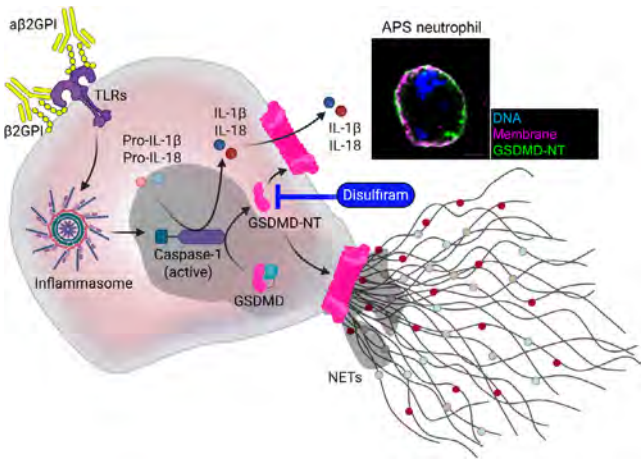


Figure 1. Schematic illustration depicting the role of active GSDMD in promoting the release of mature interleukins and NETs in APS neutrophils.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: NETosis was measured with the SYTOX Green assay and/or citrullinated histone H3-based quantification. Cleaved, pore-forming N-terminal GSDMD (**GSDMD-NT**) was identified using flow cytometry, immunoblotting, and confocal microscopy. Caspase-1 activity was measured with a luminescent assay. Plasma IL-1β, IL-18, and calprotectin were quantified by ELISA. *In vitro*, neutrophils were treated with inhibitors of GSDMD (disulfiram, necrosulfonamide) or caspase-1 (VX-765), followed by exposure to IgG fractions from controls or APS patients or affinity-purified anti-β2GPI. GSDMD-deficient (*Gsdmd*$^{-/-}$) mice were assessed in the context of APS IgG-accelerated venous thrombosis in the inferior vena cava (IVC).

Results: Compared with healthy controls (n=13), neutrophils from patients with primary APS (n=25) exhibited a 3-fold increase in caspase-1 activity ($p< 0.0001$), as well as a 4-fold higher formation of cleaved, pore-competent GSDMD-NT ($p< 0.01$). A 2.8-fold rise in plasma IL-18 levels ($p< 0.01$) was also appreciated in the same patient cohort. Notably, both neutrophil caspase-1 activity ($r=0.52$, $p=0.0058$) and plasma IL-18 ($r=0.41$, $p=0.031$) positively correlated with neutrophil GSDMD-NT, as did plasma calprotectin ($r=0.64$, $p=0.0024$), a biomarker of neutrophil activation and NET formation. *In vitro*, the exposure of control neutrophils to APS patient IgG significantly increased caspase-1 activity (2.5-fold, $p< 0.05$), GSDMD-NT formation (3-fold, $p< 0.01$), IL-1β secretion (3-fold, $p< 0.01$), and NETosis (3-fold, $p< 0.0001$). Confocal microscopy demonstrated that APS IgG triggered the preferential accumulation of GSDMD-NT in neutrophil plasma membranes. Furthermore, blocking GSDMD-NT cysteine-191, which is required for efficient pore formation, with either disulfiram or necrosulfonamide prevented neutrophil activation by APS IgG; the inhibition of caspase-1 with VX-765 was similarly protective. Compared with wild-type mice, *Gsdmd*$^{-/-}$ mice (n=5) exhibited a 2-fold reduction in plasma IL-1β ($p< 0.01$, n=5) and developed significantly smaller thrombi in response to APS IgG-associated thrombosis (mean 3.1 mg versus 7.6 mg, $p< 0.01$).

Conclusion: By releasing IL-1β, NETs, and other inflammatory mediators, GSDMD pores may play a crucial role in linking innate immunity to immunothrombosis in APS (**Figure 1**). Since GSDMD deficiency and inhibition (with repurposed agents like disulfiram) reduce neutrophil activation in APS models, targeting GSDMD could offer a new approach for managing inflammation-driven thrombosis that may not respond to anticoagulation alone.

Disclosure: N. Somanathapura: None; **T. Newman**: None; **C. Liu**: None; **S. Yalavarthi**: None; **C. Sarosh**: None; **J. Madison**: None; **A. Tambralli**: None; **Y. Zuo**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

Abstract Number: 0135

Rituximab in Antiphospholipid Syndrome: aPL Titer Decline and Clinical Outcomes

Omer Uludag[1], Soner Altın[2], Gamze Kemec[2], yasemin yalcinkaya[3], Ahmet Gul[3], Murat Inanc[3] and Bahar Artim Esen[4], [1]Istanbul University, Istanbul Faculty of Medicine, Division of Rheumatology, Istanbul, Turkey, [2]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Istanbul, Turkey, [3]Istanbul University, Istanbul Faculty of Medicine, Division of Rheumatology, Istanbul, Istanbul, Turkey, [4]Istanbul University, Istanbul, Istanbul, Turkey

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Baseline demographic, clinical, and laboratory characteristics and rituximab indications of the cohort

	Patients (*n*=43)		Patients (*n*=43)
Age at diagnosis (years), mean ± SD	30.6 ± 11.1	**Pregnancy morbidity, *n* (%)**	
Duration of disease (years), median (IQR)	12 (10.3)	<16w, ≥3 abortus	52 (100)
Female, *n* (%)	35 (81.4)	16-34 w, ≥1 feral death	46 (88.5)
Recurrent thrombosis, *n* (%)	28 (65.1)	Preeclampsia	12 (23.1)
Venous thrombosis, *n* (%)	28 (65.1)	Placental insufficiency	48 (92.3)
Arterial thrombosis, *n* (%)	28 (65.1)	**aPL serology, *n* (%)**	
Microvascular thrombosis, *n* (%)	16 (37.2)	Lupus anticoagulant	38 (88.4)
Livedo racemosa	2 (4.7)	aCL IgG	29 (67.4)
Livedoid vasculopathy	3 (7)	aCL IgM	9 (20.9)
aPL-nephropathy	10 (23.2)	aβ2GPI IgG	22 (51.2)
Pulmonary hemorrhage	6 (13.9)	aβ2GPI IgM	9 (20.9)
Myocardial disease	3 (7)	Triple aPL positive	21 (48.8)
Non-thrombotic manifestations, *n* (%)		**Rituximab indications, *n* (%)**	
Heart valve disease	26 (60.5)	Lupus nephritis	7 (16.3)
Thrombocytopenia	14 (32.6)	Thrombocytopenia	5 (11.6)
Autoimmune hemolytic anemia	6 (14)	Autoimmune hemolytic anemia	1 (2.3)
Livedo reticularis	10 (23.3)	Non-renal SLE activity	11 (25.6)
		Thrombotic APS	28 (65.1)

Table 2 Details of aPL-related events after rituximab

Patient	aPL titers before RTX	aPL titers after RTX	Event	Post-RTX duration	INR at event
1	aCL IgG: 264, IgM: 0 aβ2GPI IgG: 0, IgM: 0	aCL IgG: 264, IgM: 0 aβ2GPI IgG: 300, IgM: 0	Pulmonary hemorrhage	38 months	2.4
2	aCL IgG: 194, IgM: 0 aβ2GPI IgG: 100, IgM: 0	aCL IgG: 274, IgM: 0 aβ2GPI IgG: 85, IgM: 0	Myocardial infarction	24 months	1.4
3*	aCL IgG: 0, IgM: 0 aβ2GPI IgG: 0, IgM: 0	aCL IgG: 0, IgM: 0 aβ2GPI IgG: 0, IgM: 0	Stroke	19 months	Use only aspirin
4	aCL IgG: 86, IgM: 23 aβ2GPI IgG: 0, IgM: 0	aCL IgG: 0, IgM: 0 aβ2GPI IgG: 0, IgM: 0	Recurrence of digital ischemia	10 months	1**
5	aCL IgG: 0, IgM: 120 aβ2GPI IgG: 0, IgM: 150	aCL IgG: 0, IgM: 15 aβ2GPI IgG: 0, IgM: 13	Skin necrosis	81 months	Use only aspirin

* Only lupus anticoagulant positive
** Before the event, an INR of 7.6 was converted to an INR of 1 with K-vit due to vaginal bleeding.

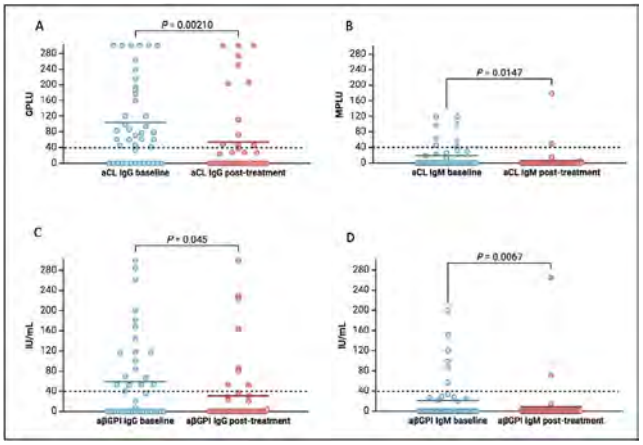


Figure 1 Change in aPL titers 6-12 months after rituximab

Background/Purpose: Rituximab treatment has been shown to be effective in non-thrombotic manifestations of APS and refractory catastrophic APS (CAPS). However, there are conflicting results regarding the change in aPL titers and limited data on the effect on thrombotic recurrence. The aim of this study was to evaluate the change in aPL titers over time, thrombotic recurrence and mortality rates, and treatment-related adverse events in APS patients treated with rituximab.

Methods: This retrospective single center study included 43 patients with thrombotic APS (11 with primary APS, 32 with SLE+APS) who received at least 1 cycle of rituximab (1000 mg on days 0 and 15). Baseline demographic, clinical, and serologic characteristics, aCL IgG/IgM and anti-β2-glycoprotein-I (aβ2GPI) IgG/IgM titers at 6 to 12 months of rituximab treatment were reviewed. The positivity threshold for aCL and aβ2GPI IgG/IgM was accepted as >40 GPL/MPL units or >99th percentile.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The demographic, clinical, and serologic characteristics of the patients are summarized in Table 1. The median follow-up period after rituximab was 3.5 (IQR: 5.8) years. Whilst the majority of patients were treated with rituximab for thrombotic APS, there were also patients who were received rituximab for lupus nephritis or non-renal SLE (Table 1). After 6-12 months of rituximab treatment, aPL positives decreased: aCL IgG from 29 (67.4%) to 13 (30.2%), aCL IgM from 9 (20.9%) to 2 (4.7%), aβ2GPI IgG from 22 (51.2%) to 9 (20.9%), and aβ2GPI IgM from 9 (20.9%) to 2 (4.7%). There was also a statistically significant decrease in aPL antibody titers (Figure 1). Five patients developed new events after rituximab and details are shown in Table 2. Five patients died during follow-up. Causes of death were sepsis in 1, traumatic intracranial hemorrhage in 1, and lupus nephritis in 1. One patient died due to recurrence of pulmonary hemorrhage 38 months after rituximab and 1 patient was lost due to treatment-refractory CAPS at 6th month of rituximab. Bacterial infections were observed in 15 patients (4 required hospitalization and 1 lost after ICU admission), COVID infections in 7 (2 required hospitalization), herpes zoster in 3. Finally, 2 patients developed allergic reactions, none of which were considered anaphylaxis.

Conclusion: In patients with thrombotic APS, rituximab treatment may prevent thrombotic recurrence with a significant decrease in aPL titers. It is noteworthy that 4 of 5 patients who developed recurrence after rituximab were not receiving effective anticoagulant therapy. These data suggest that under consideration of infectious complications, rituximab may be an effective alternative in high-risk APS patients with recurrent thrombosis.

Disclosure: O. Uludag: None; **S. Altın**: None; **G. Kemec**: None; **y. yalcinkaya**: None; **A. Gul**: None; **M. Inanc**: None; **B. Artim Esen**: None.

Abstract Number: 0136

Beyond Thrombosis: Histological Spectrum, Predictors and Outcomes of Renal Involvement in Primary Antiphospholipid Syndrome: A Single-Centre Cohort Study

RITESH KUMAR MISHRA[1], SUBIN PHILIP[2], RIZWANA NAUSHAD[2], AISHWARYA GOPAL[3], Chengappa Kavadichanda[2], CHRISTINA MARIASELVAM[2], RAJESH N G[2], Molly mary Thabah[3] and VIR SINGH NEGI[2], [1]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, Bhubaneswar, India, [2]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, PUDUCHERRY, Puducherry, India, [3]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, PUDUCHERRY, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Renal involvement in primary APS is underrecognized and histologically diverse, encompassing both vascular and glomerular pathology. We aimed to describe the histopathology, outcomes of biopsy-proven renal disease among primary APS and predictors of renal involvement.

Methods: Among 233 patients with primary APS (revised Sapporo criteria, 2006), Renal abnormalities defined as proteinuria >0.5 g/day and/or elevated serum creatinine with or without hematuria—were identified. Clinical, serological, histopathological and direct immunofluorescence (DIF) data were analyzed. Renal lesions were classified as per the Renal Pathology Society-2023 consensus definitions for aPL- nephropathy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Nineteen patients (8.15%) had renal abnormalities, Of these, 11 patients underwent kidney biopsy (Table 1). The median age of the biopsied cohort was 27 years (23.5-38), with 63.6% female. Hypertension was present in 63.6%. Median serum creatinine was 1.6 mg/dL (0.75-2.35), and UPCR was 4.4 g/g (1.76-7.5).

Renal biopsy findings were diverse (Figure 1A), with glomerular injury more frequent than aPL nephropathy. The major glomerular finding was glomerulosclerosis and ischemic wrinkling of GBM (a sequela of TMA) seen in 27%, followed by basement membrane thickening, while interstitial inflammation was present in 64% and mesangial expansion in 73% (Table 2).

S. No	Age/ Sex	Extra-renal APS manifestation	HTN	UPCR/ S. Creatinine	anti-β2GP1 anti-cardiolipin IgG/IgM titers	LAC	Renal biopsy findings	Treatment	Outcomes	Follow-up duration
1	36F	Recurrent pregnancy losses, AIHA, Thrombocytopenia, Stroke, DVT, Mitral regurgitation	+	10/2.3	High/Neg Low/Neg	+	Membranous nephropathy, Hypertensive vascular changes	Pulse Steroids, Inj CYC, MMF maintenance, Warfarin	50% proteinuria reduction at 6 months	1y
2	21M	Cutaneous Ulcers, Thrombocytopenia	+	0.3/1.6	Low/Neg Low/Neg	+	Immune complex GN-mesangioproliferative	Warfarin, Enalapril	eGFR improved on follow up	1y
3	33M	MCA Infarct, Thrombocytopenia, AIHA	+	3.3/2.4	Mod/Neg Mod/Low	+	Membranoproliferative GN, with blood vessel changes secondary to APLA	MPS Pulse, On high dose Pred and tapering, Warfarin	Expired during COVID-19	3m
4	19M	Stroke followed by Pulmonary thrombus, right atrial thrombus, splenic and renal infarcts as part of CAPS	+	5/0.5	High/Neg High/Neg	+	Immune complex glomerulonephritis-mesangioproliferative, endocapillary	Received Pulse Steroids and Pred, Warfarin for CAPS, Mycophenolate Mofetil	Urine PCR <0.5 after 15 months	4y
5	40F	Recurrent pregnancy losses, Mitral regurgitation	+	4.8/3.5	Mod/Neg Low/Neg	+	Ischemic Nephropathy with blood vessel changes secondary to APLA	Warfarin, anti-HTN	CKD G5A3: Non-oliguric	3y
6	22F	Stroke	+	10.6/0.6	Mod/High Mod/Neg	0	Class III + V Lupus Nephritis	Warfarin, Steroids, Mycophenolate mofetil	Urine PCR <0.5 after 16 months	4y
7	40F	CVT, Stroke, Recurrent DVT, AHA, Thrombocytopenia	+	0.8/1	Neg/Mod Neg/Low	+	Immune complex GN-mesangioproliferative with blood vessel changes secondary to APLA	Warfarin, Mycophenolate mofetil	Urine PCR <0.5 at 6 months	1y
8	26F	Pre-eclampsia	+	10.6/0.5	Neg/Neg Neg/Neg	+	Minimal change disease	Enalapril	Urine PCR <0.5 at 6 months	2y
9	27M	Cutaneous Ulcers	+	2.6/1.6	High/Neg Neg/Neg	+	Malignant hypertension in the setting of immune complex GN	Lost to follow-up	Lost to follow-up	3m
10	50F	Stroke	-	0.93/5.4	Neg/Neg Neg/Neg	+	Prominent blood vessel changes secondary to APLA	Warfarin	CKD G5A3: on Hemodialysis	7y
11	25F	Stroke, Recurrent pregnancy loss	+	4.4/0.9	Neg/Neg Low/Neg	+	Immune complex GN-mesangioproliferative with TMA	Warfarin, Enalapril	50% proteinuria reduction at 6 months	2y

Renal Involvement in Primary APS: Clinical Characteristics, Biopsy Findings, and Outcomes in 11 Patients

Table 2: Renal biopsy light microscopic findings (n=11)

Compartment	Injury pattern	n (%)
Glomerular	Glomerulosclerosis	3 (27%)
	Ischemic wrinkling	3 (27%)
	Uniform GBM thickening	3 (27%)
	Irregular GBM thickening	1 (9%)
	Membranoproliferative	1 (9%)
	Endocapillary hypercellularity	1 (9%)
	No changes	2 (18%)
Tubulointerstitial	Interstitial inflammation	7 (64%)
	Mild-Moderate IFTA	8 (73%)
	Mild ATN	4 (37%)
	Hyaline/RBC/WBC casts	6 (55%)
	Tubular thyroidisation	1 (9%)
	No changes	3 (27%)
Vascular	Fibrin thrombi in arteriole	1 (9%)
	Fibrin thrombi & Fibro-intimal hyperplasia	1 (9%)
	Fibro-intimal hyperplasia	4 (37%)
	Hypertensive vascular changes	1 (9%)
	No changes	4 (37%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

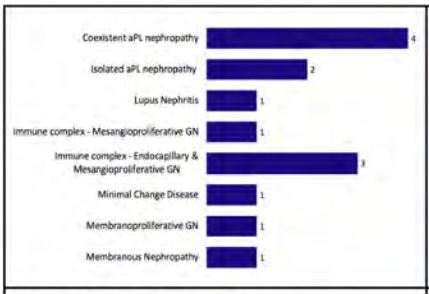


Figure 1A: Spectrum of renal biopsy diagnosis in primary APS

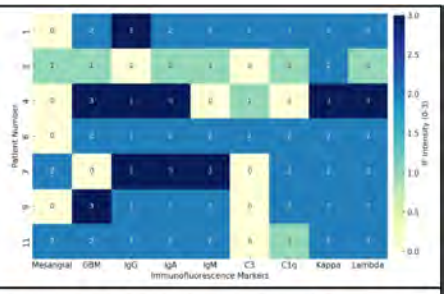


Fig 1B: Heatmap depicting DIF staining pattern in primary APS with proliferative GN

Isolated Antiphospholipid nephropathy (aPL-N) was seen in 2/11 patients. Acute or chronic TMA like lesions with immune deposits or inflammatory cells seen in 4/11 patients (54.5%). Acute TMA lesions were seen in one patient, chronic lesions seen in four, while one patient had acute with chronic TMA change (Table 2). DIF was positive in most, with a full-house pattern observed in two patients, despite no lupus manifestations (Figure 1B).

Treatment included warfarin (n=9, 81.8%), RAAS blockade (n=10, 90.9%), corticosteroids (n=4, 36.4%), and MMF (n=3, 27.3%). In the biopsied group (n=11), at a median 2-year follow-up, four (36.4%) achieved complete proteinuria remission (UPCR < 0.5 g/g), two (18.2%) had partial reduction, and one (9%) patient showed resolution of AKI.

Of all 19 APS with renal manifestations, five had CKD and only one progressed to dialysis-dependent ESRD.

On univariate analysis, arterial thrombosis ($p = 0.002$) and cutaneous ulcers ($p = 0.0009$) were significantly associated with renal involvement. On multivariable logistic regression, cutaneous ulcers independently predicted renal involvement (OR:19.5, 95% CI: 1.37-277.8, p=0.028), suggesting microvascular skin–renal overlap.

Conclusion: Renal abnormalities were identified in 8.2% of patients with primary APS. Only a minority of biopsied patients met strict histological criteria for aPL nephropathy. Most biopsies showed glomerular immune deposits or interstitial inflammation, pointing to immune-mediated renal injury in APS patients. The histologic overlap with SLE supports a pathologic continuum. Given the multitude of renal biopsy findings in Primary APS, it calls for individualized, pathology-driven treatment. Renal outcomes were favorable, with a low incidence of dialysis-requiring CKD.

Disclosure: R. MISHRA: None; **S. PHILIP**: None; **R. NAUSHAD**: None; **A. GOPAL**: None; **C. Kavadichanda**: None; **C. MARIASELVAM**: None; **R. N G**: None; **M. Thabah**: None; **V. NEGI**: None.

Abstract Number: 0137

Landscape of Primary Antiphospholipid Syndrome: Clinical Spectrum, Serology, and Predictors of Damage in a Single Center Cohort of 233 Patients

RITESH KUMAR MISHRA[1], SUBIN PHILIP[2], JAIDEV MENON[2], RIZWANA NAUSHAD[2], AISHWARYA GOPAL[3], CHRISTINA MARIASELVAM[2], Chengappa Kavadichanda[2], Molly mary Thabah[3] and VIR SINGH NEGI[2], [1]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, Bhubaneswar, India, [2]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, PUDUCHERRY, Puducherry, India, [3]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, PUDUCHERRY, India

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Antiphospholipid Syndrome (APS) a systemic autoimmune prothrombotic disorder with long-term consequences. While secondary APS is well studied, large real-world cohorts of primary APS remain scarce. We characterised the clinical, serological, and damage profiles of patients with primary APS and identified predictors of irreversible damage using the Damage Index for APS (DIAPS).

Methods: This retrospective study included 233 primary APS patients meeting the 2006 Sydney criteria for primary APS. Clinical features, antibody profiles, obstetric outcomes, and DIAPS were analyzed. High damage was defined as DIAPS ≥3. Subgroup analyses were performed in thrombotic APS (n=185) and obstetric-only APS (n=48). Multivariable logistic regression was used to identify predictors of high damage.

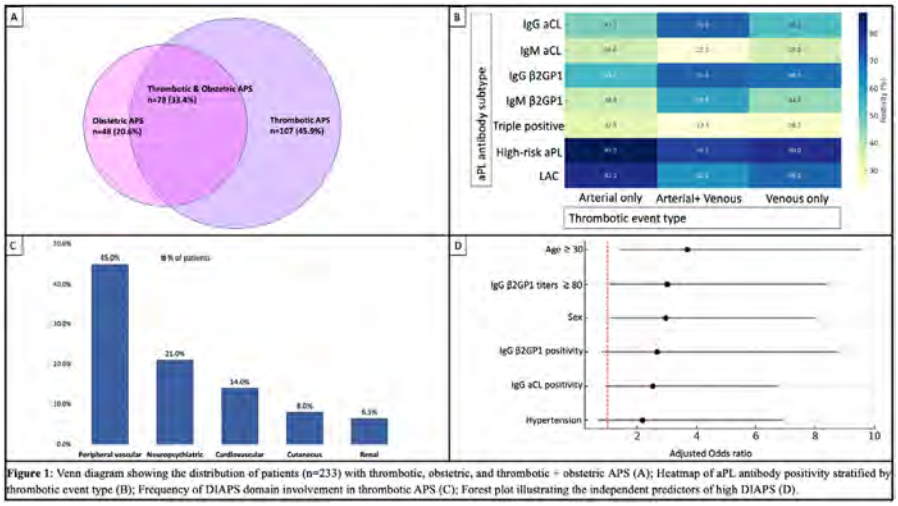


Figure 1: Venn diagram showing the distribution of patients (n=233) with thrombotic, obstetric, and thrombotic + obstetric APS (A); Heatmap of aPL antibody positivity stratified by thrombotic event type (B); Frequency of DIAPS domain involvement in thrombotic APS (C); Forest plot illustrating the independent predictors of high DIAPS (D).

TABLE 1: Manifestations of primary APS in a single center cohort of 233 patients, grouped as per the 2023 ACR/EULAR classification for APS

Domain 1 manifestations	N=185	Domain 2 manifestations	N=185	Domain 3 manifestations	N=233	Domain 4 manifestations	N=126	Other manifestations	N=233
Venous Thrombosis*	N (%)	Arterial Thrombosis*	n (%)	Micro-vascular***	n (%)	Obstetric morbidity**	n (%)	Others***	n (%)
DVT	72 (38.9)	Stroke/TIA	39 (21.1)	aPL nephropathy	10 (4.2)	≥3 Pre-fetal death (<10 weeks)	27 (21.4)	Cardiac valve -Domain 5	19 (8.13)
PTE	26 (14.1)	MI	8 (4.3)	Livedoid vasculopathy	10 (4.2)	At-least 1 Fetal death	63 (50)	Thrombocytopenia -Domain 6	65 (27.8)
CVT	27 (14.6)	Gangrene of digit	12 (6.5)	Adrenal Hemorrhage	3 (1.2)	Pre-eclampsia	15 (11.9)	AIHA	16 (6.8)
CRVO	5 (2.7)	CRAO	4 (2.2)	Pulmonary hemorrhage	1 (0.04)	Low Birth Weight	13 (10.3)	Cutaneous ulcers	15 (6.4)
Budd Chiari syndrome	6 (3.2)	Splanchnic artery thrombosis	4 (2.1)	--	--	--	--	Chorea	3 (1.2)
Splanchnic thrombosis	4 (2.1)	Organ infarcts	4 (2.1)	--	--	--	--	Osteonecrosis	5 (2.1)

Abbreviations: DVT, Deep Venous Thrombosis; PTE, Pulmonary Thromboembolism; CVT, Cerebral venous thrombosis; CRVO, Central Retinal Vein Occlusion; MI, Myocardial Infarction; CRAO, Central Retinal Artery Occlusion; TIA, Transient Ischemic attack; AIHA, Autoimmune hemolytic anemia. *-n (% among thrombotic APS, n=185), **-n (% among obstetric APS, n=126), ***-n (% among total APS, n=233)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: APS disease manifestations in high versus low damage index for APS (DIAPS)

Variable	High DIAPS (≥3) (n=31)	Low DIAPS(<3) (n=154)	p-value
Age ≥30 years	22 (71.0)	69 (44.8)	**0.01***
Male	11 (35.5)	22 (14.3)	**0.01***
Comorbidities, n (%)			
Hypertension	7 (22.6)	14 (9.1)	**0.03***
Diabetes Mellitus	1 (3.2)	12 (7.8)	0.60
APS Disease manifestations			
Venous event	17 (54.8)	89 (57.8)	0.91
Arterial event	24 (77.4)	39 (25.3)	**0.00***
Microvascular	18 (58.1)	9 (5.8)	**0.00***
Thrombocytopenia	8 (25.8)	57 (37)	0.16
Autoimmune hemolytic anemia	4 (13)	12 (7.7)	0.31
Cardiac valvular involvement	10 (32.2)	9 (5.8)	**0.00***
aPL profile, n (%)			
IgG aCL	23 (74.2)	73 (47.4)	**0.01***
IgG aCL High titers (≥80)	10 (32.3)	27 (17.5)	0.10
IgM aCL	9 (29.0)	63 (40.9)	0.30
IgM aCL High titers (≥80)	0 (0.0)	8 (5.2)	0.41
IgG β2GP1	26 (83.9)	89 (57.8)	**0.01***
IgG β2GP1 High titers (≥80)	15 (48.4)	21 (13.6)	**0.00***
IgM β2GP1	11 (35.5)	67 (43.5)	0.53
IgM β2GP1 High titers (≥80)	0 (0.0)	5 (3.2)	0.68
Lupus anticoagulant	14 (45.2)	82 (53.2)	1.0
Triple positive	13 (41.9)	39 (25.3)	0.08
High risk aPL	27 (87.1)	121 (78.6)	0.30
Single aPL positive	5 (16.1)	43 (27.9)	0.26

Results: Clinical spectrum: Over a median follow-up of 5.1 years (range 0.5–12.7), 107 (45.9%) had thrombotic-only APS, 78 (33.4%) had both thrombotic and obstetric APS, and 48 (20.6%) had obstetric-only APS (Fig. 1A). In the thrombotic subgroup (n=185), median age was 29 years (range 14–63), and 82.2% were female. Venous thrombosis occurred in 106 (57.8%), arterial events in 63 (34%), microvascular involvement in 27 (14.5%), and CAPS in 4 (1.7%) patients. Neurological manifestations seen were stroke/TIA: n=39 (21.1%); CVT: n=27 (14.6%); Chorea in n=3 (1.2%). Cardiac involvement included valvular lesions in 19 (8.1%), MI in 8 (4.3%). Hematological features included thrombocytopenia in 65 (27.8%) and AIHA in 16 (6.8%) (Table 1). Renal involvement (n=19, 8.2%) included aPL nephropathy (n=10) and immune-mediated glomerular injury (n=9).

MI, cutaneous ulcers, and arterial thrombosis were more frequent in males ($p< 0.05$). Arterial events were numerically more common in patients with triple positivity, LAC, or high-risk aPL profiles (Fig.1B).

In obstetric-only APS (n=48), the median number of pregnancies was 3 (IQR 2–3.25), with a high burden of first-trimester loss and adverse outcomes such as preeclampsia or low birth weight in 22.2%.

Serological: Of the total 233 patients, 178 (76.4%) had high-risk aPL profiles, 57 (24.5%) were triple-positive, and 83 (35.6%) had single aPL positivity.

Damage Index: The median DIAPS score was 1.0 (IQR 0–2, range 0–6); 65.9% had some damage and 17.8% had high damage. The most frequently involved domains were peripheral vascular (44.9%), neuropsychiatric (21.1%), cardiovascular (14.1%), and cutaneous (8.1%) (Figure 1C).

On multivariable analysis, age ≥30 (OR 3.9, 95% CI 1.5–10.1), male sex (OR 3.0, 95% CI 1.1–8.0), and IgG β2GP1 high titers (OR 3.0, 95% CI 1.1–8.4) independently predicted high DIAPS (Figure 1D). Hypertension showed a trend in the univariate analysis (table 2) but did not retain statistical significance in the multivariate model for prediction of high damage index.

Conclusion: This large single-center cohort highlights the clinical heterogeneity and damage burden in primary APS. Notably, CVT rates were higher than reported in international APS cohorts. Older age, male sex, and high IgG β2GP1 titers independently predicted irreversible damage. These findings underscore the need for early risk stratification to guide personalized monitoring and care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. MISHRA: None; **S. PHILIP**: None; **J. MENON**: None; **R. NAUSHAD**: None; **A. GOPAL**: None; **C. MARIASELVAM**: None; **C. Kavadichanda**: None; **M. Thabah**: None; **V. NEGI**: None.

Abstract Number: 0138

Evaluating Artificial Intelligence for Diagnosing Antiphospholipid Syndrome in Pulmonary Embolism Case Reports: A Prompt-Based Analysis

Sami Rabah and Xiangyi Kang, Lincoln Medical Center, New York, NY

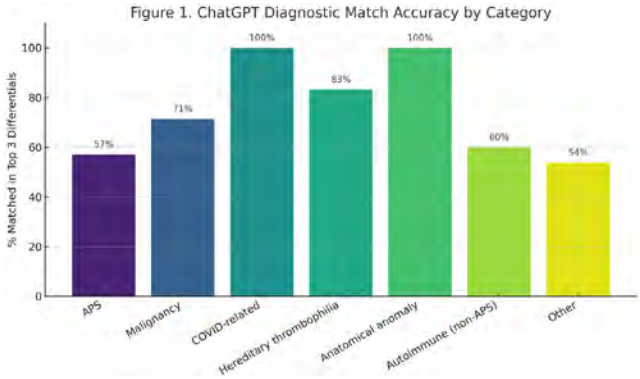
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid syndrome (APS) is a complex autoimmune prothrombotic disorder that can present with venous or arterial thromboses, often masquerading as unprovoked pulmonary embolism (PE). The use of artificial intelligence (AI) to assist in diagnostic reasoning is expanding, but its precision in recognizing rare or overlapping disorders like APS remains underexplored.

Methods: We reviewed 958 PubMed entries related to pulmonary embolism and included only English-language case reports with full-text access, adequate clinical detail, and documented APS-related diagnostic testing. Fifty cases met the inclusion criteria. Each case was blinded to the final diagnosis and analyzed using GPT-4 (ChatGPT), which was instructed to list its top three differential diagnoses, assess the likelihood of APS, and indicate whether APS antibody testing was warranted. Final diagnoses were recorded separately for performance assessment.

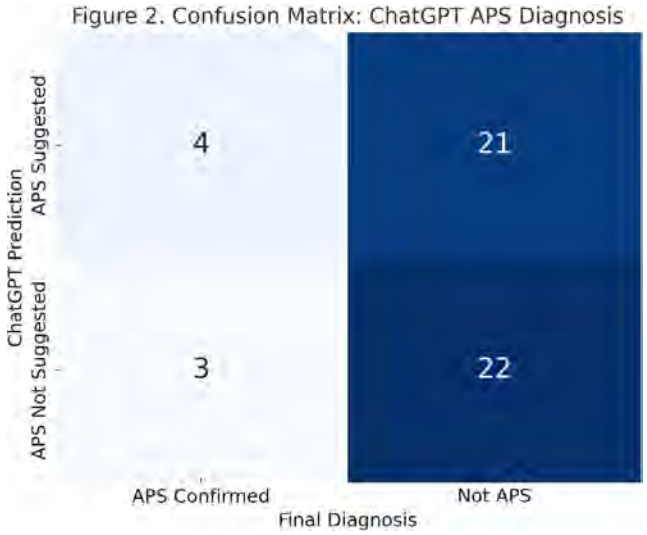
Results: Among the 50 included cases, 7 had a confirmed diagnosis of APS. ChatGPT correctly identified APS in 4 of 7 cases (sensitivity 57%) and incorrectly suggested APS in 21 non-APS cases (specificity 51%). Overall diagnostic accuracy was 52%, with a positive predictive value (PPV) of 16%, a negative predictive value (NPV) of 88%, and an F1 score of 0.25.

ChatGPT also correctly recommended APS antibody testing in all 7 APS cases and withheld testing in 19 of 43 non-APS cases, yielding a testing recommendation sensitivity of 100% and specificity of 44.2%. Additionally, in 73% of all cases, ChatGPT correctly included the final diagnosis—APS or otherwise—within its top three differential diagnoses,



Bar chart showing the percentage of cases in which ChatGPT correctly included the final diagnosis category within its top three differentials. Categories include APS, malignancy, hereditary thrombophilia, anatomical anomalies, COVID-related thrombosis, autoimmune (non-APS), and other causes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heatmap illustrating true positives, false positives, true negatives, and false negatives based on whether ChatGPT suggested APS in each case. The matrix is based on 50 PE case reports, 7 of which were confirmed to be APS.

demonstrating consistent clinical reasoning across a wide range of thrombotic etiologies including hereditary thrombophilia, malignancy, infection, and anatomical anomalies. Performance by diagnosis category is summarized in Figure 1, and APS classification performance is illustrated in the confusion matrix (Figure 2).

Conclusion: ChatGPT-4 demonstrates potential in supporting differential diagnosis generation in complex PE cases. While it overcalls APS in some instances, it consistently identifies relevant thrombotic mechanisms and reliably flags cases warranting APS testing. These findings support the growing role of artificial intelligence in complex diagnostic workflows and highlight the importance of structured prompt design in enhancing model accuracy and clinical relevance.

Disclosure: S. Rabah: None; **X. Kang**: None.

Abstract Number: 0139

When One Isn't Enough: Does Adding IgM Worsen the Antiphospholipid Syndrome Phenotype?

Santiago Dans Caballero[1], Massimo Radin[2], Chary López pedrera[3], MARIA ANGELES AGUIRRE ZAMORANO[4], Christian Merlo-Ruiz[5], Ismael Sanchez-Pareja[4], Irene Cecchi[6] and Savino Sciascia[7], [1]Reina Sofia University Hospital, Lebrija, Andalucia, Spain, [2]University of Turin, Turin, Turin, Italy, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [4]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [5]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [6]University of Turin, Turin, Piemonte, Italy, [7]University of Turin, Torino, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0115–0144) Antiphospholipid Syndrome Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by the persistent presence of antiphospholipid antibodies (aPL) along with clinical manifestations such as venous or arterial thrombosis and obstetric morbidity, including recurrent pregnancy loss and preeclampsia. Among aPL isotypes, IgG antibodies (particularly those targeting cardiolipin and β2-glycoprotein I) are well established as the primary pathogenic drivers and are central to current classification criteria. In contrast, the clinical relevance of IgM antibodies (especially when coexisting with IgG) is less well understood and often underrecognized in clinical settings. Determining whether concurrent IgM positivity confers additional clinical risk is key to enhancing diagnostic precision, prognostic evaluation, and clinical management in APS.

To determine whether the added aPL IgM positivity is associated with a more severe clinical phenotype in patients with aPL IgG positive APS.

Methods: A cross-sectional, multicenter study was conducted at two European tertiary care centers: Reina Sofía University Hospital (Cordoba, Spain) and Ospedale San Giovanni Bosco (Turin, Italy). Patients with confirmed APS, according to the revised Sydney classification criteria, were included and stratified based on the presence or absence of concurrent IgM positivity. Clinical, immunological, and therapeutic data were collected from electronic medical records. Valvular involvement (valvulopathy) was assessed by transthoracic echocardiography in accordance with institutional protocols. Univariate

Table 1. Clinical, immunological, and treatment characteristics of IgG+ versus IgG+IgM+ APS patients. ANA: antinuclear antibody; ASA: acetylsalicylic acid; VKA: vitamin K antagonist; HTN: hypertension; HCQ: hydroxychloroquine. Valvulopathy was assessed by transthoracic echocardiography according to institutional protocols.

Variable	IgG+ (n = 65)	IgG+IgM+ (n = 35)	p-value
Demographic factors			
Age (years), mean (SD)	51.6 (13.2)	53.5 (10.6)	0.45
Age at diagnosis (years), mean (SD)	39.9 (13.8)	42 (11.8)	0.44
Sex (female), n (%)	40 (61.5)	21 (60)	1.00
SLE, n (%)	24 (36.9)	10 (28.6)	0.50
Thrombotic and obstetric history			
Thrombosis ever, n (%)	58 (89.2)	27 (77.1)	0.14
Arterial thrombosis, n (%)	28 (43.1)	17 (48.6)	0.67
Venous thrombosis, n (%)	35 (53.8)	15 (42.9)	0.47
Obstetric morbidity, n (%)	13 (20.0)	12 (34.3)	0.18
Recurrent thrombosis on anticoagulation, n (%)	13 (20)	9 (25.7)	0.68
Immunologic profile			
Lupus anticoagulant, n (%)	55 (84.6)	27 (77.1)	0.51
Anti-β2GPI positivity, n (%)	51 (78.5)	31 (88.6)	0.32
Anticardiolipin positivity, n (%)	59 (90.8)	35 (100)	0.08
GAPSS, median (IQR)	10 (1.5)	13 (4)	**0.04**
ANA positivity, n (%)	43 (66.2)	23 (65.7)	1
Extrathrombotic aPL-associated manifestations			
≥1 extrathrombotic manifestation, n (%)	26 (40)	14 (40)	1
Thrombocytopenia, n (%)	12 (18.5)	9 (25.7)	0.55
Hemolytic anemia, n (%)	5 (7.7)	1 (2.9)	0.66
Valvulopathy, n (%)	1 (1.5)	6 (17.1)	**< 0.01**
Comorbidities			
Hypertension, n (%)	30 (46.2)	15 (42.9)	0.91
Dyslipidemia, n (%)	21 (32.3)	12 (34.3)	1
Smoking ever, n (%)	15 (23.1)	11 (31.4)	0.85
Treatment (ever used)			
ASA, n (%)	28 (43.1)	13 (37.1)	0.72
VKA, n (%)	42 (64.6)	20 (57.1)	0.60
HCQ, n (%)	23 (35.4)	12 (34.3)	1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

analyses were followed by multivariate logistic regression to identify independent associations, adjusting for the Global Antiphospholipid Syndrome Score (GAPSS), a validated tool for APS risk stratification.

Results: Among the 100 patients included, 65 were classified as IgG+ only and 35 as IgG+IgM+. No statistically significant differences were found between groups in age, sex, systemic lupus erythematosus (SLE) prevalence, or thrombotic burden. However, the IgG+IgM+ group had a significantly higher median GAPSS (13 vs. 10; p=0.04) and a markedly increased prevalence of echocardiographically confirmed valvulopathy (17% vs. 2%; p< 0.01). Detailed clinical and serological comparisons are shown in Table 1. In multivariable analysis, IgM positivity remained independently associated with valvulopathy (OR: 12.5; 95% CI: 1.73–274.5; p=0.03), after adjusting for potential confounders including GAPSS and the presence of SLE. The wide confidence interval highlights statistical uncertainty, limiting the precision and interpretability of this association.

Conclusion: The presence of IgM aPL in patients with IgG-positive APS defines a clinically distinct subgroup, characterized by greater valvular involvement despite similar thrombotic profiles. These findings suggest that IgM antibodies may contribute to a more complex, organ-specific disease phenotype and support their inclusion in APS risk stratification and therapeutic decision-making. Future research should explore the role of other isotypes, such as IgA, to comprehensively characterize their contribution to APS manifestations.

Disclosure: S. Dans Caballero: None; **M. Radin**: None; **C. López pedrera**: None; **M. AGUIRRE ZAMORANO**: None; **C. Merlo-Ruiz**: None; **I. Sanchez-Pareja**: None; **I. Cecchi**: None; **S. Sciascia**: None.

Abstract Number: 0140

Outcome Of Patients With Non-Criteria Manifestations Of Primary Antiphospholipid Syndrome Treated With Immunosuppressants -A Single Centre Study

Sindhuja Rajendran[1], ashish mathew[2], sukesh chandran nair[3], john mathew[2] and ruchika goel[2], [1]Christian Medical College ,Vellore, Madurai, Tamil Nadu, India, [2]Christian Medical college , Vellore , India, Vellore, Tamil Nadu, India, [3]Christian,Medical College ,Vellore ,India, Vellore, Tamil Nadu, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Non-criteria manifestations occur in 24% in Primary antiphospholipid syndrome (PAPS) . The efficacy of immunosuppressants in patients with above condition is not certain due to paucity of evidence. This stuyd aims to evaluate the outcome of patients who have been treated with immunosuppressive drugs for treatment of non-criteria manifestations of PAPS.

Methods: Patients with the diagnosis of APS or probable APS, attending our clinics between 2010 to 2024 were screened. Among these those satisfying the APL domain of ACR/EULAR 2023 criteria and had at-least one non criteria manifestation not attributable to any other defined CTD or disease and have been treated with immunosuppressive therapy were included. Data regarding clinical presentation, laboratory abnormality, treatment and response were included.

The primary outcome was the clinical improvement or resolution of the presenting manifestation after initiation of therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1:

Non -criteria Manifestations	Frequency n(%)
Thrombocytopenia	24 (54%)
Autoimmune haemolytic anaemia	12(27%)
APS Nephropathy	6 (13%)
Non Healing Ulcers	5(11%)
Lupus Anticoagulant Hypoprothrombinemia Syndrome	2(4.5%)
CAPS	2(4.5%)
Diffuse alveolar haemorrhage	2(4.5%)
Thrombotic thrombocytopenia purpura	1(2%)
Choreoathetosis	1(2%)
Laboratory domain (Antiphosphoilipid antibodies)	
Single positivity	8(18%)
Double Positivity	7 (15%)
Triple Positivity	28 (66%)
Lupus Anticoagulant	41(93%)
Anti cardiolipin	32(72%)
IgG β2 glycoprotein	30(68%)
Treatment received at initiation	
Steroid-Prednisolone equivalent (mean dose /day)	181 mg /day
Immunosuppression	
Rituximab, n (%)	19(43%)
Mycophenolate, n (%)	18(40%)
Azathioprine n (%)	7(15%)

Table 2

Non criteria manifestations	RITUXIMAB(n/total no receiving Rituximab)%	MYCOPHENOLATE+AZATHIOPRINE(n/total no receiving mycophenolate/azoran)%	Total Response
Thrombocytopenia	9/11 (81%)	11/15 (73%)	83%
AIHA	2/3 (66%)	8/9 (88%)	83%
APS Nephropathy	2/4 (50%)	1/2 (50%)	50%
Ulcers	3/3 (100%)	1/3 (33%)	66%
LAHPS	1/1 (100%)	0/2 (0%)	50%
CAPS	2/2 (100%)	-	100%
DAH	-	2/2 (100%)	100%
TTP	1/1 (100%)	-	100%
Choreoathetosis	1/1 (100%)	-	100%
Total response	80%	69%	-

80-100
60-79
40-59
20-39
0-19

Comparison of response to therapy in patients receiving Rtx and mycophenolate/ azathioprine

Results: Of the 334 patients screened ,a total of 44 patients 28 females, mean age 38±13 (SD) years satisfied the inclusion criteria. The most common non-criteria manifestation was thrombocytopenia (24, 54%) followed by AIHA (12,27%) (Table-1). Rituximab was the most common immunosuppressant used in 19(43%) followed by mycophenolate (18 (40%). 90% received antiplatelet and anticoagulants. During a median follow up of 32 months (IQR: 20-63), 80% patients responded to treatment. The best response was noted among patients with thrombocytopenia. Response rates of all manifestations is depicted in Table 2.

Major adverse events included death in 2 patients due to sepsis and pneumocystis carinii pneumonia, in patients receiving rituximab and 1 death due to sepsis, disseminated TB, Ca breast in patients receiving MMF

Conclusion: Among the patients with PAPS with non criteria manifestation, the best response to immunosuppression was observed in those presenting with AIHA and thrombocytopenia. All manifestions except LAHPS and skin ulcers showed similar response with rituximab as well as mycophenolate/ azathioprine

Disclosure: S. Rajendran: None; **a. mathew**: None; **s. chandran nair**: None; **j. mathew**: None; **r. goel**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0141

Cytokine profiles in antiphospholipid syndrome

Xiangjun Liu[1], Yuzhou Gan[2], Chun Li[3], Jianping Guo[4], lei zhu[5] and yuan jia[3], [1]Peking University, Beijing, Beijing, China, [2]University of Michigan, Ann Arbor, MI, [3]Peking University People's Hospital, Beijing, China (People's Republic), [4]Peking University People's Hospital, Beijing, Beijing, China, [5]Affiliated Nantong Rehabilitation Hospital of Nantong University, Nantong, China (People's Republic)

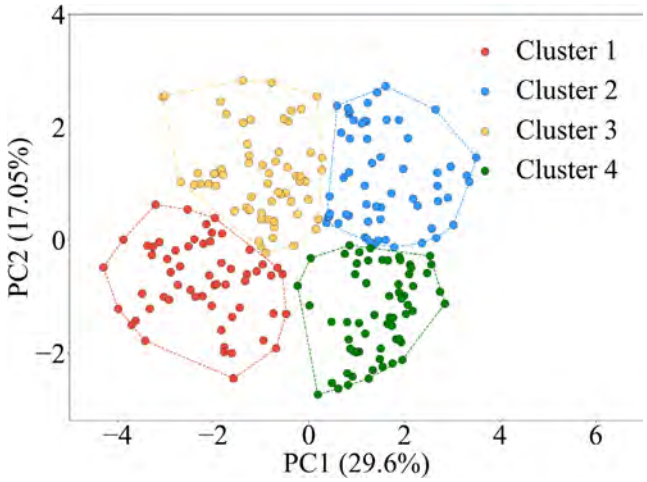
SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid syndrome (APS) is an autoimmune disease with unknown etiology. Inflammatory-mediated tissue damage plays an important role in APS. This study aimed to investigate the cytokine profiles in patients with APS.

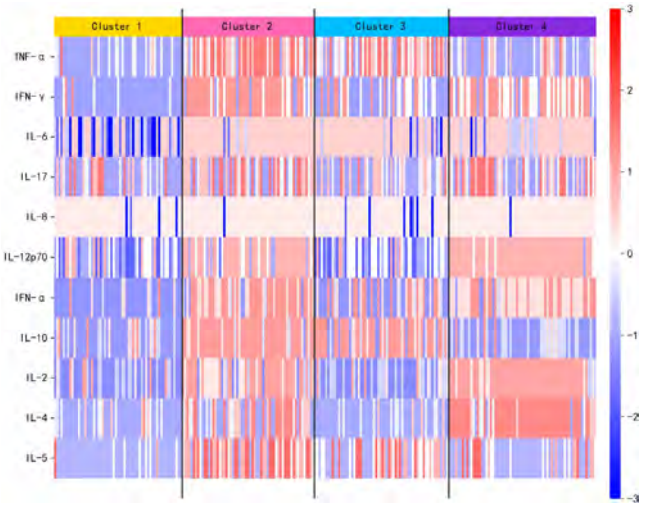
Methods: Serum samples were collected from 250 patients with APS and 129 healthy controls (HCs). Serum concentrations of 11 cytokines, including interleukin (IL)-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-17, interferon (IFN)-α, tumour necrosis factor (TNF) -a, and IFN-γ,were measured by multiplex bead array assay. Principal component analysis (PCA) and K-means clustering were performed to stratify APS patients into distinct subgroups based on their cytokine profiles. Subsequent comparative analyses assessed differences in clinical manifestations and laboratory parameters across the identified clusters.

Results: Compared withHCs, APS patients displayed significantly increased levels of IL-2 (p = 0.040), IL-1β (p<0.001), IL-12p70 (p <0.001), IL-8 (p <0.001), IL-6 (p <0.001) and IFN-γ(p=0.012), and significantly decreased levels of IL-5 (p<0.001), IL-17 (p=0.007) and TNF-α (p=0.002). The patients with thrombotic APS had significantly higher levels of IL-6 (p < 0.0001), IL-10 (p = 0.005) and TNF-α (p = 0.01), compared to patients with obstetric APS. Unsupervised clustering identified four distinct subgroups (**Fig. 1**): Cluster 1 (N=59) with globally suppressed cytokines except moderate IL-8; Cluster 2 (N=61) exhibiting pan-hypercytokinemia; Cluster 3 (N=62) showing elevated TNF-α/IL-6/IL-10/IL-5 with suppressed IFN-γ/IL-17/IL-12p70/IFN-α/IL-2/IL-4; and Cluster 4 (N=68) characterized by IL-2/IL-4 overexpression (**Fig. 2**). Clinically, Cluster 2 correlated with higher aGAPSS scores, while Cluster 4 was enriched for primary APS (p< 0.05).



PCA scatter plot in patients with APS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heatmap of cytokine expression profiles across APS patient clusters.

Conclusion: APS patients show distinct cytokine patterns with thrombotic cases displaying stronger inflammation. Cytokine clustering identifies high-risk subgroups, suggesting utility for patient stratification.

Disclosure: X. Liu: None; **Y. Gan**: None; **C. Li**: None; **J. Guo**: None; **l. zhu**: None; **y. jia**: None.

Abstract Number: 0142

Risk Factors for Antiphospholipid Syndrome-associated Nephropathy: A Retrospective Cohort Analysis

Xiaohan Wei[1], Zhixia Yang[2], Haoyu Pan[2], Yuying Fan[2], Jinyi Qian[2], Shuyi Yu[2] and Hui Shi[3], [1]Shanghai JiaoTong University, Shanghai, China (People's Republic), [2]Department of Rheumatology and Immunology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [3]Shanghai Jiaotong University Affiliated Ruijin Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: To identify independent clinical and laboratory risk factors associated with antiphospholipid syndrome-associated nephropathy (APSN) and highlight the clinical importance of early screening in high-risk patients.

Methods: This retrospective cohort study included patients with antiphospholipid syndrome (APS) consecutively enrolled in the APS-Shanghai database between January 2021 and March 2025. All patients were classified based on the 2023 ACR/EULAR criteria. Biopsy-confirmed APSN was used as the diagnostic endpoint. Clinical and laboratory data were extracted from the electronic medical record system. Differences between APSN and non-APSN groups were analyzed, and multivariate logistic regression was performed to identify independent risk factors. All statistical analyses were conducted using SPSS version 29.0.

Results: Among 208 APS patients included, 32 (15.4%) were diagnosed with biopsy-confirmed APSN. Compared with patients without renal involvement, those with APSN had a significantly higher prevalence of hypertension, valvular heart

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

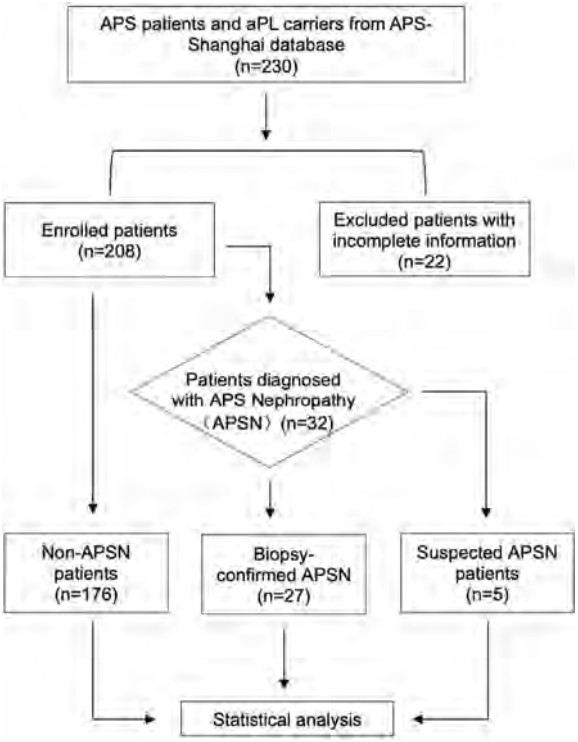


Figure 1. Study flowchart.

Table 1 Demographic and clinical characteristics at baseline in Antiphospholipid Syndrome (APS) patients

	non-APSN (n=176)	APSN (n=32)	p value
Demographics			
Age（Mean ± SD）	46.47 (16.25)	43.74 (14.17)	0.329
Female	132 (75%)	25 (78.1%)	0.705
Clinical history			
aPL carrier	23 (13.1%)	0 (0%)	**0.030**
PAPS	93 (52.8%)	15 (46.9%)	0.534
SAPS	60 (34.1%)	16 (50.0%)	**0.086**
Arterial thrombosis	52 (29.5%)	10 (31.3%)	0.846
Venous thrombosis	47 (26.7%)	5 (15.6%)	0.183
Pregnancy morbidity	31 (17.6%)	3 (9.4%)	0.246
Value Heart Disease	20 (11.4%)	10 (31.3%)	**0.003**
PAH	6 (3.4%)	1 (3.1%)	0.935
Livedo	21 (11.9%)	5 (15.6%)	0.561
Thrombocytopenia	40 (22.7%)	17 (53.1%)	**<0.001**
Stroke	29 (16.5%)	14 (43.8%)	**<0.001**
Cerebrovascular Stenosis	15 (8.5%)	7 (21.9%)	0.024
Complications			
Arterial hypertension	30 (17%)	14 (43.8%)	**<0.001**
Hyperlipidemia	12 (6.8%)	2 (6.3%)	0.906
Diabetes Mellitus	13 (7.4%)	1 (3.1%)	0.376
aPL profile			
IgG aCL	44.23 (52.38)	46.00(48.74)	0.859
IgM aCL	35.86 (57.67)	31.66 (49.72)	0.702
IgA aCL	12.82(29.04)	26.55 (55.98)	0.040
IgG b2GP1	49.68 (64.38)	43.38 (58.41)	0.607
IgM b2GP1	30.55 (64.84)	35.95 (81.29)	0.678
IgA b2GP1	41.88 (110.04)	34.17 (52.81)	0.349
LAC	1.70 (0.57)	1.83 (0.71)	0.243
Immunoglobulin and complement			
IgG	12.63 (3.75)	12.85 (5.57)	0.781
IgM	1.52 (1.36)	1.36 (0.97)	0.528
IgA	2.44 (1.70)	2.37 (0.98)	0.821
C3	1.02 (0.20)	0.93 (0.33)	**0.035**
C4	0.23 (0.12)	0.19 (0.13)	0.101
hepatic and renal function			
ALT	21.41 (14.01)	28.44 (32.73)	0.045
AST	24.68 (8.05)	30.72 (29.85)	0.023
Crea	72.98 (19.66)	110.00 (50.04)	**<0.001**
eGFR	95.33 (22.53)	69.59 (28.98)	**<0.001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 Possible risk factors for developing APSN among APS patients.

	β	P	OR (95%CI)
Univariate analysis			
Arterial thrombosis	-0.521	**0.350**	0.594(0.199-1.773
Venous thrombosis	-0.331	0.578	0.718(0.223-2.310)
Pregnancy morbidity	-0.399	0.572	0.716(0.168-2.674)
Value Heart Disease	1.372	**0.019**	3.942(1.247-12.463)
PAH	-0.328	0.815	0.720(0.046-11.310)
Livedo	0.199	0.766	1.220(0.330-4.514)
Thrombocytopenia	1.341	**0.005**	3.824(1.489-9.825)
Stroke	1.417	**0.010**	4.126(1.408-12.096)
Cerebrovascular Stenosis	0.776	0.227	2.172(0.616-7.658)
IgG aCL	-0.002	0.818	0.998(0.982-1.014)
IgM aCL	-0.009	0.157	0.991(0.978-1.004)
IgA aCL	0.012	0.127	1.012(0.997-1.028)
IgG b2 GP1	-0.008	0.240	0.992(0.979-1.005)
IgM b2 GP1	0.003	0.489	1.003(0.995-1.011)
IgA b2 GP1	-0.003	0.497	0.997(0.987-1.006)
LAC	0.380	0.350	1.462(0.659-3.245)
Multivariate analysis			
Value Heart Disease	1.001	**0.040**	2.720(1.049-7.055)
Thrombocytopenia	1.298	**0.002**	3.664(1.601-8.386)
Stroke	1.373	**0.002**	3.948(1.673-9.313)

disease, thrombocytopenia, ischemic stroke, and cerebrovascular stenosis. Laboratory differences included higher serum creatinine, lower estimated glomerular filtration rate (eGFR), reduced complement C3 levels, and a higher positivity rate for IgA anti-cardiolipin antibodies. Multivariate logistic regression identified three independent clinical predictors of APSN: valvular heart disease (OR = 2.720, 95% CI: 1.049–7.055, P = 0.04), thrombocytopenia (OR = 3.664, 95% CI: 1.601–8.386, P = 0.002), and stroke (OR = 3.948, 95% CI: 1.673–9.313, P = 0.002). These findings suggested that APS patients with these features are at increased risk of developing APSN and may benefit from early screening, including renal function monitoring and consideration for renal biopsy, even in the absence of overt renal symptoms.

Conclusion: This study identified valvular heart disease, thrombocytopenia, and stroke as independent risk factors for APSN. These findings underscore the importance of vigilant renal evaluation in APS patients with systemic vascular involvement and support the role of renal biopsy in clarifying occult nephropathy in high-risk individuals.

Disclosure: X. Wei: None; **Z. Yang**: None; **H. Pan**: None; **Y. Fan**: None; **J. Qian**: None; **S. Yu**: None; **H. Shi**: None.

Abstract Number: 0143

High-dimensional Spectral Flow Cytometry Reveals a Unique Distribution of Circulating B Cells in Patients with Antiphospholipid Syndrome

Yuzhou Gan[1], Srilakshmi Yalavarthi[2], Yiran Shen[1], Cyrus Sarosh[3], Xiangjun Liu[4], Ajay Tambralli[1], Jacqueline Madison[1], Yu (Ray) Zuo[1] and Jason S. Knight[1], [1]University of Michigan, Ann Arbor, MI, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, [3]University of Michigan, Temperance, MI, [4]Peking University, Beijing, Beijing, China

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

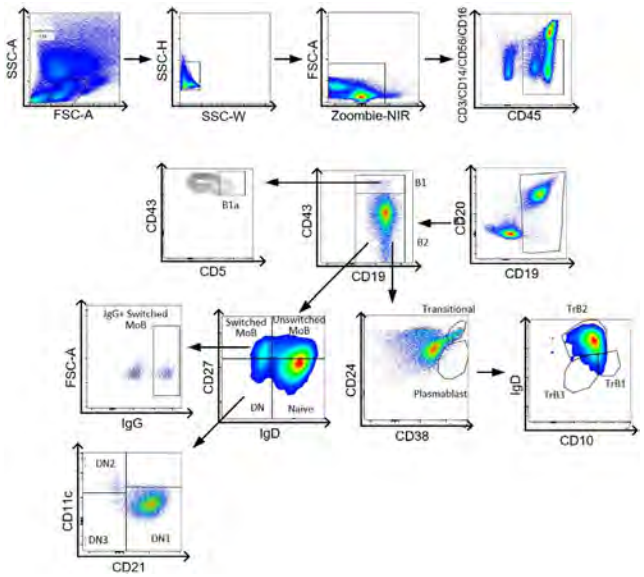


Figure 1. Gating strategies of peripheral B cells from PBMCs.

Background/Purpose: Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by the presence of pathogenic antiphospholipid antibodies (aPL) in the setting of venous or arterial thrombosis, pregnancy morbidity, and other morbid manifestations. B cells are central to APS pathogenesis through their role in aPL production. However, despite their pathogenic importance, the phenotypic and functional characteristics of circulating B cells in APS remain incompletely understood. In this study, we applied high-dimensional spectral flow cytometry to comprehensively characterize the activation profiles of circulating B cells in patients with APS.

Methods: Methods: We developed a 26-color spectral flow cytometry panel to deeply characterize circulating B cell subsets and their activation states in patients with APS. The panel was designed based on established literature and included markers for B cell development, activation, memory, homing, and regulatory phenotypes. Peripheral blood mononuclear cells (PBMCs) were isolated from APS patients (n=37) fulfilling the 2023 ACR/EULAR APS classification criteria and age-

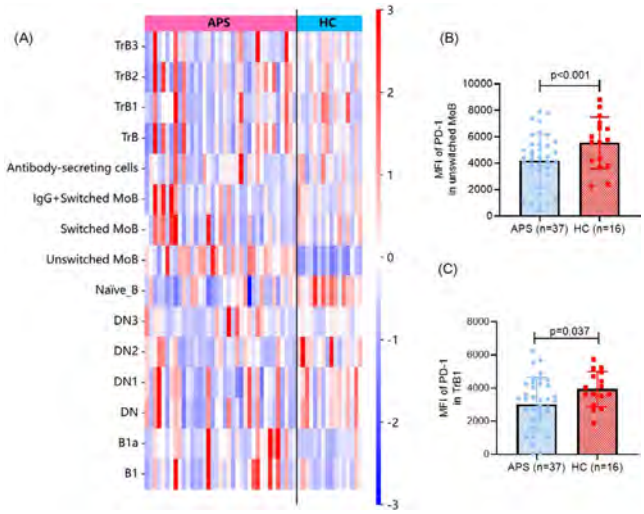


Figure 2. Altered proportions of B cell subsets and reduced PD-1 expression on unswitched memory and transitional B1 cells in APS patients. (A) Heatmap showing the relative percentages (Z-score normalized) of B cell subsets in peripheral blood from patients with antiphospholipid syndrome (APS, n = 37) and healthy controls (HC, n = 16). Subsets include transitional B cells (TrB, TrB1–TrB3), memory B cells (MoB, switched and unswitched), antibody-secreting cells, naïve B cells, double-negative B cells (DN, DN1-DN3), and B1 cells (B1, B1a). (B) Median fluorescence intensity (MFI) of PD-1 on unswitched memory B cells is significantly lower for APS patients versus HCs. (C) PD-1 MFI on transitional B1 cells is also reduced in APS patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographic Characteristics of APS Patients and Healthy Controls

	APS (n=37)	HC (n=16)	p
Gender (Female, n%)	33 (89.2)	14 (87.5)	1
Age (mean± SD)	47.9±13.5	43.2±17.9	0.353

and sex-matched healthy donors (n=16). Samples were stained and analyzed using a 5-laser Cytek Aurora spectral flow cytometer. Manual gating was performed using FlowJo software to define major B cell subsets, including naïve, transitional, memory, double-negative, and plasmablast populations. Activation markers such as CD86, CD95, CD69, and HLA-DR were assessed across subsets. Statistical analyses were conducted using SPSS to compare APS patients with healthy controls, with significance defined as $p < 0.05$.

Results: Among the patients, 25 (67.6%) were diagnosed with primary APS, while 12 (32.4%) had APS associated with systemic lupus erythematosus (SLE). Gating strategies were shown in **Fig. 1**. Compared with healthy controls, patients with APS exhibited an increased proportion of B1a cells ($CD5^+CD43^+$) (0.30% of $CD19^+CD20^+$B cells [0.15, 0.44] vs. 0.14 [0.08, 0.22], p=0.010) and unswitched memory B cells ($CD27^+IgD^+IgM^+$) (30.52% of $CD19^+CD20^+$B cells [21.68, 36.79] vs. 12.19 [9.59, 17.58], p< 0.001). In contrast, the proportion of naïve B cells ($CD27^-IgD^+IgM^+$) was significantly reduced in APS patients (46.21% of B cells [42.34, 58.44] vs. 63.01 [57.51, 72.64], p< 0.001) (**Fig. 2A**). Moreover, the expression of the key checkpoint regulator PD-1 was reduced on transitional B1 cells ($CD10^{hi}IgD^{hi}CD24^{hi}CD38^{hi}$) and unswitched memory B cells in APS patients (**Fig. 2B-C**).

Conclusion: High-dimensional profiling of circulating B cells in APS patients reveals distinct alterations in subset distribution and activation states, including increased B1a and unswitched memory B cells and reduced naïve B cells, alongside diminished PD-1 expression on key populations. These results provide novel insights into B cell dysregulation in APS and raise the possibility that augmenting PD-1 signaling or modulating specific B cell subsets could represent future therapeutic strategies for this complex autoimmune disorder.

Disclosure: Y. Gan: None; **S. Yalavarthi**: None; **Y. Shen**: None; **C. Sarosh**: None; **X. Liu**: None; **A. Tambralli**: None; **J. Madison**: None; **Y. Zuo**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

Abstract Number: 0144

Duration of Anticoagulation in Antiphospholipid Antibody-positive Patients: Results from an AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Survey

Zeynep Belce Erton[1], Joann Vega[2], Hannah Cohen[3] and Doruk Erkan[2], on Behalf of the APS ACTION Duration of Anticoagulation Working Group, [1]Hospital for Special Surgery, Brooklyn, NY, [2]hospital for special surgery, New York, NY, [3]University College London Hospitals NHS Foundation Trust, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0115–0144) Antiphospholipid Syndrome Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: APS ACTION is a multidisciplinary, international research network focused on developing collaborative studies to improve antiphospholipid syndrome (APS) diagnosis and management. There is limited prospective evidence guiding the optimal duration of anticoagulation in thrombotic APS, particularly across varied antibody profiles, levels, and thrombosis risk

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: APS ACTION Survey Responses on Anticoagulation Discontinuation in Standardized Venous Thromboembolism (VTE) and Arterial Thrombosis (AT) Scenarios, Stratified by aPL Profile and VTE and AT Risk Factors

VTE Scenario: 50-year-old female; with no other systemic autoimmune disease; with history of lower extremity deep vein thrombosis without pulmonary embolism 12 months ago, which was treated with low-molecular-weight-heparin transitioned to warfarin. For scenarios with concomitant VTE risk factors, i.e., high-risk profile or no high-risk profile, the risk factor is no more present.

AT Scenario: 55-year-old male; with no other systemic autoimmune disease; with history of acute ischemic stroke 12 months ago, treated with low-dose aspirin followed by warfarin; with no evidence of atherosclerosis or cardiac embolic source. For scenarios with concomitant cardiovascular disease risk factors, i.e., high-risk profile or no high-risk profile, the risk factor is well-controlled.

aPL Profile (Units)	% of Respondents who Would Stop Anticoagulation For VTE Scenarios Median (range)*	% of Respondents who Would Stop Anticoagulation For AT Scenarios Median (range)*
Triple aPL-positive		
-IgG (+/- IgM) 40-79 or ≥80	10 (3-13)	5 (3-13)
-IgM Only 40-79 or ≥80	13 (6-29)	5 (3-17)
Double aPL-positive		
-LA + aCL or aβ$_2$GPI IgG (+/- IgM) 40-79 or ≥80	10 (3-17)	7 (4-14)
-LA + aCL or aβ$_2$GPI IgM Only 40-79 or ≥80	16 (7-31)	9 (4-21)
-aCL and aβ$_2$GPI IgG (+/- IgM) 40-79 or ≥80	23 (10-42)	12 (7-25)
-aCL and aβ$_2$GPI IgM Only 40-79 or ≥ 80	42 (20-58)	24 (10-46)
Single aPL-positive		
-LA	18 (13-27)	15 (3-20)
-aCL IgG (+/- IgM) 40-79 or ≥80	30 (17-45)	20 (13-37)
-aCL IgM Only 40-79 or ≥80	43 (33-63)	27 (20-63)
-aβ$_2$GPI IgG (+/- IgM) 40-79 or ≥80	30 (13-43)	18 (10-33)
-aβ$_2$GPI IgM Only 40-79 or ≥80	41 (28-69)	30 (20-63)

*The number of respondents for each scenario ranged from 26 to 31; the median and range of responses were calculated based on different VTE/AT risk profiles and/or aCL/aβ$_2$GPI levels, in accordance with 2023 ACR/EULAR APS Classification Criteria. **LA:** lupus anticoagulant; **aCL / aβ$_2$GPI**: anticardiolipin antibodies / anti-β$_2$-glycoprotein-I antibodies

factors. The objective of this survey was to evaluate clinical decision-making practices among APS ACTION members regarding the duration of anticoagulation for secondary thrombosis prevention in APS, using standardized clinical scenarios.

Methods: A cross-sectional electronic survey was distributed to APS ACTION members in April 2025. Participants were asked to assess whether they would discontinue long-term anticoagulation in patients with different scenarios designed, based on the clinical and laboratory domains of the 2023 ACR/EULAR APS Classification Criteria. Each scenario was stratified by aPL profile (triple, double, or single-positive), aCL/aβ$_2$GPI isotype (IgG +/-IgM, or IgM only), and aCL/aβ$_2$GPI level (40–79U or ≥80U), as well as by venous thromboembolism (VTE) and arterial thrombosis (AT) risk profiles (Table 1). Descriptive statistics summarize the proportion of clinicians favoring discontinuation across scenarios.

Results: Fifty-nine APS ACTION members involved in patient care received the survey, and 31 (53%) (mean years in practice 25 ± 12, rheumatologists: 21 [68%], hematologists: 3 [10%],and other: 7 [22%]) responded. When stratified by aPL profile, anticoagulation discontinuation rates were the lowest in triple aPL-positive patients, with only 10–16% willing to stop in different VTE and 7% in AT scenarios. In double aPL-positive patients, discontinuation rates were lower for lupus anticoagulant (LA)-positivity, and higher when LA was negative, particularly for IgM-only profiles (10-42% would stop anticoagulation for different VTE and 7-28% for AT profiles). Single aPL-positive patients demonstrated the highest likelihood of discontinuation (lowest for LA-positive patients); depending on the aPL and thrombosis risk profiles, rates of discontinuation of anticoagulation were 13-69% for VTE and 3-63% for AT (Table 1).

Conclusion: Among APS ACTION members, anticoagulation discontinuation decisions in thrombotic APS vary significantly depending on the aPL profile, thrombosis type, and concomitant thrombosis risk factors at the time of the event. Clinicians were more likely to stop anticoagulation in VTE than AT scenarios, in patients with IgM-only profiles, and in the absence of a positive LA test. These findings highlight areas of variability in clinical practice and underscore the need for risk-stratified controlled studies to inform anticoagulation duration in diverse APS phenotypes.

Disclosure: Z. Erton: None; **J. Vega**: None; **H. Cohen**: GlaxoSmithKlein(GSK), 6, Roche, 2, Roivant, 2; **D. Erkan**: Chugai, 5, GlaxoSmithKlein(GSK), 1, 5, 6, Merida Biosciences, 2, NIH, 5, Roche, 1, Roivant Sciences, 2, Star Therapeutics, 1, Up-To-Date, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0145

Population Assessment of Cancer Incidence among Patients with Idiopathic Inflammatory Myopathies in North Carolina

Astia Allenzara[1], Ben Albright[2], Xi Zhou[2], Amanda Nelson[3], Laura Green[4], Katherine Reeder-Hayes[4], Jennifer Lund[4], Caroline Thompson[4] and Chris Baggett[4], [1]UNC, Chapel Hill, NC, [2]University of North Carolina, Chapel Hill, NC, [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, [4]University of North Carolina, Chapel Hill

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Cancer is highly prevalent and a leading cause of death for patients with Idiopathic Inflammatory Myopathies (IIM). Evaluating cancer type and stage at diagnosis for patients with IIM is paramount to identify and target critical factors to decrease cancer morbidity. Prior work in the US has focused on assessment of cancer risk by comparing

Table 1: Demographics of patients with IIM ICD code(s) who had cancer by NCCR (n=876)

Description	Number	%
Sex		
Male	361	41.2
Female	515	58.8
Race		
Non-Hispanic black	226	25.8
Non-Hispanic white	612	69.9
Other	38	4.3
Marital Status		
Married	408	46.6
Not Married	291	33.2
Unknown	177	20.2
Cancer sequence		
First and only tumor	774	69.1
First of multiple	102	9.1
First IIM ICD code relative to Cancer Diagnosis		
IIM code prior to Cancer	373	42.6
IIM ICD on/after cancer	503	57.4
SEER Stage		
In situ	75	8.6
Localized	349	39.8
Regional	174	19.9
Distant	223	25.5
Un-staged	55	6.3

Abbreviations: IIM: Idiopathic inflammatory myopathies, ICD: international classification of disease, SEER: Surveillance, Epidemiology and End Result; North Carolina Central Cancer Registry (NCCR)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: The Most Frequent Cancer Type, Overall and by Sex

Overall	N	%
Female breast	166	18.95
Lung and bronchus	110	12.56
Prostate	102	11.64
Melanoma	50	5.71
Colorectal	47	5.37
Non-Hodgkins Disease	42	4.79
Oral cavity	30	3.42
Kidney	29	3.31
Leukemia	29	3.31
Bladder	25	2.85
Female		
Breast	166	32.2
Lung and bronchus	67	13.0
Colorectal	29	5.6
Non-Hodgkins Disease	25	4.9
Melanoma	23	4.5
Uterine	18	3.5
Endocrine	17	3.3
Kidney	16	3.1
Oral cavity	13	2.5
Leukemia	13	2.5
Ovary	13	2.5
Male		
Prostate	102	28.3
Lung and bronchus	43	11.9
Melanoma	27	7.5
Colorectal	18	5.0
Non-Hodgkins Disease	17	4.7
Oral cavity	17	4.7
Leukemia	16	4.4
Bladder	16	4.4
Kidney	13	3.6
Pancreas	12	3.3

subgroups within IIM, from clinical settings. This study seeks to use a statewide population-based approach to assess cancer incidence and stage at diagnosis in patients with IIM compared to the general population.

Methods: The Cancer Information and Population Health Resource (CIPHR) is a linked dataset of the North Carolina Central Cancer Registry (NCCR) and insurance claims that cover approximately 55% of the total population of NC from Medicaid, Medicare fee for service, Medicare advantage and private insurance plans (2003-2020). Patients with IIM were selected from administrative datasets utilizing prior validated methodologies (i.e., 1 ICD-9 [710.3-4] or -10 [M36.0, M33.0-2,9, M60.8, M60.9 if associated with J99.1, J84.9 or J84.1] associated with a hospitalization or two codes [ICD-9 (710.3-4) or -10 (M33.0-2,9, G72.4]) which are between 30 days to 365 days. Once identified in claims the IIM cohort was linked to the NCCR. This abstract is focused on description of the linked cohort.

Results: A total of 6531 patients with IIM were identified from claims, of whom 876 developed an initial cancer with a mean age of 64 years. Most patients had a first and only tumor (69%) and almost half developed cancer after the first IIM ICD code date (43%). Of patients with IIM who developed cancer, the majority were female (59%), non-Hispanic white (70%), and had an urban residence (67%). A quarter (26%) of patients with IIM had a Surveillance, Epidemiology and End Result (SEER) stage of distant, although the most frequent stage was localized (40%, Table 1). The most common type of cancer for

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

women was breast cancer (19%) followed by lung (13%) then colorectal. The most frequent cancer for men was prostate (28%), then lung (12%) followed by melanoma (8%, Table 2).

Conclusion: A NC population-based assessment of cancer development in patients with IIM (a rare disease), is feasible and will enable the calculation of standardized incidence ratios which will identify those cancer types that are more likely to occur in patients with IIM, enabling future efforts for targeted screening.

Disclosure: A. Allenzara: None; **B. Albright**: None; **X. Zhou**: None; **A. Nelson**: Novo Nordisk, 1; **L. Green**: None; **K. Reeder-Hayes**: None; **J. Lund**: None; **C. Thompson**: None; **C. Baggett**: None.

Abstract Number: 0146

Association Between Frailty and Delirium and Hospitalization Outcomes Among Older Adults with Rheumatic Diseases

Bhavik Bansal[1], Yehseo Jung[2], Abdulla Damluji[3], Parag Goyal[4] and Namrata Singh[5], [1]UT Southwestern Medical Centre, Dallas, TX, [2]University of Washington, Seattle, WA, [3]Johns Hopkins, Baltimore, [4]Weill Cornell, New York, [5]University of Washington, Bellevue, WA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: We investigated the association of frailty and delirium, both independently and in combination, with in-hospital mortality and non-routine discharge (i.e. when a patient is discharged to a destination other than their home, such as transfers to rehabilitation centers, or nursing homes) among hospitalized older adults with rheumatic diseases.

Methods: We performed a retrospective study using data from the Nationwide Inpatient Sample (NIS), spanning 2016 to 2022. Adults aged 65 and older with a primary diagnosis of select rheumatic diseases (rheumatoid arthritis. systemic lupus, polymyalgia rheumatica, psoriatic arthritis, giant cell arteritis, spondyloarthropathy) were identified using ICD-10 codes. Frailty and delirium were ascertained using the Hospital Frailty Risk Score (HFRS) (categorized into three levels: low (< 5), moderate (5–15), and high (>15) frailty risk) and ICD-10 diagnostic codes, respectively. Multivariable logistic regression was used to assess the association of delirium and frailty both individually and combined with co-primary outcomes: in-hospital mortality and non-routine discharge. Each model was adjusted for demographic characteristics (age, sex, race and insurance status) and comorbidities. In a subgroup analysis, we evaluated these associations among patients with RA.

Results: Among 938,595 weighted hospitalizations of older adults with rheumatic diseases, 2.6% were classified as highly frail and 3.5% experienced delirium (**Table 1**). The mean age was 76.0 years, and 74.6% were female. Patients with RA comprised 70% of the cohort (**Table 2**). Both delirium and high frailty independently increased the odds of in-hospital mortality: delirium was associated with an OR of 4.99 (95% CI: 4.16–5.99) and high frailty with an OR of 6.80 (95% CI: 5.45–8.48). The combined presence of delirium and high frailty conferred the highest risk of mortality (OR: 16.2, 95% CI: 11.5–22.9). A similar pattern was observed for non-routine discharge, with elevated odds for delirium alone (OR: 3.14, 95% CI: 2.95–3.35), high frailty alone (OR: 5.69, 95% CI: 5.26–6.16), and both together (OR: 11.1, 95% CI: 8.78–14.0) (**Figure 1**). These associations remained significant across subgroup analyses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of the cohort by delirium status.

Characteristic	Overall, N = 938,595[1]	No Delirium, N = 905,865[1]	Delirium, N = 32,730[1]	p-value
Age (years)				**<0.001**[2]
65-69	223,445.0 (23.8)	218,410.0 (24.1)	5,035.0 (15.4)	
70-74	238,684.9 (25.4)	232,104.9 (25.6)	6,580.0 (20.1)	
75-79	197,939.9 (21.1)	191,114.9 (21.1)	6,825.0 (20.9)	
80-84	143,714.9 (15.3)	137,389.9 (15.2)	6,325.0 (19.3)	
85-89	88,615.0 (9.4)	83,615.0 (9.2)	5,000.0 (15.3)	
90 or older	46,195.0 (4.9)	43,230.0 (4.8)	2,965.0 (9.1)	
Sex				**0.001**[2]
Female	700,194.7 (74.6)	675,154.7 (74.5)	25,040.0 (76.5)	
Male	238,399.9 (25.4)	230,709.9 (25.5)	7,690.0 (23.5)	
Race				**<0.001**[2]
Asian or Pacific Islander	15,930.0 (1.7)	15,515.0 (1.7)	415.0 (1.3)	
Black	85,675.0 (9.1)	82,210.0 (9.1)	3,465.0 (10.6)	
Hispanic	62,335.0 (6.6)	60,615.0 (6.7)	1,720.0 (5.3)	
Native American	4,660.0 (0.5)	4,505.0 (0.5)	155.0 (0.5)	
Other	18,190.0 (1.9)	17,625.0 (1.9)	565.0 (1.7)	
White	751,804.6 (80.1)	725,394.7 (80.1)	26,410.0 (80.7)	
Insurance				**<0.001**[2]
Medicaid	9,280.0 (1.0)	9,010.0 (1.0)	270.0 (0.8)	
Medicare	843,409.6 (89.9)	813,374.6 (89.8)	30,035.0 (91.8)	
No charge	160.0 (0.0)	155.0 (0.0)	5.0 (0.0)	
Other	10,730.0 (1.1)	10,355.0 (1.1)	375.0 (1.1)	
Private insurance	71,415.0 (7.6)	69,515.0 (7.7)	1,900.0 (5.8)	
Self-pay	3,600.0 (0.4)	3,455.0 (0.4)	145.0 (0.4)	
Frailty Risk				**<0.001**[2]
High	24,785.0 (2.6)	20,340.0 (2.2)	4,445.0 (13.6)	
Low	575,709.7 (61.3)	568,274.7 (62.7)	7,435.0 (22.7)	
Moderate	338,099.9 (36.0)	317,249.9 (35.0)	20,850.0 (63.7)	

[1] n (%)
[2] chi-squared test with Rao & Scott's second-order correction

Table 2. Breakdown of the cohort by rheumatic disease and delirium status.

Characteristic	Overall, N = 938,595[1]	No Delirium, N = 905,865[1]	Delirium, N = 32,730[1]
RA	658,269.7 (70.1)	637,119.7 (70.3)	21,150.0 (64.6)
AS	14,355.0 (1.5)	13,925.0 (1.5)	430.0 (1.3)
PsA	45,815.0 (4.9)	44,530.0 (4.9)	1,285.0 (3.9)
SLE	124,145.0 (13.2)	118,640.0 (13.1)	5,505.0 (16.8)
GCA	42,600.0 (4.5)	40,235.0 (4.4)	2,365.0 (7.2)
PMR	100,945.0 (10.8)	97,065.0 (10.7)	3,880.0 (11.9)
GCA with PMR	6,310.0 (0.7)	5,940.0 (0.7)	370.0 (1.1)

[1] n(%)
AS: Ankylosing spondylitis; GCA: Giant cell arteritis; RA: rheumatoid arthritis; PsA: Psoriatic Arthritis; SLE: systemic lupus erythematosus; PMR: Polymyalgia rheumatica

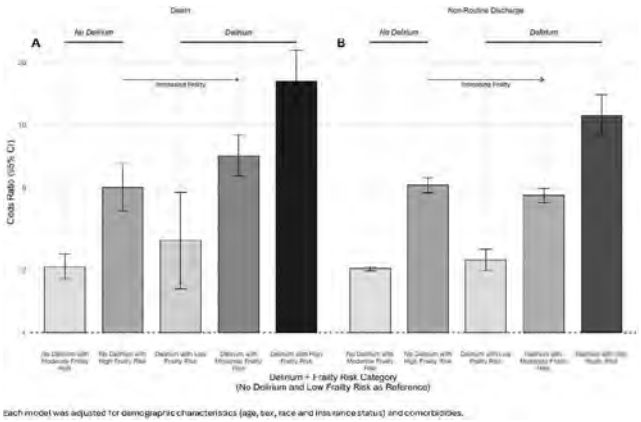


Figure 1. Multivariable analyses evaluating the association between frailty and delirium on a) in-hospital mortality and b) non-routine discharge among hospitalized older adults with rheumatic diseases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Among hospitalized older adults with rheumatic diseases, both frailty and delirium were independently linked to poorer outcomes, including higher in-hospital mortality and increased likelihood of discharge to a non-home setting. Notably, patients with both conditions faced the greatest risk. These findings underscore the potential value of proactively identifying frailty and delirium during hospitalization, as doing so could help clinicians better support safe transitions out of the hospital.

Disclosure: B. Bansal: None; **Y. Jung**: None; **A. Damluji**: None; **P. Goyal**: None; **N. Singh**: None.

Abstract Number: 0147

Rheumatoid Arthritis prevalence estimation in France using care pathways in the National Health Data System: opportunities and limitations - PREST study

cécile gaujoux-viala[1], adeline Ruyssen-Witrand[2], Laurent arnaud[3], clélia Bignon-Favary[4], Lauren Inchboard[4] and Bruno Fautrel[5], [1]Department of Rheumatology - CHU Nîmes, IDESP UM1318 INSERM – Univ. Montpellier, Nîmes, France, Nîmes, France, [2]Department of Rheumatology, C.H.U. de Toulouse, CIC 1436, Inserm, Université Paul Sabatier Toulouse III, Toulouse, France, Toulouse, France, [3]Service de rhumatologie, Hôpitaux Universitaires de Strasbourg, INSERM UMR-S 1109, Strasbourg, France, Strasbourg, France, [4]Horiana, Statistiques, Bordeaux, France, Bordeaux, France, [5]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: A total of 98.8% of French citizens are registered in the National Health Data System (SNDS), which includes claims data of all reimbursed health-related expenditures such as medication, professional healthcare services, and eligibility for full reimbursement of care related to chronic diseases (named Long-Term Disease (LTD) status).

The identification of rheumatoid arthritis (RA) patients in the SNDS is generally based on the presence of at least one RA-related ICD-10 code (International Classification of Diseases, 10th Revision) recorded during hospitalization and/or as part of an LTD status. Based on these criteria, annual mapping by the French health insurance system estimated an RA prevalence of 0.47% in the adult population in 2022. (1)

However, inclusion based on a single RA code may lack specificity, potentially leading to an overestimation of RA prevalence. Conversely, RA patients who are neither hospitalized nor covered by LTD status may not be identifiable using these criteria.

The PREST study aims to refine algorithms for improving the estimation of RA prevalence in France. Additionally, it seeks to analyze care pathways of identified patients and explore factors associated with disease management.

Methods: Data were extracted from the SNDS covering the period 2010–2022, using the following criteria: hospitalization records and/or LTD status with ICD-10 codes M05 or M06, and/or the dispensing of csDMARDs (conventional synthetic Disease-Modifying Antirheumatic Drugs) or b/tsDMARDs (biologic/targeted synthetic DMARDs).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Different RA identification algorithms were applied including additional criteria based on disease-management pathways.

Various combinations of these criteria were applied to define multiple subgroups. Corresponding RA prevalences were estimated for 2019.

Results: The data extraction identified 914,278 adult patients alive on January 1, 2019, who met at least one of the following criteria: RA LTD status (N=281,441), hospitalization with RA ICD-10 code (N=205,232), or treatment for RA without differential diagnosis (N=390,564). Patients without RA coding but with a differential diagnosis were excluded.

Among them, 355,350 met the standard definition corresponding to a prevalence of 0.70%. The new algorithms yielded highly variable prevalence estimates depending on the criteria.

The most stringent combination (patients with M05 or M06 codes receiving RA treatment) identified 249,240 cases (0.49%). Broadening the criteria to include untreated patients with at least two RA ICD-10 codes identified 275,694 patients (0.54%). Including previously excluded patients who had diagnostic procedures associated with an RA code or treatment further increased the number of identified patients to 392,974 (0.77%).

Conclusion: Depending on the identification criteria, RA prevalence in the French adult population in 2019 ranges from 0.49% to 0.82%, with the true prevalence most likely falling within this range. A previous study, EPIRHUM, conducted a general population survey in 2000 and reported an underestimated prevalence of 0.31% (2).

The significant variation in prevalence based on the identification criteria highlights the complexity of identifying RA in the SNDS.

Disclosure: c. gaujoux-viala: Amgen, 2, Biocon, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, Celtrion, 2, Chugai, 2, Eli Lilly, 2, Fresenius kabi, 2, Galapagos, 2, Gilead, 2, Janssen, 2, Medac, 2, Merck-Serono, 2, Mylan, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Sandoz, 2, Sanofi, 2, UCB, 2, Viatrix, 2; **a. Ruyssen-Witrand**: Abbvie, 2, Amgen, 2, Biocon, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celtrion, 2, Eli Lilly, 2, Fresenius kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, Nordic Pharma, 2, Novartis, 2, Pfizer, 2, Roche-Chugai, 2, Sandoz, 2, Sanofi, 2, UCB, 2; **L. arnaud**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, 6, Eli Lilly, 2, 6, Grifols, 2, 6, GSK, 2, 5, 6, Janssen, 2, 6, Kezar, 2, LFB, 2, 6, Medac, 2, 6, Merck, 2, Nordic Pharma, 2, Novartis, 2, 6, Pfizer, 2, 6, Roche-Chugaï, 2, 6, UCB, 2, 6; **c. Bignon-Favary**: Nordic Pharma, 7; **L. Inchboard**: Nordic Pharma, 7; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2.

Abstract Number: 0148

Air Pollution as a Trigger for Flares in Chronic Inflammatory Rheumatic Diseases: A Prospective Single-center Study in the South of France

Coralie Cruzel[1], antonio Iannelli[2], Alexandre Armengaud[3], Sonia Oppo[3], Marie Charlotte Trojani[4], Stephanie Ferrero[4], Veronique Breuil[4], Eric Fontas[5], Christian Roux[4] and **Clément Viala**[4], [1]2. Department of Clinical Research, Cimiez Hospital, CHU Nice, Université Côte d'Azur, Nice, France, France, France, [2]3. Centre Hospitalier Universitaire de Nice-Digestive Surgery and Liver Transplantation Unit, Archet 2 Hospital, 06202 Nice, France., NIce, France, [3]1. University Cote d'Azur, Rheumatology department, CHU Nice, France, Marseille, France, [4]1. University Cote d'Azur, Rheumatology department, CHU Nice, France, NIce, France, [5]2. Department of Clinical Research, Cimiez Hospital, CHU Nice, Université Côte d'Azur, Nice, France, NIce, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) and spondyloarthritis (SpA), are chronic inflammatory rheumatic diseases. Despite significant advancements in their management through novel therapies, some patients continue to experience flares or therapeutic resistance. Environmental factors, particularly smoking and air pollution, are known contributors to disease activity and progression. However, the role of air pollutants in exacerbating these diseases remains debated, especially in SpA.

Methods: This prospective study included 94 patients with stable RA (DAS28 < 3.2) or SpA (BASDAI < 4) recruited between January and May 2023. All patients were on stable biological therapies. Air pollutant levels (PM2.5, PM10, NO2, and O3) were obtained from AtmoSud, a regional air quality monitoring body. Exposure was calculated based on the patient's residential location over a 6-month period, with a focus on the 2 months preceding the first flare for patients experiencing disease exacerbations. Statistical analyses, including logistic regression and ROC curve analysis, were used to explore the relationship between pollutant levels and disease flares.

Results: : Sixty-one patients (65%) experienced at least one flare during the study period. Patients with flares had significantly higher exposure to PM10 (29 μg/m3 vs. 18.4 μg/m3, p=0.0003) and PM2.5 (11.7 μg/m3 vs. 8.5 μg/m3, p=0.0004). Conversely, lower exposure to ozone (O3) was associated with flares (71.9 μg/m3 vs. 104.6 μg/m3, p=0.0004). No significant differences were found for NO2 exposure. The multivariate analysis confirmed these associations, and ROC curves identified flare thresholds of 20.6 μg/m3 for PM10 and 9.5 μg/m3 for PM2.5.

Conclusion: Our findings highlight the role of air pollution, particularly particulate matter (PM2.5 and PM10), in triggering disease flares in patients with RA and SpA. These results support the need for stricter air quality standards to mitigate the impact of environmental factors on inflammatory rheumatic diseases.

Disclosure: C. Cruzel: None; **a. Iannelli**: None; **A. Armengaud**: None; **S. Oppo**: None; **M. Trojani**: None; **S. Ferrero**: None; **V. Breuil**: None; **E. Fontas**: None; **C. Roux**: None; **C. Viala**: None.

Abstract Number: 0149

Effect Of Osteoporosis And Opioid Use On Mortality And Unplanned Healthcare Utilization Among Patients With Rheumatoid Arthritis

Viengneesee Thao, Molly Moore Jeffery, Nafisseh Warner and **Elena myasoedova**, Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (**RA**) have a 2-fold increase in risk for osteoporosis compared to the general population. About 30-50% of RA patients experience fragility fractures, while pain management frequently includes prescription opioids, despite a paucity of long-term data on safety and efficacy. The impact of osteoporosis and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

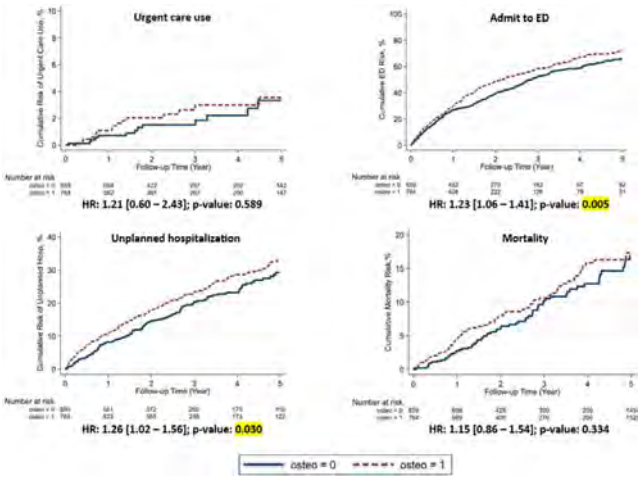


Figure 1: Cumulative risk of mortality and unplanned healthcare utilization among individuals with RA, 1:1 matched osteoporosis vs. no osteoporosis

opioid use on healthcare utilization and mortality in persons with RA is not well defined. We aimed to 1) compare mortality and unplanned healthcare use in those with RA with vs. without osteoporosis, and 2) compare 30-day mortality and unplanned healthcare use in those with RA and osteoporosis with vs. without opioid use.

Methods: This is a retrospective cohort analysis using the OptumLabs Data Warehouse, a large administrative claims database containing de-identified health information. We included commercially insured and Medicare Advantage beneficiaries, ≥50 years old, with RA. The outcomes included mortality and unplanned healthcare use, i.e. ED use, unplanned hospitalization, and urgent care. We identified persons with a diagnosis of RA between 1/1/2005-12/31/2023. For aim 1, we categorized those with RA by osteoporosis diagnosis status (1 inpatient or 2 outpatient claims with a diagnosis of osteoporosis, or at least 1 medication fill for an antiosteoporotic medication). For aim 2, we included everyone with a diagnosis of RA and osteoporosis, and categorized individuals by whether or not they had at least one opioid fill.

We 1:1 propensity score (PS) matched individuals based on the following variables: age, sex, race/ethnicity, geographic location, insurance type, comorbid conditions of interest, including the Elixhauser comorbid index, and use of glucocorticoids. After matching, a standardized mean difference < 0.10 was deemed acceptable. Cox proportional hazards regression was used to compare individuals with osteoporosis and without, in terms of mortality and unplanned healthcare use. Logistic regression was used to compare individuals with an opioid fill to those without a fill, in terms of 30-day mortality and unplanned healthcare use. As a sensitivity check we repeated our analysis using inverse probability of treatment weighting (IPTW) instead of propensity score matching.

Results: Among individuals with RA (862 matched pairs), those with osteoporosis had higher ED use [hazard ratio (HR): 1.23, 95% confidence interval (CI): 1.06 – 1.41; p-value = 0.005] and unplanned hospitalizations [HR: 1.26, 95% CI: 1.02 – 1.56; p-value = 0.03] compared to those without osteoporosis (Figure 1). The IPTW model showed similar results. Among individuals with RA and osteoporosis; the PS matched model did not yield any differences in mortality or healthcare utilization; however, the IPTW model (644 with an opioid fill vs. 189 without a fill) showed that those with an opioid fill had higher 30-day ED use [HR: 5.82, 95% CI: 1.77 – 19.19; p-value = 0.004] compared to those without a fill.

Conclusion: The presence of osteoporosis in RA and opioid use in patients with osteoporosis and RA pose a significant risk for unplanned healthcare utilization. Effective prevention and management of osteoporosis in RA, as well as judicious use of opioids can help prevent these unfavorable outcomes.

Disclosure: V. Thao: None; **M. Jeffery**: None; **N. Warner**: None; **E. myasoedova**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0150

Mortality in Anca-associated Vasculitis

Fabricio Benavides Villanueva[1], Vanesa Calvo-Río[2], Diana Prieto-Peña[3], Monica Renuncio-García[4], Adrian Martin-Gutierrez[5], Amparo Sanchez-Lopez[6], Claudia Poo-fernandez[7], Clara Escagedo-Cagigas[8], maria Rodríguez-Vidriales[8] and Ricardo Blanco[2], [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Immunopathology Group,Santander, Spain, Santander, Spain, [2]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [4]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain, [5]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Piélagos, Spain, [6]Division of Dermatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain, [7]Division of Pneumology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain, [8]Division of Nephrology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), include Granulomatosis with Polyangiitis (GPA), Microscopic Polyangiitis (MPA), and Eosinophilic Granulomatosis with Polyangiitis (EGPA).

Mortality rates are scare, Sims et al observed a morality rate of 38.4/1000 person-years (PY) between 2002-2017 (during 3385 PY of follow-up). Moreover, this depends on the AVV subtype, severity of the cohorts studied and their different classification criteria.

Our aim is to determine the mortality rate and the main causes of death in patients with GPA, MPA, and EGPA in a region of northern Spain.

Methods: Observational study of AAV from January 1, 2000, to December 31, 2024, in a northern Spanish. Classification of AAV was based on the 2022 ACR/EULAR criteria. Mortality rates were expressed as cases by 10^6 habitants/year (95% IC) and the Case Fatality rate expressed as percentage (95% IC) of deceased patients. Rates of mortality are expressed as the exposure-adjusted incidence rate (EAIR) per 100 person-years (PY). We defined two patient groups: **1) Study group** (deceased patients) and **2) Control group** (surviving patients) to compare the main clinical characteristics between these two groups. In addition, we evaluated the principal causes of death among the different types of ANCA-associated vasculitis.

	MPA	GPA	EGPA
MORTALITY RATE cases/10^6 inhabitants/ year (95% CI)	2.8 (1.7-4)	1.8 (0.9-42.7)	0.1 (-0.1-0.2)
CASE-FATALITY RATE (%), 95% CI	38.8% (20.1-57.5)	31.9% (14-49.9)	1% (-1-3)
EAIR cases/100 PY	7.9	3.86	0.6

TABLE. Comparison of Mortality and Case-Fatality Rates by ANCA Vasculitis Subtypes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

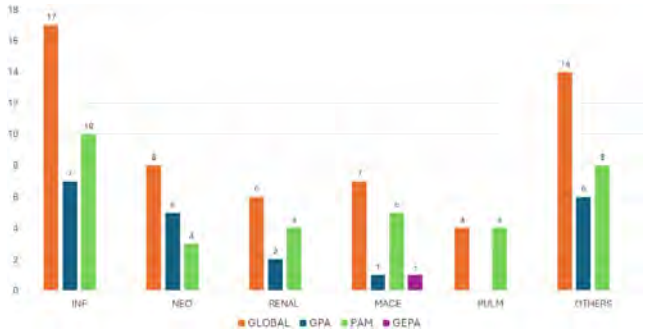


FIGURE. Main causes of death by ANCA Vasculitis Subtypes.

Results: We included 194 patients (99 men/95 women); mean age, 63.7±14.6 years, distributed as follows: GPA (n=67; 34.5%), MPA (n=69; 35.6%), and EGPA (n=28; 14.4%). Death was observed in 56 patients (28.9%); MPA (n=34; 60.7%), GPA (21; 37.5%), and EGPA (1; 3.5%).

After a mean of 6±5.4 years of follow up; in AAV group the overall mortality rate was 5.5 per 10^6 inhabitants/year (95% CI: 3.8-7.1); EAIR of 4.6/100 PY and the overall case-fatality rate was 32.5% (95% CI: 21.9-43.1).

Among the AAV subtypes, MPA showed the highest mortality and case-fatality rates with 2.8/10^6 inhabitants/year (95% CI: 1.7-4); EAIR: 7.9/100 PY and 38.8% (95% CI: 20.1-57.5), respectively. GPA followed with a mortality rate of 1.8/10^6 inhabitants/year (95% CI: 0.9-42.7); EAIR: 3.86/100 PY and a case-fatality rate of 31.9% (95% CI: 14-49.9). EGPA had low rates: a mortality rate of 0.1/10^6 habitants/year (95% CI: –0.1-0.2); EAIR: 0.6/100 PY and a case-fatality rate of 1% (95% CI: –1-3) **(Table)**.

The main causes of death were infections (n=17; 30%), neoplasia (n=8; 14%), major adverse cardiac events (MACE); (n=7; 13%), renal complications (n=6; 11%), and non-infectious pulmonary complications (n= 4; 7%). Infections were the most frequent cause of death in both GPA and MPA. In EGPA, the only cause of death was MACE.

Statistically significant differences were observed between the study group (deceased patients) and the control group (survivors), particularly regarding clinical manifestations associated with a higher risk of mortality, such as pulmonary and renal involvement.

Conclusion: Mortality rates and case-fatality rates in patients with AAV remain relatively high. mortality rate was higher in MPA and lower in EGPA. The most common causes of death were infections (30%), neoplasia (14%), and MACE (13%). Life-threatening organ involvement, such as pulmonary or renal disease, increases mortality risks.

Disclosure: F. Benavides Villanueva: None; **V. Calvo-Río**: AstraZeneca, 6, MSD, Roche, AbbVie, Lilly, Celgene, Grünenthal, and UCB Pharma, 2, 6; **D. Prieto-Peña**: None; **M. Renuncio-García**: None; **A. Martin-Gutierrez**: None; **A. Sanchez-Lopez**: None; **C. Poo-fernandez**: None; **C. Escagedo-Cagigas**: None; **m. Rodríguez-Vidriales**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0151

Post-COVID Decline in Systemic Lupus Erythematosus Mortality in the United States: A National Analysis from 2014 to 2023

Ghassan Makhoul[1], Aziz-ur-Rahman Khalid[2], Islam Rajab[1], Hasan Munshi[1], Emmanuel Olumuyide[3], MD Walid Akram Hussain[1], Aqsa Sorathia[1], Reshma John[1], Ahmed Huzien[1], ivan Mercado[1], Nargis Mateen[4] and Robert Lahita[2], [1]St. Josephs University Medical Center, Paterson, [2]St. Josephs University Medical Center, Wayne, NJ, [3]Advocate Illinois Masonic Medical Center, Chicago, [4]St. Josephs University Medical Center, Paterson, NJ

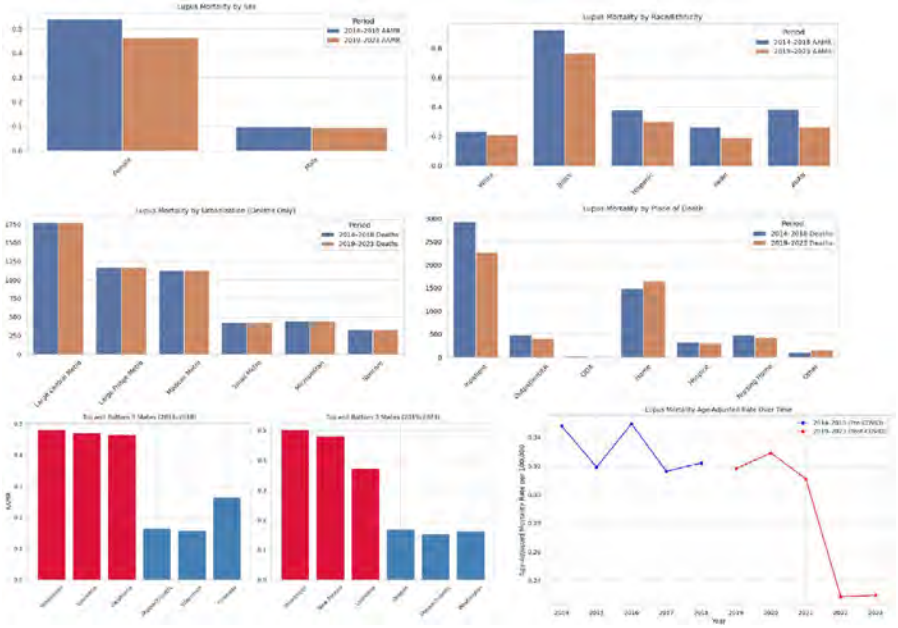
SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease with high morbidity and mortality. The impact of the COVID-19 pandemic on SLE-related deaths in the United States has not been comprehensively evaluated.

Methods: : We analyzed national mortality data from the CDC WONDER database for all deaths attributed to SLE (ICD-10 code M32) from 2014 to 2023. Data were stratified by sex, race/ethnicity, age group, state, urbanization level, and place of death. We defined two periods for analysis: pre-COVID (2014–2018) and post-COVID (2019–2023), and compared age-adjusted mortality rates (AAMRs) between periods.

Results: A total of 11,150 SLE-related deaths occurred, with 5,889 pre-COVID and 5,261 post-COVID. The national AAMR declined from 0.3496 to 0.2828 per 100,000, a 19.1% reduction. Women comprised over 85% of deaths, with AAMRs decreasing from 0.5399 to 0.4629. Male AAMRs remained lower (0.0981 to 0.0936). By race, Black individuals consistently had the highest AAMRs (0.9245 to 0.7649), followed by Hispanic (0.3820 to 0.3019), American Indian/Alaska Native (0.3846 to 0.2638), Asian (0.2632 to 0.1906), and White individuals (0.2323 to 0.2103). Mortality rates increased with age,



Graphs showing differences in pre vs post COVID state, urbanization, gender, race and place of death Lupus Mortality

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

peaking at 1.10 per 100,000 among those ≥85. Home deaths increased from 25.2% to 31.3%, while inpatient deaths declined from 49.9% to 43.3%. The highest AAMRs were observed in Mississippi and Louisiana; the lowest were in Washington and Massachusetts.

Conclusion: SLE mortality declined in the post-COVID era, with persistent disparities by sex and race. The shift in place of death suggests changes in healthcare access and utilization. These findings underscore the need for targeted, equitable strategies to improve lupus outcomes across populations.

Disclosure: G. Makhoul: None; **A. Khalid**: None; **I. Rajab**: None; **H. Munshi**: None; **E. Olumuyide**: None; **M. Hussain**: None; **A. Sorathia**: None; **R. John**: None; **A. Huzien**: None; **i. Mercado**: None; **N. Mateen**: None; **R. Lahita**: None.

Abstract Number: 0152

Exploring internet use and health information behaviour in patients with inflammatory rheumatic musculoskeletal diseases (RMD)

Ioana Andreica[1], Sulafa Chikh Mohamad[2], Dieter Wiek[3], Birgit Barten[3], Iulia Roman[4], Anja Kremser[5], David Kiefer[6], Philipp Sewerin[1], Uta Kiltz[7] and Xenofon Baraliakos[7], [1]Rheumazentrum Ruhrgebiet Herne; Ruhr-Universität Bochum, Germany, Herne, Germany, [2]Rheumazentrum Ruhrgebiet, Ruhr-Universität Bochum, Herne, Germany, [3]Deutsche Rheuma Liga, Germany, Bonn, [4]Rheumazentrum Ruhrgebiet, Ruhr-Universitét Bochum, Herne, Germany, [5]Rheumazentrum Ruhrgebiet, Herne, Germany, [6]Ruhr-Universitét Bochum; Private practice of rheumatology, Hattingen, Germany, Herne, Germany, [7]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Digital health literacy has recently become a focus of patient-centred recommendations, not only as a key social determinant of health, but also as a tool for evaluating the successful implementation and accessibility of eHealth interventions (1). In line with the overarching goal of empowering patients in their disease management, telemedicine and digital health tools are gaining ground (2). However, there is a gap in understanding the accessibility, usability and comprehensibility of available digital resources and the actual level of digital health literacy among patients with RMD. This study aims to assess the ability of patients with RMD to search for and select relevant disease-related information for self-management.

Methods: In this cross-sectional study, patients diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (SpA) were consecutively recruited from a tertiary centre. Patients completed a structured questionnaire covering internet access, search strategies, understanding and use of online disease-related information. Patients were

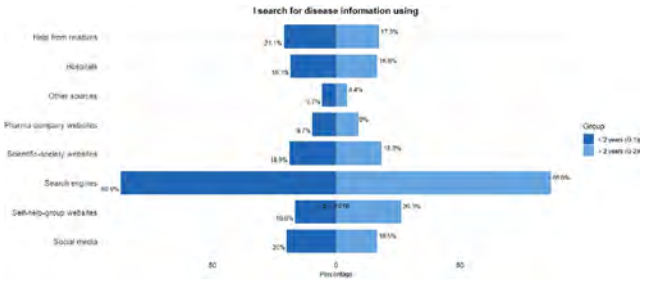


Figure 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

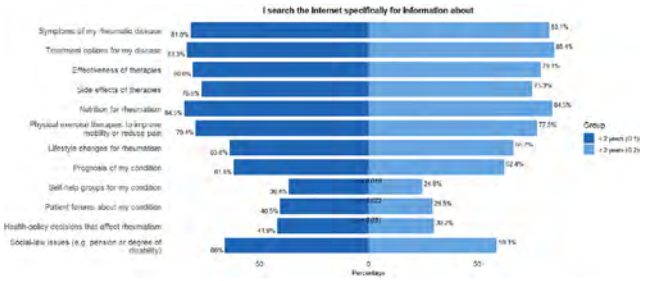


Figure 2.

categorised according to disease duration: early disease (< 2 years; Group 1, G 1) and long-standing disease (> 2 years from diagnosis; Group 2, G 2). Descriptive statistics and chi-squared tests were used for group comparisons. The study was conducted in collaboration with the patient's research partners from the German Rheumatology Patient Association (Deutsche Rheumaliga).

Results: A total of 705 patients were recruited (53.8% RA, 25.5% axSpA and 20.7% PsA) with a mean disease duration of 9.7 ± 10.5 years and a mean age of 53.7 years. The majority were female (62.7%).

Out of 705 patients, 552 (78.3%) indicated that they had searched for disease-related information on the internet. Most patients reported mainly using their smartphones (80.3%), with higher use of smartphones among patients with early vs. long-standing disease duration (86.5% vs 77.4%, respectively, $p < 0.05$). The predominance of information sources accessed is shown in Figure 1. Patients with early disease (G1) consulted the internet more frequently, with 19.3% searching several times a week, compared to 8.2% of patients with a long-standing disease (G 2). The majority found online content understandable (79.8%) and would seek clarification from their rheumatologist if in doubt (83.7%). Two-thirds (68.2%) reported using the information in their daily lives, with no significant difference between groups. Notably, patients in G 1 were more likely to investigate community, social and regulatory issues ($p< 0.05$), with 36.4% (G1) vs 24.8% (G2) looking for self-help groups, 40.5% (G1) vs 29.5% (G2) for patient forums and 41.9 % (G1) vs 30.2 % (G2) for health policy decisions, Figure 2.

Conclusion: Searching for health information online is common among patients with RMD and is used as a supplement to regular outpatient consultations. The vast majority of recruited patients, especially those in the early stages of their disease, actively seek online information and feel competent to use it. High smartphone usage highlights the need for mobile-optimised, evidence-based resources

Disclosure: I. Andreica: Boehringer-Ingelheim, 6, Chugai, 2, 5, 12, Consulting fees, Eli Lilly, 2, 5, 6, 12, Consulting fees, Galapagos, 2, 5, 12, Consulting fees, Gilead, 2, 5, GSK, 2, 5, Janssen, 2, 5, MSD, 2, 5, 6, Novartis, 5, 12, Consulting fees, received payments for other services, Pfizer, 2, 5, Sobi, 2, 5, 6, takeda, 2, 5, UCB, 2, 6, 12, Consulting fees; **S. Chikh Mohamad**: None; **D. Wiek**: None; **B. Barten**: None; **I. Roman**: None; **A. Kremser**: None; **D. Kiefer**: AbbVie/Abbott, 2, 5, Alpha sigma, 2, 6, UCB, 1, 2, 6; **P. Sewerin**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Axiom Health, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Chugai, 2, 5, Deutscher Psoriasis-Bund, 2, 5, Eli Lilly, 2, 5, Gilead, 2, 5, Hexal, 2, 5, Janssen, 2, 5, Johnson & Johnson, 2, 5, Medical Communication, 2, Medici GmbH, 2, 5, medi-login, 2, 5, Novartis, 2, 5, Onkowissen GmbH, 2, 6, Pfizer, 2, 5, Roche, 2, 5, Sanofi-Genzyme, 2, 5, Swedish Orphan Biovitrum, 2; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor.

Abstract Number: 0153

Patient Experience and Implementation of an Electronic Patient-Reported Outcome Measures (ePROM) System for Remote Monitoring in BIOBADASER

Isabel Castrejón Fernández[1], Lucia Otero[2], Antonio Mera-Valera[3], Alicia Garcia[4], Silvia Gomez-Sabater[5], Raquel Martín-Domenech[6], Jose Alvaro-Gracia[7], Juan Camilo Sarmiento-Monroy[8], Beatriz Ventosa[2], Fernando Sánchez-Alonso[9] and BIOBADASER, [1]Department of Rheumatology. Hospital General Universitario Gregorio Marañon. IiSGM. Universidad Complutense Madrid, Madrid, Spain, [2]Spanish Society of Rheumatology, Madrid, Spain, [3]H. Clínico Universitario de Santiago, Santiago de Compostela, [4]Rheumatologist, La Laguna, Spain, [5]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [6]H. Universitario de Elda, Elda, Spain, [7]Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Department of Rheumatology, Hospital General Universitario Gregorio Marañón and Faculty of Medicine, Complutense University of Madrid, Madrid, Spain, [8]Hospital Clnic Barcelona, Barcelona, Spain, [9]Sociedad Española de Reumatología, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Patient-Reported Outcome Measures (PROMs) are integral to shared decision-making and quality improvement in rheumatology. They are recommended for monitoring treatment response, assessing quality of life, and supporting clinical care. Scientific societies as EULAR have promoted standardized of PROM collection through data set recommendations and an Outcome Measures Library with instruments and validation data https://oml.eular.org/. This study aimed to: (1) develop and implement an electronic PROM (ePROM) system within BIOBADASER, a multicenter registry of advanced therapies; (2) analyze initial results post-implementation; and (3) evaluate usability and patient satisfaction.

Methods: A core set of validated and feasible PROMs was selected based on the International Consortium for Health Outcomes Measurement (ICHOM) recommendations and expert consensus. These were incorporated into a web-based application designed for patient self-completion via internet-enabled devices (smartphone, tablet, computer). Patients initiating advanced therapies were invited to participate. A pilot phase involving six centres was conducted from December 2023 to June 2024, followed by full-scale implementation across all centres. Descriptive statistics summarized demographic, clinical, and PROM data.

Results: From December 2023 to November 2024, 136 patients were invited to participate; 95 (70%) accessed the system, and 81 (60%) completed the questionnaires. Participants were predominantly female (64.2%) with a mean age of 50.9 years. The most common diagnoses were rheumatoid arthritis (35.8%), spondyloarthritis (19.8%), and psoriatic arthritis (17.3%). TNF inhibitors were the most frequently initiated therapy (72.8%). RAPID3 scores indicated high disease activity (mean 13.3 ± 6.8). Most patients reported minimal problems with mobility (69.1%), self-care (82.7%), usual activities (59.2%), and anxiety/depression (67.9%). The mean global health score was 55.6. Regarding usability, 81% experienced no or slight difficulty using the system, 79% found the instructions clear or very clear, and 80.2% were quite or very satisfied. A majority (66.7%) preferred online reporting over paper-based methods, and 87.6% felt comfortable using digital devices.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of patients using the ePROMs system

		Total
Number of patients, n		81
Female (%)		52 (64.2)
Age, mean (SD)		50.9 (10.2)
Diagnoses, n (%)		
Rheumatoid arthritis		29 (35.8)
Spondyloarthritis		29 (19.8)
Psoriatic arthritis		14 (17.3)
Other		32 (27.1)
Comorbidities		
Smoking habit, n (%)		
Never smoker		47 (58.0)
Current smoker		20 (24.7)
Former smoker		11 (13.6)
Body mass index, n (%)		
Underweight		6 (7.4)
Normal weight		28 (34.6)
Overweight		25 (30.9)
Obesity		14 (17.3)
Unknown		8 (9.9)
Hypercholesterolemia, n (%)		14 (17.3)
Hypertension, n (%)		15 (18.5)
Charlson comorbidity index, n (%)		
0		46 (56.8)
1		27 (33.3)
2		8 (9.9)
Initiated b/tsDMARD treatments, n (%)		
Anti TNFs		59 (72.8)
JAK inhibitors		9 (11.1)
Anti IL17A		7 (8.6)
Anti 12/23		2 (2.5)
Inhib Blys		1 (1.2)
CTLA4-Ig		3 (3.7)
PROMs		
Pain VAS (0-10), mean (SD)		5.6 (2.9)
Fatigue VAS (0-10), mean (SD)		4.9 (3.4)
Patient Global Assessment VAS (0-10), mean (SD)		4.9 (2.9)
MDHAQ (0-3), mean (SD)		2.7 (1.8)
RAPID3, mean (SD)		13.3 (6.8)
Tender joint count, mean (SD)		7.8 (7.9)
Quality of life (EQ5D-5L), n (%)		
Mobility	I have no problems in walking about	27 (33.3)
	I have slight problems in walking about	29 (35.8)
Self-care	I have no problems washing or dressing myself	41 (50.6)
	I have slight problems washing or dressing myself	26 (32.1)
Usual activities (work, study,	I have no problems doing my usual activities	15 (18.5)
housework, family or leisure)	I have slight problems doing my usual activities	33 (40.7)
Pain / discomfort	I have no pain/slight or discomfort	37 (44.9)
	I have moderate pain or discomfort	18 (22.2)
	I have severe/extreme pain or discomfort	22 (26.1)

Table 2. Patient experience with the electronic PROMs system and level of satisfaction

Usability and level of satisfaction		
Do you think PROMs help improve your care?	Somewhat	19 (23.5)
	Quite	27 (33.3)
	Very much	13 (16.1)
Number of questions	Appropriate	31 (38.3)
	Many questions but manageable	42 (51.9)
	Too many questions	2 (2.5)
Difficulty to complete	No difficulty	54 (66.7)
	Sligh difficulty	12 (14.8)
	Too difficult	2 (2.5)
Clarity of questions	Slightly	6 (7.4)
	Quite	43 (53.1)
	Very much	21 (25.9)
Level of satisfaction with questionnaires	Quite satisfied	50 (61.7)
	Very satisfied	15 (18.5)
Online reporting system better or worse	Same	10 (12.4)
than paper reporting	Somewhat better	9 (11.1)
	Better	54 (66.7)
Level of comfort using technology and	Quite comfortable	35 (43.2)
electronic devices	Very comfortable	36 (44.4)
Do you feel it is adequate to complete the PROMs every 3 months?	Yes	63 (77.8)

Conclusion: The ePROM system was feasible, well accepted, and effective for remote disease monitoring. Patients expressed high satisfaction and a preference for digital tools, supporting the integration of ePROMs into rheumatology registries to enhance personalized, patient-centred care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: I. Castrejón Fernández: None; **L. Otero**: None; **A. Mera-Valera**: None; **A. Garcia**: None; **S. Gomez-Sabater**: None; **R. Martín-Domenech**: None; **J. Alvaro-Gracia**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Galapagos, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **J. Sarmiento-Monroy**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6; **B. Ventosa**: None; **F. Sánchez-Alonso**: None.

Abstract Number: 0154

Incidence and Prevalence of Connective Tissue Diseases with Interstitial Lung Disease (CTD-ILD) in the United States

Diana Martins[1], George Mu[2], Elaine Irving[3], Roger A. Levy[4], Nisha Bhatt[5] and **Keele E. Wurst**[6], [1]GSK, Epidemiology, Toronto, ON, Canada, [2]GSK, Statistics, Collegeville, PA, [3]GSK, Clinical, Stevenage, United Kingdom, [4]GSK, Specialty Care, Global Medical Affairs, Collegeville, PA, [5]GSK, Global Medical Affairs, Collegeville, PA, [6]GSK, Immunology and Emerging Epidemiology, Durham, NC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite the high disease burden and reduced quality of life for patients with CTD-ILD, data on its incidence and prevalence – particularly by CTD subtype (RA, SSc, SLE, IIM, MCTD and pSS) – remains limited. This study describes the incidence and prevalence of CTD-ILD and its subtypes in the US.

Methods: This retrospective cohort study (GSK Studies 223907, 224023) of two large US databases (Optum® de-identified Electronic Health Record data set [Optum® EHR], and MarketScan® Commercial and Medicare Databases [MarketScan]) identified adults with CTD-ILD subgroups of interest between January 2018 and December 2023, using ICD-10 diagnosis codes and algorithms, in a two-step process: 1) identifying individuals with CTD, and 2) identifying ILD on or within 365 days before or after the CTD diagnosis. Index date: the later date of the first CTD or ILD diagnosis. Identified CTD-ILD cases were classified as prevalent. Of those, incident cases required a 1-year enrolment prior to index with no ILD claims during this "washout" period. Incidence was presented per 100,000 person-years (PY) and prevalence per 100,000 persons (comprising crude rates, including stratification by age and sex, and age- and sex-adjusted rates).

Table 1. Crude and adjusted incidence (per 100,000 person-years) of CTD-ILD – overall and in CTD-ILD subgroups of interest – in US Optum® EHR and MarketScan databases. *Overall captures any CTD-ILD (no duplicates), using ICD-10 diagnosis codes. Patients may be captured in more than 1 CTD subtype but will contribute only once to the CTD-ILD overall column. CI, confidence interval; CTD, connective tissue diseases; EHR, electronic health record; ICD-10, International Classification of Diseases 10th Revision; IIM, idiopathic inflammatory myositis; ILD, interstitial lung disease; MCTD, mixed connective tissue disease; pSS, primary Sjögren's syndrome; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

	CTD-ILD overall*	RA-ILD	SSc-ILD	SLE-ILD	IIM-ILD	MCTD-ILD	pSS-ILD
Optum® EHR							
Patients, N (%)	**10,455**	**6228 (59.6)**	**1699 (16.3)**	**1877 (18.0)**	**973 (9.3)**	**752 (7.2)**	**1831 (15.6)**
Crude incidence (95% CI)	10.0 (9.8, 10.2)	6.0 (5.8, 6.1)	1.6 (1.6, 1.7)	1.6 (1.5, 1.7)	0.9 (0.9, 1.0)	0.7 (0.7, 0.8)	1.6 (1.5, 1.6)
Female	12.8 (12.5, 13.1)	7.3 (7.1, 7.5)	2.3 (2.2, 2.4)	2.4 (2.3, 2.5)	1.1 (1.0, 1.2)	1.0 (1.0, 1.1)	2.3 (2.2, 2.4)
Male	6.1 (5.9, 6.3)	4.1 (3.9, 4.3)	0.7 (0.6, 0.8)	0.5 (0.4, 0.6)	0.7 (0.6, 0.8)	0.3 (0.2, 0.3)	0.5 (0.4, 0.6)
Age 18–64	6.5 (6.3, 6.7)	3.3 (3.2, 3.5)	1.3 (1.2, 1.4)	1.4 (1.3, 1.5)	0.8 (0.8, 0.9)	0.7 (0.6, 0.7)	1.0 (1.0, 1.1)
Age 65+	21.9 (21.3, 22.5)	14.9 (14.4, 15.3)	2.2 (2.1, 2.5)	2.3 (2.1, 2.5)	1.3 (1.2, 1.5)	0.9 (0.8, 1.1)	1.5 (1.1, 1.5)
Age- and sex-adjusted incidence (95% CI)	9.4 (9.1, 9.8)	5.6 (5.4, 5.9)	1.5 (1.4, 1.6)	1.5 (1.3, 1.6)	0.9 (0.8, 1.0)	0.7 (0.6, 0.8)	1.4 (1.3, 1.6)
MarketScan							
Patients, N (%)	**2512**	**1444 (57.5)**	**425 (16.9)**	**548 (21.8)**	**385 (15.3)**	**228 (9.1)**	**468 (18.6)**
Crude incidence (95% CI)	7.3 (7.0, 7.6)	4.2 (4.0, 4.4)	1.2 (1.1, 1.4)	1.6 (1.5, 1.7)	1.1 (1.0, 1.2)	0.7 (0.6, 0.8)	1.4 (1.2, 1.5)
Female	10.5 (10.1, 11.0)	5.9 (5.6, 6.3)	1.9 (1.8, 2.2)	2.6 (2.4, 2.9)	1.4 (1.3, 1.6)	1.1 (1.0, 1.3)	2.2 (2.0, 2.5)
Male	3.7 (3.4, 4.0)	2.3 (2.1, 2.5)	0.5 (0.4, 0.6)	0.4 (0.4, 0.6)	0.8 (0.6, 0.9)	0.2 (0.1, 0.3)	0.4 (0.3, 0.5)
Age 18–64	6.5 (6.2, 6.8)	3.6 (3.4, 3.8)	1.2 (1.1, 1.3)	1.5 (1.4, 1.7)	1.1 (1.0, 1.2)	0.7 (0.6, 0.8)	1.2 (1.1, 1.2)
Age 65+	26.4 (23.8, 29.3)	17.8 (15.6, 20.2)	2.9 (2.1, 4.0)	3.1 (2.3, 4.2)	2.0 (1.4, 3.0)	0.7 (0.4, 1.4)	5.0 (3.9, 6.3)
Age- and sex-adjusted incidence (95% CI)	10.7 (10.0, 11.4)	6.6 (6.1, 7.2)	1.5 (1.3, 1.8)	1.8 (1.6, 2.1)	1.3 (1.1, 1.5)	0.7 (0.5, 0.8)	2.0 (1.7, 2.3)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Crude and adjusted prevalence (per 100,000 persons) of CTD-ILD – overall and in CTD-ILD subgroups of interest – in US Optum® EHR and MarketScan databases. *Overall captures any CTD-ILD (no duplicates), using ICD-10 diagnosis codes. Patients may be captured in more than 1 CTD subtype but will contribute only once to the CTD-ILD overall column. CI, confidence interval; CTD, connective tissue diseases; EHR, electronic health record; ICD-10, International Classification of Diseases 10th Revision; IIM, idiopathic inflammatory myositis; ILD, interstitial lung disease; MCTD, mixed connective tissue disease; pSS, primary Sjögren's syndrome; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

	CTD-ILD overall*	RA-ILD	SSc-ILD	SLE-ILD	IIM-ILD	MCTD-ILD	pSS-ILD
Optum® EHR							
Patients, N (%)	**20,276**	**11,644 (57.4)**	**3852 (19.0)**	**3202 (15.8)**	**2050 (10.1)**	**1597 (7.9)**	**3095 (15.3)**
Crude prevalence (95% CI)	46.1 (45.4, 46.7)	26.5 (26.0, 26.9)	8.8 (8.5, 9.0)	7.3 (7.0, 7.5)	4.7 (4.5, 4.9)	3.6 (3.5, 3.8)	7.0 (6.8, 7.4)
Female	61.4 (60.4, 62.4)	33.6 (32.9, 34.4)	12.8 (12.4, 13.3)	11.4 (11.0, 11.8)	5.7 (5.4, 6.0)	5.4 (5.1, 5.7)	10.8 (10.4, 11.2)
Male	26.9 (26.2, 27.6)	17.5 (16.9, 18.1)	3.7 (3.4, 3.9)	2.1 (1.9, 2.3)	3.4 (3.2, 3.7)	1.4 (1.2, 1.5)	2.3 (2.1, 2.6)
Age 18–64	28.9 (28.3, 29.4)	13.8 (13.4, 14.2)	6.9 (6.7, 7.2)	6.2 (6.0, 6.5)	4.1 (3.9, 4.3)	3.3 (3.1, 3.5)	4.5 (4.3, 4.7)
Age 65+	108.8 (106.7, 110.9)	72.7 (71.0, 74.5)	15.4 (14.6, 16.2)	11.1 (10.4, 11.7)	6.8 (6.3, 7.3)	4.7 (4.3, 5.1)	16.3 (15.5, 17.2)
Age- and sex-adjusted prevalence (95% CI)	45.1 (44.0, 46.1)	26.1 (25.2, 26.9)	8.4 (8.0, 8.9)	6.9 (6.5, 7.3)	4.6 (4.2, 4.9)	3.5 (3.2, 3.8)	6.8 (6.4, 7.2)
MarketScan							
Patients, N (%)	**9342**	**4972 (53.2)**	**1942 (20.8)**	**1875 (20.1)**	**1463 (15.7)**	**866 (9.3)**	**1501 (16.1)**
Crude prevalence (95% CI)	24.7 (24.2, 25.2)	13.2 (12.8, 13.5)	5.1 (4.9, 5.4)	5.0 (4.7, 5.2)	3.9 (3.7, 4.1)	2.3 (2.1, 2.5)	4.0 (3.8, 4.2)
Female	36.2 (35.3, 37.0)	16.6 (16.0, 17.2)	8.2 (7.8, 8.6)	8.4 (7.9, 8.9)	5.1 (4.8, 5.4)	3.7 (3.5, 4.0)	6.6 (6.2, 6.9)
Male	12.4 (11.9, 12.9)	7.3 (6.9, 7.7)	1.9 (1.7, 2.1)	1.3 (1.1, 1.5)	2.5 (2.3, 2.8)	0.7 (0.6, 0.9)	1.2 (1.0, 1.4)
Age 18–64	20.7 (19.8, 20.7)	10.0 (9.7, 10.4)	4.6 (4.4, 4.8)	4.6 (4.3, 4.8)	3.6 (3.4, 3.8)	2.2 (2.0, 2.3)	3.3 (3.1, 3.5)
Age 65+	134.8 (128.9, 140.7)	89.4 (84.6, 94.2)	17.9 (15.7, 20.0)	15.2 (13.2, 17.2)	10.0 (8.4, 11.6)	5.6 (4.4, 6.9)	20.8 (18.5, 23.1)
Age- and sex-adjusted prevalence (95% CI)	44.5 (43.8, 45.6)	27.0 (26.1, 27.8)	7.3 (6.9, 7.8)	6.7 (6.3, 7.1)	5.0 (4.6, 5.3)	2.9 (2.6, 3.1)	6.9 (6.5, 7.4)

Results: Among all patients with CTD-ILD identified (N=20,276 Optum® EHR and N=9342 MarketScan), most were female (Optum® EHR: 74.1%; MarketScan: 76.0%), with median (interquartile range) age of 65 (56, 73) years (Optum® EHR) and 56 (49, 63) (MarketScan), and had RA-ILD (Optum® EHR: 57.4%, MarketScan: 53.2%). In Optum® EHR, race of patients was 73.2% Caucasian, 16.8% Black, 2.6% Asian, and 7.4% had missing race. Race of patients was not captured in MarketScan.

Age- and sex-adjusted rates for CTD-ILD overall were 9.4 (Optum® EHR) and 10.7 (MarketScan) per 100,000 PY for incidence (**Table 1**), and 45.1 (Optum® EHR) and 44.5 (MarketScan) per 100,000 persons for prevalence (**Table 2**). Age- and sex- adjusted incidence varied by CTD subtype in Optum® EHR (0.7 [MCTD-ILD] to 5.6 [RA-ILD]) and MarketScan (0.7 [MCTD-ILD] to 6.6 [RA-ILD]) (**Table 1**). This variation also existed for adjusted prevalence rates (**Table 2**). Crude stratified rates were approximately double in females versus males, and ≥3 × higher in ages 65 and older versus 18–64 years, across all CTD-ILD subtypes (**Tables 1** and **2**). Incidence and prevalence rates increased over the study period.

Conclusion: The scarcity of US data on CTD-ILD epidemiology underscores the importance of investigating ILD in patients with CTD, and vice versa, to aid diagnosis and intervention, particularly in older patients and females, where CTD-ILD incidence and prevalence rates are highest. Overall, CTD-ILD incidence and prevalence rates were highest for RA-ILD, corresponding to the higher rates of RA compared with other CTD subtypes. Importantly, findings for age- and sex-adjusted rates were similar between these two large US databases capturing different US patient populations. These prevalence data suggest that 116,000–118,000 individuals in the US have CTD-ILD (based on 2023 adult population estimated at 262.1 million). These novel data highlight a substantial healthcare burden, especially in older patients and females.

Funding: GSK

Original presentation: EULAR 2025

Disclosure: D. Martins: GSK, 12, 3; **G. Mu**: GSK, 12, 3, 8; **E. Irving**: GSK, 12, 3; **R. Levy**: GSK, 3, 8; **N. Bhatt**: Amgen, 12, GSK, 12, 3; **K. Wurst**: GSK, 12, 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0155

Effect Modification of Cigarette Smoking on the Relationship between Post Traumatic Stress Disorder and Rheumatoid Arthritis Risk

Kelsey Coziahr[1], Harlan Sayles[1], Tate Johnson[1], Joshua Baker[2], Punyasha Roul[3], Grant Cannon[4], Gary Kunkel[5], Bryant England[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pennsylvania, Philadelphia, PA, [3]UNMC, Omaha, NE, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]Salt Lake City VA, Salt Lake City, UT

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Post-traumatic stress disorder (PTSD) is associated with increased systemic inflammation that may increase the risk of developing autoimmune disorders such as rheumatoid arthritis (RA). The prevalence of cigarette smoking, an established risk factor in RA, is substantially higher in patients with PTSD than in the general population. We aimed to quantify the association between PTSD and the risk of developing RA in U.S. veterans, examining whether this association is confounded or modified by smoking.

Methods: We conducted a nested, case-control study using national Veteran Health Administration data from 2006-2019, identifying patients with incident RA (≥2 diagnostic codes, rheumatologist diagnosis, positive autoantibody or DMARD fill, plus ≥365 days in VA care before a DMARD fill or RA ICD code). Cases were matched to non-RA controls on the date the RA algorithm was fulfilled, at a ratio up to 1:10 by age, sex and year of VA enrollment. PTSD and other mental health disorders (OMH; i.e., bipolar disorder, depression, anxiety and substance use) were identified retrospectively and defined by the presence of ≥2 ICD9/10 codes. Conditional multivariable logistic regression was used to examine the association of PTSD (± OMH) and OMH (without PTSD) with RA, adjusting for race, ethnicity, urban/rural residence, smoking status, and BMI and including an interaction term for RA status and smoking. Based on initial results, additional models were stratified by ever vs. never smoking status and included age, sex, and year of VA enrollment as covariates in addition to those noted. Separate models were used to examine associations in subgroups defined by sex and seropositivity status (RF and/or aCCP).

Results: Patients included in this analysis (n=357,361; n=32,884 with RA) had a mean age of 53 years, 87% were male, and 70% had ever smoked. Among RA cases, 76% were RF or aCCP positive. PTSD, OMH, and smoking were all more frequent in patients with RA than controls (**Table 1**). In multivariable analyses, there was evidence of a highly significant smoking-PTSD interaction (p< 0.001). In subsequent multivariable analyses stratified by ever smoking status, the association of PTSD (vs. no PTSD or OMH) with RA was higher in never smokers (aOR 1.54; 95% CI 1.41, 1.69) than ever smokers (aOR 1.20;

Table 1: Frequency of PTSD and smoking status in RA cases and non-RA controls with unadjusted associations shown

	RA	Non-RA	OR (95% CI)*
Mental Health Diagnosis			
No MH Diagnosis	16,541 (50)	195,971 (60)	*Referent*
Other MH (No PTSD)	10,241 (31)	84,985 (26)	1.49 (1.45, 1.53)
PTSD	6,102 (19)	43,521 (13)	1.80 (1.74, 1.86)
Smoking Status			
Never	4,583 (14)	56,602 (17)	*Referent*
Former	10,406 (32)	77,546 (24)	1.73 (1.67, 1.79)
Current	17,410 (53)	143,212 (44)	1.58 (1.52, 1.63)
Missing	485 (1)	47,117 (15)	0.13 (0.11, 0.14)

*Conditional logistic regression accounting for matching on age, sex, and VA enrollment year
Abbreviations: PTSD, post-traumatic stress disorder; MH, mental health; RA, rheumatoid arthritis; OR, odds ratio (unadjusted)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Multivariable logistic regression models examining association of PTSD and Other Mental Health diagnoses (vs. No PTSD or OMH) with RA in Ever and Never Smokers

	RA	Non-RA	aOR (95% CI)*
Ever Smoking			
No MH Diagnosis	13,516 (49)	115,027 (52)	*Referent*
Other MH (No PTSD)	8,948 (32)	69,408 (31)	1.09 (1.06, 1.12)
PTSD	5,352 (19)	36,323 (16)	1.20 (1.16, 1.25)
Never Smoking			
No MH Diagnosis	2,668 (58)	38,724 (68)	*Referent*
Other MH (No PTSD)	1,209 (26)	11,760 (21)	1.40 (1.30, 1.51)
PTSD	706 (15)	6,118 (11)	1.54 (1.41, 1.69)

* Models adjusted for age, sex, year of VA enrollment, race, ethnicity, urban/rural residence, BMI
Abbreviations: PTSD, post-traumatic stress disorder; MH, mental health; RA, rheumatoid arthritis; OMH, Other Mental Health; aOR, adjusted odds ratio

Table 3: Multivariable logistic regression models examining association of PTSD and Other Mental Health diagnoses (vs. No PTSD or OMH) with RA in Ever and Never Smokers in subgroups defined by sex and seropositivity status

	RA	Non-RA	aOR (95% CI)*
Men - Ever Smoking			
No MH Diagnosis	12,560 (51)	106,148 (54)	*Referent*
Other MH (No PTSD)	7,635 (31)	60,463 (31)	1.07 (1.03, 1.10)
PTSD	4,569 (18)	31,299 (16)	1.19 (1.15, 1.24)
Men - Never Smoking			
No MH Diagnosis	2,106 (63)	31,150 (72)	*Referent*
Other MH (No PTSD)	776 (23)	8,088 (19)	1.36 (1.25, 1.49)
PTSD	468 (14)	4,238 (10)	1.55 (1.39, 1.73)
Women – Ever Smoking			
No MH Diagnosis	956 (31)	8,879 (39)	*Referent*
Other MH (No PTSD)	1,313 (43)	8,945 (39)	1.32 (1.21, 1.44)
PTSD	783 (26)	5,024 (22)	1.36 (1.23, 1.51)
Women – Never Smoking			
No MH Diagnosis	562 (46)	7,574 (58)	*Referent*
Other MH (No PTSD)	433 (35)	3,672 (28)	1.49 (1.30, 1.71)
PTSD	238 (19)	1,880 (14)	1.55 (1.32, 1.82)
Seropos. – Ever Smoking			
No MH Diagnosis	8,656 (49)	115,027 (52)	*Referent*
Other MH (No PTSD)	5,621 (32)	69,408 (31)	1.06 (1.02, 1.10)
PTSD	3,330 (19)	36,323 (16)	1.16 (1.11, 1.21)
Seropos. – Never Smoking			
No MH Diagnosis	1,140 (58)	38,724 (68)	*Referent*
Other MH (No PTSD)	632 (26)	11,760 (21)	1.38 (1.25, 1.53)
PTSD	382 (16)	6,118 (11)	1.55 (1.38, 1.74)
Seroneg. – Ever Smoking			
No MH Diagnosis	2,255 (43)	115,027 (52)	*Referent*
Other MH (No PTSD)	1,818 (35)	69,408 (31)	1.29 (1.21, 1.37)
PTSD	1,144 (22)	36,323 (16)	1.47 (1.38, 1.58)
Seroneg. – Never Smoking			
No MH Diagnosis	575 (53)	38,724 (68)	*Referent*
Other MH (No PTSD)	308 (29)	11,760 (21)	1.61 (1.40, 1.86)
PTSD	197 (18)	6,118 (11)	1.94 (1.64, 2.29)

* Models adjusted for age, sex, year of VA enrollment, race, ethnicity, urban/rural residence, BMI; Abbreviations: PTSD, post-traumatic stress disorder; MH, mental health; RA, rheumatoid arthritis; OMH, Other Mental Health; aOR, adjusted odds ratio

95% CI 1.16, 1.25). Similar associations, though lower in magnitude, were observed for OMH (**Table 2**). PTSD-related risk remained quantitatively higher in never vs. ever smokers in subgroups defined by sex and seropositivity with a higher risk observed for seronegative RA (**Table 3**).

Conclusion: In addition to validating prior reports demonstrating an increased risk of RA attributable to both PTSD and cigarette smoking, these results suggest that the relationship of PTSD with RA disease susceptibility is modified, rather than being confounded, by smoking status with a greater contribution to RA risk in never smokers. PTSD also appears to be more closely associated with the development of seronegative RA. These results highlight a complex relationship between PTSD and OMH with RA development and call for research into how mental health may influence the development of distinct RA phenotypes.

Disclosure: K. Coziahr: None; **H. Sayles**: None; **T. Johnson**: None; **J. Baker**: None; **P. Roul**: None; **G. Cannon**: None; **G. Kunkel**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0156

Heat Exposure and Acute Care Utilization among Individuals with Rheumatic Conditions: A Time Series Framework for Identifying Delayed Associations

Leah Santacroce[1], Jamie Collins[1], Ana Valle[2], Rebecca Summit[3], Paul Dellaripa[4] and Candace Feldman[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Brookline, MA, [3]Brigham & Women's Hospital, Boston, MA, [4]Brigham and Womens Hospital, Boston, MA

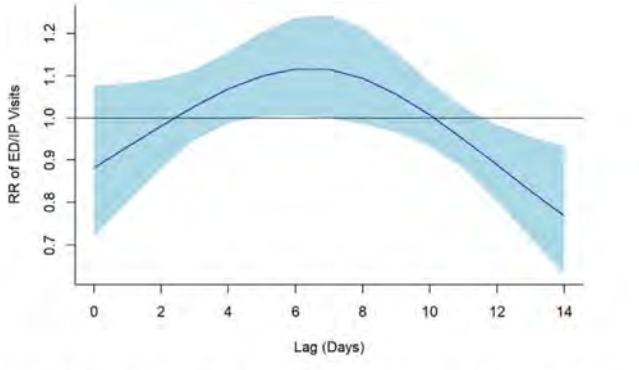
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Temperature and air pollution are increasing each year across the US. There is growing interest in studying how the effects of high temperature impact patients with rheumatic conditions. We aimed to provide a framework using time series methods to assess whether specific days of high heat contributed to acute care utilization (emergency department [ED] and inpatient [IP] visits) among individuals with rheumatic conditions.

Methods: We identified patients with ≥ 2 ICD-10 codes for rheumatic conditions in a multi-hospital center in Massachusetts. We obtained temperature and relative humidity from the National Oceanic Atmospheric Administration and air quality data from the Environmental Protection Agency. Acute care use was defined as ED or IP visits with a primary diagnosis code for a rheumatic condition or heat related illness (e.g. heat stroke, dehydration) from January 1, 2022, to October 1, 2024.

We used distributed lag non-linear time series models to estimate the effects of high temperature on risk of acute care utilization. These models allow for non-linear associations between exposures and outcomes and delayed effects using lags. We allowed the effect of temperature to be distributed over 14 days (lag days) with a cubic spline and fit a quasi-Poisson model adjusted for relative humidity, air quality index, day of week and time.

Results: 16,131 patients met inclusion criteria. 79% were white, 71% female, and the median age was 63. There was an average of 1.2 (SD 1.1) ED and IP visits with a primary diagnosis of rheumatic condition or heat related illness per day across all patients. Over the 3 summers in the study period there were 38 days that reached 90+ Fahrenheit (°F) and 12 days that reached 95+ °F. In the distributed lag non-linear models, we found significant associations between temperatures of 87°F



The dark blue line represents the relative risk and the light blue shading represents the 95% confidence interval at a day where the temperature reaches 95°F compared to 60°F.

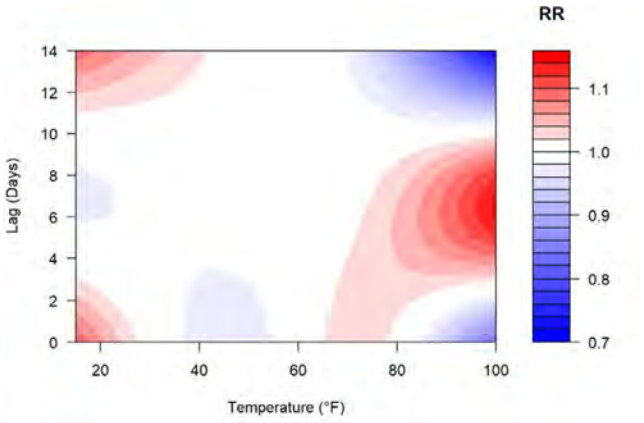
Figure 1. Relative risk of acute care utilization among individuals with rheumatic conditions at each lag day after the temperature reaches 95°F.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Relative Risk of acute care utilization among individuals with rheumatic conditions at different temperatures and lag days.

Temperature (°F)	Day 5	Day 6	Day 7
	Relative Risk (95% CI)		
92	1.09 (1.005, 1.176)	1.10 (1.005, 1.203)	1.10 (0.998, 1.206)
93	1.09 (1.005, 1.185)	1.10 (1.005, 1.214)	1.10 (0.999, 1.218)
94	1.10 (1.004, 1.194)	1.11 (1.005, 1.226)	1.11 (0.999, 1.230)
95	1.10 (1.004, 1.204)	1.12 (1.006, 1.238)	1.11 (0.999, 1.243)
96	1.10 (1.003, 1.214)	1.12 (1.006, 1.251)	1.12 (0.999, 1.256)
97	1.11 (1.002, 1.224)	1.13 (1.005, 1.263)	1.13 (0.999, 1.270)
98	1.11 (1.001, 1.234)	1.13 (1.005, 1.276)	1.13 (0.999, 1.284)
99	1.12 (1.001, 1.245)	1.14 (1.005, 1.290)	1.14 (0.999, 1.298)

Snapshot of relative risk and 95% confidence interval at various temperatures and lag days, revealing a small but statistically significant increase in risk of acute care use as temperatures increase, and higher risk ratios at higher temperatures.



Red coloring indicates a higher relative risk of acute care use, white represents a null risk, and blue coloring indicates a lower relative risk. Colors are shown at all possible temperatures and lag days after exposure day, compared to 60°F.

Figure 2. Contour plot with relative risk of temperature effects on acute care utilization among individuals with rheumatic conditions.

to 99°F with increased risk of acute care utilization at lag days 5 and 6. **Figure 1** shows the lag-response curve at 95°F which provides relative risks for each lag day. When the maximum temperature reaches 95°F on a given day, we see that there is no effect on utilization on that day or the next few days, but there is a trend toward higher risk of utilization on days 4-9 with statistical significance at days 5 and 6, which decreases around day 10. The relative risk of an ED or IP visit 6 days after the temperature reached 95°F was 1.12 (95% CI 1.01, 1.24) **(Table 1)** compared to a day when the temperature was 60 °F. **Figure 2** shows a contour plot of the relative risks at all possible lag days and temperatures, with darker red indicating higher risk of acute care utilization.

Conclusion: In this population of patients with rheumatic conditions, we found a modest delayed effect of high temperature on increased risk of acute care use for heat related illness and rheumatic conditions. The geographic areas where these patients lived have milder summers than other parts of the US, which may have limited our ability to detect risks associated with persistently high heat. As temperatures rise further, modeling approaches such as distributed lag non-linear models will become increasingly important to assess climate-related health risks among individuals with rheumatic conditions.

Disclosure: L. Santacroce: None; **J. Collins**: None; **A. Valle**: None; **R. Summit**: None; **P. Dellaripa**: None; **C. Feldman**: American College of Rheumatology, 2, Arthritis Foundation, 5, 12, Task Force Member, Bain Capital, 2, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 1, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0157

Influence of Outpatient Clinic Visits on Receipt of the COVID-19 Vaccine among People with Autoimmune Rheumatic Diseases

Lesley Jackson[1], Nicole Wright[2], Rahima Begum[3], Fazlur Rahman[1], Rena Patel[1], Kenneth Saag[4], Jeffrey Curtis[5] and Maria I. (\"Maio\") Danila[6], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Tulane University School of Medicine, New Orleans, LA, [3]University of Alabama at Birmingham, Birmingham, [4]The University of Alabama at Birmingham, Birmingham, AL, [5]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [6]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatologists and primary care providers (PCPs) are some of the most trusted clinicians for people living with autoimmune rheumatic diseases (AIRD), and they may influence the vaccine decision-making process during outpatient visits. We aimed to determine the factors associated with receipt of a COVID-19 vaccine during the immediate follow-up interval after either rheumatology or PCP clinic visits.

Methods: We used electronic health records (EHR) to conduct a retrospective cohort study of established patients with AIRD at our institution seen from 12/8/2020 through 1/8/2024. We conducted two separate cohort analyses in patients who had 2+ clinic visits in the observation period with (1) rheumatology or (2) a PCP. The primary outcome of "post-visit vaccination" was defined as receipt of a dose of the COVID-19 vaccine during the 8-day interval after a rheumatology or a PCP clinic visit (i.e., the day of visit + 7 days post-visit). We built multivariable logistic regression models to identify factors independently associated with post-visit vaccine receipt. Secondarily, we conducted a self-controlled case series (SCCS) analysis to

Table 1. Characteristics of individuals with a rheumatology clinic visit stratified by presence or absence of a COVID-19 vaccine occurring during the post-visit interval. Bold denotes p<0.05 for comparisons between the 2 groups.

Characteristic	Presence of clinic visit without associated vaccine post-visit, N=2188	Presence of clinic visit and receipt of vaccine post-visit, N=440	p-value
Sex, female, N(%)	1781 (81.4)	367 (83.4)	0.3
Age, mean (SD)	58.1 (14.7)	60.6 (13.4)	**0.0004**
Age groups (years), N (%)			0.08
<50	598 (27.3)	96 (21.2)	
50 - <65	838 (38.3)	173 (39.3)	
65 - <75	509 (23.3)	118 (26.8)	
≥75	243 (11.1)	53 (12.0)	
Race/ Ethnicity[α]			**0.001**
White	1580 (73.2)	283 (64.9)	
Black or African American	528 (24.5)	134 (30.7)	
American Indian or Alaska Native	5 (0.2)	0 (0.0)	
Asian	29 (1.3)	15 (3.4)	
Hispanic or Latinx	17 (0.8)	4 (0.9)	
Rheumatic condition			0.8
Inflammatory arthritis	982 (44.9)	194 (44.1)	
Systemic lupus erythematosus	776 (35.5)	153 (34.8)	
Other connective tissue disease	311 (14.2)	64 (14.5)	
Vasculitis	119 (5.4)	29 (6.6)	
Medication use (binary, Yes/No)[β]			
Conventional synthetic DMARDs, Yes	1777 (81.2)	367 (83.4)	0.3
Biologic DMARDs, Yes	884 (40.4)	179 (40.7)	0.9
Glucocorticoids, Yes	1456 (66.5)	344 (78.2)	**<0.0001**
Immunosuppressives, Yes	314 (14.4)	85 (19.3)	**0.01**
JAK inhibitors, Yes	206 (9.4)	55 (12.5)	0.05
CD20 inhibitors, Yes	136 (6.2)	46 (10.5)	**0.002**
IVIG, Yes	68 (3.1)	25 (5.7)	**0.01**
Phosphodiesterase inhibitors, Yes	57 (2.6)	12 (2.7)	0.9
No. of Rheumatology visits, mean (SD)	5.9 (2.6)	7.3 (2.6)	**<0.0001**
Total COVID vaccine doses received, mean (SD)	3.0 (1.3)	3.8 (1.5)	**<0.0001**
Charlson Comorbidity Index, mean (SD)	1.2 (1.1)	1.4 (1.1)	**0.007**
Smoking currently, N (%)[γ]	190 (9.5)	29 (7.3)	0.2
Overall SVI, mean (SD)[δ]	0.4 (0.3)	0.5 (0.3)	0.8

αmissing for 33 individuals. βcategories are not mutually exclusive. γmissing for 222 individuals. δmissing for 266 individuals. Rheumatology visits were defined as an outpatient visit occurring with a rheumatologist during the timeframe from Dec. 8, 2020 through Jan. 8, 2024. AIRD, autoimmune rheumatic diseases; DMARDs, disease-modifying antirheumatic drugs; IVIG, intravenous immunoglobulin; JAK, janus kinase; SD, standard deviation; SVI, social vulnerability index.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

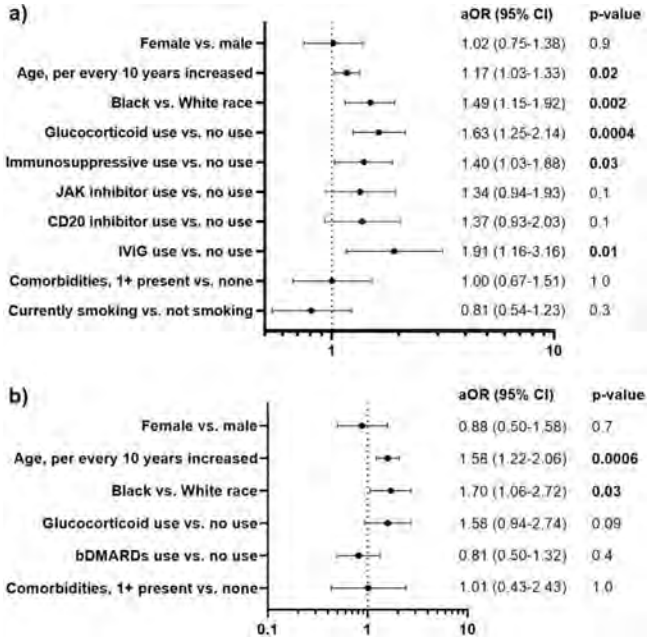


Figure 1. Results of multivariable logistic regression model with odds ratio (OR) and 95% confidence intervals (CI) for covariates associated with receipt of a COVID-19 vaccine during the 8-day post-visit interval after an outpatient a) rheumatology clinic visit or b) primary care clinic visit. Model includes all relevant covariates of biological significance (e.g., sex, age) and those with p<0.25 in the univariable analysis. OR and CI presented on a logarithmic scale. aOR, adjusted odds ratio; IVIG, intravenous immunoglobulin; JAK inhibitor, janus kinase inhibitor.

compare receipt of COVID-19 vaccination during the 8-days post-visit "hazard interval" vs. 8-days pre-visit "control interval", and censored at the time of their vaccine receipt or death during these intervals.

Results: We identified 2,628 individuals with rheumatology (**Table 1**) and 493 individuals with PCP clinic visits, of whom 440 (16.7%) and 119 (24.1%) received a COVID-19 vaccine in the 8-day post-visit interval, respectively. In the multivariable logistic regression model examining the outcome following rheumatology visits, older age (OR=1.17, 95% CI 1.03 – 1.33, for every 10-year increase), Black race (OR=1.49, 95% CI 1.15 – 1.92), and use of glucocorticoids (OR=1.63, 95% CI 1.25 – 2.14), immunosuppressives (OR=1.40, 95% CI 1.03 – 1.88), and intravenous immunoglobulin (OR=1.91, 95% CI 1.16 – 3.16) were associated with higher odds of post-visit vaccine receipt (**Figure 1a**). Among eligible patients with PCP clinic visits, only older age (OR=1.58, 95% CI 1.22 – 2.06) and Black race (OR=1.70, 95% CI 1.06 – 2.72) were associated with a post-visit vaccine receipt (**Figure 1b**). In the SCCS analysis, there were significantly higher rates of vaccine receipt during the post-visit hazard interval compared to each person's control interval following rheumatology (IRR=1.87, 95% CI 1.62 – 2.18, p< 0.0001) and PCP clinic visits (IRR=3.81, 95% CI 2.75 – 5.36, p< 0.0001); among only patients who received a vaccine, the rates were similar.

Conclusion: In this cohort study of patients with AIRD, we found that older age, Black race, and use of certain high-risk medications were associated with higher odds of COVID-19 vaccination in close proximity to a visit with a rheumatologist or PCP. While both PCP and rheumatology clinic visits were associated with more post-visit COVID-19 vaccinations, our results suggest that rheumatologists may be focusing vaccination efforts among those with certain high-risk patient characteristics such as older age or greater immunosuppression burden. Effective interventions aimed at improving vaccine uptake could be implemented at or soon after a clinic visit.

Disclosure: L. Jackson: None; **N. Wright**: None; **R. Begum**: None; **F. Rahman**: None; **R. Patel**: None; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5.

Abstract Number: 0158

Association Between Newer COVID-19 Vaccines and COVID-19 Related Hospitalizations Among People with Autoimmune Rheumatic Diseases in the U.S. National COVID Cohort Collaborative (N3C)

Lesley Jackson[1], jerrod anzalone[2], Rahima Begum[3], Fazlur Rahman[1], Namrata Singh[4], Londyn Robinson[5], Kaleb Michaud[2], Kenneth Saag[6], Jasvinder Singh[7], Rena Patel[1] and Maria I. (\"Maio\") Danila[8] On Behalf of the National Clinical Cohort Collaborative (N3C) Consortium, [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Alabama at Birmingham, Birmingham, [4]University of Washington, Bellevue, WA, [5]University of Washington, Seattle, WA, [6]The University of Alabama at Birmingham, Birmingham, AL, [7]Baylor College of Medicine, Houston, TX, [8]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1. Baseline characteristics of total cohort by COVID-19 vaccination status (as of study end in December 2023).

Characteristics	Total N=54,848	*Vaccination Status Groupings* Unvaccinated 15,467 (28%)	Initial Series Vaccination 9,483 (17%)	Boosted 24,124 (44%)	Updated 5,775 (11%)	P-value
Sex, female, N(%)	41,383 (75%)	11,609 (75%)	7,343 (77%)	18,098 (75%)	4,333 (75%)	**<0.001**
Age Groups (yrs.), N(%)						**<0.001**
<50	13,576 (25%)	4,799 (31%)	2,973 (31%)	4,769 (20%)	1,035 (18%)	
≤50 to <65	17,205 (31%)	5,051 (33%)	3,071 (32%)	7,455 (31%)	1,628 (28%)	
≤65 to <75	12,488 (23%)	2,956 (19%)	1,824 (19%)	6,041 (25%)	1,667 (29%)	
>=75	11,579 (21%)	2,661 (17%)	1,614 (17%)	5,859 (24%)	1,445 (25%)	
Race/Ethnicity, N (%)						**<0.001**
White non-Hispanic	39,766 (73%)	11,074 (72%)	6,620 (70%)	17,769 (74%)	4,303 (75%)	
Black/ African American Non-Hispanic	7,363 (13%)	1,954 (13%)	1,348 (14%)	3,155 (13%)	906 (16%)	
Hispanic or Latino Any Race	4,794 (9%)	1,581 (10%)	967 (10%)	1,915 (8%)	351 (6%)	
Multiple races, other races	2,925 (5%)	878 (6%)	547 (6%)	1,285 (5%)	215 (4%)	
Rheumatic disease, N (%)						**<0.001**
Inflammatory Arthritis	29,104 (53%)	8,330 (54%)	5,073 (53%)	12,775 (53%)	2,926 (51%)	
SLE	8,365 (15%)	2,662 (17%)	1,608 (17%)	3,337 (14%)	758 (13%)	
Vasculitis	6,485 (12%)	1,770 (11%)	1,151 (12%)	2,867 (12%)	697 (12%)	
Sjögrens	4,589 (8%)	1,096 (7%)	725 (8%)	2,108 (9%)	660 (11%)	
PMR	3,811 (7%)	860 (6%)	541 (6%)	1,959 (8%)	451 (8%)	
Other CTD	2,494 (5%)	749 (5%)	384 (4%)	1,078 (5%)	283 (5%)	
Broad Drug Category, N (%)						
CD20 inhibitors, yes	1,391 (3%)	348 (2%)	222 (2%)	608 (3%)	213 (4%)	**<0.001**
Biologic DMARDs, yes	6,390 (12%)	1,553 (10%)	982 (10%)	2,995 (12%)	860 (15%)	**<0.001**
JAK inhibitors, yes	903 (2%)	255 (2%)	137 (1%)	391 (2%)	120 (2%)	**0.03**
Conventional synthetic DMARDs, yes	13,404 (24%)	3,508 (23%)	2,078 (22%)	6,222 (26%)	1,596 (28%)	**<0.001**
Immunosuppressives, yes	4,240 (8%)	1,091 (7%)	648 (7%)	1,950 (8%)	551 (10%)	**<0.001**
Apremilast, yes	276 (1%)	93 (1%)	37 (0.4%)	112 (1%)	34 (1%)	0.07
Glucocorticoids, yes	17,217 (31%)	4,770 (31%)	2,895 (31%)	7,602 (32%)	1,950 (34%)	**<0.001**
Tobacco use, N (%)	6,422 (12%)	2,129 (14%)	1,238 (13%)	2,397 (10%)	658 (11%)	**<0.001**
Hypertension, N (%)	34,019 (62%)	8,777 (57%)	5,581 (59%)	15,829 (66%)	3,832 (66%)	**<0.001**
CCI, Median (IQR)	2 (1, 4)	2 (0, 4)	2 (1, 4)	2 (1, 4)	2 (1, 4)	**<0.001**
SVI Category, N (%)						**<0.001**
High	12,542 (23%)	3,590 (23%)	2,399 (25%)	5,360 (22%)	1,193 (21%)	
Medium	20,469 (37%)	6,078 (39%)	3,722 (39%)	9,161 (38%)	1,508 (26%)	
Low	21,837 (40%)	5,799 (37%)	3,361 (35%)	9,603 (40%)	3,074 (53%)	
Obesity based on BMI ≥30, N (%)	33,698 (61%)	9,433 (61%)	5,961 (63%)	14,862 (62%)	3,442 (60%)	**<0.001**

Inflammatory arthritis includes rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, enteropathic arthritis, and reactive arthritis. Other CTD includes polymyositis, dermatomyositis, and systemic sclerosis. Vasculitis includes Behcet's disease, ANCA-vasculitis, giant cell arteritis, and polyarteritis nodosa. CCI, Charlson Comorbidity Index; CTD, connective tissue disease; JAK inhibitor, janus kinase inhibitor; PMR, polymyalgia rheumatic; SLE, systemic lupus erythematosus; SVI, social vulnerability index. P<0.05 indicated in bold.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

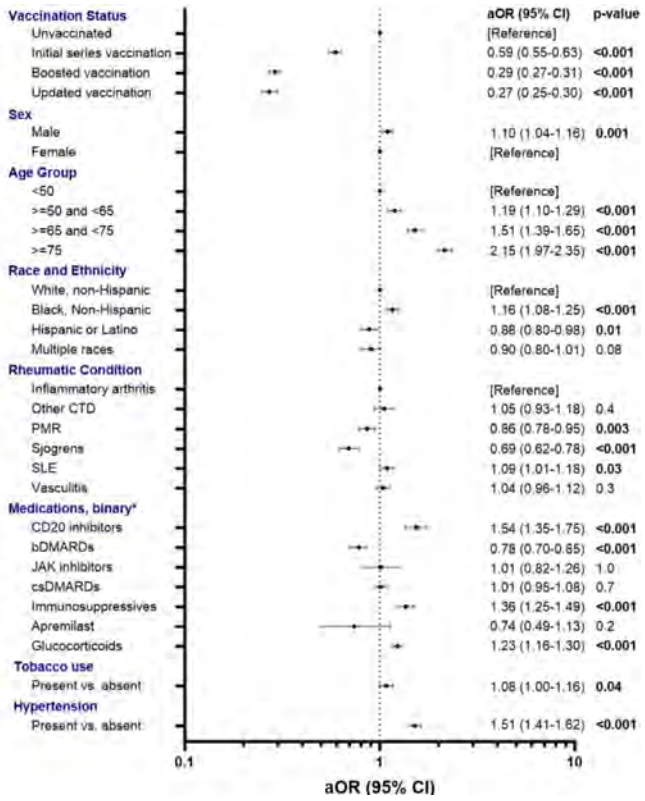


Figure 1. Results of multivariable logistic regression model with odds ratio (aOR) and 95% confidence intervals (CI) adjusted for covariates associated with COVID-19 related hospitalization. OR and CI presented on a logarithmic scale. Model was adjusted for: vaccination status, sex, age, race and ethnicity, rheumatic condition, medication use, tobacco use, presence of hypertension, Charlson Comorbidity Index, and social vulnerability index. *categories defined by presence vs. absence of medication. bDMARDs, biologic disease modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease modifying anti-rheumatic drugs; JAK inhibitor, janus kinase inhibitor; PMR, polymyalgia rheumatic; SLE, systemic lupus erythematosus.

Background/Purpose: People with autoimmune rheumatic diseases (AIRD) are at higher risk for serious complications and poor outcomes from COVID-19 infection. Data is lacking on outcomes related to the 2023-2024 updated COVID-19 vaccine in this population. We aimed to assess the association between vaccination status and COVID-19-related hospital admissions.

Methods: We conducted a retrospective cohort analysis using electronic health record (EHR) data from the National Clinical Cohort Collaborative (N3C) COVID-19 Enclave among people with AIRD and incident positive COVID-19 testing (i.e., positive SARS-CoV-2 polymerase chain reaction (PCR), antigen, or antibody test or COVID-19 diagnostic code) between December 2020 and December 2023. Eligible patients were adults age ≥18 years with ≥2 International Classification of Diseases (ICD)-10 codes for AIRD occurring at least 30-days apart. We defined time-varying vaccination status as: unvaccinated (i.e., no vaccine record on file), initial series completed (i.e., received two mRNA vaccine doses or 1 Janssen dose of the COVID-19 vaccine), boosted (i.e., received initial vaccination series and a booster or bivalent dose), or updated vaccinated (with 1+ updated 2023–2024 COVID-19 vaccine). We defined the primary outcome as presence of an inpatient hospitalization occurring during the period 3 days before and up to 14 days after positive SARS-CoV-2 testing, and allowed for repeat hospitalizations. We conducted a multivariable logistic regression model and adjusted for repeating measures and participating site. Covariates included sex, age, race and ethnicity, AIRD category, AIRD-related medication use, tobacco use, presence of hypertension, obesity, modified Charlson comorbidity index (excluding AIRD), and social vulnerability index (SVI).

Results: Our cohort included 54,848 people with AIRD, including 41,383 (75%) females, with median (IQR) age 62 (50-73) and 39,766 (73%) White non-Hispanic race (**Table 1**). Of these, 5,775 (11%) had received an updated 2023-2024 COVID-19 vaccine. After adjusting for relevant covariates, people with AIRD who had received a booster or an updated vaccine dose had 71% (adjusted odds ratio [AOR]=0.29, 95% confidence interval [CI] 0.27-0.31) and 73% (AOR=0.27, 95% CI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

0.25-0.30) lower odds of COVID-19-related hospitalization compared to unvaccinated people, with similar odds comparing to those with initial series alone (**Figure 1**). In addition, male sex, older age, Black non-Hispanic race, having systemic lupus erythematosus, exposure to CD20 inhibitors, immunosuppressives, or glucocorticoids, current tobacco use, having hypertension, more comorbidities, and higher SVI were associated with an increased odds of COVID-19-related hospitalization.

Conclusion: After accounting for important covariates, we observed a substantially decreased independent odds of COVID-related hospitalization among people with AIRD that received a booster or updated 2023-2024 COVID-19 vaccine compared to initial series alone or unvaccinated statuses. Updated vaccinations appear to continue to provide significant protection for this vulnerable population and should be supported by providers, policy makers, and patient advocacy groups.

Disclosure: L. Jackson: None; **j. anzalone**: None; **R. Begum**: None; **F. Rahman**: None; **N. Singh**: None; **L. Robinson**: None; **K. Michaud**: None; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **J. Singh**: American College of Rheumatology, 2, Atai life sciences, Kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 11, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Putnam associates, Focus forward, Navigant consu, 2, GeoVax Labs, Adaptimmune Therapeutics, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp., Aebona Pharma, 11, Intuitive Surgical Inc./Philips Electronics North America, 12, food and beverage payments, ROMTech, Atheneum, Clearview healthcare partners, Yale, Hulio, Horizon Pharmaceuticals/DINORA, ANI/Exeltis, USA Inc., Frictionless Solutions, Schipher, 2, Spherix, MedIQ, Jupiter Life Science, UBM LLC, Trio Health, Medscape, WebMD, and Practice Point communications; the National Institutes of Health, 2, Zimmer Biomet Holdings, 5; **R. Patel**: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5.

Abstract Number: 0159

Prenatal and Early-Life Environmental Exposures in Juvenile-Onset Systemic Autoimmune Rheumatic Diseases

Takuma Ohnishi[1], Megan Zhao[1], Min Shi[2], Adam Schiffenbauer[3], Sharon Jackson[3], Anna Jansen[1], Nastaran Bayat[4], Payam Farhadi[1], Christine Parks[2], Clarice Weinberg[2], Frederick Miller[5] and **Lisa Rider**[6], [1]National Institutes of Health/National Institute of Environmental Health Sciences, Bethesda, MD, [2]National Institutes of Health/National Institute of Environmental Health Sciences, Research Triangle Park, NC, [3]National Institute of Health/National Institute of Dental and Craniofacial Research, Bethesda, MD, [4]National Institutes of Health/National Institute of Environmental Health Sciences, Gaithersburg, MD, [5]National Institutes of Health/National Institute of Environmental Health Sciences, Chapel Hill, NC, [6]National Institute of Environmental Health Sciences/National Institutes of Health, Environmental Autoimmunity Group, Bethesda, MD

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic autoimmune rheumatic diseases (SARDs), including juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), idiopathic inflammatory myopathies (IIM), and systemic sclerosis (SSc), are characterized by immune dysregulation. While genetic predisposition contributes to disease susceptibility, environmental exposures, including those during the prenatal period and early childhood, may potentially influence disease risk. Evidence regarding these early-life factors is limited and inconsistent. This study aimed to examine associations between early-life environmental exposures and juvenile-onset SARDs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Associations between prenatal and early-life environmental factors and participant role

	Probands vs Unrelated controls Odds ratio (95% Confidence Interval)
Prenatal factors	
Delivery by Cesarean section	1.31 (0.68-2.58)
Premature birth (< 37 weeks)	2.08 (0.74-6.73)
Gestational hypertension	4.81 (0.80- 92.59)
Preeclampsia, eclampsia, or toxemia	8.72 (0.98-1150)
Gestational diabetes	2.00 (0.62-7.72)
Rho(D) immune globulin usage	1.06 (0.32-3.77)
Flu or fever for more than 5 days	0.75 (0.15-4.16)
Placenta previa or placental abruption	5.46 (0.53-737)
Total number of pregnancy complications	1.57 (1.14-2.24)†
Prenatal parental smoking	4.81 (1.30-24.29)‡
Maternal smoking	1.81 (0.25-36.95)
Paternal smoking	7.43 (1.66-55.68)†
Early-life factors	
Birth order	1.00 (0.78-1.30)
Breast feeding	1.02 (0.41-2.45)
Soy formula (≥ 2 weeks)	1.06 (0.48-2.46)
Passive smoke exposure*	4.88 (1.38-23.51)‡
Active cigarette smoking	2.13 (0.10-326.7)

*Household smoking before age at diagnosis for probands or reference age for unrelated controls. Reference date is the proband's date of diagnosis.

†P ≤ 0.01, ‡P ≤ 0.05

Methods: A case-control study included 124 probands with juvenile-onset SARDs diagnosed within 5 years (99 with juvenile IIM, 16 with JIA, 5 with SSc, and 4 with SLE), their same gender, close-in-age unaffected siblings (n=121), and demographically matched unrelated controls without autoimmune disease (n=90). The proband's date of diagnosis served as the reference date for their siblings and matched controls. Participants resided in the United States or Canada. Parents of pediatric patients completed questionnaires on pregnancy complications, parental smoking during pregnancy, early-life exposures, and active smoking history. Paired analyses between probands and their siblings were performed using conditional logistic regression models adjusted for age. Probands and controls were compared by logistic regression analysis, adjusting for potential confounding variables including age, sex, race, ethnicity, and education level.

Results: The median age at reference date was 7.4 years for probands, 8.4 years for siblings, and 9.2 years for controls. Sex and race distributions did not differ significantly among groups: 62% of probands and siblings were female compared to 66% of controls; 85% of probands and siblings were White compared to 87% of controls. No significant differences in pregnancy complications or early-life exposures were observed between probands and their siblings. However, compared to controls, juvenile-onset SARDs were associated with multiple pregnancy complications (OR 1.57, CI:1.14–2.24), but not with any specific complication (Table). Prenatal parental smoking was also significantly associated with juvenile-onset SARDs (OR 4.81, CI:1.30–24.29). While maternal smoking rates were similar between groups, paternal smoking was more frequent in probands compared to controls (OR 7.43, CI:1.66–55.68). Early-life exposures, such as birth order, breastfeeding and soy formula use, did not differ significantly between probands and controls. Passive smoke exposure before reference age was also associated with juvenile-onset SARDs (OR 4.88, CI:1.38–23.51). Active smoking was uncommon, with one proband and two siblings reporting tobacco use.

Conclusion: The number of pregnancy complications was associated with juvenile-onset SARDs, without an association with a specific complication. Parental smoke exposure during prenatal and early-life periods was strongly associated with SARDs. These findings highlight the importance of pregnancy and early-life factors in these diseases.

Disclosure: T. Ohnishi: None; **M. Zhao**: None; **M. Shi**: None; **A. Schiffenbauer**: AstraZeneca, 11, Hope Pharmaceuticals, 5; **S. Jackson**: None; **A. Jansen**: None; **N. Bayat**: None; **P. Farhadi**: None; **C. Parks**: None; **C. Weinberg**: None; **F. Miller**: None; **L. Rider**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0161

Risk Factors and Clinical Predictors of Lung Cancer in Systemic Sclerosis: A Matched Case-Control Study from a Michigan Cohort

Madiha Naqsh Siddiqui[1], Yen Chen[1], Rosemary Gedert[2], Suiyuan Huang[2], Dinesh Khanna[2] and John Varga[2], [1]University of Michigan, Ann Arbor, [2]University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Malignancies are one of the leading causes of non-systemic sclerosis-related mortality in patients with systemic sclerosis (SSc)[1], with lung cancer being the most common type[2,3,4]. Although factors such as prolonged immunosuppression[4], family history of malignancy[5], and smoking[6] have been implicated, findings have been inconsistent. We conducted a matched case-control study to investigate clinical, serological, and treatment-related risk factors associated with lung cancer among patients with SSc in a Michigan-based cohort.

Methods: Data were extracted retrospectively using DataDirect, a self-service tool that retrieves information from the electronic medical record system by identifying relevant International Classification of Diseases (ICD) 9 and 10 codes for SSc and lung cancer (710.1, 162.9 and M34.0, M34.1, M34.2, M34.8, M34.9, C34.00-C34.92, respectively) and/or listed diagnosis in the medical record. Inclusion criteria included adults aged 18 or older who were actively followed by rheumatology at the University of Michigan and had a confirmed diagnosis of SSc, either by fulfillment of the ACR classification criteria or through clear documentation in a rheumatologists' note. Exclusion criteria were patients aged under 18, lack of active follow-up at the University of Michigan, localized scleroderma, or secondary lung cancer (metastatic, with a primary site other than lung). Using these criteria, we identified 102 patients: 51 SSc patients with lung cancer (cases) and 51 age-

Table 1a: Baseline Characteristics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1b: Baseline Characteristics

	Sjogren	1/102 (1.0%)	0/51 (0.0%)	1/51 (2.0%)	NA*
	SLE (including overlap)	4/102 (3.9%)	3/51 (5.9%)	1/51 (2.0%)	0.1573[b]
	SSc – overlap	2/102 (2.0%)	1/51 (2.0%)	1/51 (2.0%)	1.0000[b]
	Ulcerative colitis	2/102 (2.0%)	0/51 (0.0%)	2/51 (3.9%)	NA*
Clinical Variables (Lung cancer)					
Tumor histology, n (%)	Non-small cell carcinoma	-	44/51 (86.3%)	-	NA
	Small cell carcinoma	-	7/51 (13.7%)	-	
Stage, n (%)	Stage 1	-	9/49 (18.4%)	-	NA
	Stage 2	-	2/49 (4.1%)	-	
	Stage 3	-	11/49 (22.4%)	-	
	Stage 4	-	27/49 (55.1%)	-	
SUV, n (%)	Low (<2.5)	-	1/33 (3.0%)	-	NA
	Moderate (2.5-7)	-	7/33 (21.2%)	-	
	High (>7)	-	25/33 (75.8%)	-	
Death, n (%)		51/99 (51.5%)	38/48 (79.2%)	13/51 (25.5%)	<0.0001[b]
* Test is not applicable due to fewer than 2 non-missing levels in case or control, or both. [a] Paired T test. [b] McNemar test. [c] Bowker's symmetry test.					

Table 1: Baseline Characteristics.

matched SSc patients without lung cancer (controls). Paired t-tests, McNemar's and Bowker's symmetry tests were used to assess baseline differences. Conditional logistic regression was then performed to examine associations with lung cancer.

Results: Baseline patient data characteristics are summarized below in table 1. Compared to controls, cases had significantly higher rates of diffuse cutaneous SSc (72.5% vs. 39.2%, p=0.0036), former smoking (64.7% vs. 27.5%, p=0.0009), presence of lung nodules on CT chest (87.5% vs. 61.2%, p=0.0164), and immunosuppressive therapy use (89.4% vs. 56.9%, p=0.0006). Mean DLCO% was significantly lower in cases (48.7% vs. 61.1%, p=0.0011). In multivariable

Table 2: Conditional Logistic Regression

Variables	Subcategory	Odds Ratio (95% CI)	p-value
Demographic variables			
Age (yrs)	-	0.84 (0.57, 1.22)	0.3540
Race (ref=Caucasian)	African American	1.04 (0.30, 3.65)	0.9490
	Asian and Other	1.51 (0.25, 9.21)	0.6536
Gender (ref=Female)	-	1.00 (0.38, 2.66)	1.0000
Clinical Variables			
SSc type, (ref=Diffuse)	Limited	0.14 (0.04, 0.49)	0.0017
	Sine	1.23 (0.10, 16.00)	0.8725
Disease duration of SSc (ref=0-1 year)	>1-5 years	0.31 (0.03, 3.66)	0.3489
	>5 years	0.34 (0.04, 3.38)	0.3590
ILD (ref=No)	-	1.80 (0.83, 3.90)	0.1361
ILD on chest CT (ref=No)	-	2.00 (0.90, 4.45)	0.0895
Nodules on chest CT (ref=No)	-	3.2 (1.17, 8.74)	0.0232
Pulmonary Function Testing	FVC-%	0.99 (0.97, 1.01)	0.2187
	FEV1-%	0.98 (0.96, 1.00)	0.0717
	TLC-%	0.99 (0.96, 1.03)	0.7480
	DLCO-%	0.95 (0.92, 0.99)	0.0065
ANA (ref=Negative)	-	1.00 (0.25, 4.00)	1.000
ANA titer (ref=Moderate [1:160, 1:320])	High (1:640 or higher)	0.25 (0.04, 1.42)	0.1179
	Very high (1:2560 or higher)	0.31 (0.06, 1.52)	0.1473
SCL-70 (ref=Negative)	-	2.00 (0.68, 5.85)	0.2057
RNA Pol3 (ref=Negative)	-	>999 (<0.001, >999)	0.9964
ACA (ref=Negative)	-	0.86 (0.29, 2.55)	0.7817
Tobacco history (ref=Never)	Former	8.22 (2.19, 28.27)	0.0008
	Current	4.95 (0.75, 32.65)	0.0965
Packs of tobacco (ref=<15 PPY)		2.00 (0.73, 5.33)	0.1657
Alcohol use (ref=No)	Former	0.73 (0.15, 3.50)	0.6932
	Yes	0.95 (0.43, 2.13)	0.9065
Frequency of alcohol use (ref=≤8 ounces)		0.27 (0.06, 0.98)	0.0461
BMI (ref=Underweight (<18.5))	Normal weight (18.5-24.9)	2.83 (0.50, 15.98)	0.2381
	Overweight (25-29.9)	2.68 (0.46, 15.54)	0.2709
	Obesity (>30)	1.97 (0.33, 11.58)	0.4540
Family history of lung cancer (ref=No)		3.09 (0.18, 22.06)	0.5714
Family history of other cancers (ref=No)	-	0.61 (0.29, 1.29)	0.1982
	Bladder (ref=No)	0.50 (0.05, 5.51)	0.5714
	Breast (ref=No)	0.80 (0.22, 2.98)	0.7394
	Colon (ref=No)	0.20 (0.02, 1.71)	0.1418
	Not Otherwise Specified (ref=No)	0.60 (0.26, 1.37)	0.2257
	Ovarian (ref=No)	2.00 (0.18, 22.06)	0.5714
	Prostate (ref=No)	1.00 (0.20, 4.96)	1.0000
Family history of other cancers –degree level (ref=First degree)	Second degree	>999 (<0.001, >999)	0.9961
	Both	3.00 (0.31, 28.84)	0.3414
Immunosuppressive agent	Azathioprine	2.50 (0.49, 12.89)	0.2734
	Cyclophosphamide	2.67 (0.71, 10.05)	0.1474
	Glucocorticoids	14.50 (3.46, 60.77)	0.0003
	Mycophenolate Mofetil	0.82 (0.34, 1.97)	0.6553
	Methotrexate	0.55 (0.20, 1.48)	0.2354
	Others	0.67 (0.27, 1.63)	0.3744
Personal history of other cancers (ref=No)	-	1.25 (0.49, 3.17)	0.6380
	Breast (ref=No)	3.00 (0.31, 28.84)	0.3414
	Hematologic malignancies	1.00 (0.06, 15.99)	1.0000
	Non-melanoma skin cancers	3.33 (0.92, 12.11)	0.0674
Other autoimmune disease (ref=No)	-	1.09 (0.48, 2.47)	0.8349
	Arthritis/RA	0.75 (0.26, 2.16)	0.5943
	SLE (including overlap)	>999 (<0.001, >999)	0.9914
*Death	-	14.00 (3.34, 58.77)	0.0003
*For this variable, "lung cancer" has been used as covariate			

Table 2: Conditional logistic regression results

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

analysis (table 2), former smoking (OR 8.22, 95% CI: 2.39 – 28.27, p=0.0008), glucocorticoid use (OR 14.50, 95% CI: 3.46 – 60.77, p=0.0003), and nodules on chest CT (OR 3.2, 95% CI: 1.17 – 8.74, p=0.0232) were independently associated with lung cancer. Diffuse cutaneous subtype was a risk factor, while limited cutaneous SSc was protective (OR 0.14, 95% CI: 0.04 – 0.49, p=0.0017). DLCO% was inversely associated with lung cancer risk (OR 0.95 per % increase, 95% CI: 0.92 – 0.99, p=0.0065). Cases had 1300% higher odds of death (OR 14%, 95% CI: 3.34 – 58.77, p=0.0003).

Conclusion: In this matched cohort, lung cancer in SSc was significantly associated with diffuse cutaneous subtype, prior smoking history, nodules on CT chest, reduced DLCO, and glucocorticoid exposure. In contrast, limited cutaneous SSc conferred a protective effect. These findings underscore the importance of clinical phenotype and treatment history in assessing malignancy risk in SSc patients and support the need for targeted cancer screening protocols.

Disclosure: M. Siddiqui: None; **Y. Chen**: None; **R. Gedert**: None; **S. Huang**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **J. Varga**: None.

Abstract Number: 0162

Clinical Relevance of Systematic Comorbidity Screening in Autoimmune and Inflammatory Diseases

Martin Michaud, Caroline Arlet, Jean Alain Bournazeau, François de Maupeou, Julie Gaston, Stephanie Mermet, Helene Coulier, Marie Oustalet, Christophe Raspaud, Cédric Maurice, Sophie Recipon, Claire Verplancken, Kim Paricaud and Leonardo Astudillo, Clinique Saint Exupery, TOULOUSE, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic autoimmune and inflammatory diseases are associated with an increased prevalence of various comorbidities, which may impact both prognosis and therapeutic strategies. EULAR recommends systematic identification, prevention and screening of key comorbid conditions in this population.

Methods: Since January 1st, 2025, the PREDIRE cohort has included consecutive adult patients with chronic autoimmune or inflammatory diseases undergoing a multimorbidity assessment during a one-day hospitalization. Collected data include sociodemographic and anthropometric characteristics, medical history, current treatments, cardiovascular risk factors, osteoporosis risk, and infectious risk evaluation (including dental follow-up and vaccination status). At the end of the assessment, individualized recommendations are issued for both the patient and their primary care physician.

Results: A total of 46 patients were included, with a mean age of 64.2 (±15.2) years . Autoimmune or inflammatory diseases were giant cell arteritis (26%), polymyalgia rheumatica (13%), sarcoidosis (8.7%), Behçet's disease, systemic lupus erythematosus, systemic sclerosis , spondyloarthritis (6.5%), Sjogren disease (4.3%), ANCA-associated vasculitis (4.3%), or rheumatoid arthritis, familial mediterranean fever, or retroperitoneal fibrosis (2.17% each). The median duration of the disease was 2 years (IQR: 1–7).

Regarding cardiovascular comorbidities, 21.7% had a history of major cardiovascular event, 38.1% had hypertension and 10.9% had diabetes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	All patients (n=46)
Age (years)	64,15 ± 15,17
Female (%)	58,7
Precariousness (%)	30,4
Diseases (%)	
Giant cell arteritis	26
Polymyalgia rheumatica	13
Sarcoidosis	8,69
Behcet disease	6,5
Systemic lupus erythematosus	6,5
Systemic sclerosis	6,5
Spondylarthritis	6,5
Siogren disease	4,3
ANCA associated vasculitis	4,3
Rheumatoid arthritis	2,17
Familial Mediterranean fever	2,17
Retroperitoneal fibrosis	2,17
Disease duration, median (years)	2 (1-7)
Body mass index, median (kg/m2)	25,89 (22,7-30,11)
Obesity (%)	26
Overweight (%)	28,2
Smoking (%): current/past	19,5 / 28,2
Previously diagnosed (%)	
Major Cardiovascular Event	21,7
Hypertension	39,1
Diabetes	10,8
Cancer	8,69
Osteoporosis	13
Lipid lowering therapy (%)	28,2
Anti-platelet therapy (%)	19,5
Anti-osteoporotic drug (%)	15,2

Patient Characteristics

Obesity was observed in 26% of patients, while 28.2% were overweight. Physical inactivity was reported in 34.7% of patients.

Active smoking was reported in 19.5% of cases and 28.2% had a history of smoking.

	All patients (n=46)
Metabolic syndrome (%)	19,5
Undiagnosed diabetes (%)	0
Undiagnosed or uncontrolled Hypertension (%)	36,9
Cardiovascular disease risk (%)	
Very High	34,7
High	30,47
Low to moderate	26
Very low	8,7
LDL-cholesterol target levels achievement (%)	19,5
Undiagnosed risk to sleep apnea (%)	21,7
Physical activity profile (%)	
Inactive	34,7
Active	60,8
Very active	4,3
Undiagnosed osteopenia (%)	30,4
Undiagnosed osteoporosis (%)	15,2
Vitamin D insufficency (%)	65
Low calcium intake (%)	71,7
Anti-osteoporotic drug need (%)	26
Dental care to complete (%)	21,7
Cancer screening to complete (%)	54,3
Vaccine calendar to complete (%)	84,7

Screening Outcomes

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cardiovascular risk, estimated using the SCORE2 algorithm, showed that 65.2% of patients were at high or very high risk. Target LDL cholesterol levels were achieved in only 19.5% of patients.

A risk of sleep apnea was identified in 21.2% of patients.

While osteoporosis was previously known in 13% of patients, the assessment revealed newly diagnosed osteopenia in 34% and osteoporosis in 15.2%. Vitamin D deficiency was identified in 65% of patients, and inadequate calcium intake was noted in 71.7% of cases. Despite being indicated, osteoporosis treatment was lacking in 26% of patients.

Dental follow-up was indicated in 21.7% of patients. Vaccination schedules needed updating in 84.7% of patients.

In 54.3% of cases, cancer screening was outdated or incomplete, warranting an update of the recommended evaluations

Conclusion: The first data from the PREDIRE cohort highlight the high burden of comorbidities among patients with chronic autoimmune and inflammatory diseases. The implementation of a standardized, one-day multimorbidity screening approach allowed for the early identification of unrecognized or under-managed comorbid conditions, particularly in cardiovascular, bone, infectious, and cancer-related domains. These findings support the clinical utility of systematic comorbidity screening in improving patient care and guiding personalized preventive strategies.

Disclosure: M. Michaud: None; **C. Arlet**: None; **J. Bournazeau**: None; **F. de Maupeou**: None; **J. Gaston**: None; **S. Mermet**: None; **H. Coulier**: None; **M. Oustalet**: None; **C. Raspaud**: None; **C. Maurice**: None; **S. Recipon**: None; **C. Verplancken**: None; **K. Paricaud**: None; **L. Astudillo**: None.

Abstract Number: 0163

Trends in hospitalization and outcomes among patients admitted with Adult-onset Still's disease in the United States: INSIGHTS FROM THE NATIONAL INPATIENT SAMPLE (2016-2022)

Mohammed Akram[1], Muhammad Sohaib Asghar[2], Woo Joo Lee[2], Basmah Fayaz Yousuf[3], Carmen Tormo Carillo[4] and Savier Aleman Rama[4], [1]HCA Aventura, Aventura, FL, [2]AdventHealth Sebring, Sebring, FL, [3]SUNY Downstate Health Sciences University, New York, NY, [4]HCA Florida Aventura Hospital, Aventura, FL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Adult-onset Still's Disease is a rare systemic autoinflammatory disorder characterized by spiking fever, arthralgia/arthritis, skin rash, and elevated inflammatory markers (ferritin). Estimated incidence ranges from 0.16 to 0.4 cases per 100,000 persons and is associated with significant morbidity during systemic flares requiring inpatient management. There is a lack of research related to hospitalization trends and outcomes of patients with this disease within the United States. Hence, we conducted this analysis from national databases to investigate the hospitalization trends of Adult Onset Still's Disease pre and post COVID-19 pandemic era.

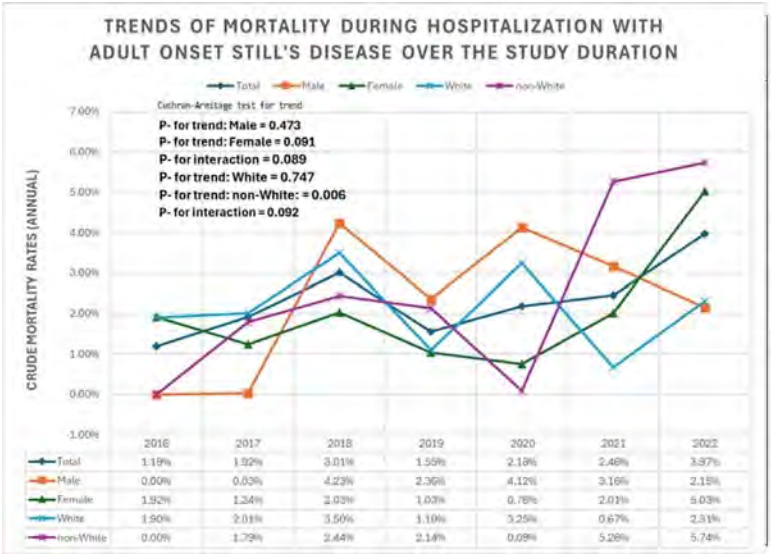
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of the study populations (n=9,135).

Variables	Total (n=9,135)	Male (n=3,630)	Female (n=5,505)	p-value	White (n=5,175)	Non-white (n=3,960)	p-value
Age mean (SD)	48.76 (17.26)	51.92 (17.41)	46.68 (16.85)	<0.001	52.70 (16.97)	43.61 (16.26)	<0.001
Females n(%)	5505 (60.26%)	-	5505 (100%)	-	2895 (55.9%)	2610 (65.9%)	<0.001
Males n(%)	3630 (39.74%)	3630 (100%)	-		2280 (44.1%)	1350 (34.1%)	
In-hospital Mortality n(%)	210 (2.3%)	100 (2.8%)	110 (2.0%)	0.293	105 (2.0%)	105 (2.7%)	0.376
Elective admission n(%)	910 (10%)	325 (9.0%)	585 (10.6%)	0.246	640 (12.4%)	270 (6.8%)	<0.001
Weekend admission n(%)	2085 (22.8%)	855 (23.6%)	1230 (22.3%)	0.548	1185 (22.9%)	900 (22.7%)	0.932
ED admission n(%)	2680 (73.8%)	4040 (73.4%)	2680 (73.8%)	0.836	3580 (69.2%)	3140 (79.3%)	<0.001
LOS mean (SD)	7.16 (8.67)	7.37 (7.74)	7.02 (9.21)	0.006	6.62 (7.65)	7.86 (9.78)	0.005
Total hospital charges in $ mean (SD)	88710.6 (185023.9)	92052.6 (175786.1)	86496.0 (190941.6)	0.008	72946.6 (94944.2)	109348.3 (257975.8)	<0.001
Total cost (adjusted) in $ mean (SD)	24363.7 (44019.0)	24775.0 (37439.9)	24091.4 (47895.0)	0.001	20925.8 (26928.6)	28864.6 (59095.1)	0.001
Discharge disposition n(%)				0.110			<0.001
Routine (alive)	6405 (70.2%)	2405 (66.3%)	4000 (72.7%)		3425 (66.2%)	2980 (75.3%)	
Short-term facility	420 (4.6%)	185 (5.1%)	235 (4.3%)		235 (4.5%)	185 (4.7%)	
Intermediate or SNF	845 (9.3%)	385 (10.6%)	460 (8.4%)		580 (11.2%)	265 (6.7%)	
Home health	1160 (12.7%)	520 (14.3%)	640 (11.6%)		775 (15.0%)	385 (9.7%)	
AMA	90 (1.0%)	35 (1.0%)	55 (1.0%)		50 (1.0%)	40 (1.0%)	
Died	210 (2.3%)	100 (2.8%)	110 (2.0%)		105 (2.0%)	105 (2.7%)	
Health Insurance n(%)				0.001			<0.001
Medicare	2775 (30.4%)	1245 (34.3%)	1530 (27.9%)		1970 (38.1%)	805 (20.4%)	
Medicaid	1695 (18.6%)	515 (14.2%)	1180 (21.5%)		485 (9.4%)	1210 (30.7%)	
Private including HMO	3985 (43.7%)	1605 (44.3%)	2380 (43.4%)		2425 (46.9%)	1560 (39.5%)	
Self pay	400 (4.4%)	140 (3.9%)	260 (4.7%)		155 (3%)	245 (6.2%)	
No charge or others	260 (2.9%)	120 (3.3%)	140 (2.6%)		135 (2.6%)	125 (3.2%)	
NCHS urbanization scheme n(%)				0.082			<0.001
Large 'central' metropolitan/Fringe metropolitan	5460 (59.9%)	2050 (56.7%)	3410 (62.1%)		2760 (53.4%)	2700 (68.5%)	
Medium metropolitan/ Small metropolitan	2690 (29.5%)	1145 (31.7%)	1545 (28.1%)		1675 (32.4%)	1015 (25.8%)	
Micropolitan/ Non-micropolitan	960 (10.5%)	420 (11.6%)	540 (9.8%)		735 (14.2%)	225 (5.7%)	
Race n(%)				0.001			-
White	5175 (58.2%)	2280 (64%)	2895 (54.4%)		5175 (100%)	-	
Black	1130 (12.7%)	385 (10.8%)	745 (14%)		-	1130 (30.5%)	
Hispanic	1535 (17.3%)	475 (13.3%)	1060 (19.9%)		-	1535 (41.4%)	
Asian or Pacific Islander	570 (6.4%)	220 (6.2%)	350 (6.6%)		-	570 (15.4%)	
Native American, others	475 (5.3%)	200 (5.6%)	275 (5.2%)		-	475 (12.8%)	
Median household income quartiles per area zip code n(%)				0.470			<0.001
1st quartile ($1 – $ 55999)	2285 (25.3%)	905 (25.3%)	1380 (25.3%)		1000 (19.6%)	1285 (32.8%)	
2nd quartile ($ 56000 – $ 70999)	2110 (23.4%)	775 (21.6%)	1335 (24.5%)		1180 (23.1%)	930 (23.8%)	
3rd quartile ($ 71000 - $ 93999)	2290 (25.4%)	910 (25.4%)	1380 (25.3%)		1325 (25.9%)	965 (24.6%)	
4th quartile ($ 94000 – or more)	2345 (26%)	990 (27.7%)	1355 (24.9%)		1610 (31.5%)	735 (18.8%)	
Hospital bed size n(%)				0.387			<0.001
Small	1555 (17%)	650 (17.9%)	905 (16.4%)		1050 (20.3%)	505 (12.8%)	
Medium	2115 (23.2%)	880 (24.2%)	1235 (22.4%)		1225 (23.7%)	890 (22.5%)	
Large	5465 (59.8%)	2100 (57.9%)	3365 (61.1%)		2900 (56%)	2565 (64.8%)	
Hospital location							

Methods: We used the National Inpatient Sample (NIS), a database that includes a subset of hospital discharges in 50 states, to identify patients with adult-onset Still's disease who were admitted to the hospital due to any cause. Patients who were admitted in the years 2016 to 2022 (including the COVID-19 pandemic) were enrolled in the study. Adult-onset Still's disease was defined based on the ICD-10 code M06.1. Patients were excluded based on age cut-off of < 15 years,



Top 20 listed primary reasons of admission (Unweighed)

1.	2895	M061	Adult-onset Still's disease
2.	1044	A419	Sepsis, unspecified organism
3.	125	J189	Pneumonia, unspecified organism
4.	124	R509	Fever, unspecified
5.	119	D761	Hemophagocytic lymphohistiocytosis
6.	100	U071	COVID-19
7.	94	N179	Acute kidney failure, unspecified
8.	65	N390	Urinary tract infection, site not specified
9.	60	A4189	Other specified sepsis
10.	55	L03116	Cellulitis of left lower limb
11.	50	I214	Non-ST elevation myocardial infarction (NSTEMI)
12.	49	I130	Hypertensive heart disease and CKD stage 1-4
13.	40	A4151	Sepsis due to Escherichia coli [E. coli]
14.	39	K529	Noninfective gastroenteritis and colitis, unspecified
15.	39	I110	Hypertensive heart disease with heart failure
16.	35	I2699	Pulmonary embolism without acute cor pulmonale
17.	35	Z5111	Encounter for antineoplastic chemotherapy
18.	34	M1712	Unilateral primary osteoarthritis, left knee
19.	30	K7200	Acute and subacute hepatic failure without coma
20.	29	I313	Pericardial effusion (noninflammatory)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and as well as juvenile rheumatoid arthritis identified as M08.2 were not included in the analysis. Discharge weights were applied to estimate national level representation. Adjusted hospital costs were reported for inflation in the year 2022 according to the U.S. Department of Labor inflation index for Medical Care Consumer Price Index (CPI) for cost-based analysis. Cochrane-armitage and Jonckheere-Terpstra test were applied as indicated to analyze the trends over the study period for in-hospital mortality rates, length of stay, inflation adjusted hospitalization costs respectively.

Results: There were a total of 1827 unweighted and 9135 weighted hospital discharges reported with a history of adult onset's still disease on payer information through healthcare cost and utilization project (HCUP). Among these admissions over a span of 7 years within NIS databases, 40% were males and 60% females, 58% were white by ethnicity. In-hospital mortality rate was 2.3%, and the trend shows an increase amongst non-White population, especially after the COVID-19 pandemic (P=0.006). The most common primary reason of admission remains sepsis following adult-onset Still's disease complications. Hospitalization costs and length of stay were found higher with male gender (p=0.001 & 0.006 respectively), and non-White population (p=0.001 & 0.005 respectively). Among non-White population, length of stay and hospitalization costs were found highest in Asians/Pacific Islanders population. Also, the mean age of these patients were comparatively higher than other races (50 vs 42 years), as opposed to White population with a mean age of 52 years (p< 0.001).

Conclusion: Sepsis was the most common primary reason for admission. Overall in-hospital mortality was low (2.3%) but increased significantly among non-White populations. Male gender and non-White race were associated with higher hospitalization costs and lengths of stay. Among subgroups, Asian/Pacific Islander patients had the highest resource use and were older at admission than other non-White groups.

Disclosure: M. Akram: None; **M. Asghar**: None; **W. Lee**: None; **B. Yousuf**: None; **C. Carillo**: None; **S. Rama**: None.

Abstract Number: 0164

Online Patient Survey on the Impact of Extreme Weather Events on Autoimmune and Rheumatic Diseases

Iazsmin Ventura[1], Tamiko Katsumoto[2], **Natasha Powell**[3], Elena Adams[4] and Olivia Casey[5], [1]Section of Rheumatology, University of Chicago, Chicago, [2]Division of Immunology and Rheumatology, Stanford University, Millbrae, CA, [3]University of Chicago Pritzker School of Medicine, Chicago, [4]New Rochelle High School, New Rochelle, [5]Autoimmune Association, Eastpointe

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The impact of climate change on autoimmune and rheumatic diseases remains poorly understood. However, emerging evidence suggests extreme weather events, often related to climate change, may be associated with disease flares, hospitalizations, and disruptions in access to medical care. This pilot study, the first retrospective online survey of its kind, investigates associations between extreme weather events, patient demographics, and self-reported disease flares.

Methods: An online survey was distributed to U.S. individuals with autoimmune and rheumatic diseases, collecting data on demographics, diagnoses, self-reported flares, and exposure to extreme weather events (e.g., floods, wildfires). It also assessed healthcare utilization, treatment disruptions, mental health impacts, and barriers to medical access post-extreme

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

weather. Respondents were grouped based on whether their disease flare occurred within 90 days of their most severe extreme weather event or not. Chi-square analyses examined associations between flares, demographics, weather events, and healthcare access.

Results: Among 155 participants, 88 participants (57%) reported having a disease flare within the period investigated. Participants with polymyalgia rheumatica (50% vs. 10.5%, p = 0.004) and rheumatoid arthritis (24% vs. 9.8%, p = 0.045), were more likely to experience flares within 90 days of their most severe extreme weather event exposure when compared with individuals who did not have the specified disease. Conversely, those with Raynaud's phenomenon (2.7% vs. 14.9%, p = 0.046) and Sjogren's disease (2.8% vs 14.8%, p = 0.052) were less likely to experience a flare within 90 days of their most severe extreme weather event.

Additionally, participants who were unable to store medication safely (75% vs. 10.4%, p < 0.001) or who had trouble remembering key details of the event (60% vs. 20.8%, p = 0.044) following their most severe extreme weather event were more likely to experience flares within 90 days of this event compared to individuals who did not have those characteristics.

Finally, participants who identified as Black (33.3% vs. 10.3%, p = 0.018) were more likely to experience flares within 90 days of their most severe extreme weather event compared to individuals who did not identify as Black.

Conclusion: Difficulty storing medication, specific diseases (polymyalgia rheumatica, rheumatoid arthritis), and identifying as Black were associated with increased flare risk within 90 days following extreme weather events. These findings point to possible mechanisms—like improper medication storage—and reinforce evidence that climate change disproportionately affects vulnerable populations, including racial and ethnic minorities. This exploratory project lays the foundation for future research and education aimed at improving patient resilience to climate change. Next steps include developing a shorter survey focused on the timing and location of severe weather events and flares, and expanding survey dissemination in the U.S. and internationally to better understand the link between severe weather and autoimmune disease flares.

Disclosure: I. Ventura: None; **T. Katsumoto**: Beyond Meat, 12, Unrestricted grant, Sanofi, 5; **N. Powell**: None; **E. Adams**: None; **O. Casey**: None.

Abstract Number: 0165

Per-Protocol Analysis of the Effectiveness of GLP1 Agonists Against SGLT2 Inhibitors on Osteoarthritis Outcomes

Nene Ukonu[1], David Felson[2], Michael LaValley[3] and S. Reza Jafarzadeh[4], [1]Boston University School of Public Health, Boston, MA, [2]Boston University, Boston, MA, [3]Boston University School of Public Health, Arlington, MA, [4]Boston University Chobanian & Avedisian School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-diabetic medications often have effects on other conditions. GLP1 agonists (GLP1a) have shown protective effects on OA outcomes in trials and short-term trial emulations, but many patients stop treatment and long-term outcomes are unknown. To assess the effectiveness of GLP1a accounting for treatment discontinuation or switching, we selected SGLT2 inhibitors (SGLT2i) as an active comparator, which have pleiotropic effects and are

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Five-Year Risk Ratios, and Risk Differences for Knee Replacement (KR) and Osteoarthritis (OA) Outcomes

Comparison	Outcome	Analysis	Risk Ratio (95% CI)	Risk Difference per 1,000 (95% CI)
GLP1a vs. SGLT2i	KR	PP	1.18 (1.05, 1.33)	8.5 (15.4, 2.5)
		ITT	1.00 (1.00, 1.00)	0.0 (0.0, 0.0)
	OA	PP	1.16 (1.10, 1.23)	23.3 (33.2, 15.1)
		ITT	1.00 (1.00, 1.00)	0.2 (0.1, 0.3)
Semaglutides vs. SGLT2i	KR	PP	1.05 (0.78, 1.12)	-2.5 (-14.5, 5.2)
		ITT	1.00 (1.00, 1.00)	0.0 (0.0, 0.0)
	OA	PP	0.96 (0.88, 1.10)	-6.4 (-19.7, 14.2)
		ITT	1.00 (1.00, 1.00)	0.1 (0.0, 0.2)
Non-Semaglutide GLP1a vs. SGLT2i	KR	PP	1.23 (1.09, 1.41)	11.4 (4.8, 17.9)
		ITT	1.00 (1.00, 1.00)	0.1 (0.0, 0.1)
	OA	PP	1.19 (1.12, 1.27)	27.1 (16.9, 35.5)
		ITT	1.00 (1.00, 1.00)	0.2 (0.1, 0.3)

Risk ratios and risk differences estimates were adjusted for baseline and time-varying confounders that included demographics, diabetes, hypertension, hyperlipidemia, chronic kidney disease, COPD, obesity, knee pain, ACL/meniscus injury history, and use of NSAIDs/opioids, insulin, metformin, statins, and DPP4 inhibitors.

efficacious in several diseases. We compared the effectiveness of GLP1a vs. SGLT2i on the 5-year risk of knee replacement (KR) and OA, using per-protocol analyses to account for treatment discontinuation or switching, addressing limitations of prior intention-to-treat (ITT) analyses that assumed sustained treatment and ignored time-varying confounding.

Methods: We emulated a target trial using 2015–2022 Merative MarketScan Commercial Claims data, including persons aged 45-65 initiating GLP1a or SGLT2i GLP1a with at least 1 year of continuous enrollment and a washout period (with no prior use of either drug). Exclusions included a prior diagnosis of fibromyalgia, rheumatoid arthritis, or any claims for KR (the primary outcome) or OA (the secondary outcome) before drug initiation. Baseline and time-varying confounders included in the model are shown in the Table 1. We used parametric g-formula for per-protocol analyses, modeling time-varying hazards with pooled logistic regression to estimate cumulative risks of treatment with GLP1a SGLT2i vs. SGLT2i. GLP1a, accounting for censoring due to discontinuation, switching, loss to follow-up, or study end (5 years). Of GLP1a, because semaglutides cause greater weight loss than earlier GLP1a, they may be uniquely beneficial in OA. Thus, we carried out sensitivity analyses to assess 5-year outcome risk comparing semaglutides vs. SGLT2i and non-semaglutide GLP1a drugs vs. SGLT2i. We further carried out ITT analyses to highlight the impact of non-adherence on risk estimates.

Results: Among 323,445 eligible individuals (129,603 GLP1a initiators and 193,842 SGLT2i initiators, mean age 55, 49% male, 61% with diabetes [72% GLP1a, 53% SGLT2i]), per-protocol analyses showed that 5-year risk of KR was 18% greater in GLP1a users vs. SGLT2i users (Table 1; risk ratio = 1.18, risk difference: 8.5 more KR cases per 1,000 in GLP1a initiators). For OA, GLP1a users had a 16% greater risk (Table 1: risk ratio = 1.16; risk difference: 23.3 more OA cases per 1,000 in GLP1a initiators). In contrast, sensitivity analyses showed no significant KR or OA risk differences for semaglutides vs. SGLT2i, whereas non-semaglutatides vs. SGLT2i showed reduced risks in SGLT2i users (Table 1). ITT analyses, ignoring drug discontinuation or switching, showed no significant differences for either outcome (Table 1).

Conclusion: GLP1a's increased risk of KR and OA onset compared with SGLT2i, suggesting SGLT2i may have previously unrecognized therapeutic effects in OA. Semaglutides and SGLT2i showed similar effects on KR and OA despite semaglutide's well-recognized weight loss effects. Our results also suggest that ITT analyses may not accurately reflect long term risks of drugs on OA outcomes, especially for drugs where discontinuation or switching is common.

Disclosure: N. Ukonu: None; **D. Felson**: None; **M. LaValley**: None; **S. Jafarzadeh**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0166

Effect of Air Pollution on Prevalence and Disease Activity of Rheumatoid Arthritis in the German Middle-aged Population from the NAKO Baseline Examination

Tim Filla[1], Gamal Chehab[1], Jutta Richter[2], Jrg Distler[3], **Oliver Sander**[1] and The NAKO Health Study, [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [2]Clinic for Rheumatology and Hiller Research Unit, Heinrich-Heine-University Duesseldorf, Medical Faculty, Duesseldorf, Germany, Dsseldorf, Germany, [3]University Hospital Duesseldorf and HHU, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Environmental influences affect the human body throughout life, from conception to old age. The influence of air pollution and fine dust particles on systemic diseases, particularly rheumatoid arthritis (RA), has been studied in various regions, but has not yet been comprehensively recorded for Germany. Therefore, the aim of this study is to describe the associations between air pollution and the prevalence and disease activity of RA in Germany.

Methods: In the German National Cohort (NAKO) Health Study, medical histories and examination findings were collected from a total of 204,729 individuals (18-69 years of age) in a population sample from 18 study centers between 2014 and 2019. In addition, 23,456 individuals underwent a clinical hand examination of 20 joints for pain and swelling by trained examiners (Level 2 subcohort), enabling the calculation of DAS28 as a measure of rheumatic disease activity. Cumulative and daily air pollution levels were made available for the NAKO study regions by the Environmental Data Unit in Munich (air pollutants (UBA: particulate matter particle size (PM) 2.5, PM10, nitrogen oxide (NO2), and ozone (O3)) to the nearest 1 km from the place of residence on a daily basis; air pollutants (ELAPSE: PM2.5, NO2, O3, black carbon (BC)) to the nearest 100 m for 2010. The analyses were adjusted for age, sex, smoking status, BMI, and income.

Results: RA was known in 4033 individuals of the total cohort (1.97%) and 426 individuals (1.82%) of the Level 2 cohort. Disease activity in the cohort was low (mean DAS28 1.37, standard deviation 1.03). The occurrence of RA was positively associated with age (10-year OR = 1.65 [95% CI: 1.59-1.71]) and female sex (OR = 2.67 [2.46-2.90]). Individuals with RA were on average 57 years old (vs. 50 years old in those without RA), and 71% were female (50%). 39% (vs. 44%) reported never smoking, 36% (vs. 32%) reported previously smoking, and 18% (vs. 20%) were currently smoking.

Table 1

Table 1: Effect sizes of environmental influences on the incidence of RA evaluated in the Level 1 cohort (n = 204,729) and the DAS28 evaluated in the Level 2 RA cohort (n = 426). All effect sizes refer to scaled variables (mean 0, variance 1).

Variables with 95% confidence interval	Odds Ratio for RA n= 204,729 (Level 1 Cohort)	Mean change DAS28 n=426 (Level 2 RA Cohort)
PM2.5 (2010)	0.99 [0.95;1.03]	0.13 [0.03;0.22]
NO2 (2010)	0.93 [0.90;0.97]	0.08 [-0.01;0.17]
O3 (2010)	1.02 [0.98;1.06]	-0.08 [-0.19;0.03]
Black Carbon (2010)	0.94 [0.90;0.98]	0.07 [-0.02;0.17]
PM2.5 (2017)	1.01 [0.97;1.05]	0.14 [0.02;0.25]
PM10 (2017)	1.01 [0.97;1.05]	0.14 [0.03;0.26]
NO2 (2017)	0.93 [0.89;0.97]	0.10 [0.01;0.19]
O3 (2017)	1.03 [0.99;1.07]	-0.12 [-0.21;-0.03]

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The historical (ELAPSE) and daily (UBA) environmental pollution levels of the respective place of residence showed a strong association with DAS28. Fine dust particle pollution for PM2.5 and PM10, NO2, and BC were positively associated with RA disease activity. In contrast, ozone pollution showed a negative association with disease activity. There was no clinically relevant effect of particulate matter pollution on the frequency of RA for PM2.5 and PM10, NO2, and BC for either the current or historical measurements, although the frequency was lower at higher ozone levels.

Conclusion: A clinically relevant association of disease activity with all air pollutant exposures for RA was demonstrated in the population sample of over 200,000 individuals. However, a relevant association between air pollutant exposure at the current place of residence and the occurrence of RA could not be demonstrated. The cross-sectional results presented here will also be prospectively examined in the NAKO cohort for 20 years to provide stronger conclusions regarding causality, particularly with regard to the different frequencies observed in the study centers.

Disclosure: T. Filla: None; **G. Chehab**: None; **J. Richter**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **O. Sander**: None.

Abstract Number: 0167

Geographic and Demographic Patterns of Rheumatoid Arthritis in the United States: Insights from GBD 2021

Punith Chirumamilla[1], Sameer Kumar Majety[2], Rithish Nimmagadda[3], Ravi Medarametla[4], Priya Sunkara[5], Pranathi Bandarupalli[6], Anjani Mahesh Kumar Cherukuri[7] and Himaja Anne[8], [1]Baptist Memorial Hospital North Mississippi, Oxford, MS, [2]School of Medicine, Xiamen University, China, Kakinada, Andhra Pradesh, India, [3]One Brooklyn Health, New York, NY, [4]Mamata Medical College, Guntur, Andhra Pradesh, India, [5]White River Health, Batesville, AZ, [6]Mercy St Vincent Medical Center, Toledo, OH, [7]Guntur Medical College, Guntur, Andhra Pradesh, India, [8]Hind Institute of Medical Sciences, Sitapur, Uttar Pradesh, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune, systemic disease with a rising U.S. healthcare burden. Utilizing Global Burden of Disease (GBD) 2021 estimates, we analyzed sex, age, and state specific trends in prevalence, incidence, Disability-Adjusted Life Year (DALY), and death, including attributable smoking burden.

Methods: We performed a descriptive analysis with GBD 2021 estimates for RA in all 50 U.S. states and District of Columbia from 1990 to 2021. Age-standardized prevalence, incidence, DALY, and death rates were stratified by sex and age group. Choropleth maps were created to display geographic disparities, and box plots were employed to compare inter-state variation and gender differences. States were also grouped based on the magnitude and temporal trends of smoking-attributable RA DALY percentages.

Results: Montana, Wyoming, and New Mexico consistently ranked among the top three states for overall RA burden, with Montana showing highest age-standardized prevalence (464.73 per 100,000) and DALY rate (73.17). The District of Columbia, California, and Mississippi reported the lowest prevalence and DALY rates. RA burden increased progressively with age.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

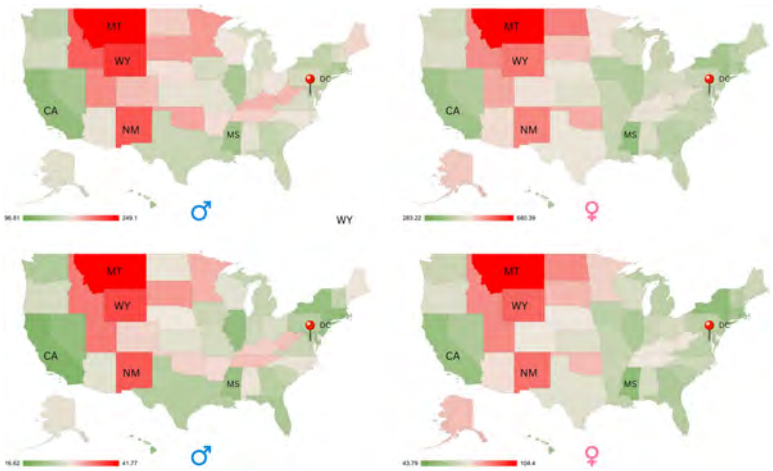


Figure 1: U.S. state-level choropleth maps showing the age-standardized burden of rheumatoid arthritis (RA) by sex. The top row depicts age-standardized prevalence rates in males (left) and females (right). The bottom row shows age-standardized DALY (disability-adjusted life year) rates in males (left) and females (right). Color gradients range from green (lower burden) to red (higher burden). Montana consistently shows the highest burden across both prevalence and DALY measures, especially among females. In contrast, states such as California and the District of Columbia demonstrate lower burden. Across all maps, females show higher RA burden compared to males, highlighting persistent sex-based disparities.

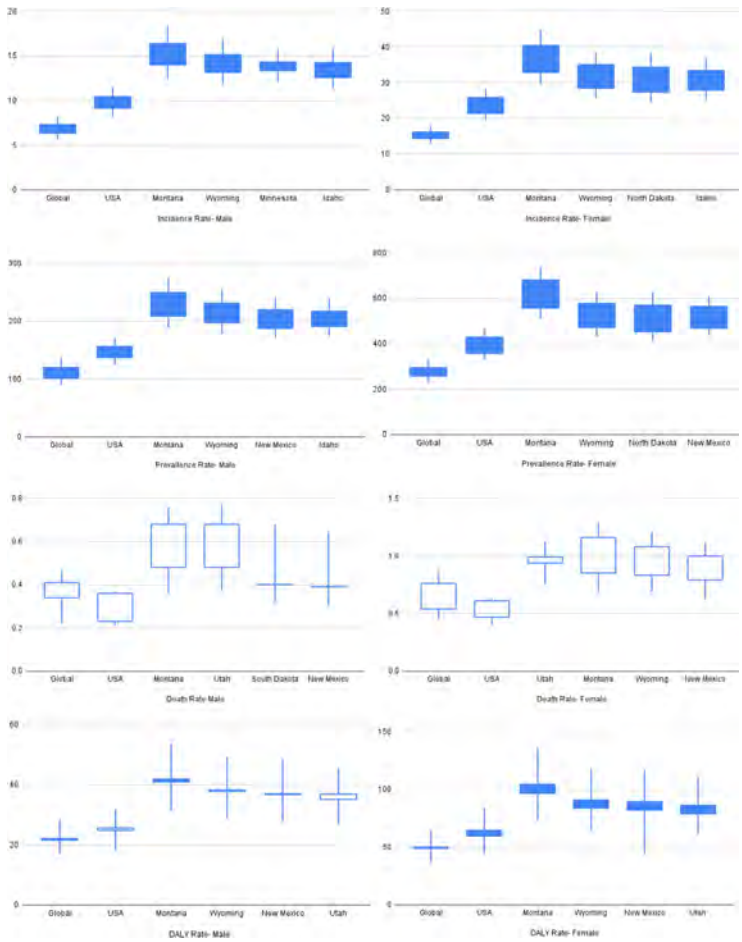


Figure 2: Boxplots illustrating age-standardized burden of rheumatoid arthritis (RA) from 1990 to 2021 across global, U.S., and high-burden states by sex and metric. The plots compare male (left column) and female (right column) data across six domains: incidence rate, prevalence rate, death rate, and DALY rate. Each box represents the interquartile range (IQR) of the metric, with the filled boxes indicating an increase and unfilled boxes indicating a decrease between 1990 and 2021. The central vertical whisker spans the widest confidence interval limits (i.e., from the lowest lower bound to the highest upper bound of both years), indicating the maximum possible uncertainty range over time. The x-axis includes Global, USA, and the top four high-burden U.S. states identified for each metric. Notably, Montana and Wyoming appear consistently among the highest for most metrics, particularly in females, who show greater overall burden across incidence, prevalence, DALY, and death.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

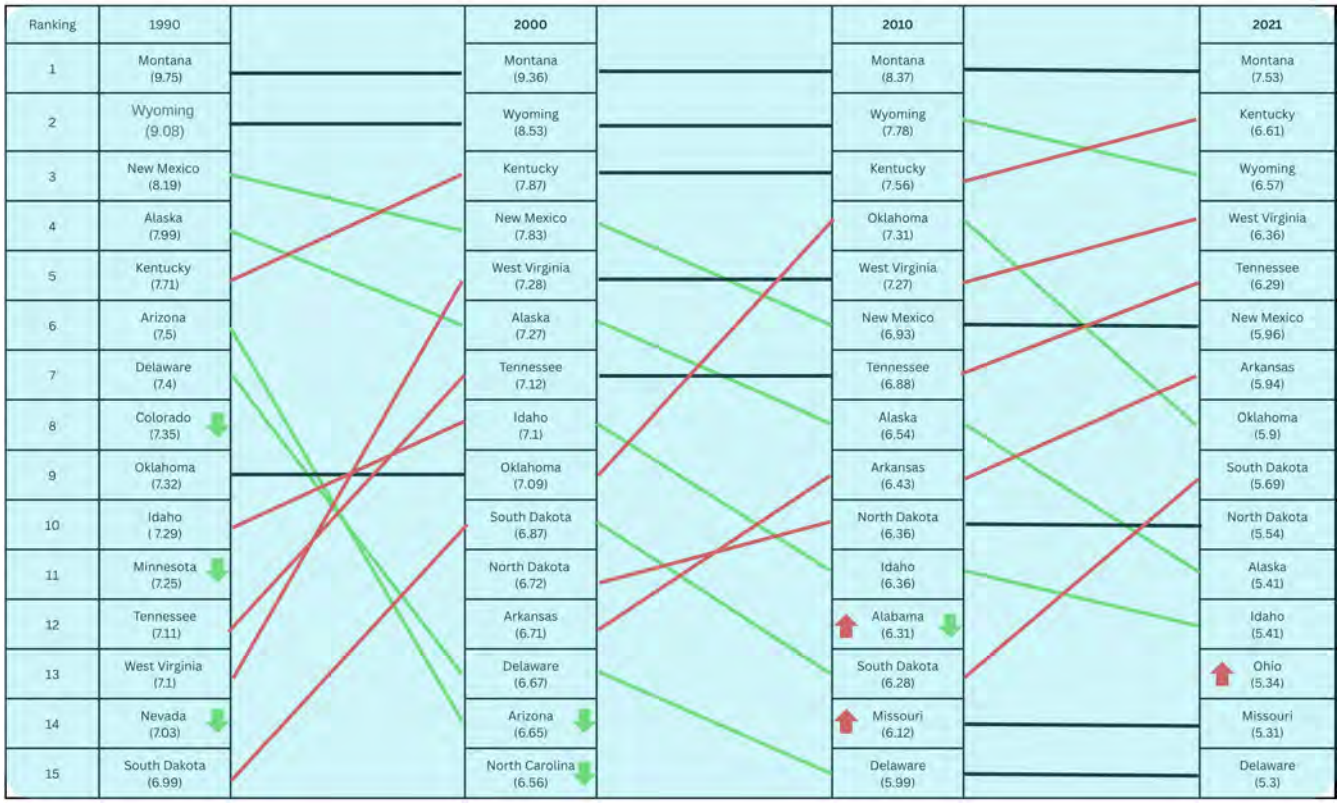


Figure 3: Trends in the top 15 U.S. states by age-standardized DALY rate attributable to smoking-related rheumatoid arthritis (RA) from 1990 to 2021. Each column represents rankings by year (1990, 2000, 2010, 2021), with corresponding DALY rates in parentheses. Black lines indicate unchanged rank from one time point to the next. Green lines indicate a decrease in rank (i.e., improvement/lower disease burden). Red lines indicate an increase in rank (i.e., worsening disease burden). Green downward arrows denote states that were ranked in the top 15 in respective time frame but dropped out by 2021. Red upward arrows denote states that entered the top 15 in respective time frame by 2021. This visualization reflects geographic and temporal disparities in smoking-attributable RA burden across the U.S., highlighting states with persistently high burden (e.g., Montana, Kentucky) and those showing worsening trends (e.g., Arkansas, South Dakota).

The 55+ group had the highest rates across all parameters (DALY: 162.8; incidence: 46.98; prevalence: 1014.63; death: 2.16), while individuals under 20 had minimal burden (DALY: 4.44; death: 0.00).Females had consistently higher burden than males across all states and age groups. For example, Montana's female DALY rate was 104.4 compared to 41.77 for males.

Smoking-attributable RA DALY rates showed an overall national decline but remained highest in states such as Montana, Kentucky, and Wyoming, which consistently ranked in the top three from 1990 to 2021. West Virginia, Tennessee, and New Mexico remained within the top 10, highlighting regions of persistent burden. Meanwhile, states such as Colorado, Minnesota, and Nevada showed significant improvement, dropping out of the top 15. In contrast, Arkansas, Kentucky and South Dakota climbed the ranks, reflecting worsening trends in smoking-related RA burden in those regions.

Conclusion: Substantial disparities in RA burden exist across U.S. states, with consistently high rates observed in Montana, Wyoming, and Kentucky. These differences are further amplified by sex- and age-specific trends, with older adults and females bearing a disproportionate burden. While smoking-attributable RA DALY percentages have declined nationally, several states—particularly Kentucky, Arkansas, and Missouri—continue to show persistently high or worsening burden, suggesting gaps in tobacco control. Conversely, states such as Colorado and Minnesota demonstrate improving trends.

These findings highlight the urgent need for state-specific, gender- and age-sensitive strategies to mitigate RA burden and address modifiable risks like smoking. Targeted interventions may include stricter tobacco control policies, tailored public health campaigns, improved telehealth access for rheumatologic care, and early screening integrated into primary care for high-risk groups. Focused, equitable efforts are critical to narrowing geographic and demographic disparities in RA outcomes across the U.S.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Chirumamilla: None; **S. Majety**: None; **R. Nimmagadda**: None; **R. Medarametla**: None; **P. Sunkara**: None; **P. Bandarupalli**: None; **A. Cherukuri**: None; **H. Anne**: None.

Abstract Number: 0168

Risk of hospitalization in patients with rheumatoid arthritis-associated interstitial lung disease or bronchiectasis: A matched cohort study

QIANRU ZHANG[1], Ying Qi[2], Xiaosong Wang[3], Gregory McDermott[4], Sung Hae Chang[5], Liya Sisay Getachew[6], Mark Chaballa[7], Vadim Khaychuk[8], Misti Paudel[9], Katherine Liao[10] and Jeffrey Sparks[6], [1]Brigham and Women's Hospital/ Beijing Tsinghua Changgung Hospital, Cambridge, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, Natick, MA, [4]Brigham and Women's Hospital, Brookline, MA, [5]Soonchunhyang University College of Medicine, Cheonan, MA, South Korea, [6]Brigham and Women's Hospital, Boston, MA, [7]Bristol Myers Squibb, Princeton, NJ, [8]Bristol Myers Squibb, Pennington, NJ, [9]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [10]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, USA, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: RA-associated lung disease (RA-LD), including RA-associated interstitial lung disease (RA-ILD) and RA-associated bronchiectasis (RA-BR), is a serious extra-articular manifestation of RA that significantly contributes to morbidity and mortality. Although previous studies have documented the adverse clinical outcomes associated with RA-LD, its impact on hospitalization risk is insufficiently investigated, particularly for RA-BR.

Methods: We conducted a retrospective matched cohort study of patients enrolled in the biobank of a large U.S. health care system, comparing RA-LD cases to RA comparators without lung disease (RA-no LD), matched by calendar date, age, sex, and RA duration at the index date. The index date was defined as the later date of the RA or ILD/BR diagnosis for RA-LD cases, and the matched date for RA-no LD comparators. Patients with RA met the 2010 ACR/EULAR classification criteria. RA-LD cases were verified by medical record review and chest imaging for clinically-apparent RA-ILD and/or RA-BR. The primary outcomes were overall and respiratory hospitalizations. Secondary outcomes included emergency department (ED) visits and intensive care unit (ICU) admissions. Incidence rates were calculated per 100 person-years. Incidence rate ratios (IRRs) with 95% confidence intervals (CI) were estimated using multivariable Poisson regression models, comparing RA-LD cases vs. RA-no LD comparators as well as for RA-ILD and RA-BR cases vs. RA-no LD comparators, with adjustment for the propensity score as a covariate.

Results: We analyzed 221 RA-LD cases (151 RA-ILD and 70 RA-BR) and 980 matched RA-no LD comparators (**Table 1**). RA-LD patients had higher rates of overall hospitalization (60% vs. 41%, p< 0.001) and respiratory hospitalization (23% vs. 6%, p< 0.001), along with higher proportions of ED visits (57% vs. 48%, p=0.02) and ICU admissions (36% vs. 20%, p< 0.001, **Table 2**). RA-LD patients had a shorter time from the index date to first hospitalization (median 922 vs. 1,217 days, p=0.01) compared to RA-no LD comparators. They also had a shorter time to first respiratory hospitalization (median 1,588 vs. 2,253 days, p=0.009), including RA-ILD (median 1,707 vs. 2,253 days, p=0.03) and RA-BR (median 1,436 vs. 2,253 days, p=0.04). RA-LD, including RA-ILD and particularly RA-BR, had higher risks of overall hospitalization (adjusted IRR 1.73, 95%CI 1.57-1.91) and respiratory hospitalization (adjusted IRR 5.13, 95%CI 3.80-6.94, **Table 3**). RA-ILD was associated with an increased risk of ICU admissions (adjusted IRR 1.99, 95%CI 1.81-2.18).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of RA-LD cases and RA-no LD comparators

Characteristics	RA-LD cases (n=221)	RA-no LD comparators (n=980)
Demographics		
Age, years (mean and SD)	63.9 (11.3)	62.3 (10.5)
Female sex, n (%)	165 (75)	743 (76)
Race		
Asian	3 (1)	13 (1)
Black	14 (6)	54 (6)
White	191 (86)	853 (87)
Other	8 (4)	37 (4)
Frailty Index, mean (SD)	0.2 (0.04)	0.1 (0.04)
Smoking		
Smoking status, n (%)		
Past	126 (57)	454 (46)
Current	15 (7)	61 (6)
Pack-years, median (IQR)	5 (0-22.5)	0 (0-12.1)
Comorbidities		
Diabetes	9 (4)	49 (5)
Heart failure	15 (7)	31 (3)
Cardiovascular disease	20 (9)	44 (4)
Solid tumor cancer	7 (3)	6 (1)
Leukemia or lymphoma	17 (8)	36 (4)
RA characteristics		
RA duration, years (median and IQR)	9.0 (0.7-18.9)	6.4 (1.8-15.0)
Seropositive	180 (81)	618 (63)
Glucocorticoids, n (%)	113 (51)	355 (37)
Any DMARDs, n(%)	136 (62)	542 (56)
csDMARDs, n (%)	108 (49)	411 (42)
bDMARDs, n (%)	82 (37)	283 (29)
tsDMARDs, n (%)	5 (2)	23 (2)
Serious infection within 365 days prior to index date, n (%)	10 (5)	18 (2)
Health care utilization		
Any hospitalization within 365 days before index, n (%)	47 (21)	107 (11)
Number of outpatient visits within 365 days before index, Median (IQR)	11 (4-23)	6 (2-15)

bDMARDs, biological disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; DMARDs, disease-modifying antirheumatic drugs; IQR, interquartile range; RA-LD, rheumatoid arthritis-associated lung disease; RA-no LD, rheumatoid arthritis without lung disease; SD, standard deviation; TNFi, tumor necrosis factor inhibitor; tsDMARDs, targeted synthetic disease-modifying antirheumatic drug

Table 2. Acute care outcomes, comparing RA-LD cases and RA-no LD comparators

Variable	RA-LD (n=221)	RA-no LD (n=980)	P value
Emergency Department			
Any visit, n (%)	127 (57)	474 (48)	**0.02**
Overall Hospitalization			
Any hospitalization, n (%)	132 (60)	401 (41)	**<0.001**
Number of hospitalizations, median (IQR)	3 (1-5)	2 (1-3)	**0.001**
Time to first hospitalization (days), median (IQR), among those with any hospitalization	922 (269-1,959)	1,217 (430-2,231)	**0.01**
Length of stay of first hospitalization, median (IQR), among those with any hospitalization	4 (2-7)	3 (2-6)	0.15
Total length of stay of all hospitalizations, median (IQR), among those with any hospitalization	14 (5-33)	6 (4-21)	**0.001**
Respiratory Hospitalization			
Any respiratory hospitalization, n (%)	50 (23)	62 (6)	**<0.001**
Number of respiratory hospitalizations, median (IQR)	1 (1-2)	1 (1-1)	**0.009**
Time to first respiratory hospitalization (days), median (IQR), among those with respiratory hospitalization	1,588 (624-2,409)	2,253 (1,170-3,951)	**0.009**
Length of stay of first respiratory hospitalization, mean (SD), among those with respiratory hospitalization	6 (3-11)	4 (2-9)	0.25
Intensive Care Unit			
Any intensive care unit hospitalization, n (%)	79 (36)	196 (20)	**<0.001**
Invasive ventilation, n (%)	20 (9)	39 (4)	**0.002**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Incidence rate ratios for acute care outcomes, comparing RA-LD cases to RA-no LD comparators

	Incidence rate (per 100 patient-years)	Multivariable** RR (95%CI)
Outcome: ED visit		
RA-no LD comparators	22.2	1.0 (Ref)
RA-LD cases	29.0	0.95 (0.86-1.04)
RA-no LD comparators	22.2	1.0 (Ref)
RA-ILD cases	28.3	0.94 (0.84-1.05)
RA-BR cases	30.8	0.96 (0.82-1.12)
Outcome: Hospitalization		
RA-no LD comparators	14.9	1.0 (Ref)
RA-LD cases	32.9	**1.73 (1.57-1.91)**
RA-no LD comparators	14.9	1.0 (Ref)
RA-ILD cases	33.2	**1.78 (1.59-1.98)**
RA-BR cases	32.3	**1.63 (1.39-1.90)**
Outcome: Respiratory hospitalization		
RA-no LD comparators	0.9	1.0 (Ref)
RA-LD cases	5.4	**5.13 (3.80-6.94)**
RA-no LD comparators	0.9	1.0 (Ref)
RA-ILD cases	5.6	**5.36 (3.88-7.40)**
RA-BR cases	5.0	**4.59 (2.93-7.01)**
Outcome: Intensive care unit		
RA-no LD comparators	12.9	1.0 (Ref)
RA-LD cases	41.5	**1.68 (1.53-1.84)**
RA-no LD comparators	12.9	1.0 (Ref)
RA-ILD cases	54.6	**1.99 (1.81-2.18)**
RA-BR cases	11.8	**0.62 (0.48-0.79)**

*RA-LD cases and RA-no LD comparators were matched by calendar date, age, sex, and RA duration at index date of RA-LD diagnosis.
**Adjusted for propensity score that included smoking status, pack-years, Frailty Index, Charlson Comorbidity Index score, serostatus, glucocorticoids, csDMARDs, bDMARDs, previous serious infection, previous hospitalization, and health care utilization.

Conclusion: RA-LD was associated with higher risks of overall hospitalization, respiratory hospitalization, and ICU admissions than RA-no LD comparators. RA-BR had a similarly elevated hospitalization risk as RA-ILD, illustrating an unreported unmet need in this population. These findings highlight the need for targeted strategies to prevent and manage acute care utilization in RA patients with lung involvement.

Disclosure: Q. ZHANG: None; **Y. Qi**: None; **X. Wang**: None; **G. McDermott**: None; **S. Chang**: None; **L. Getachew**: None; **M. Chaballa**: Bristol-Myers Squibb(BMS), 3, 11; **V. Khaychuk**: Bristol-Myers Squibb(BMS), 3, 11; **M. Paudel**: None; **K. Liao**: Merck, 2; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 0169

The High Disease Burden of Connective Tissue Disorder-Interstitial Lung Disease in the USA Demonstrates an Unmet Need for Earlier Diagnosis and Treatment

Sally Wetten[1], George Mu[2], Keele E. Wurst[3], Roger A. Levy[4], Ben Newth[5], Svetlana I. Nihtyanova[6] and Elaine Irving[7], [1]GSK, Epidemiology, Stevenage, United Kingdom, [2]GSK, Statistics, Collegeville, PA, [3]GSK, Immunology and Emerging Epidemiology, Durham, NC, [4]GSK, Specialty Care, Global Medical Affairs, Collegeville, PA, [5]GSK, Specialty Care, Global Medical Affairs, London, United Kingdom, [6]GSK, Clinical Sciences, Research & Development, London, United Kingdom, [7]GSK, Clinical, Stevenage, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a serious pulmonary manifestation that can occur across all connective tissue disorders (CTD). Aberrant immune-mediated inflammation and fibrosis leads to symptoms like dyspnea, cough, and respiratory failure, making ILD a major contributor to CTD morbidity and mortality. To better understand unmet therapeutic needs, characterization of real-world patient burden and treatment patterns is required. While epidemiologic studies have typically focused on single CTD populations, this study describes patient characteristics, comorbidities, and treatment utilization across a broad range of CTD-ILDs using a large electronic health record (EHR) database.

Methods: This retrospective cohort study (GSK Study 219992) used an Optum® de-identified EHR dataset of an incident cohort of patients with CTD-ILD diagnosed from 2018–2023. Published definitions and algorithms were used to identify CTD subtypes (RA, SSc, SLE, idiopathic inflammatory myopathies [IIM], MCTD, SS). Diagnoses of ILD after or within 365 days prior to CTD diagnosis were identified, with index being the first valid ILD diagnosis date within the study period. Baseline was 1 year prior to index. Patient follow-up was until death, discontinuation, or end of study period (Dec 31, 2023). Outcomes included baseline comorbidities and clinical characteristics, and treatment use.

Results: Baseline characteristics of eligible US patients with CTD-ILD by CTD subtype are shown in **Table 1**. ILD was diagnosed within ±1 year of CTD diagnosis in most patients (54–83%). Patients with RA and SLE were most likely to receive an ILD diagnosis >1 year after CTD (46% and 41%, respectively). Overlap with other CTD subtypes occurred in 11–38% of patients. The most frequently reported ILD symptom during the baseline period was dyspnea across all CTD subtypes (56–66%).

Around 25% of patients in each CTD subtype had ≥3 comorbidities (**Table 2**). There was a high burden from infections requiring hospitalization (29–45% by CTD subtype), of which ∼60% were due to acute respiratory infection.

Table 1. Patient and clinical characteristics at baseline. IQR, interquartile range.

		IIM ILD	MCTD ILD	RA ILD	SLE ILD	SSc ILD	SS ILD
	N	987	768	6455	1722	1863	1691
Age	Median age, (IQR)	59 (49–70)	59 (48–68)	69 (61–76)	60 (49–70)	62 (53–70)	67 (57–74)
Sex, n (%)	Female	667 (67.58)	637 (82.94)	4571 (70.81)	1515 (87.98)	1540 (82.66)	1459 (86.28)
	Missing	0	0	6 (0.09)	2 (0.12)	2 (0.11)	2 (0.12)
Race, n (%)	Asian	35 (3.55)	31 (4.04)	174 (2.70)	50 (2.90)	78 (4.19)	47 (2.78)
	African American	237 (24.01)	248 (32.29)	895 (13.87)	533 (30.95)	299 (16.05)	274 (16.20)
	Caucasian	646 (65.45)	431 (56.12)	5044 (78.14)	1026 (59.58)	1353 (72.62)	1269 (75.04)
	Missing	69 (6.99)	58 (7.55)	342 (5.30)	113 (6.56)	133 (7.14)	101 (5.97)
Ethnicity, n (%)	Hispanic	90 (9.12)	72 (9.38)	520 (8.06)	158 (9.18)	157 (8.43)	144 (8.52)
	Not Hispanic	847 (85.82)	651 (84.77)	5715 (88.54)	1492 (86.64)	1607 (86.26)	1461 (86.40)
	Missing	50 (5.07)	45 (5.86)	220 (3.41)	72 (4.18)	99 (5.31)	86 (5.09)
History of smoking, n (%)		197 (19.96)	132 (17.19)	1832 (28.38)	372 (21.60)	276 (14.81)	330 (19.52)
Timing of ILD diagnosis, n (%)	Prior to CTD	296 (29.99)	287 (37.37)	1045 (16.19)	346 (20.09)	413 (22.17)	512 (30.28)
	<1 year after CTD	449 (45.49)	352 (45.83)	2452 (37.99)	667 (38.73)	868 (46.59)	662 (39.15)
	1–3 years after CTD	183 (18.54)	97 (12.63)	1898 (29.40)	461 (26.77)	426 (22.87)	351 (20.76)
	3+ years after CTD	59 (5.98)	32 (4.17)	1060 (16.42)	248 (14.40)	156 (8.37)	166 (9.82)
ILD symptoms, n(%)	Dyspnea	367 (58.91)	283 (57.99)	2333 (56.61)	706 (56.12)	626 (65.55)	643 (58.67)
	Cough	41 (6.58)	28 (5.74)	343 (8.32)	71 (5.64)	60 (6.28)	85 (7.76)
	Chest pain	155 (24.88)	122 (25.00)	1087 (26.38)	354 (28.14)	194 (20.31)	278 (25.36)
	Fever	60 (9.63)	55 (11.27)	358 (8.69)	127 (10.10)	75 (7.85)	90 (8.21)
CTD overlap at ILD diagnosis, n (%)	Any other CTD	216 (21.88)	295 (38.41)	701 (10.86)	517 (30.02)	352 (18.89)	560 (33.12)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Selected comorbidities at ILD diagnosis. CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; GERD, gastro-esophageal reflux disease; MI, myocardial infarction.

	IIM ILD	MCTD ILD	RA ILD	SLE ILD	SSc ILD	SS ILD
N	987	768	6455	1722	1863	1691
Number of selected comorbidities, n (%)						
None	411 (41.64)	325 (42.32)	2247 (34.81)	589 (34.20)	860 (46.16)	559 (33.06)
1 or 2	337 (34.14)	256 (33.33)	2164 (33.52)	571 (33.16)	638 (34.25)	626 (37.02)
3 or more	239 (24.21)	187 (24.35)	2044 (31.67)	562 (32.64)	365 (19.59)	506 (29.92)
Selected comorbidities, n (%)						
GERD	449 (45.49)	399 (51.95)	3454 (53.51)	915 (53.14)	999 (53.62)	892 (52.75)
Hospitalization for infections	386 (39.11)	285 (37.11)	2815 (43.63)	772 (44.83)	533 (28.61)	718 (42.46)
Acute respiratory infections	230 (23.30)	183 (23.83)	1759 (27.25)	466 (27.06)	293 (15.73)	412 (24.36)
COPD / asthma	160 (16.21)	131 (17.06)	1657 (25.67)	384 (22.30)	199 (10.68)	378 (22.35)
Diabetes	134 (13.58)	76 (9.90)	1084 (16.79)	201 (11.67)	113 (6.07)	201 (11.89)
Anxiety	133 (13.48)	100 (13.02)	1030 (15.96)	292 (16.96)	189 (10.14)	277 (16.38)
Peripheral vascular disease	119 (12.06)	118 (15.36)	829 (12.84)	282 (16.38)	362 (19.43)	230 (13.60)
Raynaud phenomenon	35 (3.55)	80 (10.42)	140 (2.17)	119 (6.91)	293 (15.73)	107 (6.33)
Nausea, vomiting, or diarrhea	106 (10.74)	84 (10.94)	719 (11.14)	240 (13.94)	144 (7.73)	201 (11.89)
CKD	89 (9.02)	69 (8.98)	686 (10.63)	235 (13.65)	124 (6.66)	156 (9.23)
Heart failure	68 (6.89)	58 (7.55)	643 (9.96)	174 (10.10)	134 (7.19)	125 (7.39)
Fatigue	52 (5.27)	43 (5.60)	320 (4.96)	87 (5.05)	68 (3.65)	102 (6.03)
Malignancies	51 (5.17)	26 (3.39)	465 (7.20)	104 (6.04)	62 (3.33)	128 (7.57)
Depression	49 (4.96)	34 (4.43)	373 (5.78)	89 (5.17)	68 (3.65)	108 (6.39)
Liver disease	49 (4.96)	31 (4.04)	232 (3.59)	58 (3.37)	58 (3.11)	68 (4.02)
Acute MI	28 (2.84)	16 (2.08)	98 (1.52)	35 (2.03)	16 (0.97)	16 (0.95)
Stroke	10 (1.01)	8 (1.04)	101 (1.56)	26 (1.51)	10 (0.54)	21 (1.24)
Pulmonary hypertension	8 (0.81)	12 (1.56)	38 (0.59)	24 (1.39)	47 (2.52)	15 (0.89)
Suicidality	<5	0	5 (0.08)	<5	0	0
Progressive multifocal leukoencephalopathy	0	0	0	0	0	0

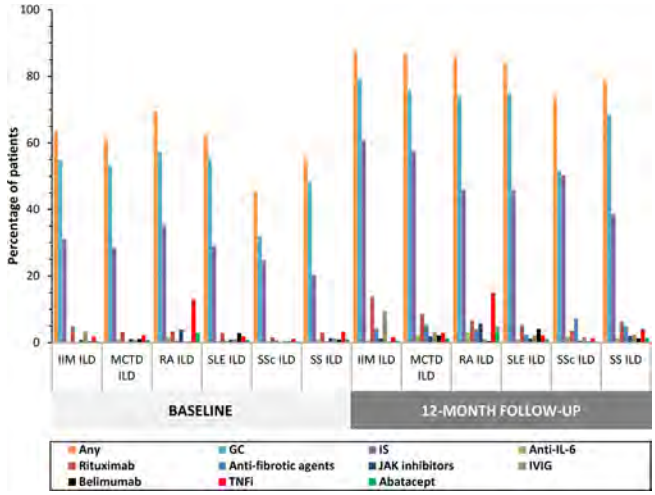


Figure. Treatment use by CTD-ILD type at baseline and 12 months. IS comprised cyclophosphamide, mycophenolate, azathioprine, methotrexate, calcineurin inhibitors, leflunomide; TNFi comprised etanercept, adalimumab, infliximab, golimumab, certolizumab pegol; anti-IL-6 comprised tocilizumab, sarilumab; anti-fibrotic agents comprised pirfenidone, nintedanib; JAK inhibitors comprised tofacitinib, baricitinib, upadacitinib. IVIG, intravenous immunoglobulin; JAK, Janus kinase; TNFi, tumor necrosis factor inhibitor.

At baseline, 31–55% of patients were not receiving any oral/IV glucocorticoids (GC), immunosuppressants (IS), or advanced therapies across CTD subtypes. GC and IS were the most common treatments across all CTD-ILDs at any time (**Figure**). There was an increase in therapy following ILD diagnosis, with the proportion of patients receiving any treatment increasing from 45–70% at baseline to 74–88% in the first year. Even at the peak of treatment use in the first year, 12–26% of patients did not receive any oral/IV GC, IS, or advanced therapies. A trend of decreasing proportions of patients receiving any treatment was observed after the first year.

Conclusion: Patients with CTD-ILD suffer considerable chronic comorbidities that often have overlap with other CTDs, leading to high disease burden on healthcare systems and complex clinical management. Symptom burden and infections requiring hospitalization were high, highlighting a need for earlier diagnosis and treatment initiation. The observation that treatment use tended to decrease after the first year suggests an unmet need for optimal therapeutic management remains.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Wetten: GSK, 3, 8, 11; **G. Mu**: GSK, 12, 3, 8; **K. Wurst**: GSK, 12, 3; **R. Levy**: GSK, 3, 8; **B. Newth**: GSK, 12, 3; **S. Nihtyanova**: GSK, 3, 8; **E. Irving**: GSK, 12, 3.

Abstract Number: 0170

Rheumatoid arthritis, serologic status and risk of heart failure: A national cohort study

Seonyoung Kang[1], Kyungdo Han[2], Yeonghee Eun[3], Jinhyung Jung[4], Seulkee Lee[1], Hoon-Suk Cha[1], Jaejoon Lee[5], Seonghye Kim[1], Se Yun Kim[6], Dong Wook Shin[1] and Hyungjin Kim[7], [1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [2]Soongsil University, Seoul, Republic of Korea, [3]Kangbuk Samsung Hospital, seoul, Republic of Korea, [4]Sungkyunkwan University School of Medicine, Suwon, Republic of Korea, [5]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [6]Sungkyunkwan University, Seoul, Republic of Korea, [7]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0145–0174) Epidemiology & Public Health Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Although rheumatoid arthritis (RA) is a known risk factor for heart failure (HF), a limited number of studies has explored the association based on HF subtype (ischemic and non-ischemic), RA serostatus, or use of biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs).

We aimed to evaluate the association between RA and subsequent risk of HF, focusing on ischemic and non-ischemic HF, as well as the role of RA serostatus (seropositive RA [SPRA] , seronegative RA[SNRA]) and the use of b/tsDMARDs.

Methods: This retrospective cohort study utilized nationwide population data from the National Health Insurance Service (NHIS) of Korea. The study analyzed 46,975 RA patients (33,424 SPRA, 13,551 SNRA) diagnosed in 2010–2017, along with 140,925 matched non-RA patients in a control group. Participants were followed from 1 year after RA diagnosis (to mitigate surveillance bias) until December 31, 2020. The primary outcome was newly diagnosed HF, classified as ischemic or non-ischemic.

Results: During follow-up, 615 new HF cases were identified (238 in the RA group, 377 in the control group). The RA patients had a higher risk of overall HF (adjusted hazard ratio (aHR) 1.97, 95% confidence interval (CI) 1.64-2.26), and risk was more prominent for ischemic HF (aHR 2.24, 95% CI 1.86-2.71) than non-ischemic HF (aHR 1.36, 95% CI 0.97-1.90). SPRA was associated with a higher risk than SNRA for overall HF (aHR 2.13, 95% CI 1.78-2.55 for SPRA and 1.59, 1.19-2.11 for SNRA compared to the control group) and non-ischemic HF (aHR 2.31, 95% CI 1.03-5.17 for SPRA and 0.71, 0.32-1.51 for SNRA) but not for ischemic HF (aHR 2.37 for SPRA and 1.94 for SNRA). Risk for HF was more prominent for bDMARD users than non-users for overall (aHR 3.16 vs. 1,89), ischemic (3.53 vs. 2.16), and non-ischemic HF (2.39 vs. 1.28). The effect of tsDMARDs could not be determined due to an insufficient number of HF events in these users.

Conclusion: This study demonstrates that RA was associated with both ischemic and non-ischemic HF, and that the association was stronger for ischemic HF. While the risk for ischemic HF was higher for both SPRA and SNRA, the risk for non-ischemic HF was higher only for SPRA and not for SNRA. bDMARDs do not seem to reduce but may instead increase the risk of HF.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Kang: None; **K. Han**: None; **Y. Eun**: None; **J. Jung**: None; **S. Lee**: None; **H. Cha**: None; **J. Lee**: Samsung Bioepis, 5; **S. Kim**: None; **S. Kim**: None; **D. Shin**: None; **H. Kim**: None.

Abstract Number: 0171

The Association Between Short-Term Trajectory Of Atmospheric Particulate Matter 10 (PM10) Concentration And Hyperuricemia

Sunggun Lee[1], Minyoung Her[1], Seong-HO Kim[1], Yong-Gil Kim[2] and Ji Seon Oh[2], [1]Department of Internal Medicine, Haeundae Paik Hospital, Inje University College of Medicine, Busan, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The association between high atmospheric particulate matter concentration and gout flare has been reported[1], but the causality and mechanism of this association remain unknown. We studied the association between trajectories of particulate matter concentration and hyperuricemia.

Methods: The seventh Korean National Health and Nutrition Examination Survey (2016–2018) linked air pollution concentration data was used. Trajectories of atmospheric particulate matter ≤10 μm (PM_{10}) concentrations from the day of serum uric acid measurement to 14 days prior (a total of 15 days) were clustered based on measures selected from principal component analysis. Hyperuricemia was defined as ≥7.0 mg/dL for men and ≥6.0 mg/dL for women. The association between the prevalence of hyperuricemia and quartiles of mean PM_{10} concentration or trajectories of PM_{10} concentration in the previous 15 days was modeled using generalized additive models, including age, sex, household income, obesity, chronic kidney disease, alcohol intake, mean temperature (spline), and mean relative humidity (spline). The associations were tested using weighted logistic regression models.

Results: The prevalence of hyperuricemia was 20.5% (95% confidence interval [CI], 19.2%–21.9%) in men and 6.1% (95% CI 5.5%–6.8%) in women. Mean PM_{10} concentration in the 15 days was 48.6 ng/mL (95% CI 47.4–49.9). There were three short-term trajectories of atmospheric PM_{10} concentrations: decreasing (N=4289, 32%), increasing (N=4724, 34%), and rapidly increasing (N=4688, 34%) (figure 1). There was no significant association between hyperuricemia and quartiles of mean PM10 concentration in prior 15 days; Q1: reference, Q2: odds ratio [OR] 0.81 (95% CI 0.69–0.96), Q3: OR 0.89 (95% CI 0.74–1.07), and Q4: OR 0.86 (95% CI 0.71–1.04). However, the short-term trajectory of PM10 levels was significantly associated with hyperuricemia. Compared with the decreasing trajectory, the increasing (OR 0.88 [95% CI 0.76–1.00], P = 0.056) and rapidly increasing (OR 0.85 [95% CI 0.74–0.97], P = 0.018) trajectories were negatively associated with hyperuricemia. When the association was analyzed using weighted generalized linear models, there was a similar trend for negative association between hyperuricemia and the rapidly increasing trajectory; decreasing trajectory: reference, increasing trajectory: OR 0.93 (95% CI 0.79–1.09, P-value 0.251), rapidly increasing trajectory: OR 0.89 (95% CI 0.75–1.07, P-value 0.081). In the receiver operating characteristic curve analysis, model discrimination was significantly better using the GAM model (Model 1 in figure 2, $P < 0.001$).

Conclusion: Compared with decreasing trajectory, rapidly increasing trajectory of atmospheric PM_{10} concentration was associated with lower prevalence of hyperuricemia. The results suggest that the mobilization of urate crystals may be the cause of gout flares associated with air pollution. This hypothesis must be validated through longitudinal studies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

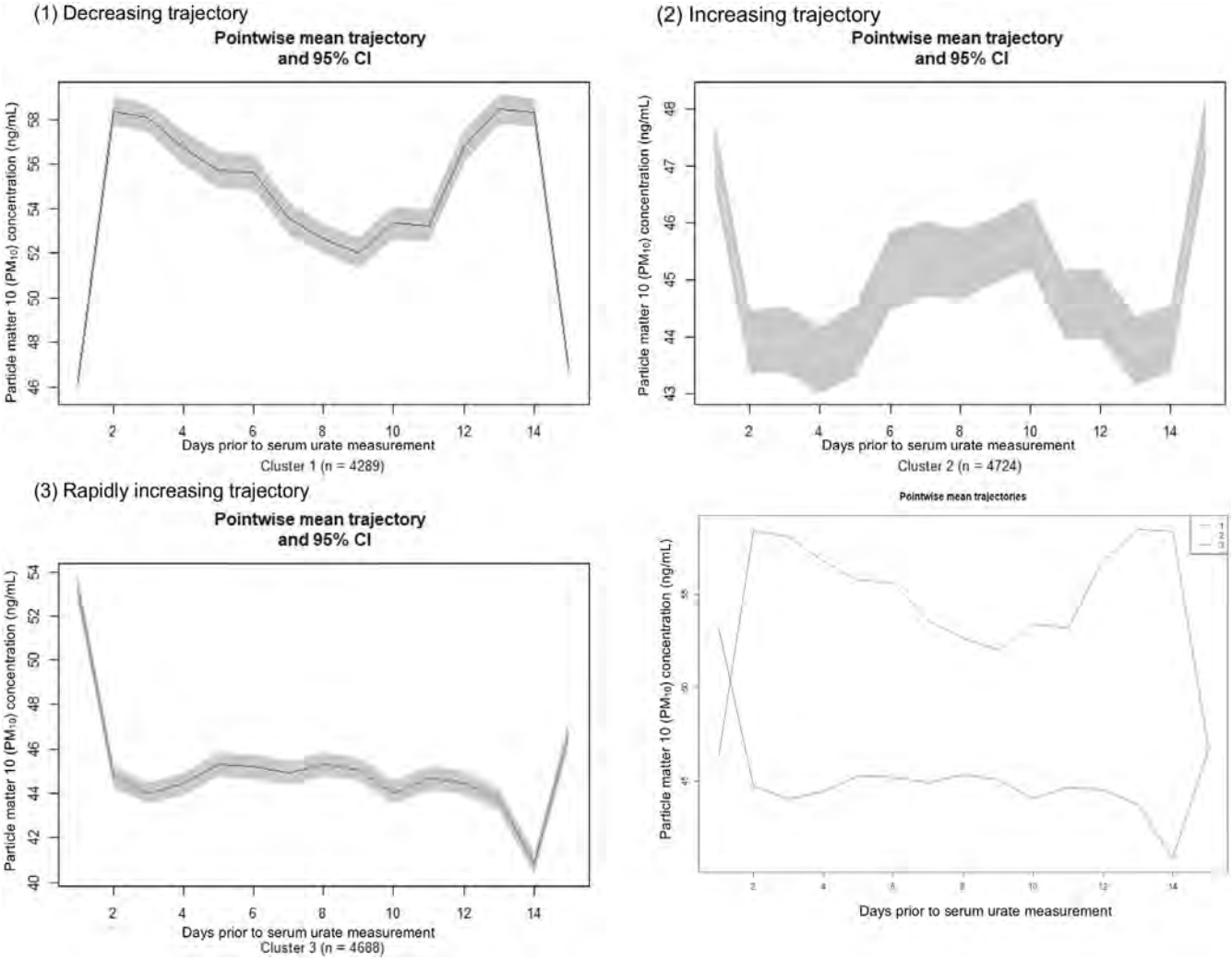


Figure 1. Pointwise mean trajectories and 95% confidence intervals of particulate matter 10 concentration from the day of serum uric acid measurement to 14 days prior (The day when blood samples were obtained is 1 on the X-axis)

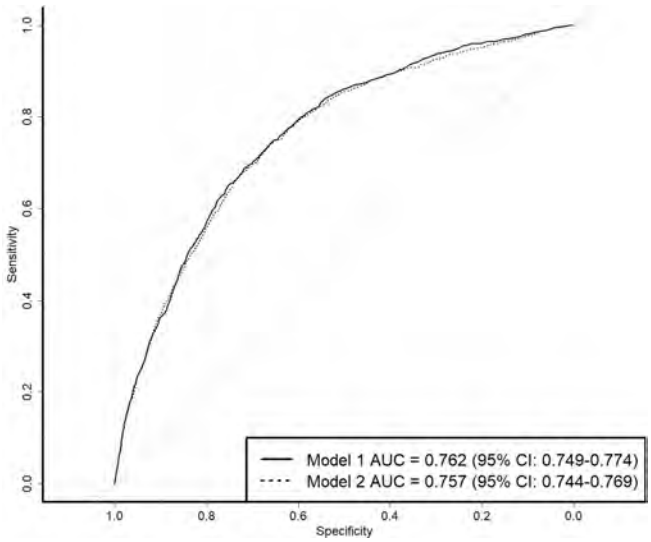


Figure 2. The receiver operating characteristic curve analysis of model discrimination by the generalized additive model (Model 1) and the logistic regression model (Model 2)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Reference

1. Ryu HJ, Seo MR, Choi HJ, Cho J, Baek HJ. Particulate matter (PM(10)) as a newly identified environmental risk factor for acute gout flares: A time-series study. Joint Bone Spine. 2021;88(2):105108.

Disclosure: S. Lee: None; **M. Her**: None; **S. Kim**: None; **Y. Kim**: None; **J. Oh**: None.

Abstract Number: 0172

Cancer Screening for Patients with Rheumatic Diseases: A Scoping Review

Teresa Xiao[1], Namrata Singh[2] and Pankti Reid[3], [1]University of Chicago, Chicago, IL, [2]University of Washington, Bellevue, WA, [3]University of Chicago Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: There is minimal guidance on specific cancer screening practices for rheumatic diseases (RDs) other than for myositis. The aim of this scoping review was to evaluate the available evidence on the risk of cancer for various RDs and associated risk factors.

Methods: We evaluated cancer associations and risk factors associated with incident cancer development for key systemic RDs: RA, SSc, and SS. We conducted a comprehensive literature search via PubMed to identify relevant publications with the following search terms: ''systemic sclerosis'' or ''Sjogren's disease'' or ''rheumatoid arthritis'' and ''cancer'' or ''malignancy'' or ''risk'' or ''risk factors.'' Data for cancer associations was limited to meta-analyses. Associated risk factors for incident cancer were obtained from meta-analyses and retrospective/prospective observational studies.

Results: We reviewed 19 manuscripts: 6 for cancer associations and 13 for risk factors. There were 3 meta-analyses for RA, 3 for SSc, and 1 for SS that reflected standardized incidence ratios (SIRs) for cancer. SS had 6 publications describing risk factors associated with cancer, followed by SSc (4) and RA (3). SSc was most commonly associated with liver cancer or lung cancer, RA with lymphoma and SS with hematologic malignancies, in particular non-Hodgkin's lymphoma (Table 1). Incident cancer risk for SSc was most commonly associated with anti-transcriptional intermediary factor 1 (TIF-1γ) positivity (Table 1).

Table 1. Cancer associations and risk factors for incident cancer in SSc, RA, and SS.

Rheumatic Disease	Cancer Associations	Risk factors for Incident Cancer	References
SSc	Liver cancer (SIR 4.36) Lung cancer (SIR range 3.14-3.18)	Anti-TIF-1-γ (OR 19.5) Anti-RNA polymerase III (OR 10.9) Anti-Scl-70 (OR 2.55) Anti-U1 RNP (OR 5.54) ILD (HR 2.85)	Onishi et al., 2013 Zhang et al., 2013 Sieiro Santos et al., 2022 Sakr et al., 2018 Hsu et al., 2021
RA	Lymphoma (SIR range 2.26-3.21)	RF and anti-CCP positivity (HR 6.29)* ILD (HR 3.25)*	Simon et al., 2015 Chatzidionysiou et al., 2022 Brooks et al., 2024
SS	Non-Hodgkin's lymphoma (SIR 13.71)	Low C3 levels (HR 36.65) Low C4 levels (HR 39.70) Lymphocytopenia (HR 16.47)	Zhang et al., 2022 Solans-Laque et al., 2011

*associated with lung cancer specifically
SSc = systemic sclerosis; RA = rheumatoid arthritis; SS = Sjogren's syndrome; Anti-TIF-1-γ = anti-transcriptional intermediary factor 1 gamma antibody; anti-Scl-70 = scleroderma antibody or anti-topoisomerase I antibody; Anti-U1 RNP = anti-U1 ribonucleoprotein antibody; ILD = interstitial lung disease; RF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide antibody

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

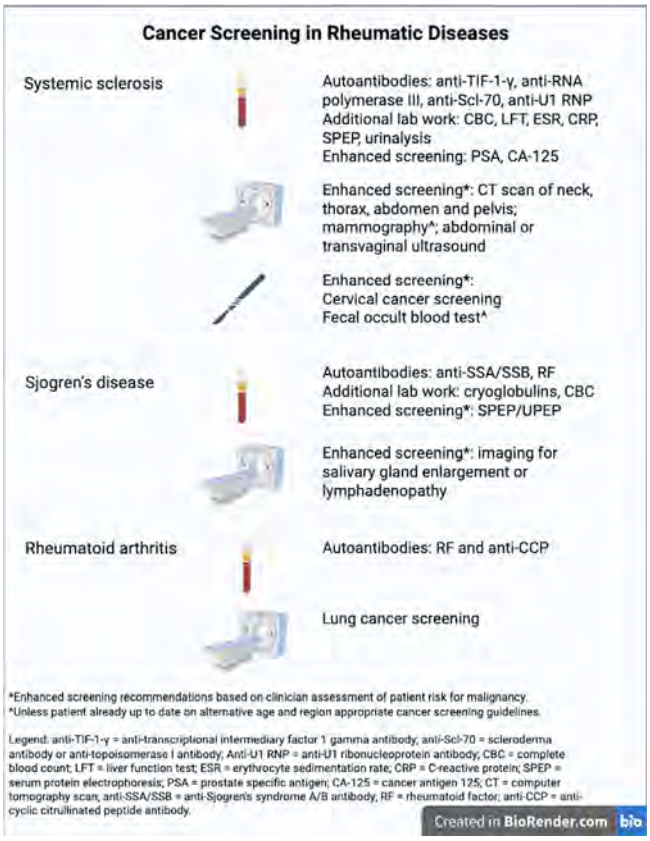


Figure 1. Cancer screening in rheumatic diseases.

RF and anti-CCP positivity were associated with lung cancer for patients with RA (Table 1). SS literature identified the highest cancer association with low complement levels and lymphocytopenia (Table 1). For RA and SSc, interstitial lung disease (ILD) was identified for both as a risk factor associated with malignancy.

Conclusion: RA, SSc, and SS are uniquely associated with different cancers. High-powered prospective studies to inform evidence-based, expert driven screening guidelines are needed to identify effectiveness of various cancer screening recommendations and guide appropriate clinical care.

Disclosure: T. Xiao: None; **N. Singh**: None; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1.

Abstract Number: 0173

Association Between the Ratio of Non-high-density Lipoprotein Cholesterol to High-density Lipoprotein Cholesterol and All-cause Mortality Risk in Patients with Rheumatoid Arthritis: A Survival Analysis Based on NHANES Data

Tingting Wang[1], Siying Xiong[1], Yuanli Wei[1], Dongmei Wang[1], Weihua Zhang[1], Caizhen Liu[2], Fanxin zeng[3] and Jianhong Wu[1], [1]Department of Rheumatology and Immunology, Dazhou Central Hospital, Dazhou, China (People's Republic), [2]Department of Rheumatology and Immunology, Dazhou Central Hospital, Dazhou, [3]Departmant of Clinical Research Center, Sichuan Clinical Research Center for Medical Imaging, Dazhou Central Hospital; Medical School, Sichuan University of Arts and Sciences; School of Basic Medical Science, Chengdu University of Traditional Chinese Medicine, Dazhou, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Table 1: Baseline Characteristics of the Study Participants

Characteristic	N	Overall N = 5,083	Q1 N = 1,290	Q2 N = 1,244	Q3 N = 1,284	Q4 N = 1,265	p-value
Age(years)	5,083	61.00 (51.00, 70.00)	65.00 (55.00, 74.00)	61.00 (52.00, 71.00)	60.00 (51.00, 69.00)	57.00 (47.00, 66.00)	<0.001
Gender,n(%)	5,083						<0.001
Male		2,165 (41%)	431 (31%)	481 (35%)	597 (46%)	656 (53%)	
Female		2,918 (59%)	859 (69%)	763 (65%)	687 (54%)	609 (47%)	
Race,n(%)	5,083						<0.001
Mexican American		554 (4.1%)	116 (3.4%)	138 (4.0%)	155 (4.6%)	145 (4.4%)	
Other Hispanic		482 (3.6%)	84 (2.3%)	111 (3.1%)	150 (4.4%)	137 (4.6%)	
Non-Hispanic White		2,827 (80%)	698 (79%)	676 (79%)	698 (80%)	755 (80%)	
Non-Hispanic Black		959 (8.4%)	325 (11%)	250 (9.0%)	227 (7.8%)	157 (5.5%)	
Other Race		261 (4.4%)	67 (3.8%)	69 (5.2%)	54 (3.0%)	71 (5.4%)	
Education,n(%)	5,083						<0.001
Less Than 9th Grade		630 (6.2%)	138 (6.1%)	157 (5.9%)	183 (6.9%)	152 (5.9%)	
9-11th Grade		767 (12%)	182 (10%)	181 (11%)	179 (11%)	225 (15%)	
High School Grad		1,225 (23%)	316 (23%)	256 (21%)	316 (24%)	337 (25%)	
Some College or AA degree		1,496 (33%)	350 (28%)	377 (34%)	386 (34%)	383 (35%)	
College Graduate or above		965 (26%)	304 (32%)	273 (29%)	220 (23%)	168 (19%)	
Marital Status,n(%)	5,083						0.026
Married		2,714 (60%)	613 (56%)	670 (60%)	712 (61%)	719 (62%)	
Widowed		818 (12%)	262 (16%)	211 (12%)	192 (12%)	153 (9.3%)	
Divorced		767 (13%)	193 (12%)	187 (14%)	199 (14%)	188 (14%)	
Separated		176 (2.5%)	53 (3.1%)	40 (2.3%)	42 (2.4%)	41 (2.2%)	
Never married		405 (7.6%)	121 (9.2%)	96 (7.3%)	89 (6.3%)	99 (7.6%)	
Living with partner		203 (3.9%)	48 (3.4%)	40 (3.9%)	50 (3.4%)	65 (5.1%)	
BMI(kg/m^2)	5,083	29.00 (25.50, 32.93)	26.80 (23.90, 30.80)	28.40 (25.00, 32.82)	29.52 (26.30, 33.70)	30.43 (27.40, 33.70)	<0.001
Total Cholesterol (mg/dL)	5,083	196.00 (168.00, 226.00)	175.00 (153.00, 200.00)	189.00 (162.00, 212.00)	198.00 (176.00, 224.00)	226.00 (196.00, 254.00)	<0.001
Smoking,n(%)	5,083						0.064
Yes		2,809 (56%)	672 (53%)	669 (54%)	700 (57%)	768 (59%)	
No		2,274 (44%)	618 (47%)	575 (46%)	584 (43%)	497 (41%)	
Drinking,n(%)	5,083						0.285
Yes		3,533 (76%)	890 (75%)	857 (75%)	874 (74%)	912 (78%)	
No		1,550 (24%)	400 (25%)	387 (25%)	410 (26%)	353 (22%)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

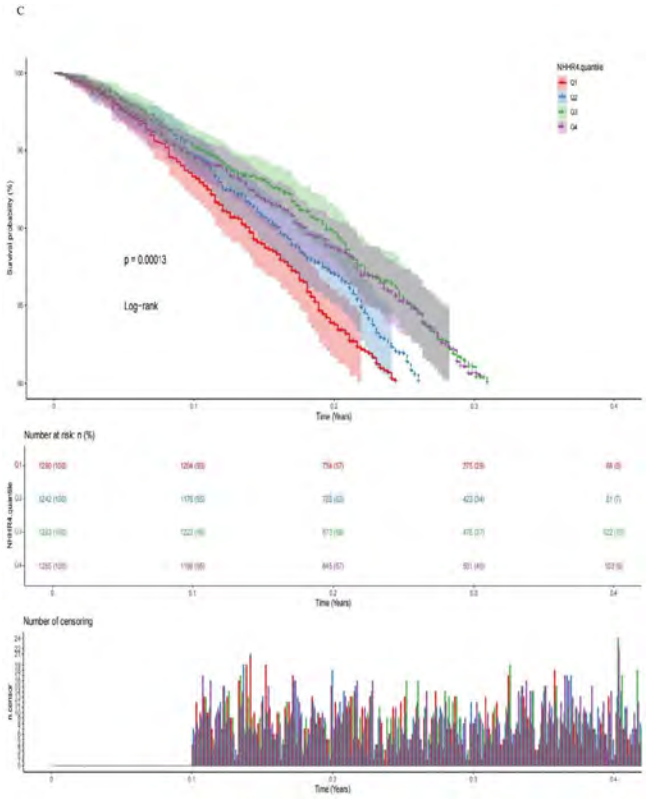


Figure 2 presents the survival analysis of RA patients. Panel A shows the survival area plot, illustrating the survival probabilities of RA patients over time. Panel B displays the survival contour plot, showing the survival probability at specific time points for RA patients. Panel C presents the survival curves by NHHR quartiles (Q1-Q4), highlighting the impact of different groups on survival probability. In Panel A, the color gradient (from red to blue) reflects changes in RA values over time. Higher RA values (red) are associated with higher survival probabilities, while lower RA values (blue) correspond to lower survival probabilities. In Panel B, S(t) represents the survival probability at various time points, ranging from 0 to 1. The color bar indicates different intervals of the survival function, with colors transitioning from purple to yellow, representing survival probabilities from low to high. Panel C features survival curves at the top: Q1 in red, Q2 in blue, Q3 in green, and Q4 in purple. The middle section shows the risk table, displaying the number of individuals at risk for each group (Q1, Q2, Q3, Q4) at each time point, with the remaining proportion for each group in parentheses. The bottom section represents censored events, with a histogram displaying the censoring status at different time points, color-coded by quartile group. Differences between survival curves across groups were tested using the Log-rank test.RA,Rheumatoid arthritis.

Background/Purpose: The Non-High-Density Lipoprotein Cholesterol to High-Density Lipoprotein Cholesterol Ratio (NHHR) has emerged as a promising marker for atherosclerosis, yet its relationship with all-cause mortality in individuals with rheumatoid arthritis (RA) remains poorly understood. This study aims to explore the association between NHHR and mortality in adults with RA.

Methods: Data from the National Health and Nutrition Examination Survey (NHANES) spanning 2007 to 2016 were analyzed, with participants stratified into quartiles based on their NHHR levels. Key covariates included age, gender, body mass index (BMI), C-reactive protein (CRP), and the presence of comorbidities. Subgroup analyses were conducted to assess how the association between NHHR and mortality risk varied across different age groups, sexes, and comorbidity profiles, with interaction effects tested using likelihood ratio tests. Multivariable Cox proportional hazards models were applied to estimate the relationship between NHHR and all-cause mortality risk. Kaplan-Meier survival curves were generated to visualize survival differences among NHHR quartiles, and restricted cubic spline models were employed to explore potential non-linear associations. Sensitivity analyses were also performed to evaluate the robustness of the findings by excluding extreme NHHR values.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

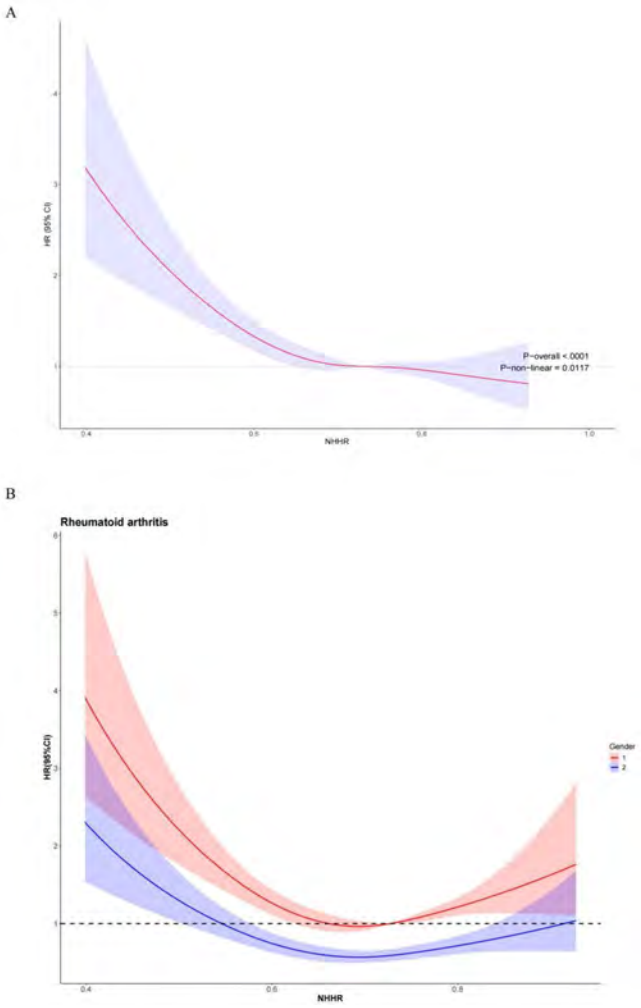


Figure 4 illustrates the relationship between NHHR and all-cause mortality in patients with rheumatoid arthritis using restricted cubic splines (A), with stratified analyses by gender (B), race (C), and education level (D). The analysis was adjusted for age, gender, race/ethnicity, marital status, education level, household poverty-to-income ratio, BMI, CRP, smoking, alcohol consumption, hypertension, diabetes, stroke, coronary heart disease, and cancer history. Solid and dashed lines represent the estimated values and their corresponding 95% confidence intervals, respectively. BMI: Body Mass Index; CRP:C-reactive protein,HR: Hazard Ratio. Gender group: 1 represents Male, 2 represents Female. Race group: 1 represents Mexican American, 2 represents Non-Hispanic Black, 3 represents Non-Hispanic White, 4 represents Other Hispanic, 5 represents Other Race. Education level group: 1 represents Less than 9th grade, 2 represents 9-11th grade, 3 represents High School, 4 represents Some college or AA degree, 5 represents College graduate or above.

Results: Significant variations in baseline characteristics were observed across NHHR quartiles, including differences in age, BMI, cholesterol levels, and comorbidities. Higher NHHR values were associated with increased BMI, total cholesterol, and CRP levels, while individuals in the lowest NHHR quartile showed a higher prevalence of hypertension, diabetes, and coronary heart disease (CHD). NHHR was inversely associated with CHD and showed a positive association with diabetes, though the latter lost significance after adjusting for covariates. A U-shaped relationship was identified between NHHR and all-cause mortality in RA patients, with a risk threshold around 0.575. Kaplan-Meier analysis indicated improved survival with increasing NHHR levels (Log-rank P=0.00013), particularly among older adults (HR = 0.18) and cancer survivors (HR = 0.18). The initial associations were attenuated after covariate adjustment, and sensitivity analyses confirmed the robustness of the findings (bias = −0.024).

Conclusion: NHHR has emerged as a valuable prognostic marker in RA, demonstrating a U-shaped relationship with all-cause mortality, with a critical threshold of 0.575. Its predictive capacity supports the early identification of high-risk individuals, enabling personalized interventions to enhance patient survival and optimize RA management strategies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Wang: None; **S. Xiong**: None; **Y. Wei**: None; **D. Wang**: None; **W. Zhang**: None; **C. Liu**: None; **F. zeng**: None; **J. Wu**: None.

Abstract Number: 0174

Genetic and Environmental Risk Factors and Incident Rheumatoid Arthritis

Xuesen Zhao[1], Puran Nepa[2], Hui Yu[3], Laura Daniel[2], Vivian Kawai[4], Michael Stein[5], Yan Guo[3] and Cecilia Chung[3], [1]University of Miami, Miami, FL, [2]University of Miami, Research Service, Miami VA Healthcare System, Miami, FL, [3]University of Miami, Miami, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0145–0174) Epidemiology & Public Health Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: While some studies have linked air pollution to risk for rheumatoid arthritis (RA), U.S.-based studies utilizing nationwide exposure data remain limited and often exclude the combined effect of genetic factors. Given the rising pollution level, it is essential to integrate environmental and genetic factors to better identify individuals at risk for RA and to inform prevention strategies.

Methods: This case-control study used data from NIH *All of Us v8* (AoU). We included participants with short read whole genome sequencing (srWGS) data. A case of RA was defined by three criteria: a) 3 or more encounters with RA-related ICD-9/10 codes, b) prescription of RA-specific medications, c) exclusion of patients with other concurrent autoimmune diseases. Incident RA cases required at least 1 year of electronic health record (EHR) preceding their earliest RA diagnosis. Control subjects did not meet any of the three criteria and had at least 1 year of EHR before their last recorded ICD codes. Cases and controls were 1:10 frequency-matched on age, sex, race, and the duration from the earliest to the latest recorded encounter. Genetic risk was quantified by a polygenic risk score (PRS) based on 92 RA-related genetic variants.

Table 1. Multivariate Cox Regression Analyses of Risk Factors for RA onset adjusted for demographics and smoking history

Variable	Unit	HR (95% CI)	P
PRS		1.25 (1.12, 1.40)	<0.001
Age	Year	1.00 (0.99, 1.01)	0.822
Sex: Male vs Female		1.05 (0.78, 1.42)	0.738
Race: White vs Black		2.10 (1.55, 2.83)	<0.001
Income: 100-150 vs <25	Thousands per year	0.35 (0.22, 0.56)	<0.001
Income: ≥150 vs <25	Thousands per year	0.35 (0.20, 0.60)	<0.001
Income: 25-50 vs <25	Thousands per Year	0.63 (0.45, 0.88)	0.007
Income: 50-100 vs <25	Thousands per Year	0.45 (0.32, 0.64)	<0.001
Education: Advanced Degree vs Less than High School		0.51 (0.26, 0.99)	0.048
Education: College Graduate vs Less than High School		0.64 (0.34, 1.20)	0.164
Education: High School vs Less than High School		0.79 (0.43, 1.43)	0.435
Education: Some College vs Less than High School		0.81 (0.45, 1.44)	0.469
Smoked 100 cigarettes: Yes vs No		1.19 (0.93, 1.51)	0.16
PM2.5 - Local Conditions	Micrograms/cubic meter (LC)	1.38 (1.30, 1.46)	<0.001
Sulfur dioxide	Parts per billion	1.10 (1.06, 1.15)	<0.001
Ozone	Parts per billion	1.10 (1.03, 1.17)	0.003
Lead (TSP) STP	Micrograms/cubic meter (25 C)	6.76 (2.00, 22.82)	0.002
Average Ambient Pressure	Millimeters (mercury)	1.00 (0.99, 1.01)	0.405
Nitrogen dioxide (NO2)	Parts per billion	0.93 (0.90, 0.96)	<0.001

*PRS: Polygenic Risk Score; TSP: Total Suspended Particles; STP: Standard Temperature Pressure; LC: Local Conditions; HR: Hazard Ratio; CI: Confidence Interval; P: P-value

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

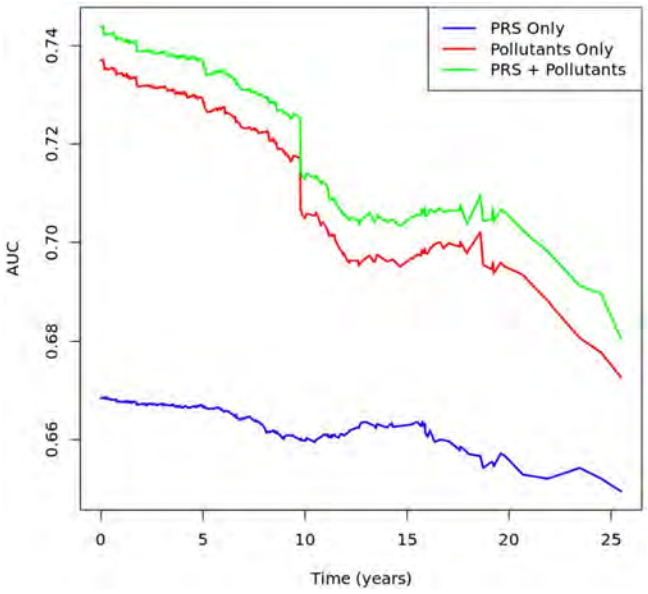


Figure 1. Time-Dependent AUC curves comparing the predictive performance of PRS-only, air pollutants-only, and the combined models for RA risk, adjusted for demographics and smoking history. All models exhibited a general decline in AUC over time. The combined model and air pollutants-only model showed notable decreases around years 10 and 20, whereas the PRS-only model maintained a relatively stable AUC throughout the follow-up period. *PRS: Polygenic Risk Score; AUC: Area Under Curve.

Environmental exposures were assessed using annual average air pollutant concentrations from Environmental Protection Agency AirData (1980–2024), aggregated at the 3-digit ZIP code level. Only exposure data preceding RA diagnosis for cases and prior to the last condition entry for controls were included. Variables selected by the LASSO and Elastic Net Cox models using 5-fold cross-validation were used to fit the final Cox model, adjusting for demographics and smoking history. Integrated Area Under the Curve (iAUC) was computed by the weighted average of time-dependent AUCs with 95% bootstrap confidence intervals (CI) in R v4.4.0.

Results: 283 cases of incident RA and 2,830 matched controls were included. PRS was significantly associated with increased risk of incident RA (HR = 1.25, CI: 1.12-1.40). Among air pollutants, lead showed the strongest association (HR = 6.76, CI: 2.00-22.82), followed by particulate matter ($PM_{2.5}$) (HR = 1.38, CI: 1.30-1.46), SO_2 (HR = 1.10, CI: 1.06-1.15) and ozone (HR = 1.1, CI: 1.03-1.17). Conversely, NO_2 exposure was associated with a reduced RA risk (HR = 0.93, CI: 0.90-0.96). Higher income levels and more advanced education were linked to reduced risk of RA incidence. Smoking history and ambient pressure showed no significant association. The combined model of PRS and air pollutants achieved the highest integrated AUC (iAUC = 0.72, CI: 0.70-0.76), outperforming models with PRS only (iAUC = 0.66, CI: 0.64-0.70).

Conclusion: Integrating PRS with air pollutants enhances the prediction of RA incidence. Notably, lead and $PM_{2.5}$ exhibited the strongest associations with increased risk for RA. These findings underscore the importance of combined genetic and environmental assessments in identifying individuals at elevated risk for RA.

Disclosure: X. Zhao: None; **P. Nepa**: None; **H. Yu**: None; **L. Daniel**: None; **V. Kawai**: None; **M. Stein**: None; **Y. Guo**: None; **C. Chung**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0175

Patient Satisfaction with a New Patient Video Triage Program

Adam Dore[1] and Yue Yin[2], [1]Allegheny Health Network, Pittsburgh, PA, [2]Allegheny Health Network, Pittsburgh

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: To assist with lowering new rheumatology patient appointment wait times, our division initiated a New Patient Video Triage Program in 2023. In this program, we found the average wait time for a new video triage appointment was less than half of an in-person new patient appointment. However, it was not understood if patients had a positive experience with a new patient video triage visit. Given this, we initiated a patient questionnaire to better understand the patients' satisfaction of the new patient video triage visit.

Methods: Patients completing a video visit through our New Patient Video Triage Program between March, 2024 and February, 2025 were asked to complete a patient satisfaction questionnaire. The questionnaire (Table 1) included 7 questions and basic demographic information. The answers were received anonymously. Descriptive statistics were initially reported. Continuous variable was reported as mean and standard deviation, while categorical variables were reported as frequency and percentage. ANOVA or t-test were conducted to compare continuous variables between groups. Fisher's exact test was conducted to examine the association between categorical variables. To control the Type I error rate, Benjamini-Hochberg correction was used to adjust *p* values. All statistical analyses were conducted under alpha level .05 via SAS 9.4.

Results: 208 surveys were completed. Most of those responding were female (83%) and identified as white/Caucasian (95%). The majority were extremely satisfied with the overall experience of the appointment (81%), the timeliness of the appointment being scheduled (67%), the attentiveness shown towards the patients' concerns (89%), the amount of time spent with the provider (86%), and the outcome of the appointment (74%). Almost all who responded would recommend a similar new patient video visit to others (96%) and only 14% of patients had technology issues during the visit (Table 2).

Table 1: Patient Questionnaire

How satisfied are you with your overall experience with this appointment?
☐ Extremely Satisfied ☐ Satisfied ☐ Somewhat Satisfied ☐ Disappointed

How satisfied are you with the timeliness of your appointment being scheduled?
☐ Extremely Satisfied ☐ Satisfied ☐ Somewhat Satisfied ☐ Disappointed

How satisfied are you with the attentiveness shown towards your concerns?
☐ Extremely Satisfied ☐ Satisfied ☐ Somewhat Satisfied ☐ Disappointed

How satisfied are you with the amount of time you spent with the provider?
☐ Extremely Satisfied ☐ Satisfied ☐ Somewhat Satisfied ☐ Disappointed

How satisfied are you with the outcome of your appointment?
☐ Extremely Satisfied ☐ Satisfied ☐ Somewhat Satisfied ☐ Disappointed

Would you recommend a similar New patient video visit to other patients?
☐ Yes ☐ No

Did you experience any technology issues during your visit?
☐ Yes ☐ No

If willing to share, please provide the following:

Age

Sex

Race

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Descriptive Statistic Results

Variable	Mean(std)/frequency(percent)
Age	53.15(14.68)
Sex	
Female	171(83.41%)
Male	34(16.59%)
Race	
Black	8(4.85%)
White	157(95.15%)
Overall experience	
Disappointed	7(3.38%)
Somewhat satisfied	3(1.45%)
Satisfied	29(14.01%)
Extremely satisfied	168(81.16%)
Scheduling timeliness	
Disappointed	9(4.35%)
Somewhat satisfied	11(5.31%)
Satisfied	47(22.71%)
Extremely satisfied	140(67.63%)
Attentiveness towards patients' concerns	
Disappointed	5(2.42%)
Somewhat satisfied	1(0.48%)
Satisfied	17(8.21%)
Extremely satisfied	184(88.89%)
Provider time spent with patient	
Disappointed	2(0.97%)
Somewhat satisfied	3(1.45%)
Satisfied	23(11.11%)
Extremely satisfied	179(86.47%)
Outcome of appointment satisfaction	
Disappointed	8(3.85%)
Somewhat satisfied	8(3.85%)
Satisfied	39(18.75%)
Extremely satisfied	153(73.56%)
Recommendation of a similar appointment to others	
No	9(4.35%)
Yes	198(95.65%)
Any technology issue	
No	178(85.58%)
Yes	30(14.42%)

According to Table 3, except the timeliness of scheduling, all survey items were significantly associated with the patients' overall recommendation of a similar appointment to others (all $p = .0008$), indicating that patients who would not recommend the video visit to others were more likely to be disappointed in the other four aspects and patients who would

Table 3: Variable Comparison for Patients' Recommendation to Others

Variable	Recommend to others		P value
	No	Yes	
Age	53.50(16.95)	53.10(14.66)	1.0000
Sex			
Female	9(100%)	161(82.56%)	1.0000
Male	0(0%)	34(17.44%)	
Race			
Black	0(0%)	8(5.06%)	1.0000
White	6(100%)	150(94.94%)	
Overall experience			
Disappointed	5(55.56%)	2(1.02%)	.0008
Somewhat satisfied	2(22.22%)	1(0.51%)	
Satisfied	2(22.22%)	27(13.71%)	
Extremely satisfied	0(0%)	167(84.77%)	
Scheduling timeliness			
Disappointed	2(22.22%)	7(3.55%)	.0558
Somewhat satisfied	2(22.22%)	9(4.57%)	
Satisfied	2(22.22%)	45(22.84%)	
Extremely satisfied	3(33.33%)	136(69.04%)	
Attentiveness towards patients' concerns			
Disappointed	4(44.44%)	1(0.51%)	.0008
Somewhat satisfied	1(11.11%)	0(0%)	
Satisfied	4(44.44%)	13(6.60%)	
Extremely satisfied	0(0%)	183(92.89%)	
Provider time spent with patient			
Disappointed	1(11.11%)	1(0.51%)	.0008
Somewhat satisfied	3(33.33%)	0(0%)	
Satisfied	5(55.56%)	18(9.14%)	
Extremely satisfied	0(0%)	178(90.36%)	
Outcome of appointment satisfaction			
Disappointed	6(66.67%)	2(1.01%)	.0008
Somewhat satisfied	2(22.22%)	6(3.03%)	
Satisfied	1(11.11%)	38(19.19%)	
Extremely satisfied	0(0%)	152(76.77%)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

recommend the video visit to others were more likely to be satisfied in the other four areas. Experiencing a technological issue during the video visit was not significantly associated with the satisfaction of the appointment (all $p > .05$).

Conclusion: Our New Patient Video Triage Program previously showed success in lowering rheumatology new patient wait times. Reassuringly, in this study we have shown that most patients completing the new patient video triage visit and questionnaire were extremely satisfied with the visit and would recommend a similar appointment to others. Having technological issues during the appointment did not impact the patient's satisfaction and there was not one area that led to overall satisfaction or dissatisfaction. Given these findings, we plan to continue utilizing new patient video triage appointments.

Disclosure: A. Dore: AbbVie/Abbott, 2, 6, Janssen, 6, Novartis, 2, UCB, 6; **Y. Yin**: None.

Abstract Number: 0176

Development and Validation of an Accurate Patient Reported Outcome Measure-based Disease Activity Score to Enable Remote Monitoring in RA

Agnes Looijen[1], Paco Welsing[2], Sytske Anne Bergstra[3], Annette van der Helm-van Mil[3] and Pascal de Jong[4], [1]Erasmus MC, Rotterdam, Netherlands, [2]Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, Utrecht, Netherlands, [3]LUMC, Leiden, Netherlands, [4]Erasmus University Medical Center, Rotterdam, the Netherlands, Rotterdam, Netherlands

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: For RA patients, regular monitoring of disease activity is essential, but in-person assessments may not always be feasible due to the increasing pressure on our healthcare system. One solution might be the implementation of 'patient-reported outcome measures' (PROMs) to remotely monitor the disease activity. Previous research combining multiple PROMs showed moderate diagnostic accuracy ('Area Under the Receiver Operating Characteristic curve' (AUC-ROC) of 0.76) in detecting a disease flare. However, these individual PROMs may include items unrelated to disease activity, hindering optimal discrimination.

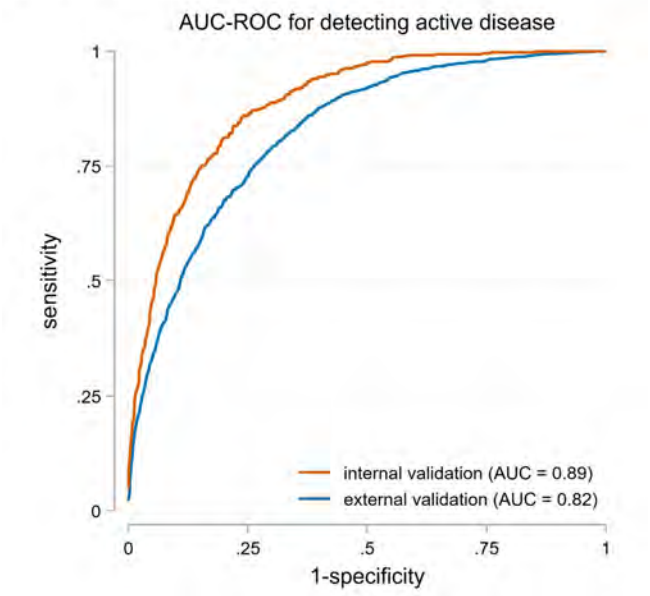
Therefore, our aim was to develop a model composed of a selection of independent PROM-items, that accurately represents the disease activity score in patients with RA.

Methods: Data from early and established RA patients in the 'treatment in the Rotterdam Early Arthritis Cohort' and 'TApering strategies in Rheumatoid Arthritis' trials were used and randomly split (1:1) into development and internal validation cohorts. For external validation data from RA patients in the 'Leiden Early Arthritis Clinic' were used. Patients were included if they met the 1987 or 2010 RA criteria and had at least one PROM-item and the DAS44 measured at the same time point.

With 'Least Absolute Shrinkage and Selection Operator' regression, a model was developed using age, sex, disease duration, and individual PROM-items (HAQ-items, pain (numeric rating scale (NRS) 0-10), general health (visual analogue (VAS) 0-100 millimeters (mm)), and fatigue (VAS 0-100mm)) to predict the DAS44. The final model was evaluated for its ability to detect active disease (DAS44 >2.4) using the AUC-ROC. Sensitivity and specificity where then assessed across thresholds based on: (I) the Youden index, (II) DAS44 >2.4, and thresholds for (III) 95% sensitivity and (IV) 95% specificity in the development cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Receiver operating characteristic curve for the internally and externally validated model which adequately reflects the disease activity score in patients with RA.



Abbreviations AUC, area under the curve; RA, rheumatoid arthritis

Table 1. Sensitivity and specificity for different thresholds of the model in the internal validation cohort

	Threshold[1]	Sensitivity	Specificity
Youden index	1.93	78	82
DAS44 threshold	2.40	52	94
95% sens[1]	1.40	97	53
95% spec[1]	2.43	49	94

[1]*Defined in the development cohort*
Abbreviations: DAS, disease activity index; Sens, sensitivity; Spec, specificity

Results: The development and internal validation cohorts included, 423 early and 187 established RA patients with 5802 visits; active disease was present in 20% of these visits. The external validation cohort included 793 patients with 2467 visits, and in 38% of those visits active disease was present. The final model included 12 of the 26 potential variables (age, sex, disease duration, 7 HAQ-items, NRS pain, and VAS general health) and showed an excellent discriminative ability (AUC-ROC=0.89 for internal validation, 0.82 for external validation) (**see figure 1)**. **Table 1** summarizes the sensitivity and specificity for the different thresholds. Using the Youden index (1.93), the sensitivity for detecting active disease is 78% and the specificity is 82%.

Conclusion: A combination of age, sex, disease duration, VAS general heath, NRS pain and seven HAQ-items is able to adequately differentiate between well-controlled and active disease with excellent diagnostic accuracy, even after validation in an external dataset. This could support remote monitoring of RA patients.

Disclosure: A. Looijen: None; **P. Welsing**: None; **S. Bergstra**: Benecke, 6, Pfizer, 5; **A. van der Helm-van Mil**: None; **P. de Jong**: AbbVie/Abbott, 1, 5, 6, Eli Lilly, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0177

Artificial Intelligence in Adult and Paediatric Rheumatology Practice and Research: Pilot Results from an International Survey

Ana Isabel Rebollo-Gimenez[1], Saverio La bella[2], Krystel Aouad[3], Latika Gupta[4], Davide Cangelosi[5], Thomas Hügle[6], Johannes Knitza[7], Nicolino Ruperto[8], Vincenzo Venerito[9], Abdellah El Maghraoui[10], Alessandra Alongi[11], Wilson bautista molano[12], Deniz Bayraktar[13], Thomas Davergne[14], Dzifa Dey[15], Ihsane Hmamouchi[16], Alison Hoens[17], Linda Li[17], Angela Migowa[18], Erin Treemarcki[19], Nelly Ziade[20], Tue Kragstrup[21] and Diego Benavent[22], [1]Department of Rheumatology, Gregorio Marañon University Hospital, Gregorio Marañon Health Research Institute, Madrid, Spain, [2]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [3]Department of Rheumatology, Saint George Hospital University Medical Center, Beirut, Lebanon, [4]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom, [5]Unità di Bioinformatica Clinica, Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [6]Department of Rheumatology, University Hospital Lausanne (CHUV) and University of Lausanne, Lausanne, Switzerland, [7]Institute for Digital Medicine, University Hospital Gießen-Marburg, Philipps University, Marburg, Germany, [8]Université Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy, [9]Univeristy of Bari \"Aldo Moro\", Italy, Bari, Bari, Italy, [10]Department of Rheumatology, Military Hospital Mohammed V, Rabat, Morocco, [11]Università Milano Bicocca, Milano, MILAN, Italy, [12]University Hospital Fundacion Santa Fe de Bogota, Bogota, Colombia, [13]Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Izmir Katip Celebi University. Arthritis Research Canada, Vancouver, British Columbia., Izmir, Turkey, [14]Department of rehabilitation.Team METHODS, CRESS UMR 1153 – University of Paris Cité, Paris, France, [15]Rheumatology Unit Department of Medicine and Therapeutics, Korle bu Teaching Hospital, University of Ghana Medical School, Accra, Ghana, [16]Health Sciences Research Center (CReSS).Faculty of Medicine, International University of Rabat, Rabat, Morocco, [17]Department of Physical Therapy, University of British Columbia, Vancouver, BC, Canada, [18]Aga Khan University Medical College East Africa, Nairobi, Kenya, [19]Department of Pediatrics, Division of Pediatric Rheumatology, University of Utah, Salt Lake City, UT, [20]Department of Rheumatology, Saint-Joseph University and Hotel-Dieu de France, Beirut, Lebanon, [21]Department of Biomedicine, Aarhus University & Rheumatology Sector, Medical Diagnostic Center, Silkeborg Regional Hospital, Silkeborg, Aarhus C, Denmark, [22]Hospital Universitari de Bellvitge, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Artificial intelligence (AI) is transforming rheumatology care, with innovative tools now empowering physicians and health professionals (HPRs). Our survey examines how adult and pediatric rheumatologists, and HPRs

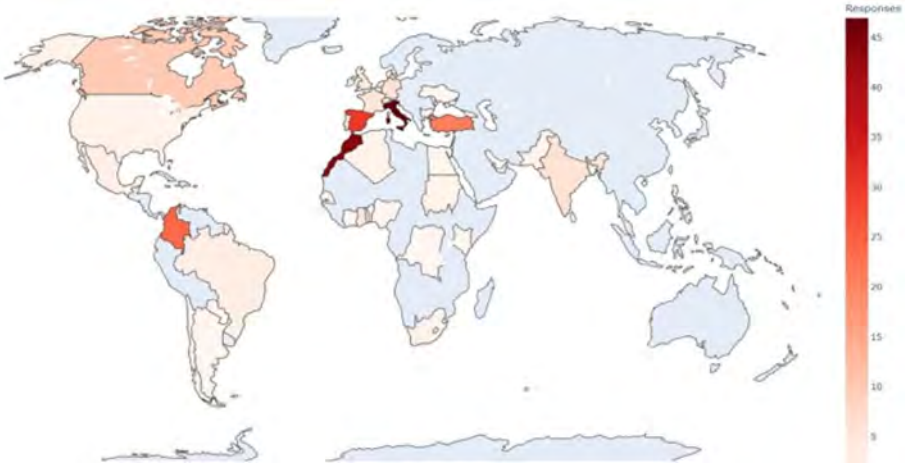


Figure 1 . Geographic distribution of survey respondents

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

currently perceive and utilize AI tools in rheumatology clinical and research environments, by identifying their experiences, concerns, and unmet needs.

Methods: An international, cross-continental online survey following CROSS & CHERRIES frameworks was shared in March 2025 to gather perspectives from the adult and paediatric rheumatology community. The questionnaire included 27 questions, both multiple-choice and open-ended, in four sections: sample characteristics, AI usage and applications, opinions and concerns, and expectations for AI implementation in clinical practice and research.

Results: By early May 2025, a total of 263 respondents (63.5% female) from 43 countries completed the survey, including rheumatologists, paediatric rheumatologists, and HPRs (figure 1). Median age of responders was 38 [IQR 32–48.5] years; only a minority of participants primarily worked in paediatric rheumatology (52, 19.8%), as HPRs (24, 9.1%), or mainly in research rather than clinical practice (54, 20.5%).

Most respondents (220, 83.7%) reported using large language models (LLMs) for medical purposes, commonly for text editing (176, 66.9%), brainstorming (137, 52.1%), summarizing papers (133, 50.6%), and manuscript writing assistance (115, 43.7%); only 30 (11.4%) respondents had never used LLMs. Attitudes towards AI were predominantly positive, with 204 (81.4%) expressing optimism regarding AI's efficacy and safety. However, up to 151 (58.1%) participants emphasized the need for strict AI regulation in medicine.

AI literacy was highly valued, with 214 (81.6%) rating it as very or extremely important, with 92 (35.5%) having or having had subscriptions to AI models/tools. Respondents favoured LLM use for practical tasks: email drafting (191, 72.9%), copy-editing (191, 74%), generating manuscript sections (136, 51.9%), and facilitating reference access (157, 59.9%). Substantial support existed for integrating AI into peer review, assisting reviewers (118, 45%) and editors (112, 42.7%). Respondents indicated AI's greatest future impact in research (212, 80.6%), diagnosis (183, 69.6%), and administrative tasks (177, 67.3%).

Key concerns included ethical issues (176, 67.2%), lack of trust in AI-generated decisions (181, 69.1%), and insufficient training (156, 59.5%). Respondents supported AI integration into rheumatology practice, with only 5 (1.9%) not recommending AI tools to colleagues.

Conclusion: Pilot results suggest the rheumatology community is recognizing AI's transformative potential whilst acknowledging the need for appropriate governance frameworks. AI tools are widely used and positively perceived by rheumatology and pediatric rheumatology professionals. However, concerns about ethics, trust, and training highlight the need for clear guidance and targeted education to support safe integration into clinical and research practice.

Disclosure: A. Rebollo-Gimenez: None; **S. La bella**: None; **K. Aouad**: None; **L. Gupta**: None; **D. Cangelosi**: None; **T. Hügle**: None; **J. Knitza**: GAIA, 2, Vila Health, 12, 2; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6; **V. Venerito**: None; **A. El Maghraoui**: None; **A. Alongi**: None; **W. bautista molano**: None; **D. Bayraktar**: None; **T. Davergne**: None; **D. Dey**: None; **I. Hmamouchi**: None; **A. Hoens**: None; **L. Li**: None; **A. Migowa**: None; **E. Treemarcki**: None; **N. Ziade**: None; **T. Kragstrup**: None; **D. Benavent**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 6, Savana, 7, UCB, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0178

Prevalence and factors associated with virtual rheumatology care utilization in a national population of Veterans with RA

Beth Wallace[1], Yuqing Gao[2], Shirley Cohen-Mekelburg[2] and Akbar Waljee[2], [1]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [2]VA Ann Arbor Healthcare Center, Ann Arbor

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Up to half of RA patients receive virtual rheumatology care, which is associated with high satisfaction but potentially lower quality. We aimed to identify factors associated with virtual RA care utilization in a real-world cohort seen at the Veterans' Health Administration, where telehealth services are established, well-integrated, and available across sites.

Methods: This retrospective cross-sectional study used national VA administrative claims to identify patients who a) met a validated claims-based definition of RA, b) had ≥1 rheumatologist visit for RA in 2022-2023 (study period). We compared demographics and treatment characteristics stratified by proportion of rheumatology care for RA received virtually (virtual proportion: 0, < 0.2, 0.2-0.5, 0.51-0.9, >0.9). To investigate factors associated with virtual proportion, we used zero-one inflated beta regression to account for the bounded nature of proportion data and excess zeros/ones. We estimated average marginal effects of age, sex, RA duration, log-transformed cumulative glucocorticoid (GC) dose and distance to rheumatologist's VA site, number of unique DMARDs, all-cause in-person office visits, MTX and biologic use. We performed a sensitivity analysis limited to those with ≥2 rheumatologist RA visits.

Results: We analyzed 11,703 patients, of whom 4964 (42.4%) had a virtual rheumatology visit, 3895 (33.2%) had virtual proportion >0.2, and 1661 (14.2%) had virtual proportion >0.5. As virtual proportion increased, age and distance to rheumatologist increased, and proportion of male patients, MTX, biologic, and GC use, number of DMARDs, and rheumatology and

Table 1: Population characteristics stratified by proportion of rheumatology care for RA received virtually

	Virtual Proportion					P for trend
	0	≤ 0.2	0.2-0.5	0.51-0.9	>0.9	
N (%)	6739 (57.5)	1069 (9.1)	2234 (19.1)	909 (7.8)	752 (6.4)	–
Age, mean (SD) years	65.9 (11.3)	66.2 (10.8)	65.1 (11.8)	65.1 (11.8)	66.8 (12.2)	0.0005
Male sex, N(%)	5306 (79)	845 (79)	1690 (76)	701 (77)	600 (80)	0.0193
Distance to rheumatologist, mean (SD) miles†	79 (74)	72 (69)	78 (72)	87 (71)	108 (83)	<0.0001
RA duration, mean (SD) years	7.1 (2.6)	7 (2.5)	7.1 (2.6)	7 (2.5)	7.2 (2.5)	0.2218
MTX use, N (%)	2586 (38)	495 (46)	878 (39)	443 (49)	253 (34)	<0.0001
Biologic use, N (%)	3601 (53)	713 (67)	1388 (62)	534 (59)	378 (50)	<0.0001
GC use, N (%)	2911 (43)	600 (56)	1023 (46)	435 (48)	265 (35)	<0.0001
Cumulative GC dose, mean (SD) mg prednisone equivalent	524 (1188)	818 (1500)	607 (1278)	644 (1258)	502 (1198)	<0.0001
Cumulative GC days' supply, mean (SD)	74 (171)	111 (197)	83 (177)	88 (179)	72 (166)	<0.0001
Unique DMARDs, mean (SD)	1.5 (1)	1.9 (1)	1.6 (1)	1.7 (1)	1.3 (1)	<0.0001
Rheumatologist visits*, mean (SD)	4.1 (2.2)	7 (2.3)	5.3 (2.8)	6.4 (3.3)	3.2 (2.7)	<0.0001
Total in-office visits, mean (SD)	24 (18)	31 (20)	24 (20)	22 (18)	15 (15)	<0.0001

†missing for 200 patients *in-person and virtual combined
GC: glucocorticoid

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Variables significantly associated with virtual care proportion in a zero-inflated beta regression

	Primary analysis		Sensitivity analysis	
	Average effect on proportion	95% CI	Average effect on proportion	95% CI
Age, per year	0.14	0.06 – 0.22	0.12	0.05 – 0.20
In-office visits, per visit	-0.55	-0.65 – -0.44	-0.42	-0.52 – -0.32
Driving distance, per log unit increase	4.2	3.3 – 5.1	3.8	3.0 – 4.6
DMARD use, per additional medication added	-2.3	-3.5 – -1.1	-1.4	-2.5 – -0.4

All variables assessed during 2022-2023

in-office visits decreased. However, distance to rheumatologist and MTX use did not differ significantly for virtual proportion 0.2-0.5 vs 0 (p=0.17, 0.43 respectively), and biologic use, GC days' supply, and GC dose did not differ significantly for virtual proportion >0.9 vs 0 (p=0.10, 0.72, 0.61 respectively).

The average change in virtual proportion per incremental increase in each predictor was examined (Table 2). Virtual proportion was associated with an average increase of 0.14 percentage points per year of age (95% CI 0.06-0.22), and 4.2 points per unit increase in log-transformed site distance (approximately 2.7-fold increase in miles, 95% CI 3.3-5.1). Virtual proportion was associated with an average decrease of 2.3 percentage points per additional unique DMARD (95% CI 3.5 to -1.1) and 0.55 points per additional all-cause in- office visits (95% CI: -0.65 to -0.44). Sex, GC dose, RA duration, and MTX and biologic use did not show significant associations. Our sensitivity analysis showed similar findings.

Conclusion: In a real-world cohort of RA patients with access to telehealth, virtual RA care was common and associated with older age, female sex, greater distance from rheumatology site, fewer in-office visits, and lower DMARD and GC use. Initial findings suggest trends may vary across levels of utilization. Limitations include those associated with claims data (e.g. confounding by indication) and cross-sectional design limiting causal inferences. Further work is needed to identify factors affecting virtual care utilization for RA and their impact on clinical outcomes.

Disclosure: B. Wallace: None; **Y. Gao**: None; **S. Cohen-Mekelburg**: None; **A. Waljee**: None.

Abstract Number: 0179

Digital Divide in Rheumatology: Patterns of Technology and AI Adoption Across Generations of Specialists

CARLA F DIONELLO[1], ANA F PADUA[2], Claudia Marques[3], BRUNA L PORTO[4], LEONARDO R CAMPOS[5], RODRIGO OLIVEIRA[6], GUSTAVO GM BALBI[7], RODRIGO LUPPINO-ASSAD[6], YURE G AZEVEDO[8], LUIZ F DIPE[9], BRUNO BORDALLO[5], Cleandro Pires[10], Licia Maria Henrique da Mota[10] and PAULA MONTINA[10], [1]FEDERAL UNIVERSITY OF RIO DE JANEIRO - UFRJ, RIO DE JANEIRO, Rio de Janeiro, Brazil, [2]SANTA CASA MG, BELO HORIZONTE, Minas Gerais, Brazil, [3]Hospital das Clinicas - Universidade Federal de Pernambuco - UFPE, Recife, Pernambuco, Brazil, [4]UNIVATES, SÃO LEOPOLDO, Rio Grande do Sul, Brazil, [5]UFF, Rio de Janeiro, Rio de Janeiro, Brazil, [6]FMRP-USP, Ribeirão Preto, Sao Paulo, Brazil, [7]UFJF, JUIZ DE FORA, Minas Gerais, Brazil, [8]SCR, SOBRAL, Ceara, Brazil, [9]GRUPO AMIL, SÃO PAULO, Sao Paulo, Brazil, [10]UNB, Brasilia, Distrito Federal, Brazil

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The integration of digital tools and artificial intelligence (AI) in rheumatology practice has advanced rapidly. However, disparities in adoption across generations of specialists remain underexplored. This study investigates patterns of digital technology and AI usage among Brazilian rheumatologists, stratified by years since medical graduation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A nationwide, self-administered, anonymous questionnaire was distributed to rheumatologists affiliated with the Brazilian Society of Rheumatology. The survey included 14 binary-use items related to electronic health records (EHR), AI-assisted tasks, telemedicine, cloud-based collaboration, and scheduling tools. Respondents were categorized into four groups based on time since graduation: 3–10, 10–20, 20–30, and >30 years. Descriptive statistics, Pearson's correlations, one-way ANOVA, chi-square tests, principal component analysis (PCA), and K-means clustering were performed.

Results: A total of 454 responses were analyzed. EHR usage demonstrated a significant negative correlation with years since graduation ($r = –0.33$, $p < 0.001$). Use of AI for text generation was also inversely correlated ($r = –0.17$, $p < 0.01$). ANOVA revealed significant variation across graduation strata in EHR usage ($p < 0.0001$), AI-assisted writing tools ($p < 0.001$), and cloud-based collaboration platforms ($p < 0.01$). Chi-square testing confirmed an association between experience level and AI writing tool adoption ($\chi^2 = 26.2$, $p < 0.0001$).

PCA explained 57.9% of the variance (PC1 = 34.9%, PC2 = 23.1%), and K-means clustering identified three distinct user profiles:

- **Cluster 0** (n=49): Low digital engagement, with 83.7% having >30 years since graduation.
- **Cluster 1** (n=96): High engagement across EHR and AI, predominantly 10–30 years since graduation (69.8%).
- **Cluster 2** (n=179): Intermediate engagement, with mixed generational representation (35.2% >30 years).

A regression model between EHR use and graduation time showed $R^2 = 0.11$ ($p < 0.001$), supporting a generational trend.

Conclusion: A digital divide exists in rheumatology, with more recent graduates demonstrating greater engagement with EHRs and AI tools. These findings highlight the importance of targeted training and support for senior rheumatologists to bridge gaps in digital literacy and optimize care delivery.

Disclosure: C. DIONELLO: None; **A. PADUA**: None; **C. Marques**: None; **B. PORTO**: None; **L. CAMPOS**: None; **R. OLIVEIRA**: None; **G. BALBI**: None; **R. LUPPINO-ASSAD**: None; **Y. AZEVEDO**: None; **L. DIPE**: None; **B. BORDALLO**: None; **C. Pires**: None; **L. Henrique da Mota**: None; **P. MONTINA**: None.

Abstract Number: 0180

Digital Transformation in IMID Care: Results from the Implementation of IMIDOC

JOSE INIESTA-CHAMORRO[1], Marta Novella-Navarro[2], Diego Benavent[3], HELENA BORREL-PAÑOS[4], Xabier Michelena Vegas[5], Javier Bachiller[6], Verónica García García[7], ESTHER ESPARTAL[4], LETICIA LOJO-OLIVEIRA[8], Enrique Calvo-Aranda[9], José Rodríguez gago[10], Gema Bonilla[11], Irene Monjo Henry[2], Victoria Navarro-Compan[12], Jaime Arroyo[10], Eugenio de Miguel[2], Mariana Díaz-Almirón[13], cARMEN ALEGRE[10], ENRIQUE J GÓMEZ[14] and **Chamaida Plasencia-Rodríguez**[2], [1]1Biomedical Engineering and Telemedicine Centre, ETSIT, Center for Biomedical Technology, Universidad Politéctica de Madrid, TELEMEDICINE, MADRID, [2]Hospital Universitario La Paz, Madrid, Spain, [3]Hospital Universitari de Bellvitge, Madrid, Spain, [4]4HOSPITAL UNIVERSITARIO VALL D´HEBRON, RHEUMATOLOGY, BARCELONA, Spain, BARCELONA, [5]Hospital Universitari Vall Hebron, Barcelona, Spain, [6]Hospital Ramon y Cajal, Madrid, Madrid, Spain, [7]Ramón y Cajal University Hospital, MADRID, Spain, [8]Hospital Universitario Infanta Leonor, Madrid, Spain, [9]Department of Rheumatology, Hospital Universitario Infanta Leonor / Universidad Complutense de Madrid, Madrid, Spain, madrid, [10]Hospital Universitario La Paz, MADRID, [11]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [12]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [13]LIMA, Advanced Medical Informatics Lab, La Paz Research Institute, IdiPAZ, Madrid, Spain, [14]1Biomedical Engineering and Telemedicine Centre, ETSIT, Center for Biomedical Technology, Universidad Politéctica de Madrid, TELEMEDICINE, MADRID, Spain, MADRID

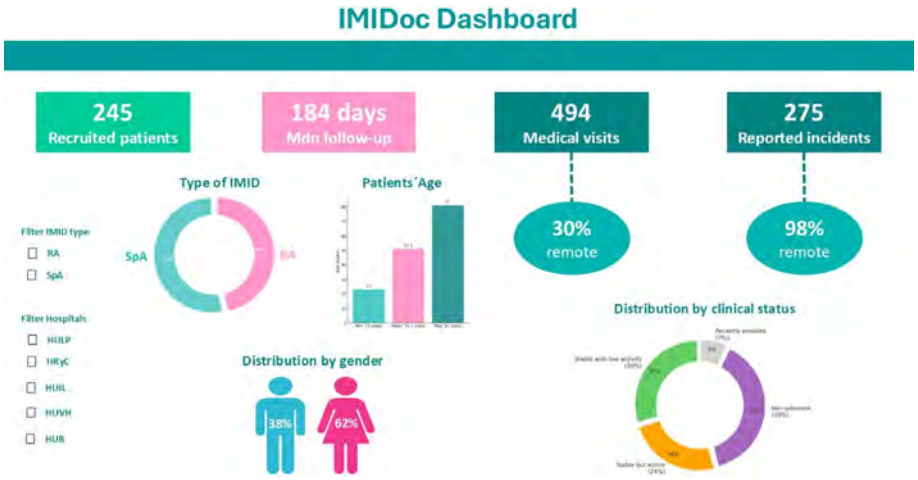
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) and spondyloarthritis (SpA) are immune-mediated inflammatory diseases (IMIDs) characterized by joint and spinal inflammation, leading to functional impairment. Their management requires close monitoring and effective communication between patients and healthcare providers. Digital health tools can help overcome current gaps in care by facilitating follow-up and interaction, especially within mixed care models that combine in-person and remote visits. Our aim was to evaluate the clinical implementation of a mixed care model using a digital tool called IMIDOC®, designed for both patients and healthcare professionals.

Methods: This prospective, multicenter study was conducted under the FIS PI22/00777 project. In its initial phase, IMIDOC was developed as a mobile app for patients and a web-based platform for clinicians. Patients can report health-related outcomes (PROs), clinical incidents, access educational content, and manage appointments and medication reminders. The clinician interface allows tracking of patient progress and timely intervention. In the clinical phase, 260 patients with RA or SpA receiving biological or targeted synthetic DMARDs (b/tsDMARDs) were scheduled for protocolized mixed follow-up for up to 12 months.

Results: Between April and October 2024, 245 patients were recruited (62% women; mean age 51.5 ±11.5 years; 47% RA, 53% SpA). The median follow-up time was 184 days (IQR 75–229). A total of 275 clinical incidents were reported (19% flares, 11% infections, 29% medication-related, 41% other), 98% of which were resolved remotely (77% via messaging, 23% via phone); only 2% required in-person visits. The median resolution time was 1 day (IQR 0–3). Among 494 medical visits, 29% were conducted remotely and 71% in person. A total of 15,011 PRO questionnaires were completed (6324 for RA, 8687 for SpA). In RA, the most frequent PROs were p-NAD (15%), p-NAT (14%), and p-VAS (14%); in SpA, p-NAD (11%), p-painful entheses (11%), and p-VAS (12%). Based on PRO-derived disease activity, 30% of patients were stable with low activity, 24% were stable but active, 39% were non-adherent, and 7% were recently enrolled. There were 609 consultations with educational materials, and at least 63% of patients accessed these resources, most commonly those related to joint self-assessment, the role of the rheumatologist, and early signs of disease. The app's usability was rated 81 on the System Usability Scale (SUS).



IMIDoc Dashboard

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The mixed care model supported by the IMIDOC tool represents a feasible and effective strategy for managing RA and SpA, combining digital and clinical components to enhance real-time monitoring, patient empowerment, and remote resolution of incidents

Disclosure: J. INIESTA-CHAMORRO: None; **M. Novella-Navarro**: None; **D. Benavent**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 6, Savana, 7, UCB, 2, 6; **H. BORREL-PAÑOS**: None; **X. Michelena Vegas**: None; **J. Bachiller**: None; **V. García García**: None; **E. ESPARTAL**: None; **L. LOJO-OLIVEIRA**: None; **E. Calvo-Aranda**: None; **J. Rodríguez gago**: None; **G. Bonilla**: None; **I. Monjo Henry**: None; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **J. Arroyo**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **M. Díaz-Almirón**: None; **c. ALEGRE**: None; **E. GÓMEZ**: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6.

Abstract Number: 0181

Launch of the National Tele-Rheumatology Program (NTRP) to Expand Rheumatology Care to Rural Veterans

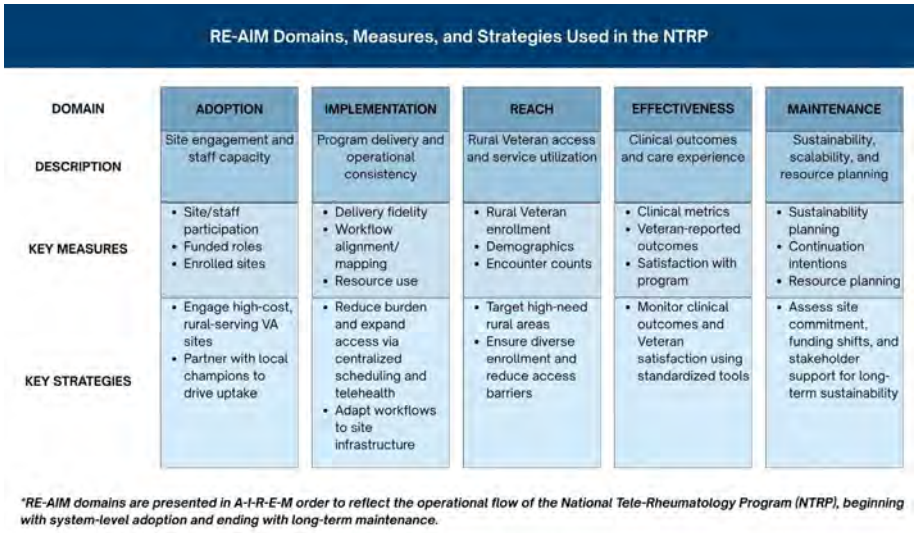
Cherish Wilson[1], Catherine Nasrallah[2], Gary Tarasovsky[3], Alicia Hamblin[4], Asia Williams[5], Broderick Flynn[5], Bernard Ng[6] and gabriela Schmajuk[7], [1]UCSF / SFVA, San Francisco, CA, [2]University of California San Francisco (UCSF), San Francisco, CA, [3]SFVA, San Francisco, [4]UCSF, San Francisco, CA, [5]Lexington VA, Lexington, [6]Lexington VA, University of Washington, Seattle, [7]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Given the nationwide shortage of rheumatologists, particularly in rural areas, many Veterans Affairs (VA) facilities have struggled to hire or retain specialists, resulting in greater reliance on non-VA (i.e., community-based) care. While non-VA care can expand access, it also increases costs for the VA and contributes to fragmented care for Veterans. To address these challenges, we launched the VA National Tele-Rheumatology Program (NTRP) in collaboration with the VA Office of Rural Health. In this study, we describe the implementation and early evaluation of the NTRP using the RE-AIM framework.

Methods: The NTRP is a centrally-managed and scalable telehealth model designed to deliver virtual rheumatology care across the country. The program launched in July 2024 with 3 clinical teams, each consisting of a rheumatologist and a Telehealth Clinical Technician with a shared nurse and pharmacist. The NTRP coordinates services and care delivery from a single site that triages and manages care for multiple outlying facilities. To recruit facilities into the program, NTRP leaders targeted sites with a high proportion of Veterans living in rural areas (according to Rural-Urban Commuting Area codes) and high expenditures on non-VA rheumatology care. Our initial evaluation used program records and data from the VA Corporate Data Warehouse to report on facility participation and characteristics (Adoption), Veteran enrollment and demographics (Reach), and non-VA care cost metrics (Implementation; **Figure 1**).

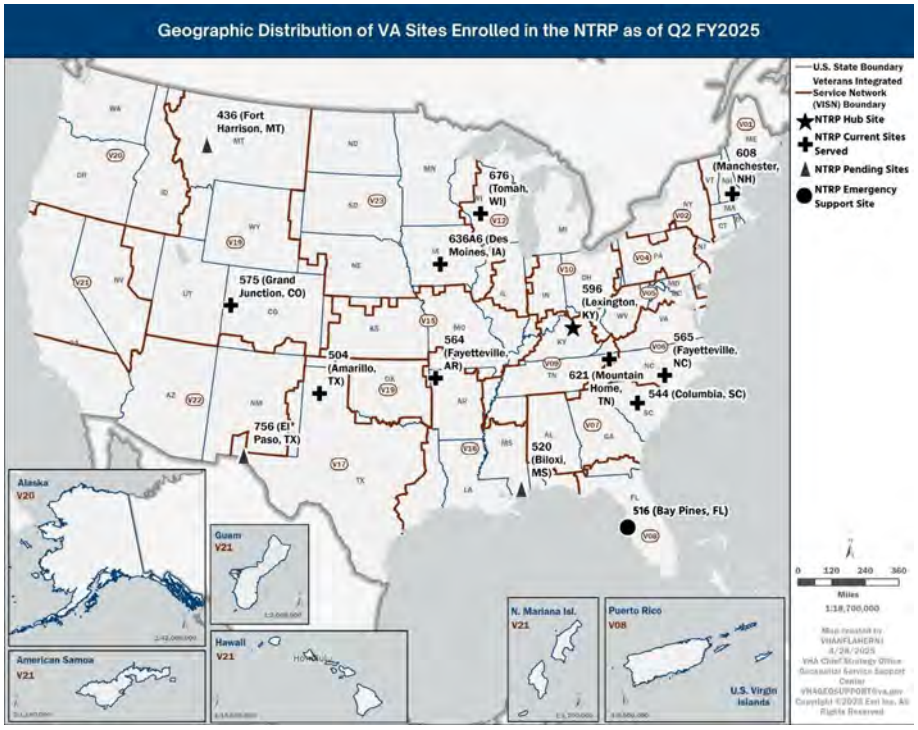
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



RE-AIM Domains, Measures, and Strategies Used in the NTRP

DOMAIN	ADOPTION	IMPLEMENTATION	REACH	EFFECTIVENESS	MAINTENANCE
DESCRIPTION	Site engagement and staff capacity	Program delivery and operational consistency	Rural Veteran access and service utilization	Clinical outcomes and care experience	Sustainability, scalability, and resource planning
KEY MEASURES	• Site/staff participation • Funded roles • Enrolled sites	• Delivery fidelity • Workflow alignment/ mapping • Resource use	• Rural Veteran enrollment • Demographics • Encounter counts	• Clinical metrics • Veteran-reported outcomes • Satisfaction with program	• Sustainability planning • Continuation intentions • Resource planning
KEY STRATEGIES	• Engage high-cost, rural-serving VA sites • Partner with local champions to drive uptake	• Reduce burden and expand access via centralized scheduling and telehealth • Adapt workflows to site infrastructure	• Target high-need rural areas • Ensure diverse enrollment and reduce access barriers	• Monitor clinical outcomes and Veteran satisfaction using standardized tools	• Assess site commitment, funding shifts, and stakeholder support for long-term sustainability

*RE-AIM domains are presented in A-I-R-E-M order to reflect the operational flow of the National Tele-Rheumatology Program (NTRP), beginning with system-level adoption and ending with long-term maintenance.

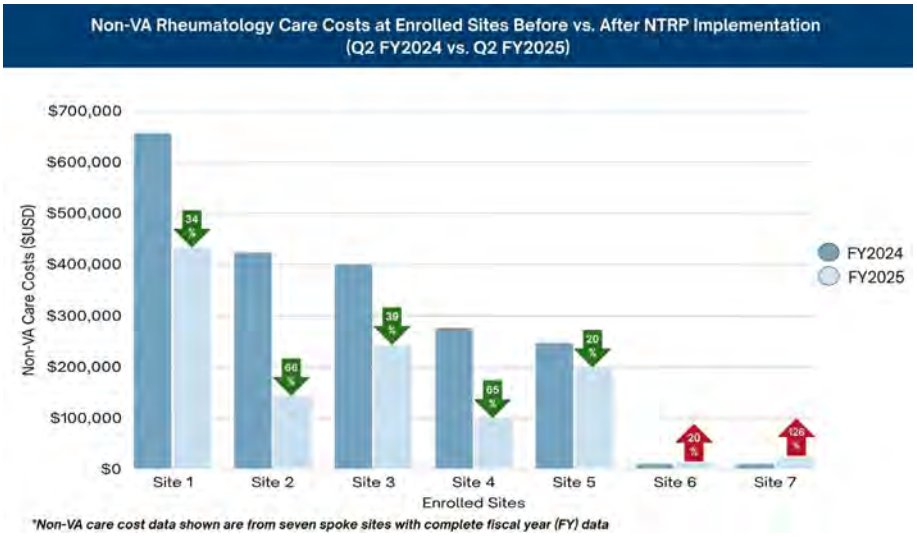


Geographic Distribution of VA Sites Enrolled in the NTRP as of Q2 FY2025

Results: Adoption: 13 facilities were recruited, most of which were located in the Southern U.S. (61.5%). Facility-level rurality ranged from 9.0% to 75.0% (**Figure 2**). Reach: 1,099 Veterans (83.2% male, 83.6% White, and mean (SD) age of 63.6 (15.1) years) received care through NTRP, 47.6% of whom lived in rural or very rural areas. Implementation: Among 7 enrolled sites with complete cost data, non-VA care expenditures for rheumatology care in Quarter 2 (Q2) of Fiscal Year (FY) 2024 averaged $289,361. These expenditures dropped by 43.2% in Q2 FY2025 (**Figure 3**).

Conclusion: In its first year, NTRP had significant adoption and reach across rural geographies. Early evaluation suggests that non-VA care expenditures rapidly decrease at participating facilities. Although we anticipate that the NTRP will lead to reduction in total costs for rheumatology care, additional evaluation is needed to determine whether savings in non-VA care

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



outweigh the costs of NTRP implementation and maintenance, and whether these cost reductions are sustained over time. Future work will also assess additional clinical and maintenance outcomes according to the RE-AIM framework.

Disclosure: C. Wilson: None; **C. Nasrallah**: None; **G. Tarasovsky**: None; **A. Hamblin**: None; **A. Williams**: None; **B. Flynn**: None; **B. Ng**: None; **g. Schmajuk**: None.

Abstract Number: 0182

A Joint Effort: Implementing Depression Screening in a Safety-net Rheumatology Clinic

Clare Grossman[1], Jay Chhabra[1], Ximena Gonzalez Sanchez[1], Karina Brito[1], Jacqueline Friskey[1], Brent Abel[2] and Mary Margaretten[2], [1]University of California San Francisco, San Francisco, CA, [2]Zuckerberg San Francisco General Hospital, UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Comorbid depression is common in patients with autoimmune diseases and is associated with increased healthcare utilization and death. Despite American College of Rheumatology recommendations for annual depression screening, it is often lacking in rheumatology practices, particularly in safety-net settings. We aimed to implement workflows for depression screening with appropriate mental health follow-up referrals in an urban, safety-net rheumatology clinic using the Institute for Healthcare Improvement's Model for Improvement.

Methods: This was a quality improvement project conducted by an interprofessional team of medical students, nurses, medical assistants (MAs), and a rheumatologist. Data were collected from workflow observations, stakeholder interviews, and Patient Health Questionnaire-9 (PHQ-9) forms, a validated tool to screen for depressive symptoms in multiple languages used by primary care at our institution. Patients literate in English, Spanish, or Chinese presenting to rheumatology clinics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

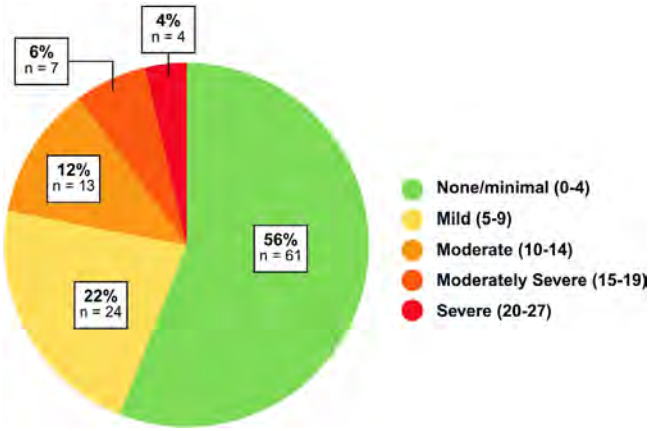


Figure 1. Severity of Depressive Symptoms Among 109 Patients Screened with PHQ-9

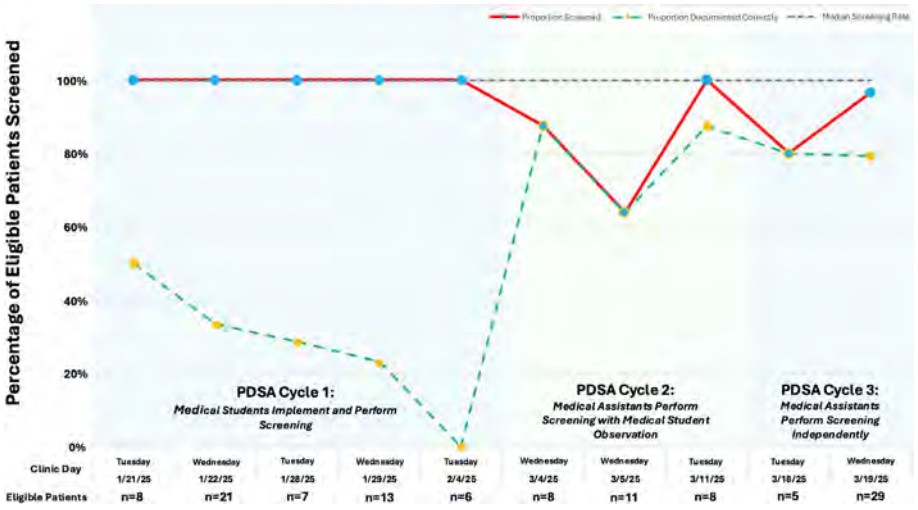


Figure 2. Rates of PHQ-9 Screening and Documentation After Workflow Implementation in a Safety-net Rheumatology Clinic Across Three PDSA Cycles (Jan - Mar 2025)

were eligible for screening, unless screened within the past 12 months. A standardized protocol for PHQ-9 collection, documentation, and follow-up was developed. PHQ-9 scores were documented in the electronic medical record (EMR) and a retrospective chart review was conducted to assess accuracy and completeness of documentation. Language concordant educational materials were created for patients who scored >4 on the PHQ-9. Referrals to behavioral health and primary care notification were made for scores ≥10; patients endorsing suicidal ideation were assessed for immediate safety needs and brought to psychiatric emergency services if needed. Implementation occurred over three plan-do-study-act (PDSA) cycles: first by students, then by MAs with student observation, and finally by MAs independently.

Results: We identified 117 patients eligible for screening. One patient declined screening and was excluded. Of the remaining 116 patients, 109 (94%) were screened for depressive symptoms and 48 (44%) screened positive (PHQ-9 >4), with 24 (22%) having PHQ-9 scores ≥ 10 that corresponded to moderate or severe symptoms (Fig. 1). Ten patients endorsed passive suicidal ideation and received timely safety assessments. All patients who screened positive were offered appropriate follow-up based on their PHQ-9 scores. Screening rates varied across PDSA cycles: 100% in the first, 82% in the second, and 94% in the third cycle. Correct documentation in the EMR went from 29% to 96% to 84% across the three cycles (Fig. 2). In qualitative follow-up interviews, clinic staff reported high acceptability of the new workflow and confidence in managing depression screening.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Screening for depressive symptoms in patients with rheumatic diseases and providing appropriate mental health follow-up in rheumatology clinics at a safety-net hospital is feasible. Although managing positive screens required staff training and interdepartmental coordination, clear protocols allowed for smooth implementation. Iterative workflow improvements can enable screening rates to remain high and improve documentation.

Disclosure: C. Grossman: None; **J. Chhabra**: None; **X. Gonzalez Sanchez**: None; **K. Brito**: None; **J. Friskey**: None; **B. Abel**: None; **M. Margaretten**: None.

Abstract Number: 0183

Optimizing the Clinical Application of Rheumatology Guidelines Using Large Language Models: A Retrieval-Augmented Generation Framework Integrating EULAR and ACR Recommendations

Alfredo Madrid[1], Diego Benavent[2], Chamaida Plasencia-Rodríguez[3], Zulema Rosales-Rosado[4], Beatriz Merino-Barbancho[5] and **DALIFER FREITES**[6], [1]Roche, Global Data Science and Analytics, Madrid, Spain., Madrid, Madrid, Spain, [2]Hospital Universitari de Bellvitge, Madrid, Spain, [3]Hospital Universitario La Paz, MADRID, Spain, [4]Grupo de Patología Musculoesquelética. Hospital Clínico San Carlos. Instituto de Investigación Sanitaria San Carlos (IdISSC), Madrid, Spain, Madrid, Madrid, Spain, [5]Escuela Técnica Superior de Ingenieros de Telecomunicación. Universidad Politécnica de Madrid. Avenida Complutense, Madrid, Spain, Madrid, Madrid, Spain, [6]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Timely access to current rheumatology guidelines at the point of care presents a significant challenge. Large Language Models (LLMs) offer potential solutions, but their propensity for "hallucinations" raises safety concerns. The primary objective of this study was to develop and evaluate a novel Retrieval-Augmented Generation (RAG) system, the first of its kind specifically for adult rheumatology, integrating European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) guidelines to provide clinicians with timely, evidence-based recommendations.

Methods: Seventy-four clinically relevant EULAR and ACR management guidelines for adult rheumatology were selected and processed. A RAG system was implemented using the LangChain framework, voyage-3 embedding model, and a Qdrant vector database, see **Figure 1**. For evaluation, 740 guideline-specific questions were generated. Answers were produced by an LLM (ChatGPT-o3-mini) with context retrieval (RAG) and without (baseline). Performance was assessed by an LLM-as-a-judge (Gemini 2.0 Flash) using a 5-point Likert scale across five dimensions (relevance, factual accuracy, safety, completeness, conciseness) and by determining preference. Wilcoxon signed-rank and Binomial tests were used for statistical analysis. Two blinded rheumatologists independently validated a random 15% sample of questions.

Results: The LLM-as-a-judge evaluation revealed that the RAG system significantly outperformed the baseline system across all criteria ($p < 0.001$). The RAG system was significantly preferred by the LLM-as-a-judge in 92.8% of comparisons ($p < 0.001$), **Table 1** Manual evaluation by rheumatologists confirmed these findings, with significant improvements in accuracy, safety, and completeness for the RAG system ($p < 0.001$), which was preferred in 71.2%-74.8% of comparisons ($p < 0.001$), **Table 2**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

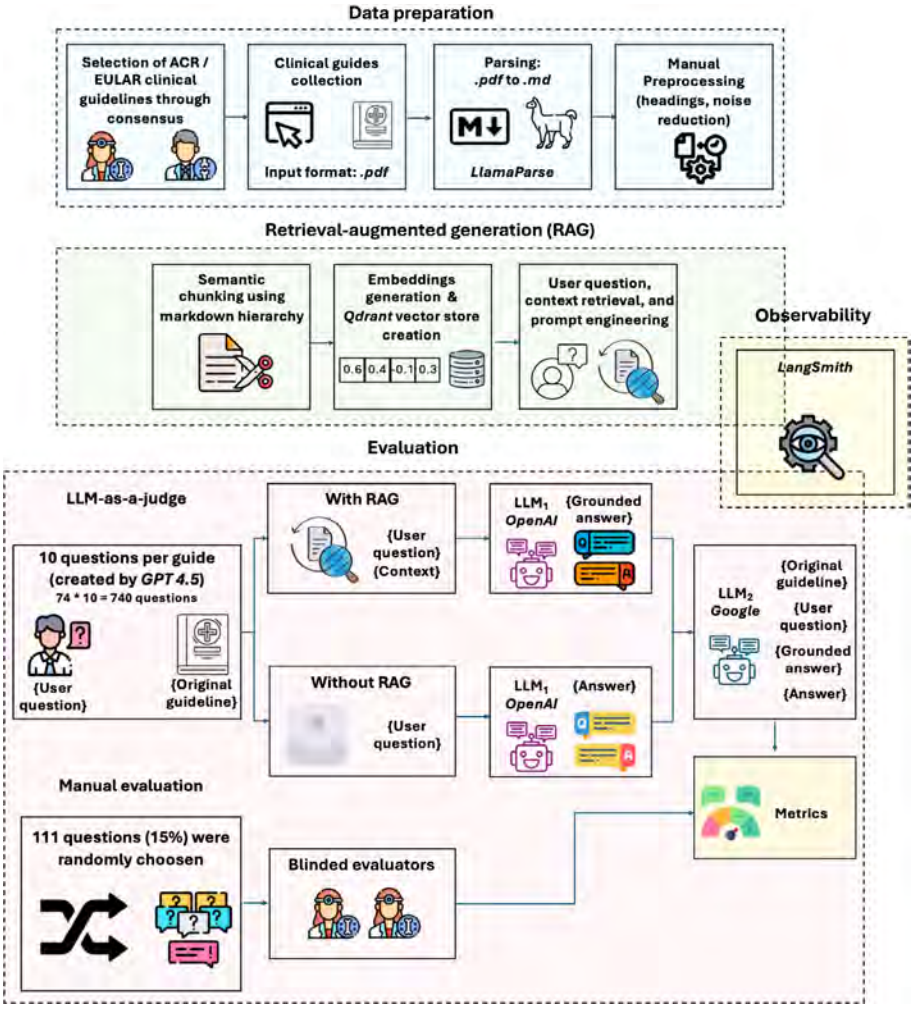


Figure 1: Walkthrough of the entire process—from initial creation to final evaluation—of the RAG architecture proposed

Conclusion: This study successfully developed and validated a RAG system integrating EULAR and ACR guidelines for adult rheumatology. The system significantly enhances the quality and reliability of LLM-generated answers, providing a robust foundation for AI-driven clinical decision support tools. Such tools have the potential to improve guideline adherence and evidence-based practice in rheumatology by offering clinicians rapid, context-aware access to recommendations.

Table 1: LLM-as-a-judge evaluation results.

Experiment: voyage-3 / Gemini 2.0 Flash / 7 sentences					
	A – Without RAG		B – With RAG		
Criteria	Median (Q1-Q3)	Mean (SD)	Median (Q1-Q3)	Mean (SD)	p-value
Relevance	5.0 (5.0-5.0)	4.8 ± 0.5	5.0 (5.0-5.0)	5.0 ± 0.3	2.01E-23
Factual Accuracy	5.0 (4.0-5.0)	4.4 ± 0.7	5.0 (5.0-5.0)	4.9 ± 0.3	1.68E-57
Safety	5.0 (4.0-5.0)	4.7 ± 0.6	5.0 (5.0-5.0)	5.0 ± 0.2	4.80E-41
Completeness	4.0 (4.0-4.0)	4.0 ± 0.7	4.0 (4.0-5.0)	4.3 ± 0.8	1.05E-25
Conciseness	5.0 (5.0-5.0)	4.8 ± 0.4	5.0 (5.0-5.0)	4.9 ± 0.3	7.52E-11
Preference	44 (7.2%)		570 (92.8%)		1.18E-117

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Manual evaluation results.

Evaluator 1					
	A – Without RAG		B – With RAG		
Criteria	Median (Q1-Q3)	Mean (SD)	Median (Q1-Q3)	Mean (SD)	p-value
Relevance	4.0 (3.0-5.0)	3.8 ± 1.2	4.0 (3.0-5.0)	3.8 ± 1.2	4.55E-02
Factual Accuracy	4.0 (3.0-4.0)	3.8 ± 1.1	5.0 (4.0-5.0)	4.4 ± 0.9	8.58E-08
Safety	5.0 (5.0-5.0)	4.7 ± 0.7	5.0 (5.0-5.0)	4.9 ± 0.4	6.45E-03
Completeness	4.0 (3.0-4.5)	4.0 ± 0.7	5.0 (4.0-5.0)	4.6 ± 0.6	2.30E-08
Conciseness	4.0 (4.0-5.0)	4.0 ± 0.8	4.0 (3.0-4.0)	3.5 ± 0.9	2.44E-06
Preference	28 (25.2%)		83 (74.8%)		1.68E-07
Evaluator 2					
	A – Without RAG		B – With RAG		
Criteria	Median (Q1-Q3)	Mean (SD)	Median (Q1-Q3)	Mean (SD)	p-value
Relevance	5.0 (5.0-5.0)	4.9 ± 0.3	5.0 (5.0-5.0)	5.0 ± 0.2	2.09E-02
Factual Accuracy	4.0 (4.0-5.0)	4.0 ± 0.8	5.0 (4.0-5.0)	4.5 ± 0.6	3.05E-09
Safety	5.0 (4.0-5.0)	4.7 ± 0.5	5.0 (5.0-5.0)	4.9 ± 0.3	1.01E-04
Completeness	4.0 (4.0-4.0)	4.0 ± 0.6	5.0 (4.0-5.0)	4.5 ± 0.6	4.08E-08
Conciseness	5.0 (4.0-5.0)	4.6 ± 0.5	4.0 (4.0-5.0)	4.5 ± 0.5	8.96E-02
Preference	21 (18.9%)		79 (71.2%)		4.34E-09

Disclosure: A. Madrid: Roche, 3; **D. Benavent**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 6, Savana, 7, UCB, 2, 6; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **Z. Rosales-Rosado**: None; **B. Merino-Barbancho**: None; **D. FREITES**: None.

Abstract Number: 0184

Neurocognitive Complications of Lupus: A Multidisciplinary Program Model for Advanced Diagnostics, Management, and Clinical Research

Douglas Wilcox[1], Matthew Baum[2], Sophie Lebiedz[2], John Sullivan[2], Margaret Naclerio[2], Jonathan Zurawski[2], Bonnie Glanz[2], Rohit Bakshi[2], Tanuja Chitnis[2], Shamik Bhattacharyya[3] and Karen H. Costenbader[4], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, Malden, MA, [4]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Neurological symptoms in lupus are common and occur in the majority of patients with SLE. Although neuropsychiatric lupus (NPSLE) can involve the entire nervous system, cognitive slowing and fatigue are more common and functionally limiting symptoms. There is currently no clear standardized, multidisciplinary approach to the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

evaluation and management of these patients. Further, there is an urgency to better understand the features and potential mechanisms of cognitive changes in patients with lupus to open new therapeutic avenues and standards of care.

Our objective was to create a multidisciplinary Neuro-Lupus Program to comprehensively assess patients through advanced second-tier diagnostics, manage patients through multidisciplinary collaborations, and to build a clinical research database to investigate cognitive concerns in patients with SLE.

Methods: Patients with a diagnosis of SLE and any neurocognitive symptoms or concerns can be referred to the Neuro-Lupus Program. Patients are initially evaluated by a dedicated lupus neurologist, where they undergo a standardized neurologic history and exam. This is followed by referral for a full neurocognitive evaluation by a clinical psychologist and evaluation by a trained expert autoimmune disease psychiatrist. Patients then undergo advanced brain imaging using a high-resolution 7T MRI scan to evaluate for subtle inflammatory changes, including leptomeningeal enhancement, cortical atrophy, and brain lesions. Patients with abnormalities on MRI are evaluated further with CSF studies through a dedicated lumbar puncture clinic. We additionally have access to refer appropriate lupus patients for FDG PET-CT brain, TSPO-PET CT brain, vascular imaging, and EEG. For the clinical research arm, following patient consent, matched serum and CSF samples are added to a biorepository for future studies investigating cognitive changes in NPSLE.

Results: At our center, we have recruited and evaluated 30 patients with lupus and neurocognitive concerns in a 6-month period (Table 1). Full neurocognitive evaluation revealed previously undiagnosed mild cognitive impairment and dysexecutive function in a significant portion (88%) of patients presenting with "fatigue" or "cognitive fog". Advanced imaging demonstrated previously undescribed leptomeningeal enhancement in 26% of patients with cognitive symptoms who underwent a 7T MRI brain scan. Despite the presence of significant cognitive changes and leptomeningeal enhancement, none of the CSF studies revealed an abnormally high white cell count or protein. Similarly, median neurofilament light chain (NfL) values, a serum biomarker for neuronal injury, was within the reference range.

Conclusion: In conclusion, our novel multidisciplinary Neuro-Lupus Program brings together neurologists, psychiatrists, rheumatologists, clinical psychologists, and radiologists to better support, evaluate, manage, and understand the complex but important cognitive impact of SLE on our patients. Future work will be aimed at leveraging our unique biobank and diagnostic studies to better understand the cellular and molecular pathways that may underly cognitive impairment in patients with lupus.

Table 1. Demographics and clinical characteristics of patients with SLE referred to the Neuro-Lupus Program

	Total number of patients (n=30)
Demographics	
Age, years (median [IQR])	41 [21.25]
Sex, n (%)	
Female	28 (93%)
Male	2 (7%)
Race and ethnicity, n (%)	
Black	6 (20%)
White	20 (67%)
Hispanic	5 (17%)
Clinical characteristics	
Presenting symptoms	
Cognitive fog	20 (67%)
Headache	14 (47%)
Fatigue	11 (37%)
Language difficulty	5 (17%)
Full neurocognitive testing, n (%)	8 (27%)
Abnormality on neurocognitive testing, n (% test)	7 (88%)
7T MRI performed, n (%)	19 (63%)
Leptomeningeal enhancement on MRI, n (% MRI)	5 (26%)
Lumbar puncture performed, n (%)	6 (20%)
CSF WBC, cells/uL (median [IQR])	1 [0.75]
CSF protein, mg/dL (median [IQR])	23.5 [9.975]
CSF glucose, mg/dL (median [IQR])	53 [0]
CSF oligoclonal bands (median [IQR])	0 [0]
Neurofilament light chain, pg/mL (median [IQR])	7.6 [8.125]

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: D. Wilcox: None; **M. Baum**: oxford university press, 9; **S. Lebiedz**: None; **J. Sullivan**: None; **M. Naclerio**: None; **J. Zurawski**: Bristol-Myers Squibb(BMS), 5, Elizabeth A. Kremer Research Foundation, 5, I-Mab Biopharmaceuticals, 5, NIH, 5, Novartis, 5; **B. Glanz**: None; **R. Bakshi**: Bristol-Myers Squibb(BMS), 5, EMD Serono, 5, 6, Novartis, 5, Sanofi, 1; **T. Chitnis**: Novartis, 2, Roche-Genentech, 1, 2, 5, Sanofi, 1, 5; **S. Bhattacharyya**: Alexion Pharmaceuticals, 1, 5, Amgen, 1, Roche, 5, UCB, 5; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 0185

Promoting Health Services Research Rigor and Reproducibility using CodeMapper: A novel tool for harmonization, collaboration, and precision

Emily Holladay[1], Nick McCormick[2], Robert Matthews[3], Shanette Daigle[4], Fenglong Xie[5], Tapan Mehta[1] and Jeffrey Curtis[6], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Auburn University, Auburn, AL, [3]Foundation for Advancing Science Technology Education and Research, Hoover, [4]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [5]The University of Alabama at Birmingham, Birmingham, AL, [6]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

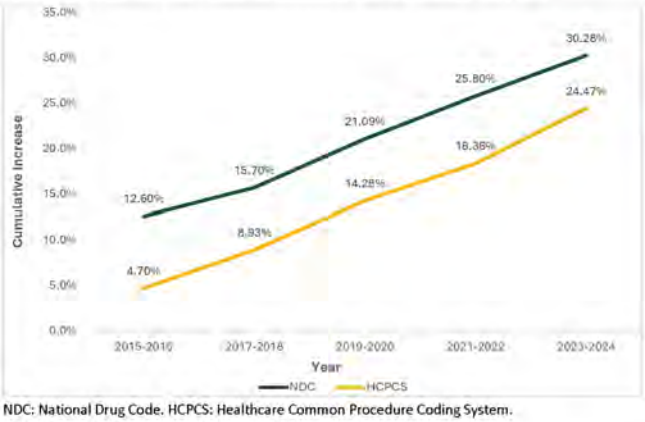
Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Medication, procedure, and diagnosis coding using structured data is fundamental to using real-world data to support clinical research, impacting cohort selection, patient recruitment, and outcome measurement. Source vocabulary systems (e.g. ICD-10-CM, HCPCS, RxNorm) are updated regularly, and incorporating these changes into existing code sets is essential yet challenging to manage, particularly in multidisciplinary settings. To address this need, we developed CodeMapper, an informatics tool designed to facilitate routine code updates and interdisciplinary collaboration. Our objective was to quantify medication, procedure, and diagnosis changes over time to assess the importance of maintaining updated code sets and provide a foundation for tool development.

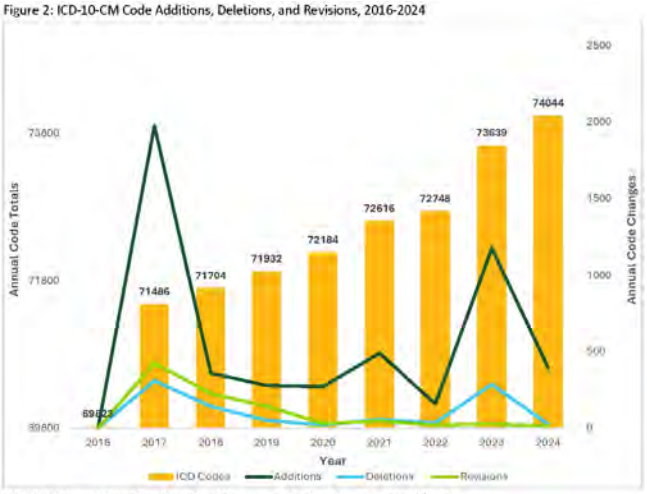
Figure 1: HCPCS and NDC Code Cumulative Increases by Two-Year Intervals, 2015-2024



NDC: National Drug Code. HCPCS: Healthcare Common Procedure Coding System.
Note: Percent increases do not include deleted or revised codes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: ICD-10-CM Code Additions, Deletions, and Revisions, 2016-2024



ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification.

Figure 3: CodeMapper Interface

Methods: We analyzed codes using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes from the National Center for Health Statistics and National Drug Codes (NDC) from First Data Bank (2015 to 2024). We also assessed Healthcare Common Procedure Coding System (HCPCS) codes from Centers for Medicare & Medicaid Services from inception through 2024. We summarized code changes over time and visualized trends using figures.

Results: Between 2015 to 2024, 2,911 new HCPCS codes were added. These additions accounted for approximately 25% of all HCPCS codes (Figure 1). Similarly, notable increases in the number of NDC codes occurred from 2016-2024 with a median (IQR) of 20510.0 (20424.0, 22275.0) NDC codes added per two-year period (Figure 1). Similar changes were also observed for ICD-10-CM codes with a median of 377.5 (276.0, 833.0) additions, 54.5 (30.0, 214.5) deletions, and 38.5 (24.0, 184.5) revisions occurring annually (Figure 2). Revisions describe the changes occurring in naming, coding granularity, and numbering.

Given these substantial changes over time in standardized coding systems, we developed CodeMapper, a new web-based informatics tool integrating current and historical diagnostic, procedural, medication, and laboratory codes. With semi-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

annual source vocabulary updates, this tool helps maintain the code sets described above and offers the ability for interdisciplinary teams to collaborate and refine code lists for use in current or future research (Figure 3).

Conclusion: Regular updates to medical coding systems are essential to support accurate research findings. The potential to under-ascertain codes within structured data is high, particularly in multi-year longitudinal studies where code sets may be fixed at the time of protocol development yet will under-capture medications, procedures, and diagnoses as they change over time. Maintenance and integration of current and complete source vocabularies are critical for rigorous and generalizable clinical research both for trials and real-world evidence using observational electronic health record or claims data.

Disclosure: E. Holladay: None; **N. McCormick**: None; **R. Matthews**: None; **S. Daigle**: None; **F. Xie**: None; **T. Mehta**: Heart Rhythm Clinical Research Solutions., 2; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 0186

Validation of Asynchronous Telehealth Visit for Adults and Children with Inflammatory Arthritis and Feasibility of Applying Thermal Imaging during Visits

Jenna Thomason[1], Rajdeep Pooni[2], Erin Sullivan[3], Adriel Liau[3], Sadie Van den Bogaerde[1], Iris Hamilton[3], Sriya Paluvayi[3], Megan Tran[4], Janeth Robles-Navarro[4], Ian Muse[5], Audrey Luey[4], Ava Klein[3], Debosmita Biswas[4], Savannah Partridge[4], Tzielan Lee[6], Alison Bays[1], Grant Hughes[7], Elizabeth Ferucci[8] and Yongdong (Dan) Zhao[9], [1]University of Washington, Seattle, WA, [2]Stanford University, Berkeley, CA, [3]Seattle Children's Hospital, Seattle, [4]University of Washington, Seattle, [5]University of Washington, Department of Pediatrics, Seattle Children's Hospital, Seattle, [6]Stanford University School of Medicine, Palo Alto, CA, [7]University of Washington, Lynnwood, WA, [8]Alaska Native Tribal Health Consortium, Anchorage, AK, [9]Seattle Children's Research Institute, Redmond, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Use of telemedicine has increased substantially. Our overall goal was to assess the utility of a standardized video joint exam and infrared thermal imaging as virtual tools to determine joint status during telemedicine visits.

Methods: Adults and children aged ≥4 and with an established diagnosis of inflammatory arthritis and suspected active inflammation in at least one knee, ankle/subtalar, elbow, or wrist joint were enrolled. A joint exam performed by the in-person clinician during routine visits was recorded as the gold standard of joint status. On the same day, participants completed a clinical research visit consisting of completion/obtainment of: 1. a questionnaire, 2. thermal images of hands, wrists, elbows, knees, ankles and feet, and 3. a standardized video joint exam. A follow-up research visit was conducted along with a clinical visit ≥3 months later. All the data collected except the clinical joint exam and assessment recorded by the in-person clinician was used to simulate "virtual visits" for "virtual" physicians to review. In order to determine the added value of each component of patient-generated data, the virtual physicians recorded their impression of the 72 joint exam and physician global assessment (PGA) sequentially: 1. after viewing the results of the patient questionnaire, primary rheumatologist's interval history, and lab results (if available), 2. after viewing the video joint exam, and 3. after viewing the thermal images and thermal imaging report. Interrater reliability statistics were calculated by cohort, joint, and review type (history only, history + video,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Characteristics

	Adults (N=100)	Children (N=101)
Patient demographics/disease characteristics		
Age (Median IQR)	56 (42 - 64)	13 (9 - 16)
Sex, Female (%)	73 (73)	77 (76)
Race/Ethnicity (%)		
American Indian/Alaska Native	5 (5)	1 (1)
Asian non-Hispanic	4 (4)	3 (3)
Black non-Hispanic	10 (10)	2 (2)
Hispanic	29 (29)	24 (24)
Native Hawaiian Pacific Islander	2 (2)	3 (3)
White non-Hispanic	46 (46)	54 (54)
Other	4 (4)	14 (14)
Length of Disease in years (Median IQR)	7 (2 - 11)	4 (1 - 8)
Height (cm) (Mean SD)	167 (10)	152 (20)
Weight (kg) (Mean SD)	80 (19)	52 (24)
Arthritis Category (%)		
Oligo persistent JIA	-	55 (54)
Extended oligo JIA	-	9 (9)
RF+ poly JIA	-	9 (9)
RF- poly JIA	-	16 (16)
ERA	-	2 (2)
Psoriatic JIA	-	7 (7)
Undifferentiated JIA	-	2 (2)
Systemic JIA	-	1 (1)
Rheumatoid arthritis	60 (60)	-
Psoriatic arthritis	16 (16)	-
Axial Spondyloarthritis	2 (2)	-
Other inflammatory arthritis	22 (22)	0 (0)
Comorbidities (%)		
Psoriasis	17 (17)	6 (6)
Crohn's or Ulcerative Colitis	4 (4)	2 (2)
Data collected from in-person physician		
Confirmed Active Arthritis (%)	78 (78)	84 (83)
Confirmed Arthritis status per patient: 1 or both joints (%)		
Knee	21 (21)	56 (55)
Ankle	21 (21)	24 (24)
Elbow	16 (16)	8 (8)
Wrist	31 (31)	24 (24)
Fingers	38 (38)	20 (20)
Toes	6 (6)	3 (3)
Total Joint Count (Median IQR)	2 (1-5) Range: 0 – 29	1 (1-3) Range: 0 - 57
Physician Global Assessment (Mean SD)	4 (2)	3 (2)
Data collected from patients		
Number of Patients with Self-Reported inflamed joints(%)	97 (97)	89 (88%)
Number of Self-reported inflamed joints (Median IQR)	12 (5 – 25)	2 (1 – 4)
RAPID3 (Mean SD)	13 (7)	-
RAPID3 (Weighted) (Mean SD)	4 (2)	-
Lab results		
Serologies (%)		
ANA Positive	16/62 (26)	58/90 (64)
RF Positive	47/87 (54)	21/90 (23)
CCP Positive	47/83 (57)	19/86 (22)
HLA-B27 Positive	5/22 (23)	6/85 (7)
CRP Category (%)	0.0 (0.0 - 0.23)	0.0 (0.0 - 0.0)
Greater than 1 mg/dL	12 (12)	7 (7)
Less than 1 mg/dL	27 (27)	53 (53)
Not done	61 (61)	41 (41)
ESR (mm/hr)	13 (6 – 23) (N=39)	12.5 (4.5 - 23.0) (N=60)

history + video + thermal), and include both baseline and follow-up assessments. Sensitivity and specificity were calculated by joint, cohort, review type, time (baseline and follow-up) and reviewer seniority.

Results: We enrolled 100 adults and 101 children (Table 1). At every virtual assessment (history only, history + video, and history + video + thermal report), there was a significant positive correlation between in-person and virtual physicians regarding the PGA. Regarding total active joint counts, there was a significantly positive correlation between in-person and virtual physicians at every assessment, except for when the adult virtual doctors were provided with history only (Table 2). Regarding the sensitivity and specificity for detecting inflammatory arthritis in the virtual setting, sensitivity was low and generally did not improve as more information was provided (13-83% for pediatric providers, and 0-58% for adult providers). However, specificity was high at nearly every time point assessed (57-97% for pediatric providers and 52-86% for adults). Agreement between the virtual physicians generally decreased as more information was added (Figure 1).

Table 2. Correlation of PGA and Joint Count by Virtual Physicians with In-person Physician by Seniority and Review Type

			Sr MD History Only	Jr MD History Only	Sr MD History + Video	Jr MD History + Video	Sr MD History + Video + Thermal	Jr MD History + Video + Thermal
Joint Count	Adult	PCC	0.129	0.127	0.305	0.188	0.372	0.208
		p-value	0.093	0.098	**<.0001**	**0.014**	**<.0001**	**0.006**
	Peds	PCC	0.726	0.702	0.489	0.634	0.283	0.448
		p-value	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**0.001**	**<.0001**
PGA	Adult	PCC	0.576	0.610	0.612	0.499	0.434	0.430
		p-value	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
	Peds	PCC	0.598	0.489	0.416	0.632	0.674	0.632
		p-value	**<.0001**	**<.0001**	**0.0002**	**<.0001**	**<.0001**	**<.0001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

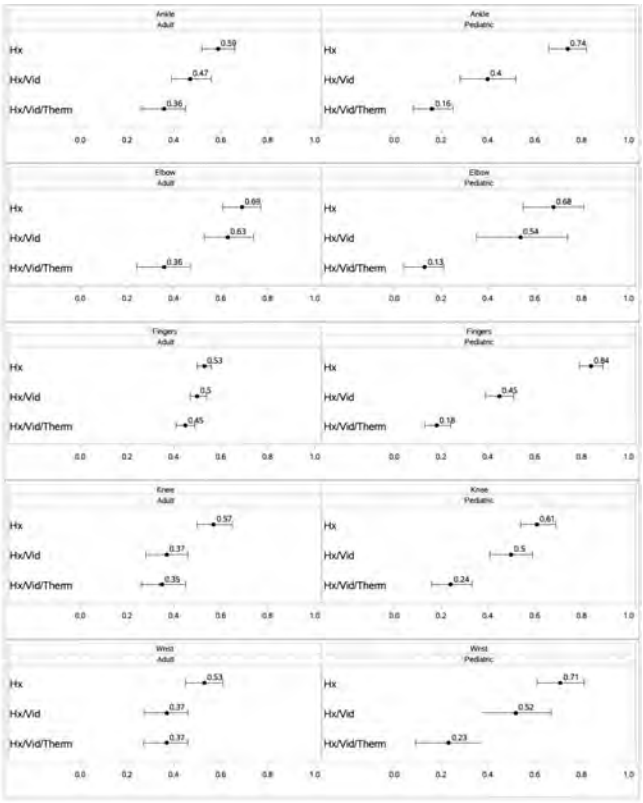


Figure 1. Kappa (95% CI) By Level of Information Among Adult and Pediatric Patients

Conclusion: Our study showed that history complemented with asynchronous video exam reviewed by rheumatologists led to moderately consistent assessment as in-person providers. Thermal imaging results did not yield additional benefit towards accurate joint assessment in the present study.

Disclosure: J. Thomason: None; **R. Pooni**: None; **E. Sullivan**: None; **A. Liau**: None; **S. Van den Bogaerde**: None; **I. Hamilton**: None; **S. Paluvayi**: None; **M. Tran**: None; **J. Robles-Navarro**: None; **I. Muse**: None; **A. Luey**: None; **A. Klein**: None; **D. Biswas**: None; **S. Partridge**: GE Healthcare, 5, Guerbet LLC, 5, Philips Healthcare, 5; **T. Lee**: None; **A. Bays**: None; **G. Hughes**: None; **E. Ferucci**: None; **Y. Zhao**: american board of pediatrics, 4, Bristol-Myers Squibb(BMS), 5, UpToDate, 9.

Abstract Number: 0187

Message Testing in Online Recruitment Advertisements for a National Rheumatoid and Psoriatic Arthritis Study

Matthew Kearney[1], Sarah Hopkins Gillespie[1], Stephanie Chen[1], Tyler Cavin[2], Christine Lindsay[3], Christopher Ritchlin[4], Jennifer Seifert[5], Susan Goodman[6], Jessica Fishman[1] and Alexis Ogdie[7], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Rochester, Rochester, NY, [3]Self, prosper, TX, [4]University of Rochester Medical Center, Canandaigua, NY, [5]University of Colorado and Oklahoma Medical Research Foundation, Aurora, CO, [6]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [7]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

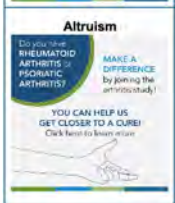
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Study recruitment procedures have increasingly included paid advertisements using social media. However, it is unclear which types of message framing will be the most effective for recruitment. The most common types of messages use an altruistic messages (contribute to the study out of a desire to help others) or simple informational message. **We aimed to** compare the effectiveness of two social media message frames - altruism and empowerment - versus attention-matched control in recruiting participants into the Accelerating Medicines Partnership Autoimmune and Immune-Mediated Diseases (AMP AIM) study, a multi-site study focused on rheumatoid arthritis, psoriatic arthritis, and psoriasis.

Methods: Between September 2024 and February 2025, we posted three Facebook advertisements to recruit study participants. Ads featured the question "Do you have RHEUMATOID ARTHRITIS or PSORIATIC ARTHRITIS?" and used one of three messages: 1) Altruism ("Make a difference by joining the arthritis study!"); 2) Empowerment ("Become a partner. Your voice matters!"); and 3) Attention-matched control ("Consider joining the arthritis study,"). Ads were linked to recruitment websites with matching messages. After pilot testing with altruism ads to focus the scope of impressions, all three ad sets were run concurrently. Facebook users randomly received one of the three ads, but not multiple. Outcomes included impressions (ad views), clicks, engagement (website visitors), and completed submissions. Regression modeling evaluated predictors of completed submissions and website visits. Analyses were conducted using StataSE (version 15).

Results: Over 39 total ad-days (pilot phase=18 days; final phase=21 days, 7 days/ad type), AMP AIM recruitment advertisements collectively generated 1,332,969 views and reached 617,206 unique Facebook users. Across both phases, 13 individuals submitted their information to learn more about the study through the AMP AIM website. Although altruism ads received 7 submissions, the most of any ad group, these submissions were all during the pilot phase. During the final phase when all three ads were run concurrently, all 6 submissions received were from individuals shown the attention-matched control ads – and zero from the altruism or empowerment ads. However, when compared to the attention-matched control ads and after controlling for study phase, regression modelling suggested that both the empowerment and altruism ads received significantly more Facebook impressions ($p < .001$), more ad clicks ($p < .001$), and more AMP AIM website visits ($p = .017$).

Conclusion: Message framing significantly affects attention, engagement, and recruitment. We learned that altruism and empowerment frames increased impressions and clicks but, ultimately, did not improve recruitment. All submissions during the final phase came from attention-matched control ads, suggesting simpler messages may better prompt action. In

Advertisement	Impressions (# of views)	Engagement (# of clicks)	Reach (# of sessions)	Contacts (# of submissions)
Attention-matched control	228,056	2,015	453	6
Altruism 	271,870	2,145	442	7 (only in pilot)
Empowerment	216,816	1,968	428	0

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

addition, traditional engagement metrics alone may not fully capture recruitment effectiveness. Additional research to compare these and other message frames among additional subpopulations could help to better inform effective strategies for recruitment.

Disclosure: M. Kearney: None; **S. Hopkins Gillespie**: None; **S. Chen**: None; **T. Cavin**: None; **C. Lindsay**: None; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **J. Seifert**: None; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2; **J. Fishman**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11.

Abstract Number: 0188

Investigating Canadians' information needs related to lupus: A Google Trends analysis of online search query data

Taylor Williamson[1], Emily Shantz[1], Susan Elliott[1], Christine Sperling[2], Karen H. Costenbader[3] and **May Choi**[4], [1]University of Waterloo, Waterloo, Canada, [2]None, Calgary, Canada, [3]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [4]University of Calgary, Calgary, AB, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: A lack of knowledge surrounding SLE has been identified as a main challenge for patients, particularly those seeking a diagnosis or recently diagnosed. Subsequently, many turn to online sources for information, where they risk encountering misleading or even endangering mis- or disinformation. Hence, we investigated the public awareness of SLE and how this varies spatially across Canada using health geographical approaches to examine Google Trends (GT) data, a tool for assessing public knowledge and information.

Methods: This research employs a health geographical approach to exploring spatial and temporal trends in information-seeking behaviours and associated knowledge gaps related to SLE in Canada. Using GT, relative search volumes (RV), associated topics and queries were collected from 2004-2024, using keywords for "lupus" (Fig1). The top 25 search terms were collected from each province and territory, and these search terms were analyzed thematically. The research process leveraged an integrated knowledge translation approach, in which a patient partner living with SLE was a key part of the research team.

Results: Search volumes for the search term "lupus" in Canada hit an all-time peak in October 2015 (RV=1.0) (Fig2,Table). This peak occurred in all provinces simultaneously, correlating with celebrity Selena Gomez's SLE diagnosis. Additional peaks were observed across Canada in July 2009 (RV=0.58), September 2016 (RV=0.69), and September 2017 (RV=0.78), all of which were correlated with milestones in the development and eventual approval of belimumab for SLE. Similarly, a peak in August 2016 (RV=0.66) was associated with positive Phase II trials for voclosporin. A national peak in June 2010 (RV=0.60) was associated with the 9th International Congress on SLE held in Vancouver, Canada. There was a marked trough across all Canadian provinces in November and December 2020 (RV=0.28), perhaps reflecting that SLE-related concerns were overshadowed by the ongoing COVID-19 pandemic. Overall, interest was highest in Newfoundland (RV=1.0), New Brunswick (RV=0.83), and Manitoba (RV=0.80), though the top related topics and queries varied spatially among provinces. The most frequently searched terms typically fell within the following themes: causes of lupus, diagnosis,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig. 1.0 Search Interest Over Time: Comparing "Lupus" and "SLE" on Google Trends

Fig. 1.1 Regional Distribution of search interest for "lupus" across Canada and Related Queries

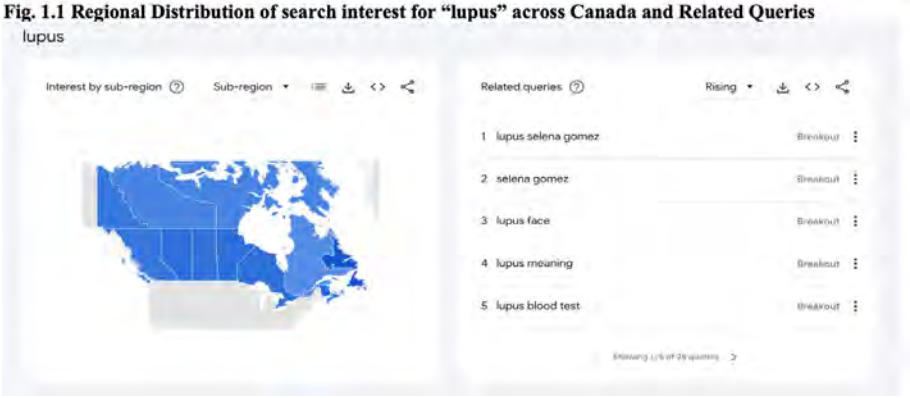


Figure 1. Google Trends dashboard displaying 1.0) search interest over time and 1.1) regional distribution across Canada

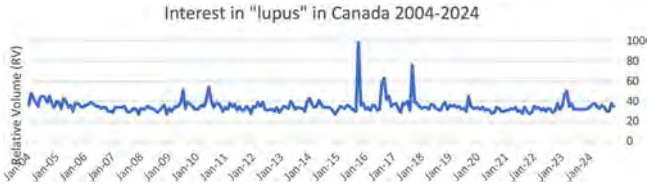


Figure 2. Relative Volume (RV) for the search term "lupus" across Canada (2004-2024)

symptoms, medication, and treatment. Some search terms were spatially unique, only appearing in one province, including search terms in French ("lupus maladie", Quebec), and Indonesian ("penyakit lupus", Newfoundland) languages.

Conclusion: An understanding of the information needs of the general public related to SLE, and how they vary spatially, is critical for designing and implementing targeted and effective patient education interventions. To this end, these research results will be shared and triangulated with the knowledge needs of advocacy organizations and the realities of lived SLE experience, through a deliberative dialogue with key stakeholders from across Canada. This research and deliberative

Table. Timeline, Key Events & Major Peaks, Search for "Lupus" (Canada 2004–2024)

Time Period	Peak/Trough	Associated News/Events
July 2009	Peak (0.58)	GSK announces positive Phase 3 study results for Benlysta News headlines speculate that musician Michael Jackson struggled with lupus prior to his death
June 2010	Peak (0.60)	9th International Congress on SLE held in Vancouver, BC
October 2015	Peak (1.0)	Selena Gomez announces diagnosis with lupus
August 2016	Peak (0.66)	Positive Phase II trials for voclosporin announced
September 2016	Peak (0.69)	Selena Gomez makes news headlines as she announces she is taking time off due to her lupus diagnosis Civil Servants' Walk for lupus awareness in Washington, DC
September 2017	Peak (0.78)	Selena Gomez undergoes kidney transplant surgery on September 14, 2017, which she shares on social media Benlysta (belimumab) autoinjectors approved in Europe and Japan
March 2023	Peak (0.50)	Lupus Nexus study begins enrolling patients at 24 sites across the Lupus Clinical Investigators Network (LCIN)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

dialogue will set a foundation for the design and implementation of relevant interventions to effectively reduce SLE-related health disparities and improve SLE-related quality of life nationwide.

Disclosure: T. Williamson: None; **E. Shantz**: None; **S. Elliott**: None; **C. Sperling**: None; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **M. Choi**: AstraZeneca, 2, 5, 6, Celltrion, 2, MitogenDx, 2, Organon, 6, Werfen, 2.

Abstract Number: 0189

"try It, You'll Love It": Patterns of AI Scribes Use Among Rheumatologists

Megan Creasman[1], Jing Li[2], Augusto Garcia-Agundez[3], gabriela Schmajuk[4] and Jinoos Yazdany[3], [1]UC San Francisco, San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]UCSF, San Francisco, CA, [4]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Heavy documentation contributes to clinician workload and burnout. Rheumatology carries one of the highest documentation burdens among Internal Medicine (IM) subspecialties. While recent advances in artificial intelligence (AI) have led to the development of AI scribes that can produce structured clinical notes in real time, little is known about how rheumatologists use these tools. The implementation of AI scribes across a large ambulatory academic health system provided a unique opportunity to compare the adoption, retention, and utilization patterns of AI scribes by rheumatologists compared to other physicians.

Methods: Data from Dec 2024-May 2025 was collected to capture AI scribes use. Ambulatory physicians were eligible to access AI scribes and became "live users" after completing a training; live users became "active users" if they used AI scribes at least once in the preceding 30 days. Provider adoption was defined as the ratio of live users to all eligible providers. Retention was defined as the ratio of active to live users in the preceding 30 days. To assess utilization, live users were categorized based on the percentage of eligible encounters that used AI scribes in the past 30 days: low (< 30%), medium (30–70%), and high (>70%). Fisher's exact test was used to compare the proportion of high utilizers between rheumatology vs. IM physicians and rheumatology vs. non-IM physicians. Outcome measures tracked the average weekly time spent on EHR activities per provider, comparing the 90 days prior to the date each physician became a "live user" to the post AI scribes period.

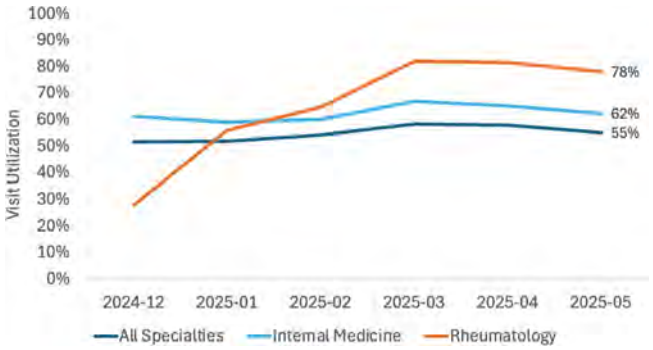


Figure 1. Visit Utilization in in Rheumatology, IM and Non-IM Specialties

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

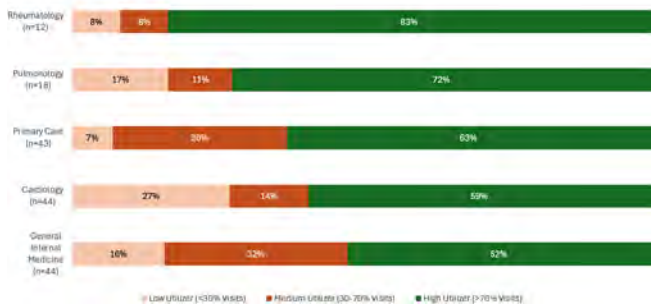


Figure 2. Top Five IM Specialties by Provider Visit Utilization

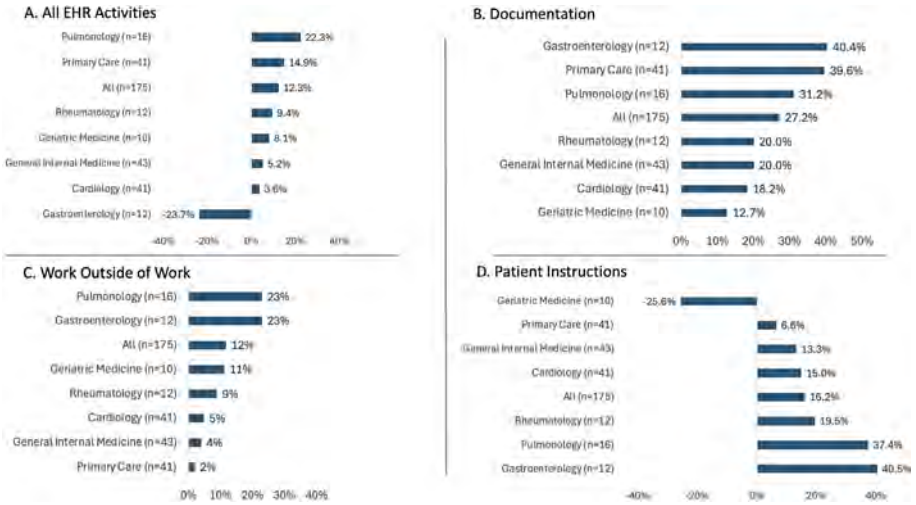


Figure 3. Outcomes by IM Specialty

Results: 2477 physicians were eligible to start using AI scribes; by the end of the observation period 888 (37%) had become live users. Adoption by rheumatologists was 41% (12/29) compared to 49% for all other IM physicians (224/455, 15 specialties). Of IM sub-specialties Rheumatology was 10th by adoption rate. Among rheumatologists, retention was 100%, slightly higher than the 94% retention seen across IM. Rheumatology live users used AI scribes for more of their encounters (78%) than any other IM specialty (62%) and non-IM physicians (55%; see Figure 1). Rheumatology had the largest percentage of high utilizers of all IM specialties (83% vs. 52%; see Figure 2). By Fisher's exact test Rheumatology had a numerically higher but not statistically significant proportion of high utilizers than IM (83% vs. 72%, p=0.5) and a significantly higher proportion than non-IM physicians (83% vs. 42%, p=0.006). Live users from IM specialties and rheumatology decreased mean time spent in all EHR activities, documentation, work outside of work, and patient instructions; rheumatologists had slightly less time savings except in patient instructions (see Figure 3).

Conclusion: Approximately half of rheumatologists adopted AI scribes, emerging as the highest users per encounter among IM subspecialties. Retention was consistently high across all specialties, including rheumatology, underscoring sustained engagement. Rheumatologists enjoyed time savings across all four outcome measures. Future research should investigate the implications of AI scribes on rheumatologist well-being and the patient experience.

Disclosure: M. Creasman: None; **J. Li**: None; **A. Garcia-Agundez**: None; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0190

Health literacy and comorbidity burden: a cluster analysis in a national cohort of people with inflammatory arthritis

Mrinalini Dey[1], James Galloway[2], Andrew Cope[2], MAYA BUCH[3], Richard Osborne[4], Sam Norton[2] and Elena Nikiphorou[2], [1]Centre for Rheumatic Diseases, King's College London, London, United Kingdom, [2]King's College London, London, United Kingdom, [3]UNIVERSITY OF MANCHESTER, MANCHESTER, United Kingdom, [4]La Trobe University, Melbourne, Victoria, Australia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Health literacy is a social determinant of health in people with chronic diseases, including inflammatory arthritis (IA). We aimed to assess the association between health literacy and comorbidity burden.

Methods: The National Early Inflammatory Arthritis Audit (NEIAA) is an observational cohort comprising adults with IA, recruited since 2018. Patients with confirmed IA, within NEIAA, were invited to complete an online survey (March to May 2024), including the Health Literacy Questionnaire (HLQ); Work Productivity and Activity Impairment questionnaire; Generalised Anxiety Disorder (GAD-2); Patient Health Questionnaire (PHQ-2); socio-demographics, employment and education; self-reported disease activity. Comorbidity data were extracted from the NEIAA for: diabetes mellitus, hypertension, lung disease, depression, and stomach ulcers.

The survey was distributed to 3300 individuals with those responding matched to original records within NEIAA.

Agglomerative hierarchical clustering using Ward's method was applied. Health literacy, socio-demographics and comorbidity profile were compared between clusters.

Results: A total of 995 patients with IA were included. The median age was 59 years (IQR 50-67) and 66% were female.

A five-cluster approach was deemed optimal for characterising the sample. The cohort was clustered according to normalised HLQ scores: "Highest" n=90; "High" n=190; "Moderate" n=296; "Low" n=270; "Lowest" n=149 (Figure 1 and Table 1).

The "highest" health literacy cluster had highest mean age (63.4, SD 11.4), lowest proportion of females, and least likely to have ever smoked. The cluster with "lowest" health literacy had the lowest mean age (53.9, SD 11.8) and highest proportion of females (Table 1).

Table 1: Outcomes presented by health literacy cluster. Higher mean scores for Patient Health Questionnaire (PHQ-2) and Generalised Anxiety Disorder (GAD-2) denote higher levels of depression and anxiety, respectively. SD= standard deviation.

Cluster by health literacy	Highest n=90	High n=190	Moderate n=296	Low n=270	Lowest n=149
Age (Mean, SD)	63.4 (11.4)	57.1 (14.7)	57.9 (13.4)	56.9 (12.6)	53.9 (11.8)
Gender (% female)	62.2	65.8	65.6	66.0	69.8
Smoking status (%)					
Current smoker	8.9	5.3	3.7	11.5	10.7
Ex-smoker	22.2	23.7	30.4	30.0	26.2
Never smoker	53.3	45.3	44.3	39.3	42.3
Unknown	15.6	25.8	21.6	19.3	20.8
PHQ-2 (Mean, SD)	0.7 (1.3)	0.9 (1.3)	1.5 (1.6)	1.8 (1.6)	2.5 (1.9)
GAD-2 (Mean, SD)	0.9 (1.4)	1.0 (1.4)	1.5 (1.7)	1.8 (1.7)	2.6 (2.0)
Self-reported disease activity (0-100; Mean, SD)	27.9 (26.6)	29.5 (26.4)	35.5 (27.7)	40.3 (26.9)	59.4 (28.2)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

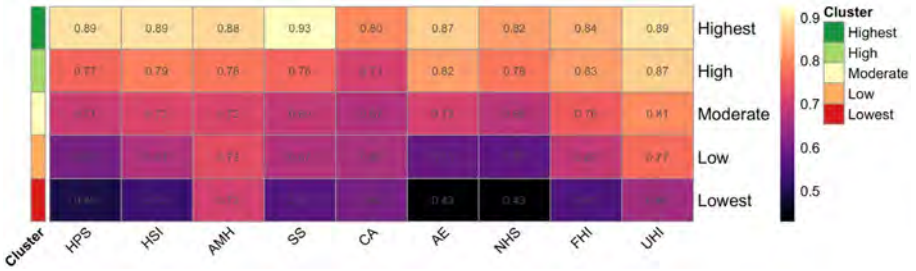


Figure 1: Normalised Health Literacy Questionnaire (HLQ) scores by cluster (0-1 scale). The HLQ has nine domains: 1. HPS: Feeling understood and supported by healthcare providers; 2. HSI: Having sufficient information to manage health; 3. AMH: Actively managing my health; 4. SS: Social support for health; 5. CA: Appraisal of health information; 6. AE: Ability to actively engage with healthcare providers; 7. NHS: Navigating the health-care system; 8. FHI: Ability to find good health information; 9. UHI: Understanding health information well enough to know what to do.

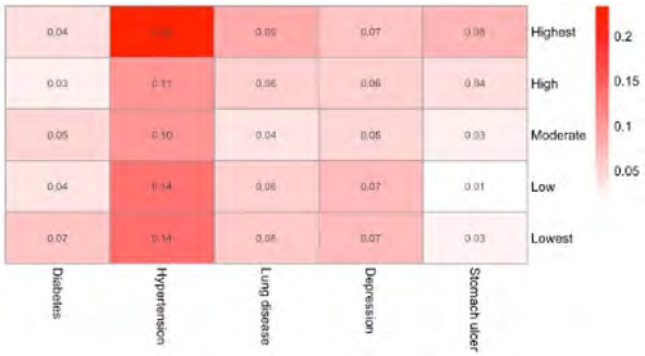


Figure 2: Mean comorbidity prevalence by health literacy cluster.

Anxiety and depression (as measured by GAD-2 and PHQ-2) were 3.6x and 2.9x higher respectively in the "lowest" compared to "highest" health literacy cluster. Self-reported disease activity was also twice as high in the "lowest" compared to "highest" health literacy cluster.

The "highest" health literacy cluster had the highest prevalence of all comorbidities, aside from diabetes, which was most frequent in the "lowest" health literacy cluster (Figure 2). The two lowest health literacy clusters had relatively high prevalence of hypertension and depression. Of the recorded comorbidities, only prevalence of hypertension and stomach ulcer were significantly different between the five clusters (p=0.02 and p=0.05 respectively).

Conclusion: The "lowest" health literacy cluster had almost four times greater anxiety and depression and twice as high self-reported disease activity, compared to the "highest" health literacy cluster. Our results suggest higher health literacy associated with older age, greater comorbidity prevalence, but lower likelihood of smoking, mental health symptoms and disease activity.

Older individuals likely have more comorbidities and more frequent contact with healthcare services which may increase overall engagement and understanding of health information. Our results will inform policy and management strategies in assessing and modifying health literacy, as well as multimorbidity, in the context of IA.

Disclosure: M. Dey: None; **J. Galloway**: AbbVie, 2, 6, Alfasigma S.p.A., 2, Eli Lilly, 2, 6, Gilead, 2, Janssen-Cilag, 2, 5, 6, Novartis, 6, Pfizer, 2, 5, 6, Takeda, 2, UCB, 6; **A. Cope**: Bristol-Myers Squibb(BMS), 2, 5, 6; **M. BUCH**: Bristol-Myers Squibb(BMS), 5; **R. Osborne**: None; **S. Norton**: None; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0191

Advanced Therapy Use in RA Patients with Moderate Disease Activity in a Large NHS Foundation Trust in South London, UK

Aoibhinn Kelly[1], Maddalena Rupnik[2], Nasra Ahmed[1], **Mrinalini Dey**[3] and Elena Nikiphorou[4], [1]King's College Hospital NHS Foundation Trust, London, United Kingdom, [2]Faculty of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, [3]Centre for Rheumatic Diseases, King's College London, London, United Kingdom, [4]King's College London, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Moderate disease in rheumatoid arthritis (RA) is defined as a 28-joint disease activity score (DAS28) of 3.2-5.1(MDAS). As per the National Institute for Health and Care Excellence (NICE, TA 715, TA 744 & TA 676), patients with moderate RA failing ≥2 conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) should be assessed for eligibility for a TNF-inhibitor, upadacitinib or filgotinib [1].

We aimed to assess compliance with NICE guidance on moderate RA management in a diverse area of London.

Methods: All patients with confirmed RA (EULAR/ACR 2010 criteria [2]) seen in the last 18 months were extracted from the electronic records (Epic) of King's College Hospital NHS Foundation Trust. Patients with recorded MDAS and previously receiving ≥2 csDMARDs were included. Exclusion criteria were: temporarily stopping advanced therapy (eg due to malignancy or infection); commencing a biologic or targeted synthetic DMARD (b/tsDMARD) not specified in TA 715, 744 or 676; no recorded DAS28 or components.

Patients were analysed in two groups:

i) those on a biologic via the moderate RA pathway;

ii) those not on a biologic.

All patients in group I were automatically eligible for inclusion.

Table 1: Summary of characteristics of included patients with rheumatoid arthritis (RA), including those commenced on advanced therapy via the moderate RA pathway during the 18-month study period.

	Patients on advanced therapy via moderate RA pathway n=87	Patients not on advanced therapy		
		Moderate RA (DAS28 3.2-5.1) n=6	DAS28 <3.2 or >5.1 n=224	No face-to-face assessment n=20
Gender				
Female (%)	53 (55)	3 (50)	165 (73)	11 (55)
Age (SD)	53 (14.7)	63 (8.0)	61.7 (16.1)	58 (17.0)
Hospital site (% total in column)				
Tertiary hospital (n=162)	47 (54.0)	1 (16.7)	105 (46.9)	9 (45)
District general hospital (n=175)	40 (46.0)	5 (83.3)	119 (53.1)	11 (55)
Advanced therapy (%)				
Adalimumab	70 (80.5)			
Certolizumab pegol	2 (2.3)			
Benepali	2 (2.3)			
Filgotinib	12 (13.8)			
Upadacitinib	1 (1.1)			

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

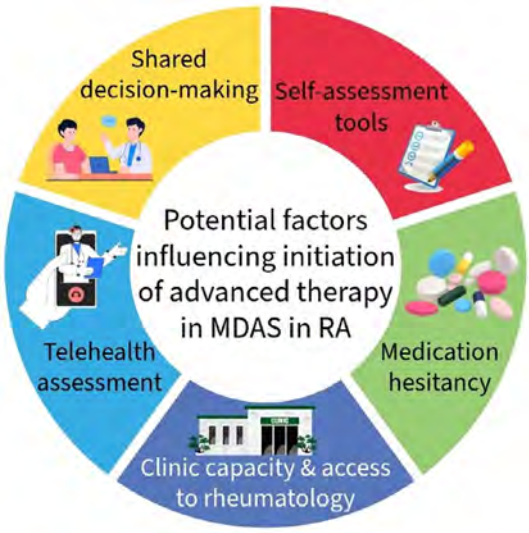


Figure 1: Summary of potential reasons for commencing or delaying advanced therapy in the setting of moderate disease activity (MDAS) in people with rheumatoid arthritis (RA). Possible reasons identified from this study include medication hesitancy (due to previous side-effects), telehealth assessments with no disease activity scores completed, and delays in accessing clinic appointments especially in rural or district hospitals. Mitigating factors may include the use of self-assessment tools in conjunction with telehealth and increased shared decision-making.

For group II, a random sample of 250 patients were reviewed in depth for encounters in which MDAS was recorded. If MDAS was present, reasons for not starting advanced therapy were extracted from Epic, if available. Other data extracted included demographics, DAS28, comorbidities and treatment history.

Results were summarised using descriptive statistics. Reasons for delaying therapy were summarised using narrative synthesis.

Results: In total, 87 patients commenced advanced therapy via the moderate RA pathway (mean age [SD]: 53 [14.7]; 55% female), most commonly adalimumab (n=70) (Table 1).

Of the 250 patients not on a b/tsDMARD, 20 had no recorded DAS (5% (n=13) did not attend a rheumatology appointment; 3% (n=7) had telephone encounters). 2% (n=6) had MDAS documented on ≥1 occasions (3.23-4.23), 50% female and mean age 63 (SD 8.0).

In all six MDAS cases, no offer of advanced therapy was recorded. One patient with MDAS had "apprehension about starting new medications" due to previous DMARD side-effects. Three patients with MDAS were subsequently assessed via telephone, precluding DAS assessment (Figure 1).

Conclusion: Our results demonstrate good compliance with NICE on escalation to advanced therapies in patients with MDAS. Increased telehealth usage limits assessment of joints and suitability for treatment escalation, especially in district hospitals. Self-assessment tools, to complete prior to telephone appointments, may mitigate this. Clinicians may be reluctant to discuss advanced therapies if patients demonstrate medication hesitancy.

Shared decision-making, appropriate triage for telehealth assessment and greater use of self-assessment tools are vital in facilitating discussions and commencement of advanced therapy in moderate RA.

References

1. National Institute for Health and Care Excellence. 2021. TA715, TA744 & TA676. Available at https://www.nice.org.uk/.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2. Aletaha, D et al. 2010 Rheumatoid arthritis classification criteria: An ACR/EULAR collaborative initiative. Arthritis & Rheumatism.

Disclosure: A. Kelly: None; **M. Rupnik**: None; **N. Ahmed**: None; **M. Dey**: None; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

Abstract Number: 0192

Digital Empowerment on Hold: Adoption Gaps in Prescribable Digital Health Applications – A National Cross-Sectional Study from Germany

Phillip Kremer[1], Daniel Fink[2], Harriet Morf[3], Hannah Labinsky[4], Karolina Gente[5], Peer Aries[6], Martin Krusche[1], Sebastian Kuhn[7], Axel Hueber[8] and Johannes Knitza[9], [1]Division of Rheumatology and Systemic Inflammatory Diseases, III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [2]Rheumazentrum Mittelhessen, Bad Endbach, Germany, [3]Department of Medicine 3 - Rheumatology & Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [4]University Hospital of Wuerzburg, Würzburg, Germany, [5]Department of Internal Medicine V - Hematology, Oncology and Rheumatology, University Hospital Heidelberg, Heidelberg, Baden-Wurttemberg, Germany, [6]Department of Rheumatology, Immunologikum, Hamburg, Germany, [7]Institute for Digital Medicine, University Hospital of Giessen and Marburg, Philipps University Marburg, Marburg, Germany, [8]Klinikum Nuernberg, Nuernberg, Germany, [9]Institute for Digital Medicine, University Hospital Gießen-Marburg, Philipps University, Marburg, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatic and musculoskeletal diseases (RMDs) are chronic conditions that require complex, multidisciplinary care. Since 2020, digital health applications (DiGAs) have been available for prescription and reimbursement in Germany, offering potential support for patient self-management. However, data on patient awareness, willingness to use,

Table 1: Patient demographics.

Characteristic	Group	Total n (%)
Gender	Female	175 (71.1)
	Male	70 (28.5)
	Other	1 (0.4)
Age, years	18-39	70 (28.5)
	40-59	96 (39.0)
	≥ 60	79 (32.1)
	Mean (SD)	50.4 (15.3)
Rheumatology setting	University Hospital	147 (59.8)
	General Hospital	27 (11.0)
	Practice	67 (27.2)
Disease	Rheumatoid Arthritis	101 (41.1)
	Psoriatic Arthritis	45 (18.3)
	Axial Spondyloarthritis	25 (10.2)
	Gout	0 (0)
	Polymyalgia rheumatica	3 (1.2)
	Osteoarthritis	1 (0.4)
	Other	65 (26.4)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

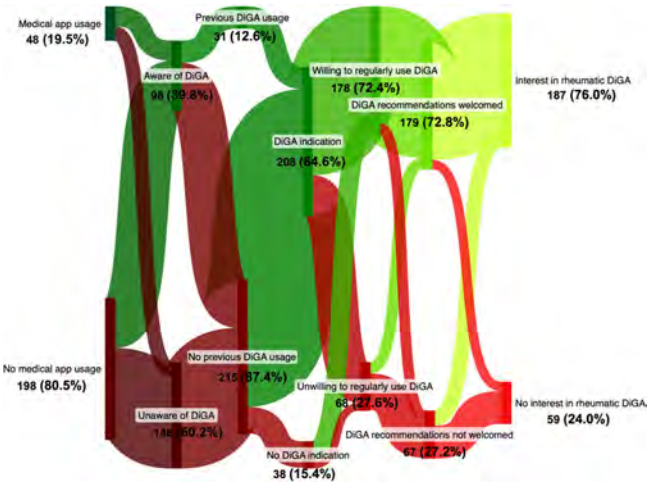


Figure 1: Sankey diagram illustrating patients' medical app usage, DiGA awareness, DiGA usage, DiGA indications, willingness to use DiGAs, interest in receiving DiGA recommendations, and interest in a rheumatology-specific DiGA.

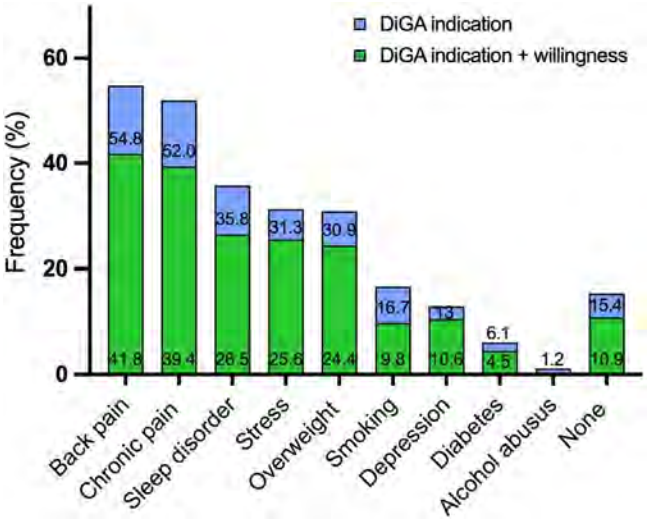


Figure 2: Patient-reported comorbidities that represent indications for approved prescribable digital health applications (DiGAs). Participants were allowed to select multiple comorbidities. Light blue depicts the proportion of patients with the reported respective indication. Green depicts the proportion of patients with the reported respective indication and reported willigness to regularly use a DiGA.

suitability, and actual adoption of DiGAs among individuals with RMDs remain limited. This study aimed to evaluate both the potential and actual adoption of DiGAs by patients with RMDs.

Methods: A national cross-sectional survey was conducted between February 17 and April 8, 2025, across multiple German rheumatology outpatient clinics. Adult patients presenting to the clinics were invited to complete an anonymous electronic REDCap questionnaire.

Results: A total of 246 patients completed the survey (mean age 50.4 years; 71.1% female). Most participants were treated at a university hospital (59.8%), primarily for rheumatoid arthritis (41.1%), psoriatic arthritis (18.3%), or axial spondyloarthritis (10.2%) (**Table 1**). Regarding digital health usage (**Figure 1**), 9.5% of patients reported prior medical app usage, 39.8% were aware of DiGAs, and 12.6% had previously used a DiGA. Additionally, 84.6% of patients reported at least one comorbidity corresponding to an approved DiGA indication; the most frequently reported indications were back pain (54.8%), chronic pain (52.0%), and sleep disorders (35.8%), see **Figure 2**. Importantly, 72.4% of patients expressed willingness to regularly use a DiGA, and 72.8% would welcome active DiGA recommendations from their rheumatologists or insurance providers. Finally, 76.0% expressed interest in a rheumatology-specific DiGA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The majority of patients reported comorbidities potentially addressable with DiGAs and expressed interest in regular use. However, only a minority had previously used a DiGA. These findings highlight the need for enhanced implementation strategies to fully leverage the potential of digital health applications.

Disclosure: P. Kremer: None; **D. Fink**: None; **H. Morf**: AbbVie/Abbott, 6, Fimo Health GmbH, 2, Galapagos, 1, Novartis, 6; **H. Labinsky**: None; **K. Gente**: None; **P. Aries**: None; **M. Krusche**: None; **S. Kuhn**: None; **A. Hueber**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos/Alfasigma, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **J. Knitza**: GAIA, 2, Vila Health, 12, 2.

Abstract Number: 0193

Evaluation of electronic health record and efficiency tool utilization by pediatric subspecialists

Samantha Coss[1], Alison Brittain[2], Jennifer Lee[3], Julie Young[1], Ivana Stojkic[1], John Mahan[4] and Alysha Taxter[5], [1]Nationwide Children's Hospital, Columbus, OH, [2]Nationwide Children's Hospital, Canal Winchester, OH, [3]Department of Gastroenterology, Nationwide Children's Hospital, Columbus, OH, [4]Department of Nephrology, Nationwide Children's Hospital, Columbus, OH, [5]Nationwide Children's, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Excessive interaction with the electronic health record (EHR) is frequently cited as a common source of physician burnout. The administrative burden and extended documentation time required by EHR systems can significantly contribute to physician fatigue and discontent. This study evaluated EHR utilization across pediatric subspecialties.

Methods: This is a cross-sectional study evaluating EHR utilization data from 8 pediatric subspecialties at a quaternary medical center. Three months of outpatient EHR provider action logs from spring 2024 were evaluated. We assessed factors associated with EHR utilization including the percentage of time reviewing the chart, writing notes, addressing in-basket tasks, managing orders as well as measures of efficient EHR usage including the percentage of notes manually typed, percentage of same day chart closure, and the use of efficiency tools were recorded. Time actively using the EHR was

Table 1: Rheumatology and Pediatric Subspecialist Electronic Health Record Utilization Metrics

	Rheumatology	Other Pediatric Subspecialists	p-value
Time in EHR[a]	53 [48, 56]	34 [23, 44]	<0.01
% time writing notes	54% [52, 60]	53% [44, 59]	0.71
% time chart review	17% [17, 20]	18% [15, 23]	0.89
% time in Basket	16% [13, 18]	13% [9, 18]	0.23
% time Orders	12% [11, 13]	13% [10, 17]	0.33
Non-business work hours[b]	296 [228, 327]	90 [33, 323]	0.11
% notes manually typed	22% [15, 22]	14% [8, 22]	0.2
% same day chart closure	51% [40, 61]	61% [31, 89]	0.64

Legend:

EHR: Electronic Health Record

[a]Time in EHR is calculated by minutes spent actively using the system (clicking, scrolling, typing)/Number of appointment

[b]Non-business work hours measured by average minutes per month outside of 7AM to 530PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: EHR utilization metrics by pediatric specialty and clinic sessions per week

	Number of Clinics per Week	Time in EHR[a]	Time writing notes (%)	Time in chart review (%)	Time in In Basket (%)	Time in Orders (%)	Notes manually typed (%)	Same day chart closure (%)	Non-business work hours[b]
Adolescent	Less than 5	17 [13, 22]	47 [41, 51]	21 [18, 26]	13 [9, 19]	22 [18, 25]	20 [15, 29]	51 [32, 78]	101 [55, 143]
	5 or More	27 [14, 32]	50 [35, 55]	23 [17, 29]	11 [10, 12]	16 [8, 24]	22 [16, 28]	38 [24, 45]	63 [52, 124]
Allergy and Immunology	Less than 5	36 [24, 43]	60 [51, 65]	15 [12, 18]	14 [10, 17]	11 [1, 12]	15 [11, 15]	73 [70, 88]	48 [18, 78]
	5 or More	25 [16, 40]	56 [54, 62]	17 [10, 18]	13 [10, 15]	13 [8, 14]	14 [12, 23]	72 [42, 92]	11 [7, 323]
Developmental Behavioral Pediatrics	Less than 5	48 [37, 92]	52 [52, 52]	20 [18, 22]	12 [10, 14]	15 [10, 20]	18 [11, 24]	9 [8, 47]	1478 [325, 2632]
	5 or More	75 [39, 85]	60 [52, 74]	19 [13, 24]	6 [4, 14]	10 [9, 15]	30 [27, 32]	41 [31, 62]	617 [13, 1243]
Endocrinology	Less than 5	38 [20, 80]	56 [47, 84]	19 [15, 24]	17 [13, 17]	8 [7, 9]	8 [6, 12]	45 [24, 84]	347 [24, 782]
	5 or More	39 [32, 45]	52 [49, 58]	22 [21, 32]	16 [9, 20]	9 [7, 12]	14 [12, 16]	50 [21, 77]	811 [405, 838]
Gastroenterology	Less than 5	38 [29, 46]	44 [42, 52]	17 [15, 25]	21 [14, 24]	13 [12, 16]	15 [3, 21]	65 [38, 96]	84 [24, 281]
	5 or More	35 [26, 39]	48 [30, 51]	22 [16, 27]	21 [18, 26]	14 [11, 17]	10 [5, 16]	89 [39, 90]	127 [42, 428]
Neurology	Less than 5	35 [28, 54]	59 [53, 64]	18 [16, 22]	11 [6, 13]	11 [10, 16]	13 [5, 30]	44 [11, 86]	72 [13, 90]
	5 or More	33 [32, 39]	60 [56, 67]	17 [13, 24]	10 [6, 13]	12 [10, 15]	19 [16, 26]	78 [72, 93]	37 [15, 142]
Rheumatology	Less than 5	54 [48, 56]	58 [52, 62]	17 [16, 21]	14 [11, 18]	12 [11, 13]	22 [10, 24]	54 [39, 66]	240 [158, 301]
	5 or More	50 [40, 60]	48 [45, 52]	19 [17, 20]	21 [18, 23]	12 [11, 14]	19 [13, 22]	46 [41, 51]	360 [327, 393]
Sports Medicine	Less than 5	NA	NA	NA	NA	NA	NA	NA	NA
	5 or More	12 [10, 13]	53 [46, 57]	13 [12, 16]	5 [4, 6]	27 [26, 33]	11 [7, 13]	93 [72, 99]	224 [93, 576]

Legend:
[a]Time in EHR is calculated by minutes spent actively using the system (clicking, scrolling, typing)/Number of appointments
[b]Non-business work hours measured by average minutes per month outside of 7AM to 530PM
EHR: Electronic Health Record

normalized by number of clinic appointments. Non-business work hours were measured by average minutes per month utilizing the EHR outside of 7AM to 530PM. Providers were stratified by greater than or less than 5 half-day sessions of clinic per week to assess differences in EHR utilization based on clinical load. Summary statistics are reported. Comparisons were made between groups using Wilcoxon rank-sum test.

Results: 127 provider logs were assessed across 8 specialties, with a median of 17 [10, 33] providers per specialty. Nine pediatric rheumatologists spent a median of 53 [48, 56] minutes within the EHR per patient appointment, whereas other subspecialists spent a median of 34 [23, 44] minutes ($p< 0.01$) (Table 1). The percentage of time completing non-documentation tasks within the EHR and rates of same day chart closure were similar between rheumatology and other subspecialists. The use of diagnosis and level of service speed buttons, quick actions, and chart review filters did not differ between rheumatologists and other subspecialists. All rheumatologists but only 68% of other subspecialists utilized chart search ($p=0.04$). There was no difference in EHR utilization metrics when stratifying by the number of clinic sessions within subspecialty departments (Table 2).

Conclusion: Pediatric rheumatologists spend significantly more time per appointment within the EHR than other subspecialty providers, and the majority of this extra time is spent on documentation. Leveraging new tools such as ambient listening and other artificial intelligence tools may lessen documentation burden and improve EHR utilization, potentially decreasing burnout rates and improving workforce retention.

Disclosure: S. Coss: None; **A. Brittain**: None; **J. Lee**: None; **J. Young**: None; **I. Stojkic**: None; **J. Mahan**: None; **A. Taxter**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0194

Evaluation of a Home-based Therapeutics Service: Feasibility, Patient and Caregiver Experience, and Cost

Xiaohui Xin, Andrea Low, Sow Ling Yee, Miao Miao Liu, Christina Tan, Daphne Ng and **Siaw Ing Yeo**, Singapore General Hospital, Singapore, Singapore

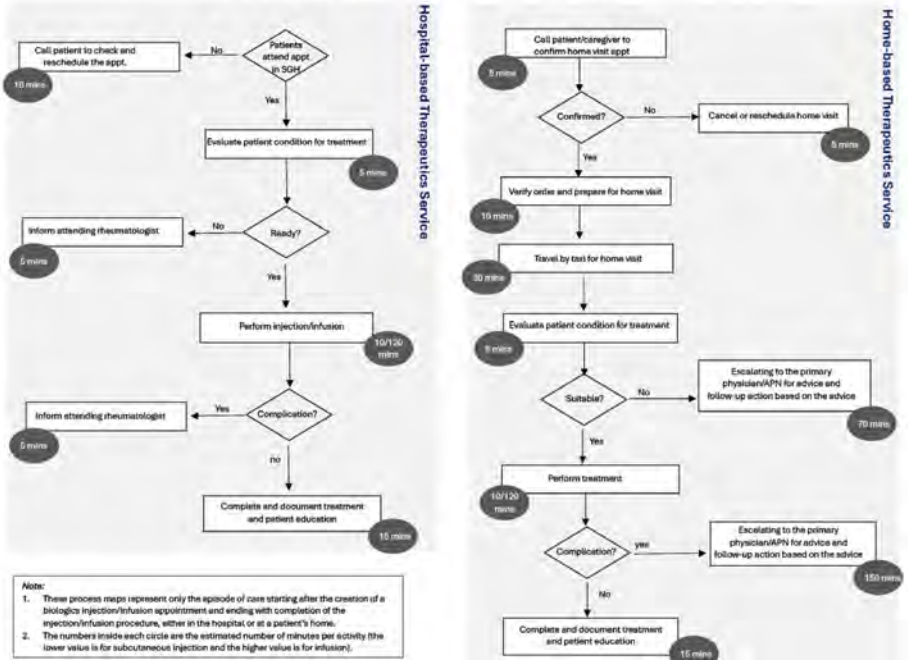
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The home-based therapeutics service (HTS) by a community nurse is part of an ongoing larger initiative—Community Therapeutics Programme (CTP)—spearheaded by the Rheumatology and Immunology Department in Singapore General Hospital. CTP is an innovative healthcare initiative designed to deliver specialist therapeutic infusions (e.g. anti-TNF inhibitors, tocilizumab, zoledronic acid) and subcutaneous injections (e.g. anti-TNF inhibitors, denosumab) within community settings by providing direct HTS and empowering primary care providers (General Practitioners and Polyclinics) to offer these treatments. It aims to address several challenges faced by patients and by healthcare systems: long waiting times for procedures, inconvenience, higher cost of frequent hospital visits for patients and their caregivers, and the strain on inpatient hospital resources.

This observational study assesses the feasibility, patient and caregiver experience, and cost of the HTS.

Methods: This evaluation included all patients referred to the HTS by their attending rheumatologists from March 2023 (the start of the CTP) to February 2025. Feasibility was assessed by tracking patients requiring urgent return to hospital-based therapeutics. Patient and caregiver feedback on their experience with the HTS was collected via anonymous online surveys,

FIGURE 1. PROCESS MAPS OF HOSPITAL-BASED VERSUS HOME-BASED THERAPEUTICS SERVICES



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

rating overall experience and specific aspects (convenience, timeliness, scheduling, and comfort) of the HTS. Cost comparison between the HTS and hospital-based care was conducted using time-driven-activity-based-costing (TDABC) method (process maps shown in Figure 1).

Results: The HTS served 230 patients during the evaluation period, administering 867 treatments: 623 subcutaneous injections to 185 patients and 244 therapeutic infusions to 45 patients. No patient needed urgent transfer to hospital-based care. Only three infusions out of the 867 procedures (0.3%) needed rheumatologist consultation: two for pre-infusion stabilisation of blood pressure and one for post-infusion monitoring of side effects that resolved within three days.

We received 258 completed service evaluation survey responses (223 by patients and 35 by caregivers), covering 111 intravenous infusion and 147 subcutaneous injection procedures, respectively. The feedback was overwhelmingly positive with 95-98% of respondents agreeing that HTS was convenient, timely, comfortable, and easy to arrange.

Cost analysis using TDABC revealed significant savings: the average HTS cost was SGD136 for a subcutaneous injection and SGD260 for a therapeutic infusion, compared to SGD286 and SGD915 respectively for hospital-based alternatives. This translated into total savings of SGD253,270 (SGD93,450 from 623 injections and SGD159,820 from 244 infusions). Even in the three rare cases requiring rheumatologist consultation, the average cost of an infusion in HTS remained more than SGD300 cheaper than that of a hospital-based infusion.

Conclusion: HTS is a safe and less costly service compared to hospital-based therapeutics with overwhelming satisfaction from both patients and caregivers.

Disclosure: X. Xin: None; **A. Low**: None; **S. Yee**: None; **M. Liu**: None; **C. Tan**: None; **D. Ng**: None; **S. Yeo**: None.

Abstract Number: 0195

Utility of Repeat ANA Testing

Michael Luggen[1] and **Sila Mateo Faxas**[2], [1]University of Cincinnati College of Medicine, Cincinnati, OH, [2]Good Samaritan Hospital, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The ANA by immunofluorescence is a sensitive screening test for most systemic auto-immune rheumatic diseases (SARDs). A negative result is oftentimes sufficient to exclude a diagnosis. However, when diagnostic uncertainty persists, repeat testing is sometimes performed. The utility of a subsequent positive result is not clear. Only one previous study has examined the predictive value of a subsequent positive test after an initial negative result and found that only 1.1% of such patients developed a SARD. The purpose of this study was to attempt to validate this result in a different population of patients followed longitudinally and specifically evaluated by a rheumatologist, something that had not been done previously.

Methods: All patients aged ≥18 years seen at the University of Cincinnati Medical Center who tested negative for ANA initially and subsequently tested positive and who were evaluated by a rheumatologist on one or more occasions between April 2015 and April 2024 constituted the study population. Clinical diagnoses were established by board-certified

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

rheumatologists and independently verified through comprehensive electronic medical record review by a second rheumatologist.

Results: Of 4129 patients who underwent ANA testing and were evaluated by a rheumatologist during the study period, 296 (7.2%) had discordant results. Among these, 103 patients (2.5% of total cohort) had an initially negative ANA followed by a subsequent positive one. Records were reviewed before and after the positive result to determine if the diagnoses had been revised. In only 4 patients or 3.8% of cases did a positive result lead to a change in diagnosis. The revised diagnoses in these 4 patients were: UCTD (1), SLE (1), Sjogren's (1), undifferentiated inflammatory arthritis (1).

Conclusion: Repeat ANA testing after a negative result in patients suspected of having connective tissue disease infrequently results in a new diagnosis. Such testing is not cost-effective and should be discouraged in clinical practice guidelines.

Disclosure: M. Luggen: AbbVie/Abbott, 5, Biogen, 5, Priovant, 5, Sun Pharma, 2; **S. Mateo Faxas**: None.

Abstract Number: 0196

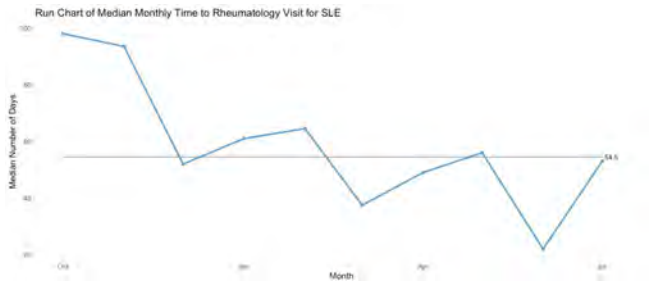
Increasing Timely Rheumatology Evaluation for High Risk Lupus Patients

Steven Taylor[1] and Elena Weinstein[2], [1]University of Colorado, Denver, CO, [2]University of Colorado, Englewood, CO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The rheumatology workforce shortage presents many challenges to the delivery of rheumatology care. Improving timely access to rheumatology for patients with life or organ threatening conditions such as SLE is one of the most important challenges. Our institution has a significant mismatch between number of referrals for new evaluation and number of new patient spots within our clinic. Further complicating the challenge of scheduling a prompt evaluation for these patients is the complex and multisystem nature of SLE. Literature

suggests less than half of these referrals have inflammatory rheumatic disease (Feuchtenberger, 2016) and delays in SLE care lead to worse outcomes (Kernder, 2021). Therefore, we developed a quality improvement (QI) project to improve the time from referral to first rheumatology appointment, in this report we describe the results of our first iteration of the project.



Run Chart of monthly days until rheumatology appointment for lupus patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Our study was deemed IRB exempt as a QI initiative. We implemented the Model for Improvement framework in our project (Langley, 2009). The aim statement of the project is to reduce the time from referral entry to first visit with a rheumatologist by 20% in which a diagnosis of SLE is coded. Data was collected from the medical record including ICD10 codes associated with the initial visit, date of initial visit, and date of the referral order. The first Plan, Do, Act, Study (PDSA) cycle focused on referral management. In the baseline state referrals were evaluated by a registered nurse (RN) reviewing the chart for appropriateness for rheumatology visit. That protocol did not include a mechanism to identify high risk phenotypes. Therefore, the referral process was changed to a hybrid of RN and rheumatologist review. The rheumatologist was instructed to evaluate appropriateness of referral and to risk stratify timing of the appointment. Statistical analysis was performed in R, tests of significance were Student's T and Mann-Whitney-Wilcoxon.

Results: The first PDSA cycle was started in February of 2024, with the addition of physician review on February 19th. From October 1, 2023, to July 1, 2024, there were 4,405 referrals to rheumatology, of which 123 had a diagnosis of SLE on the first visit. The median time from referral order to first appointment was 60.5 (±59.2) days for all referrals, and 60 (±57.2) days for SLE appointments. From October 1 to February 19 the median time to appointment was 70 (±67.3) days (n 707), and from February 19 to July 31 it is 5a5 (±42.5) days (n 539) $p \leq 0.05$. For SLE appointments the median time to appointment was 69±63 days (n 73) before intervention while the time after intervention was 51±38.9 (n 50) $p \leq 0.05$. A run chart for monthly time to evaluation is included in figure 1.

Conclusion: By incorporating physician review into the referral evaluation process, we were able to decrease the time to appointment by 26% for SLE patients. Confounding our study was an expansion of our clinical faculty in January 2024 and April 2024 by 1 full time equivalent. The next iterations of our project will focus on alternative processes to further improve access for patients with high-risk disease states while reducing reliance on manual chart review. This is an area of critical need in rheumatology.

Disclosure: S. Taylor: None; **E. Weinstein**: AbbVie/Abbott, 5, Amgen, 5, Argenx, 5, Immunovant, 5, Priovant, 5, UCB, 5.

Abstract Number: 0197

Rheumatoid arthritis (RA) patients who screen positive for anxiety, depression, and/or fibromyalgia are more likely to report problems with sleeping, memory, and/or social activities than to have an abnormal rheumatoid factor or ACPA

Theodore Pincus[1], Juan Schmukler[1] and Tengfei Li[2], [1]Rush University Medical Center, Chicago, IL, [2]Rush, chicago, IL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0175–0198) Health Services Research Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: A symptom checklist and screening indices for anxiety (ANX), depression (DEP), and/or fibromyalgia (FM) on patient questionnaires such as a multidimensional health assessment questionnaire (MDHAQ) facilitate recording symptoms as formal medical history data, not available prior to information technology. MDHAQ data may be informative to address two problems in RA: a. primary RA symptoms of joint pain and functional disability may be seen in patients with comorbid joint damage and/or patient distress, which may elevate RA core data set measures and indices in the absence

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Order of 60 symptoms among all patients	Symptom	All patients	ANX, DEP, and/or FM pos	ANX, DEP, and FM neg
2	Back pain	46%	62%	38%
3	Problems with sleeping	43%	75%	25%
5	Neck pain	38%	60%	40%
7	Headaches	33%	57%	43%
8	Unusual fatigue	28%	73%	27%
10	Anxiety	28%	100%	0%
15	Shortness of breath	25%	74%	26%
17	Depression	22%	100%	0%
18	Problems with memory	21%	81%	19%
21	Dizziness	19%	77%	23%
22	Problems with thinking	18%	87%	13%
25	Heartburn	17%	73%	27%
26	Cough	17%	56%	44%
27	Palpitations	15%	75%	25%
28	Problems with social activities	15%	92%	8%

Prevalence of self-report of symptoms in 173 patients with rheumatoid arthritis on a multidimensional health assessment questionnaire (MDHAQ), including the order in all patients (symptoms reflecting inflammatory activity are such as joint pain as #1 are excluded) according to positive screening on 1 of 3 MDHAQ indices for anxiety (ANX), depression (DEP) and or fibromyalgia (FM)

of inflammatory activity; b. rheumatoid factor (RF) or anti-cyclic citrullinated proteins (ACPA) are found in only 67-69% of RA patients (Meta-analysis: Nishimura et al Ann Int Med. 2007;146(11):797-808). Formal recording of specific symptoms may be analogous to laboratory testing to inform management decisions. The prevalence of non-inflammatory symptoms in RA patients with positive versus negative screens on MDHAQ ANX, DEP, and FM indices was analyzed.

Methods: All patients seen in the study setting complete an MDHAQ, which includes a 60-symptom checklist to record a review of systems and screen for adverse events of high-risk medications. The prevalence of each symptom was computed in all patients and compared in those who screened positive versus negative for any of the 3 MDHAQ indices, MAS2 (MDHAQ anxiety screen), MDS2 (MDHAQ depression screen) and/or FAST4 (fibromyalgia assessment screening tool). The 15 most common non-inflammatory-based symptoms reported by all patients were identified, after excluding symptoms likely to result from inflammation, e.g., joint swelling, muscle pain, muscle weakness, dry eyes, dry mouth, although recognizing that the included and excluded symptoms might have an inflammatory or noninflammatory origin in certain individual patients. The prevalence of each symptom was then compared in patients who screened positive for MAS2 for ANX , MDS2 for DEP, and/or FAST4 for FM versus negative for all 3 indices.

Results: Among all 173 RA patients, 40-50% reported neck pain, headaches, unusual fatigue, anxiety (by definition), dyspnea, depression (by definition), and problems with memory, 20-40% reported dizziness, problems with thinking, heartburn, cough, palpitations, and 15-19% problems with social activities (Table). Each of these symptoms was reported by more than 50% of patients who screened positive for ANX , DEP, or FM, and by fewer than 50% in those who screened negative (Table). More than 70% of patients who screened positive for ANX, DEP, and/or FM reported problems with thinking, memory, sleeping, and unusual fatigue, in addition to anxiety and depression (by definition), higher than the prevalence of rheumatoid factor or ACPA in RA.

Conclusion: Symptoms on a computer checklist can function as clues to the likelihood of ANX , DEP, or FM in patients with RA who may have elevated DAS28, CDAI, or RAPID3, but little or no inflammation, analogous to laboratory tests. The prevalence of symptoms in >70% of RA patients with ANX, DEP, and/or FM is higher than the prevalence of RF or ACPA in RA in a meta-analysis. This information can inform more rational patient management toward improved care and outcomes.

Disclosure: T. Pincus: Medical history services, LLC, 8, 9, 10; **J. Schmukler**: None; **T. Li**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0198

Variation in RA disease activity measure assessment and treatment change documentation in virtual vs in-office rheumatology visits

Yasmin Khader[1], Rocio Bautista Sanchez[2], Arati Kelekar[2], Marianne Kerski[2], David Wallace[2], Olivia Dickinson[3], Shirley Cohen-Mekelburg[3], Bryant England[4], Joshua Baker[5], Grant Cannon[6], Daniel Clauw[7] and Beth Wallace[8], [1]University of Michigan/VA Ann Arbor, Ann Arbor, [2]VA Ann Arbor/University of Michigan, Ann Arbor, [3]VA Ann Arbor, Ann Arbor, [4]University of Nebraska Medical Center, Omaha, NE, [5]University of Pennsylvania, Philadelphia, PA, [6]University of Utah and Salt Lake City VA, Salt Lake City, UT, [7]University of Michigan, Whitmore Lake, MI, [8]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0175–0198) Health Services Research Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: RA requires resource-intense management, with a joint exam recommended every 3-6 months to monitor disease activity. Frequent in-person visits are burdensome for patients and exacerbate access issues, contributing to long wait times and suboptimal care. Up to half of RA patients receive virtual rheumatology care, which can improve access and treatment adherence when added to office care. We know little about virtual care practices of RA management and how they compare to in-office practices. We aim to compare documentation of disease activity measure (DAM) assessment and treatment changes at virtual vs in-office RA visits in a large academic health system.

Methods: We conducted a retrospective cross-sectional study of a convenience sample of RA patients seen at University of Michigan rheumatology clinic from 2021-2024. We required a) a documented RA diagnosis in a clinical note by an attending rheumatologist during the study period, b) ≥1 office and ≥1 virtual visit during the study period to limit selection bias by

Table 1: Characteristics of the study cohort, stratified by virtual care utilization (ratio of virtual rheumatology visits to all rheumatology visits)

	Low virtual care (≤0.33)	High virtual care (>0.33)	p value
N	31	33	–
Rheumatology visits, median (IQR)	5 (4-5)	5 (3-6)	0.36
In-person	**4 (3-5)**	**2 (2-4)**	**<0.0001**
Virtual	**1 (1-1)**	**2 (1-3)**	**<0.0001**
Age, mean (SD) years	69.3 (9.5)	69.2 (12.5)	0.87
Phone contacts with rheumatology, median (IQR)	20 (7-40)	19 (7-36)	0.59
Other concurrent autoimmune disease, N (%)	**3 (9.7)**	**6 (18.1)**	**0.004**
Distance to rheumatologist, median (IQR) miles	12.3 (6.3-19.2)	11.4 (7.5-18.7)	0.08
RA duration, median (IQR) years	**14 (9-28)**	**21 (11-33)**	**0.0002**
Seropositive, N (%)	**25 (80.7)**	**29 (87.9)**	**<0.0001**
Erosive, N%	**10 (32.2)**	**6 (18.1)**	**0.03**
Fibromyalgia diagnosis, N(%)	**1 (3.2)**	**3 (9.0)**	**<0.0001**
Disease activity measures, mean (SD)*			
TJC	0.9 (1.8)	0.7 (2.4)	0.72
SJC	0.8 (1.4)	0.5 (1.3)	0.47
ESR	24.6 (20.6)	21.0 (20.6)	0.33
CRP	1.4 (3.6)	0.8 (1.7)	0.15
Rheumatologist seen, N (%)			
Attending 1	4 (12.9	5 (15.2)	0.73
Attending 2	15 (48.4)	14 (42.4)	0.60
Attending 3	13 (41.9)	16 (48.5)	0.60
Treatment during study period, N (%)			
No DMARD	2 (6.5)	3 (9.1)	0.69
Methotrexate	18 (58.1)	18 (54.5)	0.77
TNF inhibitor	17 (54.8)	10 (30.3)	0.05
Non-TNF biologic or JAKi	7 (22.6)	8 (24.2)	0.87
Opioids	5 (16.1)	7 (21.2)	0.60
Any GC	11 (35.5)	7 (21.2)	0.20
Long-term GC	7 (22.6)	6 (18.2)	0.27

*Patient and provider global assessments and HAQ not presented due to missingness

TJC: tender joint count; SJC: swollen joint count; PtGA: patient global assessment; ProvGA: provider global assessment; GC: glucocorticoid

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Virtual and office disease activity and treatment change documentation, stratified by treating rheumatologist

		Attending 1	Attending 2	Attending 3	p value
Mean (SD) virtual care frequency		0.35 (0.19)	0.30 (0.14)	0.36 (0.18)	0.24
Virtual visits	Number of visits	20	38	53	--
	Any DAM, N(%)	10 (50.0)	24 (63.2)	36 (67.9)	0.36
	TJC	0 (0)	12 (31.5)	0 (0)	0.006
	SJC	0 (0)	11 (28.9)	0 (0)	0.015
	PtGA, ProvGA, or HAQ	0 (0)	0 (0)	0 (0)	
	ESR or CRP	8 (40.0)	21 (55.3)	36 (67.9)	0.09
	Mean (SD) TJC*	0 (0)	0.4 (0.8)	0(0)	0.48
	Mean (SD) SJC*	0(0)	0.4 (0.8)	0(0)	0.59
	Mean (SD) ESR, mm/h	23.6 (10.1)	28.6 (16.6)	18.9 (22.5)	0.22
	Mean (SD) CRP, mg/dL	2.7 (6.3)	0.7 (0.8)	1.4 (3.8)	0.41
	Any treatment change, N (%)	**9 (45.0)**	**10 (26.3)**	**9 (17.0)**	**0.003**
	Change in DMARD	**8 (40.0)**	**4 (7.6)**	**9 (23.6)**	**0.004**
	Change in GC	**5 (25.0)**	**3 (7.9)**	**1 (1.8)**	**0.005**
Office visits	Number of visits	37	91	91	--
	Any DAM, N(%)	**34 (91.9)**	**88 (96.7)**	**77 (84.6)**	**0.018**
	TJC	**32 (86.5)**	**83 (91.2)**	**62 (68.1)**	**<0.0001**
	SJC	**32 (86.5)**	**83 (91.2)**	**62 (68.1)**	**<0.0001**
	PtGA, ProvGA, or HAQ	**1 (2.7)**	**0 (0)**	**0 (0)**	**<0.0001**
	ESR or CRP	**15 (40.5)**	**65 (71.4)**	**44 (48.3)**	**0.001**
	Mean (SD) TJC*	**3.2 (4.6)**	**0.6 (1.4)**	**0.08 (0.32)**	**<0.0001**
	Mean (SD) SJC*	**1.75 (2.3)**	**0.4 (1.50**	**0.3 (1.3)**	**0.0002**
	Mean (SD) ESR	26.1 (16.8)	25.0 (19.1)	18.9 (14.3)	0.18
	Mean (SD) CRP	2.0 (5.6)	0.8 (1.1)	0.8 (1.0)	0.14
	Any treatment change, N (%)	**17 (45.9)**	**21 (23.0)**	**20 (22.0)**	**0.013**
	Change in DMARD	**12 (32.4)**	**14 (15.4)**	**13 (14.3)**	**0.038**
	Change in GC	7 (18.9)	9 (9.9)	8 (8.8)	0.229

TJC: tender joint count; SJC: swollen joint count, PtGA: patient global assessment, ProvGA: provider global assessment, HAQ: health assessment questionnaire; GC: glucocorticoid

disease activity/severity. We extracted patient- and visit-level data from the electronic medical record using a standardized collection form. We used descriptive statistics to evaluate a) patient-level characteristics stratified by virtual care utilization (at/below vs above the mean ratio of virtual to total visits), b) visit-level documentation of disease activity measures (DAMs) and DMARD or glucocorticoid (GC) changes.

Results: We reviewed 330 visit notes (111 virtual, 219 office) for 64 RA patients seen by 3 rheumatology attendings during the study period. At the patient level, median (IQR) office and virtual visit counts were 1 (1-2) and 4 (2-4) respectively (Table 1). Mean (SD) virtual care utilization was 0.34 (0.16) and similar across attendings. Demographics and rheumatology clinic contact were similar across levels of virtual care utilization. Patients with higher virtual care utilization had higher rates of fibromyalgia (3.2 vs 9.0%, $p < 0.0001$), seropositivity (80.7 vs 87.9%, $p < 0.0001$), RA duration (median 14 vs 21 years, p 0.0002), and TNF inhibitor use (54.8 vs 30.3%, p 0.05).

All attendings were less likely to document DAMs at virtual vs. office visits ($p < 0.0001$) (Table 2). Patient-reported DAM documentation was low in both settings (total N = 1). We saw significant between-provider differences in joint count documentation at both virtual and office visits, inflammatory marker and treatment change documentation at virtual visits (p 0.004 DMARD, 0.005 GC), and DMARD change documentation at office visits (P 0.038). Attending 3 was less likely to change treatment at virtual vs in-office visits (p 0.05); documentation was consistent across settings for attendings 1 and 2 (all $p \geq 0.1$).

Conclusion: In a sample of RA patients seen both virtually and in-office, we saw variation in DAM and treatment change documentation a) between settings across attendings, b) across attendings in each setting. Patient-reported DAM collection was low overall. Further work is needed to confirm these findings, and to develop and test provider-facing interventions to improve DAM collection and treatment optimization in the virtual setting.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Y. Khader: None; **R. Bautista Sanchez**: None; **A. Kelekar**: None; **M. Kerski**: None; **D. Wallace**: None; **O. Dickinson**: None; **S. Cohen-Mekelburg**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Baker**: Amgen, 5; **G. Cannon**: None; **D. Clauw**: AbbVie/Abbott, 2, Allergan Sales LLC, 2, Aptinyx, Inc, 2, Eli Lilly, 2, H. Lundbeck A/S, 2, Heron Therapeutics, Inc, 2, Neumentum, Inc, 2, Pfizer, 12, 2, Regeneron Pharmaceuticals, Inc, 2, Samumed, LLC, 2, Swing Therapeutics, Inc, 2, Tonix Pharmaceuticals, Inc, 2, Virios Therapeutics, Inc, 2; **B. Wallace**: None.

Abstract Number: 0199

Pain Phenotypes and Social Determinants of Health in Chronic Chikungunya Arthritis: A Cross-Sectional Study

Abebawork Adem[1], Alfonso Sucerquia[2], Jose Forero[3], Juan Alzate[2], Larry Moreland[4], Gary Firestein[5], Andres Cadena[6] and Aileen Chang[7], [1]George Washington University, Washington, DC, DC, [2]The George Washington University, Arlington, [3]The George Washington University, Arlington, VA, [4]University of Colorado, Denver, CO, [5]University of California, San Diego, San Diego, CA, [6]Clinica de la Costa, Barranquilla, Colombia, [7]The George Washington University, Washington

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0199–0209) Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic chikungunya arthritis (CCA) is a long-term sequela of chikungunya virus infection marked by persistent pain, disability, and reduced quality of life. While nociplastic, neuropathic and nociceptive pain types have been described in other diseases, they remain understudied in CCA. This study aimed to classify pain phenotypes and evaluate clinical and social determinants associated with each phenotype among individuals with CCA.

Methods: We conducted a cross-sectional analysis of 117 participants enrolled in a clinical trial for CCA in an underserved population. Pain types were categorized using the PainDETECT Questionnaire and the Nociplastic-Based Fibromyalgia Features (NFF) tool. Disease activity and function were assessed using the Chikungunya Disease Activity Score (CHIK-DAS), Disease Activity Score-28 (DAS-28), Health Assessment Questionnaire (HAQ), and arthritis flare score. Social determinants

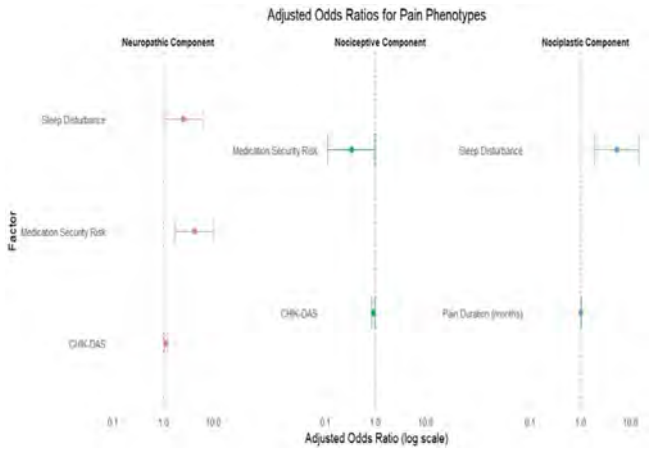


Figure 1. Adjusted Odds Ratios (AORs) for Factors Associated with Pain Phenotypes in Chronic Chikungunya Arthritis. Forest plot showing multivariable-adjusted associations between clinical and social factors and the presence of neuropathic, nociceptive, and nociplastic pain components. Odds ratios are plotted on a log scale with 95% confidence intervals. Medication insecurity and higher CHIK-DAS scores were significantly associated with neuropathic pain, while nociplastic pain was linked to longer pain duration and sleep disturbance. Nociceptive pain was inversely associated with CHIK-DAS and medication security risk.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of health (SDOH) were measured using a validated 10-item instrument. Bivariate analyses and multivariable logistic regression were used to examine associations between pain phenotypes and clinical/SDOH variables.

Results: Participants were predominantly female (78.6%), with a median age of 58 years and a median pain duration of 8.6 years. Nociplastic pain was the most prevalent phenotype (79.5%), followed by neuropathic (48.7%) and nociceptive (25.6%) pain. Nociplastic pain was significantly associated with longer pain duration (aOR = 1.02, 95% CI: 1.00–1.04) and sleep disturbance (aOR = 5.27, 95% CI: 1.92–14.44). Neuropathic pain was linked to higher disease activity (aOR = 1.12, 95% CI: 1.03–1.21), sleep disturbance (aOR = 2.47, 95% CI: 1.02–5.96), and medication insecurity (aOR = 4.17, 95% CI: 1.69–10.27). Nociceptive pain was inversely associated with CHIK-DAS (aOR = 0.91, 95% CI: 0.84–0.98) and less frequent among participants with medication insecurity (aOR = 0.33, 95% CI: 0.11–0.96) (Figure 1). Clinical burden was highest in those with nociplastic pain, while social vulnerability was more prominent in those with neuropathic components.

Conclusion: Pain in CCA is multidimensional, with nociplastic and neuropathic phenotypes predominating and associated with greater disease activity and functional impairment. Medication insecurity and sleep disturbance were key predictors of neuropathic pain, while nociplastic pain appeared more driven by chronicity and central sensitization. Incorporating SDOH screening and phenotype-specific assessments like CHIK-DAS may improve pain management strategies in post-viral arthritis.

Disclosure: A. Adem: None; **A. Sucerquia**: None; **J. Forero**: None; **J. Alzate**: None; **L. Moreland**: None; **G. Firestein**: Eli Lilly, 5; **A. Cadena**: None; **A. Chang**: None.

Abstract Number: 0200

Severe infections and malignancies in patients with cranial and extracranial giant cell arteritis treated with tocilizumab. National multicenter study of 471 patients of clinical practice

Adrian Martin-Gutierrez[1], Javier Loricera[2], Vicente Aldasoro Cáceres[3], Olga Maiz[4], Eugenio de Miguel[5], Eva Galíndez Agirregoikoa[6], Ivan Ferraz Amaro[7], Santos Castañeda[8] and Ricardo Blanco[9], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Piélagos, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Hospital Universitario de Navarra, Pamplona, Spain, [4]Hospital Universitario de Donosti, Donostia, Spain, [5]Hospital Universitario La Paz, Madrid, Spain, [6]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [7]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [8]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [9]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Infections and malignancies are two of the most feared side effects of biologic therapies. Giant cell arteritis (GCA) is a vasculitis which affects older people in whom the risk of infection and malignancies is higher.

Our aim was to assess severe infections and malignancies that occurred during the follow-up of a series of patients with (GCA) treated with tocilizumab (TCZ).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	All series (n=471)	cGCA (n=217)	ecGCA (n=80)	mixGCA (n=174)	cGCA vs ecGCA p-value	cGCA vs mixGCA p-value	ecGCA vs mixGCA p-value
Infections (EAIR/100 PY)	6.4	10.1	2.4	3.9	**0.0015**	**0.0021**	0.4092
Infections, n (%)	63 (13.4)	44 (20.3)	3 (3.7)	16 (9.2)	**0.005**	**0.004**	0.59
Urinary tract infection	14 (3.0)	10 (4.6)	0 (0)	4 (2.3)	0.067	0.28	0.31
Bacteremia/sepsis	9 (1.9)	5 (2.3)	1 (1.2)	3 (1.7)	0.99	0.99	0.99
Varicella zoster virus infection	6 (1.3)	4 (1.8)	0 (0)	2 (1.1)	0.56	0.70	0.99
Pneumonia	6 (1.3)	5 (2.3)	1 (1.2)	0 (0)	0.99	0.070	0.32
Upper respiratory tract infection	5 (1.1)	4 (1.8)	0 (0)	1 (0.6)	0.58	0.39	0.99
Cellulitis	5 (1.1)	3 (1.4)	0 (0)	2 (1.1)	0.57	0.99	0.99
Abscess	4 (0.8)	2 (0.9)	1 (1.2)	1 (0.6)	0.99	0.99	0.54
COVID-19	4 (0.8)	4 (1.8)	0 (0)	0 (0)	0.58	0.13	-
Septic arthritis	2 (0.4)	2 (0.9)	0 (0)	0 (0)	0.99	0.51	-
Osteomyelitis	2 (0.4)	1 (0.4)	0 (0)	1 (0.6)	0.99	0.99	0.99
Septic bursitis	1 (0.2)	1 (0.4)	0 (0)	0 (0)	0.99	0.99	-
Meningitis	1 (0.2)	1 (0.4)	0 (0)	0 (0)	0.99	0.99	-
Pyelonephritis	1 (0.2)	1 (0.4)	0 (0)	0 (0)	0.99	0.99	-
Pericarditis due to *Lysteria*	1 (0.2)	1 (0.4)	0 (0)	0 (0)	0.99	0.99	-
Candidiasis	1 (0.2)	0 (0)	0 (0)	1 (0.6)	-	0.44	0.99
Cytomegalovirus infection	1 (0.2)	0 (0)	0 (0)	1 (0.6)	-	0.19	0.99
Neoplasia per 100 patients-year	0.4	0.4	0	0.6	-	0.8580	
Neoplasia, n (%)	4 (0.8)	2 (0.9)	0 (0)	2 (1.1)	0.99	0.99	0.99

TABLE. Severe infections and malignancies documented in the 471 GCA patients treated with tocilizumab.

Methods: Multicentre study of 471 patients diagnosed with GCA and treated with TCZ. The diagnosis of GCA was performed between 2014 and 2020 according to: a) 1990 ACR criteria, b) temporal artery biopsy, and/or **c)** imaging evaluation techniques. Rate of infections and malignancies are expressed as the exposure-adjusted incidence rate (EAIR) per 100 person years (PY).

Results: We studied 471 patients (342 women; mean age, 74±9 years) treated with TCZ. The phenotypic distribution was: cranial GCA (cGCA) (n=217; 46%), mixed GCA (mixGCA) (n=174; 37%), and extracranial GCA (ecGCA) (n=80; 17%).

After 25.3±21.7 months of follow-up, 63 (13.4%) patients had severe infections (6.4 EAIR/100 PYs), which were more frequent in cGCA (n=44; 20.3%) **(Table)**. The most frequent infections were: urinary tract infection (n=14; 3%), bacteriemia/sepsis (n=9; 1.9%), varicella zoster virus infection (n=6; 1.3%), pneumonia (n=6; 1.3%), upper respiratory tract infection (n=5; 1.1%), cellulitis (n=5; 1.1%), abscess (n=4; 0.8%), septic arthritis (n=2; 0.4%), osteomyelitis (n=2; 0.4%), septic bursitis (n=1; 0.2%), meningitis (n=1; 0.2%), pyelonephritis (n=1; 0.2%), pericarditis due to *Lysteria* (n=1; 0.2%), candidiasis (n=1; 0.2%), and *Cytomegalovirus* infection (n=1; 0.2%).

Four (0.8%) patients developed a neoplasia (0.4 EAIR/100 PYs). The most frequent malignancies were: bladder cancer (n=1), colon cancer (n=1), lung cancer (n=1), and myelodysplastic syndrome (n=1).

Conclusion: In this wide series of TCZ in GCA of clinical practice, although TCZ is a relatively safe therapy in GCA, in our series, severe infections were observed in a non-negligible percentage rate of patients, being more frequent in cGCA. Neoplasms were rarer.

Disclosure: A. Martin-Gutierrez: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **V. Aldasoro Cáceres**: None; **O. Maiz**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **E. Galíndez Agirregoikoa**: None; **I. Ferraz Amaro**: None; **S. Castañeda**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0201

Real-World study of immunogenicity and safety of the adjuvant recombinant vaccine against varicella zoster virus in patients with immune-mediated inflammatory diseases treated with Janus Kinase Inhibitors in comparison with healthy individuals

Ana Victoria Esteban Vázquez[1], Martina Steiner[2], Cristina Vergara[2], Elisabet Castañeda Estavez[3], Maria Beatriz Paredes Romero[4], Isabel De La Camara-Fernandez[1], Laura Trives[1], Tatiana Cobo[1], Patricia Richi[5], Maria liz Romero[5], Marta De San Segundo[3], Antonio Sanchis[3], Carolina Marín[6], Maria Teresa Navio Marco[7] and Santiago Muñoz[1], [1]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Spain, [2]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Madrid, Spain, [3]Hospital Universitario Infanta Sofía, Madrid, Spain, [4]Infanta Sofia University Hospital, Madrid, Spain, [5]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, San Sebastian de Los Reyes, Madrid, Spain, [6]Department of Rheumatology, Hospital Universitario Infanta Leonor / Universidad Complutense de Madrid, Madrid, Spain, Madrid, Spain, [7]Infanta Leonor Universitary Hospital, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0199–0209) Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with immune-mediated inflammatory diseases (IMIDs) receiving Janus Kinase Inhibitors (JAKi) are at increased risk of herpes zoster reactivation. The adjuvanted recombinant zoster vaccine (HZ/su) was recently approved in Europe; however, IMID patients were not included in the pivotal clinical trials. This study presents the largest real-world analysis of the immunogenicity and safety of HZ/su in IMID patients, compared to healthy controls.

Methods: We conducted a prospective, multicenter cohort study in Madrid, Spain, between March 2022 and March 2025. Vaccine response was defined as a fourfold or greater increase in antibody titers at follow-up compared to pre-vaccination levels, in line with clinical trial criteria.

Results: A total of 93 IMID patients and 107 healthy controls were enrolled. The mean age was 54 ± 10 years in the patient group and 61.8 ± 1.5 years among controls. Previous herpes zoster reactivation was reported in 9% of participants. A humoral immune response was observed in 51.4% of healthy controls, compared to 30% of patients. Immunogenicity was not influenced by other factors, including concomitant treatment with methotrexate, prednisolone, or the treatment line. No serious adverse events or major disease flares were reported.

Conclusion: IMID patients receiving JAKi therapy showed a reduced immunogenic response to the HZ/su vaccine compared to healthy individuals, likely influenced by concurrent immunosuppression. The vaccine was well tolerated, with a very low rate of adverse events. These findings support a strong recommendation for HZ/su vaccination in this vulnerable patient population, and advocate for varicella zoster vaccination prior to starting JAKi treatment.

Disclosure: A. Esteban Vázquez: None; **M. Steiner**: None; **C. Vergara**: None; **E. Castañeda Estavez**: None; **M. Paredes Romero**: None; **I. De La Camara-Fernandez**: None; **L. Trives**: None; **T. Cobo**: None; **P. Richi**: None; **M. Romero**: None; **M. De San Segundo**: None; **A. Sanchis**: None; **C. Marín**: None; **M. Navio Marco**: None; **S. Muñoz**: Janssen, 1, 2, 5, 6, 7.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0202

Saudi Society for Rheumatology Consensus Recommendation on Vaccination Strategies in Adults Saudi with Autoimmune Rheumatic Disorders

Fahidah Alenzi[1], Hanan Alrayes[2], Khawla K Alghanim[3], FEHAID ALANAZI[4], Mohammed Attar[5], Mansour Alazmi[6], Suzan Attar[7], Nisreen Alsherbeeni[8], Azzam Alotaibi[9] and Fayssal M Farahat[10], [1]Associate Professor and Consultant Rheumatology, Department of Internal Medicine, College of Medicine, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia, Riyadh, Saudi Arabia, [2]Riyadh Military - Prince Soltan Military Medical City (PSMMC) - Olaya, Riyadh, Saudi Arabia, [3]Consultant Rheumatologist and lupus specialist, Department of Internal Medicine, Rheumatology Unit, King Fahad Military Medical Complex, Dhahran, Saudi Arabia, Dhahran, Saudi Arabia, [4]King Khaled university Hospital, Riyadh, Saudi Arabia, [5]Al hada armed forces hospital, Taif, Saudi Arabia, [6]Internal Medicine and Rheumatology Consultant , Prince Mohammed Medical City, Aljouf , Saudi Arabia, Sakaka- Aljouf, Saudi Arabia, [7]King Abdulaziz University, Saudi Arabia, Jeddah, Saudi Arabia, [8]Consultant Internal Medicine & Infectious Disease, Infectious Disease Division Department of Medicine at Prince Sultan Military Medical City, Riyadh, Saudi Arabia, [9]Consultant Internal Medicine, Allergy, and Immunology, Division of Allergy and Immunology, Department of Medicine at Prince Sultan Military Medical City, Riyadh, Saudi Arabia, [10]Infection Prevention and Control Program, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, P.O. Box 22490, Riyadh 11426, Saudi Arabia; College of Public Health and Health Informatics, King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, P.O. Box 3660, Riyadh 11481, Saudi Arabia; King Abdullah International Medical Research Center, Ministry of National Guard Health Affairs, P.O. Box 3660, Riyadh 11481, Saudi Arabia, Riyadh, Saudi Arabia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0199–0209) Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with autoimmune inflammatory rheumatic diseases (AIIRD) are at increased risk of infections due to both immune system dysfunction and the use of immunosuppressive therapies. Vaccination is a key preventive strategy to reduce infection-related morbidity and mortality in this population. This study aimed to develop evidence-based vaccination recommendations for adults with AIIRD in Saudi Arabia, based on international guidelines (ACR, EULAR, CDC, WHO), current literature on vaccine safety and efficacy, and expert consensus. The recommendations address vaccine timing, safety, and immunogenicity, covering both live and non-live vaccines, and emphasize a personalized approach that balances optimal protection with the risk of disease flares and treatment considerations.

Methods: A Delphi consensus method was used to develop expert-based vaccination recommendations for patients with AIIRD. A multidisciplinary panel comprising rheumatology, infectious disease, and immunology specialists participated in a structured, three-round process. This included an initial open-ended survey, followed by quantitative rating of statements on a 10–100 scale, with ≥70% agreement required to establish consensus. Statements not reaching consensus were revised and re-evaluated. Data collection was conducted via Word documents and Google Sheets, and both online and in-person meetings supported iterative discussion and finalization of recommendations.

Results: A review of current literature and consensus guidelines revealed that inactivated influenza vaccination is safe and generally effective in patients with AIIRD, even while receiving immunosuppressive therapy. Patients on methotrexate demonstrated improved vaccine immunogenicity when the drug was withheld for 1–2 weeks post-vaccination, without a significant increase in disease flares. For those on rituximab, delaying therapy for at least 2 weeks after vaccination may enhance immune response if disease activity permits. Vaccination is strongly recommended for patients on prednisone ≤10 mg/day and conditionally recommended at higher doses due to potentially reduced efficacy. Use of TNF inhibitors and JAK inhibitors did not significantly impair immune responses, supporting vaccine administration without treatment interruption. Despite

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

modest reductions in immunogenicity in certain subgroups, partial protection remains clinically beneficial, reinforcing the importance of annual influenza vaccination in our population.

Conclusion: Vaccination plays a vital role in reducing infection-related risks in patients with AIIRD. We present comprehensive recommendations aligned with international guidelines, highlighting the preference for non-live vaccines, the contraindication of live vaccines in immunosuppressed patients, and the importance of individualized vaccination plans. It underscores the need to enhance physician awareness and patient education to improve vaccine uptake and calls for future research to optimize vaccine responses and expand immunization strategies in Saudi population.

Disclosure: F. Alenzi: None; **H. Alrayes**: None; **K. Alghanim**: None; **F. ALANAZI**: None; **M. Attar**: None; **M. Alazmi**: None; **S. Attar**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 5, 6, Gilead, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Hikma, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Organon, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Sandoz, 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6; **N. Alsherbeeni**: None; **A. Alotaibi**: None; **F. Farahat**: None.

Abstract Number: 0203

Risk Factors for Cytomegalovirus Infection in Patients Receiving Prolonged High-Dose Corticosteroids for Rheumatic Diseases: A Retrospective Cohort Study

Sung Ik Cho[1], Jin Kyun Park[2], **Hee Won Cho**[3], Eun Young Lee[4], Eun Bong Lee[1] and Jun Won Park[1], [1]Seoul National University Hospital, Seoul, South Korea, [2]Seoul National University College of Medicine, Jongno-gu, Seoul, South Korea, [3]Seoul National University, Seoul, Seoul-t'ukpyolsi, Republic of Korea, [4]Seoul National University College of Medicine, Seoul, South Korea

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cytomegalovirus (CMV) infection is a well-recognized complication in immunocompromised individuals, yet there islimited evidence guiding surveillance strategies in patients with rheumatic diseases on immunosuppressants. This study aimed to identify risk factors for CMV infection and define a high-risk subgroup warranting active screening among patients receiving prolonged, high-dose glucocorticoids.

Methods: We retrospectively analyzed 2,343 patients with rheumatic diseases who received ≥30 mg/day of prednisolone-equivalent glucocorticoids for ≥28 consecutive days at nationwide tertiary referral centers in South Korea. Clinical, laboratory, and immunosuppressant data were collected during a 28-day lead-in period from the high-dose glucocorticoid initiation. The observation period was one year following the lead-in period. Quantitative CMV PCR or pp65 antigenemia tests were performed at the discretion of the treating physician. Cox proportional hazard model was used to identify independent predictors of 1-year CMV infection. Kaplan–Meier curves were used to present a CMV infection-free survival by risk group.

Results: During the follow-up of 2131 person-years, 223 (9.7%) patients underwent CMV testing. Of these, 104 (46.6%) were diagnosed with CMV infection, and 33 (31.7%) of them met criteria for CMV disease. Multivariable analysis identified female sex (HR 0.53 [95% CI 0.33–0.83]), Sjögren's syndrome (HR 3.17[1.35–7.44]), hypertension (HR 1.66 [1.10–2.51]), diabetes (HR 1.96 [1.29–2.98]), interstitial lung disease (HR 3.21 [2.09–4.92]), renal impairment (azotemia: HR 2.02 [1.27–

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Univariable and Multivariable Cox Regression Analyses of Risk Factors for CMV Infection Abbreviations: AAV, ANCA associated vasculitis; IIM, Idiopathic inflammatory myopathy; IPAF, interstitial pneumonia with autoimmune features; SLE, Systemic Lupus erythematosus; AST, aspartate aminotransferase; * Included variables with significant association in the univariable analysis. Final variable selection was performed using backward selection based on AIC † Anemia defined as Hb < 8 g/dL; leukopenia as WBC < 800/μL; thrombocytopenia as PLT < 150 × 10^3/μL. ‡ Removed from the final model based on variable selection process § HR and 95% CI was not calculated due to complete separation of the outcome. ¶ Cumulative steroid dose (based on prednisone) administered over the 6 months prior to index date. £ Lymphocyte-targeting immunosuppressants include tacrolimus, cyclosporine, and mycophenolate mofetil.

Variable	Univariable HR (95% CI)	Univariable P	Multivariable HR (95% CI)	Multivariable P
Sex : Female	0.50 (0.32–0.77)	0.002	0.53 (0.33 - 0.83)	0.006
Age ≥ 60	1.64 (1.10–2.44)	0.015	‡	
AAV	1.29 (0.72–2.31)	0.387		
Adult Onset Still Disease	0.64 (0.20–2.02)	0.447		
Bechet's Disease	0.19 (0.05–0.75)	0.018	‡	
IIM	1.21 (0.73–1.99)	0.457		
IPAF	2.09 (0.91–4.75)	0.081		
Rheumatoid Arthritis	0.93 (0.30–2.94)	0.903		
Sjogren's Syndrome	2.73 (1.20–6.23)	0.017	3.17 (1.35 - 7.44)	0.008
SLE	1.33 (0.89–1.99)	0.162		
Systemic Sclerosis	1.88 (0.60–5.92)	0.282		
Other Rheumatic Disease	0.75 (0.18–3.02)	0.680		
Disease Duration (years)	1.04 (1.01–1.08)	0.006	‡	
Hypertension	2.55 (1.73–3.77)	<0.001	1.66 (1.10 - 2.51)	0.016
Diabetes	2.46 (1.66–3.66)	<0.001	1.96 (1.29 - 2.98)	0.002
Azotemia, non-dialysis	2.36 (1.54–3.62)	<0.001	1.80 (1.14 - 2.86)	0.012
Hemodialysis	10.77 (6.08–19.07)	<0.001	6.16 (3.08 - 12.32)	<0.001
Liver Cirrhosis	2.43 (0.90–6.61)	0.081	‡	
Interstitial Lung Disease	2.95 (1.98–4.39)	<0.001	3.21 (2.09 - 4.92)	<0.001
Prior Solid Organ Transplantation	12.59 (3.99–39.70)	<0.001	8.79 (2.60 - 29.75)	<0.001
Starting Steroid Dose (mg)	1.00 (1.00–1.01)	0.483		
Prior Steroid Use (mg)¶	1.00 (1.00–1.00)	0.979		
Steroid Pulse	2.12 (1.39–3.22)	<0.001	‡	
Lymphocyte-targeting IS£	2.73 (1.84–4.06)	<0.001	2.49 (1.62 - 3.83)	<0.001
Oral Cyclophosphamide	1.24 (0.51–3.05)	0.639		
IV Cyclophosphamide	2.58 (1.59–4.21)	<0.001	‡	
Rituximab	3.53 (2.07–6.02)	<0.001	2.18 (1.21 - 3.92)	0.009
Lymphopenia †	2.51 (1.69–3.72)	<0.001	1.87 (1.21 –2.89)	0.005
Anemia †	5.33 (3.24–8.77)	<0.001	3.04 (1.75 - 5.30)	<0.001
Thrombocytopenia †	2.39 (1.58–3.61)	<0.001	2.06 (1.29 - 3.31)	0.003
AST	1.00 (1.00–1.00)	0.643		
Total Bilirubin	0.93 (0.62–1.39)	0.714		
Total Protein	0.64 (0.55–0.75)	<0.001	‡	
Albumin	0.50 (0.38–0.65)	<0.001	‡	

3.21]; hemodialysis: HR 53.79 [1.84–7.81]), previous solid organ transplantation (HR 14.43 [5.44–38.31]), use of lymphocyte-targeting immunosuppressants (HR 2.16 [1.39–3.35]), rituximab (HR 2.02 [1.11–3.68]), leukopenia (lymphocyte < 800/μL; HR 1.96 [1.25–3.07]), anemia (Hb < 8 g/dL; HR 3.10 [1.76–5.46]), and thrombocytopenia (platelet< 150k; HR 1.68 [1.04–2.73]) as independent risk factors (Table 1). The final model demonstrated strong discriminatory performance with AUCs ranging from 0.799 to 0.891 throughout the follow-up period. High-risk patients identified by the model showed a significantly higher incidence of CMV infection than those in the low-risk group (HR 14.82 [9.687 – 22.67]) (Figure 1). Of 34 CMV disease cases, 11 (32.4%) died within one year. Disease risk was significantly associated with lymphopenia and elevated CMV titers (antigenemia >10 or PCR >1000).

Conclusion: This risk stratification model identifies patients at increased risk for CMV infection who may benefit from active surveillance. Prospective validation is needed to optimize CMV monitoring strategies in this high-risk population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

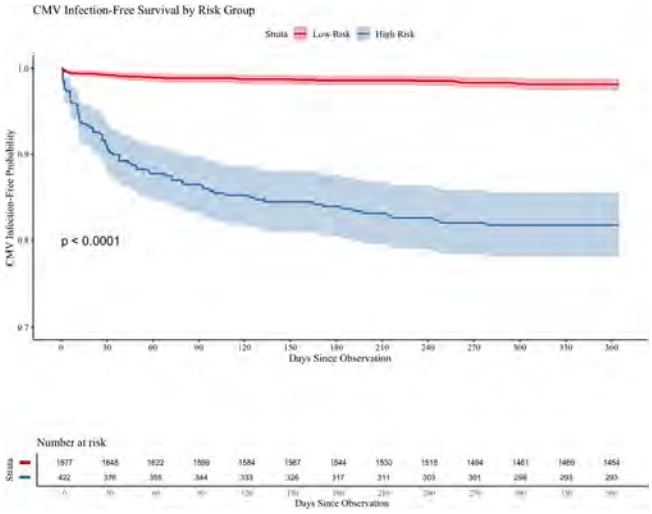


Figure 1. Kaplan–Meier estimates of CMV infection–free survival by predicted risk group. Risk stratification was based on a multivariable Cox proportional hazards model incorporating female sex, Sjögren's syndrome, hypertension, diabetes, interstitial lung disease, renal impairment (azotemia or hemodialysis), prior solid organ transplantation, lymphocyte-targeting immunosuppressants, rituximab, leukopenia (lymphocytes <800/μL), anemia (hemoglobin <8 g/dL), and thrombocytopenia (platelets <150×10^3/μL). Time zero represents 28 days after initiation of high-dose corticosteroids (lead-in period). Shaded bands indicate 95% confidence intervals. Log-rank test $p < 0.001$.

Disclosure: S. Cho: None; **J. Park**: None; **H. Cho**: None; **E. Lee**: IMbiologics, 1, Samsung Bioepis, 5; **E. Lee**: None; **J. Park**: Samsung Bioepis, 5.

Abstract Number: 0204

Immunogenicity and safety summary for the chikungunya virus-like particle vaccine development programme

Lauren Tindale[1], Jason Richardson[1], Deborah Anderson[1], Jason Mendy[2], Sufia Muhammad[2], Tobi Loreth[1], Victoria Jenkins[3], **Krystal Valenzuela**[4], Benedetto Simone[5], Patrick Ajiboye[2] and Lisa Bedell[4], [1]Bavarian Nordic Canada Inc., Toronto, Canada, [2]Bavarian Nordic, Inc., San Diego, [3]Bavarian Nordic Belgium, Brussels, Belgium, [4]Bavarian Nordic, Inc., Durham, [5]Bavarian Nordic Berna GmbH, Thoerishaus, Switzerland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chikungunya virus (CHIKV) is a threat to public health and a risk for travellers to endemic countries. Typical acute symptoms include fever, arthralgia, myalgia, fatigue, and headache. Debilitating arthralgias may persist for months or years. We report aggregated safety and immunogenicity data from five clinical trials for a CHIKV virus-like particle (VLP) vaccine, which has been approved for use by the US FDA in February 2025.

Methods: To date, the CHIKV VLP vaccine development programme has included three phase 2 and two phase3 trials across multiple sites in the US, which enrolled participants 12 to 95 years of age. Participants received a single dose of CHIKV VLP vaccine or placebo. The safety population included 3141vaccinated and 675 placebo participants from five trials and the immunogenicity evaluable population included 2829 vaccinated and 607 placebo participants from four trials. Immunogenicity was assessed by measuring CHIKV serum neutralising antibody (SNA) titres (NT80) at selected time points; SNANT80 ≥100 is the surrogate marker likely to predict protection. Immunogenicity and safety were assessed through Day 183 post vaccination.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Immunogenicity findings showed robust responses, with a seroresponse (SNA NT80 ≥100) as early as Day 8 (47%), peaking at Day 15 (96%) and Day 22 (97%; primary endpoint), and lasting through Day183 (85%).In phase 3 trials, the seroresponse rate and geometric mean titre was significantly higher in the vaccine group than the placebo group at all time points. CHIKV VLP vaccine demonstrated a favourable safety profile across trials. Most AEs were mild or moderate; events primarily consisted of injection site pain, headache, fatigue, and myalgia. Solicited and unsolicited events of arthralgia were reported at similar rates between vaccinated and placebo participants. SAEs occurred in < 1% of participants, with no vaccine-related deaths. Overall, no safety signals were detected.

Conclusion: CHIKV VLP vaccine offers a VLP-based vaccine option for immunisation against CHIKV disease. The data analysed demonstrate the strong immunogenicity and favourable safety profile of CHIKV VLP vaccine; rapid and durable SNA NT80 responses support the potential for this vaccine to protect individuals ≥12 years of age from disease caused by CHIKV.

Disclosure: L. Tindale: Bavarian Nordic, 3; **J. Richardson**: Bavarian Nordic, 3; **D. Anderson**: Bavarian Nordic, 3; **J. Mendy**: Bavarian Nordic, 2, 3; **S. Muhammad**: Bavarian Nordic, 3; **T. Loreth**: Emergent BioSolutions Inc., 12, stock holder; **V. Jenkins**: Bavarian Nordic, 3; **K. Valenzuela**: Bavarian Nordic, 3, Baxter, 3, Kaleo, 3; **B. Simone**: Bavarian Nordic, 3; **P. Ajiboye**: Bavarian Nordic, 3; **L. Bedell**: Bavarian-Nordic, 2, 7.

Abstract Number: 0205

Implementation of the *Varicella Zoster* virus vaccine and its Real-World effectiveness

Laura Mas Sanchez[1], ELENA GRAU GARCIA[2], Carlos Valera Ribera[3], Pablo Muñoz-Martínez[4], Daniel Ramos Castro[5], Alba Maria Torrat Noves[6], Belen Villanueva Manes[7], Iago Alcantara Álvarez[8], Miguel Simeo Vinaixa[9], Andres Perez Hurtado[10] and José Andrés Román Ivorra[11], [1]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [2]HUP La Fe, Valencia, Comunidad Valenciana, Spain, [3]Hospital Universitario Doctor Peset, Valencia, Spain, [4]Hospital Universitario y Politécnico La Fe, Sagunto, Spain, [5]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [6]Hospital Universitari i Politècnic La Fe de Valencia, Valencia, Spain, [7]Hospital La Fe, Valencia, Spain, [8]Hospital Universitari i Politècnic La Fe, Valencia, Spain, [9]Rheumatology Department. HUP La Fe, Valencia, Spain, [10]Hospital Universitario y Politècnico La Fe, Valencia, Comunidad Valenciana, Spain, [11]Hospital Universitari i Politècnic La Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In 2023, Spain approved the inactivated varicella zoster virus (VZV) vaccine in individuals over 50 years of age with immunosuppressive conditions, including rheumatology patients due to both immune system alterations and immunosuppressive therapies. It is anticipated that the proportion of vaccinated patients will increase in the coming years, resulting in fewer herpetic events and associated complications.

Our objective is to describe a population of rheumatology patients eligible for VZV vaccination and to analyze vaccination uptake and incidence of herpetic events.

Methods: We conducted a retrospective, observational, descriptive study of patients followed at a tertiary care Rheumatology Department. Between January 2021 and June 2024, patients were referred for vaccination prior to initiating biologic,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of patients

	Results, n (%) N=431
Female sex	285 (66.13)
Cardiovascular Risk Factors:	
Hypertension	104 (24.13)
Diabetes mellitus	33 (7.66)
Dyslipidemia	100 (23.2)
Mean follow-up time, years (SD)	10.81 ± 10.65
Mean age at treatment initiation, years (SD)	51.49 ± 13.81
Diagnosis:	
Rheumatoid Arthritis	147 (34.1)
Spondyloarthritis	98 (22.7)
Psoriatic Arthritis	82 (19)
Systemic Lupus Erythematosus	14 (3.2)
Seronegative Arthritis	13 (3)
Systemic Sclerosis	14 (3.2)
Juvenile Idiopathic Arthritis	7 (1.6)
Polymyalgia Rheumatica	8 (1.9)
Vasculitis	10 (2.3)
Uveitis	7 (1.6)
Others	31 (7.2)
Treatment initiated:	
Biologic therapies	233 (54.1)
Anti-TNF	109 (25.29)
Anti-IL17	43 (9.98)
Anti-IL6	24 (5.57)
Anti-CD20	19 (4.41)
Anti-IL23	16 (3.71)
Anti-CTLA4	13 (3.02)
Anti-BLyS	5 (1.16)
Anti-IFN tipo 1	3 (0.7)
Anti-IL1	1 (0.23)
JAKinib	89 (20.6)
Anti-PD4	6 (1.4)
Combination	2 (0.5)
Inmunosupressors	5 (1.2)
DMARDs	23 (5.3)
None	73 (16.9)
Vaccinated / Non vaccinated	171 (39.7) / 260 (60.3)

targeted synthetic, or immunosuppressive therapy. Demographic and clinical characteristics were recorded. A subanalysis of herpetic events and their incidence before and after the vaccine was performed.

Results: 431 patients (66.1% female) were referred for VZV vaccination, most commonly with Rheumatoid Arthritis (34.1%). The mean age at treatment initiation was 51.49 ± 13.81 years (Table 1). The most frequently initiated therapy was anti-TNF agents (25.29%), followed by JAK inhibitors (20.6%).

Of these, 171 patients (39.7%) received the VZV vaccine, primarily women with rheumatoid arthritis. Among vaccinated patients, JAK inhibitors were the most commonly initiated treatment (41.52%), with Upadacitinib used in 31 cases. The annual proportion of patients vaccinated against VZV increased from 10.87% in 2021 to 66.67% in 2024 (Figure 1).

29 herpetic events occurred in 23 patients, yielding an incidence of 0.06 events per patient over a mean follow-up of 10.81 years. Of these, 21 were women and 8 were receiving JAK inhibitors.

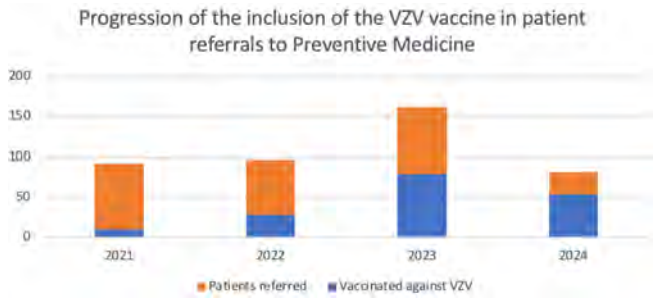


Figure 1. Annual Proportion of Patients Referred to Preventive Medicine Who Received VZV Vaccination.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Among vaccinated individuals, 22 herpetic events were recorded, with 18 occurring prior to vaccine administration and 4 events reported post-vaccination. The majority of herpetic episodes were cutaneous monometameric (60.7%), followed by multimetameric cutaneous involvement (10.7%).

The incidence of herpetic events in the vaccinated group was 0.02 events per patient (2.33% of vaccinated patients). In contrast, the incidence in unvaccinated patients was higher, at 0.05 events per patient (5.8% of the unvaccinated population).

Conclusion: 39.7% of patients referred for pre-biologic varicella zoster virus (VZV) vaccination received it, with uptake increasing progressively over the study period. The most frequent treatment initiated were JAK inhibitors.

29 herpetic events were documented in 23 patients, most of which were mild. Among these 23 patients, 18 had been vaccinated, with only 4 herpetic events occurring after vaccine administration.

The incidence of herpetic events among unvaccinated patients was 0.05 events per patient, corresponding to 5.8% of that subgroup. In contrast, the incidence in the vaccinated cohort was reduced to 0.02 events per patient, affecting 2.33% of vaccinated individuals. These findings support a potential protective role of VZV vaccination in reducing herpes zoster events in immunocompromised rheumatology patients.

Disclosure: L. Mas Sanchez: None; **E. GRAU GARCIA**: None; **C. Valera Ribera**: None; **P. Muñoz-Martínez**: None; **D. Ramos Castro**: None; **A. Torrat Noves**: None; **B. Villanueva Manes**: None; **I. Alcantara Álvarez**: None; **M. Simeo Vinaixa**: None; **A. Perez Hurtado**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6.

Abstract Number: 0206

Prospective Controlled Study of Humoral Response to Recombinant Zoster Vaccine in Cyclophosphamide-Treated Autoimmune Rheumatic Disease Patients: No Additional Impairment Compared to Other Immunosuppressive Therapies

Nadia Emi Aikawa[1], Julia Medeiros[2], Sandra G Pasoto[3], Ana C Medeiros-Ribeiro[3], Luciana Parente Costa Seguro[4], Ana Paula Luppino-Assad[5], Emily Figueiredo Neves Yuki[6], Lissiane Guedes[7], Clovis Artur Silva[8] and Eloisa Bonfa[4], [1]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, SAO PAULO, Brazil, [6]Faculdade de Medicina da USP, São Paulo, São Paulo, Brazil, [7]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, [8]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Recombinant zoster vaccine (RZV), represents a major advancement in the prevention of herpes zoster in autoimmune rheumatic diseases (ARD) patients. However, RVZ efficacy depends on strong cellular and humoral

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

immune response. Intravenous cyclophosphamide (IVCYC) is a potent immunosuppressive agent known to impair both arms of the immune system. Therefore, it is important to evaluate the impact of IVCYC on RVZ humoral immunogenicity in ARD patients, and to explore factors that may influence vaccine response.

Methods: This was a subgroup analysis of ARD patients (≥18 years) currently receiving IVCYC (ARD-IVCYC) enrolled in a phase 4 randomized placebo-controlled prospective study. Healthy immunocompetent adults ≥50 years (CG) and patients not treated with IVCYC (ARD-No IVCYC) were included as comparison groups (1:4 ratio). ARD-IVCYC patients were randomized in two groups: P1 (vaccine) and P2 (placebo). CG and P1 received RZV (D0 and D42); P2 initially received placebo, followed by RZV (D84 and D126). Humoral response to RZV was defined as anti-gE concentration (ELISA) ≥4-fold the pre-vaccination level and evaluated at baseline and 6 weeks after second dose. GMT was also calculated. Disease activity was assessed using ARD-specific activity indices. Adverse events (AEs) were recorded.

Results: 42 ARD-IVCYC, 168 CG and 168 ARD-no IVCYC individuals were included. Among ARD-IVCYC, 34% were treated according to the EuroLupus protocol, 54% National Institutes of Health (NIH) regimen, and 10% followed the CYCLOPS protocol for vasculitis. The median cumulative dose of IVCYC was 3 g (3-4.5). Groups were comparable for sex ($p< 0.05$), although ARD-IVCYC and ARD-No IVCYC were younger than CG (40 vs. 40 vs. 52 years, $p< 0.001$). ARD diagnoses were similar between ARD-IVCYC and ARD-No IVCYC groups ($p >0.05$), except for a higher frequency of vasculitis in the former (10.8% vs. 0%, $p< 0.001$). Regarding immunogenicity, ARD-IVCYC and ARD-No IVCYC had comparable humoral response but lower than CG (91.9% vs. 91.1% vs. 99.4%, $p < 0.002$). Post-immunization GMT were alike in ARD-IVCYC and ARD-No IVCYC groups but both significantly lower than CG [7.53 (95% CI 5.09–11.15) vs. 6.64 (95% CI 5.58-7.91) vs. 13.2 (95% CI 12.0–14.58) mUI/mL, $p < 0.001$]. Among ARD-IVCYC patients, those with post-RZV anti-gE titers < 7.53 mUI/mL more frequently used mycophenolate mofetil (33% vs 5.3%, p=0.042), with no differences in age, diagnosis, glucocorticoid, or other therapies compared to those with titer ≥7.53 mUI/mL ($p >0.05$). Flare rates were similar between vaccine (P1) and placebo (P2) groups (25% vs. 22.7%, p=0.592). Local and systemic AEs were less frequently reported by ARD-IVCYC compared to CG after both RZV doses ($p< 0.05$). No severe AEs were reported.

Conclusion: Our findings demonstrate that IVCYC is safe and, unexpectedly, does not exert a more detrimental effect on the humoral response to RZV than other immunosuppressive agents used in ARD, particularly MMF. Although the response rate was high, the lower immunogenicity compared to controls, despite the younger age, reinforces the need for close surveillance for HZ risk. (ClinicalTrials NCT05879419).

Disclosure: N. Aikawa: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **J. Medeiros**: None; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Costa Seguro**: AstraZeneca, 6, GlaxoSmithKlein(-GSK), 5, 6; **A. Luppino-Assad**: GlaxoSmithKlein(GSK), 5; **E. Figueiredo Neves Yuki**: GlaxoSmithKlein(GSK), 5; **L. Guedes**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0207

The Feasibility and Clinical Effects of Anti-Inflammatory Diet Intervention In Patients Diagnosed With Long COVID (Post-Acute Sequelae of SARS CoV-2, PASC)

Suzi Hong[1], Marcos Monteon[2], Kathleen Bundy[3], Chloe Delgado Ramirez[3], Phoebe Senowitz[3], Monica Guma[4], Nina Acebo[5], Chris Pruitt[6], Tanya Shekhtman[3], Shahrokh Golshan[7] and **Susan Lee**[8], [1]Herbert Wertheim School of Public Health and Human Longevity Science UCSD; Department of Psychiatry UCSD, San Diego, [2]University of California, San Diego, San Diego, [3]Department of Family Medicine, Center for Integrative Health, Krupp Endowment Fund, UCSD, La Jolla, [4]University of California San Diego, San Diego, CA, [5]University of California, San Diego, La Jolla, [6]Herbert Wertheim School of Public Health and Human Longevity Science, UCSD, La Jolla, [7]Department of Pyschiatry, UCSD, La Jolla, [8]Department of Medicine, University of California, San Diego, La Jolla, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0199–0209) Infection-related Rheumatic Disease Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: There have been over 777 million cases of acute COVID-19 infections worldwide as of April 2025. Although many patients recover, an estimated 10-30% of patients continue to experience a constellation of symptoms labelled "Long COVID" or PASC. Major symptoms include fatigue, cognitive dysfunction, post-exertional malaise, and sleep disturbances. Exact pathophysiology of PASC remains unclear but there are data suggesting a potential role of inflammation and autoimmunity in persistence of symptoms. In the absence of effective treatments, patients are inquiring about the role of diet given burgeoning data linking microbiome dysbiosis to dysregulated host immune responses and autoimmune diseases. We assessed the feasibility of a 12-week anti-inflammatory diet (Long COVID Anti-Inflammatory, LC-ITIS) among patients with PASC and explored diet-induced changes in clinical symptoms and inflammatory makers.

Methods: Patients with a confirmed COVID-19 infection and persistence of $\geq$2 of the 3 new symptoms (sleep disturbances, brain fog, fatigue $\geq$ 5 on VAS) for $\geq$ 12 weeks after the infection were recruited. LC-ITIS diet was similar to previously established RA anti-inflammatory (RA-ITIS) diet from our group which has shown correlation between gut microbiome/metabolome and clinical response [Coras R et al. Clin Transl Med 2022;12:e959]. LC-ITIS diet emphasized foods rich in anti-inflammatory nutrients and those with favorable omega-6:Omega-3 fatty acid profile (e.g. flax/chia seeds, miso). Foods such as highly processed foods, added sugar, and nightshade vegetables were restricted. Clinical outcomes, dietary adherence, and inflammatory makers were measured (Table 1). Data were analyzed using ANOVA and mixed-effects model. Statistical analyses were performed in SPSS.

Table 1. LC-ITIS Diet Regimen and Assessment Timeline

Activities	Wk -2	Wk 0	Wk 2	Wk 5	Wk 8	Wk 12
Diet Regimen	Usual Diet	LC-ITIS diet with defined meal plan	LC-ITIS diet with defined meal plan	LC-ITIS diet without defined meal plan	LC-ITIS diet without defined meal plan	LC-ITIS diet without defined meal plan
Anthropometric Measures	X	X	X			X
Diet Counseling		X	X	As needed	As needed	
Diet Log, 24-hour Diet Recall, Self-Assessment of Compliance	Daily Log	Daily Log	Daily Log	24-hour Recall	24-hour Recall	Daily Log
Fatigue Assessment Survey (FAS)	X	X	X	X	X	X
Pittsburg Sleep Quality Index (PSQI)	X	X	X	X	X	X
Beck Depression Index (BDI)	X	X	X	X	X	X
PROMIS Sleep Disturbances 8B	X	X	X	X	X	X
Montreal Cognitive Assessment (MOCA)	X		X			X
Plasma Inflammatory Markers	X	X	X			X
Stool Collection for future microbiome/metabolomics	X	X	X			X

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical Outcomes

	Wk -2	Wk 0	Wk 2	Wk 5	Wk 8	Wk 12	F
Total FAS	35.1 ± 6.7	32.9 ± 7.4	32.7 ± 8.4	30.1 ± 8.2	29.1 ± 6.8	28.4 ± 7.9	$F_{(5,41)}$ = 10.45**
BDI	17.9 ± 7.7	14.7 ± 8.0	13.1 ± 6.9	12.9 ± 8.3	12.8 ± 7.0	12.6 ± 6.8	$F_{(5,53)}$ = 7.84**
PROMIS IB Sleep Disturbances T score	58.6	57.5	55.9	54.7	54.7	53.2	$F_{(3,33)}$ = 3.31*
MOCA	26.1 ± 2.9		27.6 ± 2.1			27.5 ± 1.8	$F_{(2,31)}$ = 8.50*

Means and standard deviations are reported. FAS 10-35 (10-21: no fatigue; 22-50: substantial fatigue; Minimally important difference: 4 points); BDI 0-63 (0-13: minimum depression; 14-19: mild depression; 20-28: moderate depression; 29-63: severe depression); PROMIS 8B Sleep Disturbances T score 50 = average US population, higher T = worse sleep; MOCA no cognitive dysfunction >26; **p<0.001; *p<0.01

Results: Two patients dropped out at Week 0 (Wk0) before starting the diet. All remaining 21 patients completed 2 weeks of LC-ITIS diet with pre- and post-assessments. Majority (71%) completed 12 weeks of diet and assessments. Patients were 66% women, 57% Caucasians, and 24% Hispanics with a mean age of 53.3 ±15 (range 25-78). By the end of the study, 50% reported that they changed their dietary habits significantly. The self-reported adherence rate was high at 91% at Wk2 and maintained at 94% through Wk12 (≥6 on a 0-10 scale; moderate to very well). The mean BMI decreased from 28.8 to 27.8 over 12 weeks. Many, 69% and 49%, found diet instruction and diet easy/very easy to follow, respectively. There were significant clinical improvements in fatigue, sleep, cognitive function, and depressive mood with LC-ITIS diet (Table 2). Inflammatory marker results are excluded in this report.

Conclusion: This is the first pilot study assessing the effect of anti-inflammatory diet on clinical outcomes in patients with PASC. The diet adherence rate was very high among these patients despite significant fatigue and brain fog. Our initial findings demonstrate feasibility and potential symptom relief benefits of anti-inflammatory diet in a disease with no effective treatment. This finding should be evaluated in a larger randomized controlled trial.

Disclosure: S. Hong: None; **M. Monteon**: None; **K. Bundy**: None; **C. Delgado Ramirez**: None; **P. Senowitz**: None; **M. Guma**: AbbVie, 5, Sonoma, 5; **N. Acebo**: None; **C. Pruitt**: None; **T. Shekhtman**: None; **S. Golshan**: None; **S. Lee**: None.

Abstract Number: 0208

Current practices and challenges in tuberculosis screening and preventive treatment among patients with rheumatic diseases: A multiregional physician survey in China

Xu Wang, Lifan Zhang and Lidan Zhao, Peking Union Medical College Hospital, Beijing, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aimed to assess the current clinical practices of tuberculosis (TB) infection screening and TB preventive treatment (TPT) among patients with rheumatic diseases, identify challenges physicians face during diagnosis and treatment, and explore potential strategies for improvement.

Methods: A well-structured questionnaire was designed and distributed to nationwide physicians from multiple disciplines, including but not limited to rheumatology, infectious diseases, and tuberculosis departments.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 443 valid responses were collected and analyzed. 76% of the respondents were from general hospitals, and 71% of the respondents had treated patients with rheumatic diseases complicated by active TB in the past year. Approximately 60% of the respondents reported routinely performing TB infection screening at the initial visit of patients with rheumatic diseases. Target populations primarily included those scheduled to receive tumor necrosis factor-alpha inhibitors or Janus kinase inhibitors, and those with a history of TB exposure or previous TB infection. Common preferred screening methods included chest imaging (15.58%), the tuberculin skin test (18.06%), and interferon-gamma release assays (58.69%). Reasons for not conducting routine screening included patients' financial burden (50.57%), perceived low risk of infection (53.45%), and minimal impact on treatment decisions (46.55%). The majority of physicians (74.49%) indicated they would recommend TPT for patients with latent TB infection, and a 3-month combination regimen of isoniazid with rifampicin was mostly preferred (60.95%). However, poor treatment adherence due to long duration and adverse drug reactions was frequently reported. Although most physicians acknowledged the necessity and safety of TPT, concerns remained regarding individualized efficacy and potential risks. Key barriers identified included poor patient compliance, drug-related side effects, and a lack of robust clinical evidence.

Conclusion: Implementing TB infection screening and preventive treatment in patients with rheumatic diseases remains suboptimal, with multiple practical challenges. Enhancing professional training, improving awareness of clinical guidelines, strengthening patient education, and optimizing screening and treatment strategies may improve feasibility and effectiveness in clinical settings. Future efforts should focus on multicenter studies and policy support to standardize and promote TB infection management, thereby improving the overall quality of care for patients with rheumatic diseases.

Disclosure: X. Wang: None; **L. Zhang**: None; **L. Zhao**: None.

Abstract Number: 0209

A Retrospective Safety Analysis Based on Platelets in Arthrocentesis and Joint Injections in Cancer Patients

Yuanteng Li[1], Cheuk Leung[2], Heather Lin[2], Angeles Lopez-Olivio[3] and Jean Tayar[3], [1]MD Anderson Cancer Center, Houston, TX, [2]MD Anderson Cancer Center, Houston, [3]The University of Texas, MD Anderson Cancer Center, Houston, TX

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0199–0209) Infection-related Rheumatic Disease Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

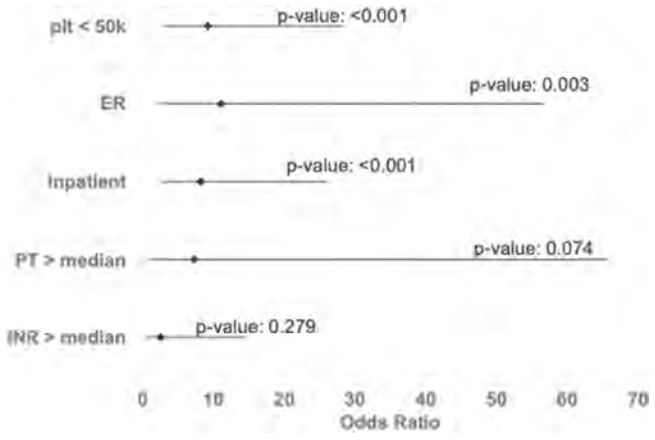
Background/Purpose: Arthrocentesis and joint injections are commonly performed to diagnose and to treat rheumatic conditions such as crystal-induced arthritis, septic arthritis, and inflammatory arthritis. While generally safe, these procedures carry risks of iatrogenic infection and bleeding (Courtney 2005, Dooley 2002), particularly in cancer patients, who often have leukopenia and thrombocytopenia from chemotherapy or are on anticoagulation therapy (Ahmed 2012). Despite proposed thresholds for prophylactic transfusions (e.g., 20,000 and 10,000/microliter) in more invasive procedures, specific guidelines on the safety of arthrocentesis in cancer patients remain lacking (Kaufman 2015, Avvisaati 2003).

Methods: We conducted a retrospective cohort study of patients who underwent arthrocentesis or joint injections between 2006 and 2016 at MD Anderson Cancer Center. Baseline demographic information, clinical characteristics (e.g. primary cancer diagnosis, smoking status, comorbidities and etc), and clinical outcomes were collected up to 12 weeks post-procedure. The primary outcome was bleeding, and the secondary outcome was iatrogenic infection. To evaluate the safety

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

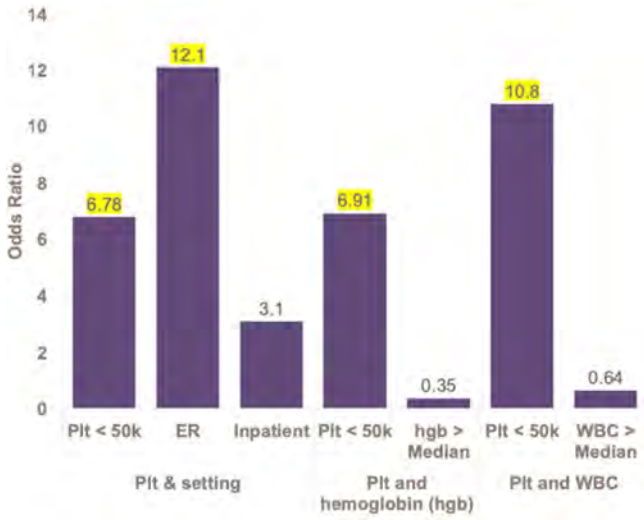
Characteristics	Category	Platelet ≤ 50 (89 patients)	Platelet ≥ 140 (174 patients)
		n (%)	n (%)
Gender	Female	30 (33.7)	60 (34.5)
	Male	59 (66.3)	114 (65.5)
Age group	18 – 30	3 (3.4)	5 (2.9)
	31 – 40	3 (3.4)	6 (3.4)
	41 – 50	7 (7.9)	14 (8.0)
	51 – 60	18 (20.2)	35 (20.1)
	61 – 70	31 (34.8)	60 (34.5)
	> 70	27 (30.3)	54 (31.0)
Cancer type	Non-solid	33 (37.1)	64 (36.8)
	Solid	56 (62.9)	110 (63.2)
Anti-platelet	No	88 (98.9)	173 (99.4)
	Yes	1 (1.1)	1 (0.6)
Anti-coagulant	No	85 (95.5)	167 (96.0)
	Yes	4 (4.5)	7 (4.0)
Race	American Indian/ Alaska native	1 (1.1)	0 (0.0)
	Black	6 (6.7)	17 (9.8)
	Hispanic	6 (6.7)	16 (9.2)
	Other	4 (4.5)	14 (8.1)
	White	72 (80.9)	126 (72.8)
Marital Status	Divorced	4 (4.5)	13 (7.6)
	Married	70 (79.5)	123 (72.4)
	Separated	0 (0.0)	2 (1.2)
	Single	9 (10.2)	17 (10.0)
	Widowed	5 (5.7)	15 (8.8)
Setting	Emergency room	3 (3.4)	11 (6.3)
	Inpatient	58 (65.2)	20 (11.5)
	Outpatient	28 (31.5)	143 (82.2)
Image guidance	No	75 (84.3)	115 (66.9)
	Yes	14 (15.7)	57 (33.1)
Aspiration	No	33 (37.1)	148 (85.5)
	Yes	56 (62.9)	25 (14.5)
DVT	No	86 (96.6)	165 (95.4)
	Yes	3 (3.4)	8 (4.6)
Median Hgb (Min, Max)		9 (5.9, 13.5)	12.3 (7.2, 17.8)
Median WBC (Min, Max)		3.2 (0, 58)	6.5 (1, 33.5)
Median ANC (Min, Max)		1.56 (0, 18.6)	3.91 (0.09, 26.2)
Median INR (Min, Max)		1.32 (1, 1.64)	1.08 (0.88, 2.04)
Median PT (Min, Max)		16.1 (13.4, 18.4)	14.1 (11.1, 23.2)

Demographics after exact matching 1:2. The absolute standardized differences were less than 10% for all 5 categories after exact matching, indicating good balances on the matching factors.



Odds of septic arthritis vs. patient characteristics based on univariable logistic regression with 95% confidence interval

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Odds of Septic Arthritis based on low platelet count and setting, hemoglobin, and WBC based on multivariable analysis with α at 0.05. Highlighted Odds Ratio have a p-value < 0.05.

of arthrocentesis and joint injections in thrombocytopenic patients (platelet count ≤50,000/μL), we performed exact matching on sex, age, cancer type, anti-platelet, and anti-coagulant drugs use in a 1:2 ratio with patients with normal platelet count (≥140,000/μL) to compare the outcomes between the two patient groups.

Results: Among 95 arthrocentesis in thrombocytopenic patients and 760 in patients with normal platelet counts, no cases of bleeding or iatrogenic infection were observed in either group. After matching, thrombocytopenic patients (n=89) and controls (n=174) were comparable in demographic and clinical characteristics. Univariable analysis showed that initial visits to the ER and inpatient were associated with higher risk of septic arthritis. However, hemoglobin greater than the median and white blood cell greater than the median are associated with a lower risk of septic arthritis. Finally, thrombocytopenic patients had a higher risk of initial septic arthritis, while even adjusting for white blood count (OR 10.8; 95% CI: 2.9-39.8; P< 0.001).

Conclusion: Arthrocentesis and joint injections appear safe in cancer patients with thrombocytopenia, as no bleeding or iatrogenic infections were observed. However, the higher incidence of septic arthritis in thrombocytopenic patients underscores the importance of microbiological analysis of synovial fluid. These findings support the safety of these procedures while highlighting the need for vigilance in high-risk patients.

Disclosure: Y. Li: None; **C. Leung**: None; **H. Lin**: None; **A. Lopez-Olivio**: None; **J. Tayar**: None.

Abstract Number: 0210

Improving Recombinant Zoster Vaccine Uptake in Younger Adults with Rheumatoid Arthritis through a Partnership with Specialty Pharmacy

Akhil Sood[1], Srijana Davuluri[2], Sheila Haidar[3], De Suan Huang[3], April Ochoa[3], Christy Bill[1] and Janice Lin[1], [1]Stanford University, Palo Alto, CA, [2]Stanford University, Stanford, CA, [3]Stanford Health Care, Palo Alto, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

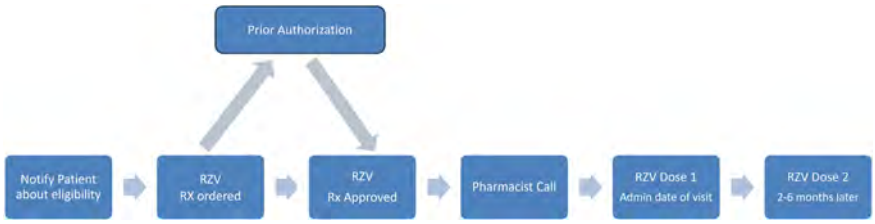


Figure 1: Process Map for RZV Dose 1 Adminstration

Background/Purpose: Despite guideline recommendations, recombinant zoster vaccine (RZV) uptake remains low among immunocompromised individuals younger than 50 years of age, notably those with rheumatoid arthritis (RA). Previous institutional efforts, including patient and physician education, demonstrated increased willingness to receive the vaccine but the impact was limited. Additional strategies to increase uptake were warranted. Our aim was to increase RZV uptake among RA patients ages 18-49 from 10% to 15% by January 2025 through a targeted partnership with specialty pharmacy.

Methods: We defined our baseline cohort as RA patients ages 18-49 years seen at a tertiary care clinic from July 2023 to December 2023. Prior patient and physician educational interventions increased baseline RZV uptake from 6.7% to 10.3% (January 2024 to May 2024). Root cause analysis identified vaccine access as a major barrier. Starting June 2024, we partnered with Stanford Specialty Pharmacy, that is located near the clinic, to develop a coordinated vaccine delivery pathway aligned with rheumatology visits. Our improvement team included clinic nurses, patient care coordinators (PCC), pharmacists, and rheumatologists. A comprehensive workflow was established including communication regarding eligibility, RZV prescription with obtaining prior authorization, pre-visit vaccine counseling, and RZV administration on date of clinic visit (Figure 1). In November 2024, a separate workflow was created to coordinate the second vaccine dose within 2-6 months post-first dose (Figure 2). To minimize barriers to vaccine access, validated parking was provided in collaboration with Stanford Medicine Transportation Services. The primary outcome was the proportion of eligible patients to receive at least 1 dose of RZV following intervention during June 2024 to January 2025. The secondary outcome was completion of 2 dose series following implementation (November 2024). Barriers to RZV were collected from telephone encounters between patient and pharmacist.

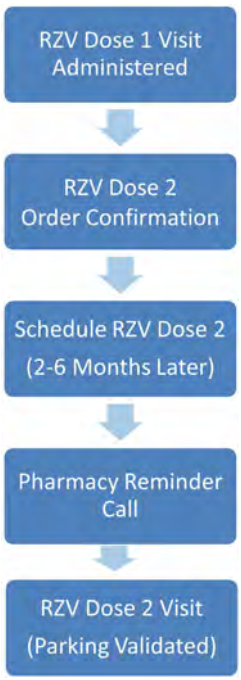


Figure 2: Process Map for RZV Dose 2 Adminstration

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among the baseline cohort (n=137), 15.3% received at least one RZV dose between June 2024 and January 2025, meeting the intervention goal. Following implementation of the workflow for dose #2 of RZV, 5 of 9 eligible patients (55.5%) completed the two-dose series by May 2025. Common barriers to vaccination included reproductive considerations (n=5) including in vitro fertilization, pregnancy, or breastfeeding as well as insurance authorization issues (n=5), and vaccine hesitancy (n=3).

Conclusion: A targeted partnership with specialty pharmacy significantly improved RZV uptake among RA patients ages 18-49 years, which included direct outreach to the patients from the pharmacists. Prior to scaling the intervention to patients with various rheumatologic conditions, it is critical to investigate and address population-specific barriers to enhance vaccine uptake in this high-risk group.

Disclosure: A. Sood: None; **S. Davuluri**: None; **S. Haidar**: None; **D. Huang**: None; **A. Ochoa**: None; **C. Bill**: None; **J. Lin**: None.

Abstract Number: 0211

Initial Results From a Single-Center Quality Improvement Initiative Using the Shingrix Rheumatology Immunization Dashboard Within the Veterans Health Administration

Alexandra Do[1], Lisa Matsumoto[1], Cherish Wilson[2], Gary Tarasovsky[3], gabriela Schmajuk[4] and Jennifer Barton[5], [1]Oregon Health and Science University, Portland, [2]UCSF / SFVA, San Francisco, CA, [3]UCSF, San Francisco, [4]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [5]VA Portland Health Care System/OHSU, Portland, OR

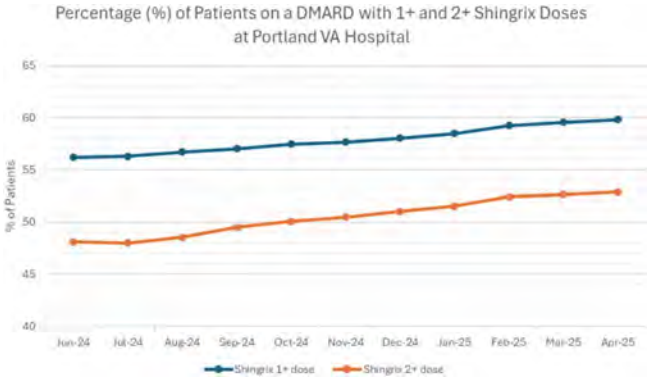
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

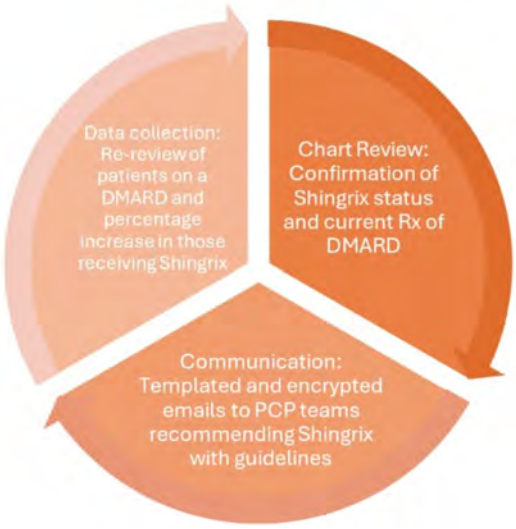
Background/Purpose: Disease-modifying antirheumatic drugs (DMARDs) are used to treat many rheumatologic diseases by modulating the patient's immune system. However, patients on DMARDs are more susceptible to infection, including varicella zoster or shingles. ACR guidelines state adults aged 19 and older who are prescribed DMARD therapy should receive two doses of the Shingrix vaccine to protect against shingles. We aimed to improve Shingrix vaccine immunization among Veterans on DMARDs at the VA Portland Health Care System (VAPORHCS) using a medication safety dashboard.

Methods: We accessed the Rheumatology Medication Safety Shingrix Dashboard developed by the San Francisco VA Measurement Science QUERI, which was available to us as part of a wait-list control randomized trial. Using data from the dashboard, we identified patients who received a DMARD through the VA Portland Health Care System and reviewed EHR charts to confirm medication use and Shingrix vaccination status or refusal. Templated, secure emails were sent to the patients' VA primary care providers and nurse care managers, highlighting the importance of Shingrix (Figure). Progress was tracked from June 2024 to April 2025 via the dashboard to monitor changes in the proportion of patients with immunizations and through chart review of patients whose PCPs were emailed, to confirm whether they received the Shingrix vaccine.

Results: From June 2024 to April 2025, the percentage of patients on a DMARD who received at least one dose of Shingrix increased from 56.2% to 59.8%—an overall rise of 3.6% (Graph). The percentage of patients fully vaccinated (both doses) increased from 48.1% to 52.9%, representing a 4.8 percentage point gain over the same period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





Study design

On a monthly basis, the proportion of patients receiving only one dose rose by 0.013%, while those completing both doses increased by about 0.018% per month. Over the 11-month period, there is an increase of 6.4% in one-dose coverage and a 9.9% increase in two-dose coverage. The gap between the first and second Shingrix doses steadily declined over 11 months, from 8.1% in June 2024 to 7.0% in April 2025, demonstrating that patients who received the first dose of the vaccine also went on to get the second dose. During the period when the majority of emails to PCP teams were sent out — November to April 2025 — we observed an increased proportion of patients receiving at least one dose of Shingrix. This suggests that outreach to PCPs was effective, as many reported they were unaware of the lowered age recommendation for Shingrix in patients on a DMARD.

Conclusion: The use of a safety dashboard, combined with targeted outreach to primary care providers was associated with a steady increase in the administration of Shingrix among Veterans on DMARDs. We plan to expand the use of these dashboards to promote other recommended immunizations within this population. Prompt implementation of EHR-based dashboards can boost quality improvement efforts by delivering key metrics and actionable insights directly to clinicians.

Disclosure: A. Do: None; **L. Matsumoto**: None; **C. Wilson**: None; **G. Tarasovsky**: None; **g. Schmajuk**: None; **J. Barton**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0212

Biomarker-Guided Therapeutic Calculator for Personalized Management in Pregnant Patients with Autoimmune Rheumatic Diseases

Noe Macias-Segura[1], Rodolfo Martinez-Canales[1], **Andres M. Ortiz-Rios**[2], Braulio R. Avalos-Garcia[2], Eva Abigaid Galindo-Calvillo[2], Mario Cesar Salinas-Carmona[1], Lorena Perez-Barbosa[2], Dionicio A. Galarza-Delgado[3] and Cassandra Michele Skinner-Taylor[2], [1]Immunology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Therapeutic decisions during pregnancy in women with autoimmune rheumatic diseases (ARDs) such as SLE, APS, RA, and Sjögren's syndrome require a personalized approach due to heterogeneous risk profiles and complex disease interactions. We developed and validated a treatment recommendation algorithm based on a comprehensive meta-analysis of over 100 studies assessing predictive biomarkers, clinical factors, and treatment outcomes during pregnancy in ARDs.

Methods: Using PRISMA guidelines, we performed a systematic review and meta-analysis to identify evidence-based therapeutic associations across ARDs. Key biomarkers were mapped to treatment responses, including lupus anticoagulant (LAC), anti-β2GP1, anti-cardiolipin, anti-SSA/Ro, anti-dsDNA, complement components (C3/C4, sC5b-9), NLR, disease activity indices, and prior pregnancy loss or thrombosis. We assigned intervention thresholds and created a decision matrix matching biomarker-risk profiles with pharmacologic and non-pharmacologic strategies, including hydroxychloroquine (HCQ), low-dose aspirin (AAS), low molecular weight heparin (LMWH), corticosteroids, and immunosuppressives.

Table 1. Biomarker-Guided Therapeutic Recommendations in Pregnant Patients with Autoimmune Rheumatic Diseases

Biomarker/Clinical Factor	Recommended Therapy	Justification (Effect Size / Evidence)
Lupus Anticoagulant (LAC) + high-titer aPLs	Low-dose aspirin (AAS) + LMWH	OR 1.29 for reducing adverse pregnancy outcomes (APOs)
Anti-SSA/Ro positive	Hydroxychloroquine (HCQ)	Reduces fetal AV block recurrence risk from 18% to 7.5%
SLEDAI > 4 or hypocomplementemia	Corticosteroids ± Azathioprine	Controls lupus activity and prevents flares during pregnancy
Elevated NLR or Chemerin	Consider an anti-inflammatory adjustment or close monitoring	Indicators of subclinical inflammation
Prior pregnancy loss or thrombosis	AAS ± LMWH depending on aPL profile	Secondary prophylaxis in obstetric APS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The calculator integrates 9 core biomarker-based indications for treatment. For instance, the presence of LAC and high-titer antiphospholipid antibodies indicated LMWH+AAS (OR for APO reduction: 1.29); anti-Ro positivity triggered HCQ to prevent fetal AV block (risk reduction from 18% to 7.5%). Active lupus (SLEDAI >4 or hypocomplementemia) prompted corticosteroid and azathioprine use; elevated NLR or chemerin levels served as adjunctive inflammation markers. Each therapeutic output is supported by published OR/RR values and is adjustable to disease context and trimester.

Conclusion: We present a personalized therapeutic calculator to optimize pregnancy outcomes in ARD patients. It translates biomarker profiles into actionable treatment recommendations with literature-based justification. The tool is undergoing academic licensing and is not publicly available. Future trials will evaluate its implementation impact in multidisciplinary care models.

Disclosure: N. Macias-Segura: None; **R. Martinez-Canales**: None; **A. Ortiz-Rios**: None; **B. Avalos-Garcia**: None; **E. Galindo-Calvillo**: None; **M. Salinas-Carmona**: None; **L. Perez-Barbosa**: None; **D. Galarza-Delgado**: None; **C. Skinner-Taylor**: None.

Abstract Number: 0213

Development of a Predictive Tool for Obstetric Risk Stratification in Autoimmune Rheumatic Diseases: A Meta-Analysis-Based Model

Noe Macias-Segura[1], Rodolfo Martinez-Canales[1], **Braulio R. Avalos-Garcia**[2], Andres M. Ortiz-Rios[2], Eva Abigaid Galindo-Calvillo[2], Mario Cesar Salinas-Carmona[1], Lorena Perez-Barbosa[2], Dionicio A. Galarza-Delgado[3] and Cassandra Michele Skinner-Taylor[2], [1]Immunology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune rheumatic diseases (ARDs) such as systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), rheumatoid arthritis (RA), and Sjögren's syndrome significantly increase the risk of adverse pregnancy outcomes (APOs), including preeclampsia, fetal restriction (intrauterine growth restriction (IUGR)), fetal loss, and preterm birth. Traditional risk factors do not fully explain these complications. We aimed to develop and validate a predictive model for obstetric risk stratification in pregnant women with ARDs, using a systematic review and meta-analysis of over 150 studies.

Methods: We conducted a systematic search across PubMed, Embase, Web of Science, and Scopus, selecting studies that evaluated biomarkers and clinical predictors of APOs in pregnant women with ARDs. Key variables included lupus anticoagulant (LAC), anti-β2GP1, anti-cardiolipin, complement activation (C3/C4, sC5b-9), neutrophil-to-lymphocyte ratio (NLR), anti-SSA/Ro antibodies, disease activity indices (SLEDAI, DAS28), and clinical history (nephritis, chronic hypertension, prior fetal loss). Data from eligible studies were pooled using random-effects meta-analysis. Predictive weights were assigned to variables based on odds ratios and integrated into a point-based risk calculator.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Predictive Biomarkers and Clinical Variables Included in the Obstetric Risk Stratification Model for Autoimmune Rheumatic Diseases

Predictor	Effect Size (OR)	Clinical Interpretation
Lupus anticoagulant (LAC)	~12.5	Strongest predictor of adverse pregnancy outcomes
Chronic hypertension	5.8	Strong risk factor for preeclampsia
Active lupus (SLEDAI >4)	2.9	Associated with preterm birth
Prior lupus nephritis	↑	Increases APO risk, esp. with proteinuria
Hypocomplementemia (C3/C4 low)	↑	Reflects active immune complex deposition
NLR >2.9	AUC = 0.71	Predicts maternal-fetal complications
Anti-SSA/Ro positivity	–	Indicates risk for fetal heart block, integrated if present
History of pregnancy loss	↑	Included as cumulative clinical risk

Results: The model incorporates 12 high-evidence predictors. LAC conferred an OR of ∼12.5 for APOs >12 weeks; chronic hypertension an OR of 5.8 for preeclampsia; and active lupus an OR of 2.9 for preterm birth. The presence of nephritis and low complement levels significantly increased APO risk. NLR >2.9 yielded an AUC of 0.71 for predicting maternal-fetal complications. Each variable was scored to produce a cumulative risk score, stratifying patients into low, moderate, or high-risk categories. Internal validation showed a sensitivity of 81% and a specificity of 74% for predicting APOs. (Table 1)

Conclusion: We developed a robust, evidence-based calculator that stratifies obstetric risk in pregnant women with ARDs. This tool integrates clinical, serologic, and inflammatory markers and has potential to guide early interventions and personalized monitoring. The model is currently under academic licensing and not yet publicly available. Future prospective validation is planned to support clinical implementation.

Disclosure: N. Macias-Segura: None; **R. Martinez-Canales**: None; **B. Avalos-Garcia**: None; **A. Ortiz-Rios**: None; **E. Galindo-Calvillo**: None; **M. Salinas-Carmona**: None; **L. Perez-Barbosa**: None; **D. Galarza-Delgado**: None; **C. Skinner-Taylor**: None.

Abstract Number: 0214

Systematic Comorbidity Screening in Inflammatory Arthritis: The Experience of a Tertiary-Care Centre

Camille Bourgeois[1], Alexandra Kobza[2], Olivier Fogel[3], Maxime Dougados[4] and Anna Molto[5], [1]Hospital general universitario Gregorio Marañon, Madrid, Madrid, Spain, [2]University of Calgary, North Vancouver, BC, Canada, [3]AP-HP, Paris, France, [4]Department of Medicine, Hopital Cochin, Universite de Paris, Paris, France, [5]Assistance Publique Hôpitauxde Paris, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with inflammatory arthritis (IA), including rheumatoid arthritis (RA) and spondyloarthritis (SpA), are at elevated risk for comorbidities, complicating disease management. Despite rheumatology societies recommending periodic comorbidity reviews, their integration into routine care remains challenging. This study aimed to (i) assess baseline compliance with comorbidity management recommendations among patients with IA, and (ii) identify clinical action items resulting from a physician-led global review.

Methods: We conducted a retrospective cohort study of adults with RA or SpA who underwent a standardized global review at Hôpital Cochin, Paris, between June 2017 and March 2025. The review adhered to EULAR recommendations for comorbidity management in rheumatic diseases and included assessments for cardiovascular risk, bone health, infections, and malignancy (1). Descriptive statistics were used to summarize patient characteristics and actions taken.

Results: The cohort included 458 patients (RA: 187, SpA: 271) with a mean disease duration of 17.4 years (SD 12.9) as detailed in Table 1. Among RA patients, 84.5% were female, with a mean age of 55.0 years (SD 15.4) and mean DAS28 of 2.7 (SD 1.3). Among SpA patients, 42.8% were female, mean age 48.6 years (SD 13.3), and mean ASDAS 1.8 (SD 1.0). Among all patients, corticosteroids were used by 14.7%, and biologics by 63.1%.

Cardiovascular history included ischaemic heart disease in 3.5%, diabetes in 4.8%, and hypertension in 22.5% of the total population, with comparable rates across the RA and SpA subgroups. Active smoking was reported in 19.3% of RA and 24.0% of SpA patients. LDL levels were above target in 40.5% and 47.5%, and obesity (BMI >30 kg/m^2) affected 10.9%

Table 1: Baseline Characteristics

Characteristic	n	Total (n=458)	n	RA (n=187)	n	SpA (n=271)
Age, years, mean (SD)	458	51.2 (14.5)	187	55.0 (15.4)	271	48.6 (13.3)
Gender, female	458	274 (59.8%)	187	158 (84.5%)	271	116 (42.8%)
Diseases duration, years, mean (SD)	449	17.4 (12.9)	185	17.0 (12.2)	264	17.7 (13.5)
Disease activity, mean (SD)						
DAS28-CRP	-	-	180	2.7 (1.3)	-	-
BASDAI (0-10)	-	-	-	-	260	2.8 (1.9)
ASDAS	-	-	-	-	244	1.8 (1.0)
Current Therapy						
Conventional DMARD	455	176 (38.7)	184	123 (66.8)	271	53 (19.6)
Biologic DMARD	455	287 (63.1)	185	108 (58.4)	270	179 (66.3)
Corticotherapy	456	67 (14.7)	186	60 (32.3)	270	7 (2.6)
Cardiovascular comorbidities						
Ischemic Heart Disease	458	16 (3.5)	187	7 (3.7)	271	9 (3.3)
Cerebrovascular Accident	458	8 (1.7)	187	6 (3.2)	271	2 (0.7)
Peripheral Arterial Disease	458	3 (0.7)	187	3 (1.6)	271	0 (0)
Renal insufficiency (moderate to severe)	458	12 (2.6)	187	6 (3.2)	271	6 (2.2)
Diabetes, Type 1 or 2	458	22 (4.8)	187	15 (8.0)	271	7 (2.6)
Hypertension	457	103 (22.5)	186	41 (22.0)	271	62 (22.9)
Modifiable Cardiovascular risk factors						
Heart Score, median (IQR)	311	1.0 (0,3.0)	123	1.5 (0,4.0)	188	1.0 (0,2.3)
Active Smoking	458	101 (22.1)	187	36 (19.3)	271	65 (24.0)
LDL above target	413	184 (44.6)	173	70 (40.5)	240	114 (47.5)
Triglycerides ≥1.7 mmol/L	420	78 (18.6)	176	18 (10.2)	244	60 (24.6)
Hypertensive in clinic (>140/90 mmHg or >130/80mmHg in case of diabetes)	430	85 (19.8)	171	38 (22.2)	259	47 (18.1)
BMI≥25 kg/m^2	451	198 (43.9)	183	68 (37.2)	268	130 (48.5)
BMI≥30 kg/m^2	451	57 (12.6)	183	20 (10.9)	268	37 (13.8)
Osteoporosis management						
Vitamin D Deficiency (<75nmol/L)	393	295 (75.1)	156	113 (72.4)	237	182 (76.8)
BMD screening	458	363 (79.3)	187	143 (76.5)	271	220 (81.2)
History of fracture	457	45 (9.8)	187	27 (14.4)	270	18 (6.7)
T score ≤ -2.5 (either spine or femur)	363	60 (16.5)	143	26 (18.2)	220	34 (15.5)
Infection prevention						
Dentist follow-up	456	326 (71.5)	186	128 (68.8)	270	198 (73.3)
Influenza vaccination	426	230 (54.0)	178	95 (53.4)	248	135 (54.4)
Pneumococcal vaccination	414	221 (53.4)	174	90 (51.7)	240	131 (54.6)
DTP vaccination	445	248 (55.7)	183	96 (52.5)	262	152 (58.0)
Cancer screening						
Colon	204	98 (48.0)	89	38 (42.7)	115	60 (52.2)
Skin	454	179 (39.4)	185	65 (35.1)	269	114 (42.4)
Breast	116	97 (83.6)	75	61 (81.3)	41	36 (87.8)
Cervical	219	191 (87.2)	114	102 (89.5)	105	89 (84.8)

*Unless otherwise specified, values represent number (percentage).
Abbreviations: DAS28-CRP= disease activity score-28 with c-reactive protein, BASDAI= Bath Ankylosing Spondylitis Disease Activity Index, ASDAS= Ankylosing Spondylitis Disease Activity Score, DMARD= disease modifying antirheumatic drug, HLAB27= human leukocyte antigen B27, RF= rheumatoid factor, CCP= cyclic citrullinated peptide, LDL= low-density lipo-protein, BMI= body mass index, BMD= bone mineral density, DTP= diphtheria-tetanus-polio

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Clinical Actions Triggered by Global Review Findings

Action Item	n	Total (n=458)	n	RA (n=187)	n	SpA (n=271)
New Cardiology Referral for Symptoms of Cardiac Insufficiency	454	16 (3.5)	186	8 (4.3)	268	8 (3.0)
New Cardiology Referral for increased risk of ischemic heart disease	444	25 (5.6)	182	13 (7.1)	262	12 (4.6)
Recommended family physician follow-up for blood pressure management	438	78 (17.8)	174	32 (18.4)	264	46 (17.4)
Referral to Dietician	452	71 (15.7)	184	32 (17.4)	268	39 (14.6)
Referral to Physiotherapy	453	57 (12.6)	185	19 (10.3)	268	38 (14.2)
Vaccination prescribed	456	285 (62.5)	186	120 (64.5)	270	165 (61.1)

*Unless otherwise specified, values represent number (percentage).

and 13.8% in RA and SpA patients, respectively. New cardiology referrals were initiated for 25 (5.6%) patients due to high ischaemic risk as seen in Table 2.

Regarding bone health, vitamin D deficiency was present in 75.1% of the overall population. Fractures were reported in 14.4% of RA patients and 6.7% of SpA patients, while a DXA-based definition of osteoporosis was seen in 18.2% vs. 15.5% respectively.

In terms of vaccination coverage, adherence was 54.0% for influenza, 53.4% for pneumococcal, and 55.7% for diphtheria-tetanus-polio (DTP) vaccines, as per French recommendations. The global review led to a vaccine prescription in 62.5% of cases.

Malignancy screening adherence was 48.0% for colon, 39.4% for skin, 83.6% for breast, and 87.2% for cervical cancer.

Conclusion: Our findings underscore the gap between recommended and actual comorbidity management in IA. The global review revealed areas needing intervention and generated actionable steps to address care gaps. Importantly, this model demonstrates that systematic screening can be feasibly implemented in routine rheumatology clinical practice.

Reference:

1. Baillet A, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Annals of the rheumatic diseases. 2016 Jun 1;75(6):965-73.

Disclosure: C. Bourgeois: None; **A. Kobza**: Novartis, 6; **O. Fogel**: None; **M. Dougados**: None; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6.

Abstract Number: 0215

Impact of Global Review on Comorbidity Management in Inflammatory Arthritis Patients

Alexandra Kobza[1], **Camille Bourgeois**[2], Olivier Fogel[3], Maxime Dougados[4] and Anna Molto[5], [1]University of Calgary, North Vancouver, BC, Canada, [2]Hospital general universitario Gregorio Marañon, Madrid, Madrid, Spain, [3]AP-HP, Paris, France, [4]Department of Medicine, Hopital Cochin, Universite de Paris, Paris, France, [5]Assistance Publique Hôpitauxde Paris, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1- Baseline Characteristics

Characteristic	n	Total (n=63)	n	RA (n=17)	n	SpA (n=46)
Age at baseline, years, mean (SD)	63	53.4 (13.3)	17	58.0 (16.5)	46	51.8 (11.7)
Gender, female	63	30 (47.6)	17	16 (94.1)	46	14 (30.4)
Diseases duration, years, mean (SD)	62	21.2 (14.2)	16	21.2 (17.0)	46	21.3 (13.4)
Time between visits, years, mean (SD)	63	4.1 (1.5)	17	3.6 (1.7)	46	4.3 (1.4)
Disease activity, mean (SD)						
DAS28-CRP	-	-	16	2.7 (1.8)	-	-
BASDAI	-	-	-	-	46	2.3 (1.7)
ASDAS	-	-	-	-	41	1.7 (0.8)
Current Therapy						
None	62	14 (22.6)	17	0 (0)	45	14 (31.1)
Conventional DMARD	63	19 (30.2)	17	11 (64.7)	46	8 (17.4)
Biologic DMARD	63	40 (63.5)	17	12 (70.6)	46	28 (60.9)
Corticotherapy	62	3 (4.8)	17	3 (17.6)	45	0 (0)
HLAB27 positivity	-	-			44	37 (84.1)
RF positivity	-	-	16	14 (87.5)	-	-
CCP positivity	-	-	16	14 (87.5)	-	-
Cardiovascular domain						
Ischemic Heart Disease	63	1 (1.6)	17	0 (0)	46	1 (2.2)
Cerebrovascular Accident	63	1 (1.6)	17	1 (5.9)	46	0 (0)
Peripheral Arterial Disease	63	0 (0)	17	0 (0)	46	0 (0)
Renal insufficiency (moderate to severe)	63	1 (1.6)	17	0 (0)	46	1 (2.2)
Diabetes, Type 1 or 2	63	3 (4.8)	17	1 (5.9)	46	2 (4.3)
Hypertension	63	16 (25.4)	17	2 (11.8)	46	14 (30.4)
Osteoporosis domain						
Bone fracture	63	8 (12.7)	17	3 (17.6)	46	5 (10.9)

*Unless otherwise specified, values represent number (percentage).
Abbreviations: DAS28-CRP= disease activity score-28 with c-reactive protein, BASDAI= Bath Ankylosing Spondylitis Disease Activity Index, ASDAS= Ankylosing Spondylitis Disease Activity Score, DMARD= disease modifying antirheumatic drug, HLAB27= human leukocyte antigen B27, RF= rheumatoid factor, CCP= cyclic citrullinated peptide

Background/Purpose: Patients with inflammatory arthritis (IA), including rheumatoid arthritis (RA) and spondyloarthritis (SpA), face elevated risk for comorbidities that complicate disease management. Although rheumatology societies recommend periodic comorbidity reviews, few studies have assessed the effectiveness of this resource- and time-intensive intervention. This study aimed to assess the impact of a structured global review on comorbidity management in patients with IA.

Methods: We conducted a retrospective cohort study of adult patients with RA or SpA who completed two global reviews at Hôpital Cochin, Paris, between June 2017 and March 2025. The global review followed a standardized protocol aligned with EULAR recommendations for comorbidity management in rheumatic diseases, assessing cardiovascular, bone, infection, and malignancy risk (1). For cardiovascular and malignancy domains, recommendations were provided to the general practitioner, while specific prescriptions were issued when vaccination or bone health interventions were indicated.

Table 2- Comparison of Comorbidity Management at Baseline and Follow-up, N=63

	Baseline	F/U	P value
Cardiovascular domain			
Heart Score, median (IQR)	**1.3 (0.9, 3.0)**	**4.3 (1.5, 7.0)**	**<0.001**
LDL above target	52.7	62.3	0.149
Triglycerides >1.7 mmol/L	21.8	21.8	1.000
Hypertensive in clinic	26.7	32.8	0.724
BMI≥25 kg/m^2	**43.5**	**54.0**	**0.046**
BMI≥30 kg/m^2	14.5	19.0	0.248
Active Smoking	23.8	19.0	0.371
Osteoporosis domain			
Vitamin D deficiency (<75nmol/L)	**81.5**	**43.1**	**<0.001**
Patients with BMD testing	88.9	96.8	0.074
T score spine, median	-1.0 (-2.1, 0.2)	-0.8 (-1.9, 4.5)	0.506
T score hip, median	-1.1 (-2.2, -0.4)	-1.0 (-1.8, -0.6)	0.684
Medication Use			
Lipid-lowering agent	10.9	15.4	0.134
Anti-hypertensive medications	23.8	25.8	1.000
Osteoporosis medication	4.8	4.8	1.000
Infection prevention in agreement with recommendations			
Dentist follow-up	75.8	82.5	0.423
Influenza vaccination	**40.7**	**66.1**	**0.004**
Pneumococcal vaccination	58.9	66.1	0.472
DTP vaccination	**57.4**	**73.0**	**0.037**
Malignancy screening in agreement with recommendations			
Colon cancer screening	51.4	57.5	0.424
Dermatology follow-up	**45.2**	**58.7**	**0.043**
Mammography	100	94.4	1.00
Pap smears	87.0	84.0	1.00

*Unless otherwise specified, values represent percentages.
Results that are bolded are significant.
Abbreviations: LDL– low-density lipo-protein, BMI– body mass index, BMD– bone mineral density, DTP= diphtheria-tetanus-polio

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Baseline characteristics were determined using simple statistics. Comorbidity management at the second review was compared to the first using McNemar's test for categorical variables and Wilcoxon signed-rank test for continuous non-normally distributed data.

Results: The cohort included 63 patients (RA: 17, SpA: 46) with a mean disease duration of 21.2 years (SD 14.2), and mean time between visits of 4.1 years (SD 1.5). Among RA patients, 94.1% were female, mean age 58.0 years (SD 16.5), mean DAS28 2.7 (SD 1.8). Among SpA patients, 30.4% were female, mean age 51.8 years (SD 11.7), and mean ASDAS 1.7 (SD 0.8). Corticosteroids use was low (4.8%), while 63.5% of patients received biologics.

Despite 52.7% of patients having elevated LDL, 26.7% being hypertensive, and 43.5% being overweight at baseline, no significant improvement was seen in cardiovascular risk management at follow-up. In contrast, with respect to bone health, there was a significant improvement in rates of vitamin D deficiency from 81.5 to 43.1% ($p< 0.001$). Vaccination adherence improved: influenza coverage increased from 40.7% to 66.1% ($p=0.004$), and DTP from 57.4% to 73.0% ($p=0.037$). Compliance with skin cancer screening rose from 45.2% to 58.7% ($p=0.043$). Adherence to mammography and Pap smear guidelines remained high (>80%) at both time points, suggesting a ceiling effect. No change was observed in colorectal cancer screening rates.

Conclusion: A single structured global review led to meaningful improvements in vaccination coverage, vitamin D deficiency correction, and skin cancer screening among IA patients. However, cardiovascular risk management did not improve, potentially due to the absence of direct prescriptions. These findings support the utility of global reviews while highlighting the need for better coordination in managing complex comorbidities in patients with IA.

Reference: 1. Baillet A, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Annals of the rheumatic diseases. 2016 Jun 1;75 (6):965-73.

Disclosure: A. Kobza: Novartis, 6; **C. Bourgeois**: None; **O. Fogel**: None; **M. Dougados**: None; **A. Molto**: AbbVie/ Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6.

Abstract Number: 0216

Evaluation of oral treatment adherence in Systemic Lupus Erythematosus patients: indentification of risks profiles

Carmen Lasa Teja[1], Carolina Aguirre-Portilla[2], Virginia Portilla González[3], Carmen Bejerano-Herreria[2], Alfonso Corrales-Martínez[4] and Ricardo Blanco[5], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, [4]Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, Santander, Spain, [5]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the sample (n = 115), variables studied, and statistical analysis results.

Variable	Mean ± SD	n (%)	Adherence CQR≥80 (n, %)	p - value
Age (years)	53,35 ± 14,27			
SLE duration (years)	14,27 ± 14			
Overall adherence			67 (58,26)	
Sex				0,0278
Women		105 (91,30)	77 (73,33)	
Men		10 (8,70)	7 (60,0)	
Study level				0,0439
No formal studies		1 (0,87)	0 (0)	
Elementary school studies		18 (15,65)	9 (50,0)	
Secondary school studies		69 (60,0)	44 (63,77)	
University studies		27 (23,48)	22 (81,48)	
Marital status				0,0944
Single		30 (26,09)	16 (53,33)	
Married		69 (60,0)	52 (75,36)	
Divorced		12 (10,43)	6 (50,0)	
Widowed		4 (3,48)	1 (25,0)	
Employment status				0,0316
Employed		55 (47,83)	44 (80,0)	
Unemployed - Retired		60 (52,17)	39 (65,0)	
Comorbidities				0,0402
With comorbidities		99 (86,09)	70 (70,71)	
Without comorbidities		16 (13,91)	13 (81,25)	
Number of oral medications for LES				0,2959
1		73 (63,48)	55 (75,34)	
2		28 (24,35)	20 (71,43)	
3		13 (11,30)	8 (61,54)	
4		1 (0,87)	0 (0)	

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic and complex autoimmune disease that requires adequate treatment adherence to control disease activity and prevent complications. However, adherence rates among SLE patients are generally low, influenced by multiple personal, social, and clinical factors. This study aims to evaluate adherence to oral pharmacological treatment in SLE patients, analyze factors associated with therapeutic compliance, and identify patient profiles with low adherence levels.

Methods: This was an observational, cross-sectional, analytical study conducted on a cohort of 115 SLE patients followed at the Rheumatology outpatient clinic of a tertiary hospital in northern Spain. Adherence to oral treatment was assessed using the Compliance Questionnaire on Rheumatology (CQR), a validated tool for evaluating therapeutic adherence in rheumatologic diseases. Good adherence was defined as a CQR score ≥ 80. Statistical analysis included descriptive statistics and Chi-square tests to identify significant associations between adherence and the studied variables.

Results: Among 115 SLE patients, 105 were women (91.30%), with a mean age of 53.35 ± 14.27 years and an average disease duration of 14.27 ± 14 years. Sociodemographic and clinical factors influencing adherence were analyzed (Table 1), identifying risk profiles with lower compliance. Overall adherence was suboptimal, with only 58.26% achieving a CQR score ≥ 80. Women had higher adherence (73.33%) than men (60.0%). University-educated patients adhered better (81.48%) than those with primary education (50.0%). Married individuals showed the highest adherence (75.36%), while divorced and widowed patients had the lowest (50.0% and 25.0%, respectively). Employment favored adherence (80.0%), surpassing unemployed or retired patients (65.0%). Patients without comorbidities adhered better (81.25%) than those with comorbidities (70.71%). Medication burden influenced adherence, with higher rates in those taking one (75.34%) or two drugs (71.43%) compared to those on three or more. Significant associations were found between adherence and sex ($p = 0.0278$), education ($p = 0.0439$), employment ($p = 0.0316$), and comorbidities ($p = 0.0402$). Marital status ($p = 0.0944$) and medication count ($p = 0.2959$) showed no significant correlation. Low adherence profiles included male sex, lower education, unemployment, comorbidities, and divorced/widowed marital status.

Conclusion: This study highlights the low treatment adherence rates among SLE patients, driven by sociodemographic and clinical factors. Findings emphasize the need for targeted interventions in vulnerable subgroups, including men, individuals with lower educational attainment, unemployed patients, and those with comorbidities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Lasa Teja: None; **C. Aguirre-Portilla**: None; **V. Portilla González**: None; **C. Bejerano-Herreria**: None; **A. Corrales-Martínez**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0217

Development of the American College of Rheumatology Implementation Guide for Integrating Patient Reported Systemic Lupus Erythematosus Quality Measures

Catherine Nasrallah[1], Christine Hariz[2], Shanthini Kasturi[3], Wambui Machua[4], Jinoos Yazdany[5], Christie Bartels[6], Kate Chiseri[7], Starla Blanks[7], Patti Katz[8], Cherish Wilson[9], April Jorge[10], Beth Radtke[11], Tom Tack[7] and Shivani Garg[12], [1]University of California San Francisco (UCSF), San Francisco, CA, [2]University of California San Francisco (UCSF, San Francisco, CA, [3]Tufts Medical Center, Boston, MA, [4]Piedmont Healthcare, Atlanta, GA, [5]UCSF, San Francisco, CA, [6]University of Wisconsin School of Medicine and Public Health, Madison, WI, [7]American College of Rheumatology, Atlanta, GA, [8]UCSF, San Rafael, CA, [9]UCSF / SFVA, San Francisco, CA, [10]Massachusetts General Hospital, Boston, MA, [11]ACR, Atlanta, GA, [12]University of Madison, School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex disease that presents unique care challenges. To improve high-quality patient-centered care, the American College of Rheumatology (ACR), developed evidence-based quality measures related to using patient reported outcome measures (PROMs) in SLE. This study aimed: 1) To conduct qualitative interviews with practices that had implemented ACR-recommended SLE PROMs as part of the pilot evaluation, using the Consolidated Framework for Implementation Research (CFIR) and 2) To synthesize implementation findings to inform the development of the SLE Quality Measures Implementation Guide for national dissemination.

Methods: Using purposive sampling, we invited five community-based rheumatology practices representing geographically diverse clinical settings to pilot the routine collection of SLE PROMs, including measures of physical function (RAPID-3 or MDHAQ) and depression (PHQ-8). After the pilot, rheumatologists and medical staff from each practice participated in qualitative virtual interviews, guided by the CFIR, to identify barriers and facilitators to implementing SLE PROMs and explore resources needed to improve the collection and use of the measures in clinical care. Recorded interviews were transcribed and analyzed thematically using deductive and inductive techniques to identify themes. Subsequently, insights from

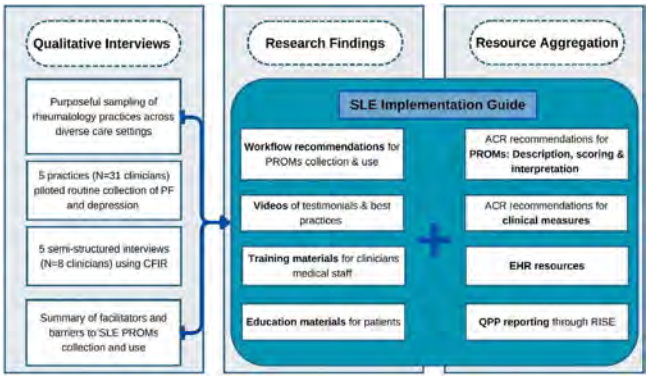


Figure1: Workflow for Developing the SLE Implementation Guide

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of Pilot Practices.

	P1	P2	P3	P4	P5
Geographic region	East South Central	West South Central	South Atlantic	East South Central	South Atlantic
EHR type	NextGen	NextGen	NextGen	NextGen	NextGen
Total number of clinicians at the practice	3	9	12	6	24
Number of clinicians engaged in the pilot	3	8	12	6	2
Number of patients with SLE diagnosis	566	703	883	999	771
Physical function (PF)					
Measure	RAPID3	Full MDHAQ	HAQ	Full MDHAQ	Full MDHAQ
Unique patients PF collected per practice report	>150	65	50	>150	35
Range of scores	0-8	1-8	0-8	1-10	0-8
Depression					
Depression Measure	PHQ8	PHQ8	PHQ8	PHQ8	PHQ8
Unique patients PHQ8 Responses	12	41	30	183	0
Unique patients' depression tools collected per practice report	>150	65	58	>150	35

Table 2: Barriers and Opportunities of SLE PROMs Collection: Findings from Qualitative Interviews

CFIR domain	Barriers	Opportunities
Process	1. Patient identification gaps in check-in workflow 2. Inconsistent collection of PROMs by medical staff 3. Staff oversight in recording scores in EHR 4. Inconsistent discussion of survey results with patients 5. Increased administrative burden	1. Standardizing PROMs integration into SLE patient check-in 2. Scheduling reports to flag upcoming SLE visits 3. Improving patient education about care process 4. Streamlining PROM training and workflows 5. Maintaining consistent PROM collection
Innovation	1. Patient difficulty with score and statement interpretation 2. Physician difficulty interpreting survey score 3. Engaging older patients in mental health discussion 4. Length of the PF forms 5. PHQ-8 questions potentially triggering for patients	1. Normalizing mental health discussions among clinicians 2. EHR templates supporting data entry in the EHR 3. Short questionnaires (PHQ8) 4. Enhancing clinical decision-making 5. Promoting patient-centered care 6. Strengthening patient-clinician rapport 7. Improving patient satisfaction and wellbeing
Individual characteristics	1. Patient survey fatigue 2. Patient privacy concerns and data-sharing resistance	1. Staff commitment and collaboration 2. Reinforcing mental health care and symptom awareness.
Inner setting	1. Unstructured EHR documentation 2. Manual data entry and scoring 3. Communication gaps between MAs and physicians 4. Physicians time constraints 5. Staff turnover and training burden	1. Electronic collection of measures (Phreesia, iPad) 2. Automatic data transmission into structured EHR fields 3. Automatic PROM reminder alerts 4. Enhancing patient awareness of PROM collection 5. Providing mental health resources for patients with high PHQ8 scores
Outer setting	1. Referral delays to mental health care 2. Limited availability of local mental health facilities 3. High cost of physical and occupational therapy 4. Insurance limitations for mental health coverage	1. Proactive referrals for mental health and therapy based on scores 2. Data collection supporting insurance authorization of treatment

interviews, combined with ACR guidelines and other resources, informed the development of an SLE Quality Measures Implementation Guide (Figure 1).

Results: Thirty-one clinicians engaged in the pilot evaluation across five practices (Table 1). Qualitative Interviews with representatives from each practice (N=8) revealed key insights into the innovations, resources, recommendations, best practices, and challenges related to SLE PROMs collection and use (Table 2). Despite challenges with workflow integration, clinician and medical staff engagement, and limited resources, both patients and clinicians supported using PROMs in routine care. PROMs effectively assessed mental health and physical function through standardized workflows, enhanced communication, and EHR integration. These findings informed the development of an online SLE Quality Measures Implementation Guide, designed to aide clinicians and care teams with implementing the recommended measures into clinical practice. Sections include recommended detailed instructions for use of ACR-recommended SLE PROMs, downloadable PROMs, workflow recommendations and scoring guidance. Reflecting themes from interviews, the guide also includes videos on best practices, patient education materials, staff training resources, and validated translations of PROMs in Spanish and Chinese.

Conclusion: This study assessed the implementation of ACR-recommended SLE PROMs in five rheumatology practices and used the findings to develop the SLE Quality Measures Implementation Guide. This guide supports rheumatologists and care teams with integrating PROMs into routine practice by offering guidance and practical strategies for collecting the measures to guide clinical decisions and advance patient-centered care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Nasrallah: None; **C. Hariz**: None; **S. Kasturi**: GlaxoSmithKlein(GSK), 1; **W. Machua**: Aurinia, 2, BMS Foundation, 5, Genentech, 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 1; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5; **C. Bartels**: None; **K. Chiseri**: None; **S. Blanks**: None; **P. Katz**: None; **C. Wilson**: None; **A. Jorge**: Bristol-Myers Squibb(BMS), 5; **B. Radtke**: None; **T. Tack**: None; **S. Garg**: None.

Abstract Number: 0218

Creating an EHR Lupus Outreach Workbench to Address Care Gaps

Ross Gilbert[1], Starla Blanks[2], Joy Buie[3], Mary Cronin[4], Jake Decker[5], Laura Dickmann[6], Cristina Drenkard[7], Sancia Ferguson[8], Shivani Garg[9], David Gazeley[5], Andrea Gilmore-Bykovskyi[10], Gale Johnson[11], Patti Katz[12], Tristan Lazewski[13], S. Sam Lim[14], Jenna McGoldrick[15], Katrina Phelps[10], Edmond Ramly[16], Rosalind Ramsey-Goldman[17], Ann Rosenthal[18], Dawn Thomas-Semanko[19], Sarah Stoltz[13], Patricia Tellez-giron[20], Amannda Weber[21], Andrea Wipperfurth[13] and **Christie Bartels**[10], [1]Johns Hopkins University, Baltimore, MD, [2]American College of Rheumatology, Atlanta, GA, [3]Lupus Foundation of America, Washington, DC, [4]retired, Fox Point, WI, [5]Medical College of Wisconsin, Milwaukee, WI, [6]Froedtert Health, Waukesha, WI, [7]Rollins School of Public Health, Emory University, Atlanta, Georgia, USA, Acworth, GA, [8]University of Wisconsin School of Medicine and Public Health, Madison, Madison, WI, [9]University of Madison, School of Medicine and Public Health, Madison, WI, [10]University of Wisconsin School of Medicine and Public Health, Madison, WI, [11]Wisconsin Department of Health Services, Madison, WI, [12]UCSF, San Rafael, CA, [13]UW Health, Madison, WI, [14]Emory University School of Medicine, Atlanta, GA, [15]SSM Health, Madison, WI, [16]Indiana University - Bloomington, Bloomington, IN, [17]Northwestern University Feinberg School of Medicine, Chicago, IL, [18]Department of Medicine, Division of Rheumatology, Medical College of Wisconsin, Wisconsin, [19]WI Chapter - LFA, Milwaukee, WI, [20]University of Wisconsin, School of Medicine and Public Health, Madison, Madison, WI, [21]University of Wisconsin (UW), UW Health, Madison, WI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus affects up to 1.5 million people in the US with significant health disparities in care and outcomes that call for care delivery innovation. Similar disparities in HIV were addressed using a globally-endorsed Care Continuum model with steps including measuring linkage and retention in specialty care by visits and labs. The Continuum led to evidence-based interventions that improved disease control including an effective Electronic Health Record (EHR) outreach intervention. Given prior success, we aimed to adapt a care retention intervention for SLE. Our objectives were to convene patients, clinicians, public health leaders, and community partners to adapt and design a pilot intervention to address SLE Care Continuum gaps.

Methods: We convened 8 focus groups (3 patient, 3 healthcare, and 2 external rheumatology/public health advisory group meetings) to discuss interventions for care retention in lupus. Participants included 10 patients with SLE, 7 rheumatologists, 2 RNs, 2 primary care physicians, 2 patient advocates, and 3 public health experts. Groups spanned 4 US states, 5 academic centers, 2 countries. Focus groups were a series of 60–90-minute virtual meetings. Transcripts were analyzed using NVivo software for content analysis.

Based on suggestions, experts at one academic center co-designed an EHR (Epic) workbench to highlight clinic patients with SLE lacking: (a) rheum clinic visit scheduled or completed in > 6 months or (b) recent laboratory tests (CBC, creatinine, urinalysis protein, complement, dsDNA every 6 months for SLE, 3 months for lupus nephritis. We added hydroxychloroquine (HCQ) and steroid indicators per 2023 ACR SLE clinical quality measures. Inclusion required age ≥18 and at least 1 rheumatologist lupus code; patients without any rheumatology clinic visits (e.g., receiving outside care) were excluded.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

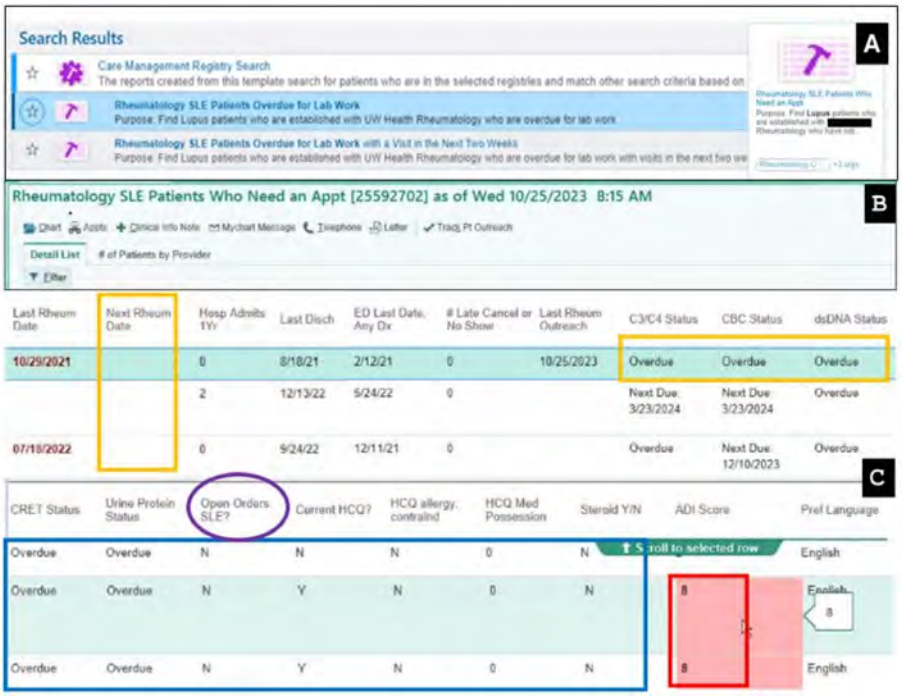


Figure 1: Three Workbench views include 34 columns with selected features shown in A-C. (A) Search panel to specify visit or lab list, (B) Overdue visit and lab list (yellow) with next and last visit dates plus ER and hospital dates, and (C) Other indicators for nephritis, open orders (purple circle), kidney test, HCQ, and steroid indicators (blue box), and adverse Area Deprivation Index (ADI) neighborhood (red) plus preferred language for instance.

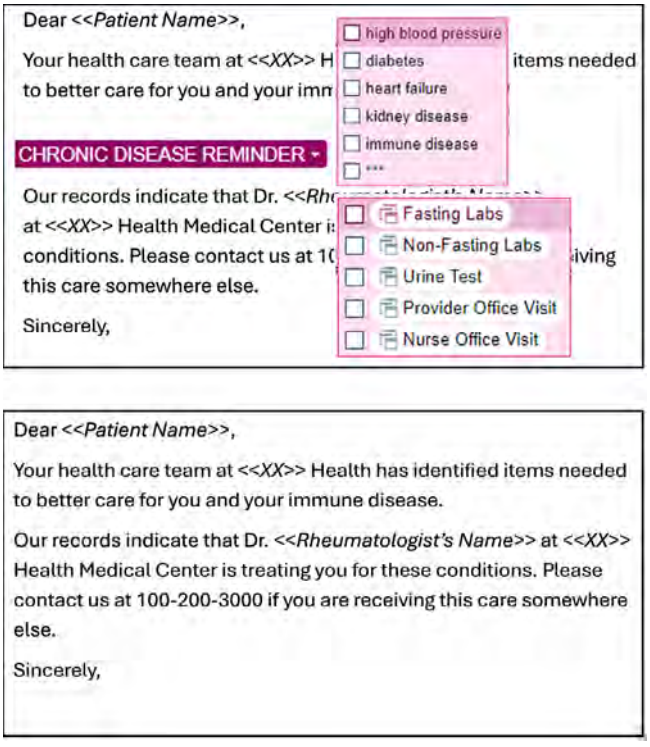


Figure 2: Chronic Disease Outreach Letter staff view (top) and patient view (bottom).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

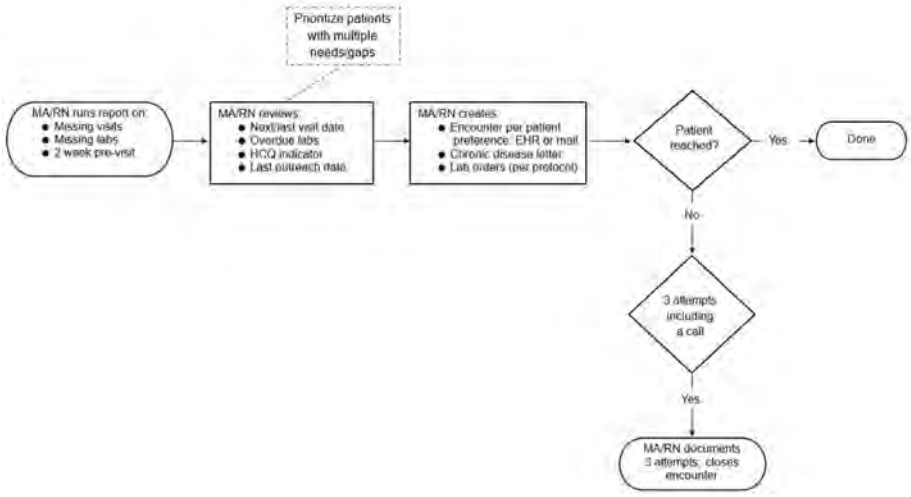


Figure 3: Process flow diagram for using the Lupus Outreach Workbench

Results: Advisors shared desires for patient reminders and outreach for due visits, labs and refills and consistent clinical personnel to address potential barriers (i.e., "patient navigator"). While many supported dedicated patient navigators, clinicians noted low resources and staff turnover as limitations. Based on this input, we designed an EHR staff outreach intervention with potential to scale to other clinics and staff.

Three workbench views (Fig 1a-c) included those lacking: 1) visits, 2) lupus labs, or 3) lacking labs with upcoming visits within 2 weeks (to aid pre-visit planning). The workbench also displays all three 2023 ACR lupus clinical quality measures: hydroxychloroquine use, kidney lab testing, and prednisone reduction.

Outreach tools consisted of modifying an existing chronic disease outreach letter to indicate a need to call for a visit or labs (*Fig 2*). Letters could be sent via EHR portal or mail by patient preference; subsequent contacts included calls by RN/MA outreach staff workflow (*Fig 3*).

Conclusion: Advisors guided adapting a proven EHR outreach intervention for care retention in SLE. Using an EHR workbench and a staff workflow with a simple chronic disease outreach letter, we created tools to address SLE care retention. The workbench also displays all three 2023 ACR lupus quality measures for use in future studies.

Disclosure: R. Gilbert: None; **S. Blanks**: None; **J. Buie**: Bristol-Myers Squibb(BMS), 1, Fate Therapeutics, 1, Genentech, 1, Novartis, 1; **M. Cronin**: None; **J. Decker**: None; **L. Dickmann**: None; **C. Drenkard**: None; **S. Ferguson**: None; **S. Garg**: None; **D. Gazeley**: None; **A. Gilmore-Bykovskyi**: None; **G. Johnson**: None; **P. Katz**: None; **T. Lazewski**: None; **S. Lim**: Accordant, 2, AstraZeneca, 2, Biogen, 5, BMS, 5, Genentech, 2, Gilead, 5, GSK, 2, Novartis, 5, UCB, 5; **J. McGoldrick**: None; **K. Phelps**: None; **E. Ramly**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **A. Rosenthal**: None; **D. Thomas-Semanko**: None; **S. Stoltz**: None; **P. Tellez-giron**: None; **A. Weber**: None; **A. Wipperfurth**: None; **C. Bartels**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0219

Increased Engagement With the RISE Registry Clinician Dashboard Is Associated With Improving Performance on Some but Not All Rheumatology Quality Measures

Jing Li[1], Jessica Fitzpatrick[2], Jinoos Yazdany[2] and **gabriela Schmajuk**[3], [1]University of California, San Francisco, San Francisco, CA, [2]UCSF, San Francisco, CA, [3]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Previous studies have shown that quality measure performance tends to improve after practices join the ACR's Rheumatology Informatics System for Effectiveness (RISE) registry, but the underlying drivers of this improvement remain unclear. One potential factor is access to the RISE web-based clinician dashboard, which provides detailed performance data to support quality improvement. Although many practices access the dashboard, its impact on quality improvement is not well understood. This study evaluated whether year-over-year changes in dashboard engagement were associated with changes in performance on 6 rheumatology-specific quality measures.

Methods: We included practices that reported any of the 6 selected measures in both 2021 and 2022. Included measures are shown in **Table 1**. Using audit log data, dashboard engagement was categorized into 4 levels: Most engaged: ≥2 sessions/month and ≥1 measure-action/month for ≥6 months; Moderately engaged: Some sessions and measure-actions, but below "most" threshold; Minimally engaged: >1 session, 0 actions; No engagement: 0 – 1 session, no actions. Practices were classified based on change in engagement level from 2021 to 2022 (increased, decreased, or no change). For each measure, we calculated performance change and visualized differences across engagement change groups using box plots. Analyses were stratified by baseline performance (above or below the 2021 median). We conducted linear regression analyses to test the association between engagement change and performance change, adjusting for baseline performance, EHR vendor, and an interaction term between engagement change and baseline performance.

Results: Among the 181 practices, most were single-specialty groups, and nearly half used the NextGen EHR (**Table 2**). At baseline, 13% were most engaged, 44% were moderately engaged, 23% were minimally engaged, and 20% had no dashboard engagement. Between 2021 and 2022, 57% of practices had no change in engagement, 26% decreased, and 17%

Table 1. Rheumatology-specific measures included in this study

Measure ID	Measure short name	Measure description
ACR10	Hepatitis B (HBV) screening	Percentage of patients initiating a new conventional or biologic DMARD with HBV screening (HBV surface antigen) in the preceding 12-month period.
ACR14	Gout Serum Urate (SU) target	Percentage of patients with gout on urate lowering therapy for at least 12 months with most recent serum urate at target of < 6 mg/dL.
ACR15	Hydroxychloroquine (HCQ) dosing	Percentage of patients receiving HCQ with an average daily dose at ≤ 5 mg/kg/day.
QPP176	TB screening	Percentage of new biologic DMARD users with a TB test completed in the preceding 12-month period.
QPP177	RA disease activity assessment	Percentage of RA patients with disease activity assessments at ≥ 50% of visits during the measurement year.
QPP178	RA functional status assessment	Percentage of RA patients with at least one functional status assessment during measurement year.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

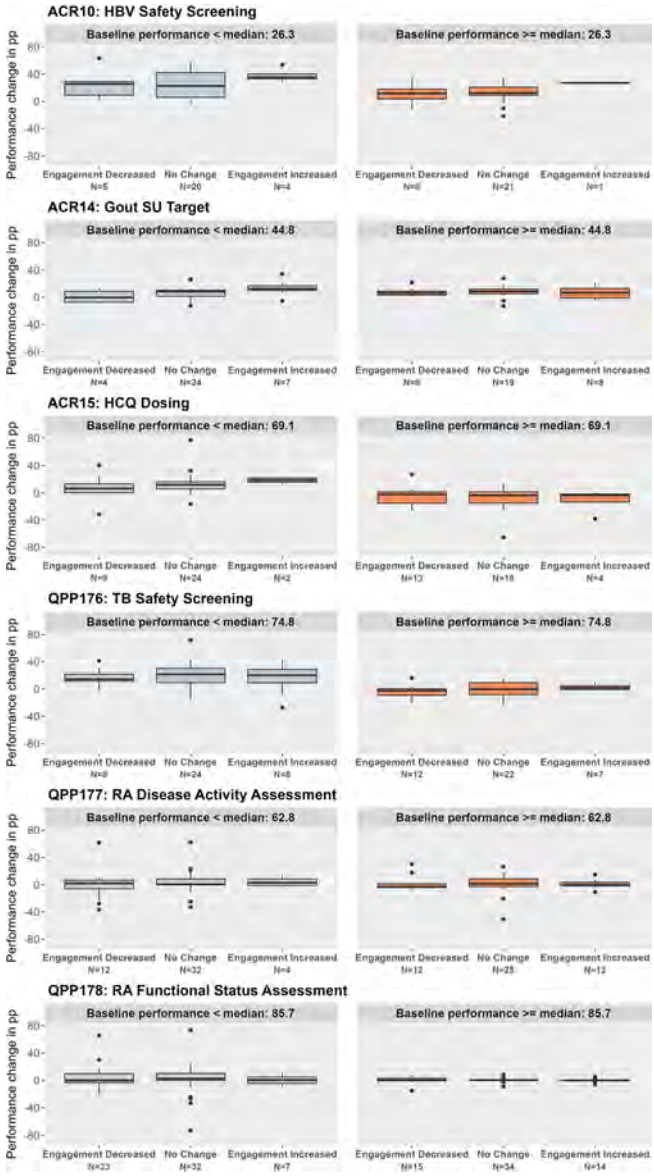


Figure. Distribution of performance change in percentage points (pp) by quality measure and 2021 performance above vs. below the median

Table 2. Characteristics of included RISE practices, according to change in engagement with the RISE clinician dashboard from 2021 to 2022

	Total	Engagement increased	No change	Engagement decreased
N	181	30	104	47
Practice Type				
Single-Specialty Group Practice	107 (59.1)	17 (56.7)	62 (59.6)	28 (59.6)
Solo Practitioner	53 (29.3)	10 (33.3)	32 (30.8)	11 (23.4)
Multi-Specialty Group Practice	21 (11.6)	3 (10.0)	10 (9.6)	8 (17.0)
Region				
South	88 (48.6)	17 (56.7)	50 (48.1)	21 (44.7)
West	41 (22.7)	9 (30.0)	20 (19.2)	12 (25.5)
Northeast	27 (14.9)	2 (6.7)	20 (19.2)	5 (10.6)
Midwest	25 (13.8)	2 (6.7)	14 (13.5)	9 (19.1)
EHR vendor				
Nextgen	85 (47.0)	18 (60.0)	49 (47.1)	18 (38.3)
eClinicalWorks	24 (13.3)	2 (6.7)	13 (12.5)	9 (19.1)
eMDs	23 (12.7)	3 (10.0)	14 (13.5)	6 (12.8)
Amazing Charts	13 (7.2)	3 (10.0)	6 (5.8)	4 (8.5)
Other	36 (19.9)	4 (13.3)	22 (21.2)	10 (21.3)

Disclaimer: This data was supported by the ACR's RISE registry. Views expressed represent those of the authors, not necessarily the ACR.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

increased. Practices that increased their engagement showed greater improvements in performance on certain measures, specifically HBV safety screening, gout serum urate (SU) target, and HCQ dosing (**Figure**). These effects were most evident among practices with below-median baseline performance. Linear regression results aligned with these findings, showing increased engagement to be associated with greater improvements in gout and HCQ measures, although these associations did not reach statistical significance.

Conclusion: Increased engagement with the RISE dashboard from one year to the next was associated with modest performance gains in selected rheumatology quality measures. Prior studies have shown steady improvements in multiple measures after practices join the registry, and these findings suggest that greater use of the dashboard may support quality improvement efforts, especially among lower-performing practices. Additional studies with larger sample sizes are needed to clarify causal pathways and identify strategies to maximize the dashboard's impact on clinical performance.

Disclosure: J. Li: None; **J. Fitzpatrick**: None; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5; **g. Schmajuk**: None.

Abstract Number: 0220

National Implementation of a Medication Safety Dashboard to Improve HLA-B*58:01 Testing Among Allopurinol Users in the Veterans Health Administration

Alissa Becerril[1], Jing Li[2], Cherish Wilson[3], Gary Tarasovsky[4], Abimbola Fadairo-Azinge[5], Mary Whooley[4] and **gabriela Schmajuk**[6], [1]UCSF, san francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]UCSF / SFVA, San Francisco, CA, [4]SFVA, San Francisco, [5]UCSF, San Francisco, [6]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Allopurinol can cause life-threatening severe cutaneous adverse reactions, especially in patients who carry the HLA-B58:01 allele. Because this allele is more common among Southeast Asian and African American individuals, the 2020 American College of Rheumatology Gout Guidelines conditionally recommend genetic testing for these groups before starting allopurinol. To support safer prescribing, we developed and evaluated a national electronic dashboard to promote HLA-B58:01 testing among at-risk allopurinol users in the U.S. Veterans Health Administration (VHA).

Methods: We identified allopurinol users in the VHA using data from the Corporate Data Warehouse. A dashboard was built using Microsoft PowerBI to display patient identifiers, HLA-B58:01 testing status, and self-reported race/ethnicity (**Figure 1**). The dashboard launched nationally in April 2023, and all VHA rheumatologists were notified by email. Dashboard use at each facility was tracked through PowerBI activity logs. Facilities were excluded if they were pilot sites (n=6), used a different EHR (Cerner; n=6), lacked structured fields for HLA-B58:01 testing (n=50), or had no recorded dashboard sessions (n=11).

The main outcome was the weekly percentage of allopurinol users with self-reported Asian or African American race who had completed HLA-B*58:01 testing, between October 2022 and April 2023 (pre-launch) and May 2023 to April 2024 (post-launch). Facilities were categorized as high or low engagement based on how often they used the dashboard after launch (≥20% of weeks vs. < 20%). We used a two-group interrupted time series (ITS) analysis to compare trends in testing between high- and low-engagement facilities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Percentage of HLA-B*58:01 testing among allopurinol users with self-reported Asian and African American race, overall and by engagement group, at the beginning and the end of the study period.

Facility	Week 1 Mean (SD)	Week 80 Mean (SD)
All Facilities (N=57)	1.57 (5.20)	3.00 (6.31)
High Engagement (n=18)	3.09 (8.98)	5.06 (10.08)
Low Engagement (n=39)	0.87 (1.47)	2.05 (3.21)

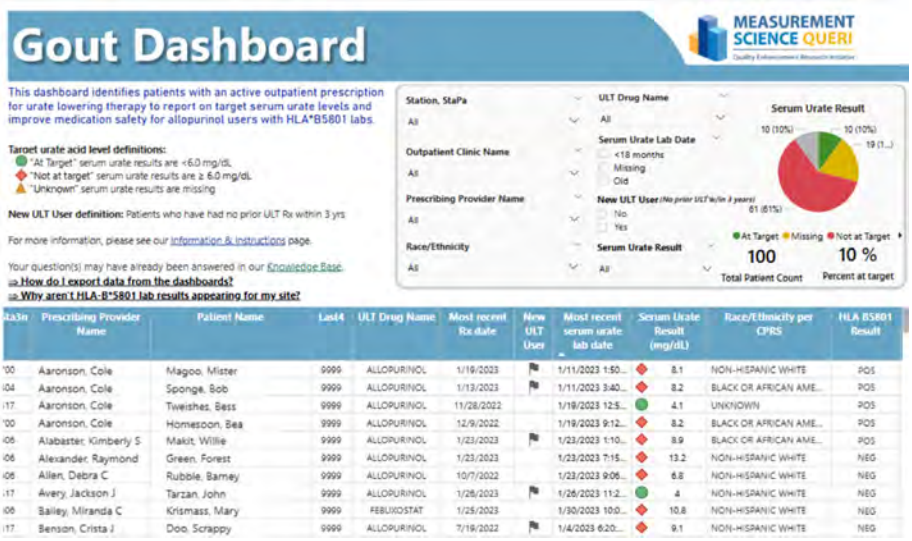


Figure 1. Simulated gout dashboard displaying fictitious patient data for monitoring HLA-B*58:01 testing and serum urate levels. This example shows how users can filter and visualize patient-level data, including urate-lowering therapy use, recent lab results, and HLA-B*58:01 testing status.

Results: The analysis included 57 VHA facilities (86% classified as high complexity), serving 45,500 at-risk allopurinol users. Patients were 97% male, with a mean age of 67.3 years; 88.5% were African American and 11.5% were Asian. Overall, HLA-B*58:01 testing increased from 1.6% at baseline to 3.0% at the end of the study (**Table**). ITS analysis showed a significantly faster increase in testing at high-engagement sites compared to low-engagement sites (post-intervention trend difference: +0.024 percentage points/week, 95% CI: 0.002–0.047; p = 0.03; **Figure 2**).

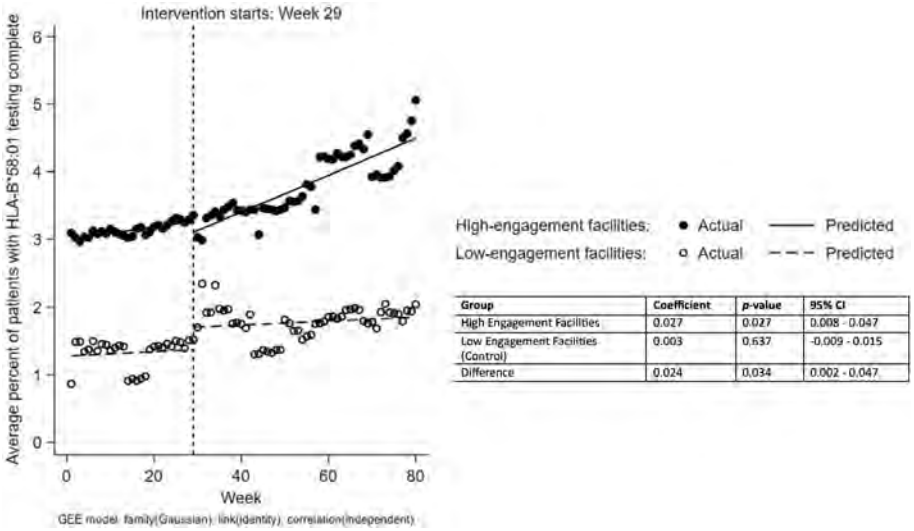


Figure 2. Interrupted time series (ITS) assessing HLA-B*58:01 testing pre- and post-dashboard launch for high vs low-engagement facilities.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Although overall testing rates remained low, implementation of a national dashboard was associated with modest but significant increases in HLA-B*58:01 testing—especially at facilities that regularly used the tool. Future studies should assess testing in an incident user cohort of patients. Ongoing work should focus on maintaining clinician engagement, improving dashboard usability, and assessing the long-term impact on patient safety.

Disclosure: A. Becerril: None; **J. Li**: None; **C. Wilson**: None; **G. Tarasovsky**: None; **A. Fadairo-Azinge**: None; **M. Whooley**: None; **g. Schmajuk**: None.

Abstract Number: 0221

A Multimodal Intervention Improves the Quantity and Quality of Disease Activity Measures Collection in a Multi-centered National Rheumatoid Arthritis Network

Grant Cannon[1], Beth Wallace[2], Deana Lazaro[3], Pascale Schwab[4], Paul Monach[5], Ankoor Shah[6], Gail Kerr[7], Andreas Reimold[8], Joshua Baker[9], Gary Kunkel[10], Katherine Wysham[11], Liron Caplan[12], John Richards[13], Aleksander Lenert[14], Andrew Jones[15], Ted Mikuls[16], Maria I. (\"Maio\") Danila[17], Bryant England[16], Brian Sauer[18], Jorge Rojas[19] and Isaac Smith[20], [1]University of Utah and Salt Lake City VA, Salt Lake City, UT, [2]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [3]VA New York Harbor Healthcare system, Short Hills, NJ, [4]VA Portland and Oregon Health & Science University, Portland, OR, [5]VA Boston Healthcare System, Boston, MA, [6]Duke University, Durham, NC, [7]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [8]Dallas VA Medical Center, Dallas, TX, [9]University of Pennsylvania, Philadelphia, PA, [10]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [11]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [12]Rocky Mountain Regional VAMC, Aurora, CO, [13]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [14]University of Iowa, Iowa City, IA, [15]VA Saint Louis and Washington University, Saint Louis, [16]University of Nebraska Medical Center, Omaha, NE, [17]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [18]Salt Lake City VA/University of Utah, Salt Lake City, UT, [19]VA Puget Sound Health Care System, Seattle, WA, [20]Duke University Hospital, Durham, NC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical guidelines recommend the use of disease activity measures (DAMs) in rheumatoid arthritis (RA) management. Measurement of DAMs is also a critical component of clinical and epidemiologic research in RA. The Veterans Affairs RA (VARA) registry is a prospective cohort study of Veterans with RA that is active at 16 VA Medical Centers. A VARA goal is to systematically collect and document eight DAM components for participants at each in-person clinic visit **(Table1)**. A multimodal intervention was initiated to enhance DAMs collection. This report details preliminary results following three months of implementation of this planned 12-month program.

Methods: This intervention involved three phases: 1) baseline; 2) development: and 3) implementation (**Table 1**). Key activities included qualitative interviews with site investigators to confirm availability of electronic health record (EHR) tools for DAM collection, provision of additional EHR tools if needed, development of monthly just-in-time lists of VARA participant appointments, and monthly provider-specific feedback on DAMs collection performance and comparison to VARA registry overall performance. Verification and retrieval of documented DAM components in the EHR was accomplished through data extraction of note text form the VA Corporate Data Warehouse. Performance at each encounter, by provider and by VARA site over the 3-month implementation phase was compared to baseline performance using chi square testing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic Information and Quality Improvement Program Study Design to Improve Collection of Disease Activity Measures (DAMs) in Clinic Notes for RA Patients in VARA Registry

Phase	Baseline	Program Development	Implementation*
Dates	March - August 2024	September - December 2024	January - March 2025
Phase Duration	6 Months	4 Months	3 months
Clinic Notes	1750	1057	769
Unique Patients	1231	916	728
Unique Providers	119	97	98
Age Project Start	67.2±10.4	67.3±10.5	66.7±10.4
Male Gender (%)	80.2%	81.8%	79.9%
Disease Duration	17.3±13.0	17.0±12.8	16.9±12.3
Activities	▪ Baseline Data Collection ▪ No other Activities	▪ Meeting with VARA Principal Investigators to discuss project goals ▪ Interviews of VARA Site Principal Investigators by Projected Director ▪ Protocol Development ▪ Development of Monthly Patient Lists of Future Rheumatology Clinic Appointments for RA patients Enrolled in VARA ▪ Development of Monthly Site Reports of DAMs collections on individual RA Patients aggregated by Provider	▪ Distribution of Monthly Pending Clinic Visit Reports ▪ Distribution of Monthly Performance Reports ▪ Continuous Feedback ▪ Review of Provider Performance by VARA Site Principal Investigator ▪ Provider Survey of Barriers and Facilitators of DAMs Collection

Outcome Measure Analysis of Each Electronic Medical Record Clinic Note for Each of the Following Factors		
Disease Activity Measure (DAM) Components	**Summary DAM Components**	**Composite DAMs**
Clinical DAM Components	Any DAM Element	DAS_28
Tender Joint Count	All Clinical DAM Element	DAS_28-CRP
Swollen Joint Count	Both ESR & CRP	CDAI
Patient Global Assessment	All 8 DAM Elements	RAPID_3
Provider Global Assessment		Any Composite DAM
Global Pain Score		
Multi-Dimensional Health Assessment Questionnaire		
2 Laboratory DAM Components		
Erythrocyte Sedimentation Rate (ESR)		
C-reactive Protein (CRP)		

*First 3 months of 12-month quality improvement process to improve DAMs collection in RA Patients Enrolled in the VARA registry.

Results: Between March 2024 through March 2025, 3,576 in-person rheumatology clinic visits occurred in 1,436 RA patients enrolled in VARA who were seen by 135 unique providers. The distribution of these visits and basic demographic information on these patients during the baseline, development, and implementation phases are listed (**Table 1**). Compared to baseline values, there was a significant increase in the documentation of individual DAM components, combined DAM components, and composite DAMs during the implementation phase with increases ranging from 5.8% to 10.4% (**Table 2**). Analyses limited to the 44 providers completing ≥5 clinical notes during both the baseline and implementation phases demonstrated an increase in the number of providers successfully documenting DAMs in >50% of encounters (**Table 3**). A separate analysis of DAMs collection by all providers at each VARA site also showed improvement in the number of VARA sites successfully documenting DAMs (**Table 3**).

Conclusion: This multimodal intervention increased DAM collection and documentation in clinical notes, expanded the number of providers consistently collecting DAMs, and enhanced the performance at VARA registry sites during an initial 3-month intervention phase. Ongoing monitoring will determine if additional performance improvement occurs through sustained intervention over a 12-month follow-up. This work demonstrates that collaborative actions in a multi-center registry

Table 2. Documentation of Specific Disease Activity Measure (DAM) Components and Composite DAMs in Clinic Notes During Baseline and Implantation Phases

	Study Time Period			
	Baseline (N=1750)	Intervention (n=769)	Change from Baseline	p-value*
DISEASE ACTIVITY MEASURE (DAM) COMPONENTS				
Clinical DAM Components				
Tender Joint Count	62.6%	68.4%	5.8%	0.0049
Swollen Joint Count	62.6%	68.4%	5.8%	0.0054
Patient Global Assessment	54.9%	61.5%	6.7%	0.0020
Provider Global Assessment	56.3%	62.7%	6.3%	0.0006
Global Pain Score	55.0%	65.4%	10.4%	<0.00001
Multi-Dimensional Health Assessment Questionnaire	44.7%	54.4%	9.6%	<0.00001
Laboratory DAM Components				
Erythrocyte Sedimentation rate (ESR)	43.0%	49.4%	6.4%	0.0028
C-reactive Protein (CRP)	40.1%	48.0%	7.9%	0.0002
Combined DAM Component Measures				
One or more DAM components documented	64.5%	71.8%	7.3%	0.0003
All Clinic DAM components documented	41.9%	50.1%	8.1%	0.0004
All Laboratory DAM components documented	38.1%	46.3%	8.2%	0.0001
All Clinic and Laboratory DAM components documented	29.0%	36.3%	7.3%	0.0003
COMPOSITE DISEASE ACTIVITY MEASURES (DAM)				
Disease Activity Score 28 Joint Count (DAS-28)	38.2%	44.2%	6.0%	0.0044
Disease Activity Score 28 Joint Count-CRP (DAS28-CRP)	36.5%	44.1%	7.6%	0.0004
Clinical Disease Activity Index (CDAI)	52.6%	58.0%	5.4%	0.0120
Routine Assessment of Patient Index Data 3 (RAPID3)	32.8%	39.9%	7.1%	0.0006
Any Composite DAM	54.5%	61.0%	6.5%	0.0025

*Comparison by chi square test

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Comparison of Numbers of Providers and VARA Registry Sites Documenting Disease Activity Measures (DAM) Components at Baseline and During Intervention Phases

Providers*

	Baseline (n=44)	Intervention (n=44)	Change from Baseline	p-value**
One or More DAM Components Documented in Note				
Outcome Documented in ≥50% of Notes	30 (68.1%)	36 (81.8%)	13.6%	0.130
Outcome Documented in <50% of Notes	14 (31.8%)	8 (18.1%)		
All Six Clinical DAM Components Documented in Note				
Outcome Documented in ≥50% of Notes	14 (31.8%)	23 (52.2%)	20.5%	0.051
Outcome Documented in <50% of Notes	30 (68.1%)	21 (47.7%)		
All Clinical and Laboratory DAM Components Documented in Note				
Outcome Documented in ≥50% of Notes	6 (13.6%)	15 (34%)	20.5%	0.025
Outcome Documented in <50% of Notes	38 (86.3%)	29 (65.9%)		

VARA Sites

	Baseline (n=16)	Intervention (n=16)	Change from Baseline	p-value**
One or More DAM Components Documented in Note				
Outcome Documented in ≥50% of Notes	9 (56.2%)	13 (81.2%)	25.0%	0.124
Outcome Documented in <50% of Notes	7 (43.7%)	3 (18.7%)		
All Six Clinical DAM Components Documented in Note				
Outcome Documented in ≥50% of Notes	3 (18.7%)	7 (43.7%)	25.0%	0.127
Outcome Documented in <50% of Notes	13 (81.2%)	9 (56.2%)		
All Clinical and Laboratory DAM Components Documented in Note				
Outcome Documented in ≥50% of Notes	2 (12.5%)	5 (31.2%)	18.8%	0.120
Outcome Documented in <50% of Notes	14 (87.5%)	11 (68.7%)		

* Limited to the 44 Providers with ≥5 Clinical Notes during Both the Baseline and Intervention Phases.
** Comparison by chi square test

can improve both the quantity and quality of high-yield clinical data collected to facilitate patient care and research. These methods may be applied in additional clinical settings to improve real-world collection of DAMs.

Disclosure: G. Cannon: None; **B. Wallace**: None; **D. Lazaro**: None; **P. Schwab**: None; **P. Monach**: Boehringer-Ingelheim, 2; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **A. Reimold**: None; **J. Baker**: Amgen, 5; **G. Kunkel**: None; **K. Wysham**: None; **L. Caplan**: None; **J. Richards**: None; **A. Lenert**: None; **A. Jones**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5; **B. England**: Boehringer-Ingelheim, 2, 5; **B. Sauer**: None; **J. Rojas**: None; **I. Smith**: None.

Abstract Number: 0222

Evaluating the Barriers and Facilitators for Collecting and Documenting Rheumatoid Arthritis Disease Activity Measures Using a Rheumatology Provider Survey

Isaac Smith[1], Linda Tovar[2], Michael Battistone[2], Andrea Barker[3], Bryant England[4], Ankoor Shah[5], Joshua Baker[6], Katherine Wysham[7], Beth Wallace[8], Ted Mikuls[4], Deanna Lazaro[9], Pascale Schwab[10], Paul Monach[11], Gail Kerr[12], Andreas Reimold[13], Gary Kunkel[2], Liron Caplan[14], John Richards[15], Aleksander Lenert[16], Andrew Jones[17], Maria I. (\"Maio\") Danila[18], Brian Sauer[19], Jorge Rojas[20] and Grant Cannon[21], [1]Duke University Hospital, Durham, NC, [2]Salt Lake City VA, Salt Lake City, UT, [3]Salt Lake City VA, Cottonwood Heights, UT, [4]University of Nebraska Medical Center, Omaha, NE, [5]Duke University, Durham, NC, [6]University of Pennsylvania, Philadelphia, PA, [7]VA PUGET SOUND/ UNIVERSITY OF WASHINGTON, Seattle, WA, [8]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [9]VA New York Harbor Healthcare System, Brooklyn, NY, [10]Oregon Health & Science University, Portland, OR, [11]VA Boston Healthcare System, Boston, MA, [12]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [13]Dallas VA Medical Center, Dallas, TX, [14]University of Colorado, Denver, CO, [15]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [16]Iowa Carver College of Medicine, Iowa City, IA, [17]VA Saint Louis and Washington University, Saint Louis, [18]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [19]Salt Lake City VA/University of Utah, Salt Lake City, UT, [20]VA Puget Sound Health Care System, Seattle, WA, [21]University of Utah and Salt Lake City VA, Salt Lake City, UT

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Disease Activity Measurement Components Ranked by Difficulty of Collection based on Rheumatology Provider Responses. CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate; MDHAQ, Multi-Dimensional Health Assessment Questionnaire; VARA, Veterans Affairs Rheumatoid Arthritis Registry

	Full Population N = 64		Provider Response by VARA Site Performance				
			High-Performing Sites n = 29		Low-Performing Sites n = 35		
How difficult is it for you to collect the...	Some Difficulty†	No Difficulty‡	Some Difficulty†	No Difficulty‡	Some Difficulty†	No Difficulty‡	p-value*
MDHAQ	67.2%	32.8%	55.2%	44.8%	77.1%	22.9%	0.06
Erythrocyte Sedimentation Rate (ESR)	53.1%	46.9%	48.3%	51.7%	57.1%	42.9%	0.48
C-Reactive Protein (CRP)	53.1%	46.9%	48.3%	51.7%	57.1%	42.9%	0.48
Patient Global Assessment	42.2%	57.8%	27.6%	72.4%	54.3%	45.7%	0.03
Patient Pain Score	23.4%	76.6%	17.2%	82.8%	28.6%	71.4%	0.29
Swollen Joint Count	21.9%	78.1%	17.2%	82.8%	25.7%	74.3%	0.41
Tender Joint Count	20.3%	79.7%	17.2%	82.8%	22.9%	77.1%	0.58
Physician Global Assessment	18.8%	81.3%	17.2%	82.8%	20.0%	80.0%	0.78

† "Some Difficulty" includes the following survey responses: slightly difficult, moderately difficult, very difficult, extremely difficult.
‡ "No Difficulty" includes the following survey response: not difficult at all.
* Chi-square comparison of provider responses at high- versus low-performing VARA sites.

Background/Purpose: Collection of disease activity measures (DAMs) is a key component of high-quality care for rheumatoid arthritis (RA) patients. This study surveyed rheumatology providers at Veterans Affairs RA (VARA) registry sites to identify barriers and facilitators for collecting and documenting DAMs.

Methods: The VARA registry is multicenter, prospective cohort study of US Veterans with RA who receive care within the Veterans Health Administration. A provider survey was developed to investigate barriers and facilitators for collecting and documenting DAMs [tender joint count (TJC), swollen joint count (SJC), Physician Global Assessment (PGA), Patient Global Assessment (PtGA), pain score (PS), Multi-Dimensional Health Assessment Questionnaire (MDHAQ), Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP)] for RA patients at each VARA site. Survey questions were then independently evaluated and refined by 5 expert reviewers. The final 42-question survey was administered to 92 VA rheumatology providers at 16 VARA sites. Sites were designated as high- or low-performing based on whether the percentage of site notes that documented all 6 clinical DAMs (TJC, SJC, PGA, PtGA, PS, MDHAQ) for VARA participants was above or below the mean of the 16 VARA sites from 3/2024 to 3/2025. Responses were scored using 5-point Likert scales. Responses were grouped into "no difficulty or barrier" and "some difficulty or barrier" categories for DAM barrier questions and "very helpful" and "less helpful" categories for DAM facilitator questions due to clustering of responses at the low and high ends of the barrier and facilitator scales respectively. Results were reported as descriptive statistics, and provider responses from high- and lower-performing sites were compared using chi-square testing.

Table 2. Barriers to Collecting Disease Activity Measures Ranked by Provider Response Frequency. CPRS, Computerized Patient Record System; CRP, C-Reactive Protein; DAMs, Disease Activity Measures; ESR, Erythrocyte Sedimentation Rate; VARA, Veterans Affairs Rheumatoid Arthritis Registry.

	Full Population N = 64		Provider Response by VARA Site Performance				
			High-Performing Sites n = 29		Low-Performing Sites n = 22		
In your clinical setting, how significant are the following barriers to collecting DAMS?	Some Barrier†	No Barrier‡	Some Barrier†	No Barrier‡	Some Barrier†	No Barrier‡	p-value*
ESR and CRP labs are not drawn prior to clinic visit.	90.6%	9.4%	93.1%	6.9%	88.6%	11.4%	0.54
DAMs forms are available but not completed.	75.0%	25.0%	72.4%	27.6%	77.1%	22.9%	0.66
There is insufficient time to collect DAMs data.	70.3%	29.7%	58.6%	41.4%	80.0%	20.0%	0.06
Rheumatology fellows do not consistently collect or document DAMs for VARA patients they see in clinic.	65.6%	34.4%	55.2%	44.8%	74.3%	25.7%	0.11
Lack of research support staff in clinic to assist with collecting DAMs.	65.6%	34.4%	51.7%	48.3%	77.1%	22.9%	0.03
There is insufficient time to document DAMs in CPRS.	59.4%	40.6%	51.7%	48.3%	65.7%	34.3%	0.26
Veterans who require DAMs assessments are not identified.	53.1%	46.9%	37.9%	62.1%	65.7%	34.3%	0.03
VARA patients who require DAMs are seen by non-VARA providers.	46.9%	53.1%	44.8%	55.2%	48.6%	51.4%	0.77
DAM forms are not available in the clinic.	40.6%	59.4%	31.0%	69.0%	48.6%	51.4%	0.16
Templates for DAMs entry are not available for use in CPRS notes.	26.6%	73.4%	17.2%	82.8%	34.3%	65.7%	0.12
I am not aware of the goal to collect DAMs for all VARA patients.	14.1%	85.9%	10.3%	89.7%	17.1%	82.9%	0.44
I am not adequately trained to assess and document DAMs.	4.7%	95.3%	3.4%	96.6%	5.7%	94.3%	0.67

† "Some Barrier" includes the following survey responses: slightly significant, moderately significant, very significant, extremely significant.
‡ "No Barrier" includes the following survey response: not a barrier.
* Chi-square comparison of provider responses at high- versus low-performing VARA sites.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Facilitators of Collecting Disease Activity Measure Ranked by Provider Response Frequency. Note: the "N" and "n" of the full population and high- and low-performing sites excludes providers who responded, "not currently available at my site." CPRS, Computerized Patient Record System; CRP, C-Reactive Protein; DAMs, Disease Activity Measures; ESR, Erythrocyte Sedimentation Rate; VARA, Veterans Affairs Rheumatoid Arthritis Registry.

	Full Population			Provider Response by VARA Site Performance						
				High-Performing Sites*			Low-Performing Sites*			
At your VARA site, how helpful are the following facilitators in completing DAMs?	N	Very Helpful†	Less Helpful‡	n	Very Helpful†	Less Helpful‡	n	Very Helpful†	Less Helpful‡	p-value*
VARA patients are seen in a rheumatoid arthritis specific clinic.	22	72.7%	27.3%	14	100.0%	0.0%	8	25.0%	75.0%	<0.01
Having standardized templates for VARA patients within CPRS.	57	66.7%	33.3%	26	76.9%	23.1%	31	58.1%	41.9%	0.13
Having printed DAM forms available in clinic.	62	66.1%	33.9%	28	71.4%	28.6%	34	61.8%	38.2%	0.42
ESR and CRP labs are routinely drawn on all VARA patients prior to clinic visit.	45	64.4%	35.6%	23	69.6%	30.4%	22	59.1%	40.9%	0.46
Having research support staff assisting with collecting DAMs.	34	61.8%	38.2%	16	56.3%	43.8%	18	66.7%	33.3%	0.53
Having research support staff assisting with documenting DAMs.	35	60.0%	40.0%	18	50.0%	50.0%	17	70.6%	29.4%	0.21
Identifying upcoming VARA patient appointments prior to the visit.	49	51.0%	49.0%	23	39.1%	60.9%	26	61.5%	38.5%	0.12
Ensuring providers are made aware of the goals to collect DAMs on all VARA patients.	61	50.8%	49.2%	28	57.1%	42.9%	33	45.5%	54.5%	0.36
Routine provider training on the collection of DAMs.	56	42.9%	57.1%	26	46.2%	53.8%	30	40.0%	60.0%	0.64
Ensuring that VARA patients are only seen by VARA providers.	41	36.6%	63.4%	19	42.1%	57.9%	22	31.8%	68.2%	0.50
The availability and usability of the VARA Rheumatoid Arthritis Dashboard.	53	30.2%	69.8%	27	25.9%	74.1%	26	34.6%	65.4%	0.49

† "Very Helpful" includes the following survey responses: quite helpful, essential.
‡ "Less Helpful" includes the following survey response: not helpful, slightly helpful, moderately helpful.
* Chi-square comparison of provider responses at high- versus low-performing VARA sites.

Results: 66 providers (71.7%) from 15 sites (93.8%) submitted survey responses. Providers at both high-and low-performing sites reported the MDHAQ, ESR, CRP, and PtGA were the most difficult DAMs to collect (**Table 1**). Providers at both high- and low-performing sites reported the most common DAM barriers were labs not being drawn prior to clinic visits, DAM forms not being completed, insufficient time, inconsistent DAMs assessment by fellows, and lack of research support staff (**Table 2**). Providers at low-performing sites cited two barriers more often than high-performing sites: lack of research support staff (77.1% vs. 51.7%; p=0.03) and failure to identify Veterans requiring DAMs assessments (65.7% vs. 37.9%; p=0.03). Among all respondents, the most common DAM facilitators were having an RA-specific clinic, using standardized DAM templates, using printed DAM forms, drawing labs before clinic visits, and having research support staff (**Table 3**). Providers at high-performing sites noted having an RA-specific clinic as a facilitator more often than low-performing sites (100.0% vs. 25.0%; p< 0.01).

Conclusion: Our rheumatology provider survey identified several modifiable barriers and facilitators for DAMs collection and documentation for RA patients. These results will inform future VARA registry QI efforts and may provide useful information to improve DAMs collection and documentation in other healthcare systems.

Disclosure: I. Smith: None; **L. Tovar**: None; **M. Battistone**: None; **A. Barker**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **J. Baker**: None; **K. Wysham**: None; **B. Wallace**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **D. Lazaro**: None; **P. Schwab**: None; **P. Monach**: Boehringer-Ingelheim, 2; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **A. Reimold**: None; **G. Kunkel**: None; **L. Caplan**: None; **J. Richards**: None; **A. Lenert**: None; **A. Jones**: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5; **B. Sauer**: None; **J. Rojas**: None; **G. Cannon**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0223

Timely Dermatologic Diagnosis and Management Changes in Systemic Collagen Vascular Diseases: Experiences from the Rheumatology-Dermatology Combined Clinic

Gopisree Peringeth[1], Benedict Wu[1], Shudan Wang[2], Beth McLellan[3], Clement Tagoe[4] and **Jeanie Lee**[1], [1]Albert Einstein College of Medicine - Montefiore Medical Center, Bronx, NY, [2]Montefiore Medical Center, Bronx, NY, [3]Albert Einstein College of Medicine - Montefiore Medical Center, Bronx, [4]Albert Einstein College of Medicine, FRESH MEADOWS, NY

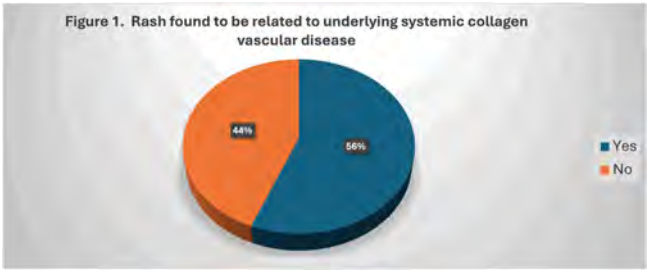
SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Collagen vascular diseases (CVD) often present with skin manifestations, but it is not always clear whether these changes are directly related to the underlying autoimmune condition. Therefore, a collaborative effort between rheumatologists and dermatologists is imperative to distinguish dermatoses related to systemic CVD versus dermatoses unrelated to systemic CVD. By promptly identifying systemic CVD with skin involvement, early changes in therapies can lead to better outcomes. The goals of this study were to 1) identify the percentage of dermatoses that were associated with systemic CVD, 2) identify and describe the frequency of immunosuppressive therapy modifications after patients' first rheumatology-dermatology combined clinic (RDCC) visit.

Methods: All patients who were evaluated at the RDCC between February 2023 to February 2025 were included in this study. Patients were assessed simultaneously by one of two rheumatologists and one dermatologist. A retrospective study chart review was performed using the electronic medical records. Data collection included RDCC pre-clinic diagnosis and systemic CVD treatment, as well as post-clinic diagnosis and systemic CVD treatment. Secondary outcomes were autoimmune serologies, skin biopsy frequency, rates of clinical photography, and topical therapies. The data was analyzed using descriptive statistics. The IRB reviewed and approved the study (#2023-15460).

Results: A total of 98 patients were identified. Of these, 56% had dermatoses related to systemic CVD, while 44% had dermatoses unrelated to systemic CVD (Figure 1). At the end of the first RDCC visit, 43% of the patients had a change in immunosuppressive therapy, with the majority receiving an additional immunosuppressant or dose escalation of current therapy (Figure 2). Of the 62 patients with positive autoimmune serologies, the most common was antinuclear antibody (ANA), followed by anti-SSA antibody and anti-RNP antibody (Figure 3). Skin biopsies were performed in 22% of the cases, and clinical photography was recorded in 91% of the cases.



The post-clinic diagnoses include Systemic lupus erythematosus/ Cutaneous lupus erythematosus (25.6%), non-CVD (17.4%), Rheumatoid arthritis (10.2%), Scleroderma (10.2%), Psoriatic arthritis (9.18%), Dermatomyositis (8.2%), Undifferentiated connective tissue disease (6.1%), Sjogren's syndrome (3.1%), Sarcoidosis (3.1%), Mixed connective tissue disease (2%), Erythema nodosum (1.0%), Panniculitis (1.0%), Morphea (1.0%), Raynaud's (1.0%), Ankylosing spondylitis (1.0%).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

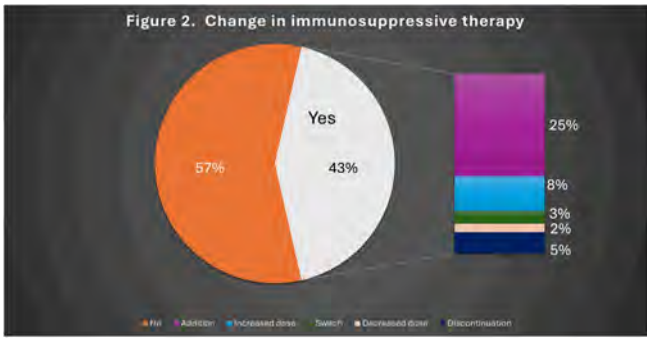


Figure 3. The serologies of patients seen in the RDCC

Positive autoimmune serology	N=62
ANA	50
SSA	21
RNP	16
RF	9
Centromere	8
CCP	4
MDA5	1
PR3	1
MPO	1

ANA: Anti-nuclear antibody, SSA: anti-SSA/Ro antibody, RNP: anti-RNP antibody, RF: Rheumatoid factor, Centromere: anti-centromere antibody, CCP: anti-cyclic citrullinated peptide, MDA5: anti-melanoma differentiation-associated protein 5, PR3: anti-proteinase 3 antibody, MPO: anti-myeloperoxidase antibody

Conclusion: The RDCC was designed to streamline communications between rheumatologists and dermatologists, to improve diagnostic accuracy and timely management in patients with suspected systemic CVD with skin involvement. Based on our clinic experience, over half of the patients referred for dermatoses had underlying systemic CVD. This finding suggests there may be some diagnostic uncertainty when either field refers to the other and highlights the benefit of a combined clinic. The diagnostic uncertainty becomes more evident in patients with positive ANA or anti-SSA antibodies. Moreover, there was a change in immunosuppressive therapy in almost half of the patients after their initial RDCC visit, demonstrating the importance of timely management changes made possible through our RDCC.

Disclosure: G. Peringeth: None; **B. Wu**: None; **S. Wang**: None; **B. McLellan**: Bristol-Myers Squibb(BMS), 5, Daiichi Sankyo, 1, Johnson & johnson, 1; **C. Tagoe**: None; **J. Lee**: None.

Abstract Number: 0224

Improving Adherence to Pulmonary Hypertension Screening in Systemic Sclerosis Patients: Post-Intervention Analysis

John Hickernell[1] and Zineb Aouhab[2], [1]Loyola Univeristy Medical Center, Chicago, IL, [2]Loyola University Medical Center, Oak Brook, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic data of patients in post-intervention analysis.

Demographic	Count (n=48)	Percentage
Sex		
Female	44	91.7%
Male	4	8.3%
Race		
White	33	68.8%
Black	5	10.4%
Latino	10	20.8%

Background/Purpose: Annual screening for pulmonary hypertension (PH) in patients with Systemic Sclerosis (SSc) reduces mortality. The American College of Radiology, European Society of Cardiology/European Respiratory Society, and the 6th World Symposium of PH all recommend yearly screening with 1) Pulmonary Function Testing (PFT) with diffusing capacity for carbon monoxide (DLCO), 2) Transthoracic Echocardiogram (TTE), and 3) B-natriuretic peptide (BNP). However, clinician adherence is variable, with one study reporting rates as low as 34% (Pauling JD *et al*.).

We previously conducted a retrospective study assessing PH screening in our quaternary medical center, presented at ACR 2024. Based on these findings, we implemented a quality improvement (QI) intervention consisting of a departmental presentation outlining our adherence rates and a streamlined electronic order set for all three tests.

Methods: To evaluate the impact of this intervention, we analyzed screening compliance over a six-month period (September 17, 2024 to March 17, 2025). Inclusion criteria matched our prior study: 1) rheumatologist-diagnosed SSc, 2) age over 18 years at diagnosis, 3) seen in our rheumatology clinics, and 4) no prior PH diagnosis.

We reviewed charts for completed PFTs, TTEs, and BNPs. "Full compliance" was defined as completion of all three tests within 12 months prior or 6 months after an outpatient visit. "Ever compliant" was defined as completion of at least one of these tests, maintaining consistency with our prior methodology.

Results: A total of 48 patients met these criteria, accounting for 70 outpatient visits. Demographically, 91% (44) of patients were female, 68.8% (33) White, 10.4% (5) Black, and 20.8% (10) Latino (Table 1). At the visit level, 74% (52) had at least one screening test completed, and 20% (14) had all three tests completed. Individually, 48.6% (34) of visits had a PFT, 67.1% (47) a TTE, and 30% (21) a BNP (Figure 1).

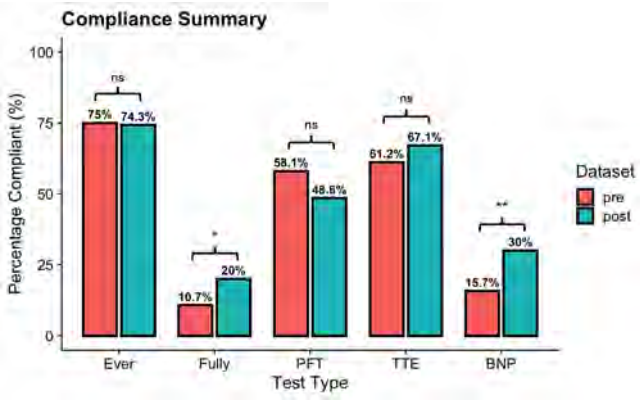


Figure 1: Percentage compliance with recommended testing per appointment. "Ever" indicates completion of at least one of the three tests (PFT, TTE, BNP), while "Fully" indicates completion of all three within 12 months prior to or 6 months after the visit. Compliance is also shown for each individual test. Bars represent pre-intervention (red) and post-intervention (teal) proportions. p-values reflect two-proportion Z-tests comparing pre- and post-intervention groups. *$p < 0.05$, **$p < 0.01$

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Pre- & post-intervention analysis using two-proportion Z test. *p < 0.05, **p < 0.01

Metric	Pre (%)	Post (%)	Difference (%)	z-stat	p-value
Ever Compliant	75	74.3	–0.7	0.125	0.90
Fully Compliant	10.7	20	+9.3	-2.234	0.0255*
PFT	58.1	48.6	–9.5	1.529	0.126
TTE	61.2	67.1	+5.9	-0.981	0.326
BNP	15.7	30	+14.3	-2.619	0.009**

Comparing pre- and post-intervention periods using a two-proportion Z test (Table 2), full compliance increased significantly from 10.7% to 20% (z=-2.234, p=0.0255), and BNP testing improved from 15.7% to 30% (z=-2.619, p=0.009). Changes in PFT, TTE, and ever-compliant rates were not statistically significant.

Conclusion: Our QI intervention significantly improved adherence to full, guideline-based PH screening and BNP testing in SSc patients. Barriers remain for PFT and TTE completion, which require additional efforts in patient scheduling and follow-through. Future interventions will target these challenges through patient education materials and streamlined coordination support.

Disclosure: J. Hickernell: None; **Z. Aouhab**: None.

Abstract Number: 0225

Positive anxiety, depression and/or fibromyalgia screening on validated MDHAQ indices is seen in 30-50% of routine care patients with all rheumatic diagnoses

Juan Schmukler[1], Tengfei Li[2] and Theodore Pincus[1], [1]Rush University Medical Center, Chicago, IL, [2]Rush, chicago, IL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Comorbid anxiety (ANX), depression (DEP), and fibromyalgia(FM) are reported as more common in patients with rheumatoid arthritis (RA) and other rheumatic diagnoses than in the general population. These comorbidities are associated with elevated RA indices such as DAS28 and CDAI designed to assess inflammatory activity. However, formal recognition of ANX, DEP, and/or FM is largely limited to research studies, as multiple patient questionnaires are not feasible in busy routine care. Three validated indices within a multidimensional health assessment questionnaire (MDHAQ), MAS 2 - MDHAQ anxiety screen, MDS2 - MDHAQ depression screen, and FAST4 - fibromyalgia assessment screening tool, agree >80% with reference questionnaires. We analyzed the prevalence of positive MDHAQ screening for comorbid ANX, DEP, and/or FM on MDHAQ indices in unselected routine care patients with any rheumatic diagnosis seen at an academic medical center.

Methods: All patients with all diagnoses at the study site are asked to complete an MDHAQ at each rheumatology visit prior to seeing a health professional. The prevalence of positive screening on the MDHAQ indices for ANX, DEP, and FM was computed according to ICD-10 diagnoses. Diagnoses with fewer than 20 patients were grouped as "other inflammatory" (other inflam) or "other noninflammatory" (other non-inflam).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table: Proportion of patients in each category who screen positive or negative for any of the 3 MDHAQ indices for anxiety, depression, and/or fibromyalgia and each individual index

1º Diagnosis	n	% ANX, DEP, &/or FM pos	% Anxiety pos	% Depression pos	% FM pos	% ANX, DEP, & FM neg
Inflammatory diagnoses						
Myositis	21	48%	38%	33%	10%	52%
Sjogren syndrome	45	47%	33%	27%	24%	53%
Polymyalgia rheumatica	22	45%	18%	27%	27%	55%
Systemic lupus erythematosus	215	45%	33%	23%	22%	55%
Psoriatic arthritis	40	45%	33%	30%	25%	55%
Rheumatoid arthritis	366	43%	25%	23%	27%	57%
Spondyloarthropathy	29	38%	31%	21%	28%	62%
Other inflammatory	54	37%	17%	15%	26%	63%
Systemic sclerosis	23	35%	35%	9%	9%	65%
Vasculitis	27	30%	19%	22%	7%	70%
Crystal arthritis	50	30%	20%	20%	12%	70%
Non-inflammatory diagnoses						
Other non-inflammatory	152	52%	39%	31%	24%	48%
Osteoarthritis	238	46%	32%	25%	31%	54%
Bone mineral disorders	55	42%	36%	24%	18%	58%
Total without primary FM	1337	44%	30%	24%	25%	56%
Primary FM	60	78%	55%	55%	53%	22%
Totals – all pts	1397	45%	31%	25%	26%	55%

Results: In 1337 patients, excluding 60 with primary FM, positive screening for MAS2 ANX, MDS2 DEP and/or FAST4 FM was seen in 587 (44%), including 399 (30%) for MAS2 ANX, 321 (24%) for MDS2 DEP, 328 (25%) for FAST4 FM; 750 patients (56%) screened negative for all the 3 indices (Table). Among diagnosis categories, a positive screen for **any** of the 3 indices ranged from 52% in patients with "other non-inflammatory" diagnoses, excluding primary fibromyalgia, to 30% in crystal diseases and vasculitis, for ANX from 39% in “other non-inflammatory" diagnoses to 19% in “other-inflammatory” diagnoses, for DEP from 33% in myositis to 9% in systemic sclerosis to, and for FM from 31% in OA to 7% in vasculitis (Table). The totals were raised by only 1% with inclusion of 60 patients with primary FM, reflecting a high prevalence of 1 , 2, or 3 positive screens in all other diagnosis categories (Table). Among all patients with a positive MDHAQ screening index for ANX, DEP, and/or FM, one of the 3 was positive in 271 (43%), 2 of the 3 in 214 (34%), and all 3 in 149 (24%) (Figure).

Conclusion: In 1337 patients seen in routine care (excluding 60 with primary FM), positive screening on MDHAQ indices was seen in 30% for ANX, 24% for DEP, 25% for FM, and 44% for any of the 3 indices. Positive screening is common, and affects assessment, management, and outcomes of all rheumatic diseases. An important limitation involves data from only one setting, as variation is likely according to cultural and socioeconomic variables in different settings. An MDHAQ, completed by most patients in 5-10 minutes prior to seeing a rheumatologist and available in the February 2025 release of the Epic electronic medical record (EMR), provides a feasible strategy to screen for ANX, DEP, and FM in all patients.

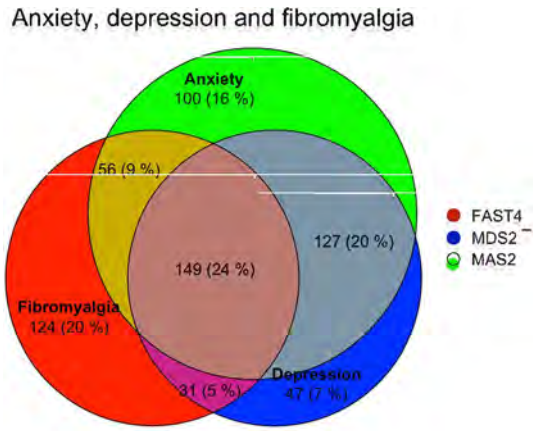


Figure: positive screening for anxiety, depression and fibromyalgia in rheumatology patients with all diagnoses seen in routine rheumatology care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Schmukler: None; **T. Li**: None; **T. Pincus**: Medical history services, LLC, 8, 9, 10.

Abstract Number: 0226

Integration of the 5Ms of Geriatrics in a Novel Geri-Rheumatology Clinic

Justin Levinson[1] and Christie Bartels[2], [1]University of Wisconsin- Madison, Madison, WI, [2]University of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Geriatric integrative care models, such as the Perioperative Optimization of Senior Health (POSH) initiative, have shown improved outcomes (PMID: 29299599), yet there remains limited adoption in specialty clinics such as Rheumatology. This study aims to assess the findings of a novel Geri-Rheumatology clinic by a dual rheumatologist-geriatrician at an academic medical center. To test our hypothesis that an interplay of chronic inflammation and cardiovascular disease (CVD) risks impact rheumatology patients who have been shown to have higher rates of cognitive impairment (PMID: 39542002), we aimed to evaluate associated risk factors in older patients compared to peers without inflammatory conditions.

Methods: In this quality improvement pilot from August 2023 through November 2025, new Geri-Rheumatology referrals for ages >55 years were offered a geriatric evaluation using validated screening tools performed by Montreal Cognitive Assessment (MoCA) certified practitioners preceding their rheumatology visit (Figure1). The 5M's of Geriatrics were integrated through clinical assessments of Mobility (Short Physical Performance Battery [SPPB]), Mind (MoCA), Medications (polypharmacy and anti-cholinergic burden), Multicomplexity (medical and social history assessment), and Matters Most, by appropriate counseling and referrals. Patients could opt-in to the full geriatric assessment or certain elements. Cognitive risk factors of sleep apnea, depression, anxiety, and disease activity were assessed along with CVD medical history. Patients with primary diagnosis codes for rheumatologic diseases (ex. SLE, RA) were compared to those with non-inflammatory codes (ex. OA, Positive ANA, Osteoporosis).

Table 1. Geriatric Assessment of Rheumatologic vs Non-Inflammatory Cohorts by MoCA Score

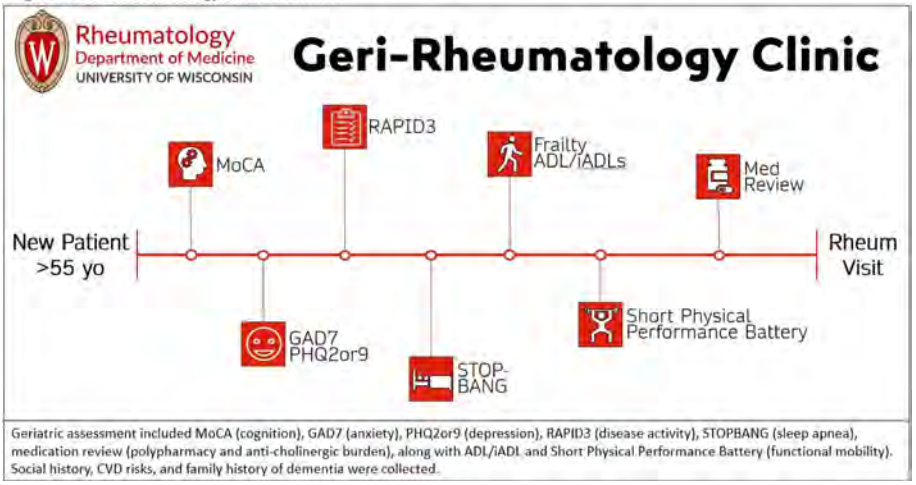
	Normal Cognition (MoCA >25)		Mild Cognitive Impairment (MoCA 18-25)		Moderate Cognitive Impairment (MoCA 10-17)		Overall	
	Rheumatologic Diagnosis	Non-Inflammatory Diagnosis	Rheumatologic Diagnosis	Non-Inflammatory Diagnosis	Rheumatologic Diagnosis	Non-Inflammatory Diagnosis	Rheumatologic Diagnosis	Non-Inflammatory Diagnosis
Geriatric Assessment								
Mean Age (n)	69.9 (33)	72.2 (17)	73.35 (16)	71.13 (8)	76.5 (2)	87 (1)	71.42 (51)	72.46 (26)
Mean StopBang (n)	3.22(9)	3.14 (7)	3.78 (8)	4 (1)	2 (2)	-	3.53 (19)	3.25 (8)
Mean PHQ2 (n)	0.56(9)	1.42 (7)	0.75 (8)	0 (1)	0 (2)	-	0.61 (19)	1.25 (8)
Mean GAD7 (n)	1.78(9)	3.14 (7)	1.63 (8)	0 (1)	1 (2)	-	1.72 (19)	2.75 (8)
Mean RAPID3 (n)	3.35 (33)	3.24 (17)	3.46 (16)	3.84 (8)	2.3 (2)	6 (1)	3.34 (51)	3.55 (26)
Mean SPPB (n)	11.67(9)	9.71 (7)	9 (8)	12 (1)	10 (1)	-	10.39 (18)	10 (8)
Past Medical History								
Hypertension (%)	19 (57.6%)	6 (35.3%)	10 (62.5%)	4 (50%)	1 (50%)	0	30 (58.8%)	10 (38.5%)
Hyperlipidemia (%)	17 (51.5%)	6 (35.3%)	8 (50%)	4 (50%)	0	0	25 (49%)	10 (38.5%)
Diabetes (%)	5 (15.2%)	2 (11/8%)	1 (6.3%)	1 (12.5%)	0	0	6 (11.8%)	3 (11.5%)
Chronic kidney disease (%)	1 (3%)	0	4 (25%)	1 (12.5%)	0	0	5 (9.8%)	1 (3.8%)
Stroke history (%)	1 (3%)	0	1 (6.3%)	0	0	0	2 (3.9%)	0
Coronary Artery Disease (%)	4 (12.1%)	1 (5.9%)	1 (6.3%)	0	0	0	5 (9.8%)	1 (3.8%)
Mean MoCA Score (n)	**28.2 (33)**	**27.76 (17)**	**22.7 (16)**	**22.75 (8)**	**15.5 (2)**	**17 (1)**	**25.98 (51)**	**25.81 (26)**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Montreal Cognitive Assessment Scores by Age

Age (years)	N	Overall	MoCA Domains						
			Visual/ Exec	Naming	Attention	Language	Abstraction	Recall	Orientation
55-<60	9	27.7	4.4	3.0	5.6	2.8	2.0	3.9	6.0
60-69	13	26.7	4.4	3.0	5.4	2.9	2.0	3.0	6.0
70-79	48	25.8	4.2	2.8	5.3	2.7	1.9	3.0	6.0
80-85	7	23.3	3.3	2.4	5.0	2.6	1.6	2.9	5.6
Overall	**77**	**25.9**	**4.2**	**2.8**	**5.3**	**2.8**	**1.9**	**3.1**	**6.0**

Figure 1. Geri-Rheumatology Clinic Workflow



Geriatric assessment included MoCA (cognition), GAD7 (anxiety), PHQ2or9 (depression), RAPID3 (disease activity), STOPBANG (sleep apnea), medication review (polypharmacy and anti-cholinergic burden), along with ADL/iADL and Short Physical Performance Battery (functional mobility). Social history, CVD risks, and family history of dementia were collected.

Results: A total of 77 patients completed a MOCA assessment and are included in this evaluation. With a cut off for Cognitive Impairment of ≤25, 35% (27) showed cognitive impairment with 3.9%(3) showing moderate impairment. While cognitive impairment frequencies were similar between rheumatologic and non-inflammatory cohorts, rheumatologic patients had higher baseline rates of CVD comorbidities (Table1). Lower MOCA scores were similar between cohorts and inversely related to age. The most common impairments were in Visuospatial, Attention, and Recall domains (Table2).

Polypharmacy (≥ 5 medications) was found in 73% vs 62% (p=0.44) of the rheumatologic and non-inflammatory cohorts, respectively. The average overall anti-cholinergic burden was 2.2 medications. The geriatric assessment led to 24 memory clinic, 12 physical therapy, and 15 sleep study referrals.

Conclusion: With a growing geriatric population, this study adds to the body of knowledge informing care for older rheumatology patients. Nearly 1/3 of patients were offered referral to memory clinic for further evaluation. Clinicians should consider cognitive screening for this high-risk group as dementia affects patient outcomes, counseling, and medication adherence. Limitations were small cohort size and that patients self-selected involvement; no patients had severe impairment likely due to difficulties with visit attendance or consent. Future studies should expand this cohort to evaluate long-term outcomes.

Disclosure: J. Levinson: None; **C. Bartels**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0227

Malignancy Screening of Dermatomyositis Patients in the Penn State Registry of Inflammatory Myopathies (PRIMO)

Katrina Gonzales[1], William DeKryger[2], Deepika Pugalenthi Saravanan[2], Esha Tulsian[2], Peri Newman[3], Jacob Colello[2], Galen Foulke[4] and Nancy Olsen[5], [1]Penn State College of Medicine, Hummelstown, PA, [2]Penn State College of Medicine, Hershey, PA, [3]Penn State Health/ Penn State College of Medicine, Hershey, PA, [4]Penn State Health, Hershey, PA, [5]Penn State University/Milton S Hershey, Hershey, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is an immune-mediated myopathy characterized by muscle weakness and skin rash that carries an elevated risk of associated malignancy within 5 years of diagnosis [1]. While the link between DM and malignancy is well established, no consensus guidelines exist regarding advanced malignancy screening beyond standard age appropriate US Preventive service task force (USPSTF) and American Cancer Society recommendations. Given the variability of practices among providers, we sought to explore institutional trends and barriers to obtaining malignancy screenings for adult DM patients.

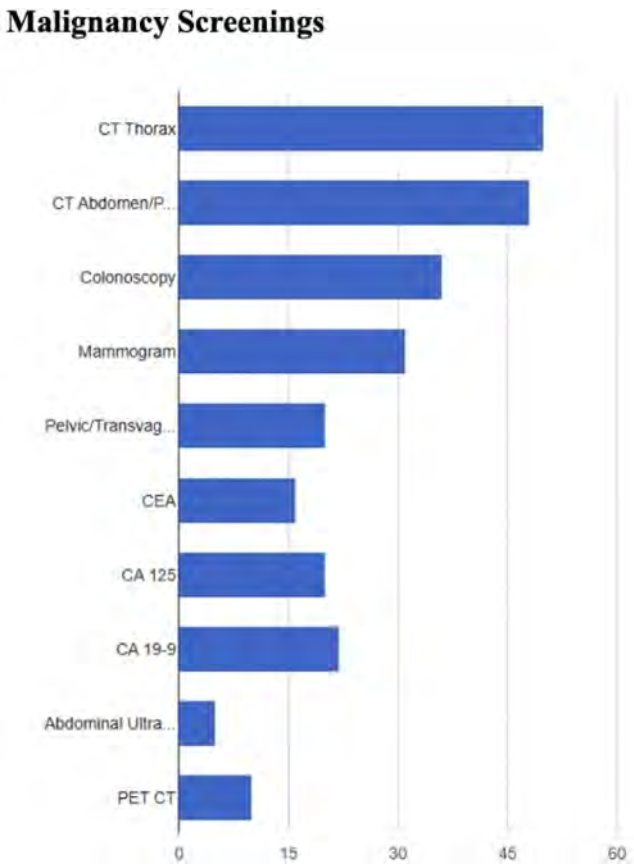
Methods: We conducted a retrospective review of patients enrolled from 2010-2020 in our previously established registry, the Penn State Registry of Inflammatory Myopathies (PRIMO). Inclusion criteria were diagnosed at age >18, DM diagnosis confirmed through ACR/EULAR criteria, and presentation within 3 years of diagnosis. Descriptive statistics were used to summarize results.

Table 1 - Demographics and Antibody Panel

Demographics and Antibody Panel Labs

Demographics		**Antibody Panel**	
Sex	Number of patients (%)	**ANA**	
Female	51 (78.5%)	Positive	44 (67.7%)
Male	14 (21.5%)	Negative	18 (27.7%)
Ethnicity		Unknown/Not Done	3 (4.6%)
Hispanic or Latino/a	7 (10.8%)	**Anti-TIF1γ antibody**	
Non-Hispanic or Latino/a	55 (84.6%)	Positive	12 (18.5%)
Race		Negative	11 (16.9%)
White	52 (80.0%)	Unknown/Not Done	42 (64.6%)
African-American	5 (7.7%)	**Anti-MJ/NXP-2 antibody**	
Other	6 (9.2%)	Positive	1 (1.5%)
Unknown	2 (3.1%)	Negative	21 (32.3%)
Disease Subtype		Unknown/Not Done	43 (66.2%)
DM	53 (81.5%)	**Anti-SAE antibody**	
Amyopathic DM	9 (13.8%)	Positive	1 (1.5%)
Hypomyopathic DM	3 (4.62%)	Negative	16 (24.6%)
		Unknown/Not Done	48 (73.8%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Malignancy Screenings: X-axis = Malignancy Screening Type, Y-axis = Number of tests ordered

Results: A total of 65 patients met inclusion criteria. Patients were predominantly female (78.5%), with mean age at diagnosis of 55.3 years. In 69.8% of initial encounters, malignancy risk and/or need for screening was documented. CT thorax (72.3%) and CT abdomen/pelvis (66.2%) were the most commonly completed screenings with 42.8% undergoing PET CT. Regarding USPSTF screenings, 29% and 37.4% of eligible patients completed colonoscopy and mammogram respectively. All patients with high risk antibody profiles received advanced screening. Notably, 15.4% of patients had no advance testing completed or documented. Rheumatologists (25, 43.1%), dermatologists (29, 50.0%), and primary care physicians (19, 32.8%) were the most common ordering providers. Insurance approval and financial concerns were leading reasons why ordered tests were not completed. Malignancy was present in 18.8% of patients and included breast, lung, gastrointestinal, hematologic, and gynecologic cancers. The average time between first DM evaluation and malignancy diagnosis was 27.6 months.

Conclusion: Our data highlights the variability that exists among cancer screening practices in DM. While those with the highest risk disease subtypes were identified and screened, many others were not recommended for advanced screening and clinical decision making was not well documented. Furthermore, USPSTF screenings were not commonly ordered by specialists, drawing attention to the need for collaboration. Given the morbidity and mortality that accompanies malignancy, efforts should be made to overcome barriers to screening. Future efforts should focus on collaborations with other institutions to expand participant diversity, adopting insights from primary care screening practices, assessing patient and provider perspectives, and developing practical quality improvement initiatives to trial in the clinical environment.

Disclosure: K. Gonzales: None; **W. DeKryger**: None; **D. Pugalenthi Saravanan**: None; **E. Tulsian**: None; **P. Newman**: None; **J. Colello**: None; **G. Foulke**: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0228

Bridging the Gap: Leveraging Econsultation to Improve Access to Quality Gout Care

Laura Nichols[1] and Steven Taylor[2], [1]University of Colorado, Aurora, CO, [2]University of Colorado, Denver, CO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In the context of the rheumatology workforce shortage, eConsultation holds significant potential to address some challenges through supporting primary care providers in managing rheumatologic conditions. Gout is a useful prototype for implementation of eConsults considering uric acid as a biomarker, the common nature of gout, and well-defined treatment regimens. This quality improvement project aimed to evaluate the current impact of gout eConsults on improvements in uric acid, consistency of consultation, conversion to in-person visits, and milage and travel cost savings.

Methods: Data from 93 gout consults received between 5/18/2018 – 9/16/2024 at a single academic site were reviewed. Data was collected regarding uric acid levels, the type of recommendation provided, as well as whether the patient was seen in-person by rheumatology. Consults were categorized based on whether patients were evaluated with eConsult only, immediately converted to in-person visit, or subsequently converted to an in-person visit. Duplicate eConsults and patients who were never seen due to cancellations or scheduling errors were excluded from analysis. Milage saved and travel cost saved were calculated based on the distance between the patient's zip code and the medical center and the average IRS milage compensation from 2018-2024 ($0.599/mile).

Results: Forty-nine eConsults did not require an in-person visit.Twenty-five patients were converted to an initial in-person visit. Six additional patients were subsequently converted to an in-person visit. Average uric acid levels decreased over the monitoring period in patients treated by all three pathways (Table 1). Patients triaged to in-person visits compared to eConsult generally had a higher baseline uric acid level (8.2 versus 7.9), but lower levels (5.1 versus 6.0) at 1 year. Average 2-way milage saved for patients with eConsult was 45.6 miles. Average cost savings was $27.31 (Figure 1). Formal categorization of qualitative data was not performed for this quality improvement study. However, there was notable heterogeneity in responses, such as interval of checking uric acid. Limitations include missing values for uric acid.

Conclusion: eConsults resulted in decreased uric acid from baseline as well as both mileage and travel cost savings for patients. Though there were likely intrinsic differences between in-person and eConsult patient populations at baseline, the lower uric acid levels with in-person visits suggest there is room for improvement with current eConsultation practices.

Table 1: Change in uric acid over time for eConsultation and in-person visits

	BASELINE URIC ACID	URIC ACID AT 6 MONTHS	URIC ACID <6 AT 6 MOS N (%)	URIC ACID AT 1 YEAR	URIC ACID <6 AT 1 YEAR N (%)	MOST RECENT URIC ACID
E-CONSULTATION ONLY N=49	7.9	6.5	11 (22%)	6.0	14 (29%)	6.7
INITIAL IN-PERSON EVALUATION N=25	8.2	5.9	9 (36%)	5.1	14 (56%)	5.8
CONVERSION TO IN-PERSON EVALUATION N=6	8.7	7.2	1 (17%)	6.6	2 (33%)	6.1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Travel distance (2-way) and associated travel costs for patients

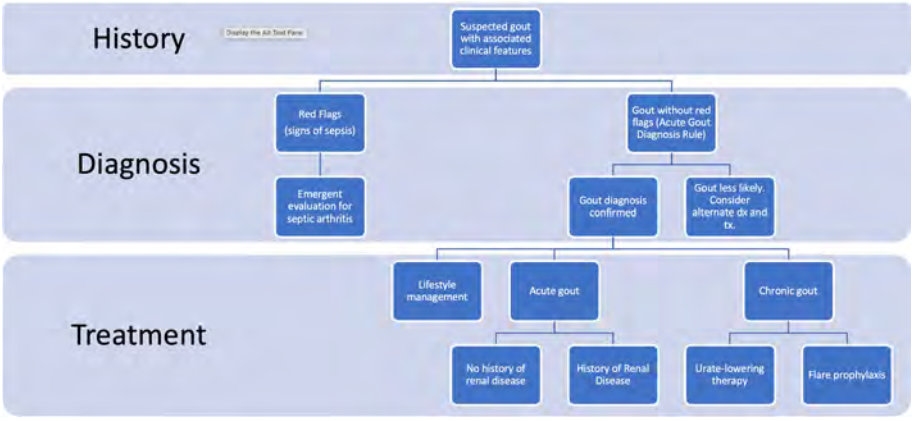


Figure 2: Schematic for point-of-care diagnostic and therapeutic algorithm

Future quality improvement directions include: standardization of gout eConsult recommendations utilizing tools such as a division-wide consult smart phrases, point-of-care treatment algorithms for referring clinicians such as in Figure 2, and pairing of eConsults with other care-delivery models such as pharmacy or nursing-led gout clinics. Analysis of cost savings and milage savings represent unique metrics for monitoring quality improvement.

Disclosure: L. Nichols: None; **S. Taylor**: None.

Abstract Number: 0229

Leveraging the Electronic Medical Record to Improve the Rate of Discrete Data Collection in a Pediatric Rheumatology Clinic

Lisa Buckley[1] and Eli Lourie[2], [1]Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN, [2]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

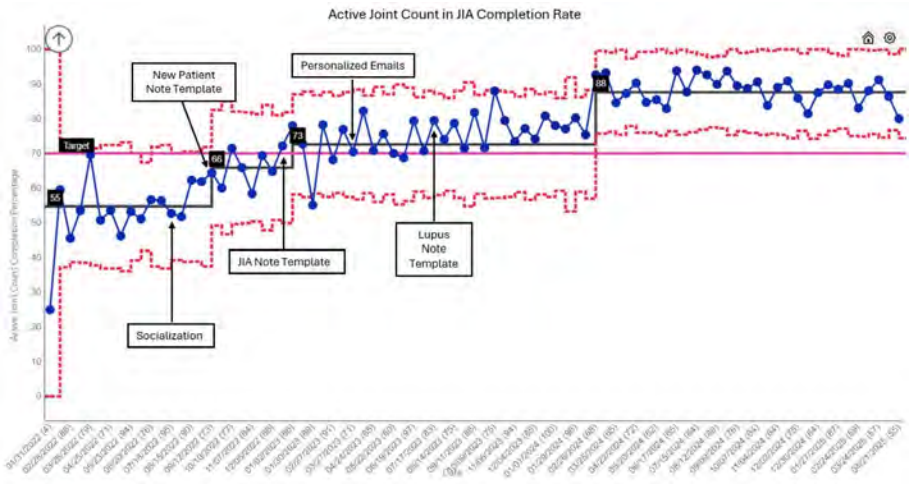


Figure 1: Active Joint Count in JIA Completion Rate P chart

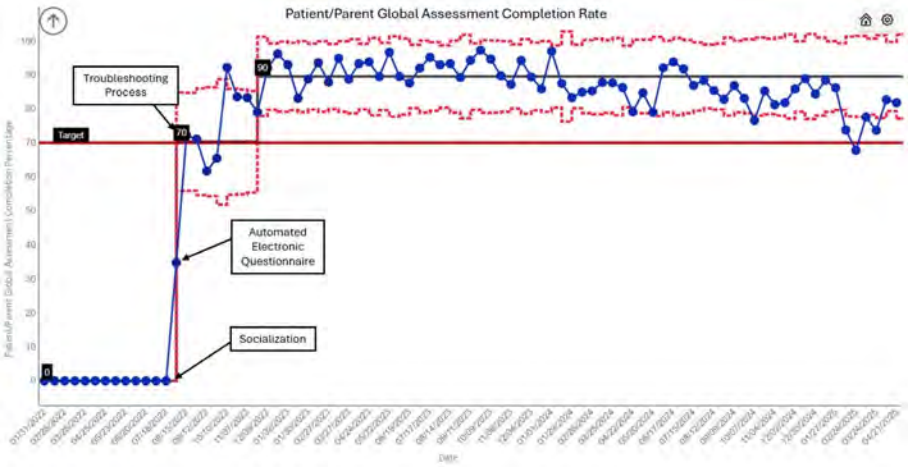


Figure 2: Patient/Parent Global Assessment Completion Rate P Chart

Background/Purpose: A systematic approach to clinical data collection is critical to enhancing patient outcomes, enabling research and quality improvement initiatives, and benchmarking performance. This quality improvement project aimed to increase the rate of discrete data captured during eligible outpatient visits in a pediatric rheumatology clinic from a mean documentation rate of 0-55% of visits to 70% of visits for each data element.

Methods: Division-wide consensus identified data variables essential for patient care and research, including active joint count in JIA, physician global assessment of disease activity in JIA, patient/parent global assessment, clinical juvenile arthritis disease activity score (cJADAS) in JIA, and patient health questionnaire-9 (PHQ-9) score for depression screening in lupus. Patient-reported data were collected via an automated paperless workflow using a virtual interface, with discrete storage in the electronic medical record (EMR). A semi-structured documentation strategy incorporating hyperlinks, disappearing reminders, and auto-populated fields was created to prompt provider-reported data collection. A flexible "choose your own adventure" approach provided structure for data collection while maintaining the personalization providers desired. The essential data elements were grouped as exam data and outcomes data relevant to specific disease and were easily accessed as a link in the EMR. Providers had the options of using a standard note template with embedded data elements or a personalized template or copied forward note to which the essential data elements could be manually added. The EMR automatically calculated cJADAS from its components utilizing an existing functionality. Other interventions included consensus meetings, provider education and individual provider performance feedback. The Model for Improvement guided implementation through Plan-Do-Study-Act cycles, and outcomes were analyzed using statistical process control (SPC).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

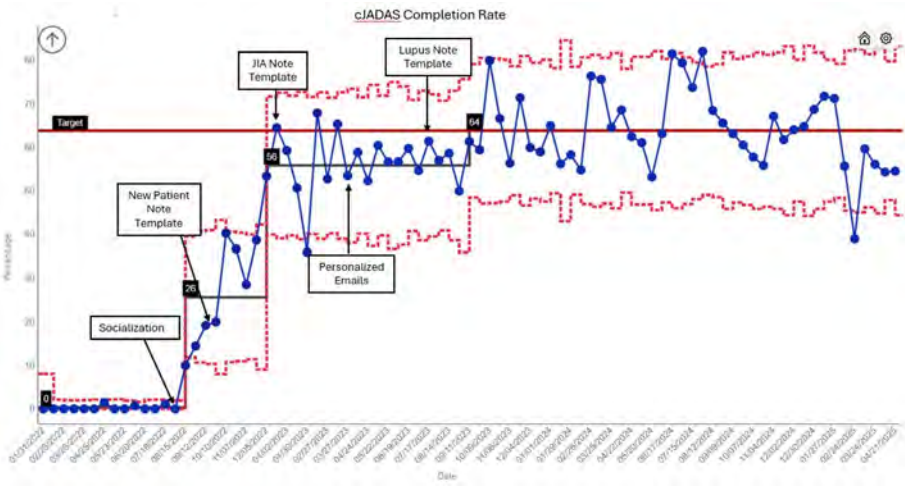


Figure 3: cJADAS Completion Rate P Chart

Results: From January 2022 to March 2024, completion rates improved significantly: active joint count in JIA rose from 55% to 88% (Figure 1), physician global assessment in JIA from 32% to 76%, patient/parent global assessment from 0% to 90% (Figure 2), cJADAS in JIA from 0% to 64% (Figure 3), and PHQ-9 in lupus from 57% to 84% of visits. All mean shifts met criteria for special cause variation using SPC methods. The target completion rate of 70% was achieved in all but one data element (cJADAS). All gains were sustained through April 2025.

Conclusion: A high rate of standardized discrete data collection in a pediatric rheumatology clinic was achieved and maintained using automated electronic patient questionnaires, a flexible documentation strategy, and existing EMR functionalities. These interventions have potential to be adapted to other data elements and across institutions to improve rates of discrete data collection for patient care, research, and quality improvement in pediatric rheumatology.

Disclosure: L. Buckley: None; **E. Lourie**: None.

Abstract Number: 0230

An Epic Journey – Therapeutic Drug Monitoring at an Academic Center

Puja Khanna[1] and Michael Rice[2], [1]Division of Rheumatology, University of Michigan, Ann Arbor, MI, [2]Division of Gastroenterology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Non-oncologic use of immunomodulatory agents is increasing. These drugs have a narrow, patient-specific therapeutic index, making therapeutic drug monitoring essential for safe prescribing. However, monitoring parameters vary widely, often influenced by the managing clinician's expertise and the complexity of patients with multiple comorbidities (1). In rheumatology, this challenge is compounded by ambiguous guidelines from professional societies and regulatory bodies, as well as high monitoring costs and frequency that affect patient preferences (2). Inconsistency in recommendations about how best to monitor for adverse effects impacts which ones clinicians adhere to. Our objective

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Patients being monitored by Specialty

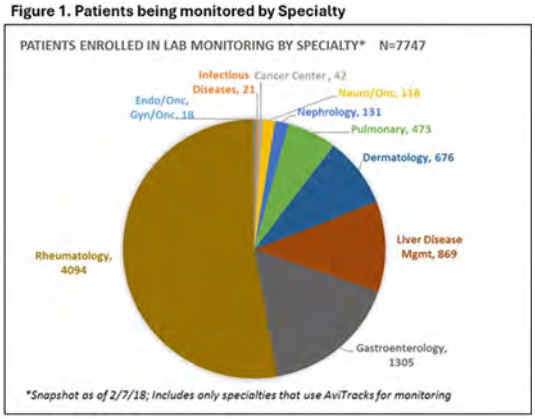
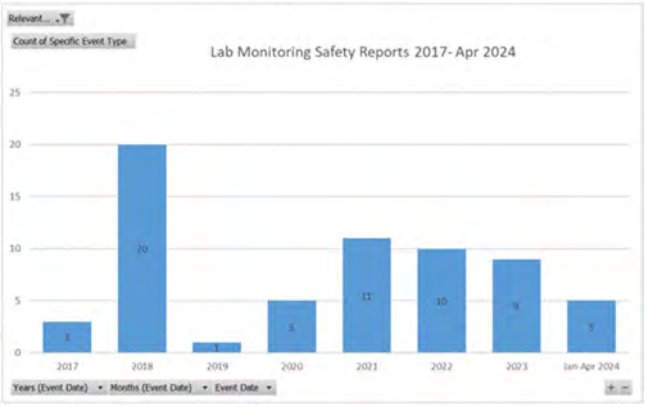


Table 1. Medication Monitoring Root Cause Analysis

GAPS IN Workflows
Significant process variability across sites and within specialties
Multiple management structures; work decentralized across multiple clinics
Accountability for work not well defined
Roles often not clearly defined; no overall process owner
Communication gaps arise due to fragmented documentation systems and absence of of standardized workflows
Lab results retrieval and entry can be time consuming as several patients have their labs done in the community
Significant inefficiencies emerge as workload increases
No best practice to share

Figure 2. Rates of Safety Reports



was to create an evidence-based best practice paradigm for clinicians and operationalize a dynamic program for supporting care teams to avoid adverse outcomes at a tertiary care academic practice.

Methods: A large interdisciplinary steering committee was formed to assess laboratory monitoring across eight Internal Medicine specialties, with Rheumatology taking the lead due to its high patient volume. Stakeholder focus groups were conducted (among clinicians, nursing, IT, pathology, pharmacists, medical assistants and patient support advocates) to identify gaps, areas of improvement, and achieve consensus on a minimum standard of streamlined processes. A standardized laboratory monitoring policy was instituted to establish the workflows unique to each subspecialty and then operationalized at

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the height of COVID in 2021. Epic©, the electronic medical record (EMR), was leveraged to build a single unified platform. Smartsets were designed to facilitate efficient lab ordering, reduce manual data retrieval for staff and attain timely review of integral results.

Results: Baseline data revealed 7,747 patients enrolled in various inconsistently monitored programs across IM specialties in 2020 (Figure 1). Root cause analysis identified approximately 5 % missed enrollments and several workflow gaps in the medication monitoring (Table 1). In the followup PDCA, over 16,000 patients are now being monitored for both medication safety and disease activity at our institution. We saw an incremental decline in the volume of safety events (Figure 2) from the inception of this initiative.

Conclusion: Ensuring patient safety is essential to delivering optimal care for patients with complex conditions requiring high-risk medications. Our experience at a large academic center demonstrates how the EMR can be leveraged with the support of a multi-disciplinary collaborative team to ensure successful implementation of a standardized platform to attain this longitudinal goal. A dashboard is in development for each specialty to explore the quality of key monitoring metrics in a sustainable manner.

References:

1. Tsakas et al. Attitudes and practices in the laboratory monitoring of conventional synthetic disease modifying anti-rheumatic drugs by rheumatologists and rheumatology trainees BMC Rheumatology (2022) 6:59.
2. Rigby WFC, Lampl K, Low JM, Furst DE. Review of routine laboratory monitoring for patients with rheumatoid arthritis receiving biologic or nonbiologic DMARDs. Int J Rheumatol. 2017;2017:9614241.

Disclosure: P. Khanna: Arthrosi, 5, Olatec, 5, Selecta Biosciences, 5, Sobi, 2; **M. Rice**: ANX Robotics, 1, Medtronic, 1.

Abstract Number: 0231

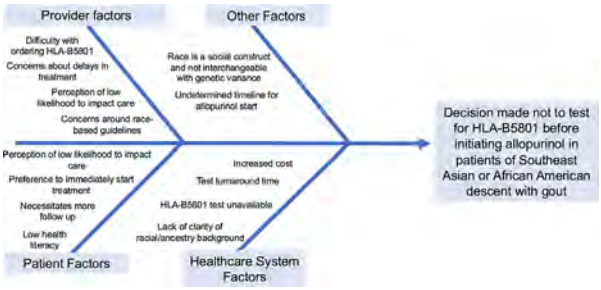
A Quality Improvement Project to Explore the Implications of the 2020 ACR Gout Guideline Recommendations for HLA-B5801 Testing

Sarah Anstett[1], Brian Coburn[2], Carlos Garcia-Gonzalez[3], Max Krall[1], Akash Gupta[4], Riya Madan[5], Stephanie Lee[6], Tania Aguila[1], Adam Mayer[7], Elise Breed[2], Preethi Thomas[8], Nora Sandorfi[1], Anupama Shahane[1] and Rachel Dayno[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Hospital of the University of Pennsylvania, Philadelphia, PA, [3]University of Pennsylvania, Philadelphia, [4]Hospital of University of Pennsylvania, Philadelphia, PA, [5]University of Pennsylvania Medical Center, Philadelphia, PA, [6]University of Pennsylvania and Children's Hospital of Philadelphia, Philadelphia, PA, [7]University of Pennsylvania/Children's Hospital of Philadelphia, Philadelphia, PA, [8]UNIVERSITY OF PENNSYLVANIA, Conshohocken, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The presence of the HLA-B5801 allele increases the risk of life-threatening allopurinol hypersensitivity syndrome (AHS). The 2020 ACR gout management guidelines conditionally recommend HLA-B5801 testing before starting allopurinol in populations more likely to have this allele, including African Americans and individuals of Southeast Asian descent (FitzGerald et al, Arthritis Care Res 2020). While intended to reduce harm, these guidelines could result in delayed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Fishbone diagram examining barriers to testing HLA-B5801

or untreated gout in these high-risk populations if appropriate systems are not in place. This project aims to identify beliefs, practices, and consequences of HLA-B5801 testing to inform future strategies that ensure prompt urate-lowering therapy (ULT) initiation for all individuals.

Methods: Data collection included a chart review and provider survey. The chart review was conducted at two academic rheumatology clinics from October 1, 2023 to September 30, 2024. All new patients and hospital discharge visits with a diagnostic code for gout (M10.XX, M1A.XX) during this period were reviewed. Manual chart review collected self-identified race as listed in the electronic health record, consideration of ULT, length of allopurinol treatment, HLA-B5801 testing, and ULT prescribing/dispensing details. A local survey of rheumatology providers assessed HLA-B5801 testing practices, perceived testing frequency, barriers, and future testing intentions. The chart review and survey results informed the creation of a fishbone diagram to identify targets for quality improvement interventions (Figure 1).

Results: We identified 78 patients who fit our criteria (Table 1). Of those, 47% of Black patients (n=14) and 75% of Asian patients (n=3) had HLA ordered (Table 2). Among Black and Asian patients who started allopurinol, HLA-B5801 testing was ordered for 50% (n=7) of patients on allopurinol for ≤6 months and for 57% (n=8) who had never received allopurinol. Of the patients who had never received allopurinol, 25% (n=2) started low dose allopurinol the same day HLA-B5801 testing was ordered while the remainder waited for results. Of the 20 survey responses, 100% reported awareness of ACR guidelines; 60% reported consistently ordering HLA-B5801 testing. The majority (85%) felt comfortable discussing race/ancestory to guide testing. Among the 8 providers who did not routinely order testing, there were concerns about delaying ULT initiation, thought that testing would not impact management, and challenges with ordering the test.

Conclusion: Providers demonstrated variable practices and beliefs surrounding HLA-B5801 testing. This may reflect uncertainty about implementing a race- or ancestry-based recommendation in clinical practice. Future goals for our quality improvement project are to reduce barriers for HLA-B5801 ordering so high-risk populations for the HLA-B5801 allele may be promptly and safely started on appropriate ULT.

Characteristic	N = 78[1]
Age	57 (16)
Race	
Black	30 (38%)
Asian	4 (5.1%)
White	40 (51%)
American Indian or Alaskan Native	0 (0%)
Native Hawaiian or Other Pacific Islander	1 (1.3%)
Other	3 (3.8%)
ULT	
Allopurinol	68 (87%)
Febuxostat	2 (2.6%)
None	7 (9.0%)
Other	1 (1.3%)

[1] Mean (SD); n (%)

Baseline Patient Characteristics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Characteristic	Black N = 30[1]	Asian N = 4[1]	White N = 40[1]
HLA-B5801 Ordered	14 / 30 (47%)	3 / 4 (75%)	0 / 40 (0%)
HLA-B5801 Drawn			
Yes	10 / 14 (71%)	3 / 3 (100%)	0 / 0 (NA%)
No	3 / 14 (21%)	0 / 3 (0%)	0 / 0 (NA%)
Unknown	1 / 14 (7.1%)	0 / 3 (0%)	0 / 0 (NA%)
HLA-B5801 Result			
Negative	10 / 10 (100%)	3 / 3 (100%)	0 / 0 (NA%)

[1] n / N (%)

Assessment of HLA-B5801 testing in high-risk populations as defined by the ACR gout guidelines by self-identified race

Disclosure: S. Anstett: None; **B. Coburn**: None; **C. Garcia-Gonzalez**: None; **M. Krall**: None; **A. Gupta**: None; **R. Madan**: None; **S. Lee**: None; **T. Aguila**: None; **A. Mayer**: None; **E. Breed**: None; **P. Thomas**: None; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 2, Janssen, 2, Novartis, 1; **A. Shahane**: None; **R. Dayno**: None.

Abstract Number: 0232

Hydroxychloroquine Blood Testing in Lupus: The Michigan Medicine Experience

Zeinab Saleh[1], Michelle Kahlenberg[2], Wendy Marder[1], Emily Somers[1] and Internal Medicine Clinical Experience & Quality team, [1]University of Michigan, Ann Arbor, MI, [2]Michigan Medicine, Ann Arbor, MI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0210–0232) Measures & Measurement of Healthcare Quality Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

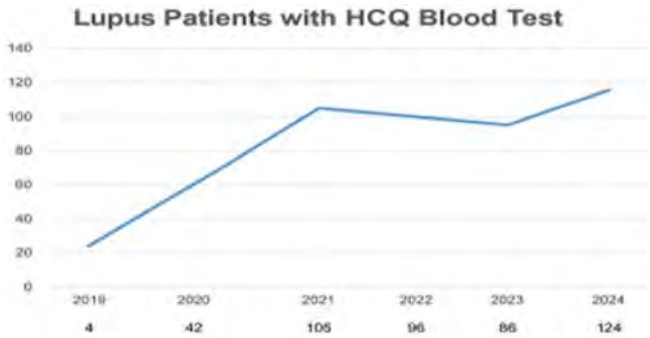
Background/Purpose: Measuring hydroxychloroquine (HCQ) blood levels in patients with systemic lupus erythematosus (SLE) can assess medication adherence and determine whether concentrations fall within the therapeutic or toxic ranges. Despite this potential, HCQ monitoring has not been incorporated into routine SLE care, largely due to the absence of standardized clinical cut-offs and formal guidelines from rheumatology associations (e.g, the American College of Rheumatology and the European Alliance of Associations for Rheumatology). Our objectives are twofold: (1) to provide evidence-informed recommendations for monitoring HCQ blood levels in adult SLE patients on therapy for at least six months, and (2) to evaluate HCQ levels in our lupus population at Michigan Medicine (MM).

Methods: We conducted a systematic review using PubMed, Embase, and Cochrane databases (from inception to October 2024), applying MeSH terms and keywords related to lupus and hydroxychloroquine. A multidisciplinary team—including representatives from rheumatology, dermatology, ophthalmology, nursing, pharmacy, pathology, the Internal Medicine Clinical Experience & Quality team, and a patient advisor—held six teleconferences, reached consensus, and developed institutional recommendations for HCQ blood level monitoring. In parallel, our continuous improvement specialist and data analyst assisted in extracting data from our adult lupus patient population.

Michigan Medicine HCQ Blood Level Target Range Guidelines		
	Whole Blood	Serum
Severen non-adherence	< 200 ng/mL	< 100 ng/mL
Partial non-adherence or Sub-therapeutic	200-750 ng/mL	100-400 ng/mL
Therapeutic or Target range	750-1200 ng/mL	400-600 ng/mL
Supra-therapeutic	> 1200 ng/mL	> 600 ng/mL

Michigan Medicine HCQ Blood Level Target Range Guidelines

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Number of Michigan Medicine lupus patients with HCQ blood tested between 2019 and 2024

	Number of Patients (Total 457, from 2019-2024)
Severe non-adherence	65
Partial non-adherence or Sub-therapeutic	284
Therapeutic or Target range	68
Supra-therapeutic	40

HCQ Blood Level Distribution in Our Patient Cohort

Results: (1) Our team defined target HCQ blood level ranges for four clinical categories: severe non-adherence (frequent interruptions or complete discontinuation), partial non-adherence (occasional missed doses) or subtherapeutic levels, therapeutic levels, and supra-therapeutic levels (associated with potential retinal toxicity). These guidelines are now posted on PolicyStat, Michigan Medicine's centralized platform for institutional policies, procedures, and guidelines (Figure 1).

(2) From January to July 2024, only 4% of adult lupus patients managed by MM Rheumatology had their HCQ blood levels tested. However, utilization has steadily increased since the test was introduced in 2019 (Figure 2). Figure 3 illustrates the distribution of HCQ levels among our tested patients.

Conclusion: Our work provides clinicians with practical, consensus-based guidance for monitoring HCQ blood levels in patients with SLE. We are actively engaging stakeholders- including rheumatologists, ophthalmologists, dermatologists, nurses, and patients- to raise awareness of the benefits of HCQ level monitoring in improving long-term outcomes. Our goal is to increase testing among HCQ-treated lupus patients from 4% to 25% within the next six months.

Disclosure: Z. Saleh: None; **M. Kahlenberg**: None; **W. Marder**: None; **E. Somers**: None.

Abstract Number: 0233

Differential Effects of GLP-1 Receptor Agonists versus SGLT2 Inhibitors on Hypoglycemia and Infection Risk in Diabetic Patients with Inflammatory Arthritis

Godbless Ajenaghughrure[1], Sila Mateo Faxas[2], **Gurjot Singh**[3], Nirys Mateo Faxas[4], Kim Nguyen[3], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Trihealth Good Samaritan Hospital, Cincinnati, OH, [2]Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: While both SGLT2 inhibitors and GLP-1 receptor agonists improve glycemic control in type 2 diabetes (T2D), their safety profiles, particularly regarding hypoglycemia and infection risk, may differ in patients with inflammatory conditions. This study compared these outcomes in patients with T2D and inflammatory polyarthropathy treated with either drug class.

Methods: This retrospective cohort study analyzed data from the TriNetX global health research network, identifying adult patients with T2D and inflammatory polyarthropathy receiving either SGLT2 inhibitors (n=3,377) or GLP-1 receptor agonists (n=4,733). After propensity score matching (n=2,838 per group), we evaluated the incidence of hypoglycemia, respiratory infections, urinary tract infections, sepsis, and other infection-related outcomes over a 5-year follow-up period.

Results: Patients treated with SGLT2 inhibitors experienced higher rates of sepsis (8.1% vs 5.9%, HR 1.609, 95% CI 1.318-1.965, p< 0.001) and acute kidney injury (16.9% vs 13.6%, HR 1.371, 95% CI 1.216-1.547, p< 0.001) compared to those on GLP-1 receptor agonists. Hypoglycemic events were more common in the SGLT2 inhibitor group (1.8% vs 1.1%, HR 1.594, 95% CI 1.028-2.472, p=0.036). The SGLT2 inhibitor cohort also showed higher rates of endocarditis/valve disorders (3.8% vs 2.9%, HR 1.478, 95% CI 1.098-1.990, p=0.043) and bacteremia (3.4% vs 2.4%, HR 1.627, 95% CI 1.205-2.196, p=0.001). Pneumonia incidence was similar between groups. Acute respiratory distress was more frequent with SGLT2 inhibitors (11.0% vs 6.7%, HR 1.699, 95% CI 1.480-1.949, p< 0.001).

Conclusion: In patients with T2D and inflammatory polyarthropathy, treatment with GLP-1 receptor agonists was associated with lower risks of serious infections, acute kidney injury, and hypoglycemia compared to SGLT2 inhibitors. These findings suggest that GLP-1 receptor agonists may offer a more favorable safety profile in this specific patient population. Clinicians should consider these differences when selecting glucose-lowering agents for patients with T2D and inflammatory arthritis.

Disclosure: G. Ajenaghughrure: None; **S. Mateo Faxas**: None; **G. Singh**: None; **N. Mateo Faxas**: None; **K. Nguyen**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 0234

Use of Corneal Confocal Microscopy to Assess Small Fiber Neuropathy in Patients with Sarcoidosis

Philip Bucur[1], Kelly Gwathmey[2], **Huzaefah Syed**[2], Aamer Syed[2], Thomas Iden[3], Neha Gupta[2], Jessica McLaughlin[2], Jordana Kron[2], Ryan Canissario[2], Shanshan Chen[1], Hoda Gad[4], Rayaz Malik[4], Sai Patel[2] and Vaishali Patel[2], [1]VCU Health, Richmond, VA, [2]Virginia Commonwealth University Medical Center, Richmond, VA, [3]Virginia Commonwealth University Medical Center, Richmond, [4]Weill Cornell Medicine-Qatar, Doha, Qatar

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Small fiber neuropathy (SFN) is a common complication of sarcoidosis, affecting about one third of patients. The current gold standard for diagnosis combines patient history and a skin biopsy to quantify small nerve fibers. Corneal confocal microscopy (CCM) is now being used with more frequency to evaluate nerve fibers in the cornea, specifically in diabetic neuropathy. However, further research is needed to validate the role of CCM in sarcoidosis. Our study focused on CCM and how it can be utilized as an accurate, non-invasive diagnostic tool for SFN in patients with sarcoidosis.

Methods: This study is a subset analysis of a larger study to better characterize SFN in sarcoidosis. A total of 12 patients with sarcoidosis who completed CCM analysis were included in the study. We categorized sarcoidosis patients into two groups: those with a physician impression of neuropathy (PIN) and those without a physician impression of neuropathy (non-PIN). A third group, healthy age-matched controls without sarcoidosis from a database, were added for comparison. CCM was performed to determine corneal nerve fiber density, length and tortuosity and corneal nerve branch density.

Results: CCM data was collected on 12 patients with sarcoidosis, 8 of who had PIN and 4 of who had non-PIN. The mean age of patients in the PIN group was 52.8 years with 87.5% females. The non-PIN group averaged 47.25 years old with 50% females. The healthy control group had a mean age of 51.3 years with no data on sex. One-way ANOVA analysis revealed a difference in corneal nerve fiber density (CNFD) approaching significance (p = 0.05) between the three groups. Post-hoc comparison using two-sample t-test to assess for between-group differences revealed a statistically significant difference in CNFD (p = 0.03), and a difference in corneal nerve branch density approaching statistical significance (p = 0.05) between

Table 1. One-way ANOVA test analyzing group differences in corneal nerve fiber density (CNFD), corneal nerve branch density (CNBD), corneal nerve fiber length (CNFL), and corneal nerve fiber tortuosity (CNFT) among three groups: health controls (HC), patients without a clinical impression of peripheral neuropathy (non-PIN), and patients with a clinical impression of neuropathy (PIN). The difference in CNFD is approaching statistical significance between the groups (p = 0.05).

	HC (N=12)	Non-PIN (N=4)	PIN (N=8)	P-value
CNFD				
Mean (SD)	30.0 (4.99)	23.4 (5.98)	20.3 (11.0)	0.0543
Median [Min, Max]	29.2 [22.3, 39.6]	21.9 [18.7, 31.2]	15.6 [12.5, 37.5]	
CNBD				
Mean (SD)	73.1 (25.9)	59.4 (16.5)	39.8 (38.1)	0.0696
Median [Min, Max]	69.5 [43.8, 125]	56.2 [43.7, 81.2]	28.1 [0, 106]	
CNFL				
Mean (SD)	22.7 (3.76)	19.8 (4.60)	16.8 (8.48)	0.11
Median [Min, Max]	22.3 [18.6, 29.0]	18.4 [16.1, 26.2]	16.3 [5.18, 29.7]	
CNFT				
Mean (SD)	13.8 (1.98)	18.8 (7.95)	14.3 (5.26)	0.21
Median [Min, Max]	13.6 [9.63, 16.9]	16.2 [12.9, 29.8]	12.7 [9.00, 23.5]	
Missing	2 (16.7%)	0 (0%)	0 (0%)	

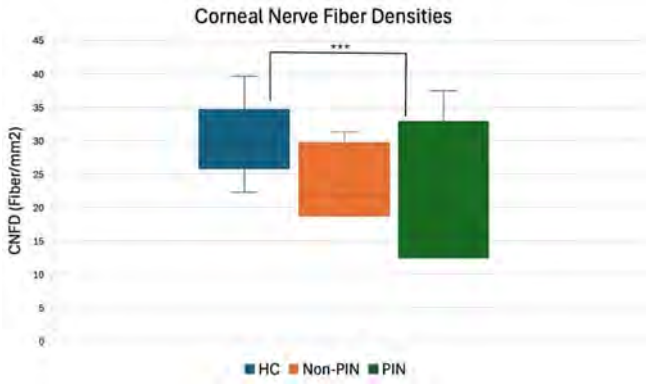


Figure 1. Corneal nerve fiber densities (CNFD) among healthy controls (HC), patients without a clinical impression of peripheral neuropathy (non-PIN), and patients with a clinical impression of neuropathy (PIN). A statistical difference was noted between healthy controls and PIN groups (p= 0.03).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

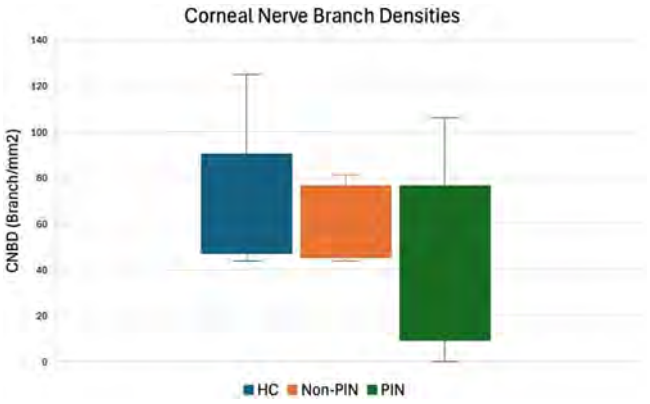


Figure 2. Corneal nerve branch densities (CNBD) among healthy controls (HC), patients without a clinical impression of peripheral neuropathy (non-PIN), and patients with a clinical impression of neuropathy (PIN). Though no statistically significant difference was found among the groups, there was a trend towards significance between HC and PIN groups (p = 0.05).

age-matched controls and PIN patients. However, there was not a difference in corneal nerve fiber length or corneal nerve fiber tortuosity between the two groups. There was no statistical difference noted in any of the measures between healthy controls and the non-PIN group or when comparing the PIN and the non-PIN groups.

Conclusion: CCM is a non-invasive method to capture images of small nerve fibers as a marker for SFN. Primarily used in diabetic neuropathy, our study findings indicate CCM can provide diagnostic data in patients with sarcoidosis and features of SFN, especially when analyzing CNFD. Interestingly, though not statistically significant, non-PIN patients trended toward having low corneal nerve fiber and branch densities, similar to PIN patients. Due to the low number of patients in our study, further research will be needed to validate the use of CCM as a screening tool for SFN in sarcoidosis patients.

Disclosure: P. Bucur: None; **K. Gwathmey**: None; **H. Syed**: None; **A. Syed**: None; **T. Iden**: None; **N. Gupta**: None; **J. McLaughlin**: None; **J. Kron**: None; **R. Canissario**: None; **S. Chen**: None; **H. Gad**: None; **R. Malik**: None; **S. Patel**: None; **V. Patel**: None.

Abstract Number: 0235

Mortality Trends due to Hypertension Related Deaths in Elderly Patients with Inflammatory Polyarthropathy: A CDC WONDER Analysis of 21 Years

ZAUHA FAWAD MEMON[1], Sibgha Fawad Memon[2], Matia Fawad Memon[2], **REHAN ISHAQUE**[3], AHMAD SANAN[4] and MUHAMMAD MUGHEES[5], [1]Peoples University of Medical and Health Sciences for Women, Tando Allahyar, Sindh, Pakistan, [2]Peoples University of Medical and Health Sciences for Women, Tando Allahyar, Pakistan, [3]LIAQUAT UNIVERSITY OF MEDICAL AND HEALTH SCIENCES, Jam Shoro, Sindh, Pakistan, [4]KHYBER MEDICAL COLLEGE, Peshawer, Pakistan, [5]Bahria University health Sciences, KARACHI, Pakistan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory polyarthropathy (IPA) is a group of chronic autoimmune disorders, common among older adults and contribute significantly to systemic inflammation and cardiovascular risk . These conditions are associated with systemic inflammation, which leads to an elevated risk of cardiovascular diseases, notably hypertension (HTN). Recent

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

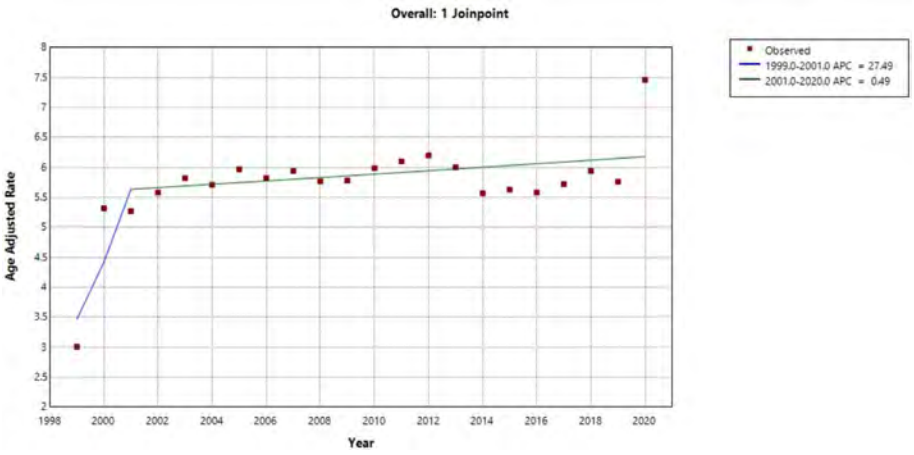


Figure 1: showing an overall increase in mortality trend due to Inflammatory Polyarthropathy and Hypertension

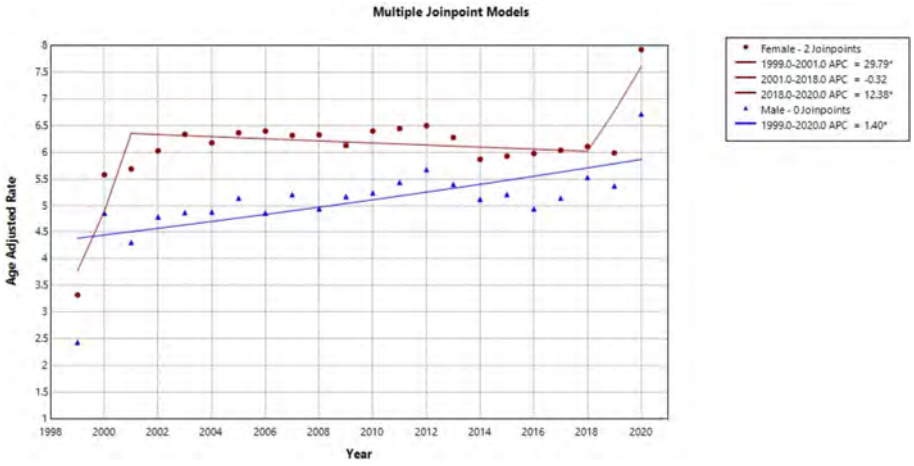


Figure 2: Showing disparities in mortality trends between sexes, with constant rise seen in males, and females demonstrating a biphasic pattern

studies suggest that people with IPA like rheumatic arthritis (RA) are 48% more likely to develop cardiovascular disorders than the general population. Emerging research underscores the role of immune-mediated inflammation in pathogenesis of HTN among patients with IPA. This study explores mortality rates due to IPA in patients with (HTN) patients aged 55 or above to inform prevention and care strategies.

Methods: We conducted a retrospective population-based study using the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research system (CDC WONDER) death certificate data (1999-2020). Subjects with Inflammatory polyarthropathy and Hypertension (HTN) were selected. Age-adjusted mortality rates (AAMRs) per 100,000 were calculated, and trends were assessed using Joinpoint regression to estimate annual and average annual percent changes (APC, AAPC). Rates were stratified by year, gender, race/ethnicity, region, and urbanization.

Results: A total of 91,168 deaths were reported to be associated with Inflammatory polyarthropathy and hypertension between 1999-2020, of which males accounted for 35.68% and female accounted for 64.32%. The overall age-adjusted mortality rate (AAMR) increased from 3.01 in 1999 to 7.46 in 2020 (AAPC: 2.78, $p < 0.050810$). Females had a higher age-adjusted mortality rate than males (6.15 vs 5.17).

Racial/ethnic disparities were apparent. Black or African American population had the highest AAMR (10.97 in 2020) (AAPC: 1.12, $p < 0.565390$). Asian or Pacific Islander had an overall similar trend (AAPC: -0.67, $p < 0.170487$). The trend in White people (AAPC: 2.90, $p < 0.017643$) remained almost consistent with sudden spike in 2020 (AAMR 7.18). Hispanic people had an overall upward trend (AAPC: 3.03, $p < 0.013721$).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Geographically, all four U.S. Census regions showed statistically significant incline, most prominent in the Northeast (AAPC: 4.03) and South (AAPC: 2.75) regions.

Both Urban and rural populations witnessed a substantial rise, however, it was more pronounced in rural population (AAPC: 3.30, $p < 0.021351$) as compared to urban (AAPC: 2.50, $p < 0.083213$)

Conclusion: Over the last 2 decades, mortality due to inflammatory polyarthropathy in patients with hypertension has remarkably increased. These findings highlight the need for targeted public health interventions and equitable access to address these disparities.

Disclosure: Z. MEMON: None; **S. Memon**: None; **M. Memon**: None; **R. ISHAQUE**: None; **A. SANAN**: None; **M. MUGHEES**: None.

Abstract Number: 0236

Safety and Efficacy of T Cell Engager Therapy in patients with refractory Autoimmune Disease

Laura Bucci[1], Sebastian Böltz[1], Melanie Hagen[1], Danae-Mona Nöthling[1], Tobias Rothe[2], Carlo Tur[1], Andreas Wirsching[1], Janina Auth[3], jochen wacker[1], Markus Eckstein[4], Stefano Alivernini[5], Aline Bozec[1], Christina Bergmann[1], Maria Antonietta D'Agostino[6], Maria Gabriella Raimondo[1], Georg Schett[7] and **Ricardo Grieshaber-Bouyer**[8], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlagen, Germany, [3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Bayern, Germany, [4]Institute of Pathology and Comprehensive Cancer Center EMN, Friedrich-Alexander- Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [5]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [6]Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [7]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [8]University Hospital Erlangen, Erlangen, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: T cell engagers (TCEs) are a promising therapeutic strategy to treat autoimmune diseases (AID). However, long-term data remain limited.

Methods: Patients with treatment-refractory AID were treated with the CD19 TCE blinatumomab or the BCMA TCE teclistamab. Eligibility criteria for blinatumomab were (i) diagnosis of rheumatoid arthritis (RA), (ii) ACPA/RF positivity or B-cell infiltration of the synovium, (iii) DAS28-ESR >3.2 and (iv) failure of ≥ 3 bDMARDs/tsDMARDs. Eligibility criteria for teclistamab: (i) diagnosis of AID according to respective diagnostic criteria, (ii) presence of characteristic autoantibodies, (iii) active disease based on respective criteria and ascertained by three specialists and (iv) failure of ≥ 2 immunosuppressants.

Results: 24 patients received TCE therapy. Most (18/24) had previously failed B cell depletion. 14 RA patients received blinatumomab (2–3 cycles, cumulative dose 77–189µg). 10 patients received teclistamab [systemic sclerosis (SSc), N=3, idiopathic inflammatory myositis (IIM) N=2, IgG4-related disease (IgG4-RD) N=2, primary Sjogren's-Syndrome (SjS) N=1,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

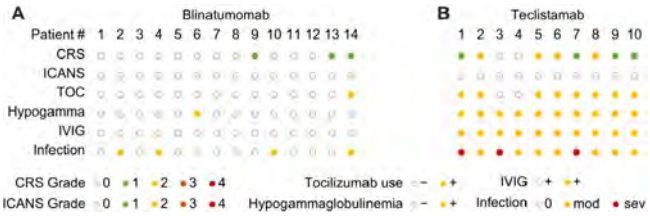


Figure 1. Safety of blinatumomab and teclistamab in autoimmune disease. (A) Overview of adverse events during blinatumomab therapy. (B) Overview of adverse events during teclistamab therapy.

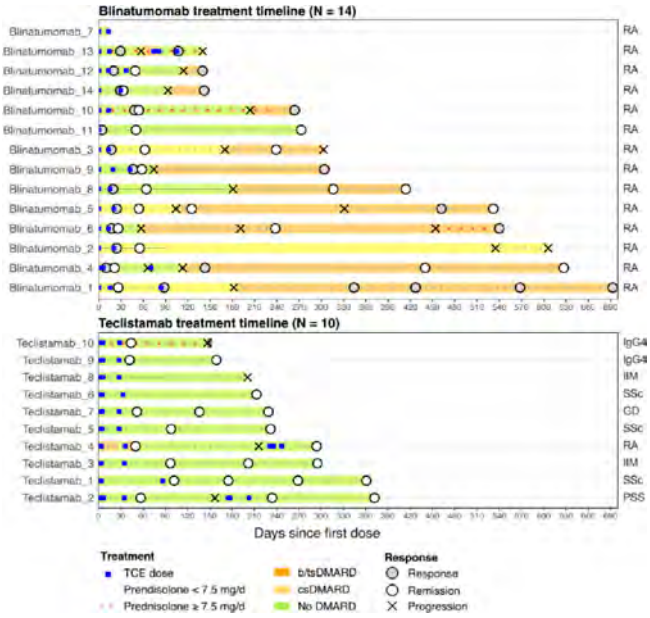


Figure 2. Durability of response. (A) Blinatumomab and (B) teclistamab treatment timeline.

Graves disease (GD) N=1, RA N=1]. Teclistamab was administered s.c. (d1: 0.06 mg/Kg; d3: 0.3 mg/Kg; d5: 1.5 mg/Kg, week 4: 1.5 mg/Kg). Treatment with TCEs was well tolerated (Fig. 1). No high-grade CRS and no ICANS occurred.

In patients treated with blinatumomab, low-grade (1-2) CRS was observed in 3/14 cases.

Transient hypogammaglobulinemia occurred in one patient. Mild infections occurred in 4 patients; no severe infections were observed. In patients treated with teclistamab, low-grade CRS occurred in 8/10 cases and resolved upon tocilizumab infusion. Hypogammaglobulinemia occurred in 9/10 patients and resolved after a median of 2 [range: 1-5] immunoglobulin infusions. 3 severe infections were observed, which fully resolved (viral gastroenteritis, *Clostridium difficile* infection, urinary tract infection). Mild upper respiratory tract infections occurred in 8/10 patients.

All patients showed initial clinical and serological response. In blinatumomab-treated RA patients, average DAS28-CRP decreased from 5.13 to 2.6, leading to DAS remission in 9/14 patients at month 3. After a median response to blinatumomab of 3.8 months, 13/14 patients progressed and required further therapy; one patient stayed in remission (Fig. 2).

In patients treated with teclistamab, disease specific autoantibodies seroconverted or markedly decreased. Serum IgG4 and CRP normalized and organ manifestations of IgG4-RD improved. At 3-month follow-up, mRSS decreased on average by 10, ESSDAI decreased from 34 to 12, CDASI improved from 22 to 5 and MMT8 increased from 138 to 150. DAS28 decreased from 5.59 to 2.1. Interstitial lung disease improved (median KCO of 45% to 53% at month-3 follow up). In the patient with GD, endocrine orbitopathy reverted.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6/10 patients treated with teclistamab maintained clinical response (median: 9 months), 3/10 patients progressed after a median of 5.2 months, one patient showed initial non-response (Fig. 2).

Conclusion: Our data substantiate an overall favorable safety profile and clinical efficacy of TCEs, warranting further investigation as treatments in different AIDs.

Disclosure: L. Bucci: None; **S. Böltz**: None; **M. Hagen**: None; **D. Nöthling**: None; **T. Rothe**: None; **C. Tur**: Sanofi, 2; **A. Wirsching**: None; **J. Auth**: None; **j. wacker**: None; **M. Eckstein**: None; **S. Alivernini**: None; **A. Bozec**: None; **C. Bergmann**: None; **M. D'Agostino**: Bristol-Myers Squibb(BMS), 5; **M. Raimondo**: UCB, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6.

Abstract Number: 0237

Monogenic autoinflammatory diseases and undefined autoinflammatory syndrome in Western Mediterranean adults: clinical, genetic, and therapeutic insights

Alba Maria Torrat Noves[1], José Ivorra Cortes[2], Alejandro Jose Mateo Vendrell[2], ELENA GRAU GARCIA[3], Pablo Muñoz Martinez[2], Laura Mas Sanchez[4], Daniel Ramos Castro[5], Iago Alcantara Álvarez[6], Belen Villanueva Manes[7], Andres perez Hurtado[2], Miguel Simeo Vinaixa[2], inmaculada Calvo Penades[8], Berta López Montesinos[8], Lucia Lacruz-perez[8] and José Andrés Román Ivorra[9], [1]Hospital Universitari i Politècnic La Fe de Valencia, Valencia, Spain, [2]Rheumatology Department. HUP La Fe, Valencia, Spain, [3]HUP La Fe, Valencia, Comunidad Valenciana, Spain, [4]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [5]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [6]Hospital Universitari i Politècnic La Fe, Valencia, Spain, [7]Hospital La Fe, Valencia, Spain, [8]Pediatric Rheumatology Department. HUP La Fe, Valencia, Spain, [9]Hospital Universitari i Politècnic La Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Monogenic autoinflammatory diseases are rare innate immunity disorders characterized by recurrent episodes of fever and systemic inflammation. They are most often described in childhood, although adult-onset cases have been reported. Clinical, genetic, and phenotypic expression varies by geographic region, and correlations between genotype and symptomatology have been described.

Undefined autoinflammatory syndrome (uSAID) is characterized by recurrent episodes of inflammation similar to monogenic autoinflammatory diseases with no diagnosis or genetic alterations detected.

The purpose of this study is to describe the characteristics of autoinflammatory diseases managed in rheumatology and to analyze genotype–phenotype correlations in patients with Familial Mediterranean Fever (FMF).

Methods: Descriptive, longitudinal, retrospective study of patients with monogenic autoinflammatory diseases and uSAID in the Rheumatology Department of a tertiary hospital. Demographic, diagnostic and clinical data were registered throughout the disease course. Laboratory, Autoinflammatory Disease Activity Index (AIDAI) and therapeutic data at the last visit were collected. Student's T-test and Pearson correlation matrix were applied for analytical modeling.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, clinical and laboratory features of the patients studied by diagnosis.

	FMF (n=36)	Undefined autoinflammatory syndrome (n=18)	TRAPS (n=6)	HIDS (n=6)	APLAID (n=1)	PFAPA (n=1)	SAVI (n=1)	BLAU (n=1)
Demography								
SEX(female) n(%)	21(59)	12(66)	1(16)	4(11)	1(100)	1(100)	1(100)	1(100)
MEDIAN AGE AT ONSET (±SD)	9.8(±13.5)	19.1 (±17)	7.05(±4.1)	0.7(±0.86)	46.1	14.6	1.2	29.9
MEDIAN AGE AT DIAGNOSIS (± SD)	14.9(±13.4)	27.4(±16.8)	13.6(±5.32)	9.05(±16.37)	48.4	-	38.4	40.7
Symptoms n(%)								
FEVER	31(86)	15(83)	5(83)	6(100)	1(100)	1(100)	1(100)	1(100)
ARTHRALGIA	32(88)	14(77)	5(83)	4(66)	1(100)	1(100)	1(100)	1(100)
ARTHRITIS	18(50)	8(44)	2(33)	2(33)	-	-	1(100)	-
SEROSITIS n(N%)								
• Abdominal Pain	29(80)	9(50)	3(50)	6(100)	-	1(100)	1(100)	1(100)
• Confirmed peritonitis	2(5)	-	-	-	-	-	-	-
• Chest Pain	14(38)	4(22)	1(16)	1(16)	-	1(100)	-	-
• Pericarditis	4(11)	2(11)	1(16)	-	-	-	-	-
ORAL APHTOUS LESIONS	18(50)	10(55)	3(50)	4(66)	-	1(100)	1(100)	-
LYMPHADENOPATHY	2(5)	3(16)	6(100)	5(83)	-	1(100)	-	-
ODYNOPHAGIA	2(5)	8(44)	4(66)	3(50)	-	1(100)	-	-
GENITAL APHTOUS LESIONS	1(3)	1(5)	-	2(33)	-	-	-	-
OCULAR HYPEREMIA	-	5(27)	3(50)	2(33)	-	-	-	-
Laboratory Median (±SD)								
AMYLOID mg/L	6.05 (±3.8)	6.47(±58.4)	3.72 (±3)	13.5 (16.5±)	8.23	5.31	-	18.7
CRP* mg/L	1.05 (±3)	2.8 (±14.2)	1 (±1)	8.2 (±7.8)	2.3	4.8	2	10.4
ESR* mm/h	2.5 (±14.8)	3(±21.7)	2.5(±5.5)	6 (±14.9)	5	-	18	39

*CRP: C reactive protein.
*ESR: Erythrocyte Sedimentation Rate

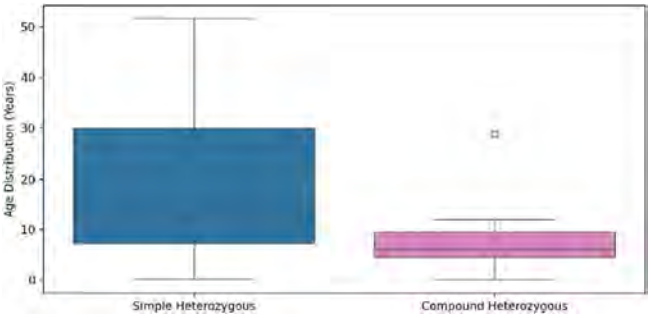


Figure 1. Distribution of symptom onset age according to FMF patient genotype.

Results: 70 patients were studied (60% female), with a median age at symptom onset of 10.3 years (±14.9) and at diagnosis of 18.4 years (±15.3). Table 1 describes their demographic, clinical and laboratory features.

A positive correlation was observed between amyloid levels and ESR, and more strongly with CRP. Higher levels of amyloid, CRP, and ESR were associated with older age at symptom onset, diagnosis, and beginning of follow-up. Female sex was linked to higher ESR levels and later diagnosis (median in males 13 vs. 31 years in females). Additionally, higher AIDAI scores were associated with requirement for anti-IL1 therapy.

Table 2. Classification criteria and treatment according to FMF patient genotype.

Variable	Compound Heterozygous (n=15) n(%)	Simple Heterozygous (n=17) n(%)	Homozygous (n=3) n(%)
Meets Eurofever/PRINTO classification criteria	12(80)	7(41)	2(67)
Meets new Eurofever/PRINTO classification criteria	14(93)	9(52)	3(100)
Treatment with Colchicine	9(60)	3(17)	-
Treatment with Colchicine+canakinumab	2(13)	7(41)	2(67)
Treatment with Colchicine +anakinra	1(6)	1(5)	1(33)
Without treatment	1(6)	2(11)	-
Treatment with Canakinumab	-	2(11)	-
Other treatments	2(13)	2(11)	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Among FMF patients, 15 (41%) were compound heterozygotes (symptom onset at 5.6 years [SD 6.8]), 17 (47%) simple heterozygotes (symptom onset 12.8 years [SD 16]), and 3 (8%) homozygotes (symptom onset 13 years [SD 14.5]). Table 2 shows FMF patient characteristics according to genotype. Symptom onset was statistically significantly earlier in compound than in simple heterozygotes (p = 0.0137; see Figure 1).

18 MEFV gene mutations were identified in FMF patients. The most frequent were c.2082G >A (p.Met694Ile) (25%), c.442G >C (p.Glu148Gln) (19%), and c.2080A >G (p.Met694Val) (16%).

Among patients with uSAID, 22% were in remission without treatment, 11% received colchicine, and 61% required biologic therapy.

Conclusion: -Amyloid levels were correlated with the need for anti-IL1 therapy; female sex was associated with later diagnosis and higher ESR levels.

-FMF was the most frequent disease, being c.2082G >A (p.Met694Ile) the most common MEFV mutation observed.

-FMF patients with compound heterozygosity showed more typical clinical features with a higher proportion of patients meeting classification criteria, and symptom onset was statistically significantly earlier than in simple heterozygotes.

-Most patients uSAID did not respond to colchicine and required biologic therapy, mainly anakinra.

Disclosure: A. Torrat Noves: None; **J. Ivorra Cortes**: None; **A. Mateo Vendrell**: None; **E. GRAU GARCIA**: None; **P. Muñoz Martinez**: None; **L. Mas Sanchez**: None; **D. Ramos Castro**: None; **I. Alcantara Álvarez**: None; **B. Villanueva Manes**: None; **A. perez Hurtado**: None; **M. Simeo Vinaixa**: None; **i. Calvo Penades**: None; **B. López Montesinos**: None; **L. Lacruz-perez**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6.

Abstract Number: 0238

Real-World Effectiveness of Mepolizumab on Gastrointestinal Involvement in Eosinophilic Granulomatosis with Polyangiitis and Hypereosinophilic Syndrome: A Multicenter Retrospective Study

Alessia Gatti[1], Francesca Regola[1], Giulia Fontana[2], Jacopo Mora[2], Mario Andrea Piga[3], Gianluca Moroncini[3], Rossella Acquaviva[4], Palma Carlucci[4], Silvia Noviello[4], Angelo Vacca[4], Paolo Delvino[5], Enrico Heffler[6], Emanuele Nappi[6], Jakub Moll[7], Jan Schroeder[7], Laura Losappio[7], Federica Davanzo[8], Roberto Padoan[9], Paolo Cameli[10], Edoardo Conticini[11], Greta Pacini[12], Alvise Berti[12], Lorenzo Vrola[13], Paola Tomietto[13], Benedetta Fazzi[14], elena treppo[15], Luca Quartuccio[14], Jan Willem Cohen Tervaert[16], Sabrina Arnold[17], Prof. Dr. med. Peter Lamprecht[18], Florence Roufosse[19], Ilaria Cavazzana[1], Franco Franceschini[20], Giacomo Emmi[21], Paola Toniati[22] European EGPA Study Group (EESG), [1]Rheumatology and Clinical Immunology Unit – ERN ReCONNET, ASST Spedali Civili of Brescia and University of Brescia, Brescia, Italy, [2]Rheumatology and Clinical Immunology Unit – ERN ReCONNET, ASST Spedali Civili and University of Brescia, Brescia, Lombardia, Italy, [3]Università Politecnica delle Marche and Azienda Ospedaliero Universitaria delle Marche, Ancona, Italy, [4]Section of Internal Medicine 'Guido Baccelli', Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari 'Aldo Moro', Bari, Italy, [5]Rheumatology Unit, IRCCS San Gerardo dei Tintori, Monza, Italy, [6]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI) and Personalized Medicine, Asthma and Allergy, IRCCS Humanitas Research Hospital, Milano, Italy, [7]Division of Allergy and Clinical Immunology, ASST GOM Niguarda, Milano, Italy, [8]Rheumatology Unit, Department of Medicine DIMED, University of Padua, Padova, Italy, [9]Rheumatology Unit, Department of Medicine DIMED, University of Padua, Padua, Italy, [10]University of Siena, Siena, Italy, [11]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Italy, Siena, Italy, [12]Santa Chiara Hospital and University of Trento, Unit of Rheumatology, Trento, Italy, [13]UCO Medicina Clinica, ASUGI, Cattinara Teaching Hospital, Trieste, Italy, [14]Division of Rheumatology, Department

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of Medicine (DMED), University of Udine, Udine, Italy, [15]Division of Rheumatology, Department of Medicine, University of Udine, Udine, Italy, [16]University of Alberta, Edmonton, AB, Canada, [17]Department of Rheumatology and Clinical Immunology, University of Lübeck, Lubeck, Germany, [18]University of Lbeck, Lbeck, Germany, [19]Department of Internal Medicine, Hôpital Universitaire de Bruxelles - Erasme, Université Libre de Bruxelles, Bruxelles, Belgium, [20]University of Brescia, Brescia, Brescia, Italy, [21]Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, Italy, [22]Rheumatology and Clinical Immunology Unit – ERN ReCONNET, ASST Spedali Civili of Brescia, Brescia, Lombardia, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic gastrointestinal disorders (EGIDs) are a group of disorders characterized by marked eosinophilic infiltration of the gastrointestinal (GI) tract resulting in organ dysfunction and onset of GI symptoms. They may present isolated or as part of systemic diseases including eosinophilic granulomatosis with polyangiitis (EGPA) and hypereosinophilic syndrome (HES).

Table 1. Patients' characteristics and clinical, laboratory, and treatment data before MEPO

PATIENTS' CHARACTERISTICS			
	EGPA (n=23)	HES (n=25)	TOTAL (n=48)
Male sex, n (%)	15 (65)	12 (48)	27 (56)
Smoking status, n (%)			
Never	13 (57)	20 (80)	33 (69)
Former	6 (26)	4 (16)	10 (21)
Current	4 (17)	1 (4)	5 (10)
Age at disease onset (y), median (IQR)	44 (37-53)	34 (24-44)	38 (30-51)
Age at disease diagnosis (y), median (IQR)	47 (40-56)	36 (27-45)	43 (33-55)
HES subtype, n (%)			
Myeloid	-	0 (0)	-
Reactive		1 (4)	
Lymphocytic		1 (4)	
Idiopathic		20 (80)	
NA		3 (12)	
Diagnostic delay (months), median (IQR)	20 (5-51)	8 (2-42)	12 (3-44)
Time from onset to MEPO initiation (months), median (IQR)	47 (16-111)	46 (13-97)	46 (13-106)
Time from diagnosis to MEPO initiation (months), median (IQR)	6 (1-49)	4 (1-45)	5 (1-49)
CLINICAL AND LABORATORY DATA BEFORE MEPO INITIATION			
GI involvement before MEPO initiation, n (%)	23 (100)	25 (100)	48 (100)
Esophagitis	6 (26)	4 (16)	10 (21)
Gastritis	8 (35)	11 (44)	19 (40)
Enteritis	11 (48)	15 (60)	26 (54)
Colitis	15 (65)	17 (68)	32 (67)
Ascites	2 (9)	6 (24)	8 (17)
Cholecystitis	4 (17)	2 (8)	6 (13)
Ischemic	2 (9)	-	2 (4)
Eosinophilic GI infiltration confirmed by biopsy, n (%)	19 (83)	20 (80)	39 (81)
GI inflammation confirmed by imaging, n (%)	13 (57)	14 (56)	27 (56)
GI flares before MEPO initiation (from disease onset), n (%)			
0 flares	9 (39)	5 (20)	14 (29)
1 flare	5 (22)	5 (20)	10 (21)
2 flares	3 (13)	4 (7)	7 (15)
= 3 flares	1 (4)	10 (40)	11 (23)
NA	5 (22)	1 (5)	6 (13)
AEC highest documented peak (n/µL), median (IQR)	3200 (1470-6360)	4000 (2010-10000)	3857 (1593-9743)
THERAPY BEFORE MEPO INITIATION			
Corticosteroids, n (%)	21 (91)	24 (96)	46 (96)
Intravenous	10 (43)	12 (48)	22 (46)
Topic	2 (9)	9 (36)	11 (23)
Oral	19 (83)	22 (88)	41 (85)
Cytotoxic/Immunosuppressive therapy, n (%)			
CYA	0 (0)	2 (8)	2 (4)
MTX	4 (17)	3 (12)	7 (15)
AZA	5 (22)	2 (8)	7 (15)
MMF	3 (13)	0 (0)	3 (6)
CYC	5 (22)	0 (0)	5 (10)
IVIG	0 (0)	1 (4)	1 (2)
IFNα	0 (0)	1 (4)	1 (2)
Biologic drugs other than MEPO, n (%)			
Rituximab	3 (13)	0 (0)	3 (6)
Dupilumab	1 (4)	1 (4)	2 (4)
Benralizumab	2 (9)	0 (0)	2 (4)

Legend: EGPA: Eosinophilic Granulomatosis with Polyangiitis; HES: Hypereosinophilic Syndrome; NA: Not Assessed; MEPO: Mepolizumab; AEC: Absolute Eosinophil Count; CYA: Cyclosporine A; MTX: Methotrexate; AZA: Azathioprine; MMF: Mycophenolate Mofetil; CYC: Cyclophosphamide; IVIG: Intravenous Immunoglobulins; IFNα: Interferon alfa

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical, laboratory, and treatment data collected at MEPO initiation and during follow up

	MEPO START	MEPO FOLLOW UP				
	t0 (n=48)	t1 (n=39)	t3 (n=46)	t6 (n=44)	t12 (n=37)	t24 (n=26)
MEPO dose, n (%)						
100 mg/4w sc	15 (31)	14 (36)	14 (30)	12 (27)	12 (32)	8 (31)
300 mg/4w sc	31 (65)	23 (59)	31 (67)	30 (68)	23 (62)	16 (62)
750 mg/4w iv	2 (4)	2 (5)	2 (4)	1 (2)	0 (0)	0 (0)
Other	0 (0)	0 (0)	0 (0)	1 (2)*	2 (5)†	2 (8)‡
Active GI involvement, n (%)	31 (65)	14 (36)	13 (28)	4 (9)	3 (8)	3 (12)
Esophagitis	7 (15)	3 (8)	2 (4)	2 (5)	0 (0)	0 (0)
Gastritis	11 (23)	3 (8)	5 (11)	2 (5)	0 (0)	1 (4)
Enteritis	17 (35)	5 (13)	4 (9)	2 (5)	2 (5)	2 (8)
Colitis	24 (50)	8 (21)	10 (22)	1 (2)	2 (5)	1 (4)
Ascites	4 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Cholecystitis	2 (4)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)
Ischemic	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
AEC (n/µL), median (IQR)	805 (482-1805)	115 (60-223)	75 (50-110)	70 (37-100)	65 (38-90)	70 (23-108)
Glucocorticoids, n (%)	44 (92)	35 (90)	37 (80)	28 (64)	19 (51)	12 (46)
Intravenous, n (%)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Topic for GI, n (%)	7 (15)	3 (8)	37)	2 (5)	2 (5)	0 (0)
Oral, n (%)	41 (85)	33 (85)	35 (76)	28 (64)	18 (49)	12 (46)
Oral PDN equivalent daily dose (mg), median (IQR)	11.3 (5-25)	7.5 (5-12.5)	5 (2.5-7.5)	5 (0-5)	0 (0-3.8)	0 (0-2.5)

*167 mg/4w iv; †125 and 214 mg/4w iv; ‡187 and 200 mg/4w iv
Legend: MEPO: Mepolizumab; sc: subcutaneous; iv: intravenous; GI: gastrointestinal; AEC: Absolute Eosinophil Count; IQR: Interquartile Range; PDN: Prednisone

Table 3. Summary of disease flare characteristics and related treatments

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Diagnosis	EGPA	EGPA	EGPA	EGPA	HES	HES	HES	HES
Time to event (months)	2	21	28	4	10	7	3	171
Type of GI flare	Colitis	Colitis	Colitis	Cholecystitis	Colitis	Esophagitis Gastritis Enteritis	Gastritis Enteritis Colitis	Esophagitis Gastritis Enteritis Ascites
AEC (n/µL)	NA	0	80	300	100	110	900	140
Ongoing therapy								
MEPO dose (mg/4w)	100	100	300	100	300	300	100	300
OCS (mg/d)	12.5	-	-	-	2.5	-	5	-
Other	-	-	MMF	-	-	-	-	-
Therapeutic management of flare	Switch to MEPO 300, add OCS 25 mg/d	Increase OCS to 25 mg/d, add MTX and RTX	Add OCS 25 mg/d, add topic CS for GI	Add OCS 40 mg/d and MMF	Increase OCS to 10 mg/d	Add CS (iv bolus followed by OCS 50 mg/d)	Switch to MEPO 300, increase OCS to 25 mg/d	Add OCS 40 mg/d (short course)

Legend: EGPA: Eosinophilic Granulomatosis with Polyangiitis; HES: Hypereosinophilic syndrome; GI: gastrointestinal; AEC: Absolute Eosinophil Count; OCS: Oral Corticosteroids; MMF: Mycophenolate Mofetil; RTX: Rituximab; iv: intravenous

Mepolizumab (MEPO), an anti-interleukin 5 monoclonal antibody, is approved for both of these conditions; however, data are limited regarding its role in managing GI involvement.

The aim of this study is to retrospectively evaluate the efficacy of MEPO on EGPA and HES-related GI involvement.

Methods: This was a retrospective cohort study conducted among centres referring to the European EGPA Study Group. Inclusion criteria: age $\geq$ 18 years; diagnosis of EGPA ([1], [2]) or HES ([3]); GI manifestations confirmed by histology or imaging; start of MEPO any dosage (ie 100 mg/month sc, 300 mg/month sc, 750 mg/month iv) for uncontrolled GI manifestations.

Data were collected from disease onset until MEPO start (t0), at 1 (t1), 3 (t3), 6 (t6), 12 (t12), and 24 (t24) months, as well as during flares (defined as exacerbations of GI symptoms requiring therapeutic escalation).

Outcomes included symptom improvement, absolute eosinophil count (AEC) reduction, flare occurrence, and corticosteroid (CS)-sparing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Data are presented as n (%) or median (IQR). Wilcoxon or McNemar tests were used as appropriate. Flare rates (flares/patient-month) pre- and post-MEPO were compared using incidence rate ratio (IRR) with 95% CI ($p< .05$).

Results: Forty-eight patients were included [23 EGPA, 25 HES; median age at onset: 38 (30-51) years; median age at diagnosis: 43 (33-55) years; median diagnostic delay: 12 (3-44) months]. At baseline, all the patients had active GI involvement, with a median peak AEC of 3857 (1593-9743) cells/μL. Overall, 46 patients (96%) had a history of CS use prior to MEPO. Median time from diagnosis to MEPO start was 5 (1-49) months (Table 1).

Median AEC significantly decreased by t1 [t0: 805 (482-1805) cells/μL; t1: 115 (60–223); $p< .001$] and remained low through t24 [70 (23–108) cells/μL; $p< .001$]. By t24, a significant decrease in the proportion of patients with active GI symptoms (65% to 12%, $p< .001$) and oral CS (OCS) use (85% to 46%, $p=.001$) were seen. Median prednisone equivalent daily dose decreased from 11.3 (5-25) mg/day at t0 to 0 (0-2.5) mg/day at t24 ($p< .001$) (Table 2).

During follow up, 8 patients experienced a GI relapse [4 EGPA, 4 HES; median time to event: 9 (4-23) months]. All were on a stable MEPO dose, 3 were on OCS (2 tapering) and 1 on MMF. The AEC increased AEC in only 1 case. All flares were managed by adjusting CS therapy; additionally, MEPO dose was increased in 2 cases and immunosuppressive therapy was added in 2 others (Table 3). The flare rate decreased from 0.021 to 0.0049 flares per patient-month after MEPO initiation (IRR 0.23, 95% CI 0.11–0.49, $p=.0001$), representing a 77% reduction.

Conclusion: MEPO effectively controlled GI symptoms and reduced CS use in the majority of EGPA and HES patients.

References:

[1] Grayson et al., Ann Rheum Dis 2022;81:309–14
[2] Wechsler et al., N Engl J Med 2017;376:1921–32
[3] Valent et al., Allergy 2023;78:47–59

Disclosure: A. Gatti: None; **F. Regola**: GlaxoSmithKlein(GSK), 6; **G. Fontana**: None; **J. Mora**: None; **M. Piga**: None; **G. Moroncini**: None; **R. Acquaviva**: None; **P. Carlucci**: None; **S. Noviello**: None; **A. Vacca**: None; **P. Delvino**: None; **E. Heffler**: None; **E. Nappi**: None; **J. Moll**: None; **J. Schroeder**: None; **L. Losappio**: None; **F. Davanzo**: None; **R. Padoan**: None; **P. Cameli**: GlaxoSmithKlein(GSK), 6; **E. Conticini**: GlaxoSmithKlein(GSK), 2, 6; **G. Pacini**: None; **A. Berti**: None; **L. Vrola**: None; **P. Tomietto**: None; **B. Fazzi**: None; **e. treppo**: None; **L. Quartuccio**: None; **J. Cohen Tervaert**: AbbVie/Abbott, 6, GlaxoSmithKlein(GSK), 6, Hoffmann-La Roche, 6, IDMC InflaRx, 12, Chair, Mallinckrodt Pharmaceuticals, 2, Medexus, 6, Merck/MSD, 2, Novartis, 2, Pfizer, 6, Sanofi, 6; **S. Arnold**: None; **P. Lamprecht**: AstraZeneca, 1, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Bundesministerium für Bildung und Forschung, 5, Deutsche Forschungsgemeinschaft, 5, GlaxoSmithKlein(GSK), 1, 6, Janssen, 6, John Grube Foundation, 5, Novartis, 6, UCB, 1, 6, Vifor, 1, 5, 6; **F. Roufosse**: None; **I. Cavazzana**: None; **F. Franceschini**: None; **G. Emmi**: None; **P. Toniati**: GlaxoSmithKlein(GSK), 6.

Abstract Number: 0239

Safety of Rilzabrutinib, a BTK Inhibitor, in Adult Patients with IgG4-related disease (IgG4-RD) in a 52-week Phase 2 Open-label Study

Alireza Meysami[1], Mollie Carruthers[2], John Stone[3], Fernando Martinez-Valle[4], nicolas schleinitz[5], Daniela Ghetie[6], Robert Spiera[7], Jeea Choi[8], Leda Mannent[9] and Owen Hagino[8], [1]Henry Ford Health, Detroit, MI, [2]Vancouver General Hospital, Vancouver, BC, Canada, [3]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [4]Vall d'Hebron Hospital, Barcelona, Spain, [5]Aix Marseille university, AP-HM, Marseille, France, [6]Oregon Health and Science

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University, Portland, OR, [7]Scleroderma, Vasculitis, and Myositis Center, Hospital for Special Surgery, Weill Cornell Medical College, New York, NY, [8]Sanofi, Morristown, NJ, [9]Sanofi, Gentilly, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4- related disease (IgG4-RD) is a chronic, progressive, immune-mediated fibrotic disease with limited treatment options. Rilzabrutinib is an orally available, reversible, inhibitor of Bruton's tyrosine kinase (BTKi). We conducted an open label proof-of-concept safety and efficacy study of rilzabrutinib orally twice daily in patients diagnosed with active IgG4-RD. As of Jan 2, 2025, the cumulative exposure to rilzabrutinib in interventional clinical trials is estimated to be 1186 participants and 672 patient-years (PY). Across the completed and ongoing studies in multiple indications (IgG4-RD, immune thrombocytopenia, warm autoimmune hemolytic anemia, focal segmental glomerulosclerosis/minimal change disease, pemphigus vulgaris, asthma, atopic dermatitis, and chronic spontaneous urticaria) rilzabrutinib was well tolerated, including at single and multiple doses

Methods: The safety of rilzabrutinib was evaluated in a 52-week, phase 2 proof-of-concept study (NCT04520451) including adult patients with active IgG4-RD. Two cohorts were included. Cohort A included participants in the United States and Cohort B included participants in Canada, France, Italy, and Spain. Safety parameters included spontaneously reported treatment emergent adverse events (TEAE), serious TEAE, TEAE leading to discontinuation, adverse events of special interest (AESI), and death

Results: The most frequently reported TEAEs by primary SOC (≥20% of participants) were: Gastrointestinal disorders (16 of 27 [59.6%], infections and infestations (12 of 27 [44.4%]), skin and subcutaneous tissue disorders (11 of 27 [40.7%]) and nervous system disorders (8 of 27 [29.6%]) (Table). Overall, 2 of 27 (7.4%) participants experienced serious TEAE (1 participant with campylobacter infection; and 1 death due to aspiration pneumonitis while hospitalized for acute kidney injury, reported as not related to study intervention, in a participant with history of chronic kidney failure, oesophagitis, and hiatal hernia). Overall, 5 of 27 (18.5%) reported TEAEs leading to permanent treatment discontinuation (Table). There were no reports of pregnancy, symptomatic overdose, tuberculosis, or uveitis; nor drug related AESI associated with other BTKi: major hemorrhagic events, severe or serious cytopenia, or atrial fibrillation.

Table: Summary of adverse events and the most common adverse events (>20%) reported during the study

Summary of adverse events	Cohort A (N = 13)	Cohort B (N = 14)	Overall (N = 27)
Participants with at least one TEAE	10 (76.9)	13 (92.9)	23 (85.2)
Participants with at least one Serious TEAE	1 (7.7)	1 (7.1)	2 (7.4)
Participants with TEAE leading to death	0 (0.0)	1 (7.1)	1 (3.7)
Participants with TEAE leading to permanent Study intervention discontinuation	2 (15.4)	3 (21.4)	5 (18.5)
Participants with treatment emergent AESI	4 (30.8)	3 (21.4)	7 (25.9)
TEAE reported in ≥20% of participants			
System Organ Class (SOC)			
Participants with at least one TEAE	10 (76.9)	13 (92.9)	23 (85.2)
Gastrointestinal disorders	8 (61.5)	8 (57.1)	16 (59.3)
Infections and infestations	5 (46.2)	6 (42.9)	12 (44.4)
Skin and subcutaneous tissue disorders	3 (23.1)	8 (57.1)	11 (40.7)
Nervous system disorders	4 (30.8)	4 (28.6)	8 (29.6)

Treatment emergent adverse events that started on or after the first dose of rilzabrutinib.
Adverse events are coded using the MedDRA 27.1
n (%) = number and percentage of participants with at least one TEAE by SOC and PT.
Percentages are based on the number of Participants in the Rilzabrutinib Treated Population.
TEAEs: Treatment emergent adverse events (TEAEs) AESI: Adverse event of special interest
NB: 1 participant accounts 1 serious TEAE, 1 TEAE leading to permanent study intervention discontinuation and 1 death

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Although this study included participants with a multi-organ, chronic, relapsing disease, with the exception of the unrelated fatal event, the safety profile was consistent with that reported for other clinical trials of rilzabrutinib. No participant experienced a TEAE associated with other BTKi, e.g., bleeding, cytopenia, or atrial fibrillation.

Disclosure: A. Meysami: Amgen, 1, 2, 6, AstraZeneca, 1, GlaxoSmithKlein(GSK), 1, Janssen, 1, Zenas, 1; **M. Carruthers**: AbbVie, 2, Amgen, 2, Janssen, 2, Pfizer, 2, Roche, 2, Sanofi, 2, UCB, 2, Zenas, 2; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **F. Martinez-Valle**: Amgen, 1; **n. schleinitz**: Amgen, 1, 2; **D. Ghetie**: None; **R. Spiera**: Abbvie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Certa, 2, Chemocentryx, 2, 5, Corbus, 5, Cytori, 2, 5, Galderma, 2, GlaxoSmithKlein(GSK), 2, 5, Horizon, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Regeneron, 2, Roche-Genentech, 2, 5, Sanofi, 2, Vera Therapeutic, 2; **J. Choi**: Sanofi, 3; **L. Mannent**: Sanofi, 3; **O. Hagino**: Sanofi, 3.

Abstract Number: 0240

Behçet's Disease in a Diverse Urban Single-Center Cohort in the United States: HLA-B Alleles and Clinical Features

Amir Razmjou[1], Alexandra Klomhaus[2], David Kellner[3], Meika Fang[4], Michael Weisman[5] and John FitzGerald[3], [1]UCLA / Veterans Affairs, Los Angeles, CA, [2]UCLA, Los Angeles, [3]UCLA, Los Angeles, CA, [4]VA Greater Los Angeles/UCLA, Los Angeles, CA, [5]Cedars-Sinai Medical Center, LOS ANGELES, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

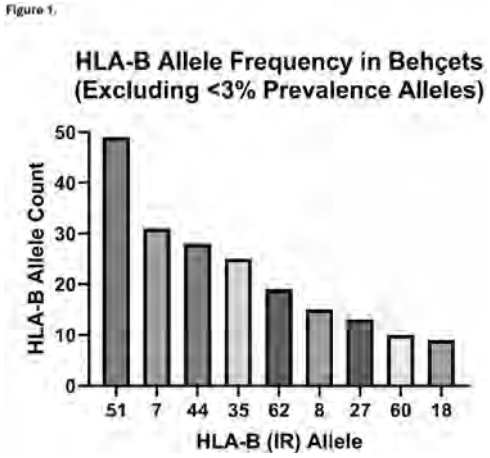
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's disease (BD) is a chronic systemic disease with heterogenous clinical presentations. The strongest genetic risk factor and diagnostic biomarker for BD is the class I major histocompatibility complex antigen HLA-B51. Although best studied in 'Silk-Road' populations, B51's prevalence in BD varies considerably across different racial/ethnic groups (Capittini, et al. *Dis Markers*, 2021). The genetic risks in American populations with BD are limited. This study

Figure 1.



Values represent HLA-B allele count from total of 285 alleles (144 Behçet's patients, 3 missing copies). Excluded the following HLA-B alleles representing <3% prevalence, but still present at least once: HLA-B: 13, 37, 38, 39, 41, 42, 45, 46, 47, 48, 49, 50, 55, 56, 57, 58, 61, 63, 65, 67, 71, 72, 75, 77.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics, and genetic HLA-B frequencies in Behçet's patients stratified by B51(+) status.

Total N=144	B51(+): N=48 (33%)	B51(-): N=96 (67%)
Age (Years)	45.4 (15.5)	46.1 (16.5)
Gender (Female)	38 (79.2)	77 (80.2)
Race		
White	17 (35.4)	40 (41.7)
Non-White	31 (64.6)	56 (58.3)
AAPI	4 (8.3)	8 (8.3)
Middle Eastern	3 (6.3)	4 (4.2)
Black	0 (0.0)	1 (1.0)
Multi-race	5 (10.4)	6 (6.3)
Other	14 (29.2)	22 (22.9)
Refused	5 (10.4)	15 (15.6)
Ethnicity		
Hispanic	7 (14.6)	12 (12.5)
csDMARD	21 (43.8)	39 (40.6)
bDMARD (RA)	11 (22.9)	30 (31.3)
bDMARD (SpA)	10 (20.8)	28 (29.2)
tsDMARD	2 (4.2)	2 (2.1)
Glucocorticoids	38 (79.2)	77 (80.2)
B27+	2 (4.2)	10 (10.4)
B44+	3 (6.3)	**22 (22.9)***
B7+	5 (10.4)	**25 (26.0)***
B35+	6 (12.5)	18 (18.8)
B8+	1 (2.1)	12 (12.5)

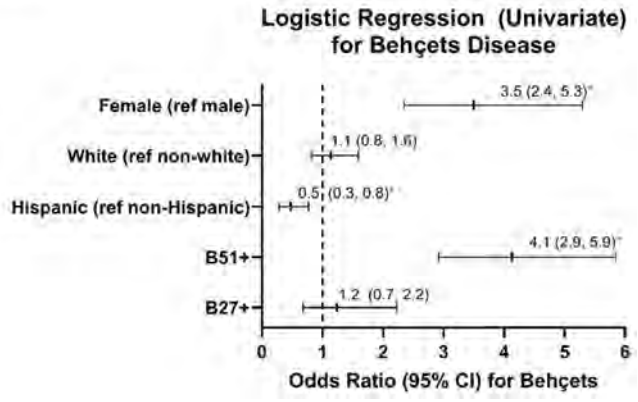
Values represent n (%) for categorical variables, and mean (SD) for continuous variables. Race, ethnicity, and gender are self-reported by the patient. *p<0.05, by Chi-Squared testing comparing B51(+) vs (-) AAPI=Asian American/Pacific Islander, DMARD=disease modifying anti-rheumatic drug, csDMARD=conventional synthetic DMARD, bDMARD=biologic DMARD (RA=bDMARDs for RA, SpA=bDMARDs for spondyloarthritis, including IL17i, IL12/23i, IL23i), tsDMARD=targeted synthetic DMARD.

describes the associations between HLA-B alleles and demographics in a diverse BD population from a large urban academic medical center in Los Angeles County.

Methods: Inclusion criteria required that patients had HLA-B allele testing (by sequence-specific oligonucleotide-polymerase chain reaction typing) conducted in routine clinical care, and were identified as having BD with ≥2 ICD-9/10 codes for BD. A sensitivity analysis with a more restrictive cohort (≥2 ICD-9/10 codes for BD, plus ≥1 rheumatology encounter, plus ≥1 DMARD prescription) was performed, and had similar demographic/genetic features. HLA-B alleles evaluated in the analysis included known relevant alleles (B51, B27), and the other 3 alleles of highest frequency.

Results: There were 144 identified BD patients, with B51 positivity in 33% (48 patients), versus a B51 prevalence of 11% among 2614 non-rheumatic controls (p< 0.0001). Amongst the BD patients, the alleles of highest frequency were B51 (49), B7 (31), B44 (28), and B35 (25) (Figure 1). Comparing B51(+) versus B51(-) BD patients, the groups were similar by age, gender, race/ethnicity and use of disease modifying agents (Table 1). However, there were higher percentages of B7(+) and B44(+) patients in the B51(-) group (Table 1). 35% of BD patients identified as white and compared to non-white BD patients had similar rates of B51(+), but a higher rate of B27(+) (16% vs 4%, p=0.01). White BD patients compared to white non-rheumatic controls had significantly higher B51(+) and B27(+). Non-white/Hispanic BD patients compared to

Figure 2.



Univariate logistic regressions for the outcome of Behçet's Disease diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

non-white/Hispanic controls had significantly higher B51(+). The unadjusted odds ratios (OR) for BD (yes/no) demonstrated B51(+) 4.13 (95% CI 2.92, 5.85), female gender 3.5 (2.35, 5.30), and Hispanic ethnicity 0.48 (0.29, 0.77) (Figure 2). B51, gender, and Hispanic ethnicity remained significant in a multivariate model, and interaction terms were non-significant.

Conclusion: In a large diverse U.S. urban academic medical center, BD was significantly associated with B51(+) and was present in ~1/3 of BD patients. B51(+) did not differ significantly between race or ethnicity. White BD patients had significantly higher rates of B27(+) than non-rheumatic white controls, and non-white BD patients. This data shows that U.S. BD patients may have lower B51(+), and higher female prevalence than in Silk-Road BD populations, which may reflect different genetic/environmental risks for BD. Limitations include selection bias (patients had to have clinically indicated HLA-B allele testing), and misclassification bias utilizing ICD codes (though sensitivity analysis demonstrated similar baseline/genetic features).

Disclosure: A. Razmjou: None; **A. Klomhaus**: None; **D. Kellner**: None; **M. Fang**: None; **M. Weisman**: Spyre Therapeutics, 1, 2; **J. FitzGerald**: None.

Abstract Number: 0241

Efficacy and Safety of JAK Inhibitors in Behçet's Syndrome: A Systematic Literature Review

Bercemhan Sulu[1], Sinem Nihal Esatoglu[1], Ibrahim Hatemi[2], Aykut Ferhat Celik[3] and Gulen Hatemi[1], [1]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa / Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Gastroenterology, Istanbul, Turkey, [3]Istanbul University-Cerrahpasa / Cerrahpasa Medical Faculty / Department of Internal Medicine / Division of Gastroenterology, Istanbul, Turkey

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) are a key treatment modality for major organ involvement, one of the main contributors to morbidity and mortality, as well as for resistant mucocutaneous and articular manifestations that significantly impair quality of life in Behçet's Syndrome (BS). In cases of inadequate response, and with emerging evidence on the involvement of multifactorial immune mediators and activation of the Janus kinase (JAK) signaling pathway in BS, JAK inhibitors (JAKi) have been introduced through pilot studies and case reports. We aimed to investigate the efficacy and safety profile of JAKi through a systematic literature review.

Methods: The systematic literature review was registered in PROSPERO under the identification number CRD420251000172. All articles published in PubMed, EMBASE, and the Cochrane Library up to March 6, 2025, that reported the use of JAKi in patients with BS and provided treatment outcomes were included. The search was conducted using the keywords: "Behçet AND (JAK OR tofacitinib OR baricitinib OR upadacitinib OR filgotinib OR Janus)." Two independent investigators (BS and SNE) screened 306 articles, and a total of 18 articles, reporting on 91 patients, along with one case report from our center, were included. Four patients (4.3%) had a prior history of JAKi use.

Results: Among the included patients, 16 (17.4%) received upadacitinib, 49 (53.3%) received tofacitinib, and 31 (33.7%) received baricitinib. The primary indication for initiating JAKi therapy was uveitis in 18 patients (19.6%), vascular involvement in 22 (23.9%), and gastrointestinal involvement in 46 (50%). The remaining 5 patients received JAK inhibitors due to refractory mucocutaneous and/or articular involvement. Nearly all patients had previously failed conventional treatments and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and clinical characteristics of patients with BS who used JAKi identified by systematic review including our case

Variable*	Overall (n=92)	Tofacitinib (n=49)	Baricitinib (n=31)	Upadacitinib (n=16)
Age at JAK initiation, years, mean (SD)	38.5 (13.5)	38.4 (14.4)	38 (12.8)	37.9 (11.5)
Male, n (%)	47 (51.6)	24 (53.3)	18 (58.1)	5 (33.3)
Disease duration, mean (SD)	129.8 (89.7)	141.2 (105.8)	142.1 (64.8)	88.0 (84.2)
Follow-up (months)	10 (6.00-19.50)	12.50 (6-24)	10 (9.0-15.0)	6.5 (3.75-9.0)
Classification/diagnostic criteria, n/N (%)				
ISG	48/83 (57.8)	24/48 (50)	22 (71)	6/8 (75)
ICBD	28/83 (33.7)	20/48 (41.7)	8 (25.8)	0
Unmet criteria	6/83 (7.2)	4/48 (8.3)	1 (3.2)	2/8 (25)
Indication for JAKi initiation				
Eye	19 (20.6)	15 (30.6)	0	4 (25)
Vascular	22 (23.9)	5 (10.2)	17 (54.8)	0
Gastrointestinal	46 (50)	27 (55.1)	14 (45.2)	9 (56.3)
Mucocutaneous and/or articular	5 (5.4)	2 (4.1)	0	3 (18.8)
Treatment n/N (%)				
Prior use of TNFi	52/91(57.1)	25/49 (51.0)	17 (54.8)	15/15 (93.3)
Concomitant IS therapy	50/82 (61.0)	22/47 (46.8)	28 (90.3)	3/8 (37.5)
The Remission Rates n/N (%)				
Gastrointestinal				
Clinical	38/46 (82.6)	19/27 (70.4)	11/14 (78.6)	9/9 (100)
Endoscopic	19/38 (50)	12/22 (54.5)	6/9 (66.7)	1/7 (14.3)
Ocular	15/18 (83.3)	12/15 (80)	N/A	3/3 (100)
Vascular	20/22 (90.9)	5/5 (100)	15/17 (88)	N/A

57.1% at least one anti-TNF monoclonal antibody. The remission rates were 82.6% and 50% for gastrointestinal involvement in terms of clinical and endoscopic remission, respectively; 83.3% for ocular involvement; and 90.9% for vascular involvement. The relapse rates were 2.2% for gastrointestinal and 16.7% for ocular involvement (Table 1). Serious adverse events were reported in 6 patients (6.5%), including two cases of anemia, one of pneumonia, and three cases of herpes zoster. No thrombotic events were reported in any patient.

Conclusion: JAK inhibitors are promising targeted synthetic DMARDs for patients with BS who show inadequate response to TNF inhibitors, particularly in cases with major organ involvement. However, randomized controlled trials are needed to establish their true efficacy and safety profile.

Disclosure: B. Sulu: None; **S. Esatoglu**: None; **I. Hatemi**: None; **A. Celik**: None; **G. Hatemi**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 2, Novartis, 6, Pfizer, 6, UCB, 6.

Abstract Number: 0242

Contemporary Recurrent Pericarditis Management – Real-world Evidence of Limited Cardiac Magnetic Resonance Imaging Prior to Initiating Rilonacept

Brittany Weber[1], Paul Cremer[2], Michael Garshick[3], Sushil Allen Luis[4], Ajit Raisinghani[5], Vidhya Parameswaran[6], Allison Curtis[6], Allan Klein[7], John Paolini[6] and RESONANCE Study Group, [1]Brigham and Women's Hospital, DEDHAM, MA, [2]Cleveland Clinic, Shaker Heights, OH, [3]NYU Langone Health, Tenafly, NJ, [4]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, [5]Division of Cardiology, Department of Medicine, Sulpizio Cardiovascular Center, University of California San Diego, San Diego, CA, [6]Kiniksa Pharmaceuticals, LEXINGTON, MA, [7]Cleveland Clinic, Cleveland, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

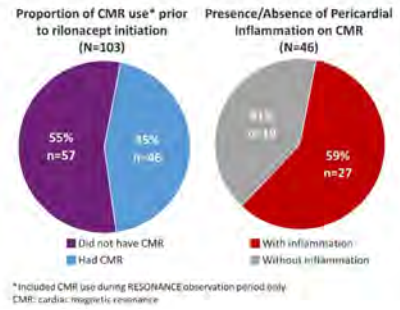
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure: Pericardial characterization prior to rilonacept initiation in RESONANCE



	Patients who had CMR prior to rilonacept initiation (N=46)	Patients who did not have CMR prior to rilonacept initiation (N=57)
Type of institution		
Academic medical center, patients, % (n/N)	46% (45/97)	54% (52/97)
Non-Academic medical center, patients, % (n/N)	17% (1/6)	83% (5/6)
Disease characteristics		
Number of recurrences prior to rilonacept initiation, median [Q1, Q3]	2 [1,3]	1 [1,2]
Steroid use prior to rilonacept initiation, patients, %	52%	32%
Disease duration at rilonacept initiation, years, median [Q1, Q3]	1.0 [0.5, 2.9]	0.9 [0.4, 2.9]

Background/Purpose: Recurrent pericarditis (RP) is a chronic autoinflammatory disease (mediated by IL-1) that requires long-term treatment, and selection of therapy is guided by multiple factors. Cardiac magnetic resonance (CMR) imaging characterizes pericardial inflammation and may inform RP management. Rilonacept, an IL-1α and IL-1β cytokine trap, is the only FDA-approved treatment for RP. We analyzed all CMR use prior to rilonacept initiation in RESONANCE, a US observational RP registry.

Methods: CMR use data were analyzed from 103 active pts at 22 sites (19 academic medical centers [AMCs], n=97; 3 non-AMC sites, n=6) who initiated rilonacept during RESONANCE up to Sep 9, 2024 (223.9 pt-yrs in median [Q1:Q3] 2.2 [1.4, 3.0] yrs).

Results: In 103 pts initiating rilonacept (mean [SD] age 49.7 [17.0] yrs, 56% female; median observation 0.8 [0.4, 1.0] yrs), median disease duration was 1.0 [0.4, 2.9] yr, with 1.5 [1, 2] prior recurrences. 45% (46/103) of pts had CMR before rilonacept initiation, 98% (45/46) of whom were managed at AMCs; 59% (27/46) showed pericardial inflammation. 54% (52/97) of rilonacept initiators at AMCs and 83% (5/6) at non-AMCs did not have CMR (**Figure**). Those having CMR had similar disease duration (1.0 [0.5,2.9] yr) but more prior recurrences (2 [1, 3]) and more prior steroid use (52%) than those not having CMR (0.9 [0.4, 2.9] yrs; 1 [1, 2]; 32%).

Conclusion: Recurrent pericarditis is a chronic disease that requires long-term treatment, and selection of therapy is guided by multiple factors. While CMR has utility amongst expert cardiologists in diagnosis, pericardial characterization, and monitoring, it was obtained in more clinically complex RP pts; real-world data indicate that pericardial imaging with CMR prior to rilonacept initiation was performed primarily at AMCs but in less than half of AMC patients (pericardial inflammation was present in approximately half); clinical criteria informed rilonacept initiation in the remainder.

Disclosure: B. Weber: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **P. Cremer**: Kiniksa Pharmaceuticals, 2, 5, Sobi, 5; **M. Garshick**: Agepha, 2, Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2; **S. Luis**: Cardiol Therapeutics, 2, Kiniksa Pharmaceuticals, 2, Medtronic, 2; **A. Raisinghani**: Kiniksa Pharmaceuticals, 2; **V. Parameswaran**: Kiniksa Pharmaceuticals, 3, 11; **A. Curtis**: Kiniksa Pharmaceuticals, 3, 11; **A. Klein**: Cardiol Therapeutics, 2, 5, Kiniksa Pharmaceuticals, 2, 5, Pfizer, 2, 5; **J. Paolini**: Kiniksa Pharmaceuticals, 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0243

Epidemiology of adult-onset Systemic Autoinflammatory Diseases in a well-defined population from northern spain

Carmen Lasa Teja[1], Laura Muñoz-Llopis[2], Diana Prieto-Peña[3], Isla Morante Bolado[4], José Luis Martín-Varillas[5], Nerea Paz-Gandiaga[6] and Ricardo Blanco[7], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [4]Rheumatology, Hospital General Sierrallana, Torrelavega, Spain., Santander, [5]Rheumatology Division, Hospital de Laredo. IDIVAL, Immunopathology Group. Santander, Spain., Laredo, Spain, [6]Rheumatology, Hospital Comarcal de Laredo, Laredo, Spain., Santander, [7]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic autoinflammatory diseases (SAIDs) are rare disorders characterized by recurrent episodes of fever, serositis, gastrointestinal symptoms, arthritis, and/or skin lesions. In adult-onset SAIDs, clinical manifestations are often less pronounced and differ from typical pediatric features. The incidence and prevalence of adult-onset SAIDs remain unknown due to variations in classification criteria and heterogeneous population samples.

Our objectives were: (a) to estimate the incidence of adult-onset SAIDs in a well-defined population, (b) to describe their demographic and clinical features, and (c) to document associated genetic variants.

Methods: We included all patients diagnosed with SAIDs with onset in adulthood (≥16 years of age) from January 1st, 2000 to December 31st, 2024 in Cantabria, Northern Spain. Patients were classified according to Yamaguchi and/or Fautrel criteria for adult-onset Still disease (AOSD) and Eurofever/PRINTO classification criteria for the remaining SAIDs. Annual incidence rates were calculated as cases per 100,000 inhabitants.

Table. Demographic, clinical, and laboratory characteristics of 45 patients with adult-onset SAIDs

	Adult-onset SAIDs (n=45)
Demographic features	
Age at diagnosis (years), *mean±SD*	45.2 ± 16.4
Sex (women), *n (%)*	24 (53.3%)
Clinical manifestations	
Duration of symptoms after diagnosis (months), median [IQR]	3 [1-24]
Fever, n(%)	40 (88.9%)
Skin rash, n(%)	35 (77.8%)
Mucocutaneous ulcers, n(%)	7 (15.6%)
Arthralgia/arthritis, n(%)	40 (88.9%)
Ocular, n(%)	8 (17.8%)
Pleuropericarditis, n(%)	7 (15.6%)
Neurologic, n(%)	6 (13.3%)
Gastrointestinal, n(%)	12 (26.7%)
Asthenia, n(%)	37 (82.2%)
Constitutional syndrome, n(%)	16 (35.6%)
Lymphadenopathies n(%)	17 (37.8%)
Macrophage activation syndrome n(%)	0 (0%)
Laboratory parameters	
CRP (mg/dL), median [IQR]	54 [19-120]
ESR (mm/1st hour), median [IQR]	45 [13-75]

Abbreviations: CRP (creatinine reactive phosphate), ESR (erythrocyte sedimentation rate).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

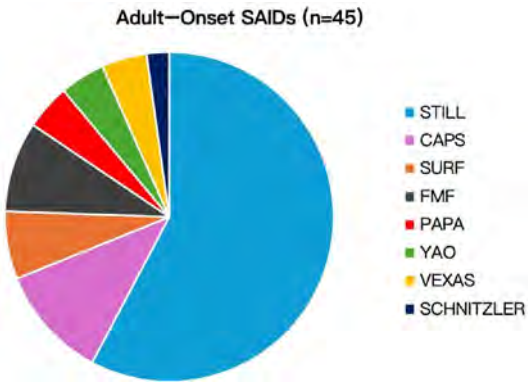


Figure. Classification of 45 patients with adult-onset SAIDs.

Results: We included 45 patients (24 women/21 men; mean age: 45.2±16.4 years). The mean annual incidence was 0.32 cases per 100,000 inhabitants, and the prevalence was 7.6 cases per 100,000. Patients were classified into the following SAIDs (Figure): AOSD (n=26), Cryopyrin-Associated Periodic Syndromes (CAPS) (n=5), Syndrome of Undifferentiated Recurrent Fever (SURF) (n=3), Familial Mediterranean Fever (FMF) (n=4), Pyogenic Arthritis, Pyoderma Gangrenosum, and Acne Syndrome (PAPA) (n=2), YAO Syndrome (n=2), VEXAS (n=2), Schnitzler Syndrome (n=1). The demographic and clinical features are summarized in Table.

The most common manifestations were recurrent fever (88.9%), arthralgia/arthritis (88.9%), asthenia (82.2%), and rash (77.8%). The median time from symptom onset to diagnosis was 3 [1-24] months. Genetic variants were identified in the following genes: NLRP12 (n=3), NOD2 (n=2), NLRP3 (n=2), MEFV (n=4), CD2BP1 (n=2), UBA1 (n=2), WDR1 (n=1), TNFAIP3 (n=1), BTD (n=1), SCL40A1 (n=1), SLC29A3 (n=1), NLRC4 (n=1).

Conclusion: Over a 20-year period, the mean annual incidence of adult-onset SAIDs was 0.46 cases per 100,000 inhabitants, with a prevalence of 11 cases per 100,000 in a well-defined population in Northern Spain. A similar gender distribution was observed, with AOSD being the most common condition.

Disclosure: C. Lasa Teja: None; **L. Muñoz-Llopis**: None; **D. Prieto-Peña**: None; **I. Morante Bolado**: None; **J. Martín-Varillas**: AbbVie, Pfizer, Lilly, Celgene, Janssen, and UCB Pharma, 5; **N. Paz-Gandiaga**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0244

Effectiveness and safety of Anifrolumab in Non-Systemic Cutaneous Lupus

Carmen Lasa Teja[1], Javier Loricera[2], Marcos López-Hoyos[3], Carmen Bejerano-Herreria[4], Andrea Estébanez[5], Mireia Sanmartin Martínez[6], Marta González-Fernández[7], Ivan Ferraz Amaro[8] and Ricardo Blanco[9], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [4]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [5]Department of Dermatology, Hospital Universitario Doctor Peset, Valencia, Spain, Valencia, Spain, [6]Hospital General Universitario de Valencia, Valencia, Comunidad Valenciana, Spain, [7]Basurto University Hospital, Bilbao, Pais Vasco, Spain, [8]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [9]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Anifrolumab is a human monoclonal antibody targeting the type I interferon receptor, approved for the treatment of systemic lupus erythematosus (SLE), with demonstrated efficacy in managing cutaneous involvement. However, its potential role in non-systemic subacute and chronic cutaneous lupus remains undefined, as its use in this setting is off-label.

This study aimed to assess the effectiveness and safety of anifrolumab in patients with non-systemic subacute or chronic cutaneous lupus in routine clinical practice.

Methods: This multicenter study evaluated patients with non-systemic subacute or chronic cutaneous lupus treated with anifrolumab. Given that non-systemic lupus represents an off-label indication, informed consent was obtained from all participants.

Cutaneous involvement was assessed using the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), evaluating both disease activity (CLASI-A, score range: 0–70) and damage (CLASI-D, score range: 0–56). The primary outcome was the reduction in CLASI-A and CLASI-D scores. Comparisons were conducted between baseline and months 1, 3, and 6 using Wilcoxon's signed-rank test.

Furthermore, considering the role of natural killer (NK) cells in the pathogenesis of cutaneous lupus, we analyzed NK cell dynamics in three patients over the study period.

Results: A total of 10 patients (8 females, 2 males) with cutaneous lupus treated with anifrolumab were included in the analysis (TABLE). The diagnoses were discoid lupus (n=7) and subacute lupus (n=3). The mean disease duration prior to anifrolumab initiation was 32.9±30.2 months.

Patient	Age/sex	Type of cutaneous lupus	Prior therapies	Systemic therapies concomitant with anifrolumab	Baseline CLASI-A score	CLASI-A score at last follow-up (months)	CLASI-A score change (% change)	Baseline CLASI-D score	CLASI-D score at last follow-up (months)	CLASI-D score change (% change)	Adverse events
1	61/M	Discoid lupus	Topical glucocorticoids, hydroxychloroquine	None	9	0 (3)	9 (100)	14	14 (3)	0 (0)	None
2	44/M	Discoid lupus	Topical glucocorticoids, hydroxychloroquine	Hydroxychloroquine	33	11 (3)	22 (66.7)	25	23 (3)	2 (8)	None
3	66/F	Discoid lupus	Topical glucocorticoids, oral glucocorticoids, hydroxychloroquine, methotrexate	Oral glucocorticoids	22	10 (2)	12 (54.5)	3	2 (2)	0 (0)	None
4	56/F	Discoid lupus	Topical glucocorticoids, hydroxychloroquine, methotrexate, azathioprine, belimumab, rituximab	Hydroxychloroquine, azathioprine	20	1 (14)	19 (95)	8	2 (14)	6 (75)	None
5	29/F	Discoid lupus	Topical glucocorticoids, hydroxychloroquine, chloroquine, mepacrine, methotrexate, thalidomide, apremilast, belimumab, rituximab	Hydroxychloroquine, methotrexate	16	1 (14)	15 (93.7)	10	6 (14)	4 (40)	None
6	46/F	Subacute lupus	Topical glucocorticoids, hydroxychloroquine	hydroxychloroquine	10	1 (3)	9 (90)	4	4 (3)	0 (0)	None
7	48/F	Discoid lupus	Topical glucocorticoids, oral glucocorticoids, hydroxychloroquine, chloroquine, methotrexate, azathioprine, mycophenolate mofetil	Hydroxychloroquine, mycophenolate mofetil	17	1 (3)	16 (94.1)	9	7 (3)	2 (22.2)	None
8	57/F	Subacute lupus	Topical glucocorticoids, oral glucocorticoids, hydroxychloroquine, methotrexate	Hydroxychloroquine, methotrexate	15	0 (3)	15 (100)	5	4 (3)	1 (20)	None
9	65/F	Discoid lupus	Topical glucocorticoids, oral glucocorticoids, hydroxychloroquine, chloroquine, methotrexate	Hydroxychloroquine	12	1 (6)	11 (91.7)	1	1 (6)	0 (0)	None
10	70/F	Subacute lupus	Topical glucocorticoids, oral glucocorticoids, hydroxychloroquine, methotrexate	Oral glucocorticoids, hydroxychloroquine	31	4 (5)	27 (87.1)	8	4 (5)	4 (50)	None

TABLE. Main features of the 8 patients with cutaneous lupus treated with anifrolumab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

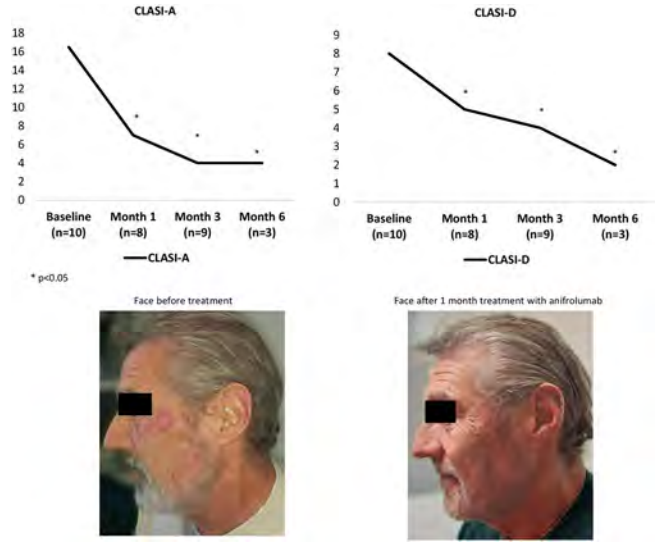


FIGURE 1. Clinical improvement of cutaneous lupus in patients treated with anifrolumab.

Before starting anifrolumab, patients had received the following treatments: topical glucocorticoids (n=10), hydroxychloroquine (n=10), methotrexate (n=7), oral glucocorticoids (n=5), chloroquine (n=3), azathioprine (n=2), belimumab (n=2), rituximab (n=2), mepacrine (n=1), thalidomide (n=1), apremilast (n=1), and mycophenolate mofetil (n=1).

Anifrolumab was administered at a dose of 300 mg intravenously every 4 weeks, either in combination with other therapies (n=9) or as monotherapy (n=1). All patients experienced a rapid and significant improvement in cutaneous disease activity (CLASI-A and CLASI-D) following anifrolumab initiation (FIGURE 1).

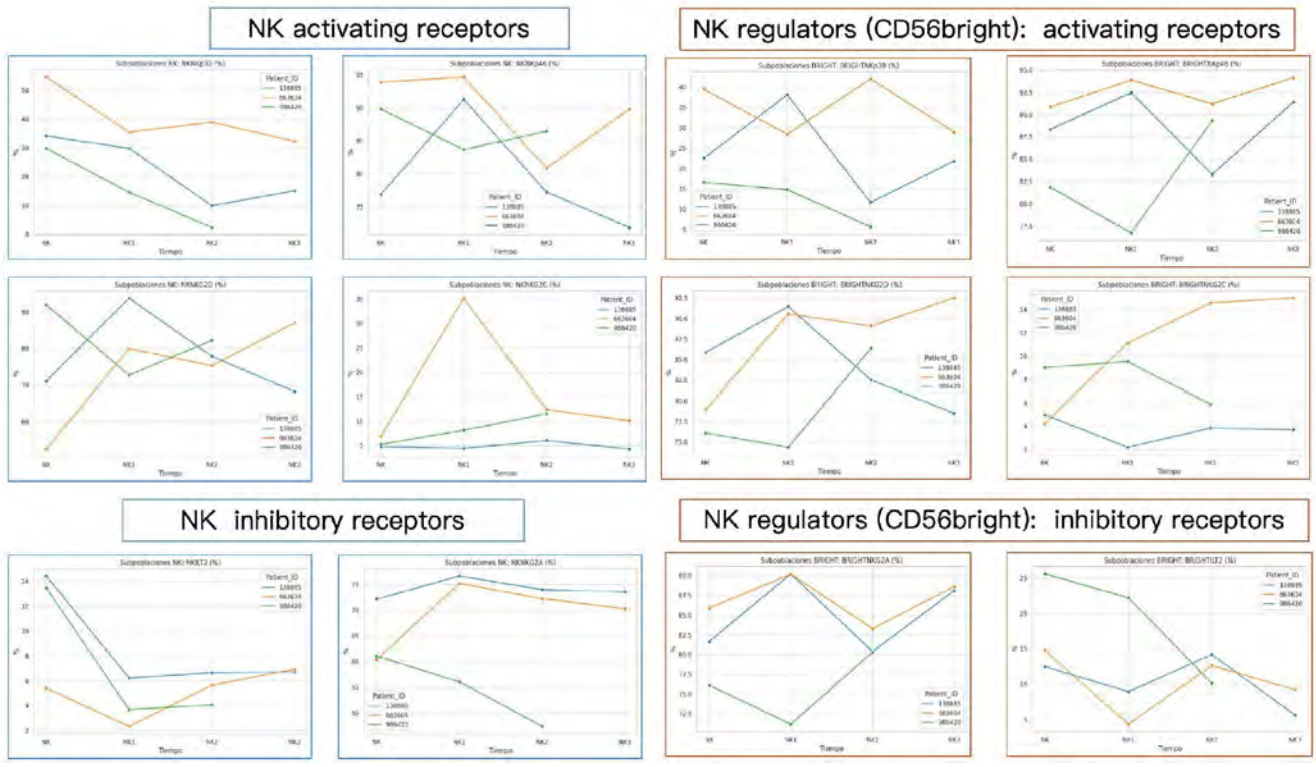


FIGURE 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

During a mean follow-up of 5.3±4.6 months, the median [IQR] CLASI-A score decreased from 16.5 [12.7–21.5] to 1 [1–3.2] (p=0.032), while the median [IQR] CLASI-D score decreased from 8 [4.2–9.7] to 4 [2.5–6.7] (p=0.044). No adverse effects were reported during follow-up. Additionally, an upregulation trend in inhibitory markers was observed in NK cell subtypes among the three patients in whom this analysis was performed (FIGURE 2).

Conclusion: Anifrolumab appears to be an effective and well-tolerated treatment for patients with refractory non-systemic cutaneous lupus.

Disclosure: C. Lasa Teja: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **M. López-Hoyos**: None; **C. Bejerano-Herreria**: None; **A. Estébanez**: None; **M. Sanmartin Martínez**: None; **M. González-Fernández**: None; **I. Ferraz Amaro**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0245

Predictors of Arterial Stiffness in Connective Tissue Diseases: Insights from the Lupus Extended Autoimmune Phenotype (LEAP) Cohort Study

cristiana Sieiro[1], Sarah Dyball[2], Ellen Bruce[3], Ben Parker[4] and Ian Bruce[5], [1]Univrsity of Manchester, Manchester, United Kingdom, [2]University of Manchester, Manchester, United Kingdom, [3]Manchester University NHS FT, The Kellgren Centre of Rheumatology, Manchester, United Kingdom, Manchester, [4]NIHR Manchester CRF, Manchester Royal Infirmary, Manchester, United Kingdom, [5]Centre for Public Health, Faculty of Medicine, Health and Life Sciences, Queen's University, Belfast, Manchester, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Connective tissue diseases (CTDs), including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and Sjögren's disease (SjD), are associated with an increased risk of cardiovascular disease (CVD), driven by chronic inflammation and immune dysregulation. Arterial stiffness, measured by carotid-femoral pulse wave velocity (cfPWV) and augmentation index (AIx), serves as a reliable marker of cardiovascular health and a predictor of adverse cardiovascular events. However, factors associated with arterial stiffness in CTD populations remain poorly defined.

This study aimed to assess arterial stiffness, measured by pulse wave velocity (PWV) and augmentation index (AIx), in individuals with CTDs including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), primary Sjögren's disease (SjD), undifferentiated connective tissue disease (UCTD), mixed connective tissue disease (MCTD), and/or overlap and idiopathic inflammatory myositis (IIM), compared to healthy controls (HC) and to identify factors associated with arterial stiffness in this population.

Methods: Participants from the Lupus Extended Autoimmune Phenotype (LEAP) cohort were enrolled in the study, which included patients with a diagnosis of a CTD and age- and gender-matched healthy controls. Sociodemographic data, CVD risk factors, and treatment details were collected for each participant. To identify independent associations with carotid-femoral pulse wave velocity (cfPWV) and brachial and aortic augmentation index (Aix), multivariate linear regression models were used.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We enrolled 382 CTD patients (167 with SLE, 75 with SjD, 53 with UCTD, 25 with SSc, 17 with overlap/MCTD, and 17 with myositis) and 28 healthy controls. Median age was 51 ± 21 years old. 357 (93%) patients were female. SLE patients were prescribed immunosuppressive treatment, antimalarial and oral steroids treatment significantly more often ($p < 0.0001$) than those with other diagnoses.

Patients with SSc diagnosis had a higher cfPWV compared with other CTDs ($\beta = 0.40$, $p = 0.04$). Across all CTDs, increased cfPWV was associated with age ($\beta = 0.04$, $p = 0.002$), systolic blood pressure (SBP) ($\beta = 0.01$, $p = 0.001$), diastolic blood pressure (DBP) ($\beta = 0.09$, $p = 0.002$), and aortic AIx ($\beta = 0.09$, $p < 0.0001$). Aortic Aix was associated with male gender ($\beta = 6.73$, $p < 0.0001$), age ($\beta = 0.32$, $p < 0.0001$), DBP ($\beta = 0.39$, $p = 0.01$) and mean arterial pressure (MAP) ($\beta = 0.73$, $p < 0.0001$). In addition, AIx brachial ($\beta = 0.08$, $p < 0.0001$), cfPWV ($\beta = 0.15$, $p = 0.03$), and central blood pressure ($\beta = 0.49$, $p < 0.0001$) were positively correlated with aortic AIx. Conversely, heart rate ($\beta = -0.44$, $p < 0.0001$) and diastolic reflection area ($\beta = -0.13$, $p < 0.0001$) showed significant negative associations. Brachial AIx was associated with age ($\beta = 0.46$, $p = 0.02$) as was a diagnosis of SSc SSc was ($\beta = 12.67$, $p = 0.03$). Of note, anti-Scl70 antibodies across all CTDs had a negative association with brachial AIx ($\beta = -1.64$, $p = 0.08$).

Conclusion: Arterial stiffness in patients with CTDs are particularly associated with blood pressure parameters, heart rate, and a diagnosis of SSc diagnosis.

Disclosure: c. Sieiro: None; **S. Dyball**: None; **E. Bruce**: None; **B. Parker**: Autolus Therapeutics, 1, LUPUS UK, 5, Otsuka, 6, UCB, 12, Conference attendance; **I. Bruce**: AstraZeneca, 2, 5, 6, BMS, 2, Cabaletta Bio, 2, GSK, 2, 5, 6, Janssen, 5, 6, Lilly, 2, Novartis, 5, Otsuka, 5, UCB, 2.

Abstract Number: 0246

Fracture Risk in Intestinal Autoimmune-mediated Diseases Patients: Clinical Insights from REMS

Marco Di Paola[1], Fiorella Anna Lombardi[1], **Edmund J MacLaughlin**[2], Maurizio Muratore[3], Kathleen Methric[4], Gianmarco Del Vecchio[5], Giusy Peluso[6], Chiara Stomaci[7], Roberto Franchini[1], Francesco Conversano[1], Paola Pisani[1] and Sergio Casciaro[1], [1]Institute of Clinical Physiology, National Research Council, Lecce, Puglia, Italy, [2]Rheumatology Associates of Delmarva and BoneVue Diagnostics, Easton, MD, [3]ASL- LE, "Vito Fazzi" Hospital, Lecce, Puglia, Italy, [4]BoneVue Diagnostics, Catonsville, MD, [5]Department of Research and Development, Echolight S.p.a., Lecce, Puglia, Italy, [6]Department of Innovative Engineering, University of Salento, Lecce, Puglia, Italy, [7]Department of Biological and Envinronmental Sciences and Technologies, University of Salento, Lecce, Puglia, Italy

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Intestinal Bowel Diseases (IBD), including Crohn's (ChD), and Ulcerative Colitis (UCD), along with Celiac (CID), diseases are chronic inflammatory conditions that primarily affect the gastrointestinal tract with systemic complications such as compromised bone health. These disorders are frequently associated with malabsorption of essential nutrients critical for bone metabolism. Chronic inflammation further exacerbates bone loss by promoting osteoclast activation and impairing osteoblast function through elevated levels of pro-inflammatory cytokines leading to higher prevalence of osteopenia, osteoporosis, and fragility fractures, even at a younger age. Additionally, long-term corticosteroid therapy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

contributes to reduced BMD and increased fracture risk Understanding the interplay between intestinal immune activity and skeletal health is essential for effective prevention and monitoring strategies. This study primary aims to assess the innovative 5-year fracture risk (FR) in these patients using the Radiofrequency Echographic Multi-spectrometry (REMS) technology and, secondarily, determine which condition has the greatest impact on fracture risk.

Methods: The 5-year FR was assessed using a REMS-based algorithm that automatically integrates both quantity and quality parameters. Specifically, by combining the REMS T-score with the Fragility Score (FS), the system identifies 7 distinct risk categories, each corresponding to a progressively increasing probability of fracture. To ascertain the impact of each pathology on the likelihood of experiencing an incident fracture, a logistic regression was performed.

Results: A cohort of 63 Caucasian patients (both genders), with ChD (n = 19, median age: 61 yo, 42.1% women < 65 yo), CID (n = 38, median age: 47.8 yo, 73.7% women < 65 yo), and UCD (n = 6, median age: 71 yo, 25% women < 65 yo) diseases underwent REMS scans at femoral neck. The FR analysis on hips showed that in ChD and UCD patients were mostly classified into high-risk classes (R5-R7), as follows: 21.1% (R5), 10.5% (R6), and 21.1% (R7), and 33.3% (R5 and R7), respectively. Conversely, in CID, patients were never classified in the high-risk level: R1 (23.7%), R3 (44.7%), and R4 (5.3%)). The logistic regression revealed a strong and statistically significant association between IBD and CID and high-risk fracture, with UCD OR = 5.5 (95% CI = 5.5, $p < 0.001$), followed by ChD (OR = 3.1% CI = 3.1-3.1, $p < 0.0001$) and by CID (OR = 1.3, 95% CI = 1.3-1.3, $p < 0.0001$) groups. Notably, the FS was higher in the IBD patients compared to CID group (42.51 and 29.2 for ChD and UCD, respectively), thus supporting the hypothesis that a steroids-based therapy in these patients can negatively affect the trabecular architecture.

Conclusion: This study highlights a significant link between these conditions and increased fracture risk, with UCD having the greatest impact, followed by ChD, while CID posed a comparatively lower risk. Furthermore, these findings emphasize the importance of early, targeted monitoring of bone health in these patients. The integration of bone quantity and quality parameters could enhance fracture risk prediction and support cost-effective strategies to prevent osteoporotic fractures in USA.

Disclosure: M. Di Paola: None; **F. Lombardi**: None; **E. MacLaughlin**: None; **M. Muratore**: None; **K. Methric**: None; **G. Del Vecchio**: None; **G. Peluso**: None; **C. Stomaci**: None; **R. Franchini**: None; **F. Conversano**: None; **P. Pisani**: None; **S. Casciaro**: None.

Abstract Number: 0247

Use of Nintedanib in Patients with Progressive Pulmonary Fibrosis

Elizabeth Volkmann[1], Steven Nathan[2], Karen Coeytaux[3], Yanni Fan[4], Jill Curran[3], Haikun Bao[3], Kamila Sroka-Saidi[5], Ann Chauffe[6] and Jeffrey J Swigris[7], [1]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA, [2]Inova Advanced Lung Disease and Transplant Program, Falls Church, VA, USA, Falls Church, [3]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, Ridgefield, [4]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, Ridgefield, CT, [5]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany, Ingelheim am Rhein, Germany, [6]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, Newberry, FL, [7]Center for Interstitial Lung Disease, Division of Pulmonary, Critical Care and Sleep Medicine, National Jewish Health, Denver, CO, USA, Denver

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Nintedanib was approved in the US for the treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype (progressive pulmonary fibrosis [PPF]) in 2020. We used US claims data to evaluate the characteristics and treatment patterns of patients with PPF treated with nintedanib.

Methods: We analysed claims data from 2019 to 2022 in the Optum Clinformatics Data Mart database. PPF was identified based on ≥1 of these criteria: a) ≥2 encounters with ICD-10 diagnosis code for 'interstitial lung disease with progressive fibrotic phenotype', ≥1 to 365 days apart; b) fibrotic ILD (≥2 encounters with relevant ICD-10 diagnosis codes, ≥1 to 365 days apart) and a progressive fibrosing phenotype (met ≥1 proxy criterion for progression after diagnosis of fibrotic ILD). Patients with idiopathic pulmonary fibrosis were not included. Analyses were based on data from patients who were newly prescribed nintedanib after identification of PPF in 2020 or 2021. Patients were followed from nintedanib initiation until death, the end of continuous insurance coverage (30-day gap permitted), or the end of the study.

Results: Among the 333 patients newly prescribed nintedanib after identification of PPF in 2020 or 2021, mean age was 72 years; 55.9% were male; 65.5% were White; 81.7% had Medicare. The nintedanib dose at initiation was 150 mg twice daily in 74.8% of patients. Among the patients for whom information on provider was available, the provider at initiation of nintedanib was a pulmonologist in 72.8%, internist in 17.4%, a rheumatologist in 1.8%, a family practitioner in 0.9%, and a different provider in 7.0% of patients. Over a mean follow-up of 463 days, nintedanib was discontinued in 47.2% of patients and interrupted in 40.5% of patients. The mean time to first interruption or discontinuation of nintedanib was 134 days. The mean time between the first interruption and re-starting nintedanib was 34 days. After initiating nintedanib, oxygen therapy was prescribed for 72.1% of patients, systemic corticosteroids for 45.4%, mycophenolate for 13.2%, hydroxychloroquine for 6.9%, methotrexate for 2.4%, rituximab for 2.1%, and tocilizumab for 1.8%; 1.5% underwent lung transplantation. Among patients who initiated nintedanib, 79 (23.7%) died during the follow-up period.

Conclusion: This analysis of a claims database showed that among US patients with PPF prescribed nintedanib, comedication use was high, with 72.1% of patients later prescribed oxygen. Almost half of patients initiated on nintedanib discontinued it over a mean follow-up of about 15 months.

Disclosure: E. Volkmann: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **S. Nathan**: Boehringer Ingelheim, 2, 6, 12, Medical writing support provided by Fleishman Hillard, United Therapeutics, 2, 6; **K. Coeytaux**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **Y. Fan**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **J. Curran**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **H. Bao**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **K. Sroka-Saidi**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **A. Chauffe**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **J. Swigris**: Boehringer Ingelheim, 2, 12, Medical writing support provided by Fleishman Hillard, Bristol Myers Squibb, 2, CSL Behring, 2, Dr. Swigris and National Jewish Health receive royalties related to use of copyrighted patient-reported outcome questionnaires, 9, Live Fully, 12, Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, patientMpower, 1, PF Warriors, 1, PureTech, 2, Tvardi, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0248

Clinical and serological characteristics of anti-Ku autoantibodies in a Hispanic cohort

Emmanuel Dominguez-Chapa[1], Angel Kevin Garza-Elizondo[2], Karina Deciderio-Pavon[3], Rosa Arvizu-Rivera[4], Jesus Alberto Cardenas-de la Garza[5], Miguel Villarreal-Alarcon[6] and Dionicio A. Galarza-Delgado[7], [1]Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [2]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo Leon, Mexico, [4]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico, [5]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [6]Hospital Universitario UANL, Monterrey, Nuevo León, Mexico, [7]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-Ku antibodies are rare myositis-associated antibodies directed against a DNA-binding heterodimer involved in DNA repair. Anti-Ku positivity may be associated with a distinct clinical phenotype in autoimmune diseases and, when present in isolation from other autoantibodies, may represent a distinct clinical syndrome. The current literature primarily includes studies on Asian and Caucasian populations, with limited data available on Hispanic individuals. We aim to describe the clinical and serological characteristics of Hispanic patients with anti-Ku positivity.

Methods: We conducted a cross-sectional study at the "Dr. José Eleuterio González" University Hospital in Monterrey, Mexico, between February 2016 and December 2023. Patients were identified by moderate or strong positivity for anti-Ku antibodies using the EUROLINE Autoimmune Inflammatory Myopathies panel. Demographic, clinical, and serological data were obtained from medical records. Patients with weak or borderline positivity, duplicated entries, or insufficient follow-up were excluded. This study was approved by our institution's ethics committee (RE24-00004).

Results: Eight patients were included, with a median age of 46 (IQR: 32.5 – 64.75). Seven (87.5%) were women. Three patients were diagnosed with anti-Ku syndrome. Other rheumatic diagnoses included overlap syndrome (systemic lupus erythematosus (SLE)/rheumatoid arthritis (RA), n=3), systemic sclerosis (SSc), and SLE (n=1 each). Clinical characteristics are detailed in Table 1.

In our cohort, all patients reported articular involvement during their clinical evolution. Skin involvement (alopecia, malar rash, and hyperpigmentation) appeared in seven patients. Sicca symptoms and Raynaud's were present in five (62.5%) and four (50%) patients, respectively. Cardiac and lung involvement each occurred in two patients.

Anti-Ro52 was the most common overlapping antibody (50%). We identified three antibody subgroups: anti-Ro-52 ± MDA5/NXP2/U1-RNP (n=4), often associated with Raynaud's and cardiac involvement, including the cohort's only death; isolated anti-Ku (n=3), with predominantly articular and sicca symptoms, and anti-cN1A (n=2), associated with SLE and cutaneous features.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of patients with moderate or strong positivity for anti-Ku antibodies.

Sex	Age	Diagnosis	Manifestations at onset	Age at disease onset	Skin manifestations	Fatigue	Raynaud's phenomenon	Arthralgia	Dysphagia	Sicca symptoms	Lung involvement	Cardiac involvement	Overlap antibodies	Treatment	Death	Follow-up (years)
Woman	68	SSc	Arthralgia Fatigue	65	Periungual lesions Skin hyperpigmentation	Yes	No	Yes	No	Yes	Yes	No	Ro-52 NXP2	Mycophenolate mofetil Prednisone Nintedanib	No	3
Man	64	Anti-Ku syndrome	Arthralgia Muscle weakness	63	No	Yes	No	Yes	No	No	No	No	No	Cortisone	No	1
Woman	37	Overlap syndrome (DM, RA, SLE)	Myalgias Arthralgia	36	Skin hyperpigmentation Alopecia Facial erythema	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Ro-52 MDA5	Indomethacin Betamethasone Methocarbamol	Yes	1
Woman	42	Anti-Ku syndrome	Pruriginous lesions in face, neck and thorax Polyarthralgia	40	Alopecia Photosensitivity Facial erythema	Yes	No	Yes	No	Yes	No	No	No	Methotrexate Prednisone	No	2
Woman	21	Overlap syndrome (RA, SLE) PM	Polyarthralgia Fatigue	13	Livedo reticularis Malar rash Alopecia	Yes	Yes	Yes	No	No	No	Yes	Ro-52 CN-1a U1-RNP	Chloroquine Celecoxib Gabapentin Prednisone	No	3
Woman	50	Overlap syndrome (RA, SLE, SSc)	Polyarthralgia Lower back pain	48	Digital ulcers Malar rash	Yes	Yes	Yes	Yes	No	No	No	Ro-52	Methotrexate Hydroxychloroquine Azathioprine Prednisone	No	1
Woman	65	Anti-Ku syndrome	Arthralgia	59	Alopecia	No	No	Yes	Yes	Yes	No	Yes	No	Leflunomide Prednisone	No	5
Woman	31	SLE	Paresthesia Lower extremity muscle weakness	29	Photosensitivity Malar rash Skin hyperpigmentation	Yes	Yes	Yes	No	Yes (oral ulcers)	No	No	CN-1A	Hydroxychloroquine Leflunomide Prednisone Azathioprine Methotrexate	No	7

Compared to international cohorts, our patients shared similar articular symptom prevalence (France: 83%, Italy: 86%, Germany: 80%) and Raynaud's rates (Portugal: 40.7%, France: 43%, Italy: 66.7%, ours: 50%). However, ILD was less frequent (25%) than in other international cohorts (up to 58%). All patients received corticosteroids. Immunosuppressants included methotrexate (n=3), azathioprine, mycophenolate mofetil, hydroxychloroquine, and leflunomide (n=2 each).

Conclusion: Clinical manifestations largely mirrored data from other international cohorts, particularly in articular and Raynaud's symptoms. Antibody clustering may reveal phenotypes with distinct prognoses. Our findings highlight the need to consider autoantibody profiles in risk stratification and individualized treatment. Larger studies are needed to better define clinical implications in this population.

Disclosure: E. Dominguez-Chapa: None; **A. Garza-Elizondo**: None; **K. Deciderio-Pavon**: None; **R. Arvizu-Rivera**: None; **J. Cardenas-de la Garza**: None; **M. Villarreal-Alarcon**: None; **D. Galarza-Delgado**: None.

Abstract Number: 0249

Obesity as a possible confusion factor in the scleroderma pattern

Eva Álvarez Andrés[1], Marta Novella-Navarro[2], Paloma García de la Peña Lefebvre[3], Eugenio de Miguel[2] and Paz Collado Ramos[4], [1]Hospital Severo Ochoa de Madrid, Madrid, Spain, [2]Hospital Universitario La Paz, Madrid, Spain, [3]Facultad ciencias de la Salud HM de la UCJC, Madrid, Spain, [4]Department of Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain, MADRID, Madrid, Spain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The 2023 EULAR criteria for systemic sclerosis reaffirm the diagnostic value of nailfold videocapillaroscopy (NVC), particularly the presence of giant capillaries and capillary loss to detect scleroderma pattern. However, their presence in non-rheumatic patients with cardiovascular risk factors (CVRFs), such as overweight/ obesity (OBE), remains underexplored.

The main objective of the study was to evaluate the existence of differences in capillaroscopic findings, in patients with OBE compared to patients with normal weight.

Methods: Longitudinal unicentric observational study carried out in 2020 and 2025, in which the frequency of pathological findings in capillaroscopy is estimated in subjects without rheumatic disease or Raynaud's phenomenon and compared by presence of OBE (body mass index >26) and normal weight. Exclusion criteria included having Raynaud's phenomenon or any rheumatological disease, as well as having a CVRF other than OBE.The variables collected were: sociodemographic, weight, height and body mass index, cardiovascular complications, autoimmunity, lipid profile, treatments, tortuosities and NVC alterations (ramified capillaries, enlarged capillaries, giant capillaries, haemorrhages and density loss). The NVC was performed again after 5 years, in 2025, to verify evolution.

For the statistics, measures of central tendency and dispersion were used for quantitative variables, and frequencies and percentages for qualitative variables. The outcome variable was OBE yes/no, and the X^2 test and Fisher's test were used to compare variables.

Results: 78 subjects were included (78,2% men, mean age 48±13 years), 39 with only obesity as a CVRF and 39 healthy controls without CVRF. The predominant vascular or thrombotic complication was abortion in 15.4% of the subjects, followed by stroke in 2,6% of participants. The presence of tortuosities was observed in 82.1% of the participants, subsequently 44.9% ramified capillaries, 35.9% enlarged capillaries, 33.3% haemorrhages, 28.2% density loss and 26.6% giant capillaries.

A statistically significant association was found between OBE and the presence of all the NVC findings, especially giant capillaries and density loss ($p < 0,001$).

These OBE patients were classified as having a scleroderma pattern and remained asymptomatic throughout. Five years later, the analytical and capillaroscopic studies were repeated, revealing the same NVC changes, with no development of rheumatologic pathology in any of them.

Conclusion: Scleroderma-pattern capillaroscopic findings may occur in non-rheumatic patients with OBE. These results underscore the importance of clinical context in interpreting NVC findings and suggest a potential overlap between metabolic and autoimmune microvascular damage.

Disclosure: E. Álvarez Andrés: None; **M. Novella-Navarro**: None; **P. García de la Peña Lefebvre**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **P. Collado Ramos**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0250

Autoinflammatory diseases in adult patients. Spanish registry.

Eztizen Labrador-Sanchez[1], Diana Prieto-Peña[2], Carlota L Iñiguez[3], Rafael B. Melero-González[4], Alberto Ruiz-Roman[5], Clara Moriano[6], Paula García-Escudero[7], Anahy Maria Brandy[8], Marta López[9], Fred Anton Pages[10], Maria Camila Osorio-SanJuan[11], Nahia Plaza-Aulestia[12], Bryan Josué Flores Robles[13], Estibaliz Andres Trashaedo[14] and Ricardo Blanco[15], [1]Hospital Universitario San Pedro, Laguardia, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [3]Hospital del Bierzo, Ponferrada, Castilla y Leon, Spain, [4]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [5]Hospital Juan Ramon Jimenez, Huelva, Spain, [6]Hospital León, LEON, Castilla y Leon, Spain, [7]Hospital Universitario Álava, Bilbao, Spain, [8]Hospital Germans Trias i Pujol, Badalona, Spain, [9]Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain, [10]Hospital General de Segovia, Segovia, Spain, [11]Hospital Clínico Lozano Blesa, Zaragoza, Spain, [12]Rheumatology division. Galdakao-Usansolo University Hospital, Galdakao, Spain, [13]Hospital San Pedro, Logroño, Spain, [14]Hospital San Pedro, Logroño, Spain, [15]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Autoinflammatory diseases(AIDs) are characterized by recurrent inflammatory episodes resulting from alterations in regulatory genes, activating the innate immune system. Although these diseases primarily occur in children, an increasing number of cases are reported in adults.

This study aimed to identify demographic, clinical, analytical, and therapeutic response factors contributing to diagnosing AIDs in adults in a clinical setting. Additionally, we sought to establish a correlation between these variables and the outcomes of genetic analysis.

Methods: A multicenter observational study was conducted involving adult patients (≥16 years) diagnosed with AID and followed up in rheumatology departments in Spain. Demographic, clinical, genetic, analytical, and therapeutic response data were collected. Genetic analysis was performed using Sanger or exome sequencing. Descriptive and relational comparative analyses were conducted using IBM SPSS statistical software.

Results: The study included 117 patients (57 females) with a mean age at diagnosis of 45.3±18.1 years and a mean time to diagnosis of 62 months; 15.4% had a family history of AID.

The most frequently diagnosed conditions (table)were adult-onset Still disease(AOSD) (43.6%), undifferentiated AID(UAID) (12.8%), and familial mediterranean fever(FMF)(12.8%).

The most common clinical manifestations included musculoskeletal symptoms(88%), fever(83.8%), asthenia(76.1%), cutaneous manifestations(75.2%), constitutional syndrome(40.2%), abdominal pain(30.8%), lymphadenopathy(29.9%), atypical chest pain(29.1%), oral aphthosis(25.6%) and ocular abnormalities(17%).

The mean C-reactive protein (CRP) level was 88.1 mg/L.

Genetic sequencing was performed for 93 patients(79.3%), with 64.4% of them showing heterozygous findings, including variants of uncertain significance (VUS)(n=35) and pathogenic variants(n=22).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Clinical Characteristics	Still n=51	PAPA n=4	UAID n=15	FMF n=15	CAPS n=7	VEXAS n=6	Yao n=2	Schnitzler n=3	BLAU n=1	CANDLE n=1	COPA n=1	HA20 n=1	NLRP12 n=1	MAIEED n=1	SAVI n=2	SURF n=2	TRAPS n=4
Female gender n (%)	24 (47.1)	2 (50)	8 (53.3)	6 (40)	3 (42.8)	0	0	2 (66.7)	1	0	1	1	0	1	2	2	4
Age at diagnosis in years±STD	45.75 ± 17.6	49.3±11.8	45.9±17.6	35.6±12.7	33.6 ±13.25	72.67 ±4.5	41.5± 20.5	64.7± 17.2	36	56	60	37	43	30	46.50± 37.47	30± 18.38	41.5± 37.5
Family history, n (%)	1 (2)	2 (50)	2 (13.3)	8 (72.6)	0	0	0	0	0	0	0	1	0	0	0	1(50)	2 (50)
CRP in mg/L, median	85.5	11	58	24.5	4	42.2	120,5	23	10	24	129	3	203	99	53.45	9	122,5
Musculoskeletal, n(%)	49(96.1)	4(100)	13(86.6)	12(80)	5(71.4)	6(100)	2(100)	2(66.7)	1	1	1	1	1	1	1(50)	0	3(75)
Fever, n (%)	51 (100)	2 (50)	12 (80)	10 (66.7)	5 (71.4)	4 (66.7)	2 (100)	2 (66.7)	0	1	1	1	0	1	2(100)	2(100)	3 (75)
Cutaneous, n (%)	44 (86.3)	3 (75)	9 (60)	10 (66.7)	5 (71.4)	5 (83.3)	2 (100)	3 (100)	0	1	0	0	0	1	2(100)	0	4 (100)
Digestive, n (%)	10 (19.6)	2 (50)	9 (60)	9 (60)	5 (71.4)	0	1 (50)	0	0	0	0	1	0	0	2(100)	0	3 (75)
Atipical chest pain, n (%)	14 (17.5)	0	7 (46.7)	5 (33.3)	0	2 (16.7)	1 (50)	0	1	0	1	0	0	1	0	0	2 (50)
Neurological, n (%)	8 (15.7)	0	6 (40)	6 (40.0)	6 (85.7)	0	0	1 (33.3)	0	0	0	0	0	1	0	1(50)	2 (50)
Oral aphthosis, n (%)	7 (13.7)	1 (25)	8 (53.3)	7 (46.7)	4 (57.1)	0	0	0	0	0	0	1	0	0	0	0	2 (50)
Ocular, n (%)	6 (11.8)	2 (50)	3 (20)	1 (6.7)	2 (28.6)	3 (50)	1 (50)	0	0	0	0	0	0	1	0	1(50)	1 (25)
Patients with variants, n (%)	6 (11.8)	3 (75)	6 (40)	15 (100)	7 (100)	4 (66.7)	1 (50)	2 (66.7)	1	1	1	1	1	1	2(100)	1(50)	4

Abbreviations: Autoinflammatory disease (AID), adult-onset Still disease(AOSD), undifferentiated autoinflammatory disease (UAID), familial mediterranean fever(FMF), cryopyrin-associated periodic syndrome(CAPS), syndrome of undifferentiated recurrent fever (SURF), tumor necrosis factor receptor periodic syndrome(TRAPS), STING-associated vasculopathy with onset in infancy (SAVI).

Treatment approaches included corticosteroids (GC)(82.1%) with a complete response(CR) of 43.7%, NSAIDs(54.7%) with a CR of 6.2%, methotrexate (MTX)(51.3%) with a CR rate of 31.6%, colchicine(49.6%) with a CR of 15.4%, anakinra(33.3%) with a CR of 38.5%, anti-IL-6(20.4%) with a CR of 58.3%, anti-TNF(19.6%) with a CR of 26.1%, canakinumab(10.2%) with a CR of 58.3%, and JAK inhibitors(6.7%) with a CR of 37.5%.

A significant relationship ($p < 0.05$) was found between carriers of VUS or pathogenic genetic variants and the presence of affected relatives, oral aphtosis, testicle pain, neurological and digestive manifestations. CR to GC and MTX was significantly higher in non-carriers.

Conclusion: This study identified AOSD, UAID and FMF as the most common in adults. Nevertheless, the genetic analysis was not performed in all patients, therefore monogenic AIDs may be underdiagnosed. Musculoskeletal symptoms, fever, asthenia and cutaneous manifestations were prevalent and anti-IL6 and canakinumab treatments showed the highest CR rates.

Genetic variants were linked to family history, oral aphtosis, testicle pain, neurological and digestive manifestations while non-carriers had higher CR to GC and MTX. Although the sample size was limited, these findings may assist in detecting monogenic AIDs in adults

Disclosure: E. Labrador-Sanchez: None; **D. Prieto-Peña**: None; **C. Iñiguez**: None; **R. Melero-González**: None; **A. Ruiz-Roman**: None; **C. Moriano**: None; **P. García-Escudero**: None; **A. Brandy**: None; **M. López**: None; **F. Anton Pages**: None; **M. Osorio-SanJuan**: None; **N. Plaza-Aulestia**: None; **B. Flores Robles**: None; **E. Andres Trashaedo**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0251

Impact of Mepolizumab on Idiopathic Hypereosinophilic Syndromes: Preliminary Analysis of a Monocentric Retrospective Cohort

Jacopo Mora[1], Francesca Regola[1], Paola Toniati[2], Giulia Fontana[1], Alessia Gatti[1], Ilaria Cavazzana[3] and Franco Franceschini[4], [1]Rheumatology and Clinical Immunology Unit – ERN ReCONNET, ASST Spedali Civili and University of Brescia, Brescia, Lombardia, Italy, [2]Rheumatology and Clinical Immunology Unit – ERN ReCONNET, ASST Spedali Civili of Brescia, Brescia, Lombardia, Italy, [3]Rheumatology and Clinical Immunology Unit, Clinical and Experimental Sciences Department, ERN ReCONNET, ASST Spedali Civili of Brescia and University of Brescia, Brescia, Italy, Brescia, Lombardia, Italy, [4]University of Brescia, Brescia, Brescia, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic hypereosinophilic syndromes (iHES) are a group of disorders characterized by persistent eosinophilia and eosinophil-mediated organ damage. Mepolizumab, an anti-interleukin-5 monoclonal antibody, has proven effective in reducing eosinophilic burden, controlling clinical manifestations in various forms of iHES, and decreasing the reliance on glucocorticoids (GCs). This study aims to evaluate the clinical and steroid-sparing efficacy of mepolizumab in a monocentric retrospective cohort of patients with iHES.

Methods: We analyzed a cohort of patients diagnosed at our Center according to the 2023 refined diagnostic criteria and classification for HES (1). Only patients diagnosed with iHES and treated with mepolizumab were included. Descriptive statistics included medians (1st-3rd IQR). Differences were assessed using the Wilcoxon test (significance: $p \leq 0.05$). Variables were analyzed immediately prior to mepolizumab initiation (t0) and at 1 (t1), 3 (t3), 6 (t6), 12 (t12), 18 (t18), and 24 (t24) months post-treatment.

Table 1. Clinical manifestations from iHES onset to diagnosis. Abbreviations: ENT = Ear, Nose, and Throat; SVT = superficial venous thrombosis; PTE = pulmonary thromboembolism; BAL = bronchoalveolar lavage; DVT = deep venous thrombosis.

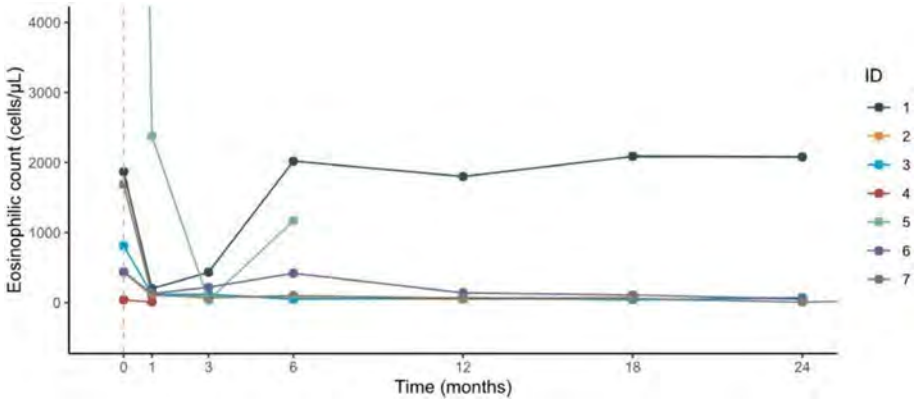
Symptoms	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
General	Fever		Fever		Fever		Loss of weight > 5%
ENT		Rhinorrhea Nasal crusts		Rhinorrhea			
Skin	Papules	Lichenified eczema	Urticaria				
Pulmonary	Pulmonary infiltrates Pleuritis	Nodular infiltrates Pleuritis	Asthma Pulmonary infiltrates		Pulmonary infiltrates Pleuritis		Pulmonary infiltrates Pulmonary fibrosis
Cardiac					Pericarditis Myocarditis		
Neurological					Polyneuropathy		
Digestive			Gastritis Enteritis	Gastritis Enteritis Ascites		Gastritis Enteritis Ascites	Esophagitis Gastritis Colitis Ascites
Thrombotic	Small saphenous vein SVT PTE				Intracardiac thrombosis	Right gemellar vein DVT	Ischemic colitis
Biopsy site	Lung	Skin	Stomach Duodenum Bone marrow	Stomach Duodenum	N/A	Stomach Duodenum Bone marrow	Esophagus Stomach Colon Bone marrow
Eosinophilic inflammation in other sites	BAL Pleural fluid			Ascitic fluid	Pleural fluid Pericardial fluid	Ascitic fluid	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Eosinophil count and glucocorticoid daily dosage at t0 (immediately prior to mepolizumab initiation) and at different time points (each representing the number of months) after mepolizumab initiation.

Time points	t0	t1	t3	t6	t12	t18	t24
	Eosinophil count (cells/μl)						
Patient 1	1871	200	435	2020	1800	2090	2080
Patient 2	436	100	100	70	48	80	
Patient 3	810	120	120	50	70	40	70
Patient 4	40	10					
Patient 5	25010	2380	32	1170			
Patient 6	440	130	220	420	140	110	50
Patient 7	1690	112	69	101	60	60	10
Median (1st-3rd IQR)	810 (438-1250)	120 (106-125)	110 (77-117)	260 (76-380)	70 (60-70)	80 (60-80)	60 (40-62)
	Glucocorticoid daily dosage (mg/day)						
Patient 1	0	0	0	0	0	25	5
Patient 2	5	5	5	0	0	0	
Patient 3	55	5	2.5	0	0	0	0
Patient 4	38.5	5					
Patient 5	50	50	25	0			
Patient 6	37.5	37.5	0	10	2.5	2.5	2.5
Patient 7	12.5	10	7.5	7.5	2.5	0	0
Median (1st-3rd IQR)	27 (2-51)	5 (5-9)	2.5 (0-10)	0 (0-0)	0 (0-0)	0 (0-6)	0 (0-2.5)

Results: Seven patients were enrolled [3 males, 4 females; median age at HES onset: 49 (35-59) years; median age at diagnosis: 49 (37-59) years; median diagnostic delay: 4 (1-26) months]. Clinical features at onset are reported in Table 1. At HES onset, median eosinophil count (EC) was 6910 (5685-16525) cells/μl and all patients showed hypereosinophilia. The median time from diagnosis to mepolizumab initiation was 5 (1-18) months, with a median follow-up of 24 (12-24) months. Six patients had received GCs prior to mepolizumab and were still on steroid therapy at the time of initiation. Furthermore, patient 2 had been treated with cyclosporine A for lichenified trunk eczema. At t0, 1 patient showed eosinophilia and 3 hypereosinophilia. A marked decrease in EC was observed as early as t1 [median t0: 810 (438-1250) cells/μl; median t1: 120 (106-125) cells/μl; p: 0.0156], which was maintained at the last available follow-up [median at last follow-up: 70 (30-625) cells/μl; p: 0.0469]. At t6, 2 patients showed a significant rebound in ECs. In patient 1, hypereosinophilia persisted from t6 onward, and both GCs and dupilumab were introduced at t18. Patient 6 was hospitalized at t6 and later died from septic shock (notably, with a history of substance abuse) (Table 2; Graphic 1). Overall, the median percentage reduction in EC was 89 (78-92) % (p: 0.0469). During follow-up, GCs were discontinued in 5 patients and later reintroduced in 3 cases due to HES relapses. The comparison of GC daily dose at t0 and at the last available follow-up showed a significant reduction [median at t0: 27 (2-51) mg/day; median at last follow-up: 0 (0-4) mg/day; p: 0.0469] (Table 2). The number of HES



Graphic 1. Eosinophil count trend over time, from t0 (immediately prior to mepolizumab initiation) to t24. For Patient 5, an outlier value of 25010 cells/μl was excluded to improve graphical readability; however, the overall trend line was maintained to reflect the general trajectory.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

relapses before (n: 9) and after (n: 4) initiation of mepolizumab showed a trend toward statistical significance, although not reaching it (p: 0.0780).

Conclusion: Preliminary findings from our cohort suggest that mepolizumab may be effective in achieving clinical control and reducing GC dependence in patients with iHES.

References:

(1) Valent P, et al. Proposed refined diagnostic criteria and classification of eosinophil disorders and related syndromes. Allergy. 2023 Jan;78(1):47-59

Disclosure: J. Mora: None; **F. Regola**: GlaxoSmithKlein(GSK), 6; **P. Toniati**: GlaxoSmithKlein(GSK), 6; **G. Fontana**: None; **A. Gatti**: None; **I. Cavazzana**: None; **F. Franceschini**: None.

Abstract Number: 0252

Capillaroscopic Signatures in Autoimmune Rheumatic Diseases: Unveiling Patterns in Systemic Sclerosis, Polyautoimmunity, and PAH

María Paula Carrillo[1], Juan Esteban Bedoya-Loaiza[1], Claudia Ibáñez-Antequera[1], Laura Gallego[1], Alejandro Escobar[1], Adriana Rojas-Villarraga[2] and **Jairo Cajamarca-Baron**[3], [1]Fundacion universitaria de ciencias de la salud, Bogota, Distrito Capital de Bogota, Colombia, [2]Fundacion Universitaria de Ciencias de la salud, Bogota, Distrito Capital de Bogota, Colombia, [3]Fundacion universitaria de ciencia de la Salud, Bogota, Distrito Capital de Bogota, Colombia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Nailfold capillaroscopy is a fundamental tool in rheumatology for assessing capillary morphology, allowing the differentiation between primary and secondary Raynaud's phenomenon, identifying risks associated with systemic sclerosis, and exploring vascular alterations in various autoimmune diseases. This study aimed to describe capillaroscopic patterns in a cohort of patients with autoimmune disorders.

Methods: A cross-sectional, observational, and descriptive study was conducted in 136 patients with autoimmune rheumatic diseases. Sociodemographic, clinical, and capillaroscopic data were collected using the RedCap platform; images were obtained with the Smart G-Scope device and processed using Capillary.io software. Statistical analysis was performed using STATA 18.

TABLE . Summary of the frequencies of the most relevant capillaroscopic findings in autoimmune diseases

Disease	Reduced density	Avascular areas	Giant capillaries	Microhemorrhages	Tortuosities	Flame-shaped or helmet hemorrhage	Perivascular edema
Systemic sclerosis	+++	+	+++	+++	++	++	+
Inflammatory myopathy	+++	+	+++	+++	+++	+++	+
Sjögren's syndrome	++	-/+	+++	+++	+	+	+
Systemic lupus erythematosus	++	-	++	+++	+	+	+
Rheumatoid arthritis	+	-	+	++	++	-/+	+
Vasculitis	-	-	+	++	+	-	-

Frequency -: 0%; -/+: 0–10%; +: 10–30%; ++: 30–50%; +++: >50%

Summary of the frequencies of the most relevant capillaroscopic findings in autoimmune diseases

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The cohort included 136 patients, mostly women (86.76%), with a median age of 59 years. Systemic sclerosis was the most prevalent disease (50.74%), followed by Sjögren's syndrome and systemic lupus erythematosus; 24.2% presented with polyautoimmunity. Pulmonary arterial hypertension (PAH), confirmed or suspected, was found in 25 patients (18.3%). Capillary dilations (91.91%), giant capillaries (51.47%), and decreased capillary density (41.98%) were documented, particularly in systemic sclerosis. Microhemorrhages were observed in 58.82% of patients, most frequently in those with systemic sclerosis (49 out of 69 patients, 71.01%), followed by inflammatory myopathy (3 out of 5 patients, 60%) and Sjögren's syndrome (16 out of 29 patients, 55.17%). Tortuosity was the most frequent morphological abnormality (26.47%) (See Table). In inflammatory myopathy, all patients exhibited at least one type of abnormal capillary morphology, with arborized capillaries being the most common. Systemic sclerosis, in turn, showed the greatest diversity and number of abnormal capillary forms. The most frequently observed pattern was nonspecific, followed by the active pattern in systemic sclerosis and inflammatory myopathies. The nonspecific pattern (n=50, 36.76%) was the most common overall, prevalent in all diseases except systemic sclerosis and inflammatory myopathy, where the active pattern predominated (n=27, 39.13% and n=3, 60%, respectively), reflecting greater microvascular aggressiveness in these conditions. Patients with positive ANAs had reduced capillary density (Fisher's exact = 0.018), as did those with polyautoimmunity (p = 0.043), who also showed a higher number of microhemorrhages per millimeter (p = 0.020). Patients with PAH exhibited a higher number of capillary dilations per millimeter (p = 0.022) and reduced capillary density (≤6 capillaries/mm; p = 0.0444).

Conclusion: These findings support the use of videocapillaroscopy as a diagnostic and prognostic tool not only in systemic sclerosis but also in broader autoimmune contexts like polyautoimmunity and PAH.

Disclosure: M. Carrillo: None; **J. Bedoya-Loaiza**: None; **C. Ibáñez-Antequera**: None; **L. Gallego**: None; **A. Escobar**: None; **A. Rojas-Villarraga**: None; **J. Cajamarca-Baron**: None.

Abstract Number: 0253

Ophthalmology Screening for Asymptomatic Uveitis in Sarcoidosis Patients: A Single-Center Investigation

Justin Nguyen[1], Philip Bucur[2], Sai Patel[2], Aamer Syed[2], Thomas Iden[3], Jessica McLaughlin[2], Neha Gupta[2], Jordana Kron[2], Kelly Gwathmey[2], Ryan Canissario[2], Vaishali Patel[2] and Huzaefah Syed[2], [1]Virginia Commonwealth University Medial Center, Richmond, VA, [2]Virginia Commonwealth University Medical Center, Richmond, VA, [3]Virginia Commonwealth University Medical Center, Richmond

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Asymptomatic ocular involvement must be considered in any patient with sarcoidosis. If left untreated, severe complications, including vision loss, can occur. As a result, sarcoidosis patients without ocular symptoms are frequently referred to ophthalmology for uveitis screening. However, the frequency of these patients being diagnosed with asymptomatic uveitis remains uncertain. Additional referrals may burden the healthcare system, leading to longer wait times. In this retrospective, descriptive analysis, our primary objective was to determine how many patients with non-ocular sarcoidosis developed asymptomatic uveitis after their new-patient sarcoidosis visit. Secondary objectives included determining the number of referrals made to ophthalmology, the number of patients following ophthalmology or optometry, and the number of patients who developed any ocular manifestations of sarcoidosis over time.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

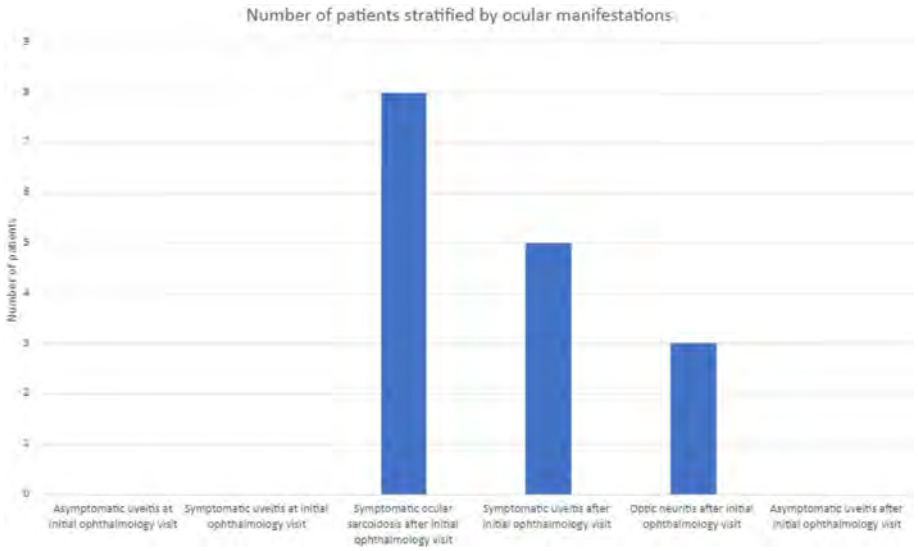


Table 1: Patient Demographics and Ophthalmologic Outcomes

Category	Variable	Patients with Sarcoidosis (N = 856)	Percentage (%) of Total
Age	Years, mean ± SD	53.3 ±12.6	
Sex	Male, n (%)	360	57.9
	Female, n (%)	496	42.1
Race	White	407	47.5%
	Black	420	49.1%
	Hispanic	2	0.2%
	Asian	2	0.2%
	Other	25	2.9%
Ophthalmology Stats	Total Internal Ophthalmology Referrals	158	18.5 %
	Total Patients Established with Ophthalmology	419	48.9 %
	Patients Established with Internal Ophthalmology	43	5.0 %
	Patients Established with External Ophthalmology	376	43.9 %

Methods: Using our institution's Data Repository of Pulmonary Sarcoidosis (DROP Sarcoidosis) database, we filtered 2,387 sarcoidosis patients for those with ocular involvement, resulting in 998 patients. This list was further filtered to exclude patients with new patient visit notes mentioning ocular disease not reflected in the database, patients with optic neuritis, and those who eventually received a diagnosis other than sarcoidosis. We then reviewed new and follow-up patient visits occurring from Oct 10, 2019, until November 8, 2024. We searched key phrases in the electronic medical record to determine if patients had a history of ocular involvement and manually reviewed our institution's internal ophthalmology records.

Results: Our study consisted of 856 patients, with an average age of 53.3 ± 12.6 years. Among our patients, 57.9% were female and 42.1% male, with demographics of 49.1% black, 47.5% white, 0.2% Hispanic, 0.2% Asian, and 2.9% other races. Over an average of 34 months, no patients had asymptomatic uveitis on referral to ophthalmology. However, 8 of the 856 (0.9%) patients developed symptomatic manifestations of ocular sarcoidosis. This included 5 patients developing symptomatic uveitis and 3 patients developing optic neuritis. Additionally, 158 (18.5%) patients were referred internally to ophthalmology. Meanwhile, 419 (48.9%) patients were already following either internal ophthalmology or eye care (ophthalmology or optometry) externally.

Conclusion: Our analysis challenges the necessity of ophthalmology referral for primary screening of uveitis in newly diagnosed sarcoidosis patients. However, some patients subsequently developed ocular manifestations, which may support an indication for new patient referrals when symptoms occur. Patients who are established with ophthalmology may benefit from timely evaluation when ocular symptoms do arise.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Nguyen: None; **P. Bucur**: None; **S. Patel**: None; **A. Syed**: None; **T. Iden**: None; **J. McLaughlin**: None; **N. Gupta**: None; **J. Kron**: None; **K. Gwathmey**: None; **R. Canissario**: None; **V. Patel**: None; **H. Syed**: None.

Abstract Number: 0254

Comparative Outcomes in MAGIC Syndrome versus Relapsing Polychondritis Alone: A Propensity-Matched Analysis

Justin Riley Lam[1], Emmanuel Otabor[2], Laith Alomari[2], Michael Hamilton[2], Maxim Barnett[2], Shahrzad Abdollahi[3] and Irene Tan[4], [1]Albert Einstein Medical Center, Philadelphia, PA, [2]Jefferson Einstein Hospital Philadelphia, Philadelphia, PA, [3]Jefferson Einstein Hospital, Philadelphia, PA, [4]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: MAGIC syndrome, a rare overlap of relapsing polychondritis (RP) and Behçet's disease manifestations, remains poorly characterized compared to isolated RP. Behçet's-associated features such as recurrent mucosal ulcerations and ocular inflammation may amplify systemic inflammatory burden. Given its hybrid nature involving vascular, mucosal, and cartilaginous inflammation, MAGIC may carry heightened risk for both airway and systemic complications. We aimed to compare clinical outcomes between patients with MAGIC syndrome and those with RP alone.

Methods: Using the TriNetX Global Collaborative Network, we conducted a retrospective cohort study identifying adults (≥18 years) diagnosed with RP. Cohort 1 (n=374) included patients with RP and concomitant features of Behçet's disease, identified using ICD-10 codes for iridocyclitis or uveitis, recurrent oral ulcers, and genital ulcers (MAGIC syndrome). Cohort 2 (n=3,313) included patients with RP without these features. After 1:1 propensity score matching for demographics and comorbidities, 361 patients per cohort were analyzed. Outcomes over three years included thrombosis, vision loss, stroke, tracheal stenosis, gastrointestinal (GI) bleeding, inflammatory markers (CRP, ESR), and immunosuppressive or biologic therapy utilization. Risk analyses and Kaplan-Meier survival curves were performed.

Results: Following matching, baseline characteristics were well-balanced. Rates of thrombosis (3.3% vs 3.3%; p=0.994), vision loss (2.9% vs 2.9%; p=0.953), stroke (3.4% vs 4.3%; p=0.571), and GI bleeding (3.9% vs 3.1%; p=0.539) were similar between MAGIC and RP groups. Tracheal stenosis occurred more frequently in MAGIC (3.9% vs 3.0%) and was associated with a significantly increased hazard ratio (HR 4.18, 95% CI 1.19–14.66; p=0.015). Median CRP levels trended higher in MAGIC (31.3 vs 19.1 mg/L; p=0.055), while ESR was similar (24.6 vs 22.5 mm/hr; p=0.501). Use of non-biologic immunosuppressants (e.g., mycophenolate mofetil, azathioprine) was more common in RP, whereas biologic therapy (e.g., infliximab, tocilizumab) use was higher in MAGIC, though neither difference reached statistical significance.

Conclusion: Patients with MAGIC syndrome demonstrated similar risks of thrombosis, stroke, vision loss, and GI bleeding compared to matched RP patients. However, the significantly increased incidence of tracheal stenosis in MAGIC highlights a possible pathophysiologic overlap involving vasculitis, mucosal inflammation, and cartilaginous involvement—potentially accounting for increased airway compromise. These findings support vigilant airway surveillance and raise the possibility that MAGIC represents a more aggressive RP phenotype with unique clinical considerations.

Disclosure: J. Lam: None; **E. Otabor**: None; **L. Alomari**: None; **M. Hamilton**: None; **M. Barnett**: None; **S. Abdollahi**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0255

Clearing the Smoke: Association Between Cannabis Use and Autoimmune Disease Incidence in a Retrospective Cohort Analysis

Justin Riley Lam[1], Emmanuel Otabor[2], Laith Alomari[2], Esteban Kosak Lopez[2], Maxim Barnett[2] and Shahrzad Abdollahi[3], [1]Albert Einstein Medical Center, Philadelphia, PA, [2]Jefferson Einstein Hospital Philadelphia, Philadelphia, PA, [3]Jefferson Einstein Hospital, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cannabis use has increased substantially in the past decades, with legalization expanding across the U.S. Despite its known therapeutic potential, the immunomodulatory effects of cannabis remain unclear. Prior studies suggest cannabis may influence immune responses, potentially affecting autoimmune disease risk. However, epidemiological evidence on its long-term impact on autoimmune disease incidence is limited. We evaluate the association between cannabis, use and the incidence of autoimmune diseases, inflammatory markers, and major adverse health outcomes, including all-cause mortality and cardiovascular events, using a large-scale retrospective cohort analysis.

Methods: A retrospective cohort study was conducted using TriNetX Global Collaborative Network data. Two cohorts were defined: cannabis users (ICD-10: F12) and non-users, matched 1:1 via propensity scoring based on demographics, comorbidities, and social determinants. The primary outcomes included the incidence of autoimmune diseases (e.g., rheumatoid arthritis), inflammatory markers (CRP, ESR), major adverse cardiovascular events (MACE), and all-cause mortality. Statistical analyses included risk ratios, Kaplan-Meier survival analysis, and t-tests for laboratory outcomes.

Results: Among 229,366 matched patients, cannabis use was associated with a lower incidence of certain autoimmune conditions, including Hashimoto's thyroiditis (RR: 0.512, $p < 0.001$), rheumatoid arthritis (RR: 0.817, $p = 0.020$), type 1 diabetes (RR: 0.810, $p = 0.002$), and vitiligo (RR: 0.735, $p = 0.046$). (Figure 1.) However, inflammatory markers (CRP, ESR) were significantly elevated in cannabis users ($p < 0.001$), and cannabis use was linked to an increased risk of MACE (RR: 1.195, $p < 0.001$) and all-cause mortality (RR: 1.670, $p < 0.001$). (Figure 2.)

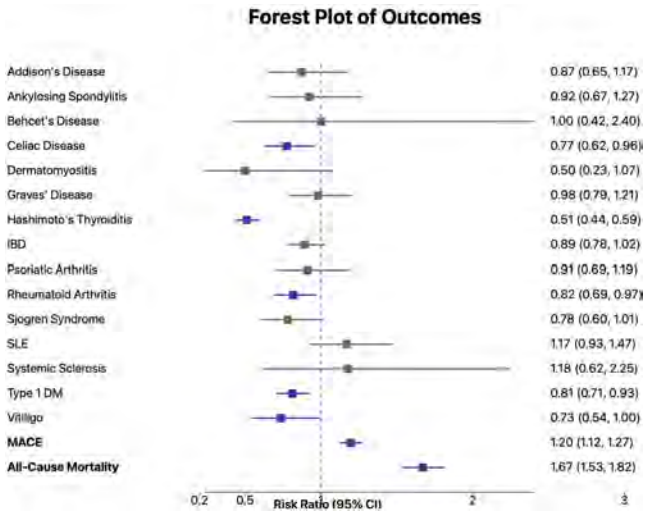


Figure 1. Forest Plot of Outcomes

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

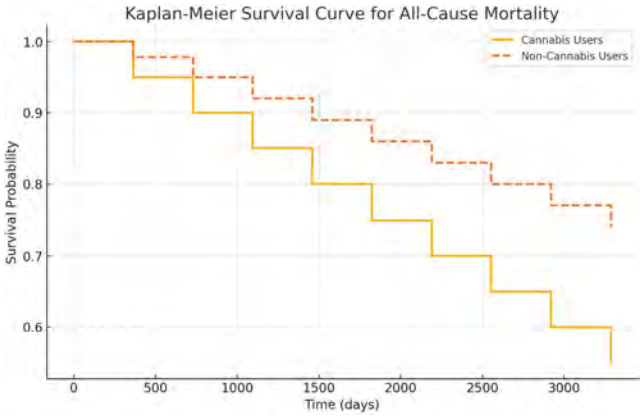


Figure 2. Kaplan-Meier Curve for All Cause Mortality

Conclusion: Cannabis use was associated with significantly increased inflammatory markers, higher risk of major adverse cardiovascular events (MACE), and elevated all-cause mortality. While there appeared to be a decreased incidence of certain autoimmune diseases among cannabis users, this finding should be interpreted with caution. The lower observed rates may reflect underdiagnosis or underreporting, potentially influenced by changing patterns of healthcare engagement amid rising cannabis legalization and widespread use. As cannabis use becomes increasingly normalized, it is essential to critically evaluate both its potential harms and the risk of diagnostic oversight. Prospective research is needed to clarify causality and guide evidence-based clinical and public health recommendations.

Disclosure: J. Lam: None; **E. Otabor**: None; **L. Alomari**: None; **E. Kosak Lopez**: None; **M. Barnett**: None; **S. Abdollahi**: None.

Abstract Number: 0256

The Role of Extracorporeal Membrane Oxygenation in Cardiopulmonary Dysfunction Due to Rheumatologic Diseases: A Systematic Review

Kari Falaas[1], Lyubov Tiegs[2] and Elie Gertner[3], [1]University of Minnesota, Minneapolis, [2]University of Minnesota, Mineapolis, [3]Regions Hospital, St. Paul, MN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatologists are increasingly involved in the management of patients with severe manifestations of rheumatologic disease treated with Extracorporeal Membrane Oxygenation (ECMO). A 2020 systematic review, reviewing the use of ECMO in rheumatology from 1999 to 2018, found a survival rate of 93% (in 27 of 29 patients). The use of ECMO has steadily increased since then. This systematic review documents the current status of ECMO use in patients with complications of rheumatologic diseases.

Methods: A systematic review was conducted following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, covering studies from January 2019 to January 2025 (Figure 1). The initial search identified 2,695 studies from 4 different databases. Inclusion criteria included patients requiring ECMO for rheumatologic disease complications with documented outcomes. Studies were excluded if they lacked outcome data, were not published in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

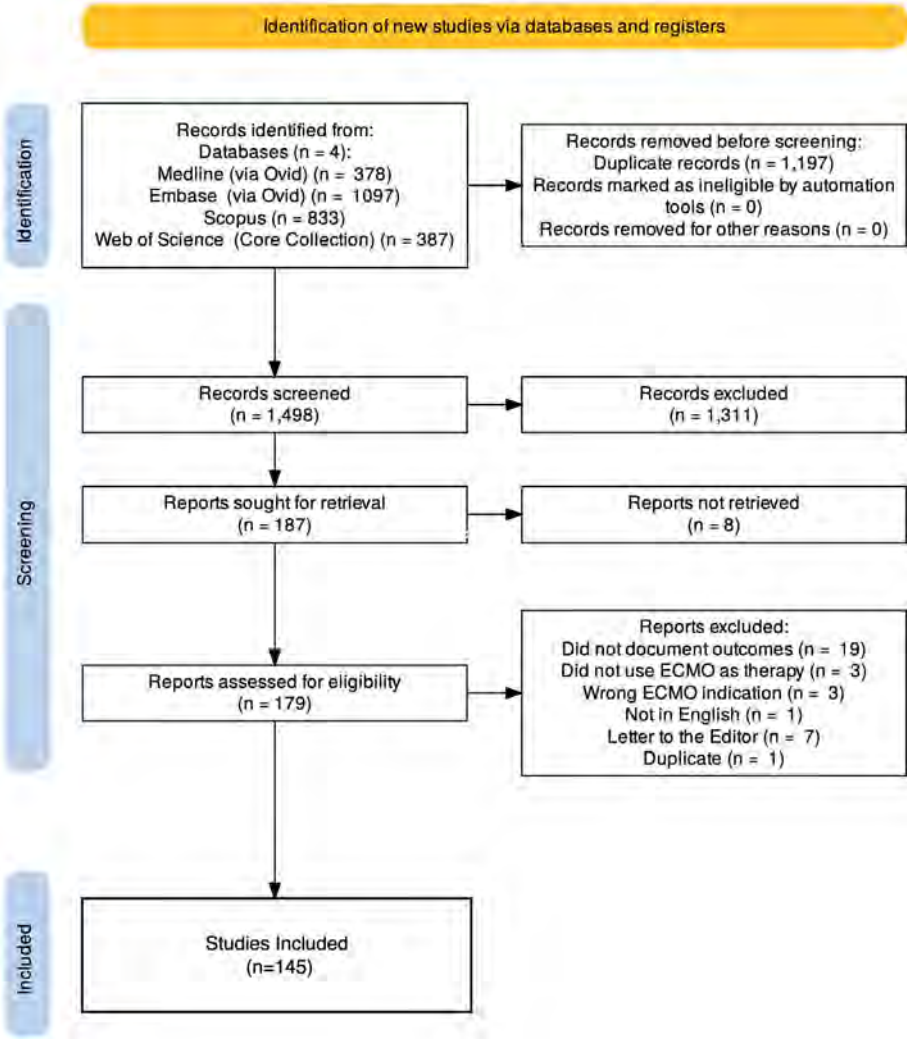


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart outlining the process of screening and selection.

English, letters to the editor, secondary sources, or ECMO for non-rheumatologic indications. Data extracted included patient characteristics, ECMO indications and details, therapy type, outcomes, and complications.

Results: A total of 145 studies were included in the final analysis, encompassing 734 patients who received ECMO. The average age of patients was 32.2 years (range: 7 weeks to 70 years), with 340 (46%) females. The most common indications for ECMO were diffuse alveolar hemorrhage, severe interstitial lung disease, myocarditis, cardiac arrest, and massive pulmonary embolism. The most frequent rheumatologic diagnoses were anti-neutrophil cytoplasmic antibody (ANCA) vasculitis, inflammatory myositis, systemic lupus erythematosus (SLE), anti-glomerular basement membrane disease, and antiphospholipid syndrome. There were 482 patients treated with venovenous (VV) ECMO, 236 with venoarterial (VA) ECMO, and 10 were transitioned between VA and VV. ECMO duration ranged from 1 day to 123 days. Common therapies included glucocorticoids, cyclophosphamide, and plasmapheresis. Infection was the most frequent complication during hospitalization. In terms of outcomes, 362 patients were successfully bridged to recovery, 54 patients underwent successful transplants and survived, 304 patients died, and 3 patients remained on ECMO at the time of publication.

Conclusion: ECMO remains a potential and viable option for the severe manifestations of rheumatologic disease, serving as a bridge to either recovery or transplant. In this review, 416 patients survived due to ECMO who likely would have otherwise

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Summary of ECMO results (Part 1)

Table 1. Summary of ECMO Results

Disease	# of Case Reports	# of Other Studies	# of Patients	Age (years)	Female/ Male	Patients on VV/VA	Most Common ECMO Indication	Treatments (most common)	Alive/Alive with Transplant	Died	Complications
Systemic Rheumatic Disease (pediatrics)	0	1	207	9.3	57/49	83/111	DAH	Steroids	104	103	Infection, Hematologic
ANCA Vasculitis, Undifferentiated	17	4	179	43.6	86/74	161/18	DAH	Steroids, CYC, RTX, PLEX	127/4	48	Renal Failure, Hematologic
Myositis, Undifferentiated	0	3	143	44.4	80/63	123/20	RP-ILD	Steroids, CYC, RTX, IVIG	35/19	89	Hematologic, Renal Failure
Systemic Rheumatic Disease (adults)	0	1	69	41	43/26	31/38	Myocarditis	Steroids	24/7	27	Infection
Dermatomyositis	28	1	35	48.9	17/18	32/3	RP-ILD	Steroids, CYC, PLEX, RTX, IVIG	4/9	20	2 Remain on ECMO, Infection
GPA	16	0	16	32.3	9/7	16/0	DAH	Steroids, CYC, RTX, PLEX	14/2	0	Infection, Bleeding
SLE	12	1	13	32.8	12/1	5/8	Myocarditis	Steroids, CYC, RTX, IVIG	7/2	3	1 remains on ECMO, Infection
APS	11	0	11	32.9	7/4	2/9	Cardiogenic shock from PE	Steroids, RTX, IVIG, anticoagulation	6	5	Hematologic
Anti-GBM	8	0	8	23	3/5	8/0	DAH	Steroids, RTX, CYC, PLEX	7/0	1	Renal failure, thrombosis
Kawasaki	7	0	7	8.7	3/4	1/6	Cardiac arrest	Steroids, IVIG, anticoagulation, aspirin	6/1	0	Neurologic symptoms
MPA	6	0	6	55.2	4/2	5/1	DAH	Steroids, CYC, RTX, PLEX	5/0	1	Infection, Renal Failure
AOSD	5	0	5	29.6	3/2	1/4	Myocarditis	Steroids, Anakinra, Canikinumab	5	0	CMV, coagulopathy
ASSD	5	0	5	49.6	3/2	5/0	RP-ILD	Steroids, CYC, RTX	2/2	1	Ileus
Takayasu Arteritis	5	0	5	18	4/1	0/5	Cardiogenic shock	Steroids, MMF, TAC, Tocilizumab	0/2	3	Renal failure, CABG

Table 1. Summary of ECMO results (Part 2 including glossary)

Disease	# of Case Reports	# of Other Studies	# of Patients	Age (years)	Female/ Male	Patients on VV/VA	Most Common ECMO Indication	Treatments (most common)	Alive/Alive with Transplant	Died	Complications
EGPA	4	0	4	30.8	2/2	1/3	Myocarditis	Steroids, CYC	4/0	0	Infection
Juvenile Dermatomyositis	3	0	3	6	2/1	2/1	RP-ILD	Steroids, CYC, RTX, IVIG	2/0	1	CMV viremia, pneumomediastinum
RA	3	0	3	41.3	3/0	3/0	ILD	Steroids, RTX,CYC	1/1	1	Infection, Acute cellular rejection
Sarcoidosis	3	0	3	52.3	0/3	0/3	Cardiogenic shock	Steroids, MMF, TAC	1/2	0	None
MCTD	2	0	2	40	2/0	1/1	RP-ILD, Cardiac arrest	Steroids, CYC, MMF	2/0	0	Infection
Polymyositis	2	0	2	52.5	0/2	1/1	Respiratory Failure /Myocarditis	Steroids, CYC, TAC, IVIG, AZA	1/1	0	None
Scleroderma	2	0	2	50	1/1	1/1	RP-ILD, Cardiac arrest	Steroids, CYC, TAC, IVIG, MMF	0/2	0	Infection
Behçet's disease	1	0	1	54	1/0	0/1	Massive PE	anticoagulation	1/0	0	None
HSS	1	0	1	26	0/1	1/0	DAH	Steroids, AZA, IFX, Plasmapheresis	1/0	0	None
IgG4 Related Disease	1	0	1	34	0/1	0/1	Myocarditis	steroids	1/0	0	Multiple
Necrotizing Myositis	1	0	1	41	0/1	0/1	Myocarditis	Steroids, CYC	1/0	0	None
RPC	1	0	1	51	1/0	1/0	Tracheal Stenosis	Steroids	1/0	0	None
sJIA	1	0	1	2	0/1	0/1	Myocarditis	Steroids, IVIG, Anakinra	1/0	0	Anemia, Thrombocytopenia

Glossary: ANCA: anti-neutrophil cytoplasmic antibody; Anti-GBM: anti-glomerular basement membrane disease; APS: antiphospholipid syndrome; AOSD: adult-onset Still's disease; ASSD: anti- synthetase syndrome; AZA: azathioprine; CABG: coronary artery bypass grafting; CMV: cytomegalovirus; CYC: cyclophosphamide; DAH: diffuse alveolar hemorrhage; ECMO: extracorporeal membrane oxygenation; EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; HSS: Hughes-Stovin syndrome; IFX: infliximab; ILD: interstitial lung disease; IVIG: intravenous immunoglobulin; MCTD: mixed connective tissue disease; MMF: mycophenolate mofetil; MPA: microscopic polyangiitis; PE: pulmonary embolism; PLEX: plasma exchange (plasmapheresis); RA: rheumatoid arthritis; RP-ILD: rapidly progressive interstitial lung disease; RPC: relapsing polychondritis; RTX: rituximab; sJIA: systemic juvenile idiopathic arthritis; SLE: systemic lupus erythematosus; TAC: tacrolimus; VA: veno-arterial; VV: veno-venous.

died. Overall, ECMO provides significant survival benefits, allows for organ recovery, and serves as a bridge to additional therapies, especially when used early and in carefully selected patients.

Disclosure: K. Falaas: None; **L. Tiegs**: None; **E. Gertner**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0257

Safety of Guselkumab in Inflammatory Bowel Disease Up to 1 Year: Integrated Safety Analysis of Phase 2 and 3 Studies in Crohn's Disease and Ulcerative Colitis

Bruce E. Sands[1], Remo Panaccione[2], Silvio Danese[3], Julián Panés[4], Tadakazu Hisamatsu[5], Geert D'Haens[6], Rian Van Rampelbergh[7], Mobolaji Olurinde[8], Jacqueline Yee[8], **Karissa Lozenski**[9], Thomas Baker[8], Shadi Yarandi[8], Matthew Germinaro[8], Marion L. Vetter[8], Hewei Li[8], Mauricio Rosas Ballina[10], Jessica R. Allegretti[11], Anita Afzali[12] and David T. Rubin[13], [1]Icahn School of Medicine at Mount Sinai, New York, NY, USA, NY, [2]University of Calgary, Calgary, AB, Canada, AB, Canada, [3]Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milan, Italy, Milano, Italy, [4]Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain, Barcelona, Spain, [5]Kyorin University School of Medicine, Tokyo, Japan, Tokyo, Japan, [6]Amsterdam University Medical Centers, Amsterdam, The Netherlands, D'Haens, Swaziland, [7]Johnson & Johnson, Antwerp, Belgium, Antwerp, Belgium, [8]Johnson & Johnson, Spring House, PA, USA, PA, [9]Johnson & Johnson, Horsham, PA, [10]Actelion Research & Development, Allschwil, Switzerland, Allschwil, Switzerland, [11]Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, MA, [12]University of Cincinnati, College of Medicine, Cincinnati, OH, USA, OH, [13]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, IL, USA, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Guselkumab (GUS), a dual-acting interleukin (IL)-23 inhibitor that potently neutralizes IL-23 and binds to CD64 (a receptor on cells that produce IL-23), is currently approved in the United States for treatment of ulcerative colitis (UC) and worldwide for the treatment of plaque psoriasis and psoriatic arthritis. While GUS has been shown to be safe in Crohn's disease (CD) and UC, safety results have only been reported in individual trials to date. To characterize the overall

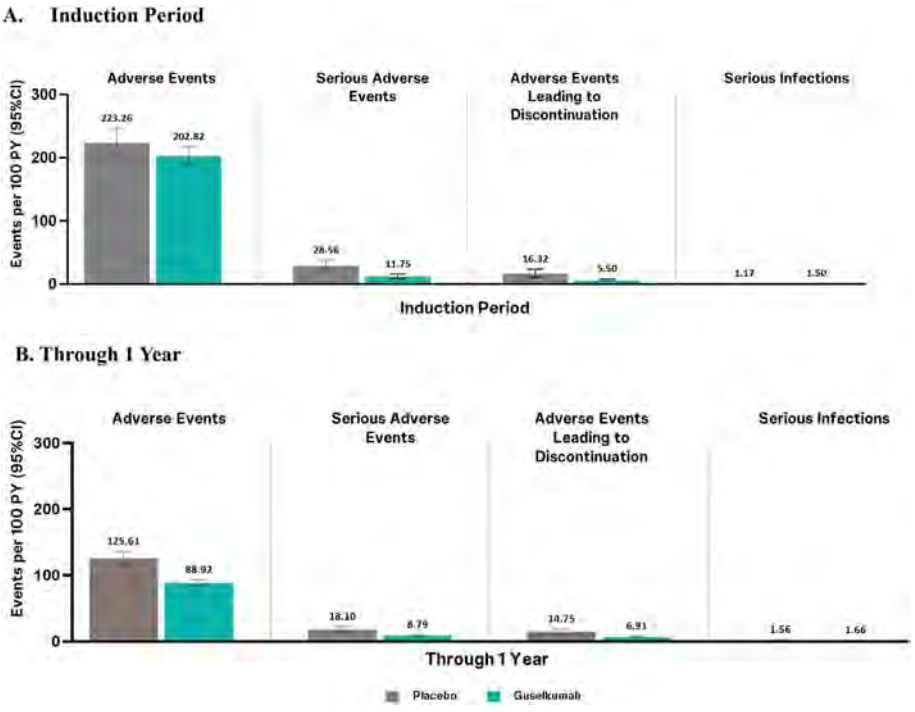


Figure 1. Key safety events in phase 2/3 IBD clinical studies during the induction period (Week 0-12) (A) and through 1 year (B)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

safety profile of GUS in inflammatory bowel disease (IBD), we evaluated pooled safety data from Phase 2 and 3 clinical trials of GUS in CD and UC.

Methods: Participants with moderately to severely active CD (n=1492; GALAXI 1, 2, & 3, and GRAVITI studies) or UC (n=1514; QUASAR Induction Study 1, Induction Study 2, & Maintenance Study and VEGA-GUS monotherapy arm only) were assigned to GUS 200 mg intravenous (IV) or 400 mg subcutaneous (SC) induction (GRAVITI only) at Weeks 0, 4, and 8, followed by GUS 100 mg SC every 8 weeks or 200 mg SC every 4 weeks; or placebo (PBO). SC maintenance treatment continued through approximately 1 year. GUS studies were pooled for the induction period (GALAXI, GRAVITI, & QUASAR;

Table 1: Targeted adverse events during the induction period and through 1 year; exposure-adjusted rates of events per 100 participant-years (PY) of follow-up and 95% confidence intervals (CI)

	Pooled IBD			
	Induction Period (Weeks 0-12)[a]		Through 1 Year	
	PBO (n=743)	GUS (n=1703)	PBO[b] (n=886)	GUS[c] (n=2057)
Total PYs of follow-up	171.6	399.9	447.4	1752.1
Events/100 PY (95% CI)[d]				
Deaths	1.17 (0.14, 4.21)	0.50 (0.06, 1.81)	0.45 (0.05, 1.61)	0.11 (0.01, 0.41)
Active TB	0.00 (0.00, 1.75)	0.00 (0.00, 0.75)	0.00 (0.00, 0.67)	0.06 (0.00, 0.32)
Malignancies	0.00 (0.00, 1.75)	1.25 (0.41, 2.92)	0.89 (0.24, 2.29)	0.74 (0.40, 1.27)
Anaphylactic or serum sickness-like reactions	0.00 (0.00, 1.75)	0.00 (0.00, 0.75)	0.00 (0.00, 0.67)	0.00 (0.00, 0.17)
Opportunistic infections	1.75 (0.36, 5.11)	0.50 (0.06, 1.81)	0.67 (0.14, 1.96)	0.23 (0.06, 0.58)
Major adverse cardiovascular events	1.17 (0.14, 4.21)	0.50 (0.06, 1.81)	0.45 (0.05, 1.61)	0.29 (0.09, 0.67)
Clinically important hepatic disorders[e]	0.00 (0.00, 1.75)	0.75 (0.15, 2.19)	0.22 (0.01, 1.25)	0.40 (0.16, 0.82)

Abbreviations: AEs=adverse events; CI=confidence interval; GUS=guselkumab; IBD=inflammatory bowel disease; MedDRA=Medical Dictionary for Regulatory Activities; PBO=placebo; PY=participant-years; SAE=serious AE; TB=tuberculosis.

[a]Ulcerative colitis: (0-12 weeks) CNTO1959UCO3001 QUASAR Induction Study 1 and Induction Study 2 (VEGA not included due to no PBO control); Crohn's disease (0-12 weeks): CNTO1959CRD3001 GALAXI 1, GALAXI 2, GALAXI 3 and CNTO1959CRD3004 GRAVITI.

[b]Ulcerative colitis: includes data up to the first dose of guselkumab for participants who were initially treated with placebo; includes data at or after 12 weeks from the last induction dose of guselkumab for participants who were treated with guselkumab in induction and were rerandomized to placebo in the Maintenance Study, up to the dose adjustment for participants who had a dose adjustment. Crohn's disease: includes data up to the time of rescue or crossover.

[c]Ulcerative colitis: CNTO1959UCO3001 QUASAR (through induction Week 20 for participants who did not enter the Maintenance Study and did not receive treatment at induction Week 12; through induction Week 32 for participants who did not enter the Maintenance Study and received treatment at induction Week 12; through maintenance Week 44 for participants who entered the Maintenance Study); CNTO1959UCO2002 VEGA through Week 38 (guselkumab monotherapy arm only); includes all guselkumab data and data up to 12 weeks from the last induction dose of guselkumab for participants who were randomized to placebo in the Maintenance Study. Crohn's disease: CNTO1959CRD3001 GALAXI 1, GALAXI 2 and GALAXI 3, and CNTO1959CRD3004 GRAVITI through Week 48; includes data from the first dose of guselkumab onward for participants who were rescued or crossed over from placebo.

[d]Confidence interval based on an exact method assuming that the observed number of events follows a Poisson distribution.

[e]Clinically important hepatic disorders are defined as hepatic disorder AEs reported as SAEs or AEs leading to discontinuation of study intervention.

Note: Includes all participants who were treated.

Note: Participants are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 26.0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

IV and SC, Weeks 0-12 [VEGA excluded due to no PBO control]) and through 1 year (GALAXI, GRAVITI, QUASAR, & VEGA). In this pooled analysis, safety events were normalized to 100 participant-years (PY) of follow-up with corresponding confidence intervals.

Results: Through Week 12, 1703 participants were treated with GUS with 399.9 PY of follow-up. Rates of adverse events (AEs) were similar between participants treated with GUS (200 mg IV or 400 mg SC) and PBO (**Figure 1A**). AEs occurred at a rate of 202.82/100 PY and 223.26/100 PY, serious AEs at 11.75/100 PY and 28.56/100 PY, AEs leading to study agent discontinuation at 5.50/100 PY and 16.32/100 PY, and serious infections at 1.50/100 PY and 1.17/100 PY, for GUS and PBO, respectively.

Through 1 year, 2057 participants were treated with GUS, with 1752.1 PY of follow-up. Rates of AEs, serious AEs, AEs leading to discontinuation, and serious infections, were no higher in GUS-treated than PBO-treated participants (**Figure 1B**). Through 1 year, no anaphylactic or serum sickness reactions were reported, and rates of malignancy, opportunistic infection, major adverse cardiovascular event, and clinically important hepatic disorders were low (**Table 1**). In GUS-treated participants, one participant (from an endemic region) reported active tuberculosis, and 2 deaths (acute myocardial infarction in a participant with pre-existing cardiovascular risk factors and non-suicidal gunshot wound, respectively) occurred.

Conclusion: Through 1 year of treatment, GUS demonstrated a favorable safety profile comparable to PBO in participants with CD and UC. No new safety concerns were identified.

Disclosure: B. Sands: AbbVie, 2, Abivax, 2, 6, Adiso Therapeutics, 2, Agomab, 2, Alimentiv, 2, Amgen, 2, AnaptysBio, 2, Arena Pharmaceuticals, 2, Artugen Therapeutics, 2, AstraZeneca, 2, Biolojic Design, 2, Biora Therapeutics, 2, Boehringer Ingelheim, 2, Boston Pharmaceuticals, 2, Bristol Myers Squibb, 2, 5, 6, Calibr, 2, Celgene, 2, Celltrion, 2, ClostraBio, 2, Eli Lilly, 2, 6, Enthera, 2, Envied Biosciences, 2, Equillium, 2, Evommune, 2, Ferring, 2, Fiat, 2, Fresenius Kabi, 2, Galapagos, 2, Genentech (Roche), 2, Gilead Sciences, 2, Gossamer Bio, 2, GSK, 2, Imhotex, 2, Index Pharmaceuticals, 2, Innovation Pharmaceuticals, 2, Inotrem, 2, Janssen, 2, 5, 6, Kaleido, 2, Kallyope, 2, Merck, 2, Microba, 2, Mobius Care, 2, Morphic Therapeutics, 2, MRM Health, 2, Nexus Therapeutics, 2, Nimbus, 2, Odyssey, 2, Pfizer, 2, 5, 6, Progenity, 2, Prometheus Biosciences, 2, Prometheus Laboratories, 2, Protagonist Therapeutics, 2, Q32 Bio, 2, Rasayana Therapeutics, 2, Recludix Therapeutics, 2, Reistone Biopharma, 2, Sanofi, 2, Spyre Therapeutics, 2, Sun Pharma, 2, Surrozen, 2, Takeda, 2, 5, 6, Target RWE, 2, Teva, 2, Theravance Biopharma, 2, 5, 6, TLL Pharmaceutical, 2, Tr1X, 2, Union Therapeutics, 2, Ventyx Biopharma, 2, 11; **R. Panaccione**: AbbiVax, 2, Abbott, 2, AbbVie, 2, Alimentiv, 2, Amgen, 2, AnaptysBio, 2, Arena Pharmaceuticals, 2, AstraZeneca, 2, Biogen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Celgene, 2, Cosmos Pharmaceuticals, 2, Eisai, 2, Elan, 2, Eli Lilly, 2, Ferring, 2, Fresenius Kabi, 2, Galapagos, 2, Genentech, 2, Gilead Sciences, 2, GSK, 2, JAMP Bio, 2, Janssen, 2, Merck, 2, Mylan, 2, Novartis, 2, Oppilan Pharma, 2, Organon, 2, Pandion Pharma, 2, Pendopharm, 2, Pfizer, 2, Progenity, 2, Prometheus Biosciences, 2, Protagonist Therapeutics, 2, Roche, 2, Sandoz, 2, Satisfai Health, 2, Shire, 2, Spyre Therapeutics, 2, Sublimity Therapeutics, 2, Takeda, 2, Theravance Biopharma, 2, Trellus, 2, UCB, 2, Union Biopharma, 2, Ventyx Biopharma, 2, Viatris, 2; **S. Danese**: AbbVie, 2, 6, Alimentiv, 2, Allergan, 2, Amgen, 2, 6, AstraZeneca, 2, Athos, 2, Biogen, 2, Boehringer Ingelheim, 2, Celgene, 2, Celltrion, 2, Eli Lilly, 2, Enthera, 2, Ferring, 2, 6, Gilead, 2, 6, Hospira, 2, Inotrem, 2, Janssen, 2, 6, Johnson & Johnson, 2, MSD, 2, Mundipharma, 2, Mylan, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, Sublimity Therapeutics, 2, Takeda, 2, 6, TiGenix, 2, UCB, 2, Vifor, 2; **J. Panés**: AbbVie, 2, Alimentiv, 2, 12, has served on a data safety monitoring board, Athos, 2, Atomwise, 2, Boehringer Ingelheim, 2, Celsius, 2, Ferring, 2, Galapagos, 2, Genentech/Roche, 2, GSK, 2, Janssen, 2, Mirum, 2, 12, has served on a data safety monitoring board, Nimbus, 2, Pfizer, 2, Progenity, 2, Prometheus, 2, Protagonist Therapeutics, 2, Revolo, 2, Sanofi, 2, 12, has served on a data safety monitoring board, Sorriso, 2, 12, has served on a data safety monitoring board, Surrozen, 2, 12, has served on a data safety monitoring board, Takeda, 2, Wasserman, 2; **T. Hisamatsu**: AbbVie GK, 2, 5, 6, Abivax, 2, Boston Scientific Corporation, 5, Bristol Myers Squibb, 2, EA Pharma Co. Ltd, 2, 5, 6, Gilead, 2, Janssen Pharmaceutical K.K., 2, 6, JIMRO

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Co. Ltd., 5, 6, Kissei Pharmaceutical Co. Ltd., 5, 6, Kyorin Pharmaceutical Co. Ltd., 5, 6, Lilly, 2, Mitsubishi Tanabe Pharma Corporation, 2, 5, 6, Mochida Pharmaceutical Co. Ltd., 5, 6, Nippon Kayaku Co. Ltd., 5, Pfizer Inc., 2, 5, 6, Takeda Pharmaceutical Co. Ltd., 5, 6, Zeria Pharmaceutical Co. Ltd., 5; **G. D'Haens**: AbbVie, 2, 6, 12, data monitoring board activities, Agomab, 2, AMT, 2, AstraZeneca, 2, 12, data monitoring board activities, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 6, 12, data monitoring board activities, Celltrion, 2, Eli Lilly, 2, Exeliom, 2, Galapagos, 2, 6, 12, data monitoring board activities, Gossamerbio, 2, GSK, 2, Immunic, 2, Index, 2, Johnson & Johnson, 2, Kaleido, 2, Origo, 2, Pfizer, 2, 6, Polpharma, 2, Procise Diagnostics, 2, Progenity, 2, Prometheus Biosciences, 2, Prometheus Laboratories, 2, Protagonist Therapeutics, 2, Seres Health, 12, data monitoring board activities, Takeda, 6; **R. Rampelbergh**: Johnson & Johnson, 3, 11; **M. Olurinde**: Johnson & Johnson, 3, 11; **J. Yee**: Johnson & Johnson, 3, 11; **K. Lozenski**: BMS, 11, Johnson & Johnson, 3, 11; **T. Baker**: Johnson & Johnson, 3, 11; **S. Yarandi**: Johnson & Johnson, 3, 11; **M. Germinaro**: Johnson & Johnson, 3, 11; **M. Vetter**: Johnson & Johnson, 3, 11; **H. Li**: Johnson & Johnson, 3, 11; **M. Ballina**: Actelion Research & Development, 3, 11; **J. Allegretti**: AbbVie, 2, 6, Adiso, 2, Bristol Myers Squibb, 2, 6, Ferring, 2, Genentech, 2, GlaxoSmithKline, 2, Janssen, 12, 2, 5, 6, 12, Steering committee member, Merck, 2, 5, Pfizer, 2, 5, Roivant, 2, Seres Therapeutics, 2; **A. Afzali**: AbbVie, 12, potential conflicts of interest, Bristol Myers Squibb, 12, potential conflicts of interest, Celgene, 12, potential conflicts of interest, DiaSorin, 12, potential conflicts of interest, Eli Lilly, 12, potential conflicts of interest, Gilead Sciences, 12, potential conflicts of interest, IBD Horizons, 12, potential conflicts of interest, Janssen, 12, potential conflicts of interest, Pfizer, 12, potential conflicts of interest, Takeda, 12, potential conflicts of interest, TLL Pharmaceuticals, 12, potential conflicts of interest; **D. Rubin**: AbbVie, 1, 2, 6, Altrubio, 1, 2, 6, 11, Apex, 1, 2, 6, Avalo, 1, 2, 6, 12, reports potential conflicts of interest, Bristol Myers Squibb, 1, 2, 6, Buhlmann Diagnostics Corp, 1, 2, 6, Celgene, 1, 2, 6, Connect BioPharma, 1, 2, 6, Cornerstones Health, Inc, 12, Membership on the Board of Directors, Crohn's & Colitis Foundation, 12, Board of Trustees, Datos Health, 11, Intouch Group, 1, 2, 6, Iterative Health, 1, 2, 6, 11, Janssen (Johnson & Johnson), 1, 2, 6, 12, reports potential conflicts of interest with, Lilly, 1, 2, 6, Pfizer, 1, 2, 6, Samsung Neurologica, 1, 2, 6, Takeda, 1, 2, 5, 6.

Abstract Number: 0258

Performance characteristics of anti-Collagen II antibodies for diagnosing inflammatory and non-inflammatory diseases: a systematic review and meta-analysis

Karyssa Stonick[1], Marcela ferrada[2], Alice Fike[3], Kaitlin Quinn[3], Benjamin Turturice[3], Casey Stein[4] and Peter Grayson[5], [1]National Insitute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [2]University of Maryland, Bethesda, MD, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [4]NIAMS, NIH, Chevy Chase, MD, [5]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-collagen II (Col2) antibodies have been clinically and experimentally associated with relapsing polychondritis (RP), rheumatoid arthritis (RA), and other diseases. Whether anti-Col2 antibodies are directly involved in disease pathogenesis in humans or represent a marker of cartilage disease remains unknown. The purpose of this study was to synthesize and evaluate the current evidence in the literature on the prevalence and diagnostic performance of anti-Col2 antibodies across all the diseases in which it has been studied.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A systematic review and meta-analysis was performed on diagnostic performance of anti-Col2 antibodies across a broad spectrum of diseases and studies in accordance with the recommendations of the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The study was registered in PROSPERO (April 1, 2025; CRD# 1023286). A PubMed search for articles measuring anti-Col2 antibodies in human serum was completed using the terms ((anti-collagen II) OR (collagen II antibodies)) AND (human)). Additionally, snowballing was used to identify articles not captured in the original search. Two independent investigators classified each article into one of four categories: inflammatory diseases with cartilage involvement, inflammatory diseases without cartilage involvement, non-inflammatory

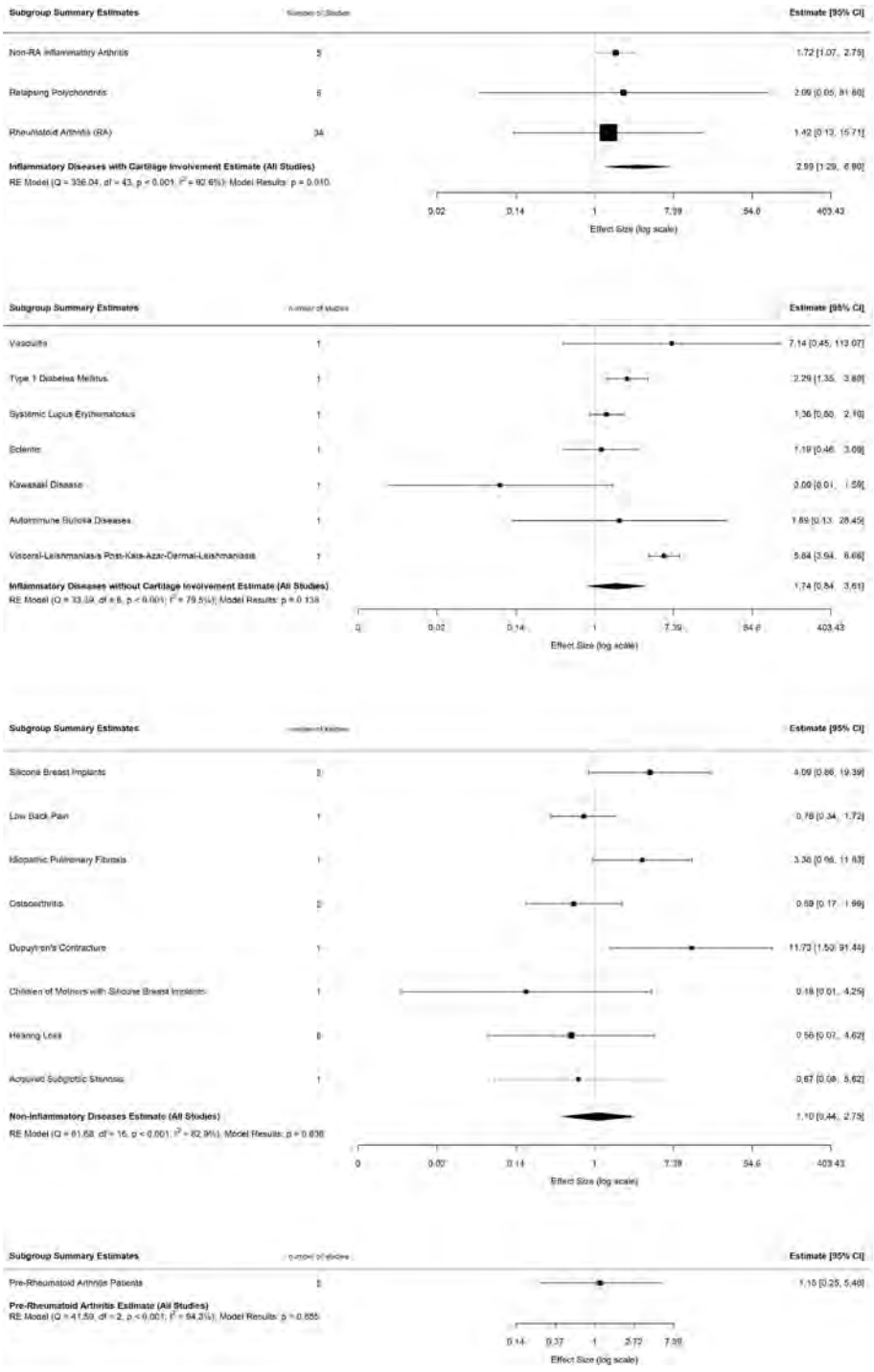


Figure 1: Forest plots summarized by disease within each composite disease subgroup. The risk ratio (RR) is the probability of anti-col2 antibody positivity in the disease versus control groups.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

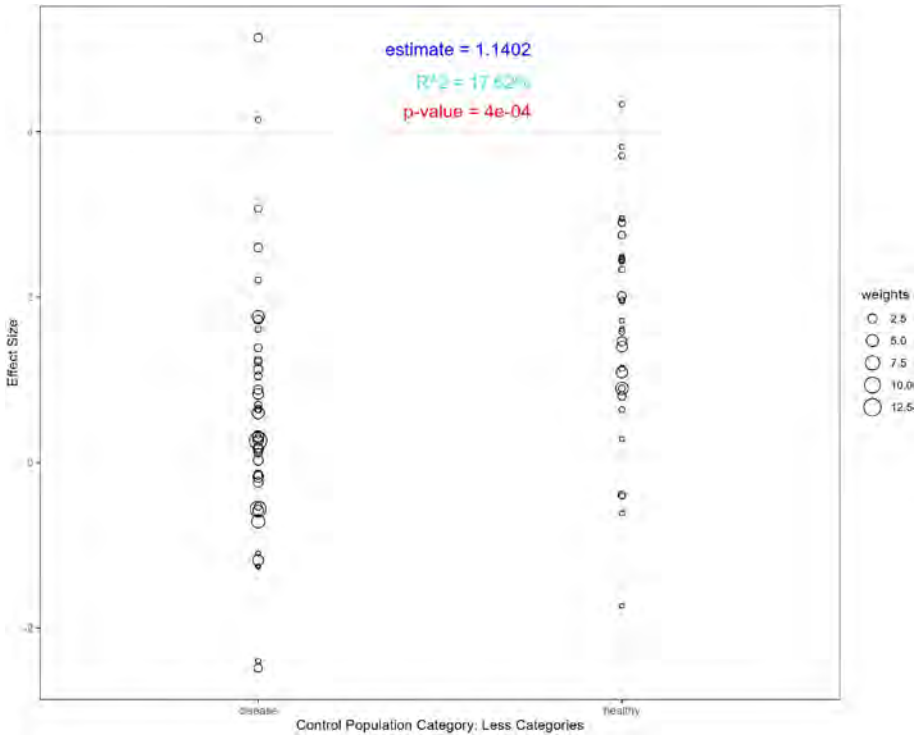


Figure 2: Differences in Composition of the Control Population Explains a Proportion of Heterogeneity Between Studies

diseases, and pre-RA patients. Forest, funnel, and meta-regression plots were generated to evaluate individual study risk ratios (RR) and pooled disease category RR, study bias, and inter-study heterogeneity.

Results: Out of 2443 reviewed articles, 72 were selected for analysis. Prevalence of anti-Col2 antibodies was significantly associated with the group of inflammatory diseases with cartilaginous involvement (RR 2.99; 95% CI: 1.29, 6.91; p=0.01); however, it was not significantly associated with most of the specific diseases contained in this category, including RP or RA (**Figure 1**). There was no significant association between anti-Col2 antibody positivity and inflammatory diseases without cartilage involvement (RR: 1.74, 95% CI: 0.84, 3.61, p = 0.138), non-inflammatory diseases (RR: 1.10, 95% CI: 0.44, 2.75, p = 0.84) or the pre-RA group (RR: 1.15, 95% CI: 0.25, 5.40, p = 0.86) (**Figure 1**). Studies that used healthy rather than disease controls reported increased effect sizes (Beta-estimate = 1.14, I^2=17.08%, p=0.0004) (**Figure 2**).

Conclusion: Anti-Col2 antibodies have been indiscriminately detected in several diseases where there is inflammation of cartilage. As such, Anti-Col2 antibodies are more likely a marker of inflammatory cartilage damage rather than a driver of disease pathogenesis. Clinical use of these antibodies to diagnose specific conditions, such as RP, is not advisable.

Disclosure: K. Stonick: None; **M. ferrada**: UpToDate, 9; **A. Fike**: None; **K. Quinn**: None; **B. Turturice**: None; **C. Stein**: None; **P. Grayson**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0259

Inhaled pirfenidone as an innovative therapeutic approach to treat autoimmune ILD and other forms of Progressive Pulmonary Fibrosis: Phase 2b Study Design

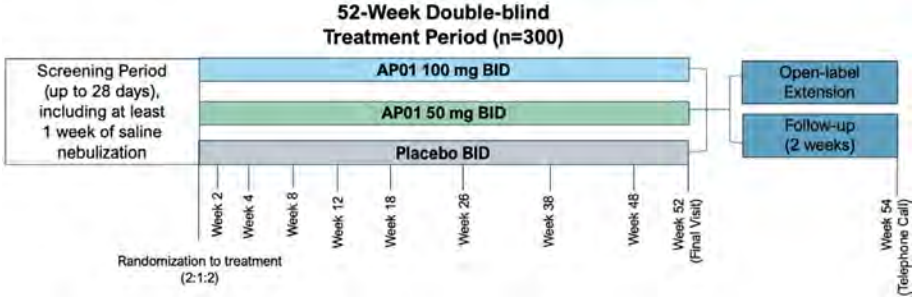
Kristin Highland[1], Colin Reisner[2], Allison Trucillo[3], Deepthi Nair[4], Felix Woodhead[4], Howard Lazarus[4], Craig Conoscenti[4] and Martin Kolb[5], [1]Cleveland Clinic, Shaker Heights, OH, [2]DevPro Biopharma, Basking Ridge, NJ, [3]Avalyn Pharma, Austin, TX, [4]Avalyn Pharma, Cambridge, MA, [5]McMaster University, Hamilton, ON, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Progressive Pulmonary Fibrosis (PPF) is an increasingly recognized condition, defined in 2022 to address the progression of pulmonary fibrosis in patients with interstitial lung diseases (ILDs) other than idiopathic pulmonary fibrosis (IPF). PPF is a characteristic feature of autoimmune ILD. Oral pirfenidone has shown positive signals in some studies without reaching the primary endpoint, but treatment with oral pirfenidone is also associated with significant adverse events and a poor tolerability profile. This study aims at exploring the efficacy and safety of inhaled pirfenidone which might be a promising therapeutic approach considering the local drug delivery into the lungs and the subsequent reduced systemic exposure.

Data from the AP01-002 (ATLAS) Study of inhaled pirfenidone in IPF demonstrated efficacy and improved safety compared to that seen historically with oral pirfenidone. The AP01-005 long term extension study allowed new patients with PPF to enter the study and showed a trend toward FVC stabilization. The AP01-007 (MIST Study) is designed to study the efficacy and safety of AP01 (inhaled pirfenidone) in patients with PPF including autoimmune ILD patients.

Methods: MIST is a prospective randomized placebo-controlled trial comparing two doses (100mg BID and 50mg BID) of inhaled pirfenidone with placebo over 52 weeks. Patients will be eligible if they meet at least one of the following criteria for progression of ILD within the 24 months prior to screening: a relative decline in the FVC of at least 10% of the predicted value, a relative decline in the FVC of ≥5% to less than < 10% of the predicted value accompanied by worsening of respiratory symptoms or an increased extent of fibrosis on HRCT; or worsening of respiratory symptoms and an increased extent of fibrosis on HRCT. Patients will remain on stable background immunosuppression, and up to 30% of patients will remain on background nintedanib therapy. 300 patients will be recruited in 14 countries, including the US.



MIST phase 2b Study Design

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The AP01-007 (MIST Study) is designed to study the efficacy and safety of AP01 (inhaled pirfenidone) in patients with PPF including autoimmune ILD patients. The primary endpoint is the change in the annual rate of decline in FVC in the AP01 treatment groups as compared to placebo. In addition, efficacy will be measured in secondary endpoints of time to progression, change in fibrotic scores via quantitative HRCT, and change from baseline QoL. Safety outcomes will be assessed as well. Cough will be analyzed through cough questionnaires, which should allow differentiation of cough related to PPF vs. aerosol inhalation via nebulization.

Conclusion: MIST is the first study to analyze the novel concept of inhaled medications in autoimmune ILD. In addition to the safety and efficacy endpoints, MIST will examine the presence of cough in this population of patients.

Disclosure: K. Highland: Atyr Pharmaceuticals, 2, 5, Avalyn, 2, 5, Boehringer-Ingelheim, 2, 5, 6, Forsee, 2, Gossamer Bio, 2, 5, Johnson & Johnson, 2, 5, 6, Merk, 2, 5, 6, Mitsubishi, 2, United Therapeutics, 2, 5, 6; **C. Reisner**: Avalyn Pharma, 2; **A. Trucillo**: Avalyn Pharma, 3; **D. Nair**: Avalyn Pharma, 3; **F. Woodhead**: Avalyn Pharma, 3; **H. Lazarus**: Avalyn Pharma, 3; **C. Conoscenti**: Avalyn Pharma, 3; **M. Kolb**: Avalyn, 1, 2, Boehringer-Ingelheim, 1, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 6.

Abstract Number: 0260

Development of a Consensus Definition of VEXAS Flare for Use in Clinical Research

Lachelle D. Weeks[1], Danielle Hammond[2], Sinisa Savic[3], Mael Heiblig[4], Onima Chowdhury[5], Arsène Mekinian[6], Carmelo Gurnari[7], Radhakrishanan Ramchandren[8], Sophie georgin-Lavialle[9], Marcela ferrada[10], Sarah A. Buckley[11], Bryan G. harder[11], Sandra Goble[11], David Beck[12] and Matthew Koster[13], [1]Dana Farber Cancer Institute, Boston, MA, [2]The University of Texas MD Anderson Cancer Center, Houston, TX, [3]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [4]Lyon-Sud Hospital, Hospices Civils de Lyon, Paris and Université Claude Bernard, Lyon, France, [5]Oxford University Hospitals' NHS Foundation Trust and Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, United Kingdom, [6]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [7]Department of Biomedicine and Prevention, University of Rome Tor Vergata and Translational Hematology and Oncology Research Department, Taussig Cancer Center, Cleveland Clinic, Clevland, OH, Rome, Italy, [8]University of Pittsburgh Medical Center, Pittsburgh, PA, [9]Sorbonne university, Tenon hospital, DMU3ID, CEREMAIA, ERN RITA, Paris, France, [10]University of Maryland, Bethesda, MD, [11]Sobi Inc., Waltham, MA, [12]Center for Human Genetics and Genomics, NYU Grossman School of Medicine. Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine. Department of Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, New York, NY, USA, New York, NY, [13]Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: VEXAS syndrome is a recently identified, severe systemic hemato-inflammatory disease with a complex and heterogeneous clinical presentation. The disease is associated with significant morbidity and mortality, with most patients experiencing recurrent flares or persistent symptoms despite anti-inflammatory therapy. Accurate and standardized measures of disease activity are critical for understanding disease progression, optimizing management, and conducting effective clinical trials. Before developing a disease activity instrument, it is essential to define disease activity, such as VEXAS flare. The absence of universally accepted definitions of VEXAS flare has significantly hindered these efforts. Developing consensus criteria for a VEXAS flare will promote consistency in research, the evaluation of therapeutic interventions, and most importantly will improve patient care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A 9-member international expert advisory committee, including both hematologists and rheumatologists, developed a consensus definition of VEXAS flare using modified Delphi methodology. Clinical manifestations of VEXAS syndrome were identified by a systematic literature review. Committee members developed a conceptual framework for flare definition, proposed revisions, and voted on changes until consensus was reached (defined as ≥75% concurrence). To facilitate revisions, a moderator amended VEXAS flare definition text, synthesizing similar proposed changes, and providing multiple drafts for consideration for dissimilar proposals.

Results: A total of 4 revision rounds were conducted from May to July of 2024, and consensus was reached on the definition of VEXAS flare as an active inflammatory manifestation of VEXAS syndrome requiring escalation in glucocorticoid therapy. Three categories of flare were established: **A)** recurrence of a prior documented VEXAS manifestation; **B)** development of a new VEXAS-defining inflammatory sign; or **C)** development of an inflammatory sign not meeting criteria for categories A or B. The panel agreed upon the need for an independent adjudication committee to aid in the determination of flares, particularly in the context of category C manifestations, during clinical trials.

Conclusion: A consensus definition of VEXAS flare provides uniform criteria for defining and characterizing recurrence of VEXAS disease activity. Future efforts will focus on refining this definition through its application and performance in clinical trials.

This abstract has been accepted for publication by the European Alliance of Associations for Rheumatology (EULAR). The definitive copyedited version is available online at: www.ard.eular.org

---

Disclosure: L. Weeks: AbbVie, 2, Sobi, 2, Vertex, 2; **D. Hammond**: None; **S. Savic**: BioCryst, 2, Celldex, 2, CSL Behring, 2, 5, KalVista, 2, 6, Novartis, 2, 5, 6, Pharming, 2, 6, Phavaris, 2, Sobi, 2, Takeda, 2, 6; **M. Heiblig**: AbbVie, 2, Astellas, 2, Blueprint, 2, BMS/Celgebe, 2, Jazz Pharmaceuticals, 2, Servier, 2; **O. Chowdhury**: Jazz Pharmaceuticals, 6, Novartis, 6; **A. Mekinian**: Roche, 5; **C. Gurnari**: Alexion, 5, Genesis Therapeutics, 2; **R. Ramchandren**: Curis, 2, GSK, 6, Incyte, 2, Sobi, 2; **S. georgin-Lavialle**: Novartis, 2, Sobi, 2; **M. ferrada**: UpToDate, 9; **S. Buckley**: Sobi, Inc., 3; **B. harder**: Sobi, Inc., 3; **S. Goble**: Sobi, Inc., 3; **D. Beck**: Alexion, 2, Genesis Therapeutics, 2, GSK, 2, Novartis, 2, Sobi, 2; **M. Koster**: Amgen, 2.

Abstract Number: 0261

Randomized Confirmatory Basket Trial: Performance Evaluation of a Simulated Application Example in Rare Disease Using Real World Data

Daphne Guinn[1], **Linchen He**[2], Yuru Ren[1], Valeriy Korostyshevskiy[1] and Robert Beckman[1], [1]Georgetown University, Washington, [2]Novartis, East Hanover

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Basket trials group together participants who share a common biomarker or disease pathway across several diseases or phenotypes in a single clinical study. Such trial designs may substantially increase efficiency of clinical development, especially in rare diseases with the challenges of limited resources and high operation costs. Rituximab, a monoclonal antibody targeting the CD20 antigen on B-cells, is used as a treatment option for several rare

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

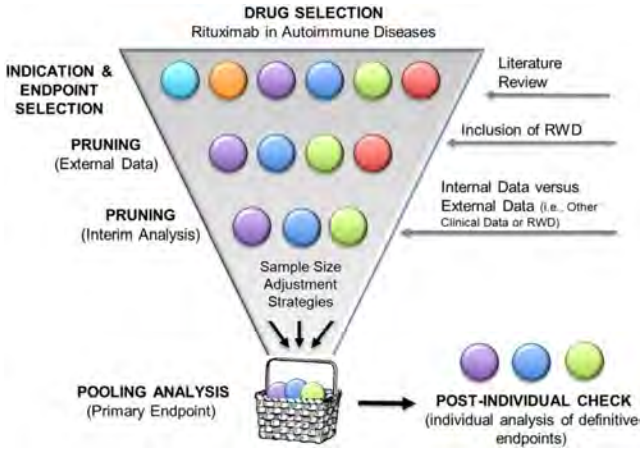


Figure 1. Randomized confirmatory basket designs. Cartoon shapes represent putative indications. The design is a funnel proceeding from top to bottom with the indicated steps shown on the side of the funnel. After indication and endpoint selection by literature review, RWD is used to optimize the choice of indications and other detailed study design features. A pruning process subjects possible indications to a high interim bar to decrease heterogeneity. After this pruning, the resulting pooled indications continue until study maturity. A pooled analysis on pooled data by the definitive endpoint is applied and followed by an additional pruning step to individual indications if the pooled analysis is positive, which enables stricter control of the false positive rate by individual indications.

autoimmune diseases including autoimmune hemolytic anemia (AIHA), thrombotic thrombocytopenic purpura (TTP), and idiopathic thrombocytopenic purpura (ITP), as it effectively depletes B-cells which are often implicated in the production of autoantibodies causing these conditions.

Methods: We utilized real world data (RWD) of off-label use of rituximab together with literature data for a design of a randomized confirmatory basket trial of steroid therapy +/- rituximab in multiple rare auto-immune diseases. The adaptive basket design removes disease indications where the therapy does not appear to be benefitting patients at interim analysis, pools the remaining indications in the primary analysis, and then performs an indication-by-indication post check, again discarding indications that do not appear to benefit patients (Figure 1). We simulated this basket design under numerous scenarios varying design parameters based on RWD and literature information and assessed power, efficiency, and benefit of a basket trial investigating k indications compared to k parallel, independent Phase 3 designs, given the false positive rate of the entire trial controlled at 0.025k. Efficiency was defined as the number of true positive results confirmed per patient enrolled. A false positive event was considered to have occurred if the study resulted in approval of one or more indications where experimental therapy was not beneficial.

Results: Information from RWD influenced our selection of indications for the simulated trial and led us to increase the sample size due to more realistic estimates of clinical benefit. Literature information alone resulted in poor study performance. Using the RWD information together with literature information, we were able to design a basket trial of three auto-immune indications that had robust performance across plausible clinical scenarios, and up to a 46-132% improvement in development efficiency with comparable control of the false positive rate when compared to parallel clinical studies.

Conclusion: RWD can be useful when performing design optimization of complex basket trial designs in rare auto-immune disease. Rigorous, efficient confirmatory basket trial designs are feasible.

Disclosure: D. Guinn: None; **L. He**: Novartis, 3; **Y. Ren**: Amarex Clinical Research, 3; **V. Korostyshevskiy**: None; **R. Beckman**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0262

Preclinical Characterization of ABB071 – a Humanized anti-CD180 Antibody that Modulates Multiple Pro-inflammatory Immune Pathways for the Treatment of Autoimmune and Inflammatory Disorders

Margaret McDaniel, Brenda Stevens, Socheath Khim, Alan Wahl, Che-Leung Law and Edward Clark, Abacus Bioscience, Seattle, WA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: CD180 is a Toll-like receptor (TLR) homolog expressed on antigen-presenting cells (APCs): B cells, dendritic cells, monocytes, and macrophages. While the extracellular domain of CD180 is structurally similar to other TLRs, intracellular signaling is distinct from classical TLRs as CD180 lacks a TIR domain. Instead, CD180 signaling leads to pleiotropic downstream immune responses, including PI3K activation and downregulation of type I interferon (IFN)-associated inflammation. In mice, treatment with an agonistic anti-CD180 antibody is therapeutic in multiple models of lupus.

Methods: We utilize RNA-sequencing and transcriptional analysis of human B cells stimulated with humanized anti-CD180 monoclonal antibody to characterize CD180 signaling and predict diseases that may show therapeutic effect with anti-CD180 treatment. Mouse models of rheumatic disease are used to support these disease predictions.

Results: To support clinical development of anti-CD180 therapy, we have humanized G28-8, a mouse anti-human CD180 monoclonal antibody. Humanized G28-8 (hzG28-8), including the lead drug candidate ABB071, have retained primate CD180 cross-reactivity and functional profiles of the parent G28-8.

RNAseq analysis revealed an inverse correlation between genes regulated by ABB071 in B cells from normal donors to genes differentially expressed in B cells from patients with rheumatic disease. Several genes upregulated in B cells from lupus patients, e.g., TLR7 and IRF5, were downregulated in ABB071 treated B cells. In contrast, genes downregulated in B cells from lupus patients, e.g., PNPT1 and DNASE1L3, were induced by ABB071. These results suggest a genetic connection between CD180 biology and the pathogenesis of autoimmune and inflammatory disorders.

Suppression of IFN-stimulated genes (ISGs) was used to evaluate the therapeutic potential of ABB071. ABB071 inhibited ISGs induced by ligands for TLR7, TLR8, TLR9, cGAS-STING, as well as IFNα in B cells from normal donors. The effects of ABB071 against TLR7/8 ligand and IFNα was also observed in B cells from SLE patients. In addition, ABB071 down-modulated baseline expression of several genes in the type I IFN pathway including IFNAR1/2, IRF5, and IL-15.

A mouse model of imiquimod-induced psoriasis was used to validate the role of CD180 signaling in suppressing inflammatory disease. Mice treated with anti-CD180 had reduced overall PASI scoring (psoriasis severity scoring), as well as reduced levels of key inflammatory cytokines in the skin. The safety margin of CD180 targeting in mice was confirmed by the finding that anti-CD180, up to 50 mg/kg, did not result in observable clinical side effects or increase in circulating proinflammatory cytokines such as IL-6, TNFα, and IFNɣ.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In contrast to most current approved therapies designed to neutralize individual cytokines or their receptors globally in patients, targeting CD180 is a novel strategy focusing the therapeutic actions on one of the most relevant subsets of immune cells, the APCs, to simultaneously suppress multiple key pro-inflammatory pathways. This study provides the rationale for clinical development of ABB071 in the treatment of autoimmune and inflammatory diseases.

Disclosure: M. McDaniel: None; **B. Stevens**: None; **S. Khim**: None; **A. Wahl**: Abacus Bioscience, Inc., 12, 3, 4, 8; **C. Law**: Abacus Bioscience, Inc., 3, 4, 8, 11; **E. Clark**: None.

Abstract Number: 0263

A Multicenter Retrospective Case Series of Patients with Susac Syndrome Treated with Rituximab

Michelle Benjamin[1], Mattia Wruble Clark[2], Shamik Bhattacharyya[3], Audra Horomanski[1] and Kristin Galetta[4], [1]Stanford University, Palo Alto, CA, [2]Mass General Brigham, Somerville, MA, [3]Brigham and Women's Hospital, Malden, MA, [4]Stanford Medical Center, Palo Alto

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Susac Syndrome (SuS) is a rare immune-mediated vasculo-occlusive disease characterized by a triad of encephalopathy, hearing loss, and branched retinal artery occlusions. Deficits can be permanent and there is limited data to guide treatment. Here, we describe the treatment trajectories of a series of patients with SuS treated with rituximab.

Methods: A retrospective chart review of patients with SuS treated with rituximab and followed in neurology and/or rheumatology clinics at three tertiary care centers in the United States was performed.

Results: Eight patients -- 4 (50%) females, 7 (87.5%) with the complete SuS triad, median age of 47 years (range 21-66 years) -- were included. There were 11 instances of rituximab treatment (1 patient received 3 distinct courses) -- 8 (72.7%) for ≥ 6 months (3 are ongoing) and 3 (27.3%) for < 6 months. Co-treatment with prednisone occurred in 10 (90.9%) instances -- all 7 instances of rituximab ≥ 6 months reached steroid freedom; all 3 instances of rituximab < 6 months saw a decrease in daily prednisone dose by ≥ 30mg, but none reached steroid freedom. Mycophenolate mofetil (MMF) co-treated patients continued at the same dose, decreased, and weaned off MMF completely over 4 (36.4%), 2 (18.2%), 4 (36.4%) instances of rituximab treatment respectively. In the 4 (36.4%) rituximab instances involving co-treatment with intravenous immunoglobulin G (IVIg), the total monthly IVIg dose was decreased over 2 (50.0%) rituximab instances and weaned off completely over 1 (25.0%) instance. Additional co-treatments included methotrexate and azathioprine in 1 instance each, both of which were weaned off completely during rituximab treatment. No patients were co-treated with cyclophosphamide (though 1 was treated cyclophosphamide before rituximab initiation).

Conclusion: In this case series of patients with SuS, rituximab facilitated steroid freedom and tapering of other immunotherapeutic agents. These initial findings provide evidence supporting the use of rituximab in SuS.

Disclosure: M. Benjamin: None; **M. Wruble Clark**: Alexion, 5, Roche, 5; **S. Bhattacharyya**: Alexion Pharmaceuticals, 1, 5, Amgen, 1, Roche, 5, UCB, 5; **A. Horomanski**: Gilead, 5, VielaBio, 5, Zenas, 5; **K. Galetta**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0264

Seeing Beyond the Eye: Subclinical Audio-Vestibular Involvement in Vogt-Koyanagi-Harada Disease

Mohamed Tharwat Hegazy, Rania Yacoub, Sarah Sheta, Rana Hussein Amin and Noha Khalil, Faculty of Medicine, Cairo University, Cairo, Egypt

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Vogt-Koyanagi-Harada disease (VKH) is a systemic disease that affects the central nervous system, ocular, and integumentary system. It causes bilateral granulomatous uveitis, dysacusia ranging from tinnitus, vertigo to hearing loss, and skin abnormalities such as poliosis, vitiligo, and alopecia. The present criteria only mention tinnitus as an ear finding, despite some studies reporting vestibular and cochlear involvement in individuals with VKH. Also, the diagnostic criteria for VKH do not include hearing loss as an auditory finding

Methods: Our study is one of the unique prospective studies in VKH. We aimed to evaluate the clinical and sub-clinical audio-vestibular (AV) involvement in VKH, and to compare between eye and AV response to treatment. Our patients were recruited and followed for 6 months. All our patients were assessed with emphasis on eye and AV evaluation {using Pure Tone Audiometry (PTA), Transient Evoked Otoacoustic Emission (TEOAE), positioning, spontaneous nystagmus, and caloric tests}. Laboratory investigations included CBC, ALT, AST, Creatinine, ESR, and CRP

Results: 100 patients with VKH were included. 63 cases with Active uveitis: Anterior 23/63 (35.5%), intermediate 10/63 (15.9%), posterior 4/63(6.3%), pan uveitis **40.3%25/63 (**, symptomatic patients had symptomatic (clinical) AV involvement either audiological 18/26 (69.2%), vestibular 1/26 (3.8%), or both 7/26 (27%), while **40 asymptomatic patients had subclinical AV involvement:** audiological 26/40 (65%), vestibular 2/40 (5%), both 12/40 (30%). The 63 cases with active uveitis). 26 55.5% (35/63**) had subclinical**, and 15/63 (24.2%) had clinical AV involvement. The 37 patients with no uveitis, **14/37 (40.5%)** had subclinical and 11/37 (29.7%) had clinical AV involvement. This group with subclinical AV involvement and no eye activity is very important, as without evaluating the AV system, those patients would have been missed without treatment till damage occurs. Patients received treatment according to the activity by different lines of management **(Table 1). After 6 months:** Follow-up (F/U) for ocular response: Complete response in 33/63 (52.4%), Partial response in 12/63 (19%), No response in 6/63 (9.5%), Worsening in 8/63 (12.7%), Lost F/U in 4/63 (6.3%). Follow up for AV response:

Table 1: The medications used as single treatments or in combinations.

Medication	Number of patients using this medication
Low dose steroid <10 mg/day	17
Medium dose steroid (10-20 mg/day)	35
High dose steroid >20 mg/day	33
Methotrexate	50
Mycophenolate mofetil	7
Azathioprine	23
Cyclosporine	9
Leflunomide	1
Adalimumab	14
Infliximab	1
Rituximab	3

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Base line characteristics of Uveitis and Audio-vestibular involvement and follow-up

	Baseline							Follow-up of organ involvement								
Uveitis	Active Uveitis						No Uveitis	Complete response	Partial response	No response	Worsening	Lost F/U				
	63 (%)						37 (%)									
	Anterior	Intermediate	Posterior	Panuveitis				33/63 (52.4%)	12/63 (19%)	6/63 (9.5%)	8/63 (12.7%)	4/63 (6.3%)				
	23 (35.5%)	10 (15.9%)	4 (6.3%)	35 (55.5%)												
Audio-vestibular involvement (AV)	AV involvement 66 (%)						No AV 34 (%)									
	Symptomatic 26/66 (39.4%)			Subclinical 40/66 (60.6%)				Symptomatic 26/66 (39.4%)				Subclinical 40/66 (60.6%)				
	Audio	Vestibular	Both	Audio	Vestibular	Both		Improve	No Improve	Worsening	Lost F/U	Improve	No Improve	Worsening	Lost F/U	
	18/26 (69.2%)	1/26 (3.8%)	7/26 (27%)	26/40 (65%)	2/40 (5%)	12/40 (30%)		15/26 (57.7%)	6/26 (23.1%)	4/26 (15.4%)	1/26 (3.8%)	28/40 (70%)	4/40 (10 %)	3/40 (7.5%)	5/40 (12.5 %)	

subclinical improvement 28/40 (70%), subclinical no improvement 4/40 (10%), subclinical worsening 3/40 (7.5%), lost F/U 5/40 (12.5%), clinical improvement 15/26 (57.7%), clinical no response 6/26 (23.1%), clinical worsening 4/26 (15.4%), lost F/U 1/26 (3.8%). Regarding the group of patients with normal eyes at base line with AV involvement and received treatment: subclinical improvement 10/14 (71.4%), subclinical no improvement 1/14 (7.1%), subclinical worsening 1/14 (7.1%), lost F/U 2/14 (14.3%), clinical improvement 8/11 (72.8%), clinical no response 1/11 (9%), clinical worsening 2/11 (18.2%) **(Table 2)**

Conclusion: Subclinical AV (40%) involvement is common and more than symptomatic cases and even present in about 40% of cases without uveitis. So, early detection of subclinical AV involvement is important to allow early treatment before damage. We recommend adding AV involvement in the diagnostic criteria of VKH and not only tinnitus

Disclosure: M. Hegazy: None; **R. Yacoub**: None; **S. Sheta**: None; **R. Amin**: None; **N. Khalil**: None.

Abstract Number: 0265

Influence of Menopausal Status on Coronary Artery Calcium Burden and Cardiovascular Computed Tomography Abnormalities in Inflammatory Arthritis

Mohammed Mohammed[1], Bindee Kuriya[2], Lihi Eder[1], Elsie Nguyen[3], Shadi Ahktari[4], Paula Harvey[5], Wei Wu[6] and Sohan Shahab[7], [1]University of Toronto, Toronto, ON, Canada, [2]University of Toronto - Toronto, Toronto, ON, Canada, [3]University of Toronto, Toronto, [4]University of Toronto Department of Medicine and Women's College Hospital, Toronto, Canada, [5]University of Toronto Department of Medicine and Women's College Hospital, Toronto, ON, Canada, [6]University of Toronto, Toronto, Canada, [7]Women's College Research Institute, Women's College Hospital, Toronto, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with inflammatory arthritis (IA) have increased cardiovascular risk. Coronary artery calcium (CAC) scoring by computed tomography (CT) detects early coronary disease and structural abnormalities. While sex and menopause influence CVD risk, their impact on coronary and extra-coronary CT findings in IA is unclear

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Multivariable-adjusted odds ratios for elevated coronary artery calcium score in post-menopausal women compared to men with inflammatory arthritis patients.

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Post-menopausal status	0.541 (0.367-0.798)	***0.314 (0.188-0.526)***
Age, years	1.085 (1.061-1.110)	***1.113 (1.081-1.147)***
Disease duration, years	1.017 (1.001-1.034)	1.007 (0.989-1.026)
CRP, mg/L	1.024 (0.999-1.050)	***1.034 (1.006-1.063)***
Hypertension	2.739 (1.800-4.167)	1.682 (0.998-2.835)
Diabetes	4.221 (1.970-9.041)	***2.453 (1.001-6.014)***
Dyslipidemia	2.277 (1.475-3.515)	1.475 (0.818-2.659)
Smoking History	1.975 (1.341-2.910)	***2.028 (1.283-3.204)***
Obesity (BMI>30)	1.567 (1.058-2.320)	1.308 (0.814-2.103)

Methods: We conducted a cross-sectional analysis using data from the U of T CardioRheum Network (2017–2023). Eligible participants were aged >40 years with confirmed IA, and no prior CVD. The primary outcome was total CAC category (0, 1–100, >100); secondary outcomes included plaque distribution and other CT-detected abnormalities. Multivariable logistic regression assessed associations with post-menopausal status, adjusting for confounders.

Results: Among 594 IA patients, 31% were male (mean age 57.3), 14% pre-menopausal female (46.1), and 54% post-menopausal female (61.7). Males were more likely to have AS/PsA (71%) compared to pre-menopausal (38%) and post-menopausal females (30%), while RA was more prevalent in post-menopausal females (70%, $p< 0.001$). Males had more CVD risk factors and higher Framingham scores (44% vs. 11% post- and 1.5% pre-menopausal females, $p< 0.0001$). Both female groups had higher joint counts, global, and pain scores (all $p< 0.05$). DMARD use was highest in post-menopausal females (92%), though biologics were more common in males (58%) and pre-menopausal females (54%) than post-menopausal females (45%) ($p=0.01$). Corticosteroid use was also higher in post-menopausal females (25%, $p=0.01$). CAC >100 occurred in 28% of males, 19% of post-, and 1.4% of pre-menopausal females ($p< 0.0001$). Post-menopausal females had more aortic calcification (44%), aortic enlargement (23%), and pericardial effusion (8%) (all $p\leq0.001$), while males had more left main and right coronary calcification ($p\leq0.001$). In multivariable models, post-menopausal females had lower odds of elevated CAC vs. males (OR 0.31, 95% CI 0.19–0.53). Independent predictors of CAC >100 included older age, higher CRP, smoking, and diabetes. Post-menopausal women had lower odds of CAC in specific coronary territories (left main, right, and circumflex arteries), but there were no adjusted differences in aortic involvement.

Conclusion: Sex and menopausal status significantly influence both coronary and extra-coronary abnormalities detected by CT in IA patients. While men exhibit greater coronary plaque burden, post-menopausal women show a distinct pattern of vascular and structural abnormalities. These findings support a sex-specific approach to cardiovascular risk stratification in IA.

Disclosure: M. Mohammed: None; **B. Kuriya**: AbbVie/Abbott, 1, Pfizer, 1, UCB, 1; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **E. Nguyen**: None; **S. Ahktari**: None; **P. Harvey**: None; **W. Wu**: None; **S. Shahab**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0266

Chronic PPI Use Association with Development of Autoimmune Conditions: Retrospective Cohort Study

Nanuka Tsibadze[1], Irakli Tskhakaia[1], Rusudan Tskitishvili[2] and Fabian Rodriguez[3], [1]Jefferson Health - Einstein, Philadelphia, PA, [2]Virtua Health, Camden, NJ, [3]Jefferson Health - Einstein, Philadelphia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1. Baseline Patient Characteristics of Study Groups, before and after Propensity Score Matching

Characteristics	PPI Group (N=948,767)	No PPI Group (N=1,427,586)	*p*-value	PPI Group (N=383,505)	No PPI Group (N=383,505)	*p*-value
	Before Propensity Score Matching			After Propensity Score Matching		
Demographics						
Age, mean ±SD	29.5 ± 8.26	26.9 ± 8.96	<0.0001	28.2 ± 8.47	27.8 ± 8.73	<0.0001
Female, %	59.815	61.184	<0.0001	62.73	63.701	<0.0001
Male, %	36.601	35.786	<0.0001	34.047	33.261	<0.0001
White, %	61.884	55.884	<0.0001	59.965	59.651	<0.0001
Black, %	13.261	12.728	<0.0001	13.403	13.704	<0.0001
Asian, %.	28.947	57.027	<0.0001	3.588	3.76	<0.0001
Unknown Race, %	15.489	20.406	<0.0001	16.694	16.309	<0.0001
Diagnoses						
Digestive System Diseases, %	93.226	24.462	<0.0001	83.327	82.86	<0.0001
Endocrine Diseases, %	54.421	22.388	<0.0001	45.226	44.409	<0.0001
Nervous System Diseases, %	48.572	19.908	<0.0001	40.638	40.142	<0.0001
Neoplasms, %	17.276	7.649	<0.0001	15.508	15.413	<0.0001
Medications						
CNS, %	76.166	37.173	<0.0001	63.03	65.7	<0.0001
Dermatological, %	72.638	33.954	<0.0001	61.827	62.601	<0.0001
Gastrointestinal, %	79.855	25.676	<0.0001	58.074	57.964	<0.0001
Hormones, Synthetic, Modifiers, %	60.229	27.611	<0.0001	50.346	50.395	<0.0001
Musculoskeletal, %	53.86	25.737	<0.0001	46.779	47.585	<0.0001
Genitourinary, %	49.736	20.608	<0.0001	41.001	41.153	<0.0001
Cardiovascular, %	51.446	19.013	<0.0001	39.248	38.631	<0.0001
Antineoplastics, %.	7.223	3.119	<0.0001	6.501	6.421	<0.0001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Proton pump inhibitors (PPIs) are one of the most prescribed medications around the world. Recent research has increasingly identified adverse reactions in patients with long-term prescription of PPIs, including the risks of enteric infection with Clostridium difficile, osteoporosis, malignancy, ischemic stroke, myocardial infarction, and dementia. Autoimmune diseases (ADs) comprise disorders caused by an imbalance of the immune system, which leads to damage to individual tissues. The administration of medications is one of the most important factors in the induction of ADs. Some medications change the composition of the gastrointestinal microbiota, which may cause development of various diseases. Alteration of the gut microbiome can play a pathogenic role in the development of ADs.

Methods: This is a nationwide, retrospective study. We used the global, multicenter research network (TrinetX) database from 83 large healthcare organizations across multiple countries. We included patients within the age of 18-45 with a diagnosis of gastroesophageal reflux disease (GERD), or dyspepsia, from January, 2000 through September, 2024, using the International Classification of Disease-10 codes. We compared GERD, or dyspepsia patients on PPIs (Esomeprazole, Dexlansoprazole, Lansoprazole, Pantoprazole, Omeprazole, Rabeprazole, Vonoprazan), with GERD, or dyspepsia patients not on PPIs. We used 1:1 propensity score matching that accounted for demographic variables (age, gender, race); diagnoses (gastrointestinal, endocrine, nervous system, neoplastic); medication use (CNS, cardiovascular, dermatological, gastrointestinal, hormonal, musculoskeletal, genitourinary, antineoplastic agents). Index event was determined as simultaneous appearance of dyspepsia, or GERD, and PPI use in patients' charts. Outcome of interest was the incidence of autoimmune conditions, including Sjogren's Syndrome, Scleroderma, Rheumatoid Arthritis, Dermatomyositis, Polymyositis, SLE,

Table 2. Risks of autoimmune conditions in patients (18-45) who were on chronic PPI therapy versus not on PPI therapy

Outcome	Groups	Overall Risk, %	Risk Ratio	Overall Risk, %	Risk Ratio
	Before Propensity Score Matching			After Propensity Score Matching	
Systemic Sclerosis	PPI	0.117 (1,124/ 958,503)	3.562 (3.196-3.97) p-value < 0.0001	0.122 (471/387,262)	2.591 (2.184-3.075) p-value < 0.0001
	No PPI	0.033 (460/ 1,397,208)		0.047 (182/387,764)	
Sjogren's Syndrome	PPI	0.397 (3,801/956,641)	2.705 (2.564-2.854) p-value < 0.0001	0.379 (1,467/386,723)	1.814 (1.665,1-1.976) p-value < 0.0001
	No PPI	0.147 (2,050/1,395,706)		0.209 (809/386,869)	
Rheumatoid Arthritis	PPI	0.719 (6,826/ 949,840)	2.417 (2.326-2.512) p-value < 0.0001	0.707 (2,716/385,267)	1.699 (1.597-1.805) p-value < 0.0001
	No PPI	0.297 (4,138/ 1,391,943)		0.416 (1.602/384,989)	
Dermatomyositis	PPI	0.033 (318/960,432)	3.533 (2.883-4.331) p-value < 0.0001	0.03 (118/387,999)	2.36 (1.696-3.286) p-value < 0.0001
	No PPI	0.009 (131/1,397,962)		0.013 (50/388,063)	
Polymyositis	PPI	0.03 (290/960,340)	4.589 (3.629-5.801) p-value < 0.0001	0.028 (110/387,970)	2.974 (2.09-4.316) p-value < 0.0001
	No PPI	0.007 (92/1,397,957)		0.01 (37/388,058)	
Systemic Lupus Erythematosus	PPI	0.434 (4,118/949,245)	2.421 (2.303-2.544) p-value < 0.0001	0.42 (1,614/384,067)	1.794 (1.654-1.946) p-value < 0.0001
	No PPI	0.179 (2,496/ 1,392,738)		0.234 (903/385,577)	

Table 2. Risks of autoimmune conditions in patients (18-45) who were on chronic PPI therapy versus not on PPI therapy (Ctd.)

Outcome	Groups	Overall Risk, %	Risk Ratio	Overall Risk, %	Risk Ratio
	Before Propensity Score Matching			After Propensity Score Matching	
Antiphospholipid Syndrome	PPI	0.292 (2,793/956,287)	2.64 (2.481-2.809)	0.257 (994/386,716)	1.657 (1.498-1.834) p-value < 0.0001
	No PPI	0.111 (1,544/1,395,778)		0.155 (600/386,821)	
Granulomatosis with Polyangiitis (GPA)	PPI	0.035 (337/960,165)	3.634 (2.977-4.437)	0.031 (120/387,938)	2.034 (1.49-2.778) p-value < 0.0001
	No PPI	0.01 (135/1,397,903)		0.015 (59/388,020)	
Giant Cell Arteritis	PPI	0.038 (369/960,559)	2.285 (1.94,2-2.691)	0.034 (131/388,043)	1.236 (0.957,1-1.596) p-value: 0.1045
	No PPI	0.017 (235/1,397,935)		0.027 (106/388,015)	
Psoriatic Arthritis	PPI	0.195 (1,872/958,328)	2.326 (2.162,2-2.502)	0.185 (715/387,260)	1.615 (1.434-1.818) p-value < 0.0001
	No PPI	0.084 (1,173/1,396,608)		0.114 (443/387,416)	
Behcet's Disease	PPI	0.028 (270/960,346)	2.933 (2.384,3-3.608)	0.028 (108/387,953)	1.8 (1.313-2.468) p-value 0.0002
	No PPI	0.01 (134/1,397,831)		0.015 (60/387,956)	
Ankylosing Spondylitis	PPI	0.156 (1,496/958,804)	2.24 (2.066,2-2.428)	0.152 (588/387,392)	1.504 (1.323-1.709) p-value < 0.0001
	No PPI	0.07 (973/1,396,735)		0.101 (391/387,416)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Antiphospholipid Syndrome, Granulomatosis with Polyangiitis (GPA), Giant Cell Arteritis, Psoriatic Arthritis, Behcet Disease, Ankylosing Spondylitis. Patients displaying these outcomes before the index event were excluded from the analysis. Risk ratios with 95% confidence intervals were calculated for each outcome. A two-sided p-value less than 0.05 was considered statistically significant.

Results: We identified 948,767 GERD, or dyspepsia patients taking proton pump inhibitors (PPIs) and 1,427,586 patients not taking PPIs. At baseline, the mean age of diagnosis was 29.5 ±8.26 years for those on PPIs and 26.9±8.96 not on PPIs. Female patients were predominant in PPI group. After propensity score matching, patients on PPIs showed higher risk of developing autoimmune conditions compared to those not using PPIs (Table 2).

Conclusion: Patients with GERD, or dyspepsia, using PPI therapy have higher risks for autoimmune disease development, compared to those patients, not on PPI therapy. Further research is warranted to elucidate the pathways through which alterations in the gut microbiota contribute to the pathogenesis of autoimmune diseases.

Disclosure: N. Tsibadze: None; **I. Tskhakaia**: None; **R. Tskitishvili**: None; **F. Rodriguez**: None.

Abstract Number: 0267

Pharmacosurvellience study of FDA Adverse Event Reporting System (FAERS) events of Secukinumab and Guselkumab

NUR BARLAS[1], Sait Barlas[1] and Emre Adalier[2], [1]Florida State University College of Medicine, Cape Coral, [2]University of Pavia School of Medicine & Surgery, Pavia, Italy

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

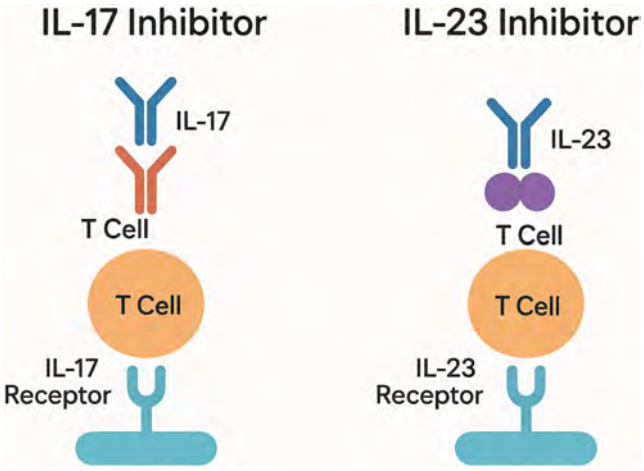
Background/Purpose: Interleukin-17 (IL-17) and interleukin-23 (IL-23) inhibitors have revolutionized treatment for psoriatic arthritis, axial spondyloarthritis, and moderate-to-severe plaque psoriasis. IL-17 inhibitors block the pro-inflammatory cytokine IL-17, while IL-23 inhibitors target the Th17 pathway via IL-23. Secukinumab (Cosentyx), an IL-17 inhibitor, was FDA-approved in 2015, and Guselkumab (Tremfya), an IL-23 inhibitor, received approval in 2017. Both classes are highly effective, but their distinct mechanisms lead to different safety profiles, guiding treatment choices—especially in patients with comorbidities.

Methods: The FAERS system gathers information on adverse events and medication errors.

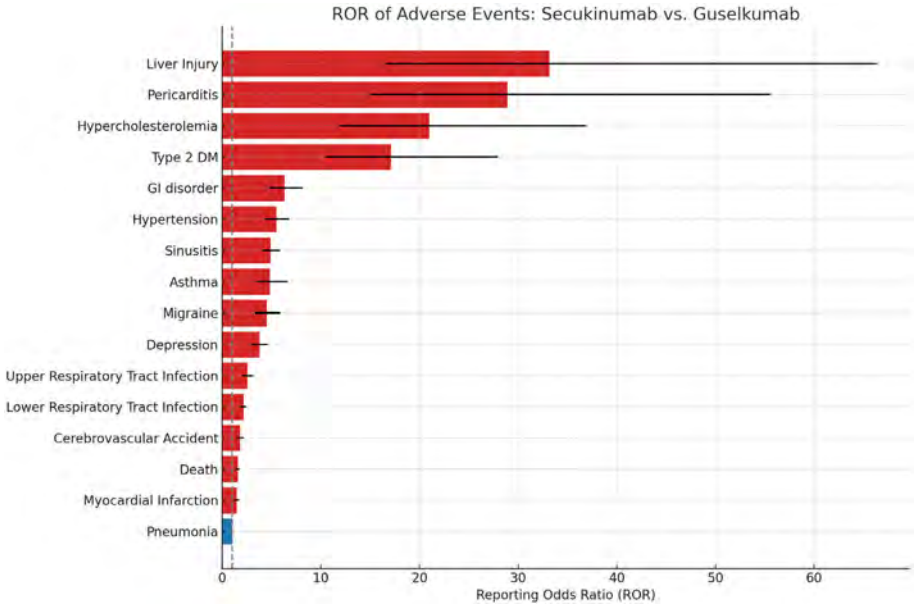
We conducted a pharmacovigilance study using the FAERS database to evaluate adverse events (AEs) associated with Secukinumab and Guselkumab. Post-marketing reports from 2015 to 2024 were analyzed using disproportionality analysis. Reporting odds ratios (RORs) were calculated to assess drug-event associations. An ROR >1 indicates a stronger association of the drug with the adverse event compared to the other. An ROR < 1 indicates a weaker association of the drug with the adverse event.

Results: As of December 2024, there were a total of 143,401 and 23,064 reported adverse events (AEs) for Secukinumab and Guselkumab, respectively. Secukinumab was associated with a significantly higher ROR of several adverse events compared to Guselkumab, including liver injury (ROR 13.01, 95% CI 6.41–26.42), pericarditis (ROR 12.78, 95% CI 6.41–

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Interleukin-17 and interleukin-23 inhibitors mechanism of action



ROR Results of Secukinumab and Guselkumab

25.47), hypercholesterolemia (ROR 9.31, 95% CI 5.00–17.35), type 2 diabetes mellitus (ROR 8.49, 95% CI 4.97–14.48), gastrointestinal disorder (ROR 6.26, 95% CI 4.79–8.18), hypertension (ROR 5.42, 95% CI 4.34–6.78), sinusitis (ROR 4.85, 95% CI 4.02–5.85), depression (ROR 2.99, 95% CI 2.34–3.83), asthma (ROR 2.24, 95% CI 1.55–3.24), and lower respiratory tract infection (ROR 2.11, 95% CI 1.83–2.43). Notably, Guselkumab showed higher odds of cerebrovascular accident (ROR 0.68, 95% CI 0.55–0.85) and myocardial infarction (ROR 0.45, 95% CI 0.36–0.57), indicating these were more frequently reported with Guselkumab. There was no statistically significant difference in the risk of pneumonia (ROR 0.97, 95% CI 0.89–1.06) or death (ROR 1.14, 95% CI 0.99–1.31) between the two agents.

Conclusion: This FAERS-based analysis highlights the distinct adverse event profiles of Secukinumab and Guselkumab. Secukinumab showed higher RORs for liver injury, pericarditis, hypercholesterolemia, type 2 diabetes, GI disorders, hypertension, sinusitis, and depression. Guselkumab was more strongly associated with cerebrovascular accidents and myocardial infarctions. No significant differences were found for pneumonia or mortality. These findings underscore the need for individualized risk assessment when choosing between IL-17 and IL-23 inhibitors and highlight the importance of further research into their long-term safety.

Disclosure: N. BARLAS: None; **S. Barlas**: None; **E. Adalier**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0268

Multicenter study and literature review of JAK inhibitor treatment in refractory uveitis due to different immune-mediated inflammatory pathologies

Nuria Barroso Garcia[1], Lara Sánchez Bilbao[2], José Luis Martín-Varillas[3], Vanesa Calvo-Río[2], Mar Esteban Ortega[4], Santiago muñoz Fernández[5], José Luis Álvarez-Vega[6], Emma Beltran[7], Vega Jovaní[8], Olga Maiz Alonso[9], raúl Veroz González[10], Angel Garcia-Aparicio[11], marta Garijo Bufort[12] and Ricardo Blanco[2], [1]Rheumatology, Hospital Regional Universitario, Universidad de Málaga UMA, Málaga, Spain, Malaga, Spain, [2]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [3]Rheumatology Division, Hospital de Laredo. IDIVAL, Immunopathology Group. Santander, Spain., Laredo, Spain, [4]Rheumatology and Ophthalmology. Hospital Infanta Sofía. Madrid. Spain, Madrid, Spain, [5]Rheumatology and Ophthalmology. Hospital Infanta Sofía, Madrid. Spain, Madrid, [6]Rheumatology. Complejo Hospitalario Universitario de Badajoz, Badajoz, Spain., Badajoz, Spain, [7]Rheumatology. Hospital del Mar. Barcelona, Spain., Barcelona, Spain, [8]Hospital General Universitario de Alicante, Reumatología, Alicante, Alicante, Comunidad Valenciana, Spain, [9]Rheumatology. Hospital de Donostia. San Sebastián, Spain., San Sebastián, Spain, [10]Rheumatology. Hospital de Mérida. Mérida, Spain., Mérida, Spain, [11]Hospital Universitario de Toledo, Toledo, Spain, [12]Rheumatology Department, Hospital de Sagunto, Spain, Valencia, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Study, year (Ref)	Cases	Age/Sex	Underlying Disease	JAKINIB	Ocular involvement	Previous IS/biological treatment	Ocular Evolution
Bauermann et al. 2018	1	22, F	Juvenile idiopathic Arthritis	TOFA	Anterior uveitis, CME	MTX, ADA, RTX, GOLI, IFX, CsA, TCZ, MMF	Complete improvement
Paley et al. 2019	1	45, F	Idiopathic	TOFA	Anterior uveitis, CME	MTX, LFN, AZA, MMF, ADA, IFX, CZP, intravitreal fluocinolone acetonide	Complete improvement
Majumder et al. 2020	1	26, F	Vogt-Koyanagi-Harada disease	TOFA	Posterior uveitis	IVMP	Complete improvement
Miserocchi et al. 2020	4	1. 9, F 2. 1, F 3. 2, F 4. 10, M	Juvenile Idiopathic Arthritis	1. TOFA 2. BARI 3. BARI 4. BARI	1. Panuveitis 2. Panuveitis 3. Panuveitis 4. Panuveitis	1. IFX, ADA, LFN, ABA, RTX, TCZ. 2. MTX, ADA, IFX, RTX, ABA. 3. MTX, AZA, IFX, ADA, TCZ. 4. ETN, MTX, CsA, IFX, ADA, ABA, TCZ, RTX.	1. Complete improvement 2. Complete improvement 3. Complete improvement 4. Complete improvement
Kaneko et al. 2022	1	35, M	Rheumatoid Arthritis	BARI	Panuveitis	MTZ, SSZ, ADA, IFX	Complete improvement
Xiao-Bao et al. 2022	1	18, F	Idiopathic	TOFA	Panuveitis	MTX, MMF, CsA, ADA	Complete improvement
Tac et al. 2023	2	1. 16, F 2. 30, M	1.Behçet syndrome 2.Behçet syndrome	1.UPA 2.UPA	1. Panuveitis 2. Panuveitis	1. MTX, CsA, MMF, ADA 2.MTX, CsA, MMF, ADA	1. Complete improvement 2. Complete improvement
Blaquet-Walscheid et al. 2023	1	24, F	Juvenile Idiopathic Arthritis	UPA	Anterior uveitis	IVMP, MTX, AZA, CsA, ADA, IFX, TCZ, TOFA	Complete improvement
Kraev et al. 2024	1	42, F	Behçet syndrome and Ankylosing Spondylitis	UPA	Panuveitis	Local and systemic corticosteroids	Complete improvement
Present study, 2024	18	1. 26, F 2. 54, M 3. 67, F 4. 65, F 5. 69, M 6. 40, F 7. 55, M 8. 58, M 9. 48, F 10. 62, F 11. 8, F 12. 53, F 13. 53, F 14. 61, F 15. 42, F 16. 31, F 17. 45, F 18. 54, F	1. Blau Syndrome 2. Spondyloarthritis and Chron's disease 3. Ankylosing Spondylitis 4. Idiopathic 5. Ankylosing Spondylitis 6. Spondyloarthritis and ulcerative colitis 7. Ankylosing Spondylitis 8. Ankylosing Spondylitis 9. Ankylosing Spondylitis 10.Ankylosing Spondylitis 11. Idiopathic 12.Ankylosing Spondylitis 13.Ankylosing Spondylitis 14. Spondyloarthritis 15.Spondyloarthritis, Chron's disease and psoriasis 16. Idiopathic 17. Spondyloarthritis 18. Ankylosing Spondylitis	1. TOFA/BARI 2. UPA 3. UPA 4. BARI 5. UPA 6. TOFA 7. UPA 8. UPA 9. UPA 10. UPA 11. BARI 12. UPA 13. UPA 14. UPA 15. TOFA 16. UPA 17. UPA 18. UPA	1. Panuveitis 2. Anterior uveitis 3. Anterior uveitis 4. Panuveitis 5. Anterior uveitis 6. Anterior uveitis 7. Anterior uveitis, CME 8. Anterior uveitis 9. Anterior uveitis 10.Anterior uveitis 11 Intermediate uveitis 12.Anterior uveitis 13.Anterior uveitis 14.Anterior uveitis 15.Anterior uveitis 16. Panuveitis 17.Anterior uveitis 18.Anterior uveitis	1.MTX, ETN, ANA, ABA, ADA 2.MTX, AZA, IFX, ADA 3.SZP, ADA 4. MTX, AZA 5. MTX, ADA 6. MTX, AZA, ADA 7. MTX, IFX, GOLI 8. GOL, ADA 9. ADA 10. SSZ, ADA 11. MTX, ADA 12. SSZ, CsA, LFN IFX 13. SSZ, CsA, LFN IFX 14. DLQ, LFN, IFX, CZP, ADA, BIME 15. MTX, SSZ, ADA, IFX, SECU 16. ADA, CsA 17. SSZ, ADA, CZP 18. SSZ, IFX, ADA, SECU, GOL	1. Complete improvement 2. Complete improvement 3. Complete improvement 4. Complete improvement 5. Complete improvement 6. Complete improvement 7. Complete improvement 8. Complete improvement 9. Partial improvement 10. Complete improvement 11. Partial improvement 12. Complete improvement 13. Complete improvement 14. Complete improvement 15. Complete improvement 16. Complete improvement 17. Complete improvement 18. Complete improvement

TABLE. Case reports and literature review of patients with uveitis treated with Janus Kinase Inhibitors

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

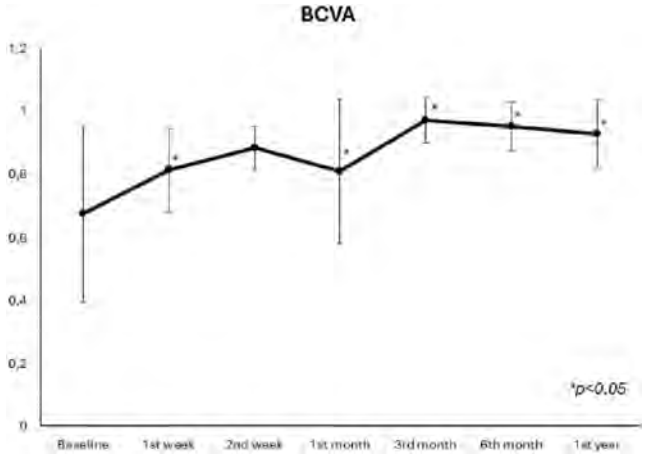


FIGURE 1. Rapid improvement of best corrected visual acuity (BCVA) following the start of JAKINIB

Background/Purpose: Non-infectious uveitis may be related to several immune-mediated diseases (IMIDs). Those that are refractory to conventional therapy or biologics may lead to severe ocular damage. Janus Kinase inhibitors (JAKINIB) had shown efficacy in refractory cases.

The objectives were to assess the efficacy and safety of JAKNIBs in patients with refractory uveitis due to IMIDs, and to review the updated literature.

Methods: Multicenter study of 18 patients with refractory uveitis due to IMIDs treated with different JAKNIBs. Our ocular variables evaluated were best corrected visual acuity (BCVA), anterior chamber cells and presence of cystoid macular edema, and they were recorded from baseline up to 1 year treatment.

We included patients with non-infectious uveitis treated with JAKNIBs for the literature review searched on PubMed, Embase and the Cochrane library up to 1st December 2024.

Results: We studied 18 patients from Spain and 13 cases from the literature were reviewed. They were 24 women and 7 men. There were panuveitis (n=12), anterior (n=17;), intermediate (n=1) and posterior uveitis (n=1).

26 patients with uveitis were secondary to IMIDs while 5 cases were idiopathic. The main underlying IMIDs were spondylarthritis (n=14) and juvenile idiopathic arthritis (n=6) **(Table)**.

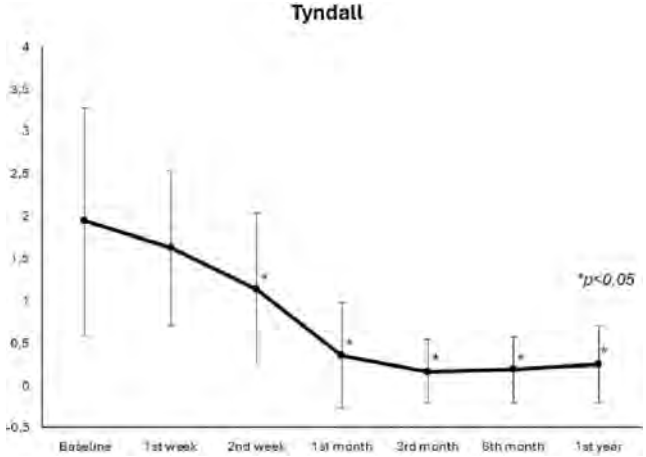


FIGURE 2. Decrease of Tyndall following the initiation of JAKNIB

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

They received treatment with conventional (n=26) or biological immunosuppressive drugs (n=27) before the JAKNIBs therapy. The JAKINIB most widely used was Upadacitinib (n= 17).

Complete clinical improvement was recorded after starting JAKNIBs treatment. 28 patients presented a complete improvement while the remaining patients showed partial improvement.

In the multicenter study, BCVA showed a rapid and maintained improvement **(Figure 1)** after 13 months of follow-up. From 14 patients with Tyndall + at baseline, 4 of them had a partial decrease in the first month (n=4) and resolved by the sixth month **(Figure 2)**. Two patients had cystic macular edema at baseline, resolved at 3 months of follow-up. No serious adverse effects were found.

Conclusion: Treatment with JAKNIBs in uveitis due to different IMIDs may be effective and safe, even in refractory to previous biological drugs patients.

Disclosure: N. Barroso Garcia: None; **L. Sánchez Bilbao**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **J. Martín-Varillas**: AbbVie, Pfizer, Lilly, Celgene, Janssen, and UCB Pharma, 5; **V. Calvo-Río**: AstraZeneca, 6, MSD, Roche, AbbVie, Lilly, Celgene, Grünenthal, and UCB Pharma, 2, 6; **M. Esteban Ortega**: None; **S. muñoz Fernández**: None; **J. Álvarez-Vega**: None; **E. Beltran**: Abbvie, Amgen, Janssen, MSD, Pfizer, Lilly, Novartis and UCB, 6; **V. Jovaní**: None; **O. Maiz Alonso**: None; **r. Veroz González**: None; **A. Garcia-Aparicio**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 1, 2, 6, UCB, 6; **m. Garijo Bufort**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0269

Clinical Landscape and Severity Markers of VEXAS Syndrome in a Spanish Cohort: Findings from VEXASSER Study Group

Paula Garca-Escudero[1], Marta Lpez[2], Berta Magallares[3], Dolly Viviana Fiallo Suárez[4], Diego Dios Santos[5], César Antonio Egües Dubuc[6], Santos Castañeda[7], Alicia Garcia[8], Isla Morante Bolado[9], Elena María Oliver García[10], Clara Garcia Belando[11], Cristina Corrales[12], Francisco Javier Toyos[13], Judit Font-Urgelles[14], Meritxell Salles Lizarzaburu[15], Carolina Merino[16], Irene Carrion[17], Jose Angel Hernandez[18], Lourdes Villalobos[19], Alina-Lucica Boteanu[20], Beatriz Frade Sosa[21], cristiana Sieiro[22], Irene Monjo Henry[23], Ernesto Trallero[24], Eugenia Enriquez[25], Maria Rodriguez[26], Elena Riera Alonso[27], Marta Ibañez[28], Delia Reina[29], Rafael Benito Melero González[30], Giuliano Boselli[31], Alberto Mariano[32], Ignacio Vázquez Gómez[33], Jose Alberto Miranda[34], Clara Moriano[35], Elena Aurrecoechea[36], Paloma Vela Casasempere[37], Iñigo Rúa-Figueroa[38], Jaime Calvo[39] and VEXASSER Study Group, [1]Hospital Universitario lava, Bilbao, Spain, [2]Complex Hospitalari Universitari Moiss Broggi, Barcelona, Spain, [3]Hospital de Sant Pau, Bareclona, [4]H.U. Doctor Negrín, Gran Canarias, [5]C. H. U. A Coruña, A Coruña, Spain, [6]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [7]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [8]Rheumatologist, La Laguna, Spain, [9]Rheumatology, Hospital General Sierrallana, Torrelavega, Spain., Santander, [10]H.C. U. Lozano Blesa, Zaragoza, [11]H.C. U. Virgen de la arrizaca, Murcia, [12]HOSPITAL UNIVERSITARIO MARQUES DE VALDECILLA, Santander, Spain, [13]Virgen Macarena University Hospital, Sevilla, Spain, [14]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [15]Rheumatology Department, Althaia Xarxa Assistencial Universitària Manresa Manresa (Spain)., Manresa, Spain, [16]Rheumatology department. Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda (Madrid), Madrid, Spain, [17]Hospital del Mar, Barcelona, Spain, [18]Hospital Universitario Insular de Gran Canaria, Las Palmas de Gran CanariaHospital, Spain, [19]Ramon y Cajal Hospital, MADRID, Spain, [20]H.U. Ramn y Cajal, Madrid, Spain, [21]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [22]Univrsity of Manchester, Manchester, United Kingdom, [23]Hospital Universitario La Paz, Madrid, Spain, [24]H. U. Vall d'Hebron, Barcelona, [25]Clnica Universidad de Navarra, Madrid, Spain, [26]H. Clínico San Carlos, Madrid, Spain, [27]Hospital Universitari Mùtua Terrassa, Terrassa, Spain, [28]Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [29]Complex Hospitalari Moisès Broggi, Barcelona, Spain, [30]C. H. U. de Ourense, Ourense, [31]Rheumatology Division, Hospital Universitario Miguel Servet, Zaragoza, Spain, Zaragoza, Aragon, Spain, [32]Virgen del Rocío University Hospital, Sevilla, Spain, [33]H.U. Doctor Peset, Valencia, [34]C. H. U. Lucus Augusti, Lugo, Spain, [35]Hospital Len, LEON, Castilla y Leon, Spain, [36]H. Sierrallana, Santander, [37]Hospital General

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [38]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [39]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: VEXAS syndrome is a rare disease caused by somatic mutations in *UBA1* gene. Different mutations in this gene appear to be associated with specific phenotypes, potentially influencing disease severity and progression. This work aims to describe the clinical, phenotypic, and laboratory characteristics of a Spanish cohort of patients with confirmed VEXAS syndrome and to evaluate associations between *UBA1* mutations, manifestations and mortality.

Methods: An observational, ambispective study conducted across rheumatology units in Spain, identifying patients with genetically confirmed VEXAS syndrome. Demographic, clinical, laboratory, and outcome data were collected. Statistical analyses were performed using standardized tests (significance set at $p < 0.05$).

Results: A total of 50 patients with VEXAS syndrome were identified, all male and of Caucasian origin. The mean age at symptom onset was 68.05 years (SD±10.24) and the mean age at diagnosis was 73.49 years (SD±8.72). The mean diagnostic delay was 5.79 years (SD±4.4). "*Table 1*" summarizes the most common initial misdiagnoses.

The most frequent clinical manifestations included cutaneous lesions (88%), arthritis, constitutional symptoms, non-infectious fever, (76% respectively), and chondritis (48%). Other hallmark features of the syndrome, such as pulmonary involvement, thromboembolic disease associated with VEXAS, and renal impairment, were observed in 38%, 32%, and 22% of the patients (see "*Table 2*").

Laboratory findings revealed anemia in 47 patients (94%), with macrocytosis in 41. The mean hemoglobin level was 9.89 g/dL (SD±2), and the mean MCV was 107.3 fL. Additionally, 23 patients (46%) presented with leukopenia (mean leukocyte count 5337/mm^3) and 22 (44%) with thrombocytopenia (mean platelet count 136950/mm^3). MDS was present in 44% of the cases, while MGUS was identified in 26% (see "*Table 2*").

Genetic analysis identified the leucine variant as the most frequent UBA1 mutation (40%, n=20), followed by threonine (36%, n=18) and valine (16%, n=8). Four patients harbored other UBA1 mutations, two of which were classified as VUS (c.1798A >G, p.Thr600Ala and c.209T >A, p.Leu70His), previously unreported. Significant associations were found between leucine and MGUS, threonine and thrombocytopenia, and valine and renal involvement. Non-significant numerical trends included leucine with Sweet's syndrome (inverse with medium-vessel vasculitis), threonine with thromboembolic disease, and valine with multisystemic involvement ("*Image 1*").

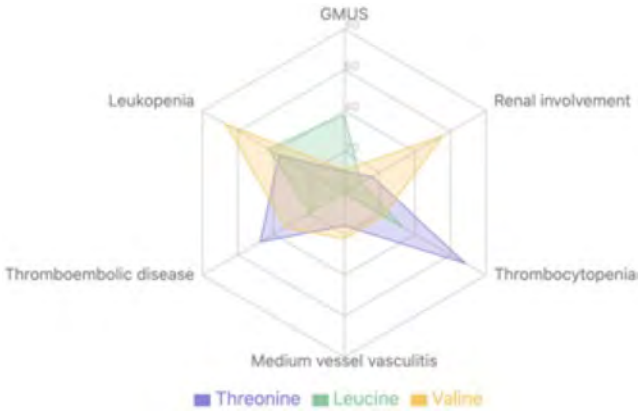
"Table 1". Most common initial misdiagnoses.

Previous diagnosis	*n*
Seronegative arthritis	9
Relapsing polychondritis	7
Rheumatic polymyalgia	5
Sweet's síndrome	4
Systemic lupus erythematosus	3
Medium vessel vasculitis	3

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

"Table 2". Clinical characteristics and laboratory findings according to main mutations.

	Total *n=50* (%)	Leucine *n*=20	Threonine *n*=18	Valine *n*=8	*p*-value
Skin lesions	44 (88%)	18 (90%)	16 (88.88%)	8 (100%)	
Neutrophilic dermatosis	25 (50%)	13 (65%)	14 (77.77%)	4 (50%)	
LCV	10 (20%)	5 (35%)	3 (16.66%)	2 (25%)	
Constitutional syndrome	38 (76%)	14 (70%)	15 (83,33%)	6 (75%)	
Non infectious fever	38 (76%)	13 (65%)	14 (77.77%)	8 (100%)	
Arthritis	38 (76%)	17 (85%)	14 (77.77%)	4 (50%)	
Chondritis	24 (48%)	11 (55%)	11 (61.11%)	2 (25%)	
Perichondritis	24 (48%)	11 (55%)	11(61.11%)	2 (25%)	
Nasal chondritis	8 (16%)	3 (15%)	4 (22.22%)	1 (12.5%)	
Ocular lesions	28 (56%)	8 (40%)	9 (50%)	2 (25%)	
Pulmonary involvement	19 (38%)	6 (30%)	7 (38.88%)	5 (62.5%)	
Tromboembolic disease	16 (32%)	4 (20%)	9 (50%)	3 (37.5%)	
Periorbital edema	13 (26%)	3 (15%)	7 (38.88%)	3 (37.5%)	
Renal involvement	11 (22%)	2 (10%)	4 (22.22%)	**5 (62.5%)**	**<0.01**
Splenomegaly	9 (18%)	5 (25%)	3 (16.66%)	1 (12.5%)	
Hepatomegaly	5 (10%)	1 (5%)	3 (16.66%)	1 (12.5%)	
Hypoacusis	9 (18%)	2 (10%)	5 (27.77%)	1 (12.5%)	
Medium vessel vasculitis	7 (14%)	0 (0%)	3 (16.66%)	2 (25%)	
Orchitis	5 (10%)	1 (5%)	3 (16.66%)	1 (12.5%)	
Epididymitis	4 (8%)	0 (0%)	3 (16.66%)	1 (12.5%)	
Cardiac involvement	3 (6%)	1 (5%)	1 (5.55%)	1 (12.5%)	
Anemia	47 (94%)	18 (90%)	18 (100%)	7 (87.5%)	
Leukopenia	23 (46%)	10 (50%)	7 (38.88%)	6 (75%)	
Thrombocytopenia	22 (44%)	7 (35%)	**13 (72.22%)**	2 (25%)	**<0.05**
MDS	22 (44%)	7 (35%)	8 (44.44%)	4 (50%)	
MGUS	13 (26%)	**8 (40%)**	2 (11.11%)	1 (12.5%)	**<0.05**
MM	7 (14%)	4 (20%)	1 (5.55%)	2 (25%)	



"Image 1". Mutations and main clinical associations.

Mortality occurred in 11 patients (22%), with only 6 deaths (12%) related to VEXAS activity. Periorbital edema was significantly associated with VEXAS-related death (5/6, p=0.006). No significant mortality differences were found between UBA1 variants.

Conclusion: Patients with VEXAS syndrome in this cohort are predominantly older males presenting with cutaneous, constitutional, and articular symptoms, reflecting a "*rheumatologic profile*". Specific genotype-phenotype correlations were identified (leucine: MGUS, threonine: thrombocytopenia, valine: renal involvement), along with potential severity markers (periorbital edema: mortality).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Garcia-Escudero: None; **M. Lopez**: None; **B. Magallares**: None; **D. Fiallo Suárez**: None; **D. Dios Santos**: None; **C. Egües Dubuc**: None; **S. Castañeda**: None; **A. Garcia**: None; **I. Morante Bolado**: None; **E. Oliver García**: None; **C. Garcia Belando**: None; **C. Corrales**: None; **F. Toyos**: None; **J. Font-Urgelles**: None; **M. Salles Lizarzaburu**: None; **C. Merino**: None; **I. Carrion**: None; **J. Hernandez**: None; **L. Villalobos**: None; **A. Boteanu**: GSK, 5, 6; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **c. Sieiro**: None; **I. Monjo Henry**: None; **E. Trallero**: None; **E. Enriquez**: None; **M. Rodriguez**: None; **E. Riera Alonso**: None; **M. Ibañez**: None; **D. Reina**: None; **R. Melero González**: None; **G. Boselli**: None; **A. Mariano**: None; **I. Vázquez Gómez**: None; **J. Miranda**: None; **C. Moriano**: None; **E. Aurrecoechea**: None; **P. Vela Casasempere**: None; **I. Rúa-Figueroa**: None; **J. Calvo**: None.

Abstract Number: 0270

Diagnostic Challenge of IgG4-related Disease: Comparison Between ACR/EULAR, Umehara, and Okazaki Criteria

Rafael Gálvez Sánchez[1], Ivan Ferraz Amaro[2], Fernando Lopez Gutierrez[3], Javier Loricera[4], Pablo Martínez Calabuig[5], Jorge Juan Fragío Gil[6], Roxana González Mazarí[7], Cristina Hormigos Martín[8], DALIFER FREITES[9], Maria Rodríguez Laguna[8], Patricia Moya Alvarado[10], Marta López I Gómez[11], Hector Corominas Macia[10], Maite Silva Díaz[12], Guillermo González Arribas[12], Angel García Aparicio[13], Judit Font-Urgelles[14], Ivette Casafont Solé[15], Elisabet Castaneda[16], Carolina Merino Argumánez[17], Raquel Zas Vaamonde[18], Juan Molina Collada[19], Sergio Rodríguez Montero[20], Rafael Melero Gonzalez[21], Eva Galíndez Agirregoikoa[22], Andrea Hernández[23], Lucia Pantoja Zarza[24], Ignacio Braña Abascal[25], Vega Jovaní[26], Elia Valls Pascual[27], Natalia Mena Vázquez[28], ADELA MARIA GALLEGO FLORES[29], Noelia Cabaleiro Raña[30], Raúl Veroz González[31], Mariano Andrés[32], Santos Castañeda Sainz[33], Ricardo Blanco[34] and Grupo de cooperación nacional de enfermedad relacionada con IgG4, [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [2]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [3]Hospital Universitario Marqués de Valdecilla, Immunopathology Group -IDIVAL, Reumatología, Santander, Santander, Spain, [4]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [5]Hospital General Universitario de Valencia, Spain/ Uversidad Catolica de Valencia San Vicente Martir, Valencia, Spain, Ontinyent, Spain, [6]Hospital General Universitario, Valencia, Spain, [7]Hospital General Universitario de Valencia, Reumatología, Valencia, Valencia, Spain, [8]Hospital Clínico San Carlos, Reumatología, Madrid, Madrid, Spain, [9]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [10]Hospital de Sant Pau, Reumatología, Barcelona, Barcelona, Spain, [11]Hospital Universitario de Araba, Reumatología, Vitoria, Vitoria, Spain, [12]Complejo Hospitalario Universitario de A Coruña, Reumatología, A Coruña, Spain, [13]Hospital Universitario de Toledo, Reumatología, Toledo, Toledo, Spain, [14]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [15]Hospital German Trias i Pujol, Reumatología, Badalona, Badalona, Spain, [16]Hospital Universitario Infanta Sofía, Reumatología, Madrid, Madrid, Spain, [17]Hospital Universitario Puerta del Hierro, Reumatología, Madrid, Madrid, Spain, [18]Hospital Universitario 12 de Octubre, Reumatología, Madrid, Madrid, Spain, [19]Hospital General Universitario Gregorio Marañón, Reumatología, Madrid, Madrid, Spain, [20]Hospital Universitario de Valme, Reumatología, Sevilla, Sevilla, Spain, [21]Hospital Alvaro Cunqueiro, Reumatología, Vigo, Vigo, Spain, [22]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [23]Hospital Universitario de Gran Canaria Dr Negrin, Reumatología, Palmas de Gran Canaria, Gran Canaria, Spain, [24]Hospital General de Segovia, Reumatología, Segovia, Segovia, Spain, [25]Hospital Universitario Central de Asturias, Reumatología, Oviedo, Oviedo, Spain, [26]Hospital General Universitario de Alicante, Reumatología, Alicante, Alicante, Comunidad Valenciana, Spain, [27]Hospital General de Valencia, Reumatología, Valencia, Valencia, Spain, [28]Hospital Regional Universitario de Málaga, Reumatología, Málaga, Malaga, Spain, [29]Complejo Hospitalario don Benito Villanueva, Reumatología, Badajoz, Badajoz, Extremadura, Spain, [30]Hospital Universitario Montecelo, Reumatología, Pontevedra, Pontevedra, Spain, [31]Hospital de Mérida, Reumatología, Mérida, Mérida, Spain, [32]Hospital General Universitario de Alicante, Reumatología, Alicante, Alicante, Spain, [33]Hospital Universitario La Princesa, Reumatología, Madrid Grupo de cooperación nacional de enfermedad relacionada con IgG4: Blanca García Magallón (Hospital Universitario Puerta del Hierro), Maite Odriozola Gil (Hospital Universitario de Valme), Cristina Arciniega (Hospital de Mérida), Maria Lourdes Mateo Soria (Hospital German Trias i Pujol), Santiago Muñoz (Hospital Universitario Infanta Sofía), Iñigo Jesús Rua Figueroa, (Hospital Universitario de Gran Canaria Dr Negrin), Sabela Fernández Aguado, (Hospital de Montecelo)., Madrid, Spain, [34]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a rare immune-mediated condition characterized by fibrosclerosing inflammation, elevated serum and tissue IgG4 levels, and heterogeneous clinical manifestations. Several classification criteria have been proposed, including ACR/EULAR (2019) (1), Umehara (2011) (2), and Okazaki (2012) (3). The objective of this study is to analyze the concordance and differences among the main IgG4-RD classification criteria.

Methods: Observational multicenter study of patients diagnosed with IgG4-RD by expert rheumatologists across 25 Spanish hospitals. The ACR/EULAR, Umehara, and Okazaki classification criteria were applied to determine which patients fulfilled each set. Concordance between the criteria was assessed using PABAK index (prevalence- and bias-adjusted kappa). A Venn diagram was used to represent the overlap among the different criteria, illustrating how many patients fulfilled only one, shared more than one, or met none. Notably, patients who did not fulfill any of the established classification criteria but were diagnosed with IgG4-RD based on expert clinical judgment were categorized as having an exclusive clinical diagnosis. In addition, clinical, demographic, and laboratory data were analyzed for each subgroup.

Results: We include 68 patients (43 men/25 women) diagnosed as IgG4-RD by expert rheumatologists; mean age was 54.4 years. Of them 37 (54.4%) met Okazaki and ACR/EULAR criteria; 16 (23.5) were classified based exclusively on clinical criteria and 13 (19.1%) met Umehara. Concordance between criteria was variable. PABAK showed low-moderate agreement between ACR/EULAR and Umehara (PABAK 0.264), and between Umehara and Okazaki (PABAK 0.441), while the exclusive clinical criterion showed significant discordance, with negative PABAK values (**Table 1**). Patients classified according to Umehara showed a higher prevalence of pancreatic involvement (47.1%), whereas those classified by ACR/EULAR had more glandular involvement (32.4%). In contrast, the exclusive clinical group exhibited a less typical profile, with lower prevalence of pancreatic involvement (6.2%). Serum IgG4 levels were highest in the Umehara group (303.4 mg/dL). Additional clinical, laboratory, and complementary characteristics are shown in **Table 2**. When comparing the two most recent criteria, ACR/EULAR and Okazaki, no statistically significant differences were observed. According to the Venn diagram (**Figure**), only 8 patients met the three criteria simultaneously, 14 met only the Okazaki criteria, 9 met only ACR/EULAR, and none met exclusively Umehara criteria. The greatest overlap was between ACR/EULAR and Okazaki, with 15 patients meeting both sets of criteria.

Conclusion: Concordance among classification criteria was low. These results highlight the inherent challenges in diagnosing IgG4-related disease. Currently available criteria appear to prioritize different aspects of the disease, which may limit their ability to capture the complexity of the clinical picture and hinder their consistent application in clinical practice. A new universally accepted classification criteria for IgG4-related disease are still an unmet need.

Table 1. Concordance of Classification Criteria: PABAK (95% CI) Between ACR/EULAR, Umehara, Okazaki, and Exclusive Clinic

PABAK IC 95%	ACR/EULAR	Umehara	Okazaki	Exclusive Clinic
ACR/EULAR	-			
Umehara	0.264 (0.03 – 0.49)	-		
Okazaki	0.176 (-0.06 – 0.40)	0.441 (0.22 – 0.65)	-	
Exclusive Clinic	-0.558 (-0.68 – -0.29)	-0.294 (-0.45 – -0.05)	-0.558 (-0.68 – -0.29)	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Comparison of the Different Classification Criteria for IgG4-Related Disease (Umehara, Exclusive Clinical, Okazaki, and ACR/EULAR), Including Demographic Data, Clinical Manifestations, and Complementary Tests

	Total Patients (N=68)	Umehara Definitive (N=13)	Exclusive Clinical (N=16)	Okazaki (N=37)	ACR/EULAR (N=37)	ACR vs Okazaki p value
Demographic Data						
Age at Diagnosis (SD)	54.4 ± 15.2	54 ± 14.7	56.2 ± 17.4	53.4 ± 16.8	52.7±15.3	0.85
Sex (Male %)	43 (63.2)	8 (61.5)	14 (87.5)	17 (45.9)	24 (64.8)	0.10
Clinical Manifestations n (%)						
Glandular	14 (20.6)	4 (30.7)	1 (6.2)	7 (18.9)	12 (32.4)	0.18
Lacrimal	9 (13.2)	3 (23.1)	1 (6.2)	6 (16.2)	8 (21.6)	0.56
Submandibular	1 (1.5)	0	0	1 (2.7)	1 (2.7)	0.99
Parotid	11 (16.1)	3 (23.1)	0	6 (16.2)	10 (27)	0.26
Sinusal	0	0	0	0	0	0.99
Pleuro/Pulmonary	15 (22.1)	3 (23.1)	3 (18.7)	7 (18.9)	9 (24.3)	0.57
Pancreatic	12 (17.6)	6 (47.1)	1 (6.2)	4 (10.8)	10 (27)	0.08
Hepatic	2 (2.9)	0	0	2 (5.4)	1 (2.7)	0.55
Biliary Tract	10 (14.7)	6 (47.1)	1 (6.2)	4 (10.8)	8 (21.6)	0.21
Renal	17 (25)	6 (47.1)	3 (18.7)	9 (24.3)	12 (32.4)	0.44
Peritoneal	23 (33.8)	2 (15.4)	7 (43.7)	10 (27)	12 (32.4)	0.61
Aortic	14 (20.6)	2 (15.4)	5 (31.2)	4 (10.8)	9 (24.3)	0.13
Orbital	15 (22.1)	2 (15.4)	5 (31.2)	6 (16.2)	6 (16.2)	0.99
Lymphadenopathy	30 (44.1)	9 (69.2)	6 (37.5)	15 (40.5)	17 (45.9)	0.64
N° of organs affected (SD)	2.88 ±1.68	3.90 ±1.67	2.4 ± 1.45	2.82 ± 1.57	3.36 ± 1.79	0.17
Lab Test at Diagnosis						
IgG (SD)	1389.7 ± 461	1692.9 ± 743	1289.3 ± 637	1435.4 ± 739	1449.1 ± 713	0.94
IgG4 (SD)	181.5 ± 315	303.4 ± 205	109.8 ± 123	242.4 ± 387	163.6 ± 387	0.39
CPR (SD)	10.7 ± 20.9	10.4 ± 24.1	15.3 ± 29.6	7.4 ±10.9	9.6 ± 10.9	0.54
ESR (SD)	40.1 ± 20.9	25.6 ± 17.1	37.1 ± 35.6	41.55 ± 35.1	40.7 ± 35.1	0.94
Pathological Complementary Tests n (%)						
CT	57 (83.8)	13 (100)	12 (75)	32 (86.5)	33 (89.1)	0.73
PET	33 (48.5)	3 (23.1)	11 (68.7)	15 (40.5)	17 (45.9)	0.64
MRI	26 (38.2)	8 (61.5)	8 (50)	13 (35.1)	11 (29.7)	0.62
Compatible biopsy	32 (47.1)	7 (53.8)	3 (18.7)	21 (56.7)	20 (54)	0.82

Abbreviations (in alphabetical order): n: number; SD: standard deviation

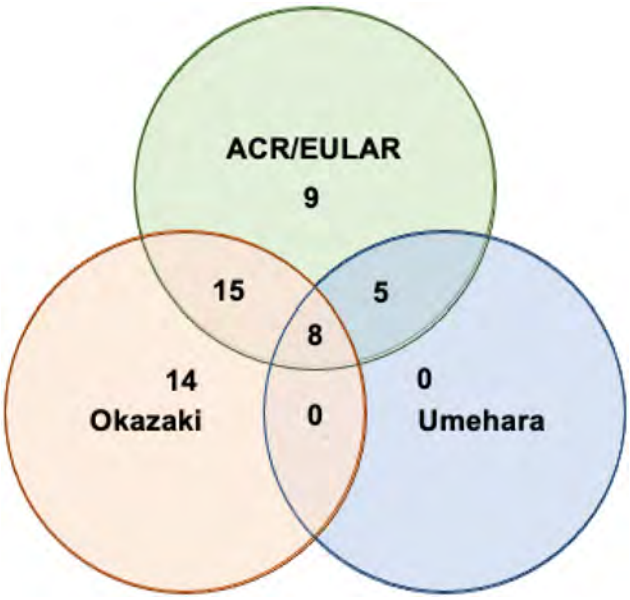


Figure: Venn diagram showing the overlap of patients classified as IgG4-RD according to each of the ACR/EULAR, Umehara, and Okazaki criteria.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Gálvez Sánchez: None; **I. Ferraz Amaro**: None; **F. Lopez Gutierrez**: Roche, Galápagos, Novartis, UCB Pharma, MSD, Celgene, Astra Zeneca, Grünenthal, Janssen, Abbvie, Lilly, Pfizer, 12, support for attending meetings and/or travel; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **P. Martínez Calabuig**: None; **J. Fragío Gil**: Quibim, 1; **R. González Mazarí**: None; **C. Hormigos Martín**: None; **D. FREITES**: None; **M. Rodríguez Laguna**: None; **P. Moya Alvarado**: None; **M. López I Gómez**: None; **H. Corominas Macia**: None; **M. Silva Díaz**: None; **G. González Arribas**: None; **A. García Aparicio**: None; **J. Font-Urgelles**: None; **I. Casafont Solé**: None; **E. Castaneda**: None; **C. Merino Argumánez**: None; **R. Zas Vaamonde**: None; **J. Molina Collada**: None; **S. Rodríguez Montero**: None; **R. Melero Gonzalez**: None; **E. Galíndez Agirregoikoa**: None; **A. Hernández**: None; **L. Pantoja Zarza**: None; **I. Braña Abascal**: None; **V. Jovaní**: None; **E. Valls Pascual**: None; **N. Mena Vázquez**: None; **A. GALLEGO FLORES**: None; **N. Cabaleiro Raña**: None; **R. Veroz González**: None; **M. Andrés**: None; **S. Castañeda Sainz**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0271

Clinical Presentation of Igg4-Related Disease. Multicenter Study and Literature Review

Rafael Gálvez Sánchez[1], Fernando Lopez Gutierrez[2], Javier Loricera[3], Pablo Martínez Calabuig[4], Jorge Juan Fragío Gil[5], Roxana González Mazario[6], Cristina Hormigos Martin[7], DALIFER FREITES[8], Maria Rodriguez Laguna[9], Patricia Moya Albarado[10], Marta López i Gómez[11], Hector Corominas[12], Maite Silva-Diaz[13], GUILLERMO GONZALEZ ARRIBAS[14], Angel Garcia-Aparicio[15], Judit Font-Urgelles[16], Ivette Casafont-Solé[16], elisabeth Castañeda[17], Carolina Merino[18], Raquel Zas[19], Juan Molina-Collada[20], Sergio Rodríguez Montero[21], Rafael B. Melero-González[22], Eva Galíndez Agirregoikoa[23], Andrea Hernández[24], Lucia Pantoja[25], Ignacio Braña[26], Vega Jovaní[27], Elia Valls-Pascual[28], Natalia Mena Vzquez[29], Adela Gallego[30], Noelia Cabaleiro Raña[31], Raul Veroz[32], Mariano Andrs Collado[33], Santos Castañeda[34], Ricardo Blanco[35] and IgG4 Related Disease National Collaborative Group, [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, Immunopathology Group -IDIVAL, Reumatología, Santander, Santander, Spain, [3]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [4]Hospital General Universitario de Valencia, Spain/ Uversidad Catolica de Valencia San Vicente Martir, Valencia, Spain, Ontinyent, Spain, [5]Hospital General Universitario, Valencia, Spain, [6]Hospital General de Valencia, Valencia, Spain, [7]Hospital Clínico San Carlos, Madrid, Spain, [8]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [9]Hospital Clinico San Carlos, Madrid, Spain, [10]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [11]Hospital Universitario de Araba, Vitoria, Pais Vasco, Spain, [12]Hospital de Sant Pau, Barcelona, Spain, [13]Complexo Hospitalario Universitario A Corua, A Corua, Galicia, Spain, [14]Facultativo especialista, PALMA DE MALLORCA, Galicia, Spain, [15]Hospital Universitario de Toledo, Toledo, Spain, [16]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [17]Hospital Universitario Infanta Sofía, Madrid, Madrid, Spain, [18]Rheumatology department. Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda (Madrid), Madrid, Spain, [19]Hospital Universitario Doce de Octubre, Madrid, Spain, [20]Department of Rheumatology, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Spain, [21]Hospital Universitario de Valme, Sevilla, Andalucia, Spain, [22]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [23]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [24]Hospital Universitario de Gran Canaria Dr Negrin, Palmas de Gran Canaria, Canarias, Spain, [25]Complejo Hospitalario Segovia, Segovia, Spain, [26]Hospital Universitario Central de Asturias, Oviedo, Spain, [27]Hospital General Universitario de Alicante, Reumatología, Alicante, Alicante, Comunidad Valenciana, Spain, [28]Hospital General de Valencia, Valencia, Comunidad Valenciana, Spain, [29]Hospital Regional Universitario de Malaga, Malaga, Spain, Mlaga, Spain, [30]Complejo Hospitalario don Benito Villanueva, Badajoz, Spain, [31]Hospital Universitario Montecelo, Rheumatology, Pontevedra, Galicia, Spain, [32]Hospital de Merida, Merida, Extremadura, Spain, [33]Hospital General Universitario de Alicante, Madrid, Comunidad Valenciana, Spain, [34]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [35]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory entity that can involve almost every organ, with characteristic histological features. Its pathogenesis remains poorly understood, clinical features are heterogeneous and unspecific, and recently released classification criteria have poorer performance in early recognition of the disease. Therefore, regrettably IgG4-RD continues to be underdiagnosed. Our objetives were a) To evaluate the clinical characteristics of patients diagnosed with IgG4-RD; and b) to compare it with other large series.

Reference	Cases	Sex Female (F)/ Male (M)	Age, median [IQR] or mean±SD	Diagnosis criteria	Number of organs affected	Level of serum IgG4 (mg/dL), median [IQR]
Lanzillotta et al. Rheumatology 2020	131	F (n=36), M (n=95)	62 [53-70]	-Umehara: possible (46%), probable (2%), definitive (52%)	-1 organ (26%) -More of 1 organ (74%)	224 [115-382]
An et al. Orphanet J Rare Dis 2022	127	F (n=35), M (n=92)	63 [55-69]	-Umehara: possible (82.6%), probable (2.3%), definitive (11.8%)	-1 organ (20%) -2-4 organs (68%) -More of 5 organs (9%)	980 [390-1520]
Zongfei et al. Clin Rheumatol 2021	102	F (n=25), M (n=77)	62 [54.1-65.8]	-Okazaki (100%)	Median [IQR]: 2 [1-3]	399 [199-776]
Wang et al. Arthritis Res Ther 2018	215	F (n=67), M (n=148)	54 [46-62]	-Umehara: possible (47.9%), probable (4.7%), definitive (47.4%)	-1-2 organs (36%) -3-4 organs (47%) -5 or more organs (17%)	896 [350-1860]
Inoue et al. Medicine (Baltimore) 2015	235	F (n=189), M(n=46)	67	-Symptoms+laboratory+image/ Compatible histology (100%)	-1 organ (41%) -2 or more organs (59%)	470 [ND]
Wallace et al. Arthritis Rheumatol 2015	125	F (n=49), M (n=76)	50,3±14.9	- Symptoms+laboratory+image/ Compatible histology (100%)	-1 organ (38%) -2 organs (24%) -3 or more organs (38%)	ND
Current series	68	F (n=25), M (n=48)	54 ± 15,16	-Okazaki: 51,4% -Umehara: possible (5,9%), probable (5%), definitive (45,6%) -ACR/EULAR 2020 (51.4%) -Symptoms+laboratory+image/ Compatible histology (23,6%)	-1 organ (26%) -2 organs (26%) -3 or more organs (46%)	109 [49.5-188]

TABLE. Main features of the patients with IgG4-RD in series of more than 100 patients and in current series

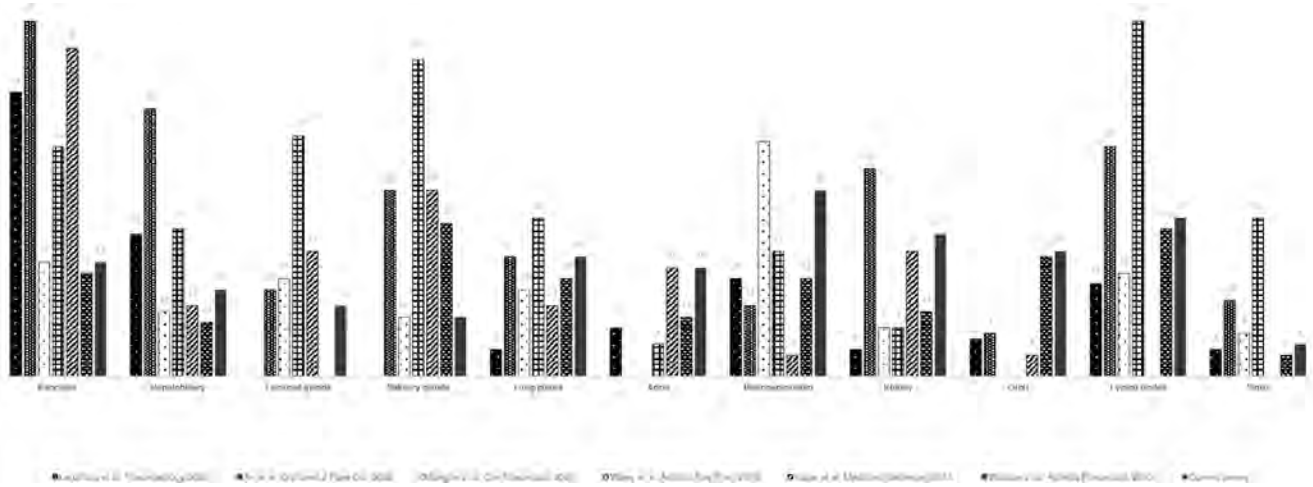


FIGURE. Involved organs in series of more than 100 patients and in current series. Data are in %

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Observational multicenter study of patients diagnosed with IgG4-RD and literature review. Diagnosis was made accordingly to these criteria: a) Okazaki; b) Umehara; c) ACR/EULAR 2020; and/or d) clinical, laboratory and imaging suggestive findings (1-3). For the literature review, we searched PubMed and the Cochrane library from its inception until 30 November 2024, selecting those series with the largest number of patients.

Results: We studied 78 patients diagnosed with IgG4-RD (48 males/25 females, mean±SD age; 54.4±15 years). The main affected organs were lymph nodes (n=29; 42,6%), retroperitoneum (n=23; 33.8%), kidney (n=18; 26.5%), orbit (n=16; 23.5%), aorta (n=14; 20.5%), lung/pleura (n=15; 22.%), pancreas (14; 20.6%), salivary glands (n=11; 16.1%), ear nose and throat (n=9; 16.6%), lacrimal glands (n=9; 13.2%), liver/biliary duct (n=11; 16.1%), pachymeninges (n=3; 5.5%), mesenterium (n=2; 3.7%) and other 9 (n=16.6%). IgG4 values were above 135mg/dL in 23 (33,8%) patients (median 109 mg/dL [IQR 49,5-188]). Median values of CRP and ESR were 2.6 mg/dL [IQR 0.77-13.6] and 29 mm/h [IQR 11-56], respectively. In the literature review, 6 series of more than 100 patients each were selected. The main data from the different series are listed in table. The figure shows the most frequently affected organs in the different series. The pancreas and salivary glands were less frequently involved in our series. In contrast, aortic, retroperitoneum and lung/pleura were more frequently involved than in most of the other series.

Conclusion: IgG4-RD is a very heterogeneous disease with involvement of virtually every organ of the anatomy, usually presenting with involvement of more than one organ. Despite the name of the entity, serum IgG4 is not always elevated.

References:

1. Okazaki K et al. Int J Rheumatol. 2012. PMID: 22690221
2. Umehara H, et al. Mod Rheumatol. 2012. PMID: 21881964
3. Wallace ZS et al. Arthritis Rheumatol. 2020. PMID: 3179325

Disclosure: R. Gálvez Sánchez: None; **F. Lopez Gutierrez**: Roche, Galápagos, Novartis, UCB Pharma, MSD, Celgene, Astra Zeneca, Grünenthal, Janssen, Abbvie, Lilly, Pfizer, 12, support for attending meetings and/or travel; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **P. Martínez Calabuig**: None; **J. Fragío Gil**: Quibim, 1; **R. González Mazario**: None; **C. Hormigos Martin**: None; **D. FREITES**: None; **M. Rodriguez Laguna**: None; **P. Moya Albarado**: None; **M. López i Gómez**: None; **H. Corominas**: None; **M. Silva-Diaz**: None; **G. GONZALEZ ARRIBAS**: None; **A. Garcia-Aparicio**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 1, 2, 6, UCB, 6; **J. Font-Urgelles**: None; **I. Casafont-Solé**: None; **e. Castañeda**: None; **C. Merino**: None; **R. Zas**: None; **J. Molina-Collada**: None; **S. Rodríguez Montero**: Abbvie, Pfizer, Roche, UCB, Novartis, 12, Financial supporto for attending meetings or travel; **R. Melero-González**: None; **E. Galíndez Agirregoikoa**: None; **A. Hernández**: None; **L. Pantoja**: None; **I. Braña**: None; **V. Jovaní**: None; **E. Valls-Pascual**: None; **N. Mena Vazquez**: None; **A. Gallego**: None; **N. Cabaleiro Raña**: None; **R. Veroz**: None; **M. Andres Collado**: Grünenthal, Menarini, 6, 12, Attending meetings or travel; **S. Castañeda**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0272

Ocular Involvement in Behçet's Disease: Comparative Study of Two Classification Criteria in Clinical Practice

Rafael Gálvez Sánchez[1], José Luis Martín-Varillas[2], Lara Sánchez Bilbao[3], Ivan Ferraz Amaro[4], Elena Aurrecoechea[5] and Ricardo Blanco[3], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [2]Rheumatology Division, Hospital de Laredo. IDIVAL, Immunopathology Group. Santander, Spain., Laredo, Spain, [3]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [4]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [5]Hospital Sierrallana, CANTABRIA, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Ocular involvement is a potential severe complication of Behçet's Disease (BD). The traditional classification, by the International Study Group (ISG, 1990) requires the mandatory presence of recurrent painful oral ulcers, whereas the International Criteria for BD (ICBD, 2013) uses a scoring system without mandatory oral ulcers.

Our objective was to assess the frequency and type of ocular manifestations accordingly to these classification criteria and compare the sensitivity and concordance of ISG versus ICBD, focusing on the impact of including or excluding ophthalmologic involvement and highlighting therapeutic implications.

Methods: Observational study of 142 BD, diagnosed by expert rheumatologists in Northern Spain (January 1980-November 2023). ISG and ICBD criteria were applied to these patients. Ocular manifestations included anterior, intermediate and posterior uveitis, panuveitis, dry eye, scleritis, episcleritis, and peripheral ulcerative keratitis (PUK). Proportions for each ocular manifestation were compared between the two classification sets, and p-values were provided to assess statistical significance. We calculated proportions for each ocular feature, assessed statistical significance (p-values), and evaluated sensitivity and concordance (Cohen's Kappa, Prevalence and Bias Adjusted Kappa - PABAK) when ocular involvement was included or excluded.

ICBD criteria showed greater sensitivity than ISG, specially due to the absence of oral ulcers in certain patients. Classifying these additional patients by ICBD facilitated the initiation of on-label biologic treatments (e.g., monoclonal anti-TNF), potentially improving the management of BD, particularly for those with ocular involvement and without oral ulcers.

Results: We studied 142 patients diagnosed as BD by expert rheumatologists, 84 met the ISG criteria while 116 met the ICBD criteria. Therefore, there were 32 additional patients with ICBD (**Table 1)**.

Among ISG-classified patients (n=84), ocular lesions were present in 49 patients (58.3%), while among ICBD-classified patients (n=116), 55 patients (47.4%) had ocular involvement (p=0.13). The frequency of uveitis (n=42; 50% ISG vs. n=47; 40.5% ICBD; p=0.18), and subtype (anterior, posterior, or panuveitis) were similar in both groups. With ocular inclusion, the non-adjusted Kappa was 0.405 (95% CI: 0.176–0.634), and the PABAK was 0.788, indicating strong agreement; without ocular inclusion, these values decreased to 0.443 (95% CI: 0.326–0.561) and 0.408 respectively, as shown on **Table 2**. Of the 32 patients classified as BD exclusively by ICBD, 7 were on anti-TNF therapy (3 infliximab, 4 adalimumab) and 2 on apremilast; 5 had uveitis and not oral ulcers with 1 receiving infliximab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Main clinical features according to different diagnosis criteria focusing on the ocular manifestations and biological treatments.

	Expert Diagnosis (N=142)	ISG criteria (N=84)	ICBD criteria (N=116)	ISG vs ICBD p value
Demographic data				
Age, mean (SD)	36.4 (13.9)	35 (12.8)	37 (13.2)	
Gender, n (%)				
Male	73 (51.4)	41 (48.8)	57 (49.1)	0.80
Female	69 (48.6)	43 (51.2)	59 (50.9)	0.59
Clinical Manifestations n (%)				
Oral aphthosis	135 (95.1)	84 (100)	115 (99.1)	0.99
Recurrent (3 times/year)	115 (81)	72 (85.7)	102 (87.9)	0.80
Genital aphthosis	88 (62)	67 (79.7)	88 (75.8)	0.63
Skin manifestations	91 (64.1)	74 (88.1)	79 (68.1)	0.01
Ocular lesions	60 (42.3)	49 (58.3)	55 (47.4)	0.13
Uveitis	52 (36.6)	42 (50)	47 (40.5)	0.18
Anterior	20 (14.1)	20 (23.8)	20 (17.2)	0.25
Intermediate	3 (2.1)	0	2 (1.7)	0.51
Posterior	14 (9.9)	11 (13.1)	13 (11.2)	0.68
Panuveitis	14 (9.9)	10 (11.9)	11 (9.5)	0.58
Unilateral	29 (20.4)	25 (29.8)	28 (24.1)	0.37
Bilateral	23 (16.2)	17 (20.2)	19 (16.4)	0.49
Dry Eye	8 (5.6)	7 (8.3)	8 (6.9)	0.71
Scleritis	0	0	0	0.99
Episcleritis	4 (2.8)	3 (3.6)	4 (3.4)	0.99
PUK	1 (0.7)	1 (1.2)	1 (0.86)	0.90
Joint manifestations	87 (61.3)	52 (61.9)	71 (61.2)	0.99
Neurological manifestations	29 (20.4)	13 (15.4)	22 (18.9)	0.65
Vascular manifestations	19 (13.4)	9 (10.7)	17 (14.6)	0.54
Complementary tests n (%)				
Pathergy test positive	7 (5)	6 (7.1)	6 (5.1)	0.78
HLA 51 Positive	51 (36)	25 (29.7)	38 (32.7)	0.76
Treatment n (%)				
Anti- TNF treatment	36 (25.3)	28 (33.3)	35 (30.1)	0.63
Infliximab	15 (10.5)	12 (14.2)	15 (12.9)	0.78
Adalimumab	20 (14.1)	15 (17.8)	19 (16.3)	0.78
Etanercept	1 (0.7)	1 (1.2)	1 (0.8)	0.99
Apremilast	10 (7)	7 (8.3)	9 (7.7)	0.88
Anti-IL6r (Tozilizumab)	1 (0.7)	0	0	0.99

Conclusion: ICBD criteria showed greater sensitivity than ISG, specially due to the absence of oral ulcers in certain patients. Classifying these additional patients by ICBD facilitated the initiation of on-label biologic treatments (e.g., monoclonal anti-TNF), potentially improving the management of BD, particularly for those with ocular involvement and without oral ulcers.

Table 2: Metrics for Modified Classification Criteria: Concordance Analysis After the Addition or Exclusion of Ocular Manifestations in All Patients.

	With Ocular Involvement	Without Ocular Involvement
Non adjusted Kappa (CI 95%)	0.405 (0.176 - 0.634)	0.443 (0.326 - 0.561)
Specific agreement + (CI 95%)	94.2% (72.1% - 83.1%)	74.4% (67.2% - 80.5%)
Specific agreement - (CI 95%)	44.4% (22.1% - 43.6%)	65.0% (56.1% - 72.9%)
Global agreement + (CI 95%)	89.4% (58.8% - 74.1%)	70.4% (62.5% - 77.3%)
Bias and prevalence indices		
Bias index	-10.6%	-29.6%
Bias adjusted Kappa	0.386	0.393
Prevalence index	81.0%	15.5%
Prevalence and bias adjusted Kappa (PABAK)	0.788	0.408

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Gálvez Sánchez: None; **J. Martín-Varillas**: AbbVie, Pfizer, Lilly, Celgene, Janssen, and UCB Pharma, 5; **L. Sánchez Bilbao**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **I. Ferraz Amaro**: None; **E. Aurrecoechea**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0273

Effector CD8+ T cells and PD-1hi CXCL13hi CD4+ T cells contribute to recurrent immune checkpoint inhibitor mediated inflammatory arthritis

Synat Keam[1], Yuanteng Li[2], Yanshuo Chu[1], Jean Tayar[3], Huifang Lu[4], Michael Wu[5], Sandeep Agarwal[6], Nitin Jain[7], Pavlos Msaouel[1], Adi Diab[2], Cara Haymaker[1], Linghua Wang[1], Roza Nurieva[8] and **Sang Kim**[9], [1]The University of Texas MD Anderson Cancer Center, houston, [2]MD Anderson Cancer Center, Houston, TX, [3]The University of Texas, MD Anderson Cancer Center, Houston, TX, [4]UT MD Anderson Cancer Center, Houston, TX, [5]Baylor College of Medicine, Houston, [6]Baylor College of Medicine, Houston, TX, [7]The Universty of Texas MD Anderson Cancer Center, Houston, [8]University of Texas MD Anderson, Houston, TX, [9]Yale University, Branford, CT

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitor (ICI) therapy is associated with life- and/or organ-threatening immune-related adverse events, including inflammatory arthritis (ICI-IA). However, the mechanisms behind ICI-IA, especially when it recurs, have not been fully elucidated. Thus, longitudinal sample analyses provide valuable information to understand disease pathogenesis. The purpose of the study is to elucidate mechanisms of ICI-IA by analyzing longitudinal synovial fluid (SF) samples.

Methods: SF samples were collected from six ICI-IA patients at the first and second occurrences of the IA flare and analyzed with single-cell RNA sequencing (scRNAseq), scTCRseq, scBCRseq, and flow cytometry. SF samples from cancer-naïve osteoarthritis (OA) patients were used as negative controls.

Results: SF effector $CD8^+$ T cells and PD-1^{hi} $CXCL13^{hi}$ $CD4^+$ T cells were clonally expanded, implying their role in ICI-IA pathogenesis. Ninety three % of the top 10 expanded effector $CD8^+$ T cell clones were shared between the first and second ICI-IA flare, with 47% of them are being expanded in the second IA flare. For PD-1^{hi} $CXCL13^{hi}$ $CD4^+$ T cells, half of the top 10 clones were shared between first and second ICI-IA flares, and 60% of shared clones were expanded in the second IA flare. Effector $CD8^+$ T cells and PD-1^{hi} $CXCL13^{hi}$ $CD4^+$ T cells produced inflammatory cytokines including IFNg, TNFa, and IL-21, especially in the second ICI-IA. Trajectory inference analysis demonstrated that effector $CD8^+$ T cells were positioned after tissue-resident memory T cells and effector memory T cells. The trajectory within the $CD4^+$ T cells indicated that recently activated $CD4^+$ T cells have the developmental potential to become PD-1^{hi} $CXCL13^{hi}$ $CD4^+$ T cells. Effector $CD8^+$ T cells and PD-1^{hi} $CXCL13^{hi}$ $CD4^+$ T cells interact with each other and with myeloid immune cells via chemokines (CXCL9/10/11/13, CCL5) and cytokines (MIF, IL-2/7/15/21). Age-associated B cells, B cell population expanded in autoimmune diseases, were seen expanded in the second ICI-IA flare.

Conclusion: Effector $CD8^+$ T cells and PD-1^{hi} $CXCL13^{hi}$ $CD4^+$ T cells play a pivotal role in ICI-IA disease pathogenesis. These cells were more clonally expanded and produced more inflammatory cytokines in the second ICI-IA flare, implying immune memory responses. Understanding of these cells will shed light on therapeutic targets for ICI-IA and biomarkers to predict development or recurrence of ICI-IA, an emerging disease entity in rheumatology and oncology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Keam: None; **Y. Li**: None; **Y. Chu**: None; **J. Tayar**: None; **H. Lu**: None; **M. Wu**: None; **S. Agarwal**: None; **N. Jain**: None; **P. Msaouel**: None; **A. Diab**: None; **C. Haymaker**: None; **L. Wang**: None; **R. Nurieva**: None; **S. Kim**: None.

Abstract Number: 0274

Transplant-free survival in patients with systemic autoimmune rheumatic diseases and progressive pulmonary fibrosis in the ILD-PRO Registry

Sonali Bracken[1], Aparna Swaminathan[2], Jeremy M Weber[3], Megan L Neely[4], Scott Palmer[4], Erin Wilfong[5], Ann Chauffe[6], Elizabeth Volkmann[7] and ILD-PRO Registry investigators, [1]Duke University Medical Center, Durham, NC, USA, Apex, NC, [2]Duke University Medical Center and Duke Clinical Research Institute, Durham, NC, USA, Durham, NC, [3]Duke Clinical Research Institute, Durham, NC, USA, Durham, [4]Duke University Medical Center and Duke Clinical Research Institute, Durham, NC, USA, Durham, [5]Vanderbilt University Medical Center, Nashville, TN, USA, Nashville, TN, [6]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, Newberry, FL, [7]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Progressive pulmonary fibrosis (PPF) is known to be associated with high mortality, but there are few data on the course of PPF in patients with interstitial lung disease (ILD) due to systemic autoimmune rheumatic diseases (SARDs). We evaluated time to death or lung transplant among patients with SARDs and PPF.

Methods: The ILD-PRO Registry enrolled patients who had an ILD other than idiopathic pulmonary fibrosis, reticular abnormality and traction bronchiectasis (with or without honeycombing) on HRCT, and met criteria for ILD progression within the prior 24 months. Patients were followed prospectively while receiving usual care. The Kaplan–Meier method was used to analyze time to death or lung transplant over 24 months in patients with the following SARDs: rheumatoid arthritis (RA), systemic sclerosis (SSc), idiopathic inflammatory myopathies (IIMs), interstitial pneumonia with autoimmune features (IPAF), mixed or undifferentiated connective tissue disease (CTD), Sjögren's disease, and other SARDs.

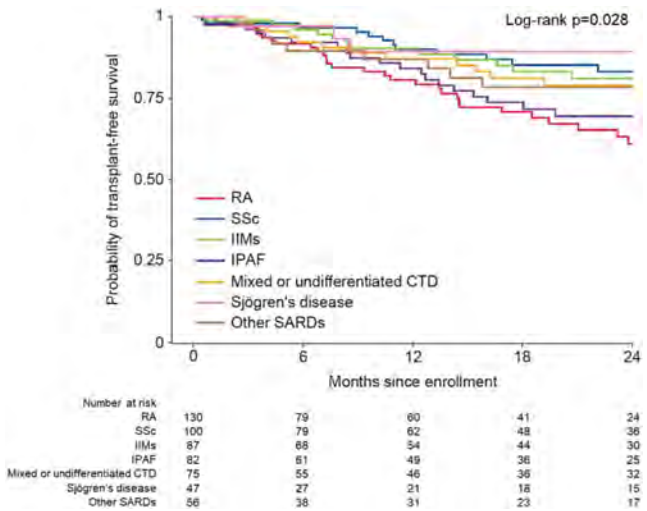


Figure. Kaplan-Meier estimate of time to death or lung transplant among patients with SARDs and PPF in the ILD-PRO Registry.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Characteristics of patients with SARDs and PPF at enrollment in the ILD-PRO Registry

	RA (n=130)	SSc (n=100)	IIMs (n=87)	IPAF (n=82)	Mixed or undifferentiated CTD (n=75)	Sjögren's disease (n=47)	Other SARDs (n=56)
Age, years	70 (62, 75)	60 (52, 70)	62 (53, 72)	74 (65, 77)	61 (54, 69)	71 (59, 76)	65 (51, 70)
Female	56.2	77.0	64.4	51.2	80.0	78.7	80.7
Ever smoker	48.5	26.0	39.1	47.6	36.0	31.9	39.3
FVC % predicted	61.7 (49.4, 71.5)	67.5 (53.2, 78.7)	62.0 (47.0, 72.7)	62.2 (47.6, 75.5)	60.6 (49.4, 69.8)	65.3 (55.9, 79.4)	66.7 (48.2, 76.9)
DLco % predicted	38.8 (29.6, 48.3)	38.2 (29.7, 51.8)	35.6 (27.4, 46.4)	36.3 (29.5, 47.3)	36.2 (25.9, 46.8)	45.4 (33.9, 55.4)	40.2 (30.4, 51.9)

Data are median (Q1, Q3) or % of patients with available data.

Results: A total of 577 patients in the ILD-PRO Registry had SARDs: 130 (22.5%) RA, 100 (17.3%) SSc, 87 (15.1%) IIMs, 82 (14.2%) IPAF, 75 (13.0%) mixed or undifferentiated CTD, 47 (8.1%) Sjögren's disease, and 56 (9.7%) other SARDs. Patient characteristics at enrollment are summarized in the Table. The probability of transplant-free survival at 24 months was 60.8% for RA, 83.0% for SSc, 80.9% for IIMs, 69.3% for IPAF, 78.8% for mixed or undifferentiated CTD, 89.2% for Sjögren's disease and 78.2% for other SARDs (Figure).

Conclusion: Patients with SARDs and PPF enrolled in the ILD-PRO Registry had a high probability of death or lung transplant over the following two years. The probability of transplant-free survival varied by type of SARD, with the worst survival in patients with RA and IPAF.

Disclosure: S. Bracken: None; **A. Swaminathan**: Boehringer Ingelheim, 12, Medical writing support provided by Fleishman Hillard, Duke Clinical Research Institute, 3, Duke University Medical Center, 3; **J. Weber**: Boehringer Ingelheim, 12, Medical writing support provided by Fleishman Hillard, Duke Clinical Research Institute, 3; **M. Neely**: Boehringer Ingelheim, 12, Medical writing support provided by Fleishman Hillard, Duke Clinical Research Institute, 3, Duke University Medical Center, 3; **S. Palmer**: Boehringer Ingelheim, 12, Medical writing support provided by Fleishman Hillard, Duke Clinical Research Institute, 3, Duke University Medical Center, 3; **E. Wilfong**: Allogene, 2, AstraZeneca, 2, Boehringer Ingelheim, 1, 5, 12, Medical writing support provided by Fleishman Hillard, Capstan Therapeutics, 2, Merck, 1, UpToDate, 9; **A. Chauffe**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5.

Abstract Number: 0275

A Snapshot of Subcutaneous Infliximab Use in Inflammatory Rheumatic Diseases: A Multicenter Italian Study

Stefano Gentileschi[1], Carla Gaggiano[1], Francesco Placido[1], Riccardo Terribili[1], Laura Cometi[2], Giuseppe Lopalco[3], Greta Dipetrangelo[3], Giacomo Cozzi[4], Roberto Padoan[5], Riccardo Bixio[6], Simone Parisi[7], Maria Chiara Ditto[8], Gemma Lepri[9], Caludia Fabiani[10], Luca Cantarini[1], Florenzo Iannone[11], Roberta Ramonda[12], Bruno Frediani[1] and Serena Guiducci[2], [1]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University Hospital of Siena, Siena, Italy, Siena, Italy, [2]Division of Rheumatology, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, Florence, Italy, [3]Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University o f Bari, Bari, Italy, Bari, Italy, [4]Rheumatology Unit, Department of Medicine, University of Padua, Padua, Italy, Padua, Italy, [5]Rheumatology Unit, Department of Medicine DIMED, University of Padua, Padua, Italy, [6]Rheumatology Unit, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Verona, Italy, Verona, Italy, [7]Ospedaliera Universitaria Città della Salute e della Scienza di Torino, Turin, Italy, [8]SC Reumatologia, AOU Città della Salute e della Scienza, Torino, Italy, Turin, Italy, [9]Department of Experimental and Clinical Medicine, University of Florence, Division of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rheumatology Scleroderma Unit, AOU Careggi Hospital, Florence, Italy., Florence, Italy, [10]Ophthalmology Unit, Department of Medical Sciences, Surgery and Neuroscience, University of Siena, Siena University Hospital [European Reference Network (ERN) for Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases (RITA) Center], Siena, Italy, Siena, Italy, [11]Rheumatology DiMePReJ, University of Bari, School of Medicine, Bari, Italy, Bari, Italy, [12]Rheumatology Unit-DIMED-University of Padova ITALY, Padova, Padua, Italy

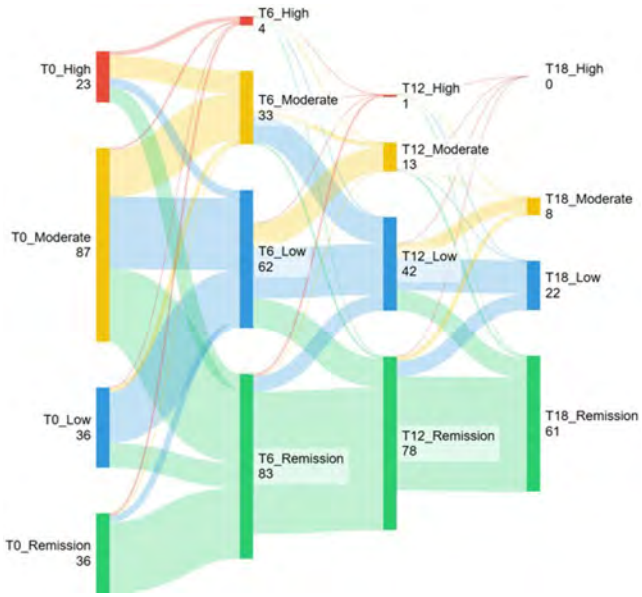
SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: A new subcutaneous formulation of infliximab (CT-P13) has recently become available for the treatment of inflammatory rheumatic diseases (IRDs), psoriasis and inflammatory bowel diseases. To date there are no real-life data on the use of this product nor is any real-world effectiveness evidence available in rheumatological settings. This study aims to provide a snapshot of subcutaneous infliximab (scIFX) use in IRDs evaluating treatment persistence and any factor able to influence drug retention rate (DDR).

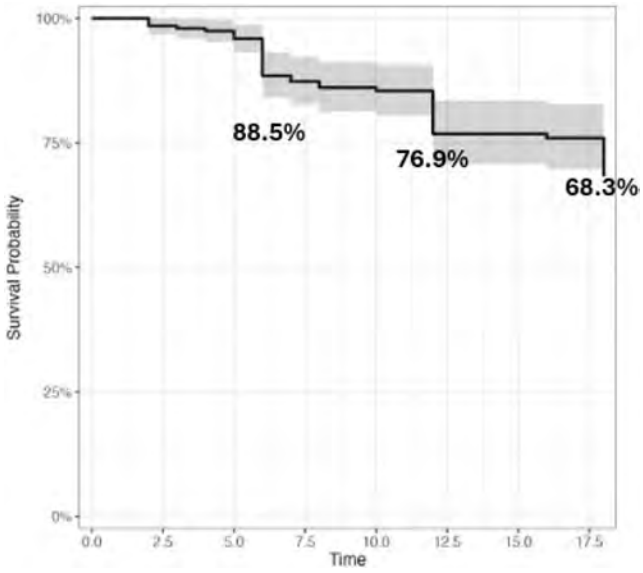
Methods: We conducted a multicentric observational retrospective study enrolling consecutive adult patients with immune-mediated diseases treated with scIFX for at least 6 months. Disease status was assessed with standard activity indexes according to diagnosis (i.e. DAS28 for rheumatoid arthritis (RA), DAPSA for Psoriatic Arthritis (PsA), ASDAS-CRP for Axial Spondyloarthritis and clinician's evaluation for the other conditions). Treatment persistence was assessed using the DRR at 6, 12, and 18 months. Factors influencing DRR were identified using the Log-Rank test.

Results: A total of 201 patients were included [134 women (66.7%), mean±SD age 49.9±13.8 years (range 18-82)]. Sixty-six (32.8%) patients had a diagnosis of AxSpA, 68 (33.8%) of PsA, 18 (9%) of RA, 18 (9%) of Behçet's disease (BD), 10 (5%) of Takayasu arteritis (TA), 16 (8%) of Juvenile Idiopathic Arthritis (JIA) (16; 8%) and 5 (2.5%) of other IRDs. Patients were treated with scIFX for a median duration of 14.0 months (IQR 13). Among them, 71 (35.3%) were treated with IFX as first-line biologic, 75 (37.3%) as second-line biologic and 55 subjects were treated as third or more line of treatment. Ninety-five (47.3%) patients were treated with intravenous (iv)IFX before switching to scIFX. Figure 1 shows our cohort disease status variations after scIFX start at the different timepoints. While starting scIFX, an induction regimen was used in 74 patients (78.3%), while 32 patients started scIFX every other week without any loading dose. The DRR for scIFX (Figure 2) was



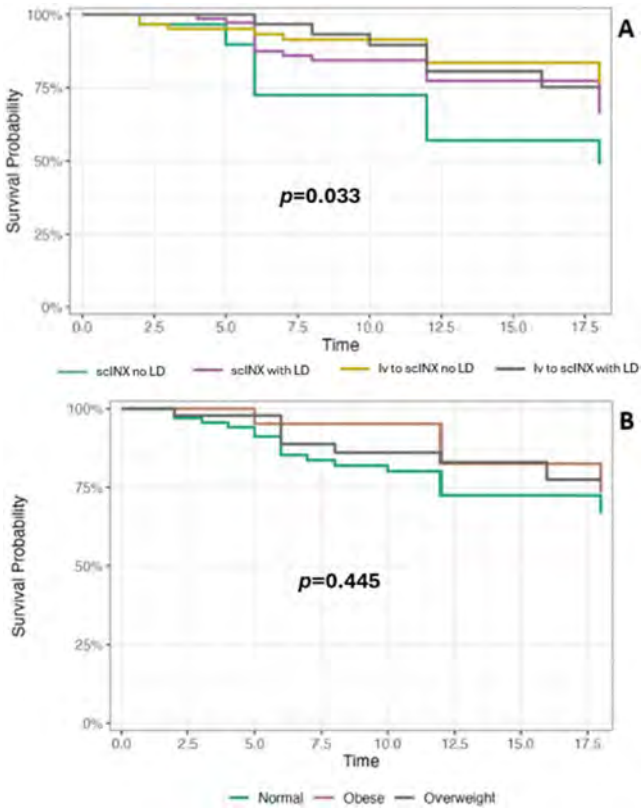
Disease status variation during the observation period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



scIFX drug retention rate of the whole cohort

88.5% at 6 months, 76.9% at 12 months, and 68.3% at 18 months (Figure 2). DRR was significantly higher in patients switching from ivIFX than directly stating with scIFX (p=0.038). Patients starting scIFX without loading dose had a significant lower DRR (p=0.033) than those who underwent a loading dose both subcutaneously or intravenously (Figure 3A). Patients starting scIFX (no previous ivIFX) had a similar DRR regardless of the line of biologic treatment (p=0.066). Similarly, there were no differences in DRR among BMI classes in the whole cohort (p=0.445) (Figure 3B). Forty-seven subject (23.4%) discontinued scIFX during the observation time. Concerning safety, 21 patients (10.4 %) experienced adverse events.



A: Drug Retention rate according to scIFX initiation (switchers from ivIFX vs new scIFX treatments) and according to the performance of a loading dose (LD vs no-LD) at the start of treatment. B: Drug retention rate according to BMI classes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The study results suggest that scIFX provides sustained effectiveness over time for the treatment of IRDs. While factors such as line of treatment or BMI class do not affect DRR, the use of an induction dose appears to predict better treatment persistence.

Disclosure: S. Gentileschi: None; **C. Gaggiano**: None; **F. Placido**: None; **R. Terribili**: None; **L. Cometi**: None; **G. Lopalco**: None; **G. Dipetrangelo**: None; **G. Cozzi**: None; **R. Padoan**: None; **R. Bixio**: None; **S. Parisi**: None; **M. Ditto**: None; **G. Lepri**: None; **C. Fabiani**: None; **L. Cantarini**: None; **F. Iannone**: None; **R. Ramonda**: None; **B. Frediani**: None; **S. Guiducci**: None.

Abstract Number: 0276

Plasma Proteomic Profiling Identifies Inflammatory Proteins and Pathways Associated With Non-idiopathic and Idiopathic Retroperitoneal Fibrosis

Thomas Pelowitz, Benjamin Hur, Kenneth Warrington, Jaeyun Sung and Matthew Koster, Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Retroperitoneal fibrosis (RPF) is a rare fibroinflammatory disease of the retroperitoneum that can lead to obstructive uropathy and other life-threatening complications. While RPF can arise secondary to malignancy, IgG4-related disease, or vascular inflammation, many cases remain idiopathic. Despite increasing awareness, diagnosis remains challenging due to reliance on non-specific imaging or invasive biopsy. Blood-based biomarkers capable of accurately distinguishing RPF from healthy individuals are needed to facilitate earlier and less invasive diagnosis.

Methods: Plasma from 45 individuals with RPF (Non-idiopathic: IgG4-related = 9, malignancy-associated = 3, Erdheim-Chester disease = 4, inflammatory abdominal aortic aneurysm = 4; Idiopathic = 19) and 6 healthy (non-disease) controls were profiled using the SomaLogic SomaScan 7K Assay, which quantifies over 7,000 proteins per sample. Differential abundance analysis was performed using linear regression analysis, adjusting for clinical and demographic covariates (e.g., age, sex, BMI, creatinine levels, platelet counts, hemoglobin, and IgG4 levels). Proteins significantly more or less abundant in RPF cases compared to control as well as idiopathic RPF compared to non-idiopathic RPF (significance criteria: $P < 0.05$ and mean fold-change $\geq 25\%$) were identified. A machine learning pipeline was trained to distinguish RPF cases, and its performance was estimated across 100 bootstrap iterations.

Results: A total of 176 plasma proteins were differentially abundant between RPF patients and controls while controlling potential confounders. Proteins notably elevated in RPF included those associated with inflammation and immune dysregulation (e.g., Ferritin, Serum amyloid A [SAA], and T-cell immunoglobulin and mucin domain-containing protein 3 [TIMD3]). Pathway enrichment analyses found that these differentially abundant proteins mainly participated in fibrosis-related inflammatory tissue remodeling processes, such as cytokine-chemokine signaling, apoptosis, interleukin signaling, and integrin-mediated cell adhesion pathways. We also identified protein differences amongst etiological subtypes of non-idiopathic RPF. Additionally, 80 proteins showed differential abundance between idiopathic and non-idiopathic forms of RPF, including chemokine ligand 7 (CCL7) and junction adhesion molecule-like 1 (JAML1). Non-idiopathic RPF subtype-specific analyses further identified proteins uniquely elevated within subtypes compared to controls. Finally, an Extra-Trees classifier trained on these plasma protein profiles demonstrated potential in distinguishing RPF cases from controls, achieving a mean ROC-AUC of 0.81.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study identifies key inflammatory proteins and immune-related pathways significantly associated with RPF. In all, these plasma-derived proteins offer promising candidates for minimally invasive diagnostics, as well as provide insight into systemic inflammatory mechanisms underlying RPF pathology. Looking ahead, follow-up studies incorporating disease controls will be necessary to further validate specificity and clinical utility.

Disclosure: T. Pelowitz: None; **B. Hur**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **J. Sung**: Rheumasense, 1, 9, 10; **M. Koster**: Amgen, 2.

Abstract Number: 0277

A Phase 1, Randomized Study to Evaluate the Safety, Tolerability, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Single and Multiple Ascending Doses and Food Effects of BGB-45035, a Chimeric Degradation Activating Compound (CDAC), in Healthy Participants

Vaibhav Mundra[1], Cunjing Yu[2], Roland Morley[1], Yuan Yuan[3], Yifan Qin[3], Jingjing Schneider[1], Shengnan Chen[3], Zhenyuan Zhou[3] and Zhen Yao[2], [1]BeOne Medicines USA, Inc., San Carlos, CA, [2]BeOne Medicines (Beijing) Co, Ltd., Beijing, China (People's Republic), [3]BeOne Medicines (Shanghai) Co, Ltd., Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin 1 receptor associated kinase 4 (IRAK4) degradation may modulate toll-like receptor signaling and alleviate symptoms in rheumatoid arthritis and atopic dermatitis.[1,2] BGB-45035, an orally administered CDAC, targets IRAK4 and in animal models, demonstrated a PK/PD association with suppression of IL-33–induced skin inflammation.

Table 1. TEAEs Occurring in ≥3 Participants by Preferred Term (Parts A-C; Safety Analysis Set [N=116])

Preferred term, n (%)	Cohort A1-6, X-30X (n=48)	Cohort B1, X (n=8)	Cohort B2 + C1, 2X (n=20)	Cohort B3 + C2, 4X (n=20)	Cohort B4 + C3, 6X (n=20)
Participants with any TEAE	**22 (45.8)**	**7 (87.5)**	**13 (65.0)**	**16 (80.0)**	**18 (90.0)**
Upper respiratory tract infection	4 (8.3)	0	2 (10.0)	3 (15.0)	6 (30.0)
Headache	4 (8.3)	2 (25.0)	0	1 (5.0)	2 (10.0)
Blood triglycerides increased	0	0	3 (15.0)	4 (20.0)	1 (5.0)
Catheter site pain	3 (6.3)	1 (12.5)	0	2 (10.0)	2 (10.0)
Alanine aminotransferase increased	0	0	3 (15.0)	1 (5.0)	2 (10.0)
Blood pressure increased	0	0	4 (20.0)	2 (10.0)	0
Monocyte count increased	0	0	2 (10.0)	3 (15.0)	1 (5.0)
Sinus bradycardia	0	0	0	3 (15.0)	1 (5.0)
Vessel puncture site bruise	3 (6.3)	0	0	0	0

TEAE, treatment-emergent adverse event.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. BGB-45035 Geometric Mean (CV% GM) PK Parameters After Single- and Multiple-Dose Administration

Cohort A1-6: SAD		
Dose	C_{max}, ng/mL	$AUC_{0\text{-}inf}$, ng·h/mL
X	44.1 (48.4)	2560 (40.3)
3X	103 (67.6)	6370 (59.2)
6X	149 (57.6)	11,300 (57.6)
12X	202 (64.6)	15,400 (12.2)
18X	350 (35.4)	28,500 (41.1)
30X	388 (36.1)	33,700 (42.2)

Cohort B1-4: MAD				
Dose	T_{max}, h	C_{max}, ng/mL	$AUC_{0\text{-}tau}$, ng·h/mL	AR AUC
X	4.00	190 (34.1)	2680 (26.5)	6.05 (17.6)
2X	4.00	265 (36.6)	4130 (18.1)	5.18 (54.5)
4X	4.00	455 (39.5)	6790 (22.8)	5.03 (30.1)
6X	4.00	369 (68.7)	5920 (55.2)	5.20 (10.5)

Cohort C1-3: MAD				
Dose	T_{max}, h	C_{max}, ng/mL	$AUC_{0\text{-}tau}$, ng·h/mL	AR AUC
2X	4.00	340 (40.7)	5100 (20.4)	6.38 (18.9)
4X	4.00	596 (28.8)	9810 (28.8)	6.86 (43.7)
6X	4.00	658 (26.6)	11,783 (30.0)	7.67 (45.2)

Geometric mean (CV% GM) values are rounded to three significant digits. T_{max} values are presented as median.

AR AUC, accumulation ratio for day 14/day 1 area under the plasma concentration-time curve over the last 24-hour dosing interval; $AUC_{0\text{-}inf}$, area under the plasma concentration-time curve from time zero extrapolated to infinity; $AUC_{0\text{-}tau}$, area under the plasma concentration-time curve over a dosing interval; C_{max}, maximum observed plasma concentration; CV% GM, geometric coefficient of variation; MAD, multiple ascending dose; PK, pharmacokinetic; SAD, single ascending dose; T_{max}, time to maximum plasma concentration.

This first-in-human study of BGB-45035 has 6 parts, data from parts A–C are reported. Parts A (single ascending dose [SAD]) and B (multiple ascending dose [MAD]) were in healthy participants; part C assessed MAD in healthy Chinese participants (China only). Objectives were to assess the safety, tolerability, PK, and PD of BGB-45035.

Methods: Participants were aged 18-55 years, with a body mass index of 18-32 kg/m^2. Parts A-C were double-blind and placebo controlled. Part A (SAD) comprised 6 cohorts (X, 3X, 6X, 12X, 18X, 30X dosages); in each cohort, 6 participants received BGB-45035, and 2 participants received placebo. Participants were randomized (5:1) to BGB-45035 or placebo. Parts B and C (MAD) comprised 4 cohorts (X, 2X, 4X, 6X dosages) and 3 cohorts (2X, 4X, 6X dosages), respectively. Participants in both parts were randomized (3:1) to BGB-45035 or placebo once daily (QD) for 14 days. Adverse events and serious adverse events (SAEs) were monitored. PK parameters were estimated from plasma concentration data. PD assessments included IRAK4 protein concentration extracted from whole blood and cytokine production from ex vivo stimulated from whole blood.

Results: As of April 7, 2025, 80 participants (all men) were enrolled in parts A (n=48; median age 29 [range, 20-54] years) and B (n=32; median age 28 [range, 19-54] years) and 36 were enrolled in part C (median age 27 [range, 18-44] years). All active doses were generally well tolerated. No dose-dependent toxicity was observed; no safety signals were identified. Upper respiratory tract infection was the most common treatment-emergent adverse event, all were mild in severity (**-Table 1**). One SAE, delirium, was considered severe but not treatment-related, and led to treatment discontinuation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

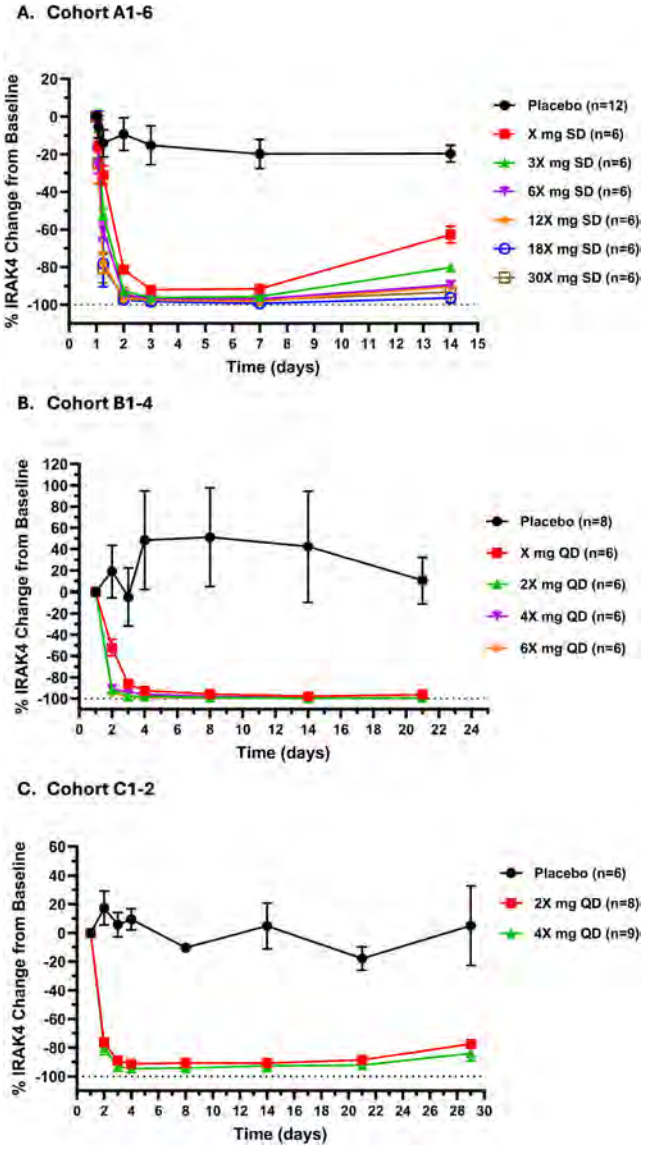


Figure 1. Mean Percent Reduction of IRAK4 in Part A-C

Dose-dependent PK increases were observed with doses of X-30X, with maximum concentration observed at a median of 4 hours and a mean terminal half-life ($t_{1/2}$) ranging from 58.5 to 95.6 hours across dosage groups (**Table 2**). Consistent with $t_{1/2}$, a ≈5-6–fold increase in exposure was observed on day 14 with BGB-45035 QD dosing. Substantial IRAK4 degradation was observed via whole blood assay after BGB-45035 dosing (**Figure 1**).

Conclusion: BGB-45035 is a potent IRAK4 degrader that was generally well tolerated in healthy participants, with a favorable safety and PK profile over a 14-day dosing period. This supports continued evaluation of BGB-45035 as a therapy for autoimmune diseases.

References:

1. Ackerman L, et al. *Nat Med*. 2023;29(12):3127-3136.
2. Lavazais S, et al. *Sci Transl Med*. 2023;15(683):eabj3289.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Mundra: BeOne Medicines, Ltd., 3, 11; **C. Yu**: BeOne Medicines, Ltd., 3, 11; **R. Morley**: BeOne Medicines, Ltd., 3, 11, 12, Travel, accommodation, expenses, Gilead, 3, 11, 12, Travel, accommodation, expenses; **Y. Yuan**: BeOne Medicines, Ltd., 3, 11; **Y. Qin**: BeOne Medicines, Ltd., 7, Caidya, 3; **J. Schneider**: BeOne Medicines, Ltd., 3, 11, 12, Travel, accommodations, or expenses; **S. Chen**: BeOne Medicines, Ltd., 3, 11; **Z. Zhou**: BeOne Medicines, Ltd., 3, 11; **Z. Yao**: BeOne Medicines, Ltd., 3, 11.

Abstract Number: 0278

Classic and Clinically Amyopathic Dermatomyositis: Autoantibody Positivity

Xiwei Yang[1], Shae Chambers[2], Aretha On[1], Hammad Ali[2], Touraj Khosravi[3], Lais Lopes Almeida Gomes[2], Rui Feng[4] and Victoria Werth[5], [1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Department of Dermatology, Perelman Shool of Medicine, University of Pennsylvania, Philadelphia, PA, [4]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, Pennsylvania, Philadelphia, PA, [5]University of Pennsylvania, Wynnewood, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is an idiopathic inflammatory myopathy subclassified as classic (CDM) and clinically amyopathic (CADM). It can involve myositis-associated (MAA) and myositis-specific (MSA) autoantibodies. Many MSA are associated with specific DM subsets, which helps in disease monitoring and prognostication. However, few studies have compared the positivity rates of all commonly tested MAA and MSA in CDM versus CADM.

Methods: We performed a retrospective cross-sectional review of CDM and CADM patients in our IRB-approved DM database at the University of Pennsylvania who had myositis autoantibody testing between April 01, 2016 and October 31, 2024. MAA included anti-SSA, -Pm-Scl, -Ku, -U1-RNP, -U2-RNP, and -U3-RNP. MSA included anti-Jo-1, -PL-7, -PL-12, -EJ, -OJ, -Mi-2, -SRP, -TIF-1γ, -NXP-2, -MDA5, and -SAE. ANA status was also recorded. The relation between DM subtype and autoantibody positivity rate was assessed using chi-square and Fisher's exact tests with $\alpha = 0.05$.

Results: We identified 320 patients tested at mean age 52.6 ± 14.4 years; 198 (62%) were CDM and 122 (38%) CADM. MSA positivity rate was 47% (94/198) in CDM vs. 40% (49/122) in CADM, $p = 0.20$. Though typically seen in CADM, anti-MDA5 was comparably positive in CDM (8%, 13/166) and CADM (10%, 10/97), $p = 0.49$. Although anti-NXP2 was more common in CDM (10%, 16/162) than in CADM (5%, 5/94), the difference was not statistically significant ($p = 0.20$). Anti-TIF-1γ was the most common MSA in both subtypes (CDM 17%, 29/169; CADM 22%, 21/97). MAA positivity rate was 29% (48/168) in CDM vs. 26% (26/100) in CADM, $p = 0.65$. Anti-SSA was the most common MAA in both subtypes (CDM 21%, 33/159; CADM 19%, 18/94). ANA was positive in 63% (90/143) CDM vs. 49% (42/85) CADM, $p = 0.045$. Of the patients with negative myositis panels, 26/53 (49%) CDM and 13/36 (36%) CADM were ANA positive.

Conclusion: We found that MSA and MAA positivity rates did not differ significantly between CDM and CADM ($p > 0.05$), whereas ANA was significantly more common in CDM ($p < 0.05$). A sizeable portion of DM was ANA positive despite negative MSA and MAA, which suggests that there may be other DM-related autoantibodies not yet discovered. These results reiterate that DM management requires integrating clinical and lab findings and should not solely depend on autoantibody status.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Testing Laboratories, Tested Antibodies, and Detection Assays of Myositis Autoantibody Panels Performed in the Study Cohort

Laboratory	Panel name	No. (%) performed (n = 373)	Type of tested abs	No. of tested abs	Tested abs (for No. of tested abs < 10)	Untested abs (for No. of tested abs ≥ 10)	Assay
ARUP		**191 (51)**					Immunoblot, IP, multiplex bead assay[a]
	MYOSITIS EXTENDED PANEL	170 (46)	MSA, MAA	16	N/A	Anti-U2-RNP	
	MYOSITIS ANTIBODY COMPREHENSIVE	11 (3)	MSA, MAA	14	N/A	Abs to TIF-1γ, MDA-5, NXP-2, SAE	
	MYOSITIS SPECIFIC ANTIBODY	5 (1)	MSA	11	N/A	Abs to SSA, Pm-Scl, Ku, U1-RNP, U2-RNP, U3-RNP	
	POLYMYOSITIS AND DERMATOMYOSITIS PANEL	5 (1)	MSA	11	N/A	Abs to SSA, Pm-Scl, Ku, U1-RNP, U2-RNP, U3-RNP	
LABCORP		**97 (26)**					ELISA, RIPA gel radiography[b]
	MYOMARKER 3 PLUS PROFILE	67 (18)	MSA, MAA	17	N/A	N/A	
	MYOSITIS PANEL III	13 (3)	MSA, MAA	11	N/A	Abs to TIF-1γ, MDA5, NXP-2, SAE, U2-RNP, U3-RNP	
	MYOSITIS PANEL VI	7 (2)	MSA, MAA	17	N/A	N/A	
	MYOSITIS PANEL I	4 (1)	MSA, MAA	7	Abs to Mi-2, SRP, PL-7, PL-12, EJ, OJ, Ku	N/A	
	MYOSITIS PANEL II	3 (1)	MSA, MAA	7	Abs to Mi-2, SRP, PL-7, PL-12, EJ, OJ, Ku	N/A	
	MYOSITIS PANEL IV	3 (1)	MSA, MAA	8	Abs to Mi-2, SRP, PL-7, PL-12, EJ, OJ, Ku, U1-RNP	N/A	
QUEST		**68 (18)**					Chemiluminescence, ELISA, line blot
	MYOSITIS SPECIFIC 11 AB PANEL	29 (8)	MSA	10	N/A	Abs to SAE, SSA, Pm-Scl, Ku, U1-RNP, U2-RNP, U3-RNP	
	MYOSITIS PANEL COMPREHENSIVE	25 (7)	MSA	6	Abs to PL-7, PL-12, Mi-2, Jo-1, EJ, OJ	N/A	
	EXTENDED MYOSITIS SPECIFIC AB PANEL	9 (2)	MSA	12	N/A (includes anti-HMGCR, anti-cN-1A)	Abs to SAE, SSA, Pm-Scl, Ku, U1-RNP, U2-RNP, U3-RNP	
	MYOSITIS ASSESSR PLUS JO-1	5 (1)	MSA, MAA	8	Abs to Mi-2, SRP, PL-7, PL-12, EJ, OJ, Jo-1, Ku	N/A	
OMRF	MYOSITIS PANEL	**12 (3)**	MSA, MAA	12	N/A	Abs to TIF-1γ, MDA-5, NXP-2, SAE, U3-RNP	IP, ID, IF
MAYO	MYOMARKER PANEL 3	**5 (1)**	MSA, MAA	10	N/A	Abs to TIF-1γ, MDA-5, NXP-2, Jo-1, SAE, Pm-Scl, SSA	ELISA, RIPA gel radiography

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Positivity Rates of Myositis-specific (MSA), Myositis-Associated (MAA), and Anti-nuclear Autoantibodies (ANA) by Dermatomyositis (DM) Subtype

		No. (%)		
		Classic DM (n = 198)	Clinically amyopathic DM (n=122)	P-value
	Any MSA positive	94/198 (47)	49/122 (40)	.20
	Any MAA positive	48/168 (29)	26/100 (26)	.65
	Any ANA positive	90/143 (63)	42/85 (49)	**.045 (< .05)**
	Either MSA or MAA positive	118/198 (60)	63/122 (52)	.16
	Both MSA and MAA negative	80/198 (40)	59/122 (48)	.16
	Both MSA and MAA negative but ANA positive	26/53 (49)	13/36 (36)	.23
MSA	Anti-TIF-1γ	29/169 (17)	21/97 (22)	.37
	Anti-MDA-5	13/166 (8)	10/97 (10)	.49
	Anti-NXP-2	16/162 (10)	5/94 (5)	.20
	Anti-SAE	10/137 (7)	7/79 (9)	.68
	Anti-Mi-2	12/197 (6)	6/119 (5)	.70
	Anti-PL-7	10/197 (5)	2/119 (2)	.22
	Anti-Jo-1	9/192 (5)	1/118 (1)	.10
	Anti-SRP	3/187 (2)	3/109 (3)	.67
	Anti-PL-12	2/197 (1)	1/119 (1)	1
	Anti-OJ	1/197 (1)	1/119 (1)	1
	Anti-EJ	0/197 (0)	0/119 (0)	1
MAA	Anti-SSA	33/159 (21)	18/94 (19)	.76
	Anti-SSA-52	26/159 (16)	15/94 (16)	.93
	Anti-SSA-60	11/159 (7)	6/94 (6)	.89
	Anti-SSA-52 positive with CT-proven ILD	11/26 (42)	5/15 (33)	.57
	Anti-Pm-Scl	13/160 (8)	5/94 (5)	.40
	Anti-U1-RNP	12/160 (8)	3/93 (3)	.27
	Anti-Ku	1/166 (1)	3/100 (3)	.15
	Anti-U2-RNP	0/91 (0)	1/57 (2)	.39
	Anti-U3-RNP	2/139 (1)	1/84 (1)	1
ANA	Anti-RNP	5/42 (12)	1/20 (5)	.65
	Anti-Smith	0/72 (0)	0/37 (0)	1

Disclosure: X. Yang: None; **S. Chambers**: None; **A. On**: None; **H. Ali**: None; **T. Khosravi**: Pfizer, 1; **L. Lopes Almeida Gomes**: None; **R. Feng**: None; **V. Werth**: AbbVie/Abbott, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta Bio, 2, Calyx, 2, CSL Behring, 5, Cugene, 2, Eli Lilly, 2, EMD Serona, 2, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 5, Immunovant, 2, Janssen, 2, Kwoya Kirin, 2, Merck/MSD, 2, Novartis, 2, Nuvig, 2, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, Rome Pharmaceuticals, 5, Sanofi, 2, Takeda, 2, UCB, 2, 2, Ventus, 2, Viela, 5.

Abstract Number: 0279

Assessment of Baseline igg4-rd Disease Characteristics and Impact upon Safety and Efficacy of Inebilizumab: Results from the MITIGATE Study

Yoshiya Tanaka[1], Emma Culver[2], Arezou Khosroshahi[3], Wen Zhang[4], Kazuichi Okazaki[5], Matthias Lohr[6], nicolas schleinitz[7], Xinxin Dong[8], melissa rosen[9], Sue Cheng[8], Daniel Cimbora[8] and John Stone[10], [1]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [2]John Radcliffe Hospital; University of Oxford, Oxford, United Kingdom, [3]Emory University, Atlanta, GA, [4]Peking Union Medical College Hospital, Dong Cheng Qu, China (People's Republic), [5]Kansai Medical University Kori Hospital, Osaka, Japan, [6]Karolinska Institutet, Stockholm, Sweden, [7]Aix Marseille university, AP-HM, Marseille, France, [8]Amgen, Thousand Oaks, CA, [9]Amgen Inc., Thousand Oaks, CA, [10]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0233–0279) Miscellaneous Rheumatic & Inflammatory Diseases Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: IgG4-related disease (IgG4-RD) is a progressive, systemic, fibroinflammatory disease characterized by unpredictable and recurring flares, leading to organ damage and decreased quality of life. Inebilizumab is a humanized, glycoengineered, CD19-directed, monoclonal antibody that depletes CD19+ B cells, including plasmablasts and some plasma cells, effectively in a targeted manner. MITIGATE (NCT04540497) is an international, randomized, blinded, placebo-controlled Phase 3 trial that evaluates the safety and efficacy of inebilizumab as treatment for IgG4-RD. The aim is to evaluate the safety and efficacy of inebilizumab across various baseline disease characteristic subgroups of participants enrolled in the study.

Methods: Adult participants who met the ACR/EULAR Classification Criteria for IgG4-RD with a score ≥20 were enrolled in the study. Eligible participants had a history of multiorgan IgG4-RD and had experienced an IgG4-RD flare that required glucocorticoid treatment during the screening period. Additional eligibility criteria and study design have been previously reported (Stone et al, 2024). The primary endpoint (time to first adjudication committee (AC)-determined and investigator-treated IgG4-RD flare during the RCP) and all key secondary endpoints were met in the overall study population. This post

Table 1: Baseline Disease Characteristics

Subgroup	PBO, N=67	INEB, N=68	Overall, N=135
Disease Duration, y (SD)	2.5 (3.1)	2.6 (3.7)	2.6 (3.4)
<2 years, n (%)	38 (56.7)	40 (58.9)	78 (57.8)
≥2 years, n (%)	29 (43.3)	28 (41.1)	57 (42.2)
IgG4-RD Manifestation			
Newly Diagnosed, n (%)	31 (46.3)	31 (45.6)	62 (45.9)
Recurrent, n (%)	36 (53.7)	37 (54.4)	73 (54.1)
Highest known IgG4 Serum Level (mg/dL), Median (Q1, Q3)	642.6 (313.8, 1780.0)	713.0 (321.1, 1384.0)	653.0 (320.0, 1604.0)
ACR/EULAR Score, Median (Q1, Q3)	36.3 (29.2, 44.7)	38.7 (31.0, 46.5)	36.7 (30.0, 46.2)
CD20 B cell count (cells/μL), Median (Q1, Q3)	239.1 (128.8, 375.2)	306.9 (171.4, 507.8)	273.6
Prior Maintenance Therapy			
Yes	12 (17.9)	11 (16.2)	23 (17.0)
No	55 (82.1)	57 (83.8)	112 (83.0)

Table 2: Subgroup Analysis of Time to the First Treated and Adjudication Committee-determined IgG4-RD Flare During RCP

Subgroup	PBO, N=67 n (%)	INEB, N=68 n (%)	HR (95% CI)
Disease Duration			
<2 years	18/38 (47.4)	3/40 (7.5)	0.13 (0.04, 0.44)
≥2 years	22/29 (75.9)	4/28 (14.3)	0.12 (0.04, 0.34)
IgG4-RD Manifestation			
Newly Diagnosed	17/31 (54.8)	1/30 (3.2)	<0.1 (0.0, 0.3)
Recurrent	23/36 (63.9)	6/37 (16.2)	0.2 (0.1, 0.4)
Highest known IgG4 Serum Level			
< Median	18/34 (52.9)	4/33 (12.1)	0.19 (0.06, 0.55)
≥ Median	22/33 (66.7)	3/35 (8.6)	0.09 (0.03, 0.30)
ACR/EULAR Score			
< Median	20/34 (58.8)	5/31 (16.1)	0.16 (0.05, 0.48)
≥ Median	20/33 (60.6)	2/37 (5.4)	0.07 (0.02, 0.30)
CD20 B cell count			
< Median	21/33 (63.6)	3/26 (11.5)	0.13 (0.04, 0.44)
≥ Median	14/24 (58.3)	3/35 (8.6)	0.08 (0.02, 0.34)
Prior Maintenance Therapy			
Yes	8/12 (66.7)	4/11 (36.4)	0.43 (0.13, 1.46)
No	32/55 (58.2)	3/57 (5.3)	0.07 (0.02, 0.22)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Subgroup Analysis of The Proportion of Subjects Achieving Flare-Free, Corticosteroid-Free Complete Remission[a] at Week 52 (RCP)

Subgroup	PBO, N=67 n (%)	INEB, N=68 n (%)	Odds ratio (95% CI)	Nominal P-value[b]
Disease Duration				
<2 years	12/38 (31.6)	23/40 (57.5)	2.93 (1.16, 7.41)	.0233
≥2 years	3/29 (10.3)	17/28 (60.7)	13.36 (3.23, 55.28)	.0003
IgG4-RD Manifestation				
Newly Diagnosed	8/31 (25.8)	18/31 (58.1)	3.98 (1.36, 11.67)	.0118
Recurrent	7/36 (19.4)	22/37 (59.5)	6.08 (2.12, 17.44)	.0008
Highest known IgG4 Serum Level				
< Median	10/34 (29.4)	22/33 (66.7)	4.76 (1.69, 13.41)	.0031
≥ Median	5/33 (15.2)	18/35 (51.4)	5.90 (1.84, 18.99)	.0029
ACR/EULAR Score				
< Median	7/34 (20.6)	17/31 (54.8)	4.62 (1.53, 14.00)	.0068
≥ Median	8/33 (24.2)	23/37 (62.2)	5.02 (1.77, 14.24)	.0025
CD20 B cell count				
< Median	6/33 (18.2)	16/26 (61.5)	7.54 (2.25, 25.21)	.0010
≥ Median	5/24 (20.8)	21/35 (60.0)	5.72 (1.73, 18.91)	.0043
Prior Maintenance Therapy				
Yes	0/12 (0.0)	6/11 (54.5)	N/A[c]	N/A[c]
No	15/55 (27.3)	34/57 (59.6)	3.94 (1.78, 8.72)	.0007

[a]Flare-free, corticosteroid-free complete remission is defined as the absence of evident disease activity at week 52; defined as an IgG4-RD Responder Index score of 0 or determination by the investigator that no disease activity is present (on the basis of physical, laboratory, pathology, or other evidence), no AC-determined flare during the RCP of the trial, and no corticosteroid treatment for flare or disease control beyond the protocol required prednisone taper.
[b]P-values should be interpreted with caution due to the questionable reliability of the statistical test based on the small sample sizes.
[c]Not estimable due to 0% response in placebo arm.

hoc subgroup analysis evaluated safety and efficacy of inebilizumab across baseline characteristics: disease duration, IgG4 serum level, ACR/EULAR score, CD20 B-cell count, and prior maintenance therapy.

Results: 135 participants were randomized and received at least one dose of inebilizumab (n=68) or placebo (n=67). Baseline disease characteristics were generally well balanced between the 2 treatment groups for subgroups (Table 1). Inebilizumab treatment substantially reduced the risk of flare relative to placebo in all subgroups (Table 2), with each subgroup exhibiting a hazard ratio similar to the overall study population. Annualized flare rates were reduced by inebilizumab relative to placebo in all subgroups. Proportions of participants achieving flare-free, treatment-free complete remission or flare-free, corticosteroid-free complete remission at Week 52 were increased by inebilizumab in all subgroups with sufficient representation to permit analysis (Table 3). No subgroup exhibited safety findings that were substantially different from those observed in the overall population.

Conclusion: The MITIGATE trial demonstrates the consistent benefit and safety of inebilizumab across all baseline disease characteristic subgroups analyzed. Inebilizumab represents a viable treatment option for all patients, regardless of their IgG4-RD baseline disease characteristics.

Disclosure: Y. Tanaka: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **E. Culver**: Amgen, 1, 2, Zenus, 2; **A. Khosroshahi**: Amgen, 1, 2; **W. Zhang**: None; **K. Okazaki**: Amgen, 1; **M. Lohr**: Amgen, 1; **n. schleinitz**: Amgen, 1, 2; **X. Dong**: Amgen, 3, 11; **m. rosen**: Amgen, 3, 11; **S. Cheng**: Amgen, 3, 11; **D. Cimbora**: Amgen, 3, 11; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0280

Sera from dermatomyositis patients induce muscle weakness via activation of type I interferon (IFN) receptors

Suchada Kaewin[1], Cecilia Leijding[2], Kristofer Andreasson[2], Helene Alexanderson[3], Stefano Gastaldello[1], Ingrid Lundberg[2] and **Daniel C. Andersson**[2], [1]Karolinska Institutet, inst fysiologi och farmakologi, Stockholm, Sweden, [2]Karolinska Institutet, Stockholm, Sweden, [3]Karolinska University Hospital, Stockholm, Sweden

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is a major subtype of idiopathic inflammatory myopathies (IIMs) and characterized by muscle weakness, systemic inflammation and cutaneous lesions. Expression of type I interferon (IFN)-stimulated genes have been found in muscle, skin tissue and peripheral blood cells which links to disease activity in DM patients. However, the mechanisms of muscle weakness in DM are incompletely understood. For instance, it is unclear to what degree systemic factors, eg IFN signalling, contribute to muscle weakness and disease phenotypes. This study aims to investigate whether inhibition of type I IFN signaling protects DM serum-induced muscle weakness and to determine the effects of IFN-a and/or IFN-b on muscle force generation.

Methods: An experimental platform was used in which isolated mouse muscles were exposed to DM patient serum or healthy control serum. Flexor digitorum brevis (FDB) muscles were isolated from healthy C57BL/6JRj mice and exposed to 10% dilution of serum from healthy controls or serum from DM patients for 24 hours. To determine whether inhibition of type I IFN protect DM serum-induced muscle weakness, an IFN-a/b receptor 1 (IFNR) blocking antibody was used. Isolated FDB muscles were pre-incubated with IFNAR1 antibody for 2 h and thereafter muscles were incubated in serum from DM patients with or without IFNAR1 antibody. To investigate the effect of IFN-a and/or IFN-b on muscle force generation, FDB muscles were incubated in 10% healthy control serum containing of 1,000U/ml of IFN-a and/or IFN-b. Muscle force was measured before and after incubation in a paired fashion.

Results: Serum from DM patients, but not from healthy controls, induced a decline in FDB muscle force. Treatment with an anti-IFN1R antibody protected from the DM serum-induced muscle force decline. Surprisingly, neither IFN-a nor IFN-b affected force production when incubated for 24h in isolation with the muscles. However in combination, IFN-a together with IFN-b, induceed a marked reduction in muscle force, which was rescued with addition of an IFN1R blocking antibody.

Conclusion: Serum from DM patients contain factors that can induce muscle weakness. One mechanism for this effect is mediated by pathways dependent on type I IFN Receptor signaling.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

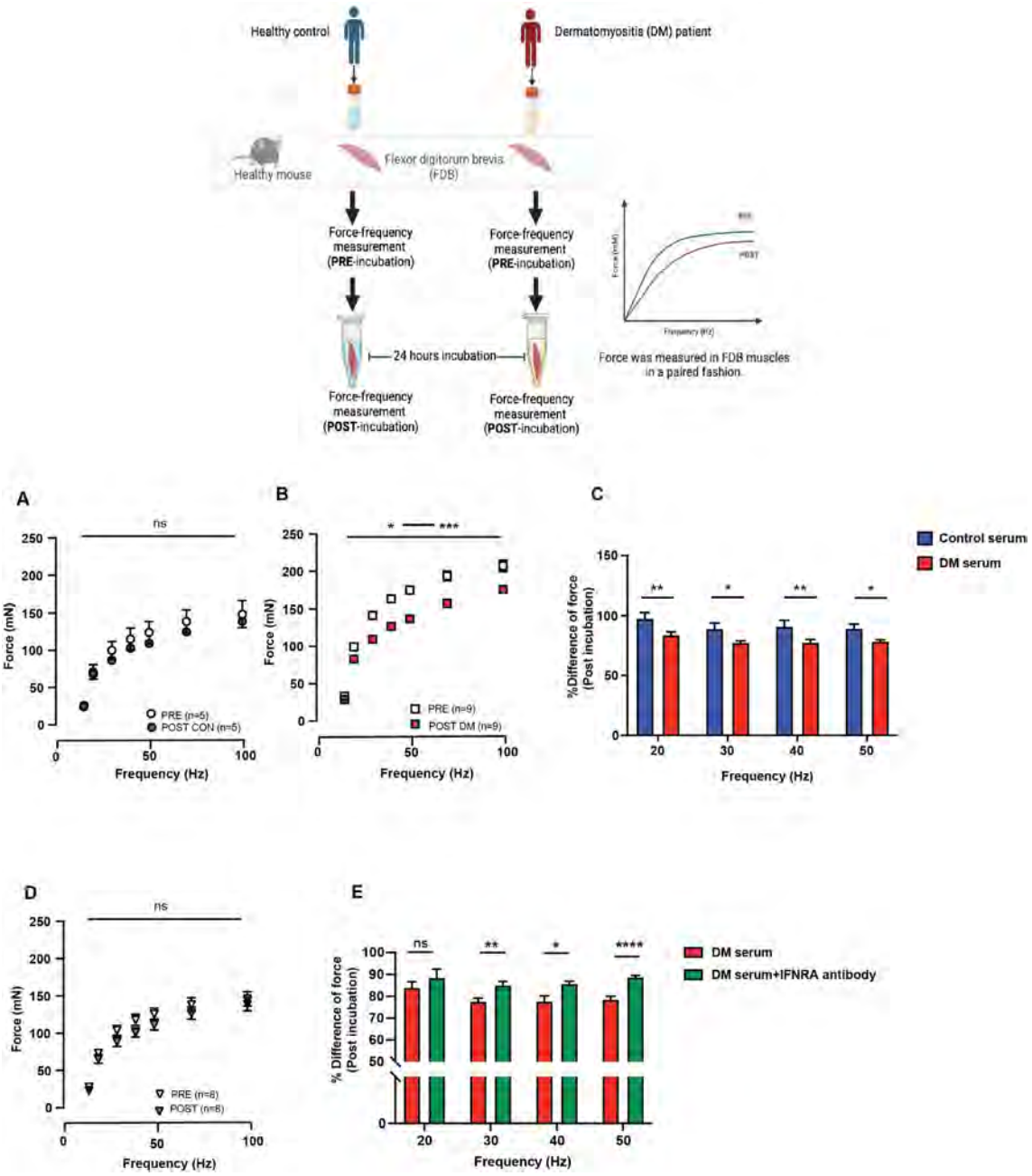
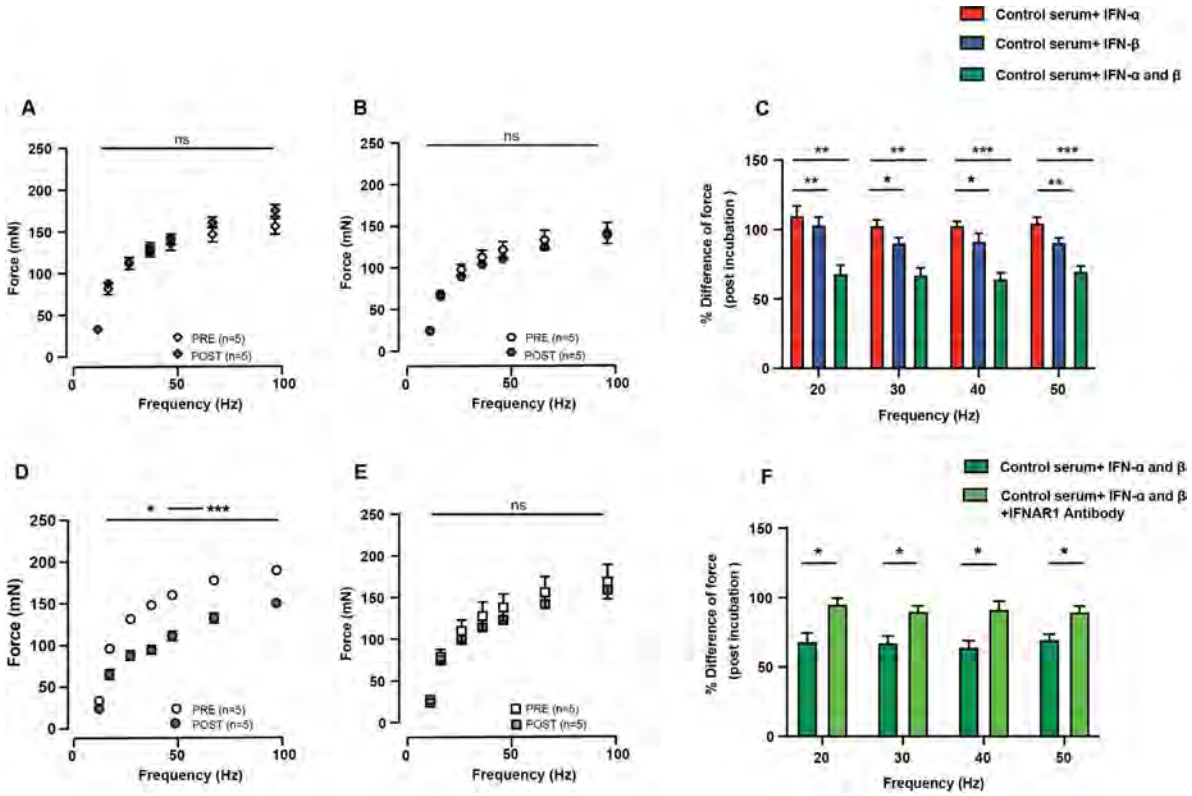


Figure 1 Inhibition of type I IFN pathway protects the effect of DM serum-induced muscle weakness in isolated skeletal muscles from healthy mice. (A) Force-frequency curve from isolated flexor digitorum brevis (FDB) muscles before (PRE) and after (POST) incubation with 10% serum from healthy control. Isolated FDB muscles were incubated with serum from healthy control and repeated in difference muscles for five times. (B) Force-frequency curve from FDB muscles before (PRE) and after (POST) incubation with 10% serum from dermatomyositis (DM) patients. Serum from nine DM patients were used in the experiments. Force measurement was performed in isolated FDB muscle in a paired fashion. (C) The bar graph demonstrates the percentage of differences of force after exposed to serum from healthy control (blue) or DM serum (red) at 20-50 Hz. (D) Force-frequency curve from FDB muscles were incubated with serum form DM patients in the presence of IFNAR1 antibody. (E) The bar graph demonstrates the percentage of differences of force after exposed to serum from DM patients (red) or DM serum with IFN-a/b receptor 1 (IFNAR1) antibody (dark green) at 20-50 Hz. Data were presented as mean +/−SEM, *p<0.05, **p< 0.01 ***p<0.0001, Bonferroni multiple comparison test was performed for data analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



IFN-a and IFN-b decline contractile force in isolated FDB muscle. (A) Force-frequency curve from FDB muscle before (PRE) and after (POST) incubated with 10% healthy serum containing IFN-a (1,000U/ml) for 24 hours. (B) Force-frequency curve from FDB muscle before (PRE) and after (POST) exposed to 10% healthy serum containing IFN-b (1,000U/ml). (C) The bar graph demonstrates the percentage of differences of force after exposed to serum from healthy serum containing of IFN-a (red) or IFN-b (blue) and combination of IFN-a plus IFN-b (green) at 20-50 Hz. (D) Force-frequency curve from FDB muscle before (PRE) and after (POST) exposed to 10% of healthy serum containing IFN-a together with IFN-b (1,000U/ml). (E) Force-frequency curves from FDB muscle before (PRE) and after (POST) incubated with 10% healthy serum containing of IFN-a and IFN-b (1,000U/ml) and treated with type I IFN-a/b receptor1 (IFN1R) antibody at the final concentration of 10 g/ml (green). (F) The bar graph demonstrates the percentage of differences of force after exposed to serum from healthy serum containing of IFN-a and IFN-b (dark green) or IFN-a and IFN-b plus IFN1R blocking antibody (light green) at 20-50 Hz. Data were presented as mean +/–SEM, *p<0.05, **p< 0.01 ***p<0.0001, two way ANOVA, Bonferroni multiple comparison test was performed for the data analysis.

Disclosure: S. Kaewin: None; **C. Leijding**: None; **K. Andreasson**: None; **H. Alexanderson**: None; **S. Gastaldello**: None; **I. Lundberg**: AstraZeneca, 1, Chugai, 1, Johnson & Johnson, 5, Novartis, 1, 11, Pfizer, 1, Roche, 11; **D. Andersson**: Bristol-Myers Squibb(BMS), 6.

Abstract Number: 0281

anti-il-6 Autoantibodies and IL-6 Signalling in Idiopathic Inflammatory Myopathies

Anja Srpcic[1], Manca Ogric[1], Sasa Cucnik[1], Sergej Pirkmajer[2], Katja Lakota[1] and **Katja Perdan Pirkmajer**[1], [1]University Medical Centre Ljubljana, Ljubljana, Slovenia, [2]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of systemic autoinflammatory diseases that affect muscle tissue, often leading to muscle atrophy, weakness and myalgia. While IIM patients frequently present with myositis-specific or myositis-associated autoantibodies, less is known about the presence and function of natural anti-cytokine autoantibodies (ACAAs). Some studies report their presence in healthy individuals, suggesting a role in tissue homeostasis and regeneration, while others have found elevated levels in autoimmune diseases. The aim of this study was to measure serum levels of ACAAs directed against interleukin-6 (anti-IL-6) in IIM patients and assess their potential impact on IL-6 signalling, a pathway associated with inflammation-induced muscle wasting.

Methods: Serum samples were collected from 44 consecutive IIM patients treated at the Department of Rheumatology, University Medical Centre Ljubljana, and from 36 healthy controls (HC, Fig. 1). Patients were stratified into treatment-naive (n=13) and previously treated groups (n=31). ELISA was used to quantify serum IL-6 (BioLegend), soluble IL-6 receptor (sIL-6R, Proteintech), and anti-IL-6 levels (in-house ELISA). To assess the functional effects of anti-IL-6 antibodies, sera were mixed with recombinant human IL-6 (rhIL-6) and applied to a reporter gene assay (RGA, SVAR Life Science) that detects IL-6 signalling pathway activity. In treatment-naive patients, the relationship between RGA activity and markers of muscle damage was evaluated.

Results: Serum IL-6 levels were significantly higher in IIM patients than in HC, while sIL-6R levels showed no significant difference. Anti-IL-6 levels tended to be lower in IIM patients, but this difference did not reach statistical significance (p=0.08). RGA activity, indicating IL-6 signalling pathway activation, was markedly higher in IIM patients (p< 0.0001) and tended to be higher in individuals with low anti-IL-6 levels (Fig. 2). To rule out interference from endogenous IL-6 present in serum samples, control experiments were performed without the addition of recombinant human IL-6 (rhIL-6), confirming that the observed increase in RGA activity was not due to endogenous IL-6. Treatment status had no significant effect on the measured parameters, although treatment-naive patients exhibited higher IL-6 and lower anti-IL-6 levels. Among these patients, those with higher RGA activity tended to have lower manual muscle test scores and higher serum creatine kinase (CK) levels (Fig. 3).

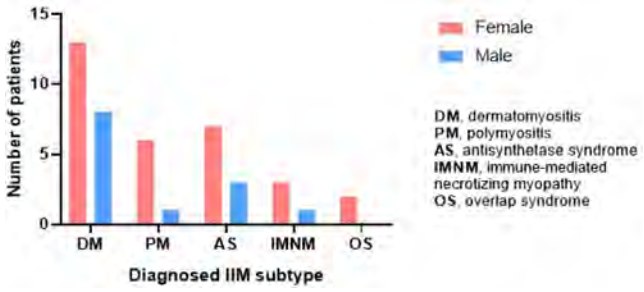


Figure 1: Number of IIM patients included in the study.

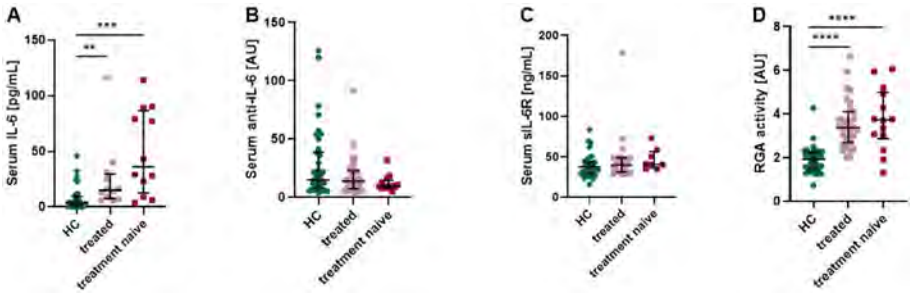


Figure 2: Serum levels of IL-6 (Fig. 2A), anti-IL-6 autoantibodies (Fig. 2B), soluble IL-6 receptor (Fig. 2C) and serum RGA activity (Fig. 2D) in treatment-naive or treated IIM patients and healthy controls. Kruskal-Wallis test: ** p<0.01; *** p<0.001; **** p<0.0001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

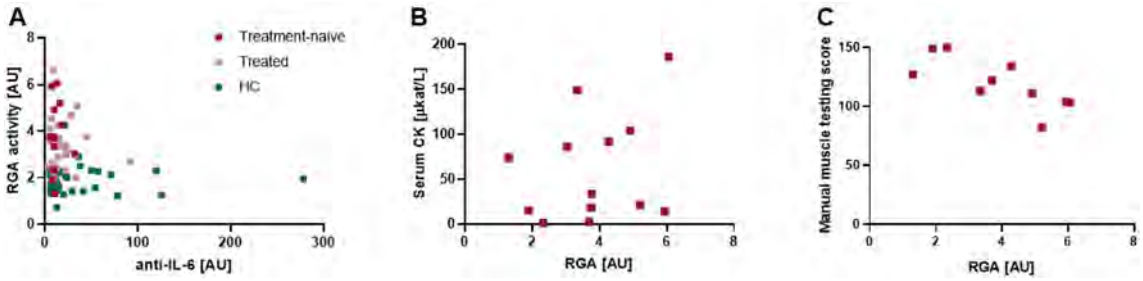


Figure 3: Correlation of RGA activity with anti-IL-6 autoantibodies in serum of treatment-naive or treated patients and healthy controls (Fig. 3A). Correlation of serum creatine kinase levels (Fig. 3B) and manual muscle testing score (Fig. 3c) with RGA activity in treatment-naive patients.

Conclusion: Sera from IIM patients showed enhanced IL-6 signalling activity, independent of the treatment status and serum IL-6, or sIL-6R levels. Based on the inverse relationship between anti-IL-6 levels and RGA activity, we hypothesise that these autoantibodies may neutralise IL-6 signalling. In treatment-naive patients, elevated RGA activity was associated with markers of muscle damage, indicating a pathological role of IL-6 signalling activity in muscle function in these patients.

Disclosure: A. Srpcic: None; **M. Ogric**: None; **S. Cucnik**: None; **S. Pirkmajer**: None; **K. Lakota**: None; **K. Perdan Pirkmajer**: None.

Abstract Number: 0282

Clinical Meaningfulness and Improvement Thresholds of Myositis Core Set Measures: Association with Patient-Reported Outcomes

Shiri Keret[1], **Raisa Lomanto Silva**[2], Irada Choudhuri[3], Eugenia Gkiaouraki[3], Tanya Chandra[3], Nantakarn Pongtarakulpanit[3], Shreya Sriram[3], Niladri Bhowmick[3], Vaidehi Kothari[3], Kaushik Sreerama Reddy[3], Eaman Alhassan[4], Anushka Aggarwal[5], Maha Almackenzie[6], Siamak Moghadam-Kia[4], Dana Ascherman[7], Chester V. Oddis[7] and Rohit Aggarwal[8], [1]Bnai Zion Medical Center, Atlit, Israel, [2]Massachusetts General Hospital, Boston, MA, [3]University of Pittsburgh Medical Center, Pittsburgh, [4]University of Pittsburgh Medical Center, Pittsburgh, PA, [5]Indraprastha Apollo Hospital, New Delhi, India, [6]Medical Cities of the Ministry of the Interior, Riyadh, Saudi Arabia, [7]University of Pittsburgh, Pittsburgh, PA, [8]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The six myositis core set measures (CSMs) are widely utilized to assess disease activity in idiopathic inflammatory myopathies (IIM). However, their association with how the patient feels and functions, and minimal thresholds for clinically meaningful improvement, remain undefined.

We aimed to evaluate the validity, meaningfulness, and minimal clinical thresholds of change in CSMs in relation to symptoms, function, and quality of life in patients with IIM.

Methods: Adults with IIM were enrolled in a 6-month prospective observational study. Monthly data collected included CSMs (patient global assessments, Health Assessment Questionnaire [HAQ] and creatine kinase [CK]) and patient-reported outcome measures (PROMs) such as pain and fatigue (VAS), Short Form-36 (SF-36), and PROMIS-Physical Function (PROMIS-PF). Physician measures, including MMT-8 (scale 0-80), MDAAT, and physician global assessments, were

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Longitudinal correlations between core set measures (CSMs) and outcome measures using linear mixed models adjusted for age, sex, and race. Most CSMs showed strong associations with patient-reported outcomes and other clinical metrics, supporting their validity in tracking disease activity in IIM.

Table 1. The correlation of the myositis CSMs with other myositis CSMs and outcome measures during the follow-up period, using a linear mixed model, adjusted for sex, age, and race.

Variable	CK	Patient-global	HAQ-DI	Physician-global	MMT	EXGLB
CK	-	0.06*	0.04	0.04*	-0.18*	-0.004
Patient-global	0.06*	-	2.13**	0.19**	-0.19**	0.48**
HAQ-DI	0.04	2.13**	-	1.07**	-3.37**	0.19**
Physician-global	0.04*	0.19**	1.07**	-	-0.09**	0.78**
MMT	-0.18*	-0.19**	-3.37**	-0.09**	-	-0.09
EXGLB	-0.004	0.48**	0.19**	0.78**	-0.09	-
Muscle disease	0.03*	0.69**	0.22**	0.97**	-2.44**	0.36**
PROMIS- PF T score	-0.03	-0.19**	-0.06**	-0.11**	0.19*	-1.55**
Pain (VAS)	0.06*	0.32**	0.04**	0.078	-0.08*	0.007
Fatigue (VAS)	0.07*	0.42**	0.02*	0.09*	-0.04	0.06
SF36- Physical functioning	-0.43	-0.05**	-0.01**	-0.024**	0.04*	-0.02**
PCS (physical summary score)	-0.17*	-0.15**	-0.02**	-0.06**	0.13*	-0.04**
MCS (mental summary score)	-0.11	-0.03*	-0.003	-0.02*	0.15	-0.01

* Correlation is significant at the **0.05** level
** Correlation is significant at the **0.01** level

(**Bold** indicates significance).

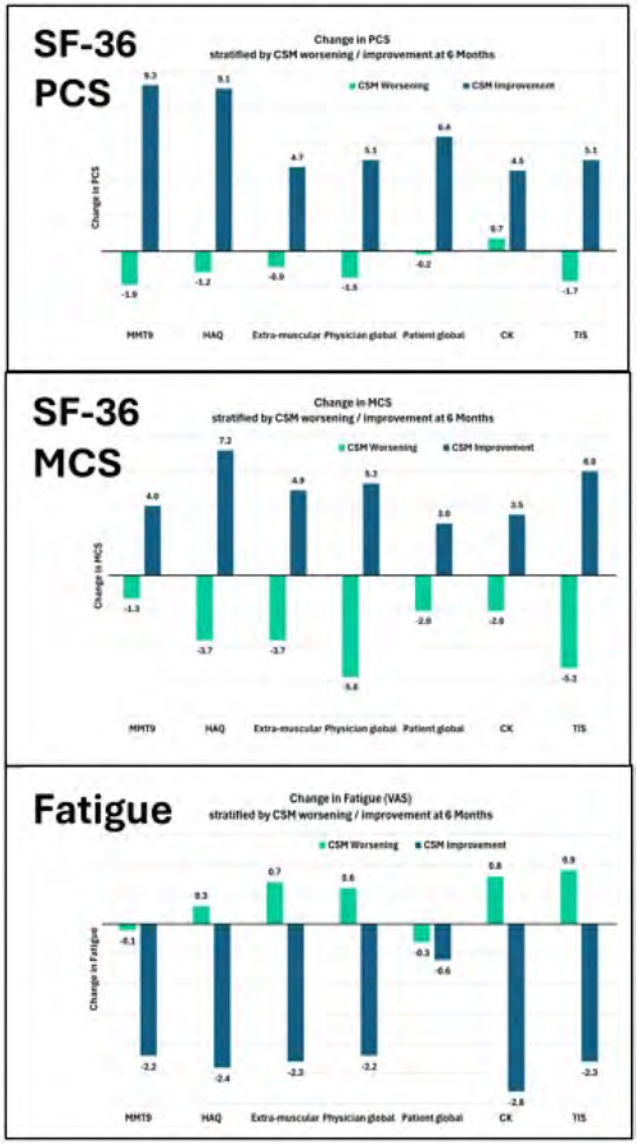


Figure 1. Changes in patient-reported outcomes (PCS, MCS, and Fatigue VAS) stratified by levels of improvement in CSMs and TIS over 6 months. Greater improvements in core measures were associated with meaningful gains in quality of life and symptom burden, as perceived by patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Change over 6 months, effect size, and clinically important difference (CID) of CSMs, in physician-reported change and patient-reported change groups.

Anchor used	Patient assessment of change		Physician assessment of change	
Variable (mean± SD)	Disease improved n=19	No change/ worsening in disease n=16	Disease improved n=21	No change/ worsening in disease n=17
Physician global disease activity				
Mean difference (6 Months to baseline)	-2.69±1.99	-0.56±0.89	-3.11±1.35	0.18±0.66
P value	**<0.001**	0.72	**<0.001**	0.39
Effect size	-1.35	-0.06	-2.31	0.27
CID		2.1		3.3
Patient global disease activity				
Mean difference (6 Months to baseline)	-1.26±2.56	0.47±1.36	-1.24±2.42	0.32±1.89
P value	0.06	0.26	0.053	0.29
Effect size	-0.49	0.35	-0.51	0.17
CID		1.7		1.6
Muscle manual testing (MMT)				
Mean difference (6 Months to baseline)	4.32±4.72	0.13±1.09	7.19±9.34	-0.11±1.05
P value	**0.003**	1.00	**<0.001**	1.0
Effect size	0.92	0.12	0.77	-0.11
CID		4.2		7.3
HAQ-DI				
Mean difference (6 Months to baseline)	-0.42±0.55	0.12±0.30	-0.47±0.55	0.12±0.28
P value	**0.006**	0.099	**0.005**	0.09
Effect size	-0.77	0.39	-0.85	0.43
CID		0.5		0.6
Creatine kinase (CK)				
Mean difference (6 Months to baseline)	-945.4±2345.9	530.1±1161.9	-1106.5±2315.4	556.5±1061.2
P value	**0.03**	0.099	**0.007**	**0.033**
Effect size	-0.40	0.47	-0.48	0.53
CID		1475		1663
Extra-muscular global disease activity				
Mean difference (6 Months to baseline)	-1.48±1.71	-0.06±1.04	-1.77±1.42	0.19±0.89
P value	**0.003**	0.40	**<0.001**	0.59
Effect size	-0.87	-0.05	-1.25	0.22
CID		1.4		2.0

gathered every three months. Baseline and longitudinal associations were evaluated using Spearman correlation and linear mixed models. Responsiveness, effect sizes, and clinically important differences (CID) were assessed using patient- and physician-reported change at 6 months as anchors.

Results: Fifty patients (mean age 51.6 ± 14.9, 60% females) were enrolled, including 48% dermatomyositis, 12% polymyositis, 18% necrotizing myopathy, and 22% anti-synthetase syndrome. Most CSMs demonstrated strong baseline and longitudinal associations with key patient- and clinician-reported outcome measures, including pain, fatigue, physical function, and quality of life. CK showed weaker associations at baseline, but significant longitudinal correlations with most outcome measures (**Table 1**). In patients with improvement in absolute percentage change in the CSMs and TIS over 6 months, corresponding positive trends were observed in quality of life (PCS, MCS), fatigue (VAS), pain (VAS), and physical function (PROMIS-PF) (**Figure 1**). Specifically, greater improvements in patient and physician global assessments, disability (HAQ-DI), and muscle strength (MMT) were associated with incremental gains in quality of life and physical function measures, along with reductions in fatigue and pain).In patients who improved based on the patient global impression of change (PtGIC) and physician global impression of change (PhGIC) anchors, significant improvements were observed in physician global disease activity, MMT, HAQ-DI, CK, and extra-muscular disease activity, with moderate to large effect sizes. The CIDs according to PtGIC were 2.1 for physician global disease activity, 1.4 for extra-muscular disease activity, 1.7 for patient global disease activity, 4.2 for MMT, 0.5 for HAQ, and 1475 IU/L for CK levels. Similar results were observed for physician-reported improvement (**Table 2**.

Conclusion: Myositis CSMs showed strong validity and responsiveness, reflecting meaningful changes in patient symptoms, function, and quality of life, and supporting their utility in IIM clinical trials and practice. CIDs were defined for all CSMs, improving their interpretability and application in clinical trials and routine care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Keret: None; **R. Lomanto Silva**: None; **I. Choudhuri**: None; **E. Gkiaouraki**: None; **T. Chandra**: None; **N. Pongtarakulpanit**: None; **S. Sriram**: None; **N. Bhowmick**: None; **V. Kothari**: None; **K. Sreerama Reddy**: None; **E. Alhassan**: None; **A. Aggarwal**: None; **M. Almackenzie**: None; **S. Moghadam-Kia**: None; **D. Ascherman**: None; **C. V. Oddis**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

Abstract Number: 0283

The Performance of Rule-Based Algorithms to Identify Patients With Idiopathic Inflammatory Myopathies in Electronic Health Records

Ana Valle[1], Amy Vo[2], Rochelle Castillo[1], Yumeko Kawano[3], Leah Santacroce[3], Daniel Solomon[4], Katherine Liao[3] and Candace Feldman[3], [1]Brigham and Women's Hospital, Brookline, MA, [2]Harvard Medical School, Boston, [3]Brigham and Women's Hospital, Boston, MA, [4]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM; including dermatomyositis, polymyositis, and inclusion body myositis) are heterogenous systemic inflammatory conditions that cause significant disability and morbidity. The study of these rare diseases (prevalence of 10-20/100,000) is limited by our ability to accurately classify cases with a high positive predictive value (PPV). Rule-based algorithms that rely on ICD codes have been used to identify IIM prevalence based on administrative claims and IIM hospitalizations with reported PPVs of 90% or higher. The objective of this study was to apply published rule-based ICD-based algorithms to electronic health record (EHR) data to identify IIM cases to build an IIM cohort.

Methods: Data was extracted from a multihospital EHR system. We identified patients with $\geq$1 ICD 9/10 codes for IIM (359.7*, 710.3, 710.4, G72.4*, M33.*, M36.*) between 1/1/2000 - 9/6/2024; from this set, a random sample of 250 patients were selected for chart review. Subjects were classified as having "definite", "probable", "possible", or "unlikely" IIM per the 2017 EULAR/ACR Classification Criteria. ICD codes were extracted for all subjects. The performance of 8 previously published rule-based algorithms for IIM were compared against "definite" cases of IIM from chart review. Algorithms developed using ICD-9 codes were updated to map to ICD-10 codes. Reviews were performed by two independent reviewers (ALV, AV) and discrepancies were adjudicated by a blinded third reviewer (RLC). As the goal was to create an IIM cohort for study, the key performance characteristic of interest was PPV. Specificity, sensitivity, and negative predictive value (NPV) were also calculated.

Results: We identified 5706 patients with $\geq$1 IIM ICD 9 or 10 code from the EHR. The prevalence of definite IIM in this cohort was 34.8% (Table 1). M33.* (dermatopolymyositis) was the most common code (35.2%) in the cohort. The highest PPV achieved was 65% with $\geq$2 IIM ICD codes in the outpatient setting within 2 months (Algorithm 1) and IIM ICD codes used $\geq$2 times between 30 and 365 days (Algorithm 7, Table 2). Algorithm 7 classified 67.8% of definite IIM cases. The algorithm achieving the highest specificity at 94% had low sensitivity (16%) (Algorithm 5, Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of individuals with ≥1 ICD9/10 codes for IIM, N=250		
Median age – Years (IQR)		64 (56, 78)
Sex – N (%)	Female	165 (66.0)
	Male	84 (33.6)
	Other	1 (0.4)
Race – N (%)	White	182 (72.8)
	Black	29 (11.6)
	Asian	10 (4.0)
	Other	6 (2.4)
	Not disclosed	23 (9.2)
Ethnicity – N (%)	Hispanic/Latinx	19 (7.6)
	Not Hispanic/Latinx	169 (67.6)
	Not disclosed	62 (24.8)
EULAR/ACR 2017 IIM Classification – N (%)	Definite	87 (34.8) (47 DM, 18 PM, 22 IBM)*
	Probable	28 (11.2) (6 DM, 18 PM, 4 IBM)
	Possible	3 (1.2) (1 DM, 2 PM)
	Unlikely	132 (52.8)
Jo-1 Antibody Status – N (%)	Positive	7 (2.8)
	Negative	148 (59.2)
	Not assessed	95 (38)
Muscle Biopsy– N (%)	Performed	75 (30)

*DM = dermatomyositis, PM = polymyositis, and IBM = inclusion body myositis.

Table 2. Description and performance of the algorithms compared to chart review definite IIM among n=250 subjects.

	Algorithms	# Cases as defined by algorithm	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
1	Any ICD code ≥2 from outpatient physician visit <2 months	82	61 (50-71)	82 (75-88)	65 (53-75)	80 (73-86)
2	Any ICD code billed ≥1 by rheumatologist, regardless of setting	68	39 (29-50)	79 (72-85)	50 (38-62)	71 (64-77)
3	Any ICD code billed ≥1 by rheumatologist, dermatologist, or neurologist, regardless of setting	126	82 (72-89)	66 (58-73)	56 (47-65)	87 (80-92)
4	Any ICD code during hospitalization	46	24 (16-35)	85 (78-90)	46 (31-61)	68 (61-74)
5	Primary hospitalization ICD code	23	16 (9-26)	94 (90-97)	61 (39-80)	68 (61-74)
6	≥2 ICD codes during hospitalization	19	13 (6-21)	95 (91-98)	58 (33-80)	67 (61-73)
7	Any ICD code ≥2 frequency at least 30 days and less than 365 days apart	91	68 (57-77)	80 (73-86)	65 (54-75)	82 (75-88)
8	Any ICD code ≥3 frequency from any physician in any setting	94	67 (56-76)	78 (71-84)	62 (51-72)	81 (74-87)

* Algorithms 1, 2, 5 based on Bernatsky S et al. Ann Rheum Dis. 2009;68(7):1192-1196; mapped to ICD 10 codes. Algorithms 4, 6, based on Hannah JR et al. Rheumatol Adv Pract. 2022;6(3):rkac102; with the exclusion of interstitial lung disease and less specific codes (M60.8 for Other Myositis, M60.9 for Myositis unspecified). Algorithms 3, 4, 7 based on Smoyer-Tomic et al. BMC Musculoskelet Disord. 2012;13:103; mapped to ICD 10 codes.

Conclusion: The best performing rule-based IIM algorithms correctly classified 65% of definite IIM cases. The lower performance from prior reports may be due to the different patient populations and lack of direct mapping of ICD-9 codes to ICD-10 codes. Future directions include considering a broader range of EHR data including IIM treatments or data extracted using natural language processing related to IIM characteristics to improve the ability to accurately classify IIM cases at high PPV (≥80%); a crucial first step for IIM studies.

Disclosure: A. Valle: None; **A. Vo**: None; **R. Castillo**: Chronicle Medical Software, Inc., 2; **Y. Kawano**: None; **L. Santacroce**: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9; **K. Liao**: Merck/MSD, 2, UCB, 2; **C. Feldman**: American College of Rheumatology, 2, Arthritis Foundation, 5, 12, Task Force Member, Bain Capital, 2, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 1, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0284

Glucocorticoid Tapering and Relapse Risk in Anti-ARS Antibody-Positive Myositis: A Retrospective Study in a Single-Center Cohort Treated with Immunosuppressants

Ayaka Inoue[1], Takashi Yamane[2], Noriaki Yasuda[3] and Takahisa Ohnishi[1], [1]Kakogawa Central City Hospital, Kakogawa, Japan., kakogawa-cho, kakogawa city, Hyogo, Japan, [2]Kakogawa Central City Hospital, Kobe, Hyogo, Japan, [3]Kakogawa Central City Hospital, Kakogawa, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti–synthetase syndrome is generally responsive to glucocorticoid (GC) therapy, though relapse frequently complicates tapering. Prolonged GC use is associated with adverse events and decreased quality of life, yet the optimal maintenance dose to prevent relapse remains unclear. While immunosuppressants (IS) are often used in combination with GC to prevent disease recurrence, the risk of flare in patients treated with both remains insufficiently understood.

Methods: We retrospectively reviewed patients with anti–aminoacyl–tRNA synthetase (anti–ARS) antibody-positive myositis, identified by enzyme immunoassay (LSI Medience), treated at our institution between April 2018 and September 2024. Among 45 patients identified, 37 who received GC and had ≥26 weeks of follow-up were included. Clinical characteristics, relapse, GC tapering, and IS use were analyzed. Multivariate Cox proportional hazards, ROC curve, and Kaplan–Meier analyses were performed.

Results: Of the 37 patients, 21 were female (57%) with a mean age of 64 years; 33 had interstitial lung disease. Methylprednisolone pulse therapy was given in 10 cases; the average initial prednisolone (PSL) dose was 39 mg/day (0.7 mg/kg). IS was used in 36 of 37 cases (97%).

Table 1. Predictive Factors for Relapse in Patients with Anti-ARS Antibody Syndrome: Univariate and Multivariate Cox Proportional Hazards Models

Table 1. Predictive Factors for Relapse in Patients with Anti-ARS Antibody Syndrome: Univariate and Multivariate Cox Proportional Hazards Models

A. Baseline Clinical and Disease Characteristics

Variable	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Disease duration (days)	1.00 (0.99 – 1.001)	0.18	—	—
Arthritis	1.25 (0.53 – 2.97)	0.61	0.93 (0.37 – 2.35)	0.88
Mechanic's hands	1.10 (0.43 – 2.93)	0.83	1.47 (0.53 – 4.00)	0.46
Raynaud's phenomenon	3.89 (1.33 – 11.40)	0.013	3.80 (1.18 – 12.30)	0.026
Fever	3.61 (1.27 – 10.27)	0.016	—	—
ILD	25.66 (0.07 – 10093)	0.36	0 (N/A)	0.98

* Multivariate for ILD, arthritis, mechanic's hand, and Raynaud's phenomenon

B. Initial Treatment-Related Factors

Treatment	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Days to concomitant IS initiation	1.01 (1.00 – 1.02)	0.029	1.01 (1.00 – 1.03)	0.018
mPSL pulse therapy	1.28 (0.47 – 3.53)	0.63	1.63 (0.52 – 5.06)	0.401
Daily PSL dose at baseline	1.58 (0.29 – 8.74)	0.6	—	—
Daily PSL dose at 26 weeks	1.06 (0.91 – 1.26)	0.44	1.06 (0.88 – 1.26)	0.546
Daily PSL dose at 52 weeks	1.15 (0.90 – 1.47)	0.28	—	—

*Multivariate for age, Days until concomitant IS induction, mPSL pulse therapy, and Daily PSL(mg/kg).

Abbreviations: IS:immunosuppressants, mPSL:methylprednisolone:, PSL:prednisolone, HR:hazard ratio, CI:confidence interval

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Prednisolone Dose at Relapse in Anti-Jo-1 and Non-Jo-1 Anti-ARS Antibody Groups

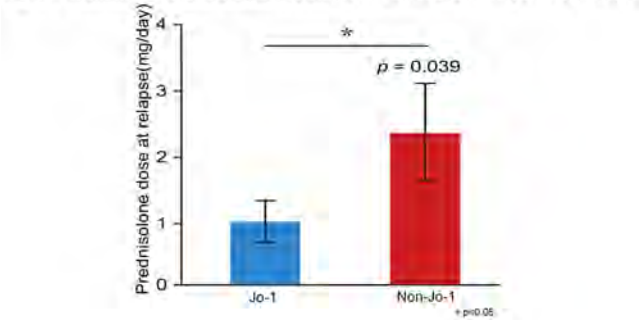
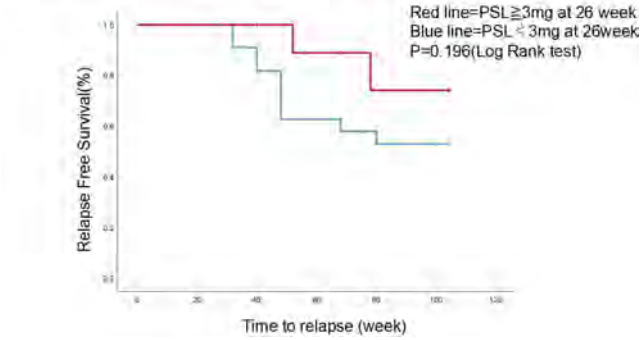


Figure2:Kaplan–Meier Curve for Relapse-Free Survival According to Prednisolone Dose at Week 26 (<3 mg/day vs ≥3 mg/day)



Anti–Jo–1 antibodies were positive in 9 patients, non–Jo–1 in 26, and untyped in 2. Relapse occurred in 5 Jo–1-positive (56%) and 16 non–Jo–1 (62%) patients (p = 1.00). No relapses were observed in the Jo–1 group when PSL reached 5 mg/day, while 5 relapses occurred in the non–Jo–1 group. The mean PSL dose at relapse was significantly lower in the Jo–1 group (1.0 vs. 4.3 mg/day; p = 0.039).

In multivariate Cox analysis, Raynaud's phenomenon (HR 3.8; 95% CI 1.18–12.3; p = 0.026) and longer interval until IS initiation (HR 1.01; 95% CI 1.00–1.03; p = 0.018) were independently associated with relapse. ROC analysis identified 1.55 mg/day as the optimal PSL cutoff to predict non-relapse (sensitivity 66.7%, specificity 68.8%). Relapse was more common in patients tapered to < 5 mg/day than those on ≥5 mg/day. KM analysis from week 26 to 104 showed a trend toward more relapse in patients < 3 mg/day (log-rank p = 0.196).

Conclusion: In this IS-treated cohort, Jo–1-positive patients were able to maintain remission on lower GC doses, with no relapses observed when PSL was tapered to 5 mg/day. However, relapse was more frequent in patients tapered below 5 mg/day, and a possible trend toward increased relapse was also observed below 3 mg/day. Although nearly all patients received IS, delayed initiation was associated with increased relapse risk. These findings support early immunosuppressant use and strategic tapering guided by clinical risk factors such as the presence of Raynaud's phenomenon and timing of IS initiation. Tapering GC doses to 3 mg/day may be possible with caution, although relapse risk should be carefully monitored in anti–synthetase syndrome.

Disclosure: A. Inoue: None; **T. Yamane**: GlaxoSmithKlein(GSK), 6; **N. Yasuda**: None; **T. Ohnishi**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0285

Delayed-Onset Myopathy in Dermatomyositis: A Retrospective Cohort Study

Connor Buechler[1], Nawang Singhe[2], Lindsey Wanberg[2], Cody Rasner[2], Joseph McGrath[2], Karen Baker-James[2], Rebecca Freese[2] and David Pearson[3], [1]University of Minnesota, Mendota Heights, MN, [2]University of Minnesota, Minneapolis, MN, [3]Department of Dermatology, University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Amyopathic dermatomyositis (ADM) is a subset of DM in which cutaneous findings occur without muscle disease for >6 months after diagnosis. However, there is limited data on the mean time to onset of muscle symptoms in classic DM (CDM). Differentiating ADM and CDM may affect treatment, screening for comorbidities including malignancy and interstitial lung disease, and clinical trial inclusion.

Methods: We performed a retrospective cohort study of adult DM patients at an academic tertiary referral center to determine the mean time to onset of muscle symptoms in CDM and characterize the presentation of patients who develop muscle symptoms >6 months after diagnosis. Patients were reviewed to confirm diagnostic and demographic details, including the timing of muscle symptom onset relative to first cutaneous or pulmonary symptom onset and the time from presentation to formal diagnosis.

Results: 223 patients with DM were identified, of which the majority had CDM (172; 77%). 154 CDM patients had a clearly identifiable date of symptom onset. Median time to muscle symptoms was 0 months, with 24 (15.6%) developing muscle symptoms >6 months after first symptom onset. The onset of muscle symptoms in the delayed group ranged from 6.4 months to 42.4 months (median 13.3 months). Those with late onset muscle symptoms did not differ demographically from typical CDM or ADM patients, but they experienced a higher rate of ILD (33%) than either typical CDM (29%) or ADM (18%) patients and lower rate of DM-related death (0%) than either typical CDM (11%) or ADM (5.8%) patients. Those with late onset muscle symptoms also experienced a longer mean delay from presentation to diagnosis (8.4 months) than either ADM (4.3 months) or typical CDM (1.9 months) patients (ANOVA p=0.024).

Conclusion: Our results suggest that even patients diagnosed with ADM should be monitored for muscle weakness and pain. This study sheds further light on a subpopulation of DM patients with potentially disparate outcomes from either CDM or ADM, which could affect counseling, treatment, and clinical trial inclusion.

Disclosure: C. Buechler: None; **N. Singhe**: None; **L. Wanberg**: None; **C. Rasner**: None; **J. McGrath**: None; **K. Baker-James**: None; **R. Freese**: None; **D. Pearson**: Biogen Inc, 2, Daiichi Sankyo Inc, 5, EMD Serono, Billerica, MA, US, 5, Merck KGaA, Darmstadt, Germany, 2, Pfizer Inc, 2, Priovant Therapeutics, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0286

Anifrolumab for Treatment of Refractory Juvenile Dermatomyositis in Adult Patients

Connor Buechler[1] and David Pearson[2], [1]University of Minnesota, Mendota Heights, MN, [2]Department of Dermatology, University of Minnesota, Minneapolis, MN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is an autoimmune connective tissue disorder with a chronic, relapsing course that can persist into adulthood. Current therapies exhibit widely variable efficacy. While JDM pathogenesis remains incompletely understood, continuous activation of type-I interferon (IFN) signaling is thought to play a key role, leading to changes including activation and infiltration of CD4+ and CD8+ T-cells, mitochondrial dysfunction, microvascular remodeling, and reduced muscle stem-cell repair and proliferation. IFN activity has been shown to correlate with histological and clinical measures of disease activity. Anifrolumab, a monoclonal antibody that blocks the type I IFN receptor IFNAR1, has been approved for treatment of SLE and is currently undergoing a phase III trial in adult DM, with some case reports and series showing encouraging prospects.

Methods: Clinical data were extracted to complete a retrospective case series.

Results: Three female patients with JDM, ages 22, 24, and 48, were seen in the adult dermatology clinic. They had failed to obtain durable control of cutaneous JDM through combinations of methotrexate, mycophenolate, hydroxychloroquine, intravenous/subcutaneous immune globulin, or prednisone. Two had also failed systemic janus kinase inhibitors (JAKi), two had failed rituximab, one had failed quinacrine, one had failed azathioprine, one had failed cyclophosphamide, and one had failed cyclosporine. After initiation of anifrolumab at 300 mg per month alongside existing therapies, each patient saw remarkable improvement in cutaneous disease. Each patient was able to reduce systemic glucocorticoids and taper other therapies, including cessation of prior intravenous or subcutaneous immune globulin in two cases and JAKi in one case.

Conclusion: These encouraging results illustrate the relationship between type-I IFN modulation and JDM as well as the promise of anifrolumab as a rescue medication for refractory cases. As there are no current FDA-approved therapies for refractory cutaneous JDM, these cases also highlight the need for further systematic investigation into type-I IFN modulation in JDM therapy.

Disclosure: C. Buechler: None; **D. Pearson**: Biogen Inc, 2, Daiichi Sankyo Inc, 5, EMD Serono, Billerica, MA, US, 5, Merck KGaA, Darmstadt, Germany, 2, Pfizer Inc, 2, Priovant Therapeutics, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0287

Comprehensive Profiling of Neutrophil Subsets Reveals Functional Signatures Linked to Vasculopathic Features in Patients with Inflammatory Myopathies

Daniel Alberto Carrillo-Vázquez[1], Beatriz Alcalá-Carmona[1], Jennifer Tiare Balderas Miranda[2], Yatzil Reyna Juarez[3], María José Ostos Prado[1], Samuel Govea-Peláez[1], Nancy R Mejía Domínguez[4], Guillermo Juárez Vega[4], Karina Santana-De Anda[1], Jiram Torres-Ruiz[5] and Diana Gomez-Martin[6], [1]Instituto Nacional De Ciencias Médicas Y Nutrición Salvador Zubirán, Mexico City, Distrito Federal, Mexico, [2]Universidad Nacional Autónoma de México, Coyoacan, Federal District, Mexico, [3]Instituto Politecnico Nacional, Tultitlán de Mariano Escobedo, Mexico State, Mexico, [4]Universidad Nacional Autónoma de México, Mexico City, Distrito Federal, Mexico, [5]INCMNSZ, Ciudad de Mexico, Mexico, [6]INCMNSZ, Mexico city, Federal District, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

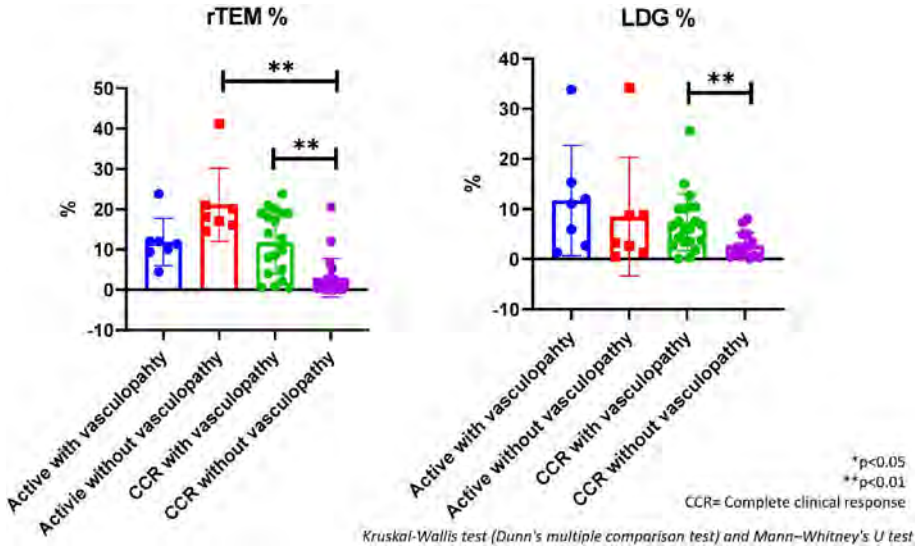
Session Time: 10:30AM–12:30PM

Background/Purpose: Vasculopathic manifestations of idiopathic inflammatory myopathies (IIM) such as interstitial lung disease (ILD), calcinosis, skin ulcers, mechanic's hands, are characterized by immune-mediated vascular damage. However, operational definitions of activity/complete clinical response (CCR) underscore vasculopathy as a domain that impacts therapeutic decisions. Different subsets of neutrophils had been described as key regulators of activity in IIM. The "low-density granulocytes" (LDGs) in patients with vasculopathy, produce higher amount of neutrophil extracellular traps (NETs), correlate with IL18 and are found more frequently in different tissues from patients anti-MDA5 positive; a clinical subtype with predominance of vasculopathic features. A different unexplored subset are the neutrophils that migrate from sites of inflammation to the vascular system, known as reverse transendothelial migration (rTEM), characterized by the expression of CD54high, CXCR1low. The role of innate immune cells subsets in immune-mediated IM vasculopathy is unknown. The aim of this study was to address the role of neutrophil and monocyte subsets in the vasculopathic features of patients with IIM.

	Active with vasculopathy (n= 7)	Active without vasculopathy (n= 7)	Inactive with vasculopathy (n= 18)	Inactive without vasculopathy (n= 18)	P value
Myositis Specific Antibodies (MSA)	MDA5 (50%), TIF 1γ (20%) Jo1 (20%)	TIF 1γ (33.3%), MI2 (33.3%) PL12 (16.6%) ,Jo1 (16.6%)	MDA5 (55%), NXP 2 (11%) PL7 (5.5%), PL12 (5.5%), Jo1 (5.5%), SRP (5.5%, Mi2 (5.5%), SAE (5.5%)	Mi2 (16.5%), NXP2 (16.5%) MDA5 (11%) PL12 (5.5%), Ku (5.5%)	
Myositis Associated Antibodies (MAA)	Ro52 (20%), PMScl75(20%), Ku (20%)	Ro52 (33.3%), PMScl100(16.6%)	Ro52 (44%), PMScl75 (11%), PMScl100 (5.5%)	Ro52 (5.5%), PMScl75(5.5%)	
Age (years)	48 (42-60)	45 (39-53)	53 (49-63)	39 (31-56.5)	0.1709
MMT8	**142 (136-149)**	**84 (42-148)**	150(150-150)	150(150-150)	0.03
CDASI activity	3 (0-14)	**10 (0.5-11.5)**	0 (0-3)	**0 (0-1)**	0.073
Leucocytes (x10^3/mcL)	6850 (5700-7875)	5500 (4900-7700)	5000 (4400-6700)	6450 (5400-7525)	0.144
Neutrophils (x10^3/mcL)	4435 (3330-7250)	3850 (3060-6370)	2980 (2580-4470)	4290 (3438-5283)	0.065
Lymphocytes (x10^3/mcL)	1305 (700-1946)	1060 (620-2380)	1240 (850-1840)	1460 (1135-1940)	0.472
Neutrophil/lymphocytes rate	3.91 (1.8-6.49)	3.46 (1.95-9.71)	2.56 (1.79-4.5)	2.71 (2.07-3.67)	0.84
CPK (U/L)	72 (26.5-586)	**346 (47-1167)**	**58.5 (35-79.5)**	115 (68.5-170)	0.041
Ferritin (ng/mL)	**126.5 (26.6-208.5)**	**501 (120-1311)**	49 (9 (14.68-100.6)	50.45 (23.65-95.5)	0.073
DHL (U/L)	200 (132.5-269.8)	**332 (184-577)**	154.5 (135.5-182.3)	**156 (142.-172.5)**	0.0161
Aldolase (U/L)	2.8 (1.42-5.8)	**9.4 (3.6-27.4)**	**5.15 (1.6-3.7)**	4.1 (2.8-6.32)	0.017
C reactive protein (mg/dL)	0.29 (0.11-7.1)	0.16 (0.09-0.36)	0.2 (0.077 -0.55)	0.2 (0.04-0.65)	0.84
Prednisone (mg/d)	8.75 (0-20)	50 (10-60)	0 (0-5)	0 (0-0)	0.089
AZA	0	0	22%	27.5%	
MTX	0	16.6%	55%	71.5%	
MMF	100%	66.4%	58.5%	33%	
HCQ	80%	83%	94%	80.5%	
Tacrolimus	40%	**16.6%**	16.5%	5.5%	
RTX	80%	**49.8%**	33%	5.5%	
CYC	20%	0	5.5%	0	
IIM	0	0	11%	0	
IVIg	40%	**83%**	5.5%	0	
PLEX	20%	0	0	0	

Clinical features of the fifty patients included in the study

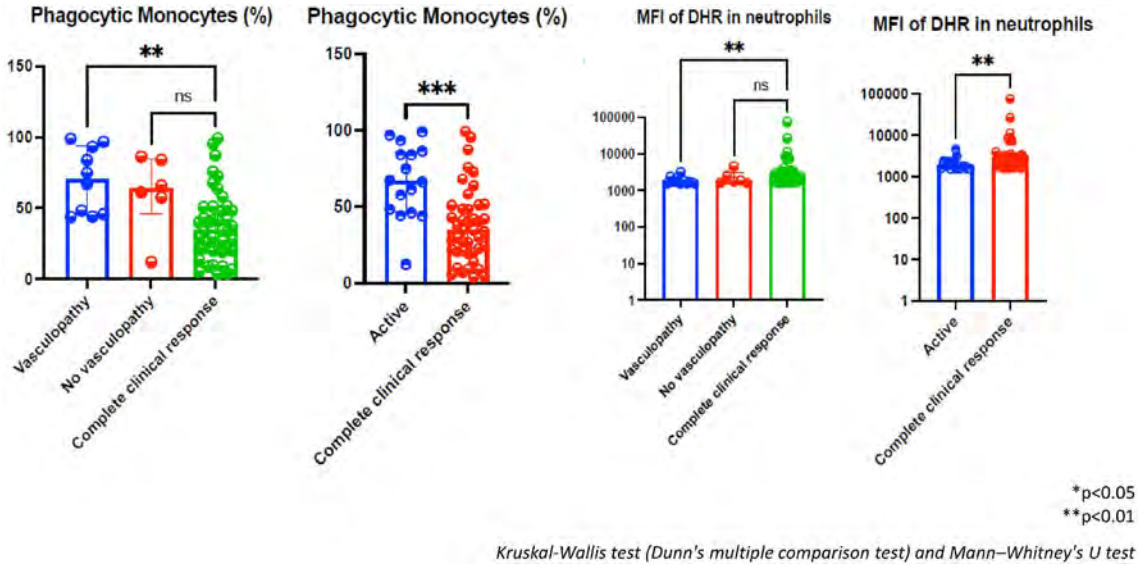
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



IIM patients with CCR and vasculopathy exhibit a significantly increased percentage of LDGs and rTEM compared with patients in CCR without vasculopathy (9.54% (2.9-29.18) vs 0.7% (0.48-2.32); p=0.0092) / (19.7% (9.85-23.8) vs 2.4% (0.99-2.88)

Methods: : A single-tertiary center cross-sectional study was performed. Fifty patients with definite IIM diagnosis according to ACR/EULAR 2017 criteria from the institutional (MYOTReCSZ) cohort were included, 25 patients with vasculopathy (7 with active IIM and 18 with CCR) who were compared with 25 patients without vasculopathy (7 with active IIM and 18 with CCR). Vasculopathy was defined as the presence of interstitial lung disease, calcinosis, ulcers, mechanic's hands or hiker's feet. Disease activity was defined as MMT8 < 136 and/or CDASI >6. Immunophenotyping of neutrophils (LDGs: $CD66b^{pos}CD14^{neg}$, rTEM: $CD15^{pos}CD16^{hi}CD54^{hi}CXCR1^{lo}$) and monocytes (Classical monocytes: $CD14^{hi}CD16^{neg}$, Non-classical monocytes: $CD14^{pos}CD16^{hi}$, Intermediate Monocyte: $CD14^{hi}CD16^{pos}$) was performed using flow cytometry, as well as phagocytosis and respiratory burst assays evaluation with pHRhodo and DHR123 assays, respectively.

Results: IIM patients with CCR and vasculopathy exhibit a significantly increased percentage of LDGs and rTEM compared with patients in CCR without vasculopathy (9.54% (2.9-29.18) vs 0.7% (0.48-2.32); p=0.0092) / (19.7% (9.85-23.8) vs 2.4% (0.99-2.88); furthermore, monocyte's phagocytosis is increased in vasculopathy group compared with CCR patients (70%



Monocyte's phagocytosis is increased in vasculopathy group compared with CCR patients (70% (45.35-94.08) vs 34.5% (20.3-50.7); p=0.0012). IIM patients with vasculopathy displayed a markedly greater reduction in respiratory burst activity compared with patients, IN CCR, indicating a distinct functional impairment in this subgroup. (1703 IMF (1547-2279) vs 2736 IMF (1946-3217); p=0.005).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(45.35-94.08) vs 34.5% (20.3-50.7); p=0.0012). IIM patients with vasculopathy displayed a markedly greater reduction in respiratory burst activity compared with patients, IN CCR, indicating a distinct functional impairment in this subgroup. (1703 IMF (1547-2279) vs 2736 IMF (1946-3217); p=0.005).

Conclusion: The expansion of LDGs and rTEM, along with the increased monocyte phagocytosis and reduced respiratory burst in neutrophils, phenotypically and functionally differentiate the innate immune profiles of IIM patients with vasculopathy.

Disclosure: D. Carrillo-Vázquez: None; **B. Alcalá-Carmona**: None; **J. Balderas Miranda**: None; **Y. Reyna Juarez**: None; **M. Ostos Prado**: None; **S. Govea-Peláez**: None; **N. Mejía Domínguez**: None; **G. Juárez Vega**: None; **K. Santana-De Anda**: None; **J. Torres-Ruiz**: None; **D. Gomez-Martin**: None.

Abstract Number: 0288

Predictors and Characteristics of Objective Flares in Adult Dermatomyositis

Didem Saygin[1], York Wang[2], Kathryn C. Fitzgerald[3], Jemima Albayda[4], Julie Paik[5], Eleni Tiniakou[6], Brittany L Adler[2], Andrew Mammen[7], Lisa Christopher-Stine[4] and Chris Mecoli[2], [1]Rush University Medical Center, Chicago, IL, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, [4]Johns Hopkins University, Baltimore, MD, [5]Johns Hopkins Rheumatology, Baltimore, MD, [6]UT Health Science Houston, Houston, TX, [7]NIH, Bethesda, MD

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is a chronic systemic autoimmune disease with a heterogenous clinical course. Flares often lead to increased morbidity, health care utilization, and reduced quality of life. Understanding risk factors and clinical features of flares can inform individualized therapeutic and monitoring strategies. In this study, we aim to determine the predictors and characteristics of flares in patients with DM.

Methods: Patients who were seen at the Myositis Center outpatient clinic and fulfilled the 2017 EULAR/ACR Classification Criteria for DM were included. Two authors manually reviewed all notes to ascertain any increase in disease activity and the context in which it occurred. Patient symptoms, physical exams, labs, imaging findings, and medication changes were recorded for each encounter. Objective flare was defined as evidence of active disease on exam or ancillary testing (worsening/new weakness, rash, inflammatory arthritis, pulmonary function test [PFT] or lung imaging findings concerning for worsening/new myositis-related lung disease) that resulted in an increase in immunosuppressive therapy. Increased disease activity within 6 months of diagnosis were not counted, nor were increases in disease activity within 3-6 months after tapering immunosuppression. The characteristics of participants and flares were summarized using descriptive statistics. We assessed the association between covariates and time to first flare using Cox proportional hazards models.

Results: A total of 637 patients with DM (75.4% female; 77.1% White; average age at diagnosis of 48.7 [±13.7]) were included. The patients had an average follow up of 7.9 years (± 4.6), during which time 35.5% (n=226) had at least one flare. Among patients with flare, DM rash documented on exam was the most common finding (75.7%), followed by muscle weakness (58.4%), new/worsening findings on PFTs and/or lung imaging (19.0%) and inflammatory arthritis (12.4%). The

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Risk factors for flare in patients with DM on univariate and multivariable cox proportional hazards models.

	Univariate cox proportional hazards model			Multivariable cox proportional hazards model		
	Hazard ratio	CI	p value	Hazard ratio	CI	p value
Age at diagnosis	0.99	0.99, 1.00	0.3	0.99	0.98, 1.00	0.3
Time to diagnosis	0.90	0.83, 0.99	0.03*	0.89	0.81, 0.99	0.02*
Sex (male)	0.82	0.60, 1.12	0.2	0.91	0.66, 1.25	0.6
Race						
White	1.00	-	-	1.00	-	-
Black	1.63	1.15, 2.30	0.006*	1.55	1.07, 2.24	0.02*
Asian	0.63	0.26, 1.54	0.3	0.59	0.24, 1.44	0.3
Other	0.72	0.37, 1.40	0.3	0.55	0.26, 1.19	0.1
Autoantibodies						
Anti-MDA-5	1.15	0.70, 1.88	0.6	-	-	-
Anti-Mi-2	0.62	0.37, 1.05	0.08	-	-	-
Anti-TIF1γ	0.97	0.73, 1.29	0.8	-	-	-
Anti-NXP-2	0.98	0.63, 1.53	0.9	-	-	-
Anti-SAE	0.45	0.14, 1.41	0.2	-	-	-
Anti-Jo-1	1.24	0.87, 1.78	0.2	-	-	-
Anti-PL-7	1.88	0.89, 4.01	0.1	-	-	-
Anti-PL-12	2.59	1.37, 4.89	0.003*	-	-	-
Anti-EJ	0.53	0.07, 3.78	0.5	-	-	-
Anti-OJ	0.94	0.39, 2.29	0.9	-	-	-
Anti-PM/Scl	1.10	0.60, 2.02	0.8	-	-	-
Anti-Ku	1.43	0.46, 4.48	0.5	-	-	-
Autoantibodies (categorical)						
ASYS	1.44	1.07, 1.95	0.02*	1.37	0.99, 1.88	0.06
DM	0.86	0.63, 1.17	0.3	0.93	0.67, 1.28	0.7

majority of the patients who self-reported rash, weakness, dyspnea, joint swelling and dysphagia fulfilled the definition of objective flare (**Figure 1)**. In univariate Cox proportional hazards model, Black race, anti-synthetase (ASYS) autoantibody and shorter time to diagnosis were significantly associated with increased flare risk. On multivariable model, Black race and time to diagnosis remained associated with flare risk **(Table 1)**. Among patients who experienced a flare, the odds of being diagnosed with cancer within 6, 12, or 24 months were significantly lower, suggesting that most flares do not herald a cancer diagnosis. Of the 71 patients diagnosed with cancer after their dermatomyositis diagnosis, 5 (7%) experienced a flare within 6 months of their cancer diagnosis, 8 (11%) within 12 months, and 10 (14%) within 24 months.

Conclusion: In this tertiary care center cohort of patients with DM, approximately one third of the patients experienced at least one flare. Patient-reported symptoms of increased disease activity are often indicative of objective flare. Black race and shorter time to diagnosis were associated with increased risk of flares. Understanding these factors can inform clinicians about timely intervention and improved patient outcomes.

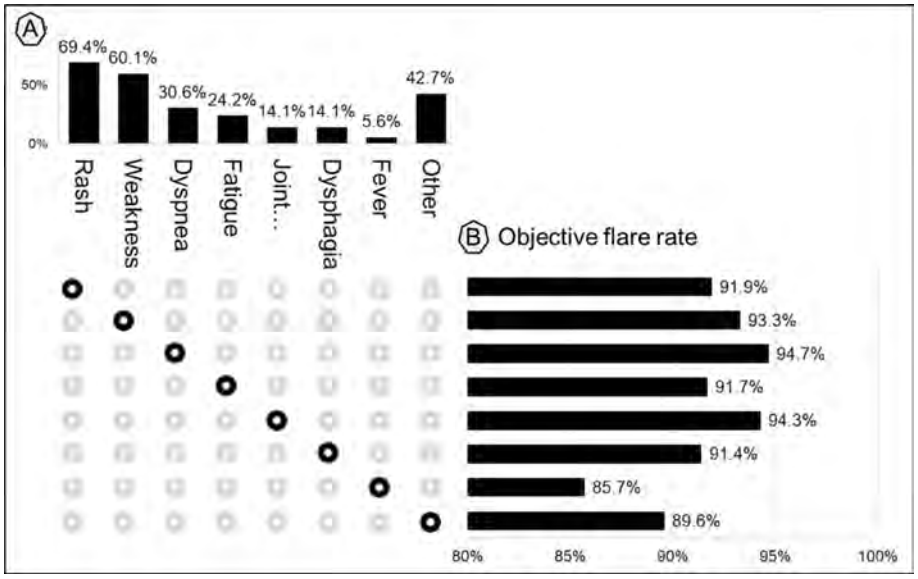


Figure 1. Frequency of symptoms reported by patients with DM (A) and proportion of patients who met the objective flare criteria based on self-reported symptom (B).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: D. Saygin: None; **Y. Wang**: None; **K. Fitzgerald**: None; **J. Albayda**: None; **J. Paik**: ArgenX, 12, Priovant, 12,; **E. Tiniakou**: None; **B. Adler**: None; **A. Mammen**: None; **L. Christopher-Stine**: Amgen, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Octapharma, 1, 5, Pfizer, 5, Priovant, 1; **C. Mecoli**: None.

Abstract Number: 0289

Standardized Interoperable Data Collection for Myositis Research: Developing Common Data Elements for Myositis Disease Activity Core Set Measures

Didem Saygin[1], Matthew Diller[2], Varsha Surampudi[3], Mark Bodkin[3], Payam Farhadi[4], Adam Schiffenbauer[5], Audrey Kessel[3], Chris Mecoli[6], Rohit Aggarwal[7], Helene Alexanderson[8], Michelle Best[9], Olivier Benveniste[10], Hector Chinoy[11], Brian Feldman[12], Linda Kobert[13], Manuel Lubinus[14], Liza McCann[15], Chester V. Oddis[16], Nicolino Ruperto[17], Jens Schmidt[18], Victoria Werth[19], Christie Bartels[20], Hanna Kim[21], Andrew Mammen[22], Julie Paik[23], Ellen M. Werner[13], Ingrid de Groot[24], Pedro Machado[25], Susan Kim[26], Tahseen Mozaffar[27], Adam M Huber[28], Angelo Ravelli[29], Richard Scheuermann[2] and Lisa Rider[30], [1]Rush University Medical Center, Chicago, IL, [2]National Library of Medicine, National institutes of Health, Bethesda, MD, [3]Social Scientific System Inc, a DLH holding company, Baltimore, MD, [4]National Institutes of Health/National Institute of Environmental Health Sciences, Bethesda, MD, [5]National Institute of Health/National Institute of Dental and Craniofacial Research, Bethesda, MD, [6]Johns Hopkins University School of Medicine, Baltimore, MD, [7]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA, [8]Karolinska University Hospital, Stockholm, Sweden, [9]Cure JM Foundation, Lessburg, VA, [10]Sorbonne Unierisite, Hopital de la Pitie-Salpetriere, Paris, France, [11]The University of Manchester, Manchester, United Kingdom, [12]The Hospital for Sick Children, Toronto, ON, Canada, [13]The Myositis Association, Columbia, MD, [14]Myositis Support and Understanding, Lincoln, DE, [15]Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom, [16]University of Pittsburgh, Pittsburgh, PA, [17]University Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy, [18]Immanuel University Hospital Ruedersdorf, Brandenburg Medical School, Rudersdorf, Germany, [19]University of Pennsylvania, Philadelphia, PA, [20]University of Wisconsin School of Medicine and Public Health, Madison, WI, [21]NIAMS, NIH, Bethesda, MD, [22]NIH, Bethesda, MD, [23]Johns Hopkins Rheumatology, Baltimore, MD, [24]The Myositis Association, Rotterdam, Netherlands, [25]University College London, London, United Kingdom, [26]UCSF Benioff Children's Hospital, San Francisco, CA, [27]University of California, Irvine, Orange, CA, [28]IWK Grace Health Centre, Halifax, NS, Canada, [29]IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genoa, Genoa, Italy, [30]National Institute of Environmental Health Sciences/National Institutes of Health, Environmental Autoimmunity Group, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Recent progress has been made in developing myositis outcome assessments, response and classification criteria, and consensus in the design and conduct of clinical trials through the International Myositis Assessment and Clinical Studies Group (IMACS). However, critical deficiencies remain for data standardization across myositis registries. While the National Institute of Health (NIH) Common Data Elements (CDEs) Repository has been developed to facilitate consistent data collection and data sharing, few myositis-specific or autoimmune disease CDEs currently exist. Here, we developed CDEs for myositis core set activity measures (CSMs) using novel data science strategies to support myositis research interoperability.

Methods: Dictionaries of several myositis registries were examined to understand how myositis CSMs are captured across databases. We used the Linked data Modeling Language (LinkML), an open-source data modeling framework for creating schemas for structured, linked data to develop computable CDEs. Information and metadata of CDEs were captured in a machine-readable format that leverages existing standards for data standardization and reuse. The Observational Health Data Science and Informatics (OHDSI) application Athena-OHDSI Vocabularies Repository (Odysseus Data Services, Inc.)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

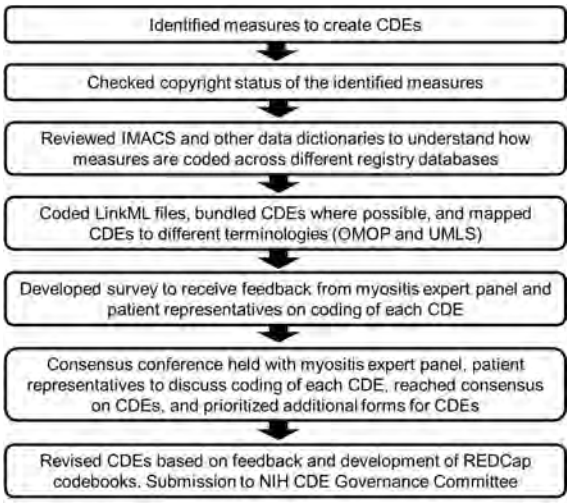


Figure 1. Flow diagram of the project steps.

Table 1. Myositis Core Set Activity Measure CDEs: Comments received, solutions presented, and consensus rating for CSM CDEs

CSM	CSM characteristics	Comments Received on CDEs	Planned Solutions	Consensus on CDEs
Physician/ Patient/Parent global disease activity	10-cm VAS on overall disease activity	- Add numeric rating scale: used more than VAS - Change nomenclature from Likert to ordinal scale - Likert scale rarely used	- 21-point numeric rating scale added - Ordinal scale terminology used and made optional	100%
HAQ/CHAQ	20-item patient-reported daily-life activities questionnaire assessing disability	- Include scoring of domains when aides/devices are used - Pain VAS not used in Europe	- Adjusted scoring to include aides/devices - Made pain VAS an optional element	100%
MMT-8	Muscle strength measure by manual muscle testing, assessing eight key muscle groups	- Include instructions on how to perform the test - Specify left/right and dominant side - Include image or URL of the form	- Added instructions - Added a question to specify the dominant side and laterality of the test -Plan to create persistent URL of IMACS website with detailed instructions and link to it in CDE	100%
Extra-muscular Global Disease Activity/MDAAT	10-cm VAS on overall disease activity excluding muscle disease	No comments	No revision	100%
Serum muscle enzymes	Laboratory results of serum creatine kinase, aldolase, AST, ALT, LDH, and creatinine	- SGOT and SGPT terminology used more commonly in Europe than AST and ALT - Aldolase not commonly available in Europe - Change form name or remove creatinine, as it is not a muscle enzyme - Add age, sex, and race of the individual	- SGOT and SGPT added to the naming of AST and ALT - Results of enzymes were made optional - Form name changed to Serum muscle enzymes and metabolites - Age and sex were added	100%
CMAS	Performance-based tool assessing muscle strength, endurance, and	No comments	No revision	100%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Myositis measures prioritized by expert panelists (n=22) for future CDE development

Form Name	% Endorsement for CDE Development (n/N)
ACR-EULAR IIM Response Criteria	100.0% (22/22)
EULAR-ACR IIM Classification Criteria	72.7% (16/22)
Myositis Damage Index	72.7% (16/22)
PROMIS Pain Interference Short Form 6a	68.2% (15/22)
Physician Patient/Parent Global Damage	59.1% (13/22)
Functional Index-3	54.6% (12/22)
Timed Up-and-Go and Sit-to-Stand tests	54.6% (12/22)
Swallowing Questionnaire	50.0% (11/22)
PROMIS FACIT Fatigue	45.5% (10/22)
PROMIS Fatigue Short Form 7a	45.5% (10/22)
Preliminary Criteria for Worsening of Myositis (Disease Flare Criteria)	45.5% (10/22)
IBM Functional Rating Scale	36.4% (8/22)
Six-minute Walk test, Two-minute Walk test	33.3% (7/22)
ENMC Classification Criteria for IBM	31.8% (7/22)
Provider and Patient Skin Activity	31.8% (7/22)
Cancer screening form	31.8% (7/22)
Initial muscle magnetic resonance imaging and biopsy	27.3% (6/22)
PROMIS-57 Adult profile	27.3% (6/22)
Quantitative muscle testing	23.8% (5/22)
Thigh muscle magnetic resonance imaging	23.8% (5/22)
PROMIS 49 Pediatric Profile	22.7% (5/22)
PROMIS Physical Function Shore Form 8b	22.7% (5/22)
IMACS Core-01A and 01B form (core demographics, clinical subgroups, myositis autoantibodies, clinical features, medications)	22.7% (5/22)
Dermatomyositis Disease Symptom Questionnaire	19.1% (4/22)
SkinDex29	13.6% (3/22)

Abbreviations: FACIT: Functional Assessment of Chronic Illness Therapy; IBM: Inclusion Body Myositis; ENMC: European Neuromuscular Centre.

was utilized to map CDEs to the Observational Medical Outcomes Partnership (OMOP) vocabulary. After development of draft CDEs for myositis CSMs, a hybrid conference was held to discuss results, reach consensus on the coding of myositis CSM CDEs, and to prioritize additional forms for development of CDEs. An international panel of 13 myositis experts and 11 discussants, including adult/pediatric rheumatologists, neurologists, dermatologists, physical therapists, and patients/patient advocates, attended the consensus conference. The Delphi method and modified nominal group technique were used in tandem as consensus methods for each CDE. Comments from participants were received via an open survey on REDCap and discussed, followed by electronic voting to reach consensus. Participants also ranked additional myositis measures for future CDE development.

Results: A standardized workflow has been established for creation of CDEs in myositis and other autoimmune diseases (Figure). CDEs for all myositis CSMs were drafted, except CHQ-P50 due to its restrictive licensing. After receiving several comments on each CDE and holding discussions to improve the coding of the CSM CDEs, 100% agreement among participants was reached for all CDEs (Table 1). The prioritized measures for future CDEs included IIM Response, Classification and Flare Criteria, damage measures, task-oriented physical function measures, and patient-reported outcome measures via PROMIS instruments among others (Table 2).

Conclusion: Leveraging broad multispecialty expertise in myositis and patient communities through IMACS and data science expertise of the National Library of Medicine (NLM), the first myositis-specific CDEs have been developed to accelerate the ability to conduct interoperable myositis clinical studies and therapeutic trials.

Disclosure: D. Saygin: None; **M. Diller**: None; **V. Surampudi**: None; **M. Bodkin**: None; **P. Farhadi**: None; **A. Schiffenbauer**: AstraZeneca, 11, Hope Pharmaceuticals, 5; **A. Kessel**: None; **C. Mecoli**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2; **H. Alexanderson**: None; **M. Best**: None; **O. Benveniste**: None; **H. Chinoy**: argenx, 2, AstraZeneca, 1, Pfizer, 2, 5; **B. Feldman**: Cabelleta, 1, Pfizer, 12, DSMB; **L. Kobert**: None; **M. Lubinus**: None; **L. McCann**: None; **C. V. Oddis**: None; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6; **J. Schmidt**: None; **V. Werth**: AbbVie/Abbott, 2, Alpine Immune Sciences, 2, Amgen, 2, 5, AnaptysBio, 2, argenx, 2, AstraZeneca, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Calyx, 2, Caribou, 2, CESAS Medical, 6, Corbus Pharmaceuticals, 5, Crisalis, 2, CSL Behring, 2, 5, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 2, 5, Immunovant, 2, Innovaderm, 2, Janssen, 2, Kyowa Kirin, 2, MAPI Trust, 9, Merck KGaA, Darmstadt, Germany, 2, N/A, 12, The University of Pennsylvania owns the copyright for the CLASI., Nektar, 2, Nuvig Pharmaceuticals, 2, Pfizer, 2, 5, Priovant, 5, Regeneron, 2, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Takeda, 2, UCB, 2, Ventus, 2, 5, Viela Bio, 2, 5, Xencor, 2; **C. Bartels**: None; **H. Kim**: Bristol-Myers Squibb(BMS), 12, CRADA, providing drug for clinical study, Cabaletta Bio, 1, 12, Cellular Therapy Product and Research Support, Eli Lilly, 12, CRADA, providing drug and research support; **A. Mammen**: None; **J. Paik**: ArgenX, 12, Priovant, 12,; **E. Werner**: None; **I. de Groot**: None; **P. Machado**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **S. Kim**: Cabaletta, 1; **T. Mozaffar**: None; **A. Huber**: None; **A. Ravelli**: AbbVie, 2, 5, 6, Alexion, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, SOBI, 2, 5, 6; **R. Scheuermann**: None; **L. Rider**: None.

Abstract Number: 0290

Comparison of Organ Damage and Survival in Anti-synthetase Syndrome and Other Idiopathic Inflammatory Myopathies: An Analysis of Patients from Turkey

Ezgi Sahin[1], Omer Uludag[2], yasemin yalcinkaya[3], Bahar Artim Esen[4], Ahmet Gul[3] and Murat Inanc[3], [1]Istanbul University Istanbul Faculty of Medicine, Istanbul, Turkey, [2]Istanbul University, Istanbul Faculty of Medicine, Division of Rheumatology, Istanbul, Turkey, [3]Istanbul University, Istanbul Faculty of Medicine, Division of Rheumatology, Istanbul, Istanbul, Turkey, [4]Istanbul University, Istanbul, Istanbul, Turkey

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are rare autoimmune diseases characterized by muscle weakness, often involving other organs such as the skin, lungs, and heart. Defined subtypes include dermatomyositis (DM), anti-synthetase syndrome (ASS), polymyositis (PM), immune necrotizing myopathy (IMNM), and inclusion body myositis (IBM). ASS exhibits distinct clinical, serological, and prognostic features.This study aims to compare the prognosis and clinical characteristics of patients with ASS and other IIMs (OIMM) in our cohort.

Methods: Data of 122 IIM patients fulfilled Bohan and Peter criteria and 2017 myositis classification criteria with myositis-specific antibody results who were followed up in our clinic between 1991 and 2024 were retrospectively analysed. The patients were divided into two groups, those with ASS and those with OIMM and their clinical and laboratory characteristics damage progress and survival rates were compared.

Results: A total of 35 patients (28.7%) were diagnosed with ASS. In this cohort, 85.7% of ASS and 59.8% of OIIM were female (p = 0.011). The median age at diagnosis was 47 years in ASS and 46 years in OIMM. The mean follow-up period

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

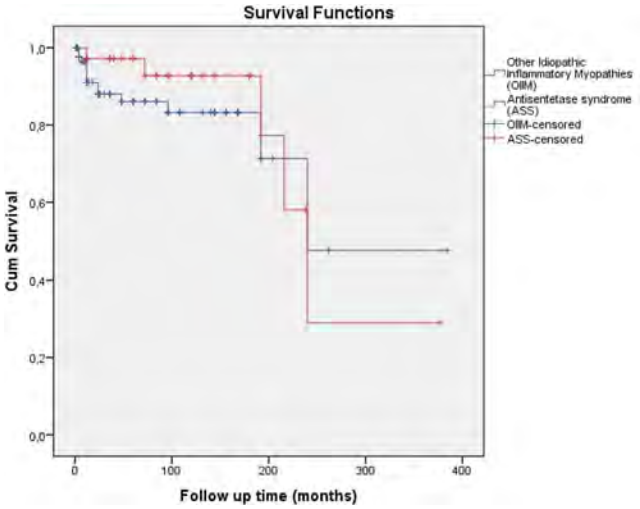


Figure 1: Comparison of survival rates by Kaplan-Meier analysis (Mantel Cox Log Rank test χ^2=0.679 df=1, p=0.410).

was 84.48±77.95 months. In these patients, anti-Jo-1 was positive in 88.6%, anti-PL-7 in 8.6%, and anti-KS in 2.8%. The frequency of mechanic's hand (ASS: 11.4%; OIMM: 1.1%; p = 0.024), arthritis (ASS: 51.4%; OIMM: 21.8%; p = 0.003), and ILD (ASS: 68.6%; OIMM: 21.8%; p< 0.001) were significantly higher in the ASS. Dysphagia was frequent in the OIMM (ASS: 8.6%; OIIM: 37.9%; p = 0.003). Anti-Ro-52 positivity was also higher in the ASS (ASS: 42.9%; OIIM: 21.8%; p = 0.034). At the time of diagnosis, median CRP, leukocyte, and neutrophil values were higher in the ASS. The median myositis damage index (MDI) of the ASS group was higher than the OIMM in the sixth month of the follow-up (median MDI: 3 vs. 2, p = 0.046) Comparing the ASS group with other autoantibody based subgroups, a difference was observed between the ASS and the TIF-1 gamma-positive patients in terms of damage progression at the sixth month (median MDI: 3 vs 1.5, p = 0.033) While ILD was observed at a high prevalence in the ASS malignancy was predominant in anti-TIF-1gamma positive patients (ILD: 72.7% vs 3%, p < 0.001; malignancy: 20% vs 35.3%, p = 0.045) In the last assessment there was no difference between the OIMM and ASS for MDI. The mortality rate was 14.3% in the ASS and 14.9% in the OIIM **(Figure 1)** It was found that there was no difference in survival rates between the ASS and OIMM.

Conclusion: The ASS has significant clinical differences from OIMM. Among these patients, mechanic's hand, arthritis, and ILD are more prevalent, whereas dysphagia is less common. Inflammatory markers like CRP, leukocyte, neutrophil levels, and anti-Ro-52 positivity are more frequent at baseline in the ASS. In the early follow-up period, higher organ damage was developed in patients with the ASS compared to the OIIM. This difference was due to the rapid development of significant ILD in most of the patients with ASS. These findings highlight the unique clinical features and different disease progression trajectories of ASS, providing insight into possible differences in the management strategies for IIM subtypes.

Disclosure: E. Sahin: None; **O. Uludag**: None; **y. yalcinkaya**: None; **B. Artim Esen**: None; **A. Gul**: None; **M. Inanc**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0291

Acute Onset Inflammatory Myositis: Clinical Features and Survival

Gollakota Nandita[1], Madhuri Challa[2], Phani Kumar D[3], Meghna Gavali[4] and Liza rajasekhar[5], [1]NIMS, Hyderabad, Hyderabad, Telangana, India, [2]Nizams institute of medical sciences, hyderabad, Andhra Pradesh, India, [3]NIMS, Hyderabad, Telangana, India, [4]nizam's institute of medical sciences ,Hyderabad, Hyderabad, Telangana, India, [5]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are characterized by subacute onset symmetric proximal muscle weakness, with occasional extra-muscular involvement, leading to significant morbidity and mortality. Acute onset inflammatory myositis with seasonal variation has been documented[1], but the role of infectious or environmental triggers in temporal clustering remains uncertain. We report on cases of acute myositis observed over a two-year period, with temporal clustering .

Methods: Records of patients admitted with acute-onset (< 8 weeks), severe, symmetrical proximal muscle weakness between January 2023 and April 2025, unrelated to toxin exposure were reviewed and patients followed up. Demographics, clinical features, antibody profile (Euroimmun line immunoblot, 16 antigens), muscle biopsy, diagnosis, and outcomes were recorded. Patients with a dermatomyositis (DM) specific rash and/or myositis specific antibodies

Table 1- Survivors versus Non survivors

	Non- Survivors(11)	Survivors (22)	P
Age	48.00 28.22 to 57.58	41.00 29.86 to 47.00	0.2071
CPK	10000.00 4091.73 to 19257.85	9027.50 5460.81 to 12046.75	0.9848
Duration of symptoms	4.00 2.00 to 4.00	3.50 2.00 to 4.00	0.8488
LDH	1200.00 869.28 to 1821.34	1122.00 849.11 to 1491.96	0.3593
MMT8	46.50 40.37 to 74.93	78.00 68.00 to 83.42	0.0072
Gender(Proportion of Males)	27%	50%	0.215
Arthritis	36%	13%	0.157
Prodrome	70%	72%	0.9
Myocarditis	9%	27%	0.178
Dysphagia	81%	54%	0.125
MSA positivity	27%	13.6%	0.35
MHC 1 positivity	90%	100%	0.138
Mx A positivity	30%	44%	0.47
Necrosis on Biopsy	81%	63%	0.29
Endomysial inflammation	18%	0	0.04
Perivascular inflammation	27%	31%	0.78
Perifascicular Atrophy	27%	18%	0.55

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2- Patients with Clinical improvement versus Worsening

	Clinical Worsening n = 4	Clinical Improvement n = 17	P
Age	40.00	40.00 27.05 to 46.97	0.8225
Duration of symptoms in weeks	3.50	4.00 3.00 to 4.00	0.9261
MMT8	65.50	79.00 68.02 to 91.85	0.0484
SGOT	547.50	315.00 186.05 to 660.31	0.3616
SGPT	154.00	126.00 68.06 to 196.73	0.5170
CPK	11666.50	8634.00 5256.51 to 11319.68	0.4618
LDH	1351.00	1100.00 810.34 to 1529.53	0.5744
Dysphagia	100%	41%	0.038
Arthritis	0%	23%	0.5
Prodrome	75%	76%	0.9
Myocarditis	0	11%	0.48
MSA positivity	75%	0	0.0002
MHC 1 positivity	100%	100%	
Mx A positivity	42%	33%	0.7
Necrosis on Biopsy	50%	75%	0.34
Endomysial inflammation	0	6%	0.6
Perivascular inflammation	50%	29%	0.43
Perifascicular Atrophy	50%	11%	0.07

(MSA), perifascicular atrophy (PFA), or MXA staining on muscle biopsy were classified as dermatomyositis. Those not meeting 2016 ACR/EULAR subtypes were labeled unclassified acute myositis.

Categorical data were reported as percentages, continuous as means/medians. Cox regression identified factors associated with survival and outcomes.

Results: Of 51 incident inflammatory myositis cases admitted, 33 (19 female) had acute-onset myositis, with clustering noted during September 2023–January 2024 and October–December 2024. The median (IQR) MMT-8 score was 68 (52–83). 9 patients were classified as DM. 3 of 11 non-survivors had DM and 8 unclassified acute myositis. Survivors had higher baseline MMT-8 scores and less frequent endomysial inflammation on biopsy (Table 1).

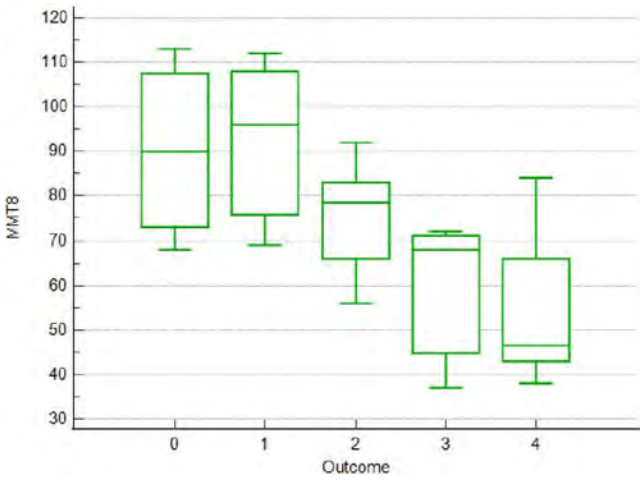


Figure 1- Box and Whisker Plot Depicting MMT-8 amongst various groups(0-Off all medication, 1- Tapering doses of DMARDs, 2- Tapering doses of Steroids, 3-Hiking in IS, 4- Non-Survivors

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Survivors were followed for a median (IQR) 61.2 (25–73) weeks. At follow-up, 4 patients were off therapy, 13 remained stable on tapering steroids or immunosuppressants, and 4 experienced flares requiring treatment escalation. Follow-up data were unavailable for 1 patient. Lower baseline MMT-8, presence of dysphagia, and MSA positivity were associated with flares or clinical worsening (Table 2).

There was higher frequency of Gottron's lesions and PFA positivity in the DM group ;prodromal symptoms and clinical improvement in the unclassified myositis group.

Conclusion: Two clusters of acute myositis observed over two years included 9 patients with dermatomyositis . There was considerable mortality which was linked to lower MMT-8 scores and endomysial inflammation . In most survivors immunosuppression was either being tapered off or stopped. Lower MMT-8, dysphagia, and MSA positivity predicted the need for escalating therapy.

Disclosure: G. Nandita: None; **M. Challa**: None; **P. D**: None; **M. Gavali**: None; **L. rajasekhar**: None.

Abstract Number: 0292

Patterns and Predictors of Longitudinal Trajectories of Pain in Individuals with Inflammatory Myopathies

Haley Zimmerman[1], Ethan Ritz[2], Kristin Wipfler[3], Kaleb Michaud[4] and Didem Saygin[1], [1]Rush University Medical Center, Chicago, IL, [2]Rush Research Informatics Core, Rush University Medical Center, Chicago, IL, [3]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [4]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) have historically been considered a disease of painless weakness. However, recent studies indicate that most patients with IIM experience pain that interferes with their daily activities. Despite the high prevalence and burden of pain, longitudinal pain trajectories of patients with IIM are currently unknown. Understanding the temporal course of pain in these patients can inform clinicians about risk stratification and assist with long-term pain management. In this study, we aimed to explore longitudinal changes in pain levels and to examine the relationship between changes in pain and various clinical variables in individuals with IIM.

Methods: The FORWARD Databank is a longitudinal prospective registry of adults in the US with rheumatic diseases. The Databank includes patient-reported biannual forms related to their socio-demographics, disease activity and subtypes, comorbidities, symptoms including pain levels (21-point numeric rating scale), and medications. We identified participants with IIM diagnosis in FORWARD who had pain scores at ≥2 time points. Pain trajectories over time were fit using latent class mixed models with the lcmm package in R version 4.4.3. Pain was modeled as an ordinal outcome, using the "thresholds" link function. The model included a fixed effect for time and included random intercepts and slopes for each participant. Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to determine the optimal number of latent classes. We compared the baseline characteristics of the two groups with chi square test and t test/Fisher's exact test where appropriate. To further examine the factors associated with change in pain levels over time, univariate and multivariable linear mixed models were performed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

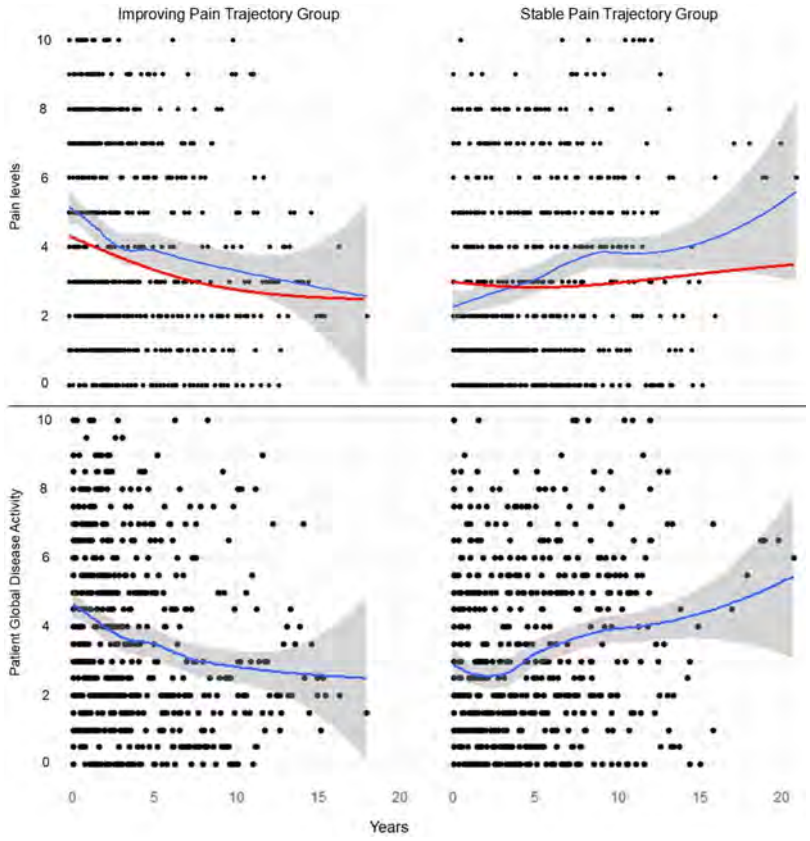


Figure 1. Longitudinal pain trajectories of adults with IIM and the corresponding change in patient global disease activity in each group (Blue line with grey area: LOESS line with confidence interval; Red line: Trajectory line).

Table 1. Baseline characteristics of participants by improving and stable pain trajectories.

Variables	Improving pain trajectory (n=84)	Stable pain trajectory (n=63)	P value
Sociodemographic features			
Age	53.9 (13.8)	55.6 (13.8)	0.4
Sex (male)	16 (19.0%)	12 (20.0%)	0.9
Race (White)	62 (79.5%)	54 (91.5%)	0.053
Smoking history	42 (50.0%)	25 (39.7%)	0.2
Body mass index	28.1 (6.7%)	28.6 (6.7%)	0.7
Years of education	14.0 (2.1%)	14.4 (2.0%)	0.2
Total annual income ($1,000s)	51.7 (31.3)	58.6 (31.0)	0.2
Number of study visits	8.1 (7.1)	10.2 (8.1)	0.1
Rheumatology visits (≥ 3 visits)	43 (58.1%)	23 (49.0%)	0.03*
IIM subtype			
DM	30 (35.7%)	19 (30.2%)	0.6
PM/IMNM	26 (31.0%)	24 (38.1%)	
Other	28 (33.3%)	20 (31.7%)	
Clinical outcomes			
Pain (0-10)	4.9 (2.6)	2.0 (2.4)	<0.001*
Fatigue (0-10)	5.7 (3.1)	3.5 (3.1)	<0.001*
Pt global disease activity (0-10)	4.8 (2.6)	2.8 (2.3)	<0.001*
HAQ-II (0-3)	1.2 (0.6)	0.9 (0.8)	0.02*
SF-36 PCS (0-100)	33.2 (9.3)	39.1 (11.8)	0.002*
SF-36 MCS (0-100)	45.1 (12.7)	50.5 (10.9)	0.01*
Health satisfaction (0-4)	1.8 (1.4)	2.4 (1.2)	0.004*
Comorbidities			
Rheum dz comorbidity index	2.3 (1.8)	1.9 (1.5%)	0.2
Fibromyalgia	32 (41.0%)	15 (26.8%)	0.09
Osteoarthritis	14 (16.7%)	13 (20.6%)	0.5
Raynaud's	15 (20.5%)	12 (19.7%)	0.9
Depression	28 (37.8%)	10 (16.4%)	0.006*
Anxiety	20 (27.0%)	11 (17.7%)	0.2
Fracture history	8 (9.5%)	8 (12.7%)	0.5
GI disorder	48 (57.1%)	25 (39.7%)	0.04*
Pulmonary disorder	7 (8.3%)	4 (6.3%)	0.8
Symptoms (last 6 months)			
Joint swelling	33 (44.6%)	11 (18.0%)	0.001
Joint pain	57 (77.0%)	28 (45.9%)	<0.001*
Muscle pain	58 (78.4%)	27 (44.3%)	<0.001*
Muscle weakness	60 (81.1%)	39 (61.9%)	0.01*
Sun sensitivity	22 (30.6%)	10 (16.1%)	0.05*
Pleurisy	12 (16.7%)	4 (6.6%)	0.07
Rash	29 (39.7%)	12 (19.7%)	0.01*
Medications			
NSAIDs	35 (44.3%)	11 (17.5%)	0.001*
Opioids	24 (30.4%)	8 (12.7%)	0.01*
Glucocorticoids	43 (54.4%)	34 (54.0%)	0.9
Non-biologic immunosuppression	59 (67.3%)	50 (79.3%)	0.7
Biologics	13 (16.4%)	4 (6.3%)	0.1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Univariable and multivariable linear mixed models to examine longitudinal associations between pain levels and other variables in individuals with myositis.

Variables	Univariable linear mixed model			Multivariable linear mixed model		
	β	SE	p value	β	SE	p value
Age	-0.03	0.01	0.001*	-0.02	0.01	0.04*
Symptom duration (years)	-0.02	0.01	0.09			
Sex (male)	-0.36	0.49	0.5			
Race (white)	-1.63	0.55	0.003*	-0.62	0.44	0.2
Smoking (yes)	0.12	0.32	0.7			
Body mass index	0.05	0.02	0.008*	0.05	0.02	0.002*
Education level (years)	-0.27	0.09	0.003*	-0.1	0.07	0.2
Total income ($1,000s)	0.002	0.003	0.463			
Non-DM subtype (vs DM)	0.12	0.45	0.8			
Patient global disease activity	0.36	0.02	<0.0001*	0.33	0.03	<0.0001*
Comorbidities						
Rheum dis comorb index	0.07	0.04	0.115			
Osteoarthritis	0.32	0.52	0.5			
Depression	0.51	0.17	0.002*	0.18	0.17	0.3
Anxiety	0.37	0.16	0.02*	0.25	0.17	0.1
Pulmonary disorder	-0.46	0.17	0.007*	-0.15	0.19	0.4
Gastrointestinal disorder	0.08	0.2	0.7			
Medications						
NSAIDs	0.43	0.14	0.003*	0.49	0.15	0.001*
Opioids	0.91	0.18	<0.0001*	0.79	0.18	<0.0001*
Glucocorticoids	0.07	0.14	0.6			
Non-biologic immunosuppressants	-0.19	0.16	0.2			

Results: A total of 147 individuals with IIM (mean age of 54.6 [±13.8], female 78.9%) were included in the study. Two groups were identified: improving (57%; n=84) and stable longitudinal pain trajectories (43%; n=63) **(Figure 1)**. Pain levels of the improving group started at 4.31 and improved by 0.14 per year. The pain trajectories were in line with longitudinal change in patient global disease activity. The participants with improving pain trajectory had worse baseline pain levels, patient global disease activity, fatigue and disability, and more commonly reported joint swelling, rash, photosensitivity, and muscle weakness than those in stable group **(Table 1)**. Baseline demographics, disease subgroups, socioeconomic variables, and comorbidities, including osteoarthritis and fibromyalgia, were generally comparable between the two trajectory groups. Younger age, higher BMI, analgesic use and higher patient global disease activity were significantly associated with increase in pain levels over time in multivariable models **(Table 2)**.

Conclusion: Pain levels improved over time in nearly 60% of the individuals with IIM, while the rest had stable pain levels. Individuals with improving pain trajectory were more likely to have active disease. A close link between pain trajectories and myositis disease activity suggests that pain could be a clinical manifestation of IIM.

Disclosure: H. Zimmerman: None; **E. Ritz**: None; **K. Wipfler**: None; **K. Michaud**: None; **D. Saygin**: None.

Abstract Number: 0293

Presence of Anti-cN-1A (Mup44, NT5c1A) IgG is Specific for Sporadic Inclusion Body Myositis

Jackie Weiss[1], Miriam Mende[2], EunByul Cho[3], Guo Shen[3], Dmitry Karayev[3], Allan L. Metzger[3], Robert I. Morris[3], Sabine L. Kramp[2], Cornelia Dähnrich[2] and Wolfgang Schlumberger[2], [1]EUROIMMUN US, Mountain Lakes, NJ, [2]Institute for Experimental Immunology, affiliated with EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany, [3]RDL Reference Laboratory Inc., Los Angeles, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sporadic inclusion body myositis (sIBM) is an autoimmune disease manifesting with muscle degeneration, inflammatory infiltrates and inclusion vacuoles. Diagnosis of sIBM is hampered by its imprecise characteristics, at times indistinguishable from other Idiopathic Inflammatory Myopathies, but may now be assisted by detection of sIBM-specific autoantibodies targeting muscle antigen Mup44, identified as cytosolic 5'-nucleotidase 1A (cN-1A; Mup44; NT5c1A). This study evaluated sensitivity and specificity of an anti-cN-1A IgG serological assay in sera from patients with and without sIBM.

Methods: Serum from patients with clinically and pathologically diagnosed sIBM (n=68) and from suspected sIBM (encompassing biopsy readings of possible, probable and doubtful sIBM patients, n=15), as well as from patients with other forms of myositis [including dermatomyositis (DM; n=4), polymyositis (PM; n=7); unspecified myositis without sIBM (n=94), muscle atrophy (n=1), myonecrosis (n=4)], systemic lupus erythematosus (n=33), scleroderma (n=20), Sjögren's syndrome (n=20), rheumatoid arthritis (n=20) and from healthy controls (n=254) were tested for anti-cN-1A IgG using an anti-cN-1A ELISA (full-length antigen, EUROIMMUN).

Results: Anti-cN-1A was most frequent among definite sIBM (41.2%). The overall specificity was 96.3% with individual specificities from 90% (scleroderma) to 100% (PM or DM).

Conclusion: The presence of anti-cN-1A in serum appears to be disease-specific for sIBM. These antibodies are found at a moderate prevalence but are only rarely detected in other autoimmune conditions. Thus, anti-cN-1A ELISA may support the diagnostics of sIBM and accelerate the diagnosis, where muscle biopsy is delayed or unfeasible.

Disclosure: J. Weiss: EUROIMMUN, 3; **M. Mende**: EUROIMMUN, 3; **E. Cho**: None; **G. Shen**: None; **D. Karayev**: None; **A. Metzger**: None; **R. Morris**: None; **S. Kramp**: EUROIMMUN, 3; **C. Dähnrich**: EUROIMMUN, 3; **W. Schlumberger**: EUROIMMUN, 3.

Abstract Number: 0294

Clinical relevance of low titer positive myositis-specific autoantibodies and myositis-associated autoantibodies in patients with an underlying malignancy.

Jocelyn Hui Ching Chow[1], Nikola Wilk[2], Ian Smith[3], Ronald A. Booth[4], Nancy Maltez[2], Catherine Ivory[2] and Jodi Warman-Chardon[5], [1]Department of Medicine, Division of General Internal Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [2]Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [3]Department of Medicine, Division of Neurology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [4]Department of Pathology and Laboratory Medicine, The Ottawa Hospital, University of Ottawa & Eastern Ontario Regional Laboratory Association, Ottawa, ON, Canada., Ottawa, ON, Canada, [5]Department of Medicine, Division of Neurology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada. Department of Medicine and Cellular and Molecular Medicine, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, ON, Canada., Ottawa, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune connective tissue diseases that often present with multisystem involvement. Autoantibodies such as myositis-specific

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 | Demographics

	Clinically True Positive ($n = 7$)	Clinically False Positive ($n = 31$)
Demographics		
Age (years)	78.4 (12.2)	68.7 (13.8)
Sex (female)	6 (86%)	17 (55%)
Weight (kg)	74.1 (8.7)	77.2 (20.7)
Height (cm)	159.9 (3.7)	167.1 (11.6)
Body Mass Index [kg/m^2]	28.5 (4.2)	27.6 (6.3)
IIM - Diagnosis		
Cancer associated	2 (29%)	
Amyopathic dermatomyositis	1 (14%)	
Dermatomyositis	2 (29%)	
Antisynthetase syndrome	1 (14%)	
Immune mediated necrotizing myopathy	1 (14%)	
Overlap myositis	0	
Malignancy		
Gastrointestinal	1 (14%)	5 (16%)
Skin	2 (29%)	7 (23%)
Breast	2 (29%)	6 (19%)
Lung	1 (14%)	1 (3%)
Cervical	0	1 (3%)
Hematological	1 (14%)	2 (6%)
Prostate	0	3 (10%)
Other	0	6 (19%)

autoantibodies (MSA) and myositis-associated autoantibodies (MAA) can now be identified in up to 70% of IIM patients. Clinical validation of multi-specific immunoassays, especially regarding the clinical relevance of low-titer positive MSA/MAA in the setting of a malignancy, remains to be determined.

Methods: Using an electronic database, we identified all patients for whom a myositis panel was assessed through the Eastern Ontario Regional Laboratory Association from June 2019 to October 2024. This myositis panel included 18 autoantibodies detected by a semi-quantitative (autoantibodies are reported in terms of low, moderate and high titers) immunoblot assay (EUROIMMUN Medizinische Labordiagnostika AG, Lübeck Germany). We performed a retrospective chart review examining clinical characteristics of the subset of patients with low titers of MSA/MAA and a history of malignancy.

Results: We identified 166 patients with low titer positive MSA or MAA antibodies from 1478 patients with a myositis panel result. In total, 38 patients had a history of malignancy and 7 patients (18%) were clinically true positives, meaning their positive MSA/MAA was clinically associated with a diagnosis of IIM [Table 1]. IIM diagnoses included cancer-associated (n=2), amyopathic dermatomyositis (n=1), dermatomyositis (n=2), antisynthetase syndrome (n=1), and immune mediated necrotizing myopathy (n=1). The majority (58%) of underlying malignancies in clinically false positives (n=31) were gastrointestinal (n=5), skin (n=7) and breast (n=6). Proximal weakness was present in 71% of clinically true positive cases, whereas interstitial

Table 2 | Clinical Characteristics

Presentation	Clinically True Positives n (%)	Clinically False Positives n (%)
Weakness	Upper extremities	5 (71%)	0
Weakness	Lower extremities	5 (71%)	2 (6%)
Dysphagia	2 (29%)	1 (3%)
Heliotrope rash:	2 (29%)	1 (3%)
Gottron's papules:	3 (43%)	0
Subcutaneous calcifications:	0	2 (6%)
Raynaud's phenomenon:	0	3 (10%)
Cutaneous ulcerations:	1 (14%)	2 (6%)
Interstitial lung disease	1 (14%)	10 (32%)
Arthralgias:	2 (29%)	9 (31%)
Synovitis:	1 (14%)	2 (6%)
Laboratories:	**Median (Interquartile range)**	**Median (Interquartile range)**
Creatinine kinase closest to myositis panel	206 (71 – 878)	80 (50-120)
Alanine aminotransferase	31 (19-66.5)	16.5 (11.25-35.5)
Aspartate transaminase	63.5 (17.25-132.25)	25.5 (18-47.5)
Lactate Dehydrogenase	234 (189.5-252)	275 (221.25-335.25)
Creatinine	77 (71.5-96)	95 (67-112)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 | Antibody Profile

ANA titers (*n*=7,30)	Clinically True Positives	Clinically False Positives	Anti-Mi2-beta (*n*=7,31)	Clinically True Positives	Clinically False Positives
Negative	1 (14%)	7 (23%)	Low	0	5 (16%)
1:80	1 (14%)	3 (10%)	High	0	1 (3%)
1:160	2 (29%)	9 (30%)	**Anti-MDA5 (*n*=7,31)**		
1:320	2 (29%)	8 (27%)	Low	0	1 (3%)
1:640	0	0	**Anti-HMGCR (*n*=7,30)**		
1:1280	1 (14%)	2 (7%)	Low	1 (14%)	1 (3%)
1:2560	0	1 (3%)	**Anti-SRP (*n*=7,31)**		
ANA Pattern (*n*=7,30)			Low	0	1 (3%)
Homogeneous	4 (57%)	13 (43%)	High	0	1 (3%)
Speckled	2 (29%)	9 (30%)	**Anti-TIF1-Gamma (*n*=7,31)**		
Nucleolar	0	1 (3%)	Low	1 (14%)	3 (10%)
Anti-Ro (*n*=7,31)			High	1 (14%)	0
Low	0	0	**Anti-NXP2 (*n*=7,31)**		
Medium	1 (14%)	1 (3%)	Low	0	4 (13%)
High	1 (14%)	3 (10%)	**Anti-5NT1A (*n*=7,31)**		
Anti-La (*n*=2,15)			Low	1 (14%)	1 (3%)
Low	0	0	**Anti-Mitochondrial (*n*=2,4)**		
Anti-Smith (*n*=2,17)			Low	0	0
Low	0	1 (6%)	**Anti-Scl-100 (*n*=7,31)**		
Anti-RNP (*n*=2,15)			Low	0	1 (3%)
Low	0	1 (7%)	**Anti-Ku (*n*=7,31)**		
Anti-Scl70 (*n*=2,15)			Low	0	2 (6%)
Low	0	1 (7%)	**Anti-EJ (*n*=7,31)**		
Anti-Jo1 (*n*=7,31)			Low	0	1 (3%)
Low	1 (14%)	4 (13%)	**Anti-OJ (*n*=7,31)**		
Anti-PL7 (*n*=7,31)			Low	0	1 (3%)
Low	1 (14%)	7 (23%)	**Anti-SAE (*n*=7,31)**		
Anti-PL12 (*n*=7,31)			Low	2 (29%)	3 (10%)
Low	0	2 (6%)	**Anti-Mi2-alpha (*n*=7,31)**		
High	1 (14%)	0	Low	0	1 (3%)

lung disease presented most commonly (32%) among those with clinically false positives [Table 2]. A large proportion of clinically false positives were found to be anti-Mi2-alpha (3%) or -beta (19%) positive, anti-PL7 positive (23%), or anti-NXP2 positive (13%) [Table 3]. From the 11 patients (29%) identified with multiple positive MSA/MAA, 2 had clinically true positives.

Conclusion: In patients with an underlying malignancy, a positive MSA/MAA at low titer identified by multi-specific immunoassay had a corresponding clinical positive in only 18% (n=7/38) of cases, and 18% (n=2/11) of those with multiple positive MSA/MAA. The most common false positives identified were anti-Mi2-beta (19%), anti-PL7 (23%) and anti-NXP2 (13%). Further studies are needed to understand the clinical significance of low positive titer MSA/MAA in the setting of a past or present malignancy.

Disclosure: J. Chow: None; **N. Wilk**: None; **I. Smith**: None; **R. Booth**: None; **N. Maltez**: None; **C. Ivory**: None; **J. Warman-Chardon**: None.

Abstract Number: 0295

Multidimensional Analysis of Fatigue in Idiopathic Inflammatory Myopathies: Clinical, Psychological, and Sociodemographic Determinants

Manali Sarkar[1], Meera Shah[2], Vincenzo Venerito[3], Vikas Agarwal[4], Latika Gupta[5] and CoVAD Study Group, [1]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India., Mumbai, Maharashtra, India, [2]Indraprastha Apollo Hospital, New Delhi, Mumbai, Maharashtra, India, [3]Univeristy of Bari \"Aldo Moro\", Italy, Bari, Bari, Italy, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [5]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Fatigue significantly impacts quality of life in idiopathic inflammatory myopathies (IIM) but remains poorly understood. This study aimed to identify the key determinants of fatigue in IIM through comprehensive analysis of disease-specific, psychological, and sociodemographic factors.

Methods: Cross-sectional data from the global e-survey "Collating the Voice of people living with autoimmune diseases" were analysed. Fatigue was measured using the Visual Analogue Scale for Fatigue (VAS-F) and reported as mean±SD. Regression models were constructed to identify factors influencing fatigue across three domains: disease-associated, psychological, and sociodemographic **[Fig 1 A]**. Hierarchical cluster analysis using Euclidean distance and Ward's D2 linkage was performed to identify distinct patient subgroups.

Results: Among 11,541 respondents **[Fig 1 B]**, 1,193 (10.33%) had IIM, with fatigue significantly higher in IIM (6.04 ± 2.36) compared to healthy controls (4.11± 2.64), p< 0.001) **[Fig 1 C]**. Within IIM subtypes, overlap myositis (OM) reported the highest fatigue (6.63±2.29) and antisynthetase syndrome (ASyS) the lowest (5.25± 2.28) **[Fig 1 D]**. Disease factors explained the greatest variance in fatigue (R^2=0.43), with disease activity, disease damage, pain, lung involvement, dermatomyositis (DM), inclusion body myositis (IBM), necrotizing autoimmune myositis (NAM), OM, polymyositis (PM) significantly associated with higher fatigue **[Fig 2 A]**. Younger age reduces fatigue risk. Among psychological factors (R^2=0.31), depression, fibromyalgia, and chronic fatigue syndrome increased fatigue; while greater self-efficacy and subjective well-being were protective **[Fig 2 B]**. For sociodemographic variables (R^2=0.19), female gender was associated with higher fatigue while non-Caucasian ethnicity, higher family functioning and household income were protective **[Fig 2 C]**. A

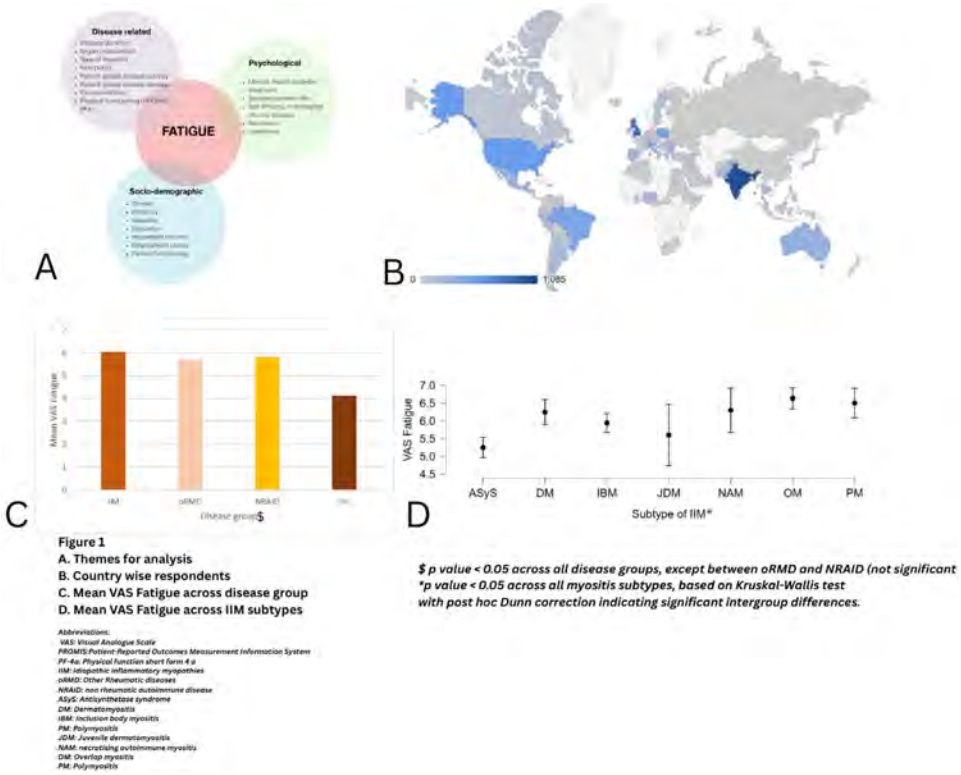


Figure 1 A. Themes for analysis B. Country wise respondents C. Mean VAS Fatigue across disease group D. Mean VAS Fatigue across IIM subtypes

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

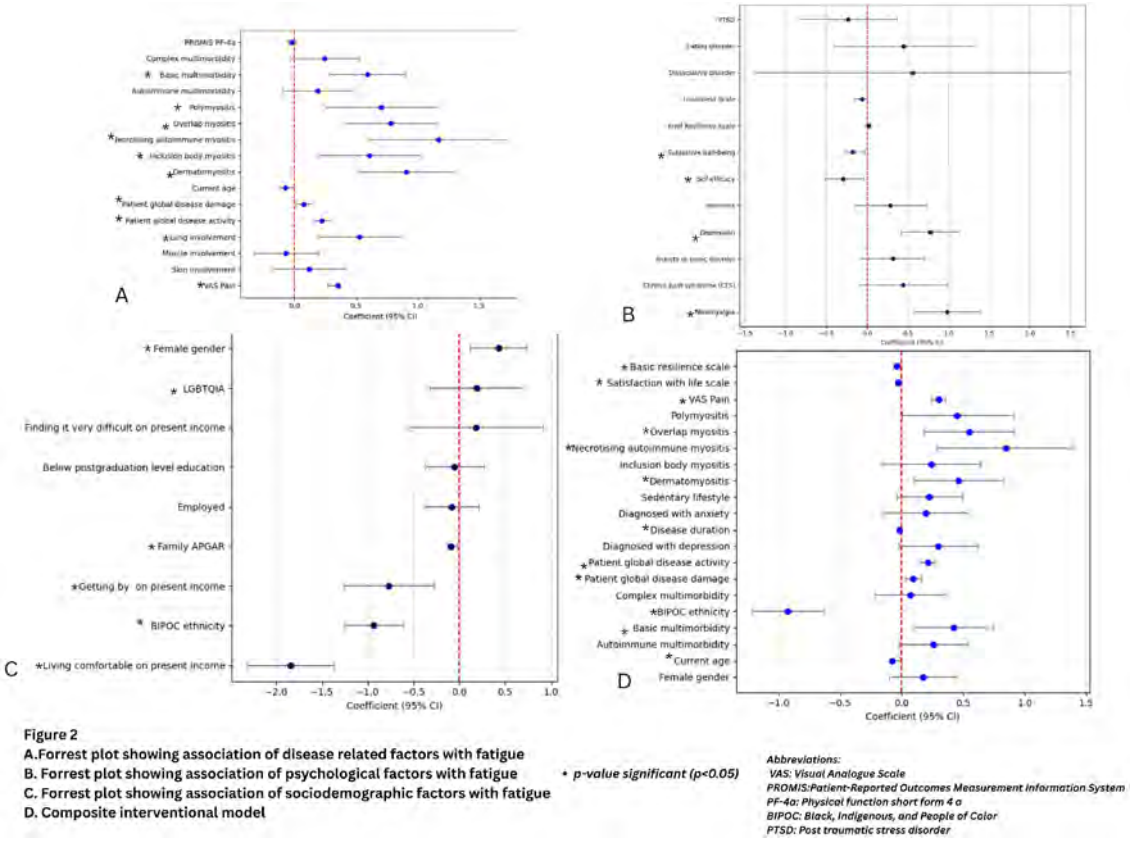


Figure 2 A.Forrest plot showing association of disease related factors with fatigue B. Forrest plot showing association of psychological factors with fatigue C. Forrest plot showing association of sociodemographic factors with fatigue D. Composite interventional model

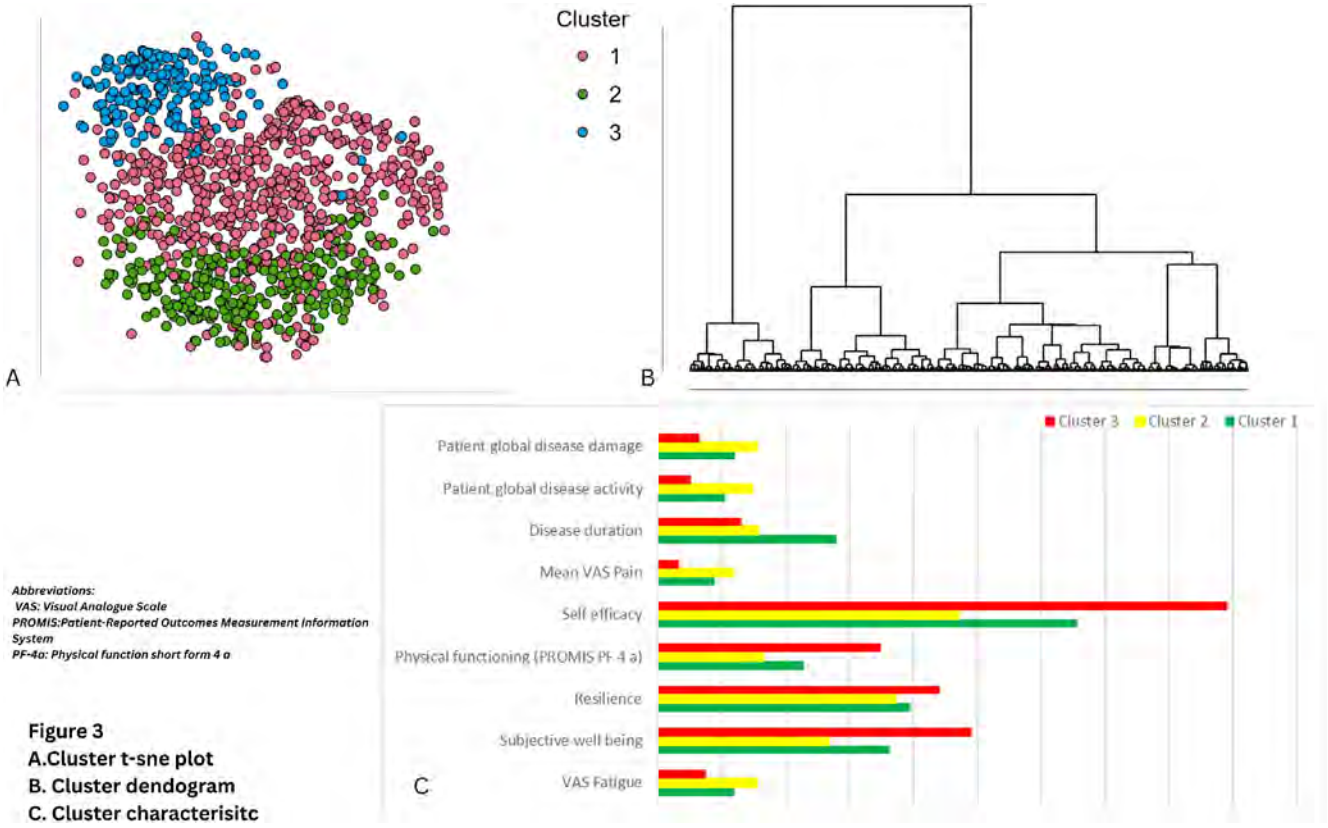


Figure 3 A.Cluster t-sne plot B. Cluster dendogram C. Cluster characterisitc

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

composite interventional model was made where younger age, presence of basic co-morbidity, higher disease activity and damage, certain IIM subtypes (DM, NAM, OM) and high pain scores had higher fatigue scores. Shorter disease duration, higher self-efficacy, better satisfaction with life, higher resilience and non Caucasian ethnicity had lower fatigue scores **[Fig.2D]**. Cluster analysis **[Fig 3]** identified three distinct patient subgroups: Cluster 3 (predominantly DM) showed lower fatigue (3.76±2.21) and comorbidity burden, while Clusters 1 and 2 (primarily IBM, OM, and ASyS) demonstrated intermediate (6.01±2.04) and high (7.74±1.70) fatigue and disease burden, respectively.

Conclusion: Fatigue in IIM emerges as a complex multidimensional phenomenon driven by disease-specific, psychological, and sociodemographic factors. Our findings highlight the importance of integrating these domains in clinical assessment and developing targeted interventions to address fatigue in IIM patients.

Disclosure: M. Sarkar: None; **M. Shah**: None; **V. Venerito**: None; **V. Agarwal**: None; **L. Gupta**: None.

Abstract Number: 0296

Aggregation of HARS1 and Internalized Antibodies in Muscle Biopsies of Patients with Antisynthetase Syndrome and anti-jo1(hars) Autoantibodies

maria Casal-Dominguez[1], Iago Pinal Fernandez[2], Katherine Pak[2], Travis Kinder[1], Jon Musai[1], Ana Matas-Garcia[3], Gloria Garrabou[4], Iban aldecoa[5], Albert Selva-O´callaghan[6], Jose Milisenda[7] and Andrew Mammen[8], [1]National Institutes of Health, Bethesda, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [3]Muscle Research Unit, Internal Medicine Service, Hospital Clinic, Barcelona, Spain., Barcelona, Spain, [4]Muscle Research Unit, Internal Medicine Service, Hospital Clinic, Barcelona, Spain., Barcelona, [5]Pathology, Neurological Tissue Bank. Hospital Clinic of Barcelona-CDB-IDIBAPS/FCRB-University of Barcelona, Barcelona, Spain., Barcelona, [6]Systemic Autoimmune Disease Section, Vall d'Hebron Institute of Research, Barcelona, Spain, Barcelona, [7]Hospital Clinic de Barcelona, Barcelona, Spain, [8]NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

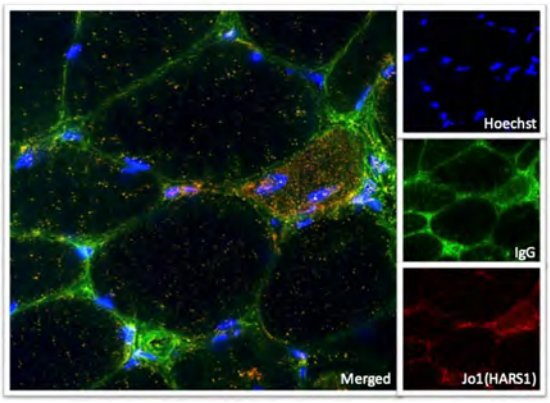
Background/Purpose: Autoimmune inflammatory myopathies (IMs) comprise a diverse group of diseases that primarily affect the muscles and often involve the lungs, skin, and joints. Among them, patients with autoantibodies against aminoacyl-tRNA synthetases develop a distinct clinical entity known as antisynthetase syndrome (ASyS), characterized by inflammatory myopathy, pulmonary fibrosis, arthritis, Raynaud's phenomenon, and mechanic's hands. The most common antisynthetase autoantibody, anti-Jo1, targets histidyl-tRNA synthetase (HARS).

Recent studies have demonstrated that autoantibodies can penetrate muscle fibers and disrupt the function of their target autoantigens. In ASyS patients, this process induces a distinct transcriptomic profile that recapitulates the effects of pharmacologic inhibition of HARS with histidinol.

This study aims to examine the localization of anti-Jo1 antibodies and their cognate antigen, HARS1, in muscle biopsies from anti-Jo1–positive ASyS patients and diseased controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1.



Direct immunofluorescence showing the aggregation of HARS1 and internalized antibodies in a muscle biopsy of a patient with antisynthetase syndrome and anti-Jo1 (HARS1) autoantibodies

Methods: We performed direct immunofluorescence for IgG and HARS1 staining on 10 µm-thick unfixed muscle sections from patients with anti-Jo1 autoantibodies and those with other forms of inflammatory myopathy. Images were acquired using a Leica SP8 high-resolution confocal microscope.

Results: We observed co-aggregation of HARS1 and internalized IgG in muscle biopsies from ASyS patients with anti-Jo1 autoantibodies (Figure 1). This pattern was not detected in samples from patients with other forms of myopathy.

Conclusion: Our data suggest that antibodies from anti-Jo1 patients induce HARS1 aggregation in the cytoplasm of muscle fibers. Notably, similar HARS1 aggregation has been observed in patients with HARS1 mutations and Charcot-Marie-Tooth (CMT) disease. In CMT, this aggregation disrupts HARS1 function, resulting in errors in peptide translation.

Disclosure: m. Casal-Dominguez: None; **I. Pinal Fernandez**: None; **K. Pak**: None; **T. Kinder**: None; **J. Musai**: None; **A. Matas-Garcia**: None; **G. Garrabou**: None; **I. aldecoa**: None; **A. Selva-O´callaghan**: None; **J. Milisenda**: None; **A. Mammen**: None.

Abstract Number: 0297

Longitudinal Serum Proteomic Profiles – A Step Closer to Personalized Monitoring in Dermatomyositis

Natasha Le Blanc[1], Marie Hudson[1], Ana Cristina Gonzalez Sanchez[2], Lina Marcela Diaz Gallo[2], Valerie Leclair[3] and Canadian Inflammatory Myopathy Study (CIMS) Group, [1]McGill University, Montral, QC, Canada, [2]Karolinska Institutet, Stockholm, Sweden, [3]McGill University, Montral, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is a multisystemic immune mediated disease presenting with heterogeneous clinical features. Disease monitoring in DM relies in part on biomarkers of muscle disease activity such as creatinine kinase (CK) which may be unreliable especially in patients with predominant extra-muscular involvement. Novel proteomic platforms have the potential to identify inflammatory biomarkers for personalized monitoring.The objective of this study was to determine whether the Olink Target 96 Inflammation panel could identify proteins associated with disease activity in DM.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

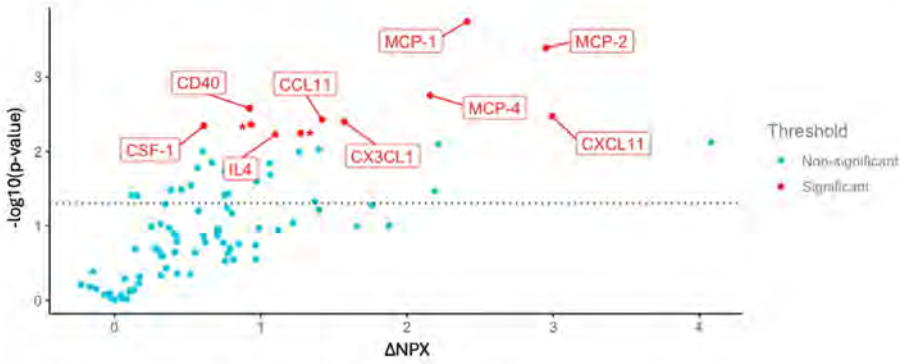
Table 1. Clinical characteristics of the six DM patients included in study

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age at study entry *years*	38	34	50	53	47	42
Sex	Female	Female	Female	Female	Female	Female
Autoantibodies*	anti-TIF1y 2+ anti-Ku 1+	anti-Ro52 2+ anti-Mi2-a/b 2+	None	anti-MDA5 3+ anti-Ro52 2+	anti-MDA5 3+	anti-MDA5 3+ anti Ro52 3+ anti-Ku 2+
Clinical features at timepoint 1						
Rash	Yes	Yes	Yes	Yes	Yes	Yes
Raynaud	No	No	No	Yes	Yes	Yes
Arthritis	No	No	No	No	No	Yes
Dysphagia	No	Yes	No	No	No	No
ILD	No	Yes	Yes	Yes	Yes	Yes
Myocarditis	Yes	No	No	No	No	No
Muscle weakness	Yes	Yes	Yes	No	Yes	Yes
Max CK (U/L)	330	6039	1800	41	252	321
Malignancy	No	No	No	No	No	Yes
Disease activity						
PhGA timepoint 1	5	5	3	6	6	7
PhGA timepoint 2	1	1	3	4	2	3
TIS	55	35	0	27.5	52.5	50
Treatment						
Timepoint 1	None	None	HCQ, AZA	MTX	None	MMF, HCQ, Prednisone
Timepoint 2	TOF, MTX	MTX	HCQ, AZA	MMF, TAC	TOF, TAC, IVIG	TAC, HCQ, Prednisone

Abbreviations: ILD, interstitial lung disease; MTX, methotrexate; HCQ, Hydroxychloroquine; AZA, azathioprine; TOF, Tofacitinib; TAC, tacrolimus; CK, creatinine kinase; PhGA, Physician Global Assessment; TIS, Total Improvement Score
*Autoantibodies measured with Euroimmun line immunoassay

Methods: Six DM patients from a multicenter inflammatory myopathy registry with available longitudinal biobanked sera were identified. All patients met the 2017 EULAR/ACR criteria for adult idiopathic inflammatory myopathy. Disease activity at each timepoint was categorized based on the International Myositis Assessment and Clinical Study (IMACS) physician global assessment (PhGA) as low (PhGA 0-3) or moderate/high (PhGA 4-10). The IMACS core set measures necessary to calculate the 2016 ACR/EULAR Total Improvement Score were extracted. Serum samples were analyzed using proximity

Figure 1. Volcano plot demonstrating the 11 proteins with significant NPX fold change comparing low vs. moderate/high disease activity



* 2 proteins unlabeled with significant NPX fold change: IL-15RA, PDL1

Abbreviations : NPX, normalized protein expression; **MCP-1**, Monocyte Chemoattractant Protein-1 (CCL2); **MCP-2**, Monocyte Chemoattractant Protein-2 (CCL8); **MCP-4**, Monocyte Chemoattractant Protein-4 (CCL13); **CXCL11**, C-X-C Motif Chemokine Ligand 11; **CX3CL1**, Fractalkine (C-X3-C Motif Chemokine Ligand 1); **CD40**, CD40 Molecule; **CCL11**, C-C Motif Chemokine Ligand 11 (Eotaxin-1); **CSF-1**, Colony Stimulating Factor 1 (Macrophage Colony-Stimulating Factor); **IL-4**, Interleukin 4; **IL-15RA**, Interleukin 15 Receptor Alpha; **PDL1**, Programmed Death Ligand 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

extension technology (Olink Proteomics Inc., Watertown, MA), simultaneously targeting 92 proteins involved in inflammatory processes. Results were reported as normalized protein expression (NPX) values (log2 scale) with higher NPX values representing higher protein concentration in the sample. Paired comparisons of NPX results were made using t-tests with Benjamini-Hochberg correction for multiple testing.

Results: Six female DM patients with ages ranging from 34 to 53 years were included (**Table 1**). Clinical features at timepoint 1 included rash (n=6), muscle weakness (n=5), interstitial lung disease (n=5), Raynaud's (n=3), arthritis (n=1) and dysphagia (n=1). Median CK was 326 U/L (range 41-6039 U/L). Autoantibodies included anti-MDA5, -TIF1y, -Mi2, -Ro52, and -Ku. At the first timepoint, 5 patients had moderate/high disease activity and at the second timepoint, 5 patients had low disease activity. Eleven proteins were significantly upregulated when results were compared based on disease activity status (moderate/high vs. low) (**Figure 1**). The strongest modulation (ΔNPX) was observed for monocyte chemoattractant proteins, MCP-2 (3.0, adj. p=0.02), MCP-1 (2.4, adj. p=0.02), MCP-4 (2.2, adj. p=0.02), and C-X-C motif chemokine 11 (CXCL11, –3.0, adj. p=0.05). Additional upregulated proteins (ΔNPX) included PD-L1 (1.27, adj. p=0.05) and CD40 (0.92, adj. p=0.05). Other proteins with significant upregulation (all adj. p=0.05) were CX3CL1 (1.57), CCL11 (1.42), IL-4 (1.1), IL-15RA (0.9) and CSF-1 (0.61).

Conclusion: Using longitudinal serum inflammatory profiles, we identified proteins upregulated when patients with DM have moderate/high disease activity. Those included chemokines involved in monocyte and T-cell recruitment that could represent potential biomarkers for disease monitoring. Further studies on a larger number of DM patients are required to understand the potential of longitudinal proteomic analyses to improve personalized monitoring in DM.

Disclosure: N. Le Blanc: None; **M. Hudson**: Astra Zeneca, 5, 6, Boehringer-Ingelheim, 5, Merck, 1, Pfizer, 5; **A. Gonzalez Sanchez**: None; **L. Diaz Gallo**: None; **V. Leclair**: None.

Abstract Number: 0298

Inter-rater Reliability of Hand-Held Dynamometry in Patients with Idiopathic Inflammatory Myopathy

Niladri Bhowmick[1], Shashank Suresh[2], Didem Saygin[3], Siamak Moghadam-Kia[4], Dana Ascherman[5], Chester V. Oddis[5] and Rohit Aggarwal[6], [1]University of Pittsburgh Medical Center, Pittsburgh, [2]Atrium Health, Charlotte, NC, [3]Rush University Medical Center, Chicago, IL, [4]University of Pittsburgh Medical Center, Pittsburgh, PA, [5]University of Pittsburgh, Pittsburgh, PA, [6]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are characterized by symmetrical proximal muscle weakness. Accurate and reliable assessment of muscle strength is important for diagnosis, monitoring, and clinical trials. Manual Muscle Testing (MMT) is widely used due to its simplicity but has notable limitations, particularly in inter-rater reliability. (1) Isokinetic dynamometry, the gold standard, is accurate but impractical for routine use. Hand-held dynamometry (HHD) offers a portable and objective alternative, and studies have shown that HHD outperforms MMT in intra-rater reliability and clinical responsiveness in IIM. However, prior studies were limited by homogenous evaluator profiles. (2)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

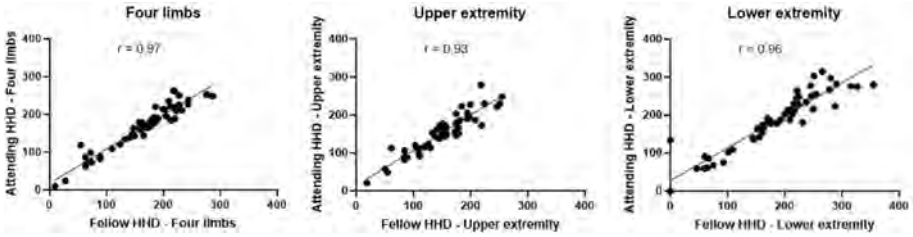


Figure 1:- Correlation plots for handheld dynamometry measurements of fellows and attending for upper and lower extremities as well as four-limb measurement.

Severity of weakness (n)	MMT9 score	Combined* handheld dynamometry in lbs of force, mean± SD (range)
Normal (20)	160	218 ± 30 (156-267)
Mild (12)	150 to <160	174 ± 38 (89-241)
Moderate (9)	140 to <150	126 ± 41 (74-183)
Severe (5)	<140	50 ± 31 (10-86)

* Mean of four-limb combined fellow and attending readings

Figure 2:- Combined fellow and attending handheld dynamometry readings across four MMT9 scores grading severity of weakness

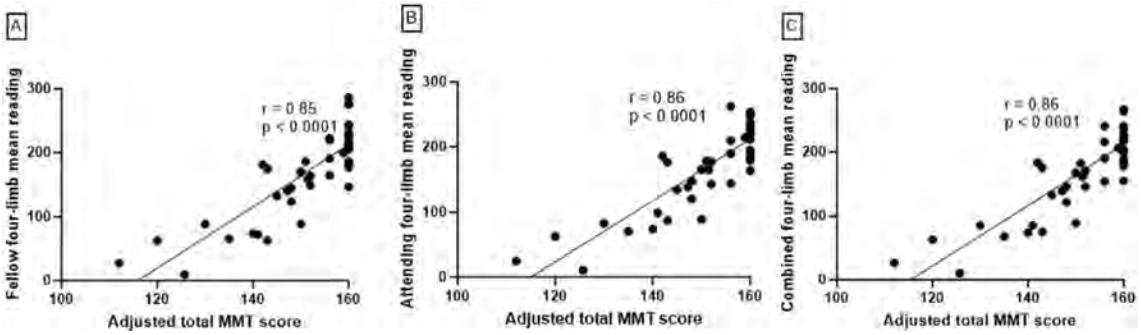


Figure 3: Correlation of adjusted total MMT score with four-limb HHD readings performed by fellow (A), attending (B), and the mean of both (C).

Methods: This study was aimed to evaluate the inter-rater reliability of HHD and its correlation with MMT scores. Forty-six patients who were evaluated at the University of Pittsburgh Myositis Center between July 2020 and March 2021 and classified as IIM (DM/PM/NM) as per 2017 EULAR/ACR Classification criteria were included. Muscle strength of bilateral deltoid and iliopsoas groups was assessed using a Micro FET2 dynamometer and MMT of 9 muscle group (MMT-9). HHD was conducted sequentially by two blinded examiners—one experienced male attending and one female rheumatology fellow who underwent a 20 minute training on assessing HHD. Inter-rater reliability was analysed using intraclass correlation coefficients (ICCs) and Pearson correlation.

Results: In the cohort of 46 patients, the mean age was 56 years with 80% (n=37) females and 80% (n=37) Caucasians. Dermatomyositis (n=23) and necrotizing myopathy (n=12) were the most common subtypes of IIM. The mean MMT score in the combined cohort was 151.Physician assessment showed excellent inter-rater reliability: ICCs were 0.92 (upper extremity), 0.93 (lower extremity), and 0.95 (four-limb) among the fellow and attending. Correlation coefficients were strong across patient subgroups stratified by sex and race. The correlation between HHD and MMT scores was also strong [r = 0.85 (fellow), r=0.86 (attending)], with consistent findings for both upper and lower extremity muscle groups. A ceiling effect was noted with MMT, as HHD captured a wide range of values even at maximum MMT score. Variability was greater in iliopsoas testing, likely due to the influence of examiner strength when assessing stronger muscle groups. Subgroup analysis of DM and non-DM patients revealed similar reliability and correlation patterns.

Conclusion: This study confirms the high inter-rater reliability of HHD in assessing muscle strength in IIM, even among raters with different levels of clinical experience and gender. HHD correlated well with MMT and demonstrated additional utility in detecting subtle strength variations, supporting its clinical application in myositis care and research.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References-

1. Rider LG, et al; International Myositis Assessment and Clinical Studies Group. Defining Clinical Improvement in Adult and Juvenile Myositis. J Rheumatol. 2003 Mar;30(3):603-17
2. Saygin D, et al. Hand-held dynamometry for assessment of muscle strength in patients with inflammatory myopathies. Rheumatology (Oxford). 2021 May 14;60(5):2146-2156

Disclosure: N. Bhowmick: None; **S. Suresh**: None; **D. Saygin**: None; **S. Moghadam-Kia**: None; **D. Ascherman**: None; **C. V. Oddis**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

Abstract Number: 0299

Interpreting Myositis Autoantibody Line-Blot Immunoassays in Real-World Settings: Implications for Diagnostic Accuracy for Inflammatory Myopathies

pei-Hsinq lai[1], TING-YUAN LAN[2], Chiao-Feng Cheng[3], Tai-Ju Lee[4], Ting-Wei Chang[5], Jui-Hung Kao[6], Kuan-Yen Lin[7], Cheng-Hsun Lu[8], Chiehyu Shen[9], Ko-Jen Li[8] and Song-Chou Hsieh[10], [1]Taipei City Hospital, Taichung, Taiwan, [2]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan, [3]National Taiwan University Hospital, Taipei City, Taiwan (Republic of China), [4]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan (Republic of China), [5]National Taiwan University Hospital Hsinchu Branch, Taichung, Taiwan, [6]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, Taipei, Taiwan (Republic of China), [7]National Taiwan University Hospital, Hsin-Chu Branch, Hsin-Chu City, Taiwan (Republic of China), [8]National Taiwan University Hospital, Taipei, Taiwan, [9]National Taiwan University Hospital, Taipei city, Taiwan, [10]National Taiwan Unuversity Hospital, Taipei City, Taiwan (Republic of China)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) present with diverse clinical features and disease courses. The myositis autoantibody line blot immunoassay (LIA) has advanced IIM diagnostics and is widely adopted across multiple specialties. We explored its predictive value in real-world, broader clinical settings.

Methods: A retrospective observational study of consecutive patients received the myositis autoantibody LIA testing in the National Taiwan University Hospital (NTUH) System from April 2021 to March 2023. All patients received the LIA testing via EUROLINE Autoimmune Inflammatory Myopathies 16 Ag kit. Patient demographics, including the presenting symptoms and IIM diagnosis subtypes, LIA details and the associated diagnostic work-up results were extracted from the electronic medical records (EMR). Two adult rheumatologists (TY and PH) were involved for the clinical review.

Based on the presence of IIM and the LIA results, we categorized the autoantibody status of the each patients into: true-positive (TP, IIM+Autoantibody+), false-positive (FP, IIM-Autoantibody+), false-negative (FN, IIM+Antoantibody-), true-negative (TN, IIM-Antoantibody-) and calculated the clinical predictive values.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the included cases.

Characteristics, N= 677	
Age	64 (49, 74)
Gender	
Female	383 (56.5%)
Testing indications	
Suspected IIM	113 (16.7%)
Single Clinical Domain	
Pulmonary	289 (42.9%)
Muscular	115 (19.6%)
Skin	29 (4.3%)
Joint	6 (0.8%)
Cardiovascular	1 (0.1%)
Autoimmune	124 (18.3%)
IIM Disease Subtypes	
Dermatomyositis	73 (45.1%)
Anti-synthetase syndrome	45 (27.8%)
Polymyositis	24 (14.8%)
Immune mediated necrotizing myopathy	12 (7.4%)
Juvenile dermatomyositis	5 (3.1%)
Immune checkpoint inhibitor related inflammatory myositis	2 (1.2%)
Inclusion body myositis	1 (0.6%)
Predictive Values	
True positive	130 (28.0%)
False positive	173 (25.6%)
False negative	32 (4.7%)
True negative	342 (50.5%)

Variables of the study population: median (Q1, Q3) or number (%).

IIM: idiopathic inflammatory myopathy.

We further determined the LIA testing indications for each patients into: *suspected IIM* (presented with manifestations across multiple clinical domains), *single clinical domain* (*pulmonary, muscular, joint, skin, cardiovascular*) and *autoimmune work-ups*. We then analyzed autoantibody positive predictive value (PPV) based on the LIA testing indication categories. All analysis were performed using R software.

Results: A total of 677 patients were included. One hundred sixty-two patients were diagnosed with IIM and the most common subtypes ere dermatomyositis (73, 45.1%), anti-synthetase syndrome (45, 27.8%) and polymyositis

Figure 1. Myositis Autoantibody Line Blot Immunoassay (LIA) Clinical Performances, Stratified by Testing Indications. Heatmap demonstrating positive predictive value and positive likelihood ratio of myositis LIA, stratified by testing indications. Both the highest PPV and LR+ were seen in the suspected IIM category. IIM: idiopathic inflammatory myopathy. PPV: positive predictive value. LR+: positive likelihood ratio.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

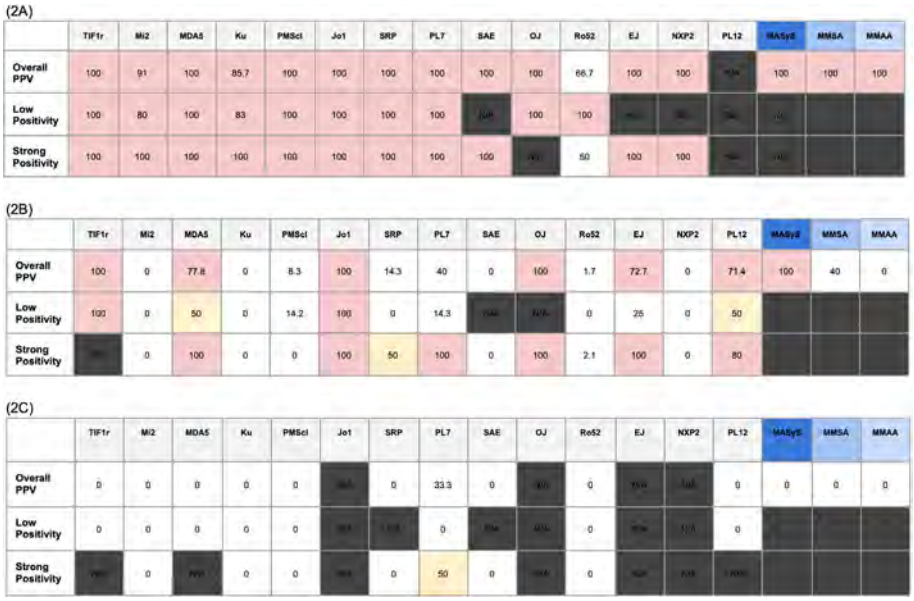


Figure 2. Myositis Autoantibody Positive Predictive Value (PPV), Stratified by LIA Testing Indications. Heatmap demonstrating PPV for individual autoantibody PPV(%) among the cases with LIA tested for (2A) Suspected IIM, (2B) Pulmonary manifestations and (2C) autoimmune work-ups. Multiple autoantibody positivity was distinguished from single antibody positivity. Overall positivity PPV included PPV of both low and strong positivity. MMSA: presence of more than one myositis specific antibody. MASyS: presence of more than one anti-aminoacyl-tRNA synthetase antibody. MMAA: presence of more than one myositis associated antibody. N/A: non-applicable.

(24, 14.8%)(Table 1). LIA demonstrated overall sensitivity 80.2% and specificity 66.4%. *Suspected IIM* exhibited the highest PPV (95.9%) and positive likelihood ratio than any entities from *single clinical domain* or *autoimmune work-ups* (Figure 1)

Among patients diagnosed with IIM, 19.7% were LIA negative while MDA5 (11.1%), multiple MSA (9.9%) and TIF1r (9.3%) were the most commonly positive autoantibodies. While PPV of most autoantibodies were high for *suspected IIM* even at low positivity (Figure 2A), autoantibodies with higher PPV for *pulmonary manifestations* (Figure 2B) were multiple coexisting anti-aminoacyl-tRNA synthetase antibodies, TIF1r and MDA5. Autoantibody PPV was low for cases tested for *joint, skin manifestations* and *autoimmune work-ups* (Figure 2C).

Conclusion: Pre-test clinical assessment is valuable under wider clinical applications as the diagnostic accuracies increase with pre-test probability. Autoantibody positive predictive values vary with specific autoantibodies and clinical Indications. Further studies are necessary to elucidate whether myositis autoantibody positivity in cases tested for single clinical domain manifestations, in particular the pulmonary manifestations, would predict and/or associate with disease course and treatment response.

Disclosure: p. lai: None; **T. LAN**: None; **C. Cheng**: None; **T. Lee**: None; **T. Chang**: None; **J. Kao**: None; **K. Lin**: None; **C. Lu**: None; **C. Shen**: None; **K. Li**: None; **S. Hsieh**: None.

Abstract Number: 0300

Exploring Malignancy in Anti-synthetase Syndrome: A Multisite Retrospective Study

Reena Yaman[1], Archit Srivastava[2], Alejandro Arango Martinez[3], Caroyln Harvey[4], Ronald Butendieck[5], Vikas Majithia[6] and Florentina Berianu[1], [1]Mayo Clinic Florida, Jacksonville, FL, [2]Mayo Clinic, Florida, Jacksonville, FL, [3]Universidad Pontificia Bolivariana, Medellín, Colombia, [4]Mayo Clinic, Phoenix, AZ, [5]Mayo Clinic Florida, Jacksonville, [6]Mayo Clinic Hospital, Jacksonville, FL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-synthetase syndrome (ASyS) is a rare, heterogeneous inflammatory myopathy characterized by presence of anti-aminoacyl transfer RNA synthetase autoantibodies with multisystem disease manifestations including myositis, inflammatory arthritis, and "mechanic's hands" rash.1 Other forms of idiopathic inflammatory myopathy, mainly dermatomyositis, are associated with increased risk of malignancy.2 Although ASyS has been presumed to have low associated malignancy risk, reports of malignancy have been presented.3 The goal of this study was to describe the incidence and types of malignancy in a cohort of ASyS patients.

Methods: A retrospective observational study was conducted by reviewing medical records of adults diagnosed with ASyS across 3 sites at the same institution. Charts were reviewed to identify whether malignancy of any type was diagnosed around the time of ASyS diagnosis defined as up to 5 years before or after. Demographic, clinical, radiologic, and immunologic data, including ILD patterns and myositis-specific antibodies, were collected and descriptive statistics were performed. Incidence rates per person-years are calculated for three intervals: 5 years before, 5 years after, and 5 years before and after ASyS diagnosis.

Characteristic	Total (N=40)
Age	
Age at ASyS diagnosis, mean (SD)	61.7 (13.86)
Sex, n (%)	
Male	19 (47.5%)
Female	21 (52.5%)
Ethnicity, n (%)	
White	36 (90.0%)
Black or African American	3 (7.5%)
Asian	1 (2.5%)
Smoking, n (%)	
Current	3 (7.5%)
Never	26 (65.0%)
Former	11 (27.5%)
Alcohol use, n (%)	
Current	11 (27.5%)
Never	25 (62.5%)
Prior history	4 (10.0%)
Family history, n (%)	
Positive	
Autoimmune Disease	3 (7.5%)
Malignancy	16 (40.0%)
Negative	18 (45.0%)
Occupational exposure, n (%)	
Yes	8 (20.0%)
No	32 (80.0%)
Human immunodeficiency virus, n (%)	
Negative	40 (100.0%)
Infectious hepatitis, n (%)	
Negative	40 (100.0%)
Arthritis, n (%)	
Present	32 (82.1%)
Absent	7 (17.9%)
Myositis, n (%)	
Present	32 (82.1%)
Absent	7 (17.9%)
Mechanic's hands, n (%)	
Present	17 (43.6%)
Absent	22 (56.4%)
Other rash or skin involvement, n (%)	
Present	14 (35.9%)
Absent	25 (64.1%)
Raynaud's phenomenon, n (%)	
Present	19 (48.7%)
Absent	20 (51.3%)
Interstitial lung disease, n (%)	
Present	40 (100.0%)
Interstitial lung disease pattern, n (%)	
Nonspecific interstitial pneumonia	14 (35.0%)
Fibrotic nonspecific interstitial pneumonia	14 (35.0%)
Organizing pneumonia	5 (12.5%)
Nonspecific interstitial pneumonia/organizing pneumonia overlap	4 (10.0%)
Fibrotic usual interstitial pneumonia	3 (7.5%)
Autoantibody positivity, n (%)	
Antinuclear	23 (57.5%)
Anti-Jo1	27 (67.5%)
Anti-PL7	9 (22.5%)
Anti-PL12	4 (10.0%)
Anti-EJ	1 (2.5%)
Anti-OJ	1 (2.5%)
Anti-Ro/SSA 52-kD	16 (40.0%)
Anti-La/SSB	3 (7.5%)
Anti-U1 RNP	5 (12.5%)
Anti-Ku	1 (2.5%)
Anti-melanoma differentiation-associated gene 5	1 (2.5%)
Anti-polymyositis/scleroderma 100	1 (2.5%)
Treatment, n (%)	
Prednisone	39 (97.5%)
Mycophenolate mofetil	29 (72.5%)
Azathioprine	13 (32.5%)
Rituximab	11 (27.5%)
Methotrexate	6 (15.0%)
Cyclophosphamide	4 (10.0%)
Intravenous immunoglobulin	4 (10.0%)
Hydroxychloroquine	2 (5.0%)
Tacrolimus	2 (5.0%)
Tocilizumab	1 (2.5%)
Plasmapheresis	1 (2.5%)

Characteristics of patients diagnosed with malignancy within 5 years of anti-synthetase syndrome diagnosis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Incidence type	Numerator	Denominator (person-years)	Incidence Rate (cases per person-year)	Incidence Rate (cases per 100 person-years)
Total incidence before/after ASyS (10-year span)	40	2225.66	0.0180	1.80
Incidence before ASyS (5-year span)	18	1146.62	0.0157	1.57
Incidence after ASyS (5-year span)	22	1084.05	0.0203	2.03

Incidence rates of malignancy in anti-synthetase syndrome (5 years before diagnosis, 5 years after diagnosis, and 5 years before and after diagnosis)

	Total (N=40)
Malignancy Category, n (%)	
Solid organ	19 (47.5%)
Skin	17 (42.5%)
Hematological	3 (7.5%)
Both solid organ and skin	1 (2.5%)
Malignancy Type, n (%)	
Squamous cell carcinoma (skin)	9 (22.5%)
Basal cell carcinoma	6 (15.0%)
Lung adenocarcinoma	3 (7.5%)
Melanoma	3 (7.5%)
Colon adenocarcinoma	3 (7.5%)
Papillary thyroid cancer	3 (7.5%)
Breast cancer	2 (5.0%)
Prostate cancer	2 (5.0%)
Multiple myeloma	2 (5.0%)
Renal cell carcinoma	2 (5.0%)
Lymphoma	1 (2.5%)
Glioblastoma multiforme	1 (2.5%)
Cervical cancer	1 (2.5%)
Seminoma	1 (2.5%)
Bladder cancer	1 (2.5%)
Leiomyosarcoma	1 (2.5%)

Malignancy categories and types in the cohort of patients with anti-synthetase syndrome diagnosed with malignancy within 5 years of anti-synthetase diagnosis

Results: A total of 236 patients diagnosed with ASyS were identified with 40 (17%) receiving a diagnosis of malignancy within 5 years of ASyS diagnosis. Of these, 18 (45%) and 22 (55%) occurred before and after ASyS diagnosis, respectively. Demographics, disease characteristics, potential malignancy risk factors, and trialed therapies of the identified cohort with concurrent malignancy are outlined in Table 1. The incidence of malignancy was 1.8 per 100 person-years, slightly higher post-ASyS diagnosis (2.03/100 person-years) than pre-ASyS diagnosis (1.57/100 person-years) (Table 2). The most common category of malignancy was solid tumors (47.5%) followed by skin cancer (42.5%). The most common individual cancer type was squamous cell carcinoma (20%), followed by basal cell carcinoma (12.5%), of the skin. Identified malignancies and their frequencies are shown in Table 3.

Conclusion: Malignancy was seen in 17% of ASyS within a period of 5 years prior to and 5 years after diagnosis of their rheumatic disease with incidence 1.8 cases per 100 person-years. Comparison to rates in the general population and further elucidation of disease and treatment characteristics associated with risk of malignancy is warranted.

1. Mahler M, Miller FW, Fritzler MJ. Idiopathic inflammatory myopathies and the anti-synthetase syndrome: a comprehensive review. *Autoimmun Rev*. 2014;13(4-5):367-371.
2. Olazagasti JM, Baez PJ, Wetter DA, Ernste FC. Cancer risk in dermatomyositis: a meta-analysis of cohort studies. *Am J Clin Dermatol*. 2015; 16:89-98.
3. Rozelle A, Trieu S, Chung L. Malignancy in the setting of the anti-synthetase syndrome. *J Clin Rheumatol*. 2008;14(5):285-288.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Yaman: None; **A. Srivastava**: None; **A. Arango Martinez**: None; **C. Harvey**: None; **R. Butendieck**: None; **V. Majithia**: None; **F. Berianu**: None.

Abstract Number: 0301

Novel HMGCS1 Deficiency Expands Proinflammatory Monocytes and Cytotoxic Populations with Increased Cytokine Release

Sabrina Helmold Hait[1], Mary Maclean[2], Cindy Phung[3], Gustaf wigerblad[4], Iago Pinal Fernandez[4], Carl Esperanzate[5], hongying Wang[5], Andrew Mammen[6], willian Gahl[5], Daniel L. Kastner[7], Stefania Dell'orso[4], Danica Novacic[5], massimo Gadina[4] and Ivona Aksentijevich[8], [1]NIAMS/NIH, Bethesda, MD, [2]NIH-NIAMS, Rockville, MD, [3]National Institute of Arthritis, Musculoskeletal, and Skin Diseases (NIAMS), Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [5]National Human Genome research Institute (NHGRI), National Institutes of Health (NIH), Bethesda, MD, [6]NIH, Bethesda, MD, [7]National Human Genome research Institute (NHGRI), National Institutes of Health (NIH), Bethesda, [8]100, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

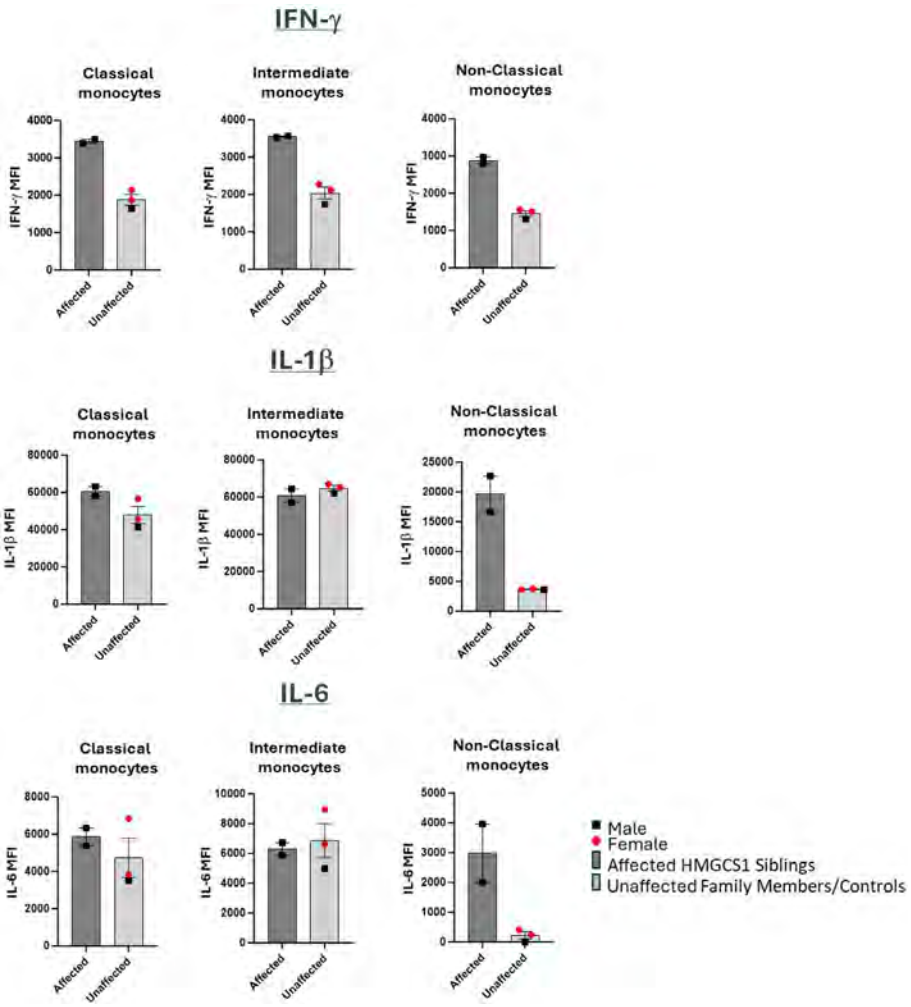
Session Time: 10:30AM–12:30PM

Background/Purpose: The mevalonate (MVK) pathway synthesizes isoprenoids that mediate post-translational protein modifications via prenylation. Deficient protein prenylation due to decreased mevalonate kinase (MK) activity leads to innate immune activation and autoinflammatory disorders. Patients using statins, HMG-CoA reductase inhibitors, may present with myopathy. However, the precise pathogenesis of prenylation deficiency-associated inflammation and myotoxicity remains unclear. We identified a rare homozygous pathogenic variant in the *HMGCS1* gene (c.265C >T, p. Arg89Trp), encoding for HMG-CoA synthase, the first enzyme in the MVK pathway, in two siblings presenting with necrotizing myopathy, arthropathy/arthritis, and susceptibility to infections.

Methods: Single-cell RNA sequencing **(**scRNA-seq) was conducted on PBMCs obtained from affected siblings, an unaffected sibling (wild-type), the mother (heterozygous) and unrelated healthy control. Muscle biopsies from affected siblings were used for bulk RNA sequencing. Using spectral flow cytometry, whole blood and/or PBMCs from affected individuals were assessed for IFN-g, IL-1b and IL-6 expression in monocytes, while IFN-g, granzyme B and perforin were assessed on NK and T cells.

Results: ScRNA-seq data evidenced an expansion of activated monocyte and cytotoxic populations in the affected but not in the unaffected brother, suggesting monocytes, T and NK cells as drivers of inflammation. Since muscle biopsies of the affected brothers revealed a strong IFN-g signature and IL-1 and IL-6 are crucial for inflammasome formation, we investigated these cytokines and inflammatory markers in LPS-stimulated myeloid subsets, and IL-12-stimulated NK cells and T cells of affected and unaffected controls. Percentage of IL-1b^{+} and IL-6^{+} non-classical monocytes (NCM) were significantly elevated in the affected siblings. IFN-g levels were increased in all monocyte subpopulations of the affected siblings, consistent with the IFN-g signature observed in the muscle biopsies. Monocytes expressing inflammatory markers, such as CD64, Siglec-1, and CD11c, were increased with a marked expression in NCM. Classical monocytes (CM), intermediate monocytes (IM), and NCM of the affected siblings presented lower PSGL-1 levels, aligned with the observed inflammatory responses, suggesting an infiltration of activated monocytes into muscle tissues. We observed a decrease in NK cells in affected donors, while T cells, specifically Th1 and Th17 cells, were expanded. Further, T cells presented elevated IFN-g expression in affected siblings, correlating with T cells infiltration seen in muscle tissue. Notably, T cells of the affected donors showed higher expression of granzyme B and perforin but decreased CD107a, indicating these cells were activated but with diminished degranulation activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



IFN-g, IL-1 and IL-6 release is increased in non-classical monocytes of HMGCS1 homozygous siblings.

Conclusion: Our data provide strong evidence that monocytes and T cells may play a pivotal role in the pathogenesis of inflammation and necrotizing myositis in patients with *HMGCS1* deficiency, with NCM and cytotoxic T cells presenting the most proinflammatory profile suggesting an important role of these cells in sustaining *HMGCS1* mutation-associated auto-inflammatory disorder.

Disclosure: S. Helmold Hait: None; **M. Maclean**: None; **C. Phung**: None; **G. wigerblad**: None; **I. Pinal Fernandez**: None; **C. Esperanzate**: None; **h. Wang**: None; **A. Mammen**: None; **w. Gahl**: None; **D. Kastner**: None; **S. Dell'orso**: None; **D. Novacic**: None; **m. Gadina**: None; **I. Aksentijevich**: In Vitro Diagnostics, 9.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0302

Urine Kynurenine Pathway Biomarkers Correlate with Disease Activity and Damage Core Set Measures in JDM

Shannon O'Connor[1], Hermine Brunner[1], Josh Gunn[2], Payam Farhadi[3], Carley Phillips[4], Lisa Rider[5], Alexei Grom[1] and Sheila Angeles-Han[6], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Ethos R&D, Newport, KY, [3]National Institutes of Health/National Institute of Environmental Health Sciences, Bethesda, MD, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, [5]National Institute of Environmental Health Sciences/National Institutes of Health, Environmental Autoimmunity Group, Bethesda, MD, [6]Cincinnati Children's Hospital, Cincinnati, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is an autoimmune vasculopathy affecting muscle, skin, and vasculature. Core set measures (CSM) assess disease activity and damage, and guide treatment. However, CSMs can be time consuming and provider dependent. Type I and II interferon (IFN) signatures correlate with disease activity. Some metabolites in the urine of children with rheumatic diseases reflect IFN activity. We aim to assess correlations between CSMs of disease activity and damage and urinary metabolites reflective of IFN activity kynurenine pathway, oxidative stress, intracellular micronutrient status, or neurotransmitter production in JDM. We hypothesize that urine metabolite concentrations correlate with JDM clinical disease.

Methods: This was a cohort study at the National Institutes of Health in collaboration with Cincinnati Children's. Inclusion criteria: a) definite or probable JDM per Bohan and Peter criteria in patients ≤18 yrs; and b) disease activity and damage CSMs performed within 3 days of urine and blood collection. Ethos R&D measured concentrations of 10 urine metabolites via mass spectrometry, normalized by urine creatinine. Absolute values of Spearman's rank correlation coefficient were calculated for each urine biomarker-CSM pair and each serum/plasma biomarker-CSM pair then sorted by the root mean square (RMS) to determine individual strongest disease predictors. Activity and damage CSMs were separated, and RMS calculated to determine predictors for activity and damage.

Table. Patient demographics and clinical characteristics at time of sample collection. Patients were in varying stages of their disease course.

Characteristics	Category	Frequency (n=33)	Percentage
Mean Age (years) (Standard Deviation)		11.6 (4.8)	
Mean disease duration (years) (Standard Deviation)		3.2 (3.6)	
Sex	Female	25	75.8
Race	White	27	81.8
	African American	3	9.1
	Asian	3	9.1
Ethnicity	Not Hispanic or Latino	29	87.9
	Hispanic or Latino	4	12.1
Myositis Specific Autoantibodies	TIF1	10	30.3
	NXP2	10	30.3
	MDA5	9	27.3
	Jo1	2	6.1
	Mi2	1	3.0
Myositis Associated Autoantibodies	Ro	7	21.2
	U1RNP	1	3.0
	PM/Scl	1	3.0
Calcinosis	Present	15	45.5

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

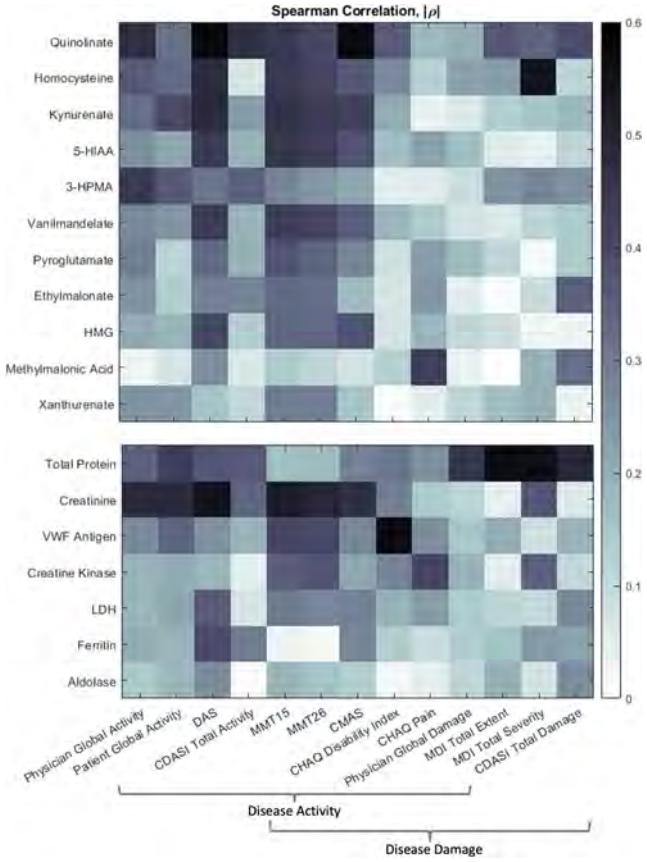


Figure 1. Heatmap of the absolute value of Spearman's rank correlation coefficient calculated for each urine biomarker-core set measure (CSM) pair (top block), and each serum or plasma biomarker-CSM pair (bottom block) for comparison. Urine metabolites are sorted from top to bottom by the root mean square (RMS) of Spearman's rank correlation coefficient to demonstrate the individually strongest predictors of disease activity and damage. VWF = von Willebrand Factor; LDH = lactate dehydrogenase. CDASI = Cutaneous Dermatomyositis Disease Area and Severity Index; CHAQ = Childhood Health Assessment Questionnaire; CMAS = Childhood Myositis Assessment Scale; DAS = Disease Activity Score; MDI = Myositis Damage Index; MMT = Manual Muscle Testing.

For each CSM, we performed linear regression with independent coefficients for each urine metabolite. CSM values were plotted against predicted CSM values and R^2 was calculated. We excluded patients with urine metabolite concentrations with a Z-score >5 (n=1).

Results: Demographics and clinical characteristics of 33 patients are shown in Table.

Figure 1 shows urine metabolites and plasma biomarkers predictive of disease activity and damage across the CSMs. Quinolinate (QA) (RMS=0.42), homocysteine (HYCS) (RMS=0.35) kynurenate (KYNA) (RMS=0.34), and 5-HIAA (RMS=0.31) are most predictive of disease activity and damage. QA (RMS=0.44,0.38), KYNA (RMS=0.36. 0.28), HYCS (RMS=0.34, 0.33), 5-HIAA (RMS=0.32, 0.27), and vanilmandelate (VMA) (RMS=0.31, 0.25) correlate best with activity and damage measures, respectively.

Creatinine (RMS=0.44, 0.33), von Willebrand Factor Antigen (VWF Ag) (RMS=0.35, 0.32), and total protein (RMS=0.31, 0.39) correlate best with disease activity and damage measures, respectively. Urine biomarkers outperform serum/plasma biomarkers, namely total protein (RMS=0.36) and VWF Ag (RMS=0.31).

Urine biomarkers showed strong correlations with CSMs in linear regression models (Figure 2), highest for MMT26 (R^2=0.74), DAS (R^2=0.70), MMT15 (R^2=0.67), and Physician Global Activity (R^2=0.65).

Conclusion: We report strong correlations between clinical measures of JDM disease activity and damage and 10 urine metabolites, many in the kynurenine pathway. 5 of these reflect disease status individually. This first step toward identifying

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

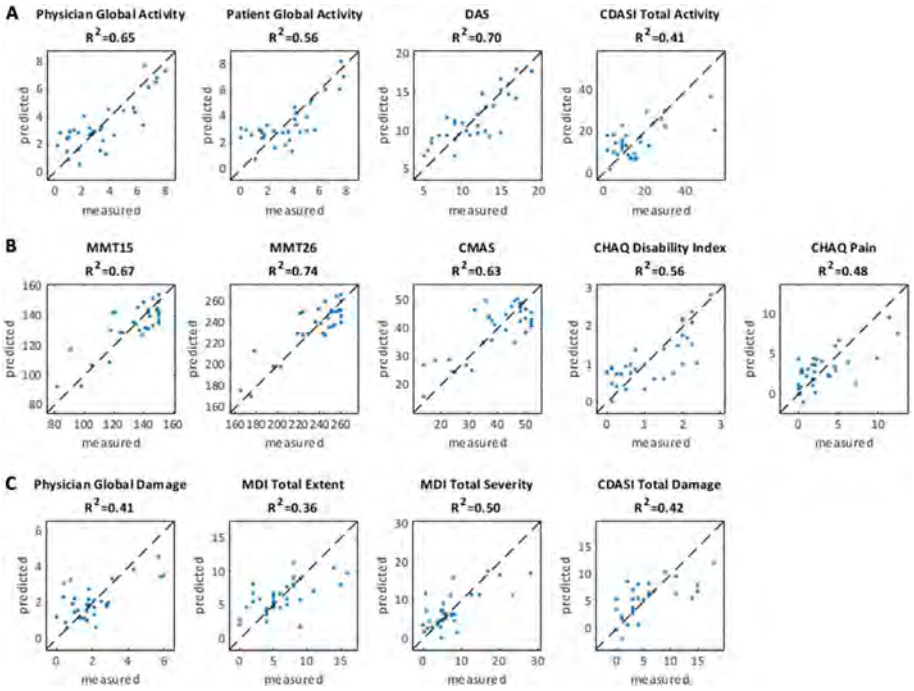


Figure 2. For each core set measure (CSM), linear regression models were calculated with independent coefficients for each of the urine biomarkers, normalized by urine creatinine. Measured CSM values on the x axes were plotted against model-predicted CSM values on the y axes, and an R2 was calculated based on goodness of fit to the ideal model y=x (dotted line). CDASI = Cutaneous Dermatomyositis Disease Area and Severity Index; CHAQ = Childhood Health Assessment Questionnaire; CMAS = Childhood Myositis Assessment Scale; DAS = Disease Activity Score; MDI = Myositis Damage Index; MMT = Manual Muscle Testing. A. Disease Activity CSMs: Physician Global Activity, Patient Global Activity, DAS, CDASI Total Activity. B. Muscle Strength and Function CSMs: MMT15, MMT26, CMAS, CHAQ Disability Index, CHAQ Pain. C. Disease Damage CSMs: Physician Global Damage, MDI Total Extent, MDI Total Severity, CDASI Total Damage.

urine biomarkers of disease activity and damage in JDM may facilitate non-invasive methods for disease monitoring and clinical decision-making.

Disclosure: S. O'Connor: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **J. Gunn**: None; **P. Farhadi**: None; **C. Phillips**: None; **L. Rider**: None; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9; **S. Angeles-Han**: None.

Abstract Number: 0303

A Predictive Model for Liver Enzyme Elevations Based on Creatine Kinase in Idiopathic Inflammatory Myopathies

Shiri Keret[1], Tanya Chandra[2], Nantakarn Pongtarakulpanit[2], Kaushik Sreerama Reddy[2], Jesse Wilkerson[3], Siamak Moghadam-Kia[4], Dana Ascherman[5], Chester V. Oddis[5] and Rohit Aggarwal[6], [1]Bnai Zion Medical Center, Atlit, Israel, [2]University of Pittsburgh Medical Center, Pittsburgh, [3]DLH, Bethesda, MD, [4]University of Pittsburgh Medical Center, Pittsburgh, PA, [5]University of Pittsburgh, Pittsburgh, PA, [6]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Ratios of Muscle Enzymes to CK during the study

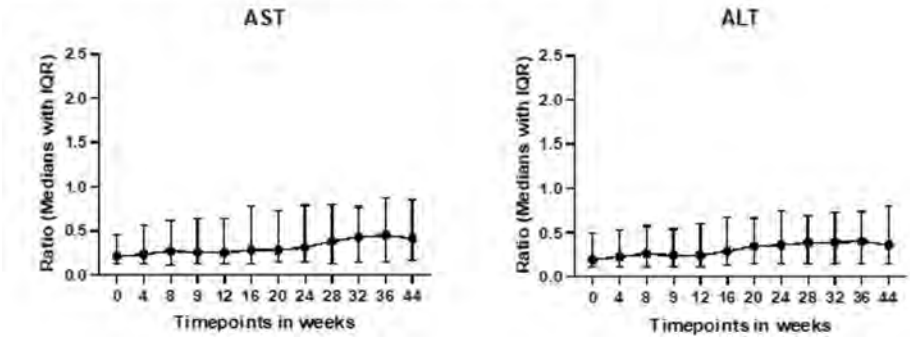


Figure 1. Stability of Muscle Enzyme-to-CK Ratios Over Time in IIM Patients. Median enzyme-to-CK ratios (AST/CK and ALT/CK) remained consistent throughout the study, supporting proportional enzyme release from muscle.

Table 1. Comparison of Muscle Enzyme Abnormalities Based on Hepatotoxic Medication Use. Median values of CK, AST, ALT, and corresponding enzyme-to-CK ratios in patients on hepatotoxic medications versus those not on such medications, including a sub-analysis by methotrexate use. No significant differences were observed between groups.

Table 1: Comparison of Muscle Enzyme Abnormalities Based on Hepatotoxic Medication Use:

Muscle enzyme level (x ULN)	Patients on any hepatotoxic medications (n=109)	Patients not on hepatotoxic medications (n=38)	P value (Mann-Whitney Test)
CK	3.32 (1.23-10.49)	4.07 (0.58-7.85)	0.42
AST	1.18 (0.79-2.29)	1.28 (0.63-1.85)	0.65
ALT	1.2 (0.7-2.1)	1.1 (0.6-1.9)	0.35
AST/CK	0.35 (0.2-0.75)	0.42 (0.22-1)	0.32
ALT/CK	0.32 (0.19-0.79)	0.41(0.2-0.87)	0.52
	Patients *on* Methotrexate (n=83)	**Patients *not* on Methotrexate (n=19)**	
CK	3.4 (1.4-10)	4.8 (0.5-10)	0.84
AST	1.3 (0.8-2.1)	1.5 (0.61-2.3)	0.73
ALT	1.2 (0.8-2.1)	1.1 (0.6-1.9)	0.31
AST/CK	0.34 (0.21-0.64)	0.42 (0.14-0.93)	0.78
ALT/CK	0.32 (0.19-0.67)	0.33 (0.11-1)	0.97

Table 2. Model-Predicted AST and ALT Levels Based on CK Values in IIM Patients. Estimated AST and ALT (in xULN) across CK categories, derived from a predictive model using $\log_{10}$-transformed CK values. Values include means, 95% confidence intervals of the mean, and expected value ranges.

Table 2: Expected Muscle Enzyme Values Based on Continuous CK Levels

Continuous CK (xULN)	AST (xULN)		ALT (xULN)	
	Mean (95% CI of mean)	95% CI of Expected Values	Mean (95% CI of mean)	95% CI of Expected Values
< 1	0.63 (0.58 – 0.68)	0.28 – 1.42	0.60 (0.54 – 0.66)	0.20 – 1.79
1-2	0.84 (0.77 – 0.93)	0.38 – 1.88	0.84 (0.75 – 0.94)	0.34 – 2.03
2-3	0.96 (0.87 – 1.07)	0.41 – 2.26	1.00 (0.88 – 1.13)	0.38 – 2.61
3-4	0.98 (0.87 – 1.10)	0.19 – 5.08	0.95 (0.82 – 1.10)	0.35 – 2.54
4-5	1.11 (0.97 – 1.26)	0.52 – 2.38	1.12 (0.96 – 1.30)	0.42 – 2.99
5-10	1.42 (1.29 – 1.57)	0.65 – 3.10	1.41 (1.25 – 1.58)	0.48 – 4.15
10-15	2.01 (1.81 – 2.24)	0.96 – 4.23	1.97 (1.74 – 2.25)	0.69 – 5.61
15-20	2.70 (2.35 – 3.09)	1.08 – 6.75	2.63 (2.24 – 3.10)	0.90 – 7.73
≥20	4.08 (3.78 – 4.42)	1.59 – 10.52	3.03 (2.76 – 3.32)	0.97 – 9.42

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are characterized by elevated muscle enzymes, including creatine kinase (CK), aldolase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH). While CK is a relatively specific marker of muscle injury, AST and ALT are also indicators of liver damage, complicating interpretation- particularly in patients receiving potentially hepatotoxic medications. Distinguishing muscle-related enzyme elevations from true liver injury remains a key clinical challenge.

We aimed to develop a predictive model for estimating liver enzyme levels based on CK values in IIM patients, assisting in the differentiation between muscle-derived enzyme elevations and true hepatotoxicity.

Methods: This study analyzed data from adult participants in the Rituximab in Myositis (RIM) trial, a multicenter, randomized, double-blind, placebo-controlled trial in patients with refractory dermatomyositis (DM) or polymyositis (PM). Patients with known liver disease were excluded. Data on CK, AST, and ALT were collected across 11 visits over 44 weeks. Enzyme values were standardized as multiples of the upper limit of normal (xULN). Concurrent medication use, including potentially hepatotoxic agents such as methotrexate, acetaminophen, and NSAIDS, was documented.

All enzyme values were incorporated into a repeated measures mixed model as $\log_{10}$-transformed variables to normalize distributions and satisfy model assumptions. Predicted enzyme levels and their 95% confidence intervals (CI) were derived from the model and subsequently back-transformed to xULN to facilitate clinical interpretation.

Results: The study included 147 patients (49% DM, 51% PM), with a mean age of 49 ± 11.3 years; 75% were female and 71% were White. Muscle enzyme-to-CK ratios remained stable over time (median range 0.19–0.87), reflecting consistent proportional release **(Figure 1)**.

There were no significant differences in CK, AST, ALT, or enzyme-to-CK ratios between patients receiving hepatotoxic medications and those who were not. Similar results were observed in a sub-analysis comparing methotrexate users to non-users (**Table 1**).

ALT and AST levels were predicted from CK using model-derived formulas: $ALT = 0.480 \times \log_{10}(CK) + 0.186$ ($R^2 = 0.78$) and $AST = 0.598 \times \log_{10}(CK) + 0.204$ ($R^2 = 0.82$). Expected enzyme levels across CK categories are summarized in **Table 2**. For example, for CK levels between 2 and 3 times the ULN, the estimated ALT and AST values were 1.0 and 0.96 xULN, respectively. Estimated AST and ALT based on CK levels were similar in DM vs. PM patients.

Conclusion: A CK-based predictive model can allow reliable estimation of AST and ALT in IIM patients, providing a valuable framework for distinguishing muscle-related enzyme elevations from potential liver injury. The use of hepatotoxic medications did not significantly influence liver enzyme levels in this cohort. This model can potentially aid clinicians in interpreting liver enzyme elevations in the context of active muscle disease.

Disclosure: S. Keret: None; **T. Chandra**: None; **N. Pongtarakulpanit**: None; **K. Sreerama Reddy**: None; **J. Wilkerson**: None; **S. Moghadam-Kia**: None; **D. Ascherman**: None; **C. V. Oddis**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0304

Concordance for myositis-specific autoantibody detection between commercial enzyme-linked immunosorbent assay and line blot assay: a multi-center study across the Asia-Pacific region

Takahisa Gono[1], Vidya Limaye[2], Latika Gupta[3], Vikas Agarwal[4], Ho So[5], JASMIN RAJA[6], Warren Weng Seng Fong[7], Supraporn Wangkaew[8], Andrea Low[9], Akihiro Murakami[10], Kimiko Hasegawa[10], Takuya Isayama[11] and Masataka Kuwana[1], [1]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [2]Royal Adelaide Hospital, Adelaide, South Australia, Australia, [3]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [5]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, [6]University Malaya, Subang Jaya, Malaysia, [7]Singapore General Hospital, Singapore, [8]Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand, [9]Singapore General Hospital, Singapore, Singapore, [10]Medical & Biological Laboratories co., ltd., Tokyo, [11]Medical & Biological Laboratories co., ltd., Tokyo, Japan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: RNA/protein immunoprecipitation (IP) assays remain the "gold standard" for myositis-specific autoantibody (MSA) detection. However, the requirements for large-scale cell culture and radioisotopes limit its availability to specialized laboratories. Clinical practice has shifted toward commercial enzyme-linked immunosorbent assay (ELISA) and multianalyte line blot assay (LBA), yet their reliability is inadequately established. Our study provides the comprehensive evaluation of concordance between two widely used commercial assays against IP assays, establishing evidence-based guidelines for MSA testing in clinical practice.

Table 1

Table1. Comparison of MSA results between ELISA and LBA

	Cutoff value of LBA	Positive percentage agreement	Negative percentage agreement	Total percentage agreement	Cohen's kappa	Grade of agreement*
Anti-synthetase (n=521)						
Anti-Jo-1	LBA 1+	0.96	0.99	0.98	0.92	Almost perfect
	LBA 2+	0.89	0.99	0.99	0.93	Almost perfect
	LBA 3+	0.80	1	0.98	0.88	Almost perfect
Anti-PL-7	LBA 1+	0.89	0.97	0.97	0.62	Substantial
	LBA 2+	0.83	0.98	0.98	0.74	Substantial
	LBA 3+	0.81	1	0.98	0.66	Substantial
Anti-PL-12	LBA 1+	0.83	0.99	0.99	0.84	Almost perfect
	LBA 2+	0.70	0.99	0.98	0.79	Substantial
	LBA 3+	0.61	1	0.98	0.75	Substantial
Anti-EJ	LBA 1+	0.95	0.99	0.99	0.95	Almost perfect
	LBA 2+	0.91	0.99	0.99	0.93	Almost perfect
	LBA 3+	0.78	1	0.99	0.85	Almost perfect
Anti-MDA5 (n=491)**	LBA 1+	0.93	0.99	0.99	0.91	Almost perfect
	LBA 2+	0.74	0.99	0.97	0.83	Almost perfect
	LBA 3+	0.59	0.99	0.96	0.70	Substantial
Anti-Mi-2 (n=521)	LBA 1+	0.67	0.98	0.97	0.52	Moderate
	LBA 2+	0.53	0.99	0.98	0.58	Moderate
	LBA 3+	0.20	0.99	0.98	0.31	Fair
Anti-TIF1-γ (n=491)**	LBA 1+	0.89	0.99	0.99	0.90	Almost perfect
	LBA 2+	0.79	0.99	0.98	0.84	Almost perfect
	LBA 3+	0.68	0.99	0.98	0.78	Substantial

* The grade of the agreement was defined based on a previous manner: the kappa values were 0-0.2 in slight agreement, 0.21-0.4 in fair agreement, 0.41-0.6 in moderate agreement, 0.61-0.8 in substantial agreement, and 0.81-1.0 in almost perfect agreement.
**Thirty samples were unable to be tested because of limited serum volume.
MSAs, myositis specific autoantibodies; ELISA, enzyme-linked immunosorbent assay; LBA, multianalyte line-blot assay; ARS, aminoacyl-tRNA synthetase; MDA5, melanoma differentiation-associated gene 5; TIF1, transcriptional intermediary factor

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Sera from patients with idiopathic inflammatory myopathies (IIMs) were collected across the Asia-Pacific region. Anti-Jo-1, anti-PL-7, anti-PL-12, anti-EJ, anti-melanoma differentiation-associated gene 5 (MDA5), anti-Mi-2, and anti-transcriptional intermediary factor (TIF) 1-γ antibodies were centrally measured using commercial ELISA kits (MBL, Tokyo, Japan) and LBA systems (EuroImmun, Lübeck, Germany). Positive percentage agreement (PPA), negative percentage agreement (NPA), and Cohen's kappa were calculated to assess concordance between the two assays. Discordant results were further validated using RNA/protein IP assays.

Results: A total of 521 sera from patients with dermatomyositis (DM; n = 180), amyopathic DM (n = 44), juvenile DM (n = 7), polymyositis or immune-mediated necrotizing myopathy (n = 197), inclusion body myositis (n = 57), and IIM-not-otherwise-specified (n = 36) were collected from Australia (n = 200), India (n = 83), Hong Kong (n = 35), Japan (n = 152), Malaysia (n = 21), Singapore (n = 20), and Thailand (n = 10). The highest PPA at the 1+ cutoff value for LBA was observed for anti-Jo-1 (0.96), followed by anti-EJ (0.95), anti-MDA5 (0.93), anti-TIF1-γ (0.89), anti-PL-7 (0.89), anti-PL-12 (0.83), and anti-Mi-2 (0.67). Kappa values indicated strong agreement for anti-Jo-1, anti-PL-12, anti-EJ, anti-MDA5, and anti-TIF1-γ, but lower agreement for anti-PL-7 and anti-Mi-2 (Table 1). PPA at the cutoff value of 2+ or 3+ for LBA was numerically lower for all MSAs, whereas NPA remained high in all (0.99-1). The validation analysis using IP assays in sera with discordant results between ELISA and LBA at the 1+ cutoff value revealed a high rate of false-positives for anti-PL-7 (7/9 samples) and anti-Mi-2 (6/6 samples) antibodies with LBA. The false-positive rates decreased at the 3+ cutoff value for anti-PL-7 (0/9) and anti-Mi-2 (1/6).

Conclusion: LBA demonstrates discordance in PPA based on the cutoff values across all MSAs. Clinicians should interpret LBA results with caution, particularly when evaluating antibodies to PL-7 and Mi-2.

Disclosure: T. Gono: Boehringer-Ingelheim, 6, Medical and Biological Laboratories, 5; **V. Limaye**: None; **L. Gupta**: None; **V. Agarwal**: None; **H. So**: None; **J. RAJA**: None; **W. Fong**: None; **S. Wangkaew**: None; **A. Low**: None; **A. Murakami**: None; **K. Hasegawa**: None; **T. Isayama**: None; **M. Kuwana**: AbbVie, 2, Asahi Kasei Pharma, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 6, GlaxoSmithKlein(GSK), 2, Medical and Biological Laboratories, 5, 9, Mochida, 2, Novartis, 2, Ono Pharmaceuticals, 6.

Abstract Number: 0305

From Movement to Meaning: Exploring Physical Function in IBM with Actigraphy

Vaidehi Kothari[1], Eaman Alhassan[2], Kevin Renz Ambrocio[1], Bonny Rockette-Wagner[3], Chester V. Oddis[1], Kendrea (Focht) Garand[1] and Rohit Aggarwal[4], [1]University of Pittsburgh, Pittsburgh, PA, [2]University of Pittsburgh Medical Center, Pittsburgh, PA, [3]University of Pittsburgh, PITTSBURGH, [4]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0280–0305) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Inclusion body myositis (IBM) is a progressive and severe inflammatory muscle disease that primarily affects adults over 50 years of age. It presents with asymmetric weakness, particularly in the quadriceps and finger flexors, and leads to significant disability over time. Standard clinical measures may not fully capture real-world activity and function. Actigraphy, a non-invasive tool for monitoring continuous physical activity, has been utilized in other myopathy subtypes but

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of enrolled patients

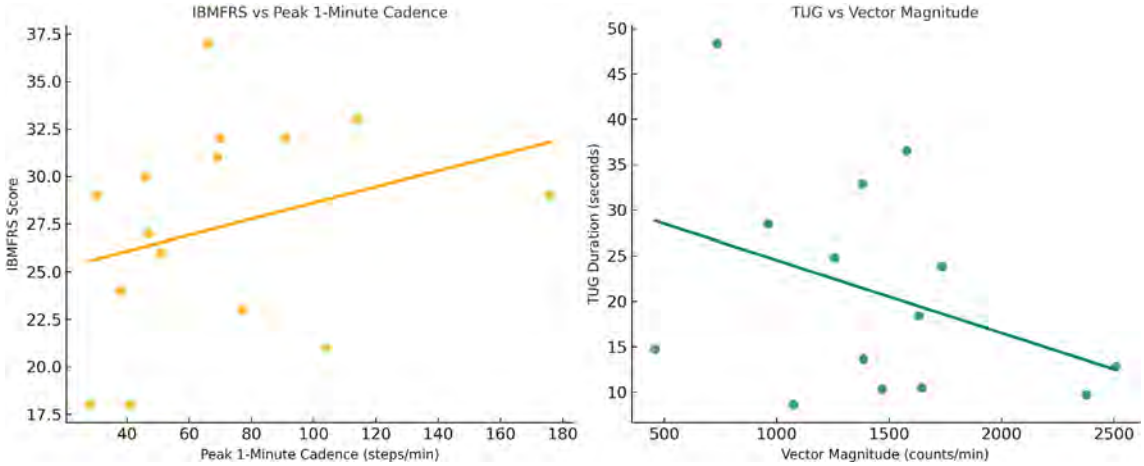
Parameter	n	Median (IQR)	Mean ± SD	95% CI	Min	Max
Demographics						
BMI (kg/m²)	15	26.00 (24.50–29.00)	26.40 ± 2.95	24.77–28.03	21	31
Age at visit (years)	15	73.00 (69.50–76.00)	72.53 ± 5.91	69.26–75.81	60	83
Age at symptom onset (years)	15	65.00 (60.00–69.00)	65.13 ± 5.90	61.86–68.40	57	74
Age at diagnosis (years)	15	69.00(65.50–74.00)	68.93 ± 5.62	65.82–72.05	60	77
Disease Duration (years)	15	8.00 (6.00–9.50)	8.60 ± 3.76	6.52–10.68	4	17
Physical Function Outcome measures						
IBMFRS Score	15	29.00 (23.50–31.50)	27.33 ± 5.61	24.22–30.44	18	37
TUG (seconds)	14	16.57 (11.05–27.55)	20.97 ± 12.02	14.02–27.91	8.61	48.33
Actigraphy						
MVPA (%)	15	19.55 (13.68–25.00)	19.72 ± 9.80	14.29–25.14	0.18	36.97
Vector Magnitude counts per minute	15	1386.20 (1165.65–1638.60)	1436.21 ± 539.63	1137.37–1735.05	458.7	2507.5
Steps per minute	15	7.40 (4.75–7.80)	6.91 ± 2.69	5.42–8.40	2.6	11.7
Peak 1 min cadence	15	66.00 (43.50–84.00)	69.87 ± 39.22	48.15–91.58	28	176

Table 2: Correlations between clinical assessment outcomes and Actigraphy parameters

Measure	MVPA (%)	Vector Magnitude counts per minute	Steps per minute	Peak 1-min cadence
IBMFRS	0.25 (p=0.37)	0.26 (p=0.34)	0.29 (p=0.30)	0.41 (p=0.13)
TUG	-0.30 (p=0.26)	-0.36 (p=0.20)	-0.32 (p=0.26)	-0.31 (p=0.28)

remains understudied in IBM, where it may offer valuable additional insights. This study examined the relationship between clinical assessments and actigraphy-derived activity metrics in individuals with IBM.

Methods: We conducted a pilot prospective cohort study at an academic center. Participants met the European Neuromuscular Center Classification (2024) and the ACR classification criteria (2017) for IBM. Assessments included the IBM Functional Rating Scale (IBMFRS), Timed Up and Go (TUG), and wrist-worn actigraphy (24/7 for seven consecutive days). Using Spearman's rank-order correlation, we assessed relationships between the clinical assessments (IBMFRS and TUG) and four actigraphy-derived metrics: percentage of time in moderate-to-vigorous physical activity (%MVPA), vector magnitude counts per minute (VM), average daily steps per minute, and peak 1-minute cadence.



Correlation Graphs

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Fifteen participants (60% male, mean age 72.5 ± 5.9 years) completed the study. The mean age of symptom onset was 65.1 years, and the mean age at diagnosis was 68.9 years, indicating a diagnostic delay of ~3.8 years. The average disease duration at enrollment was 8.6 years. Participants' IBMFRS scores averaged 27.3 ± 5.6, and mean TUG time was 21.0 ± 12.0 seconds, indicating moderate impairment. Actigraphy revealed substantial limitations in daily activities, with a mean MVPA of 19.7%, VM of 1436.2 counts/min, average daily steps of 6.9/min, and peak 1-minute cadence of 69.8 steps/min (Table 1).

IBMFRS was moderately correlated with peak 1-minute cadence ($\rho = 0.41$, $p = 0.13$) and average daily steps per minute ($\rho = 0.29$, $p = 0.30$). TUG duration was inversely correlated with VM ($\rho = -0.36$, $p = 0.20$) and steps per minute ($\rho = -0.32$, $p = 0.26$), suggesting that higher physical activity is associated with better mobility (Table 2).

Conclusion: Actigraphy metrics, particularly peak 1-minute cadence and steps per minute, demonstrated promising correlations with functional outcomes in IBM. These findings support the potential of accelerometry to capture real-world physical function and highlight the need for validation in larger, diverse myositis cohorts to establish clinical relevance and utility.

Disclosure: V. Kothari: None; **E. Alhassan**: None; **K. Ambrocio**: None; **B. Rockette-Wagner**: None; **C. V. Oddis**: None; **K. (Focht) Garand**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

Abstract Number: 0306

Direct Assessment of Intestinal Permeability as a Risk Factor for Multiple Joint Osteoarthritis in Community Cohorts of Humans and Pet Dogs

Liubov Arbeeva[1], Virginia Kraus[2], Richard Loeser[3], Yvonne Golightly[4], Hiroko Enomoto[5], Masataka Enomoto[5], Duncan Lascelles[5] and **Amanda Nelson**[6], [1]University of North Carolina, Chapel Hill, Carrboro, NC, [2]Duke University, Durham, NC, [3]University of North Carolina, Chapel Hill, NC, [4]University of Nebraska Medical Center, Omaha, NE, [5]North Carolina State University, Raleigh, NC, [6]University of North Carolina at Chapel Hill, Chapel Hill, NC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Increased intestinal permeability (IP) is common in chronic inflammatory diseases, and can be measured indirectly (e.g., with blood markers such as lipopolysaccharide, LPS), or directly (through measurement of ingested and excreted sugars). The goal was to determine cross-sectional associations between directly measured IP and radiographic multiple joint osteoarthritis (rMJOA) in community cohorts of humans and pet dogs.

Methods: Data were from the Johnston County Health Study (JoCoHS) and a parallel study in pet dogs from North Carolina State University (NCSU). JoCoHS participants (n=96, mean age 55 yrs, 63% females, 57% White) provided radiographs, clinical, and demographic data. Similar data were collected from an independent cohort of pet dogs (N=110, mean age 8 yrs). rMJOA was defined as 3+ unique appendicular joint sites involved in both cohorts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Multivariable Associations of mannitol excretion* at 5 hours with rMJOA and clinical characteristics. Multiple R-squared of the model: 0.16; p-value=0.03

Variable	Beta**	Standard Error	p-value
rMJOA	0.28	0.30	0.35
BMI	0.01	0.01	0.53
Age	-0.01	0.01	0.13
Female Sex	-0.59	0.21	0.01
Number of Medications	0.03	0.03	0.36
Charlson Index	0.13	0.12	0.29
LPS	-0.003	0.002	0.17

* log transformed
**beta coefficients with standard errors from linear regression
BMI= Body Mass Index; MJOA; rMJOA= radiographic multiple joint osteoarthritis; LPS=lipopolysaccharide

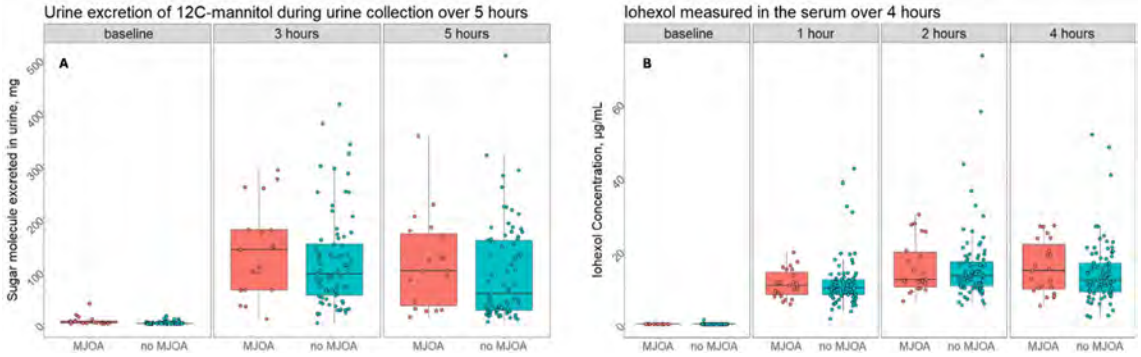
For direct IP assessment, humans fasted overnight followed by ingestion of 10g lactulose and 5g 12C-mannitol; sugars excreted in urine at baseline, 3- and 5-hours post-ingestion were measured using high-performance liquid chromatography (HPLC)–tandem mass spectrometry (Mayo). Lactulose:mannitol (L:M) ratio was calculated based on the percentage of administered dose of each sugar molecule in urine at 3- and 5-hours post-ingestion.

IP in dogs was also assessed after an overnight fast, followed by oral iohexol at a dose of 2.0 mL/kg (Omnipaque-350, GE Healthcare Ireland, Ireland). HPLC was used to analyze iohexol concentration in serum at baseline, 1, 2, and 4 hours post-iohexol ingestion (NCSU).

Sugars excreted at each time point and L:M at 5 hours in humans, and iohexol absorbed in dogs, were evaluated for participants with and without rMJOA using boxplots, comparing those with and without MJOA and by number of sites with rOA. Regression models adjusted for sex, age, body mass index (BMI), Charlson Index, and medications were used to examine the association of the mannitol excretion (log transformed) at 5 hours with rMJOA in humans; a similar approach used body composition score (BCS), age and rMJOA status in pet dogs.

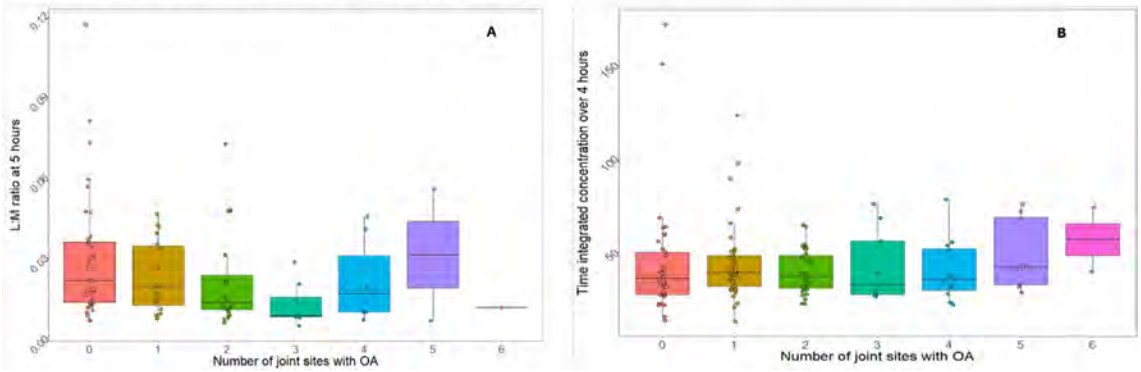
Results: The overall prevalence of increased IP (L:M ≥ 0.1, PMID33865841) was low in JoCoHS participants. The expected associations between IP (L:M ratio) and LPS, age, and BMI were seen in humans, indicating that the test performed as expected (data not shown). Mannitol excretion was slightly higher in those with rMJOA at 3 and 5 hours (**Fig1**). In regression models, mannitol excretion at 5 hours was lower in women but not statistically significantly associated with rMJOA (**Table 1**).

In dogs, higher serum iohexol was not associated with BCS (a measure of obesity), age, or rMJOA status. IP measured by serum iohexol was numerically but not significantly increased at 4 hours (**Fig1**). IP (L:M ratio at 5 hours for humans; total time-integrated serum iohexol at 4 hours in dogs) was increased when more joint sites were involved (**Fig2**).



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Radiographic osteoarthritis joint count vs (A) urine L:M ratio at 5 hours in 96 humans and (B) serum iohexol time integrated concentrations at 4 hours in 110 dogs



Conclusion: No associations were observed between increased IP and rMJOA in humans or pet dogs, likely due to limited sample size and cross-sectional data. Increased IP was infrequent in both cohorts, although a few outliers were noted (primarily in individuals with comorbidities and medication use).

Disclosure: L. Arbeeva: None; **V. Kraus**: 4-P Pharma, 1, Genascence, 1, Pacira, 1, Paradigm Biopharma, 1; **R. Loeser**: None; **Y. Golightly**: None; **H. Enomoto**: None; **M. Enomoto**: None; **D. Lascelles**: None; **A. Nelson**: Novo Nordisk, 1.

Abstract Number: 0307

Cytokine Profiling of Molecular Endotypes of Knee Osteoarthritis: Insights from the IMI-APPROACH cohort

Monica T. Hannani[1], Jaume Bacardit[2], Jonathan Larkin[3], Virpi Glumoff[3], Morten A. Karsdal[1], **Anne-Christine Bay-Jensen**[1], Ali Mobasheri[3] and Christian Thudium[4], [1]Nordic Bioscience A/S, Herlev, Denmark, [2]Newcastle University, Newcastle upon Tyne, United Kingdom, [3]University of Oulu, Oulu, Finland, [4]Nordic Bioscience, Herlev, Denmark

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: There has been a surging interest in characterizing subpopulations of osteoarthritis (OA) to facilitate recruitment of the right subgroups for drug development. The APPROACH consortium discovered three biomarker-based endotypes driven by i) structural damage to bone and cartilage, ii) connective tissue inflammation, and iii) low tissue turnover in 295 knee OA (KOA) participants at baseline. There is a need to gain a deeper understanding of the endotypes of OA to unveil the clinically actionable potential of such patient subgroups. The purpose of this study was to further characterize the three endotype subgroups through cytokine-profiling.

Methods: 277 participants from APPROACH fulfilling the ACR criteria for KOA were included. The three endotypes of structural damage, inflammation, and low tissue turnover previously defined by 19 serum and urine biomarkers reflecting bone and cartilage turnover and inflammation were considered at the month six, 12, and 24 visits. 24 cytokines were measured with Luminex Multiplex Immunoassays. Cytokines with ≤ 50% missing values were considered, resulting in 15 included

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

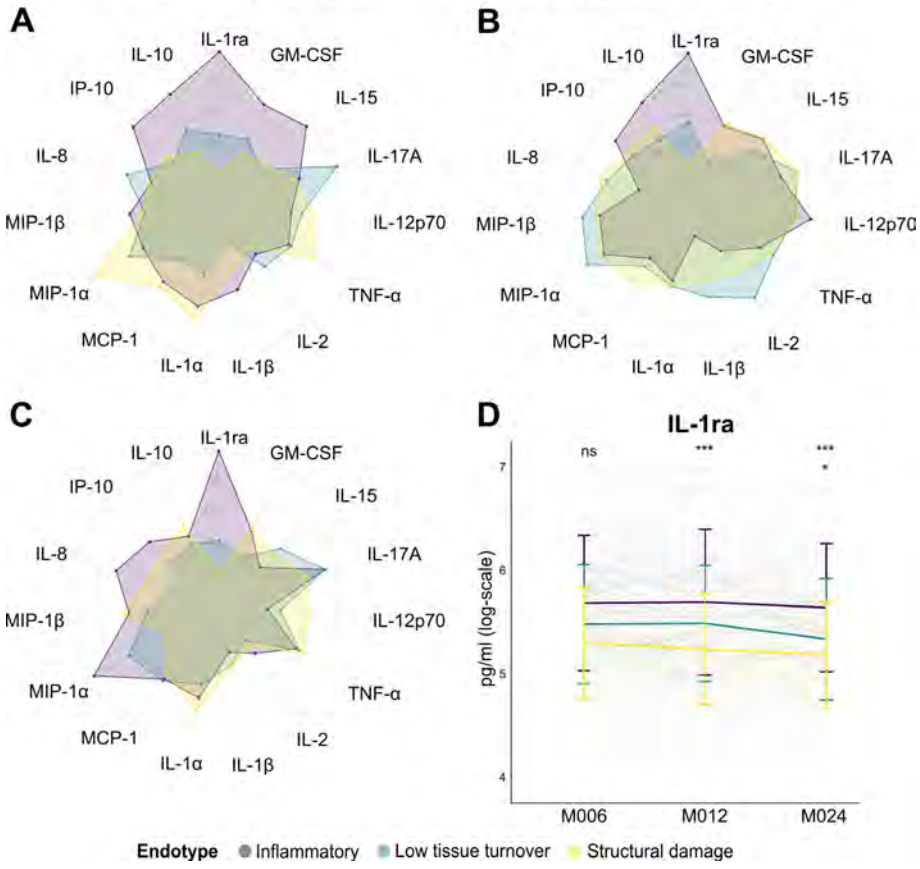


Figure 1. **Cytokine profiles of molecular endotypes of knee osteoarthritis participants from APPROACH at the A) six (M006), B) 12 (M012), and C) 24 (M024) month visits. Log-transformation and sex-specific z-score scaling was performed on the measurements (min-max normalized values shown). D) Longitudinal measurements of interleukin-1 receptor antagonist (IL-1ra) for each participant and endotype means with standard deviations. Differences between endotypes were estimated with a linear-mixed model, adjusting for age, sex, and BMI. P-values were Benjamini-Hochberg-adjusted for multiple testing. ns, no significance between any comparisons; *, p = 0.047 between inflammatory and low tissue turnover endotypes; ***, p < 0.001 between inflammatory and structural damage endotypes.**

markers. Cytokine levels were log-transformed, trimmed for extreme outliers (Winsor's and Tukey's rule), and sex-specific z-score scaling was performed. Cytokine-profiles of each endotype and visit were visualized using min-max normalized median concentrations. Percent changes in geometric mean cytokine concentrations between the endotypes were computed with linear mixed-effects models (LMMs), adjusting for age, sex, and BMI based on non-z-score scaled, log-transformed cytokine levels. P-values were Benjamini-Hochberg-adjusted for multiple testing. Intra-class correlations (ICCs) of the cytokines levels over time were estimated.

Results: Cytokine-profiling across the visits of the KOA endotypes revealed fluctuating longitudinal cytokine expression patterns (Fig. 1A-C). 8/15 cytokines exhibited good longitudinal stability (ICC > 0.75), with the highest ICCs achieved for MCP-1 of 0.89 (95% CI: 0.87, 0.91) and the anti-inflammatory cytokine interleukin-1 receptor antagonist (IL-1ra) of 0.88 (95% CI: 0.85, 0.90). IL-1ra was the only cytokine with differential levels between the endotypes (Fig. 1D). At month 12, a mean change of IL-1ra of 36% (95% CI: 19%, 54%; p-value < 0.001) was found for the inflammatory endotype relative to structural damage, while it was 40% (95% CI: 22%, 59%; p-value < 0.001) at month 24. At month 24, a mean change of IL-1ra of 21% (95% CI: 10%, 31%; p-value = 0.047) was found for the inflammatory endotype relative to low tissue turnover.

Conclusion: This study further characterized the three KOA by an independent modality from which the endotypes were originally defined. We showed that the cytokine panel was associated with longitudinal fluctuations across the endotype

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

subgroups but found that IL-1ra was persistently and differentially associated with the inflammatory endotype. These results may indicate an intriguing pathobiological involvement of the anti-inflammatory cytokine IL-1ra in OA subgroups driven by an inflammatory molecular endotype.

Disclosure: M. T. Hannani: Nordic Bioscience A/S, 11; **J. Bacardit**: None; **J. Larkin**: None; **V. Glumoff**: None; **M. A. Karsdal**: Nordic Bioscience A/S, 3, 11; **A. Bay-Jensen**: Nordic Bioscience A/S, 3, 11; **A. Mobasheri**: Ampio Pharmaceuticals, 2, Aptissen, 2, Consumer Healthcare at Sanofi, 2, Contura, 2, Enlivex, 2, Grünenthal, 2, 6, HALEON, 2, Janssen, 6, Kolon TissueGene, 2, Nestlé, 2, Novartis, 6, Orion Corporation, 2, 6, Pacira Biosciences, 2, Rottapharm, 2, Sanofi, 2, Sanofi-Aventis, 2, Synartro, 2, Viatris, 6; **C. Thudium**: Nordic Bioscience A/S, 3, 11.

Abstract Number: 0308

Artificial Intelligence Assisted Extraction of Patient-reported Pain Outcomes in Osteoarthritis Using Prompt Engineering of Large Language Models

Jainesh Doshi[1], Stephen Batter[1], Yiyuan Wu[2], Alice Santilli[1], Sandhya Kannayiram[3], Susan Goodman[4] and **Bella Mehta**[5], [1]Hospital for Special Surgery, New York, [2]Weill Cornell Medicine, New York, NY, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Unstructured data in physician notes can be incredibly valuable, especially for understanding patient-reported outcomes (PROs), which are often mentioned in these notes.

In this study, we explore an Artificial Intelligence technique to efficiently extract patient-reported pain in Osteoarthritis (OA) patients by prompt engineering Large Language Models (LLMs). Prompt engineering is the process of designing inputs in LLMs to help to get insights from unstructured data. Our objective is to apply prompt engineering techniques to extract/predict patient-reported pain in physician notes in OA patients.

Table 1:

Table 1: Patient Characteristics	N = 159
Age (years), Mean (SD)	65 years (SD ± 7)
Sex	
Female	63 (40%)
Male	96 (60%)
Race	
White	127 (80%)
Asian	8 (5%)
Black	16 (10%)
More than one race/Other/Unknown	8 (5%)
Not Hispanic Ethnicity	151 (96%)
Patient Reported Pain Continuous	5.88 (SD ± 2.20)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

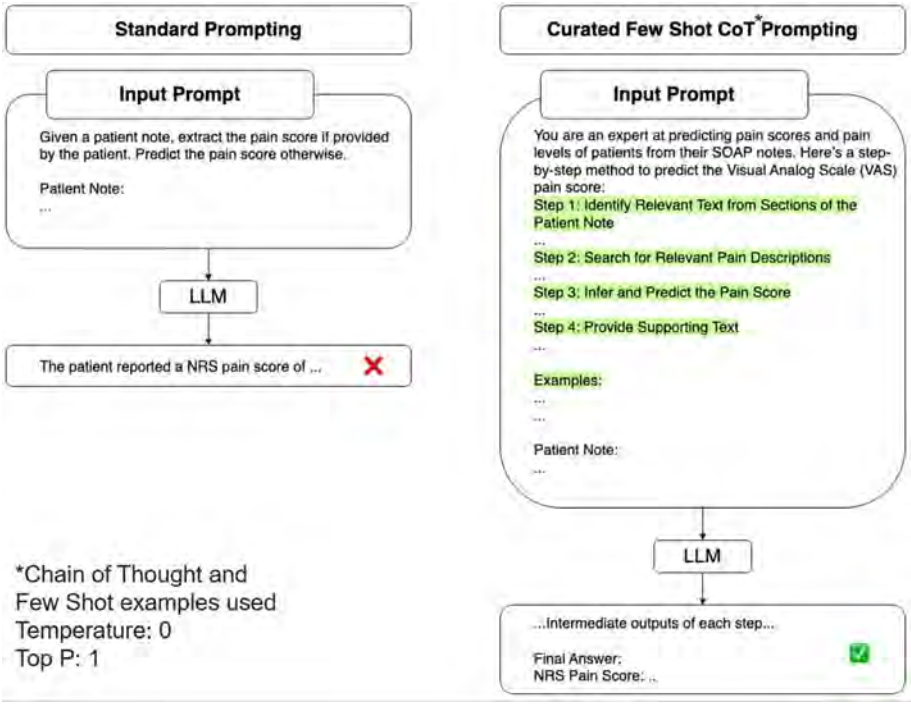


Figure 1

Methods: We used notes from patients with osteoarthritis at Internal Medicine screening (IM) and Orthopedic visits(ortho) enrolled in a registry before Total Knee Arthroplasty. A trained abstractor extracted pain scores (0-10) where they were explicitly stated. For notes without explicit scores, a board-certified IM physician estimated it based on the content. Notes were processed using the Llama 3.2-90B model, with a prompt engineered to extract 0-10 pain scores. **(Figure 1)**. Prompt engineering techniques, such as Chain of Thought and Few Shot examples, were employed. Outside of the visits, patients reported a 0–10 pain score **(Table 1)**. We calculated Kendall's Tau-b to measure ordinal correlation between the LLM predictions, abstractor scores when present and patient reported pain. Physician predictions were analyzed for notes without scores.

Results: There were 159 patients in this study with corresponding ortho and IM notes. We identified 133 IM notes and 66 ortho notes that explicitly stated pain scores **(Figure 2)**. In comparisons between pain scores extracted via a trained abstractor and the LLM, we observed a strong correlation in IM notes ($\tau = 0.81$) and an even stronger correlation in ortho

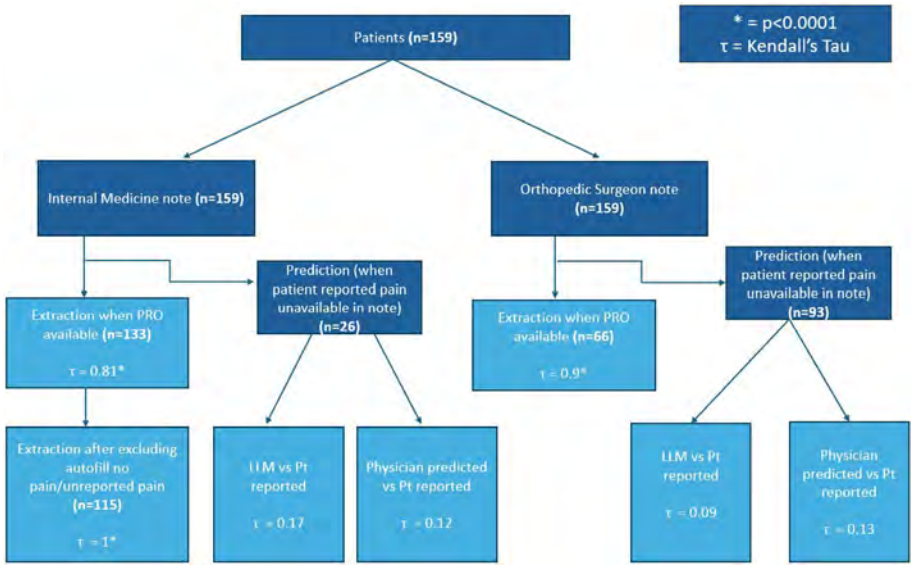


Figure 2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

notes (τ = 0.99). In IM notes, 18 had a pain score written as 0 because the question was unanswered by patients, causing the EMR system to default to zero. In most cases, the LLM recognized and flagged these abnormalities. We then excluded the default zero and had a perfect correlation (τ = 1).

For notes lacking explicit pain scores, the LLM predicted scores for 26 IM notes and 93 ortho notes. When comparing LLM-predicted pain scores to patient-reported pain scores obtained outside of the visit, the correlations were weak (IM: τ = 0.17, p = 0.30) (Ortho: τ = 0.09, p = 0.30). When a board-certified physician was asked to predict the scores, the correlation remained weak (IM: τ = 0.12, p = 0.46) (Ortho: τ = 0.13, p = 0.12).

Conclusion: When patient pain is explicitly documented in the chart, large language models (LLMs) can accurately extract this information, offering a potential time-saving tool for abstracting data from clinical notes. In contrast, when pain scores are not explicitly documented, LLM predictions are less accurate but still comparable to the performance of physicians attempting to infer scores from the same unstructured text. LLMs represent an efficient method for extracting information from clinical notes which may have variability in documentation when relevant data exist in unstructured form, opening new pathways for leveraging this information in both clinical care and research.

Disclosure: J. Doshi: None; **S. Batter**: None; **Y. Wu**: None; **A. Santilli**: None; **S. Kannayiram**: None; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2; **B. Mehta**: Amgen, 1, Horizon, 1.

Abstract Number: 0309

A Composite Cumulative Cartilage Damage Metric Predicts Incident Symptomatic Knee OA: Data from the Osteoarthritis Initiative

Julieann Patarini[1], Timothy McAlington[2], Jonggyu Baek[1], Emily Kirillov[3], Nhung Vo[3], Michael Richard[3], Ming Zhang[4], Matthew Harkey[5], Grace Lo[6], Shao-Hsien Liu[1], Kate Lapane[1], Charles Eaton[7], James Mackay[8] and **Jeffrey Driban**[9], [1]UMass Chan Medical School, Worcester, MA, [2]UMass Chan School of Medicine, Arlington, MA, [3]Tufts Medical Center, Boston, MA, [4]Boston University, Westford, MA, [5]Michigan State University, East Lansing, MI, [6]Baylor College of Medicine / MEDVAMC, Houston, TX, [7]Brown University, Pawtucket, RI, [8]University of Cambridge; Norwich Medical School, San Diego, CA, [9]University of Massachusetts Chan Medical School, Marlborough, NH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cartilage defects are a hallmark of OA progression. We previously developed a composite MRI-based metric that combines cartilage damage from 6 anatomical regions throughout a knee. This cumulative damage metric relates to radiographic knee OA severity and reflects the accumulation of damage attributable to OA over the course of the disease. Cumulative damage is a sensitive biomarker for detecting cartilage changes; however, morphological cartilage changes typically occur later in the disease process. It remains unclear whether this composite score represents clinically meaningful pathways relevant to early stages of OA and can identify people before the onset of OA. We evaluated whether our cumulative damage composite metric is prognostic of incident symptomatic knee OA over the subsequent three years.

Methods: We analyzed a convenience sample within the Osteoarthritis Initiative of participants without symptomatic knee OA. Pain assessments and radiographs were collected annually. Using Magnetic resonance images from the initial visit, we combined 6 regional cartilage damage index measures (intra-reader ICC ≥ 0.84) to calculate a composite score, referred

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Worse Cumulative Damage is Associated with a Greater Risk of Incident Symptomatic OA

Table 1. Worse Cumulative Damage is Associated with a Greater Risk of Incident Symptomatic OA

	Incident Symptomatic OA			
	Absent	Present	Unadjusted Relative Risk (RR)	Adjusted RR[a]
Overall Study Sample	n= 630	n = 283	(95% CI)	(95% CI)
Cumulative Damage (mean (SD))	0.64 (3.29)	1.95 (3.41)	**1.09 (1.06 - 1.13)[b]**	**1.08 (1.04 - 1.12)[b]**
Cumulative Damage – Tertiles Low (-9.40 to -0.49)	230 (37%)	72 (25%)	REFERENCE	
Moderate (-0.45 to 2.69)	227 (36%)	79 (28%)	1.12 (0.84 - 1.51)	1.09 (0.81 - 1.48)
High (2.70 to 13.25)	173 (27%)	132 (47%)	**1.90 (1.46 - 2.46)**	**1.73 (1.31 - 2.29)**
No Symptoms, No Radiographic OA	Incident Symptomatic OA			
(n = 277)	Absent	Present	Unadjusted RR*	
	n= 259	n = 18	(95% CI)	
Cumulative Damage (continuous)	0.14 (3.07)	0.14 (2.31)	1.03 (0.92 - 1.15)	
Cumulative Damage –Tertiles Low (-9.40 to -0.49)	110 (42%)	10 (56%)	REFERENCE	
Moderate (-0.45 to 2.69)	95 (37%)	5 (28%)	0.64 (0.23 - 1.75)	
High (2.70 to 13.25)	54 (21%)	3 (17%)	0.81 (0.24 - 2.80)	
Radiographic OA Only (No Symptoms)	Incident Symptomatic OA			
(n = 459)	Absent	Present	Unadjusted RR*	
	n= 211	n = 248	(95% CI)	
Cumulative Damage (continuous)	1.44 (3.57)	2.09 (3.50)	1.03 (1.00 - 1.05)	
Cumulative Damage –Tertiles Low (-9.40 to -0.49)	61 (29%)	59 (24%)	REFERENCE	
Moderate (-0.45 to 2.69)	67 (32%)	67 (27%)	0.97 (0.75 - 1.24)	
High (2.70 to 13.25)	83 (39%)	122 (49%)	1.18 (0.95 - 1.47)	
Symptoms Only (No Radiographic OA)	Incident Symptomatic OA			
(n = 175)	Absent	Present	Unadjusted RR*	
	n= 158	n = 17	(95% CI)	
Cumulative Damage (continuous)	0.43 (3.05)	1.97 (2.53)	1.17 (0.99 - 1.37)	
Cumulative Damage –Tertiles Low (-9.40 to -0.49)	57 (36%)	3 (18%)	REFERENCE	
Moderate (-0.45 to 2.69)	65 (41%)	7 (41%)	1.65 (0.43 - 6.27)	
High (2.70 to 13.25)	36 (23%)	7 (41%)	2.83 (0.77 - 10.41)	

Notes. (a). Relative risks adjusted for age, gender, and body mass index. (b). Relative risks for disease activity as a continuous measurement are per 1 unit. Bold = statistically significant associations. * Only unadjusted relative risks are reported because of the limited sample size within each stratum.

to as the cumulative damage metric. A cumulative damage metric of 0 approximated the average value for a reference sample (n=197, 53% had moderate-severe radiographic knee OA, average [SD] WOMAC pain score = 5.0 [3.6]); lower (negative) values indicate milder disease, while greater values indicate worse disease. The outcome was incident symptomatic knee OA (the combined state of frequent knee pain and radiographic OA [Kellgren-Lawrence Grade ≥ 2]) within three years after the cumulative damage measurement. We used logistic regression with repeated measures to assess the association between cumulative damage (continuous measure and tertiles) and incident symptomatic knee OA, adjusting for gender, age, and body mass index.

Results: Among 913 knees (n=572 participants), most were female (56%), white (82%), and had a mean age of 61 (SD=9) and body mass index of 29.4 (SD=4.5) kg/m^2. Cumulative damage ranged from -9.4 to 13.3 (higher values = worse cartilage damage). Knees that developed incident symptomatic OA had greater cumulative damage (2.0 [3.4] vs. 0.6 [3.3]); the adjusted relative risk per 1 unit increase was 1.09 (95% confidence interval: 1.06-1.13; Table). More specifically, the tertile with the worst cumulative damage – analogous to damage typically observed among knees with radiographic OA (Table) – was associated with a greater risk for incident symptomatic knee OA.

Conclusion: Greater cumulative damage, especially severe damage typical of knees with radiographic OA, is associated with a higher risk of incident symptomatic OA.

Disclosure: J. Patarini: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **J. Baek**: None; **E. Kirillov**: None; **N. Vo**: None; **M. Richard**: None; **M. Zhang**: None; **M. Harkey**: None; **G. Lo**: None; **S. Liu**: None; **K. Lapane**: None; **C. Eaton**: None; **J. Mackay**: AstraZeneca, 3, Blue Earth Diagnostics, 3; **J. Driban**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0310

Evaluate Safety, Tolerability, and Pharmacodynamics of a Single Intra-Articular Injection of GNSC-001 Gene Therapy in Subjects with Knee Osteoarthritis: 12-month Results from DONATELLO

Annahita Keravala[1], Philip Conaghan[2], shanna jackson[1], sharmila Vijay[1], Thomas Chalberg[3], **Jeyanesh Tambiah**[4] and Laurie Halligan[1], [1]Genascence, Palo Alto, CA, [2]University of Leeds, Leeds, United Kingdom, [3]Genascence Corp, Palo Alto, CA, [4]Genascence, San Diego, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IL-1 contributes significantly to osteoarthritis (OA) pathology, driving inflammation and cartilage degradation. Prior therapies targeting IL-1 have shown limited success due to inadequate drug delivery and retention in joints. GNSC-001, a recombinant adeno-associated virus (rAAV) encoding the IL-1 receptor antagonist (IL-1Ra) transgene, is designed to provide sustained, local inhibition of IL-1 activity after a single intra-articular (IA) injection. The DONATELLO Phase 1b trial was initiated to evaluate the safety, dosing and pharmacodynamic effects of GNSC-001. Effects of immune conditioning with short regimens of corticosteroids (CS) were also investigated. Results from the 12-month primary follow-up period are reported.

Methods: Consented participants (40-75 years, Kellgren Lawrence grades 2-3, target knee pain WOMAC ≥20/50) were randomized (1:1:1:1:1) into five groups: (1: n=12) GNSC-001 $1x10^{12}$ vector genomes (vg); (2: n=11)) GNSC-001 $1x10^{12}$ vg + oral CS (prednisone 60mg/day tapered over 6 weeks); (3: n=10) GNSC-001 $1x10^{13}$ vg; (4: n=10) GNSC-001 $1x10^{13}$ vg + oral CS and (5: n=10) placebo (PBO). An open-label group (6: n=14) with target knee effusions at baseline, received GNSC-001 $1x10^{13}$ vg with IA methylprednisolone (80mg) plus oral prednisone (60mg/day for 3 days). All subjects received ultrasound-guided IA injections on Day 1. Visits, including synovial fluid (SF) draws to measure IL-1Ra expression and exploratory patient reported outcomes (PROs) occurred at Months 1, 3, 6, and 12, with planned 48-month safety follow-up.

Table 1: Treatment Emergent and Target Knee Adverse Events, Groups 1-6. * Related AE are all AE classified as either Possibly, Probably or Definitely related. ** Only applies to cohorts receiving oral steroids.

	Placebo (N=10)	GNSC-001 (1*10^12 vg) (N=12)	GNSC-001 (1*10^12 vg, steroids) (N=11)	GNSC-001 (1*10^13 vg) (N=10)	GNSC-001 (1*10^13 vg, steroids) (N=10)	GNSC-001 (1*10^13 vg, steroids IA) (N=14)
No of subjects with at least one TEAE	6 (60.0%)	6 (50.0%)	7 (63.6%)	7 (70.0%)	6 (60.0%)	10 (71.4%)
No of TEAEs	**21**	**17**	**29**	**17**	**28**	**58**
No of subjects with at least one						
Severe TEAE (Grade 3-5 CTCAE)	1 (10.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	1 (10.0%)	2 (14.3%)
Serious TEAE	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
TEAE related to study treatment *	1 (10.0%)	1 (8.3%)	1 (9.1%)	2 (20.0%)	2 (20.0%)	**7 (50.0%)**
Severe (Grade 3-5 CTCAE)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
TEAE related to study procedure *	2 (20.0%)	1 (8.3%)	0 (0.0%)	2 (20.0%)	2 (20.0%)	4 (28.6%)
Severe (Grade 3-5 CTCAE)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
TEAE requiring concomitant medication	5 (50.0%)	5 (41.7%)	6 (54.5%)	5 (50.0%)	4 (40.0%)	10 (71.4%)
TEAE requiring medical procedure	1 (10.0%)	2 (16.7%)	1 (9.1%)	1 (10.0%)	2 (20.0%)	**7 (50.0%)**
TEAE requiring hospitalization	1 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
Target Knee Adverse Events (TKAEs)						
No of subjects with at least one TKAE	3 (30.0%)	2 (16.7%)	2 (20.0%)	3 (27.3%)	4 (40.0%)	8 (57.1%)
No of TKAEs	**4**	**3**	**4**	**6**	**15**	**24**
No of subjects with at least one						
Severe TKAE (Grade 3-5 CTCAE)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	1 (7.1%)
TKAE related to study treatment *	1 (10.0%)	1 (8.3%)	2 (20.0%)	1 (9.1%)	2 (20.0%)	7 (50.0%)
Severe (Grade 3-5 CTCAE)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
TKAE related to study procedure *	2 (20.0%)	1 (8.3%)	2 (20.0%)	0 (0.0%)	2 (20.0%)	4 (28.6%)
Severe (Grade 3-5 CTCAE)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)
TKAE related to study steroids*, **	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
TKAE requiring concomitant medication	2 (20.0%)	1 (8.3%)	0 (0.0%)	3 (27.3%)	2 (20.0%)	6 (42.9%)
TKAE requiring medical procedure	0 (0.0%)	1 (8.3%)	0 (0.0%)	1 (9.1%)	2 (20.0%)	5 (35.7%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: IL-1Ra Expression. Numbers denote % subjects expressing IL-1Ra in synovial fluid in target range (>500pg/ml)

Time following GNSC-001 injection	Placebo (N=10)	GNSC-001 (1*10^12 vg) (N=12)	GNSC-001 (1*10^12 vg, steroids) (N=11)	GNSC-001 (1*10^13 vg) (N=10)	GNSC-001 (1*10^13 vg, steroids) (N=10)	GNSC-001 (1*10^13 vg, steroids IA) (N=14)
Baseline	0	0	25	0	0	0
1 month	0	50	83	20	100	92
3 months	0	67	88	17	100	83
6 months	0	75	86	14	80	92
12 months	0	67	86	0	100	71

Results: At study completion (Month 12), 67 subjects (78% female, mean age 60.9 ± 8.5 years, mean BMI 28.6 ± 4.3 kg/m^2) had been dosed across the 6 groups. No deaths or related treatment-emergent serious adverse events were reported. Treatment-Emergent Adverse Events (TEAEs) were balanced in Groups 1-5, trending higher in Group 6. Target knee AEs (TKAEs) across Groups 1-6 were mostly mild-moderate, with one graded as a 'severe' event (recurrent knee effusion in Group 6). TKAEs included arthralgia, swelling, effusion, and stiffness. TEAEs and TKAEs at 12 months are summarized in Table 1. GNSC-001 treated groups 1, 2, 4 and 5 had elevated SF IL-1Ra levels compared to baseline and PBO (Table 2). PROs in GNSC-001 treated groups showed sustained improvement from baseline in most subjects.

Conclusion: This trial met its primary and secondary objectives, with GNSC-001 demonstrating a favorable safety profile and sustained IL-1Ra expression in SF. Corticosteroid immune conditioning was associated with increased IL-1Ra expression. Exploratory PROs in GNSC-001 treated groups showed improvements from baseline in a majority of subjects. These data support further clinical development of GNSC-001 as a promising therapeutic strategy addressing unmet clinical needs for treatment of knee OA.

Disclosure: A. Keravala: Genascence, 3, 8, 11; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6; **s. jackson**: Genascence, 2; **s. Vijay**: Genascence, 2; **T. Chalberg**: Genascence, 3, 4, 8, 11; **J. Tambiah**: Genascence, 3, 8, 11; **L. Halligan**: Genascence, 3, 11.

Abstract Number: 0311

Time series analysis of continuous accelerometry data to determine the impact of symptomatic multiple joint osteoarthritis (MJOA) in the naturally occurring canine model

Elizabeth Kawecki-Wright[1], **Liubov Arbeeva**[2], Christina Stevens[1], Masataka Enomoto[1], Amanda Nelson[3], Margaret Gruen[1] and Duncan Lascelles[1], [1]North Carolina State University, RALEIGH, NC, [2]University of North Carolina, Chapel Hill, Carrboro, NC, [3]University of North Carolina at Chapel Hill, Chapel Hill, NC

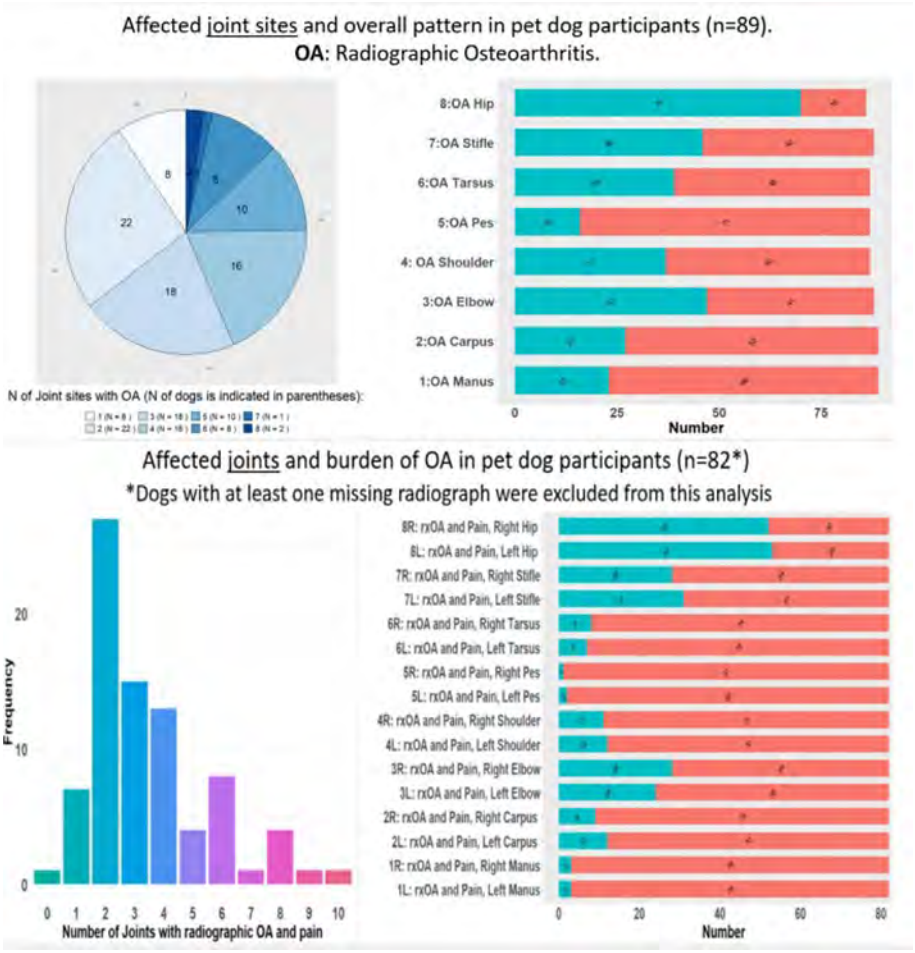
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Pet dogs are a promising translational model for naturally occurring multiple joint osteoarthritis (MJOA). We characterized the impact of symptomatic (sx) MJOA, over the non-MJOA phenotype, on weekday physical activity (PA) patterns in pet dogs with OA pain using accelerometer-based data.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

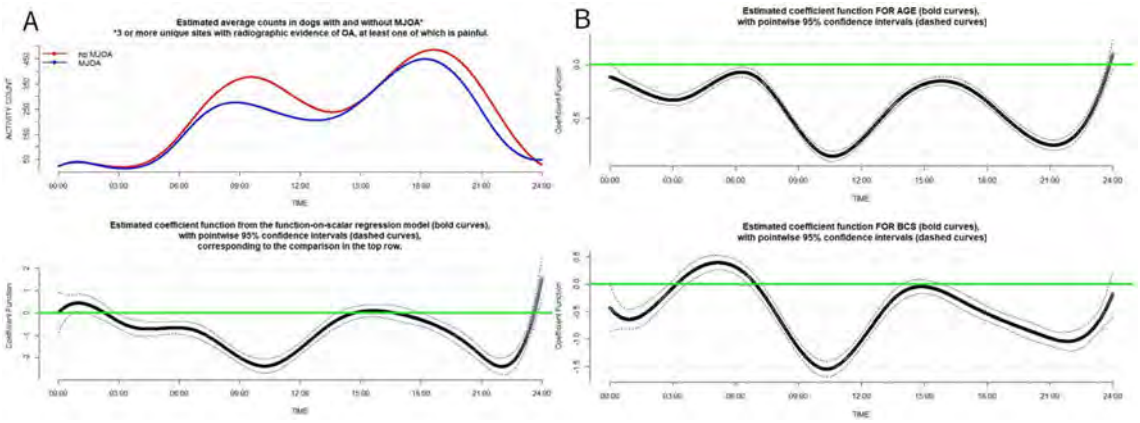
Methods: Full-body radiographs and orthopedic assessments were collected from pet dogs with evidence of OA (N=99). MJOA was defined as radiographic OA (rxOA) in 3+ unique appendicular joint sites (bilateral joints=single site) with at least one painful rxOA joint. Missing radiographs were allowed if N of OA joint sites from available images was >=3. Burden of OA was defined only for dogs with complete radiographs as the total number of **joints** with both OA **and** pain. Dogs wore a collar-mounted activity monitor (Actigraph GT3X) for at least 7 days. Per minute average vector magnitudes were recorded on weekdays and used to create composite 24-h PA profiles. Function on scalar regression (FoSR) was used to examine the association of 24-h PA (outcome) with MJOA and with burden of OA (total number of **joints** with both OA **and** pain) adjusting for age and body condition score (BCS). Coefficients and 95% confidence intervals (CIs) are interpreted analogously to a simple linear regression but **estimated per minute**. To provide an intuitive interpretation, we created the "averaged" coefficients and 95% CIs by integrating the beta and CI curves over time.

Results: Of 99 dogs, 89 had sufficient data to define MJOA and were included (48% male, 52% female, mean age 9 years). Fifty-nine (66%) dogs had MJOA; distribution of joints is shown in **Fig1**. All dogs with rxMJOA were symptomatic (sxMJOA). Age, BCS, and MJOA had negative effects on PA patterns (averaged βs [95% CIs]: -0.40 [-0.44, -0.35], -0.52 [-0.67, -0.37], and -0.86 [-1.19, -0.54]**)**. **Fig2A** shows 24-h average activity. Dogs without MJOA (red line) showed higher activity during peak hours. The CIs were below 0 from 3 am to 2 pm and from 6 pm to ~11 pm, suggesting that dogs with MJOA (blue line) are less active than those without in these time windows. The coefficient function and CI for MJOA and age were below 0 during most of the 24-h period, suggesting older dogs and those with MJOA are less active (**Fig2B**). A short period of PA around and after midnight in older dogs and those with MJOA (curves and CIs above the green line) suggests pain-related sleep interference. Similarly, dogs with higher OA-pain burden (n=82 dogs with complete radiographs) displayed less

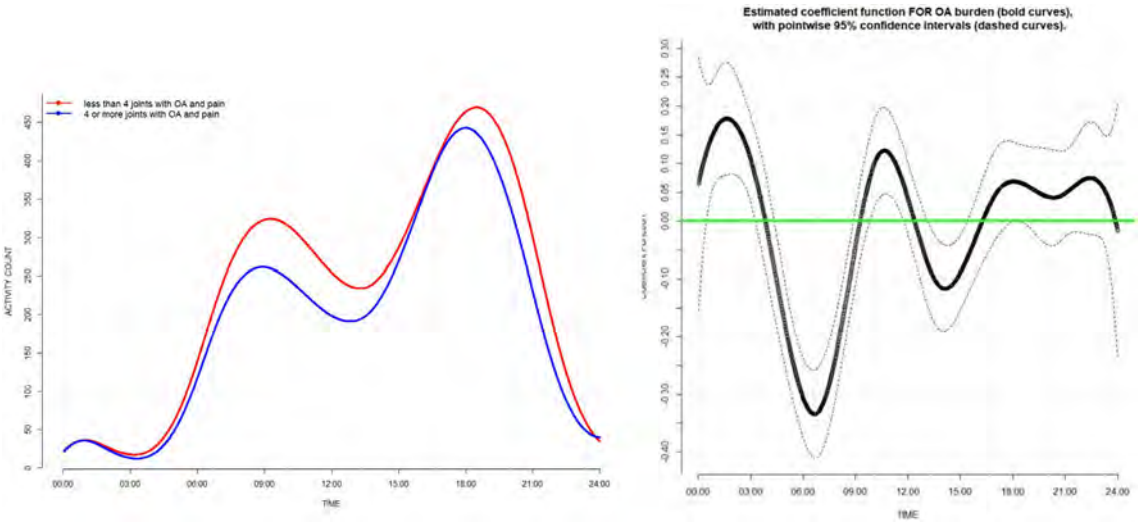


Radiographic OA and painful joints and joint sites in client canine population.

23265203, 2025, S9, Downloaded from https://acvjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparison of mean activity distributions between dogs with and without multiple joint osteoarthritis (MJOA) over time. The green lines correspond to beta=0, which indicates that there is no difference between groups at the corresponding time point.



Estimated mean activity in dogs with different N of joints with rxOA and pain (<4 and >=4) and estimated coefficient function for OA burden derived from the function on scalar regression model of accelerometer data on continuous N of joints adjusted forage and BCS. The green line corresponds to beta=0, which indicates that there is no effect of OA burden on PA at the corresponding time point.

PA during daytime hours **(Fig3)**. These associations were not seen when data were collapsed to average per-minute activity (averaged β [95% CIs]: -0.01 [-0.09, -0.07]).

Conclusion: Analysis of 24-h PA patterns clearly demonstrates the negative influence of MJOA on weekday PA, as well as the greater negative influence on PA patterns when more OA joints are painful. If similar effects are seen in humans with symptomatic MJOA, our results would further support the use of the naturally occurring pet dog model of OA pain, and of PA patterns as a clinically relevant outcome measure. The FoSR approach to evaluating PA patterns identified timeframes with lower PA in dogs with MJOA which were not evident if sum scores of PA were used.

Disclosure: E. Kawecki-Wright: None; **L. Arbeeva**: None; **C. Stevens**: None; **M. Enomoto**: None; **A. Nelson**: Novo Nordisk, 1; **M. Gruen**: None; **D. Lascelles**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0312

Efficacy and Safety of Tocilizumab in Children with Juvenile Idiopathic Arthritis: A Systematic Review and Meta-Analysis

Kainat Jahangir[1], Meer Murtaza[2], **Rida Ul Jannat**[3], Muhammad Arham[4], Najam Gohar[5], Faseeh Haider[6], Rohma Ahmed[7], FNU Raja[8], Rabie Habib[9], Mahnoor Umar[10], Hira Saleem[11], Faizan Ahmed[12], Tehmasp Mirza[13], Momina Siddiqui[14], Muhammad Umer[15], Haziq Ahmed[16], Maryam Anwar[17], Rehab Bint e Tahir[18], Yusra Junaid[19] and Ramsha Ali[20], [1]Dow Medical College, Karachi, Pakistan, [2]Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan, [3]Wake Forest University, Winston Salem North Carolina, Winston-Salem, NC, [4]Sheikh Zayed Medical College, Lahore, Pakistan, [5]Ameer Ud Din Medical College, Sialkot, Pakistan, [6]Allama Iqbal Medical college, Lahore, Punjab, Pakistan, [7]Fatima Jinnah Medical University, Lahore, Pakistan, [8]Federal Medical and Dental College, Islamabad, Pakistan, [9]Baylor College of Medicine, Texas, Pakistan, [10]Nassau University Medical Center, New York, [11]Houston Methodist Hospital, Texas, [12]Corewell health, dearborn, MI, [13]Shalamar Medical and Dental College, Lahore, Pakistan, [14]Rawalpindi Medical Univeristy, Rawalpindi, Punjab, Pakistan, [15]King Edward Medical College, Lahore, Pakistan, [16]Sheikh Khalifa bin zayed Alnahyan Medical College, Lahore, Punjab, Pakistan, [17]Baqai Medical University, Karachi, Pakistan, [18]-, lahore, [19]Dow University of health and sciences, karachi, Pakistan, [20]Peoples University of Medical and Health Sciences SBA, NawabShah, Pakistan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

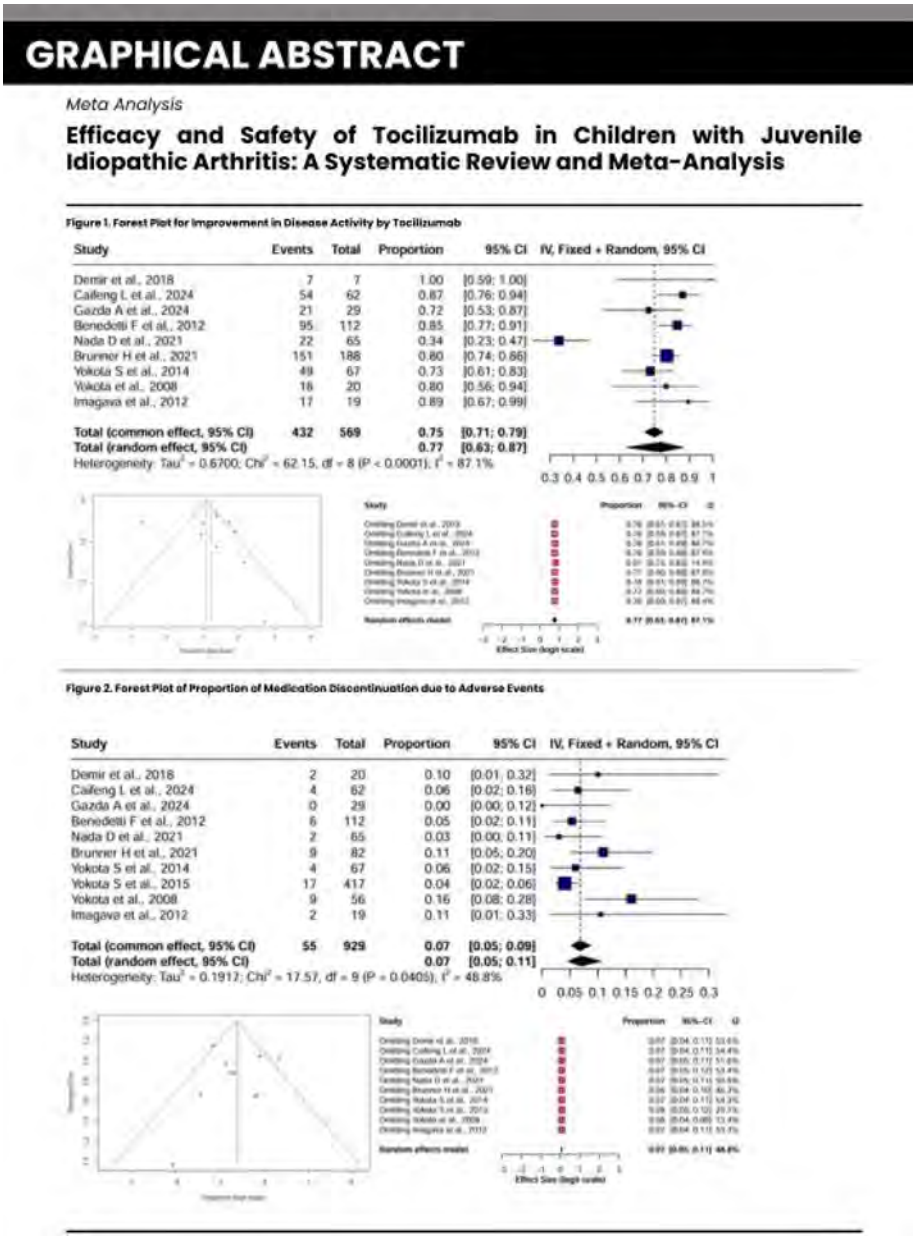
Background/Purpose: Juvenile idiopathic arthritis (JIA) encompasses various chronic inflammatory conditions in children that lead to joint discomfort and potential disability. Tocilizumab, an antibody targeting interleukin-6, has shown effectiveness in treating rheumatoid arthritis and may also help children with JIA. Due to the distinct characteristics of the disease, its efficacy and safety in children require assessment.

Methods: A systematic literature review was conducted by searching PUBMED, EMBASE, COCHRANE, SCIENCE DIRECT, and SCOPUS for RCTs and non-RCTs assessing the efficacy and safety of Tocilizumab in Juvenile Idiopathic Arthritis up to 2025. The primary outcomes assessed were disease activity improvement, joint inflammation reduction, Functional enhancements (i.e., CHAQ score), and QOL scores. Statistical analysis was conducted in R (v2025.05.0+496).

Results: A meta-analysis involving 11 studies with a total of 929 children diagnosed with Juvenile Idiopathic Arthritis (JIA) indicated that Tocilizumab led to improved disease activity, achieving a pooled risk ratio of 3.77 (95% CI 2.32-6.13, p=0.060) when compared to the control group. When examining study types, the subgroup analysis revealed proportions of 0.04 (95% CI 0.03-0.07) for non-RCTs and 0.10 (95% CI 0.07-0.14) for RCTs (p=0.0040). The average Childhood Health Assessment Questionnaire (CHAQ) score was 1.67, indicating functional improvement; the quality of life score was 45.74. In terms of JIA subtypes, the proportions were 0.11 (95% CI 0.06-0.18) for polyarticular JIA and 0.06 (95% CI 0.04-0.08) for systemic JIA (p=0.0502). Adverse events were reported in 7% of the participants (pooled proportion 0.07, 95% CI 0.05-0.09), primarily mild infections, with no serious adverse events noted. Sensitivity analysis demonstrated the stability of the results (range 0.06-0.07), with moderate heterogeneity (I^2=48.8%).

Conclusion: Our findings support using Tocilizumab in managing Juvenile Idiopathic Arthritis, demonstrating improved outcomes without significantly increasing adverse events. These results offer a clearer understanding of its clinical value and underscore the need for further high-quality randomized trials.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Graphical Abstract

Disclosure: K. Jahangir: None; **M. Murtaza**: None; **R. Jannat**: None; **M. Arham**: None; **N. Gohar**: None; **F. Haider**: None; **R. Ahmed**: None; **F. Raja**: None; **R. Habib**: None; **M. Umar**: None; **H. Saleem**: None; **F. Ahmed**: None; **T. Mirza**: None; **M. Siddiqui**: None; **M. Umer**: None; **H. Ahmed**: None; **M. Anwar**: None; **R. Bint e Tahir**: None; **Y. Junaid**: None; **R. Ali**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0313

People with Knee Osteoarthritis Infrequently Seek Medical Care for Arthritis, Even Those With Severe Disease

Grace Lo[1], **Shunshun Yan**[2], Julieann Patarini[3], Timothy McAlington[4], Charles Eaton[5] and Jeffrey Driban[6], [1]Baylor College of Medicine / MEDVAMC, Houston, TX, [2]Baylor College of Medicine, Houston, [3]UMass Chan Medical School, Worcester, MA, [4]UMass Chan School of Medicine, Arlington, MA, [5]Brown University, Providence, RI, [6]University of Massachusetts Chan Medical School, Marlborough, NH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is the most common form of arthritis, a condition associated with substantial disability. Providers are often uncomfortable managing arthritis, and patients with OA often do not seek care within the healthcare system. The lack of engagement with medical care for OA has yet to be quantified.

Methods: Using data from the Osteoarthritis Initiative (OAI), a cohort recruited originally to facilitate the identification of biomarkers for knee OA, we evaluated engagement of arthritis care at the baseline visit of the study. Participants were recruited into the study if they were healthy controls, were at risk for symptomatic radiographic knee OA (SOA), or already had SOA. At the baseline visit, participants had PA knee radiographs scored for Kellgren and Lawrence (KL) grade (0-4) and were asked whether they had frequent knee pain in each knee. Study staff measured each participant's weight and height and asked about their gender, race, and age. They were also asked, "Are you currently seeing a doctor or other health care professional for arthritis?" that allowed for a dichotomous response of yes or no. We performed frequency evaluations for this question for the whole cohort, then cross-tabulated based on maximal KL grade (those with a prosthetic were grouped separately). We also performed a cross-tabulation with the number of knees with frequent knee pain and chi-squared test to evaluate significant differences between groups.

Results: Of the 4796 participants within the OAI cohort, the mean age was 61.5 (9.2) years, the mean BMI was 28.6 (4.8) kg/m^2, and 58% were female. 57% had at least one knee with radiographic OA (KL$\geq$2). 58 had an arthroplasty in one knee. In this cohort, only 12% answered that they currently see a doctor or other health care professional for arthritis. Females, those with a prior diagnosis of OA, greater BMI, greater KL grade, more knee pain, and SOA were more likely to seek care for their arthritis. Those with insurance and lower income were more likely to seek care for OA.

Conclusion: In a cohort recruited to study knee OA, 56% of whom had radiographic evidence of knee OA in at least one knee, only 12% were currently seeking care for their arthritis. Those with greater disease severity, symptoms, and SOA were more likely to seek care, but even among those groups, participation was low. Interestingly, those with a lower income were more likely to seek care for knee OA. These findings confirm a substantial gap in the provision of care for knee OA using traditional healthcare systems and provide important impetus for identifying novel strategies for management of OA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Percentage of Participants in Difference

Table 1. Percentage of Participants in Difference		
	Seek Care for Arthritis	Chi-squared p-value
All participants	12%	
Female (58%)	14%	p<0.0001
Male (42%)	9%	
Age		
<50 (12%)	9%	p=0.03
50 – 59 (36%)	11%	
60 – 69 (32%)	13%	
>70 (21%)	19%	
BMI		
low (<20) (9%)	9%	p=0.001
Normal (20-24) (23%)	10%	
Overweight (25-29) (33%)	11%	
Obese (>30) (36%)	14%	
Race		
White (79%)	11%	p=0.004
Black (18%)	15%	
Other (3%)	13%	
Max KL Grade		
0 (28%)	7%	p<0.0001
1 (15%)	10%	
2 (29%)	11%	
3 (20%)	16%	
4 (7%)	29%	
Arthroplasty (1%)	38%	
Number of knees with frequent knee pain		
0 (51%)	7%	p<0.0001
1 (26%)	16%	
2 (22%)	17%	
Symptomatic KOA		
No (72%)	9%	p<0.0001
Yes (28%)	20%	
Ever been given a diagnosis of degenerative knee arthritis?		
No (76%)	7%	p<0.0001
Yes (24%)	27%	
Income		
<$10K (4%)	24%	p<0.0001
$10K to < $25K (10%)	12%	
$25K to < $50K (26%)	13%	
$50K to < $100K (36%)	11%	
$100K or greater (24%)	10%	
Have Medical Insurance		
No (12%)	9%	p=0.04
Yes (88%)	12%	
Clinic Site		
A (16%)	13%	p<0.0001
B (21%)	10%	
C (27%)	13%	
D (24%)	9%	
E (11%)	26%	

Disclosure: G. Lo: None; **S. Yan**: None; **J. Patarini**: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **C. Eaton**: None; **J. Driban**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0314

What changes in quality of life can be observed in patients with knee or hip OA prior to total hip or total knee replacement surgery ? data from the KHOALA cohort

Anne-Christine Rat[1], LATOURTE Augustin[2], Maud Wieczorek[3], Jérémie sellam[4], willy Ngueyon Sime[5], Jacques Pouchot[6], Christian Roux[7], Alain SARAUX[8], Francis Guillemin[9] and Joel Coste[10], [1]Caen University hospital, UMR 1075 Caen normandy university, Caen, France, [2]Rheumatology Department, Lariboisiere Hospital, Paris, France, [3]Lausanne Univserty, Lausanne, Switzerland, [4]Saint-Antoine hospital, Assistance Publique – Hôpitaux de Paris, Paris, France, Sorbonne University, Paris, France, [5]CIC, Epidémiologie Clinique, CHRU-Nancy, Inserm, Université de Lorraine, Nancy, France, nNancy, France, [6]HEGP hospital, Assistance Publique-Hopitaux de Paris, Paris, France, [7]CHU Nice, Nice, France, [8]CHU Brest, Brest, France, [9]CHU Nancy, Nancy, France, [10], Assistance Publique – Hôpitaux de Paris, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

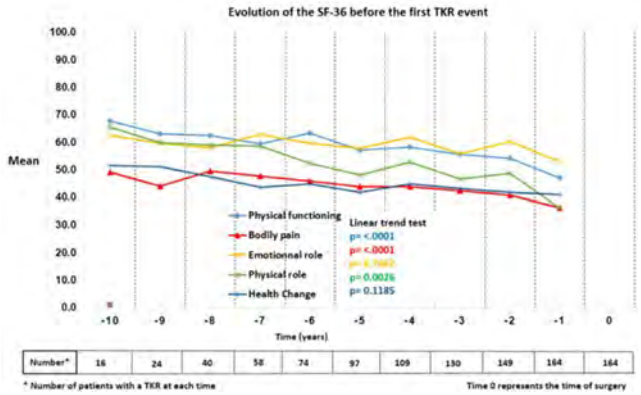
Background/Purpose: Few studies have examined how the quality of life (QoL) evolves in patients with osteoarthritis (OA) before undergoing total hip or total knee replacement surgery (THR/TKR). Although quality of life (QoL) appears to be stable in OA cohorts, patients undergo THR or TKR. This raises the question of whether it is deterioration in QoL that motivates intervention, and which specific dimensions deteriorate and lead to intervention.

The aim of the study was to analyze changes in various dimensions of QoL (especially pain, functional capacity, mental status, and social functioning) prior to THR/TKR in patients with symptomatic hip and/or knee OA.

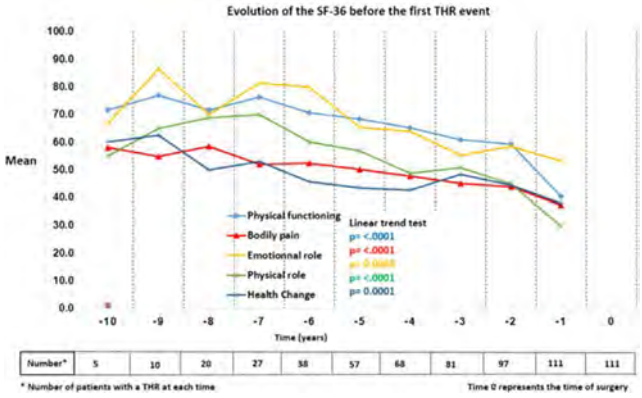
Methods: The Knee and Hip OsteoArthritis Long-term Assessment (KHOALA) cohort is a French multicenter, population-based cohort of 878 patients with symptomatic hip or knee OA. Patients were followed annually for up to 10 years using self-administered questionnaires. QOL was assessed using the SF36.

The evolution of QoL before the first THR/TKR is described by the mean (standard deviation) up to 10 years before surgery.

Results: Of the 878 patients in the cohort, 164 (18.7%) underwent TKR and 111 (12.6%) underwent THR over the 10-year follow-up: 196 (71.3%) were female, mean (SD) age 62.8 (7.5) years, mean body mass index 29.8 (6.0). 83 patients had more than one THR or TKR during follow-up.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



The evolution of SF-36 before the first incident THR and TKR are shown in the 2 graphs (Figure).

Prior to TKR for knee OA, deterioration in QoL was statistically significant over the entire period for physical function, bodily pain and physical role. Prior to THR for hip OA, deterioration in QoL was statistically significant over the entire period for physical function, bodily pain, physical role, and also emotional role and health change.

Changes in QoL differ from one dimension to another: rather stable trajectories until accelerated deterioration in QoL for physical function, physical pain and physical role dimensions, 2 years before TKR. Slow deterioration in the different dimensions of QoL before THR, with a sharp acceleration in the deterioration of QoL two years before surgery for the dimensions of physical function, bodily pain, physical role, emotional role, and change in health. Deterioration was greater for physical function and physical role than for pain.

Mental health, vitality, and social functioning were not found to change over time.

Conclusion: In the KHOALA cohort, impairment of physical function, pain, and physical or emotional role were well observed prior to surgery.

For hip OA, these impairments occurred progressively during several years with a sharp acceleration 2 years prior to surgery in particular for physical functional and role dimensions. For knee OA, trajectories are pretty stable up to 2 years prior to surgery.

Deterioration in QoL appears to be more gradual for THR than TKR and greater in the two years prior to surgery, particularly for functional abilities dimensions.

Disclosure: A. Rat: AbbVie/Abbott, 6, Eli Lilly, 6, Galapagos, 6, Merck/MSD, 6; **L. Augustin**: None; **M. Wieczorek**: None; **J. sellam**: None; **w. Ngueyon Sime**: None; **J. Pouchot**: None; **C. Roux**: None; **A. SARAUX**: Novartis, 6; **F. Guillemin**: None; **J. Coste**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0315

Cross-sectional analysis of association between erosive hand osteoarthritis and cardiovascular disease.

Avanika Mahajan[1], Caroyln Harvey[2], Andy Abril[3] and Megan Sullivan[4], [1]Mayo Clinic, Scottsdale, [2]Mayo Clinic, Phoenix, AZ, [3]Mayo Clinic Florida, Jacksonville, [4]Mayo Clinic Arizona, Scottsdale, AZ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Erosive hand osteoarthritis (EHOA) is an inflammatory subtype of hand OA that causes subchondral bone erosion and cortical destruction, often resulting in debilitating symptoms. The association between inflammation,

Table 1: Baseline patient characteristics with Descriptive stats and univariate comparison (case vs control). Case=EOA patient, Control=non-EOA patient.

Covariate	Control (N=636)	Case (N=212)	Total (N=848)	P-value
Age				0.9301
Missing	0	0	0	
Mean (SD)	72.5 (8.49)	72.6 (8.66)	72.5 (8.53)	
Median (IQR)	73.0 (67.0, 78.0)	73.0 (67.0, 78.0)	73.0 (67.0, 78.0)	
Range	46.0, 102.0	46.0, 97.0	46.0, 102.0	
Age (at 07May2025)				0.9911
Missing	0	0	0	
Mean (SD)	74.4 (8.49)	74.4 (8.60)	74.4 (8.52)	
Median (IQR)	74.9 (68.7, 79.9)	74.8 (68.8, 79.9)	74.9 (68.8, 79.9)	
Range	48.0, 104.2	48.2, 99.0	48.0, 104.2	
BMI				0.5271
Missing	10	4	14	
Mean (SD)	25.4 (8.31)	25.9 (8.31)	25.5 (8.31)	
Median (IQR)	25.8 (22.6, 29.3)	26.1 (23.4, 30.0)	26.0 (22.8, 29.5)	
Range	0.0, 49.4	0.0, 53.7	0.0, 53.7	
Ethnicity, n (%)				0.5642
Hispanic or Latino	26 (4.1%)	6 (2.8%)	32 (3.8%)	
Not Hispanic or Latino	604 (95.0%)	205 (96.7%)	809 (95.4%)	
Unknown	6 (0.9%)	1 (0.5%)	7 (0.8%)	
Race, n (%)				0.8323
Asian	9 (1.4%)	3 (1.4%)	12 (1.4%)	
Black/African	6 (0.9%)	2 (0.9%)	8 (0.9%)	
Other/Unknown	5 (0.8%)	3 (1.4%)	8 (0.9%)	
White	616 (96.9%)	204 (96.2%)	820 (96.7%)	
Sex, n (%)				>0.9992
Female	525 (82.5%)	175 (82.5%)	700 (82.5%)	
Male	111 (17.5%)	37 (17.5%)	148 (17.5%)	
Estrogen use, n (%)	63 (9.9%)	24 (11.3%)	87 (10.3%)	0.5562
Smoking history, n (%)	225 (35.4%)	70 (33.0%)	295 (34.8%)	0.5322
Statin use, n (%)	423 (66.5%)	144 (67.9%)	567 (66.9%)	0.7052
Diabetes, n (%)	83 (13.1%)	38 (17.9%)	121 (14.3%)	0.0792
Any CV dx, n (%)	422 (66.4%)	161 (75.9%)	583 (68.8%)	0.0092
Arterial Disease, n (%)	305 (48.0%)	129 (60.8%)	434 (51.2%)	0.0012
Atherosclerosis, n (%)	88 (13.8%)	59 (27.8%)	147 (17.3%)	<.0012
Cerebral Infarction, n (%)	25 (3.9%)	14 (6.6%)	39 (4.6%)	0.1082
Ischemic Heart Disease, n (%)	178 (28.0%)	69 (32.5%)	247 (29.1%)	0.2062
HTN, n (%)	179 (28.1%)	83 (39.2%)	262 (30.9%)	0.0032
MI, n (%)	25 (3.9%)	10 (4.7%)	35 (4.1%)	0.6182

[1]Equal variance two sample t-test; [2]Chi-Square p-value; [3]Fisher Exact p-value;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Univariate and multivariable logistic regression modeling (adjusted for BMI, smoking history, statin use, diabetes). Odds ratios and 95% CIs for the case/control status variable listed. Each outcome is modeled separately. N=848 for each univariate model. N=834 for each multivariable model (14 pts are missing BMI and excluded from multivariable analysis).

Outcome	Unadjusted OR (95% CI)	p-value	Adjusted OR* (95% CI)	p-value
Any CVD	1.60 (1.12-2.28)	0.009	1.65 (1.14-2.41)	0.009
Arterial Disease	1.69 (1.23-2.32)	0.001	1.71 (1.24-2.37)	0.001
Atherosclerosis	2.40 (1.65-3.50)	<.001	2.44 (1.65-3.60)	<.001
Cerebral Infarction	1.73 (0.88-3.39)	0.111	1.66 (0.84-3.28)	0.146
Ischemic Heart Disease	1.24 (0.89-1.74)	0.206	1.25 (0.87-1.78)	0.227
HTN	1.64 (1.19-2.27)	0.003	1.63 (1.16-2.29)	0.005
MI	1.21 (0.57-2.56)	0.619	1.10 (0.51-2.38)	0.811

dysregulated immunity and cardiovascular event (CVE) risk is well established[1]. Specifically, several previous studies have found an increased risk of CVE in patients with rheumatoid arthritis (RA)[2]. Given the common denominator of inflammation in RA and EHOA, we hypothesized that EHOA is associated with increased CVE risk.

Methods: Patients with EHOA were identified from the electronic medical record by ICD code or by utilizing radiograph reports containing the term "erosive osteoarthritis". Radiographs were reviewed to confirm the characteristic changes of EHOA, namely central erosions and joint space narrowing within the distal and middle interphalangeal joints. Patients with autoimmune arthritis were excluded. Age and gender matched controls were identified in a 1:3 ratio. Study variables included BMI, smoking history, Type II diabetes and statin use. The primary outcome was any cardiovascular disease, while secondary outcomes were myocardial infarction (MI), hypertension (HTN), arterial disease, atherosclerosis, ischemic heart disease or cerebral infarction that were identified using ICD-9 and ICD-10 codes. EHOA and control groups were univariately compared using equal variance two-sample t-tests for continuous variables and Chi-square tests for categorical variables. Differences between cases and controls was estimated using logistic regression modeling adjusted for BMI and smoking history.

Results: We observed a positive association between EHOA and history of 1) any CVE, 2) arterial disease, 3) atherosclerosis, and 4) HTN. The adjusted odds ratio (OR) calculated using multivariate regression analysis was 1.65 (95% CI: (1.15-2.38); p-value 0.007) for overall prevalence of CVE, 1.71 ((95% CI: 1.24-2.37); p-value 0.001) for arterial disease, 2.51 ((95% CI: 1.70-3.69); p-value< 0.001) for atherosclerosis and 1.68 ((95% CI: 1.21-2.34); p-value 0.002) for HTN . The OR was similar without adjusting for covariates.

Conclusion: Our study shows that patients with EHOA have a higher prevalence of any CVE compared with age and gender matched controls with and without adjustment for potential confounders. Within CVEs, it shows higher prevalence of arterial disease, atherosclerosis and HTN. Our findings are in agreement with prior studies performed with RA patients, thus reinforcing the link between inflammation and increased cardiovascular link. Further studies are warranted to explore this association between EHOA and cardiovascular disease.

Disclosure: A. Mahajan: None; **C. Harvey**: None; **A. Abril**: None; **M. Sullivan**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0316

Increased Synovial Inflammation, Xist Escape Gene Expression and Knee Pain in Females with Osteoarthritis

Bella Mehta[1], Miguel Otero[2], Michael Mazzucco[3], Jenelys Ruiz-Ortega[4], Caryn Hale[4], Fuadur Omi[4], Syed Henah Balkhi[5], Purva Singh[3], Samantha Lessard[3], Wei Wang[4], Maryam Aslam[4], Tristan Maerz[6], Peter Sculco[3], Anne-Marie Malfait[7], Xiaoshun Li[8], Yiyuan Wu[9], Shady Younis[10], William Robinson[11], Daniel Ramirez[12], Edward DiCarlo[12] and Dana Orange[5], [1]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ, [2]Hospital For Special Surgery, New York, [3]Hospital For Special Surgery, New York, NY, [4]The Rockefeller University, New York, [5]The Rockefeller University, New York, NY, [6]University of Michigan, Ann Arbor, MI, [7]Rush University Medical Center, Chicago, [8]Hospital For Special Surgery, Ridgewood, NY, [9]Weill Cornell Medicine, New York, NY, [10]Stanford University, Stanford, CA, [11]Stanford University, Palo Alto, CA, [12]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1: Clinical OA characteristics according to sex

Characteristic	Total N (%) = 135	Female, N = 82	Male, N = 53	p-value
Age (IQR)	66 (61, 70)	67 (61, 71)	65 (61, 69)	0.2
BMI (IQR)	30 (27, 34)	31 (27, 35)	29 (27, 32)	0.6
Race				0.2
White	109 (81)	62 (76)	47 (89)	
Black or African American	13 (9.6)	10 (12)	3 (5.7)	
Other	13 (9.6)	10 (12)	3 (5.7)	
Duration of Diagnosis in years (IQR)	8 (3, 15)	8 (4, 15)	7 (3, 13)	0.3
Duration of Symptoms in years (IQR)	11 (6, 20)	11 (5, 19)	11 (6, 21)	0.5
Duration of Pain in years (IQR)	8 (5, 16)	8 (4, 15)	9 (5, 20)	0.4
CRP (Median IQR)	1.50 (0.78, 3.43)	1.70 (0.90, 4.10)	1.20 (0.70, 1.90)	0.015
Elevated ESR**	37 (30)	33 (43)	4 (8.9)	<0.001
ESR (Median IQR)	14 (8, 24)	16 (8, 29)	8 (5, 16)	<0.001
Kellgren and Lawrence Grade				0.5
1-2	19 (14)	13 (16)	6 (12)	
3-4	115 (86)	69 (84)	46 (88)	
Macroscopically most eroded location				0.3
Lateral	33 (24)	22 (27)	11 (21)	
Medial	86 (64)	48 (59)	38 (72)	
Other – tricompartmental / patellofemoral etc	16 (12)	12 (15)	4 (8)	
ICOAP Constant Pain Subscale (IQR)	40 (15, 55)	50 (21, 60)	30 (10, 45)	0.016
ICOAP Intermittent pain subscale (IQR)	50 (33, 58)	54 (42, 63)	42 (21, 54)	<0.001
ICOAP Total pain score (IQR)	45 (25, 57)	50 (36, 61)	36 (20, 48)	<0.001
KOOS pain score (IQR)	53 (43, 67)	49 (42, 60)	56 (47, 72)	0.010
VAS pain score (IQR)	6.00 (4.75, 7.00)	6.50 (5.00, 7.38)	5.00 (3.50, 7.00)	0.004
PROMIS Pain Intensity Score (IQR)	10.00 (8.00, 11.00)	10.50 (9.00, 11.00)	9.00 (8.00, 10.00)	0.002
Have you ever been diagnosed with gout?	10 (9.8)	5 (7.9)	5 (13)	0.5

All group comparisons were made using the Pearson's Chi-squared test or Fisher's exact test as appropriate. Differences between medians and distributions were made using the Wilcoxon rank sum test. IQR: interquartile range.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: MRI evidence of synovitis and bone marrow lesions, but not cartilage degeneration associate with pain in osteoarthritis (OA). In this work, we integrated clinical, histological, and transcriptomic analyses of synovial tissue from patients with knee OA to explore correlations of OA pain and sex related pain differences.

Methods: We enrolled 135 patients undergoing total knee arthroplasty who met 1986 ACR classification criteria for knee OA. Demographic, clinical data, patient-reported pain outcomes, and Osteoarthritis Research Society International (OARSI) cartilage scores and synovial histology features measured by board-certified pathologists were collected and analyzed (Table 1). Cell density and cell aggregate number and size were quantified using a previously established computer vision pipeline. Bulk RNA-seq was performed on RNAlater-preserved synovial tissues, using a KAPA-Stranded RNAseqKit with RiboErase for library preparation, and sequenced on a NovaSeq with 150 base pair paired-end reads targeting 100M

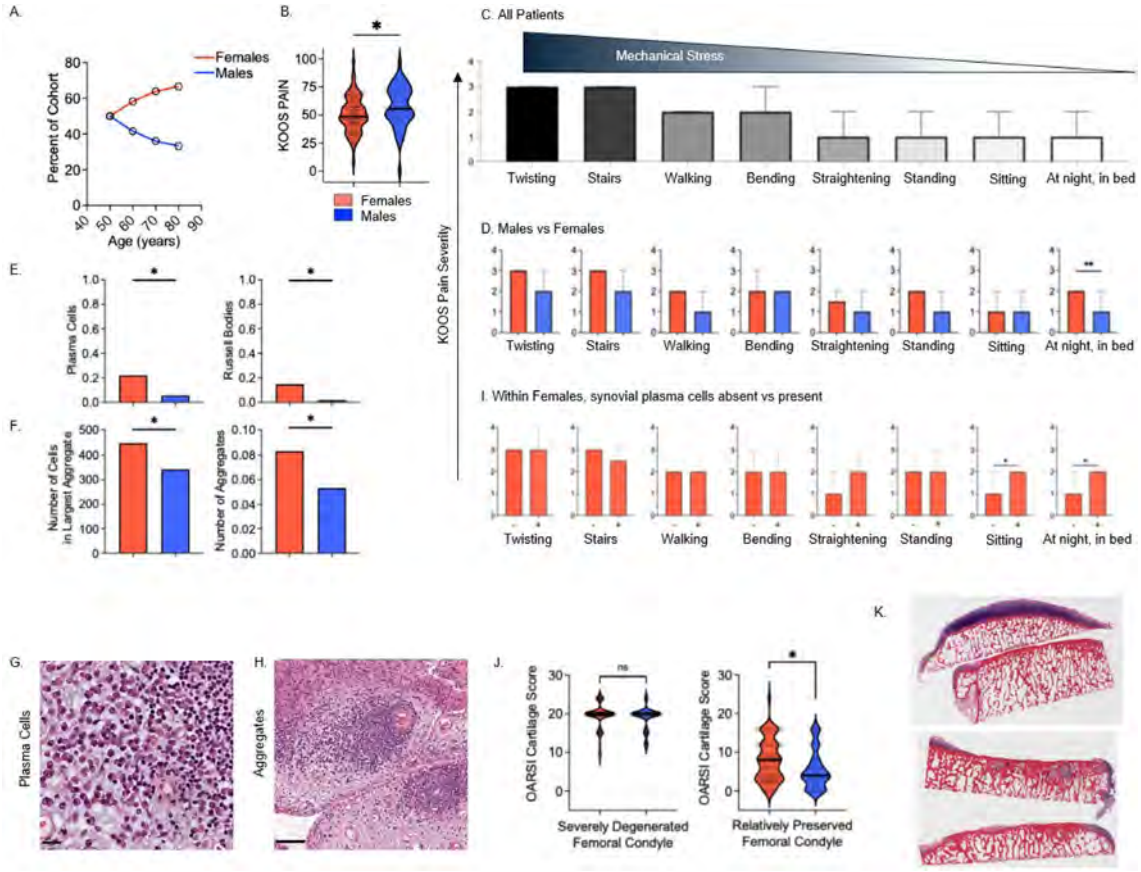


Figure 1: Percentage age distribution across different age groups. Figure B: Sex differences in knee pain as measured by the KOOS pain subscale. Females reported significantly worse knee pain compared to males mean KOOS pain score. Figure C: KOOS pain scores reported by all patients for specific activities. Pain was highest during activities involving greater mechanical stress on the knee and progressively decreased during lower-stress activities such as sitting or lying down. A mechanical stress gradient is illustrated above, highlighting the inverse relationship between stress level and pain intensity. Figure D: KOOS pain scores reported by females and males across different activities. While no significant sex differences were found in most categories, females reported significantly greater pain "at night, in bed" compared to males. Figure E: The proportion of plasma cells (left) and Russell bodies (right) in synovial tissue from females and males. Females exhibited significantly higher levels of both plasma cells and Russell bodies compared to males. Figure F: The number of cells in the largest synovial cell aggregate (left) and the number of aggregates per tissue area (right) in females and males. Females exhibited significantly larger and more numerous synovial aggregates compared to males. Figure G: High-magnification image of Hematoxylin and eosin (H&E) stain synovial tissue with plasma cell infiltrates. Figure H: Low-magnification image of Hematoxylin and eosin (H&E) stain synovial tissue with aggregates within the synovium. Figure I: KOOS pain scores for individual activities in female patients with and without synovial plasma cell infiltration. Pain during low mechanical stress activities of sitting and at night in bed was significantly higher in females with plasma cells present in their synovial tissue. Figure J: OARSI cartilage scores for male and female patients in both severely degenerated (left) and relatively preserved (right) femoral condyles. No significant differences were observed in the severely degenerated regions, females exhibited significantly higher cartilage damage in the relatively preserved condyles compared to males. Figure K: Representative low-magnification images of Hematoxylin and eosin (H&E) stained cartilage of males (top) and females (bottom) described in Figure J

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

reads per sample. Reads were pseudoaligned to Hg38 with Kallisto, and Limma was used to test for differentially expressed genes (DEGs). Gene set enrichment analysis (GSEA) was used to test for enrichment in GO pathways.

Results: Kellgren Lawrence (KL) grades, BMI, and symptom duration were similar between sexes. Females had higher Erythrocyte Sedimentation Rate (ESR) and reported worse Knee Injury and Osteoarthritis Outcome Score (KOOS) pain scores (p=0.01), particularly rest pain (at night, while in bed) (p=0.02) (Table 1). Rest pain was less common than mechanical pain (e.g., with twisting or stair use) but, when present, it correlated with higher total KOOS pain scores. Synovial histology revealed increased plasma cells, binucleate plasma cells, Russell bodies, and size and number of cellular aggregates in females. Females with synovial plasma cells reported increased rest pain. OARSI cartilage scores were similar in the most severely eroded femoral condyles between sexes, but females had significantly higher scores in the less eroded condyles (Figure 1). RNA-seq revealed 25 DEGs between sexes, and a pronounced enrichment in Xist escape genes in females. GSEA identified 132 pathways significantly enriched in females, including "adaptive immune response" and "complement activation". Among females, genes associated with inflammation, fibrosis, and neurogenesis pathways were positively

Figure 2A

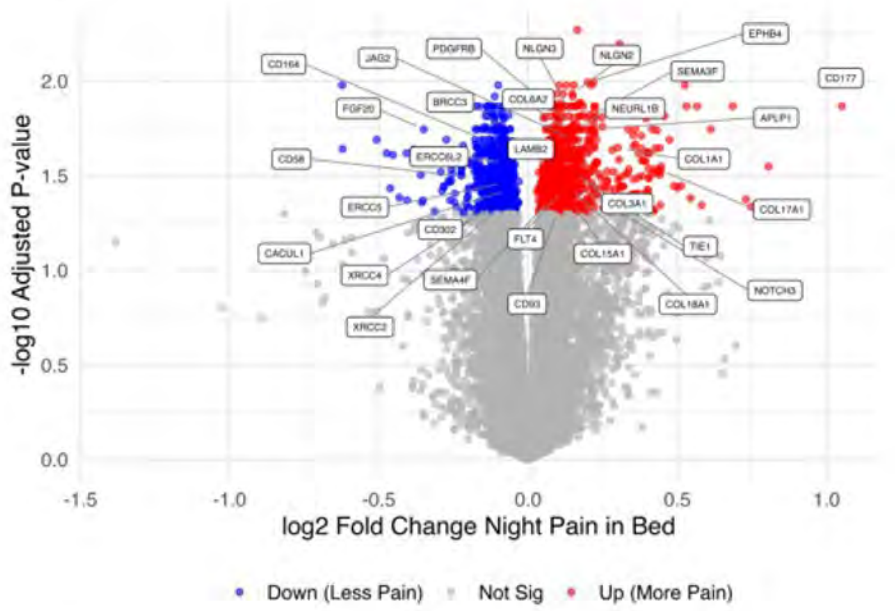


Figure 2B

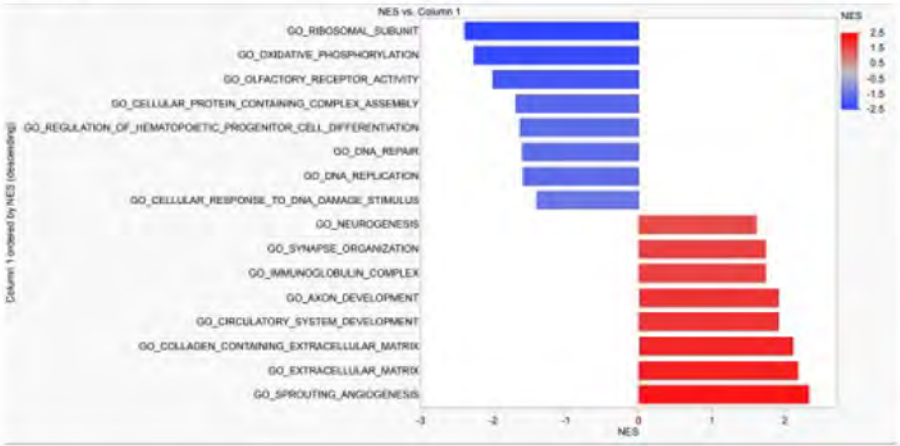


Figure 2A. Volcano plot of differential gene expression of rest pain (night pain in bed). Figure 2B. Gene Set Enrichment Analysis (GSEA) displaying pathway associated with rest pain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

associated with rest pain, while genes associated with DNA damage response and progenitor cells were negatively associated with rest pain. There were no genes associated with rest pain in males.

Conclusion: Compared to males, females have significantly increased systemic and synovial tissue inflammation, along with increased multicompartmental cartilage degeneration. Among females, rest pain is positively associated with synovial inflammation, fibrosis, and neurogenesis pathway gene expression and negatively associated with DNA damage response and progenitor cell gene expression. This analysis provides insights into the molecular underpinnings of the clinical observation that MRI evidence of synovitis is associated with pain in knee OA.

Disclosure: B. Mehta: Amgen, 1, Horizon, 1; **M. Otero**: Jannu Therapeutic, 1; **M. Mazzucco**: None; **J. Ruiz-Ortega**: None; **C. Hale**: None; **F. Omi**: None; **S. Balkhi**: None; **P. Singh**: None; **S. Lessard**: None; **W. Wang**: None; **M. Aslam**: None; **T. Maerz**: None; **P. Sculco**: BetterPT, 8, Enovis, 2, 9, HS2, LLC, 8, HSS ASC Development Network, LLC, 8, Intellijoint Surgical, Inc, 8, Joint Effort Administrative Services Organization, 8, Osgenic, 1, 8, Parvizi Surgical Innovation, LLC, 8, Zimmer Biomet, 2, 5, 9; **A. Malfait**: Asahi Kasei Pharma Corporation, 23andMe, Orion, 2; **X. Li**: None; **Y. Wu**: None; **S. Younis**: None; **W. Robinson**: None; **D. Ramirez**: None; **E. DiCarlo**: None; **D. Orange**: AstraZeneca, 2, Pfizer, 2.

Abstract Number: 0317

"No Matter How Great My Doctor Is, He Hasn't Had a Knee Replacement, He Doesn't Understand All That Pain" Program Evaluation of the *Moving Well* Peer Coach Intervention for Total Knee Replacement

Cara Murphy[1], Sarah Young[2], Vanessa Madrigal[3], Noelia Hernandez[4], Daniel Garcia[5], Yuliana Dominguez Paez[6], Monika Safford[3], Iris Navarro-Millan[7] and Mackenzie Brown[8], [1]HSS, New York, NY, [2]Weill Cornell Medicine, Johnson City, NY, [3]Weill Cornell Medicine, New York, [4]Weill Cornell Medicine, New York, NY, [5]Weill Cornell, Brooklyn, NY, [6]Albert Einstein College of Medicine, The Bronx, NY, [7]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY, [8]Weill Cornell Medicine, Brooklyn, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: *Moving Well* was a pre-habilitation peer coach intervention aimed at reducing levels of anxiety, depression, and pain among individuals undergoing total knee replacement (TKR)[1]. A peer coach was a person who had knee osteoarthritis and TKR who was trained[2] to guide another person in the preparation and recovery from TKR. The goal of this study was to evaluate the experience of the participants in both *Moving Well* and its attention control arm *Staying Well* to refine the interventions in preparation for a fully powered trial.

Methods: We conducted semi-structured interviews of participants in *Moving Well* and *Staying Well*. Interviews were offered regardless of completion of the intervention. The topic guide focused on barriers and facilitators to completing the intervention, the experience with the curriculum, logistics of the program, and the experience of working with a peer coach (*Moving Well*) or healthy coach (*Staying Well*). Data were analyzed thematically with two coders (CM and SRY) using NVivo software.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Ninety-two participants completed the trial (52 in *Moving Well* and 40 in *Staying Well*). Eighteen participants completed the evaluation interviews (10 from *Moving Well* and 8 from *Staying Well*). Table 1 includes their demographic information. Five themes emerged (Table 2). These were: 1) *The peer coach was a highly valued aspect of the intervention* (Tables 2 and 3 with sub-themes); 2) *Participants value the breathing exercises, mindfulness, and exercise program but have mixed feelings about the mood component and principles of cognitive behavioral therapy*; 3) *The Staying Well curriculum had mixed reviews, while there was strong appreciation for the paired healthy coach as a guide*; 4) *Perceived facilitators to completing the interventions included being motivated, being structured, and wishing for a good surgical outcome*; 5)*Time constraints and comorbidities were the perceived barriers to engage or complete either intervention*. The *Moving Well* peer coach was influential for participants due to their shared experience and their ability to act as a motivator and allow for vulnerability. The curricular components combined with the peer coaches were tools to empower participants to exercise.

Table 1: Demographic data of participants

Characteristic	Moving Well Arm (N = 10)	Staying Well Arm (N = 8)
Age, Mean (SD)	66.5 (5.64)	70 (8.18)
Sex, n		
Female	7	6
Male	2	2
Prefer not to say	1	0
Race/Ethnicity, n		
Black or African American	2	3
Hispanic/Latino	1	1
Asian/Pacific Islander	0	0
Native American or Alaskan Native	0	0
White	5	4
Prefer not to say	1	0
Other	1	0
Education, n		
High School	0	0
Some College	0	0
Associate's Degree	0	2
Bachelor's Degree	3	2
Advanced Degree (doctorate, masters)	7	3
Other	0	1
Insurance, n		
Public	3	5
Private	7	3
Income, n		
Less than $24,000	0	0
$25,000-$50,000	2	3
$51,000 - $100,000	2	1
Greater than $100,000	6	4
Work Status, n		
Unemployed	0	0
Disabled	0	1
Working, Full Time	6	3
Working, Part Time	1	0
Retired	3	4

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Themes that Emerged from Interview Evaluations of Participants of *Moving Well* and the Attention Control Arm *Staying Well*

The peer coach was a highly valued aspect of the intervention (See Table 3 for sub-themes)	"What I found helpful was that someone who had done it and did it for similar reasons to me and was now doing what I wanted to be able to do." "I think the coach was really the most vital element of it all... compassion, understanding, and personalization in the whole approach to preparing for recovery"
Participants value the breathing exercises, mindfulness, and exercise program, but have mixed feelings about the mood component and principles of cognitive behavioral therapy	"And then I sit there, and it used to be that you pushed and then took that pain away by going back to a regular position, but now I just breathe into it, and it's interesting. I relax and I breathe into the pain and relax my body and then you can push farther" "But those things really reinforced me to just work on, what we call prehab, a little bit harder and do a little bit more and that gave me a tremendous edge over other friends of mine that had their surgery done by different physicians at different hospitals." "I didn't spend a lot of time doing it because I really couldn't analyze how my mood affected my pain. I could only analyze how my pain affected my mood." "And then working on replacing my fears with better ideas...And so it was the whole idea of identifying the problem and then coming up with a better way of 1. How to handle it so I wasn't freaking myself out and then 2. To focus on what was better for what was going to happen in the future. And I thought this really worked and it really helped."
The *Staying Well* curriculum had mixed reviews, while there was a strong appreciation for the paired healthy coach as a guide.	"It should be like a curriculum of life" "What the Staying Well program really needs is an exercise component for sure. Because to be honest, I didn't get anything out of the eating part." "Oh yeah, I wouldn't have done it if it wasn't for her (the coach) haha" "...the human touch, the human part of it, of both interacting with somebody, a live person, I think is very important."
Perceived facilitators to completing the *Staying Well* or *Moving Well* intervention included being motivated, being structured, and wishing for a good surgical outcome	"I wanted to be successful and preparing for my surgery. I really wanted to be prepared as possible, and I wanted to have the best outcome. So that was my total objective." "I have a grandbaby, and I said I really need this knee replacement because I don't want to be in a wheelchair, while he's running around saying, come on, grandma."
Time constraints and comorbidities were the perceived barriers to engage or complete either intervention	"Just keep in mind that if somebody is working full time, you don't always have the time to read and answer all the questions like the assignments" "The only problem I ran into was time constraints in my own life"

While the *Staying Well* (control arm), was not intended to have an exercise program, the fact that individuals were eager to engage in exercising supports that the focus of *Moving Well* aligns with the needs of this population.

Conclusion: Peer coaching for preparation and rehabilitation from TKR was a highly valued aspect of *Moving Well* because of the role modeling, motivation, vulnerability, and shared experiences. The major barrier for completion was time constraints, which could be an area for improvement in the next iteration of *Moving Well*.

References:

1. Jabri A, et al. A single-center, open-label, randomized, parallel-group trial to pilot the effectiveness of a peer coach behavioral intervention versus an active control in reducing anxiety and depression in patients scheduled for total knee replacement. BMC Musc Disord. 2023 PMID: 37147587
2. Paez YD, et al. Training of Peer Coaches to Assist Individuals with Knee Osteoarthritis Prepare and Recover From Total Knee Replacement. ACR Open Rheum. 2024 PMID: 39254264

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Theme and Sub-themes on the Evaluation of the Peer Coach Experience within *Moving Well*

Theme:	Associated Quotes:
Having a shared experience was valuable from an empathy, motivation, and preparation standpoint	*"We talked about some of her ski trips, and it was both a connection and a recognition that I was going to get to where I wanted to go"* *"I thought the biggest benefit was having somebody who had been through it before and could tell me what to expect and answer the questions that I had"* *"I don't want to just read something in the abstract as opposed to talking to somebody who can relate to your own goals and progress"*
The peer coach served as a motivator to prepare the participant for a good surgical outcome	*"I think the coach does keep you accountable."* *"I think the combination of the two really makes the most out of the program because I think just the program alone, it would be OK, but it wouldn't be as valuable as having the coach to facilitate and ask questions and get feedback on how things are going."*
The peer coach allowed for vulnerability and human connection which impacted improved well-being	*"I've never gone to a psychologist or a psychiatrist, it was nice talking to someone. I think it was sort of that kind of experience."* *"I have friends, but you don't want to bore them with all your physical troubles. There's nothing more boring, try friends my age, everybody's got a series of maladies, and it's really boring. I didn't feel bad boring him. Not that he acted bored, but he was very sympathetic and understanding and it was good to have someone to talk to, in a way I couldn't do otherwise."*
Desire to continue contact with the peer coach	*"I got a little sad when she said, oh, this is the last time we're going to talk"* *"It was wonderful...I'm really sad that I can't ever talk to her. For, was it two or three years now? I don't know if she has this experience with everybody, but it was great, I felt like I had a whole new friend"* *"And so, I understand not being able to talk to her, but it's like I want to know how the chickens are doing, you know? So, it worked out really well for us, you know. Could you just let her know that I am going to have surgery on the other knee. I don't know when yet, but he will do my other knee, just, could you forward that information to her?"*

Disclosure: C. Murphy: None; **S. Young**: None; **V. Madrigal**: None; **N. Hernandez**: None; **D. Garcia**: None; **Y. Dominguez Paez**: None; **M. Safford**: MedExplain Health, 1; **I. Navarro-Millan**: None; **M. Brown**: None.

Abstract Number: 0318

Plasma Lipoprotein Subclasses and Risk of Incident Knee Osteoarthritis: A Population-Based Cohort Study

Cheng Li[1], Jing wu[2], Yuqing Zhang[3], Hongyi He[4], Ying Hu[5], Jie Wei[6], Guanghua Lei[6] and Chao Zeng[6], [1]Xiangya Hospital, Changsha, China (People's Republic), [2]Xiangya Hospital, chagnsha, Hunan, China (People's Republic), [3]Massachusetts General Hospital, Quincy, MA, [4]Xiangya Hospital Central South University, Changsha, China (People's Republic), [5]Xiangya School of Public Health Central South University, changsha, China (People's Republic), [6]Xiangya Hospital, Central South University, Changsha, Hunan, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Lipoprotein subclasses play diverse roles in health and disease. Although lipoproteins have been implicated in knee osteoarthritis (KOA), the relationship between lipoprotein subclasses and KOA remains unexplored.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

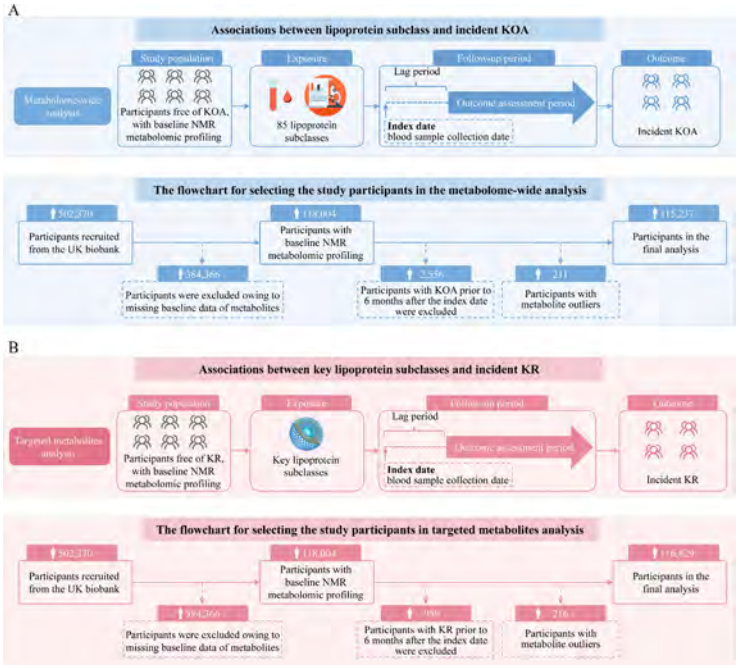


Figure 1: The schematic illustration of this study. (A) Part 1: Metabolome-wide analysis for the associations of 85 lipoprotein subclass and the risk of incident KOA; Part 2: Flowchart for the selection of the study population for metabolome-wide analysis. (B) Part 1: Targeted analysis for the associations of key lipoprotein subclass and the risk of incident KR; Part 2: Flowchart for the selection of the study population for targeted analysis. The date of blood sample collection was designated as the index date for each participant. Key lipoprotein subclasses were defined as those that showed consistent significant associations with KOA across both models in the metabolome-wide analysis. KOA, knee osteoarthritis; KR, knee replacement; NMR, nuclear magnetic resonance.

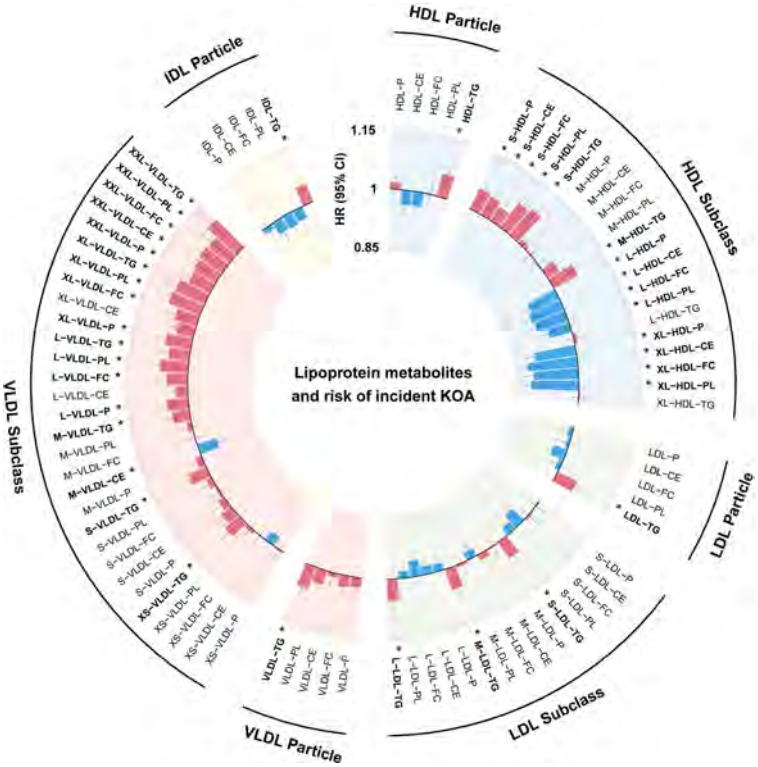


Figure 2: Associations of individual lipoprotein metabolites with risk of incident KOA. HRs (per SD) were adjusted for age, sex, Townsend Deprivation Index score, body mass index, drinking status, smoking status, fasting time, lipid-lowering medication, and history of knee joint injury. The red bars indicate HR>1, while the blue bars represent HR<1. The significant lipoprotein metabolites are highlighted in bold. *P<5.6×10-3 (0.05/9). KOA, knee osteoarthritis; HR, hazard ratios; SD, standard deviation; -CE, cholesteryl ester; -FC, free cholesterol; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; L-, large; LDL, low-density lipoprotein; M-, medium; -P, particle concentration; PL, phospholipids; S-, small; TG, triglycerides; VLDL, very-low-density lipoprotein; XL-, very-large; XS-, very-small; XXL-, extremely-large.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

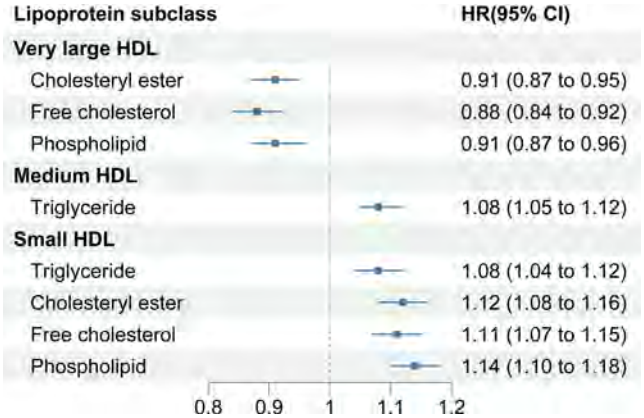


Figure 3: Associations of the key lipoprotein subclass with the risk of incident knee replacement. HRs (per SD) were adjusted for age, sex, Townsend Deprivation Index score, body mass index, drinking status, smoking status, fasting time, lipid-lowering medication, and history of knee joint injury. HR, hazard ratio; SD, standard deviation; CI, confidence interval; HDL, high-density lipoprotein.

Methods: We conducted a cohort study of 115,237 participants from the UK Biobank to examine the associations of 85 plasma lipoprotein subclasses, defined by combinations of density (high, low, intermediate, very-low), size (extremely-large, very-large, large, medium, small, very-small), and composition (triglyceride, free cholesterol, cholesteryl ester, phospholipid), with incident KOA in the metabolome-wide analysis (**Figure 1A**). Data were analyzed using Cox proportional hazards models, correcting for multiple tests (0.05/9). We conducted the analyses using two models. Model 1 adjusted for age, sex, Townsend Deprivation Index score, body mass index (BMI; as a categorical variable), drinking status, smoking status, fasting time, lipid-lowering medication, and history of knee joint injury. Model 2 included the same covariates as Model 1, except that BMI was adjusted as a continuous variable. We subsequently conducted targeted analyses to examine the association between the key lipoprotein subclasses, which consistently showed significant associations with KOA across both models, and knee replacement, as the outcome may reflect severe OA (**Figure 1B**).

Results: During a median follow-up period of 12.8 years, 6,782 incident cases of KOA were identified. A total of 38 lipoprotein subclasses were statistically significantly associated with incident KOA (**Figure 2**). Specifically, higher concentrations of very-large and large high-density lipoproteins (HDL), excluding triglyceride, were associated with a lower risk of incident KOA (hazard ratios [HRs] range 0.87-0.94). Conversely, higher concentrations of small HDL, irrespective of composition, were associated with a higher risk of incident KOA (HRs range 1.04-1.09). Extremely-large very-low-density lipoprotein (VLDL) across all compositions, very-large VLDL excluding cholesteryl ester, and large VLDL excluding cholesteryl ester showed positive associations with incident KOA (HRs range 1.05-1.10). Additionally, medium, small, and very-small VLDL, and intermediate-density lipoprotein, as well as large, medium and small low-density lipoprotein, combined with triglyceride, were consistently positively associated with incident KOA (HRs range 1.04-1.06). After adjusting for BMI as a continuous variable, differential effects among HDL subclasses remained evident, except for the association between large HDL and KOA. Conversely, the associations between other lipoprotein subclasses and KOA become non-statistically significant. Similar findings were observed for the associations between HDL subclasses and the risk of knee replacement in the targeted analysis (**Figure 3**).

Conclusion: We provided novel evidence of diverse associations between lipoprotein subclasses and incident KOA, indicating the distinct effects of HDL subclasses.

Disclosure: C. Li: None; **J. wu**: None; **Y. Zhang**: None; **H. He**: None; **Y. Hu**: None; **J. Wei**: None; **G. Lei**: None; **C. Zeng**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0319

Glucagon-like Peptide-1 Receptor Agonists in Management of Knee Osteoarthritis: A Meta-Analysis

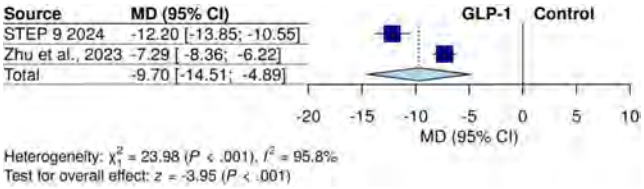
Danielle Madison[1], Adriana Morales Rivera[2], Dylon Collins[2], Isabel Lam[2], Daniel Khokhar[2], Garrett Snyder[2], Anthony Thompson[2], Mark Soliman[2], Daniela Carralero Somoza[2] and Michael Sabina[2], [1]Lakeland Regional Medical Center, Lakeland, FL, [2]Lakeland Regional Medical Center, Lakeland

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

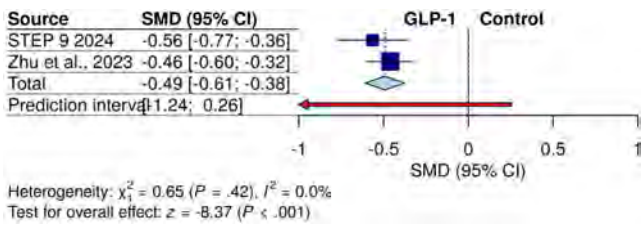
Background/Purpose: Knee osteoarthritis (KOA) is a leading cause of disability and the most common rheumatological condition worldwide. Weight management has been recognized as a key modifiable factor in disease progression and symptom burden. Glucagon-like peptide-1 receptor agonists (GLP-1RAs), primarily used for diabetes and weight loss, may offer additional benefits in KOA through weight reduction and improved joint function. We conducted a meta-analysis of GLP-1RAs versus control interventions in patients with KOA.

Methods: We included two studies — Semaglutide Treatment Effect in People with obesity (STEP) 9, a randomized controlled trial, and the Shanghai Osteoarthritis Cohort (SOC), a large observational cohort — reporting outcomes in body weight and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) domains. Both studies utilized GLP-1RAs as their experimental variable. Data was pooled using random-effects models and heterogeneity was assessed using the I^2 statistic.

Results: GLP-1RA therapy led to a pooled reduction in body weight of -9.70 kg (95% CI -14.51 to -4.89; I^2 = 95.8%). For the WOMAC pain score, the pooled mean difference (MD) was -0.49 points (95% CI -0.61 to -0.38; I^2 = 0.0%), reflecting improvement in symptoms. Physical function demonstrated a pooled standardized mean difference (SMD) of –1.29 (95% CI -3.79 to 1.21; I^2 = 99.6%). For the total WOMAC score, the pooled SMD was –0.30 (95% CI -0.77 to 0.17; I^2 = 92.9%), and for WOMAC stiffness, the pooled SMD was -0.23 (95% CI –0.64 to 0.18; I^2 = 90.9%). Despite variable heterogeneity, the direction of benefit consistently favored GLP-1RAs across all domains.



The aggregate mean difference between GLP-1RA use and control for body weight. Presented as a forest plot.



The aggregate mean difference between GLP-1RA use and control for reported pain on WOMAC index. Presented as a forest plot.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Graphic depicting the focus of the meta-analysis and its primary end-points.

Conclusion: GLP-1RAs appear to reduce pain in patients with knee osteoarthritis, likely through weight reduction. Changes in physical function and stiffness have been reported with varying significance and should be assessed more in-depth. While the magnitude of effect varied across primary end-points and studies, the consistent direction of benefit supports further investigation of GLP-1RAs as adjunctive therapy in KOA management.

Disclosure: D. Madison: None; **A. Morales Rivera**: None; **D. Collins**: None; **I. Lam**: None; **D. Khokhar**: None; **G. Snyder**: None; **A. Thompson**: None; **M. Soliman**: None; **D. Carralero Somoza**: None; **M. Sabina**: None.

Abstract Number: 0320

Transcriptomic profiling of the skeletal muscle of knee OA patients uncovers elevated glucocorticoid and GABA signaling as mediators of skeletal muscle dysfunction in advanced disease

Gina Many[1], Tyler Mansfield[2], Tyler Sagendorf[3], Daniel Evans[2], Sameneh Farsijani[4], Bret Goodpaster[5], Lauren Sparks[5] and NANCY LANE[6], [1]Pacific Northwest National Laboratory, Richland, WA, Richland, WA, [2]California Pacific Medical Research Institute, San Francisco, CA, [3]Pacific Northwest National Laboratory, Richland, WA, [4]University of Pittsburgh, Pittsburgh, PA, [5]Translational Research Institute, AventHealth, Orlando, FL, [6]University of California at Davis, School of Medicine, Sacramento, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Age-related declines in muscle mass and function are leading causes for hospitalizations and mortality in elderly individuals. The risk of developing knee osteoarthritis also increases with age and those affected display reductions in skeletal muscle mass, quality and function yet the mechanisms behind these changes are broadly unknown. Characterizing the transcriptional landscape of skeletal muscle from patients with knee OA to identify molecular targets of skeletal muscle dysfunction and then formulate a targeted treatment approach.

Methods: Study participants (n=528, 56% Female; mean age 76.6 ± 4.9 years) were enrolled in the Study of Muscle, Mobility and Aging (SOMMA), a longitudinal cohort study of subjects, >70 years of age, free of life-threatening diseases and mobile. Study subjects had obtained a muscle biopsy at the baseline study visit and knee radiographs at the year 1 follow-up visit. Radiographic OA (ROA) was determined by Kellgren and Lawrence scores (0-4), and knee pain was self-reported to be at least monthly in the right knee. RNA sequencing data were analyzed using DESeq2 to assess differential

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

gene expression, contrasting a control group (Kellgren-Lawrence (KL) score 0–1, n=322) with three nested "case" groups: (1) all KL ≥2 (n=206), (2) KL ≥2 with pain (n=114), and (3) KL ≥3 with pain (n=74). Covariates in the statistical models included sex, race/ethnicity, age, weight, waist circumference, abdominal adiposity from MRI, right anterior thigh fat free muscle volume, clinical site, batch, steps per day (using GGIR actigraph), and pain medications. Resulting pathway enrichment analysis was performed using CAMERA.

Results: DESeq2 revealed differential transcript expression across the three case-control contrasts, with 20, 10 and 22 differentially expressed genes for contrasts 1-3 respectively. Two genes, Mettl21c, a methyltransferase, and pseudogene Rpl29p11 displayed differential expression in all three contrasts. Pathway enrichment analysis revealed significant differences between the three contrasts, with gene expression regulatory terms and pathways related to ribosomes and translation being downregulated in groups 2&3. Group 3 also displayed unique enrichment of GABA secretion (z-score: 3.6, FDR=0.03) and glucocorticoid (GC) signaling (z-score: 3.4, FDR< 0.05).

Conclusion: Gene expression profiling of ROA skeletal muscle reveals differential molecular profiles based on KL grade and self-reported knee pain. Patients presenting with KL 3+ and pain displayed unique pathway enrichments indicative of transcriptional and translational repression, GC signaling and GABA secretion. Given adjustment for physical activity in statistical modeling, these findings suggests that elevated GC and GABA signaling may be potential mechanisms for skeletal muscle dysfunction and atrophy in advanced stage ROA.

Disclosure: G. Many: None; **T. Mansfield**: None; **T. Sagendorf**: None; **D. Evans**: None; **S. Farsijani**: None; **B. Goodpaster**: None; **L. Sparks**: None; **N. LANE**: ANI, 1.

Abstract Number: 0321

Per- and Polyfluoroalkyl Substances and Hand Osteoarthritis: Data from the Osteoarthritis Initiative

Jeffrey Driban[1], Lisa Rokoff[2], Bing Lu[3], Timothy McAlington[4], Charles Eaton[5], Mary Roberts[6], Diana Mathes[7], Colleen Lestician[7], Zhijin Carrie Xu[7], Zhihua Tina Fan[7], Shawn O'Leary[7] and Abby Fleisch[8], [1]University of Massachusetts Chan Medical School, Marlborough, NH, [2]Center for Interdisciplinary and Population Health Research, MaineHealth Institute for Research, Westbrook, ME, [3]UConn Health Center, Newton, MA, [4]UMass Chan School of Medicine, Arlington, MA, [5]Brown University, Pawtucket, RI, [6]Center for Primary Care and Prevention, Kent Hospital, Pawtucket, RI, [7]Environmental and Chemical Laboratory Services, Public Health & Environmental Laboratories, New Jersey Department of Health, Ewing, NJ, [8]Maine Medical Center; 2. Center for Interdisciplinary and Population Health Research, MaineHealth Institute for Research, Westbrook, ME

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The prevalence of hand osteoarthritis (OA) has doubled in the United States over the past half century – a finding that cannot be solely explained by increases in longevity, raising the possibility that environmental factors play a role. In cross-sectional studies, exposure to per- and polyfluoroalkyl substances (PFAS; "forever chemicals"), synthetically produced water-, grease-, or stain-resistant chemicals, has been associated with self-reported OA diagnosis. Given the ongoing use of PFAS and the scale of contamination, there is an urgent need for longitudinal studies to clarify the relationship between PFAS and specific phenotypes of OA (e.g., symptomatic hand OA) to inform public health policies and

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Associations [OR (95%CI)] of baseline serum PFAS concentration with symptomatic hand OA incidence among 1,729 participants without baseline hand osteoarthritis

	Unadjusted OR (95%CI)	Adjusted OR (95%CI)[a]
PFOS		
IQR (8.90 ng/mL)	1.01 (0.93, 1.09)	0.97 (0.89, 1.06)
Q1 (0.10 – 9.00 ng/mL)	Reference	Reference
Q2 (9.01 – 12.73 ng/mL)	0.98 (0.79, 1.21)	0.87 (0.69, 1.10)
Q3 (12.74 – 17.90 ng/mL)	1.08 (0.87, 1.34)	1.03 (0.82, 1.30)
Q4 (17.91 – 85.50 ng/mL)	0.92 (0.74, 1.14)	0.81 (0.64, 1.03)
PFOA		
IQR (3.01 ng/mL)	0.99 (0.92, 1.06)	0.95 (0.87, 1.02)
Q1 (0.33 – 3.87 ng/mL)	Reference	Reference
Q2 (3.88 – 5.18 ng/mL)	0.86 (0.69, 1.07)	0.80 (0.64, 1.01)
Q3 (5.19 – 6.88 ng/mL)	0.86 (0.69, 1.07)	**0.74 (0.59, 0.93)**
Q4 (6.89 – 66.30 ng/mL)	1.00 (0.81, 1.23)	0.88 (0.70, 1.11)
PFNA		
IQR (0.74 ng/mL)	1.03 (0.98, 1.09)	**1.07 (1.00, 1.13)**
Q1 (0.07 – 0.76 ng/mL)	Reference	Reference
Q2 (0.77 – 1.05 ng/mL)	1.18 (0.95, 1.46)	1.19 (0.95, 1.49)
Q3 (1.06 – 1.50 ng/mL)	1.00 (0.80, 1.24)	0.98 (0.78, 1.24)
Q4 (1.51 – 13.40 ng/mL)	1.08 (0.87, 1.34)	1.17 (0.92, 1.48)
PFHxS		
IQR (2.62 ng/mL)	0.99 (0.93, 1.04)	**0.94 (0.88, 1.00)**
Q1 (0.10 – 1.96 ng/mL)	Reference	Reference
Q2 (1.97 – 2.97 ng/mL)	1.09 (0.88, 1.36)	0.91 (0.72, 1.15)
Q3 (2.98 – 4.58 ng/mL)	1.11 (0.90, 1.38)	0.93 (0.74, 1.18)
Q4 (4.59 – 66.70 ng/mL)	1.04 (0.84, 1.29)	0.84 (0.66, 1.06)
MeFOSAA		
IQR (0.46 ng/mL)	1.03 (0.98, 1.08)	1.01 (0.96, 1.06)
Q1 (0.03 – 0.25 ng/mL)	Reference	Reference
Q2 (0.26 – 0.43 ng/mL)	1.13 (0.91, 1.41)	1.10 (0.87, 1.38)
Q3 (0.44 – 0.72 ng/mL)	**1.25 (1.00, 1.55)**	1.18 (0.94, 1.49)
Q4 (0.73 – 16.30 ng/mL)	1.23 (0.99, 1.53)	1.10 (0.87, 1.38)
PFHpS		
IQR (0.34 ng/mL)	1.02 (0.93, 1.12)	0.91 (0.82, 1.00)
Q1 (<LOD – 0.21 ng/mL)	Reference	Reference
Q2 (0.22 – 0.36 ng/mL)	0.92 (0.73, 1.14)	**0.75 (0.59, 0.95)**
Q3 (0.37 – 0.55 ng/mL)	1.20 (0.97, 1.49)	0.92 (0.73, 1.16)
Q4 (0.56 – 2.97 ng/mL)	1.00 (0.80, 1.24)	**0.74 (0.58, 0.94)**
PFDA		
IQR (0.25 ng/mL)	1.05 (0.99, 1.11)	**1.12 (1.05, 1.20)**
Q1 (<LOD – 0.15 ng/mL)	Reference	Reference
Q2 (0.16 – 0.25 ng/mL)	1.10 (0.89, 1.36)	1.25 (1.00, 1.56)
Q3 (0.26 – 0.40 ng/mL)	0.89 (0.72, 1.11)	1.06 (0.84, 1.33)
Q4 (0.41 – 3.54 ng/mL)	1.07 (0.86, 1.32)	**1.30 (1.03, 1.64)**
PFUnA		
IQR (0.24 ng/mL)	1.01 (0.94, 1.07)	1.05 (0.98, 1.12)
Q1 (<LOD – 0.08 ng/mL)	Reference	Reference
Q2 (0.09 – 0.16 ng/mL)	0.90 (0.72, 1.12)	0.93 (0.74, 1.16)
Q3 (0.17 – 0.32 ng/mL)	1.02 (0.83, 1.27)	1.15 (0.92, 1.44)
Q4 (0.33 – 3.41 ng/mL)	0.95 (0.77, 1.18)	1.05 (0.83, 1.32)

Bolded estimates indicate p<0.05

[a] Adjusted for gender/menopause status (male, pre-menopausal female, peri-menopausal female, post-menopausal female), race (Black, yes/no), education level (college graduate, yes/no), age at baseline, and BMI at baseline.

Note: The analyses had inverse probability weighting to account for oversampling of cases with the case-cohort study design.

Abbreviations: confidence interval (CI); interquartile range (IQR); limit of detection (LOD); odds ratio (OR); quartile 1-4 (Q1-4); Perfluorooctane sulfonoic acid (PFOS); Perfluorooctanoic acid (PFOA); Perfluorononanoic acid (PFNA); Perfluorohexane sulfonoic acid (PFHxS); 2-(N-Methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA); Perfluoroheptanesulfonic acid (PFHpS); Perfluorodecanoic acid (PFDA); Perfluoroundecanoic acid (PFUnA)

clinical monitoring. Hence, we explored whether specific PFAS and a mixture of PFAS – reflecting the joint effects and correlations among each PFAS – relate to incident hand OA and progression.

Methods: We leveraged a case-cohort sample (n = 1,878) from the Osteoarthritis Initiative among participants with hand radiographs at the baseline and 48-month visits. We assayed baseline serum samples for 12 PFAS via online solid-phase extraction liquid chromatography tandem mass spectrometry. For analyses, we a priori included only 8 PFAS for which 60% of samples were above the limits of detection. Our 2 primary outcomes were incident symptomatic hand OA and an increased number of joints with radiographic OA (Kellgren-Lawrence≥2; yes/no). We classified a participant as having incident symptomatic hand OA if at the 48-month visit, but not at baseline, they had ≥2 finger joints (distal interphalangeal, proximal interphalangeal, or metacarpophalangeal joints) on at least 2 separate digits with at least a small osteophyte or mild joint space narrowing (modified Kellgren-Lawrence grade≥2) on radiograph and reported on a questionnaire hand/finger pain, aching, or stiffness on more than half of the 30 days prior to the radiograph. We used covariate-adjusted weighted logistic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Associations [OR (95%CI)] of baseline serum PFAS concentration with having an increase (vs. not) in total number of joints with a KL grade ≥2 between baseline and the 48-month follow-up visit (N=1,878)

	Unadjusted OR (95%CI)	Adjusted OR (95%CI)[a]
PFOS		
IQR (8.90 ng/mL)	0.96 (0.88, 1.05)	0.98 (0.90, 1.08)
Q1 (0.10 – 9.00 ng/mL)	Reference	Reference
Q2 (9.01 – 12.73 ng/mL)	1.05 (0.83, 1.32)	1.03 (0.81, 1.31)
Q3 (12.74 – 17.90 ng/mL)	0.98 (0.77, 1.24)	1.02 (0.80, 1.30)
Q4 (17.91 – 85.50 ng/mL)	0.95 (0.75, 1.21)	1.01 (0.79, 1.30)
PFOA		
IQR (3.01 ng/mL)	1.04 (0.96, 1.11)	1.04 (0.96, 1.12)
Q1 (0.33 – 3.87 ng/mL)	Reference	Reference
Q2 (3.88 – 5.18 ng/mL)	0.84 (0.66, 1.08)	0.84 (0.65, 1.08)
Q3 (5.19 – 6.88 ng/mL)	**1.29 (1.03, 1.63)**	**1.32 (1.04, 1.67)**
Q4 (6.89 – 66.30 ng/mL)	1.03 (0.81, 1.31)	1.06 (0.83, 1.36)
PFNA		
IQR (0.74 ng/mL)	0.98 (0.92, 1.04)	0.99 (0.93, 1.05)
Q1 (0.07 – 0.76 ng/mL)	Reference	Reference
Q2 (0.77 – 1.05 ng/mL)	0.79 (0.63, 1.01)	0.80 (0.63, 1.01)
Q3 (1.06 – 1.50 ng/mL)	1.08 (0.87, 1.36)	1.08 (0.86, 1.36)
Q4 (1.51 – 13.40 ng/mL)	**0.77 (0.61, 0.98)**	0.81 (0.63, 1.04)
PFHxS		
IQR (2.62 ng/mL)	1.01 (0.95, 1.06)	1.01 (0.95, 1.06)
Q1 (0.10 – 1.96 ng/mL)	Reference	Reference
Q2 (1.97 – 2.97 ng/mL)	**1.28 (1.01, 1.62)**	**1.31 (1.02, 1.67)**
Q3 (2.98 – 4.58 ng/mL)	1.06 (0.83, 1.35)	1.11 (0.87, 1.43)
Q4 (4.59 – 66.70 ng/mL)	1.13 (0.89, 1.44)	1.17 (0.91, 1.50)
MeFOSAA		
IQR (0.46 ng/mL)	0.99 (0.93, 1.05)	0.98 (0.92, 1.04)
Q1 (0.03 – 0.25 ng/mL)	Reference	Reference
Q2 (0.26 – 0.43 ng/mL)	1.27 (1.00, 1.61)	1.24 (0.97, 1.58)
Q3 (0.44 – 0.72 ng/mL)	**1.27 (1.00, 1.62)**	1.27 (1.00, 1.62)
Q4 (0.73 – 16.30 ng/mL)	1.17 (0.92, 1.50)	1.13 (0.89, 1.45)
PFHpS		
IQR (0.34 ng/mL)	0.94 (0.85, 1.04)	0.96 (0.86, 1.07)
Q1 (<LOD – 0.21 ng/mL)	Reference	Reference
Q2 (0.22 – 0.36 ng/mL)	1.17 (0.93, 1.47)	1.13 (0.90, 1.44)
Q3 (0.37 – 0.55 ng/mL)	0.91 (0.71, 1.16)	0.91 (0.70, 1.17)
Q4 (0.56 – 2.97 ng/mL)	0.92 (0.73, 1.18)	0.95 (0.74, 1.23)
PFDA		
IQR (0.25 ng/mL)	0.98 (0.91, 1.04)	0.99 (0.92, 1.06)
Q1 (<LOD – 0.15 ng/mL)	Reference	Reference
Q2 (0.16 – 0.25 ng/mL)	1.10 (0.87, 1.39)	1.13 (0.89, 1.43)
Q3 (0.26 – 0.40 ng/mL)	0.96 (0.76, 1.22)	1.01 (0.80, 1.28)
Q4 (0.41 – 3.54 ng/mL)	0.91 (0.72, 1.16)	0.94 (0.73, 1.21)
PFUnA		
IQR (0.24 ng/mL)	0.98 (0.91, 1.04)	0.98 (0.91, 1.06)
Q1 (<LOD – 0.08 ng/mL)	Reference	Reference
Q2 (0.09 – 0.16 ng/mL)	1.19 (0.94, 1.49)	1.18 (0.93, 1.49)
Q3 (0.17 – 0.32 ng/mL)	0.94 (0.74, 1.19)	0.96 (0.75, 1.22)
Q4 (0.33 – 3.41 ng/mL)	0.94 (0.74, 1.20)	0.94 (0.74, 1.21)

Bolded estimates indicate p<0.05

[a] Adjusted for gender/menopause status (male, pre-menopausal female, peri-menopausal female, post-menopausal female), race (Black, yes/no), education level (college graduate, yes/no), age at baseline, BMI at baseline.

Note: The analyses had inverse probability weighting to account for oversampling of cases with the case-cohort study design

Abbreviations: confidence interval (CI); interquartile range (IQR); limit of detection (LOD); odds ratio (OR); quartile 1-4 (Q1-4); Perfluorooctane sulfonoic acid (PFOS); Perfluorooctanoic acid (PFOA); Perfluorononanoic acid (PFNA); Perfluorohexane sulfonoic acid (PFHxS); 2-(N-Methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA); Perfluoroheptanesulfonic acid (PFHpS); Perfluorodecanoic acid (PFDA); Perfluoroundecanoic acid (PFUnA)

regression models to assess single PFAS (continuous and quartiles) and quantile-based g-computation to assess the PFAS mixture in relation to our primary outcomes.

Results: rticipants were mostly female (58%), White (83%), and on average 61 years of age and overweight (mean BMI = 28.6 kg/m^2). Participants with higher serum PFDA and PFNA had greater odds of incident symptomatic hand OA [OR (95%CI) per interquartile-range increment: 1.12 (1.05, 1.20) for PFDA; 1.07 (1.00, 1.13) for PFNA], but the associations were not monotonic when represented in quartiles (Table 1). Participants with higher PFHxS had lower odds of hand OA [e.g., OR (95%CI): 0.93 (0.86, 1.00) per interquartile-range increment]. Participants in the highest quartile of PFHpS (vs. quartile 1) had lower odds of hand OA. We observed no other monotonic associations between individual PFAS or the PFAS mixture with either primary outcome (Tables 1 and 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: We observed possible associations of PFDA and PFNA with symptomatic hand OA incidence that warrant further study in cohorts with more nuanced measures of hand OA symptoms, but we otherwise found no consistent evidence that greater serum PFAS concentrations relate to a greater chance of developing hand OA incidence or progression.

Disclosure: J. Driban: None; **L. Rokoff**: None; **B. Lu**: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **C. Eaton**: None; **M. Roberts**: None; **D. Mathes**: None; **C. Lestician**: None; **Z. Xu**: None; **Z. Fan**: None; **S. O'Leary**: None; **A. Fleisch**: None.

Abstract Number: 0322

Metabolites Reflective of the Gut Microbiome Relate to Future Incident Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Jeffrey Driban[1], Shike Xu[2], Timothy McAlington[3], John Haran[4], Julieann Patarini[4] and Bing Lu[5], [1]University of Massachusetts Chan Medical School, Marlborough, NH, [2]University of Connecticut Health Center, Farmington, CT, [3]UMass Chan School of Medicine, Arlington, MA, [4]UMass Chan Medical School, Worcester, MA, [5]UConn Health Center, Newton, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Numerous cross-sectional and animal studies have linked an altered gut microbiome to osteoarthritis (OA). Human studies are needed to explore the association between the gut microbiome and incident OA. Assessing microbiomes can be challenging; however, blood measures (e.g., metabolites) have offered insights into the gut microbiome and its relationship with prevalent OA. Hence, we explored whether blood-based metabolites, reflective of the gut microbiome, relate to incident knee OA during the subsequent 7 years.

Methods: We performed a secondary analysis of a case-cohort study that included 603 participants from the Osteoarthritis Initiative, comprising 237 incident knee OA cases and 366 non-cases from a randomly selected sub-cohort over an 8-year follow-up. Plasma metabolomes were analyzed using liquid chromatography-tandem mass spectrometry. Among the measured metabolites, 47 were previously identified in the literature as microbial metabolites (Rushing BR et al., 2021). We averaged metabolite levels at baseline and year 1 as the exposure and identified incident OA cases as knees with a Kellgren and Lawrence grade ≥2 in subsequent follow-ups. Weighted logistic regression, which accounted for the study design and adjusted for age and gender with and without body mass index (BMI), was used to examine associations between these metabolite concentrations and knee OA incidence. As an exploratory analysis, multiple comparison correction was not applied.

Results: Among the 603 participants, 70% of OA cases (mean [SD] age = 60 [9] years, BMI = 28.6 [4.7] kg/m^2), and 55% of non-cases were female (age = 58 [9], BMI = 26.9 [8.0] kg/m^2). When adjusting only for age and gender, the upper quartile of 4 metabolites had a statistically significant association with greater odds of incident knee OA (2 had a significant p for trend; Table 1): 3-(3-Hydroxyphenyl)propanoic acid (OR = 1.90, p trend = 0.048), N,N-Dimethylglycine (OR = 1.65, p trend = 0.016), Kynurenic acid (OR = 1.51), N-Acetyl-L-phenylalanine (OR = 1.62). Only 3-(3-Hydroxyphenyl)propanoic acid remained statistically significant after adjusting for BMI (OR = 1.90, Table 2). Three metabolites had evidence suggestive that higher levels related to lower odds of incident OA: Benzoic acid (ORs range = 0.54-0.74), Butyric acid (OR range =

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Association between microbial metabolites and knee osteoarthritis risk (adjusted for age and gender).

Compound Name	Quartile 2 (OR [95% CI])	Quartile 3 (OR [95% CI])	Quartile 4 (OR [95% CI])	p-value
4-hydroxyphenylacetylglutamine	0.78 [0.52, 1.16]	0.81 [0.54, 1.21]	1.01 [0.67, 1.52]	0.883
phenylacetylglutamine	1.14 [0.77, 1.69]	0.92 [0.62, 1.38]	0.87 [0.58, 1.32]	0.619
2-hydroxy-4-(methylthio)butanoic acid	1.22 [0.84, 1.77]	**0.46 [0.30, 0.71]**	0.77 [0.51, 1.17]	0.227
deoxycholic acid 12-sulfate	1.06 [0.71, 1.58]	1.39 [0.94, 2.06]	1.05 [0.70, 1.57]	0.917
deoxycholic acid glucuronide	1.11 [0.75, 1.64]	0.87 [0.58, 1.31]	1.18 [0.79, 1.76]	0.538
3-(3-Hydroxyphenyl)propanoic acid	0.81 [0.53, 1.24]	1.16 [0.77, 1.73]	**1.90 [1.29, 2.81]**	**0.048**
3-Phenylpropionic acid	0.73 [0.49, 1.09]	0.86 [0.58, 1.26]	0.73 [0.49, 1.09]	0.414
4-Hydroxyphenylacetic acid	1.03 [0.68, 1.56]	1.37 [0.92, 2.04]	1.41 [0.94, 2.12]	0.213
Allantoin	1.23 [0.84, 1.83]	1.12 [0.74, 1.68]	1.09 [0.72, 1.63]	0.781
Benzoic acid	**0.60 [0.40, 0.89]**	0.74 [0.51, 1.09]	**0.54 [0.36, 0.80]**	0.092
Betaine	1.01 [0.68, 1.50]	1.18 [0.79, 1.76]	1.01 [0.67, 1.52]	0.646
Butyric acid	0.72 [0.48, 1.06]	0.84 [0.57, 1.24]	**0.63 [0.42, 0.94]**	0.228
Choline	1.17 [0.78, 1.75]	1.12 [0.74, 1.70]	1.23 [0.81, 1.87]	0.514
Caprylate	1.00 [0.66, 1.52]	1.47 [0.99, 2.19]	0.93 [0.61, 1.42]	0.772
Hippuric acid	1.07 [0.72, 1.57]	0.73 [0.49, 1.10]	0.95 [0.64, 1.41]	0.713
Malic acid	0.96 [0.65, 1.43]	0.99 [0.66, 1.48]	0.85 [0.56, 1.28]	0.648
N,N-Dimethylglycine	1.24 [0.82, 1.86]	1.20 [0.79, 1.84]	**1.65 [1.09, 2.51]**	**0.016**
Hypoxanthine	1.20 [0.82, 1.77]	0.89 [0.59, 1.32]	0.90 [0.60, 1.35]	0.954
Indole-3-acetic acid	0.84 [0.56, 1.24]	0.93 [0.63, 1.38]	1.07 [0.72, 1.58]	0.587
myo-Inositol	1.07 [0.71, 1.60]	1.34 [0.90, 1.99]	0.78 [0.51, 1.18]	0.939
Nicotinamide	1.12 [0.75, 1.66]	1.24 [0.83, 1.84]	1.10 [0.73, 1.67]	0.815
4-hydroxyphenylpyruvic acid	0.77 [0.52, 1.13]	0.77 [0.52, 1.14]	0.83 [0.55, 1.23]	0.196
Palmitic acid	0.81 [0.55, 1.21]	0.81 [0.55, 1.21]	0.75 [0.50, 1.12]	0.589
Phenylpyruvic acid	1.25 [0.86, 1.83]	0.75 [0.49, 1.13]	0.93 [0.60, 1.44]	0.849
Phenylacetic acid	0.87 [0.59, 1.29]	**0.66 [0.44, 0.99]**	0.86 [0.58, 1.28]	0.766
Pyruvic acid	1.12 [0.76, 1.65]	0.93 [0.63, 1.39]	0.89 [0.59, 1.33]	0.442
Sarcosine	0.85 [0.58, 1.25]	0.77 [0.52, 1.15]	0.86 [0.57, 1.28]	0.683
Succinic acid	1.31 [0.88, 1.96]	1.36 [0.91, 2.04]	0.78 [0.51, 1.20]	0.68
Trimethylamine N-oxide	0.76 [0.50, 1.15]	0.88 [0.58, 1.32]	1.03 [0.69, 1.54]	0.304
Homovanillic acid	1.08 [0.72, 1.63]	1.00 [0.66, 1.50]	1.46 [0.99, 2.18]	0.264
Indolepropionate	0.92 [0.62, 1.36]	0.75 [0.50, 1.11]	0.75 [0.50, 1.12]	0.299
Kynurenic acid	0.96 [0.64, 1.44]	1.31 [0.88, 1.97]	**1.51 [1.01, 2.29]**	0.061
2-Hydroxy-3-phenylpropanoic acid	1.07 [0.72, 1.59]	**1.60 [1.07, 2.39]**	1.02 [0.63, 1.66]	0.780
Glucose	1.04 [0.71, 1.53]	0.82 [0.55, 1.23]	0.79 [0.52, 1.19]	0.325
Xylitol	1.01 [0.69, 1.49]	0.72 [0.48, 1.07]	0.78 [0.52, 1.16]	0.592
4-Hydroxyphenyllactate	1.35 [0.92, 1.98]	1.16 [0.76, 1.75]	1.10 [0.70, 1.73]	0.865
Suberate	1.11 [0.74, 1.68]	1.48 [0.99, 2.22]	1.35 [0.90, 2.03]	0.543
Myristic acid	1.19 [0.80, 1.79]	1.37 [0.92, 2.04]	0.83 [0.54, 1.27]	0.898
4-Ethylphenol	1.14 [0.77, 1.68]	0.82 [0.54, 1.23]	0.97 [0.65, 1.44]	0.644
N-Acetyl-L-phenylalanine	1.45 [0.96, 2.19]	1.63 [1.07, 2.48]	**1.62 [1.05, 2.52]**	0.342
3-Hydroxybutyric acid	0.94 [0.63, 1.40]	0.93 [0.62, 1.38]	0.92 [0.62, 1.36]	0.641
L-Lactic acid	0.93 [0.63, 1.38]	1.06 [0.71, 1.57]	1.03 [0.69, 1.54]	0.976
Xylose	0.87 [0.59, 1.28]	0.76 [0.51, 1.12]	0.68 [0.45, 1.01]	0.272
Fructose	1.08 [0.73, 1.62]	0.89 [0.60, 1.34]	1.07 [0.72, 1.60]	0.884
L-Threonic acid	1.24 [0.85, 1.83]	0.86 [0.58, 1.29]	0.67 [0.44, 1.01]	0.333
L-Prolyl-glycine	0.73 [0.49, 1.09]	0.72 [0.48, 1.08]	1.23 [0.83, 1.82]	0.543

Bold: $p \leq 0.05$

0.63-0.84), and Phenylacetic acid (OR range = 0.66-0.87). Benzoic acid (OR range = 0.62-0.74) and Butyric acid (OR range = 0.66-0.88) remained statistically significant after adjusting for BMI (Table 2). Furthermore, after adjusting for BMI, 10 other metabolites had evidence that higher levels related to lower odds of incident OA, including 3 with a p for trend < 0.05: 4-hydroxyphenylpyruvic acid, Pyruvic acid, and Glucose.

Conclusion: Our results complement a prior cross-sectional analysis using fecal metabolomes, which suggested OA was associated with perturbed pathways, including amino acid metabolism (e.g., glycine, serine, tryptophan, phenylalanine), fatty acid metabolism, dietary polyphenol metabolism, and pyruvate metabolism. Unlike the prior study, we offer longitudinal evidence that these metabolites are altered before the onset of knee OA and may be modifiable risk factors, which can be monitored in blood samples.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Association between microbial metabolites and knee osteoarthritis risk (adjusted for age, gender, and body mass index).

Compound Name	Quartile 2 (OR [95% CI])	Quartile 3 (OR [95% CI])	Quartile 4 (OR [95% CI])	p-value
4-hydroxyphenylacetylglutamine	**0.66 [0.44, 0.99]**	0.67 [0.44, 1.01]	0.74 [0.48, 1.13]	0.443
phenylacetylglutamine	1.14 [0.77, 1.71]	0.99 [0.66, 1.49]	0.90 [0.60, 1.37]	0.717
2-hydroxy-4-(methylthio)butanoic acid	1.31 [0.90, 1.92]	**0.50 [0.33, 0.77]**	0.75 [0.49, 1.15]	0.187
deoxycholic acid 12-sulfate	0.97 [0.64, 1.46]	1.34 [0.90, 2.00]	0.89 [0.59, 1.34]	0.668
deoxycholic acid glucuronide	1.11 [0.75, 1.66]	0.90 [0.59, 1.35]	1.22 [0.81, 1.83]	0.582
3-(3-Hydroxyphenyl)propanoic acid	0.79 [0.51, 1.21]	1.12 [0.74, 1.68]	**1.90 [1.29, 2.83]**	**0.037**
3-Phenylpropionic acid	0.79 [0.53, 1.18]	0.95 [0.64, 1.41]	0.90 [0.60, 1.36]	0.843
4-Hydroxyphenylacetic acid	0.98 [0.65, 1.49]	1.29 [0.86, 1.93]	1.17 [0.77, 1.77]	0.502
Allantoin	1.37 [0.92, 2.04]	1.01 [0.66, 1.53]	0.94 [0.62, 1.42]	0.341
Benzoic acid	**0.66 [0.44, 0.99]**	0.74 [0.50, 1.10]	**0.62 [0.41, 0.92]**	0.158
Betaine	1.15 [0.77, 1.72]	1.25 [0.83, 1.87]	1.14 [0.76, 1.73]	0.468
Butyric acid	0.71 [0.47, 1.06]	0.88 [0.60, 1.31]	**0.66 [0.44, 0.99]**	0.301
Choline	1.20 [0.80, 1.80]	1.12 [0.74, 1.71]	1.03 [0.67, 1.59]	0.947
Caprylate	0.98 [0.64, 1.49]	1.46 [0.98, 2.20]	0.99 [0.65, 1.51]	0.892
Hippuric acid	1.21 [0.81, 1.80]	0.77 [0.51, 1.17]	1.09 [0.73, 1.65]	0.918
Malic acid	0.97 [0.65, 1.44]	1.00 [0.66, 1.50]	0.89 [0.59, 1.35]	0.641
N,N-Dimethylglycine	1.20 [0.80, 1.82]	1.01 [0.66, 1.56]	1.46 [0.96, 2.23]	0.053
Hypoxanthine	1.09 [0.74, 1.61]	0.83 [0.55, 1.24]	0.79 [0.52, 1.19]	0.710
Indole-3-acetic acid	0.97 [0.64, 1.45]	1.01 [0.67, 1.50]	1.10 [0.74, 1.65]	0.693
myo-Inositol	1.03 [0.68, 1.55]	1.31 [0.87, 1.96]	0.79 [0.51, 1.20]	0.796
Nicotinamide	1.04 [0.70, 1.55]	1.04 [0.69, 1.56]	1.05 [0.69, 1.60]	0.948
4-hydroxyphenylpyruvic acid	0.73 [0.49, 1.08]	**0.65 [0.43, 0.97]**	**0.56 [0.37, 0.86]**	**0.036**
Palmitic acid	0.71 [0.47, 1.07]	**0.66 [0.43, 0.99]**	**0.60 [0.40, 0.91]**	0.242
Phenylpyruvic acid	1.14 [0.78, 1.68]	0.67 [0.44, 1.02]	0.79 [0.50, 1.23]	0.474
Phenylacetic acid	0.98 [0.66, 1.47]	0.75 [0.50, 1.13]	1.06 [0.70, 1.59]	0.750
Pyruvic acid	1.06 [0.71, 1.57]	0.73 [0.48, 1.10]	**0.59 [0.38, 0.90]**	**0.038**
Sarcosine	0.80 [0.54, 1.19]	**0.66 [0.44, 1.00]**	0.82 [0.54, 1.23]	0.587
Succinic acid	1.31 [0.87, 1.97]	1.45 [0.96, 2.18]	0.87 [0.56, 1.34]	0.908
Trimethylamine N-oxide	**0.65 [0.43, 1.00]**	0.76 [0.50, 1.16]	0.82 [0.54, 1.24]	0.652
Homovanillic acid	1.01 [0.67, 1.53]	0.89 [0.59, 1.35]	1.38 [0.93, 2.07]	0.361
Indolepropionate	1.03 [0.69, 1.53]	0.93 [0.62, 1.41]	0.92 [0.61, 1.40]	0.681
Kynurenic acid	0.83 [0.55, 1.26]	1.14 [0.75, 1.72]	1.11 [0.72, 1.71]	0.329
2-Hydroxy-3-phenylpropanoic acid	0.98 [0.66, 1.47]	1.48 [0.98, 2.22]	1.00 [0.61, 1.63]	0.641
Glucose	0.93 [0.63, 1.38]	0.69 [0.46, 1.05]	**0.52 [0.33, 0.80]**	**0.016**
Xylitol	0.97 [0.66, 1.44]	**0.52 [0.34, 0.79]**	**0.57 [0.38, 0.87]**	0.117
4-Hydroxyphenyllactate	1.22 [0.83, 1.80]	0.90 [0.59, 1.38]	0.86 [0.54, 1.37]	0.333
Suberate	1.02 [0.67, 1.55]	1.35 [0.90, 2.04]	1.30 [0.86, 1.97]	0.602
Myristic acid	1.09 [0.72, 1.65]	1.27 [0.84, 1.91]	0.73 [0.48, 1.13]	0.688
4-Ethylphenol	1.24 [0.83, 1.84]	0.88 [0.58, 1.33]	1.08 [0.72, 1.61]	0.986
N-Acetyl-L-phenylalanine	1.25 [0.83, 1.90]	1.35 [0.88, 2.08]	1.24 [0.79, 1.95]	0.995
3-Hydroxybutyric acid	0.75 [0.50, 1.14]	0.93 [0.62, 1.39]	0.94 [0.62, 1.39]	0.892
L-Lactic acid	0.88 [0.59, 1.31]	1.06 [0.71, 1.57]	1.03 [0.69, 1.54]	0.442
Xylose	0.87 [0.59, 1.29]	0.71 [0.51, 1.12]	**0.60 [0.40, 0.90]**	0.139
Fructose	1.16 [0.77, 1.74]	0.92 [0.61, 1.39]	1.05 [0.72, 1.58]	0.982
L-Threonic acid	1.24 [0.80, 1.75]	0.85 [0.58, 1.28]	0.67 [0.44, 1.01]	0.475
L-Prolyl-glycine	0.73 [0.49, 1.09]	0.72 [0.48, 1.08]	1.23 [0.83, 1.82]	0.543

Bold: $p \leq 0.05$

Disclosure: J. Driban: None; **S. Xu**: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **J. Haran**: None; **J. Patarini**: None; **B. Lu**: None.

Abstract Number: 0323

Automated Effusion-Synovitis Volume is Prognostic and Responsive to Knee Osteoarthritis Progression: Data from the Osteoarthritis Initiative

Jeffrey Driban[1], Kate Lapane[2], Shao-Hsien Liu[2], Jonggyu Baek[2], Grace Lo[3], Matthew Harkey[4], Charles Eaton[5], James Mackay[6], Timothy McAlington[7], Mohammad Chowdhury[8], Zhen Cao[9], Juan Shan[10] and Ming Zhang[11], [1]University of Massachusetts Chan Medical School, Marlborough, NH, [2]UMass Chan Medical School, Worcester, MA, [3]Baylor College of Medicine / MEDVAMC, Houston, TX, [4]Michigan State University, East Lansing, MI, [5]Brown University, Pawtucket, RI, [6]University of Cambridge; Norwich Medical School, San Diego, CA, [7]UMass Chan School of Medicine, Arlington, MA, [8]Pace University, New York City, NY, [9]Boston University, Boston, MA, [10]Pace University, New York, NY, [11]Boston University, Westford, MA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Semi-quantitative and semi-automated quantitative measurements of effusion-synovitis (ES) are prognostic for knee OA progression. Changes in these metrics relate to changes in knee pain. However, these traditional methods require readers to review or measure MRIs, leading to reader variability and significant time demands. An automated approach could enable quantitative ES volume measurements that can be rapidly deployed on large datasets without variations between readers. Hence, we evaluated the prognostic and construct validity of an automated quantitative measurement of ES volume by comparing its relationship to knee OA progression against that of a well-established semi-automated ES volume.

Methods: We conducted knee-based analyses among participants in the Osteoarthritis Initiative with bilateral knee MRIs and at least one knee with Kellgren-Lawrence (KL) grade ≥ 1 and a WOMAC pain score ≥ 10/100. We included participants with ES measurements at the 12- and 36-month OAI visits. A trained reader measured whole-knee ES volume on MRIs using our semi-automated software. To develop an automated measurement, we implemented a deep neural network approach based on the 3D U-Net architecture developed with the Medical Open Network for Artificial Intelligence (MONAI) framework. The model was trained using a different dataset with data augmentation techniques, including random affine transformations, spatial flips, and intensity shifts to enhance robustness. We calculated Pearson Correlation Coefficients between the automated and semi-automated ES volumes (cross-sectionally and 2-year change) and created Bland-Altman plots. To assess prognostic validity, we examined how ES volumes at the 12-month visit related to changes in radiographic severity (KL and joint space narrowing [JSN] progression) over the subsequent 3 years. To assess construct validity, we examined concurrent change in ES volumes with 2-year progression in KL grade, JSN grade, or WOMAC knee pain scores (change > 10/100 points). We performed knee-based analyses using logistic regression with repeated measures to adjust for correlations between knees within each person.

Results: Among the 506 participants (1,011 knees), 56% were female with a mean (SD) age = 61 (9) years and BMI = 29.3 (4.3) kg/m^2. The sample included 82 (8%) knees with KL progression, 103 (10%) with medial JSN progression, and 126 (12%) with knee pain worsening. Cross-sectionally, the automated method yielded smaller volumes than the semi-automated method (Figure 1B); however, these differences were attenuated when assessing longitudinal change (Figure 1D). Despite these differences, the automated ES volume strongly correlated with the semi-automated volume (r = 0.89; Figure 1A) and volume change (r = 0.84; Figure 1C). The table shows that the automated and semi-automated ES volumes had consistent statistically significant associations with every outcome.

Table. Automated quantitative measurements of effusion-synovitis volume (cm3) have similar prognostic and construct validity as well-established semi-automated effusion-synovitis volumes.

Table 1. Automated quantitative measurements of effusion-synovitis volume (cm^3) have similar prognostic and construct validity as well-established semi-automated effusion-synovitis volumes.

	Semi-automated Effusion-Synovitis Volume			Automated Effusion-Synovitis Volume		
	Outcome Absent M (SD)	Outcome Present M (SD)	Odds Ratio (95% CI) Per SD	Outcome Absent M (SD)	Outcome Present M (SD)	Odds Ratio (95% CI) Per SD
Prognostic validity (relating 12-month effusion-synovitis volume with change over the subsequent 3 years)						
Kellgren-Lawrence Progression	12.7 (8.5)	15.3 (10.2)	1.27 (1.08, 1.49)	6.2 (4.3)	7.8 (6.0)	1.32 (1.13, 1.54)
Joint Space Narrowing Progression	12.6 (8.6)	16.0 (9.1)	1.33 (1.14, 1.54)	6.2 (4.4)	8.0 (5.2)	1.35 (1.15, 1.57)
Construct validity (relating 2-year change to 2-year change)						
Kellgren-Lawrence Progression	1.4 (5.8)	4.7 (9.1)	1.58 (1.26, 1.97)	0.2 (3.2)	1.9 (5.5)	1.52 (1.20, 1.93)
Joint Space Narrowing Progression	1.4 (5.7)	3.9 (9.1)	1.41 (1.12, 1.77)	0.2 (3.1)	1.8 (5.5)	1.46 (1.15, 1.85)
WOMAC Knee Pain Worsening	1.4 (6.0)	3.8 (7.1)	1.52 (1.26, 1.83)	0.2 (3.3)	1.4 (4.1)	1.45 (1.19, 1.78)

M = Mean, SD = Standard deviation, 95% CI = 95% confidence interval

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

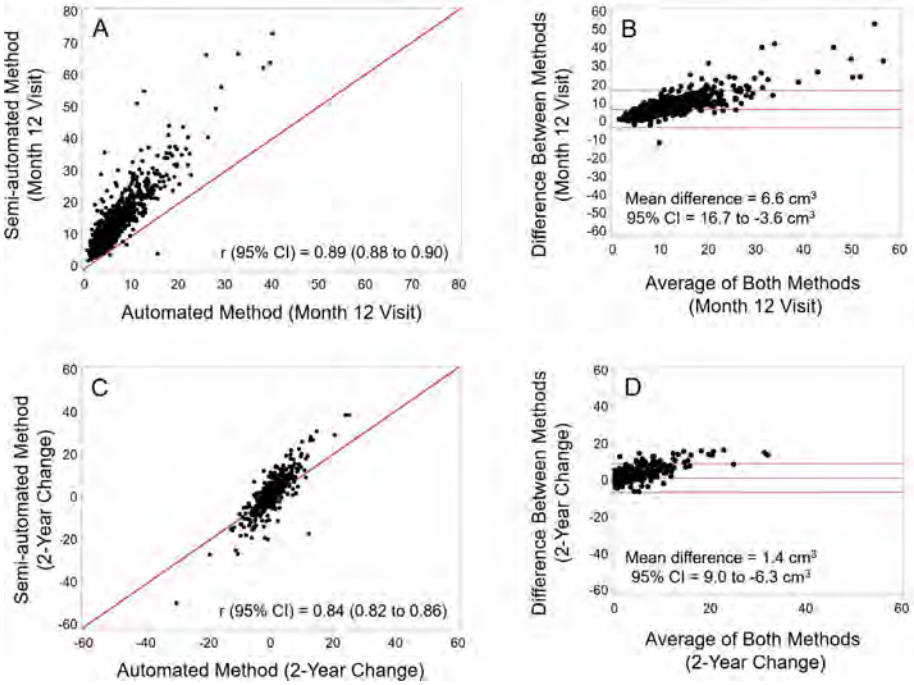


Figure 1. Cross-sectionally, the automated effusion-synovitis volumes (cm^3) are typically smaller than the semi-automated effusion-synovitis volumes (A [Scatter Plot], B [Bland-Altman Plot]); however, these differences are attenuated when examining the two-year change in both measures (C [Scatter Plot], D [Bland-Altman Plot]). In Figures A and C, the red line is the line of identity/equality, and correlations are reported with 95% confidence intervals (CI). In Figures B and D, the middle red line is the mean difference between the methods. The upper and lower red lines represent the upper and lower bounds of the 95% confidence interval, respectively.

Conclusion: The automated ES volume had strong prognostic and construct validity regarding radiographic and pain outcomes. The automated method offers an efficient strategy to quantify ES in studies with large sample sizes. It may provide a cost-effective approach to screen MRIs in future clinical trials.

Disclosure: J. Driban: None; **K. Lapane**: None; **S. Liu**: None; **J. Baek**: None; **G. Lo**: None; **M. Harkey**: None; **C. Eaton**: None; **J. Mackay**: AstraZeneca, 3, Blue Earth Diagnostics, 3; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **M. Chowdhury**: None; **Z. Cao**: None; **J. Shan**: None; **M. Zhang**: None.

Abstract Number: 0324

Bile Acids Metabolism in Symptomatic Hand Osteoarthritis: Data from the Xiangya Osteoarthritis Study and Genetics of OA Consortium

Jiatian Li[1], Jing Ye[1], Tuo Yang[1], david Hunter[2], Weiya Zhang[3], Michael Doherty[3], Yuqing Zhang[4], Zidan Yang[1], Hui Li[1], Yilun Wang[1], Dongxing Xie[1], Ziying Wu[5], Wei Li[1], Zeqin Wen[1], Changjun Li[1], Chao Zeng[1], Guanghua Lei[1] and Jie Wei[1], [1]Xiangya Hospital, Central South University, Changsha, Hunan, China (People's Republic), [2]Sydney Musculoskeletal Health, University of Sydney, St Leonards, New South Wales, Australia, [3]School of Medicine, University of Nottingham, Nottingham, United Kingdom, [4]Massachusetts General Hospital, Quincy, MA, [5]Xiangya Hospital, Central South University, Chang Sha, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Although gut microbiome dysbiosis has been implicated in symptomatic hand OA (SHOA), the potential contribution of bile acids (BAs), key metabolites in host-microbiota interactions, to SHOA pathogenesis remains unexplored. This study examined the association between plasma BA metabolism and SHOA using data from multiple cohorts, aiming to elucidate potential pathogenic mechanisms underlying SHOA and investigate potential therapeutic targets.

Methods: Participants in the discovery cohort were drawn from the Xiangya Osteoarthritis (XO) Study, a community-based observational study. SHOA was defined as the presence of both self-reported hand symptoms and radiographic hand OA in at least one hand. Individuals without SHOA in either hand served as controls. 71 SHOA and 1,288 control participants were identified in the discovery cohort. The associations between plasma BAs and SHOA were examined using logistic regression model. We replicated the analysis to validate the association between key BAs and SHOA using a case-control design that include 71 SHOA and 71 age-, sex-, and body mass index-matched control participants, who were identified in an independent validation cohort. Multi-omics analyses were conducted to explore links between SHOA-related microbes and key BAs, while mediation analysis assessed the role of BAs in the gut microbiome-SHOA relationship. Finally, to explore the potential underlying mechanisms of the associations, we conducted gene-based meta-analyses to assess the associations between key BA receptors and SHOA using data from the XO Study and Genetics of OA Consortium.

Results: In the discovery cohort, the plasma BA profiles were primarily dominated by glycochenodeoxycholic acid (GCDCA), chenodeoxycholic acid (CDCA), cholic acid (CA), glycocholic acid (GCA), and deoxycholic acid (DCA) (**Figure 1A**).

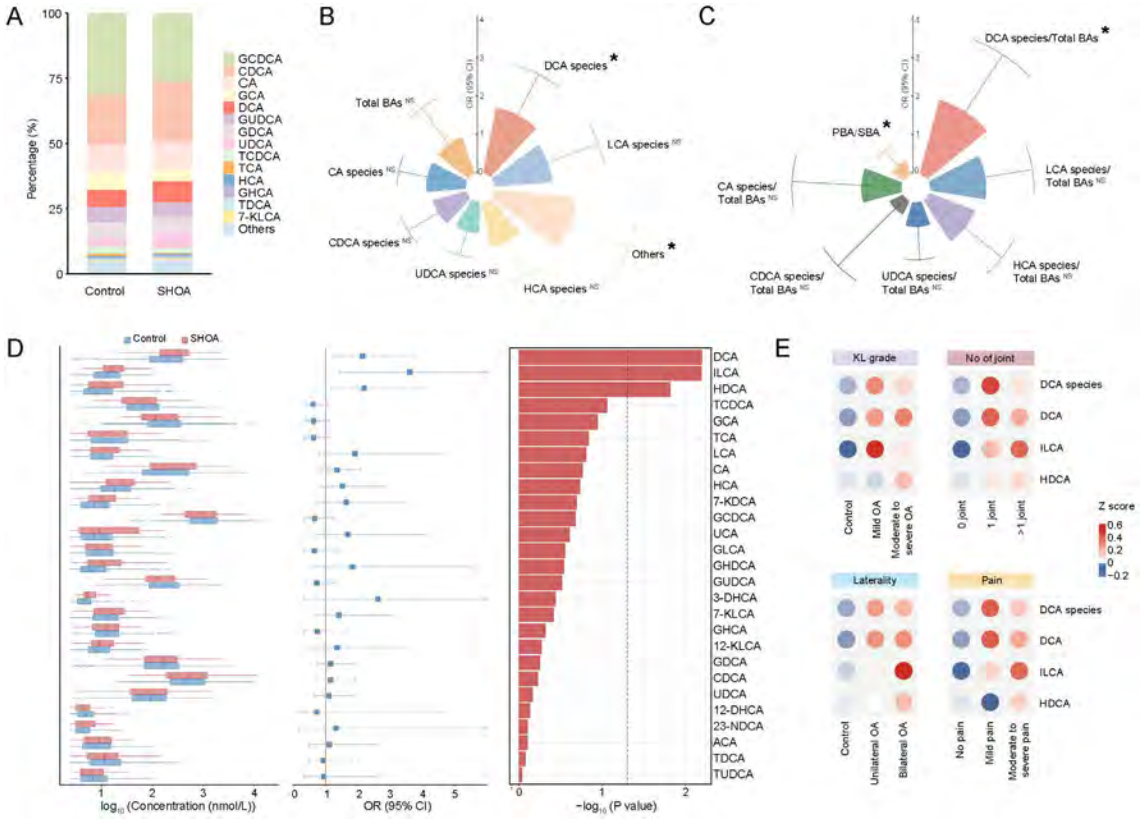


Figure 1. Associations of plasma bile acids with symptomatic hand OA in the discovery cohort. (A) Top 15 most abundant plasma bile acid categories identified in participants with SHOA and controls. (B) Associations of bile acid species, (C) bile acid species ratios, (D) and individual plasma bile acids with SHOA, adjusting for age, sex, body mass index, smoking status, alcohol consumption, and dietary intake of meat/eggs, dairy, and vegetables. (E) Associations between key plasma bile acids and the severity of SHOA. SHOA, symptomatic hand OA; GCDCA, glycochenodeoxycholic acid; CDCA, chenodeoxycholic acid; CA, cholic acid; GCA, glycocholic acid; DCA, deoxycholic acid; GUDCA, glycoursodeoxycholic acid; GDCA, glycodeoxycholic acid; UDCA, ursodeoxycholic acid; TCDCA, taurochenodeoxycholic acid; TCA, taurocholic acid; HCA, hyocholic acid; GHCA, glycohyocholic acid; TDCA, taurodeoxycholic acid; 7-KLCA, 7-Ketolithocholic acid; DCAs, deoxycholic acid species; LCAs, lithocholic acid species; HCAs, hyocholic acid species; UDCAs, ursodeoxycholic acid species; CDCAs, chenodeoxycholic acid species; CAs, cholic acid species; BA, bile acids; KL grade, Kellgren-Lawrence grade; No of joint, number of affected joints.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Elevated levels of deoxycholic acid (DCA) species (odds ratio [OR]=1.75, 95% confidence interval [CI]: 1.03–2.96), DCA (OR=2.14, 95% CI: 1.24–3.70), isolithocholic acid (OR=3.60, 95% CI: 1.43–9.04), and hyodeoxycholic acid (OR=2.20, 95% CI: 1.17–4.15) were positively associated with SHOA (**Figure 1B-D**) and its severity (**Figure 1E**). Similar associations between BAs and SHOA were found in the independent validation cohort (**Figure 2**). Multi-omics analyses revealed significant correlations between DCA species, DCA, and the DCA species/total BAs ratio with SHOA-related microbial species (**Figure 3A**).[1] Mediation analysis showed that DCA mediated the relationships of four SHOA-related microbial species, with the mediation effects ranged from 7.0% to 24.1% (**Figure 3B-E**). Gene-based meta-analyses identified a significant association between the gene encoding the Farnesoid X receptor (FXR), a key BA receptor, and SHOA.

Conclusion: Dysregulated BA metabolism, particularly elevated DCA levels, is associated with SHOA and key SHOA-related microbiomes. DCA mediates the link between gut microbiota dysbiosis and SHOA, while FXR could be a treatment target for SHOA.

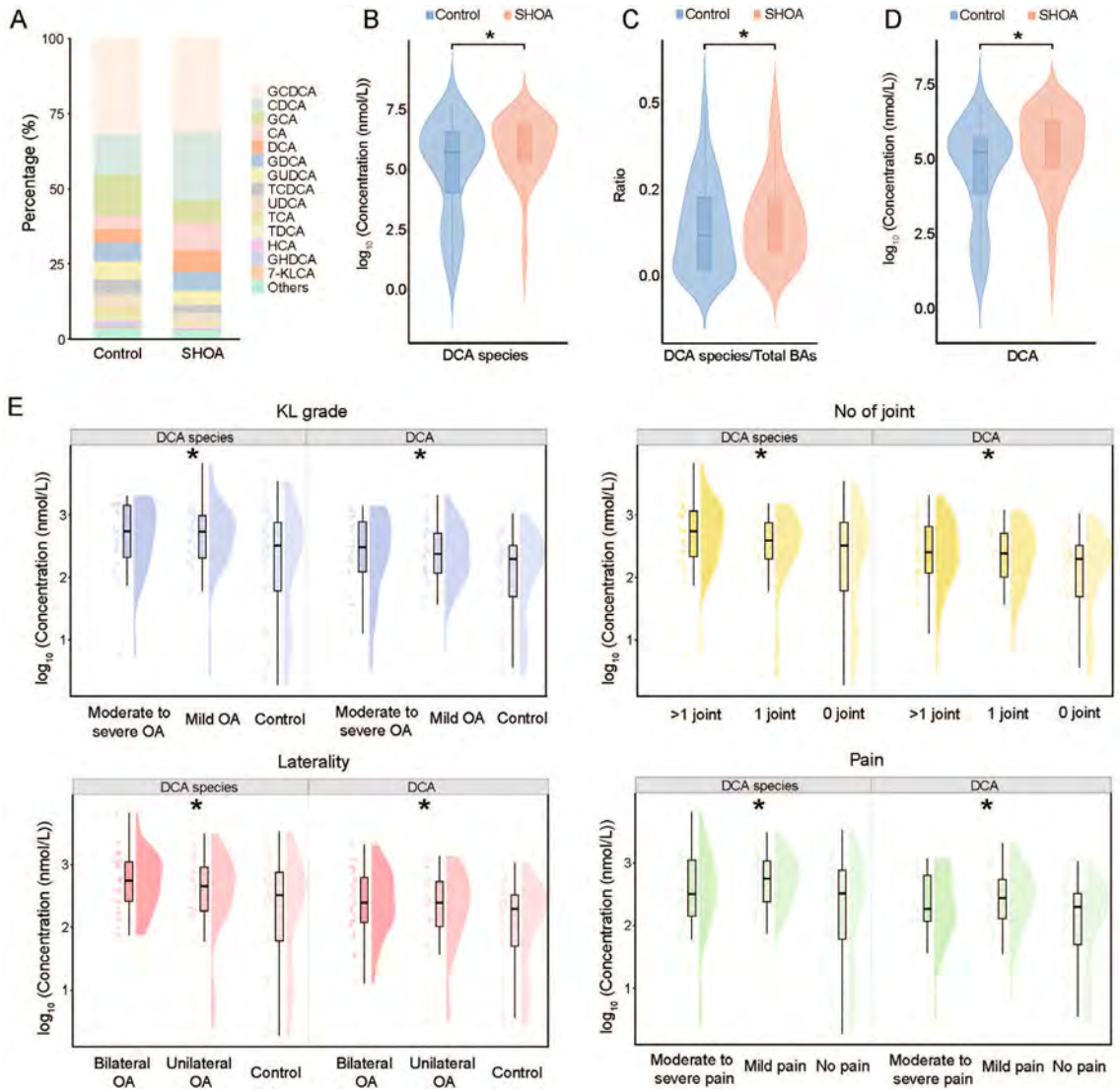


Figure 2. Associations of plasma bile acids with symptomatic hand OA in the Validation cohort. (A) Top 15 most abundant plasma bile acid categories identified in participants with SHOA and controls. (B) Bile acid species validated in the validation cohort. (C) Bile acid species ratios validated in the validation cohort. (D) Individual plasma bile acid validated in the validation cohort. (E) Associations between key plasma bile acids and the severity of SHOA. SHOA, symptomatic hand OA; GCDCA, glycochenodeoxycholic acid; CDCA, chenodeoxycholic acid; GCA, glycocholic acid; CA, cholic acid; DCA, deoxycholic acid; GDCA, glycodeoxycholic acid; GUDCA, glycoursodeoxycholic acid; TCDCA, taurochenodeoxycholic acid; UDCA, ursodeoxycholic acid; TCA, taurocholic acid; TDCA, taurodeoxycholic acid; HCA, hyocholic acid; GHDCA, glycohyodeoxycholic acid; 7-KLCA, 7-ketolithocholic acid; DCAs, deoxycholic acid species; KL grade, Kellgren-Lawrence grade; No of joint, number of affected joints.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

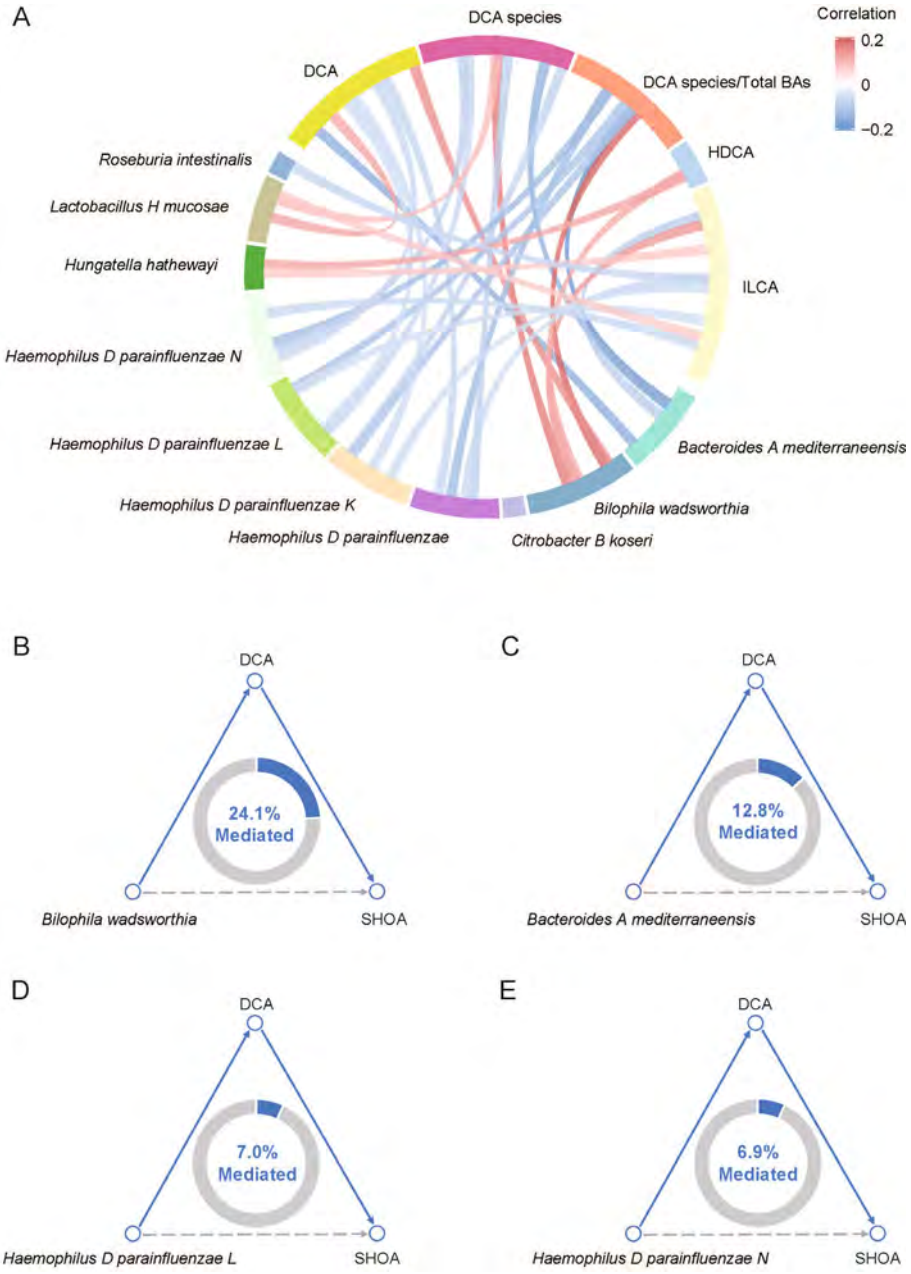


Figure 3. Correlations between gut microbial species to plasma bile acids in symptomatic hand OA. (A) Correlations between SHOA-related plasma bile acids and SHOA-related microbiome species. The correlations were calculated by partial Spearman's rank correlation test. (B) Mediation effect of DCA on the association between Bilophila wadsworthia and SHOA. (C) Mediation effect of DCA on the association between Bacteroides A mediterraneensis and SHOA. (D) Mediation effect of DCA on the association between Haemophilus D parainfluenzae L and SHOA. (E) Mediation effect of DCA on the association between Haemophilus D parainfluenzae N and SHOA.The proportions of the indirect effect (mediation effect) are labeled at the center of the ring charts. SHOA, symptomatic hand OA; DCA, deoxycholic acid.

REFERENCES

1. Wei J, et al. EBioMedicine 2023;98:104892.

Disclosure: J. Li: None; **J. Ye**: None; **T. Yang**: None; **d. Hunter**: None; **W. Zhang**: None; **M. Doherty**: None; **Y. Zhang**: None; **Z. Yang**: None; **H. Li**: None; **Y. Wang**: None; **D. Xie**: None; **Z. Wu**: None; **W. Li**: None; **Z. Wen**: None; **C. Li**: None; **C. Zeng**: None; **G. Lei**: None; **J. Wei**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0325

Knee Symptom Phenotyping Incorporating Pain and Function across Different Levels of WOMAC Function in Two Cohorts: Data from the Multicenter Osteoarthritis Study (MOST) and the Osteoarthritis Initiative (OAI)

C. Kent Kwoh[1], Amanda Nelson[2], Rongrong Tang[3], Edward J. Bedrick[3], Yong Ge[1], Yvonne Golightly[4], Zong-Ming Li[3], Jean Liew[5], Xiaoxiao Sun[1], Jeffrey Duryea[6] and Tuhina Neogi[5], [1]The University of Arizona Arthritis Center, University of Arizona, Tucson, AZ, [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]The University of Arizona Arthritis Center, University of Arizona, Tucson, [4]University of Nebraska Medical Center, Omaha, NE, [5]Boston University School of Medicine, Boston, MA, [6]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

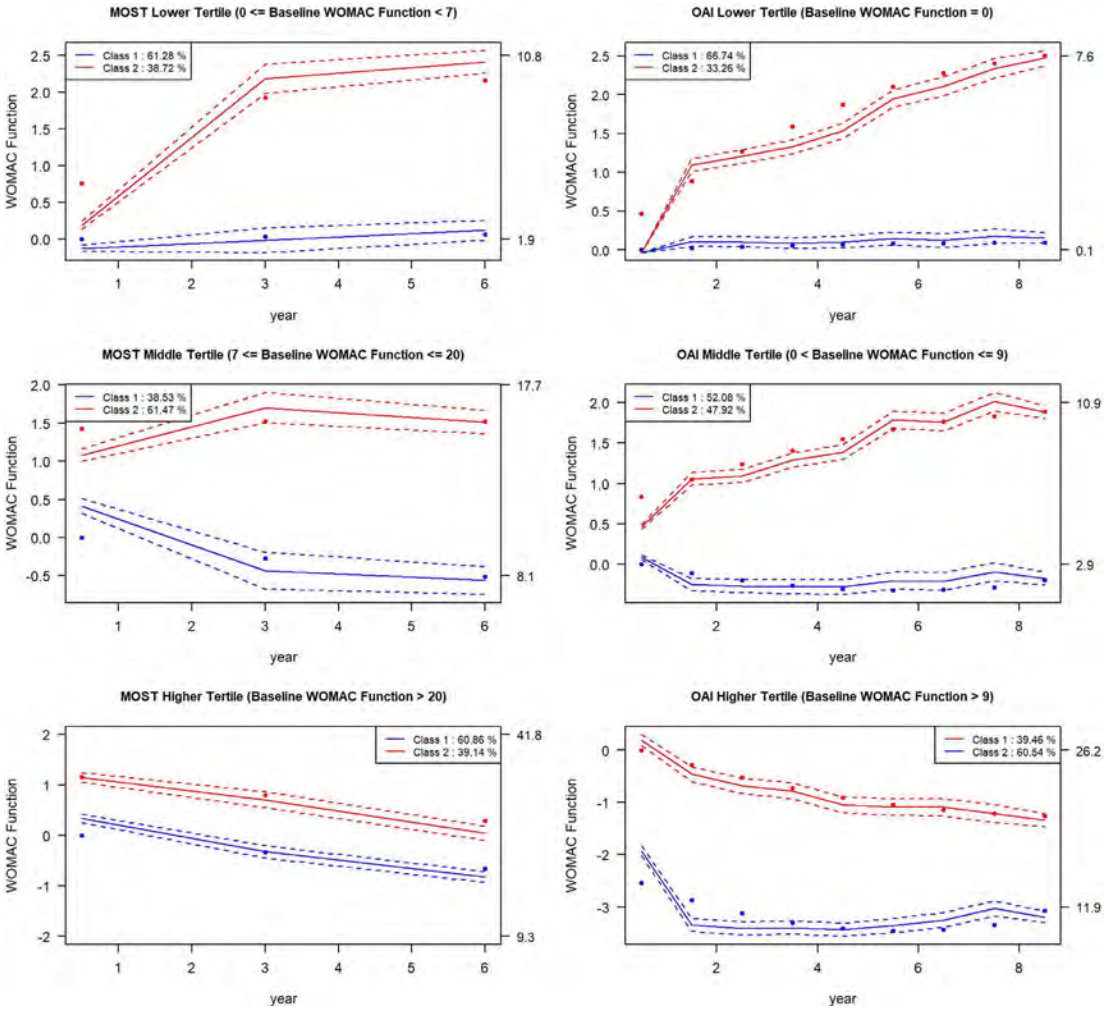


Figure 1. Knee symptom phenotyping by tertiles of baseline WOMAC function score for OAI and MOST The average trajectory (solid line) and confidence intervals (dashed lines) for WOMAC function are shown. The left column shows the trajectory results for OAI, and the right column show the trajectory results for MOST. Each row shows the tertile-specific cluster trajectories by strata of baseline WOMAC function score by tertile. The left-sided y-axis is the latent process WOMAC function score transformed using the link function. The right-sided y-axis is the actual WOMAC function score.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Knee pain and functional limitations are the most common symptoms of knee OA. Understanding the various patterns of symptoms (i.e., pain and function changes over time) can help identify individuals most in need of targeted interventions. Using OAI data, we have previously shown that there are distinct symptom trajectories for knees that start with no symptoms at baseline and there are specific predictors of a worse symptom trajectory. Our objective was to analyze knee symptoms among individuals with or at risk for knee OA with varying degrees of symptoms to identify temporal knee pain and function phenotypes using two large cohorts.

Methods: We selected 2965 knees from MOST, and 9491 knees from OAI that had the following knee pain/function measures available at baseline to develop the knee symptom phenotypes based upon trajectories of these measures over time: WOMAC function, WOMAC pain, and the Numerical Rating Scale (NRS) for knee pain severity. We used data from 0 to the 7^{th} year in MOST, and from 0 to the 9^{th} year in OAI to develop the trajectories. Knees that were already replaced at the baseline visit were excluded. Latent Class Mixed Models (LCMM) were employed to cluster the selected knees into distinct knee pain/function progression trajectories, while simultaneously using logistic regression to identify predictors associated with each trajectory. The response covariance matrix was allowed to be different for each latent class. We used tertiles of the baseline WOMAC function score as strata for LCMM analyses for each of the symptom measures.

Results: In both cohorts, two trajectories for each model were identified as optimal. For each tertile of baseline WOMAC function, the patterns of the trajectories were similar for each of the pain and function outcomes. As a sample illustration, the clusters for WOMAC function by tertile for MOST and OAI are shown in Figure 1. For the lowest tertile, there was a stable

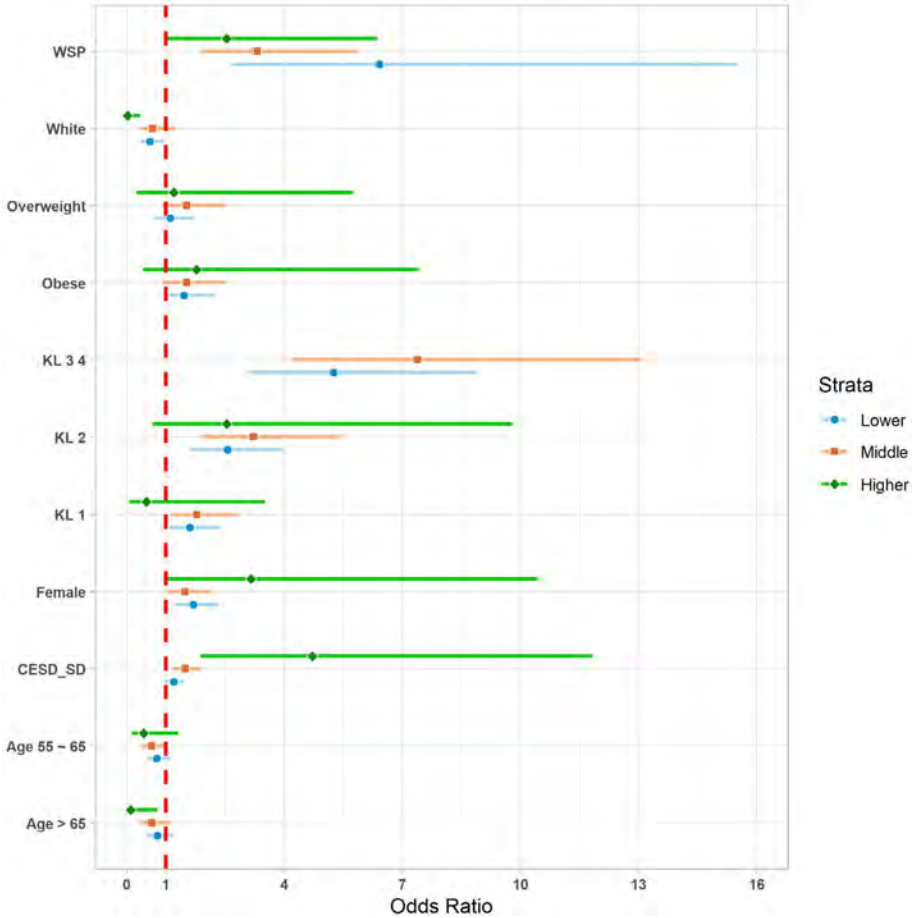


Figure 2. Summary of the predictors for being in the Red Trajectory (i.e., worse/worsening) vs. the Blue Trajectory (i.e., stable/improving) [in Figure 1] by tertiles of baseline WOMAC function score for MOST WSP = widespread pain; KL = Kellgren-Lawrence; CES-D_SD = Center for Epidemiologic Studies Depression scale by standard deviation OR of KL 3, 4 for the highest tertile is 99.48, with CI [5.26, 1881.83]. This information was not included in the plot due to scale issues.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

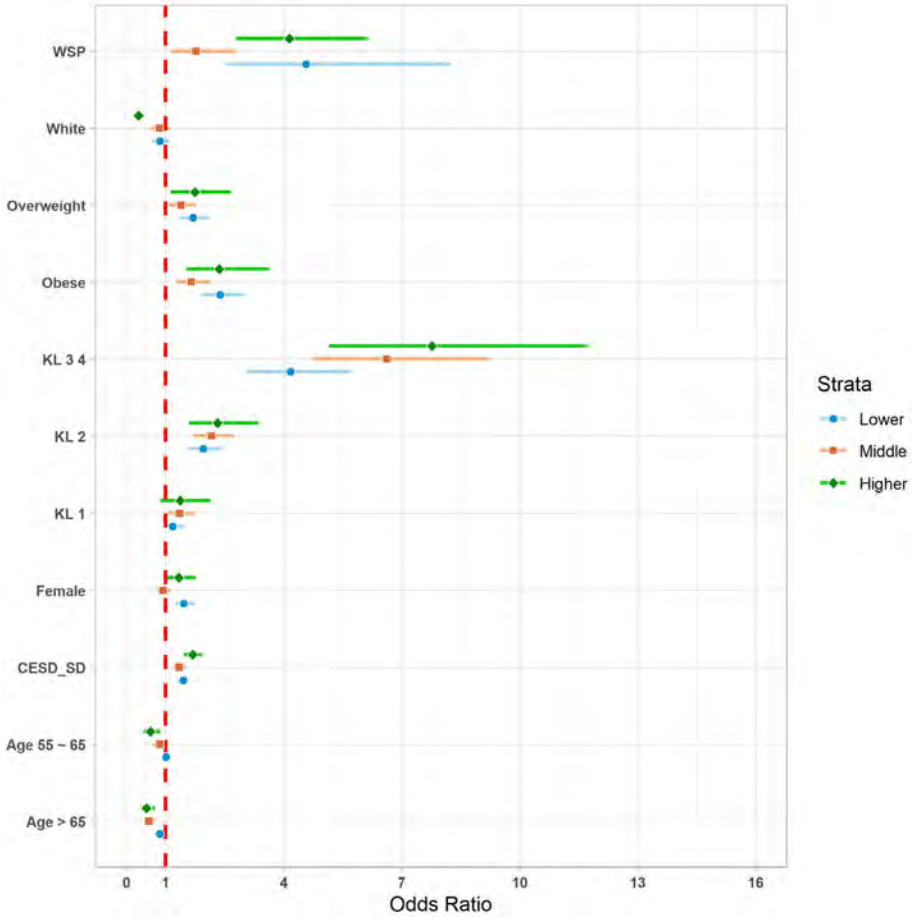


Figure 3. Summary of the predictors for being in the Red Trajectory (i.e., worse/worsening) vs. the Blue Trajectory (i.e., stable/improving) [in Figure 1] by tertiles of baseline WOMAC function score for OAI WSP = widespread pain; KL = Kellgren-Lawrence; CES-D_SD = Center for Epidemiologic Studies Depression scale by standard deviation

trajectory (blue) vs. a rapidly worsening trajectory (red). For the middle tertile, there was an improving trajectory (blue) vs. a worsening trajectory (red). For the highest tertile, both the red and blue clusters showed improving trajectories, but starting at different baseline scores. The ORs for being in the red (i.e., worse/worsening) vs. the blue (i.e., stable or improving) clusters for each tertile are summarized in Figure 2 for MOST and Figure 3 for OAI. The predictors in common across models associated with being in the red (i.e., worse) cluster were widespread pain, overweight/obese, higher Kellgren-Lawrence Grade (KLG), and more depressive symptoms (i.e., Center for Epidemiologic Studies Depression scale, CES-D).

Conclusion: For both MOST and OAI, similar symptom trajectories were identified when the cohorts were stratified using the tertile of the baseline WOMAC function score. We have also identified readily assessable predictors of the worse symptom trajectories. The trajectories with worse symptom progression may represent a group to target with interventions earlier in their disease course.

Disclosure: C. Kwoh: Apos Health, 1, 2, Express Scripts, 1, 2, Kolon Tissue Gene, 2, Mobieus Sun, 1, 2, TLC, 1, 2, Xalud, 1, 2; **A. Nelson**: Novo Nordisk, 1; **R. Tang**: None; **E. Bedrick**: None; **Y. Ge**: None; **Y. Golightly**: None; **Z. Li**: None; **J. Liew**: None; **X. Sun**: None; **J. Duryea**: None; **T. Neogi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0326

Gender Disparities in Clinical Outcomes Among Older Adults with Knee Osteoarthritis: A Retrospective Cohort Study

Kinga Grzybowski[1], Ahmer Khan[2], Samuel Bonomo[3] and Arthur Lau[4], [1]Jefferson Einstein Montgomery Hospital, Maspeth, NY, [2]Jefferson Einstein Philadelphia Hospital, Philadelphia, [3]Jefferson Einstein Montgomery Hospital, East Norriton, PA, [4]Jefferson Einstein Hospital, Maple Glen, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is the most common type of arthritis which classically affects multiple joints, mainly the knees. About 595 million people worldwide suffer from OA which affects older individuals after the age of 50; females more frequently affected than males. The reason for the increased risk in females is suspected to be multifactorial and possibly related to genetics and environment. Many studies have found that women suffer from more severe disease compared to men. An observational, retrospective cohort study was conducted using the TriNetX database, which uses electronic health records from over 140 global collaborative networks, to explore gender differences in the diagnostic evaluation, treatment, and outcomes in patients with OA of the knees.

Methods: Inclusion criteria were limited to patients above the age of 65, assigned the ICD-10 code M17 for the diagnosis of OA of the knee. Individuals with RA, osteoporosis, gout, FM, polymyalgia rheumatica, AS and patients on steroids were excluded. Two cohorts were studied: females and males over the age of 65. The index event was defined as the initial appearance of the diagnosis of OA of the knee. Propensity matching was used for age, race/ethnicity and other comorbidities at the time of the index event. The outcomes evaluated included falls, fractures, depression, anxiety, PCP Visits, hospitalizations, mortality, chronic pain, opioid use, sleep disturbances, and visits to skilled nursing facilities (SNF Visits). Patients who experienced any of these outcomes prior to the index event were excluded and both risk and risk ratio calculations were measured.

Results: The dataset included 354,678 males, and 521,319 females. After propensity matching the average age was 70. Most males and females were White, of unknown race, or Black/African American. After propensity matching, a total of 219,227 patients were excluded from both groups and the outcomes were calculated. Analysis showed a statistically significant difference for falls (RR 1.141, 95% CI 1.105-1.178, P< 0.0001), fractures (RR 1.349, 95% CI 1.29-1.41, P< 0.0001),

Table 1: Baseline Characteristics of Both Cohorts Before (Left) and After (Right) Propensity Matching

Characteristics	Males	Females	p-value	Males	Females	p-value
Demographics						
Age at Index; mean ± SD	70.0 ± 8.89	70.8 ± 9.12	<0.0001	70.0 ± 8.89	70.0 ± 8.92	0.6920
White	59.7%	51.1%	<0.0001	59.4%	59.5%	0.6674
Unknown Race	23.4%	27.3%	<0.0001	23.6%	23.6%	0.8547
Black/African American	8.0%	11.5%	<0.0001	8.0%	8.1%	0.8418
Hispanic/Latino	4.8%	5.0%	<0.0001	4.8%	4.9%	0.0131
Diagnoses (%)						
Hypertension	32.1%	29.1%	<0.0001	31.5%	31.6%	0.6403
Obesity	8.6%	8.9%	<0.0001	8.5%	8.5%	0.9648
Diabetes	14.3%	11.9%	<0.0001	13.8%	13.9%	0.2985
Cerebral Infarction	2.3%	1.7%	<0.0001	2.1%	2.0%	0.1530
Acute MI	2.1%	0.99%	<0.0001	1.4%	1.4%	0.7944

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Differences in Diagnosis, Treatment, and Clinical Outcomes of Both Cohorts

Outcomes		Males (328,385)	Females (328,385)	RR (95% CI), P-value
Falls	*n* after matching in cohort	6,991	7,895	RR 1.141 (95% CI 1.105-1.178)
	Patients with outcome (%)	2.2%	2.5%	P<0.0001
Fractures	*n* after matching in cohort	3,356	4,489	RR 1.349 (95% CI 1.29-1.41)
	Patients with outcome (%)	1.1%	1.4%	P<0.0001
Depression	*n* after matching in cohort	7,587	10,355	RR 1.409 (95% CI 1.369-1.451)
	Patients with outcome (%)	2.4%	3.4%	P<0.0001
Anxiety	*n* after matching in cohort	9,494	13,753	RR 1.507 (95% CI 1.469-1.546)
	Patients with outcome (%)	3.1%	4.6%	P<0.0001
PCP Visits	*n* after matching in cohort	16,744	16,489	RR 0.972 (95% CI 0.952-0.992)
	Patients with outcome (%)	5.8%	5.7%	P 0.0074
Hospitalizations	*n* after matching in cohort	307	198	RR 0.645 (95% CI 0.539-0.771)
	Patients with outcome (%)	0.094%	0.06%	P<0.0001
Mortality	*n* after matching in cohort	4,395	3,760	RR 0.855 (95% CI 0.819-0.893)
	Patients with outcome (%)	1.35%	1.15%	P<0.0001
Chronic Pain	*n* after matching in cohort	15,684	15,793	RR 1.002 (95% CI 0.98-1.023)
	Patients with outcome (%)	5.3%	5.3%	P 0.8908
Opioid Use	*n* after matching in cohort	390	253	RR 0.648 (95% CI 0.554-0.76)
	Patients with outcome (%)	0.1%	0.08%	P<0.0001
Sleep Disorders	*n* after matching in cohort	14,789	12,510	RR 0.821 (95% CI 0.803-0.841)
	Patients with outcome (%)	5.0%	4.1%	P<0.0001
SNF Visits	*n* after matching in cohort	306	375	RR 1.226 (95% CI 1.054-1.426)
	Patients with outcome (%)	0.09%	0.114%	P 0.0080

depression (RR 1.409, 95% CI 1.369-1.451, P< 0.0001), anxiety (RR 1.507, 95% CI 1.469-1.546, P< 0.0001), and SNF visits (RR 1.226, 95% CI 1.054-1.426, P 0.0080) in females. Additionally, PCP visits (RR 0.972, 95% CI 0.952-0.992, P 0.0074), hospitalizations (RR 0.645, 95% CI 0.539-0.771, P< 0.0001), mortality (RR 0.855, 95% CI 0.819-0.893, P< 0.0001), opioid use (RR 0.648, 95% CI 0.554-0.76, P< 0.0001), and sleep disorders (RR 0.821, 95% CI 0.803-0.841, P< 0.0001) were determined to be statistically significant in males.

Conclusion: The study shows that females with OA are at higher risk for falls, fractures, depression, anxiety, and SNF visits. Men with OA are more likely to face sleep disorders, seek PCP visits, require more hospitalizations, have a higher mortality, and are more likely to be prescribed opioids, indicating that both genders face different consequences of OA, and that gender discrepancies exist. Additional research should be conducted specifically focusing on gender differences in osteoarthritis to explore potential contributive or causative factors that may explain these findings.

Disclosure: K. Grzybowski: None; **A. Khan**: None; **S. Bonomo**: None; **A. Lau**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0327

Structural Severity Assessment of Hand Osteoarthritis Using Radiomic Analysis: Correlation with the Kellgren-Lawrence Score – Results from the DIGICOD Cohort

Laetitia Perronne[1], SELLAM JEREMIE[2], Antoine Decoux[3], Loïc Duron[4], Constance de Margerie[5], Maxime Dougados[6], Simo Saarakala[7], Emmanuel Maheu[8], Michel Crema[8], Anne Miquel[8], Francis BERENBAUM[9], Armelle Arnoux[3], Jean Denis Laredo[10] and Laure Fournier[3], [1]Northwestern University, Chicago, IL, [2]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, F-75012 Paris, France, /Rheumatology Department, AP-HP Saint-Antoine Hospital, 184, rue du Faubourg Saint-Antoine, 75012, Paris, France., Paris, France, [3]Université paris Cité, Paris, France, [4]Hôpital Fondation Adolphe de Rothschild, Paris, France, [5]Hôpital Saint Louis, Paris, France, [6]Department of Medicine, Hopital Cochin, Universite de Paris, Paris, France, [7]University of Oulu, Oulu, Finland, [8]Hôpital Saint Antoine, Paris, France, [9]Sorbonne University/Inserm/AP-HP/4Moving Biotech, Paris, France, [10]Hôpital Lariboisière, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Radiomics involves the high-throughput extraction of quantitative data from medical imaging. This study aimed to develop a radiomic analysis pipeline applied to hand radiographs and evaluate its ability to classify joints according to the Kellgren-Lawrence (KL) score, a grading system for hand osteoarthritis severity. The goal was to assess whether radiomic features could enable automated and standardized KL classification, complementing expert visual assessment.

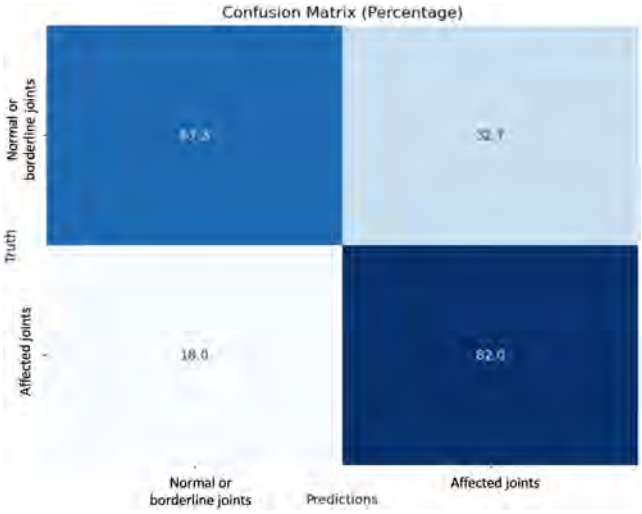
Methods: The study was based on 436 hand radiographs from the DIGICOD cohort, a prospective study of patients with hand osteoarthritis according to American College of Rheumatology criteria. After excluding 30 radiographs not found in PACS and 25 with artifacts or surgical hardware, 381 radiographs were analyzed, representing 10,531 joints (trapeziometacarpal [TMC], metacarpophalangeal [MCP], proximal interphalangeal [PIP], and distal interphalangeal [DIP] joints). KL grading was performed by an experienced radiologist at baseline.

Radiomic analysis involved several steps: (1) joint segmentation using an algorithm developed for the study. Manual segmentations from 20 patients served as ground truth to train a U-Net model with iterative training and correction; (2) extraction of 179 radiomic features (4 shape, 45 intensity histogram, and 130 texture features); (3) exclusion of texture features with relative variation < 0.05 after pixel shuffling (deemed non-informative); (4) dimensionality reduction by removing highly correlated features (Spearman > 0.9), resulting in 86 features. A random forest model with stratified cross-validation selected the 20 most relevant features for predicting KL scores. Classification performance was evaluated by comparing predicted vs. expert-assigned KL scores, using area under the curve (AUC), accuracy, and balanced accuracy. Accuracy reflects the proportion of correctly classified joints, while balanced accuracy adjusts for class imbalance.

Overview of the radiomic pipeline used in this study, from image acquisition and joint segmentation to feature extraction and classification modeling. The pipeline was designed to automate Kellgren-Lawrence scoring from standard hand radiographs in patients with hand osteoarthritis (DIGICOD cohort).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Comparison Between Manual and Automated Segmentation of Hand Joints. Comparison between manual segmentation by the radiologist (in orange) and automated segmentation using a U-Net-based model (in light blue). Concordant areas between both segmentations are shown in dark blue, indicating high overlap and supporting reliable feature extraction for radiomic modeling.



Confusion Matrix for Binary Classification of Joint Osteoarthritis Severity. Confusion matrix illustrating the performance of the radiomic model in predicting affected (KL 2–4) versus non-affected (KL 0–1) joints.

Results: The radiomic model achieved good classification performance for KL grading. Differentiation between affected joints (KL 2–4) and normal or borderline joints (KL 0–1) yielded an AUC of 0.81 and accuracy of 0.74. Discrimination between non/mildly affected (KL 0–2) and severely affected joints (KL 3–4) achieved an AUC of 0.83 and accuracy of 0.68. Considering all KL classes, the overall AUC was 0.76, with balanced accuracy of 0.37. Joint-type specific analysis (affected vs. normal/borderline) showed lower performance, with AUCs of 0.67, 0.71, and 0.49 and balanced accuracies of 0.34, 0.35, and 0.39 for MCP, PIP, and DIP joints, respectively. A downsampling strategy was applied to mitigate class imbalance, slightly improving overall classification, especially for the most frequent classes.

Conclusion: This study is the first to evaluate radiomic analysis in hand osteoarthritis. Radiomics enabled, to some extent, automated reproduction of KL classification. However, performance varied depending on joint type and severity. While this approach shows promise as a complementary tool for assessing hand osteoarthritis, external validation on an independent cohort is required before clinical application.

Disclosure: L. Perronne: None; **S. JEREMIE**: None; **A. Decoux**: None; **L. Duron**: None; **C. de Margerie**: Bracco, 12, travel support; **M. Dougados**: None; **S. Saarakala**: None; **E. Maheu**: None; **M. Crema**: None; **A. Miquel**: None; **F. BERENBAUM**: 4Moving Biotech, 2, 8, 10; **A. Arnoux**: None; **J. Laredo**: None; **L. Fournier**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0328

High synovial fluid leukocyte counts and markers of TLR activation correlate with poorer response to injections in patients with knee OA

Lance Murphy[1], Baofeng Hu[2], Vu Nguyen[3], Bryant England[4], Katherine Wysham[5], Mercedes Quinones[6], Joshua Baker[3] and Carla Scanzello[3], [1]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [2]University of Pennsylvania, Wynnewood, PA, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Nebraska Medical Center, Omaha, NE, [5]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [6]Washington DC VA Medical Center, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Toll-like receptors (TLRs) are pattern-recognition receptors of the innate immune response and are important in driving the initial activation of myeloid lineage cells to both pathogenic and non-pathogenic challenges. Deficiency of TLR3, TLR4, or CD14 (a TLR co-receptor) have been shown to mitigate OA progression and pain in animal models. However, the role of TLR signaling in human knee OA (KOA) is less studied. We evaluated the levels of synovial fluid (SF) markers including sTLR4 and sCD14 from patients enrolled in a clinical trial testing the impact of corticosteroid injections to determine if these markers could predict those that are most likely to respond to injections.

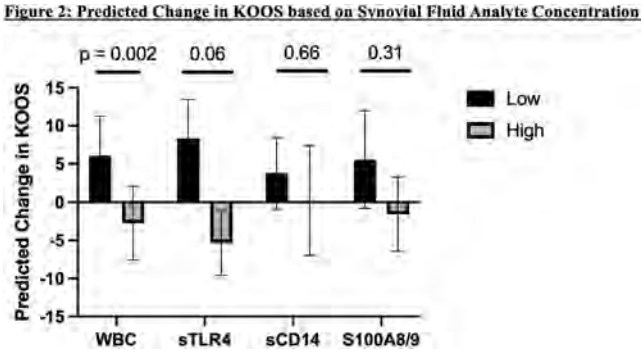
Methods: The MOVE-OK trial was a VA-funded, a multi-center blinded crossover randomized trial, comparing the effects of corticosteroid + lidocaine vs. lidocaine-only injections in Veterans with KOA . Inclusion criteria included a clinical diagnosis of KOA with a K-L X-ray grade ^{3}1, aged 40-80 years, and a clinical indication for joint injection according to the treating provider. 221 participants were randomized to receive blinded corticosteroid (CS) injections plus lidocaine (LC) (40 mg methylprednisolone) or LC-only injections then crossed-over to the other injection at 16 weeks. The primary outcome was the change in the total KOOS measured bi-weekly between 0 and 12 weeks after each injection. 196 participants received both injections, and SF was collected at the time of injection from a total of 40 patients with 14 patients having fluid collected at both injection time-points. We performed ELISAs on SF from these 14 patients measuring sTLR4, sCD14, and S100A8/9. Associations between SF biomarkers and the change in KOOS was assessed using linear regression incorporating generalized estimating equations to evaluate all time-points (2-12 weeks) after each injection, adjusting for the baseline KOOS score.

Results: Patients included in this subanalysis exhibited similar demographics to those enrolled in the main study (Table 1). SF from 4 patients had sTLR4 concentration below the limit of detection, but otherwise analytes were detectable in all samples.

Figure 1: Demographics of patients

Factor	SF subgroup	Large MOVE-OK group
N	14	221
Age	67 (8)	64 (9)
# Female Patients	1 (7%)	36 (16.3%)
BMI	32.2 (5.6)	32.6 (6.7)
KOOS Baseline	47.0 (20.8)	43.4 (16.6)
SF WBC concentration	250 (189, 340)	-
sCD14 concentration (ng/mL)	604.4 (365.5, 745.1)	-
S100A8/9 Concentration (ng/mL)	47.6 (22.8,102.3)	-
sTLR4 Concentration (pg/mL)	336.9 (0, 543.8)	-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



The median (IQR) concentrations of sCD14, S100A8/9 and sTLR4 are shown in Table 1. Patients with high SF WBC counts at baseline were less likely to show improvement in their KOOS scores over the course of the study (Figure 2). A similar trend was shown for sTLR4 concentration in SF. While there was numerically less improvement in KOOS over time between patients with high vs. low concentrations of sCD14 and S100A8/9, differences were not significant. There were no interactions to suggest that the association between biomarkers and the change in KOOS score differed between those receiving a CS v. LC-only injection.

Conclusion: Our results suggest that patients with higher SF levels of WBC and sTLR4 demonstrate less improvement in response to knee injection. Future proteomic analyses of these samples are planned and may provide additional insights. Analysis of these markers in larger cohorts are needed to validate these findings, but our results point to a potential importance of inflammation and the innate immune response in the joint in predicting symptom improvement in response to interventions.

Disclosure: L. Murphy: None; **B. Hu**: None; **V. Nguyen**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **K. Wysham**: None; **M. Quinones**: None; **J. Baker**: Amgen, 5; **C. Scanzello**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10.

Abstract Number: 0329

Machine Learning-Based Model to Predict Rapid Structural Progression in Knee Osteoarthritis

Maria Fernanda Gonzalez Hernandez[1], Ignacio rego Pérez[2], Isabel Rodríguez Valle[3], Jorge Vázquez García[4], Vanesa Balboa[5], Sara Relaño Fernández[4], María C. de Andrés[6], Lucía Lourido[7], Valentina Calamia[7], Rocio Paz González[4], Patricia Quaranta[7], Patricia Fernández-Puente[4], Nicola Veronese[8], Cristina Ruiz-Romero[9], Natividad Oreiro[10] and francisco J Blanco[11], [1]Instituto de Investigacion Biomedica de A Coruna (INIBIC), A coruna, Galicia, Spain, [2]Department of Rheumatology, Rheumatology Research Group (GIR) Biomedical Re-search Institute (INIBIC), A Coruna, Spain, [3]Instituto de Investigacion Biomedica de A Coruna (INIBIC), Coruña, Galicia, Spain, [4]Instituto de Investigacion Biomedica de A Coruna (INIBIC), coruña, Spain, [5]Grupo de Investigación de Reumatología (GIR). Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, coruña, Spain, [6]Instituto de Investigación Biomédica de A Coruña (INIBIC), Grupo de Investigación de Reumatología (GIR), A Coruña, Spain, [7]Instituto de Investigacion Biomedica de A Coruna (INIBIC), coruna, Spain, [8]Geriatric Unit, Department of Internal Medicine and Geriatrics, University of Palermo, palermo, Italy, [9]Department of Rheumatology, Rheumatology Research Group (GIR) Biomedical Re-search Institute (INIBIC), A Coruña, Spain, [10]CHUAC, La Coruna, Spain, [11]INIBIC-University of A Coruna, A Coruna, Galicia, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

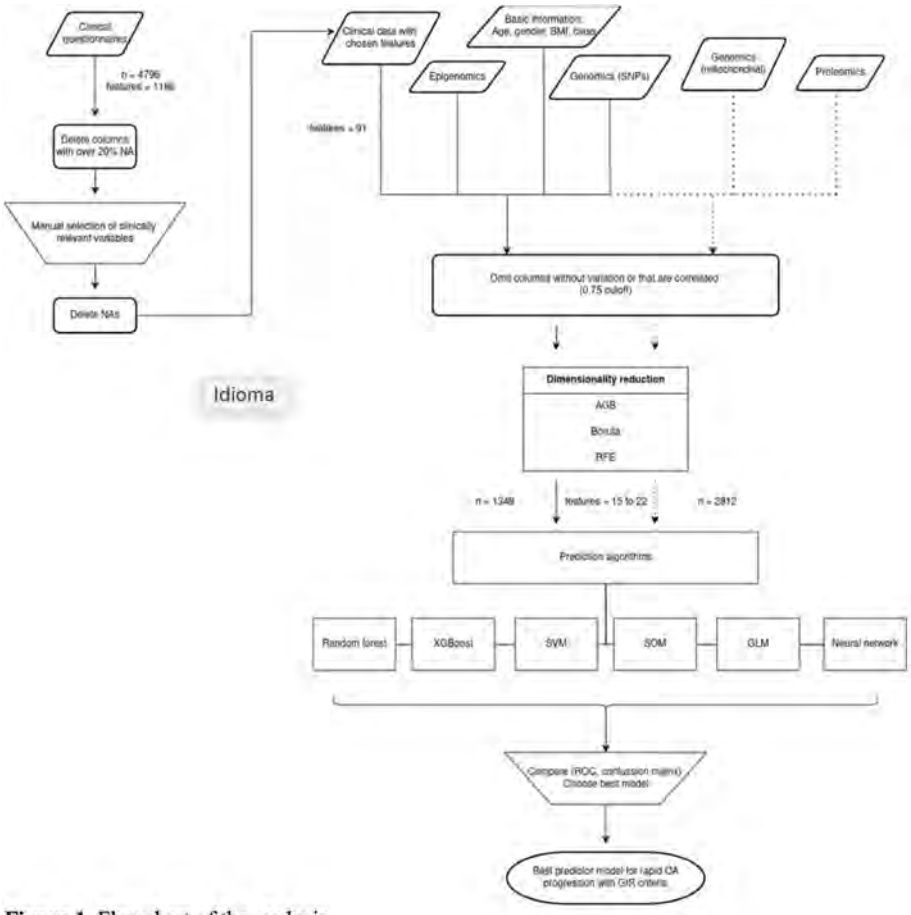


Figure 1. Flowchart of the analysis

Background/Purpose: Osteoarthritis (OA) is the most common chronic joint disorder, characterized by structural cartilage and bone damage that often causes pain and disability. However, the severity of joint damage does not always correlate with the level of pain. The limited effectiveness of current treatments may stem from difficulties in identifying patients at high risk of rapid structural progression. The Rheumatology and Health Research Group (GIR-S) defines progression as moving from a Kellgren and Lawrence (KL) grade 0–1 to ≥3, or from KL 2 to KL 4 or total knee replacement (TKR) within 48 months.

Our group has identified molecular biomarkers that, together with clinical and imaging data, may enhance the application of machine learning (ML) to detect patterns associated with OA subgroups. Advanced statistical tools enable us to extract multivariate signatures to differentiate patient phenotypes more precisely.

Our objective is to develop a predictive model for the rapid structural progression of osteoarthritis by integrating various machine learning techniques and using clinical, genomic, proteomic, and epigenetic data to predict structural progression over time in well-characterized prospective patient cohort, Osteoarthritis Initiative (OAI).

Methods: Rapid structural progression was defined according the GIR criteria, patients with an increase in the Kellgren-Lawrence (KL) score from ≤1 to ≥3, or from KL = 2 to KL = 4, or joint replacement over a follow-up period of 48 months. We used clinical, imaging, molecular biomarkers (including 20 proteins, 8 nuclear SNPs, and 3 mitochondrial haplogroups). The selected features were subsequently filtered using Recursive Feature Elimination (RFE) for dimensionality reduction. Using this data, we generated six machine learning models, dividing the data into 75% for training and 25% for testing. Figure 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

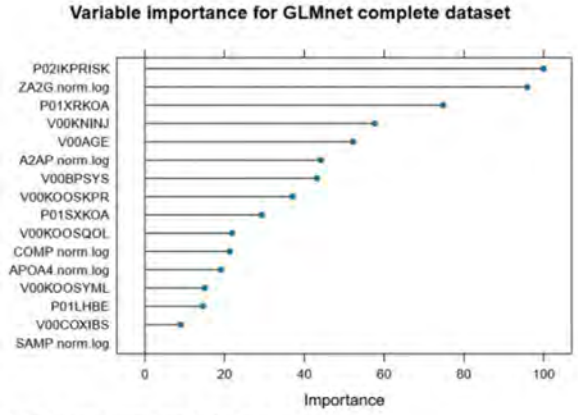


Figure 2a. Variable importance for GLMnet complete dataset.

Abbreviations: *P02IKPRISK* (Either knee symptom status at IEI); *ZA2G.norm.log* (normalized values of protein ZA2G (Alpha-2-Glycoprotein 1, Zinc- Binding); *P01XRKOA* (Baseline radiographic knee OA status by person); *V00KNINJ* (Either knee, injections for treatment of arthritis, past 6 months); *V00AGE* (Age when entering study); *A2AP.norm.log* (normalized values of protein A2AP (Alpha 2-antiplasmin); *V00BPSYS* (Blood pressure: systolic); *V00KOOSKPR* (Right knee, KOOS Pain Score); *P01SXKOA* (Baseline symptomatic knee OA status by person); *V00KOOSQOL* (KOOS Quality of Life Score); *COMP.norm.log* (normalized values of protein COMP (Cartilage oligomeric matrix protein); *APOA4.norm.log* (normalized values of protein APOA4 (Apolipoprotein A4); *V00KOOSYML* (KOOS Symptoms Score); *P01LHBE* (Left hand exam: total number of bony enlargements); *V00COXIBS* (Used COXIBS for joint pain or arthritis more than half the days of the month, past 30 days). *SAMP.norm.log* (normalized values of protein SAMP (Small Archaeal Modifier Protein).

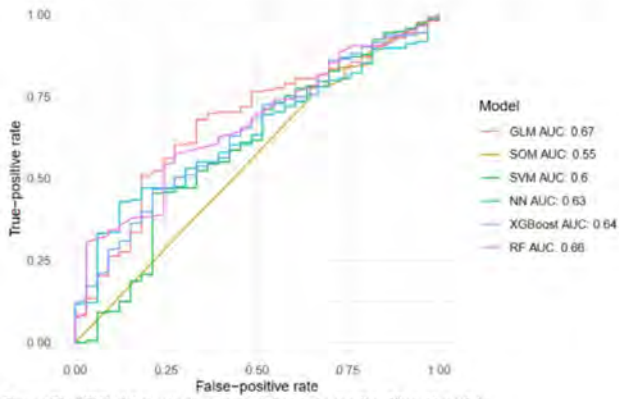


Figure 2b. *ROC plot comparison for test data between the different models.*

Figure 2. Variable importance for GLMnet dataset. Figure 2b. ROC comparison for test in the dataset.

Results: After applying Recursive Feature Elimination (RFE), the dataset included 2812 individuals and 20 variables, with 240 rapid progressors. We then applied various machine learning algorithms and compared their performance across training and testing subsets in both datasets. Among the models tested, the GLMnet model demonstrated the best performance with AUC of 0.67 (Figure 2a and 2b).

Conclusion: While promising, its full potential requires validation with additional cohorts to ensure robustness. This tool could prove invaluable for the early identification of patients at risk of rapid structural progression of OA, enabling timely interventions that could significantly improve both patient outcomes and the effectiveness of early treatment strategies.

Funding: This work was funded by Pfizer inc & Elli Lilly and Company through the 3rd Global Awards for Advancin Chronic Pain Reserah, ADVANCE (Grand ID#64122119)

Disclosure: M. Gonzalez Hernandez: None; **I. rego Pérez**: None; **I. Rodríguez Valle**: None; **J. Vázquez García**: None; **V. Balboa**: None; **S. Relaño Fernández**: None; **M. de Andrés**: None; **L. Lourido**: None; **V. Calamia**: None; **R. Paz González**: None; **P. Quaranta**: None; **P. Fernández-Puente**: None; **N. Veronese**: None; **C. Ruiz-Romero**: None; **N. Oreiro**: None; **f. Blanco**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0330

Prevalence of Radiographic and Symptomatic Osteoarthritis, and Ultrasound Features at the Knee: The Johnston County Health Study

Maya Patel[1], Carolina Alvarez[2], Todd Schwartz[3], Tessa Walker[1], Serena Savage-Guin[1], Jordan Renner[1], Jonathan Samuels[4], Janice Lin[5], Minna Kohler[6], Catherine Bakewell[7], Yvonne Golightly[8] and Amanda Nelson[1], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]University of North Carolina-Chapel Hill, Chapel Hill, NC, [4]NYU Langone, Rye Brook, NY, [5]Stanford University, Palo Alto, CA, [6]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [7]Intermountain Healthcare, Salt Lake City, UT, [8]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To report sex and BMI differences among ultrasound (US) features of knee osteoarthritis (KOA), patient-reported symptoms (Ksx), radiographic KOA (rKOA), and symptomatic KOA (sxKOA), in a general population.

Methods: Johnston County Health Study participants (JoCoHS, 2019-24, n=902) provided data on demographics, comorbidities, clinical features and symptoms, along with imaging using standardized acquisition and scoring. Prevalence (weighted to the 2020 census population for Johnston County, North Carolina) estimates and 95% confidence intervals (CI) for Ksx, rKOA, sxKOA, severe rKOA, and US features were calculated overall and for sex and BMI subgroups, at the person-level under a stratified sampling design. No formal testing is performed for differences among subgroups, instead CI indicate precision of estimates and the overlap among subgroups. RKOA was defined as Kellgren-Lawrence grade ≥ 2, severe rKOA as grades 3-4, and sxKOA as both rKOA and Ksx in the same knee. Standardized US features were obtained as previously reported (PMID39989271).

Results: The population was majority female (67%), non-Hispanic white (66%) with an average age of 55 ± 10 years and average BMI of 33 ± 8 kg/m^2. Of these, 861 individuals had US imaging (no major demographic differences existed compared to the overall group). The overall weighted prevalence of Ksx, rKOA, sxKOA, and severe rKOA, were 61%, 36%, 27%, and 21%, respectively, and all were higher among females and participants with overweight/obesity (Table 1). Among both sexes, rKOA, sxKOA, and severe rKOA were more prevalent among those with severe obesity compared to those with

Table 1. Weighted* knee prevalence estimates (%) and corresponding 95% confidence intervals by sex and BMI category in the JoCoHS cohort 2019-2024, N=902

Sex	BMI group	Ksx	rKOA	Severe rKOA	sxKOA
	kg/m^2	% (95% CI)			
Female					
	Overall (range 17-71)	62.1 (57.4, 66.8)	37.1 (32.4, 41.7)	22.7 (18.7, 26.8)	27.8 (23.6, 32.0)
	Normal (18.5-24.9)	44.0 (31.8, 56.3)	12.5 (5.3, 19.8)	7.2 (1.1, 13.4)	7.3 (2.4, 12.2)
	Overweight (25-29.9)	53.3 (43.1, 63.6)	21.9 (12.5, 31.2)	11.8 (3.3, 20.3)	11.8 (4.4, 19.3)
	Obesity (30-39.9)	63.9 (56.6, 71.2)	42.5 (35.0, 50.1)	23.7 (17.2, 30.2)	32.3 (25.1, 39.5)
	Severe obesity (40+)	84.2 (77.4, 91.0)	63.7 (53.9, 73.5)	46.6 (37.0, 56.3)	54.7 (44.8, 64.6)
Male					
	Overall (range 17-71)	58.9 (52.6, 65.1)	35.2 (29.3, 41.1)	19.9 (15.1, 24.6)	26.0 (20.7, 31.3)
	Normal (18.5-24.9)	58.7 (38.9, 78.5)	23.7 (8.7, 38.6)	14.3 (1.3, 27.4)	20.1 (5.9, 34.4)
	Overweight (25-29.9)	49.7 (37.0, 62.5)	30.4 (19.1, 41.7)	14.4 (6.4, 22.5)	19.2 (10.1, 28.2)
	Obesity (30-39.9)	63.8 (55.2, 72.4)	35.1 (26.6, 43.6)	20.0 (13.2, 26.8)	27.1 (19.1, 35.2)
	Severe obesity (40+)	58.6 (42.2, 74.9)	52.1 (35.2, 69.0)	32.5 (17.7, 47.4)	37.7 (22.9, 52.6)

*Weighted to the 2020 target population for Johnston County, NC; ne=not estimable due to cross-tabulation cell sizes<5

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 Weighted* knee US prevalence estimates (%) and corresponding 95% confidence intervals (CI) by sex, of the of the JoCoHS cohort 2019-2024, N=861

US features (not mutually exclusive)	Female	Male
	Weighted % (95% CI)	Weighted % (95% CI)
GS effusion/synovitis 1: a small hypo/anechoic line beneath the capsule	47.4 (42.5, 52.3)	54.8 (48.5, 61.1)
GS effusion/synovitis 2: elevated joint capsule parallel to joint area	25.3 (21.1, 29.6)	40.5 (34.3, 46.7)
GS effusion/synovitis 3: convex distension of the joint capsule	3.5 (1.8, 5.2)	8.9 (5.5, 12.4)
GS synovitis 1: minimal distention of recess by hypo/anechoic material	42.5 (37.7, 47.4)	49.7 (43.4, 56.1)
GS synovitis 2: moderate distention with flat or concave limit	26.9 (22.5, 31.3)	40.7 (34.4, 46.9)
GS synovitis 3: severe or bulging distention of joint recess	2.7 (1.4, 4.0)	8.8 (5.4, 12.2)
GS effusion: abnormal hypo/anechoic intra-articular material	41.9 (37.1, 46.7)	64.0 (57.8, 70.1)
Suprapatellar PD for synovitis 1: trace to 10% intra-articular color signal	31.1 (26.8, 35.4)	37.7 (31.5, 43.9)
Suprapatellar PD for synovitis 2: 10% or more intra-articular color signal	5.7 (3.5, 7.9)	7.1 (3.9, 10.2)
Osteophytes, medial tibiofemoral 1: small but distinct	35.2 (30.6, 39.9)	32.6 (26.7, 38.5)
Osteophytes, medial tibiofemoral 2: medium/larger	18.3 (14.5, 22.1)	16.6 (12.3, 21.0)
Osteophytes, medial tibiofemoral 3: large, bulky, prominent	5.4 (3.8, 7.0)	7.3 (4.2, 10.4)
Osteophytes, lateral tibiofemoral 1: small but distinct	36.8 (32.0, 41.6)	34.3 (28.4, 40.2)
Osteophytes, lateral tibiofemoral 2: medium/larger	17.5 (14.0, 21.0)	13.7 (9.5, 18.0)
Osteophytes, lateral tibiofemoral 3: large, bulky, prominent	2.6 (1.3, 4.0)	2.0 (0.6, 3.3)
Meniscal extrusion, medial tibiofemoral	22.7 (18.6, 26.9)	15.6 (11.2, 19.9)
Meniscal extrusion, lateral tibiofemoral	31.3 (26.7, 35.8)	25.8 (20.6, 31.1)
Cartilage damage, medial femur/trochlea 1: hyperechoic, loss of sharpness	71.1 (66.6, 75.5)	61.5 (55.4, 67.7)
Cartilage damage, medial femur/trochlea 2: localized thinning	41.7 (36.9, 46.5)	28.3 (22.6, 33.9)
Cartilage damage, medial femur/trochlea 3: complete cartilage loss	7.1 (4.8, 9.4)	3.1 (1.1, 5.1)
Cartilage damage, lateral femur/trochlea 1: hyperechoic, loss of sharpness	68.0 (63.3, 72.7)	59.2 (53.0, 65.5)
Cartilage damage, lateral femur/trochlea 2: localized thinning	34.4 (29.8, 39.0)	22.5 (17.5, 27.5)
Cartilage damage, lateral femur/trochlea 3: complete cartilage loss	5.9 (4.0, 7.8)	5.5 (2.6, 8.3)
Popliteal cyst 1: small/possible	53.9 (48.9, 58.9)	51.9 (45.4, 58.4)
Popliteal cyst 2: definite	6.5 (4.4, 8.5)	6.3 (3.6, 9.0)
Calcium crystal deposition, any view	21.3 (17.1, 25.5)	19.1 (14.5, 23.7)

*Weighted to the 2020 target population for Johnston County, NC; ne=not estimable due to cross-tabulation cell sizes<5
GS: greyscale; PD: power doppler

obesity (Table 1). Among those with severe obesity, the prevalence of Ksx was greater among females than males with non-overlapping confidence intervals (Table 1).

Mild (grade 1) US features were seen in one-third to one-half of knees. Grey-scale (GS) effusion and synovitis were more prevalent among males compared with females, particularly when moderate or severe (Table 2). In contrast, US findings of medial and lateral cartilage damage were more prevalent in females than males (Table 2). With increasing levels of obesity, effusion/synovitis were less prevalent while osteophytes and medial cartilage damage were more prevalent (Table 3).

Table 3 Weighted* knee US prevalence estimates (%) and corresponding 95% confidence intervals (CI) by BMI group, of the of the JoCoHS cohort 2019-2024, N=861

US features (not mutually exclusive)	BMI: normal	BMI: overweight	BMI: obesity	BMI: severe obesity
	Weighted % (95% CI)	Weighted % (95% CI)	Weighted % (95% CI)	Weighted % (95% CI)
GS effusion/synovitis 1: a small hypo/anechoic line beneath the capsule	57.8 (46.8, 68.9)	55.5 (47.6, 63.4)	47.3 (41.2, 53.4)	46.6 (37.3, 56.0)
GS effusion/synovitis 2: elevated joint capsule parallel to joint area	30.3 (21.4, 39.2)	38.5 (30.6, 46.3)	32.7 (27.0, 38.3)	25.5 (17.5, 33.5)
GS effusion/synovitis 3: convex distension of the joint capsule	5.5 (1.2, 9.8)	4.7 (1.3, 8.1)	7.3 (4.1, 10.6)	5.2 (1.8, 8.6)
GS synovitis 1: minimal distention of recess by hypo/anechoic material	46.2 (34.8, 57.7)	53.4 (45.5, 61.3)	42.1 (36.0, 48.1)	43.1 (33.7, 52.6)
GS synovitis 2: moderate distention with flat or concave limit	33.1 (24.0, 42.2)	37.5 (29.8, 45.3)	35.0 (29.2, 40.8)	24.1 (16.4, 31.9)
GS synovitis 3: severe or bulging distention of joint recess	5.7 (1.3, 10.1)	5.1 (1.6, 8.6)	5.8 (3.0, 8.7)	5.4 (2.0, 8.9)
GS effusion: abnormal hypo/anechoic intra-articular material	67.1 (57.0, 77.2)	56.2 (48.4, 64.0)	49.2 (43.0, 55.4)	43.3 (33.9, 52.6)
Suprapatellar PD for synovitis 1: trace to 10% intra-articular color signal	50.7 (39.9, 61.4)	31.8 (24.8, 38.8)	33.6 (27.5, 39.7)	26.6 (19.6, 33.6)
Suprapatellar PD for synovitis 2: 10% or more intra-articular color signal	6.1 (0.9, 11.3)	7.2 (3.1, 11.3)	6.9 (3.8, 10.0)	4.1 (1.5, 6.8)
Osteophytes, medial tibiofemoral 1: small but distinct	19.7 (11.5, 28.0)	31.2 (23.7, 38.6)	39.3 (33.4, 45.2)	36.8 (27.9, 45.7)
Osteophytes, medial tibiofemoral 2: medium/larger	4.9 (0.6, 9.2)	11.0 (5.9, 16.2)	19.0 (14.3, 23.7)	33.0 (24.3, 41.7)
Osteophytes, medial tibiofemoral 3: large, bulky, prominent	ne	1.8 (0.3, 3.3)	5.6 (2.9, 8.4)	17.2 (11.4, 23.0)
Osteophytes, lateral tibiofemoral 1: small but distinct	26.4 (17.4, 35.5)	31.8 (24.4, 39.2)	37.7 (31.8, 43.6)	43.5 (34.4, 52.5)
Osteophytes, lateral tibiofemoral 2: medium/larger	4.8 (1.4, 8.2)	13.3 (7.8, 18.8)	16.4 (12.2, 20.6)	28.4 (18.3, 34.5)
Osteophytes, lateral tibiofemoral 3: large, bulky, prominent	ne	2.1 (0.0, 4.4)	1.5 (0.5, 2.5)	4.7 (1.6, 7.8)
Meniscal extrusion, medial tibiofemoral	15.3 (7.7, 22.9)	14.6 (8.8, 20.4)	20.3 (15.4, 25.1)	27.8 (20.5, 35.0)
Meniscal extrusion, lateral tibiofemoral	31.1 (21.0, 41.2)	22.7 (16.2, 29.3)	31.9 (26.5, 37.3)	27.4 (19.8, 34.9)
Cartilage damage, medial femur/trochlea 1: hyperechoic, loss of sharpness	69.5 (60.1, 78.8)	66.5 (59.0, 73.9)	64.7 (58.5, 70.8)	68.9 (61.4, 76.3)
Cartilage damage, medial femur/trochlea 2: localized thinning	24.1 (15.6, 32.6)	37.4 (29.7, 45.1)	34.2 (28.7, 39.7)	45.4 (36.6, 54.3)
Cartilage damage, medial femur/trochlea 3: complete cartilage loss	4.4 (0.4, 8.4)	3.9 (1.3, 6.5)	5.7 (3.1, 8.3)	6.8 (3.5, 10.1)
Cartilage damage, lateral femur/trochlea 1: hyperechoic, loss of sharpness	53.7 (42.4, 65.0)	59.2 (51.3, 67.1)	68.7 (62.9, 74.5)	66.7 (58.0, 75.5)
Cartilage damage, lateral femur/trochlea 2: localized thinning	31.1 (21.9, 40.3)	28.5 (21.4, 35.7)	27.6 (22.4, 32.8)	30.7 (23.3, 38.0)
Cartilage damage, lateral femur/trochlea 3: complete cartilage loss	ne	6.7 (2.9, 10.5)	4.3 (2.3, 6.3)	10.7 (5.2, 16.3)
Popliteal cyst 1: small/possible	56.5 (45.6, 67.4)	44.3 (36.5, 52.2)	56.1 (50.0, 62.2)	56.5 (47.0, 66.0)
Popliteal cyst 2: definite	5.7 (1.8, 9.5)	5.6 (2.5, 8.7)	6.3 (3.7, 8.8)	7.1 (3.0, 11.2)
Calcium crystal deposition, any view	20.4 (12.9, 27.8)	24.4 (17.6, 31.2)	22.0 (17.1, 26.9)	11.2 (6.1, 16.2)

*Weighted to the 2020 target population for Johnston County, NC; ne=not estimable due to cross-tabulation cell sizes<5; GS: grayscale; PD: power doppler

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Additionally, among knees with rKOA compared to those without, osteophytes, meniscal extrusion, calcium crystals, and moderate to severe cartilage damage were much more prevalent (data not shown).

Conclusion: We identified differences in the prevalence of US features of KOA, Ksx, rKOA, sxKOA, and severe rKOA particularly among females with severe obesity. Prior prevalence studies have not distinguished between obesity and severe obesity, due to the relatively small proportion of the population within the severe obesity category. The data above reveals non-overlapping 95% confidence intervals in outcome prevalence among levels of obesity, which should be investigated further. This differentiation could lead to the development of more effective prevention and treatment strategies, as well as a better understanding of the distinct mechanisms driving knee OA in individuals with severe obesity.

Disclosure: M. Patel: None; **C. Alvarez**: None; **T. Schwartz**: None; **T. Walker**: None; **S. Savage-Guin**: None; **J. Renner**: None; **J. Samuels**: None; **J. Lin**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **C. Bakewell**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 2, 6, UCB, 2, 6; **Y. Golightly**: None; **A. Nelson**: Novo Nordisk, 1.

Abstract Number: 0331

Safety and Efficacy of Colchicine in Osteoarthritis: A Systematic Review and Meta-Analysis of 6,965 Patients

Mohamed Abdelsalam[1], Bassant Elaraby Elsayed Badwy[2], Menat Alla Ayman Ali Mahdy[2], Maryam Lasheen[3], Hadeer Hafez[4], Omar Sameh Nabil El Sedafy[1] and Mohamed Reda Awad[5], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [3]Misr University For Science and Technology, Helwan, Al Qahirah, Egypt, [4]6th October University, 6 october, Al Jizah, Egypt, [5]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is the most common joint disease, that leads to significant pain and affects quality of life, particularly in older adults. Current treatments primarily focus on symptom relief, as no treatment has yet demonstrated the ability to modify disease progression or restore damaged joint structures. Colchicine, a medication traditionally used to treat gout, has attracted interest as a potential therapy for OA due to its anti-inflammatory effects. Despite growing interest, the evidence regarding colchicine efficacy and safety in OA management remains inconclusive. This study aims to assess the safety and efficacy of colchicine in treating OA.

Methods: We conducted a systematic search across multiple databases, such as PubMed, Web of Science, and Scopus from inception till April 5th, 2025. We included randomized clinical trials evaluating the efficacy and safety of colchicine in OA (Fig 1). The main outcome was pain measured by visual analogue scale (VAS). We stratified the outcome into three follow-up intervals: short-term (4 and 8 weeks), medium-term (10, 12 and 16 weeks), and long-term (20 and 24 weeks or longer). We used Rayyan for identifying duplicates, title, abstract and full-text screening and Review Manager (RevMan) software Version 5.4 for meta-analysis.

Results: This systematic review and meta-analysis incorporates data from a total of 21 clinical trials encompassing 6,965 participants, with 13 contributing to the meta-analysis including 879 participants. The main objective was to assess the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

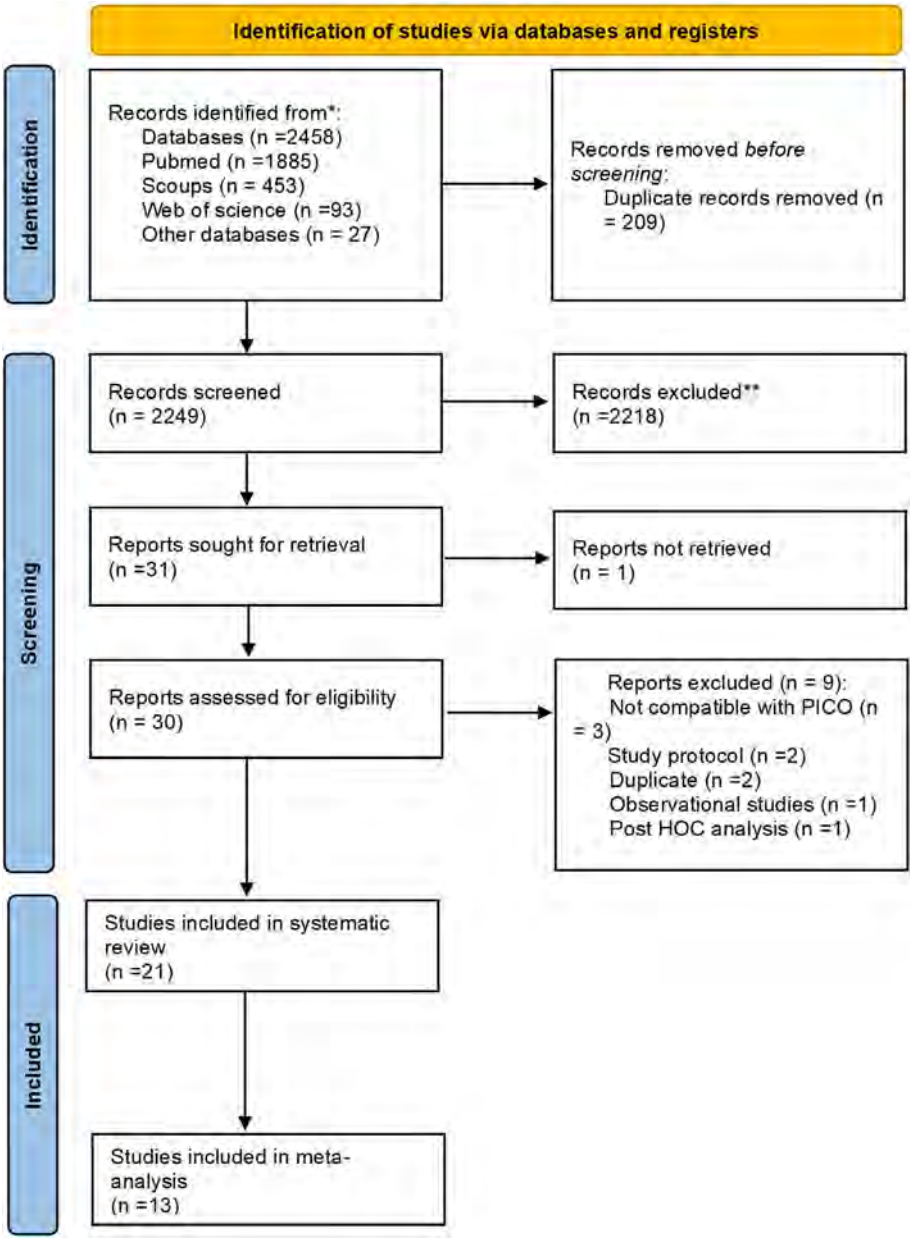


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

efficacy of colchicine across multiple outcome measures. Pain relief, assessed by VAS, exhibited a significant short-term improvement at week 8 (standardized mean difference [SMD] = -1.03, 95% confidence interval [CI]: -2.01, -0.06, p=0.04), and a non-significant improvement at medium-term follow-up at week 12 (SMD = -0.34, 95% CI: -0.78, 0.10, p=0.75), and a significant long-term improvement at week 20 follow-up (SMD = -1.24, 95% CI: -1.73, -0.76, p< 0.00001), with an overall significant improvement (SMD = -0.73, 95% CI:-1.06, -0.41, p < 0.00001) (Fig 2). Similarly, quality of life indicated significant impact of colchicine treatment (SMD = -0.48, 95% CI: -0.83, -0.12, p =0.008). However, for physical dysfunction, the analysis reveals no statistically significant difference (SMD = -0.21, 95% CI: -0.45, 0.04, p=0.09), with significant difference in adverse events (AEs) (risk ratio [RR]: 1.27; 95% CI:1.07, 1.50, p=0.007) between colchicine and control groups (Fig 3).

Conclusion: This is the most recent and comprehensive systematic review and meta-analysis showing that colchicine is an effective therapeutic option for OA, with significant pain relief measured by VAS score. Additionally, it contributes to improved quality of life in patients with OA. However, physical dysfunction did not show significant differences. Future

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

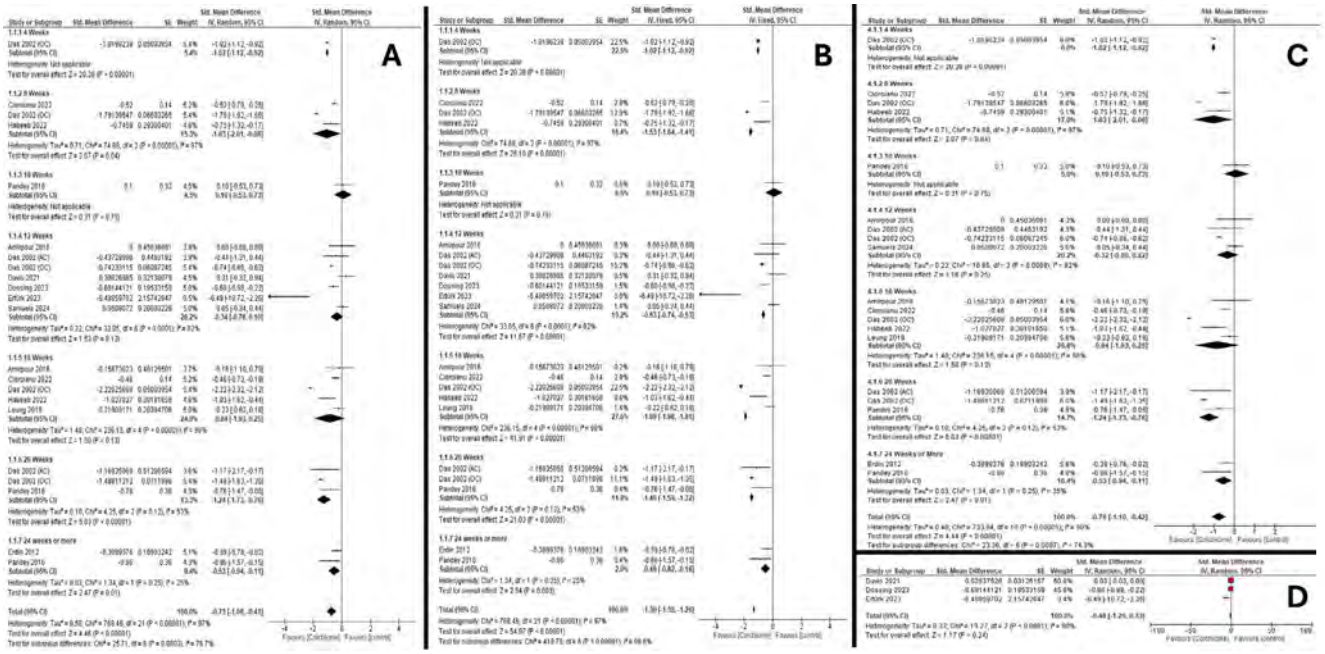


Figure (2) (A) Forest Plot of Pain Reduction (VAS) at Various Time Points (Random-Effects Model. Forest plot of pain reduction measured using VAS at various time points. The plot includes subgroups based on follow-up duration. Subgroup at 4 Weeks: Studies included: Das 2002 (OC). Subgroup at 8 Weeks: Studies included: Cioroianu 2022, Das 2002 (OC), Habeeb 2022. Subgroup at 10 Weeks: Studies included: Pandey 2016. Subgroup at 12 Weeks: Studies included: Amirpour 2016, Das 2002 (AC), Das 2002 (OC), Davis 2021, Dossing 2023, Erturk 2023, Samuel 2024. Subgroup at 16 Weeks: Studies included: Amirpour 2016, Cioroianu 2022, Das 2002 (OC), Habeeb 2022, Leung 2018. Subgroup at 20 Weeks: Studies included: Das 2002 (OC), Pandey 2016. Subgroup at 24 Weeks or More: Studies included: Erdin 2012, Pandey 2016. Overall: The plot shows a significant SMD in pain reduction of -0.73 (95% CI: -1.06 to -0.41), with considerable heterogeneity (I^2 = 97%). Test for overall effect: Z = 4.46 (P < 0.00001). Test for subgroup differences: Chi^2 = 25.71, df = 6 (P = 0.0003), I^2 = 76.7%. (B). Forest Plot of Pain Reduction (VAS) at Various Time Points (Fixed-Effects Model) Studies Included same as the Random effect model. Overall: The plot shows a significant SMD in pain reduction of -1.30 (95% CI: -1.35 to -1.26), with considerable heterogeneity (I^2 = 97%). Test for overall effect: Z = 64.97 (P < 0.00001). Test for subgroup differences: Chi^2 = 418.79, df = 6 (P < 0.00001), I^2 = 98.6%. (C) Forest Plot of KOA Pain Reduction (VAS) at Various Time Points (Random-Effects Model): The plot includes subgroups based on follow-up duration: Subgroup at 4 Weeks: Studies included: Das 2002 (OC). Subgroup at 8 Weeks: Studies included: Cioroianu 2022, Das 2002 (OC), Habeeb 2022. Subgroup at 10 Weeks: Studies included: Pandey 2016. Subgroup at 12 Weeks: Studies included: Amirpour 2016, Das 2002 (AC), Das 2002 (OC), Samuel 2024. Subgroup at 16 Weeks: Studies included: Amirpour 2016, Cioroianu 2022, Das 2002 (OC), Habeeb 2022, Leung 2018. Subgroup at 20 Weeks: Studies included: Das 2002 (AC), Das 2002 (OC), Pandey 2016. Subgroup at 24 Weeks or More: Studies included: Erdin 2012, Pandey 2016. Overall: The plot shows a significant mean difference in pain reduction of -0.76 (95% CI: -1.10 to -0.42), with high heterogeneity (I^2 = 98%). Test for overall effect: Z = 4.44 (P < 0.00001). Test for subgroup differences: Chi^2 = 23.36, df = 6 (P < 0.0007), I^2 = 74.3%. (D): Forest Plot of HOA Pain Reduction (VAS) (Random-Effects Model) Studies included: Davis 2021, Dossing 2023, Erturk 2023. Overall: The plot shows a non-significant SMD in pain reduction of -0.48 (95% CI: -1.29 to 0.33), with high heterogeneity (I2=90%). Test for overall effect: Z=1.17(P=0.24). Heterogeneity Tau2=0.33, Chi2=19.22, df=2 (P<0.0001) CI, confidence interval; df, degrees of freedom; IV, inverse variance; SMD, standardized mean difference; VAS, Visual Analog Scale.

research should focus on optimal dosing, long-term safety, and larger randomized controlled trials to validate these findings.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

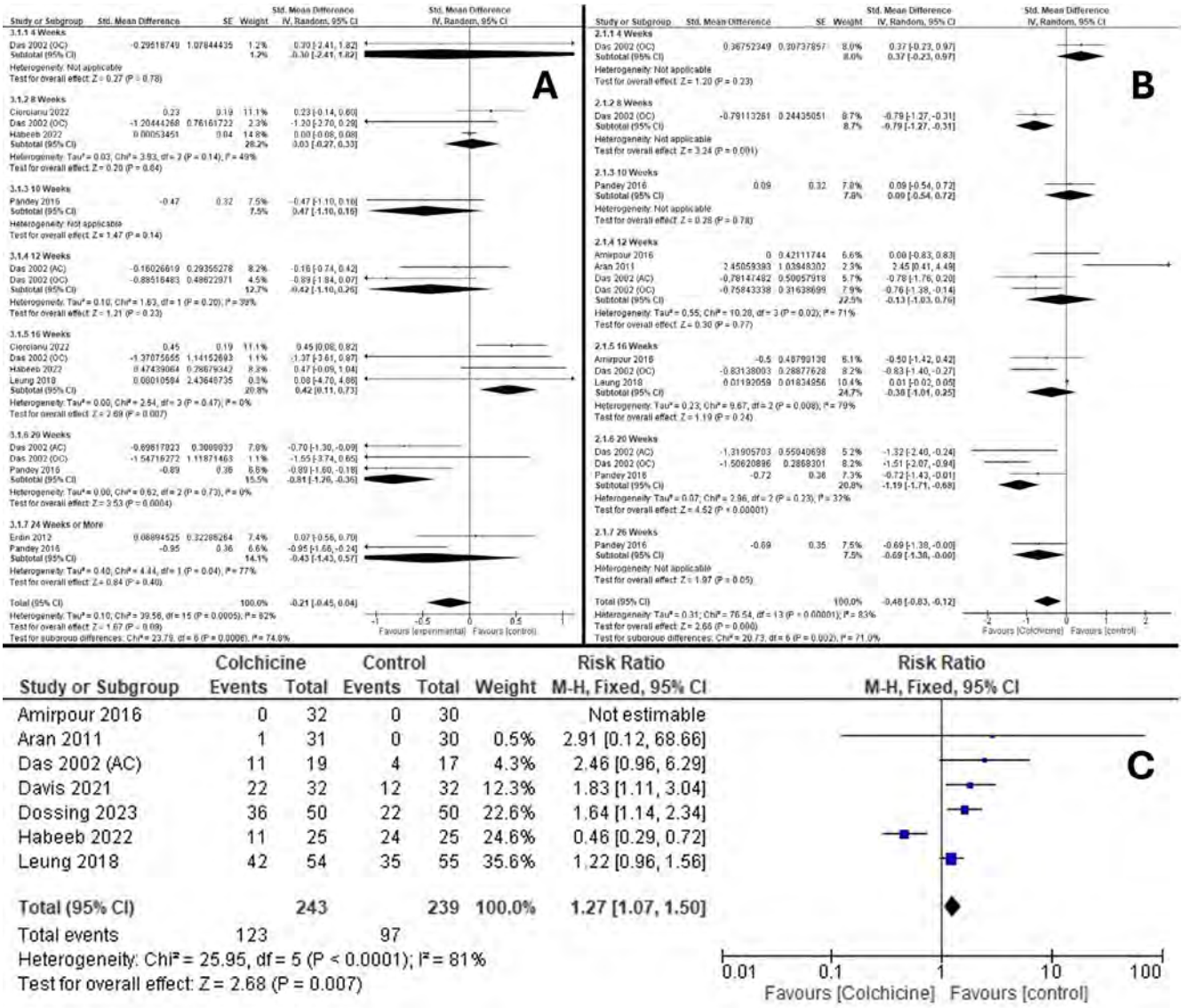


Figure (3) (A): Forest Plot of Physical Dysfunction Improvement (WOMAC) (Random-Effects Model) The plot includes subgroups based on follow-up duration: Subgroup at 4 Weeks: Studies included: Das 2002 (OC). Subgroup at 8 Weeks: Studies included: Cioroianu 2022, Das 2002 (OC), Habeeb 2022. Subgroup at 10 Weeks: Studies included: Pandey 2016. Subgroup at 12 Weeks: Studies included: Das 2002 (AC), Das 2002 (OC). Subgroup at 16 Weeks: Studies included: Cioroianu 2022, Das 2002 (OC), Habeeb 2022, Leung 2018. Subgroup at 20 Weeks: Studies included: Das 2002 (AC), Das 2002 (OC), Pandey 2016. Subgroup at 24 Weeks or More: Studies included: Erdin 2012, Pandey 2016. Overall: The plot shows a non-significant standardized mean difference (SMD) in physical dysfunction improvement of -0.21 (95% CI: -0.45 to 0.04), with moderate heterogeneity (I2=62%). Test for overall effect: Z=1.67(P=0.09). Heterogeneity: Tau2=0.10,Chi2=39.56,df=15(P=0.0005). Test for subgroup differences: Chi2=23.79,df=6(P=0.0006),I2=74.8%. (B): Forest Plot of Quality of Life (QoL) Improvement (Random-Effects Model) The plot includes subgroups based on follow-up duration: Subgroup at 4 Weeks: Studies included: Das 2002 (OC). Subgroup at 8 Weeks: Studies included: Das 2002 (OC). Subgroup at 10 Weeks: Studies included: Pandey 2016. Subgroup at 12 Weeks: Studies included: Aminpour 2016, Aran 2011, Das 2002 (AC), Das 2002 (OC). Subgroup at 16 Weeks: Studies included: Aminpour 2016, Das 2002 (OC), Leung 2018. Subgroup 20 Weeks: Studies included: Das 2002 (AC), Das 2002 (OC), Pandey 2016. Subgroup at 26 Weeks: Studies included: Pandey 2016. Overall: The plot shows a significant SMD in QoL improvement of -0.48 (95% CI: -0.83 to -0.12), with considerable heterogeneity (I2=83%). Test for overall effect: Z=2.66(P=0.008). Heterogeneity: Tau2=0.31,Chi2=76.54,df=13(P<0.00001). Test for subgroup differences: Chi2=20.73, df=6 (P=0.002), I2=71.0%. (C): Forest Plot of Adverse Events in Colchicine vs Control groups (Fixed-Effects Model) Studies included: Amirpour 2016, Aran 2011, Das 2002 (AC), Davis 2021, Dossing 2023, Habeeb 2022, Leung 2018. Overall: The plot shows a significant RR in pain reduction of -1.27 (95% CI: 1.07 to 1.50), with Considerable heterogeneity (I2=81%). CI, confidence interval; df, degrees of freedom; IV, inverse variance; SMD, standardized mean difference; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; RR, Risk Ratio; QoL, Quality of Life.

Disclosure: M. Abdelsalam: None; **B. Badwy**: None; **M. Mahdy**: None; **M. Lasheen**: None; **H. Hafez**: None; **O. El Sedafy**: None; **M. Awad**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0332

Safety, Short- and Long-Term Efficacy of Methotrexate in Osteoarthritis: A Systematic Review and Meta-Analysis

Mohamed Abdelsalam[1], Maryam Lasheen[2], Hadeer Hafez[3], Bassant Elaraby Elsayed Badwy[4], Omar Sameh Nabil El Sedafy[1] and Mohamed Reda Awad[5], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]Misr University For Science and Technology, Helwan, Al Qahirah, Egypt, [3]6th October University, 6 october, Al Jizah, Egypt, [4]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [5]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate (MTX), traditionally used for inflammatory conditions like rheumatoid arthritis, has well-established anti-inflammatory properties, recently gained interest as a potential therapeutic option for osteoarthritis (OA). Current treatments largely focus on symptom management, with limited options for altering disease course. This study aims to evaluate the safety and efficacy of MTX in reducing OA symptoms in both the short and long term.

Methods: We systematically searched PubMed, Web of Science, Embase, Ovid, and Scopus from inception to April 22, 2025. Studies evaluating the safety and efficacy of MTX in OA were included (Fig. 1). The primary outcome was pain, measured by the Visual Analogue Scale (VAS) or Numeric Rating Scale (NRS). Outcomes were stratified by follow-up duration: short-term (less than 6 months), medium-term (6 months and 9 months), and long-term (12 months). Data were extracted and analyzed using Review Manager 5.4 (RevMan) software.

Results: This systematic review and meta-analysis included 14 studies in the qualitative synthesis and 8 in the meta-analysis, encompassing 1251 and 649 patients, respectively. MTX significantly reduced pain (SMD: –0.47; 95% CI: –0.68 to –0.26). Subgroup analyses by treatment duration showed SMDs of –0.46 (95% CI: –0.75 to –0.17) at < 6 months, –0.75 (95% CI: –1.2 to –0.29) at 6 months, –0.42 (95% CI: –1.35 to 0.51) at 9 months, and –0.06 (95% CI: –0.46 to 0.34) at 12 months. For the WOMAC score, MTX had a significant overall effect (SMD: –0.71; 95% CI: –1.2 to –0.22), with subgroup SMDs of –0.45 (95% CI: –0.88 to –0.01) at < 6 months, –1.81 (95% CI: –4.56 to 0.94) at 6 months, –0.37 (95% CI: –0.78 to 0.04) at 9 months, and –0.27 (95% CI: –0.68 to 0.13) at 12 months. For physical function, the overall effect was significant (SMD: –0.53; 95% CI: –0.84 to –0.23), with subgroup SMDs of –0.46 (95% CI: –0.76 to –0.16) at < 6 months, –0.88 (95% CI: –1.73 to –0.03) at 6 months, –0.35 (95% CI: –0.81 to 0.12) at 9 months, and –0.19 (95% CI: –0.58 to 0.19) at 12 months. On stiffness, MTX also had an overall significant effect (SMD: –0.44; 95% CI: –0.65 to –0.23). Subgroup SMDs were –0.33 (95% CI: –0.68 to 0.01) at < 6 months, –0.52 (95% CI: –0.81 to –0.24) at 6 months, –0.39 (95% CI: –1.49 to 0.72) at 9 months, and –0.34 (95% CI: –1.43 to 0.75) at 12 months (Fig. 2). Our results stated that there is an overall significant difference in adverse events (AEs) (RR, 0.75; 95% CI, 0.60 to 0.94), with a significant difference in mild AEs (RR, 0.77; 95% CI, 0.61 to 0.97) and no significant difference in serious AEs (RR, 0.65; 95% CI, 0.31 to 1.34) (Fig. 3).

Conclusion: MTX provides significant short- and medium-term improvements in pain, stiffness, and physical function in OA, with the most pronounced benefit observed at 6 months. However, its safety profile in real-world settings requires more thorough investigation. Further large-scale randomized controlled trials are needed to confirm these findings and assess long-term efficacy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

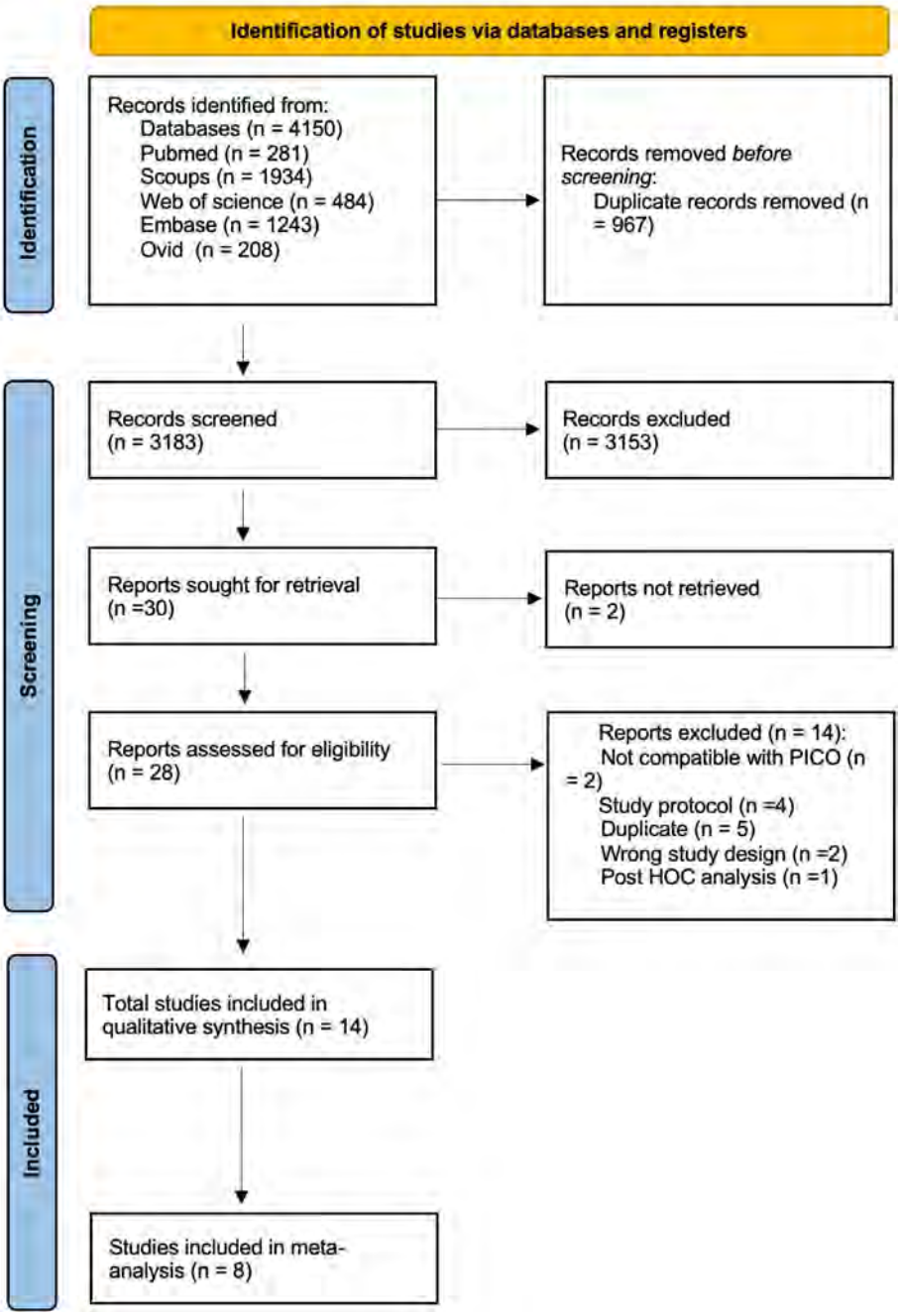


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

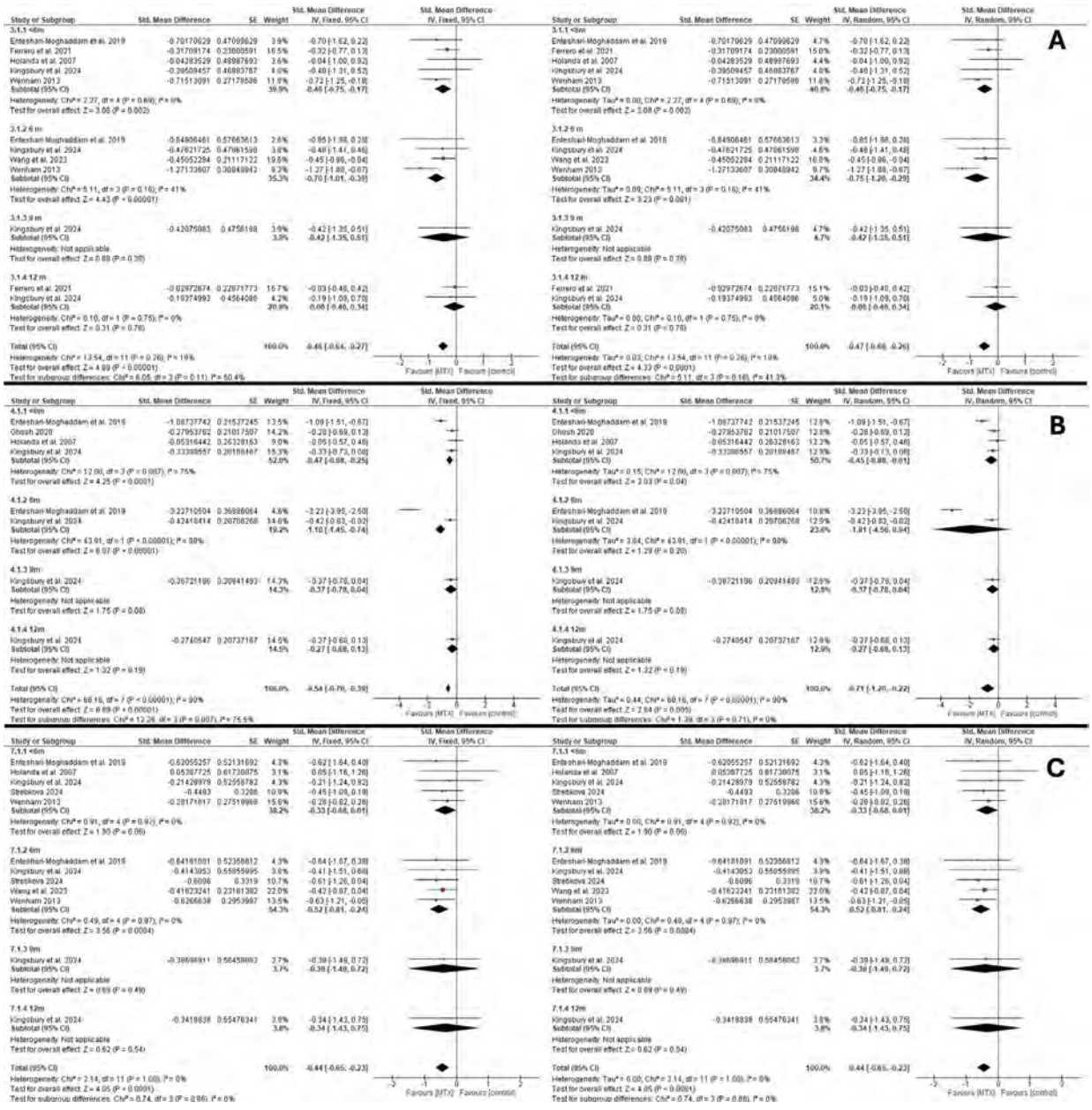


Figure (2) Forest Plots of Treatment Effects for MTX in OA by Follow-Up Duration. (A) Pain Reduction (Fixed-Effects Model): Subgroups:<6 months: Studies included: Enteshari-Moghaddam et al. 2019, Ferrero et al. 2021, Holanda et al. 2007, Kingsbury et al. 2024, Wenham 2013. 6 months: Studies included: Enteshari-Moghaddam et al. 2019, Kingsbury et al. 2024, Wang et al. 2023, Wenham 2013. 9 months: Studies included: Kingsbury et al. 2024. 12 months: Studies included: Ferrero et al. 2021, Kingsbury et al. 2024. Overall: Significant standardized mean difference (SMD) in pain reduction: -0.46 (95% CI: -0.64 to -0.27), with low heterogeneity (I2=19%). Test for overall effect: Z=4.89 (P<0.00001). Test for subgroup differences: χ2=6.05, df=3 (P=0.11), I2=50.4%. (A) Pain Reduction (Random-Effects Model): Studies included: Same as fixed-effects model. Overall: Significant SMD: -0.47 (95% CI: -0.68 to -0.26), with a heterogeneity of (I2=19%). Test for overall effect: Z=4.33 (P<0.0001). Test for subgroup differences: χ2=5.11, df=3 (P=0.16), I2=41.3%. (B) WOMAC Improvement (Fixed-Effects Model): Subgroups:<6 months: Studies included: Enteshari-Moghaddam et al. 2019, Ghosh 2020, Holanda et al. 2007, Kingsbury et al. 2024. 6 months: Studies included: Enteshari-Moghaddam et al. 2019, Kingsbury et al. 2024. 9 months: Studies included: Kingsbury et al. 2024. 12 months: Studies included: Kingsbury et al. 2024. Overall: Significant SMD in WOMAC improvement: -0.54 (95% CI: -0.70 to -0.39), with Considerable heterogeneity (I2=90%). Test for overall effect: Z=6.89 (P<0.00001). Test for subgroup differences: χ2=12.26, df=3 (P=0.007), I2=75.5%. (C) Stiffness Reduction (Fixed-Effects Model): Subgroups: <6 months: Studies included: Enteshari-Moghaddam et al. 2019, Holanda et al. 2007, Kingsbury et al. 2024, Strebkova 2024, Wenham 2013. 6 months: Studies included: Enteshari-Moghaddam et al. 2019, Kingsbury et al. 2024, Strebkova 2024, Wang et al. 2023, Wenham 2013. 9 months: Studies included: Kingsbury et al. 2024. 12 months: Studies included: Kingsbury et al. 2024. Overall: Significant SMD in stiffness reduction: -0.44 (95% CI: -0.65 to -0.23), with no heterogeneity (I2=0%). Test for overall effect: Z=4.05 (P<0.0001). Test for subgroup differences: χ2=0.74, df=3 (P=0.86), (I2=0%) Pain, WOMAC and stiffness reduction showed consistent benefits across time points, with the largest effects at 6 months. Heterogeneity was negligible for stiffness and pain but substantial for WOMAC. CI, confidence interval; SMD, standardized mean difference; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; I2, heterogeneity index; df, degrees of freedom.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

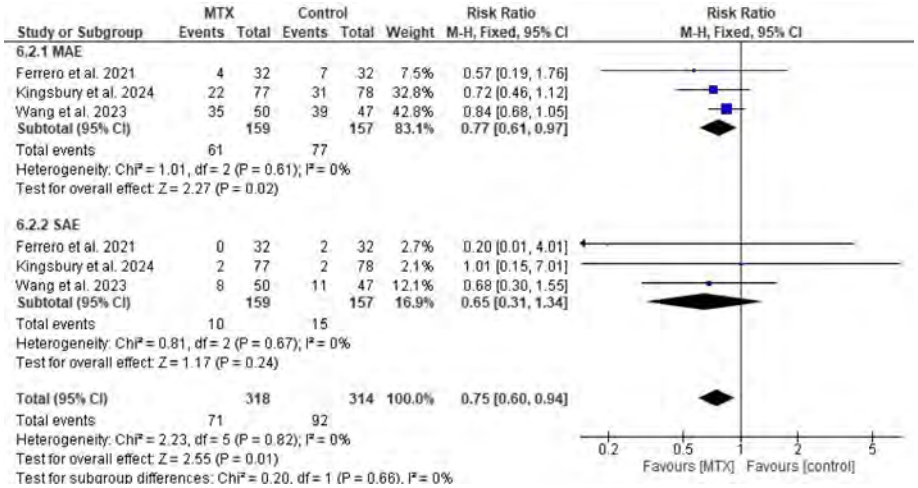


Figure (3) Forest Plot of Adverse Events (AEs) Associated with MTX in Osteoarthritis. MAEs: Subgroup: Studies included: Ferrero et al. 2021, Kingsbury et al. 2024, Wang et al. 2023. Overall: Significant reduction in MAEs with MTX (RR = 0.77; 95% CI: 0.61–0.97), with no heterogeneity (I2=0%). Test for overall effect: Z=2.27 (P=0.02). SAEs: Subgroup: Studies included: Ferrero et al. 2021, Kingsbury et al. 2024, Wang et al. 2023. Overall: Non-significant reduction in SAEs with MTX (RR = 0.65; 95% CI: 0.31–1.34), with no heterogeneity (I2=0%). Test for overall effect: Z=1.17 (P=0.24). Total (MAEs + SAEs): Overall: Significant reduction in total AEs with MTX (RR = 0.75; 95% CI: 0.60–0.94), with no heterogeneity (I2=0%). Test for overall effect: Z=2.55 (P=0.01). Test for subgroup differences (MAE vs. SAE): $\chi 2=0.20$, df=1 (P=0.66), I2=0%. MTX demonstrated a significant reduction in total adverse events, driven primarily by MAEs. SAEs showed a non-significant trend toward reduction and also studies reported that SAEs were not related to MTX. No heterogeneity was observed across studies, and subgroup differences were negligible. CI, confidence interval; MAE, mild adverse event; SAE, serious adverse event; RR, risk ratio; I2, heterogeneity index; df, degrees of freedom.

Disclosure: M. Abdelsalam: None; **M. Lasheen**: None; **H. Hafez**: None; **B. Badwy**: None; **O. El Sedafy**: None; **M. Awad**: None.

Abstract Number: 0333

Diagnostic Test Accuracy of Artificial Intelligence in Early Diagnosis of Osteoarthritis: A Systematic Review and Meta-Analysis of 45,588 Knees

Mohamed Abdelsalam[1], Hadeer Hafez[2], Omar Sameh Nabil El Sedafy[1], Nourhan Abouelella[3], Ahmed Abdulhafeez Hamza[3], Omnia Samy El-Sayed[4], Mohamed Reda Awad[5], Gihan Omar[3] and Hazem E. Mohammed[6], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]6th October University, 6 october, Al Jizah, Egypt, [3]Faculty of Medicine, Misr University for Science and Technology, 6 october, Al Jizah, Egypt, [4]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [5]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt, [6]Faculty of Medicine, Assiut university, Assiut, Egypt, assyut, Asyut, Egypt

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Artificial intelligence (AI) rapid advancement opens new opportunities in the field of rheumatology. With better imaging, AI may help find early osteoarthritic changes that would not have been otherwise detected and help physicians with the diagnosis of early stage of knee osteoarthritis (KOA). The early diagnosis and timely intervention ultimately results in more favorable outcomes for the patients. This study aims to assess the diagnostic accuracy of AI detection and classification of radiographic Kellgren–Lawrence (KL) grades for KOA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

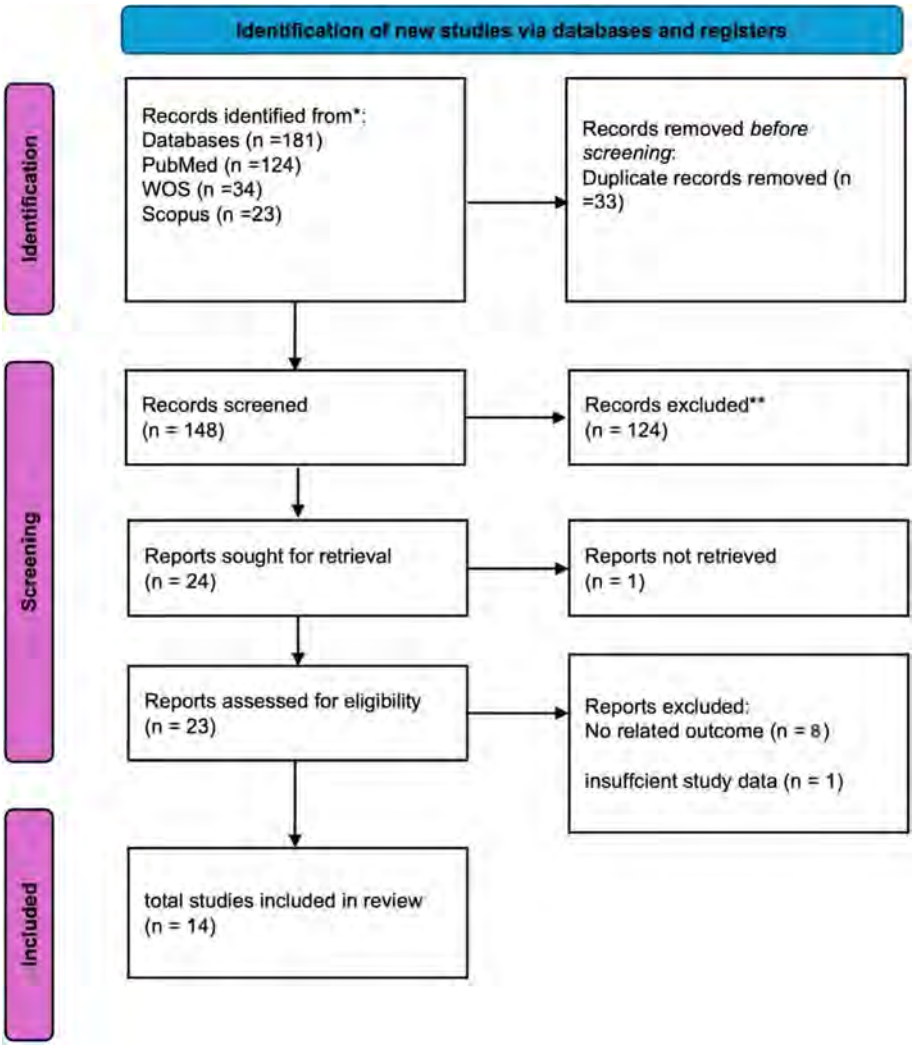


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

Methods: We conducted a systematic search across PubMed, Web of Science, and Scopus databases, covering all available literature up to March 1st, 2025. Following the PRISMA guidelines (Figure 1), we screened and evaluated the methodological quality of the eligible studies, selecting only those deemed to be of high quality and excluding studies without outcome data or insufficient quality. We performed a meta-analysis to estimate pooled sensitivity, pooled specificity, and diagnostic likelihood ratios (LR+/LR-). All analyses were conducted using RStudio version 4.4.2.

Results: A total of 14 studies were included in the systematic review and meta-analysis, encompassing 45588 radiographs. As for KL grading, AI showed robust diagnostic performance across all grades. In KL Grade 0, specificity was 0.954 (95% CI: 0.877–0.984) and sensitivity was 0.829 (95% CI: 0.488–0.961) with Pre Test Probability (PP) of 30%, Post Test Probability +ve (PTP +ve) of 88%, and Post Test Probability -ve (PTP -ve) of 7%. For KL Grade 1, specificity remained high at 0.956 (95% CI: 0.880–0.984), with modest sensitivity of 0.680 (95% CI: 0.392–0.875) and (PP: 20%, PTP +ve: 79%, PTP -ve: 8%). For KL Grade 2, specificity was 0.937 (95% CI: 0.883–0.967), sensitivity was 0.850 (95% CI: 0.733–0.921) and (PP: 25%, PTP +ve: 82%, PTP -ve: 5%). KL Grade 3 yielded a specificity of 0.977 (95% CI: 0.937–0.992), sensitivity of 0.906 (95% CI: 0.793–0.961) and (PP: 15%, PTP +ve: 87%, PTP -ve: 2%). in KL Grade 4, specificity reached 0.995 (95% CI: 0.984–0.999), sensitivity 0.938 (95% CI: 0.800–0.983) and (PP: 10%, PTP +ve: 96%, PTP -ve: 1%).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

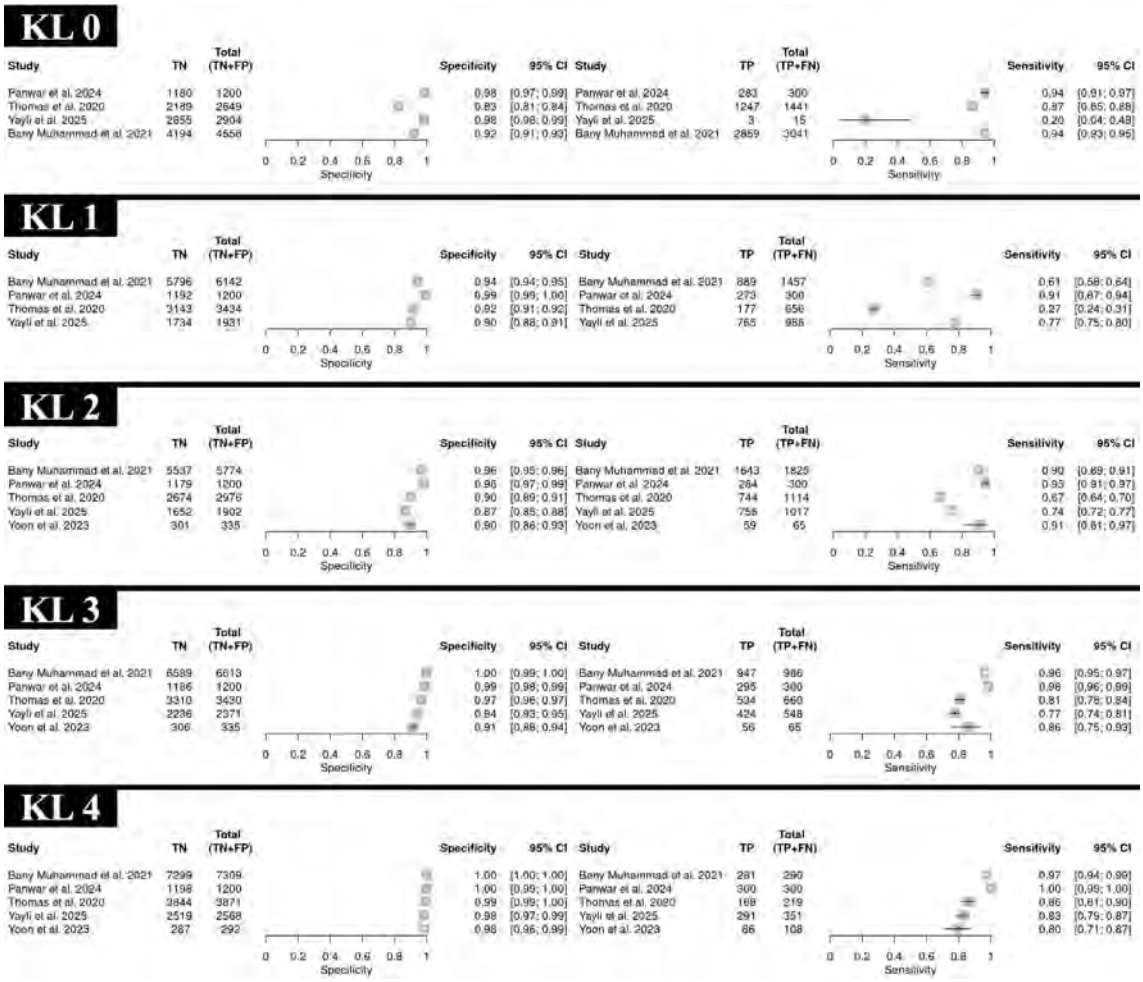


Figure (2) (A) and (B):Forest Plots of Sensitivity and Specificity for KL0 and KL1, Se and Sp Forest Plot: Studies included: Panwar et al. 2024, Thomas et al. 2020, Yayli et al. 2025, Bany Muhammad et al. 2021. (C), (D) and (E) :Forest Plots of Se and Sp for KL2-4, Se Forest Plot: Studies included: Panwar et al. 2024, Thomas et al. 2020, Yayli et al. 2025, Bany Muhammad et al. 2021, and Yoon et al 2023. AI showed robust diagnostic performance across all grades. CI, confidence interval; KL, Kellgren-Lawrence; TP, true positives; TN, true negatives; FP, false positives; FN, false negatives; Se, Sensitivity; Sp, specificity.

Conclusion: This is the first systematic review and meta-analysis to evaluate the use of AI in the early diagnosis of KOA. AI demonstrates consistently good sensitivity and specificity across all KL grades. These findings support the use of AI as a valuable assistant for rheumatologists in the early diagnosis of KOA. However, further research is needed to focus on

Table (1): Pooled Diagnostic Performance Metrics of AI for OA Stratified by KL Grade. The table summarizes sensitivity (Se), specificity (Sp), area under the curve (AUC), likelihood ratios (LR), diagnostic odds ratios (DOR), and post-test probabilities for AI-based classification of OA severity across KL grades (0–4). AI was superior to the index test in most metrics (Pooled Se , Sp, AUC. Positive likelihood ratio (LR+), post-test probability) and notably had a significant post-test probability in all KL Grades with DOR increase progressively with higher KL grades. CI, confidence interval; KL, Kellgren-Lawrence.

	Pooled Se (CI 95%)	Pooled Sp (CI 95%)	AUC (CI 95%)	Prior Probability	Post Test Probability +ve	Post Test Probability -ve	LR +ve (CI 95%)	LR -ve (CI 95%)	DOR (CI 95%)
KL 0	0.83 (0.49-0.96)	0.95 (0.88-0.98)	0.97 (0.95-0.98)	30%	88%	7%	17.94 (6.96-46.28)	0.18 (0.05-0.68)	99.8 (20.65-482.27)
KL 1	0.68 (0.39-0.88)	0.96 (0.88-0.98)	0.94 (0.92 -0.96)	20%	79%	8%	15.304 (4.07-57.55)	0.34 (0.14-0.78)	45.67 (5.65-369.08)
KL 2	0.85 (0.73-0.92)	0.94 (0.88-0.97)	0.96 (0.94-0.97)	25%	82%	5%	13.47 (6.51-27.9)	0.16 (0.08-0.31)	84.21 (21.82-324.99)
KL3	0.91 (0.79-0.96)	0.98 (0.94-0.99)	0.99 (0.97-0.99)	15%	87%	2%	38.92 (13.17-115.08)	0.1 (0.04-0.23)	406.09 (63.27-2606.41)
KL 4	0.94 (0.8-0.98)	1.0 (0.98-1.0)	1.00 (0.99-1.00)	10%	96%	1%	204.74 (54.16-774.07)	0.06 (0.02-0.22)	3290.31 (263.03-41159.94)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

developing, training, and validating of a unified model capable of accurate KOA diagnosis, especially the early stages of the disease.

Disclosure: M. Abdelsalam: None; **H. Hafez**: None; **O. El Sedafy**: None; **N. Abouelella**: None; **A. Hamza**: None; **O. El-Sayed**: None; **M. Awad**: None; **G. Omar**: None; **H. Mohammed**: None.

Abstract Number: 0334

Diagnostic Test Accuracy of Ultrasound for Detecting Knee Osteoarthritis: A Systematic Review and Meta-Analysis

Mohamed Abdelsalam[1], Hadeer Hafez[2], Maryam Lasheen[3], Bassant Elaraby Elsayed Badwy[4], Omar Sameh Nabil El Sedafy[1], Menat Alla Ayman Ali Mahdy[4], Hazem E. Mohammed[5] and Mohamed Reda Awad[6], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]6th October University, 6 october, Al Jizah, Egypt, [3]Misr University For Science and Technology, Helwan, Al Qahirah, Egypt, [4]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [5]Faculty of Medicine, Assiut university, Assiut, Egypt, assyut, Asyut, Egypt, [6]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Ultrasound (US) is an emerging, promising imaging modality offering a safe, radiation-free, and cost-effective option for diagnosing and assessing structural changes in knee osteoarthritis (KOA), potentially overcoming limitations of current gold-standard modalities such as X-ray and MRI. Despite growing interest in US capabilities, its diagnostic performance remains variable across studies, with no clear agreement on its accuracy compared to standard reference methods. This systematic review and meta-analysis aims to evaluate the diagnostic accuracy of US in detecting KOA and related parameters.

Methods: We conducted a systematic review and meta-analysis following PRISMA guidelines (Fig 1). PubMed, Web of Science, and Scopus were searched from inception to April 4th 2025, for studies evaluating US diagnostic accuracy in detecting KOA. Studies were included if they provided sufficient data to construct 2×2 tables and used a valid reference standard. A meta-analysis estimated pooled sensitivity (Se), specificity (Sp), and the summary receiver operating characteristic (SROC) curve of US for diagnosing KOA and related parameters. All analyses were performed using R software 4.4.2.

Results: We included 27 studies in the qualitative synthesis and 17 in the meta-analysis, encompassing 7,187 and 3,871 knee radiographs, respectively. US achieved a pooled Se of 0.94 (95% CI: 0.71–0.99) and Sp of 0.79 (95% CI: 0.48–0.94) for total KL grading (Fig. 2). For KL grade 0, Se was 0.47 (95% CI: 0.12–0.85) and Sp was 0.98 (95% CI: 0.19–1.00). For KL grade 1, Se was 0.95 (95% CI: 0.53–1.00) and Sp was 0.89 (95% CI: 0.44–0.99). For KL grade 2, Se was 0.99 (95% CI: 0.69–1.00) and Sp was 0.86 (95% CI: 0.48–0.97). For KL grade 3, Se was 0.87 (95% CI: 0.82–0.91) and Sp was 0.90 (95% CI: 0.67–0.98). For KL grade 4, Se was 0.94 (95% CI: 0.84–0.98) and Sp was 0.97 (95% CI: 0.42–1.00) (Fig. 3). For osteophyte detection, Se was 0.86 (95% CI: 0.76–0.92) and Sp was 0.76 (95% CI: 0.65–0.84). For cartilage degeneration, Se was 0.88 (95% CI: 0.71–0.95) and Sp was 0.76 (95% CI: 0.73–0.79). For medial meniscus protrusion (MMP), Se was 0.77 (95% CI: 0.56–0.90) and Sp was 0.70 (95% CI: 0.47–0.86) (Fig. 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

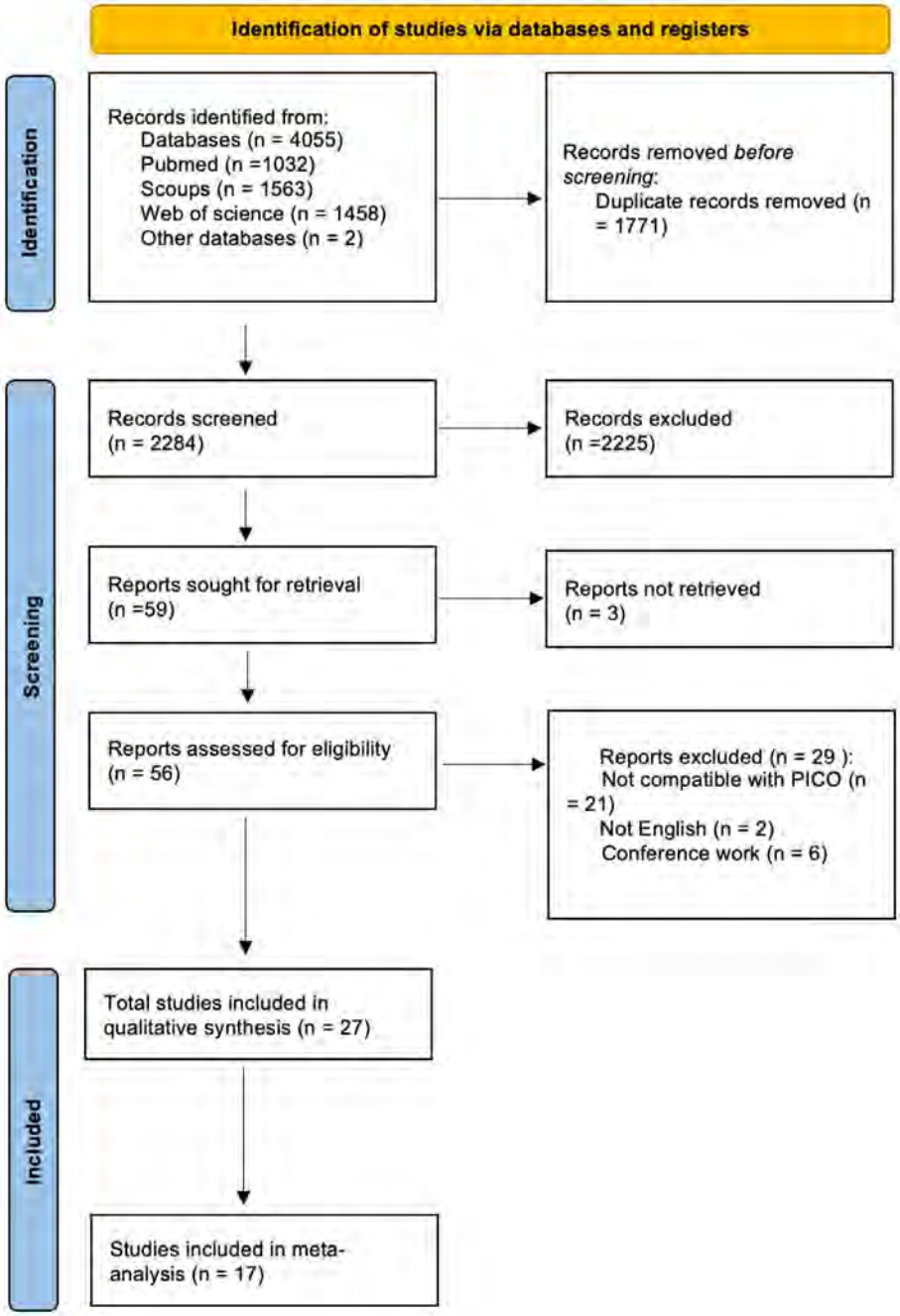


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

Conclusion: This systematic review and meta-analysis is the first to assess US diagnostic accuracy in detecting KOA and KOA-related structural changes, showing high pooled sensitivity and specificity for overall KL grading, individual KL grades, and the detection of osteophytes, cartilage degeneration, and MMP. Future research should focus on enhancing early stage KOA detection by US for more timely diagnosis and intervention, and explore the link between clinical symptoms and ultrasound findings to better understand how imaging correlates with patient reported outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

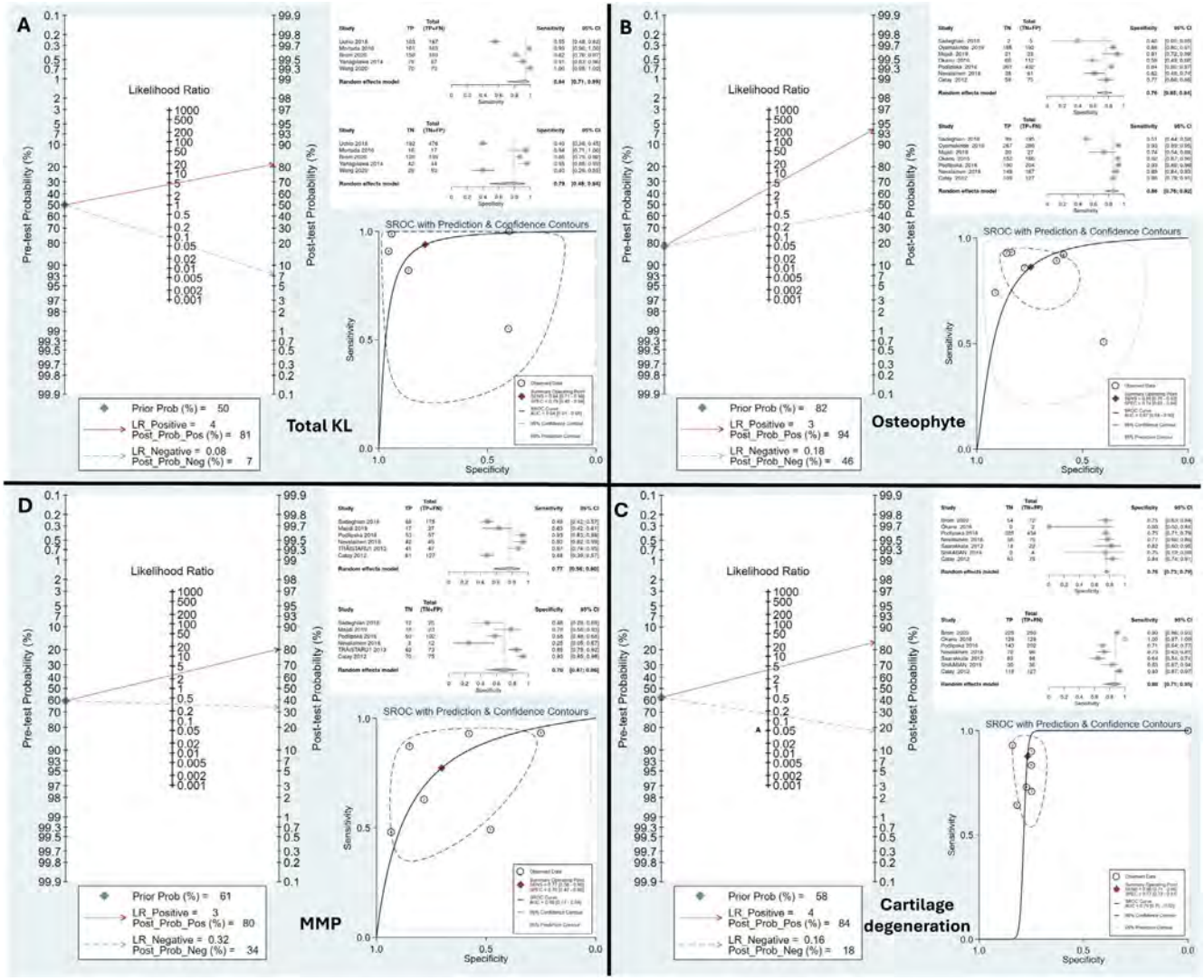


Figure (2) Diagnostic Accuracy of Ultrasound for Osteoarthritis Features. (A) Total KL Grade: Pooled Se: 0.94 (95% CI: 0.71–0.99); Pooled Sp: 0.79 (95% CI: 0.48–0.94). Studies included: Uchio 2018, Mortada 2016, Brom 2020, Yanagisawa 2014, Wang 2020. SROC AUC: 0.94 (95% CI: 0.91–0.95). LR+ = 4; LR– = 0.08. Post-Test Probabilities: Post_Prob_Pos = 81%; Post_Prob_Neg = 7%. (B) Osteophytes: Pooled Se: 0.86 (95% CI: 0.76–0.92); Pooled Sp: 0.76 (95% CI: 0.65–0.84). Studies included: Sadeghian 2018, Oyamakinde 2019, Majidi 2019, Okano 2016, Podlipská 2016, Nevalainen 2018, Catay 2012. SROC AUC: 0.87 (95% CI: 0.84–0.90). LR+ = 3; LR– = 0.18. Post-Test Probabilities: Post_Prob_Pos = 94%; Post_Prob_Neg = 46%. (C) Cartilage Degeneration: Pooled Se: 0.88 (95% CI: 0.71–0.95); Pooled Sp: 0.76 (95% CI: 0.73–0.79). Studies included: Brom 2020, Okano 2016, Podlipská 2016, Nevalainen 2018, Saarakkala 2012, SHAABAN 2019, Catay 2012. SROC AUC: 0.79 (95% CI: 0.75–0.82). LR+ = 4; LR– = 0.16. Post-Test Probabilities: Post_Prob_Pos = 84%; Post_Prob_Neg = 18%. Total KL grade classification demonstrated the highest diagnostic accuracy (AUC = 0.94), with near-perfect Se (0.94) and moderate Sp (0.79). (D) MMP: Pooled Se: 0.77 (95% CI: 0.56–0.90); Pooled Sp: 0.70 (95% CI: 0.47–0.86). Studies included: Sadeghian 2018, Majidi 2019, Podlipská 2016, Nevalainen 2018, TRÄIS-TARU1 2013, Catay 2012. SROC AUC: 0.80 (95% CI: 0.77–0.84). LR+ = 3; LR– = 0.32. Post-Test Probabilities: Post_Prob_Pos = 80%; Post_-Prob_Neg = 34%. Osteophytes and cartilage degeneration showed strong Se (0.86–0.88) but weaker Sp (0.74–0.76). MMP-based detection had lower pooled Se (0.77) and Sp (0.70), reflecting challenges in disease progression follow up. All SROC curves indicated robust discriminative capacity (AUC >0.75), with LRs supporting clinical utility. AUC, area under the curve; CI, confidence interval; KL, Kellgren-Lawrence; LR+, positive likelihood ratio; LR–, negative likelihood ratio; MMP, Medial Meniscal Protrusion; Post_Prob_Pos/Neg, post-test probability (positive/negative); SROC, summary receiver operating characteristic; Sp, Specificity; Se, Sensitivity.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

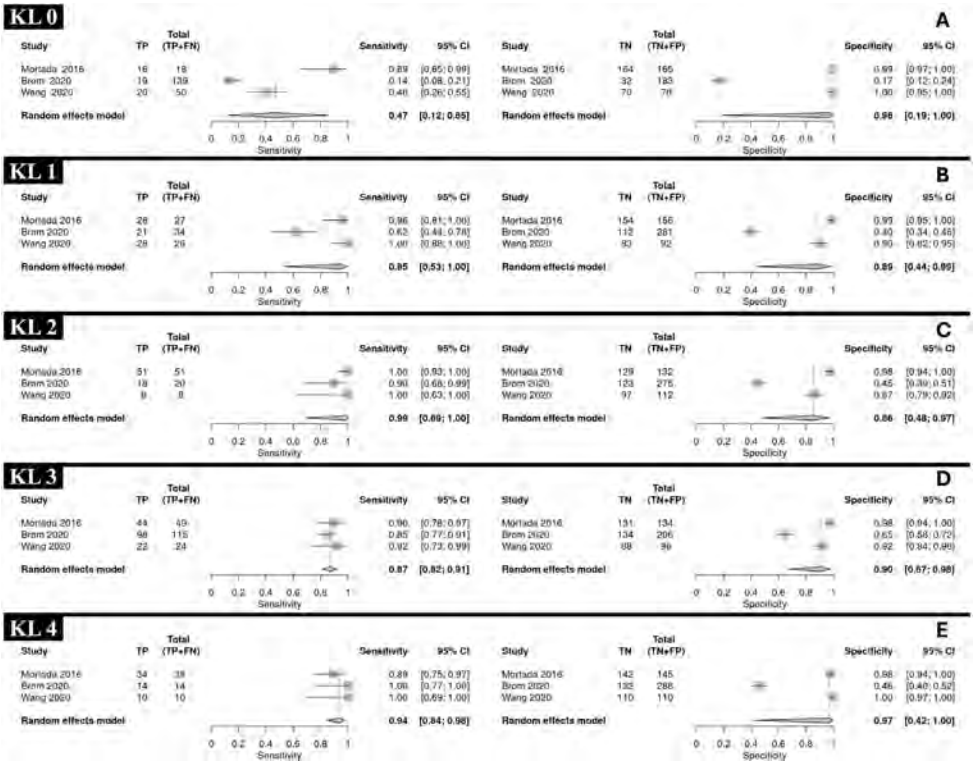


Figure (3) Forest Plots of Sensitivity and Specificity for US Detection of OA Severity by KL Grade (A) , (B), (C), (D), and (E): Forest Plots For KL grade 0, Se was 0.47 (95% CI: 0.12–0.85) and Sp was 0.98 (95% CI: 0.19–1.00). Studies included: Mortada 2016, Brom 2020, Wang 2020. For KL grade 1, Se was 0.95 (95% CI: 0.53–1.00) and Sp was 0.89 (95% CI: 0.44–0.99). Studies included: Mortada 2016, Brom 2020, Wang 2020. For KL grade 2, Se was 0.99 (95% CI: 0.69–1.00) and Sp was 0.86 (95% CI: 0.48–0.97). Studies included: Mortada 2016, Brom 2020, Wang 2020. For KL grade 3, Se was 0.87 (95% CI: 0.82–0.91) and Sp was 0.90 (95% CI: 0.67–0.98). Studies included: Mortada 2016, Brom 2020, Wang 2020. For KL grade 4, Se was 0.94 (95% CI: 0.84–0.98) and Sp was 0.97 (95% CI: 0.42–1.00). Studies included: Mortada 2016, Brom 2020, Wang 2020. Se and Sp improved with higher KL grades, reaching near-perfect performance for KL4 (Se = 0.94, Sp = 0.97). KL0 exhibited the lowest pooled Se (0.47) and widest CIs, indicating variability in early-stage detection. Abbreviations: CI, confidence interval; KL, Kellgren-Lawrence; TP, true positives; TN, true negatives; FP, false positives; FN, false negatives; Sp, Specificity; Se, Sensitivity.

Disclosure: M. Abdelsalam: None; **H. Hafez**: None; **M. Lasheen**: None; **B. Badwy**: None; **O. El Sedafy**: None; **M. Mahdy**: None; **H. Mohammed**: None; **M. Awad**: None.

Abstract Number: 0335

Discontinuation and Non-Publication of Osteoarthritis Clinical Studies: A Cross-Sectional Analysis of 10,686,413 Patients

Mohamed Abdelsalam[1], Hadeer Hafez[2], Maryam Lasheen[3], Bassant Elaraby Elsayed Badwy[4], Omar Sameh Nabil El Sedafy[1], Abdelrahman M Hafez[5], Omnia Samy El-Sayed[4], Menat Alla Ayman Ali Mahdy[4], Ali Tarek Hassanin[3], Mohamed Reda Awad[6] and Mohammed Safwat Kamal Hamza[7], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]6th October University, 6 october, Al Jizah, Egypt, [3]Misr University For Science and Technology, Helwan, Al Qahirah, Egypt, [4]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [5]Faculty of medecine, Damietta university, Mansoura, Ad Daqahliyah, Egypt, [6]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt, [7]Faculty of Medicine, Misr University for Science and Technology, 6 october, Al Jizah, Egypt

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0306–0336) Osteoarthritis – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Osteoarthritis (OA) is rising at an alarming rate, affecting millions worldwide and threatening mobility, independence, and quality of life. High-quality evidence is essential to guide clinical decision-making and ensure the best patient outcomes. The discontinuation and non-publication of clinical studies are major contributors to research waste and incomplete data synthesis in evidence-based medicine. This study aims to assess the prevalence, characteristics, and publication history of OA clinical studies and investigate the causes for their non-publication or discontinuation.

Methods: We searched OA-related clinical trials registered in ClinicalTrials.gov using NCT identifiers up to January 2nd, 2025. We excluded the last 24 months to account for ongoing peer reviews. Studies were considered discontinued if terminated, withdrawn, or suspended and unpublished if their results were not available in a peer-reviewed journal. Data on gender, age, study type, funding, intervention, enrollment, and location were extracted. Multiple logistic regression analyzed characteristics linked to unpublished or discontinued trials. All statistical analyses were performed using Jamovi 2.6.24 software.

Results: A total of 3,818 studies were included, comprising 2,706 (70.9%) completed, 425 (11.1%) discontinued, and 687 (17.9%) with unknown status (Fig. 1). Of the completed and discontinued studies, 2,588 were interventional and 538 were observational. Among the 425 discontinued studies, 9.4% of them were published despite being discontinued, and 34.8% of unknown studies were also found published. Also, nearly half (43.3%) of completed studies remained unpublished (table 1). Logistic regression analysis revealed that non-industry-funded studies had lower odds of discontinuation than industry-funded ones (OR = 0.380, 95% CI: 0.279–0.518, $p < 0.001$). Device-based interventions were nearly three

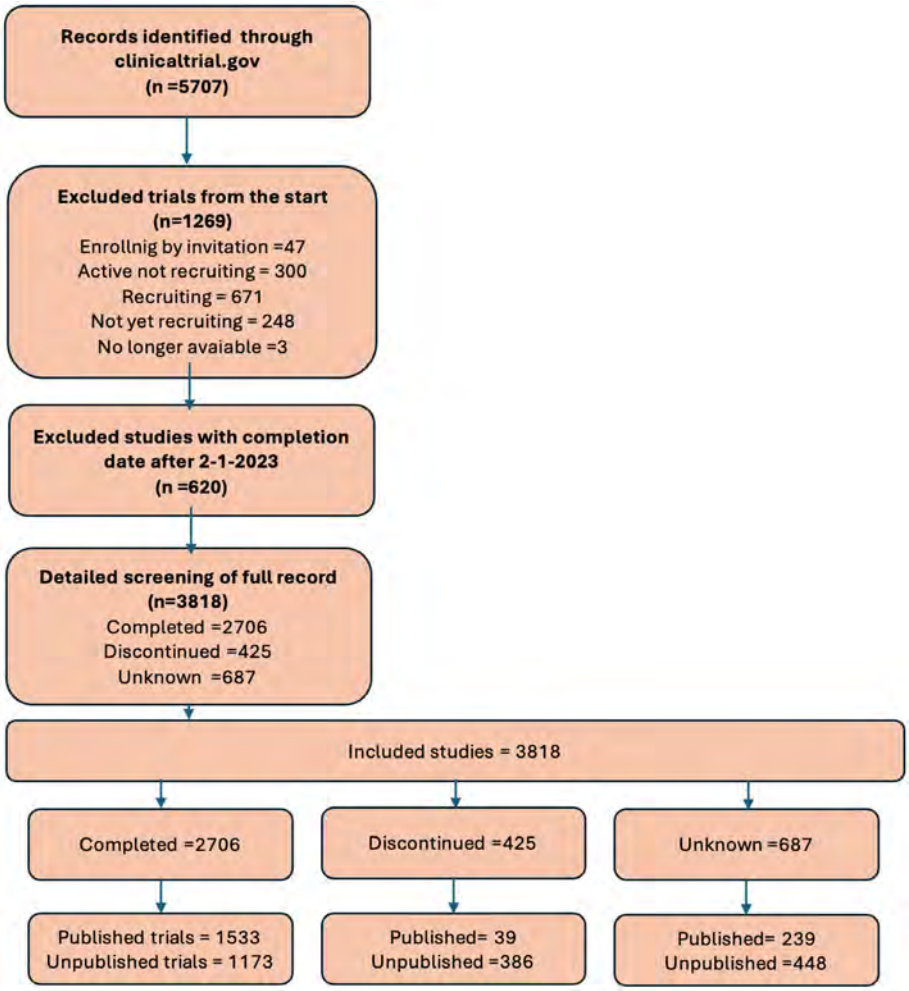
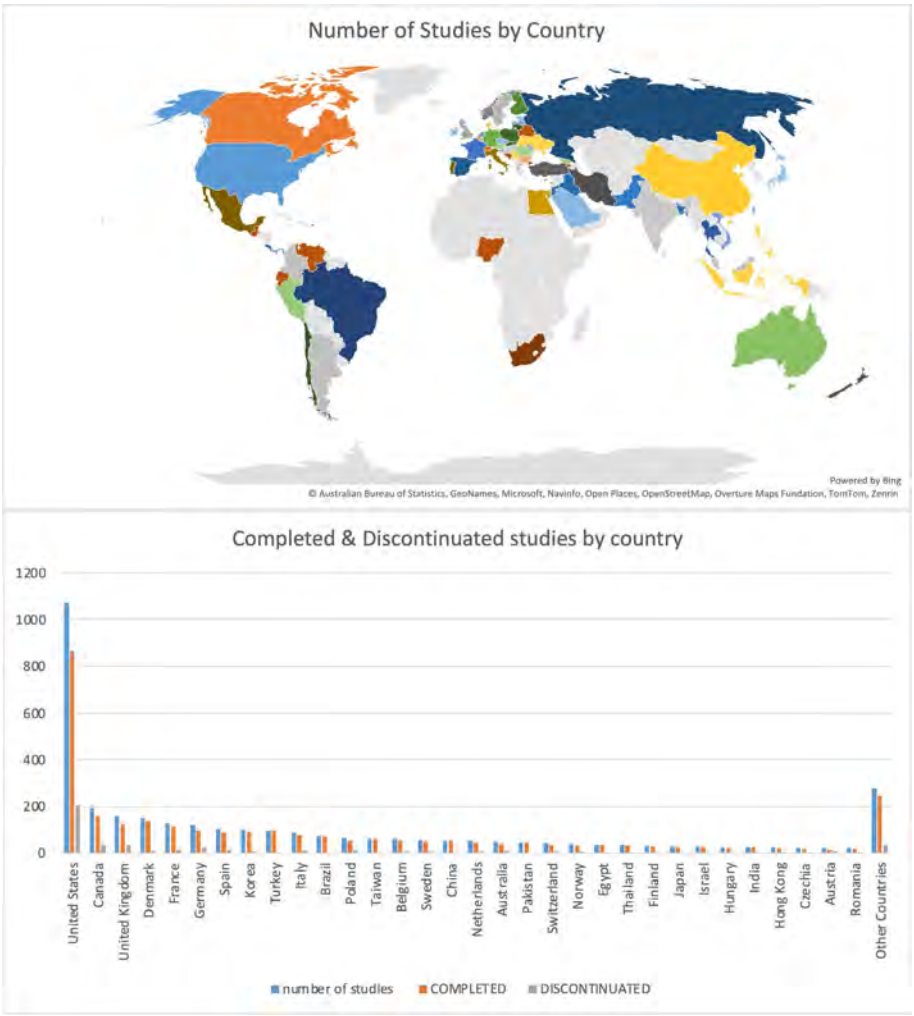


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(Figure 2) Global Distribution of Total, Completed and Discontinued clinicals studies by Country.

times more likely to be discontinued than behavioral interventions (OR = 2.977, 95% CI: 1.445–6.133, $p = 0.003$). Trials with >100 participants had lower odds of discontinuation than those < 100 (OR = 0.371, 95% CI 0.278, 0.495, $p < 0.001$). As for publication, behavioral interventions were significantly more likely to be published compared to device intervention (OR = 2.346, 95% CI: 1.594 to 3.451, $p < 0.001$), enrollment sizes >100 were more likely to be published than those < 100 (OR = 0.575, 95% CI: 0.479 to 0.690), and non-industry-funded studies were more likely to be published than industry-funded ones (OR = 0.409, 95% CI: 0.326 to 0.513). Notably, the United States was the most common location for conducting OA clinical trials 1,072 (28.4%), and also had the highest discontinuation rate globally (39.2%) (Fig. 2).

Conclusion: OA clinical trials are frequently discontinued and often remain unpublished, restricting access to valuable research findings. This lack of transparency not only hinders scientific progress but also raises ethical concerns about participant contributions. Ensuring transparency through mandatory reporting and stricter policies can help address publication bias and ensure that patients efforts contribute meaningfully to medical knowledge.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(Table 1) Characteristics and outcomes of OA clinical Studies by completed, discontinued, published and nonpublished status

	COMPLETED (N=2706)	Discontinued (N=425)	p value	Published (N=1572)	Unpublished (N=1559)	p value	Total (N=3131)
Study Results			0.7671			0.8861	
NO	2135.0 (78.9%)	338.0 (79.5%)		1240.0 (78.9%)	1233.0 (79.1%)		2473.0 (79.0%)
YES	571.0 (21.1%)	87.0 (20.5%)		332.0 (21.1%)	326.0 (20.9%)		658.0 (21.0%)
Interventions			< 0.001[1]			< 0.001[1]	
N-Miss	167	37		83	121		204
BEHAVIORAL	180.0 (7.1%)	10.0 (2.6%)		133.0 (8.9%)	57.0 (4.0%)		190.0 (6.5%)
BIOLOGICAL	116.0 (4.6%)	23.0 (5.9%)		67.0 (4.5%)	72.0 (5.0%)		139.0 (4.7%)
COMBINATION_PRODUCT	14.0 (0.6%)	0.0 (0.0%)		8.0 (0.5%)	6.0 (0.4%)		14.0 (0.5%)
DEVICE	533.0 (21.0%)	162.0 (41.8%)		281.0 (18.9%)	414.0 (28.8%)		695.0 (23.7%)
DIAGNOSTIC_TEST	26.0 (1.0%)	0.0 (0.0%)		16.0 (1.1%)	10.0 (0.7%)		26.0 (0.9%)
DIETARY_SUPPLEMENT	76.0 (3.0%)	3.0 (0.8%)		49.0 (3.3%)	30.0 (2.1%)		79.0 (2.7%)
DRUG	732.0 (28.8%)	98.0 (25.3%)		394.0 (26.5%)	436.0 (30.3%)		830.0 (28.4%)
GENETIC	5.0 (0.2%)	0.0 (0.0%)		1.0 (0.1%)	4.0 (0.3%)		5.0 (0.2%)
OTHER	495.0 (19.5%)	33.0 (8.5%)		320.0 (21.5%)	208.0 (14.5%)		528.0 (18.0%)
PROCEDURE	348.0 (13.7%)	57.0 (14.7%)		211.0 (14.2%)	194.0 (13.5%)		405.0 (13.8%)
RADIATION	14.0 (0.6%)	2.0 (0.5%)		9.0 (0.6%)	7.0 (0.5%)		16.0 (0.5%)
Interventions-coded			< 0.001[1]			< 0.001[1]	
N-Miss	167	37		83	121		204
BEHAVIORAL	180.0 (7.1%)	10.0 (2.6%)		133.0 (8.9%)	57.0 (4.0%)		190.0 (6.5%)
BIOLOGICAL	116.0 (4.6%)	23.0 (5.9%)		67.0 (4.5%)	72.0 (5.0%)		139.0 (4.7%)
DEVICE	533.0 (21.0%)	162.0 (41.8%)		281.0 (18.9%)	414.0 (28.8%)		695.0 (23.7%)
DRUG	732.0 (28.8%)	98.0 (25.3%)		394.0 (26.5%)	436.0 (30.3%)		830.0 (28.4%)
OTHER	630.0 (24.8%)	38.0 (9.8%)		405.0 (27.1%)	265.0 (18.4%)		668.0 (22.8%)
PROCEDURE	348.0 (13.7%)	57.0 (14.7%)		211.0 (14.2%)	194.0 (13.5%)		405.0 (13.8%)
Sex			0.0471			0.0011	
N-Miss	5	1		6	0		6
ALL	2620.0 (97.0%)	420.0 (99.1%)		1513.0 (96.6%)	1527.0 (97.9%)		3040.0 (97.3%)
FEMALE	69.0 (2.6%)	4.0 (0.9%)		50.0 (3.2%)	23.0 (1.5%)		73.0 (2.3%)
MALE	12.0 (0.4%)	0.0 (0.0%)		3.0 (0.2%)	9.0 (0.6%)		12.0 (0.4%)
Age			0.0821			0.1511	
N-Miss	4	1		5	0		5
ADULT	97.0 (3.6%)	7.0 (1.7%)		46.0 (2.9%)	58.0 (3.7%)		104.0 (3.3%)
ADULT, OLDER_ADULT	2368.0 (87.6%)	388.0 (91.5%)		1386.0 (88.4%)	1370.0 (87.9%)		2756.0 (88.2%)
CHILD, ADULT	4.0 (0.1%)	2.0 (0.5%)		2.0 (0.1%)	4.0 (0.3%)		6.0 (0.2%)
CHILD, ADULT, OLDER_ADULT	180.0 (6.7%)	23.0 (5.4%)		97.0 (6.2%)	106.0 (6.8%)		203.0 (6.5%)
OLDER_ADULT	52.0 (1.9%)	4.0 (0.9%)		36.0 (2.3%)	20.0 (1.3%)		56.0 (1.8%)
CHILD	1.0 (0.0%)	0.0 (0.0%)		0.0 (0.0%)	1.0 (0.1%)		1.0 (0.0%)
Phases			0.0031			0.9191	
N-Miss	1708	256		1034	930		1964
EARLY_PHASE1	13.0 (1.3%)	4.0 (2.4%)		8.0 (1.5%)	9.0 (1.4%)		17.0 (1.5%)
PHASE1	121.0 (12.1%)	9.0 (5.3%)		55.0 (10.2%)	75.0 (11.9%)		130.0 (11.1%)
PHASE1|PHASE2	49.0 (4.9%)	9.0 (5.3%)		27.0 (5.0%)	31.0 (4.9%)		58.0 (5.0%)
PHASE2	231.0 (23.1%)	41.0 (24.3%)		121.0 (22.5%)	151.0 (24.0%)		272.0 (23.3%)
PHASE2|PHASE3	40.0 (4.0%)	3.0 (1.8%)		22.0 (4.1%)	21.0 (3.3%)		43.0 (3.7%)
PHASE3	281.0 (28.2%)	37.0 (21.9%)		153.0 (28.4%)	165.0 (26.2%)		318.0 (27.2%)
PHASE4	263.0 (26.4%)	66.0 (39.1%)		152.0 (28.3%)	177.0 (28.1%)		329.0 (28.2%)
Enrollment			< 0.001[1]			0.2942	
N-Miss	32	6		25	13		38
<100	1521.0 (56.9%)	319.0 (76.1%)		5972.6 (211418.7)	324.6 (2741.4)		1840.0 (59.5%)
>100	1153.0 (43.1%)	100.0 (23.9%)		0.0 - 8308821.0	0.0 - 79189.0		1253.0 (40.5%)
Funder Type			< 0.001[1]			< 0.001[1]	
N-Miss	4	1		25	13		5
INDUSTRY	858.0 (31.8%)	222.0 (52.4%)		862.0 (55.7%)	978.0 (63.3%)		1080.0 (34.5%)
Non-industry	1844.0 (68.2%)	202.0 (47.6%)		685.0 (44.3%)	568.0 (36.7%)		2046.0 (65.5%)
Study Type			0.0181			< 0.001[1]	
N-Miss	4	1		5	0		5
Interventional	2254.0 (83.4%)	334.0 (78.8%)		392.0 (25.0%)	688.0 (44.1%)		2588.0 (82.8%)
Observational	448.0 (16.6%)	90.0 (21.2%)		1175.0 (75.0%)	871.0 (55.9%)		538.0 (17.2%)
Locations			0.0171			< 0.001[1]	
N-Miss	303	69		5	0		372
Multicenter	689.0 (28.7%)	124.0 (34.8%)		1352.0 (86.3%)	1236.0 (79.3%)		813.0 (29.5%)
Single Center	1714.0 (71.3%)	232.0 (65.2%)		215.0 (13.7%)	323.0 (20.7%)		1946.0 (70.5%)
Pub/nonPub			< 0.001[1]			< 0.001[1]	
Published	1533.0 (56.7%)	39.0 (9.2%)					1572.0 (50.2%)
Unpublished	1173.0 (43.3%)	386.0 (90.8%)					1559.0 (49.8%)
Study Status						< 0.001[1]	
COMPLETED				1533.0 (97.5%)	1173.0 (75.2%)		2706.0 (86.4%)
Discontinued				39.0 (2.5%)	386.0 (24.8%)		425.0 (13.6%)

P -values < 0.05 were considered statistically significant.
1. Pearson's Chi-squared test
2. Linear Model ANOVA

Disclosure: M. Abdelsalam: None; **H. Hafez**: None; **M. Lasheen**: None; **B. Badwy**: None; **O. El Sedafy**: None; **A. Hafez**: None; **O. El-Sayed**: None; **M. Mahdy**: None; **A. Hassanin**: None; **M. Awad**: None; **M. Hamza**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0336

Does Baseline Physical Function Moderate Change in Steps/day Following a Telephone-Delivered Walk With Ease Program?

Nurten Gizem Tore[1], Daniel K. White[2] and Christine Pellegrini[3], [1]University of Delaware, Newark, [2]University of Delaware, Newark, DE, [3]Arnold School of Public Health, Columbia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0306–0336) Osteoarthritis – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Adults with knee osteoarthritis with worse physical function are known to benefit more from therapeutic exercise than those with less limitation. However, there is limited evidence on whether those with worse physical function also have more improvement in physical activity in response to physical activity interventions. This study aimed to examine the interaction effects of baseline physical function on changes in steps/day among individuals participating in the 6-week Walk With Ease by Phone (WWE-P) intervention compared to a control group.

Methods: Baseline physical function was assessed using the 30-Second Chair Stand Test (30-CST) total repetitions. Study participants in the intervention received 6 weeks of WWE-P while those in the waitlist control received no intervention until 12 months. Daily step count were measured using an Actigraph GT9X Link, collecting at the baseline, and 6 months. We examined the interaction effects between baseline physical function categorized as high and low using mean 30-CST time and treatment group with changes in steps/day from baseline to 6 months.

Table 1. Daily step count according to function level

	Steps/day	
High Function	Mean	Standard Deviation
Baseline		
Intervention	4460	1806
Control	4595	2616
6 months		
Intervention	3947	2520
Control	4149	3127
Low Function		
Baseline		
Intervention	3603	1966
Control	3822	2132
6 months		
Intervention	2499	2399
Control	3003	2480

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 267 participants (mean age = 64.1 years old, 92% female, 49.4% in the WWE-P group) were included in the overall analytic sample. The mean baseline 30-CST score for the WWE-P and control group were 8.83 ± 2.88 and 8.88 ± 3.02, respectively. No statistically significant differences were observed between groups at baseline. Baseline 30-CST significantly interacted with time and group in predicting changes in daily step count (p = 0.001). Those in the intervention and control groups with low 30-CST walked 1104 and 819 fewer steps/day over 6 months, while those with high 30-CST in the intervention and control walked 513 and 446 fewer steps/day.

Conclusion: The results of this research indicate the significant interaction between baseline 30-CST and changes in daily step count over time, such that those with low physical function walked fewer steps/day regardless of the intervention group over 6 months, while those with high physical function had less decline. These findings suggest that those with worse physical function may have the greatest decline in physical activity regardless of receiving a physical activity intervention.

Disclosure: N. Tore: None; **D. White**: None; **C. Pellegrini**: None.

Abstract Number: 0337

Bridging the Bone Gap: A Quality Improvement Project on Osteoporosis Screening Practices in a Teaching Institution

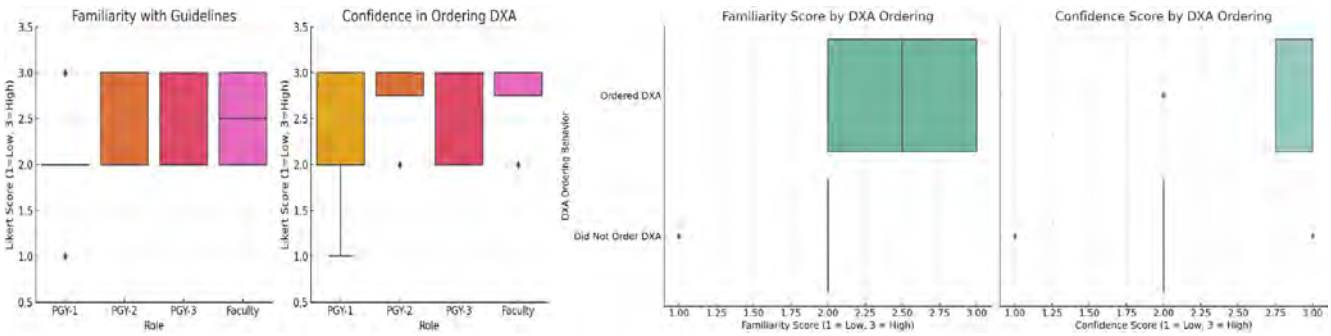
Aakanksha Pitliya[1], Alexandra Georgiana Boc[2], Hema Latha Anam[2], Richard Oletsky[2], Dipabali Chaudhuri[2] and Rajesh Thirumaran[2], [1]Mercy Catholic Medical Center, Darby, PA, Clifton Heights, PA, [2]Mercy Catholic Medical Center, Darby, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

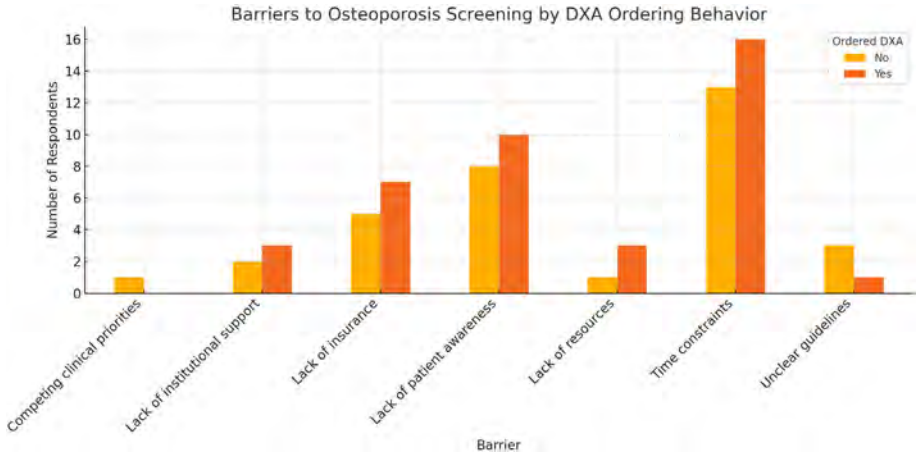
Background/Purpose: Osteoporosis remains underdiagnosed despite clear guidelines. As primary care physicians and trainees are key to preventive care, this quality improvement (QI) project aimed to assess provider knowledge, confidence in ordering Dual-energy X-ray absorptiometry (DEXA) scans, and perceived barriers to inform strategies for improving osteoporosis screening.

Methods: We conducted an anonymous survey with 44 physicians, including internal medicine residents (PGY-1 to PGY-3) and faculty members. The survey evaluated baseline knowledge of guidelines, perceived barriers and facilitators, and confidence in ordering DEXA scans. A knowledge score of 0-6 was calculated using the answers to questions based on



Comparison of familiarity and confidence scores by role and DXA ordering behavior; confidence was the stronger predictor of ordering; confidence was the stronger predictor of ordering behavior (p < 0.005).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



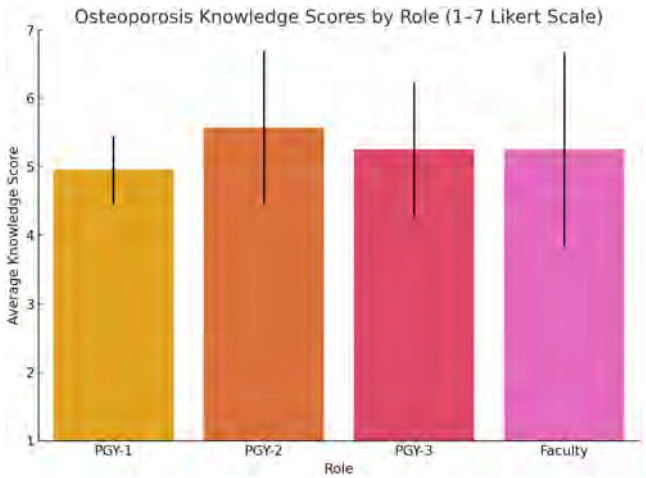
Reported barriers to osteoporosis screening, stratified by DXA ordering behavior, with both groups citing time constraints and patient awareness most frequently.

guidelines. Familiarity and confidence were scored on a 3-point Likert scale. ANOVA was used for assessing statistical significance, t-tests were used for the continuous variables (confidence and familiarity scores), Chi-square tests for evaluating categorical variables (provider role vs DEXA ordering), and logistic regression was used to evaluate the predictors of ordering behaviour. Multivariate logistic regression assessed whether confidence or familiarity predicted DEXA ordering behavior. All statistical analyses were conducted in R (v4.3.2) with $\alpha = 0.05$.

Results: A total of 44 providers participated in the survey, including PGY-1 (47.7%), PGY-2 (15.9%), PGY-3 (27.3%), and faculty (9.1%). Most worked in ambulatory care (56.8%) or academic hospitals (29.5%). The mean knowledge scores were high (mean = 4.95 ± 0.88), highest among faculty (5.5 ± 0.58), lowest among PGY-1s (4.00 ± 1.05), but not statistically different (ANOVA F = 0.55, p = 0.65). Participants reported being somewhat familiar with guidelines (2.36 ± 0.53) and very confident in ordering DEXA (2.51 ± 0.55).

Providers who had ordered DEXA were significantly more confident (t = 7.05, $p < 0.000001$) and more familiar with guidelines (t = 4.51, p = 0.00005). Logistic regression showed confidence to be an independent predictor of ordering behavior ($\beta = 3.52$, p = 0.0047), while familiarity was not ($\beta = 1.09$, p = 0.405). No association was found between provider role and ordering behavior ($\chi^2 = 0.64$, p = 0.42).

Top barriers included lack of patient awareness (54.5%), time constraints (31.8%), and insurance issues (31.8%). Requested improvements included Electronic Health Record (EHR) based reminders (52.3%), clearer guidelines (40.9%),



Average osteoporosis knowledge scores by role showing no statistically significant difference across PGY levels and faculty (ANOVA p = 0.65).*

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and improved DEXA access (40.9%). Most participants supported standardized protocols (72.7%) and integration into routine preventive care (65.9%).

Conclusion: Residents and faculty members had good awareness of osteoporosis screening, but confidence, rather than familiarity, is the strongest predictor of DEXA ordering. Providers experience both practical and systemic barriers, notably those linked to patient engagement and time. EHR reminders, clearer institutional protocols, and educational support could significantly enhance screening behavior, especially among trainees.

Disclosure: A. Pitliya: None; **A. Boc**: None; **H. Anam**: None; **R. Oletsky**: None; **D. Chaudhuri**: None; **R. Thirumaran**: None.

Abstract Number: 0338

Fractures and Changes in Bone Mineral Density During Two Years of Low Dose Glucocorticoid Treatment for Rheumatoid Arthritis: A Systematic Literature Review and Individual Participant Data Meta-Analysis

Andriko Palmowski[1], Tobias Haugegaard[2], Ingiäld Hafstörm[3], Henning Bliddal[4], Judith Oldenkott[5], Siegfried Wassenberg[6], Ernest Choy[7], John Kirwan[8], Robin Christensen[9], Maarten Boers[10] and FRANK BUTTGEREIT[11], [1]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [2]The Parker Institute, Kopenhagen, Denmark, [3]Karolinska Institutet, Stockholm, Sweden, [4]The Parker Institute, Frederiksberg, Denmark, [5]Charité, Berlin, Germany, [6]Rheumazentrum Ratingen, Ratingen, Germany, [7]Division of Infection and Immunity, CREATE Centre, Cardiff University, Cardiff, United Kingdom, [8]University of Bristol, Bristol, United Kingdom, [9]Musculoskeletal Statistics Unit, The Parker Institute, Copenhagen, Hovedstaden, Denmark, [10]Amsterdam UMC, Vrije Universiteit, Amersfoort, Netherlands, [11]Charite University Medicine Berlin, Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: It is unclear to what extent low dose glucocorticoids (GCs) impact bone health in patients with rheumatoid arthritis (RA). RA leads to bone loss which might be mitigated with GC via disease control, but GCs themselves can negatively affect the bone. Observational studies are prone to bias and randomized controlled trials (RCTs) possibly underpowered for safety signals. We performed a protocolized (dx.doi.org/10.17504/protocols.io.6qpvr3ombvmk/v1) systematic literature review and individual participant data (IPD) meta-analysis to overcome these limitations.

Methods: MEDLINE (via PubMed), Embase (via Ovid) and the Cochrane Central Register of Controlled Trials (via Cochrane Library) were searched for RCTs that compared low dose GC (≤ 7.5 mg/d prednisone equivalent) with placebo or any other control treatment (e.g., standard of care). Search results were screened separately by two reviewers. There were two co-primary endpoints: Participants with ≥ 1 fractures (clinical/symptomatic) and change in bone mineral density (BMD; in g/cm^2, as measured by dual x-ray absorptiometry); both over two years. BMD was analysed separately for lumbar spine and femoral (total hip or femoral neck) measuring sites. Analyses were based on one-stage models and the intention-to-treat approach. Missing outcome data were handled via multiple imputations by chained equations. I^2 was estimated from standard random-effects meta-analysis models. To identify subgroups especially vulnerable to bone loss at the lumbar spine, various baseline characteristics were assessed as effect modifiers. A sensitivity analysis used data 'as observed'.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

	Glucocorticoids n = 548	Control n = 564
Age, years	60.7 (14.8)	62.0 (14.2)
Female	346 (69.2)	345 (66.4)
ACPA positive	193 (62.3)	209 (65.7)
RF positive	324 (65.9)	343 (67.4)
Smoking status		
Never smoked	155 (45.2)	158 (44.5)
Previous smoker	119 (34.7)	128 (36.1)
Current smoker	69 (20.1)	69 (19.4)
BMI, kg/m²	26.4 (4.5)	26.6 (4.4)
Weight, kg	73.0 (13.5)	73.6 (15.2)
DAS28, score	4.8 (1.2)	5.0 (1.2)
Disease duration, years	1.0 [0.4 – 8.0]	1.0 [0.5 – 7.0]
Pain (0-10)	5.2 (2.4)	5.2 (2.3)
ESR, mm/h	30 [16 – 48]	30 [16 – 48]
CRP, mg/l	10.0 [3.5 – 23.5]	10.0 [4.0 – 28.0]
HAQ, score	1.5 (0.8)	1.4 (0.9)
BMD lumbar spine, g/cm²	1.08 (0.20)	1.07 (0.20)
BMD femur, g/cm²	0.88 (0.15)	0.88 (0.16)

Values are mean (SD), median [IQR] or n (%). Percentages are based on patients with available data. Values are based on individual participant data that were available to the study team. Pain was measured on the visual or numerical analogue scale. In one trial, a positive latex agglutination text was considered positive for rheumatoid factor [18]. In one trial, the Hannover Functional Ability Questionnaire (FFbH) was used to evaluate disability – the scores were converted to HAQ scores according to the original publication with the following formula: HAQ = 3.16 – (0.028 x FFbH) [16]. ACPA, anti-citrullinated protein antibody, RF, rheumatoid factor, BMI, body mass index, DAS28, disease activity score 28 joints, ESR, erythrocyte sedimentation rate, CRP, C-reactive protein, HAQ, health assessment questionnaire, BMD, bone mineral density.

Results: Out of 2,336 articles, five RCTs conducted in twelve countries in Europe with 1,112 participants were included and shared IPD: [1-5]. All studies allowed concomitant treatment with DMARDs. Baseline characteristics, including lumbar spine and femoral BMD, were well balanced across groups (**Table 1**). Regarding femoral BMD, four trials provided femoral neck BMD, one trial had only total hip data available. BMD decreased in both groups over two years (**Table 2**). There was an increase in bone loss in the GC compared to the control group at the lumbar spine but not at the femur. 24 participants experienced at least one fracture, with similar odds in both groups. Sensitivity analyses yielded consistent results. Subgroup

Table 2. 2-Year changes in bone density at the lumbar spine and the femur and number of fractures in the glucocorticoid and control groups*

	Glucocorticoids (n=548)	Control (n=564)	Contrast (95%CI)	p	I² §
Change in lumbar spine BMD, g/cm²	-0.032 (0.009)	-0.011 (0.010)	-0.021 (-0.032 to -0.010)	0.001	28 %
Change in femur BMD, g/cm²	-0.016 (0.010)	-0.023 (0.009)	0.007 (-0.005 to 0.020)	0.272	0 %
Participants with fractures during the study period	0.084 (0.557) †	0.076 (0.546) †	1.111 (0.739 to 1.670) ‡	0.614	0 %

95%-CI, 95% confidence interval; GC, Glucocorticoid; BMD, bone mineral density.

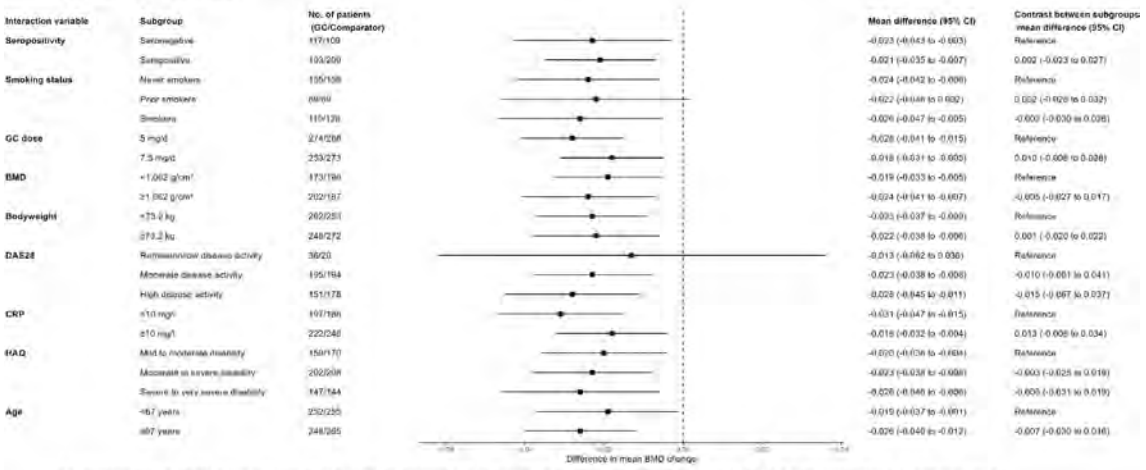
*Missing data was handled using multiple imputation. Values are reported as least squares means (standard error) unless otherwise stated.

† Values are odds (SE)

‡ Values are OR (CI)

§ I^2 signifies the percentage of variation across studies due to heterogeneity between trials rather than due to chance. It stems from additionally computed two-stage models.

Figure 2. Subgroup analyses



GC, glucocorticoid, BMD, bone mineral density, DAS28, disease activity score 28 joints, CRP, C-reactive protein, HAQ, health assessment questionnaire, CI, confidence interval

analyses did not reveal groups particularly susceptible to GC-induced bone loss at the lumbar spine (**Figure 1**). Data on anti-osteoporotic medication was available for one trial where 13% were treated with anti-osteoporotic drugs at baseline (bisphosphonates or denosumab). In those who were randomized to GC and used anti-osteoporotic drugs at baseline (n = 28), there was no bone loss at the lumbar spine.

Conclusion: Low dose GCs, used for two years to treat RA, lead to bone loss at the lumbar spine but not at the femur. Anti-osteoporotic drugs may prevent GC-induced bone loss at the lumbar spine. There was no subgroup identified to be especially vulnerable to GC-induced bone loss.

References

1. Boers Ann Rheum Dis 2022
2. Choy Ann Rheum Dis 2005
3. Wassenberg Arthritis Rheum 2005
4. Svensson Arthritis Rheum 2005
5. Kirwan NEJM 1995

Disclosure: A. Palmowski: Novartis, 1; **T. Haugegaard**: None; **I. Hafstörm**: None; **H. Bliddal**: None; **J. Oldenkott**: None; **S. Wassenberg**: None; **E. Choy**: AbbVie, 2, 6, Alfasigma, 6, Bio-Cancer, 2, 5, Biocon, 2, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 6, Fresenius Kabi, 2, 6, Gedeon Richter, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 6, Viatris, 2, 6; **J. Kirwan**: None; **R. Christensen**: None; **M. Boers**: MBCelltrion, AbbVieunrelated., 12, MBCelltrion, AbbVieunrelated.; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0339

Evaluating Discordance between Bilateral Hip Bone Density Measurements in Individuals with Low Bone Mass

Anupama Shahane[1], Nora Sandorfi[2] and Alexis Ogdie[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, USA, Philadelphia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Bone mineral density (BMD) measurement by dual X-ray absorptiometry (DXA) is the basis of World Health Organization (WHO) classification criteria for osteoporosis. Traditionally unilateral hip bone density has been measured and the utility of bilateral reporting remains unclear. Recent data have shown that a significant difference may be noted in bone density measurements between left and right hips with resultant failure to identify and treat individuals at high risk of fracture. In the 2023 Position Statement, the International Society of Clinical Densitometry (ISCD) noted that the impact of discordant hip bone density on diagnosis and monitoring of osteoporosis is a significant knowledge gap. This study aims to examine concordance vs discordance between left and right hip bone density measurement at a large hospital system. Results of this study may be helpful to further evaluate the impact and need for bilateral hip BMD testing as standard of care for osteoporosis screening.

Methods: A retrospective cohort study was performed using data from electronic medical record at the University of Pennsylvania. After IRB approval, patients with bilateral DXA were identified. A subset of charts with the following criteria were randomly selected for review: age 50 years or older, DXA report within the past 4 years within the health system, and diagnosis of osteopenia or osteoporosis. Manual chart review was conducted for capture of T scores for lumbar spine, left femoral neck, left total hip, right femoral neck and right total hip. We descriptively report baseline characteristics. Scatter plots were used to assess correlation between the right and left sides. Paired T tests were employed to test whether the left was significantly different from the right side for both the total hip and femoral neck.

Table 1. Demographics

Demographics	N (%)
Gender	
Male	27 (14.2%)
Female	163 (85.7%)
Race	
White	164 (81%)
Asian	4 (2.1%)
Black	23 (12.1%)
Other	9 (4.8%)
DXA reports	
Bilateral	137 (72.1%)
Unilateral	50 (26.3%)
No hips	2 (1%)
Other	1 (0.5%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Difference between left and right femoral neck and total hip T scores

	Mean T-score	Std error	Std deviation	CI	
Left FN	-1.737	.091	1.049	-1.917	-1.556
Right FN	-1.704	.090	1.039	-1.883	-1.525
Difference	-.032	.042	.484	-.115	.050
Left TH	-1.409	.102	1.138	-1.613	-1.206
Right TH	-1.397	.093	1.036	-1.582	-1.212
Difference	-.012	.033	.366	-.0775	.0531

TH – total hip. FN – femoral neck.

Results: Within the health system, 29,258 patients > age 50 years had received a DXA scan at 3 primary sites between 2021 and 2024. The initial search was then narrowed to limit patients to those seen by Rheumatology providers (N=1171). Among these, 85.7% patients were female and 81% were White. 200 charts were randomly selected among these and reviewed manually. 143 (71.5%) patients had DXA results reporting bilateral hip BMD. 27 (19%) patients had a T score difference of 0.5 between left and right femoral neck or total hip. 13 patients were classified into a different category: 2 patients with normal T score on one side vs low bone mass on the other side, and 11 patients with low bone mass on one side vs

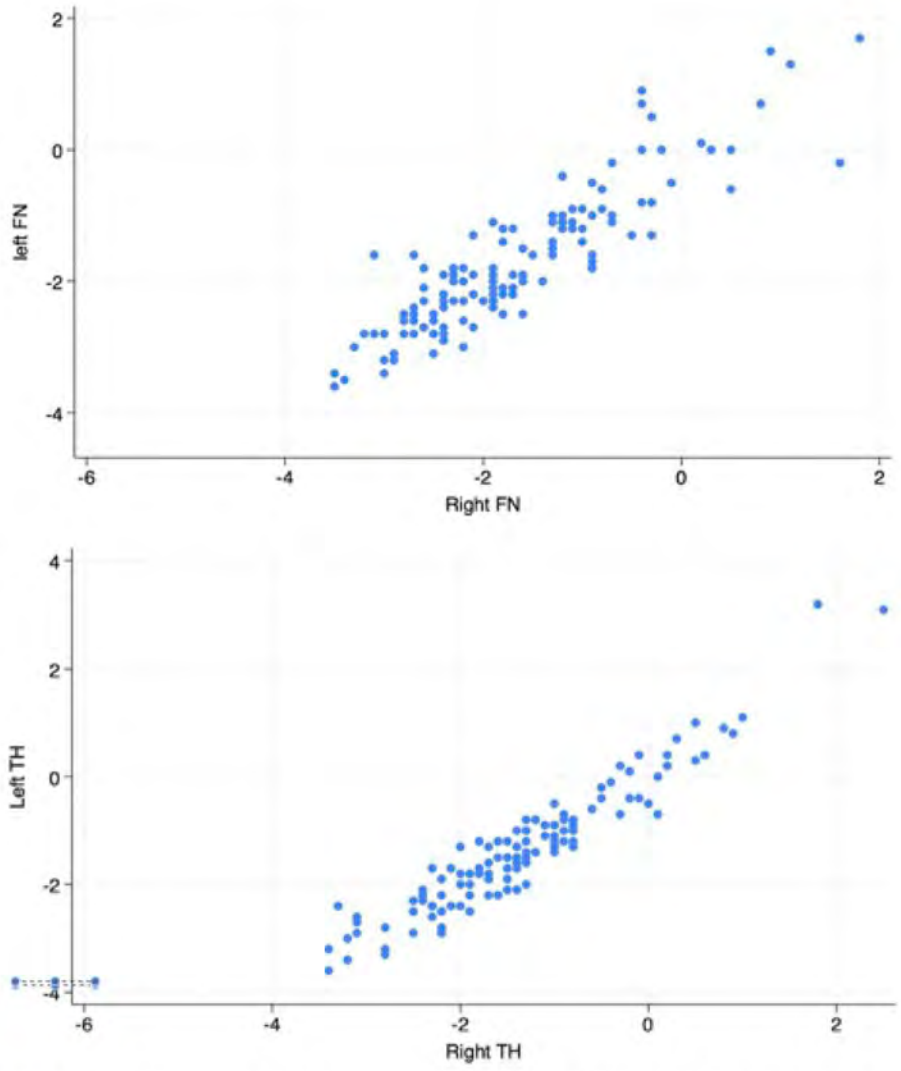


Figure 1A and 1B: Scatter plots comparing right and left sides for FN (A) and total hip (B)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

osteoporosis on the other side. This resulted in a reclassification rate of 7.8%, with 7% of patients with missed diagnosis of osteoporosis. Correlation between the two sides was high (Figure 1A and B) and there were no statistically significant differences between the left and right sides (Table 2).

Conclusion: In this retrospective study of patients >50 years, measurement of bilateral hip bone density demonstrated a high overall correlation between the two sides but resulted in a reclassification rate of 7% from low bone mass into osteoporosis when compared to measuring only one side. There may be a significant missed opportunity for primary fracture prevention which needs further examination.

Disclosure: A. Shahane: None; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 1, Johnson & Johnson, 1, 2, Novartis, 1; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5.

Abstract Number: 0340

Associations with fragility fractures in a population with inflammatory bowel disease (IBD): An observational study.

Chern Lee Choy[1], Hamzah Amin[2] and marwan Bukhari[3], [1]University Hospitals of Morecambe Bay NHS Foundation Trust, Barrow-In-Furness, United Kingdom, [2]Lancaster University, Lancaster, United Kingdom, [3]University Hospitals of Morecambe bay NHS foundation trust, Lancaster, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: It is well recognized that inflammatory bowel disease (IBD) is associated with osteoporosis and fragility fractures, likely due to multiple factors, including systemic inflammation, corticosteroid use, malabsorption etc. Nonetheless, the exact mechanism for fractures in IBD patients is still unclear. There are multiple studies working with small cohorts, supporting different predictors for fracture risk, yet it remains to be elucidated. This study aims to evaluate the association of demographic and various predictors with fracture risk in IBD patients on and off steroids.

Methods: A retrospective observational study was conducted in IBD patients who had a dual-energy X-ray absorptiometry (DEXA) scan done in the North West of England between 2004 and 2019. Data analysed included demographics, family history of fractures, FRAX™ risk factors, total femur BMD, L1-L4 BMD, fat percentages at different sites including total body, abdomen and both femurs. Chi-square tests were used to assess statistically significant associations between categorical variables, while Student's t-tests were used for continuous variables. Univariate and multivariate logistic regression models were then utilised to identify significant predictors associated with the development of fractures. Results are shown in both Table 1 and 2.

Results: A total of 1827 patients with IBD were analysed, in which 1495 (81.8%) were female. The mean age at DEXA scan was 65.2 (SD 13.17) years. Fractures occurred in 674 (36.9%) patients, including 573 (31.4%) females and 101 (5.5%) males. Patient with fractures had a higher fat percentage in total, abdominal and femoral regions. Fractures were also associated with lower BMD at all measured sites including L1-L4, femoral necks and total femur.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of IBD patients

Variables	All patients with IBD (n=1827)	IBD with fracture (n=674)	IBD without fracture (n=1153)	*p*-value
Mean age at DEXA scan (SD), years	65.2 (13.17)	66.4 (12.92)	64.4 (13.26)	0.002
Male, n (%)	332 (18.2)	101 (30.4)	231 (69.6)	0.007
Female, n (%)	1495 (81.8)	573 (38.3)	922 (61.7)	0.007
Height (cm)	162.1	161.6	162.4	0.064
Weight (kg)	72.00	71.41	71.23	0.823
BMI (kg/m^2)	27.07	27.27	26.95	0.258
Total fat percentage (%)	39.21	41.19	38.04	<0.001
Abdominal fat percentage (%)	31.80	32.55	31.36	0.035
Right femur fat percentage (%)	29.70	32.03	28.4	<0.001
Left femur fat percentage (%)	30.29	32.83	28.86	<0.001
Dual femur fat percentage (%)	29.80	32.24	28.49	<0.001
L1 -L4 BMD (g/cm^2)	1.099	1.059	1.122	<0.001
Right femur neck BMD (g/cm^2)	0.8690	0.8257	0.8929	<0.001
Right femur total BMD (g/cm^2)	0.9092	0.8639	0.9338	<0.001
Left femur neck BMD (g/cm^2)	0.8621	0.8178	0.8865	<0.001
Left femur total BMD (g/cm^2)	0.9084	0.8595	0.9352	<0.001
Previous fractures	69	64 (92.8%)	5 (7.2%)	<0.001
Family history of fractures	440 (24.1%)	177 (40.2%)	263 (59.8%)	0.096
Rheumatoid arthritis	146 (8.0%)	65 (44.5%)	81 (55.5%)	0.046
Secondary osteoporosis	29 (1.6%)	12 (41.4%)	17 (58.6%)	0.614
Any steroid use	575 (31.5%)	173 (30.1%)	402 (69.9 %)	<0.001
Current steroid use	361 (19.8%)	88 (24.4%)	273 (75.6%)	<0.001
Previous steroid use	220 (12.0%)	87 (39.5%)	133 (60.5%)	0.384
Any alcohol use	145 (7.9%)	54 (37.2%)	91 (62.8%)	0.927
Current excess alcohol use	123 (6.7%)	45 (36.6%)	78 (63.4%)	0.942
Previous excess alcohol use	30 (1.6%)	13 (43.3%)	17 (56.7%)	0.461
Any smoking	629 (34.4%)	231 (36.7%)	398 (63.3%)	0.915
Current smoker	163 (8.9%)	59 (36.2%)	104 (63.8%)	0.847
Previous smoker	481 (26.3%)	181 (37.6%)	300 (62.4%)	0.696

Table 2. Univariate and Multivariate model analysis for predictors of fracture in IBD patients

	Unadjusted OR		Adjusted OR	
Variables	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Mean age at DEXA scan	1.012 (1.004, 1.019)	0.002	1.007 (0.997, 1.018)	0.160
Gender	0.704 (0.545, 0.909)	0.007	0.766 (0.512, 1.146)	0.195
Height (cm)	0.989 (0.978, 1.001)	0.064	0.980 (0.910, 1.055)	0.585
Weight (kg)	1.001 (0.995, 1.006)	0.823	1.041 (0.958, 1.130)	0.342
BMI (kg/m^2)	1.010 (0.993, 1.026)	0.258	0.911 (0.734, 1.132)	0.402
Total fat percentage (%)	1.039 (1.027, 1.050)	<0.001	1.006 (0.973, 1.041)	0.713
Abdominal fat percentage (%)	1.009 (1.001, 1.018)	0.035	0.980 (0.962, 0.999)	0.038
Right femur fat percentage (%)	1.062 (1.048, 1.077)	<0.001	1.414 (1.112, 1.799)	0.005
Left femur fat percentage (%)	1.065 (1.052, 1.079)	<0.001	1.582 (1.248, 2.006)	<0.001
Dual femur fat percentage (%)	1.065 (1.051, 1.080)	<0.001	0.477 (0.300, 0.759)	0.002
L1 -L4 BMD (g/cm^2)	0.161 (0.095, 0.275)	<0.001	0.778 (0.324, 1.870)	0.575
Right femur neck BMD (g/cm^2)	0.034 (0.016, 0.072)	<0.001	0.069 (0.003, 1.358)	0.079
Right femur total BMD (g/cm^2)	0.053 (0.027, 0.104)	<0.001	36.401 (1.132, 1170.669)	0.042
Left femur neck BMD (g/cm^2)	0.029 (0.014, 0.064)	<0.001	1.543 (0.081, 29.501)	0.773
Left femur total BMD (g/cm^2)	0.039 (0.019, 0.078)	<0.001	0.021 (0.001, 0.676)	0.029
Previous fractures	24.089 (9.644, 60.169)	<0.001	95.398 (11.270, 807.509)	<0.001
Family history of fractures	1.205 (0.967, 1.502)	0.096	1.062 (0.800, 1.409)	0.679
Rheumatoid arthritis	1.413 (1.004, 1.987)	0.047	1.252 (0.795, 1.971)	0.332
Secondary osteoporosis	1.211 (0.575, 2.552)	0.614	0.069 (0.007, 0.719)	0.025
Any steroid use	0.645 (0.522, 0.797)	<0.001	1.874 (0.015, 235.572)	0.799
Current steroid use	0.484 (0.372, 0.629)	<0.001	0.322 (0.003, 40.085)	0.645
Previous steroid use	1.137 (0.852, 1.517)	0.385	0.403 (0.003, 49.942)	0.712
Any alcohol use	1.016 (0.716, 1.444)	0.927	0.472 (0.065, 3.440)	0.459
Current excess alcohol use	0.986 (0.674, 1.442)	0.942	1.885 (0.279, 12.727)	0.516
Previous excess alcohol use	1.314 (0.634, 2.723)	0.462	1.912 (0.364, 10.038)	0.444
Any smoking	0.989 (0.810, 1.208)	0.915	0.571 (0.142, 2.297)	0.430
Current smoker	0.968 (0.692, 1.352)	0.847	1.632 (0.434, 6.132)	0.469
Previous smoker	1.044 (0.842, 1.295)	0.696	1.929 (0.491, 7.576)	0.346

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Of the 1252 (68.5%) patients not using steroids, 501 (40.0%) reported fractures, while 88 (24.1%) of the 361 current steroid users had fractures. 65 (44.5%) of the 146 (8.0%) patients with rheumatoid arthritis also reported fractures. 64 out of the 647 patients with fractures reported previous fractures.

The multivariate model identified abdominal fat percentage, both right and left femur fat percentages, dual femur fat percentages, both right and left total femur BMD, to be significant predictors of fractures in IBD patients. The right femur fat percentage showed a wide confidence interval (OR 36.40, 95% CI: 1.13–1170.67, p = 0.042), possibly due to sample variability or multicollinearity, though the association remains statistically significant and may be clinically relevant.

Conclusion: Our study showed that lower total femoral BMD is associated with an increased fracture risk in patients with IBD, reinforcing the association between reduced BMD and higher fracture likelihood. Moreover, higher fat percentages in both femoral regions elevate fracture risk, suggesting that body fat composition at different sites may play a role in the development of fragility fractures. It is notable that fractures occurred in a significant proportion of steroid-naive patients with IBD, suggesting that IBD itself contributes to the development of fragility fractures.

Disclosure: C. Choy: None; **H. Amin**: None; **m. Bukhari**: None.

Abstract Number: 0341

Romosozumab in patients with Osteoporosis: Safety and Efficacy analysis in Clinical Practice

Daniel Ramos Castro[1], SAMUEL LEAL[2], ELENA GRAU GARCIA[3], Pablo Muñoz-Martínez[4], Laura Mas Sanchez[5], Alba Maria Torrat Noves[6], Belen Villanueva Manes[7], Iago Alcantara Alvarez[8], Andres perez Hurtado[9], Miguel Simeo Vinaixa[9] and José Andrés Román Ivorra[10], [1]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [2]Rheumatology Department. HUP La Fe, Valencia, Comunidad Valenciana, Spain, [3]HUP La Fe, Valencia, Comunidad Valenciana, Spain, [4]Hospital Universitario y Politécnico La Fe, Sagunto, Spain, [5]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [6]Hospital Universitari i Politecnic La Fe de Valencia, Valencia, Spain, [7]Hospital La Fe, Valencia, Spain, [8]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [9]Rheumatology Department. HUP La Fe, Valencia, Spain, [10]Hospital Universitari i Politècnic La Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoporosis is the most common bone metabolism disorder in developed countries. It increases the risk of fragility fractures, impairing quality of life, increasing disability, mortality, and healthcare costs. Recently approved, Romosozumab is the only treatment with dual antiresorptive and bone-forming effects.

The aim of this study is to characterize the profile of patients treated with romosozumab, as well as its safety and efficacy.

Methods: This is a retrospective, longitudinal, descriptive study of patients with osteoporosis treated with romosozumab. Baseline clinical data on bone metabolism (PTH, β-CTX, P1NP, ALP, and vitamin D) and densitometry (T-score/BMD) were collected at the start of treatment, at 6 months, and after completing 1 year.

Results: A total of 49 patients (100% women) with a mean age of 71.8 years were included. Primary osteoporosis was diagnosed in 75.5% of cases, and 70.2% had a history of fractures, most commonly vertebral (57.6%). The most frequent

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. BMD and bone biomarkers evolution during Romosozumab treatment.

	Month 0	Month 6	Month 12	
N	49	36	28	Delta BMD (%)
BMD Lumbar spine	0.72 (0.16)	0.75 (0.16)	0.81 (0.19)	+12,5%
BMD Femoral neck	0.56 (0.09)	0.56 (0.09)	0.6 (0.11)	+7,14%
BMD Total hip	0.68 (0.11)	0.7 (0.11)	0.75 (0.15)	+10,29%
Vit. D	35.01 (14.41)	40.79 (17.7)	37.02 (12.7)	
P1NP	47.94 (33.81)	70.85 (68.63)	59.18 (34.57)	
β-CTX	0.33 (0.34)	0.39 (0.85)	0.23 (0.22)	
PTH	88.49 (48.33)	152.63 (190.42)	83.8 (46.01)	
Alkaline phosphatase	134,24 (121,88)	145.24 (137.99)	78.8 (18.01)	

cardiovascular risk factors were dyslipidemia (42.9%), hypertension (40.8%), and diabetes (8.2%). Active smoking was reported by 8.2% of patients, and none reported habitual alcohol consumption. A history of malignancy was recorded in 10 patients (3 non-melanoma skin cancer, 3 breast, 1 lung, 1 kidney, 1 hematologic, and 1 parotid), and 5 patients had a history of radiotherapy.

Prior to romosozumab, the most commonly used treatments were oral bisphosphonates (38.8%), denosumab (20.4%), and teriparatide (16.3%). The mean duration of romosozumab treatment was 10.51 months (median: 12 months). A total of 5 adverse events were recorded: 1 case each of arthromyalgia, heart failure decompensation, dizziness, blurred vision, and local reaction. No pulmonary embolism (PE), major adverse cardiovascular events (MACE), or strokes were reported. Of the 49 patients who initiated treatment, 28 completed the full 12-month course. The most frequently used medications after romosozumab were denosumab (44.4%), risedronic acid (27.8%), zoledronic acid (13.9%), alendronate (5.6%), and teriparatide (2.8%).

Renal function markers and general biochemical markers remained stable throughout treatment. Regarding bone metabolism markers, β-CTX decreased from 0.33 to 0.23, as did ALP (100.12 to 90.85). Conversely, P1NP increased (from a mean of 47.94 to 59.18). PTH increased at 6 months but returned to normal by the end of treatment. Vitamin D levels remained unchanged.

For densitometry, the mean baseline T-scores were: lumbar spine -3.05, femoral neck -2.63, and total hip -2.15. Among patients who completed 12 months of treatment, BMD increased at all three sites. This resulted in a reduction in the proportion of patients with osteoporosis: from 70.45% to 46.67% at the lumbar spine, from 60% to 50% at the femoral neck, and from 34.88% to 21.43% at the total hip.

Conclusion: Romosozumab is a safe bone-forming treatment option for elderly patients with established classic cardiovascular risk factors. An increase in bone formation markers and a reduction in bone resorption were observed in blood tests, along with an increase in BMD. The most frequently used therapy after romosozumab was denosumab, followed by bisphosphonates.

Disclosure: D. Ramos Castro: None; **S. LEAL**: None; **E. GRAU GARCIA**: None; **P. Muñoz-Martínez**: None; **L. Mas Sanchez**: None; **A. Torrat Noves**: None; **B. Villanueva Manes**: None; **I. Alcantara Alvarez**: None; **A. perez Hurtado**: None; **M. Simeo Vinaixa**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0342

Comparison of Cortical Backscatter Ultrasound, Reference-Point Indentation and Bone Mineral Density in Discriminating Prevalent Fragility Fractures in Inflammatory Rheumatic Diseases: A Pilot Study

Edgar Wiebe[1], Benjamin Kuntz[2], Angela Galindo Santos[3], Zhivana Boyadzhieva[3], Sandra Hermann[1], Burkhard Muche[2], Andriko Palmowski[2], Gerhard Krönke[4], Ralf Schmidmaier[5], Kay Raum[3] and FRANK BUTTGEREIT[6], [1]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Berlin, Germany, [4]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Berlin, Germany, [5]Klinikum der Universität München, Medizinische Klinik und Poliklinik IV, München, Bayern, Germany, [6]Charite University Medicine Berlin, Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with inflammatory rheumatic and musculoskeletal diseases (iRMDs) are at elevated risk for osteoporotic fragility fractures. Standard assessment via dual-energy X-ray absorptiometry (DXA) does not fully capture fracture risk. Cortical Backscatter (CortBS) ultrasound is a radiation-free technique assessing viscoelastic and microstructural cortical bone properties and has shown high accuracy in detecting prior fractures in postmenopausal women. Bone material strength index (BMSi), derived from reference-point indentation, reflects mechanical bone properties. However, their comparative performance in fracture discrimination in iRMDs is unclear.

This study aimed to evaluate the performance of CortBS in detecting prevalent fragility fractures in iRMD patients, compared to DXA and BMSi.

Methods: Consecutive iRMD patients from our outpatient osteoporosis clinic, with and without prior fragility fractures and no prior anti-osteoporotic treatment, were analyzed. CortBS was measured at the anteromedial tibia using a custom ultrasound scanner. DXA-based T-scores and BMSi (via 8 indentations) were obtained at the same visit.

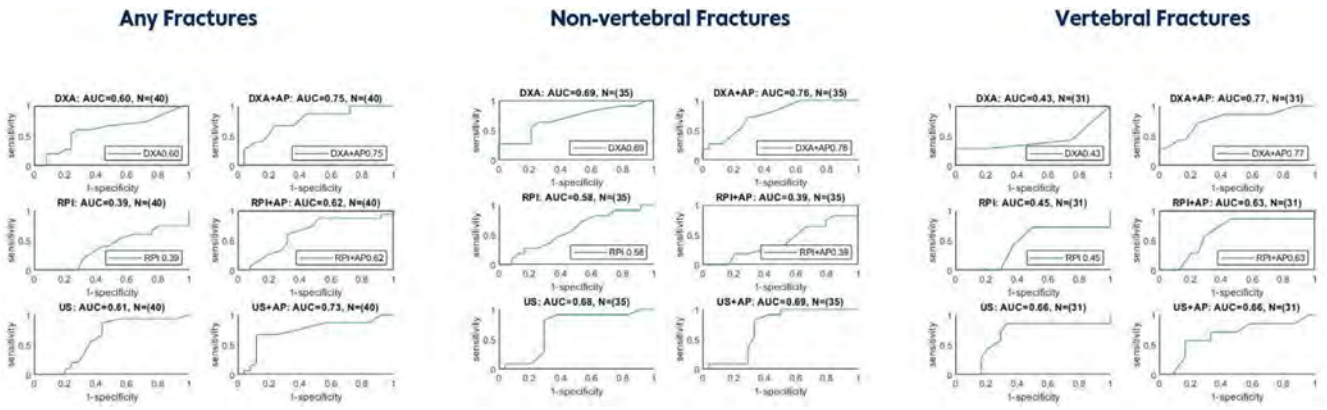


Figure 1: ROC-AUC with 5-fold cross-validation for any (left), non-vertebral (center) and vertebral (right) fragility fractures for DXA, BMSi and CortBS. AP (anthropometric data: weight, height, body mass index)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

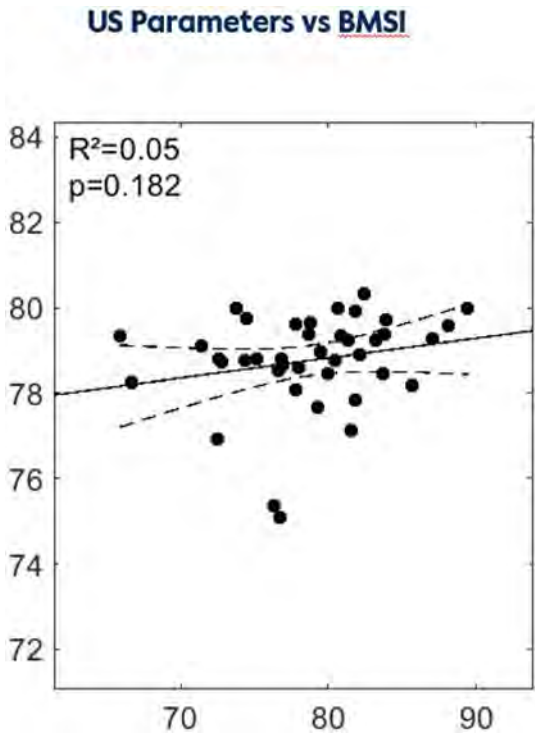


Figure 2: Predictions of aBMD at spine (A), femur neck (B), and total femur (C) based on ultrasound backscatter and anthropometric parameters using multivariate PLS regression Spearman correlation

Fracture discrimination models for vertebral, non-vertebral, and any fragility fracture were developed using multivariate partial least squares linear discrimination analysis with Leave-One-Out Cross-Validation (PLS-LDA LOOCV). For each method, the area under the curve (AUC) of the receiver operating characteristics (ROC), sensitivity, and accuracy were calculated, with and without anthropometric data (weight, height, BMI). CortBS-BMSi correlation was assessed using PLS regression with threefold cross-validation.

Results: 97 iRMD patients (mean age 64 ± 10 years) were included: 42% with rheumatoid arthritis, 23% spondyloarthritides, and 19% connective tissue diseases. 44 patients (45%) had fragility fractures (19 vertebral, 34 non-vertebral, 9 both). Complete CortBS data were available in 40 patients (15 with fractures). CortBS showed comparable discrimination to DXA for any fracture (AUC 0.61 vs. 0.60) and non-vertebral fractures (AUC 0.68 vs. 0.69). For vertebral fractures, CortBS (AUC 0.66) outperformed both DXA (0.43) and BMSi (0.45), though small sample size limits interpretation.

Adding anthropometric data improved prediction for all tools (CortBS AUC 0.73, DXA 0.75, BMSi 0.62). No significant correlation was found between CortBS and BMSi (R^2 = 0.05, p = 0.18).

Conclusion: CortBS demonstrated fracture discrimination comparable to DXA and even superior performance for vertebral fractures. In contrast, BMSi showed limited discriminatory ability. As a radiation-free and accessible technique, CortBS holds promise for improving fracture risk assessment in iRMDs. Larger and longitudinal studies are needed to evaluate whether CortBS can enhance fracture prediction by capturing cortical porosity and structural bone properties.

Disclosure: E. Wiebe: Sobi, 6; **B. Kuntz**: None; **A. Galindo Santos**: None; **Z. Boyadzhieva**: None; **S. Hermann**: None; **B. Muche**: AbbVie/Abbott, 6, Amgen, 6, Celltrion, 6, Theramex, 6, UCB, 6; **A. Palmowski**: Novartis, 1; **G. Krönke**: None; **R. Schmidmaier**: None; **K. Raum**: None; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

Abstract Number: 0343

Impact of Janus Kinase Inhibitors on Bone Mineral Density and Microarchitecture in Rheumatoid and Psoriatic Arthritis: Insights from a Real-World Cohort

Edgar Wiebe[1], Dörte Huscher[2], Zhivana Boyadzhieva[3], Andriko Palmowski[4], Sandra Hermann[1], Burkhard Muche[4], Arnd Kleyer[5], David Simon[6], Gerhard Krönke[7], Paula Hoff[8] and FRANK BUTTGEREIT[9], [1]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [5]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [6]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Germany, [7]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Berlin, Germany, [8]Endokrinologikum Berlin, Medizinisches Versorgungszentrum (MVZ) am Gendarmenmarkt, Berlin, Berlin, Germany, [9]Charite University Medicine Berlin, Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Janus kinase (JAK) inhibitors are an important treatment option for rheumatoid arthritis (RA) and psoriatic arthritis (PsA). By disrupting pro-inflammatory cytokine signaling (e.g., IL-6, TNF-α), they reduce inflammation and may potentially mitigate bone loss. Chronic inflammation in RA and PsA leads to systemic and local imbalances in bone remodeling, characterized by increased osteoclast activity and decreased osteoblast function. While JAK inhibitors have shown promise in counteracting these processes *locally*, clinical evidence regarding their effects on systemic bone health remains limited.

Table 1: Results from the multivariable linear regression model with backward selection for minimum T-Score and trabecular bone score (TBS) forcing JAK inhibitors into the model JAK : Janus kinase, BMI : Body Mass Index, CI : confidence interval, CRP : C-reactive Protein, DAS28 : Disease-activity score 28, GC : Glucocorticoids

	T-Score		TBS	
	β (95% CI)	p-value	β (95% CI)	p-value
JAK-inhibitors	-0.095 (-0.322;0.132)	0.413	**0.061 (0.021;0.101)**	**0.003**
Glucocorticoid treatment	-0.257 (-0.405;-0.109)	<0.001		
Family history for fractures	-0.395 (-0.627;-0.164)	<0.001		
Female sex			0.085 (0.058;0.111)	<0.001
Diabetes mellitus (Typ I or II)			-0.034 (-0.067;0)	0.048
DAS28-CRP			-0.012 (-0.021;-0.003)	0.010
BMI	0.049 (0.036;0.061)	<0.001	-0.015 (-0.017;-0.012)	<0.001
Age (in years)	-0.027 (-0.034;-0.021)	<0.001	-0.003 (-0.004;-0.002)	<0.001
Active smoking	-0.278 (-0.455;-0.101)	0.002	-0.047 (-0.077;-0.016)	0.003
Prevalent osteoporotic fractures	-0.272 (-0.417;-0.127)	<0.001		
GC cumulative dose	-3.74E-03 (-6.94E-03;-5.42E-04)	0.022		

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We aimed to quantify the impact of JAK inhibitors on bone health in a real-world cohort of patients with RA and PsA.

Methods: Baseline data from patients with RA or PsA from the Rh-GIOP study, a prospective observational cohort at Charité–Universitätsmedizin Berlin, were included in this cross-sectional analysis. Bone health was assessed using DXA for bone mineral density (expressed as the minimum T-Score from lumbar spine and hip measurements), trabecular bone score (TBS; enCORE V18 iNsight®, Med-Imaps SA), and 3D structural parameters of the femur (3D-Shaper v2.12, 3D-Shaper Medical). Multivariable linear regression models were used to identify clinical, serological, and treatment-related factors associated with T-Score and TBS. JAK inhibitors were included in these models to evaluate their impact on outcomes, provided that a prior stable treatment period had been established. Missing data were addressed using multiple imputation with 10 replications.

Results: The study included 856 patients (mean age 64 years, 77% female, 92% postmenopausal), with 89 receiving JAK-inhibitors (33 baricitinib, 25 tofacitinib, 21 upadacitinib, 10 filgotinib). Osteoporosis was prevalent in 24% of patients, while the majority had either normal bone mineral density (BMD) or osteopenia. Treatment with JAK inhibitors was not significantly associated with T-Score (table 1). However, vertebral trabecular microarchitecture expressed by TBS, showed that JAK-inhibition was positively associated with TBS (β (95%CI)= +0.061 (0.021;0.101), p=0.003), suggesting a potential positive impact on trabecular microarchitecture.

Conclusion: In this real-world cohort, JAK inhibitors were associated with positive impact on trabecular microarchitecture. These findings suggest that a broad cytokine inhibition may support bone health. Longitudinal studies are required to confirm these observations and evaluate their implications for fracture prevention and individualized treatment strategies.

Disclosure: E. Wiebe: Sobi, 6; **D. Huscher**: None; **Z. Boyadzhieva**: None; **A. Palmowski**: Novartis, 1; **S. Hermann**: None; **B. Muche**: AbbVie/Abbott, 6, Amgen, 6, Celltrion, 6, Theramex, 6, UCB, 6; **A. Kleyer**: AbbVie/Abbott, 1, 6, Alfasigma, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, 6, Gilead, 1, Janssen, 1, 6, Novartis, 1, 6, UCB, 1, 6; **D. Simon**: AbbVie, 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, Janssen-Cilag, 2, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Lilly, 2, 6, Medac, 2, 6, Novartis, 2, 6, UCB, 2, 6; **G. Krönke**: None; **P. Hoff**: None; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

Abstract Number: 0344

Inpatient Zoledronic Acid for Glucocorticoid-Induced Osteoporosis Prevention

Gregory Challener[1], Zandra E. Walton[1], Christine M. Parsons[1], Aakash V. Patel[2], Alex Tinianow[3], Molly E. Griffin[1], Raisa Lomanto Silva[3], Avira Som[1], Laura J. Yockey[4], WuQiang Fan[5], Sheila L. Arvikar[1] and Marcy Bolster[6], [1]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, [2]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [3]Massachusetts General Hospital, Boston, MA, [4]MGH, Charlestown, MA, [5]Division of Endocrinology, Department of Medicine, Massachusetts General Hospital, Boston, [6]Massachusetts General Hospital, Concord, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Glucocorticoids are widely used in rheumatology and are associated with increased fracture risk. The 2022 ACR Guideline for the Prevention and Treatment of Glucocorticoid-induced Osteoporosis (GIOP) strongly recommends assessment of fracture risk for patients initiating prolonged glucocorticoid treatment with pharmacologic treatment for GIOP prevention depending on risk stratification. While many patients with new diagnoses or flares of giant cell arteritis (GCA) or idiopathic inflammatory myopathies (IIM) meet criteria for GIOP prevention, initiation of such therapy is often delayed or missed. We hypothesized that a standardized inpatient screening protocol with administration of inpatient zoledronic acid (ZA) for appropriate patients would improve timely GIOP prevention.

Methods: This project evaluated a new screening protocol for addressing GIOP prevention in hospitalized patients with active GCA or IIM (**Figure 1**). The protocol, based on the 2022 ACR Guideline, was implemented by the Massachusetts General Hospital Rheumatology Consult Service from February 2024 to January 2025 and compared to a historical cohort from February 2022 to January 2023. The primary outcome was GIOP treatment initiation within 3 months of diagnosis. Secondary outcomes included inpatient ZA use and DXA completion within 6 months of initial evaluation. Patients were

GIOP prophylaxis decision aid
(please check appropriate boxes by placing an x in the brackets [x])

Inclusion criteria (must meet all 4):
[] 40 years of age or older
- diagnosis or suspected diagnosis of:
  [] GCA, or
  [] myositis
- started on high-dose steroids during the index hospitalization with plan for either:
  [] ≥ 30 days of ≥ 30 mg qd prednisone (or equivalent), or
  [] ≥ 3 months of ≥ 2.5 mg qd of prednisone (or equivalent)
- "moderate" (or higher) fracture risk per the 2022 ACR GIOP guideline (https://assets.contentstack.io/v3/assets/bliee37abb6b278ab2c/blt8c68fa62e5f70069/giop-guideline-summary-2022.pdf):
- FRAX calculator here: https://frax.shef.ac.uk/FRAX/tool.aspx?country=9
- Patient's FRAX score is (ensure glucocorticoid use risk factor selected in calculator question #8):
  _____ % 10-y risk for major osteoporotic fracture (MOF)
  _____ % 10-y risk for hip fracture
  - FRAX score corrected for GC use (applicable if > 7.5 mg/d prednisone equiv.) is:
    (Above x 1.15) _____ % 10-y risk for major osteoporotic fracture (MOF)
    (Above x 1.2) _____ % 10-y risk for hip fracture
  - Patient is:
    [] very high fracture risk
    [] high fracture risk
    [] moderate fracture risk

PATIENT MEETS INCLUSION CRITERIA:
[] YES (meets all 4 above requirements)
[] NO

Important considerations
(please check the boxes by placing an x in the brackets [x] if any of the following apply to this patient):
[] previously treated with antiresorptive or anabolic therapy for bone health within the last 2 years (may be reasonable to continue holiday if on holiday or continue current therapy)
[] have enough uncertainty in their diagnoses at the time of discharge (e.g., still awaiting biopsy result) that it precludes reasonable estimation of duration of steroid exposure (may be reasonable to defer decision on GIOP prophylaxis)
[] women of childbearing potential (do not use bisphosphonate)
[] CrCl <35 cc/min (do not use bisphosphonate)
[] 25-OH vitamin D <28 ng/mL (replete first)
[] hypocalcemia (uncorrected) (rectify first)
[] planned invasive dental work (avoid anti-resorptive)

Treatment:
[] optimize vitamin D and calcium intake through supplements and diet. Recommend calcium and vitamin D supplementation
- consider oral (alendronate) or IV (zoledronic acid). Reasons to choose IV over oral include GERD, difficulty with adherence to oral medication, patient preference.
- for those with very high fracture risk, consider also PTH analogs (teriparatide, abaloparatide) for anabolic benefit. Reasons to avoid include elevated PTH or MGUS (send PTH and SPEP/SFLC if considering), hx of Paget's, other risk factor for osteosarcoma (hx of radiation to skeleton, skeletal mets), insurance coverage, cost.
- for those with high fracture risk, consider also denosumab. Reasons to avoid include patient at risk of adherence interruption (should not be abruptly stopped).
- for those with very high fracture risk, consider romosozumab for anabolic benefit. Reasons to avoid include CV risk (increased risk of MI, stroke, and death; absolute contraindication if MI or stroke in last yr), cost, insurance coverage.

PATIENT WILL BE STARTED ON:
[] alendronate
[] zoledronic acid
[] other: _____

THIS IS PLANNED TO START:
[] inpatient (please record date if known _____)
[] outpatient

Figure 1. GIOP Screening Protocol

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Intervention and Historical Cohorts

	Intervention cohort (N=19)	Historical cohort (N=20)
Demographics		
Female, n (%)	15 (78.9%)	13 (65%)
Age, mean (SD)	71.9 (12.1)	70.1 (10.5)
Race/ethnicity		
Asian	1 (5.3%)	0
Black	1 (5.3%)	0
White	17 (89.5%)	19 (95%)
Unknown	0	1 (5%)
Comorbidities		
Inpatient diagnosis		
Inflammatory myopathy	3 (15.8%)	5 (25%)
Giant cell arteritis	16 (84.2%)	15 (75%)
Known osteopenia (preceding)	6 (31.6%)	3 (15%)
Known osteoporosis (preceding)	3 (15.8%)	3 (15%)
Prior fragility fracture	3 (15.8%)	4 (20%)
Chronic kidney disease	5 (26.3%)	5 (25%)
Other		
Prior history of antiresorptive or anabolic therapy (>2y prior)	3 (15.8%)	3 (15%)
On aromatase inhibitor	1 (5.3%)	0
Tobacco use		
Never	9 (47.4%)	14 (70%)
Past	9 (47.4%)	5 (25%)
Current	1 (5.3%)	1 (5%)
EtOH use >=3 drinks/day	0	1 (5%)

identified by billing codes and chart review, with exclusions for factors including age < 40, prior anabolic or antiresorptive therapy (within the preceding 2 years), renal insufficiency with eGFR < 35 mL/min/1.73 m^2, and 25-hydroxy vitamin D < 20 ng/mL, noting the latter two factors were uncommon reasons for exclusion, resulting in only 3 excluded patients in each cohort. Fisher's exact test *p*-values were used to compare categorical outcomes between the intervention and historical cohorts.

Results: A total of 39 patients were included (19 intervention, 20 historical). Baseline characteristics were similar with respect to age (mean 71.9 versus 70.1 years, respectively), race/ethnicity, and prevalence of comorbidities (**Table 1**). GIOP preventative therapy within 3 months was more frequent in the intervention group (52.6% vs 40%, p=0.53) with higher rates of inpatient ZA administration (26.3% vs 15%, p =0.45). There were similar rates of other GIOP preventative therapy (26.3% vs 25%, p=1.00) and DXA completion within 6 months (52.6% vs 45%, p=0.75) (**Table 2**).

Conclusion: Implementation of a systematic inpatient screening protocol and provision of ZA in the inpatient setting for patients with active GCA or IIM has the potential to improve timely initiation of GIOP management. While our outcomes did not reach statistical significance, likely due to a limited sample size over a 12-month period, the increased rate of timely GIOP

Table 2. Patient Outcomes

	Intervention cohort (N=19)	Historical cohort (N=20)	*p*-value
Received GIOP within 3 months	10/19 (52.6%)	8/20 (40%)	$p = 0.53$
Received ZA inpatient	5/19 (26.3%)	3/20 (15%)	$p = 0.45$
Received other GIOP	5/19 (26.3%)	5/20 (25%)	$p = 1.00$
Alendronate	3[1]	4	
ZA outpatient	2[1]	1	
Denosumab	1	0	
Teriparatide	0	0	
Did not receive GIOP within 3 months	9/19 (47.4%)	12/20 (60%)	$p = 0.53$
Patient declined inpatient ZA and other GIOP	5	1	
GIOP discussed but not started for unclear reason	2	0	
GIOP not addressed in medical record	2	11	
DXA performed within 6 months	10/19 (52.6%)	9/20 (45%)	$p = 0.75$

[1]Note that one patient received alendronate before transitioning to ZA treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

prophylaxis (noting an already-high baseline rate), particularly with inpatient ZA administration, suggests a potential clinical benefit for an undertreated patient population at risk for significant morbidity. Given its ease of implementation and potential to reduce fracture risk, this intervention will continue as part of our routine inpatient care.

Disclosure: G. Challener: None; **Z. Walton**: Bristol-Myers Squibb(BMS), 2; **C. Parsons**: None; **A. Patel**: None; **A. Tinianow**: None; **M. Griffin**: None; **R. Lomanto Silva**: None; **A. Som**: None; **L. Yockey**: None; **W. Fan**: None; **S. Arvikar**: None; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5.

Abstract Number: 0345

Association Between Deprivation and Fracture Risk in a Regional UK Cohort

Hashem Cheema[1], Hamzah Amin[2] and marwan Bukhari[3], [1]University Hospitals of Morecambe bay NHS foundation trust, Manchester, United Kingdom, [2]Lancaster University, Lancaster, United Kingdom, [3]University Hospitals of Morecambe bay NHS foundation trust, Lancaster, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Low socioeconomic status is associated with.an increase in osteoporosis and fracture risk respectively. A multitude of factors have been proposed including income, educational attainment and cohabitation status. However, the mechanisms that drive the disparity between social deprivation and osteoporosis remain unclear. We aim to identify key socioeconomic factors that could explain the association between deprivation and osteoporosis.

Methods: We conducted a retrospective cohort study on 31,170 patients referred for Dual-Energy X-ray Absorptiometry (DEXA) between April 2006 and February 2024 in the

Table 1 outlines baseline demographics, risk factors for fragility fracture and bone mineral density between the least and most deprived cohorts.

Table 1:

Characteristic	Most deprived N = 10,278	Least deprived N= 10,388	P value	95% CI
Age (yrs)[a]	66 ± 12.4	64 ±13.3		64.60 – 64.96
Height(cm)[a]	162.3 ±8.36	161.3 ±8.73		161.70- 161.93
Female[b]	8,609 (50.06%)	8,588 (49.94%)		
Ever smoked[b]	3,157 (30.66%)	4,729 (45.35%)	0.00	
BMI (kg/m2)[a]	26.7 ± 6.5	27.7 ±27.6		27.09- 27.28
Body fat (%)[a]	29 ±7.3	30 ±7.7		2.97 – 2.99
Fragility fracture[b]	3, 931 (38.17%)	3, 918 (37.57%)	0.37	
Fracture of radius[b]	1,836 (17.83%)	1,751 (16.79%)	0.048	
Bone mineral density (t-Score)[a]	-0.94 ±1.22	-0.94 ±1.29		
Steroid use[b]	2,447 (23.76%)	2,813 (26.98%)	0.00	
excess alcohol[b]	700 (6.80%)	810 (7.77%)	0.007	
Family history of fracture[b]	2,042 (19.83%)	1,894 (18.16%)	0.002	

[a]Mean ± standard deviation
[b]n (%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

North West of England. The cohort was divided into deciles based on the Index of Multiple Deprivation (IMD). The 3 most deprived deciles were compared to the 3 least deprived deciles respectively. Patient demographics, risk factors for fracture risk and bone mineral density from the femoral neck and lumbar spine were recorded. Data was analysed using chi-squared and two-sample t-test. P values of less than 0.05 were considered statistically significant.

Results: The least deprived cohort had a greater steroid use (26.98%), excess alcohol intake (7.77%) and had ever smoked (45.3%). The more deprived had a higher family history of fracture (17.83%) but a lower BMI and percentage body fat. There were no differences in bone density and total fracture rates, however, the more deprived cohorts had a greater rate of radius fracture (17.83%).

Conclusion: These results suggest that whilst there are differences in traditional risk factors for developing fractures between the most and least deprived in society, however, this does not translate towards an increase in total fracture risk nor a reduction in bone mineral density in the least deprived. This supports the evidence that there are unmeasured confounders that could predict fracture risk in groups with greater deprivation. Some limitations include that this is data on referrals to a regional scanner and not population data. Further research is needed to clarify the mechanisms between deprivation and socioeconomic status and fracture risk.

Disclosure: H. Cheema: None; **H. Amin**: None; **m. Bukhari**: None.

Abstract Number: 0346

Fibroblast Growth Factor-23 and Bone Status in Patients with Chronic Kidney Disease Compared to a Healthy Control Group and Its Relationship with Cardiovascular Risk

José Rodríguez gago[1], Carolina Tornero[2], Lina León[3], María Luisa González-Casaus[3], Luisa Fernanda Giraldo[3], Gloria del Peso[3], Diego Garrido[3], Teresa López[3], Mónica Coronado[3], María Auxiliadora Bajo[4], Sara García[3], María Gema Serrano[3], Marta Ossorio[3], Alejandro Balsa[3] and Pilar Aguado[3], [1]Hospital Universitario La Paz, MADRID, [2]Hospital La Paz, Madrid, Spain, [3]Hospital Universitario La Paz, Madrid, Spain, [4]Hospital Universitario de la Princesa - ISS Princesa, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic kidney disease (CKD) is linked to increased vascular comorbidity and fracture risk. This study aims to assess bone status in CKD patients versus healthy controls and its relationship with intact fibroblast growth factor 23 (iFGF-23). A secondary aim is to evaluate cardiovascular risk (CVR) in CKD and its associations with bone status and iFGF-23.

Methods: Adults with CKD stages 2–4 (normal phosphate levels) were assessed for bone metabolism, iFGF-23, and bone density using DXA. Bone quality was evaluated via Trabecular Bone Score (TBS) at the lumbar spine and 3D-DXA at the proximal femur. FRAX scores and vertebral fractures were recorded. Carotid ultrasound and Kauppila vascular calcification scores assessed subclinical CVR. A matched control group (age, sex, BMI) was used for bone quality comparison via propensity score matching.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics and densitometric results from DXA-3D and Trabecular Bone Score (TBS) in CKD patients and controls

Characteristic		Total. N=158	Controls. n=7G	Cases. n=7G	p-value
Male Sex, n/N (%)		118 (74.7)	57 (72.2)	61 (77.2)	0.583
Age (years), median (IQR)		65 (55-72)	63.00 (53-74)	66 (60-71.5)	0.337
BMI (kg/m²), median (IQR)		27.85 (25.18 - 30.77)	27.43 (25.01 - 29.75)	28.17 (25.24 - 32.23)	0.211
Lumbar BMD, median (IQR)		1.06 (0.95 - 1.19)	0.99 (0.91 - 1.06)	1.17 (1.05 - 1.31)	<0.001
Lumbar T-score, median (IQR)		-0.41 [-1.26 - 0.49]	-0.49 [-1.25 - 0.09]	-0.40 [-1.25 - 0.78]	0.173
Femoral BMD, median (IQR)		0.91 (0.82 - 1.02)	0.93 (0.86 - 0.99)	0.90 (0.79 - 1.03)	0.229
Femoral T-score, median (IQR)		-1.05 [-1.75 - (-0.30)]	-0.91 [-1.48 - (-0.28)]	-1.30 [-2.00 - (-0.30)]	0.090
WHO Osteoporosis criteria (%)	Normal	93 (59.2)	66 (83.5)	27 (34.6)	<0.001
	Osteopenia	50 (31.8)	12 (15.2)	38 (48.7)	
	Osteoporosis	14 (8.9)	1 (1.3)	13 (16.7)	
Trabecular bone score (TBS)	Normal	85 (57.8)	47 (63.5)	38 (52.1)	0.301
	Partially degraded	44 (29.9)	18 (24.3)	26 (35.6)	
	Degradaded	18 (12.2)	9 (12.2)	9 (12.3)	
Cortical cBMD (mg/cm²), median (IQR)		167.48 (148.43 - 185.11)	162.51 (148.10 - 184.47)	170.37 (149.22 - 186.15)	0.684
Cortical vBMD (mg/cm³), median (IQR)		822.08 (747.44 - 868.41)	818.45 (746.41 - 883.54)	833.29 (766.05 - 889.65)	0.517
Integral vBMD (mg/cm²), median (IQR)		316.33 (273.96 - 351.24)	316.53 (282.60 - 350.15)	316.13 (260.42 - 352.38)	0.438
Trabecular vBMD (mg/cm³), median (IQR)		165.85 (139.03 - 191.07)	169.45 (147.86 - 190.45)	164.50 (129.40 - 191.43)	0.187
Cortical thickness (mm), median (IQR)		2.01 (1.90 - 2.11)	2.02 (1.90 - 2.11)	2.01 (1.89 - 2.12)	0.786

Results: A total of 79 CKD patients were included. Osteoporosis and osteopenia prevalence was higher in CKD patients (16.7% and 48.7%) compared to controls (15.2% and 1.3%,p=0.001). Among CKD patients with vertebral fractures (n=7;10.6%), TBS was lower (1.256 vs. 1.362,p=0.046), and trabecular volumetric BMD (vBMD) by 3D-DXA was reduced (126.5 vs. 166.6 mg/cm^3,p=0.019). iFGF-23 inversely correlated with cortical vBMD (ρS: -0.82,p=0.02).

Table 2. Demographic characteristics and densitometric results from DXA-3D and TBS sub-analysis in CKD G2-G3a, CKD G3b-G4 patients and controls

Characteristics		(1) Controls. n=7G	(2) CKD G2-G3a. n=3G	(3) CKD G3b-G4. n=40	p-value 2 vs 3	p-value 2 vs 1	p-value 3 vs 1
Male sex, n/N (%)		57 (72.2)	34 (87.2)	27 (67.5)	0.069	0.111	0.754
Age (years), median (IQR)		63.00 (53-74)	65.00 (56.50-69.50)	69.00 (65.50-75.25)	0.009	0.843	0.081
BMI (kg/m²), median (IQR)		27.43 (25.01 - 29.75)	28.17 (25.76- 31.11)	28.02 (25.12 - 32.43)	0.945	0.336	0.281
Lumbar BMD, median (IQR)		0.99 (0.91 - 1.06)	1.17 (1.10 - 1.30)	1.13 (1.02 - 1.30)	0.289	<0.001	<0.001
Lumbar T-score, median (IQR)		-0.49 (-1.25 - 0.09)	-0.10 (-1.10 - 0.70)	-0.50 (-1.45 - 0.63)	0.310	0.062	0.706
Femoral BMD, median (IQR)		0.93 (0.86 - 0.99)	0.94 (0.80 -1.05)	0.89 (0.78 - 0.99)	0.101	0.921	0.043
Femoral T-score, median (IQR)		-0.91 [-1.48 - (-0.28)]	-1.25 [-1.95 - (-0.20)]	-1.30 [-2.00 - (-0.50)]	0.592	0.348	0.073
WHO Osteoporosis Criteria (%)	Normal	66 (83.5)	17 (44.7)	15 (37.5)	0.370	<0.001	<0.001
	Osteopenia	12 (15.2)	16 (42.1)	18 (45.0)			
	Osteoporosis	1 (1.3)	5 (13.2)	7 (17.5)			
Trabecular bone score (TBS)	Normal	47 (61.5)	20 (52.6)	18 (51.4)	1.0	0.364	0.321
	Partially degraded and degraded	27 (36.5)	18 (47.4)	17 (48.6)			
Cortical cBMD (mg/cm²), median (IQR)		162.51 (148.10 - 184.47)	172.87 (150.38 - 189.67)	168.73 (148.70 - 182.56)	0.389	0.422	0.666
Cortical vBMD (mg/cm³), median (IQR)		818.45 (746.41 - 883.54)	853.58 (747.86 - 889.41)	817.16 (778.45 - 886.34)	0.740	0.478	0.742
Integral vBMD (mg/cm²), median (IQR)		316.53 (282.60 - 350.15)	322.69 (280.79 - 356.86)	298.60 (264.19 - 332.48)	0.208	0.816	0.124
Trabecular vBMD (mg/cm³), median (IQR)		169.45 (147.86 - 190.45)	169.04 (134.89 - 201.66)	161.90 (119.34 - 179.07)	0.055	0.977	0.030
Cortical thickness (mm), median (IQR)		2.02 (1.90 - 2.11)	2.02 (1.94 - 2.17)	2.00 (1.86 - 2.11)	0.270	0.439	0.715

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Demographics, laboratory results, ultrasound-based cardiovascular risk assessment, stratified BMD and TBS parameters, and DXA-3D parameters by presence or absence of subclinical cardiovascular risk (SCVR) and/or major adverse cardiovascular events (MACE)

Characteristics		Total. N=62	SCVR and or MACEs. N=45	No SCVR or MACEs. N=17	p-value
Male sex. n/N (%)		46/62 (74.2%)	37/45 (82.2%)	9/17 (52.9%)	0.024
Age (years), median (IQR)		67 (61-73.25)	68 (64-76)	58 (47-70)	0.007
BMI (kg/m²), median (IQR)		25.11 (28.20-31.66)	68 (64-76)	25.22 (22.14-33.76)	0.348
Hypertension, n/N (%)		42/62 (67.7%)	37/55 (82.2%)	5/17 (29.4%)	<0.001
Dyslipidemia, n/N (%)		43/62 (69.4%)	31/45 (71.1%)	10/17 (58.8%)	0.211
Glomerular filtration rate (mL/min/1.73m²)		43.5 (34.75-57)	45 (36-50.5)	37 (31-51)	0.134
FGF-23 (pg/mL)		96.9 (70.9-137.9)	100 (70.3-138)	83 (65.8-142.3)	0.502
Serum calcium (mg/mL)		9.7 (9.5-10)	9.7 (9.5-10)	9.6 (9.4-9.9)	0.306
Serum phosphate (mg/dL)		3.5 (3.1-4)	3.5 (3.4)	3.3 (3.2-4)	0.538
Serum phosphate (mg/dL)		28.5 (23.8-39.3)	28 (21.5-41)	32 (26-38.5)	0.331
PTH (pg/mL)		93.2 (62.3-136.2)	92.4 (57.4-132.3)	98.6 (64.2-153)	0.538
Right carotid IMT, median (IQR)		0.73 (0.62-0.80)	0.75 (0.68-0.81)	0.62 (0.56-0.70)	<0.001
Left carotid IMT,median (IQR)		0.73 (0.61-0.81)	0.76 (0.66-0.84)	0.60 (0.56-0.67)	<0.001
Average carotid IMT, median (IQR)		0.62 (0.62-0.80)	0.75 (0.69-0.81)	0.60 (0.56-0.70)	<0.001
Kauppila index, median (IQR)		2 (0-6.25)	4 (1-7)	0 (0-1)	0.001
Bone densitometry (WHO)	Normal. n/N (%)	20/62 (32.3%)	15/45 (33.3%)	5/17 (29.4%)	0.951
	Osteopenia. n/N (%)	31/62 (50%)	22/45 (48.9%)	9/17 (52.9%)	
	Osteoporosis. n/N (%)	11/62 (17.7%)	8/45 (17.8%)	3/17 (17.6%)	
Femoral BMD (g/cm²), median (IQR)		0.89 (0.79-1.02)	0.89 (0.79-1.02)	0.84 (0.78-1.008)	0.365
Femoral Z-Score, median (IQR)		-0.5 (-0.9-0.50)	0.2 (-0.8-0.55)	-0.6 (-1.2-0.4)	0.099
Lumbar BMD (g/cm²), median (IQR)		1.14 (1.01-1.26)	1.15 (1.04-1.28)	1.06 (1.00-1.26)	0.468
Lumbar Z-Score, median (IQR)		0.05 (-0.72-0.95)	0.1 (-0.56-1.3)	-0.6 (-1.35-0.70)	0.297
Trabecular bone score (TBS)	Normal. n/N (%)	29/59 (50%)	21/43 (48.8%)	8/15 (53.3%)	0.757
	Partially degraded	22/43 (37.9%)	16/43 (37.2%)	6/15 (40%)	
	Degradaded. n/N (%)	7/43 (12.1%)	6/43 (14%)	1/15 (6.7%)	
TBS, median (IQR)		1.349 (1.233-1.422)	1.347 (1.221-1.42)	1.356 (1.246-1.438)	0.5
Cortical vBMD (mg/cm³),median (IQR)		168.72 (140.29-191.84)	170.37 (150.15-192.40)	152.63 (136.17-178.70)	0.220
Cortical vBMD (mg/cm³), median (IQR)		820.98 (744.66-888.68)	833.29 (744.66-889.65)	785.67 (736.05-869.81)	0.701
Trabecular vBMD (mg/cm³), median (IQR)		161.9 (119.68-185.95)	163.76 (129.40-185.95)	131.42 (109.97-192.52)	0.453
Cortical thickness (mm), median (IQR)		1.98 (1.85-2.11)	2.00 (1.86-2.13)	1.94 (1.83-2.09)	0.365
FRAX without TBS	Major	2.6 (1.88-4.78)	3 (1.8-4.7)	2.1 (1.4-5.4)	0.576
	Hip	0.6 (0.2-1.43)	0.6 (0.2-1.6)	0.5 (0.2-1.1)	0.742
FRAX with TBS	Major	3 (1.8-4.85)	3.3 (2-4.9)	2.3 (1.3-6.4)	0.329
	Hip	0.7 (0.2-1.45)	0.7 (0.2-1.65)	0.4 (0.1-1.75)	0.491

Abbreviations: aIMT: Average of right and left carotid intima-media thickness; BMD: Bone mineral density; MACE: Major adverse cardiovascular event; CKD: Chronic kidney disease; IMT: Intima-media thickness; IFGF-23: Intact fibroblast growth factor 23; BMI: Body mass index; PTH: Parathyroid hormone; SCVR: Subclinical cardiovascular risk; TBS: Trabecular Bone Score.

No significant differences in BMD, TBS, or 3D-DXA were found between CKD stages G2-G3a and G3b-G4. However, when comparing G2-G3a to controls, osteoporosis and osteopenia were more prevalent (44.7% and 13.2% vs. 15.2% and 1.3%,p=0.001). In G3b-G4 patients versus controls, lower femoral BMD (0.89 vs. 0.93,p< 0.043) and trabecular vBMD by 3D-DXA (161.90 vs. 169.45,p< 0.03) were found, with higher osteoporosis and osteopenia prevalence (52.5% and 20% vs. 15.2% and 1.3%;p=0.001).

Table 1 compares demographics and DXA, TBS, and 3D-DXA between CKD patients and controls. Table 2 presents results by CKD stage and controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In 62 patients undergoing carotid ultrasound (Table 3), 67.7% had low BMD and 50% showed altered TBS. Patients with subclinical CVR and/or cardiovascular disease (CVD) (n=45) were older (p=0.007), with higher carotid intima-media thickness (cIMT, p< 0.001) and Kauppila index (p< 0.001) compared to those without (n=17). DXA, TBS, 3D-DXA did not differ significantly.

iFGF-23 inversely correlated with eGFR (r: -0.38, p=0.002). cIMT correlated inversely with 25(OH) vitamin D (r: -0.25, p=0.047), and directly with lumbar BMD (r: 0.485,p< 0.001), cortical vBMD (r: 0.27, p=0.038), cortical surface BMD by 3D-DXA (r: 0.25, p=0.053), and the Kauppila index (r: 0.42,p=0.001).

In patients with subclinical CVR and/or CVD and fragility fractures, iFGF-23 was inversely correlated with cortical vBMD (ρS: -0.9,p=0.037).

Conclusion: CKD patients show reduced bone mass compared to healthy individuals, evident even in early stages of the disease. Bone quality alterations assessed by TBS and 3D-DXA may help identify those at risk for vertebral fractures. iFGF-23 appears to contribute to both bone quality deterioration and vascular damage. In the subgroup of patients with subclinical cardiovascular disease and/or major adverse cardiovascular events (MACE) and fragility fractures, impaired bone quality parameters were observed by 3D-DXA.

Disclosure: J. Rodríguez gago: None; **C. Tornero**: None; **L. León**: None; **M. González-Casaus**: None; **L. Giraldo**: None; **G. del Peso**: None; **D. Garrido**: None; **T. López**: None; **M. Coronado**: None; **M. Bajo**: None; **S. García**: None; **M. Serrano**: None; **M. Ossorio**: None; **A. Balsa**: None; **P. Aguado**: None.

Abstract Number: 0347

Identifying Risk Factors for Fragility Fractures in Patients with Coeliac Disease: An Observational Study

Kabyar Cho[1], Hamzah Amin[2] and marwan Bukhari[3], [1]University Hospitals of Morecambe Bay NHS Foundation Trust, Barrow-In-Furness, United Kingdom, [2]Lancaster University, Lancaster, United Kingdom, [3]University Hospitals of Morecambe bay NHS foundation trust, Lancaster, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Coeliac disease (CD) is an autoimmune disease, which has been widely reported to be associated with reduced bone mineral density (BMD), leading to an increased risk of fragility fractures. The lower bone mineral density observed in coeliac disease patients may be attributed to several factors including malabsorption, vitamin D deficiency, chronic inflammation, and associations with inflammatory conditions such as osteoporosis or rheumatoid arthritis.

Recent studies have found different risk factors of fragility fractures which are not currently recognised in FRAX™ tool. This observational study aims to evaluate parameters strongly associated with fracture risk in coeliac patients.

Methods: Data was collected from patients with coeliac disease who were referred for dual-energy X-ray absorptiometry (DEXA) scans in the North West of England between 2004 and 2019. Variables include patient demographics, FRAX™ risk factors, L1-L4 BMD, fat percentages of the whole body, abdomen and both femurs. Data analysis was conducted using a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of patients with coeliac disease

Variables	All patients with coeliac disease (n=1220)	Patients with fracture (n=285)	Patients without fracture (n=935)
Mean age at scan (SD)	63.971 (14.1)	64.313 (13.5)	63.867 (14.3)
Male (n, %)	229 (18.7%)	46 (20%)	183 (79.9%)
Female (n, %)	991 (81.2%)	239 (24%)	752 (75.9%)
Height (cm)	162.663	161.780	162.932
Weight (kg)	70.722	70.166	70.891
BMI (kg/m2)	26.672	26.740	26.651
L femur neck BMD (g/cm2)	0.886	0.830	0.901
R femur neck BMD (g/cm2)	0.887	0.832	0.903
L1 BMD (g/cm2)	0.996	0.926	1.018
L2 BMD (g/cm2)	1.077	0.993	1.103
L3 BMD (g/cm2)	1.141	1.062	1.165
L4 BMD (g/cm2)	1.130	1.068	1.149
L1-L4 BMD (g/cm2)	0.890	0.562	0.561
Left femur fat percentage (%)	26.627	29.159	25.846
Right femur fat percentage (%)	26.129	28.497	25.406
Abdominal Fat Percentage (%)	27.018	28.378	26.582
Total fat Percentage (%)	35.388	36.966	34.875
Any alcohol use	70 (5.7%)	21 (30%)	49 (70%)
Previous excess Alcohol use	20 (1.6%)	7 (35%)	13 (65%)
Current Excess Alcohol use	53 (4.34%)	16 (30.2%)	37 (69.8%)
Any smoking history	326 (26.7%)	73 (22.4%)	253 (77.6%)
Previous smoking history	219 (17.9%)	56 (25.6%)	163 (74.4%)
Current smoking history	113 (9.3%)	20 (17.7%)	93 (82.3%)
Any steroid use	106 (8.7%)	34 (32.1%)	72 (67.9%)
Previous steroid use	36 (2.95%)	12 (33.3%)	24 (66.7%)
Current steroid use	72 (5.9%)	22 (30.6%)	50 (69.4%)
Secondary Osteoporosis	31 (2.54%)	10 (32.3%)	21 (67.7%)
Rheumatoid arthritis	27 (2.21%)	12 (44.4%)	15 (55.6%)
Previous fracture	25 (2.05%)	5 (20%)	20 (80%)
Family history of fracture	241 (19.75%)	49 (20.3%)	192 (79.7%)

chi-square test for categorical variables, and student t-test for continuous variables. Subsequently, univariate and multivariate logistic regression analyses were performed to identify parameters independently associated with outcomes of fracture. Baseline characteristics included are tabulated by fracture status as shown in Table 1.

Results: A total of 1220 patients were analysed. Mean age at DEXA scan was 63.9 years (SD 14.1). 285 (23.4%) patients sustained a fracture, among which 239 (83.9%) patients were females. Patients with a fracture had a significantly lower BMD at both the femoral necks, across the entire femur, and the lumbar spine (all $p< 0.001$), as well as a higher fat percentage in both femurs ($p< 0.001$), abdomen ($p=0.027$), and total body fat percentage ($p=0.017$). Fractures were also significantly associated with steroid use ($p=0.026$), rheumatoid arthritis ($p=0.009$), and family history of fracture ($p=0.047$).

Our univariate regression model established that a lower BMD and higher fat percentage at all measured sites were significantly associated with an increased risk of fractures. The results can be seen in Table 2.

The multivariate model, adjusted for other covariates, revealed that lumbar spine BMD, abdominal fat percentage, total fat percentage, left femoral fat percentage, and positive family history were strong predictors of fracture in this group of patients. This is shown in Table 3.

Conclusion: Our study concluded that lower lumbar spine BMD is significantly associated with increased prevalence of fractures, a relationship that has not been widely recognised in larger cohort studies. In addition, abdominal fat percentage, total fat percentage, and left femoral fat percentage were found to be significant factors predisposing to increased fracture in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Univariate regression analysis of demographics and clinical factors predicting fragility fracture in patients with coeliac disease

Variables	Crude OR (95% CI)	*p*-value
Mean age at scan	1.002 (0.993 - 1.012)	0.640
Gender	1.264 (0.887 - 1.802)	0.195
Height (cm)	0.985 (0.970 - 1.000)	0.051
Weight (kg)	0.997 (0.989 - 1.005)	0.514
BMI (kg/m^2)	1.003 (0.980 - 1.027)	0.814
Left femur neck BMD (g/cm^2)	0.026 (0.009 - 0.075)	<0.001
Right femur neck BMD (g/cm^2)	0.026 (0.009 - 0.075)	<0.001
Left femur total BMD (g/cm^2)	0.029 (0.011 - 0.074)	<0.001
Right femur total BMD (g/cm^2)	0.026 (0.010 - 0.068)	<0.001
L1 -L4 BMD (g/cm^2)	0.047 (0.021 - 0.105)	<0.001
Left femur fat percentage (%)	1.065 (1.044 - 1.086)	<0.001
Right femur fat percentage (%)	1.062 (1.041 - 1.084)	<0.001
Abdominal fat percentage (%)	1.013 (1.001 - 1.025)	0.027
Total fat percentage (%)	1.023 (1.008 - 1.038)	0.003
Any alcohol use	1.438 (0.847 - 2.442)	0.178
Previous excess alcohol use	1.786 (0.7006 - 4.520)	0.221
Current excess alcohol use	1.444 (0.791 - 2.636)	0.232
Any smoking	0.928 (0.686 - 1.256)	0.629
Previous smoker	1.158 (0.826 - 1.623)	0.394
Current smoker	0.683 (0.413 - 1.129)	0.137
Any steroid use	1.624 (1.055 - 2.499)	0.028
Previous steroid use	1.668 (0.824 - 3.380)	0.155
Current steroid use	1.481 (0.880 - 2.490)	0.139
Secondary osteoporosis	1.583 (0.736 - 3.401)	0.239
Rheumatoid arthritis	2.696 (1.247 - 5.893)	0.012
Family history of fractures	1.380 (1.004 - 1.898)	0.047

Table 3. Significant fracture predictors in patients with coeliac disease (univariate and multivariate model)

Variables	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Left femur neck BMD (g/cm^2)	0.026 (0.009 - 0.075)	<0.001	30.606 (0.208 - 4499.1)	0.179
Right femur neck BMD (g/cm^2)	0.026 (0.009 - 0.075)	<0.001	0.365 (0.003 - 47.576)	0.685
Left femur total BMD (g/cm^2)	0.029 (0.011 - 0.074)	<0.001	0.093 (0.000 - 20.749)	0.389
Right femur total BMD (g/cm^2)	0.026 (0.010 - 0.068)	<0.001	0.174 (0.001 - 41.283)	0.531
L1 -L4 BMD (g/cm^2) *	0.047 (0.021 - 0.105)	<0.001	0.200 (0.048 - 0.842)	0.028
Left femur fat percentage (%) *	1.065 (1.044 - 1.086)	<0.001	1.113 (1.025 - 1.208)	0.011
Right femur fat percentage (%)	1.062 (1.041 - 1.084)	<0.001	1.025 (0.945 - 1.112)	0.554
Abdominal fat percentage (%) *	1.013 (1.001 - 1.025)	0.027	1.028 (1.001 - 1.056)	0.039
Total fat percentage (%) *	1.023 (1.008 - 1.038)	0.003	0.933 (0.891 - 0.977)	0.003
Rheumatoid arthritis	2.696 (1.247 - 5.893)	0.012	1.060 (0.388 - 2.891)	0.910
Family history of fractures*	1.380 (1.004 - 1.898)	0.047	1.586 (1.057 - 2.381)	0.026

Asterisk denotes significant predictors in multivariate analysis

coeliac patients. This implies the need to re-evaluate the clinical utility of fracture risk assessment tools like FRAX™ and consider incorporating additional parameters to improve fracture risk stratification in coeliac patients.

Disclosure: K. Cho: None; **H. Amin**: None; **m. Bukhari**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0348

Correlation between Bone Mineral Density by Dual-energy X-ray Absorptiometry at the Radius and Radius Cortical Bone Thickness using Routine Hand Radiographs in Rheumatoid Arthritis Patients

Karla Miller[1], Amani Jridi[2] and Tina Basak[3], [1]University of Utah School of Medicine, Salt Lake City, UT, [2]University of Utah, Salt Lake City, UT, [3]University of Utah Department of Radiology, Salt Lake City, UT

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) patients are at higher risk of having generalized osteoporosis of the axial and appendicular skeleton assessed by dual-energy x-ray absorptiometry (DXA) but are also known to have local periarticular bone loss on hand radiographs as a typical manifestation of disease. DXA is the most common method to assess general bone mineral density (BMD) and is recommended for osteoporosis screening in RA patients, while hand radiographs are routinely obtained for RA diagnosis and monitoring. It is unknown if radius cortical bone thickness (CBT) by radiograph correlates with bone mineral density at the radius by DXA in RA patients. The aim of this study is to assess the correlation of distal radius cortical bone thickness (CBT) measurements by routine hand radiographs with DXA BMD and T-score results for osteoporosis screening in RA patients.

Methods: For this Institutional Review board approved retrospective study, RA patients who underwent a distal radius DXA scan and had a hand radiograph taken within a 5-year period were included. Distal radius CBT was ascertained by measuring the outside diameter and the inside diameter of the cortical shell at the metaphyseal/diaphyseal junction and their ratio was calculated (Figure 1). Correlation between CBT of the distal radius and the DXA bone mineral density (BMD) values and T-scores of the distal radius, spine, and femurs were analyzed using Pearson correlation coefficient. Subgroup analyses of the correlation of distal radius CBT with the overall distal radius, ultra-distal radius (UD), mid-distal radius (MD), and one-third distal radius (OT) BMD and T-scores were also performed.

Results: 27 total patients were included for this study (mean age 63.9 years, 81% women). There was moderate positive correlation ($p \leq 0.05$) between the distal radius CBT and the MD ($r = 0.44$), OT ($r = 0.38$), and overall distal radius BMD ($r=0.41$). Weak correlation was seen between the distal radius cortical thickness and the overall, UD, MD, and OT T-scores and the ultra-distal BMD without statistical significance. No significant correlation was seen between the distal radius CBT and the T-scores and BMD of the femurs or lumbar spine.

Conclusion: Opportunistic use of routine hand radiographs to measure the distal radius CBT can provide modest correlation to the BMD at the MD, OT, and overall distal radius in RA patients. Larger study population and prospective study could provide confirmation of this correlation.

Distal Radius Cortical Bone Thickness Measurement

Disclosure: K. Miller: None; **A. Jridi**: None; **T. Basak**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0349

Underrecognized Glucocorticoid-Induced Osteoporosis in a Polymyalgia Rheumatica Patient Cohort

katherine Loomba[1], Emily Campbell[1], Nisha Khubchandani[1], chih Fang[1], William Rigby[2] and Vivekanand Tiwari[1], [1]Dartmouth Hitchcock Medical Center, Lebanon, NH, [2]Dartmouth-Hitchcock, Norwich, VT

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyalgia Rheumatica (PMR) and Giant Cell Arteritis (GCA) are systemic inflammatory disorders treated with prolonged corticosteroid therapy. Prolonged use of corticosteroids is a significant risk factor for developing osteoporosis and subsequent fractures. In adults over 40, osteoporosis is defined as the presence of a fragility fracture or a T-score < -2.5, or a high fracture risk as defined by FRAX scoring of >20% for a major osteoporotic fracture or >3% for a hip fracture. It is also suggested to increase the FRAX estimates for hip fracture and overall fracture by 20% and 15%, respectively, for patients on doses > 7.5 mg/d prednisone for at least three months. If the FRAX score is not considered or corrected for glucocorticoid exposure, this may lead to the underdiagnosis of osteoporosis. This study aimed to explore this risk by reanalyzing the FRAX scores of an osteopenic cohort of Polymyalgia Rheumatica (PMR) patients and comparing them to their original classification.

Methods: We conducted a retrospective review of PMR patients at a rheumatology clinic, focusing on those diagnosed with PMR or PMR with GCA and excluding patients with other rheumatological disorders. The study included 459 patients from 2011 to 2021. We retrospectively assessed the osteopenic patients and calculated each patient's FRAX with glucocorticoid correction, if applicable

Results: The original study included 459 PMR patients, with documentation showing that 171 (37.2%) had osteoporosis, 70 (15.3%) had osteopenia, 121 (26.4%) had normal bone mineral density, and 98 (21.4%) had no available DXA data. In the original cohort, screening for osteoporosis using DXA scans was conducted for 64.4% of patients. Among the total PMR patients, 37.3% were diagnosed with osteoporosis, and 16% had osteopenia. In the present analysis, after

Table 1. Addended Baseline Characteristics of PMR Cohort Regarding Bone Mineral Density

Classification	Variable	Value
PMR patients	Total	459
Osteoporotic	Total	200
	Mislabeled as osteopenic	14.5% *
	Mean Age	73.6
	Gender (F, M)	74%, 26%
	On Bisphosphonates	65.5%
	On Ca + Vit D	86%
Osteopenic	Total	43
	Mean Age	68.6
	Gender (F, M)	18.8%, 81.2%
	On Bisphosphonates	13.9%
	On Ca + Vit D	44.4%
No DXA available	Total	98
	Mean Age	70.1
	Gender (F, M)	33.7%, 66.3%
Normal DXA	Total	26.4%

*14.5% of osteoporotic patients were misdocumented as osteopenic; this made up 41.4% of the original osteopenic cohort (29/70) and was comprised of 15 women/14 men.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

considering FRAX scoring and glucocorticoid correction, 41.4% of the documented osteopenic patients were found to qualify for osteoporosis diagnosis, increasing the total osteoporotic subset of our PMR cohort to 200 (43.6%).

Conclusion: The FRAX calculation and glucocorticoid correction should be included in the osteoporosis diagnosis rather than relying solely on the T score; otherwise, osteopenic patients may inadvertently remain untreated.

Disclosure: k. Loomba: None; **E. Campbell**: None; **N. Khubchandani**: None; **c. Fang**: None; **W. Rigby**: None; **V. Tiwari**: sanofi, 1.

Abstract Number: 0350

Perioperative Evaluation of Blood Tests Including Bone Turnover Markers in Patients Undergoing Surgery for Proximal Femur Fractures

KEN NAKASEKO, KUWANA CITY MEDICAL CENTER, KUWANA, Mie, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoporosis treatment is essential to prevent fractures. However, few patients with proximal femur fractures receive osteoporosis treatment before injury. Initiating treatment postoperatively is critical to reduce the risk of subsequent fractures, such as contralateral hip and vertebral fractures. Our institution proactively initiates osteoporosis treatment during hospitalization after proximal femur fracture surgery.

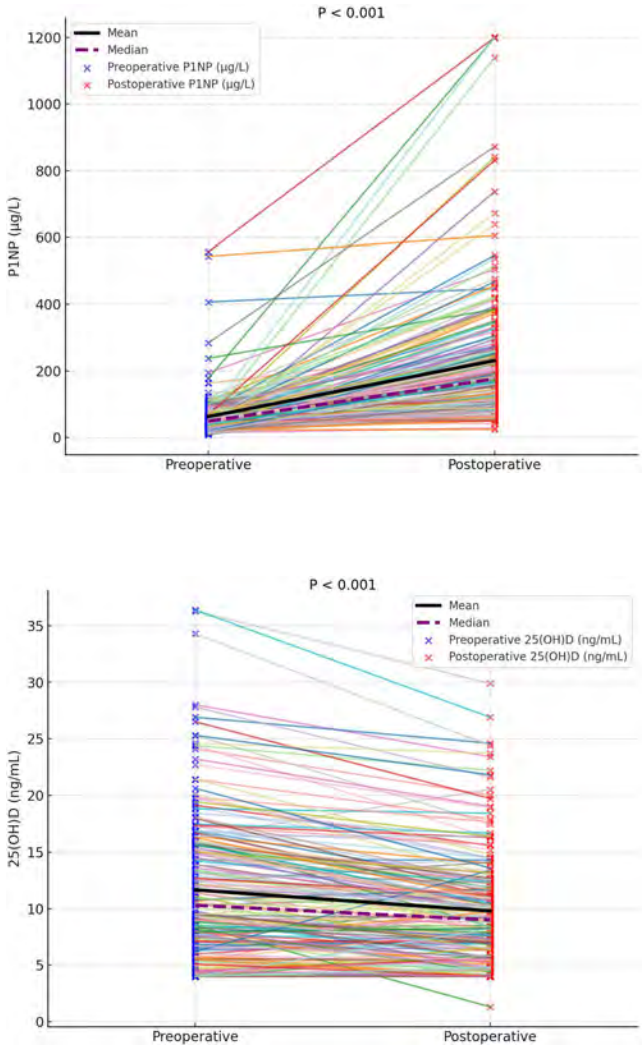
We perform bone mineral density measurements, spinal and pelvic X-rays, and blood tests, including bone turnover markers, to guide medication selection. Although bone turnover markers should ideally be measured within 24 hours of injury, postoperative measurement is sometimes unavoidable. This study evaluated differences in blood test parameters between pre- and postoperative periods, assessed differences by fracture type, and examined considerations when bone turnover markers cannot be measured early.

Methods: We included 179 patients (41 males, 138 females; mean ages 82.6, 82.8 years) hospitalized within 24 hours of a proximal femur fracture. Of these, 81 had femoral neck fractures (18 males, 63 females; mean ages 82.5, 82.7), and 98 had trochanteric fractures (23 males, 75 females; mean ages 82.9, 83.0).

All patients underwent preoperative blood tests at admission, followed by surgery (osteosynthesis, bipolar hip arthroplasty, or total hip arthroplasty). We measured procollagen type 1 N-terminal propeptide (P1NP), tartrate-resistant acid phosphatase-5b (TRACP-5b), 25-hydroxyvitamin D, alkaline phosphatase, calcium, and phosphorus at admission and 1–2 weeks postoperatively. Changes before and after surgery, and differences by fracture type, were analyzed using t-tests.

Results: Postoperative P1NP levels increased in 171 of 179 patients (76 of 81 femoral neck, 95 of 98 trochanteric fractures), averaging a 3.7-fold increase. Preoperative 25-hydroxyvitamin D levels were < 20 ng/mL in 163 patients (76 femoral neck, 87 trochanteric), declining further postoperatively in 170 patients (78 femoral neck, 92 trochanteric). A postoperative decrease was seen in 137 patients (63 femoral neck, 74 trochanteric).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Significant differences ($P < 0.001$) were observed in P1NP and 25-hydroxyvitamin D between pre- and postoperative measurements, regardless of fracture type. No significant changes were seen in TRACP-5b, alkaline phosphatase, calcium, or phosphorus, and no fracture type differences were detected.

Conclusion: We observed a marked postoperative increase in P1NP, highlighting the importance of early measurement to avoid overestimation due to fracture-induced elevation. These findings were consistent across fracture types, supporting uniform management.

When early assessment is not feasible, clinicians should interpret P1NP cautiously and consider alternative markers, recognizing that elevated P1NP alone should not preclude anabolic therapy. The postoperative decline in 25-hydroxyvitamin D underscores the need for early active vitamin D supplementation. These findings provide practical guidance for optimizing osteoporosis management in acute fracture care.

Disclosure: K. NAKASEKO: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0351

Experience with romosozumab in women with osteoporosis at high risk of fracture in real-world clinical practice

MARIA DEL CARMEN ORTEGA DE LA O[1], Laura Gonzalez Hombrado[2], Marina Salido Olivares[3], Carolina Marin[4], Angel Aragon[5], Celia arconada[6], Maria Carmen Ortega de la O[7], Alvaro Garcia[8], elisabeth Castañeda[9], Patricia Castro Perez[10], alberto diaz Oca[11] and Eva Andres Esteban[12], [1]HOSPITAL UNIVERSITARIO GETAFE, GETAFE, Madrid, Spain, [2]Hospital Universitario del Tajo, Aranjuez (MADRID), Madrid, Spain, [3]Hospital Clinico San Carlos, Madrid, Madrid, Spain, [4]Hospital Infanta Leonor, Madrid, Madrid, Spain, [5]Hospital Universitario Quironsalud Madrid, Pozuelo de Alarcon, Madrid, Spain, [6]Hospital universitario de Getafe, Getafe, Madrid, Spain, [7]Hospital Universitario Getafe, Madrid, Madrid, Spain, [8]Hospital Universitario del Tajo, Aranjuez, Madrid, Spain, [9]Hospital Universitario Infanta Sofía, Madrid, Madrid, Spain, [10]Hospital de Getafe, Madrid, Madrid, Spain, [11]Hospital de Fuenlabrada, Fuenlabrada, Madrid, Spain, [12]Universidad Rey Juan Carlos, Fuenlabrada, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Romosozumab (RMZ) is a recently approved dual-acting drug which has been shown to reduce fracture risk in patients with osteoporosis (OP) in clinical trials. However, data on its use in actual clinical practice remain limited. Our purposes are:

-Describe the profile of patients treated with RMZ in realworld clinical practice.
-Evaluate its efficacy based on densitometric changes and the incidence of new fractures.
-Assess the safety profile of the drug and patient satisfaction.

Methods: This multicentre retrospective observational study aimed to assess the use of RMZ and its efficacy in patients with OP in real-world clinical settings. Data were collected from the medical records of patients treated by their regular rheumatologist at the participating centres and entered into an anonymous electronic database. Demographic data, comorbidities, risk factors for OP development, the number and location of previous fractures and prior treatments performed on the patients were gathered. Laboratory tests and densitometry were conducted before and after treatment. The FRAX index was calculated for all patients prior to starting treatment. The study was approved by the ethics committee at Hospital 12 de Octubre.

Results: A total of 128 women from six centres in the Region of Madrid were included, of whom 81 have completed treatment to date. Baseline patient data are shown in Table 1. The mean age was 69.7 ±12.9 years. The mean BMI was 26.1 ± 6.8, while 39.5% were classified as obese. The most common comorbidities were hypertension and dyslipidaemia (both 35.8%). Most of the patients had no toxic habits. 88.9% had experienced one or more previous fractures, the majority of which were vertebral fractures. The mean FRAX data for hip fracture risk were 9.2 ± 11.1 and for major osteoporotic fracture they were 21.4 ± 14.7. RMZ was used as a second-line treatment in most patients (43.4%). No laboratory test changes were observed during treatment. The densitometric changes found are shown in Table 3, which illustrates the statistically significant differences between the baseline and post-treatment DEXA values for the lumbar spine and hip. Chart 1 shows the treatments after completing RMZ

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of patients at the start of the study

BASELINE CHARACTERISTICS	N=81 patients
Age	69.7 +/- 12.9
BMI	26.1 +/- 6.8
Menopausal age	47.6 +/- 5.7
Surgical menopause	5 (6.2%)
HBP	29 (35.8%)
Dyslipidaemia	29 (35.8%)
Diabetes mellitus	5 (6.2%)
Cardiovascular disease	4 (4.9%)
Drinker	2 (2.5%)
Smoker	10 (12.3%)
PREVIOUS FRACTURES	72 (88.9%)
1 fracture	26.50%
2 or more fractures	73.50%
Hip fracture	11.80%
Rheumatoid arthritis	7 (8.6%)
Hyperparathyroidism	1 (1.2%)
LINE OF TREATMENT	
1st line	17 (22.4%)
2nd line	33 (43.4%)
3rd line	14 (18.4%)
4th or more lines	12 (15.8%)
Concomitant osteopenia treatments	13 (16.1%)

Six patients reported adverse effects. The most common were local reactions at the injection site. Treatment was discontinued in two patients due to adverse effects, one due to a severe skin reaction and the other due to a stroke. None of the patients experienced a new fracture during the follow-up period. Patient satisfaction was rated at 4.6 ± 0.6 (scale 0-5).

Table 3. Densitometric data before and after RMZ

	BASELINE	AFTER RMZ	p value
LUMBAR SPINE			
LUMBAR BMD	705.1 (308.5)	769.6 (234.5)	0.002
LS TS	-3.1 (1.5)	-2.3 (1.3)	<0.001
FEMORAL NECK			
FN BMD	541.5 (215.8)	626.6 (124.2)	0.002
FN TS	-2.6 (0.9)	-2 (1.8)	0.002
TOTAL HIP			
TH BMD	500.1 (285.5)	679.5 (123.7)	0.001
TH TS	-2.5 (1.1)	-2.2 (1.1)	<0.001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

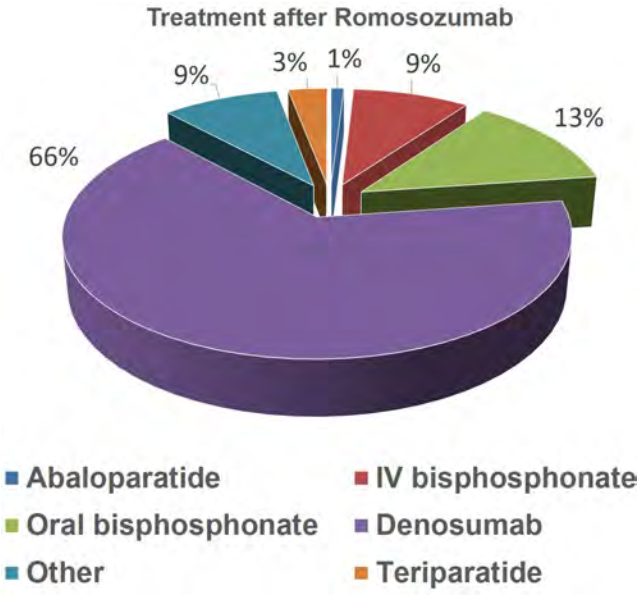


Chart 1

Conclusion: RMZ is mainly used in women with severe OP, most of whom have experienced several previous fractures and are receiving second or subsequent lines of treatment. It has shown statistically significant improvements in densitometric measurements in the lumbar spine and hip. The majority of adverse effects were mild and no patients experienced new fractures during the follow-up period

Disclosure: M. ORTEGA DE LA O: None; **L. Gonzalez Hombrado**: None; **M. Salido Olivares**: None; **C. Marin**: None; **A. Aragon**: None; **C. arconada**: None; **M. Ortega de la O**: None; **A. Garcia**: None; **e. Castañeda**: None; **P. Castro Perez**: None; **a. diaz Oca**: None; **E. Andres Esteban**: None.

Abstract Number: 0352

Complication Rates of Typical Hip Fractures, Subtrochanteric Femoral Fractures, and Atypical Femoral Fractures

Marshall Weber[1], William Obremskey[2], Jared Huling[3], Nitya Shah[3], Emily Budde[4], Zhiping Huo[4], Reside Jacob[4], Brinda Basida[1], Colton Hoffer[1], Binni Makkar[5] and Laura Carbone[1], [1]Augusta University, Augusta, GA, [2]Vanderbilt University, Nashville, TN, [3]University of Minnesota School of Public Health, Minneapolis, MN, [4]Center of Innovation for Complex Chronic Healthcare, Washington DC, DC, [5]University of Kentucky, Lexington, KY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Atypical femoral fractures (AFFs) are a rare complication of bisphosphonate use and a major reason that drug holidays are recommended following bisphosphonate use. However, the extent to which post-fracture complications occur in AFFs compared to subtrochanteric femoral fractures (SFF) and typical hip fractures (THF) is not clear. This study aims to determine if time without complication differs among AFF, SFF and THF.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective study of adults aged > 50 years old who used oral or IV bisphosphonates between October 1, 1999 and December 31, 2022 in the VHA Corporate Data Warehouse who had AFF, SFF, or THF. Those with ESRD, metabolic bone diseases other than osteoporosis, cancer, a filled prescription for etidronate, pamidronate or tiludronate or those whose dose of zoledronic acid was or $\leq$ 273 days from the initial dose were excluded. Among these patients, we used ICD-9-CM and ICD-10-CM codes to find complications of fractures including osteomyelitis, pressure ulcers, fracture nonunion, and fracture malunion within 12 months of diagnosis. We then used an unadjusted semiparametric accelerated failure time (AFT) model to determine the time to complication among each cohort. We adjusted the results for age at first prescription of bisphosphonate script (FPOS), White vs. non-White racial identity, ethnicity, BMI, Charleston Comorbidity Index, VA Frailty Index, and smoking status.

Results: Of the 5,650 patients who met inclusion criteria, 21 experienced an AFF (with a median age of 68 at FPOS, and 9.52% non-White), 255 experienced a SFF (with a median age of 70 at FPOS, and 11.7% non-White), and 5,374 experienced a THF (with a median age of 75 at FPOS, and 8.19% non-White). Within 12 months of the fracture, only 1 person (4.76%) with an AFF experienced a complication (a fracture nonunion), compared to 22 (8.63%) with SFF and 283 (5.27%) with a THF. The number of complications in each group were too small to compare rates for each complication directly.

Overall time to complication did not differ between the three groups. The average time without complication following SFF was 0.520 times that for THF (95% CI: 0.455 to 0.596, $p \approx 0$). The average time without complication following AFF did not differ from THF (95% CI: 0.186 to 23.584, $p = 0.549$).

After adjusting for the above covariates, the average time without any complication following SFF was 0.381 times the estimated time without any complication following THF (95% CI: 0.190 to 0.765, $p = 0.007$). Adjusting for the same variables, the estimated time without complication following AFF did not differ from estimated time without complication following THF (95% CI: 0.056 to 35.875, $p = 0.831$).

Conclusion: The adjusted average time to complication is shorter in patients with SFF compared to THF. However, the adjusted average time to complication in patients with AFF does not differ from those with THF.

Disclosure: M. Weber: None; **W. Obremskey**: None; **J. Huling**: None; **N. Shah**: None; **E. Budde**: None; **Z. Huo**: None; **R. Jacob**: None; **B. Basida**: None; **C. Hoffer**: None; **B. Makkar**: None; **L. Carbone**: None.

Abstract Number: 0353

Incidence of Clinical Fragility Fractures and Mortality in Patients with Rheumatoid Arthritis Treated with Rituximab

Montserrat Roig Kim[1], Carla Marco-Pascual[2], Martí Aguilar-Coll[1], Javier Narváez[3], Joan Miquel Nolla[1] and Carmen Gomez Vaquero[4], [1]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [2]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [3]Hospital Universitario de Bellvitge, Barcelona, Spain, [4]Hospital Universitari de Bellvitge, 08907 L'Hospitalet, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with Rheumatoid Arthritis (RA) have an increased risk of osteoporosis and fragility fractures. Bone loss in RA is multifactorial and mainly determined by classical risk factors for fracture (age, previous fracture, parental hip fracture, postmenopausal period duration, proximal femur bone mineral density (BMD)), factors associated with RA (disease activity, erosions, disability) and use of glucocorticoids (GC). A recent study (*Bone. 2023;168:116654*) suggested that patients with RA treated with Rituximab (RTX) may have a higher incidence of clinical fragility fractures (CFF), compared to those receiving other DMARDs. However, this association has not been thoroughly studied.

Methods: Retrospective, single-centre observational study in patients with RA diagnosis, according to the ACR/EULAR 2010 RA classification criteria, who received at least one dose of RTX between 1 January 2010 and 31 December 2019. Two comparator groups matched by sex, age, and disease duration were included: one treated with conventional synthetic DMARDs (group 1), and the other with biological or targeted synthetic DMARDs (group 2). Patients treated with RTX were assigned to group 3. Hospital and primary care medical records were reviewed up to 31 December 2024 or until loss of follow-up. We defined CFF as those resulting in the absence of external injury, such as from falls from one's own height or walking at normal speed. Date and location of CFF were recorded, as well as the date and reason for the end of follow-up, together with data on RA characteristics and fracture risk factors.

Results: A total of 204 patients were included (68 per group), of whom 71% were women, with a mean age of 53.6 years and a mean disease duration of 2.0 years, with no significant differences between groups. The indication for RTX was RA disease activity in 62% of cases and interstitial lung disease (ILD) in 38%. Baseline characteristics of the groups are summarised in Table 1.

Fifty-eight patients had 90 CFF (39 vertebral fractures, 13 humerus, 10 distal forearm, 4 hip fractures, and 24 other locations). The incidence of CFF was 2.1, 2.4 and 2.3 per 100 person-years (ppy), in groups 1, 2 and 3 respectively, with no statistically significant differences. Patients with CFF showed a significantly higher prevalence of erosions, parental history of hip fracture, use of GC, WHO osteoporosis diagnostic category, lower BMD at lumbar spine, femoral neck and total hip, and higher FRAX scores.

Table 1: RA characteristics and fracture risk factors, at baseline.

	Group 1: csDMARD (n=68)	**Group 2:** bDMARD (n=68)	**Group 3:** Rituximab (n=68)	**Total sample** (n=204)	p-value
Erosions	31 (45.58%)	47 (69.11%)	43 (63.23%)	121 (59.31%)	0.015
RF					
Positive	45 (66.17%)	52 (76.47%)	54 (79.41%)	151 (74.01%)	ns
Titre, UI/mL	122 [49.1-318.0]	107 [50.0-288.0]	95.6 [46.5-363.0]	109 [48.9-330.0]	ns
Anti-CCP					
Positive	42 (61.76%)	52 (76.47%)	57 (83.82%)	151 (74.01%)	0.017
Titre, UI/mL	56.0 [2.50-342.0]	145 [2.50-526.0]	167 [34.5-484.0]	120 [2.50-458.0]	0.034
BMI, *kg/m²*	26.7 ± 4.5	27.0 ± 4.0	27.8 ± 4.5	27.2 ± 4.3	ns
Active smoker	12 (17.64%)	22 (32.35%)	24 (35.29%)	58 (28.43%)	ns
Alcohol use	3 (4.41%)	1 (1.47%)	4 (5.88%)	8 (3.92%)	ns
Age of menopause	49.4 ± 4.30	49.1 ± 4.38	49.1 ± 4.66	49.2 ± 4.40	ns
Previous fracture	1 (1.47%)	4 (5.88%)	5 (7.35%)	10 (4.90%)	ns
Parental hip fracture	8 (11.76%)	4 (5.88%)	4 (5.88%)	16 (7.84%)	ns
Lumbar spine BMD, *g/cm²*	0.952 ± 0.164	0.944 ± 0.201	0.965 ± 0.157	0.950 ± 0.178	ns
Femoral neck BMD, *g/cm²*	0.768 ± 0.134	0.789 ± 0.163	0.767 ± 0.132	0.774 ± 0.140	ns
Total femur BMD, *g/cm²*	0.945 ± 0.156	0.938 ± 0.163	0.889 ± 0.379	0.921 ± 0.245	ns
WHO osteoporosis diagnostic category	14 (20.58%)	17 (25.00%)	10 (14.70%)	41 (20.09%)	ns
FRAX (MOF), %	6.5 [2.9-11.0]	4.7 [3.5-8.6]	5.4 [3.5-8.7]	5.3 [3.5-9.0]	ns
FRAX (HF), %	1.1 [0.2-2.7]	0.8 [0.2-2.3]	1.1 [0.4-2.4]	1.0 [0.2-2.5]	ns
Use of GC	26 (38.23%)	45 (66.17%)	35 (51.47%)	106 (51.96%)	0.005

Results are presented as number of patients (%) for categorical variables, as mean ± standard deviation for normally distributed continuous variables and as median [interquartile range] for non-normally distributed continuous variables.
***Abbreviations**: RF: Rheumatoid Factor; Anti-CCP: anti-cyclic citrullinated peptide antibodies; BMI: Body Mass Index; BMD: Bone Mineral Density; WHO: World Health Organization; FRAX: Fracture Risk Assessment Tool; MOF: Major Osteoporotic Fracture; HF: Hip Fracture; GC: Glucocorticoid; nS: non-significant.*

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The mortality rate was 0.7, 0.7 and 2.8 ppy ($p < 0.001$), respectively. In group 3, mortality was particularly high when RTX was indicated for ILD (53.9%) rather than for RA disease activity (11.9%) and in patients with vertebral fractures.

Conclusion: In our sample, there were no differences in the incidence of CFF between groups treated with RTX or other DMARDs. CFF were associated with classical fracture risk factors and erosive disease. The group treated with RTX showed higher mortality, particularly when the indication was ILD and in patients with vertebral fractures.

Disclosure: M. Roig Kim: None; **C. Marco-Pascual**: None; **M. Aguilar-Coll**: None; **J. Narváez**: None; **J. Nolla**: None; **C. Gomez Vaquero**: None.

Abstract Number: 0354

Greater Neighborhood Walkability is Associated with Lower Incidence of Hip Fracture in Older, Community-dwelling Women in the United States: The Cardiovascular Health Study

Rachel Elam[1], Petra Buzkova[2], Howard Fink[3], Joshua Barzilay[4], Eric Roseen[5], Jane Cauley[6], John Robbins[7], Laura Carbone[1], Gina Lovasi[8] and Kenneth Mukamal[9], [1]Augusta University, Augusta, GA, [2]University of Washingon, Seattle, WA, [3]University of Minnesota, Minneapolis, MN, [4]Kaiser Permanente of Georgia, Atlanta, GA, [5]Boston University, Boston, MA, [6]University of Pittsburgh, Pittsburgh, PA, [7]University of California Davis, Davis, CA, [8]Drexel University, Philadelphia, PA, [9]Beth Israel Deaconess Medical Center, Brookline, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Higher physical activity is linked to reduced fracture risk in older adults, especially for hip fractures. Emerging evidence demonstrates a potential role for the physical and built environment in promoting physical activity in community-dwelling, older adults. We aimed to evaluate whether neighborhood walkability and greenspace are associated with incident hip fracture in a large, community-dwelling, older adult population in the United States.

Methods: We conducted a retrospective analysis of 1992-2005 data from the prospective longitudinal Cardiovascular Health Study, a large cohort of community-dwelling adults aged ≥ 65 years from Winston-Salem, NC; Sacramento, CA; Hagerstown, MD; and Pittsburgh, PA. We included participants with a geocoded residential address at baseline (1992-1993 study visit) who were deceased as of July 2016 (to limit risks related to unintentional data disclosure). A participant's neighborhood was defined as a 1-km Euclidean radial buffer surrounding their residential address at baseline. Neighborhood walkability was the sum of the standardized population density and density of walkable destinations for daily living, truncated at 5 due to a heavy upper tail. Neighborhood greenspace was the proportion of land uses classified as green or vegetated in the 1992 National Land Cover Dataset. Incident hip fractures were identified by participant report every six months from baseline, confirmed by hospital medical record review. Participants were followed for up to 12 years or until the occurrence of hip fracture, death, or loss to follow-up, whichever occurred first. Cox hazard models were used to evaluate associations of neighborhood walkability and greenspace with incident hip fracture in sex-stratified and combined analyses, adjusting for numerous fracture risk factors and socioeconomic metrics for the individual (marital status, education, annual household income) and neighborhood (median household income, median value of housing units, and proportion of persons in managerial or professional occupations), using study site as a random effect.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Association of neighborhood walkability and greenspace with incident hip fracture: hazard ratios per 1 unit higher exposure in unadjusted, minimally adjusted, and fully adjusted Cox hazard models using study site as a random effect, overall and by sex

Table 1: Association of neighborhood walkability and greenspace with incident hip fracture: hazard ratios per 1 unit higher exposure in unadjusted, minimally adjusted, and fully adjusted Cox hazard models using study site as a random effect, overall and by sex

		Overall (n=3,676)		Women (n=2,118)		Men (n=1,558)	
Neighborhood metric	**Model**	**HR**	**(95% CI)**	**HR**	**(95% CI)**	**HR**	**(95% CI)**
Walkability	Unadjusted	0.99	(0.93, 1.06)	0.99	(0.91, 1.07)	1.02	(0.90, 1.15)
	Minimally adjusted[1]	0.99	(0.92, 1.05)	0.98	(0.91, 1.06)	0.99	(0.88, 1.12)
	Fully adjusted[2]	0.90	(0.79, 1.03)	0.84	(0.72, 0.99)	1.07	(0.84, 1.36)
Greenspace[3]	Unadjusted	0.92	(0.63, 1.35)	0.97	(0.63, 1.51)	0.75	(0.36, 1.56)
	Minimally adjusted[1]	0.96	(0.66, 1.40)	0.99	(0.64, 1.54)	0.87	(0.42, 1.83)
	Fully adjusted[2]	0.84	(0.48, 1.47)	0.90	(0.45, 1.79)	0.72	(0.27, 1.91)

HR: Hazard ratio; CI: Confidence interval

[1]Adjusted for participant age, sex, and race

[2]Adjusted for participant age, sex, race, weight, height, smoking status, current heavy alcohol use, oral corticosteroid use, osteoporosis medication use (vitamin D, calcium, selective estrogen receptor modulators, estrogens, and bisphosphonates), and other medication use affecting bone metabolism and/or fracture risk (loop diuretics, thiazide diuretics, selective serotonin reuptake inhibitors, anticonvulsants, benzodiazepines, sedative/hypnotics, proton pump inhibitors, thiazolidinediones, and thyroid medications), prevalent diabetes, estimated glomerular filtration rate, marital status, education level, annual household income, neighborhood median household income, neighborhood median value of housing units, and neighborhood proportion of persons in managerial/professional occupations

[3]Proportion of land uses consistent with greenspace (13 green or vegetated land uses included: deciduous, evergreen, or mixed forest, shrubland, orchards/vineyards, grassland/herbaceous, pasture/hay, row crops, small grains, fallow, urban/recreational grasses, woody wetlands, emergent herbaceous wetlands)

Results: Among 3,676 participants (mean age 75±5.5 years, 83% White/17% Black, 58% women) over a median 10 years of follow-up, we observed 506 hip fractures (365 in women, 141 in men). Greater neighborhood walkability was statistically significantly associated with lower incidence of hip fracture in women in fully adjusted models (hazard ratio: 0.84 per 1 unit higher neighborhood walkability, 95% confidence interval: 0.72-0.99) (Table 1). In contrast, neighborhood walkability was not statistically significantly associated with hip fracture in men (Table 1). There were no statistically significant associations between neighborhood greenspace and hip fracture (Table 1). Penalized spline plots revealed no significant non-linear relationships.

Conclusion: In this large, community-based cohort of older adults, greater neighborhood walkability was associated with lower hip fracture risk in women, highlighting a potential opportunity for urban planners to decrease fracture burden through walkable community design. No significant association was observed between neighborhood greenspace and hip fracture risk.

Disclosure: R. Elam: None; **P. Buzkova**: None; **H. Fink**: None; **J. Barzilay**: None; **E. Roseen**: None; **J. Cauley**: None; **J. Robbins**: None; **L. Carbone**: None; **G. Lovasi**: None; **K. Mukamal**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0355

Changes in scanographic bone mineral density in melanoma patients treated with immunotherapy

Soukayna Baddi[1], Suarez Dimitri[1], Alexis Ruet[1], Theo Van Butsel[1], Damiano Cerasuolo[1], Jean-Matthieu L'Orphelin[1] and Anne-Christine Rat[2], [1]Caen University Hospital, Caen, France, [2]Caen University hospital, UMR 1075 Caen normandy university, Caen, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The use of immune checkpoint inhibitors (ICIs) is becoming increasingly important in the management of melanoma. However, although ICIs are associated with various immune-related adverse events (irAEs), their potential effect on the skeleton—particularly on bone mineral density (BMD) and the occurrence of fractures—has been little described.

The aim of this study is to assess the changes in BMD on CT scans in patients with melanoma treated with ICIs at one and two years and to investigate the factors associated with these changes.

Methods: We conducted a real-world, retrospective cohort study. Patients were recruited from outpatient dermatology clinic between October 2014 and 1 December 2023. Inclusion criteria for patients were: male or female, age ≥ 18 years, histologically confirmed melanoma, first treatment with immunotherapy (according to current treatment guidelines and after discussion in a multidisciplinary tumor board), with CT imaging follow-up both before and after initiation of immunotherapy, and follow-up of at least one year after initiation of immunotherapy. Patients were excluded if they met any of the following criteria: history of bone fragility disorders or osteoporotic fractures, spinal surgery, vertebral metastases. BMD was measured at baseline (T0), 1 year (T1) and 2 years (T2) at the L1 vertebrae. Changes in CT-based BMD over time were analyzed using paired Student's t-tests, and risk factors for BMD changes were analyzed using linear regression models.

Results: 165 patients (mean age: 65 years; 44.2% women) were included. BMD decreased significantly over 2 years (mean difference: 14.02 HU, 95% CI 10.31-17.74, $p < 0.001$), with bone loss rates of 5.15% and 11.91% at 1 and 2 years, respectively.

Male gender (β 8.87; [95%CI 3.62 to 14.11]; p=0.001) and younger age (β -0.34; [95%CI -0.5 to -0.09]; p=0.005) were associated with greater BMD loss at 1 year.

Compared with patients in complete remission, those with disease progression (β 8.25 [95% CI 2.27 to 19.75]; p=0.002) or partial response (β 8.25 [95% CI 2.98 to 13.53]; p=0.002) experienced a greater decrease in BMD at 2 years.

Conclusion: ICIs are associated with significant BMD loss, particularly in men. These findings underscore the importance of osteoporosis prevention and routine BMD monitoring during ICI therapy

Disclosure: S. Baddi: None; **S. Dimitri**: None; **A. Ruet**: None; **T. Van Butsel**: None; **D. Cerasuolo**: None; **J. L'Orphelin**: None; **A. Rat**: AbbVie/Abbott, 6, Eli Lilly, 6, Galapagos, 6, Merck/MSD, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0356

An Analysis of Osteoporosis Screening in Males 50 and Older with Rheumatic Disease Across Stony Brook Medicine Network

Stephen Poos[1], Hoang Nguyen[2], Samuel Greenberg[3], Marcus Lee[2], Heidi Roppelt[1] and Asha Patnaik[2], [1]Stony Brook Southampton Hospital, Southampton, NY, [2]Stony Brook University Hospital, Stony Brook, NY, [3]Renaissance School of Medicine at Stony Brook University, Stony Brook, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0337–0356) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoporosis is under screened in men. The United States Preventive Services Task Force (USPSTF) does not publish guidelines for osteoporosis screening in men. Other professional societies only recommend screening when certain risk factors are present. The Fracture Risk Assessment Tool cites risk factors including rheumatoid arthritis (RA), smoking, alcohol use, glucocorticoid use, and family history of hip fracture. In addition to RA, literature evidence links low bone mineral density to autoimmune connective tissue disease (CTD) and seronegative spondyloarthropathy (SpA) [1]. Our study assesses provider recognition of rheumatic disease as a risk for osteoporosis by examining the prevalence of dual-energy X-ray absorptiometry (DXA) screening in men with rheumatic disease. We hypothesized that osteoporosis is under screened among men with rheumatic diseases.

Methods: We conducted a retrospective cohort study using electronic health record data from the Stony Brook system from 1/1/2000 to 12/15/2024. We identified 38,970 men with current age 50 and older with ICD-10 codes mapped to RA, SpA, osteoarthritis (OA), polymyalgia rheumatica (PMR), crystal arthropathy (CA), vasculitis, and CTD. Osteoporosis screening was defined as at least one CPT code corresponding to a DXA scan after initial documentation of a disease or risk factor. We performed bivariate logistic regression to assess the unadjusted association between DXA screening and disease groups, smoking, family history of osteoporosis, alcohol abuse/dependence, long-term systemic steroid use, and demographics. Variables meeting a relaxed Wald $p \leq 0.2$ were included in a multivariate logistic regression model to identify independent predictors of screening.

Results: The percentage of patients with DXA was low in all disease cohorts, with an average screening rate of 4.05%. The highest rates were seen in PMR (8.33%) and RA (5.10%) and the lowest in CA (1.59%). The yield of osteoporosis among those screened ranged from 20.95% (CTD) to 41.91% (SpA) with the average yield being 31.51% (Figure 1). Increasing age, long-term steroid use, RA, PMR, SpA, and CTD were all significantly associated with DXA screening (Figure 2).

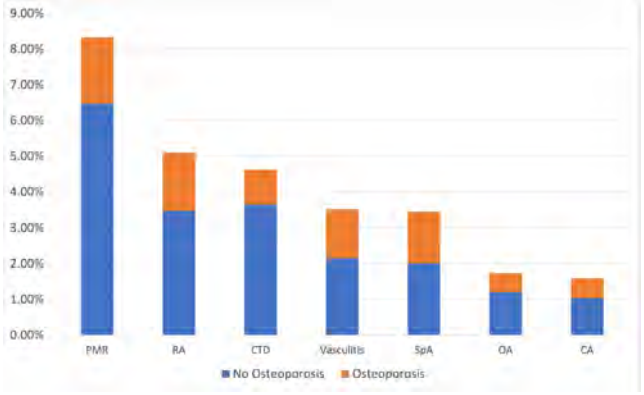


Figure 1. Total percentage of screened patients within each disease cohort, along with the percentage of those patients found to have osteoporosis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

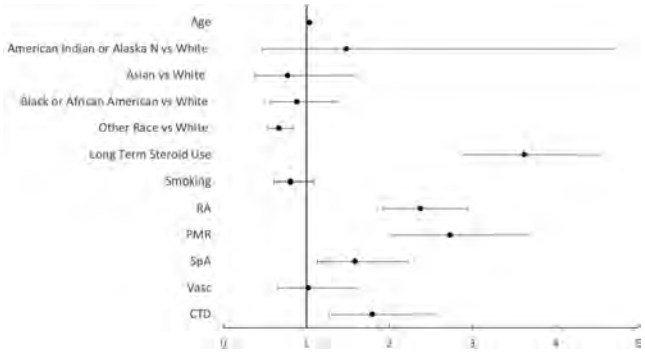


Figure 2.Variables meeting a relaxed Wald p ≤ 0.2 in bivariate logistic regression with the outcome of DXA screening were included in a multivariate logistic regression model. The resulting odds ratios and confidence intervals are displayed in this forest plot.

Conclusion: Providers screened patients with autoimmune diseases in greater percentages than patients with OA or CA, and autoimmune diseases except vasculitis were significantly associated with DXA screening. Long-term steroid use was the only significant non-disease predictor of DXA screening. One limitation is the undefined duration of "long-term" use in the associated ICD-10 code, though chronicity is implied. Family history of osteoporosis was excluded; its wide confidence interval (OR 7.6, 95% CI 1.7–33.3) reflects low documentation, likely during DXA referrals, limiting its reliability as an independent predictor. Despite low screening rates, the yield of osteoporosis among screened patients was substantial. With growing recognition of autoimmunity as an osteoporosis risk factor, we are optimistic that more patients will receive timely diagnosis and treatment.

1. Bultink, I.E.M. *et al*. Inflammatory Rheumatic Disorders and Bone. *Curr Rheumatol Rep* **14**, 224–230 (2012). doi.org/10.1007/s11926-012-0252-8

Disclosure: S. Poos: None; **H. Nguyen**: None; **S. Greenberg**: None; **M. Lee**: None; **H. Roppelt**: None; **A. Patnaik**: None.

Abstract Number: 0357

Content validation of patient-reported outcome (PRO) measures for fatigue, physical function and disease activity in Polymyositis (PM)

Jason Xenakis[1], **Esther Yi**[1], Iyar Mazar[2], Sarah Knight[3], Harriet Makin[3], Samantha Wratten[3], Rohit Aggarwal[4] and Stephanie McKee[3], [1]Pfizer Inc., New York, United States of America, New York, [2]Pfizer, US, New York, [3]Clarivate, London, United Kingdom, [4]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyositis (PM) is a subtype of idiopathic inflammatory myopathy (IIM) characterized by muscle inflammation and muscle weakness. Extra muscular manifestations like interstitial lung disease (ILD), joint pain or skin rashes may also be experienced.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

This study aimed to evaluate the content validity of patient-reported outcome (PRO) measures used in PM (encompassing ASyS, OM, Others, IMNM), i.e., whether the content of these measures 1) captures symptoms or impacts that are important to adults with PM and 2) is comprehensible to respondents.

Methods: Adult (≥18 years) patients in the US with a clinical diagnosis of PM were recruited by a clinical site to take part in individual, semi-structured, 90-minute online interviews conducted from September 2023 to June 2024. Osteoarthritis, fibromyalgia, neurological disorders, cardiac conditions, and lung conditions unrelated to IIM were excluded. The IRB-

Table 1. Overeview of findings from cognitive debriefing interviews

PRO (n participants who debriefed the measure) and response options	Instruction and item understanding	Relevance	Recall	Meaningful change
HAQ-DI (n=33) Participants selected from four options for each item ranging from 'Without ANY difficulty' (0) to 'UNABLE to do' (3). The highest score applied to each category (dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities) represents the overall score for that category, with higher scores representing greater difficulty. One item assessing pain in the past week uses a 15cm VAS anchored with 'no pain' (0) to 'very severe pain' (100). Most participants were able to use the response options appropriately.	All participants interpreted the instructions and most items (23/25 items) correctly.	Most items were relevant to more than half of participants.	Most participants correctly understood the recall period.	Meaningful change was explored at the item-level. An item-level improvement of 1- or 2-points was considered meaningful to nearly all participants.
FACIT-Fatigue (n=26) Participants selected from five response options for each item ranging from 'Not at all' (0) to 'Very much' (4). Items form two domain scores or a total score ranging from 0 to 52. The Experience domain includes five items ranging in total scores from 0 to 20. The Impact domain includes the remaining eight items with scores ranging from 0 to 32, with higher scores representing greater fatigue. Most participants were able to use the response options appropriately.	All participants interpreted the instructions and most items (8/13 items) correctly.	Almost all items were relevant to more than half of participants.	Most participants correctly understood the recall period.	Meaningful change was explored at the item-level. An item-level improvement of 2-points was considered meaningful to most participants.
PGA-VAS/NRS (VAS n=26, NRS n=27)† Participants selected a response on the 10cm VAS measure by marking on a line anchored at either end by 'No evidence of disease activity' to 'Extremely active or severe disease activity.' The NRS measure used the same anchors on a scale ranging from 0 to 10, with higher scores indicating more severe activity. All participants were able to use the VAS and NRS response options correctly.	All participants interpreted the VAS and NRS versions of the item correctly.	Items were relevant to all participants.	Most participants correctly understood the recall period.	A 2-point improvement and 1-point worsening on the NRS were considered meaningful.
PROMIS-PF (n=25) Participants selected from five response options for each item ranging from 'Without any difficulty' or 'Not at all' (5) to 'Unable to do' or 'Cannot do' (1). Higher scores indicate better physical function. Items assess function capability in the upper and lower extremities and central regions, and activities of daily living. Most participants were able to use the response options appropriately.	All participants interpreted the instructions and nearly all items (19/20 items) correctly.	Most items were relevant to more than half of participants.	A range of timeframes were reported (this measure does not specify a timeframe).	Meaningful change was explored at the item-level.An item-level 1- or 2-point improvement was considered meaningful
PGA-VRS (n=8) Participants selected from five response options ranging from 'None' (0) to 'Very severe' (4). Most participants were able to use the response options appropriately.	All participants interpreted the item correctly.	Item was relevant to all participants.	All participants correctly understood the recall period.	A 1-point improvement or worsening was considered meaningful.
PGIS-PA (n=8) Participants selected from five response options ranging from 'None' (0) to 'Very severe' (4). All participants were able to use the response options appropriately.	All participants interpreted the item correctly.	Item was relevant to all participants.	All participants correctly understood the recall period.	A 1-point improvement or worsening was considered meaningful.
PGIC-PA (n=8)‡ Participants selected from five response options ranging from 'Much better' to 'Much worse.' All participants understood the response options.	All participants interpreted the item correctly.	*N/A*	All participants correctly understood the recall period.	Most participants indicated that improving to 'Much better' would be meaningful after taking a new medication.

Abbreviations: ASyS, Anti-synthetase syndrome; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; IMNM, Immune Mediated Necrotizing Myopathy; OM, Overlap myositis; PGA-VRS, Patient Global Activity assessment-Verbal Rating Scale; PGIC-PA, Patient Global Impression of Change – Physical Activity; PGIS-PA, Patient Global Impression of Symptoms-Physical Activity; PROMIS-PF, Patient-Reported Outcome Measurement Information System-Physical Function.
†Exploration of meaningful change was completed using the participant's NRS response.
‡Participants were asked to imagine they were taking part in a clinical trial of a new treatment while completing the patient global impression of change items.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

approved interview guide included open-ended questions to explore the content validity (i.e., relevance, comprehensiveness, and comprehensibility) of 8 PRO measures which assess physical functioning, fatigue and disease activity (Table 1). Participants were also asked about their perceptions of meaningful changes in scores. Purposive sampling with recruitment targets were used to recruit a diverse sample in terms of age, sex, race, ethnicity, and education level. Interviews were audio-recorded, transcribed, anonymized and analyzed using qualitative framework analysis in Atlas.ti v9.

Results: Participants were mostly female (n=21/34, 62%) and/or white (n=30/34, 88%) with a mean age of 58 years (range 32 – 77 years). Most participants had a graduate/postgraduate (n=14/34, 41%) or bachelor's degree (n=10/34, 29%). Due to time constraints, not all measures were debriefed by all participants.

An overview of findings is presented in Table 1. The instructions and item wording were interpreted as intended by the majority of participants for all PRO measures debriefed. The measures were conceptually relevant to the majority of the sample. Most participants interpreted the recall periods correctly. The response options/scales were correctly interpreted by participants. Participant feedback indicated that none of the suggested changes were critical for understanding.

Meaningful change was assessed at the item level for multi-item PRO measures. For the HAQ-DI and the PROMIS-PF items, participants considered an improvement of 1- or 2-points as meaningful. A 2-point improvement on FACIT-Fatigue item(s) was considered meaningful to most participants.

A 2-point improvement on the single-item PGA-NRS and PGIC-PA, or 1-point worsening on the PGA-NRS was considered by most participants to be meaningful. A 1-point improvement or worsening on the PGA-VRS and PGIS-PA was considered meaningful.

Conclusion: All 8 PRO measures demonstrated content validity for use in research with adults with PM. For multi-item and single-item PROs, a 1- to 2-point item-level change was considered meaningful, demonstrating the value of small improvements for individuals with this debilitating condition. These insights are valuable for interpreting quantitative within-patient changes when evaluating treatments for PM.

Disclosure: J. Xenakis: Pfizer, Inc., 3, 11; **E. Yi**: Pfizer, Inc., 3, 11; **I. Mazar**: Pfizer, Inc., 3, 11; **S. Knight**: Clarivate Analytics, 3, 11; **H. Makin**: Clarivate Analytics, 3, 11; **S. Wratten**: Clarivate, 3, 11; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2; **S. McKee**: Clarivate, 3, 11.

Abstract Number: 0358

Different Perspectives between Physicians and Patients on Treatment Priorities and Challenges in Still's Disease

Gisella Beatrice Beretta[1], Luciana Pereira[2], **Greta Rogani**[3], Francesco Baldo[4], Claudia Bracaglia[5], Dirk Foell[6], Marco Gattorno[7], Marija Jelusic[8], Sebastiaan Vastert[3], Rashmi Sinha[9], Francesca Minoia[10] and PReS MAS/sJIA Working Party and the Systemic JIA Foundation, [1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, Milan, Italy, [2]Systemic JIA Foundation, Cincinnati, [3]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [4]ASST-Pini-CTO, Milano, Milan, Italy, [5]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Rome, Italy, [6]University Hospital Muenster, Muenster, Germany, [7]IRCCS G. Gaslini, Genova, Genoa, Italy, [8]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Zagreb, Croatia, [9]Systemic JIA Foundation, Cincinnati, OH, [10]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Milan, Italy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite therapeutic advances, major concerns and disparities persist in the care of Still's Disease (SD). Capturing both patient/caregiver and physician perspectives is essential to optimize patient-centered care. This real-life study aims to assess and compare the perspective of both groups regarding treatment goals, challenges, and unmet needs related to the treatment of SD.

Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize SD and Macrophage Activation Syndrome (MAS) management, 2 surveys, 1 addressed to physicians and 1 to patients/caregivers, were developed by a core team, involving physicians and patients representatives. The physician survey was forwarded through the PReS/PRINTO network, while the patient survey via the Systemic JIA Foundation to all their members. Responses were analyzed using chi-square tests to assess group differences.

Results: 197 physicians and 139 patients/caregivers participated. Most patient respondents were parents or legal guardians (94%), primarily from the United States (64%) and Europe (19%). Physicians were mainly pediatric rheumatologists (90%), from 56 countries worldwide.

Regarding treatment goals, both groups prioritized complete symptom control (84% vs 79%, p=0.28) and achieving a quality of life similar to peers (63% vs 73%, p=0.44). However, patients considered pain control a key objective more often than physicians (43% vs 13%, p< 0.001), whereas physicians placed greater emphasis on glucocorticoid reduction (79% vs 54%, p< 0.001).

In terms of glucocorticoid-related concerns, mood changes were predominantly reported by patients (65% vs 14%, p< 0.001), whereas physicians were more concerned about osteoporosis (66% vs 32%, p< 0.001), glucose intolerance (52% vs 27%, p< 0.001), and hypertension (51% vs 37%, p=0.02). Both groups highlighted growth delay and infection risk as shared concerns.

Regarding fears at treatment initiation, both groups were concerned about treatment failure (82% patients vs 66% physicians, p=0.001) and adverse events (77% vs 72%, p=0.27). However, physicians were more worried about treatment duration (57% vs 21%, p< 0.001), while patients emphasized infection risk (52% vs 27%, p< 0.001) and lack of clear information about the treatment (34% vs 23%, p=0.03).

As for future challenges, both groups stressed the need to reduce the burden of glucocorticoid use (68% patients vs 59% physicians, p=0.10). Physicians more frequently cited the inability to prevent MAS (52% vs 40%, p=0.03), while patients highlighted limited physician expertise (57% vs 15%, p< 0.001) and lack of access to psychological support (33% vs 10%, p< 0.001) as major unmet needs.

Conclusion: Besides shared perspectives, patients and physicians show relevant differences in prioritizing treatment outcomes and concerns in SD. Including patient priorities early in the disease course is essential to advancing truly patient-centered care.

Disclosure: G. Beretta: None; **L. Pereira**: None; **G. Rogani**: None; **F. Baldo**: None; **C. Bracaglia**: None; **D. Foell**: None; **M. Gattorno**: Fresenius Kabi SwissBioSim GmbH, 6, Novartis, 1, 2, 5, 6, SOBI, 2, 6; **M. Jelusic**: None; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **R. Sinha**: None; **F. Minoia**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0359

VA Is a Slow-moving Ship, but You Can Steer It": Clinician Views on Navigating Shared Decision-making and Anticipated Use of an RA Decision Aid

Alicia Hamblin[1], Dylan Waller[2], Anaïs Tuepker[2], Catherine Nasrallah[3], Alexandra Bennett[2], Brooke Jespersen[2], Joshua Baker[4], Madhavi Valiveti[5], gabriela Schmajuk[6] and **Jennifer Barton**[2], [1]UCSF, San Francisco, CA, [2]Center to Improve Veteran Involvement in Care (CIVIC) and VA Portland Health Care System, Portland, OR, [3]University of California San Francisco (UCSF), San Francisco, CA, [4]Corporal Michael J. Crescenz VA Medical Center (CMCVAMC) and University of Pennsylvania, Philadelphia, PA, [5]VAMC Wilmington, Wilmington, DE, [6]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Shared decision-making (SDM) is the first overarching principle of the treat-to-target guidelines for rheumatoid arthritis (RA). The quality of SDM varies widely, and its adoption in practice remains limited. To address this gap, a decision aid tool for RA "RA Choice" was introduced as part of a multicomponent intervention (e.g., clinician communication training, medication summary guide, patient activation brochure) in a stepped-wedge, randomized controlled trial (RCT; NCT05530694) across multiple rheumatology clinics within the Veterans Health Administration (VHA). Prior to the launch of the intervention, during the usual care phases of the trial across multiple sites, we aimed to explore clinician attitudes and beliefs regarding SDM and the use of RA Choice.

Methods: Between June 2023 and October 2024, we conducted semi-structured interviews with clinicians prior to the implementation of the multicomponent intervention which included RA Choice. The Consolidated Framework for Implementation Research (CFIR) provided a framework for interview question development. Recorded Interviews were transcribed verbatim and analyzed using a hybrid deductive/inductive qualitative content approach, guided by iterative Rapid Research Evaluation and Appraisal Lab (RREAL) sheets. The results were then organized using the CFIR.

Results: 16 semi-structured interviews were conducted with VHA rheumatologists (n=14) and nurse practitioners (n=2) across three intervention sites: Philadelphia (n=6), Portland (n=5), and San Francisco (n=5). Many clinicians were familiar with the concept of SDM and perceived it as beneficial to patient well-being. Participants stated that an ideal RA-focused decision aid should help patients describe their symptoms, including pain levels and mobility difficulties, support clinicians in explaining medical concepts, enhance the efficiency of SDM, and be accessible in a paper format.

Participants also identified factors that would affect successful implementation of an RA-focused decision aid. These factors aligned with CFIR domains, including: Outer Setting issues like bureaucratic hurdles and national vs. clinic-level implementation, Inner Setting elements such as the VHA's culture of innovation, and Intervention Characteristics like the tool's simplicity for Veteran comprehension. They also emphasized Characteristics of the Individual, including clinician buy-in, patients' willingness to engage in decision-making, and clinicians' perceived value of the tool.

Conclusion: In this qualitative study, we identified patient, clinician, and institutional factors that may influence the use of the RA Choice decision aid during the pre-intervention phase of a multi-site, stepped-wedge RCT. This pre-intervention qualitative data identified clinician buy-in to the general usefulness of SDM as a concept and a cautious optimism around leveraging a tool to improve SDM, however this was tempered by perceptions of challenges encountered by large system bureaucracy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Factors with exemplary quotes corresponding to the CFIR

CFIR Constructs	Factors	Quotes
Outer setting	Bureaucratic hurdles	*"They have elevated these goals of safety and quality... that have helped them overcome the bureaucratic barriers to implementing new health IT systems like that... so I think that it's a very slow-moving ship, but you can steer it." (9)*
	Nationwide vs. clinic implementation	*"...In our little microsystem of our rheumatology clinic and division I think there have actually been quite a few small changes that have been affected. I think changing the whole VA, that's another story." (7)*
Inner setting	VHA culture of innovation	*"I think there's a common bond behind education and wanting to provide a good learning environment... also a culture of life-long learning where we're open to new ideas and new things." (4)*
Intervention characteristics	Simplicity in the RA decision aid for Veteran comprehension	*"...it would be overwhelming to have a single tool that would communicate all of the potential options and facilitate that shared decision-making conversation in some... I think a decision tool is best if it has a concise focus on what it's trying to support in the communication." (9)*
Characteristics of the individual	Clinician buy in (to SDM and/or RA Choice)	*"...The buy-in that you get from every person within the department is also very variable. There's some people that are very, very entrenched in their ways and have no interest in changing the way that they've done practice for the last 15, 20, 30 years. Others have more stakes in it and are more willing to change..." (16)*
	Perceived patient desire to participate in SDM	*"There are Veterans who really want to know everything and make a choice, and others who say, 'You're the doctor- just tell me what to do.'" (10)*
	Clinician's perceived value of the tool	"In theory, this tool could help patients make better choices and improve adherence, but if *it's too wordy or overwhelming, it could do more harm than good." (7)*

and patient-level factors of limited literacy or low levels of engagement. Future research will focus on impacts of the intervention on Veterans' experience of SDM.

Disclosure: A. Hamblin: None; **D. Waller**: None; **A. Tuepker**: None; **C. Nasrallah**: None; **A. Bennett**: None; **B. Jespersen**: None; **J. Baker**: None; **M. Valiveti**: None; **g. Schmajuk**: None; **J. Barton**: None.

Abstract Number: 0360

Assessing Content Validity of a New Questionnaire Evaluating Glucocorticoid Toxicity

Timothy Howell[1], anne Skalicky[2], Louis Matza[1], **John Stone**[3], Martha Stone[4], Vijayaraghava Rao[5] and Glenn Phillips[5], [1]evidera, Washington, DC, [2]evidera, Seattle, WA, [3]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [4]Steritas, LLC, Concord, MA, [5]argenx, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

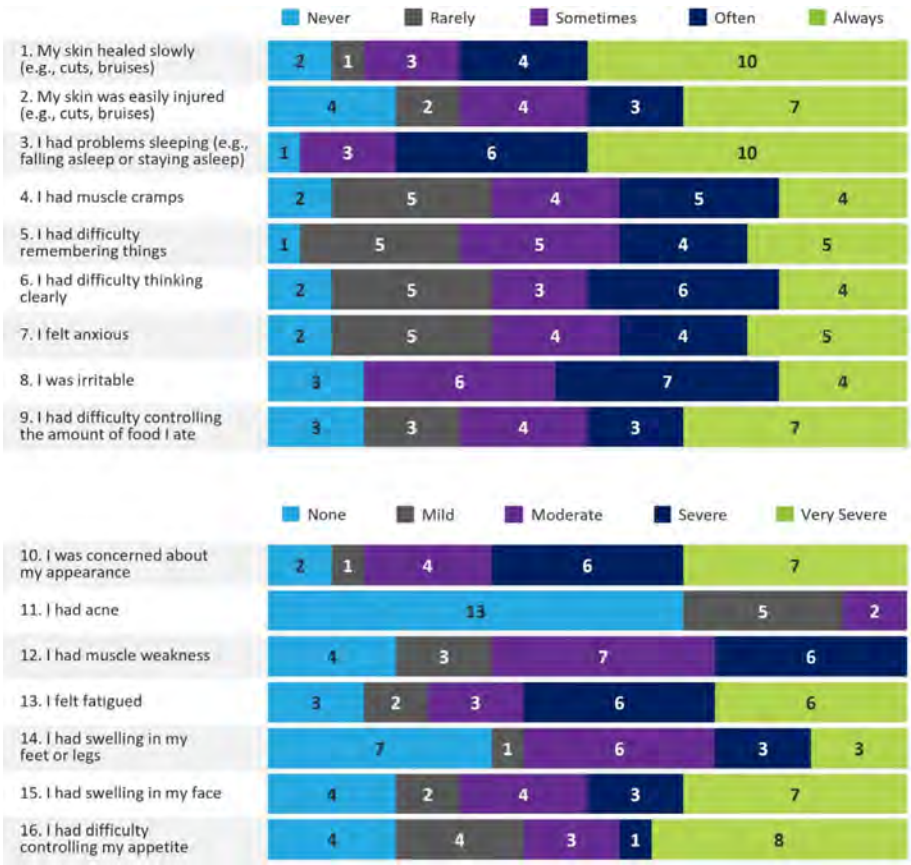
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: While glucocorticoids (GCs) are commonly used to treat a range of inflammatory diseases, the burden of toxicities associated with these medications is significant. The Glucocorticoid Toxicity Index is a clinician-reported outcome measure that quantifies change in steroid toxicity over time. A robust complementary patient-reported outcome measure (PRO) is needed to capture the patient perspective of steroid treatment. The purpose of this study was to develop and assess the content validity of a PRO, the Patient Reported Outcome of Steroid Experience (PRO-SE), to evaluate GC toxicity. The PRO-SE was developed following established PRO guidance.

Methods: The draft PRO-SE was developed from a pool of concepts derived from one-on-one virtual patient interviews. Individual hybrid concept elicitation/cognitive interviews were conducted with patients with a range of conditions for which GCs are prescribed. Patients were recruited through patient advocacy organizations and interviewed via telephone or video conference. During the concept elicitation portion of the interview, participants shared symptoms associated with their illness as well as toxicities associated with GC medication. Participants then completed the PRO-SE and provided feedback on their comprehension of the instrument as well as the clarity and relevance of the items.

Results: Interviews were completed with 20 participants (n=3 IgG4-related disease; n=4 vasculitis; n=1 bullous pemphigoid; n=3 systemic lupus erythematosus; n=3 chronic inflammatory demyelinating polyradiculoneuropathy; n=6 myasthenia gravis). Toxicities commonly experienced by participants included difficulty sleeping/insomnia (n=10, 50%), swelling in the face ("moon face"; n=8, 40%), weight gain (n=7, 35%), difficulty with skin healing, increased appetite, and mood swings (all n=5, 25%). Participant responses to the PRO-SE are shown in Figure 1. When asked to assess the measure, all participants (n=20, 100%) provided positive feedback, describing it as "good," "comprehensive," "easy," "simple," or "clear." Participants also demonstrated understanding of the instructions, 7-day recall period, and response options (n=20, 100%). There were no major item comprehension issues, with 95-100% of the participants clearly demonstrating



Participant Responses to the PRO-SE

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

understanding of each of the 16 items. Participants stated that the most important items were fatigue (n=16, 80%), sleep problems (n=15, 75%), facial swelling, and difficulty controlling appetite (both n=11, 55%; not mutually exclusive).

Conclusion: The PRO-SE demonstrated good content validity in this population. Participants found the PRO-SE comprehensive, easy to complete and relevant to their experience with GC toxicity. Further research should be conducted to assess psychometric validity and determine a scoring algorithm for this new instrument. The PRO-SE is a potentially useful tool for assessing patients' experience of GC toxicity in clinical practice and may serve as either a stand-alone instrument or as a complement to clinician ratings of steroid toxicity, for example, the Glucocorticoid Toxicity Index.

Disclosure: T. Howell: argenx, 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck/MSD, 2; **a. Skalicky**: None; **L. Matza**: None; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **M. Stone**: argenx, 2; **V. Rao**: argenx, 3; **G. Phillips**: Argenx, 3, 11.

Abstract Number: 0361

Transition in Focus: Health Care Utilization and Disease Status in Youth with Connective Tissue Diseases— A Single-Center Experience in British Columbia, Canada

Mercedes Chan[1], Lori Tucker[1], **Jude AlMasoud**[1], Jaime Guzman[2], Andrea Human[1], David Cabral[3], Angela How[4], Wendy Wong[5] and Jennifer Corpuz[6], [1]BC Children's Hospital, Vancouver, BC, Canada, [2]University of British Columbia and BC Children's Hospital, Vancouver, BC, Canada, [3]BC Children's Hospital and University of British Columbia, Vancouver, BC, Canada, [4]UBC, Vancouver, BC, Canada, [5]University of British Columbia, Surrey, BC, Canada, [6]UBC, New Westminster, BC, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Graduating from child and family-oriented to adult-oriented health care is a vulnerable time when youth with chronic disease drop out of, or disengage from, the healthcare system. For young adults with connective tissue diseases (CTD) in Vancouver, we developed a 3-phase "transition program" beginning in the multidisciplinary pediatric clinic; at end of high school patients transfer to a Young Adult Rheumatic Disease (YARD) clinic – a pediatric-adult hybrid-care transition clinic with no parental involvement; in 3-4 years they then transfer to adult care. This study describes healthcare use and disease outcomes of youth with CTD during the early phase of their transition through to the YARD clinic.

Methods: We conducted a retrospective chart review of patients who transitioned from pediatric care to the YARD clinic between 2013 and 2023. Comparative statistics were used to assess demographics, disease activity, and healthcare utilization (FU = follow-up visits, ED = emergency department, HA = hospital admission) one year pre- and post-transition. For study purposes, the first "transition" time point equates to the first YARD clinic visit.

Results: 42 patients were included (85.7% female) with systemic lupus erythematosus (SLE) (28/42), 66.7% juvenile dermatomyositis (14.3% linear scleroderma, 4.8% mixed connective tissue disease, and one patient each with cutaneous lupus, undifferentiated connective tissue disease, primary Sjogren's, and systemic sclerosis. Mean transition age: 18 years (17.9-18).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Disease Activity, and Healthcare Utilization Across Transition Intervals

	12-month period prior to transition	Time from last pediatric visit to 1st YARD visit (Median 4 / (IQR 3-5.5)	12-month period post transition
Number of patients	42	40	30
Visits attended Median (IQR)	4 (3-4.25)	NA	3 (2-4)
Visits missed Median (IQR)	0 (0-1)	0 (0)	0 (0-0.5)
SLEDAI (N=28) Median (IQR)*	4 (0-6)	2 (0-4)	2 (0-4)
PGA (Mean)*	1.14	0.75	0.57
ED visits %:	26.2%	7.5%	27.5%
Disease activity	41.67%	0%	33.33%
Non-rheumatological (mental health or trauma)	41.67%	66.7%	66.67%
Infection	16.66%	33.3%	0%
Admissions %:	11.9%	2.5%	7.7%
Disease activity	60%		66.7%
Non-rheumatological (Mental health, trauma, or surgery)	40%	100%	33.3%

*Scores for SLEDAI and PGA correspond to the clinical evaluations at the 12-month pre-transition, transition, and post-transition time points.

Patients attended an average of 4.19 FU visits pre-transition and 2.90 post-transition. The mean of missed rheumatology visits was 0.38 pre- and 0.41 post-transition (Table 1).

For SLE patients, the median SLE Disease Activity Index (SLEDAI) scores were 4 pre- and 2 post-transition. Physician Global Assessment (PGA) scores were 1.14 pre- and 0.57 post-transition for all patients.

Table 2: Physician Global Assessment at the 12-month pre-transition, transition, and post-transition time points

PGA (Scale 0-10)	12 Months Prior To transition (n=42)	Time from last pediatric visit to 1st YARD visit (n=40)	12 months post transition (n=30)
0	45.2%	57.5	70.3%
1-3	50%	40%	29.7%
≥ 4	4.8%	2.5%	0%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ED visits occurred in 26.2% and 27.5% of patients pre- and post-transition, respectively, with 41.67% and 33.3% due to disease flare (Table 1). HA occurred in 11.9% and 7.7% pre- and post-transition, respectively, with 60% and 66.7% due to disease activity. There was no significant difference in ED or HA in the 12 months pre- vs. post-transition (p = 1.33 and 0.518).

The YARD clinic received 40/42 (95.2%) patient referrals sent to the clinic. Post-transition, 30 patients remained in follow-up, 7 relocated or were transferred to a local physician, and 3 failed to show up despite repeated appointments.

Conclusion: In this cohort, initial transition from pediatric care to the YARD clinic was associated with stable ED use and HA rates. These findings suggest that our structured transition process is initially effective with minimal loss to follow-up and stable clinical outcomes. Our results highlight the need to evaluate the longer-term success of the YARD transition and subsequently after transfer to adult care.

Disclosure: M. Chan: None; **L. Tucker**: None; **J. AlMasoud**: None; **J. Guzman**: None; **A. Human**: None; **D. Cabral**: None; **A. How**: None; **W. Wong**: None; **J. Corpuz**: None.

Abstract Number: 0362

Drug Persistence of IL-17A Inhibitors Among Patients with PsA: Real-World Data from the CorEvitas PsA/SpA Registry

Philip J. Mease[1], Nicole Middaugh[2], Maya Marchese[3], Skyler Peterson[3], Burcu Ertugrul Vardar[4], Russel Burge[5], **Natalia Bello**[6], Marcus Ngantcha[7], Joseph F Merola[8], Louis Bessette[9] and Alexis Ogdie[10], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]CorEvitas, LLC, Waltham, MA, [3]CorEvitas, LLC, Waltham, [4]Eli Lilly Cork GBS Ltd, Dublin, Dublin, Ireland, [5]Eli Lilly and Company, Indianapolis, [6]Eli Lilly, Indianapolis, IN, [7]Eli Lilly GBS Cork Ltd, Cork, Ireland, [8]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [9]Centre de l'Osteoporose et de Rhumatologie de Quebec, Quebec, QC, Canada, [10]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IL-17A inhibitors (IL-17Ai) are considered recommended biologic therapies for PsA per current treatment guidelines[1,2]. Real-world evidence (RWE) studies on IL-17Ai drug persistence among patients with PsA are limited[3]. RWE data on long-term use of biologics can support more informed treatment strategies and improve patient outcomes[4]. Here, we analyse RWE data to assess the persistence of IL-17Ai therapy in patients with PsA.

Methods: This observational study included adult patients with a diagnosis of PsA enrolled in the CorEvitas PsA/SpA Registry. Primary and sensitivity analyses were conducted among IL-17Ai initiators, defined as patients who initiated ixekizumab or secukinumab as first use within the IL-17Ai mechanism of action (MOA) and had at least 1 follow-up registry visit. The primary outcome was drug persistence defined as time from treatment initiation of a specific MOA to discontinuation (DC) of that MOA. For sensitivity analysis, persistence was redefined as continuous use of initiated therapy without DC, with cycling to another IL-17Ai therapy considered as DC. Each outcome was censored at the last available study visit or 12 months (M12), whichever occurred first. Drug persistence at M12, with corresponding 95% confidence intervals (CI), was estimated using the Kaplan-Meier method. Unadjusted Cox proportional hazards models were used to estimate hazard ratios (HR) and corresponding 95% CI between patient characteristics and DC.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

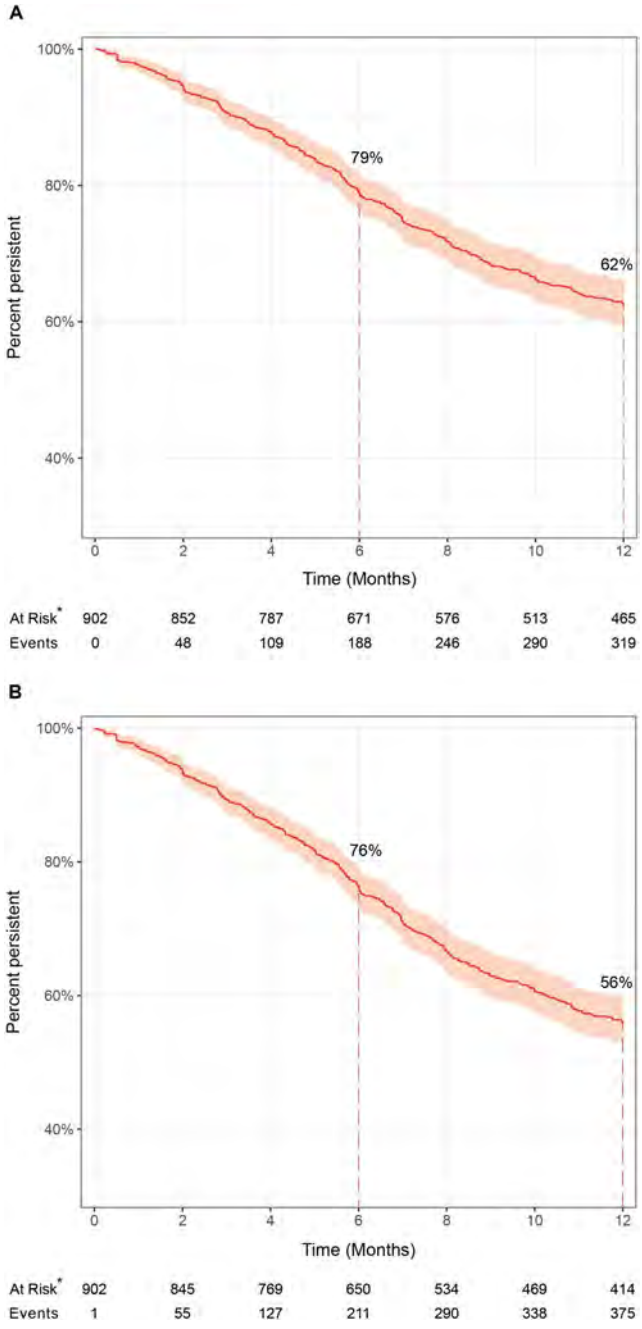


Figure 1: Kaplan-Meier plots of drug persistence among IL-17Ai initiators for the (A) primary analysis and (B) sensitivity analysis *This does not represent the outcome of interest, rather the number of patients remaining at risk for the outcome at each timepoint. The pink shaded area represents the 95% confidence interval.

Results: A total of 902 patients with PsA initiated a first IL-17Ai. Demographic, disease and treatment characteristics at index are presented in **Table 1**. Secukinumab was initiated by the majority (74.9%) of the IL-17Ai cohort, with ixekizumab accounting for 25.1%. **(Table 1)**. For the primary outcome, proportion persistent with a specific MOA at M12 was estimated to be 62.4% (95% CI: 59.2, 65.8) **(Figure 1)**. Median persistence was not reached at M12. Persistence was numerically lower in the sensitivity analysis (55.7% [95% CI: 52.4, 59.2]). Unadjusted univariate analysis showed that numerically some factors including female sex, history of fibromyalgia, depression, current smoker, >2 comorbidities, axial involvement among others had an increased risk of IL-17Ai DC (HR >1) **(Table 2)**, with similar results in the sensitivity analysis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient demographics and health characteristics at index[a] for IL-17Ai initiators (N=902)

Demographic Characteristics	
Age (years)	N=902
Mean (SD)	53.3 (12.2)
Female	N=901
n (%)	516 (57.3)
White	N=886
n (%)	811 (91.5)
Hispanic	N=789
n (%)	65 (8.2)
Health Characteristics	
Smoking history, n (%)	N=897
Never	519 (57.9)
Former	276 (30.8)
Current	102 (11.4)
BMI, n (%)[b]	N=892
Underweight/Normal (BMI < 25 kg/m²)	111 (12.4)
Overweight (BMI 25 – 30 kg/m²)	234 (26.2)
Obese 1 (BMI 30 – 35 kg/m²)	238 (26.7)
Obese 2 (BMI 35 – 40 kg/m²)	150 (16.8)
Obese 3 (BMI ≥ 40 kg/m²)	159 (17.8)
History of comorbidities, n (%)	N=902
Anxiety	118 (13.1)
Depression	178 (19.7)
Fibromyalgia	146 (16.2)
Number of comorbidities, n (%)[c]	N=902
0:	314 (34.8)
1:	265 (29.4)
2+:	323 (35.8)
Treatment Characteristics	
Prior use of IL-23i	N=902
n (%)	36 (4.0)
Current therapy, n (%)	N=902
Ixekizumab	226 (25.1)
Secukinumab	676 (74.9)
Number of prior csDMARDs/APR, n (%)[d]	N=902
0:	222 (24.6)
1:	397 (44.0)
2+:	283 (31.4)
Number of prior b/tsDMARDs, n (%)[e]	N=902
0:	259 (28.7)
1:	287 (31.8)
2+:	356 (39.5)
Concomitant therapy, n (%)	N=902
Monotherapy	626 (69.4)
Combination with cDMARDs/APR	276 (30.6)
Disease Characteristics	
Axial PsA	N=902
n (%)	372 (41.2)
Duration of PsA disease (years)	N=894
Mean (SD)	6.9 (8.0)
Disease Activity	
Tender joint count	N=891
Mean (SD)	7.2 (9.9)
Swollen Joint Count (66)	N=891
Mean (SD)	2.8 (5.1)
PhGA VAS 0-100	N=897
Mean (SD)	32.5 (24.2)
BSA (0 – 100%)	N=884
Mean (SD)	6.9 (12.8)
DAPSA	N=576
Mean (SD)	20.7 (15.4)
cDAPSA	N=882
Mean (SD)	19.9 (15.7)
mPASDAS	N=568
Mean (SD)	4.5 (1.4)
Patient-Reported Outcomes	
PtGA VAS (0-100)	N=894
Mean (SD)	45.5 (26.6)
Patient pain VAS (0-100)	N=899
Mean (SD)	51.7 (28.1)
Patient fatigue VAS (0-100)	N=899
Mean (SD)	50.8 (29.0)
EQ-5D-3L	N=889
Mean (SD)	0.6 (0.2)
EQ (VAS 0-100)	N=898
Mean (SD)	61.5 (21.1)
WPI[f]	N=426
Mean (SD)	4.9 (3.8)
FSS[f]	N=379
Mean (SD)	10.5 (5.9)

APR: Apremilast, BMI: Body Mass Index, BSA: Body Surface Area, cDAPSA: Clinical Disease Activity Index for Psoriatic Arthritis, csDMARDs: Conventional Synthetic Disease-Modifying Antirheumatic Drug, PhGA: Physician Global Assessment, PtGA: Patient Global Assessment, SD: Standard Deviation, VAS: Visual Analog Scale.

[a]The index visit corresponds to the registry visit where baseline variables associated with initiation of IL-17Ai are ascertained.
[b]Based on the CDC cut-offs for normal/underweight (under 25); Overweight (25.0 – 30); and Obese (30.0 and above).
[c]Comorbidities include history of cardiovascular disease, malignancies, depression, anxiety, fibromyalgia, hypertension, diabetes, uveitis, and inflammatory bowel disease
[d]csDMARDs include methotrexate, Plaquenil, Arava, Azulfidine.
[e]b/tsDMARDs include Cimzia, Humira, Remicade, Enbrel, Simponi, Taltz, Cosentyx, Skyrizi, Tremfya, Stelara, Orencia, Xeljanz, Rinvoq and biosimilars.
[f]WPI and FSS data collected as of May 1, 2020.

Conclusion: Findings from this observational study of patients with PsA demonstrate the persistence of IL-17Ai, as a class, in a real-world setting. Persistence estimates at M12 align with patient retention rates observed in clinical trials[5] and previous registry-based studies[6] for IL-17Ai cohorts. Numerous factors demonstrated a higher risk of decreased persistence, with CIs not suggesting statistical significance. This underscores the effect that disease burden in patients with PsA can have on treatment outcomes, affecting the persistence of treatments[7].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Unadjusted hazard ratios estimating the association between patient characteristic and risk of IL-17Ai discontinuation

	Primary Analysis HR (95% CI)	Sensitivity* Analysis HR (95% CI)
Demographic Characteristics		
Age (years) (5-year increase):	1.00 (0.96, 1.05)	1.00 (0.96, 1.04)
Female:	1.26 (1.01, 1.58)	1.35 (1.09, 1.67)
White:	1.15 (0.76, 1.74)	1.22 (0.82, 1.80)
Hispanic:	0.76 (0.51, 1.14)	0.83 (0.57, 1.21)
Health Characteristics		
Smoking history		
Never:	—	—
Former:	0.82 (0.64, 1.06)	0.92 (0.73, 1.16)
Current:	1.08 (0.77, 1.52)	1.05 (0.76, 1.44)
BMI		
Underweight/Normal (BMI < 25 kg/m^2):	—	—
Overweight (BMI 25 – 30 kg/m^2):	0.71 (0.49, 1.02)	0.81 (0.57, 1.14)
Obese 1 (BMI 30 – 35 kg/m^2):	0.68 (0.47, 0.98)	0.74 (0.52, 1.04)
Obese 2 (BMI 35 – 40 kg/m^2):	0.88 (0.60, 1.30)	0.91 (0.63, 1.32)
Obese 3 (BMI ≥ 40 kg/m^2):	0.82 (0.56, 1.21)	1.02 (0.71, 1.46)
Anxiety:	1.42 (1.06, 1.91)	1.48 (1.13, 1.94)
Depression:	1.27 (0.98, 1.64)	1.23 (0.97, 1.56)
Fibromyalgia:	1.25 (0.94, 1.67)	1.42 (1.10, 1.84)
Number of comorbidities		
0:	—	—
1:	0.94 (0.71, 1.24)	1.00 (0.77, 1.29)
2+:	1.13 (0.87, 1.46)	1.17 (0.92, 1.48)
Treatment Characteristics		
Prior use of IL-23i:	1.21 (0.71, 2.06)	1.01 (0.59, 1.73)
Number of prior csDMARDs/APR		
0:	—	—
1:	1.08 (0.82, 1.43)	1.06 (0.82, 1.37)
2+:	0.99 (0.73, 1.34)	1.03 (0.78, 1.36)
Number of prior b/tsDMARD		
0:	—	—
1:	0.91 (0.69, 1.20)	0.97 (0.75, 1.25)
2+:	0.84 (0.64, 1.10)	0.90 (0.70, 1.15)
Concomitant therapy		
Monotherapy:	—	—
Combination with cDMARDS/APR:	1.21 (0.96, 1.52)	1.11 (0.90, 1.38)

	Primary Analysis HR (95% CI)	Sensitivity* Analysis HR (95% CI)
Disease Characteristics		
Axial PsA:	1.33 (1.06, 1.65)	1.19 (0.97, 1.46)
Duration of PsA disease (years):	1.01 (0.99, 1.02)	1.00 (0.99, 1.02)
Disease (PsA/SpA) duration based on symptoms:	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
Disease activity		
Tender joint count (68):	1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
Swollen joint count (66):	1.01 (0.98, 1.03)	1.00 (0.98, 1.02)
PhGA (VAS 0-100) (5-unit increase):	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)
BSA (0-100%) (5-unit increase):	0.97 (0.93, 1.02)	0.98 (0.93, 1.02)
DAPSA (5-unit increase):	1.04 (1.00, 1.08)	1.04 (1.00, 1.08)
cDAPSA (5-unit increase):	1.04 (1.00, 1.07)	1.03 (1.00, 1.07)
mPASDAS:	1.10 (1.00, 1.21)	1.11 (1.02, 1.22)
Patient-reported outcomes		
PtGA VAS (0-100):	1.04 (1.02, 1.06)	1.03 (1.01, 1.05)
Patient pain (VAS 0-100) (5-unit increase):	1.03 (1.01, 1.05)	1.03 (1.01, 1.05)
Patient fatigue (VAS 0-100) (5-unit increase):	1.03 (1.01, 1.05)	1.03 (1.01, 1.05)
EQ-5D-3L (0.1-unit increase):	0.94 (0.90, 0.99)	0.94 (0.90, 0.98)
EQ (VAS 0-100) (5-unit increase):	0.96 (0.94, 0.98)	0.96 (0.93, 0.98)
WPI:	1.04 (1.00, 1.08)	1.05 (1.01, 1.09)
FSS:	1.03 (1.00, 1.05)	1.03 (1.01, 1.06)

APR: Apremilast, BMI: Body Mass Index, BSA: Body Surface Area, b/tsDMARD: Biologic and Targeted Synthetic Disease-modifying Antirheumatic Drug, cDAPSA: Clinical Disease Activity Index for Psoriatic Arthritis, CI: Confidence Interval, csDMARDs: Conventional Synthetic Disease-Modifying Antirheumatic Drug, EQ-5D-3L: European Quality of Life 5 Dimensions 3 Level Version, FSS: Fibromyalgia Severity Scale, HR: Hazard Ratio, IL-23i: Interleukin-23 inhibitor, mPASDAS: Modified Psoriatic Arthritis Disease Activity Score, PhGA: Physician Global Assessment, PtGA: Patient Global Assessment, VAS: Visual Analog Scale, WPI: Widespread Pain Index

— Reference level

*Sensitivity analysis was conducted using an alternative definition of persistence: continuous use of initiated therapy without discontinuation (where switch to another drug of the same MOA was considered a discontinuation).

References

1. Coates, LC, *Nat Rev Rheumatol*, 18 (2022) 465
2. Gossec, L, *Ann Rheum Dis*, 83 (2024) 706
3. Joven, B, Adv Ther, 40 (2023) 5415
4. Rohekar, S, *ACR Open Rheumatol*, 6 (2024) 440
5. VD-Heijde, D, *J Rheumatol*, 45 (2018) 367
6. López-Medina, C, *Ann Rheum Dis*, 83 (2024) 1494
7. Campanholo, CB, *J Rheumatol*, 50 (2023) 426

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **N. Middaugh**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

UCB.; **M. Marchese**: None; **S. Peterson**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **B. Ertugrul Vardar**: Eli Lilly Cork Ltd, 3; **R. Burge**: Eli Lilly and Company, 3; **N. Bello**: Eli Lilly, 3, 11, Eli Lilly and Company, 3; **M. Ngantcha**: Eli Lilly, 3; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, 5, 6, Fresenius Kabi, 2, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, TEVA, 2, 6, UCB, 2, 5, 6; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5.

Abstract Number: 0363

Assessing Whole Health Needs in Systemic Lupus Erythematosus

Amanda Eudy[1], Megan Clowse[2], Dana Burshell[3], Connor Drake[3], Tamara Somers[4], David Pisetsky[5], Rebecca Sadun[6], Ralph Snyderman[7], Kai Sun[6], Lisa Criscione-Schreiber[3], Mithu Maheswaranathan[3], Nathaniel Harris[5], Jayanth Doss[8] and Jennifer Rogers[3], [1]Duke University, Raleigh, NC, [2]Duke University, Chapel Hill, NC, [3]Duke University School of Medicine, Durham, [4]Duke University School of Medicine, Durham, NC, [5]Duke University Medical Center, Durham, NC, [6]Duke University, Durham, NC, [7]Duke Center for Personalized Health Care, Durham, NC, [8]Division of Rheumatology and Immunology, Duke University Department of Medicine, Durham, NC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Care models that take a 'Whole Health' perspective by emphasizing personalized care focused on the individual's values, needs, and goals, rather than solely on medical conditions are sorely needed for patients with SLE. Enhancing self-care can significantly improve overall well-being but is often missing from SLE management. This study aims

Table 1. The Whole Health Self-Assessment completed by patients with SLE.

People find different components of their life make living with lupus a bit easier. We'd like to learn which of the following components are currently working for you. Rate yourself in each area.	
Movement and Exercise	0 = I have trouble moving my body or exercising 100 = I move my body or exercise regularly
Rest	0 = I have trouble sleeping and relaxing 100 = I sleep well
Nutrition	0 = I eat an unhealthy diet 100 = I eat a very healthy diet
Purpose and Meaning in Life	0 = I lack purpose & meaning in my life 100 = I have a clear sense of purpose
Personal and Professional Goals	0 = I am unable to pursue my personal and/or professional goals, 100 = I am very able to pursue my personal and/or professional goals
Stress	0 = I am frequently stressed, anxious, or depressed 100 = I manage my stress and emotions well
Relationships	0 = I do not have open, supportive relationships with the people in my life 100 = I have open, supportive relationships with the people in my life
Physical Environment	0 = My surroundings are unsafe, unstable, and/or stressful 100 = I have a safe, and comfortable home and workplace
Lupus Medications	0 = I don't take my lupus medications 100 =I always take my lupus medications
Trust in Healthcare	0 = I don't trust healthcare providers 100 = I always trust healthcare providers

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Correlation of Whole Health Assessment Domains with Type 1 & 2 SLE Measures.

	Movement & Exercise	Rest	Nutrition	Purpose & Meaning in Life	Personal and Professional Goals	Stress	Relationships	Physical environment	Lupus Medications	Trust in healthcare
Type 1 SLE Activity Measures										
Type 1 PGA	-0.16	-0.20	-0.11	**-0.23**	**-0.23**	-0.19	-0.15	-0.11	-0.12	-0.19
SLEDAI	-0.04	0.01	0.01	-0.02	-0.06	-0.06	0.02	-0.03	0.03	-0.21
Clinical SLEDAI	-0.05	-0.04	0.01	0.00	-0.08	-0.04	0.02	0.02	-0.01	-0.17
Type 2 SLE Activity Measures										
Type 2 PGA	**-0.26**	**-0.37**	**-0.26**	**-0.29**	**-0.46**	**-0.26**	**-0.26**	-0.15	-0.09	-0.05
Polysymptomatic Distress Score (PSD)	**-0.26**	**-0.35**	-0.15	-0.22	**-0.44**	**-0.29**	-0.20	-0.14	-0.04	-0.07
Widespread Pain Index (WPI)	-0.20	**-0.26**	-0.09	-0.09	**-0.28**	-0.17	-0.10	-0.05	0.03	0.002
Symptom Severity Score (SSS)	**-0.27**	-0.39	-0.20	**-0.34**	**-0.54**	**-0.39**	**-0.30**	-0.23	-0.12	-0.15
FACIT Fatigue Score	**0.38**	**0.42**	**0.27**	**0.36**	**0.61**	**0.41**	**0.41**	0.22	0.13	0.13
PROMIS Measures										
Self-efficacy for medications	0.10	0.09	0.12	0.16	**0.28**	**0.23**	**0.28**	0.15	**0.24**	**0.27**
Self-efficacy for symptom management	**0.24**	0.20	0.11	**0.23**	**0.49**	**0.33**	**0.29**	0.17	0.14	0.21
Pain interference	**-0.23**	**-0.33**	-0.19	**-0.27**	**-0.46**	**-0.26**	**-0.36**	-0.21	-0.11	-0.09
Pain intensity	-0.19	**-0.30**	-0.19	**-0.24**	**-0.38**	-0.18	**-0.33**	-0.21	-0.11	-0.10

Correlation	
Strong	>|0.5|
Moderate	|0.3-0.5|
Weak	|0.1-0.3|
Absent	<|0.1|

to identify the greatest self-care needs for individuals with SLE using a modified Whole Health Self-Assessment survey, focusing on differences by subgroups of Type 2 SLE activity (Intermittent and Persistent).

Methods: Patients with SLE enrolled in a lupus registry completed the Polysymptomatic Distress Score (PSD), FACIT Fatigue scale, PROMIS measures, and a modified Whole Health Self-Assessment, rating their health on a visual analog scale across 10 domains (Table 1). Participants also selected their three most important areas for self-care. Rheumatologists scored the SLEDAI and Type 1 & 2 physician's global assessments (PGA). Spearman's correlation coefficients measured the correlation of Whole Health domain scores with disease activity and PROMIS measures. Correlations were classified as strong (>0.5), moderate (0.3-0.5), weak (0.1-0.3), or absent (< 0.1).

High Type 1 SLE activity was defined as SLEDAI ≥6, clinical SLEDAI ≥4, Type 1 PGA ≥1, or active nephritis. High Type 2 SLE activity was defined as PSD ≥8 or Type 2 PGA ≥1. Among patients with ≥3 visits in the registry, Type 2 SLE patterns were classified as:

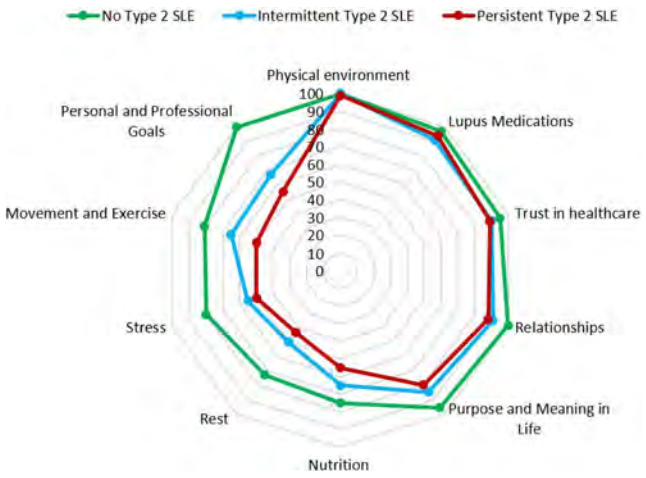


Figure 1. Differences in Median Whole Health Domain Scores by Type 2 SLE Pattern.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

- No Type 2 SLE
- Intermittent Type 2 SLE: Type 2 SLE activity at ≤2 visits and Type 1 SLE activity at ≥1 visit
- Persistent Type 2 SLE: Type 2 SLE activity at 3 visits and Type 1 SLE activity at < 3 visits, or Type 2 SLE activity at ≥2 visits and Type 1 SLE activity at 0 visits

Differences in median Whole Health Assessment scores across Type 2 pattern groups were compared using the Kruskal-Wallis test.

Results: We included 295 patients with SLE (mean age 44 years, 92% female, 60% Black, 33% White). Strong correlations were observed between Personal & Professional Goals with the SSS (r=-0.54) and FACIT Fatigue score (r=0.61; Table 2). Type 2 SLE activity measures were moderately correlated with Movement & Exercise, Rest, Purpose & Meaning in Life, Personal & Professional Goals, Stress, and Relationships. Weak correlations were found between Type 1 PGA and Purpose & Meaning in Life (r=-0.23) and Personal & Professional Goals (r=-0.23). Among 194 patients with ≥3 visits, patients with Persistent Type 2 SLE had worse scores across several Whole Health domains (Figure 1). When asked to indicate the areas of self-care most important to them, all groups selected "Rest" as the top domain (67-79%), followed by Movement & Exercise (42-51%), Nutrition (35-47%), and Purpose & Meaning in Life (39-40%).

Conclusion: Significant correlations were observed between Whole Health domains and Type 2 SLE activity measures, with scores decreasing as Type 2 SLE activity worsened. These findings helped support our development of a curriculum for a 'Whole Health' program aimed at improving self-care and quality of life for patients with SLE through education, peer support, and goal setting outside of the clinical setting. Incorporating these insights into routine care can help address what matters most to patients.

Disclosure: A. Eudy: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **M. Clowse**: None; **D. Burshell**: Immunovant, 5; **C. Drake**: ZealCare, 12, 10; **T. Somers**: None; **D. Pisetsky**: Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(-GSK), 2, Immunovant, 2, 5; **R. Sadun**: The Expert Institute, 12,; **R. Snyderman**: DNAnexus, 4, Heartland Whole Health Institute, 4, iRhythm Technologies, 4, OrthoTheapeutics, Inc., 1, ZealCare, 4; **K. Sun**: Aurinia, 2; **L. Criscione-Schreiber**: UCB, 5; **M. Maheswaranathan**: AstraZeneca, 2, UCB, 2; **N. Harris**: None; **J. Doss**: None; **J. Rogers**: AstraZeneca, 1, 1, Aurinia, 2, 5, Exagen, 5, Immunovant, 2, 5.

Abstract Number: 0364

Group-Based Medical Mistrust and Logistical Factors Influencing Rheumatology Clinical Trial Enrollment: A Single-Center Cross-Sectional Survey

Andreina Martinez Paulino[1], Miles King[2], Danny Arias Diaz[1], Asma Cheema[3] and Muznay Khawaja[4], [1]Jersey City Medical Center, Jersey City, NJ, [2]Albert Einstein College of Medicine, New York, NY, [3]Montefiore Einstein , Wakefield Campus, Woodbridge Township, NJ, [4]Jersey City Medical Center, Hoboken, NJ

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical trials are the cornerstone of evidence-based rheumatology, yet enrolling and retaining a representative patient cohort remains challenging. While underrepresentation of underserved minorities is well documented,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics of Participants

Characteristics	Participants (n = 47) n (%)
Age	
18–35 years	10 (21.28)
36–45 years	9 (19.15)
46–65 years	24 (51.06)
66+ years	4 (8.51)
Sex	
Female	37 (78.72)
Male	10 (21.28)
Race/Ethnicity	
White	13 (27.66)
Black/African American	11 (23.40)
Latino/a	10 (21.28)
Asian/Pacific Islander	7 (14.89)
Other	6 (12.76)
Rheumatic Diseases	
Rheumatoid Arthritis	22 (46.80)
Systemic Lupus Erythematosus	7 (14.89)
Psoriatic Arthritis	3 (6.38)
Undifferentiated Connective Tissue Disease	3 (6.38)
Gout	2 (4.26)
Sacroiliitis	2 (4.26)
Sjögren Syndrome	2 (4.26)
Other	6 (12.77)
Trial Willingness	
Yes	31 (65.96)
No	16 (34.04)

Table 2. Mean (SD) Scores on Individual Group-Based Medical Mistrust Scale Items for All Participants and by Willingness to Participate in a Clinical Trial

Items	All	Willing	Unwilling	p
		Item Mean (SD)		
Mean GBMMS Score	**24.91 (12.10)**	**24.74 (11.62)**	**25.25 (13.36)**	**0.893**
1. Doctors sometimes hide information from patients who belong to my ethnic group.	2.55 (1.61)	2.74 (1.71)	2.19 (1.38)	
2. Doctors have the best interests of people in my ethnic group.[a]	2.15 (1.43)	2.16 (1.39)	2.13 (1.54)	
3. People of my ethnic group should not confide in doctors because it will be used against them.	1.74 (1.24)	1.58 (1.23)	2.06 (1.24)	
4. People of my ethnic group should be suspicious of information from doctors.	1.60 (1.10)	1.52 (1.06)	1.75 (1.18)	
5. People of my ethnic group cannot trust doctors.	1.55 (1.05)	1.48 (1.00)	1.69 (1.20)	
6. People of my ethnic group should be suspicious of modern medicine.	1.74 (1.19)	1.71 (1.13)	1.81 (1.33)	
7. Doctors treat People of my ethnic group like 'guinea pigs.'	2.21 (1.52)	2.10 (1.58)	2.44 (1.41)	
8. People of my ethnic group receive the same medical care from doctors as people from other groups.[a]	2.23 (1.62)	2.23 (1.61)	2.25 (1.69)	
9. Doctors do not take the medical complaints of my ethnic group seriously.	2.79 (1.69)	2.81 (1.74)	2.75 (1.65)	
10. People of my ethnic group are treated the same as people of other groups by doctors.[a]	2.34 (1.67)	2.29 (1.68)	2.44 (1.71)	
11. In most hospitals, people of different ethnic groups receive the same kind of care.[a]	2.21 (1.60)	2.13 (1.57)	2.38 (1.71)	
12. I have personally been treated poorly or unfairly by doctors because of my ethnicity.	1.89 (1.58)	2.03 (1.66)	1.63 (1.41)	

Scale: 1 Strongly Disagree – 5 Strongly Agree. SD = Standard Deviation.

[a]Reverse scored.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Mean (SD) Importance Ratings of Logistical Factors for All Participants and by Willingness to Participate in a Clinical Trial

Table 3. Mean (SD) Importance Ratings of Logistical Factors for All Participants and by Willingness to Participate in a Clinical Trial

Factors	All	Willing	Unwilling
		Factor Mean (SD)	
1. Travel/Transportation	5.14 (1.47)	5.67 (1.45)	**4.13 (0.89)**
2. Scheduling/Time commitment	3.13 (1.39)	3.42 (1.31)	2.56 (1.41)
3. Prospect of getting a new treatment	3.45 (2.14)	3.90 (2.18)	2.56 (1.82)
4. Blood draws	3.38 (1.26)	3.81 (1.01)	2.56 (1.31)
5. Having personal health information stored/shared	3.96 (0.81)	4.03 (0.91)	3.81 (0.54)
6. Level of compensation/payment	4.72 (2.01)	5.38 (1.73)	3.44 (1.97)
7. Prospect of stopping worsening disease	6.08 (1.59)	6.45 (1.56)	**5.38 (1.40)**
8. Trial encouragement from doctor	5.42 (1.54)	5.87 (1.31)	**4.56 (1.63)**
9. Prospect of patient education by doctor	4.49 (1.12)	4.70 (1.32)	4.06 (0.25)
10. Shared ethnic group with doctor	4.40 (1.15)	4.58 (1.29)	4.06 (0.77)
11. Shared language with doctor	4.38 (1.05)	4.52 (1.26)	**4.13 (0.34)**

Scale: 1 Extremely Unlikely – 7 Extremely Likely. SD = Standard Deviation.

patients across all demographic groups may face medical mistrust or logistical barriers that affect trial participation. Prior research using the Thompson et al. (2004) Group-Based Medical Mistrust Scale (GBMMS) has linked higher mistrust to reduced engagement in preventive care, but its impact on rheumatology trial enrollment has not been studied. This study therefore examines whether GBMMS scores predict adult patients' willingness to enroll in a rheumatology clinical trial and, among those who decline, identifies the logistical concerns that most strongly influence their decision.

Methods: Between November 2024 and February 2025, we conducted a cross-sectional survey in a rheumatology clinic. After informed consent, adults (≥18 years) with physician-confirmed rheumatoid arthritis (2010 ACR/EULAR), systemic lupus erythematosus (2012 SLICC), or other rheumatic conditions completed the 12-item GBMMS (score range 12–60, higher score = more mistrust), 11 logistical-concern items, each rated 1 ("extremely unlikely to influence me") to 7 ("extremely likely"); and a yes/no question on willingness to participate in a clinical trial. We evaluated GBMMS reliability (Cronbach's α), compared mean mistrust by willingness status using Welch's t test, and ran a univariable logistic regression to assess whether mistrust predicted trial willingness. Among those unwilling, we ranked logistical factors by mean importance and calculated Pearson correlations between GBMMS total and each logistical rating (two-tailed $\alpha = 0.05$).

Results: Forty-seven patients (79 % women, mean age = 49.23 ± 13.63 years) participated; 66 % reported they would enroll in a clinical trial (Table 1). Internal consistency of the GBMMS was $\alpha = 0.90$. Mean mistrust scores did not differ among the groups (willing 24.74 ± 11.62 and unwilling 25.25 ± 13.36; Welch's $t(26) = 0.13$, $p = 0.893$) (Table 2) and did not predict willingness in the logistic regression model (OR = 0.996, 95 % CI 0.95 – 1.05, $p = 0.89$). Among the 16 unwilling to participate in clinical trials, the top-rated logistical factors were: stopping disease progression (mean = 5.38), doctor encouragement (4.56), travel/transportation (4.13) and shared language with doctor (4.13) (Table 3). Across the full sample, mistrust correlated most strongly (though non-significantly) with lower importance on a novel treatment option ($r = -0.28$; $p = 0.056$) and doctor encouragement ($r = -0.23$; $p = 0.11$).

Conclusion: Group-based medical mistrust did not predict patients' self-reported willingness to join a clinical trial. Instead, expectation of concrete disease improvement and personal endorsement by one's treating rheumatologist emerged as the strongest drivers of participation. These findings suggest that recruitment efforts focused on highlighting clear clinical benefits and enlisting rheumatologists to personally invite patients may outperform strategies aimed solely at reducing mistrust.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Martinez Paulino: None; **M. King**: None; **D. Arias Diaz**: None; **A. Cheema**: None; **M. Khawaja**: None.

Abstract Number: 0365

Clinical Characteristics and Psychosocial Outcomes of Patients with UCTD Compared to SLE

Caroline Siegel[1], Yongjay Kim[2], Lucy Masto[3], Neha Nagpal[1], Amaya Smole[4], Dongmei Sun[1], Haley Slosberg[1], Margaret Minett[5], Joann Vega[1], Deanna Jannat-Khah[1], Jane Salmon[1], Michael Lockshin[6], Lisa Sammaritano[1] and Medha Barbhaiya[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Englewood Cliffs, NJ, [3]Hospital for Special Surgery, San Francisco, CA, [4]Hospital for Special Surgery, Brooklyn, NY, [5]Hospital for Special Surgery, New York, [6]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: While UCTD is considered less clinically severe than SLE, our prior qualitative study reported that patients with UCTD experience significant psychosocial challenges (*J Clin Rheumatol* 2022). Here, we describe a large UCTD cohort and quantify psychosocial challenges in comparison to SLE.

Methods: This retrospective cohort study included patients aged ≥18 years enrolled in a UCTD or SLE academic hospital-based registry, January 2022-March 2025. Participants in the UCTD registry had a positive ANA, ≥1 sign/symptom of a CTD, and did not meet ACR/EULAR-endorsed classification criteria for SLE, RA, SSc, SS, Idiopathic Inflammatory Myopathy, or 2006 Revised Sapporo Criteria for APS. Participants in the SLE registry fulfilled 1997 ACR or 2019 ACR/EULAR SLE Classification Criteria. We administered the 36-Item Short Form Health Survey (SF-36) to assess health-related quality of life (HRQoL), Fatigue Severity Scale (FSS), General Anxiety Disorder-7 (GAD-7), and Beck Depression Inventory (BDI). We compared demographic and clinical variables and psychosocial questionnaire scores between patients with UCTD and SLE, and performed multivariable regression to evaluate the association between diagnosis and each psychosocial outcome, adjusting for demographic and treatment variables.

Results: Compared to individuals with SLE (N=225), those with UCTD (n=114) were older (median [IQR] age 43.1 [32.1, 53.7] vs. 38.0 [29.8, 50.3], p=0.03), more frequently White race (70.2% vs. 40.0% p< 0.01), and less frequently Hispanic/Latino ethnicity (16.4% vs. 28.9%, p=0.02). Overall, patients with UCTD had fewer CTD manifestations. The most frequent clinical and serologic manifestations in UCTD, as compared to SLE, included: Raynaud's (46.5% vs. 46.2%, p=1.00), arthritis (27.2% vs. 76.0%, p< 0.01), and lymphopenia (19.3% vs. 48.0%, p< 0.01). Patients with UCTD versus SLE were less frequently prescribed antimalarials (54.4% vs. 82.2%, p< 0.01) and immunosuppressive medications (9.6% vs. 52.4%, p< 0.01) [**Table 1**]. Compared to patients with SLE, those with UCTD had better SF-36-defined physical functioning (median [IQR] score 80.0 [60.0, 95.0] vs. 75.0 [50.0, 90.0], p< 0.05); other measures of HRQoL, fatigue, anxiety, and depression did not differ [**Table 2**].

After multivariable adjustment, no association was demonstrated for diagnosis (UCTD vs. SLE) and HRQoL (based on SF-36 physical and mental component summary scores), FSS-defined fatigue severity, GAD-7-defined anxiety, or BDI-defined depression. In the overall group, female sex and non-Hispanic/Latino ethnicity were associated with worse SF-36 mental component summary scores. Female sex was associated with worse fatigue severity, and Hispanic/Latino ethnicity with increased odds of anxiety. Lastly, immunosuppressive treatment was associated with increased odds of depression [**Table 3**].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics of Patients with UCTD vs. SLE

Characteristic	Overall (N=339)	UCTD (N=114)	SLE (N=225)	p-values
Demographics				
Age (years)	*40.1 (30.0, 51.9)*	*43.1 (32.1, 53.7)*	*38.0 (29.8, 50.3)*	*0.03*
Female Sex	314 (92.6)	108 (94.7)	206 (91.6)	0.40
Race				*<0.01*
• White	170 (50.1)	80 (70.2)	90 (40.0)	
• Black/African American	63 (18.6)	8 (7.0)	55 (24.4)	
• Asian	33 (9.7)	11 (9.6)	22 (9.8)	
• *Other/Unknown*	*73 (21.5)*	*15 (13.2)*	*58 (25.8)*	
Hispanic/Latino Ethnicity	83 (25.2)	18 (16.4)	65 (28.9)	0.02
BMI (kg/m²)	24.6 (21.2, 29.3)	24.1 (21.1, 29.0)	24.8 (21.3, 29.4)	0.55
CTD Manifestations[1]				
Positive ANA	339 (100)	114 (100)	225 (100)	N/A
Immunologic Disorder[2]	204 (60.2)	29 (25.4)	175 (77.8)	*<0.01*
• Anti-dsDNA antibody	158 (46.6)	8 (7.0)	150 (66.7)	*<0.01*
• Anti-Sm antibody	76 (22.4)	*See footnote**	72 (32.0)	*<0.01*
• Antiphospholipid antibody	54 (15.9)	21 (18.4)	33 (14.7)	0.46
Nonerosive Arthritis	202 (59.6)	31 (27.2)	171 (76.0)	*<0.01*
Hematologic Disorder[2]	166 (49.0)	28 (24.6)	138 (61.3)	*<0.01*
• Leukopenia	80 (23.6)	12 (10.5)	68 (30.2)	*<0.01*
• Lymphopenia	130 (38.3)	22 (19.3)	108 (48.0)	*<0.01*
• Thrombocytopenia	21 (6.2)	*See footnote**	20 (8.9)	*<0.01*
Raynaud's	157 (46.3)	53 (46.5)	104 (46.2)	1
Alopecia	139 (41.0)	20 (17.5)	119 (52.9)	*<0.01*
Photosensitivity	114 (33.6)	11 (9.6)	103 (45.8)	*<0.01*
Malar Rash	99 (29.2)	9 (7.9)	90 (40.0)	*<0.01*
Renal Disorder	76 (22.4)	*See footnote**	76 (33.8)	*<0.01*
Pleuritis or Pericarditis	85 (25.1)	*See footnote**	82 (36.4)	*<0.01*
Oral ulcers	89 (26.3)	12 (10.5)	77 (34.2)	*<0.01*
Discoid Rash	30 (8.8)	*See footnote**	29 (12.9)	*<0.01*
Neurologic Disorder	11 (3.2)	*See footnote**	11 (4.9)	*0.02*
Other Related Condition				
Fibromyalgia	39 (11.5)	12 (10.5)	27 (12.0)	0.82
Medications (Current)				
Systemic corticosteroids	123 (36.3)	18 (15.8)	105 (46.7)	*<0.01*
Antimalarial	247 (72.9)	62 (54.4)	185 (82.2)	*<0.01*
Immunosuppressive[3]	129 (38.1)	11 (9.6)	118 (52.4)	*<0.01*

Data are represented by median (IQR) or n (%); p-values are for UCTD vs. SLE, <0.05 was statistically significant.
**Values <5 were not listed.*
1. All criteria-based manifestations defined as per 1997 ACR Classification Criteria for SLE.
2. Sub-categories not mutually exclusive. No participant had hemolytic anemia.
3. Azathioprine, Cyclophosphamide, IVIG, Methotrexate, Mycophenolate, Rituximab, TNF-alpha inhibitor.

Table 2. Health-Related Quality of Life, Anxiety, Depression, and Fatigue in Patients with UCTD vs. SLE Based on Validated Psychosocial Questionnaires

Metric	UCTD (N=114)	SLE (N=225)	p-value
36-Item Short Form Health Survey (SF-36) – Range 1-100[1]			
Physical Component Summary	41.8 (32.5, 51.8)	39.8 (32.0, 49.5)	0.51
• Physical functioning	80.0 (60.0, 95.0)	75.0 (50.0, 90.0)	*<0.05*
• Role-Physical	50.0 (0.0, 100.0)	50.0 (0.0, 100.0)	0.74
• Bodily Pain	51.0 (41.0, 63.5)	51.0 (41.0, 74.0)	0.32
• General Health	46.0 (32.0, 67.0)	45.0 (27.0, 62.0)	0.36
Mental Component Summary	44.4 (34.6, 52.0)	41.9 (33.9, 50.8)	0.52
• Vitality	45.0 (20.0, 65.0)	40.0 (30.0, 55.0)	0.96
• Social Functioning	75.0 (50.0, 87.5)	62.5 (50.0, 87.5)	0.24
• Role-Emotional	100.0 (0.0, 10.0)	66.7 (0.0, 100.0)	0.61
• Mental Health	72.0 (56.0, 84.0)	72.0 (56.0, 80.0)	0.39
Generalized Anxiety Disorder-7 (GAD-7) – Range 0-21[2]	4.0 (1.25, 10.0)	5.0 (2.0, 10.0)	1.00
None [0-5]	67 (58.8)	130 (57.8)	
Mild [6-10]	22 (19.3)	61 (27.1)	
Moderate/Severe [11-21]	25 (21.9)	34 (15.1)	
Beck Depression Inventory (BDI) – Range 0-63[2]	8.5 (4.0, 15.0)	10.0 (5.0, 15.0)	0.71
Minimal [0-13]	77 (67.5)	161 (71.6)	
Mild [14-19]	24 (21.1)	34 (15.1)	
Moderate/Severe [20-63]	13 (11.4)	30 (13.3)	
Fatigue Severity Scale (FSS) – Range 1-7[2]	40.5 (28.3, 53.8)	44.0 (32.0 54.0)	0.50

Data are represented by median (IQR) or n (%); p-value <0.05 was statistically significant.
1. Higher number indicates better health state. 2. Higher number indicates greater severity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Regression Models Evaluating the Association Between Diagnostic Category (UCTD vs. SLE), Demographic Characteristics, and Psychosocial Outcomes

	Model Outcomes									
	SF-36 Physical Component Summary[1]		SF-36 Mental Component Summary[1]		Fatigue Severity Score[1]		GAD-7 Anxiety[2]		BDI Depression[2]	
	β coefficient [95% CI]	p-value	β coefficient [95% CI]	p-value	β coefficient [95% CI]	p-value	Odds Ratio [95% CI]	p-value	Odds Ratio [95% CI]	p-value
Diagnosis										
• SLE	*Referent*									
• UCTD	-2.88 [-11.24 – 5.48]	0.50	-0.34 [-3.38 – 2.70]	0.83	0.027 [-3.80 – 3.85]	0.99	1.39 [0.81 – 2.39]	0.23	1.55 [0.85 – 2.82]	0.15
Age	-0.07 [-0.31 – 0.17]	0.56	0.06 [-0.03 – 0.15]	0.19	-0.05 [-0.16 – 0.06]	0.37	***0.98 [0.97 – 1.00]***	***0.02***	0.99 [0.97 – 1.00]	0.08
Sex										
• Male	*Referent*									
• Female	-3.69 [-16.32 – 8.93]	0.57	***-7.08 [-11.67 – -2.49]***	***<0.01***	***8.41 [2.63 – 14.19]***	***<0.01***	2.42 [0.95 – 6.17]	0.07	2.00 [0.71 – 5.64]	0.19
Race										
• White	*Referent*									
• Black/ African American	-6.08 [-15.53 – 3.37]	0.21	0.57 [-2.88 – 4.00]	0.75	-1.96 [-6.29 – 2.36]	0.37	0.65 [0.34 – 1.22]	0.17	1.0 [0.51 –1.97]	>0.99
• Asian	0.57 [-11.50 – 12.64]	0.93	3.95 [-0.44 – 8.34]	0.08	-5.30 [-10.83 – 0.22]	0.06	0.49 [0.21 – 1.15]	0.10	0.75 [0.31 – 1.85]	0.53
• Other/ Unknown	-4.14 [-14.58 – 6.30	0.44	-0.47 [-4.47 – 3.12]	0.73	-0.23 [-5.00 – 4.55]	0.93	0.92 [0.48 – 1.77]	0.81	0.93 [0.46 – 1.91]	0.85
Ethnicity										
• Non-Hispanic/ Latino	*Referent*									
• Hispanic/ Latino	4.88 [-4.49 – 14.26]	0.31	***3.71 [0.30 – 7.11]***	***0.03***	-3.70 [-7.99 – 0.59]	0.09	***1.83 [1.02 – 3.27]***	***0.04***	1.52 [0.81 – 2.84]	0.19
Antimalarial										
• No	*Referent*									
• Yes	1.73 [-6.26 – 9.71]	0.67	0.46 [-2.45 – 3.37]	0.75	1.22 [-2.44 – 4.87]	0.51	1.35 [0.79 – 2.28]	0.27	0.89 [0.50 – 1.56]	0.68
Immuno-suppressive										
• No	*Referent*									
• Yes	-0.38 [-7.94 – 7.19]	0.92	-1.57 [-4.32 – 1.18]	0.26	2.19 [-1.27 –5.65]	0.21	1.21 [0.74 – 1.99]	0.44	***1.77 [1.02 – 3.07]***	***0.04***

p<0.05 was statistically significant.
1. For continuous variables, we conducted generalized linear regression analysis.
2. For categorical variables, we conducted ordinal logistic regression analysis. GAD-7 categories were defined as: None [0-5], Mild [6-10], Moderate/Severe [11-21]; BDI categories were defined as: Minimal [0-13], Mild [14-19], Moderate/Severe [20-63].

Conclusion: Patients with UCTD have fewer disease manifestations, less frequently require immunomodulatory/immunosuppressive treatment, and report better physical function than SLE comparators. Nonetheless, UCTD patients experience a similar degree of impaired HRQoL, fatigue, anxiety, and depression, suggesting they may benefit from dedicated psychosocial support.

Disclosure: C. Siegel: None; **Y. Kim**: None; **L. Masto**: None; **N. Nagpal**: None; **A. Smole**: None; **D. Sun**: None; **H. Slosberg**: None; **M. Minett**: None; **J. Vega**: None; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **J. Salmon**: UCB, 1, 5; **M. Lockshin**: None; **L. Sammaritano**: None; **M. Barbhaiya**: None.

Abstract Number: 0366

Dental Findings in Patients with Rheumatic Diseases and Its Association with Self-perceived Oral Health

Fernanda M. Garcia-Garcia[1], Margarita Isabel Alarcon-Jarquin[2], Vanessa L. Lopez-Flores[2], Gabriel P. Castro-Cruz[3], Carlos I. Estrada-Anguiano[3], Jennifer Garcia-Bravo[3], Aleydis Gonzalez-Melendez[3], Gabriel Figueroa-Parra[3], Dionicio A. Galarza-Delgado[1] and Janett C. Riega-Torres[4], [1]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [2]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, [4]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Oral health conditions are frequent in patients with rheumatic diseases and can impact daily function and quality of life. Factors such as chronic inflammation and immunosuppressive therapies may contribute to dental complications, including caries, xerostomia, and temporomandibular dysfunction. While clinical assessments are essential, patient-reported outcomes offer additional perspective on perceived oral health needs. Understanding the relationship between self-perceived oral health and clinical findings can enhance screening and support integrated management in rheumatology care.

Methods: We conducted a cross-sectional study including adult patients with rheumatic diseases, consecutively recruited from a tertiary care rheumatology clinic. Patients were categorized into good perceived oral health and poor perceived oral health groups according to General Oral Health Assessment Index (GOHAI) score-based thresholds. Clinical characteristics, comorbidities, and treatments were documented. Oral health status was evaluated using the GOHAI, International Caries Detection and Assessment System (ICDAS) caries assessment, salivary parameters (pH and flow rate), xerostomia, and

Table 1. Clinical and treatment characteristics of patients with rheumatic diseases with poor and good perceived oral health

Variable	Patients with poor perceived oral health n= 101	Patients with good perceived oral health n= 100
Age, mean ± SD	52.27 ± 14.17	53.97 ± 14.10
Women, n (%)	91 (90.09)	95 (95.00)
Rheumatic diseases		
Rheumatoid arthritis	52 (51.48)	45 (45.00)
Systemic lupus erythematosus	17 (16.83)	18 (18.00)
Sjögren's syndrome	12 (11.88)	10 (10.00)
Other rheumatic diseases	2 (19.80)	27 (27.00)
Comorbidities		
DM, n (%)	21 (20.79)	8 (8.00)
Hypertension, n (%)	39 (38.61)	29 (29.00)
Smoker, n (%)	5 (4.95)	7 (7.00)
Alcohol consumption, n (%)	10 (9.90)	11 (14.00)
Treatments		
Glucocorticoids, n (%)	28 (27.72)	36 (36.00)
DMARDs, n (%)	73 (72.27)	80 (80.00)
Methotrexate, n (%)	48 (47.52)	49 (49.00)
Bisphosphonates, n (%)	9 (8.91)	9 (9.00)

SD, Standard Deviation; DM, Diabetes Mellitus; DMARDs, Disease-Modifying Antirheumatic Drugs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Self-perceived oral health and quality of life measures of patients with rheumatic diseases with poor and good oral perceived oral health.

Variable	Patients with poor perceived oral health n= 101	Patients with good perceived oral health n= 100	p-value
Aware of dental impact, n (%)	34 (33.66)	40 (40.00)	0.352
Rheumatologist dental advice	28 (27.72)	34 (34.00)	0.335
Desire of dental referral, n (%)	85 (84.15)	72 (72.00)	**0.037**
Oral Health Quality of Life Domains			
Physical function, mean ± SD	14.00 ± 2.49	17.85 ± 2.07	**< .001**
Psychosocial function, mean ± SD	17.62 ± 2.63	21.91 ± 2.29	**< .001**
Pain discomfort, mean ± SD	9 ± 2.25	13.21 ± 1.53	**< .001**

SD, Standard Deviation

Table 3. Clinical and behavioral oral health assessment of patients with rheumatic diseases with poor and good perceived oral health.

Variable	Patients with poor perceived oral health n= 101	Patients with good perceived oral health n= 100	p-value
ICDAS			
Caries-free, n (%)	1131 (39.99)	1360 (48.57)	**< .001**
Initial caries, n (%)	492 (17.39)	504 (18.00)	0.554
Moderate caries, n (%)	407 (14.39)	382 (13.64)	0.418
Severe caries, n (%)	108 (3.81)	55 (1.96)	**< .001**
Missing tooth, n (%)	690 (24.39)	499 (17.82)	**< .001**
Salivary parameters and xerostomia			
Salivary pH, mean ± SD	6.50 ± 0.55	6.38 ± 0.58	0.319
Salivary flow rate (mL/min), mean ± SD	0.20 ± 0.28	0.40 ± 0.58	**0.019**
Xerostomia, n (%)	58 (57.42)	45 (45.00)	**0.05**
Temporomandibular joint			0.210
Pain/ Dysfunction	30 (29.70)	21 (21.00)	
Time since last dental visit			0.215
Within the past year, n (%)	49 (48.51)	44 (44.00)	
1-5 years ago, n (%)	27 (26.73)	35 (35.00)	
Over 5 years ago, n (%)	18 (17.82)	10 (10.00)	
Never, n (%)	7 (6.93)	11 (11.00)	
Dental visit frequency			0.599
Once a year, n (%)	11 (10.89)	12 (12.00)	
Twice or more per year, n (%)	16 (15.84)	11 (11.00)	
Never, n (%)	74 (73.26)	77 (77.00)	
Daily toothbrushing frequency			0.631
Once	17 (16.82)	15 (15.00)	
Twice	55 (54.45)	50 (50.00)	
Three or more	29 (28.71)	35 (35.00)	

SD, Standard Deviation; ICDAS, International Caries Detection and Assessment System

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

temporomandibular joint examination. All oral examinations were performed by a board-certified dentist trained in standardized assessment protocols. Behavioral data included dental visit frequency and toothbrushing habits. Statistical comparisons were performed using chi-square and Student's t-tests, with significance defined as $p < 0.05$.

Results: A total of 201 patients with rheumatic diseases were included, divided into poor perceived oral health (n=101) and good perceived oral health (n=100) groups. The mean age was 52.27 ± 14.17 and 53.97 ± 14.10 years, respectively, with a higher proportion of women in both groups (90.09% vs. 95.00%). Rheumatoid arthritis was the most prevalent diagnosis, additional demographic and clinical characteristics are displayed in **Table 1**. The poor perceived oral health group reported a greater desire for dental referral (84.15% vs. 72.00%; p=0.037, **Table 2**). The poor perceived oral health group showed lower scores in physical function (14.00 ± 2.49 vs. 17.85 ± 2.07; p< 0.001), psychosocial function (17.62 ± 2.63 vs. 21.91 ± 2.29; p< 0.001), and pain/discomfort (9.00 ± 2.25 vs. 13.21 ± 1.53; p< 0.001, **Table 3**).

Clinically, the poor perceived group had a lower percentage of caries-free teeth (39.99% vs. 48.57%; p< 0.001), and a higher prevalence of severe caries (3.81% vs. 1.96%; p< 0.001) and missing teeth (24.39% vs. 17.82%; p< 0.001), while initial and moderate caries stages showed no significant differences between groups. Salivary flow rate was higher in the good perceived group (0.40 ± 0.58 mL/min vs. 0.20 ± 0.28 mL/min; p=0.019).

Conclusion: Poor self-perceived oral health was associated with greater impairment in oral health–related quality of life, higher prevalence of severe caries and tooth loss, and increased demand for dental referral. These results highlight the importance of combining patient-reported oral health measures with clinical evaluations to enhance detection and management of oral health issues in rheumatic patients.

Disclosure: F. Garcia-Garcia: None; **M. Alarcon-Jarquin**: None; **V. Lopez-Flores**: None; **G. Castro-Cruz**: None; **C. Estrada-Anguiano**: None; **J. Garcia-Bravo**: None; **A. Gonzalez-Melendez**: None; **G. Figueroa-Parra**: None; **D. Galarza-Delgado**: None; **J. Riega-Torres**: None.

Abstract Number: 0367

Differences in Self-Reported Medication Nonadherence and its Drivers in Young Adults versus Older Adults with Systemic Lupus Erythematosus

Hannah Concannon[1], Kai Sun[2], Jennifer Rogers[3], Megan Clowse[4], Rachel Randell[2], Mithu Maheswaranathan[5], Lisa Criscione-Schreiber[5], Nathaniel Harris[6], Amanda Eudy[7] and Rebecca Sadun[2], [1]Duke University School of Medicine, Chapel Hill, NC, [2]Duke University, Durham, NC, [3]Duke, Durham, NC, [4]Duke University, Chapel Hill, NC, [5]Duke University School of Medicine, Durham, NC, [6]Duke University Medical Center, Durham, NC, [7]Duke University, Raleigh, NC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Medication adherence poses a challenge for patients with SLE, especially younger patients, who often experience both more active disease and more intensive treatments than their older counterparts. Risk factors associated with nonadherence in patients with SLE have been described; however, modifiable adherence barriers specific to young adults under 30 years old remain poorly understood. Thus, this study compared medication nonadherence and drivers of nonadherence by age group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

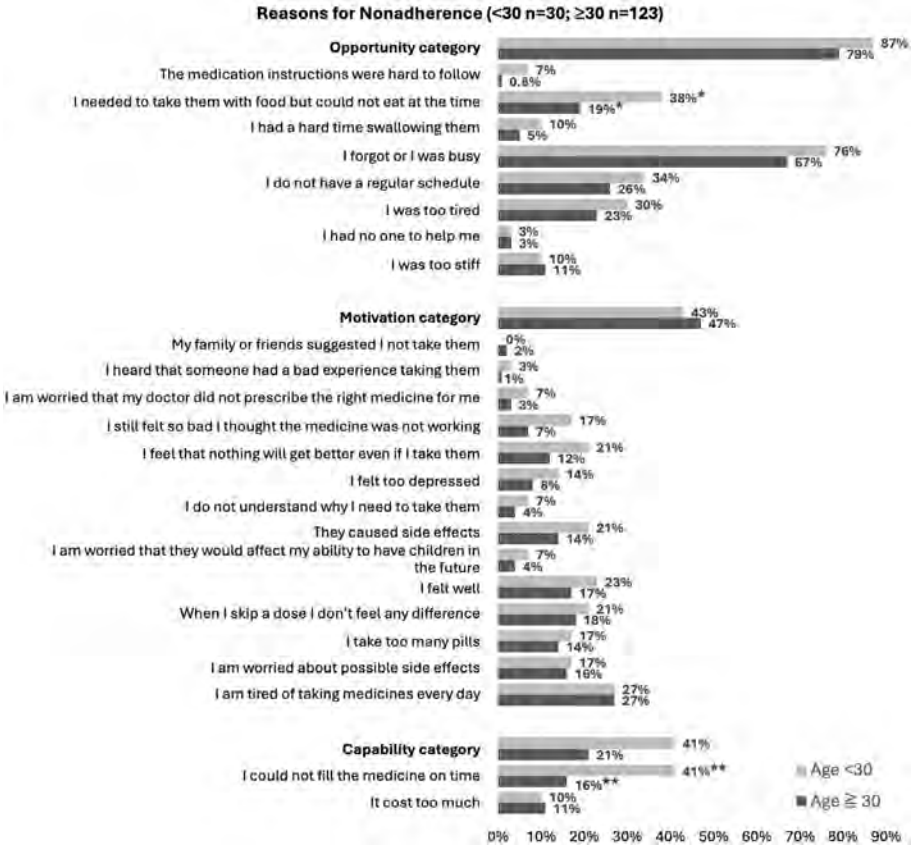


Figure 1. Reasons for nonadherence per DOSE-nonadherence-SLE self-reports for patients <30 vs. patients 30 years old and over. Reasons for nonadherence are organized by reason category (Capability, Opportunity, or Motivation) and listed in descending order by odds ratios within each category. *denotes p<0.05, **denotes p<0.005

Methods: Participants in this study were enrolled in an academic SLE Registry at a large academic medical center in the United States. From February 2020 to June 2024, we prospectively collected responses to the DOSE-Nonadherence-SLE questionnaire, a clinical tool validated to measure both the *extent of* and the *reasons for* medication nonadherence in SLE. The questionnaire organizes reasons for nonadherence into Capability, Opportunity, and Motivation categories. We defined nonadherence as binary: Patients were considered nonadherent if they reported missing or skipping at least one dose of lupus medication over the past seven days in the *extent of nonadherence* domain. We calculated proportions and odds ratios for *extent of nonadherence* by decade of life and for *reasons for nonadherence* across age groups < 30 and ≥30 years old. We also used logistic regression to determine relationships of nonadherence with age and other covariates.

Table 1. Cohort demographics and characteristics. Values presented as n (%) unless otherwise indicated.

	All ages	≥30	<30
n	336	281	55
Age, years, mean (SD)	44.4 (13.4)	48.1 (11.3)	25.4 (2.7)
Race (n=335)			
Black	188 (56%)	158 (56%)	30 (56%)
Other	29 (9%)	20 (7%)	9 (16%)
White	118 (35%)	102 (36%)	16 (29%)
Hispanic	17 (5%)	11 (4%)	6 (11%)
Female	312 (93%)	262 (93%)	50 (91%)
Married or living with partner (n=329)	158 (48%)	149 (54%)	10 (18%)
Medicare, Medicaid, or Uninsured (n=324)	149 (46%)	127 (47%)	22 (42%)
Annual household income <$50,000 (n=312)	172 (55%)	140 (54%)	32 (62%)
Number of lupus medications, mean (SD)	2.0 (1.1)	2.0 (1.1)	2.3 (1.1)
Nonadherent	153 (46%)	123 (44%)	30 (55%)
Number of reasons for nonadherence reported, mean (SD)	3.4 (3.5)	3.2 (2.9)	4.5 (5.2)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Results of logistic regression for extent of nonadherence. Significant odds ratios are bolded. *Multivariable analysis includes only those variables with p-value <0.05 in the univariate models.

	Univariate OR (95% CI)	Multivariable OR (95% CI)*
Age, years	**0.97 (0.95-0.99)**	**0.98 (0.96-0.99)**
Race		
Black	**2.05 (1.27-3.29)**	**1.94 (1.19-3.16)**
Other	1.53 (0.67-3.48)	0.78 (0.30-2.04)
White	1.0 (ref)	1.0 (ref)
Hispanic	**4.16 (1.33-13.02)**	**4.37 (1.22-15.64)**
Not married or living with partner	1.38 (0.89-2.14)	--
Medicare, Medicaid, or Uninsured	1.07 (0.69-1.66)	--
Annual household income <$50,000	1.50 (0.96-2.36)	--

Results: Of the 336 completed unique DOSE-Nonadherence-SLE questionnaires, 55 (16%) were from patients < 30 years old (Table 1). Medication nonadherence differed significantly across age groups 18-30, 30-40, 40-50, and 50+ ($p< 0.01$); for each increased year of age, self-reported nonadherence decreased by 2% ($p< 0.05$). Black race and Hispanic ethnicity were also predictive of nonadherence (Table 2). Across age groups, the most common reasons for nonadherence were "I forgot or I was busy" (69%), "I do not have a regular schedule (28%), and "I am tired of taking medicines every day" (27%). Patients < 30 were more likely to report nonadherence due to inability to fill a medication on time (41% vs. 16%, OR 3.72; 95% CI: 1.53, 9.02) and due to needing to take a medicine with food but not being able to eat (38% vs. 19%, OR 2.55; 95% CI: 1.06, 6.13) (Figure 1).

Conclusion: Younger patients reported greater extent of medication nonadherence, often due to logistical impediments. In addition to counseling on the importance of medication adherence, rheumatologists should, when possible, provide support to help young adults with SLE overcome challenges in obtaining and taking medicines. Approaches to understanding and intervening on medication nonadherence in SLE may need to be tailored by age.

Disclosure: H. Concannon: None; **K. Sun**: Aurinia, 2; **J. Rogers**: AstraZeneca, 1, 1, Aurinia, 2, 5, Exagen, 5, Immunovant, 2, 5; **M. Clowse**: None; **R. Randell**: biogen, 12, My husband is employed at Biogen and owns a small amount of stock <$10,000; **M. Maheswaranathan**: AstraZeneca, 2, UCB, 2; **L. Criscione-Schreiber**: UCB, 5; **N. Harris**: None; **A. Eudy**: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **R. Sadun**: The Expert Institute, 12.

Abstract Number: 0368

Factors Associated with Patient Acceptability of Rheumatology Care Delivered by Telemedicine

Hareem Farooq[1], Lesley Jackson[1], Rahima Begum[2], Gary Cutter[2], Kenneth Saag[3], Jinoos Yazdany[4] and Maria I. (\"Maio\") Danila[5], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, [3]The University of Alabama at Birmingham, Birmingham, AL, [4]UCSF, San Francisco, CA, [5]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and socioeconomic characteristics of study participants.

Characteristics	N=233
Age, Mean (SD), years	54.8 ± 13.7
Sex, N (%)	
Male	34 (14.59)
Female	199 (85.41)
Race, N (%)	
White	121 (51.93)
Other (Black, Asian, Hispanic, Native American)	112 (48.07)
Education, N (%)	
4 years degree or more	87 (38.50)
Some college or less	139 (61.50)
Health Literacy*, N (%)	
Adequate	197 (87.95)
Inadequate	27 (12.05)
Medication Adherence, N (%)**	
Always Adherent	164 (72.89)
Nonadherent	61 (27.11)
Telemedicine Visit Type, N (%)	
Video	103 (44.59)
Phone-only	128 (55.41)
Distance to Clinic, N (%)	
Less than 22 miles	109 (51.90)
Equal to or more than 22 miles	101 (48.10)

*Health literacy was assessed by asking, "How confident are you filling out medical forms by yourself?" 'Adequate' is defined by grouping the following answers: 'extremely' and 'quite a bit'. 'Inadequate' is defined by grouping 'somewhat', 'a little bit', and 'not at all'.
**Medication adherence was assessed by asking, "How frequently do you take your medications exactly as prescribed?" 'Always adherent' is defined by 'you always take your medication exactly as prescribed'. 'Nonadherent' is determined by grouping the answer choices 'there are some days you don't take your medication exactly as prescribed,' and 'you often don't take your medication exactly as prescribed'
Data from a total of 233 patients were analyzed. Education is missing 7 responses; health literacy is missing 9 responses; medication adherence is missing 8 responses; telemedicine visit type is missing 2 responses; distance to clinic is missing 23 responses.

Background/Purpose: Home-based telemedicine is an efficient healthcare delivery approach. A recent randomized clinical trial (RCT) found that in-person visits may be preferred among rheumatology patients. Thus, it is key to understand factors influencing patient acceptability of telemedicine. We aimed to identify socioeconomic and demographic factors associated with patient acceptability of rheumatology care via telemedicine.

Methods: We utilized data from an RCT (August 2021-January 2023) comparing telemedicine to in-person rheumatology care at two U.S. academic medical centers. The primary outcome was patient acceptability of telemedicine using a 17-item validated Telemedicine Perception Questionnaire (TMPQ). TMPQ measures usefulness, reliability, ease of use, interaction quality, and satisfaction with telemedicine. Responses were scored 1-5 and summed for each respondent; higher scores represented higher acceptability. We excluded data from patients answering < 50% of the questions. For other

Table 2. Univariable and multivariable linear regression analysis of factors associated with the acceptability of telemedicine using the TMPQ score. Bolded p<0.05 represents statistical significance.

Variable	Univariable Analysis	Multivariable Linear Regression			
	p value	β	95% Confidence Interval		p value
Age (per 1 year increase)	0.13	-0.09	-0.19	0.02	0.11
Sex (Female vs Male)	0.44	-1.28	-5.38	2.83	0.54
Race (White vs Other races*)	**0.03**	**3.00**	**0.12**	**5.89**	**0.04**
Education (≥4-year degree vs ≤Some college)	0.09	2.10	-0.85	5.05	0.16
Health Literacy (Adequate vs Inadequate)	**0.01**	4.19	-0.35	8.73	0.07
Medication Adherence (Adherent vs Nonadherent)	**0.03**	**4.11**	**1.01**	**7.21**	**0.01**
Telemedicine Visit Type (Phone-only vs Video)	0.52	0.99	-1.98	3.96	0.51

*Other races include Black, Asian, Hispanic, and Native Americans.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

missing data, we used the patient's mean score for answered questions, scaled to the full scale of items (sum of items answered multiplied by 17 divided by the number of questions answered). Our independent variables were age, sex, race, telemedicine visit type (audio-only vs video), geocoded distance from patient's home to clinic, education level (≥4 years degree vs ≤some college), health literacy (adequate vs inadequate) and medication adherence (always vs non-adherent) (**-Table 1** footnote for details). We used frequencies (proportions) to describe categorical variables and means (SD) for continuous variables. We created univariable and multivariable linear regression models to analyze the association between independent variables and telemedicine acceptability via TMPQ (continuous). Statistical significance was defined as $p < 0.05$.

Results: We analyzed data from 233 patients who had telemedicine visits with TMPQ scores available. Our study population included 85.4% female and 51.9% White patients. The mean (SD) age was 54.8 (13.7) years. The mean (SD) TMPQ score was 65.9 (10.7) (**Table 1**). In univariable analysis, White (vs other) race (p=0.03), adequate (vs inadequate) health literacy (p=0.01), and high medication adherence (vs non-adherence) (p=0.03) were significantly associated with higher TMPQ scores (**Table 2**). Multivariable linear regression (**Table 2**) confirmed that high medication adherence (β=4.11, 95% CI 1.01-7.21, p=0.01) and White race (β=3.00, 95% CI 0.12-5.89, p=0.04) were associated with higher TMPQ scores. Adequate health literacy was not statistically significant but had a consistent trend toward higher TMPQ scores.

Conclusion: We observed variation in telemedicine acceptability by patient characteristics and identified high medication adherence, White race, and adequate health literacy as positive predictors. Our findings provide insight into factors associated with telemedicine acceptability in rheumatology patients and can help clinicians predict who might be receptive to telemedicine and inform future research to better understand how lower telemedicine acceptability can be mitigated in certain populations, thus enhancing a patient-centered approach to care delivery.

Disclosure: H. Farooq: None; **L. Jackson**: None; **R. Begum**: None; **G. Cutter**: Consulting or Advisory BoardsAlexion, Antisense Therapeutics/Percheron, Avotres, Biogen, Clene Nanomedicine, Clinical Trial Solutions LLC, Endra Lif, 1, 2, Data and Safety Monitoring BoardsApplied Therapeutics, AI therapeutics, AMO Pharma, Argenx, Astra-Zeneca, Avexis Pharmaceuticals, Bristol Meyers Squ, 2, Pythagoras, Inc., 4, 8; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5.

Abstract Number: 0369

Real-World Persistence of Janus Kinase Inhibitors in Biologic-Experienced Patients with Rheumatoid Arthritis

Jeffrey Curtis[1], Emily Holladay[2], Nick McCormick[3], Yujie Su[4], Fenglong Xie[1] and Alexis Dineen[5], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Edmond, OK, [3]Auburn University, Auburn, AL, [4]University of Alabama at Birimingham, Birmingham, AL, [5]Self, Portola Valley, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Over the last decade, Janus kinase inhibitors (JAKs) for RA have been increasingly used as a treatment option for patients who do not respond to biologic DMARD (bDMARD) treatments. The introduction of orally administered drugs, like JAKs, was expected to address poor therapy persistence rates associated with self-administered,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of JAK initiators for Medicare and Marketscan claims-based persistence analysis

Characteristic	Medicare N = 11,170	Marketscan N = 9,458
Age at index date in years		
Mean (SD)	63.2 (12.2)	53.6 (10.8)
Female: N (%)	9,512 (85.2)	7,814 (82.6)
Number of prior biologic DMARDS		
Mean (SD)	2.1 (1.2)	2.0 (1.1)
Number of prior conventional DMARDS		
Mean (SD)	1.8 (1.0)	1.7 (1.0)

JAK: Janus kinase; SMD: Standard mean difference; SD: Standard deviation; IQR: Interquartile range; DMARD: Disease-modifying antirheumatic drug.

Table 2: Persistence with JAK inhibitors at 1 and 2 years

	Medicare		Marketscan	
	1 year	2 years	1 year	2 years
Overall, % (95% CI)	42.0 (41.1, 43.0)	27.2 (26.4, 28.1)	43.7 (42.6, 44.7)	26.9 (25.9, 28.0)
Baricitinib, % (95% CI)	27.4 (21.1, 35.6)	10.6 (5.8, 19.5)	41.9 (33.4, 52.6)	22.1 (14.8, 32.9)
Tofacitinib, % (95% CI)	42.2 (41.3, 43.2)	27.4 (26.6, 28.3)	43.1 (42.0, 44.2)	26.8 (25.7, 27.9)
Upadacitinib, % (95% CI)	41.1 (33.4, 50.5)	— (—, —)	50.8 (47.0, 54.9)	20.1 (13.8, 29.2)

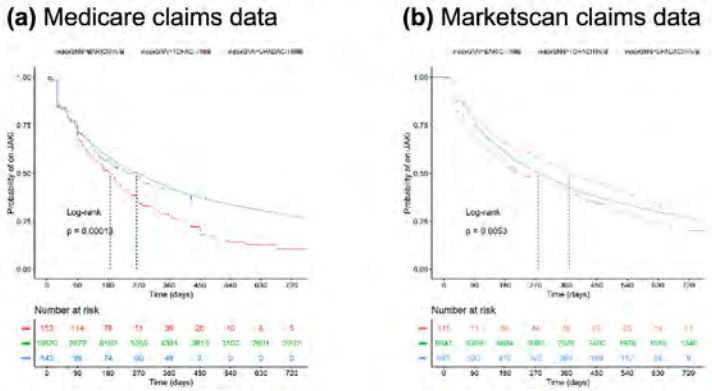
injectable bDMARDs. The purpose of this analysis is to evaluate the persistence of JAKs used to treat RA in the United States using real-world commercial (Marketscan) and government (Medicare) insurance claims data.

Methods: We conducted a retrospective analysis of patients initiating their first JAK for RA using 2006-2021 Marketscan data (commercial health plan claims data) and 2010-2020 Medicare fee for service (FFS) data to assess 2-year JAK persistence. The last index date in the claims data that was allowable was 12/31/2019 for Medicare and 12/31/2020 for

Marketscan, enabling the analysis to have the potential for at least 1 year of follow-up . Drug persistence was measured at 1 and 2 years using the following definition: continuous use of JAK without gap of >90 days (next prescription fill date is no later than previous prescription fill date + days of supply + 90) and did not switch to another JAK or bDMARD.

Results: In the Medicare cohort, there were 11,170 RA patients with an index date on or before 12/31/2019. Individuals had mean prior use of 2.1 ± 1.2 bDMARDs and 1.8 ± 1.0 cDMARDs. JAK persistence was 42.0% (95% CI: 41.1, 43.0) at 1 year and 27.2% (95% CI: 26.4, 28.1) at 2 years. Drug persistence differed across individual drugs with 1-year persistence of

Figure 1: Persistence with JAK inhibitors at 1 and 2 years for (a) Medicare data (b) Marketscan data



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

27.4% (95% CI: 21.1, 35.6), 42.2% (95% CI: 41.3, 43.2), and 41.1% (95% CI: 33.4, 50.5) for baricitinib, tofacitinib and upadacitinib, respectively. At 2 years, 10.6% (95% CI: 5.8, 19.5) and 27.4% (95% CI: 26.6, 28.3) continued baricitinib and tofacitinib, respectively. There were no patients taking upadacitinib at 2 years, which was not unexpected given the end of the Medicare data (12/31/2020) and the timing of FDA approval of upadacitinib (2019).

In the Marketscan cohort, there were 9,458 patients with an index date on or before 12/31/2020. Patients had mean prior use of 2.0 ± 1.1 bDMARDs and 1.7 ± 1.0 cDMARDs. Among these, 43.7% (95% CI: 42.6, 44.7) initiating a JAK were persistent at 1 year, and 26.9% (95% CI: 25.9, 28.0) were persistent at 2 years. At 1 year, 41.9% (95% CI: 33.4, 52.6), 43.1% (95% CI: 42.0, 44.2), and 50.8% (95% CI: 47.0, 54.9) of patients continued baricitinib, tofacitinib and upadacitinib, respectively. At 2 years, 22.1% (95% CI: 14.8, 32.9) of patients continued baricitinib, 26.8% (95% CI: 25.7, 27.9) continued tofacitinib, and 20.1% (95% CI: 13.8, 29.2) continued upadacitinib.

Conclusion: Persistence with initial JAK for RA in real-world settings was poor for all FDA-approved JAKs as measured in two independent data sources, and 2-year estimates were comparable between commercial and government health claims sources. Drug persistence differed across individual JAKs, with lower persistence rates for baricitinib compared to tofacitinib and upadacitinib. Compared to historical data, the introduction of oral JAKs does not appear to have improved therapy persistence, with < 30% treatment persistence at 2 years.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **E. Holladay**: None; **N. McCormick**: None; **Y. Su**: None; **F. Xie**: None; **A. Dineen**: SetPoint Medical, 3, 8.

Abstract Number: 0370

Patient Preferences for Treatments of Rheumatoid Arthritis: A Discrete Choice Experiment Evaluating Preference for Advanced Drug Therapies and Neuroimmune Modulation Device

Jeffrey Curtis[1], Joshua Baker[2], Shilpa Venkatachalam[3], Sherry Danese[4], Julie Ulloa[5] and Ankit Shah[6], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Pennsylvania, Philadelphia, PA, [3]Global Healthy Living Foundation, New York, NY, [4]OutcomesInsights, Calabasas, CA, [5]OutcomesInsights, Calabasas, [6]SetPoint Medical, Valencia, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite broadening treatment options for RA, several challenges and unmet needs remain. The 2021 ACR guideline for the treatment of RA marked a significant step in expanding the integration of patient voices in guideline development, incorporating patient perspectives to inform treatment decisions based on their preferences. This study aimed to characterize patient satisfaction with, and preferences for, current RA treatments as well as a novel vagus nerve-mediated neuroimmune modulation device, which recently demonstrated safety and effectiveness in treating biologic-experienced RA patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Participant Characteristics

	Total (n=354)	Biologic Naive (n=103)	Biologic Experienced I (n=151)	Biologic Experienced II (n=100)
% Female	74%	83%	72%	69%
Mean Age	47.8	48.0	47.6	48.0
Years with RA Symptoms (mean)	11	10	11	11
Disease Severity (RAPID3)				
Near Remission	7%	9%	7%	5%
Low Severity	7%	9%	7%	5%
Moderate Severity	27%	23%	27%	29%
High Severity	60%	59%	59%	61%
Current Treatment (% of patients)				
cDMARDs	53%	88%	43%	35%
TNF Inhibitors	52%	-	46%	61%
JAK Inhibitors	18%	-	15%	22%
IL Inhibitors	4%	-	5%	4%
T-cell Inhibitors	3%	-	2%	4%
TSQM Score				
Dissatisfied (35 or less)	6%	8%	7%	5%
Somewhat Satisfied (36 to 79)	62%	68%	61%	56%
Satisfied (80 to 100)	32%	24%	32%	39%

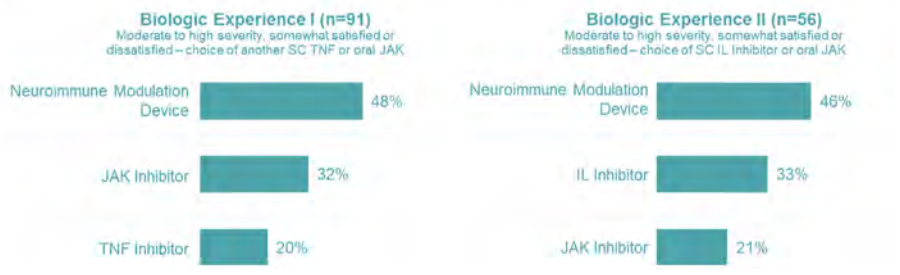
Methods: A web-based patient survey was conducted in combination with a discrete choice experiment (DCE) to capture the experiences, perspectives, and preferences of patients living with RA in the US. Patient satisfaction with current RA pharmacologic therapies was determined using the Treatment Satisfaction Questionnaire for Medication (TSQM), a validated instrument to measure patient satisfaction. DCEs are widely utilized tool in economics research that can elicit an individual's distinct valuation of several options and account for trade-offs between them based on their personal experiences. The DCE in this study included 12 choice sets which contained a device profile and drug profile featuring 8 clinically relevant attributes for RA patients.

Results: 354 completed surveys were included in the analysis. Participants were stratified into three subgroups, Biologic Naïve (n=103); Biologic Experienced I, those on their first biologic (n=151); and Biologic Experienced II, those who had a history of multiple biologics (n=100). Disease severity, as measured by RAPID3, indicated 27% had 'Moderate Disease Activity' (RAPID3 > 6, ≤12) and 60% with 'High Disease Activity' (RAPID3 > 12). Based on the TSQM, only 32% were satisfied with their RA treatment; dissatisfaction increased with exposure to a greater number of biologics or JAKs (**Table 1**).

The initial impression of implantable device-based treatment option was regarded as "Positive" or "Extremely Positive" by 45%. Patient preferences were modeled for biologic-experienced patients with moderate to high disease severity who were dissatisfied or only somewhat satisfied with their current RA treatment. Neuroimmune modulation therapy was preferred over trying another drug treatment options for both Biologic Experienced I and II groups (**Figure 1**). Key drivers of treatment preference included out-of-pocket treatment cost, proportion of improvement in symptoms, level of physical function and fatigue, and effectiveness in protection from irreversible joint damage **(Table 2)**.

Conclusion: These results indicate that RA patients are accepting of a novel neuroimmune modulation approach using a surgically implanted device. Preference for neuroimmune modulation device over another biologic or JAK was particularly

Figure 1: Patient preferences based on prior biologic or JAK exposure



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Choice-Based Conjoint Utilities and Importance Summary

Attributes and Levels	Average Utility[a]	Standard Deviation	Average Importance	Standard Deviation
Drug Cost to Patient[b]				
$0 every month	98.5	53.3	15.8	6.6
$25 every month ($300 per year)	24.0	38.8		
$50 every month ($600 per year)	11.9	30.9		
$200 every month ($2,400 per year)	-43.7[c]	40.9		
$500 every month ($6,000 per year)	-90.6	60.0		
Device Cost to Patient				
$600 one-time cost for surgery followed by $0 per month	79.3	51.4	15.0	6.0
$2,000 one-time cost for surgery followed by $0 per month	53.8	29.2		
$5,000 one-time cost for surgery followed by $0 per month	-34.8	41.9		
$5,000 one-time cost for surgery followed by $50 per month ($600 per year	-98.2	50.8		
Percent of patients that would have improved in RA symptoms, physical function or fatigue after 3 months with device				
60%	36.9	50.7	10.8	5.7
50%	31.9	61.3		
40%	-8.3	39.3		
30%	-12.4	34.8		
20%	-48.1	60.1		
Drug Dosage				
Subcutaneous injection you give yourself every 2 weeks	37.1	25.6	7.8	2.4
Subcutaneous injection you give yourself once per week	26.0	37.4		
Oral tablet once per day	-2.9	22.7		
A series of two 3-4-hour infusions administered by a healthcare provider every 6 months	-26.9	28.3		
60-minute infusion that is administered to you by a healthcare provider every 4 weeks	-33.3	27.1		
Percent of patients that would have improvement in RA symptoms, physical function, or fatigue after 3 months with drug				
50%	36.4	26.6	6.7	3.3
40%	8.6	23.7		
30%	-11.2	21.1		
20%	-33.8	34.0		

Attributes and Levels	Average Utility[a]	Standard Deviation	Average Importance	Standard Deviation
The percent of patients protected from irreversible joint damage after 12 months				
95%	29.7	27.1	6.2	2.6
85%	-4.6	31.3		
70%	-11.7	29.8		
60%	-13.3	29.6		
Drug Non-serious side effects				
Infusion side effects	16.3	22.6	5.3	2.0
Oral side effects	15.8	23.3		
Sub-Q side effects	-32.2	20.0		
Drug Risk of shingles				
None	15.7	29.1	4.3	2.0
15 in 1000 patients	-5.1	17.6		
45 in 1000 patients	-10.6	22.8		
Drug Risk of serious infection				
None	16.1	22.4	4.1	2.2
2 in 100 patients	5.3	17.0		
6 in 100 patients	-21.4	21.0		
Drug Risk of blood clot				
None	11.8	22.2	3.5	1.8
2 in 1000 patients	-3.5	19.0		
7 in 1000 patients	-8.3	19.7		
Drug Risk of GI perforation				
None	5.6	19.8	2.8	1.9
3 in 1000 patients	-0.7	15.6		
1 in 1000 patients	-4.9	18.8		
Device Risk of serious infection				
None	3.6	15.2	1.8	1.6
2 in 100 patients	-3.6	15.2		

[a]The relative importance of each treatment attribute is characterized by considering how much difference each attribute could make in the total utility of a treatment. That difference is the range in the attribute's utility values. Percentages are calculated from relative ranges, obtaining a set of attribute importance values that total 100%.

[b]While we understand the FDA does not consider cost of therapies, this data is included to provide complete data that were collected.

[c]A negative number indicates it is highly undesired

high for those who had previous exposure to, and dissatisfaction with, currently available advanced RA therapies. These results underscore the importance of discussing patients' personal preferences, their experiences with prior therapies and the attributes of treatment that are most important to them in making future treatment selections.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **J. Baker**: Amgen, 5; **S. Venkatachalam**: None; **S. Danese**: None; **J. Ulloa**: None; **A. Shah**: SetPoint Medical, 3, 8, 11.

Abstract Number: 0371

Lifestyle Coaching in Psoriatic Arthritis: Pilot Findings from an Online eCoaching Program

Judy Zhang[1], Leonard Calabrese[2], Shilpa Venkatachalam[3], angela Degrassi[4], Yuxuan Jin[2] and M. Elaine Husni[5], [1]Cleveland Clinic, Cleveland, United States, Cleveland, OH, [2]Cleveland Clinic, Cleveland, OH, [3]Global Healthy Living Foundation, New York, NY, [4]Global Healthy Living Foundation, Upper Nyack, NY, [5]Department of Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

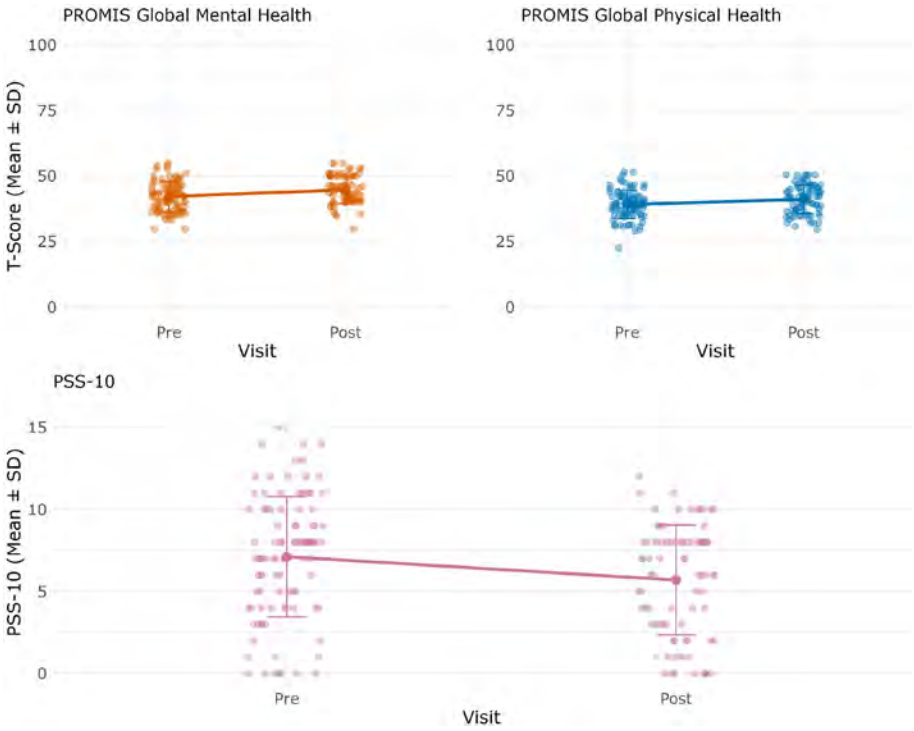
Background/Purpose: As healthcare shifts towards patient-centered care, multifactorial lifestyle interventions, though effective, often impose time and resource burdens on patients. An online program like IMMUNE STRENGTH can streamline delivery of mindfulness, sleep, nutrition and exercise support, reduce patient burden and enhancing self-management in psoriatic arthritis (PsA).

Methods: A prospective, single-arm pilot study evaluated the feasibility and preliminary efficacy of IMMUNE STRENGTH, a 10-week online, coach-led program targeting lifestyle interventions in adults (≥18 years) with PsA per ACR criteria. To enhance external validity, participants were recruited from an academic rheumatology clinic and a national patient advocacy group. Key exclusions included concomitant systemic autoimmune diseases and inability to engage in remote coaching.

The program featured weekly modules focused on four core lifestyle pillars (mindfulness, sleep hygiene, nutrition, and exercise) delivered via a platform with videos, self-guided exercises, and tracking tools such as sleep logs and dietary journals. Certified health coaches led weekly communication and provided individualized support with emails or phone calls, delivering targeted education, answering questions, and gathering feedback in real time.

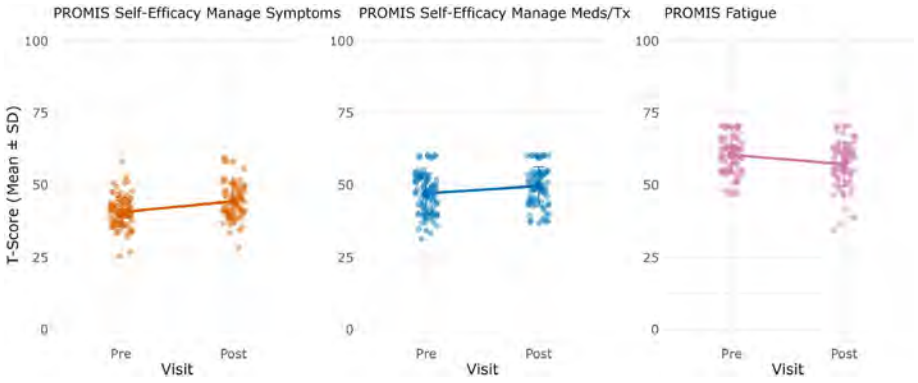
Engagement was measured via module completion and coaching session attendance. Patient-reported outcomes were measured using validated PROMIS scales including pain, fatigue, and global health at baseline and post-intervention (Week 10). Feasibility was evaluated based on enrollment and retention rates. Continuous and categorical variables were described using means ± standard deviations and counts (%), respectively. Changes from baseline to Week 10 were analyzed using paired t-tests. All analyses were performed in R (v4.3.1), with a two-sided $\alpha = 0.05$.

Results: Of the 143 enrolled, 86 (60.1%) completed the program and were included in the Week 10 analysis. PROMIS Global Mental Health T-scores rose from 42.2 to 44.7 (SD = 5.20, $p < 0.001$) and Global Physical Health T-scores from 39.1 to 41.1 (SD = 4.44, $p = 0.001$), approaching the 3-point minimal clinically important difference (MCID) commonly cited for PROMIS measures. Perceived stress, as measured by the 10-item Perceived Stress Scale (PSS-10), declined from 7.12 to 5.70 (SD = 3.04, $p < 0.001$). Self-efficacy also improved: symptom-management T-scores increased by 3.45 points (SD =



Change in PROMIS Global Mental and Physical Health and PSS 10 scores from baseline to post intervention

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Change in PROMIS Self Efficacy and Fatigue from baseline to post intervention.

4.89, $p < 0.001$) and medication-management scores by 3.00 points (SD = 6.55, $p < 0.001$). Participants also experienced reductions in symptom burden, with fatigue scores falling from 60.4 to 57.2 (SD = 6.38, $p < 0.001$) and pain-interference scores from 61.8 to 58.5 (SD = 5.89, $p < 0.001$). Finally, 90.6% of completers reported being "satisfied" or "very satisfied," and 87.5% would recommend IMMUNE STRENGTH to others.

Conclusion: The IMMUNE STRENGTH pilot showed significant improvements in mental and physical health, self-efficacy and symptom burden, supporting the potential of an online, coach-led lifestyle intervention as an adjunctive approach for managing PsA. Further research is needed to confirm these preliminary outcomes and evaluate long-term benefits.

Disclosure: J. Zhang: None; **L. Calabrese**: AbbVie, 2, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, Fate Therapeutics, 2, Galvani, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, 6, Mymee, 2, Open Evidence, 2, PPD, 2, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6; **S. Venkatachalam**: None; **a. Degrassi**: None; **Y. Jin**: None; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2.

Abstract Number: 0372

Development and Implementation of a Remote Educational Program to Optimize Safe Medication Use in Older Veterans with Rheumatic Diseases

Maria Romero Noboa[1], Hannah Howell[2], Angelo Gaffo[3] and Maria I. (\"Maio\") Danila[4], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, [3]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [4]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Symptomatic treatment in rheumatic and musculoskeletal diseases (RMDs) – including glucocorticoids (GCs) and non-steroidal anti-inflammatory drugs (NSAIDs) – can result in improved quality of life but also increase the rates of polypharmacy. GCs and NSAIDs combination is associated with a higher risk of serious adverse events such as acute kidney injury, cardiovascular disease, dyspepsia, and gastrointestinal (GI) bleeding. This is an important safety concern for Veterans with RMDs. The aim of this project is to create and evaluate a patient-directed informational program,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

entitled ScaLable Medication Deprescribing (SLIM-D). This program combines written education and case management to optimize safe medication use in older Veterans with RMDs and use GCs and NSAIDs in combination.

Methods: The SLIM-D program was developed in partnership with rheumatology clinic staff in preparation for its implementation at the Birmingham VA Medical Center. Existing educational materials from the VA-funded "Eliminating Medications through Patient OWnership of End Results" (EMPOWER) program were reviewed and used as template for the SLIM-D Veteran-facing informational booklet (Figure 1). We also created additional materials including program invitations for Veterans (Figure 2), scripts for Veteran calls, and provider electronic messages. Veteran-facing materials were assessed for readability level using Flesch-Kincaid Reading Ease (FKRE >60 representing being easily understood by 13 to 15 year olds) and Flesch Kincaid Grade Level (FKGL), with FKGL = 8-9 being an acceptable readability goal. Veterans seen at Birmingham VA Rheumatology clinic were invited to review the materials and complete the validated Patient Education Materials Assessment Tool (PEMAT-P) to determine the understandability and actionability scores of the written materials (highest score =100%, goal ≥ 80%).

Results: The FKGL readability of the invitation brochure was 8th grade with FKRE of 60.2 and the FKGL readability for the informational booklet was 9th grade with FKRE of 50.9. The invitation brochure and informational booklet were presented to 22 Veterans, 77% were men and 50% were ≥ 60 years of age. The invitation brochure had a mean (SD) understandability score 81.8% (19.8) and 82.4% (22.2) actionability score. The informational booklet had a mean (SD) 96.6% (5.8) understandability score and 98.5% (5.0) actionability score (Table 1).

Conclusion: The materials created for the SLIM-D program had a high understandability and actionability score. The SLIM-D program will offer a structured approach to reducing the combined use of GCs and NSAIDs in older Veterans with RMD. Providing information materials to the Veteran will encourage a discussion of safe medication use with their clinician

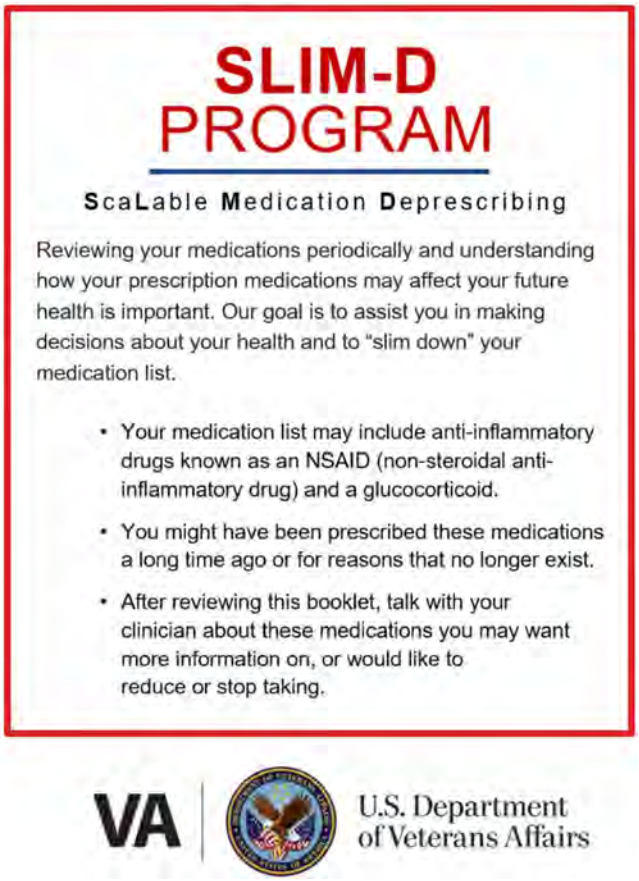


Figure 1: SLIM-D Program Informational Booklet Cover Page

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: SLIM-D Program Informational Brochure

and might promote a decrease in polypharmacy among this population. We will implement the SLIM-D program at Birmingham VA Medical Center to determine rates of Veteran participation, and evaluate its feasibility, acceptability, and appropriateness from the Veterans perspective.

Table 1: Assessment of Understandability, Actionability Scores and Readability for SLIM-D Educational Materials In Veterans with Rheumatic and Musculoskeletal Diseases.

Variable	Invitation Brochure Review	Informational Booklet Review
	N = 11	N = 11
Sex		
Male	9	8
Female	2	3
Age Range, years	50 - 79	30 - 89
PEMAT-P Understandability Score, Mean (SD)	81.8% (19.8)	96.6% (5.8)
PEMAT-P Actionability Score, Mean (SD)	82.4% (22.2)	98.5% (5.0)
Flesch-Kincaid Reading Ease	60.2	50.9
Flesch-Kincaid Grade Level	7.9	9.0

PEMAT-P (Patient Education Materials Assessment Tool for Printed Materials)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Romero Noboa: None; **H. Howell**: None; **A. Gaffo**: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5.

Abstract Number: 0373

Implementation of a Lupus Self-Management mHealth App: Using Incentives to Drive Engagement

Melissa French[1], Katherine Carpenter[2], Eric Johnson[2], Melicent Miller[2] and Mary Crimmings[2], [1]Lupus Foundation of America, Alexandria, VA, [2]Lupus Foundation of America, Washington, DC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: As part of a five-year cooperative agreement with the Centers for Disease Control and Prevention, the Lupus Foundation of America (LFA) has implemented the digital lupus self-management (SM) education program, "Strategies to Embrace Living with Lupus Fearlessly (SELF)." Launched online in January 2022, and as a mobile app in September 2023, SELF offers user-tailored SM education, tracking tools, and support. As engagement is a primary challenge for mobile health (mHealth) apps generally[1], this effort used social media promotion as a way to explore incentives to improve app engagement.

Methods: In January 2025, we launched a social media promotion to incentivize engagement by offering a gift box of lupus self-care items to new and existing SELF users who used the app at least four times during the month. Users were asked to complete any of the following actions on any four days: an SM skill-building activity, an entry in the symptom tracker, or an entry in the medication tracker. We compared this to a previous social media promotion period in September 2024 when new users were incentivized to sign-up for SELF with a similar gift.

Across the two promotion periods, September 2024 (P1) and January 2025 (P2) we examined new user sign-ups, retention beyond the initial day in new users, and engagement for four or more days in new and existing users. Categorical comparisons of new user sign-ups, retention beyond the initial day, and engagement for four plus days were assessed using Chi Square test. User feedback was evaluated qualitatively.

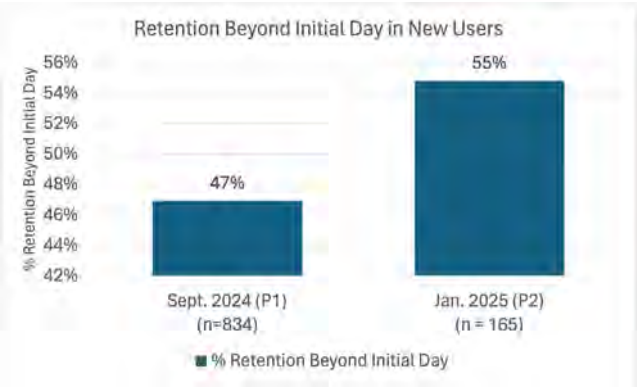
Results: Likely due to wider promotional efforts, total SELF users was higher in P1 (n = 1946) than P2 (n = 455). The proportion of new user sign-ups decreased from P1 (91%; n = 1777) to P2 (61%; n = 301), while the proportion of existing users increased over the same period (p = 0.00) (Fig 1.). In new users, retention beyond the initial day increased from 47% in P1 to 55% in P2 (p = 0.00) (Fig. 2.). In all users, engagement for four or more days increased from P1 (4%) to P2 (16%) (p = 0.00) (Fig. 3).

During both promotion periods, the most popular areas of focus for SM skill-building activities were managing symptoms and managing stress. Satisfaction with the app was high.

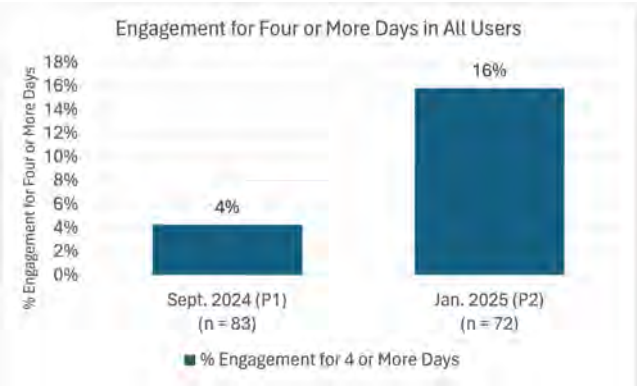
Conclusion: New users in P1 were higher because of the focus on sign-ups, but the P2 effort was more effective at increasing retention and engagement. Including all users the promotion and focusing on the behavior we aimed to improve, brought more existing users back to SELF in P2. By linking the incentive to retention and engagement rather than sign-ups, we prompted users to do more in the app, use the program as intended, and depart satisfied.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The proportion of new user sign-ups decreased from P1 (91%; n = 1777) to P2 (66%; n = 301), while the proportion of existing users increased from P1 (9%; n = 169) to P2 (34%; n = 154) (p = 0.00).



In new users, retention beyond the initial day increased from 47% in P1 (n = 834) to 55% in P2 (n = 165) (p = 0.00).



In all users, engagement for four or more days increased from 4% in P1 (n = 83) to16% in P2 (n = 72) (p = 0.00).

[1]Amagai, S. et al. (2022). Challenges in Participant Engagement and Retention Using Mobile Health Apps: Literature Review. Journal of medical Internet research, 24(4), e35120. https://doi.org/10.2196/35120

Disclosure: M. French: None; **K. Carpenter**: None; **E. Johnson**: None; **M. Miller**: None; **M. Crimmings**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0374

Assessing Attitudes and Barriers to Vaccination in Pediatric Rheumatic

Merav Heshin Bekenstein[1], Rebecca Hetrick[2], Vidya Sivaraman[3], Beth Rutstein[4], Albert Chow[5], Peter Chiraseveenuprapund[6], Vincent Del Gaizo[7], Melanie Kohlheim[8], guy Brock[9], Sapuni Chandrasena[9], Chloé Janse van Rensburg[10], Marina Gad El Sayed[11] and the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Vaccination Workgroup, [1]Tel Aviv Medical Center Israel, Binyamina, Tel Aviv, Israel, [2]Indiana University School of Medicine, Indianapolis, IN, [3]Nationwide Children's Hospital/ The Ohio State University, Columbus, OH, [4]The Children's Hospital of Philadelphia, Wynnewood, PA, [5]Loma Linda University, Loma Linda, CA, [6]University of Utah, Salt Lake City, UT, [7]Childhood Arthritis & Rheumatology Research Alliance (CARRA), Whitehouse Station, NJ, [8]CARRA, Granville, OH, [9]The Ohio State University Wexner Medical Center, Columbus, OH, [10]Max Rady College of Medicine, University of Manitoba, Winnipeg, MB, Canada, [11]University of California, Riverside School of Medicine, Riverside, CA

Table 1: Independent variables stratified by caregiver-reported vaccination status

	All Respondents N = 163[1]	Unimmunized, Partially Immunized, or Unsure N = 59[1]	Fully Immunized N = 104[1]	p-value[2]
Age	11.5 (5.2)	9.8 (4.9)	12.5 (5.1)	0.002
Age Category				0.014
<5	18 (11.0%)	11 (18.6%)	7 (6.7%)	
5-10	49 (30.1%)	21 (35.6%)	28 (26.9%)	
>10	96 (58.9%)	27 (45.8%)	69 (66.3%)	
Location				0.6
United States	134 (82.2%)	51 (86.4%)	83 (79.8%)	
Canada	12 (7.4%)	3 (5.1%)	9 (8.7%)	
Other	10 (6.1%)	2 (3.4%)	8 (7.7%)	
Europe	7 (4.3%)	3 (5.1%)	4 (3.8%)	
Diagnosis				0.034
sJIA or AOSD	70 (42.9%)	34 (57.6%)	36 (34.6%)	
JIA (non-systemic forms)	38 (23.3%)	9 (15.3%)	29 (27.9%)	
CRMO/CNO	29 (17.8%)	6 (10.2%)	23 (22.1%)	
Vasculitis	11 (6.7%)	3 (5.1%)	8 (7.7%)	
JDM	9 (5.5%)	5 (8.5%)	4 (3.8%)	
Morphea or Linear Scleroderma	4 (2.5%)	2 (3.4%)	2 (1.9%)	
SLE	1 (0.6%)	0 (0.0%)	1 (1.0%)	
Other	1 (0.6%)	0 (0.0%)	1 (1.0%)	
General vaccine hesitancy (PACV-SF score)				<0.001
Not hesitant (score <2)	86 (52.8%)	15 (25.4%)	71 (68.3%)	
Hesitant (score ≥ 2)	77 (47.2%)	44 (74.6%)	33 (31.7%)	
Vaccine hesitancy related to rheumatic disease				0.02
Absent	56 (34.4%)	13 (22.0%)	43 (41.3%)	
Present	107 (65.6%)	46 (78.0%)	61 (58.7%)	
Caregiver reports PCP is well-informed on vaccination in rheumatic disease				0.12
No or Partially	96 (58.9%)	40 (67.8%)	56 (53.8%)	
Yes	67 (41.1%)	19 (32.2%)	48 (46.2%)	
Financial barriers to vaccination				0.6
No	160 (98.2%)	59 (100.0%)	101 (97.1%)	
Yes	3 (1.8%)	0 (0.0%)	3 (2.9%)	

[1]Mean (SD); n (%)

[2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Abbreviations: sJIA (Systemic Juvenile Idiopathic Arthritis); AOSD (Adult-onset Still's Disease); JIA (Juvenile Idiopathic Arthritis); CRMO (Chronic Recurrent Multifocal Osteomyelitis); CNO (Chronic Non-bacterial Osteomyelitis); JDM (Juvenile Dermatomyositis); SLE (Systemic Lupus Erythematosus); PACV-SF (Parent Attitudes about Childhood Vaccines – Short Form)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

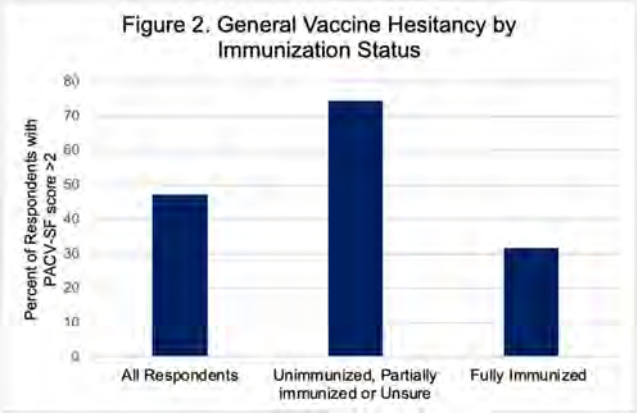
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Vaccine-preventable diseases pose greater risk to children with rheumatic diseases treated with immunosuppressive therapies and to those with underlying immune dysregulation. Despite the importance of vaccine protection, children with rheumatic disease often have lower vaccination rates compared to healthy populations. The drivers of decreased vaccine uptake in pediatric rheumatic disease (PRD) are poorly understood. This study examines the caregiver attitudes and barriers surrounding immunization in PRD patients.

Methods: This study included a voluntary online survey of caregivers of PRD patients recruited through online parent support groups for PRD patients from June – July 2024. General vaccine hesitancy was assessed via a modified Parental Attitudes about Childhood Vaccines – Short Form (PACV-SF), a 4-question scale designed to screen for vaccine hesitant caregivers.[1] Additional questions on barriers to vaccination were developed by the CARRA Vaccination Work Group. The

Figure 1. Modifications to the Parental Attitudes about Childhood Vaccines – Short Form (PACV-SF)[5] for Pediatric Rheumatic Disease Patients

Original Question	Modified Question	Scoring
1. Have you ever delayed having your child get a shot for reasons other than illness or allergy?	1. Have you ever delayed having your child get a vaccine for reasons other than illness or allergy?	"No" or "Not sure" = 0 "Yes" = 1
2. How concerned are you that a shot might not prevent the disease?	2. How concerned are you that a vaccine might not prevent the disease?	"Not at all concerned" or "Not too concerned" = 0 "Somewhat concerned" or "Very concerned" or "Not sure" = 1
3. Overall, how hesitant about childhood shots would you consider yourself to be?	3. Overall, how hesitant about childhood vaccines would you consider yourself to be?	"Not at all hesitant" or "Not too hesitant" = 0 "Somewhat hesitant" or "Very hesitant" or "Not sure" = 1
4. I trust the information I receive about shots.	4. I trust the information I receive about vaccines from healthcare providers.	"Strongly agree" or "Agree" = 0 "Disagree" or "Strongly disagree" or "Not sure" = 1



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

primary outcome was caregiver report of immunization status. Associations with explanatory variables were assessed using chi-squared tests and Fisher's exact test for categorical variables and Wilcoxon rank-sum tests for continuous variables. Univariable and multivariable logistic regression analyses were used to examine the association between vaccination status and explanatory variables. Multivariable Model 1 includes all explanatory variables while multivariable Model 2 includes only those found to be significant in the univariable analysis.

Results: Of the 163 respondents, 104 (64%) reported that their child had received all recommended immunizations and 59 (36%) reported partial immunization, no immunization, or uncertain immunization status (Table 1). General vaccine hesitancy, as indicated by a score $\geq$2 on the PACV-SF (Figure 1), was strongly associated with a lower odds of immunization uptake (OR 0.16, 95% CI 0.08-0.32, $p < 0.001$) in all models (Figure 2). Age was associated with increased odds of immunization uptake in the univariable model and multivariable Model 1. Vaccine hesitancy related to rheumatic disease was associated with decreased odds of immunization uptake in the univariable model but this association became non-significant in the multivariable models.

Conclusion: General vaccine hesitancy in caregivers strongly predicted decreased odds of fully immunized status in children. While not surprising, this was the only factor undiminished in all multivariable models, suggesting a strong independent relationship. In contrast, vaccine hesitancy related to the child's rheumatic disease diagnosis was not significant in the multivariable models. The study's limitations include unknown generalizability due to convenience sampling and relatively small sample size. Nevertheless, this study suggests that general vaccine hesitancy may play a stronger role in caregiver immunization decisions than other types of barriers.

Disclosure: M. Heshin Bekenstein: None; **R. Hetrick**: None; **V. Sivaraman**: None; **B. Rutstein**: None; **A. Chow**: None; **P. Chiraseveenuprapund**: None; **V. Del Gaizo**: None; **M. Kohlheim**: None; **g. Brock**: None; **S. Chandrasena**: None; **C. van Rensburg**: None; **M. Gad El Sayed**: None.

Abstract Number: 0375

Association of Glucocorticoid Toxicity Index Scores with Quality-of-life and Healthcare Resource Utilization at 6 Months in a Real-world Cohort of Individuals Receiving Glucocorticoids

Naomi Patel[1], Jiaqi Wang[1], Isha Jha[2], Grace McMahon[1], Tania Chiha[3], Hyon K. Choi[4] and John Stone[5], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Mount Auburn Hospital, Boston, [4]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [5]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Glucocorticoids (GCs) are used long-term by approximately 1% of the adult population and contribute to excess morbidity and mortality. We prospectively assessed Glucocorticoid Toxicity Index (GTI) scores at 6 months in a real-world cohort of individuals using GCs in rheumatology clinic given the limited published real-world data involving GTI scores.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, Disease, and Treatment Characteristics of Participants in LONG-TOX at Enrollment (Baseline) and 6 Months

Characteristic at time of enrollment	Baseline (N=90)	6 months (N=74)
Age, years, mean (SD)	60.0 (16.6)	n/a
Female, n (%)	56 (62.2)	n/a
Race, n (%)		n/a
White	81 (90.0)	n/a
Black	6 (6.7)	n/a
Asian	2 (2.2)	n/a
More than one race	1 (1.1)	n/a
Hispanic ethnicity, n (%)	3 (3.3)	n/a
Rheumatic disease diagnosis or category, n (%)		n/a
PMR/GCA	37 (41.1)	n/a
AAV	9 (10.0)	n/a
Other vasculitis	7 (7.8)	n/a
Myositis	6 (6.7)	n/a
IgG4-RD	5 (5.6)	n/a
Sarcoidosis	6 (6.7)	n/a
Multiple	2 (2.2)	n/a
Other	17 (18.9)	n/a
Disease activity, n (%)		
Remission	17 (18.9)	38 (51.4)
Mild	29 (32.2)	21 (28.4)
Moderate	32 (35.6)	11 (14.9)
Severe	12 (13.3)	4 (5.4)
GC-free, n (%)	n/a	28 (37.8)
Current glucocorticoid dose among those still on, prednisone-equivalent mg, mean (SD)	33.4 (19.1)	10.7 (10.1)
Concomitant immunomodulatory therapy, n (%)*		
Conventional synthetic DMARD	18 (20.0)	18 (24.3)
Biologic DMARD	46 (51.1)	43 (58.1)
Targeted synthetic DMARD	1 (1.1)	2 (2.7)
IVIG	5 (5.6)	5 (6.8)
None	32 (35.6)	19 (25.7)
Cumulative GC exposure (baseline to 6 months), prednisone-equivalent mg, median (IQR)	n/a	2114.0 (1185.0, 3080.0)

PMR, polymyalgia rheumatica; GCA, giant cell arteritis, IgG4-RD, IgG4-related disease; GC, glucocorticoid; DMARD, disease-modifying antirheumatic drug; IVIG, intravenous immune globulin

Methods: We developed a prospective cohort of adult patients with rheumatic diseases in a large academic hospital and prospectively assessed GC toxicity as measured by the GTI, patient-reported quality-of-life (including the 36-Item Short Form Survey [SF-36] scale and component scores, and EQ5D-visual analogue scale [VAS]), and physician clinic visits. Data on healthcare utilization are obtained by manual medical record review. We evaluated overall GTI (Cumulative Worsening Score [CWS], a measure of any toxicity, and Aggregate Improvement Scores [AIS], which assess both worsening [increasing scores] and improvement [decreasing scores]) and individual domains at 6 months. We evaluated the relationship of

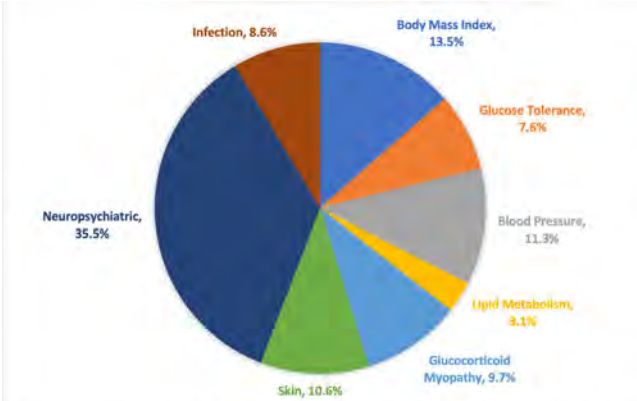


Figure 1. Contribution of Glucocorticoid Toxicity Index (GTI) Domain Scores to Overall GTI Scores at 6 months

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Association of 6-month Glucocorticoid Toxicity Index Cumulative Worsening Scores with Quality-of-Life, Cumulative Glucocorticoid Exposure, and Healthcare Resource Utilization

Variable at or over 6 months	GTI CWS, unadjusted correlation coefficient (95% CI)	GTI CWS, adjusted correlation coefficient (95% CI)*
Cumulative 6-month GC exposure	**0.28 (0.06, 0.48)**	0.20 (-0.09, 0.46)
SF-36#		
Physical Functioning	-0.17 (-0.42, 0.10)	-0.14 (-0.41, 0.16)
Role limitations due to physical health	-0.18 (-0.43, 0.09)	-0.16 (-0.43, 0.13)
Role limitations due to emotional problems	-0.20 (-0.44, 0.08)	-0.11 (-0.38, 0.19)
Energy/Fatigue	-0.18 (-0.42, 0.09)	-0.14 (-0.41, 0.16)
Emotional well-being (n = 56)	-0.05 (-0.31, 0.21)	0.01 (-0.28, 0.29)
Social functioning (n = 56)	-0.24 (-0.47, 0.03)	-0.20 (-0.46, 0.09)
Pain	-0.20 (-0.44, 0.07)	-0.18 (-0.44, 0.12)
General health	-0.20 (-0.44, 0.07)	-0.16 (-0.43, 0.13)
Physical Component Summary	-0.22 (-0.47, 0.07)	-0.19 (-0.45, 0.10)
Mental Component Summary	-0.11 (-0.37, 0.18)	-0.07 (-0.35, 0.22)
EQ-5D Visual Analogue Scale#	-0.20 (-0.43, 0.07)	-0.17 (-0.43, 0.13)
Clinic visits	0.09 (-0.14, 0.31)	0.03 (-0.26, 0.32)

SF-36, 36-Item Short-Form Survey; GTI CWS, Glucocorticoid Toxicity Index Cumulative Worsening Score
*Adjusted model adjusted for age, sex, categorical disease activity
#SF-36 scale and component scores range from 0-100, with mean (SD) of 50 (10) in the general population, and higher scores representing better health-related quality-of-life. EQ-5D VAS ranges from 0-100, with higher scores representing better health-related quality-of-life.

6-month GTI scores to cumulative GC exposure, quality-of-life measures, and clinic visits using unadjusted and multivariable (adjusted for age, sex, and disease activity) Pearson correlation coefficients (rho).

Results: We evaluated the first 90 patients enrolled (mean age 60 years, 62% female, 90% White, 41% with PMR and/or GCA) and the first 74 who completed 6-month follow-up (**Table 1**). The majority of patients (81%) had active disease at enrollment. The mean (SD) current GC dose was 33.4 (19.1) prednisone-equivalent mg, and most were also receiving a DMARD (65, 72%). Over the 6-month follow-up period, the median (IQR) cumulative GC exposure was 2114 (1185, 3080) prednisone-equivalent mg, or approximately 11.6 mg/day. The median (IQR) overall 6-month GTI CWS was 44 (20, 93) and GTI AIS was 3 (-42, 54). The most common GTI domain in which individuals experienced worsening was the Neuropsychiatric domain, followed by the Body Mass Index, Blood Pressure, and Skin domains (**Figure**).

The unadjusted correlation coefficient between GTI CWS scores and 6-month GC exposure was 0.28 (95% CI: 0.06-0.48); this was diminished in the adjusted analysis (**Table 2**). Higher GTI CWS was associated with numerically lower (i.e., worse) SF-36 scale and component scores. There was a weak positive association between the GTI CWS and the number of clinic visits though this was not statically significant.

Conclusion: In this real-world prospective cohort of individuals with autoimmune diseases receiving GCs, most people experienced various GC toxicities over 6 months with a predominant proportion with neuropsychiatric toxicities. Improvement in some GC toxicities was also observed, as evidenced by the markedly lower 6-month AIS value compared to the 6-month CWS value. Higher GTI CWS scores were numerically associated with worse quality-of-life. Presence of any GC toxicities correlated more strongly with outcomes than net overall change in toxicity. As shown in other studies, the relationship between cumulative GC exposure and GC toxicity is imperfect, emphasizing the importance of measuring GC toxicity directly.

Disclosure: N. Patel: Amgen, 5; **J. Wang**: None; **I. Jha**: None; **G. McMahon**: None; **T. Chiha**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0376

An Internet-delivered, Arthritis-tailored Cognitive Behavioral Therapy for Insomnia Program for People with Co-morbid Sleep Disturbance: Comparing Baseline Characteristics of Cannabis Users and Non-users

Nicole Andersen[1], Diane Lacaille[2], Josee Savard[3], Elham Rahme[1], Paul Fortin[4] and Deborah Da Costa[5], [1]McGill University, Montreal, QC, Canada, [2]Arthritis Research Canada, University of British Columbia, Vancouver, BC, Canada, [3]Université Laval, Quebec, Canada, [4]Centre ARThrite - CHU de Quebec - University Laval, Quebec, QC, Canada, [5]McGill University, Pointe-Claire, QC, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1. Characteristics of the Sample

Means (SD) or N (%)	Users (n=13)	Non-Users (n=41)	Sig.
Age			
Mean (SD)	55 (11)	43 (15)	.713
Female	13 (100%)	40 (98%)	
Disease duration			
Mean (SD)	10 (10)	10 (14)	.852
Comorbidities			
Mean (SD)	2 (2)	2 (2)	.902
Education			
High School or less	7 (54%)	17 (45%)	
Post secondary	5 (38%)	12 (32%)	.456
Graduate/Professional	1 (8%)	9 (24%)	
Work Status			
Full-time	4 (31%)	10 (26%)	
Part-time	4 (31%)	3 (8%)	
Student	0 (0%)	2 (5%)	.461
On disability leave due to illness/injury	3 (23%)	9 (24%)	
Retired	2 (15%)	12 (31%)	
Arthritis Type			
RA	10 (77%)	31 (76%)	
PsA	3 (23%)	3 (10%)	
AS	0 (0%)	1 (2%)	.490
SLE	0 (0%)	2 (5%)	
Polymyalgia Rheumatica	0 (0%)	1 (2%)	
Undisclosed	0 (0%)	3 (7%)	
Self-rated health			
Excellent	0 (0%)	1 (3%)	
Very good	3 (23%)	5 (13%)	
Good	5 (39%)	15 (40%)	.306
Fair	1 (8%)	12 (32%)	
Poor	4 (31%)	5 (13%)	
Pain Intensity (0-10 VAS)	5.3 (2.5)	4.1 (2.7)	.332
PROMIS-29 T-Scores			
Anxiety	**61.4 (4.9)**	**57.3 (9.2)**	**.046**
Depression	**58.5 (6.7)**	**52.4 (8.5)**	**.023**
Fatigue	61.8 (6.2)	61.5 (8.9	.911
Pain Interference	61.2 (8.3)	60.6 (9.1)	.830
Social participation	46.1 (7.3)	46.2 (8.1)	.964
Physical function	33.4 (5.2)	32.5 (6.2)	.611
Sleep disturbance	52.3 (3.8)	51.1 (3.2)	.156

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. PROMIS-29 Outcomes Associated with Cannabis Use

	B	Sig.	Exp(B)
Anxiety	.014	.874	1.014
Depression	.150	.072	1.162
Fatigue	-.023	.744	0.977
Pain	-.071	.441	0.931
Participation	-.065	.375	0.937
Physical function	.115	.358	1.122
Sleep disturbance	.063	.604	1.065

Background/Purpose: The use of cannabis among individuals with rheumatologic conditions has gained increasing attention due to potential effects on pain, mood, and overall quality of life. However, data on its frequency of use, motivations, and patient-reported outcomes remain limited. We compared cannabis users and non-users by sociodemographic and arthritis characteristics and HRQL, and explored motivations for use, and assessed differences in HRQL among people with rheumatic diseases.

Methods: Data are from the baseline visit of a pilot study of people with inflammatory rheumatic diseases who volunteered for an internet-based intervention to improve sleep. Participants self-reported cannabis use, reasons for consumption, and completed the PROMIS-29 questionnaire (physical function, anxiety, depression, fatigue, sleep disturbance, pain interference, and social participation). Characteristics were compared between cannabis users and non-users using t-test and chi-square. Associations between cannabis use, demographics, and clinical characteristics were examined using multivariable regression.

Results: Our sample had a mean (SD) age of 54 (14) and 98% were female. Most had RA or PSA, with a mean disease duration of 10 (11) years; many also had OA (30%; Table 1). One third reported using cannabis use in the past year, and 24% in the past 3 months (of which 38% used weekly and 31% daily/almost daily). All participations indicated they were using for medicinal reasons only (100%), with primary motivations being to improve pain (19%), sleep (17%), fatigue (< 5%) or anxiety (< 5%). Nearly half (46%) reported a little improvement in arthritis symptoms with use, with 15% reporting a lot of improvement, 31% no change, and 8% were unsure. Compared to Non-Users, Users reported significantly higher anxiety (p=.046) and depression (p=.014). However, logistic regression results suggested cannabis use was not associated with differences in PROMIS-29 outcomes.

Conclusion: One in three participants in an online intervention to improve sleep reported using cannabis in the past year to improve their arthritis symptoms, with nearly a quarter using cannabis regularly to improve pain, sleep, fatigue and anxiety. User did not report different PROMIS-29 outcomes, although 61% reported a little to a lot of symptom improvement. Understanding the motivations and health impact of cannabis use can help guide patient counseling and future research on alternative management strategies for pain and mood disorders.

Disclosure: N. Andersen: None; **D. Lacaille**: None; **J. Savard**: None; **E. Rahme**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1; **D. Da Costa**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0377

New efforts to incorporate patient-reported outcomes into clinical trials for lupus therapeutics

Patti Katz[1], Anca Askanase[2], Nandan Baruah[3], Wen-Hung Chen[4], Nicole Cooper[5], Anna Fisch[3], Lili Garrard[6], Meenakshi Jolly[7], Veronica Vargas Lupo[8], Carla Menezes[9], Judith Mills[3], Hoang Nguyen[10], Teodora Staeva[5], Josephine Park[11], Zahi Touma[12] and The Lupus Voices Council of Lupus Accelerating Breakthroughs Consortium, [1]UCSF, San Rafael, CA, [2]Columbia University Medical Center, New York, NY, [3]Lupus Voices Council, Lupus Accelerating Breakthroughs Consortium, New York, [4]GlaxoSmithKline, Philadelphia, PA, [5]Lupus Research Alliance, New York, [6]FDA, CDER, SIlver Spring, MD, [7]Rush University, Chicago, [8]Lupus Voices Council, Lupus Research Alliance, New York, NY, [9]Lupus Therapeutics, New York, NY, [10]Lupus Research Alliance, New York, NY, [11]EMDSerono, Boston, MA, [12]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1. Summary of small group discussions

What to measure and why? • Pain, fatigue, and cognitive function/brain fog were the most frequently recommended primary domains. • The next most frequent mentions were skin issues (e.g., photosensitivity, hair loss, rashes), physical functioning, mental health (depression, anxiety, and anger), treatment side effects, and quality of life. • Social functioning (e.g., work, family, "showing up") was woven through a number of responses.
What should the questionnaire burden be for trial participants? What mode of administration? Other considerations? • Most common response: 15 minutes. Acceptable questionnaire time depended on whether respondents could take breaks while completing questionnaires, whether questionnaires could be completed at home vs. at a study visit, whether questionnaires could be completed over multiple days. • Improve presentation of questionnaires (e.g., font size, screen contrast) • Electronic administration strongly preferred • Make adaptations as necessary to facilitate clinical trial participation and completion of materials by trial participants
Should PRO results and/or trial results be returned to participants? If so, when? • General agreement that trial results should be provided to participants without them having to seek them out. • Acknowledgement of the issues around participant privacy (e.g., pharma does not have participant information), but it was felt that trial sites could manage this communication • Information about trial results should be provided at appropriate health literacy levels and in accordance with plain language guidelines (e.g., length, multiple formats) • Need for real-time evaluation of some PROs, such as measures of depression • Make it clear to participants if providers do not see information from PRO measures in real time
How should PROs for a trial be selected; specifically, what are the roles of pharma, researchers, scientific evidence, and patients? • Ultimately, industry will select PROs, ideally with input from researchers and patients; be responsive to regulators and to payors to facilitate reimbursement for product • PRO selection will depend on the drug's mechanism of action.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Steps needed to advance incorporation of PROs into endpoints for regulatory decision-making
• Advocate the value and importance of PROs to pertinent stakeholders
• Promote greater sharing of PRO data from clinical trials; encourage that PRO data be made public and accessible to researchers and/or published
• Involve people living with lupus in selection of PRO domains and measures.
• Come to a consensus on core domains and appropriate measures for those domains and develop an evidence package for these domains/measures

Background/Purpose: Lupus Accelerating Breakthroughs Consortium (Lupus ABC) was formed by the Lupus Research Alliance as a public private partnership of people living with lupus, investigators, pharmaceutical companies, and the FDA to accelerate lupus drug development in a precompetitive, collaborative setting and ensure that the perspectives of people with lived experience of lupus are incorporated into the drug development process. We report on the first meeting to convene broad representation of lupus community voices to focus on better integration of patient-reported outcomes (PROs) in lupus clinical trials.

Methods: A public meeting with representatives from all Lupus ABC stakeholders was held October 16-17, 2024. The current use of PROs in lupus clinical trials was presented and breakout groups discussed 4 primary topics: 1) the important concepts of interest or PRO domains to measure; 2) questionnaire burden, modes of administration, and sharing results; 3) selection of reliable and valid PRO measures for trials; and 4) steps needed to advance the goal of wider PRO incorporation into trials. Results from breakout groups were presented and discussed; these are summarized below.

Results: Pain, fatigue, and cognitive function/brain fog were the most frequently recommended primary domains by participants with lupus and were corroborated with other stakeholders (Table 1). Ideas on questionnaire burden varied, and persons with lupus suggested potential adaptations of how PRO measures are currently administered depending on frequency, mode of administration and context, including a preference for electronic administration. There was strong consensus to return information on PROs and trial results to participants and involve all stakeholders early in the trial design process to identify the appropriate PRO domains and measures. While PROs are collected in most lupus clinical trials, participants felt that they may be underutilized as primary or secondary/exploratory endpoints. A desire to change the focus in trials from disease activity and signs to include PROs to highlight patients' voices was noted. The need for balance between the mechanisms of action of a product, what is important to patients, and what aspect(s) of disease that could be changed from treatment was also discussed as a critical issue. The potential lack of concordance between standard clinical measures and PROs was felt to be a challenge to the acceptance of PROs as potential endpoints. The group noted specific steps that are needed to incorporate PROs into endpoints for regulatory decision-making: encourage PRO data to be made public and accessible to researchers; come to consensus on domain(s) and best measure(s) of those domains; and involve people living with lupus in selection of PRO domains and measures and trial design (Table 2).

Conclusion: The group, with broad lupus community representation, identified a number of steps needed to incorporate PRO measures into endpoints for regulatory decision-making. For these actions, collaborations among industry, researchers, regulators, payors, and people living with lupus are needed.

Disclosure: P. Katz: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **N. Baruah**: None; **W. Chen**: AstraZeneca, 3, GlaxoSmithKlein(GSK), 3; **N. Cooper**: None; **A. Fisch**: None; **L. Garrard**: None; **M. Jolly**: LRA, 1, Rush University, 9, 10; **V. Vargas Lupo**: None; **C. Menezes**: None; **J. Mills**: None; **H. Nguyen**: None; **T. Staeva**: None; **J. Park**: EMD Serono, 3, GlaxoSmithKlein(GSK), 3, Novartis, 3; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0378

Identifying Patterns of Telemedicine Readiness and Digital Health Literacy in Rheumatoid Arthritis Patients: A Latent Class Analysis

Preeti Dhanasekaran[1], Bryant Lim[2], Qai Ven Yap[2], Hafizah Ahmad[3], Siew Hwa Chong[3], Ginny Goh[3], Manjari Lahiri[4], Amelia Santosa[4], Gim Gee Teng[3], Peter Cheung[4], Siriwan Lim[1] and Margaret Ma[4], [1]National University of Singapore, Singapore, Singapore, [2]National University of Singapore, Singapore, [3]National University Hospital, Singapore, [4]National University Hospital, Singapore, Singapore

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The COVID-19 pandemic accelerated telemedicine adoption, yet readiness and digital literacy vary widely across patient populations. Understanding these differences is crucial to designing equitable and effective telehealth systems for chronic disease management.

Methods: Latent class analysis (LCA) was performed on 138 RA patients enrolled at National University Hospital, Singapore using 18 items from a Telemedicine Readiness Survey [1] and the eHealth Literacy Scale [2]. Age, sex, race, education, employment, and marital status were not part of the clustering but were compared. Cluster solutions were evaluated based on model fit indices and interpretability.

Results: We identified four distinct clusters ranging from those who were digitally disengaged and resistant to telehealth to those who were confident and ready adopters of remote care (Figure 1).

Cluster 1 (C1) (n=26, 16.3%) was digitally disengaged. Patients in this cluster demonstrated the lowest levels of telemedicine engagement and digital confidence. 95.8% reported lacking confidence in accessing or using online health information. Half of the participants found telemedicine too complicated.

Cluster 2 (C2) (n=38, 23.8%) had moderate digital literacy and occasional telemedicine use, and remained ambivalent due to concerns about communication quality during teleconsultations. Approximately 65.8% expressed difficulty or dissatisfaction with communicating effectively during virtual consultations.

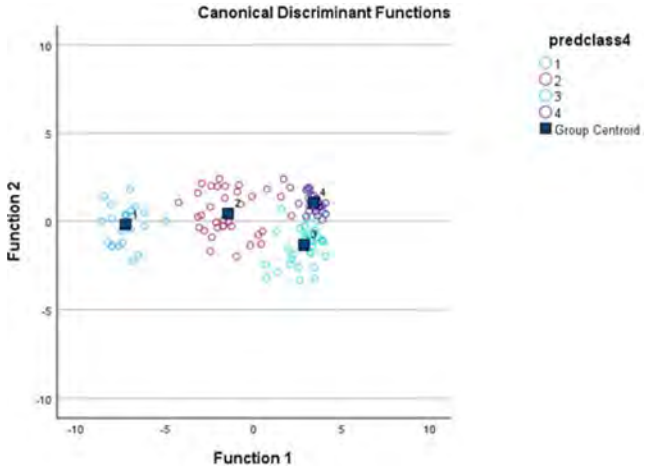


Figure 1. Canonical discriminant analysis of the 4 clusters and their group centroids. The plot shows the clear discrimination of the 4 clusters based on the discrimination functions 1 and 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Cluster distribution and baseline characteristics among the different subgroups. Data are presented as n (%) or mean (SD).

Variable	Cluster 1 *Seniors with Limited Digital Engagement* (n = 26)	Cluster 2 *Moderate Digital Adopters* (n = 38)	Cluster 3 *Digital Novices with Potential* (n = 38)	Cluster 4 *Confident Digital Adopters* (n = 36)	p-value
Age, mean ± SD	68.0 ± 10.4	58.9 ±15.2	58.0 ± 12.7	51.5 ± 15.7	<0.001
Race					0.025
Chinese	18 (69.2)	20 (54.1)	21 (55.3)	15 (42.9)	
Malay	4 (15.4)	7 (18.9)	3 (7.9)	12 (34.2)	
Indian	4 (15.4)	9 (24.3)	11 (28.9)	3 (8.6)	
Others	0 (0.0)	1 (2.7)	3 (7.9)	5 (14.3)	
Female	19 (73.1)	31 (81.6)	32 (84.2)	31 (86.1)	0.586
Ever-married	22 (84.6)	31 (81.6)	31 (81.6)	31 (83.3)	0.940
Education					<0.001
None/ Primary	13 (50.0)	11 (30.6)	3 (7.9)	0 (0.0)	
Secondary	10 (38.5)	10 (27.8)	8 (21.1)	9 (25.7)	
Tertiary	3 (11.5)	13 (36.1)	22 (57.9)	25 (74.1)	
Others	0 (0.0)	2 (5.6)	5 (13.2)	1 (2.9)	
English-speaking	18 (69.2)	31 (81.6)	34 (89.5)	34 (94.4)	0.038
Employment					0.171
Part-time	3 (12.5)	2 (5.9)	2 (5.9)	3 (8.6)	
Full-time	7 (29.2)	13 (38.2)	17 (50.0)	20 (57.1)	
Retired	12 (50.0)	9 (26.5)	9 (26.5)	8 (22.9)	
Homemaker/ Others	2 (8.3)	10 (29.4)	6 (17.6)	4 (11.4)	
Previous telemedicine experience	8 (11.3)	19 (26.8)	27 (38.0)	17 (23.9)	0.009

*Between-cluster differences were assessed using the one-way ANOVA for continuous variables and the chi-square test for categorical variables.

Cluster 3 (C3) (n=38, 23.8%) was open to remote care but demonstrated low digital self-efficacy. 38.0% reported active use of telemedicine but 97.3% lacked confidence in navigating online health information effectively. This cluster reflected a mismatch between willingness to engage with telemedicine and the digital skills required to do so.

Cluster 4 (C4) (n=36, 22.5%) demonstrated high telemedicine literacy, minimal difficulty using digital tools, and strong preference for remote care when appropriate. Notably, 94.4% agreed that time and cost savings positively influenced their decision to use telemedicine, and 97.2% preferred remote consultations over delays in care. This cluster exemplified a confident, proactive user group capable of navigating digital healthcare environments.

Demographic comparisons revealed differences between clusters. C1, the oldest group (mean age: 68.0±10.4 years), had the highest proportion of participants with only primary or no formal education (50.0%). In contrast, C4, the youngest group (mean age: 51.5±15.7 years) had the highest proportion of participants with tertiary education (74.1%). Additionally, English proficiency differed across clusters, ranging from 69.2% in C1 to 94.4% in C4 (p=0.038).

Conclusion: Four distinct patient clusters were identified, reflecting a spectrum of telemedicine readiness. Cluster membership was primarily shaped by patients' digital confidence and eHealth literacy. Our findings support targeted efforts to boost digital literacy and confidence, especially among older adults and those with less formal education.

[1] Gurupur V et al. Health Informatics Journal. 2016;23(3):181-196
[2] Norman CD, Skinner HA. J Med Internet Res. 2006 Nov 14;8(4):e27

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Responses to selected items from the Telemedicine Readiness Survey and eHealth Literacy Scale across patient clusters. Data are presented as n (%) or mean (SD).

Variable	Cluster 1 *Seniors with Limited Digital Engagement* (n = 26)	Cluster 2 *Moderate Digital Adopters* (n = 38)	Cluster 3 *Digital Novices with Potential* (n = 38)	Cluster 4 *Confident Digital Adopters* (n = 36)	p-value
The time and money saved from travelling and taking leave from work to attend face to face visit with my doctor/nurse would influence my decision to use telemedicine.					<0.001
Disagree	11 (42.3)	7 (18.4)	7 (18.4)	0 (0.0)	
Neutral	9 (34.6)	9 (23.7)	7 (18.4)	2 (5.6)	
Agree	6 (23.1)	22 (57.9)	24 (63.2)	34 (94.4)	
I am concerned about being able to understand what the doctor says through telemedicine video					0.041
Disagree	3 (11.5)	11 (28.9)	11 (28.9)	14 (38.9)	
Neutral	7 (26.9)	2 (5.3)	10 (26.3)	8 (22.2)	
Agree	16 (61.5)	25 (65.8)	17 (44.7)	14 (38.9)	
If I needed an earlier appointment, I would agree to see a doctor or nurse by telemedicine rather than wait longer to see them in person.					<0.001
Disagree	15 (57.7)	8 (21.1)	6 (15.8)	1 (2.8)	
Neutral	5 (19.2)	9 (23.7)	7 (18.4)	0 (0.0)	
Agree	6 (23.1)	21 (55.3)	25 (65.8)	35 (97.2)	
The idea of telemedicine sounds too complicated.					<0.001
Disagree	7 (26.9)	19 (50.0)	18 (47.4)	31 (86.1)	
Neutral	6 (23.1)	9 (23.7)	10 (26.3)	0 (0.0)	
Agree	13 (50.0)	10 (26.3)	10 (26.3)	5 (13.9)	
How useful do you feel the Internet is in helping you in making decisions about your health?					<0.001
Disagree	7 (29.2)	4 (10.8)	0 (0.0)	0 (0.0)	
Neutral	3 (12.5)	20 (54.1)	30 (81.1)	36 (100.0)	
Agree	14 (58.3)	13 (35.1)	7 (18.9)	0 (0.0)	
I know how to find helpful health resources on the Internet					<0.001
Disagree	23 (95.8)	5 (13.5)	2 (5.4)	0 (0.0)	
Neutral	0 (0.0)	11 (29.7)	35 (94.6)	35 (100.0)	
Agree	1 (4.2)	21 (56.8)	0 (0.0)	0 (0.0)	
I know how to use the health information I find on the Internet to help me					<0.001
Disagree	23 (95.8)	5 (13.9)	0 (0.0)	0 (0.0)	
Neutral	0 (0.0)	8 (22.2)	36 (97.3)	36 (100.0)	
Agree	1 (4.2)	23 (63.9)	1 (2.7)	0 (0.0)	
I feel confident in using information from the Internet to make health decisions					<0.001
Disagree	24 (100.0)	10 (28.6)	7 (19.4)	6 (17.1)	
Neutral	0 (0.0)	3 (8.6)	22 (61.1)	28 (80.0)	

*Between-cluster differences were assessed using chi-square test for categorical variables.

Disclosure: P. Dhanasekaran: None; **B. Lim**: None; **Q. Yap**: None; **H. Ahmad**: None; **S. Chong**: None; **G. Goh**: None; **M. Lahiri**: AbbVie/Abbott, 12, conference support, Eisai, 6; **A. Santosa**: None; **G. Teng**: None; **P. Cheung**: None; **S. Lim**: None; **M. Ma**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0379

Do Rheumatoid Arthritis Patients have Residual Fatigue Without Swollen Joints and Laboratory Inflammation? A Multicenter Study

Rosa Maria Morlà Novell[1], Enrique González-Dávila[2], Beatriz Frade Sosa[3], Maria López-Lasanta[4], Noemí Busquets Pérez[5], Marta Valls Roc[6], Meritxell Sallés Lizarzáburu[7], Georgina Salvador Alarcón[8], Virginia Ruiz-Esquide[9], Lola Tobalina Mastre[10], José Gomez-Puerta[11] and Raimon Sanmartí[9], [1]Hospital Clínic de Barcelona, Barcelona, Spain, [2]Departamento de Matemáticas. Universidad de La Laguna, Tenerife, Spain, [3]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [4]Hospital Universitari Vall d´Hebron, Barcelona, Spain, [5]Hospital de Granollers, Granollers, Spain, [6]Hospital Universitari Dr Trueta, Girona, Sudan, [7]Xarxa Sanitària Althaia Manresa, Manresa, Spain, [8]Hospital Universitari Mùtua Terrassa, Terrassa, Spain, [9]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [10]IDIBAPS. Hospital Clinic de Barcelona, Barcelona, [11]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Residual fatigue highlights an unmet prevalent[1] need in rheumatoid arthritis (RA) patients despite achieving remission of disease activity according to activity indices (DAS28).

We examine associated factors that may explain residual fatigue in RA patients according to two types of predefined clinical remission and compare them.

Methods: Patients with RA (EULAR/ACR, 2010), excluding chronic fatigue syndrome, were collected for 6 months from different Rheumatology Services throughout Catalonia (ARCat study group), fulfilling 3 questionnaires:

Table. Associated factors to residual fatigue in patients with remission by SJC/CRP compared with patients in remission by DAS28, only significant data (p<0.05).

	SJC/CRP REM				DAS28 REM			
VARIABLES	VAS Fatigue < 5 (N = 74)	VAS Fatigue ≥ 5 (N = 28)	*p*-value	OR ($IC_{95\%}$)	VAS Fatigue < 5 (N = 74)	VAS Fatigue ≥ 5 (N = 18)	*p*-value	OR ($IC_{95\%}$)
SOCIODEMOGRAPHICS								
Women, n (%)	53 (71,6)	27 (96,4)	**0,006**	10,69(1,36; 83,84)	53 (71,6)	17 (94,4)	0,062	6,74 (0,84; 53,87)
Active smoker, n (%)	7 (9,7)	8 (29,6)	**0,025**	3,91 (1,25; 12,17)	9(12,2)	5(27,8)	0,139	2,78 (0,80;9,65)
CONCOMITANT NON-RHEUMATIC DISEASE								
Depression, n (%)	4 (5,6)	6 (22,2)	**0,023**	**4,85 (1,21; 18,85**	5(6,8)	3 (16,7)	0,186	2,76 (0,9;12,83)
TREATMENT, n (%)								
bDMARD, n (%)	38 (52,8)	18 (66,7)	0,259	1,79 (0,71; 4,51)	36(48,6)	14(77,8)	**0,035**	**3,69 (1,11;12,28)**
Antidepressant, n (%)	8 (11,1)	8 (29,6)	**0,035**	**3,37 (1,11; 10,17)**	7(9,6)	2(11,8)	0,676	1,26 (0,24;6,67)
DISEASE ACTIVITY								
TJC28, median (IQR)	0 (0; 0)	0 (0; 1,5)	**0,021**	**1,56 (1,08; 2,26)**	6 (8,1)	5 (27,8)	**0,036**	**4,36 (1,16; 16,43)**
SJC28, median (IQR)	-	-			4 (5,4)	4 (22,2)	**0,044**	**5,00 (1,12; 22,41)**
DAS28ESR, median (IQR)	2,07 ± 0,75	2,69 ± 0,83	**<0,001**	**2,83 (1,50; 5,32)**	10 (6; 17)	6,5 (4; 9)	**0,028**	**0,92 (0,84; 0,99)**
DAS28CRP, median (IQR)	1,82 ± 0,42	2,38 ± 0,61	**<0,001**	**8,06 (3,06; 21,19)**	1,79 ± 0,42	2,17 ± 0,56	**0,002**	**4,62 (1,60; 13,36)**
CDAI, median (IQR)	2 (1; 5)	6,5 (4; 10)	**<0,001**	**1,32 (1,15; 1,52)**	2 (0,5; 4)	4,5 (3; 7)	**0,011**	**1,20 (1,03; 1,41)**
SDAI, median (IQR)	2,4 (1,1; 5,4)	6,8 (4,4; 10,3)	**<0,001**	**1,32 (1,15; 1,53)**	2,4 (0,9;4,1)	5 (3,1; 7,4)	**0,016**	**1,19 (1,02; 1,40)**
QUESTIONNAIRES								
Pain (0-10), median (IQR)	1 (0,4; 2,6)	4,5 (3; 7,4)	**<0,001**	**1,85 (1,44; 2,39)**	1 (0; 3)	4,5 (2,5; 7)	**<0,001**	**1,74 (1,33; 2,27)**
PGA (0-10), median (IQR)	1 (0,5; 3)	5,3 (3,5; 7,8)	**<0,001**	**1,87 (1,46; 2,41)**	1,5 (0,5; 3)	5,3 (4; 7)	**<0,001**	**1,75 (1,35; 2,29)**
sRADAI(0-48),median (IQR)	3 (1; 7)	14 (6; 23)	**<0,001**	**1,22 (1,11; 1,33)**	2,5 (1; 7)	11,5 (5; 26)	**<0,001**	**1,13 (1,06; 1,22)**
RO560, median (IQR)	5 (3; 8)	13 (7,3; 21)	**<0,001**	**1,16 (1,08; 1,248)**	5 (3; 9)	13 (8; 21)	**<0,001**	**1,16 (1,07; 1,26)**
RAPID3, median (IQR)	4,1 (1,5; 7,5)	12 (9,8; 18,5)	**<0,001**	**1,402 (1,22; 1,61)**	3,6 (1,3;7,8)	13(7,3;17,8)	**<0,001**	**1,29 (1,15; 1,46)**
MDS2 +, n (%)	13 (18,3)	16 (57,1)	**<0,001**	**5,94 (2,27; 15,54)**	16 (22,2)	10 (55,6)	**0,009**	**4,38 (1,48; 12,92)**
FAST3 Pain+, n (%)	1 (1,4)	12 (42,9)	**<0,001**	**54,75(6,63;451,82)**	3 (4,1)	6 (33,3)	**0,001**	**11,83 (2,60; 3,83)**
FAST3 Fatigue+, n (%)	1 (1,4)	14 (50,0)	**<0,001**	**73,00 (8,87;600,80)**	3 (4,1)	6 (33,3)	**0,001**	**11,83 (2,60; 3,83)**
FAST4 Fatigue+, n (%)	-	11 (39,3)	**<0,001**		-	5 (27,8)	**<0,001**	
FACIT, median (IQR)	41,7 ± 7,2	23,2 ± 9,3	**<0,001**	**0,79 (0,72; 0,86)**	42,2 ± 7,0	24,2 ± 9,4	**<0,001**	**0,78 (0,70; 0,88)**
RAID, median (IQR)	1,8 ± 1,6	5,3 ± 1,7	**<0,001**	**3,03 (1,93; 4,75)**	1,8 ± 1,6	5,0 ± 1,8	**<0,001**	**2,49 (1,66; 3,74)**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1. MDHAQ: Function (FN, modified HAQ)(1-10), VAS_Pain (0-10), PGA (0-10), VAS_Fatigue (0-10, significant fatigue=VAS_-Fatigue≥5)[2], Review of 60 symptoms (ROS60), self-assessment 48 joint count (sRADAI) and integrated indices: RAPID3 (0-30), FAST3_Pain, FAST3/FAST4_Fatigue, and MDS2.

2. Global FACIT_Fatigue, for fatigue(0-64, indirect score).

3. Global RAID, for the impact of the disease (0-10).

They were studied according to 1. Remission by DAS28ESR< 2.6 (DAS28 REM) and 2. A defined "Inflammatory remission" by SJC=0 and CRP< 0.4mg/dL (=SJC/CRP REM).

Sociodemgraphics variable, evolution of the disease, concomitant rheumatic diseases and comorbidities (depression, anemia, anxiety, hypothyroidism, and diabetes mellitus), and treatments (glucocorticoids, DMARDs, antidepressants) were analyzed. Patient outcomes from questionnaires (PROMs) and joint examinations (TJC28, SJC28), laboratory markers (RF, ACPA, ESR, and CRP), and disease activity composite indices (CDAI, SDAI, and DAS28CRP/ESR) were assessed.

A univariate analysis of the different variables studied was performed on whether VAS_fatigue is ≥5 or not in these patients according to two described types of remission (SJC/CRP REM vs DAS28 REM).

Results: A total of 246 RA non-selected patients were recruited, 77,1% females, mean age of 61.3 ±10.5 years, 17.19 (20.39) years of disease, BMI of 26.5±5 kg/m2, and DAS28ESR=3.47 (1.37). Osteoarthritis (17.1%) and Sjögren Syndrome (11.4%) as concomitant rheumatic diseases, and glucocorticoids (37.4%), bDMARD (45%), Jak inhibitors (13.6%) and antidepressants (15%) treatments were the most frequent.

SJC/CRP REM definition was observed in 102 patients; 28 of them (27.4%) experienced residual fatigue, and 92 patients met remission according to DAS28 REM, 18 (19.5%) reporting residual fatigue.

In clinical disease activity, TJC and SJC, and the composite indices, PROMs scores, were significantly associated with residual fatigue even in both types of studied remission (Table). And SCJ/CRP REM patients showed a significantly higher prevalence of female sex, active smokers, and a history of depression and antidepressants, but not in DAS28 REM. However, antirheumatic DMARDb treatment was associated with fatigue in DAS28 REM (Table).

Conclusion: Clinical disease activity and PROMs scores factors are similar in explaining residual fatigue in both types of defined clinical remission. Moreover, in the group of patients without SJC and with normal CRP, we also must take into account: female sex, smoking, and history of depression.

References: 1. Druce K, *et al*. Rheumatology 2016. 2. Tournadre, *et al*. Joint Bone Spine, 2019.

Disclosure: R. Morlà Novell: None; **E. González-Dávila**: None; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **M. López-Lasanta**: None; **N. Busquets Pérez**: None; **M. Valls Roc**: None; **M. Sallés Lizarzáburu**: None; **G. Salvador Alarcón**: None; **V. Ruiz-Esquide**: None; **L. Tobalina Mastre**: None; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **R. Sanmartí**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Eli Lilly, 5, 6, Merck/MSD, 5, 6, Pfizer, 5, 6, Roche, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0380

Multidimensional Health Assessment Questionnaire (MDHAQ)/RAPID3, is an Useful Tool to Assess Comorbid and Residual Fatigue in Rheumatoid Arthritis Patients

Rosa Maria Morlà Novell[1], Beatriz Frade Sosa[2], Maria López-Lasanta[3], Meritxell Sallés Lizarzáburu[4], Noemí Busquets Pérez[5], Georgina Salvador Alarcón[6], Marta Valls Roc[7], Virginia Ruiz-Esquide[8], Lola Tobalina Mastre[9], Raimon Sanmarti[8] and José Gomez-Puerta[10], [1]Hospital Clínic de Barcelona, Barcelona, Spain, [2]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [3]Hospital Universitari Vall d´Hebron, Barcelona, Spain, [4]Xarxa Sanitària Althaia Manresa, Manresa, Spain, [5]Hospital de Granollers, Granollers, Spain, [6]Hospital Universitari Mùtua Terrassa, Terrassa, Spain, [7]Hospital Universitari Dr Trueta, Girona, Sudan, [8]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [9]IDIBAPS. Hospital Clinic de Barcelona, Barcelona, [10]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Fatigue is a highly prevalent (40%-70%)[1] comorbidity in rheumatoid arthritis (RA) patients, and residual fatigue has been described in a significant proportion of patients who achieve low or remission disease activity[2].

Table 1. Associated factors in fatigued vs non-fatigued patients; only significant differences (p <0.05) are shown.

Variables	Patients	Non-fatigued (VAS_Fatigue<5) (n=140)	Fatigued (VAS_Fatigue>5) (n=106)	*p*-value
SOCIODEMOGRAPHIC AND DISEASE CHARACTERISTICS				
Sex, females, n (%)	205 (83.3%)	108 (77.1%)	97 (91.5%)	**0.003**
Educational levels (basic and medium), n (%)	78 (31.7%)	89 (63.6%)	71 (67%)	**0.016**
Active smoker, n (%)	39 (15.9%)	15 (10.7%)	24 (22.9%)	**0.023**
Depression, n (%)	8 (5.7%)	8 (5.7%)	18 (17.0%)	**0.032**
JOINT COUNT EXAMINATION				
TJC (0-28), mean (SD)	2.51 (4.63)	1.07 (1.68)	4.50 (5.65)	**<0.001**
SJC (0-28), mean (SD)	2.00 (4.33)	0.86 (1.86)	3.06 (4.97)	**0.007**
DISEASE ACTIVITY INDICES				
DAS28-ESR, mean (SD)	3.47 (1.37)	3.02 (1.10)	4.02 (1.51)	**<0.001**
DAS28-CRP, mean (SD)	3.08 (1.29)	2.46 (0.90)	3.65 (1.32)	**<0.001**
CDAI, mean (SD)	11.65 (11.49)	7.68 (6.12)	16.63 (13.55)	**<0.001**
SDAI, mean (SD)	12.47 (11.75)	8.23 (6.07)	17.47 (13.62)	**<0.001**
QUESTIONNAIRES				
FN (0-10), mean (SD)	2.96 (2.04)	1.78 (1.76)	3.83 (1.66)	**<0.001**
VAS_Pain (0-10), mean (SD)	5.27 (3.28)	3.38 (3.18)	6.72 (2.59)	**<0.001**
PGA (0-10), mean (SD)	5.03 (2.82)	2.98 (2.53)	6.81 (1.82)	**<0.001**
RAPID3 (0-30), mean (SD)	12.85 (7.32)	8.14 (6.39)	17.36 (5.19)	**<0.001**
FAST3_Pain+, n (%)	9 (6.4%)	62 (58.5%)	71 (28.9%)	**<0.001**
FAST_3 Fatigue+, n (%)	6 (4.3%)	62 (58.5%)	68 (27.6%)	**<0.001**
FAST_4 Fatigue+, n (%)	2 (1.4%)	56 (52.8%)	58 (23.6%)	**<0.001**
MDS2, n (%)	26 (19.1%)	53 (50.5%)	79 (32.1%)	**<0.001**
sRADAI (0-48), mean (SD)	13.98 (12.19)	9.79 (11.63)	19.06 (10.47)	**<0.001**
ROS60 (0-60), mean (SD)	11.09 (9.65)	7.68 (5.91)	15.50 (7.81)	**<0.001**
FACIT_Fatigue (0-64), mean (SD)	21.68 (12.79)	12.93 (8.85)	27.50 (8.23)	**<0.001**
RAID global (0-10), mean (SD)	4.63 (2.40)	3.21 (2.61)	6.52 (1.37)	**<0.001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Correlation VAS_ Fatiga and FACIT_Fatigue with the clinical study variables.

Variables	VAS_Fatigue	*p-value*	FACIT _Fatigue	*p-value*
VAS Fatigue	1.000	-	0.823	**<0.001**
FACIT_Fatigue global	0.823	<0.001	1.000	-
TJC	0.376	<0.001	0.352	**<0.001**
SJC	0.337	<0.001	0.233	**<0.001**
CRP	0.039	0.541	0.025	0.694
ESR	0.058	0.364	0.020	0.756
DAS28ESR	0.434	<0.001	0.370	**<0.001**
CDAI	0.502	<0.001	0.451	**<0.001**
SDAI	0.492	<0.001	0.430	**<0.001**
FN	0.617	<0.001	0.617	**<0.001**
PN	0.666	<0.001	0.608	**<0.001**
PATGL	0.721	<0.001	0.660	**<0.001**
RAPID3	0.749	<0.001	0.683	**<0.001**
ROS60	0.583	<0.001	0.608	**<0.001**
sRADAI	0.650	<0.001	0.620	**<0.001**
RAID global	0.796	<0.001	0.756	**<0.001**

We describe and study the characteristics of fatigued patients compared to non-fatigued using the VAS_Fatigue scale (testing in advance as a good tool), and we assessed residual fatigue according to different activity indices in a group of RA patients.

Methods: RA patients (ACR/EULAR criteria, 2010), excluding Chronic Fatigue Syndrome, were included consecutively in different hospitals across Catalonia (ARcat study group) during 6 months, fulfilling 3 qüestionnaires (PROMs):

1. MDHAQ: Function (FN, modified HAQ) (1-10), VAS_Pain (0-10), PGA (0-10), VAS_Fatigue (0-10; fatigue=VAS_Fatigue≥ 5[3]), Review of 60 symptoms (ROS60), self-assessment 48 joint count (sRADAI) and integrated indices: RAPID3 (0-30) for disease activity, FAST3_Pain and FAST3/FAST4_Fatigue for fybromialgia, and MDS2 for depression.

2. FACIT_Fatigue (0-64, indirect score).

3. RAID for impact of the disease (0-10).

Sociodemographic and clinical variables: history of depression, disease duration, treatment (DMARDs and glucocorticoids), joint count exam (TJC, SJC: 0-28), acute reactants (ESR, CRP), immunology (RF, ANA) and activity composite indices (DAS28 CRP/ESR, CDAI, SDAI) were assessed.

Descriptive and bivariate statistical analyses of variables (quantitatives: Student's test, categorical: Chi[2]) comparing fatigued/non-fatigued patients, with a previously Spearman correlation (VAS with FACIT) were performed, and we assessed the frequency of residual fatigue according to disease activity indices.

Results: A total of 246 RA patients (77,1% females) were collected; 61.3±10,5 years, BMI of 26.5±5 kg/m2, disease duration:17.19 (SD:20.39) years and DAS28ESR=3.47 (SD:1.37), treated with glucocorticoids in 52 (37.4%), bDMARD in 63 (45.0%), and Jak inhibitors in 19 (13.6%).

Table 3. Prevalence of fatigued patients in low activity according to the different activity indices studied; (p<0.001).

Patients	DAS28≤3.2 (n=146)	DAS28>3.2 (n=86)	CDAI≤10 (n=185)	CDAI>10 (n=60)	SDAI≤11 (n=183)	SDAI>11 (n=63)	RAPID3≤6 (n=79)	RAPID3>6 (n=167)
Fatigued	**41 (28,1%)**	60 (69.8%)	**61 (33%)**	45 (75%)	**58 (31.7%)**	48 (76,2)%	**5 (6.3%)**	101 (60.5%)
Non Fatigued	105 (71,9%)	26 (30,2%)	124 (67%)	15 (25%)	125 (68.3%)	15 (23.8%)	74 (93.7%)	66 (39.5%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A significant level of fatigue (VAS_Fatigue≥5) was found in 106 (43.1%) patients with significant differences ($p< 0.05$) compared to non-fatigued patients in: sex, educational levels, smoking, depression history, disease activity indices, and all of the PROMs scores (Table 1).

A strong negative correlation ($r=-0.82$, $p< 0.001$) was observed between VAS_Fatigue (0-10) and FACIT_Fatigue (0-54), also good for FN, PN, PATGL, sRADAI, ROS60, RAPID3, RAID, and a moderate for TJC and SJC and composite activity indices, and no correlation for ESR and CRP. A similar level of correlation was obtained for FACIT_Fatigue (Table 2).

The presence of residual fatigue (VAS≥5) is less frequent (6,3%; $p< 0.001$) when measuring activity with RAPID3 ≤ 6 than in the rest of the indices. In all of the cases, the differences between the presence or not of fatigue in remission patients were significant (Table 3)

Conclusion: Comorbid fatigue associated with clinical activity, sociodemographics, and PROMs is prevalent in RA patients, and it is feasibly measured by a simple VAS scale included in the MDHAQ. Moreover, the RAPID3 index seems to be the more stringent index to examine residual fatigue.

References:1. Hewlett S, 2011. 2. Michaud K, 2020. 3. Tournadre A, 2019.

Disclosure: R. Morlà Novell: None; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **M. López-Lasanta**: None; **M. Sallés Lizarzáburu**: None; **N. Busquets Pérez**: None; **G. Salvador Alarcón**: None; **M. Valls Roc**: None; **V. Ruiz-Esquide**: None; **L. Tobalina Mastre**: None; **R. Sanmartí**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Eli Lilly, 5, 6, Merck/MSD, 5, 6, Pfizer, 5, 6, Roche, 5, 6; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6.

Abstract Number: 0381

Improving Participation in The Lupus Foundation of America's Research Accelerated by You (RAY) Patient Registry By Understanding Patient Preference in Communication Strategies

Safoah Agyemang[1], Melicent Miller[1], Tori Justin[2], Lydia Oberholtzer[2] and Joy Buie[1], [1]Lupus Foundation of America, Washington, DC, [2]Sharp Insight LLC, Montgomery County, MD

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The purpose of Research Accelerated by You (RAY) is to amplify awareness about clinical research and trials and ensure lupus patient partnership in therapeutic development. However, Black/ African Americans (B/AA) make up only 16% of RAY participants, a notable disparity as B/AAs account for 30-43% of the lupus population. To address the lack of representativeness in race/ethnicity amongst B/AA in RAY, we explored B/AA motivations and communications preferences driving registry enrollment decision-making.

Methods: We conducted two focus groups with people living with lupus (PWL) who were already enrolled in RAY or a part of the Lupus Research Action Network (LRAN), a patient peer-to-peer network, but not enrolled in RAY. All focus group (FG) participants were B/AA females aged 25-46 years (n=4 each). Key informant (KI) interviews were also conducted with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. How KIs navigate barriers to enrollment

To boost RAY enrollment of the target audience (i.e., B/AA ages 18-35) KIs offered a wide range of suggestions such as:

	Promoting RAY at historically black colleges and universities (HBCUs) and partnering with student health services to reach potential patients: *"Considering working with HBCUs and student health services on campus."* – KI 2
	Showcasing how the RAY and clinical trials are useful for the Black/African American population: *"Some of my patients were reluctant until I mentioned the results or research in Black patients."* –KI 1
	Engaging pediatric rheumatologists: *"One more thing about that transitioning pediatric population. If RAY is not already being advertised and promoted with pediatric rheumatology, I would do so. They actually do see a lot of those patients that are 18 to 21, [and] sometimes they see them until they're 26 and that's when you are removed from your parent's insurance. So, I would certainly engage pediatric rheumatologists and getting the word out about [RAY]."* – KI 2

When promoting RAY, participants also suggested:

	Letting users know what LFA is doing with the data and providing feedback to those who complete surveys: "People are more likely to respond to survey if they get feedback. Let them know what they're doing with the data." —KI 1
	Writing promotional messages that illustrate how the patient benefits from enrollment. These messages should be person-centered and emphasize how participation helps the patient and their community, not the research team: *"RAY needs to be clear that it serves the patients, not the research objectives."* –KI 3

PWL with no affiliation with the Lupus Foundation of America (LFA)(n=1) and registry directors at academic medical centers (n=3). Audio-recordings were transcribed and cleaned using Otter.ai. Manual content analysis followed an inductive approach, allowing themes to emerge from data rather than predetermined categories for FGs and KIs. Resulting themes with exemplary quotes are presented in Tables 1-4.

Table 2. Perceptions of RAY Communication Materials and RAY Marketing Infographics

Model Images	Likes	Recommendations for Improvement
	"Purple and white stand out nicely. Language feels welcoming." – RAY participant *"I like the word "share" and "lupus experience". The model looks like the target audience."* –KI 3	*"Hard to depict if the woman has lupus".* – RAY participant *"Looks racially ambiguous. Looks like trying to please everyone not Black people."* –LRAN participant *"Use a Black lupus patient. I have a friend where lupus is affecting the face, to me that would make me want to share my experience."* –LRAN participant *"Consider showing external lupus features."* – KI 1 *"This may be too many words, but I want to add in something at the end, 'sharing your lupus experience so we can conquer lupus!'"* – KI 2
	"This woman doesn't seem smiley which is good. I would click on this. It is vague but the picture is more inviting."— RAY participant *"This would appear more targeted to Lupus community. And, I like the "Share Your Lupus Experience." She is more focused and looking at the lupus itself and trying to tackle it."* – RAY participant	
	"It is important to show different ethnic backgrounds so this caters to everyone." – RAY participant	*"Not sure if that's freckles or rash or scar; I would not pick freckled person. Not the right model for this demographic; need to have hat or something to show that they are protecting their skin."* –KI 1 *"Maybe have a model with rash and show it on different black skin shades with texture; thinning of the hair, swelling around eyes. Show an activity of mom having to stay in shade but kids are in the sun."*–KI 3

Infographics	Likes	Recommendations for Improvement
	"I like the information better than the models. The words make me want to help in some way. I like the data approach. This makes me feel like I'm not doing my part." – LRAN participant *"I like the 10% especially."* – LRAN participant	*"The test tube is a symbol of research but it looks like you are asking them to give blood; participation is survey related. Add pen to paper instead of test tube image."* – KI 1 *"The first image is incorrect, there are 5 FDA approved treatments not 3."* –KI 3
	"I like the information; this would make me want to sign up." – LRAN participant. *"I like the quick facts; they can educate someone in less than 10 seconds."*— LRAN participant	*"There should be a conclusion image here. Put the call to action here. Missing how lupus makes you feel."*— Non-affiliated participant *"Add other organs like kidneys; add cognition and brain function. I would like to see other non-common factors. Add sex drive and sexual organs that are less talked about."* – LRAN participant *"Include kidney, more frequent than eye and muscles. Skin, joints and kidney will capture most patients."* – KI 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Digital Advertising Copy

Digital Advertising Copy	Likes	Recommendations for Improvement
RAY: Research Accelerated by You is an online research platform where people with lupus and caregivers share their experiences to help develop new treatments. Sign up today for this online lupus registry and help accelerate lupus research.	*"I like that it [the message] has caregivers."* – LRAN participant *"I like that it [the message] is straight forward."* –Non-affiliated participant	*"Bullet the messages, make them more concise."* – KI 2
Lupus is a cruel mystery—but together, we can solve it. With RAY: Research Accelerated by You, people with lupus and caregivers can share their experiences on an online data platform to help develop new treatments. Sign up today to be the solution to lupus!	*"This message shows community and teamwork."*—KI 2 *"This resonates with me. I like how it says 'develop new treatments'."*—LRAN participant	*"[This message is] not patient focused for this group; there is no trust here. The primary benefactor is the researchers, not the people with lupus."* – KI 3
We're on a mission to end the brutal impact of lupus. And YOU are the key to developing better treatments. We created a data platform called RAY: Research Accelerated by You to help develop new treatments. Sign up for RAY today and share your lupus experience to guide research.	*"I like how this message centers 'YOU'."* – LRAN participant *"[It is] important to have various messages that speak to a variety of people."*—KI 2	*"Brutal is a strong word. Don't replace it just state 'impact'."* – Non-affiliated participant
#DYK: 7 in 10 survey participants responded that lupus has impacted multiple organs. What about you? Share your experience through our online research platform, RAY: Research Accelerated by You. When you sign up today, see how your experience compares to others and help advance lupus research!	*"I like the comparison aspect."* – RAY participant	*"I don't like the DYK. The older Black PWL may not get the DYK."* –LRAN participant *"DYK is not a popular hashtag, so many may not know what this means."* – KI 2
You can help advance lupus research and treatments! And it's easy. Join our online lupus registry, RAY: Research Accelerated by You, and share your lupus experience to help researchers develop new treatments. Sign up today!	*"Sounds more conversational. Like the conversational approach. More energy here."* – LRAN participant	*"RAY needs to be clear that it serves the patients, not the research objectives. Especially about depression, brain fog, and fatigue. Consider clearly stating the clinical trial measures, such as suicide, quality of life, and sometimes depression."* – KI 3 *"Take out 'easy'."* –RAY participant *"Add specific language and facts related to target population."*—KI 2

Results: Three overarching themes emerged:

1.Communication Preferences: Participants receive most of their lupus information from the LFA's emails, social media, and website, in addition to email/text alerts from other research institutions. Furthermore, some participants also noted that their family members/friends have sent them lupus materials; however, most shared they **prefer** to receive lupus-related information from their healthcare team.

2.Building Trust and Rapport: KIs mentioned this theme as essential to encouraging registry and clinical trial enrollment. To build rapport, KIs discussed the importance of speaking with patients face-to-face about enrollment, educating potential participants about patient protections, and explaining the history of mistrust as it relates to the medical profession and the B/AA community in the U.S.

3.Curating Messages/Imagery that Resonate: After reviewing RAY marketing materials, participants stated models who look indisputably like the target audience (i.e., B/AA PWL) are preferred. Additionally, some participants mentioned they prefer the models to feature lupus symptoms such as having a "rash" or "swelling around the eyes." Participants preferred messaging demonstrating how RAY benefited the patient rather than the researcher, and they favored clear and straightforward content. To improve messaging, participants suggested avoiding the notion that lupus is "easy" and adding language centering the target population.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: B/AA PWL may be more inclined to enroll in registries and clinical trials if they receive clear and transparent information from their healthcare team about the benefits and risks of participation, particularly as they relate to B/AA PWL. Centering the experience of B/AA PWL in registry and clinical communication materials is a key theme of importance to potential study participants and may improve enrollment in the registry.

Disclosure: S. Agyemang: None; **M. Miller**: None; **T. Justin**: None; **L. Oberholtzer**: None; **J. Buie**: Bristol-Myers Squibb(BMS), 1, Fate Therapeutics, 1, Genentech, 1, Novartis, 1.

Abstract Number: 0382

Preventative Health Screening Practices Among 666 Women with Systemic Rheumatic Diseases from the Hospital for Special Surgery Rheumatology Women's Reproductive Health and Wellness Cohort: A Cross-Sectional Analysis

Sandhya shri Kannayiram[1], Amaya Smole[2], Lucy Masto[3], Yongjay Kim[4], Neha Nagpal[1], Naiva Manuela Piatchou Donfack[1], Deanna Jannat-Khah[1], Lisa Mandl[1], Sarah Lieber[1], Caroline Siegel[1], Michael Lockshin[5], Lisa Sammaritano[1] and Medha Barbhaiya[1], [1]HOSPITAL FOR SPECIAL SURGERY, New york, NY, [2]Hospital for Special Surgery, Brooklyn, NY, [3]Hospital for Special Surgery, San Francisco, CA, [4]Hospital for Special Surgery, Englewood Cliffs, NJ, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Timely preventative health screenings in women with systemic rheumatic diseases (SRDs), especially those with other chronic conditions or who are on immunosuppressive therapy, may improve outcomes through early detection. This study aimed to identify demographic, lifestyle, disease-related, and healthcare utilization factors associated with delayed preventative health screenings in this population.

Methods: We included women aged 18-65 evaluated at Hospital for Special Surgery (HSS) by a rheumatologist ≥2 times who enrolled in the HSS Rheumatology Women's Reproductive Health and Wellness Cohort between 12/2022- 5/2024 and completed a standardized questionnaire on their preventative health screening status. Patients reported being "due or overdue" for six screenings: colon, breast, cervical, and skin cancers; bone density; and retinal (eye) toxicity screening. We evaluated the degree of delay and the reasons for delay. Descriptive analyses compared demographics, lifestyle factors, SRD status, medication use, and healthcare utilization for patients "due/overdue" versus those not due/overdue for the screenings. Multivariable logistic regression analyzed factors associated with being due/overdue for each screening.

Results: Among 666 women included in this cross-sectional analysis, increased age was associated with being due/overdue for colon, breast, and skin cancer, as well as bone density screening, and patients with 'other' or Black race, but not White race were more frequently due/overdue for bone density screenings **(Table 1)**. Hispanic versus non-Hispanic women were more frequently due/overdue for breast (21% vs. 11%) and eye toxicity screenings (20% vs. 11%). Ever smokers were also more likely to be due/overdue for breast, cervical, skin cancer, bone density, and eye toxicity screenings than non-smokers, and SRD status was significantly different only for eye toxicity screenings**(Table 1)**.In multivariable analyses, factors associated with being due/overdue for a particular screening test included: increased age (OR=1.04, 95%CI 1.02–1.07) for colon cancer; increased age (OR=1.04, 95%CI 1.02–1.06), Hispanic ethnicity (OR=2.40, 95% CI 1.27–

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, Socioeconomic, Lifestyle, Disease, and Health Utilization Factors in 666 women with Systemic Rheumatic Diseases Enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort between 2022 and 2024, by their Preventative Health Screening Status for Six Screening Evaluations

Table 1. Demographic, Socioeconomic, Lifestyle, Disease and Health Utilization Factors in 666 Women with Systemic Rheumatic Diseases Enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort between 2022-2024, by their Preventative Health Screening Status for Six Screening Evaluations[a1]

	Colon Cancer Screening			Breast cancer Screening			Cervical Cancer Screening			Skin cancer Screening			Bone Density Screening			Retinal toxicity Screening		
Characteristics	Due/ overdue N = 101	Not Due/ overdue N = 565	P-Value	Due/ overdue N = 131	Not Due/ overdue N = 535	P-Value	Due/ overdue N = 115	Not Due/ overdue N = 551	P-Value	Due / overdue N = 137	Not Due/ overdue N = 529	P-Value	Due/ overdue N = 67	Not Due/ overdue N = 599	P-Value	Due/ overdue N = 84	Not Due/ overdue N = 582	P-Value
Demographic Factors, N (%) except age																		
Age(years); median (IQR)	**52 (47,60)**	**49 (37,59)**	**<0.01**	**54 (45,60)**	**49 (36,59)**	**<0.01**	53 (41,59)	49 (38,59)	0.10	**53 (42, 59)**	**49 (37,59)**	**<0.01**	**56 (45, 62)**	**49 (38,59)**	**<0.01**	48 (38,56)	50 (39,59)	0.4
Race																		
• White	72(72.7)	420 (76.1)	0.6	92(72.4)	400(76.3)	0.5	81(70.4)	411(76.7)	0.3	105(80.1)	387(74.4)	0.4	**35(53.8)**	**457(78)**	**<0.01**	55(66.2)	437(76.9)	0.09
• Black	11(11.1)	47(8.5)		11(8.6)	47(9)		14(12.2)	44(8.2)		10(7.6)	48(9.2)		**10(15.4)**	**48(8.2)**		11(13.2)	47(8.3)	
• Other	16(16.2)	85(15.4)		24(18.9)	77(14.7)		20(17.4)	81(15.1)		16(12.2)	85(16.3)		**20(30.8)**	**81(13.8)**		17(20.5)	84(14.8)	
Hispanic Ethnicity	12(11.9)	72(12.8)	0.8	**20(20.8)**	**57(10.7)**	**<0.01**	18(15.6)	66(12)	0.3	23(16.8)	61(11.6)	0.1	**19(28.4)**	**65(10.9)**	**<0.01**	**17(20.2)**	**67(11.6)**	**0.03**
Insurance, N (%)																		
• Commercial/Private	86(85.1)	496(88.6)	0.3	115(88.5)	467(87.9)	0.9	104(90.4)	478(87.5)	0.4	124(90.5)	458(87.4)	0.3	56(84.8)	526(88.4)	0.4	71(85.5)	511(88.4)	0.5
• Medicare/Medicaid	15(14.8)	64(11.4)		15(11.5)	64(12)		11(9.6)	68(12.4)		13(9.5)	66(12.6)		10(15.1)	69(11.6)		12(14.5)	67(11.6)	
Employed[2]	64(64.0)	396(71.1)	0.2	88(68.7)	372(70.3)	0.7	76(66.1)	384(70.8)	0.3	92(69.7)	368(70.1)	>0.9	45(68.2)	415(70.2)	0.8	**46(56.1)**	**414(72.0)**	**<0.01**
Ever Smoker	30(29.7)	117(21)	0.05	**39(30.7)**	**108(20.3)**	**0.01**	**40(35.4)**	**107(19.6)**	**<0.01**	**40(29.4)**	**107(20.5)**	**0.03**	21(31.3)	126(21.3)	0.06	**28(33.7)**	**119(20.7)**	**<0.01**
Rheumatology Diagnosis, N (%)																		
• IA[3]	53(60.9)	301(60.3)	>0.9	67(59.8)	287(60.5)	0.9	54(56.8)	300(61.1)	0.4	83(65.9)	271(58.9)	0.2	34(54.8)	320(61.1)	0.3	**26(37.7)**	**328(63.4)**	**<0.01**
• Systemic CTD[4]	34(39.1)	198(39.7)		45(40.2)	187(39.4)		41(43.2)	191(38.9)		43(34.1)	189(41.1)		28(45.2)	204(38.9)		**43(62.3)**	**189(36.6)**	
Medications (Current versus Not Current), N (%)																		
• Immunosuppressive meds	63(65.6)	328(64.2)	0.8	70(58.8)	321(65.8)	0.2	64(62.1)	327(64.9)	0.6	88(67.7)	303(63.5)	0.4	40(65.6)	351(64.3)	0.8	43(57.3)	348(65.4)	0.2
• Steroids	12(11.8)	71(12.6)	0.8	20(15.3)	63(11.8)	0.3	16(13.9)	67(12.2)	0.6	20(14.6)	63(11.9)	0.4	13(19.4)	70(11.7)	0.07	11(13.1)	72(12.4)	0.9
• Antimalarials*	35(34.6)	220(39.2)	0.4	47(36.2)	208(39.1)	0.5	50(43.8)	205(37.4)	0.2	52(37.7)	203(38.7)	>0.9	33(49.2)	222(37.3)	0.06	N/A		-
Healthcare Utilization, N (%)																		
PCP visit <1/year	28(27.7)	123(21.8)	0.2	**39(29.8)**	**112(20.9)**	**0.03**	34(29.6)	117(21.3)	0.05	38(27.7)	113(21.4)	0.13	17(25.4)	134(22.4)	0.6	26(30.9)	125(21.5)	0.05
Gynecologist visit <1/year	30(29.7)	134(23.7)	0.2	**52(39.7%)**	**112(20.9)**	**<0.01**	**56(48.70)**	**108(19.6)**	**<0.01**	**43(31.4)**	**121(22.9)**	**0.04**	22(32.8)	142(23.7)	0.10	26(31.0)	138(23.7)	0.15

1. All p-values calculated using Welch Two Sample t-test; Fisher's exact test; Pearson's Chi-squared test. Bold p- value <0.05 =statistically significant.
2. Unemployed includes disability, retired, students.
3. I.A.-Inflammatory arthritis diagnoses include Ankylosing spondylitis, Enteropathic arthritis, Juvenile idiopathic arthritis, Palindromic rheumatism, Polymyalgia rheumatica, Polyarthritis, Psoriatic arthritis, and Rheumatoid arthritis.
4. CTD- Connective tissue disease diagnoses include Antiphospholipid syndrome, Eosinophilic fasciitis, Mixed connective tissue disease, Myositis, Overlap connective tissue disease, Sjogren's syndrome, Systemic lupus erythematosus, Systemic sclerosis
*Patients not on antimalarials cannot be checked for delay in eye toxicity screening, hence not included here; N/A- not applicable
a –Total of number of patients may not add up in some columns as patients who preferred not to answer were excluded.

Table 2. Logistic Regression Results Estimating the Association of Demographic, Medication, and Healthcare Utilization Factors with Being Due/Overdue for a Preventative Health Screening Study Among 666 women with Systemic Rheumatic Diseases enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort between 2022 and 2024

TABLE 2. Logistic Regression Results Estimating the Association of Demographic, Medication, and Healthcare Utilization Factors with Being Due/Overdue for a Preventative Health Screening Study Among 666 women with Systemic Rheumatic Diseases enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort between 2022-2024

Screening	Colon Cancer Screening		Breast Cancer Screening		Cervical Cancer Screening		Skin Cancer Screening		Bone Density Testing		Retinal toxicity screening	
Factors (Reference variable)	OR (95 % CI)	P-value	OR (95 % CI)	P-value	OR (95 %CI)	P-value	OR (95% CI)	P-value	OR (95 %CI)	P-value	OR (95 %CI)	P-value
Sociodemographics												
Age	**1.04 (1.02, 1.07)**	**<0.01**	**1.04 (1.02,1.06)**	**<0.01**	1.00 (0.98,1.02)	0.9	1.01 (0.99,1.03)	0.2	**1.06 (1.03,1.09)**	**<0.01**	0.98 (0.96, 1.01)	0.15
Race (White)												
• Black or African American	1.26 (0.5, 2.75)	0.6	0.72 (0.2, 1.61)	0.4	1.69 (0.7, 3.59)	0.2	0.57 (0.2, 1.29)	0.2	2.30 (0.9, 5.39)	0.07	1.21 (0.4, 2.93)	0.7
• Other	1.23 (0.58, 2.47)	0.6	1.10 (0.56,2.06)	0.8	0.95 (0.47,1.83)	0.9	0.75 (0.38,1.38)	0.4	**4.36 (2.13,8.87)**	**<0.01**	1.78 (0.86, 3.53)	0.11
Ethnicity (non-Hispanic)												
• Hispanic	0.74 (0.31, 1.57)	0.5	**2.40 (1.27,4.47)**	**<0.01**	1.55 (0.77,2.99)	0.2	1.62 (0.85,3.03)	0.14	1.99 (0.95, 4.02)	0.06	1.58 (0.73, 3.27)	0.2
Insurance (Private)												
• Medicare/Medicaid/ Other types	0.87 (0.41, 1.74)	0.7	0.56 (0.25,1.13)	0.12	0.59 (0.25,1.29)	0.2	0.64 (0.30, 1.28)	0.2	0.75 (0.31, 1.68)	0.5	1.09 (0.4, 2.48)	0.8
Diagnosis (Inflammatory Arthritis)												
• Connective Tissue Disease	1.24 (0.72, 2.11)	0.4	1.17 (0.70,1.95)	0.5	1.06 (0.62, 1.83)	0.8	0.65 (0.40, 1.06)	0.09	1.02 (0.53, 1.95)	>0.9	**2.30 (1.3, 4.03)**	**<0.01**
Employment Status (Employed)*												
• Unemployed	N/A		N/A		N/A		N/A		N/A		**1.97 (1.3–4.8)**	**<0.01**
Medications												
Steroids (No)												
• Yes	0.57 (0.22, 1.25)	0.2	1.24 (0.62,2.37)	0.5	1.10 (0.51, 2.21)	0.8	1.30 (0.67,2.42)	0.4	1.60 (0.69, 3.44)	0.2	0.86 (0.33, 1.99)	0.7
Antimalarials (No)*												
• Yes	0.64 (0.36, 1.12)	0.12	0.79 (0.47,1.33)	0.4	1.35 (0.79,2.31)	0.3	1.03 (0.64, 1.66)	0.9	1.44 (0.75,2.73)	0.3	**N/A**	**N/A**
Lifestyle factor - Smoking(no)												
• Ever smoker	1.27 (0.73, 2.14)	0.4	1.40 (0.83, 2.31)	0.2	**1.96 (1.14,3.35)**	**0.01**	1.49 (0.91,2.40)	0.11	1.33 (0.69, 2.51)	0.4	**2.57 (1.37, 4.81)**	**<0.01**
Healthcare utilization												
PCP seen ≥1/year (Yes)												
• No	1.39 (0.76, 2.46)	0.3	1.25 (0.71,2.13)	0.4	1.06 (0.59, 1.85)	0.8	1.45 (0.87, 2.39)	0.2	1.21 (0.59, 2.38)	0.6	1.31 (0.69, 2.39)	0.4
Gynecologist seen ≥1/year (Yes)												
• No	1.02 (0.58, 1.77)	>0.9	**2.03 (1.24,3.32)**	**<0.01**	**3.70 (2.23, 6.17)**	**<0.01**	1.32 (0.81, 2.14)	0.3	0.94 (0.48, 1.77)	0.8	N/A	N/A

*Due/overdue for Eye toxicity screening cannot be checked for patients not on antimalarials and hence not included in that respective analysis. Bold p- value <0.05 =statistically significant.
+ Retinal toxicity screening was additionally adjusted for employment status based on significance achieved in bivariate analyses (Table 1)
Abbreviations: N/A =Not applicable; OR=Odds ratio; 95% CI=95% Confidence Interval.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

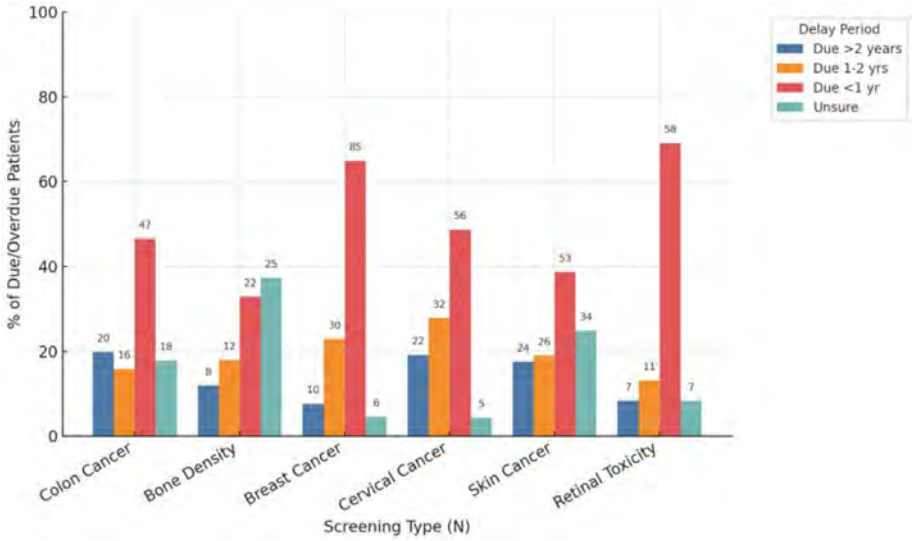


Figure: Degree of Delay in Health Screenings Among 666 Women with Systemic Rheumatic Diseases Enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort between 2022 -2024

4.47), and < 1/year gynecology visits (OR=2.03, 95% CI 1.2–3.3) for breast cancer; ever smoking (OR=1.96, 95% CI 1.14-3.35) and < 1/year gynecology visits (OR=3.70, 95% CI 2.2–6.1) for cervical cancer; increasing age (OR=1.06, 95% CI 1.03–1.09) and 'Other' vs. white race (OR=4.36, 95% CI 2.13-8.87] for bone density; and ever smoking(OR=2.57, 95 % CI 1.37-4.81), CTD status (OR=2.30, 95% CI 1.3–4.03) and unemployment(OR=1.97, 95% CI 1.3–4.8) for eye toxicity screening **(Table 2)**. Degrees of self-reported delays were most typically < 1 year **(Figure)**. The most common reasons for delay were forgetfulness and scheduling difficulty (data not shown).

Conclusion: Preventative health screening delays in a cohort of women with SRDs were influenced by age, Race, Ethnicity, smoking history, CTD diagnosis, employment status, and infrequent gynecology visits. Targeted strategies are needed to improve adherence to suggested screenings and thereby reduce health risks in this vulnerable population.

Disclosure: S. Kannayiram: None; **A. Smole**: None; **L. Masto**: None; **Y. Kim**: None; **N. Nagpal**: None; **N. Piatchou Donfack**: EMD Serono, 3; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **L. Mandl**: ACP, 12, Associate Editor Annals of Internal Medicine, Wolters, 9; **S. Lieber**: None; **C. Siegel**: None; **M. Lockshin**: None; **L. Sammaritano**: None; **M. Barbhaiya**: None.

Abstract Number: 0383

Hidden Risk in Low Frailty: Impact of Elixhauser Comorbidities on In-Hospital Mortality Among Osteoporosis Patients — A Nationwide Analysis

Simran Bhimani[1], Anand Reddy Maligireddy[2], Sameer Bhimani[3], Birju Bhatt[4] and Nevena Barjaktarovic[5], [1]The Wright Center for graduate medical education, Scranton, PA, [2]The Wright Center GME, Scarnton, PA, [3]The Wright Center for GME, scranton, PA, [4]Solara Health NJ, New Jersey, NJ, [5]The Wright Center, GME, Scranton, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

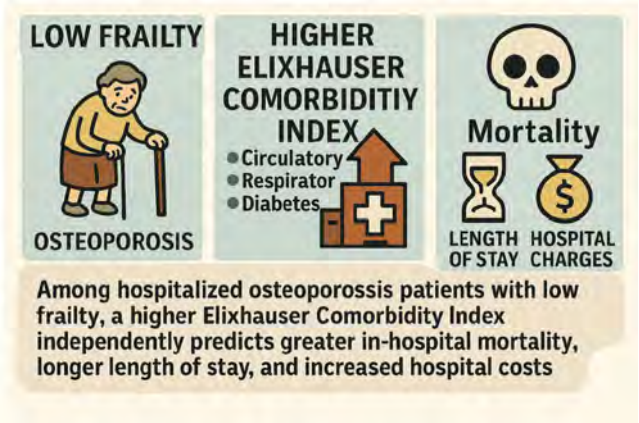
Table 1

	Low Elixhauser Comorbidity index (< 3)	High Elixhauser Comorbidity Index (≥3)	P-value
Age ,years (95% CI)	71.43 (71.36-71.52)	74.23 (74.15-74.31)	<0.05
Female	89.40%	87%	<0.05
Elixhauser Comorbidities			
Congestive Heart Failure	1.40%	26.40%	<0.05
Cardiac Arrhythmias	7.7%	36.8%	<0.05
Valvular Disease	2.3%	17.9%	<0.05
Pulmonary Circulation Disorders	0.8%	8.9%	<0.05
Peripheral Vascular Disorders	2.5%	15.0%	<0.05
Hypertension, Uncomplicated	45.0%	55.4%	<0.05
Paralysis	0.5%	1.2%	<0.05
Other Neurological Disorders	2.5%	5.8%	<0.05
Chronic Pulmonary Disease	13.6%	39.9%	<0.05
Diabetes, Uncomplicated	4.3%	15.4%	<0.05
Diabetes, Complicated	1.8%	14.6%	<0.05
Hypothyroidism	12.6%	32.7%	<0.05
Renal Failure	1.8%	14.9%	<0.05
Liver Disease	1.3%	6.1%	<0.05
Peptic Ulcer Disease	0.3%	1.2%	<0.05
AIDS/HIV	0.0%	0.2%	<0.05
Lymphoma	0.7%	1.7%	<0.05
Metastatic Cancer	1.1%	5.1%	<0.05
Solid Tumor Without Metastasis	3.6%	10.5%	<0.05
Rheumatoid Arthritis	4.9%	13.6%	<0.05
Coagulopathy	1.4%	7.2%	<0.05
Obesity	5.2%	19.2%	<0.05
Weight Loss	1.7%	7.3%	<0.05
Fluid and Electrolyte Disorders	3.1%	9.9%	<0.05
Blood Loss Anemia	0.4%	1.4%	<0.05
Deficiency Anemia	1.3%	6.6%	<0.05
Alcohol Abuse	0.6%	2.4%	<0.05
Drug Abuse	0.8%	2.9%	<0.05
Psychoses	0.4%	1.3%	<0.05
Depression	8.7%	23.6%	<0.05
Hypertension, Complicated	2.0%	28.7%	<0.05

Background/Purpose: Osteoporosis is a common condition associated with increased morbidity, particularly in older adults. While frailty is a known predictor of adverse outcomes, the independent impact of comorbidities in patients with low frailty is not well defined. This study evaluated the association between the Elixhauser Comorbidity Index and in-hospital mortality among hospitalized osteoporosis patients with low frailty and examined differences in hospital utilization and demographics.

Methods: We conducted a retrospective, survey-weighted analysis using the Nationwide Readmissions Database (2016–2022) to identify hospitalized adult (>18 years) patients with osteoporosis and low frailty scores (≤5). A total of 1,378,142 patients met inclusion criteria and were categorized by the Elixhauser Comorbidity Index: < 3 vs. ≥3. Multivariable logistic regression, adjusted for sex and weekend admission, was used to evaluate the association between comorbidity burden and in-hospital mortality.

Results: Of the 1,378,142 patients included, 775,034 (56.2%) had a high Elixhauser Comorbidity Index (≥3), of whom 88.0% were female. Table 1 outlines the distribution of individual Elixhauser comorbidities across both groups. In-hospital mortality was significantly higher in the high comorbidity group (0.71% vs. 0.23%; p< 0.001). In adjusted analysis, a higher Elixhauser Comorbidity Index was significantly associated with increased odds of in-hospital death (aOR 1.31; 95% CI: 1.29–1.33; p< 0.001). Patients with greater comorbidity burden had longer hospital stays (3.8 vs. 3.1 days; p< 0.001) and higher mean hospital charges ($61,938 vs. $59,837; p< 0.001) Figure 1.



Conclusion: Among hospitalized osteoporosis patients with low frailty, a higher Elixhauser Comorbidity Index independently predicts greater in-hospital mortality, longer length of stay, and increased hospital costs. These findings emphasize the importance of comorbidity assessment for risk stratification and care planning, even in patients considered low-risk by frailty measures.

Disclosure: S. Bhimani: None; **A. Maligireddy**: None; **S. Bhimani**: None; **B. Bhatt**: None; **N. Barjaktarovic**: None.

Abstract Number: 0384

Hip Fracture Hospitalization Trends in Osteoporotic Patients (2016–2022): National Data Insights

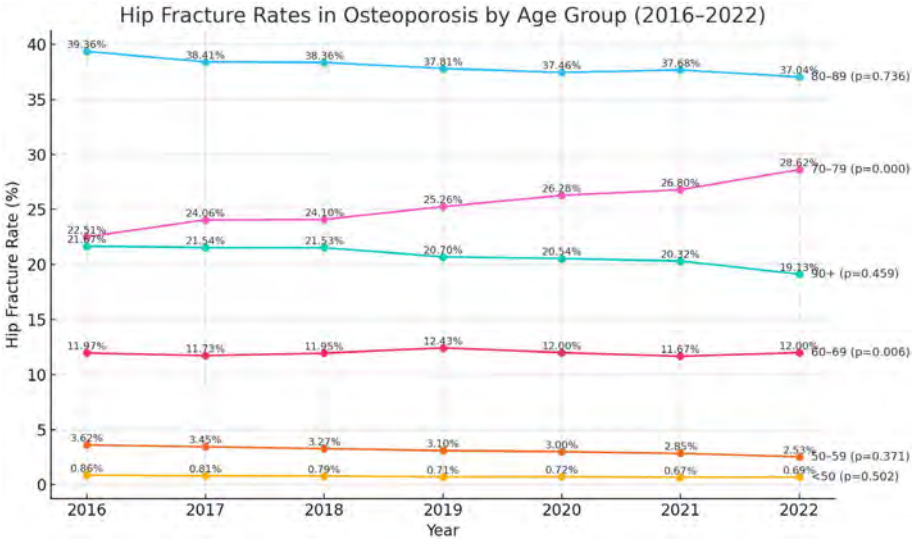
Simran Bhimani[1], Anand Reddy Maligireddy[2], Sameer Bhimani[3] and Birju Bhatt[4], [1]The Wright Center for graduate medical education, Scranton, PA, [2]The Wright Center GME, Scarnton, PA, [3]The Wright Center for GME, scranton, PA, [4]Solara Health NJ, New Jersey, NJ

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Hip fractures in patients with osteoporosis are a major contributor to morbidity, mortality, and healthcare costs. While classically associated with the oldest patients, emerging trends suggest that younger elderly adults may now bear a growing share of the burden. We evaluated age-stratified trends in hip fracture hospitalizations and in-hospital mortality among osteoporotic adults in the United States.

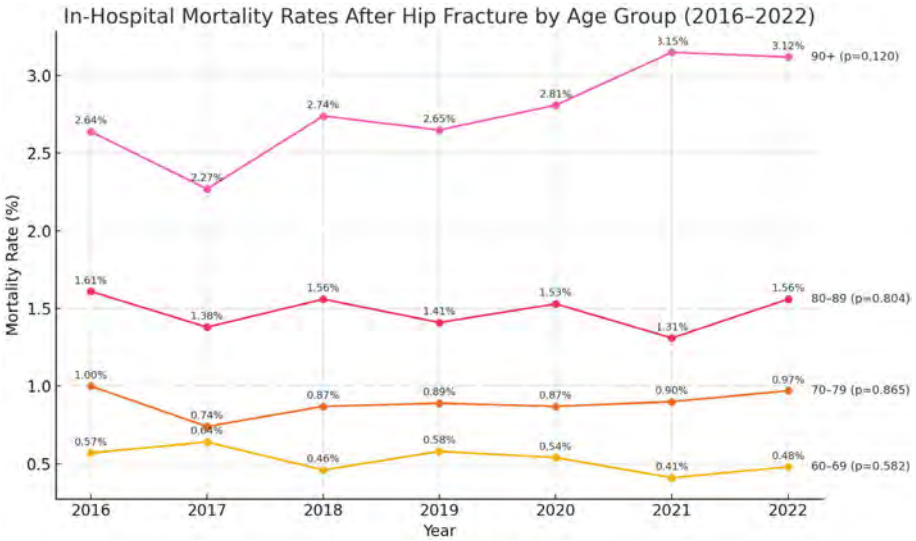
Methods: We conducted a retrospective cohort study using the National Readmissions Database (NRD) from 2016 to 2022. We included adult patients hospitalized with osteoporosis and identified those with a primary discharge diagnosis of hip fracture using ICD-10 codes. Patients were stratified into age groups: < 50, 50–59, 60–69, 70–79, 80–89, and ≥90 years. Survey-weighted logistic regression was used to evaluate temporal trends in hip fracture hospitalizations and in-hospital mortality, comparing 2022 to 2016 within each age group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

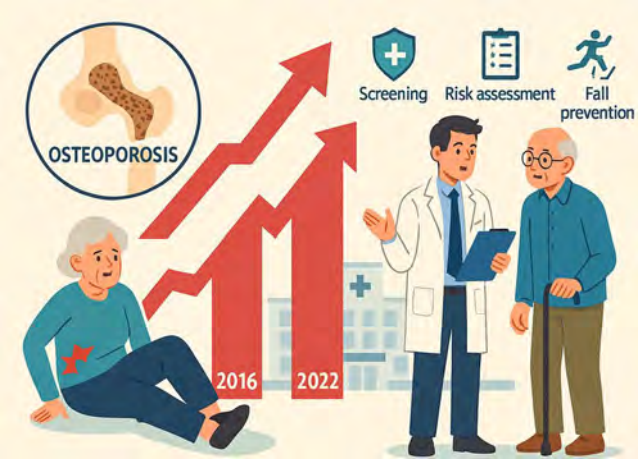


Results: Among 5,040,169 weighted osteoporosis-related hospitalizations, 392,615 (7.8%) were for hip fractures. The 70–79 age group showed the most significant increase in hip fracture hospitalizations, rising from 22.5% in 2016 to 28.6% in 2022. Odds of hip fracture rose by 13% in this group (OR: 1.13, 95% CI: 1.06–1.20, $p < 0.001$). The 60–69 group also demonstrated a significant increase (OR: 1.12, $p = 0.006$) Figure 1. Despite these increases, in-hospital mortality rates remained unchanged across all groups Figure 2.

Conclusion: From 2016 to 2022, adults aged 70–79 with osteoporosis experienced a significant rise in hip fracture hospitalizations without increased in-hospital mortality, reflecting improved acute care. Proactive screening, earlier risk assessment, and fall prevention efforts targeting adults in their 60s and 70s may be critical in curbing the growing hospitalization burden in this increasingly vulnerable population Figure 3.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: S. Bhimani: None; **A. Maligireddy**: None; **S. Bhimani**: None; **B. Bhatt**: None.

Abstract Number: 0385

Musculoskeletal Ultrasound Enhances Patient Insight and Clinical Decisions: A Multi-Center Study

Simran Nimal[1], Meridith Balbach[2], Aslam Fawad[1], Midori Nishio[3] and Erin Chew[2], [1]Mayo Clinic Arizona, Scottsdale, AZ, [2]Vanderbilt University, Nashville, TN, [3]John Muir Specialty Medical Group, Lafayette, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal ultrasound (MSKUS) is a valuable tool for early detection and management of inflammatory arthritis.(1) Although integrated into rheumatology guidelines, training programs, and classification criteria, its impact on patient perceptions and shared decision-making is underexplored.(2, 3) We hypothesized that MSKUS improves patient understanding of disease and enhances provider confidence in management.

Methods: This prospective cohort study at 2 academic centers enrolled patients with undifferentiated joint pain referred for MSKUS between August 2023 and June 2024. Institutional review board (IRB) approval was obtained at one site and deemed exempt at the other. Patients completed pre- and post-MSKUS visit surveys assessing understanding of joint pain etiology, perceived need for treatment change, evaluation thoroughness, and treatment adherence likelihood. Referring providers completed pre- and post-surveys on MSKUS indication, immunosuppression, confidence in treatment plan, and perceived MSKUS utility. Responses, recorded on a 5-point Likert scale, were analyzed using descriptive statistics and paired t-tests.

Results: A total of 109 patients and 53 provider surveys were analyzed. Table 1 shows the rheumatologic disease diagnoses and MSKUS referral indications. The mean scores and standard deviations (SD) for key outcomes are as follows: Post-MSKUS, understanding of the ultrasound purpose significantly improved, with scores (1 = very poorly, 5 = very well) increasing from 4.339 (SD = 0.841) to 4.688 (SD = 0.588), $p < 0.001$. Understanding of joint pain cause improved, with scores rising from 3.449 (SD = 1.312) to 4.046 (SD = 1.109), $p < 0.001$. Most patients felt their problem had been more thoroughly

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Rheumatologic diagnosis and purpose of musculoskeletal ultrasound (MSKUS) referral.

Table 1a: Breakdown of diagnosis

Diagnosis	n (%)
Rheumatoid arthritis	20.8%
Undiagnosed	17.9%
Osteoarthritis	15.5%
Systemic sclerosis	11.9%
Carpal tunnel syndrome	7.7%
Trigger finger	6.0%
Psoriatic arthritis	4.2%
Fibromyalgia	3.6%
Osteoporosis	3.6%
Gout	3.0%
Sjogren's syndrome	3.0%
Systemic lupus erythematosus	2.4%
De Quervains tenosynovitis	1.8%
Pseudogout	1.8%
Ankylosing spondylitis	1.2%
Reactive arthritis	1.2%
Baker's cyst	0.6%
Juvenile idiopathic arthritis	0.6%
Overlap syndrome	0.6%
Vasculitis	0.6%

Table 1b: Purpose of MSKUS referral

(Percentages >100% due to multiple indications)

Purpose	n (%)
Assess disease activity and/or therapeutic response	39.6%
Help make, confirm, or clarify a specific diagnosis	58.5%
Improve patient's disease understanding, medication compliance, or assist with shared decision making	15%

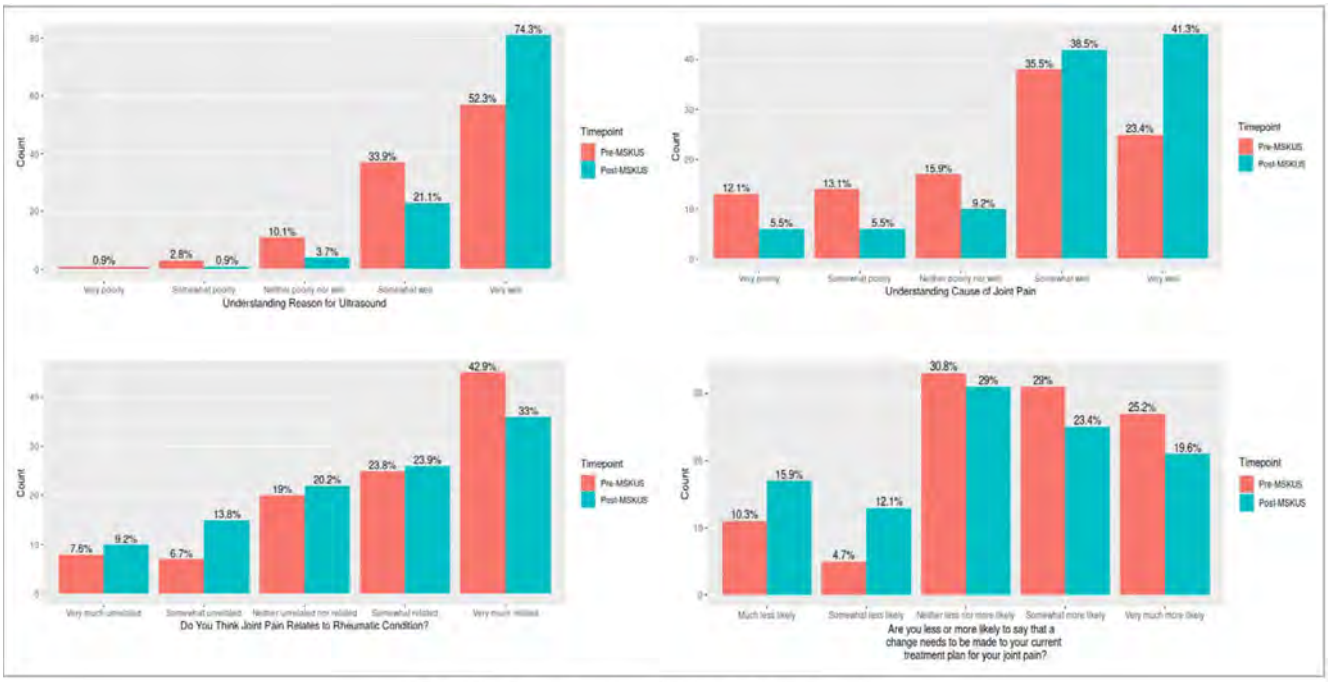


Figure 1: Effect of musculoskeletal ultrasound on patient perceptions

Figure 1: Effect of musculoskeletal ultrasound on patient perceptions.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

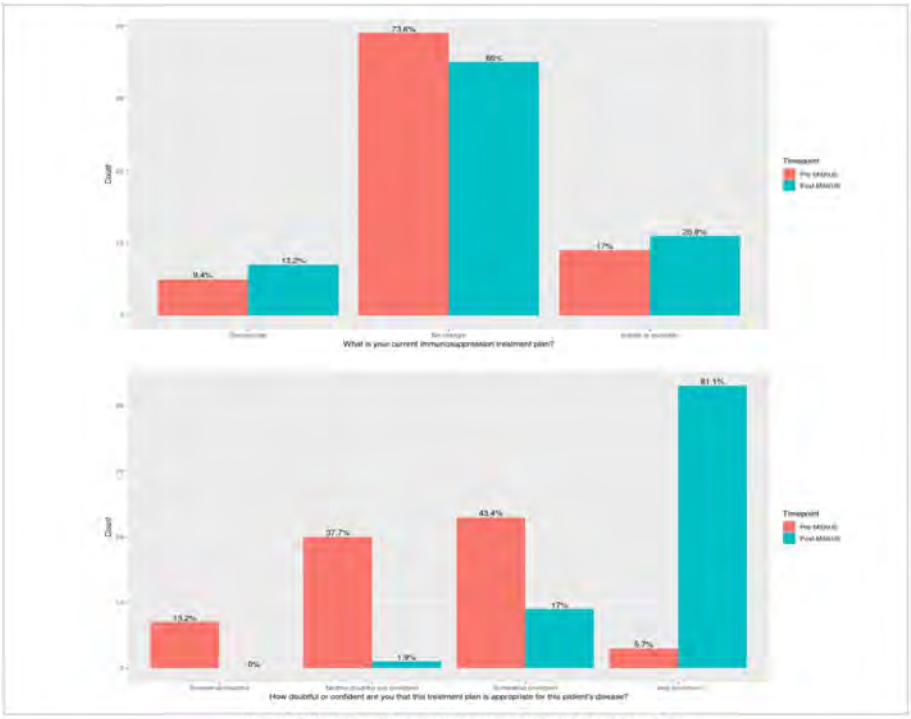


Figure 2: Effect of musculoskeletal ultrasound on provider treatment plans

Figure 2: Effect of musculoskeletal ultrasound on provider treatment plans.

examined (94.4%) and reported to be more likely to adhere to their provider's treatment plan (75.7%). Post-MSKUS, patients were less likely to feel a need for treatment change, with scores (1 = much less likely, 5 = very much more likely) decreasing from 3.542 (SD = 1.215) to 3.187 (SD = 1.326), p = 0.006. There was a modest decline in attributing joint pain to rheumatic disease, with scores (1 = very much unrelated, 5 = very much related) decreasing from 3.876 (SD = 1.253) to 3.578 (SD = 1.321), p = 0.047. Among 15 referring providers reporting on 53 patients referred for MSKUS, confidence in treatment plans increased from 3.415 (SD = 0.795) to 4.792 (SD = 0.454), $p < 0.001$. with 32.1% changing management based on ultrasound findings.

Conclusion: Real-time MSKUS is an effective educational tool that supports shared decision-making and strengthens provider confidence in personalized treatment planning. These findings support its broader integration into routine rheumatologic care.

References

1. Cannella AC KE, Torralba KD, Higgs JB, Kaeley GS. Evolution of musculoskeletal ultrasound in the United States: implementation and practice in rheumatology. Arthritis Care Res 2014.
2.Patil P DB. Role of diagnostic ultrasound in the assessment of musculoskeletal diseases. Musculoskeletal Dis. 2012.
3. Płaza M N-PA, Pracoń G, Sudoł-Szopińska I. Role of ultrasonography in the diagnosis of rheumatic diseases in light of ACR/EULAR guidelines. J Ultrason. 2016.

Disclosure: S. Nimal: None; **M. Balbach**: None; **A. Fawad**: None; **M. Nishio**: None; **E. Chew**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0386

Introducing the Multidimensional Pain Inventory as a Comprehensive Tool or Assessing Pain in Patients With Axial Spondyloarthritis

David Kiefer[1], Yade Sonkaya[2], Dietmar Krause[3], Markus Voglau[4], Bernhard Mintrop[5], Imke Redeker[6], Xenofon Baraliakos[7] and **Uta Kiltz**[7], [1]Ruhr-Universityt Bochum; Private practice of rheumatology, Hattingen, Germany, Herne, Germany, [2]Ruhr-Universität Bochum, Herne, Germany, [3]Elisabeth-Gruppe, Herne, Germany, Essen, Germany, [4]myself, Oldenburg, Germany, [5]Private rheumatology practice, Hattingen, Germany, [6]Ruhr University Bochum, Bochum, Germany, [7]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0357–0386) Patient Outcomes, Preferences, & Attitudes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The West Haven-Yale Multidimensional Pain Inventory (MPI) is a validated tool designed to assess the multidimensional aspects of chronic pain, including the 5 dimensions of pain: pain-related life interference, pain severity, affective distress, social support and life control. Originally developed in the US, the MPI has been successfully adapted and validated in German-speaking populations [1]. Chronic pain in rheumatic diseases often involves nociplastic and central sensitization mechanisms components. Therefore, the MPI, with its biopsychosocial framework, offers an opportunity to explore dimensions of pain in patients with axial spondyloarthritis (axSpA).

Our aim was to assess the construct validity of the MPI by examining its correlations with patient-reported outcomes (PRO) in the Assessment of SpondyloArthritis international Society-Outcomes Measures in Rheumatology (ASAS-OMERACT) core domain set for clinical trials in axSpA [2].

Methods: The five MPI dimensions were assessed in axSpA patients with a pain score ≥ 4 (NRS 0-10) and results were correlated with the ASAS-OMERACT core domain set, including disease activity (ASDAS, CRP, BASDAI, patient global assessment (PtGA) of disease activity, physical function (BASFI), health-related quality of life (ASAS Hi, of the SF36 MCS/PCS), total back pain, morning stiffness, and spinal mobility (BASMI) as well as demographic and clinical data using Pearson´s correlations. Correlations were classified as weak (r≥0.1), moderate (r≥0.3), and strong (r≥0.5).

Results: 136 patients with axSpA were included and the MPI was completed by 109 (80.2%) patients (table 1). Pain-related life interference showed significant strong correlations with ASDAS, BASDAI, BASFI, PCS, fatigue and total back pain while moderate correlations were found for PtGA of disease activity, MCS, morning stiffness, and BASMI. For pain severity, significant strong correlations were observed with ASDAS, BASDAI and total back pain. Moderate correlations were found with PtGA of disease activity, BASFI, PCS and fatigue, weak correlations were found with MCS, ASAS HI and morning stiffness. Affective distress showed strong correlations only with MCS and weak or moderate correlations with all other assessments, while social support only showed a weak correlation with the PCS and the BASMI. For life control, a strong positive correlation was only found with MCS whereas moderate negative correlations were found with PtGA of disease activity and total back pain and weak negative correlations with ASDAS, BASDAI, BASFI, ASAS HI and fatigue.

Conclusion: The MPI provides valuable insights into the multidimensional aspects of pain in axSpA. Pain-related life interference and severity demonstrated strong correlations, while affective distress and life control showed weak to moderate correlations with the ASAS core domain set and thereby demonstrating construct validity. Apart from a weak correlation of social support with the PCS, the domains of social support and life control are not yet fully captured in the axSpA core domain set or other commonly used PROs in axSpA trials.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic and clinical data of baseline patients

Characteristics		n=136
Age (years)		48.7 (11.9)
Gender female, n (%)		63 (46.4)
Time (years) since axSpA symptoms		19.2 (13.8)
Time (years) since axSpA diagnosis		14.1 (12.9)
BMI, kg/m^2		28.8 (6.7)
CRP, mg/dl		0.6 (1.1)
HLA-B 27, n (%)		90 (66.1)
Charlson Comorbidity Index, 0-29		1.1 (1.3)
NSAID index, 0-100		18.9 (29.6)
No. of patients on csDMARD, n (%)		8 (5.9)
No. of patients on bDMARD, n (%)		89 (65.5)
No. of patients on tsDMARD, n (%)		10 (7.4)
MPI(D)	Pain severity (0-6)	3.6 (1.2)
	Pain-related life interference (0-6)	3.5 (1.1)
	Affective distress (0-6)	3.2 (1.2)
	Social support (0-6)	3.6 (1.7)
	Life control (0-6)	3.6 (1.1)
ASDAS, 0-10		2.8 (0.8)
BASDAI, 0-10		5.3 (1.8)
Fatigue (BASDAI 1), 0-10		6.5 (2.3)
Morning stiffness (BASDAI 5+6), 0-10		4.4 (2.7)
Total back Pain (BASDAI 2), 0-10		6.1 (2.0)
Patient global assessment (PtGA) of disease activity, 0-10		5.0 (2.2)
BASFI, 0-10		4.8 (2.3)
SF-36 (PCS), 0-100		33.0 (7.9)
SF-36 (MCS), 0-100		41.8 (12.6)
ASAS Health Index, 0-17		8.1 (3.6)
BASMI, 0-10		3.2 (1.5)

Values are presented as mean (standard deviation), unless otherwise indicated; ASAS: Assessment of Spondyloarthritis International Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; NRS: Numerical rating scale; NRS; NSAID: Nonsteroidal anti-inflammatory drug; MPI (D): Multidimensional Pain Inventory; HADS: Hospital Anxiety and Depression Scale; FIQ: Fibromyalgia Impact Questionnaire: PAM 13: Patient Activation Measure-13

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Correlations of MPI domains with axSpA assessments

Characteristics	Pain-related life interference	Pain severity	Affective distress	Social support	Life control
Age (years)	0.09	0.05	-0.13	-0.03	0.05
Time (years) since axSpA symptoms	0.13	0.05	-0.08	0.01	-0.02
Time (years) since axSpA diagnosis	0.03	0.03	-0.06	-0.01	0.01
BMI, kg/m²	0.21*	0.16	0.04	0.01	0.03
CRP, mg/dl	0.04	0.03	0.05	0.05	-0.1
Charlson Comorbidity Index, 0-29	0.13	0.17	-0.19*	-0.15	0.13
NSAID index, 0-100	0.02	-0.01	-0.09	0.14	-0.05
No. of previous b-DMARDs	0.05	0.12	-0.04	0.14	0.14
ASDAS, 0-10	0.55**	0.5**	0.32**	0.08	-0.27**
BASDAI, 0-10	0.7**	0.55**	0.4**	0.1	-0.29**
Fatigue (BASDAI 1), 0-10	0.55**	0.4**	0.4**	0.02	-0.24*
Morning stiffness (BASDAI 5+6), 0-10	0.39**	0.27**	0.19	0.13	-0.16
Total back Pain (BASDAI 2), 0-10	0.59**	0.52**	0.38**	0.12	-0.3**
Patient global assessment of disease activity	0.43**	0.4**	0.32**	0.02	-0.31**
BASFI, 0-10	0.59**	0.4**	0.33**	0.2*	-0.27**
SF-36 (PCS), 0-100	-0.52**	-0.33**	-0.18	-0.25**	0.15
SF-36 (MCS), 0-100	-0.44**	-0.27**	-0.64**	0.12	0.5**
ASAS Health Index, 0-17	0.54**	0.26**	0.47**	-0.09	-0.29**
BASMI, 0-10	0.36**	0.22*	0.18	0.27*	-0.1

Values are presented as correlation coefficient (r) and p-value; ASAS: Assessment of Spondyloarthritis International Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; NSAID: Nonsteroidal anti-inflammatory drug

**Correlation is significant at the 0.01 level *Correlation is significant at the 0.05 level

Disclosure: D. Kiefer: AbbVie/Abbott, 2, 5, Alpha sigma, 2, 6, UCB, 1, 2, 6; **Y. Sonkaya**: None; **D. Krause**: None; **M. Voglau**: None; **B. Mintrop**: None; **I. Redeker**: None; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0387

Association Between Juvenile Arthritis and Physical Activity Levels in U.S. Children: A Cross-sectional Study Using the 2016–2021 National Survey of Children's Health

William Soulsby[1] and **Carolina Tamashiro**[2], [1]University of California, San Francisco, San Francisco, CA, [2]UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile arthritis (JA) is characterized by joint pain, stiffness, and decreased mobility, potentially affecting participation in physical activity (PA). Current guidelines from the CDC and WHO recommend that children engage in at least 60 minutes of PA daily. While research in PA level and JA has been conducted in European countries, data on physical activity levels among children with arthritis in the United States remain limited. It is not well understood whether U.S. children with arthritis meet recommended PA targets or how PA engagement relates to their broader health outcomes. This study aims to assess whether a current diagnosis of arthritis is associated with lower PA levels among a nationally representative sample of U.S. children and adolescents.

Methods: This cross-sectional analysis assessed adherence to daily PA recommendations among U.S. children with JA compared to peers without JA, using 2016–2021 National Survey of Children's Health (NSCH) data, a nationally representative survey that investigates health of pediatric population in the U.S. Univariable and multivariable logistic regression models examined the association between JA and meeting daily PA recommendations. A sensitivity analysis using ordinal logistic regression assessed PA frequency ("0 days," "1–3," "4–6," "daily"). Models were adjusted for potential confounders like age, sex, race, ethnicity, and socioeconomic status.

Results: Children with JA were less likely to meet daily PA recommendations than peers without arthritis (13.5% vs. 17.0%; $p = 0.05$) and had higher rates of obesity (23.3% vs. 13.9%; $p < 0.001$), physical limitations, pain (69.9% vs. 10.3%; $p < 0.001$) and comorbidities (55.2% vs. 30.6%; $p < 0.001$). However, in adjusted analyses, arthritis was not significantly associated with meeting PA guidelines (aOR = 1.34; 95% CI: 0.78–2.32; $p = 0.29$). Similarly, arthritis was not significantly associated with PA level in ordinal logistic regression (aOR = 1.17; 95% CI: 0.81–1.69; $p = 0.41$). Female sex, older age, presence of mental health conditions, and obesity (aOR for ≥95th percentile = 0.64; 95% CI: 0.52–0.78), were negatively associated with PA. Sports participation was strongly associated with meeting guidelines for PA (aOR = 1.58; 95% CI: 1.44–1.74; $p < 0.001$)

Conclusion: In a large nationally representative U.S. sample, children and adolescents with and without arthritis demonstrated low adherence to the CDC and WHO-recommended PA levels. Overall, arthritis was not found to be a statistically significant predictor of PA levels in unadjusted or adjusted analyses. These findings might suggest that while arthritis poses challenges, it may not be a key independent barrier to PA. Efforts to increase PA should address modifiable barriers like obesity and mental health, and promote sports participation, especially among older children with JA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

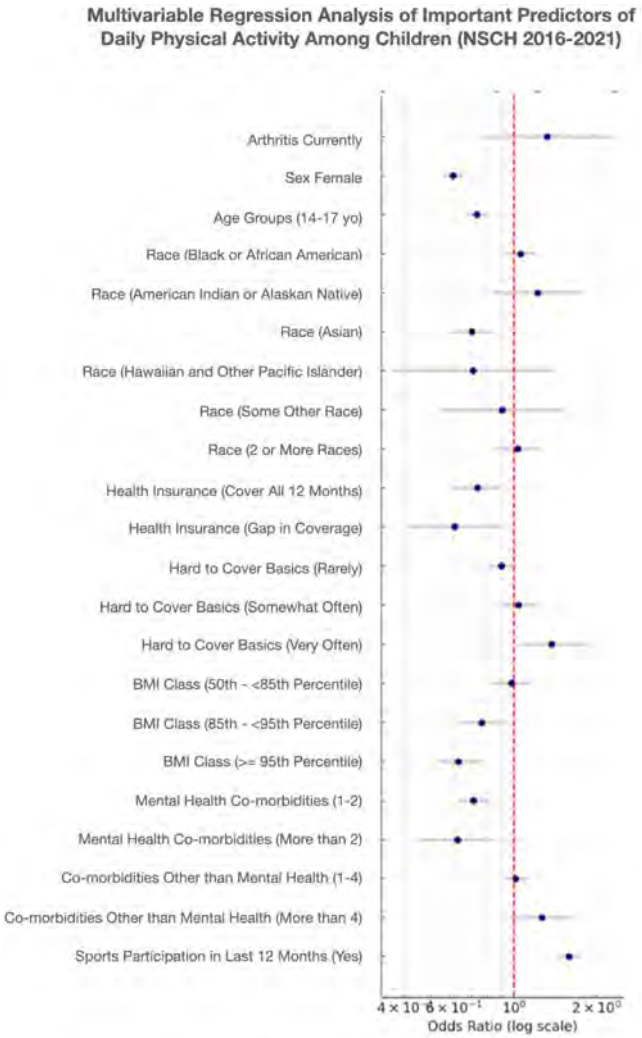
Table 1: Sociodemographic and clinical characteristics of children and adolescent participants in the National Survey of Children's Health (NSCH) from 2016-2021

		No Arthritis (N=85,153)	Arthritis (N=469)	p-value
Sex	Male	44,263 (52.0%)	184 (39.2%)	<0.001
	Female	40,890 (48.0%)	285 (60.8%)	
Age group (years)	10-13	37,861 (44.5%)	132 (28.1%)	<0.001
	14-17	47,292 (55.5%)	337 (71.9%)	
Race	White	65,847 (77.3%)	374 (79.7%)	0.001
	Black or African American	6,365 (7.5%)	47 (10.0%)	
	American Indian or Alaska Native	862 (1.0%)	7 (1.5%)	
	Asian	4,681 (5.5%)	6 (1.3%)	
	Native Hawaiian or Other Pacific Islander	462 (0.5%)	2 (0.4%)	
	Some other race alone	769 (0.9%)	3 (0.6%)	
	Two or more races	6,167 (7.2%)	30 (6.4%)	
Parental nativity	1st generation household	1,962 (2.3%)	5 (1.1%)	<0.001
	2nd generation household	12,736 (15.2%)	30 (6.5%)	
	3rd generation household	64,508 (77.0%)	383 (83.4%)	
	Other (parents are not listed)	4,621 (5.5%)	41 (8.9%)	
Highest level of parental education	Less than high school	2,545 (3.0%)	21 (4.5%)	<0.001
	High school	11,957 (14.0%)	91 (19.6%)	
	More than high school	70,649 (83.0%)	352 (75.9%)	
Health insurance coverage in the past 12 months	No	3,330 (3.9%)	19 (4.1%)	0.60
	Yes, covered all 12 months of the year	79,479 (93.7%)	430 (92.9%)	
	Yes, gap in coverage in last 12 months	1,974 (2.3%)	14 (3.0%)	
Hard to cover basics (e.g. food, housing)	Never	44,343 (53.1%)	142 (31.2%)	<0.001
	Rarely	28,185 (33.8%)	160 (35.2%)	
	Sometimes	8,861 (10.6%)	93 (20.4%)	
	Very Often	2,110 (2.5%)	60 (13.2%)	
Neighborhood has a park/playground	No	22,791 (27.4%)	143 (31.4%)	0.054
	Yes	60,413 (72.6%)	312 (68.6%)	
Neighborhood has sidewalks and walking paths	No	23,617 (28.3%)	149 (32.5%)	0.046
	Yes	59,757 (71.7%)	309 (67.5%)	
Child is safe in neighborhood	Definitely agree	59,440 (71.6%)	296 (65.2%)	<0.001
	Somewhat agree	21,028 (25.3%)	131 (28.9%)	
	Somewhat disagree	1,867 (2.2%)	14 (3.1%)	
	Disagree	682 (0.8%)	13 (2.9%)	
Child participates in sports team/lessons in the past 12 months	No	33,642 (40.1%)	247 (53.7%)	<0.001
	Yes	50,157 (59.9%)	213 (46.3%)	
Child participates in physical activity for at least 60 minutes per day	0 days of the week	9,996 (11.9%)	98 (21.4%)	<0.001
	1-3 days of the week	35,048 (41.7%)	178 (38.9%)	
	4-6 days of the week	24,801 (29.5%)	120 (26.2%)	
	Every day of the week	14,282 (17.0%)	62 (13.5%)	
BMI, Percentile	<5th percentile	5,235 (6.4%)	31 (7.0%)	<0.001
	5th – 85th percentile	53,427 (65.0%)	232 (52.4%)	
	85th – 95th percentile	12,129 (14.7%)	77 (17.4%)	
	≥95th percentile	11,449 (13.9%)	103 (23.3%)	
Number of comorbidities [a] (excluding mental health conditions)	None	57,147 (67.1%)	145 (30.9%)	<0.001
	1-4	26,035 (30.6%)	259 (55.2%)	
	More than 4	1,971 (2.3%)	65 (13.9%)	
Number of mental health comorbidities [b]	None	67,913 (79.8%)	252 (53.7%)	<0.001
	1-2	15,389 (18.1%)	177 (37.7%)	
	More than 2	1,851 (2.2%)	40 (8.5%)	

[a] Comorbidities included: Asthma, Brain injury, Cerebral palsy, Diabetes, Epilepsy, Cardiac diseases, Headache, Down syndrome, Cystic fibrosis, Hematological disorders, Genetic disorders, Developmental delay, Intellectual disability, Speech delay, Learning disability, Autism spectrum disorder, Attention-Deficit/Hyperactivity disorder

[b] Mental Health Comorbidities included: Anxiety, Depression, Substance Abuse, Behavior Problems

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot

Disclosure: W. Soulsby: None; **C. Tamashiro**: None.

Abstract Number: 0388

A Scoping Review of Outcomes of Adults with Childhood-onset Systemic Autoimmune Rheumatic Diseases

Michael Moore[1], **Kaien Gu**[2], Carol Cooke[1], Annaliese Tisseverasinghe[1] and Lily Lim[1], [1]University of Manitoba, Winnipeg, MB, Canada, [2]Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic autoimmune rheumatic diseases (SARD) include systemic lupus erythematous (SLE), idiopathic inflammatory myositis (IIM), systemic sclerosis (SSc), Sjögren syndrome (SS), and systemic vasculitis (SV). Patients with childhood-onset SARD (ChildSARDs) develop disease during years of growth and organ maturation, which can result in unique influences on outcomes. We aim to assess disease outcomes of adults with ChildSARDs.

Methods: With an academic librarian, we developed a peer-reviewed search strategy using MEDLINE and Embase for English articles (1 January 1990 to 30 June 2023). We tested our searches against 26 known articles on adult outcomes in ChildSARDs to confirm and refine search coverage. Childhood-onset of disease was defined by authors (< 14-18 years old). Studies with mixed populations (e.g. adolescent-adult, childhood, adult-onset) were excluded if: i) ChildSARDs adult outcomes were not reported separately, ii) studies primarily focused on non-clinical outcomes. Studies were graded for risk-of-bias using the Quality in Prognosis Studies (QuiPS) tool. Two reviewers independently graded studies before meeting to reach consensus. Any disputes were resolved by a third reviewer.

Results: The search identified 6848 papers, of which 40 met study criteria. No study meeting criteria was published before 2000, 4 (10%) between 2001-2010, 24 (60%) between 2011-2020, and 12 (30%) between 2021-2024. Most studies were conducted in Europe (43%) and North America (28%). 60% of studies were SLE, 25% IIM, 8% SSc, 5% SV, and 0% SS. 27 (68%) publications were cross-sectional in design. Commonly reported outcomes included disease activity (48%), accumulated damage (40%), cardiovascular (33%), and mortality (23%). Mean disease duration ranged from 5.5-23.9 years (N=18), and median disease duration ranged from 8.08-29 years (N=11). QuiPS identified a moderate to high risk-of-bias in the following domains: 95% of study participation, 92% of study attrition (N=13, non-cross-sectional studies), 40% of prognostic factors, 70% of outcomes, 95% of confounding, 73% of statistical analysis.

Conclusion: There is growing interest in adult outcomes of ChildSARDs but data is still relatively scarce. The majority of studies demonstrated moderate to high risk-of-bias in multiple study domains. Researchers should commit to reporting outcomes using standard disease outcome measurements to help accumulate evidence. Investigators planning studies of adult outcomes of ChildSARDs should consider bias reduction measures during the design stage and acknowledge limitations where biases cannot be substantially reduced. Readers should be aware of design limitations when interpreting results from current studies.

Disclosure: M. Moore: None; **K. Gu**: None; **C. Cooke**: None; **A. Tisseverasinghe**: None; **L. Lim**: Pfizer, 12, Speaker.

Abstract Number: 0389

An International Delphi Survey for the Definition of New Classification Criteria for Juvenile Idiopathic Arthritis

Alessandra Alongi[1], Hermine Brunner[2], Angelo Ravelli[3], Tadej Avcin[4], Michael Beresford[5], RUBEN BURGOS-VARGAS[6], Ruben Cuttica[7], Raju Khubchandani[8], Ronald laxer[9], Seza zen[10], Ross Petty[11], Carol Wallace[12], Nico Wulffraat[13], Silvia Magni-Manzoni[14], Marija Jelusic[15], Alessandro Consolaro[16], Jordi anton[17], Gerd Horneff[18], Mia Glerup[19], Giovanni Filocamo[20], Gabriele Simonini[21], ADELE CIVINO[22], Agustin Remesal[23], Silvia Scala[24], Angela Pistorio[25], Daniel Lovell[2], Alberto Martini[26] and **Nicolino Ruperto**[27], For the Pediatric Rheumatology International Trials Organization (PRINTO) and the Pediatric Rheumatology Collaborative Study Group, [1]Università Milano Bicocca, Milan, Italy, Milano, Italy, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genoa, Genoa, Italy, [4]University Children's Hospital, University Medical Center Ljubljana, Ljubljana, Slovenia, [5]Alder Hey Children's NHS Foundation Trust Hospital, Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [6]Department of Rheumatology, Hospital General de Mexico, Faculty of Medicine, Universidad Nacional Autonoma de Mexico, Ciudad de Mxico, Mexico, [7]Hospital Pedro de Elizalde, Buenos Aires, Argentina, [8]Jaslok Hospital and Research Center, Mumbai, India, [9]The Hospital for Sick Children, Toronto, ON, Canada, [10]Hacettepe University Medical Faculty, Ankara, Turkey, [11]British Columbia Children's Hospital, University of British Columbia, Vancouver, ON, Canada, [12]Seattle Children's Hospital, University of Washington,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Seattle, WA, [13]Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, Netherlands, [14]Bambino Gesù IRCCS Children's Hospital, Rome, Italy, [15]University Hospital Centre Zagreb, Zagreb, Croatia, [16]IRCCS Istituto Giannina Gaslini, Genoa, Italy, [17]Hospital Sant Joan de Du. Universitat de Barcelona, Barcelona, Spain, [18]Asklepios Klinik, Hamburg, Germany, [19]Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark, [20]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [21]Rheumatology Unit, ERN-ReCONNET center, Meyer Children's Hospital IRCCS, Firenze, Firenze, Italy, [22]Department of Pediatric Immunology and Rheumatology, LECCE, Italy, [23]Hospital Universitario La Paz, Madrid, Spain, [24]Clinica Pediatrica e Reumatologia, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [25]Servizio di Epidemiologia e Biostatistica, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [26]Università degli Studi di Genova, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [27]Universit Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To improve the current classification criteria for juvenile idiopathic arthritis (JIA), a multi-step initiative coordinated by PRINTO was launched in 2015, starting with a consensus process that culminated in the proposal of the preliminary PRINTO JIA classification criteria. The steps include a large-scale prospective data collection of patients with new-onset JIA and the ongoing validation of evidence-based criteria. To initiate the validation phase, an international Delphi survey was conducted among pediatric rheumatologists to identify the most relevant categories and candidate variables for subsequent data collection.

To identify consensus-based categories and variable sets for the evidence-based revision of JIA classification criteria.

Methods: An invitation to participate in two Delphi rounds was sent to PRINTO/PRCSG membership starting in 2020.

In Round 1, participants evaluated each ILAR category plus the additional category 'Early Onset ANA Positive Arthritis', indicating whether to retain or discard it, and suggesting revised names. They also listed variables used in practice to diagnose each category.

In Round 2, participants re-evaluated each category for retention and ranked the top three preferred names and the ten most useful variables for the category-specific diagnosis among those identified in Round 1. Based on the ranking, a median score for each variable was calculated. Variables falling above the 75th percentile of the score were identified for each category.

Results: 434 physicians responded in Round 1 and 884 in Round 2. Votes to retain the ILAR categories were 236 (73%) for Systemic arthritis, 218 (70%) for Oligoarthritis, 209 (69%) for Polyarthritis Rheumatoid Factor (RF) negative, 276 (92%) for Polyarthritis RF positive, 188 (66%) for Psoriatic arthritis, 225 (78%) for Enthesitis-related arthritis (ERA), 183 (67%) for Early-onset ANA-positive JIA, and 142 (53%) for Other arthritis.

Top ranking labels for each new category were 'Juvenile-onset Still disease', 'Oligoarticular JIA', 'Juvenile polyarthritis', 'JIA RF positive or anti-CCP positive', 'Juvenile psoriatic arthritis', 'Early onset spondyloarthritis', 'ANA positive juvenile arthritis' and 'Unclassified JIA'.

The variables identified as most useful for the diagnosis (in the top quartile of the score) were 15 for Systemic arthritis, 31 for Oligoarthritis, 33 for Polyarthritis RF negative, 33 for Polyarthritis RF positive, 45 for ERA, 26 for Psoriatic arthritis, 27 for Early-onset ANA-positive JIA and 19 for Other arthritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The study yielded consensus-based categories to be considered in the new classification criteria and identified candidate variables to be included in the ongoing step of the project, namely the evidence-based validation of new classification criteria for JIA based on real new-onset patients' data.

Disclosure: A. Alongi: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **A. Ravelli**: AbbVie, 2, 5, 6, Alexion, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, SOBI, 2, 5, 6; **T. Avcin**: Novartis, 6, Octapharma, 1, 6, Pfizer, 6, Takeda, 6; **M. Beresford**: Novartis, 5; **R. BURGOS-VARGAS**: None; **R. Cuttica**: None; **R. Khubchandani**: None; **R. laxer**: Akros pharma, 2, Eli Lilly Canada, 2, Novartis, 2, Sanofi, 2; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **R. Petty**: None; **C. Wallace**: None; **N. Wulffraat**: None; **S. Magni-Manzoni**: None; **M. Jelusic**: None; **A. Consolaro**: None; **J. anton**: Sobi, 1, 5, 6; **G. Horneff**: Janssen, 5, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, Sanofi, 6; **M. Glerup**: None; **G. Filocamo**: None; **G. Simonini**: None; **A. CIVINO**: None; **A. Remesal**: None; **S. Scala**: None; **A. Pistorio**: None; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **A. Martini**: None; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6.

Abstract Number: 0390

Radiographic Assessment in Juvenile Spondyloarthritis: Evaluating the axJSpA Criteria Using Radiographs Alone Versus MRI

David M. Biko[1], Nancy A. Chauvin[2], Michael Francavilla[3], Nele Herregods[4], Walter P. Maksymowych[5], Robert G. W. Lambert[6], Timothy Brandon[1], Ozgur Kasapcopur[7], Mehmet YILDIZ[8], Hemalatha Srinivasalu[9], **Pamela Weiss**[10] and the Juvenile Axial Spondyloarthritis Research Taskforce (JAxSpRT), [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]The Cleveland Clinic, Hummelstown, PA, [3]Department of Pediatric Radiology, Children's Hospital Philadelphia, Philadelphia, PA, [4]Ghent University Hospital, Ghent, Belgium, [5]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [6]University of Alberta, Department of Radiology & Diagnostic Imaging, Edmonton, AB, Canada, [7]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey, [8]Istanbul University-Cerrahpasa Department of Pediatric Rheumatology, Istanbul, Turkey, [9]Children's National Hospital, Washington, DC, [10]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Radiographs are neither sensitive nor reliable for assessing axial disease in juvenile spondyloarthritis (JSpA), though they are still used in some settings due to limited access to magnetic resonance imaging (MRI). The recently validated axial JSpA (axJSpA) classification criteria include inflammatory and structural imaging domains. When both imaging modalities are available, MRI findings are prioritized over radiographic data in the structural domain. This study evaluated the performance of the axJSpA criteria when using pelvic radiographs alone and compared these results with those based on MRI.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective analysis of an international cohort of patients with JSpA and symptom onset before age 18. All participants underwent anteroposterior (AP) pelvic radiography and dedicated pelvic MRI during axial disease evaluation. A centralized panel independently reviewed cases for unequivocal sacroiliitis: structural lesions on radiograph and both inflammatory and/or structural lesions on MRI typical of axial disease (Table 1). Imaging criteria were considered met when the majority of raters agreed. Agreement between radiograph- and MRI-defined structural lesions was assessed using Cohen's kappa coefficient. For each subject, fulfillment of the axJSpA criteria was assessed using MRI data and radiographic data alone, in addition to non-imaging domains. For the assessment of radiographic data alone, the inflammatory lesions on imaging domain for criteria defaulted to a score of "0".

Results: A total of 137 subjects (59.1% male; median age 14.3 years) were included. Imaging criteria were met in 40 (29.2%) cases for MRI-defined inflammatory lesions, 33 (24.1%) for MRI-defined structural lesions, and 29 (21.2%) for radiographic sacroiliitis. Agreement between MRI- and radiograph-defined structural lesions yielded a kappa coefficient of 0.54, indicating moderate concordance (Table 2). Using MRI data, 40 subjects met axJSpA classification criteria, compared to 12 using radiographic data alone. Relying on radiographic findings altered classification status in 32 (23.4%) subjects, with 2 additional cases meeting criteria and 30 cases no longer fulfilling them (Figure 1).

Table 1. Validated definitions for axJSpA Imaging Classification Criteria.

Imaging type	AxJSpA Classification Criterion	Definition
Pelvic Radiograph	Unequivocal sacroiliitis in skeletally immature youth	Unequivocal lesion (erosion, sclerosis, or ankylosis [partial or complete]) that must include at least one iliac bone. When sclerosis is present in isolation, if measurable, should extend ≥5mm from the joint surface. The decision may be influenced by the presence of other lesions, which in themselves do not suffice to meet the criterion.
Pelvic MRI	Unequivocal inflammatory lesion typical of axJSpA	Bone marrow edema in ≥3 SIJ quadrants across all SIJ MRI slices
Pelvic MRI	Unequivocal structural lesion typical of axJSpA	Erosion in at least 3 quadrants *or* at least one of the following lesions in at least 2 SIJ quadrants across all SIJ MRI slices: sclerosis, fat lesion, backfill, ankylosis

Table 2. Agreement between radiograph- and MRI-defined structural lesions.

		Unequivocal sacroiliitis on radiograph	
		No	Yes
Unequivocal SIJ structural lesions on MRI	No	95	9
	Yes	13	20

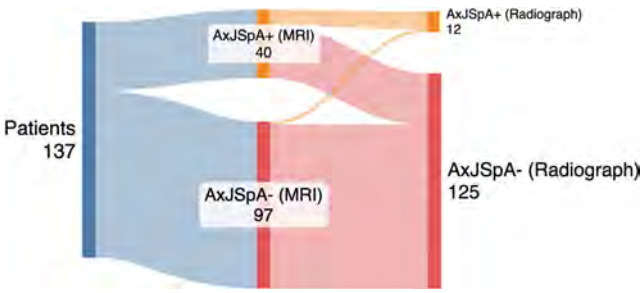


Figure 1. Re-classification of axJSpA status using MRI and radiograph as sources for imaging domain weighting. Patient classification by axJSpA status using the different imaging modality combinations were AxJSpA+ (MRI)/AxJSpA+ (Radiograph): n=10, AxJSpA+ (MRI)/AxJSpA- (Radiograph): n=30, AxJSpA- (MRI)/AxJSpA+ (Radiograph): n=2, and AxJSpA- (MRI)/AxJSpA- (Radiograph): n=95. Using radiograph-only data excluded scoring from the inflammatory lesions domain. AxJSpA+ = axial juvenile spondyloarthritis classification criteria met; AxJSpA- = axial juvenile spondyloarthritis classification criteria not met.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Although pelvic radiographs moderately align with MRI in identifying structural lesions, reliance on radiographic findings alone can misclassify a subset of patients under the axJSpA criteria. These findings underscore the importance of obtaining and prioritizing MRI for accurate classification and assessment of axial disease in JSpA when available. Nevertheless, in settings where MRI is unavailable, the criteria still perform reasonably when based solely on radiographic findings, supporting their utility in resource-limited contexts.

Disclosure: D. Biko: None; **N. Chauvin**: None; **M. Francavilla**: None; **N. Herregods**: None; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Lambert**: AbbVie, 2, CARE Arthritis and Image Analysis Group, 2; **T. Brandon**: None; **O. Kasapcopur**: None; **M. YILDIZ**: None; **H. Srinivasalu**: Otsuka, 3; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

Abstract Number: 0391

Which score fits best? Correlation of clinical indices of Disease Activity and Ultrasound findings in Juvenile Idiopathic Arthritis during Transitional Care

Andrea Pilato[1], Giusyda Tarantino[2], Maria Isabella Petrone[2], Angela Aquilani[2], Emiliano Marasco[2], Rebecca Nicolai[2], Fabrizio De Benedetti[3], Roberto Giacomelli[4], Luca Navarini[1] and **Silvia Magni-Manzoni**[2], [1]University of Rome Campus Bio-Medico, Rome, Italy, [2]Bambino Gesù IRCCS Children's Hospital, Rome, Italy, [3]Bambino Gesu Children's Hospital, Rome, Rome, Italy, [4]i) Clinical and Research Section of Rheumatology and Clinical Immunology, Fondazione Policlinico Campus Biomedico; ii) Rheumatology and Clinical Immunology, Department of Medicine, School of Medicine, University of Rome "Campus Bio-Medico", Rome, Italy

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Monitoring disease activity is a crucial aspect of the treat to target paradigm in the management of rheumatic diseases. There are no standardized protocols for monitoring disease activity levels in patients with Juvenile Idiopathic Arthritis (JIA) during the transition of care.

The aim of this study is to compare different disease activity indices for all JIA category (excluding systemic JIA), to evaluate their discriminative validity in a real-life setting.

Methods: Young adult JIA patients eligible for transition of care underwent a prospective clinical evaluation by both paediatric and adult rheumatologists. Disease activity was assessed using validated clinical indices. The cJADAS, JADAS10, JADAS27, and JADAS71 were applied to all patients. SDAI, CDAI, and DAS28 were used for persistent oligoarticular (oJIA-p), extended oligoarticular (oJIA-e), and RF-positive and RF-negative polyarticular JIA (polyJIA RF^-/RF^+). The DAPSA was applied to patients with juvenile psoriatic arthritis (JPsA), while jSPADA, ASDAS-CRP, and BASDAI were used for patients with enthesitis-related arthritis (ERA). Ultrasound data were collected as an additional marker of articular inflammation in all cases of clinical suspicion of arthritis or for disease monitoring, to detect active synovitis according to OMERACT paediatric definitions. Spearman's rank correlation was used to assess associations between the disease activity indices. ROC analyses were used to compare the ability of different clinical indices to reflect ultrasound-detected synovitis in selected JIA subgroups. Statistical analysis was performed using R software (version 4.5.0, released April 11, 2025; R Core Team).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of the study cohort (total N = 124)

Age, years, median (IQR)	19 (17-23)
Sex, no. (%)	
Female	93 (75.6)
Male	30 (24.4)
JIA category, no. (%)	
Persistent oligoarthritis	27 (22)
Extended oligoarthritis	40 (32.5)
RF-positive Polyarticular JIA	4 (3.3)
RF-negative Polyarticular JIA	23 (18.7)
ERA	9 (7.3)
jPsA	19 (15.4)
Undifferentiated	1 (0.8)
Patients on csDMARDs, no. (%)	67 (54.5)
Patients on bDMARDs, no. (%)	90 (73.2)
Patients on combination therapy, no. (%)	52 (42.3)
Patients undergoing ultrasound, no. (%)	105 (84.7)
Number of joints assessed per patient, median (IQR)*	4 (3-27)
Ultrasound-detected synovitis, no. (%)	53 (43)

*The number of joints assessed refers to each individual joint scanned (e.g., MCP, PIP, and DIP joints counted separately). This approach may result in higher counts in patients with detailed hand or foot examinations.

Table 2. Summary of Disease Activity indices by JIA category. Values are expressed as median (IQR), except where indicated. RF: rheumatoid factor; PCR: C-reactive protein.

Disease Activity Index	Median (IQR)
Extended oligoarticular and RF-negative polyarticular JIA	Total N=73
cJADAS	2.50 (1.25–5.00)
JADAS10-PCR	2.50 (1.25–5.40)
JADAS27-PCR	2.50 (1.25–5.40)
JADAS71-PCR	2.57 (1.49–5.72)
DAS28	1.89 (1.42–2.41)
SDAI	3.20 (1.49–7.03)
CDAI	3.00 (1.00–6.50)
Persistent oligoarticular JIA	Total N=27
cJADAS	2.00 (0.50–8.50)
JADAS10-PCR	3.00 (0.73–8.50)
JADAS27-PCR	3.00 (0.73–8.50)
JADAS71-PCR	3.19 (1.12–8.75)
DAS28	1.96 (1.53–2.74)
CDAI	2.00 (0.50–9.00)
SDAI	3.40 (1.12–9.28)
jPsA	Total N=19
cJADAS	3.50 (2.25–5.50)
JADAS10-PCR	3.80 (2.25–5.50)
JADAS27-PCR	3.80 (2.25–5.50)
JADAS71-PCR	4.03 (2.38–5.83)
DAPSA	5.03 (2.13–10.67)
ERA	
jSpADA, median (IQR)	1.00 (0.00–2.50)
BASDAI, mean ± SD	2.58 ± 2.25
ASDAS-PCR, mean ± SD	1.37 ± 0.85

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Comparison of AUC values of the Disease Activity indices by JIA subgroups.

Comparison AUC values for oJIA-e and polyJIA-FR- group	
Indices	**AUC**
cJADAS	0.836
JADAS10-PCR	0.837
JADAS27-PCR	0.837
JADAS71-PCR	0.844
SDAI	0.845
CDAI	0.803
Comparison AUC values for oJIA-p group	
cJADAS	0.935
JADAS10-PCR	0.926
JADAS27-PCR	0.926
JADAS71-PCR	0.926
CDAI	0.926
SDAI	0.932
Comparison AUC values for JPsA group	
cJADAS	0.744
JADAS10-PCR	0.744
JADAS27-PCR	0.744
JADAS71-PCR	0.784
DAPSA	0.818

Results: A total of 124 JIA patients were included (median age 19 years, IQR 17–23). Disease activity was highest in jPsA (N=19; median JADAS10 3.8, DAPSA 5.0), compared to lower values in oJIA-e/polyJIA RF$^-$ (JADAS10 2.5) and oJIA-p (JADAS10 3.0). In oJIA-p, oJIA-e, and polyJIA RF$^-$, strong correlations were observed among JADAS scores, CDAI, and SDAI ($\rho > 0.87$; $p < .001$), with slightly lower values for DAS28. In the jPsA subgroup, a moderate-to-strong correlation was observed between JADAS scores and DAPSA ($\rho \approx 0.87$, $p < .001$). In ERA, jSpADA correlated moderately with ASDAS-PCR ($\rho = 0.51$; $p = 0.161$), but not with BASDAI.

Ultrasound was performed in 84.7% of patients, with a total of 1612 assessed joints. In oJIA-e and polyJIA RF$^-$, JADAS71-PCR and SDAI yielded the highest AUCs (0.844–0.845) for ultrasound-detected synovitis. In oJIA-p, all indices performed well (AUCs ≥ 0.926). In jPsA, DAPSA showed the best discrimination (AUC 0.818).

Conclusion: In this real-life transition cohort, both paediatric (JADAS scores and jSPADA) and adult-derived indices (SDAI, CDAI, DAPSA, ASDAS-PCR, BASDAI) showed good correlation and comparable performance in assessing disease activity, in all JIA subtypes. These findings support the integration of selected adult indices into transitional care to ensure consistent and reliable disease monitoring.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Pilato: None; **G. Tarantino**: None; **M. Petrone**: None; **A. Aquilani**: None; **E. Marasco**: None; **R. Nicolai**: None; **F. De Benedetti**: AbbVie, 2, 5, Apollo, 2, 5, Elixiron, 2, 5, Kiniksa, 2, 5, Novartis, 2, 5, Sanofi, 2, 5, Sobi, 2, 5; **R. Giacomelli**: None; **L. Navarini**: None; **S. Magni-Manzoni**: None.

Abstract Number: 0392

Clinical Indicators of Methotrexate Response in Juvenile Idiopathic Arthritis (JIA) and JIA with Uveitis (JIA-U)

Abigale Jagger[1], Mara Becker[2], Susan Thompson[3], Mekibib Altaye[4], John Bohnsack[5], Hermine Brunner[6], Margaret Chang[7], Ashley Cooper[8], Stefanie Davidson[9], Alexandra Duell[6], Bharti Gangwani[7], Carl Langefeld[10], Melissa Lerman[11], Mindy Lo[7], Serena Pastore[12], Mariia Pavlenko[13], Sampath Prahalad[14], Megan Quinlan-Waters[15], Laura Ramsey[16], Grant Schulert[6], Gabriele Simonini[17], Erin Stahl[8], Gabriele Stocco[18], Marc Sudman[19], Andrea Taddio[18], Virginia Miraldi Utz[6], Rae Yeung[20] and Sheila Angeles-Han[1], [1]Cincinnati Children's Hospital, Cincinnati, OH, [2]Duke University Medical Center/ Duke Clinical Research Institute, Chapel Hill, NC, [3]Cincinnati Children's Hospital Medical Center/Univ of Cincinnati College of Medicine, BLUE ASH, OH, [4]Cincinnati Children's Hospital, Cincinnati, [5]University of Utah, Salt Lake City, UT, [6]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [7]Boston Children's Hospital, Boston, MA, [8]Children's Mercy Kansas City, Kansas City, MO, [9]University of Pennsylvania/CHOP, Philadelphia, PA, [10]Wake Forest University School of Medicine, Winston Salem, NC, [11]Children's Hospital of Philadelphia, Philadelphia, PA, [12]Institute of Child and Maternal Health - IRCCS "Burlo Garofolo", Trieste, Italy, [13]Cincinnati Children`s Hospital Medical Center, Cincinnati, OH, [14]Emory + Children's Pediatric Institute, Atlanta, GA, [15]Cincinnati Children's Hospital Medical Center, CCHMC, [16]Children's Mercy, Kansas City, MO, [17]Rheumatology Unit, ERN-ReCONNET center, Meyer Children's Hospital IRCCS, Firenze, Firenze, Italy, [18]Insitute for Maternal and Child Health IRCCS Burlo Garofolo, Trieste, Italy, [19]Cincinnati Children's Hospital Medical Center, Cincinnati, [20]The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with JIA are at high risk for development of chronic anterior uveitis (CAU), impacting 10-20% of this population. Although methotrexate (MTX) is the first-line systemic treatment for JIA-U patients, only 50% respond to therapy. Poor MTX response and delayed escalation of therapy can lead to sight-threatening complications. Non-white race, male sex, ANA positivity, and young age at JIA diagnosis have been associated with a lack of response. We aim to identify clinical risk factors associated with non-response to MTX in JIA-U patients.

Methods: This is a multicenter, prospective study – PEDIA-U and PROMOTE. Patients diagnosed with JIA or JIA-U who were prescribed MTX and who had 12 months follow-up were included. Patients were grouped as MTX non-responders (MTX-NR) vs responders (MTX-R). MTX-NR for CAU was defined as active or worse CAU by Standardization of Uveitis Nomenclature (SUN) criteria, presence of new or worsening complications, and/or need for > 2 drops/day of topical or oral steroids after 3 months. MTX-NR for arthritis was defined as no change in active joint count after 3 months. Clinical phenotypes were compared between MTX-NR and MTX-R using Chi-square and two sample tests. Odds ratios were calculated by multiple logistic regression.

Results: A total of 635 patients with JIA were identified, 187 (29.4%) of whom had JIA-U (Table 1). The overall cohort was predominately white (73.7%) and female (74.9%), with 298 (46.9%) being identified as MTX-NR. Average MTX oral and subcutaneous dose was similar at 16.5 mg/m^2 (SD 6.6) and 17.4 mg/m^2 (SD 5.7), respectively. White race was associated with MTX-NR on bivariate (X^2=20.0, p=0.0012) and multivariate (OR 2.429, CI 1.512-3.904) analysis, with no other significant clinical variables identified. Of the 187 JIA-U patients, 91 (48.6%) were identified as being MTX-NR (Table 2). Of the 91 JIA-U MTX-NR, a majority were non-responders due to arthritis activity (61.5%), followed by both CAU and arthritis activity (26%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics assoicated with MTX reponse in patients with JIA

		All Cohort, N	Non-responders, N (%)	Responders, N (%)
Total number of patients		635	298 (46.9)	337 (53.1)
JIA Patients		448	207 (46.2)	241 (53.8)
JIA-U Patients		187	91 (48.7)	96 (51.3)
Sex at birth, p=0.6842[1]				
	Male	148	73 (49.3)	75 (50.7)
	Female	476	219 (46.0)	257 (54.0)
	Unknown	11	6 (54.6)	5 (45.5)
Race, p=0.0012[1]				
	White	468	239 (51.1)	229 (48.9)
	Other	55	22 (40.0)	33 (60.0)
	Unknown	112	37 (33.0)	75 (67.0)
JIA subtype, p=0.4512[1]				
	Oligo	288	132 (45.8)	156 (54.2)
	Polyarctular	290	134 (46.2)	156 (53.8)
	Psoriatic	43	23 (53.5)	20 (46.5)
	Undiffrentiated	14	9 (64.3)	5 (35.7)
ANA, p= 0.7998[1]				
	Negative	222	104 (46.9)	118 (53.2)
	Positive	377	179 (47.5)	198 (52.5)
	Unknown	36	15 (41.7)	21 (58.3)
Uveitis Laterality, p=0.4206[1]				
	Both	101	55 (54.5)	46 (45.5)
	Unilateral	50	23 (46.0)	27 (54.0)
	Unknown	6	2 (33.3)	4 (66.7)
MTX PO only, 0.8827[1]				
	Yes	307	145 (47.2)	162 (52.8)
	No	328	153 (46.7)	175 (53.4)
MTX Intolerance, p=0.1155[1]				
	Yes	173	90 (52.0)	83 (48.0)
	No	462	208 (45.0)	254 (55.0)
Age at JIA Diagnosis, Mean (SD), p=0.3968[2]			5.9 (4.4)	6.1 (4.6)
Age at Uveitis DX, Mean (SD), p=0.2197[2]			5.3 (3.5)	6.0 (3.3)
Days between MTX start & JIA diagnosis, Mean (SD), p=0.5778[2]			247.1 (1328)	187.4 (1350)
Days between MTX start & CAU diagnosis, Mean (SD),p=0.1251[2]			-111 (1485.2)	-450.7 (1027.7)
[1]Chi-square testing completed for categorical variable (ie. Race)				
[2]T-test used for continuous variable (ie. Age)				

Table 2. Demographic and clinical characteristics associated with MTX response in patients with JIA-U

		JIA-U, N (%)	Non-responders, N (%)	Responders, N (%)
Number of patients		187	91 (48.7)	96 (51.3)
Sex at birth, p=0.9078[1]				
	Male	32	15 (46.9)	17 (53.1)
	Female	144	70 (48.6)	74 (51.4)
	Unknown	11	6 (54.6)	5 (45.5)
Race, p=0.3373[1]				
	White	148	76 (51.4)	72 (48.7)
	Other	17	6 (35.3)	11 (64.7)
	Unknown	22	9 (40.9)	13 (59.1)
JIA subtype, p=0.4854[1]				
	Oligo	114	54 (47.4)	60 (52.6)
	Polyarctular	66	32 (48.5)	34 (51.5)
	Psoriatic	5	3 (60.0)	2 (40.0)
	Undiffrentiated	2	2 (100)	0 (0.0)
ANA, p= 0.1747[1]				
	Negative	49	19 (38.8)	30 (61.2)
	Positive	132	70 (53.0)	62 (47.0)
	Unknown	6	2 (33.3)	4 (66.7)
Uveitis Laterality, p=0.4206[1]				
	Both	101	55 (54.5)	46 (45.5)
	Unilateral	50	23 (46.0)	27 (54.0)
	Unknown	6	2 (33.3)	4 (66.7)
MTX Intolerance, p=0.0023[1]				
	Yes	40	28 (70.0)	12 (30.0)
	No	147	63 (42.9)	84 (57.1)
Age at JIA Diagnosis, Mean (SD), p=0.644[2]			4.0 (3.1)	4.3 (3.4)
Age at Uveitis DX, Mean (SD), p=0.2197[2]			5.3 (3.5)	6.0 (3.3)
Days between MTX start & JIA diagnosis, Mean (SD), p=0.3996[2]			561 (1485.2)	390.5 (1215.3)
Days between MTX start & CAU diagnosis, Mean (SD), p=0.1251[2]			-111 (1485.2)	-450.7 (1027.7)
Duration of arthritis at CAU DX, N, Mean days (SD), p=0.106[2]			70/91, 132.5 (364.6)	70/96, 189.9 (270.1)
[1]Chi-square testing completed for categorical variable (ie. Race)				
[2]T-test used for continuous variable (ie. Age)				

and isolated CAU activity (12%). In contrast to the overall cohort, MTX intolerance (MTX-IT) was associated with MTX-NR (X^2=9.3, p=0.00023) in the JIA-U group. The most common reason for MTX-IT being GI symptoms (76.2%), followed by laboratory abnormalities (11.9%). The most initiated biological DMARD in MTX-NR patients was adalimumab (37.9%). No significant differences in predictors of response were found between JIA and JIA-U groups across clinical and demographic variables.

Conclusion: Patients of white race and those who experience MTX-IT were significantly more likely to be MTX-NR in the combined and JIA-U cohorts, respectively. Risk factors of MTX-NR from previously reported smaller cohorts were not significant in our population. Our study does not support evidence of using clinical criteria alone to identify at-risk populations for MTX-NR. Future investigation could include ocular findings on novel imaging modalities, biomarkers, and genetics as risk factors of MTX-NR, with the potential for developing individualized JIA-U therapy plans while minimizing ophthalmic morbidity.

Disclosure: A. Jagger: None; **M. Becker**: None; **S. Thompson**: None; **M. Altaye**: None; **J. Bohnsack**: Bristol-Myers Squibb(BMS), 5, Janssen, 5, Pfizer, 5; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **M. Chang**: None; **A. Cooper**: None; **S. Davidson**: None; **A. Duell**: None; **B. Gangwani**: None; **C. Langefeld**: None; **M. Lerman**: None; **M. Lo**: None; **S. Pastore**: None; **M. Pavlenko**: None; **S. Prahalad**: None; **M. Quinlan-Waters**: None; **L. Ramsey**: BTG Specialty Pharmaceuticals, 2, 5; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **G. Simonini**: None; **E. Stahl**: Sydnexis, 2; **G. Stocco**: None; **M. Sudman**: None; **A. Taddio**: None; **V. Miraldi Utz**: None; **R. Yeung**: AstraZeneca, 5, SOBI, 6; **S. Angeles-Han**: None.

Abstract Number: 0393

Effects of Self-Reported Medication Barriers on Medication Adherence and Disease Activity in a Cohort of Patients with Juvenile Idiopathic Arthritis

Aditi Shaily[1], Allison R. Eckard[2], Paul Nietert[3], Emily Vara[1], Natasha Ruth[4] and Mileka Gilbert[3], [1]Division of Rheumatology, Medical University of South Carolina, Charleston, SC, [2]Departments of InternDivision of Infectious Diseases, Medical University of South Carolina, Charleston, SC, [3]Medical University of South Carolina, Charleston, SC, [4]Medical University South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Medications used to manage juvenile idiopathic arthritis (JIA) are highly effective in preventing joint damage and provide a favorable prognosis. Many patients, however, struggle with treatment adherence. Yet, little data exist on self-reported medication barriers and how they may affect treatment adherence and disease activity in this vulnerable population.

Methods: Retrospective cross-sectional analysis was used to examine medication barriers in a cohort of patients with JIA seen in an ambulatory rheumatology clinic at a quaternary care academic institution in Charleston, SC. Pediatric Rheumatology Care and Outcomes Improvement Network Barriers Assessment Tool (BAT) was used to obtain patient/caregiver-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Medication Adherence and Disease Activity Assessments in Patients with Juvenile Idiopathic Arthritis

	All patients (n= 90)	Patients reporting ≥1 medication barriers (n= 36)	Patients not reporting any medication barriers (n= 54)	*p*-value
Currently taking JIA medication(s)?				0.37
No (%)	22 (24.4)	7 (19.4)	15 (27.8)	
Yes (%)	68 (75.6)	29 (80.6)	39 (72.2)	
If yes, how often are you taking your medication(s)?				0.40
0-25% (%)	3 (4.4)	2 (6.9)	1 (2.6)	
26-50% (%)	1 (1.5)	1 (3.5)	0 (0.0)	
51-75% (%)	6 (8.8)	3 (10.3)	3 (7.7)	
76-100% (%)	51 (75.0)	19 (65.5)	32 (82.1)	
Unable to specify (%)	7 (10.3)	4 (13.8)	3 (7.7)	
Disease Activity Assessment				
Disease duration, months	48 (17.0-96.0)	42.5 (15.5- 6.5)	55.0 (19.0- 100.0)	0.47
Patient Global Assessment score	0 (0-1.8)	0 (0-2.0)	0 (0-1.8)	0.83
Physician Global Assessment score	0 (0-1.0)	0 (0-1.0)	0 (0-1.0)	0.54
Active Joint Count	0 (0-1.0)	0 (0-1.0)	0 (0-1.0)	0.12
cJADAS-10 score	0.5 (0-4.0)	1 (0-3.5)	0.0 (0-4.0)	0.83

Data are presented as N (%) or median (interquartile range). cJADAS-10, 10-point Clinical Juvenile Arthritis Disease Activity Score.

Table 2: Sociodemographic characteristics & JIA subtypes

	All patients (n= 90)	Patients reporting ≥1 medication barriers (n= 36)	Patients not reporting medication barriers (n= 54)	*p*-value
Age, years	14 (8.0-17.0)	13 (6.0-17.0)	14 (9.0-17.0)	0.08
Sex				0.21
Female (%)	66 (73.3)	29 (80.6)	37 (68.5)	
Male (%)	24 (26.7)	7 (19.4)	17 (31.5)	
Race and ethnicity (self-reported)				0.61
White, non-Hispanic (%)	59 (65.6)	26 (72.2)	33 (61.1)	
Black, non-Hispanic (%)	11 (12.2)	4 (11.1)	7 (13.0)	
Hispanic (%)	9 (10.0)	4 (11.1)	5 (9.3)	
Other, non-Hispanic (%)	8 (8.9)	2 (5.6)	6 (11.1)	
Asian (%)	3 (3.3)	0 (0.0)	3 (5.6)	
Health insurance				0.36
Private (%)	48 (53.3)	18 (50.0)	30 (55.6)	
Medicaid (%)	29 (32.2)	10 (27.8)	19 (35.2)	
Tricare (%)	10 (11.1)	6 (16.7)	4 (7.4)	
Uninsured (%)	3 (3.3)	2 (5.6)	1 (1.9)	
Distance of primary living residence to rheumatology clinic (study site)				0.40
<50 miles (%)	50 (55.6)	22 (61.1)	28 (51.9)	
50-100 miles (%)	8 (8.9)	4 (11.1)	4 (7.4)	
101-150 miles (%)	24 (26.7)	7 (19.4)	17 (31.5)	
151-200 miles (%)	4 (4.4)	1 (2.8)	3 (5.6)	
>200 miles (%)	4 (4.4)	2 (5.6)	2 (3.7)	
JIA Subtype				0.98
Oligoarticular, extended (%)	2 (2.2)	1 (2.8)	1 (1.9)	
Oligoarticular, persistent (%)	28 (31.1)	13 (36.1)	15 (27.8)	
Polyarticular, RF- (%)	26 (28.9)	10 (27.8)	16 (29.6)	
Polyarticular, RF+ (%)	7 (7.8)	3 (8.3)	4 (7.4)	
Enthesitis-related (%)	14 (15.6)	5 (13.9)	9 (16.7)	
Psoriatic (%)	5 (5.6)	1 (2.8)	4 (7.4)	
Systemic (%)	3 (3.3)	1 (2.8)	2 (3.7)	
Undifferentiated (%)	5 (5.6)	2 (5.6)	3 (5.6)	

Data are presented as N (%) or median (interquartile range).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Secondary Analysis of Medication Adherence and Medication Barrier Types in Patients with Juvenile Idiopathic Arthritis Responding "Yes" vs. "No" to Question about Medication Barriers on the Survey

	All patients (n= 90)	Patients responding "yes" to medication barriers (n= 15)	Patients responding "no" to medication barriers (n= 75)	*p*-value
Currently taking JIA medication(s)?				**0.03**
No (%)	22 (24.4)	7 (46.7)	15 (20.0)	
Yes (%)	68 (75.6)	8 (53.3)	60 (80.0)	
Medication Barriers				
The pills are hard to swallow	5 (5.6)	2 (13.3)	3 (4.0)	0.19
I forget to do the treatment	9 (10.0)	4 (26.7)	5 (6.7)	**0.04**
We run out of the medicine	9 (10.0)	2 (13.3)	7 (9.3)	0.64
I do not like the side effects of the treatment (e.g., nausea)	10 (11.2)	5 (33.3)	5 (6.7)	**0.01**
I refuse to do the treatment	4 (4.4)	1 (6.7)	3 (4.0)	0.52
I feel I do not need the treatment	7 (7.7)	3 (20.0)	4 (5.3)	0.09
I do not want others to know that I take/do the treatment	5 (5.5)	1 (6.7)	4 (5.3)	0.99
The treatment is painful	15 (16.6)	7 (46.7)	8 (10.7)	**<0.01**
The treatment does not work	6 (6.7)	2 (13.3)	4 (5.3)	0.26
The treatment is inconvenient	4 (4.4)	1 (6.7)	3 (4.0)	0.52
The treatment gets in the way of our other activities	4 (4.4)	1 (6.7)	3 (4.0)	0.52
The treatment makes me uncomfortable or upset	13 (14.4)	9 (60.0)	4 (5.3)	**<0.01**
The treatment has instructions that are hard to understand or follow through with	4 (4.4)	1 (6.7)	3 (4.0)	0.52
The treatment costs too much	7 (7.7)	4 (26.7)	3 (4.0)	**0.01**
The treatment makes me worry about future side effects/consequences	9 (10.0)	4 (26.7)	5 (6.7)	**0.04**
The treatment makes me worry about my ability to have children in the future	4 (4.4)	0 (0.0)	4 (5.3)	0.99
Other	3 (3.3)	1 (6.7)	2 (2.7)	0.43

Data are presented as N (%) or median (interquartile range). p-values in bold depict those <0.05.

reported medication barriers. Treatment adherence rates were estimated using a patient/caregiver-driven survey. 10-point clinical Juvenile Arthritis Disease Activity Score (cJADAS-10) assessed disease activity. Primary objectives were to investigate relationships among medication barriers, medication adherence, and disease activity. Secondary objective was to evaluate for health disparities associated with medication barriers. Fisher's exact or Wilcoxon rank-sum tests were used to make between-group comparisons.

Results: 90 patients were included (median age 14 years; 73.3% female); 75.6% reported taking ≥1 JIA medication. 36 of 90 patients (40%) reported the presence of at least one medication barrier; 54 (60%) reported not having any barriers. "Treatment is painful," "treatment makes me uncomfortable or upset," and "I do not like the side effects of the treatment" were the most reported barriers. Comparison groups were based on the selection of one or more medication barriers from the BAT in primary analysis; and on the response to the survey question "Do you have any barriers to, challenges with, or concerns about taking your medication(s)?" in secondary analysis. Associations between medication barriers and medication adherence rates, disease activity and sociodemographic variables were not statistically significant in the primary analysis (Tables 1 & 2). However, medication barriers were found to decrease adherence rates in the secondary analysis with a different operational definition of medication barriers (Table 3).

Conclusion: No differences were observed in treatment adherence rates, disease activity and sociodemographic factors in patients reporting medication barriers versus not reporting any barriers. However, medication adherence varied with different operational definitions of medication barriers. Hence, additional investigation is warranted to further delineate perceived medication barriers and their effects on long-term disease outcomes.

Disclosure: A. Shaily: None; **A. Eckard**: None; **P. Nietert**: None; **E. Vara**: None; **N. Ruth**: None; **M. Gilbert**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0394

Predictors of quality of Life in a longitudinal cohort of patients with Uveitis, Juvenile Idiopathic Arthritis, and JIA-associated uveitis

andressa Guariento Ferreira Alves[1], Amy Cassedy[2], Virginia Miraldi Utz[3], Alexandra Duell[3], Megan Quinlan-Waters[4], Nicole Reitz[5], Sheila Angeles-Han[6] and Melissa Lerman[7], [1]The Children's Hospital of Philadelphia, Philadelphia, PA, [2]Cincinnati Children's hospital medical center, cincinnati, OH, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]Cincinnati Children's Hospital Medical Center, CCHMC, [5]Department of Mental Health, St. Louis, MO, [6]Cincinnati Children's Hospital, Cincinnati, OH, [7]Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Uveitis, juvenile idiopathic arthritis (JIA), and JIA-associated uveitis (JIA-U) greatly influence children's quality of life (QOL). Our aim is to identify demographic, disease, and treatment features that may impact patient-reported outcomes (PROs) over time.

Methods: Patients with Uveitis, JIA, and JIA-U, and their caregivers enrolled in Longitudinal Outcomes of Childhood Uveitis Study (LOCUS) registry completed PROs as age-appropriate. The Effects of Youngsters' Eyesight on Quality of Life (EYE-Q) measures vision-related QOL and function, and Pediatric Quality of Life Inventory (PedsQL) measures overall QOL. Scores range 0 -100 (higher scores: better QoL). The Revised Childhood Anxiety and Depression Scale (RCADS) assesses anxiety and depression. Scores >70 indicate anxiety or depression. The Childhood Health Assessment Questionnaire (C-HAQ) measures functional disability from JIA with scores range 0 -3 (higher scores: worse function). Generalized estimating equation models were used to identify predictors of QOL.

Results: A total of 19 (21.6%) patients with uveitis, 34 (38.7%) JIA-U and 35 (39.7%) JIA completed 5 visits. The median time between baseline and last visit was 19.7 mo (IQR:15.8-28.6). There was a predominance of female sex in JIA 23 (26.2%) and JIA-U 28 (31.8%) compared to Uveitis 8 (9.1%) (< 0.001). Disease duration was longer in JIA-U 5.2 (IQR: 1.5-9.0) vs. Uveitis 0.8 (IQR: 0.2-2.8) and JIA 1.2 (IQR: 0.5-2.5) (p< 0.001). Patients with uveitis alone and active JIA had worse EYE-Q scores ($p < 0.01$) compared to JIA-U. Not being on a DMARD, being > 10 y/o, and subsequent visits from baseline were significantly associated with better EYE-Q for parents only. Predictors of better PedsQL were not being on DMARD or NSAIDs, and male sex for parents and children. Those with any form of uveitis had worse PedsQL although only for parents. Patients >10 y/o with inactive arthritis or uveitis had better CHAQ for parents and patients. The use of DMARDs was not associated with CHAQ. RCADS better outcome predictors were male sex, for parents and patients, age < 10 y/o for patients and inactive JIA disease for parents.

Conclusion: Having a diagnosis of uveitis, even more so if it was an isolated disease, was associated with worse physical functioning and vision-related QOL/function and PedsQL. Overall predictors were similar between parents and patients with few differences. Male sex, not being on DMARDS or NSAID, and having inactive JIA were associated with better outcomes. Being >10 y/o was associated with better physical functioning and vision-related QOL/function but worse RCAD. Identification of key predictors that impact quality of life over time will help us begin to tailor interventions to enhance the wellbeing of patients with chronic arthritis and uveitis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of baseline patient characteristics per disease group.

Characteristics	JIA-U N= 34	Uveitis N= 19	JIA N=35	p
Sex (female), n (%)	28 (82)	8 (42)	23 (66)	**0.01**
Race, n (%)				0.1
American Indian/Alaska native	1 (3)	0	0	
Asian	2 (6)	0	0	
Black	1 (3)	4 (21)	2 (6)	
White	30 (88)	14 (74)	33 (94)	
No race described	0	1 (5)	0	
Disease duration (yrs), median (IQR)	5.2 (1.5-9.0)	0.8 (0.2-2.8)	1.2 (0.5-2.5)	**<0.001**
Age (years)	9.5 (5.2-12.7)	11 (8-14.5)	6 (4-10)	**0.004**
Arthritis subtype				**0.002**
Oligo persistent	10 (29)	0	25 (71)	
Oligo extended	10 (29)	0	2 (6)	
Poly FR negative	12 (35)	0	8 (23)	
Psoriatic arthritis	1 (3)	0	0	
Undifferentiated arthritis	1 (3)	0	0	
Medication				0.1
Abatacept	1 (3)	0	1 (3)	
Adalimumab	3 (9)	0	1 (3)	
Etanercept	0	0	4 (11)	
Infliximab	6 (18)	1 (5)	0	
leflunomide	1 (3)	0	3 (8)	
Methotrexate	15 (44)	10 (53)	16 (46)	
Mycophenolate	1 (3)	0	0	
Tocilizumab	2 (6)	0	2 (6)	
Oral steroids	0	2 (10)	2 (6)	0.1
Topical steroids	24 (71)	16 (84)	N/A	0.3
NSAID	9 (26)	N/A	12 (34)	**0.01**

Juvenile idiopathic arthritis associated uveitis (JIA-U); Juvenile idiopathic arthritis (JIA); nonsteroidal anti-inflammatory (NSAID); years (yrs); Intervale interquartile (IQR)
Bonferroni correction was used for multiple analysis

Juvenile idiopathic arthritis associated uveitis (JIA-U); Juvenile idiopathic arthritis (JIA); nonsteroidal anti-inflammatory (NSAID); years (yrs); Intervale interquartile (IQR) Bonferroni correction was used for multiple analysis

Table 2: Least Square Mean scores for patient-reported total score of EYE-Q and PedsQL.

Predictors	EYE-Q				PedsQL			
	Patient n= 242 LS mean (95%CI)		Parent n=308 LS mean (95%CI)		Patient n= 365 LS mean (95%CI)		Parent n=409 LS mean (95%CI)	
	Total score	p	Total score	p	Total score	p	Total score	p
Disease group		**0.002***		**<0.001***		0.428		**0.047 ‡**
JIA-U	90.4 (86.2-94.8)		96.0 (92.9-99.4)		84.7 (78.8-91.2)		87.4 (81.1-94.2)	
Uveitis	84.7 (79.0-90.9)		87.2 (83.7-91.0)		84.4 (79.5-89.7)		80.0 (73.4-87.2)	
JIA	96.8 (91.8-102.1)		99.9 (96.1-103.9)		80.9 (74.7-87.6)		90.6 (83.6-98.2	
Time from baseline visit (months)		0.700		**0.041 §**		0.389		0.225
Baseline	87.8 (82.9-93.0)		90.7 (87.4-94.3)		81.2 (76.0-86.9)		81.3 (75.2-87.9)	
< 7 months	89.1 (84.0-94.4)		92.7 (89.6-96.1)		82.2 (76.4-88.4)		87.3 (80.5-94.8)	
7 < 12 months	91.3 (87.0-95.9)		95.5 (92.2-98.9)		83.8 (78.9-89.1)		85.0 (79.2-91.1)	
12 <18 months	91.4 (87.7-95.3)		95.1 (91.9-98.6)		86.2 (81.3-91.4)		88.2 (82.6-94.2)	
18 < 24 months	90.1 (83.7-96.9)		95.6 (92.0-99.6)		83.5 (78.0-89.4)		84.7 (78.2-91.9	
≥ 24 months	93.5 (88.1-99.2)		94.9 (90.9-99.3)		83.1 (78.4-88.1)		89.1 (83.2-95.4)	
Age at visit		0.157		**0.017**		0.059		0.248
≤10 year old	88.9 (84.3-93.7)		92.6 (89.5-95.8)		80.6 (75.0-86.6)		84.4 (79.0-90.2)	
>10 year old	92.2 (87.9-96.6)		95.6 (92.4-99.0)		86.1 (81.8-90.7)		87.4 (81.6-93.6)	
Sex		0.108		0.115		**0.001**		**0.046**
Male	92.2 (88.2-96.4)		95.1 (92-98.5)		87.5 (83.0-92.2)		88.6 (83.0-94.5)	
Female	88.9 (84.3-93.6)		93.2 (90-96.8)		79.4(74.3 -84.9)		83.3 (77.6-89.4)	
Active JIA		**0.031**		**<0.001**		0.100		0.120
Yes	88.4 (83.6-93.4)		92.2 (89.0-95.6)		81.3 (75.9-87.0)		84.0 (78.1-90.4)	
No	92.7 (89.1-96.4)		96.3 (93.1-99.7)		85.4 (81.1- 90.0)		87.8 (82.7-93.3)	
Active uveitis		0.751		0.823		0.953		0.481
Yes	90.2 (85.6-95.0)		94.5 (90.1-99.2)		83.4 (78.6-88.5)		84.9 (78.6-91.7)	
No	90.8 (86.9-94.9)		93.9 (90.8-97.2)		83.3(78.8-88.1)		86.9 (81.9-92.1)	
On topical steroids		0.349		0.253		0.895		0.773
Yes	88.4 (81.9-95.5)		92.2 (87.0-97.9)		83.7 (76.4-91.7)		86.7 (78.6-95.6)	
No	92.6 (88.0-97.6)		96.3 (92.7-100.1)		83.0 (77.4-89.0)		85.1 (79.0-91.7)	
On DMARD		0.252		**0.021**		**0.632**		**0.040**
Yes	89.2 (85.4-93.2)		92.7 (89.5-96.2)		82.8 (78.4-87.4)		82.9 (77.5-88.6)	
No	91.9 (86.9-97.1)		95.7 (92.4-99.1)		83.9 (78.7-89.4)		89.0 (82.8-95.7)	
On oral steroids		0.274		0.284		0.859		0.944
Yes	92 (86.6-97.8)		95.8 (90.5-101.3)		83.0 (76.4-90.1)		85.7(77.4-95.0)	
No	89 (85.4-92.8)		92.9 (90.5-95.4)		83.7 (79.4-88.1)		86.1 (81.9 -90.4)	
On NSAID		0.139		0.086		**0.051**		**0.157**
Yes	88.5 (83.0-94.5)		93.1 (89.2-97.2)		80.0 (73.6 -86.9)		83.6 (77.0-90.8)	
No	92.5 (89.4-95.8)		95.5 (92.8-98.4)		86.8 (83.1-90.8)		88.2 (83.2-93.5)	

Effects of Youngsters' Eyesight on Quality of Life (EYE-Q); Pediatric Quality of Life Inventory (PedsQL); Juvenile idiopathic arthritis associated uveitis (JIA-U); Juvenile idiopathic arthritis (JIA); Disease-modifying antirheumatic drug (DMARD); nonsteroidal anti-inflammatory (NSAID); Least Square Mean scores (LS mean)
Pairwise analyses with Tukey's correction for multiple analysis were significant for:
* JIA vs U and JIA-U vs U; ‡JIA vs U; § Time since baseline significant 7-11 and 18-24 in comparison with baseline

Effects of Youngsters' Eyesight on Quality of Life (EYE-Q); Pediatric Quality of Life Inventory (PedsQL); Juvenile idiopathic arthritis associated uveitis (JIA-U); Juvenile idiopathic arthritis (JIA); Disease-modifying antirheumatic drug (DMARD); nonsteroidal anti-inflammatory (NSAID); Least Square Mean scores (LS mean) Pairwise analyses with Tukey's correction for multiple analysis were significant for: * JIA vs U and JIA-U vs U ‡JIA vs U § Time since baseline significant 7-11 and 18-24 in comparison with baseline

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Least Square Mean scores for patient-reported total score of CHAQ and RCADS

Predictors	CHAQ				RCADS			
	Patient n= 167 LS mean (95%CI)		Parent n= 411 LS mean (95%CI)		Patient n= 268 LS mean (95%CI)		Parent n=250 LS mean (95%CI)	
	Total score	p	Total score	p	Total score	p	Total score	p
Disease group		0.517		0.778		0.509		0.510
JIA-U	0.34 (0.20-0.49)		0.11 (-0.03-0.25)		34.2 (30.9-37.8)		39.9 (37.4-42.5)	
Uveitis	0.26 (0.09-0.42)		0.13 (-0.06-0.32)		36.8 (32.8-41.4)		41.5 (38.4-44.8)	
JIA	0.30 (0.14-0.46)		0.09 (-0.07-0.25)		34.2 (30.9-37.8)		39.2 (36.1-42.5)	
Time from baseline visit (months)		0.753		**0.01**‡		**0.030**‡		0.100
Baseline	0.30 (0.17-0.43)		0.22 (0.048-0.39)		37.3 (34.0-40.8)		41.8 (39.5-44.3)	
< 7 months	0.29 (0.13-0.46)		0.12 (-0.03-0.28)		35.3 (31.9-39.0)		40.3 (37.8-42.9)	
7 < 12 months	0.29 (0.15-0.43)		0.11 (-0.06-0.27)		34.2 (31.3-37.4)		40.2 (37.8-42.9)	
12 <18 months	0.28 (0.13-0.44)		0.06 (-0.10-0.21)		34.9 (32.1-38.0)		39.3 (37.0-41.8)	
18 < 24 months	0.34 (0.18-0.50)		0.12 (-0.05-0.27)		34.1 (30.3-38.3)		40.8 (37.7-44.0)	
≥ 24 months	0.29 (0.12-0.46)		0.04 (-0.12-0.21		34.7 (30.5-39.4)		38.7 (33.6-44.6)	
Age at visit		**0.003**		<0.001				0.387
≤10 year old	0.2 (0.05-0.30)		0.20 (0.05-0.36)		80.6 (75.0-86.6)	**0.036**	40.6 (38.3-43.1)	
>10 year old	0.1 (0.00-0.20)		0.01 (-0.14-0.17)		86.1 (81.8-90.7)		39.7 (37.3-42.3)	
Sex		0.210		0.593		**<0.001**		**<0.001**
Male	0.26 (0.14-0.38)		0.12 (-0.03-0.27)		37.4 (35.0-39.9)		37.4 (35.0-39.9)	
Female	0.34 (0.19-0.49)		0.10 (-0.06-0.26)		43.1 (40.6-45.8)		43.1 (40.6-45.8)	
Active JIA		**0.045**		0.761		0.130		**0.014**
Yes	0.20 (0.1-0.31)		0.10 (-0.05-0.26)		35.9 (32.8-39.3)		41.5 (38.9-44.3)	
No	0.10 (0.03-0.21)		0.11 (-0.03-0.26)		34.2 (31.8-36.9)		38.9 (36.8-41.1)	
Active uveitis		0.462		0.960		0.228		0.634
Yes	0.33 (0.16-0.49)		0.11 (-0.04-0.26)		34.2 (31.2-37.5)		40.4 (38.0-43.0)	
No	0.27 (0.16-0.38)		0.11(-0.05-0.28)		35.9 (33.1-39.0)		39.9 (37.7-42.3)	
On topical steroids		0.167		0.966		0.495		0.590
Yes	0.22 (0.07-0.36)		0.11 (-0.15-0.37)		35.9 (32.1-40.1)		39.5 (35.9-43.4)	
No	0.382 (0.20-0.57)		0.12 (-0.02-0.24)		34.2 (31.1-37.6)		40.9 (38.0-43.9)	
On DMARD		0.704		0.528		0.292		0.789
Yes	0.28 (0.18-0.38)		0.12 (-0.04-0.29)		34.3 (32.0-36.7)		40.3 (38.1-42.7)	
No	0.32 (0.13-0.50)		0.09 (-0.06-0.25)		35.8 (32.3-39.8)		40.0 (37.3-42.8)	
On oral steroids		0.641		0.488		0.858		0.184
Yes	0.28 (0.13-0.43)		0.06 (-0.24-0.35)		34.9 (30.8-39.4)		38.9 (35.5-42.6)	
No	0.32 (0.18-0.46)		0.16 (0.10-0.22)		35.2 (33.2-37.4)		41.5 (39.5-43.5)	
On NSAID		**0.010**		0.010		0.910		0.923
Yes	0.20 (0.10- 0.35)		0.20 (0.00-0.35)		36.3 (32.7-40.3)		40.2 (37.2-43.5)	
No	0.10 (0.01-0.17)		0.05 (-0.10-0.20)		33.8 (31.7-36.1)		40.1 (37.9-42.4)	

Childhood Health Assessment Questionnaire (C-HAQ); The Revised Childhood Anxiety and Depression Scale (RCADS); Juvenile idiopathic arthritis associated uveitis (JIA-U); Juvenile idiopathic arthritis (JIA); Disease-modifying antirheumatic drug (DMARD); nonsteroidal anti-inflammatory (NSAID); Least Square Mean scores (LS mean)
Pairwise analyses with Tukey's correction for multiple analysis were significant for:
* Baseline x 7-11 months visit; ‡Baseline x 12-17 months visit

Childhood Health Assessment Questionnaire (C-HAQ); The Revised Childhood Anxiety and Depression Scale (RCADS); Juvenile idiopathic arthritis associated uveitis (JIA-U); Juvenile idiopathic arthritis (JIA); Disease-modifying antirheumatic drug (DMARD); nonsteroidal anti-inflammatory (NSAID); Least Square Mean scores (LS mean) Pairwise analyses with Tukey's correction for multiple analysis were significant for: * Baseline x 7-11 months visit ‡Baseline x 12-17 months visit

Disclosure: a. Guariento Ferreira Alves: None; **A. Cassedy**: None; **V. Miraldi Utz**: None; **A. Duell**: None; **M. Quinlan-Waters**: None; **N. Reitz**: None; **S. Angeles-Han**: None; **M. Lerman**: None.

Abstract Number: 0395

Association Between Body Mass Index (BMI) and JIA Inactive Disease at One Year

Anna Sutton[1] and Susan Shenoi[2], [1]University of Washington, Seattle, WA, [2]Seattle Children's Hospital and Research Center, Mercer Island, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic characteristics of patients with JIA from 2008 -2020 by BMI category[1]

	Underweight (N=31)	Healthy weight (N=573)	Overweight (N=122)	Obese (N=96)
Age at first visit, mean (sd)	9.3 (4.3)	9.4 (4.4)	10.5 (3.6)	9.9 (3.9)
Sex n(%)				
Female	15 (48)	386 (67)	79 (65)	51 (53)
Race and Ethnicity, n(%)				
White, non-Hispanic	20 (65)	380 (66)	64 (52)	46 (50)
White, Hispanic	-	19 (3)	6 (5)	9 (9)
Black	-	11 (2)	-	5 (5)
Asian	-	29 (5)	-	-
AIAN/NHPI	-	12 (2)	6 (5)	-
Other, Hispanic	-	50 (9)	20 (16)	12 (13)
Other, non-Hispanic	-	16 (3)	6 (5)	5 (5)
Missing	-	56 (10)	13 (11)	12 (13)
ILAR Category, n(%)				
Oligo	-	196 (34)	25 (20)	21 (22)
Oligo extended	-	21 (4)	6 (5)	-
Poly RF+	-	20 (3)	-	6 (6)
Poly RF-	-	77 (13)	16 (13)	11 (11)
Poly, unknown RF	14 (45)	108 (19)	23 (19)	18 (19)
ERA	-	81 (14)	18 (15)	22 (23)
Psoriatic	-	51 (9)	22 (18)	14 (15)
Systemic	-	14 (2)	7 (6)	-
Undifferentiated	-	5 (1)	-	-
TNFi use,[2] n(%)	9 (29)	116 (20)	31 (25)	26 (27)

Cells < 5 were not reported.
[1]BMI categories defined according to US CDC guidelines for BMI percentile by age and sex: underweight <5 percentile; healthy weight 5 to <85 percentile; overweight 85 to <95%; obese ≥95 percentile
[2]TNFi prescribed within 9 months of initial rheumatology visit; includes infliximab, etanercept, and adalimumab

Background/Purpose: Among adults, higher BMI contributes to worse outcomes and reduced response to treatment in rheumatoid arthritis (RA), but this relationship is understudied among those with Juvenile Idiopathic Arthritis (JIA). We investigated the relationship between BMI and disease activity 1-year post-diagnosis in JIA. Given that TNF inhibitors are the most commonly prescribed biologic DMARDs in JIA, we further assessed the impact of BMI category on response to treatment among those who were prescribed TNF inhibitors.

Methods: This is a retrospective cohort study from a single large quaternary center. Inclusion criteria were JIA (ages 2-16 years) diagnosed between November 2008 and September 2020 and followed for at least 12 months. Patients were identified using ICD-10 codes for JIA. Exclusion criteria were treatment with immunosuppressants before JIA diagnosis, inflammatory bowel disease, or missing data for height, weight, or disease activity at 12 months. Demographic characteristics, including height, weight, and BMI at initial rheumatology visit were extracted from a central patient database and patient clinic records. Age- and gender-specific BMI percentile was calculated for each patient and categorized according to CDC definitions as: underweight (< 5th percentile), healthy weight (5th to < 85th percentile), overweight (85th to < 95th

Table 2: Odds of active disease at 12 months among children with JIA by BMI category

	Active Disease	Inactive Disease	Odds Ratio (95% CI)[2]
Overall (N= 822)			
BMI Categories,[1] n(%)			
Healthy Weight	221 (38)	352 (62)	reference
Underweight	6 (19)	25 (81)	0.38 (0.15, 0.96)*
Overweight	50 (41)	72 (59)	1.04 (0.69, 1.57)
Obese	38 (40)	58 (60)	0.98 (0.62, 1.54)
Among TNF users[3] (N=182)			
BMI Categories,[1] n(%)			
Healthy Weight	36 (31)	80 (69)	reference
Underweight	<10	<10	0.27 (0.03, 2.28)
Overweight	13 (42)	18 (58)	1.59 (0.68, 3.71)
Obese	13 (50)	13 (50)	2.09 (0.86, 5.05)

[1]BMI categories defined according to US CDC guidelines for BMI percentile by age and sex: underweight <5 percentile; healthy weight 5 to <85 percentile; overweight 85 to <95%; obese ≥95 percentile
[2]Adjusted for ILAR category
[3]TNF prescription within 9 months of initial rheumatology visit; includes infliximab, etanercept, and adalimumab
*Statistically significant at α=0.05

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

percentile), or obese (≥ 95th percentile). Disease activity status at 12 months was extracted from patient records. Logistic regression was used to evaluate the association between BMI category and disease status overall and among those who were prescribed a TNF inhibitor (infliximab, etanercept, and adalimumab).

Results: Among 822 included patients, the majority (70%) were healthy weight (underweight: 4%, overweight: 15%, obese: 12%). Among 182 patients using TNF inhibitors, 64% were healthy weight (underweight: 5%, overweight: 17%, obese: 14%). Those who were underweight had lower odds of active disease at 12 months when compared to those with healthy weight, both overall (OR=0.38, 95%CI: 0.15-0.96) and among those taking TNF inhibitors (OR=0.30, 95%CI: 0.03-2.28). Among those taking TNF inhibitors, those who were overweight (OR=1.59, 95%CI: 0.68-3.71) or obese (OR=2.09, 95% CI: 0.86-5.05) had higher odds of active disease at 12 months compared to those with healthy weight.

Conclusion: Although it has been established in adults with RA that higher BMI contributes to worse disease outcomes, our analysis suggests that this may not be the case among children with JIA, as those who were overweight or obese had similar odds of active disease to those with healthy weight. Our study was likely underpowered to detect significant differences among those taking TNF inhibitors, but results suggest a trend, with higher likelihood of active disease found in each successively higher category of BMI. Further research in a larger cohort of JIA patients taking TNF inhibitors would elucidate the validity of this observed trend.

Disclosure: A. Sutton: None; **S. Shenoi**: AbbVie/Abbott, 2, Pfizer, 2, sobi, 2.

Abstract Number: 0396

Quantifying Burden of Uveitis Care for Pediatric Uveitis Patients and Caregivers

Catherine Lavallee[1], Samuel Garfinkle[2], Devlin Eckardt[3], Stefanie Davidson[4], Melissa Lerman[5], Nicole Reitz[6] and Kerry Hurlbut[5], [1]St. Christopher's Hospital for Children, Philadelphia, PA, [2]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, [3]Children's Hospital of Philadelphia, Philadelphia, [4]University of Pennsylvania/CHOP, Philadelphia, PA, [5]Children's Hospital of Philadelphia, Philadelphia, PA, [6]Department of Mental Health, St. Louis, MO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic noninfectious uveitis (CU) in pediatric patients is often asymptomatic and can cause vision loss, requiring frequent ophthalmologist visits and long-term treatment. This survey aimed to evaluate perception of the overall impact of CU on patients and their families and to describe the relative contributions of financial costs, healthcare access, and treatment adherence to perceived burden.

Methods: With input from patient representatives, a questionnaire was developed including ~65 questions: multiple-choice, Likert-scale, and open-ended. It was administered via REDCap at a pediatric tertiary center between April-June 2024. Participants included English-speaking guardians or adult patients (≥ 18 yo) diagnosed with CU < age 18, who received care in a coordinated ophthalmology/rheumatology clinic. Patients were asked to score "overall burden"; to categorize factors (eg. dollars spent per month, commute time to appointments), and to score perceived burdens from each category (cost, travel, obtaining medicine, giving medicine, impact on work/school/family, and emotional concerns). Data was analyzed using descriptive statistics, Wilcoxon rank sum tests, and Spearman's rank correlations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Cohort demographics.

Demographics			
	Total (N=46)	**Patient Reported (N=10)**	**Guardian Reported (N=36)**
Patient Sex			
Male	19 (41.3%)	4 (40.0%)	15 (41.7%)
Female	25 (54.3%)	6 (60.0%)	19 (52.8%)
Missing	2 (4.3%)	0 (0%)	2 (5.6%)
Patient Age (years)			
Median [Min, Max]	13.0 [5.00, 20.0]	18.0 [6.00, 20.0]	12.0 [5.00, 18.0]
Uveitis Subtype			
Anterior	15 (32.6%)	3 (30.0%)	12 (33.3%)
Intermediate	3 (6.5%)	1 (10.0%)	2 (5.6%)
Pan	6 (13.0%)	1 (10.0%)	5 (13.9%)
Unknown	22 (47.8%)	5 (50.0%)	17 (47.2%)
Age at Uveitis Diagnosis			
Median [Min, Max]	8.00 [1.00, 20.0]	11.5 [1.00, 17.0]	7.50 [1.00, 20.0]
Systemic Disease			
Idiopathic Uveitis	21 (45.7%)	5 (50.0%)	16 (44.4%)
Unknown	6 (13.0%)	2 (20.0%)	4 (11.1%)
JIA	13 (28.3%)	2 (20.0%)	11 (30.6%)
Other Systemic Disease	6 (13%)	1 (10%)	5 (13.9%)
Household Income			
< $25,000	6 (13.6%)	2 (20.0%)	4 (11.8%)
$25,000 - $50,000	7 (15.9%)	2 (20.0%)	5 (14.7%)
$51,000 - $75,000	6 (13.6%)	3 (30.0%)	3 (8.8%)
$76,000 - $100,000	0 (0%)	0 (0%)	0 (0%)
$101,000 - $150,000	10 (22.7%)	1 (10.0%)	9 (26.5%)
> $150,000	6 (13.6%)	0 (0%)	6 (17.6%)
No Response	9 (20.5%)	2 (20.0%)	7 (20.6%)
Insurance Status			
Uninsured	1 (2.3%)	0 (0%)	1 (2.9%)
Public	15 (34.1%)	4 (40.0%)	11 (32.4%)
Private	25 (56.8%)	5 (50.0%)	20 (58.8%)
Public and Private	3 (6.8%)	1 (10.0%)	2 (5.9%)
Monthly Medication Cost			
< $50	13 (29.5%)	1 (10.0%)	12 (35.3%)
$50 - $100	3 (6.8%)	1 (10.0%)	2 (5.9%)
$101 - $200	2 (4.5%)	0 (0%)	2 (5.9%)
> $200	4 (9.1%)	1 (10.0%)	3 (8.8%)
Unknown	22 (50.0%)	7 (70.0%)	15 (44.1%)

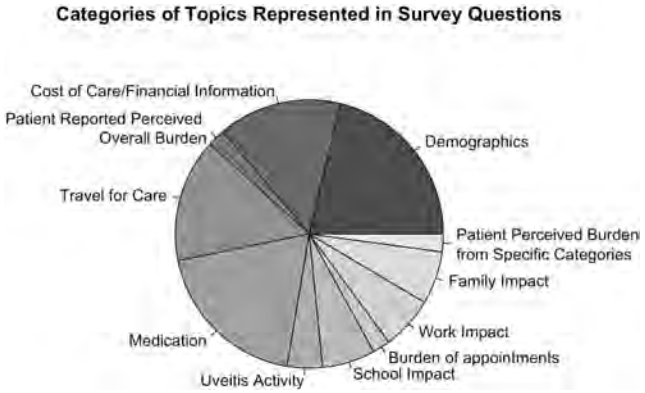
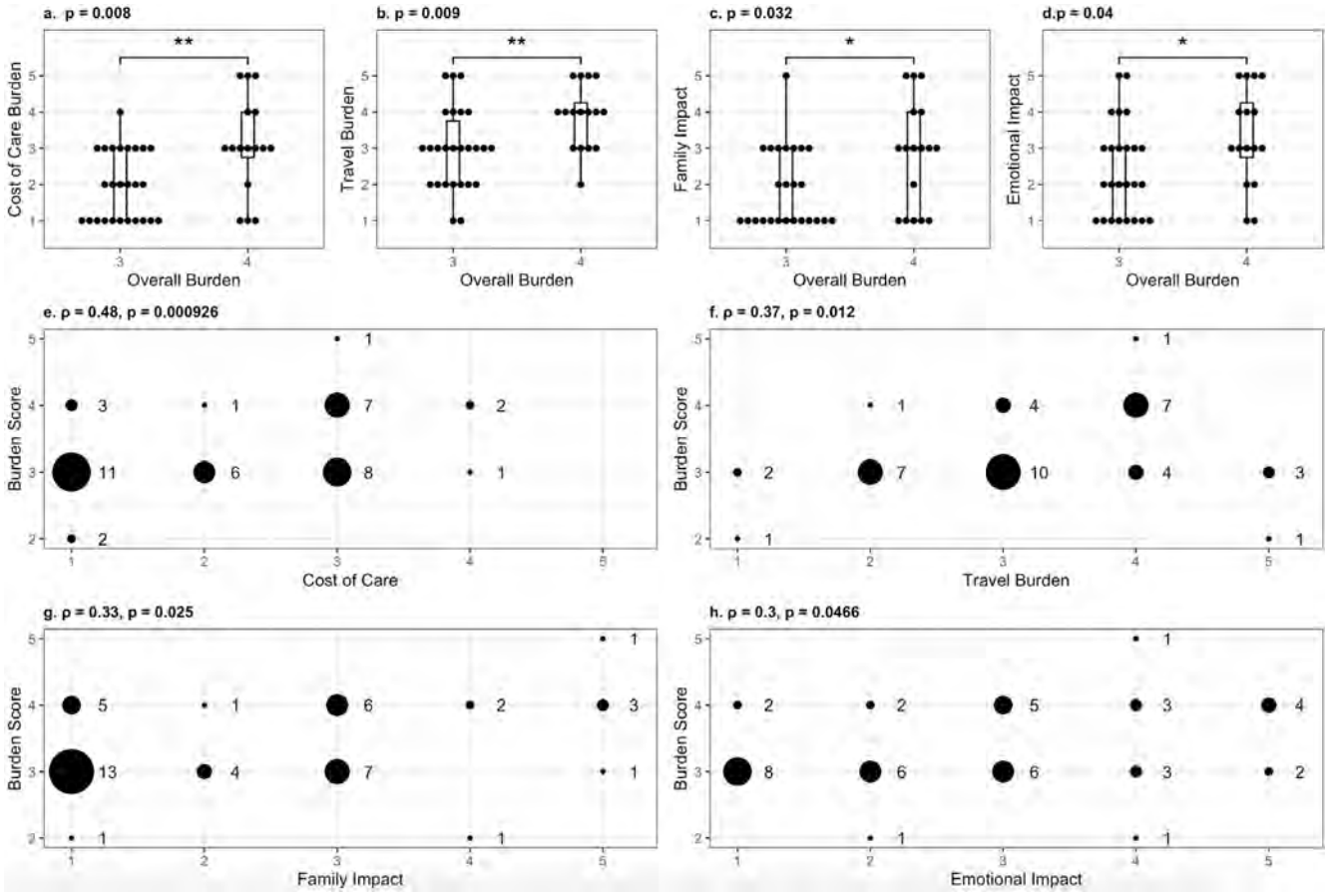


Figure 1. Categories Represented in Survey Questions. Each segment in this pie chart represents a category assessed in the survey, including Demographic information, Patient Reported Perceived Overall Burden, Patient Reported Perceived Burden from Specific Categories, Family Impact, Work Impact, School Impact, Burden of Appointments, Uveitis Activity, Medication, Travel for Care, and Cost of Care/Financial Information. The size of each segment corresponds to the proportion of survey questions dedicated to the category.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Panels a-d: Wilcoxon rank-sum tests of association of Overall burden (x-axis) and burden from individual categories (y-axis). Overall burden: "Considering the ways uveitis affects your life and finances, how difficult is receiving uveitis care on the patient and their family/caretaker(s)? (Note, in this survey we are not focusing on emotional burden)"; scoring: Very easy (1), Easy (2), Neutral (3), Difficult (4), Very Difficult (5). Every dot represents a patient. Panels e-h: Spearman's rank correlations of patient reported burden from individual categories (x-axis) and perceived overall burden (y-axis). Burden of individual categories: "Please rank what factors of uveitis care are most burdensome for the patient and guardian"; scoring: Not a Burden (1), Neutral (3), a Great Burden (5). Individual categories include Cost of care (E), Burden from travel to appointments (F), Burden on Family (G), Emotional Concerns (H). Rho: represents strength of correlation. P-value represents statistical significance. Larger dot size represents more patients.

Results: A total of 46 participants completed the survey. 93% of respondents (n=43) answered the question of their perceived overall burden of uveitis care. 61% reported a perceived overall burden sentiment of "neutral" while 40% reported "difficult". Higher burden (difficult vs. neutral) was significantly associated with patient reported higher burdens from categories: cost of care (p = 0.008), burden from travel to appointments (p=0.009), burden on family (p=0.032) and emotional concerns (p=0.04). There was no correlation between burden and participant age. Nearly half of participants were unaware of their uveitis subtype, and many did not know their monthly medical expenses. Spearman correlation confirmed significant positive associations of perceived overall burden with patient reported higher burdens from categories: cost of care (rh=0.48, p=0.001), burden from travel to appointments (rh=0.37, p=0.012), burden on family (rh=0.33, p=0.025), and emotional concerns (rh=0.30, p=0.047).

Conclusion: The study describes the burden faced by pediatric CU patients and their families. Cost and travel requirements were perceived as the greatest contributors. Limitations of this pilot study include it being performed at a single center and survey being restricted to patients in a coordinated uveitis clinic. Further directions include quantifying burden in a larger cohort and evaluating whether these same factors are the greatest contributors.

Disclosure: C. Lavallee: None; **S. Garfinkle**: None; **D. Eckardt**: None; **S. Davidson**: None; **M. Lerman**: None; **N. Reitz**: None; **K. Hurlbut**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0397

Paediatric uveitis - Retrospective comparison of cataract surgery outcomes with or without intraocular lens implantation from two tertiary centres in United Kingdom

Chaitra Govardhan[1], Ashwini Batchu Prithvi[1], Bushra Aladaileh[1], Elizabeth Cattermole[2], Farrag Abdelsattar[2], Catherine Guly[2], Jessy Choi[3], Johannes Keller[2] and Athimalaipet V Ramanan[1], [1]Bristol Royal Hospital for Children, Bristol, United Kingdom, [2]Bristol Eye Hospital, Bristol, United Kingdom, [3]Sheffield Children's Hospital, Sheffield, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cataract is one of the most common and visually debilitating complications of paediatric uveitis developing as a consequence of chronic inflammation and steroid use. Cataract surgery can be technically challenging in patients with uveitis and the outcomes less certain.(1) Inserting an intraocular lens (IOL) is controversial for paediatric uveitis patients leading to variable practice across different institutions. This study compares the outcomes of cataract surgery associated with paediatric uveitis with or without IOL implantation.

Methods: A retrospective comparison study was conducted at two centres, Bristol Eye Hospital (Centre 1-Cataract surgery with IOL implantation) and Sheffield Children's Hospital (Centre 2-Cataract surgery without IOL implantation). All children below 18 years of age with uveitis who underwent cataract surgery between year 2011 and 2024 were included. Pre and post operative outcomes from the two groups were compared, including best corrected visual acuity(BCVA), LogMAR lines of improvement, ocular inflammation and complications. Follow up data upto 2 years post-surgery where available were recorded. Data was analysed using descriptive statistics.

Table:1 Demographic and Clinical comparison of the study groups

	Intra-ocular lens group (Centre-1)	No Intra-ocular lens group (Centre-2)
Total number of children	25	10
Total number of eyes (R:L)	30 (18:12)	13 (7:6)
Gender (M:F)	10:15	8:5
Median age at diagnosis of uveitis (years) (IQR)	5.5 (IQR 4-8)	5 (IQR 3.5 – 8.5)
Median age at surgery (years) (IQR)	9 (IQR 6.75-13)	5 (IQR 3.25 – 11.5)
Median time between diagnosis of uveitis and cataract surgery (months)	34 months (9.25 – 70.5)	10 months (6-29.5)
Diagnosis, n(%) JIA Idiopathic Others	(n=25) 15 (60) 8 (32) 2 (8)	(n=10) 9 (90) 1 (10) 0
Subtype of uveitis n(%) Anterior Intermediate Posterior	(n=30) 29 3 2	(n=13) 9 0 4
Immunomodulatory therapy n(%)	Topical steroids-2(6.6) Systemic-28(93.3)	Topical steroids- 4(30.7) Systemic- 2(15.3) Combined-7(53.8)
Associated intraocular pathologies (n) Vitreous haze Cystoid macular oedema Epiretinal membrane Macular scarring Band Keratopathy Anterior capsule fibrosis Glaucoma	 1(3.3) 1(3.3) 0 0 5(16.6) 6(20) 14(46.6)	 2(15.3) 1(7.6) 1(7.6) 2(15.3) 10(76.9) 10(76.9) 2(15.3)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table-2: Grading of anterior chamber inflammation in eyes with and without IOL

	Eyes n (%)							
	Preoperative n(%)		Post-operative n(%)					
			3 months		12 months		24 months	
AC cells	IOL	No IOL	IOL	No IOL	IOL	No IOL	IOL	No IOL
<1+	30 (100)	11 (84.6)	20 (66.7)	12 (92.2)	22 (73.3)	10 (76.9)	22 (72.3)	10 (76.9)
1+	0	0	6 (20.0)	0	7 (23.3)	1 (7.7)	4 (13.3)	0
2+	0	1 (7.7)	4 (13.3)	1 (7.7)	1 (7.7)	0	1 (7.7)	0
>2+	0	1 (7.7)	0	0	0	1 (7.7)	0	1 (7.7)
NA	0	0	0	0	0	1 (7.7)	3 (10)	2 (15.4)

AC= Anterior chamber; IOL= Intraocular lens; NA= Not available or not measured

Table-3 Comparison of pre- and post-operative best corrected visual acuity and lines of improvement at 3, 12 and 24 months.

	Eyes n(%)							
	Preoperative		3 months		12 months		24 months	
BCVA	IOL	No IOL	IOL	No IOL	IOL	No IOL	IOL	No IOL
≤0.38	0	0	21 (70)	7 (53.8)	25 (83.3)	5 (38.5)	19 (63.3)	6 (46.2)
0.4-0.54	4 (13.3)	0	3 (10)	2 (15.4)	1 (3.3)	2 (15.4)	2 (6.7)	0
0.6-1.0	16 (53.3)	4 (30.8)	4 (13.3)	1 (7.7)	3 (10)	1 (7.7)	5 (16.7)	1 (7.7)
>1.0	10 (33.3)	9 (69.2)	1 (3.3)	3 (23.1)	1 (3.3)	4 4 (30.8)	0	4 4 (30.8)
NA	0	0	1 (3.3)	0	0	1 (7.7)	4 (13.3)	2 (15.4)
LogMAR lines of improvement								
Median lines of improvement (IQR)	Baseline	Baseline	5(2.75-11.25)	7 (4-11.5)	6(3.5 - 13.5)	5(-0.5 – 10.5)	6(1 – 10)	7(0 – 12)
No. of children >2 lines of improvement n/total (%)	N=30	N=13	24/29 (82.8)	11/13 (84.6)	27/29 (93.1)	9/12 (75)	21/26 (80.8)	9/11 (81.8)
Mean BCVA (Range)	1.16 ± 0.75	1.64 ± 0.78	0.35± 0.52	0.89± 1.03	0.25± 0.35	0.93± 1.11	0.21± 0.29	0.80± 1.07
Median BCVA (IQR)	0.84 (0.60 - 1.43)	1.60 (0.92 – 2.48)	0.20 (0.10 – 0.40)	0.38 (0.24 – 1.56)	0.20 (0.04 – 0.30)	0.50 (0.14 – 1.99)	0.10 (0.00 – 0.35)	0.15 (0.05-1.69)

NA= Not available or not measured

Results: There were total 35 children (43 eyes) identified from both centres, 25 children (30 eyes) from centre-1 and 10 children (13 eyes) from centre 2. The median age at diagnosis in years was 5.5years(centre 1) and 5years (centre 2) and median age at surgery was 9 and 5 years with M:F=2:3 and 1.6:1 respectively. JIA was the most common etiology at both centres (60% and 90% respectively). Anterior uveitis was the most common subtype of uveitis at both centres (29 eyes, 9 eyes respectively)-Table1. Surgical capsulotomy was required in 3 eyes (10%) by 24 months at centre 1. Active anterior chamber inflammation >1+ cells was recorded in 10(33%), 8(36.4%), 5(16.7%) in centre-1 and 1(7.7%), 2(15.4%), 1(7.7%) in centre-2 at 3,12 and 24 months.(Table2) Median preoperative BCVA (IQR) was 0.84 (0.60-1.43) and 1.6 (0.92- 2.48) respectively. The median post-operative BCVA at 3 months, 12 months and 24 months at centre 1 was 0.20,0.2 and 0.10 and at centre 2 was 0.38, 0.50 and 0.15. Percentage of children with 2 or more lines of improvement at 3,12 and 24 months at centre 1 was 82.8%, 93.1% and 80.8% whereas at centre 2 was 84.6%, 75% and 81.8%.(Table3)

Conclusion: Good visual improvement following cataract surgery in children with uveitis with and without IOL would support either of the practices. However, a caveat being that IOL insertion could potentially be associated with active inflammation.

References:

1. Quiñones K, Cervantes-Castañeda RA, Hynes AY, Daoud YJ, Foster CS. Outcomes of cataract surgery in children with chronic uveitis. J Cataract Refract Surg. 2009 Apr;35(4):725–31.

Disclosure: C. Govardhan: None; **A. Batchu Prithvi**: None; **B. Aladaileh**: None; **E. Cattermole**: None; **F. Abdelsattar**: None; **C. Guly**: None; **J. Choi**: None; **J. Keller**: None; **A. V Ramanan**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0398

Efficacy of Tumor Necrosis Factor Inhibitors in Children Diagnosed With Non-Systemic Juvenile Idiopathic Arthritis ≤ 2 Years Old Using The Childhood Arthritis and Rheumatology Research Alliance Registry

Christina Gulla[1], Tara Lozy[2] and Ginger Janow[3] For The CARRA Registry Investigators, [1]Hackensack University Medical Center, Hackensack, NJ, [2]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Nutley, [3]Joseph M. Sanzari Children's Hospital at Hackensack Meridian Health, Hackensack, NJ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1: Demographics and Clinical Disease Characteristics For All Patients Diagnosed With Non-sJIA 0-23 Months and Those Enrolled in CARRA Registry More and Less Than 6 Months From Diagnosis

Demographics	Entire cohort (total diagnosed non-sJIA 0-23mo) n=949	Enrolled at >6 mo from diagnosis n=671	Subcohort (enrolled at <6 mo from diagnosis) n=278	Effect Size	P value
Female, n (%)	815 (85.9)	580 (86.4)	235 (84.5)	0.02	0.44
Age at diagnosis (mo), median (IQR)	19 (17 - 21)	19 (17 - 21)	19.5 (18 - 22)	0.06	0.08
Disease duration at baseline visit (mo), median (IQR)	40 (4 - 99)	72 (34 - 118)	2 (0 - 3)		
Race, n(%)					
Asian	33 (3.5)	18 (2.7)	15 (5.4)	0.07	0.27
Black	12 (1.3)	5 (0.8)	7 (2.5)	0.07	0.18
Hispanic	55 (5.8)	40 (6.0)	15 (5.4)	0.01	1.00
White	761 (80.3)	549 (81.9)	212 (76.3)	0.06	0.35
Other	41 (4.3)	31 (4.6)	1 (0.4)	0.07	0.16
Multiracial	48 (5.1)	29 (4.3)	19 (6.8)	0.05	0.76
Prefer not to answer	10 (1.1)	3 (0.4)	7 (2.5)	0.09	**0.03**
JIA subtype at baseline, n (%)					
Oligoarthritis	512 (54.0)	337 (50.2)	175 (63.0)	0.12	**0.002**
Polyarthritis (RF-)	333 (35.1)	257 (38.3)	76 (27.3)	0.10	**0.01**
Polyarthritis (RF+)	13 (1.4)	10 (1.5)	3 (1.1)	0.02	1.00
Psoriatic arthritis	64 (6.7)	45 (6.7)	19 (6.8)	0.00	1.00
Enthesitis related arthritis	8 (0.8)	8 (1.2)	0 (0.0)	0.06	0.41
Undifferentiated arthritis	19 (2.0)	14 (2.1)	5 (1.8)	0.01	1.00
Labs, n (%)					
ANA positive	638 (71.3)	438 (69.0)	200 (76.9)	0.08	**0.02**
HLAB27 positive	28 (7.9)	24 (9.2)	4 (4.2)	0.05	0.12
CCP positive	20 (5.7)	11 (4.7)	9 (7.7)	0.03	0.26
RF+	11 (1.6)	10 (2.1)	1 (0.5)	0.03	0.15
Uveitis (ever)	287 (32.0)	252 (39.6)	35 (13.4)	0.25	**<.001**
Baseline Total Active joint count, median (IQR)	0 (0 - 2)	0 (0 - 1)	2 (1 - 4)	0.42	**<.001**
Total number of joints ever affected, n (%)				0.15	**<.001**
< 5 joints	444 (47.1)	257 (38.5)	187 (68.0)		
>= 5 joints	498 (52.9)	410 (61.5)	88 (32.0)		
Baseline PGA, median (IQR)	1 (0 - 3)	0 (0 - 2)	2 (0.75 - 5)	0.28	**<.001**
Baseline CHAQ, median (IQR)	0.125 (0 - 0.575)	0 (0 - 0.375)	0.375 (0.1075 - 1)	0.33	**<.001**
Baseline cJADAS10, median (IQR)	3 (0 - 8)	2 (0 - 5)	8 (3 - 13)	0.37	**<.001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

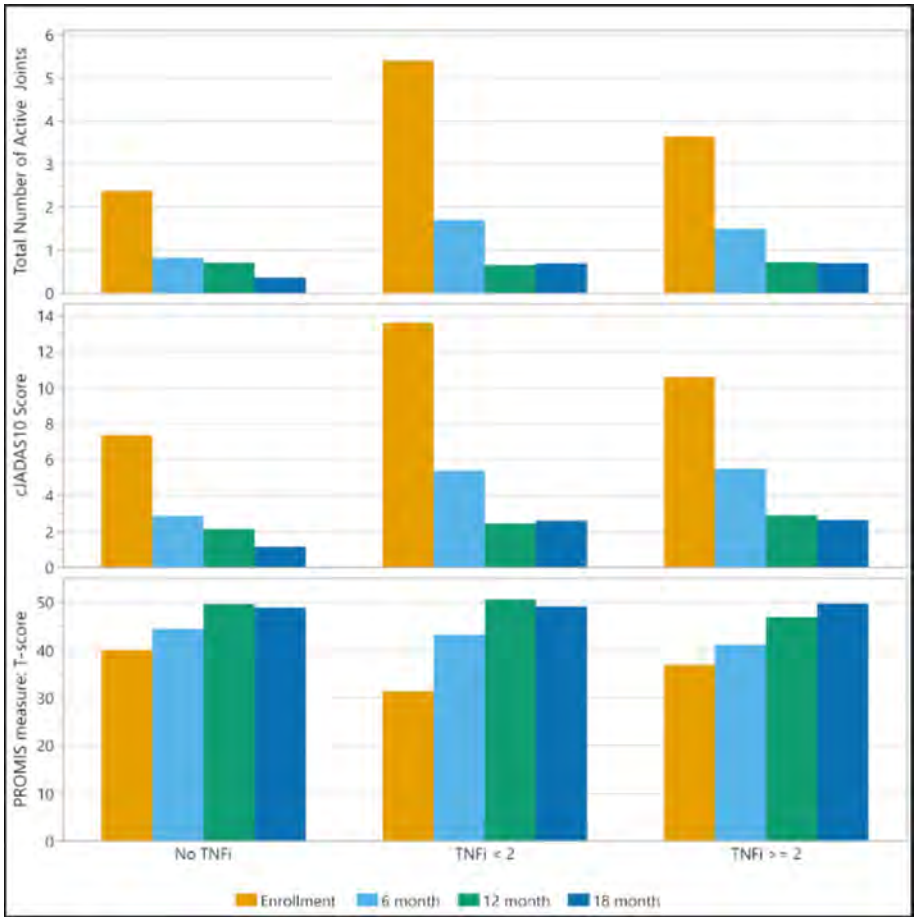


Figure 1: Disease Activity Over Time in Those That Started TNFi <2 Years Old, TNFi ≥ 2 Years Old, and Never Used TNFi

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is the most common pediatric rheumatic disease. Tumor necrosis factor inhibitors (TNFi) are key treatments in non-systemic JIA (sJIA), but patients diagnosed ≤2 years old have been underrepresented in studies thus far. Despite widespread clinical use, limited data exists on TNFi efficacy in this cohort, often leading to treatment delays. Early disease control is critical to optimize long-term outcomes and prevent damage. This study aimed to (1) describe demographics of children diagnosed with non-sJIA 0-23 mo and (2) evaluate TNFi effectiveness in improving disease activity in these patients using data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, a national multicenter observational database.

Methods: Demographic and disease characteristics were described for all patients diagnosed with non-sJIA 0-23 mo from 2015-2023 in the CARRA Registry using descriptive statistics. Efficacy was analyzed in patients enrolled within 6 months of diagnosis with ≥2 follow-up visits at 0-3, 4-8, 10-14, or 16-20 months using total active joint count, clinical Juvenile Arthritis Disease Activity Score (cJADAS-10), and Patient-Reported Outcomes Measurement Information System (PROMIS) T-scores. Bivariate analysis comparing the subcohort to the entire cohort was performed using Mann Whitney U and Chi-Square tests with a significance of 0.05. Effects size was reported based on the type of statistical test used.

Results: 949 children were diagnosed with non-sJIA 0-23 mo in the CARRA registry; 29.3% were enrolled within 6 months of diagnosis and had ≥2 follow-ups. Most common subtypes at enrollment were oligoarticular JIA (54.0%) then Rheumatoid Factor (RF)-negative polyarticular JIA (35.1%). Early enrollees had higher baseline disease activity based on active joint counts (2 vs 0), physician global assessments (PGA) (2 vs 0), childhood health assessment questionnaires (CHAQ) (0.375 vs 0.125), and cJADAS10 (8 vs 3) ($p< 0.001$). They also had higher ANA positivity rates (76.9% vs. 71.3%, $p=0.02$) and lower uveitis rates (13.4% vs 32.0%, $p< 0.001$) (Table 1). At baseline, the TNFi ≤2 patients had higher mean active joint

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

counts (4 vs 3 vs 2), cJADAS10 scores (14.5 vs 10 vs 7), and lower PROMIS scores (30.5 vs 25.5 vs 39) compared to the TNFi >2 and never-TNFi groups respectively. Improvements were seen through 16-20 mo with similar joint counts (0 vs 0 vs 0), cJADAS10 (0.75 vs 1 vs 0), and PROMIS (56 vs 56 vs 45) across all 3 groups (Fig 1).

Conclusion: Patients enrolled closer to diagnosis had higher baseline disease activity, reinforcing that they represent an "enriched" cohort and more severe phenotype. Despite this, patients who started TNFi ≤2 demonstrated significant and sustained improvements in all disease activity measures by 12 months, ultimately reaching similar values as those who started TNFi >2 and did not use TNFi. This suggests that early initiation of TNFi therapy has a significant impact on disease course as it essentially corrected for the initial dramatically higher values in disease activity. These Improvements across clinical and functional measures strongly support the efficacy and early initiation of TNFi in the youngest children with non-sJIA.

Disclosure: C. Gulla: None; **T. Lozy**: Eli Lilly & Company, 11; **G. Janow**: None.

Abstract Number: 0399

External Validation of Claims-based Algorithms for Newly Diagnosed Juvenile Idiopathic Arthritis

Daniel Horton[1], Lauren Parlett[2], Yuyang Zhu[3], Sanika Rege[4], Patricia Hoffman[5], Daniel Reiff[6], Sarah McGuire[7], Sonia Pothraj[8], Cynthia Salvant[9], Lakshmi Moorthy[1], Cecilia Huang[4], Dawn Koffman[4], Matthew Iozzio[3], Alicia Iizuka[4], Kevin Schott[2], Stephen Crystal[10], Amy Davidow[11], Tobias Gerhard[4], Kevin Haynes[12], Brian Strom[13], Daniel Beachler[2] and Carlos Rose[14], [1]Department of Pediatrics, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [2]Carelon Research, Inc, Wilmington, DE, [3]Rutgers Center for Pharmacoepidemiology and Treatment Science, Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ, USA, New Brunswick, [4]Rutgers Center for Pharmacoepidemiology and Treatment Science, Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ, USA, New Brunswick, NJ, [5]Hospital for Special Surgery, New York, NY, [6]Boys Town National Research Hospital, Boys Town, [7]Department of Obstetrics and Gynecology, Cooper Medical School, Camden, Camden, NJ, [8]Washingtonville Pediatrics, Washingtonville, NY, [9]Albany Medical Center, Albany, NY, [10]Rutgers Center for Health Services Research, Institute for Health, Health Care Policy and Aging Research, New Brunswick, NJ, [11]New Jersey Medical School, Newark, NJ, [12]Janssen Research & Development, Titusville, NJ, [13]Rutgers Biomedical and Health Sciences, New Brunswick, [14]Thomas Jefferson University, Wilmington, DE

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Administrative claims databases enable research in large populations with JIA. We previously showed that machine learning (ML)-based algorithms accurately identify new JIA diagnoses within US commercial insurance claims data. We externally validated these algorithms within US public insurance claims data.

Methods: We performed a cross-sectional validation study using US commercial health plan data (2013-20) and national US Medicaid data (2013-18). We identified children diagnosed with JIA (ICD-9-CM: 696.0, 714, 720; ICD-10-CM: L40.5, M05, M06, M08, M45) before age 18 after ≥12 months' continuous enrollment without JIA diagnosis or immunosuppression. JIA diagnoses were based on 3 previously validated definitions: 1) rheumatologist's diagnosis plus ≥2 specific lab test orders; 2) ≥2 outpatient diagnoses 8-52 weeks apart; or 3) 1 inpatient diagnosis. A random set of available qualifying charts were abstracted and independently adjudicated as definite, probable, possible, or unlikely JIA by clinical experts; discrepancies were resolved by consensus. Incident JIA was defined as definite or probable JIA diagnosed ≤4 months before first JIA claim. ML-based algorithms used simulation-based balancing and logistic regression regularization hyperparameters with 10-fold

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Accuracy of optimal machine-learning based algorithms for incident JIA

	Commercial, commercial insurance data-derived					Medicaid, commercial insurance data-derived					Medicaid, Medicaid data-derived				
ICD type	N. vars	Se (%)	Sp (%)	PPV (%, 95% CI)	AUC	N. vars	Se (%)	Sp (%)	PPV (%, 95% CI)	AUC	N. vars	Se (%)	Sp (%)	PPV (%, 95% CI)	AUC
ICD-9	30[1,2]	100	96	97 (93-100)	1.00	30[2]	97	19	67 (55-80)	0.76	24[1,2]	70	90	88 (82-94)	0.93
ICD-10	9[2,3]	100	97	97 (94-100)	1.00	9[2]	100	29	70 (57-83)	0.87	12[2,3]	100	96	96 (93-100)	1.00

AUC, area under the receiver operating characteristic curve; N. vars, number of variables; PPV, positive predictive value; Se, sensitivity; Sp, specificity

[1] 2 variables in common between commercial and public insurance data-derived algorithms

[2] 1 variable in common between ICD-9- and ICD-10-based algorithms within each database

[3] 1 variable in common between commercial and public insurance data-derived algorithms

Table 2. Accuracy of rule-based algorithms for incident JIA based on rheumatologist's diagnosis and JIA-specific labs[1]

Claims type	Commercial insurance data				Medicaid insurance data			
Diagnosis code type	ICD-9-CM (n=37)		ICD-10-CM (n=35)		ICD-9-CM (n=1)		ICD-10-CM (n=7)	
JIA diagnosis by rheumatologist plus	PPV	Se	PPV	Se	PPV	Se	PPV	Se
≥2 lab orders (original)	76%	100%	51%	100%	100%	100%	57%	100%
≥3 lab orders	77%	82%	81%	72%	100%	100%	60%	75%
≥4 lab orders	81%	61%	91%	56%	100%	100%	60%	75%
≥5 lab orders	88%	25%	100%	17%	-	0	67%	50%
≥2 lab orders + treatment[2]	77%	86%	59%	89%	100%	100%	67%	100%
≥2 lab orders + non-GC treatment	76%	80%	61%	78%	100%	100%	67%	100%
≥2 lab orders + DMARD treatment	79%	39%	69%	61%	100%	100%	75%	75%
≥2 lab orders, excl. non-specific JIA codes[3]	76%	89%	53%	100%	-	0	67%	100%
≥3 lab orders, excl. non-specific JIA codes[3]	77%	71%	87%	72%	-	0	100%	100%
≥4 lab orders, excl. non-specific JIA codes[3,4]	83%	54%	100%	56%	-	0	100%	75%
≥5 lab orders, excl. non-specific JIA codes[3]	88%	25%	100%	17%	-	0	100%	50%

DMARD, disease-modifying antirheumatic drug; GC, glucocorticoid; ICD-9/10-CM, International Classification of Diseases, Version 9/10, Clinical Modification; PPV, positive predictive value; Se, sensitivity

[1] ≥1 rheumatologist's diagnosis plus orders for specific labs (antinuclear antibody, rheumatoid factor, anti-cyclic citrullinated protein antibody, or HLA-B27) within ±4 months

[2] Nonsteroidal anti-inflammatories, oral or intra-articular glucocorticoids, or synthetic or biologic DMARDs within 4 months

[3] Excluding ICD-9 714.0, 714.1, 714.4, or 714.8 used before age 16, or 714.9 (any age); ICD-10 M05 or M06 used before age 16

[4] Suggested algorithm in bold font

Table 3. Accuracy of rule-based algorithms for incident JIA based on ≥2 JIA-related visits[1]

Claims type	Commercial insurance data				Medicaid insurance data			
Diagnosis code type	ICD-9-CM (n=52)		ICD-10-CM (n=50)		ICD-9-CM (n=60)		ICD-10-CM (n=47)	
Definition[2]	PPV	Se	PPV	Se	PPV	Se	PPV	Se
≥2 visits (any provider)	46%	100%	36%	100%	52%	100%	51%	100%
≥2 visits (not ophtho)[3]	48%	96%	41%	100%	52%	94%	52%	92%
≥5 visits (not ophtho)[3]	65%	83%	50%	100%	77%	55%	75%	88%
≥14 visits (not ophtho)[3]	76%	54%	63%	67%	88%	23%	67%	25%
≥2 visits, 16-52 weeks apart (not ophtho)[3]	54%	92%	41%	94%	55%	77%	58%	88%
≥2 visits, 30-52 weeks apart (not ophtho)[3]	68%	71%	41%	78%	53%	58%	61%	83%
≥2 visits, any JIA treatment (not ophtho)[3,4]	66%	96%	48%	89%	66%	81%	71%	92%
≥2 visits, non-GC treatment (not ophtho)[3]	71%	83%	47%	83%	68%	81%	71%	83%
≥2 visits, DMARD treatment (not ophtho)[3]	87%	54%	35%	39%	84%	68%	80%	67%
≥5 visits, any JIA treatment (not ophtho)[3,4]	83%	83%	53%	89%	83%	48%	78%	88%
≥2 visits, DMARD treatment (not ophtho), excl. non-specific JIA codes[4,5]	92%	50%	39%	39%	90%	61%	79%	63%
≥5 visits, any JIA treatment (not ophtho), excl. non-specific JIA codes[3,4,5,6]	89%	71%	57%	89%	88%	45%	81%	88%

DMARD, disease-modifying antirheumatic drug; GC, glucocorticoid; ICD-9/10-CM, International Classification of Diseases, Version 9/10, Clinical Modification; ophtho, ophthalmologist; PPV, positive predictive value; Se, sensitivity

[1] Original algorithm: ≥2 visits with JIA diagnosis (any provider), 8-52 weeks apart

[2] Visits 8-52 weeks apart unless otherwise noted

[3] Index diagnosis not from an ophthalmologist

[4] Nonsteroidal anti-inflammatories, oral or intra-articular glucocorticoids, or synthetic or biologic DMARDs within 4 months

[5] Excluding ICD-9 714.0, 714.1, 714.4, or 714.8 used before age 16, and 714.9 (any age); ICD-10 M05 or M06 used before age 16

[6] Suggested algorithm in bold font

cross-validation. We used optimal predictive model variables to assess sensitivity (Se), specificity (Sp), and positive predictive value (PPV) (95% confidence interval [CI]). We also tested rule-based algorithms refined based on provider type, JIA diagnosis counts, laboratory test counts, and documented JIA treatment. We compared results across databases and ICD types.

Results: Of 298 eligible charts reviewed (182 commercial, 116 public), 151 had incident JIA (ICD-9 commercial 58%, public 53%; ICD-10 commercial 41%, public 52%). Optimal ML-based algorithms derived within commercial claims data enabled excellent discrimination between incident JIA and unlikely JIA (ICD-9: Se 100%, Sp 96%, PPV 97%; ICD-10: Se 100%, Sp 97%, PPV

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

97%) (Table 1). However, the same algorithm was not accurate within the Medicaid sample (ICD-9: Se 97%, Sp 19%, PPV 67%; ICD-10: Se 100%, Sp 29%, PPV 70%), and more accurate algorithms derived within Medicaid data used distinct sets of predictive variables (Table). Moreover, optimal ML-based algorithms differed in number and types of predictors across ICD-9 and ICD-10 data. Rule-based algorithms had lower specificity and/or sensitivity, but refined algorithms were more accurate and consistent across databases and ICD types (Table 2-3). Preferred rule-based algorithms required either: 1) rheumatologist's outpatient diagnosis plus ≥4-5 specific lab orders, or 2) ≥5 outpatient JIA visits (first diagnosis not for eye care) plus any JIA treatment.

Conclusion: While ML-based diagnostic algorithms for incident JIA performed well within each database and ICD type, results differed across databases and ICD types. In contrast, refined rule-based algorithms had better external validity, with similarly high PPVs across databases and ICD code types. These preferred rule-based algorithms will improve the quality of future claims-based research on the diagnosis, management, and outcomes of newly diagnosed JIA.

Disclosure: D. Horton: None; **L. Parlett**: Bristol-Myers Squibb(BMS), 5, Novartis, 5, Pfizer, 5, Teva, 5; **Y. Zhu**: None; **S. Rege**: None; **P. Hoffman**: None; **D. Reiff**: None; **S. McGuire**: None; **S. Pothraj**: None; **C. Salvant**: None; **L. Moorthy**: None; **C. Huang**: None; **D. Koffman**: None; **M. Iozzio**: None; **A. Iizuka**: None; **K. Schott**: None; **S. Crystal**: None; **A. Davidow**: None; **T. Gerhard**: Genentech, 1; **K. Haynes**: Janssen, 3, 11; **B. Strom**: None; **D. Beachler**: None; **C. Rose**: None.

Abstract Number: 0400

Recent Antibiotic Exposure and Response to Treatment of Juvenile Idiopathic Arthritis

Daniel Horton[1], Charu Verma[2], Sanika Rege[2], Alicia Iizuka[2], Matthew Iozzio[3], Dawn Koffman[3], Stephen Crystal[4], Amy Davidow[5], Tobias Gerhard[2], Lauren Parlett[6], Carlos Rose[7] and Brian Strom[8], [1]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [2]Rutgers Center for Pharmacoepidemiology and Treatment Science, Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ, USA, New Brunswick, NJ, [3]Rutgers Center for Pharmacoepidemiology and Treatment Science, Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ, USA, New Brunswick, [4]Rutgers Center for Health Services Research, Institute for Health, Health Care Policy and Aging Research, New Brunswick, NJ, [5]New Jersey Medical School, Newark, NJ, [6]Carelon Research, Inc, Wilmington, DE, [7]Thomas Jefferson University, Wilmington, DE, [8]Rutgers Biomedical and Health Sciences, New Brunswick

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile idiopathic arthritis (JIA), the most common pediatric rheumatic disease, has been tied to microbiome disruption (dysbiosis). Dysbiosis in adults with arthritis affects response to methotrexate, a common disease-modifying antirheumatic drug (DMARD), but the effects of microbiome-altering drugs (e.g., antibiotics) on methotrexate response for JIA are unknown. We tested if antibiotic exposure is associated with response to methotrexate for JIA, hypothesizing shorter times to treatment change after antibiotic exposure and larger effects with more recent, frequent, and disruptive exposures.

Methods: We conducted a retrospective cohort study using national US public insurance administrative claims data (2001-2019). We included children ages 1-17 diagnosed with JIA who were initiating methotrexate monotherapy or, for comparison, tumor necrosis factor inhibitor (TNFi) monotherapy, after ≥10 months of continuous enrollment without

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

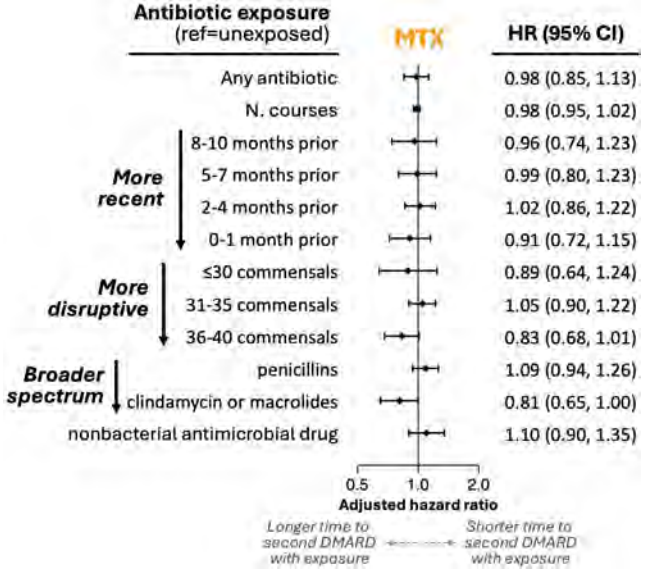
Table. Baseline characteristics of the study population

Characteristic	MTX users		TNFi users	
Demographics, N (%)	**Exposed N=3,067**	**Unexposed N=2,443**	**Exposed N=640**	**Unexposed N=634**
Age, years				
0-5	957 (31.2)	533 (21.8)	108 (16.9)	68 (10.7)
6-11	997 (32.5)	835 (34.2)	173 (27.0)	163 (25.7)
12-17	1,113 (36.3)	1,075 (44.0)	359 (56.1)	403 (63.6)
Female sex	2,107 (68.7)	1,673 (68.5)	408 (63.8)	381 (60.1)
Race/ethnicity				
White non-Hispanic	1,512 (49.3)	949 (38.9)	298 (46.6)	245 (38.6)
Black non-Hispanic	390 (12.7)	385 (15.8)	63 (9.8)	84 (13.3)
Hispanic/Latino	697 (22.7)	658 (26.9)	155 (24.2)	165 (26.0)
Other	468 (15.3)	451 (18.4)	124 (19.4)	140 (22.1)
Region, N (%)				
Northeast	456 (14.9)	367 (15.0)	126 (19.7)	108 (17.0)
Midwest	826 (26.9)	634 (26.0)	118 (18.4)	142 (22.4)
South	1,179 (38.4)	711 (29.1)	274 (42.8)	211 (33.3)
West	606 (19.8)	731 (29.9)	122 (19.1)	173 (27.3)
Comorbidities, N (%)				
Allergic or asthma	1,019 (33.2)	614 (25.1)	213 (33.3)	161 (25.4)
Autoimmune (besides uveitis)	251 (8.2)	163 (6.7)	112 (17.5)	68 (10.7)
Uveitis	65 (2.1)	66 (2.7)	9 (1.4)	10 (1.6)
Down or Turner syndrome	55 (1.8)	21 (0.9)	13 (2.0)	8 (1.3)
Treatment, N (%)				
NSAID or GC	2,808 (91.6)	2,091 (85.6)	540 (84.4)	455 (71.8)
Folic acid	1,671 (54.5)	1,396 (57.1)	116 (18.1)	92 (14.5)
Healthcare utilization[1]				
Outpatient visits, mean (SD)	28.4 (23.3)	21.5 (16.8)	32.8 (30.7)	21.3 (14.6)
ED visits, mean (SD)	2.3 (4.5)	1.2 (2.8)	3.1 (9.0)	1.6 (3.9)
Hospitalization, N (%)	478 (15.6)	141 (5.8)	93 (14.5)	45 (7.1)

ED: Emergency department; GC: glucocorticoid; MTX: methotrexate; NSAID: non-steroidal anti-inflammatory drug; SD: standard deviation; TNFi: tumor necrosis factor inhibitor

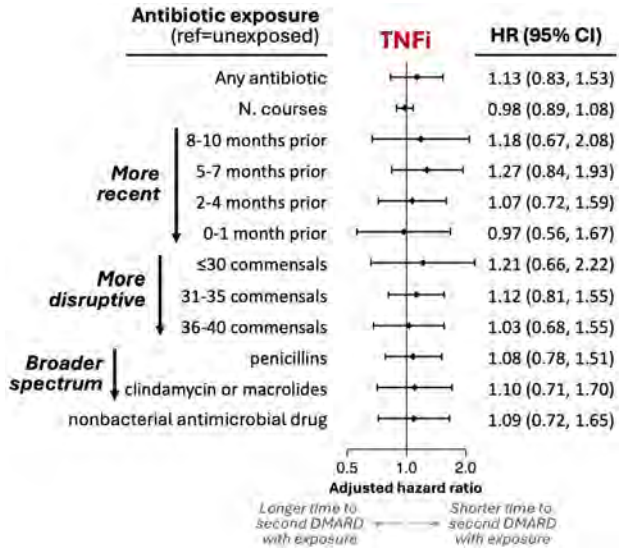
[1] Healthcare utilization during the 10-month baseline period

Figure 1. Associations between antibiotic exposure and MTX ineffectiveness. Forest plot shows associations between antibiotic exposure within 10-months before methotrexate (MTX) initiation and MTX ineffectiveness, as represented by initiation of a second DMARD after ≥1 month. Models were adjusted for baseline demographic, clinical, treatment, and healthcare-related covariates (see Table) and expressed as adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). HRs >1 signify shorter times to initiation of a second DMARD with antibiotic exposure.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Associations between antibiotic exposure and TNFi ineffectiveness. Forest plot shows associations between antibiotic exposure within 10-months before tumor necrosis factor inhibitor (TNFi) initiation and TNFi ineffectiveness, as represented by initiation of a second DMARD after ≥1 month. Models were adjusted for baseline demographic, clinical, treatment, and healthcare-related covariates (see Table) and expressed as adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). HRs >1 signify shorter times to initiation of a second DMARD with antibiotic exposure.



DMARDs. Antibiotic exposure during the 10-month baseline period was assessed and characterized by timing, number of courses, and type. Nonbacterial antimicrobial drugs were evaluated as a negative control exposure. As a proxy of treatment ineffectiveness, the primary outcome was initiation of a second DMARD after at least 1 month, a lag representing hypothetical induction time between antibiotic-induced dysbiosis and altered DMARD response, allowing for delayed initiation of a DMARD intended for use in combination. Censoring occurred after a 60-day gap in DMARDs, completion of 10 months of follow-up, loss of enrollment, or death. Associations between antibiotic exposure and treatment change were estimated using Cox regression, adjusting for baseline demographic, disease, treatment, and health utilization covariates (Table), and represented by adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). In sensitivity analyses, we considered outcomes occurring after a 2-month lag after initial DMARD exposure.

Results: We identified 5510 new methotrexate users (mean age 9.5±4.9 years, 68.6% female, 55.6% exposed to antibiotics, 15.9% with outcomes) and 1274 new TNFi users (mean age 11.6±4.5 years, 61.9% female, 50.2% exposed to antibiotics, 15.6% with outcomes). Children with antibiotic exposure tended to be younger and more likely to be White non-Hispanic, live in the South, and have more comorbidities, more anti-inflammatory exposure, and more baseline healthcare utilization (Table). No relationship was observed between baseline antibiotic exposure and treatment change in methotrexate users (HR 0.98, 95% CI 0.85, 1.13) or TNFi users (HR 1.13, 95% CI 0.83, 1.53). Antibiotic timing, number of courses, and type of antibiotic exposure, as well as nonbacterial antimicrobial drug exposure, were also not associated with treatment changes in methotrexate or TNFi users (Figures 1-2). Findings from sensitivity analyses were consistent.

Conclusion: Recent antibiotic exposure is not associated with changes in DMARD treatment in children with JIA, suggesting that dysbiosis does not play a major role in response to methotrexate or TNFi for JIA.

Disclosure: D. Horton: None; **C. Verma**: None; **S. Rege**: None; **A. Iizuka**: None; **M. Iozzio**: None; **D. Koffman**: None; **S. Crystal**: None; **A. Davidow**: None; **T. Gerhard**: Genentech, 1; **L. Parlett**: Bristol-Myers Squibb(BMS), 5, Novartis, 5, Pfizer, 5, Teva, 5; **C. Rose**: None; **B. Strom**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0401

Longitudinal Effectiveness of Abatacept in JIA: Results From an Ongoing JIA Registry

Daniel Lovell[1], Nicolino Ruperto[2], Jennifer Huggins[3], Ekaterina Alexeeva[4], Colleen Correll[5], John Bohnsack[6], Stacey Tarvin[7], Gabriele Simonini[8], Thomas Griffin[9], Andrew Zeft[10], Gerd Horneff[11], Pierre Quartier[12], Iionka Orban[13], Heather Walters[14], Valda Stanevica[15], Julisa Patel[16], Adam M Huber[17], Margalit Rosenkranz[18], Daniel Kingsbury[19], Rosie Scuccimarri[20], Gabriel Vega Cornejo[21], Joost Swart[22], Robert Carroll[23], Hermine Brunner[1], Tina Sherrard[24], Chiara Pallotti[25], Clara Malattia[26], Alberto Martini[26] and PRINTO and PRCSG Coordinating Centers, [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Università degli Studi Milano-Bicocca, Milan, Italy, [3]Cincinnati Children's Medical Center, Cincinnati, OH, [4]National Medical Research Center for Children's Health Federal State Autonomous Institution of the Russian Federation Ministry of Health and I.M. Sechenov First Moscow State Medical University (Sechenovskiy University), Moscow, Russia, [5]University of Minnesota, Minneapolis, MN, [6]University of Utah, Salt Lake City, UT, [7]Riley Hospital for Children at Indiana University, Indianapolis, IN, [8]Rheumatology Unit, ERN-ReCONNET center, Meyer Children's Hospital IRCCS, Firenze, Firenze, Italy, [9]Atrium Health Levine Children's Hospital, Charlotte, NC, [10]Cleveland Clinic, Cleveland, OH, [11]Asklepios Klinik, Hamburg, Germany, [12]Hôpital Necker-Enfants Malades, Paris, France, [13]Department of Rheumatology and Clinical Immunology of Semmelweis University, Budapest, Hungary, [14]Northwell, New Hyde Park, NY, [15]Riga Stradiņš University, Riga, Latvia, [16]Children's Hospital of Georgia, Augusta University, Augusta, GA, [17]IWK Grace Health Centre, Halifax, NS, Canada, [18]University of Pittsburgh, Pittsburgh, PA, [19]Randall Children's Hospital at Legacy Emanuel, Portland, OR, [20]McGill University Health Centre, Montreal, QC, Canada, [21]Clinica de reumatología Guadalajara, Guadalajara, Jalisco, Mexico, [22]Wilhelmina Children's Hospital / UMC Utrecht, Utrecht, Utrecht, Netherlands, [23]Bristol Myers Squibb, London, United Kingdom, [24]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [25]Istituto G. Gaslini, Servizio di Sperimentazioni Cliniche Pediatriche, Genova, Italy, [26]Istituto G. Gaslini Pediatria II Reumatologia and University of Genova, Genova, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Abatacept is a selective T-cell co-stimulation modulator approved for use in JIA. Efficacy and safety of abatacept in patients (pts) with JIA have been demonstrated previously in 2 phase 3 trials[1,2] and earlier results from this phase 4 Abatacept JIA Registry (NCT01357668).[3] The objective of this analysis was to provide data from a real-world setting for longitudinal safety and effectiveness of intravenous (IV) and subcutaneous (SC) abatacept in pts with JIA.

Table 1. Assessment of disease activity and impact. Data are mean (SE), unless otherwise indicated. a: Visual analog scale 0–10; 0=inactive; b: Range 0–15, 0=no functional limitation; c: Range 0–15, 0=best possible HRQoL. HRQoL, health-related quality of life; JAMAR, Juvenile Arthritis Multidimensional Assessment Report; SE, standard error.

Endpoint	BL (n=701)	3 months (n=533)	6 months (n=522)	1 year (n=502)	2 years (n=385)	3 years (n=275)	4 years (n=193)	5 years (n=146)
Physician Global Disease Activity[a]	2.0 (0.1)	1.6 (0.1)	1.6 (0.1)	1.2 (0.1)	1.1 (0.1)	1.1 (0.1)	1.0 (0.1)	0.9 (0.1)
Clinically inactive disease (Wallace criteria), %	32	33	37	46	53	51	50	55
Joints with active arthritis	2.8 (0.2)	2.0 (0.2)	2.0 (0.2)	1.5 (0.2)	1.4 (0.2)	1.5 (0.2)	1.2 (0.2)	1.0 (0.2)
JAMAR functional scale[b]								
Child	4.9 (0.3)	4.1 (0.3)	4.0 (0.3)	3.8 (0.3)	3.2 (0.3)	3.4 (0.4)	3.1 (0.4)	3.0 (0.5)
Parent	5.3 (0.3)	4.8 (0.3)	4.4 (0.3)	3.6 (0.3)	3.2 (0.3)	3.3 (0.5)	3.6 (0.7)	1.9 (0.5)
JAMAR HRQoL[c]								
Child	7.0 (0.2)	6.0 (0.2)	5.8 (0.3)	5.3 (0.3)	4.9 (0.3)	5.2 (0.4)	4.9 (0.4)	4.5 (0.5)
Parent	6.8 (0.2)	6.0 (0.3)	5.9 (0.3)	5.1 (0.3)	4.7 (0.3)	4.2 (0.4)	4.0 (0.6)	3.3 (0.6)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: By protocol, clinical sites in the Pediatric Rheumatology Collaborative Study Group and Pediatric Rheumatology International Trial Organization enrolled pts meeting the ILAR criteria for 1 of the categories of JIA and currently taking or starting IV or SC abatacept. Planned duration of follow-up (FU) is 10 years; data were collected up to March 31, 2024. Effectiveness was assessed at day of entry into registry (baseline [BL]), 3 and 6 months, and 1, 2, 3, 4, and 5 years. Safety data were collected at each visit.

Results: Of the 740 pts enrolled, 701 were included in the analysis (476 IV, 225 SC); 561/701 (80%) were female. At BL, median age was 13.6 years and 28 (4%) pts were aged 2–5 years; JIA disease duration was 4.5 years. Median abatacept treatment duration was 6.1 months and number of active joints was 1.0 (mean 2.7). JIA categories were systemic (2%), oligo (25%), polyarticular RF-negative (48%), polyarticular RF-positive (10%), psoriatic (5%), enthesitis-related (4%), and undifferentiated (6%). Total abatacept exposure was 1513.2 pt-years with a mean/median duration of abatacept treatment of 25.9/19.7 months. At 1-year FU, pts had low Physician Global Disease Activity, low Juvenile Arthritis Multidimensional Assessment Report scores, and improvement in the number of joints with active arthritis compared with BL (Table 1). A higher percentage of pts achieved clinically inactive disease after 1 year of FU vs BL (46% vs 32%; Table 1). This trend continued despite low numbers of pts with 4 and 5 years of FU. There were 11 serious infections reported (incidence rate [IR] 0.52/100 pt-years of FU, 95% CI: 0.26, 0.92; IR 0.73/100 pt-years on treatment, 95% CI: 0.36, 1.30). There were 17 autoimmune events (IR 0.80/100 pt-years of FU, 95% CI: 0.46, 1.28; IR 1.12/100 pt-years on treatment, 95% CI: 0.65, 1.80). There were 2 adverse event malignancies (n=1 each: medulloblastoma, T-cell lymphoma). No cases of tuberculosis were reported. There was 1 unrelated death (pre-existing cardiac problems).

Conclusion: In this real-world JIA cohort, abatacept was safe and well-tolerated with no new safety risks identified. This longitudinal analysis further supports the persistent effectiveness of abatacept in pts with JIA.

References:

1. Brunner HI, et al. *Arthritis Rheumatol* 2018;70:1144-1154.
2. Ruperto N, et al. *Lancet* 2008;372:383-391.
3. Lovell DJ, et al. *Rheumatology* 2024;63:S1195-S1026.

Medical writing: Alexus Shirk, PhD (Caudex, an IPG Health Company), funded by Bristol Myers Squibb.

Disclosure: D. Lovell: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **N. Ruperto**: AbbVie/Abbott, 2, AClaris, 2, AlfaSigma, 2, Amgen, 2, AstraZeneca, 2, Aurinia, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Galapagos, 2, Genentech, 2, Guidepoint, 2, Idorsia, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Takeda, 2; **J. Huggins**: None; **E. Alexeeva**: Amgen, 12, 5, AstraZeneca, 6, Biocad, 12, 5, Eli Lilly, 12, 5, Generium, 5, 6, Johnson & Johnson, 5, 6, Novartis, 5, 6, Pfizer, 12, 5, Roche, 6, R-Pharm JSC, 5, 6, Sanofi, 12, 5, Skopinpharm, 6, Sobi, 6, Swixx Biopharma, 6, UCB, 12, 5; **C. Correll**: None; **J. Bohnsack**: Bristol-Myers Squibb(BMS), 5, Janssen, 5, Pfizer, 5; **S. Tarvin**: AbbVie/Abbott, 5, American Academy of Pediatrics, 12, Editor, Amgen, 5, Childhood Arthritis Rheumatology Research Alliance, 5, Roche, 5, UCB, 5; **G. Simonini**: None; **T. Griffin**: None; **A. Zeft**: GE Healthcare, 12, Merck/MSD, 12, Opko, 12, Sobi, 1, Teva, 12,; **G. Horneff**: Janssen, 5, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, Sanofi, 6; **P. Quartier**: AbbVie, 2, 6, Chugai-Roche, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 1, 2, Sobi, 2, 6; **I. Orban**: None; **H. Walters**: None; **V. Stanevica**: None; **J. Patel**: None; **A. Huber**: None; **M. Rosenkranz**: None; **D. Kingsbury**: None; **R. Scuccimarri**: Bristol-Myers Squibb(BMS), 5, Sobi, 12, Attendee of sponsored CME; **G. Vega Cornejo**: None; **J. Swart**: None; **R. Carroll**: Bristol-Myers Squibb(BMS), 3; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **T. Sherrard**: None; **C. Pallotti**: None; **C. Malattia**: None; **A. Martini**: Pfizer, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0402

Risk Factors for Anti-Adalimumab Antibody Development in Pediatric Patients Using Adalimumab for Rheumatic Disease and Associated Conditions

Dawn Gist[1], Andrea Ramirez[1], Jamie Lai[2], Duc Nguyen[1] and Kexin Guo[1], [1]Baylor College of Medicine, Houston, TX, [2]Baylor College of Medicine, The Woodlands, TX

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Adalimumab is a monoclonal antibody against TNF-α that is commonly used to treat JIA, hidradenitis suppurativa (HS), chronic uveitis, sarcoidosis, and chronic nonbacterial osteomyelitis (CNO). Anti-drug antibodies (ADAs) have been frequently reported in patients receiving adalimumab, leading to decreased therapeutic efficacy of the drug. Identifying clinical factors associated with ADA formation is essential to optimize long-term outcomes. This study aims to evaluate differences in treatment duration, flare frequency, and methotrexate use between patients with and without ADAs to adalimumab.

Methods: With IRB approval, a retrospective cohort study was done to evaluate ADA formation in pediatric patients receiving adalimumab for JIA, CNO, uveitis, sarcoidosis, or HS at a tertiary care center. A total of 119 patients were stratified into two groups based on presence or absence of ADAs. Data collected included duration of adalimumab therapy, dose frequency, flare frequency, methotrexate co-therapy, and treatment interruptions. Differences between groups were determined by chi-square test for categorical variables and Kruskal-Wallis test for continuous variables. A p-value of < 0.05 was considered statistically significant.

Results: Among 119 patients, 88 received adalimumab every 14 days, 21 every 7 days, and 10 at other frequencies. Patients on treatment every 7 days had less antibody formation than those on every 14 days ($p = 0.04$). Further analysis was done on the 88 patients on every 14-day regimen. Of those, 42 (37.17%) developed ADAs (Table 1). Patients with ADAs were of younger age than those without ADAs (12 years vs. 14 years, $p = 0.02$) (Figure 1). Flare rates were higher in patients with ADAs (69.86% vs. 97.6%; $p = 0.001$). The median duration of adalimumab use was not statistically different, though still greater in those with ADAs compared to those without (24 months [IQR 13–47] vs. 13 months [IQR 7–33]; $p = 0.02$) (Figure 2). Methotrexate was used more frequently in the ADA-negative group (43.5% vs. 21.4%, $p = 0.049$). Dosing of methotrexate in mg/m^2 was not different between the groups. Treatment interruptions of >1 month occurred in 33.3% of ADA-positive patients vs. 17.4% of ADA-negative patients ($p = 0.14$), and use of methotrexate during these interruptions did not differ.

Conclusion: ADA development was more common in patients not receiving methotrexate and was associated with increased disease flares. Although length of therapy and treatment interruption did not differ significantly, the data suggests a possible role in immunogenicity risk. Patients with frequent adalimumab dosing regimens were less likely to develop ADAs, though use of methotrexate was not analyzed in this increased frequency group and needs exploration. Younger age was associated with increased risk of antibody development. Results suggest that early use of ADA monitoring, particularly in younger patients and those on less frequent adalimumab regimens, may be helpful. The addition of methotrexate therapy or increasing the dosing frequency in patients who cannot tolerate DMARDs may help reduce immunogenicity and improve clinical outcomes in pediatric rheumatology.

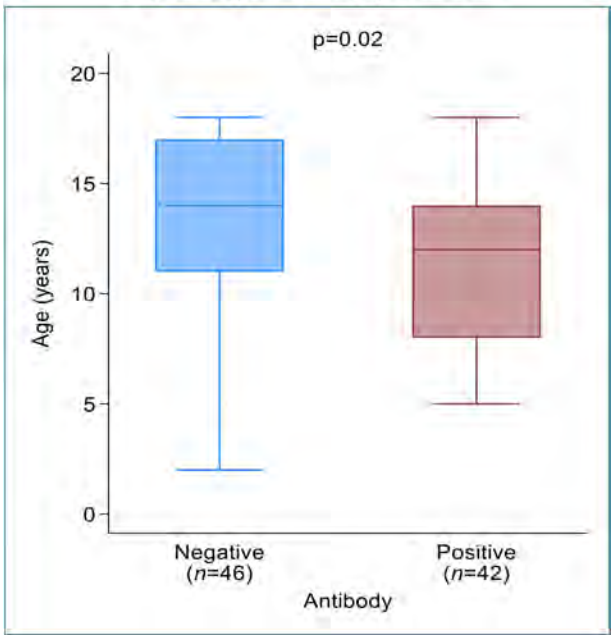
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1. CHARACTERISTICS OF PATIENTS ON ADALIMUMAB EVERY 14 DAYS, BY ADALIMUMAB ANTIBODY POSITIVITY

	TOTAL (n=88)	ANTIBODIES ABSENT (n=46)	ANTIBODIES PRESENT (n=42)	p-value
AGE (MEDIAN [IQR])	13.00 [9.00, 15.25]	14.00 [11.00, 16.75]	12.00 [8.00, 14.00]	0.02
FEMALE, N (%)	64 (72.7)	33 (71.7)	31 (73.8)	1.00
RACE, N (%)				0.03
ASIAN	5 (5.7)	5 (10.9)	0 (0.0)	
BLACK	3 (3.4)	1 (2.2)	2 (4.8)	
MULTIPLE	2 (2.3)	2 (4.3)	0 (0.0)	
UNKNOWN	7 (8.0)	1 (2.2)	6 (14.3)	
WHITE	71 (80.7)	37 (80.4)	34 (81.0)	
RACE2, N (%)				0.06
MULTIPLE	2 (2.3)	2 (4.3)	0 (0.0)	
NON-WHITE	8 (9.1)	6 (13.0)	2 (4.8)	
UNKNOWN	7 (8.0)	1 (2.2)	6 (14.3)	
WHITE	71 (80.7)	37 (80.4)	34 (81.0)	
ETHNICITY, N (%)				0.08
HISPANIC	37 (42.0)	17 (37.0)	20 (47.6)	
NON-HISPANIC	47 (53.4)	29 (63.0)	18 (42.9)	
UNKNOWN	4 (4.5)	0 (0.0)	4 (9.5)	
DIAGNOSIS, N (%)				0.68
CNO	5 (5.7)	3 (6.5)	2 (4.8)	
ENTHESITIS-RELATED ARTHRITIS (ERA)	10 (11.4)	7 (15.2)	3 (7.1)	
HIDRADENITIS SUPPURATIVA	4 (4.5)	2 (4.3)	2 (4.8)	
INFLAMMATORY BOWEL DISEASE-RELATED ARTHRITIS	2 (2.3)	1 (2.2)	1 (2.4)	
MULTIPLE	7 (8.0)	2 (4.3)	5 (11.9)	
OLIGOARTICULAR JIA	17 (19.3)	10 (21.7)	7 (16.7)	
POLYARTICULAR JIA, RF NEGATIVE	16 (18.2)	8 (17.4)	8 (19.0)	
POLYARTICULAR JIA, RF POSITIVE	11 (12.5)	4 (8.7)	7 (16.7)	
PSORIATIC JIA	9 (10.2)	6 (13.0)	3 (7.1)	
SARCOIDOSIS	1 (1.1)	1 (2.2)	0 (0.0)	
UNSPECIFIED JIA	1 (1.1)	1 (2.2)	0 (0.0)	
UVEITIS	4 (4.5)	1 (2.2)	3 (7.1)	
MONTHS ON ADALIMUMAB (MEDIAN [IQR])	19.00 [7.75, 41.50]	13.00 [6.00, 34.50]	24.00 [12.25, 42.50]	0.14
CONCURRENT METHOTREXATE USE, N (%)	29 (33.0)	20 (43.5)	9 (21.4)	0.049
METHOTREXATE DOSE IN MG/M2 (MEDIAN [IQR])	12.00 [10.00, 14.25]	12.50 [9.50, 14.25]	11.60 [10.80, 14.00]	0.90
FLARE, N (%)	73 (83.0)	32 (69.6)	41 (97.6)	0.001
INTERRUPTION IN ADALIMUMAB THERAPY >1 MONTH, N (%)	22 (25.0)	8 (17.4)	14 (33.3)	0.14
ON METHOTREXATE DURING ADALIMUMAB INTERRUPTION, N (%)	2 (9.1)	0 (0.0)	2 (14.3)	0.73

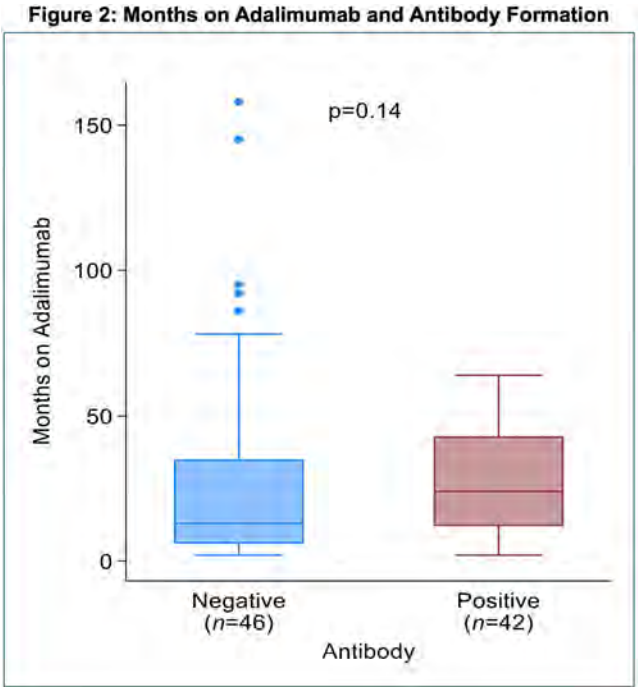
Patient characteristics by adalimumab antibody positivity, including age, sex, race, ethnicity, diagnosis, months on adalimumab, concurrent methotrexate use, dosing of methotrexate, flare rate, interruptions in adalimumab therapy, and use of methotrexate during adalimumab therapy interruptions.

Figure 1: Age and Antibody Formation



Box and whisker plot of age (in years) at the time of antibody testing compared between positive and negative adalimumab antibody groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Box and whisker plot of the number of months on adalimumab compared between positive and negative adalimumab antibody groups.

Disclosure: D. Gist: None; **A. Ramirez**: None; **J. Lai**: None; **D. Nguyen**: None; **K. Guo**: None.

Abstract Number: 0403

IL-6 as a Predictor of Response to Olokizumab in Polyarticular-Course Juvenile Idiopathic Arthritis: Results of the Phase 2 Clinical Trial

Ekaterina Alexeeva[1], Tatiana Dvoryakovskaya[1], Elena Zholobova[2], Elizaveta Krekhova[3], Valeria Matkava[4], Rinat Raupov[5], Daria Bukhanova[6], Alina Egorova[6], Sergey Grishin[6], Mikhail Samsonov[6], Mikhail Kostik[7] and Irina Nikishina[4], [1]National Medical Research Center for Children's Health Federal State Autonomous Institution of the Russian Federation Ministry of Health and I.M. Sechenov First Moscow State Medical University (Sechenovskiy University), Moscow, Russia, [2]I.M.Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russia, [3]National Medical Research Center for Children's Health Federal State Autonomous Institution of the Russian Federation Ministry of Health, Moscow, Russia, [4]V.A.Nasonova Research Institute of Rheumatology, Moscow, Russia, [5]H.Turner National Medical Research Center for Childrens Orthopaedics and Trauma Surgery, Saint-Petersburg, Russia, [6]R-Pharm JSC, Moscow, Russia, [7]Saint-Petersburg State Pediatric Medical University, Saint Petersburg, Russia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Olokizumab (OKZ) is a direct interleukin-6 (IL-6) inhibitor. IL-6 is an attractive target for the treatment of pJIA. The aim of the study was to identify the subpopulation of patients with polyarticular-course juvenile idiopathic arthritis (pJIA) who can be expected to have a better treatment response compared to the whole pJIA population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Adolescent patients with active pJIA who had failed methotrexate were included in the Phase 2 open-label multicenter study in Russia and received OKZ in a dose of 64 mg every 4 weeks (q4w) subcutaneously (SC) during the main 24-week part of the study. The following outcomes were analyzed: JIA American College of Rheumatology 30/50/70% responses (JIA ACR 30/50/70 responses), Juvenile Arthritis Disease Activity Score-71 (JADAS-71), adverse events (AEs), the associations between the baseline C-reactive protein (CRP) and IL-6 values and effectiveness outcomes. IL-6 was detected in blood with the non-commercial ELISA assay (lower limit of quantification [LLOQ] =2 pg/ml). The significance of change from baseline was tested using the Wilcoxon signed-rank test, and the difference between groups was tested using Fisher exact test.

Results: A total of 16 patients - 9 (56.3%) girls and 7 (43.8%) boys - were enrolled; the median (25%; 75%) age at inclusion was 14.0 (13.0; 16.5) years, at pcJIA onset 11.8 (5.4; 13.7) years, and pcJIA duration was 3.4 (0.4; 8.9). Baseline IL-6 level was >LLOQ in 8 patients, median 87.9 (8.0; 106.9) pg/ml; and in 7 patients was ≤LLOQ. Baseline CRP was >10 mg/l in 8 patients and ≤10 mg/l in 7 patients.

By 24 weeks of treatment, median (25%; 75%) JADAS-71 significantly decreased from 20.8 (18.4; 32.6) at baseline to 9.5 (2.65; 20.8) points, p< 0.001. JIA ACR 30/50/70 response was achieved in 80%, 73.3%, 46.7% of patients, respectively. Both JADAS-71 and JIA ACR 30/50/70 outcomes had an insignificant trend toward better results in patients with higher baseline IL-6, with a significant difference for JIA ACR70 (**Table 1, Figure 1**). In 5 (33.3%) patients inactive disease status was achieved. AEs were reported in 12 (75%) patients, mostly mild to moderate ordinary infections (37.5%), which resolved without complications. No Grade 3-4 AEs, serious AEs,or deaths were reported. One patient discontinued treatment at Week 12 due to *de novo* psoriasis.

Table 1. Baseline IL-6 and CRP levels vs JIA ACR 30/50/70 responses at Week 24

IL-6 at Baseline	**JIA ACR30**	**JIA ACR50**	**JIA ACR70**
≤LLOQ (N=7)	4 (57.1)	4 (57.1)	1 (14.3)
>LLOQ (N=8)	8 (100.0)	7 (87.5)	6 (75.0)
p-value (Fisher exact test)	0.077	0.214	0.041
CRP at Baseline	**JIA ACR30**	**JIA ACR50**	**JIA ACR70**
CRP ≤10 mg/l (N=8)	5 (62.5)	5 (62.5)	2 (25.0)
CRP >10 mg/l (N=7)	7 (100.0)	6 (85.7)	5 (71.4)
p-value (Fisher exact test)	0.200	0.569	0.132

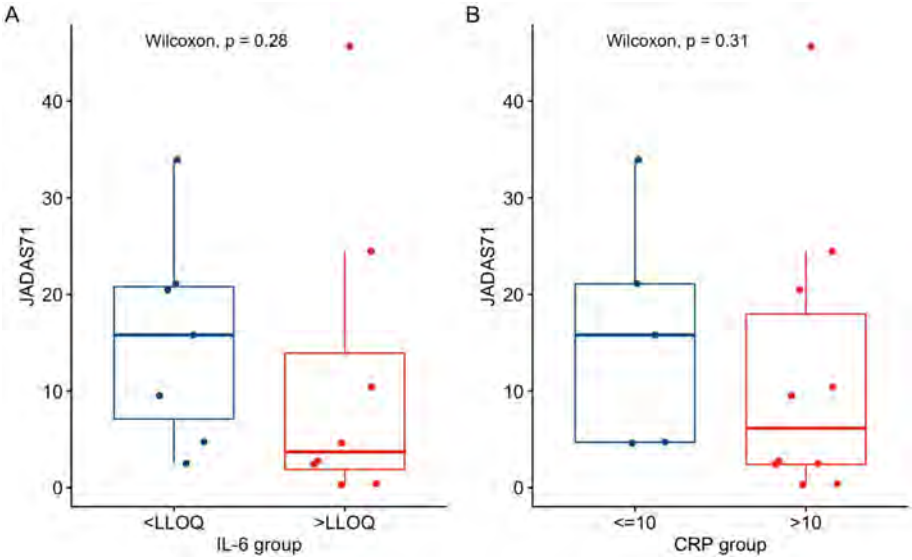


Figure 1. Baseline IL-6 and CRP levels vs JADAS-71 at Week 24

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: OKZ is a good therapeutic option for the pcJIA that leads to improvement in disease activity and has acceptable safety. It seems that OKZ response may be more successful in patients with higher baseline IL-6 levels.

Disclosure: E. Alexeeva: Amgen, 12, 5, AstraZeneca, 6, Biocad, 12, 5, Eli Lilly, 12, 5, Generium, 5, 6, Johnson & Johnson, 5, 6, Novartis, 5, 6, Pfizer, 12, 5, Roche, 6, R-Pharm JSC, 5, 6, Sanofi, 12, 5, Skopinpharm, 6, Sobi, 6, Swixx Biopharma, 6, UCB, 12, 5; **T. Dvoryakovskaya**: Amgen, 12, 5, Generium, 5, 6, Johnson & Johnson, 6, Novartis, 6, R-Pharm JSC, 5, 6, Sobi, 6, Swixx Biopharma, 6; **E. Zholobova**: Novartis, 6, Pfizer, 6; **E. Krekhova**: Johnson & Johnson, 6, Novartis, 6, R-Pharm JSC, 5, 6, Swixx Biopharma, 6; **V. Matkava**: Ipsen, 6, Novartis, 6, Pfizer, 6, R-Pharm JSC, 5; **R. Raupov**: Biocad, 5, Generium, 5, R-Pharm JSC, 5; **D. Bukhanova**: R-Pharm, JSC, 3; **A. Egorova**: R-Pharm, JSC, 3; **S. Grishin**: R-Pharm JSC, 3; **M. Samsonov**: R-Pharm, JSC, 3; **M. Kostik**: None; **I. Nikishina**: Ipsen, 6, Janssen, 6, Novartis, 6, Pfizer, 6, R-Pharm JSC, 5.

Abstract Number: 0404

Disease Extension in Children with Limited Juvenile Arthritis in the Childhood Arthritis and Rheumatology Research Alliance Registry

Eveline Wu[1], Stephen Balevic[2], Angel Marks[3], Manjushri Bhapkar[4], Baoshan Zhang[3], Alex Fist[4], Melanie Kohlheim[5], Vincent Del Gaizo[6], Laine Thomas[3], Laura Schanberg[7] and the CARRA Registry Investigators, [1]UNC Chapel Hill, Chapel Hill, NC, [2]Department of Pediatrics, Duke University, Durham, [3]Department of Biostatistics & Bioinformatics, Duke University, Durham, [4]Duke Clinical Research Institute, Duke University, Durham, [5]CARRA, Granville, OH, [6]Childhood Arthritis & Rheumatology Research Alliance (CARRA), Whitehouse Station, NJ, [7]Duke University Medical Center, DURHAM, NC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: For children with limited juvenile idiopathic arthritis (JIA), defined as ≤4 affected joints and without uveitis, psoriasis, or sacroiliitis at presentation, it is unknown how often disease extends to polyarthritis or uveitis. The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry is the largest prospective registry of children with JIA in North America, collecting longitudinal clinical and treatment data. The current study aimed to describe the natural history of limited JIA by estimating the proportion of recently diagnosed children who progress to develop polyarthritis, uveitis, or the need for systemic disease-modifying anti-rheumatic drugs (DMARDs), stratified by treatment status at the baseline Registry visit.

Methods: We conducted a retrospective analysis of data collected from the CARRA Registry between June 30, 2015 to July 16, 2021. Eligible children were 2-16 years at enrollment with a diagnosis of JIA within 6 months of enrollment and arthritis affecting ≤4 joints. Exclusion criteria included systemic JIA, sacroiliitis, inflammatory bowel disease, psoriasis, or uveitis. Patients were stratified based on systemic treatment status at the baseline Registry visit, defined as receipt of systemic DMARDs and/or systemic glucocorticoids for >14 days. The primary outcomes were incidence of disease extension within 12 and 18 months of enrollment, defined as the occurrence of polyarthritis (≥5 joints), uveitis, or need for systemic medications (e.g., conventional or biologic DMARDs or oral or intravenous glucocorticoids). We calculated the proportion of patients meeting each individual and the composite endpoint and conducted a Kaplan-Meier analysis.

Results: A total of 1,599 children with limited JIA were included (Table 1). At enrollment, 53% were receiving systemic treatment, including systemic steroids (9%), methotrexate (83%), and biologic DMARDs (28%). Among children who were treatment-naïve at enrollment, 7% developed polyarthritis, 5% developed uveitis, and 37% initiated new systemic treatment

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline patient characteristics by overall population and analysis subgroups

	No Treatment at Baseline N=760	Systemic Treatment at Baseline N=839	Overall N=1599
Age at diagnosis (years) Median (IQR)	6.4 (3.4, 11.2)	8.2 (3.9, 12.6)	7.4 (3.6, 12.0)
Time from diagnosis to baseline (months) Median (IQR)	1.4 (0, 2.8)	2.0 (0.4, 3.6)	1.8 (0, 3.2)
Female	499 (66%)	533 (64%)	1259 (79%)
Race/Ethnicity			
White	573 (75%)	631 (75%)	1204 (75%)
Black	28 (4%)	28 (3%)	56(4%)
Hispanic	47 (6%)	54 (6%)	101 (6%)
ANA positive	404 (53%)	411 (49%)	815 (51%)
Systemic steroids at baseline		79 (9%)	79 (5%)
Conventional DMARDs at baseline		747 (89%)	747 (47%)
Methotrexate		699 (45%)	699 (44%)
Biologic DMARDs at baseline		233 (28%)	233 (15%)
Targeted synthetic DMARDs at baseline		0 (0%)	0 (0%)
Polyarthritis at 12 months	52 (7%)	49 (6%)	101 (6%)
Uveitis at 12 months	35 (5%)	15 (2%)	50 (3%)
Systemic DMARDs at 12 months	278 (37%)	510 (61%)	788 (49%)
Composite endpoint at 12 months	297 (39%)	528 (63%)	825 (52%)
Polyarthritis at 18 months	60 (8%)	61 (7%)	121 (8%)
Uveitis at 18 months	38 (5%)	18 (2%)	56 (4%)
Systemic DMARDs at 18 months	308 (41%)	557 (66%)	865 (54%)
Composite endpoint at 18 months	325 (43%)	568 (68%)	893 (56%)

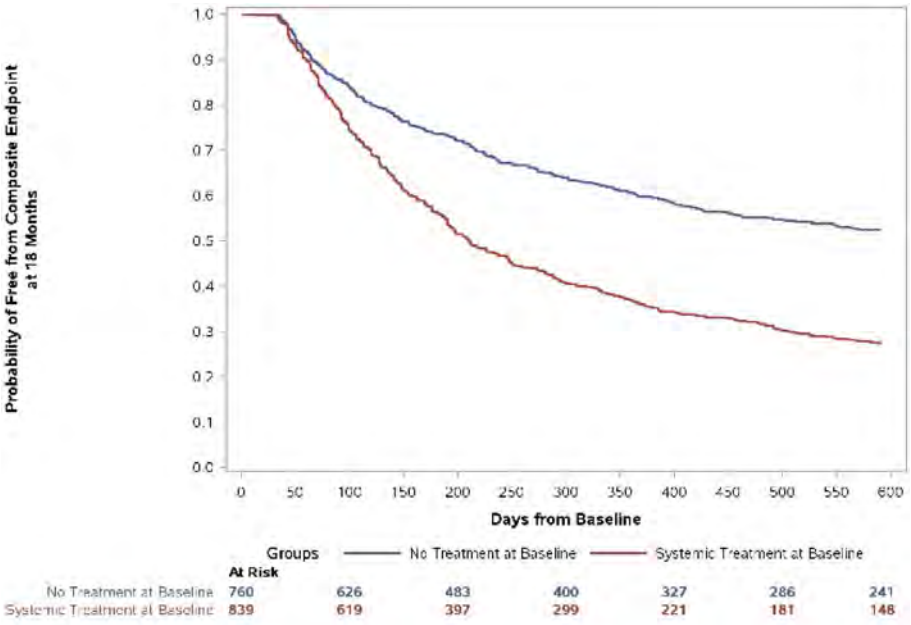


Figure 1. Kaplan-Meier Estimate for Composite Endpoint By Subgroups at 18 months.

within 12 months. By 18 months, 8% had developed polyarthritis, 5% uveitis, and 41% required new systemic treatment. The Kaplan-Meier estimate for the composite endpoint was 48% (Figure 1). Among those receiving systemic treatment at enrollment, 6% developed polyarthritis, 2% developed uveitis, and 61% were on systemic treatment at 12 months. At

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

18 months, 7% had developed polyarthritis, 2% uveitis, and 66% were on systemic treatment. The Kaplan-Meier estimate for the composite endpoint was 73% (Figure 1).

Conclusion: Among children with recently diagnosed limited JIA, nearly half received systemic DMARD within the first 6 months following disease diagnosis. Systemic medication use was not related to presence of polyarthritis or uveitis, suggesting clinicians are initiating systemic treatment early to manage persistent disease activity or prevent disease extension in limited JIA. Around 2 in 5 children who were treatment-naïve at Registry enrollment started systemic medication within 12 months. Over an 18-month period, the incidence of polyarthritis and uveitis was low across both treatment groups, with most extension occurring within the first 12 months.

Disclosure: E. Wu: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **S. Balevic**: Purdue Pharma, 5, ReveraGen, 2, UCB, 2; **A. Marks**: None; **M. Bhapkar**: None; **B. Zhang**: None; **A. Fist**: None; **M. Kohlheim**: None; **V. Del Gaizo**: None; **L. Thomas**: None; **L. Schanberg**: Bristol-Myers Squibb(BMS), 5, Sanofi, 12, DSMB, UCB, 12, DSMB.

Abstract Number: 0405

Juvenile Psoriatic Arthritis and Enthesitis-Related Arthritis: 4-Year Results From the JUNIPERA Extension Study

Hermine Brunner[1], Ivan Foeldvari[2], Gerd Horneff[3], Antonio Mera Varela[4], Angelo Ravelli[5], Sharonjeet Kaur[6], Swapnil Suhas Dahale[7], Ruvie Martin[8], Daniel Lovell[1], Alberto Martini[9] and Nicolino Ruperto[10] on behalf of Paediatric Rheumatology INternational Trials Organization (PRINTO) and Pediatric Rheumatology Collaborative Study Group (PRCSG), [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Hamburger Zentrum fuer Kinder und Jugendrheumatologie, Rheumatology, Hamburg, Germany, [3]Asklepios Klinik, Hamburg, Germany, [4]Rheumatology Division. Hospital Clínico Universitario de Santiago and Instituto de Investigaciones Sanitarias (IDIS), School of Medicine, Santiago de Compostela, Spain, [5]IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genoa, Genoa, Italy, [6]Novartis Pharma AG, Basel, Switzerland, [7]IQVIA, Mumbai, India, [8]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [9]Università di Genova, Genova, Italy, [10]Universit Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

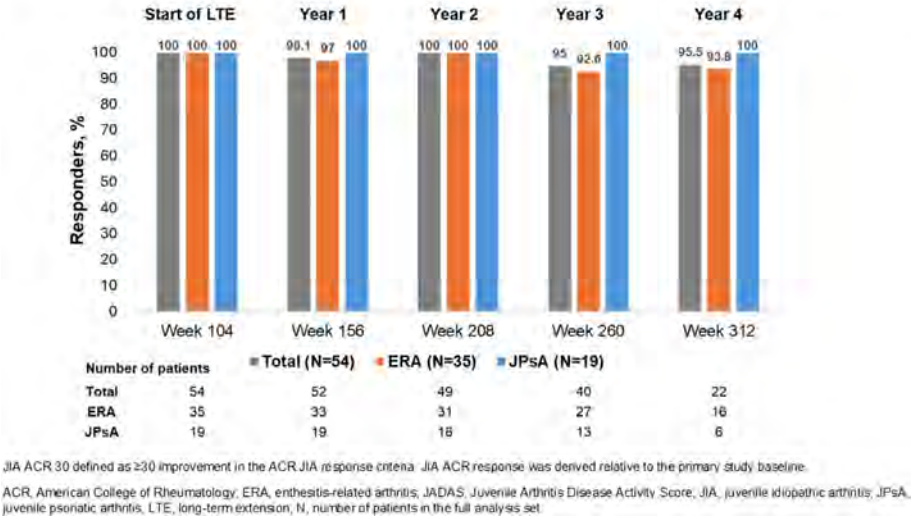
Background/Purpose: Secukinumab demonstrated efficacy and safety in patients with juvenile idiopathic arthritis (JIA), including enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA), for up to 2 years in the JUNIPERA study.[1] The JUNIPERA clinical program included an extension study to assess the long-term efficacy and safety of secukinumab in patients with ERA and JPsA. Here we report the 4-year efficacy and safety results of the long-term extension (LTE) study.

Methods: Of 86 patients in the primary study, 55 deemed by the investigator to benefit from secukinumab therapy opted to enter the LTE study. Of these, 54 received secukinumab treatment (subcutaneous; 75/150 mg in patients < 50/≥50 kg) every 4 weeks up to 4 years. Secukinumab dose could be escalated from 75 to 150 mg or 150 to 300 mg, based on the investigator judgment of disease activity. Efficacy outcomes were presented as observed for JIA American College of Rheumatology (JIA ACR) 30/50/70/90/100 responses, inactive disease (ID) status over time (from weeks 104 to up to 312), and change from baseline in Juvenile Arthritis Disease Activity Score (JADAS-27 and JADAS-71) along with adverse events (AEs).

Results: The mean (SD) age of the overall JIA population was 12.5 (3.4) years, and 66.7% were male. A total of 22 patients (40%) underwent dose escalation. Most patients achieved JIA ACR 30 responses (>93%) at all visits during the LTE (-**Figure 1**). The JIA ACR 50/70/90/100 (**Figure 2**), JADAS-27 and JADAS-71 responses (**Figure 3**), as well as the ID status

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: JIA ACR 30 response in the overall population and in each JIA subtype, ERA, and JPsA



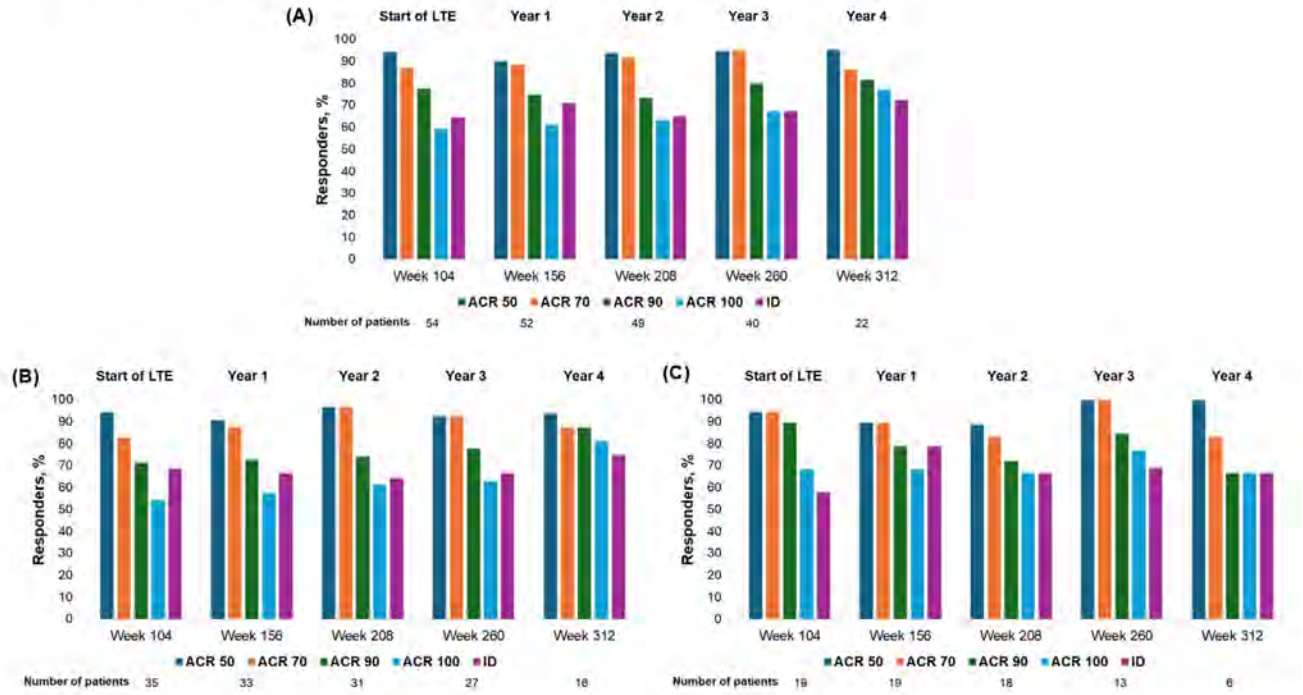
JIA ACR 30 defined as ≥30 improvement in the ACR JIA response criteria. JIA ACR response was derived relative to the primary study baseline.

ACR, American College of Rheumatology; ERA, enthesitis-related arthritis; JADAS, Juvenile Arthritis Disease Activity Score; JIA, juvenile idiopathic arthritis; JPsA, juvenile psoriatic arthritis; LTE, long-term extension; N, number of patients in the full analysis set.

Figure 1

achieved during the primary study, were maintained in the overall population and the ERA and JPsA subtypes in the LTE. Of note, the JIA ACR complete response (JIA ACR 100) was achieved by ≥50% of patients at all visits during the LTE.

Figure 2: JIA ACR 50/70/90/100 response and inactive disease status in the overall JIA population (N=54, [A]), and in the ERA (N=35, [B]) and JPsA (N=19, [C]) subtypes



JIA ACR 30/50/70/90/100 defined as ≥30%/ 50%/70%/90%/100% improvement in the ACR JIA response criteria. Clinical inactive disease definition was adapted from the ACR criteria of Wallace et al [1] which requires all the following criteria to be met: no joints with active arthritis, no uveitis, CRP (local) value within normal limits for the laboratory where tested or, if elevated, not attributable to ERA/JPsA. Physician's global assessment of disease activity score of best possible on the scale used (i.e. best possible score is defined as ≤ 10mm), and the absence of patient-reported morning stiffness attributable to JPsA or ERA lasting ≥15 minutes. JIA ACR response was derived relative to the primary study baseline.

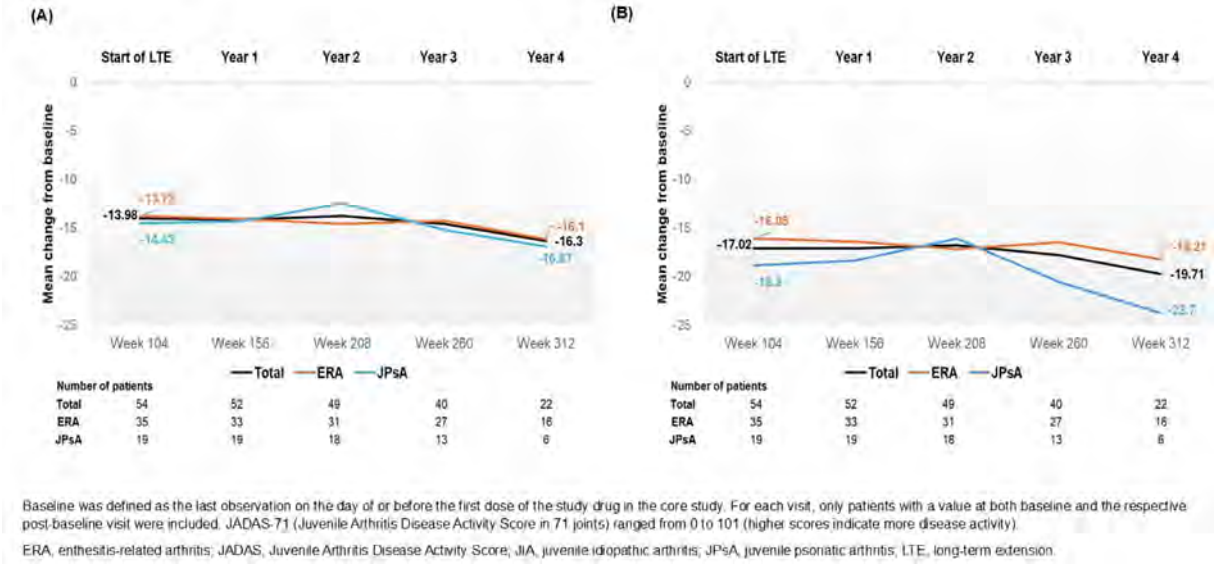
ACR, American College of Rheumatology; CRP, C-reactive protein; ERA, enthesitis-related arthritis; JADAS, Juvenile Arthritis Disease Activity Score; JIA, juvenile idiopathic arthritis; JPsA, juvenile psoriatic arthritis; LTE, long-term extension; N, number of patients in the full analysis set.

1. Wallace CA, et al. *Arthritis Care Res (Hoboken)*. 2011;63:929-936.

Figure 2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3: JADAS-27 (A) and JADAS-71 (B) change from baseline in the overall JIA population and in each JIA subtype



Baseline was defined as the last observation on the day of or before the first dose of the study drug in the core study. For each visit, only patients with a value at both baseline and the respective post-baseline visit were included. JADAS-71 (Juvenile Arthritis Disease Activity Score in 71 joint(s) ranged from 0 to 101 (higher scores indicate more disease activity).

ERA, enthesitis-related arthritis; JADAS, Juvenile Arthritis Disease Activity Score; JIA, juvenile idiopathic arthritis; JPsA, juvenile psoriatic arthritis; LTE, long-term extension.

Figure 3

With 182.2 patient-years of secukinumab exposure during the LTE, 46 patients (85.2%) experienced at least one AE. Most AEs were considered not related to the study treatment and were generally mild (n=25, 46.3%) to moderate (n=17, 31.5%) in severity. A total of 9 non-fatal serious AEs (SAEs) were experienced by 4 (7.4%) patients, and except for 1 event of Crohn's disease (1.9%) that led to treatment discontinuation, all SAEs were considered not related to secukinumab treatment and were recovered/resolved during study participation. The most common treatment-emergent AEs by system organ class were infections and infestations (n=33, 61.1%). No deaths were reported during the LTE period or during primary study.

Conclusion: Long-term sustained clinical benefits of secukinumab were observed in patients with JIA (ERA and JPsA subtypes) for up to 4 years of exposure in the LTE study, along with a favorable long-term safety profile.

Reference:

1. Brunner HI, et al. *Ann Rheum Dis*. 2023;82(1):154-160.

Disclosure: H. Brunner: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **I. Foeldvari**: Abbvie, 2, Bayer, 2, BMF, 2, Bristol-Myers Squibb(BMS), 2, Chugai, 2, Genentech, 2, Medac, 2, Novartis, 2, Pfizer, 2, Sanofi, 2; **G. Horneff**: Janssen, 5, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, Sanofi, 6; **A. Mera Varela**: None; **A. Ravelli**: AbbVie, 2, 5, 6, Alexion, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, SOBI, 2, 5, 6; **S. Kaur**: Novartis, 3, 12, Shareholder; **S. Suhas Dahale**: IQVIA, 3, Novartis, 12, Funded by Novartis to provide statistical analysis support; **R. Martin**: Novartis, 3, 12, Shareholder; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **A. Martini**: Abbvie, 2, Eli Lilly, 2, EMD Serono, 2, Janssen, 2, Novartis, 2, Pfizer, 2; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0406

Comparing biomarkers associated with uveitis in tear fluid and serum samples of children with Juvenile Idiopathic Arthritis

Ilaria Maccora[1], Mariia Pavlenko[2], Mekibib Altaye[3], Hermine Brunner[4], Margaret Chang[5], Ashley Cooper[6], Stefanie Davidson[7], Alexandra Duell[4], Bharti Gangwani[5], Aimee Hersh[8], Gary Holland[9], Carl Langefeld[10], Melissa Lerman[11], Mindy Lo[5], Virginia Miraldi Utz[4], Sampath Prahalad[12], Grant Schulert[4], Megan Quinlan-Waters[13], Erin Stahl[6], Edmund Tsui[9] and Sheila Angeles-Han[14], [1]Rheumatology Unit, ERN ReCoNNET Center, Meyer Children's Hospital IRCCS, Florence, Italy, Firenze, Florence, Italy, [2]Rheumatology Division, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, Cincinnati, OH, [3]Cincinnati Children's Hospital, Cincinnati, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [5]Boston Children's Hospital, Boston, MA, [6]Children's Mercy Kansas City, Kansas City, MO, [7]Department of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, Philadelphia, PA, [8]University of Utah, Salt Lake City, UT, [9]UCLA Jules Stein Eye Institute and the Department of Ophthalmology, UCLA David Geffen School of Medicine, Los Angeles, [10]Wake Forest University School of Medicine, Winston Salem, NC, [11]Children's Hospital of Philadelphia, Philadelphia, PA, [12]Emory + Children's Pediatric Institute, Atlanta, GA, [13]Cincinnati Children's Hospital Medical Center, CCHMC, [14]Cincinnati Children's Hospital, Cincinnati, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic anterior uveitis (CAU) develops in 15-20% of juvenile idiopathic arthritis (JIA) cases. Early detection may prevent vision loss. However, known clinical risk factors do not accurately predict CAU. We and others report that 50% of the same protein biomarkers detected in tear fluid of patients overlapped in paired aqueous humor. Non-invasive biomarkers that reflect eye inflammation and are easily implemented in clinic may improve prediction of CAU and influence screening. We aim to compare inflammatory mediators in tear fluid and serum of children with JIA with and without CAU.

Methods: The prospective multicenter PEDIA-U study enrolled JIA children without (JIA-no-U) and with CAU (JIA-U) ≥4 y/o. Serum was paired with tear fluid collected from both eyes at same study visit using Schirmer strips. S100A8/A9 and A12 were measured by ELISA, and IL-8, CXCL-10 (IP-10), MCP-1, sICAM-1, APRIL and VEGF-A by Luminex assays in all samples. We compared levels between JIA-no-U and JIA-U per sample type, then between serum and tear fluid where we calculated tear/blood ratios to assess the difference in abundance between both samples. As samples were collected from both eyes, we used a mixed model analysis with individuals and eyes as random effects. Data was log-transformed prior to analyses.

Results: Forty-two patients (31 JIA-no-U, 11 JIA-U) contributed 84 tear (62 JIA-no-U, 22 JIA-U) and 20 serum samples (16 JIA-no-U, 4 JIA-U) (Table 1). Two JIA-no-U patients at time of collection later developed CAU but were grouped as JIA-U.

In serum, S100A12 (JIA-no-U LS mean 76,807.11 vs JIA-U LS mean 27,455.02, p=0.0027) and S100A8/A9 (JIA-no-U LS mean 5,608.29 vs JIA-U LS mean 2,217.52, p=0.0008) were elevated in JIA-no-U (Table 2). In tears, CXCL-10 (JIA-no-U LS means 5.1 vs JIA-U LS means 4.01, p=0.001) and MCP1 (JIA-no-U LS Means 2.18 vs JIA-U LS means 1.31, p= 0.0083) were elevated in JIA-no-U (Table 2).

Comparing paired serum and tears levels in 19 patients (Table 3), S100A12 (serum mean 4.67 vs tears mean 3.09, ratio 0.66 p< 0.001) and sICAM-1 (4.24 vs 3.55, 0.83 p< 0.001) were significantly elevated in serum. Conversely, CXCL10 (serum 0.09 vs tear 2.14, ratio 22.76 p< 0.001), APRIL (1.88 vs 3.55, 1.86 p< 0.001), and VEGF (2.2 vs 2.69, 1.22 p< 0.003) were elevated in tear fluid. MCP-1 and S100A8/9 were similar in both samples (21.06 vs 0.86, 0.811 p=0.292 and 3.54 vs 3.66, 0.393 p=0.393 respectively).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1. Demographic and Clinical Characteristics			
	All Cohort N (%)	JIA-no-U N (%)	JIA-U N (%)
Number of patients	**42 (100)**	**31 (74)**	**11 (26)**
Number of tear samples	**84 (100)**	**62 (100)**	**22 (100)**
Number of blood samples	**20 (47.6)**	**16 (51.6)**	**4 (36.3)**
Sex at birth			
Female	27 (64)	17 (55)	10 (91)
Male	13 (31)	12 (39)	1 (9)
Unknown	2 (5)	2 (6.4)	0
Race			
White	37 (88)	26 (84)	11 (100)
Black and African American	1 (2)	1 (3.2)	0
Asian	2 (5)	2 (6.4)	0
American Indian or Alaska Native	0	0	0
Unknown	2 (5)	2 (6.4)	0
Ethnicity			
Non-Hispanic	36 (86)	26 (84)	10 (91)
Hispanic	3 (7)	2 (6.4)	1 (9)
Unknown	3 (7)	3 (10)	0
Age at sample collection in years Median (range)	12 (4-17)	12 (4-17)	12 (8-15)
Duration of JIA in years Median (range)	1 (0-12.8)	2 (0-4.3)	3.1 (0.2-12.8)
JIA Subtype			
Oligoarticular	24 (57)	20 (64.5)	4 (36.3)
Polyarticular RF-	9 (21.4)	6 (19.3)	3 (27)
Undifferentiated arthritis	2 (4.7)	2 (6.4)	0
Psoriatic	1 (2.4)	0	1 (9)
Other	1 (2.4)	1 (3.2)	1 (9)
Unknown	3 (7.2)	2 (6.4)	2 (18)
Arthritis activity			
Active	15 (35.7)	14 (45.2)	1 (9)
Inactive	24 (57.1)	15 (48.4)	9 (81.8)
Unknown	3 (7)	2 (6.4)	1 (9)
Uveitis location			
Anterior	11 (26)	N/A	11 (100)
Uveitis Activity			
Active	3 (7.2)	N/A	3 (27)
Inactive	7 (16.6)	N/A	7 (73)
Corticosteroids eye drops use at time of visit			
Yes	4 (5)	N/A	4 (18.2))
No	8 (10)	N/A	8 (36.3)
Systemic medications			
Methotrexate	28 (66.6)	20 (64.5)	8 (72.7)
Etanercept	3 (7.2)	1 (3.2)	2 (18)
Adalimumab	15 (35.7)	10 (32.2)	5 (45.5)
Abatacept	1 (2)	0	1 (9)
Leflunomide	3 (7.2)	1 (3.2)	2 (18)
None	11 (26.2)	9 (29)	2 (18)
List of abbreviations: JIA - Juvenile Idiopathic Arthritis; JIA-no-U - JIA without uveitis; JIA-U - JIA-associated uveitis; N number; N/A non-applicable.			

Table 2: Cytokine and chemokines in serum and tears of children with JIA-U and JIA-no-U, Based on natural logarithm transferred analysis, using Wilcoxon Two Sample Exact Test. In bold the significant cytokines and chemokines

Variable	Diagnosis	Mean	SE	P
SERUM				
APRIL (pg/ml)	JA-no-U	1.904	0.804	0.5655
	JA-U	1.985	0.914	
BDNF (pg/ml)	JA-no-U	1.095	0.491	0.2553
	JA-U	1.445	0.640	
CXCL10/IP-10 (pg/ml)	JA-no-U	-0.104	0.759	0.1189
	JA-U	0.847	0.336	
MCP-1 (pg/ml)	JA-no-U	0.883	0.538	0.8078
	JA-U	1.776	0.210	
VEGF-A (pg/ml)	JA-no-U	199.12	135.00	0.8916
	JA-U	264.20	245.94	
s100A12 (pg/ml)	**JA-no-U**	**4.610**	**0.313**	**0.0027**
	JA-U	**4.970**	**0.214**	
s100A8/A9 (pg/ml)	**JA-no-U**	**3.467**	**0.324**	**0.0008**
	JA-U	**3.850**	**0.208**	
sICAM-1 (pg/ml)	JA-no-U	4.282	0.216	0.4941
	JA-U	4.170	0.323	
TEARS				
APRIL (pg/ml)	JA-no-U	7.9233	0.2692	0.534
	JA-U	8.253	0.4513	
IL8 (pg/ml)	JA-no-U	3.5877	0.1423	0.0585
	JA-U	3.047	0.2383	
CXCL10/IP-10 (pg/ml)	**JA-no-U**	**5.0976**	**0.156**	**0.001**
	JA-U	**4.0159**	**0.2614**	
MCP-1 (pg/ml)	**JA-no-U**	**2.1812**	**0.1603**	**0.0083**
	JA-U	**1.3132**	**0.2685**	
VEGF-A (pg/ml)	JA-no-U	6.367	0.1129	0.6233
	JA-U	6.2579	0.1891	
s100A12 (pg/ml)	JA-no-U	7.5608	0.4262	0.1201
	JA-U	8.8819	0.7144	
s100A8/A9 (pg/ml)	JA-no-U	8.5467	0.1616	0.3392
	JA-U	8.2418	0.2706	
sICAM-1 (pg/ml)	JA-no-U	8.1372	0.1581	0.7458
	JA-U	8.0366	0.2646	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Comparison between tears and blood level of logarithmic value of biomarkers

Variable	Mean in tears	Mean in Blood	Ratio tears/blood	P value
APRIL (pg/ml)	3.51	1.88	1.86	**<0.001**
BDNF (pg/ml)	0.00	1.14	0	**<0.001**
CXCL10/IP-10 (pg/ml)	2.14	0.094	22.76	**<0.001**
MCP-1 (pg/ml)	0.86	1.06	0.811	0.292
VEGF-A (pg/ml)	2.69	2.20	1.22	**0.003**
s100A12 (pg/ml)	3.09	4.67	0.66	**<0.001**
s100A8/A9 (pg/ml)	3.66	3.54	1.033	0.393
sICAM-1 (pg/ml)	3.55	4.24	0.83	**<0.001**

Conclusion: We compared levels of tear and serum-based biomarkers in children with JIA with and without CAU. Differences in S100 proteins in serum may reflect systemic inflammation. CXCL10, APRIL and VEGF were highly enriched in tear fluid, while MCP-1 and S100 proteins were similar in both samples. These tear-based biomarkers may reflect damage from inflammation, allowing an influx of inflammatory mediators into the eye. Importantly, biomarkers reported in JIA and JIA-U were detected in both sample types. Elevated baseline S100A12 in JIA children who develop CAU has been noted, as well as VEGF in cystoid macular edema. Tear and blood-based biomarkers are easily measured in various clinical settings, may complement known CAU risk factors, and improve screening. Our future studies will consider disease activity and topical and systemic treatment.

Disclosure: I. Maccora: None; **M. Pavlenko**: None; **M. Altaye**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **M. Chang**: None; **A. Cooper**: None; **S. Davidson**: None; **A. Duell**: None; **B. Gangwani**: None; **A. Hersh**: None; **G. Holland**: None; **C. Langefeld**: None; **M. Lerman**: None; **M. Lo**: None; **V. Miraldi Utz**: None; **S. Prahalad**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **M. Quinlan-Waters**: None; **E. Stahl**: Sydnexis, 2; **E. Tsui**: None; **S. Angeles-Han**: None.

Abstract Number: 0407

The SOS project: to Switch Or to Swap After Adalimumab failure for the management of childhood non-infectious uveitis in an international cohort

Ilaria Maccora[1], Margaret Chang[2], Sheila Angeles-Han[3], Andrea Taddio[4], Lampros Fotis[5], Cinzia de Libero[6], Madison Mangin[7], Alexandra Duell[8], Marco Gabrielli[9], Kyveli Chiotopoulou[5], Lillian Sutton[10], Virginia Miraldi Utz[8] and Gabriele Simonini[11], [1]Rheumatology Unit, ERN ReCoNNET Center, Meyer Children's Hospital IRCCS, Florence, Italy, Firenze, Florence, Italy, [2]Boston Children's Hospital, Boston, MA, [3]Cincinnati Children's Hospital, Cincinnati, OH, [4]Insitute for Maternal and Child Health IRCCS Burlo Garofolo, Trieste, Italy, [5]Division of Pediatric Rheumatology, Department of Pediatrics, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece, Athene, Greece, [6]Ophthalmology Unit, Meyer Children's Hospital IRCCS, Florence, Italy, Florence, Italy, [7]Boston Children's Hospital, St Simons Island, GA, [8]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [9]University of Trieste, Trieste, Italy, Trieste, Italy, [10]Division of Immunology, Boston Children's Hospital, Boston, MA, USA, Boston, [11]Rheumatology Unit, ERN-ReCONNET center, Meyer Children's Hospital IRCCS, Firenze, Firenze, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Childhood chronic non-infectious uveitis (cNIU) is a sight-threatening condition that can lead to blindness if not appropriately treated. cNIU is typically associated with Juvenile Idiopathic Arthritis or can occur in isolation when idiopathic. Adalimumab (ADA) is the only approved treatment for cNIU and TNF inhibitors (TNFi) are the recommended first line-biologic treatment of cNIU. However, 25% of patients do not achieve disease remission. In these cases, there is no consensus whether switching to another TNFi or swapping drug class is more effective. We aim to evaluate the efficacy of the switch OR swap therapeutic approach to treating cNIU refractory to primary TNFi and the efficacy of the different drugs in these patients.

Methods: In a multicentre international retrospective study involving pediatric rheumatology centres in Florence, Boston, Cincinnati, Athens and Trieste, we enrolled children with a diagnosis of cNIU unresponsive to ADA and required the use of another biologic. Remission on treatment was determined according to the grading of ocular inflammation using the

Table1: demographic and clinical characteristics of the population in study. Comparison between the population that switched and swapped the treatment. In bold the significant differences.

Variables	*Whole cohort*	*Switch*	*Swap*	*Test and p value*
Number of patients, N	*79*	*41*	*38*	
Florence	*27*	*1*	*26*	
Boston	*28*	*24*	*4*	
Cincinnati	*13*	*10*	*3*	-
Trieste	*6*	*3*	*3*	
Athene	*5*	*3*	*2*	
Age at uveitis onset, median IQR	*60 m (25.8-103.9)*	*80.8(46.7-129)*	*35.6 (24-78)*	***<0.001***
Duration of follow-up in months, median IQR	*106 (60-150)*	*82.5 (51.5-136)*	*120 (78-157.5)*	*0.09*
Disease				
JIA-U	*57*	*28*	*29*	***χ² 3.38***
Idiopathic	*19*	*1*	*18*	***p 0.036***
TINU	*2*	*2*	-	
Behçet	*1*	*0*	*1*	
Female, N	*55*	*27*	*28*	*χ²0.57 p 0.45*
ANA positivity, available in 71	*42*	*12*	*30*	***χ² 15.37 p <0.001***
Bilateral Uveitis	*56*	*29*	*27*	*χ²0.001 p0.97*
Anatomical location uveitis				
Anterior	*64*	*33*	*31*	*χ² 1.73*
Intermediate	*8*	*3*	*5*	*p0.42*
Panuveitis	*7*	*5*	*2*	
Presence of complications, N	*23*	*13*	*10*	*χ² 0.35 p0.55*
N of complications at onset median IQR	*0 (0-1)*	*0 (0-2)*	*0 (0-0.5)*	*p0.0271*
I systemic treatment				
Methotrexate	*68*	*37*	*31*	*χ² 1.43*
Adalimumab	*9*	*4*	*5*	*p 0.48*
Mycophenolate	*1*	*0*	*1*	
Response to the I treatment	*13*	*3*	*10*	***χ² 4.62 p0.031***
I TNFi: ADA	*79*	*41*	*38*	*χ²0.93 p0.33*
Time for the administration of TNFi	*9 (3-36)*	*8.5 (3-21.5)*	*14 (3-55.5)*	*0.099*
Duration of the first TNFi	*18 (9.7-36)*	*16 (6-32)*	*28.5(12.7-44.2)*	*0.052*
Response to the I TNFi: absence/partial Loss of response	*35* *42*	*21* *19*	*14* *23*	*χ²2.58* *p0.27*
Drug administered after I TNFi				
Tocilizumab	*20*	-	*20*	
Infliximab	*38*	*38*	-	
Golimumab	*3*	*3*	-	
Baricitinib	*2*	-	*2*	
Tofacitinib	*2*	-	*2*	
Abatacept	*11*	-	*11*	-
Canakinumab	*1*	-	*1*	
Time for administration	*49 (19.25-92.5)*	*31 (14-75)*	*62 (32-114)*	***0.004***
Duration of treatment	*20 (8-36)*	*22 (12-36)*	*17 (7-40)*	*0.915*
Achievement of remission on treatment	*56*	*29*	*27*	*χ² 0.078 p 0.78*
Time to achieve remission on treatment	*6 (5-9)*	*6 (5.5-9)*	*6 (5-7.7)*	*0.326*
Relapse on treatment	*16*	*7*	*9*	*χ²0.47 p0.49*
Time to first relapse on treatment		*6.5 (2.25-9)*	*14 (4-32.5)*	*0.112*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

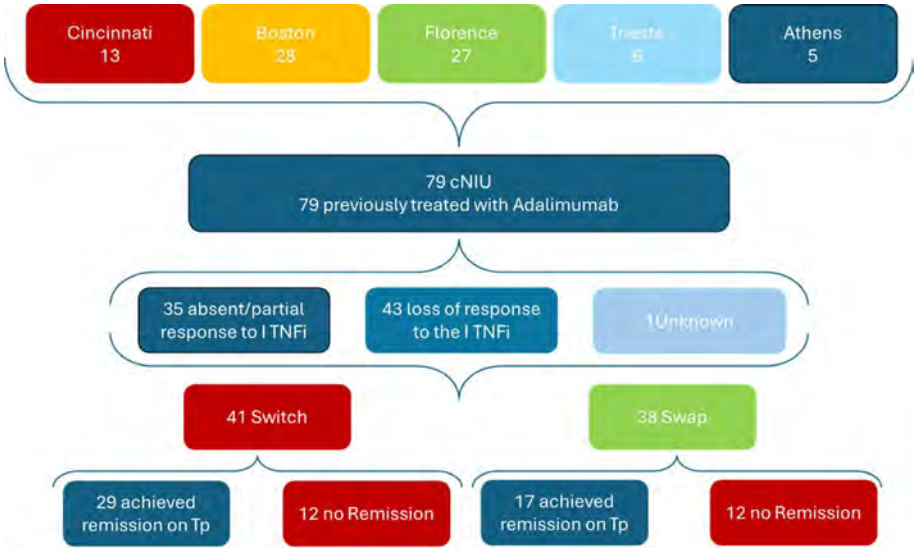


Figure 1: Figurative representation of the population included and achievement of remission with the two treatments approach

Standardization of Uveitis Nomenclature (SUN) criteria. Statistical analysis was performed using Spss 29 for windows. A p-value < 0.05 was considered significant.

Results: We collected the data of 79 children with cNIU, of whom 57 had JIA-associated uveitis (JIA-U) and 17 had idiopathic uveitis (IU) (Table 1). Seventy-nine were treated with ADA as first-line TNFi. Forty-one children did not respond to treatment and were "switched" to a second TNFi (38 infliximab, 3 golimumab), and 38 "swapped" to a non-TNFi biologic (20 tocilizumab, 2 baricitinib, 2 tofacitinib, 11 abatacept, 1 canakinumab). We identified a significant difference in treatment approach, European swapped more frequently than American (χ^2 0.078 p 0.78). We did not find significant differences in remission between switching TNFi and swapping drug class (χ^2 0.078 p 0.78) or among the different drugs (χ^2 32.87p < 0.001). On sub-analysis of the different sub-types of uveitis (JIA-U and Idiopathic), we did not find significant differences in remission of patients for either switching TNFi or swapping to non-TNFi ($\chi^2$0.021 p0.88 and χ^2 0.016 p 0.90 respectively) or for the different drugs regardless of switch/swap ($\chi^2$5.03 p0.754 and $\chi^2$2.57 p 0.463 respectively). There were no significant differences based on anatomical location- anterior NIU (switch vs swap $\chi^2$0.219 p0.64 and based on the drugs $\chi^2$4.97 p0.760) and non-anterior NIU ($\chi^2$0.117 p0.733 and $\chi^2$2.97 p0.395)., Furthermore no significant differences were assessed considering the responder to the primary TNFi ($\chi^2$0.012 p0.912 and $\chi^2$3.35 p0.851) and non-responder ($\chi^2$0.024 p0.877 and $\chi^2$5.4 p0.24)

Conclusion: Management of childhood cNIU is challenging and evidence is scarce on treatment after ADA failure. This is one of the largest multicentre international cohorts that showed that switch and swap are reasonable next treatment and there is no preference for a specific class of biologics and all are reasonable therapeutic approach for the management of cNIU. The use of the European and US cohort allowed us to make a comparison between the two treatments approach. Further data are needed to make specific comparison among drugs.

Disclosure: I. Maccora: None; **M. Chang**: None; **S. Angeles-Han**: None; **A. Taddio**: None; **L. Fotis**: None; **C. de Libero**: None; **M. Mangin**: None; **A. Duell**: None; **M. Gabrielli**: None; **K. Chiotopoulou**: None; **L. Sutton**: None; **V. Miraldi Utz**: None; **G. Simonini**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0408

Implementing Social Drivers of Health Screening for Patients with Pediatric Systemic Lupus Erythematosus

Julia Harris[1], Susan Parish[2], Michelle Manaskie[2] and Ashley Cooper[2], [1]Children's Mercy Kansas City, Overland Park, KS, [2]Children's Mercy Kansas City, Kansas City, MO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: There is a profound need to improve outcomes in children with systemic lupus erythematosus (SLE) given this disease is complicated by significant morbidity. Disparities in pediatric SLE (pSLE) outcomes are also rampant and may be better understood through a social drivers of health (SDOH) framework. SDOH are conditions in the environment where patients live, work, learn, and play, and they have been found to have a significant influence on health outcomes. Children's Mercy Integrated Care Solutions (CMICS), our hospital's population health management subsidiary, has created Lift Up KC, a social care platform linking patients and families to community resources. Our patients with SLE have low disease activity at 85.7% of visits, and 67.7% of SLE visits have a low patient/parent global assessment of overall wellbeing. We aimed to increase the percent of patients with SLE seen in the rheumatology clinic who receive screening of SDOH at follow-up clinic visits from 0% to 50% by June 30, 2025. We also aimed to increase the percent of patients with SLE who have low disease activity (based on SLEDAI-2k) from 85.7% to 90% by June 30, 2025.

Methods: We utilized quality improvement (QI) methodology including QI tools such as a key driver diagram (Figure 1), fishbone diagram, process map, and failure modes effects analysis. Our outcome measures include percent of SLE visits with low disease activity (SLEDAI-2k ≤4) and low patient/parent global assessment of overall wellbeing score (≤2). Process measures include SDOH screening being sent, completion of screening form, screen positive rate, patients/parents wanting

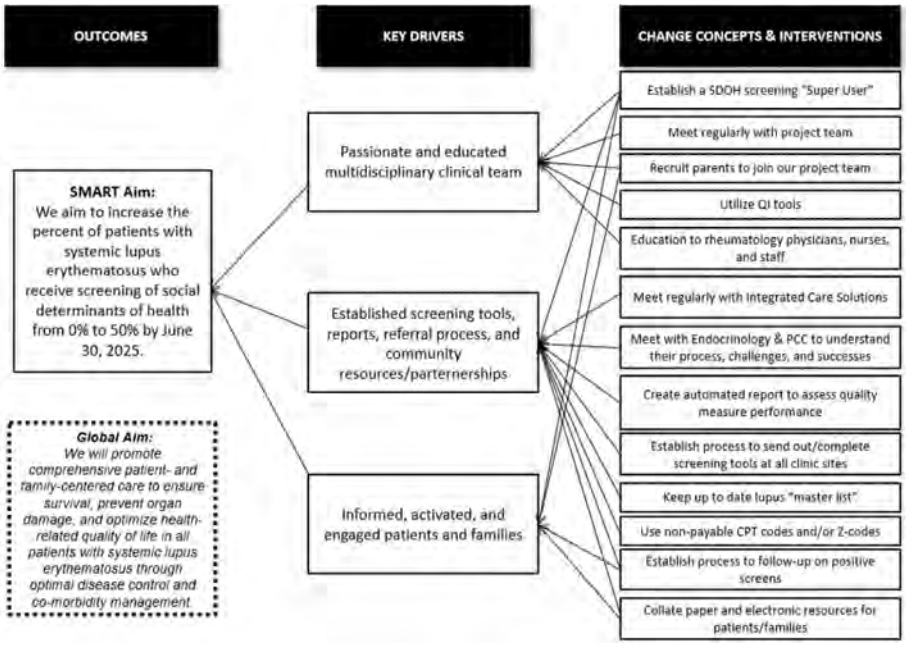


Figure 1. Key driver diagram for social drivers of health screening in patients with SLE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

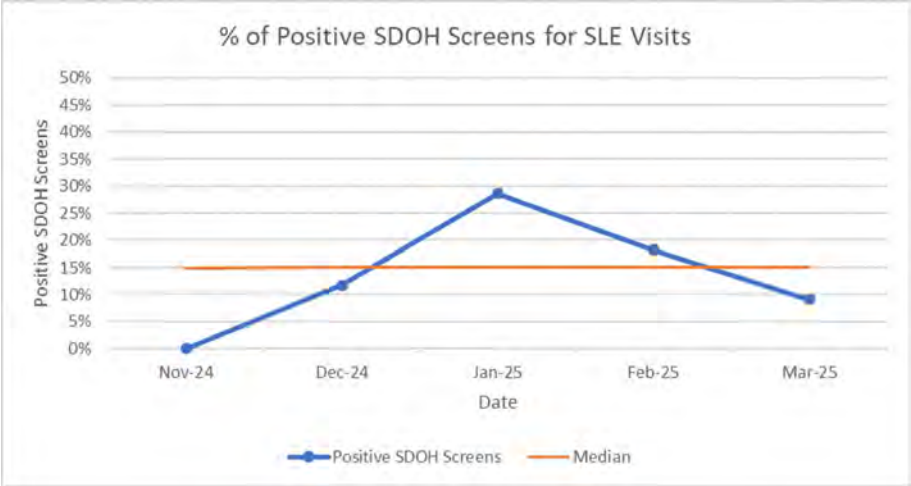


Figure 2. Run chart of positive SDOH screens.

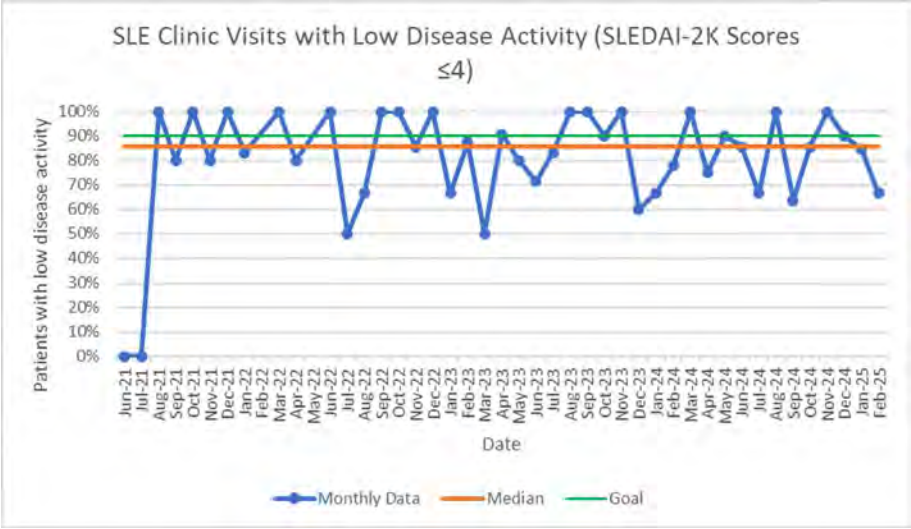


Figure 3. Annotated run chart of SLE visits with low disease activity.

assistance, successful referral to a community-based organization, and no-show rate. Our balancing measure is an average physician satisfaction score. Interventions included meeting with local experts, education on our screening tool and referral process, identification of a super user, education to physicians and nurses, and partnership with social work. We evaluated our data on run charts.

Results: SDOH screening started in November 2024 and the screening tool has been sent to 100% of patients/families since this time. The form completion rate is 63.9%. Social needs identified in 1-3 screens per month and help wanted 0-4 times per month for a positive screen rate of 9.1-28.6% (median 15%) (Figure 2). All families wanting assistance were referred to a partner community organization. No show visits and last-minute cancellations occurred in 16.7% of scheduled SLE visits. Our outcome measures remained stable – 85.7% of visits with low disease activity (Figure 3) and 67.7% with low patient/parent global assessment of overall wellbeing.

Conclusion: We have successfully implemented SDOH screening in our SLE population. Although outcomes remain stable at this point, we hope to improve the care of SLE patients over time by addressing social needs that can have a significant impact on their disease and overall health.

Disclosure: J. Harris: None; **S. Parish**: None; **M. Manaskie**: None; **A. Cooper**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0409

Discordance Between Disease Activity and Patient-Reported Outcomes in Patients with Juvenile Idiopathic Arthritis

Julia Harris[1], Leslie Favier[2], Emily Fox[3], Jordan Jones[2], Michael Holland[3], Cara Hoffart[2], Maria Ibarra[3] and Ashley Cooper[2], [1]Children's Mercy Kansas City, Overland Park, KS, [2]Children's Mercy Kansas City, Kansas City, MO, [3]Children's Mercy Hospital, Kansas City, MO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Outcome assessment is essential to optimize care for patients with juvenile idiopathic arthritis (JIA). Although disease activity and patient-reported outcomes (PROs) are different measures, patients commonly report pain and suboptimal overall wellbeing with no active arthritis on exam. We also note the converse with patients denying pain or suboptimal wellbeing with active disease being noted on physical exam. Therefore, in order to ascertain this and determine appropriate future interventions, the objective of this study was to assess for concordance between disease activity outcomes and PROs in patients with non-systemic JIA.

Methods: Data was assessed from January to August 2024. Patients with systemic JIA were excluded. Disease activity outcomes include the 10-joint clinical Juvenile Arthritis Disease Activity Score (cJADAS10), active joint count, and physician global assessment of disease activity (PhGA) value (0-10; 0=no disease activity). PROs include the Childhood Health Assessment Questionnaire (CHAQ) (0-3; 0 is optimal), arthritis-related pain intensity score (0-10; no or mild pain ≤3), and patient/parent global assessment of overall wellbeing (PtGA) (0-10; low value if ≤2).

Results: Data from 584 patients across 1149 visits were analyzed. Active arthritis was present at 31.2% of visits with a mean joint count of 1.19 (Table 1). Mean cJADAS10 was 3.5 (range 1.15 [in patients with inactive arthritis and PhGA=0] to 8.53 [in patients with active arthritis]). Mean PhGA was 0.82, and this value increased to 2.43 for those with active arthritis. Mean PROs were all lower in those with inactive arthritis although ranges remained the same. For those with no active arthritis, 34.4% had functional limitations, 37.5% had pain, and 19.4% had a moderate-high PtGA (Table 2). Conversely, for those with active arthritis, 29.5% reported no pain, 37.5% reported a CHAQ of 0, and 22.8% reported PtGA of 0.

Conclusion: For a considerable percent of patients with JIA with inactive arthritis, there are reports of pain, functional limitations, and suboptimal overall wellbeing. Additionally, many patients with JIA and active arthritis report no pain and optimal wellbeing, which suggests that PROs may be misleading if taken in isolation and physical assessment of arthritis is still paramount

Table 1. Disease activity and patient-reported outcome values.

	Overall Mean (range)	Active arthritis* mean (range)	Inactive arthritis mean (range)	Inactive arthritis & PhGA=0 mean (range)
cJADAS10	3.50 (0-27)	8.53 (0-10)	1.38 (0-10)	1.15 (0-10)
Joint Count	1.19 (0-33)	3.80 (1-33)	0	0
PhGA	0.82 (0-8)	2.43 (0-8)	0.09 (0-7)	0
CHAQ	0.32 (0-3)	0.53 (0-3)	0.23 (0-3)	0.21 (0-3)
Pain	1.70 (0-10)	2.95 (0-10)	1.18 (0-10)	1.01 (0-10)
PtGA	1.82 (0-10)	2.92 (0-10)	1.29 (0-10)	1.15 (0-10)

*Active joint count >0; cJADAS10, 10-joint clinical Juvenile Arthritis Disease Activity Score; PhGA, physician global assessment of disease activity; CHAQ, Childhood Health Assessment Questionnaire; pain, arthritis-related pain intensity; PtGA, patient/parent global assessment of overall wellbeing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Proportion of patients with disease activity and patient-reported outcome cut-offs based on the presence or absence of active arthritis.

	Overall visits n=1149 n† (%)	Active arthritis* n=340 n† (%)	Inactive arthritis n=750 n† (%)	Inactive arthritis & PhGA=0 n=646 n† (%)
cJADAS10=0	356 (35.4%)	0 (0.0%)	355 (50.3%)	355 (55.9%)
cJADAS10 ≤2.5	588 (58.4%)	22 (7.4%)	565 (80.0%)	530 (83.5%)
cJADAS10 3-5	174 (17.3%)	80 (26.8%)	94 (13.3%)	82 (12.9%)
cJADAS10 >5	244 (24.3%)	197 (65.9%)	47 (6.7%)	23 (3.6%)
PhGA=0	656 (62.5%)	6 (1.9%)	646 (90.0%)	646 (100%)
PhGA 0-2	910 (86.7%)	187 (58.8%)	714 (99.4%)	0 (0.0%)
PhGA >2	140 (13.3%)	131 (41.2%)	4 (0.6%)	0 (0.0%)
CHAQ=0	554 (57.3%)	102 (37.5%)	442 (65.6%)	402 (68.8%)
CHAQ>0	413 (42.7%)	170 (62.5%)	232 (34.4%)	182 (31.2%)
Pain=0	550 (52.6%)	88 (29.5%)	445 (62.5%)	414 (66.5%)
Pain 0-3	823 (78.8%)	178 (59.7%)	622 (86.9%)	554 (88.9%)
Pain >3	222 (21.2%)	120 (40.3%)	94 (13.1%)	69 (11.1%)
PtGA=0	475 (43.5%)	73 (22.8%)	382 (52.5%)	355 (55.9%)
PtGA 0-2	764 (69.9%)	150 (46.9%)	587 (80.6%)	526 (82.8%)
PtGA >2	329 (30.1%)	170 (53.1%)	141 (19.4%)	109 (17.2%)

*Active joint count >0. †Not all denominators in each category are the same due to missing data. cJADAS10, 10-joint clinical Juvenile Arthritis Disease Activity Score; PhGA, physician global assessment of disease activity; CHAQ, Childhood Health Assessment Questionnaire; pain, arthritis-related pain intensity; PtGA, patient/parent global assessment of overall wellbeing.

to determine active disease. Limitations include not stratifying data by JIA subtype, disease duration, uveitis status, medication use, and/or other comorbidities such as chronic pain syndromes. Continued self-management support is imperative to address factors impacting patient wellbeing. Further studies are needed to determine why this discordance exists and to assess demographic and disease characteristics associated with the discordance between disease activity and PROs.

Disclosure: J. Harris: None; **L. Favier**: None; **E. Fox**: Pfizer, 2; **J. Jones**: Pfizer, 2; **M. Holland**: None; **C. Hoffart**: None; **M. Ibarra**: None; **A. Cooper**: None.

Abstract Number: 0410

Improving Outcomes in Patients with Juvenile Idiopathic Arthritis through a Novel Chronic Condition Value-Based Care Program

Julia Harris[1], Emily Fox[2], Leslie Favier[3], Michael Holland[2], Susan Parish[4], Cara Hoffart[4], Maria Ibarra[2], Jordan Jones[4], Luke Harris[4], Kristy Diederich[4], Rachel Moran[4], Amy Vickers[4], Hannah Maasen[4], Lydia Ottaviano[4], Carlie Baldus[4], Krysten Potter[4], Melissa Erpelding[4], Stephanie Quinn[4] and Ashley Cooper[4], [1]Children's Mercy Kansas City, Overland Park, KS, [2]Children's Mercy Hospital, Kansas City, MO, [3]Childrens mercy Hospital - Kansas City, Leawood, KS, [4]Children's Mercy Kansas City, Kansas City, MO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Outcomes for patients with juvenile idiopathic arthritis (JIA) are suboptimal with many patients having active disease, functional limitations, significant pain, and decreased health-related quality of life. We partnered with Integrated Care Solutions (ICS), our population health management subsidiary, on a chronic condition value-based care program with upfront infrastructure funding and an additional performance-based funding opportunity. ICS has 250,000 value-based pediatric lives, which encompasses about 50% of children in the Kansas City metro area. Our aim was to decrease the mean 10-joint clinical Juvenile Arthritis Disease Activity Score (cJADAS10) for patients with JIA from 2.6 to 2.55 in addition to decreasing the gap between patients with commercial insurance and Medicaid from 1.4 to 0.8 by December 31, 2025.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

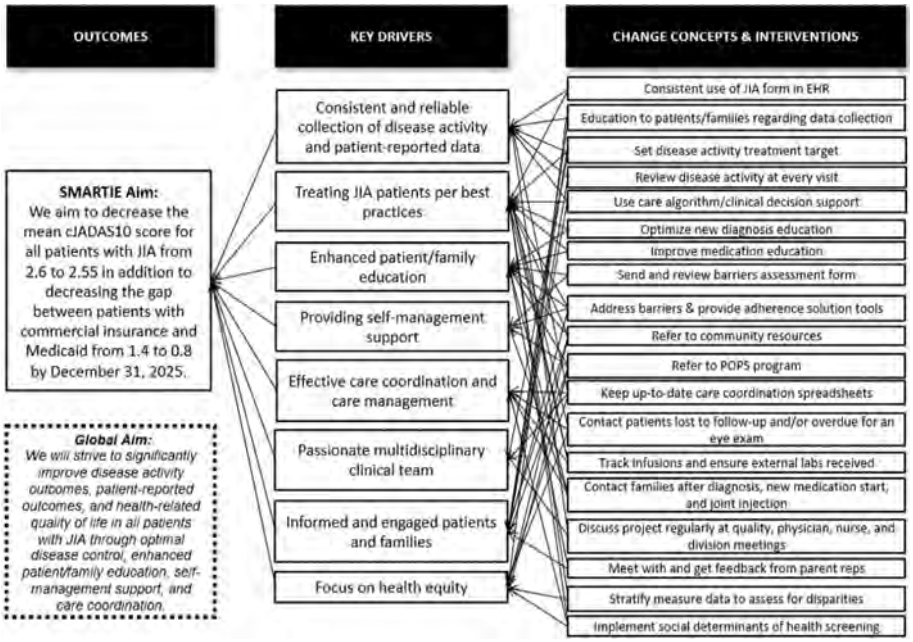


Figure 1. Key driver diagram for improving outcomes in patients with JIA.

Methods: Three outcome measures were identified – mean cJADAS10 score, active joint count, and patient/parent global assessment of overall wellbeing (PtGA). Interventions were established as our process measures: setting a treatment target of disease activity, JIA care coordination, and ICS care management. Balancing measures of physician and nurse satisfaction were established. Data from our ICS and entire JIA population were portrayed on run/control charts and stratified by insurance type, race, and ethnicity to assess for disparities.

Results: A key driver diagram was created (Figure 1). 184 patients (24.5% of our JIA population) are covered under an ICS network. Targets were established based off of baseline data and performance of a pediatric rheumatology learning health network. A cost and utilization measure was omitted this year due to the low volume of hospitalizations and the lack of reliable attribution of emergency department visits to a patient's JIA diagnosis. A quality measure dashboard for ICS patients

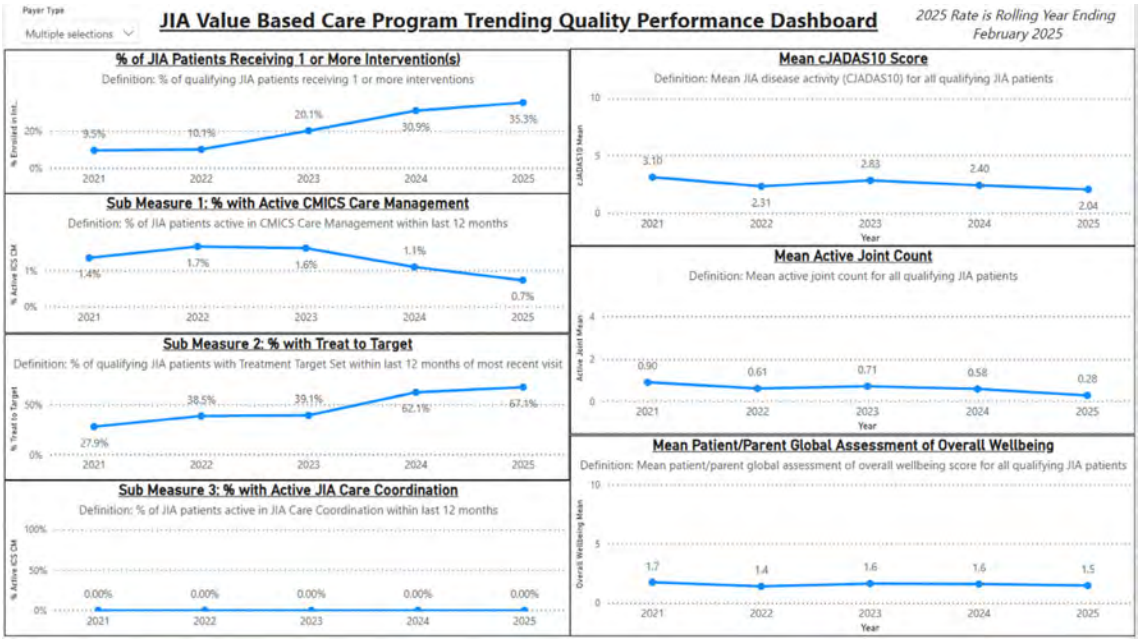


Figure 2. JIA quality measure dashboard.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

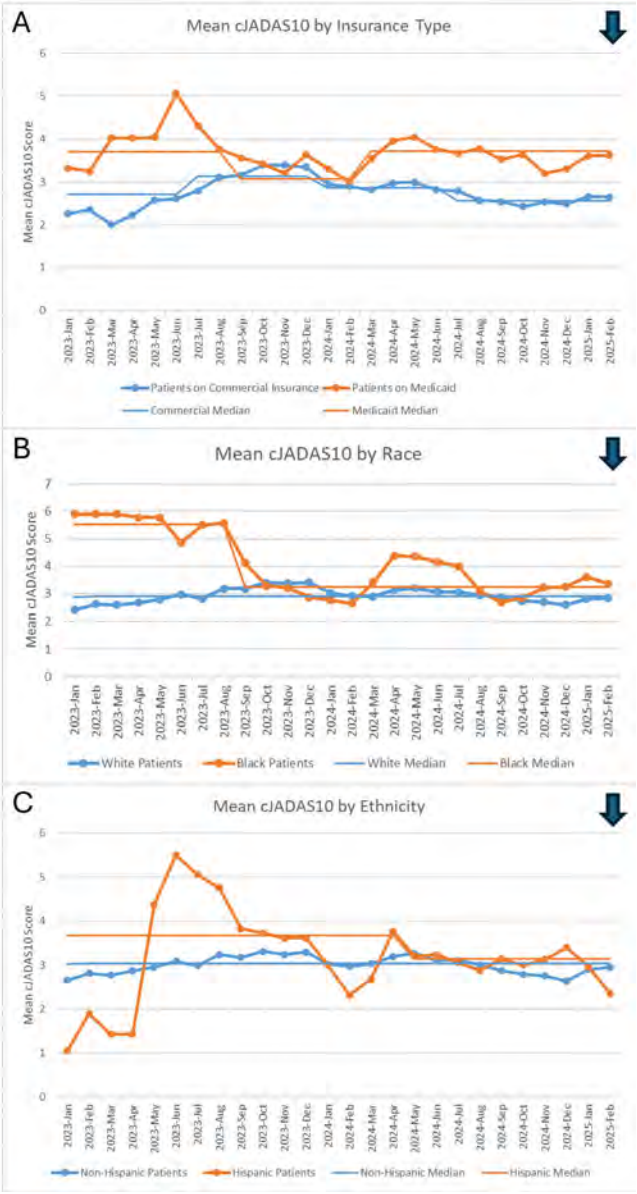


Figure 3. Run charts assessing for disparities in mean cJADAS10 by insurance type (A), race (B), and ethnicity (C).

was created (Figure 2), and additional run/control charts for the entire JIA population are tracked monthly. Our team established a new care coordination process to track patients overdue for a rheumatology appointment and to reach out to patients/families after a new JIA diagnosis, new medication start, and/or a joint injection. Baseline disparity assessment noted significant gaps in mean cJADAS10 by insurance type (0.98), race (0.36), and ethnicity (0.1) (Figure 3). Disparities based on insurance type (commercial insurance compared to Medicaid) also noted in mean active joint count (gap=0.82) and mean PtGA (gap=0.2).

Conclusion: We have partnered with our population health management subsidiary to improve outcomes in patients with JIA through a novel value-based care program. We will continue to monitor our quality measures and provide care coordination and care management in hopes of optimizing care delivery and mitigating disparities. We plan to review full cost data for JIA patients to establish a future cost and utilization metric to fully advance value-based care. Furthermore, we hope with achieving our quality measure goals, we will receive funding to support future efforts including enhanced patient/family education, social drivers of health screening, optimization of self-management support, and more.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Harris: None; **E. Fox**: Pfizer, 2; **L. Favier**: None; **M. Holland**: None; **S. Parish**: None; **C. Hoffart**: None; **M. Ibarra**: None; **J. Jones**: Pfizer, 2; **L. Harris**: None; **K. Diederich**: None; **R. Moran**: None; **A. Vickers**: None; **H. Maasen**: None; **L. Ottaviano**: None; **C. Baldus**: None; **K. Potter**: None; **M. Erpelding**: None; **S. Quinn**: None; **A. Cooper**: None.

Abstract Number: 0411

Outcomes in Juvenile Idiopathic Arthritis Based on Geographic Region in the Pediatric Rheumatology Care and Outcomes Improvement Network Registry

Julia Harris[1], Sheetal Vora[2], Catherine Bingham[3], Cagri Yildirim-Toruner[4], Kerry Ferraro[5], Erik Friedrichsen[6], Katelyn Banschbach[7], Jon Burnham[8], Danielle Fair[9], Mileka Gilbert[10], Beth Gottlieb[11], Tzielan Lee[12], Melissa Mannion[13], Edward Oberle[14], Nancy Pan[15], Natalie Rosenwasser[16], Mary Toth[17], Jennifer Weiss[18] and Esi Morgan[16], for the Pediatric Rheumatology Care and Outcomes Improvement Network, [1]Children's Mercy Kansas City, Overland Park, KS, [2]Atrium Health Levine Children's Hospital, Charlotte, NC, [3]Penn State Children's Hospital, Hershey, PA, [4]Baylor College of Medicine/ Texas Children's Hospital, Houston, TX, [5]Pediatric Rheumatology Care and Outcomes Improvement Network, Cincinnati, [6]Seattle Children's Hospital, Burien, WA, [7]cincinnati Children's hospital, Villa Hills, KY, [8]Children's Hospital of Philadelphia, Bryn Mawr, PA, [9]Medical College of Wisconsin/Children's Wisconsin, Wauwatosa, WI, [10]Medical University of South Carolina, Charleston, SC, [11]Cohen Children's Medical Center, Northwell Health, Lake Success, NY, [12]Stanford University School of Medicine, Palo Alto, CA, [13]University of Alabama at Birmingham, Birmingham, AL, [14]Nationwide Children's Hospital, Columbus, OH, [15]Hospital for Special Surgery, New York, NY, [16]Seattle Children's Hospital, seattle, WA, [17]Nemours Foundation, Orlando, FL, [18]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is a learning health network focused on improving healthcare delivery and outcomes in patients with juvenile idiopathic arthritis (JIA). Measured disease activity outcomes include inactive or low disease activity by the 10-joint clinical Juvenile Arthritis Disease Activity Score (cJADAS10), active joint count, and physician global assessment of disease activity (PhGA) score. PR-COIN also tracks patient-reported outcomes (PROs) including a patient/parent global assessment of overall wellbeing (PtGA) score, pain, and physical function. We sought to assess for any differences in disease activity and PROs based on geographic location of the PR-COIN sites.

Methods: We assessed PR-COIN registry data from 1/2023-2/2025. Geographical cohorts from the United States were divided into the following: Northeast, Midwest, South, and West. Cohort patient count, race, ethnicity, and insurance status were assessed. Run charts were created to portray data over time and medians were calculated. A low PtGA value indicates a score of ≤2 (0=very well, 10=very poor). No or mild pain is a value of ≤3 on the arthritis-related pain intensity scale (0=no pain,

Table 1. Current patient count and characteristics of patients by geographic region.

Geographic Region	Number of Sites*	Active Patients†	Race			Ethnicity			Insurance Type		
			White	Black	Other/Unknown	Non Hispanic	Hispanic	Unknown	Commercial	Medicaid	Other/Unknown
Northeast	5	2245	1646 (73.3%)	123 (5.5%)	476 (21.2%)	1747 (77.8%)	273 (12.2%)	225 (10.0%)	1246 (55.5%)	189 (8.4%)	810 (36.1%)
Midwest	4	2613	1832 (70.1%)	122 (4.7%)	659 (25.2%)	2020 (77.3%)	111 (4.2%)	482 (18.4%)	1009 (38.6%)	347 (13.3%)	1257 (48.1%)
South	4	1207	930 (77.0%)	130 (10.8%)	147 (12.2%)	1001 (82.9%)	162 (13.4%)	44 (3.6%)	719 (59.6%)	342 (28.3%)	146 (12.1%)
West	2	800	522 (65.2%)	14 (1.8%)	264 (33.0%)	569 (71.1%)	188 (23.5%)	43 (5.4%)	655 (81.9%)	52 (6.5%)	93 (11.6%)

*as of 2/2025, †as of 4/2025

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Overall median performance by geographic region from January 2023 to February 2025.

Geographic Region	Inactive or Low Disease Activity	Active Joint Count	Physician Global Assessment	Low Patient/Parent Global Assessment	No or Mild Pain	Optimal Physical Function
Northeast	85.5%	0.51	0.60	80.6%	83.2%	85.5%
Midwest	79.9%	0.81	0.66	75.5%	77.9%	60.8%
South	74.9%	0.80	0.68	75.1%	85.8%	61.0%
West	78.4%	0.33	0.22	74.0%	84.1%	92.9%

10=severe pain). Optimal physical function is a score of 0 on the Childhood Health Assessment Questionnaire (CHAQ) or ≥40 on Patient-Reported Outcomes Measurement Information System (PROMIS) Mobility or Upper Extremity Function.

Results: There are 2-5 sites and 800-2613 patients per geographic region (Table 1). White patients were a majority of the reported race (65.2-77.0%), with a sizable percentage being other or unknown (12.2-33.0%). Run charts stratified by geographic region are depicted in Figure 1. Medians for each disease activity measure and PRO varied by geographic region (Table 2). The percent of patients in inactive or low disease activity ranged from 74.9% (South) to 85.5% (Northeast). The West had the lowest active joint count (0.33), and the Midwest and South had the highest (0.80-0.81). The Midwest and South also had the highest PhGA values (0.66-0.68) with the West having a considerably lower value at 0.22. The West also

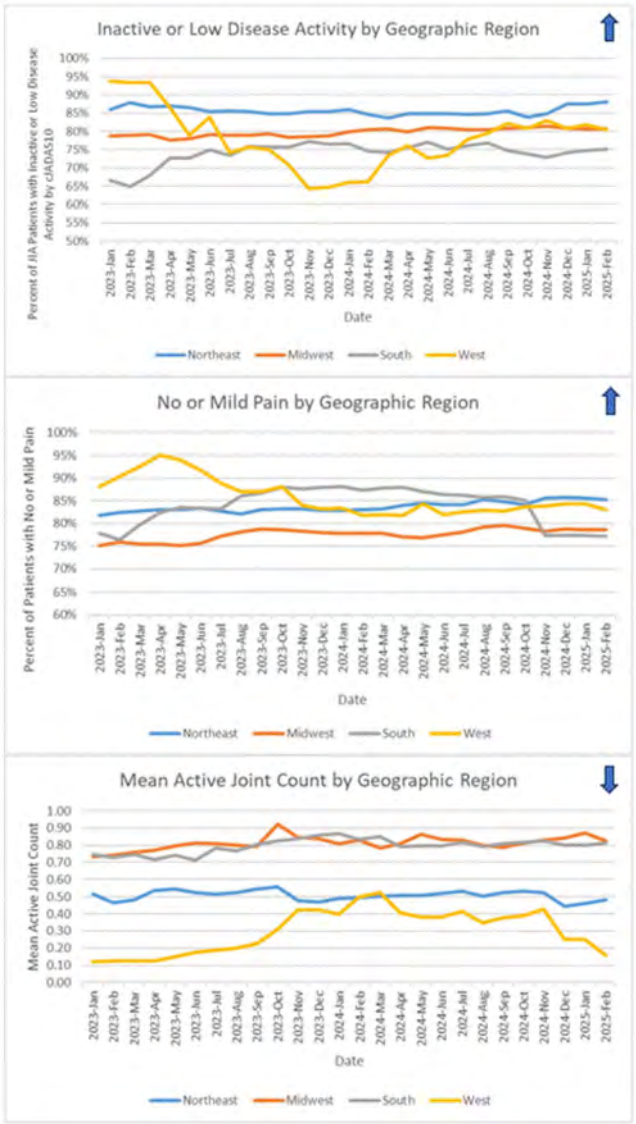


Figure 1. Examples of stratified run charts of quality measures by geographic region.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

had the least percentage of patients with a low PtGA (74.0%), and the Northeast had the highest percent (80.6%). No or mild pain ranged from 77.9% (Midwest) to 85.8% (South). Optimal physical function was bimodal with the Midwest and South ranging from 60.8-61.0% and the Northeast and West with 85.5-92.9% of their patients satisfying this measure.

Conclusion: Overall, a large proportion of patients with JIA in the PR-COIN registry are doing well with inactive or low disease activity, no or mild pain, and optimal physical function. We found differences in disease activity and PROs by geographic region. Limitations include missing data, variable data quality in relation to the percent of a site's JIA population enrolled in the PR-COIN registry, and no control for patient mix (including JIA subtype and disease duration). Next steps include assessing processes of care by geographic region, patients in rural versus urban areas, variation in medication use, impact of social drivers of health, and considering geographic-specific workgroups and/or interventions.

Disclosure: J. Harris: None; **S. Vora**: None; **C. Bingham**: None; **C. Yildirim-Toruner**: None; **K. Ferraro**: Abby's Army, 3, 8, 12, President; **E. Friedrichsen**: None; **K. Banschbach**: None; **J. Burnham**: Cabaletta Bio, 5; **D. Fair**: None; **M. Gilbert**: None; **B. Gottlieb**: None; **T. Lee**: None; **M. Mannion**: None; **E. Oberle**: Pfizer, 1; **N. Pan**: None; **N. Rosenwasser**: None; **M. Toth**: None; **J. Weiss**: None; **E. Morgan**: None.

Abstract Number: 0412

The Association of Obesity with Juvenile Spondyloarthritis

Katelyn Baggett[1], Timothy Brandon[2] and Pamela Weiss[3], [1]Johns Hopkins University, Newtown Square, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Childhood obesity is a global public health concern that impacts the health and wellbeing of all children and particularly negatively affects children living with chronic autoimmune disease. Studies in adults have shown a significant association between obesity and ankylosing spondylitis (AS); however, the association of obesity with juvenile spondyloarthritis (JSpA) is unknown. Obesity may be a risk factor for or a consequence of JSpA. This study aims to evaluate the prevalence of obesity in children with JSpA compared to a healthy control population.

Table 1. Characteristics of children with JSpA versus healthy controls. ^ Subjects with sacroiliitis had MRI-defined inflammation but did not fulfill ILAR criteria for ERA or PsA. * Subjects with undifferentiated arthritis met ERA criteria but had a first-degree relative with psoriasis or met PsA criteria but had a diagnosis of sacroiliitis and inflammatory bowel disease.

Characteristic	All	Controls	JSpA
No. of subjects	950	760	190
Age in years, median		15 (12 to 17)	15 (12 to 17)
Female, n (%)	565	348 (45.8%)	87 (45.8%)
Disease duration (days)	--	--	56.5 (0-216)
JSpA category	--	--	
Enthesitis-related arthritis	--	--	88 (46.3%)
Psoriatic Arthritis	--	--	29 (15.3%)
Sacroiliitis^	--	--	28 (14.7%)
Undifferentiated JIA*	--	--	10 (5.3%)
IBD-associated arthropathy	--	--	35 (18.6%)
Race, n (%)			
African American	75 (7.9%)	60 (7.9%)	15 (7.9%)
Asian American	35 (3.7%)	28 (3.7%)	7 (3.7%)
Multiracial/Other	170 (17.8%)	136 (17.9%)	34 (17.9%)
White	670 (70.5%)	536 (70.5%)	134 (70.5%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of BMI Categories in children with JSpA versus healthy controls.

BMI Categories	All	Controls	JSpA	*P*-value
				< 0.001
Underweight	83 (8.7%)	32 (4.2%)	51 (26.8%)	
Normal weight	527 (55.5%)	431 (56.7%)	96 (50.5%)	
Overweight	149 (15.7%)	128 (16.8%)	21 (11.1%)	
Obese	191 (20.1%)	169 (22.2%)	22 (11.6%)	

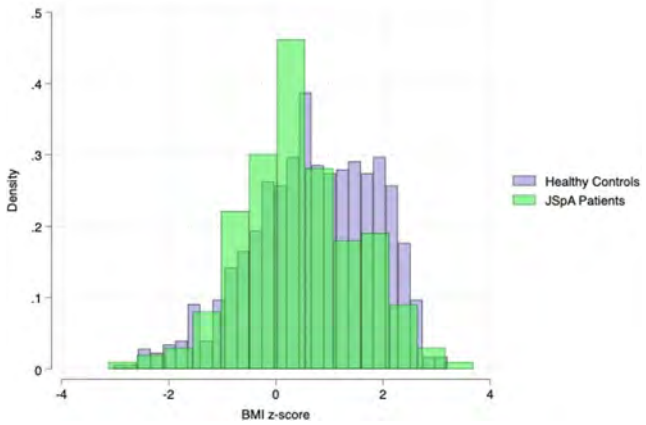


Figure 1. Histograms comparing BMI-for-age z-scores between children with juvenile spondyloarthritis (JSpA) and healthy controls. The median BMI z-score was 0.37 (IQR -0.22 to 1.13) for JSpA cases and 0.76 (IQR -0.06 to 1.63) for healthy controls (P = 0.01).

Methods: This retrospective cohort study included 190 children with JSpA and 760 healthy controls. Data on JSpA cases were drawn from a preexisting disease registry and included patients at their initial visit who met one of the following criteria: magnetic resonance imaging (MRI)-defined sacroiliitis, enthesitis-related arthritis (ERA), psoriatic arthritis (PsA), or undifferentiated arthritis. The healthy control group consisted of children without juvenile arthritis derived from the CDC National Center for Health Statistics' National Health and Nutrition Examination Survey. Cases and controls were matched by sex, race, and age, at a 4:1 ratio. Body mass index (BMI) categories were defined using CDC percentiles: obese (≥95th), overweight (85th–94th), healthy weight (5th–84th), and underweight (< 5th). BMI-for-age z-scores were calculated using the CDC 2000 growth reference in Stata and adjusted for age and sex. A Wilcoxon rank-sum test was used to compare BMI z-scores and chi-square tests assessed differences in BMI categories between children with JSpA and controls.

Results: A total of 950 children were included in the study, of whom 190 had JSpA and 760 were healthy controls. Cohort demographics are presented in Table 1. The distribution of BMI categories was significantly different between JSpA and the matched controls ($P < 0.001$). As shown in Table 2, a higher proportion of children with JSpA were underweight (26.8% in JSpA vs. 4.2% in controls), while fewer were classified as obese (11.6% in JSpA vs. 22.2% in controls). Histograms comparing BMI-for-age z-scores between children with JSpA and healthy controls are shown in Figure 1. The median BMI z-score was 0.37 (IQR -0.22 to 1.13) for JSpA cases and 0.76 (IQR -0.06 to 1.63) for healthy controls ($P = 0.01$).

Conclusion: Children with JSpA had significantly lower BMI z-scores compared to age, sex, and race-matched controls. More children with JSpA were underweight when compared with a control population. The impact of disease duration, disease activity, and concurrent medications on BMI in JSpA should be further explored.

Disclosure: K. Baggett: None; **T. Brandon**: None; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0413

Improving Access to Timely Joint Injections for Pediatric Rheumatology Patients – A Quality Improvement Initiative

Kendra Lauer[1], Vidya Sivaraman[2], Melissa Argraves[3], Ysabella Esteban[4], Laura Pratt[5], Alysha Taxter[6], Shoghik Akoghlanian[3], Kelly Wise[7], Kathryn Anliker[3], Jonnie Hughes[3], James Booker[3], Ashlee Leone[3] and Edward Oberle[3], [1]Nationwide Children's Hospital, Dublin, OH, [2]Nationwide Children's Hospital/ The Ohio State University, Columbus, OH, [3]Nationwide Children's Hospital, Columbus, OH, [4]Nationwide Children's Hospital, Plain City, OH, [5]Nationwide Children's Hospital/The Ohio State University College of Medicine, Columbus, OH, [6]Nationwide Children's, Columbus, OH, [7]Nationwide Children's Hospital, Hilliard, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Timely treatment for juvenile idiopathic arthritis (JIA) is essential for disease remission and decreasing risk of long-term morbidity. Intra-articular corticosteroid joint injections can treat active arthritis. If a joint injection cannot be completed in the outpatient clinic due to sedation needs, additional steps must be made to schedule the procedure, often delaying treatment. Using quality improvement (QI) methodology, this study aims to reduce the time to completion of joint injection for patients in our pediatric rheumatology clinic.

Methods: Our QI team reviewed all clinic encounters of JIA patients from September 2023 to March 2025. We obtained a baseline number of joint injections per month for the initial 8 months and the percentage of those that were completed within 30 days. A new monthly joint injection clinic was started in collaboration with the surgery center for sedated joint injections. Scheduling processes for joint injections were implemented as standardized forms for nursing and provider workflows within the electronic health record (EHR). The number of patients receiving joint injections and the time to completion were tracked monthly using control charts. To further evaluate the new workflows, a survey was administered to providers, trainees, and nurses.

Results: During the study period, 166 patients received joint injections, and 137 (82%) were completed within 30 days. During the baseline period, there was a mean completion rate of 90%. As we continued standardization processes and

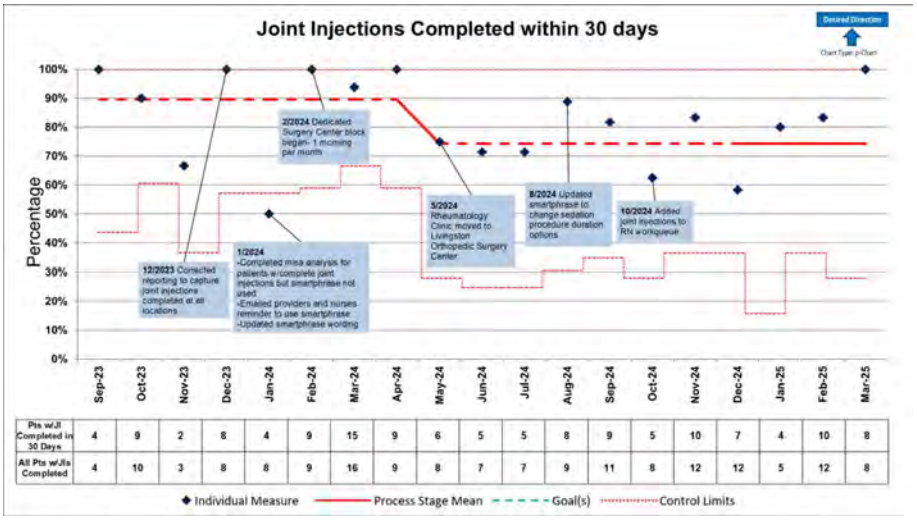


Figure 1: Control chart showing percentage of joint injections completed per month.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

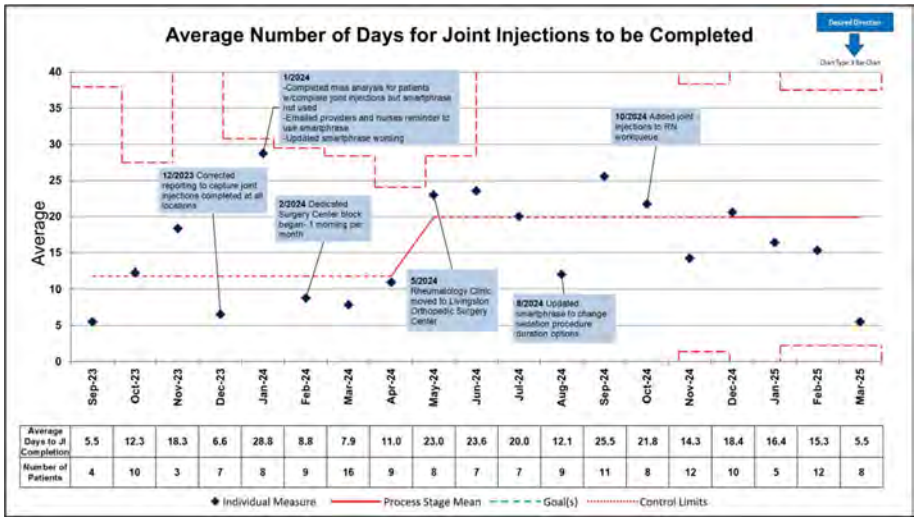


Figure 2: Control chart showing number of days for joint injections to be completed per month.

implementing interventions, there was a decrease in joint injections completed in 30 days resulting in a new process stage mean of 74% (**Figure 1**). When looking at average number of days until joint injection completion, the initial baseline mean was 12 days but increased to 20 days after the new process stage mean was established. The median average of days until injection completion was 15.5 days (**Figure 2**). Factors contributing to decrease in mean included: 1) transition to a new surgery center location in May 2024 and 2) decreased availability of sedated procedures over the holiday months of November-December 2024. Provider and staff survey results showed agreement that our new workflows have streamlined communication for details of the procedures to surgery center staff, simplified the scheduling process, decreased the number of messages needed to schedule procedures, and increased the procedure opportunities for fellow trainees. Respondents felt that length of time to schedule a joint injection was closely split between decreased (46%) and no difference (47%) (**Figure 3**).

Conclusion: This ongoing QI study demonstrates that implementation of a standardized form used by nursing and physician workflows within the EHR helped create a streamlined process for scheduling and completing corticosteroid joint injections within a 30-day window.

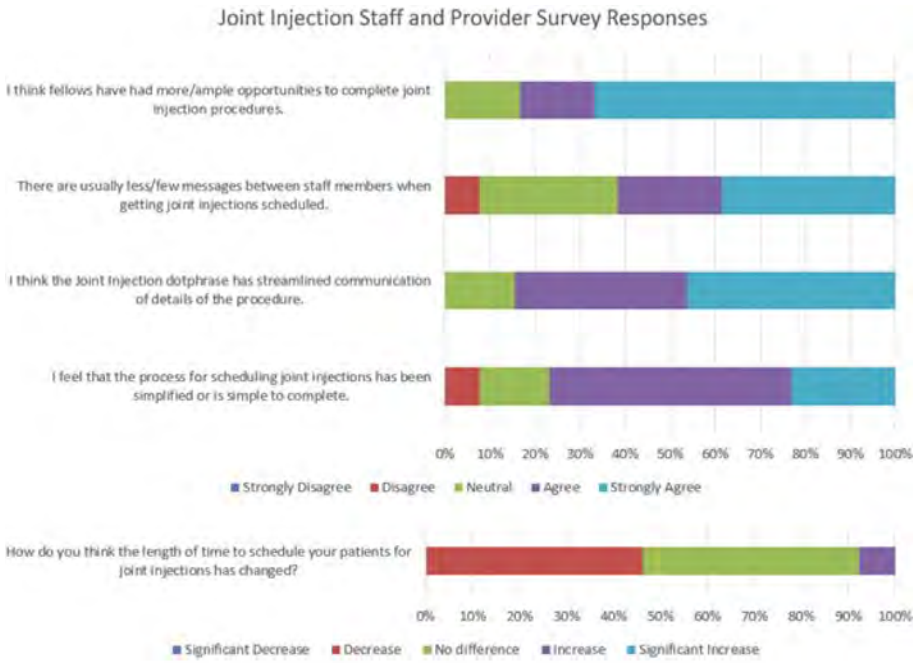


Figure 3: Survey results regarding usefulness of standardized form for joint injections within the electronic health record.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Lauer: None; **V. Sivaraman**: None; **M. Argraves**: None; **Y. Esteban**: None; **L. Pratt**: None; **A. Taxter**: None; **S. Akoghlanian**: None; **K. Wise**: None; **K. Anliker**: None; **J. Hughes**: None; **J. Booker**: None; **A. Leone**: None; **E. Oberle**: Pfizer, 1.

Abstract Number: 0414

Predicting JIA-Associated Uveitis Using Tear Fluid Biomarkers: A Prospective Multicenter Study

Mariia Pavlenko[1], Mekibib Altaye[2], Hermine Brunner[3], Margaret Chang[4], Ashley Cooper[5], Stefanie Davidson[6], Alexandra Duell[3], Bharti Gangwani[4], Aimee Hersh[7], Gary Holland[8], Carl Langefeld[9], Melissa Lerman[10], Mindy Lo[4], Virginia Miraldi Utz[3], Sampath Prahalad[11], Grant Schulert[3], Megan Quinlan-Waters[12], Erin Stahl[5], Edmund Tsui[8] and Sheila Angeles-Han[13], [1]Cincinnati Children`s Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital, Cincinnati, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]Boston Children's Hospital, Boston, MA, [5]Children's Mercy Kansas City, Kansas City, MO, [6]Department of Ophthalmology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, Philadelphia, PA, [7]University of Utah, Salt Lake City, UT, [8]UCLA Jules Stein Eye Institute and the Department of Ophthalmology, UCLA David Geffen School of Medicine, Los Angeles, [9]Wake Forest University School of Medicine, Winston Salem, NC, [10]Division of Rheumatology, Children's Hospital of Philadelphia and Department of Pediatrics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, Philadelphia, PA, [11]Emory + Children's Pediatric Institute, Atlanta, GA, [12]Cincinnati Children's Hospital Medical Center, CCHMC, [13]Cincinnati Children's Hospital, Cincinnati, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Uveitis is the most common extra-articular manifestation of juvenile idiopathic arthritis (JIA) and can lead to vision loss if not detected early. Current clinical risk factors are insufficient for the reliable prediction of uveitis development. Tear fluid represents a non-invasive source for biomarker discovery. In this prospective study, we investigated tear-based biomarkers to enhance early prediction and monitoring of uveitis in patients with JIA.

Methods: This prospective multicenter study included children with JIA without uveitis (JIA-no-U) diagnosed within the first 4 years of JIA and JIA-associated uveitis (JIA-U) from the Predicting Eye Disease in Childhood Arthritis - Uveitis Study (PEDIA-U) cohort. Tear samples were collected from both eyes by Schirmer strips at baseline (BL) and at 4 follow-up visits (FU1-4), approximately every 3 months. Levels of s100A8/A9 and A12 were measured by ELISA; IL-8, CXCL10, MCP-1, sICAM-1, APRIL and VEGF-A by Luminex assays. Biomarker levels between JIA-U and JIA-no-U were compared at 1) BL and 2) longitudinally, including FU1 and FU2 visits only. The log-transformed data were used in mixed model analysis with individuals and eyes as random effects, adjusting for arthritis activity and testing for a time-by-uveitis status interaction for repetitive sample collection. Least square (LS) means comparisons are adjusted for multiple testing using the Tukey-Kramer method. Multivariate analysis was performed using PROC GLIMMIX.

Results: Forty-two patients (31 JIA-no-U and 11 JIA-U) contributed 142 tear samples (102 JIA-no-U and 40 JIA-U) (Table 1). All patients had a BL visit and 17 had at least one FU. Of 11 JIA-U patients, 2 had active and 9 had inactive uveitis at BL; two JIA-no-U patients developed uveitis during FU. Only two patients changed their uveitis activity status over time.

At baseline, MCP-1 and CXCL-10 levels were significantly decreased in the JIA-U group compared to JIA-no-U (LS mean MCP-1: 1.31 vs. 2.18, p=0.008; CXCL-10: 4.01 vs. 5.1, p=0.001) (Figure 1). Over time, MCP-1 levels in the JIA-U group significantly increased from BL to FU2 (LS mean: BL = 1.2, FU = 3.1, p=0.027), while no significant change was observed in JIA-no-U. In contrast, CXCL-10 levels significantly decreased in JIA-no-U group from BL to FU2 (LS mean: BL = 4.9, FU =

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics at Baseline

Table 1. Demographic and Clinical Characteristics at Baseline

	All Cohort N (%)	JIA-no-U N (%)	JIA-U N (%)	JIA with developed uveitis N (%)
Number of patients	**42 (100)**	**31 (74)**	**9 (21)**	**2 (5)**
Number of tear samples	**142**	**102**	**28**	**12**
Sex at birth				
Female	27 (64)	17 (55)	8 (89)	2 (100)
Male	13 (31)	12 (39)	1 (11)	0
Unknown	2 (5)	2 (6)	0	0
Race				
White	37 (88)	26 (84)	9 (100)	2 (100)
Black and African American	1 (2)	1 (3)	0	0
Asian	2 (5)	2 (6)	0	0
American Indian or Alaska Native	0	0	0	0
Unknown	2 (5)	2 (6)	0	0
Ethnicity				
Non-Hispanic	36 (86)	26 (84)	8 (89)	2 (100)
Hispanic	3 (7)	2 (6)	1 (11)	0
Unknown	3 (7)	3 (10)	0	0
Age at sample collection in years Median (range)	13 (4-18)	12 (4-18)	14 (8-18)	14 (8-17)
Duration of JIA in years Median (range)	1 (0-12.8)	1 (0-4.3)	3.5 (0.2-12.8)	1.1 (0.2-0.5)
JIA Subtype				
Oligoarticular	24	20	4	0
Polyarticular RF-	9	6	3	0
Undifferentiated arthritis	2	2	0	0
Psoriatic	1	0	1	0
Other	1	1	0	1
Unknown	3	2	1	1
Arthritis activity				
Active	15 (35.7)	14	1	0
Inactive	24 (57.1)	15	7	2
Unknown	3 (7.2)	2	1	0
Uveitis location				
Anterior	11	N/A	9	2
Uveitis activity				
Active	2	N/A	2	N/A
Inactive	7	N/A	7	N/A
Corticosteroids eye drops use at time of visit				
Yes	4	N/A	4	0
No	8	N/A	6	2
Systemic medications				
Methotrexate	29 (69)	21 (68)	7 (78)	1 (50)
Adalimumab	19 (45)	11 (35)	7 (78)	1 (50)
Infliximab	5 (12)	2 (6)	3 (33)	0
Tocilizumab	7 (17)	2 (6)	5 (55)	0
Abatacept	2 (5)	0	2 (22)	0
Golimumab	3 (7)	0	3 (33)	0
Etanercept	5 (12)	2 (6)	3 (33)	0
Leflunomide	5 (12)	3 (10)	2 (22)	0

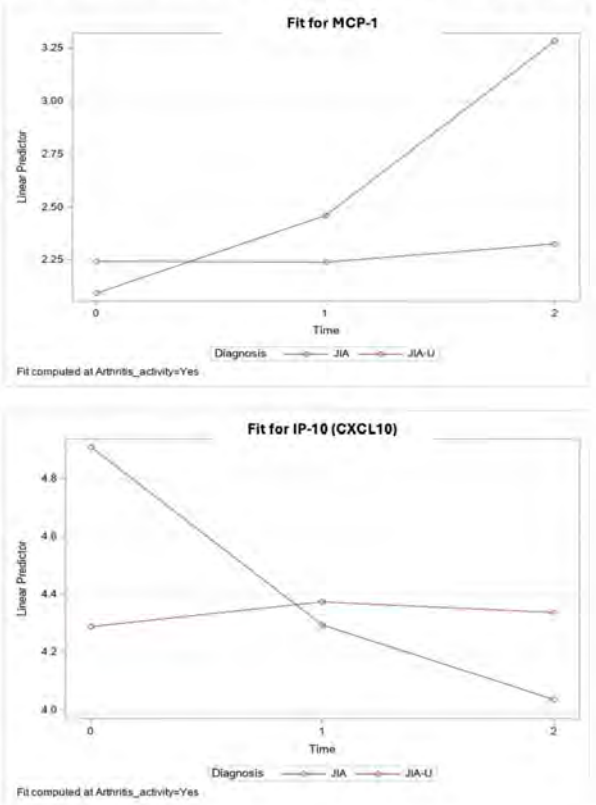
List of abbreviations: JIA - Juvenile Idiopathic Arthritis; JIA-no-U - JIA without uveitis; JIA-U - JIA-associated uveitis; N number; N/A non-applicable.

4.0, p=0.0002), with no distinct change in JIA-U. For two patients who developed uveitis during FU visits, their MCP-1 and CXCL-10 levels followed the same trajectory as JIA-U group. In multivariate analysis, we found that levels of CXCL-10 (p=0.0036) and APRIL (p=0.026) were significantly associated with JIA-U diagnosis, and MCP-1 (p=0.008) showed a trend to significance. Additionally, S100A12 and VEGF-A significantly increased from BL to FU for both JIA-U and JIA-no-U groups (p=0.024, p=0.044, respectively). These changes might be related to JIA progression itself.

Conclusion: This is the first prospective study evaluating tear-based biomarkers over time in JIA. We found a distinct difference in MCP-1 and CXCL10 levels in tear fluid between JIA-U and JIA-no-U patients at BL and FU. This data might be used for early uveitis prediction in JIA patients and potential treatment enhancement.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Predicted means of MCP-1 and CXCL10 (IP-10) by group and time



Time 0 – baseline visit, time 1 – first follow-up, time 2 – second follow-up
JIA- Juvenile Idiopathic Arthritis; JIA-U – JIA-associated uveitis

Disclosure: M. Pavlenko: None; **M. Altaye**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **M. Chang**: None; **A. Cooper**: None; **S. Davidson**: None; **A. Duell**: None; **B. Gangwani**: None; **A. Hersh**: None; **G. Holland**: None; **C. Langefeld**: None; **M. Lerman**: None; **M. Lo**: None; **V. Miraldi Utz**: None; **S. Prahalad**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **M. Quinlan-Waters**: None; **E. Stahl**: Sydnexis, 2; **E. Tsui**: None; **S. Angeles-Han**: None.

Abstract Number: 0415

The Impact of Social Vulnerability Index Scores in Pediatric Uveitis

Minal Aundhia[1], Pankaj Rajdeo[2], Michael Wagner[1], Alexandra Duell[1], Megan Quinlan-Waters[3], Virginia Miraldi Utz[1] and Sheila Angeles-Han[4], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, [3]Cincinnati Children's Hospital Medical Center, CCHMC, [4]Cincinnati Children's Hospital, Cincinnati, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Demographics and Clinical Characteristics of JIA-Only and Uveitis Cohorts.

N (%) unless otherwise indicated	JIA-no-U N=357	JIA-U N=127	Uveitis-Only N=25	P-value
Gender (N=509)				
Female	230 (64.4)	99 (78.0)	2 (8.0)	**<0.0001**
Male	127 (35.6)	28 (22.0)	23 (92.0)	
Race/ethnicity (N=496)				
Black, Hispanic or Latino	1 (0.3)	0 (0.0)	0 (0.0)	
Black, Not Hispanic or Latino	23 (6.4)	19 (15.0)	8 (32.0)	
White, Hispanic or Latino	10 (2.8)	2 (1.6)	0 (0.0)	**0.0040**
White, Not Hispanic or Latino	296 (82.9)	102 (80.3)	17 (68.0)	
Other/Multiethnic	16 (4.5)	2 (1.6)	0 (0.0)	
JIA Subtype (N=379)				
ERA	13 (4.6)	0 (0.0)	-	
Oligoarticular, extended	9 (3.2)	19 (19.59)	-	
Oligoarticular, persistent	103 (36.6)	54 (55.67)	-	
Oligoarticular, unspecified	6 (2.1)	0 (0.0)	-	
Polyarticular RF (+)	1 (0.4)	0 (0.0)	-	**<0.0001**
Polyarticular RF (-)	60 (21.3)	16 (16.49)	-	
Psoriatic Arthritis	13 (4.6)	0 (0.0)	-	
Undifferentiated Arthritis	16 (5.7)	7 (7.22)	-	
Systemic JIA	60 (21.2)	1 (1.03)	-	
Other	1 (0.4)	0 (0.0)	-	
Age at uveitis onset (N=96)	-	5.0 ± 2.4 (N=95)	8.0 (N=1)	
Age at arthritis onset (N=170)	4.8 ± 3.0 (N=84)	4.4 ± 2.9 (N=86)	-	0.378
Uveitis Laterality (N=125)				
Bilateral uveitis	-	70 (55.1)	23 (92.0)	**<0.0001**
Unilateral uveitis	-	30 (23.6)	2 (8.0)	
Years between JIA and uveitis onset (N=74)	-	0.3 ± 0.5		-
Years between JIA and uveitis diagnosis (N=78)	-	0.6 ± 1.6		-
Treated with methotrexate (N=200)	69 (19.3)	108 (85.0)	23 (92.0)	**<0.0001**
Time to start methotrexate from JIA onset (N=140)	3.4 ± 1.8 (N=54)	1.3 ± 1.8 (N=86)	-	**<0.0001**
Treated with biologic (in addition to methotrexate) (N=156)	61 (17.1)	82 (64.6)	13 (52.0)	**<0.0001**
ANA positivity (N=157)	94 (26.33)	63 (49.6)	0 (0.0)	**<0.001**
ESR Status (N=264)				-
Elevated ESR (>11 mm/hr)	142 (83.5)	61 (70.1)	7(100.0)	**0.0165**
Not Elevated (<11 mm/hr)	28 (16.5)	26 (29.9)	0 (0.0)	

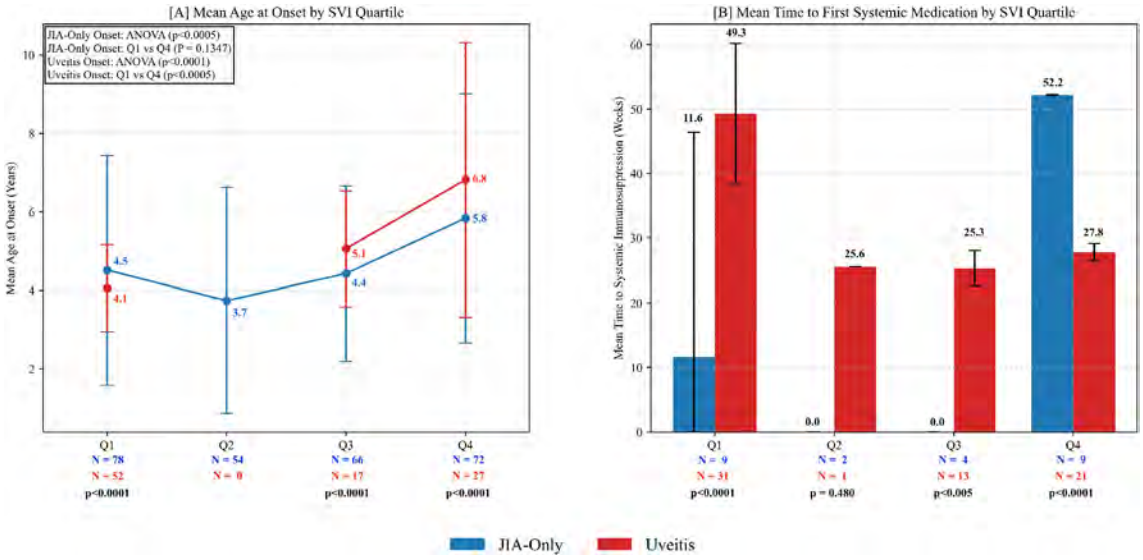


Figure 1. Impact of Social Vulnerability Index (SVI Q1=Low, Q4=High) on Disease Onset and Treatment Timing. (A) Mean age at JIA-Only and Uveitis onset by SVI Quartile. (B) Mean time to systemic immunosuppression in JIA-only and Uveitis patients by SVI Quartile. *P-values shown for comparisons.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

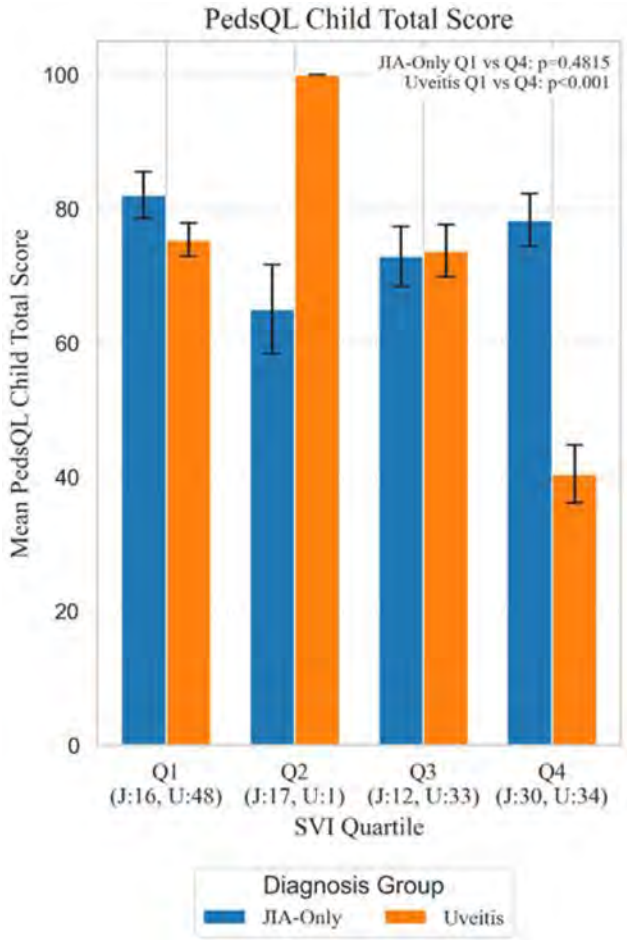


Figure 2. Association of Social Vulnerability Index (SVI Q1=Low, Q4=High) with mean PedsQL Child Total Score. Higher scores indicate better QoL. *P-values shown for comparisons.

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children with uveitis as the most common extra-articular manifestation. Uveitis can lead to sight-threatening complications and vision loss. While outcomes are influenced by disease phenotype and clinical risk factors, social determinants of health may significantly impact disease burden. The CDC's Social Vulnerability Index (SVI) is a composite measure of socioeconomic and demographic stressors and has not previously been applied to pediatric uveitis. This study investigates whether higher SVI is associated with delayed diagnosis, worse quality of life (QoL), and poorer clinical outcomes in affected children.

Methods: This retrospective single-center study included children diagnosed with JIA without uveitis (JIA-no-U), JIA-associated uveitis (JIA-U), and uveitis-only (Uveitis) from the Longitudinal Outcomes of Childhood Uveitis Study (LOCUS) registry. For SVI analyses, JIA-U and uveitis-only were combined as a single group (Uveitis). SVI scores (0 = low, 1 = high) were derived from addresses in the Electronic Medical Record using deGAUSS software and divided into quartiles (Q1–Q4). Analyses compared Q1 (low) and Q4 (high). Variables included demographics, age at diagnosis, time to systemic immunosuppression, and Pediatric QoL Inventory (PedsQL-Child Total) scores, an age-appropriate outcome measure. Analyses used t-tests and ANOVA. Some dates were recorded only by year, limiting precision.

Results: Of 509 patients, 357 had JIA-no-U, 127 JIA-U, and 25 uveitis-only (Table 1). Compared to JIA-only, JIA-U patients were more likely to be ANA-positive (49.6% vs 26.3%, p< 0.001) and female (78.0% vs 64.4%, p< 0.0001).

SVI Q4 was linked to later mean uveitis onset (Q4: 6.8 vs Q1: 4.1 yrs; p=0.0004) but not JIA-only onset (Q4: 5.8 vs Q1: 4.5 yrs; p=0.1347) (Figure 1A). Time to systemic immunosuppression showed opposite SVI associations (Figure 1B): in JIA-only,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

systemic treatment for Q4 was delayed (52.2 vs 11.6 weeks; p=0.000); for the Uveitis group, Q4 had shorter time to systemic treatment (27.8 vs 49.3 weeks; p=0.000).

For QoL, Uveitis patients in Q4 reported significantly worse PedsQL scores (Q4: ∼40 vs Q1: ∼75; p< 0.01). In JIA-only, scores did not differ significantly (Q4: ∼79 vs Q1: ∼82; p=0.4815) (Figure 2).

Conclusion: Social vulnerability significantly impacts key clinical outcomes and QOL in pediatric uveitis. Higher SVI patients with uveitis received systemic therapy more quickly, perhaps indicating severity at onset and rapid need for treatment escalation to prevent vision loss. Further, they are at risk for delayed uveitis diagnosis and poorer QOL. The SVI may serve as a valuable risk stratification tool to guide early intervention and targeted care coordination in at-risk children. Further study is warranted to evaluate subtype-specific mechanisms and treatment adherence patterns.

Disclosure: M. Aundhia: None; **P. Rajdeo**: None; **M. Wagner**: None; **A. Duell**: None; **M. Quinlan-Waters**: None; **V. Miraldi Utz**: None; **S. Angeles-Han**: None.

Abstract Number: 0416

Outcomes Of Children with Juvenile Idiopathic Arthritis Receiving Biological Disease-Modifying Anti-Rheumatic Drugs: Retrospective Analysis of A Real-World Experience From A Resource-Limited Setting

Narendra Bagri[1], Pavneet Kaur[2], Farheen KS[2], Bala Siva rama Krishna J[2], Banoth Sreesanth[2], Ayisha KP[2], Bareddy Sai Thrisha Reddy[2], ASHISH DATT UPADHYAY[2], RAKESH LODHA[2] and Sushil Kumar kabra[2], [1]All India Institute of Medical Sciences(AIIMS), New Delhi, Delhi, India, [2]All India Institute of Medical Sciences, New Delhi, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: We aimed to study the outcomes (remission, flare, and adverse events) of biological disease-modifying anti-rheumatic drugs (bDMARD) in children with JIA from a low-middle-income country setting, and explore the factors associated with these outcomes.

Methods: The Pediatric Rheumatology Clinic bDMARD register (2009 to August 2024) was screened to enrol children with JIA and at least 3 months of follow-up whilst on bDMARDs. Participant characteristics and clinical responses were collected in a pre-designed proforma to evaluate the primary objective i.e. studying outcomes among children with JIA on bDMARDs. The secondary objective was to study factors associated with time-to-remission (TTR) and flare-after-stopping-bDMARDs. The study was approved by the Institute Ethics Committee (IECPG-596/20/09.2023, RT-02/21.02.2024). Consent was waived for this retrospective study.

Results: One-hundred-fifteen children (59.1% boys) with 168 patient-years of bDMARD use were enrolled for this study. Enthesitis-related-arthritis was the commonest subtype of JIA (n=44, 38.3%). The most commonly used bDMARD was adalimumab (n=43, 37.3%). The median (IQR) delay to initiation of bDMARD from the perceived need was 2 (0-6) months, primarily due to financial impediments (n=81, 70.4%). Fifteen (13%) children screened positive for tuberculosis infection. One hundred ten (95.6%) children achieved remission on bDMARD, after a median (IQR) of 7.5 (4-12) weeks. Macrophage

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Key characteristics

Characteristic	N=115
Male	68 (59.1)
Age:	
at symptom onset, years	6.6 (3.5)
at diagnosis, years	8.7 (5.8)
Delay in diagnosis, months	12 (9-18)
Juvenile idiopathic arthritis subtype	
Enthesitis-related arthritis	44 (38.2)
Systemic onset	35 (30.4)
Polyarthritis	29 (25.2)
Rheumatoid factor positive	10/29
Rheumatoid factor negative	19/29
Oligoarthritis	5 (4.3)
Psoriatic	2 (1.7)
Follow up duration, months	54.5 (38.1)
patient-years of follow-up	522.5
Follow-up duration whilst on bDMARDs, months	32 (7-71)
patient-years of bDMARD use	188
Time from disease onset to bDMARD initiation, years	5.6 (1.9-5.8)
Symptoms at initiation of bDMARD, n(%)	
Fever*	45 (39.1)
Rash*	24 (20.9)
Macrophage activation syndrome*	4 (3.5)
Uveitis	9 (7.8)
Active joints at initiation	0 (4, 8)
Restricted joints at initiation	2 (0, 4)
Sacroiliitis^ at initiation, n(%)	11/44 (70.5)
Concomitant csDMARDs, n(%)*	
Methotrexate	95 (82.6)
Sulfasalazine	33 (28.7)
Leflunomide	11 (9.6)
Pre-existing TB infection requiring prophylaxis^, n(%)	15 (13)
Delay in prescribed bDMARDs, months	2 (0-6)
Range, months	0-66
bDMARDs funding sources, n(%)	
Public sector schemes	73 (63.4)
Philanthropic organization	26 (22.6)
Self-funded	16 (13.9)
Proportion achieving remission on bDMARD, n(%)	110 (95.7)
Time to achieve remission, weeks	7.5 (4-12)
Reduction in active joints at follow-up	5 (2 to -4)
Reduction in restricted joints at follow-up	0 (0 to -2)
Failure of bDMARD, n(%)	7 (6%)
Proportion in whom bDMARDs stopped, n(%)	68 (59.1)
Proportion of flare after stopping, n(%)	33/68 (48.5)
Time to flare after stopping BDMARDs, months	6 (3.5-12)
Reasons for stopping BDMARDs, n(%)	
Adverse Event	27 (39.7%)
Financial constraint	23 (33.8%)
Controlled disease activity	13 (19.1%)
Patient Defaulted	5 (7.4%)
Proportion with poor adherence to therapy, n(%)	33 (28.6%)
Proportion of adverse events while on BDMARDs, n(%)	43 (36.5)
Serious infection episodes requiring hospitalization	13 (11.3)
Varicella infection	2 (1.7)
Tuberculosis	4 (3.5)
Scabies infestation	2 (1.7)
Injection site reaction	2 (1.7)
Infusion-associated events	1 (0.9)
Azathioprine neutrop	1 (0.9)
Leucopenia	1 (0.9)
Thrombocytopenia	4 (3.5)
Anaemia	4 (3.5)
Tuberculosis	6 (5.2)
Neoplastic/lymphoproliferative events	2 (1.7)
Other adverse events, including minor infections	6 (5.2)

Categorical data was presented as proportions, normal continuous data as mean (with standard deviation) and skewed continuous data as median (with interquartile range).

**In children with systemic onset juvenile idiopathic arthritis*

** There were children who received more than one csDMARD.*

^In children with enthesitis related arthritis

^ As suggested by a positive TST or IGRA or chest X ray abnormalities without any active TB disease.

Key characteristics

activation syndrome at initiation was significantly associated (HR 3.1 (1.1-8.8), p=0.03) with a longer time-to-remission. bDMARDs were stopped in n=68/115 (59.1%) after a median (IQR) 15 (9.6-26.5) months, of whom n=33/68 (48.5%) flared during the next 6 (3.5-12) months. Longer time-to-remission (OR 1.12 (1-1.2), p=0.02) was significantly associated with flare after stopping bDMARDs. Forty-two (36.5%) patients experienced adverse events. The most striking

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Analyses for factors associated with time-to-remission (A), flare after stopping (B)

A. Time to remission	Hazard Ratio (HR)	Confidence Interval (95%CI)	P value	Multivariable regression HR (95% CI), p value
Male	1.09	0.7-1.6	0.65	
Age of symptom onset	1	0.9-1.0	0.85	
Age at diagnosis	0.99	0.9-1.0	0.76	
Time to diagnosis	0.99	0.9-1.0	0.64	
Time to initiation of biologicals	0.99	0.9-1.0	0.37	
Prior steroid use	1.02	0.7-1.5	0.88	
JIA subtype (pJIA)	0.62	0.4-2.7	0.3	
bDMARD class (IL-6i)	0.65	0.4-0.9	0.04	
Active joints at initiation	0.97	0.9-1.0	0.35	
Fever at initiation	1.3	0.9-2.0	0.10	1.3 (0.8-1.9), p=0.19
Macrophage activation syndrome	3.6	1.3-10.0	0.03	**3.1 (1.1-8.8), p=0.03**
Flares during therapy	0.85	0.5-1.4	0.52	
Therapy interruption	1.14	0.7-1.7	0.69	
B. Flare after stopping	**Odds Ratio (OR)**	**Confidence Interval (95%CI)**	**P value**	**Multivariable regression OR (95%CI), p value**
Age of symptom onset	0.99	0.9-1	0.10	
Age at diagnosis	1.01	0.9-1.0	0.34	
Time to diagnosis	0.99	0.9-1.0	0.37	
Time to biologicals	1.02	0.98-1.05	0.38	
Active joints at initiation	1.05	0.9-1.1	0.71	
JIA subtype (sJIA)	0.83	0.6-1.2	0.23	
Fever at initiation	1.00	0.4-2.6	0.95	
Time to remission	1.12	1.02-1.23	0.01	**1.12 (1.0-1.2), p=0.015**
Flares during therapy	2.60	0.78-8.6	0.11	2.3 (0.6-8.5) p=0.2

Analyses for factors associated with time-to-remission (A), flare after stopping (B)

adverse events were serious infections requiring hospitalisation (n=13, 11.3%) and tuberculosis (n=4, 3.4%). All children who developed tuberculosis were on TNFi (Adalimumab).

Conclusion: : Though children on bDMARDs showed comparable remission rates, we noted a higher frequency of serious infections and tuberculosis, compared to the experience described from high-income countries. These observations highlight the need for further surveillance of outcomes of bDMARD use in JIA in an LMIC setting.

Disclosure: N. Bagri: None; **P. Kaur**: None; **F. KS**: None; **B. Krishna J**: None; **B. Sreesanth**: None; **A. KP**: None; **B. Thrisha Reddy**: None; **A. DATT UPADHYAY**: None; **R. LODHA**: None; **S. kabra**: None.

Abstract Number: 0417

Implementation of a Communication Aid in Juvenile Idiopathic Arthritis Patient Visits, a Quality Improvement Study

Nazlican Civilibal Tang[1], Rachel Guess[2], Ran Hazan[3], Amy Monahan[4] and Maleewan Kitcharoensakkul[5], [1]WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST.LOUIS, MISSOURI, St.Louis, MO, [2]WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST.LOUIS, MISSOURI, st.louis, [3]WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST.LOUIS, MISSOURI, Saint Louis, MO, [4]WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST.LOUIS, MISSOURI, St. Louis, MO, [5]Washington University/B-JH/SLCH Consortium, St. Louis, MO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

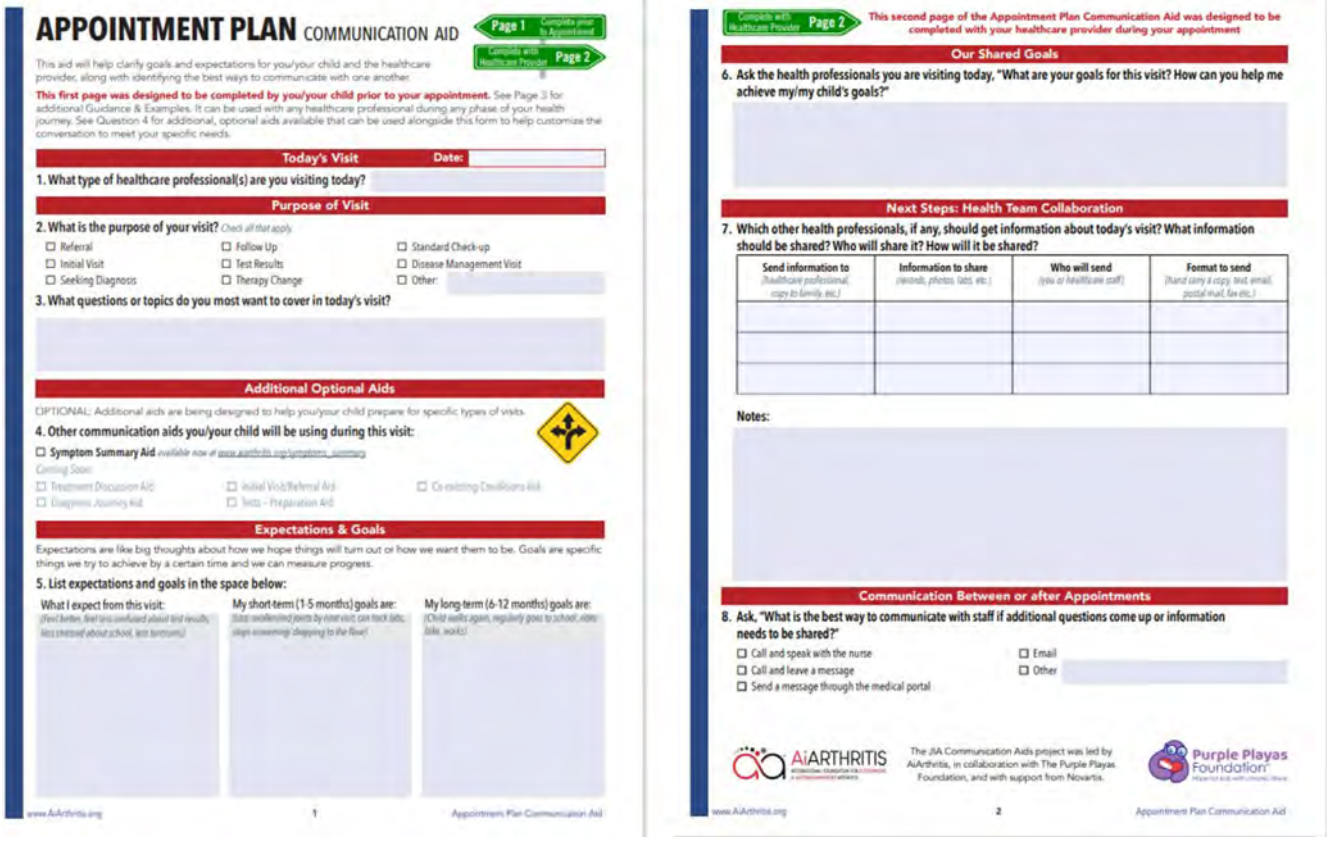
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Juvenile idiopathic arthritis (JIA) is a childhood onset autoimmune disease requiring long-term care and personalized treatment. Through a rigorous series of mixed patient and provider workgroups, AiArthritis developed communication aids to improve communication and decision making between JIA families and their providers. The aid clarifies the patient's clinical questions, and their short- and long-term goals of care (Fig 1). We aimed to evaluate the feasibility and effectiveness of this communication aid in pediatric rheumatology clinics.

Methods: Following approval from the Washington University Institutional Review Board, this quality improvement (QI) study enrolled patients through the pediatric rheumatology clinic with JIA and suspected JIA of any age, with parental consent. The communication aid was provided at check-in for the patient (age ≥12) or the parent to complete. The provider reviewed the responses during the visit. Afterward, both the patient/parent and the provider team completed anonymous surveys. Primary outcome measures were set at ≥ 50% of patients finding the aid easy to use, helpful in communicating goals, and improving the quality of experience, and ≥75% of provider responses indicating an improved therapeutic alliance without adversely affecting clinic workflow. The first Plan-Do-Study-Act cycle enrolled 10 patients, and the second enrolled 20. The third cycle has ongoing enrollment.

Results: Of 31 patient/parent participants, 93% found the handout very easy to use. Majority of participants (64%) felt the aids greatly or somewhat helpful in preparing their appointment goals (Fig 2). Two-thirds reported an improved overall experience during their appointment, and 70% wanted the aid used in future visits. Among 56 provider responses, 50%, 30%, and 19% were from attending physicians, fellows, and nurses, respectively. The majority (93%) reported that the aid did not adversely affect workflow (Fig 3); none indicated a negative impact. Moreover, 79% of the providers felt the communication aid improved therapeutic relationship with patients, and 91% of the respondents supported the continued use of the communication aid in the clinic.

Figure 1- Communication aid



APPOINTMENT PLAN COMMUNICATION AID

Page 1 Complete prior to Appointment

Complete with Healthcare Provider Page 2

This aid will help clarify goals and expectations for you/your child and the healthcare provider, along with identifying the best ways to communicate with one another.

This first page was designed to be completed by you/your child prior to your appointment. See Page 3 for additional Guidance & Examples. It can be used with any healthcare professional during any phase of your health journey. See Question 4 for additional, optional aids available that can be used alongside this form to help customize the conversation to meet your specific needs.

Today's Visit Date:

1. What type of healthcare professional(s) are you visiting today?

Purpose of Visit

2. What is the purpose of your visit? *Check all that apply*

☐ Referral ☐ Follow Up ☐ Standard Check-up
☐ Initial Visit ☐ Test Results ☐ Disease Management Visit
☐ Seeking Diagnosis ☐ Therapy Change ☐ Other:

3. What questions or topics do you most want to cover in today's visit?

Additional Optional Aids

OPTIONAL: Additional aids are being designed to help you/your child prepare for specific types of visits.

4. Other communication aids you/your child will be using during this visit:

☐ **Symptom Summary Aid** *available now at* www.aiarthritis.org/symptoms_summary

Coming Soon:

☐ Treatment Discussion Aid ☐ Initial Visit/Referral Aid ☐ Co-existing Conditions Aid
☐ Diagnosis Journey Aid ☐ Tests – Preparation Aid

Expectations & Goals

Expectations are like big thoughts about how we hope things will turn out or how we want them to be. Goals are specific things we try to achieve by a certain time and we can measure progress.

5. List expectations and goals in the space below:

What I expect from this visit:	My short-term (1-5 months) goals are:	My long-term (6-12 months) goals are:
(Feel better, Brief less confused about test results, less stressed about school, less tantrums)	*(Make weekend/work plans by next visit, can track labs, stops screaming/dropping to the floor)*	*(Child walks again, regularly goes to school, rides bike, works)*

www.AiArthritis.org 1 Appointment Plan Communication Aid

Complete with Healthcare Provider Page 2

This second page of the Appointment Plan Communication Aid was designed to be completed with your healthcare provider during your appointment

Our Shared Goals

6. Ask the health professionals you are visiting today, "What are your goals for this visit? How can you help me achieve my/my child's goals?"

Next Steps: Health Team Collaboration

7. Which other health professionals, if any, should get information about today's visit? What information should be shared? Who will share it? How will it be shared?

Send information to *(healthcare professional, copy to family, etc.)*	Information to share *(records, photos, labs, etc.)*	Who will send *(you or healthcare staff)*	Format to send *(hand carry a copy, text, email, postal mail, fax etc.)*

Notes:

Communication Between or after Appointments

8. Ask, "What is the best way to communicate with staff if additional questions come up or information needs to be shared?"

☐ Call and speak with the nurse ☐ Email
☐ Call and leave a message ☐ Other
☐ Send a message through the medical portal

AiARTHRITIS

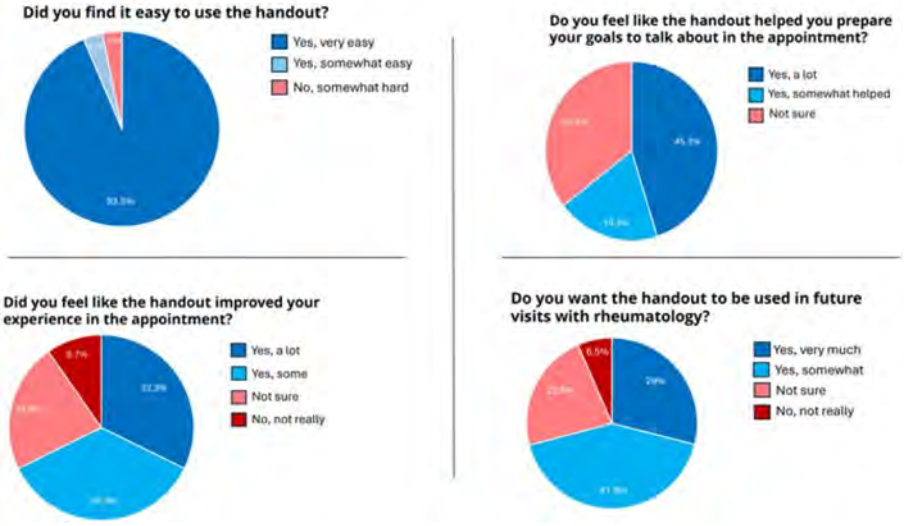
The JIA Communication Aids project was led by AiArthritis, in collaboration with The Purple Playas Foundation, and with support from Novartis.

Purple Playas Foundation

www.AiArthritis.org 2 Appointment Plan Communication Aid

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2- Patient responses

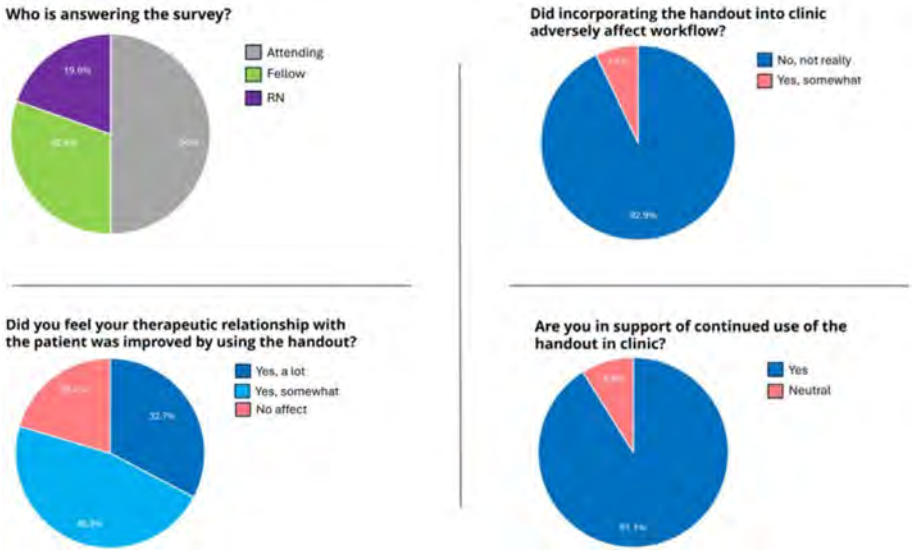


Conclusion: This QI study has met the primary outcome measures. We have found that the communication aid was feasible to use in outpatient clinic for patients with JIA or suspected JIA. It facilitates development of personalized treatment plans and should be considered for implementation more widely in the pediatric rheumatology clinic.

Areas for improvement include providing communication aid in advance of the appointment. Limitations of the study are lack of long-term follow up to assess for durable communication improvement and progress towards reaching patient-made goals.

Acknowledgement: AiArthritis (International Foundation for Autoimmune & Autoinflammatory Arthritis) for developing the JIA Health Journey Communication Aids and allowing us to use these aids for the study. AiArthritis would also like to acknowledge Purple Playas Foundation for their role in co-designing the aids.

Figure 3- Provider responses



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Civilibal Tang: None; **R. Guess**: None; **R. Hazan**: None; **A. Monahan**: None; **M. Kitcharoensakkul**: None.

Abstract Number: 0418

Evaluation of Disease Activity in the Knee Joint Through Clinical, Radiologic, Synovial Fluid and Histopathologic Measurements of Inflammation in Children with Juvenile Idiopathic Arthritis

Patricia Vega-Fernandez[1], Kelly Rogers[2], Alyssa Sproles[2], Sherry Thornton[1], Lexi Auld[3], Jackeline Rodriguez-Smith[1], Ekemini Ogbu[1], Kara Murphy Schmidt[4], McKenzie Vater[5], Katelyn Banschbach[6], Grant Schulert[1], Alexei Grom[1], Sheila Angeles-Han[2], Hermine Brunner[1], Jennifer Huggins[7], Daniel Lovell[1], Amy Cassedy[8], Yuriy Baglaenko[2], Tracy Ting[1] and Sara Szabo[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital, Cincinnati, OH, [3]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [4]Cincinnati Children's Hospital Medical Center, Louisville, KY, [5]Cincinnati Children's Hospital Medical Center, Fort Thomas, KY, [6]cincinnati Children's hospital, Villa Hills, KY, [7]Cincinnati Children's Medical Center, Cincinnati, OH, [8]Cincinnati Children's hospital medical center, cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical, radiologic and biomarker data are measurements used in the assessment of juvenile idiopathic arthritis (JIA) disease activity. The development of ultrasound-guided synovial biopsy (USGSB) in children has accelerated synovial histopathology research. Investigate the relationship between clinical features of arthritis, radiologic synovitis, synovial fluid (SF) biomarkers of inflammation, and histologically confirmed synovitis in children with JIA.

Methods: JIA patients requiring a knee joint injection were enrolled. Patients underwent standardized clinical assessment (cJADAS, range 0-30), a musculoskeletal ultrasound (MSUS) examination, and USGSB of the affected knee with collection of synovial fluid (SF). MSUS images were collected and scored by pediatric MSUS experts. MSUS synovitis was scored using a validated semiquantitative MSUS scoring system for the knee joint (MSUS-knee score, range 0-6). Synovial biopsy inflammation was determined by Krenn's score (KS, which examines for synovial hyperplasia, stromal cellularity/reactivity and inflammatory infiltrate, range 0 to 9, higher scores indicating greater severity. Biomarkers measured in SF included: TNFR1, IL-6, IL-10, MCP-1, ANG-1, ANG-2, MMP-2, MMP-8, CCL18, CCL20, IFNg, IL-17a, IL-2Ra, IL-23, IL-18, resistin, CXCL9, VEGF, TIMP-1 by Luminex, and S100A12, S100A8/A9 by ELISA. Wilcoxon Rank Sum test was used to compare group differences. Spearman correlation (r_s) was used to assess the relationship between the studiedvvariables

Results: Thirty-four patients [mean age 10 (SD 5.1)] were enrolled. Their median cJADAS score was 4 (IQR 2-8) while 32% of them had no pain at the affected joint (Table 1). All patients had presence of MSUS synovitis with a median MSUS-knee score of 5 (IQR 4-6). Median KS was 6 (IQR: 4-7). Children receiving conventional and/or biologic disease modifying medications (DMARDs) had similar median KS compared to children not on these treatments [6, (IQR 3-7) and 6 (IQR 5-8), respectively] (p=0.962). Children with polyarticular JIA had a median KS of 5 (IQR 5-6) while the KS for children with oligoarticular was 6 (IQR 4-8) (p=0.725). Children with oligoarticular JIA taking NSAIDs at the time of the USGSB had a significantly lower KS than oligoarticular JIA children not on an NSAID [median 3.5 (IQR 3-4) v 6.5 (IQR 4.2-7.7), respectively] (p=0.033). A significant moderate correlation was found between the MSUS-knee score and the KS r_s: 0.45 (0.12 -0.7), with the highest association being between the KS stroma domain and the MSUS-knee score [r_s: 0.5 (0.17-0.720] (Table 2). Strong significant correlations (r_s>0.8, p< 0.05) were found between SF levels of S100A12, S100A8A9, CCL18, IL-6, MMP-8 and the KS (Table 3). S100A8A9 also had a significant correlation with the MSUS-knee score [r_s 0.55 (0.08-0.82)].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical Characteristics of Patients Involved (n=34)

Demographics	
Age in years, mean (SD)	10.0 (5.1)
Sex, n (%)	
Female	25 (73.5)
Male	9 (26.5)
Race, n (%)	
Black/African-American	3 (8.8)
White	31 (91.2)
Hispanic, n (%)	1 (2.9)
Clinical	
Time since diagnosis in months, median (IQR)	2.3 (0.8-13.4)
Diagnosis, n (%)	
Crohn's related arthritis	1 (2.9)
Oligoarthritis, extended	1 (2.9)
Oligoarthritis, persistent	22 (64.8)
Polyarthritis, RF negative	8 (23.5)
Psoriatic	2 (5.9)
ANA, n (%)	
Negative	26 (76.5)
Positive	8 (23.5)
RH Factor, n (%)	
Negative	29 (85.3)
Not done	5 (14.7)
HLA-B27, n (%)	
Negative	12 (35.3)
Positive	1 (2.9)
Not done	21 (61.8)
Total number of active joints by clinical examination, median (IQR)	1 (1-2)
cJADAS score, median (IQR)	4 (2-8)
ESR, median (IQR)	13 (8-33)
CRP, median (IQR)	0.5 (0.4-1.0)
Treatment at the time of biopsy* – yes, n (%)	24 (70.6)
Conventional and/or biologics DMARDs, n (%)	10 (29.4)
Steroid, n (%)	3 (8.8)
NSAID, n (%)	18 (52.9)
Total number of USGSB-knees	40
cJADAS: clinical Juvenile Arthritis Disease Activity Score; MTX: methotrexate, DMARDs: disease modifying drugs; NSAIDs: Nonsteroidal Anti-Inflammatory drugs *Medications are not mutually exclusive	

Table 2. Relationship between MSUS-knee score and Krenn's scores (n=34)

	B-Mode Complexity	
Total Krenn's Score	0.45 (0.12-0.7)	**0.010***
Synovial lining hyperplasia/enlargement	0.38 (0.03-0.65)	**0.033***
Stromal Cell Density/pannus formation	0.50 (0.17-0.72)	**0.004***
Inflammatory infiltrate	0.23 (-0.14-0.54)	0.221
*Strength of the correlation calculated using Spearman correlation (rs). p-value significant (<0.05)		

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Relationship between Synovial Fluid Biomarkers and Krenn's scores (n=16)

	Total Krenn Score	
Synovial Fluid Biomarkers		
S100A12	0.79 (0.35-0.94)	**0.003***
s100A8A9	0.74 (0.33-0.92)	**0.002***
MMP-2	0.15 (-0.44-0.65)	0.632
CCL18	0.87 (0.6-0.96)	**<0.001***
TIMP-1	0.67 (0.18-0.89)	**0.011***
IL-6	0.86 (0.59-0.96)	**<0.001***
MCP-1	0.58 (0.04-0.86)	**0.038***
Ang-2	0.55 (0-0.85)	0.050
MMP-8	0.84 (0.54-0.95)	**<0.001***
INF-Gamma	0.32 (-0.28-0.74)	0.294
CCL20	0.66 (0.18-0.89)	**0.012***
IL-17a	0.34 (-0.26-0.75)	0.270
CD25	0.5 (-0.07-0.82)	0.083
Resistin	0.68 (0.2-0.89)	**0.009***
CXCL9	0.63 (0.11-0.88)	**0.020***
VEGF	0.6 (0.07-0.86)	**0.029***
TNFRI	0.35 (-0.25-0.75)	0.255
IL-23	0.62 (0.11-0.87)	**0.022***
IL-18	0.77 (0.39-0.93)	**0.001***
Protein	0.25 (-0.35-0.7)	0.418

Matrix metalloproteinases (MMP), Chemokine ligand (CCL), Angiopoeitin (Ang), Tissue inhibitor of metalloproteinases 1 (TIMP-1), Interleukin (IL), monocyte chemoattractant protein (MCP), interferon (IFN), monokine induced by gamma interferon/chemokine (C-X-C motif) ligand (CXCL9), vascular endothelial growth factor (VEGF), tumor necrosis factor receptor 1(TNFR1). *Strength of the correlation calculated using Spearman correlation (rs). p-value significant (<0.05).

Conclusion: This pilot study suggests that the degree of inflammation as measured by the KS does not associate with JIA disease category or DMARDs use but may be modified by concomitant NSAID use The association of the MSUS-knee score and SF biomarkers of inflammation with the KS detected in this study suggest that these measurements may have a role as surrogate markers of histologically confirmed active synovitis.

Disclosure: P. Vega-Fernandez: None; **K. Rogers**: None; **A. Sproles**: None; **S. Thornton**: None; **L. Auld**: None; **J. Rodriguez-Smith**: None; **E. Ogbu**: Cartesian Therapeutics, 2; **K. Schmidt**: None; **M. Vater**: None; **K. Banschbach**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9; **S. Angeles-Han**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **J. Huggins**: None; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **A. Cassedy**: None; **Y. Baglaenko**: None; **T. Ting**: None; **S. Szabo**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0419

Ultrasound-Guided Synovial Biopsy in Children and Adolescents with Juvenile Arthritis: Initial Results

Patricia Vega-Fernandez[1], Kelly Rogers[2], Megan Quinlan-Waters[3], Sheila Angeles-Han[2], Alexei Grom[1], Daniel Lovell[1], Jennifer Huggins[4], Ekemini Ogbu[1], Amy Cassedy[5], Sara Szabo[1], Tracy Ting[1], Grant Schulert[1], McKenzie Vater[6], Hermine Brunner[1], Jackeline Rodriguez-Smith[1] and Katelyn Banschbach[7], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital, Cincinnati, OH, [3]Cincinnati Children's Hospital Medical Center, CCHMC, [4]Cincinnati Children's Medical Center, Cincinnati, OH, [5]Cincinnati Children's hospital medical center, cincinnati, OH, [6]Cincinnati Children's Hospital Medical Center, Fort Thomas, KY, [7]cincinnati Children's hospital, Villa Hills, KY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Ultrasound-guided synovial biopsy (USGSB) has been recently implemented for clinical and research purposes in adults with inflammatory arthritis. The current use of USGSB in the pediatric population is very limited. Here we report our USGSB experience at Cincinnati Children's Hospital Medical Center (CCHMC).

Methods: Children with a diagnosis of Juvenile Idiopathic Arthritis (JIA) that were to receive a clinically indicated therapeutic knee joint injection were eligible for this study. USGSB was approved by the CCHMC IRB, and all patients/parents provided informed consent. At the time of the joint injection, a musculoskeletal ultrasound (MSUS), USGSB and steroid injection of the affected joint was performed by a pediatric rheumatologist. Clinical and procedure data were collected to determine feasibility. Synovial biopsy inflammation was determined by Krenn's score. To evaluate procedural safety and tolerability, a questionnaire was administered to the patient/family 2-4 days after the procedure.

Results: A total of 34 children [mean age 10 years (SD 5.1)] with JIA were enrolled in this study. The majority of participants had oligoarticular JIA (68%) with the youngest patient in which an USGSB was completed being 2 years old. While 58% (n=20) of the procedures were done in the operative room under general anesthesia, 42% (n=14) were completed in clinic under local anesthesia. The USGSB and steroid injection was completed in all participants. In general, USGSB were well tolerated. One patient developed a subcutaneous hematoma that resolved within 1 week. The median Krenn's score was 6 (IQR: 4-7). When patients/families were asked about knee joint pain after the USGSB and steroid injection, they reported that the joint pain had improved in 73% of the cases, while 27% felt the pain after the procedure was the same or worse. After the procedure, all participants/family reported feeling glad being a part of the study and 93% (14 of 15 responders) felt that other children could tolerate the biopsy while pain during the procedure is under control. Of note, 2 patients had a repeat biopsy with no complications.

Conclusion: USGSB are safe and well-tolerated in children. USGSB has been successfully implemented for research purposes in children and adolescents with JIA in our center.

Disclosure: P. Vega-Fernandez: None; **K. Rogers**: None; **M. Quinlan-Waters**: None; **S. Angeles-Han**: None; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **J. Huggins**: None; **E. Ogbu**: Cartesian Therapeutics, 2; **A. Cassedy**: None; **S. Szabo**: None; **T. Ting**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **M. Vater**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **J. Rodriguez-Smith**: None; **K. Banschbach**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0420

Long-term efficacy of intra-articular triamcinolone hexacetonide injections in juvenile idiopathic arthritis patients starting tumor necrosis factor inhibitor therapy: 48 weeks results from a randomized, open-label, blinded-assessor multicenter phase 4 trial - the MyJIA trial

Pernille Boyesen[1], Anna-Birgitte Aga[1], Vibke Lilleby[1], Maiju Pesonen[1], Marite Rygg[2], Ellen Nordal[3], Bjørn Barstad[4], Karin Tylleskär[5], Helga Sanner[1], Siri Hetlevik[1], Nina Martine Sande[1], Inge Christoffer Olsen[1], Siri Lillegraven[6], Espen Haavardsholm[7], Athimalaipet Ramanan[8], Oyvind Molberg[9] and Berit Flatø[1], [1]Oslo University Hospital, Oslo, Norway, [2]Department of Clinical and Molecular Medicine, NTNU - Norwegian University of Science and Technology and Department of Pediatrics, St. Olavs Hospital, Trondheim, Norway., Trondheim, Norway, [3]University Hospital of North Norway, Tromsø, Nepal, [4]Stavanger University Hospital, Stavanger, Norway, [5]Haukeland University Hospital, Bergen, Norway, [6]Diakonhjemmet Hospital, Oslo, Norway, [7]Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [8]Bristol Royal Hosp for Children, Bristol, United Kingdom, [9]Oslo University Hospital, Oslo, Nepal

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Modern therapies have improved outcomes in patients with JIA, but up to 60% of patients treated with TNF-α inhibitors (TNFi) have persisting disease activity underscoring the need for improved therapeutical approaches. Intra-articular (IA) triamcinolone hexacetonide injections are often used as adjunctive therapy to TNFi treatment even though no controlled studies have examined their potential added benefit. We aim to assess the efficacy and safety of IA triamcinolone hexacetonide injections compared to no injections in children with JIA starting TNFi therapy.

Table 1. Baseline demographics and disease characteristics.

	Intra-articular triamcinolone hexacetonide injections (intervention) (n=92)	No intra-articular injections (control) (n=95)
Age at randomization, years	10.5 (4.3)	10.4 (4.5)
Disease duration, years	2.0 (3.7)	1.7 (2.9)
Female gender	58 (63%)	61 (64%)
JIA category		
Oligoarticular persistent	29 (32%)	25 (26%)
Oligoarticular extended	13 (14%)	12 (13%)
Polyarticular RF positive	8 (9%)	10 (11%)
Polyarticular RF negative	23 (25%)	22 (23%)
Enthesitis-related arthritis	8 (9%)	13 (14%)
Psoriatic arthritis	4 (4%)	3 (3%)
Undifferentiated arthritis	7 (8%)	10 (11%)
Concurrent methotrexate therapy at baseline	80 (87%)	80 (84%)
Previous biologic DMARD therapy	6 (7%)	6 (6%)
Number of joints with active arthritis, 0-71. Median (IQR)	3 (5)	2 (4)
Physician's global assessment of disease activity, 0-100 mm.	43.7 (21.9)	41.5 (18.8)
Disease activity assessed by the Juvenile arthritis disease activity score 10, 0-40.	13.9 (7.4)	12.9 (6.1)
Erythrocyte sedimentation rate, mm/hr. Median (IQR)	10 (18)	12 (17)
C-reactive protein, mg/L. Median (IQR)	2.2 (8.6)	1.7 (8)

Data are mean (SD) or n (%) unless otherwise stated.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The MyJIA trial (NCT 04614311) is a randomized, controlled, multicenter, parallel group, blinded-assessor, open-label, phase 4 clinical trial. Main inclusion criteria were non-systemic JIA, age 1 to 18 years, clinical indication for TNFi therapy, and at least one joint with arthritis suited for IA steroid injection. Participants were assigned by a computer randomization procedure (1:1) to IA triamcinolone hexacetonide injections of active joints or no joint injections. Core outcome variables for JIA were collected at baseline, weeks 6, 12, 24, 36 and 48. Participants randomized to IA injections had joints with arthritis injected at baseline and if clinically indicated at follow-up visits with triamcinolone hexacetonide (large joints 0.5-1 mg/kg (max 40mg), medium joints 0.3-0.5 (max 20mg), small joints, 0.1-0.3 (max 15mg), maximum total dose per visit 3.5mg/kg or < 140mg). Primary endpoint was the proportion of patients in sustained inactive disease, as defined by the JIA-ACR/Wallace 2011 criteria, at both weeks 24 and 36, analysed using logistic regression adjusted for study site.

Results: In total 187 children with non-systemic JIA were randomized; 92 (49%) to the injection group, and 95 (51%) to the no-injection group. Baseline characteristics are summarized in **Table 1**. The primary endpoint, the proportion of patients achieving JIA-ACR inactive disease at weeks 24 to 36, was 35% in the IA steroid injection group compared to 33% in the no-injection group (risk difference (RD) 0.02, 95% CI -0.12-0.15, p 0.80) (**Figure 1**). The mean time to JIA-ACR inactive disease was similar between groups (mean difference -4.5 days, 95% CI -37.4-28.5). JIA-ACR30 response rates were significantly higher in the IA steroid injection group when compared to the no-injection group with a risk difference of 12% (95% CI 0.01-0.24, p=0.03) at week 6, 16% at week 12 (95% CI 0.06-0.26, p< 0.01), 9% (95% CI 0.01-0.17, p=0.03) at week

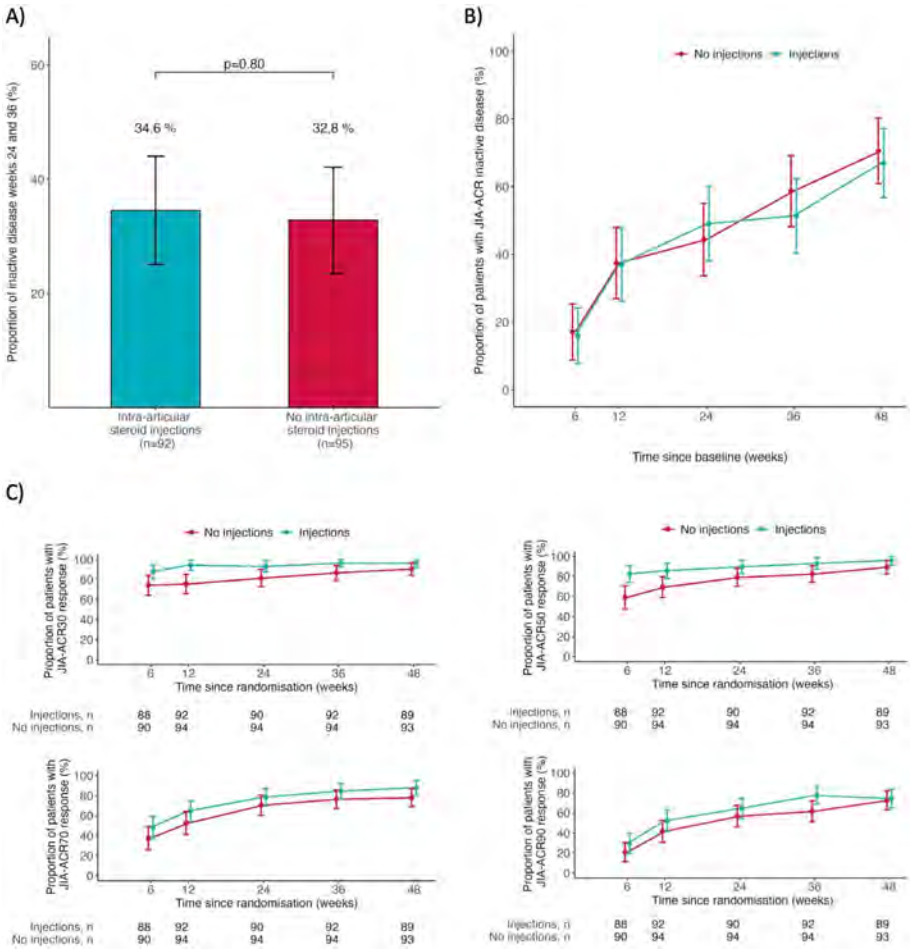


Figure 1. Efficacy of intra-articular triamcinolone hexacetonide injections in juvenile idiopathic arthritis (JIA) patients starting tumor necrosis factor inhibitor (TNFi) therapy. A) Primary endpoint: Bar chart of the proportion of patients in sustained JIA-ACR/Wallace inactive disease at both weeks 24 and 36 for patients receiving intra-articular steroid injections versus no injections (n=187). Estimates (95% CI) from logistic regression model adjusted for study center. B) JIA-ACR inactive disease response rates with estimates (95% CIs) from logistic mixed model including weeks 6, 12, 24, 36 and 48 by treatment group (n=163). C) JIA-ACR30, 50, 70, and 90 response rates with estimates (95% CIs) from logistic mixed model including weeks 6, 12, 24, 36 and 48 by treatment group (n=163).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

24, and 6% (95% CI 0.00-0.13, p=0.04) at week 36. At week 48, JIA-ACR30 response rates were similar (RD 0.03, 95% CI -0.01-0.08, p=0.08). (**Figure 1**). JIA-ACR 70/90 and JIA-ACR core set variables showed no between-group differences at any time point. AEs/SAEs occurred in 67%/7% in the injection group, and in 75%/8% in the no-injection group. Subcutaneous atrophy occurred in 8 of 288 steroid injected joints (3%).

Conclusion: IA triamcinolone hexacetonide injections did not increase the proportion of JIA patients with sustained inactive disease up to 48 weeks after starting TNFi therapy. These findings show that added intra-articular steroid injections is redundant in children with JIA starting TNFi therapy.

Disclosure: P. Boyesen: None; **A. Aga**: None; **V. Lilleby**: None; **M. Pesonen**: None; **M. Rygg**: None; **E. Nordal**: None; **B. Barstad**: None; **K. Tylleskär**: None; **H. Sanner**: None; **S. Hetlevik**: None; **N. Sande**: None; **I. Olsen**: None; **S. Lillegraven**: None; **E. Haavardsholm**: None; **A. Ramanan**: None; **O. Molberg**: None; **B. Flatø**: None.

Abstract Number: 0421

Inflammatory Orbital Diseases: Pediatric Case Series From a Tertiary Care Center

Rasha Elrefai[1], Katherine Williams[2] and Hannah Bradfield[3], [1]Baylor College of Medicine, Houston, TX, [2]Texas Children's Hospital, Houston, TX, [3]Baylor College of Medicine/Texas Children's Hospital, Houston, TX

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Orbital inflammatory diseases in the pediatric population present diagnostic and therapeutic challenges due to variable clinical manifestations, limited prospective data, and lack of standardized treatment protocols. This case series describes clinical features and outcomes in children with orbital inflammatory disease, with particular attention to recurrence, therapeutic approaches, and visual prognosis.

Methods: We retrospectively reviewed the medical records of 12 pediatric cases (ages 3–18 years; all female) with orbital inflammatory disease seen at Texas Children's Hospital between October 2015 and June 2024. Data collected includes clinical presentation, laterality, lacrimal gland and optic nerve involvement, treatment regimens, recurrence, and outcomes. All patients underwent biopsy by an oculoplastic surgeon with histopathology reviewed with an ocular pathologist.

Results: The most common presenting symptoms were eyelid swelling (75%), proptosis (50%), ptosis (42%), and blurry vision (33%) (Table 1). The presenting symptoms were bilateral in 5 patients. Lacrimal gland involvement was common (75%), particularly in patients with ANCA vasculitis or IgG4-related disease. Optic nerve involvement was noted in 2 cases.

Treatment regimens varied by diagnosis and response. Most ANCA-associated cases were managed with methotrexate and glucocorticoids, with escalation to rituximab, surgery, or additional immunosuppressant. Among these, 3 of 4 patients experienced disease recurrence, and one had progressive vision loss requiring a change in therapy. Patients with IgG4-related disease were primarily managed with rituximab or mycophenolate, with favorable outcomes and no recurrences reported (Figure 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table (1): Demographics and clinical characteristics of patients

Case	Diagnosis	Age (years)/ Gender	Follow Up in months	Presenting Symptoms	Laterality	Lacrimal gland involvement	Optic nerve involvement	Treatment	Recurrence	Outcome
1	ANCA vasculitis	15/ Female	39	Eyelid swelling Ptosis Blurry vision Diplopia	Unilateral	Yes	Yes	Methotrexate and steroids (failed) Surgery Rituximab Mycophenolate mofetil	Yes	Decreased vision in left eye Mycophenolate mofetil
2	IgG4	3/ Female	116	Eyelid swelling Proptosis	Unilateral	Yes	No	Rituximab	No	Stable disease Off treatment
3	IgG4	11/ Female	97	Eyelid swelling	Bilateral	Yes	No	Mycophenolate mofetil	No	Stable disease Off treatment
4	ANCA vasculitis	12/ Female	10	Eyelid swelling Ptosis	Unilateral	Yes	No	Methotrexate (failed)	Yes	Worsening eye swelling Plan to switch to rituximab
5	NSOI*	8/ Female	13	Eye pain Conjunctival injection Ptosis Proptosis Blurry vision	Unilateral	No	No	Mycophenolate mofetil (failed) Rituximab	Yes	Worsening eye swelling Plan to switch to infliximab
6	IgG4	14/ Female	17	Proptosis	Bilateral	Yes	No	Rituximab and steroids	No	Improved proptosis Rituximab (off steroid)
7	ANCA vasculitis	11/ Female	75	Eyelid swelling Proptosis Ptosis	Bilateral	Yes	No	Methotrexate and steroids (failed) Surgery Rituximab Hydroxy - chloroquine Azathioprine	Yes	Stable disease Azathioprine
8	ANCA vasculitis	7/ Female	17	Eyelid swelling	Bilateral	No	No	Rituximab	No	Resolved swelling Rituximab for extra-ocular vasculitis
9	NSOI	13/ Female	6	Eyelid swelling Pain Conjunctival injection Blurry vision	Bilateral	No	Yes	Steroids	No	No improvement in eyelid swelling or pain Plan to start a steroid sparing agent
10	NSOI	12/ Female	10	Pain Proptosis Ptosis	Unilateral	Yes	No	Methotrexate and steroids	No	No improvement in proptosis
11	Right Dacryo-adenitis	18/ Female	11	Eye swelling Redness	Unilateral	Yes	No	Mycophenolate mofetil	No	Improved eye swelling and pain Mycophenolate mofetil
12	NSOI	12/ Female	21	Eye swelling Pain Proptosis Blurry vision	Unilateral	Yes	No	Methotrexate and steroid (failed) Rituximab	Yes	Improved lacrimal gland swelling and resolution of intraocular muscle inflammation Off treatment

*NSOI: Nonspecific orbital inflammation

Nonspecific orbital inflammation (NSOI) cases demonstrated a heterogeneous response. Three of 4 patients required escalation beyond methotrexate and glucocorticoids, with rituximab leading to partial improvement in 2.

Overall, recurrence occurred in 42% of cases predominantly in ANCA and NSOI diagnoses. Patients with IgG4-related disease did not require escalation of therapy.

Conclusion: Pediatric orbital inflammatory diseases exhibit diverse clinical presentations and outcomes. ANCA-associated orbital disease demonstrates a higher risk of recurrence and treatment escalation compared to IgG4-related disease. Of note, ANCA-associated vasculitis in pediatric patients did not manifest the bony sinonasal obliteration observed in adult patients. Lacrimal gland involvement is frequent; optic nerve compromise is rare. Rituximab appears effective across etiologies, particularly in refractory cases. This case series highlights the rarity of these diseases in children, importance of early recognition, and close longitudinal follow-up in managing these complex disorders.

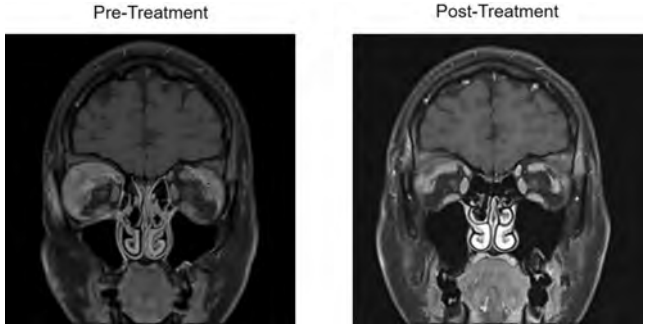


Figure 1. MRI Brain and Orbits Coronal T1 FS images showing bilateral inflammatory orbital masses pre- and post-treatment with rituximab and glucocorticoids in a patient with IgG4-related ocular disease.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Elrefai: None; **K. Williams**: None; **H. Bradfield**: None.

Abstract Number: 0422

Clinical Outcomes of Ultrasound Guidance for Corticosteroid Injections of the Ankle and Midfoot Joints and Tendon Sheaths in Children with Juvenile Idiopathic Arthritis

Rina Ferguson[1], Xing Wang[2], Erin Balay-Dustrude[3], Ramesh Iyer[3], Natalie Rosenwasser[1], Susan Shenoi[4] and Yongdong (Dan) Zhao[5], [1]Seattle Children's Hospital, Seattle, WA, [2]Seattle Children's Hospital, Seattle, [3]University of Washington, Seattle, WA, [4]Seattle Children's Hospital and Research Center, Mercer Island, WA, [5]Seattle Children's Research Institute, Redmond, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1: Clinical characteristics of the study population by injections

		Ultrasound-guided (n = 64)	Non-ultrasound-guided (n = 77)	p-value
Number of distinct patients		37	54	
Sex	Female	39 (61)	51 (66)	0.80
	Male	24 (38)	25 (33)	
ILAR JIA category	Oligoarticular	35 (55)	18 (23)	<0.001
	Extended oligoarticular	14 (22)	22 (29)	
	Polyarticular	8 (13)	32 (42)	
	Enthesitis-related	2 (3)	5 (7)	
	Psoriatic	2 (3)	0 (0)	
	Undifferentiated	0 (0)	0 (0)	
	Systemic	3 (5)	0 (0)	
Age at diagnosis of JIA in years (median [IQR])		3.6 [2.0, 6.2]	5.1 [2.2, 8.7]	0.13
Symptom onset prior to diagnosis in months (median [IQR])		3 [2, 8]	3 [2, 7]	0.67
Anti-nuclear antibody (ANA)	Positive	43 (67)	43 (56)	0.23
	Negative	18 (28)	32 (42)	
HLA-B27	Positive	4 (6)	15 (20)	0.02
	Equivocal	3 (5)	0 (0)	
	Negative	44 (69)	43 (56)	
Rheumatoid factor (RF)	Positive	3 (5)	4 (5)	0.17
	Negative	59 (92)	64 (83)	
Cyclic citrullinated peptide (CCP) antibody	Positive	1 (2)	6 (8)	0.02
	Negative	58 (91)	55 (71)	
Co-existing conditions	IBD	2 (3)	2 (3)	1.00
	Psoriasis	1 (2)	0 (0)	0.45
	Celiac disease	3 (5)	0 (0)	0.09
	Hypothyroidism	6 (9)	0 (0)	<0.01
	Immune dysregulation	4 (6)	1 (1)	0.18
	Type I diabetes mellitus	1 (2)	1 (1.3)	1.00

All values are represented as number (%) unless otherwise specified. Some patients had unknown status for ANA, HLA-B27, RF, and/or CCP antibody. ILAR = International League of Associations for Rheumatology, IBD = inflammatory bowel disease (that was diagnosed either before or after JIA was diagnosed); IQR = interquartile range.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Characteristics of injections that were performed

		Ultrasound-guided (n = 64)	Non-ultrasound-guided (n = 77)	p-value
Ankle or midfoot compartment that was injected	Ankle joint*	47 (73)	77 (100)	<0.001
	Midfoot joint	6 (9)	0 (0)	
	Medial (flexor) tendon	8 (13)	0 (0)	
	Lateral (evertor) tendon	2 (3)	0 (0)	
	Anterior (extensor) tendon	1 (2)	0 (0)	
	Posterior tendon	0 (0)	0 (0)	
*Ankle joint that was injected	Subtalar	19 (40)	4 (5)	<0.001
	Tibiotalar	28 (60)	73 (95)	
Injected medication	Triamcinolone	51 (81)	21 (28)	<0.001
	Triamcinolone hexacetonide	1 (2)	55 (72)	
	Methylprednisolone acetate	11 (18)	0 (0)	

All values are represented as number (%).

Background/Purpose: Intra-articular corticosteroid injections (IACI) are used to treat active ankle or midfoot inflammation in juvenile idiopathic arthritis (JIA). Ultrasound (US) can help identify the specific joint or periarticular tendon that is inflamed and facilitate precise delivery of the medication. This study compared short-term clinical efficacy between US-guided and non-US-guided injections performed by rheumatologists.

Methods: This retrospective case-control study compared clinical outcomes between US-guided and non-US-guided IACI of the ankle and midfoot joint or tendon sheath in patients with JIA at a single quaternary center. We included patients who received an injection between January 1, 2009 and January 1, 2024, without a systemic medication change 28 days before or after the injection, and with at least 1 clinic follow-up visit. Fisher's exact test was used to compare proportion of arthritis or tenosynovitis resolution at the immediate post-injection clinic visit (within 6 months). Resolution was defined as absence of swelling, warmth, and/or decreased range of motion thought to be due to active inflammation on a rheumatologist's documented physical exam. Mann–Whitney U test was applied to analyze the change in physician global assessment (PGA).

Results: 64 US-guided and 77 non-US-guided IACI, from 37 and 54 patients respectively, were included. Polyarticular JIA patients were less likely to have US-guided IACI (**Table 1**). Non-US-guided IACI were more likely to have been done in patients with a positive cyclic citrullinated peptide (CCP) antibody or positive HLA-B27 antigen. No tendon sheaths were injected in the non-US-guided group (**Table 2**). In the US-guided group compared to the non-US-guided group, subtalar joints were more likely to be injected, and triamcinolone was more likely to be used than triamcinolone hexacetonide

Table 3: Clinical outcomes observed at first follow up visit within 6 months of injection

	Ultrasound-guided (n = 64)	Non-ultrasound-guided (n = 77)	p-value
Days between injection and clinic visit	50 [37, 65]	44 [37, 61]	0.14
Inflammation resolved in injected compartment (%)	50 (78)	51 (67)	0.19
PGA before injection	30 [20, 50]	20 [20, 30]	0.01
PGA after injection	8 [0, 30]	5 [0, 10]	0.35
Change in PGA after injection	-20 [-30, -10]	-20 [-30, -10]	0.65

All values are represented as median [IQR] unless otherwise specified. IQR = interquartile range; PGA = physician global assessment (range 0 – 100).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(**Table 2**). **Table 3** demonstrates that arthritis and tenosynovitis clinically resolved at the follow up visit in 78% of US-guided and 67% of non-US-guided IACI, which was not statistically significant (p = 0.19). Evaluation of change in PGA after injection demonstrated that both groups had an average decrease of 20/100 (p = 0.65).

Conclusion: Our study found no significant difference in post-injection remission between US-guided and non-US-guided IACI into the ankle and midfoot from a single center over a 15-year span. The results of this study support our current institutional guidelines which do not explicitly recommend diagnostic and procedural US during IACI for all patients with ankle and midfoot inflammation. A multicenter trial with randomization will be preferred to validate our findings.

Disclosure: R. Ferguson: None; **X. Wang**: None; **E. Balay-Dustrude**: None; **R. Iyer**: None; **N. Rosenwasser**: None; **S. Shenoi**: AbbVie/Abbott, 2, Pfizer, 2, sobi, 2; **Y. Zhao**: american board of pediatrics, 4, Bristol-Myers Squibb(BMS), 5, UpToDate, 9.

Abstract Number: 0423

Macrophage activation syndrome-associated proteins and enhanced interferon gamma responsiveness characterize the plasma proteome of patients with Multisystem Inflammatory Syndrome in Children (MIS-C) in a pre-treatment replication single center cohort

Sarah McCuaig[1], Cara Toland[2], Katharine Konvinse[3], Emily Yang[3], Paul Utz[4], Laura Vella[1], Audrey R. Odom John[1], Hamid Bassiri[1] and Edward Behrens[5], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, [3]Stanford University School of Medicine, Palo Alto, CA, [4]Stanford University, Stanford, CA, [5]CHOP, West Chester, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Multisystem inflammatory syndrome in children (MIS-C) is a rare hyperinflammatory syndrome that follows SARS-CoV-2 infection. Prior plasma proteomic analysis from a 2020 cohort of MIS-C patients at our center revealed a profile characterized by macrophage-activation syndrome (MAS)-associated proteins, dysregulated interferon gamma responses and thrombotic microangiopathy. However, a limitation of that study, as well as most others at the time, was that samples were often acquired post-treatment. In this study, we interrogate the plasma proteome in untreated MIS-C patients versus pediatric patients with other viral syndromes in an independent cohort to identify signatures that uniquely define MIS-C unconfounded by treatment effects.

Methods: Plasma samples were collected from patients presenting to the Children's Hospital of Philadelphia Emergency Department with fever upon their first blood draw and prior to any therapies. Samples were subsequently annotated based on final hospital diagnosis of MIS-C (N=12) or viral syndrome (N=30) as adjudicated by an expert panel. Analysis of 5400 plasma proteins was performed using the O-link Explore HT platform. Plasma auto-antibody analysis was performed using a customized Luminex auto-antibody array. Differential protein expression and pathway analysis were performed in R.

Results: Differential protein expression analysis confirmed that the MIS-C plasma proteome is distinct from that of patients with viral syndromes (Figure 1A) and pathway analysis revealed up-regulation of cytokine signaling pathways (Figure 1B).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

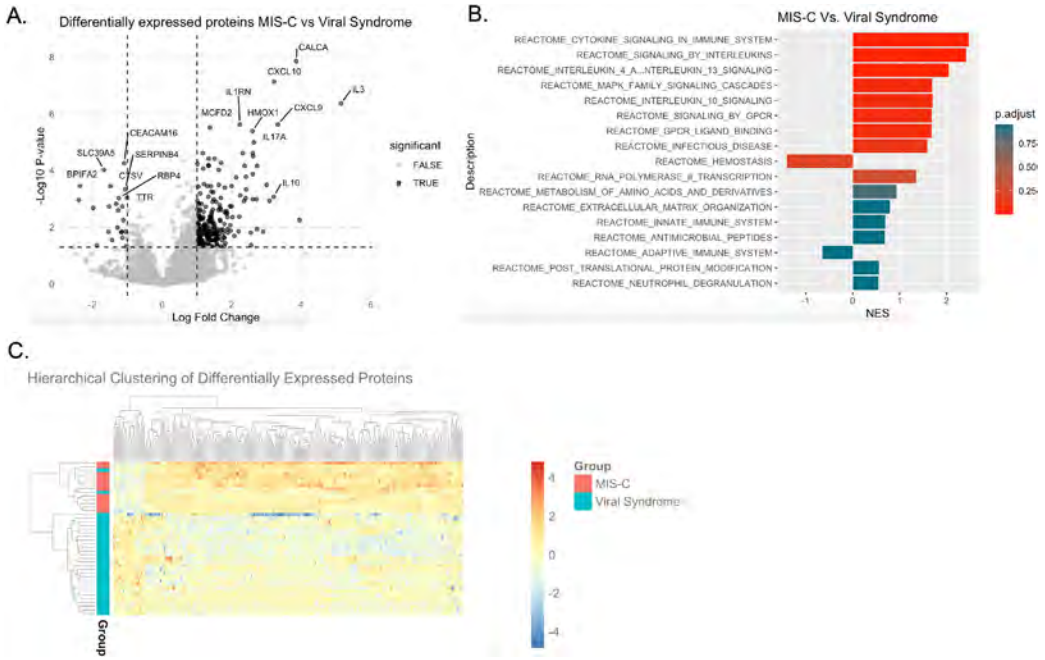


Figure 1 – The plasma proteome of MIS-C is distinct from other viral syndromes. (A) Differential protein expression analysis comparing plasma from patients with MIS-C (N=12) and viral syndromes (N=30). Differentially expressed proteins were considered significant when absolute log2 fold change was greater than 1 and Benjamini-Hochberg adjusted p-value less than 0.05. (B) Reactome pathway analysis of significantly differentially expressed proteins. (C) Hierarchical clustering of significantly differentially expressed proteins.

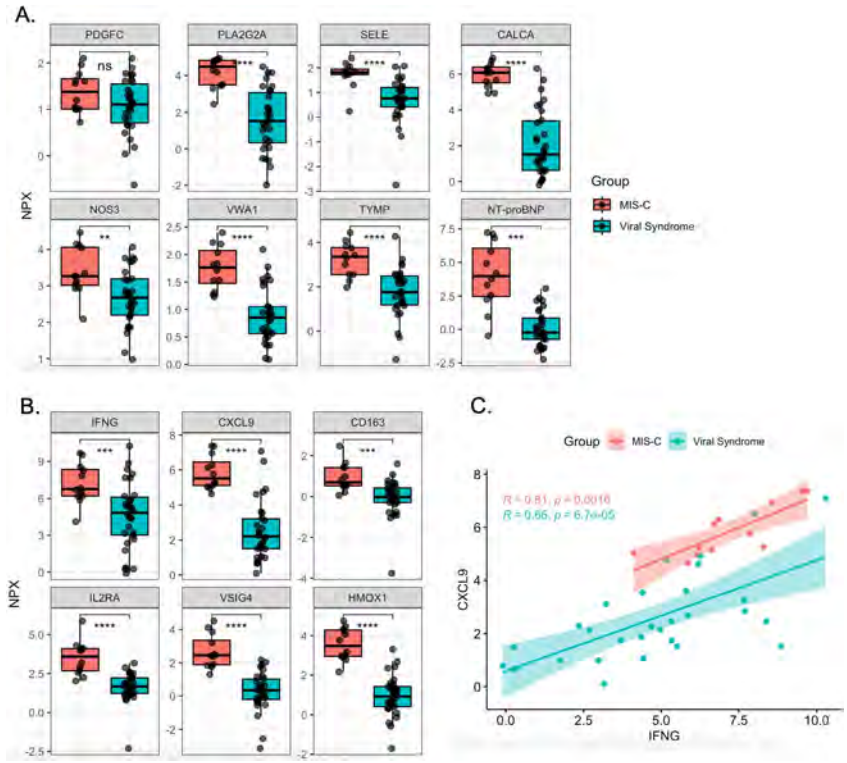


Figure 2 – sC5b9 and macrophage activation syndrome (MAS)-associated plasma protein expression in MIS-C patients compared to patients with other viral syndromes. (A) Box and whisker plots of sC5b9-related proteins and NT-proBNP comparing MIS-C to other viral syndromes. p-values computed using Welsh's T-test. Dots are individual patient normalized protein expression (NPX) values. (B) Box and whisker plots of MAS-associated proteins comparing MIS-C to other viral syndromes. p-values computed using Welsh's T-test. Dots are individual patient NPX values. (C) Pearson correlation analysis between IFNg and CXCL9. Dots are individual patients colored by disease state. Colored areas represent 95% confidence intervals. ****p<0.0001, ***p<0.001, **p<0.01.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

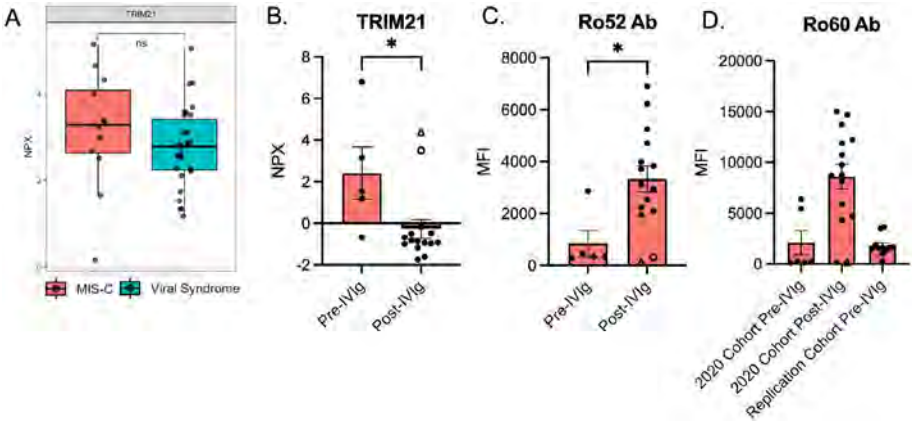


Figure 3 – TRIM21/Ro52 expression and anti-Ro52, anti-Ro60 autoantibody levels in MIS-C patients stratified by IVIg treatment status. (A) Box and whisker plots of TRIM21 comparing MIS-C to other viral syndromes. P-value computed using Welsh's t-test. Dots are individual patient NPX values. (B) TRIM21 expression in MIS-C patients in 2020 cohort stratified by IVIg treatment status (untreated [pre-IVIg], treated [post-IVIg]). P-value computed using Welsh's t-test. Dots are individual patient normalized protein expression (NPX) values. (C) Anti-Ro52 Ab MFI in MIS-C patients in 2020 cohort stratified by IVIg treatment status. Patients denoted by open triangles and open circles are the same patient in the TRIM21 and Ro52 Ab plot. (D) Anti-Ro60 Ab MFI in MIS-C patients in 2020 cohort stratified by IVIg treatment status (untreated [pre-IVIg], treated [post-IVIg]) and in replication cohort (all patients untreated [pre-IVIg]). *p<0.05.

Unsupervised hierarchical clustering of differentially expressed proteins classified MIS-C from viral syndrome (Figure 1C). Consistent with findings in the 2020 cohort, sC5b9-associated proteins and MAS-associated proteins are more highly expressed and there is a disproportionally higher CXCL9 response to IFNg in MIS-C compared to viral infection (Figure 2A, B, C). Patients with MIS-C had lower expression of the IFNg suppressive protein TRIM21 in the 2020 cohort, however this was not reproduced in the current cohort (Figure 3A). Closer inspection revealed that only patients who received IVIg treatment prior to sampling had low TRIM21 expression in the 2020 cohort (Figure 3B). TRIM21 (also known as Ro52/SSA) is the antigen for anti-Ro52 autoantibodies. Plasma autoantibody profiling revealed anti-Ro52 antibodies in patients who had received IVIg (Figure 3C). Related anti-Ro60/SSA antibodies were low in samples collected prior to IVIg treatment and high in those sampled after IVIg (Figure 3D).

Conclusion: We have validated several unique features of the plasma proteome of MIS-C patients first identified in 2020. MIS-C plasma show high sC5b9 and MAS-associated protein expression and enhanced IFNg responsivity. Discrepant TRIM21 expression in these two cohorts is due to the presence of anti-Ro52 autoantibodies in IVIg-treated patients. These data support the use of plasma cytokine profiling and possibly a CXCL9/IFNg ratio to rapidly identify MIS-C patients. Furthermore, they highlight the presence of autoantibodies in IVIg and the need to interpret plasma proteomic data with caution in patients with prior IVIg exposure.

Disclosure: S. McCuaig: None; **C. Toland**: None; **K. Konvinse**: None; **E. Yang**: None; **P. Utz**: None; **L. Vella**: None; **A. Odom John**: None; **H. Bassiri**: Johnson & Johnson Innovative Medicine, 3; **E. Behrens**: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0424

Juvenile Idiopathic Arthritis Mimics: A Case Series on Progressive Pseudo-Rheumatoid Dysplasia and CACP Syndrome in Pediatric Patients from a Tertiary Center in South India

Sreelekha Kambhampati[1], keerthi vardhan yerram[2], Kavitha Meesala[1], Phani Kumar Devarasetti[2] and Liza rajasekhar[3], [1]Nizams institute of medical sciences, hyderabad, India, [2]Nizams institute of medical sciences, hyderabad, Andhra Pradesh, India, [3]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is the most prevalent chronic arthritis in children, but its diagnosis is often challenging due to overlapping symptoms with other conditions that mimic it.Among these mimics, Progressive Pseudo-Rheumatoid Dysplasia (PRD) and Camptodactyly - Arthropathy-Coxa Vara-Pericarditis (CACP) syndrome are particularly noteworthy due to their potential to cause significant diagnostic confusion and subsequent mismanagement.

Methods: This study aims to elucidate the clinical and genetic characteristics of pediatric patients diagnosed with PRD and CACP syndrome, highlighting the critical need for accurate differential diagnosis to avoid misdiagnosis and improve management strategies.–A retrospective case series was conducted at NIMS Hospital, Hyderabad,reviewing pediatric patients who presented to the outpatient department over a two-year period with symptoms initially suggestive of JIA.Seven patients with clinical presentations, including multiple joint pains and back pain, were evaluated. Comprehensive clinical assessments, imaging studies, and Whole Exome Sequencing (WES) were utilized to establish definitive diagnoses.

Results: RESULTS - Out of the seven patients evaluated, five were diagnosed with PPD and two with CACP syndrome.The age of onset ranged from 1 to 10 years, with a mean age of 4.7 years.3 rd degree consanguinity was found in all patients, and 2 nd brothers were of same family, 2 females and 3 male children in PPD and 1 male and 1 female child in CACP cluster Clinically, all patients presented with chronic joint pain; additional features included back pain, bilateral knee joint swelling, and, in CACP patients, characteristic

camptodactyly, joint contractures.Inflammatory markers were normal Genetic analysis done for 5 patients , it identified mutations in the CCN6 gene in three PRD patients and in the PRG4 gene in the two CACP patients.

Conclusion: PPD and CACP syndrome are critical differential diagnoses in pediatric patients presenting with JIA-like symptoms, especially in cases that deviate from typical JIA presentations or are unresponsive to standard treatments. These disorders were inherited in

WHOLE EXOME SEQUENCING

PRG	EXON 7	c. 983 dup, c.619 del.	Homozygous	AR
CCN6	EXON 4	c. 762dup	Homozygous	AR

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

PPD SYNDROME- ENLARGED EPIPHYSES, WIDENED METAPHYSES, PLATYSPONDYLY WITH ANTERIOR BEAKING OF VERTEBRAE

CACP – CLINICAL AND RADIOLOGY IMAGES - CAMPTODACTYLY , KNEE AND WRIST SWELLING, KNEE EFFUSION , OSTEOPENIA, COXAVARA

AR pattern with non-inflammatory arthropathy and deformities with early age of onset and atypical radiological features.This case series underscores the importance of a thorough diagnostic approach that includes detailed clinical assessment, imaging, and genetic testing. In all of these cases the correct diagnosis was made due to careful, longitudinal clinical phenotyping and a close working relationship between rheumatology, radiology and clinical genetics; highlighting the importance of the multidisciplinary team in managing complex patients

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Kambhampati: None; **k. yerram**: None; **K. Meesala**: None; **P. Devarasetti**: None; **L. rajasekhar**: None.

Abstract Number: 0425

High Density Lipoprotein Dysfunction in Juvenile Idiopathic Arthritis as Compared to Children without Rheumatologic Disease

Tahnee Spoden[1], Samira Nazzar Romero[2], Deborah McCurdy[3], Alice Hoftman[4], Sangmee Bae[5], Jennifer Wang[4], Ani Shahbazian[4] and Christina Charles-Schoeman[6], [1]UCLA, Los Angeles, CA, [2]Nemours Children's Health, Orlando, [3]UCLA Medical Center, Los Angeles, CA, [4]UCLA, Los Angeles, [5]UCLA Rheumatology, Los Angeles, CA, [6]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular disease remains the leading cause of mortality in patients with Rheumatoid Arthritis (RA). Normally, high density lipoprotein (HDL) acts in a cardioprotective capacity through various anti-inflammatory and anti-oxidative functions. Research has shown that the antiinflammatory capacity of HDL is impaired in states of chronic inflammation, such as RA. Abnormal lipid profiles have been described in patients with JIA, however, qualitative studies on HDL in this population are lacking. We aim to investigate if the antiinflammatory function of HDL is impaired in JIA patients as compared to healthy controls. We also aim to investigate if HDL dysfunction correlates with JIA subtype and disease activity.

Baseline Characteristics (cases, n= 30; controls, n= 15)

		cases		controls		
		median (IQR)	mean (SD)	median (IQR)	mean (SD)	p-value
Age		14 (12-15.5)	13.6 (2.4)	12 (10.5-16.0)	13.0 (3.0)	0.507
		N	percentage	N	percentage	
Sex	female	23	77%	10	63%	0.032*
	male	7	23%	5	33%	
Race	latino	13	43%	5	33%	
	caucasian	10	33%	6	40%	
	mixed	4	13%	2	13%	0.96
	african american	1	3%	1	7%	
	Other	2	7%	1	7%	
Medications	Taking vitamin D	7	23%	5	33%	
	Current or recent steroids	7	23%	1	7%	0.245
	Contraceptives	3	10%	3	20%	
Cardiovascular risk factors	Family history of CVD	17	57%	6	40%	0.282
	Family history of Early CVD	5	17%	1	7%	0.352
	Overweight/Obesity	14	47%	7	47%	1
	Systolic BP > 90th percentile	3	10%	1	7%	0.711
	Diastolic BL > 90th percentile	6	20%	2	13%	0.497
	Physical inactivity	6	20%	3	20%	1
	Vaping+	1+	5% +	0+	0%+	0.516
	Alcohol+	3+	17%+	2+	29%+	0.504
	Second-hand smoke exposure	1	3%	3	20%	0.064
Physical activity	Recommended by CDC**	11	37%	11	73%	0.02*
	Moderate	13	43%	7	47%	0.832
	Vigorous	14	47%	10	67%	0.205
		median (IQR)	mean (SD)	median (IQR)	mean (SD)	p-value
Lipid Profile	HDL (mg/dl)	55.5 (44.9-69.2)	60.2 (23.9)	61.6 (78.3-42.3)	62.7 (23.6)	0.744
	Total Cholesterol (mg/dl)	235.6 (211-262.3)	235.3 (32.1)	240.5 (269.9-252.7)	236.7 (40.4)	0.906
	ApoA1 (ug/mL)	125 (111-153)	132 (31)	119 (116-132)	118 (25)	0.526
HETE/HODE (ng/mL)	13 HODE	10.0 (5.9-21.3)	15.8 (14.4)	5.5 (4.6-9.4)	8.6 (4.6)	0.0314*
	9HODE	12.0 (4.8-24.4)	18.8 (20.9)	4.7 (4.2-11.7)	9.8 (10.5)	0.0617
	15HETE	1.3 (0.7-2.6)	1.9 (1.9)	0.5 (0.2-1.1)	1.1 (0.8)	0.0134*
	14S-HDHA	3.9 (1.3-8.6)	5.4 (4.7)	0.9 (9.5-2.9)	2.4 (2.9)	0.0111*
	11HETE	2.8 (1.4-8.6)	6.3 (7.6)	1.2 (0.4-2.9)	2.7 (3.8)	0.0382*
	12HETE	31.8 (15.2-118.3)	67.9 (63.6)	20.2 (11.6-35.0)	26.4 (23.1)	0.0026*
	5HETE	22.7 (0.3-146.)	67.6 (84.0)	0.2 (0.2-22.6)	37.2 (77.9)	0.2381

+ Percentages are based on subjects who were 13 and above and answered the confidential questions about substance use which were 19 cases and 7 controls.** CDC recommended physical activity is 60 min of moderate-vigorous activity daily. * Statistically significant differences by chi-squared analysis designated by p value <0.05

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Characteristics of JIA Patients				
			N	percentage
JIA Subtype	Poly-JIA		22	73%
	Other		8	27%
		ERA	5	73%
		Psoriatic JIA	3	38%
Immunomodulation	cDMARD		18	60%
	Biologic		20	67%
	anti-TNF		12	40%
	anti-IL6		6	20%
	JAK inhibitor		2	7%
	Biologic + cDMARD		15	50%
	None		4	13%
ANA	positive		17	47%
	negative		13	53%
Anti-CCP	positive		6	33%
	negative		21	60%
	not available		3	7%
RF	positive		8	40%
	negative		22	60%
HLA B27	positive		4	11%
	negative		20	68%
	not available		6	21%
JADAS10 (disease activity score)	Inactive		3	4%
	Minimal		2	4%
	Moderate		9	41%
	High		16	52%
Duraiton of disease activity (months)	<13		5	17%
	13-36		13	43%
	>36		11	37%
	Poly-JIA	Other	p value	
ESR	17.6 (18.9)	5.6 (5.8)		**0.013***
CHAQ disability index (standard)	0.73 (0.62)	0.70 (0.78)		0.93
JADAS10 (disease activity score)	14.5 (8.1)	7.8 (4.9)		**0.012***
Active Joint Count	4.1 (3.9)	1.1 (1)		0.0036*

Methods: We performed a cross-sectional study on 30 patients with JIA and 15 controls between 9 and 17 years of age. Disease activity was assessed based on the juvenile arthritis disease activity score (JADAS-10) and the childhood health assessment questionnaire (CHAQ). HDL's antiinflammatory function (HII) was measured using a cell-free assay assessing the ability of the patient's HDL to inhibit oxidation of low-density lipoprotein. Circulating oxidized biproducts of arachidonic and linoleic acid were measured by liquid chromatography-electrospray ionization, tandem mass spectroscopy. HDL-associated apoprotein A-1 (ApoA1) levels were measured by sandwich ELISA. Levels and activity of HDL associated antioxidant enzymes PON-1 (paraoxonase, arylesterase and lactonase) were quantified using spectrophotometry.

Results: Total HDL and total cholesterol were not significantly different between cases and controls. Joint count in the 22 patients with poly-JIA was higher than the 8 patients with other subtypes of JIA (63% ERA, 38% psoriatic JIA) [mean (s.d.)] (4.5 (4.3), 1.1 (1), p=0.002). ESR was significantly higher in the poly JIA group (17 (19), 6 (6), p=0.022). The HII was

	Poly JIA	Other JIA	Control	P
HII	0.422 (0.181)	0.581 (0.207)	0.38 (0.185)	**P vs O: 0.0447** P vs C: 0.5062 **O vs C: 0.0179**
Paraoxonase (nmol/ml/min)	1170 (696)	2993 (2947)	1236 (659)	**P vs O: 0.0022** P vs C: 0.8837 **O vs C: 0.0050**
Arylesterase (umol/ml/min)	271 (93)	316 (39)	299 (60)	P vs O: 0.1551 P vs C: 0.2804 O vs C: 0.5997
Lactonase (umol/ml/min)	30 (9)	40 (7)	31 (8)	**P vs O: 0.0069** P vs C: 0.6078 **O vs C: 0.0273**
ApoA1 (ug/mL)	119 (29)	149 (27)	118 (25)	**P vs O: 0.0160** P vs C: 0.8211 **O vs C: 0.0338**
Values are represented in mean (SD); Statistically significant differences based on student's T-test p<0.05				

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

higher JIA subtypes associated with spondyloarthropathy as compared to poly-JIA and controls (p=0.0447, p=0.0179). HDL concentration correlated significantly with the HII (r_s= -0.63, p= 0.0003) in all JIA patients and correlated with disease activity. Several circulating bioactive lipid mediators were significantly higher in JIA patients compared with controls with 9HODE,15HODE and 11HETE showing positive correlation with the HII (r_s = 0.36-0.44, p= 0.05-0.02). Arylesterase and Lactonase activity negatively correlated with joint count (r_s= -0.41, p=0.026; r_s=-0.38, p=0.041) and ESR (r_s=-0.40, p=0.027; r_s=-0.41, p= 0.023) respectively in all JIA patients.

Conclusion: This pilot study demonstrates that chronic inflammation in patients with JIA may contribute to HDL dysfunction, particularly in patients with axial involvement. Larger cohort studies are needed to further characterize patients with axial disease as well as aide in our understanding of how PON-1 changes over time in children with chronic inflammation.

Disclosure: T. Spoden: None; **S. Nazzar Romero**: None; **D. McCurdy**: None; **A. Hoftman**: None; **S. Bae**: None; **J. Wang**: None; **A. Shahbazian**: None; **C. Charles-Schoeman**: AbbVie/Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Immunovant, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2, Sana Biotechnology, 2.

Abstract Number: 0426

Tofacitinib in Juvenile Idiopathic Arthritis: efficacy and safety in a clinical practice setting.

Vicenç Torrente-Segarra[1], Andrea Zacarias[2], Cynthia Rojas[3], Jordi Antón-López[2], Judith Sanchez[4] and Meritxell Salles Lizarzaburu[5], [1]Hospital Comarcal Alt Penedés Garraf, Vilafranca del Penedas, Spain, [2]Pediatric Rheumatology Department, Hospital Sant Joan de Déu, Barcelona (Spain)., Barcelona, Spain, [3]Rheumatology Department, Hospital Comarcal Alt Penedès Garraf, Vilafranca del Penedès (Spain)., Vilafranca del Penedes, Spain, [4]Pediatric Rheumatology Department, Taulí Hospital Universitari-Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Sabadell (Spain)., Sabadell, Spain, [5]Rheumatology Department, Althaia Xarxa Assistencial Universitària Manresa Manresa (Spain)., Manresa, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aims to evaluate the efficacy and safety of tofacitnib, a JAK inhibitor, in a multicentric cohort of patients with juvenile idiopathic arthritis (JIA).

Methods: Patients with JIA attending a pediatric rheumatology clinic who were treated with tofacitnib at some point of their follow-up were retrospectively included. Data collection: at Baseline, sociodemographics, JIA features and subtype and immunology status, JIA disease course of treatments and time on tofacitinib and number of previous therapies, JIA disease status variables and ongoing treatment/discontinuation were collected at 3 and 12 months of follow-up (Wallace criteria); and overall time on tofacitinib (drug survival). Descriptive and comparative statistical analysis comparing baseline and 3- and 12- months variables (JAMOVI (R)) were performed.

Results: N=23 (60% female), mean age 16.5 years (SD 5.02), age at diagnosis 7 years (SD 5.02), mean disease duration 114 months (SD 71.1), age at tofacitinib onset 13.8 years old (SD 4.61). JIA subtypes: RF- poly 26%, ERA 21%, persistent

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. JIA activity status at baseline, 3 and 12 months. *p <0.005 (Baseline vs 3-months) **p<0.005 (Baseline vs 12-months) ^p<0.005 (3-months vs 12-months). *Abbreviations: RF, rheumatoid factor; ANA, anti-nuclear antibodies; CCP, anti-citrulline antibodies; B27, HLA B27 positive; TJC, tender joint count; SJC, swollen joint count;PGA, physician global assessment; ESR, erythrocite sedimentation rate; CPR, C reactive protein*.

	Baseline	3-months	12-months
TJC	3.57	0.85*	0.61**
SJC	2.57	1.15*	0.53**
PGA	4.0	1.9*	0.69**^
JADAS-71	10.1	4*	2.67**
ESR	8.57	6.63*	5.0
CRP	7.43	2.05	3.5

oligo 17%, RF+ polyarthritis 13%, soJIA 13% and psoriatic 4%; 65% ANA positive. Previous failure to biologicals (BT): 48%, 2; 26%, 1; 22%, 3; 4%, 5. Mean time on last therapy: 21.1 months (SD 18.8), 95% innefficacy.

Concomitant therapy: at baseline, 65% DMARD, 43% oral steroids; at 3 months, 58% DMARD, 30% oral steroids; at 12 months, 54% DMARD, 15% oral steroids.

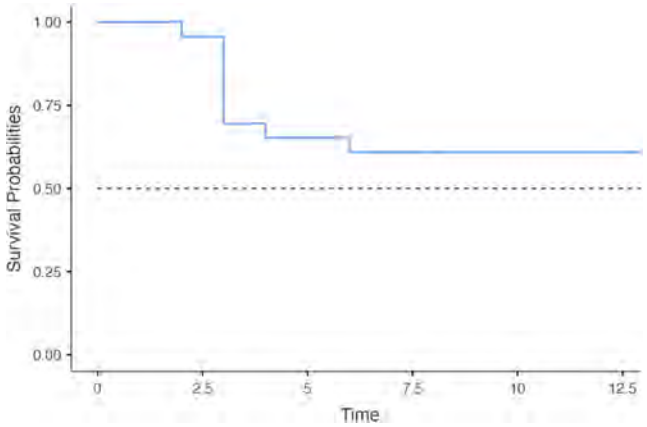
At 12 months, 56% were still receiving tofacitinib, 58% fulfilled inactivity criteria, 58% clinical remission on treatment, 8% clinical remission off treatment.

No adverse event were recorded.

Drug survival (from onset to current date): median of 13 months (range: 2-96).

No differences were found among all variables, except for the significant reduction on oral steroids intake from baseline to 12-months follow-up (p=0.040).

Conclusion: Our results show that very refractory JIA patients who received tofacitinib after biological therapy failure (75% failed to ≥2 biologicals), either combined (DMARD) or in monotherapy, showed clinical statistical significant benefit in all JIA assessments (TJC, SJC, PGA, JADAS-71), both at 3 and 12 months of follow-up. Drug retention was 13 months



1st-year Survival tofacitinib rate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(2-96). Safety profile was very positive with no adverse events recorded, specially with the higher rates of combined therapy (tocilizumab and canakinumab). Both an 11% and 28% of patients were allowed to discharge DMARD and oral steroids through follow-up, respectively. No particular subsets of patients were found to predict tofacitinib response. Further studies with larger cohorts are recommended to confirm our data.

Disclosure: V. Torrente-Segarra: None; **A. Zacarias**: None; **C. Rojas**: None; **J. Antón-López**: None; **J. Sanchez**: None; **M. Salles Lizarzaburu**: None.

Abstract Number: 0427

Maternal Smoking During Pregnancy and Risk of Juvenile Idiopathic Arthritis (JIA): Triangulating Evidence from Polygenic Risk Scores and Meta-Analysis in Scandinavian Birth Cohorts

Vilde Øverlien Dåstøl[1], Kristine Løkås Haftorn[2], Maria Christine Magnus[3], Sigrid Hestetun[4], Siri Eldevik Håberg[5], Lisa Rider[6], Karen H. Costenbader[7], Ida Henriette Caspersen[8], Sjurdur Frodi Olsen[9], Ketil Størdal[10] and Helga Sanner[1], [1]Oslo University Hospital, Oslo, Norway, [2]Oslo University Hospital, Department of Rheumatology, Oslo, Norway, [3]Norwegian Institute of Public Health, Centre for Fertility and Health, Oslo, Norway, [4]Oslo University Hospital, Department of Rheumatology/University of Oslo, Oslo, Norway, [5]Norwegian Institute of Public Health, Centre for Fertility and Health/University of Bergen, Oslo, Norway, [6]National Institute of Environmental Health Sciences/National Institutes of Health, Environmental Autoimmunity Group, Bethesda, MD, [7]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [8]Norwegian Institute of Public Health, Centre for Fertility and Health/Oslo University Hospital, Oslo, Norway, [9]Statens Serum Institut,Biobank, congenital disorders, and vaccines preparedness/Harvard T.H. Chan School of Public Health, Copenhagen, Denmark, [10]Oslo University Hospital, Department of Pediatric and Adolescent Medicine/University of Oslo, Oslo, Norway

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Maternal smoking during pregnancy has been associated with a seemingly lower risk of juvenile idiopathic arthritis (JIA) in the child (1), contrasting with smoking's established role as a risk factor for rheumatoid arthritis (RA) (2). Using large pregnancy and birth cohorts, we investigated the association between in-utero tobacco exposure and JIA and assessed the role of unmeasured confounding using a Mendelian Randomization (MR) framework.

Methods: We used three Scandinavian cohorts:

1) The Norwegian Registry Linkage Cohort (NRC): All births in Norway from 2004-2020 (n >1 million children).

2) The Norwegian Mother, Father, and Child Cohort Study (MoBa): A pregnancy cohort from 1999-2009 (n >110 000 mother-infant pairs).

3) The Danish National Birth Cohort (DNBC): A pregnancy cohort from 1996-2002 (n >90 000 mother-infant pairs).

JIA cases were identified by ≥2 ICD-10 codes (M08/M09) by linking each cohort to national patient registries. Smoking was self-reported during pregnancy, and categorized as "none", "1st trimester only", and "beyond 1st trimester". In MoBa, maternal genotyping data (n=41,887) enabled estimation of the association between maternal polygenic risk scores (PRS) for smoking initiation (3) and JIA in the child based on MR principles.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Results of Analyses of Maternal Smoking Exposure and Child Risk of Developing JIA

Maternal Smoking During Pregnancy	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
NRC[1]	**JIA n= 976, non-JIA n= 782,769**	
None	Reference	Reference
Only 1st trimester	1.69 (1.29-2.23)	1.09 (0.82-1.44)
Beyond 1st trimester	1.71 (1.38-2.12)	1.20 (0.96-1.50)
MoBa[1]	**JIA n= 281, non-JIA n= 86,669**	
None	Reference	Reference
Only 1st trimester	0.86 (0.60-1.23)	0.81 (0.56-1.17)
Beyond 1st trimester	1.01 (0.70-1.47)	0.87 (0.59-1.29)
Polygenic risk score for smoking	N/A	0.97 (0.84-1.13)
DNBC	**JIA n= 221, non-JIA n= 58,813**	
None	Reference	Reference
Only 1st trimester	1.02 (0.60-1.61)	1.01 (0.60-1.60)
Beyond 1st trimester	1.07 (0.75-1.50)	1.04 (0.72-1.48)

[1]There is an overlap of 221 JIA patients in these two cohorts and result should therefore be interpreted with caution

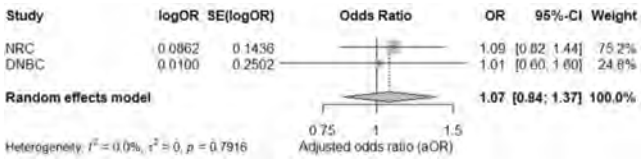


Figure 1. Meta-analysis of NRC and DNBC: Associations between maternal smoking in 1st trimester and JIA (both sexes combined)

Associations were estimated using logistic regression, adjusting for maternal education, parity, inflammatory rheumatic disease (MoBa and DNBC), region of birth (NRC and MoBa), and birth year. In the PRS-analyses, we only adjusted for the first 10 principal components. NRC and DNBC were meta-analyzed to increase precision, here excluding MoBa due to partial overlap with NRC (~220 JIA cases).

Results: 9.5% infants in the NRC, and 25% in both MoBa and DNBC, were exposed to in-utero tobacco exposure. We found no robust evidence that maternal smoking influenced JIA-risk in the child, with meta-analysis yielding an aOR of 1.07 (95% CI 0.84–1.37) for exposure only during the 1st trimester, and 1.15 (95% CI 0.95–1.39) for exposure beyond 1st trimester (**Table 1; Figures 1 and 2**). Maternal PRS for smoking initiation was strongly associated with self-reported smoking during pregnancy in MoBa ($p < 0.001$), supporting its validity as an instrument, but showed no associations with JIA (**Table 1**).

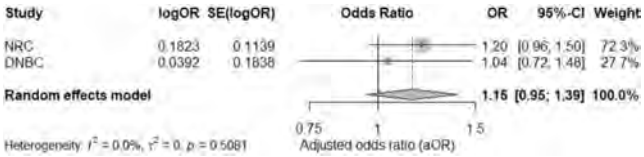


Figure 2. Meta-analysis of NRC and DNBC: Associations between maternal smoking beyond 1st trimester and JIA (both sexes combined)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Across three prospective birth cohorts, using a triangulation approach, we find no evidence of a protective effect of maternal smoking during pregnancy on JIA risk, as previously reported. These findings underscore the importance of prospective designs and multiple approaches when investigating complex, confounding-prone exposures.

References:

1) Clarke SLN, et al. Rheumatology (Oxford). 2022;61(2)
2) Costenbader KH, et al. Am J Med. 2006;119(6)
3) Liu M, et al. Nat Genet. 2019;51

Disclosure: V. Dåstøl: None; **K. Haftorn**: None; **M. Magnus**: None; **S. Hestetun**: None; **S. Håberg**: None; **L. Rider**: None; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **I. Caspersen**: None; **S. Olsen**: None; **K. Størdal**: None; **H. Sanner**: None.

Abstract Number: 0428

The OMERACT Juvenile Idiopathic Arthritis MRI Score for Active and Structural Lesions in the Sacroiliac Joints: Development and Validation in Two Longitudinal Cohorts

Walter P. Maksymowych[1], Michael Francavilla[2], Nele Herregods[3], Robert G. W. Lambert[4], Arthur Meyers[5], Joel Paschke[6], Jennifer Stimec[7], Pamela Weiss[8] and Dax Rumsey[9], [1]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [2]Department of Pediatric Radiology, Children's Hospital Philadelphia, Philadelphia, PA, [3]Department of Pediatric Radiology, Ghent University Hospital, Ghent, Belgium, [4]University of Alberta, Department of Radiology & Diagnostic Imaging, Edmonton, AB, Canada, [5]Department of Radiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [6]CARE Arthritis Limited, Edmonton, AB, Canada, [7]Department of Diagnostic Imaging, SickKids, University of Toronto, Toronto, Canada, [8]Childrens Hospital of Philadelphia, Philadelphia, PA, [9]Department of Pediatrics, University of Alberta, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The OMERACT Juvenile Idiopathic Arthritis MRI (JAMRIS) Working group has defined a spectrum of MRI lesions in the sacroiliac joint (SIJ) in youth with spondyloarthritis and axial disease (axJSpA) that can be included in a scoring method. Previous reports have described the application of Spondyloarthritis Research Consortium of Canada (SPARCC) methodology to quantify MRI SIJ lesions in axJSpA, where assessment of inflammation is limited to bone marrow edema (BME) and lesions are assessed in a limited number of semicoronal slices. We aimed to assess the impact of including all inflammatory lesions and SPARCC methodology versus an all-slice method on the metrology of JAMRIS in two longitudinal cohorts of youth with axJSpA treated with a tumor necrosis factor inhibitor (TNFi).

Methods: The two cohorts recruited youth with axJSpA who had a rheumatologist diagnosis of axJSpA. All subjects underwent MRI as part of a diagnostic evaluation for axial disease. MRI lesions were assessed on semicoronal slices through the SIJ from the most anterior (≥1cm vertical height of cartilaginous portion) to the most posterior (≥1cm visible cartilaginous portion) slice. Structural lesions were assessed first on the T1-weighted scan followed by inflammatory lesions on a fluid-sensitive sequence. Scans were obtained at baseline and 3 months-1 year follow up after initiation of treatment with TNFi and assessed blinded-to timepoint and clinical details by 7 readers (4 pediatric and 1 adult MSK radiologists, 1 adult and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

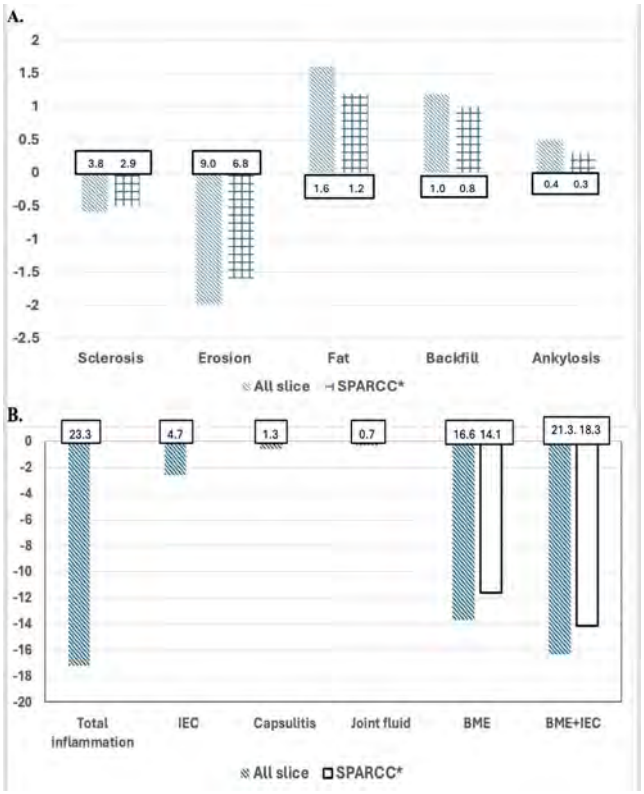


Figure 1. Change from baseline values (in boxes) in A. MRI structural lesion scores (SIJ quadrants for erosion, sclerosis, and fat lesion, SIJ halves for backfill and ankylosis) and B. MRI inflammation scores (SIJ quadrants for BME and inflammation in an erosion cavity (IEC)), after TNFi assessed across all SIJ slices or limited to the slices selected in the SPARCC methods.

1 pediatric rheumatologist) after standardized calibration using a CARE Arthritis online module. MRI lesions were recorded based on standardized lesion definitions derived from ASAS and the JAMRIS group in a standardized eCRF (ASAS MRImagine). Analyses included descriptive statistics, reliability (intraclass correlation coefficient (ICC), smallest detectable difference (SDD) or change (SDC)), and responsiveness (standardized response mean (SRM)).

Table. Reliability of change scores for MRI SIJ inflammatory and structural lesions for all 7 readers, MSK radiologists (n=5), and rheumatologists (n=2). SDC smallest detectable change.

	Overall ICC	MSK Rad overall ICC	Rheum overall ICC	Overall SDC value (% of scoring range)	MSK Rad SDC value (% of scoring range)	Rheum SDC value (% of scoring range)
Sclerosis (all slice)	0.29	0.32	0.11	1.97 (6.8%)	2.50 (8.6%)	3.05 (16.1%)
Sclerosis (SPARCC)	0.30	0.33	0.13	1.59 (6.4%)	2.02 (8.1%)	2.24 (18.7%)
Erosion (all slice)	0.35	0.44	-0.10	3.30 (6.6%)	3.74 (8.1%)	7.44 (24.8%)
Erosion (SPARCC)	0.33	0.39	-0.07	2.65 (7.4%)	3.10 (9.7%)	5.88 (23.5%)
Fat (all slice)	0.53	0.54	0.61	2.77 (3.9%)	3.64 (5.1%)	2.66 (9.5%)
Fat (SPARCC)	0.59	0.58	0.71	1.89 (4.3%)	2.50 (5.7%)	1.93 (7.7%)
Ankylosis (all slice)	0.89	0.96	0.87	0.97 (2.1%)	0.81 (1.7%)	1.27 (5.1%)
Ankylosis (SPARCC)	0.86	0.92	0.72	0.66 (2.5%)	0.63 (2.4%)	1.26 (7%)
Backfill (all slice)	0.510	0.50	0.60	1.82 (5.2%)	2.33 (6.6%)	2.21 (13%)
Backfill (SPARCC)	0.50	0.47	0.63	1.50 (6.2%)	1.95 (8.1%)	1.93 (12.8%)
Total inflammation-change	0.80	0.84	0.71	7.18 (4.3%)	8.10 (4.9%)	12.84 (13.5%)
BME (all slice)	0.85	0.89	0.70	4.70 (4.2%)	4.90 (4.4%)	11.06 (12.1%)
BME (SPARCC)	0.82	0.87	0.67	4.10 (4.5%)	4.37 (5.2%)	9.43 (12.1%)
Inflammation in erosion cavity (IEC)	0.50	0.61	0.10	2.63 (6.7%)	3.16 (8.1%)	3.49 (20.5%)
BME + IEC (all slice)	0.83	0.87	0.71	8.74 (6.2%)	9.53 (6.8%)	17.19 (17.5%)
BME + IEC (SPARCC)	0.80	0.84	0.69	7.65 (7.4%)	8.55 (8.2%)	14.76 (17.2%)
Capsulitis	0.62	0.69	0.44	1.08 (4.3%)	1.28 (5.1%)	1.59 (11.3%)
Joint space fluid	0.17	0.23	0.07	2.21 (6.1%)	2.75 (7.6%)	3.11 (13.5%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

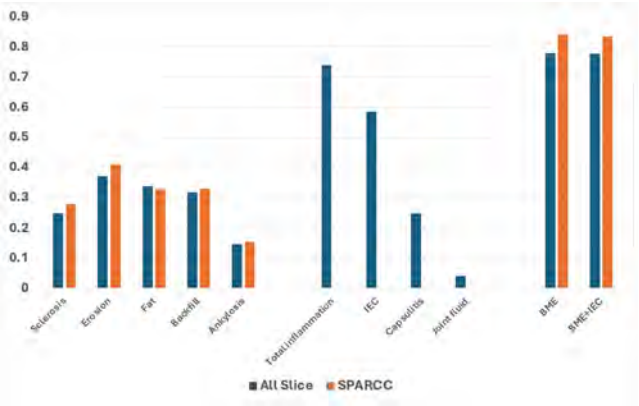


Figure 2. Standardized response means for MRI SIJ inflammatory and structural lesions scores after TNFi assessed across all SIJ slices or limited to the slices selected in the SPARCC method. IEC inflammation in an erosion cavity

Results: Pre- and post-treatment scans (mean(SD) duration between scans 46.6(47.1) weeks) were available from 60 cases, 30 from each cohort. An inflammatory lesion in addition to BME was recorded in 41(68.3%) cases by a majority of readers. But only 1 case had an inflammatory lesion without any BME. For change in structural lesion scores after TNFi treatment, minimal differences were evident between SPARCC and all slice methodologies (Figure 1A). The major contributor to change in inflammatory lesion scores was BME followed by inflammation in an erosion cavity (IEC), though differences between SPARCC and all slice methodologies were minimal (Figure 1B). Reliability for detection of change scores was comparable between SPARCC and all slice methodologies (Table). Responsiveness was comparable between methodologies and combining scores for inflammatory lesions was not superior to BME alone (Figure 2).

Conclusion: BME is the most responsive lesion to treatment with TNFi in axJSpA followed by IEC and then erosion. Responsiveness is not enhanced by assessment of all slices as compared to SPARCC nor by scoring additional inflammatory lesions beyond BME.

Disclosure: W. Maksymowych: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. Francavilla**: None; **N. Herregods**: None; **R. Lambert**: AbbVie, 2, CARE Arthritis and Image Analysis Group, 2; **A. Meyers**: Elsevier, 9, Pfizer, 2; **J. Paschke**: CARE Arthritis Limited, 3; **J. Stimec**: None; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1; **D. Rumsey**: None.

Abstract Number: 0429

Real-world experience of upadacitinib therapy in difficult-to-treat juvenile idiopathic arthritis: a case series of 24 patients

Xuemei Tang[1], Xiwen Luo[2], Xiya Luo[1], Mengwei Ding[3], Xi Yang[2], Dawei Liu[2], Li Xu[2], Zhiyong Zhang[2], Yunfei An[2] and Xiaodong Zhao[1], [1]Department of Rheumatology and Immunology, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity, Chongqing, China, Chongqing, China (People's Republic), [2]Department of Rheumatology & Immunology, Children's Hospital of Chongqing Medical University, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, National Clinical Research Center for Child Health and Disorders (Chongqing), Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Infection and Immunity, Chongqing, China., Chongqing, China (People's Republic), [3]Big Data Center for Children's Medical Care, Children's Hospital of Chongqing Medical University, Chongqing, China., Chongqing, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

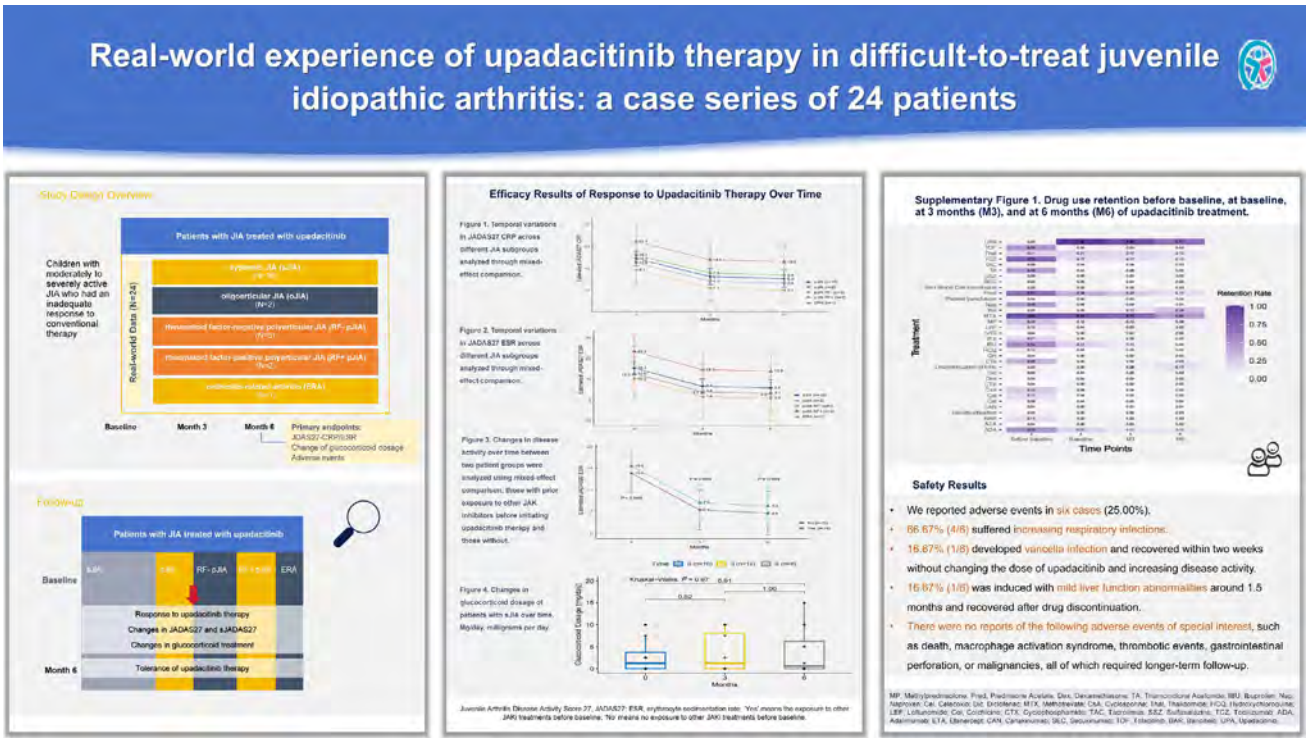
SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0387–0429) Pediatric Rheumatology – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease. Some patients experiencing active disease due to inadequate responses to conventional treatments. Studies have demonstrated effectiveness of JAK inhibitors (JAKis) among JIA patients. This study aimed to evaluate the efficacy and safety of upadacitinib in JIA patients.

Methods: We included 24 difficult-to-treat JIA patients in China treated with upadacitinib from January 1, 2024, to December 31, 2024. Juvenile arthritis disease activity scores (JADAS) and efficacy outcomes were collected. Differences between groups were analyzed using univariable and mixed-effect model analyses. A two-sided P value < 0.05 was considered statistically significant in this study.

Results: Total patients received upadacitinib for a median duration of 7.00 (range: 3.50-10.50) months. Baseline median JADAS27 CRP and JADAS27 ESR were 14.59 (range: 8.00-18.61) and 15.05 (range: 12.50-19.60), respectively. Both scores significantly decreased to 3.75 (range: 2.00, 10.00) and 3.75 (range: 2.25, 7.85) at 3 months and sustained



Graphical Abstract Image of Real-world experience of upadacitinib therapy in difficult-to-treat juvenile idiopathic arthritis a case series of 24 patients. Figure 1. Temporal variations in JADAS27 CRP across different JIA subgroups analyzed through mixed-effect comparison. Juvenile Arthritis Disease Activity Score 27, JADAS27; CRP, C-reactive protein. Figure 2. Temporal variations in JADAS27 ESR across different JIA subgroups analyzed through mixed-effect comparison. Juvenile Arthritis Disease Activity Score 27, JADAS27; ESR, erythrocyte sedimentation rate. Figure 3. Changes in disease activity over time between two patient groups were analyzed using mixed-effect comparison: those with prior exposure to other JAK inhibitors before initiating upadacitinib therapy and those without. Juvenile Arthritis Disease Activity Score 27, JADAS27; ESR, erythrocyte sedimentation rate; 'Yes' means the exposure to other JAKi treatments before baseline; 'No' means no exposure to other JAKi treatments before baseline. Figure 4. Changes in glucocorticoid dosage of patients with sJIA over time. Mg/day, milligrams per day. Supplementary Figure 1. Drug use retention before baseline, at baseline, at 3 months (M3), and at 6 months (M6) of upadacitinib treatment. MP, Methylprednisolone; Pred, Prednisone Acetate; Dex, Dexamethasone; TA, Triamcinolone Acetonide; IBU, Ibuprofen; Nap, Naproxen; Cel, Celecoxib; Dic, Diclofenac; MTX, Methotrexate; CsA, Cyclosporine; Thal, Thalidomide; HCQ, Hydroxychloroquine; LEF, Leflunomide; Col, Colchicine; CTX, Cyclophosphamide; TAC, Tacrolimus; SSZ, Sulfasalazine; TCZ, Tocilizumab; ADA, Adalimumab; ETA, Etanercept; CAN, Canakinumab; SEC, Secukinumab; TOF, Tofacitinib; BAR, Baricitinib; UPA, Upadacitinib.

improvements at 6 months ($P < 0.001$). Median prednisone dose decreased from 1.88 (range: 0.00, 7.50) mg/day to 0.63 (range: 0.00, 7.50) mg/day at 3 months and 0.00 (range: 0.00, 5.00) mg/day at 6 months. Tolerance was acceptable with several cases of elevated transaminases and increased upper respiratory tract infections.

Conclusion: This is the largest real-world study of upadacitinib in JIA to date and provides encouraging evidence of the drug's efficacy and safety. The study also indicates that irrespective of prior treatment with other JAKis, switching to upadacitinib may help regain control of disease activity in patients with difficult-to-treat JIA.

Disclosure: X. Tang: None; **X. Luo**: None; **X. Luo**: None; **M. Ding**: None; **X. Yang**: None; **D. Liu**: None; **L. Xu**: None; **Z. Zhang**: None; **Y. An**: None; **X. Zhao**: None.

Abstract Number: 0430

Retrospective evaluation of the clinical impact of democgraphic , serological , clinical , radiological parameters and treatment modalities in patients with RA-ILD

fatih ŞAhiner[1], Mine Nokay[2], funda erbasan[2], Veli Yazisiz[3] and **Ender terzioglu**[2], [1]Akdeniz University, Antalya, [2]Akdeniz University, Antalya, Turkey, [3]Akdeniz University, Faculty of Medicine, Antalya, Turkey

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: RA-ILD is significant determinants of morbidity and mortality. This study aims to evaluate the demographic and serological characteristics of RA-ILD patients and investigate the relationship with smoking, phenotypic features and lung involvement using HRCT, treatments administered, and parameters affecting mortality.

Methods: We evaluated 65 patients with RA-ILD who showed interstitial changes on HRCT imaging. We collected data on demographics, clinical findings, laboratory results, pulmonary function tests, HRCT images, and treatments from the hospital information system patient records. We analyzed the relationships between disease progression, mortality, and factors such as age, gender, smoking history, serological test results, disease duration, HRCT findings, DAS28-ESR, pulmonary function tests, and treatments.

Results: The study included 65 patients, with a mean age of 67.14 ± 9.52 years. 60% were female and 40% were male. Of the total, 26.2% had died, with 58.8% of these deaths attributed to ILD. Patients who had lung involvement exceeding 20% on HRCT had a significantly higher mortality rate. Serological evaluations showed high positivity rates for RF at 60% and ACPA at 71.4%. The mean duration between diagnoses of RA and ILD was 7.82 ± 10.16 years. The most common HRCT pattern observed was UIP, present in 46.2% of patients, while 32.3% had lung involvement exceeding 20% on HRCT. At the time of ILD diagnosis, 33.3% of patients were in remission, which increased to 71.9% at the final follow-up. The proportion of patients exhibiting high disease activity decreased from 3.5% initially to none at the last evaluation. Additionally, FVC and diffusing capacity of the lungs for DLCO values declined over time, with the final mean DLCO value recorded at 56.69 ± 21.68. In terms of treatment, 90.8% of patients received MTX, 75.4% received HCQ, and 56.9% received RTX.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Age and Gender Characteristics

Variables (n=65)	Mean±SD	Med(IQR)	Min-Max
Age (Year)	67,14±9,52	68(62-73)	39-84
	Number (n)	Percentage (%)	
Gender			
Female	39	60,0	
Male	26	40,0	

Table 2. Exitus Information

Variables	n	Number (n)	Percentage (%)
Exitus Information	65		
Alive		48	73,8
Exitus		17	26,2
Exitus due to Pulmonary Causes	17		
Yok		7	41,2
Var		10	58,8

Table 3. Smoking Status

Variables (n=61)	Number (n)	Percentage (%)
Smoking (Pack/Year)		
Never Smoker	29	47,5
<10	3	4,9
10-30	12	19,7
>30	17	27,9

Table 4. Serologic Status

Variables	n	Number (n)	Percentage (%)
RF	65		
Negative		15	23,1
Low positive		11	16,9
High positive		39	60,0
ACPA	63		
Negative		14	22,2
Low positive		4	6,3
High positive		45	71,4

Table 5. Disease Ages

Variables (n=65)	Mean±SD	Med(IQR)	Min-Max
RA Disease Age (Year)	13,48±10,29	11(7-16)	0-49
ILD Disease Age (Year)	5,66±2,8	6(4-7)	1-13
Time Between RA-ILD (Year)	7,82±10,16	5(1-10)	-13-44

Table 2. FVC and DLCO values at diagnosis and last follow-up According to ACPA positivity

	ACPA			
Variables	Negative	Low Positive	High positive	p
Diagnosis FVC	76,5(73-94)	80,5(64,5-99)	80(73-90)	0,971[£]
Last Follow-up FVC	75(63-83)	78(67-105)	72(56-82)	0,472[£]
Diagnosis DLCO	68(66-79)	58(41-65)	66(58,5-86)	0,189[£]
Last Follow-up DLCO	58(51-69,5)	58(46-69)	57(39-69)	0,862[£]
Diagnosis FVC (Categorized)				0,827*
≥80	6(42,9)	2(50)	24(53,3)	
<80	8(57,1)	2(50)	21(46,7)	
Last Follow-up FVC (Categorized)				0,886*
≥80	4(30,8)	1(33,3)	14(36,8)	
<80	9(69,2)	2(66,7)	24(63,2)	
Diagnosis DLCO (Categorized)				0,488*
≥50	10(90,9)	2(66,7)	36(90)	
30-50	1(9,1)	1(33,3)	3(7,5)	
<30	0(0)	0(0)	1(2,5)	
Last Follow-up DLCO (Categorized)				0,845*
≥50	9(75)	2(66,7)	18(54,5)	
30-50	3(25)	1(33,3)	13(39,4)	
<30	0(0)	0(0)	2(6,1)	

[£]Kruskal- Wallis H Test, *Med (IQR)*
*Pearson Chi-Square Test, Fisher's Freeman Halton Exact Test, *n (%)*

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. HRCT Pattern and Involvement Rate According to RF Positivity

Variables	RF			p*
	Negative	Low Positive	High positive	
HRCT Pattern				0,285
UIP	4(26,7)	6(54,5)	20(51,3)	
Possible UIP	1(6,7)	1(9,1)	3(7,7)	
NSIP	4(26,7)	0(0)	6(15,4)	
Fibrotic NSIP	3(20)	1(9,1)	2(5,1)	
LIP	0(0)	1(9,1)	0(0)	
Undifferentiated	3(20)	2(18,2)	8(20,5)	
HRCT Involvement Rate				0,168
<%10	4(26,7)	5(45,5)	12(30,8)	
%10-20	9(60)	3(27,3)	11(28,2)	
>%20	2(13,3)	3(27,3)	16(41)	

*Pearson Chi-Square Test, Fisher's Freeman Halton Exact Test, *n (%)*

Conclusion: Our study findings indicating that RA-ILD is more common in older patients, males, seropositive individuals, and with a smoking history. RA-ILD mortality is higher than non-ILD. Among ILD phenotypes, UIP is the most frequently observed pattern, with higher lung involvement percentages in this group. As lung involvement increases, pulmonary function declines, and mortality rises. Consistent with previous studies, no correlation was found between seropositivity, DAS28 score, and ILD phenotype. However, although numerically significant, the finding that patients with high-titer seropositivity may have more extensive lung disease was not statistically significant.

In deceased patients, pulmonary function test results were lower, disease activity was higher, and the interval between RA and ILD diagnoses was shorter. Patients with high disease activity at RA diagnosis had lower FVC values at ILD diagnosis, while those in remission had higher FVC values. Patients with UIP and NSIP patterns exhibited greater declines in pulmonary function, with UIP associated with higher mortality.

Unlike similar studies, no significant decline in FVC and DLCO values was observed with increased smoking history. Furthermore, in contrast to previous research, no statistically significant relationship was found between TNFi agents and mortality.

Disclosure: f. ŞAhiner: None; **M. Nokay**: None; **f. erbasan**: None; **V. Yazisiz**: None; **E. terzioglu**: None.

Abstract Number: 0431

Calprotectin Serum levels: a potential neutrophil activation biomarker to monitor treatment response in Rheumatoid Arthritis

Sangeeta Kumari[1], **Eric meldrum**[1], Josephine Stein[1], Tirza Bruurmijn[1], Robin de Jong[2], Katerina Pardali[1], Maarten Kraan[1], Renato Chirivi[1], Rogier Thurlings[3] and Michael Nurmohamed[2], [1]Citryll BV, Oss, Netherlands, [2]Reade, Amsterdam, Netherlands, [3]Radboudumc, Nijmegen, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Calprotectin is a protein highly expressed in myeloid cells and its elevated presence in blood, and the GI tract is associated with immune mediated inflammatory diseases. In autoimmune diseases such as rheumatoid arthritis (RA), elevated levels of calprotectin have been previously reported in patient serum. Furthermore, calprotectin is often

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

associated with neutrophil-mediated inflammation, and in RA disproportionate neutrophil activation exacerbates disease progression with associated elevated calprotectin levels in affected patients. This study aimed to evaluate the utility of calprotectin as a biomarker for monitoring response to different treatments in two longitudinal cohorts of RA patients.

Methods: Serum samples stored at -80°C were obtained from the biobanks of Reade and Radboud University Medical Centre (RUMC). A total of 231 RA serum samples from 33 participants across seven time points over a one-year follow-up period were collected from Reade, while 153 RA samples from 36 participants at various time points over a similar period were obtained from RUMC. At baseline, all samples in the Reade cohort were from treatment-naïve participants, whereas in the RUMC cohort two participants had prior treatment. Throughout consecutive sampling, patients underwent various DMARD treatments. Calprotectin levels were measured using the R&D Biosystems S100A8/A9 ELISA kit following the manufacturer's protocol. Data analysis was performed using Prism 10 and Spotfire Desktop Analyst software, and statistical analysis was performed using the Friedman test.

Results: Baseline calprotectin levels showed a gradual decline following the introduction of treatment. In both cohorts, stratification based on treatment response revealed a significantly greater reduction in calprotectin levels among responders compared to non-responders. In the Reade cohort, the median calprotectin level decreased from **4270 ng/ml at baseline to 1812 ng/ml** after one year ($p< 0.01$), while in the RUMC cohort, it dropped from **5498 to 2021 ng/ml** over a similar period ($p< 0.01$). In contrast, non-responders exhibited minimal changes, with median values shifting from **2920 to 2822 ng/ml** in the Reade cohort and from **2413 to 2670 ng/ml** in the RUMC cohort over one year. Furthermore, the change or delta calprotectin showed a positive correlation with delta CRP (R=0.55), delta ESR (R=0.61) and delta DAS28-CRP (R=0.37).

Conclusion: Our data obtained from the analyses of two longitudinal RA cohorts demonstrate that serum calprotectin and its change can be used as a biomarker for disease activity and response to treatment. Citryll is developing a novel antibody therapeutic mAb (CIT-013) that targets release of extracellular traps from neutrophils. It is our intention to further probe the utility of calprotectin, along with other conventionally used endpoints, as a marker of response to therapy in an RA phase 2a proof of concept study which will begin in 2025.

Disclosure: S. Kumari: Citryll BV, 3, 11; **E. meldrum**: Citryll BV, 3, 3, 5, 11, 11; **J. Stein**: Citryll BV, 3, 11; **T. Bruurmijn**: Citryll BV, 3, 11; **R. de Jong**: None; **K. Pardali**: Citryll BV, 3, 11; **M. Kraan**: Citryll BV, 3, 11; **R. Chirivi**: Citryll BV, 3, 5, 8, 10, 11; **R. Thurlings**: None; **M. Nurmohamed**: None.

Abstract Number: 0432

Frequency and Characteristics of Ophthalmologic Involvement in Patients with Rheumatoid Arthritis

Javier Federico Flores Trejo[1], **Joan Manuel Dapeña**[2], Florencia Micaela Pascual[3], Graciela Liliana Ghiglione[1], Juan Manuel Bande[3], María Alejandra Medina[3], José Angel Caracciolo[3] and Silvia Beatriz Papasidero[3], [1]Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [2]Sanatorio Dr Julio Méndez, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [3]Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient's characteristics (N=50)

Variable	Value
Age (years), mean (SD)	56.7 (9.9)
Female sex, n (%)	43 (86)
RA duration (months), median (IQR)	106.5 (40.5 - 168)
Erosive disease, n (%)	31 (62)
Positive RF, n (%)	47 (94)
Positive ACPA, n (%)	40 (80)
Extra-articular manifestations, n (%)	31 (62)
DAS28, median (IQR)	3.87 (3 - 4.8)
SDAI, median (IQR)	15.3 (7.2 - 19.7)
CDAI, median (IQR)	14 (6.2 - 19)
HAQ-A, median (IQR)	1.5 (1 - 2.14)
Current treatment, n (%) Glucocorticoids Dose (mg), median (IQR) Conventional synthetic DMARDs Targeted synthetic DMARDs Biologic DMARDs	 47 (94) 10 (10 - 15) 48 (96) 4 (8) 16 (32)

SD = Standard deviation; **IQR** = Interquartile range; **RF** = Rheumatoid factor; **ACPA** = Anti-citrullinated protein antibodies; **DAS28** = Disease Activity Score using 28 joints; **SDAI** = Simplified Disease Activity Index; **CDAI** = Clinical Disease Activity Index; **HAQ-A** = Health Assessment Questionnaire – Argentine version.

Background/Purpose: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease that primarily affects synovial joints but may also involve extra-articular organs. Ocular involvement is one of the most common extra-articular manifestations and may result from disease activity or treatment-related complications. The aim of this study was to describe the ophthalmologic manifestations in a cohort of patients with RA and to evaluate their association with sociodemographic and disease-related characteristics.

Methods: A cross-sectional, observational, descriptive and analytical study was conducted. Consecutive patients ≥ 18 years old with RA (2010 ACR/EULAR criteria) were included. Sociodemographic data, disease characteristics, history of ocular involvement and current treatment were recorded. All patients were asked to complete the Ocular Surface Disease Index (OSDI) and underwent a comprehensive ophthalmologic evaluation performed by the same specialist, including tear break-up time (TBUT), Schirmer's test, slit-lamp biomicroscopy, fundoscopy and intraocular pressure measurement. Descriptive statistics were used to summarize results. Associations between ocular dryness severity and clinical variables were analyzed using Chi-squared and Spearman correlation tests. A p-value ≤ 0.05 was considered statistically significant.

Results: A total of 50 patients were included. Patient's characteristics are shown in Table 1. Fifty percent reported previous sicca symptoms, with xerophthalmia being the most frequent (46%). Sjögren's syndrome associated with RA was identified in 6% of patients. The median OSDI score was 8.3 (IQR 4.2–38.0), classifying 40% of patients as having moderate-to-severe ocular dryness. Ophthalmologic examination revealed xerophthalmia in 94% of cases (78% mild, 12% moderate, 4% severe). Cataracts were observed in 46% of patients, with nuclear cataracts accounting for 32%. All ophthalmologic evaluations are detailed in Table 2. Patients with moderate-to-severe dryness based on OSDI had significantly higher disease activity by DAS28 (p = 0.025) and SDAI (p = 0.018).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Ophthalmologic evaluations (N=50)

OSDI, median (IQR)	8.3 (4.2 – 38)
OSDI category, n (%)	
• Normal	27 (54)
• Mild – Moderate	3 (6)
• Moderate – Severe	20 (40)
Dry eye tests, n (%)	
• TBUT	45 (90)
• Schirmer test	41 (82)
• Fluorescein staining	10 (20)
• Rose Bengal staining	16 (32)
Intraocular pressure, mean (SD)	
• Right eye	13.6 (1.8)
• Left eye	13.8 (1.7)
Biomicroscopy findings, n (%)	
• Incipient cataract	2 (4)
• Cortical cataract	3 (6)
• Nuclear cataract	16 (32)
• Corticonuclear cataract	2 (4)
• Tear film alteration	17 (34)
• Superficial keratitis	3 (6)
• Blepharitis	1 (2)
• Corneal leucoma	1 (2)
• Pseudophakia with posterior chamber IOL	2 (4)
• Conjunctival hyperemia (tarsal and bulbar)	2 (4)
• Meibomian gland dysfunction	1 (2)
Fundoscopy findings, n (%)	
• Normal	43 (86)
• Vascular narrowing/tortuosity	2 (4)
• Slightly pale optic nerve	1 (2)
• Degenerative myopic retinopathy	1 (2)
• Decreased macular brightness	1 (2)
• Angiosclerosis and arteriovenous crossings	1 (2)
• Media opacities	1 (2)
Ophthalmologic diagnosis, n (%)	
• No signs of xerophthalmia	3 (6)
• Mild dry eye syndrome (Grade I)	39 (78)
• Moderate (Grade II)	6 (12)
• Severe (Grade III)	2 (4)

IQR = Interquartile range; **SD** = Standard deviation; **OSDI** = Ocular Surface Disease Index; **TBUT** = Tear Break-Up Time; **IOL** = Intraocular lens.

Conclusion: In our cohort of RA patients, the most frequent ocular manifestation was xerophthalmia, which was mild in 78% of cases. Cataracts were present in 46% of patients, with the nuclear subtype being the most common. Moderate-to-severe dry eye symptoms were associated with higher disease activity. These results highlight the importance of identifying ocular symptoms in RA and suggest that ocular surface involvement may reflect a higher systemic inflammatory burden.

Disclosure: J. Flores Trejo: None; **J. Dapeña**: None; **F. Pascual**: None; **G. Ghiglione**: None; **J. Bande**: None; **M. Medina**: None; **J. Caracciolo**: None; **S. Papasidero**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0433

In-hospital outcomes of patients admitted due to First-Time Pulmonary Embolism with preexisting Rheumatoid Arthritis: A Nationwide Analysis 2016-2022

John Langley[1], **Karuna Bista**[2], Clarisse Yapp[2], Nisha Sapkota[3], Shukranta Shrestha[2] and Sulav Pyakurel[1], [1]Montefiore New Rochelle Hospital, New Rochelle, NY, [2]Montefiore New Rochelle Hospital, New Rochelle, [3]Interfaith Medical Center, One Brooklyn Health, Brooklyn, NY

SESSION INFORMATION

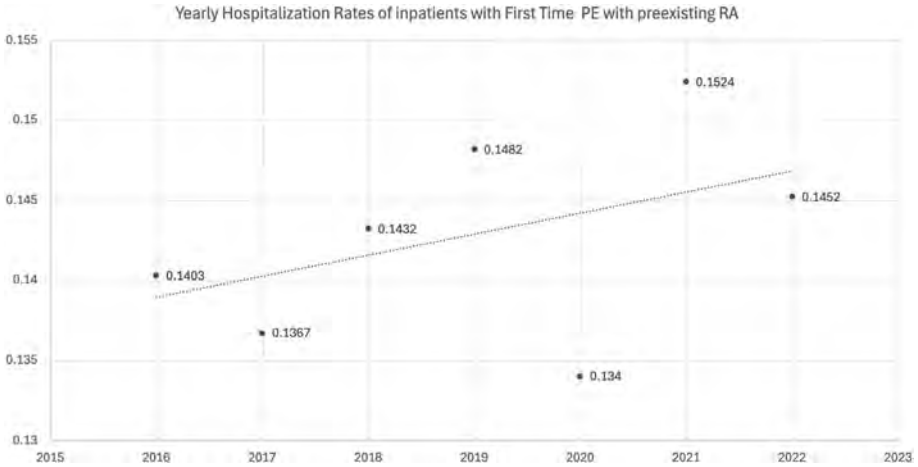
Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

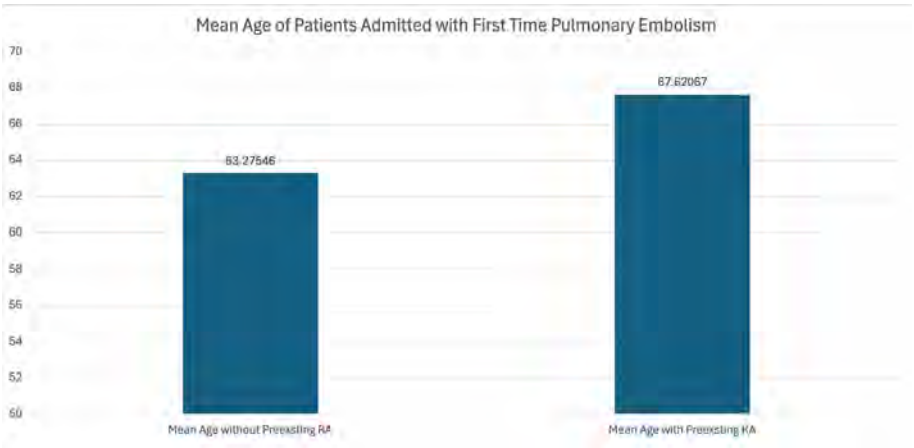
Background/Purpose: Although it has been documented that patients with Rheumatoid Arthritis may be at increased risk of Pulmonary Embolism, other inpatient outcomes remain largely unexplored. We aimed to better identify the impact of Rheumatoid Arthritis on hospital outcomes in patients admitted for first-time Pulmonary Embolism.



Hospitalization Rates of patients admitted for First Time PE with preexisting RA steadily increased from 2016 to 2022.

The majority of inpatients were White followed by Black and Hispanic individuals.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Individuals without preexisting RA were hospitalized at earlier ages.

Methods: A retrospective cohort analysis using the U.S. HCUP NIS Database from 2016-2022 was conducted. Patients admitted with a primary diagnosis of a first episode of Pulmonary Embolism with preexisting Rheumatoid Arthritis were identified using ICD-10 codes. The primary outcome was in-hospital mortality. Secondary outcomes were length of stay, resource utilization and need of various interventions. Univariate analysis was done and variables with $p< 0.2$ were considered for multivariate analysis, adjusting by age, gender, race, Charlson comorbidity index, hospital location and teaching status, size, region and insurance status. Data was considered statistically significant with p-value < 0.05.

Results: From 2016 to 2022, a total of 1,315,394 patients were admitted for a first-time pulmonary embolism (PE). Out of these, 30,474 patients, or 2.32%, had a preexisting diagnosis of rheumatoid arthritis (RA). Notably, these RA patients demonstrated a 35.19% reduction in the odds of mortality (p-value = 0.00). Additionally, they experienced an average decrease in the length of hospital stay by 0.3764 days (p-value = 0.001) and a significant reduction in mean total charges for their hospital stay, amounting to $6,886.12 (p-value = 0.00). Furthermore, RA patients had a 27.87% lower likelihood of undergoing intubation during their hospitalization (p-value = 0.001).

Conclusion: Our research revealed that Rheumatoid Arthritis is associated with improved inpatient outcomes with patients with first-time Pulmonary Embolism. These findings suggest that Rheumatoid Arthritis may confer a protective effect in this population, warranting further investigation.

Disclosure: J. Langley: None; **K. Bista**: None; **C. Yapp**: None; **N. Sapkota**: None; **S. Shrestha**: None; **S. Pyakurel**: None.

Abstract Number: 0434

The advantage of a "tight control" and "treat-to-target" strategy in new-onset rheumatoid arthritis patients in daily rheumatology practice

Katarina Friberger Pajalic[1], Jon Einarsson[1], Caroline Bengtsson[2], Elisabeth Mogard[3], Ellen Landgren[4], Carmen Roseman[3], Elisabet Lindqvist[3], Johan Karlsson Wallman[5], Tor Olofsson[6] and **Meliha Kapetanovic**[3], [1]Lunds University, Department of clinical sciences, section of Rheumatology Malmö and Skåne University Hospital Malmö, Sweden, Lund, Sweden, [2]Skåne University Hospital Lund, Sweden, Lund, Sweden, [3]Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden, [4]Lunds University, Department of clinical sciences, section of Rheumatology, Lund, Skane Lan, Sweden, [5]Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Skane Lan, Sweden, [6]Lunds University, Department of clinical sciences, section of Rheumatology, Lund, Sweden

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Since 2021, patients with new-onset rheumatoid arthritis (RA) at the Department of Rheumatology, Skåne University Hospital, Lund, Sweden, are invited to participate in a ”tight control” and ”treat-to-target” (TC+T2T) follow-up strategy (TINDRA study). This strategy includes follow-up visits to a rheumatologist (at diagnosis and 3, 6, 12, 18, 24 months) and rheumatology nurse-led physical/telephone consultations between physician visits every other week for 3 months and thereafter when needed. Visits include disease activity assessments and adjustment of anti-rheumatic treatment when needed, aiming for remission. The aim of the current study was to explore possible advantages of implementing this TC+T2T strategy over routine clinical practice in new-onset RA patients regarding achievement of remission (DAS28< 2,6, DAS28CRP< 2,4, CDAI≤2,8, and remission defined as 0 swollen joints in the 28-joint count score [“0 swollen joints of 28” remission]).

Methods: RA patients with symptom duration < 12 months at diagnosis were eligible. Data on disease-, treatment characteristics and outcome measures for patients included in the TINDRA study and controls were retrieved from the Swedish Rheumatology Quality register (SRQ). Controls comprised early RA patients followed according to routine clinical practice at the rheumatology out-patient clinics elsewhere in the Skåne region during the same period. In total, 103 patients were followed according to the TC+T2T strategy and 740 according to routine care. Achievement of remission at 1 year after diagnosis was compared between the two strategies using logistic regression, adjusted for sex, age, symptom duration, number of swollen and tender joints, CRP, ACPA status and HAQ at diagnosis.

Results: Disease and treatment characteristics at diagnosis are summarized in Table1.

Percentage females/mean age/mean symptom duration at inclusion were 73%/58 years/5,9 months (TC+T2T) and 69%/60 years/5,7 months (routine care).

Figure 1 illustrates proportion (%) of patients reaching remission (green area) according to the “0 swollen joints of 28” definition at different follow-up times in patients and controls.

Percentages of patients reaching DAS28, DAS28CRP and CDAI remission criteria increased in both groups over time, but the differences between the TC+T2T strategy and routine care were not significant. However, at 12 months of follow-up, the TC+T2T strategi was associated with significantly higher odds of reaching “0 swollen joints of 28” remission compared to routine care (Table2).

Table 1. Disease and treatment characteristics at diagnosis

	TC+T2T group (n=193)	Controls (n=143)
Swollen 28 joint count	6.1 (4)	5.8 (5)
Tender 28 join count	8.4 (6)	7.3 (6)
ESR	46.8 (29)	41.3 (28)
CRP	21.7 (30)	20.6 (32)
DAS28	5.4 (1)	4.9 (1)
DAS28CRP	4.7 (1)	4.4 (1)
CDAI	23.5 (11)	21.6 (12)
HAQ	1.0 (0.6)	1.1 (0.7)
Fatigue (VAS)	32.3 (28)	38.1 (30)
Pain (VAS)	28.8 (25)	34.1 (27)
Smoking (ever) (%)	42%	30%
Methotrexate started at diagnosis (%)	75%	66%
Prednisolone started at diagnosis (%)	68%	42%

Mean and standard deviation (SD) if not otherwise stated.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

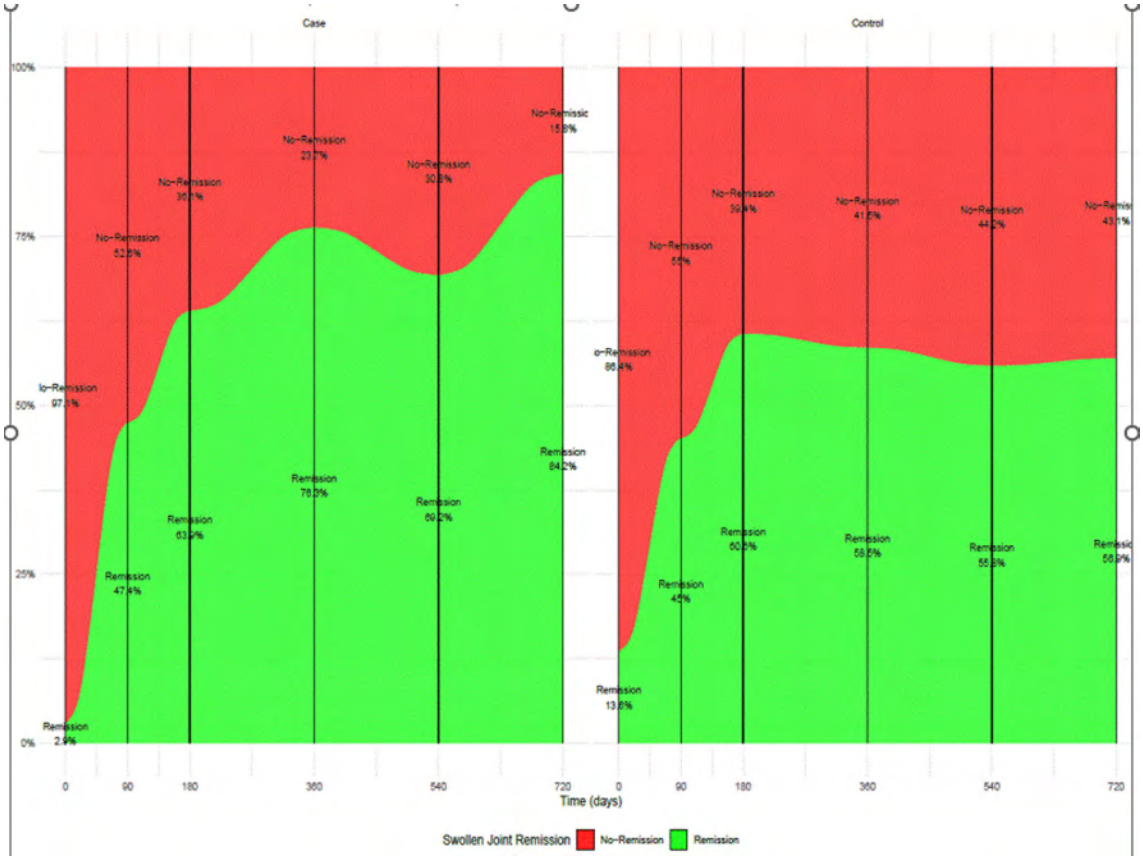


Figure. illustrates proportion (%) of patients reaching remission (green area) according to the "0 swollen joints of 28" definition at different follow-up times in patients and controls.

Table2. Predictors of achieving remission according to the "0 swollen joints of 28" definition, at 12 months of follow-up

	p-value	OR	95% CI
TC+T2T vs routine care	**0,003**	**2,4**	**1,36-4,30**
**Age (years)	0,921	1,0	0,99-1,10
Sex (men versus women)	0,084	1,6	0,94-2,73
Swollen 28-joint count at diagnosis	0,500	1,0	0,94-1,10
Tender 28-joint count at diagnosis	0,872	1,0	0,93-1,10
CRP (mg/L)	0,574	1,0	0,99-1,01
ACPA positivity	0,847	1,0	0,60-1,43
HAQ (0-3)	0,203	0,91	0,59-1,005

*TC+T2T = tight control and treat-to-target

Conclusion: Compared to routine rheumatology care, the "tight control" and "treat-to-target" follow-up strategy resulted in larger proportions of patients reaching remission throughout the first two years after RA diagnosis and a more than doubled probability of reaching the strict target of "no swollen joints" one year following the diagnosis. These findings suggest that such a strategy should be considered for implementation in routine care of patients with new-onset RA.

Disclosure: K. Friberger Pajalic: None; **J. Einarsson**: None; **C. Bengtsson**: None; **E. Mogard**: AbbVie/Abbott, 6; **E. Landgren**: None; **C. Roseman**: None; **E. Lindqvist**: None; **J. Karlsson Wallman**: AbbVie/Abbott, 5, Amgen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5; **T. Olofsson**: None; **M. Kapetanovic**: GlaxoSmithKlein(GSK), 6, UCB, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0435

Comparative Outcomes in Seropositive and Seronegative Rheumatoid Arthritis: A Retrospective Cohort Study

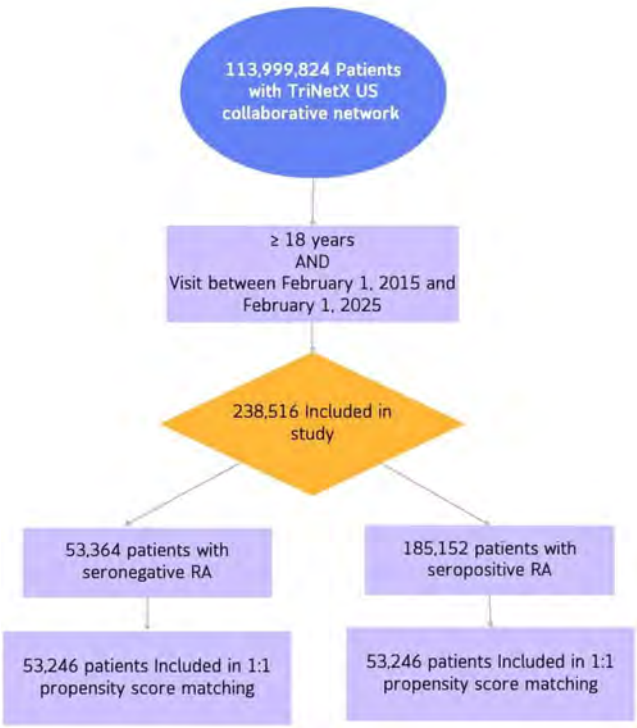
Ahmad Alomari[1], Reem Elmusa[2], Nikita Shah[3], Miguel Rodriguez[4] and Diala Alawneh[5], [1]UCF- North Florida hospital, Gainesville, FL, [2]UCF/ HCA - North florida hospital, Gainesville, FL, [3]UCF/HCA Florida North Florida Hospital, Gainesville, FL, [4]SIMED Rheumatology, Gainesville, FL, [5]University of Florida, Gainesville, FL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease that manifests as either seropositive or seronegative subtypes. Seropositive RA, characterized by the presence of autoantibodies such as RF and ACPA, is often linked to more severe joint damage and systemic complications. In contrast, seronegative RA has a less defined clinical profile but may still present with significant comorbidities. This study aims to compare clinical outcomes between these RA subtypes using real-world data from the TriNetX Research Network.

Methods: A retrospective cohort study was conducted to analyze adult patients diagnosed with rheumatoid arthritis (RA) between 2015 and 2025. Patients were categorized as either seropositive or seronegative based on the International Classification of Diseases, 10th Revision (ICD-10) codes. To reduce confounding and ensure comparability between

Figure 1. Flowchart of the Selection Process

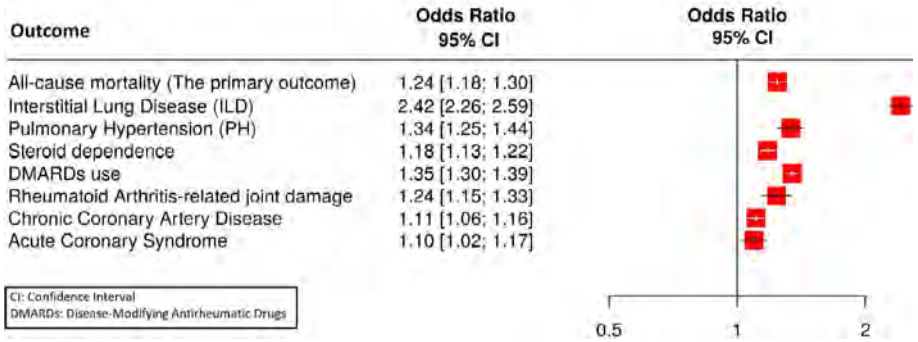


23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Outcome	Number of Patients with Event (%)		Odds Ratio (95% CI)	P Value
	Seropositive RA	Seronegative RA		
All-Cause Mortality	12,478 (23.4%)	10,048 (18.9%)	1.24 (1.16–1.27)	<0.001
DMARD Use	45,216 (84.9%)	39,872 (74.9%)	1.35 (1.30–1.40)	<0.001
Steroid Dependence	20,486 (38.5%)	17,184 (32.3%)	1.18 (1.13–1.23)	<0.001
RA-Related Joint Damage	15,927 (29.9%)	12,738 (24.0%)	1.24 (1.19–1.29)	<0.001
Interstitial Lung Disease (ILD)	7,329 (13.8%)	3,029 (5.7%)	2.42 (2.30–2.55)	<0.001
Chronic CAD	16,214 (30.5%)	14,516 (27.2%)	1.11 (1.06–1.16)	<0.001
Acute Coronary Syndrome (ACS)	5,479 (10.3%)	4,912 (9.2%)	1.10 (1.02–1.17)	0.008

Comparative Outcomes in Seropositive and Seronegative Rheumatoid Arthritis

Figure 3: Forest Plot showing Odds Ratio (OR) and Confidence Intervals (CI)



groups, propensity score matching (PSM) was applied to balance key baseline characteristics, such as age, sex, comorbidities, and other rheumatologic diseases. Following matching, outcomes were compared between the two groups over a follow-up period of 10 years. Figure 1 illustrates the selection process. The primary outcome was all-cause mortality. Other outcomes included steroid dependence, disease-modifying antirheumatic drug (DMARD) use, RA-related joint damage, interstitial lung disease (ILD), and coronary artery disease (CAD).

Results: Among 106,492 matched patients (53,246 per cohort), seropositive RA patients had significantly higher all-cause mortality (OR: 1.24; $p < 0.001$). Kaplan-Meier analysis demonstrated lower survival probabilities in the seropositive group (76.51% vs. 81.68%; log-rank $p < 0.001$), with a hazard ratio of 1.21 (95% CI: 1.16–1.27), indicating a significantly increased risk.

The use of DMARDs was more frequent in seropositive patients (OR: 1.35; $p < 0.001$), and steroid dependence was more common (OR: 1.18; $p < 0.001$). Additionally, seropositive patients had a higher risk of RA-related joint damage (OR: 1.24; $p < 0.001$). Furthermore, the incidence of ILD (OR: 2.42; $p < 0.001$), chronic CAD (OR: 1.11; $p < 0.001$), as well as acute coronary syndrome (ACS) (OR: 1.10; $p = 0.008$) were significantly higher (Table1) (Figure 2).

Conclusion: This study highlights significant differences in clinical outcomes between seropositive and seronegative RA patients. Seropositive RA was associated with higher all-cause mortality, greater steroid dependence, and more frequent use of DMARDs. Additionally, seropositive patients had a higher risk of RA-related joint damage, interstitial lung disease, and coronary artery disease. These findings highlight the more aggressive nature of seropositive disease and its extra-articular involvement, emphasizing the need for early and targeted interventions in this subgroup and reinforce the importance of autoantibody status in prognostication and risk stratification for RA patients.

Disclosure: A. Alomari: None; **R. Elmusa**: None; **N. Shah**: None; **M. Rodriguez**: None; **D. Alawneh**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0436

Why Do Patients with Rheumatic Disease Have MACE and Thrombotic Events?

Andrea Mazariego and Maria Greenwald, Desert Medical Advances, Rancho Mirage, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatic disease have an increased risk for thrombotic events and major adverse cardiac events (MACE) due to systemic inflammation. Bleeding time is a test performed in the clinic and consistently confirms a short time to clot with known risk factors such as estrogen, cox-2 inhibitors, JAK inhibitors, and factor V Leiden. Historically, a short bleeding time under 3 minutes is associated with an increased risk of thrombotic disease. We explored whether patients with rheumatic disease have a short bleeding time. This may be the physiologic mechanism leading to clotting events.

Methods: All sequential 239 patients over age 50 with rheumatic disease had a bleeding time test (BT). This included patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and lupus. Data was collected between September 2022- December 2024. Patients who began low dose aspirin 81 mg daily in 2023 had a repeat BT to confirm compliance. No patients had a history of cardiovascular disease but 15 developed MACE or a thrombotic event prior to aspirin therapy, and this resulted in death for three patients. BT at baseline (prior to the event) and BT after the event were compared. Cohorts were analyzed by assigned treatments for rheumatic disease including methotrexate, JAK inhibitors, TNF inhibitors, abatacept, secukinumab, IL-1 inhibitors, and PD-1 agonist.

Results: Rheumatic disease patients at baseline had shorter BT results compared to historical normal controls (1.52 $\pm$ 0.77) versus 4-7 minutes which is found in the normal general population ($p < 0.01$). There was no difference in the short BT among patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, or lupus. Cohorts were analyzed by treatment and BT did not discriminate between treatment assigned (Table 1). The addition of low dose aspirin 81 mg daily dramatically

Table 1

Table 1: BT at baseline before aspirin and after low dose aspirin

RA	BT without aspirin	BT with aspirin	p (compared to asp)
Methotrexate (age 70)	1.74± 1.00	2.98± 0.69	<0.0001
JAKi (age 58)	1.38± 0.51	3.47± 1.36	<0.001
TNFi (age 59)	1.10± 0.31	3.05± 0.84	<0.001
Abatacept (age 70)	1.15± 0.50	3.47± 0.11	<0.0001
IL-1i (age 60)	1.91± 1.10	3.11± 0.59	<0.01
PD-1 agonist(age 59)	1.78± 0.93	3.76± 1.16	<0.002
PsA			
Secukinumab (age 61)	1.64± 0.98	3.31± 1.30	<0.05
SLE			
JAKi (age 58)	2.34± 0.45	6.34± 4.29	<0.05
Hydroxychloro (age 59)	1.71± 0.63	4.20± 2.24	<0.03
SLE with clot*(age 60)	1.66± 0.57	4.40± 3.4	<0.05

*Legend: *There were 3 patients with MACE or thrombotic events; 2 of 3 were anti-cardiolipin positive.*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2

Table 2: BT at baseline without aspirin and after anti-coagulants for patients who developed MACE or Thrombotic events

Rheumatic disease	age/gender	event	BL BT	BT with anti-coag
PsA	72 M	PE	1.06	3.6
Lupus	63 F	TIA	1.88	2.48
RA	48 F	PE	2.48	3.44
RA	78 M	TIA	1.97	4.3
Lupus	63 F	TIA	2.88	5.01
Lupus	63 F	CVA	2.48	3.01
RA	68 M	MI	3.01	4.02
RA	73 M	MI	1.06	4.12
RA	77 M	PE	2.53	4.3
RA	78 M	MI	1.55	4.22
RA	67 M	MI	3.02	4.5
Lupus	64 F	DVT	2.39	5.3
RA	54 F	DVT	2.31	2.38
RA	60 M	MI	2.87	7.21
RA	74 F	DVT/ MI	1.99	25.5

Legend: Deep vein thrombosis (DVT), myocardial infarction (MI), pulmonary embolism (PE), transient cerebral accident (TIA). Three of these events resulted in death. N=15, average age 68.

nearly doubled BT. The patients who developed MACE or a thrombotic event had short BT test results but did not differ from those who did not have a clotting event. The only significant findings in the MACE/thrombotic group was older age by almost a decade, predominantly male gender, and 80% were smokers (Table 2).

Conclusion: All patients with rheumatic disease with systemic inflammation tested had short BT results. BT did not identify a specific individual who would develop MACE or a thrombotic event. BT tests did revert to normal with the addition of low dose aspirin 81 mg daily. Aspirin is now recommended prophylactically in all lupus with phospholipid syndrome. Perhaps it is time to consider low dose aspirin for patients over age 50 with rheumatic disease.

Disclosure: A. Mazariego: None; **M. Greenwald**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0437

Lipid Screening in Rheumatoid Arthritis: A Retrospective Cohort Study Highlighting Gaps in Cardiovascular Risk Prevention

Anokhi Saklecha[1], Amelia Khoo[2], Sierra Mendelsohn[2], Abhijeet Danve[3], Mei Xue Dong[4] and Lisa Suter[2], [1]Yale University, New Haven, CT, [2]Yale School of Medicine, New Haven, CT, [3]Section of Rheumatology, Department of Medicine, Yale School of Medicine, New Haven, CT, [4]Yale-New Haven Medical Center, new haven, CT

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is associated with a 1.5 to 2 fold increased risk of cardiovascular disease (CVD) due to systemic inflammation and endothelial dysfunction. This level of cardiovascular threat is comparable to—and may even exceed—that of traditional risk factors such as diabetes. The European Alliance of Associations for Rheumatology (EULAR) recommends adjusting CVD risk scores by a factor of 1.5 in patients with RA, emphasizing the importance of cardiovascular risk screening in this population, including lipid testing. The American College of Cardiology (ACC) and American Heart Association (AHA) recommend lipid screening every 4 to 6 years in all adults, and as often as every 2 years when risk factors are present. In this study, we aimed to assess the prevalence and patterns of lipid screening in RA patients.

Methods: We conducted a retrospective cohort study using electronic health records from a large academic health system. Adults (≥18 years) with RA who had at least one outpatient rheumatology visit between 1/1/2020 and 12/31/2024 were included. Lipid screening was defined as any recorded lipid panel over the five year period. Relevant demographic and clinical factors were extracted, including age, sex, BMI, and comorbidities. Chi-squared tests were then used to compare the rates of lipid screening across different subgroups.

Results: We analyzed 1,686 patients with RA, of whom 81.7% were female and 18.3% were male. Overall, 1,182 patients (70.1%) underwent lipid screening over the 5-year period, while 504 (29.9%) did not. Screening rates were significantly higher among patients with traditional cardiovascular risk factors. RA patients with diabetes were more likely to be screened than those without (77% vs. 60%, $p< 0.0001$), as were those with hypertension (77% vs. 60%, $p< 0.0001$). Screening was also more common among patients with obesity (BMI ≥30) compared to those with lower BMIs (76% vs. 72%, $p=0.03$). Patients under 40 were less likely to be screened than middle-aged or older patients (45% vs. 72%, $p< 0.0001$).

Conclusion: Despite the well-established cardiovascular risk, nearly one in three RA patients in our health system did not undergo lipid screening over a 5-year period. When screening did occur, it was more strongly associated with the presence of traditional risk factors, including hypertension, diabetes, and obesity, than with RA alone. This suggests that clinicians may not fully recognize RA itself as an independent driver of cardiovascular risk, leading to missed opportunities for disease prevention. To address this gap, our health system is implementing an Epic Best Practice Alert (BPA) to prompt regular lipid testing in all RA patients. Through such tools, we aim to facilitate earlier risk management and ultimately reduce cardiovascular morbidity and mortality in RA.

Disclosure: A. Saklecha: None; **A. Khoo**: None; **S. Mendelsohn**: None; **A. Danve**: AbbVie, 2, Amgen, 2, Eli Lilly, 5, Janssen, 2, Novartis, 2, 5; **M. Dong**: None; **L. Suter**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0438

Exploring the Potential for Cardiorenal-Metabolic Therapies to Target Comorbidities in Early Rheumatoid Arthritis

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiorenal-metabolic (CRM) therapies, such as SGLT-2 inhibitors and GLP-1 agonists, are medications that target interconnected pathways between cardiovascular, renal, and metabolic systems and may provide additional benefits for patients with rheumatoid arthritis (RA) by potentially reducing systemic inflammation. Our objectives were to (1) To assess the prevalence of CRM conditions and eligibility for CRM therapies based on approved indications and investigational (off-label) use in early RA (ERA). (2) To examine differences in clinical characteristics, including sex-based variations, for patients with and without CRM conditions.

Methods: Data were from the Canadian Early Arthritis Cohort, a cross-sectional study of patients recruited between 2017 and 2023, including baseline BMI, creatinine, Clinical Disease Activity Index (CDAI), and CDAI at 12 months. We estimated the baseline prevalence of approved Canadian CRM indications: (1) type 2 diabetes, (2) obesity (BMI ≥30 kg/m^2), (3) heart failure, or (4) overweight (BMI ≥27 and < 30 kg/m^2) + ≥ 1 weight-related complication of hypertension and/or dyslipidemia. Off-label indications included (5) chronic kidney disease (< eGFR < 60 mL/min/1.73 m^2), (6) overweight BMI with elevated C-reactive protein (CRP >5mg/L), or (7) large joint osteoarthritis[1]. Descriptive statistics were done for the overall cohort. Stratification by sex was used to identify differences associated with CRM conditions.

Table. Baseline prevalence of approved and off-label cardiorenal-metabolic (CRM) indications, stratified by sex.

	Approved CRM Indications				Approved and Off-Label CRM Indications			
	Total N = 278	Female N = 185	Male N = 93	P-value	Total N = 278	Female N = 185	Male N = 93	P-value
Any CRM Condition	126 (45%)	79 (43%)	47 (51%)	0.22	151 (54%)	94 (51%)	57 (61%)	0.09
Type 2 Diabetes	31 (11%)	16 (9%)	15 (16%)	0.0615	31 (11%)	16 (9%)	15 (16%)	0.06
Obesity	88 (32%)	62 (34%)	26 (28%)	0.35	88 (32%)	62 (34%)	26 (28%)	0.34
Heart Failure	0	0	0	NA	0	0	0	NA
Overweight BMI + ≥ 1 weight-related complication:	25 (9%)	14 (8%)	11 (12%)	0.24	41 (15%)	24 (13%)	17 (18%)	0.24
Hypertension	21 (8%)	12 (7%)	9 (10%)	0.34	21 (8%)	12 (6%)	9 (10%)	0.34
Dyslipidemia	16 (6%)	9 (5%)	7 (8%)	0.3686	16 (6%)	9 (5%)	7 (8%)	0.37
CRP levels (>5mg/L)	–	–	–	–	28 (10%)	17 (9%)	11 (12%)	0.49
Chronic Renal Disease	–	–	–	–	12 (4%)	9 (5%)	3 (3%)	0.76
Knee Osteoarthritis	–	–	–	–	28 (10%)	18 (10%)	10 (11%)	0.79
Number of Conditions								
0 conditions	152 (55%)	106 (57%)	46 (50%)	0.3	127 (46%)	91 (49%)	36 (39%)	0.28
1 condition	108 (39%)	66 (36%)	42 (45%)		107 (38%)	63 (34%)	44 (47%)	
2 conditions	18 (6%)	13 (7%)	5 (5%)		39 (14%)	27 (15%)	12 (13%)	
3 conditions	0	0	0		5 (2%)	4 (2%)	1 (1%)	
≥ 4 conditions	0	0	0		0	0	0	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Out of 855 recruited patients, the final sample included 278 patients and 67% were female. The mean age was 57 ± 14 years, and mean symptom duration was 5.1 ± 2.7 months. At baseline, nearly all patients (90%) had moderate or high Clinical Disease Activity Index (CDAI) scores. Overall, 54% had one CRM condition and 45% met approved indications for CRM therapy, primarily for obesity (Table). Overlapping conditions increased (14% had ≥2 CRM) when off-label indications such as knee OA or overweight BMI + elevated CRP were considered. Patients with CRM conditions were older and had more non-metabolic comorbidities. However, there were no significant differences in disease activity components beyond inflammatory makers (mean CRP 9.5 mg/L vs. 4.8mg/L, p=0.01), nor were there differences in initial DMARD or corticosteroid strategies. In sex stratified analyses, no differences were observed between male and females for the number or type of CRM conditions (Table).

Conclusion: In this real-world ERA cohort, 45% of patients met criteria for approved CRM therapy, primarily for obesity and diabetes. Obesity is known to negatively affect RA disease activity and treatment response, making it a critical target for intervention. The lack of significant sex-based differences in CRM conditions further highlights the universal relevance of CRM conditions in RA management. Future research should explore how CRM therapies, particularly those targeting obesity, could improve metabolic health and RA outcomes, warranting their study in this population.

Reference: 1. Bliddal H et al. Once-Weekly Semaglutide in Persons with Obesity and Knee Osteoarthritis. N Engl J Med. 2024 Oct 31;391(17):1573-1583.

Disclosure: B. Kuriya: AbbVie/Abbott, 1, Pfizer, 1; **S. Bartlett**: Accord, 2, Nordic, 2, PROMIS Health Organization, 4, Sandoz, 2; **M. Valois**: None; **J. Pope**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Frese, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mallinckrodt Pharmaceuticals, 2, 5, Merck/MSD, 2, Mitsubishi Tanabe Pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2, Sanofi, 2, Teva, 2, UCB, 2, Viatris, 2; **C. Thorne**: Medexus, Accord, AbbVie, Acccord, BIOGEN, Pfizer, Roche, Medexus, Nordic, Organon, 1, 2; **C. Hitchon**: Accord, 1, AstraZeneca, 2, Fresenius-Kabi, 2, Pfizer, 2, Sandoz, 2; **H. Allard-Chamard**: AbbVie, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 1, 5, 6, GlaxoSmithKlein(GSK), 1, Janssen, 1, 5, 6, Kabi, 1, 5, 6, Novartis, 1, 6, Otsuka, 1, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Sobi, 1, 5, 6; **G. Hazlewood**: None; **G. Boire**: Biocon, 5, Sanofi, 1; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, 5, 6, Fresenius Kabi, 2, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, TEVA, 2, 6, UCB, 2, 5, 6; **V. Bykerk**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, E.R. Squibb & Sons, 2, Janssen, 2, L.L.C, 2, Organon, 2, Pfizer, 2.

Abstract Number: 0439

Osteoarthritis and Other Degenerative Musculoskeletal Disorders Are Common and Often Associated with Active Inflammation in Difficult-to-Treat Rheumatoid Arthritis: A Cross-Sectional Cohort

Blanche QUERE[1], Grégoire CORMIER[2], LE GOFF Benoit[3] and Adrien LE PLUART[4], [1]CHU de Nantes, Nantes, Pays de la Loire, France, [2]Centre Hospitalier département de Vendée, La Roche Sur Yon, France, [3]CHU Nantes, Nantes, France, [4]CHU Nantes, Nantes, Pays de la Loire, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Despite advances in therapeutic strategies, a subset of patients with rheumatoid arthritis (RA) continues to experience persistent symptoms. In 2022, the EULAR proposed a standardized definition and and points to consider for the management of difficult-to-treat (D2T) RA. Distinguishing whether persistent symptoms are due to active inflammation or other conditions is essential to guide therapeutic decisions.

The aim of this study was to assess the prevalence of non-inflammatory causes of persistent joint symptoms and to explore both patient and physician perspectives on symptom origins.

Methods: This cross-sectional study was conducted from November 2023 to January 2025 in two hospital centers. Inclusion criteria were a confirmed diagnosis of RA according to the 2010 ACR/EULAR criteria and fulfillment of the 2022 EULAR definition of D2T RA.

Comprehensive assessments were performed as recommended by the EULAR "points to consider." Collected data included demographics, comorbidities, treatment history, clinical evaluation, and patient-reported outcomes (including SF-12 for quality of life, MARS-5 for treatment adherence, PCS for pain catastrophizing, and WPI for fibromyalgia symptoms).

All patients underwent a standardized diagnostic work-up, including laboratory tests, radiographic, and ultrasound assessment.

Persistent inflammatory refractory RA (PIRRA) was defined by the presence of Doppler-positive synovitis. Other patients were categorized as having non-inflammatory refractory RA (NIRRA).

Results: A total of 52 patients were included, with a median age of 61.2 years. The majority were female (76.9%) with severe, erosive disease (78.8%) and seropositivity (88.4% ACPA positive).

Methotrexate had been prescribed to 96% of patients, though only 48% were still receiving it at the time of assessment. Patients had received an average of 4.4 targeted therapies. Daily corticosteroid use was reported in 60% of patients, with a mean dose of 6.2 mg/day.

Table 1. Patient Characteristics and Perceived Causes of Articular Symptoms (Physician vs Patient Assessment)

Variable	All (n=52)	PIRRA (n=40)	NIRRA (n=12)
Patient Characteristics			
Age (years), mean	61.2	60.9	67.3
ACPA positive, n (%)	46 (88.4%)	36 (90.0%)	10 (83.3%)
Smokers, n (%)	18 (34.6%)	14 (35.0%)	4 (33.3%)
Number of targeted DMARDs, mean	4.4	4.4	4.2
DAS28-CRP, mean	4.2	4.38	3.7
Clinical synovitis count, mean	4.2	4.9	1.3
Mode B synovitis count, mean	9.2	11.2	2.3
Doppler-positive synovitis count, mean	3.7	4.8	0.0
Causes Contributing to Articular Symptoms — Physician Assessment			
RA sequelae, n (%)	27 (51.9%)	21 (52.5%)	6 (50.0%)
Osteoarthritis, n (%)	21 (40.4%)	14 (35.0%)	6 (50.0%)
Fibromyalgia, n (%)	7 (13.5%)	5 (12.5%)	2 (16.7%)
Causes Contributing to Articular Symptoms — Patient Self-Assessment			
RA sequelae, n (%)	29 (55.8%)	24 (60.0%)	5 (41.7%)
Osteoarthritis, n (%)	19 (36.5%)	12 (30.0%)	7 (58.3%)
Fibromyalgia, n (%)	2 (3.8%)	2 (5.0%)	0 (0.0%)

The mean DAS28-CRP was 4.2. Based on ultrasound findings, 41 patients (76.9%) were classified as PIRRA.

Osteoarthritis was present in 40.4% of patients and was deemed to contribute to symptoms in 35.0% of PIRRA patients. RA-related structural damage (sequelae) was observed in 51.9% of patients and contributed to symptoms in 52.5% of PIRRA cases. Fibromyalgia criteria were met by 9.6% of patients.

Most patients (94.2%) — including all PIRRA patients — perceived their disease as active, compared to 78.8% based on the physician global assessment.

Pain catastrophizing was identified in 48.1% of patients, and 17.3% had poor treatment adherence. These patterns were similarly distributed between PIRRA and NIRRA groups.

Conclusion: In this cohort, a significant proportion of patients with D2T RA experienced symptoms attributable to non-inflammatory causes, particularly osteoarthritis and RA-related joint damage, either alone or in combination with active disease. These findings underscore the importance of a comprehensive and integrated approach to the management of D2T RA.

Disclosure: B. QUERE: None; **G. CORMIER**: None; **L. Benoit**: AbbVie/Abbott, 1, Amgen, 1, Bristol-Myers Squibb(BMS), 1, 5, Fresenius-Kabi, 1, Lilly, 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, 5, Roche, 1, 5, Sandoz, 5, Viatris, 1; **A. LE PLUART**: None.

Abstract Number: 0440

The Painful Truth: Non-Articular Pain's Impact on Rheumatoid Arthritis Assessment after Initiating a new DMARD for Active Disease

Charis Meng[1], Jing Song[2], Lutfiyya muhammad[3], Caci Julia[4], Tuhina Neogi[5], Marcy Bolster[6], Wendy Marder[7], Clifton Bingham[8] and Yvonne Lee[9], [1]Hospital for Special Surgery, New York, NY, [2]Northwestern University Feinberg School of Medicine, Worthington, MN, [3]Northwestern University Feinberg School of Medicine, Chicago, IL, [4]Hospital for Special Surgery, New York, [5]Boston University School of Medicine, Boston, MA, [6]Massachusetts General Hospital, Concord, MA, [7]University of Michigan, Ann Arbor, MI, [8]Johns Hopkins University, Baltimore, MD, [9]Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: RA-related pain is typically thought of as pain in the joints. However, non-articular pain (NAP) is also common, persisting in 1/3 of patients with early RA despite treatment (1). NAP may prevent patients from achieving treatment goals by contributing to elevated pain intensity and patient global assessment (PtGA). Overestimation of disease activity may lead to changes in DMARD treatment without associated improvements in disease outcomes. Recognizing NAP as a driver of pain intensity and PtGA may help prevent overtreatment with DMARDs, lead to earlier recognition of and addressing treatment with greater specificity for different types of pain. Our aims were to evaluate the cross-sectional association of NAP with elevated pain intensity and PtGA in patients 3-months after initiating a new DMARD for active RA.

Methods: The Central Pain in Rheumatoid Arthritis study is a prospective cohort of patients fulfilling 2010 ACR/EULAR criteria for RA, who have active disease and are initiating a new DMARD. At the 3-month visit, patients indicated any areas of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics in Total Cohort and Across NAP groups (N=192)

	Overall, N = 192[1]	No NAP, N = 14[1]	Regional NAP, N = 85[1]	Widespread NAP, N = 93[1]
Age, years	55.1 (14.5)	51.9 (13.2)	57.0 (14.6)	53.8 (14.6)
Female	161 (83.9%)	10 (71.4%)	71 (83.5%)	80 (86.0%)
White	143 (74.5%)	10 (71.4%)	61 (71.8%)	72 (77.4%)
BMI (kg/m^2)	28.8 (7.1)	26.2 (6.6)	28.3 (7.5)	29.7 (6.6)
Some college or higher education	139 (72.4%)	12 (85.7%)	68 (80.0%)	59 (63.4%)
Current smoker	26 (13.5%)	0 (0.0%)	16 (18.8%)	10 (10.8%)
Comorbidity, number	1.4 (1.0)	1.2 (0.7)	1.3 (0.9)	1.4 (1.2)
RA duration, years	10.7 (12.8)	6.5 (8.5)	10.9 (14.0)	11.2 (12.1)
Seropositivity	134 (69.8%)	11 (78.6%)	67 (78.8%)	56 (60.2%)
Pain intensity (0-10) (NRS)	3.9 (2.4)	2.2 (2.2)	3.5 (2.3)	4.5 (2.4)
PtGA	3.0 (2.5)	1.5 (2.2)	2.4 (2.2)	3.7 (2.7)
CDAI at follow-up	14.9 (12.6)	6.5 (6.5)	11.9 (10.5)	19.0 (13.7)

[1]Mean (SD); n (%); baseline data shown as most variables not collected at follow-up

NRS Numerical Rating Scale, PtGA patient global assessment, CDAI Clinical Disease Activity Index

Table 2: Mean and Median Pain Intensity and PtGA levels across NAP groups

	Overall (N=192)	No NAP (N =14)	Regional NAP (N = 85)	Widespread NAP (N = 93)
*Pain Intensity**				
Mean (SD)	3.9 (2.4)	2.2 (2.2)	3.5 (2.3)	4.5 (2.4)
Median (IQR)	4.0 (2.0, 6.0)	1.5 (1.0, 3.8)	3.0 (1.0, 5.0)	4.0 (3.0, 6.0)
*Patient Global**				
Mean (SD)	3.0 (2.5)	1.5 (2.2)	2.4 (2.2)	3.7 (2.7)
Median (IQR)	2.5 (1.0, 5.0)	1.0 (0.0, 1.4)	2.0 (0.5, 4.0)	4.0 (1.2, 6.0)

*From 3 month follow-up visit after changing DMARD therapy for active RA

IQR Interquartile range

pain or tenderness that they were experiencing on a body pain diagram (BPD), derived from the Widespread Pain Index which assesses 19 body areas (jaw, neck, shoulder (girdle), upper arm, lower arm, upper back, chest, abdomen, lower back, hip (buttock), upper leg and lower leg). Prespecified NAP patterns were classified based on pain reported in 5 sections (4 quadrants and axial, excluding hands and feet) and grouped as: 1) no NAP (no sections selected), 2) regional (1-3 sections) or 3) widespread NAP (4-5 sections) (1). Patients completed synchronous assessments of pain intensity and PtGA. Separate median regression models were used to examine the associations between NAP groups and the two outcomes. Both unadjusted and adjusted models (controlling for age, sex, education, smoking status, comorbidity, seropositivity, and study site) were fitted.

Results: The 192 RA patients were mostly female (84%) with mean (SD) age of 55 (14) years; 70% were seropositive, mean RA disease duration was 10.8 (212.8) years and mean (SD) CDAI was 14.9 (12.6) (Table 1). NAP was prevalent in 92.7% (n=178), with regional NAP 44.3% (n=85) and widespread NAP 48.4% (n=93). Compared to other groups, those with widespread NAP were more frequently White women who reported more comorbidities and longer disease duration. At follow-up, NAP was associated with higher median values [IQR] for pain intensity and for PtGA in a dose-dependent fashion across

Table 3: Multivariable regression analysis showing association of NAP with elevated Pain Intensity and PtGA in RA Patients Changing DMARDs

	Pain Intensity				PtGA			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	Difference in Medians (95% CI)	p-value	Difference in Medians (95% CI)	p-value	Difference in Medians (95% CI)	p-value	Difference in Medians (95% CI)	p-value
No NAP	Reference	N/A	Reference	N/A	Reference	N/A	Reference	N/A
Regional NAP	1.0 (-0.8, 2.8)	0.281	0.8 (-0.7, 2.4)	0.304	**1.0 (0.0, 2.0)**	**0.047**	0.5 (-0.7, 1.6)	0.427
Widespread NAP	**2.0 (0.1, 3.9)**	**0.04**	**1.9 (0.3, 3.6)**	**0.025**	**3.0 (1.6, 4.4)**	**<0.001**	**2.4 (0.8, 3.9)**	**0.003**

*adjusted for age, sex, education, current smoker, comorbidity and seropositive status at follow-up visit

CI= confidence intervals

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pain groups: no NAP, regional NAP and widespread NAP (Table 2). In median regression analyses, compared to no NAP, widespread NAP was associated with higher median levels of both pain intensity and PtGA: difference in medians 95% [CI] was 1.9 (0.3, 3.6) and 2.4 [0.8, 3.9], respectively (Table 3).

Conclusion: NAP was associated with higher pain intensity and PtGA in RA in a dose-dependent fashion. Despite changing DMARD treatment to manage active RA, widespread NAP was identified as a significant driver of pain intensity and PtGA. A limitation includes a lack of validated tool to screen for NAP in RA, calling for improved reporting of NAP. Early identification and intervention of NAP may help patients to reach their treatment goals.

1. Meng et al. doi: 10.1002/art.43049.

Disclosure: C. Meng: None; **J. Song**: None; **L. muhammad**: None; **C. Julia**: None; **T. Neogi**: None; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **W. Marder**: None; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1.

Abstract Number: 0441

Charting the Course of Worsening: Utilizing Standard Outcomes to Define Worsening for Pathophysiological Insights into RA

Charis Meng[1], Caci Julia[2], Kelsey Gripp[2], Deanna Jannat-Khah[1], Yvonne Lee[3], Susan J. Bartlett[4], Clifton Bingham[5] and Vivian Bykerk[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, New York, [3]Northwestern University, Chicago, IL, [4]McGill University, Beaconsfield, QC, Canada, [5]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: RA disease worsening contributes to joint damage and cardiovascular disease. While measures of improvement are established in RA, we do not have uniform definitions for disease worsening. Robustly identifying RA disease worsening reported by clinicians and patients could facilitate future translational studies of its pathophysiology (i.e. using -omics data). The OMERACT RA-FLARE questionnaire (RAFQ) is a valid patient-reported outcome (PRO) of RA worsening. Patients reporting they were "a lot worse" had a mean RA-FQ increase of 8.9 points[1]. We aimed to evaluate associations with stringent definitions of RA disease worsening using composite clinical outcomes and the level of change in RAFQ, in order to understand if the RAFQ could be used to identify subjects with clear RA worsening and whose samples to include for translational studies.

Methods: Patients with early (e) RA (symptom duration< 2 years, CDAI >2.8) enrolled in the Consortium of Early Arthritis Cohorts US with $\geq$ two recorded CDAI or DAS28 measures from $\geq$2 separate protocolized visits. We defined stringent RA worsening using 1) DAS28: an increase in DAS28 >1.2 and worsening of disease state by $\geq$ 1 category (remission or low disease activity to moderate disease activity or moderate disease activity to high disease activity) or 2) CDAI: an increase in CDAI>10 and worsening of disease state by $\geq$1 category. To further ensure stringency, patient outcomes and change in RAFQ scores were compared between their pre-RA worsening visit (one with the lowest DAS28 or CDAI score before worsening) and their designated RA worsening visit (one with the maximal DAS28 or CDAI score) using paired t-tests. An alpha of 0.05 was used to determine statistical significance. All analyses were done using STATA version 18.0.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of real-world early RA cohort comparing those who later develop RA worsening vs not

	N=153	Later develop RA worsening* (N=41)	Do not worsen (N=112)	p-value
Age, mean (SD)	49.5 (16.7)	53.4 (16.2)	48.1 (16.8)	0.084
Female, n (%)	126 (82.4)	32 (78.0)	94 (83.9)	0.47
White, n (%)	115 (75.2)	32 (78.0)	83 (74.1)	0.68
BMI, mean (SD)	26.1 (5.8)	26.3 (6.7)	26.1 (5.4)	0.83
Regular use of tobacco products (past or present), n (%)	55 (35.9)	20 (48.8)	35 (31.2)	0.13
Comorbidities RDCI (0-9), mean (SD)	**0.88 (1.3)**	**1.3 (1.4)**	**0.73 (1.3)**	**0.02**
Osteoarthritis, n (%)	**25 (16.3)**	**12 (29.3)**	**13 (11.6)**	**0.012**
Symptom duration (months), mean (SD)	8.9 (6.7)	7.6 (5.8)	9.4 (7.0)	0.15
Seropositive (RF or CCP), n (%)	113 (73.9)	32 (78.0)	81 (72.3)	0.54
TJC28, mean (SD)	3.6 (4.6)	3.7 (5.5)	3.6 (4.2)	0.93
SJC28, mean (SD)	4.1 (5.2)	5.2 (5.8)	3.7 (4.9)	0.11
DAS28, mean (SD)	3.0 (1.4)	3.0 (1.5)	3.0 (1.4)	0.9
CDAI, mean (SD)	14.3 (11.8)	16.2 (12.7)	13.6 (11.4)	0.25
RAFQ, mean (SD)	15.8 (11.5)	16.4 (11.2)	15.6 (11.7)	0.7
Pain intensity (0-10), mean (SD)	3.5 (2.5)	3.4 (2.4)	3.5 (2.5)	0.79
MD global (0-10), mean (SD)	3.6 (2.2)	3.9 (2.0)	3.5 (2.3)	0.38
Patient global (0-10), mean (SD)	3.2 (2.5)	3.2 (2.3)	3.2 (2.6)	0.85
ESR (mm/hr), mean (SD)	18.5 (18.6)	18.7 (24.2)	18.5 (16.2)	0.95
Methotrexate, n(%)	106 (69.3)	30 (73.2)	76 (67.9)	0.69
Oral Steroids, n(%)	61 (39.9)	20 (48.8)	41 (36.6)	0.2
Advanced therapy in first 9 months, n (%)	57 (37.3)	19 (46.3)	38 (33.9)	0.19

RDCI Rheumatic Disease Comorbidity Index; TJC tender joint count; SJC swollen joint count; MDGA MD global assessment; PTGA patient global assessment; CDAI Clinical Disease Activity Index; *Stringent RA worsening denote those who meet 1) an increase in DAS28 >1.2 and worsening of disease state by > 1 category (remission or low disease activity to moderate disease activity or moderate disease activity to high disease activity) or 2) an increase in CDAI>10 and worsening of disease state by >1 category

[Δ] Treatments (biologics and Janus Kinase inhibitors) reported at later timepoint as low frequencies expected at baseline visit

Results: The 153 eRA patients were mainly White (75%) women (82%) with a mean (SD) age of 50 (17). Initial DAS28 was 3.0 (1.4), and CDAI was 14.3(11.8). Most (70%) received an MTX (Table 1). Compared with those who did not worsen, subjects who later worsened had higher baseline mean (SD) comorbidity scores 1.3(1.4) vs 0.73(1.3), (p=0.02). More had osteoarthritis, 29.3% vs 11.6% (p=0.012). Significant differences in patient outcomes including RAFQ, joint counts and pain scores were observed between pre-RA worsening and RA worsening visits (Table 2). A mean increase in RAFQ of 9.7 (95%CI 5.1, 14.3) was seen for DAS28-defined worsening and 13.2(95%CI 5.9, 20.6) for CDAI-defined worsening (Table 3).

Conclusion: Significant worsening in RA is consistently observed using multiple RA clinical outcomes and PROs between pre-worsening and worsening visits, demonstrating the stringency and clinical relevance of applied definitions of RA worsening. An increase in the RAFQ of 10-13 in patients meeting clinical definitions of worsening is similar to that of patients reporting they were "a lot worse"[1]. These findings demonstrate a consistent value of measures indicating a patient's worsening of RA between clinician- and patient-based composite measures. These data suggest that any of these measures can inform designation of clear RA disease worsening for future translational research.

Table 2: Comparing Clinical Outcomes between Pre-RA worsening and RA Worsening Visits (N=41)*

	Pre-RA worsening visit	RA worsening Visit	p-value
RAFQ, mean (SE)	13.2 (1.7)	22 (2.2)	0.000
Swollen joint count, mean (SE)	1.4 (0.6)	6.5 (1.0)	0.000
Tender joint count, mean (SE)	0.7 (0.3)	8.9 (1.2)	0.000
ESR, mean (SE)	12.4 (2.3)	22.4 (3.5)	0.000
Patient Global Assessment, mean (SE	2.2 (0.3)	4.4 (0.4)	0.000
Rapid 3, mean (SE)	1.9 (0.3)	3.7(0.4)	0.000
Pain intensity, mean (SE)	2.4 (0.3)	4.8 (0.5)	0.000

*Stringent RA worsening criteria 1) an increase in DAS28 >1.2 and worsening of disease state by > 1 category or 2) an increase in CDAI>10 and worsening of disease state by >1 category Change in outcomes determined from their pre-worsening (lowest DAS28 or CDAI score prior to worsening) visit and their designated RA worsening visit (maximal DAS28 or CDAI score) using paired t-tests using either DAS28 or CDAI flare; for those meeting both definitions, data for DAS28 was used

SE standard error

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Change in RA-FQ by stringent RA disease worsening critera*

	DAS28-defined worsening (N=25)			CDAI-defined worsening (N=21)		
	Δ	95%CI	SD	Δ	95% CI	SD
RA-FQ (range 0-50)	9.7	(5.1, 14.3)	11.1	13.2	(5.9, 20.6)	16.1
RA-FQ Components(0-10)						
Pain	2.5	(1.4, 3.6)	2.6	2.9	(1.4, 4.4)	3.4
Physical Function	2.3	(1.0, 3.6)	3.1	2.95	(1.0, 4.9)	4.2
Fatigue	1.2	(0.0, 2.4)	2.9	2	(0.4, 3.7)	3.6
Stiffness	2.1	(1.1, 3.0)	2.3	2.29	(0.5, 4.1)	4
Participation	1.7	(0.8, 2.6)	2.3	3.1	(1.7, 4.5)	3.1

*Stringent RA worsening criteria 1) an increase in DAS28 >1.2 and worsening of disease state by > 1 category or 2) an increase in CDAI>10 and worsening of disease state by >1 category

Change in RAFQ determined from their pre-worsening (lowest DAS28 or CDAI score prior to worsening) visit and their designated worsening visit (maximal DAS28 or CDAI score) using paired t-tests

1. Bartlett S et al. Qual Life Res. 2023 May;32(5):1307-18

Disclosure: C. Meng: None; **C. Julia**: None; **K. Gripp**: None; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1; **S. Bartlett**: Accord, 2, Nordic, 2, PROMIS Health Organization, 4, Sandoz, 2; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **V. Bykerk**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, E.R. Squibb & Sons, 2, Janssen, 2, L.L. C, 2, Organon, 2, Pfizer, 2.

Abstract Number: 0442

Beyond the Joints: The Impact of Non-Articular Pain on Patient-Reported Function in a Longitudinal Real-World Early RA Cohort

Charis Meng[1], Marie-France Valois[2], Caci Julia[3], Yvonne Lee[4], Bindee Kuriya[5], Gilles Boire[6], Hugues Allard-Chamard[7], Carol Hitchon[8], Louis Bessette[9], Glen Hazlewood[10], Carter Thorne[11], Susan J. Bartlett[12], Janet Pope[13] and Vivian Bykerk[1], [1]Hospital for Special Surgery, New York, NY, [2]McGill University, Pointe-Claire, QC, Canada, [3]Hospital for Special Surgery, New York, [4]Northwestern University, Chicago, IL, [5]Mount Sinai Health, Toronto, Canada, [6]Retired, Sherbrooke, QC, Canada, [7]Université de Sherbrooke, Sherbrooke, Canada, [8]University of Manitoba, Winnepeg, Canada, [9]Centre de l'Ostoporose et de Rhumatologie de Qubec, Quebec, QC, Canada, [10]University of Calgary, Calgary, AB, Canada, [11]Southlake Regional Health Centre, Newmarket, ON, Canada, [12]McGill University, Beaconsfield, QC, Canada, [13]University of Western Ontario, London, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: A third of patients with early (e)RA report pain outside the joint or non-articular pain (NAP) despite RA treatment(1). NAP, both regional and widespread, impairs HR-QOL and negatively impacts remission outcomes in eRA(1). Patients with eRA report having NAP in both upper body areas nearly twice as often as both lower body areas(1). How NAP, both regional and widespread, impacts physical function, including that of upper extremities, is not well understood. We aim to evaluate the impact of NAP, regional and widespread, on physical function using 3 instruments 1) Multi-Dimensional Health Assessment Questionnaire (MDHAQ) 2) PROMIS29 Physical Function (PF) 3) Neuro-QOL Upper Extremity (UE) Function (assesses reach function and ADLs) (2), at baseline and over the first year of RA diagnosis and treatment.

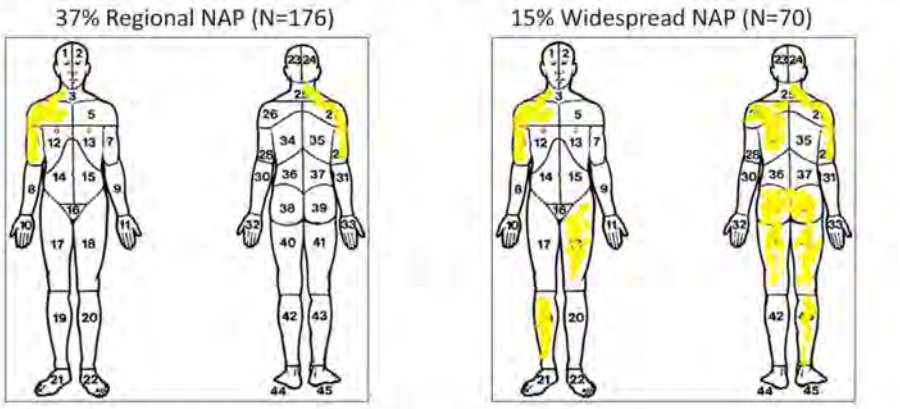
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Characteristics across NAP patterns in Early RA Cohort

	Total Sample (N = 472)	No NAP (N = 226)	Regional NAP (N = 176)	Widespread NAP (N=70)
Age (year), mean (SD)	57 (14)	58 (14)	56 (14)	56 (14)
Female, n (%)	313 (66)	146 (65)	118 (67)	49 (70)
White, n (%)	380 (81)	174 (77)	149 (85)	57 (81)
BMI (kg/m^2) mean (SD)	28.45 (7.0)	28.0 (6.9)	28.7 (6.9)	29.6 (7.5)
Rheumatic Disease Comorbidity Index (0-9), mean (SD)	1.4 (1.4)	1.2 (1.3)	1.4 (1.3)	1.8 (1.6)
Current smoker, n(%)	70 (15)	29 (13)	27 (15)	14 (20)
CDAI, mean (SD)	27.0 (14.1)	26.6 (14.9)	26.4 (12.8)	29.4 (14.5)
MDHAQ, 10 items (0-3)	0.8 (0.6)	0.7 (0.6)	0.9 (0.5)	1.2 (0.6)
PROMIS29 Physical function (T-score), mean (SD)*	40.8 (7.9)	42.4 (8.3)	39.9 (6.9)	38.1 (8.2)
NeuroQol UE Function (T-score), mean (SD)*	37.6 (10.5)	39.9 (11.1)	36.2 (9.6)	34.0 (9.4)

*Reported by MD or patient; RDCI Rheumatic Disease Comorbidity Index; CDAI Clinical Disease Activity Index; MDHAQ Multi-Dimensional Health Assessment Questionnaire; Neuro-QOL UE Neuro-Quality of Life Upper Extremity
* Lower T-scores for function reflect worse perceived function

Figure: Baseline prevalence of regional and widespread NAP in early RA cohort (N=472)



Figures are illustrative examples of regional and widespread NAP, adapted from Margolis body pain diagram
Prevalence calculated for total cohort N=472

Table 2: A Mixed Effects Model* of Mean-Change in Patient-Reported Function by 3 Instruments across NAP groups over First Year of RA

	Mean-Change	(95% CI)
MDHAQ (0-3)		
No NAP	Reference	
Regional NAP	**0.5**	**(0.3, 0.6)**
Widespread NAP	**1.3**	**(1.0, 1.6)**
PROMIS29 Physical Function T-Score		
No NAP	Reference	
Regional NAP	**-1.7**	**(-2.4, -1.0)**
Widespread NAP	**-3.5**	**(-4.8, -2.3)**
NeuroQoL Upper Extremity T-score		
No NAP	Reference	
Regional NAP	**-1.6**	**(-2.5, -0.6)**
Widespread NAP	**-5.2**	**(-6.8, -3.5)**

*fullly adjusted multivariate mixed effects model adjusted for baseline age, sex, education, smoking, comorbidities, seropositivity and time-variant CDAI
CI confidence interval; MDHAQ Multidimensional Health Questionnaire
Worse function reflected in higher MDHAQ scores and lower T-scores for PROMIS and NeuroQOL

Methods: Data were from patients with active early RA (symptoms< 1 year, CDAI >2.8) enrolled in the Canadian Early Arthritis Cohort between Jan/2017-10/2023. Patients were instructed to indicate any non-joint pain they experienced on a body pain diagram (BPD) at baseline (BL), and 6- and 12-month follow-up visits. Prespecified NAP patterns were classified based

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

on pain reported in 5 sections (4 quadrants and axial, excluding hands and feet) and grouped as: 1) no NAP (no sections selected on BPD), 2) regional (1-3 sections) or 3) widespread NAP(3+sections). Patients completed synchronous assessments of physical function: MDHAQ (0-3), PROMIS29 PF and Neuro-QoL UE function T-scores (mean is 50, 1 standard deviation is 10) over 1-year. Adjusted associations between NAP and physical function were estimated in separate multivariable mixed effects models adjusted for baseline age, sex, education, smoking, comorbidities, seropositivity and time-variant CDAI.

Results: The 472 eRA patients were mostly female (66%) with a mean (SD) age of 57(14) and had active disease at baseline, with a mean (SD) CDAI 27.0 (14.1) (Table 1). Most (79%) were treated with methotrexate. Regional NAP was more prevalent than widespread (Figure). Compared to other groups, those with widespread NAP more often had higher BMI, reported more comorbidities, smoked and had higher CDAIs. NAP was associated with worse baseline function assessed by MDHAQ, PROMIS29 PF and Neuro-QOL UE function in a dose-response manner across pain groups (none, regional and widespread NAP). The adjusted regression analyses similarly exhibited a dose-response effect of NAP on physical function with worsening in all 3 outcomes over 1-year (Table 2). All relationships were statistically significant. Neuro-QoL UE T-scores worsened by close to half a standard deviation in those with widespread NAP (Table 2).

Conclusion: NAP is common in eRA and negatively impacts physical function, including that of upper extremities, at baseline and over the first year of RA diagnosis and treatment. Worse physical function by all 3 instruments were observed with greater NAP distribution. Early identification and targeted intervention of NAP is recommended to help prevent long-term disability in patients with RA.

1. Meng C. Characterizing NAP at early RA diagnosis. A&R. 2025 Apr;77(4):405-413.
2. Bartlett SJ. The Neuro-QOL upper extremity function scale. ARD. 2021;80(Suppl 1):159-60.

Disclosure: C. Meng: None; **M. Valois**: None; **C. Julia**: None; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1; **B. Kuriya**: AbbVie/Abbott, 1, Pfizer, 1; **G. Boire**: Biocon, 5, Sanofi, 1; **H. Allard-Chamard**: AbbVie, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 1, 5, 6, GlaxoSmithKlein(GSK), 1, Janssen, 1, 5, 6, Kabi, 1, 5, 6, Novartis, 1, 6, Otsuka, 1, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Sobi, 1, 5, 6; **C. Hitchon**: Accord, 1, Astra-Zeneca, 1, Frensnius-Kabi, 1, Pfizer, 5, Sanofi, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, 5, 6, Fresenius Kabi, 2, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, TEVA, 2, 6, UCB, 2, 5, 6; **G. Hazlewood**: None; **C. Thorne**: Accord, 1, 2, Jamp, 2, 5, Medac/Medexus, 1, 2, 6, Nordic, 2, Sandoz, 1, 2, 6; **S. Bartlett**: Accord, 2, Nordic, 2, PROMIS Health Organization, 4, Sandoz, 2; **J. Pope**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Frese, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mallinckrodt Pharmaceuticals, 2, 5, Merck/MSD, 2, Mitsubishi Tanabe Pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2, Sanofi, 2, Teva, 2, UCB, 2, Viatris, 2; **V. Bykerk**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, E.R. Squibb & Sons, 2, Janssen, 2, L.L.C, 2, Organon, 2, Pfizer, 2.

Abstract Number: 0443

Association Between Pan-immune-inflammation and Synovitis as Assessed by Ultrasound in Rheumatoid Arthritis

Elvira E Aguilar-Oliva[1], Luis M Amezcua-Guerra[2], ismael valenzuela[3], Carina Soto-Fajardo[4], Karina Arias[5], Alejandra Espinosa[6], Carlos Pineda[4] and Luis H Silveira[7], [1]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, TLALPAN, Distrito Federal, Mexico, [2]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico city, [3]Instituto Nacional de Cardiología Ignacio Chávez, TLALPAN, Distrito Federal, Mexico, [4]National Rehabilitation Institute " Luis Guillermo Ibarra Ibarra ", Mexico City, Mexico, [5]Instituto Nacional de Rehabilitación Luis Guillermo Ibarra Ibarra, Tlalpan, Distrito Federal, Mexico, [6]National Rehabilitation Institute " Luis Guillermo Ibarra Ibarra ", Ciudad de Mexico, Mexico, [7]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

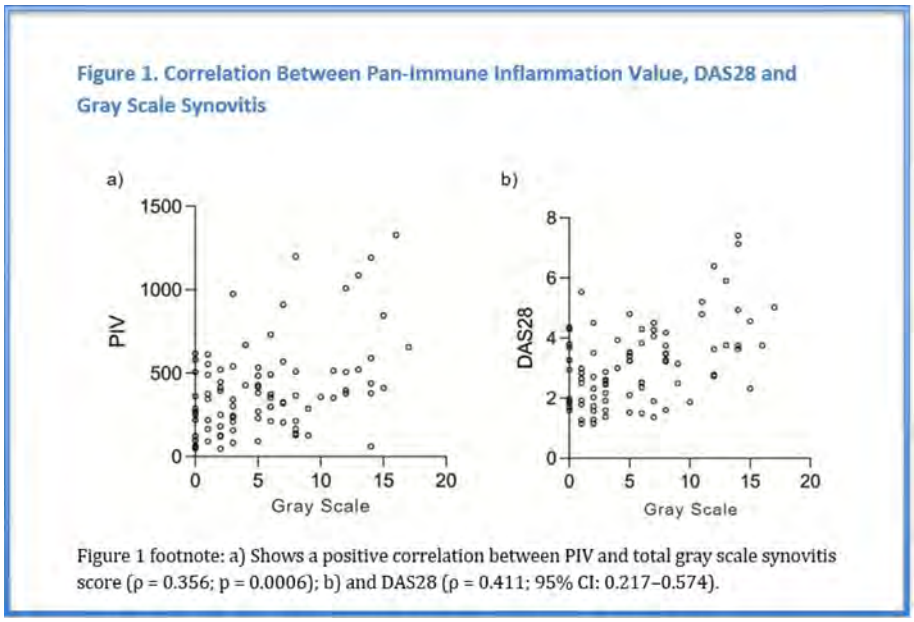
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The pan-immune-inflammation value (PIV) is a novel composite biomarker derived from blood count parameters, reflecting the systemic balance of immune-inflammatory activity. Although it has been explored in various inflammatory conditions, its association with ultrasound-detected synovitis in rheumatoid arthritis (RA) remains uncharacterized. Musculoskeletal ultrasound provides a sensitive modality for detecting synovitis through semiquantitative grading of gray scale (GS) and power Doppler (PD) signals on a 0–3 scale for each joint.

To evaluate the association between PIV and synovitis, as assessed by GS and PD scores, and to compare these correlations with clinical disease activity (DAS28) and functional disability (HAQ-DI) in patients with RA.

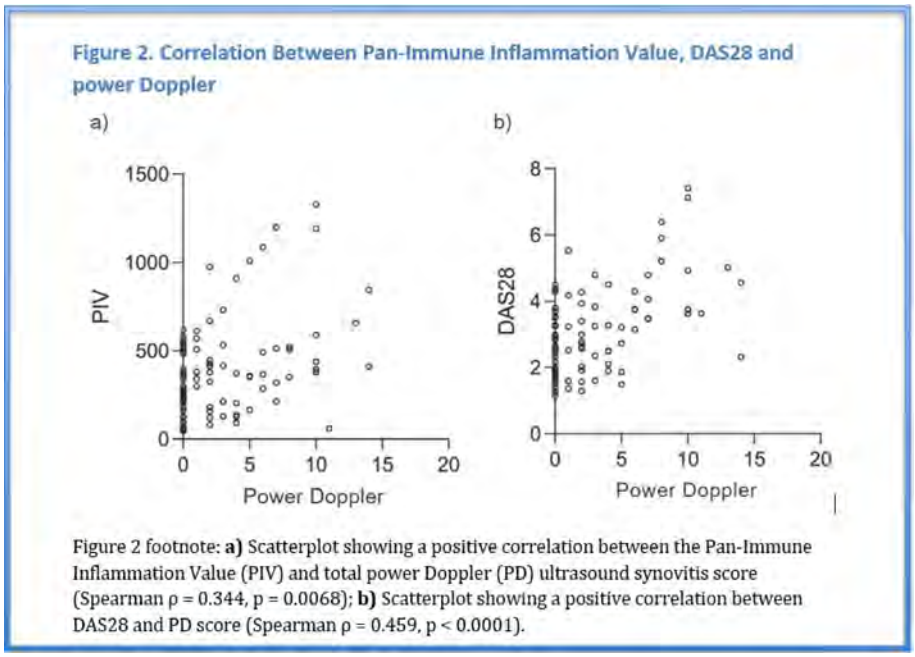
Methods: RA patients were prospectively recruited from a single-center cohort. Bilateral wrists and the second and third metacarpophalangeal (MCP) joints were assessed using the EULAR-OMERACT semiquantitative scoring system. PIV was calculated as: (neutrophils × monocytes × platelets) / lymphocytes). Spearman's ρ coefficients with 95% confidence intervals (CIs) were used to assess relationships between PIV, DAS28, HAQ-DI, and ultrasound scores. Multivariable linear regression models were developed using GS and PD scores as dependent variables. PIV values were also compared against a reference population of healthy adults from Mexico City.

Results: Seventy patients with RA were recruited and compared with 2,170 healthy adults. GS scores were significantly correlated with PIV (ρ = 0.356; 95% CI: 0.155–0.529) and DAS28 (ρ = 0.411; 95% CI: 0.217–0.574), but not with HAQ-DI (ρ = 0.027; 95% CI: –0.180 to 0.239). Similarly, PD scores correlated with both PIV (ρ = 0.344; 95% CI: 0.141–0.519) and DAS28 (ρ = 0.459; 95% CI: 0.273–0.612), but not with HAQ-DI (ρ = 0.069; 95% CI: –0.145 to 0.279). In multivariable models, PIV (β = 0.0061, p = 0.001) and DAS28 (β = 1.120, p = 0.014) were independently associated with GS scores; both PIV (β = 0.0043, p = 0.004) and DAS28 (β = 0.960, p = 0.007) also emerged as independent predictors of PD scores. Notably, 42% of RA patients had PIV values exceeding the 75th percentile (285.3) of the healthy reference population.



Correlation Between Pan-Immune Inflammation Value, DAS28 and Gray Scale Synovitis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Correlation Between Pan-Immune Inflammation Value, DAS28 and power Doppler

Conclusion: Ultrasound-detected synovitis is independently associated with systemic inflammatory activity as measured by the PIV and with clinical disease activity assessed by DAS28, but not with patient-reported functional disability. These findings suggest that PIV may represent a useful, non-invasive biomarker for quantifying inflammatory burden in RA.

Disclosure: E. Aguilar-Oliva: None; **L. Amezcua-Guerra**: None; **i. valenzuela**: None; **C. Soto-Fajardo**: None; **K. Arias**: None; **A. Espinosa**: None; **C. Pineda**: None; **L. Silveira**: None.

Abstract Number: 0444

Low Disease Activity: Good Enough?

Emily Thoman[1], Sebastiano Porcu[1] and Martin Bergman[2], [1]Lankenau Medical Center, Wynnewood, PA, [2]Drexel University College of Medicine, Philadelphia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Treat-to-target is the guiding principle and therapeutic strategy for rheumatoid arthritis (RA) treatment. Escalation of treatment is based on the regular assessment of disease activity to attain and maintain an established target. Although remission is the preferred target of treatment, low disease activity (LDA (CDAI >2.8 and ≤10)) may be an acceptable target. It remains unclear if patients attaining LDA have incremental benefit after 1 to 2 years, if they can remain with a CDAI < 10. This study aims to evaluate differences in outcomes among patients with RA treated to LDA and then followed over a two-year period.

Methods: Data were collected from 522 adult patients in a private practice with established RA treated with advanced therapies, who completed a questionnaire at every visit and were evaluated with a physical exam. Those who attained LDA at

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Study Groups

	Remission (CDAI ≤ 10 at baseline & ≤ 2.8 at Year 1 after baseline)	VLDA (CDAI ≤ 10 at baseline & ≤ 2.9-6 at Year 1)	HLDA (CDAI ≤ 10 at baseline & ≤ 6.1-10 at Year 1)
Number of subjects	47	53	43
Age	62.24±15.35	62.96±13.55	65.06±14.17
Sex (% Male)	32	28	24
Disease Duration (years)	9.99±8.66	12.73±10.86	12.15±11.68
Tender joint count	0.06±0.25	0.19±0.44	0.35±0.87
Swollen joint count	0.19±0.50	0.83±1.33	1.95±2.45
Physician global	0.48±0.60	1.16±1.03	1.59±2.45
Functional component of MDHAQ (0-3)	0.25±0.32	0.43±0.42	0.44±0.34
Pain scale (0-10)	0.80±0.88	2.42±1.64	3.77±2.23
Patient global severity (0-10)	0.74±0.66	2.47±1.59	3.98±1.92
Fatigue scale (0-10)	1.31±1.76	2.68±2.19	4.22±2.74
Damaged Joints	1.51±2.52	2.74±4.05	3.23±3.95
Replaced Joints	0.17±0.52	0.38±1.03	0.49±1.47
Depression problems (0-3)	0.19±0.45	0.25±0.62	0.21±0.47
Clinical Disease Activity Index (CDAI)	1.48±0.84	4.65±1.09	7.87±1.09
DAS28 CPR3	1.63±0.36	1.81±0.48	1.98±0.51
RAPID3	2.37±1.92	6.33±3.96	9.00±4.44

VLDA: very low disease activity; HLDA: high low disease activity; RA: rheumatoid arthritis

baseline = 1 year a low disease activity

baseline and remained with CDAI < 10 at 1 and 2 years were studied. Data included patient demographics, disease duration, smoking status, CDAI, DAS28, RAPID3, MDHAQ function (FN), pain VAS, patient global VAS (PtGlb), MDHAQ fatigue, joint replacements, depression, swollen joints, tender joints, physician global VAS (DocGlb), ESR and CRP. At Year 1 and 2, Remission was defined as CDAI < 2.8, Very Low Disease Activity (VLDA) was defined as CDAI ≥ 2.8 and ≤ 6, and High LDA (HLDA) was defined as CDAI > 6 and ≤ 10. Data were analyzed with two-sample T tests.

Results: 143 patients with established RA with low CDAI at baseline receiving DMARD therapy (CS-DMARD, B-DMARD, or TS-DMARD) were followed at 1 and 2 years. 47 (33%) patients achieved remission, 53 (37%) achieved VLDA, and 43 (30%) patients achieved HLDA at follow-up. Patients who achieved remission had improved documented global scores and MDHAQ function scores compared to patients in VLDA and HLDA at both 1 and 2 years (p< 0.05), and less damaged joints

Table 2: Unadjusted Univariate Results by Disease Activity Status at Year 1 & 2

	n	Remission (CDAI ≤ 10 at baseline & ≤ 2.8 at Year 1)	VLDA (CDAI ≤ 10 at baseline & ≥ 2.8 and ≤ 6 at Year 1)	HLDA (CDAI ≤ 10 at baseline & > 6 and ≤ 10 at Year 1)	P-value (remission vs. VLDA CDAI)	P-value (remission vs. HLDA CDAI)
Number of subjects		47	53	43		
1-Year Post Baseline Assessment						
Tender joints	143	0.06±0.25	0.19±0.44	0.35±0.87	0.0893	**0.0339**
Swollen joints	143	0.019±0.50	0.83±1.33	1.95±2.45	**0.0024**	**<0.0001**
Docglb	143	0.48±0.60	1.16±1.03	1.59±1.31	**0.0001**	**<0.0001**
MDHAQ score (0-3)	143	0.25±0.32	0.43±0.42	0.44±0.34	**0.0169**	**0.0084**
MDHAQ fatigue score	141	1.31±1.76	2.68±2.19	4.22±2.74	**0.0009**	**<0.0001**
Replaced joints	139	2 (4.26%)	4 (7.55%)	9(20.93%)	0.2028	0.1677
Damaged joints	141	9(19.15%)	15(28.3%)	13(30.23%)	0.0766	**0.0147**
2-Year Post Baseline Assessment						
Tender joints	143	0.02±0.14	0.22±0.52	0.27±0.60	**0.0102**	**0.0069**
Swollen joints	143	0.10±0.37	0.96±1.11	2.06±2.41	**<0.0001**	**<0.0001**
Docglb	143	0.48±0.53	1.07±0.84	1.64±1.25	**0.0001**	**<0.0001**
MDHAQ score (0-3)	143	0.21±0.32	0.38±0.39	0.60±0.40	**0.0236**	**<0.0001**
MDHAQ fatigue score	141	1.23±1.40	2.44±2.14	4.05±2.41	**0.0016**	**<0.0001**
Replaced joints	139	2(1.43%)	9(16.98%)	4(9.3%)	0.1619	0.3242
Damaged joints	141	11(23.4%)	15(28.3%)	15(34.88%)	0.074	0.3427

VLDA: very low disease activity; HLDA: high low disease activity; MDHAQ: Multidimensional Health Assessment Questionnaire

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

compared to patients in HLDA at 1 year ($p< 0.05$). Remission was not significant for less damaged joints compared to VLDA. There was no observable difference at 1 or 2 years in age, sex, duration of disease, self-reported joint replacements or depression scores between patients who achieved remission vs VLDA vs HLDA. Similarly, patients in VLDA did better than those in HLDA. At year 1: Swollen Count, Pain, PtGlb, Fatigue and RAPID3, and at Year 2: Swollen Count, DocGlb, Fn, Pain, PtGlb, Fatigue, DAS28-CRP and RAPID3 were all significantly better in VLDA vs. HLDA ($p< 0.05$).

Conclusion: Patients who successfully achieved remission from a baseline of low disease activity were found to have improved functional and clinical outcomes after 1 and 2 years. Patients who achieved VLDA had improvement but to a lesser degree. Finally, while remaining in LDA, patients in HLDA had worse outcomes compared to Remission or VLDA.

Disclosure: E. Thoman: None; **S. Porcu**: None; **M. Bergman**: JNJ, 12, Stock Ownership.

Abstract Number: 0445

GLP-1 Receptor Agonists Reduce Mortality and Cardiovascular Events in Patients with Rheumatoid Arthritis

Giorgos Loizidis and Ross summer, Thomas Jefferson University, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Obesity significantly increases cardiovascular morbidity and mortality in rheumatoid arthritis (RA), yet effective strategies for managing obesity-related risks in this population remain limited. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) offer substantial cardiometabolic benefits in diabetic populations, but their effects in obese RA patients without diabetes are not well defined. This study investigated whether GLP-1 RA therapy reduces one-year all-cause mortality and major adverse cardiovascular events (MACE) in non-diabetic obese RA patients.

Methods: This retrospective cohort study utilized the TriNetX platform, selecting adults (≥18 years) with RA, obesity (BMI ≥30 kg/m^2), and no history of diabetes mellitus. Patients initiating GLP-1 RA treatment (semaglutide, liraglutide, tirzepatide) were propensity score–matched (1:1) with RA controls not receiving GLP-1 RA therapy, balancing demographics, BMI categories, cardiovascular comorbidities, immunosuppressive therapies, and cardiometabolic medications. The primary endpoint was all-cause mortality at one year; secondary outcomes included new-onset MACE (heart failure, myocardial infarction, stroke) (Table 1)

Results: The matched analysis included 2,698 patients per group (Table 2). GLP-1 RA treatment was associated with significantly reduced one-year all-cause mortality compared to matched controls (0.37% vs. 0.93%; HR, 0.14; 95% CI, 0.04–0.47; p=0.0002). Additionally, MACE incidence was significantly lower in the GLP-1 RA group (1.09% vs. 2.19%; HR, 0.60; 95% CI, 0.38–0.95; p=0.026), driven primarily by fewer heart failure events (0.74% vs. 1.71%; HR, 0.52; 95% CI, 0.31–0.90; p=0.017). Myocardial infarction and cerebrovascular infarction rates were not significantly different between groups. (Table 3)

Conclusion: In obese, non-diabetic RA patients, GLP-1 RA therapy significantly reduced one-year all-cause mortality and cardiovascular events, particularly heart failure. These results highlight GLP-1 RAs as a promising therapeutic option for cardiometabolic risk reduction in RA. Prospective trials are warranted to confirm these findings.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographic and Clinical Characteristics of RA Patients With vs Without GLP-1 RA (Before Propensity Score Matching)

Characteristic	RA–GLP-1 RA(n=2,774) No. (%) or mean ± SD	RA–no–GLP1 RA(n=49,993) No. (%) or mean ± SD	p-value	Std. Diff.
Demographics				
Age (years), mean ± SD	53.7 ± 11.7	56.1 ± 14.1	<0.001	0.184
Female	2,375 (85.6)	36,423 (72.9)	<0.001	0.319
White	1,899 (68.5)	34,394 (68.8)	0.706	0.007
Black	448 (16.1)	6,834 (13.7)	<0.001	0.070
Asian	30 (1.1)	606 (1.2)	0.539	0.012
BMI (kg/m²), mean ± SD	38.4 ± 7.4	34.1 ± 5.9	<0.001	0.642
Cardiovascular Comorbidities				
Smoking	151 (5.4)	3,332 (6.7)	<0.012	0.051
Prediabetes	444 (16.0)	1,033 (2.1)	<0.001	0.501
Hypertension	1,175 (42.4)	14,909 (29.8)	<0.001	0.263
Hyperlipidemia	588 (21.2)	6,977 (14.0)	<0.001	0.191
Fatty liver disease	196 (7.1)	777 (1.6)	<0.001	0.274
Coronary artery disease	191 (6.9)	3,028 (6.1)	0.076	0.034
Heart failure	99 (3.6)	1,804 (3.6)	0.913	0.002
Myocardial infarction (acute)	15 (0.5)	489 (1.0)	0.021	0.050
History of myocardial infarction	21 (0.8)	611 (1.2)	0.028	0.047
Peripheral vascular disease	75 (2.7)	1,152 (2.3)	0.174	0.026
Atrial fibrillation	73 (2.6)	1,524 (3.0)	0.212	0.025
Cerebrovascular accident	26 (0.9)	529 (1.1)	0.544	0.012
Chronic kidney disease	115 (4.1)	1,763 (3.5)	0.087	0.032
Pulmonary Comorbidities				
Obstructive sleep apnea	659 (23.8)	3,799 (7.6)	<0.001	0.456
COPD	115 (4.1)	2,575 (5.2)	0.019	0.048
Pulmonary fibrosis	25 (0.9)	625 (1.3)	0.105	0.034
Rheumatoid lung disease	10 (0.4)	195 (0.4)	0.808	0.005
Pulmonary hypertension	55 (2.0)	693 (1.4)	0.010	0.046
Pulmonary embolism	44 (1.6)	509 (1.0)	0.004	0.050
GLP-1 Receptor Agonists				
Semaglutide	1,853 (66.8)	0 (0.0)	<0.001	2.006
Tirzepatide	550 (19.8)	0 (0.0)	<0.001	0.703
Liraglutide	379 (13.7)	0 (0.0)	<0.001	0.563

Characteristic	RA–GLP-1 RA(n=2,774) No. (%) or mean ± SD	RA–no–GLP1 RA(n=49,993) No. (%) or mean ± SD	p-value	Std. Diff.
Anti-inflammatory and Glucocorticoids				
Chronic use of NSAIDs	101 (3.6)	1,350 (2.7)	0.003	0.054
Glucocorticoids	1,780 (64.2)	29,289 (58.6)	<0.001	0.115
Immunosuppressive Agents				
Methotrexate	857 (30.9)	22,552 (45.1)	<0.001	0.296
Azathioprine	24 (0.9)	602 (1.2)	0.108	0.034
Sulfasalazine	163 (5.9)	3,890 (7.8)	<0.001	0.076
Hydroxychloroquine	788 (28.4)	16,681 (33.4)	<0.001	0.108
TNF inhibitors	585 (21.1)	8,534 (17.1)	<0.001	0.102
Abatacept	131 (4.7)	1,196 (2.4)	<0.001	0.126
JAK inhibitors	226 (8.1)	1,652 (3.3)	<0.001	0.210
Rituximab	50 (1.8)	789 (1.6)	0.358	0.017
Tocilizumab	88 (3.2)	738 (1.5)	<0.001	0.113
Sarilumab	17 (0.6)	84 (0.2)	<0.001	0.071
Psychiatric Comorbidity				
Depression	373 (13.4)	2,123 (4.2)	<0.001	0.328
Medications for Heart Disease, Hyperlipidemia, Dysglycemia				
β blockers	634 (22.9)	8,446 (16.9)	<0.001	0.150
ACE inhibitors	272 (9.8)	4,843 (9.7)	0.838	0.004
ARBs	472 (17.0)	4,405 (8.8)	<0.001	0.246
Aldosterone antagonists	170 (6.1)	1,538 (3.1)	<0.001	0.146
Sodium-glucose co-transporter 2 inhibitors	70 (2.5)	83 (0.2)	<0.001	0.206
Metformin	267 (9.6)	576 (1.2)	<0.001	0.382
Ezetimibe	56 (2.0)	454 (0.9)	<0.001	0.093
Statins	647 (23.3)	8,580 (17.2)	<0.001	0.154
Evolocumab	14 (0.5)	52 (0.1)	<0.001	0.073
Alirocumab	10 (0.4)	27 (0.1)	<0.001	0.067
Aspirin	236 (8.5)	5,492 (11.0)	<0.001	0.084
Clopidogrel	39 (1.4)	901 (1.8)	0.125	0.032
Rivaroxaban	39 (1.4)	620 (1.2)	0.444	0.015

Characteristic	RA–GLP-1 RA(n=2,774) No. (%) or mean ± SD	RA–no–GLP1 RA(n=49,993) No. (%) or mean ± SD	p-value	Std. Diff.
Apixaban	97 (3.5)	1,073 (2.1)	<0.001	0.082
Warfarin	24 (0.9)	999 (2.0)	<0.001	0.095
Loop diuretics	222 (8.0)	3,627 (7.3)	0.140	0.028
Chronic Pain Syndromes (Not Controlled for)				
Osteoarthritis	1,172 (42.2)	18,914 (37.8)	<0.001	0.090
Low back pain	420 (15.1)	4,415 (8.8)	<0.001	0.195
Fibromyalgia	376 (13.6)	4,161 (8.3)	<0.001	0.168

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Baseline Demographic and Clinical Characteristics of RA Patients With vs. Without GLP-1 RA (After Propensity Score Matching)

Characteristic	RA–GLP-1 RA (n=2,698) No. (%) or Mean ± SD	RA–no–GLP-1 RA (n=2,698) No. (%) or Mean ± SD	p-value	Std. Diff.
Demographics				
Age (years), mean ± SD	53.7 ± 11.8	53.9 ± 14.2	0.573	0.015
Female	2,305 (85.4)	2,364 (87.6)	0.019	0.064
White	1,852 (68.6)	1,853 (68.7)	0.977	0.001
Black	432 (16.0)	454 (16.8)	0.419	0.022
Asian	28 (1.0)	27 (1.0)	0.892	0.004
BMI (kg/m²), mean ± SD	38.3 ± 7.4	37.4 ± 7.1	< 0.001	0.131
Cardiovascular Comorbidities				
Smoking	146 (5.4)	155 (5.7)	0.593	0.015
Prediabetes	392 (14.5)	350 (13.0)	0.097	0.045
Hypertension	1,125 (41.7)	1,143 (42.4)	0.620	0.014
Hyperlipidemia	561 (20.8)	566 (21.0)	0.867	0.005
Fatty liver disease	176 (6.5)	178 (6.6)	0.912	0.003
Coronary artery disease	182 (6.7)	165 (6.1)	0.345	0.026
Heart failure	94 (3.5)	91 (3.4)	0.822	0.006
Myocardial infarction (acute)	15 (0.6)	19 (0.7)	0.491	0.019
History of myocardial infarction	21 (0.8)	23 (0.9)	0.762	0.008
Peripheral vascular disease	74 (2.7)	76 (2.8)	0.868	0.005
Atrial fibrillation	70 (2.6)	62 (2.3)	0.481	0.019
Cerebrovascular accident	26 (1.0)	24 (0.9)	0.776	0.008
Chronic kidney disease	111 (4.1)	113 (4.2)	0.891	0.004
Pulmonary Comorbidities				
Obstructive sleep apnea	611 (22.6)	641 (23.8)	0.333	0.026
COPD	111 (4.1)	114 (4.2)	0.838	0.006
Pulmonary fibrosis	25 (0.9)	23 (0.9)	0.772	0.008
Rheumatoid lung disease	10 (0.4)	10 (0.4)	1.000	< 0.001
Pulmonary hypertension	50 (1.9)	56 (2.1)	0.556	0.016
Pulmonary embolism	43 (1.6)	42 (1.6)	0.913	0.003
GLP-1 Receptor Agonists				
Semaglutide	1,802 (66.8)	0 (0.0)	< 0.001	2.006
Tirzepatide	537 (19.9)	0 (0.0)	< 0.001	0.705
Liraglutide	366 (13.6)	0 (0.0)	< 0.001	0.560
Anti-inflammatory and Glucocorticoids				
Chronic use of NSAIDs	100 (3.7)	101 (3.7)	0.943	0.002
Glucocorticoids	1,722 (63.8)	1,728 (64.0)	0.865	0.005
Immunosuppressive Agents				
Methotrexate	834 (30.9)	768 (28.5)	0.049	0.054
Azathioprine	24 (0.9)	17 (0.6)	0.272	0.030
Sulfasalazine	158 (5.9)	153 (5.7)	0.770	0.008
Hydroxychloroquine	776 (28.8)	818 (30.3)	0.210	0.034
TNF inhibitors	562 (20.8)	540 (20.0)	0.458	0.020
Abatacept	127 (4.7)	111 (4.1)	0.289	0.029
JAK inhibitors	216 (8.0)	227 (8.4)	0.585	0.015
Rituximab	48 (1.8)	53 (2.0)	0.615	0.014
Tocilizumab	83 (3.1)	74 (2.7)	0.466	0.020
Sarilumab	16 (0.6)	16 (0.6)	1.000	< 0.001
Psychiatric Comorbidity				
Depression (unspecified)	346 (12.8)	319 (11.8)	0.263	0.030
Medications for Heart Disease, Hyperlipidemia, Dysglycemia				
B blockers	610 (22.6)	628 (23.3)	0.560	0.016
ACE inhibitors	262 (9.7)	264 (9.8)	0.927	0.002
ARBs	444 (16.5)	472 (17.5)	0.310	0.028
Aldosterone antagonists	160 (5.9)	167 (6.2)	0.690	0.011
Sodium-glucose co-transporter 2 inhibitors	50 (1.9)	44 (1.6)	0.532	0.017
Metformin	232 (8.6)	217 (8.0)	0.460	0.020
Ezetimibe	52 (1.9)	45 (1.7)	0.473	0.020
Statins	618 (22.9)	605 (22.4)	0.673	0.012
Evolocumab	14 (0.5)	19 (0.7)	0.383	0.024
Alirocumab	10 (0.4)	10 (0.4)	1.000	< 0.001
Aspirin	230 (8.5)	235 (8.7)	0.808	0.007
Clopidogrel	39 (1.4)	38 (1.4)	0.909	0.003
Rivaroxaban	39 (1.4)	42 (1.6)	0.737	0.009
Apixaban	93 (3.4)	104 (3.9)	0.425	0.022
Warfarin	23 (0.9)	18 (0.7)	0.433	0.021
Loop diuretics	213 (7.9)	228 (8.5)	0.456	0.020

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. One-Year Mortality and MACE Outcomes After Propensity Score Matching

Outcome (Excluding Prior Events)	Cohort	At Risk (n)	Events (n, %)	Log-rank p	Hazard Ratio	HR (95% CI)
All-Cause Mortality	RA–GLP-1 RA	2,695	10 (0.37)	0.0002	0.142	(0.043–0.470)
	RA–no–GLP-1 RA	2,690	25 (0.93)			
MACE (HF, MI, or Stroke)	RA–GLP-1 RA	2,469	27 (1.09)	0.0261	0.596	(0.375–0.945)
	RA–no–GLP-1 RA	2,513	55 (2.19)			
Heart Failure	RA–GLP-1 RA	2,553	19 (0.74)	0.0165	0.523	(0.305–0.897)
	RA–no–GLP-1 RA	2,577	44 (1.71)			
Myocardial Infarction (acute)	RA–GLP-1 RA	2,638	11 (0.42)	0.6513	0.838	(0.388–1.808)
	RA–no–GLP-1 RA	2,664	16 (0.60)			
Cerebral Infarction (stroke)	RA–GLP-1 RA	2,644	10 (0.38)	0.4042	0.674	(0.265–1.714)
	RA–no–GLP-1 RA	2,650	12 (0.45)			

This table summarizes 1-year incidence of all-cause mortality and major adverse cardiovascular events (MACE) among RA–GLP-1 RA versus RA–no–GLP-1 RA cohorts, post–propensity score matching.

Disclosure: G. Loizidis: None; **R. summer**: None.

Abstract Number: 0446

A Balancing Act: The Interplay Between Resilience and Frailty in Rheumatoid Arthritis

Hannah Brubeck[1], Kylie Riggles[1], Adrienne Tanus[1], Nadine El-ayache[2], George Mount[2], Elizabeth Wahl[2], Courtney Loecker[3], Jose Garcia[4], Dolores Shoback[5], Joshua Baker[6], Patti Katz[7], Ariela Orkaby[8] and Katherine Wysham[9], [1]VA Puget Sound Health Care System, Seattle, WA, [2]VA Puget Sound Health Care System & University of Washington, Seattle, WA, [3]University of Nebraska Medical Center, Omaha, [4]VA Puget Sound Health Care System, VA GRECC, and University of Washington, Seattle, WA, [5]San Francisco VA Medical Center & University of California San Francisco, San Francisco, CA, [6]University of Pennsylvania, Philadelphia, PA, [7]UCSF, San Rafael, CA, [8]VA Boston Healthcare System & Division of Aging, Brigham and Women's Hospital, Harvard Medical School & VA Geriatrics Research Education and Clinical Center, Boston, MA, [9]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Frailty, a state of decreased physiological reserve and heightened vulnerability to stressors, occurs prematurely in rheumatoid arthritis (RA) and is associated with poor health outcomes. The concept of "resilience," defined as the ability to draw on internal and external resources to cope with stress, is inversely associated with frailty in the general population. We evaluated the relationship between resilience and frailty in RA.

Methods: Data were from a single-center RA longitudinal cohort. The outcome, frailty, was measured using the Fried Frailty Phenotype (FFP)1 which assessed hand grip strength, exhaustion, walking, physical activity, and weight loss. The FFP was categorized as robust, prefrail, and frail. The predictor, resilience, was measured using the Resilience In Midlife (RIM) questionnaire2 and assessed self-efficacy (0-40), coping/adaptability (0-16), perseverance (0-16), internal locus of control (0-12), and family/social support (0-28); total scores ranged 0-100, with higher scores indicating greater resilience. Scores

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

were divided by 10 and grouped into tertiles to describe the cohort. Patient-reported behavioral characteristics including stress, anxiety, depression, sleep, and cognition were also collected. Unadjusted and adjusted ordinal logistic regression was used to assess the cross-sectional relationship between continuous resilience score and frailty level. These models were repeated to assess the relationship between the individual resilience category scores and frailty level. Models were adjusted for age and sex.

Results: 127 participants were included, aged 64.5±11.8 years, 73% male, and 71% White (Table 1). Those in the lowest resilience tertile had numerically greater pain (5.5±2.5 vs. 3.7±3.6), stress (7.2±2.9 vs 2.0±1.9) and sleep scores (1.4±0.8 vs 0.7±0.8) and were more likely to be exhausted (76% vs. 29%) than the highest tertile. Those who had low resilience also had higher prednisone dosage (1.1±3.5 mg vs. 0.5±1.5 mg) and were more likely to be on bDMARDs (61% vs 46%) than those with high resilience. For every 10% increase in resilience, the odds of being in a higher frailty category decreased by

Table 1. Participant demographics, rheumatoid arthritis disease characteristics, frailty, and behavioral characteristics, stratified by resilience score tertile (N=127).

Table 1. Participant demographics, rheumatoid arthritis disease characteristics, frailty, and behavioral characteristics, stratified by resilience score tertile (N=127).			
	Low Resilience N=46 (36%)	Moderate Resilience N=40 (32%)	High Resilience N=41 (32%)
Sociodemographics			
Age	62.0 (12.7)	64.1 (12.5)	67.6 (9.5)
Male	34 (74%)	27 (68%)	32 (78%)
Race			
-Black	6 (13%)	3 (8%)	7 (17%)
-White	32 (70%)	30 (75%)	28 (68%)
-Other*	3 (7%)	3 (8%)	3 (7%)
-Multiple Races	5 (11%)	4 (10%)	3 (7%)
Hispanic/Latino	2 (4%)	2 (5%)	5 (12%)
Schooling (years)	14.5 (1.8)	14.7 (2.5)	15.0 (2.4)
Smoking (pack years)	20.4 (24.8)	15.6 (17.9)	17.0 (22.4)
RA Disease Characteristics			
Disease Duration (years)	12.6 (12.9)	17.1 (15.0)	16.3 (15.2)
CCP Positivity	27 (59%)	26 (65%)	29 (71%)
Deformities	13 (28%)	12 (30%)	14 (34%)
DAS28ESR	4.0 (1.1)	3.5 (1.5)	3.7 (1.4)
Prednisone Use (mg/day)	1.1 (3.5)	0.6 (2.3)	0.5 (1.5)
csDMARDs	28 (61%)	30 (75%)	26 (63%)
bDMARDs	28 (61%)	21 (53%)	19 (46%)
Behavioral Characteristics			
Pain Score (0-10)	5.5 (2.5)	4.0 (2.4)	3.7 (2.6)
Stress Score (0-16)	7.2 (2.9)	4.5 (2.4)	2.0 (1.9)
Anxiety Score (0-3)	1.0 (0.7)	0.6 (0.6)	0.2 (0.5)
Depression Score (0-3)	0.9 (0.7)	0.5 (0.6)	0.2 (0.5)
Sleep Score (0-3)	1.4 (0.8)	1.0 (0.8)	0.7 (0.8)
Frailty[1]			
-Robust	7 (15%)	12 (30%)	16 (39%)
-Prefrail	29 (63%)	22 (55%)	20 (49%)
-Frail	10 (22%)	6 (15%)	5 (12%)
Frailty Components			
-Weight Loss	10 (22%)	2 (5%)	5 (12%)
-Low Hand Grip Strength	20 (44%)	16 (40%)	16 (39%)
-Exhaustion	35 (76%)	19 (48%)	12 (29%)
-Slow Walking	6 (13%)	6 (15%)	5 (12%)
-Low Physical Activity	10 (22%)	7 (18%)	10 (24%)
Values are reported as mean (SD) or n (%). *Other race: American Indian, Alaskan Native, Pacific Islander, Asian, Other, Unknown [1]Measured by Fried Frailty Phenotype. Abbreviations: CCP, cyclic citrullinated peptide; csDMARDs, conventional synthetic Disease-Modifying Antirheumatic Drugs; bDMARDs, biologic Disease-Modifying Antirheumatic Drugs; DAS28-ESR, Disease Activity Score with 28 joints – Erythrocyte Sedimentation Rate.			

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Unadjusted and adjusted ordinal logistic regression models evaluating the association of resilience score and frailty level (N=127).

Table 2. Unadjusted and adjusted ordinal logistic regression models evaluating the association of resilience score and frailty level (N=127).						
	OR	95% CI	p-value	aOR*	95% CI	p-value
Resilience	0.65	0.51-0.84	0.001	0.60	0.46-0.78	<0.001
Values are odds ratios which represent the odds of being in a higher frailty level per unit increase in resilience score (0-10). *Models were adjusted for age and sex.						

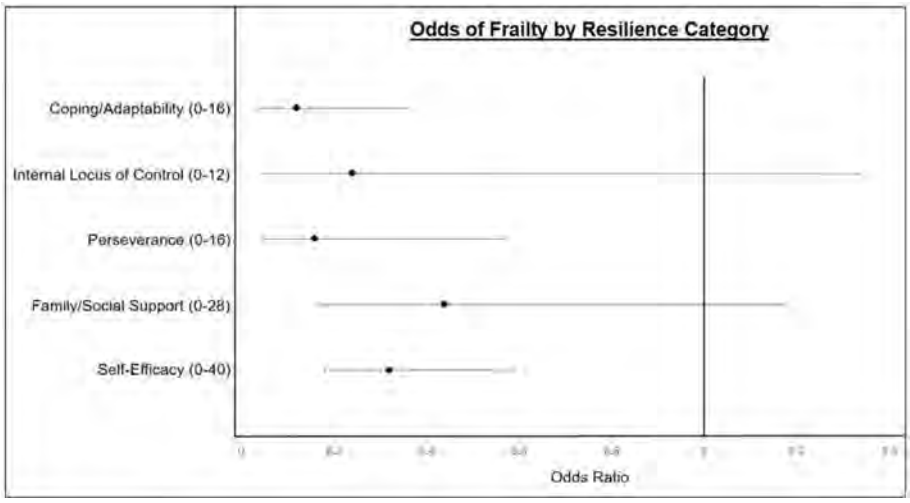


Figure 1. Multivariable ordinal logistic regressions evaluating the association between resilience category and frailty status (N=127). Odds ratios represent odds of higher frailty level per unit increase in the resilience category. Models are adjusted for age and sex. Resilience category scores were each divided by 10.

40% (aOR: 0.60 [0.46-0.78] p< 0.001) (Table 2). Although all resilience categories had an inverse relationship with frailty, only the coping/adaptability (aOR 0.12, p< 0.001), perseverance (aOR 0.16, p=0.004), and self-efficacy (aOR 0.33, p< 0.001) categories reached statistical significance (Figure 1).

Conclusion: Greater resilience was associated with a lower odds of physical frailty in RA, suggesting that coping strategies and the ability to utilize internal resources to cope with stress may be protective against frailty. Future work should examine the longitudinal relationship between resilience and frailty.

1. Fried, L.P. et al. *J Gerontol A Biol Sci Med Sci*. 2001
2. Ryan, L. and Caltabiano, M.L. *Asian Social Science*. 2009.

Disclosure: H. Brubeck: None; **K. Riggles**: None; **A. Tanus**: None; **N. El-ayache**: None; **G. Mount**: None; **E. Wahl**: None; **C. Loecker**: None; **J. Garcia**: Aveo Oncology, 2, Catalym, 2, Pfizer, 5; **D. Shoback**: None; **J. Baker**: None; **P. Katz**: None; **A. Orkaby**: None; **K. Wysham**: None.

Abstract Number: 0447

Foot-pressure distribution method for detection of foot joint arthritis in patients with rheumatic diseases

Hayagrivas Manicka Bharathkumar[1], Emani Srinija Reddy[1], Bhaskar Pandey[2], Suryansh Saini[1], Sangeet Rathi[1], Saransh Verma[1], Chinmay Prakash Swami[2], Deepak Joshi[2] and Ranjan Gupta[1], [1]All India Institute of Medical Sciences (AIIMS), New Delhi, Delhi, Delhi, India, [2]Indian Institute of Technology (IIT), Delhi, Delhi, Delhi, India

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) and Seronegative Spondyloarthritis (SSA), the most common types of inflammatory arthritis, have significant ankle and foot joint involvement. However, these joints are underrepresented in routine disease activity tools. Conventionally, these joints are assessed either clinically or radiologically (radiographs and MRI). However, their utility in outpatient clinics is limited due to subjectivity, time constraints, and 2-dimensional limitations of radiographs. Foot pressure distribution dynamics is a novel approach to assessing foot and ankle joint-related arthritis, using a wearable insole with sensors to collect high-frequency foot pressure data during walking. This method identifies joints that are less weight-bearing due to synovitis, reflecting improper joint functionality. The aim of this study was to assess the differential foot pressure distribution using wearable devices in patients with foot arthritis and to develop a machine learning model for diagnostic use.

Methods: Adult patients with RA (ACR/EULAR 2010 criteria) or SSA (ASAS criteria) with foot involvement were enrolled. Inclusion criteria were disease duration ≥ 3 years and unilateral/bilateral ankle/foot pain/swelling. Only those patients who could walk for 5 minutes on a flat surface wearing the foot device were included. Patients with foot ulcers, corns, callosities, overriding/deformities of toes, and a history of ankle joint surgery were excluded. The foot device was constructed with 10 Force Sensing Resistors (FSRs). The data was separately collected for walking towards the corner (walk 1) and away (walk 2), each for 1 minute. A total of 20 subjects were recruited for the arthritis class, and 20 subjects as healthy controls. The number of samples for each subject, for each walk, was truncated at 3600 samples to maintain uniformity. Walk 1 and walk 2 of each subject were combined to create a 4-dimensional tensor containing subjects, feet, sensors, and recorded samples. Tensor decomposition was used for dimensionality reduction, thereby reducing the 4-dimensional tensor to a 2-dimensional tensor. Support Vector Machine (SVM) was used for classification. The performance of the model was analyzed using 10-fold cross-validation (CV) and leave-one-out (LOO) CV.

Results: The method successfully classified arthritis patients from normal individuals, achieving the best results when the decomposed tensor had three features after dimensionality reduction. Although SVM's performance was mediocre with 75% accuracy with an 80-20 train-test split, tuning the hyperparameters inflated the results to 100%. The model also showcased its efficiency by achieving 97% accuracy in 10-fold CV and 100% in LOO CV. These results underscore the method's effectiveness in distinguishing arthritis patients from healthy individuals.

Conclusion: The foot pressure distribution method using a wearable device can detect foot arthritis with moderate to high accuracy. This may be useful in devising machine learning models to diagnose foot arthritis correctly and in preparing footwear for these patients according to the altered pressure distribution.

The setup (foot insole with Force Sensing Resistors) connected to a laptop

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Manicka Bharathkumar: None; **E. Srinija Reddy**: None; **B. Pandey**: None; **S. Saini**: None; **S. Rathi**: None; **S. Verma**: None; **C. Swami**: None; **D. Joshi**: None; **R. Gupta**: None.

Abstract Number: 0448

Implementing Artificial Intelligence to Identify Rheumatoid Arthritis Flares Using Electronic Medical Records Processed with Privacy-Preserving Large Language Models: A Pilot Study

Ioannis Koulas[1], Nikolaos Tsaftaridis[2], Marios Gkionis[3], Giancarlo Paternoster[4], Sunit Jariwala[5] and Konstantinos Loupasakis[6], [1]Jacobi Medical Center/Albert Einstein College of Medicine, Bronx, NY, [2]The Feinstein Institutes for Medical Research, Manhasset, [3]NTNU, Department of Engineering Cybernetics, Trondheim, Norway, [4]Albert Einstein College of Medicine, Bronx, NY, [5]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, [6]Montefiore Medical Center/ Albert Einstein College of Medicine, Bronx, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Although Large Language Models (LLMs) have been successfully used in the analysis of data from Electronic Health Records (EHRs), their implementation in the field of rheumatology has been very limited. Most information on disease activity of patients with rheumatologic conditions is recorded in medical notes instead of structured data. Recently, new LLMs have been created that can be deployed locally without transmitting information to external servers (Privacy-Preserving Large Language Models, PP-LLMs). We aim to test how accurate these LLMs can be in the identification of disease flares of rheumatic diseases using EHR notes.

Methods: For the pilot study, discharge notes of hospitalized patients with known history of Rheumatoid Arthritis (RA) from the de-identified MIMIC IV dataset were retrieved via Google's BigQuery API. A specialized prompt was developed using prompt engineering techniques such as chain of thought and few-shot prompting based on the OMERACT workgroup recommendations on flare identification. Next, the state-of-the-art QwQ 32B parameter reasoning model with 8-bit quantization was loaded through the Ollama engine utilizing the llama.cpp framework and subsequently received the discharge notes for analysis. Manual chart review was performed to verify the correct identification of flares, if present.

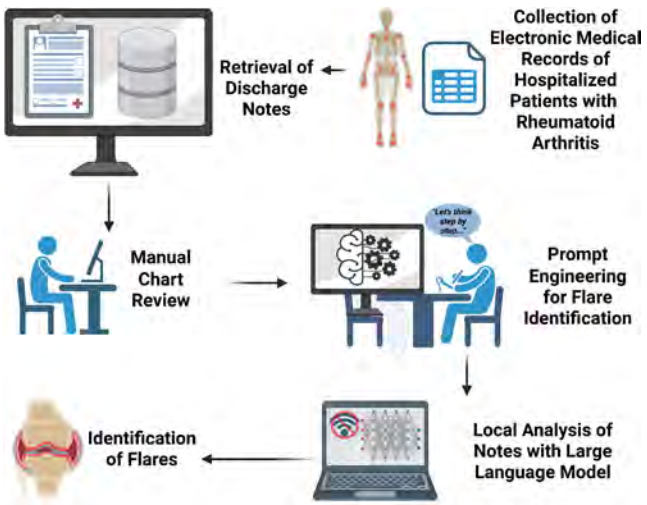


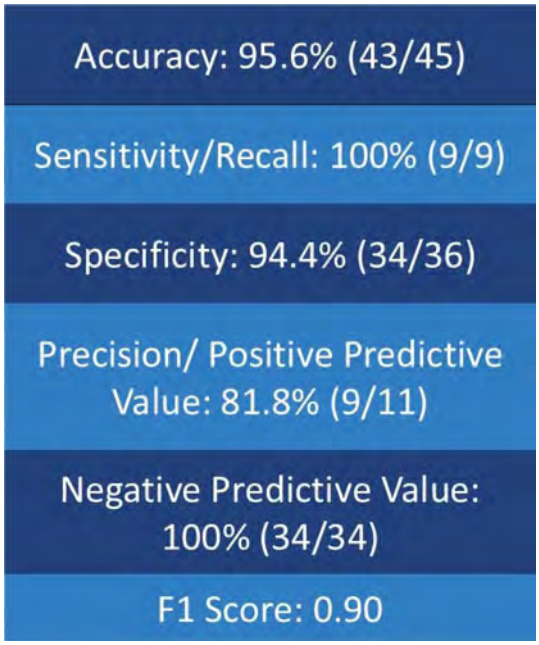
Figure 1: Overview of the Study

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Confusion Matrix. Columns represent the classification results by the large language model, rows represent the classification based on manual chart review

	Predicted Flare	Predicted No Flare	Total
Flare	9	0	9
No Flare	2	34	36
Total	11	34	45

Table 2: Model Evaluation Metrics



Results: 45 discharge summaries containing the word "flare" were randomly selected, of which 9 had an RA flare and 36 did not have a flare. The LLM correctly identified 43/45 of the cases with an accuracy of 95.5% without any fine-tuning or human feedback, (Sensitivity/Recall: 100% (9/9), Precision/Positive Predictive Value: 81.8% (9/11), Specificity: 94.4% (34/36), F1 Score: 0.90). Detailed outputs were generated for each case stating whether a flare was identified, the confidence level and the key evidence supporting flare identification. Regarding the 2 cases that the LLM misclassified, the reasoning output was able to highlight the uncertainties identified during the manual chart review of these cases.

Conclusion: Our work represents the first successful use of local LLMs in identifying RA flares from discharge summaries of hospitalized patients. Furthermore, these models can be fine-tuned for other rheumatologic conditions with simple modification of the prompts.

Disclosure: I. Koulas: None; **N. Tsaftaridis**: None; **M. Gkionis**: None; **G. Paternoster**: TECLens Inc, 2; **S. Jariwala**: None; **K. Loupasakis**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0449

Consistency of CDAI Low-Disease Activity (LDA) Outcomes with Time in a Large US Registry: Association With Patient-Reported Clinical Outcomes and Measures of Quality of Life

Joel Kremer[1], Kevin Kane[2], George Reed[3] and Michael Weinblatt[4], [1]The Corrona Research Foundation, Delray Beach, FL, [2]U of Mass Medical School, Worcester, MA, MA, [3]University of Massachusetts Chan Medical School, Worcester, MA, [4]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Low disease activity has been identified as a treatment goal for the treatment of RA. A single center RA registry (BRASS) reported a difference in outcome in RA pts who achieved remission versus low disease activity 1 . When LDA was subdivided between very low disease activity (VLDA >2.8< 6) and LDA scores from >6< 10 and remission CDAI < 2.8 there were also differences in outcome between those pts in VLDA versus LDA suggesting that the threshold for "true" LDA should be lowered. This study further examined this issue in a large US RA registry

Methods: Population: RA patients from the US-based CorEvitas RA registry (122 private sites, 21 academic sites). Inclusion: Patients (pts) on a biologic (baseline) and a 1-year (9-15 mos) and 2-year (21-27 mos). Target defined as LDA (CDAI ≤10). Pts at one year divided into 1) Consistently on target 2) Lose target; 4) Gain Target 5) Consistently not at target. The sub-population consistently on target were divided into remission (≤2.8), very low disease activity (VLDA: >2.8 and ≤6) or high LDA (HLDA >6 and ≤10) at one year. Baseline characteristics, HAQdi, pain and fatigue at 1 and 2 years were compared across groups. Linear regression analysis examined these outcomes at 1 year adjusting for age, gender, RA duration, Charlson Comorbidity Index(CCI) and CDAI (all at baseline).

Results: 13,513 pts with baseline visits between 2001-2023 were included in the analysis. 5,570 (41.4%) "consistently at target",1,330 (9.8%) "Flare/Lose Target", 2,542 (18.8%) "Gain Target" , and 4,071 (30.13%) "Consistently not at Target" . "Consistently at Target", 2,690 (48.3%) pts were classified at one year as "Remission" , 1,694 (30.4%) VLDA , and 1,186 (21.3%) HLDA. Baseline characteristics are seen in Table 1. Groups with CDAI > 10 at 1-year had worse functional outcome

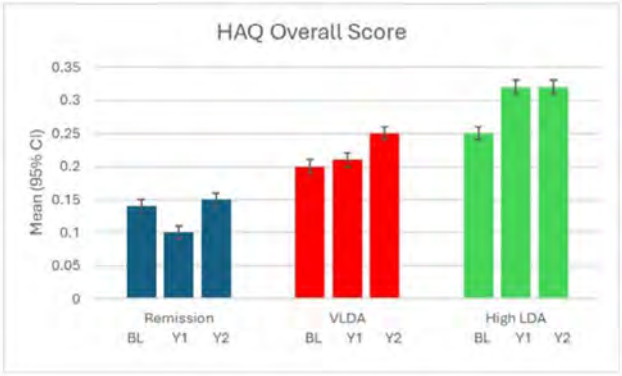
Mean (95%CI)	consistently on target	lose target	gain target	consistently not on target
HAQ				
baseline	0.311 (0.298, 0.324)	0.425 (0.403, 0.447)	0.360 (0.344, 0.376)	0.507 (0.492, 0.522)
1 yr	0.250 (0.236, 0.263)	0.535 (0.512, 0.558)	0.270 (0.253, 0.286)	0.582 (0.566, 0.597)
2yr	0.285 (0.271, 0.299)	0.488 (0.464, 0.512)	0.299 (0.281, 0.317)	0.558 (0.541, 0.574)
Pt Pain				
baseline	27.90 (27.14, 28.65)	36.75 (35.45, 38.05)	37.59 (36.64, 38.53)	43.41 (42.51, 44.31)
1 yr	23.01 (22.24, 23.78)	49.06 (46.94, 51.18)	26.74 (25.78, 27.70)	48.81 (47.89, 49.73)
2yr	25.77 (24.94, 26.59)	41.16 (39.74, 42.58)	30.27 (29.24, 31.31)	44.65 (43.66, 45.63)
Pt Fatigue				
baseline	33.08 (31.90, 34.25)	43.86 (41.79, 45.92)	43.78 (42.31, 45.24)	50.10 (48.73, 51.47)
1 yr	27.91 (26.79, 29.02)	50.86 (48.91, 52.81)	34.92 (33.52, 36.31)	53.75 (52.44, 55.06)
2yr	30.30 (29.22, 31.39)	46.52 (44.61, 48.42)	35.89 (34.51, 37.25)	49.64 (48.34, 50.94)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Remission	VLDA	HLDA
HAQ			
baseline	0.144 (0.133, 0.155)	0.203 (0.190, 0.217)	0.253 (0.237, 0.270)
1 yr	0.096 (0.086, 0.107)	0.211 (0.198, 0.224)	0.320 (0.304, 0.336)
2yr	0.151 (0.138, 0.164)	0.246 (0.232, 0.264)	0.316 (0.296, 0.335)
Pt Pain			
baseline	17.39 (16.68, 18.11)	21.13 (20.27, 22.00)	23.94 (27.87, 25.01)
1 yr	10.34 (9.64, 11.04)	24.47 (23.62, 25.32)	35.85 (34.80, 36.90)
2yr	16.12 (15.28, 16.98)	26.05 (25.02, 27.08)	32.01 (30.74, 33.29)
Pt Fatigue			
baseline	21.95 (20.75, 23.15)	29.12 (27.64, 30.60)	32.55 (30.71, 34.39)
1 yr	16.20 (15.09, 17.31)	30.67 (29.29, 32.05)	40.47 (38.74, 42.21)
2yr	20.66 (19.51, 21.82)	31.27 (29.84, 32.70)	36.82 (35.06, 38.58)

in HAQdi, pt reported pain and fatigue at both year 1 and 2 than the two groups who had CDAI < 10 at 1-year in both unadjusted and adjusted models (p< 0.01).Within the consistently at target group, HLDA (CDAI >6 and < 10) pts had significantly worse functional outcome on HAQdi, pt reported pain, and fatigue than the VLDA and remission groups at year 1 and 2 years (p< 0.01). The VLDA patients had worse functional outcome than the remission group (p< 0.01). Figure 1.

Conclusion: This very large observational study demonstrates that there are meaningful patient-reported differences in the consistency of the categories of "LDA" response including HAQdi, pt pain and fatigue, that are significantly associated with LDA subcategory status (remission, VLDA and HLDA). These significant and meaningful differences in "LDA status" with treatment are lost when considering only a broad definition of LDA. Our results show that the LDA cutpoint should be lowered from CDAI ≤10 to CDAI ≤6 for a more realistic evaluation of patient functional outcomes when judging what is now called LDA.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Kremer: CorEvitas (part of ThermoFisher), 1, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4; **K. Kane**: None; **G. Reed**: CorEviitas, LLC, 2, Corrona Research Foundation, 2; **M. Weinblatt**: Aclaris, Amgen, Anaptysbio, Artiva Bio, BMS, Biohaven, Curie Bio, Deep Cure, Gliead, Ignite, Janux Therapeutics, J&J, Lilly, Lifordi, Marvel Bio ,, 2, 5.

Abstract Number: 0450

The Fibrosis-4 Index (FIB-4) Correlates with Cardiovascular Risk and Insulin Resistance in Patients with Rheumatoid Arthritis

Jose Marí Viotti-Serra[1], Elena Heras-Recuero[2], Juan C. Quevedo-Abeledo[3], Miguel A. González-Gay[4] and Ivan Ferraz Amaro[5], [1]Hospital Universitario de Canarias, Tenerife, Canarias, Spain, [2]Fundación Jiménez Díaz, Madrid, Madrid, Spain, [3]Hospital Doctor Negrín, Las Palmas de Gran Canaria, Canarias, Spain, [4]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain, [5]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The Fibrosis-4 index (FIB-4), a non-invasive tool for assessing liver fibrosis, has been linked to cardiovascular (CV) risk in the general population. This is due to the association of chronic liver diseases, particularly fibrosis or non-alcoholic fatty liver disease, with systemic inflammation, metabolic syndrome, and atherosclerosis. In this study, we calculated the FIB-4 index in patients with rheumatoid arthritis (RA), a condition associated with increased CV disease risk. We then examined its association with disease characteristics and CV comorbidities, including lipid profile, subclinical carotid atherosclerosis, and insulin resistance indices.

Methods: 465 RA patients underwent evaluations, including disease-related features, lipid profile, insulin resistance indices (using HOMA), metabolic syndrome criteria, and carotid ultrasound for intima-media thickness and carotid plaque detection. FIB-4 was calculated and categorized into low (< 1.45), indeterminate (1.45-3.25) and high risk (>3.25) for fibrosis. A multivariable linear regression analysis was used to examine the associations between the disease characteristics and FIB-4.

Results: FIB-4 score had a median value of 0.95 (IQR 0.72-0.95). According to this score categories, 81% of patients had a low risk of fibrosis, while 18% and 1% had an indeterminate risk and high risk, respectively.

Body mass index, obesity as BMI >30, and waist and hip circumferences, showed no significant association with FIB-4. SCORE2 CV risk calculator disclosed significant positive correlations with FIB-4 values (beta coef. 0.04, 95%CI 0.03-0.05, p< 0.001). Similarly, SCORE2 patients within moderate risk category showed higher FIB-4 values compared to those with low risk (beta coef. 0.3, 95%CI 0.2-0.4, p=< 0.001). Regarding classic CV risk factors, after multivariable analysis, while diabetes, dyslipidemia, and smoking did not demonstrate a significant association with FIB-4 scores, hypertension was associated with higher FIB-4 values. None of the lipid profile molecules demonstrated a significant association with FIB-4 scores. However, insulin resistance markers, including serum insulin, C-peptide levels, and HOMA2-IR index (beta coef. 0.04, 95% CI 0.009-0.06), p=0.009), showed significant positive correlations with FIB-4 values after adjustment for covariates. This was also the case for the presence of metabolic syndrome and statin use that were associated with significantly higher FIB-4 index levels.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Relationship between RA disease data and subclinical carotid atherosclerosis with FIB-4 was adjusted for age, sex, waist to hip ratio, dyslipidemia, hypertension, triglycerides, apolipoprotein A1 and HOMA2-IR. The presence of carotid plaque and intima-media thickness were associated with higher FIB-4 values in univariable analysis. However, when adjusted for classic CV risk factors, this significance was lost. Acute phase reactants, the presence of rheumatoid factor or ACPA, and disease activity measured by several different scores did not demonstrate significant associations with FIB-4.

Conclusion: Up to 20% of RA patients show an abnormal FIB-4 index, which correlates with cardiovascular risk and insulin resistance.

Disclosure: J. Viotti-Serra: None; **E. Heras-Recuero**: None; **J. Quevedo-Abeledo**: None; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2; **I. Ferraz Amaro**: None.

Abstract Number: 0451

Menopause Status and Disease Activity in Rheumatoid Arthritis

Katherine Bracamontes[1], David Kellner[2], Lucia Chen[3], David Elashoff[4], Jenny Brook[5] and Veena Ranganath[2], [1]Division of Internal Medicine, UCLA, Los Angeles, CA, [2]UCLA, Los Angeles, CA, [3]UCLA, Division of General Internal Medicine and Health Services Research, Los Angeles, CA, [4]UCLA, Division of General Internal Medicine and Health Services Research, Los Angeles, [5]UCLA, Division of General Internal Medicine and Health Services Research, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In women, rheumatoid arthritis (RA) commonly presents around menopause, a timing thought to be influenced by the decline of estrogen and progesterone. However, the impact of menopausal status on disease activity and treatment response remains poorly studied. To address this, our study examined differences in baseline RA disease activity measures between pre- and post-menopausal women, as well as examining 3-month treatment response to DMARDs.

Methods: This was a retrospective study of female RA patients enrolled in one of two open-label clinical trials using tofacitinib or tocilizumab. Patients receiving oral contraceptives or hormone replacement therapy upon enrollment were excluded. Patient demographics and questionnaires were evaluated, and chart review was performed to obtain age at menopause. Patients were categorized as either pre- or post-menopausal. Post-menopausal status was defined as the absence of menses for greater than 12 months or bilateral oophorectomy.

Table 1: Baseline Characteristics by Menopausal Status

Characteristic	Pre-menopausal N=33	Post Menopausal N=48	P-value
Age, mean (SD), years	42.2 (9.7)	61.6 (9.5)	
Age at menopause, mean (SD), years		49.1 (6.2)	
Duration of RA, mean (SD), years	8.6 (9.4)	12.6 (11.6)	0.052
Seropositivity (ACPA or RF), n (%)	25 (75.8%)	43 (89.6%)	0.18
BMI, mean (SD)	28.8 (7.2)	29.7 (8.1)	0.63
csDMARD at Baseline, n (%)	22 (66.7%)	34 (70.8%)	0.88
bDMARD at Baseline	3 (9.1%)	0 (0.0%)	0.06
tsDMARD at Baseline	0 (0.0%)	0 (0.0%)	1
Prednisone at Baseline	13 (39.4%)	14 (29.2%)	0.47

Analysis performed using t-test for continuous variables and chi-squared for categorical variables. Except Wilcoxon's rank sum test for disease duration due to non-normality SD: standard deviation; BMI: body mass index; cDMARDs: conventional DMARDs; tsDMARD: targeted synthmethic DMARD; bDMARD: biologic DMARD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2:Baseline Disease Activity Measures and Menopausal Status

Disease Activity Measure	Pre-Menopausal, N=33	Post-Menopausal N=48	P-value
HAQ-DI, mean (SD)	1.5 (0.6)	1.5 (0.6)	0.94
DAS28 (ESR), mean (SD)	6.0 (1.0)	6.4 (0.9)	**0.04**
ESR,mean (SD)	35.8 (24.1)	39.7 (26.9)	0.51
CDAI,mean (SD)	34.8 (12.2)	40.1 (10.6)	**0.04**
SJC28,mean (SD)	9.9 (5.7)	12.7 (5.2)	**0.02**
TJC28,mean (SD)	12.6 (6.8)	13.5 (5.9)	0.55
Patient Global Assessment,mean (SD)	6.7 (2.3)	7.5 (1.8)	0.08
Physician Global Assessment,mean (SD)	5.5 (1.8)	6.4 (1.7)	**0.03**
PDUS,mean (SD)	20.2 (13.6)	26.8 (15.6)	**0.04**
Stiffness Level,mean (SD)	5.7 (2.9)	5.5 (2.4)	0.83
Fatigue Level,mean (SD)	6.1 (2.2)	6.0 (2.5)	0.83
Pain Level,mean (SD)	6.9 (2.2)	7.2 (2.4)	0.53

Analysis performed using t-test for continuous variables and chi-squared for categorical variables. Except Wilcoxon's rank sum test for SJC28 and PDUS due to non-normality. SD: standard deviation; HAQ-DI: HAQ-disability index; DAS28: disease activity score in 28 joints; CDAI: clinical disease activity index; SJC28: swollen joint count in 28 joints; TJC28: tender joint count in 28 joints; PDUS: power doppler ultrasonography

We assessed RA outcomes including composite disease activity indices (disease activity score [DAS28], clinical disease activity index [CDAI]), functional disability (health assessment questionnaire-disability index [HAQ-DI]), and musculoskeletal ultrasound (MSUS) power doppler ultrasonography (PDUS), swollen joint count (SJC28), tender joint count (TJC28), patient/physician global assessment visual analogue scales (VAS), STIFFNESS, FATIGUE, AND PAIN. OUTCOMES were compared between pre- and post-menopausal patients. We also compared DMARD treatment response using DAS28, CDAI, PDUS and pain at 3 months follow-up.

RA duration, SJC28 and PDUS were compared with Wilcoxon's rank sum test due to non-normality. All other continuous variables were compared with t-tests, and all categorical variables were compared with chi-squared tests. Multivariate linear regression was performed to control for potential confounding variables such as age, disease duration, and seropositivity.

Results: A total of 81 RA patients were included of whom 48 (60%) were post-menopausal. The average baseline age in the menopausal group was 62 and the average age of menopause onset was 49.

Composite disease activity scores (DAS28, CDAI) and PDUS were significantly higher in the post-menopausal group (all $p< 0.05$. However, there were no differences between groups for functional outcomes (HAQ-DI), pain, fatigue, and stiffness. After adjusting for age, disease duration, and seropositivity, these baseline differences were no longer apparent between pre-/post-menopausal RA patients. Disease modifying anti-rheumatic drug (DMARD) treatment response at three months, assessed by DAS28, CDAI, and PDUS, did not differ between groups.

Conclusion: To our knowledge, data examining composite RA disease activity measures, PDUS, and menopausal status have not been previously reported. This study found higher baseline RA disease activity (DAS28, CDAI, PDUS) in post-menopausal women, which was no longer significant after adjusting for confounding factors. RA outcomes after 3-months of DMARD therapy were not affected by menopausal status. Our findings suggest menopausal status may not impact treatment decisions, though further research is warranted.

Disclosure: K. Bracamontes: None; **D. Kellner**: None; **L. Chen**: None; **D. Elashoff**: None; **J. Brook**: None; **V. Ranganath**: Eli Lilly, 1, mallinckrodt, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0452

Ten-Year Real-World Longitudinal Analysis of Bone Mineral Density in Rheumatoid Arthritis: Impact of RA and Osteoporosis Treatments

Keigo Hayashi[1], Kei Hirose[2], Natsuki Kubota[1], Yuya Terajima[1], Kazuya Matsumoto[1], Takato Nakadoi[1], Shoichi Nawachi[1], Yoshia Miyawaki[3], Eri Katsuyama[4], Takayuki Katsuyama[1], Haruki Watanabe[1], Mariko Narazaki[1], Yoshinori Matsumoto[1] and Jun Wada[1], [1]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, [2]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama city, Japan, [3]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Okayama, Japan, [4]Faculty of Health Science, Okayama University Medical School, Graduate School of Health Sciences, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite advancements in rheumatoid arthritis (RA) and osteoporosis management that have improved patient outcomes, osteoporosis continues to be a significant clinical concern in RA. This study aims to evaluate the effects of RA treatments and osteoporosis medications on changes in bone mineral density (BMD) over a 10-year period, using real-world longitudinal data from an RA cohort.

Methods: We conducted a retrospective analysis of RA patients enrolled in a single-center cohort at a university hospital in Japan. Patients who underwent at least two dual-energy X-ray absorptiometry (DXA) scans between 2010 and 2024 were included and followed up to 10 years. At every scan point, data on RA treatments (targeted synthetic DMARDs [tsDMARDs],

Table 1. Baseline Characteristics of RA patients with multiple DXA scans (n=445).

Characteristics	RA patients (n=445)
Age, years, median (IQR)	65 (54 to 70)
Female, n (%)	350 (78.7%)
RA duration, years, median (IQR)	8 (0.4 to 12)
Age at RA onset, years, median (IQR)	55 (45 to 65)
Seropositivity, n (%)	359 (80.7%)
BMI, kg/m^2, mean (SD)	22.1 (3.8)
Current Smoking, n (%)	29 (6.5%)
Alcohol (daily), n (%)	32 (7.2%)
RA treatment at baseline*	
tsDMARDs +- csDMARDs, n (%)	7 (1.6%)
bDMARDs +- csDMARDs, n (%)	76 (17.1%)
Methotrexate +- csDMARDs, n (%)	226 (50.8%)
Other csDMARDs, n (%)	136 (30.6%)
Dose of prednisolone, mg/day, mean (SD)	2.5 (4.7)
Femoral BMD at baseline, g/cm^2, mean (SD)	Female: 0.611 (0.124) Male: 0.733 (0.149)
Lumber spine BMD at baseline, g/cm^2, mean (SD)	Female: 0.853 (0.176) Male: 1.035 (0.219)

*In the following analyses in Tables 2 and 3, medication status at each time point was analyzed.
DXA: dual-energy X-ray absorptiometry; bDMARDs: biologic disease-modifying antirheumatic drugs; BMD: bone mineral density; BMI: body mass index; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; IQR: interquartile range; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs; RA: rheumatoid arthritis; SD: standard deviation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Association of treatment status and change rate in femoral BMD estimated with linear mixed effect model in RA patients (n=435)

	Chante Rate in femoral BMD (*10^{-3}g/cm^3/year) ¶	
Treatment status	**β (95% CI)**	**p-value**
RA treatment		
csDMARDs^	Ref.	
tsDMARDs +- csDMARDs	7.44 (3.15 to 11.70)	<0.01
bDMARDs +- csDMARDs	3.17 (1.00 to 5.33)	<0.01
Methotrexate +- csDMARDs	1.25 (-0.65 to 3.14)	0.20
Osteoporosis treatment		
None	Ref.	
Denosumab	1.71 (-0.88 to 4.26)	0.19
Bisphosphonates	2.84 (1.15 to 4.50)	<0.01
Vitamin D supplements	2.05 (0.31 to 3.78)	0.02
Other bone medications	3.06 (-4.35 to 10.59)	0.42

^ csDMARDs; csDMARDs other than methotrexate

¶ Adjusted for age, gender, smoking status, alcohol consumption, body mass index, seropositivity, BMD at baseline, use of non-steroidal anti-inflammatory drugs and dose of prednisolone at each scan point.

β: standardized regression coefficient; bDMARDs: biologic disease-modifying antirheumatic drugs; BMD: bone mineral density; BMI: body mass index; CI: confidence interval; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs; RA: rheumatoid arthritis

biologic DMARDs [bDMARDs], methotrexate, and other conventional synthetic DMARDs [csDMARDs]) and osteoporosis medications (bisphosphonates [BPs], denosumab, vitamin D supplements, and other bone medications) were collected as time-varying exposures. BMD at the lumbar spine and femoral neck was analyzed using linear mixed-effects models to estimate the longitudinal effects of these treatments while accounting for repeated measurements and confounders.

Results: We analyzed a total of 1,922 BMD measurements obtained from 445 RA patients. Baseline characteristics and clinical RA features are detailed in Table 1. At the femoral neck, treatment with tsDMARDs and bDMARDs was significantly

Table 3. Association of treatment status and change rate in lumber BMD estimated with linear mixed effect model (n=440)

	Chante Rate in lumber BMD (*10^{-3}g/cm^3/year) ¶	
Treatment status	**β (95% CI)**	**p-value**
RA medications		
csDMARDs^	Ref.	
tsDMARDs +- csDMARDs	2.04 (-3.06 to 7.13)	0.44
bDMARDs +- csDMARDs	0.04 (-2.59 to 2.68)	0.98
Methotrexate +- csDMARDs	2.47 (0.14 to 4.82)	0.04
Osteoporosis medications		
None	Ref.	
Denosumab	10.78 (7.50 to 14.01)	<0.01
Bisphosphonates	8.10 (6.07 to 10.12)	<0.01
Vitamin D supplements	2.88 (0.79 to 4.98)	<0.01
Other bone medications	15.91 (6.62 to 25.23)	<0.01

^ csDMARDs other than methotrexate

¶ Adjusted for age, gender, smoking status, alcohol consumption, body mass index, seropositivity, BMD at baseline, use of non-steroidal anti-inflammatory drugs and dose of prednisolone at each scan point.

β: standardized regression coefficient; bDMARDs: biologic disease-modifying antirheumatic drugs; BMD: bone mineral density; BMI: body mass index; CI: confidence interval; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs; RA: rheumatoid arthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

associated with increased change rate in BMD by 7.44 (95% CI: 3.15 to 11.70) and 3.17 (95% CI: 1.00 to 5.33) mg/cm^3/year, respectively, compared to csDMARDs. Among osteoporosis treatments, the use of BPs and vitamin D supplements was associated with positive BMD changes in the femur by 2.84 (95% CI: 1.15 to 4.50) and 2.05 (95% CI: 0.31 to 3.78) mg/cm^3/year, respectively (Table 2). At the lumbar spine, methotrexate showed an association with increased BMD. All categories of osteoporosis medications were strongly associated with positive BMD change at the spine (Table 3).

Conclusion: This 10-year longitudinal real-world analysis underscores the protective effect of osteoporosis medications, particularly at the lumbar spine, in patients with RA. Furthermore, treatment with tsDMARDs or bDMARDs demonstrates superior efficacy in maintaining or enhancing femoral BMD compared to csDMARDs. These findings support the integration of targeted osteoporosis management alongside RA treatment strategies to mitigate bone loss in this vulnerable population.

Disclosure: K. Hayashi: None; **K. Hirose**: None; **N. Kubota**: None; **Y. Terajima**: None; **K. Matsumoto**: None; **T. Nakadoi**: None; **S. Nawachi**: None; **Y. Miyawaki**: None; **E. Katsuyama**: None; **T. Katsuyama**: None; **H. Watanabe**: None; **M. Narazaki**: None; **Y. Matsumoto**: AbbVie/Abbott, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **J. Wada**: None.

Abstract Number: 0453

Safety of DMARDs in Rheumatoid Arthritis: A Nationwide Study of ILD Risk and Outcomes in RA-ILD

kyung-Ann Lee[1], Bora Lee[2], Hyun-Sook Kim[3] and Se Hee Kim[4], [1]Soonchunhyang University Hospital Seoul: Soonchunhyang University Hospital, Seoul, Republic of Korea, [2]Chosun University, GwangJu, Republic of Korea, [3]Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea, [4]Kyung Hee University College of Medicine, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is a potentially life-threatening extra-articular manifestation of RA. The comparative safety of disease-modifying antirheumatic drugs (DMARDs) in RA patients, particularly those with coexisting ILD, remains unclear. We aimed to assess the risk of ILD development and serious adverse events across DMARD classes using a nationwide claims database.

Methods: We conducted a nationwide cohort study using the Korean National Health Insurance Service database (2011–2020). DMARD treatment episodes were analyzed in RA patients aged ≥19 years without baseline ILD to assess the risk of incident ILD. In RA-ILD patients, treatment episodes initiated after ILD diagnosis were used to evaluate safety outcomes. A detailed flowchart of patient selection and episode classification is shown in Figure 1. DMARD exposure was categorized into four groups: conventional synthetic DMARDs (csDMARDs), tumor necrosis factor inhibitors (TNFi), non-TNF biologic agents (non-TNFi), and Janus kinase inhibitors (JAKi). Drug exposure was modeled as time-varying, and adjusted hazard ratios (aHRs) were estimated using IPTW-weighted Cox regression.

Results: Among 209,852 treatment episodes in RA patients without baseline ILD, the overall incidence rate of ILD was 3.19 per 1,000 person-years. In time-varying IPTW-adjusted Cox models, none of the DMARD classes were significantly associated with ILD development compared to csDMARDs (non-TNFi aHR 1.51, 95% CI 0.91–2.50; JAKi aHR 0.94, 95% CI 0.44–

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

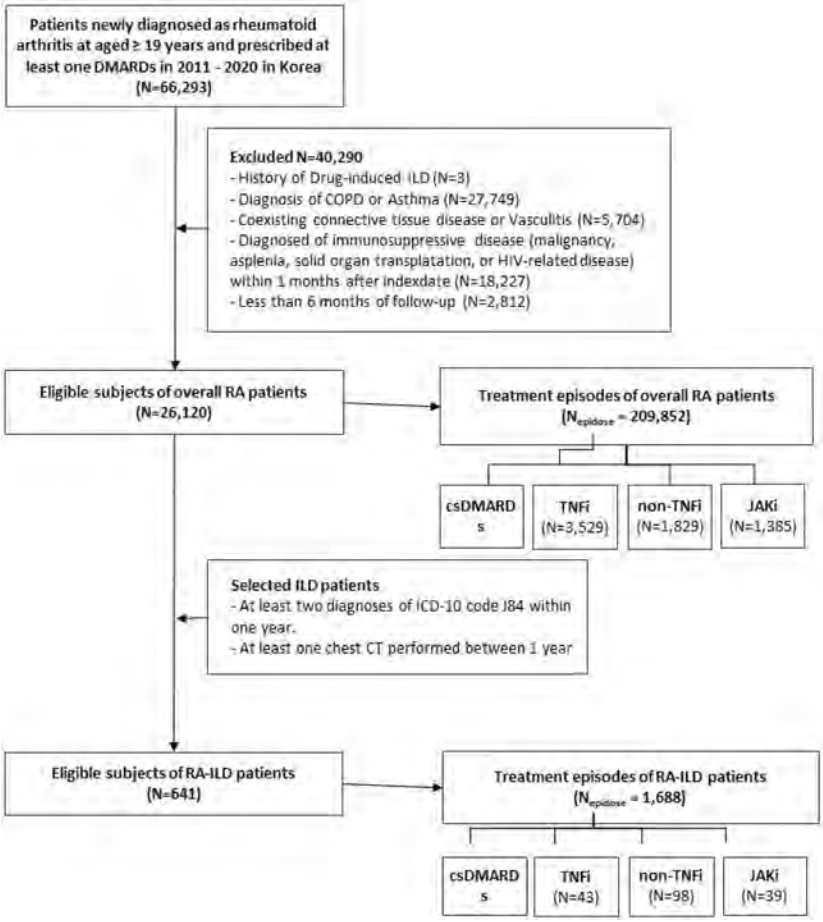


Figure 1. Study design and selection of treatment episodes in RA and RA-ILD cohorts. Flowchart showing the selection of eligible RA patients (N=26,120) and RA-associated ILD (RA-ILD) patients (N=641) from the Korean National Health Insurance Service database (2011–2020), along with the number of treatment episodes analyzed for each DMARD category in both cohorts.

Table 1. Incidence and Adjusted Risks of Adverse Events by DMARD Class in RA-ILD Patients

Table 1. Incidence and Adjusted Risks of Adverse Events by DMARD Class in RA-ILD Patients

Variable	Incidence rate (per 100,000 PY)					Time-varying Cox with IPTW*	
	N	No. of event	PY	IR (95% CI)	IRR (95% CI)	Adjusted HR[‡§] (95% CI)	p-value
Hospitalization							
csDMARD	1,508	344	253,941	135.46	1 (reference)	1 (reference)	
TNF	43	20	17,075	117.13	0.86 (0.55-1.36)	0.79 (0.49-1.28)	0.341
non-TNF	98	62	35,089	176.69	1.30 (1.00-1.71)	1.35 (1.02-1.80)	**0.039**
JAKi	39	20	19,122	104.59	0.77 (0.49-1.21)	0.79 (0.49-1.27)	0.328
Infection							
csDMARD	1,508	204	290,501	70.22	1 (reference)	1 (reference)	
TNF	43	13	20,140	64.55	0.92 (0.52-1.61)	0.84 (0.47-1.50)	0.556
non-TNF	98	40	44,855	89.18	1.27 (0.90-1.78)	1.51 (1.06-2.15)	**0.024**
JAKi	39	11	25,109	43.81	0.62 (0.34-1.14)	0.84 (0.45-1.56)	0.574
Any Malignancy							
csDMARD	1,508	105	365,563	28.72	1 (reference)	1 (reference)	
TNF	43	10	22,708	44.04	1.53 (0.80-2.93)	1.02 (0.50-2.07)	0.966
non-TNF	98	9	64,547	13.94	0.49 (0.25-0.96)	0.49 (0.25-0.98)	**0.043**
JAKi	39	5	28,873	17.32	0.60 (0.25-1.48)	0.57 (0.23-1.41)	0.221
MACE							
csDMARD	1,508	131	356,187	36.78	1 (reference)	1 (reference)	
TNF	43	14	21,538	65.00	1.77 (1.02-3.07)	1.56 (0.85-2.85)	0.15
non-TNF	98	14	58,410	23.97	0.65 (0.38-1.13)	0.93 (0.53-1.64)	0.804
JAKi	39	11	25,506	43.13	1.17 (0.63-2.17)	1.42 (0.73-2.78)	0.304
Death							
csDMARD	1,508	33	395,315	8.35	1 (reference)	1 (reference)	
TNF	43	4	26,212	15.26	1.83 (0.65-5.16)	1.18 (0.38-3.60)	0.776
non-TNF	98	15	65,448	22.92	2.75 (1.49-5.05)	4.31 (2.21-8.41)	**<0.001**
JAKi	39	5	29,541	16.93	2.03 (0.79-5.19)	2.70 (0.99-7.38)	0.052

IPTW: inverse probability of treatment weighting; HR, hazard ratio; CI, confidence interval;
*IPTW was calculated for duration RA disease, duration of prior csDMARDs, age, sex, year of enrollment, cumulative DDD of glucocorticoid, concomittant average DDD of glucocorticoid, current smoking, obesity, and CCI.
†Adjusted for duration of RA disease, duration of prior csDMARDs, age, sex, year of enrollment, cumulative DDD of glucocorticoid, concomitant average DDD of glucocorticoid, current smoking, obesity, and CCI.
‡§Adjusted for duration of prior csDMARDs, age, and year of enrollment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2.02; TNFi aHR 0.89, 95% CI 0.51–1.56). Among 1,688 treatment episodes in RA-ILD patients, non-TNF biologics were associated with significantly increased risks of all-cause hospitalization (aHR 1.35, 95% CI 1.02–1.80), infection (aHR 1.51, 95% CI 1.06–2.15), and death (aHR 4.31, 95% CI 2.21–8.41) compared to csDMARDs (Table 1). Non-TNFi use was also associated with a higher risk of infection recurrence (aHR 1.35, 95% CI 1.01–1.79) and pneumonia-related hospitalization (aHR 1.90, 95% CI 0.98–3.69). In contrast, hospitalization due to ILD exacerbation did not differ significantly across treatment groups. The risk of major adverse cardiovascular events was also comparable between groups.

Conclusion: In RA patients without baseline ILD, the risk of developing ILD did not significantly differ across DMARD classes. In RA-ILD patients, while rates of hospitalization due to ILD exacerbation were comparable across groups, non-TNFi use was associated with increased risks of infection and pneumonia-related outcomes. Given that pneumonia is a leading cause of death in RA-ILD, close infection surveillance and preventive strategies are warranted when using non-TNF biologics in this population.

Disclosure: k. Lee: None; **B. Lee**: None; **H. Kim**: None; **S. Kim**: None.

Abstract Number: 0454

Models to predict flare and sustained remission in Rheumatoid Arthritis patients on optimization treatment with bDMARDs: clinical and molecular insights

Laura Galindo Domínguez[1], Belen Acasuso[1], Vanesa Balboa[2], Juan Cañete[3], Benjamin Fernández-Gutiérrez[4], Isidoro Gonzalez-Alvaro[5], jose Luis Pablos[6], Carmen Bejerano-Herreria[7], Maite silva[8], Ignacio rego Pérez[9], Cristina Ruiz-Romero[10], Francisco J De-Toro-Santos[11], Natividad Oreiro[12] and francisco J Blanco[13], [1]Grupo de Investigación en Reumatología (GIR). INIBIC-Complejo Hospitalario Universitario A Coruña (CHUAC). SERGAS, A Coruña, Galicia, Spain, [2]Grupo de Investigación de Reumatología (GIR). Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, coruña, Spain, [3]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [4]Department of Rheumatology and Health Research Institute (IdISSC), Hospital Clínico San Carlos, Madrid, Spain., Madrid, Madrid, Spain, [5]Department of Rheumatology, Hospital Universitario La Princesa, IIS, Madrid Spain, Madrid, Spain, [6]Department of Rheumatology, Instituto de Investigación Hospital 12 de Octubre, Complutense University of Madrid, Madrid, Madrid, Spain, [7]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [8]Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, A Coruña, Spain, A Coruña, Galicia, Spain, [9]Department of Rheumatology, Rheumatology Research Group (GIR) Biomedical Re-search Institute (INIBIC), A Coruna, Spain, [10]Department of Rheumatology, Rheumatology Research Group (GIR) Biomedical Re-search Institute (INIBIC),, A Coruña, Spain, [11]Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, A Coruña, Spain, A Coruña, [12]CHUAC, La Coruna, Spain, [13]INIBIC-University of A Coruna, A Coruna, Galicia, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Optimization of biologic DMARDs (bDMARDs) in patients with rheumatoid arthritis (RA) may be feasible in those who have maintained remission for at least six months. However, this approach carries the risk of disease flare, underscoring the need for reliable predictors to guide clinical decisions. Identifying robust clinical and molecular markers can help design personalized strategies that enhance safety and therapeutic success.

The aim of this study was to identify clinical and molecular predictive variables and develop two models (one for sustained remission and another for joint flare) in RA patients undergoing bDMARD optimization. Both models integrated clinical and molecular data.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Sustained remission prediction model

Remission model	OR	(IC, 95%)	P value
Age	0.92	0.86-0.97	0.012
Rheumatoid Factor	4.86	0.98-28.67	0.060
DAS28-CRP	0.10	0.01-0.67	0.027
rs112267464 (C/A)	5.77	1.30-29.38	0.024
rs5169931244 (G/C)	2.30	0.99-5.83	0.059
rs1560011 (G/A)	3.27	1.09-11.73	0.046

Sustained remission prediction model

Table 2 Joint flare prediction model

Flare model	HR	(IC, 95%)	P value
3v-DAS28-CRP	7·28	1·43-36·95	0·016
Hb (g/dL)	1·52	0·88-2·60	0·125
SBP (mm/Hg)	1·02	1·00-1·05	0·040
Erosion	8·15	1·58-42·02	0·012
VAS pain	1·06	1·02-1·10	<0·001
rs5746065 (C/A)	0·31	0·09-1·00	0·050
rs9594987 (T/C)	0·15	0·04-0·57	0·005
Anti-IFNγ	1·00	1·00-1·00	0·031

Joint flare prediction model

Methods: Data were obtained from the OPTIBIO clinical trial (Eudra-CT 2012-004482-40) and the REMRABIT Project (PMP15/00032), a multicenter, open-label, randomized, phase IV trial. Adults with RA (1987 ACR criteria), in remission for ≥6 months on TNFi or tocilizumab, were randomized (1:1) to continue or taper bDMARD. The optimization group (n=96) was analyzed. Logistic and Cox regression models were developed for sustained remission and flare, respectively. Model performance was assessed using AUC-ROC and concordance index (C-index) over a 12-month follow-up. Analyses were performed using SPSS v28 and R v4.3.1.

Results: Of 195 randomized patients, 74/96 in the optimization group achieved successful tapering after 12 month follow up. In the remission model, older age (8% lower odds per year) and higher 3v-DAS28-CRP (90% lower odds per unit) were significant predictors. The C allele of rs5746065 (TNFRSF1B) and the G allele of rs1560011 (CLEC2D) were associated with sustained remission, with a potential role for rs6555900 (KCNIP1). This model yielded an AUC of 0.88, sensitivity 84%, specificity 83%, and NPV/PPV of 60% and 95%. In the flare model, significant predictors included higher 3v-DAS28-CRP, joint erosions, pain VAS, low hemoglobin, systolic blood pressure, anti-IFN-γ antibodies, and two SNPs. The C allele of

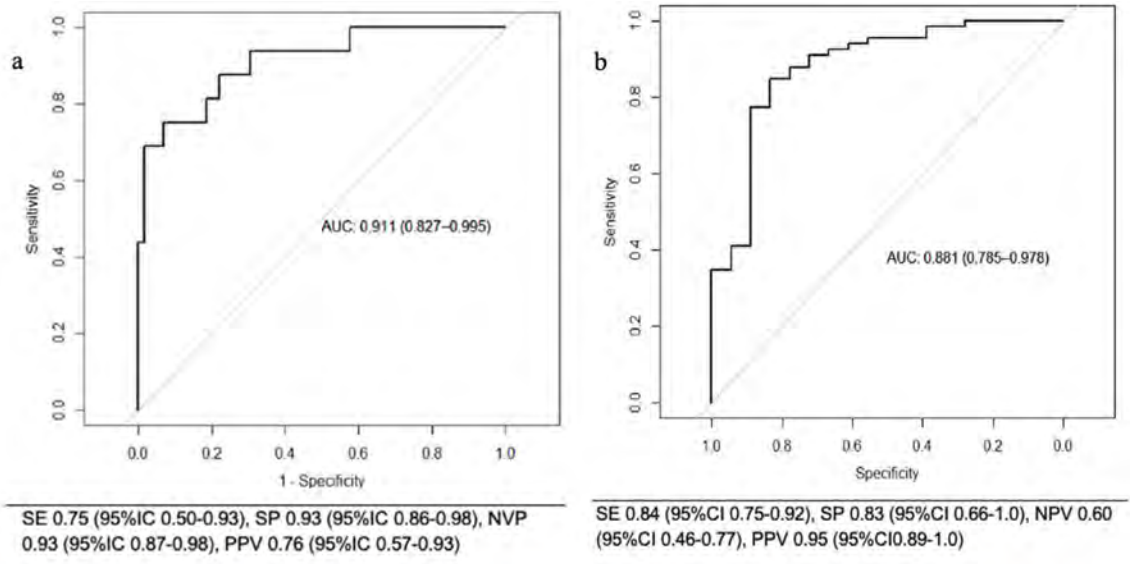


Figure 1a. AUC for joint flare prediction model b. AUC for sustained remission model

Image 1 AUC of prediction models a. Joint flare prediction model b. Sustained remission model

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

rs5746065 (TNFRSF1B) reduced flare risk by 69%, and the C allele of rs9594987 in gene ENOX1 (T/C) by 85%. The model showed a C-index of 0.884, AUC of 0.911 (95% CI: 0.82–0.99), sensitivity 75%, specificity 93%, and NPV/PPV of 93% and 76%.

Conclusion: Combination of predictive clinical, proteomic and genomic biomarkers are crucial for guiding treatment optimization in RA. These models provide promising tools to support personalized bDMARD dose reduction. Further external validation is needed to confirm their generalizability across diverse populations and clinical settings.

Disclosure: L. Galindo Domínguez: None; **B. Acasuso**: None; **V. Balboa**: None; **J. Cañete**: None; **B. Fernández-Gutiérrez**: None; **I. Gonzalez-Alvaro**: None; **j. Pablos**: None; **C. Bejerano-Herreria**: None; **M. silva**: None; **I. rego Pérez**: None; **C. Ruiz-Romero**: None; **F. De-Toro-Santos**: None; **N. Oreiro**: None; **f. Blanco**: None.

Abstract Number: 0455

Assessment of Pain Outcomes in Pooled Phase 3 Trials of a Selective, Tyrosine Kinase 2 Inhibitor, Deucravacitinib, in Patients with Active Psoriatic Arthritis

Lihi Eder[1], Philip J. Mease[2], Vibeke Strand[3], Alexis Ogdie[4], Atul Deodhar[5], Rebecca Haberman[6], April Armstrong[7], Alice B. Gottlieb[8], David Roberts[9], Laurie Eliason[10], Stefan Varga[11], Eleni Vritzali[12], Janice Li[11] and Laure Gossec[13], [1]University of Toronto, Toronto, ON, Canada, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]Stanford University School of Medicine, Palo Alto CA, Portola Valley, CA, [4]University of Pennsylvania, Philadelphia, PA, [5]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [6]NYU Langone Health, New York, NY, [7]University of California Los Angeles, Los Angeles, CA, USA, Los Angeles, CA, [8]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX, [9]Bristol Myers Squibb, Uxbridge, United Kingdom, [10]Bristol Myers Squibb,, Princeton, NJ, [11]Bristol Myers Squibb, Princeton, NJ, [12]Bristol Myers Squibb, Boudry, Switzerland, [13]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

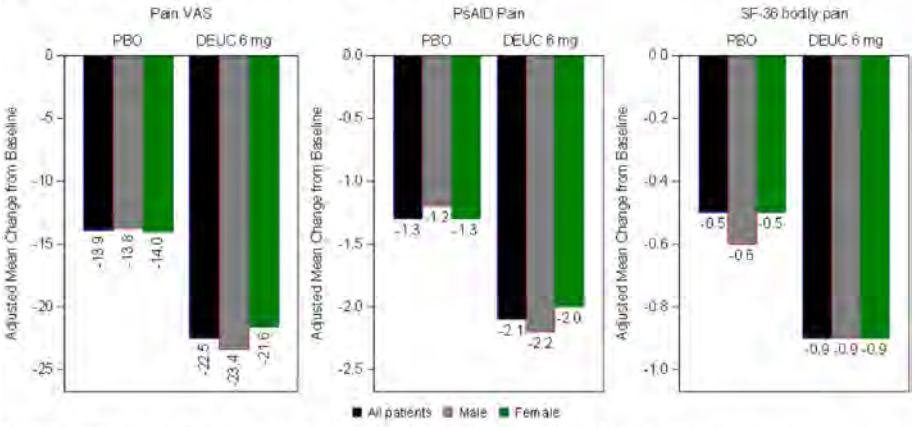
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients rate pain as one of the most important aspects of psoriatic arthritis (PsA). Pain signaling involves a series of cytokines, including those downstream of tyrosine kinase 2 (TYK2) inhibition. Deucravacitinib, an oral, selective allosteric inhibitor of TYK2, mediates signaling of key cytokines in PsA pathogenesis. Deucravacitinib was efficacious vs placebo in phase 3 trials in patients with active PsA. Deucravacitinib is approved for the treatment of adults with plaque psoriasis and is currently under investigation in two phase 3 trials in PsA (POETYK PsA-1 [NCT04908202] and POETYK PsA-2 [NCT04908189]). This analysis includes pooled data from both trials to characterize the effect of deucravacitinib on pain across 3 pain measures for the overall population and by sex to examine its relationship to pain intensity and differences in response to therapies.

Methods: Patients with PsA were randomized to receive deucravacitinib 6 mg (n = 648) or placebo (n = 646). All patients met the CASPAR classification criteria for PsA as part of study enrollment. Pain was assessed at baseline and Week 16 using the Patient Global Assessment (PGA) of Pain visual analog scale (VAS; scored from 0-100); Psoriatic Arthritis Impact of Disease (PsAID) pain instrument (scored from 0-10); and the 36-Item Short Form Survey (SF-36) Bodily Pain questionnaire (6-item Likert scale from "none" [0] to "very severe" [6]). Adjusted mean change in scores from baseline and proportion of patients with different levels of change to Week 16 were reported. Correlations among pain scales and disease activity were also evaluated.

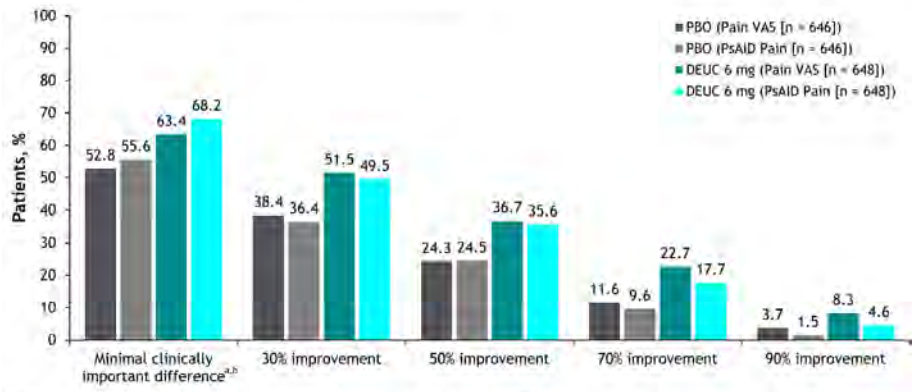
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Mean change from baseline to Week 16 in pain across instruments



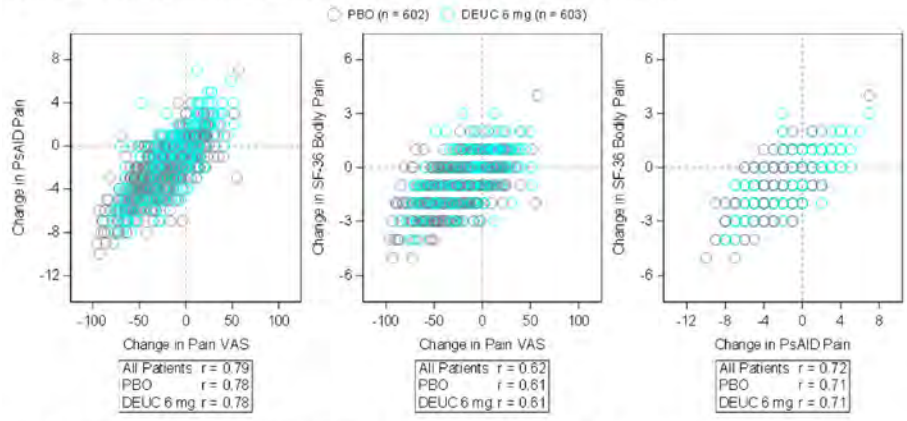
DEUC, deucravacitinib; PBO, placebo; PsAID, Psoriatic Arthritis Impact of Disease; SF-36, 36-Item Short Form Survey; VAS, visual analog scale.

Figure 2. Within-patient improvement in pain at Week 16, as measured by pain VAS and PsAID



[a]For Pain VAS, minimal clinically important difference was defined as ≥10 point reduction in change from baseline or ≥15% reduction in percentage change from baseline on a scale of 0-100.
[b]For Pain PsAID, minimal clinically important difference was defined as ≥1-point reduction in change from baseline or ≥15% reduction in percentage change from baseline on a scale of 0-10.
DEUC, deucravacitinib; PBO, placebo; PsAID, Psoriatic Arthritis Impact of Disease; VAS, visual analog scale.

Figure 3. Pearson's correlation of change from baseline to Week 16 in pain assessment



DEUC, deucravacitinib; PBO, placebo; PsAID, Psoriatic Arthritis Impact of Disease; SF-36, 36-Item Short Form Survey; VAS, visual analog scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: At baseline, mean pain scores in the deucravacitinib vs placebo groups were: pain VAS 61.8 (20.45) vs 61.4 (20.68); PsAID Pain 6.3 (2.04) vs 6.3 (2.08); and SF-36 Bodily Pain 4.3 (0.96) vs 4.3 (0.98). All assessments of pain were strongly correlated with the disease activity at baseline. Overall, mean improvements in pain at Week 16 were greater in patients treated with deucravacitinib vs placebo across all measures. No consistent differences were observed between sexes in mean improvements in pain measures (**Figure 1**). In patients treated with deucravacitinib, nearly two-thirds reported improvements ≥ minimal clinically important difference, and >20% reported a 70% improvement in pain (**Figure 2**). Mean changes in patient-reported pain were highly correlated among pain instruments, demonstrating consistency (**Figure 3**).

Conclusion: Pooled data from 2 trials demonstrated a higher proportion of patients treated with deucravacitinib reported improvement in pain vs placebo, regardless of the instrument used. Improvements were generally consistent between males and females. These findings demonstrate that the use of deucravacitinib resulted in pain relief in patients with PsA.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **V. Strand**: AbbVie/Abbott, 2, Alumis, 2, Amgen, 2, Arthrosi, 2, Artiva, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer-Ingelheim, 2, catalys, 2, contura, 2, Cullinan, 2, Fate Therapeutics, 2, Fortress Biotech, 2, genasence, 2, GlaxoSmithKlein(GSK), 2, Inmedix, 2, Lipum, 2, Longitude Capiral, 2, MED institute, 2, Novartis, 2, RAPT, 2, Royalty Pharma, 2, Sanofi, 2, scipher medcine corp, 2, SetPoint Medical, 2, Sobi, 2, Spherix, 2, Synact, 2, Takeda, 2, Topography, 2, Zoe, 2; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Haberman**: Johnson and Johnson, 1, 2, Novartis, 1, 2; **A. Armstrong**: AbbVie/Abbott, 1, 6, 12, Research Investigator, Almirall, 1, 6, 12, Research Investigator, Arcutis, 1, 6, 12, Research Investigator, Aslan, 1, 6, 12, Research Investigator, Beiersdorf, 1, 6, 12, Research Investigator, Boehringer-Ingelheim, 1, 6, 12, Research Investigator, Bristol-Myers Squibb(BMS), 1, 6, 12, Research Investigator, Dermavant, 1, 6, 12, Research Investigator, Dermira, 1, 6, 12, Research Investigator, Eli Lilly, 1, 6, 12, Research Investigator, EPI Health, 1, 6, 12, Research Investigator, Incyte, 1, 6, 12, Research Investigator, Janssen, 1, 6, 12, Research Investigator, Leo Pharma, 1, 6, 12, Research Investigator, Mindera Health, 1, 6, 12, Research Investigator, Nimbus, 1, 6, 12, Research Investigator, Novartis, 1, 6, 12, Research Investigator, Ortho Dermatologics, 1, 6, 12, Research Investigator, Pfizer, 1, 6, 12, Research Investigator, Regeneron, 1, 6, 12, Research Investigator, Sanofi, 1, 6, 12, Research Investigator, Sun Pharma, 1, 6, 12, Research Investigator, UCB, 1, 6, 12, Research Investigator; **A. Gottlieb**: Amgen, 2, 4, 6, Avalo Therapeutics, 5, BMS, 5, Eli Lilly and Company, 2, 4, 6, Highlights Therapeutics, 2, 4, 6, Janssen, 2, 4, 5, 6, MoonLake Immunotherapeutics, 5, Novartis, 2, 4, 6, Sanofi, 2, 4, 6, Sun Pharma, 2, 4, 6, Takeda, 2, 4, 6, Teva, 2, 4, 6, UCB, 2, 4, 5, 6; **D. Roberts**: Bristol-Myers Squibb, 3, 11; **L. Eliason**: Bristol-Myers Squibb, 3, 11; **S. Varga**: Bristol Myers Squibb, 3, 11; **E. Vritzali**: Bristol Myers Squibb, 3, 11; **J. Li**: Bristol-Myers Squibb, 3, 11; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0456

Impact of Rheumatoid Arthritis on mortality and other outcomes in Heart failure: A nationwide analysis.

Nisha Sapkota[1], Samuel Sule-saa[1], Yubraj Aryal[2], Mark Ntow[3], Karuna Bista[4], Parvathy Rajeev[3], jemima Alemonai[3], Esther Duodu[5], Brijesh Ghimire[3], Pyae Hein[3], Jeffrey Sackey[6], Muhanned Towfig[3], Robert Lamptey[3], Temesgen Gobena[7], Daniel Pinkrah[7] and Mona Pervil Ulysse[8], [1]Interfaith Medical Center, One Broolyn Health, Brooklyn, NY, [2]Geisinger Medical Center, Danville, PA, [3]Interfaith Medical Center, One Broolyn Health, Brooklyn, [4]Montefiore New Rochelle Hospital, New Rochelle, NY, [5]Broodale Hospital Medical Center, One Broolyn Health, Brooklyn, [6]Interfaith Medical Center,One Broolyn Health, Brooklyn, [7]Interfaith Medical Center, Brooklyn, NY, [8]Interfaith Medical Center, One Brooklyn Health, Brooklyn

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease associated with systemic inflammation and increased cardiovascular risk, particularly heart failure (HF). Patients with RA and cardiopulmonary involvement face worse outcomes, including higher HF incidence, mortality, and healthcare use. While earlier studies link RA to adverse cardiac events, large-scale, recent analyses on both mortality and resource utilization are limited. This study fills that gap by analyzing nationwide data (2016–2021) to compare in-hospital mortality in HF admissions with and without RA.

Methods: We conducted a retrospective cohort study using the Nationwide Inpatient Sample (2016–2021) to identify adult hospitalizations with a primary diagnosis of heart failure. Patients were stratified by the presence of rheumatoid arthritis involving the heart or lung (RAHL), defined by ICD-10 codes. In-hospital mortality was assessed using unadjusted and multivariable logistic regression analyses comparing RAHL and non-RA groups. Subgroup analyses were performed for systolic, diastolic, and combined heart failure types.Healthcare utilization (total charges and costs) was evaluated via

Table 1 shows Adjusted and unadjusted logistic regression models

Adjusted and unadjusted logistic regression models of mortality in Heart failure admissions in patients with RA involving the heart or lung (RAHL) vs without RA

		95% CI		
	OR	Lower limit	Upper limit	p value
Unadjusted	2.09	1.79	2.43	<.01
Adjusted	2.12	1.80	2.48	<.01

Adjusted and unadjusted logistic regression models of Combined systolic and diastolic Heart failure admissions in patients with RA involving the heart or lung (RAHL) vs without RA

		95% CI		
	OR	Lower limit	Upper limit	p value
Unadjusted	2.38	2.25	2.51	<.01
Adjusted	1.51	1.42	1.61	<.01

Adjusted and unadjusted logistic regression models of Systolic Heart failure admissions in patients with RA involving the heart or lung (RAHL) vs without RA

		95% CI		
	OR	Lower limit	Upper limit	p value
Unadjusted	1.21	1.10	1.34	<.01
Adjusted	0.91	0.81	1.01	0.09

P < 0.05 indicates statistical significance. Multivariable regression models were adjusted for age at admission, gender, race, median household income, national quartile for patient ZIP Code, Charlson Comorbidity Index, location/teaching status of the hospital, region of the hospital, patient's residence, insurance. CI: 95% confidence interval; OR: Odds ratio.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 shows Adjusted and unadjusted logistic and linear regression models

Adjusted and unadjusted logistic regression models of Diastolic Heart failure admissions in patients with RA involving the heart or lung (RAHL) vs without RA

	OR	95% CI		p value
		Lower limit	Upper limit	
Unadjusted	3.07	2.88	3.27	<.01
Adjusted	1.89	1.77	2.03	<.01

Adjusted and unadjusted linear regression model of Total Charge comparing patients with RA involving the heart or lung (RAHL) vs without RA

	Coefficient	95% CI		p value
		Lower limit	Upper limit	
Unadjusted	9242.02	2958.05	15526.0	<.01
Adjusted	9472.21	3177.60	15766.81	<.01

Adjusted and unadjusted linear regression model of total cost comparing patients with RA involving the heart or lung (RAHL) vs without RA

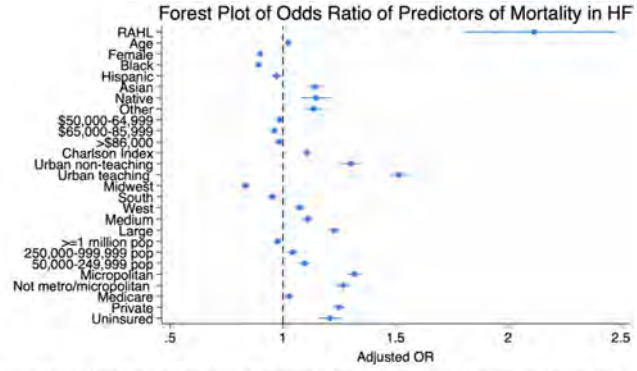
	Coefficient	95% CI		p value
		Lower limit	Upper limit	
Unadjusted	3615.93	1147.64	6084.23	<.01
Adjusted	2232.58	197.72	4662.87	<.01

P < 0.05 indicates statistical significance. Multivariable regression models were adjusted for age at admission, gender, race, median household income, national quartile for patient ZIP Code, Charlson Comorbidity Index, location/teaching status of the hospital, region of the hospital, patient's residence, insurance. CI: 95% confidence interval; OR, Odds ratio.

unadjusted and adjusted linear regression. All models adjusted for demographics, comorbidities, hospital factors, and illness severity.

Results: Logistic regression models were used to examine mortality and heart failure subtypes. In unadjusted analyses, RAHL was associated with a more than twofold increased odds of mortality (OR 2.09, 95%,$p < 0.01$). This association persisted after adjustment for confounders (adjusted OR 2.12, 95%, $p < 0.01$). For combined systolic and diastolic heart failure admissions, the unadjusted model yielded an OR of 2.38 (95%, $p < 0.01$), which was attenuated controlling for confounders resulting in an adjusted OR of 1.51 (95%, $p < 0.01$). Interestingly, while systolic heart failure admissions demonstrated a significant association in the unadjusted model (OR 1.21, 95%, $p < 0.01$), the adjusted odds ratio was not statistically significant (OR 0.91, 95%, $p = 0.09$). However, diastolic heart failure admissions remained significantly elevated in both the unadjusted (OR 3.07, 95%, $p < 0.01$) and adjusted (OR 1.89, 95%, $p < 0.01$) models. Linear regression showed that RAHL was linked to higher healthcare utilization, with significantly increased total hospital charges (adjusted coefficient: $9,472.21) and costs (adjusted coefficient: $2,232.58) in both unadjusted and adjusted models ($p < 0.01$) among RAHL patients. From the Forest plot, RAHL, hospital type, insurance type, and certain racial/ethnic groups were strong predictors of mortality, while female sex, higher income brackets, and Midwest location showed protective associations.

Table 3 shows Forest Plot of Odds Ratio of Predictors of Mortality in HF



Forest Plot of Odds Ratio of Predictors of Mortality in HF (adjusted model). The vertical dashed line represents the null value (OR = 1.0). Horizontal lines represent 95% confidence intervals for each variable

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our analysis indicates that heart failure patients with rheumatoid arthritis have more than double the odds of mortality and higher healthcare utilization than those without RA. Despite the retrospective design and reliance on ICD coding, these results underscore the need for enhanced clinical surveillance, tailored treatment strategies, and further studies incorporating detailed therapeutic and cardiac data to better guide management.

Disclosure: N. Sapkota: None; **S. Sule-saa**: None; **Y. Aryal**: None; **M. Ntow**: None; **K. Bista**: None; **P. Rajeev**: None; **j. Alemonai**: None; **E. Duodu**: None; **B. Ghimire**: None; **P. Hein**: None; **J. Sackey**: None; **M. Towfig**: None; **R. Lamptey**: None; **T. Gobena**: None; **D. Pinkrah**: None; **M. Ulysse**: None.

Abstract Number: 0457

Pulmonary Profiles: Characterizing Lung Findings in Rheumatoid Arthritis Patients Undergoing Lung Cancer Screening

Pratyusha Banik[1], Melody Andrews[1], Sudhakar Pipavath[1] and Namrata Singh[2], [1]University of Washington, Seattle, WA, [2]University of Washington, Bellevue, WA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) has been associated with an increased risk of lung cancer with shared risk factors being heavy smoking history and possibly interstitial lung disease (ILD). They highlight the importance of lung cancer screening in persons with RA that meet age and smoking history criteria. However there have not been many studies examining the radiographic findings among persons with RA that undergo chest computed tomography (CT) for lung cancer screening. The objectives of our study were to evaluate the yield of lung cancer diagnoses in those with RA that underwent lung cancer screening with low dose CT chest, and to characterize the pattern of lung nodules and pulmonary parenchymal findings in this cohort.

Methods: We identified all adults (>18 years of age) with an ICD10 diagnostic code of RA between March 2021 and October 2023, that follow with rheumatology providers at our academic center. We then used the procedure code for lung cancer screening with chest CT (72171) to identify patients with RA that met the United States Preventative Task Force (USPSTF) criteria for lung cancer screening CT, and who had undergone at least one CT scan. We conducted chart review

Table 1: Patient characteristics

Table 1

Patient Characteristics	
Age of 1st Screen, years - mean (+/- SD)	63 (+/- 6)
Sex - Male - no (%)	16 (38)
Ethnic group - Non-Hispanic or Latino/a or Latinx – no(%)	40 (95)
Ethnic group - Hispanic or Latino/a or Latinx – no (%)	2 (5)
Positive RF - no (%)	28 (66)
Positive CCP - no (%)	27 (64)
Total Smoking Pack /Year History - Median (min, max)	35(10, 104)
Smoking status at 1st screen: Former - no (%)	24 (57)
Smoking status at 1st screen: Current - no (%)	18(43)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1A

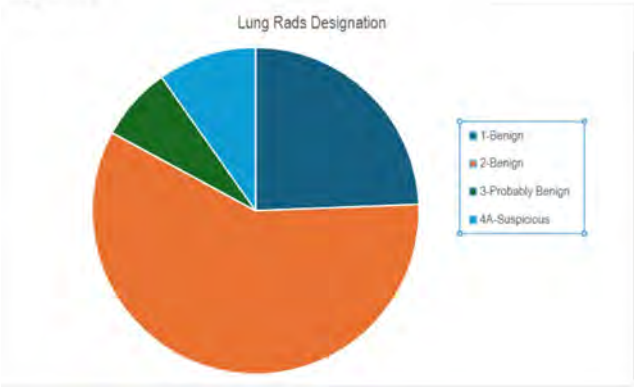


Figure 1A: Lung-RADS Category Assessment of Nodules

Figure 1B

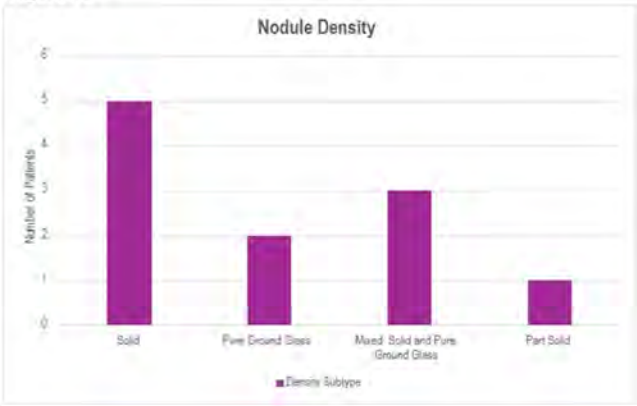


Figure 1B: Nodule Density

to extract patient characteristics and lung imaging data such as age, sex duration of RA, rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) status, smoking pack year history, nodule characteristics, presence of ILD, and lung cancer diagnosis.

Results: 42 patients met the inclusion criteria. The majority were female (62%). 66% were RF positive and 64% were CCP positive. Of the 42 patients with RA who underwent lung cancer screening, one (2.4%) was diagnosed with lung cancer (squamous cell carcinoma) on follow up imaging. The majority (80%) had benign lung nodules with Lung-RADS(Lung Imaging Reporting and Data System) category 1 or 2, and 9.5% had suspicious findings (Lung-RADS 4A). Nodules > 6 mm were found in 17% and calcified nodules suggestive of prior granulomatous disease were seen in five patients. Nodule density varied with solid, pure ground glass, part solid, and mixed patterns observed. Interstitial lung abnormalities or interstitial lung disease was seen in 17%, and showed no association with Lung-RADS category.

Conclusion: Among patients with RA who met criteria for lung cancer screening, the diagnostic yield for malignancy was low, and most lung nodules were benign. Nonetheless, a notable proportion had suspicious findings requiring follow-up. These results highlight the importance of targeted lung cancer screening in RA, particularly for individuals with significant smoking history, and support ongoing vigilance in radiographic surveillance for early detection and management.

Disclosure: P. Banik: None; **M. Andrews**: None; **S. Pipavath**: None; **N. Singh**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0458

TyG-BMI Index as a Serological Biomarker for Carotid Plaque and Cardiac Function Changes in Rheumatoid Arthritis

Rebeca L. Polina-Lugo[1], Oscar Azael Garza-Flores[2], Fernanda M. Garcia-Garcia[3], Esteban C. Garza-Gonzalez[4], Jesus Alberto Cardenas-de la Garza[5], Iris J. Colunga-Pedraza[3], Jose R Azpiri-Lopez[6], Dionicio A. Galarza-Delgado[3], Victor M Fraga-Enriquez[7] and Diego Azamat Salcedo Almanza[8], [1]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, San Nicolas de los Garza, Nuevo Leon, Mexico, [5]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [6]Cardiology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [7]Cardiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [8]Radiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The Triglyceride-Glucose-BMI index (TyG-BMI) is a reliable method for detecting insulin resistance (IR), with effectiveness comparable to the gold standard. Elevated TyG-BMI levels have been associated with subclinical atherosclerosis and cardiac dysfunction. Both IR and rheumatoid arthritis (RA) promote a state of hyperglycemia. Therefore, the use of TyG-BMI as a screening tool for CV risk assessment in this population is proposed, offering a practical and effective alternative for screening. For this reason, we aim to evaluate the association of the TyG-BMI Index with carotid plaque (CP), left ventricular geometry, and subclinical cardiac dysfunction in patients with RA.

Methods: A Cross-sectional, descriptive, comparative study was conducted. Patients aged 30 to 75 with RA criteria were included. Those with CV disease history were excluded. Carotid ultrasound and transthoracic echocardiogram were performed in 297 and 238 participants, respectively. CP was defined as a diffuse carotid intima-media thickness (IMT)

Table 1. Demographic and clinical characteristics of carotid ultrasound.

Variables	Tercile 1 (119.2-227.5) n=99	Tercile 2 (227.6-265.1) n=99	Tercile 3 (265.2-495.7) n=99	*p-value*
Age, years, ± SD	55.7 ±9.6	57.0 ±8.6	54.3 ±10.4	0.16
Women, n (%)	94 (94.9)	92 (92.9)	93 (93.9)	0.83
Comorbidities				
Diabetes, n (%)	10 (10.1)	14 (14.1)	28 (28.2)	**0.002**
Hypertension, n (%)	23 (23.2)	29 (29.2)	45 (45.4)	**0.003**
Dyslipidemia, n (%)	38 (38.3)	42 (42.4)	40 (40.4)	0.84
Active smoking, n (%)	11 (11.1)	8 (8.0)	8 (8.0)	0.77
Obesity, n (%)	1 (1.0)	11 (11.1)	88 (88.8)	**<0.001**
BMI, median (IQR)	24 (22.2-25.7)	28.1 (27.0-29.3)	33.7 (31.5-36.2)	**<0.001**
Clinical features				
Disease duration, years, median (IQR)	8.4 (3.0-14.8)	9 (3.9-15.3)	7 (2.8-11.1)	0.18
Subclinical atherosclerosis	40 (40.4)	41 (41.4)	40 (40.4)	0.98
Unilateral plaque, n (%)	20 (20.2)	22 (22.1)	23 (23.2)	0.87
Bilateral plaque, n (%)	20 (20.2)	19 (19.1)	17 (17.1)	0.85

SD, standard deviation; IQR, interquartile range; BMI, Body mass index.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Demographic and clinical characteristics of echocardiography.

Variables	Tercile 1 (119.2-227.1) n=80	Tercile 2 (227.2-266.8) n=79	Tercile 3 (266.9-462.4) n=79	*p-value*
Age, years, ±SD	55.4 ±9.7	57.5 ±8.2	53.0 ±10.0	**0.01**
Women, n (%)	73 (91.2)	74 (96.6)	75 (94.9)	0.64
Comorbidities				
Diabetes, n (%)	10 (10.1)	14 (14.1)	28 (28.2)	0.08
Hypertension, n (%)	23 (23.2)	29 (29.2)	45 (45.4)	**<0.001**
Dyslipidemia, n (%)	38 (38.3)	42 (42.4)	40 (40.4)	0.29
Active smoking, n (%)	11 (11.1)	8 (8.0)	8 (8.0)	0.92
Obesity, n (%)	1 (1.0)	11 (11.1)	88 (88.8)	**<0.001**
BMI, mean, ±SD	23.6 ±2.7	28.2±1.5	34.4 ±4.2	**0.01**
Clinical features				
Disease duration, years, median (IQR)	7 (3.0-14.0)	8.2 (3.0-14.0)	6.2 (2.5-14.5)	0.70
LV-Remodeling classification				
Normal, n (%)	34 (42.5)	30 (37.9)	32 (40.5)	0.84
Concentric remodeling, n (%)	15 (18.7)	26 (32.1)	19 (24.0)	0.11
Concentric hypertrophy, n (%)	8 (10.0)	3 (3.7)	4 (5.0)	0.23
Eccentric hypertrophy, n (%)	1 (1.2)	1 (1.2)	1 (1.2)	1.00
Subclinical diastolic dysfunction				
Normal, n (%)	45 (56.2)	48 (60.7)	49 (62.0)	0.73
Pseudonormal, n (%)	19 (23.7)	16 (20.2)	18 (22.7)	0.86
RRP, n (%)	6 (7.5)	10 (12.6)	10 (12.6)	0.67
IRP, n (%)	2 (2.5)	2 (2.5)	2 (2.5)	1.0
Subclinical systolic dysfunction				
TAPSE, median (IQR)	22 (21-25)	22 (21-24)	22 (20-24)	0.37
LVEF, median (IQR)	61 (58-64)	62 (58-65)	60 (57-64)	0.19
GLS, median (IQR)	-21 (-22 to -19)	-20 (-23 to -19)	-20 (-22 to -18)	0.17
SSD, n (%)	6 (7.5)	10 (12.6)	10 (12.6)	0.48

SD, standard deviation; IQR, interquartile range; BMI, Body mass index; LV, left ventricle; RRP, reversible restrictive pattern; IRP, irreversible restrictive pattern; TAPSE, tricuspid annular plane systolic excursion; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; SSD, subclinical systolic dysfunction

≥1.2 mm or focal thickness ≥0.8 mm. The echocardiographic assessment included left ventricular mass index (LVMI), relative wall thickness (RWT), tricuspid annular plane systolic excursion (TAPSE), and left ventricular ejection fraction (LVEF). Subclinical diastolic dysfunction (SDD) was defined according to the 2016 American College of Cardiology classification, and subclinical systolic dysfunction (SSD) of the left ventricle (LV) was defined as a global longitudinal strain (GLS) >-18%.

To calculate the TyG-BMI index, serum triglyceride (TG) levels, fasting blood glucose (FBG), and body mass index (BMI) were used with the following formula: TyG-BMI Index = Ln [TG (mg/dL) × FBG (mg/dL)/2] × BMI.

Participants were categorized into tertiles based on the TyG-BMI. Group distribution was evaluated using the Kolmogorov-Smirnov test. Comparisons were made using the Chi-square test, ANOVA, or Kruskal-Wallis test. A p-value ≤0.05 was considered statistically significant.

Results: Most patients with RA were women aged between 53 and 57 years. Among the 297 patients who underwent carotid ultrasound (Table 1), a higher prevalence of diabetes, hypertension, and obesity was observed in the third tertile. However, the prevalence of CP was similar across all groups and was not statistically significant.

Regarding the 238 patients who underwent transthoracic echocardiography (Table 2), a similar prevalence of CV risk comorbidities was observed. From the second tertile onward, there was an increase in the prevalence of subclinical diastolic dysfunction and concentric remodeling changes, although these differences were not statistically significant.

Conclusion: The TyG-BMI index was not associated with the presence of CP, significant changes in echocardiographic parameters. However, higher TyG-BMI levels were related to traditional CV risk comorbidities. Despite these findings, studies with larger sample sizes are needed to confirm these associations. Integrating echocardiographic and carotid ultrasound assessments into CV risk evaluation remains essential for the early detection of structural and functional abnormalities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Polina-Lugo: None; **O. Garza-Flores**: None; **F. Garcia-Garcia**: None; **E. Garza-Gonzalez**: None; **J. Cardenas-de la Garza**: None; **I. Colunga-Pedraza**: None; **J. Azpiri-Lopez**: None; **D. Galarza-Delgado**: None; **V. Fraga-Enriquez**: None; **D. Salcedo Almanza**: None.

Abstract Number: 0459

Risk Factors for Acute Exacerbation in Patients with Rheumatoid Arthritis-associated Interstitial Lung Disease

Rinko Katsuda[1], Akiko Kitagawa[1], Masayuki Azukizawa[2], Musuzu Fujimori[1] and Tetsuji Kawamura[3], [1]Department of Rheumatology, NHO Himeji Medical Center, Japan, Himeji, Japan, [2]Department of Orthopaedic Surgery, NHO Himeji Medical Center, Japan, Himeji, Japan, [3]Department of Respiratory Medicine, NHO Himeji Medical Center, Japan, Himeji, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is a common and serious extra-articular manifestation of RA, contributing to ∼10% of RA-related mortality. Acute exacerbation (AE) of RA-ILD is often fatal, but its clinical risk factors remain poorly defined.

Methods: We retrospectively analyzed RA-ILD patients treated at our center. The AE group included patients hospitalized for AE between 2013 and 2022. The non-AE group comprised patients attending outpatient care in 2013 who were not hospitalized for AE during the same period. Clinical variables included age, age at RA onset, RA duration, sex, smoking history, use of methotrexate (MTX) and prednisolone (PSL), DAS28-ESR, RF, and ACPA. Univariate analyses were performed using t-tests or chi-square tests. Logistic regression was used for both univariate and multivariate analyses (Forward: LR method). Given a strong correlation between age and age at RA onset ($r = 0.719$), only the latter was included in multivariate analysis.

Results: Univariate analysis identified age and age at RA onset as significantly associated with AE ($p< 0.001$ and $p=0.003$, respectively). Multivariate analysis revealed age at RA onset (OR 1.264, 95% CI 1.099–1.455, $p=0.001$) and RA duration (OR 1.226, 95% CI 1.067–1.409, $p=0.004$) as independent risk factors. The model showed moderate explanatory power (Nagelkerke $R^2 = 0.425$) and high predictive accuracy (85.7%). In-hospital AE mortality was 40%.

Conclusion: Later onset of RA and longer disease duration independently increased the risk of AE in RA-ILD. These findings highlight the importance of early risk stratification and close monitoring in susceptible patients.

Disclosure: R. Katsuda: None; **A. Kitagawa**: None; **M. Azukizawa**: None; **M. Fujimori**: None; **T. Kawamura**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0460

The Impact of Early and Artificial Menopause on Dementia Risk Among Women with Rheumatoid Arthritis

Ryan Salama[1], Cassondra Hulshizer[2], Cynthia Crowson[3] and Elena myasoedova[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, [3]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Alzheimer's disease and related dementias present an increasing global health concern, with increasing incidence and prevalence. Hormonal fluctuations associated with menopause may exacerbate inflammatory and cerebrovascular changes, contributing to neurocognitive decline. Early and artificial menopause have been linked to elevated dementia risk and neurocognitive decline in the general population. Rheumatoid arthritis (RA) has been separately established as a risk factor for dementia. However, the specific relationship between menopause characteristics and dementia in populations with RA remains unclear. We aimed to evaluate the association between artificial and early menopause on occurrence of dementia in a population with RA.

Methods: This retrospective population-based study included women /=50 years of age with incident RA in 1980-2014 who met 1987 ACR criteria and had no previous diagnosis of dementia. Age at menopause was categorically defined as the age bracket of an individual (< 45, 45–54, and ≥55 years) at 6 months post-menstruation cessation for natural cases or at the time menopause was induced for artificial cases. Menopause data was manually collected from medical records. Women with unknown age at menopause were assigned to the 45-54 age bracket; women with unknown causes of menopause were classified as natural. Artificial menopause included those with bilateral oophorectomy or chemotherapy-induced menopause. Dementia was defined as two relevant ICD-9/ICD-10 codes at least 30 days apart.

Cox proportional hazards models were used to estimate the adjusted hazard ratio (aHR) and 95% confidence intervals (CI) between menopause and dementia. Individuals with early (< 45 years) or artificial menopause were compared to referents with natural or unknown-cause menopause at ≥45 years. Primary covariates included age and index year of RA incidence. To assess effect modification by RA severity and treatment, separate interaction models were performed examining the effects of RF/CCP positivity, erosions and/or destructive changes, severe extra-articular RA manifestations, or large joint swelling within one year.

Results: A total of 458 women were included, with a median age at RA incidence of 63.2 years. Sixty-six women had an outcome of dementia following RA diagnosis. Early and/or surgical menopause was present in 82 women (17.9%). Early or surgical menopause was associated with an increased risk of dementia (aHR 1.96; CI 0.99-3.89). Results were similar when adjusting for RF/CCP positivity, obesity, smoking, and education. For the interaction analyses, no statistically significant effect modifications were observed (all interactions P >0.05).

Conclusion: In women with RA, early or surgical menopause was associated with a nearly two-fold increase in risk of dementia, suggesting the need for increased awareness of increased risk for cognitive decline in this population of patients with RA. This association was not significantly modified by RA severity factors, smoking, education, or obesity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Salama: None; **C. Hulshizer**: None; **C. Crowson**: None; **E. myasoedova**: None.

Abstract Number: 0461

Right Diagnoses For the Wrong Reasons: Limitations of Current Large-Language Model based Agentic Frameworks for Screening of Rheumatoid Arthritis

Sarthak Verma[1], Avarna Agarwal[1], Umakanta Maharana[2], Murari Mandal[3], Prasanta Padhan[1], Prakashini Mruthyanjaya[4] and Sakir Ahmed[1], [1]Department of Clinical Immunology and Rheumatology, Kalinga Institute of Medical Sciences, Bhubaneswar, Orissa, India, [2]School of Computer Engineering, KIIT University, Bhubaneswar, India, [3]School of Computer Engineering, KIIT University, Bhubaneswar, Orissa, India, [4]Department of Clinical Immunology and Rheumatology, Kalinga Institute of Medical Sciences, Bhubaneswar, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: In India, Rheumatoid arthritis (RA) is often diagnosed late. Artificial Intelligence (AI) driven Large Language models (LLMs) can be deployed via widely available mobile phone devices, offering a potential screening solution. Here, we attempted to explore various AI agentic frameworks to identify the most effective model SARA (Screening Agent for RA), and also to validate how these models arrive at a diagnosis of RA.

Methods: We had developed the PreRAID (Pre-Screening Rheumatoid Arthritis Information Database) from consenting patients with joint pain, classifying patients into RA or not RA as per treating physician diagnosis. The dataset was split into 280 cases for the knowledge base (KB) and 70 for testing. A Neo4j vector database enabled embedding-based retrieval.

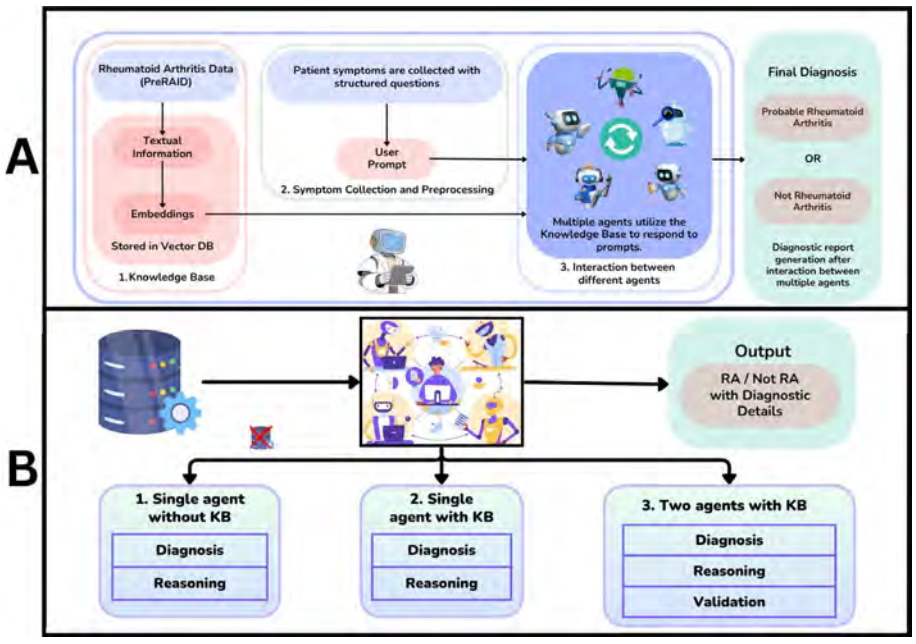


Figure 1: Agentic framework. (A) Workflow of the SARA framework and (B) Illustration of the sequential steps involved in diagnosing RA with single agent without knowledge base (KB), single agent with KB and Two agents with KB

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

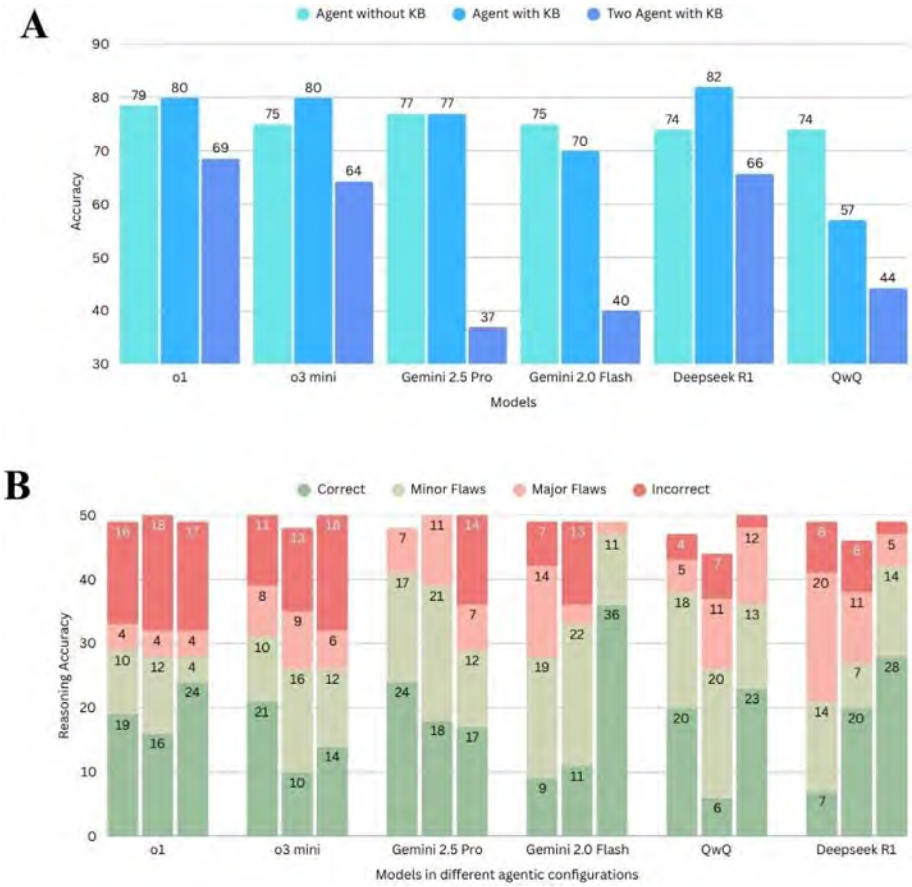


Figure 2: Validation of the different models. (A) Accuracies of different LLM models under different agentic configurations and (B) Accuracies of reasonings provided by different models as validated by clinicians

Six LLMs were evaluated—four closed-source (OpenAI o1, OpenAI o3 mini, Gemini 2.5 Pro, Gemini 2.0 Flash) and two open-source (QwQ, Deepseek R1 70B). Each model was tested under three agentic configurations: (1) a single agent without knowledge base (KB) access; (2) a single agent with retrieval-augmented generation (RAG); and (3) a dual-agent setup, where the first agent generated a diagnosis and reasoning, validated by a second agent. [Figure 1]

Each model-configuration pair was evaluated on 50 new cases. The models were also asked to explain the reasons behind each diagnosis, which was independently assessed by two fellows and one consultant rheumatologist using a four-point Likert scale.

Results: The PreRAID dataset included 84% RA-confirmed cases and 16% controls. Deepseek R1 showed the highest accuracy (82%) in the single-agent with KB setting, followed by o1 and o3 mini (80% each). Accuracy dropped in the two-agent setup, most notably in Gemini 2.5 Pro (37%) and Gemini 2.0 Flash (40%) [Figure 2].

Despite moderate to high accuracy, Gemini models underperformed in reasoning when agentic complexity increased. Reasoning quality was suboptimal across all models. Gemini 2.0 Flash (36/50) and Deepseek R1 (28/50) had the most correct justifications, while QwQ and Gemini 2.5 Pro scored the lowest (6 and 10, respectively). Many outputs showed minor or major reasoning flaws, indicating a disconnect between diagnostic accuracy and reasoning integrity.

Conclusion: Deepseek R1 achieved the highest diagnostic accuracy (82%) in the single-agent with KB configuration. However, reasoning quality across all models was suboptimal, with many correct diagnoses attributed to flawed reasons. The dual-agent setup, intended to enhance reasoning, led to decreased diagnostic performance. Though we built a robust

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

system (SARA) for screening, the lack of proper reasoning by the LLMs preclude the use as a diagnostic tool. Future directions should prioritize explainable AI approaches so that clinicians can trust the tool.

Disclosure: S. Verma: None; **A. Agarwal**: None; **U. Maharana**: None; **M. Mandal**: None; **P. Padhan**: None; **P. Mruthyanjaya**: None; **S. Ahmed**: Alkem, 6, Cipla, 6, Dr Reddy's, 6, Ipca, 6, Janssen, 1, Pfizer, 6, Sun Pharma, 6, Torrent, 6.

Abstract Number: 0462

Does Biological Sex Affect Mortality in Frail Patients with Rheumatoid Arthritis?

Sayuli Bhide[1], Hannah Brubeck[2], Punyasha Roul[3], Aaron Baraff[2], Bryant England[4], Nadine El-Ayache[1], Grant Cannon[5], Namrata Singh[6], Gary Kunkel[7], Ted Mikuls[4], Dolores Shoback[8], Kaleb Michaud[4], Patti Katz[9], Jose Garcia[10], Ariela Orkaby[11], Joshua Baker[12] and Katherine Wysham[13], [1]University of Washington, Seattle, WA, [2]VA Puget Sound Health Care System, Seattle, WA, [3]UNMC, Omaha, NE, [4]University of Nebraska Medical Center, Omaha, NE, [5]University of Utah and Salt Lake City VA, Salt Lake City, UT, [6]University of Washington, Bellevue, WA, [7]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [8]San Francisco VA Medical Center & University of California San Francisco, San Francisco, CA, [9]UCSF, San Rafael, CA, [10]VA Puget Sound Health Care System, VA GRECC, and University of Washington, Seattle, WA, [11]Veterans Affairs Boston Healthcare System & Brigham and Women's Hospital, Boston, MA, [12]University of Pennsylvania, Philadelphia, PA, [13]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Frailty predicts mortality in RA. In the general population, males have a higher risk of death than females despite lower levels of frailty.[1] We evaluated how sex modifies the relationship between frailty and mortality in RA.

Methods: Participants from the Veterans Affairs Rheumatoid Arthritis (VARA) Registry enrolled between 1/2003 to 12/2020 were included. Follow up ended in 12/2022, allowing for at least 2 years of observation for each participant. Frailty was measured annually throughout the observation period using the VA Frailty Index (VA-FI), a validated deficit accumulation score based on >6000 diagnostic codes.[2] Participants were categorized as robust or frail at enrollment using the established VA-FI cutoff of >0.2. Our primary model used multivariable Cox regression to evaluate the relationship between baseline frailty and mortality, with sex as an interaction term. A subsequent multivariable Cox model, including only those who have new onset frailty, evaluated sex differences in the risk of death starting at the time of frailty onset. Models were adjusted for baseline age (categorized by decade), race, BMI (normal/low vs. high), RF positivity, RA disease duration, DAS28-ESR, rheumatic disease comorbidity index (RDCI), prednisone use, conventional synthetic DMARDs and biologic DMARDs.

Results: 2,601 males and 344 females were included in the primary analysis, with average age 66 (10) for males and 55 (12) for females. Disease duration was 11.6 (11.5) years for males and 9.8 (9.8) years for females. An equal proportion of males and females were frail at baseline (28% and 27%, respectively). During follow-up, 1,301 (50%) males and 66 (19%) females died. Compared to robust males, robust females were less likely to die (aHR 0.45, [0.32-0.63]). Frailty was associated with an increased risk of death in frail males compared to robust males (aHR 1.37, [1.20-1.57]). The risk of death did increase in frail females, however, it was not significantly higher than that of robust males (aHR 1.01, [0.70-1.45]). The risk of death conferred by frailty was higher in females than males as represented by the significant interaction term between sex and frailty of 1.64 (p=0.051). The incident frailty analysis included 948 males with mean age 67.6

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographics by Sex in RA Patients, VARA Cohort (1/2003 – 12/2020). Values are means (standard deviations) or N (%).

	All	Males	Females
	2,945	2,601 (88%)	344 (12%)
Frail	829 (28%)	736 (28%)	93 (27%)
Died	1,367 (46%)	1,301 (50%)	66 (19%)
Age (Years)	65 (11)	66 (10)	55 (12)
Decade Enrolled			
<50	267 (9%)	157 (6%)	110 (32%)
50-60	637 (22%)	529 (20%)	108 (31%)
60-70	1,127 (38%)	1,037 (40%)	90 (26%)
70-80	712 (24%)	687 (26%)	25 (7%)
80+	202 (7%)	191 (7%)	11 (3%)
Race			
White	2,126(72%)	1,941 (75%)	185 (54%)
Non-White	485 (17%)	374 (14%)	111 (32%)
Smoking Status			
Never Smoker	610 (21%)	456 (18%)	154 (45%)
Current Smoker	728 (25%)	674 (26%)	54 (16%)
Former Smoker	1,543 (52%)	1,427 (55%)	116 (34%)
Body Mass Index (BMI)			
<25	736 (25%)	661 (25%)	75 (22%)
25+	2,071 (70%)	1,815 (70%)	256 (74%)
Disease Duration	11.4 (11.3)	11.6 (11.5)	9.8 (9.8)
Rheumatoid Factor Positive	2,175 (74%)	1,940 (75%)	235 (68%)
Anti-CCP Positive	2,187 (74%)	1,939 (75%)	248 (72%)
DAS28ESR			
Remission	580 (20%)	523 (20%)	57 (17%)
Low	356 (12%)	307 (12%)	49 (14%)
Moderate	928 (32%)	825 (32%)	103 (30%)
High	483 (16%)	426 (16%)	57 (17%)
RDCI	3.4 (2.0)	3.5 (1.9)	3.3 (2.2)
Prednisone Use	938 (32%)	862 (33%)	76 (22%)
csDMARD Use	2,138 (73%)	1,899 (73%)	239 (70%)
Biologic DMARD Use	1,200 (41%)	1,023 (39%)	177 (52%)

DAS28-ESR = Disease activity score 28 – Erythrocyte sedimentation rate, RDCI = Rheumatic disease comorbidity index, csDMARD = conventional synthetic DMARD. Percentages Missing: Race (11%), Smoking status (2%), BMI (5%), Anti-CCP (4%), RF (4%), DAS28-ESR (20%), Prednisone (6%), csDMARD (6%), Biologic DMARD (6%).

Table 2. Multivariable Cox models evaluating the relationship between baseline frailty and mortality and again with evaluating the interaction of frailty and sex on the risk of mortality in RA.

	Total	Died	aHR [95%CI]*
All Participants			
Non-Frail	2,116	862 (41%)	Ref
Frail	829	505 (61%)	1.40 [1.23-1.60]
Sex-Based Analysis*			
Males			
-Non-Frail	1,865 (72%)	827 (44%)	Ref
-Frail	736 (28%)	474 (64%)	1.37 [1.20-1.57]
Females			
-Non-Frail	251 (73%)	35 (15%)	0.45 [0.32-0.63]
-Frail	93 (27%)	31 (33%)	1.01 [0.70-1.45]

*Interaction between sex and frailty HR 1.64, p=0.051
- aHR = adjusted hazard ratio for baseline age, race, BMI, RF positivity, RA disease duration, DAS28-ESR, use of prednisone, conventional synthetic DMARDs and biologic DMARDs, and RDCI
- CI = confidence interval

Table 3. Risk of death in in males and females with incident frailty.

	Total	Died	aHR [95%CI]*	Median Time to Death (years) [95%CI]
Male	948	526 (55%)	Ref	6.50 [6.10-7.08]
Female	95	26 (27%)	0.53 [0.35-0.79]	>16.40**

- aHR = adjusted hazard ratio for baseline age, race, BMI, RF positivity, RA disease duration, DAS28-ESR, use of prednisone, conventional synthetic DMARDs and biologic DMARDs, and RDCI
- CI = confidence interval
**Median death unable to be calculated due to <50% death in females

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(0.39) and 95 females with mean age 64.9 (2.43) with 526 (55%) males and 26 (27%) females dying during follow-up. Females with incident frailty were less likely to die than males with incident frailty (aHR 0.59, [0.39-0.91]). Median survival time was shorter in newly frail males than females (6.50 vs >16.40 years, respectively); exact median could not be calculated for females due to less than 50% death among females.

Conclusion: Frailty in RA is associated with mortality and this relationship differs by sex. Males, regardless of frailty status, have a higher risk of death than females, yet frailty confers a higher relative risk of death in females. Males with incident frailty have a higher risk of death and shorter median survival times than females with incident frailty with RA, highlighting the need for early recognition and intervention in this group.

References:

(1) Gordon et al. *Exp Gerontol* **2017**
(2) Orkaby et al. T*J Gerontol A Biol Sci Med Sci* **2019**

Disclosure: S. Bhide: None; **H. Brubeck**: None; **P. Roul**: None; **A. Baraff**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **N. El-Ayache**: None; **G. Cannon**: None; **N. Singh**: None; **G. Kunkel**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **D. Shoback**: None; **K. Michaud**: None; **P. Katz**: None; **J. Garcia**: Aveo Oncology, 2, Catalym, 2, Pfizer, 5; **A. Orkaby**: None; **J. Baker**: Amgen, 5; **K. Wysham**: None.

Abstract Number: 0463

Synovial fluid is a robust biomarker of synovial tissue inflammation in rheumatoid arthritis

Solana Cushing[1], Susan Goodman[2], Michael Parides[1], Hadeel Abdul-Rehman[1], Daniel Ramirez[2], Edward DiCarlo[2], Kristine Carandang[3], Renee Davis[4], Rebecca Blank[5], Laura Donlin[1], Anna Helena Jonsson[6], Amit Lakhanpal[2], Bella Mehta[7], Dana Orange[8] and Melanie smith[2], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [3]Young Patients' Autoimmune Research & Empowerment Alliance, San Diego, CA, [4]New York, New York, NY, [5]NYU Langone Health, New York, NY, [6]University of Colorado School of Medicine, Aurora, CO, [7]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ, [8]The Rockefeller University, New York, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Synovial tissue pathotype may indicate treatment response in RA, but synovial biopsies are not widely available. Synovial fluid (SF) is a promising surrogate. We sought to identify SF features that reflect histopathological and clinical characteristics in RA.

Methods: SF and synovial tissue were prospectively collected from patients meeting RA criteria undergoing total knee replacement. SF white blood cell (WBC) count and differentials were analyzed in the clinical laboratory. Patients were stratified into three groups by medication history: "biologic naïve," "on biologic" and "refractory." Synovial Lymphocytic Inflammation (SLI) was graded from low (0-2) to high (3) inflammation by a board-certified pathologist. Descriptive statistics, correlations, ROC curve, and multivariate regressions were used to assess associations with SF cell counts.

Separately, a retrospective review of the electronic medical record (EMR) extracted SF parameters, clinical characteristics, and patient reported outcome measures (PROMs) from patients who underwent joint aspirations between 2017 and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics stratified by low (0-2)^1 and high (3)^2 synovial lymphocytic inflammation (SLI) for RA patients with paired synovial tissue histology and SF data.

Characteristic	Low SLI (N = 35)	High SLI (N = 29)	Total (N = 64)	P-value
Age, mean (SD)	65.8 (10.9)	64.8 (12.7)	65.3 (11.7)	0.56[1]
Sex, Female, n (%)	32 (91.4)	26 (89.7)	58 (90.6)	0.81[2]
Race, White, n (%)	25 (71.4)	17 (58.6)	42 (65.6)	0.28[2]
TJC, mean (SD)	4.2 (5.8)	3.9 (3.6)	4.1 (4.9)	0.34[1]
SJC, mean (SD)	3.8 (3.1)	5.7 (3.5)	4.6 (3.4)	**0.021**[1]
CRP, mean (SD)	0.6 (1.5)	2.4 (2.6)	1.4 (2.3)	**<0.0001**[1]
RF Positive, n (%)	17 (48.5)	20 (69.0)	37 (57.8)	0.062[2]
CCP Positive, n (%)	22 (62.9)	26 (89.7)	48 (75.0)	**0.035**[2]
Disease duration, mean (SD)	17.8 (14.8)	18.6 (13.1)	18.2 (13.9)	0.61[1]
CDAI, mean (SD)	16.6 (11.9)	19.5 (9.4)	17.9 (10.9)	0.19[1]
DAS28-CRP, mean (SD)	3.3 (1.4)	4.2 (0.9)	3.8 (1.3)	**0.014**[1]
SF WBC/μL, mean (SD)	934 (2841)	11365 (12191)	5661 (9889)	**<0.0001**[1]
% PMN, mean (SD)	30.7 (22.1)	56.4 (27.7)	44.8 (28.2)	**0.0006**[1]
% Lymph, mean (SD)	33.5 (17.3)	28.6 (23.5)	30.8 (20.9)	0.17[1]
% Mono, mean (SD)	29.4 (17.8)	14.1 (8.4)	21.0 (15.4)	**0.003**[1]
Fibrin[5] present in Synovial Tissue (% of specimens)	14 (40.0)	25 (86.2)	39 (60,9)	**0.0002**[2]
SLH >3 cells thick, n (%)	13 (37.1)	23 (79.3)	36 (56.3)	**0.0007**[2]
Medication group, n (%)				0.44[2]
Biologic Naive	9 (25.7)	9 (31.0)	18 (28.1)	
On Biologic	15 (42.9)	8 (27.6)	23 (35.9)	
Refractory	11 (31.4)	12 (41.4)	23 (35.9)	

TJC-Tender Joint Count, SJC- Swollen Joint Count; CRP-C-reactive protein; RF-rheumatoid factor; CCP-cyclic citrullinated peptide; CDAI-Clinical Disease Activity Index; SF WBC-synovial fluid white blood cell; PMN-polymorphonuclear; lymph – lymphocyte; mono – monocyte; SLH-synovial lining hyperplasia; DAS-28 CRP-Disease Activity Index CRP

[1]Low SLI- score of 0-2 is classified as low inflammatory (0 indicates no inflammation or less than 1 perivascular aggregate in at least 2 fields, 1 indicates mild inflammation or 1 perivascular aggregate in at least 2 fields, 2 (moderate) indicates greater than or equal to 2 perivascular aggregates or interstitial inflammation)

[2]High SLI- SLI score of 3 is classified as high inflammatory (widespread perivascular / interstitial aggregates or band-like bridging between blood vessels)

[3]Kruskal-Wallis p-value; [4]Chi-Square p-value; [5]Fibrin is measured as present or absent

2023. Infections, gout, and CPPD were defined by positive cultures or appropriate crystal identification; other diagnoses were determined using ICD-10 codes. PROMs included the Multidimensional Health Assessment Questionnaire (MDHAQ), and Routine Assessment of Patient Index Data 3 (RAPID3).

Results: In 64 RA patients with paired synovial tissue histology and SF cell counts, mean SF WBC was 5,661 cells/μL, and mean CDAI was 17.9 (Table 1). 29 (45%) had high SLI, which correlated positively with SF WBC (Figure 1A). Patients in the high SLI group had higher mean CRP (2.4 vs. 0.6, p< 0.0001), swollen joint count (5.7 vs. 3.8, p=0.021), CCP positivity (86% vs 63%, p=0.035), and DAS28-CRP (4.2 vs 3.3, p=0.014) compared to patients in the low SLI group. There were no differences in disease activity or SLI between medication groups. SF WBC ≥ 1400 cells/μL was sensitive (0.86) and specific (0.91) for high SLI (AUC 0.91) (Figure 1B).

The proportion of aspirations with WBC ≥ 1400 cells/μL varied by diagnosis in the retrospective chart review (Figure 1C). Of 2,171 aspirations, 823 were from RA patients, of whom 492 (60%) had WBC ≥ 1400 cells/μL. Septic arthritis and OA had

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

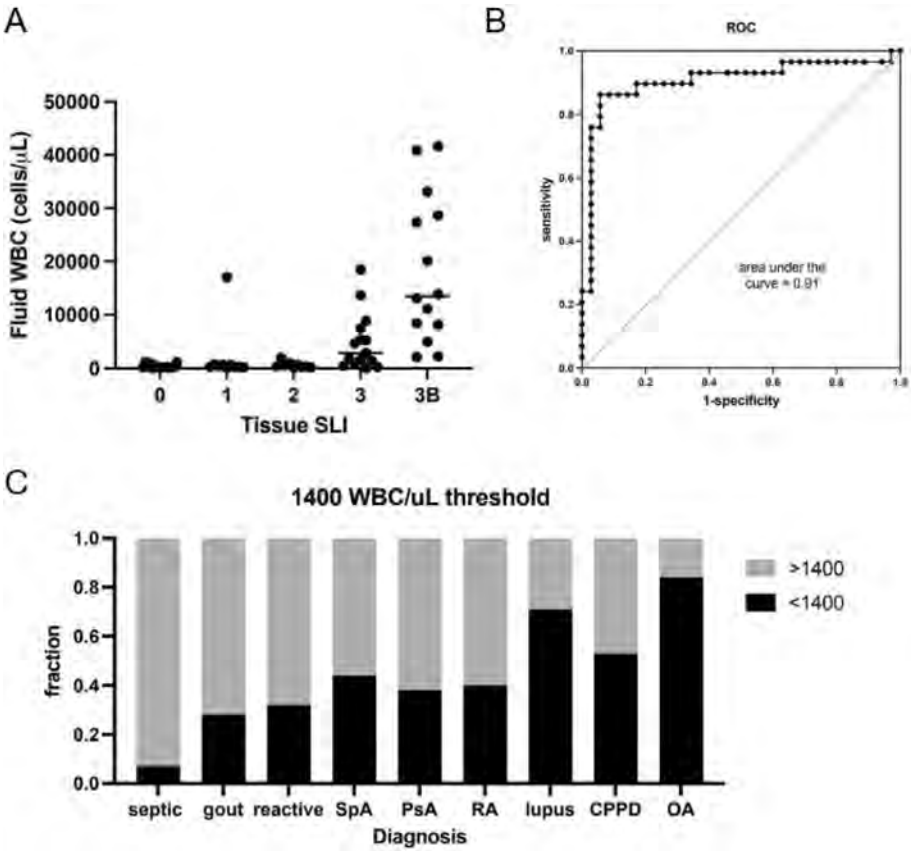


Figure 1. Synovial fluid cellularity predicts synovial tissue inflammation in RA and varies by diagnosis. 1A) Scatterplot depicting increasing synovial tissue lymphocytic inflammation (0-3B) vs. synovial fluid white blood cell (WBC) count (cells/μL). B = SLI 3-band. Kruskal-Wallis chi-square = 36.9, df = 4, p<0.001. 1B) Synovial fluid cellularity predicts the degree of tissue inflammation. Receiver Operator Curve using synovial fluid threshold ≥ 1400 WBC/μL to classify synovial tissue with grade 3 SLI. 1C) Fraction of aspirations associated with each diagnosis with > 1400 WBC/μL.

the highest and lowest proportion of WBC ≥ 1400 cells/μL, respectively. Compared to those with WBC < 1400 cells/μL, RA patients with WBC ≥ 1400 cells/μL had higher mean ESR (38.7 vs 23.0, p< 0.0001), CRP (10.9 vs 6.7, p=0.0008), and SF PMN% (61.1 vs. 17.8, p< 0.0001) (Table 2). RA patients with WBC ≥ 1400 cells/μL had significantly lower mean RAPID3 scores (11.9 vs 14.1, p=0.0213) compared to those with WBC < 1400 cells/μL. Mean MDHAQ scores did not differ significantly between the two WBC groups.

Conclusion: SF WBC is sensitive and specific for differentiating high and low SLI in RA. SF WBC ≥ 1400 cells/μL was associated with higher measures of systemic inflammation when collected intra-operatively and during routine aspiration but not with composite measures of disease activity or PROMs, suggesting that the SF WBC count provides distinct information that may be useful in selecting appropriate anti-inflammatory targeted therapy.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of clinical characteristics and patient reported outcome measures (PROMs) for Synovial Fluid (SF) aspirations of RA patients stratified by the SF white blood cell (WBC) count.

Variable	WBC < 1400 cells/μL (N=331)	WBC ≥1400 cells/μL (N=492)	Total (N = 823)	P-value
CCP				**0.231[2]**
N	217	347	564	
Positive, no (%)	68 (31.3)	132 (38.0)	200 (35.5)	
RF				**0.119[2]**
N	242	381	623	
Positive, no (%)	64 (26.4%)	132 (34.6%)	196 (31.5%)	
ESR (mm/hr)				**<.0001[1]**
N	204	325	529	
Mean	23 (20.61)	38.7 (32.48)	32.6 (29.48)	
CRP (mg/dL)				**0.0008[1]**
N	115	259	374	
Mean (SD)	6.7 (15.36)	10.9 (20.85)	9.6 (19.41)	
RAPID3				**0.0213[1]**
N	82	153	235	
Mean (SD)	14.1 (6.5)	11.9 (6.2)	12.7 (6.4)	
MDHAQ				0.0986[1]
N	82	153	235	
Mean (SD)	2.6 (1.9)	2.1 (1.7)	2.3 (1.8)	
WBC (cells/ μL)				**<.0001[1]**
N	331	492	823	
Mean (SD)	443.5 (352.1)	15194.7 (15430)	9262.0 (13951)	
PMN%				**<.0001[1]**
N	239	490	729	
Mean (SD)	17.8 (21.9)	61.1 (27.8)	46.9 (33.0)	
Mono%				**<.0001[1]**
N	238	490	728	
Mean (SD)	32.3 (24.1)	14.6 (14.2)	20.4 (19.9)	
Lymph%				**<.0001[1]**
N	239	490	729	
Mean (SD)	47.1 (25.6)	23.9 (21.5)	31.5 (25.4)	

[1]Kruskal-Wallis p-value
[2]P-values based on a logistic regression with parameter estimation via generalized estimating equations (GEE) to account for the repeated within patients

Disclosure: S. Cushing: None; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2; **M. Parides**: None; **H. Abdul-Rehman**: None; **D. Ramirez**: None; **E. DiCarlo**: None; **K. Carandang**: None; **R. Davis**: None; **R. Blank**: None; **L. Donlin**: Bristol-Myers Squibb (BMS), 2, Karius, Inc., 5, Stryker, 2; **A. Jonsson**: Arpelos Biosciences, 2, Ono Pharmaceuticals, 5, Pfizer, 6; **A. Lakhanpal**: None; **B. Mehta**: Amgen, 1, Horizon, 1; **D. Orange**: AstraZeneca, 2, Pfizer, 2; **M. smith**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0464

Synovial Inflammation is not Associated With Reoperation in Patients With Rheumatoid Arthritis Undergoing Total Hip or Knee Arthroplasty

Solana Cushing[1], Kelsey Gripp[2], Edward DiCarlo[3], Deanna Jannat-Khah[1], Yoshimi Endo[3], Jose Rodriguez[3], Mark Figgie[3], Bella Mehta[4] and Susan Goodman[3], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, New York, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [4]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Reoperations following arthroplasty are a significant burden to patients and surgeons. In patients with RA who receive total hip (THA) or knee (TKA) arthroplasty, radiographic loosening, a common cause of reoperation, has been linked to increased disease activity.[1,2] We sought to determine if synovitis in the operated joint at time of THA/TKA was associated with increased risk of reoperation.

Methods: RA patients who underwent primary THA/TKA and a reoperation on the same joint at our institution were identified via the EMR and clinical characteristics were extracted. Synovium specimens from THA/TKA were graded by a board-certified musculoskeletal pathologist for Synovial Lymphocytic Inflammation (SLI), Synovial Lining Hyperplasia (SLH), and Krenn synovitis score. SLI was graded from 0 (none) to 4 (band-like), with SLI 0–1 classified as non-inflammatory and 2–4 as inflammatory. Radiographs preceding reoperation were graded as loose or not loose by a board-certified radiologist based on a combination of periprosthetic lucency and implant position. Kaplan-Meier (KM) survival curves estimated risk of reoperation over time among subjects with a diagnosis of aseptic loosening, implant dislocation, or failure. Log rank tests were performed to assess differences in KM survival curves. Continuous and categorical variables were compared using two-tailed t-tests and Fisher's exact tests, respectively. Logistic regression models assessed odds of reoperation within 5 years. Analyses were performed using STATA 18.0 with an alpha of 0.05.

Results: Thirty-nine patients meeting eligibility criteria were included; 109 cases were excluded due to secondary surgery on a different joint and 5 because index surgery occurred at another institution. Inflammatory synovium was present in 19 cases. 34 (85%) were female with mean ± SD age of 59± 10 years, BMI 30 ± 8.4 kg/m^2; 15 (38.5%) had a loose implant, and 33 (82%) reoperations were revisions (Table 1). Time to reoperation did not differ between inflammatory and non-inflammatory groups (log-rank p-value > 0.05) (Figure 1). Neither diagnosis at reoperation (p-value = 0.24) nor radiographic loosening (53% vs. 25%, p-value = 0.10) differed between groups (Table 2). Inflammatory synovium was not associated with increased odds of reoperation within 5 years (OR 0.98, 95% CI 0.17, 5.83). Neither SLI, SLH, or Krenn score were associated with odds of reoperation within 5 years.

Conclusion: In this small cohort with a low incidence of secondary surgery, synovial inflammation at the time of primary surgery was not associated with increased risk of reoperation. Other factors, including systemic inflammation, may play a role in aseptic loosening and reoperation risk for RA patients undergoing THA or TKA and merit further investigation in a larger cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, clinical, and histologic features of study patients

	N = 39
Sex, Female, no. (%)	33 (85)
Age at Baseline, mean ± SD	58.86 ± 10.5
Race, no. (%)	
White	32 (82)
Black	6 (15)
Patient Declined to Answer	1 (3)
Ethnicity, Not Hispanic or Latino, no. (%)	30 (77)
RF Positive, no. (%)	18 (46)
CCP Positive, no. (%)	20 (51)
BMI at Primary Surgery,	N = 32
Mean ± SD	30.77 ± 8.4
Weight at Primary Surgery (kg)	N = 32
Mean ± SD	81.40 ± 23.1
BMI at Secondary Surgery	N = 38
Mean ± SD	30.21 (± 8.006)
Weight at Secondary Surgery (kg)	N = 38
Mean ± SD	82.17 (± 25.55)
Surgery Type, no. (%)	
TKA	24 (62 %)
THA	15 (38 %)
Secondary Procedure Name, no. (%)	
Revision	33 (85 %)
Irrigation and Debridement	4 (10 %)
Arthrotomy	2 (5 %)
Synovial Lymphocytic Inflammation, no. (%)	
None	12 (31 %)
Mild	8 (21 %)
Moderate	10 (26 %)
Marked	6 (15 %)
Band-like	3 (8 %)
Synovial Lymphocytic Inflammation, mean (SD)	
Mean (SD)	1.487 (± 1.295)
Synovial Mucoid Change, no. (%)	
None	12 (31 %)
Slight (perivascular or focal interstitial)	16 (41 %)
Moderate (perivascular or focal interstitial)	9 (23 %)
Marked (perivascular or focal interstitial)	0 (0 %)
Myxomatous	0 (0 %)
Missing	2 (5.1%)
Vascularity	
Normal	31 (79 %)
Slight Increase	4 (10 %)
Marked Increase	1 (3 %)
Missing	3 (7.7%)
Sclerosis/Fibrosis	
None	4 (10 %)
Focal	19 (49 %)
Widespread	14 (36 %)
Band-like	0 (0 %)
Missing	2 (5.1%)
Fibrin, no (%)	
None	30 (77 %)
Present	6 (15 %)
Missing	3 (7.7%)
Plasma Cell Inflammation (x25 mag)	
<10% plasma cells within lymphocytic aggregates	23 (58 %)
<50% plasma cells	5 (13 %)
>50% plasma cells	11 (28 %)
Binucleate Plasma Cells, no (%)	
None	28 (71 %)
Present	11 (28 %)
Russell Bodies, no (%)	
None	34 (87 %)
Present	5 (13 %)
Eosinophils, no (%)	
None	24 (62 %)
Present	2 (5 %)
Missing	13 (33.3%)
Synovial Giant Cells, no (%)	
None	25 (64 %)
Present	11 (28 %)
Missing	3 (7.7%)
Mast Cells, no (%)	
None	9 (23 %)
Present	27 (69 %)
Missing	3 (7.7%)
Synovial Lining Hyperplasia	
Normal Lining	4 (10 %)
1-3 Cells Thick	20 (51 %)
3-4 Cells Thick	8 (21 %)
>4 Cells Thick	4 (10 %)
Missing	3 (7.7%)
Detritus (Bone/Cartilage), no. (%)	
Absent	24 (62 %)
Small Particles	9 (23 %)
Large Particles	3 (8 %)
Missing	3 (7.7%)
Acute Inflammation/Neutrophil Inflammation, no. (%)	
None	32 (82 %)
Present	7 (18 %)
Inflammation Binary, no. (%)	
Non-Inflammatory	20 (51 %)
Inflammatory	19 (49 %)
Germinal Centers, no. (%)	
None	37 (95 %)
Present	2 (5 %)
Sum of Krenn Score, mean ± SD	2.189 (± 1.450)
Radiographic Loosening, no. (%)	
Not Loose	24 (61.5%)
Loose	15 (38.5%)
Loose Component, no. (%)	N = 15
Tibial	7 (18 %)
Femoral	6 (15 %)
Acetabular cup	2 (5 %)

References

1. Böhler C, Weimann P, Alasti F, Smolen JS, Windhager R, Aletaha D. Rheumatoid arthritis disease activity and the risk of aseptic arthroplasty loosening. Semin Arthritis Rheum. 2020;50(2):245-251. doi:10.1016/j.semarthrit.2019.07.011

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of clinical characteristics at time of reoperation stratified by inflammatory status at primary surgery based on Synovial Lymphocytic Inflammation (SLI) grade

	Non-Inflammatory (N=20)	Inflammatory (N=19)	p-value
Prosthesis Age, Days, mean (SD)	1979 (2971)	2208 (1903)	0.78[1]
Radiographic Loosening, no (%)			0.10[2]
Not Loose	15 (75%)	9 (47%)	
Loose	5 (25%)	10 (53%)	
Diagnosis at reoperation, no (%)			0.24[2]
Aseptic loosening	3 (15%)	10 (53%)	
Fracture	4 (20%)	1 (5%)	
PJI	3 (15%)	2 (11%)	
Dislocation	4 (20%)	2 (11%)	
Tissue Reaction	4 (20%)	3 (16%)	
Implant Failure	1 (5%)	1 (5%)	
Wound dehiscence	1 (5%)	0 (0%)	

[1]T-test; [2]Fisher's exact test

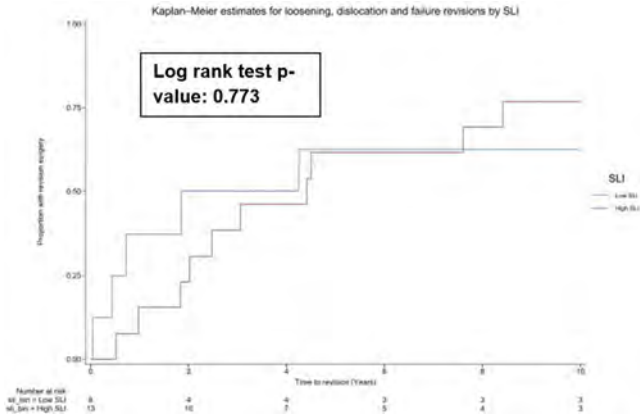


Figure 1. Kaplan-Meier survival curves for time to reoperation among patients with diagnosis at secondary surgery of implant loosening, dislocation, or failure, grouped by status as inflammatory or non-inflammatory. The proportion of patients undergoing reoperation surgery over time was not statistically different between groups (log-rank p > 0.05).

2. Anil U, Singh V, Schwarzkopf R. Diagnosis and Detection of Subtle Aseptic Loosening in Total Hip Arthroplasty. J Arthroplasty. 2022;37(8):1494-1500. doi:10.1016/j.arth.2022.02.060

Disclosure: S. Cushing: None; **K. Gripp**: None; **E. DiCarlo**: None; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **Y. Endo**: None; **J. Rodriguez**: ASS ASC Development Network, LLC, 8, BICMD, 2, 8, Exactech, Inc., 2, 9, HS2, LLC, 8, Joint Effort Administrative Services Organization, 8, Restor3d, 2, 9, Smith & Nephew, 2, 9, Wishbone, 8; **M. Figgie**: Bone Solutions, Inc, 2, Diffusion Rx, Inc., 1, 8, Enovis, 2, 9, HS2, LLC, 8, Icarus Medical, 8, Joint Effort Administrative Services Organization, 8, Mekanika, Inc., 8, Sylke, Inc., 1, 8, Wishbone Medical, 1, 2, 8, 9; **B. Mehta**: Amgen, 1, Horizon, 1; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2.

Abstract Number: 0465

Reproductive Factors and Risk of Rheumatoid Arthritis-Associated Interstitial Lung Disease or Bronchiectasis in Women

Suchita Nety[1], Xiaosong Wang[2], Misti Paudel[3], Ying Qi[4], Qianru Zhang[1], Nancy Shadick[5], Michael Weinblatt[6], Liya Sisay Getachew[7], Gregory McDermott[8] and Jeffrey Sparks[7], [1]Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Natick, MA, [3]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [4]Brigham and Women's Hospital, Boston, [5]Brigham & Women's Hospital, Boston, MA, [6]Brigham and Women's Hospital/ Harvard Medical School, Waban, MA, [7]Brigham and Women's Hospital, Boston, MA, [8]Brigham and Women's Hospital, Brookline, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: RA-associated lung diseases (RA-LD) such as RA-associated interstitial lung disease (RA-ILD) and RA-associated bronchiectasis (RA-BR) are more common in men, but risk rises with age for both men and women. However, no studies have examined the role of reproductive factors, such as time since menopause, in RA-LD risk among women.

Methods: We performed a case-control study of reproductive factors and RA-LD risk in women from two established US prospective RA cohorts (an institutional registry and a health care system biobank) who had clinically indicated high-resolution chest computed tomography (CT) imaging. All women had RA by 2010 ACR/EULAR criteria. RA-LD cases were identified using research review of chest CT images by thoracic radiologists and detailed medical record review confirming that participants met criteria for RA-LD. Controls had RA and no evidence of lung disease based on medical record review and were matched to cases by age and RA duration. The index date for cases was the date of RA-LD diagnosis and the index date was assigned to RA-noLD controls. We analyzed women who answered surveys about reproductive health. The primary analysis investigated years since menopause for RA-LD risk. Secondary analyses included age at menarche, pregnancies, ovulatory-years, type of menopause, and age at menopause as well as RA-ILD and RA-BR risk. We used logistic regression to estimate odds ratios for RA-LD, adjusting for chronological age, smoking, and serostatus.

Results: We analyzed 99 RA-LD cases (mean age 65.5 years) and 170 RA-noLD controls (mean age 63.4 years) who answered surveys about female reproductive factors. RA-LD cases had shorter duration of ovulatory-years (mean 33.8 vs. 35.4 years, p=0.037), younger age at menopause (mean 47.0 vs. 48.5 years, p=0.038), and longer time since menopause (mean 18.4 years vs. 14.8 years, p=0.013) than RA-noLD controls (**Table 1**). In the primary analysis, time since menopause was significantly associated with RA-LD (adjusted OR 1.05 per year, 95%CI 1.004 to 1.10; p=0.034) (**Table 2**). In the secondary analyses, menarche at age 10 years or younger was associated with higher RA-LD risk than menarche at

Table 1. Characteristics of female RA-LD cases and RA-noLD controls at index date of RA-LD diagnosis for cases or matched date for controls.

	RA-LD cases (n=99)	RA-noLD controls (n=170)	p-value
Mean age, years (SD)	65.5 (9.4)	63.4 (9.8)	0.10
Female sex	99 (100%)	170 (100%)	-
Race			
-Asian	1 (1.0%)	1 (0.6%)	0.98
-Black	5 (5.1%)	7 (4.1%)	
-White	87 (87.9%)	151 (88.8%)	
-Other	6 (6.1%)	11 (6.5%)	
Smoking status			0.11
-Never	38 (38.4%)	79 (46.5%)	
-Past	58 (58.6%)	78 (45.9%)	
-Current	3 (3.0%)	13 (7.6%)	
Mean smoking pack-years (SD)	11.9 (16.1)	9.4 (17.5)	0.25
Median RA duration, years (IQR)	12.2 (2.8, 20.8)	8.3 (3.2, 17.4)	0.22
Seropositive	81 (81.8%)	115 (67.7%)	**0.012**
Mean number of pregnancies (SD)	1.31 (1.50)	1.3 (1.5)	0.93
Mean ovulatory-years* (SD)	33.9 (6.3)	35.3 (5.5)	0.06
Postmenopausal	94 (94.9%)	162 (95.3%)	0.90
Mean age at menopause (SD)	47.0 (6.0)	48.5 (5.2)	**0.038**
Mean years since menopause (SD)	18.4 (11.6)	14.8 (11.3)	**0.013**

*Ovulatory-years was calculated as the years from menarche to menopause, not counting the duration of pregnancies.

CT, computed tomography; ILD, interstitial lung disease; IQR, interquartile range; RA, rheumatoid arthritis; SD, standard deviation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Reproductive factors and odds ratios for RA-LD cases vs. RA-noLD controls in women.

	Unadjusted OR (95%CI)	Multivariable* OR (95%CI)
Primary analysis		
Time since menopause (per year)	**1.03 (1.01 to 1.06) p=0.014**	**1.05 (1.004 to 1.10) p=0.034**
Secondary analyses		
Age at menarche		
-10 years or younger	2.06 (0.97 to 4.37)	**2.54 (1.15 to 5.60)**
-11 to 14 years	1.0 (Ref)	1.0 (Ref)
-15 years or older	1.03 (0.37 to 2.86)	1.11 (0.39 to 3.16)
Pregnancies (per gestation)	0.99 (0.84 to 1.17)	0.96 (0.81 to 1.14)
Ovulatory-years** (per year)	0.96 (0.92 to 1.002)	0.96 (0.92 to 1.007)
Age at menopause		
-<45 years	**2.00 (1.03 to 3.87)**	**2.06 (1.03 to 4.11)**
-45 to 49 years	1.89 (0.99 to 3.60)	1.84 (0.95 to 3.56)
-50 to 54 years	1.0 (Ref)	1.0 (Ref)
-55+ years	1.61 (0.60 to 4.33)	1.61 (0.57 to 4.51)
Type of menopause		
-Natural	1.0 (Ref)	1.0 (Ref)
-Iatrogenic (surgical, radiation, or chemotherapy)	0.72 (0.40 to 1.29)	0.70 (0.39 to 1.28)
Time from menopause to index date (categorical)		
-0 to <10 years	1.0 (Ref)	1.0 (Ref)
-10 to <20 years	1.38 (0.69 to 2.78)	1.21 (0.54 to 2.72)
-20+ years	1.93 (0.97 to 3.85)	1.42 (0.49 to 4.09)

*Matched by RA duration and adjusted for chronological age, smoking status, and RA serostatus.
**Ovulatory-years was calculated as the years from menarche to menopause, not counting the duration of pregnancies.

CI, confidence interval; LD, lung disease; OR, odds ratio; RA, rheumatoid arthritis.

Table 3. Reproductive factors and odds ratios for RA-ILD (n=72 cases) or RA-BR (n=27 cases) in women.

	Multivariable* OR for RA-ILD (95%CI)	Multivariable* OR for RA-BR (95%CI)
Primary analysis		
Time since menopause (per year)	1.05 (0.996 to 1.11) p=0.069	1.05 (0.96 to 1.15) p=0.31
Secondary analyses		
Age at menarche		
-10 years or younger	**4.22 (1.57 to 11.32)**	0.71 (0.13 to 3.88)
-11 to 14 years	1.0 (Ref)	1.0 (Ref)
-15 years or older	1.71 (0.48 to 6.11)	0.48 (0.05 to 4.51)
Pregnancies (per gestation)	0.92 (0.74 to 1.14)	1.04 (0.77 to 1.42)
Ovulatory-years** (per year)	0.97 (0.92 to 1.02)	0.95 (0.87 to 1.04)
Age at menopause		
-<45 years	**2.36 (1.03 to 5.42)**	1.49 (0.40 to 5.60)
-45 to 49 years	1.83 (0.80 to 4.20)	2.25 (0.71 to 7.10)
-50 to 54 years	1.0 (Ref)	1.0 (Ref)
-55+ years	1.76 (0.50 to 6.20)	1.63 (0.22 to 11.95)
Type of menopause		
-Natural	1.0 (Ref)	1.0 (Ref)
-Iatrogenic (surgical, radiation, or chemotherapy)	0.98 (0.48 to 2.01)	**0.24 (0.06 to 0.93)**
Time from menopause to index date (categorical)		
-0 to <10 years	1.0 (Ref)	1.0 (Ref)
-10 to <20 years	1.37 (0.51 to 3.70)	0.97 (0.23 to 4.12)
-20+ years	1.66 (0.47 to 5.88)	1.34 (0.18 to 10.1)

*Matched by RA duration and adjusted for chronological age, smoking status, and RA serostatus.
**Ovulatory-years was calculated as the years from menarche to menopause, not counting the duration of pregnancies.

BR, bronchiectasis; CI, confidence interval; ILD, interstitial lung disease; OR, odds ratio; RA, rheumatoid arthritis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

age 11 to 14 years (adjusted OR 2.54, 95%CI 1.15 to 5.60). Higher ovulatory-years had a trend towards lower RA-LD risk but was not statistically significant after adjustment (OR 0.96 per year, 95%CI 0.92 to 1.003). Younger age at menopause was associated with RA-LD risk (adjusted OR 2.06, 95%CI 1.03 to 4.11 for onset < 45 years vs. 50 to 54 years). There was no association of iatrogenic menopause (surgical, radiation, or chemotherapy) with RA-LD risk. When analyzing RA-ILD and RA-BR separately, results for RA-ILD risk were similar to RA-LD risk (**Table 3**).

Conclusion: In this first study examining reproductive factors and RA-LD risk in women, longer time since menopause was associated with higher RA-LD risk. Younger ages at menarche and at menopause were each associated with higher RA-LD risk, and results were similar for RA-ILD. Results were not explained by chronological age, RA duration, serostatus, or smoking. These findings suggest that menopausal factors, such as lack of estrogen, may place older women with RA at risk for LD.

Disclosure: S. Nety: None; **X. Wang**: None; **M. Paudel**: None; **Y. Qi**: None; **Q. Zhang**: None; **N. Shadick**: Bristol-Myers Squibb(BMS), 5, Janssen, 5; **M. Weinblatt**: aclaris, 2, amgen, 2, anaptysbio, 2, Artiva Bio, 2, Biohaven, 2, Bristol-Myers Squibb(BMS), 2, 5, Canfite, 11, Curie Bio, 2, Deep Cure, 2, Eli Lilly, 2, Gilead, 2, Ignite, 2, Inmedix, 11, Janssen, 5, Janux Therapeutics, 2, Johnson and Johnson, 2, Lifordi, 2, Marvel Bio, 2, Matchpoint, 2, Merck/MSD, 2, Neutrolis, 2, Novartis, 2, Sana, 2, Santa Ana, 2, Sci Rhom, 2, scipher medcine corp, 11, SetPoint Medical, 2, Surf Therapeutics, 2, Thymmune, 2, Xencorp, 2, ZuraBio, 2; **L. Getachew**: None; **G. McDermott**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 0466

Pilot Study Demonstrates Altered Intestinal Mucosal Microbiome in Patients with Rheumatoid Arthritis versus Control Subjects

Tulsi Joishy[1], Anastasiia Phothisane[2], Phicharmon Kulapatana[2] and Michelle Ormseth[1], [1]Vanderbilt University Medical Center, Nashville, [2]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease that is thought to originate at the mucosa. Despite the mucosa's importance, few studies have examined the microbiome of the intestinal mucosa in patients with RA, instead assessing stool microbiome as a surrogate. The purpose of this pilot study is to determine if the mucosal microbiome differs in patients with RA compared to control participants and by site.

Methods: Patients with RA and without RA or other inflammatory autoimmune disease who were undergoing routine colonoscopy were recruited at Vanderbilt University Medical Center as part of the Vanderbilt GI Repository. Mucosal tissue biopsies were obtained from terminal ileum, and ascending, transverse and descending colon. Specimens were flash frozen immediately after collection and stored at -80°C until processing. DNA was extracted from all four mucosal biopsy samples and 16S rRNA long-read DNA sequencing (V1-V8 regions) was performed using Oxford Nanopore Technology. Counts of bacterial taxa were compared using DESeq2 and the Benjamini-Hochberg method was used to adjust for multiple comparisons with a false discovery rate at 5%.

Results: This pilot study included 5 RA (mean age 56 ± 14 years, 100% female) and 5 control (mean age 44 ± 21 years, 60% female) participants. Measures of alpha diversity across sites were not significantly different in RA vs control participants;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

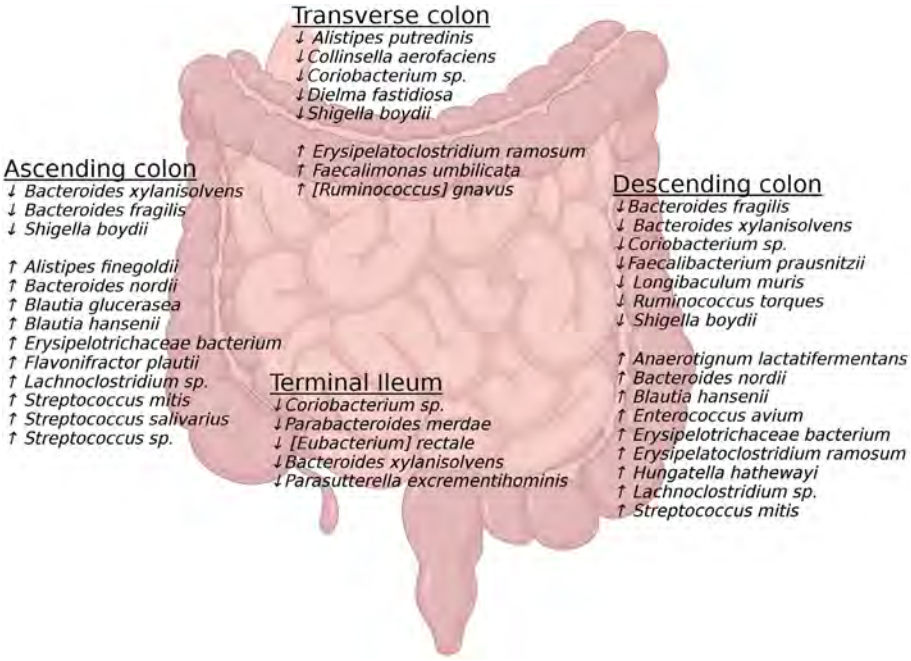


Figure: Mucosal site-specific microbiome alterations in patients with RA versus control participants

however, there were significant differences in the microbiome composition at the 4 mucosal sites. At all sites, *Prevotella*, Christensenellales, *Megaspharera massiliensis, and Odoribacter splanchnicus* were significantly decreased in RA versus control participants. Within all sites of the colon *Eubacterium callanderi*, *Veillonella* and *Bacteroides ovatus* were increased, and *Shigella dysenteriae* was decreased significantly in RA versus control participants. While there were these commonalities by site, there were many site-specific significant alterations in mucosal microbiome (Figure).

Conclusion: Several taxa including *Prevotella* and Christensenellales were decreased at all mucosal sites in patients with RA versus control participants, while there were many site-specific mucosal microbiome alterations. Further studies will be needed to validate these findings in a larger cohort and to assess whether mucosal site-specific alterations in microbiome are associated with development of RA, disease activity and features.

Disclosure: T. Joishy: None; **A. Phothisane**: None; **P. Kulapatana**: None; **M. Ormseth**: None.

Abstract Number: 0467

A Machine Learning Classifier Leveraging anti-ra33, anti-pad4, and Conventional Biomarkers Enhances Diagnostic Performance Characteristics for RA

Vasileios Kyttaris[1], Sepehr Taghavi[2], Clayton Nagle[3], Christine Schleif[3], Brittany Partain[4] and Tyler O'Malley[5], [1]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, [2]Exagen Inc, Escondido, CA, [3]Exagen, Carlsbad, CA, [4]Exagen, Boston, MA, [5]Exagen, Vista, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics

	Total (N=760)	RA Seropositive (N=205)	RA Seronegative (N=145)	AHV (N=215)	SLE (N=107)	Sjogrens (N=43)	PsA (N=45)
Ethnicity n(%)							
White	515 (68%)	145 (71%)	119 (82%)	114 (53%)	63 (59%)	37 (86%)	37 (82%)
Black	50 (7%)	14 (7%)	7 (5%)	5 (2%)	21 (20%)	2 (5%)	1 (2%)
Hispanic	114 (15%)	31 (15%)	15 (10%)	53 (25%)	10 (9%)	3 (7%)	2 (4%)
Asian	45 (6%)	5 (2%)	1 (1%)	28 (13%)	10 (9%)	1 (2%)	0 (0%)
Other	22 (3%)	7 (3%)	2 (1%)	8 (4%)	2 (2%)	0 (0%)	3 (7%)
Not Disclosed	14 (2%)	3 (1%)	1 (1%)	7 (3%)	1 (1%)	0 (0%)	2 (4%)
Subject is Female n(%)	585 (77%)	157 (77%)	122 (84%)	141 (66%)	97 (91%)	43 (100%)	25 (56%)
Age at Visit - Mean(SD)	51.3 (±15)	56.9 (±13)	57.3 (±13)	42.1 (±13)	45.4 (±15)	58.1 (±11)	53.7 (±12)
Years since Diagnosis - Mean(SD)	9.4 (±9)	10.9 (±11)	7.5 (±8)	NA	11.7 (±7)	NA	9.8 (±7)
ANA By Method Result n(%)							
By ELISA	363 (48%)	111 (54%)	52 (36%)	58 (27%)	98 (92%)	35 (81%)	9 (20%)
By HEp-2	403 (53%)	141 (69%)	71 (49%)	49 (23%)	93 (87%)	31 (72%)	18 (40%)
RA Disease Duration*							
Early	NA	34 (17%)	35 (24%)	NA	NA	NA	NA
Established	NA	48 (23%)	60 (41%)	NA	NA	NA	NA
Longstanding	NA	46 (22%)	26 (18%)	NA	NA	NA	NA
Unknown	NA	77 (38%)	24 (17%)	NA	NA	NA	NA
CDAI Interpretation							
Remission	NA	32 (16%)	9 (6%)	NA	NA	NA	NA
Low	NA	56 (27%)	48 (33%)	NA	NA	NA	NA
Moderate	NA	34 (17%)	24 (17%)	NA	NA	NA	NA
High	NA	33 (16%)	34 (23%)	NA	NA	NA	NA
Data Unavailable	NA	50 (24%)	30 (21%)	NA	NA	NA	NA
Methotrexate	176 (23%)	84 (41%)	84 (58%)	0 (0%)	4 (4%)	0 (0%)	4 (9%)
HCQ	101 (13%)	22 (11%)	23 (16%)	0 (0%)	56 (52%)	0 (0%)	0 (0%)
Prednisone	75 (10%)	17 (8%)	14 (10%)	0 (0%)	24 (22%)	12 (28%)	8 (18%)
Abatacept	6 (1%)	3 (1%)	3 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infliximab	17 (2%)	8 (4%)	8 (6%)	0 (0%)	0 (0%)	0 (0%)	1 (2%)
Tocilizumab	2 (0%)	2 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adalimumab	67 (9%)	23 (11%)	36 (25%)	0 (0%)	0 (0%)	0 (0%)	8 (18%)
Certolizumab	6 (1%)	2 (1%)	4 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Golimumab	1 (0%)	1 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Etanercept	41 (5%)	22 (11%)	16 (11%)	0 (0%)	0 (0%)	0 (0%)	3 (7%)

*RA Disease Duration: Early (0-2 years), Established (2.1-10 years), and Longstanding (> 10 years)

Background/Purpose: Early diagnosis of rheumatoid arthritis (RA) enables prompt intervention, significantly mitigating risk for disease progression, joint damage, and associated morbidity. Conventional biomarkers, anti-CCP and rheumatoid factor (RF), have high specificity but limited sensitivity. Novel biomarkers such as RA33 (heterogeneous nuclear ribonucleoprotein A2/B1) and PAD4 (peptidyl arginine deiminase 4) antibodies have demonstrated diagnostic potential, though their combined utility remains unclear. This study evaluates the performance of novel biomarkers individually and in combination with traditional markers using machine learning algorithms.

Methods: A total of 760 subjects were enrolled, including 350 RA patients meeting 2010 ACR criteria (205 seropositive, 145 seronegative), 215 apparently healthy volunteers (AHV), and 195 disease controls (107 SLE meeting 1997 ACR criteria, 43 primary Sjögrens disease, and 45 psoriatic arthritis [PsA]). Serum samples were tested for anti-CCP IgG, RF IgM and IgA,

Table 2. Performance characteristics

Marker	Sensitivity for RA: Seropositive (N=205)	Sensitivity for RA: Seronegative (N=145)	Specificity for RA: AHV (N=215)	Specificity for RA: SLE (N=107)	Specificity for RA: Sjogren (N=43)	Specificity for RA: PsA (N=45)	RA vs AHV: LR+	RA vs AHV: LR-
RA33 IgA	5%	5%	97%	93%	95%	91%	1.55	0.98
RA33 IgG	12%	13%	95%	71%	98%	89%	2.41	0.92
RA33 IgM	10%	6%	95%	90%	95%	98%	1.77	0.96
PAD4 IgA	24%	6%	96%	92%	98%	93%	4.57	0.86
PAD4 IgG	44%	7%	99%	93%	98%	91%	20.43	0.72
Anti-CCP	81%	0%	99%	98%	100%	100%	52.33	0.53
RF IgA	44%	0%	98%	93%	88%	100%	13.68	0.75
RF IgM	83%	0%	98%	88%	72%	91%	20.25	0.53

Table 2. Clinical Performance Charactristics of RA Markers

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

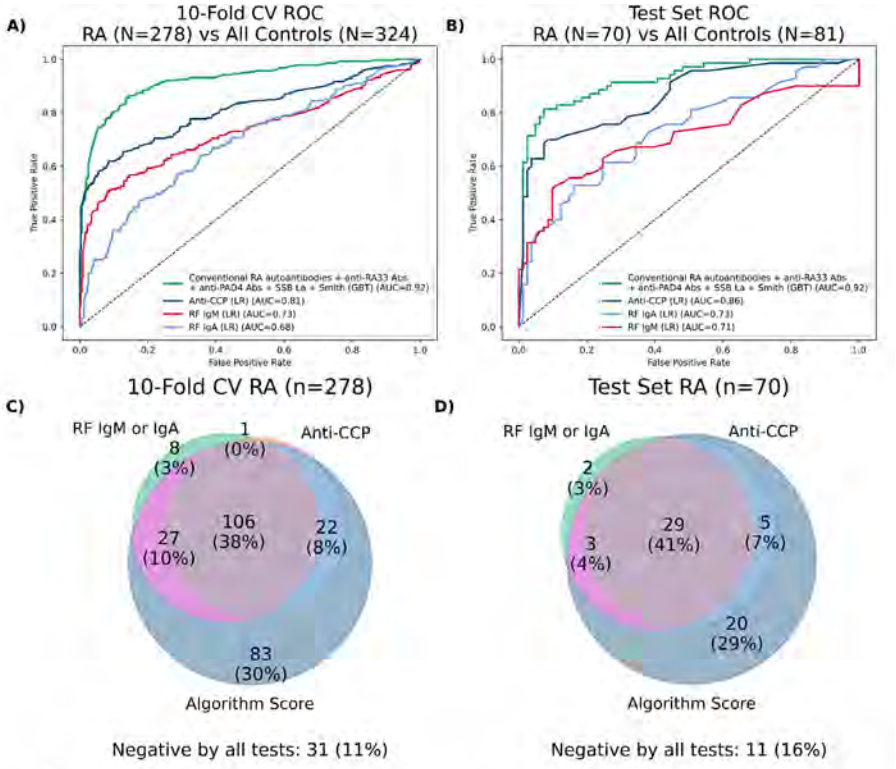


Figure 1. (A) An 80% sampling of the dataset was subjected to 10-fold cross-validation. The optimal probability cutoff achieving the maximum F1 score balancing sensitivity and specificity was 0.35. (B) The Test set reflects an independent 20% subset of the dataset that was not shown to the GBT model during training used to assess model generalizability. (C) The Venn diagram illustrates the percentage of RA patients testing positive for either RF, anti-CCP or the GBT algorithm score based on the F1 maximized threshold in the 10-fold cross validation set. (D) The Venn diagram illustrates the percentage of RA patients testing positive for either RF, anti-CCP or the GBT algorithm score based on the F1 maximized threshold in the test set.

Figure 1. ROC analysis comparing algorithm performance to conventional biomarkers and sensitivity overlap analysis

RA33 (IgA, IgG, IgM), PAD4 (IgA, IgG), anti-SSB/La, and anti-Smith. Diagnostic cutoffs for anti-CCP and RF followed manufacturer recommendations; novel biomarker cutoffs were determined based on at least 95% specificity vs. AHVs. We evaluated multiple machine learning models and biomarker combinations using 10-fold cross-validation and independent test validation. Logistic regression models were built for individual conventional markers to compare against a Gradient Boosted Tree (GBT) classifier, which was ultimately selected based on superior AUC performance. Sensitivity and specificity were calculated at the optimal F1-maximized threshold.

Results: The RA cohort was predominantly female (77%), white (68%), with a mean age of 51 years (SD = 15) and a mean disease duration of 9 years (SD = 9) (Table 1). Anti-CCP was highly specific (99–100%) and RF IgM also showed high specificity (91–98%) (Table 2). RA33 markers were generally specific (71–98%), with RA33 IgG showing the highest sensitivity among them (13% in seronegative RA). PAD4 markers also had high specificity (92–98%), with PAD4 IgG demonstrating the highest sensitivity overall (44% in seropositive RA). PAD4 IgG had the highest positive likelihood ratio (+LR = 20.43), followed by PAD4 IgA (4.57), RA33 IgG (2.41), RA33 IgM (1.77), and RA33 IgA (1.55). The GBT classifier combining conventional and novel biomarkers (RA33s, PAD4s, anti-SSB La, Smith) achieved an AUC of 0.92 in both cross-validation and test sets (Figure 1A-B). The algorithm was 86% sensitive and 86% specific in cross-validation, and 81% sensitive and 90% specific in the test set. The GBT algorithm identified an additional 30% of RA cases in cross-validation (Figure 1C) and 29% in the test set (Figure 1D) that were missed by conventional biomarkers alone, leaving only 11–16% of RA patients undetected by any marker.

Conclusion: Integrating conventional biomarkers with novel RA33 and PAD4 antibodies through machine learning improves RA diagnostic accuracy, capturing ~30% of cases missed by conventional biomarkers alone. This enhanced diagnostic performance highlights the potential of advanced classifiers for earlier identification and timely management of RA.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Kyttaris: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2; **S. Taghavi**: Exagen, 3; **C. Nagle**: Exagen, 3; **C. Schleif**: Exagen, 3; **B. Partain**: Exagen, 3; **T. O'Malley**: Exagen, 12,, 3, 11.

Abstract Number: 0468

Performance of the expanded cardiovascular risk prediction score for rheumatoid arthritis (ERS-RA) in a nationwide multicenter Chinese cohort

Xingbei Dong[1], Nan Jiang[2], Hong Li[3], Misti Paudel[4], Jiangmei Liu[5], Xinwang Duan[6], Dongmei Wu[7], Hongbin Li[8], Fen Li[9], Yongfu Wang[10], Ju Liu[11], Shengqian Xu[12], Hui Luo[13], huanzi dai[14], Shuhong Chi[15], Jian Xu[16], Lijun Wu[17], zhaohui zheng[18], Jing Xue[19], Xiaofu Yu[20], QIn Huang[21], Xiaofei Shi[22], Xiaomin Zhang[23], Yuehong Huo[24], Qian Wang[2], Xiaofeng Zeng[25], Daniel Solomon[26], Mengtao Li[2] and Xinping Tian[2], [1]Peking Union Medical College Hospital, Beijing, China (People's Republic), [2]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [3]Beijing Anzhen Hospital, Capital Medical University, Beijing, China (People's Republic), [4]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [5]Chinese Center for Disease Control and Prevention, Beijing, China (People's Republic), [6]The Second Affiliated Hospital of Nanchang University, Nanchang, China (People's Republic), [7]The People's Hospital of Yuxi City, Yuxi, China (People's Republic), [8]The Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China (People's Republic), [9]The Second Xiangya Hospital of Central South University, Changsha, China (People's Republic), [10]The First Affiliated Hospital of Baotou Medical College, Baotou, China (People's Republic), [11]Affiliated Jiujiang Hospital of Nanchang University, Jiujiang, China (People's Republic), [12]The First Affiliated Hospital of Anhui Medical University, Hefei, China (People's Republic), [13]Xiangya Hospital of Central South University, Changsha, China (People's Republic), [14]Daping Hospital & Research Institute of Surgery, Army Medical University, Chongqing, PR China., Chongqing, China (People's Republic), [15]General Hospital of Ningxia Medical University, Yinchuan, China (People's Republic), [16]The First Affiliated Hospital of Kunming Medical University, Kunming, China (People's Republic), [17]People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, China (People's Republic), [18]Department of Clinical Immunology, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China (People's Republic), [19]The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China (People's Republic), [20]Guyuan People's Hospital, Guyuan, China (People's Republic), [21]Nanfang Hospital, Guangzhou, China (People's Republic), [22]The First Affiliated Hospital of Henan University of science and Technology, Luoyang, China (People's Republic), [23]Red Flag Hospital Affiliated to Mudanjiang Medical College, Mudanjiang, China (People's Republic), [24]The Fifth People's Hospital of Datong, Datong, China (People's Republic), [25]Department of Rheumatology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Beijing, China (People's Republic), [26]Brigham and Women's Hospital, Newton, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of developing cardiovascular (CV) events compared to the general population. However, this risk is often underestimated by current CV event risk prediction algorithms that do not take the characteristics of RA into account. The expanded cardiovascular risk prediction score for rheumatoid arthritis (the ERS-RA) has been shown to be superior to models that only incorporate traditional risk factors in predicting the risk of CV in patients with RA. This study aims to externally validate the ERS-RA for predicting 10-year CV event risk in Chinese patients with RA.

Methods: Patients with RA from a Chinese nationwide, multicenter, prospective cohort, enrolled between October 2008 and May 2024 were included as the external validation cohort. Discrimination was evaluated using C-index, and calibration was examined using comparisons of observed versus predicted risks.

Results: A total of 10,721 patients with RA were included. The incidence rate of CV events was 5.65 per 1,000 person-years. The C-index of the ERS-RA in this Chinese cohort was 0.831 (95% confidence interval [CI] 0.801 – 0.861). The overall

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

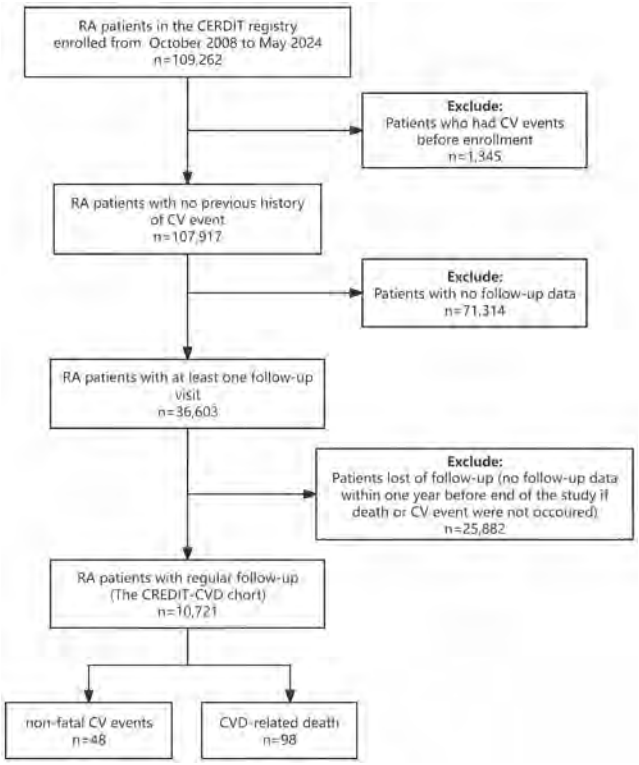


Figure 1. Study flow chart. *RA, rheumatoid arthritis; CREDIT, The Chinese Registry of Rheumatoid Arthritis; CV, cardiovascular; CVD, cardiovascular disease

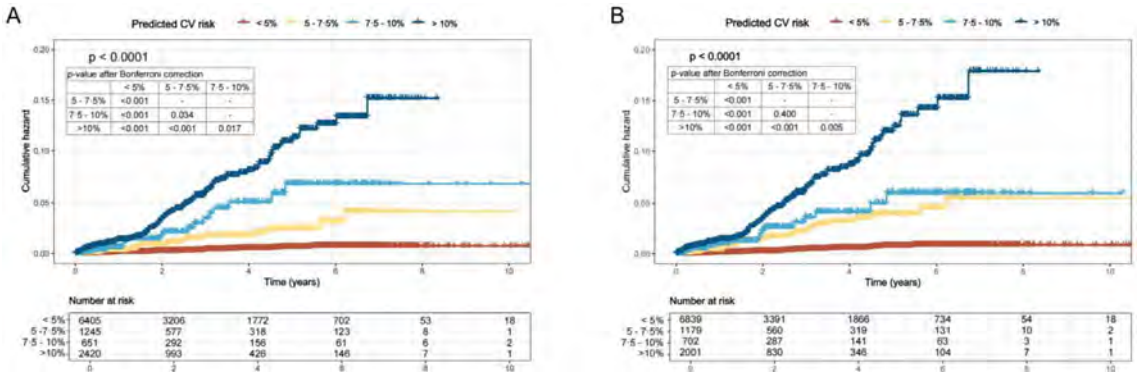


Figure 2. Comparison of cumulative hazard of cardiovascular events between four predicted 10-year cardiovascular event risk levels (<5%, 5.0-7.5%, 7.5-10%, and ≥10.0%) in the CREDIT-CVD cohort with imputed mHAQ (A) and without mHAQ (B) * CVD, cardiovascular disease.

calibration slope was 1.012 (95% CI 0.873 – 1.152), and the observed-to-expected ratio was 0.796 (95% CI 0.676 – 0.937). Across clinically relevant risk intervals, the ERS-RA slightly overestimated CV event risk by 1.41%–2.18% for patients with the predicted risks of < 5%, 5–7.5%, and 7.5–10%, but underestimated CV risk by 10.46% for patients with the predicted risk ≥10%.

Conclusion: The ERS-RA model demonstrated excellent discrimination and calibration for 10-year CV risk prediction in Chinese patients with RA. These results add to growing evidence for the clinical utility of ERS-RA in US, European, and now Chinese populations.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

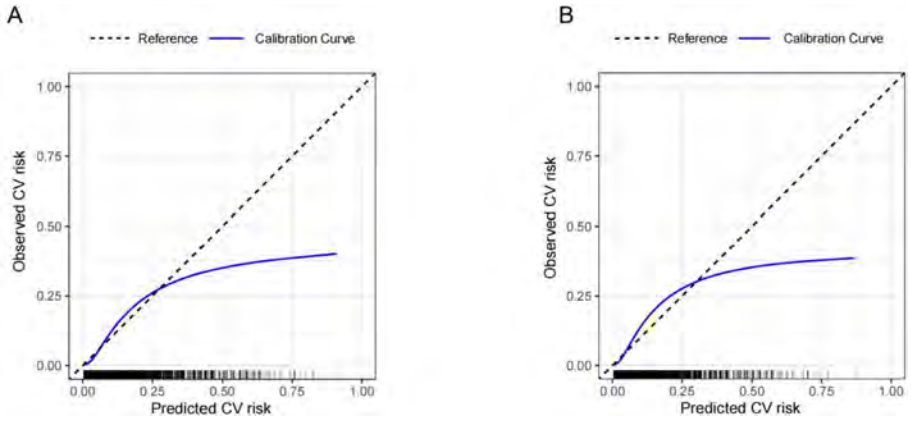


Figure 3. Calibration plots comparing the observed and predicted 10-year risk of cardiovascular event by the ERS-RA score in the CREDIT-CVD cohort with imputed mHAQ (A) and without mHAQ (B) *Short black bars at the x-axis indicate distribution of predicted risks. **ERS-RA, expanded risk score for cardiovascular disease in rheumatoid arthritis.

Disclosure: X. Dong: None; **N. Jiang**: None; **H. Li**: None; **M. Paudel**: None; **J. Liu**: None; **X. Duan**: None; **D. Wu**: None; **H. Li**: None; **F. Li**: None; **Y. Wang**: None; **J. Liu**: None; **S. Xu**: None; **H. Luo**: None; **h. dai**: None; **S. Chi**: None; **J. Xu**: None; **L. Wu**: None; **z. zheng**: None; **J. Xue**: None; **X. Yu**: None; **Q. Huang**: None; **X. Shi**: None; **X. Zhang**: None; **Y. Huo**: None; **Q. Wang**: None; **X. Zeng**: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9; **M. Li**: None; **X. Tian**: None.

Abstract Number: 0469

Evaluating Large Language Models for Automated Joint Involvement Analysis in Rheumatoid Arthritis

Xingyi Liu[1], Sunghwan Sohn[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0430–0469) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In rheumatoid arthritis (**RA**), delaying initiation of treatment for 12 weeks or longer may lead to permanent joint damage and make remission harder to achieve. Therefore, it's essential to develop strategies that improve early detection of RA in primary care setting. Joint involvement ("synovitis") is a core domain of the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for RA. Manual extraction of joint counts from unstructured clinical notes is time-consuming and labor-intensive. We evaluated Llama 3.1—a state-of-the-art large language model (LLM)—for automated identification, quantification, and dating of swollen/tender joints documented in electronic health record (EHR) notes.

Methods: We selected 200 patients meeting RA criteria by manual chart review and 200 non-RA controls. All clinic notes from 1990-01-01 to 2024-05-22 were processed by LLM prompted to act as an expert rheumatologist and provided with the exact same information used during manual chart review—including definitions of large and small joints and the exclusion criteria for certain joints—to extract counts of swollen/tender large and small joints. These counts were then mapped to the five joint involvement levels defined by the 2010 ACR/EULAR criteria (1 large joint = 0 point; 2–10 large joints = 1 point; 1–3 small joints = 2 points; 4–10 small joints = 3 points; >10 joints with at least one small joint = 5 points). Model-derived results were compared to the manual gold standard: we computed true positives (TP), true negatives (TN), false positives

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Performance Metrics of LLM for Joint Involvement Analysis.

Joint involvement	TP	FP	TN	FN	Acc	Pre	Rec	F1	Date Diff (days) Med	Q1	Q3
1 large joint	167	44	38	38	0.71	0.79	0.81	0.80	0	-187.75	8.5
2-10 large joints	95	50	100	42	0.68	0.66	0.69	0.67	0	-23.5	0
1-3 small joints	201	22	24	40	0.78	0.90	0.83	0.87	0	-152	14
4-10 small joints	107	4	82	94	0.66	0.96	0.53	0.69	0	0	57
11+ joints	22	2	172	91	0.68	0.92	0.19	0.32	0.5	0	366.5

*TP: True positive, FP: False positive, TN: True negative, FN: False negative, Acc: Accuracy, Pre: Precision, Rec: Recall, F1: F1-score, Med: Median, Q1: the 25th percentile, Q3: the 75th percentile.

(FP), false negatives (FN), accuracy, precision, recall, and F1-score for each level. For cases correctly identified (TP), we calculated the distribution of days between the LLM's first detected date and the manual review date of joint involvement.

Results: LLM achieved level-specific accuracies ranging from 0.66 (4-10 small joints) to 0.78 (1-3 small joints), with F1-scores spanning 0.32 (11+ joints) to 0.87 (1–3 small joints) (**Table**).

When we compared the LLM's first detected date and the manual review date among true positives, the median absolute difference was zero days for all levels except the 11+ joint level (0.5 days). For the 25th percentile, LLM's first detected date was 187.75 days, 23.5 days and 152 days earlier than the manual review date for 1 large joint, 2-10 large joints and 1-3 small joints, respectively, detection timing was identical for 4–10 small joints and 11+ joints. For the 75th percentile, it trailed manual review by 8.5 days for 1 large joint, 14 days for 1–3 small joints, 57 days for 4–10 small joints, and 366.5 days for 11+ joints, with 2–10 large joints detected at the same date (**Table**).

Conclusion: LLMs demonstrate potential to extract and classify joint involvement levels from unstructured EHR notes, matching manual review in both classification performance and temporal accuracy. These results support the promise of LLMs, especially with continued refinement, to accelerate and automate RA phenotyping.

Disclosure: X. Liu: None; **S. Sohn**: None; **C. Crowson**: None.

Abstract Number: 0470

Characterization of Patients With Rheumatoid Arthritis Based on Distinct Patterns of Pain Improvement Following Treatment With Filgotinib: A *Post Hoc* Analysis of FINCH 1

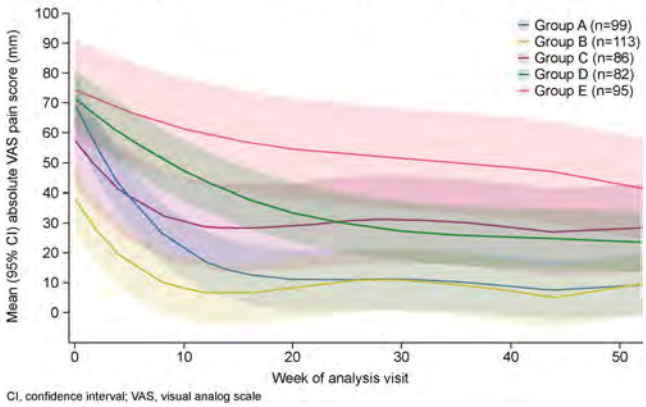
Peter Taylor[1], Yoshiya Tanaka[2], Louis Dron[3], Katrien Van Beneden[4], Gerd Burmester[5] and **Bruno Fautrel**[6], [1]University of Oxford, Oxford, United Kingdom, [2]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [3]Cytel, Toronto, Canada, [4]Alfasigma S.p.A., Bologna, Italy, [5]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [6]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Janus kinase inhibitors have been shown to ameliorate pain as well as inflammation in patients with rheumatoid arthritis (RA). Pain response trajectories were modeled in patients treated with filgotinib in the FINCH 1 trial.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure. Pain trajectories in patients from FINCH 1 receiving filgotinib 200 mg



CI, confidence interval; VAS, visual analog scale

Methods: FINCH 1 (NCT02889796) was a 52-week trial in which patients with RA and an inadequate response to methotrexate (MTX) received filgotinib 200 mg or 100 mg, adalimumab or placebo, each with MTX. Patients reported pain on a visual analog scale (VAS) ranging from 0 mm (no pain) to 100 mm (worst possible). Moderate pain was defined as a score of 40–60 mm, with scores >60 mm indicating severe pain. Group-based trajectory modeling[1] was used to identify patient groups with similar pain responses over a 12-month period.

Results: Among patients receiving filgotinib 200 mg (n=475), modeling produced five distinct groups of pain response trajectory (**Figure**). Age, disease duration and erosion score were similar across all groups at baseline. Groups A and B (45% of patients) had a rapid reduction in pain in the first 3 months, with the improvement maintained over 12 months. Group A had the greatest reduction in pain. Groups C and D (35% of patients) had a slower response but achieved a 50% pain reduction after 6 months. Group E (20% of patients) had severe pain at baseline (mean VAS pain approx. 75 mm) and persistent, moderate pain over 12 months. Mean VAS pain score was < 40 mm at Month 3 in Groups A, B and C (approx. 60% of patients) and at Month 6 in Groups A, B, C and D (80% of patients).

At Months 3, 6 and 12, the greatest absolute changes in Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP) and 36-Item Short Form Survey (SF-36) Physical Component Summary (PCS) scores were seen in patients with the most rapid pain responses (Groups A and B) (**Table**). At Month 6, 50% of patients in Group A and 53% in Group B were in remission (by Clinical Disease Activity Index), compared with 3% in Group E (noted for highest median DAS28-CRP and lowest [worst] median SF-36 PCS score at baseline). At Months 6 and 12, the greatest improvements in patient's and physician's global assessment of disease activity occurred in Group A.

Lack of efficacy was the most common reason for discontinuation in Group E (10.5%); 2.1% discontinued due to adverse events. In Groups A, B, C and D, the leading reason for discontinuation was adverse events (6.1%, 4.4%, 7.0% and 8.5%, respectively), followed by lack of efficacy (5.1%, 2.7%, 5.8% and 7.3%, respectively).

Similar pain trajectories were observed in patients receiving filgotinib 100 mg (n=480).

Conclusion: Of patients with prior inadequate response to MTX treated with filgotinib 200 mg, 80% achieved a substantial reduction in pain within 6 months. The most rapid pain responses with filgotinib were associated with the greatest improvements in other disease-related measures. Overall, these data illustrate the heterogeneity of treatment response in patients with RA and underscore the importance of communicating realistic expectations and timelines to patients.

Reference:

1. Nagin DS, et al. *Stat Methods Med Res* 2018;27:2015–23.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Efficacy outcomes from baseline to Month 12 in patients receiving filgotinib 200 mg, by pain response trajectory

		Group A (n=99)	Group B (n=113)	Group C (n=86)	Group D (n=82)	Group E (n=95)
DAS28-CRP, median (IQR)	Baseline	5.68 (5.11, 6.50)	5.33 (4.84, 5.84)	5.52 (5.05, 6.10)	5.85 (5.43, 6.46)	6.33 (5.64, 6.77)
	6-month absolute change from baseline	−3.76 (−3.09, −4.30); n=86	−3.36 (−2.53, −4.09); n=102	−2.97 (−2.05, −3.56); n=77	−3.15 (−2.57, −3.63); n=67	−2.49 (−1.55, −3.06); n=78
	12-month absolute change from baseline	−4.00 (−3.31, −4.66); n=85	−3.55 (−2.83, −4.05); n=98	−2.95 (−2.13, −3.73); n=69	−3.39 (−2.73, −4.03); n=65	−2.89 (−2.23, −3.86); n=72
SF-36 PCS score, median (IQR)	Baseline	31 (28, 34)	39 (33, 44)	33 (29, 38)	32 (28, 36); n=80	30 (27, 34)
	6-month absolute change from baseline	17 (12, 23); n=89	11 (5, 17); n=104	7 (3, 12); n=80	8 (5, 12); n=67	7 (2, 10); n=82
	12-month absolute change from baseline	17 (13, 25); n=85	12 (6, 18); n=99	10 (5, 15); n=71	11 (6, 14); n=65	8 (5, 14); n=75
SJC28, median (IQR)	Baseline	10.0 (8.0, 13.0)	9.0 (7.0, 14.0)	9.0 (6.2, 12.8)	10.0 (7.2, 14.0)	11.0 (8.0, 15.5)
	6-month absolute change from baseline	−10.0 (−7.0, −13.0); n=86	−9.0 (−6.0, −12.0); n=102	−7.0 (−6.0, −11.0); n=77	−10 (−7.0, −12.5); n=67	−9.0 (−6.0, −13.0); n=78
	12-month absolute change from baseline	−10.0 (−8.0, −13.0); n=85	−9.0 (−5.6, −13.0); n=99	−8.0 (−6.0, −10.0); n=71	−10.0 (−8.0, −13.0); n=65	−10.0 (−7.0, −14.2); n=76
TJC28, median (IQR)	Baseline	14 (10, 18)	12 (8, 17)	13 (10, 17)	16 (12, 22)	17 (13, 21)
	6-month absolute change from baseline	−12 (−9, −18); n=86	−11 (−8, −16); n=102	−10 (−7, −15); n=77	−14 (−11, −17); n=67	−11 (−7, −17); n=78
	12-month absolute change from baseline	−13 (−9, −17); n=85	−12 (−8, −15); n=99	−11 (−8, −15); n=71	−14 (−9, −19); n=65	−13 (−9, −17); n=76
CDAI responders at Month 6, n/N (%)	Remission	42/84 (50.0)	54/102 (52.9)	15/77 (19.5)	3/67 (4.5)	2/76 (2.6)
	LDA	37/84 (44.0)	43/102 (42.2)	39/77 (50.6)	36/67 (53.7)	21/76 (27.6)
	Remission or LDA	79/84 (94.0)	97/102 (95.1)	54/77 (70.1)	39/67 (58.2)	23/76 (30.3)

CDAI, Clinical Disease Activity Index; IQR, interquartile range; LDA, low disease activity; SF-36, 36-Item Short Form Survey; PCS, Physical Component Summary; S/TJC28, swollen/tender joint count based on 28 joints.

Disclosure: P. Taylor: AbbVie, 2, Acelyrin, Inc., 2, Alfasigma S.p.A., 2, 5, Biogen, 2, Eli Lilly & Co., 2, Fresenius Kabi, 2, Gilead, 2, Immunovant, 2, Moonlake, 2, Nordic Pharma, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB, 2; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **L. Dron**: None; **K. Van Beneden**: Alfasigma S.p.A., 3, Galapagos, 3; **G. Burmester**: Celltrion, 6, Chugai, 6, Fresenius, 6, Gedeon Richter, 6, Sanofi, 6; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0471

An Open-label, Randomized, Controlled Phase 1/2 Study to Assess the Safety and Efficacy of KYV-101 anti-cd19 CAR-T Cell Therapy in Active and Difficult-to-treat ACPA Positive Rheumatoid Arthritis: Preliminary Results of the COMPARE Trial

Fredrik Albach[1], **Ioanna Minopoulou**[1], Artur Wilhelm[2], Robert Biesen[1], Arnd Kleyer[1], Norman Drzeniek[3], Edgar Wiebe[4], Anja Fleischmann[3], Dominic Borie[5], Vincent Casteleyn[3], Tobias Alexander[3], Christian Furth[6], Jan Zernicke[3], Burkhard Muche[7], Sandra Hermann[4], Pfeil Alexander[8], Veronika Scholz[3], Elpida Phithak[3], Olaf Penack[9], Kamran Movassaghi[9], Eva Vanessa Schrezenmeier[10], Udo Schneider[3], Antonia Busse[11], Georg Schett[12], Ulrich Keller[11], Lars Bullinger[9], Gerhard Krönke[13], Marie Luise Hütter-Krönke[14] and David Simon[15], [1]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [2]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, [3]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, [4]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [5]Kyverna Therapeutics, Emeryville, CA, [6]Department of Nuclear Medicine, Charité-Universitätsmedizin Berlin, Berlin, Germany, Berlin, [7]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [8]Department of Internal Medicine III, Jena University Hospital - Friedrich Schiller University Jena, Jena, Germany, [9]Department of Hematology, Oncology and Tumor Immunology, Charité - Universitätsmedizin Berlin, Campus Virchow Klinikum, Berlin, Germany, Berlin, [10]Department of Nephrology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, [11]Department of Hematology, Oncology and Cancer Immunology, Charité - Universitätsmedizin Berlin, Campus Steglitz, Berlin, Germany; Max-Delbrück-Center for Molecular Medicine, Berlin, Germany; German Cancer Consortium (DKTK) partner site Charité Berlin and German Cancer Research Center (DKFZ), Heidelberg, Germany, Berlin, [12]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [13]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Berlin, Germany, [14]Department of Hematology, Oncology and Cancer Immunology, Charité - Universitätsmedizin Berlin, Campus Steglitz, Berlin, Germany, Berlin, [15]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disease characterized by autoreactive B cells that produce anti-citrullinated protein antibodies (ACPA), contributing to sustained synovial inflammation and joint destruction. Recent clinical reports indicate that anti-CD19 chimeric antigen receptor (CAR) T-cell therapy shows promise in

Table 1. Screening characteristics of apheresed RA patients

Parameter	Pat. 1	Pat. 2	Pat. 3	Pat. 4	Pat. 5	Pat. 6	Mean (SD)
Sex [m/f]	f	f	m	f	m	m	n.a.
Age [years]	49	42	60	54	31	69	50.8 (13.4)
Disease duration [years]	9	4	9	23	6	14	10.8 (6.9)
Prior b/tsDMARDs	6	5	3	6	7	8	5.8 (1.7)
DAS28-ESR	6.8	5.5	5.9	4.6	5.9	6.4	5.9 (0.8)
ACPA [U/ml]	652.4	170.6	>1000	>1000	>1000	39.6	n.a.
RF IgA [U/ml]	42.4	29.2	>500	27.1	>500	180.8	n.a.
RF IgM [U/ml]	30.3	19.5	>500	289.7	158.2	160	n.a.
HAQ-DI	1.5	2.13	1.88	1.38	1.63	0.5	1.5 (0.6)
Latest follow-up after therapy [days]	56	28	-	-	-	-	n.a.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

inducing drug-free clinical remission in difficult-to-treat RA (D2T-RA, Lidar 2025; Li 2025). The COMPARE (COMparison of B-cell dePletion by rituximAb and anti-CD 19 CAR-T therapy in Patients with rhEumatoid arthritis) trial was designed to (i) evaluate the safety and efficacy of the anti-CD19 CAR-T cell therapy KYV-101 in ACPA-positive patients with active, treatment refractory D2T-RA and (ii) to compare the impact of KYV-101 on disease activity to the standard-of-care anti-CD20 monoclonal antibody rituximab (RTX). KYV-101 is a fully human, autologous anti-CD19 CAR T-cell therapy with CD28 costimulation, which is under investigation in B-cell driven autoimmune disease. With a single administration, KYV-101 has potential to achieve durable drug-free and disease-free remission via deep B-cell depletion and immune reset. Preliminary data suggest its potential for durable effects across rheumatic (Albach 2025, Minopoulou 2025, Haase 2025) and neuroimmune indications (Haghikia 2023; Faissner 2024).

Methods: COMPARE, an open-label, randomized, controlled Phase 1/2 trial (EU CT:2024-514955-13-00) is currently enrolling the safety run-in of the trial (Phase 1; n=6) during which all participants receive 1×10^8 CAR T cells after lymphodepletion. The primary endpoint in Phase 1 is safety (Cytokine Release Syndrome (CRS), Immune Cell Associated Neurotoxicity Syndrome (ICANS), adverse events). Additional endpoints include pharmacokinetics of KYV-101, B-cell and autoantibody levels, and disease activity scores.

Results: At the time of submission, Phase 1 is fully recruited with 6 participants apheresed; two participants have received KYV-101 by 12 May 2025, with follow-ups up to 28 and 56 days. Participants had active disease for a mean of 10.8 (±6.9) years duration and 5.8 (±1.7) prior therapies (Table 1). Both treated participants experienced expected transient cytopenias due to lymphodepletion and CRS (grade I and II), which promptly resolved following tocilizumab and dexamethasone administration. No ICANS, serious adverse events or deaths occurred. CAR T-cells expanded rapidly, reaching peaks of 479 and 122 cells/mL at days 21 and 10 after KYV-101 infusion. Both patients exhibited complete peripheral B-cell depletion and a decline in ACPA values to 19% and 5% of screening values at the latest follow-up.

Conclusion: Preliminary data from the COMPARE trial suggest that KYV-101 has a favorable safety profile and leads to robust CAR T-cell expansion and complete peripheral B-cell depletion in seropositive, active, treatment refractory D2T-RA. With apheresis completed and planned KYV-101 infusion for all Phase 1 patients by July 2025 completion of safety run-in is anticipated shortly, followed by the randomized portion of the trial. Updated data summarizing Phase 1 experience with estimated follow-up post-infusion of 4 months will be presented.

Disclosure: F. Albach: Kyverna Therapeutics, 12, Financial/Material Study Support; **I. Minopoulou**: AbbVie/Abbott, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Novartis, 6; **A. Wilhelm**: None; **R. Biesen**: None; **A. Kleyer**: AbbVie/Abbott, 1, 6, Alfasigma, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, 6, Gilead, 1, Janssen, 1, 6, Novartis, 1, 6, UCB, 1, 6; **N. Drzeniek**: None; **E. Wiebe**: Sobi, 6; **A. Fleischmann**: None; **D. Borie**: Kyverna Therapeutics, 3, 8; **V. Casteleyn**: None; **T. Alexander**: None; **C. Furth**: None; **J. Zernicke**: None; **B. Muche**: AbbVie/Abbott, 6, Amgen, 6, Celltrion, 6, Theramex, 6, UCB, 6; **S. Hermann**: None; **P. Alexander**: None; **V. Scholz**: None; **E. Phithak**: None; **O. Penack**: Alexion, 1, 6, Apogepha, 1, Equillium Bio, 1, Gilead, 1, 6, Incyte, 5, Jazz, 1, 6, Merck/MSD, 1, 6, Neovii, 6, Novartis, 1, 6, Omeros, 1, Orca Bio, 1, Pfizer, 6, Priothera, 1, 5, Sanofi, 1, Shionogi, 1, SOBI, 1, Therakos, 6; **K. Movassaghi**: None; **E. Schrezenmeier**: None; **U. Schneider**: None; **A. Busse**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **U. Keller**: None; **L. Bullinger**: None; **G. Krönke**: None; **M. Hütter-Krönke**: None; **D. Simon**: AbbVie, 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, Janssen-Cilag, 2, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Lilly, 2, 6, Medac, 2, 6, Novartis, 2, 6, UCB, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0472

Detrimental Effects of Umbilical Cord Blood-derived Mesenchymal Stem Cells Intra-articular Injections on Pannus Invasiveness

Sung Eun Kim[1], Hye Lim Kang[1], Min Jung Kim[2], Hyung-Sik Kim[3] and **Kichul Shin**[4], [1]Division of Rheumatology, Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, Republic of Korea, [2]Seoul Metropolitan Government Boramae Medical center, Dongjak-gu, Seoul, South Korea, [3]Department of Oral Biochemistry, Pusan National University School of Dentistry, Yangsan, Republic of Korea, [4]Seoul National University, Seoul, South Korea

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

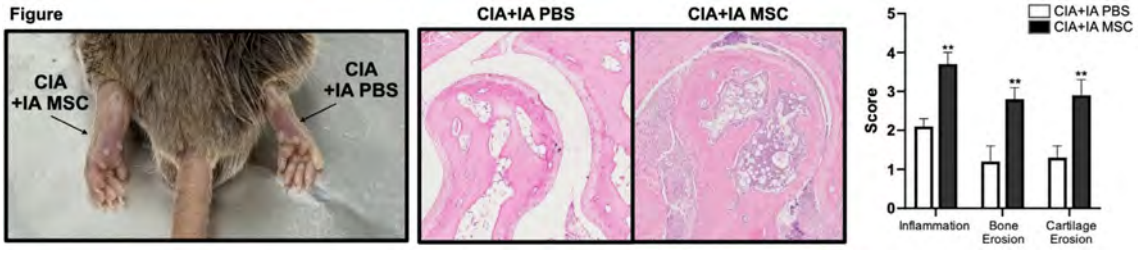
Session Time: 10:30AM–12:30PM

Background/Purpose: Studies have shown that mesenchymal stem cell (MSC) infusion ameliorates arthritis in animal models. However, the first-pass effect in the lung has directed attention to other routes of administration for MSCs. We aimed to investigate the impact of intra-articular MSC injections in mice with arthritis and its underlying mechanism.

Methods: An indirect co-culture of umbilical cord blood-derived (UCB-) MSC and fibroblast-like synoviocytes from patients with rheumatoid arthritis (RA-FLS) was conducted to study the altered traits of proliferation, migration, and invasion of RA-FLS. We utilized proteomics to analyze the outcomes of the co-culture in both cell types. CIA was induced in DBA/1 mice, followed by a single intra-articular injection in the ankle on day 28. The mice were euthanized on day 42 for histological analyses. Recombinant transforming growth factor-beta-1-induced transcript 1 (TGFB1I1) and anti-TGFB1I1 were employed in subsequent experiments to investigate the mechanisms of the transformed milieu in the synovium.

Results: The proliferation, mobility, and invasiveness of RA-FLS were enhanced when co-cultured with UCB-MSC (Figure 1). While intravenous UCB-MSC reduced the severity of arthritis in mice, intra-articular injection of UCB-MSC resulted in significant arthritis in the injected ankle compared to the contralateral side (Figure). The proteomic analysis revealed a substantial expression of TGB1I1 in RA-FLS co-cultured with UCB-MSC and even higher levels in UCB-MSCs. Indeed, TGB1I1 was highly expressed in UCB-MSC-injected ankles of CIA mice. Furthermore, TGB1I1 not only induced cytoskeletal rearrangement in RA-FLS but also promoted the gene expression of IL-1beta, IL-8, MMP-3, and MMP-13, thereby contributing to both joint inflammation and damage. TGB1I1 knockdown resulted in significantly reduced mobility of FLS co-cultured with UCB-MSC.

Conclusion: Intra-articular injection of UCB-MSCs into inflamed joints inexplicably induces detrimental effects that may expedite joint damage and perpetuate systemic inflammation. MSC therapy may act as a double-edged sword depending on its route of administration in patients with rheumatoid arthritis.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Kim: None; **H. Kang**: None; **M. Kim**: None; **H. Kim**: None; **K. Shin**: None.

Abstract Number: 0473

A Phase 2b Dose-ranging Study of Peresolimab for Adults With ra

Jay Tuttle[1], Kirstin Griffing[2], Mark Genovese[2], Hyungmin Rha[2], So Young Park[2], Pia Yachi[1], Ajay Nirula[1], LANCE PFEIFER[2], Tami Jo Rayle[2], Jesus Abraham Simón-Campos[3], Clifton Bingham[4], Kevin Winthrop[5], Daniel Aletaha[6], Iain McInnes[7], Yu Xue[8], Yoshiya Tanaka[9], Roy Fleischmann[10], Paul Emery[11] and **Michael Weinblatt**[12], [1]Lilly Biotechnology Center, San Diego, CA, [2]Eli Lilly and Company, Indianapolis, IN, [3]Köhler & Milstein Research, UADY School of Medicine, Merida, Yucatan, Mexico, [4]Johns Hopkins University, Baltimore, MD, [5]Oregon Health & Science University, Portland, OR, [6]Medical University Vienna, Wien, Austria, [7]University of Glasgow, Glasgow, United Kingdom, [8]Huashan Hospital, Fudan University, Shanghai, China (People's Republic), [9]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [10]Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, [11]University of Leeds, Leeds, England, United Kingdom, [12]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Peresolimab, a humanized IgG1 mAb, activates programmed cell death protein 1. In a phase 2a study, peresolimab demonstrated efficacy in participants (pts) with RA who had an inadequate response to prior DMARDs.[1] Here, we present data from a phase 2b dose-ranging study of peresolimab.

Methods: This double-blind, placebo (PBO)-controlled study in adults with moderately to severely active RA (N=490) randomized pts (1:2:2:2) to 100 mg (n=68), 400 mg (n=141), or 1000 mg (n=141) peresolimab or PBO (n=140) subcutaneously (SC) every 4 weeks (Q4W). At Week 12, pts receiving peresolimab continued their assigned dose; those receiving PBO switched (1:1) to 400 mg (n=67) or 1000 mg (n=73) peresolimab SC Q4W. The primary endpoint was 20% improvement in ACR response (ACR20) at Week 12; secondary endpoints included ACR50 and DAS28-CRP change from baseline (BL) at Week 12. Safety through 12 weeks and malignancies and possible major adverse cardiovascular events (MACE) through Week 60 are presented. A logistic regression model with treatment group, BL disease activity, and stratification factors as covariates was used for dichotomous endpoints. Missing data were imputed as non-response. A mixed-effects model for repeated measures with treatment group, BL disease activity, stratification factors, visit and treatment-by-visit interaction as fixed factors and pts as a random factor was used for continuous endpoints. Nominal p values are reported.

Results: At BL, the mean (SD) age was 54.0 (11.3) yrs, RA duration was 11.6 (8.2) yrs, and DAS28-CRP score was 5.97 (0.86); 92.4% were RF positive and 85.9% were anti-CCP positive, 33.5% were biological/target synthetic (b/ts) DMARD

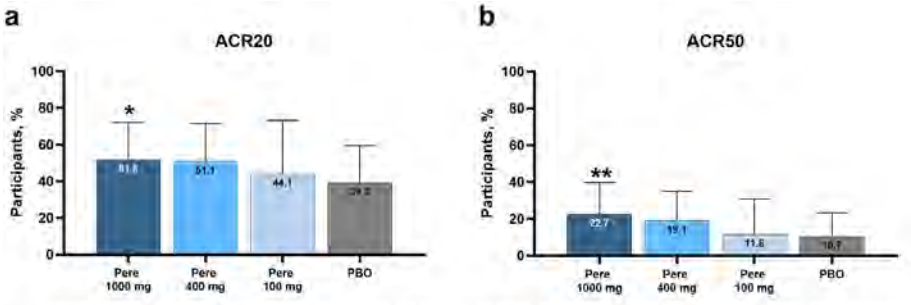


Figure 1. Proportion of participants with ACR20 and ACR50 response at Week 12.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Overview of adverse events during Weeks 0 to 12

	Peresolimab 1000 mg (n=141)	Peresolimab 400 mg (n=141)	Peresolimab 100 mg (n=68)	PBO (n=140)
TEAE	45 (31.9)	41 (29.1)	25 (36.8)	43 (30.7)
TEAE by severity[a]				
Mild	26 (18.4)	22 (15.6)	15 (22.1)	17 (12.1)
Moderate	14 (9.9)	15 (10.6)	8 (11.8)	21 (15.0)
Severe	5 (3.5)	4 (2.8)	2 (2.9)	5 (3.6)
SAE	7 (5.0)	4 (2.8)	1 (1.5)	5 (3.6)
Death	0	0	0	0
Discontinuation from study treatment due to adverse event	3 (2.1)	3 (2.1)	0	3 (2.1)
AESI				
Allergic reaction /hypersensitivity	3 (2.1)	5 (3.5)	2 (2.9)	2 (1.4)
Injection site reactions	6 (4.3)	3 (2.1)	1 (1.5)	4 (2.9)
Infections	17 (12.1)	19 (13.5)	9 (13.2)	20 (14.3)
Serious infection	2 (1.4)	1 (0.7)	0	2 (1.4)
Infection leading to permanent discontinuation	0	1 (0.7)	0	0
Potential OI	1 (0.7)	1 (0.7)	0	0
Confirmed OI	0	0	0	0
Malignancies	2 (1.4)	2 (1.4)	0	0

Data are n (%).
[a]Participants with multiple occurrences of the same event are counted under the highest severity.
AESI, adverse event of special interest; OI, opportunistic infection; SAE, serious adverse event; TEAE, treatment-emergent adverse event

naïve, and 82.4% were female. A total of 30 (44.1%; p=0.534), 72 (51.1%; p=0.098), and 73 (51.8%; p=0.014) pts who received 100, 400, or 1000 mg peresolimab, respectively, achieved ACR20 at Week 12 vs 55 (39.3%) who received PBO (Figure 1a). Similarly, ACR50 at Week 12 was significantly different (p=0.003) in pts receiving 1000 mg peresolimab vs PBO but not for 400 mg (p=0.102) or 100 mg (p=0.741) peresolimab vs PBO (Figure 1b). The least squares mean (standard error) change from BL to Week 12 in DAS28-CRP was greater for pts receiving peresolimab 100 mg (-1.29 [0.15]), 400 mg (-1.41 [0.11]; p=0.030), and 1000 mg (-1.67 [0.11]; p< 0.001) vs PBO (-1.08 [0.11]). Treatment-emergent adverse events (AEs) were similar across groups through Week 12 other than 2 malignancies in each the 400 mg and 1000 mg peresolimab dose groups (Table 1). After Week 12, an additional 4 malignancies (non-melanoma skin cancer events excluded) were reported up to Week 60; 9 possible MACEs were reported in pts receiving peresolimab through Week 60.

Conclusion: Peresolimab was superior to PBO at Week 12 for several key endpoints, but efficacy was not differentiated from existing treatment options. In context of observed efficacy combined with the number of reported malignancies and possible MACEs through week 60, the study was stopped based on the non-favorable benefit/risk profile for peresolimab in treating RA patients.

References:

1. Tuttle, et al. *N Engl J Med*. 2023;388(20):1853–62

Disclosure: J. Tuttle: Eli Lilly and Company, 3, 11; **K. Griffing**: Eli Lilly and Company, 3, 11; **M. Genovese**: Eli Lilly and Company, 3, 11; **H. Rha**: Eli Lilly and Company, 3, 11; **S. Park**: Eli Lilly and Company, 3, 11; **P. Yachi**: Eli Lilly and Company, 3, 11; **A. Nirula**: Eli Lilly and Company, 11, Recludix Pharma, 3, 11, Zura Bio, 1; **L. PFEIFER**: Eli Lilly and Company, 3, 11; **T. Rayle**: Eli Lilly and Company, 3, 11; **J. Simón-Campos**: None; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **K. Winthrop**: AbbVie/Abbott, 2, AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly and Company, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Moderna, 2, Novartis, 2, Pfizer, 2, 5, Regeneron, 2, Roche, 2, Sanofi, 2, Union Chimique

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Belge, 2; **D. Aletaha**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sanofi, 6; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **Y. Xue**: None; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **R. Fleischmann**: AbbVie/Abbott, 2, Almirall, 2, Artiva Biotherapeutics, 2, Atomwise, 2, Biohaven Pharmaceuticals, 2, Bristol-Myers Squibb(BMS), 2, Cyoxone, 2, Deep Cure, 2, Dren Bio, 2, ECOR, 2, Eli Lilly, 2, Galvani, 2, Gates Bio, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Halia, 2, ImmuneMed, 2, Immunovant, 2, InventisBio, 2, Istesso, 2, Janssen, 2, Janux, 2, Monte Rosa, 2, Novartis, 2, Overland, 2, Pfizer, 2, Synact, 2, TPG, 2, UCB, 2, Vyne, 2, Xencor, 2; **P. Emery**: Abbvie, 1, Activa, 1, Anaptysbio, 1, Astra-Zeneca, 1, BMS, 1, Boehringer Ingelheim, 1, Galapagos, 1, Gedeon Richter, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, Novartis, 1; **M. Weinblatt**: Aclaris, Amgen, Anaptysbio, Artiva Bio, BMS, Biohaven, Curie Bio, Deep Cure, Gliead, Ignite, Janux Therapeutics, J&J, Lilly, Lifordi, Marvel Bio ,, 2, 5.

Abstract Number: 0474

Real-World Experience of Janus Kinase Inhibitors; Retention and Factors Associated with Discontinuation

Joseph Nathan[1], Bayram Farisogullari[2], Nicholas Jones[3], Mohammad Ayoub[3], James Brown[3], Sarah Levy[3], James Brader[4], Ayse Ersoy[4], Blossom Israni[4], Mark Lloyd[4], Afzal Latheef[5], Diane Hill[5], Amybel Taylor[6], Darshani Arachchige[6], Hlaing Chitsu[6], Helen Linklater[6], Kunal Lather[7], Luke Gompels[7], Eman Elfar[8], Ritu Malaiya[8], Pedro Machado[9] and **Patrick Kiely**[10], [1]St George's Hospital, London, United Kingdom, [2]University College London, London, [3]Croydon Health Services NHS Trust, Croydon, England, United Kingdom, [4]Frimley Health NHS Foundation Trust, Frimley, England, United Kingdom, [5]St George's University Hospitals NHS Foundation Trust, London, England, United Kingdom, [6]Surrey and Sussex Healthcare NHS Trust, Redhill, England, United Kingdom, [7]Somerset NHS Foundation Trust, Taunton, England, United Kingdom, [8]Epsom and St Helier University Hospitals NHS Trust, Carshalton, England, United Kingdom, [9]Department of Rheumatology, University College London, and Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS Trust, Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [10]St George's University Hospitals NHS Foundation Trust, London, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The use of Janus Kinase inhibitors (JAKi) to treat RA and PsA in a real-world setting has not been well described. Our aim was to investigate the place in treatment pathway, retention and factors associated with discontinuation of JAKi prescribed for RA and PsA in routine care.

Methods: A retrospective review of all patients treated with Baricitinib (B), Filgotinib (F), Tofacitinib (T) and Upadacitinib (U) in 6 centres was conducted from time of first use of any of these agents in routine care until November 2024. Standardized data was collected including demographics, place in treatment pathway, concurrent MTX and CS use, duration of treatment and reason for discontinuation. Retention rate was calculated using Kaplan-Meier analysis. Factors associated with JAKi discontinuation were assessed by multivariable Cox regression analyses.

Results: The case notes of 985 patients were reviewed, 79.5% female, mean age 60 (range 19 - 89) years. The JAKi was B in 658 (67%), F in 127 (13%), T in 100 (10%) and U in 100 (10%). The disease indications were RA in 849 (86%; B 648, F

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

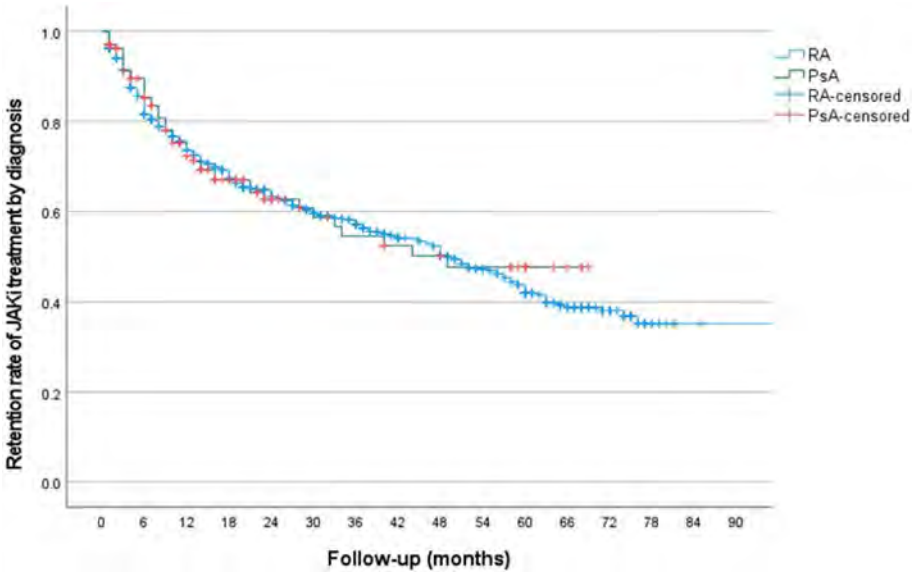


Figure 1. Kaplan Maier retention curve for patients with RA and PsA treated with any JAK inhibitor

127, T 47, U 27), PsA in 136 (14%; B 10, F 0, T 53, U 73). MTX was co-prescribed in 43%, subsequently discontinued in 6%. CS was co-prescribed in 34%, subsequently tapered in 18% and discontinued in 62%.

For all cases, JAKi were prescribed 1st line before biologic DMARD in 7.5%, 2nd line after bDMARD 13.7%, 3rd line 29% and 4th line or later in 49.8%. Median retention for all JAKi was 49 months (range 1-85, 95% C.I. 42.62-55.37), and 52.8% remained on treatment at time of analysis, with no difference between RA and PsA populations. The median retention on B was 52 months and T 24 months ($p< 0.0011$), with no difference in retention between other pairwise JAKi comparisons. See Figures 1 and 2.

Multivariable regression analyses showed a significantly higher relative risk of JAKi discontinuation for older age, female sex and treatment with Tofa compared to Bari. For RA patients co-prescription with MTX had a significantly lower risk of JAKi discontinuation, Table 1.

JAKi were discontinued in 46.4%; primary inefficacy 9.8%, secondary inefficacy 11.8%, adverse events 18.5% and 6.3% pre-emptively due to the Oral Surveillance study findings. There were no significant differences in reasons for discontinuation

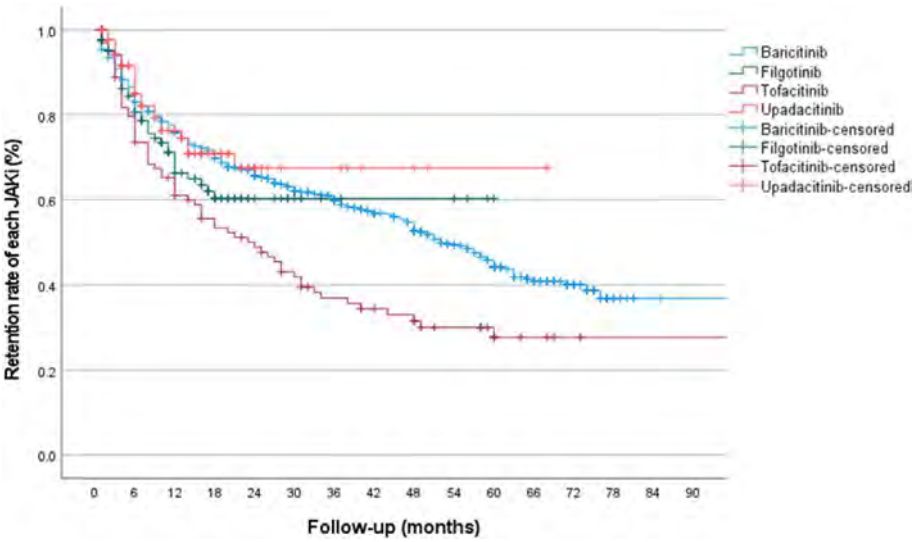


Figure 2. Kaplan Maier retention curve for all patients treated with individual JAK inhibitors

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Multivariable regression analysis showing relative risk for JAKi discontinuation; all patients and RA and PsA patients

Multivariable regression analysis for all, RA and PsA patients						
	All patients (n= 982)		RA patients (n= 847)		PsA patients (n= 135)	
Variables	RR (%95 CI)	p-value	RR (%95 CI)	p-value	RR (%95 CI)	p-value
Age	**1.01 (1.00-1.02)**	**0.044**	1.01 (1.00-1.02)	0.061	1.01 (0.98-1.03)	0.53
Gender						
Male	Reference		Reference		Reference	
Female	**1.66 (1.28-2.16)**	**<0.001**	**1.62 (1.22-2.15)**	**<0.001**	1.63 (0.82-3.23)	0.16
Diagnosis			NA	NA	NA	NA
RA	Reference					
PsA	0.70 (0.47-1.05)	0.083				
Order of Jaki						
1st	Reference		Reference		Reference	
2nd or more	1.05 (0.73-1.51)	0.79	1.09 (0.75-1.57)	0.67	**0.04 (0.004-0.39)**	**0.006**
Type of JAKi		**<0.001**		**<0.001**		0.43
Baricitinib	Reference		Reference		Reference	
Filgotinib	1.19 (0.85-1.67)	0.31	1.20 (0.85-1.69)	0.29	1.60 (0.54-4.80)	0.40
Tofacitinib	**2.27 (1.64-3.14)**	**<0.001**	**2.40 (1.69-3.40)**	**<0.001**	1.05 (0.33-3.50)	0.90
Upadacitinib	1.22 (0.74-2.02)	0.43	1.03 (0.46-2.16)	0.95		
MTX co-prescription when JAKi started (yes vs no)	0.84 (0.70-1.01)	0.066	**0.81 (0.66-0.98)**	**0.032**	1.24 (0.66-2.34)	0.51
Steroid co-prescription when JAKi started (yes vs no)	1.11 (0.91-1.34)	0.32	1.10 (0.90-1.35)	0.36	1.10 (0.55-2.20)	0.78

JAKi: Janus kinase inhibitors; PsA: Psoriatic arthritis; RA: Rheumatoid arthritis

between RA and PsA, nor individual JAKi. Venous thromboembolic events (VTE) occurred in 1.4%, event rate 0.57 / 100 patient years; 10 pulmonary embolism (PE) and 4 deep vein thrombosis (DVT), with mean time to event 29 months, range 6 – 75 months. Other adverse events included cerebrovascular events in 1.2%, 0.49 / 100 patient years, cardiac events in 0.7%, 0.29 / 100 patient years and cancer in 0.9%, 0.37 / 100 patient years.

Conclusion: JAKi are generally used late in the DMARD treatment pathway in routine care, with high retention rates and a CS sparing effect was evident. Significantly higher risks for discontinuation were female sex, older age, Bari versus Tofa treatment, and in RA patients use without MTX. The place in treatment pathway conferred no effect on retention. Adverse events were in line with this class of immune suppressive therapies including VTE, where PE outnumber DVT events.

Disclosure: J. Nathan: None; **B. Farisogullari**: None; **N. Jones**: None; **M. Ayoub**: None; **J. Brown**: None; **S. Levy**: None; **J. Brader**: None; **A. Ersoy**: None; **B. Israni**: None; **M. Lloyd**: UCB, 12, Sponsored to attend British Society for Rheumatology Conference 2024; **A. Latheef**: None; **D. Hill**: None; **A. Taylor**: None; **D. Arachchige**: None; **H. Chitsu**: None; **H. Linklater**: None; **K. Lather**: None; **L. Gompels**: None; **E. Elfar**: None; **R. Malaiya**: Novartis, 12, Attendance at educational events, UCB, 12, attendance at educational events; **P. Machado**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **P. Kiely**: Alfasigma, 6, Eli Lilly, 12, Sponsorship to attend educational meetings.

Abstract Number: 0475

Drug Discontinuation in Inflammatory Arthritis Following Mandatory Non-Medical Switching from Originator to Biosimilar in Quebec, Canada

Cristiano Moura[1], Luck Lukusa[2], Denis Choquette[3], Gilles Boire[4], Nathalie Carrier[5], Autumn Neville[2] and **Sasha Bernatsky**[6] on behalf of RHUMADATA and EUPA investigators, [1]Research Institute of the McGill University Health Center, Montral, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, Canada, [3]Institut de Rhumatologie de Montréal, Saint-Donat-de-Montcalm, Canada, [4]Retired, Sherbrooke, QC, Canada, [5]Centre integré universitaire de santé et de services sociaux de l'Estrie – Centre hospitalier universitaire de Sherbrooke (CIUSSS de l'Estrie-CHUS), Sherbrooke, Canada, [6]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of individuals transitioning from bio-originator to biosimilars.

Characteristic	N (%), mean (SD), or median (IQR)
Biosimilar, N (%)	
Adalimumab	75 (68.2)
Etanercept	22 (20.0)
Rituximab	12 (10.9)
Infliximab	1 (0.9)
Female sex, N (%)	67 (60.9)
Age in years, mean (standard deviation, SD)	56.9 (15.8)
Disease duration in years, mean (SD)	19.3 (12.6)
Body mass index, mean (SD)	29.0 (6.6)
Current smoker, N (%)	18 (16.4)
Current alcohol drinker, N (%)	21 (19.1)
Use of biologic (other than the originator) in the past year, N (%)	33 (30.0)
Current use of synthetic disease-modifying antirheumatic drugs, N (%)	58 (53.2)
Health Assessment Questionnaire (HAQ) score, median (interquartile range, IQR, Q1-Q3)	1.1 (0.6-1.6)
Modified HAQ* score, median (IQR)	1.1 (0.9-1.6)

*HAQ for the RHUMADATA cohort and Modified HAQ for EUPA cohort and USRAT

Background/Purpose: In April 2022, the Canadian province of Quebec introduced a mandatory non-medical switch to biosimilars for persons on bio-originators to manage healthcare costs. Our objective is to describe real-world experience with biosimilars used for inflammatory arthritis in the context of this policy change.

Methods: We used data from three adult clinical registries in Quebec: the RHUMADATA prospective arthritis registry, the Early Undifferentiated Polyarthritis (EUPA) cohort, and the University of Sherbrooke Registry of Advanced Therapies (USRAT). We studied individuals who transitioned from the originator biologics to their equivalent biosimilars – infliximab, etanercept (ETA), adalimumab (ADA), and rituximab– from the time of the non-medical switching policy (April 2021) through May 2023. The study period began one year before the implementation of the non-medical switching policy to capture the transition phase leading up to and following the policy's introduction.Baseline characteristics were assessed at the time of biosimilar initiation, including age, sex, underlying condition (ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis), disease duration, body mass index, alcohol and tobacco use, and quality of life (Health Assessment Questionnaire for RHUMADATA, and the Modified HAQ for EUPA and USRAT). Prior medication history, including other biologics, corticosteroids, and non-biologic immunosuppressants, was also reviewed. Reasons for discontinuation were documented by treating physicians. Discontinuation was estimated using Kaplan-Meier methods.

Results: We studied 110 individuals with inflammatory arthritis, most switching to ADA (68%) or ETA (20%) biosimilars. Females were 61% of the cohort, and at biosimilar transition, the mean age was 56.9 years (standard deviation 15.8). Additional baseline characteristics are presented in Table 1. Individuals were followed for a median of 1.5 years (interquartile range 0.5 to 1.9 years). During this time, 16 individuals discontinued their treatment, for a discontinuation rate of 115.7 (95% confidence interval, CI 66.1-187.8) events per 1,000 person-years. As seen in Figure 1, the probability of discontinuation was 11.2% (95% CI: 4.4%-17.6%) by Year 1 and 18.2% % (95% CI: 9.3% to 26.2%) by Year 2. The most common reason for discontinuation was treatment failure in 7 individuals.

Conclusion: Among individuals with arthritis who underwent mandatory non-medical switching from bio-originators to biosimilars, about 80% remain on the biosimilar at 2 years. Thus, discontinuation rates appear consistent with those observed among experienced biologic users, suggesting relative stability despite the policy-driven switch.

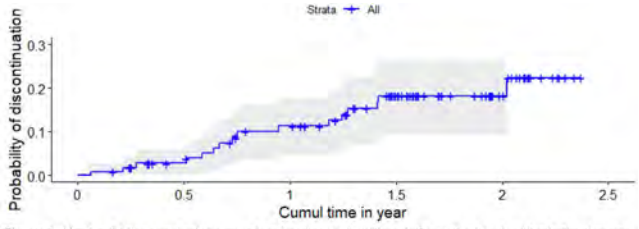


Figure 1. Kaplan-Meier survival curves showing the probability of discontinuing the biosimilar therapy over follow-up, with shaded areas representing 95% confidence intervals (95% CI).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Moura: None; **L. Lukusa**: None; **D. Choquette**: AbbVie, 5, 6, Amgen, 5, 6, Eli Lilly, 5, 6, Fresenius-Kabi, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Sandoz, 5, 6, Teva Pharmaceuticals, 5, 6, Viatris, 5, 6; **G. Boire**: Biocon, 5, Sanofi, 1; **N. Carrier**: None; **A. Neville**: None; **S. Bernatsky**: None.

Abstract Number: 0476

Impact of Comorbidity Burden on the Efficacy of, a Direct Interleukin 6 Inhibitor, Olokizumab: Real World Evidence

Maxim Korolev[1], Alexander Dubikov[2], Daria Bukhanova[3], Alina Egorova[3], Eugenyi Alekseev[4], **Sofia Kuzkina**[5] and Mikhail Samsonov[3], [1]Research Institute of Clinical and Experimental Lymphology – Branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russia, [2]Rheumatology clinic of Professor Dubikov A.I., Vladivostok, Russia, [3]R-Pharm JSC, Moscow, Russia, [4]"R-Pharm", JSC, Moscow, Russia, [5]R-Pharm, Moscow, Russia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Comorbidities may affect the efficacy of bDMARDs in rheumatoid arthritis (RA). Post-hoc analysis of the randomized clinical trial (RCT) data shows that the efficacy of the direct IL-6 inhibitor olokizumab (OKZ) does not depend on the comorbidity burden [1,2]. However, information about the impact of comorbidities on the OKZ effectiveness in routine clinical practice is lacking. The study purpose was to determine the impact of comorbidity burden on the OKZ efficacy in RA patients in the real-world data (RWD) study.

Methods: Biologic DMARDs (bDMARD)-naive patients with RA on methotrexate ± glucocorticoids (GC) inefficacy who received OKZ for at least 24 weeks were included in our retrospective RWD study.

To assess the impact of comorbid conditions on effectiveness, we used Rheumatic Disease Comorbidity Index (RDCI). Patients were stratified into two groups based on the baseline RDCI score: "RDCI-L" (RDCI ≤ 1) vs "RDCI-H" (RDCI ≥ 2). The following effectiveness variables were analyzed at Week 24 after treatment initiation: proportion of patients that achieved SDAI ≤ 3.3, CDAI ≤ 2.8 and ≤ 10, DAS28(ESR) ≤ 2.6 and ≤ 3.2. To address the imbalance in baseline parameters across comorbidity groups, an optimal 1:1 propensity score matching algorithm based on logistic regression model was employed. Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were estimated using logistic regression to present the study findings. A p value < 0.05 was considered statistically significant.

Results: In the general group of patients, 77.9% had comorbidities: cardiovascular diseases - 41.4%, osteoarthritis-24.3%, osteoporosis-16.4%, gastrointestinal diseases-11.5%, diabetes-7.4%, kidney damage-4.2%, lung damage-3.9%.

Overall, 222 patients treated with OKZ 64 mg q2w or q4w were included in the analysis (per 111 patients in RDCI-L and RDCI-H groups). The baseline characteristics were similar in both groups and are presented in the Table 1. The median values of baseline RA activity corresponded to high disease activity.

There was no significant difference in the effectiveness results between RDCI-L and RDCI-H groups (Table 2), similar proportions of patients achieved low disease activity and remission in both groups (p > 0.05). These findings align with the general trend observed in previous research of OKZ efficacy in relation to comorbidity burden in RCT.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of patients in RDCI-L ad RDCI-H Note: CDAI, Clinical Disease Activity Index; DAS28, The Disease Activity Score 28; GC, corticosteroids; Me, median; n(%), number (percentage) of patients; Q1;Q3, the first and the third quartiles; RDCI, Rheumatic Disease Comorbidity Index; SDAI, Simplified Disease Activity Index.

Characteristics	RDCI-L (N=111)	RDCI-H (N=111)
Female/Male, n (%)	82 (74)/29 (26)	80 (72)/31 (28)
Age, years, Me[Q1;Q3]	60[54;67]	61[54;67]
RA duration, month, Me[Q1;Q3]	84[41;144]	118[48;147]
GC use, n (%)	63(57)	62(56)
Baseline RA activity Me[Q1;Q2]		
DAS28-ESR	5.6[5.1;6.1]	5.6[5.0;6.0]
CDAI	38[29;45]	36[30.45]
SDAI	40[31;49]	39[32;48]

Table 2. The impact of comorbidities on efficacy in OKZ treated patients (week 24) Note: OR > 1 indicates that patients with high comorbidity have higher odds of achieving the outcome compared to those with low comorbidity. CI, confidence interval;

	RDCI-L (N=111), n (%)	RDCI-H (N=111), n (%)	OR (0.95% CI)	p
SDAI ≤ 3.3				
	13(12.0)	8(7.2)	0.59 (0.22 – 1.48)	0.300
CDAI ≤ 2.8				
	12 (11.0)	5(4.5)	0.39 (0.12 – 1.09)	0.086
CDAI ≤ 10				
	58(52.0)	46(41.0)	0.64 (0.37– 1.10)	0.110
DAS28 (ESR) ≤ 2.6				
	45(41)	34(31)	0.64 (0.36 - 1.11)	0.110
DAS28 (ESR) ≤3.2				
	73(66)	69(62)	0.81 (0.46 – 1.42)	0.500

Conclusion: There were no significant differences in effectiveness outcomes in OKZ-treated RA patients with high and low comorbidity burden over 24 observation weeks in the RWD study. Further research may clarify the impact of comorbidities on OKZ outcomes.

Disclosure: M. Korolev: AstraZeneca, 6, Biocad, 6, Johnson and Johnson, 6, Novartis, 6, R-Pharm, JSC, 6; **A. Dubikov**: None; **D. Bukhanova**: R-Pharm, JSC, 3; **A. Egorova**: R-Pharm, JSC, 3; **E. Alekseev**: R-Pharm, JSC, 3; **S. Kuzkina**: R-Pharm, JSC, 3; **M. Samsonov**: R-Pharm, JSC, 3.

Abstract Number: 0477

At the patient level, ultrasound evaluation during the follow up of rheumatoid arthritis does not modify radiographic evolution: a prospective, multicenter, randomized, pragmatic clinical trial (BCD study)

Alexandre GARMENDIA[1], Valerie Devauchelle[2], Grégoire CORMIER[3], LE GOFF Benoit[4], Aleth Perdriger[5], Saloua Mammou[6], Emannuel Hoppe[7], Emmanuelle Dernis[8], Jose Le Noach[9], Carine Salliot[10], florent garrigues[1], Raphael Auffret[1], Ichem Mohtarif[11], Mateusz Chodorowsky[11], Thierry MARHADOUR[12], Divi Cornec[13], Dewi Guellec[1], Emmanuelle Courtois Communier[1], Alain SARAUX[14] and sandrine jousse[12], [1]CHU de BREST, Brest, Bretagne, France, [2]UBO, Brest, France, [3]Centre Hospitalier département de Vendée, La Roche Sur Yon, France, [4]CHU Nantes, Nantes, France, [5]Rennes University, Rennes, France, [6]CHU TOURS, TOURS, France, [7]CHU ANGERS, Angers, France, [8]Rheumatology Department, Le Mans Central Hospital, Le Mans, France, LE MANS, France, [9]Centre Hospitalier de Lorient, Lorient, France, [10]CHR orleans, Orleans, France, [11]CHU de Brest, Brest, France, [12]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [13]Departement of Rhumatology, CHU Brest, Université de Brest, INSERM UMR1227: LBAI, Brest, France, Brest, France, [14]CHU Brest, Brest, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Previous studies, including TASER and ARTIC (1,2), failed to demonstrate a significant benefit of ultrasound (US) compared to clinical evaluation in achieving clinical remission or slowing structural progression in rheumatoid arthritis (RA). Despite these findings, the role of US in the follow-up of RA patients remains debated. This study aimed to determine whether radiographic progression at 1 year (primary end point) and 2 years, differs in RA patients followed by rheumatologists aiming for remission without synovitis (including the 28 articulations included in the SDAI and the 10 MTPs), using either Doppler-mode US, B-mode US, or clinical evaluation alone.

Methods: The BCD study (NCT02410304) was a prospective, multicenter, randomized, pragmatic clinical trial conducted across 10 hospitals in France from 2014 to 2018. RA patients, diagnosed with RA according to the 2010 ACR/EULAR criteria and on stable treatment, were randomized in a 1:1:1 ratio. Patients were followed every 3 months for 1 year with a remission target (no synovitis, no painful joints, patient visual analog scale ≤1/10, and normal C-reactive protein) assessed through:

1. **D-mode US**: Doppler evaluation of 38 joints (10 PIP, MCP, 2 wrists, 2 elbows, 2 shoulders, 2 knees, 10 MTP).
2. **B-mode US**: A combination of clinical evaluation for 26 joints and B-mode US for MTP and shoulders.
3. **C-mode**: Clinical evaluation only.

All patients underwent US and radiographic assessments (Sharp-van der Heijde scores: SvHD) at baseline, 12 months, and 24 months. Radiographic progression, the primary endpoint, was defined as an increase of >1 point in the SvHD score at 12 months. Between-group comparisons of radiographic evolution were conducted using a generalized linear model with binary distribution and log link, adjusted for center as a random effect.

Results: 545 patients were randomized, and 513 were analyzed at 12 months (169 C-mode, 171 B-mode, 173 D-mode). Baseline characteristics were similar across groups. Mean age was 58.12 (12.05 SD) years and mean RA duration was 11.79 (9.89 SD) years. 41.9% of patients were in remission according DAS-CRP. Radiographic progression (>1 point increase in Sharp score) at 12 months did not significantly differ between groups (Table 1). In contrast, B-mode US was associated with a higher proportion of global high radiographic progression compared to C-mode at 24 months.

Conclusion: Although US detect more synovitis than clinical evaluation, neither D-mode nor B-mode US guided therapy slowed radiographic progression during follow-up compared to clinical evaluation guided therapy alone.

Table 1: radiographic evolution at M12 according to the follow-up

	C-Mode N= 183	B-Mode N=179	D-Mode N= 183	RR (IC 95%) B versus C	p-value	RR (IC 95%) D versus C	p-value
Erosion and narrowing (>1pt) n (%)	40 (28.2%)	42 (30.2%)	49 (33.3%)	1.02 [0.71, 1.45]	0.9343	1.13 [0.8, 1.58]	0.4927
Erosion (>1pt) n (%)	33 (22.9%)	34 (24.3%)	38 (25.0%)	1.07 [0.7, 1.62]	0.7593	1.09 [0.73, 1.64]	0.6782
Narrowing (>1pt) n (%)	17 (11.6%)	29 (19.5%)	22 (14.8%)	1.58 [0.94, 2.66]	0.0816	1.14 [0.64, 2.01]	0.6613

REFERENCES:

1. Haavardsholm EA, Aga AB, Olsen IC, Lillegraven S, Hammer HB, Uhlig T, et al. Ultrasound in management of rheumatoid arthritis: ARCTIC randomised controlled strategy trial. BMJ. 16 août 2016;i4205.
2. Dale J, Stirling A, Zhang R, Purves D, Foley J, Sambrook M, et al. Targeting ultrasound remission in early rheumatoid arthritis: the results of the TaSER study, a randomised clinical trial. Ann Rheum Dis. juin 2016;75(6):1043-50.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. GARMENDIA: None; **V. Devauchelle**: None; **G. CORMIER**: None; **L. Benoit**: AbbVie/Abbott, 1, Amgen, 1, Bristol-Myers Squibb(BMS), 1, 5, Fresenius-Kabi, 1, Lilly, 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, 5, Roche, 1, 5, Sandoz, 5, Viatris, 1; **A. Perdriger**: None; **S. Mammou**: None; **E. Hoppe**: None; **E. Dernis**: None; **J. Le Noach**: None; **C. Salliot**: None; **f. garrigues**: None; **R. Auffret**: None; **I. Mohtarif**: None; **M. Chodorowsky**: None; **T. MARHADOUR**: None; **D. Cornec**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Pfizer, 2, Roche, 2; **D. Guellec**: None; **E. Courtois Communier**: None; **A. SARAUX**: Novartis, 6; **s. jousse**: None.

Abstract Number: 0478

Racial and Ethnic Disparities in DMARD Use and in Medicare Part B-Covered Options Among Medicare Beneficiaries with Late-Onset Rheumatoid Arthritis

ashkan ara[1], John FitzGerald[2] and Susan Ettner[2], [1]UCLA Health, Los Angeles, CA, [2]UCLA, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Biologic and targeted synthetic DMARDs can substantially improve the quality of life for Medicare beneficiaries with rheumatoid arthritis (RA). However, racial and ethnic disparities in their use, particularly those covered by Part B, have not been well studied in this population. Medicare defines any drug costing over $670 per patient per month as a "specialty" drug, which encompasses all biologic and targeted synthetic DMARDs. We examined racial and ethnic differences in 12-month use of any DMARD, specialty DMARDs, and the Part B-covered subset in a large cohort of Medicare enrollees with late-onset RA.

Methods: We used 20% Sample Medicare claims from 2016-2020 to establish an incident cohort of late-onset RA, defined as ≥2 outpatient ICD-10 RA codes 7-365 days apart following a 12-month washout. Eligible beneficiaries were ≥65 years old, continuously enrolled in Medicare Parts A/B/D, and had no other indication for DMARD use. Outcomes included receipt of (1) any DMARD, (2) specialty DMARDs, and (3) Part B-covered subset within 12 months of case identification. The main

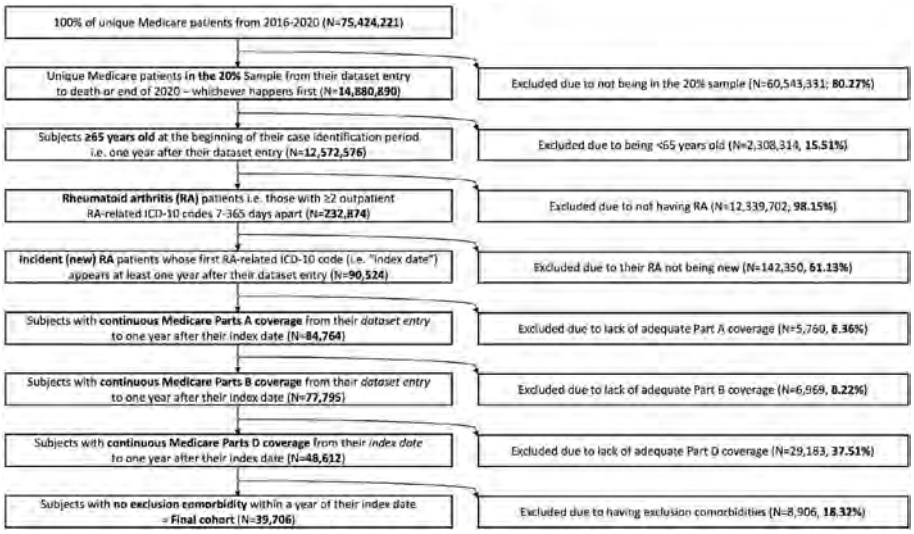


Figure: Flow diagram depicting the establishment of a cohort with incident late-onset RA among Medicare beneficiaries (2016-2020).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of the included patients, overall and by receipt of first DMARD (any), first specialty DMARD, and first Part B-covered specialty DMARD (i.e. office- or infusion-center–administered) within 12 months of case identification.

Characteristic	All Participants (N=39,706)	Received DMARD (N=14,190)	Received Specialty DMARD (N=1,906)	Received Part B-covered DMARD (N=1,363)
Race & Ethnicity: N (%)				
Non-Hispanic White	30,723 (77.4 %)	11,147 (78.6 %)	1,489 (78.1 %)	1,176 (86.3 %)
Black or African-American	3,688 (9.3 %)	1,241 (8.7 %)	171 (9.0 %)	84 (6.2 %)
Hispanic	3,201 (8.1 %)	1,057 (7.4 %)	145 (7.6 %)	61 (4.5 %)
Other	2,094 (5.3 %)	745 (5.3 %)	101 (5.3 %)	42 (3.1 %)
Sex: N (%)				
Male	10,847 (27.3 %)	3,946 (27.8 %)	586 (30.7 %)	378 (27.7 %)
Female	28,859 (72.7 %)	10,244 (72.2 %)	1,320 (69.3 %)	985 (72.3 %)
Low-income Subsidy (LIS): N (%)				
No	28,893 (72.8 %)	10,679 (75.3 %)	1,455 (76.3 %)	1,226 (89.9 %)
Yes	10,813 (27.2 %)	3,511 (24.7 %)	451 (23.7 %)	137 (10.1 %)
Age at Index Date: Mean (SD)	75.9 (7.2)	74.7 (6.7)	73.8 (6.5)	73.2 (5.6)

regressor was race and ethnicity (non-Hispanic White reference). Covariates included age, sex, and low-income subsidy status (LIS). We performed multivariable logistic regressions for each outcome, incorporating calendar-month and calendar-year fixed effects, and reporting adjusted ORs (aORs) with 95% CIs.

Results: Among 39,706 beneficiaries with incident late-onset RA (Figure), 14,190 (35.7%) received any DMARD, 1,906 (4.8%) a specialty DMARD, and 1,363 (3.4%) a Part B–covered specialty DMARD within 12 months (Table 1). The most common first DMARDs included:

- *Any DMARD*: methotrexate (6,154), hydroxychloroquine (5,229), and leflunomide (850);
- *Specialty*: abatacept (278; both formulations), certolizumab (274; both formulations), and infliximab (259);
- *Part B-covered subset*: certolizumab (270), infliximab (255), and abatacept (253).

In multivariable models (Table 2) Black patients (aOR: 0.92) had significantly lower odds of receiving any DMARD than non-Hispanic White patients. Race and ethnicity were not associated with differential receipt of specialty DMARDs. However, in the Part B-covered subset, Black (aOR 0.78), Hispanic (aOR 0.75), and Other (aOR 0.63) patients had significantly lower odds of receiving these agents compared to non-Hispanic White patients.

Also, LIS was associated with 14%, 15%, and 67% lower odds of any DMARD use, specialty DMARD use, and the Part B-covered subset, respectively. Moreover, each additional year of age was associated with 4%, 5%, and 6% lower odds of any DMARD use, specialty DMARD use, and Part B therapy use, respectively (with mild nonlinearity modeled via age^2). Furthermore, female sex was associated with 13% lower odds of specialty DMARD use.

Conclusion: Part B-covered DMARDs exhibited the most pronounced disparities: Black, Hispanic, and Other non-White patients were 22-37% less likely to receive these therapies. This gap is particularly concerning because, despite the inconvenience of office or infusion-center administration, Part B agents carry lower coinsurance than Part D's specialty tier, representing a key cost-saving opportunity that non-White beneficiaries may be missing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adjusted odds ratios (95% CI) from multivariable logistic regression models examining the association of race and ethnicity, sex, age, and low-income subsidy status (LIS: proxy for socioeconomic status) with (A) any DMARD use, (B) specialty DMARD use, and (C) Part B-covered specialty DMARD use within 12 months of case identification. Four model specifications are shown per outcome: Model 1 (race and ethnicity only), Model 2 (+ LIS), Model 3 (all covariates except LIS), and Model 4 (full model). Significant findings ($p < 0.05$) are indicated by an asterisk.

Outcome: Any DMARD Utilization

Parameter	Model 1 regressors: RTI only	Model 2 regressors: RTI plus LIS	Model 3 regressors: All except LIS	Model 4 regressors: All (full model)
Race & Ethnicity (RTI)				
Black (vs White)	0.891 (0.829–0.957)*	0.950 (0.882–1.024)	0.876 (0.815–0.942)*	0.922 (0.855–0.993)*
Hispanic (vs White)	0.866 (0.801–0.935)*	0.945 (0.871–1.024)	0.863 (0.798–0.933)*	0.924 (0.852–1.002)
Other (vs White)	0.970 (0.884–1.064)	1.033 (0.940–1.135)	0.928 (0.845–1.018)	0.975 (0.887–1.072)
Sex				
Female (vs Male)			0.998 (0.953–1.046)	1.008 (0.962–1.057)
Age (demeaned)			0.963 (0.960–0.966)*	0.963 (0.960–0.967)*
Age (demeaned) ^2			1.000 (1.000–1.000)	1.000 (1.000–1.000)
Low-income subsidy (LIS)		0.831 (0.790–0.874)*		0.863 (0.820–0.908)*

Outcome: Specialty DMARD Utilization

Parameter	Model 1 regressors: RTI only	Model 2 regressors: RTI plus LIS	Model 3 regressors: All except LIS	Model 4 regressors: All (full model)
Race & Ethnicity (RTI)				
Black (vs White)	0.955 (0.812–1.123)	1.026 (0.868–1.212)	0.941 (0.800–1.107)	0.993 (0.840–1.174)
Hispanic (vs White)	0.932 (0.782–1.109)	1.027 (0.856–1.232)	0.937 (0.787–1.116)	1.008 (0.839–1.210)
Other (vs White)	0.995 (0.809–1.223)	1.067 (0.865–1.316)	0.935 (0.760–1.151)	0.982 (0.796–1.211)
Sex				
Female (vs Male)			0.865 (0.782–0.956)*	0.874 (0.790–0.966)*
Age (demeaned)			0.951 (0.944–0.958)*	0.952 (0.945–0.959)*
Age (demeaned) ^2			1.001 (1.000–1.002)*	1.001 (1.000–1.002)*
Low-income subsidy (LIS)		0.811 (0.722–0.911)*		0.853 (0.759–0.959)*

Outcome: Part B-covered DMARD Utilization

Parameter	Model 1 regressors: RTI only	Model 2 regressors: RTI plus LIS	Model 3 regressors: All except LIS	Model 4 regressors: All (full model)
Race & Ethnicity (RTI)				
Black (vs White)	0.586 (0.468–0.733)*	0.813 (0.647–1.021)	0.571 (0.456–0.715)*	0.775 (0.616–0.974)*
Hispanic (vs White)	0.488 (0.376–0.633)*	0.779 (0.596–1.017)	0.485 (0.374–0.629)*	0.751 (0.575–0.982)*
Other (vs White)	0.514 (0.377–0.702)*	0.705 (0.515–0.965)*	0.482 (0.353–0.659)*	0.629 (0.459–0.862)*
Sex				
Female (vs Male)			1.049 (0.929–1.184)	1.106 (0.979–1.249)
Age (demeaned)			0.937 (0.928–0.946)*	0.938 (0.929–0.948)*
Age (demeaned) ^2			0.997 (0.996–0.999)*	0.998 (0.996–0.999)*
Low-income subsidy (LIS)		0.315 (0.262–0.379)*		0.332 (0.276–0.400)*

Disclosure: a. ara: None; **J. FitzGerald**: None; **S. Ettner**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0479

Risk of Arrhythmias Following IL-6 Inhibitor Use; A Pharmacosurvellience Study of FDA Adverse Event Reporting System (FAERS)

Asim Khanfar[1], Omar Hamdan[2], Shiamak Cooper[3], Sanjana Thimmannagari[1] and Anthony Ocon[4], [1]Rochester General Hospital, Rochester, NY, [2]University of Jordan, Az-Zarqa, Jordan, [3]Rochester General Hospital, Irondequoit, NY, [4]Rochester Regional Health, Fairport, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin-6 (IL-6) inhibitors, including tocilizumab and sarilumab, are immunomodulatory agents commonly used in the treatment of rheumatoid arthritis and COVID-19. Prior studies have implicated IL-6 signaling in the pathogenesis of various cardiovascular disorders, including atrial fibrillation and other arrhythmias, raising concerns about potential pro-arrhythmic effects of IL-6 inhibition. To further characterize this risk, we conducted a pharmacovigilance analysis using the FDA Adverse Event Reporting System (FAERS) to evaluate the incidence and nature of arrhythmias associated with IL-6 inhibitor use.

Methods: The FAERS database was searched for cardiac arrhythmias (Tachycardia, bradycardia, atrial fibrillation, QRS complex abnormalities, QT interval abnormalities, bundle branch block (BBB), atrioventricular blocks (AV blocks) and supraventricular tachycardia (SVT)) associated with the use of IL-6 inhibitors (tocilizumab, sarilumab, and siltuximab). Data were reported as frequencies and as reporting odds ratios (ROR) with a 95% confidence interval (95% CI).

Results: We analyzed 30,179,725 adverse event reports from the FAERS database. A total of 107,540 reports were associated with the use of the three anti-IL-6 drugs; 78.3% of them were females, with cardiac arrhythmias being reported in 1% of them. Most of the cases were associated with tocilizumab (85.5%), followed by sarilumab (13.8%). Tachycardia was the most common arrhythmia among tocilizumab users, which was reported in 668 cases, followed by bradycardia, which was reported in 134 cases. Among all arrhythmias tested, only tachycardia and BBB were significantly higher among tocilizumab users compared to all other drugs (ROR=1.959; 95% CI: 1.815 – 2.114) and (ROR=3.599; 95% CI: 2.364 – 5.479), respectively. In addition, siltuximab users had significantly higher odds of atrial fibrillation compared to all other drugs users (ROR=1.3.114; 95% CI: 1.163 – 8.339) (Table 1). When the three anti-IL-6 medications were put into a head-to-head comparison, tocilizumab had the highest ROR of causing tachycardia, bradycardia, SVT, and AV block. However, siltuximab users had the highest odds of causing QT prolongation (ROR=18.73; 95% CI: 6.770 – 51.80) (Table 2).

Conclusion: IL-6 inhibitors, particularly tocilizumab and siltuximab, are associated with increased reporting of specific arrhythmias. These findings highlight the need for arrhythmia monitoring in susceptible patients receiving IL-6 inhibitors. Further studies are needed to clarify causality and the mechanisms underlying these associations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. ROR of anti-IL 6 drugs

Adverse reaction	Frequency	Odds Ratio	95% Confidence Interval
Tocilizumab			
Tachycardia	668	1.959	1.815 – 2.114
Bradycardia	134	0.6697	0.5652 – 0.7934
Atrial Fibrillation	36	0.1206	0.08701 – 0.1673
QT prolongation	0	-	-
QRS abnormalities	2	1.603	0.3995 – 6.431
Supraventricular Tachycardia	33	0.9445	0.6711 – 1.329
Bundle Branch Block	22	3.599	2.364 – 5.479
AV Block	16	0.5561	0.3405 – 0.9081
Sarilumab			
Tachycardia	89	1.406	1.141 – 1.731
Bradycardia	9	0.2433	0.1266 – 0.4677
Atrial Fibrillation	23	0.4185	0.2780 – 0.6300
QT prolongation	18	0.8896	0.5603 – 1.412
QRS abnormalities	0	-	-
Supraventricular Tachycardia	2	0.3096	0.07742 – 1.238
Bundle Branch Block	0	-	-
AV Block	6	1.130	0.5076 – 2.517
Siltuximab			
Tachycardia	3	2.013	0.6465 – 6.269
Bradycardia	1	1.149	0.1615 – 8.178
Atrial Fibrillation	4	3.114	1.163 – 8.339
QT prolongation	0	-	-
QRS abnormalities	0	-	-
Supraventricular Tachycardia	0	-	-
Bundle Branch Block	0	-	-
AV Block	0	-	-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Head to head comparison of anti-IL 6 drugs

Adverse reaction	Odds Ratio	95% Confidence Interval
Tocilizumab		
Tachycardia	8.633	6.941 – 10.74
Bradycardia	15.93	8.378 – 30.29
Atrial Fibrillation	1.585	0.9620 – 2.610
QT prolongation	-	-
QRS abnormalities	-	-
Supraventricular Tachycardia	19.61	4.706 – 81.74
Bundle Branch Block	-	-
AV Block	3.170	1.240 – 8.101
Sarilumab		
Tachycardia	0.8539	0.6841 – 1.066
Bradycardia	0.07722	0.04001 – 0.1490
Atrial Fibrillation	1.227	0.7852 – 1.917
QT prolongation	2.582	1.494 – 4.461
QRS abnormalities	-	-
Supraventricular Tachycardia	-	-
Bundle Branch Block	-	-
AV Block	2.419	0.9463 – 6.182
Siltuximab		
Tachycardia	2.419	0.9463 – 6.182
Bradycardia	1.085	0.3476 – 3.386
Atrial Fibrillation	1.916	0.2673 – 13.73
QT prolongation	18.73	6.770 – 51.80
QRS abnormalities	-	-
Supraventricular Tachycardia	-	-
Bundle Branch Block	-	-
AV Block	-	-

Disclosure: A. Khanfar: None; **O. Hamdan**: None; **S. Cooper**: None; **S. Thimmannagari**: None; **A. Ocon**: Amgen, 2, 6.

Abstract Number: 0480

Efficacy and safety of tacrolimus and its serum concentration in patients with rheumatoid arthritis with inadequate response to methotrexate

Chan-Bum Choi, Hanyang University Hosptial for Rheumatic Diseases, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Addition of a biologic disease-modifying antirheumatic drug (bDMARD) or targeted synthetic DMARD (tsDMARD) is recommended in patients with rheumatoid arthritis (RA) with inadequate response to methotrexate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Current reimbursement, but the Korean National Health Insurance Service requires moderate to high disease activity with at least 6 months' treatment with at least two conventional synthetic DMARDs (csDMARDs). Triple therapy with the addition of hydroxychloroquine and sulfasalazine is often used. Methotrexate plus leflunomide or tacrolimus is also used. Drug levels of tacrolimus in patients with RA and their correlation with efficacy and safety were assessed

Methods: A retrospective medical record review of patients with RA who had fulfilled the 2010 ACR/EULAR classification criteria for RA and had initiated treatment with tacrolimus was performed. Serum tacrolimus concentration was measured after six months of treatment with tacrolimus. Disease Activity Score 28 (DAS28) and renal function were assessed at initiation of tacrolimus and after six months. ACR20 responses were assessed at 6 months.

Results: A total of 189 patients were assessed. The mean age was 61.4 ± 11.7 years, and 88.9% were female. Mean DAS28 at baseline was 3.48 ± 1.77 with a mean serum creatinine level of 0.7 ± 0.2 mg/dl and a mean Glomerular Filtration Rate (GFR) of 98.9 ± 15.0. Mean dose of tacrolimus was 1.3 ± 0.5 mg. At six months, the mean DAS28 was 2.98 ± 1.33 with a mean serum creatinine level of 0.7 ± 0.6 mg/dl and a mean GFR of 99.4 ± 14.8. Mean tacrolimus concentration at six months was 3.5 ± 2.6 ng/ml, with the highest being 14.8 ng/dl. A total of 117 (63.9%) patients showed tacrolimus levels below 3 ng/dl, 51 (27.9%) patients showed 3 -7 ng/d, and 21 (11.1%) showed over 7 ng/dl. ACR20 response rates at six months were 44.9% for patients with tacrolimus levels less than 3 ng/dl and 34.7% for those with greater than 3 ng/dl without significant differences. There was no significant increase in serum creatinine levels and GFR at six months, and the differences were not significant according to the serum tacrolimus drug concentration levels.

Conclusion: Tacrolimus at low doses showed clinical efficacy in patients with RA with inadequate response to methotrexate, and there was no significant increase in serum creatinine. All patients showed serum tacrolimus levels below the recommended 15 ng/dl, and there were no significant differences in efficacy and renal function by serum tacrolimus concentration.

Disclosure: C. Choi: None.

Abstract Number: 0481

Intracellular Methotrexate Polyglutamate Profiles Do Not Correlate with Early Clinical Response in Treatment-Naïve Rheumatoid Arthritis: A Prospective Study

Chandrashekara MN[1], AASTHA KHULLAR[2], Bidyalaxmi Leishangthem[3], Shankar Naidu[4], Varun Dhir[5] and Sanjay Jain[4], [1]PGIMER, Chandigarh, Chandigarh, India, [2]Postgraduate Institute of Medical Education and Research, CHANDIGARH, Chandigarh, India, [3]PGIMER, Chandigarh, India, Chandigarh, Chandigarh, India, [4]Post graduate Institute of Medical Education and Research, Chandigarh, Chandigarh, Chandigarh, India, [5]PGIMER, CHD, INDIA, CHANDIGARH, Chandigarh, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate (MTX) polyglutamates (MTX-PGs), the intracellular active forms of MTX, are hypothesized to reflect cumulative exposure and potentially predict therapeutic efficacy in rheumatoid arthritis (RA). Prior studies have shown contrasting results. This study aimed to assess association of total MTX-PG levels, PG1–PG5 with EULAR response at 16 weeks in treatment-naïve RA patients undergoing standardized MTX escalation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Univariate analysis to identify predictors of response from baseline variables and MTX-PG levels.

Variable	Responders (Mean ± SD)	Non-responders (Mean ± SD)	p-value
BMI, Kg/m	23.97 ± 5.02	27.14 ± 8.05	0.108
Duration of RA (months)	15.91 ± 12.56	24.00 ± 11.31	0.062
Age (years)	42.04 ± 11.73	41.90 ± 10.65	0.973
Baseline DAS28-CRP	6.00 ± 1.05	5.47 ± 1.67	0.189
CRP (mg/L)	26.64 ± 28.60	36.75 ± 31.77	0.316
Total MTX-PG (nM)	112.05 ± 54.08	112.26 ± 73.08	0.992
Short-chain MTX-PG (MTX PG1-2) (nM)	36.48 ± 21.97	41.38 ± 31.40	0.547
Long chain MTX PG (MTX PG3-5) (nM)	75.56 ± 43	69.86 ± 58.74	0.73

Methods: This was a prospective observational cohort study including 65 treatment-naïve RA patients initiated on oral or subcutaneous MTX using a standardized protocol. At 16 weeks, MTX-PG levels (total, PG1–PG5, short-chain-MTX PG1-2, long-chain-MTX PG3-5) were measured using HPLC. The primary outcome was EULAR response at week 16 (Good, Moderate, None). Descriptive statistics, independent t-tests, ANOVA, Tukey post hoc analysis, and logistic and linear regression were used to explore associations between MTX-PG levels and response, adjusting for age, sex, BMI, RA duration, route of administration, baseline CRP, and DAS28.

Results: A total of 65 seropositive treatment-naïve rheumatoid arthritis (RA) patients were included. The median age was 44.5 years (interquartile range [IQR]: 38–53), and 76.9% were female. 86.2% were RF-positive and 95.4% were anti-CCP–positive. The median disease duration at baseline was 17.2 months (IQR: 12–24), and the median baseline DAS28-CRP was 5.9 (IQR: 5.2–6.6)

Among 65 patients, 21 (32.3%) achieved Good response, 34 (52.3%) Moderate, and 10 (15.4%) No response. **No significant difference** was found in total MTX-PG levels between responders (good and moderate) and non-responders (112.05 ± 54.1 vs 112.26 ± 73.1 nM; p = 0.992). Also, short-chain and long-chain MTX-PG levels did not differ significantly. Univariate analysis showed a trend toward higher BMI and longer RA duration in non-responders.

Table 2. Multivariable Logistic Regression for EULAR Response at 16 Weeks

Variable	Adjusted OR (95% CI)	p-value
Total MTX-PG (nM)	1.00 (0.99–1.01)	0.831
Short-chain MTX-PG (PG1–2)	1.01 (0.97–1.06)	0.627
Long-chain MTX-PG (PG3–5)	1.01 (0.99–1.03)	0.211
BMI (kg/m²)	1.03 (0.91–1.16)	0.607
RA Duration (months)	1.00 (0.94–1.07)	0.909
MTX Route (SC vs Oral)	0.52 (0.10–2.61)	0.430
Cumulative MTX Dose (mg)	1.01 (0.99–1.03)	0.413
Baseline CRP (mg/L)	1.00 (0.97–1.03)	0.841
Baseline DAS28-CRP	1.24 (0.67–2.31)	0.487

Note: OR = Odds Ratio, CI = Confidence Interval, SC = Subcutaneous,

MTX = Methotrexate. Multivariable logistic regression model adjusted for listed variables.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

However, ANOVA revealed significant higher PG3 levels with moderate responders showing higher PG3 than good responders (p = 0.025, Tukey). Multivariable logistic regression did not identify any independent predictors of EULAR response. In linear regression, age was the only significant predictor of total MTX-PG levels (p = 0.033).

Conclusion: In this real-world prospective study, neither total MTX-PG levels nor specific PG subtypes independently predicted EULAR response at 16 weeks. Further studies incorporating longitudinal sampling, genetic polymorphisms, and safety outcomes are warranted to clarify the pharmacodynamic utility of MTX-PG monitoring in RA.

Disclosure: C. MN: None; **A. KHULLAR**: None; **B. Leishangthem**: None; **S. Naidu**: None; **V. Dhir**: None; **S. Jain**: None.

Abstract Number: 0482

R-2487, a Synthetic Biology-Based Oral Immunotherapy, Promotes Treg-Mediated Immune Rebalancing and Reduces Disease Activity in Rheumatoid Arthritis Patients

Christian Furlan Freguia[1], Janet Stephens[1], Sathya Janardhanan[1], Chuck Bourne[1], Kaitlyn Skeie[1], Hudson Lowe[1], David Pascual[2] and Gary Fanger[1], [1]Rise Therapeutics, Rockville, MD, [2]University of Wyoming, Laramie, WY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: R-2487 is a novel, orally delivered, synthetic biology-based immunotherapy that utilizes *Lactococcus lactis* as a carrier vehicle to deliver Colonization Factor Antigen I (CFA/I) to harness immune control via intestinal immune architecture. CFA/I is a recently identified bacterial adhesin, which engages dendritic cells (DCs) and promote systemic regulatory T cell (Treg) expansion. Designed to correct the dysfunctional DC–Treg axis underlying autoimmunity, R-2487 has demonstrated robust immunomodulatory activity and disease protection in the preclinical model of collagen-induced arthritis. These studies showed that oral administration of R-2487 expanded Tregs, reduced inflammatory cytokines, and improved disease outcomes via bystander tolerance in an antigen-independent manner. R-2487 was evaluated in a first-in-human Phase I clinical trial in patients with active Rheumatoid Arthritis (RA). Here, we report preliminary safety, immunological activity, and clinical efficacy data from that clinical study.

Methods: This open-label study enrolled adult patients with RA across three dosing cohorts. Clinical endpoints included DAS28-CRP, CDAI, and RAPID3 scores. Immunophenotyping assessed Treg expansion via flow cytometry. Safety was monitored through adverse event reporting and laboratory values.

Results: R-2487 was well tolerated across all cohorts with no serious adverse events or clinically meaningful laboratory abnormalities. The majority of subjects demonstrated peripheral Treg expansion, confirming the expected mechanism of action. Clinically, patients showed improvement in disease activity as early as 2 weeks post-treatment. Eleven out of 12 subjects reached low disease activity or remission per DAS28-CRP. Among Cohort 2 and 3, all the subjects exhibited robust reduction in CDAI scores (≥6 points) as well as an improvement in the RAPID3 score (>3.6 points). Upregulation of Treg populations correlated with clinical improvement and supports the hypothesized bystander tolerance mechanism.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Oral administration of R-2487 was safe, well tolerated, and induced meaningful improvements in RA disease activity. The observed peripheral Treg expansion suggests that R-2487 rebalances immune homeostasis through a tolerogenic DC–Treg pathway, illustrating the novel mechanism of action of R-2487. These findings validate the utility of a synthetic biology approach to immune modulation in autoimmune disease, highlight the potential of leveraging microbiome-associated immune control mechanisms, and support continued development of R-2487 in RA.

Disclosure: C. Furlan Freguia: Rise Therapeutics, LLC, 3; **J. Stephens**: Rise Therapeutics, LLC, 3; **S. Janardhanan**: Rise Therapeutics, LLC, 3; **C. Bourne**: Rise Therapeutics, LLC, 3; **K. Skeie**: Rise Therapeutics, LLC, 3; **H. Lowe**: Rise Therapeutics, LLC, 3; **D. Pascual**: None; **G. Fanger**: Rise Therapeutics, LLC, 3.

Abstract Number: 0483

Safety of JAK inhibitors (JAKi) in chronic inflammatory arthritis (CIA): an observational study

Clara De Miguel[1], Héctor Vega[2], Marta Sánchez[2], Esther Toledano[3], Pedro Pablo Bermejo[4], Leonor Laredo[5], José Alberto Peña[6], María Teresa Benítez[7], DALIFER FREITES[8], LETICIA LEON[9] and lydia Abasolo Alcazar[10], [1]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Spain, [2]Complutense University of Madrid, Madrid, Spain, [3]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Spain, [4]Clinical Pharmacology Service, San Carlos Clinical Hospital, MADRID, Madrid, Spain, [5]Hospital Clinico San Carlos, MADRID, Madrid, Spain, [6]Pharmacy Service San Carlos Clinical Hospital, MADRID, Madrid, Spain, [7]San Carlos Clinical Hospital, MADRID, Madrid, Spain, [8]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [9]Fundación Investigación Biomédica Hospital Clínico San Carlos, IdISSC; Universidad Camilo Jose Cela, MADRID, Madrid, Spain, [10]IdISSC. HCSC, Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA), psoriatic arthritis (PsA), and spondyloarthritis (SpA) are chronic inflammatory arthritis (CIAs). Janus kinase inhibitors (JAKis) have emerged as a promising therapeutic option for managing these conditions. However, their safety profile remains under ongoing investigation due to adverse events (AEs) reported in clinical trials and real-world data. This study aimed to evaluate the safety of JAKis in patients with CIA in a real-life setting.

Methods: A retrospective observational study was conducted on patients diagnosed with RA, PsA, or SpA who received treatment with JAKis—baricitinib (BAR), tofacitinib (TOF), upadacitinib (UPA), or filgotinib (FIL)—between 2017 and 2024. The primary outcome was the incidence and causes of treatment discontinuation due to AEs. Clinical, sociodemographic, and treatment-related variables were analyzed. Incidence rates (IR) were calculated per 100 patient-years using survival analysis techniques, along with 95% confidence intervals (CI).

Results: A total of 181 patients were included (83.4% female; mean age: 56.2 ± 12.7 years). The most common comorbidities were dyslipidemia (43%), hypertension, and thyroid disorders; 8.3% had cardiovascular disease. A total of 227 JAKi treatment courses were recorded: BAR (41.8%), TOF (15.8%), UPA (37.5%), and FIL (4.8%). Treatment was discontinued due to AEs in 49 courses among 42 patients (23%). Respiratory infections were the leading cause (36.7%), followed by general malaise (28.5%). Ten AEs were classified as serious (e.g., diverticulitis, pneumonia requiring hospitalization, gastric cancer, and pulmonary embolism), including three deaths (two due to COVID-19 pneumonia and one due to gastric cancer). The overall IR for AE-related discontinuation was 14.74 per 100 patient-years (95% CI: 11.14–19.51), with 50% of cases occurring within the first 1.65 years of therapy. Discontinuation rates were higher among women and patients with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cardiovascular disease. Compared to TOF (IR: 21.8; 95% CI: 11.7–40.5), BAR and UPA/FIL showed lower discontinuation rates (IR for UPA/FIL: 13.6; 95% CI: 8.0–21.3; IR for BAR: 13.03; 95% CI: 9.3–21.1).Multivariate analysis identified cardiovascular disease as a significant predictor of AE-related discontinuation (HR: 4.07; 95% CI: 2.17–7.63; p< 0.001). No significant differences were found based on sex, age, or specific JAKi agent.

Conclusion: JAK inhibitors showed an overall acceptable safety profile in patients with chronic inflammatory arthritis. Cardiovascular comorbidity was the most relevant risk factor associated with AE-related discontinuation, independent of JAKi type or patient demographic characteristics.

Disclosure: C. De Miguel: None; **H. Vega**: None; **M. Sánchez**: None; **E. Toledano**: None; **P. Bermejo**: None; **L. Laredo**: None; **J. Peña**: None; **M. Benítez**: None; **D. FREITES**: None; **L. LEON**: None; **I. Abasolo Alcazar**: None.

Abstract Number: 0484

Comparable Efficacy of FK-Tocilizumab and Reference Tocilizumab in Rheumatoid Arthritis Patients With and Without Prior Biologic Exposure

Ernest Choy[1], Marco Gattorno[2], Kamila Klama[3], Andras Illes[4], Peter Baker[5], Maria Romanova Michailidi[6] and Anna Zubrzycka-Sienkiewicz[7], [1]Division of Infection and Immunity, CREATE Centre, Cardiff University, Cardiff, United Kingdom, [2]IRCCS G. Gaslini, Genova, Genoa, Italy, [3]Solumed Clinical Research Center, Poznan, Poland, [4]Fresenius Kabi SwissBioSim, Eysin, Switzerland, [5]Fresenius Kabi Biopharma, Eysins, Switzerland, [6]University of Geneva, Eysins, Switzerland, [7]Reumatika - Centrum Reumatologii, Warszawa, Poland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Biosimilars offer comparable efficacy and safety to their originators, thereby improving patient access to affordable treatments. FK-Tocilizumab (FK-toci) is the first tocilizumab biosimilar approved by both FDA and EMA for the treatment of autoimmune diseases including moderate-to-severe Rheumatoid Arthritis (RA). Therapeutic equivalence of FK-toci to reference tocilizumab was shown in subjects with moderate to severe RA in APTURA-1, a randomized, double blind efficacy study. Since its launch in 2024, FK-toci has accumulated ~50,000 patient-treatment-years of exposure with no new safety information affecting its benefit-risk balance. This analysis assessed the efficacy of FK-toci in patient subgroups with and without prior biologic use to support a broader patient access, including for patients with more refractory disease histories.

Methods: Subjects (M/F) over 18 years with moderate to severe RA were randomized to subcutaneous (SC) injections of 162 mg FK-toci or reference tocilizumab (originator) for 24 weeks (W). Randomization was stratified by previous exposure to biological treatment for RA (yes/no). A cohort of patients were switched from the originator to FK-toci at W24. The primary objective was to demonstrate therapeutic equivalence, with 90% and 95% CIs for the difference in DAS28-ESR LS mean change from baseline at W24 falling within predefined equivalence intervals ([-0.6, 0.5] and [-0.6, 0.6], respectively). ACR20 response at W24 was an important secondary endpoint. Both endpoints were analyzed in the subgroups with and without previous exposure to biologic treatment for RA.

Results: 604 patients were randomized, 302 on FK-toci and 302 on originator; 54 (28 and 26, respectively) were previously exposed to biologic treatment for RA. Gender, race, ethnicity, age and disease characteristics were all well balanced at

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

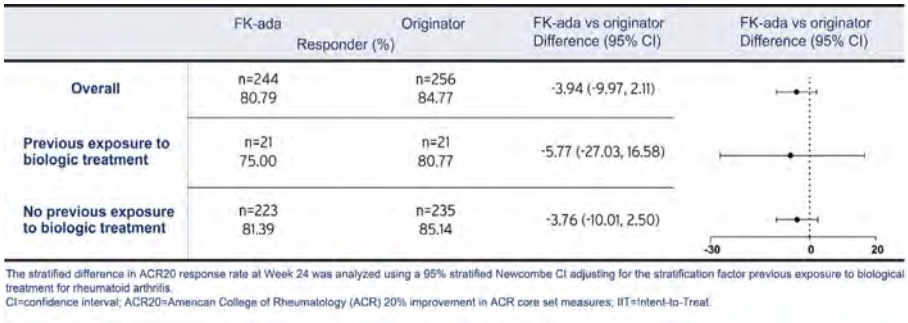


Figure 1 - ACR20 Response at Week 24 by Previous Exposure to Biologic Treatment for Rheumatoid Arthritis (ITT Analysis Set)

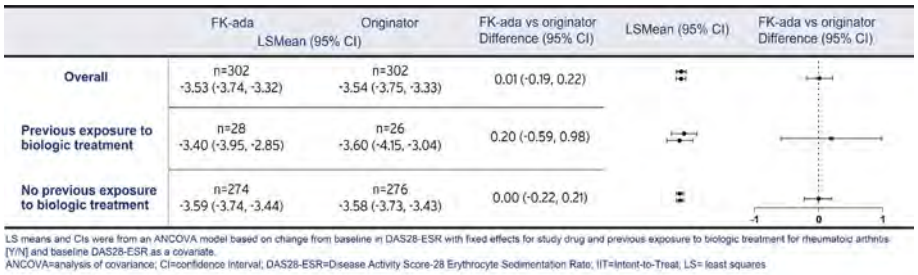


Figure 2 - DAS28-ESR Change from Baseline at Week 24 by Previous Exposure to Biologic Treatment for Rheumatoid Arthritis (ITT Analysis Set)

baseline. In total, 77.8% of patients with previous biologic exposure reached ACR20 at W24, versus 83.3% for subjects without previous biologic exposure, with similar ACR20 response rates in the two treatment groups (Figure 1). Similar reduction of DAS28-ESR at W24 were observed in both subgroups and in the two treatment groups (Figure 2).

Conclusion: Subgroup analyses by prior biologic exposure support the therapeutic equivalence of FK-tocilizumab and the originator, with no clinically meaningful differences in efficacy. These findings reinforce the reliability of FK-tocilizumab across a range of patient profiles, including those with previous biologic treatment, and underscore its potential to expand access to effective RA therapy.

Disclosure: E. Choy: AbbVie, 2, 6, Alfasigma, 6, Bio-Cancer, 2, 5, Biocon, 2, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 6, Fresenius Kabi, 2, 6, Gedeon Richter, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 6, Viatris, 2, 6; **M. Gattorno**: Fresenius Kabi SwissBioSim GmbH, 6, Novartis, 1, 2, 5, 6, SOBI, 2, 6; **K. Klama**: None; **A. Illes**: Fresenius Kabi SwissBioSim GmbH, 3; **P. Baker**: Fresenius Kabi SwissBioSim GmbH, 3; **M. Romanova Michailidi**: Fresenius Kabi SwissBioSim GmbH, 3; **A. Zubrzycka-Sienkiewicz**: None.

Abstract Number: 0485

Multicenter study on the use of Upadacitinib: Results in RA patients previously treated with Baricitinib

Guillermo Gonzalez Mozo de Rosales[1], Luis Maria Lopez-Dominguez[2], Nerea Alcorta-Lorenzo[3], oihane ibarguengoitia Barrena[4], David Montero[5], Ana Ruibal Escribano[6], estibaliz barastay Alberdi[7], Jesus Alejandro Valero Jaimes[8], Libe Ibarrola[9], Paula Garcia Escudero[10], Marta Lopez I Gomez[11], Eva Galindez Aguirregoicoa[12] and Maria Luz Garcia Vivar[13], [1]Basurto University Hospital, Bilbao, Spain, [2]Rheumatology Department, Donostia University Hospital., San Sebastián, Pais Vasco, Spain, [3]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [4]Galdakao-Usansolo University Hospital, GALDAKAO, Spain, [5]Galdakao-Usansolo University Hospital, Bilbao, Spain, [6]Urduliz Hospital, Urduliz, Pais Vasco, Spain, [7]Urduliz Hospital, Urduliz, Spain, [8]Hospital Bidasoa, Irun, Spain, [9]Galdakao-Usansolo University Hospital, Galdakao, [10]H.U.Araba, Vitoria, [11]Araba University Hospital, Vitoria, Pais Vasco, Spain, [12]Basurto University Hospital, Bilbao, Pais Vasco, Spain, [13]Basurto Hospital, Bilbao, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumathoid Arthritis (RA) is a chronic inflammatory disease that affects the musculoskeletal system. Early and effective treatment is important to improve the quality of life of patients and prevent irreversible damage. Upadacitinib (UPA) is a Janus Kinase inhibitor (JAKi) selective for JAK1, approved for RA in 2019. In the Basque Country, since May 2022, UPA has been the prioritized after Adalimumab biosimilar failure in RA patients.

The aim of this study was to evaluate the efficacy of UPA in RA patients treated with JAKi previously and to describe the characteristics of the patients and clinical response.

Methods: 7 hospitals in our region (1.5M inhabitants) participated in a multicenter, observational and ambispective study that included patients with UPA prescription from June 2021 to May 2024, with follow-up until Dec 2024.

In our study, 248 patients were divided into two groups based on who received a previous JAKi treatment or not. We used SDAI to measure the disease activity at six visits.

Results: Of the 248 RA patients included, 84.1% were women, the mean age was 55.9 years (SD 12.30). The rest of the baseline characteristics are reflected in Table 1. The first group contained 91 patients who received JAKi previously (JAKi group), 94.5% Baricitinib suspended for lack of efficacy. The other group containing 157 patients did not receive JAKi before the treatment (No JAKi group). When both groups were compared, the JAKi group showed a higher refractory rate (55% needed two or more biologicals compared to 17%) and a longer disease duration (140 months vs 107 months). At the beginning of the treatment with UPA, 91.1% (226) of the patients had a high/moderate activity (SDAI) with no difference between both groups (91.2% vs 90.4%). As shown in Figure 1, the No JAKi group achieved a higher percentage of patients with a low activity and remission. However, these differences did not reach statistical significance. Both groups showed similar trends regarding treatment continuation and reasons for discontinuation with inefficiency as the primary cause in the later visits. Most adverse effects appeared in the first 3 months. Although JAKi showed a lower suspension rate at 3 months, there were no statistically significant differences. Median UPA persistence in RA was 22.71 months (SE 1.67148 and 95%

Table 1. Patients' baseline characteristics.

Baseline Characteristics	JAKI	No JAKI	P value
Patients	91	157	
Disease duration (Months) (Mean;SD)	107.89 (91.52)	139.50 (101.01)	0,013[a]
Gender (Female %)	87.8	82.1	0,279[b]
BMI (Mean;SD)	27.00 (4.66)	27.67 (5.24)	0,466[a]
Never Smoked (%)	54.0	56.2	0,269[b]
DM (%)	18.8	22.0	0,792[b]
HTA (%)	50.0	51.4	1,000[b]
Regicor (Mean;SD)	3.79 (3.07)	3.38 (2.31)	0,295[a]
Seropositive for RF (%)	76.7	73.7	0,650[b]
Seropositive for ACPA (%)	72.2	76.3	0,543[b]
EPID (Number of patients)	4	6	1,000[b]
Herpes Zoster Vaccination (%)	82.6	89.0	0,169[b]
Corticosteroids (%)	54.4	49.0	0,832[b]
csDMARDS (%)	45.6	58.3	0,063[b]

(a:T Student test; b:Fisher test)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

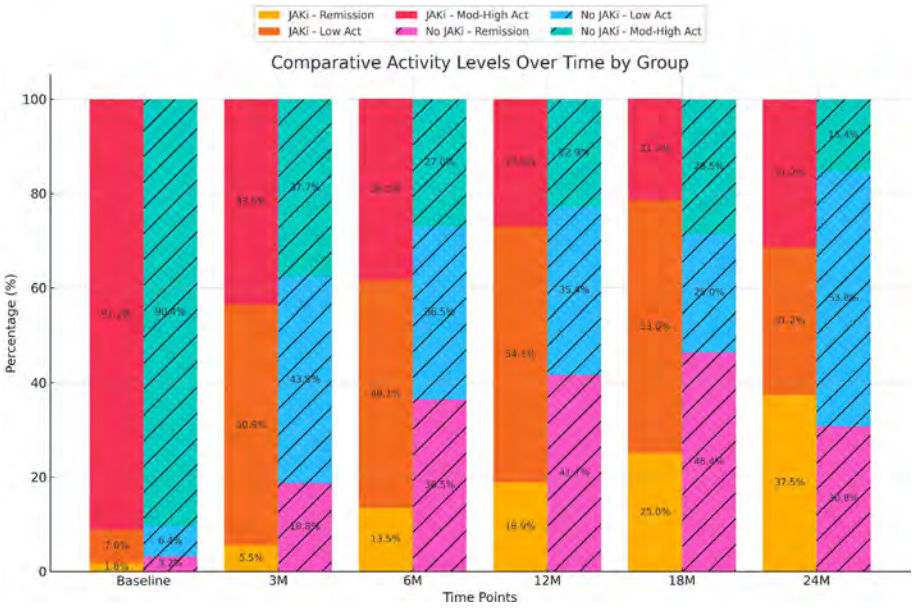


Figure 1. Comparative activity levels over time by group.

CI 18.5733), slightly shorter for the JAKI group (22.02 months; SE 1.6571 and 95% CI 18.2774), but not reaching statistical significance. No differences were found in terms of adherence to the treatment in the first two years (91% vs 93%).

Conclusion: In our study, the JAKi-experienced group showed no significant differences in terms of patient characteristics, comorbidities, baseline disease activity, or co-treatment with Prednisone and csDMARDs. Only the disease duration and refractoriness to previous biologic treatments were significantly higher in the JAKi-experienced group. Clinical response and drug persistence (median almost 2 years) were good and comparable between both groups, as were discontinuation rates and causes (inefficacy). Therefore, in our study, UPA appears to be a good treatment option for RA patients who are refractory and have been previously treated with Baricitinib.

Disclosure: G. Gonzalez Mozo de Rosales: None; **L. Lopez-Dominguez**: None; **N. Alcorta-Lorenzo**: None; **o. ibarguengoitia Barrena**: None; **D. Montero**: None; **A. Ruibal Escribano**: None; **e. barastay Alberdi**: None; **J. Valero Jaimes**: None; **L. Ibarrola**: None; **P. Garcia Escudero**: None; **M. Lopez I Gomez**: None; **E. Galindez Aguirregoicoa**: None; **M. Garcia Vivar**: None.

Abstract Number: 0486

Safety of sarilumab in more than 1000 patients with rheumatoid arthritis in Japan by age group: a post-marketing surveillance study

Hideto Kameda[1], Sadatomo Tasaka[2], Toshiya Takahashi[3], Naoki Soeda[3], Katsuhisa Suzuki[4] and Yoshiya Tanaka[5], [1]Department of Internal Medicine, Toho University, Tokyo, Japan, [2]Department of Respiratory Medicine, Hirosaki University Graduate School of Medicine, Hirosaki, Japan, [3]Medical Affairs, Asahi Kasei Pharma Corporation, Tokyo, Japan, [4]Medical Affairs, Sanofi K.K., Tokyo, Japan, [5]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sarilumab (SAR) is approved as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) for treatment of patients (pts) with moderate-to-severely active rheumatoid arthritis (RA). In this post-marketing surveillance (PMS), real-world study in Japan, safety and effectiveness of SAR therapy for pts with RA were investigated.

Methods: Pts treated with SAR (200 or 150 mg once every 2 weeks) between June 2018 and November 2021 were enrolled and followed to November 2024. This analysis stratified pts by age (< 65 years [yrs], ≥65 to <75 yrs, ≥75 yrs) and evaluated treatment emergent adverse events (TEAEs) as priority surveillance items per the risk management plan of SAR in Japan. Serious infections, for which a causal relationship to treatment could not be excluded, were analyzed by stratification of pts by their lowest absolute neutrophil count (ANC) below/above the lower limit of normal (LLN; $1.96\times10^3/\mu L$) during the observation period for pts aged < 65 or ≥65 yrs. Effectiveness was assessed by 28-joint disease activity score with C-reactive protein (DAS28-CRP).

Results: Data were collected for 1121/1125 enrolled pts, with 62.1% (696/1121) who completed 1 yr of treatment (<65 yrs, 62.6% [288/460]; ≥65 to <75 yrs, 63.9% [228/357]; ≥75 yrs, 59.2% [180/304]). Major reasons for discontinuation varied by age for insufficient clinical effect (All, 15.3% [171/1121]; <65 yrs, 17.4% [80/460]; ≥65 to <75 yrs, 14.6% [52/357]; ≥75 yrs,

Table 1. Patient background

	All patients (N=1118)	<65 yrs (n=457)	≥65 to <75 yrs (n=357)	≥75 yrs (n=304)
Mean age at baseline, yrs (SD)	65.5 (13.2)	52.7 (9.4)	69.6 (2.7)	80.0 (4.2)
Sex, n (%)				
Female	858 (76.7)	371 (81.2)	257 (72.0)	230 (75.7)
Mean body weight, kg (SD)	56.6 (13.0)	60.9 (14.4)	55.2 (11.7)	52.4 (10.1)
<55 kg, n (%)	334 (29.9)	101 (22.1)	117 (32.8)	116 (38.2)
≥55 kg, n (%)	342 (30.6)	163 (35.7)	106 (29.7)	73 (24.0)
Unknown, n (%)	442 (39.5)	193 (42.2)	134 (37.5)	115 (37.8)
Median (range) disease duration, months	90.5(1–792)	72.0 (1–432)	120.0 (1–768)	84.0 (1–792)
Steinbrocker staging system, n (%)				
Stage I	259 (23.2)	131 (28.7)	69 (19.3)	59 (19.4)
Stage II	360 (32.2)	158 (34.6)	113 (31.7)	89 (29.3)
Stage III	236 (21.1)	87 (19.0)	77 (21.6)	72 (23.7)
Stage IV	242 (21.6)	70 (15.3)	95 (26.6)	77 (25.3)
Unknown	21 (1.9)	11 (2.4)	3 (0.8)	7 (2.3)
Steinbrocker functional classification, n (%)				
Class I	248 (22.2)	135 (29.5)	75 (21.0)	38 (12.5)
Class II	613 (54.8)	253 (55.4)	195 (54.6)	165 (54.3)
Class III	193 (17.3)	49 (10.7)	64 (17.9)	80 (26.3)
Class IV	33 (3.0)	5 (1.1)	17 (4.8)	11 (3.6)
Unknown	31 (2.8)	15 (3.3)	6 (1.7)	10 (3.3)
Prior therapies, n (%)				
bDMARDs	711 (63.6)	302 (66.1)	220 (61.6)	189 (62.2)
csDMARDs, glucocorticoids or NSAIDs other than bDMARDs	984 (88.0)	411 (89.9)	312 (87.4)	261 (85.9)
Mean sarilumab treatment period, days (SD)	270.7 (132.7)	272.0 (131.8)	278.1 (128.2)	260.0 (138.5)
Initial dose of sarilumab, n (%)				
150 mg	46 (4.1)	7 (1.5)	14 (3.9)	25 (8.2)
200 mg	1072 (95.9)	450 (98.5)	279 (78.2)	279 (91.8)
Concomitant therapies, n (%)				
csDMARDs, glucocorticoids or NSAIDs	963 (86.1)	402 (88.0)	302 (84.6)	259 (85.2)
Other than for primary disease	769 (68.8)	285 (62.4)	253 (70.9)	231 (76.0)
Medical history, n (%)	311 (27.8)	96 (21.0)	114 (31.9)	101 (33.2)
Liver dysfunction	128 (11.4)	33 (7.2)	49 (13.7)	46 (15.1)
Renal dysfunction	56 (5.0)	6 (1.3)	19 (5.3)	31 (10.2)
Allergies	71 (6.4)	29 (6.3)	22 (6.2)	20 (6.6)
Other disease(s)	301 (26.9)	89 (19.5)	112 (31.4)	100 (32.9)
Comorbidities, n (%)	755 (67.5)	259 (56.7)	259 (72.5)	237 (78.0)
Liver dysfunction	241 (21.6)	77 (16.8)	89 (24.9)	75 (24.7)
Renal dysfunction	124 (11.1)	17 (3.7)	44 (12.3)	63 (20.7)
Allergies	152 (13.6)	68 (14.9)	43 (12.0)	41 (13.5)
Other disease(s)	706 (63.1)	234 (51.2)	242 (67.8)	230 (75.7)

bDMARDs, biological disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; SD, standard deviation; yrs, years

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Priority surveillance items as TEAEs

Priority surveillance item event term (PT), n	All patients (N=1118)		<65 yrs (n=457)		≥65 to <75 yrs (n=357)		≥75 yrs (n=304)	
	Total	Serious	Total	Serious	Total	Serious	Total	Serious
All events	151 (13.5)	96 (8.6)	50 (10.9)	25 (5.5)	55 (15.4)	37 (10.4)	46 (15.1)	34 (11.2)
Hepatic dysfunction[a]	60 (5.4)	3 (0.3)	27 (5.9)	0	20 (5.6)	1 (0.3)	13 (4.3)	2 (0.7)
Serious infections (including tuberculosis)[b]	42 (3.8)	42 (3.8)	10 (2.2)	10 (2.2)	15 (4.2)	15 (4.2)	17 (5.6)	17 (5.6)
Serious haematologic disorders[c]	31 (2.8)	31 (2.8)	12 (2.6)	12 (2.6)	10 (2.8)	10 (2.8)	9 (3.0)	9 (3.0)
Severe hypersensitivity reactions[d]	16 (1.4)	16 (1.4)	3 (0.7)	3 (0.7)	7 (2.0)	7 (2.0)	6 (2.0)	2 (2.0)
Interstitial lung disease[e]	8 (0.7)	8 (0.7)	0	0	6 (1.7)	6 (1.7)	2 (0.7)	2 (0.7)
Malignant tumour[f]	7 (0.6)	7 (0.6)	1 (0.2)	1 (0.2)	4 (1.1)	4 (1.1)	2 (0.7)	2 (0.7)
Cardiovascular event[g]	7 (0.6)	5 (0.5)	0	0	2 (0.6)	2 (0.6)	5 (1.6)	3 (1.0)
Intestinal perforation[h]	3 (0.3)	3 (0.3)	0	0	1 (0.3)	1 (0.3)	2 (0.7)	2 (0.7)
Hepatitis B virus	0	0	0	0	0	0	0	0

[a]Prefered term (PT) included in drug-related hepatic disorders (MedDRA SMQ) – comprehensive search
[b]Serious PT included in infection and infestations (MedDRA SOC)
[c]Serious preferred term (PT) included in haematopoietic leukopenia (MedDRA SMQ), haematopoietic thrombocytopenia (MedDRA SMQ) and blood disorder (MedDRA SOC)
[d]Serious PT included in hypersensitivity (MedDRA SMQ) and anaphylactic reaction (MedDRA SMQ)
[e]PT included in interstitial lung disease (MedDRA SMQ)
[f]PT included in malignant or unspecified tumours (MedDRA SMQ)
[g]PT included in cardiac disorders (MedDRA SOC) and vascular disorders (MedDRA SOC)
[h]PT included in gastrointestinal perforation (MedDRA SMQ) and diverticulum inflammation (MedDRA HLT)
[i]PT (hepatitis B and hepatitis B reactivation) included in infections and infestations (MedDRA SOC)
HLT, high-level terms; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; SMQ, standardised MedDRA queries; SOC, system organ class; TEAE, treatment emergent adverse event; yrs, years

Table 3. Serious infections related to the treatment, stratified by minimum ANC (above and below LLN [1.96×10³/μL])

n (%)	All patients		<65 yrs		≥65 yrs	
Priority survey item E\event term (PT)	Above LLN (n=512)	Below LLN (n=530)	Above LLN (n=196)	Below LLN (n=230)	Above LLN (n=316)	Below LLN (n=300)
Serious infections (including tuberculosis)	15 (2.9)	9 (1.7)	4 (2.0)	3 (1.3)	11 (3.5)	6 (2.0)
Bacteremia	1 (0.2)	0	0	0	1 (0.32)	0
Cellulitis	1 (0.2)	4 (0.8)	1 (.5)	1 (0.5)	0	3 (1.0)
Diverticulitis	3 (0.6)	0	0	0	3 (1.0)	0
Pneumonia	2 (0.4)	0	1 (0.5)	2 (0.9)	1 (0.3)	1 (0.3)
Urinary tract infection	1 (0.2)	0	0	0	1 (0.3)	0
Purulent	0	1 (0.2)	0	0	0	1 (0.3)
Arthritis	0	1 (0.2)	0	0	0	1 (0.3)
Mycobacterium avium complex infection	1 (0.2)	0	0	0	1 (0.3)	0
Pneumonia bacterial	2 (0.4)	0	0	0	2 (0.6)	0
Pseudomonas infection	1 (0.2)	0	0	0	1 (0.3)	0
Atypical mycobacterial infections	1 (0.2)	0	0	0	1 (0.3)	0
Herpes zoster disseminated	1 (0.2)	0	1 (0.5)	0	0	0
Infectious pleural effusion	2 (0.4)	0	1 (0.5)	0	1 (0.3)	0
COVID-19	1 (0.2)	0	0	0	1 (0.3)	0

ANC, absolute neutrophil count; COVID-19, coronavirus disease 2019; LLN, lower limit of normal; PT, preferred term; yrs, years

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

12.8% [39/304]) and TEAEs (All, 12.3% [138/1121]; <65 yrs, 9.3% [43/460]; ≥65 to <75 yrs, 12.3% [44/357]; ≥75 yrs, 16.8% [51/304]). The safety analysis included 1118 pts (female, 76.7% [858/1118]) (**Table 1**). Prior treatment with biologic DMARDs was observed in 63.6% (711/1118) of pts and was similar by age. Most pts received SAR 200 mg (95.9% [1072/1118]), with similar use of concomitant medications by age (All: 86.1% [963/1112] <65 yrs, 88.0% [402/457]; ≥65 to <75 yrs, 84.6% [302/357]; ≥75 yrs, 85.2% [259/304]). The incidence of priority surveillance items was 13.5% (151/1118) and tended to increase with age (< 65 yrs, 10.9% [50/457]; ≥65 to < 75 yrs, 15.4% [55/357]; ≥75 yrs, 15.1% [46/304]) (**Table 2**). Serious infections tended to increase slightly with age (< 65 yrs, 2.2% [10/457]; ≥65 to < 75 yrs, 4.2%, [15/357]; and ≥75 yrs, 5.6% [17/304]). Incidence of drug-related serious infections was similar when stratified by ANC (>LLN, 2.9% [15/512] and < LLN, 1.7% [9/530]) (**Table 3**), with a similar trend by age (<65 yrs: >LLN, 2.0% [4/196] and < LLN, 1.3% [3/230]; ≥65 yrs: >LLN, 3.5% [11/316] and < LLN, 2.0% [6/300]). The incidence of treatment-related grade ≥3 neutropenia was also similar (< 65 yrs: 3.5% [16/457]; and ≥65 yrs: 3.9% [26/661]). In 1037 pts eligible for effectiveness analysis, DAS28-CRP mean scores improved from 4.2 at baseline to 2.7 (low disease activity) after 1 month and to 2.3 (remission) at the final evaluation.

Conclusion: These results show that SAR treatment was well tolerated by pts in Japan with RA regardless of age, and no new safety concerns were identified. Additionally, no link was established between occurrence of neutropenia during SAR treatment and the development of serious infections.

Disclosure: H. Kameda: AbbVie, 2, 6, Amgen, 2, 6, Asahi Kasei Pharma Co., 2, 5, 6, BMS, 6, Eisai, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Mitsubishi-Tanabe, 6, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, Taisho, 2, 5, UCB, 2, 6; **S. Tasaka**: None; **T. Takahashi**: Asahi Kasei Pharma Corporation, 3; **N. Soeda**: Asahi Kasei Pharma Corporation, 3; **K. Suzuki**: Sanofi K.K., 3; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6.

Abstract Number: 0487

Efficacy of sarilumab in patients with rheumatoid arthritis of different disease activity at treatment initiation: a post-hoc analysis of a Phase 3 trial of sarilumab in Japan

Hideto Kameda[1], Toshiya Takahashi[2], Naoki Soeda[2] and Yoshiya Tanaka[3], [1]Department of Internal Medicine, Toho University, Tokyo, Japan, [2]Medical Affairs, Asahi Kasei Pharma Corporation, Tokyo, Japan, [3]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The efficacy and safety of sarilumab (SAR) and methotrexate (MTX) in patients (pts) in Japan with moderate-to-severely active rheumatoid arthritis (RA) and inadequate response to MTX have been demonstrated in the phase 3 KAKEHASI trial (NCT02293902). This *post hoc* analysis evaluated the efficacy of sarilumab in pts with RA by disease activity at treatment initiation.

Methods: In the KAKEHASI study of SAR with MTX, pts were randomized 2:2:1:1 to receive SAR 150 or SAR 200 mg every 2 wks (q2w) for 52 weeks (wks), or placebo for 24 wks followed by SAR 150 or SAR 200 mg q2w for 28 wks. Here, pts from

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

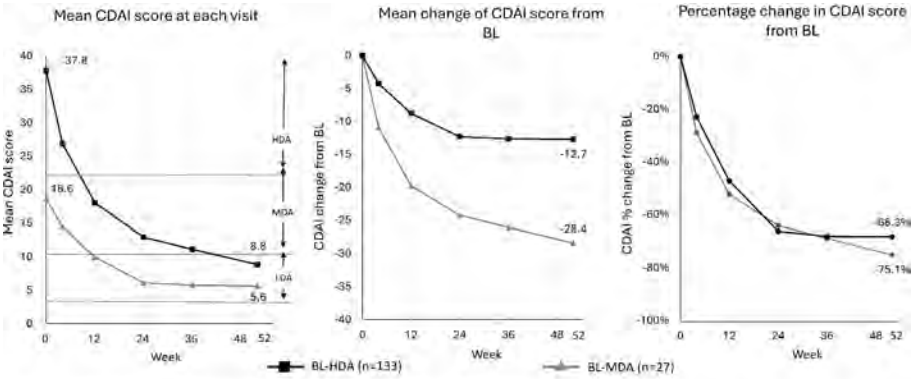


Figure 1. Mean CDAI scores, mean change in CDAI score from BL, and percentage change in CDAI score from BL for BL-HDA and BL-MDA subgroups. BL, baseline; HDA, high disease activity; LDA, low disease activity; MDA, medium disease activity.

the efficacy analysis population were stratified by Clinical Disease Activity Index (CDAI) scores at SAR initiation (baseline [BL]) as: low disease activity (BL-LDA), CDAI >2.8 and ≤10; moderate disease activity (BL-MDA), CDAI >10 and ≤22; and high disease activity (BL-HDA), CDAI >22. Differences in baseline characteristics and SAR response measured by CDAI, DAS28-CRP, American College of Rheumatology [ACR]20/50/70, HAQ-DI and visual assessment score [VAS]) were assessed. Pts with high disease activity were further stratified into two (LHDA: >22 and ≤35.7; HHDA: >35.7) and four subgroups (HDA1, CDAI >22 and ≤29.5; HDA2, CDAI >29.5 and ≤35.7; HDA3, CDAI >35.7 and ≤43.3; and HDA4, CDAI >43.3).

Results: In total, 243 pts (female, 76.3–81%; mean age, 51.9–56.1 years) were randomized to receive SAR 150 mg q2w (n=81), SAR 200 mg q2w (n=80), or placebo followed by SAR 150 mg q2w (n=42) or SAR 200 mg q2w (n=40). The pooled efficacy analysis population (n=242) was stratified as: BL-HDA, n=204 (84.3%), BL-MDA, n=37 (15.3%), and BL-LDA, n=1 (< 1%). BL characteristics were similar between BL-MDA and BL-HDA groups (female, 73.0% and 78.5%; ≥65 years, 81.1% and 77.6%, respectively). Mean CDAI scores at BL for BL-HDA and BL-MDA groups were 37.8 (n=133) and 18.6 (n=27), decreasing to 8.8 (n=105) and 5.6 (n=17), respectively, by 52 wk (**Figure 1**). Change in mean (%) CDAI scores over 52 wks was similar between groups (BL-HDA, −28.4 [−75.1%]; BL-MDA, −12.7 [−68.3%]). Of all SAR-treated pts, >50%

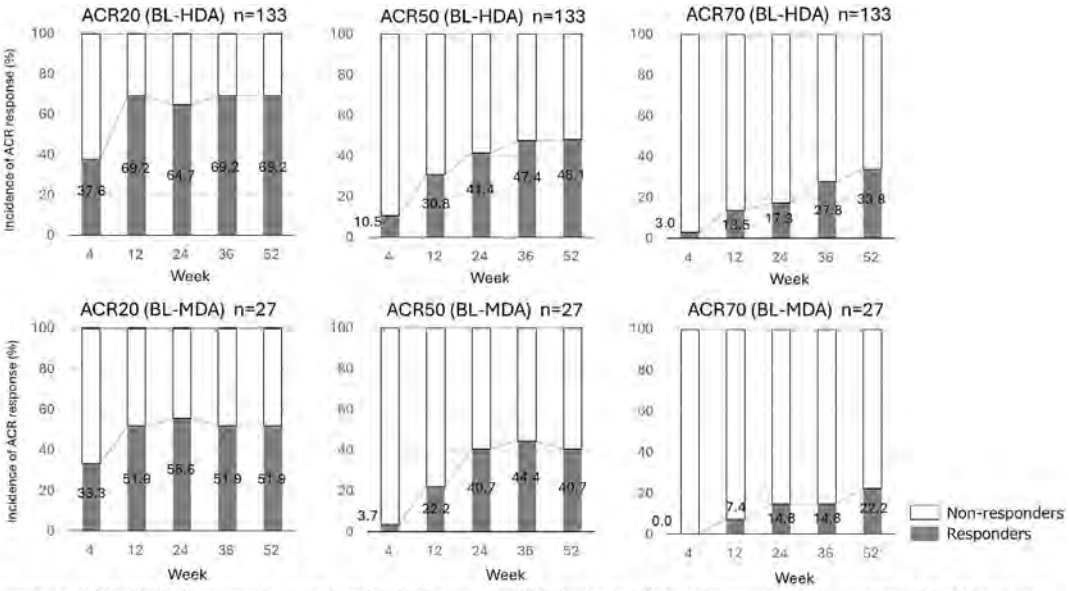


Figure 2. Incidence of ACR20/50/70 response for BL-HDA and BL-MDA subgroups. ACR, American College of Rheumatology; BL, baseline; HDA, high disease activity; LDA, low disease activity; MDA, medium disease activity.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

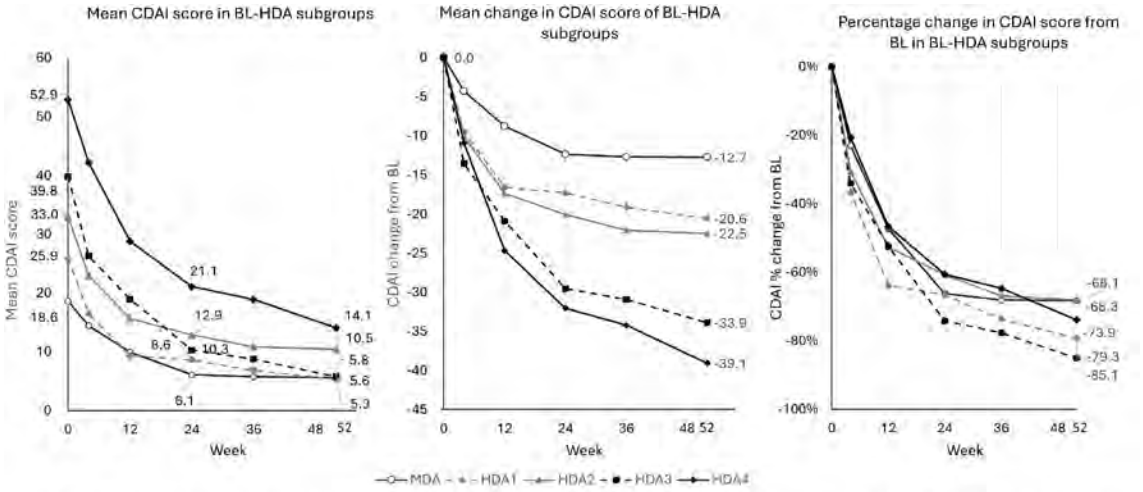


Figure 3. Mean CDAI scores, changes in mean CDAI score from BL, and percentage change in mean CDAI score from BL in the HDA-1 to HDA-4 subgroups with BL-MDA for comparison. BL, baseline; HDA, high disease activity; LDA, low disease activity; MDA, medium disease activity.

achieved LDA or remission at 52 wks (BL-HDA, 56.4% [75/133]; BL-MDA, 55.6% [15/27]). The trends in changes of mean (%) CDAI score were also reflected in those of DAS28-CRP scores (BL-MDA, –2.2 [–51.0%]; BL-HDA, –3.4 [–58.7%]) and HAQ-DI scores (BL-MDA, –0.41 [–48.6%]; BL-HDA, –0.67 [–54.2%]). Physician Global VAS also followed this trend for the BL-MDA (–34.5 [–76.0%]) and BL-HDA (–49.7 [–77.5%]) groups. Incidence of ACR20/50/70 response was similar regardless of BL-CDAI activity (HDA/MDA), but slightly higher in the BL-HDA group (**Figure 2**). In the two-subgroups, although the mean change of CDAI from BL at 52 wks was higher in the HHDA (–36.7) than the LHDA group (–21.4), the percentage change was notably similar (–72.9% and –79.1%, respectively), as per the HDA/MDA groups. In the four-subgroups, pts in HDA-3 and HDA-4 subgroups with the highest disease activity had a greater absolute decrease of CDAI than other groups with a similar percentage change, yet no plateau by 52 wks (**Figure 3**).

Conclusion: These results indicate that the efficacy of SAR is generally similar across pts with RA of different disease activity.

Disclosure: H. Kameda: AbbVie, 2, 6, Amgen, 2, 6, Asahi Kasei Pharma Co., 2, 5, 6, BMS, 6, Eisai, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Mitsubishi-Tanabe, 6, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, Taisho, 2, 5, UCB, 2, 6; **T. Takahashi**: Asahi Kasei Pharma Corporation, 3; **N. Soeda**: Asahi Kasei Pharma Corporation, 3; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6.

Abstract Number: 0488

Early and Sustained Improvements in Disease Activity and Patient-Reported Outcomes in Patients Treated with Filgotinib for Rheumatoid Arthritis: Up to 2-Year Interim Real-World Data From FILOSOPHY and PARROTFISH

Jérôme Avouac[1], Neil Betteridge[2], Karen Bevers[3], Gerd Burmester[4], Roberto Caporali[5], Ouafia Bouzid[6], Thomas Debray[6], Carole Van der Donckt[6], James Galloway[7], Susana Romero-Yuste[8] and Patrick Verschueren[9], [1]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France, [2]Neil Betteridge Associates, London, United Kingdom, [3]Sint Maartenskliniek, Nijmegen, Netherlands, [4]Department of Rheumatology and Clinical Immunology, Charité –

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Universitätsmedizin Berlin, Berlin, Germany, [5]University of Milan and ASST Gaetano Pini-CTO, Milano, Italy, [6]Alfasigma S. p.A., Bologna, Italy, [7]King's College London, London, United Kingdom, [8]University Hospital Complex of Pontevedra, Pontevedra, Spain, [9]Rheumatology, University Hospital Leuven and Skeletal Biology and Engineering Research Centre, KU Leuven, Leuven, Belgium

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: FILOSOPHY (NCT04871919) and PARROTFISH (NCT05323591) are ongoing, prospective, observational Phase 4 studies of filgotinib in patients (pts) with rheumatoid arthritis (RA) in Europe. In this interim analysis, pooled data from the studies are reported up to 2 years.

Table 1. Baseline characteristics and cardiovascular risk factors/comorbidities of interest (all treated patients)

Characteristic	N=1,423
Age, years	56.0 (49.0–64.0)
Female sex, n (%)	1,091 (76.7)
Body mass index, kg/m^2	26.4 (23.1–30.5); N=1,275
TJC28	6.0 (3.0–12.0); N=1,365
SJC28	4.0 (2.0–7.0); N=1,363
DAS28-CRP	4.5 (3.7–5.3); N=1,122
CDAI score	23.0 (16.0–32.0); N=1,118
VAS pain score	62.0 (48.0–76.0); N=475
FACIT-Fatigue score	27.0 (18.0–35.0); N=469
HAQ-DI score	1.3 (0.8–1.8); N=335
RA disease duration, years	8.1 (3.2–15.7); N=1,411
RF and/or ACPA positive, n (%)*	831 (58.4)
Smoking status, n (%)†	
Former smoker	239 (16.8)
Current smoker	244 (17.1)
Family history of myocardial infarction, n (%)‡	96 (6.7)
Comorbidities of interest/medical history, n (%)	
Hypertension	398 (28.0)
Dyslipidemia	191 (13.4)
Diabetes	100 (7.0)
Cardiovascular disease	82 (5.8)
Peripheral vascular disease	35 (2.5)
Ischemic CNS vascular disorders	33 (2.3)
Prior use of DMARDs for RA, n (%)	
At least one bDMARD	870 (61.1)
At least one tsDMARD	249 (17.5)
Study treatment at baseline, n (%)	
Filgotinib monotherapy	741 (52.1)
Filgotinib + csDMARDs for RA	663 (46.6)
Concomitant glucocorticoids at baseline, n (%)	520 (36.5)

Data are median (IQR) unless stated otherwise.
*164 patients (11.5%) were both RF and ACPA negative; data were missing for 428 patients (30.1%).
†Nonsmoker, n=642 (45.1%); data on smoking status were missing for 298 patients (20.9%).
‡Data were missing for 314 patients (22.1%).
ACPA, anti-citrullinated protein antibody; (b/cs/ts) DMARD, (biologic/conventional synthetic/targeted synthetic) DMARD; CDAI, Clinical Disease Activity Index; CNS, central nervous system; DAS28-CRP, Disease Activity Score in 28 joints using C-reactive protein; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue; HAQ-DI, Health Assessment Questionnaire–Disability Index; RF, rheumatoid factor; S/TJC28, swollen/tender joint count based on 28 joints; VAS, visual analog scale

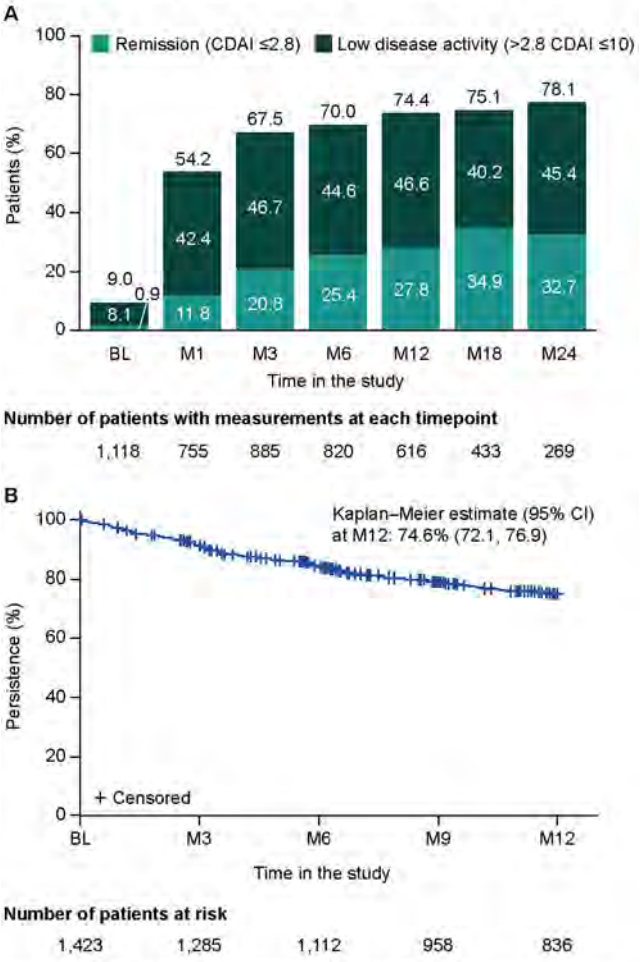
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Treatment-emergent adverse events up to Month 24

TEAE	Incidence rate per 100 patient-years of exposure (95% CI) N=1,423
Any TEAE	96.8 (90.5, 103.5)
Serious TEAE	9.8 (8.3, 11.5)
TEAE leading to premature discontinuation of filgotinib	9.6 (8.2, 11.2)
TEAEs of interest	
Fractures	1.8 (1.2, 2.6)
Herpes zoster	1.4 (0.9, 2.2)
MACE*	1.1 (0.6, 1.7)
Malignant or unspecified tumors (excluding NMSC)	0.7 (0.4, 1.3)
Pulmonary embolism	0.3 (0.1, 0.7)
Opportunistic infections	0.2 (0.1, 0.6)
Serious infections	0.1 (0.0, 0.3)
Deep vein thrombosis	0.1 (0.0, 0.4)
Cardiac failure	0.1 (0.0, 0.4)

*Non-adjudicated MACE, including acute myocardial infarction, stroke and cardiovascular death (MedDRA v26.0).
MACE, major adverse cardiovascular events; MedDRA, Medical Dictionary for Regulatory Activities; NMSC, nonmelanoma skin cancer; TEAE, treatment-emergent adverse event

Figure. Proportion of patients with CDAI remission or low disease activity up to M24 (**A**) and treatment persistence up to M12 (**B**)



As observed at the time of the data cut. No imputation of missing data was performed. The Kaplan–Meier plot (part B) illustrates time to treatment discontinuation or death within a 12-month follow-up period. In the absence of documented treatment discontinuation or death events, patients were censored at their last recorded treatment end date. Due to the interim nature of these data, some disposition records may still be incomplete. Kaplan–Meier estimates may therefore change as additional follow-up data become available.
BL, baseline; CDAI, Clinical Disease Activity Index; CI, confidence interval; M, Month

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The studies enrolled adults with moderate to severe active RA who were prescribed filgotinib for the first time in daily practice. Disease activity assessments included Clinical Disease Activity Index (CDAI) and Disease Activity Score in 28 joints using C-reactive protein (DAS28-CRP). The following patient-reported outcomes (PROs) were collected: visual analog scale (VAS) pain, Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue and Health Assessment Questionnaire–Disability Index (HAQ-DI) scores. A ≥10-mm reduction in VAS pain score or a ≥4-point increase in FACIT-Fatigue score were considered clinically meaningful changes from baseline. Outcomes were assessed in biologic (b) DMARD-naïve and -experienced pts. Treatment persistence (Kaplan–Meier estimate) and treatment adherence (5-Item Compliance Questionnaire for Rheumatology [CQR5]) were reported up to Month 12. CQR5 scores >80% indicate good adherence. Treatment-emergent adverse events (TEAEs) were reported. All data are on-treatment.

Results: From May 2021 to September 2024, 1,423 pts were treated with filgotinib (median follow-up: 550 days); baseline characteristics are shown in **Table 1**. 38.9% of pts were bDMARD naïve; 61.1% were bDMARD experienced. 91.2% received filgotinib 200 mg; 8.8% received filgotinib 100 mg. The proportion of pts with a CDAI score ≤10 increased from baseline to Month 24 (**Figure A**). In bDMARD-naïve pts, median (IQR) CDAI score decreased from 22.0 (16.0–31.0) at baseline (n=424) to 8.0 (4.0–14.0) at Month 1 (n=311) and 3.0 (0.0–7.5) at Month 24 (n=112), and in bDMARD-experienced pts from 24.0 (17.0–33.0) at baseline (n=694) to 10.5 (6.0–18.0) at Month 1 (n=444) and 6.0 (3.0–12.0) at Month 24 (n=157). Similar improvements were seen for DAS28-CRP. For PROs, median (IQR) HAQ-DI score decreased from 1.3 (0.8–1.8) at baseline (n=335) to 0.8 (0.3–1.3) at Month 1 (n=227) and 0.6 (0.3–1.1) at Month 18 (n=73). A clinically meaningful change in VAS pain score occurred in 43.9% of pts (177/403) at Week 1 and 63.5% (54/85) at Month 24; for FACIT-Fatigue, the proportions were 43.6% (175/401) at Week 1 and 55.3% (47/85) at Month 24. Improvements in PROs were seen in bDMARD-naïve and -experienced pts. At Month 12, treatment persistence (95% CI) was 74.6% (72.1, 76.9) (**Figure B**), and 79.8% of pts had a CQR5 score >80%. There were 9 deaths, 7 of which were considered unrelated to study treatment by the investigator. TEAEs of interest are shown in **Table 2**.

Conclusion: Pts treated with filgotinib in FILOSOPHY and PARROTFISH showed improvements in disease activity and HAQ-DI from Month 1, and in pain and fatigue from Week 1. Improvements were maintained up to Month 24 (Month 18 for HAQ-DI) and were seen regardless of prior bDMARD exposure. At Month 12, treatment persistence was high (75%) and 80% of pts showed good adherence. Safety data were consistent with those previously reported from randomized controlled trials of filgotinib.

Disclosure: J. Avouac: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6; **N. Betteridge**: Alfasigma S.p.A., 2, Galapagos, 2, 6, Grünenthal, 2, 6, Ipsen, 2, Sanofi, 2, 6; **K. Bevers**: Alfasigma S.p.A., 2, Galapagos, 2; **G. Burmester**: Celltrion, 6, Chugai, 6, Fresenius, 6, Gedeon Richter, 6, Sanofi, 6; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Eli Lilly & Co., 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **O. Bouzid**: Alfasigma S.p.A., 3, Galapagos, 3; **T. Debray**: Alfasigma S.p.A., 2, Biogen, 12, Advisor on methodology, Daiichi Sankyo, 2, Galapagos, 2, Gilead, 12, Advisor on methodology; **C. Van der Donckt**: Alfasigma S.p.A., 3, Galapagos, 3; **J. Galloway**: AbbVie, 2, 6, Alfasigma S.p.A., 2, Eli Lilly, 2, 6, Gilead, 2, Janssen-Cilag, 2, 5, 6, Novartis, 6, Pfizer, 2, 5, 6, Takeda, 2, UCB, 6; **S. Romero-Yuste**: AbbVie, 2, 6, AstraZeneca, 2, 6, Eli Lilly & Co., 2, 6, Galapagos, 6, UCB, 2; **P. Verschueren**: AbbVie, 6, 12, Support for attending meeting, Alfasigma S.p.A., 2, 5, Boehringer Ingelheim, 2, Citryll, 2, Eli Lilly & Co., 2, 6, Fresenius Kabi, 12, Support for attending meeting, Galapagos, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0489

Efficacy and safety profile of JAK inhibitors in current practice in rheumatoid arthritis

Omar Al Tabaa[1], Salomé Abdellaoui[1], Sophie Hecquet[1], Marion Thomas[2], Sandrine Carves[1], Alice Combier[1], Olivier Fogel[3], Yannick Allanore[4] and **Jérôme Avouac**[5], [1]Rheumatology department, Cochin Hospital, Paris, France, [2]APHP, Paris, France, [3]AP-HP, Paris, France, [4]University Paris City, Paris, France, [5]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: JAKi have been used in rheumatoid arthritis in current practice for several years now, with the progressive arrival on the market of 4 molecules. The use of JAKi has also been hindered by successive safety alerts, which have restricted their use in elderly patients or those with risk factors. The aim of this study was to assess the therapeutic maintenance of the 4 JAKIs available, as well as their efficacy and safety in current RA practice.

Methods: A retrospective study was conducted at a single center, encompassing all RA patients who received a first JAKI between April 2018 and June 2022. The primary endpoint was treatment maintenance at 12 and 24 months, as analyzed using the Kaplan-Meyer survival curve.

Table 1: Characteristics of patients treated with JAKi

	Total (n=108)	BARI (n=30)	TOFA (n=10)	UPA (n=48)	FILGO (n=20)
Baseline demographics					
Age (years), mean ± SD	57± 11	62± 11	58± 11	55± 16	55± 10
Women, n (%)	91 (84)	23 (77)	7 (70)	41 (85)	20 (100)
Baseline disease characteristics					
Disease duration (years), mean ± SD	19± 12	22± 13	17± 10	17± 12	19± 15
Positive rheumatoid factor, n (%)	91 (84)	25 (83)	8 (80)	42 (88)	16 (80)
Positive anti-CCP2 antibodies, n (%)	95 (88)	26 (87)	8 (80)	45 (94)	16 (80)
Bone erosions on hand/foot x-rays, n (%)	83 (77)	25 (83)	6 (60)	38 (79)	14 (70)
Extra-articular manifestations	37 (34)	7 (23)	3 (30)	18 (38)	9 (45)
Baseline disease activity:					
Tender joints, mean± SD	5.7± 5.8	6.3± 6.0	3.6± 4.0	6.4± 6.5	4.2± 4.1
Swollen joints, mean± SD	4.6± 5.2	4.3± 4.6	4.4± 3.8	5.0± 5.1	4.2± 6.56
Patient Global Assessment (0-100), mean±SD	62± 25	65± 23	56± 41	62± 24	59± 22
DAS28, mean±SD	4.62± 1.42	4.74± 1.00	4.06± 2.24	4.76± 1.55	4.49± 1.38
DAS28-CRP, mean± SD	4.05± 1.24	4.05± 1.07	3.66± 1.46	4.22± 1.29	3.85± 1.27
ESR (mmH1), mean ±SD	30± 25	27± 20	36± 35	30± 26	25 6±
CRP (mg/L), mean ±SD	9.1± 13.4	5.7± 7.6	19.1± 27	7.7 8.7±	12.3± 14
Baseline comorbidities					
Active Smokers / former smokers, n (%)	15 (14) / 29 (27)	3 (10) / 8 (27)	2 (20) / 3 (30)	8 (17) / 9 (19)	2 (10) / 9 (45)
High blood pressure, n (%)	23 (21)	7 (23)	4 (40)	11 (23)	1 (5)
Diabetes mellitus, n (%)	9 (8)	1 (3)	1 (10)	7 (15)	0 (0)
Hypercholesterolemia, n (%)	18 (17)	3 (10)	2 (20)	7 (16)	6 (30)
BMI, kg/m2, mean ±SD	25 5±	25.4± 5.8	24.5± 5.8	25.1± 4.8	25.2± 5.1
BMI >30 kg/m2, n (%)	22 (20)	6 (20)	2 (20)	9 (19)	5 (25)
Atherosclerotic cardiovascular disease, n (%)	3 (3)	1 (3)	1 (10)	1 (2)	0 (0)
History of ischemic stroke, n (%)	3 (3)	1 (3)	1 (10)	1 (2)	0 (0)
History of venous thromboembolism, n (%)	6 (6)	3 (10)	0 (0)	3 (6)	0 (0)
History of severe infection, n (%)	6 (6)	2 (7)	1 (10)	2 (4)	1 (5)
History of herpes zoster, n (%)	12 (11)	3 (10)	0 (0)	6 (13)	3 (15)
Previous neoplasia, n (%) (Solid/hemopathy)	13 (12)	7 (23)	1 (10)	4 (8)	1 (5)
≥65 years and/or at least one CV risk factor, n (%)	73 (68)	21 (70)	7 (70)	31 (65)	14 (70)
Treatments received at baseline					
Current corticosteroid use, n (%)	75 (69)	23 (77)	7 (70)	33 (69)	12 (60)
Corticosteroid dose, mg/day, mean± SD	3.1± 1.7	4.9± 3.3	4.5± 3.7	4.1± 3.3	3.3± 3.1
Current conventional DMARD use, n (%)	83 (77)	25 (83)	6 (60)	40 (83)	12 (60)
Current MTX use, n (%)	64 (59)	18 (60)	6 (60)	34 (71)	6 (30)
Targeted therapeutic line of the JAKi					
First line, n (%)	18 (17)	4 (14)	0 (0)	9 (19)	5 (25)
Second line, n (%)	28 (26)	7 (23)	4 (40)	12 (25)	5 (25)
Third line, n (%)	24 (22)	7 (23)	4 (40)	11 (23)	2 (10)
>3 lines, n (%)	38 (35)	12 (40)	2 (20)	16 (33)	8 (40)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Efficacy of JAKi on DAS28-CRP

	Baseline	6 months	Final	Delta baseline-6m	P-value	Delta baseline-final	P-value
JAKi	**4.05± 1.24**	**2.79± 1.00**	**2.98± 1.58**	**-1.46± 1.28**	**<0.001**	**-1.05± 1.67**	**<0.001**
BARI	4.05± 1.07	3.15± 0.69	3.26± 1.63	-0.85± 1.12	0.032	-0.79± 1.75	0.079
TOFA	4.28± 1.46	3.21± 1.77	3.57± 1.89	-1.07± 1.16	0.089	-0.85± 1.93	0.14
UPA	4.23± 1.29	2.56± 1.04	2.96± 1.57	-1.73± 1.15	<0.001	-1.01± 1.85	0.006
FILGO	3.85± 1.27	2.76± 1.13	2.44± 1.39	-1.57± 1.64	0.009	-1.53± 1.04	<0.001

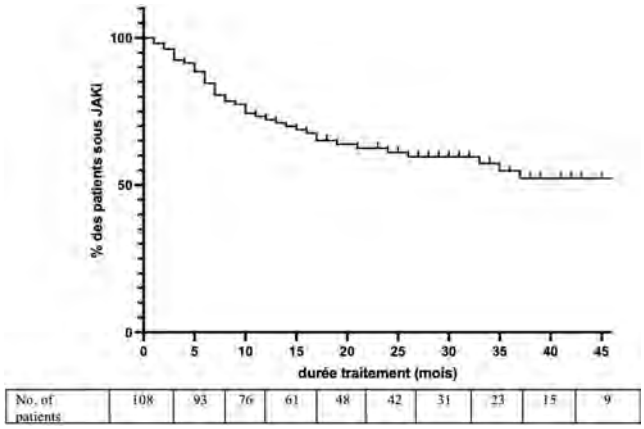


Figure 1: Therapeutic maintenance of JAKi

Secondary endpoints included the efficacy of JAKi and each molecule at 6 months and at the last available visit (until June 2024), as assessed by the DAS28-CRP (Wilcoxon) score, and the number of treatment discontinuations due to inefficacy or intolerance.

Results: We included 108 patients (91 women, 84%) treated with JAKi with a mean age of 57± 14 years and a disease duration of 19± 12 years; rheumatoid factors and ACPA were positive in 91 (84%) and 95 (88%) patients respectively, 83 (77%) had erosions and 37 (34%) extra-articular involvement (**Table 1)**. JAKi were predominantly used in combination with a csDMARD (83/108, 77%) and beyond the 3rd line of targeted therapy (**Table 1)**. The characteristics of patients treated with the 4 JAKi were comparable and are presented in **Table 1**. Therapeutic maintenance in JAKi was 72% at 12 months and 61% at 24 months. Median treatment survival was 47 months (**Figure 1)**.

A significant reduction in DAS28-CRP was observed at 6 months (-1.46± 0.28 vs. inclusion visit, p< 0.001) and at the last visit, which occurred 21± 15 months following JAKi initiation (-1.05± 1.67 vs. inclusion visit, p< 0.001) (**Table 2**). This decrease in DAS28-CRP appears to be numerically greater with the more selective JAKi (Upadacitinib, Filgotinib) than with Baricitinib and Tofacitinib.

During the follow-up period, 45 patients (42%) discontinued JAKi (including 16 patients on Baricitinib, 53%, 6 on Tofacitinib, 60%, 21 on Upadacitinib, 44% and 2 on filgotinib, 10%). The primary reasons for discontinuation included lack of efficacy (26 cases) and intolerance (15 cases). Noteworthy side effects included a myocardial infarction, three pulmonary embolisms, and the detection of breast cancer.

Conclusion: The present study demonstrated that the therapeutic maintenance of JAKi in RA exhibited a relatively high rate of occurrence at 12 and 24 months. Primarily utilized as a third-line targeted therapy, JAKi has been demonstrated to significantly improve RA activity, yielding favorable outcomes. However, a considerable proportion of patients discontinued treatment due to lack of efficacy or adverse effects, underscoring the necessity for ongoing, personalized evaluation of these therapies in routine clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: O. Al Tabaa: None; **S. Abdellaoui**: None; **S. Hecquet**: None; **M. Thomas**: None; **S. Carves**: None; **A. Combier**: None; **O. Fogel**: None; **Y. Allanore**: None; **J. Avouac**: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6.

Abstract Number: 0490

Infection Risks Associated with Monotherapy and Combination Therapies Using Biological or Targeted - DMARD in RA: A Systematic Review and Network Meta-analysis

Li Liu[1], Xue-Mei Zhang[1], Zhi-Chun Gu[1] and **Jia Li**[2], [1]Ren Ji Hospital, Shanghai Jiao Tong University School Of Medicine, Pu Dong Xin Qu, Shanghai, China (People's Republic), [2]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aimed to evaluate the infection risks in patients with rheumatoid arthritis (RA) treated with biological or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs), either as monotherapy or in combination with conventional synthetic DMARDs (csDMARDs).

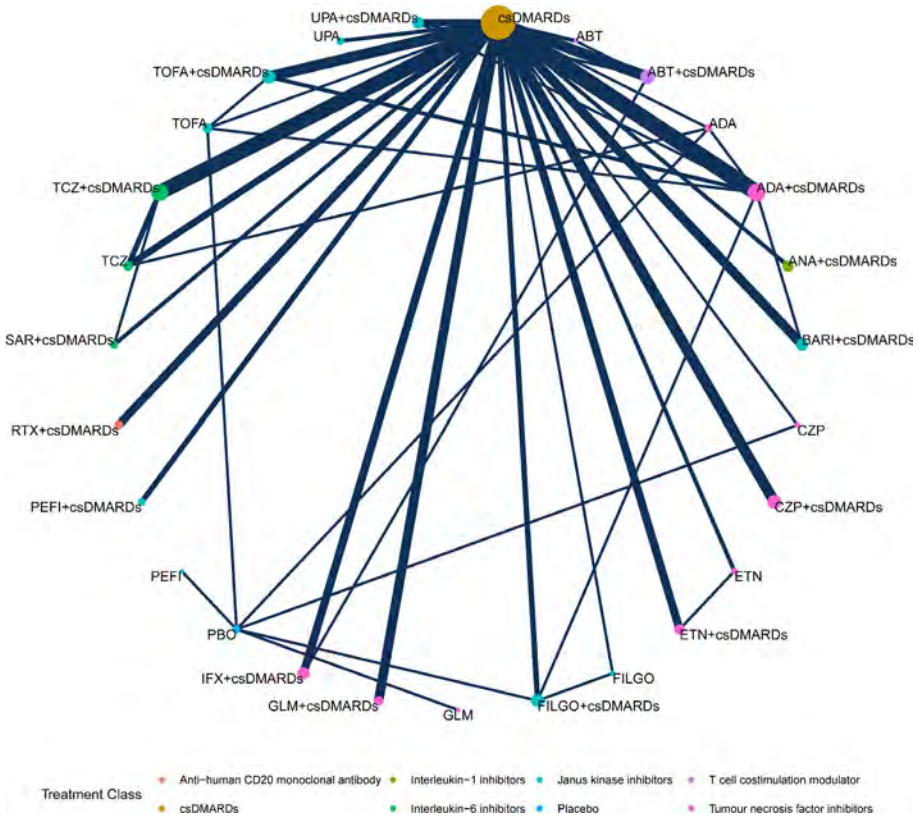


Figure 1 Network map of treatment comparisons for Serious infections Links between the nodes indicated the available direct comparisons between different treatments. ABT, Abatacept; ADA, Adalimumab, ANA, Anakinra, BARI, Baricitinib; CZP, Certolizumab; ETN, Etanercept; FILGO, Filgotinib; GLM, Golimumab; IFX, Infliximab; PEFI, Peficitinib; PBO, Placebo; RTX, Rituximab, SAR, Sarilumab; TCZ, Tocilizumab; TOFA, Tofacitinib; UPA, Upadacitinib; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 A heat map ranking b/tsDMARDs ± csDMARDs based on the risk of serious infections, any infection, and specfic infectious outcomes Numbers reflect P-score, which rank b/tsDMARDs ± csDMARDs on a continuous scale from 0 to 1. A higher P-score indicates a greater increase in risk of infection. Transverse line indicate that data were not available. ABT, Abatacept; ADA, Adalimumab, ANA, Anakinra, BARI, Baricitinib; CZP, Certolizumab; ETN, Etanercept; FILGO, Filgotinib; GLM, Golimumab; IFX, Infliximab; PEFI, Peficitinib; PBO, Placebo; RTX, Rituximab, SAR, Sarilumab; TCZ, Tocilizumab; TOFA, Tofacitinib; UPA, Upadacitinib, bDMARDs, biological disease-modifying antirheumatic drugs; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs.

P-score	Serious infections	Any infection	Upper respiratory tract infection	Bronchitis	Pneumonia	Gastroenteritis	Urinary tract infection	Herpes zoster	Tuberculosis	Sepsis
csDMARDs	0.35	0.34	0.45	0.46	0.36	0.57	0.34	0.25	0.45	0.51
PBO	0.08	0.16	0.15	0.38	-	0.39	0.70	0.35	0.46	-
FILGO	0.65	0.45	0.42	0.20	0.36	-	0.74	0.53	-	0.72
TOFA	0.54	0.32	0.36	0.81	0.68	0.50	0.52	0.52	0.46	0.52
UPA	0.49	0.24	0.54	0.52	0.24	0.44	0.21	0.83	0.47	0.51
PEFI	-	0.21	0.39	0.81	0.51	0.70	-	0.47	-	-
BARI	-	0.46	0.26	0.31	-	0.74	0.44	0.77	0.47	-
ABT	0.91	0.71	0.31	0.27	0.56	0.27	0.35	-	-	-
CZP	0.57	0.60	0.41	0.44	0.32	0.81	-	-	0.47	-
TCZ	0.52	0.35	0.50	0.59	0.36	-	0.20	-	0.40	0.29
ADA	0.34	0.27	0.38	0.19	-	0.35	0.64	-	0.40	0.54
ETN	0.26	0.85	0.46	0.81	0.44	0.17	-	-	0.43	0.25
GLM	0.09	0.28	-	-	-	-	-	-	0.48	-
SAR	-	0.34	0.09	0.51	-	-	0.69	-	-	-
TOFA+csDMARDs	0.87	0.76	0.87	0.29	0.73	0.57	0.71	0.76	0.60	0.61
UPA+csDMARDs	0.83	0.85	0.89	0.74	0.56	0.58	0.51	0.49	0.47	0.34
BARI+csDMARDs	0.39	0.79	0.56	0.44	0.20	0.76	0.77	0.72	0.43	0.67
FILGO+csDMARDs	0.33	0.59	0.76	0.37	0.74	0.13	0.75	0.38	0.48	0.42
PEFI+csDMARDs	0.18	-	0.59	-	-	-	0.45	0.40	-	-
ANA+csDMARDs	0.77	0.48	-	-	-	-	-	-	0.46	-
IFX+csDMARDs	0.73	0.70	0.65	0.35	0.77	-	0.68	0.46	0.83	0.72
SAR+csDMARDs	0.69	0.61	0.75	0.64	0.66	0.88	0.55	0.46	0.46	0.51
ADA+csDMARDs	0.65	0.59	0.64	0.25	0.77	0.54	0.60	0.54	0.55	0.58
TCZ+csDMARDs	0.61	0.64	0.45	0.93	0.40	0.79	0.48	0.22	0.50	0.28
CZP+csDMARDs	0.59	0.72	0.82	0.39	0.24	0.19	0.29	0.50	0.64	0.67
ABT+csDMARDs	0.49	0.64	0.36	0.54	0.50	0.52	0.29	0.48	0.51	0.58
GLM+csDMARDs	0.43	0.31	0.35	0.72	0.60	0.33	0.45	-	0.47	-
ETN+csDMARDs	0.35	0.43	0.38	0.61	0.50	0.28	0.68	0.42	0.62	0.27
RTX+csDMARDs	0.31	0.49	0.71	0.44	-	0.56	0.09	-	0.47	-

Methods: A comprehensive literature search of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) was conducted to identify randomized controlled trials (RCTs) assessing infection risks in RA patients treated with b/tsDMARDs. The primary outcome was the incidence of serious infections, while the secondary outcomes included any infection and specific events such as respiratory tract infections, gastroenteritis and herpes zoster. A frequentist network meta-analysis was performed to calculate odds ratios (ORs). This study was registered with PROSPERO (CRD42023435681).

Results: In this network meta-analysis of 127 RCTs involving 55,749 patients, b/tsDMARD monotherapy showed a similar risk of serious infections compared with csDMARDs. By contrast, combining csDMARDs with adalimumab, infliximab, tofacitinib, or upadacitinib (though not with other b/tsDMARDs) significantly increased the risk of serious infections (OR 1.51, 95% CI: 1.04-2.19; OR 1.75, 95% CI: 1.09-2.81; OR 2.52, 95% CI: 1.26-5.03; OR 2.31, 95% CI: 1.13-4.73, respectively). For any infection, b/tsDMARD monotherapy posed a similar risk to csDMARDs, except for etanercept. Regarding specific risks, tsDMARDs were associated with an increased incidence of herpes zoster compared to csDMARDs, except for filgotinib and peficitinib. Although rare, pneumonia, tuberculosis, and sepsis were observed more frequently with infliximab combined with csDMARDs than with other b/tsDMARD regimens.

Conclusion: Compared to csDMARDs, b/tsDMARD monotherapy showed no elevated serious infection risk, whereas specific combination therapy regimens with csDMARDs increased the risk of serious infections in RA patients. A specialized clinical pathway with detailed recommendations was developed to assess infection risks and optimize drug selection for RA patients undergoing b/tsDMARD treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

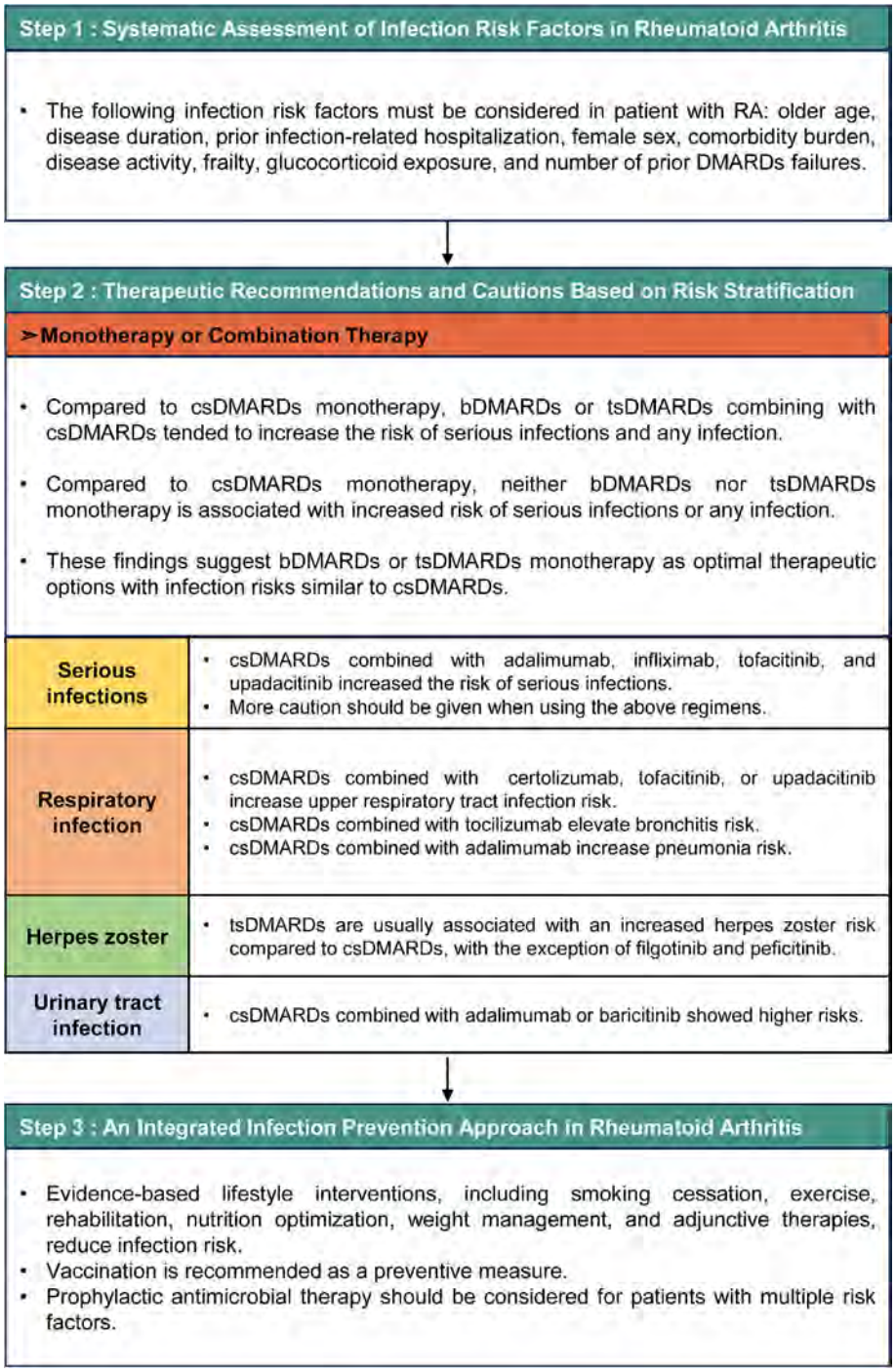


Figure 2. Infection Risk Management Protocol in Rheumatoid Arthritis RA, rheumatoid arthritis; DMARDs, disease-modifying antirheumatic drugs; csDMARDs, conven-tional synthetic disease-modifying antirheumatic drugs; bDMARDs, biological disease-modifying antirheumatic drugs; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs; IL-1Ra, interleukin-1 receptor antagonist.

Disclosure: L. Liu: None; **X. Zhang**: None; **Z. Gu**: None; **J. Li**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0491

Association Of short Chain Fatty Acids and diet with Disease Activity and Methotrexate Response in New Onset Rheumatoid Arthritis: A Proof of Principle Study

Kaci French[1], Luz Alvarado[2], Rebecca Haberman[3] and Rebecca Blank[3], [1]NYU Langone, New York, NY, [2]NYU Langone, New York, [3]NYU Langone Health, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Diet, the gut microbiome, and gut microbial metabolites have been implicated in rheumatoid arthritis (RA) development and modulation. Seafood based-omega-3 fatty acids modulate inflammatory cytokines in RA. Fiber rich diets, such as Mediterranean and vegetarian diets, are associated with increased short chain fatty acid (SCFA)-producing bacteria. In turn, SCFAs have been shown to modulate the gut microbiome, enhance anti-inflammatory mediators in murine RA models, and be associated with decreased risk of progression to clinical RA in at-risk individuals. Until now, most studies of SCFA supplementation have been in animal models. In this proof of principle study, we aimed to address this gap by analyzing the effects of diet and butyrate supplementation in new onset RA (NORA) patients, hypothesizing that butyrate supplementation in NORA with healthier diets will improve disease activity, ultimately leading to better treatment response.

Methods: Clinical, dietary, and metabolomic data were obtained from NORA patients meeting 2010 ACR/EULAR RA criteria. Participants took methotrexate (MTX) plus butyrate (1 gm butyrate, 3 times daily) over 4 months (Table 1). MTX responders (MTX-R) were defined by either a change in DAS-28 ESR of > 1.8 from baseline and/or DAS28 < 2.6 (remission) at 4 months. Clinical data, dietary data (based on a modified NHANES Food Frequency Questionnaire), and fecal samples were collected at month 1, 2, and 4. Fecal metabolite quantification was performed by 1^{H} NMR spectroscopy. Between group differences were analyzed using Mann Whitney U tests and Fischer's exact tests as appropriate. Relationships between variables were calculated using Spearman's correlations. Adherence to multiple healthy diets, including fish/seafood, Mediterranean, and vegetarian diets was assessed to examine associations between diet quality, SCFA, and disease activity.

Results: 17 patients were enrolled: 11 responders and 6 non-responders. Increase in fecal SCFA concentration correlated with improvement in DAS28 scores at 1 month (r= -0.749, p=0.001, Figure 1A). In a group of 12 patients, those with higher quality diet had an increase in fecal acetate after 4 months of butyrate supplementation, while those who had the lowest

Table 1. Characteristics of NORA cohort taking MTX and butyrate.

Characteristic	Total (n=17)	MTX Non-Responders (n=6)	MTX Responders (n=11)	p-value
Age- Median (IQR)	55 (48, 62)	46.5 (27, 62)	57 (51.5, 62)	0.216
Female- n (%)	14 (82.4)	5 (83.3)	9 (81.8)	1.000
Race- n (%)				0.102
Asian	1 (5.9)	0 (0)	1 (9.1)	
Black/African American	3 (17.6)	0 (0)	3 (27.3)	
Native American	1 (5.9)	0 (0)	1 (9.1)	
White/Caucasian	12 (70.6)	6 (100.0)	6 (54.5)	
Hispanic Ethnicity- n (%)	6 (35.3)	3 (50.0)	3 (27.3)	0.462
Methotrexate dose (mg)- Median (IQR)	15 (15, 17.5)	13.8 (10, 15)	15 (15, 18.8)	0.149

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

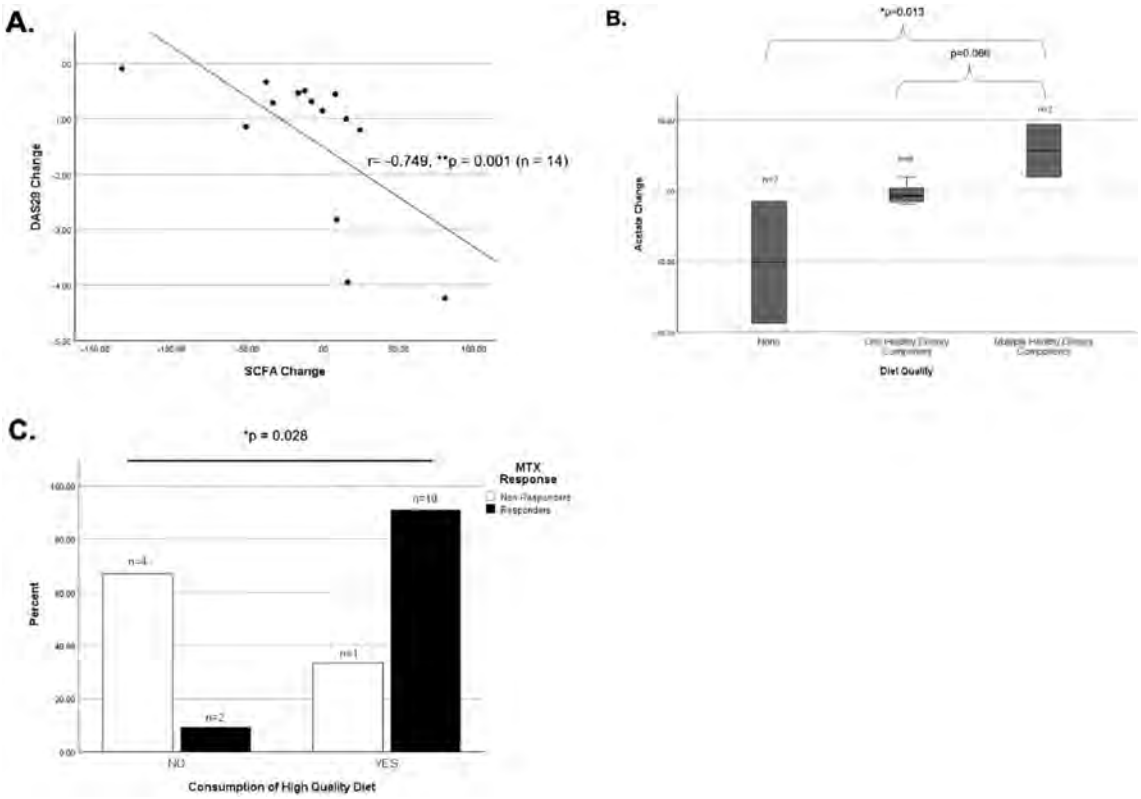


Figure 1. Associations between disease activity, SCFA, and diet. (A) Change in fecal SCFA is negatively correlated with change in DAS28 scores after 1 month of butyrate supplementation. (B) Participants who consumed multiple foods groups containing fish/omega-3, mediterranean, or vegetarian diets had increased change in fecal acetate after 4 months of MTX and butyrate supplementation when compared to those who did not consume these diets (C) MTX responders were more likely to report consumption of diets rich in fish, omega-3, legumes, whole grains, vegetables, and/or fruits compared to non-responders.

quality diet had a decrease in acetate (p=0.013, Figure 1B). Patients with high quality diets were more likely to be MTX-R (p=0.028, Figure 1C).

Conclusion: In this small, proof of principle study, we found that increased fecal SCFA concentration was associated with improvement in disease activity after only 1 month of MTX and butyrate, reinforcing the connection between SCFA and disease activity. Furthermore, only those consuming diets rich in SCFA precursors had improvement in acetate levels which may indicate that these diets are essential for butyrate supplementation to be effective. In fact, high quality diets, irrespective of SCFA changes, were associated with response. While thought provoking, larger studies are needed to explore and confirm these hypothesis-generating results.

Disclosure: K. French: None; **L. Alvarado**: None; **R. Haberman**: Johnson and Johnson, 1, 5, Novartis, 1; **R. Blank**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0492

Outcomes of Total Knee Replacement in Patients with Rheumatoid Arthritis: A National Inpatient Sample Database Analysis

karun Shrestha[1], Pravakar Parajuli[2], Anil Regmi[3], Prakriti Subedi[4], Manoj Ghimire[5], Sajana Poudel[6], Mohammed Hasan[7], Mahmoud Hashim[8], Veera Durga Vaishnavi Kurra[9] and ClementT Taoge[10], [1]Department of Internal Medicine, St. Barnabas Hospital, SBH Health System, Bronx, NY 10457, USA, BRONX, NY, [2]Patan Academy of Health Sciences-School of Medicine (PAHS-SOM), Lalitpur, Bagmati, Nepal, [3]Parkview Health, Fort Wayne, IN, [4]St. Barnabas Hospital, Bronx, NY, [5]St Barnabas Hospital, BRONX, NY, [6]Cook County Health, CHICAGO, NY, [7]Parkview Medical Center, Pueblo, CO, [8]SBH Health System, New Rochelle, NY, [9]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [10]Albert Einstein College of Medicine - Montefiore Medical Center, Bronx

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, inflammatory disease of the joints with an estimated prevalence of 0.5% of people. Nearly 25% of RA patients undergo joint replacement/arthroplasty within 22 years of diagnosis. The hip and knee are the most frequently replaced joints. Total knee replacement (TKR) effectively treats advanced joint destruction in RA patients, significantly enhancing mobility and quality of life. Other common TKR indications include symptomatic moderate-to-severe osteoarthritis, advanced symptomatic osteonecrosis with arthritis, and limb deformity correction. Studies on outcomes of TKR in RA patients are limited. This study uses the national inpatient sample (NIS) database to compare characteristics, comorbidities, perioperative complications, and outcomes in TKR patients with and without RA.

Table 1: Patient characteristics and co-morbidities

Characteristics	TKR with RA (n=127080)	TKR with out RA (n=3288610)	p-value
Age,years (mean ±SD)	65.8 ± 9.8	66.8 ±9.5	0.45
Gender			
Female, %	76.01	60.62	<0.001
Race, %			
White	75.65	81.03	
Black	11.52	8.34	
Hispanic	8.2	6.31	
Asian	1.46	1.57	
Native American	0.71	0.49	
Other	2.47	2.26	<0.001
Location, %			
Rural	8.87	10.22	
Urbam Non teachimg	26	26.49	
Urban Teaching	65.12	63.29	<0.001
Co morbidities, n(%)			
Hx of MI	3.61	3.26	0.002
CHF	5.24	3.98	<0.001
Peripheral vascular disease	3.39	2.76	<0.001
Dementia	1.02	0.08	<0.001
COPD	22.33	15.73	<0.001
Diabetes	15.31	16.97	<0.001
Diabtes with complications	5.94	5.25	<0.001
Hemi/Paraplegia	0.11	0.01	<0.001
Hx of Stroke	4.56	3.8	<0.001
Renal disease	8.68	7.61	<0.001
Mild Liver disease	1.86	1.39	<0.001
Moderate /SevereLiver disease	0.09	0.08	0.68
Cancer	0.88	0.94	0.33
Metastatic Cancer	0.12	0.11	0.56
AIDS	0.03	0.04	0.3

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Comparisons of complications between two groups

Complications, n(%)	TKR with RA (n=127080)	TKR with out RA (n=3288610)	p-value
Acute MI	3.71	3.34	0.001
Stroke	0.12	1.02	0.007
Blood Transfusion	3	1.61	<0.001
DVT	0.31	0.25	0.04
Pulmonary embolism	0.27	0.24	0.24
Periprosthetic Dislocation	1.26	0.89	<0.001
periprosthetic fracture	0.81	0.38	<0.001
periprosthetic infection	2.94	1.53	<0.001
Bloos loss anemia	19	15.02	<0.001
AKI	2.44	2.17	0.003
Superficial SSI	0.03	0.01	<0.001
Deep SSI	0.003	0.004	0.91
Post procedure sepsis	0	0.005	0.21
Cardiogenic shock	0.01	0.02	0.56
Post procedure septic shock	0	0.003	0.35

Table 3: Primary outcomes

Outcome	TKR with RA (n=127080)	TKR with out RA (n=3288610)	p-value
Mortality n (%)	105(0.08)	1405(0.04	0.003
Length of Stay (LOS), days (mean ±SD)	2.54 ±2.29	2.31 ± 2.07	0.01
Total Charges, $, (mean ±SD)	72002 ± 52750	67185 ± 50232	<0.001

Methods: A retrospective cross-sectional study was conducted using data from NIS (2016-2021). Primary and secondary diagnoses were identified using International Classification of Diseases (ICD-10) codes. All patients aged >18 years undergoing TKR were included in the study. TKR patients with and without RA were compared for demographics, comorbidities, complications, and outcomes, including mortality, length of stay, and hospitalization charges. Statistical analysis was done using STATA v.17.

Results: A total of 3,415,690 patients underwent TKR during the study period. Patients with RA undergoing TKR (n=127080) were more likely to be female (76.0% vs 60.6%, p< 0.001) and non-White. The most common sites were urban teaching hospitals. RA patients had significantly higher prevalence of comorbidities; congestive heart failure (5.2% vs 4.0%), COPD (22.3% vs 15.7%), and renal disease (8.7% vs 7.6%) - and significantly more complications including blood loss anemia (19.0% vs 15.0%, p< 0.001), blood transfusions (3.0% vs 1.6%), peri-prosthetic infection (2.9% vs 1.5%), dislocation (1.26% vs 0.89%), fracture (0.81% vs 0.38%), and superficial surgical site infection (0.03% vs 0.01%). RA patients had higher postoperative mortality (0.08% vs 0.04%, p=0.003), longer hospital stay (2.54 vs 2.31 days, p=0.01), and higher hospital charges ($72,002 vs $67,185, p< 0.001).

Conclusion: This study found that RA patients undergoing TKR experience higher perioperative complications, prolonged hospitalization, and higher costs. The study also demonstrated that patients with RA undergoing TKR had more comorbidities, with no significant age difference between those with and without RA. These findings underscore the importance of preoperative optimization and vigilant postoperative care in this vulnerable population. More studies are required to accurately identify the outcomes and complications of the TNR in RA patients.

Disclosure: k. Shrestha: None; **P. Parajuli**: None; **A. Regmi**: None; **P. Subedi**: None; **M. Ghimire**: None; **S. Poudel**: None; **M. Hasan**: None; **M. Hashim**: None; **V. Kurra**: None; **C. Taoge**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0493

Phase I Trial in Participants with Rheumatoid Arthritis and Healthy Volunteers with CIT-013, a First in Class NETosis Inhibitor

Maarten Kraan[1], Salah Hadi[2], Leonie Middelink[3], Renato Chirivi[3], Eric meldrum[3], Naomi Klarenbeek[4] and Patrick Round[3], [1]Citryll BV, Den Dolder, Netherlands, [2]ICON Netherlands BV, Groningen, Netherlands, [3]Citryll BV, Oss, Netherlands, [4]CHDR, Leiden, Netherlands

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Aberrant Neutrophil Extracellular Trap (NET) production contributes to the pathophysiology of multiple inflammatory and autoimmune diseases including rheumatoid arthritis (RA). We report data of a phase 1 trial (EudraCT number:2020-005848-36) with a humanized monoclonal antibody (CIT-013) targeting the citrullinated histones H2A and H4. CIT-013 inhibits NET formation and accelerates the clearance of NETs and netting neutrophils, thus lowering NET tissue burden with significant anti-inflammatory consequences (Chirivi et al 2021; van der Linden et al 2024).

Methods: Prospective, randomized, double-blind, placebo-controlled, phase I trial in participants with RA and healthy volunteers (HV). After obtaining informed consent and completion of baseline assessments, placebo, 25 mg or 50 mg of CIT-013 was administrated subcutaneously at days 1 and 15. Endpoints at day 29 were safety, tolerability, pharmacokinetics (PK) and effect on disease activity as measured with the disease activity score counting 28 joints and CRP (DAS28-CRP).

Results: In total 9 participants with RA and 3 HV were dosed with CIT-013, 3 participants received placebo, 3 participants 25 mg CIT-013 and 6 participants 50 mg CIT-013. Two participants with RA received placebo, 3 received 25 mg CIT-013 and 4 received 50 mg CIT-013. All 9 participants with RA met the ACR/EULAR criteria and were on stable synthetic disease modifying anti-rheumatic drugs (sDMARDs).

In general, CIT-013 was well tolerated, reported adverse events were mild (grade 1) injection site reactions (all resolved spontaneously) and headache. There was one serious adverse event in a placebo participant with RA that required surgery and hospitalization for a fracture. Anti-drug antibodies were only observed at Day 56 in 2 partcipants with RA, 1 in the 25 mg group and 1 in the 50 mg group, both with low titres (< 4).

The half life of CIT-013 was approximately 6 days and all PK parameters were comparable between HV, participants with RA in remission, and participants with RA and active disease.

Table 1. Mean DAS28-CRP ± Standard Deviation at baseline and at day 29 and DAS28-CRP response status at Day 29 for the included participants with RA.

Cohort	Disease status at baseline	n	DAS baseline	DAS Day 29	No DAS Response Day 29	DAS Response/Remission Day 29
Placebo	Remission	1	1.6	1.7	1	0
	Active	1	5.4	4.6	1	0
25 mg	Remission	3	1.9 ± 0.3	1.9 ± 0.9	3	0
50 mg	Remission	1	2.3	3.4	1	0
	Active	3	4.2 ± 0.6	2.4 ± 0.7	0	3

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

At baseline 4 out of 9 participants with RA (44%) had active disease, defined as a DAS28-CRP of 2.6 or higher. Of these, 1 participant received placebo and continued having active disease, 3 participants received 50 mg CIT-013 and all these had a clinical relevant reduction in disease activity. The clinical activity as observed on day 29 for all 9 participants with RA is captured in Table 1.

None of the HV and only 1 RA participant with active disease (8% of total, 25% of participants with active RA) had detectable serum CIT-H3 levels at baseline. In this participant the level dropped below the lowest level of detection (LLD) immediately after the 1st dose.

Conclusion: CIT-013 was well tolerated and a DAS28-CRP reduction was observed in participants with RA and active disease. These findings support further clinical development.

Disclosure: M. Kraan: Citryll BV, 3; **S. Hadi**: None; **L. Middelink**: Citryll BV, 7; **R. Chirivi**: Citryll BV, 3, 5, 8, 10, 11; **E. meldrum**: Citryll BV, 3, 3, 5, 11, 11; **N. Klarenbeek**: None; **P. Round**: Citryll B V, 3.

Abstract Number: 0494

LFD-200, an Antibody Drug Conjugate that Selectively Delivers a Glucocorticoid Payload to Immune Cells, Provides Sustained Anti-inflammatory Effects Without Systemic Toxicity in Non-human Primates

Matt McClure[1], Catherine Carriere[1], Kierstin Bell[1], Rex Williams[2], Geoff Kuesters[2], Emily Sansevere[2], Dave Nichols[2], Arthur Tzianabos[2] and Jay Rothstein[1], [1]Lifordi Immunotherapeutics, Lebanon, NH, [2]Lifordi Immunotherapeutics, Burlington, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Glucocorticoids (GCs) are the most versatile and efficacious anti-inflammatory drugs rheumatologists have available for patients. Unfortunately, prolonged systemic GC exposure leads to unacceptable toxicities, which have reduced GC use in favor of biologics that sacrifice efficacy for improved safety. LFD-200 is an antibody-drug conjugate that limits systemic toxicities through selective delivery of a modified, potent GC payload to immune cells via an antibody to VISTA, a cell surface protein mainly expressed on immune cells. In multiple prior mouse studies, including models of autoimmune disease (e.g., diabetes, asthma, arthritis), LFD-200 is rapidly internalized, resulting in reduced serum GC exposure and increased intracellular exposure in immune cells as well as enhanced efficacy compared to conventional GCs. Safety and pharmacodynamic studies of LFD-200 have now also been conducted in non-human primates (NHPs).

Methods: Three NHP studies evaluating subcutaneously administered LFD-200 were conducted in cynomolgus macaques.

Study 1: NHPs received one dose of LFD-200 (5 or 20 mg/kg). The control group received one dose of vehicle followed by 2 doses of dexamethasone (Dex; 3 mg/kg) given 6 and 7 days post vehicle. Ex vivo cytokine stimulation with lipopolysaccharides (LPS) was conducted on pre- and post-dosing tissue samples. Tissue exposure was assessed via immunohistochemistry using an antibody to the payload. **Study 2**: Toxicology study in which NHPs were dosed every 2 weeks (Q2W) with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

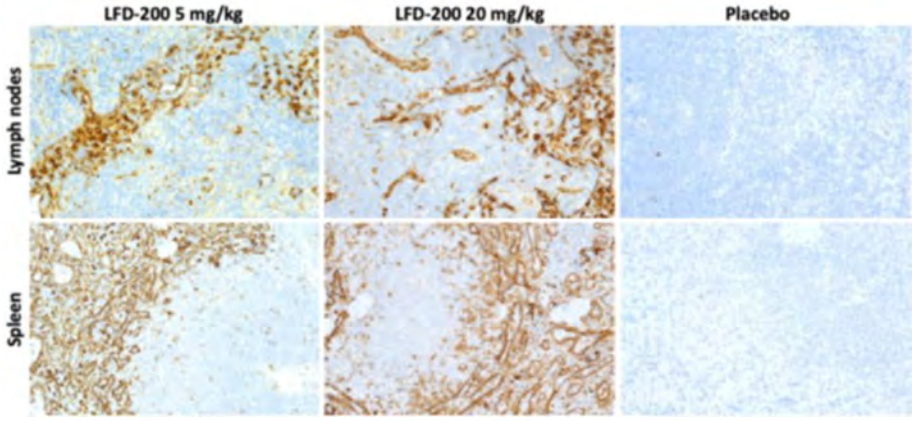


Figure 1: LFD-200 payload accumulation in lymph nodes and spleen. Immunohistochemistry for LFD-200 payload was conducted on lymph nodes and spleen that were collected 7 days after a single dose of 5 or 20 mg/kg LFD-200. Payload-specific antibody staining (brown) was detected in the spleen and lymph node at both doses but was absent in the placebo group. Slides were counterstained with hematoxylin (blue).

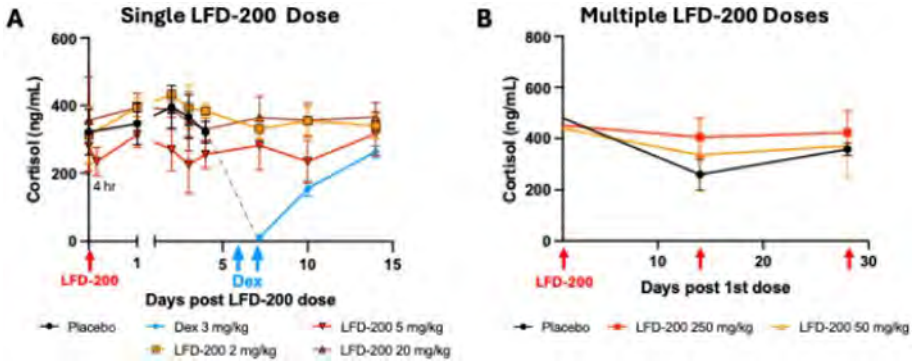


Figure 2: Serum cortisol levels following LFD-200 administration. A) Cortisol levels observed in Study 3 following a single dose (2, 5 or 20 mg/kg) of LFD-200 (n=4/group); the control group received one dose of vehicle followed by two doses of dexamethasone (3 mg/kg) 6 and 7 days post vehicle dosing (4 hrs before the final tissue collection). B) Cortisol levels (collected before each dose) observed in Study 2 following repeated doses of LFD-200 (50 or 250 mg/kg) (n=2 for the vehicle and n=4 for LFD-200). Red and blue arrows indicate LFD-200 and dexamethasone dosing, respectively.

placebo or LFD-200 at 50 or 250 mg/kg for 4 weeks. **Study 3**: Same dosing design as Study 1, but with an additional 2 mg/kg in LFD-200 group. Circulating cortisol levels were assessed in Studies 2 and 3 via ELISA or liquid chromatography/tandem mass spectrometry.

Results: LFD-200 achieves durable GC exposure in immune cells. A single dose of 5 or 20 mg/kg LFD-200 resulted in GC payload detection in immune tissues for ≥7 days post-dose (Figure 1).

LFD-200 achieves durable cytokine suppression. Compared to baseline, LFD-200 dosing resulted in up to 75% decrease in LPS-stimulated cytokines (e.g., IL-1β, IP-10, TNFa) in whole blood through 4 days post-dose, with up to 43% reduction observed 7 days post-dose.

LFD-200 treatment showed no evidence of systemic GC effects. In Study 3, after a single dose of LFD-200, no impact on cortisol levels was observed at any dose or time point tested. Comparatively, dexamethasone suppressed cortisol levels well below baseline for >3 days (Figure 2A). In Study 2, repeated high doses of LFD-200 (50 and 250 mg/kg Q2W) showed no changes in cortisol (Figure 2B) and no histopathological changes in heart, brain, liver, bone, eye, kidney, or intestine (thymic cellularity was decreased at 250 mg/kg).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In these NHP studies, LFD-200 selectively delivered sustained GC levels in immune tissues, resulting in inhibition of ex vivo induced inflammatory cytokines without evidence of systemic toxicity. LFD-200 has the potential to provide a safer, less frequently dosed GC treatment option for patients living with autoimmune or inflammatory diseases.

Disclosure: M. McClure: Lifordi Immunotherapeutics, 3, 4, 11; **C. Carriere**: Lifordi Immunotherapeutics, 12,, 3, 10; **K. Bell**: Lifordi Immunotherapeutics, 12,, 3, 10; **R. Williams**: Lifordi Immunotherapeutics, 3, 11, SpringWorks Therapeutics, 12,, 10, 11; **G. Kuesters**: Lifordi Immunotherapeutics, 3, 11; **E. Sansevere**: Lifordi Immunotherapeutics, 3; **D. Nichols**: Lifordi Immunotherauputics, 3; **A. Tzianabos**: Lifordi Immunotherapeutics, 12,, 4; **J. Rothstein**: Lifordi Immunotherapeutics, 12,, 3, 4, 10.

Abstract Number: 0495

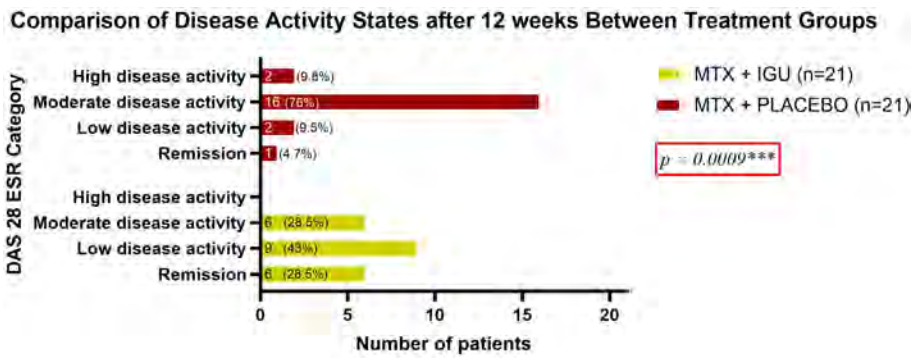
Effectiveness and Safety of Iguratimod with Background Methotrexate Therapy in Indian Patients with Rheumatoid Arthritis: A Randomized Double Blinded Placebo Controlled Study

MIDHUN SAKRAVARTHY JALANATHAN[1], Mehdi Ali Mirza[1], Vijaya prasanna Parimi[2], Seethalakshmi S[1] and Tejaswini Ramineni[3], [1]ESIC Medical College and Hospital, Sanathanagar, Hyderabad, Telangana, India, [2]ESIC Medical College and Super Specilaity Hospital, hyderabad, Telangana, India, [3]Esic Medical College And Hospital, Sanathnagar, Hyderabad, Telangana, India

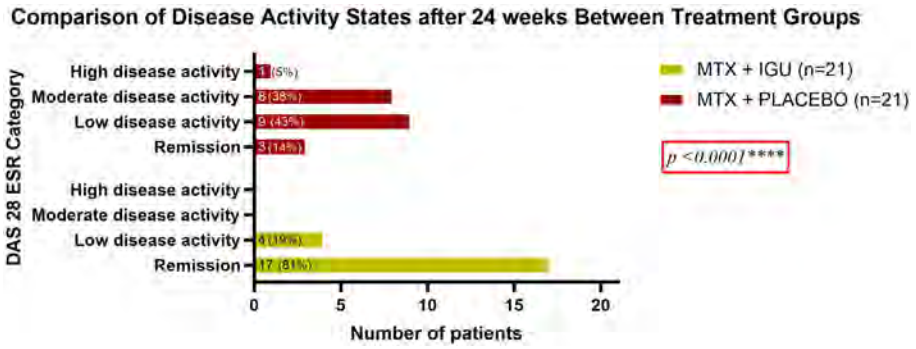
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Iguratimod (IGU), an oral synthetic disease-modifying antirheumatic drug (DMARD), has shown significant efficacy and safety in rheumatoid arthritis (RA) when combined with methotrexate (MTX) or as monotherapy in Japanese studies [Ishiguro et al, 2013]. RA is a chronic autoimmune disease that, without early intervention, leads to irreversible joint damage and disability. Prompt initiation of DMARDs is crucial to achieving remission and preventing complications. Despite IGU's therapeutic benefits, no randomized controlled trial (RCT) has evaluated its role in Indian RA patients. This study aims to assess the efficacy and safety of IGU with MTX in newly diagnosed, DMARD-naïve Indian patients with active RA.

Methods: In this randomized, double-blind, placebo-controlled, single-centre trial, eligible Indian patients (≥18 years, either gender) with DMARD-naïve, early active RA (ACR-EULAR 2010 criteria, DAS28-ESR ≥3.2, disease duration < 1 year) were



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



randomized 1:1 to receive either IGU (25 mg twice daily) plus MTX or placebo plus MTX. MTX was initiated at 20mg/week for 12weeks and increased to 25mg/week for the next 12weeks. Randomization was performed using computer-generated block randomization. The primary endpoint was the proportion of patients achieving remission or low disease activity (LDA) per DAS28-ESR at 12 and 24 weeks. Secondary endpoints included ACR20/50/70 response rates at 24 weeks and incidence of adverse events. Statistical analysis was performed using GraphPad Prism v10, with p< 0.05 considered significant.

Results: A total of 42 patients were randomized and treated. Baseline characteristics were comparable: mean age was 49 ±12 years (test) and 48±10 years (placebo); females constituted 90% and 86%, respectively. High disease activity was observed in 90% (test) and 95% (placebo). At 12weeks, remission or LDA was achieved in 71% of the test group (28% remission, 43% LDA) versus 14% (5% remission, 9% LDA) in the placebo group (p=0.0009). By 24weeks, 100% in the test group (81% remission, 19% LDA) and 57% in the placebo group (14% remission, 43% LDA) achieved remission or LDA (p< 0.0001). ACR20/50/70 responses were significantly higher in the test group (100%, 88%, 59%) than in the placebo group (71%, 57%, 9%) (p< 0.0001). Adverse events were comparable (test: 5, placebo: 4, p >0.99), including leukopenia, transaminitis, GI symptoms, and mouth ulcers.

Conclusion: Iguratimod plus methotrexate demonstrated superior efficacy and safety in newly diagnosed DMARD-naïve Indian RA patients, with incremental benefits over placebo for remission or LDA (57% at 12weeks, 43% at 24weeks) and ACR responses (ACR20:29%, ACR50:31%, ACR70:50%). These findings align with Japanese studies [Ishiguro et al, 2013].

Disclosure: M. JALANATHAN: None; **M. Ali Mirza**: None; **V. Parimi**: None; **S. S**: None; **T. Ramineni**: None.

Abstract Number: 0496

Certolizumab Pegol Shows a Higher Retention Rate Compared to JAK Inhibitors in Patients with Rheumatoid Arthritis, Regardless of Baseline Rheumatoid Factor Levels. A Multicenter Retrospective Study

Mitndbaim Parra[1], Rafaela Ortega-Castro[2], Jerusalén Calvo[3], Francisco Jose Cepas[4], Montserrat Robustillo-Villarino[5], Andres Zuniga-Vera[5], Ana Martinez-Feito[6], Chamaida Plasencia-Rodríguez[7], Ester Costa-Moya[8], Delia Taverner-Torrent[8], Luis Sainz Comas[9], Cesar Diaz-Torne[9], Virginia Ruiz-Esquide[10], Cynthia Rojas[11], Lourdes Martin-de la Sierra Lopez[12], Laura Jimenez-Rodriguez[12], David Velasco-Sanchez[12], Regina Fara Garcia[13], Antonio Juan-Mas[14], Marina soledad Moreno Garcia[15], Ana Valeria Acosta Alfaro[16], Santiago Muñoz[17], Maria Martín López[18], Raquel Zas[19], FRANCISCO JAVIER GODOY NAVARRETE[20], Isabel Anon Onate[21], Fernando Ortiz-Márquez[22], Natalia Mena Vazquez[23], Paula Estrada-Alarcón[24], Lourdes Ladehesa[25], Alejandro Escudero Contreras[3] and Clementina López Medina[26], [1]1. Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., Cordoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University of Cordoba, Spain, Cordoba, Andalucia, Spain, [3]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [4]University of Cordoba, Cordoba, Spain, [5]Department of Rheumatology, Hospital Universitario de la Plana, Vila-real, Castellón, Spain, Vila-real, Castellón, Spain, [6]Hospital Universitario La Paz, Madrid, Madrid, Spain, [7]Hospital Universitario La Paz, MADRID, Spain, [8]Hospital Sant Joan Reus, Reus, Spain, [9]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [10]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [11]Hospital Clinic, Barcelona, Spain, [12]Hospital General Universitario de Ciudad Real, Ciudad Real, Spain, [13]Hospital Son Llatzer, Palma, Spain, [14]Son Llazter University Hospital, Madrid, Spain, [15]Hospital Universitario Miguel Servet, Zaragoza, Spain, [16]Hospital Universitario Infanta Sofia; Universidad Europea de Madrid; FIIB HUIS-HUHEN, Madrid, Spain, [17]Hospital Universitario Infanta Sofía; Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Spain, [18]Hospital 12 de Octubre, Madrid, Spain, [19]Hospital Universitario Doce de Octubre, Madrid, Spain, [20]Jaen University Hospital, Spain, Jaen, Spain, [21]Hospital Universitario de Jaen, Jaen, Spain, [22]Department of Rheumatology, Hospital Regional Universitario de Málaga, Málaga, Spain, Malaga, Spain, [23]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [24]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [25]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [26]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid factor (RF) is an antibody directed against the Fc fragment of IgG that plays a key role in the development of rheumatoid arthritis (RA). Elevated RF levels have been associated with greater disease severity and higher cardiovascular risk. In this context, patients with high RF levels may present a higher inflammatory burden and a lower response to JAK inhibitors (JAKi), possibly due in part to the use of these drugs at low doses. However, previous studies have shown that certolizumab pegol (CZP) offers comparable efficacy in patients with both high and low RF levels.

The objectives of this study were: a) to compare, in RA patients with high RF levels, the efficacy of CZP vs. JAKi after 12 months of treatment and b) to compare the drug retention rate between both groups after 3 years of follow-up.

Methods: Longitudinal, retrospective, multicenter study including RA patients treated with CZP or JAKi (tofacitinib, baricitinib, upadacitinib, or filgotinib) between 2010 and 2024. Baseline RF levels and disease activity (DAS28) were collected at baseline, 6 months, and 12 months, along with treatment start and discontinuation dates. Propensity score (PS) matching was used to match CZP and JAKi groups based on age, prior use of b/tsDMARDs, and concomitant methotrexate use. Change in DAS28 was compared between groups using Student's t-test. Log-rank tests and Kaplan-Meier curves were used to evaluate treatment retention rates in both groups according to RF levels, considering RF ≥200 IU/mL as "very high" levels.

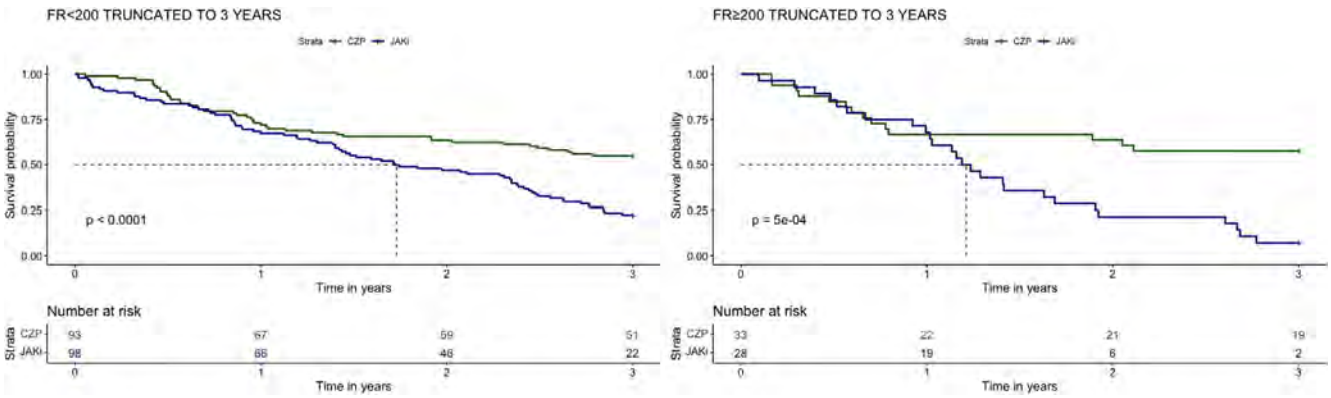


Figure 1. Three-year drug retention rate in patients with (A) RF ≥200 IU/mL and (B) RF <200 IU/mL.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 364 patients (234 CZP and 126 JAKi) with available RF titers were included. After PS matching, both groups (126 patients each) were comparable in age, sex, disease duration, baseline DAS28, concomitant methotrexate use, and prior b/tsDMARD use.

In patients with RF ≥200 IU/mL, those treated with CZP showed a greater reduction in DAS28 compared to JAKi (-2.12 ±1.29 vs. -1.41±1.38, p=0.098), although this did not reach statistical significance. In patients with RF < 200 IU/mL, the change in DAS28 was similar between groups (-1.66±1.38 vs. -1.89±1.41, p=0.339).

In patients with RF ≥200 IU/mL, the 3-year drug retention rate was significantly higher in CZP vs. JAKi (survival probability 57.6% [95%CI 43.0–77.2] vs. 7.1% [95%CI 1.9%–27.2], p< 0.001). Similarly, in patients with RF < 200 IU/mL, CZP also showed a higher retention rate (survival probability 54.8% [95%CI 45.6%–66.0%] vs. 22.5% [95%CI 15.5%–32.4%], p< 0.001).

Conclusion: In patients with high RF levels (≥200 IU/mL), CZP showed a trend toward greater clinical efficacy after 12 months compared to JAKi. In addition, CZP demonstrated a higher drug retention rate than JAKi in both high and low RF subgroups, suggesting greater persistence of CZP regardless of RF levels in the general RA patient population.

Disclosure: M. Parra: None; **R. Ortega-Castro**: None; **J. Calvo**: None; **F. Cepas**: None; **M. Robustillo-Villarino**: None; **A. Zuniga-Vera**: None; **A. Martinez-Feito**: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **E. Costa-Moya**: None; **D. Taverner-Torrent**: None; **L. Sainz Comas**: None; **C. Diaz-Torne**: None; **V. Ruiz-Esquide**: None; **C. Rojas**: None; **L. Martin-de la Sierra Lopez**: None; **L. Jimenez-Rodriguez**: None; **D. Velasco-Sanchez**: None; **R. Fara Garcia**: None; **A. Juan-Mas**: None; **M. Moreno Garcia**: None; **A. Acosta Alfaro**: None; **S. Muñoz**: Janssen, 1, 2, 5, 6, 7; **M. Martín López**: None; **R. Zas**: None; **F. GODOY NAVARRETE**: None; **I. Anon Onate**: None; **F. Ortiz-Márquez**: None; **N. Mena Vazquez**: None; **P. Estrada-Alarcón**: None; **L. Ladehesa**: None; **A. Escudero Contreras**: None; **C. López Medina**: None.

Abstract Number: 0497

Drug Survival and Discontinuation Reasons of Eight Biological Disease-Modifying Antirheumatic Drugs in 1,182 Patients with Rheumatoid Arthritis: A Retrospective Study Using the Niigata Orthopedic Rheumatoid Arthritis Database (NOSRAD)

Nariaki Hao and Naoki Kondo, Division of Orthopedic Surgery, Niigata University Medical and Dental General Hospital, Niigata, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: To retrospectively evaluate drug survival and reasons for discontinuation of eight biological disease-modifying antirheumatic drugs (bDMARDs) in rheumatoid arthritis (RA) patients using the Niigata Orthopedic Rheumatoid Arthritis Database (NOSRAD).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient backgrounds of bDMARDs-naïve group.

n=784	IFX (n=64)	ETN (n=217)	TCZ (n=253)	ADA (n=62)	ABT (n=89)	GLM (n=62)	CZP (n=26)	SAR (n=11)	*P*-value
Female, n (%)	51 (79.7)	183 (84.3)	194 (76.7)	43 (69.4)	69 (77.5)	54 (87.1)	20 (76.9)	6 (54.5)	.040
Age (years), mean±SD	55.1±14.9	56.4±15.1	56.7±16.3	57.8±13.3	70.4±10.5	67.4±13.2	56.8±14.0	68.6±9.3	<.001
Disease duration (years), mean±SD	9.8±10.0	10.5±9.6	7.1±9.1	10.9±10.5	11.2±12.5	14.6±12.0	7.6±7.5	16.0±16.0	<.001
DAS28-ESR, mean±SD	4.22±1.29	3.89±1.31	3.74±1.50	3.28±1.19	4.65±1.39	2.93±0.76	2.39±0.86	3.62±0.94	<.001
MTX use, n (%)	59 (92.2)	134 (62.2)	104 (41.1)	48 (77.4)	32 (36.0)	47 (67.7)	17 (65.4)	6 (54.5)	<.001
MTX dose (mg/week), mean±SD	7.4±1.8	7.2±2.1	7.7±2.2	8.1±2.5	7.3±3.2	7.9±2.3	7.4±2.3	6.7±0.9	.248
PSL use, n (%)	28 (43.8)	113 (52.1)	97 (38.3)	22 (35.5)	54 (60.7)	29 (46.8)	10 (38.5)	7 (63.6)	.002
PSL dose (mg/day), mean±SD	7.9±9.5	6.9±5.5	8.0±8.2	5.2±2.6	5.7±3.4	4.2±2.1	6.5±2.6	6.1±2.9	.012

Methods: Of 1,517 RA patients registered in NOSRAD from May 2001 to August 2022, 1,182 who received at least one of the following bDMARDs were included: abatacept (ABT), adalimumab (ADA), certolizumab pegol (CZP), etanercept (ETN), golimumab (GLM), infliximab (IFX), sarilumab (SAR), and tocilizumab (TCZ). We analyzed patient backgrounds, drug survival, and discontinuation reasons in three groups: the overall cohort, bDMARDs-naïve group, and switch group. The chi-square test and Kruskal–Wallis test were used for categorical and continuous variables, respectively. Drug survival was estimated using the Kaplan–Meier method, and compared by log-rank test. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

Results: In the naïve group (n = 784), significant inter-drug differences were observed in sex, age, disease duration, the 28-joint Disease Activity Score with erythrocyte sedimentation rate (DAS28-ESR), concomitant methotrexate (MTX) use, concomitant prednisolone (PSL) use, and PSL dose. In the switch group (n = 398), significant differences were found in age, disease duration, DAS28-ESR, MTX use, PSL dose, and whether the drug was used as a second or fourth-line agent.

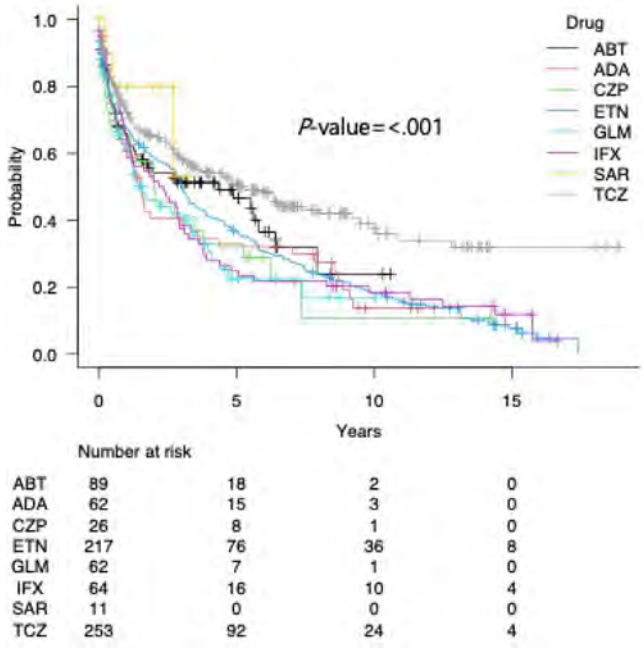


Figure 1. Kaplan-Meier drug-survival rates for each drug in bDMARDs-naïve group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Reasons for discontinuation.

n=1182	IFX (n=74)	ETN (n=280)	TCZ (n=390)	ADA (n=86)	ABT (n=145)	GLM (n=95)	CZP (n=53)	SAR (n=59)	*P*-value
Lack of effectiveness, n (%)	30 (40.5)	96 (34.3)	65 (16.7)	33 (38.4)	33 (22.8)	27 (28.4)	22 (41.5)	14 (23.7)	<.001
Adverse events, n (%)	15 (20.3)	56 (20)	65 (16.7)	15 (17.4)	19 (13.1)	16 (16.8)	13 (24.5)	5 (8.5)	.256
Infection, n (%)	3 (4.1)	27 (9.6)	29 (7.4)	3 (3.5)	8 (5.5)	4 (4.2)	5 (9.4)	0	.082
Pulmonary disorders, n (%)	0	5 (1.8)	3 (0.8)	1 (1.2)	3 (2.1)	0	0	0	.495
Hepatic disorder, n (%)	0	3 (1.1)	4 (1)	1 (1.2)	0	1 (1.1)	0	0	.830
Dermatologic disorder, n (%)	2 (2.7)	1 (0.4)	9 (2.3)	7 (8.1)	1 (0.7)	5 (5.3)	1 (1.9)	2 (3.4)	.002
Cardiovascular disease, n (%)	0	1 (0.4)	4 (1)	0	2 (1.4)	0	0	0	.633
Malignant tumour, n (%)	3 (4.1)	2 (0.7)	3 (0.8)	1 (1.2)	1 (0.7)	3 (3.2)	2 (3.8)	0	.084
Others, n (%)	7 (9.5)	17 (6.1)	13 (3.3)	2 (2.3)	4 (2.8)	3 (3.2)	5 (9.4)	3 (5.1)	.091
Remission/good response, n (%)	2 (2.7)	15 (5.4)	14 (3.6)	6 (7)	1 (0.7)	2 (2.1)	2 (3.8)	1 (1.7)	.180
Patient preference, n (%)	0	10 (3.6)	13 (3.3)	0	6 (4.1)	2 (2.1)	1 (1.9)	1 (1.7)	.409
Transfer, n (%)	15 (20.3)	64 (22.9)	47 (12.1)	5 (5.8)	13 (9)	16 (16.8)	2 (3.8)	5 (8.5)	<.001
Others, n (%)	1 (1.4)	3 (1.1)	3 (0.8)	0	0	3 (3.2)	1 (1.9)	0	.277
Unknown, n (%)	4 (5.4)	4 (1.4)	22 (5.6)	5 (5.8)	7 (4.8)	1 (1.1)	1 (1.9)	1 (1.7)	.072

Among the naïve group, TCZ showed the highest drug survival rate (50.8% at 5 years and 37.6% at 10 years). The 5-/10-year survival rates of other bDMARDs were as follows: ABT 46.6%/24.0%, IFX 25.0%/18.5%, ETN 36.6%/18.1%, GLM 22.6%/17.0%, ADA 32.3%/13.7%, and CZP 33.0%/10.8%. In the switch group, ABT had the highest survival rate (42.6% at 5 years and 21.3% at 10 years), followed by TCZ (38.2%/21.1%), ADA (18.3%/18.3%), ETN (15.1%/8.1%), CZP (17.3% at 5 years; 10-year data unavailable), GLM (14.8%; 10-year data unavailable), and IFX (10.0%; 10-year data unavailable). The proportion of discontinuation due to insufficient efficacy was 40.5% for IFX, 34.3% for ETN, 16.7% for TCZ, 38.4% for ADA, 22.8% for ABT, 28.4% for GLM, 41.5% for CZP, and 23.7% for SAR. Discontinuation due to adverse events was 20.3%, 20.0%, 16.7%, 17.4%, 13.1%, 16.8%, 24.5%, and 8.5%, respectively. Discontinuation due to non-adverse reasons (remission or good response, patient preference, transfer, others, or unknown) was 29.7%, 34.3%, 25.4%, 18.6%, 18.6%, 25.3%, 13.2%, and 13.6%, respectively.

Conclusion: In the naïve group, TCZ had the highest survival; in the switch group, ABT did. Switching was associated with lower survival. ABT was often used in older patients and had fewer discontinuations due to adverse events, suggesting its potential utility in elderly RA. This large-scale, single-center, long-term study highlights the importance of selecting and dosing bDMARDs appropriately to maintain long-term efficacy.

Disclosure: N. Hao: None; **N. Kondo**: None.

Abstract Number: 0498

Pharmacokinetic Similarity of DRL_AB, a Proposed Biosimilar Abatacept (Orencia®): Results from a Randomized, Single Dose, Double-Blind, Parallel Arm, Comparative Pharmacokinetic Study in Healthy Subjects by the Intravenous Route.

Naveen Reddy[1], Narendra Maharaj[1], Pramod Kumar Reddy[1], Mansi Dhananjaya Jakhade[1], Maria Velinova[2] and Vendel Kemény[3], [1]Biologics, Dr. Reddy's Laboratories Ltd., Hyderabad, India, Hyderabad, India, [2]ICON – Early Development Services Van Swietenlaan 6 9728 NZ, Groningen, Netherlands, Groningen, Netherlands, [3]ICON Magyarország Kft. Fázis I-es Klinikai Farmakológiai Vizsgálóhely Rottenbiller utca 13 1077, Budapest, Hungary, Budapest, Hungary

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Dr. Reddy's-abatacept (DRL_AB) is being developed as a biosimilar to the reference product (RP) (RP-US licensed Orencia®) and the reference medicinal product (RMP) (RMP-EU approved Orencia®). The primary objective of this study was to demonstrate PK similarity of DRL_AB compared to RP and RMP as well as between RP and the RMP following a single 750 mg intravenous (i.v.) dose.

Methods: This Phase I study included healthy male subjects assigned to DRL_AB, RP, or RMP in a randomized, double-blind, parallel group design. The primary objective was to demonstrate PK similarity in terms of $AUC_{0\text{-}inf}$, with secondary objectives including other PK parameters ($AUC_{0\text{-}t}$, C_{max}, t_{max}), safety, tolerability and immunogenicity comparison.

Results: A total of 114 male subjects aged 18 and 50 years with a BMI between 19.3 kg/m^2 and 29.6 kg/m^2 participated in the study. Baseline characteristics were similar between groups. The $AUC_{0\text{-}inf}$ for abatacept following treatment with DRL_AB was comparable to RP and RMP. The 90% CI of T/R ratio for $AUC_{0\text{-}inf}$ fell within the bioequivalence criteria (80.00%, 125.00%) when DRL_AB compared with RP or RMP. After correcting for the protein content differences, the 90% CI of T/R ratio for $AUC_{0\text{-}inf}$ being 105.27% [99.00%, 111.93%]) for DRL_AB compared to RP and 111.29% [105.15%, 117.78%]) for DRL_AB as compared to RMP. The 90% CIs for $AUC_{0\text{-}inf}$ were maintained within the bioequivalence criteria after excluding ADA positive subjects. The secondary PK endpoints ($AUC_{0\text{-}t}$, C_{max}, t_{max}) were also comparable between groups. The 90% CI of T/R ratios for $AUC_{0\text{-}t}$ and C_{max} fell within the bioequivalence criteria (80.00%, 125.00%) when DRL_AB was compared with RP or RMP. The tmax for abatacept was similar for DRL_AB versus RP or RMP and this was confirmed by non-parametric analysis. A total of 84 subjects experienced at least one Treatment-emergent adverse event (TEAE), with a similar proportion across the DRL_AB (68.4%), RP (81.1%), and RMP (71.8%) groups. Most of the TEAEs (222 out of 238) were of mild severity, while 16 were considered moderate. The incidence of moderate TEAEs was 15.8% in DRL_AB, 8.1% in RP, and 7.7% in RMP groups. Adverse events of special interest (AESIs) like hypersensitivity, viral infections, and other infections were similar between groups. Eight AESIs were reported in 8 subjects (7.0%); 2 (5.3%) in DRL_AB, 2 (5.4%) in RP, and 4 (10.3%) in RMP groups. No deaths or serious adverse events (SAEs) were reported, and all TEAEs resolved without sequelae. The incidence of treatment-emergent ADA positivity was 15.8% in the DRL_AB group, 8.1% in the RP group, and 10.3% in the RMP group. Number of subjects reporting ADA CTLA-4 tested positive with the treatments DRL_AB, RP and RMP were 5 (13.2%), 1 (2.7%), 3 (7.7%) on Day 85 respectively and all these were reported first time at Day 85. The number of subjects reporting neutralizing antibody (NAb) positivity with DRL_AB, RP, and RMP were 0, 1 (2.7%), 0 on Day 15, and 2 (5.3%), 2(5.4%), 3 (7.7%) on Day 85, respectively. The incidence of ADA and NAb, as well as ADA titer, were comparable following treatment with DRL_AB, RP, and RMP.

Conclusion: The study demonstrated PK similarity of DRL_AB with RP and RMP in healthy subjects, with comparable safety and immunogenicity profiles.

Disclosure: N. Reddy: Dr. Reddy's Laboratories Ltd, 3; **N. Maharaj**: Dr. Reddy's Laboratories Ltd, 3; **P. Reddy**: Dr. Reddy's Laboratories Ltd, 3; **M. Jakhade**: Dr. Reddy's Laboratories Ltd, 3; **M. Velinova**: ICON – Early Development Services Van Swietenlaan, 3; **V. Kemény**: ICON Magyarország Kft. Fázis I-es Klinikai Farmakológiai Vizsgálóhely, 3.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0499

Olokizumab Improves Patient-Reported Outcomes in Rheumatoid Arthritis MTX-IR and TNF-IR Patients up to 106 Weeks (Results from Clinical Phase III Program)

Roy Fleischmann[1], Eugen feist[2] and Josef Smolen[3], [1]Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, [2]Helios Department of Rheumatology, Vogelsang-Gommern, Germany, [3]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria, Vienna, Austria

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Olokizumab (OKZ), an interleukin-6 inhibitor approved in several countries for managing rheumatoid arthritis (RA), was evaluated in previous phase III RCTs, demonstrating changes in patient-reported outcomes (PROs) for MTX-IR and TNFi-IR patients with active disease [1-3]. This study extends those findings to assess the long-term sustainability of OKZ's effects on PROs up to 106 weeks (ClinicalTrials.gov number, NCT03120949).

Methods: We included all randomized for OKZ or PBO in phase III clinical program patients (with active rheumatoid arthritis and fulfilled the ACR/EULAR 2010 revised classification criteria). We analyzed data using the Intent-To-Treat population, utilizing a mixed model for repeated measures to assess changes from baseline. Results are expressed as least squares mean (LSM) and standard error. The proportion of patients reporting improvement from baseline at week 24 ≥ the minimal clinically important difference (MCID) in HAQ-DI scores was determined using thresholds of ≥0.22 and ≥0.3 points. Post hoc responder analyses were conducted to estimate the percentages of patients who reported improvement from baseline ≥ MCID of 10 mm for PtGA and pain VAS scores; 2.5 points for SF-36 PCS and MCS scores, 5 points for individual domains; and 4 points for the FACIT-F. Discontinuations or use of rescue medication classified subjects as non-responders.

Results: Overall 1982 patients were included. MTX-IR and TNFi-IR populations were comparable at baseline with a mean age of 53 years, mostly women (77-90%), 56-61% using glocucorticoids, and DAS28-CRP approximately 5.87-5.99 (RA duration, CDAI, intolerance to ≥15 mg/week MTX dose and HAQ-DI were numerically higher in TNFi-IR patients). At week 12, OKZ biweekly (q2w), and every four weeks (q4w), compared with placebo showed significantly greater LSM improvements in all PROs for MTX-IR patients (Table 1). For TNFi-IR patients, improvements were not as large as in MTX-

Table 1. Change from baseline in patient-reported outcome scores at weeks 12, 24 and 106 (as observed). MTX-IR #p<0.050 compared to the baseline value within the group. All p values are nominal. FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; MCS, mental component summary; PCS, physical component summary; PtGA, patient global assessment of disease activity; q2w, every 2 weeks; q4w, every 4 weeks; SF-36, Short Form 36 Health Survey; VAS, visual analogue scale.

Patient-reported outcomes	Least square mean (standard error)						
	Week 12			Week 24		Week 106	
	OKZ q2w N = 532	OKZ q4w N = 549	PBO N = 386	OKZ q2w N = 532	OKZ q4w N = 549	OKZ q2w N = 532	OKZ q4w N = 549
HAQ-DI	-0.61 (0.02)#	-0.59 (0.02)#	-0.35 (0.03)#	-0.68 (0.02)#	-0.68 (0.02)#	-0.76 (0.03)#	-0.81 (0.03)#
PtGA (VAS) (mm)	-30.97 (0.96)#	-30.86 (0.94)#	-18.23 (1.05)#	-35.54 (1.00)#	-35.81 (0.97)#	-38.38 (1.09)#	-38.37 (1.07)#
PhGA (VAS) (mm)	-41.50 (0.77)#	-42.15 (0.75)#	-22.43 (0.87)#	-46.76 (0.80)#	-48.12 (0.78)#	-53.23 (0.86)#	-54.42 (0.85)#
Pain (VAS) (mm)	-33.72 (0.97)#	-33.24 (0.96)#	-18.39 (1.06)#	-38.24 (1.02)#	-38.81 (0.99)#	-41.48 (1.10)#	-41.13 (1.08)#
FACIT Fatique	8.54 (0.38)#	8.63 (0.38)#	4.85 (0.41)#	9.63 (0.40)#	10.02 (0.39)#	10.85 (0.43)#	11.81 (0.42)#
EQ-5D	21.06 (0.91)#	21.32 (0.89)#	11.31 (1.01)#	23.41 (0.95)#	24.07 (0.92)#	28.03 (1.03)#	27.68 (1.01)#
SF-36 PCS	7.83 (0.32)#	7.46 (0.32)#	4.07 (0.33)#	9.50 (0.34)#	9.39 (0.33)#	10.86 (0.36)#	11.39 (0.36)#
SF-36 MCS	5.56 (0.38)#	5.77 (0.37)#	3.41 (0.40)#	5.71 (0.39)#	6.44 (0.38)#	6.73 (0.43)#	7.40 (0.42)#

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 Change from baseline in patient-reported outcome scores at weeks 12, 24 and 106 (as observed). TNFa-IR #p<0.050 compared to the baseline value within the group. All p values are nominal. FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; MCS, mental component summary; PCS, physical component summary; PtGA, patient global assessment of disease activity; q2w, every 2 weeks; q4w, every 4 weeks; SF-36, Short Form 36 Health Survey; VAS, visual analogue scale.

	Least square mean (standard error)						
Patient-reported outcomes	Week 12			Week 24		Week 106	
	OKZ q2w N = 124	OKZ q4w N = 127	PBO N = 69	OKZ q2w N = 124	OKZ q4w N = 127	OKZ q2w N = 124	OKZ q4w N = 127
HAQ-DI	-0.53 (0.05)#	-0.43 (0.05)#	-0.39 (0.06)#	-0.67 (0.05)#	-0.56 (0.05)#	-0.77 (0.06)#	-0.59 (0.06)#
PtGA (VAS) (mm)	-25.90 (2.04)#	-26.22 (1.98)#	-21.37 (2.56)#	-32.80 (2.17)#	-33.09 (2.08)#	-35.41 (2.31)#	-35.54 (2.30)#
PhGA (VAS) (mm)	-43.73 (1.49)#	-40.92 (1.43)#	-30.99 (2.14)#	-47.76 (1.59)#	-47.77 (1.49)#	-58.23 (1.68)#	-53.29 (1.68)#
Pain (VAS) (mm)	-29.84 (2.08)#	-29.80 (2.02)#	-18.60 (2.62)#	-34.87 (2.21)#	-34.72 (2.12)#	-40.37 (2.35)#	-39.72 (2.34)#
FACIT Fatique	9.05 (0.79)#	7.63 (0.76)#	5.19 (1.00)#	9.11 (0.83)#	8.39 (0.79)#	10.72 (0.88)#	9.34 (0.87)#
EQ-5D	20.08 (2.00)#	20.28 (1.92)#	10.98 (2.58)	24.02 (2.11)#	24.04 (2.01)#	27.46 (2.26)#	26.07 (2.24)#
SF-36 PCS	7.73 (0.68)#	6.12 (0.65)#	4.28 (0.78)#	9.44 (0.71)#	8.53 (0.68)#	11.54 (0.76)#	8.79 (0.75)#
SF-36 MCS	4.64 (0.73)#	4.12 (0.70)#	0.82 (0.92)	3.94 (0.77)#	5.18 (0.73)#	5.87 (0.82)#	6.62 (0.82)#

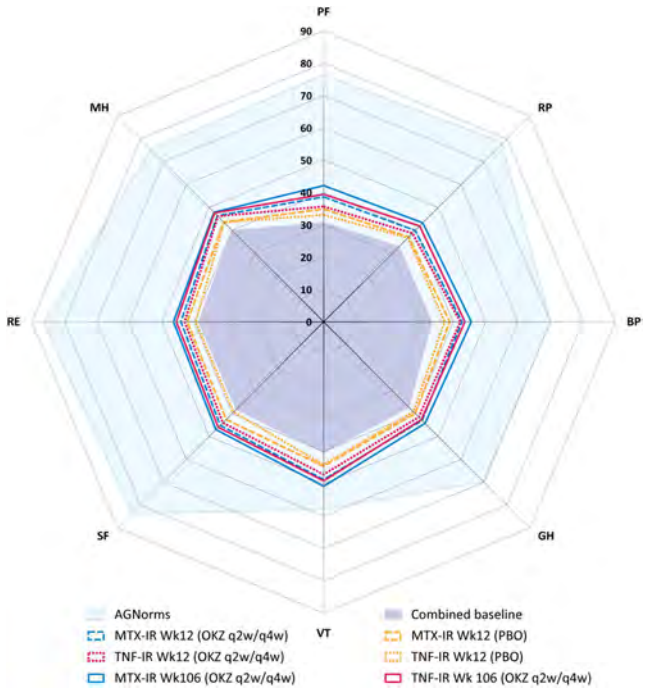


Figure 1. SF-36 domain changes from baseline to week 106 Abbreviations: AGNorms, age- and gender-matched normative values; BP, bodily pain; GH, general health; MTX-IR, methotrexate irresponsive; MH, mental health; OKZ, olokizumab; PF, physical functioning; PBO, placebo; RE, role emotional; RP, role physical; SF-36, the Short Form health survey is a 36-item, patient-reported survey; SF, social functioning; TNFi-IR, tumor necrosis factor inhibitors irresponsive; VT, vitality

IR population (Table 2). PRO improvements were sustained through week 106. Post hoc analyses demonstrated a higher proportion of patients receiving OKZ attained improvements ≥ MCID vs. placebo ($p< 0.05$) at week 12 in all (except EQ-5D) reported PROs for both MTX-IR and TNFi-IR. Numbers needed to treat (NNT) ranged from 4.6 to 11.6 with OKZ q2w vs 10.6 to 13.5 with OKZ q4w (MTX-IR), and from 7.6 to 27.8 and 7.5 to 34.5 (TNFi-IR), accordingly. SF-36 domain changes from baseline to week 106 presented (Figure 1).

References

1. Nasonov E, et al. Ann Rheum Dis. 2022;81(4):469-479.
2. Smolen JS, et al. N Engl J Med. 2022;387(8):715-726.
3. Feist E, et al. Ann Rheum Dis. 2022 Dec;81(12):1661-1668.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Treatment with OKZ over 106 weeks resulted in statistically significant and clinically meaningful improvements in PROs compared to baseline in both MTX-IR and TNFi-IR RA patients. The improvements in PRO's were observed as early as week 12, were sustained and improved further to week 106. There were no discernible differences between the two regimens of OKZ regarding patient reported outcomes.

Disclosure: R. Fleischmann: AbbVie/Abbott, 2, Almirall, 2, Artiva Biotherapeutics, 2, Atomwise, 2, Biohaven Pharmaceuticals, 2, Bristol-Myers Squibb(BMS), 2, Cyoxone, 2, Deep Cure, 2, Dren Bio, 2, ECOR, 2, Eli Lilly, 2, Galvani, 2, Gates Bio, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Halia, 2, ImmuneMed, 2, Immunovant, 2, InventisBio, 2, Istesso, 2, Janssen, 2, Janux, 2, Monte Rosa, 2, Novartis, 2, Overland, 2, Pfizer, 2, Synact, 2, TPG, 2, UCB, 2, Vyne, 2, Xencor, 2; **E. feist**: AB2Bio, 6, AbbVie/Abbott, 6, Alfasigma, 6, AstraZeneca, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Galapagos, 6, Hexal, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6, Roche/Chugai, 6, R-Pharm, JSC, 6, Sandoz, 6, Sanofi, 6, Sobi, 6, UCB, 6; **J. Smolen**: AbbVie/Abbott, 5, 6, Ananda, 6, AstraZeneca, 5, 6, Astro, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Celltrion, 6, Chugai-Roche, 6, Galapagos, 5, 6, Immunovant, 6, Janssen, 6, Lilly, 5, 6, Pfizer, 6, R-Pharma, 6, Samsung, 6, Sandoz, 6, Sanofi, 6.

Abstract Number: 0500

Is Methotrexate Tapering Possible In Stable RA? Clinical Observations of Methotrexate Tapering At Two Tertiary Care Centers

Sama Hajizadeh[1], Tarun Sharma[1], Peri Newman[2], Julio Hernandez[2], Rayford June[3], Erik Lehman[2], Nicole Wilson[1], Nancy Olsen[4] and Sharon Banks[5], [1]Allegheny Health Network, Pittsburgh, PA, [2]Penn State Health/ Penn State College of Medicine, Hershey, PA, [3]Penn State College of Medicine/Lebanon VA Medical Center, Hummelstown, PA, [4]Penn State University/Milton S Hershey, Hershey, PA, [5]Penn State Milton S. Hershey Medical Center, Hershey, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In our previous Rheumatoid Arthritis Medication TAPering (RheumTAP) cohort study of patients with stable RA in remission on biologics +/- methotrexate at Allegheny Health Network (AHN), we found that the risk of flare was the lowest and insignificant with tapering methotrexate (MTX) alone (13%) compared to tapering biologics1. This result needed to be confirmed in larger studies given that current guideline recommendations on this topic are based on low level evidence. Thus, we built a collaborative cohort between AHN and Penn State Health (PSH) of patients with stable RA on MTX. A patient and provider survey within both cohorts demonstrated interest in MTX tapering2.

Methods: A retrospective cohort of adult patients with RA in sustained remission or low disease activity for at least 6 months while on MTX was created at both centers. The data were longitudinally followed between 1/1/2020-12/31/2022. The following tapering related variables were analyzed: reasons for MTX taper (remission, conception, infection, surgery, CKD, malignancy, side effect), tapering strategy (reduction vs. discontinuation), and tapering speed (gradual vs. rapid) along with others listed in Table 1. Clinical outcomes were compared between the groups at 3 and 6 months and the end of follow-up. Flare was defined as CDAI >10 and/or any worsening of disease activity leading to initiation of rescue therapy i.e. restoration of MTX dose or change of current therapy.

Results: Our cohort included a total of 100 patients with stable RA in remission or low disease activity while on MTX. Of these, 77 underwent MTX tapering. Baseline comparisons are listed in Table 1. MTX taper was initiated by the providers in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variables	MTX taper group (N=77)	MTX continuation group (N=23)
Demographics:		
Age, yrs	61.3 ± 13.0	63.7 ± 12.4
BMI	30.5 ± 5.9	30.5 ± 4.7
Gender, female	57 (74%)	15 (65.2%)
Race, white	64 (84.2%)	21 (91.3%)
RA related:		
Duration of RA, yrs	6.0 (2.7, 12.4)	10.0 (4.2, 15.0)
Seropositivity (RF and/or CCP)	64 (84.21%)	19 (90.48%)
Erosive status	18 (23.68%)	5 (23.81%)
RF titer, U/mL	95 (45.5, 304)	38 (15, 157)
CCP titer, U/mL	250 (168.5, 292.5)	250 (56.8, 400)
Symptom onset to treatment, months	6.1 (1.3, 36)	3 (0, 22.2)
Baseline CDAI	4 (2, 6)	2 (2, 4)
End visit CDAI	2.5 (0, 5.5)	4 (3, 5)
Concurrent DMARD use	10 (27.78%)	8 (58.33%)
Taper related variables:		
Duration of MTX use, median, months	52.6 (23.1, 89.7)	120.8 (42.1, 181.8)
Improvement on MTX initiation	75 (97.4%)	20 (90.9%)

Comparison of MTX taper vs Continuation groups

Variable	MTX taper group (N=77)	MTX continuation group (N=23)	p-value (Chi-square)
Flare rate, 3 months	32 (41.55%)	3 (13.04%)	0.01
Flare rate, end of follow up period	34 (44.16%)	9 (37.5%)	0.67
Proportion in remission, 6 months	61 (79.22%)	13 (56.52%)	0.029
Re-achieved remission after flare	30 (88.24%)	5 (55.5%)	0.44

Clinical Outcomes of MTX taper vs Continuation Groups

62 (80.5%) patients with the most common reason for tapering being remission (64%), followed by side effects/transaminitis (25%). Most patients had a MTX dose reduction (85.7%) vs stoppage (4.29%). Tapering was gradual (< 50% reduction over >4 weeks) in most patients. Median reduction in MTX dose was by 25% and 24 (31.58%) patients reduced MTX by at least 50%. There was no statistically significant difference in overall flare risk between MTX taper vs continuation groups at the end of follow-up period [n=34 (44.16%) vs 9 (37.5%), p=0.67] (Table 2). However, risk of flare was significantly higher in taper vs continuation group at 3 months [32 (41.55%) vs 3 (13.04%), RR 3.1, 95%CI 1.07-9.45, p=0.036]. There was no significant difference in proportion of patients in remission at 6 months [61 (79.2%) vs 13 (56.5%), RR 1.4, 95%CI 0.96 to 2.04, p=0.078]. In the taper group, most patients (88.24%) re-achieved remission with restoration of MTX dose.

Conclusion: In our retrospective cohort study on the outcomes of MTX tapering in well-controlled RA, patients who tapered or stopped MTX were no more likely to experience a flare by end of follow up period or sustain remission at 6 months after tapering than patients that continued MTX. However, the risk of flare after 3 months of MTX tapering was 3 times higher than MTX continuation which highlights the importance of close follow up after tapering. Most patients re-achieved remission with restoration of MTX after a flare.

1. Tageldin et al, Rheumatology. 2023
2. Newman et al, Arthritis Rheumatol. 2024

Disclosure: S. Hajizadeh: None; **T. Sharma**: None; **P. Newman**: None; **J. Hernandez**: None; **R. June**: None; **E. Lehman**: None; **N. Wilson**: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5; **S. Banks**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0501

Phase 1b Study of SBT777101, an Engineered CAR-T-Regulatory Cell Product, in Patients With Rheumatoid Arthritis: Interim Demographics and Safety

Sarah Baxter[1], Ari Bitton[2], Victor Yuan[2], Fawad Aslam[3], Gregory Challener[4], Jonathan Graf[5], Melissa Griffith[6], Tamiko Katsumoto[7], Minna Kohler[8], Elena Massarotti[9], Larry Moreland[10], Allison Rosenthal[11], Jeffrey Sparks[9], Steven Vlad[12], Janeth Yinh[13], Andrew Clauw[14], Sally Arai[15], Alexander Carvidi[5], Angela Chavez[16], Olivia Gabriel[17], Rita Gyurko[17], Megan Hall[18], Jennifer Seifert[19], Emma Stainton[15], Michelle Blake[1], Sabrina Fox-Bosetti[2], Mark Fromhold[1], Mindy Jensen[20], Herve Lebrec[2], Sean O'Bryan[2], Amanda Pace[21], Mei-Lun Wang[2], Yuanyuan Xiao[2], Joseph Arron[2] and Jeffrey Bluestone[22], [1]Sonoma Biotherapeutics, Seattle, WA, [2]Sonoma Biotherapeutics, San Francisco, CA, [3]Mayo Clinic, Arizona, Scottsdale, AZ, [4]MGH, Boston, MA, [5]UCSF, San Francisco, CA, [6]University of Colorado, Aurora, CO, [7]Division of Immunology and Rheumatology, Stanford University, Millbrae, CA, [8]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [9]Brigham and Women's Hospital, Boston, MA, [10]University of Colorado, Denver, CO, [11]Mayo Clinic, Phoenix, [12]Tufts Medicine, Boston, MA, [13]Massachusetts General Hospital, Boston, MA, [14]Univ of Colorado, Aurora, CO, [15]Stanford, Palo Alto, CA, [16]Tufts, Boston, MA, [17]BWH, Boston, MA, [18]Mayo, Scottsdale, AZ, [19]University of Colorado and Oklahoma Medical Research Foundation, Aurora, CO, [20]Sonoma Bio, Seattle, [21]Sonoma Bio, Seattle, WA, [22]Sonoma Biotherapeutics, South San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Regulatory T cells (T_{regs}) modulate inflammation, maintain self-tolerance, and promote tissue repair, and thus hold promise as a versatile therapeutic tool. Autologous polyclonal T_{regs} have a favorable safety profile but equivocal efficacy in autoimmune disorders.

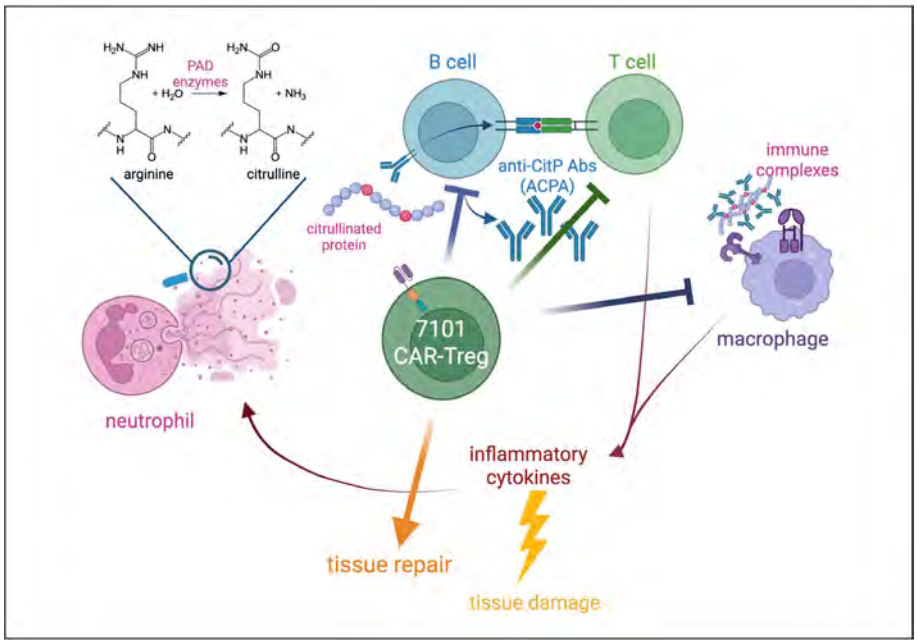


Figure 1: SBT777101 CAR-T regulatory cells target citrullinated intracellular proteins (Cit-P). Cit-P are released by activated neutrophils undergoing NETosis. Cit-P can serve as autoantigens leading to the formation of anti-CitP antibodies (ACPA), citrullinated peptides presented on HLA-DRB*01 "shared epitope" alleles activate T cells, and Cit-P-ACPA immune complexes activate macrophages. These innate and adaptive immune processes amplify inflammation leading to tissue damage. Engineered Tregs expressing a CAR reactive to Cit-P are hypothesized to down-modulate multiple inflammatory processes and promote tissue repair.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

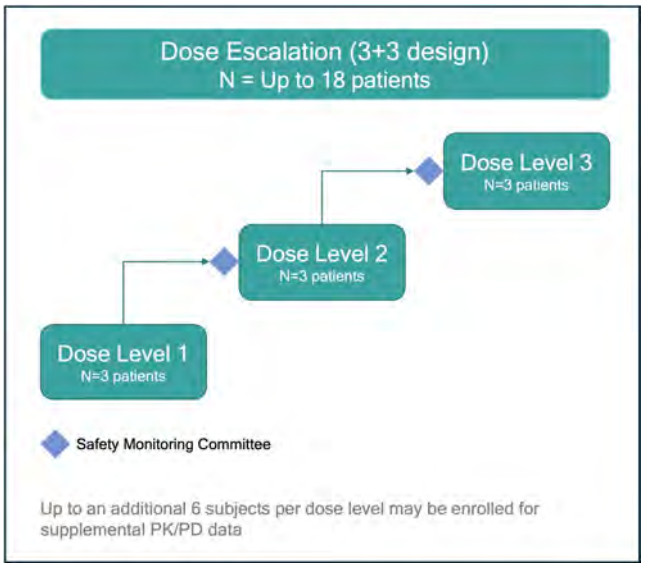


Figure 2: REGULATE-RA is a first-in-human phase 1 dose-escalation study. Each dose level cohort comprises three participants, with a safety monitoring committee evaluation prior to escalation to the next dose cohort.

Engineered T_{regs} offer a novel approach by introduction of a chimeric antigen receptor (CAR) specific for tissue- or disease-associated antigens. SBT777101 is an autologous T_{reg} product transduced with a CAR specific for citrullinated proteins (Cit-P), which are present in the inflamed synovium of participants with rheumatoid arthritis (RA, Figure 1). Unlike cytotoxic CAR-T therapies, SBT777101 may restore balance to the immune system without cell destruction. Potential mechanisms of action include bystander suppression of antigen presenting cells and effector T cells, IL2 consumption, and immunomodulatory cytokine production to promote immune homeostasis and tissue repair.

REGULATE-RA is an ongoing first-in-human, phase 1 study to evaluate the safety and tolerability of autologous CAR-T_{reg} therapy targeting Cit-P in patients with refractory RA. Exploratory endpoints include the assessment and characterization of SBT777101's pharmacokinetic (PK) profile, pharmacodynamic (PD) parameters, mechanism of action (MOA), and preliminary efficacy.

Table 1: Participant Characteristics. Eight participants have been enrolled in the study as of April 2025; four participants have received drug product. Abbreviations: Pt – Participant; AI- American Indian; AN- Alaska Native; RF- Rheumatoid Factor; ACPA- Anti-Citrullinated Protein Antibodies; CRP- C-reactive Protein; ESR- Erythrocyte Sedimentation Rate; DAS28- Disease Activity Score; DMARDs- disease modifying antirheumatic drugs; b/ts- Biologic/targeted-synthetic; MOA- Mechanism of Action

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8
Sex at birth	F	F	F	F	F	F	M	F
Age (years)	42	58	68	64	51	52	39	26
Race/Ethnicity	White, Hispanic	White, Hispanic	White, Hispanic	White, not Hispanic	White, not Hispanic	White, and AI or AN, not Hispanic	White, not Hispanic	White, not Hispanic
Disease duration (years)	18.1	4.8	2.3	28.1	7.5	14.7	3.3	10.1
RF status (titer)	Positive (35)	Positive (323)	Positive (90)	Positive (>1200)	Positive. (75)	Positive (779)	Positive. (728)	Positive (59)
ACPA status (titer)	Positive (200)	Positive (203)	Positive (32)	Positive (250)	Positive (>250)	Positive (256)	Positive (199)	Positive (250)
CRP (mg/L)	2.6	4.6	2.0	3.0	20	0.4	11	4.4
ESR (mm/hr)	ND	20	16	11	8	26	69	15
Swollen joints – 28 joint count	7	20	5	6	20	11	10	14
Tender joints – 28 joint count	4	21	7	22	27	17	19	11
DAS28-CRP	3.7	6.5	4.5	6.2	7.6	5.3	6.2	5.2
Total number of prior DMARDs	10	12	6	14	9	8	5	6
Number of prior b/ts DMARDs of different MOA	5	5	4	6	4	5	3	3

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The study includes RA participants aged 18-70 with moderate-to-severe active disease (DAS28-CRP≥3.2). Participants must have demonstrated an inadequate response to, or intolerance of, at least 3 biologic or targeted synthetic disease-modifying antirheumatic drugs with differing MOA.

SBT777101 is prepared by transduction of autologous T_{regs} with a Cit-P-specific CAR and is administered in a 3+3 dose-escalation design (figure 2).

Participants are monitored for adverse events and clinical response over a 48-week study period. PK, PD, and MOA are evaluated in peripheral blood and, where available, synovial biopsies. All participants are encouraged to enter a 15-year long-term follow-up study for safety evaluation.

Results: Prior to patient enrollment, a manufacturing process for SBT777101 was established and shown to produce consistent yield, functionality, and molecular signatures from both healthy donors and RA participants. For dosed participants, the yield and molecular signatures of manufactured products have remained consistent with the preclinical manufacturing results.

As of April 2025, four participants have received infusions of SBT777101, and no dose-limiting toxicities have been observed. Four additional participants are enrolled but are not yet dosed. Patient characteristics are summarized in Table 1.

All four dosed participants tolerated the infusion, with no cytokine release syndrome, neurotoxicity, or other immune-mediated toxicities detected. Clinical assessments and biomarker analyses are ongoing to assess changes in disease activity, systemic inflammation and T_{reg} activity.

Conclusion: To date, CAR-T_{reg} therapy targeting Cit-P demonstrates a favorable safety profile in this early phase study. Ongoing enrollment and follow-up will provide additional insights into characterization, pharmacodynamics and efficacy outcomes.

Disclosure: S. Baxter: Sonoma Biotherapeutics, 3; **A. Bitton**: None; **V. Yuan**: None; **F. Aslam**: None; **G. Challener**: None; **J. Graf**: None; **M. Griffith**: AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Sonoma, 5; **T. Katsumoto**: Beyond Meat, 12, Unrestricted grant, Sanofi, 5; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **E. Massarotti**: Argenyx, 2, Caballetta, 2, EMD Serono, 2, Janux, 2, Kezar, 2, Otsuka, 2, Pioneering Medicine Partnerships, 2, Sonoma Biotherapeutics, 5, Xencor, 2; **L. Moreland**: None; **A. Rosenthal**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **S. Vlad**: None; **J. Yinh**: Janssen, 2, Springer, 9; **A. Clauw**: None; **S. Arai**: None; **A. Carvidi**: None; **A. Chavez**: None; **O. Gabriel**: None; **R. Gyurko**: None; **M. Hall**: None; **J. Seifert**: None; **E. Stainton**: None; **M. Blake**: Sonoma Biotherapeutics, 3, 11; **S. Fox-Bosetti**: Sonoma Biotherapeutics, 3; **M. Fromhold**: Sonoma Bio, 3; **M. Jensen**: Sonoma Bio, 3; **H. Lebrec**: Amgen, 12,, 11, Sonoma Biotherapeutics, Inc., 3; **S. O'Bryan**: Sonoma Biotherapeutics, 3; **A. Pace**: None; **M. Wang**: None; **Y. Xiao**: None; **J. Arron**: Sonoma Biotherapeutics, 12,, 3, 4; **J. Bluestone**: Gilead, 4.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0502

Real-World Comparative Safety of Tocilizumab and Sarilumab in Rheumatoid Arthritis: A Multi-Center Observational Study

Satani Sharkas[1], Saeed Abughazaleh[2] and Dariush Jahandideh[3], [1]Boston Medical Center - Brighton, Brighton, MA, [2]Boston Medical Center - Brighton, Brighton, [3]Boston Medical Center - Brighton, Boston

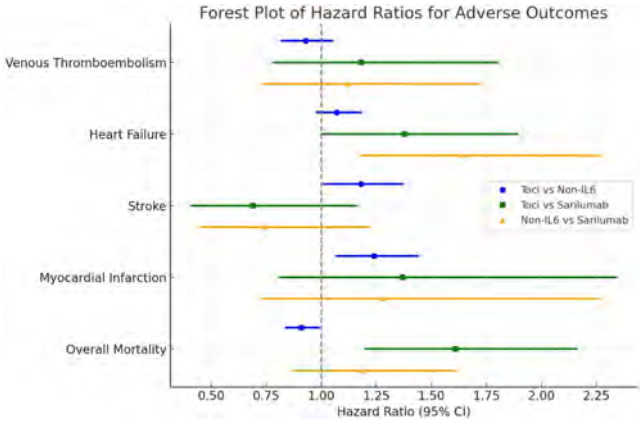
SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin-6 (IL-6) inhibitors, including tocilizumab and sarilumab, are approved treatments for rheumatoid arthritis (RA). However, comparative safety data on cardiovascular outcomes and all-cause mortality in real-world settings remain limited. We conducted a multi-cohort analysis to evaluate the safety profiles of IL-6 inhibitors compared to non-IL6 regimens, including sensitivity analyses by follow-up duration and sex.

Methods: We performed a retrospective cohort study using the TriNetX Global Collaborative Network, including adult RA patients treated with tocilizumab, sarilumab, or no IL-6 inhibitors. Patients were grouped into three matched cohorts: Non-IL6, Tocilizumab-only, and Sarilumab-only. Propensity score matching (1:1) was conducted using demographics, comorbidities, medications, and laboratory variables. Outcomes included all-cause mortality, myocardial infarction (MI), stroke, heart failure (HF), and venous thromboembolism (VTE) over a 5-year follow-up. Sensitivity analyses included a truncated 3-year window and sex-stratified comparisons.

Results: Matched cohorts included 17,958 patients per group (non-IL6 vs Tocilizumab), 1,855 per group (non-IL6 vs Sarilumab), and 1,992 per group (Tocilizumab vs Sarilumab). Tocilizumab was associated with higher mortality than Sarilumab (5.6% vs 3.7%; risk difference [RD]: 1.9%; hazard ratio [HR]: 1.61; 95% CI: 1.20–2.16; p = 0.001), and higher mortality than non-IL6 (6.4% vs 5.5%; RD: –1.0%; p < 0.001). Mortality did not significantly differ between Sarilumab and Non-IL6. MI, stroke, HF, and VTE risks were comparable across all groups, with findings consistent in the 3-year analysis. In sex-stratified analyses, mortality was significantly higher in males treated with Tocilizumab versus Sarilumab (8.3% vs 4.8%; RD: 3.5%; p = 0.049; HR: 1.86; 95% CI: 1.04–3.32), while the difference in females was not significant.



Forest Plot of Hazard Ratios for Adverse Outcomes: Tocilizumab vs Non-IL6, Tocilizumab vs Sarilumab, and Non-IL6 vs Sarilumab

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Outcome	Tocilizumab (n)	Events (%)	Sarilumab (n)	Events (%)	Risk Difference (95% CI)	Risk Ratio (95% CI)	Hazard Ratio (95% CI)	P-value
Overall Mortality	1,986	112 (5.6%)	1,985	74 (3.7%)	+0.019 (0.006–0.032)	1.51 (1.14–2.02)	1.61 (1.20–2.16)	0.001
Myocardial Infarction	1,936	31 (1.6%)	1,942	24 (1.2%)	+0.004 (–0.004–0.011)	1.30 (0.76–2.20)	1.37 (0.81–2.34)	0.242
Stroke	1,941	24 (1.2%)	1,952	37 (1.9%)	–0.007 (–0.014–0.001)	0.65 (0.39–1.09)	0.69 (0.41–1.16)	0.159
Heart Failure	1,834	86 (4.7%)	1,843	68 (3.7%)	+0.010 (–0.003–0.023)	1.27 (0.93–1.74)	1.38 (1.00–1.89)	0.049
Venous Thromboembolism	1,895	46 (2.4%)	1,908	42 (2.2%)	+0.002 (–0.007–0.012)	1.10 (0.73–1.67)	1.18 (0.78–1.80)	0.428

Clinical Outcomes: Risk Differences, Hazard Ratios, and Odds Ratios for Adverse Events Across Matched Cohorts

Conclusion: In this large real-world RA cohort, sarilumab was associated with lower all-cause mortality than tocilizumab, particularly among male patients. Cardiovascular outcomes were similar across treatments. These findings support the need for individualized IL-6 inhibitor selection, with consideration of treatment duration and patient sex.

Disclosure: S. Sharkas: None; **S. Abughazaleh**: None; **D. Jahandideh**: None.

Abstract Number: 0503

Impact of Olokizumab on Pain in Rheumatoid Arthritis: a Meta-analysis

Andrey E. Karateev[1], **Sofia Kuzkina**[2], Alina Egorova[3] and Elena Y. Polishchuk[1], [1]V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, [2]R-Pharm, Moscow, Russia, [3]R-Pharm JSC, Moscow, Russia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Pain is one of the most debilitating symptoms of rheumatoid arthritis (RA) and a major contributor to reduced quality of life. Persistent joint pain severely limits daily activities and can lead to work disability, emotional distress, and diminished overall well-being. Olokizumab (OKZ) is a humanized anti-interleukin-6 monoclonal antibody approved for RA. We aimed to evaluate the impact of OKZ on patient-reported pain in RA through a meta-analysis of clinical and observational studies.

Methods: We systematically searched PubMed and eLibrary databases for studies reporting pain outcomes in RA patients treated with OKZ (Figure 1). Eligible sources included 3 randomized controlled trials (RCTs) and 4 real-world observational studies with pain assessments at 12 and 24 weeks. 3 RCTs and 2 observational studies were included for evaluation, while other 2 observational trials were currently withdrawn due to need in recalculation of certain measures of variance. A random-effects model (DerSimonian–Laird) was used to pool mean changes from baseline and mean differences versus placebo with corresponding 95% confidence intervals. When necessary, medians were converted to means and standard deviations based on Wan et al.'s method. All analyses were conducted in R (v4.4.1).

Results: In the RCTs, OKZ treatment led to clinically meaningful pain improvement compared to placebo. At 12 weeks, the mean reduction in patient pain (VAS) from baseline was greater in OKZ groups than in placebo by –14.05 points (95% CI –19.51 to –8.58) for 64 mg q2w and –13.89 (95% CI –19.52 to –8.56) for 64 mg q4w (both $p < 0.001$). These benefits were sustained or enhanced by Week 24, with OKZ-treated patients maintaining significantly greater pain reduction than placebo.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

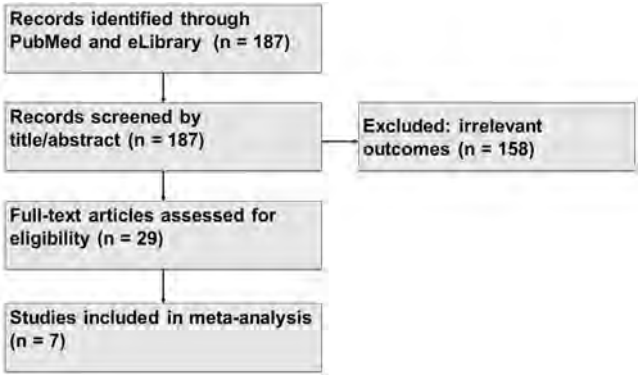


Figure 1. Literature search and study selection flowchart for pain outcomes

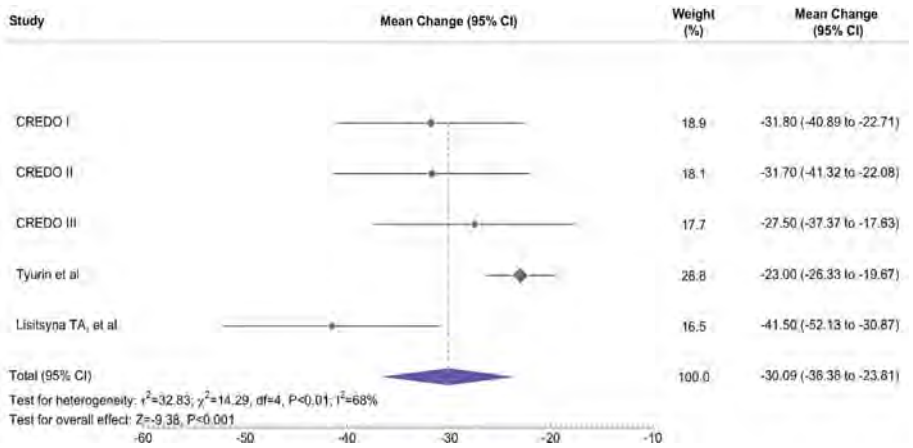


Figure 2. Pooled mean change in pain (VAS 0–100) at Week 12 with OKZ 64 mg q4w. CI- confidence interval

Due to the non-comparative nature of observational studies they only revealed changes of pain in OKZ groups vs baseline. Real-world data echoed the findings in RCTs: patients on OKZ experienced robust pain relief over 12 weeks (figure 2), and the changes were sustained through week 24 when the mean pain reduction with OKZ reached -37.13 (-42.66 – 31.59) mm from baseline (Tyurin et al had data by 12 weeks only) (figure 3). All the changes vs baseline were significant (p< 0,001).

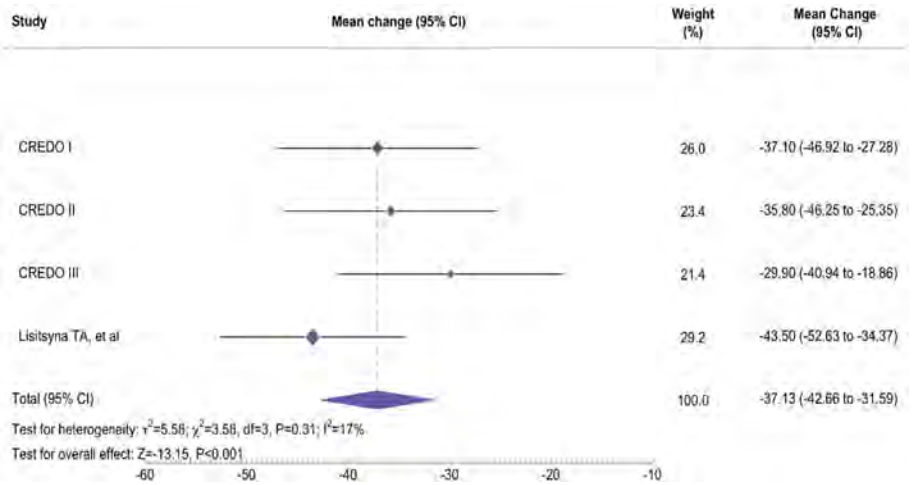


Figure 3. Pooled mean change in pain at Week 24 with OKZ 64 mg q4w CI- confidence interval

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: OKZ significantly reduces patient-reported pain in RA, with greater improvements than placebo observed in clinical trials and similarly robust pain relief reported in real-world studies. These meta-analytic findings underscore the value of OKZ as an effective therapy for managing pain in RA.

Disclosure: A. Karateev: None; **S. Kuzkina**: R-Pharm, JSC, 3; **A. Egorova**: R-Pharm, JSC, 3; **E. Polishchuk**: None.

Abstract Number: 0504

Spatial profiling of gene signatures in synovial tissue informs treatment strategy for Rheumatoid Arthritis

Vincent Wong[1], Katie Lowe[2], Annabelle Small[3], Christopher Altmann[3], Susanna Proudman[4], Malcolm Smith[2], Wittaya Suwakulsiri[5], Ranjeny Thomas[5], Chung Hoow Kok[6] and Mihir Wechalekar[7], [1]College of Medicine and Public Health, Bedford Park, South Australia, Australia, [2]Flinders University, Adelaide, South Australia, Australia, [3]Flinders University, Bedford Park, South Australia, Australia, [4]The University of Adelaide, Adelaide, Victoria, Australia, [5]Frazer Institute, University of Queensland, Brisbane, Queensland, Australia, [6]Centre for Cancer Biology, and Clinical Health Sciences, University of South Australia, Adelaide, South Australia, Australia, [7]Flinders Medical Centre and Flinders University, Bedford Park, South Australia, Australia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) shows heterogeneous therapeutic responses that may reflect diversity within synovial tissue (ST). We aimed to identify gene signatures that predict Adalimumab response and provide an initial spatial transcriptomic validation of their cellular context.

Methods: ST biopsies were obtained from 30 anti-citrullinated protein antibody–positive, treatment-naïve RA patients (symptom duration ≤ 12 months) classified by immunohistochemistry as TNF- or T-cell-dominant. Bulk RNA-seq data for all protein-coding genes were analysed with glmnet LASSO-regularised logistic regression to derive a small set of genes predictive of remission versus non-remission using baseline samples from patients targeted for Adalimumab treatment (remission and non-remission at 3 months; DAS CRP< 2.6). The resulting model was also applied on baseline samples from Abatacept and triple-DMARD non-responders. The predictive genes were mapped onto high-resolution Stereo-seq spatial transcriptomic sections. Spatially resolved expression was assessed against cell-type annotations derived from unsupervised clustering and marker genes.

Results: A concise set of genes clearly separated early-remission from non-remission cases in the Adalimumab cohort. When applied to baseline samples from other treatment arms, the predictive model identified one patient in the Abatacept cohort and six patients in the triple-DMARD cohort as having remission-like profiles, indicating scope for treatment re-stratification. Preliminary Stereo-seq analysis suggests these genes may be more locally enriched in baseline ST from early-remission cases (Figure 1).

Conclusion: This study identifies key synovial gene signature that predicts clinical response to Adalimumab and demonstrate, for the first time, its restricted spatial expression in specific ST cell populations. Although preliminary, these Stereo-seq data strengthen the biological plausibility of the signature and support future validation in larger spatial cohorts. Incorporating qPCR-based testing of these genes in routine biopsies could expedite personalised therapeutic decisions in RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

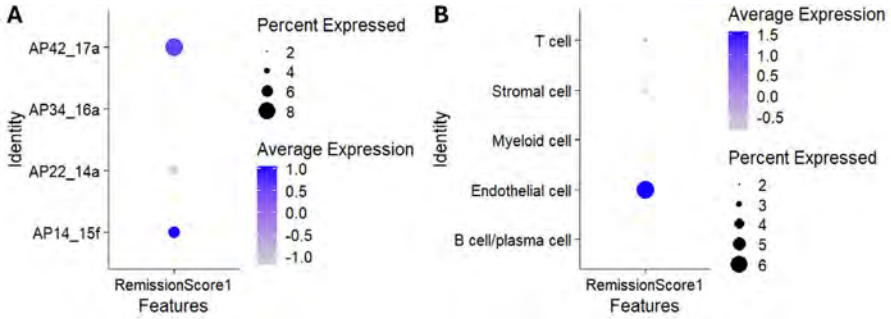


Figure 1. Spatially informed predictive-gene expression module in Rheumatoid Arthritis patients. A) Dot plot of the Adalimumab RemissionScore1 module across four Stereo-seq patient samples. Dot size denotes the percentage of spatial bins expressing the score; colour scale reflects average expression (blue = higher). Sample AP14_15f received Adalimumab and achieved early clinical remission (DASCRP < 2.6 at 3 months). B) Same score mapped to cell-type annotations. Highest expression localises to endothelial cells, with lower levels in T cells and negligible signal in other cell populations.

Spatially informed predictive-gene expression module in Rheumatoid Arthritis patients.

Disclosure: V. Wong: None; **K. Lowe**: None; **A. Small**: None; **C. Altmann**: None; **S. Proudman**: Boehringer-Ingelheim, 6, Janssen, 6; **M. Smith**: None; **W. Suwakulsiri**: None; **R. Thomas**: AbbVie/Abbott, 2, CSL, 2; **C. Kok**: None; **M. Wechalekar**: GlaxoSmithKlein(GSK), 5, Janssen, 5.

Abstract Number: 0505

Use of Upadacitinib in Real-World Clinical Practice: Patient Characteristics and Glucocorticoid-Sparing Effect

Virginia Ruiz-Esquide[1], Lourdes Mateo[2], Carolina Pérez García[3], Hye Sang-Park[4], Susana Holgado[5], María Aparicio[6], Beatriz Frade[7], Juan Camilo Sarmiento-Monroy[8], Annika Nack[9], Felipe Julio Ramirez Garcia[10], José Gomez-Puerta[11] and Raimon Sanmartí[1], [1]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [2]Hospital Trías i Pujol, Barcelona, Catalonia, Spain, [3]Hospital del Mar, Barcelona, Spain, [4]Hospital Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [5]Hospital Germans Trias i Pujol, Barcelona, Catalonia, Spain, [6]Hospital Germans Trías i Pujol, Badalona, Catalonia, Spain, [7]Hospotal Clínic de Barcelona, Barcelona, Catalonia, Spain, [8]Hospital Clinic Barcelona, Barcelona, Spain, [9]Hospital Germans Trias i Pujol, Barcelona, Spain, [10]Rheumatology Department, Hospital Clinic and IDIBAPS of Barcelona, Barcelona, Spain, [11]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0470–0505) Rheumatoid Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: While clinical trials have demonstrated the efficacy of upadacitinib (UPA), real-world data are essential to understand patient characteristics and assess its effectiveness in routine clinical practice.

This study aims to describe a real-world cohort of patients with rheumatoid arthritis (RA) initiating treatment with UPA, analyzing cohort characteristics, UPA efficacy, and its glucocorticoid (GC)-sparing effect.

Methods: This was a multicenter observational study of patients with active RA who started UPA. Prescription decisions were made at the discretion of rheumatologists, and patients were included consecutively. Epidemiological and clinical data were collected. Concomitant GC treatment was assessed at baseline and at follow-up visits after 1, 3, 6, and 12 months.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographics, RA characteristics and treatment for total cohort

	Patients n=99
Demographics	
Age	55.17 ± 12.0
Age ≥ 65 years old	19.2%
Female	89.9%
BMI	26.1 ± 5.4
Ever smoker	37.9%
RA Characteristics	
Age at diagnosis	41.61 ± 12.9
RA duration	13.52 ± 9.2
RF+	70.7%
ACPA+	67.7%
TJC	7.81 ±6.8
SJC	6.12 ± 6.0
CRP mg/L	4.9 ± 11.7
ESR mm/h	23.81 ± 20.4
DAS28-ESR	4.75 ± 1.5
CDAI	25.91 ± 14.6
Erosive disease	61.6%
Treatment	
Use of GC	69.7%
GC dose mg/d	7.37 ± 5.0
Combination with scDMARD	53.5%
Number of previous DMARD	1.59 ± 0.8
Number of previous b/tsDMARD	2.80 ± 2.0
UPA as 1st line of advanced therapy	7.0%
UPA as 2nd line of advanced therapy	22.2%
UPA as ≥3rd line of advanced therapy	70.7%
Comorbidities	
RCDI	1.07 ± 1.5
Hypertension	21.2%
DM2	6.1%
Fragility fracture	3.0%
Depression	15.2%
Lung disease	15.6%

Data presented as mean ± 1 standard deviation or n (%). BMI: body mass index, RF: rheumatoid factor, ACPA: anti-citrullinated peptides antibodies, TJC: tender joint count, SJC: swollen joint count, CRP: C reactive protein, PHS: patient global health, ESR: erythrocyte sedimentation rate, GC: glucocorticoid, b/ts DMARD: biologic or targeted synthetic Disease-Modifying Antirheumatic Drugs, RCDI: rheumatic disease co-morbidity index, DM2: diabetes mellitus type 2.

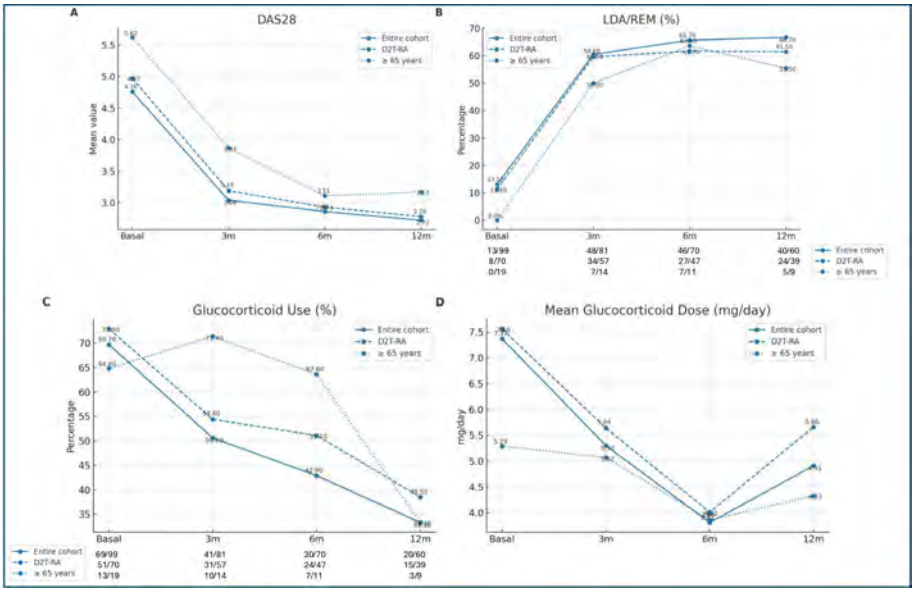
Data presented as mean ± 1 standard deviation or n (%). BMI: body mass index, RF: rheumatoid factor, ACPA: anti-citrullinated peptides antibodies, TJC: tender joint count, SJC: swollen joint count, CRP: C reactive protein, PHS: patient global health, ESR: erythrocyte sedimentation rate, GC: glucocorticoid, b/ts DMARD: biologic or targeted synthetic Disease-Modifying Antirheumatic Drugs, RCDI: rheumatic disease co-morbidity index, DM2: diabetes mellitus type 2.

Results: A total of 99 patients were included, 89.9% of whom were female, with a mean (SD) age of 55.17 (12.0) years. Among them, 19.2% were ≥65 years old. At UPA initiation, patients generally had moderate to high disease activity, with a mean (SD) DAS28 score of 4.75 ± 1.5. UPA was used in combination with csDMARDs in 53.5% of patients and with GCs in 69.7%, with a mean (SD) dose of 7.37 ± 5.0 mg/dL. Seventy percent of patients started UPA as ≥3rd-line advanced therapy (additional data in Table 1). At 3, 6, and 12 months, 82%, 71%, and 61% of patients continued UPA treatment, while 60.5%, 65%, and 67% had achieved low disease activity or remission, respectively.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Evolution of disease activity and GC use and dose

	DAS28	LDA/REM	GC	Dosis GC
Entire cohort				
Basal n=99	4.76 ± 1.5	13.1% (13/99)	69.7% (69/99)	7.37 ± 5.0 mg/d
3m n=81	3.04 ± 1.3	60,5% (49/81)	50.6% (41/81)	5.30 ± 3.4 mg/d
16m n=70	2.86 ± 1.2	65.7% (46/70)	42.9% (30/70)	3.81 ± 1.9 mg/d
12m n=60	2.72 ± 0.9	66.7% (40/60)	33.3% (20/60)	4.91 ± 3.5 mg/d
D2T-RA (UPA started as ≥3rd line of advanced therapy)				
Basal n=70	4.97± 1.4	11.4% (8/70)	72.9% (51/70)	7.56 ± 5.2 mg/d
3m n=57	3.19 ± 1.4	59.6% (34/57)	54.4% (31/57)	5.64 ± 3.6 mg/d
6m n=47	2.93 ± 1.2	61.7% (29/47)	51.1% (24/47)	4.01± 1.9 mg/d
12m n=39	2.78 ± 0.9	61.5% (24/39)	38.5% (15/39)	5.66 ± 3.8 mg/d
≥ 65 years old				
Basal n=19	5.62 ± 1.3	0%	64.8% (13/19)	5.29 ± 3.0 mg/d
3m n=14	3.87 ± 2.0	50% (7/14)	71.4% (10/14)	5.07 ± 3.8 mg/d
6m n=11	3.11 ± 1.6	63.6% (7/11)	63.6% (7/11)	3.86 ± 1.4 mg/d
12m n=9	3.17 ± 0.8	55.5% (5/9)	33.3% (3/9)	4.33 ± 1.2 mg/d



Evolution since baseline and up to 12 months of follow up of: A DAS28, B proportion of patients in LDA (low disease activity)/ REM (remission), C proportion of patients in treatment with GC and D mean dose of GC, in de entire cohort (full line), D2T-RA (dashed line) and patients ≥65 years old (dotted line).

A GC-sparing effect was observed throughout the study period. At baseline, nearly 70% of patients were receiving GC therapy. By 3 months, 20% had discontinued GC, and by 12 months, only 33% remained on GC. The mean GC dose also decreased (Table 2).

A secondary analysis compared patients who started UPA as ≥3rd-line advanced therapy (D2T-RA) with those who initiated it as 1st or 2nd-line treatment. Patients in the ≥3rd-line group had significantly longer disease duration (15.1 vs. 9.58 years, p=0.005) and had received more csDMARDs before starting advanced therapy. However, they were more likely to start UPA as monotherapy (45% in D2T-RA vs. 70% in non-D2T-RA). No significant differences were observed in baseline disease activity or GC use. Treatment response and GC-sparing effects were similar in both groups.

Among patients ≥65 years old, combination therapy with csDMARDs was used in 50% of patients, and 65% received GC, with a mean (SD) dose of 5.29 ± 3.0 mg/d. Treatment response and GC-sparing effects were comparable to those in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients ≤65 years old. Over the follow-up period, nine infections were reported, including two severe cases. UPA was discontinued in two patients.

Conclusion: Most patients in this real-world cohort initiated UPA as ≥3rd-line advanced therapy. Half started UPA in combination with csDMARDs, and 70% received concurrent GC therapy. A significant early reduction in GC use was observed, with over half of GC-treated patients discontinuing GC by 12 months. UPA was effective in both older patients and those with refractory disease.

Disclosure: V. Ruiz-Esquide: None; **L. Mateo**: None; **C. Pérez García**: None; **H. Sang-Park**: None; **S. Holgado**: None; **M. Aparicio**: None; **B. Frade**: None; **J. Sarmiento-Monroy**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6; **A. Nack**: None; **F. Ramirez Garcia**: AbbVie, 2, 6, Eli Lilly, 6, Johnson and Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, UCB, 2, 6; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **R. Sanmartí**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Eli Lilly, 5, 6, Merck/MSD, 5, 6, Pfizer, 5, 6, Roche, 5, 6.

Abstract Number: 0506

Discovery-based Identification of Non-canonical Autoantibody Specificities in Ro Seronegative Sjögren's Disease Using High-content Human Proteome Arrays

Songyuan Yao[1], Christina Lawrence[1], Hope Christakos[2], Charmaine Lopez-Davis[1], Bhuwan Khatri[1], Tommi C. Taylor[1], Astrid Rasmussen[1], Kiely Grundahl[2], R Hal Scofield[1], Blake M. Warner[3], Judith James[1], Joel Guthridge[1], Christopher J. Lessard[1] and **A. Darise Farris**[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, [3]National Institutes of Health, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical tests for Sjögren's disease (SjD) often overlook Ro-seronegative (Ro^{Neg}) cases, leading to delayed or missed diagnoses. Identifying additional serum autoantibodies could improve diagnostic accuracy and enhance disease management. Proteome-wide autoantibody screening in Ro^{Neg} SjD cases was previously reported using HuProt 3.2 arrays (CDI Labs) with 19,500 proteins[1]. This expanded study utilizes HuProt 4.0 arrays with >21,000 human proteins. The aim of the study was to identify 24 autoantibody specificities that best discriminate Ro^{Neg} SjD (n=86; 30% ESSDAI≥5) from healthy control (HC, n=24) and other rheumatic disease (OD, n=44; 45% SLE, 39% RA, 9% SSc, 7% other) groups for further development of a multiplex Luminex assay.

Methods: Arrays were probed as per the manufacturer except serum incubations were for 18h at 5°C. IgG (635 nm), and IgA (532 nm) signals were collected using anti-human, heavy chain-specific IgG and IgA secondary antibodies. After assisted alignment of signals with array templates using a novel algorithm-based alignment tool, data were quantile-normalized, and positive thresholds (avg + 3*SD of HCs) for antibody binding to each protein established. Fisher's exact tests ($p< 0.1$) identified specificities bound more commonly in the Ro^{Neg} group compared to HC and OD groups. Protein specificity enrichments were explored using STRING. A machine learning pipeline (2/3 training, 1/3 testing) incorporating chi-square selection, random forest-based feature selection, and logistic regression was used for classification.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

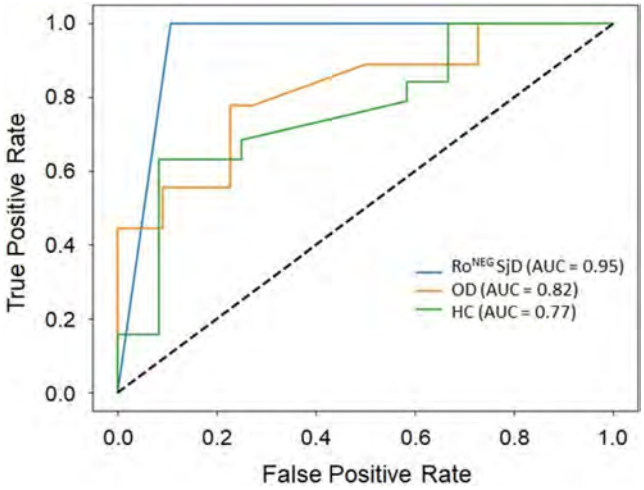


Figure 1. A panel of 24 IgG autoantibody specificities selected by machine learning and manual curation distinguishes Ro seronegative Sjögren's disease (RoNEG SjD) from healthy control (HC) and other rheumatic disease (OD) groups with ROC AUC = 0.95.

Results: Fisher's analysis revealed 27 specificities bound by IgG more commonly in RoNeg SjD (14-22%) vs HC (0-4%), with a subset of 4 (CBX3, CBX5, NAV3, NUSAP1) also bound more commonly by IgG from RoNeg SjD vs OD, and significant enrichment in specificities located in pericentric heterochromatin by STRING analysis. The RoPos SjD group bound 57 proteins more commonly than HC, with a subset of 14 recognized more commonly than in the OD group, and STRING enrichment in RNA and miRNA regulation. Common specificities overlapping between RoNeg and RoPos groups included ATAT1, CBX3, PAIP1, PNPLA1, PTK6 and SLC19A1. Machine learning was applied to RoNeg SjD, OD and HC groups.

Table 1. Panel of 24 IgG autoantibody specificities distinuishing RoNeg SjD from healthy control (HC) and other rheumatic disease (OD) groups.

	Serum IgG, % Positive				
Specificity (Gene Symbol)	Ro^{Neg} SjD N=86	Ro^{Pos} SjD N=86	OD N=44	HC N=24	Fisher's p (RoNeg SjD vs. HC) **
CBX3	20.9	18.6	4.5	0	***0.011***
NUSAP1	14	7	0	0	***0.065***
FBXO22	11.6	5.8	2.3	0	0.114
RAB11FIP5	7	2.3	18.2	0	0.336
AGO4	5.8	8.1	18.2	0	0.584
HCCS	5.8	9.3	15.9	0	0.584
NCCRP1	5.8	12.8	18.2	0	0.584
DCUN1D2	4.7	5.8	13.6	0	0.575
DDB1	4.7	15.1	20.5	0	0.575
C15orf41	3.5	3.5	13.6	0	>0.999
CYB5R3	3.5	4.7	13.6	0	>0.999
HDDC2	3.5	11.6	20.5	0	>0.999
LSM5	3.5	15.1	13.6	0	>0.999
TBC1D22A	3.5	4.7	15.9	0	>0.999
INO80E	2.3	3.5	11.4	0	>0.999
PRDX1	2.3	8.1	13.6	0	>0.999
KLHL11	1.2	4.7	13.6	0	>0.999
NDUFA3	1.2	1.2	11.4	0	>0.999
NAV3*	15.1	7	2.3	0	***0.067***
CBX5*	16.3	12.8	4.5	0	***0.037***
HNRNPD*	14	9.3	4.5	0	***0.065***
TMEM174*	17.4	9.3	15.9	0	***0.038***
FGFR4*	15.1	11.6	6.8	0	***0.067***
SRCRM*	18.6	11.6	11.4	0	***0.021***

* Specificities curated solely from manual analysis. All others were identified by the machine learning pipeline. ** p<0.1 indicates common specificiteis prevalent in RoNeg SjD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

IgG binding to 121 proteins discriminated the RoNeg group with ROC AUC=0.88. IgA and combined IgG + IgA specificities yielded lower ROC AUC values. A panel of 24 IgG specificities selected from one end of the distribution of logistic regression coefficients yielded ROC AUC=0.83. Replacement of 6 specificities with others showing high prevalence among RoNeg SjD by manual analysis yielded a ROC AUC=0.95 for distinguishing RoNeg SjD cases from HC and OD groups (Table 1; Figure 1).

Conclusion: Using proteome arrays, a novel array alignment algorithm, and machine learning pipelines, we developed an advanced approach for autoantibody biomarker discovery in Ro^{Neg} SjD, defining a curated panel of 24 autoantibodies with potential diagnostic significance.

Reference:

1. Ann Rheum Dis. 2023 Sep;82(9):1181-1190.

Funding: NIH/NIAMS 3UC2AR081032-04S1; NIH/NIAMS P30AR073750

Disclosure: S. Yao: None; **C. Lawrence**: None; **H. Christakos**: None; **C. Lopez-Davis**: None; **B. Khatri**: None; **T. Taylor**: None; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **K. Grundahl**: None; **R. Scofield**: IQVIA, 1, Jannsen Pharmaceuticals, 1; **B. Warner**: Mitobridge, subsidiary of Astellas Bio, 5, Pfizer, Inc., 5; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Guthridge**: None; **C. Lessard**: Johnson & Johnson Innovative Medicine, 2, 5; **A. Farris**: Johnson & Johnson Innovative Medicine, 5.

Abstract Number: 0507

Diagnostic performance of the lacrimal and salivary gland ultrasound in patients with primary Sjogren's disease of recent onset versus sicca controls.

Rosa Elena Cervantes[1], Carina Soto-Fajardo[2], Fabian Carranza[3], Gabriela Hernandez-Molina[4], Narlly Ruíz Quintero[5], **Daniela Rojas Abarca**[6], Ana Mora[7], Ada Rocío Morales Meza[6], Carlos Montiel Castañeda[8], Angela Maldonado Luna[9], Fabiola Sánchez Zamudio[6] and Carlos Pineda[2], [1]National Institute of Rehabilitation "Luis Guillermo Ibarra Ibarra"", Mexico City, Distrito Federal, Mexico, [2]National Rehabilitation Institute " Luis Guillermo Ibarra Ibarra ", Mexico City, Mexico, [3]National Rehabilitation Institute " Luis Guillermo Ibarra Ibarra ", Ciudad de Mexico, Mexico, [4]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Federal District, Mexico, [5]Instituto Nacional de Ciencias Medicas y Nutricion, México, city, Distrito Federal, Mexico, [6]National Institute of Rehabilitation "Luis Guillermo Ibarra Ibarra", Mexico, City, Distrito Federal, Mexico, [7]National Rehabilitation Institute " Luis Guillermo Ibarra Ibarra ", Mexico, Mexico, [8]National Institute of Rehabilitation "Luis Guillermo Ibarra Ibarra", México, city, Distrito Federal, Mexico, [9]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico, City, Estado de México, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a chronic systemic autoimmune disease primarily affecting the exocrine glands. There is an increasing use of salivary gland ultrasound in SjD due to its good diagnostic yield and noninvasive, radiation-free, low-cost, and reproducible nature. Limited information exists on lacrimal gland ultrasound. The objective was to determine the usefulness of lacrimal and salivary gland ultrasound in diagnosing patients with primary SjD of recent onset compared to primary sicca syndrome.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variables		Patients with SjD, n (%) or median (IQR 25 - 75) n=15	Sicca syndrome n (%) or median (IQR 25 -75) n=15	p
Sex		15 (50%)	15 (50%)	/
Age		49 (40-57)	49 (35-56)	1.000
Rheumatoid factor		38.6 (13.7-63.9)	/	/
SSA/Ro		443.70 (216.60-913.8)	/	/
SSB/La		36.9 (5.4-487.2)	/	/
ESSPRI		6.07 (1.3)	5 (2)	1.000
Disease symptoms onset in months		60 (48-72)	48(18-60)	0.466
Degree of dysfunction	No dysfunction	0(0)	3 (20)	0.005
	Mild	8 (53.3)	12 (80)	
	Moderate	7 (46.7)	0	
	Severe	0	0	
OSDI		35.41 (16.66-47.90)	35.41 (27.08-62.50)	1.000
lissamine stain (right eye)	0	0	9 (60)	0.004
	1	9 (60)	4 (26.7)	
	2	4 (26.7)	2 (13.3)	
	3	2 (13.33)	0	
lissamine stain (left eye)	0	0	8 (53.3)	0.009
	1	9 (60)	3 (20)	
	2	5 (33.33)	3 (20)	
	3	1 (6.7)	1 (6.67)	
Hocevar 14 points or more		13 (100)	2 (13.33)	0.000
Hocevar 17 points or more		11 (73.33)	0	0.000
OMERACT ≥2 for ≥1 glands		15 (100)	1 (6.67)	0.000
Tear gland greater than or equal to 3 points		15 (100)	0	0.000

TABLE 1. Demographic and clinical characteristics of patients with SjD and SICCA syndrome.

Methods: We included primary SjD patients of recent onset (≤5 years) who fulfilled the 2016 ACR/EULAR criteria attending a tertiary reference center. We also included sicca controls matched by age(±5 years), sex, and disease duration (±5 years). An ophthalmologist evaluated keratoconjunctivitis sicca, including Schirmer test, OSS score, and Van Bijsterveld Score. We scored the ESSPRI and the Ocular Surface Disease Index [OSDI] questionnaire. We excluded both patients and controls with diabetes mellitus or with a body mass index ≥30.

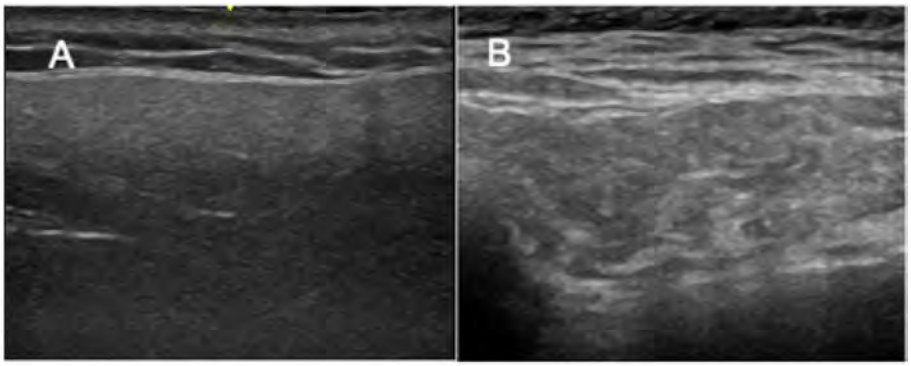
Ultrasound evaluation of the lacrimal and salivary glands (parotid and submandibular) was performed using a GE LOGIQe device with an 8-18 MHz linear probe. The OMERACT and Hocevar ultrasound scales were used for the salivary glands, and the scale reported by Kim et al. (1) for the lacrimal glands.

Results: We included 15 patients with primary SjD and 15 sicca controls. Patients and controls had similar symptoms, disease duration (60 months vs 40 months), and ESSPRI scores (6 points and 5 points). SjD patients had a higher degree of tear dysfunction than sicca controls (46.7% and 53.3% vs. 0% and 80% with moderate and mild damage, respectively; p=0.005). However, both groups had similar OSDI scores. Baseline characteristics are shown in Table 1.

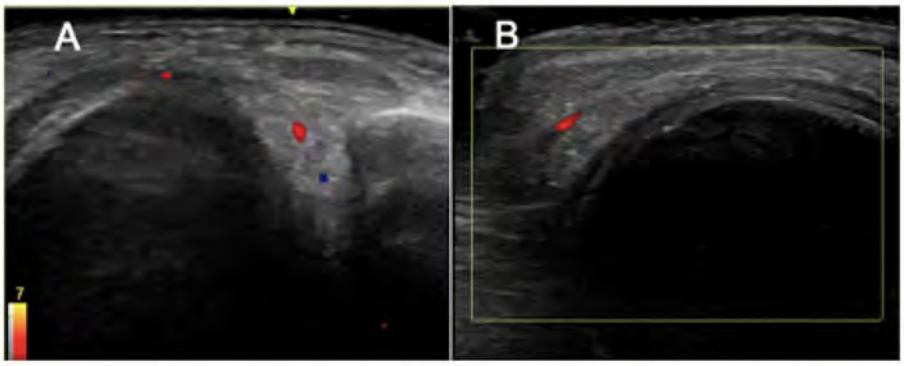
The OMERACT score had good diagnostic performance, with an AUC of 0.97 (95% CI: 0.89–1; $p < 0.0001$). The Hocevar scale, using two cut-off points of 14 and 17 points, had a good, adequate diagnostic performance, with an AUC of 0.93 (95% CI: 0.82-1; $p < 0.0001$) and 0.9 (95% CI: 0.77-1; $p < 0.0001$), respectively.

Regarding the lacrimal gland, the presence of an intraglandular arterial branch, loss of homogeneity, hypoechoic areas, hyperechoic bands, and loss of glandular demarcation were features mainly observed in patients with SjD vs sicca controls

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A) Healthy parotid gland (OMERACT 0). B) Parotid gland with moderate loss of parenchymal homogeneity with focal hypo/anechoic areas, surrounded by normal tissue (OMERACT 2).



A) Presence of intraglandular branch of the lacrimal artery. B) Extra glandular branch of the lacrimal artery.

Figure 1. Examples of glandular ultrasounds performed on patients with SjD and sicca syndrome.

($p < 0.0001$ for each of them). Finally, we observed a strong correlation between the tear gland and Hocevar scores (rho = 0.83, $p< 0.001$).

Conclusion: Ultrasonography of both the lacrimal and salivary glands is a valuable diagnostic tool for identifying patients with primary SjD of recent onset from sicca controls.

Disclosure: R. Cervantes: None; **C. Soto-Fajardo**: None; **F. Carranza**: None; **G. Hernandez-Molina**: None; **N. Ruíz Quintero**: None; **D. Rojas Abarca**: None; **A. Mora**: None; **A. Morales Meza**: None; **C. Montiel Castañeda**: None; **A. Maldonado Luna**: None; **F. Sánchez Zamudio**: None; **C. Pineda**: None.

Abstract Number: 0508

Serum immune complexes assessed using a cell-reporter assay are associated with serum IFN-alpha levels, disease activity and the risk of incident lymphoma in the ASSESS prospective cohort

Clementine Pouenat[1], Marine Vierling[2], Chiara Meier[3], Ludivine Robin[4], Philippe Kolb[5], Hartmut Hengel[6], Gaetane Nocturne[7], Divi Cornec[8], Valerie Devauchelle[9], Véronique Le Guern[10], Claire larroche[11], Damien Sène[12], Marion Couderc[13], Eric HACHULLA[14], Philippe Dieude[15], Olivier Vittecoq[16], Jacques Morel[17], Nicolas Meyer[18], Raphaele Seror[19], Reinhard Voll[20], Pierre-Marie Duret[21], Laurent Miguet[22], Xavier Mariette[23], **Jacques-eric GOTTENBERG**[24] and Investigators of the ASSESS cohort, [1]IBMC, UPR 3572, STRASBOURG, France, [2]Strasbourg University Hospital, Department of Public Health, GMRC, Strasbourg, France, Strasbourg, Alsace, France, [3]Strasbourg University Hospital,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Department of Rheumatology, STRASBOURG, France, [4]Strasbourg University Hospital, Department of pathology, 4CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire (IBMC), Strasbourg, France Strasbourg, France;, Strasbourg, Alsace, France, [5]INSTITUTE OF VIROLOGY Medical Center, Freiburg, Freiburg, Germany, [6]INSTITUTE OF VIROLOGY University Hospital Freiburg, FREIBURG, Germany, [7]University Paris Saclay, Le Kremlin Bicetre, Ile-de-France, France, [8]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, Bretagne, France, [9]UBO, Brest, France, [10]Cochin hospital, Paris, France, [11]Service de Médecine Interne, Hôpital Avicenne APHP, Bobigny, Paris, Ile-de-France, France, [12]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, Paris, Ile-de-France, France, [13]Service de Rhumatologie CHU Clermont-Ferrand, Clermont-Ferrand, [14]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-Immunes et Auto-Inflammatoires Rares du Nord, Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille, France, Lille, France, [15]Service de Rhumatologie, Hôpital Bichat APHP, Paris, Paris, Ile-de-France, France, [16]Service de Rhumatologie & CIC-CRB 1404, CHU de Rouen, Université de Rouen, Rouen, Rouen, France, [17]CHU and University of Montpellier, Montpellier, France, [18]Strasbourg University Hospital, Department of Public Health, GMRC, Strasbourg, France, Strasbourg, Alsace, France, [19]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [20]University Medical Center Freiburg, Freiburg, Germany, [21]Colmar General Hospital; Strasbourg University Hospital, Strasbourg, France, [22]Haemtology, Strasbourg University Hospital, IBMC UPR 3572, Strasbourg, France, [23]Universit Paris-Saclay, Le Kremlin Bicetre, France, [24]Hautepierre Hospital, STRASBOURG, Alsace, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Fc-gamma receptor (FcγR) activation by soluble IgG immune complexes (sICs) is considered to play a pivotal pathogenic role in B-cell-mediated autoimmune diseases, such as primary Sjögren's disease (SD). Previous indirect ELISA assays based on the affinity of sICs to C1q or C3d, were not sensitive enough and did not allow a correct discrimination between IgG monomers and sICs.

Methods: In serum at enrollment from 369 patients with primary SD prospectively followed up since 2005, FcγR activation was measured. Briefly, reporter cells transfected with human-FcγRIIA were incubated with patient's serum (1). Incubation was performed in a 96-well ELISA plate for 1 h at 4°C. Reporter cell IL-2 secretion was quantified after 20 h of incubation using ELISA. The area under curve (AUC) of IL2 secretion was compared to that resulting from incubation of synthetic ICs (hTNFa with infliximab) to obtain an equivalent quantification (pM).

Results: Serum levels of sICs were significantly correlated with serum levels of IFN-alpha assessed by digital ELISA (r=0,5 ; p= $2.5*10^{-19}$). In multivariate analysis, taking notably anti-SSA, rs9273012 (a HLA class II gene polymporphism previously reported to be associated with serum IFN-alpha level) and clinESSDAI into account, sICs remained significantly and independently associated with serum levels of IFN-alpha(p=$7,6*10^{-7}$).

Median serum levels of sICs were higher in patients with moderate or high systemic disease activity (ESSDAI≥5) at enrolment than in patients with no or low systemic disease activity (ESSDAI< 5) (121 pM/L vs 88 pM/L, p= 0.03). Median serum levels of sICs were higher in patients with B cell activation markers and no systemic disease activity or in patients with moderate to severe systemic disease activity than in patients with high symptom burden and no systemic disease activity (121 pM/L, 90 pM/L and 51 pM/L, respectively, p< 0.001), these 3 patient clusters defined as recently published (2). No association was observed between serum ICs and history of previous lymphoma. Ten incident lymphoma have occured since patients were enrolled in the cohort. Among patients with incident lymphoma, serum levels of sICs were significantly higher than in patient without lymphoma (225 vs 94, p=0,025)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Serum sICs assessed using a cell-based assay are associated with activation of type I interferon pathways, systemic disease activity, and incident lymphoma in Sjogren's disease.

References

1. Chen H, et al. EMBO Mol Med 2022
2. Nguyen Y, et al. Lancet Rheumatol 2024

Disclosure: C. Pouenat: None; **M. Vierling**: None; **C. Meier**: None; **L. Robin**: None; **P. Kolb**: None; **H. Hengel**: None; **G. Nocturne**: None; **D. Cornec**: None; **V. Devauchelle**: None; **V. Le Guern**: AstraZeneca, 12, attending meetings and travel., Bristol-Myers Squibb(BMS), 6, Novartis, 2; **C. Iarroche**: None; **D. Sène**: None; **M. Couderc**: None; **E. HACHULLA**: None; **P. Dieude**: None; **O. Vittecoq**: None; **J. Morel**: AbbVie, 2, 5, 6, Biocon, 6, Biogen, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, GlaxoSmithKline, 2, 6, Lilly, 2, 6, Medac, 6, Mylan/Viatris, 6, Nordic Pharma, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche/Chugai, 6, Sanofi, 2, 6; **N. Meyer**: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **R. Voll**: None; **P. Duret**: None; **L. Miguet**: None; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6.

Abstract Number: 0509

Functional Anti-M3R Autoantibodies in Sjögren's Disease: From Gland to Circulation

Martha Tsaliki[1], Joshua Cavett[2], Biji T Kurien[3], valerie Lewis[3], John Ice[4], Devavrat Dave[5], Sina Khosravani[5], Menerva Racy[5], Rebecca Wood[6], Seunghee Cha[7], A. Darise Farris[3], Kristi A. Koelsch[5] and **R. Scofield**[3], [1]The University of Oklahoma Health Sciences Center, Oklahoma City, OK, [2]Oklahoma Medicar Research Foundtion, Oklahoma City, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]OKC Veterans Affairs Medical Center, Oklahoma City, OK, [5]Oklahoma Medical Research Foundation, oklahoma City, [6]University of Oklahoma Health Sciences Center, Edmond, OK, [7]University of Florida, Gainesville

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a systemic autoimmune disease characterized by immune-mediated damage to salivary and lacrimal glands. While autoantibodies against muscarinic type 3 receptor (M3R) have long been implicated in disease pathogenesis, their clinical relevance remains unclear. We hypothesized that pathogenic anti-M3R antibodies originate in inflamed salivary glands and are detectable in both circulation and saliva, where their presence correlates with objective measures of disease activity.

Methods: Recombinant monoclonal antibodies (mAbs) were generated from single cells infiltrating labial salivary glands of classified SjD, NSS (non-Sjögren's sicca), and overlap SjD subjects and screened for binding to linear and conformational M3R epitopes. Monoclonal antibodies along with matched plasma and saliva samples, as well as an expanded plasma cohort, were screened using a conformational On-Cell Western assay. Functional effects were assessed via inhibition of M3R signaling in a cell-based activity assay. Associations with clinical features and disease activity were evaluated.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A subset of IgG^+ mAbs from SjD glands bound conformational M3R and inhibited signaling. These features were reflected in matched plasma and, to a lesser extent, saliva. In the larger cohort, plasma anti-M3R reactivity was significantly elevated in SjD and showed association with ocular staining scores, focus scores, and higher ESSDAI biological domain activity. ROC analysis supported moderate diagnostic potential (AUC = 0.736).

Conclusion:

These findings demonstrate that anti-M3R antibodies are functionally relevant and detectable in both salivary gland tissue and the circulation. Their association with key glandular and systemic disease features underscores the importance of conformational assays in identifying clinically meaningful autoantibodies. These results suggest that anti-M3R reactivity may define distinct immunopathologic subtype within SjD and serve as a potential biomarker of disease activity.

Disclosure: M. Tsaliki: None; **J. Cavett**: None; **B. Kurien**: None; **v. Lewis**: None; **J. Ice**: None; **D. Dave**: None; **S. Khosravani**: None; **M. Racy**: None; **R. Wood**: None; **S. Cha**: None; **A. Farris**: Johnson & Johnson Innovative Medicine, 5; **K. Koelsch**: None; **R. Scofield**: IQVIA, 1, Jensen Pharmaceuticals, 1.

Abstract Number: 0510

A Risk Estimation Tool for Clinical Practice to Improve Early ILD Detection in Sjögren Disease

Anna-Maria Hoffmann-Vold[1], Kastriot Kastrati[2], Marco Sprecher[3], Emily Violette Langballe[1], Phuong Diep[1], Havard Fretheim[1], Helena Andersson[1], Paul Studenic[4], Bojana Müller-Durovic[3], Cathrine Brunborg[1], Cosimo Bruni[5], Christian Clarenbach[3], Thomas Frauenfelder[6], Trond Mogens Aaløkken[1], Natasha Moe[1], Helmut Prosch[4], Helga Radner[2], Øyvind Molberg[7] and Oliver Distler[8], [1]Oslo University Hospital, Oslo, Norway, [2]Department of Medicine III, Division of Rheumatology, Medical University Vienna, Vienna, Austria, [3]Univeristy Hospital Zurich, Zurich, Switzerland, [4]Medical University of Vienna, Vienna, Austria, [5]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [6]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, Zurich, Switzerland, [7]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [8]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) affects 10-15% of Sjögren disease (SjD) patients, leading to increased morbidity and reduced survival. The true prevalence may be higher due to underdiagnosis, partly due to the lack of effective risk factor–based screening tools compared to other connective tissue diseases. Current guidelines recommend screening at-risk SjD patients using high-resolution computed tomography (HRCT), but effective risk factor estimation tools are lacking, leaving it unclear which patients should be referred for HRCT in practice. The objective was to develop a decision support tool for estimating the risk of ILD in SjD patients, guiding HRCT referrals in clinical practice.

Methods: We included all SjD patients from three European expert rheumatology centers (Zurich, Oslo and Vienna) with available HRCT images of the chest. All HRCT images were reviewed by expert radiologists at each site for the presence of ILD. Available data included demographic, serological and laboratory data, clinical SjD manifestations, and other comorbidities. To create the decision support tool, we developed a nomogram based on a logistic regression model (with Odds ratio (OR) and 95% confident interval (CI)) to estimate patient-specific probabilities, translating multivariable relationships into

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of patients with SjD and HRCT scans segregated by the presence of ILD

	All SjD (n=547)	SjD with ILD (n=163)	SjD no ILD (n=384)	p-value
Age, years (SD)	63 (15.1)	68 (13.01)	62 (15.4)	<0.001
Females, n (%)	491 (88)	135 (83)	346 (90)	0.017
Caucasians, n (%)	425 (94)	146 (94)	279 (94)	0.559
Smokers, n (%)	156 (36)	42 (36)	114 (36)	0.955
Anti-Ro/SSA, n (%)	412 (80)	137 (88)	275 (76)	<0.001
Anti-La/SSB, n (%)	236 (46)	96 (62)	140 (39)	<0.001
Anti-CCP, n (%)	16 (4)	8 (4)	8 (3)	0.107
Arthritis, n (%)	74 (14)	17 (11)	57 (15)	0.186
Dermal affection, n (%)	40 (17)	8 (17)	32 (17)	0.965
Polyneuropathy, n (%)	57 (11)	22 815)	35 (9)	0.081
Raynaud's phenomenon, n (%)	55 (23)	44 (23)	11 (23)	0.357
Vasculitis, n (%)	41 (8)	20 (13)	21 (6)	0.004
Lymphadenopathy, n (%)	97 (19)	38 (25)	59 (16)	0.019
Lymphoma, n (%)	20 (4)	8 (6)	8 (3)	0.011
CRP, mg/L (SD)	0.6 (1.5)	0.6 (0.9)	0.6 (1.7)	0.389
ESR, mm/h (SD)	27 (21.9)	34 (24.2)	23 (19.1)	<0.001
Lymphopenia, n (%)	124 (25)	56 (38)	68 (19)	<0.001
Hypergammaglobulinemia, n (%)	169 (34)	74 (50)	95 (27)	<0.001
C3, g/L (SD)	0.62 (0.6)	0.76 (0.6)	0.55 (0.6)	<0.001
C4, g/L (SD)	0.34 (2.3)	0.2 (0.3)	0.4 (2-7)	0.114

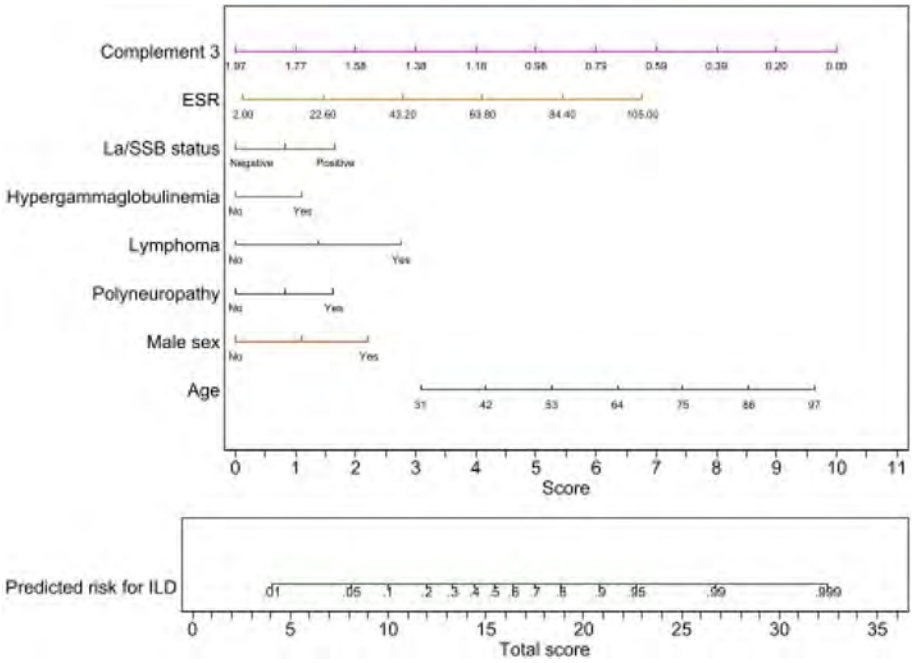


Figure 1: Nomogram estimating the ILD probability in SjD patients, informing HRCT referrals based on individual risk

a graphical tool for clinical application. Predictor variables were selected based on clinical relevance, statistical significance and the area under the ROC curve (AUC) of the final multivariable logistic model.

Results: We included 547 SjD patients with HRCT, of which 163 (29.8%) had ILD. Demographic and clinical characteristics are presented in Table 1. In multivariable regression, age (OR 1.01, 95%CI 1.01-1.07, p< 0.001), erythrocyte sedimentation rate (ESR) (OR 1.03, 95%CI 1.01-1.04, p=0.003), and complement C3 (OR 0.13, 95%CI 0.05-0.35, p< 0.001) were significantly associated with the presence of ILD, adjusted for male sex, polyneuropathy, lymphoma, hypergammaglobulinemia and anti-La/SSB antibodies. The model was deemed acceptable (AUC 0.8). Based on this multivariable model, we built a nomogram which is a practical decision support tool estimating the probability of ILD in SjD patients, informing HRCT referrals based on individual risk.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

An example patient who is female, 50 years old, positive for anti-La/SSB, has hypergammaglobulinemia, an ESR of 40 mm/hour, and C3 of 0.8g/L has a total score of 15.5, which corresponds to a 50% predicted risk of having ILD.

Conclusion: We developed a nomogram-based decision support tool that effectively estimates the risk of ILD in SjD patients using key predictors such as age, sex, hypergammaglobulinemia, antibodies, extrapulmonary organ manifestation, ESR and complement C3 levels. This tool aids clinicians in making informed HRCT referral decisions, addressing potential underdiagnosis in at-risk SjD patients and improving early detection and outcomes. Future validation in broader populations is necessary to confirm its clinical utility.

Disclosure: A. Hoffmann-Vold: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **K. Kastrati**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Novartis, 6; **M. Sprecher**: Abbvie, 5; **E. Langballe**: Boehringer-Ingelheim, 6; **P. Diep**: Boehringer-Ingelheim, 6, NordicInfu Care AB, 1; **H. Fretheim**: Boehringer-Ingelheim, 6; **H. Andersson**: None; **P. Studenic**: AbbVie, 6; **B. Müller-Durovic**: None; **C. Brunborg**: None; **C. Bruni**: Boehringer Ingelheim, 2, EMDO Foundation, 5, Iten-Kohaut Foundation, 5, Scleroderma Clinical Trials Consortium (SCTC), 5, Scleroderma Research Foundation (SRF), 2; **C. Clarenbach**: Boehringer-Ingelheim, 6, Roche, 6; **T. Frauenfelder**: AstraZeneca, 2, Bayer, 6, Siemens, 6; **T. Aaløkken**: None; **N. Moe**: Boehringer-Ingelheim, 6; **H. Prosch**: AstraZeneca, BMS, Boehringer Ingelheim, Bracco, Daiichi Sankyo, Janssen, MSD, Novartis, Roche, Sanofi, Siemens Healthineers, Takeda, 6, Boehringer Ingelheim, AstraZeneca, Siemens Healthineers and the Christian Doppler Research Association, EU Commission (EU4Health, Horizon Europe Healt, 5; **H. Radner**: None; **Ø. Molberg**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0511

Submandibular Gland Ratio Stratifies Salivary Function and Reveals a Senescence Peak in Anti-SSA Positive Sjögren's Syndrome

Chiao-Feng Cheng[1], Tseng-Cheng Chen[2], Min-Shu Hsieh[3], TING-YUAN LAN[4], Jui-Hung Kao[5], Yu Heng Lin[6], Mei-Fang Cheng[7], Yi-Chieh Chen[8], Hsiao-Sang Chu[9], Yi-Min Huang[10], Cheng-Hsun Lu[11], Ko-Jen Li[11], Chieh-Yu Shen[1] and Song-Chou Hsieh[12], [1]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, Taipei, Taiwan (Republic of China), [2]Department of Otolaryngology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan., Taipei, Taiwan (Republic of China), [3]Department of Pathology, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei 100225, Taiwan, Taipei, Taiwan (Republic of China), [4]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan, [5]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, Taipei, Taiwan (Republic of China), [6]Department of Internal Medicine, National Taiwan University Hospital Yun-Lin Branch, Yun-Lin, Taiwan, Taipei, Taiwan (Republic of China), [7]Department of Nuclear Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan., Taipei, Taiwan (Republic of China), [8]Department of Nuclear Medicine, National Taiwan University Hospital, Taipei, Taiwan., Taipei, Taiwan (Republic of China), [9]Department of Ophthalmology, National Taiwan University Hospital, Taipei City, Taiwan., Taipei, Taiwan (Republic of China), [10]Department of Internal Medicine, National Taiwan University Cancer Center, Taipei, Taiwan, Taipei, Taiwan (Republic of China), [11]National Taiwan University Hospital, Taipei, Taiwan, [12]National Taiwan Unuversity Hospital, Taipei City, Taiwan (Republic of China)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: In primary Sjögren's syndrome (pSS), the histologic focus score reflects immune infiltration but does not capture irreversible glandular damage. We evaluated a submandibular gland (SMG) gland ratio—defined as the proportion of preserved parenchyma in biopsy sections—as a marker of structural integrity, and assessed its associations with salivary function, serology, and imaging.

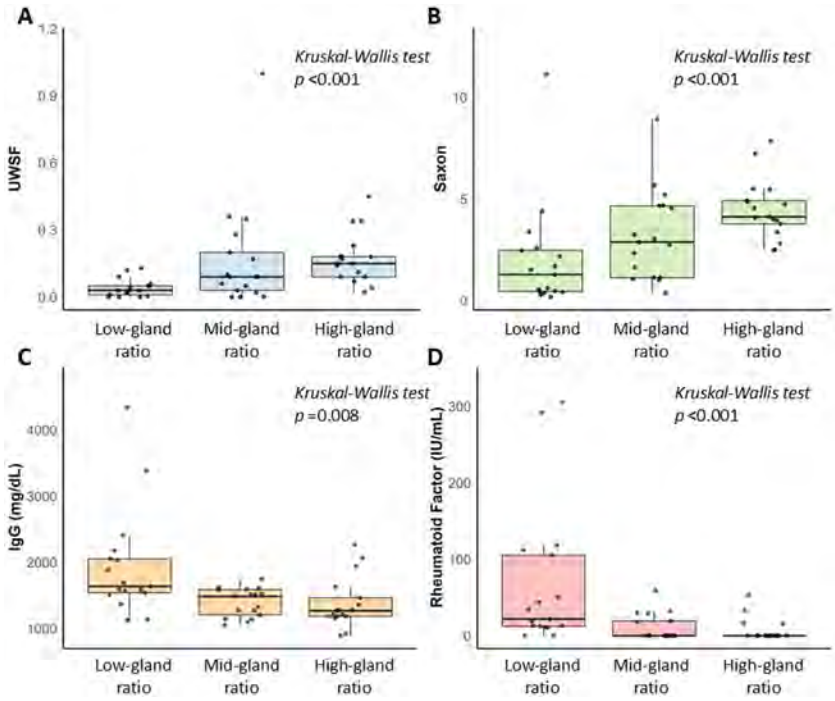


Figure 1. Salivary function and serologic activity across tertiles of submandibular gland (SMG) gland ratio. (A–B) Saxon test and unstimulated whole salivary flow (UWSF) improved with increasing gland preservation. (C–D) Serum IgG and rheumatoid factor decreased across tertiles. SMG, submandibular gland; UWSF, unstimulated whole salivary flow.

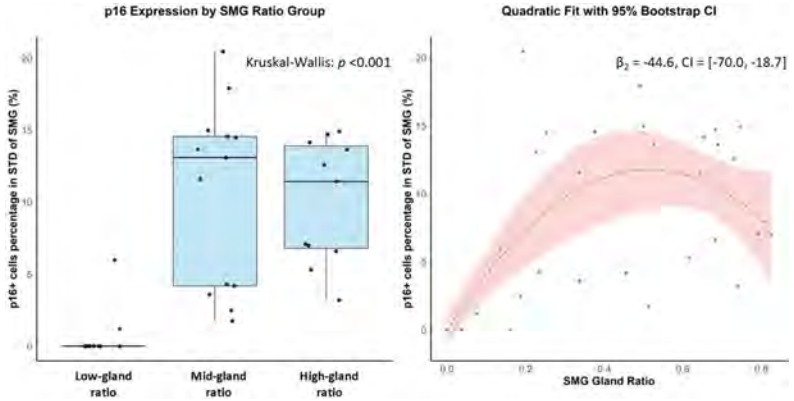


Figure 2. p16^{+} cell percentage in striated ducts (STD) across submandibular gland (SMG) gland ratio tertiles in anti-SSA^{+} pSS (n = 36). (Left) Boxplot showing increased p16^{+} burden in mid- and high-tertile groups. (Right) Quadratic regression model reveals a bell-shaped association, peaking near gland ratio 0.5 (95% bootstrap CI shaded). No similar pattern was observed in anti-SSA^{-} patients (not shown).

Table 1. Clinical, serologic, and imaging features across submandibular gland (SMG) gland ratio tertiles. Gland ratio was defined as the preserved parenchymal area over total biopsy section. p-values based on Kruskal–Wallis test. UWSF, unstimulated whole salivary flow; ESSDAI, EULAR Sjögren's syndrome disease activity index.

Characteristics	Low gland ratio (T1, n = 17)	Mid-gland ratio (T2, n = 17)	High gland ratio (T3, n = 17)	p-value
Female, n (%)	16 (94)	17 (100)	13 (76)	0.111
Age, year, median (IQR)	57.0 (16.0)	55.0 (15.0)	46.0 (20.0)	0.065
UWSF, mL/min, median (IQR)	0.0 (0.0)	0.1 (0.2)	0.2 (0.1)	<0.001*
Saxon, mL/2 mins, median (IQR)	1.3 (2.0)	2.9 (3.5)	4.1 (1.2)	<0.001*
Average Schirmer I, mm/5 mins, median (IQR)	6.0 (8.5)	6.5 (3.5)	6.0 (9.5)	0.899
Rheumatoid factor, IU/mL, median (IQR)	22.0 (93.1)	0.0 (19.4)	0.0 (0.0)	<0.001*
C3, mg/dL, median (IQR)	126.1 (22.5)	114.8 (27.6)	110.4 (24.7)	0.662
C4, mg/dL, median (IQR)	32.8 (13.8)	33.2 (16.1)	27.3 (9.9)	0.839
IgG, mg/dL, median (IQR)	1641.6 (511.5)	1488.9 (381.3)	1272.2 (280)	<0.001*
CK, U/L, median (IQR)	57.0 (27.0)	70.0 (41.0)	106.0 (59.0)	0.010*
ESSDAI, median (IQR)	2.0 (6.0)	4.0 (6.0)	0.0 (4.0)	0.392
Gland ratio of the SMG, median (IQR)	0.0 (0.0)	0.3 (0.3)	0.7 (0.2)	<0.001*
Focus score in the SMG, median (IQR)	0.0 (0.0)	0.4 (1.4)	0.6 (1.2)	0.091
OMERACT score of SMG				0.011*
Score = 0, n (%)	0 (0)	2 (11.8)	2 (11.8)	
Score = 1, n (%)	5 (29.4)	10 (58.8)	10 (58.8)	
Score = 2, n (%)	9 (52.9)	4 (23.5)	5 (29.4)	
Score = 3, n (%)	3 (17.6)	1 (5.9)	0 (0)	
Gland ratio of the PG, median (IQR)	0.1 (0.2)[a]	0.3 (0.2)[b]	0.2 (0.2)[b]	0.037*
PG gland ratio group				
Low-gland ratio, n (%)	8 (50)[a]	3 (20)[b]	5 (33)[b]	0.285
Mid-gland ratio, n (%)	5 (31)[a]	4 (27)[b]	6 (40)[b]	
High-gland ratio, n (%)	3 (19)[a]	8 (53)[b]	4 (27)[b]	
Focus score in the PG, median (IQR)	0.3 (0.9)	0.0 (0.3)	0.0 (0.6)	0.474
Other autoimmune diseases, n (%)	3 (18)	5 (29)	3 (18)	0.690

[a] One of the patients received only SMG core needle biopsy

[b] Two of the patients received only SMG core needle biopsy

*p < 0.05

ESSDAI, EULAR Sjögren's syndrome disease activity index; IQR, interquartile range; SMG, submandibular gland; PG, parotid gland; UWSF, unstimulated whole salivary flow

Methods: We analyzed 51 anti-SSA$^+$ pSS patients who underwent SMG core needle biopsy (CNB); 46 had paired parotid gland (PG) CNB. The gland ratio was calculated as the area of preserved acini and ducts divided by total tissue area, including stroma, adipose, and fibrosis. Patients were stratified by SMG gland ratio tertiles. Salivary function was assessed by unstimulated whole salivary flow (UWSF) and Saxon test. Serologic markers included IgG, rheumatoid factor (RF), complement, and CK. Among 29 patients, SMG sialoscintigraphy was performed. In 36 patients, p16$^+$ cells were quantified in striated ducts by immunohistochemistry.

Results: Lower SMG gland ratios were associated with impaired salivary function. UWSF increased from median 0.02 to 0.20 mL/min across tertiles (p< 0.001); Saxon test rose from 1.3 to 4.1 mL/2 min (p< 0.001). IgG (p=0.008) and RF (p< 0.001) decreased with greater gland preservation. Echography scores (OMERACT) also declined with increasing gland ratio (p=0.011). SMG gland ratio correlated with sialoscintigraphy uptake (ρ=0.55–0.61) and maximal secretion (ρ=0.63–0.65). PG gland ratio showed marginal association with Saxon (p=0.067) but not UWSF. In a subset (n=36), p16$^+$ cells in striated ducts showed a bell-shaped association with gland ratio, peaking near 0.5, suggesting senescence may rise before overt tissue loss.

Conclusion: The SMG gland ratio stratifies salivary function, immune activity, and imaging findings in anti-SSA$^+$ pSS, supporting its potential as a histologic anchor for structural damage staging. Preliminary findings further suggest senescence may peak in moderately preserved glands, highlighting its possible role in early irreversible injury.

Disclosure: C. Cheng: None; **T. Chen**: None; **M. Hsieh**: None; **T. LAN**: None; **J. Kao**: None; **Y. Lin**: None; **M. Cheng**: None; **Y. Chen**: None; **H. Chu**: None; **Y. Huang**: None; **C. Lu**: None; **K. Li**: None; **C. Shen**: None; **S. Hsieh**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0512

Dry Eye Disease Severity and Salivary Gland Biopsy in Patients with Primary Sjögren's Syndrome

Karina Palomo-Arnaud[1], Janett C. Riega-Torres[2], Jose Martinez-Delgado[3], Fernando Morales-Wong[3], Jesus Mohamed-Hamsho[3], Valeria Mata-Riega[1], Irma Cantu-Zapata[1], Luis Medina-Gomez[1], Miguel Betancourt-De la Torre[1], Aritze Chong-Amezcua[1], Dionicio A. Galarza-Delgado[4] and Karim Mohamed-Noriega[3], [1]Hospital Universitario "Dr. José Eleuterio González", Rheumatology, Monterrey, Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [3]Hospital Universitario "Dr. José Eleuterio González", Ofthalmology, Monterrey, Nuevo León, Monterrey, Nuevo Leon, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film. This is commonly observed in patients with rheumatic diseases, particularly among patients with Sjögren's Syndrome (SS). SS is an autoimmune disease that mainly affects exocrine glands such as the salivary and lacrimal glands, causing chronic dryness of the ocular surface resulting in inflammatory reaction and gradual destruction of conjunctival epithelium. According to the 2016 ACR/EULAR classification criteria, a positive minor salivary gland (MSG) biopsy is considered the criterion with the highest weight, along with positive serology. However, the relationship between MSG involvement and dry eye disease (DED) is poorly understood. We aimed to determine the DED severity among patients with SS with a positive or negative MSG biopsy.

Methods: We performed a cross-sectional study, including patients of 18 years or older, with DED symptoms and primary SS (according to 2016 ACR/EULAR criteria), between 2015-2024. MSG biopsy, Unstimulated Whole Salivary Flow rate (UWSF), tear film osmolarity, tear matrix metalloproteinase 9 (MMP-9), Ocular Surface Disease Index (OSDI), tear break-up time (TBUT), SICCA ocular surface staining (SICCA OSS), and Schirmer tear test with and without anesthesia (STT) were evaluated. Only the worst eye was included, which was selected based on the SICCA OSS score. We used descriptive statistics (frequencies [%], mean ± SD, median [IQR]) to present the results and compared the patients with positive or negative biopsies with Chi^2, Mann-Whitney U, or Student's tests as appropriate. A p-value < 0.05 was considered statistically significant. This study was approved by the institutional review board and all participants provided written informed consent.

Results: We included 142 patients, the mean age was 52.93 ± 12.62 years, and 97.2% (n=138) of patients were women. One hundred twenty-one (85.2%) had a positive MSG biopsy, and 21 patients were biopsy negative. Patients with positive biopsy had similar OSDI scores (39.6 [IQR: 0-100]) than those with negative biopsies (47.91 [IQR: 4-79.2]; p=0.505; Table 1). Similarly, biopsy-positive patients had similar SICCA OSS (7.0 [IQR: 0-15] vs. 6.0 [IQR: 1.0-12]; p=0.443) and tear film osmolarity (307 [IQR: 277-397] vs 307 [IQR: 284-345]; p=0.392) than biopsy-negative patients. Positivity to tear MMP-9 (29, 24.0% vs 4, 19.0%; p=0.440), STT with anesthesia (5, 1-35 vs 7.0, 1-25; p=0.399) or without anesthesia (5, 0-35 vs 7, 1-35; p=0.290), and the TBUT (4, 1-15 vs 4, 2-10; p=0.289) were no different between patients with positive or negative MSG biopsy.

Conclusion: Positive minor salivary gland biopsy was not associated with worse dry eye disease in patients with primary SS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Dry eye disease among patients with SS and positive or negative minor salivary gland (MSG) biopsy.

	All N= 142	Positive MSG Biopsy N=121	Negative MSG Biopsy N=21	p-value*
Age, years, mean ± SD	52.93 ± 12.62	53.3 ± 12.9	49.6 ± 12.3	0.234
Sex, n (%)				0.560
Female	138 (97.2%)	118 (97.5%)	20 (95.2%)	
Male	3 (2.8%)	3 (2.5%)	1 (4.8%)	
UWSF ≤ 0.5 ml/5 min, n (%)	42 (29.6%)	34 (28.1%)	8 (38.1%)	0.497
Positive MMP-9, n (%)	33 (21.9%)	29 (24.0%)	4 (19.0%)	0.440
OSDI score, median (IQR)	39.6 (0-100)	39.6 (0-100)	47.91 (4-79.2)	0.505
SICCA OSS score, median (IQR)	7 (0-15)	7 (0-15)	6 (1-12)	0.443
Schirmer's tear test w/o anesthesia, median (IQR)	6 (0-35)	5 (0-35)	7 (1-35)	0.290
Schirmer's tear test with anesthesia, median (IQR)	5 (1-35)	5 (1-35)	7 (1-25)	0.399
TBUT, median (IQR)	4 (1-15)	4 (1-15)	4 (2-10)	0.289
Tear film osmolarity, median (IQR)	309 (277-397)	307 (277-397)	307 (284-345)	0.392

UWSF= Unstimulated Whole Salivary Flow rate, MMP-9= Matrix metalloproteinase 9, OSDI= Ocular Surface Disease Index, SICCA OSS= SICCA ocular surface staining, STT= Schirmer tear test with and without anesthesia. TBUT= tear break-up time.

*Chi^2, Mann Whitney's U test and student-T test.

Disclosure: K. Palomo-Arnaud: None; **J. Riega-Torres**: None; **J. Martinez-Delgado**: None; **F. Morales-Wong**: None; **J. Mohamed-Hamsho**: None; **V. Mata-Riega**: None; **I. Cantu-Zapata**: None; **L. Medina-Gomez**: None; **M. Betancourt-De la Torre**: None; **A. Chong-Amezcua**: None; **D. Galarza-Delgado**: None; **K. Mohamed-Noriega**: None.

Abstract Number: 0513

Real-world Clinical and Diagnostic Features of Patients with Isolated Anti-SSB Antibodies Compared to Those with Combination Anti-SSA and Anti-SSB Antibodies

Massiel Jimenez Artiles[1], asim Khanfar[2], Pratibha Chaudhary[3], Roshan Subedi[4], Qi Wang[5] and Anthony Ocon[6], [1]Rhode Island Hospital, North Providence, RI, [2]Rochester Regional Health, Rochester, NY, [3]Rochester General Hospital, Rochester, NY, [4]Medstar Washington Hospital Center, Washington, DC, [5]Metrohealth System/Case Western Reserve University, Cleveland, OH, [6]Rochester Regional Health, Fairport, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variable	Anti-SSA/SSB	Anti-SSB	p-value
Hemoglobin <11.9 mg/dL	n=195 50 (26%)	n=96 5 (5%)	<0.001
White Blood Cell Count < 4 cells * 1000/uL	n=195 39 (20%)	n=96 5 (5%)	0.003
Platelet Count <150 cells * 1000/uL	n=195 15 (8%)	n=96 5 (5%)	0.733
Proteinuria	n=160 45 (28%)	n=62 6 (10%)	0.004
Elevated AST	n=197 31 (16%)	n=101 13 (13%)	0.164
Elevated ALT	n=196 11 (6%)	n=100 10 (10%)	0.314
Positive ANA screen	n=189 175 (93%)	n=95 39 (41%)	<0.001
ANA Titer	n=174	n=40	<0.001
<1:80	2 (1%)	5 (13%)	
80-160	53 (30%)	29 (73%)	
>160	119 (68%)	6 (15%)	
ANA pattern	n=172	n=35	<0.001
Homogenous	17 (10%)	15 (43%)	
Centromere	3 (2%)	1 (3%)	
Nucleolar	3 (2%)	10 (29%)	
Speckled	138 (80%)	7 (20%)	
Mixed	11 (6%)	2 (6%)	
Positive Anti-Smith	n=159 16 (10%)	n=44 0 (0%)	0.028
Positive Anti-double stranded DNA	n=179 33 (18%)	n=61 8 (13%)	0.34
Positive Anti-U1-Ribonucleoprotein	n=155 34 (22%)	n=45 4 (9%)	0.05
Positive Rheumatoid Factor	n=143 77 (54%)	n=67 4 (6%)	<0.001
Positive Anti-Cyclic Citrullinated Peptide	n=107 12 (11%)	n=64 0 (0%)	0.011
C-Reactive Protein	n=178 48 (27%)	n=86 18 (21%)	0.288

Hematologic, Chemistry, Autoantibody, and Immunologic Laboratory Comparison

Background/Purpose: While Sjögren's disease is commonly associated with anti-SSA (anti-Ro) and/or anti-SSB (anti-La) antibodies, these autoantibodies are not disease-specific and may be present in various autoimmune conditions. Emerging evidence suggests that isolated anti-SSB positivity is not strongly associated with Sjögren's or other connective tissue diseases, whereas dual positivity for anti-SSA and anti-SSB may indicate a more severe disease phenotype [1-4]. This study aimed to compare the clinical and serologic profiles of patients with isolated anti-SSB antibodies to those with concurrent anti-SSA and anti-SSB positivity in a real-world clinical setting.

Symptoms	Anti-SSA/SSB	Anti-SSB	p-value
Joint pain	1.5 (0.2 - 12.2)	0.7 (0.1 - 5.7)	0.725
Joint swelling	0.89 (0.1 - 5.3)	1.1 (0.2 - 6.8)	0.896
Joint stiffness	1.2 (0.1 - 10.3)	0.8 (0.1 - 7.0)	0.86
Xeropthalmia	21.5 (2.5 - 185.4)	0.1 (0.0 - 0.4)	0.005
Xerostomia	4.0 (0.7 - 24.1)	0.2 (0.0 - 1.5)	0.126
Hair loss	1.5 (0.2 - 14.8)	0.6 (0.1 - 6.2)	0.705
Skin rash	0.3 (0.1 - 1.7)	3.1 (0.6 - 15.9)	0.181
Serositis	5.1 (0.2 - 116.0)	0.2 (0.0 - 4.5)	0.31

Odds Ratio (OR) for Clinical Symptomology between Groups

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Diagnosis	Anti-SSA/SSB (n=206)	Anti-SSB (n=109)	p-value
Sjogren's Disease	134 (65%)	27 (24%)	<0.001
Systemic Lupus Erythematosus	68 (33%)	8 (7%)	<0.001
Rheumatoid arthritis	25 (12%)	2 (2%)	<0.001
Other rheumatologic diagnosis*	27 (13%)	19 (17%)	0.318
No rheumatologic diagnosis	62 (30%)	86 (79%)	<0.001

*Includes: polymyositis, dermatomyositis, undifferentiated connective tissue disease, mixed connective tissue disease, axial spondyloarthritis, or systemic sclerosis.

Comparison of Clinical Diagnoses between Groups

Methods: A retrospective analysis of electronic medical records from January 1, 2018, to December 31, 2022 was conducted. Adults (≥18 years) with positive serologic testing for anti-SSA and anti-SSB antibodies were included. Patients with isolated anti-SSA, negative repeat serology within six months, or insufficient clinical data were excluded. Demographic data, clinical manifestations, autoantibody profiles, and diagnostic outcomes were compared between groups. Statistical analysis included Student's t-test and chi-squared tests for group comparisons, and univariate and multivariate logistic regression to estimate odds ratios (OR), with a significance threshold of $p < 0.05$.

Results: A total of 315 patients were included: 109 with isolated anti-SSB and 206 with both anti-SSA/SSB positivity. The groups were similar in age and sex distribution (83% vs. 85% female). Compared to the dual-positive anti-SSA/anti-SSB, patients with isolated anti-SSB antibody were significantly less likely to exhibit anemia, leukopenia, proteinuria, or positive ANA. Other autoantibodies (anti-Smith, anti-RNP, RF, anti-CCP) were also less frequent in the isolated anti-SSB group. Additionally, this group had lower rates of xerophthalmia and diagnoses of Sjögren's disease, systemic lupus erythematosus, and rheumatoid arthritis, and were more often left without a rheumatologic diagnosis.

Conclusion: Isolated anti-SSB positivity is associated with a significantly lower likelihood of Sjögren's disease, SLE, and RA. These findings suggest that isolated anti-SSB may lack diagnostic utility in connective tissue diseases and could represent a benign serologic finding in many patients.

Disclosure: M. Jimenez Artiles: None; **a. Khanfar**: None; **P. Chaudhary**: None; **R. Subedi**: None; **Q. Wang**: None; **A. Ocon**: Amgen, 2, 6.

Abstract Number: 0514

Transitional Monocytes and Innate T Cell Populations Help Distinguish Ro Seropositive vs Ro Seronegative Sjögren's Disease Using Whole Blood Immunophenotyping

Nicholas Bauer[1], Rufei Lu[1], Carla Guthridge[1], Tayte Stephens[2], Benjamin Jones[3], Wade DeJager[4], Susan Macwana[1], Caroline Shiboski[5], Alan Baer[6], Christopher Lessard[1], Astrid Rasmussen[1], Stephen Shiboski[5], Judith James[1], Linda F. Thompson[1], Blake M. Warner[7], A. Darise Farris[1], Joel Guthridge[1] and Sjögren's Team for Accelerating Medicines Partnership and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM), [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Oklahoma Health Science Center, Oklahoma City, OK, [3]Oklahoma State University, Oklahoma City, OK, [4]Oklahoma Medical Research Foundation, Oklahoma City, [5]University of California San Francisco, San Francisco, CA, [6]Johns Hopkins University School of Medicine, Baltimore, MD, [7]National Institutes of Health, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Blood immunophenotyping reveals systemic immune alterations and therapeutically actionable molecular endotypes in Sjögren's Disease (SjD). Reported changes include reduced memory B cells, plasmacytoid dendritic cells (pDC), and myeloid dendritic cells (mDC). Prior studies focused on Ro seropositive (Ro^{Pos}) SjD and utilized peripheral blood mononuclear cells, which are prone to processing artifacts. To avoid this limitation, we used mass cytometry with a point-of-care whole blood assay to compare immune cell frequencies in both Ro^{Pos} and Ro seronegative (Ro^{Neg}) SjD participants.

Methods: Blood samples from multiple sites were stained using the 30-marker Maxpar Direct Immune Profiling Assay (MDIPA) for broad immune phenotyping, then shipped to a central lab for CyTOF XT acquisition. Data were processed with OMIQ software, using FlowCut for quality control. Manual gating followed manufacturer guidelines to quantify total and lineage-specific immune cell subsets. Absolute cell counts were derived using individual white blood cell (WBC) counts. This study included 10 HC, 12 Ro^{Neg} SjD, and 31 Ro^{Pos} SjD participants, with cases meeting 2016 ACR/EULAR criteria. Principal component analysis (PCA) and heatmaps were used for dimension reduction and clustering.

Results: Novel findings included increased frequencies of transitional monocytes within the monocyte lineage in Ro^{Pos} vs. Ro^{Neg} SjD (p=0.022), with selective increases in Ro^{Pos} SjD cases with elevated disease activity (ESSDAI≥5) (p=0.032). Absolute counts of transitional monocytes trended higher in Ro^{Pos} SjD (p=0.13) despite reduced WBC counts in Ro^{Pos} vs. Ro^{Neg} SjD (p=0.025). In addition, absolute numbers of TCRγδ+ T cells were selectively increased in Ro^{Neg} SjD compared to both HC (p=0.009) and Ro^{Pos} SjD (p=0.025), while numbers of $CD28^{+}CD161^{hi}$ MAIT/NKT cells were selectively reduced in Ro^{Pos} SjD (p=0.013). Based on PCA, Ro^{Pos} participants with moderate to high ESSDAI scores clustered together at least in part due to increased transitional monocyte frequencies and decreased MAIT/NKT and γδT cells. In agreement with previous studies, we also found that frequencies, but not absolute numbers of memory and naïve B cells were reduced (p=0.018) and increased (p=0.015), respectively, in Ro^{Pos} SjD compared to HC. Absolute numbers of pDC were reduced in Ro^{Pos} SjD compared to both Ro^{Neg} SjD (p=0.02) and HC (p=0.024), and these reductions were driven by Ro^{Pos} cases with ESSDAI≥5 (p=0.013). Myeloid DC showed similar results, with reductions occurring in Ro^{Pos} patients with ESSDAI≥5 (p=0.012).

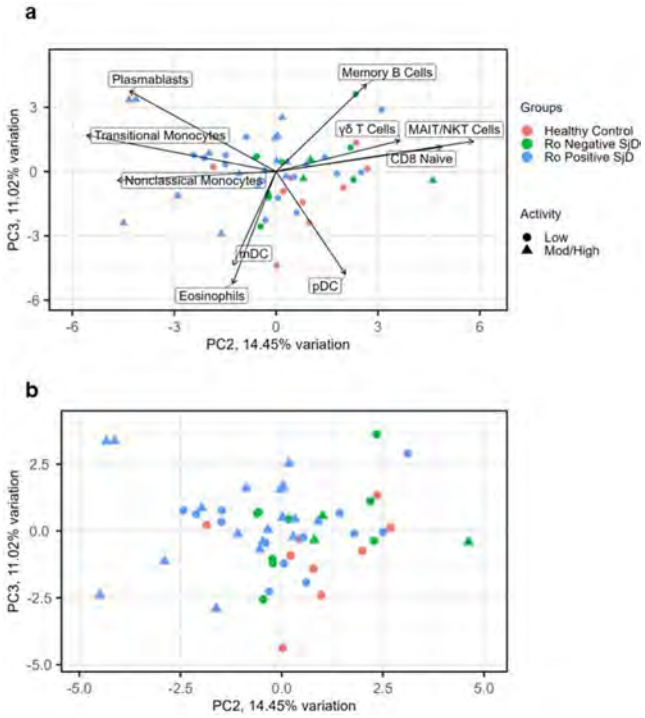


Figure 1: PCA highlights cell types important in distinguishing different endotypes of SjD. (a): PCA of SjD cases and controls using PC2 and PC3 to discriminate disease group and severity, both with the top six loadings. (b): PCA without loadings.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

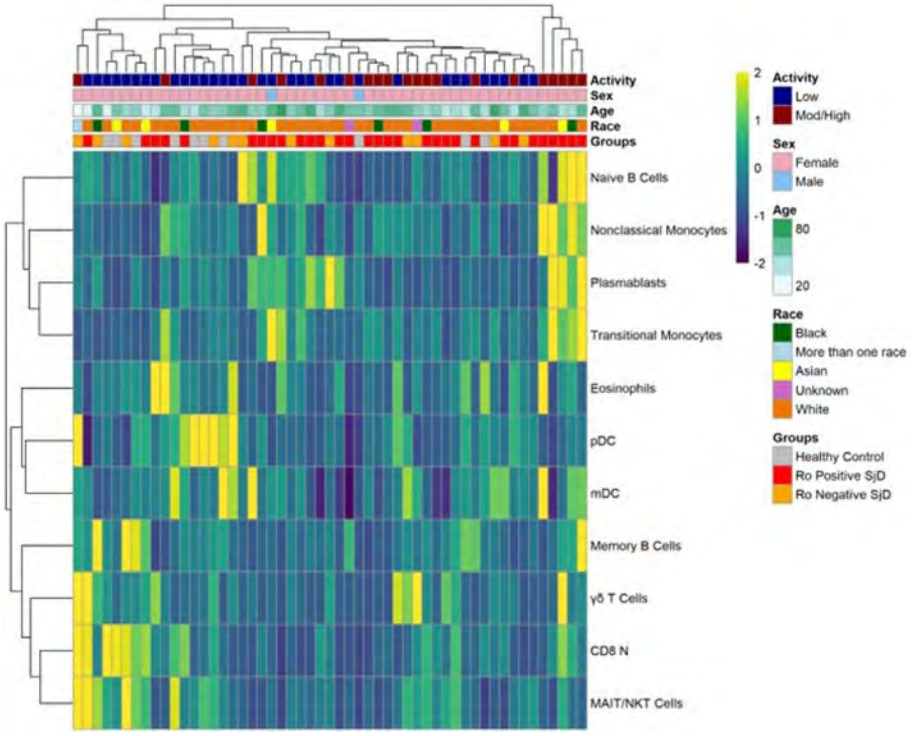


Figure 2. Unsupervised clustering showcases differences between groups in Ro positivity and disease activity. Clustered heatmap based on total percentages with disease group, sex, age, and race displayed. Both participants and features were clustered using Euclidian clustering.

Table 1. Descriptive and group statistics summarizing results from cell populations differentiating RoPos SjD and RoNeg SjD. While group statistics are listed in this table, significant pairwise comparisons are listed in the body of the abstract.

Table 1. Descriptive statistics and group significance testing among disease groups identifies populations separating Ro^{Pos} SjD from Ro^{Neg} SjD.

		Median +/- IQR			
	Cell Type	Healthy Controls N=10	Ro^{Neg} SjD N = 12	Ro^{Pos} SjD N = 31	Kruskal-Wallis p-value
% of Total	Naïve B Cell	2.951 ± 2.117	3.309 ± 1.881	3.677 ± 3.653	0.606
	Memory B Cell	0.624 ± 0.376	0.62 ± 0.41	0.413 ± 0.567	0.149
	mDC	0.19 ± 0.082	0.18 ± 0.093	0.177 ± 0.078	0.503
	pDC	0.12 ± 0.082	0.091 ± 0.083	0.067 ± 0.039	***0.042***
	Transitional Monocyte	0.13 ± 0.117	0.13 ± 0.13	0.231 ± 0.301	0.062
	MAIT/NKT	0.823 ± 0.644	0.872 ± 0.812	0.424 ± 0.454	***0.04***
	TCRγδ T Cell	0.225 ± 0.185	0.677 ± 0.601	0.295 ± 0.429	***0.038***
% of Lineage	Naïve B Cell	74.7 ± 15.236	77.689 ± 15.371	87.207 ± 13.009	***0.04***
	Memory B Cell	24.06 ± 14.508	21.04 ± 14.897	12.102 ± 12.658	***0.032***
	mDC	65.083 ± 10.786	66.116 ± 9.493	71.045 ± 13.229	0.493
	pDC	34.916 ± 10.786	33.883 ± 9.493	28.954 ± 13.229	0.493
	Transitional Monocyte	2.91 ± 0.983	2.556 ± 1.964	4.474 ± 3.401	***0.043***
Absolute	Naïve B Cell	0.144 ± 0.188	0.169 ± 0.102	0.165 ± 0.164	0.827
	Memory B Cell	0.026 ± 0.023	0.034 ± 0.021	0.018 ± 0.022	0.133
	mDC	0.009 ± 0.004	0.01 ± 0.004	0.008 ± 0.004	***0.045***
	pDC	0.005 ± 0.004	0.004 ± 0.004	0.003 ± 0.002	***0.016***
	Transitional Monocyte	0.006 ± 0.003	0.007 ± 0.003	0.011 ± 0.013	0.233
	MAIT/NKT	0.051 ± 0.038	0.039 ± 0.038	0.021 ± 0.027	***0.044***
	TCRγδ T Cell	0.013 ± 0.011	0.043 ± 0.032	0.011 ± 0.027	***0.035***

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Point-of-contact whole blood immunophenotyping reveals transitional monocytes as a novel marker of systemic disease activity in Ro^{Pos} SjD. The differential abundance of transitional monocytes, γδ T cells, and MAIT/NKT cells between Ro^{Pos} and Ro^{Neg} patients suggests distinct underlying pathogenic mechanisms. These findings enable more precise patient selection for immuomodulatory therapies targeting monocyte- and innate T cell-driven dysregulation, Planned studies aim to validate these signatures longitudinally and assess their utility in predicting treatment response or disease progression.

Disclosure: N. Bauer: None; **R. Lu**: None; **C. Guthridge**: None; **T. Stephens**: None; **B. Jones**: None; **W. DeJager**: None; **S. Macwana**: None; **C. Shiboski**: None; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **C. Lessard**: Janssen Global Services, 2, Johnson & Johnson Innovative Medicine, 2, 5; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **S. Shiboski**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **L. Thompson**: None; **B. Warner**: Mitobridge, subsidiary of Astellas Bio, 5, Pfizer, Inc., 5; **A. Farris**: Johnson & Johnson Innovative Medicine, 5; **J. Guthridge**: None.

Abstract Number: 0515

Inverse Correlation Between Type I Interferon Pathway Activation And Unstimulated Whole Salivary Flow In Sicca Patients

Nikolaos Marketos[1], Charalampos Skarlis[1], Sylvia Raftopoulou[1], Ada Gjyrezi[2], Paul Zumbo[3], Doron Betel[3], Ioanna E. Stergiou[4], Michael Voulgarelis[4], Paraskevi Giannakakou[5] and Clio Mavragani[6], [1]Molecular Physiology and Clinical Applications Unit, Department of Physiology, Medical School of Athens, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece, [2]Department of Medicine, Weill Cornell Medicine, New York, NY, USA, and Department of Physiology , National & Kapodistrian University of Athens, Athens, Greece, New York, [3]Department of Physiology & Biophysics, Applied Bioinformatics Core, Weill Cornell Medicine, New York, NY, USA, New York, [4]Outpatient Rheumatology Clinic, Department of Pathophysiology, Medical School of Athens, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece, [5]Department of Medicine, Weill Cornell Medicine, New York, NY, USA, and Meyer Cancer Center, Weill Cornell Medicine, New York, NY, USA, New York, [6]National and Kapodistrian University of Athens, Athens, Greece

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Oral and ocular dryness are hallmarks in patients with Sjögren's disease (SjD). Given that activation of interferon (IFN) pathways has been shown to be involved in SjD pathogenesis, we aimed to explore whether demographic, clinicopathological, and laboratory features, as well as type I IFN-inducible gene expression, are associated with impaired salivary secretion in a cohort of patients presenting with sicca complaints.

To exp

Methods: 623 consecutive patients with sicca symptoms that were evaluated in the Department of Physiology, Medical School of Athens, NKUA were included in this study after informed consent. Demographic, clinicopathological and laboratory data were thoroughly collected. Immune profile testing, chronic viral infections (HIV, HCV), chest X-ray and minor salivary gland (MSG) biopsy were also performed. Unstimulated whole salivary (UWS) flow rate was considered low with a threshold of ≤ 0.5 mL/5min. 110 MSG biopsies were subjected to real-time PCR to quantify IFN I and IFN II inducible genes (IFIGs). Moreover, IFIGs derived from the peripheral blood of these patients were evaluated. For ten patients with SjD, six of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

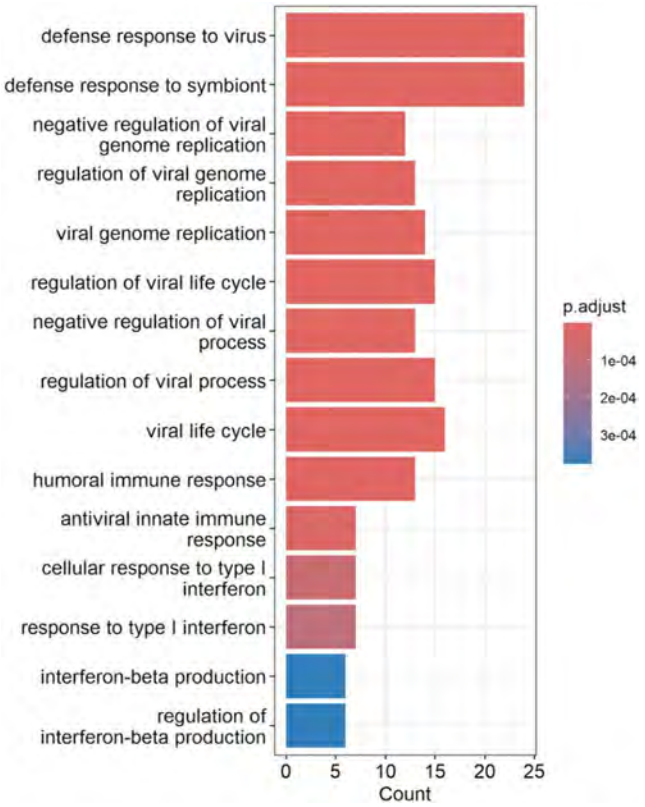


Figure 1-Gene Ontology (GO) analysis of upregulated genes in patients with low versus normal unstimulated salivary flow rates.

whom with normal and four with low UWS, besides next-generation sequencing (NGS), a pilot bulk RNA-sequencing study was performed. Total RNA was extracted from blood leukocytes, for which quality control was first performed. Statistical analysis was performed by SPSS 29.0. and bioinformatics analysis in R programming language.

Results: UWSF was inversely correlated to both type I IFIG transcripts (IFIT1: r=-0.446, p= 0.043, IFI44: r= -0.46, p=0.03, MX-1: r=-0.487, p=0.02) and IFN II (MIG: r= -0.592, p=0.006). Furthermore, this inverse correlation was detected against subjective oral dryness (r=-0.199, p=0.002), age at symptom onset (r=-0.146, p=0.046), Rose Bengal stain (r=-0.244, p=0.005), and Schirmer's test (r=-0.339, p< 0.001). Additionally, UWSF was inversely correlated to the presence of anti-Ro/SSA (r=-0.246, p< 0.001) and anti-La/SSB (r=-0.199, p=0.003) serological reactivities, as well as ESR (r=-0.170, p=0.012), IgG (r=-0.278, p=0.003) IgA (r=-0.245, p=0.01) and C4 (r=-0.161, p=0.018). Finally, MSG biopsy parameters, such as Focus score (FS) (r=-0.370, p< 0.01, Tarpley (r=-0.381, p< 0.01) and fat score (r=-0.448, p=0.013) were also inversely correlated to UWSF. Following differential gene expression (DEG) analysis, the upregulated DEGs in patients with low UWS compared to normal UWS were subjected to gene ontology analysis (GO) (Fig.1). Interestingly, the patients with low UWS had upregulated GOs regarding innate immunity such as defense response to virus and symbiont. Additionally, an upregulation of processes, such as response to type I IFN and regulation of IFN production, was illustrated.

Conclusion: These data highlight a negative correlation of UWSF to components of the IFN pathway as well as demographic, laboratory, and clinicopathological features in a cohort of patients with sicca symptoms. Furthermore, SjD patients with low UWS are characterized by upregulated antiviral defense and interferon signaling pathways in their peripheral blood, highlighting the link between IFN pathway and low UWS.

Disclosure: N. Marketos: None; **C. Skarlis**: None; **S. Raftopoulou**: None; **A. Gjyrezi**: None; **P. Zumbo**: None; **D. Betel**: None; **I. Stergiou**: None; **M. Voulgarelis**: None; **P. Giannakakou**: None; **C. Mavragani**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0516

Association Between Anti-cytosolic 5'-nucleotidase 1A (anti-cN1A) Antibodies and Lymphoma in Primary Sjögren Disease (SD)

Pierre-Marie Duret[1], Maude Bouchard-Marmen[2], Loukas Chatzis[3], Margherita Giannini[4], François Severac[5], FELTEN Renaud[6], Dan Levy[7], Benoit Nespola[8], Emmanuel Chatelus[9], Emmanuelle Dernis[10], Valerie Devauchelle[11], Philippe Dieude[12], Jean-Jacques Dubost[13], Anne-Laure Fauchais[14], Bernard Geny[15], Eric Hachulla[16], Claire larroche[17], Véronique Le Guern[18], Jacques Morel[19], Aleth Perdriger[20], Carine Salliot[21], Alain SARAUX[22], Damien Sène[23], Jean Sibilia[24], SORDET Christelle[6], Olivier Vittecoq[25], Raphaele Seror[26], Gaetane Nocturne[27], Andreas Goules[28], Athanasios G. Tzioufas[29], Xavier Mariette[30], Jacques-eric GOTTENBERG[31] and Alain Meyer[32], [1]Colmar General Hospital; Strasbourg University Hospital, Strasbourg, France, [2]CHU de Québec, Québec, QC, Canada, [3]Pathophysiology Department, Athens School of Medicine, National and Kapodistrian University of Athens, Greece, Athens, Greece, [4]Explorations fonctionnelles musculaires, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, Service de Rhumatologie, Centre de référence des maladies auto-immunes rares (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, Strasbourg, Alsace, France, [5]Département de Santé Publique, Groupe Méthodes en Recherche Clinique (GMRC), CHU de Strasbourg, Strasbourg, Strasbourg, Alsace, France, [6]Service de Rhumatologie, Centre de référence des maladies auto-immunes rares (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, Strasbourg, Alsace, France, [7]Explorations fonctionnelles musculaires, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, Strasbourg, Alsace, France, [8]Laboratoire d'Immunologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, Strasbourg, Alsace, France, [9]Department of Rheumatology, University Hospital Strasbourg, France, Strasbourg, France, [10]Service de Rhumatologie, Centre Hospitalier Le Mans, Le Mans, Le Mans, France, [11]UBO, Brest, France, [12]Service de Rhumatologie, Hôpital Bichat APHP, Paris, Paris, Ile-de-France, France, [13]Service de Rhumatologie, CHU Gabriel Montpied, Clermont-Ferrand, Clermont-Ferrand, France, [14]UR 3072, Centre de Recherche en Biomédecine, Université de Strasbourg, Strasbourg; France, Strasbourg, France, [15]UR 3072, Centre de Recherche en Biomédecine, Université de Strasbourg, Strasbourg; FranceExplorations fonctionnelles musculaires, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg;, Strasbourg, Alsace, France, [16]Service de Médecine Interne et Immunologie Clinique, CHU de Lille, Hôpital Claude Huriez, Lille, Lille, France, [17]Service de Médecine Interne, Hôpital Avicenne APHP, Bobigny, Paris, Ile-de-France, France, [18]Cochin hospital, Paris, France, [19]CHU and University of Montpellier, Montpellier, France, [20]Rennes University, Rennes, France, [21]CHR orleans, Orleans, France, [22]CHU Brest, Brest, France, [23]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, Paris, Ile-de-France, France, [24]Rheumatology Department, National Center for Rare autoimmune disease RESO,Strasbourg University Hospital, Strasbourg, Alsace, France, [25]Service de Rhumatologie & CIC-CRB 1404, CHU de Rouen, Université de Rouen, Rouen, Rouen, France, [26]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [27]University Paris Saclay, Le Kremlin Bicetre, Ile-de-France, France, [28]Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens Institute for Autoimmune Systemic and Neurologic Diseases, Athens, Athens, Greece, [29]Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens Institute for Autoimmune Systemic and Neurologic Diseases, Athens, Athens, [30]University Paris-Saclay, Le Kremlin Bicetre, France, [31]Hautepierre Hospital, STRASBOURG, Alsace, France, [32]Service de Rhumatologie, Centre de référence des maladies auto-immunes rares (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, Explorations fonctionnelles musculaires, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, UR 3072, Centre de Recherche en Biomédecine, Université de Strasbourg, Strasbourg; France, Strasbourg, Alsace, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: There is an unmet clinical need for identification of novel biomarkers of systemic complications and lymphoma in primary Sjögren disease (SD). Anti-cytosolic 5'-nucleotidase 1A (anti-cN1A) antibodies have been reported in SD but their clinical significance in this specific context is currently unknown. Anti-cN1A have been originally described in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

inclusion body myositis (IBM). Both SD and IBM are associated with hematological malignancies. The objectives of this study were to determine the clinical significance of anti-cN1A antibodies and their value as a predictive biomarker of non-Hodgkin lymphoma (NHL) in SD.

Methods: Baseline serum levels of anti-cN1A were measured in a prospective discovery cohort of 377 patients with SD, from the French ASSESS cohort, whose primary objective was to prospectively examine the incidence and predictors of systemic complications and lymphoma in SD. The significance of anti-cN1A positivity in the ASSESS cohort was analyzed in univariate and multivariate models. Multivariate analysis included variables associated with anti-cN1A positivity in univariate analyses with a p-value < 0.2.

An independent validation case-control cohort of 58 SD patients (26 patients with untreated SD-NHL at the time of blood sampling and 32 patients with SD and no lymphoma despite ≥10-year follow-up), from the Athens' University Hospital SD cohort, was also screened for anti-cN1A antibodies.

Results: Twenty-nine SD patients tested positive for anti-cN1A (29/377 [7.7 %] [95% CI: 0.05-0.11]).

Only one patient in the anti-cN1A positive group was diagnosed with myositis during the follow-up, which fulfilled IBM criteria (1/29 [3.4 %] vs. 1/348 [0.3%] in the anti-cN1A negative group, p = 0.024).

Anti-cN1A positive patients had more frequently lymphadenopathy at baseline (8/29 [27.6 %] vs. 44/346 [12.7 %], p = 0.026) and more frequently developed lymphoma during follow-up (incident NHL: 3/29 [10.3%] in the anti-cN1A positive vs. 6/348 [1.7%] in the anti-cN1A negative patients, p = 0.003). The association between SD-NHL and anti-cN1A positivity remained significant (p=0.008) in multivariate analysis taking into account some previously reported predictors of lymphoma including lymphadenopathy, beta2-microglobulin and BAFF serum levels.

In the validation cohort, patients with SD-NHL had more frequently anti-cN1A positivity as compared with SD patients and no lymphoma (4/26 [12%] vs 0/32 [0%], p= 0.039).

Conclusion: In two independent cohorts of well-phenotyped SD patients, anti-cN1A positivity was associated with lymphoma. Anti-cN1A positivity might therefore represent a novel predictive biomarker of SD-related lymphoma.

Disclosure: P. Duret: None; **M. Bouchard-Marmen**: None; **L. Chatzis**: None; **M. Giannini**: None; **F. Severac**: None; **F. Renaud**: None; **D. Levy**: None; **B. Nespola**: None; **E. Chatelus**: None; **E. Dernis**: None; **V. Devauchelle**: None; **P. Dieude**: None; **J. Dubost**: None; **A. Fauchais**: None; **B. Geny**: None; **E. Hachulla**: None; **C. Iarroche**: None; **V. Le Guern**: AstraZeneca, 12, attending meetings and travel., Bristol-Myers Squibb(BMS), 6, Novartis, 2; **J. Morel**: AbbVie, 2, 5, 6, Biocon, 6, Biogen, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, GlaxoSmithKline, 2, 6, Lilly, 2, 6, Medac, 6, Mylan/Viatris, 6, Nordic Pharma, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche/Chugai, 6, Sanofi, 2, 6; **A. Perdriger**: None; **C. Salliot**: None; **A. SARAUX**: Novartis, 6; **D. Sène**: None; **J. Sibilia**: None; **S. Christelle**: None; **O. Vittecoq**: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **G. Nocturne**: None; **A. Goules**: None; **A. Tzioufas**: None; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **A. Meyer**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0517

Gut Microbiota Dysbiosis and Clinical Predictors of Fatigue in Primary Sjögren's Syndrome: A Multi-Omics Study

Qiguo Cui[1], Pan Wang[2], Bin Zhou[1] and QIn Huang[3], [1]Southern Medical Univercity Nanfang Hospital, guang zhou, China (People's Republic), [2]southern medical university Nanfang Hospital, Guangzhou, China (People's Republic), [3]Nanfang Hospital, Guangzhou, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Fatigue affects 70% of primary Sjögren's syndrome (pSS) patients, but its mechanisms remain unclear. We investigated clinical predictors and gut microbiota associations in pSS-related fatigue.

Methods: 196 pSS patients were stratified by ESSPRI and Profile of Fatigue (ProF) scores. Univariate/multivariable logistic regression identified fatigue predictors. Fecal samples from 57 patients underwent 16S rRNA sequencing.

Results: 1.ESSPRI fatigue dimension: Fatigue was associated with SAS (OR = 1.06, 95% CI: 1.01–1.12, p = 0.032) and IFN-γ (OR = 1.72, 95% CI: 1.34–2.2, p < 0.001). Fatigue improvement was linked to the use of total glucosides of paeony (OR = 1.98, 95% CI: 1.03–3.81, p = 0.041) and IgG levels (OR = 0.94, 95% CI: 0.90–0.99, p = 0.014).

2.Profile of Fatigue-Somatic Dimension: Fatigue was associated with SAS (OR = 1.10, 95% CI: 1.04–1.16, p < 0.001), IFN-γ (OR = 1.37, 95% CI: 1.12–1.68, p = 0.003), and anti-SSB antibodies (OR = 2.72, 95% CI: 1.39–5.69, p = 0.008). Fatigue improvement correlated with total glucosides of paeony use (OR=2.32, 95%CI 1.07 ~ 5.01, p=0.032) and CH50 levels (OR=1.06, 95%CI 1.03-1.10, p<0.001).

3.Profile of Fatigue-Mental Dimension: Fatigue was associated with SAS (OR = 1.06, 95% CI: 1.01–1.11, p = 0.019) and SDS (OR = 1.05, 95% CI: 1.01–1.09, p = 0.016). Fatigue improvement was linked to male sex (OR = 0.10, 95% CI: 0.01–0.85, p = 0.035), hematologic involvement (OR = 0.44, 95% CI: 0.21–0.92, p = 0.029), CH50 (OR = 1.04, 95% CI: 1.01–1.07, p = 0.019), and anti-SSB antibody positivity (OR = 0.45, 95% CI: 0.21–0.95, p = 0.036).

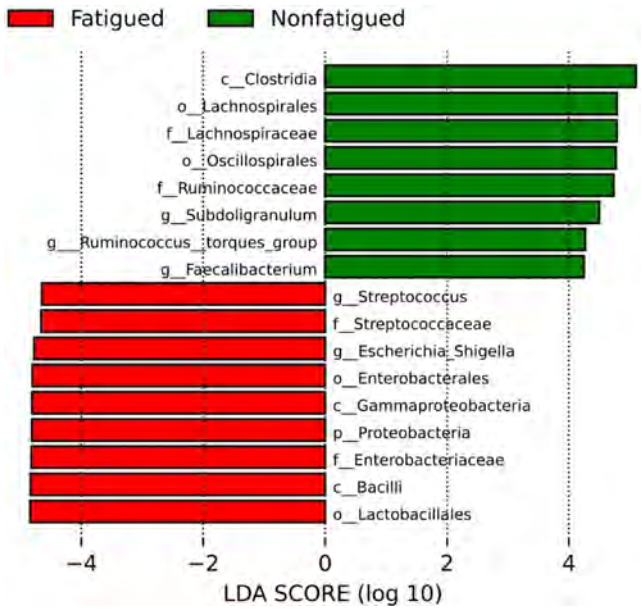
variable	univariate analysis					multivariate analysis				
	β	S.E	Z	*P*	OR (95%CI)	β	S.E	Z	*P*	OR (95%CI)
man (%)	-2.17	1.07	-2.03	**0.042**	0.11 (0.01 ~ 0.93)	-1.86	1.12	-1.66	0.097	0.15 (0.02 ~ 1.40)
Total glucosides of paeony (%)	1	0.35	2.84	**0.005**	2.73 (1.36 ~ 5.47)	0.84	0.39	2.14	**0.032**	2.32 (1.07 ~ 5.01)
CH50 (U/mL)	0.06	0.02	3.53	**<.001**	1.06 (1.03 ~ 1.10)	0.06	0.02	3.29	**0.001**	1.06 (1.03 ~ 1.10)
Hematologic involvement (%)	-0.76	0.35	-2.18	**0.03**	0.47 (0.24 ~ 0.93)	-0.65	0.38	-1.7	0.089	0.52 (0.25 ~ 1.10)

Binary logistic regression based on Profile of Fatigue-Somatic improvement grouping

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

variable	univariate analysis					multivariate analysis				
	β	S.E	Z	*P*	OR (95%CI)	β	S.E	Z	*P*	OR (95%CI)
man (%)	-2.17	1.07	-2.03	**0.042**	0.11 (0.01 ~ 0.93)	-2.33	1.11	-2.11	**0.035**	0.10 (0.01 ~ 0.85)
CH50 (U/mL)	0.04	0.01	2.76	**0.006**	1.04 (1.01 ~ 1.07)	0.04	0.02	2.34	**0.019**	1.04 (1.01 ~ 1.07)
Anti-SSB antibodies (%)	-0.74	0.35	-2.1	**0.036**	0.48 (0.24 ~ 0.95)	-0.8	0.38	-2.1	**0.036**	0.45 (0.21 ~ 0.95)
Hematologic involvement (%)	-0.83	0.35	-2.36	**0.018**	0.44 (0.22 ~ 0.87)	-0.82	0.37	-2.18	**0.029**	0.44 (0.21 ~ 0.92)

Binary logistic regression based on Profile of Fatigue-Mental improvement grouping



LEfSe analysis of gut microbiota between two groups

4.16S rRNA sequencing revealed significant differences in α- and β-diversity of gut microbiota between fatigue and non-fatigue groups. Escherichia-Shigella and Streptococcus were significantly enriched in the fatigue group, and their abundances showed a strong positive correlation with fatigue severity scores. In contrast, Ruminococcus torques group, Faecalibacterium, and Subdoligranulum were predominantly enriched in the non-fatigue group, with their abundances negatively correlated with fatigue scores.

Conclusion: This study, through a multi-dimensional assessment framework encompassing the ESSPRI fatigue dimension and the ProF physical/mental fatigue subscales, revealed that SAS, SDS, IFN-γ, and anti-SSB antibodies are associated with pSS-related fatigue. Total glucosides of paeony use, IgG levels, CH50 levels, sex(male), anti-SSB antibody status, and hematologic involvement significantly influence fatigue improvement in pSS patients. Gut microbiota may contribute to the pathogenesis of pSS-related fatigue. These findings provide critical insights into the mechanisms underlying pSS-related fatigue and suggest novel strategies for diagnosis and therapeutic intervention.

Disclosure: Q. Cui: None; **P. Wang**: None; **B. Zhou**: None; **Q. Huang**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0518

Deregulation of PSGL-1, HLA-DR and IFNα expression in peripheral innate immune cells of primary Sjögren Syndrome patients

Santos Castañeda[1], Alejandra Ramos-Manzano[2], Ines Sanchez-Abad[3], Miren Uriarte-Ecenarro[4], M. Paula Alvarez-Hernandez[4], Esther San-Antonio[4], Esther Vicente-Rabaneda[5] and Ana Urzainqui[4], [1]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [2]Hospital Unversitario de la Princesa, Madrid, Madrid, Spain, [3]Hospitla de la Princesa, Madrid, Spain, [4]Hospital de la Princesa, Madrid, Madrid, Spain, [5]Hospital Universitario de La Princesa, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Sjögren's Syndrome (pSS) is an autoimmune disease characterized by lymphocytic infiltration of exocrine glands and systemic manifestations including cutaneous and renal involvement. Phagocytes--monocytes, neutrophils, and dendritic cells-- are innate immune cells playing crucial roles in both innate defence and modulation of adaptive immunity. Dysregulation of these cells in pSS has been linked to altered inflammatory response, although the mechanisms driving disease progression remain unclear. PSGL-1 is a leukocyte adhesion molecule and a checkpoint for the immune system. High expression level of HLA-DR is a sign of immune activation. Additionally, higher production of IFNα has been related to pSS pathogenesis

Methods: We obtained the peripheral blood of 44 pSS patients and 26 healthy donors (HD). The percentage of cells expressing PSGL-1, HLA-DR and IFNα mean fluorescence intensity (MFI) was analysed by flow cytometry in neutrophils, monocytes (both classical and non-classical), and plasmacytoid dendritic cells (pDC).

Statistical differences between HD and patients were calculated using Mann-Whitney U test or Student's T-test. Association of the different variables with the presence of the disease was assessed by binary logistic regression (BLR). Then, we performed its receiver operating characteristic (ROC) curves. Statistical significance was set at $p< 0.05$. Statistical analyses were performed using SPSS 25.0 and GraphPad Prism 8 software.

Results: Compared to HD, the percentage of HLA-DR-expressing cells was increased in neutrophils, monocytes, and pDC of pSS patients. The expression level was higher in pDC and monocytes, suggesting constitutive immune activation in pSS patients. The percentage of neutrophils and pDCs expressing PSGL-1 and PSGL-1's MFI of non-classical monocytes were reduced compared to HD. This reduction may contribute to higher leukocyte activation. However, the expression level of PSGL-1 in non-classical monocytes was increased. Regarding IFN-α, we found an elevated percentage of neutrophils, classical monocytes and pDC producing IFNα in pSS patients and reduced percentage of non-classical monocytes.

BLR analyses identified percentage of neutrophils expressing HLA-DR (79.6% sensitivity, 56.7% specificity and AUC 0.756), percentage of pDC expressing IFNα (92.7% sensitivity, 13.6% specificity and AUC 0.634) and ratio of conventional dendritic cells (cDC) and pDC (83.7% sensitivity, 60% specificity and AUC 0.75) as potential biomarkers for pSS diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our findings underscore an important role of phagocytes in maintaining chronic immune activation in pSS patients. The altered expression of these molecules in innate cell populations might contribute to disease's pathogenesis. The results contribute to our understanding of phagocyte involvement in pSS and offer potential new avenues for diagnostic strategies.

Disclosure: S. Castañeda: None; **A. Ramos-Manzano**: None; **I. Sanchez-Abad**: None; **M. Uriarte-Ecenarro**: None; **M. Alvarez-Hernandez**: None; **E. San-Antonio**: None; **E. Vicente-Rabaneda**: None; **A. Urzainqui**: None.

Abstract Number: 0519

A Multi-criterion Feature Integration Framework for Accurate Diagnosis of Primary Sjögren's Syndrome Using Routine Laboratory Tests: A Multicentre, Retrospective Cohort Study

Shu Liu[1], Guanhao Wu[1], Mengge Pan[1], Qi Sun[2], Jingchen Gao[1], Xianming Long[3], Chaogui Tang[4], Xinran Yuan[1] and Lingyun Sun[1], [1]Department of Rheumatology and Immunology, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China (People's Republic), [2]Department of Endocrinology and Metabolism, Affiliated Hospital of Nantong University, Nantong, China, Nantong, China (People's Republic), [3]The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University, Suzhou, China (People's Republic), [4]The Affiliated Huaian First People's Hospital of Nanjing Medical University, Huai'an First People's Hospital, Nanjing Medical University, Huaian, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

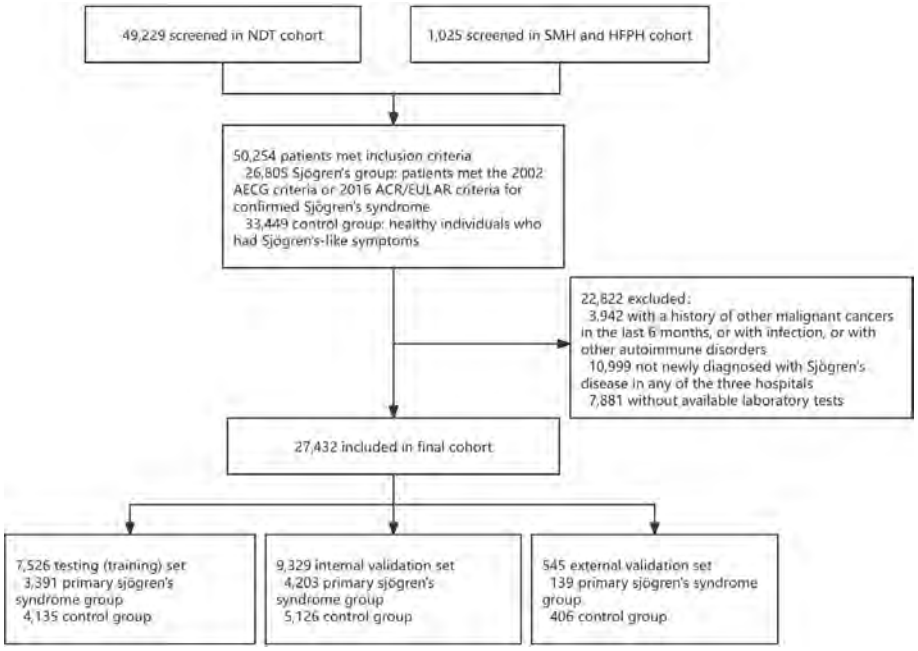
Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a prevalent systemic autoimmune disorder. However, the early and accurate diagnosis of pSS remains challenging due to its non-specific clinical manifestations, the absence of definitive molecular markers, and the limitations of current diagnostic tests. The present study aims to evaluate the diagnostic utility of routine laboratory tests for predicting pSS and to develop a robust, cost-effective and generalizable integrated artificial intelligence (AI) model to assist in the identification of pSS.

Methods: This multicentre, retrospective cohort study included data from 99 laboratory items of 27,432 patients with and without pSS who were admitted to one regional centre hospital and two local hospitals in China between January 1, 2013, and January 31, 2023. The construction of Sjögren Multi-criterion Feature Integration Framework (SMFIF) model was based on 16 optimal features, using multi-algorithm feature selection, SHAP value analysis, model performance evaluation, and ensemble learning strategies. The model was evaluated using an internal validation set comprising 9,329 individuals, and an external validation set consisting of 545 individuals. The primary outcome was the prediction accuracy of the model in identifying pSS.

Results: The SMFIF model attained an area under the receiver-operating characteristic curve (AUC) of 0.929 (95% CI, 0.923-0.935) in the testing set, 0.934 (95% CI, 0.929-0.939) in the internal validation set, and 0.964 (95% CI, 0.943-0.986) in the external validation set. The model demonstrated higher AUC, ACC and sensitivity in comparison with anti-SSA/Ro, anti-SSB/La, antinuclear antibodies (ANA), Globulin (GLO), Rheumatoid factor (RF), immunoglobulin G (IgG), and Complement (C3 and C4) in the diagnosis of pSS. The superior performance of SMFIF in pSS prediction was confirmed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Study flowchart

through calibration curves and confusion matrices. The SMFIF was developed as a publicly available prediction tool that will provide an estimated probability of pSS based on input laboratory data.

Conclusion: The SMFIF model has been shown to consistently achieve satisfactory performance in the prediction of pSS when utilising routine laboratory tests from the testing set and two validation sets. This model offers a low-cost, easily accessible, and accurate diagnostic tool for pSS.

Disclosure: S. Liu: None; **G. Wu**: None; **M. Pan**: None; **Q. Sun**: None; **J. Gao**: None; **X. Long**: None; **C. Tang**: None; **X. Yuan**: None; **L. Sun**: None.

Abstract Number: 0520

Implementation of Salivary Gland Ultrasound by General Radiology can Improve Detection of Glandular Inflammation in Patients with Sicca

Stephanie Lee[1], Chadwick Johr[2], Nora Sandorfi[2], Ali Dhanaliwala[2] and Dana DiRenzo[2], [1]University of Pennsylvania & Children's Hospital of Philadelphia, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Salivary Gland Ultrasound (SGUS) can be useful in the evaluation and management of Sjögren's Disease (SjD) but its use has been limited to trained rheumatologists. We hypothesized that implementation of a standardized scanning protocol and graded according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) scoring

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Disease characteristics of patients with sicca who had salivary gland ultrasounds scored as OMERACT grade 3 vs grade 0 at initial visit to the Sjögren's center of an academic rheumatology division.

Patient Characteristics	Grade 3	Grade 0	P value
	n=54	N=54	
Age, mean (SD)	54.9 (17.2)	52.8 (14.4)	0.49
Sex, n (%) F	48 (89%)	45 (83%)	0.40
Race, n (%)			0.021
White	31 (57%)	38 (76%)	
Asian	4 (7%)	5 (10%)	
Black	16 (30%)	3 (6%)	
Other	3 (6%)	4 (8%)	
SSA+, n (%)	49 (91%)	13 (24%)	<0.001
ANA+, n (%)	41 (85%)	11 (22%)	<0.001
RF+, n (%)	37 (73%)	7 (16%)	<0.001

system by an academic radiology department can improve sensitivity for detecting glandular inflammation that may be missed by physical exam.

Methods: This was a retrospective, case-control study of patients with sicca seen in an academic Sjogren's Center. Patient with SGUS scored as OMERACT grade 3 (≥1 parotid +/- submandibular gland) were compared to OMERACT grade 0 (all glands) with complete serologies (ANA, SSA, RF) available for review. Charts were screened consecutively. For patients with SjD, the EULAR Sjögren's Disease Activity Index (ESSDAI) and the Routine Assessment of Patient Index Data-3 (RAPID-3) were extracted with demographic, treatment, and laboratory data available either any time prior to the encounter (serologies) or completed up to 3 months after the same encounter. Descriptive statistics, including means and proportions, were calculated and comparisons made by t-test.

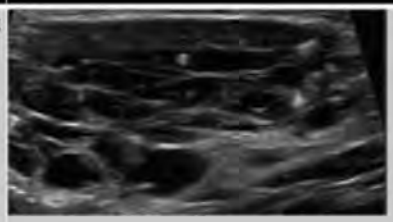
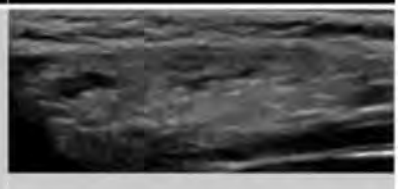
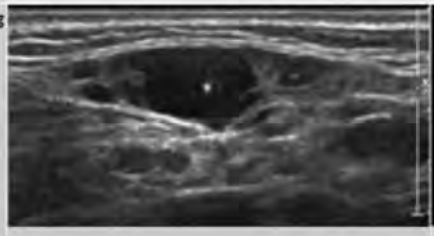
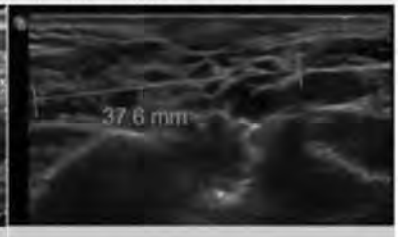
Results: Fifty–four patients with grade 3 OMERACT SGUS changes and complete antibody profiles were compared to 54 patients with grade 0 changes. Patients with grade 3 changes had a mean (SD) age of 54.9 years (17.2), were predominantly female (89%), about half met the ACR/EULAR SjD classification criteria (55.6%), and had current use of conventional

Table 2. Sjögren's Disease activity per EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) for patients with OMERACT grade 3 changes on salivary gland ultrasound at initial visit. PNS (peripheral nervous system), CNS (central nervous system).

Disease Activity (ESSDAI) n=36	No activity	Low activity	Medium Activity	High Activity
Constitutional	29 (81%)	7(19%)		
Lymphadenopathy	32 (89%)	2 (6%)	1 (3%)	1 (3%)
Glandular	26 (72%)	5 (14%)	5 (14%)	
Articular	30 (83%)	4 (11%)	2 (6%)	
Cutaneous	35 (97%)	1 (3%)		
Pulmonary	34 (94%)	2 (6%)		
Renal	35 (97%)	1 (3%)		
Muscular	36 (100%)			
PNS	35 (97%)	1 (3%)		
CNS	36 (100%)			
Hematological	35 (100%)			
Biological	27(82%)	2 (6%)	4 (12%)	
Total, median (IQR)	3 (0, 6.5)			

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Qualitative examples of echotexture changes over time from patients who completed 2 SGUSs with grade 3 OMERACT scores.

Disease Activity	Scan 1	Scan 2
Improving		
	9/3/19, right parotid sagittal views noting gland heterogeneity with diffuse anechoic lesions and hyperechoic bands, OMERACT grade 3. ESSDAI 12.	7/5/22, right parotid sagittal views noting gland heterogeneity with scattered anechoic lesions and hyperechoic bands, OMERACT grade 2. ESSDAI 0; s/p treatment with rituximab for MALT lymphoma (2/2019 to 1/2021).
Worsening		
	9/14/23, left parotid sagittal views noting a large anechoic lesion with hyperechoic density with smaller hypo-/anechoic lesions concerning for lymphoma, OMERACT grade 3. ESSDAI 12.	2/26/24, left parotid sagittal views noting severe gland heterogeneity with multiple and new, large anechoic lesions and hyperechoic densities concerning for recurrent lymphoma, OMERACT grade 3. ESSDAI 16; s/p excisional biopsy (MALT lymphoma) and radiation; no B-cell depletion received.

disease modifying agents (cDMARDs) (48.2%) (**Table 1**). Patients with grade 3 changes were more likely to have positive serologies (anti-SSA, ANA, RF). In addition, Patients with grade 3 changes had a mean (SD) RAPID-3 score of 9.4 (6.9), indicating moderate disability and symptom burden. For patients diagnosed with SjD with grade 3 changes and completed ESSDAIs (n = 36), the median (IQR) ESSDAI was 3 (0, 6.5) with low activity (>10%) present in the constitutional, glandular, and articular domains (**Table 2**). Notably, only 28% of patients with grade 3 SGUS changes had elevated activity levels on the glandular domain of the ESSDAI which is obtained through physical exam (swelling/enlargement of glands).

Conclusion: Patients with OMERACT grade 3 changes on SGUS more often had positive SSA, ANA, and RF compared to those with grade 0 changes. Despite grade 3 changes on SGUS, only 28% of patients had elevated disease activity per ESSDAI glandular domain (physical exam). This may suggest that adoption by general radiology of an SGUS scanning protocol and use of the OMERACT scoring system may improve rheumatologists' detection of glandular activity, compared to physical exam alone.

Disclosure: S. Lee: None; **C. Johr**: Bristol-Myers Squibb(BMS), 1, 2; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 2, Janssen, 2, Novartis, 1; **A. Dhanaliwala**: None; **D. DiRenzo**: Amgen, 2, Novartis, 2, Sjogren's Foundation, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0521

Umbilical cord-derived mesenchymal stem cells suppress the pathogenesis of primary Sjögren's disease by inducing Bach2 expression

Yukitomo Hagiwara[1], Goh Murayama[2], Taiga Kuga[3], Yujin Nishioka[4], Masaki Nojima[1], Takumi Saito[5], Yu Yamaji[6], Tomoko Miyashita[6], Makio Kusaoi[7], Ken Yamaji[5] and Naoto Tamura[8], [1]Juntendo University, Department of Internal Medicine and Rheumatology, Bunkyo-ku, Tokyo, Japan, [2]Department of Internal Medicine and Rheumatology, Juntendo University Graduate School of Medicine, Tokyo, Japan, [3]Juntendo University, Tokyo, Japan, [4]Juntendo University, Department of Internal Medicine and Rheumatology, Shizuoka, Japan, [5]Juntendo University, Department of Internal Medicine and Rheumatology, Tokyo, Japan, [6]Juntendo University, Department of Internal Medicine and Rheumatology, Bunkyo-ku, Tokyo, [7]Juntendo University, Department of Internal Medicine and Rheumatology, Bunkyo, Tokyo, Japan, [8]Juntendo University School of Medicine, Tokyo, Japan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0506–0521) Sjögren's Disease – Basic & Clinical Science Poster I: Etiology, Pathogenesis, Diagnosis

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Sjögren's disease (pSD) is characterized by lymphocytic infiltration of the salivary and lacrimal glands, leading to functional loss and gradually causing dry mouth and dry eyes. In this study, we investigated the anti-inflammatory effects of umbilical cord-derived mesenchymal stem cells (MSCs) on salivary gland pathology and the involvement of Bach2.

Methods: Peripheral blood mononuclear cells (PBMCs) from pSD patients were co-cultured with MSCs under various stimulatory conditions to evaluate the inhibition of cell differentiation and cytokine production. $CD4^+$ T cells and B cells were isolated from the peripheral blood of pSD patients and co-cultured with MSCs stimulated with pSD-associated autoantigens. The changes in cell subsets and the suppression of IgG production due to MSC inhibitory effects were evaluated. Cell damage was induced in human salivary gland cell lines (HSGs) using H_2O_2, and the frequency of dead cells was compared. The above experiment was performed under conditions with and without contact cell-to-cell. Bach2 expression in T cells, B cells, and monocytes was also evaluated by Western blotting.

Results: MSCs decreased the production of IFN-γ and IL-4 on T cells and TNF-α on monocytes without cell-to-cell contact with MSCs. Co-culturing B cells from pSD patients with MSCs in the presence of CpG-ODN significantly reduced the proportion of plasma cells and increased the proportion of memory B cells compared to B cell monocultures. Similar results were obtained under non-contact cell-to-cell conditions. Furthermore, when $CD4^+$T cells and B cells were co-cultured in the presence of pSD-associated autoantigen, IgG production was suppressed under cell-to-cell contact with MSCs compared to without MSCs. In the induction of cell damage against HSGs, the frequency of dead cells was significantly reduced under non-contact with MSCs. In addition, Bach2 expression in T cells, B cells, and monocytes was enhanced when co-cultured with MSCs in the presence of various stimulations.

Conclusion: In this study, we found that the critical function of MSCs is to induce Bach2 expression in target cells through cell-independent, soluble factors. MSCs control cytokine production and excessive autoantibody production in target cells by inducing Bach2 expression, and even prevent cell death in salivary gland cells. Conventional pSD therapy has not achieved sufficient improvement in salivary gland secretion flow through the use of immunosuppressive drugs. MSCs hold potential as an innovative pSD therapy, including for salivary gland disorders.

Disclosure: Y. Hagiwara: Cell Exosome Therapeutics Co., Ltd., 5; **G. Murayama**: Cell Exosome Therapeutics Co., Ltd., 5; **T. Kuga**: None; **Y. Nishioka**: None; **M. Nojima**: None; **T. Saito**: None; **Y. Yamaji**: None; **T. Miyashita**: None; **M. Kusaoi**: Cell Exosome Therapeutics Co., Ltd., 5; **K. Yamaji**: None; **N. Tamura**: AbbVie/Abbott, 6, Asahi Kasei,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

5, 6, AstraZeneca, 6, Ayumi, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, 6, Cell Exosome Therapeutics Co., Ltd., 5, Chugai, 5, 6, Daiichi Sankyo, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 6, Novartis, 6, Taisho, 5, UCB, 6.

Abstract Number: 0522

The Incidence Rate and Risk Factors of Arrhythmias in Patients with Psoriatic Arthritis

Abdulrahman Y Almansouri[1], Jiayi Li[2], Ali Alhadri[3], Keith Colaco[4], Paula Harvey[5], Shadi Ahktari[6], Vinod Chandran[7], Dafna D. Gladman[8], Richard Cook[2] and **Lihi Eder**[7], [1]King Faisal Specialist Hospital and Research Centre, University of Toronto and Women's College Hospital, Toronto, Canada, [2]University of Waterloo, Waterloo, Canada, [3]King Fahad Hospital, University of Toronto and Toronto Western Hospital, Schroeder Arthritis Institute, Toronto, Canada, [4]University of Toronto, Toronto, Canada, [5]University of Toronto Department of Medicine and Women's College Hospital, Toronto, ON, Canada, [6]University of Toronto Department of Medicine and Women's College Hospital, Toronto, Canada, [7]University of Toronto, Toronto, ON, Canada, [8]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with psoriatic arthritis (PsA) are at increased risk of developing cardiovascular diseases, including arrhythmias. Given that traditional cardiovascular disease risk factors are prevalent in patients with PsA, it remains unclear if arrhythmia development risk in this population is due to these factors or PsA disease activity. We therefore aimed to assess the incidence and risk factors for tachy- and bradyarrhythmias in patients with PsA.

Methods: We performed a retrospective cohort analysis of PsA patients followed prospectively from 1994 to 2024. Patients were assessed every 6 to 12 months following a standard protocol where demographics, measures of PsA disease activity, comorbidities and medication information were collected. Arrhythmia events were identified via review of patients charts and linkage with provincial hospitalization databases. The following arrhythmia endpoints were assessed: atrial tachyarrhythmia (defined as atrial fibrillation, atrial flutter or supraventricular tachycardia); bradyarrhythmia/pacemaker (defined as second degree atrioventricular block, complete heart block or pacemaker placement); ventricular tachyarrhythmia (defined as ventricular tachycardia, ventricular fibrillation or placement of implantable cardioverter-defibrillator). The cumulative incidence rate (CIR) of each type of arrhythmia was calculated. Cox regression hazard models were used to evaluate the association between PsA disease activity measures (either single time-point level prior to event or cumulative average over time) and arrhythmia endpoints. Each model was hierarchically adjusted for age and sex, PsA duration, cardiovascular risk factors and PsA therapies.

Results: Of 1670 PsA patients (mean age 46.3 years, 54.2% male, **Table 1**) included in this analysis, a total of 80 atrial, 17 brady and 11 ventricular arrhythmias were identified. By age 70, the overall CIRs were 7.82%, 0.45% and 0.67% for atrial, brady and ventricular arrhythmias, respectively (**Figure 1**). Arrhythmias occurred predominantly in older patients, with a marked increase in the rate of atrial tachyarrhythmias after age 60. Bradyarrhythmia and ventricular tachyarrhythmia also occurred predominantly in older population, with a marked increase in the rate of these events after age of 70. In the fully adjusted multivariable analysis (**Table 2**), remission/low vs. high disease activity state was associated with lower risk of atrial tachyarrhythmia (single-point Hazard Ratio (HR) 0.49, 95% CI 0.26, 0.92; cumulative mean HR 0.46, 95% CI 0.23, 0.91). Similarly higher 3-item Visual Analog Scale (3-VAS) was associated with higher risk of atrial tachyarrhythmia (single-point

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

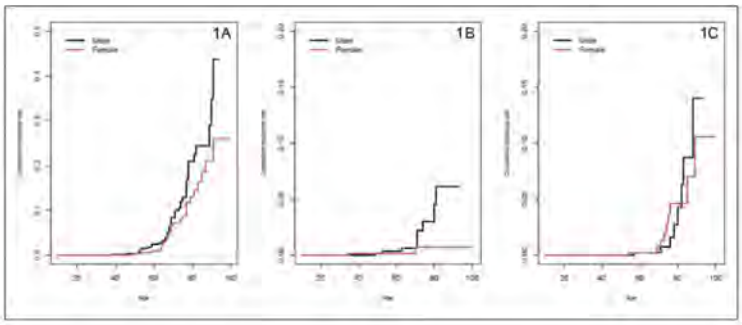
Table 1 : Baseline characteristics of the study population overall and among patients with arrhythmia

Table 1: Baseline characteristics of the study population.

	All population (N=1670)	Atrial arrhythmia (N=80)	Ventricular arrhythmia (N=11)	Bradyarrhythmia (N=17)
Age	46.4 ± 13.3	56.4 ± 12.1	52.0 ± 12.2	60.7 ± 9.2
Sex: Male (%)	902 (54.0)	50 (62.5)	9 (81.8)	8 (47.1)
Ethnicity: White (%)	1359 (81.4)	77 (96.3)	10 (90.9)	17 (100)
Psoriasis duration	17.3 ± 13.6	22.7 ± 14.7	22.6 ± 17.0	22.9 ± 16.1
PsA duration	7.17± 9.2	13.54± 11.1	11.26± 10.5	15.82± 9.2
Smoking: Current (%)	578 (34.6)	37 (46.2)	8 (72.7)	11 (64.7)
BMI (kg/m²)	28.74 (6.4)	29.5 (6.3)	28.68 (6.5)	28.43 (4.5)
Hyperlipidemia (%)	188 (11.2)	6 (7.5)	0 (0)	0 (0)
Hypertension (%)	320 (19.1)	28 (35)	3 (27.2)	3 (17.6)
Heart disease (%)	36 (2.1)	3 (3.7)	1 (9.0)	0 (0)
Thyroid disease (%)	83 (4.9)	2 (2.5)	1 (9.0)	0 (0)
Diabetes (%)	125 (7.4)	7 (8.7)	0 (0)	1 (5.8)
DAPSA category (%)				
Remission/Low	468 (28.0)	21 (26.2)	4 (36.3)	1 (5.8)
Moderate	551 (32.9)	21 (26.2)	2 (18.1)	12 (70.5)
High	651 (38.9)	38 (47.5)	5 (45.4)	4 (23.5)
PASI category (%)				
Mild	888 (53.1)	38 (47.5)	5 (45.4)	8 (47.0)
Moderate	401 (24.0)	20 (25.0)	2 (18.1)	6 (35.2)
Severe	381 (22.8)	2 (27.5)	4 (36.3)	3 (17.6)
3-VAS (0-10)	4.3 ± 2.0	4.34 ± 2.1	4.27 ± 2.2	4.28 ± 2.0
CRP, mean (mg/L)	11.03 ± 19.2	12.66 ± 23.0	15.85 ± 29.5	10.62 ± 19.2
PsA therapies (%)				
Daily NSAID use (%)	440 (26.35)	18 (22.5)	3 (27.2)	9 (52.9)
csDMARD use (%)	221 (13.23)	7 (8.75)	2 (18.1)	2 (11.7)
b/tsDMARD use (%)	110 (6.59)	3 (3.75)	0 (0)	1 (5.8)

Abbreviations: BMI, body mass index; b/tsDMARD, biologic or targeted synthetic DMARD; CRP, c-reactive protein; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; DAPSA, disease activity in psoriatic arthritis: NSAIDs, non-steroidal anti-inflammatory drug; PASI, psoriasis area severity index; PsA, psoriatic arthritis; 3-VAS, 3-component visual analogue scale.

HR 1.18, 95% CI 1.04, 1.33; cumulative mean HR 1.22, 95% CI 1.04, 1.44). Although higher PASI scores showed a trend towards increased risk of arrhythmia, these findings did not reach statistical significance.



1D: Crude cumulative incidence rate by age group for each arrhythmia endpoint in PsA

	Overall CIR%* (95% CI)		
Age, years	**Atrial Tachyarrhythmia**	**Ventricular Tachyarrhythmia**	**Bradyarrhythmia**
60	1.69 (1.05, 2.72)	0.25 (0.08, 0.78)	0.21 (0.05, 0.85)
70	7.82 (5.86, 10.43)	0.67 (0.25, 1.81)	0.45 (0.13, 1.53)
80	17.08 (13.23, 22.05)	2.64 (1.23, 5.67)	4.40 (2.36, 8.19)

* Cumulative incidence rate (number of events by age).
Abbreviations: CI, confidence interval; IR, incidence rate; PsA, psoriatic arthritis

Figure 1 - Cumulative incidence of arrhythmia events in male and female patients with PsA: 1A. Atrial Tachyarrhythmia; 1B. Ventricular Tachyarrhythmia; 1C. Bradyarrhythmia; 1D: Overall cumulative incidence rate by age (95% CI).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 - The association between PsA-related variables and the risk of atrial tachyarrhythmia in patients with PsA using Cox proportional hazards models

Table 2: The association between PsA-related factors and the risk of atrial tachyarrhythmia in patients with PsA using Cox proportional hazards models (Total population=1670 patients, n= 80 events).

Variable		Cumulative average co-variates*		Single time point co-variates*	
		HR (95% CI)	P value	HR (95% CI)	P value
DAPSA-Categories	Moderate vs. High disease activity	0.59 (0.33, 1.05)	0.076	0.65(0.34, 1.27)	0.214
	Remission/low vs. High disease activity	**0.46 (0.23, 0.91)**	**0.03**	**0.49 (0.26, 0.92)**	**0.031**
PASI-Category	Moderate vs. Mild	0.82 (0.46, 1.46)	0.498	1.29(0.73, 2.27)	0.388
	Severe vs. Mild	1.51 (0.85, 2.66)	0.165	1.44(0.75, 2.75)	0.276
3-VAS	1-unit increase	**1.22 (1.04, 1.44)**	**0.019**	**1.18(1.04, 1.33)**	**0.011**
CRP, mg/L	1-unit increase	1.01 (0.99, 1.03)	0.329	1.01(0.99, 1.02)	0.463

*Each model is adjusted for age, sex, PsA disease duration, diabetes, hypertension, dyslipidemia, thyroid disease, heart disease, smoking status and body mass index, NSAIDs, csDMARDs and b/tsDMARDs. **Significant results are bolded**

Abbreviations: CI, confidence interval; CRP, c-reactive protein; DAPSA, disease activity in psoriatic arthritis; HR, Hazard Ratio; PASI, psoriasis area severity index; PsA, psoriatic arthritis; 3-VAS, 3-component visual analogue scale.

Conclusion: Higher PsA disease activity is associated with higher atrial tachyarrhythmia risk. These findings reinforce the importance of controlling inflammation in PsA to prevent these events.

Disclosure: A. Almansouri: None; **J. Li**: None; **A. Alhadri**: None; **K. Colaco**: None; **P. Harvey**: None; **S. Ahktari**: None; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **R. Cook**: None; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5.

Abstract Number: 0523

SPECTREM: Guselkumab Significantly Improves Patient Reported Outcomes at Week 16 in Participants with Low Body Surface Area, Moderate Psoriasis with Special Sites Involvement

Jennifer Soung[1], Virginie Kelly[2], Marni Wiseman[3], Adrian Rodriguez[4], Theodore Alkousakis[5], Olivia Choi[5], Daphne Chan[5], Katelyn Rowland[5], **Linda Hou**[6], Jenny Jeyarajah[7], Nastaran Abbarin[8], Elizabeth Skobelev[5], Sancharitha Ramji[5], James Krell[9], Max Sauder[10] and David Adam[11], [1]Southern California Dermatology, Inc, Santa Ana, CA, USA, Santa Ana, [2]Saint-Louis Medical Clinic, Quebec, Canada, Quebec, Canada, [3]SkinWise Dermatology, Manitoba, Canada, Manitoba, Canada, [4]Nashville Skin Comprehensive Dermatology Center, Nashville, TN, USA, Nashville, TN, [5]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [6]Janssen Scientific Affairs, LLC, a Johnson & Johnson company, Horsham, [7]Johnson & Johnson, Horsham, PA, USA, Horsham, [8]Janssen Inc, Toronto, ON, Canada, Toronto, Canada, [9]Total Skin & Beauty Dermatology Center, Birmingham, AL, USA, Birmingham, [10]Probity Medical Research, ON, Canada; University of Toronto, ON, Canada, Toronto, Canada, [11]CCA Medical Research, ON, Canada, Toronto, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Even low body surface area (BSA) psoriasis can be extremely bothersome to patients and can have a significant impact on their lives just as much as more extensive disease. SPECTREM is an ongoing, Phase 3b, multicenter, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of guselkumab in participants with low BSA (2%-15%), moderate (Investigator's Global Assessment [IGA]=3) psoriasis involving ≥1 special site (scalp, face, intertriginous, or genital).

Methods: A total of 338 participants were randomized 2:1 to receive guselkumab 100 mg (n=225) or placebo (n=113) at Week 0 and Week 4, then every 8 weeks. Patient-reported outcomes (PROs) assessed at Week 16 included change from baseline in Psoriasis Symptoms and Signs Diary (PSSD; range, 0-100), and Dermatology Life Quality Index (DLQI; range, 0-30).

Results: At baseline, participants had mean (standard deviation [SD]) BSA of 7.6% (3.7%); mean (SD) PSSD total symptoms score of 53.8 (23.2), mean (SD) PSSD itch score of 6.8 (2.2), and a mean (SD) DLQI of 11.5 (6.7). On average, participants had a disease duration of 17 years, and the majority of participants had never received systemic therapy (86.3%). At Week 16, guselkumab-treated participants achieved significantly greater mean change from baseline in the PSSD total symptoms score (guselkumab –36.08 vs placebo 0.37; $p< 0.001$). Among participants with PSSD itch score ≥4 at baseline, a significantly greater proportion of guselkumab-treated participants achieved ≥4-point reduction at Week 16 (guselkumab 62.7% vs placebo 12.5%; $p< 0.001$). A significant proportion of guselkumab-treated participants with PSSD symptom score >0 achieved a PSSD symptom score of 0 at Week 16 (21.9% vs placebo 2.7%; $p< 0.001$). Similarly, a significantly greater proportion of guselkumab-treated participants achieved DLQI 0/1 (guselkumab 48.9% vs placebo 3.5%; $p< 0.001$) and DLQI 0 (guselkumab 28.4% vs placebo 3.5% $p< 0.001$) at Week 16. No new safety signals were identified.

Conclusion: In this low BSA, moderate psoriasis population, quality of life impact significantly improved after just 3 doses of guselkumab.

Disclosure: J. Soung: AbbVie, 5, 12, Personal fees, Dermavant, 5, Eli Lilly, 12, Non-financial support (manuscript preparation during the conduct of the study), Kyowa Kirin, 5, LEO Pharma, 5, 12, Personal fees, Pfizer, 5, 12, Personal fees, Regeneron, 5, Sanofi, 5, 12, Personal fees; **V. Kelly**: AbbVie, 12,, 1, 2, 6, Allakaos, 12,, 1, 2, 6, Amgen, 12,, 1, 2, 6, Appolo, 12,, 1, 2, 6, Aslan pharmaceuticals, 12,, 1, 2, 6, Bausch Health, 12,, 1, 2, 6, Cara, 12,, 1, 2, 6, ConCERT pharmaceuticals, 12,, 1, 2, 6, Eli Lilly, 12,, 1, 2, 6, Galderma, 12,, 1, 2, 6, GSK, 12,, 1, 2, 6, Horizon, 12,, 1, 2, 6, Incyte, 12,, 1, 2, 6, Inmagene, 12,, 1, 2, 6, Innovaderm, 12,, 1, 2, 6, Janssen, 12,, 1, 2, 6, L'Oréal, 12,, 1, 2, 6, Laroche-Posay, 12,, 1, 2, 6, LEO Pharma, 12,, 1, 2, 6, Nektar, 12,, 1, 2, 6, Novartis, 12,, 1, 2, 6, Numab, 12,, 1, 2, 6, Opsidio, 12,, 1, 2, 6, Pfizer, 12,, 1, 2, 6, RAPT, 12,, 1, 2, 6, Sanofi, 12,, 1, 2, 6, Sun pharma, 12,, 1, 2, 6, UCB, 12,, 1, 2, 6, Verasci, 12,, 1, 2, 6; **M. Wiseman**: AbbVie, 12,, 1, 2, 6, Amgen, 12,, 1, 2, 6, Arcutis, 12,, 1, 2, 6, Asana BioSciences, 12,, 1, 2, 6, AstraZeneca, 12,, 1, 2, 6, Bausch Health, 12,, 1, 2, 6, Bristol Myers Squibb, 12,, 1, 2, 6, Celgene, 12,, 1, 2, 6, Dermira, 12,, 1, 2, 6, Eli Lilly, 12,, 1, 2, 6, Galderma, 12,, 1, 2, 6, Glenmark, 12,, 1, 2, 6, Incyte, 12,, 1, 2, 6, Janssen, 12,, 1, 2, 6, La Roche-Posay, 12,, 1, 2, 6, LEO Pharma, 12,, 1, 2, 6, Novartis, 12,, 1, 2, 6, Pfizer, 12,, 1, 2, 6, PRCL Research, 12,, 1, 2, 6, Principia, 12,, 1, 2, 6, Regeneron, 12,, 1, 2, 6, Sanofi, 12,, 1, 2, 6, UCB, 12,, 1, 2, 6; **A. Rodriguez**: Arcutis, 1, 6, Dermavent, 1, 6, Eli Lilly, 1, 6, EPI Health, 1, 6, Janssen, 1, 6, LEO Pharma, 1, 6, Novartis, 1, 6, Sciton, 1, 6, Strathspey Crown, 11, Sun Pharma, 1, 6, UCB, 1, 6; **T. Alkousakis**: Johnson & Johnson, 3, 11; **O. Choi**: Johnson & Johnson, 3, 11; **D. Chan**: Johnson & Johnson, 3, 11; **K. Rowland**: Johnson & Johnson, 3, 11; **L. Hou**: Johnson & Johnson, 3, 11; **J. Jeyarajah**: Johnson & Johnson, 3, 11; **N. Abbarin**: Janssen Research & Development, 3; **E. Skobelev**: Johnson & Johnson, 3, 11; **S. Ramji**: Johnson & Johnson, 3, 11; **J. Krell**: AbbVie, 12, Support, Amgen, 12, Support, Bristol Myers Squibb, 12, Support, Eli Lilly, 12, Support, Janssen Biotech, 12, Support, Sun Pharma, 12, Support, UCB, 12, Support; **M. Sauder**: AbbVie, 2, Amgen, 2, Arcutis, 2, Bausch Health, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Eli Lilly Canada, 2, Fresenius Kabi Canada, 2, Galderma, 2, Incyte, 2, Janssen, 2, L'Oreal Canada, 2, LEO Pharma, 2, Merck, 2, Novartis, 2, Pfizer, 2, Pierre Fabre, 2, Sanofi, 2, Sun Pharma, 2, UCB Canada, 2; **D. Adam**: AbbVie, 12,, 1, 6, Actelion, 12,, 1, 6,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Amgen, 12,, 1, 6, Arcutis, 12,, 1, 6, Bausch Health, 12,, 1, 6, Boehringer Ingelheim, 12,, 1, 6, Bristol Myers Squibb, 12,, 1, 6, Celgene, 12,, 1, 6, Coherus, 12,, 1, 6, Dermavant, 12,, 1, 6, Dermira, 12,, 1, 6, Eli Lilly, 12,, 1, 6, Galderma, 12,, 1, 6, Incyte, 12,, 1, 6, Janssen, 12,, 1, 6, LEO Pharma, 12,, 1, 6, Merck, 12,, 1, 6, Novartis, 12,, 1, 6, Pfizer, 12,, 1, 6, Regeneron, 12,, 1, 6, Sanofi Genzyme, 12,, 1, 6, Sun Pharma, 12,, 1, 6, UCB, 12,, 1, 6.

Abstract Number: 0524

Radiographic progression in sacroiliac joints in five years follow up in non-radiographic axial spondyloarthritis patients and the predictive factors

Esra Erpek[1], Hasan Kocaayan[2], Elif Ediboğlu[3], Ayberk Sinci[4], Özgür Tosun[4], Dilek Solmaz[3] and **Servet Akar**[5], [1]İzmir Katip Çelebi Üniversitesi, Romatoloji Bilim Dalı, İzmir, Izmir, Turkey, [2]Izmir Katip Çelebi University School of Medicine, Rheumatology, Turkey, İzmir, Turkey, [3]Izmir Katip Çelebi University School of Medicine, Rheumatology, Turkey, İzmir, Izmir, Turkey, [4]İzmir Katip Çelebi Üniversitesi, Radyoloji Bilim Dalı, İzmir, Izmir, Turkey, [5]Department of Medicine, Izmir Katip Celebi University School of Medicine, Izmir, Turkey

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: This study aimed to assess the rate of progression in sacroiliac joints in non-radiographic axial spondyloarthritis (nr-axSpA) and to identify the predictive factors for the progression.

Table 1: Baseline demographic, disease related clinical, and laboratory characteristics of non-radiographic axSpA patients

Characteristics (N=194)	
Male sex n (%)	84/194 (43.3)
Age, years mean ± SD	44.6 ± 10.3
Symptom duration, yıl mean ± SD	16 ± 8.8
Time since diagnosis, years, mean ± SD	10.1 ± 5.5
Education duration, years mean ± SD	10.8 ± 4
Current smoking n (%)	74/181 (40.9)
BMI kg/mZ mean ± SD	28.3 ± 21.1
HLA-B27 positivity n (%)	78/159 (49.1)
C-reactive protein mg/dl mean ± SD	9.5 ± 17.9
BASDAI mean ± SD	4.3 ± 2.3
BASFI mean ± SD	3.1 ± 2.6
ASDAS-CRP mean ± SD	2.6 ± 1.1
BASMI mean ± SD	2.8 ± 1.3
ASQOL mean ± SD	8.7 ± 5.1
HAQs mean ± SD	0.8 ± 0.6
Dactylitis, n (%)	5/184 (2.7)
Peripheral arthritis n (%)	58/177 (32.8)
Heel pain n (%)	89/170 (52.4)
Radiographic hip involvement, n (%)	8/194 (4.1)
Psoriasis n (%)	8/147 (5.4)
Inflammatory bowel disease n (%)	15/166 (9)
Uveitis n (%)	19/184 (10.3)
NSAID use n (%)	140/171 (81.9)
Biologic treatment use, n (%)	88/193 (45.6)
Positive ASAS family history,n (%)	54/168 (32.1)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Univariable and multivariable longitudinal analysis results of factors influencing progression from nr-axSpA to r-axSpA

	Univariable analysis				Multivariable analysis			
	B	%95 CI		P	B	%95 CI		P
Symptom duration	0.033	-0.002	0.067	0.065	0.031	-0.008	0.115	0.088
Education level	-0.052	-0.222	-0.014	**0.026**	-0.052	-0.159	0.056	0.347
Body Mass Index	0.016	-0.002	0.034	0.075	0.014	0.000	0.028	**0.043**
BASFI score	0.169	0.031	0.307	**0.016**	0.035	-0.169	0.239	0.735
C-reaktive protein	0.023	0.003	0.044	**0.027**	0.019	0.806	1.680	**0.038**
BASMI score	0.329	-0.049	0.708	0.088	0.372	-0.240	0.983	0.195
ASAS Family History for SpA	-0.099	-1.913	-0.80	**0.033**	-0.715	-1.619	0.189	0.121

Methods: In total 321 patients classified as nr-axSpA and who had at least one follow-up pelvic radiograph among 695 patients followed in an axSpA cohort were included in the present analysis. A total of 647 radiographs were evaluated by two independent readers (blinded for the chronological order) according to the modified New York criteria. Discrepancies were resolved by a third experienced rheumatologist. Progression rates from nr-axSpA to r-axSpA and the related factors were assessed over a follow-up period of two and five years. Potential factors influencing progression to r-axSpA at the five-year follow-up were tested by using the Generalized Estimating Equations (GEE) method. Factors/covariates has a significance level of < 0.10 were included in the multivariate analysis.

Results: Of the 321 nr-axSpA patients followed in the axSpA cohort, 194 had radiographic follow-up at two years and 116 at five years. At two years follow up progression to r-axSpA was observed in 17.5% of patients at and at five years in 24.1%. In univariate analysis symptom duration, education level, body mass index, Bath Ankylosing Spondylitis Function Index score, score, C-reactive protein levels, Bath Ankylosing Spondylitis Metrology index scores and the presence of family history for SpA according to ASAS proposal were found to be associated with the radiographic progression. However in multivariate model only elevated C-reactive proteine and body mass index were identified as significant predictors of progression to r-axSpA (Table 2).

Conclusion: In our study, the 5 year progression rate from nr-axSpA to r-axSpA was 24.1%. Previous studies have reported progression rates ranging from 2% to 43.5%, depending on variations in patient selection, imaging frequency, and disease duration at diagnosis (1). The recently published PROOF study, which included axSpA patients who were diagnosed within 1 year, reported a 5-year progression rate of 16% (2). The relatively higher rate observed in our cohort may be attributed to the longer symptom duration Importantly, among the factors analyzed, body mass index (BMI) emerged as a significant predictor of radiographic progression, which has not been consistently emphasized in previous studies. Serum CRP levels was also associated with progression, in line with established risk factors. The identification of BMI as a significant factor in our cohort highlights the potential role of metabolic and mechanical stress in disease progression and warrants further investigation. Our results reinforce the importance of integrating clinical, laboratory, and imaging parameters to improve prediction of progression in nr-AxSpA.

References

1-Protopopov M, Poddubnyy D. Radiographic progression in non-radiographic axial spondyloarthritis. Expert Rev Clin Immunol. 2018 Jun;14(6):525-533.
2-Poddubnyy D. et al. Radiographic Progression in Sacroiliac Joints in Patients With Axial Spondyloarthritis: Results From a Five-Year International Observational Study. A)CR Open Rheumatol. 2024 Feb;6(2):103-110.

Disclosure: E. Erpek: None; **H. Kocaayan**: None; **E. Ediboğlu**: None; **A. Sinci**: None; **Ö. Tosun**: None; **D. Solmaz**: None; **S. Akar**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0525

Cost-of-Illness Among Newly Diagnosed Patients with Psoriatic Arthritis in Sweden

Sofia Wittgren[1], Sofia Exarchou[2], Daniela Di Giuseppe[3], Ulf Lindström[4], **Tor Olofsson**[1], Lennart T. H. Jacobsson[4], Johan Askling[3] and Johan Karlsson Wallman[1], [1]Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Skane Lan, Sweden, [2]Lund University, Akarp, Skane Lan, Sweden, [3]Karolinska Institutet, Department of Medicine Solna, Clinical Epidemiology Division, Stockholm, Stockholms Lan, Sweden, [4]Gothenburg University, Sahlgrenska Academy, Department of Rheumatology and Inflammation Research, Gothenburg, Vastra Gotaland, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Up-to-date information on the cost-of-illness of psoriatic arthritis (PsA) is important for healthcare/social insurance system budgeting and to highlight unmet needs in PsA care. Here, we aimed to estimate societal costs (for healthcare/work disability) during one year (yr) from diagnosis among all working-age (18-64yr) individuals diagnosed with PsA in Sweden 2016-2019, and to relate these to costs during the preceding yr and in the general population (GP).

Methods: Newly diagnosed PsA patients were identified from the Swedish National Patient Register (NPR) and the Swedish Rheumatology Quality register (SRQ): ≥1 ICD-10 code for PsA (L40.5/M07.0-M07.3) as main diagnosis from rheumatology/internal medicine units in NPR or PsA diagnosis registered in SRQ 2016-2019, and no prior such diagnoses. Each PsA case was matched by sex/age/county to 5 GP comparators without PsA according to NPR/SRQ, and costs (inflation-adjusted to 2019 US Dollars [$]) from 1yr before to 1yr after PsA diagnosis (and the same period for comparators) were estimated. Costs for all dispensed prescription drugs were retrieved from the Prescribed Drug Register, while intravenous bDMARDs were priced based on doses in SRQ. For specialized (non-primary) out-/inpatient care (retrieved from NPR), costs were calculated via the Swedish 2019 Diagnosis Related Group (DRG) system. Work disability costs were estimated as accumulated net sick leave/disability pension days (Social Insurance Agency) multiplied with the average daily salary (plus social fees) in

Table. Resource use and mean annual costs during the year following diagnosis of PsA (or the corresponding time-period for matched general population comparators)

	PsA (n=5196)		GP comparators (n=25 740)		Between-group cost difference
	Resource use[a]	Mean cost (SD)	Resource use[a]	Mean cost (SD)	Mean (95%CI)[b]
Total drug use	**99%**	**2560 (5052)**	**67%**	**294 (1830)**	**2265 (2135 to 2418)**
b/tsDMARDs	27%	1853 (3931)	0.1%	3.5 (169)	1849 (1743 to 1962)
csDMARDs	60%	105 (219)	0.5%	1.0 (31)	104 (98 to 110)
All other drugs	98%	602 (3116)	67%	290 (1819)	312 (234 to 407)
Total specialized healthcare utilization[e]		**3285 (5483)**		**1178 (5194)**	**2104 (1957 to 2268)**
Outpatient care visits[f]	5.4 (4.7)	2383 (2315)	1.2 (3.1)	519 (1483)	1862 (1800 to 1928)
Inpatient care days[g]	0.7 (7.9)	905 (4332)	0.5 (5.4)	659 (4481)	244 (129 to 376)
Total healthcare costs[c,e]		**5842 (8195)**		**1472 (5744)**	**4366 (4143 to 4617)**
Total work disability costs		**9272 (17 896)**		**4581 (13 968)**	**4695 (4216 to 5229)**
Sick leave days	32 (77)	5092 (12 428)	10 (45)	1611 (7278)	3481 (3156 to 3856)
Disability pension days	26 (87)	4180 (13 974)	18 (76)	2970 (12 182)	1214 (819 to 1597)
Societal costs[d,e]		**15 101 (21 505)**		**6051 (16 324)**	**9048 (8468 to 9680)**

Costs in 2019 US Dollars. [a] % with any such drug use, or mean (SD) visits/days, during the year prior to diagnosis (or the corresponding time-period for matched GP comparators). [b] Assessed by non-parametric bootstrapping (1000 iterations), accounting for the matched design. [c] Drug + healthcare utilization costs. [d] Healthcare + work disability costs. Missing data PsA/GP: [e] n=5/12; [f] n=2/0; [g] n=3/12. b/tsDMARDs, biologic or targeted synthetic disease-modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; GP, general population; PsA, psoriatic arthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

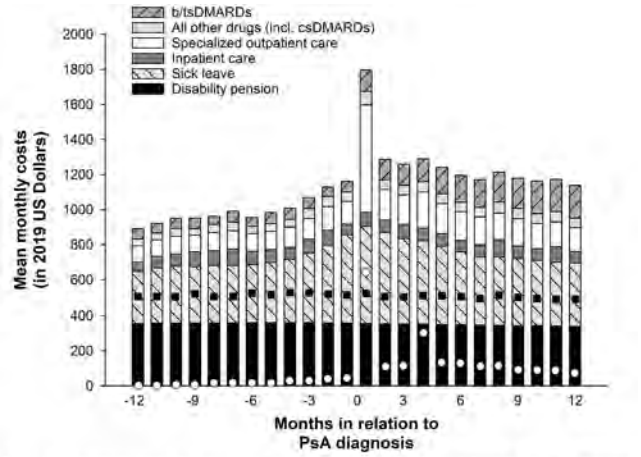


Figure 1. Mean monthly costs (by cost categories) from 12 months before until 12 months after the diagnosis of PsA among working-age (18-64 years) patients diagnosed in Sweden 2016-2019. For comparison to the mean monthly societal costs among the PsA patients (represented by the top of each bar), the corresponding mean costs in matched general population comparators (assessed during the same time-period as their respective index cases) are denoted by black squares. In the PsA group, median monthly societal costs are also indicated by white dots. b/tsDMARDs, biologic or targeted synthetic disease-modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; incl., including; PsA, psoriatic arthritis.

Figure 1

Sweden 2019. Despite skewness, costs are reported as arithmetic means, considered most informative for cost studies. Cost comparisons between PsA and comparators were done by non-parametric bootstrapping, accounting for the matched design; between subsets of PsA by Mann-Whitney U-test; and between years by Wilcoxon's matched-pair signed-rank test.

Results: During the yr following diagnosis, societal costs were significantly higher in PsA (n=5196; mean cost $15 101) than in the GP comparators (n=25 740; mean cost $6051; mean between-group difference: $9048), with elevations of all cost categories and dominated by work disability costs (61% of societal costs in PsA; **Table**). Costs were highly skewed, with 11% of cases accounting for 50% of all societal costs in PsA. The monthly costs for all categories (except inpatient care) were significantly elevated compared to the GP already 12 months prior to PsA diagnosis. Costs increased gradually (mainly

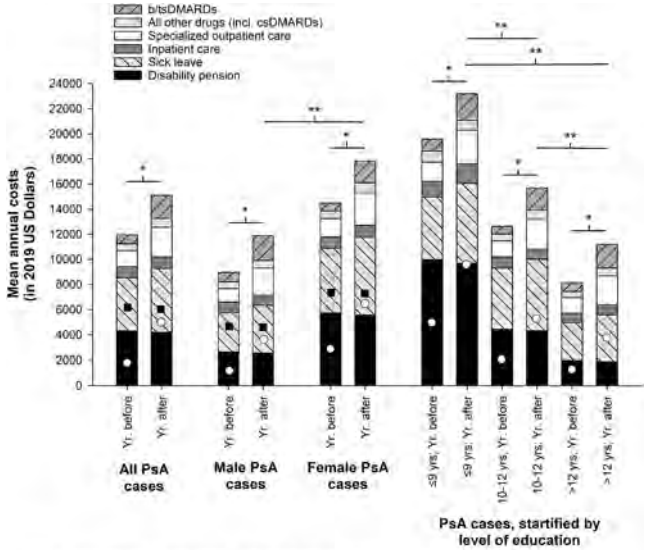


Figure 2. Mean annual costs (by cost categories) during the year before and the year following the diagnosis of PsA, respectively, among working-age (18-64 years) patients diagnosed in Sweden 2016-2019; displayed for all patients, as well as stratified by sex and level of education. For comparison to the mean societal costs among the PsA patients (represented by the top of each bar), the corresponding mean costs in matched general population comparators (assessed during the same time-period as their respective index cases) are denoted by black squares. In the PsA group, median societal costs are also indicated by white dots. * p<0.001 for comparison of yearly societal costs by Wilcoxon's matched-pair signed-rank test. ** p<0.001 for between-group comparisons of yearly societal costs by Mann-Whitney U-test. b/tsDMARDs, biologic or targeted synthetic disease-modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; incl., including; PsA, psoriatic arthritis; Yr., year.

Figure 2

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

due to rising sick leave) to a peak at diagnosis, and then slightly decreased during the following 11 months (**Figure 1**). Except for inpatient care and disability pension costs, all annual cost categories increased significantly from the yr before to the yr after diagnosis (**Figure 2**). Societal costs were higher in females and individuals with lower education (**Figure 2**).

Conclusion: Already in the year following diagnosis, PsA (at a group level) imposes a substantial health economic burden on society, with societal costs 2.5 times higher than in the GP and with work disability as the dominant cost driver. Whether earlier diagnosis/interventions could bring about a more favorable cost trajectory should be a focus of future studies.

Disclosure: S. Wittgren: None; **S. Exarchou**: AbbVie/Abbott, 1, 5, Amgen, 1, 5, Eli Lilly, 1, 5, Janssen, 1, Novartis, 1, 5, 6, Pfizer, 5, UCB, 1, 6; **D. Di Giuseppe**: None; **U. Lindström**: None; **T. Olofsson**: None; **L. Jacobsson**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, Galapagos, 2, Janssen, 2, 6, Novartis, 2, 6; **J. Askling**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Galapagos/Alfasigma, 5, Pfizer, 5, Samsung Bioepis, 5, Sanofi, 5; **J. Karlsson Wallman**: AbbVie/Abbott, 5, Amgen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5.

Abstract Number: 0526

Identification of Urine Proteomic Biomarkers Associated with Ankylosing Spondylitis

Chang-Nam Son[1], Dong-Ki Jang[2], So-Hye Nam[3], **Yoon-Jeong Oh**[4], Sungsin Jo[5], Jong-Seo Kim[6] and Tae-Hwan Kim[7], [1]UIJEONGBU EULJI MEDICAL CENTER, EULJI UNIVERSITY, UIJEONGBU, Republic of Korea, [2]School of Biological Sciences, Seoul National University, Seoul, Republic of Korea, [3]Division of Rheumatology, Department of Internal Medicine, School of Medicine, Keimyung University, Daegu, Republic of Korea, [4]Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Republic of Korea, [5]Department of Biology, Soonchunhyang University, Asan,, Republic of Korea, [6]School of Biological Sciences, Seoul National University, Seoul, [7]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Currently available diagnostic tests for inflammatory arthritis lack sufficient sensitivity and specificity, often requiring the integration of clinical manifestations with physician expertise for accurate diagnosis. Urine is a noninvasive and easily accessible specimen that represents a promising diagnostic tool. This study aimed to identify novel urinary proteomic biomarkers in ankylosing spondylitis (AS) and evaluate their associations with clinical parameters and disease activity.

Methods: Urine protein profiling was performed on samples from 20 patients with AS and 10 control subjects, each with rheumatoid arthritis (RA), gout, or healthy controls (HC), using label-free quantitative proteomics. Differentially expressed proteins were identified using MaxQuant and the UniProt database (fold change ≥ 1.5, $p < 0.05$). Selected proteins were

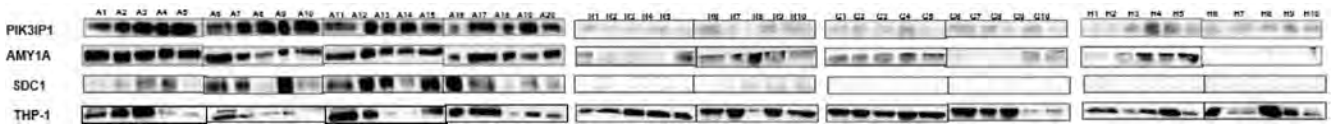


Figure 1. Verification of PIK3IP1, AMY1A and SDC1 in urine by western blot. Western blot analysis in the urine sample set: A; Ankylosing spodylitis (n=20), R; Rheumatoid arthritis (n=10), G; Gout (n=10), H; Healthy controls (n=10). THP-1 was used as an input amount control

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

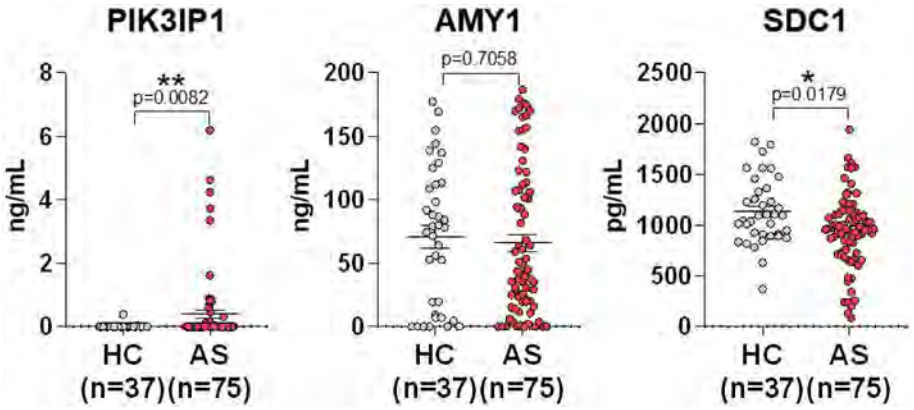


Figure 2. Validation of PIK3IP1, AMY1A and SDC1 in urine by ELISA assay. ELISA assay in the urine sample set: Ankylosing spondylitis (n=75), Healthy controls (n=37).

validated by Western blot analysis and further assessed by ELISA in an independent cohort of 75 AS patients and 37 HC. Associations between protein levels and clinical parameters, including BASDAI and ASDAS-CRP, were also analyzed.

Results: Urine proteins were analyzed by liquid chromatography and tandem mass spectrometry, identifying 1,975 proteins. Among them, AMY1A, SDC1, and PIK3IP1 were selected as candidate biomarkers based on high-fold changes and statistical significance. Western blot analysis confirmed significantly higher expression of these proteins in AS patients compared to those with RA, gout, and HC, supporting the proteomic findings (Figure 1). Receiver operating characteristic (ROC)

Table 1. Correlation analysis between urinary levels of AMY1A, SDC1, and PIK3IP1 and clinical variables in AS patients. AS; Ankylosing spondylitis, BMI; Body mass index, ESR; Erythrocyte sedimentation rate, CRP; C-reactive protein, BASDAI; Bath Ankylosing Spondylitis Disease Activity Index, ASDAS-CRP; Ankylosing Spondylitis Disease Activity Score – C-reactive protein, NSAID; Nonsteroidal Anti-Inflammatory Drug, csDMARD; Conventional synthetic Disease-Modifying Anti-Rheumatic Drug, bDMARD; Biologic Disease-Modifying Anti-Rheumatic Drug

	P - value		
Covariates	PIK3IP1	AMY1	SDC1
Age at AS diagnosis, year (mean)	0.310	0.332	0.063
AS duration, month (mean)	0.382	0.239	0.516
Height (cm)	0.648	0.622	0.945
Weight (kg)	0.345	0.968	0.093
BMI	0.205	0.836	0.099
Sacroilitis, NewYork criteria (highest grade)	0.634	0.295	0.411
Syndesmophyte	0.091	0.520	0.148
Peripheral arthritis	0.355	0.416	0.609
Enthesitis	0.939	**0.038**	0.553
Uveitis	0.953	0.077	0.742
HLA B27	0.878	0.516	0.062
ESR	0.341	0.786	0.057
CRP	0.946	0.427	0.439
BASDAI	0.524	0.094	0.648
ASDAS-CRP	0.341	0.238	0.597
NSAIDs use	0.417	0.910	0.342
csDMARDs use	0.755	0.553	0.500
bDMARDs use	0.528	0.687	0.435
Steroids use	0.964	0.634	0.757
Psoriasis	0.900	0.577	0.264
Diabetes	0.991	0.501	0.296
Hypertension	**0.008**	0.693	0.823
Dyslipidemia	0.393	0.679	0.708
Osteoporosis	0.565	0.858	0.432
Other rheumatic disease	0.565	0.761	0.141

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

curve analysis demonstrated good diagnostic performance, with the individual area under the curve (AUC) values of 0.812 (AMY1A), 0.875 (SDC1), and 0.852 (PIK3IP1). Notably, the combination of all three markers yielded an improved AUC of 0.973, indicating enhanced diagnostic accuracy with multiplexed analysis. In the validation cohort, ELISA assay confirmed that PIK3IP1 and SDC1 levels were significantly elevated in AS patients ($p = 0.0082$ and 0.0179, respectively), whereas AMY1A showed no significant difference ($p = 0.7058$) (Figure 2). No significant correlations were found between the three biomarkers and disease activity indices such as BASDAI or ASDAS-CRP. However, AMY1A levels were related to a history of enthesitis, and PIK3IP1 levels were associated with underlying hypertension (Table 1).

Conclusion: AMY1A, SDC1, and PIK3IP1 were identified as potential urinary biomarkers for AS. Among them, PIK3IP1 and SDC1 showed significantly higher levels in AS patients and demonstrated good diagnostic performance. While these markers were not associated with disease activity scores, these results suggest their potential utility in AS diagnosis.

Disclosure: C. Son: None; **D. Jang**: None; **S. Nam**: None; **Y. Oh**: None; **S. Jo**: None; **J. Kim**: None; **T. Kim**: Samsung Bioepis, 5.

Abstract Number: 0527

Gaps in Documentation of Psoriatic Arthritis Domains in General Rheumatologic Practices Compared to Rheumatology-dermatology Combined Clinics

Alexandra Lauren Rice[1], Sarah Hopkins Gillespie[2], Nikhil Sai[3], Soumya Reddy[1], Joseph Merola[4], Rebecca Haberman[5], Alexis Ogdie[6] and Jose Scher[7], [1]NYU Grossman School of Medicine, New York, NY, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [4]UT Southwestern Medical Center, Dallas, TX, [5]NYU Langone Health, New York, NY, [6]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [7]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To apply current treatment recommendations for psoriatic arthritis (PsA), clinicians must perform a comprehensive assessment of psoriatic disease domains, including a musculoskeletal exam (tender and swollen joints, dactylitis, enthesitis, axial disease) and a skin and nail exam for psoriasis (PsO). Documentation in the electronic medical record (EMR) serves as a proxy for these assessments. Additionally, ICD coding of psoriatic disease influences administrative database research. This study aimed to compare documentation of psoriatic domains and ICD coding practices between PsA specialist providers and general rheumatologists at two academic centers.

Methods: We identified patients with ICD-coded diagnoses of PsA who were seen by either general rheumatologists or PsA combined-clinic specialist providers at two established PPACMAN (Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network) sites. Clinical notes were reviewed for documentation of musculoskeletal and cutaneous PsA domains. We also evaluated the accuracy and completeness of ICD coding for PsA and/or PsO to assess the reliability of EMR-derived discrete data. Fisher's exact tests were used to assess relationships between provider type, documentation practices, and ICD coding.

Results: Across multiple academic centers, PsA combined-clinic specialist providers documented psoriatic disease domains significantly more consistently than general rheumatologists. Musculoskeletal domains—including tender and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographics for NYU, Penn, and Combined Patient Populations, grouped by provider type and institution

Table 1: Demographics for NYU, Penn, and Overall Patient Populations									
	NYU			Penn			Combined		
	Generalist (N = 35)	PsA Specialist (N=35)	p	Generalist (N = 25)	PsA Specialist (N = 25)	p	Generalist (N= 60)	PsA Specialist (N = 60)	p
Patient Age (Average)	54.8	50.0	0.208	47.7	53.2	0.232	51.25	51.6	0.903
Race, White N (%)	21 (60)	30 (85.7)	0.03*	10 (20)	0 (0)	0.0006*	31 (51.7)	30 (50)	1
Hispanic or Latino N (%)	5 (14.3)	4 (11.4)	1	1 (2)	2 (4)	1	6 (10)	6 (10)	1
Sex, Female N (%)	16 (45.7)	17 (48.6)	1	12 (24)	13 (26)	1	28 (46.7)	30 (50)	0.855
Use of Targeted or Biologic Therapy at Time of Visit N (%)	19 (54.3)	22 (62.9)	0.628	20 (40)	19 (38)	1	39 (65)	41 (68.3)	0.847

swollen joint counts (p< 0.001), assessment of spondyloarthritis (p=0.017), dactylitis (p< 0.001), and enthesitis (p< 0.001)—were more routinely documented by PsA specialists. Cutaneous domains were also more consistently documented by specialists, including PsO location (p< 0.001), phenotypic subset (p< 0.001), and use of standardized psoriasis assessment tools such as BSA, PGA, and PASI scores (p< 0.001). Furthermore, PsA specialists more frequently applied appropriate ICD codes for PsO (p< 0.001) and for both PsA and PsO (p< 0.001).

Conclusion: In this multicenter retrospective study, PsA specialist providers more thoroughly documented musculoskeletal and cutaneous disease domains and more accurately coded for PsA and PsO compared to generalists. These findings highlight gaps in documentation among general rheumatologists and underscore the need for enhanced training in psoriatic

Table 2: Documentation of Psoriatic Disease Domains, grouped by provider type and institution

Table 2: Documentation of Psoriatic Domains by Provider Type									
	NYU			Penn			Combined		
	General Rheumatologist	PsA Specialist		General Rheumatologist	PsA Specialist		General Rheumatologist	PsA Specialist	
Documentation Domain	% Documented (N = 25)	% Documented (N = 25)	P value	% Documented (N = 25)	% Documented (N = 25)	P value	% Documented (N = 25)	% Documented (N = 25)	P value
General comment on PsA joint involvement	97.1	100	1	80.0	92.0	0.42	90.0	96.7	0.272
Tender Joint Count	0.0	97.1	<0.00001*	72.0	96.0	0.049*	30.0	96.7	<0.00001*
Swollen Joint Count	0.0	97.1	<0.00001*	64.0	92.0	0.037*	26.7	95.0	<0.00001*
Assessment of Spondyloarthritis	97.1	100	1	88.0	96.0	0.023*	85.0	98.3	0.017*
Imaging of the Spine	42.9	77.1	0.0008*	52.0	92.0	0.0030*	46.7	83.3	<0.00001*
General comment on PsO skin involvement	94.3	100	0.493	92.0	100.0	0.49	93.3	100.0	0.119
Active or past hx of PsO	91.4	97.1	0.614	96.0	96.0	1	93.3	96.7	0.679
In PsO patients only: comment on location of skin involvement	87.5	100	0.05	45.8	95.8	0.0003*	69.6	98.3	<0.00001*
In PsO patients only: comment on phenotypic subset of PsO	53.1	100	<0.00001*	12.5	66.7	0.0003*	35.7	86.2	<0.00001*
In PsO patients only: documentation of BSA/PGA/PASI score	3.1	100	<0.00001*	25.0	62.5	0.019*	12.5	84.5	<0.00001*
General comment on PsO nail involvement	65.7	100	0.0002*	28.0	64.0	0.022*	50.0	85.0	0.0001*
Active or past hx of nail PsO	14.3	48.6	0.004*	32.0	64.0	<0.00001*	21.7	55.0	0.0003*
In nail PsO patients only: specific comment on nail PsO (inc. pitting, keratosis, onycholysis)	80.0	82.4	1	75.0	75.0	1	76.5	78.8	1
Assessment of Enthesitis	17.1	100	<0.00001*	16.0	100.0	<0.00001*	16.7	100.0	<0.00001*
Assessment of Dactylitis	54.3	97.1	<0.00001*	32.0	100.0	<0.00001*	45.0	98.3	<0.00001*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Documentation of ICD Coded Diagnoses, grouped by provider type and institution

Table 3: Documentation of ICD Coding by Provider Location and Type			
ICD Code Documentation – NYU	**General Rheumatologist**	**PsA Specialist**	**P values**
	% Coded of Total (N =35)	**% Coded of Total (N =35)**	
PsO	37.1	82.9	0.0002*
PsA	85.7	91.4	0.71
Both PsO and PsA	31.4	74.3	0.0007*
ICD Code Documentation – Penn	**General Rheumatologist**	**PsA Specialist**	
	% Coded of Total (N =25)	**% Coded of Total (N =25)**	
PsO	56.0	76.0	0.232
PsA	64.0	64.0	1
Both PsO and PsA	24.0	56.0	0.042*
ICD Code Documentation – Combined	**General Rheumatologist**	**PsA Specialist**	
	% Coded of Total (N =60)	**% Coded of Total (N =60)**	
PsO	45.0	80.0	0.0001*
PsA	76.7	80.0	0.825
Both PsO and PsA	28.3	66.7	<0.00001*

disease assessment. Despite significant efforts from multiple organizations, patient advocacy foundations and academics to increase awareness, improvement in both assessment and documentation are still needed. Improved documentation tools may facilitate both better clinical evaluation and more reliable research using EHR or claims-based data.

Disclosure: A. Rice: None; **S. Hopkins Gillespie**: None; **N. Sai**: None; **S. Reddy**: Bristol-Myers Squibb(BMS), 1, Janssen, 1, 5, UCB, 1; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **R. Haberman**: Johnson and Johnson, 1, 5, Novartis, 1; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2.

Abstract Number: 0528

Apolipoprotein A1 and B Levels Indicate Specific Lipid Changes in Early Treatment Naïve Psoriatic Arthritis and Correlate with 1-year Disease Activity

Alla Ishchenko[1], Margot Van Mechelen[2], Barbara Neerinkx[1], Patrick Verschueren[3], Rik Lories[1] and Kurt de Vlam[4], [1]KU Leuven, Leuven, Belgium, [2]UZA Antwerp, Antwerp, Belgium, [3]Rheumatology, University Hospital Leuven and Skeletal Biology and Engineering Research Centre, KU Leuven, Leuven, Belgium, [4]KU Leuven, UZ Gasthuisberg, Leuven, Belgium

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Psoriatic arthritis (PsA) is associated with increased cardiovascular risk and a pro-atherogenic lipid profile. We hypothesize that alterations in lipid metabolism combined with systemic inflammation are present in the early disease stages of the disease and reflect pathophysiologic, metabolic changes characteristic for PsA. We investigated serum lipid profile in early PsA and examined whether changes in the profile or apolipoproteins are specific to early disease.

Methods: Adult patients with newly diagnosed treatment naïve PsA were included in the multicenter cohort study (N=75). Clinical, demographic characteristics and comorbidities were collected. The serum lipids were measured: total cholesterol (TC), non-HDL-cholesterol (non-HDL-c), LDL-cholesterol (LDL-c), HDL-cholesterol (HDL-c), triglycerides (TAG), apolipoprotein B (ApoB) and apolipoprotein A1 (ApoA1). The results were compared to sex- and age matched healthy controls (HC) (N=61) and rheumatoid arthritis (RA) patients (N=50)(Kruskall-Wallis). The lipid measurements were re-evaluated in PsA patients after 1 year follow-up.

Results: The three groups were matched by age; HC and PsA patients were matched by age and sex. PsA patients had mainly oligoarticular disease, low PASI scores and a short symptom duration (median: 0.6 years). The mean DAPSA score (SD) was 19.5(10.8), corresponding to moderate disease activity. Early RA patients (disease duration (median: 0.5 years) all had polyarticular disease and moderate disease activity, mean(SD) DAS-28-CRP of 4.61(2.0).

Among lipid measurements, HDL-c levels were lower in PsA than in HC and RA (df2, $c^2$10, p=0.006, PsA vs HC p=0.013) (Fig 1A-E), the levels of TC, LDL-C, TAG were not different in the three groups. Significant differences in ApoA1 and ApoB levels were observed between PsA, RA and controls. ApoB was higher in PsA than in RA patients but lower than in controls (df2, $c^2$43.8; p< 0.001). ApoA1 was markedly lower in PsA patients compared to both RA and controls (df2, $c^2$118.9; p< 0.001)(Fig 1 F-H). In regression models, the levels of ApoA1, adjusted for age, sex, BMI, statin use, smoking status, CRP levels and interaction between them, were predictive of PsA diagnosis with 90.6% accuracy. In ROC analysis, ApoA1 was

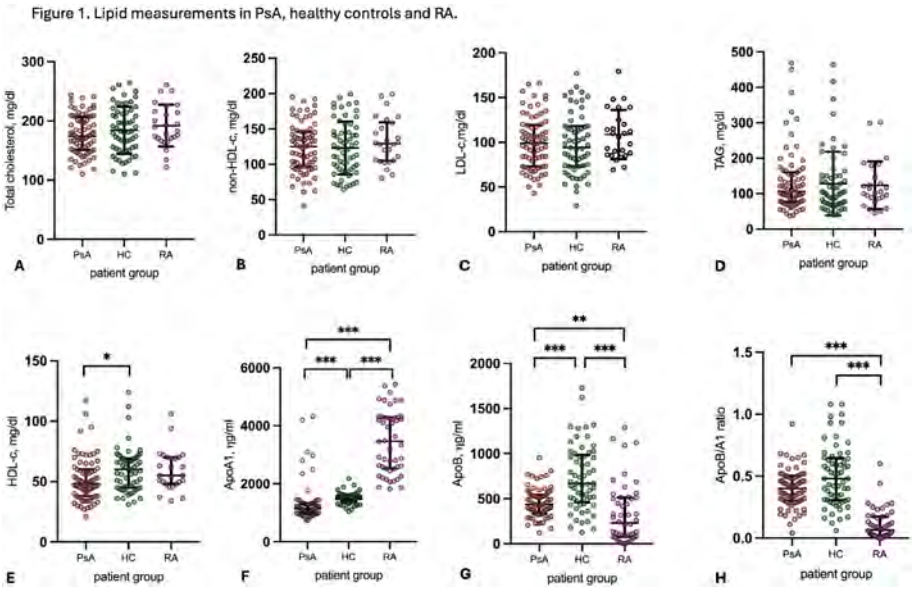


Figure 1. Lipid measurements in PsA, healthy controls and RA. A. TC measurements (mg/dl, median[IQR]) were comparable in PsA (174[56]), RA (187 [49]) and HC(183 [63]), p=0.205. B. non-HDL-c measurements (mg/dl, median[IQR]) in PsA (125 [49]), RA (129[55]) and HC (121[58]), p=0.47. C. LDL-c measurements (mg/dl, median[IQR]) in PsA (99[46]), RA (108[43]) and HC (94 [45]), p=0.291. D. TAG measurements (mg/dl, median[IQR]) in PsA (107 [83]), RA (104 [70]) and HC (99[80]), p=0.734). E. HDL-c measurements (mg/dl, median[IQR]) in PsA (48 [22]), RA (55 [22]) and HC (60 [24]), p=0.006). HDL-c levels in PsA were lower as compared to HC (p=0.013), no differnce between RA vs HC and RA-PsA was observed. F. ApoA1 levels (µg/ml, median[IQR]) were lower in PsA (1141 [317]), than in HC (1473[187]) and RA (3468[1071]), , p<0.001; p<0.001 for all pairwise). G. Apo B levels (µg/ml, median[IQR]) were higher in PsA (438 [209]) as compared to RA (231 [436]) (p<0.001) and lower as compared to HC (669 [528]), p<0.001 (pairwise: PsA vs HC and RA vs HC p<0.001, PsA vs RA p=0.009). H. ApoB/ApoA1 ratio (median(IQR] was higher in PsA (0.4 [0.2] and HC (0.5[0.3]) than in RA (0.06[0.15]), p<0.001; pairwise PsA vs RA p<0.001, RA vs HC p<0.001, PsA vs HC p=0.368). * p<0.05; ** p<0.001; *** P<0.0001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. ROC analysis for HDL-C and ApoA1 in PsA, RA and HC.

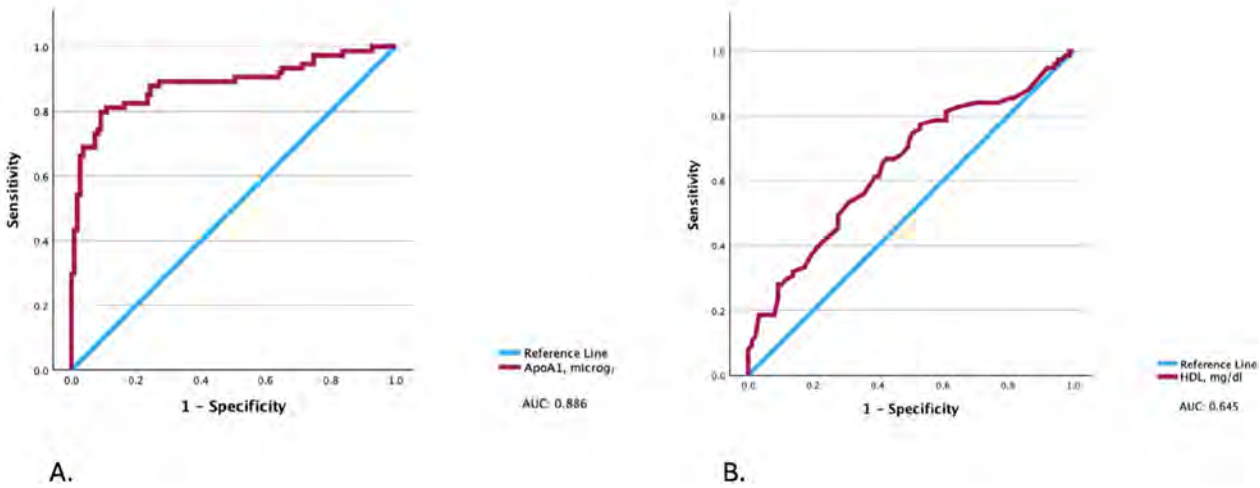


Figure 2. ROC analysis for HDL-C and ApoA1 in PsA and HC. A. ROC analysis for ApoA1 and diagnosis (PSA; RA vs HC), the diagnosis of PsA being positive classifier. AUC[95%CI] 0.886 [0.83-0.941]. Overal model quality: 0.83. Sensiticity 82.4% and specificity of 83.8 % at an optimal cut off limit of 1403 g/ml . B. ROC analysis for HDL-cholesterol and diagnosis (PSA; RA vs HC), the diagnosis of PsA being positive classifier. AUC[95%CI] 0.645 [0.83-0.941]. Overal model quality: 0.83.

predictive of the diagnosis of PsA with a specificity of 82.4% and a sensitivity of 83.8% at an optimal cut-off value of 1403 µg/ml (AUC[95%CI] 0.886[0.83-0.941]) (Fig 2). At 1 year follow-up only ApoA1 levels, but not other lipid measurements, increased in PsA patients achieving DAPSA LDA, while ApoB levels remained comparable to baseline (Fig 3).

Conclusion: Decreased levels of ApoA1 and increased levels of ApoB are specific to early and treatment naïve patients with PsA and distinguish them from early RA patients and non-arthritic controls. In particular, circulating levels of ApoA1 are strongly predictive for the diagnosis of PsA. The ApoA1 levels increase after 1 year in PsA patients achieving DAPSA low disease activity suggesting link with active disease. These findings suggest that specific changes in lipid profile are present in early stages of PsA and that apolipoprotein measurements might be better markers of pro-atherogenic profile in PsA than classical serum lipids.

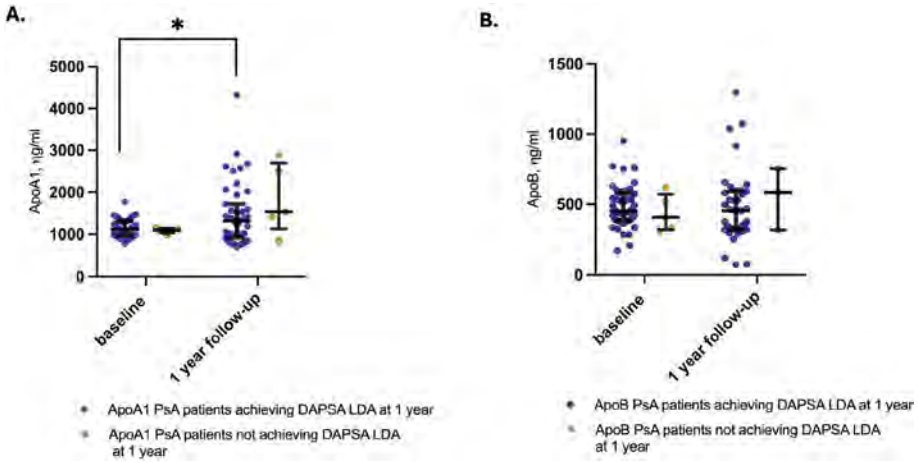


Figure 3. Change in ApoA1 and ApoB levels in patients achieving DAPSA low disease activity at 1 year-follow up. A. The levels of ApoA1 (µg/ml, mean(±SD)) increased at 1-year follow-up (1336±543) as compared to baseline (1160±217) in patients achieving DAPSA LDA (t1=2.5; p=0.016) and remained comparable to baseline in patients not-achieving DAPSA-LDA (baseline: 1052±67, 1-year: 1264±375; t=-2.01, p=0.106). B. The ApoB levels were comparable at baseline (486±162) and at 1-year (482±258) in patients achieving DAPSA LDA (t=0.114; p=0.910) and not achieving DAPSA LDA (baseline: 442±160; 1-year: 551±220; t=-0.904, p=0.461). 1 – paired samples t-test was used to compare baseline and 1-year follow-up data

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Ishchenko: Eli Lilly, 5, 12, PARTNERS group fellowship 2017-2018; **M. Van Mechelen**: None; **B. Neerinkx**: None; **P. Verschueren**: AbbVie, 6, 12, Support for attending meeting, Alfasigma S.p.A., 2, 5, Boehringer Ingelheim, 2, Citryll, 2, Eli Lilly & Co., 2, 6, Fresenius Kabi, 12, Support for attending meeting, Galapagos, 2, 5, 6; **R. Lories**: AbbVie/Abbott, 2; **K. de Vlam**: None.

Abstract Number: 0529

Anti-peptidylarginine deiminase-2 (anti-PAD2) Autoantibodies in Psoriatic Arthritis

Ana-Maria Orbai[1], Hong Wang[2], Maria Grecu[3], Ning Meng[4], Ji Soo Kim[5], Clifton Bingham[4], Uzma Haque[2], John Miller[4], Felipe Andrade[2], Erika Darrah[6] and Eleni Tiniakou[7], [1]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]River Hill High School, Clarksville, MD, [4]Johns Hopkins University, Baltimore, MD, [5]Johns Hopkins, Baltimore, MD, [6]Astra Zeneca, Gaithersburg, MD, [7]UT Health Science Houston, Houston, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Citrullinated cathelicidin (LL37), a human-derived antimicrobial peptide, is an autoantigen in psoriatic arthritis (PsA).[1] LL37 citrullination by peptidylarginine deiminase (PAD) enzymes attenuates immune activation and downregulates inflammatory responses. PAD2 is the most effective at LL37 citrullination.[2] Anti-PAD2 autoantibodies have been described in rheumatoid arthritis[3] and Lyme disease[4] and are thought to inhibit citrullination of autoantigens such as LL37. This study aimed to identify anti-PAD2 in PsA and to study their association with patient characteristics in a longitudinal PsA registry and biobank.

Methods: Participants in a PsA registry fulfilling CASPAR classification criteria and having banked serum samples were included. We assayed serum anti-PAD2 using an in-house anti-PAD2 ELISA[4] in 200 PsA patients and 75 healthy controls (HC). Anti-PAD2 positive cutoff was set at the 90-percentile of HCs. We compared the distribution of patient characteristics in the anti-PAD2 positive and negative groups, using the Wilcoxon rank-sum and Fisher's Exact tests.

Results: Anti-PAD2 were found in 29% PsA and 9.3% HC sera (p=0.004) (Figure1). 44 (of 58) anti-PAD2 positive and 124 (of 142) anti-PAD2 negative patients had clinical data for analysis. Fifty-nine sera matched with disease activity measured within 48 hours of the serum sample, an additional 9 sera within 6-months, while remaining sera matched with future clinical data (Figure 2). Patients with anti-PAD2 positive compared to negative were older, less likely to have low articular disease activity, and less likely to have active plaque psoriasis affecting the extremities (Table). Considering that 68/168 patients were assessed within 6-months of anti-PAD2 testing, these differences could be attenuated. There were no significant differences in observed treatments.

Conclusion: We discovered anti-PAD2 autoantibodies in PsA. Among PsA patients 29% were positive for anti-PAD2. Anti-PAD2 was associated with more active joint disease and less active skin disease. The clinical significance of anti-PAD2 in PsA needs evaluation in a larger sample using simultaneous measurements with musculoskeletal and skin disease activity.

References: 1. Frasca L, et al. Front Immunol. 2018;9:1936. 2. Wong A, et al. *The Journal of Immunology*. 2018;200 (7):2327-2340. 3. Darrah E, et al. Front Immunol.2018;20:9:2696. 4. Kim Y, et al. Front Neurol. 2022;13:874211.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Comparison of distributions of clinical characteristics in anti-PAD2 positive and negative study participants. Numbers and percentages and medians and interquartile ranges are shown. P-values were obtained using the Wilcoxon rank-sum and Fisher's Exact tests.

Variable	N	PAD2 Positive N(%) or Median (IQR) N = 44[1]	PAD2 Negative N(%) or Median (IQR) N = 124[1]	p-value[2]
Age[3]	168	55.0 (47.9, 68.1)	50.8 (43.1, 60.0)	**0.05**
PsA duration[3]	125	5.8 (3.0, 13.4)	3.6 (1.9, 12.5)	0.06
Registry visits	168	6.0 (3.0, 7.0)	5.0 (3.0, 7.0)	0.52
Gender	168			0.60
Female		22 (50%)	69 (56%)	
Male		22 (50%)	55 (44%)	
Race	168			0.51
Asian		2 (4.5%)	2 (1.6%)	
Black		2 (4.5%)	3 (2.4%)	
Other		2 (4.5%)	6 (4.8%)	
White		38 (86%)	113 (91%)	
Ethnicity	168			
Hispanic		2 (4.5%)	1 (0.8%)	0.08
Not Hispanic		42 (95%)	118 (95%)	
Unknown		0	5 (4.0%)	
CASPAR score	162	4.0 (4.0, 5.0)	4.0 (4.0, 5.0)	0.22
Clinical DAPSA				
Remission		11 (25%)	24 (19%)	0.52
LDA	168	6 (14%)	45 (36%)	**0.004**
MoDA		18 (41%)	35 (28%)	0.13
HDA		9 (20%)	20 (16%)	0.5
MDA	130	11 (31%)	24 (25%)	0.51
VLDA	130	2 (5.7%)	11 (12%)	0.51
Dactylitis	129	16 (52%)	38 (39%)	0.22
Enthesitis	145	21 (58%)	74 (68%)	0.32
Nail psoriasis	151	28 (78%)	97 (84%)	0.45
Plaque psoriasis	162	36 (90%)	104 (85%)	0.60
Scalp psoriasis				
Visit	81	11 (46%)	20 (35%)	0.45
Ever	162	24 (60%)	79 (65%)	0.71
Elbows plaque psoriasis				
Visit	81	4 (17%)	22 (39%)	0.070
Ever	162	25 (63%)	55 (45%)	0.069
Lower extremities plaque psoriasis				
Visit	81	5 (21%)	26 (46%)	**0.046**
Ever	162	22 (55%)	58 (48%)	0.47
Upper extremities plaque psoriasis				
Visit	81	1 (4.2%)	22 (39%)	**0.001**
Ever	162	12 (30%)	41 (34%)	0.70
HLA-B27 positive	116	2 (7.1%)	11 (12%)	0.73
Treatments	168			
MTX		18 (41%)	46 (37%)	0.72
Leflunomide		4 (9.1%)	12 (9.7%)	>0.99
Sulfasalazine		5 (11%)	13 (10%)	>0.99
Hydroxychloroquine		2 (4.5%)	3 (2.4%)	>0.99
Adalimumab		11 (25%)	31 (25%)	0.17
Etanercept		8 (18%)	12 (9.7%)	0.33
Golimumab		0	5 (4%)	0.52
Infliximab		4 (9.1%)	8 (6.5%)	0.43
Certolizumab		3 (6.8%)	5 (4%)	0.09
Secukinumab		3 (6.8%)	22 (18%)	>0.99
Ixekizumab		2 (4.5%)	8 (6.5%)	0.48
Ustekinumab		4 (9.1%)	7 (5.6%)	>0.99
Risankizumab		0	1 (0.8%)	>0.99
Abatacept		3 (6.8%)	2 (1.6%)	0.11
Apremilast		6 (14%)	17 (14%)	>0.99
Combination		25 (57%)	61 (49%)	0.48
None		1 (2.3%)	7 (5.6%)	0.68

[1]n (%)
[2]Wilcoxon rank-sum and Fisher's Exact tests
[3]Since serum sample date

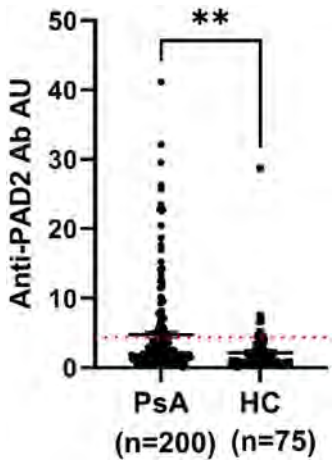


Figure 1. Anti-PAD2 in PsA (n=200) and HCs (n=75) expressed as Arbitrary Units (AU). The red dotted line represents the cut-off value for positivity at 4.393 AU. The mean ± SEM is shown for each group. **Fisher's Exact test, p = 0.004.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

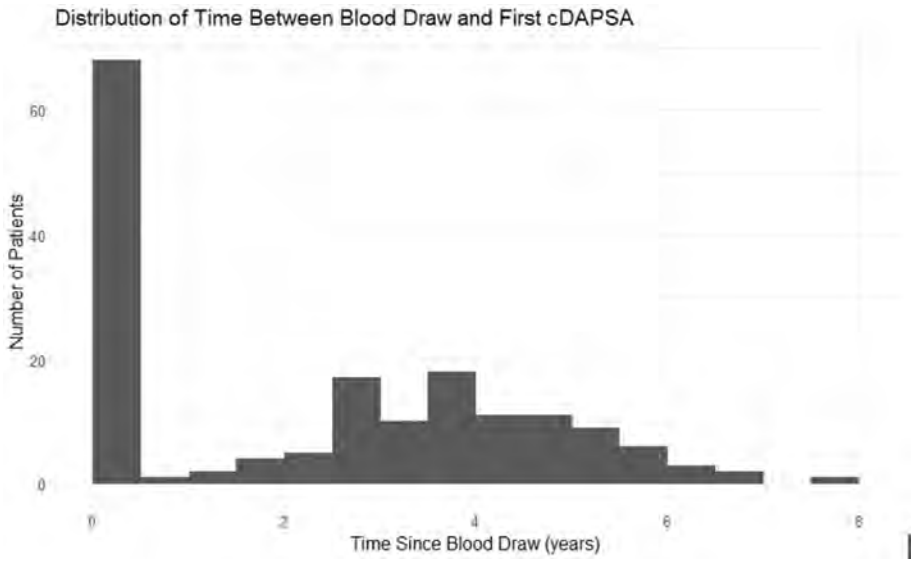


Figure 2. Histogram of time between anti-PAD2 testing and clinical assessment: 59 within 48 hours, 9 within 6-months, 100 much later, and 32 samples (not shown) without PsA-specific clinical data.

Disclosure: A. Orbai: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB, 2; **H. Wang**: None; **M. Grecu**: None; **N. Meng**: None; **J. Kim**: None; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **U. Haque**: None; **J. Miller**: None; **F. Andrade**: Advise Connect Inspire, 2, Hillstar Bio Inc, 2, Inova, 9; **E. Darrah**: AstraZeneca, 3; **E. Tiniakou**: None.

Abstract Number: 0530

Evaluating ChatGPT's Performance in Diagnosing Low Back Pain: A Comparison with Clinicians and Impact of Prompted Specialties

Annika Nack[1], Xabier Michelena Vegas[2], Pol Maymó-Paituvi[3], Cristina Calomarde-Gómez[4], david lobo[5], Asier García-Alija[6], Raquel Ugena-García[4], Maria Aparicio[1], Paola Vidal Montal[7] and Diego Benavent[8], [1]Hospital Germans Trias i Pujol, Barcelona, Spain, [2]Hospital Universitari Vall Hebron, Barcelona, Spain, [3]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [4]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [5]Doctor Josep Trueta University Hospital, Girona, Catalonia, Spain, [6]Sant Pau Hospital, Barcelona, Catalonia, Spain, [7]Bellvitge University Hospital, Barcelona, Spain, [8]Hospital Universitari de Bellvitge, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Low back pain (LBP) is a multifactorial condition managed by various specialists. AI chatbots like ChatGPT may help clinicians identify probable diagnoses. Given that query phrasing can influence outputs, we hypothesized that ChatGPT's responses may vary depending on the specialty stated in the prompt.

We aimed to evaluate whether ChatGPT's diagnostic output changes when simulating different specialties in LBP assessment, and to compare its diagnostic accuracy to that of clinicians.

Methods: A total of 10 clinical cases related to LBP were included from official public exams for rheumatologists in Spain, designed to assess expertise for permanent specialist positions. These included 5 cases of rheumatologic diseases and

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

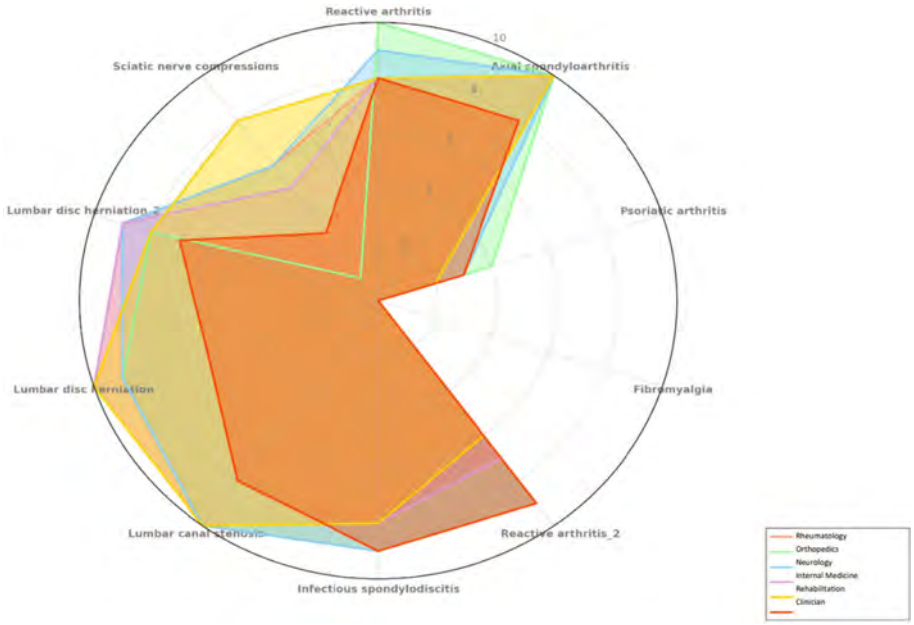


Figure 1. Percentage of the correct score for each participant and each prompted speciality

5 representing other causes. The exercise was conducted in December 2024 using ChatGPT version 4.o. Ten clinicians with at least 5 years of experience in managing rheumatic and musculoskeletal diseases (RMDs) participated in the study. Each question was answered independently by clinicians, and at a later stage by each participant asking ChatGPT, simulating five specialties (Rheumatology, Neurology, Internal Medicine, Rehabilitation, and Orthopedics). The gold standard was the official answer listed as diagnosis for each exam question. Diagnostic performance was evaluated using precision (percentage of cases where the top diagnosis matched the gold standard) and sensitivity (percentage of cases where the gold standard was included in the top three probable diagnoses). The time taken to answer all 10 clinical cases was recorded for both clinicians alone and using ChatGPT, starting when the case was reviewed and stopping when three differential diagnoses and the most probable diagnosis were finalized.

Results: In total, 528 free-text diagnoses were generated and standardized into 39 diagnostic categories. The percentage of the correct score for each participant and each prompted specialty is illustrated in Figure 1. Median precision ranged from 70% to 80% across the five specialties simulated by ChatGPT, and median sensitivity ranged from 80% to 90%. Statistical analysis revealed no significant differences in precision ($p = 0.80$) or sensitivity ($p = 0.68$) between the specialties simulated by ChatGPT, indicating consistent performance regardless of the prompted specialty. For clinicians, the median precision was 60%, and median sensitivity was 80%. When comparing ChatGPT to clinicians, ChatGPT had significantly higher diagnostic precision (median = 75% vs. 60%, $p < 0.001$) and significantly higher sensitivity (median = 85% vs. 80%, $p = 0.02$). The mean time taken by participants to complete the task was 12.35±5.62 minutes, compared to 2.33±0.03 minutes for ChatGPT ($p< 0.01$).

Conclusion: ChatGPT provides consistent diagnostic performance across simulated specialties, unaffected by the prompt's semantic framing. It may outperform clinicians in both diagnostic precision and sensitivity, highlighting its potential as a valuable complementary tool for generating fast, accurate and comprehensive differential diagnoses in cases of low back pain. Further research is needed to explore its application in clinical practice and its ability to enhance diagnostic workflows.

Disclosure: A. Nack: None; **X. Michelena Vegas**: None; **P. Maymó-Paituvi**: None; **C. Calomarde-Gómez**: None; **d. Iobo**: None; **A. García-Alija**: None; **R. Ugena-García**: None; **M. Aparicio**: None; **P. Vidal Montal**: None; **D. Benavent**: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 6, Savana, 7, UCB, 2, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0531

Evaluating the Diagnostic Utility of 14-3-3 eta Autoantibodies in Axial Spondyloarthritis: A Multiplex Assay Approach

Anthony Marotta[1], Walter P. Maksymowych[2], Stephen Bleakley[1], Stephanie Wichuk[3] and Norma Biln[4], [1]Augurex Life Sciences Corp, Vancouver, BC, Canada, [2]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [3]University of Alberta, Edmonton, AB, Canada, [4]Augurex Life Sciences, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Novel biomarkers for axSpA are urgently needed to enable earlier diagnosis and improve patient outcomes. An assay for quantifying 14-3-3η autoantibodies (AAbs) has been developed, utilizing peptides derived from the 14-3-3η protein with distinct specificities. This study aims to establish cut-off values in a training cohort and apply them to an evaluation cohort to assess the diagnostic utility of the 14-3-3η multiplex AAb assay (MAAA) alone and with HLA-B27 and C-reactive protein (CRP).

Methods: The performance of the 14-3-3η MAAA was evaluated using a training cohort of 105 axSpA patients and 74 healthy controls (HC); N=179. ROC AUCs, sensitivity, and specificity for each peptide were generated. Positivity cut-offs for each of the five peptides were defined using the Youden Index, and these were summed to yield a composite score. The strength of the association for axSpA diagnosis was assessed by comparing the composite positivity status of axSpA patients to healthy controls (HC) using Fisher's Exact test. Diagnostic utility was further assessed in an evaluation cohort of 101 axSpA patients. CRP positivity was defined as >5 mg/L. Statistical significance was set at $p < 0.05$.

Table 1. Performance Metrics of the 14-3-3η MAAA in the Training Cohort

Parameter	Peptide 1	Peptide 2	Peptide 3	Peptide 4	Peptide 5
Cut-off (U/mL)	>2.054	>0.077	>0.515	>0.031	>0.081
Sensitivity (N, %)	90 (86%)	93 (89%)	81 (77%)	79 (75%)	87 (83%)
Specificity (N, %)	37 (50%)	38 (51%)	43 (58%)	34 (46%)	44 (59%)
AUC (95% CI)	0.71 (0.63-0.79)	0.71 (0.63-0.80)	0.66 (0.58-0.74)	0.66 (0.58-0.74)	0.63 (0.54-0.71)
p-value	<0.0001	<0.0001	0.0003	0.0003	0.0035
Limit of Blank (LoB) (U/mL)	0.235	0.008	0.076	0.008	0.024
Limit of Detection (LoD) (U/mL)	0.735	0.017	0.429	0.016	0.081
Intra-assay repeatability (% CV)	11.4	6.7	8.7	6.2	4.5
Intra-laboratory precision (% CV)	14.0	11.2	12.9	11.3	8.3
Interfering Substances	None	None	None	None	None
Cross Reactivity	None	None	None	None	None
Linearity	0.9900	1.0250	1.0370	1.0205	1.0039

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Relative Risk (RR) of AxSpA Diagnosis Based on Composite Positivity: Comparison of AxSpA Patients and Healthy Controls (Results Expressed as RR and 95% CI)

	Diagnosis	
Composite Score	**axSpA (n=105)**	**Healthy (n=74)**
Positive	2.9 (1.8 - 4.8)	0.3 (0.2 - 0.5)
Negative	0.3 (0.2 - 0.6)	3.0 (2.0 - 4.5)

Table 3. Integration of 14-3-3η Autoantibody Composite with ASAS Diagnostic Markers

Positive (or for any positive)	**Training Cohort, n=105 (n,%)**	**Evaluation Cohort, n=101 (n,%)**
CRP	52 (51.5%)	53 (52.5%)
14-3-3η AAb Composite	70 (66.7%)	60 (57.7%)
HLA-B27	88 (84.6%)	85 (84.0%)
CRP and/or 14-3-3η AAb Composite	86 (81.9%)	58 (57.4%)
CRP and/or HLA-B27	98 (93.3%)	85 (81.0%)
HLA and/or 14-3-3η AAb Composite	101 (96.2%)	96 (91.4%)
CRP and/or HLA-B27 and/or 14-3-3η AAb Composite	104 (99.0%)	96 (91.4%)
HLA B27 -ve	**n=17 (n,%)**	**n=20 (n,%)**
14-3-3η AAb Composite +ve	12 (70.6%)	11 (55.0%)
CRP +ve	9 (52.9%)	6 (30.0%)
14-3-3η AAb Composite +ve and/or CRP +ve	15 (88.2%)	11 (55.0%)
14-3-3η AAb Composite +ve and CRP +ve	6 (35.3%)	6 (30.0%)

14-3-3η AAbs were positive in 23 (31%) of the 74 healthy controls. CRP was available on 68 of the 74 healthy controls. Of the 68, only 3 patients were positive for CRP, one of which was negative for 14-3-3η AAbs.

Results: All five 14-3-3η peptides exhibited significant areas under the curve (AUC) in distinguishing axSpA patients from HC in the training cohort (Table 1). The assay showed high precision, with intra-laboratory precision %CVs ranging from 8.3% to 14%. The assay showed minimal interference from normal serum elements (hemoglobin, bilirubin, triglycerides, cholesterol, and albumin), non-target antibodies (HAMA, heterophile, and infliximab), and organic chemicals (ibuprofen, sulfasalazine, and dexamethasone).

In the training cohort, the composite score yielded 67% TP and 69% TN with 33% FN and 31% FP. Fisher's Exact test produced a Chi-Square value of 31.8, with a p-value of less than 0.0001, and an Odds Ratio of 8.7 (95% CI: 3.9 - 19.6). Table 2 shows that patients with composite positivity have a significantly higher relative risk of axSpA compared to healthy controls.

Table 3 shows that adding 14-3-3η AAb composite positivity to HLA-B27 and CRP increases axSpA detection from 93.3% to 99.0% in the training cohort and from 81.0% to 91.4% in the evaluation cohort. In HLA-B27 negative patients, 14-3-3η AAb improves detection to 70.6% in the training cohort and 55.0% in the evaluation cohort. Combined with CRP, detection increases to 88.2%, highlighting its potential for early diagnosis.

Conclusion: The 14-3-3η MAAA significantly enhances the early diagnosis of axSpA, especially when combined with HLA-B27 and CRP, demonstrating its potential as a valuable diagnostic tool. This combined approach could lead to better patient outcomes through earlier and more accurate detection. Future research should focus on validating the 14-3-3η multiplex autoantibody assay in larger, diverse cohorts to confirm its diagnostic utility across different populations.

Disclosure: A. Marotta: Augurex Life Sciences Corp., 12,, 2; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **S. Bleakley**: Augurex Life Sciences Corp., 3, 11; **S. Wichuk**: None; **N. Biln**: Augurex Life Sciences Corp., 3, 4, 8, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0532

Generative artificial intelligence provides synthetic data to discriminate patients with seronegative rheumatoid arthritis versus psoriatic arthritis *sine* psoriasis

Antonio Tonutti[1], Saverio D'Amico[2], Pierandrea Morandini[2], Cosimo Faeti[2], Elisa Barone[1], Nicoletta Luciano[1], Victor Savevski[2] and Carlo Selmi[3], [1]Humanitas University, Pieve Emanuele, Italy, [2]IRCCS Humanitas Research Hospital, Rozzano, Italy, [3]Humanitas University, Milan, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

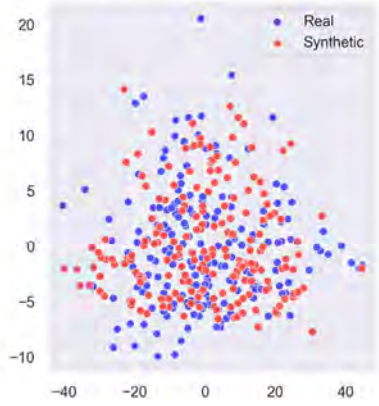
Session Time: 10:30AM–12:30PM

Background/Purpose: Distinguishing seronegative rheumatoid arthritis (RA) from psoriatic arthritis (PsA) *sine* psoriasis remains challenging, often relying on pathognomonic features (axial involvement, enthesitis) present in only few cases and causing diagnostic changes over time.

Generative artificial intelligence (AI) creates synthetic patient profiles to enhance the detection of subtle differences that may elude clinical observation. We applied generative AI for the first time in Rheumatology to evaluate statistical fidelity, privacy preservation, and clinical utility of synthetic data, and to test its potential to differentiate seronegative RA vs PsA sine psoriasis.

Methods: Leveraging data of 105 PsA sine psoriasis and 95 seronegative RA patients, a proprietary synthetic data generation platform was used to implement an optimized Conditional Tabular Wasserstein Generative Adversarial Networks (GAN) to produce 200 synthetic patients balanced across diagnostic groups. These were evaluated using Synthetic vAlidation FramEwork (SAFE) (D'Amico S, 2023). MOSAIC framework (D'Amico S, 2024) was employed for classification (PsA vs. RA), using demographic and baseline clinical variables. A Random Forest model was developed and tested on a real validation dataset using 3-fold cross-validation, then was re-evaluated after incorporating synthetic data into the training set to assess any performance enhancement using the same validation set. Model outputs were interpreted with Shapley Additive exPlanations (SHAP).

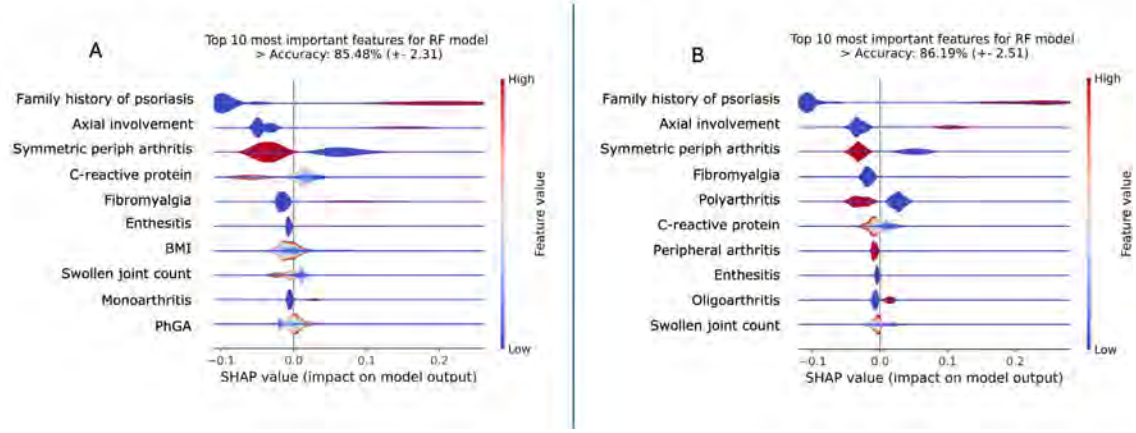
Figure 1. Principal component analysis of demographic and clinical variables of the synthetic and real cohort. While the distribution of the two principal components is similar between real and synthetic patients (mirroring clinical consistency of generated data), no overlap is observed (mirroring absence of duplication and privacy safety).



Principal component analysis of demographic and clinical variables of the synthetic and real cohort. While the distribution of the two principal components is similar between real and synthetic patients (mirroring clinical consistency of generated data), no overlap is observed (mirroring absence of duplication and privacy safety).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. SHAP summary plot showing the top 10 most influential features for the Random Forest model trained on real (Panel A) and real+synthetic (Panel B) data to distinguish PsA sine PsO (right in the plot) from seronegative RA (left in the plot). Each dot represents a patient; colors indicate feature value (red = high/high frequency, blue = low/low frequency).



SHAP summary plot showing the top 10 most influential features for the Random Forest model trained on real (Panel A) and real+synthetic (Panel B) data to distinguish PsA sine PsO (right in the plot) from seronegative RA (left in the plot). Each dot represents a patient; colors indicate feature value (red = high/high frequency, blue = low/low frequency).

Results: Generation of 200 synthetic patients had 73% privacy preservation score (nearest neighbor distance ratio; optimal 65-85) and 92% statistical fidelity, indicating that the synthetic cohort mirrored the real one without duplication with similar distributions in principal component analysis (**Fig 1**).

In the real dataset, Random Forest achieved accuracy 85.5% ± 2.3% in distinguishing PsA sine psoriasis from seronegative RA. Random Forest identified family history of psoriasis, monoarthritis, axial disease, enthesitis, fibromyalgia, and high BMI as strong PsA predictors and captured the discrepancy between inflammatory and noninflammatory mechanisms as proper of PsA (higher baseline PhGA, low swollen joint count and CRP). Symmetric arthritis favored classification as RA (**Fig 2A**).

Incorporating synthetic patients, Random Forest accuracy increased to 86.2% ± 2.5%, retained key predictors including typical PsA features (enthesitis, axial and asymmetric involvement), family history of psoriasis, and discrepancy between pain and inflammatory measures (low CRP and swollen joint count, fibromyalgia). Notably, peripheral polyarthritis vs oligoarthritis favored RA and PsA, respectively (**Fig 2B**).

Conclusion: The first-ever application of generative AI in Rheumatology provided a synthetic data cohort of seronegative RA and PsA sine psoriasis, consistent with real data and privacy-safe. Synthetic data improved classification accuracy. Key variables for intercepting PsA sine psoriasis included family history of PsO, axial/entheseal involvement and mismatch between pain measures and inflammatory markers.

Disclosure: A. Tonutti: None; **S. D'Amico**: None; **P. Morandini**: None; **C. Faeti**: None; **E. Barone**: None; **N. Luciano**: None; **V. Savevski**: None; **C. Selmi**: AbbVie, 2, 5, 6, Alfa-Wassermann, 2, 6, Amgen, 2, 5, 6, Biogen, 2, 6, Eli Lilly, 2, 6, EUSA, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 5, SOBI, 2, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0533

Reactive Arthritis Transcriptomics: Enriched Enterobacteriaceae-related Pathways in Synovial Fluid and in Blood is Associated with Drug-free Remission

Avarna Agarwal[1], Phanidhar Dhanekula[1], Sarthak Verma[1], Subham ravi Nayak[2], Prakashini Mruthyanjaya[1], Prasanta Padhan[1], A Rajkumar Patro[2], Ramnath Misra[1] and Sakir Ahmed[1], [1]Department of Clinical Immunology and Rheumatology, Kalinga Institute of Medical Sciences, Bhubaneswar, Orissa, India, [2]Department of Microbiology, Kalinga Institute of Medical Sciences, Bhubaneswar, Orissa, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In reactive arthritis (ReA) approximately a half of patients achieve drug-free remission (DFR), while others develop chronic disease. To identify predictive biomarkers for DFR, we performed a baseline transcriptomic analysis of whole blood and synovial fluid in ReA and undifferentiated peripheral spondyloarthritis (pSpA) and followed them up for 3 months each. Key differentially expressed genes (DEGs) were validated.

Methods: Fifty-seven patients meeting Braun criteria for ReA or ASAS criteria for pSpA (excluding IBD-related or psoriatic arthritis) were recruited. Baseline whole blood and synovial fluid (SF) samples from inflamed joints were collected. Drug free remission (DFR) was defined as being completely symptom-free at three months while off all medications. Patients were grouped as chronic ReA or DFR.

Transcriptomics was performed on whole blood (n=14) and paired SF (n=10) using Illumina NovaSeq for RNAseq, X Plus and DRAGEN for demultiplexing/alignment, DESeq2 for DEG analysis, and cluster Profiler for KEGG pathway enrichment in R.

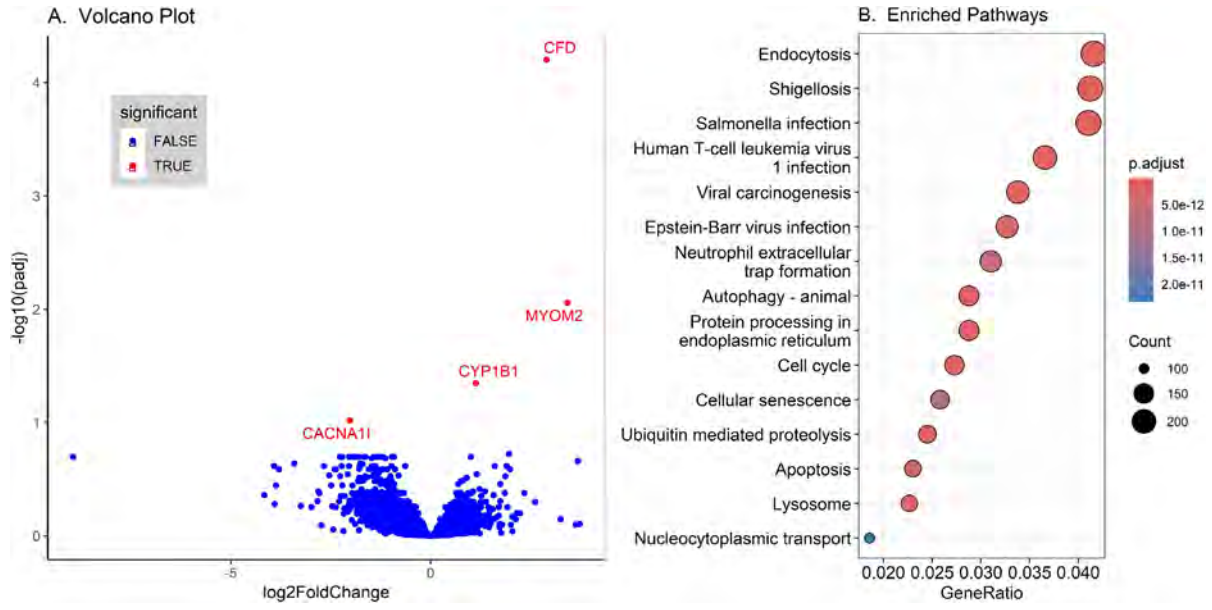


Figure 1: Comparison between whole blood transcriptome profiles of patients with chronic reactive arthritis and those with drug-free remission. (A) Volcano plot showing differentially expressed genes and (B) Showing the top 15 enriched pathways (KEGG)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

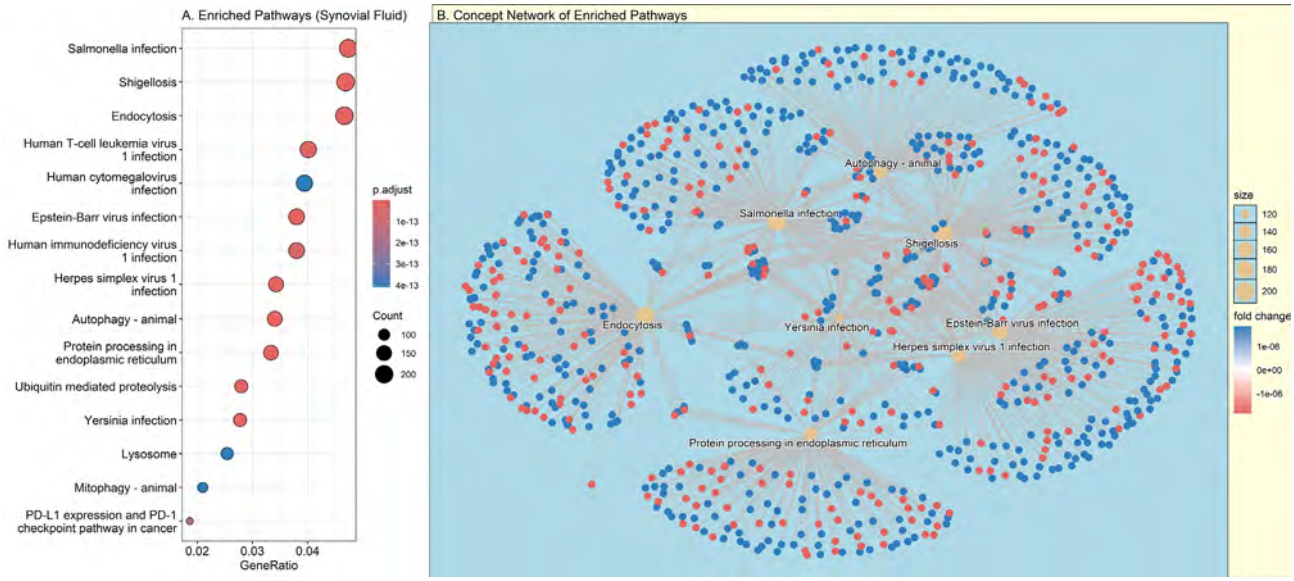


Figure 2: Comparison between synovial fluid transcriptome profiles of patients with chronic reactive arthritis and those with drug-free remission. (A) Dot plot of the top 15 enriched pathways (KEGG) and (B) showing a Concept network map between the top 8 enriched pathways.

Amongst the top differentially expressed genes, Complement factor D (CFD) and Cytochrome enzyme CYP1B1, were validated internally in the RNAseq cohort (n=14) along with another external validation (n=5) using a SYBRGreen- TaqMan system. Mann-Whitney U test compared ΔCT values between DFR and chronic groups.

Results: Out of total 57 patients [75% males; median age 32 (IQR12-40) years], 37 were ReA and 20 were undifferentiated pSpA. Fifty-two percent (n=30) of patients achieved DFR. We selected baseline whole blood (n=14) and paired synovial fluid (SF, n=10) samples based on RNA quality for RNAseq. Of these, 6 had attained DFR (SF available for 3). There was no difference in the transcriptome profiles of ReA versus undifferentiated pSpA.

Whole blood transcriptomics identified four differentially expressed genes associated with DFR (Upregulated: CFD, MYOM2, CYP1B1. Down-regulated: CACNA1I) [Figure 1A]. KEGG enrichment analysis revealed pathways related to Endocytosis, Shigellosis, Salmonellosis and certain viral-related pathways were enriched in patients who ultimately attained DFR [Figure 1B].

Differentially expressed genes in the synovial fluid were not statistically significant (not shown). However, the KEGG analysis also showed the enrichment of pathways associated with Salmonellosis, Shigellosis, Endocytosis and different viruses [-Figure 2A]. Figure 2B shows the concept maps of the top 8 upregulated pathways in the KEGG analysis.

In the preliminary validation, CFD [median ΔCT DFR: 6.48 (IQR 4.63-12.87), chronic: 9.20 (IQR 7.27-12.65); p=0.2] and CYP1B1 [median ΔCT DFR: 6.95 (IQR 6.63-8.76), chronic: 10.25 (IQR 7.98-11.69); p=0.055] did not reach statistical significance in DFR patients compared to chronic ReA.

Conclusion: Baseline whole blood gene expression profiles predict DFR in ReA. Enrichment of bacterial and viral pathways in DFR patients, despite the absence of live bacteria in SF, suggests a potential role for bacterial exosomes or other pathogen-associated molecular patterns (PAMPs) in the resolution of ReA. The role of CFD and CYP1B1 needs to be elucidated.

Disclosure: A. Agarwal: None; **P. Dhanekula**: None; **S. Verma**: None; **S. ravi Nayak**: None; **P. Mruthyanjaya**: None; **P. Padhan**: None; **A. Patro**: None; **R. Misra**: None; **S. Ahmed**: Alkem, 6, Cipla, 6, Dr Reddy's, 6, Ipca, 6, Janssen, 1, Pfizer, 6, Sun Pharma, 6, Torrent, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0534

Prevalence and Impact of Fibromyalgia on Disease Outcomes and Treatment in Axial Spondyloarthritis: 10-year Follow-up Data From the DESIR Cohort

Clementina López Medina[1], Sylvie Chevret[2], Cedric Lukas[3], Anna Molto[4] and Maxime Dougados[2], [1]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [2]Université Paris-Cité, Paris, France, [3]CHU Montpellier, Montpellier, France, [4]Assistance Publique Hôpitauxde Paris, Paris, France

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Concomitant fibromyalgia (FM) can be suspected in patients (pts) with axial SpA (axSpA) using the Fibromyalgia Rapid Screening Tool (FiRST).

The objective of this study was to evaluate the prevalence of suspected FM and its impact on the disease, including first TNFi initiation and retention rates, PROs and disability, over the first 10 years of follow-up in pts with axSpA.

Methods: This analysis included pts diagnosed with axSpA by a rheumatologist for less than 3 years. Collected data: The FiRST tool became available starting from the seventh year (M84) and was then administered annually until year 10 (M120). Statistical analysis: *a) Estimation of FM prevalence*. The percentage of FM+ pts was estimated for the entire cohort (n=708). Missing data were imputed using multiple imputation for longitudinal data at each of the four visits (M84 to M120). A patient was classified as FM+ if he/she was identified as FiRST+ at least twice during the four visits (M84-M120) after multiple imputation. *b) Impact of FM:* The impact of FM was assessed as follows: b.1.) at the start of the cohort (visit M0): by comparing objective signs of axSpA (HLA-B27 status, structural damage on X-rays, inflammation on MRI-SIJ and abnormal CRP); b.2.) over the 10 years of follow-up: by analysing disease activity, PROs and disability using mixed models for repeated measures; b.3.) therapeutic impact: by evaluating the percentage of patients treated with a first TNFi and their therapeutic maintenance using Kaplan-Meier analyses.

Results: After the multiple imputation of visits M84 to M120, the estimated prevalence of FM+ pts was 144/663 (21.7%). At baseline, the presence of FM was associated with a lower frequency of HLA-B27 positivity and radiographic sacroiliitis, but a

	FM- N = 519 Mean (SD) over 10 years	FM+ N = 144 Mean (SD) over 10 years	P-value: crude MMRM	p-value: MMRM adjusted for TNFi intake ever
BASDAI (0-100)	31.1 (20.1)	50.3 (19.7)	**<0.001**	**<0.001**
BASDAI Q1 (0-10)	4.5 (2.6)	6.3 (2.2)	**0.020**	**0.028**
BASDAI Q2 (0-10)	3.7 (2.5)	5.8 (2.3)	**0.015**	**0.009**
BASDAI Q3 (0-10)	1.9 (2.3)	3.8 (2.7)	**0.006**	**0.003**
BASDAI Q4 (0-10)	2.6 (2.7)	4.8 (2.6)	**<0.001**	**0.002**
BASDAI (Q5+Q6)/2 (0-10)	2.9 (2.3)	4.5 (2.4)	**<0.001**	**<0.001**
ASDAS (0-6)	2.0 (0.9)	2.8 (0.9)	**0.001**	**<0.001**
BASFI (0-100)	19.3 (19.3)	39.6 (22.3)	**<0.001**	**<0.001**
SF-36 MCS (0-100)	45.5 (10.6)	38.2 (11.1)	**<0.001**	**<0.001**
SF-36 PCS (0-100)	44.0 (9.5)	35.8 (8.6)	**<0.001**	**<0.001**
Days of sick leave	15.6 (49.7)	42.8 (81.6)	0.844	0.732

ASDAS: Axial Spondyloarthritis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Function Index; MM: Mixed Model for Repeated Measures; SF36-MCS: Mental Component Score from the SF-36 questionnaire; SF36-PCS: Physical Component Score from the SF-36 questionnaire; SD: Standard Deviation; TNFi: Tumour Necrosis Factor inhibitors.

Figure 1. Mixed models for Repeated Measures (MMRM) with random effects to compare disease activity and PROs over 10 years of follow-up between FM+ and FM-.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

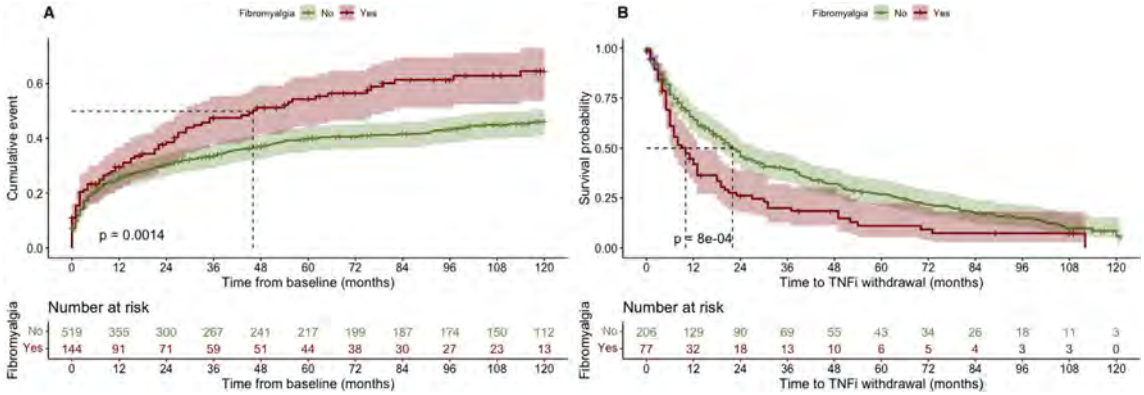


Figure 2. Impact of concomitant FM on the probability of TNFi initiation (A) and on the retention rate to the first TNFi (B).

similar prevalence of positive MRI-SIJ findings and abnormal CRP levels. Furthermore, the level of confidence in the SpA diagnosis by the rheumatologist was similar in FM+ and FM- groups (6.9 vs. 7.1 on a 0-10 scale).

The presence of FM was also associated with higher disease activity and poorer quality of life over the 10 years of follow up (Figure 1). Pts with FM showed a significant greater likelihood of reporting permanent disability after 10 years compared to FM- pts (26.4% vs. 9.4%, p< 0.001).

Finally, FM+ was associated with a higher likelihood of initiating biologic therapy during the 10 years of follow-up (64.4% vs. 46.1%). However, therapeutic maintenance was poorer in the FM+ group, with a lower percentage of pts remaining on treatment one year after initiation [FM+: 42.0% (95%CI 32.1-54.9) vs. FM-: 64.2% (95%CI 57.9-71.2)] (Figure 2).

Conclusion: This study confirms the high prevalence of FM in axSpA. The similarity of certain objective disease markers (e.g., MRI-SIJ positivity and abnormal CRP) between FM+ vs. FM- pts, as well as the comparable diagnostic confidence, suggests that FM is more likely a comorbidity than a diagnostic error. The presence of FM negatively impacts disease activity scores and quality of life, resulting in a higher likelihood of permanent disability. FM is also associated with an increased likelihood of initiating biologic therapy; however, therapeutic maintenance is lower in these pts.

Disclosure: C. López Medina: None; **S. Chevret**: None; **C. Lukas**: None; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **M. Dougados**: None.

Abstract Number: 0535

Comparing Perspectives of Physician-Assessed and Self-Reported Inflammatory Back Pain: Insights from the SHERPAS Cohort

Diego Benavent[1], Mar Tapia[2], Daniel Bernabeu[2], Victor Muley[2], Manuel Juárez[3], Chamaida Plasencia-Rodríguez[4], Alejandro Balsa[4] and Victoria Navarro-Compan[5], [1]Hospital Universitari de Bellvitge, Madrid, Spain, [2]HU La Paz, Madrid, Spain, [3]Rheumatology Unit, Hospital Universitario La Paz, IdiPAZ, Madrid, Spain, [4]Hospital Universitario La Paz, MADRID, Spain, [5]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

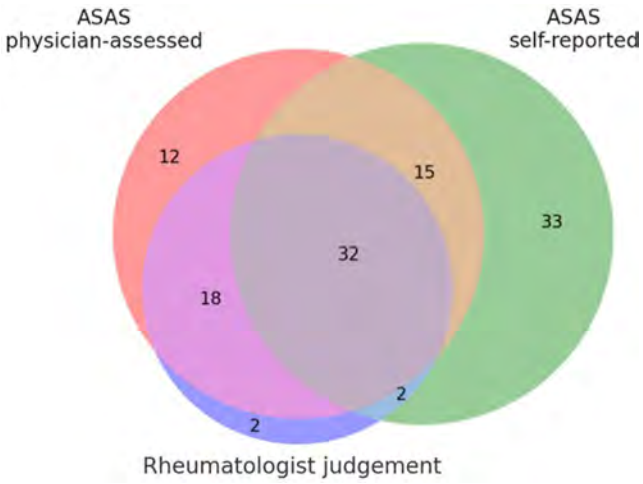


Figure 1. Number of patients with IBP according to each method of assessment

Background/Purpose: Inflammatory back pain (IBP) is very relevant for identifying patients at risk of axial spondyloarthritis (axSpA). Mounting evidence has indicated substantial variability in sensitivity and specificity among different methods of IBP assessment (1). The aim of this study is to evaluate the concordance and correlation between physician-based ASAS IBP criteria and self-reported IBP, comparing each against expert clinical judgement in a prospective cohort of patients with chronic low back pain.

Methods: A prospective, observational study was conducted at a tertiary hospital (July 2021- October 2023). Patients aged 18–40 years with chronic back pain (≥ 3 months) who underwent spine magnetic resonance imaging (MRI) requested by non-rheumatology specialists were enrolled, and completed a questionnaire capturing variables relevant to axSpA, including characteristics of IBP. Within two weeks, patients underwent a rheumatology evaluation. IBP was evaluated independently using three different approaches: physician-assessed ASAS IBP criteria as a checklist (ASAS-IBP-phy), self-reported ASAS IBP questionnaire (ASAS-IBP-self), and the rheumatologist's clinical judgement (IBP-rheumatologist). ASAS-IBP-phy and ASAS-IBP-self were evaluated through structured questionnaires completed by the physician and the patient, respectively ,while IBP-rheumatologist relied exclusively on the clinician's global assessment. Cohen's and Fleiss' kappa statistics, along with tetrachoric correlation, assessed the agreement among these methods.

Results: Among 268 enrolled patients, mean age was 35.6 years (SD 5.6), with 149 (55.6%) females. Mean duration of symptoms was 5.1 years (SD 4.6), and 64.2% had symptom duration greater than two years. ASAS-IBP criteria were positive in 79 (29.5%) patients by rheumatologist checklist evaluation (ASAS-IBP-phy), and 82 (30.6%) through self-report

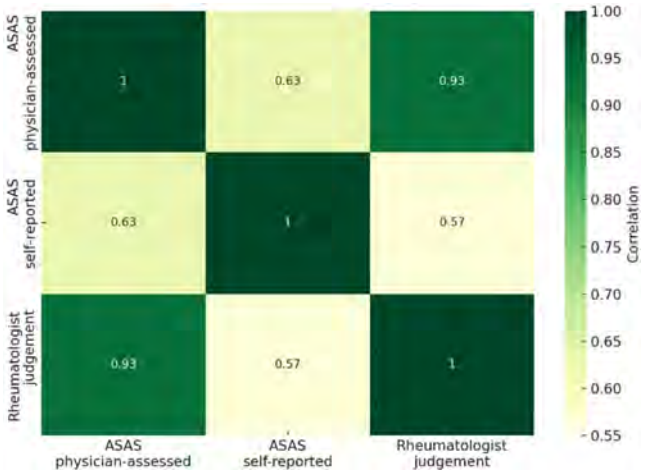


Figure 2. Correlation between IBP assessment methods

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(ASAS-IBP-self). Clinical judgement by rheumatologist identified IBP in 54 (20.1%) patients. Among patients with axSpA (n = 8), 7 (87.5%) presented IBP according to the rheumatologist, and among those without axSpA (n = 260), 47 (18.1%) did. 32 patients (11.9%) fulfilled IBP criteria across all three methods (**Figure 1**). Agreement between physician-based and self-reported IBP criteria was moderate (kappa = 0.42, p< 0.001) with a strong tetrachoric correlation (rt=0.63) (**Figure 2**). ASAS-IBP-phy showed substantial agreement with IBP according to rheumatologist clinical judgement (kappa = 0.69, p< 0.001), and a very strong tetrachoric correlation (rt=0.93). In contrast, agreement between ASAS-IBP-self and clinical IBP assessment was fair (kappa = 0.34, p< 0.001), with moderate tetrachoric correlation (rt=0.57). Fleiss' kappa for overall agreement among the three assessment methods was 0.31 (p< 0.001).

Conclusion: In this cohort, physician-based ASAS IBP criteria showed higher concordance and correlation with rheumatologist clinical judgement than self-reported criteria. Given these results, clinician-led evaluation should be prioritized when identifying IBP in clinical and research contexts, with cautious interpretation of self-reported data, particularly in remote or digital healthcare settings.

Disclosure: D. Benavent: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 6, Savana, 7, UCB, 2, 6; **M. Tapia**: None; **D. Bernabeu**: None; **V. Muley**: None; **M. Juárez**: Gebro Pharma, 6; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **A. Balsa**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, Pfizer, 6, UCB, 6; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0536

Can achieving sustained low disease activity through treat-to-target management arrest enthesiophyte progression in psoriatic arthritis? A two-year prospective study using high resolution peripheral quantitative computed tomography

Isaac Cheng[1], Ho So[1], Yingzhao jin[1], Vivian Hung[2], Ling Qin[2], James Griffith[3] and Lai Shan Tam[1], [1]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, [2]Bone Quality and Health Centre, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong, Hong Kong, Hong Kong, [3]Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Hong Kong, Hong Kong

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Enthesitis is a hallmark feature of psoriatic arthritis (PsA). Chronic inflammation in the entheses can lead to the formation of enthesiophytes (bony spurs), and this new bone formation may result in functional loss over time. Although substantial improvements in clinical response has been observed using the treat-to-target (T2T) management strategy, limited studies have demonstrated its effect on radiographic outcomes, particularly regarding new bone formation. Therefore, the objective of this study was to ascertain the effect of achieving Sustained Disease Activity in PSoriatic Arthritis (DAPSA) low disease activity (LDA) on the progression of enthesiophyte in MCP2-4 using HR-pQCT.

Methods: One hundred consecutive PsA patients were recruited to this 2-year prospective study. They received protocolized T2T treatment aiming at DAPSA-LDA. Sustained DAPSA-LDA (SDL) was defined as achievement of DAPSA-LDA at month 12, 18 and 24. HR-pQCT of the MCP2-4 were performed at baseline, one and two years,. Enthesiophytes were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

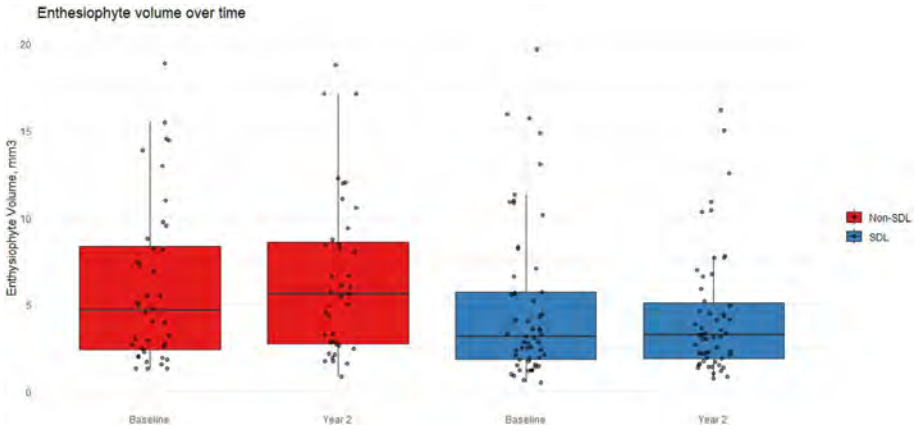


Figure 1 - Enthesiophyte volume over time between patient who achieved and did not achieve sustained LDA

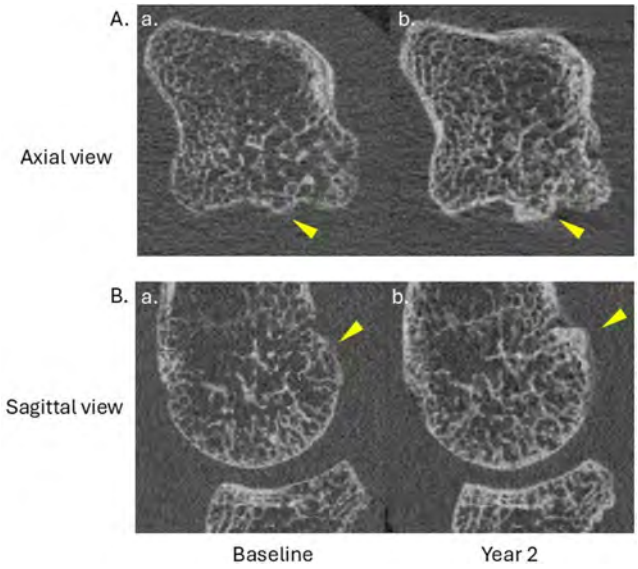


Figure 2 – Representative image showing progression of enthesiophyte from baseline to year 2 in axial and sagittal view

defined as new bone formation arising from the periosteal bone cortex at the insertion sites of the capsule, ligament, or tendons or at the location of functional enthesis.(1) Enthesiopyte volume was quantified were quantified semi-automatically. Progression of pre-existing enthesiophyte were defined as increase in enthesiophyte volume exceeding least significant change (LSC, 1.1mm^3).

Results: Ninety-five patients (age: 51±14 years, 57 (60%) male, disease duration: 3.9±6.1 years) who completed 2-year follow-up were included. After 2-years of T2T management, a significant decrease in disease activity (DAPSA - baseline: 25.1±12.7 vs Year 2: 8.4±6.8, $p< 0.001$) were observed, and 59 (62.1%) patients achieved SDL. The use of biologic disease modifying anti-rheumatic drug (bDMARDs) increased from 5% at baseline to 64% at year 2. Regarding enthesiophyte, a total of 64 and 47 enthesiophytes were identified at baseline for patients in SDL and non-SDL group respectively. After 2 years, enthesiophyte volume in non-SDL group progressed [median (IQR) of change: 0.77mm^3 (-0.19, 2.22)] and that in SDL group remained stable [median (IQR) of change: 0.08 mm^3 (-0.61, 0.73), p=0.035]. Enthesiophyte volume progression was significantly higher in non-SDL group (40% vs 19% in SDL group, (p=0.031). Using generalized estimating equation (GEE), after accounting for within subject variance, achieving SDL protected against enthesiophyte volume progression (OR=0.35, 95% CI: 0.14-0.88, p=0.025), independent of age, sex, disease duration and bDMARDs use.

Conclusion: Achievement of sustained disease activity control protects against progression of enthesiophyte in PsA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: I. Cheng: None; **H. So**: None; **Y. jin**: None; **V. Hung**: None; **L. Qin**: None; **J. Griffith**: None; **L. Tam**: None.

Abstract Number: 0537

HLA-B27 and Axial Involvement as Independent Risk Factors for Uveitis in Spondyloarthritis: New Insights from a 15-Year Real-Life Study

Kent LE[1], Hervé LOCRELLE[1], Myriam NORMAND[1], Irina COMAN[1], Louis DELENTE[1], Tiphany NEEL[1], Adamah AMOUZOUGAN[1], Thierry THOMAS[1] and Hubert Marotte[2], [1]Service Rhumatologie Hôpital Nord, Saint-Etienne, France, [2]INSERM 1059/University of Saint-Etienne, Saint-Etienne, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To assess the prevalence, risk factors and treatment-related outcomes of uveitis in patients with spondyloarthritis (SpA), using data from a 15-year real-life cohort.

Methods: We conducted a retrospective study including all patients treated for SpA at the Rheumatology Department of Saint-Etienne University Hospital, between January 2008 and July 2022. Demographic, clinical, biological, radiographic, and treatment data were collected. Patients were classified according to uveitis history and timing relative to treatment initiation (absent, recurrent, de novo). Multivariate analysis identified factors associated with uveitis and treatment outcomes.

Results: Among the 1,571 patients included (mean age 50.6 ± 14.7 years; 52.7% male; mean disease duration 13.6 ± 10.6 years), 46% were diagnosed with ankylosing spondylitis, 33.9% with non-radiographic axial SpA, and 20.1% with peripheral SpA. HLA-B27 was positive in 59.5% of patients. Uveitis prevalence was 12.3% (95% CI: 10–14%), rising to 20.7% (95% CI: 17.7–24%) among HLA-B27 positive patients. Independent risk factors for acute anterior uveitis (AAU) included axial involvement (OR = 3.34; 95% CI: 1.46–7.65; p = 0.004), HLA-B27 positivity (OR = 3.65; 95% CI: 2.30–5.82; p < 0.01), and longer disease duration (OR = 1.03/year; 95% CI: 1.01–1.05; p < 0.001). Uveitis recurrence occurred in 33.3% of patients treated with IL-17 inhibitors vs. 10.4% with anti-TNF agents (p = 0.02).

Conclusion: In this extensive cohort, our study confirmed the independent association of HLA-B27, axial phenotype, and disease duration as the key predictors of uveitis in SpA. Among bDMARDs, monoclonal anti-TNF agents were the most effective in preventing uveitis, while recurrence was significantly higher under anti-IL17 therapy. Notably, this study is the first to demonstrate the independent association between HLAB27 positivity and axial involvement, offering new insights for personalized treatment strategies.

Disclosure: K. LE: None; **H. LOCRELLE**: None; **M. NORMAND**: None; **I. COMAN**: None; **L. DELENTE**: None; **T. NEEL**: None; **A. AMOUZOUGAN**: None; **T. THOMAS**: None; **H. Marotte**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0538

Development of an Artificial Intelligence Tool for Lesion Detection in Axial Spondyloarthritis patients with Active Sacroiliitis on Magnetic Resonance Imaging

Khalid Alnaqbi[1], Jorge Juan Fragío Gil[2], Hiba Khogali[3], Gianina Statache[4], Alzahraa Abouelnadar[4], Ahlam Almarzooqi[5], Amina AlJasmi[6], Jameel Shawaqfeh[7], Manal Mashaleh[8], Maysoon Bani Hani[7], Saitah Alshammari[9], Yasser H. Alghamdi[9], Faisal Alfaisal[9], Abdulaziz Almosabihi[9], Cristina Campos Fernández[10], Roxana González Mazario[10], Jose Lozano-Montoya[11], Ana Jiménez-Pastor[11], Paula Moreno-Ruiz[11], Marta Martínez-Calle[11], Fuensanta bellvís-Bataller[11] and Almudena Fuster-Matanzo[11], [1]Sheikh Tahnoon Medical city, Al Ain, United Arab Emirates, [2]Hospital General Universitario, Valencia, Spain, [3]Madinat Zayed Hospital , Al Dhafra hospitals, Abu Dhabi, Abu Dhabi, United Arab Emirates, [4]Abu Dhabi Stem Cell Centre/Yas Clinic Hospital, Abu Dhabi, United Arab Emirates, [5]Emirates Health Services, Sharjah, United Arab Emirates, [6]Emirates Health Services, Dubai, United Arab Emirates, [7]Royal Medical Services, Amman, Jordan, [8]Al Saudi Hospital, Amman, Jordan, [9]King Saud Medical City, Riyadh, Saudi Arabia, [10]Hospital General de Valencia, Valencia, Spain, [11]Quibim, Valencia, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic immune-mediated inflammatory disease primarily affecting spine and sacroiliac joints (SIJ), leading to pain and disability. Magnetic resonance imaging (MRI) has transformed axSpA diagnosis in non-radiographic cases–undetectable on X-rays–, guiding treatment and improving long term outcomes.

As per the Assessment of Spondyloarthritis international Society (ASAS), "active sacroiliitis" requires bone marrow edema (BME) on T2-weighted MRI, indicating SIJ inflammation highly suggestive of axSpA. However, "positive MRI" definitions vary, with high inter-/intra-observer variability and frequent underdiagnosis, contributing to a mean 7-year delay. Thus, standardized, automated tools are needed. This study aimed to develop an artificial intelligence (AI)-based model to detect active axSpA on MRI.

Methods: This retrospective, observational study (NCT06591481) used real-world data from six international sites. The dataset included 684 SIJ MRIs, each with coronal-oblique T2 short tau inversion recovery (STIR) or T2 fat-saturated (FS) sequences acquired at diagnosis and follow-up. Imaging data were collected and processed using Quibim platform (Quibim SL, Valencia, Spain). All scans underwent quality checks by three radiographers with >5 years of experience on image interpretation.

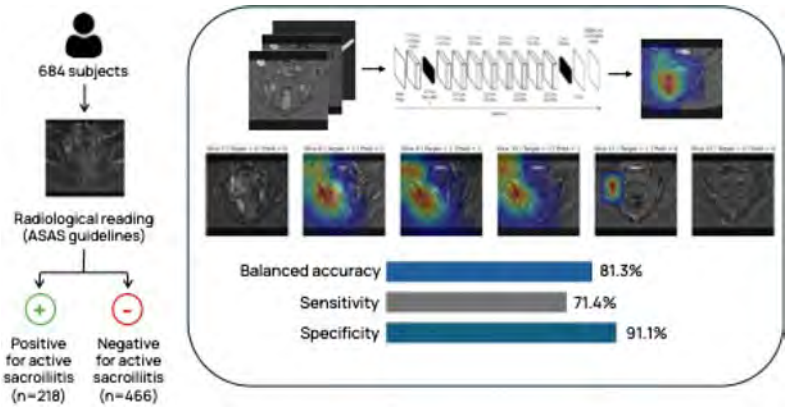


Figure 1. Development of AI-based tool for lesion detection in axSpA patients with active sacroiliitis using MRI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Following ASAS criteria, MRIs were double read by radiologists with >12 years of experience, with adjudication by a third reader. Scans were classified as positive active sacroiliitis on MRI (ASAS-positive MRI; BME on two consecutive slices) or negative, and structural damage (ankylosis, erosion and fat metaplasia) were noted. A deep-learning-based AI classification model was developed to identify axSpA patients with ASAS-positive MRI. Of the total 684 cases, 563 were used for training and validation, and 121 for testing. The model performs automated sacroiliac joint segmentation on T2 imaging to predict BME presence across patient slices. Detection of two consecutive positive slices yields a positive patient diagnosis. To enhance interpretability, heat maps highlight the regions that most influence the model's predictions.

Results: Overall, 32% of patients (*n* = 218) fulfilled the ASAS classification criteria for axSpA. The model achieved high balanced accuracy (bal acc = 81.3%), sensitivity (se = 71.4%) and specificity (sp = 91.1%) for ASAS-positive MRI detection. Performance was higher (bal acc = 89.3%; se = 84% and spe = 94.5%) in cases with consensus readings and clearly visible lesions on at least two consecutive slices. However, performance declined (bal acc = 51.5%) in cases with poor image quality, motion artifacts, or subtle lesions, highlighting the need for expert oversight. In such cases heat maps can assist in achieving a correct diagnosis.

Conclusion: We developed an AI-based classification model with high diagnostic performance in detecting MRI-positive axSpA, especially in terms of specificity (91.1%). This tool could support radiologists by standardizing MRI interpretation. Its integration into clinical workflows may enhance diagnostic accuracy and improve patient care.

Disclosure: K. Alnaqbi: None; **J. Fragío Gil**: Quibim, 1; **H. Khogali**: None; **G. Statache**: None; **A. Abouelnadar**: None; **A. Almarzooqi**: None; **A. AlJasmi**: None; **J. Shawaqfeh**: None; **M. Mashaleh**: None; **M. Bani Hani**: None; **S. Alshammari**: None; **Y. Alghamdi**: None; **F. Alfaisal**: None; **A. Almosabihi**: None; **C. Campos Fernández**: Hospital General Universitario, 2; **R. González Mazario**: None; **J. Lozano-Montoya**: Quibim, 3; **A. Jiménez-Pastor**: Quibim, 3; **P. Moreno-Ruiz**: Quibim, 3; **M. Martínez-Calle**: Quibim, 3; **F. bellvís-Bataller**: Quibim, 3; **A. Fuster-Matanzo**: Quibim, 3.

Abstract Number: 0539

Which instrument measuring structural damage progression in axial SpA is most sensitive to change? Analyses from the SPondyloArthritis Caught Early cohort

Liese de Bruin[1], Floris A. van Gaalen[1], Manouk de Hooge[2], Miranda van Lunteren[1], Mary Lucy Marques[3], Monique Reijnierse[4], Roberta Ramonda[5], Inger Jorid Berg[6], Sofia Exarchou[7], Robert Landewé[8], Désirée Van Der Heijde[1] and Sofia Ramiro[9], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [3]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [4]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [5]Rheumatology Unit-DIMED-University of Padova ITALY, Padova, Padua, Italy, [6]6Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Nepal, [7]Lund University, Akarp, Skane Lan, Sweden, [8]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [9]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The assessment of structural damage progression is an important part of outcome assessment in axial SpA (axSpA). In order to test whether interventions can potentially inhibit structural damage progression, an outcome measurement instrument that is sensitive to change is essential. We aimed at comparing the sensitivity to change of different methods assessing structural lesions on conventional radiographs and on MRI of the sacroiliac joints (SIJ) and the spine in patients with early axSpA.

Methods: Patients with chronic back pain (≥3 months; ≤2 years; onset < 45 years) from the SPondyloArthritis Caught Early (SPACE) cohort received a rheumatologist's diagnosis of axSpA or non-axSpA after two years follow-up. Only patients with an axSpA diagnosis were included in this analysis. Radiographs and MRIs of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline, 3 months, 1 and 2 years of follow-up, and scored for structural lesions (Table 1) by at least 2 and a maximum of 3 readers in two reading rounds. All patients with ≥1 score from ≥1 reader from ≥1 timepoint from ≥1 reading round were included in the analysis. To allow comparison across outcomes, the standardized rate of change was calculated using integrated multilevel generalized estimating equations while considering the individual readers and reading round. To facilitate the comparison across imaging outcomes, the relative standardized rate of change was calculated by dividing the standardized rate of change of the imaging outcome by that of an outcome chosen as the reference. Additionally, one

Table 1. Standardized yearly rate of mean change of structural outcomes over 2 years of follow-up in early axial SpA patients (N=332)*

Modality and anatomic site	Imaging outcomes	Standardized rate of change per year (95% CI)	Relative standardized rate of change	Relative standardized rate of change per anatomic site	Relative standardized rate of change per modality + anatomic site
MRI-SIJ	Total structural lesions without sclerosis (0-104)	0.090 (0.064; 0.122)	1 (ref)	1 (reference)	1 (reference)
	No. of fat lesions and/or erosions (0-80)	0.089 (0.055; 0.123)	0.988	0.988	0.988
	Total structural lesions (0-144)	0.086 (0.054; 0.118)	0.955	0.955	0.955
	No. of fat lesions (0-40)	0.079 (0.041; 0.116)	0.873	0.873	0.873
	No. of erosions (0-40)	0.067 (0.034; 0.101)	0.750	0.750	0.750
	No. of (partial) ankylosis (0-24)	0.030 (0.008; 0.053)	0.329	0.329	0.329
Radiograph SIJ	Sacroiliitis grade (mNY; 0-8)	0.040 (0.016; 0.064)	0.440	0.440	1 (reference)
	Sacroiliitis (mNY; yes/no)	0.030 (0.002; 0.057)	0.330	0.330	0.749
MRI-spine	No. of fat lesions (0-92)	0.069 (0.030; 0.107)	0.762	1 (reference)	1 (reference)
	No. of fat lesions and/or erosions and/or bone spurs (0-276)	0.068 (0.031; 0.105)	0.755	0.991	0.991
	Total structural lesions (0-322)	0.062 (0.031; 0.093)	0.693	0.909	0.909
	No. of bone spurs (0-92)	0.022 (-0.016; 0.060)	0.244	0.320	0.320
	No. of erosions (0-92)	0.009 (-0.021; 0.039)	0.102	0.134	0.134
	No. of ankylosis (0-46)	-0.003 (-0.016; 0.010)	-0.031	-0.041	-0.041
Radiograph spine	mSASSS (0-72)	0.053 (0.006; 0.099)	0.585	0.768	NA

* integrated analysis of N=332 patients, 2 reading rounds and at least 2 readers per modality

The total of structural lesions in the MRI of the sacroiliac joints is a sum of erosions, fat lesions, (partial) ankylosis, and sclerosis. The total of structural lesions in the MRI of the spine is a sum of erosions, fat lesions, bone spurs and ankylosis. CI, confidence intervals; mNY, modified New York criteria; MRI, magnetic resonance imaging; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; No, number; SIJ, sacroiliac joints; SpA, spondyloarthritis.

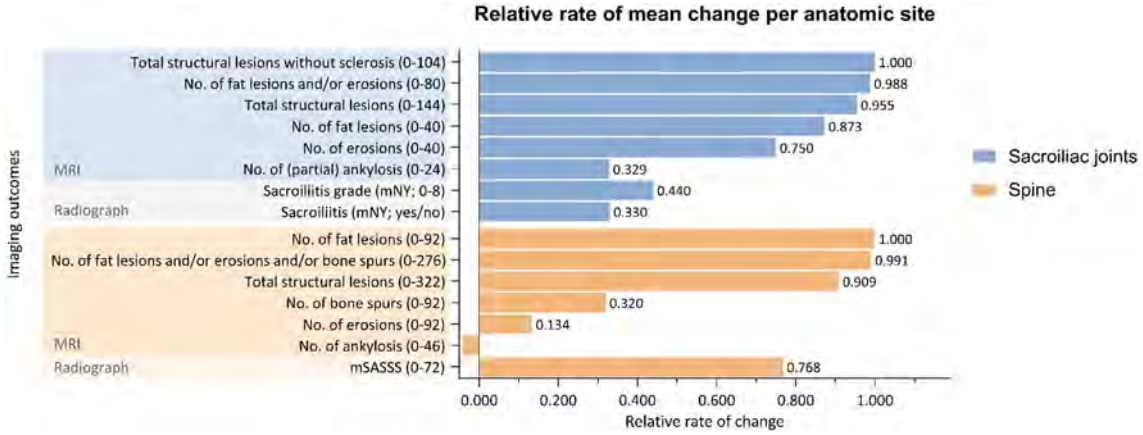


Figure 1. Relative rate of mean change using a reference per anatomic site with total structural lesions without sclerosis set as the reference. The total of structural lesions in the MRI of the sacroiliac joints is a sum of erosions, fat lesions, (partial) ankylosis, and sclerosis. The total of structural lesions in the MRI of the spine is a sum of erosions, fat lesions, bone spurs and ankylosis. mNY, modified New York criteria; No., number; mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

outcome was chosen as a reference for each anatomic site for comparison of the outcomes at the site level. The imaging outcome with the highest standardized rate of change per year was chosen as reference, both overall and for each anatomic site. A sensitivity analysis was conducted in patients with all scores from ≥2 timepoints available.

Results: In total, 332 patients with axSpA (mean age 30 (SD 8) years; 53% males) were included in the main analysis, of which 295 (89%) had all scores from ≥2 timepoints. The yearly (relative) standardized rate of change of each imaging outcome is shown in Table 1. From all outcomes, MRI-SIJ total structural lesions without sclerosis had the highest standardized rate of change per year, also meaning that SIJ structural lesions were more sensitive to change than spinal lesions. From the spine outcomes, MRI total fat lesions had highest standardized rate of change. In addition, total fat lesions were highly sensitive both in the SIJ and spine (Figure 1). In contrast, outcomes with erosions or (partial) ankylosis were less sensitive to change. The sensitivity analysis showed similar findings.

Conclusion: Compared to MRI-spine and radiographs SIJ and spine, MRI-SIJ structural lesions are generally most sensitive to change. Fat lesions are most sensitive to change, especially on the MRI-SIJ. Erosions and ankylosis are less sensitive outcomes.

Disclosure: L. de Bruin: None; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **M. de Hooge**: UCB pharma, 2; **M. van Lunteren**: None; **M. Marques**: Novartis, 2, 6; **M. Reijnierse**: None; **R. Ramonda**: None; **I. Berg**: None; **S. Exarchou**: AbbVie/Abbott, 1, 5, Amgen, 1, 5, Eli Lilly, 1, 5, Janssen, 1, Novartis, 1, 5, 6, Pfizer, 5, UCB, 1, 6; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 0540

Low-Dose CT reveals syndesmophyte progression in axial SpA, particularly in the thoracic spine: Insights from the SPACE cohort covering early and established disease

Manouk de Hooge[1], Mary Lucy Marques[2], Gizem Ayan[3], Miranda van Lunteren[4], Liese de Bruin[4], Monique Reijnierse[5], Désirée Van Der Heijde[4], Sofia Ramiro[6] and Floris A. van Gaalen[4], [1]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [3]Ankara Research and Training Hospital, Ankara, Turkey, [4]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [5]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [6]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Low-dose computed tomography (ldCT) has not previously been used to assess pt with axial spondyloarthritis (axSpA) early in their disease course, especially those with minimal structural damage at baseline. We assessed spinal damage progression using ldCT and evaluate inter-reader reliability in patients (pt) with axSpA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

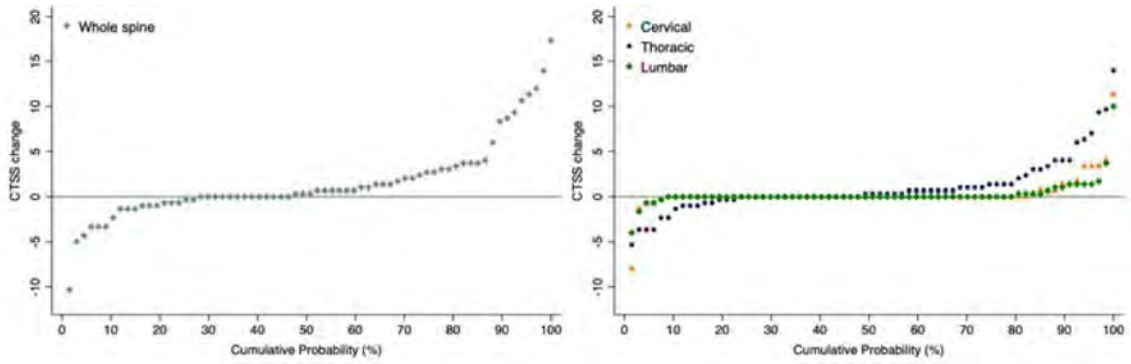


Figure 1. Cumulative probability plots of the change in computed tomography syndesmophyte score (CTSS) over 2 years for the whole spine (left) and separate spinal segments (right), based on aggregated scores derived from the average of individual reader scores

Methods: In SPondyloArthritis Caught Early (SPACE) cohort, 67 axSpA pt underwent two whole spine ldCT scans over a 2-year follow-up. First scan (T0) took place 0–10 years after inclusion, varying by pt. Regardless of T0 timing, second scan (T2) two years later.

Three central readers independently assessed CT syndesmophyte score (CTSS). Readers were blinded to image order and pt data. CTSS calculated per vertebral unit (VU) using eight quadrants, scoring syndesmophytes from 0 (absent) to 3 (bridging the intervertebral disc space), with a maximum CTSS of 552. Inter-reader reliability for CTSS change was calculated using intraclass correlation coefficients (ICC).

	Patients with new/growing syndesmophytes after 2 years				
VU	Reader 1	Reader 2	Reader 3	Consensus	Spinal level
1	0	1	3	0	C2-C3
2	1	1	1	1	C3-C4
3	1	0	1	1	C4-C5
4	2	0	1	1	C5-C6
5	1	0	2	0	C6-C7
6	3	0	5	3	C7-T1
7	0	1	2	0	T1-T2
8	3	0	4	1	T2-T3
9	4	2	9	4	T3-T4
10	6	2	6	4	T4-T5
11	5	1	6	4	T5-T6
12	6	4	6	5	T6-T7
13	10	4	11	8	T7-T8
14	7	5	7	5	T8-T9
15	6	2	14	4	T9-T10
16	7	2	8	2	T10-T11
17	6	0	11	5	T11-T12
18	5	2	8	5	T12-L1
19	5	2	5	5	L1-L2
20	2	2	3	2	L2-L3
21	4	4	4	4	L3-L4
22	1	0	1	1	L4-L5
23	3	1	2	2	L5-S1

Figure 2. Heatmap of spinal progression on ldCT: number of pt with new/growing syndesmophytes (increased red intensity reflects a higher number), based on consensus scores derived from a 2 out of 3 reader majority agreement

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Changes in CTSS (continuous data) were based on average reader scores and visualized in cumulative probability plots. Dichotomous data (new/growing syndesmophytes) were based on ≥2/3 consensus of readers at vertebral corner level. New syndesmophytes were defined by a score change from 0 to 1, 2, or 3; growth from 1 to 2 or 3, or 2 to 3. Net progression was calculated by subtracting regressors from progressors, divided by total pt, for cut-offs (≥1 to ≥5).

Results: Among 67 pt, 57% were male, 84% was HLA-B27 positive, mean age of 36 (8) years and symptom duration of 6 (3) years. 21% had early axSpA (≤2 years symptoms).

For the whole spine, the ICC for the change CTSS was 0.67 (95% CI: 0.50 to 0.78). Segment-specific ICCs showed good reliability for lumbar (0.91, 95% CI: 0.87 to 0.94) and thoracic spine (0.77, 95% CI: 0.65–0.85). Cervical spine showed poor reliability (ICC -1.69 (95% CI: -3.06 to -0.73).

Mean CTSS for whole spine increased from 9.6 (18.5) at T0 to 11.2 (20.7) at T2, resulting in a total mean change of 1.6 (4.5). When examining per spinal segments, thoracic spine showed the largest progression with a mean change of 1.0 (3.1), accounting for 63% of total change in the spine. Remaining 38% of spinal damage progression was equally accounted for by cervical and lumbar segments, each showing a mean CTSS change of 0.3 (1.9) and 0.3 (1.5), respectively. Figure 1 shows distribution of CTSS change, with smallest detectable changes of 3.93 (whole spine), 2.42 (cervical spine), 2.33 (thoracic spine) and 0.99 (lumbar spine).

Figure 2 shows number of pt with new/growing syndesmophytes per VU. Net progression of new/growing syndesmophytes (consensus) for whole spine was 22% at cut-off ≥1, 18% at cut-off ≥2, 15% at cut-off ≥3, 10% at cut-off ≥4, and 12% at cut-off ≥5.

Conclusion: Whole spine ldCT can detect progression in axSpA, even in pt with short symptom duration and minimal baseline prevalence of damage. Over two years, syndesmophyte progression occurred throughout the entire spine, with net progression rates between 10% and 22%, depending on severity cut-off. The thoracic spine showed the most change, accounting for nearly two-thirds of total progression—more than the cervical and lumbar segments combined

References

(1) Marques ML, et al. RMD Open. 2024

Disclosure: M. de Hooge: UCB pharma, 2; **M. Marques**: Novartis, 2, 6; **G. Ayan**: None; **M. van Lunteren**: None; **L. de Bruin**: None; **M. Reijnierse**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0541

Inflammatory Back Pain Is Not Associated With HLA-B27 Positivity or CRP Levels in a Nationally Representative U.S. Population

Mark Hwang[1], Seokhun Kim[2], Charles Green[1], Charles Dillon[3], Shervin Assassi[4], Michael Weisman[5] and John Reveille[6], [1]UTHealth Houston, Houston, TX, [2]UTHealth Houston, Houston, [3]NIH, Bethesda, MD, [4]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [5]Cedars-Sinai Medical Center, LOS ANGELES, CA, [6]Department of Medicine, University of Texas Medical Center, Houston, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory back pain (IBP) is a hallmark symptom of axial spondyloarthritis (axSpA) and is frequently used as a clinical entry point for further evaluation, including HLA-B27 testing and inflammatory marker assessment. However, the specificity of IBP for identifying individuals with immunogenetic or biochemical features of axSpA in the general population remains uncertain.

Methods: We analyzed data from the 2009–2010 cycle of the National Health and Nutrition Examination Survey (NHANES), a cross-sectional, nationally representative dataset. IBP was defined using Calin, ESSG, Berlin 7b, and Berlin 8a criteria, based on self-reported responses to the NHANES Arthritis Questionnaire. HLA-B27 typing and high-sensitivity CRP (hsCRP) were measured in a subset of 2,320 participants aged 20–69. We conducted logistic regression models adjusting for age, sex, race/ethnicity, smoking, alcohol use, diabetes, and hypertension. Causal mediation analysis was performed to assess whether CRP levels mediated any relationship between HLA-B27 and IBP.

Results: Among 746 participants with complete data, the prevalence of HLA-B27 was 6.1%. IBP prevalence ranged from 5.0% to 6.0% depending on the criteria used. In fully adjusted models, HLA-B27 positivity was not significantly associated with IBP by any of the criteria (e.g., Berlin 8a: OR 0.88 [95% CI 0.13–5.98], p=0.876) (Figure 1). Similarly, CRP levels were not associated with IBP (e.g., Berlin 8a: OR 0.94 [95% CI 0.63–1.39], p=0.694) (Figure 2). Mediation analysis showed no significant indirect effect of CRP on the HLA-B27–IBP relationship (indirect effect OR ≈ 1.00, p > 0.6 across all models) (Figure 3).

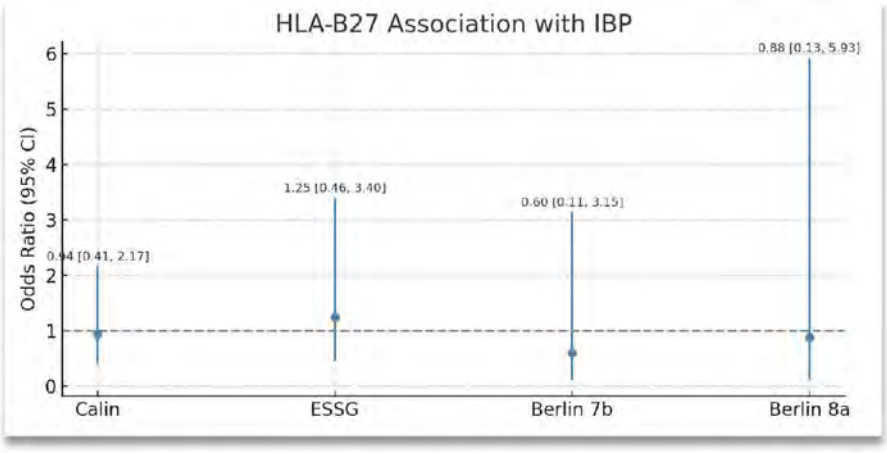


Figure 1. HLA-B27 association with Inflammatory Back Pain Criteria adjusted OR for age, sex, race, smoking, DM, HTN.

Figure 1. HLA-B27 association with Inflammatory Back Pain Criteria adjusted OR for age, sex, race, smoking, DM, HTN.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

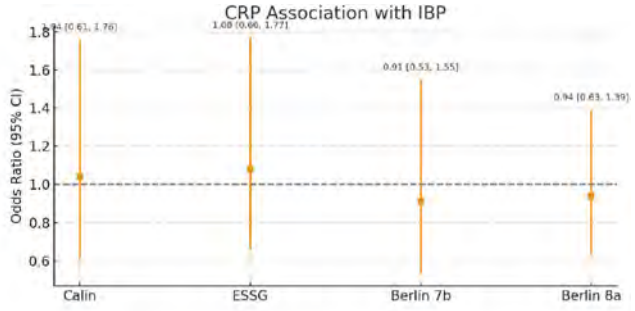


Figure 2. CRP association with Inflammatory Back Pain Criteria adjusted OR for age, sex, race, smoking, DM, HTN.

Figure 2. CRP association with Inflammatory Back Pain Criteria adjusted OR for age, sex, race, smoking, DM, HTN.

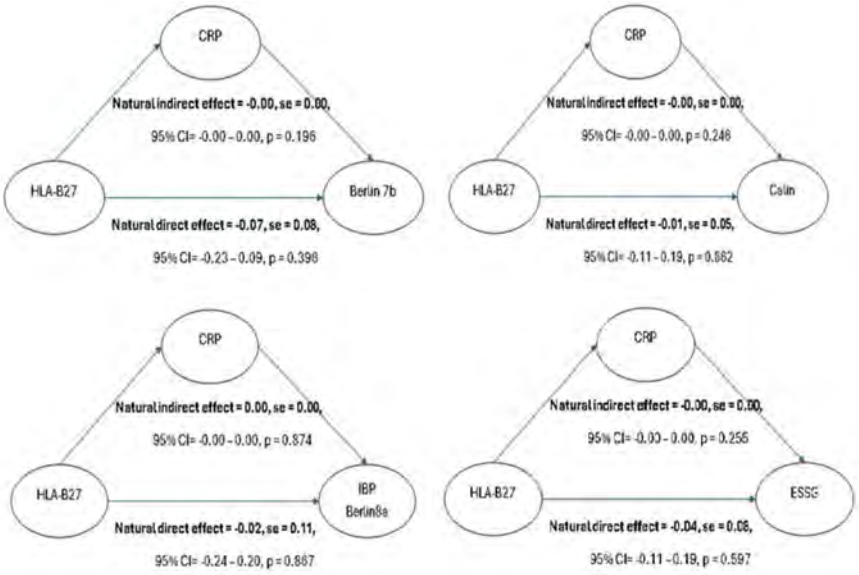


Figure 3. Causal Mediation Analyses for IBP. HLA-B27 association with IBP was not signficant after adjustment (natural direct effect). CRP does not mediate the association as well (natural Indirect effect)

Figure 3. Causal Mediation Analyses for IBP. HLA-B27 association with IBP was not signficant after adjustment (natural direct effect). CRP does not mediate the association as well (natural Indirect effect).

Conclusion: In a nationally representative U.S. sample, IBP as defined by established criteria was not associated with either HLA-B27 positivity or CRP levels. These findings suggest that IBP symptoms alone may have limited utility for identifying individuals with immunogenetic or inflammatory features of axSpA in the general population. Future strategies for early recognition of axSpA may require multimodal approaches that integrate clinical, laboratory, and imaging data beyond symptom-based screening alone.

Disclosure: M. Hwang: None; **S. Kim**: None; **C. Green**: None; **C. Dillon**: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **M. Weisman**: Spyre Therapeutics, 1, 2; **J. Reveille**: Surf Therapeutics, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0542

Transition from Psoriasis to Psoriatic Arthritis: Does Family History Influence the Time to Onset of Arthritis in Psoriasis Patients?

Marta Flores[1], Juan de Luque[2], Mitndbaim Parra[3], Alejandro Escudero Contreras[4], María Dolores López-Montilla[5] and Clementina López Medina[6], [1]1. Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., Spain, Spain, [2]Reina Sofia University Hospital, CÓRDOBA, Andalucia, Spain, [3]1. Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., Cordoba, Spain, [4]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [5]Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/ University of Cordoba., CORDOBA, Spain, [6]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a debilitating disease that occurs in up to one-third of patients with psoriasis (Pso), generally manifesting after the onset of Pso. Numerous studies have analyzed the risk factors for the development of PsA in patients with Pso, highlighting family history. However, there is little evidence about what determines the latency period between the onset of Pso and the development of arthritis.

Therefore, the following objectives have been established for this study:

a) To analyze the clinical phenotype of PsA based on the presence or absense of a family history of Pso or PsA (FH Pso/PsA)

b) To determine which factors (including FH Pso/PsA) influence the speed of onset of arthritis after the initial presentation of Pso

Methods: We conducted a retrospective analytical study including 359 patients diagnosed with PsA according to the "Classification Criteria for Psoriatic Arthritis" (CASPAR). These patients were divided based on the presence or absence of a family history of Pso/PsA (FH Pso/PsA). We collected clinical, radiographic, and treatment variables for each patient, as well as the dates of onset of Pso and arthritis. For the comparison of variables, Student's t-test (for quantitative variables) and Chi-square test (for qualitative variables) were used. We designed a survival analysis with Cox multiple regression to determine which factors influence the speed of onset of arthritis after the initial presentation of Pso.

Results: Of the 359 patients included, 37.5% had a family history of Pso/PsA (FH Pso/PsA). Patients with FH showed cutaneous-onset forms of PsA more frequently than those without FH (86.4% vs. 70%; $p< 0.001$), as well as a younger age at disease onset (Table 1). The latency period between the onset of Pso and the development of arthritis was longer in patients with FH (median time: 9.6 vs. 4.3 years; log-rank: $p< 0.001$; Figure 1). In the multivariable analysis, FH Pso/PsA (HR 0.88 (95% CI 0.78–0.99)) and a younger age at Pso onset (HR 1.03 (95% CI 1.02–1.04)) were associated with a delay in the onset of arthritis relative to Pso (Omnibus test: $p< 0.001$).

Conclusion: Family history of Pso/PsA in patients with Pso is associated with a longer time until the onset of arthritis. Therefore, patients with FH not only require a higher index of suspicion for PsA but also need longer follow-up periods to detect it. Collaboration between Dermatology and Rheumatology will be essential for early diagnosis and optimal management.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Descriptive summary of the most relevant collected variables

Variable	FH Pso/PsA (37.5%)	No FH Pso/PsA (62.5%)	P value
Gender (male)	57.6%	60.9%	0.537
Initial PsA pattern:			0.483
· DIPs	6.8%	4.5%	
· Polyarticular	17.4%	22.3%	
· Oligoarticular	62.1%	62.7%	
· Axial	13.6%	10.5%	
Age at psoriasis onset (years)	30.18 +/- 13.24	39.94 +/- 15.39	0.001
Inflammatory back pain	36.4%	29.1%	0.156
Age at arthritis onset (years)	40.69 +/- 14.17	45.94 +/- 13.38	<0.001
DIP involvement	36.4%	27.9%	0.095
Psoriasis onset type:			
· Cutaneous	86.4%	70%	<0.001
· Articular	3%	6.8%	0.128
· Simultaneous	10.6%	23.2%	0.003
Achilles enthesitis	8.3%	10%	0.604
Body surface area affected:			0.615
· <10%	14.6%	13.2%	
· 10-25%	16.9%	3.6%	
· >25%	68.5%	73.2%	
Dactylitis	25.8%	32.3%	0.196
Nail involvement	50.8%	49.1%	0.762
Radiographic sacroiliitis	40.9%	31.8%	0.084
HLA-B27 positive	6.1%	11.5%	0.097
DIP radiographic damage	26.7%	21.8%	0.296

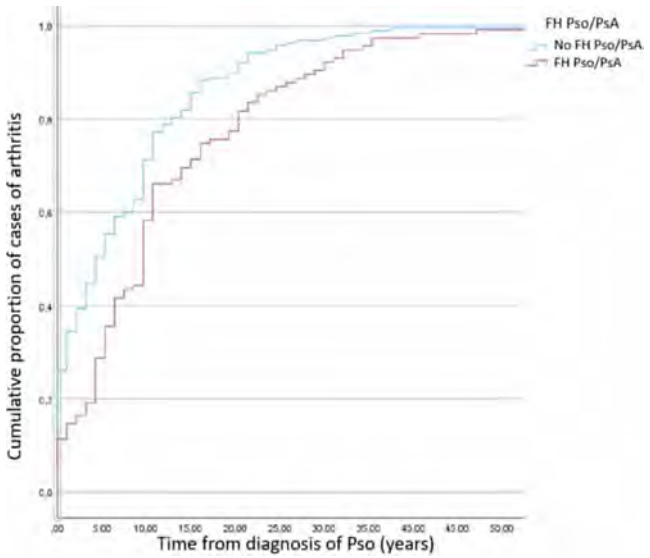


Figure 1. Longer latency to arthritis. Median time: 10 years vs. 4 years (p<0.001)

Disclosure: M. Flores: None; **J. de Luque**: None; **M. Parra**: None; **A. Escudero Contreras**: None; **M. López-Montilla**: None; **C. López Medina**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0543

Unveiling Sacroiliac Joint Involvement in Psoriatic Arthritis: MRI, Radiographic, and Clinical Insights from 581 European Routine Care Patients

Nora Vladimirova[1], Anna EF Hadsbjerg[2], Simon Krabbe[3], Adrian Ciurea[4], Kristýna Bubová[5], Monika Gregova[5], Michael Nissen[6], Burkhard Moeller[7], Raphael Micheroli[4], Susanne Pedersen[8], Jakub Zavada[5], Ziga Snoj[9], Karlo Pintaric[9], Bjorn Gudbjornsson[10], Ziga Rotar[11], iris Eshed[12], Iwona Iwona Sudol-Szopinska[13], Kasper Gosvig[14], Torsten Diekhoff[15], Robert G. W. Lambert[16], Manouk de Hooge[17], Maurice Donzallaz[18], Alexander Bernatschek[18], Merete Hetland[19], Lykke Ørnbjerg[20] and Mikkel Ostergaard[21], [1]Rigshospitalet-Glostrup, Copenhagen, Denmark, [2]Copenhagen Center for Arthritis Research, COPECARE, Glostrup, Denmark, [3]Rigshospitalet, Kobenhavn, Denmark, [4]University Hospital Zurich, Zurich, Switzerland, [5]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine Charles University, Prague, Czech Republic, [6]Rheumatology Department, Geneva University Hospital, Geneva, Switzerland, [7]Department of Rheumatology and Immunology, Inselspital, University Hospital Bern,, Bern, Swaziland, [8]Rigshospitalet, Kobenhavn, Denmark, [9]Institute of Radiology, UMC Ljubljana,, Ljubliana, Slovenia, [10]Landspitali University Hospital; Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [11]University Medical Centre Ljubljana, Ziri, Slovenia, [12]Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer affiliated with School of Medicine, Tel Aviv University, Tel Aviv, Israel, [13]Department of Radiology, National Institute of Geriatrics, Rheumatology and Rehabilitation,, Warsaw, Poland, [14]Department of Radiology, Copenhagen University Hospital Herlev-Gentofte,, Copenhagen, Denmark, [15]Charite Universitetsmedizin Berlin, Berlin, Germany, [16]University of Alberta, Department of Radiology & Diagnostic Imaging, Edmonton, AB, Canada, [17]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [18]Department of Rheumatology, University Hospital of Zurich, University of Zurich,, Zurich, Switzerland, [19]Copenhagen Center for Arthritis Research (COPECARE) and DANBIO, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; Department of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark, [20]Rigshospitalet, Glostrup, Denmark, [21]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial involvement in psoriatic arthritis (axPsA) is associated with more severe disease and greater pain compared to PsA with only peripheral disease. However, a consensus definition of axPsA is lacking, complicating diagnosis and treatment. This study aims to describe the occurrence and characteristics of MRI and radiographic sacroiliac joint (SIJ) involvement in a European cohort of patients with PsA.

Methods: Patients with a clinical diagnosis of PsA (clin-PsA) or axial spondyloarthritis with psoriasis (axSpA+Pso), who had available routine care SIJ MRIs and clinical data, were included from five European registries in the EuroSpA collaboration. SIJ MRIs and radiographs were centrally evaluated by two experienced readers for inflammatory and structural lesions, differential diagnoses, and a global assessment for SpA-indicative findings. Disagreements were adjudicated by a third expert reader. Associations between MRI-detected axPsA (defined as MRI findings indicative of SpA) and clinical characteristics were analysed using logistic regression with multiple imputations for missing data.

Results: Among the 581 included patients (Clin-PsA: n=373; axSpA+Pso: n=208), 47% were male, with a mean age of 45 years (Table 1). At the time of MRI examination, 76% had not received biological treatment.

In 31% of patients, MRI findings were indicative of SpA (MRI-axPsA). Inflammatory SpA-indicative lesions were present in 21% of patients, and structural lesions in 28%, with 76% of affected patients having both lesion types. Common differential

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics P-value <0.05 is considered significant, Chi-squared test or Fisher's test are used for categorical variables, t-test or Wilcoxon rank-sum test for continuous variables. All variables are presented as n (%) unless indicated. For each variable, available data (n) are presented in separate column (n) for all patients and for each subgroup. Pso-AxSpA: Psoriasis and axial spondyloarthritis; clin-PsA: Peripheral psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; HLA-B27: human leucocyte antigen-B27; [1]b: biological, ts: targeted synthetic Disease modifying antirheumatic drug (DMARD) received prior to or at the time of MRI examination; [2]b/tsDMARD initiated such treatment at some point after the MRI examination.

	n	All patients (n= 581)	Clinical diagnosis in the registry				
			n	PsA (n= 373)	n	axSpA+Pso (n=208)	p
Patient characteristics							
Age, mean (SD)	581	45 (13)	373	46 (13)	208	42 (12)	0.01
Sex, male	581	271(47%)	373	162(44%)	208	109(52%)	0.04
Smoking (ever)	500	385(77%)	305	239(78%)	195	146(75%)	0.5
BMI, mean (SD)	442	26.7 (4.9)	286	27.2 (5.2)	156	25.7 (4.2)	0.01
Participating countries	581		373		208		0.01
Switzerland		188(32%)		124(33%)		64(31%)	
Czech Republic		57(10%)		38(10%)		19(9%)	
Denmark		260(45%)		140(38%)		120(58%)	
Iceland		15(3%)		15(4%)		0	
Slovenia		61(11%)		56(15%)		5(2%)	
Axial symptoms							
Inflammatory back pain (ever)	479	263(55%)	299	127(43%)	180	136(76%)	0.01
BASDAI back pain ≥ 4 (current)	262	214(81%)	111	90(81%)	151	124(82%)	0.8
Extraarticular manifestations (ever)							
Skin psoriasis	559	545(98%)	352	341(95%)	207	204(99%)	0.03
Nail psoriasis	399	189(47%)	331	177(54%)	68	12(18%)	0.01
Dactylitis	547	196(36%)	350	160(46%)	197	36(18%)	0.01
Uveitis	527	46(9%)	350	16(5%)	189	30(16%)	0.01
IBD	535	28(5%)	341	16(5%)	194	12(6%)	0.5
Arthritis	556	493(89%)	362	347(96%)	194	146(75%)	0.01
Enthesitis	498	379(76%)	316	226(72%)	182	153(84%)	0.01
HLA-B27 positivity	410	151(37%)	224	57(25%)	186	94(51%)	0.01
Medication (current)							
No previous b/tsDMARD	581	442(76%)	373	270(72%)	208	172(83%)	0.01
b/tsDMARD received later[2]	443	304(70%)	270	67(23%)	208	115(55%)	0.01

diagnoses included osteitis condensans ilii (8%), probable strain-related bone marrow edema (BME) (11%), and degenerative changes (16%). In 35% of patients, SIJ MRIs were normal, showing no SpA-related lesions or alternative diagnoses.

Among patients with MRI-axPsA the SIJ MRI findings were predominantly bilateral, with BME (69%), erosion (68%), and fat lesions (58%) being the most common. BME (≥1 cm), inflammation in an erosion cavity, capsulitis, fat lesions (≥1 cm), backfill, and ankylosis were observed almost exclusively in this group (Figure 1).

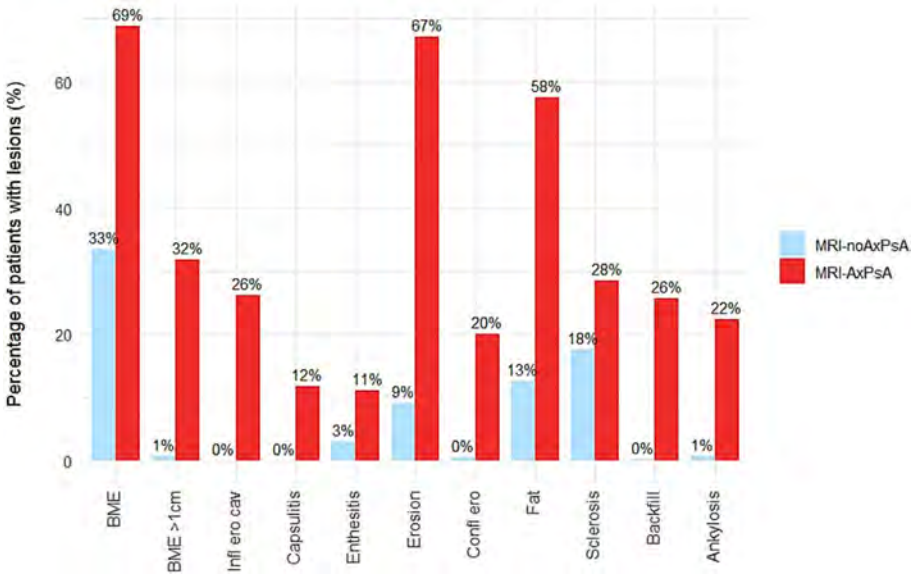


Figure 1. Inflammatory and structural MRI lesions in PsA patients with an MRI indicative of SpA (MRI-AxPsA group) versus not indicative of SpA (MRI-noAxPsA) BME, bone marrow edema; Infl Ero cav, inflammation in an erosion cavity; Confl Ero, confluent erosion; Fat, fat lesion

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Fulfilment of various definitions of axial psoriatic arthritis in all patients and in patients with (MRI-AxPsA) versus without (MRI-noAxPsA) MRI findings indicative of SpA MRI-AxPsA: patients with SIJ MRI findings indicative of SpA at the global SIJ MRI assessment; MRI-noAxPsA: patients without SIJ MRI findings indicative of SpA at the global SIJ MRI assessment. ASAS: Assessment of SpondyloArthritis International Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; mNY criteria: Modified New York criteria for ankylosing spondylitis

Various definitions of axPsA	All patients (n=581)		Central MRI assessment				
			MRI-AxPsA (n=179)		MRI-noAxPsA (n=402)		
	n		n		n		p
1. Clinical definitions (as reported by the registries):							
A. BASDAI Question 2 (back pain ≥ 4)	262	214(82%)	106	83(78%)	156	131(84%)	0.2
B. Inflammatory back pain (by ASAS criteria)	479	263(55%)	145	102(70%)	334	161(48%)	0.01
C. Fulfilment of ASAS classification criteria for axSpA	452	206(46%)	142	108(76%)	310	98(32%)	0.01
2. Radiographic definitions (central reading):							
A. Fulfilment of the radiographic part of mNY criteria	259	74(29%)	95	57(59%)	160	17(11%)	0.01
B At least grade 2 unilateral radiographic sacroiliitis	259	84(32%)	95	58(60%)	160	26(16%)	0.01
3. MRI "global" definition (central reading):							
Overall MRI findings indicative of SpA	581	179(31%)	179	100%	402	0	-
4. MRI definitions of active inflammation (central reading):							
A. ASAS-positive MRI	581	107(18%)	179	104(58%)	402	3(1%)	0.01
B Inflammatory lesions indicative of axSpA	581	121(29%)	179	114(64%)	402	7(2%)	0.01
5. MRI definition of structural lesions (central reading):							
Structural lesions indicative of axSpA	581	165(28%)	179	155(87%)	402	10(2.5%)	0.01

Among 259 patients with available radiographs, 29% met the radiographic component of the modified New York criteria (r-mNYc) for ankylosing spondylitis, while 38% had an MRI indicative of SpA. Radiographic SIJ involvement was predominantly bilateral (91%) in patients meeting the r-mNYc.

Male sex, HLA-B27 positivity, elevated CRP and history of inflammatory back pain, but not current back pain were independently associated with MRI-AxPsA, while peripheral arthritis showed a negative association.

Various clinical, radiographic, and MRI-based definitions of axial PsA were applied and compared (Table 2), using overall MRI findings indicative of SpA as the reference (Table 1, 5. MRI 'global' definition). No clinical or radiographic definition performed similarly to this MRI definition.

Conclusion: In this large European cohort, approximately one-third of routine care PsA patients had an SIJ MRI indicative of SpA. Integrating MRI into future axPsA definitions may facilitate earlier detection, and guide treatment choices in clinical practice.

Disclosure: N. Vladimirova: Merck/MSD, 6, Novartis, 5; **A. Hadsbjerg**: Novartis, 5; **S. Krabbe**: Novartis, 5; **A. Ciurea**: None; **K. Bubová**: None; **M. Gregova**: None; **M. Nissen**: Novartis, AbbVie/Abbott,Amgen, Eli-Lilly, Janssen, Novartis, Pfizer and UCB, 5; **B. Moeller**: None; **R. Micheroli**: None; **S. Pedersen**: AbbVie, UCB, Novartis, AbbVie, MSD,Novartis, and the Danish Research Foundation, 6, Novartis, 5; **J. Zavada**: Abbvie, Akord, Astra Zeneca, Celltrion, Eli-Lilly, Glaxo, Novartis, Pfizer, Sobi, 6; **Z. Snoj**: None; **K. Pintaric**: None; **B. Gudbjornsson**: None; **Z. Rotar**: None; **i. Eshed**: None; **I. Iwona Sudol-Szopinska**: None; **K. Gosvig**: None; **T. Diekhoff**: Canon MS, 5, Canon MS, Lilly, MSD, Novartis, Pfizer, and UCB, 6, UCB, Lilly, 1; **R. Lambert**: AbbVie, 2, CARE Arthritis and Image Analysis Group, 2; **M. de Hooge**: UCB pharma, 2; **M. Donzallaz**: None; **A. Bernatschek**: None; **M. Hetland**: AbbVie/Abbott, 1, 5, Alfasigma, 5, Eli Lilly, 5, Novartis, 6, Pfizer, 5, 6, Sandoz, 5, 6, UCB, 5, 6; **L. Ørnbjerg**: Novartis, UCB, 5; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0544

Prevalence and Baseline Characteristics associated with Difficult-to-Manage Axial Spondyloarthritis in the DESIR Cohort

Olivier Fakih[1], Anna Molto[2], Frank Verhoeven[1], Clément Prati[1] and WENDLING Daniel[1], [1]CHU de Besançon, Besançon, Franche-Comte, France, [2]Assistance Publique Hôpitauxde Paris, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite a choice of multiple targeted DMARDs, with different modes of action (MoA), a number of patients with axial spondyloarthritis (axSpA) have failed several treatments. This seems to correspond to a population with specific characteristics that can be termed Difficult to Manage (D2M). A definition of D2M axial spondyloarthritis (D2M-axSpA) has been proposed by the ASAS. Studies using variable definitions estimated a D2M-axSpA prevalence between 10–30%. However, no large cohort study has been conducted based on the ASAS definition. The objective of this study was to determine the prevalence of and factors associated with D2M-axSpA in the DESIR cohort of early inflammatory back pain.

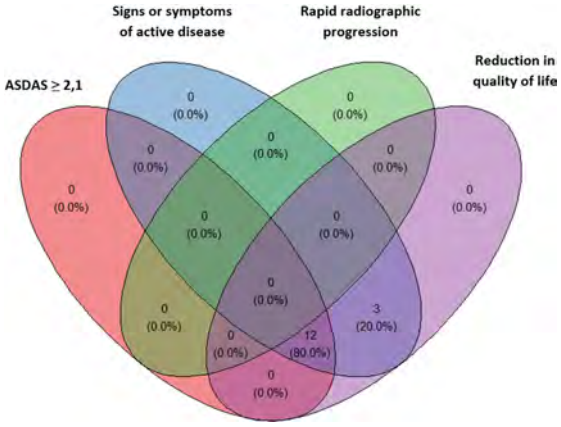
Methods: Patients from the DESIR inception cohort who met the 2009 ASAS criteria for axSpA were included. The baseline characteristics and follow-up data were collected for up to 10 years. Patients were considered to have D2M-axSpA if they failed ≥ 3 bDMARDs and at least one of the sub-criteria making up criterion 2 of the ASAS D2M-axSpA definition (ASDAS ≥ 2.1, signs or symptoms suggestive of active disease, rapid radiographic spinal progression, and reduction in quality of life). This choice reflected limited access to IL-17 inhibitors in this cohort (inclusion in the late 2000s), making it difficult to apply a definition with failure of two different MoA (criterion 1 of the ASAS D2M-axSpA definition). Perception of difficult management (criterion 3) was not assessed. The prevalence of D2M-axSpA was determined, followed by bivariate analysis of the baseline factors associated with the existence of D2M-axSpA. A multivariate analysis using logistic regression was also performed. Quantitative variables were compared using the Mann-Whitney U test and qualitative variables were compared using Fisher's exact test.

Results: A total of 420 patients were included, mean age of 31.5±7.33 years. A total of 221 (52.6%) patients were women and 368 were HLA-B27 positive (87.62%). The mean follow-up duration was 8.9±2.4 years. The mean ASDAS-crp at

Table: Comparison of characteristics between D2M-axSpA and non-D2M-axSpA patients.

Characteristics at baseline	D2M-axSpA (n=15)	Non-D2M-axSpA (n=415)	p-value
Age	33.6±8.0	31.4±7.3	0.27
Disease duration	1.73±0.99	1.58±0.89	0.53
Female sex	**12 (80.0%)**	**187 (46.2%)**	**0.02**
HLA-B27	11 (73.3%)	357 (88.4%)	0.10
Family history of SpA	3 (23.1%)	181 (46.8%)	0.16
Peripheral arthritis	6 (40%)	109 (27%)	0.26
Dactylitis	3 (20%)	51 (12.6%)	0.42
Radiographic sacro-iliitis	6 (40%)	78 (19.7%)	0.09
Radiographic spine involvement	3 (21.4%)	76 (19.9%)	1
ASDAS-crp	**3.7±1.03**	**2.57±0.96**	**<0.001**
BASFI	**55.5±20.3**	**27.8±21.9**	**<0.001**
ASQOL	**14.5±2.1**	**8.7±5.0**	**<0.001**
Inflammatory Bowel Disease	0 (0%)	20 (4.9%)	1
Psoriasis	2 (13.3%)	61 (15.1%)	1
Uveitis	1 (6.7%)	41 (10.1%)	1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Venn diagram of sub-criteria 2 of the D2M-axSpA definition.

inclusion was 2.61±0.98, BASFI was 28.8±22.4, and ASQOL 8.87±5.05. 84 (20%) patients had radiographic sacroiliitis. Fifteen patients (8.4% of bDMARD-treated; 3.6% of all) met the D2M-axSpA definition. D2M-axSpA was associated with female sex and higher ASDAS-CRP, BASFI, and ASQOL at baseline (Table). In a multivariate model adjusted for follow-up duration, only ASQOL at baseline was associated with the occurrence of D2M-axSpA (Odds-ratio 1.28 [1.04-1.63], p=0.03). All included patients met several sub-criteria of the definition, including impairment of the quality of life. None of the patients showed rapid radiographic spinal progression (Figure). A sensitivity analysis showed that seven (1.6%) patients met criteria 1 (failure of ≥ 2 bDMARDs with different MoA) and 2 of the ASAS definition of D2M-axSpA.

Conclusion: The prevalence of D2M-axSpA was low in this cohort of patients with early axSpA, although it was not possible to prescribe a class other than TNF inhibitors during the early years of follow-up. Female sex and high activity, functional, and quality of life scores at baseline were associated with a higher probability of D2M-axSpA, unlike peripheral or extra-musculoskeletal involvement.

Disclosure: O. Fakih: None; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **F. Verhoeven**: None; **C. Prati**: None; **W. Daniel**: None.

Abstract Number: 0545

Temporal trends in the phenotype and treatment outcomes in axial spondyloarthritis patients included in randomized clinical trials over 25 years: a systematic literature review and meta-regression analysis

Omar-Javier Calixto[1], Uta Kiltz[2], Brikena Lalazi[3], Franziska Neinert[3], Philipp Sewerin[4] and Xenofon Baraliakos[2], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Cellular and Molecular Immunology Group (InmuBo), Universidad El Bosque, Herne, Nordrhein-Westfalen, Germany, [2]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [3]Rheumazentrum Ruhrgebiet, Herne, Germany, [4]Rheumazentrum Ruhrgebiet Herne; Ruhr-Universität Bochum, Germany, Herne, Germany

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The phenotypes of axial spondyloarthritis (axSpA) and clinical responses to placebo and study drugs in randomized controlled trials (RCTs) have changed over time. We conducted a systematic literature review and meta-analysis to evaluate changes in phenotypes and outcomes of axSpA patients participating in RCTs over a 20-year period.

Methods: Systematic search of PubMed, EMBASE, and Cochrane Library, following PRISMA guidelines (PROSPERO registration: CRD42024621406), updated to January 2025. Baseline characteristics were summarized as weighted means or proportions and transformed into standardized mean differences or Log odds ratios for meta-analytic comparisons. To assess temporal trends, categories were based on the first year of recruitment rather than the publication year. Meta-regression was conducted across 5-year intervals (P1:1999-2003, P2:2004-2008, P3:2009-2013, P4:2014-2019). Efficacy outcomes (ASAS20 and ASAS40) were assessed using adjusted models, incorporating comparator group, treatment type, age, BASDAI, radiographic axSpA / Ankylosing Spondylitis, and ASAS classification criteria. Sensitivity analyses used the RoB2 tool.

Results: Ninety RCTs (n=20,411 participants) were included. Descriptive analysis showed that weighted mean ages were lowest during P3 (38.3±5.3 years, 95%CI: 38.1-38.5) and P4 (39.2±4.6 years, 95%CI: 39.2-39.3). Longest disease duration was in P1 (11.6±2.6 years, 95%CI: 11.3-11.6). Male proportion was lowest in P3 (69.2%, 95%CI: 67.8-70.6%) and P4 (71.2%, 95%CI: 70.4-72.0%), and highest HLA-B27 positivity in P4 (79.1%, 95%CI: 78.3-79.8%).

Meta-regression showed a significant progressive decrease in male participants (p=0.028, I^2=50.2%), A trend towards younger patients was found in recent years, with a significant age decrease in P3 compared with earlier periods (p=0.039). Although meta-analysis revealed a temporal decrease in PtGA scores and an increase in spinal inflammation, no significant temporal trends were detected in meta-regression.

Adjusted meta-regressions demonstrated significant efficacy for treatment versus comparator as expected. For ASAS20, efficacy decreased in more recent periods (P3-P4), while no such temporal decrease was observed for ASAS40 (Figure 1A-B). In both adjusted models, bDMARD use as a comparator led to a lower efficacy than placebo as comparator (p< 0.001). Additionally, Higher male proportion was associated with greater efficacy (p< 0.010 in both response criteria).

Conclusion: We report temporal changes in axSpA phenotypes in RCTs over a 20-year period. Progressive reduction in male suggests increased inclusion of women, likely reflecting greater nr-axSpA representation in recent studies. Additionally, a trend toward younger patients was observed, although disease duration remained stable.

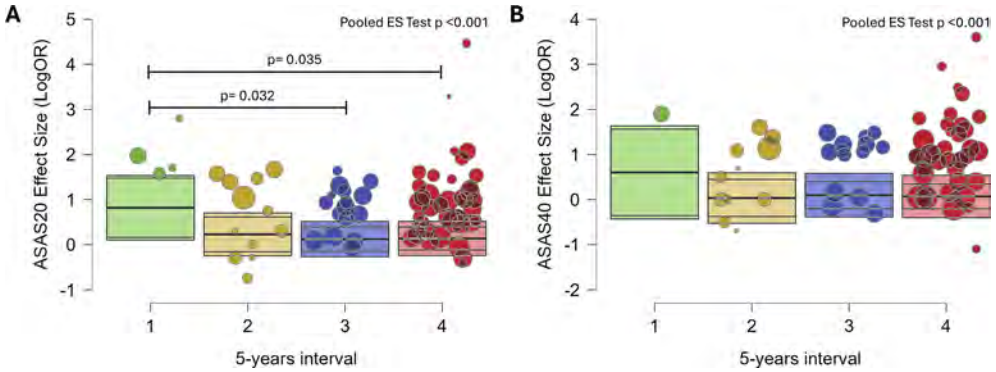


Figure 1. Temporal trends in treatment effect size for ASAS20 and ASAS40 responses across 5-year intervals. (A) Multivariable-adjusted meta-regression of ASAS20 effect sizes (log odds ratios: LogOR) stratified by 5-year recruitment intervals (P1: 1999–2003; P2: 2004–2008; P3: 2009–2013; P4: 2014–2019). (B) Multivariable-adjusted meta-regression of ASAS40 effect sizes across the same intervals. Each circle represents an individual study, with circle size proportional to study weight in the meta-regression. Boxplots indicate median, interquartile range, and variability of effect sizes within each interval. A significant decline in ASAS20 effect size was observed across periods (p for trend 0.032 and 0.035 for P3 and P4, respectively), whereas ASAS40 effect sizes remained stable over time (p≥0.05).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Despite decreased ASAS20 responses, treatment efficacy remained consistent when assessed by the stricter ASAS40 criteria, particularly after adjusting for key covariates. These findings reflect dynamic changes in recruitment patterns and diagnostic timing, with implications for cross-trial comparability and therapeutic evaluations.

Disclosure: O. Calixto: None; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **B. Lalazi**: None; **F. Neinert**: None; **P. Sewerin**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Axiom Health, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Chugai, 2, 5, Deutscher Psoriasis-Bund, 2, 5, Eli Lilly, 2, 5, Gilead, 2, 5, Hexal, 2, 5, Janssen, 2, 5, Johnson & Johnson, 2, 5, Medical Communication, 2, Medici GmbH, 2, 5, medi-login, 2, 5, Novartis, 2, 5, Onkowissen GmbH, 2, 6, Pfizer, 2, 5, Roche, 2, 5, Sanofi-Genzyme, 2, 5, Swedish Orphan Biovitrum, 2; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor.

Abstract Number: 0546

Multimorbidity clusters in psoriatic arthritis, psoriasis, and axial spondyloarthritis and their association with healthcare utilization: A population-based study

Paras Karmacharya[1], Dilli Poudel[2], Daniel Shin[3], Robert Fitzsimmons[3], Leslie Crofford[4] and Alexis Ogdie[5], [1]Vanderbilt University, Nashville, TN, Hermitage, TN, [2]Vanderbilt University Medical Center, Nashville, TN, [3]University of Pennsylvania, Philadelphia, [4]Vanderbilt University Medical Center, Melbourne, AR, [5]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Multimorbidity (≥ 2 chronic conditions) is common in inflammatory diseases such as psoriatic arthritis (PsA), psoriasis (PsO), and axial spondyloarthritis (AxSpA), increasing patient burden and healthcare costs. Understanding specific comorbidity clusters beyond simple counts is crucial for insights into disease heterogeneity and impact. The objective of this study was to identify and compare multimorbidity clusters in PsA, PsO, and AxSpA from a large population database, assess their stability, compare them with matched controls, and examine associations with healthcare utilization (HCU).

Methods: This population-based, retrospective cohort study from the UK THIN database included incident adult PsA (N=5,096), PsO (N=73,751), and AxSpA (N=2,413) patients (identified using validated Read Codes) with ≥1 year follow-up, alongside 1:5 matched controls. Morbidities chosen based on clinical relevance and prior reports were identified using Read codes. Optimal number of clusters was determined by evaluating the balance between within-cluster and between-cluster variance reduction for each level of the hierarchical clustering tree (tree method). K-median clustering identified

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

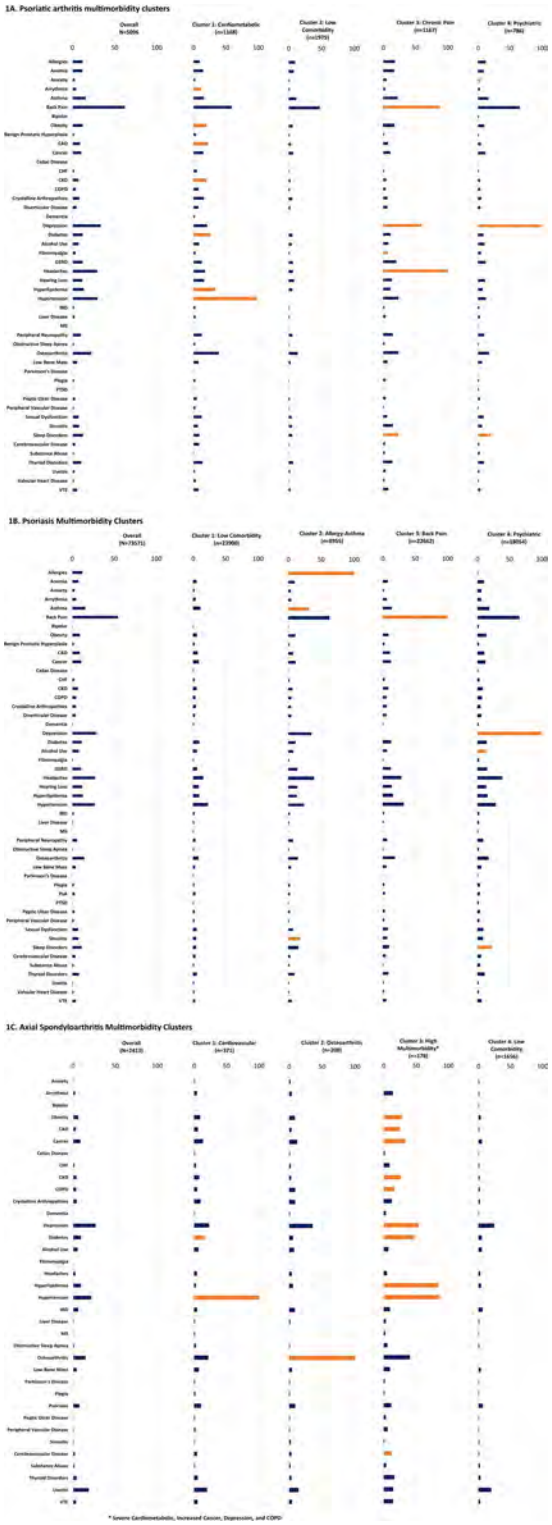


Figure 1. Prevalence of morbidities overall and in the four distinct multimorbidity clusters at 5 years following the diagnosis of A) Psoriatic Arthritis, B) Psoriasis, and c) Axial Spondyloarthritis (in their respective cohorts). Orange bars denote comorbidities considered 'cluster-defining,' indicating they have both high prevalence (>10%) within that specific cluster and a high prevalence ratio (>1.5) compared to the overall cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Healthcare utilization associated with multimorbidity clusters and substantial multimorbidity (MM5+) at 5 years following diagnosis of psoriatic arthritis, psoriasis, and axial spondyloarthritis in their respective cohorts. IRR: Incidence Rate Ratio (All IRRs are adjusted for age and sex and are presented relative to the 'Low-Comorbidity' cluster within each respective disease cohort); CI: Confidence Interval (all shown are 95% CI); IQR: Interquartile Range; MM5+: Substantial multimorbidity defined as patients with five or more morbidities; NA: Not Applicable * 'High Multimorbidity' cluster in AxSpA is characterized by severe cardiometabolic conditions, and increased cancer, depression, and COPD.

Disease Cohort and Multimorbidity Clusters (N)	Median no. of Morbidities (IQR)	Outpatient Visits IRR (95% CI)	Hospital Admissions IRR (95% CI)	Total Prescriptions IRR (95% CI)
Psoriatic Arthritis (5,096)				
Cardiometabolic (1168)	6 (4–8)	1.54 (1.45–1.64)	1.86 (1.55–2.22)	2.32 (2.14–2.52)
Chronic Pain (1167)	7 (6–9)	1.63 (1.55–1.73)	2.27 (1.91–2.69)	2.08 (1.93–2.24)
Psychiatric (786)	6 (5–7)	1.41 (1.33–1.51)	1.68 (1.38–2.04)	1.89 (1.73–2.05)
MM5+ (3197)	NA	1.74 (1.67–1.82)	2.37 (2.07–2.72)	2.35 (2.21–2.50)
Psoriasis (73,751)				
Allergy-Asthma (8955)	6 (4–8)	1.67 (1.64–1.71)	1.65 (1.55–1.76)	1.89 (1.83–1.95)
Back pain (22662)	4 (3–7)	1.38 (1.36–1.41)	1.52 (1.44–1.59)	1.33 (1.30–1.36)
Psychiatric (18054)	6 (4–8)	1.86 (1.82–1.89)	2.11 (2.01–2.22)	2.28 (2.22–2.33)
MM5+ (33126)	NA	2.21 (2.18–2.24)	2.56 (2.45–2.66)	3.15 (3.09–3.21)
Axial Spondyloarthritis (2,413)				
Cardiovascular (371)	3 (2–4)	1.42 (1.25–1.61)	1.50 (1.13–1.98)	2.02 (1.74–2.36)
Osteoarthritis (208)	2 (2–3)	1.50 (1.29–1.76)	0.97 (0.67–1.40)	1.38 (1.14–1.66)
High Multimorbidity* (178)	6 (4–7)	2.44 (2.07–2.89)	2.70 (1.88–3.89)	3.15 (2.56–3.88)
MM5+ (215)	NA	2.16 (1.86–2.50)	2.14 (1.55–2.95)	2.49 (2.07–3.00)

multimorbidity clusters at 1 and 5 years post-diagnosis. Cluster stability and comparisons with control groups were assessed. Age- and sex-adjusted negative binomial regression were performed to examine the association of year 5 clusters to HCU (outpatient visits, hospitalizations, total prescriptions).

Results: Distinct and stable multimorbidity clusters were identified in each disease cohort at years 1 and 5 (Figure 1). PsA (N=5,096) clusters included Cardiometabolic, Low-Comorbidity, Chronic Pain, and Psychiatric. The Chronic Pain cluster was unique to PsA cases versus controls. PsO (N=73,751) clusters were Low Comorbidity, Allergy-Asthma, Back Pain, and Psychiatric. The Allergy-Asthma cluster was specific to PsO cases. AxSpA (N=2,413) clusters included Cardiovascular, Osteoarthritis, High Multimorbidity (characterized by severe cardiometabolic conditions, cancer, depression, COPD), and Low Comorbidity. Osteoarthritis cluster was unique to AxSpA cases. All identified multimorbidity clusters, as well as substantial multimorbidity (MM5+; ≥5 conditions), were associated with significantly higher HCU compared to respective Low-Comorbidity reference groups (Table 1).

Conclusion: Our study reveals that PsA, PsO, and AxSpA are characterized by distinct, stable multimorbidity clusters, featuring both shared background patterns (e.g., Low-Comorbidity, Psychiatric, Cardiometabolic components) and disease-specific architectures (e.g., PsA-Chronic Pain, PsO-Allergy-Asthma, AxSpA-Osteoarthritis). In terms of healthcare utilization, the findings indicate that the total number of concurrent chronic conditions is a more significant driver than the specific type of multimorbidity cluster. Consequently, while distinct clinical phenotypes are evident, addressing the overall burden of high morbidity (such as in patients with MM5+) is crucial for mitigating excessive healthcare utilization and guiding the development of effective management strategies in these populations.

Disclosure: P. Karmacharya: None; **D. Poudel**: None; **D. Shin**: None; **R. Fitzsimmons**: None; **L. Crofford**: Argenyx, 5, Evergreen, 5, Kezar, 1, Otsaka, 1, UCB, 1; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0547

Determinants of Difficult-to-Manage Axial Spondyloarthritis: Results from a Prospective Cohort Study

Patricia Remalante-Rayco[1], Laura Passalent[2], Manal Alnasser[3], Tina Chim[1], Robert Inman[1], Nigil Haroon[4] and Denis Poddubnyy[5], [1]University Health Network, Toronto, ON, Canada, [2]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [3]King Abdulaziz Medical City, Riyadh, Saudi Arabia, [4]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada, [5]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The Assessment of SpondyloArthritis international Society (ASAS) group has recently introduced a consensus-based definition for difficult-to-manage (D2M) axial spondyloarthritis (axSpA) to identify patients with active disease despite being treated according to the current standard. This comprehensive definition incorporates not only the number of therapeutic failures but also uncontrolled disease features and the perspectives of both rheumatologists and patients on disease control. However, the real-world frequency of the problem remains unexplored, and little is known about the clinical profiles and factors associated with D2M axSpA. In this study, we aimed to determine the frequency of D2M axSpA and to identify factors associated with D2M disease in a longitudinal clinical cohort.

Methods: This retrospective analysis of a prospective cohort study included patients with a rheumatologist's diagnosis of axSpA presenting within one year of follow-up (from October 1, 2023 to September 30, 2024) at the Toronto Western Hospital Spondylitis Clinic who received at least 6 months of advanced therapy with a biological and/or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD). Variables were collected at the last follow-up visit. Since MRI was not routinely performed as part of the standard of care, data were unavailable and, therefore, excluded from the definition of "treatment-refractory" disease in this cohort. Sociodemographic and clinical profiles of patients meeting D2M criteria according to the ASAS definition were compared to non-D2M axSpA patients using bivariate analyses. Multivariate logistic regression was used to identify factors associated with D2M.

Results: Among 465 axSpA patients fulfilling the entry criteria, a total of 47 (10.1%) fulfilled all three ASAS D2M criteria. Within the D2M group, 14 (29.8%) had "treatment-refractory" disease, defined as non-response to treatment after excluding fibromyalgia and accounting for elevated CRP levels. Compared to non-D2M, D2M patients had significantly longer symptom duration, higher ASDAS, BASDAI, BASMI, and BASFI, as well as elevated CRP (in approximately 50% of the cases) (Table 1). At the same time, patients in the D2M group were less likely to be employed and had more comorbidities, higher body mass index, as well as a greater prevalence of mechanical back pain and fibromyalgia (Table 1). Logistic regression identified higher BASMI (OR 1.35, 95% CI 1.10 to 1.65, p = 0.004) and fibromyalgia (OR 3.03, 95% CI to 1.01 to 9.05, p = 0.048) as factors significantly associated with meeting D2M criteria (Figure 1).

Conclusion: The results of this study suggest that approximately 10% of patients with axSpA receiving advanced treatment have D2M disease. Half of these patients exhibit objective signs of inflammatory activity, potentially indicating the presence of treatment-refractory disease. In contrast, non-axSpA-related factors (including fibromyalgia, other comorbidities, mechanical issues in the back, and socioeconomic factors) may contribute to the D2M situation in other cases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Bivariate comparison of D2M and non-D2M axSpA patients

Variable	D2M N=47	Non-D2M N=418	p-value
axSpA classification			0.7674
r-axSpA	41 (87.2%)	358 (85.7%)	
nr-axSpA	6 (12.8%)	60 (14.4%)	
Sex (male)			0.5905
male	27 (57.5%)	257 (61.5%)	
female	20 (42.6%)	161 (38.5%)	
Symptom duration, years (mean (SD))	26.0 (10.7)	25.1 (11.8)	**<0.001**
Duration since diagnosis, years (mean (SD))	17.1 (7.7)	18.1 (10.8)	**<0.001**
HLA-B27 present	32 (68.1%)	311 (74.4%)	0.3507
Elevated CRP (≥5 mg/L)	16 (50.0%)	67 (20.9%)	**0.0002**
Extra-musculoskeletal manifestation (any in the last year)	24 (51.1%)	219 (56.3%)	0.4950
Uveitis	9 (19.2%)	135 (34.4%)	**0.0349**
Psoriasis	13 (27.7%)	82 (20.3%)	0.2414
IBD	8 (17.0%)	60 (15.3%)	0.7700
Presence of peripheral manifestations (any)	4 (9.8%)	42 (10.6%)	0.8619
Arthritis	3 (7.1%)	25 (7.3%) 26 (6.5%)	0.8728
Dactylitis	0	1 (0.3%)	0.7411
Enthesitis	1 (2.3%)	15 (4.3%)	0.6343
Comorbidities (≥1) (mean (SD))	1.9 (2.1)	1.2 (1.6)	**<0.0001**
Presence of fibromyalgia	8 (17.0%)	19 (5.1%)	**0.0016**
Mechanical back pain	21 (52.5%)	109 (28.9%)	**0.0022**
Use of NSAIDs	29 (61.7%)	206 (49.3%)	0.1064
Use of csDMARDs	14 (29.8%)	38 (9.1%)	**<0.0001**
Use of systemic corticosteroids	2 (4.3%)	3 (0.7%)	**0.0258**
Use of analgesic (opioid)	5 (15.6%)	26 (9.3%)	0.2529
Use of analgesic (non-opioid)	6 (19.4%)	22 (8.0%)	**0.0368**
ASDAS-CRP (mean, (SD))	3.3 (0.9)	1.9 (1.0)	**<0.0001**
BASDAI (mean, (SD))	6.0 (1.5)	3.4 (2.2)	**<0.0001**
BASFI (mean, (SD))	6.0 (2.0)	2.7 (2.4)	**<0.0001**
BASMI (mean, (SD))	3.7 (1.8)	2.7 (1.5)	**<0.0001**
Current/past smoker	18 (40.9%)	163 (38.9%)	0.7952
Current alcohol consumption (any)	18 (47.4%)	233 (61.2%)	0.0982
BMI (mean, (SD))	29.0 (5.5)	28.3 (5.6)	**<0.0001**
Employment status (unemployed)	26 (55.3%)	140 (33.6%)	**0.0032**
Education status (post secondary or higher)	37 (78.7%)	337 (81.6%)	0.6320
Marital status (married or common-law)	25 (54.4%)	253 (61.0%)	0.3842

axSpA, axial spondyloarthritis; r-axSpA, radiographic axSpA; nr, non-radiographic axSpA; CRP, C reactive protein; IBD, inflammatory bowel disease; NSAID, nonsteroidal anti-inflammatory drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BMI, Body Mass Index.

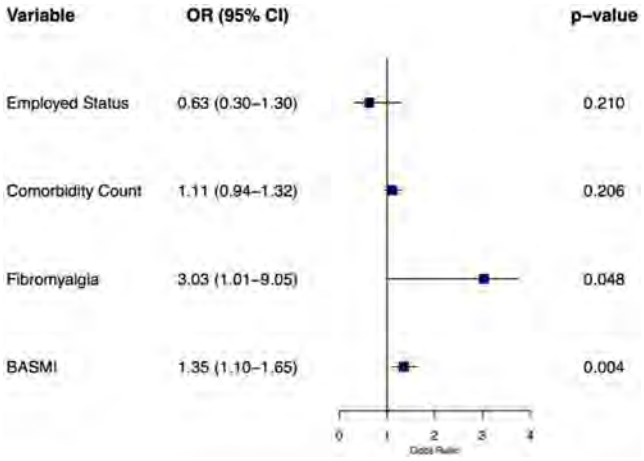


Figure 1. Factors associated with D2M in axSpA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Remalante-Rayco: None; **L. Passalent**: AbbVie/Abbott, 6, Novartis, 6, UCB, 2, 5; **M. Alnasser**: None; **T. Chim**: None; **R. Inman**: AbbVie/Abbott, 2, Janssen, 2, Novartis, 2, 5, UCB, 2, 5; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6.

Abstract Number: 0548

Artificial Intelligence in Axial Spondyloarthritis Diagnosis: Integrating Structural and Inflammatory Lesionsfrom Sacrum MRI

Seonyoung Kang[1], Yunseo Kim[2], Seulkee Lee[3], Myung Jin Chung[4], Hyungjin Kim[5], Jaejoon Lee[4], Hakje Yoo[6] and Hoon-Suk Cha[4], [1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Gangnam-gu, Seoul, Republic of Korea, [2]Samsung Medical Center, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea, [3]Samsung Medical Center, Sunkyunkwan University School of Medicine, Seoul, South Korea, [4]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [6]Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The Assessment of SpondyloArthritis International Society (ASAS) criteria define positive MRI findings based on the presence of bone marrow edema (BME) in the sacroiliac joints. However, BME may lead to false positives in situations such as post-exercise or postpartum and false negatives in chronic axial spondyloarthritis (axSpA) cases. Criteria for categorizing chronic changes as indicative of axSpA remain unclear. While artificial intelligence (AI) has shown promising performance in medical imaging diagnostics, previous studies on axSpA have mainly focused on detecting specific imaging features, particularly BME, rather than predicting clinical diagnoses. This study aims to propose a deep learning model that integrates inflammatory and structural changes in sacrum MRI to address the gap between BME detection and clinical diagnosis of axSpA.

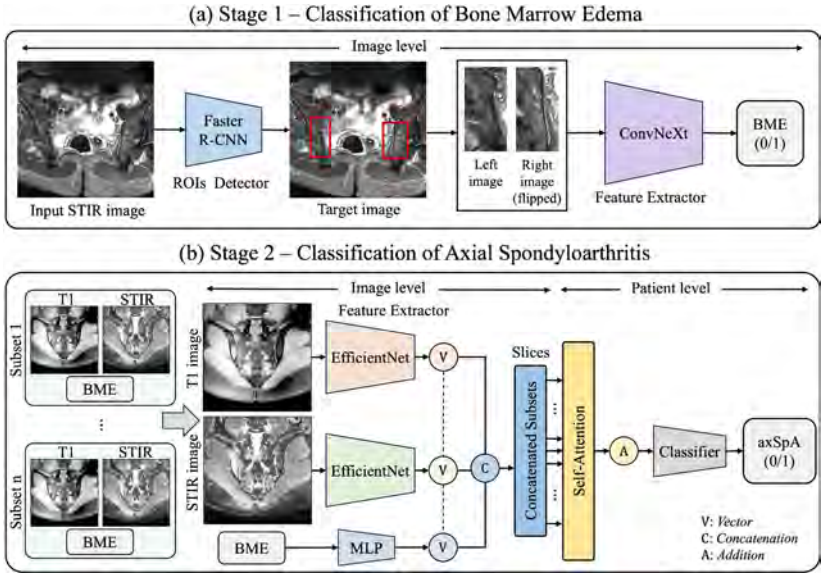


Figure 1. Overview of the proposed model.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Result of the BME classification and axSpA classification

	BME Classification	AxSpA Classification
Accuracy	0.8175 (233/285)	0.8596 (49/57)
Sensitivity	0.8162 (151/185)	0.8750 (28/32)
Specificity	0.8200 (82/100)	0.8400 (21/25)
AUROC	0.8181	0.9412

Methods: Data were collected from patients with chronic back pain who underwent sacrum MRI at Samsung Medical Center from January 2010 to December 2021. Clinical diagnosis of axSpA was defined based on ASAS criteria for axSpA. BME was identified using the ASAS definition. An end-to-end deep learning framework (Figure 1) was developed, utilizing short tau inversion recovery (STIR) and T1-weighted MRI sequences to reflect inflammatory and structural changes, respectively.

In Stage 1 (Figure 1a), Faster R-CNN detected regions of interest (ROIs) in the sacroiliac joints, and ConvNeXt identified BME within these ROIs. In Stage 2 (Figure 1b), features from STIR and T1-weighted MRI were extracted using an EfficientNet-based network to capture inflammatory and structural changes. Simultaneously, BME data were processed using a multilayer perceptron (MLP). These features were integrated to classify axSpA, combining slice-level information for final diagnosis. Model performance was evaluated using accuracy, sensitivity, specificity, and the area under the receiver operating characteristic curve (AUROC) metrics.

Results: MRI data from 291 patients, with an average of 14 slices per patient (total: 4,086 slices), were analyzed. Among the participants, 163 were clinically diagnosed with axSpA, while 128 had nonspecific back pain. The BME detection model achieved a sensitivity of 81.62%, specificity of82.00%, AUROC of 0.82, and accuracy of 81.75% (Table 1a). The axSpA classification model demonstrated a sensitivity of 87.5%, specificity of 84.0%, AUROC of 0.94, and accuracy of 85.96% (Table 1b). Notably, the model identified 6 out of 9 axSpA patients who met clinical criteria but not ASAS-defined positive MRI criteria, indicating its ability to detect features beyond conventional criteria.

Conclusion: This study demonstrated that integrating STIR and T1-weighted MRI with BME data effectively reflects both inflammatory and structural changes, enabling the AI model to predict clinical diagnoses of axSpA. Additionally, the proposed model successfully identified axSpA patients who did not meet the ASAS criteria for positive MRI. These findings highlight the potential of AI not only to detect specific imaging features but also to predict clinical diagnoses, suggesting promising applications in real-world clinical practice.

Disclosure: S. Kang: None; **Y. Kim**: None; **S. Lee**: None; **M. Chung**: None; **H. Kim**: None; **J. Lee**: None; **H. Yoo**: None; **H. Cha**: None.

Abstract Number: 0549

High Prevalence of Obstructive Sleep Apnea in Psoriatic Arthritis: A Polysomnography-Based Cross-Sectional Study

Suzan Attar[1], Siraj Walli[2], Yasser Bawazir[3], Mohammad Mustafa[4], Ayah Boudal[5], Faris alhejailli[2], Ahmad Bamagoos[2] and Omar Kanbr[2], [1]King Abdulaziz University, Saudi Arabia, Jeddah, Saudi Arabia, [2]KAU, Jeddah, Saudi Arabia, [3]King Abdulaziz University, Jeddah, Saudi Arabia, [4]Jeddah University, Jeddah, Saudi Arabia, [5]King Abdullah Medical Complex, Jeddah, Saudi Arabia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Background: Obstructive sleep apnea (OSA) is increasingly recognized in patients with psoriatic arthritis (PsA), yet few studies have used polysomnography (PSG)—the gold-standard diagnostic method. This study bridges this gap by employing PSG to definitively characterize OSA prevalence and its relationship with PsA disease activity.

Objective: To determine OSA prevalence in PsA using PSG and evaluate associations with disease activity.

Methods: This two-stage cross-sectional study included adult PsA patients.

Stage 1: Participants were screened using the STOP-BANG questionnaire for OSA risk and the Epworth Sleepiness Scale (ESS) for daytime sleepiness. Disease activity was assessed using DAPSA and DAS28-CRP, and functional status by HAQ.

Stage 2: All patients at high risk and a random 50% sample of low/intermediate-risk patients underwent overnight PSG. OSA was defined by apnea–hypopnea index (AHI) ≥5 events/hour and categorized as mild (5–14), moderate (15–29), or severe (≥

Comparison of participants with OSA to those without.

PSG variable (units)	Total (n=42)	No OSA (n=21)	OSA (n=21)	P
Female gender (%n)	71%	81%	61%	0.17
Age (years)	47 ±14	38.2 ±10.8	55.8 ±9.8	**<0.01**
BMI (kg/m^2)	30 ±5	27.8 ±6	31.5 ±3.7	**0.02**
DAPSA (score)	18 ±12	15.7 ±8.8	20.8 ±12.4	0.3
DAPSA classification (%OSA groups)				1.0
Remission to low disease	18 (43%)	9 (43%)	9 (43%)	
Moderate to high disease	24 (57%)	12 (57%)	12 (57%)	
DAS (score)	2.7 ±1.0	2.5 ±0.8	3 ±1	0.1
DAS classification (%OSA groups)				0.3
Remission to low disease	29 (69%)	16 (76%)	13 (62%)	
Moderate to high disease	13 (31%)	5 (24%)	8 (38%)	
HAQ (score)	0.7 ±0.8	0.5 ±0.7	0.8 ±0.9	0.2
HAQ classification (%OSA groups)				0.5
Remission	30 (71%)	16 (76%)	14 (67%)	
Moderate to high	12 (29%)	5 (24%)	7 (33%)	
STOPBANG (score)	3 ±2	2.2 ±1.3	4.4 ±1.5	**<0.01**
Risk of OSA development				**<0.01**
Low (%OSA groups)	14 (33%)	13 (61%)	1 (5%)	
Intermediate (%OSA groups)	15 (36%)	6 (29%)	9 (43%)	
High (%OSA groups)	13 (31%)	2 (10%)	11 (52%)	
Snoring Symptom	30 (71%)	10 (48%)	20 (95%)	**<0.01**
Tiredness Symptom	33 (79%)	15 (71%)	18 (86%)	0.3
Witnessed apnea symptom	11 (26%)	4 (19%)	7 (33%)	0.3
Any OSA symptom	37 (88%)	16 (76%)	21 (100%)	**0.017**
Any comorbidity	19 (45%)	10 (48%)	9 (43%)	0.7
ESS (score)	7 ±5	5.6 ±4.6	7.4 ±5	0.2
EDS risk				0.3
EDS low risk (%OSA groups)	33 (79%)	18 (86%)	15 (71%)	
EDS high risk (%OSA groups)	9 (21%)	3 (14%)	6 (29%)	
AHI (events/h)	13 ±15	2.5 ±1.8	23.3 ±14.4	**<0.01**
AHI REM (events/h)	25 ±26	6.4 ±7.7	43 ±25.9	**<0.01**
AHI Supine (events/h)	16 ±19	3.7 ±2.7	28.7 ±19.6	**<0.01**
Desaturation time (minutes)	35 ±38	9 ±7.2	62.5 ±38.9	**<0.01**
ODI (events/h)	10 ±9	2.8 ±2.5	16.8 ±8.6	**<0.01**

PSG: Polysomnography, OSA: Obstructive Sleep Apnea, BMI: Body Mass Index, DAPSA: Disease Activity in Psoriatic Arthritis; (Remission ≤ 4, Low Disease Activity > 4 and ≤ 14, Moderate Disease Activity > 14 and ≤ 28, High Disease Activity > 28), DAS: Disease Activity Score; (Remission < 2.6, Low Disease Activity ≥ 2.6 and < 3.2, Moderate Disease Activity ≥ 3.2 and ≤ 5.1, High Disease Activity > 5.1), HAQ: Health Assessment Questionnaire; (Mild Disability 0–1, Moderate Disability > 1–2, Severe Disability > 2–3), STOP-BANG: (Snoring, Tiredness, Observed Apnea, Blood Pressure, BMI, Age, Neck circumference, Gender); (Low Risk of OSA: 0–2, Intermediate Risk of OSA: 3–4, High Risk of OSA: ≥ 5), ESS: Epworth Sleepiness Scale; (Low Risk of EDS: <10, High Risk of EDS ≥ 10), EDS: Excessive Daytime Sleepiness, TST: Total Sleep Time, REM: Rapid Eye Movement, SE: Sleep Efficiency, AHI: Apnea-Hypopnea Index, MinO2: Minimum Oxygen Saturation, T90: Time Spent Below 90% Oxygen Saturation, ODI: Oxygen Desaturation Index.
Statistical analyses performed were independent t-test for continuous variables and chi-square test for categorical variable. P-value < 0.05 indicates statistical significance.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Sixty-eight patients (69% female, mean age 46 years, mean BMI 29 kg/m^2) were enrolled. Sleep-related symptoms were reported by 77% (snoring 53%, morning fatigue 68%). Mean disease activity scores: DAPSA 20±14, DAS28-CRP 2.8 ±1.0, HAQ 0.6±0.8. Based on STOP-BANG, 19% were high-risk, 35% intermediate, and 46% low-risk. PSG was performed in 42 patients (all high-risk and selected low/intermediate-risk). OSA was confirmed in 50%: 14% mild, 19% moderate, 17% severe. The estimated prevalence of moderate-to-severe OSA in the full cohort was 36%. Higher STOP-BANG scores (OR 2.35, p = 0.016) and older age (OR 1.13 per year, p = 0.007) were significant predictors of OSA. No significant correlation was found between OSA and PsA disease activity or comorbidities.

Conclusion: OSA is highly prevalent among PsA patients, with 50% testing positive by PSG. Despite this burden, OSA showed no association with disease activity. Routine screening and early sleep specialist referral for at-risk PsA patients may improve recognition and management. Further longitudinal, multicenter studies are needed to explore the role of psoriasis severity and treatment effects on OSA risk.

Disclosure: S. Attar: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 5, 6, Gilead, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Hikma, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Organon, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Sandoz, 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6; **S. Walli**: None; **Y. Bawazir**: None; **M. Mustafa**: None; **A. Boudal**: None; **F. alhejailli**: None; **A. Bamagoos**: None; **O. Kanbr**: None.

Abstract Number: 0550

Clinical and Genetic Factors Associated with Anti-TNF Therapy Initiation in Radiographic Axial Spondyloarthritis: A 15-Year Observational Study

Tae-jong Kim[1], Bora Nam[2], So-Young Bang[3], Youngho Park[4], Ji Hui Shin[5], Sungsin Jo[6] and Tae-Hwan Kim[7], [1]Department of Rheumatology, Chonnam National University Medical School and Hospital, Gwang-Ju, South Korea, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, South Korea, [3]Hanyang University, Seoul, Republic of Korea, [4]Department of Big Data Application College of Smart Convergence, Hannam University, Daejeon, Republic of Korea, [5]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [6]Department of Biology, Soonchunhyang University, Asan,, Republic of Korea, [7]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To identify clinical and genetic factors associated with the initiation of anti-TNF (tumor necrosis factor) therapy in patients with radiographic axial spondyloarthritis (r-axSpA) who respond poorly to NSAIDs (non-steroidal anti-inflammatory drugs).

Methods: A total of 445 Korean r-axSpA patients were enrolled and analyzed through genome-wide association studies (Table 1). The observation period started at the initial visit and continued until the initiation of anti-TNF therapy or the last follow-up, spanning 15 years. Multiple linear regression was utilized to identify clinical and genetic predictors of initiating anti-TNF therapy. Pathway analysis was also conducted.

Results: During 3658.8 person-years of observation, 277 patients initiated anti-TNF therapy. Clinical factors significantly associated with the initiation of anti-TNF therapy included younger age at symptom onset (β = -0.008, p = 3.91×10^{-5}), presence of peripheral arthritis (β = 0.181, p = 1.39×10^{-7}), and higher all-time averaged CRP levels (β = 0.022, p = 0.009). Additionally, several functional SNPs were nominally associated with anti-TNF therapy initiation. These included a synonymous

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1.

Table 1. Baseline Characteristics of Patients Initiating Anti-TNF Therapy Versus Those Not Initiating Anti-TNF Therapy in Radiographic Axial Spondyloarthritis

Variables	All patients (n=445)	Patients Initiating TNF blocker Therapy (n=277)	Patients Not Initiating TNF blocker Therapy (n=168)	p-value
Male sex, n (%)	401 (90.1)	249 (89.9)	152 (90.5)	0.841
Symptom onset age, years	20.8 (16.5-27.1)	20.4 (15.7-25.9)	21.8 (17.2-27.9)	0.036
Age at diagnosis, years	27.0 (21.6-33.6)	26.0 (21.0-32.5)	28.3 (22.0-34.9)	0.027
Age at enrollment, years	28.8 (23.2-35.4)	28.0 (23.1-34.8)	29.4 (23.3-35.8)	0.148
Symptom duration, years	6.2 (2.4-10.8)	6.8 (2.3-10.8)	6.0 (2.4-10.9)	0.880
HLAB27 positivity, n (%)	428 (96.2)	269 (97.1)	159 (94.6)	0.188
Observation period, years	8.5 (2.1-12.4)	3.9 (0.5-8.1)	12.4 (11.0-14.8)	<.0001
Family history, n (%)	38 (8.5)	27 (9.7)	11 (6.5)	0.242
Psoriasis, n (%)	15 (3.4)	13 (4.7)	2 (1.2)	0.047
IBD, n (%)	4 (0.9)	1 (0.4)	3 (1.8)	0.153
Uveitis, n (%)	186 (41.8)	123 (44.4)	63 (37.5)	0.152
Peripheral arthritis, n (%)	201 (45.2)	152 (54.9)	49 (29.2)	<.0001
Baseline CRP, mg/dL	1.7 (0.8-3.3)	2.0 (0.8-4.0)	1.1 (0.8-2.2)	<.0001
All-time averaged CRP, mg/dL	1.6 (1.0-2.8)	2.2 (1.3-3.9)	1.1 (0.9-1.5)	<.0001

Table 2.

Table 2. SNPs Associated with Anti-TNF Therapy Initiation in Radiographic Axial Spondyloarthritis

SNP	Chr	position	Beta	Gene	Function	P-value
rs117950953	1	227946825	-4.126	SNAP47	synonymous	3.69×10^{-05}
rs184281973	2	45817245	4.084	SRBD1	intronic	4.42×10^{-05}
rs17166749	5	132866184	-4.042	FSTL4	intronic	5.31×10^{-05}
rs116967760	15	80768641	4.009	ARNT2	intronic	6.11×10^{-05}
rs138455065	9	73615652	3.970	TRPM3	intronic	7.18×10^{-05}
rs141993859	5	160859293	-3.960	GABRB2	intronic	7.50×10^{-05}
rs17298221	8	59844129	-3.942	TOX	intronic	8.08×10^{-05}
rs1328452	1	78775182	-3.937	MGC27382	intronic	8.26×10^{-05}
rs7629329	3	8788336	-3.935	CAV3	3'-UTR	8.31×10^{-05}
rs10413818	19	4216910	3.931	ANKRD24	missense	8.47×10^{-05}
rs2562189	16	187429	-3.910	NPRL3	intronic	9.22×10^{-05}
rs75700106	14	34129066	3.907	NPAS3	intronic	9.35×10^{-05}
rs28479426	4	7474253	-3.895	SORCS2	intronic	9.83×10^{-05}

SNP, single nucleotide polymorphism; TNF, tumor necrosis factor; Chr, chromosome

variant in SNAP47 (rs117950953, $p = 3.69\times10^{-5}$), a missense variant in ANKRD24 (rs10413818, $p = 8.47\times10^{-5}$), and a variant in the 3'-UTR of CAV3 (rs7629329, $p = 8.31\times10^{-5}$), after adjusting for significant clinical factors (Table 2). Pathway analysis identified a significant association with the cell adhesion pathway ($p = 7.96\times10^{-5}$, Bonferroni-corrected $p = 5.88\times10^{-3}$).

Conclusion: This study highlights significant clinical and genetic factors associated with the initiation of anti-TNF therapy in r-axSpA patients with inadequate responses to NSAIDs, offering potential predictors for clinical application.

Disclosure: T. Kim: None; **B. Nam**: None; **S. Bang**: None; **Y. Park**: None; **J. Shin**: None; **S. Jo**: None; **T. Kim**: Samsung Bioepis, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0551

Enthesitis Beyond the Surface: Ultrasonographic Unmasking of Preclinical Psoriatic Arthritis in Cutaneous Psoriasis

Victor Cazac[1] and Eugeniu Russu[2], [1]Norwalk Hospital, Nuvance Health, Connecticut, [2]"Nicolae Testemitanu" State Medical and Pharmaceutical University; "Timofei Moşneaga" Republican Clinical Hospital, Chisinau, Moldova

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) develops insidiously from psoriasis (PsO), with enthesitis representing a critical initial site of inflammation. Musculoskeletal ultrasonography (MSUS) enables the identification of subclinical entheseal abnormalities and offers potential for stratifying PsA evolution into preclinical phases, long before clinical arthritis is apparent. This study aimed to determine whether inflammatory ultrasonographic changes are present in the absence of clinically overt enthesitis among patients with early PsA and PsO.

Methods: A cross-sectional observational study enrolled 153 subjects. The PsA group included 87 patients (58.6% female, mean age 44.3±8.2 years), diagnosed per CASPAR criteria within 3 years of onset. The PsO-only group comprised 66 patients (62.1% female, mean age 42.1±10.3 years) without musculoskeletal symptoms. Mean age at psoriasis onset was 27.4 ±6.1 years in the PsA group and 25.9±7.3 years in the PsO group. Mean age of arthritis onset in PsA was 41.2±7.8 years. All participants underwent clinical and MSUS evaluation of peripheral entheses (Achilles tendon, plantar fascia, patellar ligament, quadriceps tendon, lateral epicondyle), with scoring of entheseal thickness, hypoechogenicity, erosions, enthesophytes, and Power Doppler (PD) signal. Early PsA patients were subclassified as: preclinical (n=12); subclinical (n=31) and prodromal (n=44).

Results: In the PsA group, 71/87 (81.6%) had active enthesitis on MSUS, including 58.3% with PD signal. Among them, Achilles enthesitis (64.6%) and plantar fascia (48.9%) were most affected. In the PsO group, 29/66 (43.9%) had subclinical enthesitis, and 11 (16.7%) demonstrated PD positivity (Table 1).

Enthesophytes were detected in 34.2% of PsA and 19.6% of PsO (p=0.031). Bone erosions were present in 17.6% of PsA vs. 3.0% in PsO (p< 0.001). A significantly higher mean entheseal thickness (4.6 ± 0.9 mm vs. 3.2 ± 0.6 mm, p< 0.001) and frequency of bilateral involvement were found in PsA.

Conclusion: MSUS enables precise phenotyping of early PsA, detecting entheseal inflammation in both symptomatic and asymptomatic PsO patients. The stratification of patients across preclinical, subclinical, and prodromal phases supports enthesitis as an early marker of transition to PsA. Routine ultrasound surveillance in PsO may facilitate timely diagnosis and therapeutic interception of PsA progression.

Table 1. Ultrasonographic Enthesitis Features Across PsA and PsO Patients

Group/Subgroup	N (patients)	MSUS enthesitis (%)	PD (+) (%)	Enthesophytes (%)	Bone erosions (%)	Mean entheseal thickness (mm)
PsA – total	**87**	**81.6**	**58.3**	**34.2**	**17.6**	**4.6±0.9**
Preclinical	12	58.3	8.3	25.0	8,3	3.5±0.9
Subclinical	31	70.9	22.6%	32,3	12,9	3.9±0.9
Prodromal	44	95.4	97.7	45,5	31,8	4.3±0.9
PsO - total	**66**	**43.9**	**16.7**	**19.6**	**3.0**	**3.2±0.6**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Cazac: None; **E. Russu**: None.

Abstract Number: 0552

Radiographic Sacroiliitis Progression in Psoriatic Arthritis

Virginia Carrizo Abarza[1], Pankti Mehta[2], Fadi Kharouf[3], Shangyi Gao[4], Dafna D. Gladman[5], Vinod Chandran[6] and Denis Poddubnyy[7], [1]Toronto Western Hospital - University of Toronto, Toronto, ON, Canada, [2]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [3]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [4]Gladman-Krembil Psoriatic Arthritis Research Program, Centre for Prognosis Studies in the Rheumatic Diseases, Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada, [7]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I

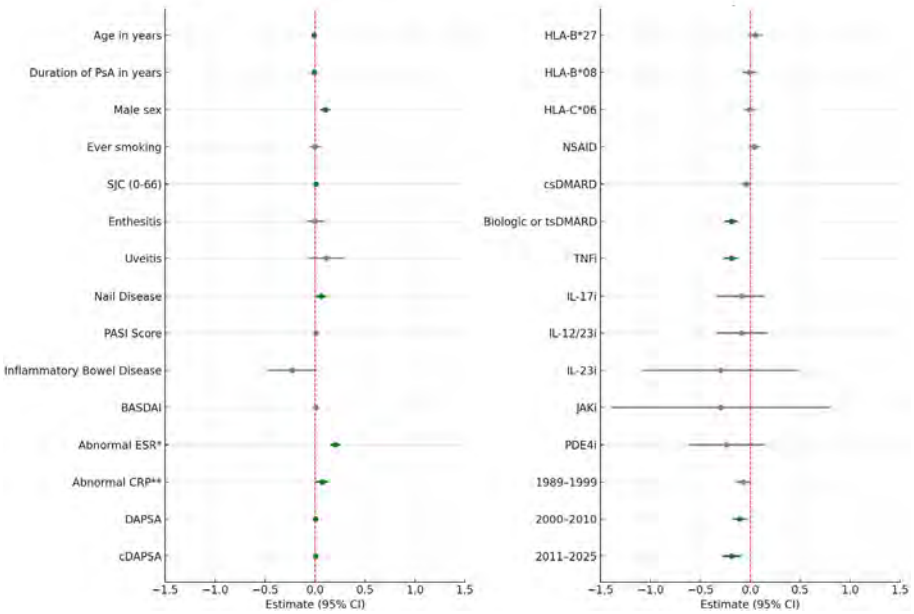
Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Radiographic sacroiliitis is an important indicator of axial involvement psoriatic arthritis (PsA), but only little is known about factors associated with progression of sacroiliitis. This study aimed to assess radiographic sacroiliitis progression in PsA and identify demographic, clinical, and genetic factors influencing its progression.

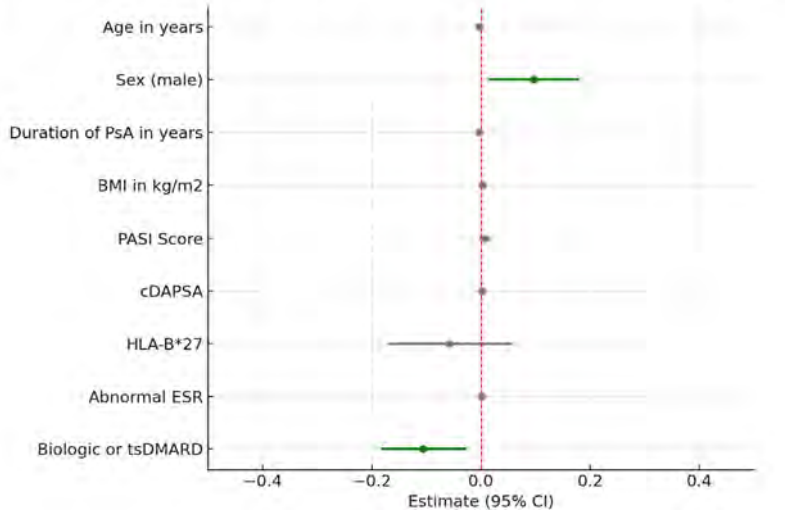
Methods: We included individuals from an observational Psoriatic Arthritis cohort (1978–2025). Pelvic radiographs were collected biannually. The Sacroiliitis Sum Score (SSS, 0–8) was calculated as the total sacroiliitis grades for the left and right sacroiliac joints, based on the modified New York (mNY) radiographic system. Radiographs were assessed by consensus.

Figure 1. Association of Demographic, Clinical and Genetic Factors with Radiographic Progression of Sacroiliitis Over Time: - Univariable Linear Mixed Model -



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Association of Demographic, Clinical and Genetic Factors with Radiographic Progression of Sacroiliitis Over Time: - Multivariable Linear



Progression was defined as an increase in the SSS by at least 1 point. Linear mixed models were used to evaluate factors influencing sacroiliitis progression, with the change in SSS as the outcome variable.

Results: A total of 1,554 patients without an SSS of 8, with a median follow-up duration of 6 years (range: 0.00–13.30), were included. Among them, 475 (30.6%) showed progression of radiographic sacroiliitis (SSS change ≥1). At baseline, 22% of all patients had sacroiliitis according to the mNY criteria, and 20% were HLA-B*27 positive.

Variables positively associated with progression included male sex, swollen joint count (SJC), Psoriasis Area and Severity Index (PASI), nail psoriasis, abnormal ESR, abnormal CRP, Disease Activity Index for PsA (DAPSA), and clinical DAPSA (Figure 1). Longer PsA duration was negatively associated with progression. HLA alleles, including HLA-B*27, were not significantly associated with progression.

Patients who received biologic or targeted synthetic DMARDs had significantly lower odds of progression. TNF inhibitors demonstrated a protective effect against sacroiliitis progression compared to other treatments. An analysis of the calendar effect showed a decline in sacroiliitis progression over time, with a greater reduction observed in the 2011–2025 period.

In multivariable analysis, male sex remained significantly associated with greater sacroiliitis progression, while biologic and targeted synthetic therapies continued to show a protective effect. (Figure 2)

Conclusion: Radiographic sacroiliitis progression occurred in one-third of patients. In univariable and multivariable analyses, male sex was associated with greater progression, while biologic and targeted synthetic therapies were protective.

Disclosure: V. Carrizo Abarza: None; **P. Mehta**: None; **F. Kharouf**: None; **S. Gao**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0553

Modified A-Tool: An online self-screening tool for axial spondyloarthritis for patients with chronic back pain

Zeyu Tang[1] and Abhijeet Danve[2], [1]Yale School of Medicine, New Haven, CT, [2]Section of Rheumatology, Department of Medicine, Yale School of Medicine, New Haven, CT

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0522–0553) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Lack of timely rheumatology referral of chronic back pain (CBP) patients with suspected axial spondyloarthritis (axSpA) is a major contributor to delayed diagnosis. We previously developed and validated an axSpA online self-screening tool (A-Tool) for patients with CBP to expedite self-referrals and evaluation [1].The original A-Tool consists of 3 pre-screening questions and 8 screening questions pertaining to high yield clinical features of axSpA without lab or imaging data. Here, we present a modified version of A-tool, that incorporates diagnostic testing and estimates post-test probability for patients.

Methods: We modified the A-tool based on the results of our prospective validation study [1]. "Unexplained joint swelling" and "Heel pain" questions were removed, while "Gradual onset" was added. We then ascribed weighted scores to each modified A-Tool item using the known positive likelihood ratios of axSpA features from literature: greater weight was put on prior diagnoses of psoriasis, inflammatory bowel disease, and uveitis (Table 1). A logarithmic model converted scores into post-test probabilities (Figure 1A). Pre-test and maximum post-test probabilities in the model were set to 5% and 45%,

Table 1. Modified A-Tool, composed of a Symptom Questionnaire (required) and Diagnostic Questionnaire (optional).

Symptom Questionnaire (Yes/No)	Score
Did your back/hip pain start gradually?	1
Does your back/hip pain improve with activities, exercise or movement	1
Does the back/hip pain wake you up at night?	1
Does your back/hip pain resolve or get much better 24 to 48 hours after taking NSAIDs (like Advil, ibuprofen, Aleve, diclofenac or meloxicam)?	1
Has a dermatologist or other physician ever diagnosed you with psoriasis of the skin or nails?	1
Has a gastroenterologist (GI doctor) ever diagnosed you with Crohn's disease or Ulcerative colitis or inflammatory bowel disease (IBD)?	1
Has an eye doctor ever diagnosed you with acute uveitis or iritis? (This is inflammatory condition of eye that causes redness, tearing, sensitivity to light and usually treated with steroid eye drops)	2
Do any of your first- or second-degree relatives have any of the following: psoriasis, IBD (Crohn's disease or ulcerative colitis), acute uveitis or ankylosing spondylitis? A first degree relevant is a parent, child, brother or sister. A second degree relative is grandparents, grandchildren, aunts, uncles, nephews, nieces or half-siblings.	1
Optional Diagnostic Questionnaire (Yes/No)	
Elevated CRP > 3.0mg/L	1
Positive HLA-B27	2
Sacroiliitis by any imaging	3

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A.

$$P_{post\text{-}test} = \frac{e^{score} \times P_{pre\text{-}test}}{P_{max} + (e^{score} - 1) \times P_{pre\text{-}test}} \times P_{max}$$

Variable	Description	Symptom-only	Diagnostics
Score	Total score	Self-Screening	Optional Diagnostic
$P_{pre-test}$	Pre-test probability	0.05	$P_{post-test}$ of Symptom-only (range 0.05 – 0.45)
P_{max}	Post-test probability	0.45	1.00

B.

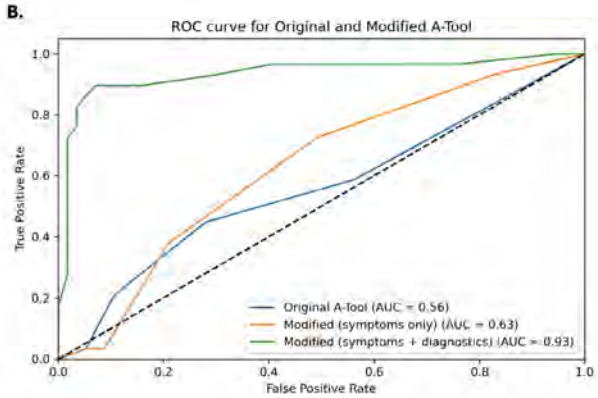


Figure 1. A) Mathematical model for post-test probability of self-screening tool. B) ROC curves for original and modified A-Tool.

respectively, based on prior literature [2]. We added an optional section for diagnostic test results: CRP, HLA B-27 and imaging sacroiliitis. When diagnostic data are included, the maximum post-test probability can increase to 100%. For analysis, we used the original A-Tool cohort to evaluate Receiver Operator Characteristic (ROC) curves, sensitivity, and specificity.

Results: There were 86 patients in the original A-Tool cohort; 29 had axSpA. All patients had CRP, HLA-B27 testing; 78 had axial MRI. ROC curves were generated for the original A-Tool, symptom-only modified A-Tool, and full modified A-Tool: area under the curve (AUC) were 0.56, 0.63, and 0.93, respectively (Figure 1B). At a post-test probability threshold of 80%, the modified A-Tool yielded a sensitivity of 86%, specificity of 95%, and positive predictive value of 89%.

Conclusion: We modified a previously validated online symptom-based axSpA self-referral tool, A-Tool, to include diagnostic testing and calculate post-test probabilities. The modified version had high sensitivity and specificity in an existing cohort. We aim to distribute the modified A-Tool as an publicly available online calculator for patients and primary care providers to facilitate rheumatology referrals (Figure 2). Future validation studies are needed to evaluate the modified A-Tool's test characteristics on a larger cohort.

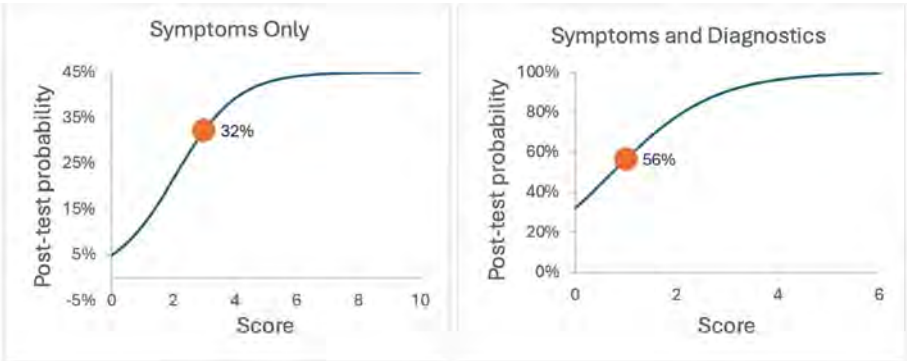


Figure 2. Example graphs generated for a hypothetical patient with symptom score of 3 and diagnostic score of 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References:

[1] Danve A. Arthritis Rheumatol. 2022; 74 (suppl 9):1514
[2] Danve A, Deodhar A. Clin. Rheumatol. 2015;34(6):987-993.

Disclosure: Z. Tang: None; **A. Danve**: AbbVie, 2, Amgen, 2, Eli Lilly, 5, Janssen, 2, Novartis, 2, 5.

Abstract Number: 0554

Real world experience with generic Tofacitinib in Axial Spondyloarthritis from North India

Sanjeev Kapoor[1], Babita Bondage[1], Niti Kedia[1], Mariya Patel[1] and **Akanksha Kapoor**[2], [1]Indian Spinal Injuries Centre (ISIC), New Delhi, India, [2]Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, Pune, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (AxSpA) is an inflammatory condition that falls under the category of spondyloarthritis (SpA) and significantly affects quality of life, causing symptoms like fatigue, sleep disturbances, depression, and sexual dysfunction, which can greatly diminish health-related quality of life and restrict work, leisure activities, and daily living.

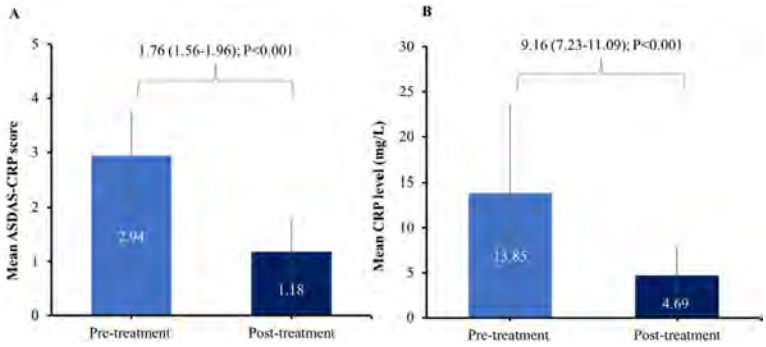


Figure 1: A) Mean ASDAS-CRP scores and B) Mean CRP level at pre-treatment and post-treatment with tofacitinib at 24 weeks (N=100)

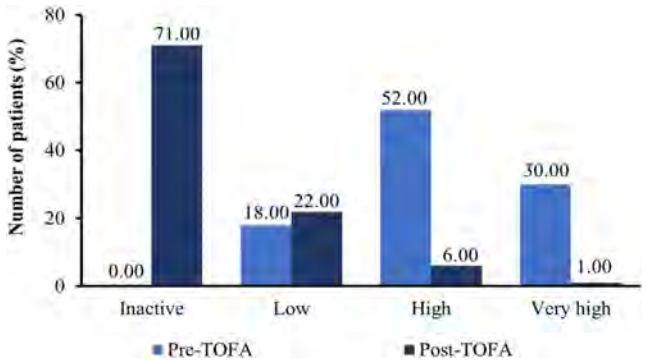


Figure 2: Disease activity at baseline and 24 weeks (post-treatment with tofacitinib) in AxSpA patients (ASDASC-CRP, axial spondyloarthritis disease activity score C-reactive protein; CRP, C-reactive protein

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics

Characteristics	No. of patients (N=100)
Gender	
Male	77 (77.00)
Female	23 (23.00)
History of Smoking	23 (23.00)
HLA B27	84 (84.00)
Presence of	
Peripheral arthritis	58 (58.00)
Uveitis	25 (25.00)
Psoriasis	1 (1.00)
Data represented as n (%). HLA, human leukocyte antigens.	

This underscores the urgent need for effective treatment strategies. Tofacitinib, a Janus kinase inhibitor, is used for various inflammatory conditions, but there is limited real-world evidence on its efficacy and safety for AxSpA in Indian patients. This retrospective study aimed to evaluate the effectiveness and safety of tofacitinib in Indian patients diagnosed with AxSpA in a real-world setting.

Methods: A single-centre, retrospective, observational study was conducted on patients with active AxSpA in India, spanning from November 2023 to April 2024. The clinical and laboratory records of AxSpA patients who were treated with generic tofacitinib at a dosage of 5 mg twice daily for 24 weeks were reviewed and analysed. The efficacy of tofacitinib was assessed based on the improvement in disease activity, specifically the change in the Ankylosing Spondylitis Disease Activity Score C-Reactive Protein (ASDAS-CRP) after 24 weeks. Adverse events (AEs) were monitored throughout the treatment period.

Results: A total of 100 patients with active AxSpA participated in the study, with a mean age of 35.95 years and an average disease duration of 8.20 years. Of these, 77 were males and 23 were females. All patients received tofacitinib 5 mg twice daily for 24 weeks. The majority of the patients were biologic-naive, with only 12 having prior biologic therapy. Additionally, 23 patients received tofacitinib monotherapy without nonsteroidal anti-inflammatory drugs (NSAIDs), while 77 patients received tofacitinib along with on-demand NSAIDs but without any concomitant conventional disease-modifying antirheumatic drug therapy. It showed a significant decrease in the ASDAS-CRP score from 2.94 to 1.18 by week 24, with a mean difference of 1.76 (95% confidence interval [CI]: 1.56-1.96, P< 0.001). The CRP levels also dropped significantly, from 13.85 mg/L to 4.69 mg/L at week 24, with a mean difference of 9.16 (95% CI: 7.23-11.09, P< 0.001). Notably, nearly 71% of patients achieved inactive disease status (ASDAS-CRP < 1.3) after 24 weeks of treatment, and tofacitinib was well tolerated in this cohort, with a low incidence of AEs like non-serious herpes zoster (6.00%), respiratory system-related infections (3.00%), and pulmonary thrombo-embolism (1.00%).

Conclusion: This retrospective real-world study supports the efficacy and safety of generic tofacitinib as an NSAID-sparing agent for Indian patients with active AxSpA. Its cost-effectiveness compared to expensive biologics and the convenience of oral administration make it an appealing option, especially in areas with limited access to biologics. Tofacitinib could improve patient outcomes and provide an affordable therapy option for managing AxSpA.

Disclosure: S. Kapoor: None; **B. Bondage**: None; **N. Kedia**: None; **M. Patel**: None; **A. Kapoor**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0555

Phase 3 Results From an Innovative Trial Design of Treating Plaque Psoriasis Involving Difficult-to-Treat, High-Impact Sites With Icotrokinra, a Targeted Oral Peptide That Selectively Inhibits the IL-23–Receptor

Melinda J. Gooderham[1], Edward Lain[2], Robert Bissonnette[3], Yu-Huei Huang[4], Charles Lynde[5], Matthias Hoffmann[6], **Joseph F Merola**[7], Eingun J. Song[8], Jessica H. Rubens[9], Amy M. DeLozier[9], Ming-Chun Hsu[9] and Richard B. Warren[10], [1]SKiN Centre for Dermatology, Queen's University, & Probity Medical Research, Peterborough, ON, ON, Canada, [2]Austin Institute for Clinical Research, Sanova Dermatology, Austin, TX, USA, Austin, TX, [3]Innovaderm Research, Montreal, QC, Canada, Montreal, QC, [4]Chang Gung Memorial Hospital & Chang Gung University, Taoyuan City, Taiwan, Taoyuan City, Taiwan (Republic of China), [5]University of Toronto, Lynde Institute for Dermatology & Lynderm Research Inc, Markham, ON, Canada, ON, Canada, [6]Dermatology Practice Dr. M Hoffmann, Witten, Germany, Witten, Germany, [7]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [8]Frontier Derm, Mill Creek, WA, USA, WA, [9]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [10]Dermatology Centre, Northern Care Alliance, NHS Foundation Trust & Division of Musculoskeletal and Dermatological Sciences, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Icotrokinra (ICO), a first-in-class, targeted oral peptide that binds and inhibits the interleukin (IL)-23R, was evaluated in ICONIC-TOTAL (NCT06095102).

Methods: This Phase 3 trial included plaque psoriasis (PsO) severity of body surface area (BSA) ≥1%/Investigator's Global Assessment (IGA) ≥2 and employed a novel basket-like design to evaluate 3 cohorts of adults & adolescents (≥12 to < 18 years) with at least moderate, difficult-to-treat, high-impact skin sites: scalp (scalp-specific [ss]-IGA ≥3), genital (static Physician Global Assessment of Genitalia [sPGA-G] ≥3), and/or hand/foot (hf-PGA ≥3). Primary (IGA 0/1: clear [0]/almost clear [1] & ≥2-grade improvement) and key secondary (ss-IGA 0/1, sPGA-G 0/1, hf-PGA 0/1) endpoints were assessed at Week 16.

Results: 311 randomized patients (ICO=208/placebo=103) with scalp (n=252), genital (n=140), and/or hand/foot (n=71) PsO received once-daily ICO 200 mg or placebo through Week 16. ICO vs placebo met primary (IGA 0/1: 57% vs 6%; P< 0.001) and scalp and genital key secondary endpoints (ss-IGA 0/1: 66% vs 11%; sPGA-G 0/1: 77% vs 21%; both P< 0.001), and showed higher hf-PGA 0/1 (42% vs 26%; P=0.144). Patient-reported scalp and genital PsO improvements were statistically significantly superior to placebo. Proportions of ICO and placebo patients with ≥1 adverse event (AE) were 50% & 42% (the most commonly reported AE was nasopharyngitis) and GI AE were 7.2% & 7.8%, respectively.

Conclusion: ICO demonstrated significantly higher rates of overall skin, scalp, and genital PsO clearance vs placebo with a favorable safety profile. Basket-like trial designs can be used to efficiently study special skin sites in patients with PsO and other diseases.

Disclosure: M. Gooderham: AbbVie, 12, 1, 6, Akros, 12, 1, 6, Amgen, 12, 1, 6, AnaptysBio, 12, 1, 6, Apogee, 12, 1, 6, Arcutis Biotherapeutics, 12, 1, 6, Aristea, 12, 1, 6, Aslan, 12, 1, 6, Bausch Health, 12, 1, 6, Boehringer-Ingelheim, 12, 1, 6, Bristol-Myers Squibb(BMS), 12, 1, 6, Celgene, 12, 1, 6, Dermavant, 12, 1, 6, Dermira, 12, 1, 6, Eli Lilly, 12, 1, 6, Galderma, 12, 1, 6, GlaxoSmithKlein(GSK), 12, 1, 6, Incyte, 12, 1, 6, Inmagene, 12, 1, 6, JAMP, 12, 1, 6, Janssen, 12, 1, 6,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kyowa Kirin, 12, 1, 6, LEO Pharma, 12, 1, 6, MedImmune, 12, 1, 6, Meji, 12, 1, 6, Merck, 12, 1, 6, MoonLake Immunotherapeutics, 12, 1, 6, Nimbus, 12, 1, 6, Novartis, 12, 1, 6, Pfizer, 12, 1, 6, Regeneron, 12, 1, 6, Roche, 12, 1, 6, Sanofi Genzyme, 12, 1, 6, Sun Pharma, 12, 1, 6, Takeda, 12, 1, 6, Tarsus Pharmaceuticals, 12, 1, 6, UCB, 12, 1, 6, Union Therapeutics, 12, 1, 6, Ventyx Biosciences, 12, 1, 6, Vyne Therapeutics, 12, 1, 6; **E. Lain**: AbbVie, 12, Personal fees, Arcutis, 12, Personal fees, Bristol-Myers Squibb(BMS), 12, Personal fees, Dermavant, 12, Personal fees, Eli Lilly, 12, Personal fees, EPI Health, 12, Personal fees, Galderma, 12, Personal fees, Incyte, 12, Personal fees, Ortho Dermatologics, 12, Personal fees, Pfizer, 12, Personal fees; **R. Bissonnette**: AbbVie, 2, 5, Amgen, 2, 5, Apogee, 2, Arcutis, 2, 5, Asana, 2, Bellus, 5, BioMimetix, 5, Bluefin, 2, Boehringer-Ingelheim, 2, Boston Pharma, 2, Cara Therapeutics, 5, Clexio, 5, Dermavant, 2, 5, Eli Lilly, 2, Escient, 2, 5, Evidera, 2, Fresh Tracks, 5, Galderma, 2, GlaxoSmithKline, 2, Incyte, 2, 5, Innovaderm, 11, Janssen, 2, 5, LEO Pharma, 2, 5, Merck, 5, Novartis, 2, Opsidio, 5, Pfizer, 2, 5, RAPT Therapeutics, 2, Sanofi Genzyme, 2, Sanofi-Aventis, 2, Target RWE, 2, 5, Vyne Therapeutics, 5, Xencor, 5; **Y. Huang**: AbbVie, 1, 6, Celgene, 1, 6, Eli-Lilly, 12, 6, Galderma, 12, Janssen-Cilag Pharmaceutica, 12, Novartis, 12, 6, Pfizer, 1, 6; **C. Lynde**: AbbVie, 12, 12, Personal Fees, Akros, 12, Amgen, 12, 12, Personal Fees, Aralez, 12, Personal Fees, Arcutis, 12, Bausch Health, 12, 12, Personal Fees, Bayer, 12, 12, Personal Fees, Bioderma, 12, 12, Personal Fees, BioJAMP, 12, 12, Personal Fees, Boehringer-Ingelheim, 12, 12, Personal Fees, Bristol-Myers Squibb(BMS), 12, 12, Personal Fees, Celgene, 12, 12, Personal Fees, Celltrion, 12, 12, Personal Fees, CeraVe, 12, 12, Personal Fees, Cipher, 12, 12, Personal Fees, Concert, 12, Dermavant, 12, 12, Personal Fees, Devonian, 12, Eli Lilly, 12, 12, Personal Fees, Evelo, 12, Fresnius Kabi, 12, Personal Fees, Galderma, 12, 12, Personal Fees, GlaxoSmithKline, 12, 12, Personal Fees, InCyte, 12, 12, Personal Fees, Innovaderm, 12, Personal Fees, Intega Skin, 12, 12, Personal Fees, Janssen, 12, 12, Personal Fees, Kyowa Kirin, 12, 12, Personal Fees, La Roche Posay, 12, 12, Personal Fees, L'Oreal, 12, 12, Personal Fees, LEO Pharma, 12, 12, Personal Fees, Medexus, 12, 12, Personal Fees, MedX, 12, Personal Fees, Merck, 12, 12, Personal Fees, MoonLake, 12, Naos, 12, 12, Personal Fees, Nimbus, 12, Novartis, 12, 12, Personal Fees, P&G, 12, 12, Personal Fees, PediaPharm, 12, 12, Personal Fees, Pfizer, 12, 12, Personal Fees, Regeneron, 12, 12, Personal Fees, Roche, 12, 12, Personal Fees, Sandoz, 12, 12, Personal Fees, Sanofi Genzyme, 12, 12, Personal Fees, Sentrex, 12, 12, Personal Fees, Skinceuticals, 12, Personal Fees, Sun Pharma, 12, 12, Personal Fees, Takeda, 12, 12, Personal Fees, TEVA, 12, 12, Personal Fees, Tribute, 12, 12, Personal Fees, UCB, 12, 12, Personal Fees, Valeant, 12, 12, Personal Fees, Viatris, 12, 12, Personal Fees, Volo Health, 12, 12, Personal Fees; **M. Hoffmann**: AbbVie, 12, 1, 2, 5, 6, Almirall, 12, 1, 2, 5, 6, Biofrontera, 12, 1, 2, 5, 6, Bristol-Myers Squibb(BMS), 12, 1, 2, 5, 6, Dermapharm, 12, 1, 2, 5, 6, Dermasence, 12, 1, 2, 5, 6, Eli Lilly, 12, 1, 2, 5, 6, Forward, 12, 1, 2, 5, 6, Galderma, 12, 1, 2, 5, 6, Incyte, 12, 1, 2, 5, 6, Janssen, 12, 1, 2, 5, 6, Kiniksa, 12, 1, 2, 5, 6, LEO Pharma, 12, 1, 2, 5, 6, L'Oréal, 12, 1, 2, 5, 6, MSD, 12, 1, 2, 5, 6, Nektar Therapeutics, 12, 1, 2, 5, 6, Novartis, 12, 1, 2, 5, 6, Pfizer, 12, 1, 2, 5, 6, Pierre Fabre, 12, 1, 2, 5, 6, Sanofi, 12, 1, 2, 5, 6, Schering-Plough, 12, 1, 2, 5, 6, Smerud Medical Research, 12, 1, 2, 5, 6, Stallergenes Greer, 12, 1, 2, 5, 6, UCB, 12, 1, 2, 5, 6, Viatris, 12, 1, 2, 5, 6; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **E. Song**: AbbVie, 12, 2, 6, Alyphn, 12, 2, 6, Amgen, 12, 2, 6, Apogee, 12, 2, 6, Arcutis, 12, 2, 6, ASLAN, 12, 2, 6, Boehringer-Ingelheim, 12, 2, 6, Bristol-Myers Squibb(BMS), 12, 2, 6, Dermavant, 12, 2, 6, Eli Lilly, 12, 2, 6, Janssen, 12, 2, 6, LEO Pharma, 12, 2, 6, Novartis, 12, 2, 6, Ortho-dermatologics, 12, 2, 6, Pfizer, 12, 2, 6, Regeneron Pharmaceuticals, 12, 2, 6, Sanofi, 12, 2, 6, Sun Pharma, 12, 2, 6, UCB, 12, 2, 6; **J. Rubens**: Johnson & Johnson, 3, 11; **A. DeLozier**: Johnson & Johnson, 3, 11; **M. Hsu**: Johnson & Johnson, 3, 11; **R. Warren**: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, Arena, 2, Astellas, 2, Avillion, 2, Biogen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 6, Celgene, 2, 5, DICE Therapeutics, 2, Eli Lilly and Company, 2, 5, 6, GSK, 2, Janssen, 2, 5, 6, LEO Pharma, 2, 5, Meiji Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, RAPT Therapeutics, 2, Sanofi, 2, Sun Pharma, 2, UCB, 2, 5, Union, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0556

Evaluating the Efficacy of Sulfasalazine Compared to Placebo in the Treatment of Psoriatic Arthritis in Adults: A Systematic Review and Meta-Analysis

Rameez Qasim[1], **Khadija Mohib**[2], Umme Abeeha Naqvi[3], Ahmad Furqan Anjum[4] and Moeeza Fatima[4], [1]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [2]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, [3]Jinnah Sindh Medical University Karachi, Karachi, Pakistan, [4]Shaikh Khalifa Bin Zayed Al-Nahyan Medical College, Shaikh Zayed Postgraduate Medical Institute (SZPGMI), Lahore, Lahore, Pakistan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

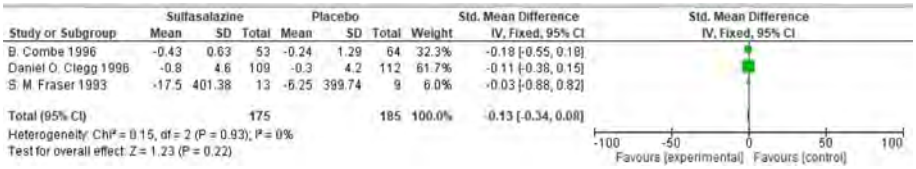
Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

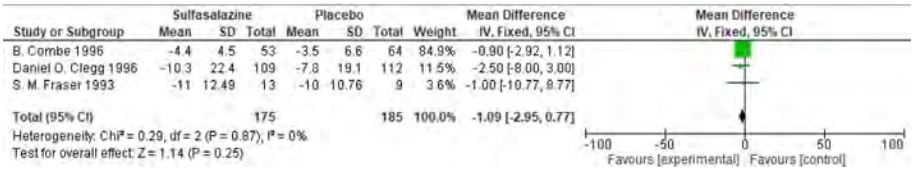
Background/Purpose: Available evidence hints towards the positive results of the use of sulfasalazine in the management of patients with psoriatic arthritis (PsA). We did a systematic review and meta-analysis to determine the possible safety and effectiveness of sulfasalazine for the treatment of PsA.

Methods: We conducted a thorough literature search using PubMed and Cochrane Library to retrieve and review all the articles through July 2024. Each of the studies in our review was to report different measures to determine the safety and efficacy of sulfasalazine by using 95% CIs. PRISMA flow guidelines were followed and used to assess the methodological quality of evidence and reporting Quality. The GRADE system was used to appraise the certainty of evidence.

Results: Our literature search produced 17 results and a final of 3 studies were included in our analysis. All the studies were prospective RCTs with a total population of 380 patients with male dominant population. There was a significant and persistent treatment effect on ESR, as evidenced by the overall standardized mean difference (SMD) of -0.47 (95% CI: [-0.68, -0.26], Z = 4.41, P < 0.0001) and low heterogeneity (Chi^2 = 1.88, P = 0.39, I^2 = 0%). The overall pooled mean difference was found to be -1.09 (95% CI: -2.95 to 0.77) and a p-value of 0.25 in case of Ritchie Index, showing no statistically significant benefit of Sulfasalazine over placebo. Based on the three studies included, overall effect size was found to be -0.13 (95% CI: -0.34 to 0.08), showing no notable variation among the groups. Heterogeneity was low (I^2 = 0%, p = 0.93), and thus result was not statistically important (Z = 1.23, p = 0.22). Two of the studied showed a low risk of bias where as one showed a high risk.

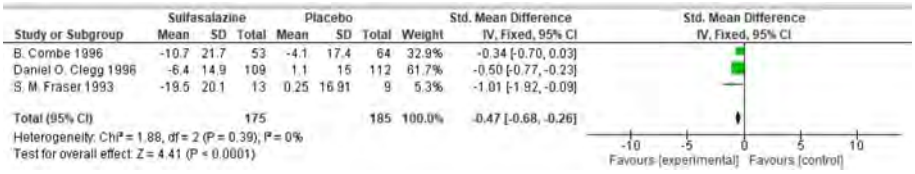


Forest Plot of effect on Morning Stiffness



Forest Plot of effect on Ritchie Articular Index

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot of effect on ESR

Conclusion: Sulfasalazine has some benefits in reducing systemic inflammation in people with psoriatic arthritis (PsA), as shown by an improved erythrocyte sedimentation rate (ESR). However, its efficacy as a stand-alone treatment is limited due to its negligible effect on important clinical symptoms such as joint pain, stiffness, and soreness. For mild to moderate PsA, sulfasalazine may be helpful as adjuvant therapy, but in more severe instances, it is not enough for complete management. To elucidate its function in PsA management, more studies involving bigger and more varied populations are required.

Disclosure: R. Qasim: None; **K. Mohib**: None; **U. Naqvi**: None; **A. Anjum**: None; **M. Fatima**: None.

Abstract Number: 0557

Efficacy of Upadacitinib in Male and Female Patients with PsA: Results from the SELECT-PsA 1 and 2 Trials

Lihi Eder[1], Axel Hueber[2], **Lucia Novelli**[3], Tianming Gao[3], Jayne Stigler[4], Zhiyuan Du[3], Rodrigo García Salinas[5], Grace Wright[6] and Sofia Ramiro[7], [1]University of Toronto, Toronto, ON, Canada, [2]Klinikum Nuernberg, Nuernberg, Germany, [3]AbbVie, North Chicago, IL, [4]AbbVie, Round Lake, IL, [5]Hospital Italiano La Plata, La Plata, Argentina, [6]Grace C Wright MD PC, New York, NY, [7]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Biologic sex can impact both clinical phenotype and therapeutic response in PsA.[1–3] Previous studies have suggested that male patients (pts) may achieve better treatment outcomes with biologic agents including TNFi and IL-17 inhibitor therapies compared with female pts.[1–3] This post hoc analysis evaluated potential differences in the efficacy of upadacitinib (UPA), an oral Janus kinase inhibitor, between male and female pts with PsA.

Methods: Data were drawn from 2 phase 3 studies, SELECT-PsA 1 (NCT03104400) and SELECT-PsA 2 (NCT03104374).[4,5] In SELECT-PsA 1, pts were randomized to UPA 15 or 30 mg once daily (QD), adalimumab 40 mg every other week, or placebo (PBO); in SELECT-PsA 2, pts were randomized to UPA 15 or 30 mg or PBO QD. In both studies, pts receiving PBO switched to UPA 15 or 30 mg QD at Week (W) 24. UPA 15 mg QD data were analyzed for the current analysis. Efficacy endpoints were assessed at W12 and W24, stratified by sex. Statistical analyses included the Cochran–Mantel–Haenszel test for binary endpoints and mixed-effect model for repeated measurement for continuous endpoints. Response rates for binary endpoints were calculated using non-responder imputation. UPA vs PBO in both studies, and UPA vs adalimumab in SELECT-PsA 1, was assessed within each sex by relative risk (RR) or mean difference, and treatment comparison between sexes was assessed by the RR ratio (RRR) or difference between differences, with 95% confidence intervals (CIs) (comparability is indicated where intervals cover 0 [RR] or 1 [RRR]).

Results: 1,386 pts were included, of whom 640 (289/351 male/female), 317 (162/155), and 429 (207/222) received UPA, PBO, and adalimumab, respectively. At baseline, male and female pts generally have comparable disease characteristics,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline patient characteristics across SELECT-PsA 1 and 2 trials

	SELECT-PsA 1						SELECT-PsA 2			
	PBO to UPA 15 mg QD		ADA 40 mg EOW		UPA 15 mg QD		PBO to UPA 15 mg QD		UPA 15 mg QD	
Baseline data	Male (n=113)	Female (n=98)	Male (n=207)	Female (n=222)	Male (n=191)	Female (n=236)	Male (n=49)	Female (n=57)	Male (n=98)	Female (n=113)
Age (years), mean (SD)	47.3 (11.7)	53.0 (12.2)	49.9 (11.6)	52.7 (12.4)	50.5 (12.4)	52.4 (12.0)	50.5 (10.9)	53.9 (12.1)	51.3 (11.5)	54.4 (12.3)
BMI, mean (SD)	29.1 (5.0)	32.0 (8.5)	30.0 (5.8)	31.3 (8.3)	28.7 (4.9)	31.3 (7.2)	30.4 (6.6)	31.6 (7.5)	31.3 (5.9)	31.6 (8.5)
TJC, mean (SD)	19.1 (13.4)	22.6 (17.8)	17.8 (13.1)	22.2 (14.2)	18.5 (14.3)	21.9 (14.9)	22.6 (17.3)	29.2 (18.2)	21.4 (15.0)	27.9 (18.6)
SJC, mean (SD)	11.5 (8.2)	11.3 (8.8)	11.5 (9.6)	11.7 (7.9)	11.7 (9.4)	11.5 (9.2)	10.8 (5.9)	12.7 (11.0)	11.0 (7.7)	11.5 (8.6)
PASI, mean (SD)	12.4 (10.3)	10.7 (11.9)	10.7 (9.7)	7.9 (6.7)	10.5 (9.9)	9.1 (10.0)	16.1 (15.1)	12.6 (11.0)	11.2 (10.1)	8.9 (7.9)
CRP, mean (SD)	13.9 (20.5)	9.9 (12.0)	12.4 (17.6)	9.5 (13.1)	13.4 (19.6)	9.1 (9.2)	15.2 (29.5)	8.9 (12.1)	11.4 (20.0)	11.0 (17.2)
FACIT-Fatigue, mean (SD)	33.1 (11.7)	29.0 (10.5)	32.9 (11.1)	26.3 (10.8)	31.3 (11.3)	27.1 (12.0)	28.6 (12.0)	23.0 (11.3)	30.9 (11.2)	24.8 (11.8)
Patient's Assessment of Pain, mean (SD)	5.7 (2.3)	6.4 (2.1)	5.4 (2.1)	6.5 (1.9)	5.8 (2.1)	6.5 (2.0)	6.1 (2.4)	7.0 (1.7)	6.3 (2.0)	6.4 (2.3)
Patient's Global Assessment of Disease Activity, mean (SD)	6.0 (2.2)	6.4 (2.1)	5.9 (2.1)	6.7 (1.9)	6.4 (1.9)	6.7 (2.1)	6.4 (1.8)	7.5 (1.7)	6.7 (1.9)	7.0 (1.9)
Physician's Global Assessment of Disease Activity, mean (SD)	6.7 (1.6)	6.5 (1.7)	6.5 (1.6)	6.6 (1.7)	6.6 (1.6)	6.7 (1.7)	6.4 (2.1)	6.6 (1.7)	6.5 (1.9)	6.4 (1.7)
HAQ-DI, mean (SD)	1.0 (0.6)	1.2 (0.6)	1.0 (0.6)	1.3 (0.6)	1.0 (0.6)	1.3 (0.7)	1.0 (0.7)	1.5 (0.7)	1.0 (0.6)	1.2 (0.6)
Dactylitis, n (%)	42 (37.2)	23 (23.5)	64 (30.9)	63 (28.4)	66 (35.6)	68 (28.6)	14 (28.6)	18 (31.6)	28 (28.6)	27 (23.9)
Enthesitis, n (%)	62 (54.9)	56 (57.1)	112 (54.1)	153 (68.9)	106 (55.5)	164 (68.9)	28 (57.1)	43 (75.4)	56 (57.7)	77 (68.1)
BASDAI, mean (SD)	5.60 (1.9)	6.09 (1.6)	4.92 (2.3)	6.3 (2.0)	5.61 (2.0)	6.28 (2.0)	6.01 (2.2)	7.17 (1.5)	5.65 (2.1)	6.15 (2.2)

ADA, adalimumab; EOW, every other week; PBO, placebo; QD, once daily; SD, standard deviation; UPA, upadacitinib.

with some numeric differences between sexes across most scores (Table 1). Higher efficacy was observed with UPA vs PBO in both sexes for the majority of endpoints (Figure & Table 2). At W12 and W24, efficacy of UPA was consistent between male and female pts for all efficacy endpoints analyzed (Figure & Table 2). The proportion of male and female pts achieving ACR20, the primary efficacy outcome, was similar in both studies and at both W12 (SELECT-PsA 1: RRR [95% CI] 1.33 [0.89–1.98]; SELECT-PsA 2: 1.69 [0.70–4.07]) and W24 (1.39 [0.99–1.95] and 1.38 [0.53–3.62], respectively). Comparable percentages of male and female pts achieved ACR50, ACR70, minimal disease activity, and Leeds Enthesitis Index=0 with similar improvements in PASI75, Visual Analog Scale pain, and HAQ-DI at both W12 and W24; numerically greater improvements for male vs female pts were observed across most endpoints (UPA vs PBO; Figure & Table 2).

Conclusion: UPA was associated with higher efficacy vs PBO in both sexes among pts with PsA. UPA was associated with consistent efficacy between male and female pts across SELECT-PsA 1 and 2 at W12 and W24 for the majority of endpoints evaluated in this post hoc analysis.

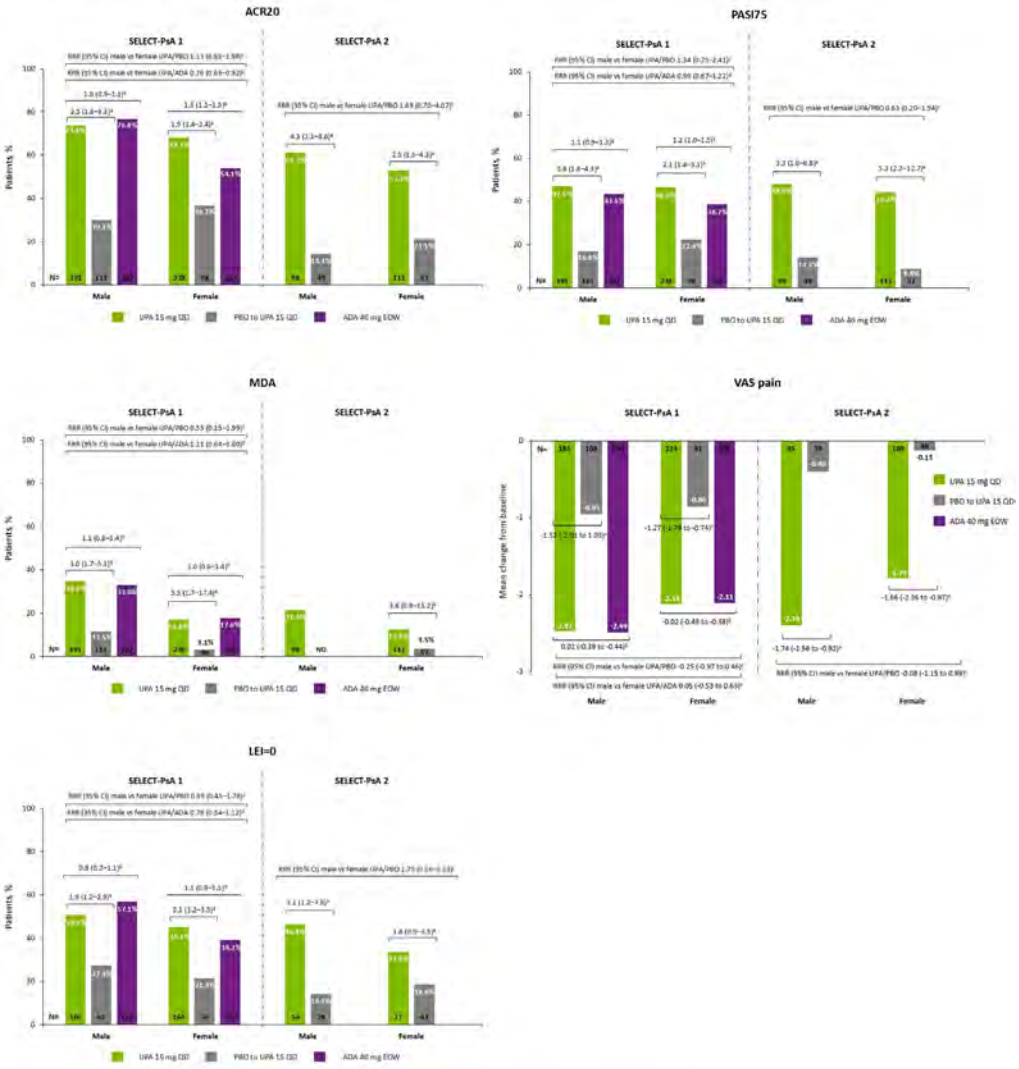
Table 2. Efficacy outcomes at W24 stratified by sex in SELECT-PsA 1 and 2 trials

Binary efficacy endpoints (% of patients)	Sex	UPA QD	PBO QD	ADA EOW	RR (95% CI) UPA vs PBO	RR (95% CI) UPA vs ADA	RRR (95% CI) male vs female UPA/PBO	RRR (95% CI) male vs female UPA/ADA
SELECT-PsA 1								
ACR20	Male	80.6	38.1	78.7	2.1 (1.7–2.7)	1.0 (0.9–1.1)	1.39 (0.99–1.95)	0.88 (0.72–1.02)
	Female	67.6	43.9	56.3	1.5 (1.2–1.9)	1.2 (1.0–1.4)		
PASI75	Male	59.7	21.2	60.4	2.8 (1.9–4.1)	1.0 (0.8–1.2)	1.47 (0.89–2.43)	0.76 (0.59–0.97)
	Female	57.1	29.6	41.7	1.9 (1.4–2.7)	1.3 (1.1–1.6)		
MDA	Male	50.3	12.4	44.0	4.1 (2.3–6.8)	1.1 (0.9–1.4)	1.80 (0.82–3.95)	1.04 (0.71–1.53)
	Female	25.6	11.2	23.4	2.3 (1.3–4.1)	1.1 (0.8–1.5)		
LEI=0	Male	67.0	35.5	68.1	1.9 (1.3–2.7)	1.0 (0.8–1.2)	1.05 (0.59–1.85)	0.77 (0.56–1.05)
	Female	51.8	28.6	39.2	1.8 (1.2–2.8)	1.3 (1.0–1.7)		
SELECT-PsA 2								
ACR20	Male	59.2	12.2	N/A	4.8 (2.2–10.4)	N/A	1.5 (2.6–6.2)	N/A
	Female	59.3	17.5	N/A	3.5 (2.0–6.2)	N/A		
PASI75	Male	51.0	12.2	N/A	4.1 (1.9–8.9)	N/A	1.62 (0.68–4.12)	N/A
	Female	52.2	21.2	N/A	2.5 (1.5–4.3)	N/A		
MDA	Male	29.6	2.0	N/A	14.4 (2.0–102.8)	N/A	1.23 (0.08–19.10)	N/A
	Female	23.2	1.8	N/A	11.8 (1.7–81.7)	N/A		
LEI=0	Male	44.6	28.6	N/A	1.5 (0.8–2.9)	N/A	0.79 (0.33–1.90)	N/A
	Female	45.5	23.3	N/A	2.0 (1.1–3.5)	N/A		
Continuous efficacy endpoints (mean change from baseline)	**Sex**	**UPA**	**PBO**	**ADA**	**Difference (95% CI) UPA vs PBO**	**Difference (95% CI) UPA vs ADA**	**Difference (95% CI) male vs female UPA/PBO**	**Difference (95% CI) male vs female UPA/ADA**
SELECT-PsA 1								
VAS pain	Male	-3.26	-1.15	-2.87	-2.11 (-2.61–-1.61)	-0.39 (0.81 to -0.04)	-0.74 (-1.49 to 0.01)	0.09 (-0.51 to 0.70)
	Female	-2.85	-1.48	-2.37	-1.37 (-1.93–-0.81)	-0.48 (0.91–0.05)		
HAQ-DI	Male	-0.54	-0.15	-0.46	-0.39 (-0.53–-0.27)	-0.09 (0.19 to -0.02)	-0.05 (-0.23 to 0.12)	0.07 (-0.07 to 0.21)
	Female	-0.49	-0.14	-0.33	-0.34 (-0.46–-0.21)	-0.15 (0.25–0.05)		
SELECT-PsA 2								
VAS pain	Male	-2.25	-0.68	N/A	-1.58 (-2.49 to -0.67)	N/A	0.01 (-1.20 to 1.23)	N/A
	Female	-2.30	-0.71	N/A	-1.59 (-2.42 to -0.77)	N/A		
HAQ-DI	Male	-0.35	-0.07	N/A	-0.28 (-0.44 to -0.12)	N/A	-0.10 (-0.33 to 0.13)	N/A
	Female	-0.32	-0.13	N/A	-0.18 (-0.35 to -0.02)	N/A		

Response rates for binary endpoints were calculated using non-responder imputation.
For continuous endpoints, an as-observed mixed-effect model for repeated measures was applied.
For binary endpoints, an RR above 1 indicated better outcomes with UPA vs PBO and UPA vs ADA. For all continuous endpoints, a between-group difference lower than 0 indicated better outcomes with UPA vs PBO and UPA vs ADA.
For binary endpoints, an RRR above 1 indicated better outcomes with males vs females; while an RRR below 1 indicated worse outcomes with males vs females. For all continuous endpoints, a between-treatment group difference above 0 indicated worse outcomes with males vs females; while a between-treatment group difference below 0 indicated better outcomes with males vs females.
ACR 20, ≥20% improvement in American College of Rheumatology response criteria; ADA, adalimumab; CI, confidence interval; EOW, every other week; LEI=0, Leeds Enthesitis Index=0; MDA, minimal disease activity; N/A, not applicable; PASI 75, 75% improvement in Psoriasis Area Severity Index score; PBO, placebo; QD, once daily; RR, relative risk; RRR, relative risk ratio; UPA, upadacitinib; VAS pain, Visual Analog Scale pain; W, Week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure. Efficacy outcomes at W12 stratified by sex in SELECT-PsA 1 and 2 trials. Response rates for binary endpoints were calculated using non-responder imputation.



Response rates for binary endpoints were calculated using non-responder imputation.
For continuous endpoints, an as-observed mixed-effect model for repeated measures was applied.
For binary endpoints, an RR above 1 indicated better outcomes with UPA vs PBO and UPA vs ADA. For all continuous endpoints, a between-group difference lower than 0 indicated better outcomes with UPA vs PBO and UPA vs ADA.
For binary endpoints, an RRR above 1 indicated better outcomes with males vs females, while an RRR below 1 indicated worse outcomes with males vs females. For all continuous endpoints, a between treatment group difference above 0 indicated worse outcomes with males vs females, while a between treatment group difference below 0 indicated better outcomes with males vs females.
[a]RR (95% CI) UPA vs PBO. [b]RR (95% CI) UPA vs ADA. [c]RRR (95% CI) male vs female UPA/PBO. [d]RRR (95% CI) male vs female UPA/ADA.
ACR 20, ≥20% in improvement in American College of Rheumatology response criteria; ADA, adalimumab; CI, confidence interval; EOW, every other week; LEI=0, Leeds Enthesitis Index=0; MDA, minimal disease activity; ND, no data; PASI 75, 75% improvement in Psoriasis Area Severity Index score; PBO, placebo; QD, once daily; RR, relative risk; RRR, relative risk ratio; UPA, upadacitinib; VAS pain, Visual Analog Scale pain; W, Week.

References

1. Koehm M, et al. *RMD OPEN*. 2023;9:e003538.
2. Eder L, et al. *Lancet Rheumatol*. 2023;5:e716–27.
3. Eder L, et al. *RMD OPEN*. 2023;9:e002718.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

4. McInnes IB, et al. *N Eng J Med*. 2021;384:1227–39.
5. Mease PJ, et al. *Ann Rheum Dis*. 2021;80:312–20.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **A. Hueber**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos/Alfasigma, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **L. Novelli**: AbbVie/Abbott, 3; **T. Gao**: AbbVie, 3, 11; **J. Stigler**: AbbVie, 3, 11; **Z. Du**: AbbVie/Abbott, 3; **R. García Salinas**: AbbVie/Abbott, 2, 5, 6, Adium, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Raffo, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **G. Wright**: AbbVie/Abbott, 2, 5, 6, AstraZeneca, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Scipher Medicine, 2, 5, 6, UCB, 2, 5, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 0558

Early Systemic and Skin Pharmacodynamic Effects of Icotrokinra in Participants with Moderate-to-Severe Plaque Psoriasis: Results Through Week 24 of the Phase 3, ICONIC-LEAD Study

Julianty Angsana[1], Marta Polak[1], Sharan Nischal[1], Elizabeth Chen[1], Deepika Balakrishna[2], Ching-Heng Chou[1], Christopher Sisk[3], Lynn Tomsho[1], Arun Kannan[1], Cynthia DeKlotz[1], Megan Miller[4], Joseph Cafone[3], Paul Newbold[1], Ya-Wen Yang[1], **Monica Leung**[1], Dawn Waterworth[1], Nina Sabins[1], Anna Perillo[5], Andreas Pinter[6] and Robert Bissonnette[7], [1]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, [2]Johnson & Johnson, San Diego, CA, USA, San Diego, USA, [3]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, CA, [4]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, CA, [5]The Rockefeller University, New York, NY, USA, New York, NY, [6]Goethe University Frankfurt, Frankfurt, Germany, Frankfurt, Germany, [7]Innovaderm Research, Montreal, QC, Canada, Montreal, QC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Icotrokinra (ICO), a first-in-class targeted oral peptide that blocks the interleukin (IL)-23R and inhibits IL-23 pathway signaling, is being evaluated in the phase 3 ICONIC-LEAD study in participants ≥12 years with moderate-to-severe plaque psoriasis (PsO). Study co-primary endpoints were met, with ICO demonstrating significantly higher Investigator's Global Assessment (IGA) 0/1 (64.7% vs 8.3%) and Psoriasis Area and Severity Index (PASI) 90 (49.6% vs 4.4%) response rates vs placebo at Week (W) 16 (both $p< 0.001$). ICO pharmacodynamics were assessed via serum protein and skin transcriptomic analyses.

Methods: Participants (N=684) were randomized 2:1 to once-daily ICO 200 mg or placebo through W16. After W16, placebo participants transitioned to ICO (placebo®ICO). Serum collected at W0, W4, and W16 from a sub-cohort (n=166 for IL-22; n=167 for other analytes) and a distinct healthy control cohort (n=30; BioIVT, Hicksville, NY) was analyzed to determine soluble IL-17A, IL-17F, IL-19, IL-22, and BD-2 concentrations. Skin biopsies collected at W0 and W24 from consenting participants of an optional sub-study (n=65) were analyzed for mRNA expression. Comparisons between ICO and placebo used linear mixed-effect modeling that included effects for W0 levels, treatment-over-time interaction, and participant random effect.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Serum IL-17A, IL-17F, IL-19, IL-22, and BD-2 levels were significantly higher in participants with PsO at baseline (W0) vs healthy control ($p< 0.05$). ICO significantly reduced serum biomarker levels vs placebo (all $p< 0.05$ at W4 and W16) and relative to W0 levels as early as W4 ($p< 0.0001$ for all analytes). Serum biomarker concentrations continued to decrease in participants receiving ICO, with levels at W16 (all $p< 0.0001$ vs W0) approaching those of healthy control. At W0, 1026 genes were significantly upregulated and 970 significantly downregulated (adjusted $p< 0.05$) in lesional vs non-lesional skin. At W24, ICO significantly reduced PsO-related gene set enrichment (MAD-3, MAD-5) and gene expression, including *IL17A, IL17F, IL22, IL19, IL23A*, and *DEFB4A* (all $p< 0.0001$ vs W0 lesional) to levels approaching those seen in W0 non-lesional skin. Similar significant reductions were observed after 8 weeks of ICO treatment in the placebo®ICO cohort (all $p< 0.0001$ vs W0 lesional).

Conclusion: Consistent with its mechanism of action of selectively and potently blocking the IL-23R, ICO significantly attenuated systemic and skin biomarkers related to IL-23 pathway activation and PsO disease severity. Findings demonstrated both early and substantial ICO effects, with levels of IL-23 pathway biomarkers of systemic and skin inflammation normalizing to a healthy state. Overall, these comprehensive biomarker findings are consistent with significant skin clearance achieved with this first targeted oral peptide to selectively inhibit IL-23 pathway activation.

Disclosure: J. Angsana: Johnson & Johnson, 3, 11; **M. Polak**: Johnson & Johnson, 3, 11; **S. Nischal**: Johnson & Johnson, 3, 11; **E. Chen**: Johnson & Johnson, 3, 11; **D. Balakrishna**: Johnson & Johnson, 3, 11; **C. Chou**: Johnson & Johnson, 3, 11; **C. Sisk**: Johnson & Johnson, 3, 11; **L. Tomsho**: Johnson & Johnson, 3, 11; **A. Kannan**: Johnson & Johnson, 3, 11; **C. DeKlotz**: Johnson & Johnson, 3, 11; **M. Miller**: Johnson & Johnson, 3, 11; **J. Cafone**: Johnson & Johnson, 3, 11; **P. Newbold**: Johnson & Johnson, 3, 11; **Y. Yang**: Johnson & Johnson, 3, 11; **M. Leung**: Johnson & Johnson, 3, 11; **D. Waterworth**: Johnson & Johnson, 3, 11; **N. Sabins**: Johnson & Johnson, 3, 11; **A. Perillo**: AbbVie, 2, 5, 6, Allergan, 2, 6, Almirall, 2, 6, Amgen, 2, 5, 6, Aristea, 2, 6, Artax Biopharma, 2, 5, 6, Avillion, 5, Biogen Idec, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Bruxelles Biopharma, 5, Calliditas, 2, 6, Eli Lilly, 2, 5, 6, Escalier, 2, 6, Exicure, 5, Immunotherapeutics, 2, 6, Incyte, 2, 5, 6, Innovaderm, 5, Janssen, 2, 5, 6, Kymera Therapeutics, 2, 6, Kyowa Kirin, 2, 5, 6, MC2 Therapeutics, 2, 6, Merck, 2, 6, MoonLake, 2, 6, Novan, 5, Novartis, 2, 5, 6, Nuvig Therapeutics, 2, 6, ONO-Pharma, 5, Oruka Therapeutics, 2, 6, Pfizer, 2, 5, 6, Provectus, 5, Regeneron, 5, Sanofi, 2, 6, SUDO Bio, 5, Sun Pharma, 2, 6, Takeda, 2, 5, 6, Target-Derm, 2, 6, UCB, 2, 5, 6, UNION Therapeutics, 2, 6, Valeant, 2, 6, Ventyx, 2, 6, Vitae Pharmaceuticals, 5; **A. Pinter**: AbbVie, 1, 5, 6, Almirall, 1, 5, 6, Amgen, 1, 5, 6, Biogen Idec, 1, 5, 6, BioNTech, 1, 5, 6, Boehringer Ingelheim, 1, 5, 6, Celgene, 1, 5, 6, Celltrion, 1, 5, 6, Eli Lilly, 1, 5, 6, Galderma, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, GmbH, 1, 5, 6, Hexal, 1, 5, 6, Johnson & Johnson, 1, 5, 6, Klinge Pharma, 1, 5, 6, LEO Pharma, 1, 5, 6, MC2 Therapeutics, 1, 5, 6, Medac, 1, 5, 6, Merck, 1, 5, 6, Mitsubishi, 1, 5, 6, MSD, 1, 5, 6, Novartis, 1, 5, 6, Pascoe, 1, 5, 6, Pfizer, 1, 5, 6, Regeneron, 1, 5, 6, Roche, 1, 5, 6, Sandoz Biopharmaceuticals, 1, 5, 6, Sanofi Genzyme, 1, 5, 6, Schering-Plough, 1, 5, 6, Tigercat Pharma, 1, 5, 6, UCB Pharma, 1, 5, 6, Zuellig Pharma, 1, 5, 6; **R. Bissonnette**: AbbVie, 2, 5, Amgen, 2, 5, Apogee, 2, Arcutis, 2, 5, Asana, 2, Bellus, 5, BioMimetix, 5, Bluefin, 2, Boehringer-Ingelheim, 2, Boston Pharma, 2, Cara Therapeutics, 5, Clexio, 5, Dermavant, 2, 5, Eli Lilly, 2, Escient, 2, 5, Evidera, 2, Fresh Tracks, 5, Galderma, 2, GlaxoSmithKline, 2, Incyte, 2, 5, Innovaderm, 11, Janssen, 2, 5, LEO Pharma, 2, 5, Merck, 5, Novartis, 2, Opsidio, 5, Pfizer, 2, 5, RAPT Therapeutics, 2, Sanofi Genzyme, 2, Sanofi-Aventis, 2, Target RWE, 2, 5, Vyne Therapeutics, 5, Xencor, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0559

Impact of Secukinumab on Cardiovascular Disease in Patients with Psoriasis, PsA, and Axial Spondyloarthritis: A Systematic Review of Existing Evidence

Javier R Godo[1], Christopher EM Griffiths[2], Miguel A. González-Gay[3], Andreas Clemens[4], Cynthia Vizcaya[4], Lara Gómez[5] and **Nehal N Mehta**[6], [1]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, [2]Centre for Dermatology Research, Manchester Academic Health Science Centre, The University of Manchester, Manchester, UK and Department of Dermatology, King's College Hospital NHS Foundation Trust, King's College London, London, United Kingdom, [3]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain, [4]Novartis Pharma AG, Basel, Switzerland, [5]Novartis Farmaceutica, Madrid, Spain, [6]The George Washington University School of Medicine and Health Sciences, Washington DC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriasis, psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) are associated with increased risk of cardiovascular (CV) disease driven by chronic systemic inflammation, with IL-17A thought to play a central pathogenic role. This inflammation contributes to endothelial dysfunction, an early and pivotal step in the development of atherosclerosis, as well as increased arterial stiffness, an important factor in its progression. Secukinumab, a selective IL-17A inhibitor approved across the three indications, may have potential implications for CV health. This review aimed to evaluate the evidence available in the scientific literature on the impact of secukinumab on CV disease in patients with psoriasis, PsA and axSpA, including its effects on vascular function, inflammatory markers, and long-term safety.

Methods: A systematic review of PubMed was performed from database inception to May 2025 according to a pre-defined search strategy (**Table 1**). Results were screened and evaluated for inclusion according to the following criteria: publications describing prospective or retrospective studies or meta-analyses; studies including at least 10 patients treated with secukinumab; studies reporting on at least one of the outcomes of interest (endothelial function, arterial stiffness, systemic inflammation, vascular imaging outcomes, and incidence of major adverse CV events [MACE] including CV death, acute myocardial infarction, stroke, unstable angina, and heart failure). Systematic reviews without meta-analysis, case studies, letters to the editor and commentaries were excluded, as were non-English language publications.

Results: From 198 articles initially returned by the search, 46 were eligible for inclusion (**Figure 1**). These comprised 9 meta-analyses or other pooled analyses, 13 randomised controlled trials, 11 retrospective studies or analyses, 9 prospective studies and 4 observational studies. Twenty publications included patients with psoriasis, 5 included patients with PsA, 11 included patients with axSpA, and 10 included multiple indications. Based on data from over twenty thousand patient-years of exposure, secukinumab did not associate with increased MACE in patients with psoriasis, PsA, or axSpA. Additionally, multiple studies reported improvements in systemic inflammatory markers including C-reactive protein, neutrophil to lymphocyte ratio and markers of oxidative stress, with others reporting favorable impact on vascular health including improvement in endothelial function, reduction in arterial stiffness, and improvement in coronary flow reserve.

Conclusion: Secukinumab was associated with a reduction in systemic inflammation and oxidative stress in multiple studies which also reported a consistent CV safety profile across psoriasis, PsA, and axSpA in terms of incidence of MACE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Emerging evidence from vascular imaging suggests that secukinumab may benefit risk factors of CV disease and markers of vascular health; however, larger, prospective randomized trials are needed to confirm this. Finally, these data suggest that secukinumab may provide benefit beyond the primary disease treatment through important reductions in systemic inflammation.

Disclosure: J. Godo: Amgen, 6, Novartis, 6, UCB, 6; **C. Griffiths**: AbbVie/Abbott, 5, 6, Almirall, 5, 6, Amgen, 5, 6, Anaptysbio, 5, 6, Artax, 5, 6, Boehringer-Ingelheim, 5, 6, Boots UK, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Celltrion, 5, 6, Eli Lilly, 5, 6, Evelo Biosciences, 5, 6, Galderma, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Inmagene, 5, 6, Janssen, 5, 6, Kyowa Kirin, 5, 6, Novartis, 5, 6, ONO Pharmaceuticals, 5, 6, Rubedo, 5, 6, Sun Pharmaceuticals, 5, 6, UCB, 5, 6; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2; **A. Clemens**: Novartis, 3; **C. Vizcaya**: Novartis, 3; **L. Gómez**: Novartis, 3; **N. Mehta**: AbbVie/Abbott, 2, 5, Abcentra, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharmaceuticals, 2, 5, Tourmaline Bio, 2, 5.

Abstract Number: 0560

Single Cell Sequencing Analysis of Tumour Necrosis Factor Inhibitor Drug Response Reveals Enrichment of Pro-inflammatory Pathway in Non-responders and Amino Acid Metabolic Pathways in Responders

Ayantika Talukdar[1], **Phuong Nguyen**[2], Neke Ibeke[3], Rohan Machhar[1], Mansi Aparnathi[1], Archita Srinath[2], Akihiro Nakamura[4], Robert Inman[3], Igor Jurisica[5], Proton Rahman[6], Nigil Haroon[7] and Sareh Keshavarazi[1], [1]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]University Health Network, Toronto, ON, Canada, [4]Queen's University, Kingston, ON, Canada, [5]University Health Network, Toronto, Canada, [6]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada, [7]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing Spondylitis (AS) is a type of chronic inflammatory arthritis affecting the spine and peripheral joints. Although tumor necrosis factor inhibitors (TNFi) substantially improve symptoms, 40% fail to respond. Predictors of treatment response could help make well-informed choices about TNFi treatment at baseline, elucidate mechanism of resistance and explore potential alternative therapeutic targets for TNFi non-responders.

This study aims to identify biomarkers correlating with TNFi treatment response using single cell sequencing in AS patients at baseline.

Methods: PBMCs derived from 7 biologic naïve AS patients (4 responders and 3 non-responders to TNFi treatment) were profiled using droplet-based single cell RNA sequencing technology (10X Genomics). Statistical analysis was carried out using Seurat R package (v5.2.0). The results were then validated using Nanostring nCounter gene expression assay, a highly reproducible and sensitive technique. The cytokines levels were validated using ELISA in the serum of AS patients and the protein expression of CXCR4 and CD74 were determined using flow cytometry on CD14+CD16- monocytes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: As compared to responders, non-responders had a higher proportions of B cells, dendritic cells and monocytes but a lower proportion of T cells. In total PBMCs, 5020 differentially expressed genes were identified among responders and non-responders. CXCR4 and CD74 were found to be upregulated in the monocytes of non-responders which has been further validated in the validation cohort using Nanostring nCounter gene expression assay. Pathway enrichment analysis (i.e., gene set enrichment analysis) of the most significantly changed genes in each response outcome revealed that regulation of osteoclast function, innate immune response, and regulation of T cell activation pathways are among the most enriched pathways in responders. Interferon regulated genes (IRGs) expression and MHC class II regulation was upregulated in non-responders at baseline compared to responders. Upregulated expression of MIF receptor, CD74, in non-responders suggests that monocytes in these patients are activated before the start of treatment and they are involved in the formation of inflammasome, resulting in enhanced inflammatory response. This has been further confirmed by assessing the levels of inflammatory cytokines and chemokines in the serum of patients before and after TNFi treatment using ELISA. We observed that after TNFi treatment, there is a decrease in the levels of CXCL10, CCL4, IL-1b, TNFa and MIF in responders, but not in non-responders.

Conclusion: In non-responders, elevated expression of inflammatory cytokines like IL-17A and IL1b, MIF and its receptors (CXCR4 and CD74)and chemokines like CXCL8, CXCL10 even prior to the commencement of the treatment may be the crucial in preconditioning the immune system towards TNFi treatment resistance in AS patients.

Disclosure: A. Talukdar: None; **P. Nguyen**: None; **N. Ibeke**: None; **R. Machhar**: None; **M. Aparnathi**: None; **A. Srinath**: None; **A. Nakamura**: AbbVie/Abbott, 6, Novartis, 6; **R. Inman**: AbbVie/Abbott, 2, Janssen, 2, Novartis, 2, 5, UCB, 2, 5; **I. Jurisica**: None; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2; **S. Keshavarazi**: None.

Abstract Number: 0561

Patient Characteristics and Treatment Patterns of Traditional and Advanced Therapies Prior to First Secukinumab Intravenous (IV) Administration in Patients with Spondyloarthritis (SpA) in US Real-World Clinical Settings

Alan Kivitz[1], Linda Grinnell-Merrick[2], Tim Nguyen[2], Ariane Faucher[3], Riley Taiji[3], Francis Vekeman[3] and Atul Singhal[4], [1]Altoona Center for Clinical Research, Duncansville, PA, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]STATLOG, Inc, Montreal, QC, Canada, [4]SouthWest Arthritis Research Group, Mesquite, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Since most approved biologics are administered subcutaneously, there is a need for alternate routes of delivery to treat patients with SpA. Secukinumab is an IL-17A inhibitor that was additionally approved for IV administration for SpA. This study described the demographic, clinical and treatment characteristics of patients with SpA who initiated IV secukinumab in real-world clinical settings.

Methods: This retrospective cohort study using HealthVerity claims database included patients who initiated IV secukinumab between Oct 6, 2023 and Oct 31, 2024 (index date = first record), with ≥1 SpA diagnosis code, including psoriatic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Demographic and Clinical Characteristics

Characteristic	IV Secukinumab (N=255)
Age, mean (SD), years[a]	55.5 (13.1)
Age groups, n (%)[a]	
18-24 years	3 (1.2)
25-34 years	9 (3.5)
35-44 years	47 (18.4)
45-54 years	54 (21.2)
55-64 years	89 (34.9)
65+ years	53 (20.8)
Female, n (%)[a]	187 (73.3)
Race, n (%)[a]	
White	88 (34.5)
Black or African American	4 (1.6)
Hispanic	25 (9.8)
Asian	2 (0.8)
Other	3 (1.2)
Unknown	133 (52.2)
Payer type, n (%)[a]	
Commercial	199 (78.0)
Medicare Advantage	27 (10.6)
Medicaid	26 (10.2)
Multiple	2 (0.8)
Unknown	1 (0.4)
SpA type, n (%)[b]	
PsA only	167 (65.5)
axSpA only	65 (25.5)
PsA and axSpA	23 (9.0)
Time from initial SpA diagnosis to index, median (IQR) months[c]	34.6 (14.7-66.7)
Deyo-Charlson Comorbidity Index, mean (SD)[a]	2.8 (2.6)
Most frequent selected comorbidities, n (%)[a]	
Osteoarthritis/osteopenia	165 (64.7)
Neurological disorder	143 (56.1)
Hyperlipidemia	136 (53.3)
Plaque psoriasis	133 (52.2)
Obese/overweight	124 (48.6)
Sleep disorder	103 (40.4)
Anxiety	98 (38.4)

axSpA, axial spondyloarthritis; IQR, interquartile range; IV, intravenous; PsA, psoriatic arthritis; SpA, spondyloarthritis. a Measured at index date or <12 months prior to index. b Measured at index date, <12 months prior to index, or up to 14 days after index date. c Measured <12 months or ≥12 months prior to index.

arthritis (PsA) and axial SpA (axSpA) in 12 months prior to or up to 14 days after index date. Patients had ≥12 months of continuous enrollment (CE) prior to the index date (baseline period) and ≥3 months post-index CE. Patient demographic, clinical, and treatment characteristics were described at the index date, within 12 months prior to index date, or beyond 12 months (baseline period), as indicated. Traditional therapies included corticosteroids, NSAIDS, or conventional synthetic (cs)

Table 2. Traditional and Advanced Therapy Characteristics

Therapy patterns[a]	IV Secukinumab (N=255)
Traditional therapies	
Traditional therapy in 12 months prior to index, n (%)	
Any traditional therapy	188 (73.7)
NSAIDs	94 (36.9)
NSAIDs and no other traditional therapy	8 (3.1)
Corticosteroids	166 (65.1)
Corticosteroids and no other traditional therapy	62 (24.3)
csDMARDs	77 (30.2)
csDMARDs and no other traditional therapy	9 (3.5)
Time from first date of supply to index, median (IQR), months	64.3 (31.0-89.9)
Time from last date of supply to index, median (IQR), months	1.9 (0.5-8.7)
Advanced therapies	
Advanced therapy in 12 months prior to index, n (%)	
Any advanced therapy	95 (37.3)
bDMARDs	85 (33.3)
bDMARDs and no other advanced therapy	72 (28.2)
≥2 bDMARDs	14 (5.49)
tsDMARDs	23 (9.0)
tsDMARDs and no other advanced therapy	10 (3.9)
≥2 tsDMARDs	1 (0.4)
bDMARDs and tsDMARDs	13 (5.1)
Time from first date of supply to index, median (IQR), months	34.2 (17.2-62.3)
Time from last date of supply to index, median (IQR), months	5.4 (2.2-14.1)

bDMARDs, biologic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; IQR, interquartile range; IV, intravenous; NSAIDs, non-steroidal anti-inflammatory drugs; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs. a Measured <12 months or ≥12 months prior to index.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

DMARDs. Advanced therapies included biologic (b)DMARDs, targeted synthetic (ts)DMARDs, or both during the baseline period. Time from the start and end of therapy prior to the index date is reported.

Results: Overall, 255 patients with SpA who initiated IV secukinumab met the eligibility criteria and were included. Most patients were diagnosed with PsA (65.5%), 25.5% of patients were diagnosed with axSpA, and 9.0% of patients had both PsA and axSpA. The mean (SD) age at index date was 55.5 (13.1.) years, and 73.3% were female (**Table 1**). During the 12 months prior to index, the mean (SD) Deyo-Charlson Comorbidity Index score (DCCI) was 2.8 (2.6), and 43.9% of patients had a score of >3.0. Common comorbidities included osteoarthritis/osteopenia (64.7%), neurological disorder (56.1%), plaque psoriasis (52.2%), and obesity (48.6%). The median (interquartile range [IQR]) time from first observed SpA diagnosis to index was 34.6 (14.7-66.7) months. During the 12 months prior to index, 73.7% of all patients used traditional therapies, which included corticosteroids (65.1%), NSAIDs (36.9%) and csDMARDs (30.2%, **Table 2**). The median (IQR) time from first supply of traditional therapy to index was 64.3 (31.0-89.9) months and from last supply was 1.9 (0.5-8.7) months. During the 12 months prior to index, advanced therapies were used by 37.3% of all patients, which included bDMARDs (33.3%), tsDMARDS (9.0%), or a combination of both (5.1%). The median (IQR) time from first supply of advanced therapy to initiation of IV secukinumab was 34.2 (17.2-62.3) months and from last supply was 5.4 (2.2-14.1) months.

Conclusion: In this population of patients with SpA who initiated IV secukinumab, patients were generally older with long-standing disease and high prevalence of comorbidities (e.g., osteoarthritis/osteopenia, neurological disorder, plaque psoriasis, or obesity), which underscores the complexity of SpA disease burden in a diverse group of patients with varied characteristics and health conditions. IV secukinumab was initiated soon after previous treatments, possibly in response to disease progression.

Disclosure: A. Kivitz: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2; **L. Grinnell-Merrick**: Novartis, 3, 11; **T. Nguyen**: Novartis, 3, 11; **A. Faucher**: STATLOG Inc., 3, 12, Employee of STATLOG Inc., which has received funding from Novartis Pharmaceuticals Corporation.; **R. Taiji**: STATLOG Inc., 3, 12, Employee of STATLOG Inc., which has received funding from Novartis Pharmaceuticals Corporation.; **F. Vekeman**: STATLOG Inc., 3, 12, Employee of STATLOG Inc., which has received funding from Novartis Pharmaceuticals Corporation.; **A. Singhal**: AbbVie/Abbott, 5, 6, Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Fujifilm, 5, Gilead, 5, Janssen, 5, Mallinckrodt, 5, MedImmune, 5, Nichi-Iko, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Roche, 5, Sanofi, 5, UCB, 5.

Abstract Number: 0562

Icotrokinra (ICO), a Novel Targeted Oral Peptide, in Patients (Pts) With Psoriatic Disease: Exploratory Assessments From a Phase 2 Psoriasis (PsO) Study Informing a Phase 3 Clinical Program in Psoriatic Arthritis (PsA)

Joseph F Merola[1], Philip J. Mease[2], Laura Coates[3], Iain McInnes[4], Peter Nash[5], **Alexis Ogdie**[6], Lihi Eder[7], mitsumasa kishimoto[8], Anna Beutler[9], Konstantina Psachoulia[9], Shihong Sheng[10], Bei Zhou[11], Mehrdad Javidi[12], Chandni Valiathan[12], Charles Iaconangelo[10], Ya-Wen Yang[13], Arun Kannan[13], Chetan S. Karyekar[9] and Tasneam Shagroni[9], [1]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [4]University of Glasgow, Glasgow, United Kingdom, [5]Griffith University and U of Queensland, Maroochydore, Queensland, Australia, Queensland, Australia, [6]University of Pennsylvania, Philadelphia, PA, [7]University of Toronto, Toronto, ON, Canada, [8]Kyorin

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University School of Medicine, Tokyo, Japan, [9]Johnson & Johnson, Spring House, PA, USA, Spring House, [10]Johnson & Johnson, Chesterbrook, PA, USA, Chesterbrook, [11]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [12]Johnson & Johnson, San Diego, CA, USA, San Diego, [13]Johnson & Johnson, San Diego, CA, USA, San Diego, CA

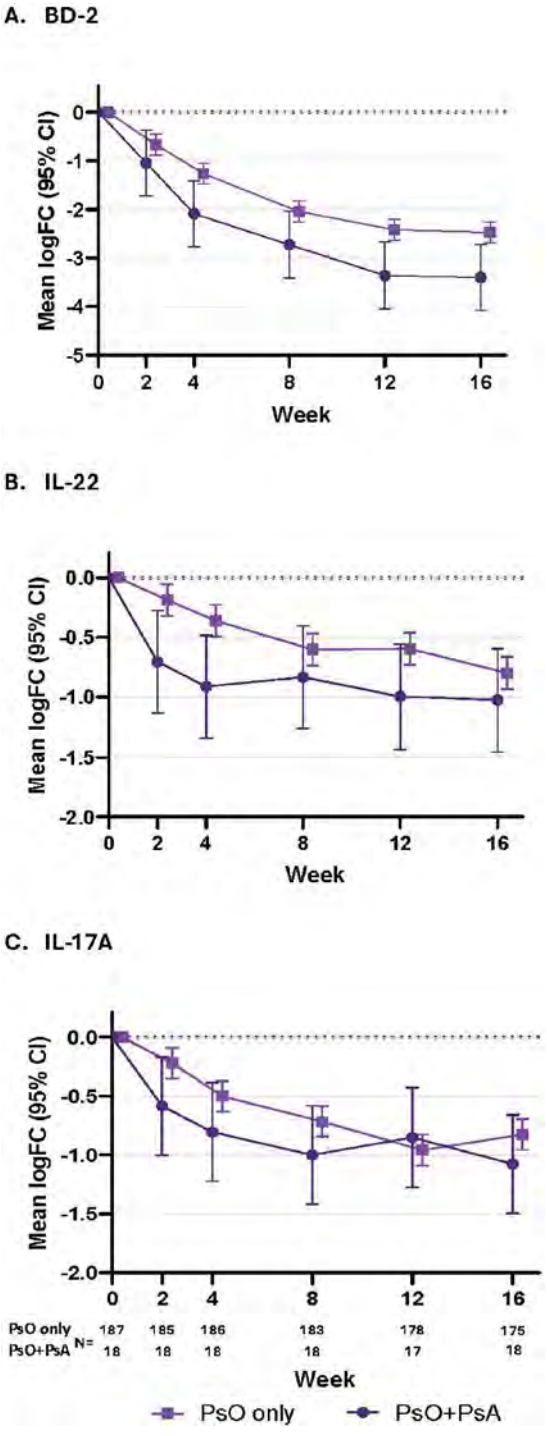
SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM



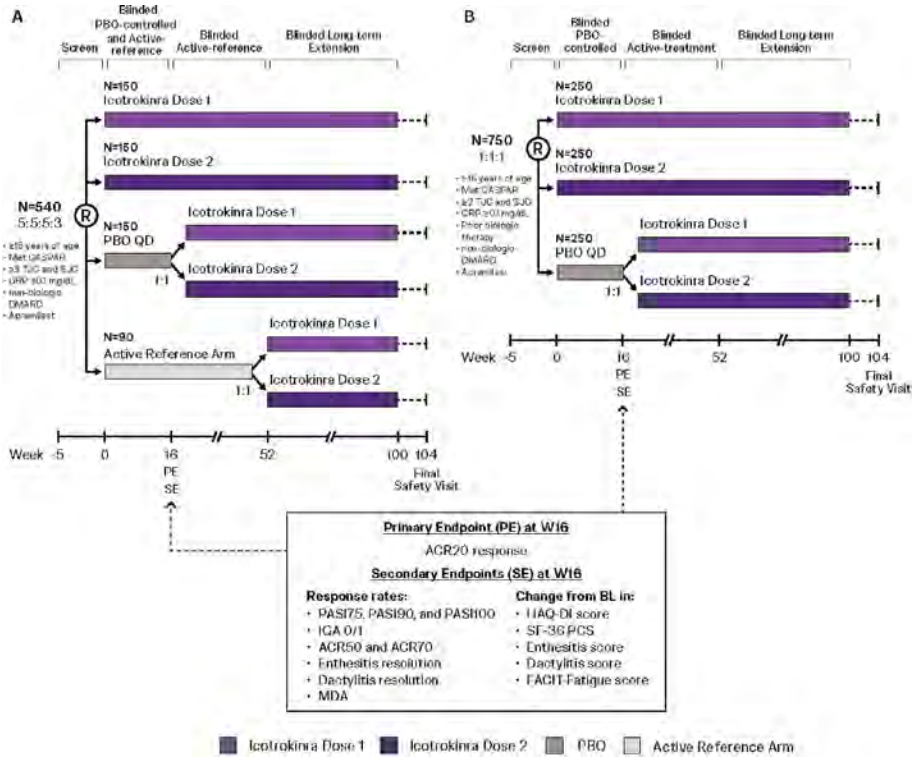
Mean change in serum BD-2 (A), IL-22 (B), and IL-17A (C) levels through W16 in FRONTIER 1 participants with PsO only and PsO+PsA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: PsA affects ~20-30% of pts with PsO, causing articular inflammation/damage, and impaired health-related quality of life (HRQoL). ICO, a novel targeted oral peptide that binds IL-23 Receptor, showed greater clinical response rates vs placebo (PBO) and a favorable safety profile in pts with moderate-to-severe plaque PsO in the Ph 2 FRONTIER 1&2 studies. We leveraged exploratory serum biomarker, Pt Reported Outcomes Measurement Information Systems (PROMIS-29), and Psoriasis Area and Severity Index 75% improvement (PASI75) data from a subset of FRONTIER 1 pts with PsO and PsA medical history (PsO+PsA) to support Ph 3 ICONIC-PsA 1 and ICONIC-PsA 2 studies.

Methods: Mean log fold-changes (logFC) in serum β-Defensin-2 (BD-2), IL-22, IL-17A, and IL-17F levels were summarized for FRONTIER pts with PsO only, and with PsO+PsA. Pts reported HRQoL via PROMIS-29 questionnaire. Improvements ≥5-points in PROMIS-29 domain scores (or ≥2 for pain), and physical/mental component summary (PCS/MCS) scores, are considered clinically meaningful. ICO PsA Ph 3 sample sizes were informed by ample safety data to support regulatory submission and estimates from model-based analyses, including a meta-analysis that bridged FRONTIER 1 PASI75 to expected American College of Rheumatology 20% improvement (ACR20) at Week (W)16 (primary endpoint) and meta-regression modeling that bridged ACR20 to secondary endpoints, ACR50/70, PASI90/100, Minimal Disease Activity.

Results: 23/91 (25%) FRONTIER 1 pts had PsO+PsA (ICO, n=20; PBO, n=3). Among pts with evaluable biomarker data, mean logFC in serum BD-2, IL-22, IL-17A (**Fig 1A-C**), and IL-17F (data not shown) over time indicated consistent ICO pharmacodynamic (PD) effect between pts with PsO only and with PsO+PsA. ICO-treated PsO+PsA pts reported numerically greater mean changes from baseline (BL) at W16 vs PBO across PsA relevant PROMIS-29 domains, ie, improvements in physical function (7.7 vs 1) and reductions in fatigue (-7.4 vs 2.3 [worsening]), pain interference (-10.7 vs -1.3), and pain intensity (- 3.5 vs -1.5). In 20 ICO-treated pts with PsO+PsA, 45% and 70% reported ≥5 point improvement from BL in PROMIS-29 PCS and MCS scores, respectively, vs no pts receiving PBO. ICONIC-PsA 1&2 sample sizes of 540 (5:5:5:3 to ICO Dose 1/2/PBO/active reference arm with no formal statistical comparisons; **Fig 2A**) and 750 (1:1:1 to ICO Dose 1/2/PBO; **Fig 2B**) were estimated to provide ≥90% power to detect significant ICO vs PBO difference between ICO and PBO. Given minorities are often under-recruited in PsA trials, the ICO PsA program aims to assess diverse pts, of different racial/ethnicities.



ICONIC PsA-1 (biologic-naïve [A]) and ICONIC PsA-2 (biologic-experienced [B]) study designs

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Exploratory assessments from the Ph 2 FRONTIER 1 study showed comparable ICO PD effects between pts with PsO only, and with PsO+PsA. ICO-treated pts with PsO+PsA reported numerically greater improvements in PsA-relevant PROMIS-29 domains vs PBO. Informed by these post hoc analyses and model-based meta-analyses that bridged data from PsO to PsA, the multicenter, double-blind, PBO-controlled ICONIC-PsA 1 and ICONIC-PsA 2 studies will comprehensively evaluate the novel targeted oral peptide ICO in diverse population of pts with active PsA.

Disclosure: J. Merola: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **P. Nash**: AbbVie, 1, 2, 5, Amgen, 1, 2, 5, Boehringer Ingelheim, 1, 2, 5, Bristol Myers Squibb, 1, 2, 5, Celgene, 1, 2, 5, Eli Lilly, 1, 2, 5, Galapagos, 1, 2, 5, GlaxoSmithKline, 1, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, Sun Pharma, 1, 2, 5, UCB, 1, 2, 5; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **A. Beutler**: Johnson & Johnson, 3; **K. Psachoulia**: Johnson & Johnson, 3, 11; **S. Sheng**: Johnson & Johnson, 3, 11; **B. Zhou**: Johnson & Johnson, 3, 11; **M. Javidi**: Johnson & Johnson, 3, 11; **C. Valiathan**: Johnson & Johnson, 3, 11; **C. Iaconangelo**: Johnson & Johnson, 3, 11; **Y. Yang**: Johnson & Johnson, 3, 11; **A. Kannan**: Johnson & Johnson, 3, 11; **C. Karyekar**: Johnson & Johnson, 3, 11; **T. Shagroni**: Johnson & Johnson, 3, 11.

Abstract Number: 0563

Efficacy and Safety of Guselkumab in Patients with Active Psoriatic Arthritis and Inadequate Response and/or Intolerance to One Prior Tumor Necrosis Factor Inhibitor

Alexis Ogdie[1], Joseph F Merola[2], Philip J. Mease[3], Christopher Ritchlin[4], Jose U. Scher[5], Kimberly Parnell Lafferty[6], Daphne Chan[7], Soumya Chakravarty[8], Wayne Langholff[9], Yanli Wang[9], Olivia Choi, MD, PhD, FAAD[7], Yevgeniy Krol[10] and Alice Gottlieb[11], [1]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [2]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [3]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [4]University of Rochester Medical Center, Canandaigua, NY, [5]New York University School of Medicine, New York, NY, [6]Johnson & Johnson, Dermatology, Horsham, PA, [7]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [8]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [9]Johnson & Johnson, Biostatistics, Spring House, PA, [10]Johnson & Johnson, Horsham, PA, [11]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Guselkumab (GUS), a fully human IL-23p19-subunit inhibitor, has demonstrated efficacy in significantly improving psoriatic arthritis (PsA) signs and symptoms with two dosing regimens: 100 mg every 4 weeks (Q4W) or 100 mg at Week (W)0, W4, then Q8W, in the pivotal Phase 3 DISCOVER-1&2 studies.[1,2] SOLSTICE, an ongoing Phase 3b, multicenter, randomized, double-blinded placebo-controlled study, was designed to evaluate the efficacy and safety of GUS Q4W and Q8W in a dedicated participant (pt) population with active PsA who were inadequate responders (IR [inadequate efficacy and/or intolerance]) to one prior tumor necrosis factor inhibitor (TNFi).

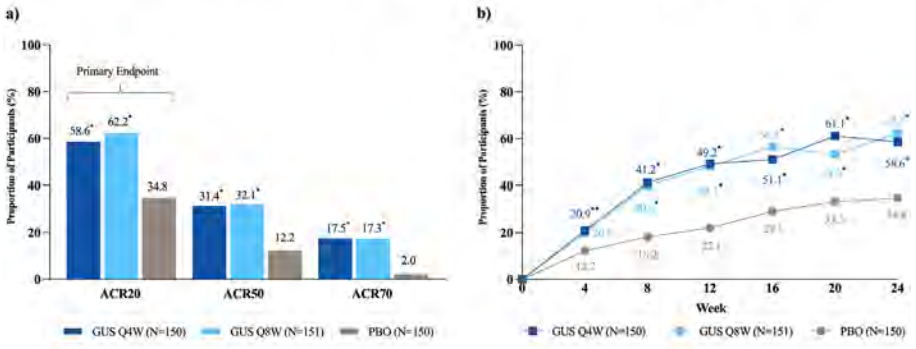
Methods: Adults (≥18 years) with active PsA (≥3 swollen joints; ≥3 tender joints; C-reactive protein [CRP] ≥0.3 mg/dL) who were TNFi-IR to one prior TNFi were eligible to be enrolled from 128 sites across 12 countries. Pts were randomized 1:1:1 to GUS 100 mg Q4W; GUS at W0, W4, then Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24. Randomization was stratified by baseline use of conventional synthetic disease-modifying antirheumatic drugs. The primary endpoint was defined as achievement of an ACR20 response at W24. Major secondary endpoints included the proportions of pts achieving ACR50/70, Investigator's Global Assessment of psoriasis response (IGA 0/1 and ≥2-grade improvement), ≥90% improvement in Psoriasis Area and Severity Index (PASI 90), and minimal disease activity (MDA) at W24.

Table. Baseline Demographics and Disease Characteristics by Treatment Group

	GUS 100 mg Q4W	GUS 100 mg Q8W	PBO
Participants, N	150	151	150
Age, years	50.6 (13.3)	51.9 (12.9)	49.2 (12.6)
Female, n (%)	75 (50.0)	77 (51.0)	85 (56.7)
Weight,[a] kg	86.5 (20.8)	89.5 (19.8)	85.9 (21.1)
SJC [0-66]	10.7 (7.8)	10.3 (6.6)	10.2 (6.4)
TJC [0-68]	18.1 (12.6)	17.1 (11.2)	16.8 (11.6)
PhGA[b] [VAS; 0-10 cm]	6.5 (1.5)	6.7 (1.6)	6.5 (1.6)
CRP [mg/dL]	1.2 (1.6)	1.3 (1.7)	1.4 (1.9)
IGA[c,d] ≥2, n (%)	106 (71.1)	105 (70.0)	111 (76.6)
PASI[d,e] [0-72]	10.4 (9.5)	10.1 (9.4)	9.0 (6.5)

Data presented as mean (standard deviation) unless otherwise noted. [a]PBO N=148. [b]GUS Q4W N=149, PBO N=147. [c]GUS Q4W N=149, GUS Q8W N=150, PBO N=145. [d]Among participants with ≥3% body surface area affected by psoriasis and IGA ≥2 at baseline. [e]GUS Q4W N=92, GUS Q8W N=89, PBO N=86. CRP=C-reactive protein; GUS=Guselkumab; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PBO=placebo; PhGA=Physician's global assessment (arthritis); Q4W=every 4 weeks; Q8W=every 8 weeks; SJC=swollen joint count; TJC=tender joint count; VAS=Visual Analog Scale.

Figure 1. a) Proportion of Participants Achieving ACR20/50/70 at Week 24; b) ACR20 Through Week 24

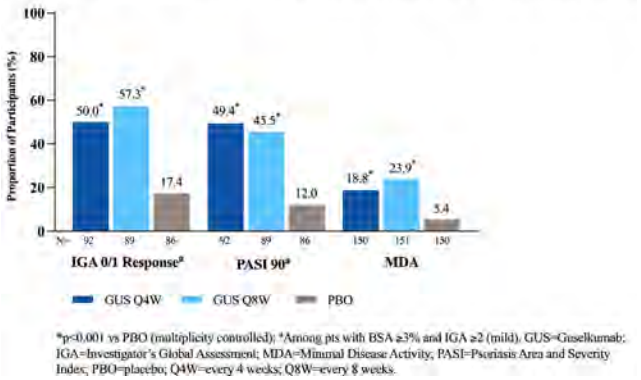


*p<0.001 vs PBO. ACR=American College of Rheumatology; GUS=Guselkumab; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks.

*p<0.001 vs PBO (only W24 is multiplicity controlled); **p=0.042 vs PBO. GUS=Guselkumab; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Proportion of Participants Achieving IGA 0/1 Response, PASI 90, and MDA at Week 24



*p<0.001 vs PBO (multiplicity controlled); *Among pts with BSA ≥3% and IGA ≥2 (mild). GUS=Guselkumab; IGA=Investigator's Global Assessment; MDA=Minimal Disease Activity; PASI=Psoriasis Area and Severity Index; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks.

Results: A total of 451 pts (Q4W n=150, Q8W n=151, PBO n=150) were included in the analysis set. Baseline characteristics were well balanced among treatment groups (mean at baseline: 50.6 years, 87.3 kg, 52.6% female; Table). Discontinuation rates were comparable between GUS Q4W (5.3% [8/150]), Q8W (4.6% [7/151]), and slightly higher for PBO (7.4%, [11/149]). Significantly greater proportions of pts in the Q4W and Q8W vs PBO groups achieved ACR20 at W24 (58.6% and 62.2% vs 34.8%, respectively), ACR50 (31.4% and 32.1% vs 12.2%, respectively), and ACR70 (17.5% and 17.3% vs 2.0%, respectively); p< 0.001 for all (Figure 1a). Through W24, Q4W and Q8W groups start achieving ACR20 as early as W4, compared to the PBO group (Figure 1b). GUS-treated pts in the Q4W and Q8W treatment groups also had significantly greater response rates at W24 vs PBO for MDA (18.8% and 23.9% vs 5.4%, respectively), IGA 0/1 response (50.0% and 57.3% vs 17.4%, respectively), and PASI 90 (49.4% and 45.5% vs 12.0%, respectively); p< 0.001 for all (Figure 2). Through W24, 49.5% of pts had ≥1 adverse event (AE), and 2.6% had ≥1 serious adverse event (SAE). Overall, the frequency of AEs and SAEs was similar across treatment groups and comparable to PBO.

Conclusion: In the TNFi-IR PsA population from SOLSTICE, GUS demonstrated superior efficacy vs PBO for improving signs and symptoms of peripheral arthritis and skin psoriasis. Both the GUS Q4W and Q8W dosing regimens were equally efficacious in this treatment refractory PsA population. Safety findings were consistent with the known safety profile of GUS in pts with psoriatic disease.[3]

References:

1. Deodhar A, et al. *Lancet*. 2020;1115-25.
2. Mease PJ, et al. *Lancet*. 2020;395:1126–36.
3. Strober, B, et al. *Drug Safety*. 2024;47, 39–57.

Disclosure: A. Ogdie: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **J. Scher**: Bristol Myers Squibb, 2, Johnson & Johnson, 2, 5, Pfizer, 2, 5, UCB, 2; **K. Parnell Lafferty**: Johnson & Johnson, 3, 11; **D. Chan**: Johnson & Johnson, 3, 11; **S. Chakravarty**: Johnson & Johnson, 3, 11; **W. Langholff**: Johnson & Johnson, 3, 11; **Y. Wang**: IQVIA, 3, Johnson & Johnson, 12, Statistical support funded by Johnson & Johnson; **O. Choi, MD, PhD, FAAD**: Apogee Therapeutics Inc., 3, Johnson & Johnson, 11, 12, Employee of Johnson & Johnson at the time study was conducted; **Y. Krol**: Johnson & Johnson,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3, 11; **A. Gottlieb**: Amgen, 1, 2, 6, Avalo Therapeutics, 5, Bristol Myers Squibb, 5, Eli Lilly, 1, 2, 6, Highlights Therapeutics, 1, 2, 6, MoonLake, 5, Novartis, 1, 2, 6, Sanofi, 1, 2, 6, Sun Pharma, 1, 2, 6, Takeda, 1, 2, 6, Teva, 1, 2, 6, UCB, 1, 2, 5, 6, Xbiotech, 1, 2, 6.

Abstract Number: 0564

Improvements in Patient Reported Outcomes Through 24 Weeks of Guselkumab Treatment in Participants with Active Psoriatic Arthritis and Inadequate Response and/or Intolerance to One Prior Tumor Necrosis Factor Inhibitor

Alice Gottlieb[1], Joseph F Merola[2], Philip J. Mease[3], Christopher Ritchlin[4], Jose U. Scher[5], Kimberly Parnell Lafferty[6], Daphne Chan[7], Soumya Chakravarty[8], Wayne Langholff[9], Yanli Wang[9], Olivia Choi, MD, PhD, FAAD[7], Yevgeniy Krol[10] and Alexis Ogdie[11], [1]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX, [2]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [3]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [4]University of Rochester Medical Center, Canandaigua, NY, [5]New York University School of Medicine, New York, NY, [6]Johnson & Johnson, Dermatology, Horsham, PA, [7]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [8]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [9]Johnson & Johnson, Biostatistics, Spring House, PA, [10]Johnson & Johnson, Horsham, PA, [11]University of Pennsylvania School of Medicine, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Guselkumab (GUS), a fully human IL-23p19-subunit inhibitor, has demonstrated efficacy in significantly improving psoriatic arthritis (PsA) signs and symptoms in participants (pts) with active PsA irrespective of prior tumor necrosis factor inhibitor (TNFi) experience. SOLSTICE is an ongoing Phase 3b, multicenter, randomized, double-blinded placebo-controlled study designed to evaluate the efficacy and safety of GUS on signs and symptoms of PsA disease specific patient reported outcomes (PROs), with two maintenance dosing regimens of 100 mg every 4 weeks (Q4W) and Q8W, in a dedicated PsA pt population who were inadequate responders (IR [inadequate efficacy and/or intolerance]) to one prior TNFi.

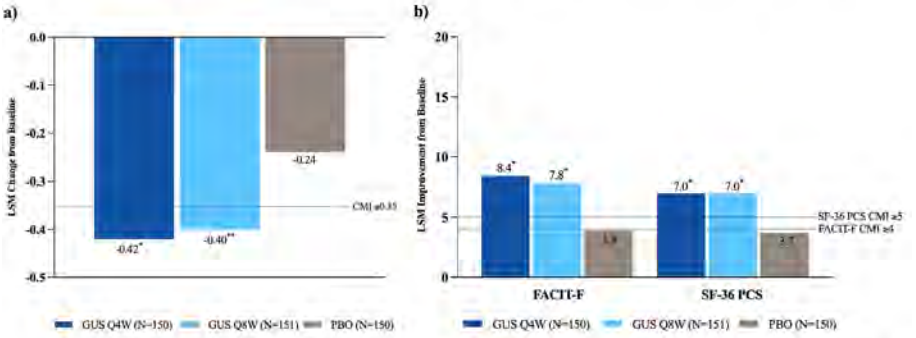
Table. Baseline Disease Characteristics and Patient Reported Outcomes by Treatment Group

	GUS 100 mg Q4W	GUS 100 mg Q8W	PBO
Participants, N	150	151	150
HAQ-DI			
Baseline (0-3)	1.3	1.3	1.3
LSM change from baseline at W24	-0.4	-0.4	-0.2
Response (improvement ≥0.35) at W24, n (%)	55.8	52.8	35.4
SF-36 PCS			
Baseline (0-100)	34.2	33.6	33.9
LSM change from baseline at W24	7.0	7.0	3.7
FACIT-F			
Baseline (0-52)	28.3	28.2	27.6
LSM change from baseline at W24	8.4	7.8	3.9
Response (improvement ≥4) at W24, n (%)	63.0	63.9	38.0

Data presented as mean (standard deviation) unless otherwise noted. FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; LSM=Least Squares Mean; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36 PCS=36-item Short-Form Health Survey Physical Component Summary; W=Week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. a) Least Squares Mean Change from Baseline in HAQ-DI at Week 24; b) Least Squares Mean Change from Baseline in FACIT-F and SF-36 PCS at Week 24



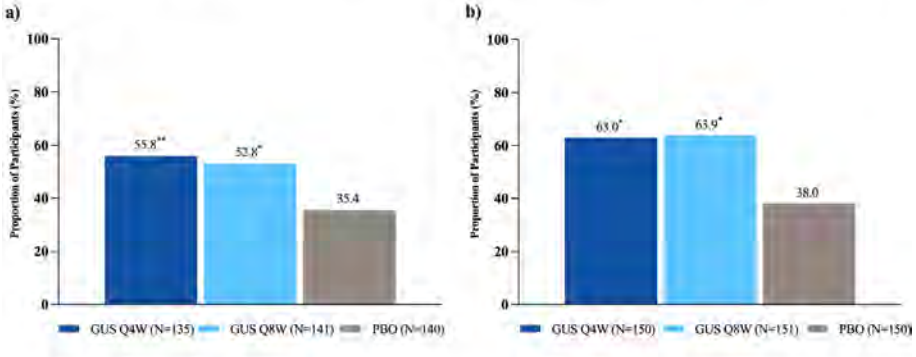
*p=0.003 vs PBO, **p=0.008 vs PBO (both multiplicity controlled); CMI=Clinically Meaningful Improvement; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; LSM=Least Squares Mean; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks.

*p<0.001 vs PBO (multiplicity controlled); CMI=Clinically Meaningful Improvement; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; GUS=Guselkumab; LSM=Least Squares Mean; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36 PCS=36-item Short-Form Health Survey Physical Component Summary.

Methods: Adults (≥18 years) with active PsA (≥3 swollen joints; ≥3 tender joints; C-reactive protein [CRP] ≥0.3 mg/dL) who were TNFi-IR to one prior TNFi were eligible to be enrolled from 128 sites across 12 countries. Pts were randomized 1:1:1 to GUS 100 mg Q4W; GUS at Week (W)0, W4, then Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24. The major secondary PRO endpoints at W24 were mean change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI; physical function), 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS; overall Health-related Quality of Life [HRQoL]), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT- F) scores. Proportions of pts achieving clinically meaningful improvements for HAQ-DI response (improvement ≥0.35) and FACIT-F response (improvement ≥4) were prespecified endpoints, but not multiplicity-controlled.

Results: A total of 451 participants (Q4W n=150, Q8W n=151, PBO n=150) were included in the analysis. On average, pts had moderate to severe impairment of physical function at baseline that is consistent with an active PsA population (Table). At W24, greater improvements in HAQ-DI, SF-36 PCS, and FACIT-F scores were observed in both treatment groups vs the PBO group (Table). A significantly greater reduction from baseline in HAQ-DI score was observed at W24 in the Q4W (-0.42, p=0.003) and Q8W (-0.40, p=0.008) groups, vs PBO (-0.24) group (Figure 1a). Furthermore, significantly greater improvement from baseline was observed in the Q4W and Q8W groups vs PBO group for SF-36 PCS (7.0 and 7.0 vs 3.7, respectively) and FACIT-F (8.4 and 7.8 vs 3.9, respectively); p< 0.001 for both (Figure 1b). Among pts with a baseline score of ≥0.35, the proportion of pts who achieved HAQ-DI response at W24 in the Q4W and Q8W groups vs PBO group were,

Figure 2. a) Proportions of Participants Achieving Clinically Meaningful Improvements in HAQ-DI Response at Week 24 Among Participants with a Baseline Score of ≥0.35; b) Proportions of Participants Achieving Clinically Meaningful Improvements ≥4 in FACIT-F Response at Week 24



*p=0.001 vs PBO, **p=0.003 vs PBO; GUS=Guselkumab; HAQ-DI=Health Assessment Questionnaire-Disability Index; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks.

*p=0.001 vs PBO; GUS=Guselkumab; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; PBO=placebo; Q4W=every 4 weeks; Q8W=every 8 weeks.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

55.8% (p< 0.001) and 52.8% (p=0.003) vs 35.4%, respectively (Figure 2a). Greater proportions of pts achieved clinically meaningful improvement in FACIT-F response in the Q4W (63.0%) and Q8W (63.9%) groups (p< 0.001 for both) vs PBO (38.0%) group (Figure 2b).

Conclusion: In the TNFi-IR PsA population from SOLSTICE, both GUS dosing regimens demonstrated superior efficacy vs PBO for improving physical function, overall HRQoL, and fatigue at W24. These data reinforce the effectiveness of GUS irrespective of dosing regimen in the TNFi-IR population across multi-domain measures of efficacy and PROs.

Disclosure: A. Gottlieb: Amgen, 1, 2, 6, Avalo Therapeutics, 5, Bristol Myers Squibb, 5, Eli Lilly, 1, 2, 6, Highlights Therapeutics, 1, 2, 6, MoonLake, 5, Novartis, 1, 2, 6, Sanofi, 1, 2, 6, Sun Pharma, 1, 2, 6, Takeda, 1, 2, 6, Teva, 1, 2, 6, UCB, 1, 2, 5, 6, Xbiotech, 1, 2, 6; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **J. Scher**: Bristol Myers Squibb, 2, Johnson & Johnson, 2, 5, Pfizer, 2, 5, UCB, 2; **K. Parnell Lafferty**: Johnson & Johnson, 3, 11; **D. Chan**: Johnson & Johnson, 3, 11; **S. Chakravarty**: Johnson & Johnson, 3, 11; **W. Langholff**: Johnson & Johnson, 3, 11; **Y. Wang**: IQVIA, 3, Johnson & Johnson, 12, Statistical support funded by Johnson & Johnson; **O. Choi, MD, PhD, FAAD**: Apogee Therapeutics Inc., 3, Johnson & Johnson, 11, 12, Employee of Johnson & Johnson at the time study was conducted; **Y. Krol**: Johnson & Johnson, 3, 11; **A. Ogdie**: AbbVie, 1, 2, 5, Amgen, 1, 2, 5, Bristol Myers Squibb, 1, 2, Celgene, 1, 2, CorEvitas, 1, 2, Eli Lilly, 1, 2, Gilead, 1, 2, Glaxo Smith Klein, 1, 2, Johnson & Johnson, 1, 2, National Psoriasis Foundation, 5, NIAMS, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, Rheumatology Research Foundation, 5, UCB, 1, 2, University of Pennsylvania, 5.

Abstract Number: 0565

Combination of Biological and Targeted Synthetic Disease-Modifying Antirheumatic Drugs in Psoriatic Arthritis: A Case-Series

Andre Lucas Ribeiro[1], Virginia Carrizo Abarza[2], Jensen Yeung[3], Khalad Maliyar[3], Siddhartha Sood[3], Ahmet Bagit[3], Muskaan Sachdeva[3], Sahil Koppikar[4], Dafna D. Gladman[5], Vinod Chandran[6] and Lihi Eder[6], [1]Hospital de Clínicas de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil, [2]Toronto Western Hospital - University of Toronto, Toronto, ON, Canada, [3]Women's College Hospital & University of Toronto, Toronto, ON, Canada, [4]Women's College Hospital & University of Toronto, Markham, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite advances in psoriatic arthritis (PsA) treatment, remission remains elusive for many patients. This has prompted growing interest in combining biologic and targeted synthetic DMARDs (b/tsDMARDs). However, real-world data on such combinations are limited. This case series evaluates clinical outcomes and safety of b/tsDMARD combinations in PsA patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and clinical characteristics of patients on combined bDMARD and JAK/TYK2i.

Clinical Characteristics	Patient ID								
	#1	#2	#3	#4	#5	#6	#7	#8	#9
Age	64	36	52	47	41	50	65	64	44
Sex	Female	Female	Female	Male	Female	Female	Male	Female	Female
Race	White	Arab	White	Asian	White	White	Asian	Mixed	White
Disease duration (years)	41	14	23	5	5	2	8	9	2
Body mass index	24.4	38.8	29.7	37.7	30.8	40.6	30.4	31.2	63.1
Fibromyalgia	No	No	No	No	No	No	Yes	No	No
Depression / Anxiety	No	No	No	No	Yes	No	Yes	No	No
Inflammatory bowel disease	No	No	No	No	No	No	No	No	No
Uveitis	No	No	No	No	No	No	No	No	No
Nº of previous csDMARDs	5	2	2	2	2	3	2	3	2
Nº of previous b/tsDMARDs	7	7	2	7	3	8	3	4	4
Combined therapy	IXE + TOFA	IXE + UPA	GUS + DEUC	BIME + DEUC	GUS + DEUC	BIME + UPA	RIS + DEUC	CER + DEUC	SEC + DEUC
Reason for combination	Peripheral arthritis	PeA + PsO	PeA + PsO	Psoriasis Nails	Ent + PsO	PeA + PPP	PeA + PPP	PeA + PsO	PeA
Tender joint count	32	13	2	0	1	1	9	3	5
Swollen joint count	0	24	0	0	1	3	0	0	5
DAPSA	47.1	52.4	8.1	11.2	9.5	18.9	25.8	NA	23.7
PASI	0	13.4	16.2	1.2	1	2.2	5.4	4.2	5.4
Follow-up duration	1751 days	239 days	189 days	259 days	200 days	748 days	322 days	324 days	214 days
Treatment outcome	Continue therapy	Continue therapy	Continue therapy	Continue therapy	Continue therapy	Continue therapy	Continue therapy	Continue therapy	Stopped therapy

BMI, body mass index; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; b/tsDMARDs, biologic/target synthetic DMARDs; TJC, tender joint count; SJC, swollen joint count; DAPSA, Disease Activity in Psoriatic Arthritis; PASI, psoriasis area and severity index; IXE, ixekizumab; TOFA, tofacitinib; UPA, upadacitinib; GUS, guselkumab; DEUC, deucravacitinib; BIME, bimekizumab; RIS, risankizumab; CER, certolizumab; SEC, secukinumab; PeA, peripheral arthritis; PsO, plaque psoriasis; Ent, enthesitis; PPP, palmoplantar psoriasis; IL23i, interleukin 23 inhibitor; IL17i, interleukin 17 inhibitor; JAKi, janus kinase inhibitor.

Methods: Case series of PsA patients receiving combined b/tsDMARD therapy, including TNFi, JAKi, TYK2i, IL17i, IL23i, IL-12/23i for effectiveness and safety. Combinations with Apremilast (APR) were analyzed for safety. Clinical and safety data were prospectively collected using standardized instruments within a longitudinal PsA cohort, and supplemented via chart review. Effectiveness was assessed by changes in joint counts, DAPSA, PASI, BSA, and patient-reported outcomes (NRS for pain, skin, and global) at 3-6 and 6-12 months. Safety outcomes included infections and non-infectious adverse events (AEs).

Results: We identified 22 patients treated with bDMARDs + JAKi or TYK2i, some with multiple regimens. Eleven (50%) were female. Complete information on PsA measure of activity was available for 9 patients (**Table 1**), while 13 had partial data, including age, sex, skin activity, and AEs. Numerical improvements were observed across disease activity measures, with **Figure 1** showing patients with visits in the prespecified timeframes, and **Table 2** showing the safety data.

Table 2. Safety analysis. IL17i, interleukin 17 inhibitor; tsDMARD, target-synthetic disease-modifying antirheumatic drug; IL23i, interleukin 23 inhibitor; TNFi, tumor necrosis factor inhibitor; IL12/23i, interleukin 12/23 inhibitor; JAKi, janus kinase inhibitor.

Drug Combination	Total Duration (days)	Total Duration (patient-years)	Adverse events (number)	Side Effect Description	Incidence Rate (per 100 patient-years)
IL17 + TYK2	3,229	8.5	2	Two upper respiratory infections (Bimekizumab + Deucravacitinib)	25.3
IL17 + JAKi	4,145	11.35	1	Infectious stomatitis (Ixekizumab + Tofacitinib)	8.81
IL23 + TYK2	3,215	9.1	4	Two upper respiratory infections One worsening of folliculitis (Guselkumab + Deucravacitinib)	32.97
IL23 + JAKi	1,337	3.7	0	None	0.00
TNF + TYK2	324	0.89	0	None	0.00

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

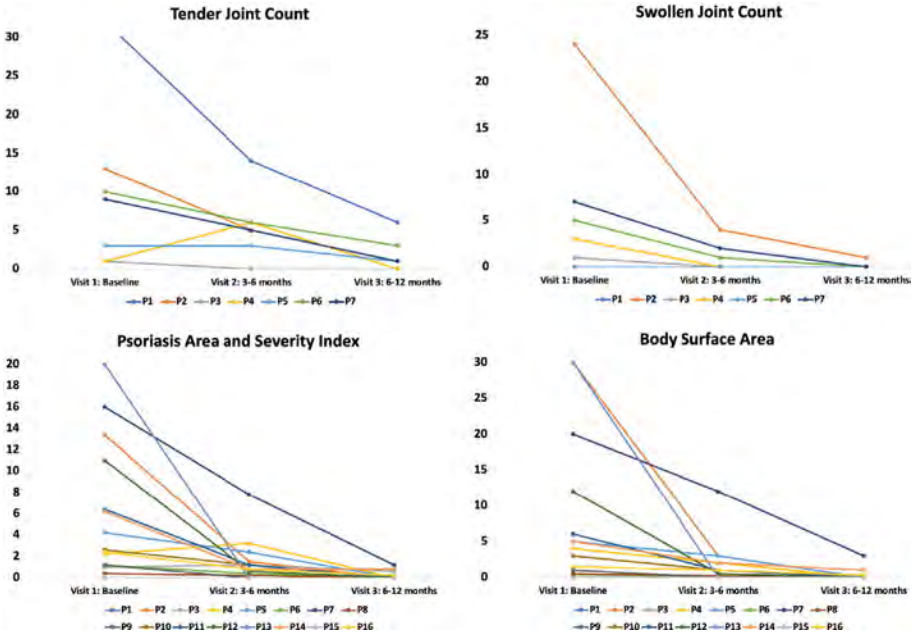


Figure 1. Individual trajectories after starting combined therapy for patients with follow-ups according to protocol.

In the bDMARD + JAKi group (n=6), IL17i + JAKi were the most frequent combinations (n=4), used for 4,145 days (11.35 patient-years [PY]). One case of mild infectious stomatitis was reported, but treatment was not discontinued. IL23i + JAKi (n=2), used for 1,337 days (3.7 PY), had no AEs.

For the bDMARD + TYK2i group (n=19), IL-17i + TYK2i (n=9) were used for 3,229 days (8.5 PY). One patient experienced two mild upper respiratory infections (URIs) on bimekizumab and deucravacitinib, prompting a switch for risankizumab with deucravacitinib. IL-23i with TYK2i (n=10) were used for 3,325 days (9.1 PY), with two cases of mild URIs leading to a switch to bimekizumab monotherapy, and one case of folliculitis, where therapy was continued. One patient received TNFi + TYK2i for 324 days (0.9 PY), with no AEs.

We identified 16 patients on bDMARDs + APR (total of 22 combinations, with a median duration of 825 days), including IL12/23i or IL23i + APR (8 combinations, duration: 360–2,250 days), IL17i + APR (8 combinations, duration: 90–2,790 days), TNFi + APR (5 combinations, duration: 180–2,340 days), and JAKi + APR (1 combination, 540 days). Two cases of diarrhea were observed, but no infections occurred.

Conclusion: Overall, the safety profile of bDMARD combinations with tsDMARDs was favorable. Infections, primarily URIs, were the most common AEs – mild in severity, non-hospitalized, and rarely requiring treatment change. Short-term improvements were observed in both musculoskeletal and skin domains. Our findings, drawn from a prospective cohort with standardized data collection, support the effectiveness and safety of combination therapy in selected PsA cases. Randomized controlled trials are needed to confirm long-term efficacy and safety.

Disclosure: A. Lucas Ribeiro: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 2, 6, Novartis, 6, UCB, 5, 6; **V. Carrizo Abarza**: None; **J. Yeung**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Janssen, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **K. Maliyar**: None; **S. Sood**: None; **A. Bagit**: None; **M. Sachdeva**: None; **S. Koppikar**: AbbVie/Abbott, 1, 2, 5, 6, Novartis, 2, 6, Pfizer, 12, Unrestricted educational grant for Northern Ontario Clinic, UCB, 2, 6; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0566

Predictor Risk Factors For Developing Difficult-to-Treat Psoriatic Arthritis in Patients Initiating a First bDMARD: a Binational Study

Astrid Goudot[1], Raphaël Hurtubise[2], Eugénie Robin[3], Laurine Cadart[4], Raghav Ramachandran[5], Federica Re[5], Tristan Pascart[6], Cécile Philippoteaux[7], René-Marc Flipo[7], Laura Coates[8] and Jean-Guillaume Letarouilly[1], [1]Université de Lille, CHU Lille, Service de rhumatologie, Lille, France, Lille, Nord-Pas-de-Calais, France, [2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK., Oxford, United Kingdom, [3]CH Valenciennes, Service de rhumatologie, Valenciennes, France, Valenciennes, France, [4]Service de biostatistiques, CHU Lille, Lille, France, Lille, France, [5]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK, Oxford, United Kingdom, [6]GHICL, Hôpital Saint-Philibert, Service de rhumatologie, Lomme, France, Lomme, France, [7]Université de Lille, CHU Lille, Service de rhumatologie, Lille, France, Lille, France, [8]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1 Baseline characteristics of patients with D2T PsA and those without PsA patients Values are expressed as number (%) unless otherwise stated. BASDAI: Bath Ankylosing Spondylitis Disease Activity; bDMARD: biological disease modifying antirheumatic drug; BMI: body mass index; CRP: C-reactive protein; D2T: difficult-to-treat; HLA: human leukocyte antigen IBD: inflammatory bowel disease; IQR: interquartile range; N: number of available observations; NA: not applicable; PsA: psoriatic arthritis; SD: standard deviation; TIA: transient ischaemic accident; TNF:Tumour Necrosis Factor.

Parameters	N	D2T PsA n = 92	N	Non D2T PsA n = 320	p value
Men	92	47 (51.1)	320	167 (52.2)	0.74
Age (years), mean ± SD	92	56.0 ± 13.5	319	55.1 ± 13.4	0.94
BMI, mean ± SD	77	28.5 ± 5.9	213	28.8 ± 6.0	0.73
PsA duration (years), median (IQR)	92	13.5 (8.5 ; 20.0)	320	11.0 (8.0 ; 17.0)	NA
Current smoker status	85	21 (24.7)	261	89 (34.1)	0.38
Clinical PsA characteristics at baseline					
Axial involvement	89	43 (48.3)	305	139 (45.6)	0.57
Peripheral involvement	92	89 (96.7)	312	289 (92.6)	0.15
Monoarthritic	90	6 (6.7)	312	33 (10.5)	-
Oligoarthritic (2-3 involved joints)	90	13 (14.4)	312	46 (14.7)	-
Polyarthritic (≥4 involved joints)	90	68 (75.6)	312	210 (67.1)	-
Dactylitis	83	14 (16.9)	301	90 (29.9)	**0.02**
Enthesitis	83	15 (18.1)	299	80 (26.8)	0.14
Tender joint count	51	5.5 ± 4.8	217	6.2 ± 6.6	0.41
Swollen joint count	51	2.5 ± 2.3	217	3.2 ± 3.0	0.37
BASDAI Baseline, mean ± SD	21	55.7 ± 20.6	73	45.7 ± 25.5	0.94
Uveitis	85	2 (2.4)	305	9 (3.0)	0.77
Psoriasis	88	70 (79.5)	311	275 (88.4)	NA
IBD	84	3 (3.6)	305	8 (2.6)	0.77
Baseline CRP (mg/L), median (IQR)	63	9.0 (3.0 ; 23.0)	267	7.0 (2.9 ; 17.3)	0.25
Positive HLA B27 status	80	12 (24.0)	148	52 (35.1)	0.15
Peripheral structural damage	80	36 (43.9)	231	92 (39.8)	0.53
Main comorbidities					
Diabete mellitus	92	15 (16.3)	317	34 (10.7)	0.34
Fibromyalgia	91	11 (12.1)	316	19 (6.0)	**0.03**
Depression	89	13 (14.6)	316	40 (12.7)	0.11
Ischaemic cardiomyopathy	92	9 (9.8)	318	11 (3.5)	**0.03**
TIA/Stroke	92	3 (3.3)	318	9 (2.8)	0.86
1st bDMARD line					
TNF inhibitors		81 (88.0)		276 (86.9)	NA
IL17 inhibitors		2 (2.2)		16 (5.0)	NA
IL12/23 inhibitor		5 (5.4)		14 (4.4)	NA
Abatacept		1 (1.1)		1 (0.3)	NA
IL 23 inhibitors		0 (0)		3 (0.9)	NA
Rituximab		1 (1.1)		0 (0)	NA
IL6 inhibitors		1 (0.3)		1 (1.1)	NA
Apremilast		1 (1.1)		7 (2.2)	NA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

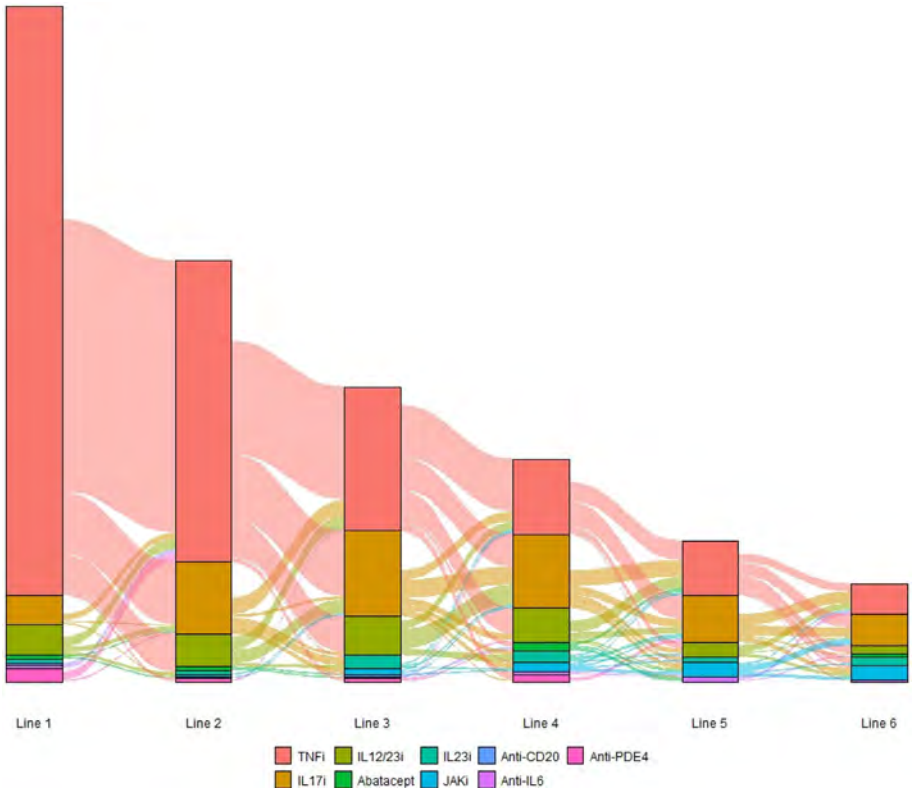


Figure 1 Treatment trajectories from first to sixth line

Background/Purpose: Risk factors to identify patients who will develop a difficult-to-treat (D2T) psoriatic arthritis (PsA) are still lacking when initiating a first bDMARD. There are ongoing GRAPPA/EULAR definitions of D2T PsA. The primary endpoint of this work was to determine the risk factors for developing D2T PsA in patients initiating a first bDMARD using the definition from Philippoteaux et al [1]. The second objective was to determine the risk factors for developing refractory PsA in the same population.

Methods: A retrospective study was conducted at three secondary and tertiary centres in France and one tertiary centre in the United Kingdom. Patients with PsA aged 18 years or older who initiated b/tsDMARDs and had at least a five-year follow-up were included. D2T PsA was defined as failure of ≥ 2 b/tsDMARDs with different mechanisms of action, including TNF, IL-

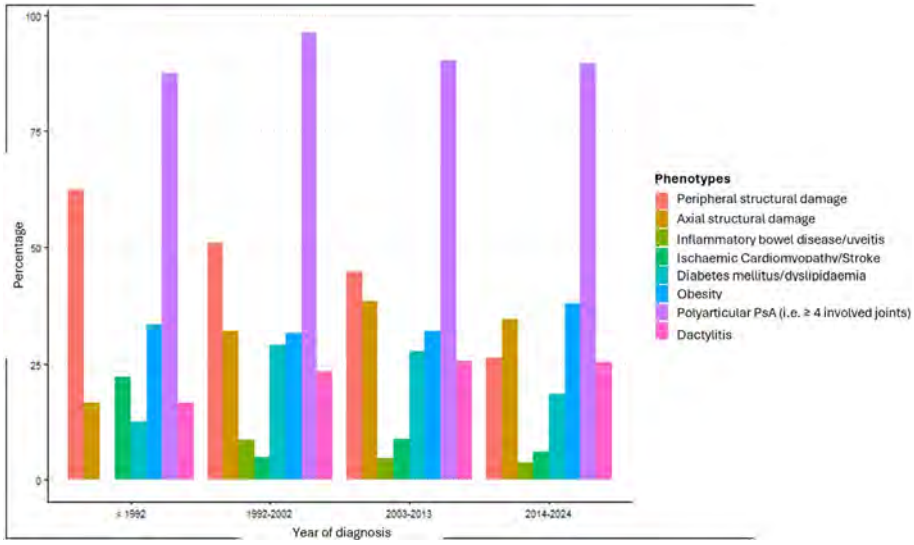


Figure 2 Evolution of phenotypes depending on the year of diagnosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

17, IL-23, and JAK inhibitors. Refractory PsA was defined as the failure of TNF, IL-17, IL-23, and JAK inhibitors. Patients with D2T PsA's characteristics were compared with patients without D2T Patients with D2T PsA's characteristics were compared with patients without D2T using logistic regression models adjusted for country (France vs. the United Kingdom). Factors significant at the 0.05 level were introduced into a multivariate logistic regression model also adjusted for country. The same methods were applied to compare patients with refractory PsA to those without refractory PsA. However, multivariate analysis was not performed due to limited sample size. The evolution of baseline characteristics was also assessed during four periods: before 1992, 1992 to 2002, 2003 to 2013, and 2014 to 2024.

Results: Four hundred and twelve patients were included: 92 with D2T PsA (22.3%; 95% confidence interval [CI], 18.3-26.7) and 320 without D2T PsA (77.7%). The median disease duration was 12.0 (8.0; 18.5). Treatment trajectories of the patients were reported from the 1st to the 6th line (**Figure 1**). A higher proportion of patients with D2T PsA had dactylitis, fibromyalgia and ischaemic cardiomyopathy (**Table 1**). In multivariate analysis, fibromyalgia (OR = 2.62; 95% CI 1.09-6.28) and ischemic cardiomyopathy (OR = 2.95; 95% CI 1.04-8.36) were found to be risk factors for D2T PsA. On the contrary, dactylitis was a protective factor for D2T PsA (OR=0.49; 95% CI 0.26-0.94). The proportion of patients with peripheral structural damage, inflammatory bowel disease, uveitis, diabetes mellitus, and dyslipidaemia at baseline decreased over time, where the proportion of patients with axial structural damage, ischaemic cardiomyopathy, stroke, obesity, polyarticular PsA (i.e ≥ four involved joints) and dactylitis were stable over time (**Figure 2**).

Fourteen patients (3.4%; 95% CI 1.9-5.6) were categorised as refractory. A refractory phenotype was associated with axial radiographic structural damage at baseline (OR = 5.65; 95% CI, 1.69-18.89).

Conclusion: In this retrospective binational study, fibromyalgia and ischaemic cardiomyopathy were found to be potential risk factors for D2T PsA, whereas dactylitis was a potential protective factor for D2T PsA. The prevalence of patients with refractory PsA was rare (< 5%) and was associated with axial radiographic structural damage at baseline.

Disclosure: A. Goudot: None; **R. Hurtubise**: Biojamp, 6, Celltrion, 6, UCB, 6; **E. Robin**: None; **L. Cadart**: None; **R. Ramachandran**: None; **F. Re**: None; **T. Pascart**: Johnson and Johnson, 6, Novartis, 6; **C. Philippoteaux**: AbbVie/Abbott, 6, Amgen, 6, Eli Lilly, 6, Galapagos, 6, Kyowa Kirin, 6; **R. Flipo**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **J. Letarouilly**: AbbVie/Abbott, 6, Amgen, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Galapagos, 6, Janssen, 6, Nordic Pharma, 6, Novartis, 6, Pfizer, 6.

Abstract Number: 0567

Sonelokimab in Biologic-Experienced Patients With Active Psoriatic Arthritis: Results From a Phase 2 Trial (ARGO) and Study Design of a Phase 3 Trial (IZAR-2) in Patients With Inadequate Response or Intolerance to Biologic TNFi, Including a Risankizumab Reference Arm

Atul Deodhar[1], Laure Gossec[2], Philip J. Mease[3], Xenofon Baraliakos[4], Lihi Eder[5], Alan Kivitz[6], Helena Marzo-Ortega[7], Frank Behrens[8], Ana-Maria Orbai[9], Georg Schett[10], Arthur Kavanaugh[11], Dennis McGonagle[12], Christopher Ritchlin[13], Nuala Brennan[14], Ben Porter-Brown[14], Eva Cullen[14], Matthew R. Thomas[14], Marius Albulescu[14], Alex Godwood[14], Kristian Reich[15] and Laura Coates[16], [1]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [2]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [3]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [4]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [5]University of Toronto, Toronto, ON, Canada, [6]Altoona Center for Clinical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Research, Duncansville, PA, [7]NIHR Leeds Biomedical Research Centre, The Leeds Teaching Hospitals NHS Trust and Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom, [8]Rheumatology, Immunology - Inflammation Medicine, University Hospital Goethe-University & Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Frankfurt am Main, Germany, [9]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [10]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [11]University of California, San Diego, School of Medicine, San Diego, CA, [12]Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom, [13]University of Rochester Medical Center, Canandaigua, NY, [14]MoonLake Immunotherapeutics AG, Zug, Switzerland, [15]MoonLake Immunotherapeutics AG and Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, Zug, Switzerland, [16]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

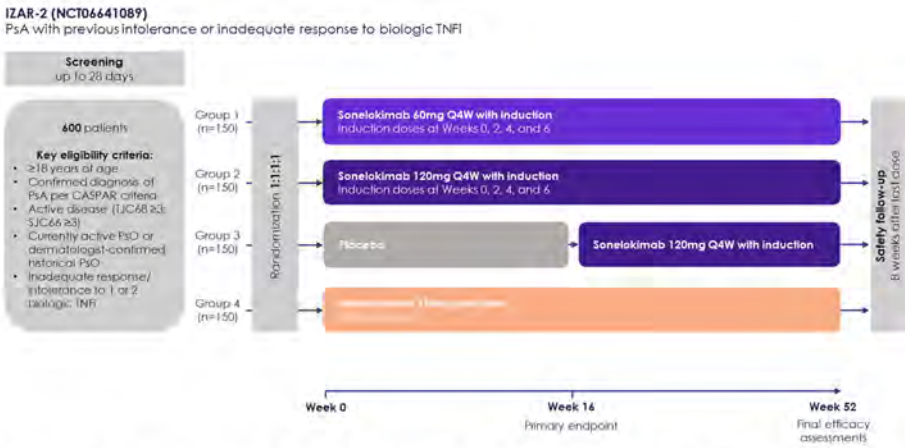
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Sonelokimab (SLK), a novel Nanobody that binds to both IL-17A and IL-17F with similarly high affinity, is designed to target difficult-to-reach sites of inflammation. The Phase 2 ARGO study demonstrated robust joint and skin responses with SLK in PsA. We report Week (W) 24 data for patients with prior biologic exposure in the ARGO trial and describe the design of the Phase 3 IZAR-2 trial that will further evaluate SLK in patients with active PsA after prior biologic TNFi therapy.

Methods: ARGO (NCT05640245) was a 24-week, global, randomized, placebo (PBO)-controlled double-blind trial of adults with active PsA. Three SLK doses were assessed: 60mg with no induction (NI; Q4W), SLK 60mg with induction (WI), and SLK 120mg WI (induction doses at W0, 2, 4, and 6; Q4W from W8). Patients with >2 prior biologics or primary failure of TNFi or IL-17i were excluded. In this exploratory analysis, W24 outcomes in patients with prior bDMARD exposure treated with SLK 120mg or 60mg WI (IZAR-2 doses) were assessed.

Results: 207 patients were enrolled. Of the 84 patients treated with SLK 120mg (n=43) or 60mg WI (n=41), 15 (17.9%) had exposure to ≥1 bDMARD (TNFi n=10, IL-23i n=7, IL-17i n=5). Among these patients, the primary endpoint of ACR50 was achieved by 53% of patients with exposure to ≥1 bDMARD and 61% of patients with no prior bDMARD exposure. Similar

Figure. Study design



CASPAR, Classification Criteria for Psoriatic Arthritis; PsA, psoriatic arthritis; PsO, psoriasis; Q4W, every 4 weeks; SJC66, 66 swollen joint count; TJC68, 68 tender joint count; TNFi, tumor necrosis factor inhibitor.

Figure. Study design

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

results were seen for minimal disease activity (MDA), which was achieved by 53% of patients with prior bDMARD exposure and 57% of patients with no prior bDMARD exposure who received SLK 120mg or 60mg WI. Of the 5 patients receiving SLK 120mg or 60mg WI with PsO at baseline (≥3% BSA) and prior bDMARD exposure, 4 (80%) achieved PASI 90 (75% for those with no prior bDMARD exposure). SLK was well tolerated, with a safety profile consistent with IL-17 inhibition. To further assess outcomes in this patient population, we designed a 52-week, global, randomized, double-blind, PBO-controlled, Phase 3 trial (IZAR-2; NCT06641089; **Figure**). An estimated 600 participants will be randomized 1:1:1:1 to SLK 60mg WI, SLK 120mg WI, PBO (SLK 120mg WI from W16), or risankizumab (RZB). Given the results from ARGO, this sample size should provide sufficient power to demonstrate a statistically significant difference vs. PBO on the primary outcome of ACR50 at W16. Eligible participants will have PsA fulfilling CASPAR criteria, active disease (TJC68 ≥3 and SJC66 ≥3), currently active or historical PsO, and inadequate response or intolerance to 1 or 2 biologic TNFi. Key secondary outcomes (all vs. PBO at W16) include ACR20, PASI 90, MDA, and HAQ-DI. RZB, an approved IL-23 p19i PsA therapy commonly used after prior inadequate response to TNFi, will be the active reference arm. A secondary endpoint of ACR50 at W16 with SLK vs. RZB will provide insights into treatment choices with IL-17A/F and IL-23i after TNFi failure.

Conclusion: In patients with active PsA and prior exposure to $\geq$1 bDMARD in the Phase 2 ARGO trial, SLK 120mg and 60mg WI showed efficacy in controlling signs and symptoms of PsA and achieving MDA response. Interpretation is limited by patient numbers; hence, a larger Phase 3 trial specifically in patients with prior inadequate response or intolerance to biologic TNFi (IZAR-2) is ongoing and actively recruiting at sites across the USA.

Disclosure: A. Deodhar: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **A. Kivitz**: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2; **H. Marzo-Ortega**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 6, UCB, 2, 5, 6; **F. Behrens**: AbbVie, 2, 6, 12, Support for attending meetings and/or travel, Acelyrin, 2, 6, Amgen, 2, 6, AstraZeneca, 6, Chugai Pharmaceuticals, 2, 5, 6, Cilag, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen Pharmaceuticals, 2, 5, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 5, Sandoz, 6, UCB, 2, 6, 12, Support for attending meetings and/or travel; **A. Orbai**: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB, 2; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, MoonLake Immunotherapeutics AG, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sobi, 2, 5, 6, UCB, 2, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **N. Brennan**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

MoonLake Immunotherapeutics AG, 3, 11; **B. Porter-Brown**: MoonLake Immunotherapetics, 3, 11, Sanofi, 3, 11; **E. Cullen**: MoonLake Immunotherapeutics AG, 3, 11; **M. Thomas**: MoonLake Immunotherapeutics AG, 3, 11; **M. Albulescu**: MoonLake Immunotherapeutics, 3, 11; **A. Godwood**: MoonLake Immunotherapeutics, 3, 11; **K. Reich**: AbbVie, 1, 6, 12, Participated in clinical trials, Almirall, 1, 6, 12, Participated in clinical trials, Amgen, 1, 6, 12, Participated in clinical trials, Boehringer Ingelheim, 1, 6, 12, Participated in clinical trials, Bristol-Myers Squibb(BMS), 1, 6, 12, Participated in clinical trials, Eli Lilly, 1, 6, 12, Participated in clinical trials, Galderma, 1, 6, 12, Participated in clinical trials, Janssen-Cilag, 1, 6, 12, Participated in clinical trials, Kyowa Kirin, 1, 6, 12, Participated in clinical trials, LEO Pharma, 1, 6, 12, Participated in clinical trials, Medac, 1, 6, 12, participated in clinical trials, MoonLake Immunotherapeutics AG, 3, 11, Novartis, 1, 6, 12, participated in clinical trials, Ocean Pharma, 1, 6, 12, participated in clinical trials, Pfizer, 1, 6, 12, participated in clinical trials, Sanofi, 1, 6, 12, participated in clinical trials, UCB, 1, 6, 12, participated in clinical trials; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0568

Drug-Free Remission in Early Peripheral Spondyloarthritis: 10-year follow-up from the CRESPA-trial

Caroline Damen[1], Philippe Carron[2], Ann-Sophie De Craemer[3], Filip Van den Bosch[3] and Dirk Elewaut[4], [1]Department of Internal Medicine and Pediatrics, Ghent University, Ghent, Belgium, [2]Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [3]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [4]VIB Center for Inflammation Research, and Ghent University Hospital, Department of Rheumatology, Ghent, Belgium

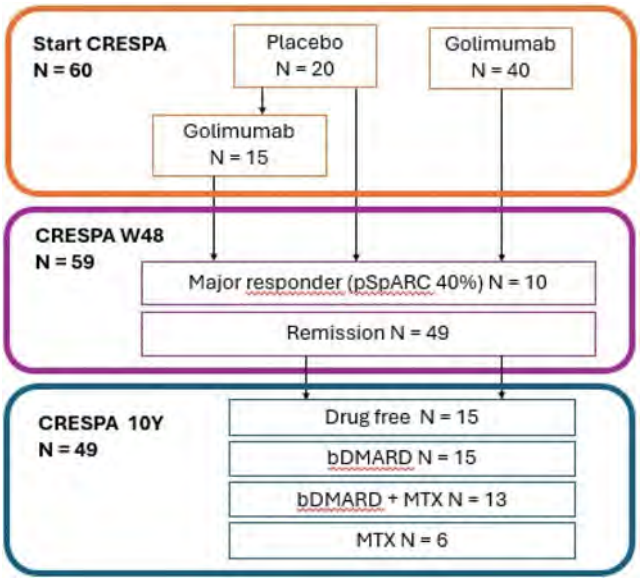
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Peripheral spondyloarthritis (pSpA) is a neglected clinical entity with few therapeutic or clinical management trials available to date. In the CRESPA-trial (1) very early pSpA patients, all fulfilling the Assessment of SpondyloArthrtis international Society (ASAS) classification criteria for pSpA and having a symptom duration ≤12 weeks, were randomized to golimumab (n=40) or placebo (n=20). Placebo-treated patients were switched to golimumab at week 24 if no sustained clinical remission was achieved (primary end point) (1). In patients achieving sustained clinical remission, treatment was stopped to assess the possibility of drug-free remission (2). In those not achieving the primary endpoint at week 48, treatment with golimumab was continued (2). The objective of this study was to determine the percentage of patients achieving a status of clinical remission after a follow-up of 10 years.

Methods: In this 10-year follow-up study patients that participated in the CRESPA-trial were evaluated through clinical examination assessing arthritis, enthesitis and dactylitis. All evaluations were done between March 2024 and September 2024. Clinical remission was defined as the absence of arthritis, enthesitis or dactylitis. A secondary aim was to identify baseline differences between patients currently in remission and those not in remission.

Results: As reported previously, sustained clinical remission was achieved in 82% (49 of 60) of patients after an induction regimen, 15 placebo treated patients needed golimumab (1) ***(figure 1)***. 1 patient was excluded due to progression to seronegative rheumatoid arthritis.

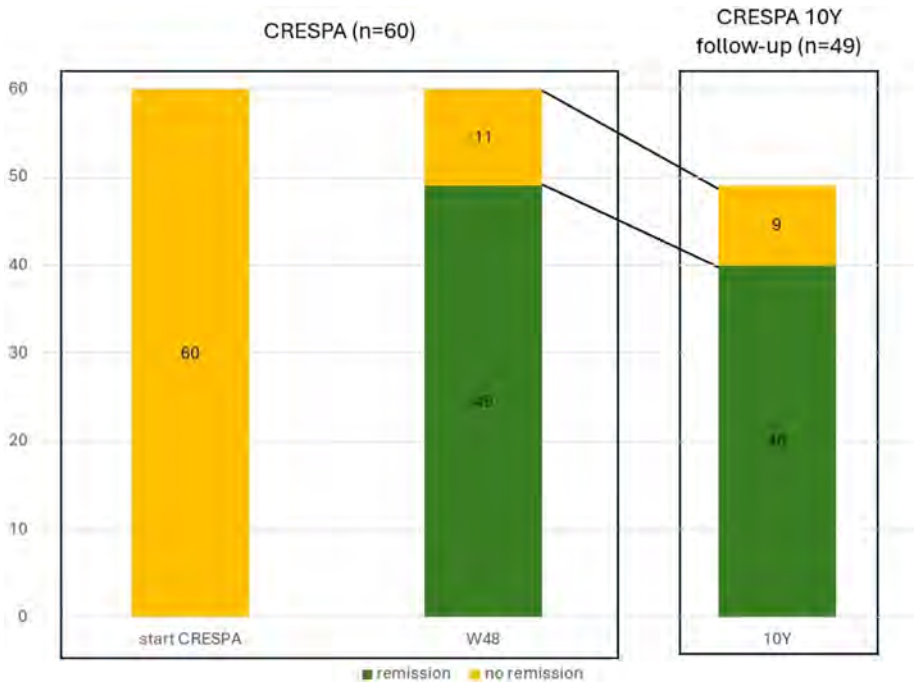
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Medication use during CRESPA trial and after 10 year follow-up

Of those 60 patients originally included in the CRESPA study, we were able to evaluate 49 patients within an average of 10.5 years (SD 0.87 years) of follow-up. Clinical remission was observed in 82% (40 of 49) patients, with 37.5% (15 of 40) of them in drug-free remission ***(figure 2)***. 6 patients were on MTX monotherapy and 28 patients on bDMARD (57% monotherapy, 43% in combination with MTX). 21 patients still use golimumab, with no unsuspected serious adverse effects reported. Of the 9 patients not in clinical remission after 10 years of follow-up, 7 experienced enthesitis, 1 arthritis and 1 both enthesitis and arthritis.

There were no baseline differences regarding sex, age, HLA B27-positivity, psoriasis, or initial treatment allocation between patients in clinical remission and those not in clinical remission. However, drug-free remission was significantly less common in patients with psoriasis compared to those without (OR = 0.11, 95% CI: 0.02–0.55, $p = 0.005$).



Remission at the end of the CRESPA trial and after 10 year follow-up

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: After 10 year follow-up, the vast majority of patients are in clinical remission with 37.5% of them even in drug-free remission. The presence of psoriasis at baseline was associated with a lower likelihood of achieving drug-free remission.

References:

1) Carron P, Varkas G, Cypers H, et al. Anti-TNF-induced remission in very early peripheral spondyloarthritis: the CRE-SPA study. Ann Rheum Dis. 2017;76(8):1389–95.
2) Carron P, Varkas G, Renson T, et al. High Rate of Drug Free Remission After Induction Therapy With Golimumab in Early Peripheral Spondyloarthritis. Arthritis Rheumatol. 2018;70(11):1769-77.

Disclosure: c. Damen: Celltrion, 5; **P. Carron**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Johnson & Johnson, 2, 6, Novartis, 2, 6, UCB, 2, 6; **A. De Craemer**: UCB, 6; **F. Van den Bosch**: AbbVie, 2, 6, Alfasigma, 2, Amgen, 2, 6, Eli Lilly, 2, Galapagos, 2, Grey Wolf Therapeutics, 2, Janssen, 2, 6, Merck, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **D. Elewaut**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6, UCB, 2, 6.

Abstract Number: 0569

ASAS Recommendations on Reporting Outcomes of Core Outcome Set Instruments in Axial Spondyloarthritis Clinical Trials

Floris A. van Gaalen[1], Victoria Navarro-Compan[2], Xenofon Baraliakos[3], Filip Van den Bosch[4], Lianne S. Gensler[5], Ihsane Hmamouchi[6], Robert Landewé[7], Pedro Machado[8], Helena Marzo-Ortega[9], Valeria Rios Rodriguez[10], Denis Poddubnyy[11], Sofia Ramiro[12] and Désirée Van Der Heijde[1], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [3]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [4]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [5]Department of Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, [6]Health Sciences Research Center (CReSS).Faculty of Medicine, International University of Rabat, Rabat, Morocco, [7]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [8]Department of Rheumatology, University College London, and Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS Trust, Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [9]NIHR Leeds Biomedical Research Centre, The Leeds Teaching Hospitals NHS Trust and Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom, [10]Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Gastroenterology, Infectious Diseases and Rheumatology (including Nutrition Medicine), Berlin, Germany, [11]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [12]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The recently updated Assessment of SpondyloArthritis international Society (ASAS) core outcome set (COS) includes an agreed minimum set of instruments that should be used in all axial spondyloarthritis (axSpA) trials. However, recommendations on how to report outcomes of the 16 COS instruments is lacking. Aim of the project is to develop expert endorsed recommendations on how outcomes of COS instruments should be reported.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table Reporting outcomes of instruments in the ASAS Core Outcome Set

Item	At baseline	At follow-up timepoint(s)
For all trials		
1. ASDAS	mean (SD)	mean (SD) + mean (SD) change from baseline + n (%) of patients with improvement of ≥1.1 and ≥2.0*
2. ASDAS disease status	n (%) per category†	n (%) per category + n (%) <2.1 and ≥2.1
3. Patient global disease activity	mean (SD)	mean (SD) + mean (SD) change from baseline
4. Total back pain (BASDAI Q2)	mean (SD)	mean (SD) + mean (SD) change from baseline
5. Mean stiffness severity (BASDAI Q5) and duration (BASDAI Q6)‡	mean (SD)	mean (SD) + mean (SD) change from baseline
6. Fatigue (BASDAI Q1)	mean (SD)	mean (SD) + mean (SD) change from baseline
7. BASFI	mean (SD)	mean (SD) + mean (SD) change from baseline
8. ASAS 20 and ASAS 40 responses	not applicable	n (%)
9. ASAS health Index	mean (SD)	mean (SD) + mean (SD) change from baseline + n (%) of patients with improvement ≥3
10. ASAS health Index status §	n (%) per category	n (%) per category
Mandatory for DMARD trials only		
11. SPARCC MRI-SIJ activity	mean (SD)	mean (SD) + mean (SD) change from baseline
12. SPARCC MRI-spine activity	mean (SD)	mean (SD) + mean (SD) change from baseline
13. Acute anterior uveitis	n (%) with history	n (%) since baseline /rate per 100 pt yrs + split by patients with and without history
14. Psoriasis	n (%) with history	n (%) new onset since baseline /rate per 100 patient years (pt yrs) + rate split by patients with and without history
15. IBD	n (%) with history	n (%) since baseline /rate per 100 pt yrs + split by patients with and without history
16. 44 swollen joint count	mean (SD)	mean (SD) + mean (SD) change from baseline ¶
17. MASES	mean (SD)	mean (SD) + mean (SD) change from baseline ¶
18. Dactylitis count	mean (SD)	mean (SD) + mean (SD) change from baseline ¶
19. mSASSS	mean (SD)	mean (SD) + mean (SD) change from baseline
20. Syndesmophytes	n (%) with ≥1	n (%) with ≥1 syndesmophyte + n (%) with a new syndesmophyte

*If flares are reported: n (%) of pts. with ASDAS of ≥0.9; † ASDAS categories: <1.3 inactive disease, ≥ 1.3 and <2.1 low disease, ≥ 2.1 and ≤3.5 high disease, >3.5 very high disease activity; ‡ BASDAI (Q5+Q6)/2; § ASAS health index categories: good ≤ 5, moderate <5 to <12, poor ≥12; ¶ in pts with swollen joint count>0, MASES>0 or dactylitis count>0 at baseline
ASAS: Assessment of SpondyloArthritis international Society; ASDAS: Axial Spondyloarthritis Disease Activity Score; BASFI: Bath Ankylosing Spondylitis Functional Index; IBD: inflammatory bowel disease; MASES: Maastricht Ankylosing Spondylitis Entheitis Score; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score ; pt: patient; Q: question; SPARCC: Spondyloarthritis Research Consortium of Canada;

Methods: A steering group (SG) (FvG, VNC, DvH) convened a workgroup (WG) consisting of thirteen ASAS members including rheumatologists, methodologists, epidemiologists, and two Young ASAS (Y-ASAS) members (all other co-authors). Recommendations on reporting instrument outcomes were developed in three steps: the SG formulated a proposal on how outcomes related to the instruments should be presented. ii) the proposal was presented, discussed and modified in a WG meeting. iii) the WG proposal was discussed and voted on by ASAS members.

Results: Reporting 20 trial outcomes at baseline and follow-up timepoints are recommended: 10 for all clinical trials and 10 for DMARD trials only (Table). The most common format is to report the mean plus the standard deviation (SD) at all timepoints while adding the mean change (SD) from baseline for each timepoint. For ASDAS it is recommended to also report the number and percentage of patient with decrease of ≥1.1 and ≥2.0 units, an increase of 0.9 for flares, and ASDAS status at all timepoints (inactive (< 1.3), low (≥1.3 and < 2.1), high (≥2.1 and ≤3.5), and very high (>3.5) plus the number and percentage of patients with scores < 2.1 and ≥2.1). For ASAS health index it is recommended to also report the number and percentage of patients with decrease in the score of ≥3 and status (good (≤ 5), moderate (< 5 to < 12), and poor (≥12)) at all timepoints. It is recommended for psoriasis, uveitis, and IBD to be reported as the number and percentage of patients with flare or (re) occurrence since baseline plus the rate per 100 patient-years while also splitting the results by patients with and without a history of that particular extra-musculoskeletal manifestations. For spinal syndesmophytes it is recommended to report the number and percentage of patients with at least one at baseline and outcomes plus the number and percentage of patients with a newly developed syndesmophyte which, if not scored separately, can be derived from the mSASSS scoring with a vertebral unit over time developing an mSASSS score of 2 or 3 from a score less than 2 counting as the development of a syndesmophyte. At the 2024 annual ASAS workshop recommendations were voted in by 81 full ASAS members with 85% in favour, 9% against, and 6% abstaining.

Conclusion: These ASAS endorsed recommendations provide a consensual approach to reporting outcomes of axSpA clinical trials. Adherence to these recommendations will standardize presentation of results and thereby provides better insight into trial outcomes and facilitate the comparison of outcomes across studies.

Disclosure: F. van Gaalen: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **F. Van den Bosch**: AbbVie, 2, 6, Alfasigma, 2, Amgen, 2, 6, Eli Lilly, 2, Galapagos, 2, Grey Wolf Therapeutics, 2, Janssen, 2, 6, Merck, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **L. Gensler**: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **I. Hmamouchi**: None; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **P. Machado**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **H. Marzo-Ortega**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 6, UCB, 2, 5, 6; **V. Rios Rodriguez**: AbbVie/Abbott, 2, 5, Eli Lilly, 5, Falk, 2, Janssen, 5, Novartis, 12, Travel support, Pfizer, 5, 12, Travel support, Takeda, 2, UCB, 5, 12, Travel support; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2.

Abstract Number: 0570

Phyto- and Endo-cannabinoids Exhibit Ex Vivo Anti-Inflammatory Effects in Refractory Rheumatic inflammatory/Autoimmune Patients: Toward Personalized Cannabinoid Therapy

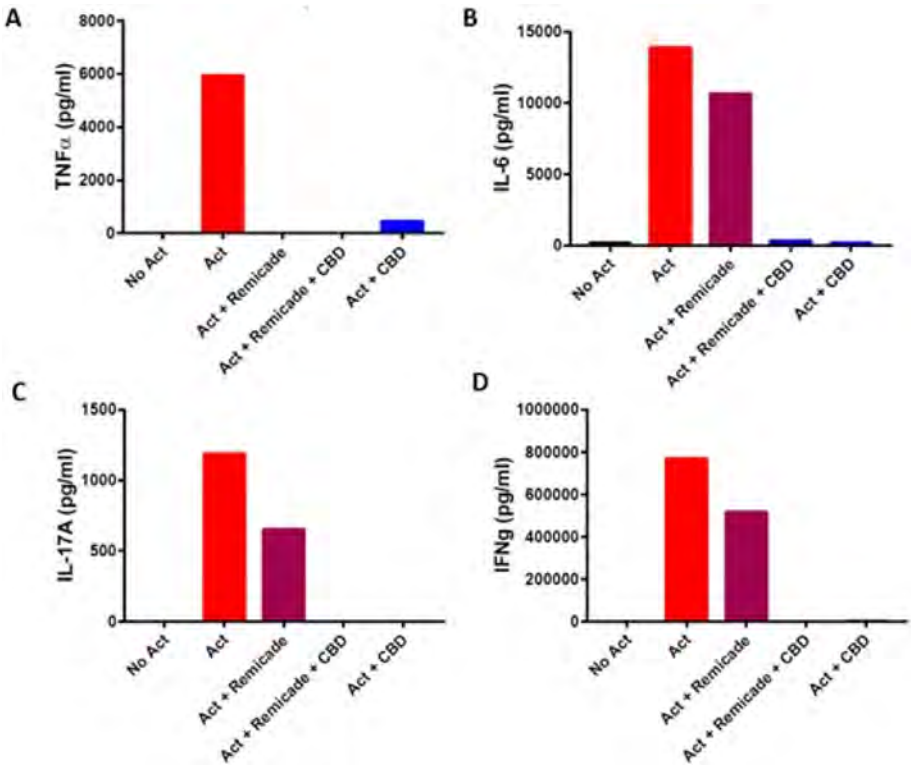
Gilad Halpert[1], Eri Govrin[1], Omer Gendelman[1], Abdulla Watad[2], Yehuda Shoenfeld[1] and Howard Amital[1], [1]Sheba Medical Center, Ramat Gan, Israel, [2]Tel Hashomer Medical Center, Ramat Gan, Israel

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: A substantial number of patients with rheumatic inflammatory/autoimmune diseases, do not achieve adequate symptom control with current standard-of-care therapies, including biologics. The endocannabinoid system may offer an alternative therapeutic target. Recently we found a significant change in the circulating level of endogenous cannabinoids (endocannabinoids) in rheumatoid arthritis (RA) and fibromyalgia syndrome (FMS) patients as compared to healthy controls. The current study aimed to evaluate *ex vivo* anti-inflammatory effects of non-psychoactive phytocannabinoids and endocannabinoids in peripheral blood mononuclear cells (PBMCs) from patients with refractory rheumatic inflammatory/autoimmune conditions.

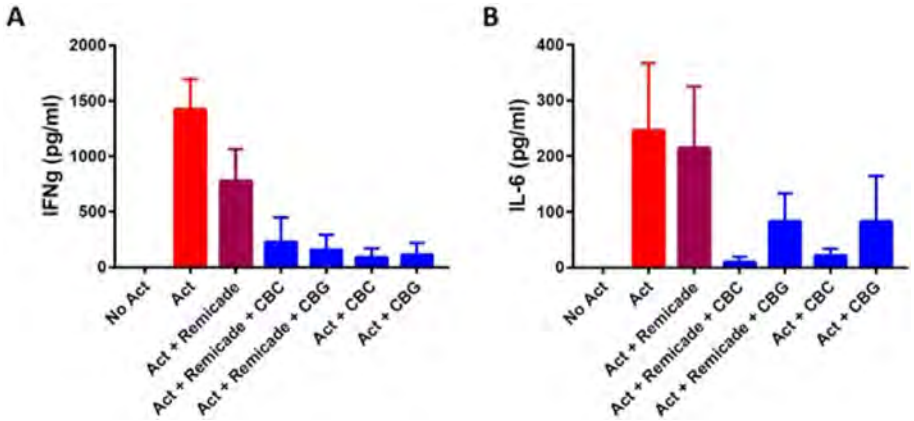
Methods: PBMCs were isolated from psoriatic arthritis (PsA) and ankylosing spondylitis (AS) patients who were unresponsive to anti-TNFα treatment, as well as from FMS patients. PBMCs were activated *ex-vivo* using PHA and LPS, and treated

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



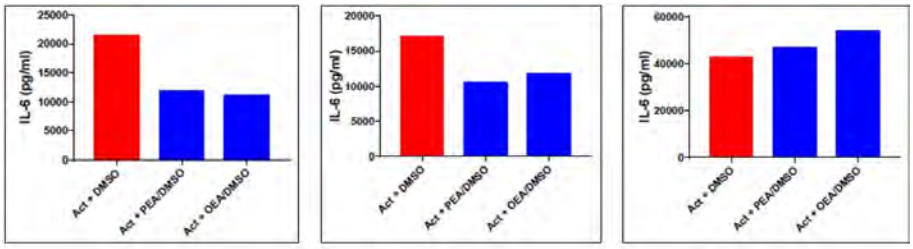
with either phytocannabinoids (CBD, CBC, CBG) or endocannabinoids (AEA, PEA, OEA). Cytokine levels (TNF-α, IFN-γ, IL-17, IL-6 and IL-1β) were measured in cell supernatants and plasma using ELISA assay.

Results: In PBMCs from severe refractory PsA patient, the phytocannabinoid CBD demonstrated superior suppression of pro-inflammatory cytokines (IL-6, IL-17, and IFN-γ) compared to the corresponding anti-TNFα biologics while both CBD and anti-TNFα abrogate TNFα secretion (Fig. 1). In PBMCs from refractory AS patients (n=3), phytocannabinoids (CBC and CBG) demonstrated superior suppression of IFN-γ and IL-6 compared to the corresponding anti-TNFα biologics (Fig. 2). In FMS patients (n=3), endocannabinoids (AEA, PEA, and OEA) modulated IL-6 secretion in a patient-specific manner, with variable cytokine responses observed (Fig. 3).



The cannabinoids (CBG and CBC) show superior reduction in the level of secreted IFNγ and IL-6 from activated PBMCs of refractory ankylosing spondylitis (AS) patients (n=3) vs. the non-effective Anti-TNFα mAb (Remicade®). Human PBMCs were isolated from severe (refractory to Anti-TNFα therapy) AS patient, seeded (500,000 cells/0.5ml/well) and activated using LPS (100ng/ml) + PHA (10μg/ml) for 24h. Anti-TNFα mAb (Remicade®) or CBC/CBG (1/3 less concentrated than Remicade) were added concomitantly to activation, for a total of 24h. IFNγ and IL-6 cytokine levels were measured in the supernatants, 24 h after activation, by ELISA assay. Act – Activation using LPS/PHA.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



The effect of N-arachidonoylethanolamine (AEA) on IL-6 secretion from LPS/PHA-induced activated PBMCs of FMS patients. Human PBMCs were isolated from FMS patients, seeded (500,000 cells/0.5ml/well) and activated using LPS (100ng/ml) + PHA (10μg/ml) for 24h. AEA (10^-6M) was added 5h after the intial activation, for a total of 24h. IL-6 cytokine level was measured in the supernatants, 24 h after activation, by ELISA assay. Act – Activation using LPS/PHA; Eth – Ethanol which used to dissolve the AEA.

Conclusion: Non-psychoactive phytocannabinoids exhibit robust *ex vivo* anti-inflammatory activity in PBMCs from refractory PsA and AS patients, surpassing anti-TNFα biologics. Additionally, individualized endocannabinoid responses in FMS support a precision medicine approach. These findings highlight the potential of integrating phytocannabinoids and endocannabinoid profiling to guide personalized therapeutic strategies in rheumatic inflammatory/autoimmune diseases.

Disclosure: G. Halpert: None; **E. Govrin**: None; **O. Gendelman**: None; **A. Watad**: AbbVie/Abbott, 1, 6, Celgene, 1, 6, Eli Lilly, 1, 6, Janssen, 1, 6, Neopharm, 1, 6, Novartis, 1, 6; **Y. Shoenfeld**: None; **H. Amital**: None.

Abstract Number: 0571

Single-cell RNA Sequencing Highlights the Role of Innate Immunity in Identifying Candidates for Early Biologics Treatment in Axial Spondyloarthritis

Jaejoon Lee[1], A-Hyun Cho[2], Yu Jin Kim[2], Seulkee Lee[3], Seonyoung Kang[4], Hyungjin Kim[5], Hoon-Suk Cha[1] and Hong-Hee Won[2], [1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [2]Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea, [3]Samsung Medical Center, Sunkyunkwan University School of Medicine, Seoul, South Korea, [4]Samsung Medical Center, Sungkyunkwan University School of Medicine, Gangnam-gu, Seoul, Republic of Korea, [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Biologics have transformed the management of axial spondyloarthritis (axSpA). Currently, it is challenging to identify patients who would benefit from early biologics, resulting in trial-and-error use of NSAIDs followed by a response evaluation over months before initiating biologics. This study aimed to characterize patients requiring early biologics through single-cell RNA sequencing (scRNA-seq) analysis of peripheral blood mononuclear cells (PBMCs) obtained from newly diagnosed axSpA patients.

Methods: PBMCs were collected at baseline from axSpA patients newly diagnosed. Patients initiating biologics within six months were categorized as early biologics users, while those who did not were categorized as non-early biologics users. Single-cell RNA sequencing data were processed using Cell Ranger, and quality control was performed using Seurat.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

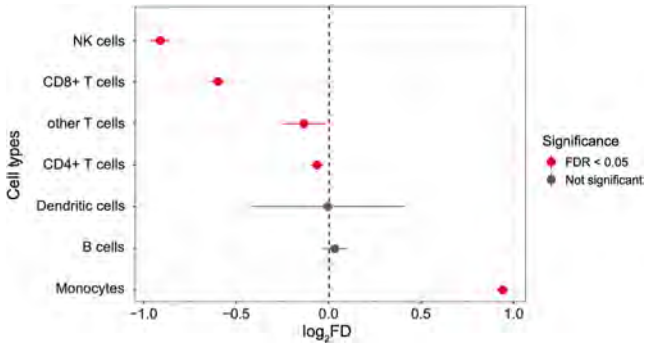


Figure 1. Single-cell proportion test results. To compare cell type proportions between early and non-early users, a single-cell proportion test was performed using the R package scProportionTest.

Differences in cell proportions were analyzed with scProportionTest, and differentially expressed genes (DEGs) were identified using the Wilcoxon Rank Sum test. Pathway enrichment analyses were conducted using KEGG and GO terms.

Results: Nineteen patients with axSpA were enrolled, of whom seven were categorized as early biologics users and twelve as non-early biologics users. A total of 157,029 single cells passed quality control and were included in subsequent analyses.

Differential cell proportion analysis revealed marked differences between early and non-early biologics users. Specifically, early biologics users exhibited a significant increase in monocyte proportions, along with a decrease in NK and CD8+ T cells, suggesting an altered balance in both innate and adaptive immunity. Monocytes had the highest number of differentially expressed genes (DEGs), highlighting the potential importance of monocytes in determining early treatment responses (Figure 1).

Enrichment analyses of monocyte-specific DEGs indicated significant activation of pathways closely linked to the pathogenesis of axSpA, including NF-κB signaling, the Toll-like receptor signaling pathway, the response to tumor necrosis factor, and MAPK signaling (Figure 2).

In CD8+ T cells, DEGs were enriched in the HIF signaling pathway in the KEGG gene set. These findings are consistent with previous reports emphasizing the necessity of increased glycolysis in supporting CD8+ T cell activation and differentiation. Similarly, NK cells in early biologics users displayed DEGs such as FPR1, XCL2, CYBB, CD14, FOS, LYZ, S100A9, AIF1, and S100A8, which are enriched in inflammatory response pathways. NK cells have been implicated in several immune-mediated diseases, and these results suggest that their dysregulation may contribute to the early disease process in axSpA.

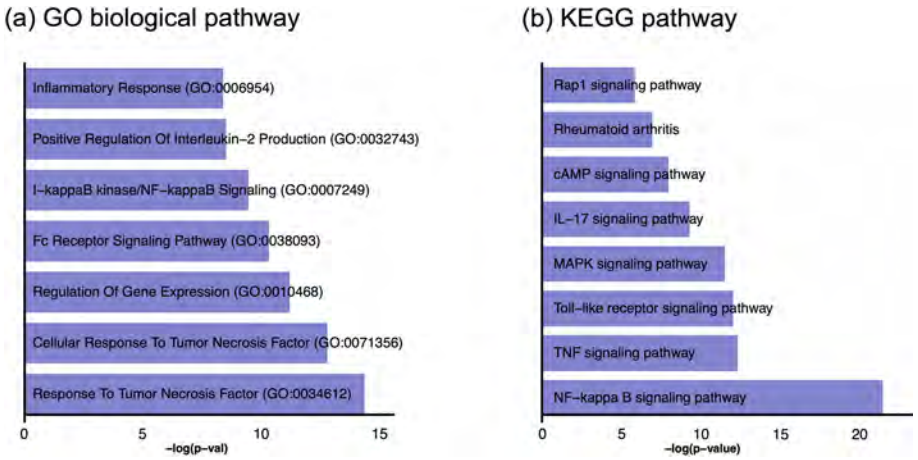


Figure 2. Results of the enrichment analysis. Enrichment analyses using (a) GO Biological Process and (b) KEGG gene sets.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: These data indicate that early biologics users exhibit a distinct immunological profile characterized by enhanced monocyte-driven inflammation and concurrent alterations in CD8+ T cell and NK cell populations. These findings underscore the critical role of innate immunity, particularly through monocyte-mediated pathways, in identifying patients who may benefit from early biologics therapy, offering a basis for personalized therapeutic strategies.

Disclosure: J. Lee: None; **A. Cho**: None; **Y. Kim**: None; **S. Lee**: None; **S. Kang**: None; **H. Kim**: None; **H. Cha**: None; **H. Won**: None.

Abstract Number: 0572

Real-World Treat-to-Target Strategy in Psoriatic Arthritis: 48-week Results from the MONITOR-PsA Cohort

Jean-Guillaume Letarouilly[1], Elnaz Saeedi[2], Raphaël Hurtubise[3], Lija James[4], Nicola Gullick[5], Deepak Jadon[6], William Tillett[7], Yvonne Sinomati[4], Laura Tucker[4], Nadia Mian[8], Sophia Massa[3] and Laura Coates[9], [1]Université de Lille, CHU Lille, Service de rhumatologie, Lille, France, LILLE, Nord-Pas-de-Calais, France, [2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK., Oxford, [3]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK., Oxford, United Kingdom, [4]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK, Oxford, United Kingdom, [5]Rheumatology Department, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, Coventry, United Kingdom, [6]Department of Medicine, University of Cambridge, Cambridge, UK, Cambridge, United Kingdom, [7]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, United Kingdom, [8]BM BS, MMedSc, Oxford, United Kingdom, [9]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: A treat-to-target (T2T) strategy in psoriatic arthritis (PsA) is supported by International PsA recommendations but not widely practiced in clinic. The aim of the Multicentre Observational Initiative in Treat-to-Target Outcomes in Psoriatic Arthritis (MONITOR-PsA) cohort was to assess clinical and patient-reported outcomes with a pragmatic implementation of a T2T approach.

Methods: Adult patients from 11 UK rheumatology departments were included if they had a clinical diagnosis of active PsA (≥ 1 tender or swollen joints or enthesis); not previously had treated with DMARDs for articular disease. The MONITOR-PsA cohort patients were assessed every 12 weeks for one year and were treated with current standard step-up care. Initial treatment consisted of methotrexate, then the addition of or switch to another csDMARD, and then potentially a switch to a bDMARD dependent on disease activity(**Figure 1**). The primary outcome was the proportion of patients achieving the PsA Disease Activity Score (PASDAS) 'good' response at 48 weeks. Key secondary endpoints were the proportion achieving PASDAS moderate response at 48 weeks and PASDAS continuous outcome 48 weeks. Exploratory outcomes included the proportion achieving MDA and DAPSA remission (≤4) at 48 weeks, the number of patients achieving a 50% decrease in 50% in dactylitis/enthesitis scores, the proportion achieving PSAID patient acceptable symptom state (≤4) and the difference between baseline and 48 weeks for radiographic outcomes (score of erosions, joint space narrowing score, modified Sharp-van der Heijde score).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table Baseline characteristics of the patients for the cohort (left, n=300) and the analysis population (right, n=234)

	Total N=300	Total N=234
Male sex	161 (53.7%)	126 (53.8%)
Age (years)	46.0 [35.0, 56.0]	44.0 [34.0, 55.0]
Current or history of psoriasis	254/272 (93.4%)	191/206 (92.2%)
Disease duration of psoriasis (years)	3.1 [0.0, 32.0]	3.1 [0.0, 24.5]
Disease duration of PsA (months)	10.9 [4.2, 28.7]	12.0 [4.8, 34.0]
Body Mass Index (kg/m²)	288, 28.5 [24.6, 32.1]	223, 28.4 [24.4, 32.2]
Underweight	4 (1.3%)	3 (1.4%)
Normal	73 (25.4%)	58 (26.0%)
Overweight	100 (34.7%)	77 (34.5%)
Obese	111 (38.6%)	85 (38.1%)
Smoker		
Never	122/225 (54.2%)	83/161 (51.5%)
Former	62/225 (27.6%)	47/161 (29.2%)
Current	41/225 (18.2%)	31/161 (19.3%)
TJC	299, 6.0 [3.0, 14.0]	233, 6.0 [2.0, 13.0]
SJC	299, 3.0 [1.0, 6.0]	233, 3.0 [1.0, 6.0]
Patients with enthesitis	145/277 (52.3%)	119/211 (56.4%)
Leeds Enthesitis Index (n/6)	101, 2.0 [1.0, 3.0]	82, 2.0 [1.0, 3.0]
Patients with dactylitis	73/277 (26.4%)	54/207 (26.1%)
Dactylitis count	73, 2.0 [1.0, 2.0]	54, 2.0 [1.0, 2.0]
PASDAS	223, 5.2 [4.4, 6.0]	159, 5.1 [4.1, 5.8]
DAPSA	229, 24.8 [17.6, 35.3]	165, 23.2 [16.0, 31.9]
cDAPSA	292, 23.5 [15.8, 34.4]	226, 21.4 [15.0, 31.1]
BASDAI	74, 5.5 [3.8, 7.3]	71, 5.5 [3.6, 7.2]
BASFI	75, 3.7 [1.2, 6.7]	72, 3.5 [1.2, 6.6]
PASI	278, 2.1 [0.6, 4.2]	213, 2.1 [0.5, 4.5]
CRP (mg/L)	230, 4.4 [2.0, 13.0]	166, 4.0 [1.7, 12.0]
PsAID-12	287, 4.9 [3.0, 6.8]	221, 4.8 [2.9, 6.8]
HAQ - Standard disability index	289, 0.9 [0.4, 1.4]	223, 0.8 [0.4, 1.4]
Erosion score	74, 3.0 [1.0, 5.0]	46, 2.5 [1.0, 5.0]
Joint Space Narrow Score	197, 5.0 [2.0, 11.0]	141, 4.0 [1.0, 9.0]
Modified Sharp-van der Heijde score	238, 4.0 [0.0, 10.0]	181, 3.0 [0.0, 8.0]

Three hundred patients with a clinical diagnosis of PsA were recruited, and 66 patients were in an embedded trial of intensive medication, so 234 patients were analysed and received step-up T2T care. Data are n (%) for categorical variables and n, median (IQR) for continuous variables. Body Mass Index (BMI) categories are defined as follows: underweight: BMI<18.5/kg/m²; normal: BMI between 18.5 and 24.9 kg/m²; overweight: BMI between 25 and 29.9kg/m² and obese: BMI ≥30kg/m². BASDAI: Bath Ankylosing Spondylitis Disease Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index. cDAPSA: clinical DAPSA. DAPSA: Disease Activity in PsA. HAQ: Health assessment questionnaire. PASDAS: PsA Disease Activity Score. PASI: Psoriasis Area and Severity Index.PsA: psoriatic arthritis. PsAID: Psoriatic Arthritis Impact of Disease. SJC: swollen joint count. TJC: tender joint count.

Results: We recruited 300 patients, 197 with polyarticular PsA and 103 with oligoarticular (< 4 active joints) PsA from 18th April 2018 to 23rd August 2022. Sixty-six patients were in an embedded trial of intensive medication, so the analysis population consisted of 234 patients receiving step-up T2T care. At baseline, PsA was moderately active with a median PASDAS of 5.1 [4.1, 5.8] and a median DAPSA of 23.2 [16.0, 31.9], and 19.7% of patients had structural damage (**Table**). At 48 weeks, 77/234 patients (33.0%) were treated with methotrexate alone and 45/234 (19.0%) were treated with bDMARDs, mainly TNFi (38/45; 84.5%) (**Figure 2**). The proportion of patients achieving the PASDAS 'moderate' and 'good' responses at 48 weeks were 49/146 (33.6%) and 54/146 (37.0%), respectively. DAPSA remission and MDA were achieved in 35/107 (32.7%) and 70/147 (47.6%) patients at 48 weeks, respectively. 37/54 (68.5%) and 68/119 (57.1%) of patients achieved a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

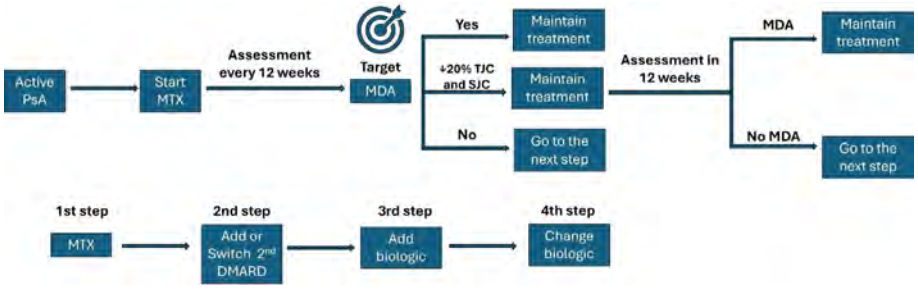


Figure 1 Treat to target strategy

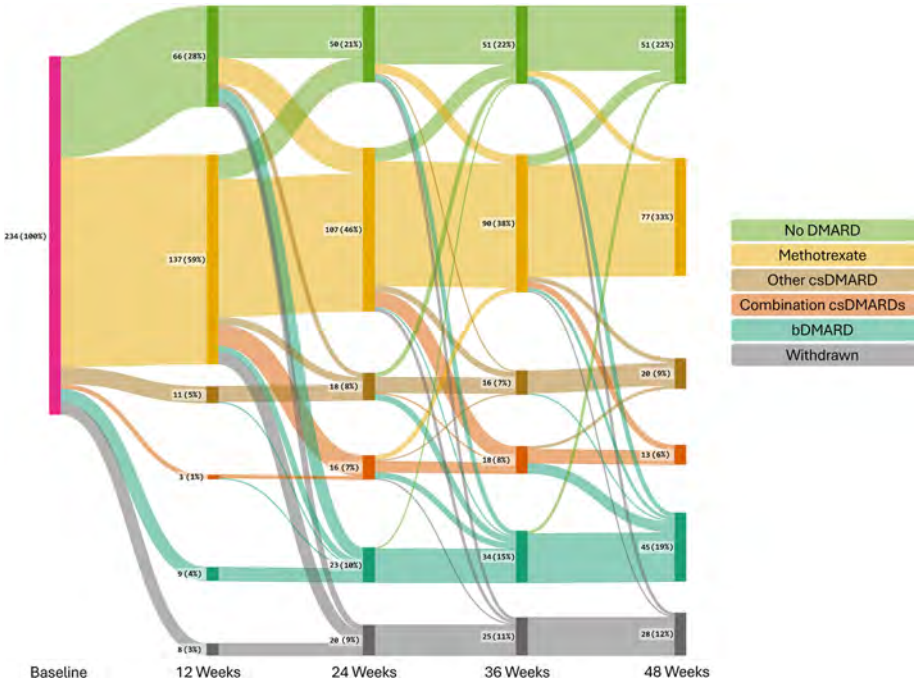


Figure 2 – Medication use in the MONITOR cohort

50% decrease in dactylitis and enthesitis counts, respectively. The majority of patients (117/168 or 69.6%) achieved PSAID patient acceptable symptom state (≤4). No structural progression was noted from baseline to 48 weeks.

Conclusion: In this pragmatic routine implementation of a T2T approach, we report results close to the T2T outcomes in the TICOPA trial (a PASDAS 'good' response, 37.0% vs 46% and or a PASDAS 'moderate' response 33.6% vs 33%), respectively MONITOR-PsA vs TICOPA), suggesting that a pragmatic T2T approach can be implemented with good outcomes in routine practice.

Disclosure: J. Letarouilly: AbbVie/Abbott, 6, Amgen, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Galapagos, 6, Janssen, 6, Nordic Pharma, 6, Novartis, 6, Pfizer, 6; **E. Saeedi**: None; **R. Hurtubise**: Biojamp, 6, Celltrion, 6, UCB, 6; **L. James**: None; **N. Gullick**: AbbVie, 2, 5, 6, Alfasigma, 2, AstraZeneca, 5, Eli Lilly, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Takeda, 2, UCB, 2, 5, 6; **D. Jadon**: None; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ono Pharma, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6; **Y. Sinomati**: None; **L. Tucker**: None; **N. Mian**: None; **S. Massa**: None; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0573

Effects of Sonelokimab, an IL-17A- and IL-17F-Inhibiting Nanobody, on Patient-Reported Symptoms and Quality of Life in Psoriatic Arthritis: Results From the Randomized, Double-Blind, Placebo-Controlled Phase 2 ARGO Trial

Joseph F Merola[1], Alexis Ogdie[2], Alice B. Gottlieb[3], Fabian Proft[4], Nuala Brennan[5], Alex Godwood[5], Matthew R. Thomas[5], Eva Cullen[5], Kristian Reich[6], Laura Coates[7] and Laure Gossec[8], [1]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [2]University of Pennsylvania, Philadelphia, PA, [3]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX, [4]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [5]MoonLake Immunotherapeutics AG, Zug, Switzerland, [6]MoonLake Immunotherapeutics AG and Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, Zug, Switzerland, [7]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [8]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

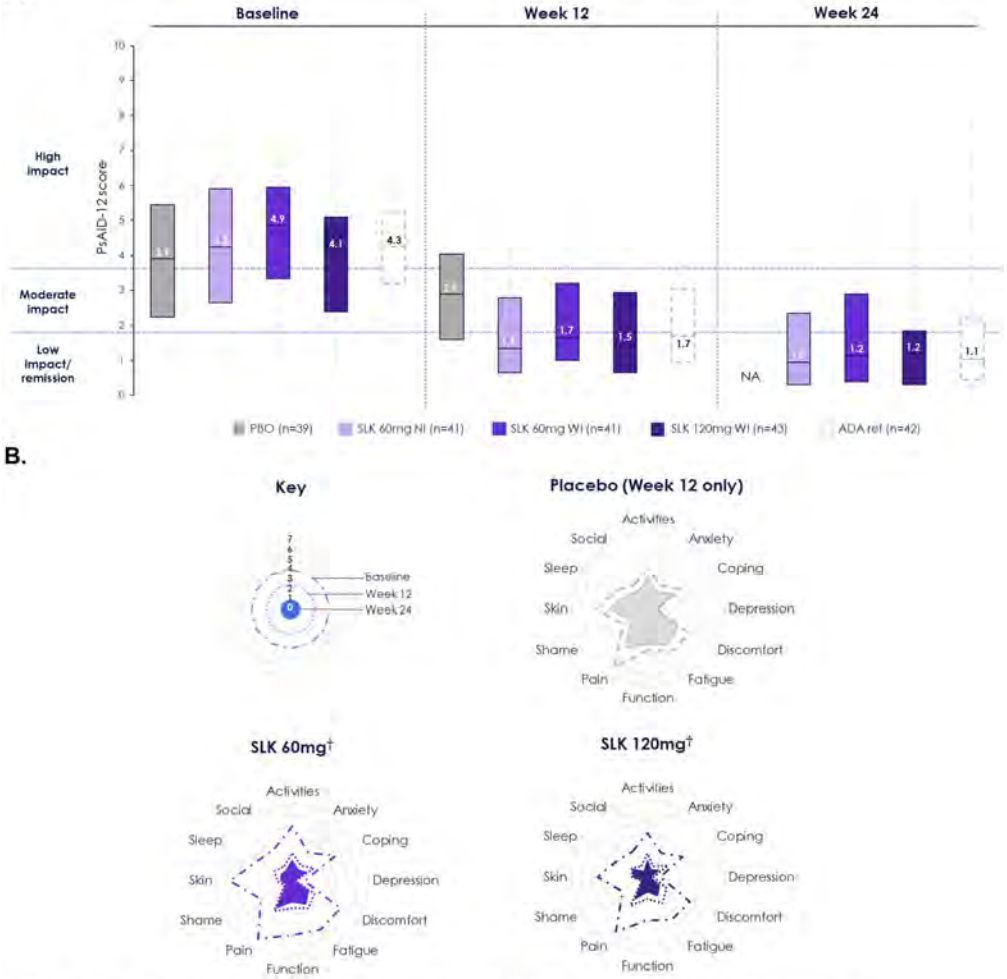
Background/Purpose: Sonelokimab (SLK) is a novel IL-17A- and IL-17F-inhibiting Nanobody designed to target difficult-to-reach sites of inflammation due to its small size and albumin-binding domain. The Phase 2 ARGO trial in patients with active PsA demonstrated the efficacy of SLK on both joint and skin outcomes (McInnes *et al*, EULAR 2024). SLK resulted in robust multidomain clinical responses that have been associated with improved QoL. We assess the effect of SLK on patient-reported outcomes (PROs) from ARGO.

Methods: ARGO (NCT05640245) was a 24-week, global, randomized, double-blind, placebo (PBO)-controlled trial that enrolled adults with active PsA. Patients were randomized to SLK 120mg Q4W (with induction [WI] doses at Weeks [W] 0, 2, 4, and 6), SLK 60mg Q4W WI, SLK 60mg Q4W with no induction (NI), PBO, or adalimumab 40mg Q2W (reference arm; not powered for statistical comparisons). W0–12 were PBO controlled, after which patients originally randomized to PBO switched to SLK 120mg NI; patients with < 20% improvement in SJC and TJC were reassigned treatment at W12 (except patients in the US who completed the study at W12). PROs including PsA Impact of Disease (PsAID)-12 (score range [SR] 0–10), Patient's Assessment of Arthritis Pain (PtAAP; SR 0–100), Patient's Global Assessment of Disease Activity (PGA; SR 0–100), and HAQ Disability Index (HAQ-DI; SR 0–3) were assessed Q4W until W24. Statistical comparisons vs. PBO were conducted at W12 using an MMRM analysis. Analyses at W24, and for patients with skin and joint responses, were observational.

Results: 207 participants were randomized. Patient-reported PsA symptom burden, as assessed by PsAID-12 score, is shown in **Figure 1A** (baseline median PsAID-12 total scores: 3.9–4.9). SLK resulted in significant improvements in PsAID-12 scores at W12, with mean improvements of 2.2–2.5 vs. 1.3 points with PBO (**Table**) and benefits across most individual domains (**Figure 1B**). Continued SLK treatment resulted in further improvements; most patients achieved PsAID-12 low impact (score >1.15–1.95) or remission (score ≤1.15) by W24 (median score: 1.0–1.2; **Figure 1A**). Improvements in PsAID-12 were pronounced (mean [SD] change from baseline [CfB] of –3.3 [1.9] points) in patients who achieved ACR50 + PASI 100, with a median score of 0.35 at W24 across pooled SLK arms. Significant improvements in pain by W12 were observed with SLK, with decreases in PtAAP scores of 30.1–30.9 vs. 18.8 points with PBO (**Table**). Improvements

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. (A) Change from baseline in PsAID-12 total score through Week 24* and (B) response across individual PsAID-12 items through Week 24



*Data show median (horizontal line), interquartile range (box), and minimum/maximum (whiskers). LOCF from Week 12 to 24 has been applied to patients who either switched treatment arm due to lack of response at Week 12 or completed the study at Week 12. All other missing data were imputed using LOCF. A score of ≤1.15 denotes remission/no symptoms/no impact, >1.15–1.95 denotes low symptom/impact severity, >1.95–3.60 denotes moderate symptom/impact severity, and >3.60 denotes high symptom/impact severity (Gossec *et al*, RMD Open 2024).
†With induction doses.
ADA ref, adalimumab reference; LOCF, last observation carried forward; NI, no induction; PBO, placebo; PsAID, Psoriatic Arthritis Impact of Disease; SLK, sonelokimab.

continued to W24, with mean CfB of –36.2 [–64.2%] to –40.0 [–65.6%] points with SLK. Significant improvements in patient-reported disease activity (PGA) scores by W12 were observed with SLK, with decreases of 27.8–31.9 vs. 18.7 points with PBO (**Table**). These improvements continued to W24, with a mean CfB ranging from –32.7 (–52.1%) to –39.7 (–35.6%) points. HAQ-DI scores improved through W24 (mean CfB at W24 of 0.47 [–47.4%] to 0.60 [–59.1%] points with SLK), although responses did not reach statistical significance vs. PBO at W12.

Conclusion: Patients treated with SLK in ARGO reported significant improvements in the symptoms and impact of PsA. Ongoing Phase 3 studies (IZAR-1: NCT06641076; IZAR-2: NCT06641089) will further assess the effect of SLK on PROs and QoL in larger patient populations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. PsAID-12, PtAAP, and PGA outcomes at Week 12

	PBO (n=40)	SLK 60mg NI (n=41)	SLK 60mg WI (n=41)	SLK 120mg WI (n=43)	ADA ref (n=42)
PsAID-12					
LSM* change from baseline (SE)	−1.3 (0.2)	−2.5 (0.2)	−2.3 (0.2)	−2.2 (0.2)	−2.2 (0.2)
P-value	-	<0.001	0.001	0.002	-
PtAAP					
LSM* change from baseline (SE)	−18.8 (3.4)	−30.4 (3.3)	−30.9 (3.3)	−30.1 (3.2)	−29.5 (3.2)
P-value	-	0.011	0.008	0.012	-
PGA					
LSM* change from baseline (SE)	−18.7 (3.3)	−31.9 (3.2)	−28.0 (3.2)	−27.8 (3.1)	−29.2 (3.2)
P-value	-	0.003	0.034	0.038	-

*MMRM including treatment arm, baseline, visit, sex, prior exposure to biologic agents, and treatment by visit interaction as fixed effects and patient as random effect. All *P*-values are nominal.
ADA ref, adalimumab reference; LSM, least squares mean; MMRM, mixed model for repeated measures; NI, no induction; PBO, placebo; PGA, Patient's Global Assessment of Disease Activity; PsAID, PsA Impact of Disease; PtAAP, Patient's Assessment of Arthritis Pain; SE, standard error; SLK, sonelokimab.

Disclosure: J. Merola: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **A. Gottlieb**: Amgen, 2, 4, 6, Avalo Therapeutics, 5, BMS, 5, Eli Lilly and Company, 2, 4, 6, Highlights Therapeutics, 2, 4, 6, Janssen, 2, 4, 5, 6, MoonLake Immunotherapeutics, 5, Novartis, 2, 4, 6, Sanofi, 2, 4, 6, Sun Pharma, 2, 4, 6, Takeda, 2, 4, 6, Teva, 2, 4, 6, UCB, 2, 4, 5, 6; **F. Proft**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Hexal, 2, 6, Janssen, 2, 6, Medscape, 2, 6, MoonLake Pharma, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 5, 6; **N. Brennan**: MoonLake Immunotherapeutics AG, 3, 11; **A. Godwood**: MoonLake Immunotherapeutics, 3, 11; **M. Thomas**: MoonLake Immunotherapeutics AG, 3, 11; **E. Cullen**: MoonLake Immunotherapeutics AG, 3, 11; **K. Reich**: AbbVie, 1, 6, 12, Participated in clinical trials, Almirall, 1, 6, 12, Participated in clinical trials, Amgen, 1, 6, 12, Participated in clinical trials, Boehringer Ingelheim, 1, 6, 12, Participated in clinical trials, Bristol-Myers Squibb(BMS), 1, 6, 12, Participated in clinical trials, Eli Lilly, 1, 6, 12, Participated in clinical trials, Galderma, 1, 6, 12, Participated in clinical trials, Janssen-Cilag, 1, 6, 12, Participated in clinical trials, Kyowa Kirin, 1, 6, 12, Participated in clinical trials, LEO Pharma, 1, 6, 12, Participated in clinical trials, Medac, 1, 6, 12, participated in clinical trials, MoonLake Immunotherapeutics AG, 3, 11, Novartis, 1, 6, 12, participated in clinical trials, Ocean Pharma, 1, 6, 12, participated in clinical trials, Pfizer, 1, 6, 12, participated in clinical trials, Sanofi, 1, 6, 12, participated in clinical trials, UCB, 1, 6, 12, participated in clinical trials; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0574

Bimekizumab 3-Year Efficacy In Patients With Psoriasis And Risk Factors For Progression To Psoriatic Arthritis Or Screening Positive For Psoriatic Arthritis: Long-Term Results From Five Phase 3/3b Trials

Richard G. Langley[1], **Joseph F Merola**[2], Diamant Thaçi[3], Emi Nishida[4], Bruce Strober[5], Richard B. Warren[6], José M. López Pinto[7], Christina Crater[8], Sarah Kavanagh[8] and Paolo Gisondi[9], [1]Dalhousie University, Halifax, NS, Canada, [2]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [3]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany, [4]Nagoya City West Medical Center, Nagoya, Japan, [5]Department of Dermatology, Yale University, New Haven, and Central Connecticut Dermatology Research, Cromwell, CT, [6]Dermatology Centre, Northern Care Alliance, NHS Foundation Trust & Division of Musculoskeletal and Dermatological Sciences, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom, [7]UCB, Madrid, Spain, [8]UCB, Morrisville, NC, [9]Section of Dermatology and Venereology, Department of Medicine, University of Verona, Verona, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) affects up to one-third of patients with psoriasis;[1] early identification and intervention for patients with psoriasis and risk factors (RFs) for progression to PsA, or those screening PsA-positive, may reduce progression.[1]

Methods: Data were pooled from the BE VIVID (NCT03370133), BE SURE (NCT03412747), and BE READY (NCT03410992) phase 3 trials, their open-label extension (OLE) BE BRIGHT (NCT03598790), and the BE RADIANT phase 3b trial (NCT03536884; including its OLE).[2–6] Included patients received bimekizumab (BKZ) 320 mg every 4 weeks (Q4W) to Week 16, then Q4W or Q8W, and entered the OLE (BKZ Total). Data are also reported for the subset of patients who received BKZ Q4W to Week 16 then Q8W continuously (Q4W/Q8W).

Achievement of 100% improvement from baseline in Psoriasis Area and Severity Index (PASI 100) was evaluated through Year 3 (OLE Week 96) in patients with baseline nail involvement (modified Nail Psoriasis Severity Index [mNAPSI] >10), and in patients screening PsA-positive at baseline (Psoriatic Arthritis Screening and Evaluation [PASE] ≥47).

Patients with ≥3 RFs, including mNAPSI >10, scalp Investigator's Global Assessment ≥3, PASI ≥20, and BMI >30 kg/m^2, were also analyzed. [7–10]

Modified non-responder imputation was used: patients discontinuing due to lack of efficacy or treatment-related adverse events were considered non-responders; multiple imputation was used for other missing data.

Results: Among 1,107 BKZ Total patients, 377, 189, and 320 had mNAPSI >10, PASE ≥47, or ≥3 RFs, respectively. Among Q4W/Q8W patients (N=374), 129, 53, and 99 had mNAPSI >10, PASE ≥47, or ≥3 RFs, respectively.

At Week 16, 61.8%, 68.8%, and 59.7% of BKZ Total patients with mNAPSI >10, PASE ≥47, or ≥3 RFs achieved PASI 100, respectively, consistent with the overall BKZ Total population (65.5%). At Year 3, 68.6%, 63.5%, and 66.9% achieved PASI 100, generally consistent with 70.2% overall.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Responses were similar in Q4W/Q8W patients with mNAPSI >10/PASE ≥47/≥3 RFs at Week 16 (72.1%/69.8%/66.7%) and Year 3 (73.8%/66.3%/70.4%), consistent with Q4W/Q8W patients overall (Week 16/Year 3: 71.5%/74.0%).

Conclusion: Rates of complete skin clearance were high through Year 3 in BKZ-treated patients with psoriasis and PsA RFs at baseline, and those screening PsA-positive at baseline, consistent with the overall BKZ-treated group. These patients may benefit from highly effective psoriasis treatment, to help prevent progression in the long term.

References:

1. Zabotti A. Ann Rheum Dis 2023;82:1162–70; **2**. Reich K. Lancet 2021;397:487–98; **3**. Warren RB. N Engl J Med 2021;385:130–41; **4**. Gordon KB. Lancet 2021;397:475–86; **5**. Strober Bl. Br J Dermatol 2023;188:749–59; **6**. Strober B. J Am Acad Dermatol 2023;486–95; **7**. Husni ME. J Am Acad Dermatol 2007;57:581–7; **8**. Yan D. Dermatol Ther (Heidelb) 2018;8:593–604; **9**. Iragorri N. Rheumatology (Oxford) 2019;692–707; **10**. Green A. Br J Dermatol 2020;182:714–20.

Previously presented at AAD 2025.

Disclosure: R. Langley: AbbVie, 1, 6, 12, Principal investigator, Amgen, 1, 6, 12, Principal investigator, Boehringer-Ingelheim, 1, 12, Principal investigator, Celgene, 1, 6, 12, Principal Investigator, Eli Lilly and Company, 1, 6, 12, Principal Investigator, LEO Pharma, 1, 6, 12, Principal Investigator, Merck, 1, 6, 12, Principal Investigator, Novartis, 1, 6, 12, Principal Investigator, Pfizer, 1, 6, 12, Principal Investigator, UCB, 1, 12, Principal Investigator; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol Myers Squibb, 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly and Company, 1, 2, 12, Investigator, Fresenius-Kabi, 2, 5, Galderma, 1, 2, 12, Investigator, Johnson & Johnson, 1, 2, 12, Investigator, Kyowa Kirin, 1, 2, 12, Investigator, L'Oreal, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, New Bridge, 1, 2, 12, Investigator, Novartis, 1, 2, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Sun-Pharma, 1, 2, 5, Target-RWE, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator, Vichy, 1, 2, 12, Investigator; **E. Nishida**: AbbVie, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Daiichi Sankyo, 2, Eli Lilly and Company, 2, Janssen, 2, Kyowa Kirin, 2, LEO Pharma, 2, Maruho, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Sanofi, 2, Sun Pharma, 2, Taiho, 2, Torii, 2, UCB, 2; **B. Strober**: AbbVie, 2, 6, Almirall, 2, 6, Alumis, 2, 6, Amgen, 2, 6, Arcutis, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Capital One, 2, 6, Connect Biopharma, 11, CorEvitas, 2, CorEvitas Psoriasis Registry, 12, Scientific Co-Director (Consulting fee) and Investgator, Dermavant, 2, 6, Eli Lilly and Company, 2, 6, Incyte, 6, Janssen, 2, 6, Journal of Psoriasis and Psoriatic Arthritis, 12, Editor-in-Chief (honorarium), LEO Pharma, 2, 6, Maruho, 2, 6, Meiji Seika Pharma, 2, 6, Mindera Health, 11, Novartis, 2, 6, Oruka, 2, 6, Pfizer, 2, 6, Protagonist, 2, 6, Rapt, 2, 6, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, Sun Pharma, 2, 6, 12, Investigator, Takeda, 2, 6, UCB, 2, 6, Union Therapeutics, 2, 6; **R. Warren**: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, Arena, 2, Astellas, 2, Avillion, 2, Biogen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 6, Celgene, 2, 5, DICE Therapeutics, 2, Eli Lilly and Company, 2, 5, 6, GSK, 2, Janssen, 2, 5, 6, LEO Pharma, 2, 5, Meiji Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, RAPT Therapeutics, 2, Sanofi, 2, Sun Pharma, 2, UCB, 2, 5, Union, 2; **J. López Pinto**: UCB, 3, 12, Shareholder; **C. Crater**: UCB, 3, 12, Shareholder; **S. Kavanagh**: Aclipse Therapeutics, 2, Aliada Therapeutics, 2, Allay Therapeutics, 2, Autobahn Therapeutics, 2, Cognition Therapeutics, 2, Colorado Prevention Center, 2, Karuna Therapeutics, 2, Kisbee Therapeutics, 2, LB Pharmaceuticals, 2, Nesos, 2, Novartis, 2, Onward Medical, 2, PharPoint Research, 2, Summit Analytical, 2, Therini Bio, 2, Tonix Pharmaceuticals, 2, Tornado Therapeutics, 2, UCB, 2, 3, Whitsell Innovations, 2, Worldwide Clinical Trials, 2, Zosano Pharma, 2; **P. Gisondi**: AbbVie, 2, Abiogen, 2, Almirall, 2, Celgene, 2, Eli Lilly and Company, 2, Janssen, 2, LEO Pharma, 2, Merck, 2, MSD, 2, Novartis, 2, Otsuka, 2, Pfizer, 2, Pierre Fabre, 2, Sanofi, 2, UCB, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0575

Why Do Some Psoriatic Arthritis Patients Fail Treatment? Exploring the Profile of D2T Patients

Laia De Daniel Bisbe[1], Jesús Rodriguez[2], Laura Berbel[3], Joan Miquel Nolla[1], Aina Fabregat[2], Monica Cubells[2] and Diego Benavent Nuñez[2], [1]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [2]Hospital Universitari de Bellvitge, Barcelona, Spain, [3]Hospital Universitari de Bellvitge, Barcelona, Catalonia, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease combining psoriasis (Pso) and arthritis. Despite the availability of multiple therapeutic options, many patients experience residual disease activity and fail to achieve remission or low disease activity. Similar to rheumatoid arthritis, where the concept of "difficult-to-treat" (D2T) has emerged, studies are exploring its application to PsA.

Methods: A retrospective analysis of patients with PsA followed during at least two years treated with at least one bDMARD between 2010 and 2024 at Bellvitge University Hospital was conducted. Patients were stratified into two groups (D2T-PsA vs. "Good Responders" (GR)). D2T was defined as failure to ≥1 conventional synthetic DMARD (csDMARD) and ≥2

Table 1. Comparison of demographic, clinical and therapeutical characteristics of good responders and D2T PsA patients

Variables	Good responders n=63	D2T n=40	p-value
Women (n,%)	30 (47.6)	21 (52.5)	0.688
Age, years, mean ± SD	58.1 ± 12.5	51.4 ± 12	**0.022**
Cardiovascular risk factors			
Smoker (ever) (n,%)	49 (78)	30 (75)	0.661
Hypertension (n,%)	17 (28)	12 (30)	1
Dyslipidemia (n,%)	26 (43)	17 (42.5)	1
Diabetes (n,%)	10 (17)	5 (12.5)	0.776
BMI (kg/m2), mean ± SD	26.2 ± 3.9	27.7 ± 6	0.206
PsA disease duration, year, median	15.7 ± 10.5	16.9 ± 10.9	0.730
Psoriasis duration, year, median	26.7 ± 13.5	27.8 ± 15	0.837
PsA types			
Axial involvement, n (%)	3 (5)	3 (8)	0.675
Polyarticular involvement, n (%)	31 (49)	18 (45)	0.683
Oligoarticular, n (%)	25 (40)	18 (45)	1
Distal interphalangeal, n (%)	26 (36)	10 (28)	0.516
Enthesitis, ever, n (%)	32 (52)	21 (52)	1
Dactylitis, ever, n (%)	28 (45)	14 (36)	0.410
Nail involvement, ever, n (%)	40 (68)	25 (68)	1
Serological features			
RF positivity, n (%)	6 (10)	4 (10)	1
Anti-CCP positivity, n (%)	3 (5)	0 (0)	0.262
HLA-B27 positivity, n (%)	4 (7)	4 (11)	0.707
Presence of fibromyalgia	5 (8)	12 (30)	**0.006**

ANA: antinuclear antibody; Anti-CCP: anti-cyclic citrullinated peptide; BMI: Body Mass index; D2T: Difficult-to-treat; RF: rheumatoid factor; PsA: psoriatic arthritis; HLA-B27: human leukocyte antigen B27; SD: standard deviation. n: number of patients.
Bold values are significant at $p<0.05$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of disease activity characteristics of good responders and D2T PsA patients

Variables	Good responders n=63	D2T n=40	p-value
DAPSA			
Before bDMARDs	28.59 ± 12.64	30.79 ± 9.73	0.628
After 6 months	11.08 ± 8.82	17.9 ± 8.40	**0.010**
After 12 months	7.31 ± 5.45	17.47 ± 13.96	**0.048**
PASI			
Before bDMARDs	9.47 ± 5.91	15.58 ± 8.45	**0.017**
After 6 months	3.2 ± 4.13	3.26 ± 3.85	0.967
After 12 months	0.98 ± 1.39	1.44 ± 2.16	0.530
CPR (mg/L)			
Before bDMARDs	8.91 ± 11.50	7.54 ± 7.09	0.824
After 6 months	5.15 ± 6.79	3.66 ± 6.17	0.142
After 12 months	2.76 ± 3.00	6.01 ± 8.36	0.416

ASDAS: Ankylosing Spondylitis Disease Activity Score; bDMARD: biologic disease-modifying antirheumatic drugs; CRP: C-reactive protein; DAPSA, Disease Activity Score for Psoriatic Arthritis; PASI: Psoriasis Area Severity Index

Bold values are significant at p<0.05. All values are expressed as mean and standard deviation

bDMARDs, and "GR" as those who failed to ≥1 csDMARD and <2 bDMARD that used during at least two years. Demographic, clinical, diagnostic, disease activity scores (including DAPSA, PASI) at baseline, 6 and 12 months, and therapeutic data were collected. Besides, bDMARDs number and reasons for their discontinuation were registered. Data were presented as frequencies and percentages for qualitative variables and as mean and standard deviation (SD) for quantitative variables. Chi-squared or Fisher's exact tests were used for the comparative analysis of qualitative variables, while the Student's t-test was applied to quantitative variables to identify differences between both groups.

Results: A total of 103 patients with PsA were included, of whom 40 (38.8%) were categorized as D2T. Clinical characteristics of both groups are shown in Table 1. While gender distribution was similar between groups (47.6 vs 51.5%), patients in the D2T group were significantly younger than the GR (p=0.022). Mean duration of Pso was around 28 years and PsA ranged 16-17 years in both groups. Cardiovascular risk factors did not differ between groups. Nonetheless, fibromyalgia (FM), as diagnosed by the rheumatologist, was more prevalent in the D2T group (p=0.006). No differences were observed in peripheral or extra-musculoskeletal manifestations, nail involvement, or serological features, including HLA-B27 positivity. Regarding disease activity, baseline DAPSA scores were similar between groups, while at 6 and 12 months post-bDMARD initiation, DAPSA scores were significantly higher in the D2T group than in GR (p=0.010 and 0.048, respectively). Baseline PASI scores were significantly higher in the D2T group at baseline (15.58 ± 8.45, p=0.017), although differences were not observed at 6 and 12 months. Tumour necrosis factor inhibitors were the most used bDMARDs in both groups. As seen in Figure 1, the most frequent reason for discontinuation was the primary inefficacy (52%) in the group of GR, while in the D2T group secondary inefficacy (40%) was the most frequent cause.

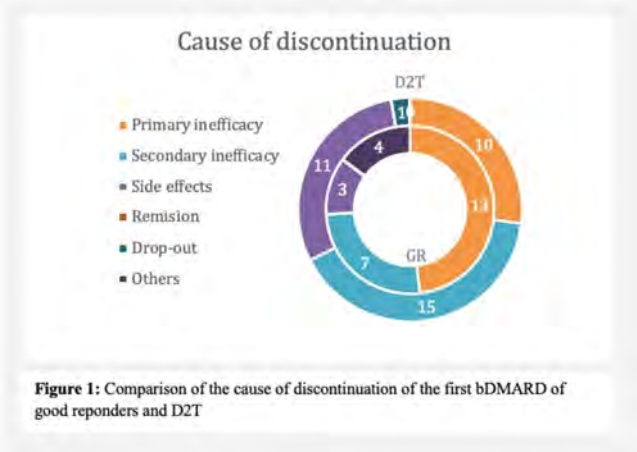


Figure 1: Comparison of the cause of discontinuation of the first bDMARD of good reponders and D2T

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Around one third of PsA patients requiring bDMARDs met D2T criteria. This subset was characterised by younger patients with higher disease activity, greater severity of Pso, and a higher prevalence of FM, while we found no differences in baseline activity by DAPSA or other variables.

Disclosure: L. De Daniel Bisbe: None; **J. Rodriguez**: None; **L. Berbel**: None; **J. Nolla**: None; **A. Fabregat**: None; **M. Cubells**: None; **D. Benavent Nuñez**: None.

Abstract Number: 0576

Factors impacting progression from oligoarticular to polyarticular PsA: Data from the FOREMOST study

Laura Coates[1], Philip J. Mease[2], Joseph Merola[3], Lourdes Perez Chada[4], Dafna D. Gladman[5], Alen Zabotti[6], Ulrich Mrowietz[7], mitsumasa kishimoto[8], Cynthia Deignan[9], Siddharth Chaudhari[10], Lichen Teng[11] and Laure Gossec[12], [1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]UT Southwestern Medical Center, Dallas, TX, [4]Harvard Medical School, Wayland, MA, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]Division of Rheumatology, Department of Medicine (DMED), Academic Hospital "Santa Maria della Misericordia", ASUFC, University of Udine, Udine, Italy, Udine, Italy, [7]Department of Dermatology, University Medical Center Schleswig-Holstein, Kiel, Germany, [8]Kyorin University School of Medicine, Tokyo, Japan, [9]Amgen, Inc., Agoura Hills, CA, [10]Amgen Inc., Thousand Oaks, CA, [11]Amgen Inc., Thousand Oaks, [12]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: FOREMOST (NCT03747939)[1] offers novel insights on early oligoarticular (oligo, ≤4 active joints) PsA. Our aim was to analyse progression to polyarticular (poly; >4 active joints) disease and predictors of progression in FOREMOST.

Table 1. Covariates included in multivariable regression of disease progression at Week 16 of the FOREMOST study

Covariate	Categories
Treatment	APR, PBO
Sex	Male, female
Age	<50 years, ≥50 years
BMI	<30 kg/m², ≥30 kg/m²
csDMARD use prior to FOREMOST	Yes, no
csDMARD use during FOREMOST	Yes, no
Baseline cDAPSA score	>4 to ≤13 (low disease activity), >13 to ≤37 (moderate disese activity)
Patient pain VAS	≤ median (=53), > median
Baseline HAQ-DI score	≤0.5 (remission/disease control), >0.5
Baseline PASS	Yes, no
Baseline PASDAS	<5.4 (low disease activity), ≥5.4
Baseline PtGA VAS	≤ 50, > 50
Baseline LEI	0 (no enthesitis), >0
Baseline SPARCC	0 (no enthesitis), >0
Baseline LDI	0 (no dactylitis), >0
Nail psoriasis at baseline	Yes, no

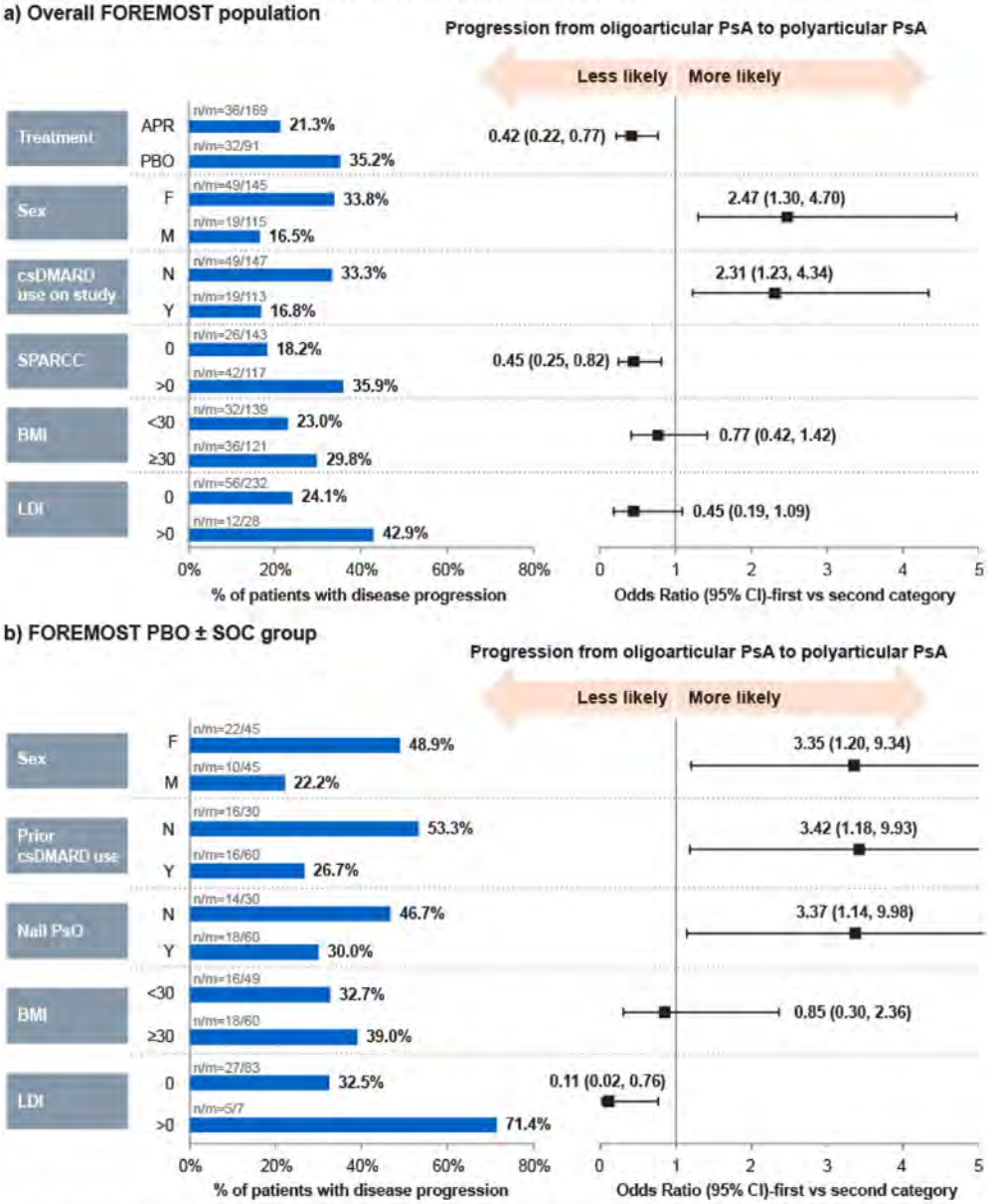
BMI, Body Mass Index; cDAPSA, clinical Disease Activity in PsA; HAQ-DI, Health Assessment Questionnaire Disability Index; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; PASDAS, Psoriatic Arthritis Disease Activity Score; PASS, Patient-Acceptable Symptom State; PtGA, Patient Global Assessment VAS; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analogue score

© Amgen 2025

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: FOREMOST is a randomized trial of 308 patients with early (duration ≤5 years) oligo PsA and limited joint involvement (>1 to ≤4 swollen and >1 to ≤4 tender joints; 66–68 joints assessed) who received apremilast (APR) (n=203) or placebo (PBO) (n=105) for 24 weeks, with a primary outcome at 16 weeks[1]. Standard of care (SoC) NSAIDs and/or conventional synthetic (cs) DMARDs were permitted if taken at a stable dose through Week 24. Progression to poly disease was defined as changing from ≤4 active (swollen and/or tender) joints at baseline to >4 active joints at Week 16. In a post hoc, multivariable regression analysis, we assessed predictors of progression in the overall FOREMOST population and the placebo (PBO)±SOC group (as a surrogate for natural history). Variables of interest were selected on clinical relevance (Table 1) and backward selection used to identify statistically significant predictors of progression ($p < 0.05$ threshold); based on clinical relevance, body mass index (BMI) and enthesitis (Leeds index, LDI) were forced to remain in the model. Missing joint data were imputed using last observation carried forward.

Figure 2. Multivariable regression of disease progression



APR, apremilast; BL, baseline; BMI, Body Mass Index (kg/m²); csDMARDs, conventional synthetic disease modifying antirheumatic drugs; F, Female; LDI, Leeds Dactylitis Index; m, number of patients in category; M, Male; n, number of patients in category with disease progression; N, No; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; Y, Yes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In FOREMOST, most patients had ≤4 active joints at baseline (overall, 268/308 [87%]; APR, 176/203 [87%]; PBO ±SOC, 92/105 [88%]) and baseline characteristics were similar between APR and PBO±SOC[1]. In the overall population, APR was associated with statistically significant lower odds of progression *vs* PBO±SOC (Odds Ratio [OR] [95% CI], 0.42 [0.22, 0.77]; Fig 2a; adjustment for other covariates). After adjusting for treatment, being female (*vs* male), not receiving (*vs* receiving) csDMARDs during the study, and enthesitis (SPARCC >0; *vs* no enthesitis) were associated with statistically significantly higher odds of progression; patients with dactylitis (LDI >0) showed a non-significant trend towards higher odds of progression *vs* patients without dactylitis. In the PBO±SOC group, being female, being csDMARD-naive (*vs* prior csDMARD use), dactylitis (LDI > 0; *vs* no dactylitis), and not having nail psoriasis (*vs* having nail psoriasis) were associated with statistically significant higher odds of progression (Fig 2b).

Conclusion: Our data provides novel insights into factors driving progression from oligo to poly PsA, with female sex, enthesitis and dactylitis found to increase the risk of progression. These data may help clinicians identify patients with poor prognosis who require close monitoring and more intensive treatment. Among patients in FOREMOST receiving PBO, prior csDMARD use decreased the likelihood of progression more than three-fold. Compared with PBO±SOC, APR more than halved the likelihood of progression. These findings highlight the importance of early intervention in oligo PsA and the benefit of APR in delaying/preventing progression to poly disease. Our results should be validated using other PsA cohorts.

1. Gossec, L., et al. Ann Rheum Dis, 2024. 83(11): p. 1480-1488.

Disclosure: L. Coates: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **L. Perez Chada**: Bristol-Myers Squibb(BMS), 2, 6, Takeda, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **A. Zabotti**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, UCB, 2, 5; **U. Mrowietz**: AbbVie, 1, 5, 6, Aditxt, 1, Almirall, 1, Amgen, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Immunic Therapeutics, 1, Janssen-Cilag, 1, LEO Pharma, 1, Merck/MSD, 1, Novartis, 1, Phi-Stone, 1, selectION, 1, Sharp & Dohme, 1, 5, 6, UCB, 1, UNION therapeutics, 1, 5, 6; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **C. Deignan**: Amgen Inc., 3, 11; **S. Chaudhari**: Amgen Inc., 3, 11; **L. Teng**: Amgen Inc., 3, 11; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0577

Persistence and Effectiveness Across PsA Patient Subgroups with Guselkumab and IL-17 Inhibitors: 6-Month Results of the PsABIOnd Observational Study

Laure Gossec[1], Mohamed Sharaf[2], Xenofon Baraliakos[3], mitsumasa kishimoto[4], Ruben Queiro[5], Ennio Lubrano[6], Emmanouil Rampakakis[7], László Köleséri[8], Karissa Lozenski[9], Enrique R. Soriano[10], Proton Rahman[11], Frank Behrens[12] and Stefan Siebert[13], [1]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [2]Janssen - Johnson & Johnson, Dubai, United Arab Emirates, [3]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [4]Kyorin University School of Medicine, Tokyo, Japan, [5]Hospital Universitario Central de Asturias, Oviedo. Asturias, Spain, [6]Department of Medicine, Università deglia Studi del Molise, CAMPOBASSO, Italy, [7]JSS Medical Research, Montreal, QC, Canada, [8]IQVIA, Budapest, Hungary, [9]Johnson & Johnson, Horsham, PA, [10]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires and University Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [11]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada, [12]Goethe-University & Fraunhofer ITMP, Frankfurt, Germany, [13]University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

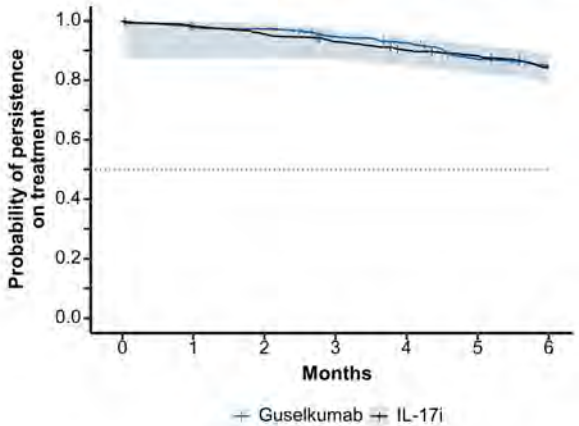
Session Time: 10:30AM–12:30PM

Background/Purpose: Randomized controlled trials have demonstrated the efficacy of IL-23 inhibitors (i) and IL-17i in PsA; however, real-world data on their effectiveness in heterogeneous patient (pt) subgroups in routine care are limited. Some subgroups, such as older, obese, or biologic-experienced pts, are of particular interest as pts in these groups report worse treatment outcomes.[1] The objective of the current analysis was to assess the 6-month persistence and effectiveness of guselkumab (GUS) and IL-17i across these subgroups of interest.

Methods: PsABIOnd (NCT05049798) is a global (20 countries) observational study in pts with PsA starting GUS or IL-17i as 1st-to-4th line of biologic therapy per their standard of care.[2] Here, the full population of the PsABIOnd study over 6 months

Fig 1. Persistence on treatment over 6 months with GUS and IL-17i

Kaplan-Meier curve of treatment persistence by initial treatment line through month 6.



Number of Patients at Risk

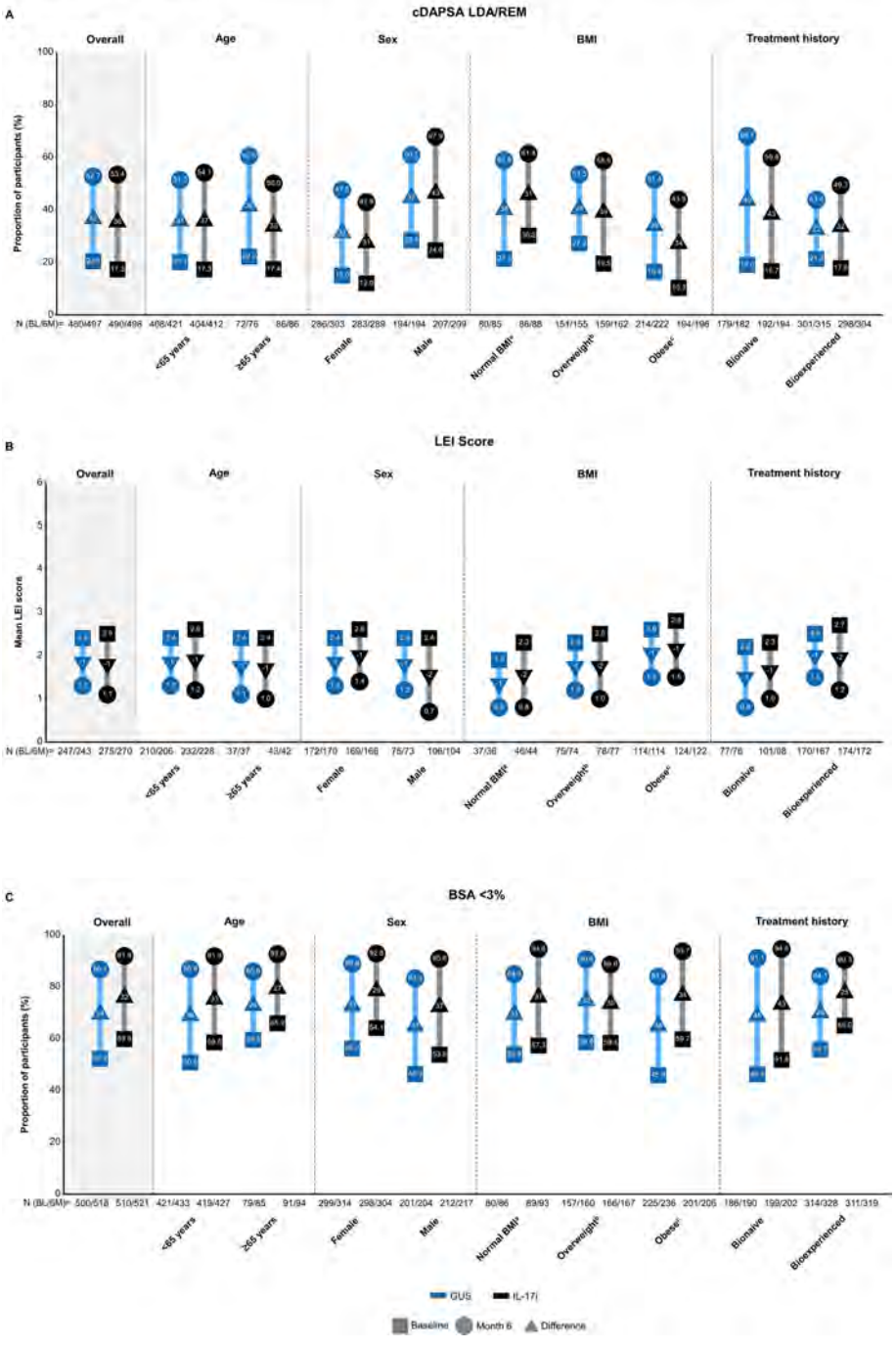
Guselkumab	555	545	540	521	509	477	461
IL-17i	579	567	552	535	516	506	480

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of follow up was analyzed. Analyses were performed according to initial treatment group allocation in the overall population and in specific subgroups defined by baseline (BL) age, sex, BMI categories, and prior biologic use. Persistence on treatment (i.e., no stop/switch) over 6 months was assessed via the Kaplan-Meier estimator function. Propensity score (PS) analysis was used to evaluate hazard ratio (HR) of GUS vs IL-17i stop/switch prior to the 6-month visit, adjusting for BL variable imbalances across cohorts. Effectiveness was descriptively assessed using rates and means at BL and 6 months of the following measures: swollen (SJC66) and tender (TJC68) joint counts, clinical Disease Activity Index for PsA (cDAPSA)-based low disease activity (LDA)/remission (REM; ≤13), the Leeds Enthesitis Index (LEI; 0-6), psoriasis body

Fig 2. PsA clinical outcomes at baseline and the 6-month visit with GUS and IL-17i across distinct participant subgroups: (A) cDAPSA LDA/REM, (B) LEI score, and (C) BSA<3%

Absolute difference between baseline and month 6 presented in triangles. Last observation carried forward was imputed for participants with no 6-month visit. [a]BMI: ≥18.5 to <25 kg/m². [b]BMI: ≥25 to <30 kg/m². [c]BMI: ≥30 kg/m².



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

surface area (BSA)< 3%, Dermatology Life Quality Index (DLQI), and number of nails affected by psoriatic disease (0-20). Dactylitis was not assessed due to the low prevalence of dactylitis at BL

Results: Of the 1134 pts analyzed, 555 and 579 pts received GUS or IL-17i, respectively, as their initial treatment. At BL, the GUS/IL-17i cohorts were generally well balanced across subgroups of interest: 83.4%/81.3% were < 65 years of age; 60.4%/59.2% were female; 48.0%/43.4% had BMI≥30 kg/m^2; and 63.4%/62.3% had previously received ≥1 targeted therapy.

Persistence on treatment up to 6 months was high in both cohorts, with 526/555 (94.8%) GUS and 539/579 (93.1%) IL-17i pts remaining on their initial treatment line at the 6-month visit (PS-adjusted HR of GUS vs IL-17i stop/switch [95% confidence interval]: 0.93 [0.75-1.16]; **Fig 1**). Persistence on GUS and IL-17i was also comparable in the different pt subgroups (data not shown). Across pt subgroups of interest, similar improvements in joint symptoms (SJC66; TJC68; cDAPSA LDA/REM; **Fig 2A**), enthesitis (LEI; **Fig 2B**), skin involvement (BSA< 3%; **Fig 2C;** DLQI), and psoriatic nail disease were observed with GUS and IL-17i at the 6-month visit.

Conclusion: Treatment with GUS or IL-17i resulted in comparable treatment persistence and effectiveness, regardless of age, sex, BMI, or treatment history, through 6 months. These results support the real-world effectiveness of GUS and IL-17i across PsA subpopulations

References

1. Haddad. Semin Arthritis Rheum. 2025;152737
2. Siebert. Rheumatol Ther. 2023;10:489

Disclosure: L. Gossec: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **M. Sharaf**: Johnson & Johnson, 3, 11; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **R. Queiro**: AbbVie, 2, 5, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Johnson & Johnson, 2, 5, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6; **E. Lubrano**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GlaxoSmithKlein, 6, Johnson & Johnson, 6, Novartis, 6, UCB, 6; **E. Rampakakis**: Johnson & Johnson, 2, JSS Medical Research, 3; **L. Kôleséri**: IQVIA, 3, Johnson & Johnson, 2; **K. Lozenski**: BMS, 11, Johnson & Johnson, 3, 11; **E. Soriano**: AbbVie, 5, 6, BMS, 5, 6, Eli Lilly, 5, 6, GSK, 5, 6, J&J, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Raffo, 5, 6, UCB, 5, 6; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **F. Behrens**: AbbVie, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genzyme, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 5, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 6, UCB, 2, 6; **S. Siebert**: AbbVie, 6, Amgen, 6, AstraZeneca, 6, BMS, 5, Boehringer-Ingelheim, 5, Eli Lilly, 5, GlaxoSmithKlein, 5, Johnson & Johnson, 5, 6, Novartis, 6, Pfizer, 6, Syncona, 6, Teijin Pharma, 6, UCB, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0578

Real-world Effectiveness of Upadacitinib on Group for Research and Assessment of Psoriasis and Psoriatic Arthritis Core Domains for Patients with Psoriatic Arthritis: Data from the CorEvitas Psoriatic Arthritis/ Spondyloarthritis Registry

Philip J. Mease[1], Xiaolan Ye[2], Christopher Saffore[3], Thomas Iyile[4], Nicole Middaugh[5], Taylor Blachley[5], Melissa Eliot[5] and Alexis Ogdie[6], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]AbbVie Inc., Mettawa, IL, [3]AbbVie Inc., waukegan, IL, [4]AbbVie Inc, North Chicago, IL, [5]CorEvitas, LLC, Waltham, MA, [6]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

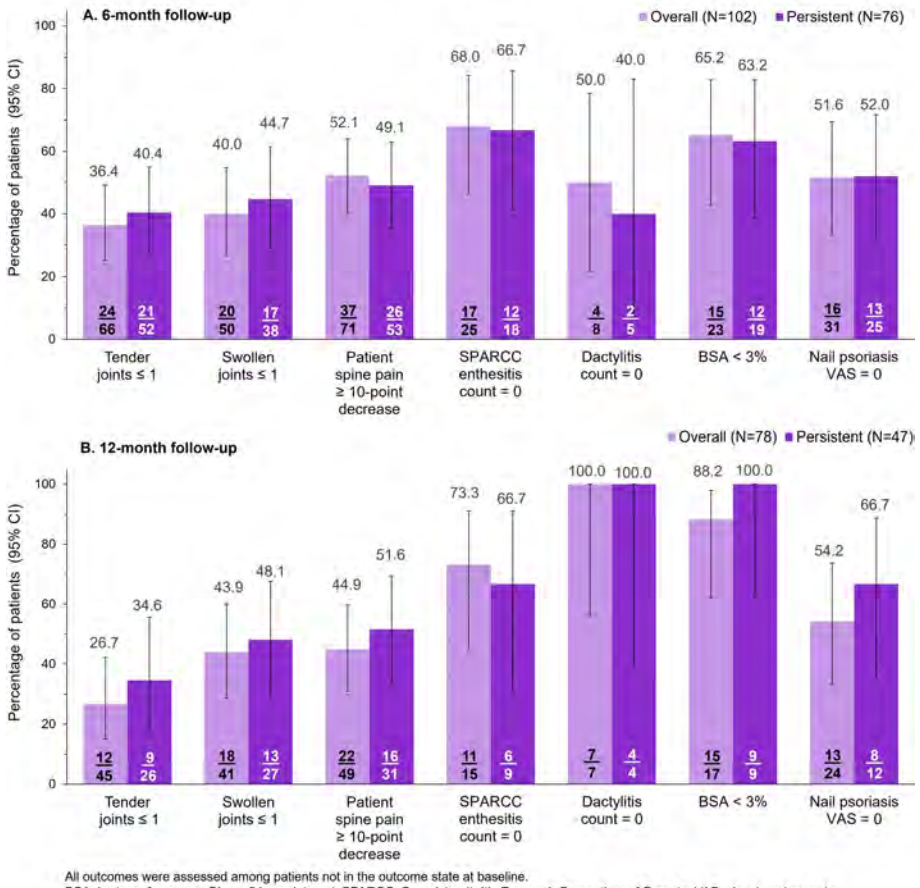
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogenous inflammatory disease that can cause substantial impairment in quality of life in affected patients. The Group for Research and Assessment of Psoriasis and PsA (GRAPPA) domain-based treatment recommendations for PsA highlight 6 key domains: peripheral arthritis, axial disease, enthesitis,

Figure 1. Response rates of clinical outcomes among patients with PsA initiating upadacitinib overall and among those persisting on therapy



All outcomes were assessed among patients not in the outcome state at baseline.
BSA, body surface area; CI, confidence interval; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale.

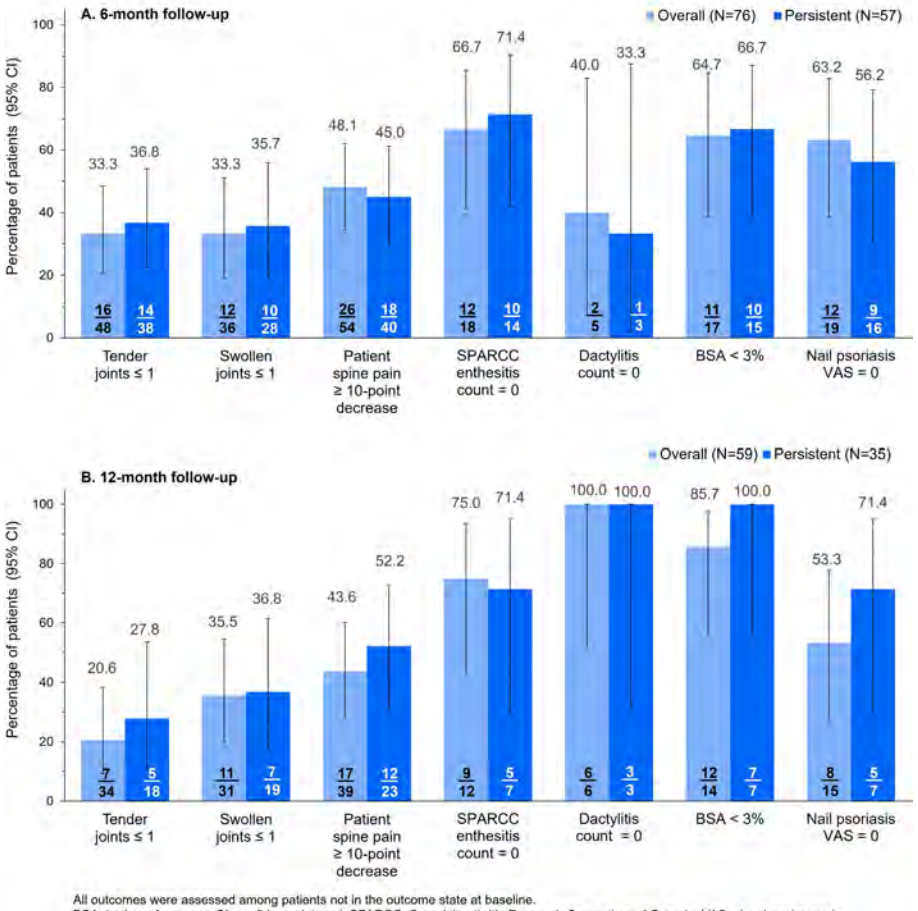
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

dactylitis, skin psoriasis, and nail disease. Upadacitinib (UPA) has demonstrated efficacy versus placebo across key domains in clinical trials in patients with PsA, but real-world data are limited. In this study, we evaluated changes in disease activity measures and patient-reported outcomes (PROs) in patients with PsA who initiated UPA and persisted on therapy for 6 and 12 months overall in a real-world setting.

Methods: Patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry who initiated UPA during or after December 2021 and had a baseline visit associated with UPA initiation were included. Disease activity and PROs were summarized at baseline; response rates (n [%]; 95% [confidence intervals] CI) for patients who were not in the outcomes state at baseline were calculated at 6 and 12 months. Outcomes included achievement of tender joint count ≤ 1, swollen joint count ≤ 1, patient spine pain (0–100 visual analog scale [VAS]) ≥ 10-point decrease, enthesitis count = 0, dactylitis count = 0, < 3% body surface area (BSA) affected by psoriasis, and nail psoriasis (0–100 VAS) = 0. Results are reported for all initiators, for those persisting on UPA treatment at 6 or 12 months, and for a subset of patients with prior TNFi-experience.

Results: This analysis included 214 patients who initiated UPA. Of these 48% (n/N, 102/214) and 36% (78/214) had 6-month and 12-month follow-up visit data available, respectively. Among all initiators, 65% (140/214) were female, mean age was 54 years, 41% (88/214) were conventional synthetic DMARD-naïve and 61% (130/214) had previously used ≥2 biologic or targeted synthetic DMARDs. Among those with respective follow-up visits, 75% (76/102) and 60% (47/78) were

Figure 2. Response rates of clinical outcomes among TNFi-experienced patients with PsA initiating upadacitinib overall and among those persisting on therapy



All outcomes were assessed among patients not in the outcome state at baseline.
BSA, body surface area; CI, confidence interval; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

persistent on therapy at 6 and 12 months. At the 6-month follow-up visit, 36% (24/66) of all initiators achieved ≤ 1 tender joint, 40% (20/50) achieved ≤ 1 swollen joint, 52% (37/71) experienced a ≥10-point decrease in spine pain, 68% (17/25) achieved resolution of enthesitis, 50% (4/8) achieved resolution of dactylitis, 65% (15/23) achieved BSA < 3%, and 52% (16/31) achieved nail psoriasis VAS = 0 (**Figure 1**). Similar trends were seen in the subset of patients who were TNF-experienced (**Figure 2**), and in those who persisted on UPA therapy for 6 and 12 months.

Conclusion: This real-world study of patients with PsA showed that those who initiated UPA had improvements in disease activity and PROs consistent with key GRAPPA domains at 6 and 12 months. Similar results were observed in the subset of TNFi-experienced patients.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **X. Ye**: AbbVie, 3, 11; **C. Saffore**: AbbVie, 3, 11; **T. Iyile**: AbbVie, 3, 11; **N. Middaugh**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **T. Blachley**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort between CorEvita, Thermo Fisher Scientific, Inc., 11; **M. Eliot**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort between CorEvita; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11.

Abstract Number: 0579

Characteristics and Treatment Patterns among Patients with Psoriatic Arthritis in the CorEvitas Psoriatic Arthritis/Spondyloarthritis Registry Initiating a Third or Higher Line of Biologic or Targeted Disease-Modifying Antirheumatic Drug Therapy

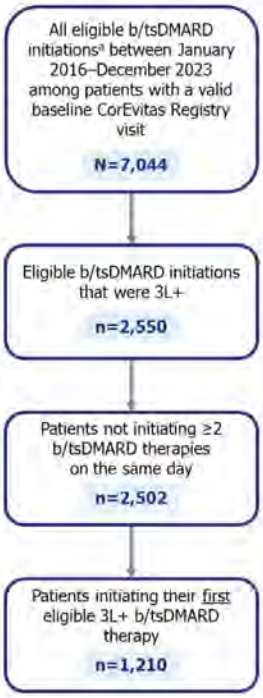
Philip J. Mease[1], Nicole Middaugh[2], Yolanda Muñoz Maldonado[2], Chao Song[3], Melissa Eliot[2], Robert Low[3] and Alexis Ogdie[4], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]CorEvitas, LLC, Waltham, MA, [3]UCB, Smyrna, GA, [4]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease affecting the joints, skin, and other regions of the body. It impacts up to 36% of patients with psoriasis in the US, often substantially impairing quality of life.[1,2] Biologic or targeted synthetic (b/ts) DMARDs, including interleukin (IL)-17, IL-12/23, tumor necrosis factor (TNF), and Janus kinase (JAK) inhibitors (i), have been effective in improving symptoms, but patients may experience suboptimal response or loss of response despite undergoing multiple lines of treatment.[2,3] This study analyzed characteristics and treatment patterns of patients with PsA upon initiation of a third-line or higher (3L+) b/tsDMARD therapy. Understanding these patterns may offer insights into the benefits of managing PsA in its early stages with effective treatments.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Selection of eligible 3L+ b/tsDMARD initiations in the CorEvitas PsA/Spondyloarthritis Registry



[a] Initiations included any line of therapy. Eligible bDMARDs included abatacept, adalimumab, bimekizumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, ustekinumab. Eligible tsDMARDs included tofacitinib and upadacitinib. 3L+: third-line or higher; b/tsDMARD: biologic or targeted synthetic disease-modifying antirheumatic drug; PsA: psoriatic arthritis.

Methods: This retrospective cohort study included patients who were ≥18 years of age, had a PsA diagnosis, and initiated a b/tsDMARD between January 2016–December 2023 as a 3L+ therapy at or after entry into the CorEvitas PsA/Spondyloarthritis Registry (baseline), a prospective, multicenter, observational US registry. Patient characteristics, treatment histories, and treatment patterns were assessed at baseline. Continuous variables were reported as means with standard deviation (SD) or medians with interquartile range (IQR), while categorical variables were described with counts and percentages.

Results: The CorEvitas registry included 7,044 initiations of b/tsDMARDs, with 2,550 (36.2%) being 3L+ initiations. This analysis included 1,210 patients initiating their first eligible 3L+ b/tsDMARD therapy (**Figure 1**). The mean (SD) age was 54.2 (12.3) years, 721 (59.7%) patients were female, and 1,105 (92.9%) patients were white. Two or more comorbidities were observed in 446 (36.9%) patients. The most common comorbidities were obesity, hypertension, and depression, reported in 734 (61.6%), 484 (40.0%), and 262 (21.7%) patients, respectively. Patients had a median (IQR) PsA duration of 7.0 (3.0, 12.0) years and symptom duration of 10.0 (5.0, 18.0) years. The median (IQR) time from first b/tsDMARD therapy to initiation of current therapy was 1.5 (0.7, 2.9) years. Most patients (813 [94.2%]) reported active disease as the reason for initiating a 3L+ therapy. Patients frequently used two prior bDMARDs (700 [57.9%]), while 1,102 (91.1%) were tsDMARDs naïve (**Table 1**). Concomitant conventional synthetic DMARDs were taken by 328 (27.1%) patients. Biologics most often used immediately prior to 3L+ therapy were TNFis (726 [68.5%]) or IL-17is (182 [17.2%]) (**Figure 2**). The most commonly initiated 3L+ b/tsDMARD class was IL-17i, used by 455 (37.6%) patients, followed by TNFis (338 [27.9%]), IL-23is (169 [14.0%]), and JAKis (148 [12.2%]).

Conclusion: These findings highlight the disease burden in this heavily pre-treated population, underscoring the need for early, more effective PsA treatments that provide a sustained response.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

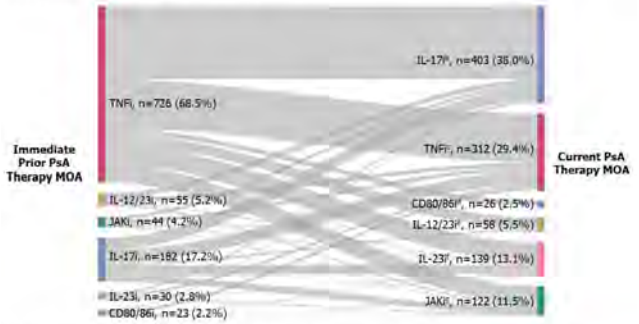
Table 1. Baseline characteristics and disease activity measures of patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry

Characteristic	Total Patients Included (N=1,210)
Demographics	
Age (years), mean (SD)	54.2 (12.3)
Sex (female; N=1,207), n (%)	721 (59.7)
Race (white; N=1,190), n (%)	1,105 (92.9)
Comorbidities, n (%)	
Obesity (BMI ≥30)	734 (61.6)
Hypertension	484 (40.0)
Depression	262 (21.7)
Fibromyalgia	226 (18.7)
Diabetes	199 (16.4)
Cardiovascular Disease	139 (11.5)
Anxiety	82 (6.8)
Malignancies	79 (6.5)
IBD	30 (2.5)
Uveitis	19 (1.6)
PsA Disease Characteristics, median (IQR)	
Duration of Disease[a] (years; N=1,202)	7.0 (3.0, 12.0)
Duration of Symptoms (years; N=1,194)	10.0 (5.0, 18.0)
PsA Disease Activity Measures	
cDAPSA: moderate (>13–≤27; N=1,149), n (%)	489 (42.6)
MDA[b] (N=1,199), n (%)	215 (17.9)
VLDA[c] (N=1,209), n (%)	51 (4.2)
SJC66 (N=1,175), mean (SD)	2.7 (4.4)
TJC68 (N=1,175), mean (SD)	7.7 (10.3)
Dactylitis Count, mean (SD)	0.4 (1.6)
LEI (N=1,007), mean (SD)	0.5 (1.1)
PGA of Arthritis (VAS-100; N=1,196), mean (SD)	31.7 (23.4)
PGA of PsA and Psoriasis (VAS-100; N=1,193), mean (SD)	36.7 (23.9)
BSA (% Involvement; N=1,178), mean (SD)	5.5 (10.5)
Patient-Reported Outcomes, mean (SD)	
PtGA of Arthritis (VAS-100; N=1,187)	47.2 (26.3)
PtGA of Arthritis and Psoriasis (VAS-100; N=1,185)	47.4 (26.6)
HAQ-DI (score: 0–3; N=1,192)	0.9 (0.7)
Pain (VAS-100; N=1,201)	54.0 (27.7)
Fatigue (VAS-100, N=1,203)	53.8 (28.0)
Time from First b/tsDMARD to Initiation of Current Therapy[d] (years; N=649), median (IQR)	1.5 (0.7, 2.9)
Prior csDMARDs, n (%)	
0	308 (25.5)
1	614 (50.7)
2+	288 (23.8)
Prior bDMARDs, n (%)	
0	5 (0.4)
1	104 (8.6)
2	700 (57.9)
3	246 (20.3)
4+	155 (12.8)
Prior tsDMARDs, n (%)	
0	1,102 (91.1)
1	104 (8.6)
2+	4 (0.3)
Prior Prednisone Use, n (%)	244 (20.2)
Prior Arthrocentesis, n (%)	421 (34.8)
Prior NSAID use, n (%)	333 (27.5)
Monotherapy[e], n (%)	861 (71.2)
Reasons for Initiating Current Therapy[f] (N=863), n (%)	
Active disease	813 (94.2)
Insurance	4 (0.5)
Safety	3 (0.3)
Lack of Efficacy[g]	3 (0.3)
Other Reasons	40 (4.6)

[a] Defined as time from the date of PsA diagnosis; **[b]** MDA was achieved if 5 out of the following 7 conditions were met: TJC68 ≤1, SJC66 ≤1, BSA ≤3%, pain (VAS-100) ≤15, PtGA of PsA and Psoriasis (VAS-100) ≤20, LEI ≤1, and HAQ-DI (score: 0–3) ≤0.5; **[c]** VLDA was achieved if all of the following conditions were met: TJC68 ≤1, SJC66 ≤1, BSA ≤3%, pain (VAS-100) ≤15, PtGA of PsA and Psoriasis (VAS-100) ≤20, LEI ≤1; **[d]** Data reported only if available; **[e]** Concomitant use did not distinguish between bridging (temporarily use [<6 months] of another b/tsDMARD) and dual therapy (addition of another b/tsDMARD to main therapy). The main therapy was the first prescribed therapy, and if two therapies were started at the same time, the patient was excluded. This applied only to the concomitant use of b/tsDMARDs and not to the concomitant use of csDMARDs; **[f]** As reported by physician; **[g]** Defined as either failure to maintain or failure to reach adequate response from prior therapy. b/tsDMARD: biologic or targeted synthetic disease-modifying antirheumatic drug; BMI: body mass index; BSA: body surface area; cDAPSA: Clinical Disease Activity Index for PsA; CI: confidence interval; csDMARD: conventional synthetic disease-modifying antirheumatic drug; HAQ-DI: Health Assessment Questionnaire Disability Index; IBD: inflammatory bowel disease; IQR: interquartile range; LEI: Leeds Enthesitis Index; MDA: minimal disease activity; NSAID: nonsteroidal anti-inflammatory drug; PGA: Physician Global Assessment; PsA: psoriatic arthritis; PtGA: Patient Global Assessment; SD: standard deviation; SJC66: swollen joint count in 66 joints; TJC68: tender joint count in 68 joints; VAS: Visual Analog Scale; VLDA: very low disease activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Current and immediate prior treatment patterns of patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry at baseline[a]



N=1,060. **[a]** Cohorts were not mutually exclusive; **[b]** Bimekizumab, ixekizumab, and secukinumab; **[c]** Adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab and its biosimilars; **[d]** Abatacept; **[e]** Ustekinumab; **[f]** Guselkumab and risankizumab; **[g]** Tofacitinib and upadacitinib. CD: cluster of differentiation; i: inhibitor; IL: interleukin; JAK: Janus kinase; MOA: mechanism of action; PsA: psoriatic arthritis; TNF: tumor necrosis factor.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **N. Middaugh**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **Y. Muñoz Maldonado**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **C. Song**: UCB, 3, 11; **M. Eliot**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort between CorEvita; **R. Low**: UCB, 3, 11; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5.

Abstract Number: 0580

Persistence and Disease Activity Control among Patients with Psoriatic Arthritis in the CorEvitas Psoriatic Arthritis/Spondyloarthritis Registry Initiating a Third or Higher Line of Biologic or Targeted Synthetic Disease-Modifying Antirheumatic Drug Therapy

Philip J. Mease[1], Nicole Middaugh[2], Yolanda Muñoz Maldonado[2], Chao Song[3], Melissa Eliot[2], Robert Low[3] and Alexis Ogdie[4], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]CorEvitas, LLC, Waltham, MA, [3]UCB, Smyrna, GA, [4]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic disease that causes inflammation of the joints, entheses, spine, skin, and nails.[1] While available advanced treatments (txs) for PsA have expanded, many patients (pts) have suboptimal responses despite undergoing multiple lines of biologic or targeted synthetic DMARDs (b/tsDMARDs).[2] This study evaluated tx persistence (time to discontinuation) and change from baseline (CfB) in disease activity and pt-reported outcomes (PROs) among pts with PsA following initiation of a third-line or higher (3L+) b/tsDMARD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

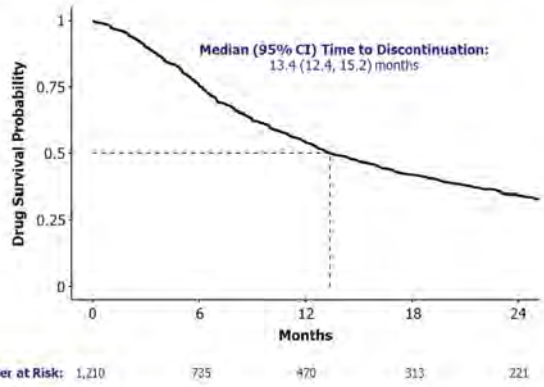
Methods: This retrospective cohort study included pts who were ≥18 years old, had a PsA diagnosis, and initiated a 3L+ b/tsDMARD between January 2016–December 2023, at or after entry into the CorEvitas PsA/ Spondyloarthritis Registry (baseline), a prospective, multicenter, observational US registry. Persistence was defined as time from therapy initiation to

Table 1. Demographics, PsA disease activity, and PRO measures at baseline among patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry

Characteristic	Total Patients Included (N=1,210)
Patient Demographics	
Age (years), mean (SD)	54.2 (12.3)
Sex (female; N=1,207), n (%)	721 (59.7)
Concomitant csDMARD Use[a], n (%)	328 (27.1)
PsA Duration (years; N=1,202), median (IQR)	7.0 (3.0, 12.0)
Class of b/tsDMARD Initiated as 3L+ Therapy[b], n (%)	
IL-17i	455 (37.6)
TNFi	338 (27.9)
IL-23i	169 (14.0)
JAKi	148 (12.2)
IL-12/23i	68 (5.6)
non-TNFi	32 (2.6)
Disease Activity	
PGA of Arthritis (VAS-100; N=1,196)	
Mean (SD)	31.7 (23.4)
Median (IQR)	30.0 (15.0, 48.0)
PGA of PsA and Psoriasis (VAS-100; N=1,193)	
Mean (SD)	36.7 (23.9)
Median (IQR)	35.0 (20.0, 51.0)
BSA (% Involvement; N=1,178)	
Mean (SD)	5.5 (10.5)
Median (IQR)	1.0 (0.0, 5.0)
BSA Category (N=1,178), n (%)	
Mild Disease (≥0–<3%)	728 (61.8)
Moderate Disease (3–<10%)	233 (19.8)
Severe Disease (10–100%)	217 (18.4)
IGA of Psoriasis (N=1,180), n (%)	
Clear (score: 0)	355 (30.1)
Almost Clear (score: 1)	248 (21.0)
Mild Disease (score: 2)	275 (23.3)
Moderate Disease (score: 3)	243 (20.6)
Severe Disease (score: 4)	59 (5.0)
cDAPSA (Score: 0–154; N=1,149)	
Mean (SD)	20.6 (15.1)
Median (IQR)	18.0 (10.5, 26.5)
cDAPSA Category (N=1,149), n (%)	
Remission (>0–≤4)	111 (9.7)
Low (>4–≤13)	284 (24.7)
Moderate (>13–≤27)	489 (42.6)
High (>27–≤154)	265 (23.1)
MDA[c] (N=1,199), n (%)	215 (17.9)
VLDA[d] (N=1,209), n (%)	51 (4.2)
BASDAI (VAS-10; N=1,184)	
Mean (SD)	5.1 (2.5)
Median (IQR)	5.5 (3.2, 7.1)
Nail Psoriasis (VAS-100) (N=1,163)	
n (%)	1,163 (96.1)
Mean (SD)	8.0 (17.5)
Median (IQR)	0.0 (0.0, 5.0)
SJC66 (N=1,175)	
Mean (SD)	2.7 (4.4)
Median (IQR)	1.0 (0.0, 4.0)
TJC68 (N=1,175)	
Mean (SD)	7.7 (10.3)
Median (IQR)	4.0 (1.0, 10.0)
mPASDAS (Score: 0–10; N=793)	
Mean (SD)	4.6 (1.4)
Median (IQR)	4.7 (3.6, 5.5)
Dactylitis Count	
n (%)	1,210 (100.0)
Mean (SD)	0.4 (1.6)
Median (IQR)	0.0 (0.0, 0.0)
SPARCC Enthesitis Index (Score: 0–16)	
Mean (SD)	1.08 (2.24)
Median (IQR)	0.0 (0.0, 1.0)
LEI (Score: 0–6; N=1,007)	
n (%)	1,007 (83.2)
Mean (SD)	0.5 (1.1)
Median (IQR)	0.0 (0.0, 0.0)
PROs	
PtGA of Arthritis (VAS-100; N=1,187)	
Mean (SD)	47.2 (26.3)
Median (IQR)	50.0 (25.0, 70.0)
PtGA of Arthritis and Psoriasis (VAS-100; N=1,185)	
Mean (SD)	47.4 (26.6)
Median (IQR)	50.0 (25.0, 70.0)
HAQ-DI (Score: 0–3; N=1,192)	
Mean (SD)	0.9 (0.7)
Median (IQR)	0.9 (0.4, 1.5)
Pain (VAS-100; N=1,201)	
Mean (SD)	54.0 (27.7)
Median (IQR)	60.0 (30.0, 75.0)
Fatigue (VAS-100; N=1,203)	
Mean (SD)	53.8 (28.0)
Median (IQR)	60.0 (30.0, 75.0)
Spine Pain (VAS-100; N=1,199)	
Mean (SD)	36.8 (30.7)
Median (IQR)	35.0 (5.0, 65.0)
Morning Stiffness (VAS-100; N=1,203)	
Mean (SD)	53.8 (29.4)
Median (IQR)	60.0 (30.0, 80.0)
Duration of Morning Stiffness (N=1,193), n (%)	
0 minutes	60 (5.0)
1–29 minutes	188 (15.8)
30–59 minutes	273 (22.9)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan-Meier curve of treatment persistence among patients with PsA initiating a 3L+ b/tsDMARD therapy



3L+: third-line or higher; b/tsDMARD: biologic or targeted synthetic disease-modifying antirheumatic drug; CI: confidence interval; PsA: psoriatic arthritis.

Table 2. CfB in disease activity and PRO measures following initiation of a 3L+ b/tsDMARD to 6-month follow-up among patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry[a]

Characteristic	n	CfB (Δ)[b] or Achievement Response Rate (%)[c]	95% CI[d]
Disease Activity			
PGA of Arthritis (VAS-100)	624	−10.0	−12.4, −7.6
PGA of PsA and Psoriasis (VAS-100)	618	−12.5	−15.0, −10.0
BSA (% Involvement)	599	−2.5	−3.5, −1.4
BSA[e] <3%	256	52.3%	46.0, 58.6
IGA 0/1[f]	329	46.2%	40.7, 51.8
cDAPSA (score: 0–154)	566	−4.8	−6.5, −3.2
cDAPSA: LDA[g]	368	37.8%	32.8, 43.0
cDAPSA: Remission[h] (>0–≤4)	504	12.7%	10.0, 16.0
mPASDAS (score: 0–10)	281	−0.5	−0.8, −0.3
MDA[i]	447	22.8%	19.1, 27.0
VLDA[j]	520	8.3%	6.1, 11.1
BASDAI (VAS-10)	612	−0.7	−0.9, −0.4
Nail Psoriasis (VAS-100)	593	−3.1	−4.9, −1.2,
SJC66	591	−1.1	−1.6, −0.7
TJC68	591	−2.2	−3.3, −1.0
Dactylitis Count	637	−0.15	−0.3, −0.01
PROs			
PtGA of Arthritis and Psoriasis (VAS-100)	618	−6.8	−9.8, −3.8
PtGA of PsA (VAS-100)	615	−6.7	−9.7, −3.7
HAQ-DI (score: 0–3)	619	−0.06	−0.13, 0.02
Pain in the Last Week (VAS-100)	628	−8.4	−11.4, −5.3
Fatigue in the Last Week (VAS-100)	630	−6.5	−9.6, −3.5
Spine Pain in the Last Week (VAS-100)	623	−3.8	−7.2, −0.5
Morning Stiffness in the Last Week (VAS-100)	630	−7.5	−10.7, −4.2
EQ-5D-3L[k]	627	0.022	−0.004, 0.048
FSS (score: 0–31)	278	−1.2	−2.1, −0.3
WPAI: Absenteeism (score: 0–100%)	293	−1.8%	−4.6, 1.0
WPAI: Presenteeism (score: 0–100%)	332	−5.0%	−8.6, −1.4
WPAI: Work Productivity Loss (score: 0–100%)	290	−6.5%	−10.7, −2.3
WPAI: Activity Impairment (score: 0–100%)	610	−6.6%	−9.9, −3.3

[a] N=1,210 pts initiating a 3L+ b/tsDMARD, of which n=637 had a 6-month follow-up. For all measurements except EQ-5D-3L, higher values indicated worse health state; thus, a negative change indicated improvement; **[b]** CfB=$\text{outcome}_{\text{6-month}} - \text{outcome}_{\text{baseline}}$; **[c]** Categorical variables were assessed by evaluating response achievement in outcomes among patients who had not achieved response at baseline; **[d]** Results are considered statistically significant if the 95% CI does not include zero for CfB or achievement response rate; **[e]** BSA <3% at follow-up among pts with BSA ≥3% at baseline; **[f]** IGA=0 or 1 at follow-up among pts with IGA >1 at baseline; **[g]** If cDAPSA ≤13 among pts with cDAPSA >13 at baseline; **[h]** If cDAPSA ≤4 among pts with cDAPSA >4 at baseline; **[i]** MDA was achieved if 5 out of the following 7 conditions were met: TJC68 ≤1, SJC66 ≤1, BSA ≤3%, pain (VAS-100) ≤15, PtGA of PsA and Psoriasis (VAS-100) ≤20, LEI ≤1, and HAQ-DI (score: 0–3) ≤0.5; **[j]** VLDA was achieved if all of the following conditions were met: TJC68 ≤1, SJC66 ≤1, BSA ≤3%, pain (VAS-100) ≤15, PtGA of PsA and Psoriasis ≤20, LEI ≤1; **[k]** For EQ-5D-3L, lower values indicated more severe disease; thus, a positive change indicated improvement. 3L+: third-line or higher; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BSA: body surface area; b/tsDMARD: biologic/targeted synthetic disease-modifying antirheumatic drug; cDAPSA: Clinical Disease Activity Index for PsA; CfB: change from baseline; CI: confidence interval; EQ-5D-3L: EuroQoL 5-dimensional, 3-level; FSS: Fibromyalgia Severity Scale; HAQ-DI: Health Assessment Questionnaire Disability Index; IGA: Investigator Global Assessment; LDA: low disease activity; MDA: minimal disease activity; mPASDAS: modified PsA Disease Activity Score; PGA: Physician Global Assessment; PRO: patient-reported outcome; PtGA: Patient Global Assessment; PsA: psoriatic arthritis; SJC66: swollen joint count in 66 joints; TJC68: tender joint count in 68 joints; VAS: Visual Analog Scale; VLDA: very low disease activity; WPAI: Work Productivity and Activity Impairment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

discontinuation (with or without switch); pts were censored at the last available registry visit within 24 months after initiation or end of the study period, whichever occurred first. CfB in PsA disease activity and PRO measures were assessed after the 6-month follow-up period. Continuous variables were reported as mean (standard deviation [SD]) and median (interquartile range [IQR] or 95% confidence intervals [CIs]). Categorical variables were described with counts and percentages.

Results: The registry included 7,044 b/tsDMARD initiations, with 2,550 (36.2%) being 3L+. This study included 1,210 pts initiating their first 3L+ b/tsDMARD; of these, 637 had a 6-month follow-up. Of the 1,210 pts included in this analysis, mean (SD) age was 54.2 (12.3) years and median (IQR) PsA duration was 7.0 (3.0, 12.0) years (**Table 1**). At b/tsDMARD initiation, mean (SD) swollen joint count (SJC) and tender joint count (TJC) were 2.7 (4.4) and 7.7 (10.3), respectively. Baseline PROs demonstrated moderate-to-high disease severity. Mean (SD) Health Assessment Questionnaire Disability Index (HAQ-DI) score was 0.9 (0.7). Mean (SD) pain and fatigue Visual Analog Scale (VAS)-100 scores were 54.0 (27.7) and 53.8 (28.0), respectively (**Table 1**).

Median (95% CI) tx persistence was 13.4 (12.4, 15.2) months (**Figure 1**); 76.0% (95% CI: 73.0, 78.0), 54.0% (95% CI: 51.0, 57.0), and 42.0% (95% CI: 39.0, 45.0) of pts remained on therapy at 6, 12, and 18 months, respectively. Among pts with 6-month follow-up (n=637), statistically significant improvements from baseline occurred in most disease activity and PRO measures except for dactylitis count, HAQ-DI, EuroQoL 5-dimensional, 3-level (EQ-5D-3L), and Work Productivity and Activity Impairment (WPAI) absenteeism (**Table 2**).

Conclusion: While median tx persistence greater than 1 year was observed, suboptimal improvements were reflected across disease activity measures and quality of life-related PROs, suggesting that pts may experience insufficient disease control even after multiple lines of tx. Therefore, earlier, more effective tx options are needed to mitigate the development of persistent symptoms and achieve disease control.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **N. Middaugh**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **Y. Muñoz Maldonado**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **C. Song**: UCB, 3, 11; **M. Eliot**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort between CorEvita; **R. Low**: UCB, 3, 11; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5.

Abstract Number: 0581

Effects of Apremilast on Body Mass Index, Weight, and HbA1c as Cardiometabolic Outcomes in Patients With Early Oligoarticular Psoriatic Arthritis in the FOREMOST Study

Philip J. Mease[1], Álvaro González Cantero[2], Jennifer Soung[3], April Armstrong[4], Joseph F Merola[5], Fabian Proft[6], Laure Gossec[7], Dafna D. Gladman[8], Laura Coates[9], Lichen Teng[10], Jimena Vázquez[11], Cynthia Deignan[12] and Arthur Kavanaugh[13], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Department of Dermatology, Ramón y Cajal University Hospital, Madrid, Spain, [3]Southern California Dermatology, Inc, Santa Ana, CA, USA, Santa Ana, [4]University of California Los Angeles, Los Angeles, [5]Department of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [6]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [7]Sorbonne Université, Pitié Salpêtrière Hospital, Paris, France, [8]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [9]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [10]Amgen Inc., Thousand Oaks, [11]Amgen Inc., Thousand Oaks, CA, [12]Amgen, Inc., Agoura Hills, CA, [13]University of California, San Diego, School of Medicine, San Diego, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

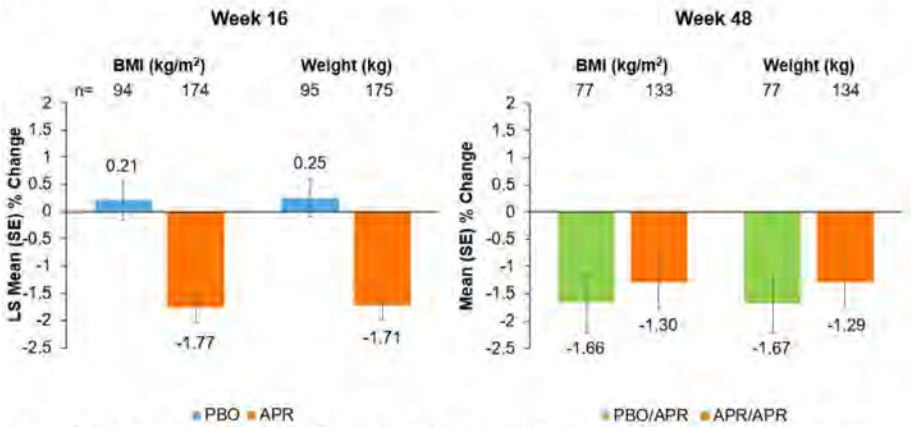
Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The prevalence of cardiometabolic diseases, including obesity and diabetes, is higher in patients with psoriatic arthritis (PsA) than those without PsA.[1,2] Metabolic syndrome is a common comorbidity of PsA that can impact treatment choice.[3] Weight loss and improvements in other cardiometabolic biomarkers have been observed with apremilast (APR) treatment in randomized controlled trials and real-world studies.[4-6] The aim of this post hoc analysis was to evaluate the effects of APR on body mass index (BMI), weight, and HbA1c over 48 weeks in patients with early oligoarticular (oligo) PsA from the FOREMOST trial (NCT03747939).

Methods: FOREMOST was a phase 4, multicenter, randomized, double-blind, placebo (PBO)-controlled trial that enrolled patients with early (duration ≤5 years) oligo PsA (>1 to ≤4 swollen joints and >1 to ≤4 tender joints; 66–68 joints assessed). Patients were randomized 2:1 to APR (n=203) or PBO (n=105) for 24 weeks (early escape at Week 16), followed by an extension phase in which all patients received APR through Week 48. Percent changes from baseline to Weeks 16 and 48 in BMI and weight were assessed. The percent change in weight from baseline to Week 48 was assessed overall and by baseline BMI category (normal: < 25 kg/m^2, overweight: ≥25 to < 30 kg/m^2, class I–II obesity: ≥30 to < 40 kg/m^2, class III obesity: ≥40 kg/m^2). Additionally, changes in BMI and HbA1c category (normal: < 5.7%, pre-diabetic: ≥5.7% to < 6.5%, and diabetic: ≥6.5%) were evaluated from baseline to Week 48.

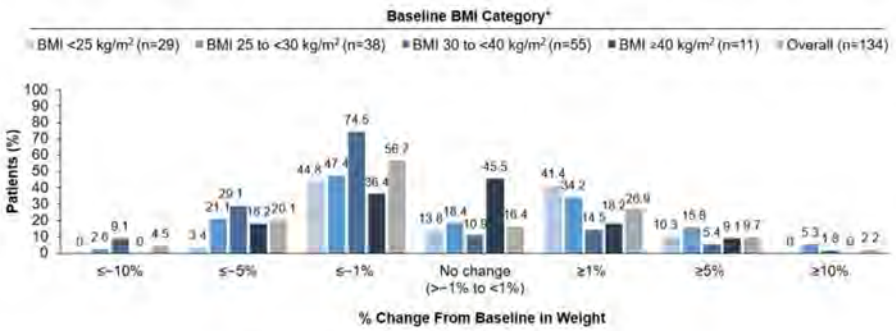
Figure 1. Percent Change From Baseline in BMI and Weight at Weeks 16 and 48



Week 16: Full analysis set (N=308). Based on an MMRM model which includes treatment group, time, treatment group by time interaction, prior/concomitant use of csDMARD (naive, prior use only, both prior and concomitant use) and baseline glucocorticosteroids use (yes/no) as factors, and baseline value as a covariate.
Week 48: APR patients as randomized (n=203) or transitioned from PBO at Week 16 or 24 (n=88). Data as observed.
APR, apremilast; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; LS, least squares; MMRM, mixed-effects model for repeated measures; PBO, placebo; SE, standard error.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Cumulative Weight Percent Change From Baseline at Week 48 Overall and by Baseline BMI



APR patients as randomized. Data as observed.
*Normal: <25 kg/m²; overweight: 25 to <30 kg/m²; class I-II obesity: ≥30 to <40 kg/m²; class III obesity: ≥40 kg/m².
APR, apremilast; BMI, body mass index.

Figure 3. Shift in BMI and HbA1c Category From Baseline at Week 48

BMI Categories at Baseline*	BMI Categories at Week 48*			
	Class III Obesity	Class I-II Obesity	Overweight	Normal
Normal (n=28)	0%	0%	3.6%	96.4%
Overweight (n=38)	0%	18.4%	65.8%	15.8%
Class I-II Obesity (n=56)	3.6%	87.5%	8.9%	0%
Class III Obesity (n=11)	81.8%	18.2%	0%	0%

Patients with ≥1 BMI category improvement
Patients with no change in BMI category
Patients with ≥1 BMI category worsening

HbA1c Categories at Baseline†	HbA1c Categories at Week 48†		
	Diabetic	Pre-diabetic	Normal
Normal (n=82)	0%	9.8%	90.2%
Pre-diabetic (n=42)	14.3%	61.9%	23.8%
Diabetic (n=16)	87.5%	12.5%	0%

Patients with ≥1 HbA1c category improvement
Patients with no change in HbA1c category
Patients with ≥1 HbA1c category worsening

APR patients as randomized. Data as observed.
*Normal: <25 kg/m²; overweight: 25 to <30 kg/m²; class I-II obesity: ≥30 to <40 kg/m²; class III obesity: ≥40 kg/m².
†Normal: <5.7%; pre-diabetic: ≥5.7% to <6.5%; diabetic: ≥6.5%.
APR, apremilast; BMI, body mass index.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Baseline BMI, weight, and HbA1c were similar between APR and PBO patients (30.2 vs 31.4 kg/m^2, 87.3 vs 91.5 kg, and 5.8 vs 5.7%, respectively). Greater percent reductions in BMI (-1.77 vs 0.21%) and weight (-1.71 vs 0.25%) were seen with APR vs PBO at Week 16 (**Figure 1**). Decreases in BMI and weight were maintained through Week 48 with continued APR treatment (APR/APR; **Figure 1**); similar improvements were seen in patients who transitioned to APR at Week 24 (PBO/APR). Over the 48-week period, a greater proportion of patients randomized to APR experienced weight loss than weight gain. More than 50% of patients had a weight reduction of ≥1% and approximately 20% achieved a reduction of ≥5% (**Figure 2**). Among patients randomized to APR, there was a general shift in BMI and HbA1c categories from baseline toward lower-risk categories after 48 weeks of treatment (**Figure 3**).

Conclusion: APR treatment through Week 48 was associated with improvements in BMI and weight in the FOREMOST study of early oligo PsA. Consistent with prior studies of APR in polyarticular PsA and psoriasis, greater changes in cardiometabolic markers were observed in patients in the highest risk categories (ie, obesity and diabetic subgroups).

References

1. Kumthekar A, Ogdie A. *Rheumatol Ther*. 2020;7(3):447–456.
2. Dubreuil M et al. *Rheumatology (Oxford)*. 2014;53(2):346–352.
3. Coates LC et al. *Nat Rev Rheumatol*. 2022;18(8):465–479.
4. Cavanaugh C et al. *JAAD Int*. 2024;16:244–251.
5. Gelfand JM et al. *JAMA Dermatol*. 2022;158(12):1394–1403.
6. Mease PJ, et al. Presented at: European Alliance of Associations for Rheumatology Annual Meeting; May 31–June 3, 2023; Milan, Italy.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **Á. González Cantero**: AbbVie, 2, 5, Almirall, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, LEO Pharma, 2, 5, Novartis, 2, 5, UCB, 2, 5; **J. Soung**: AbbVie, 5, 12, Personal fees, Dermavant, 5, Eli Lilly, 12, Non-financial support (manuscript preparation during the conduct of the study), Kyowa Kirin, 5, LEO Pharma, 5, 12, Personal fees, Pfizer, 5, 12, Personal fees, Regeneron, 5, Sanofi, 5, 12, Personal fees; **A. Armstrong**: AbbVie, 1, 12, Research Investigator, Almirall, 1, 12, Research Investigator, Arcutis, 1, 12, Research Investigator, ASLAN, 1, 12, Research Investigator, Beiersdorf, 1, 12, Research Investigator, Boehringer-Ingelheim, 1, 12, Research Investigator, Bristol-Myers Squibb(BMS), 1, 12, Research Investigator, Dermavant, 1, 12, Research Investigator, Dermira, 1, 12, Research Investigator, Eli Lilly, 1, 12, Research Investigator, EPI, 1, 12, Research Investigator, Incyte, 1, 12, Research Investigator, Janssen, 1, 12, Research Investigator, LEO, 1, 12, Research Investigator, Mindera, 1, 12, Research Investigator, Nimbus, 1, 12, Research Investigator, Novartis, 1, 12, Research Investigator, Ortho Dermatologics, 1, 12, Research Investigator, Pfizer, 1, 12, Research Investigator, Regeneron, 1, 12, Research Investigator, Sanofi, 1, 12, Research Investigator, Sun Pharma, 1, 12, Research Investigator, UCB, 1, 12, Research Investigator; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **F. Proft**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Hexal, 2, 6, Janssen, 2, 6, Medscape, 2, 6, MoonLake Pharma, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 5, 6; **L. Gossec**: AbbVie, 2, 5, 6, 12, Medical writing support, Amgen Inc., 6, 12, Medical writing support, Biogen, 5, Bristol-Myers Squibb(BMS), 2, 6, Celltrion, 2, 6, Eli Lilly, 5, 6, Galapagos, 2, 12, Medical writing support, Janssen, 2, 6, 12, Medical writing support, Merck/MSD, 2, 6, 12, Travel fees, Novartis, 2, 5, 6, 12, Travel fees, Pfizer, 2, 6, 12, Travel fees, UCB, 2, 5, 6, 12, Medical writing support; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **L. Teng**: Amgen Inc., 3, 11; **J. Vázquez**: Amgen Inc., 3, 11; **C. Deignan**: Amgen Inc., 3, 11; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2.

Abstract Number: 0582

Long-Term Efficacy and Safety of Tofacitinib in Active Axial Spondyloarthritis: Experience from a Tertiary Care Center in South India

Prabhu Vasantha Kumar[1], John Mathew[2], Ashish Jacob Mathew[3] and Ruchika Goel[2], [1]Christian Medical College, Vellore, Tamil Nadu, India, Vellore, Tamil Nadu, India, [2]Christian Medical College, Vellore, Tamil Nadu, India, [3]Christian Medical College, Vellore, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite the good efficacy of bDMARDs in nearly 60% of patients with axial spondyloarthritis (AxSpA), high costs limit their use in resource-limited settings. Few studies suggest JAK inhibitors to be more accessible and cost-effective alternative

Methods: Objective: This study aimed to evaluate the long-term effectiveness and safety of generic tofacitinib in Indian patients with active axial SpA.

Table-1: Baseline characteristics of study population

Characters	Total (N=290)
Age in Years, Mean ± SD	27 (± 5.6)
Male Patients, n (%)	247 (85.1%)
Active Smokers, n (%)	124 (42.7%)
Disease Duration since symptom onset (Median, IQR, Years)	4 (4-12)
Disease Duration since diagnosis (Median, IQR, Years)	2 (2-6)
History of Uveitis, n (%)	46 (15.9%)
Current Uveitis, n (%)	7 (2.4%)
History of IBD, n (%)	4 (1.3%)
Current IBD, n (%)	1 (0.3%)
History of Peripheral Arthritis, n (%)	147 (50.7%)
Current Peripheral Arthritis, n (%)	88 (30.3%)
HLA B27	
Positive, n (%)	141 (48.6%)
Negative, n (%)	24 (8.2%)
Not Available, n (%)	125 (43.1%)
CRP– mg/L, Mean ± SD	27.1 (±7.8)
Swollen Joint Count (SJC), Mean ± SD	5 (±2)
Tender Joint Count (TJC), Mean ± SD	7 (±3)
Presence of enthesitis based on MASES > 1, n (%)	1 (±1.4)
Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Mean ± SD	6.4 (±1.5)
Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP), Mean ± SD	3.8 (±0.8)
Prior NSAID Use, n (%)	289 (99.6%)
Prior csDMARD Use, n (%)	240 (82.8%)
Prior biological DMARD Use, n (%)	69 (23.8%)
Prior biological Inadequate Response, n (%)	11 (3.8%)
Concomitant Medication Use, n (%)	234 (80.7%)
Concomitant Medication Used	
Methotrexate, n (%)	214 (73.8%)
Sulfasalazine, n (%)	26 (9%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

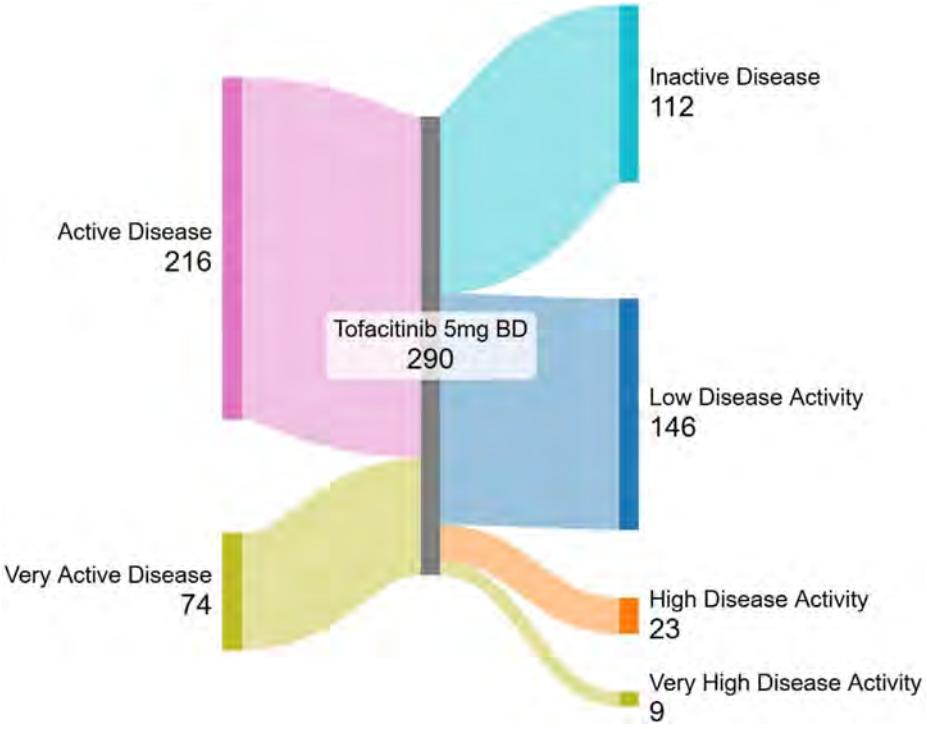


Figure-1: Sankey diagram depicting the efficacy of tofacitinib in patients with active axial SpA

Materials and Methods: This retrospective single-center study included 290 patients aged ≥18 years with active axial spondyloarthritis (axSpA), defined by BASDAI ≥4 or ASDAS ≥2.1, who were initiated on generic tofacitinib between January 2021 and March 2023, despite prior treatment with csDMARDs and/or bDMARDs. Only patients with a minimum follow-up of one year were included. Baseline data—including age, sex, disease duration, comorbidities, smoking status, HLA-B27 status, inflammatory markers (ESR, CRP), presence of uveitis, inflammatory bowel disease, enthesitis, disease activity indices (BASDAI, ASDAS), and concomitant medications—were recorded. Follow-up data on disease activity was systematically extracted from prospectively maintained electronic medical records. The primary endpoint was the proportion of patients achieving inactive disease or low disease activity (ASDAS < 2.1). Failure to meet this target within 12–24 weeks, or later in the event of disease flares, was classified as treatment failure. The details of adverse events at follow up visits were also noted

Results: Baseline characteristics of 290 patients included in the study are summarized in Table 1. After a median follow-up of 25 months (IQR 15-33), 258 of 290 patients (89%) achieved either inactive disease with ASDAS < 1.3 (n=112, 39%) or Low disease activity defined by ASDAS 1.3–2.1(n=146,50%) [Figure 1]. Tofacitinib failed in 32 patients (11%) of whom 10 (3.4%) patients had initial response but flared later. No significant predictors of non-response were identified.

Adverse events were reported in 52 patients (17.9%), most commonly transaminitis (42, 14.5%), followed by dyslipidemia (5, 1.7%), herpes zoster (3, 1%), and tuberculosis (2, 0.7%). Ten (3.4%) patients discontinued tofacitinib due to adverse effects. Transaminitis occurred at a median of 8 months and was associated with fatty liver in 29 patients (10%). Most cases of transaminitis (37, 12.7%) were mild and resolved with dose reduction. No serious infections, major adverse cardiovascular events (MACE), thromboembolic events, or deaths were observed.

Conclusion: Tofacitinib was effective and well-tolerated for controlling disease activity in active axial SpA in real life settings

Disclosure: P. Vasantha Kumar: None; **J. Mathew**: None; **A. Jacob Mathew**: None; **R. Goel**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0583

Baseline Peripheral Phenotypes Are Associated with Differential Response to TNF Inhibitors in Psoriatic Arthritis. A Cluster Analysis Approach

Raquel Granados[1], Jesús Eduardo Martín Salazar[2], María Ángeles Puche-Larrubia[3], Pedro Ortiz Buitrago[4], María Dolores López-Montilla[5], Jerusalén Calvo[6], Rafaela Ortega-Castro[7], Montserrat Romero-Gómez[8], Alejandro Escudero-Contreras[9], Nuria Barbarroja[10] and Clementina López Medina[11], [1]Hospital Universitario Reina Sofia, Cordoba, Andalucia, Spain, [2]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Rheumatology service/Department of Medical and Surgical Sciences, Cordoba, Spain, Cordoba, Andalucia, Spain, [3]Reina Sofia University Hospital, Granada, Spain, [4]Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), Cordoba, Andalucia, Spain, [5]Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., CORDOBA, Spain, [6]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [7]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [8]Reina Sofia University Hospital, Cordoba, Andalucia, Spain, [9]Reina Sofia University Hospital/Maimonides Institute of Biomedical Research of Córdoba(IMIBIC)/University of Cordoba, Cordoba, Andalucia, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [11]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

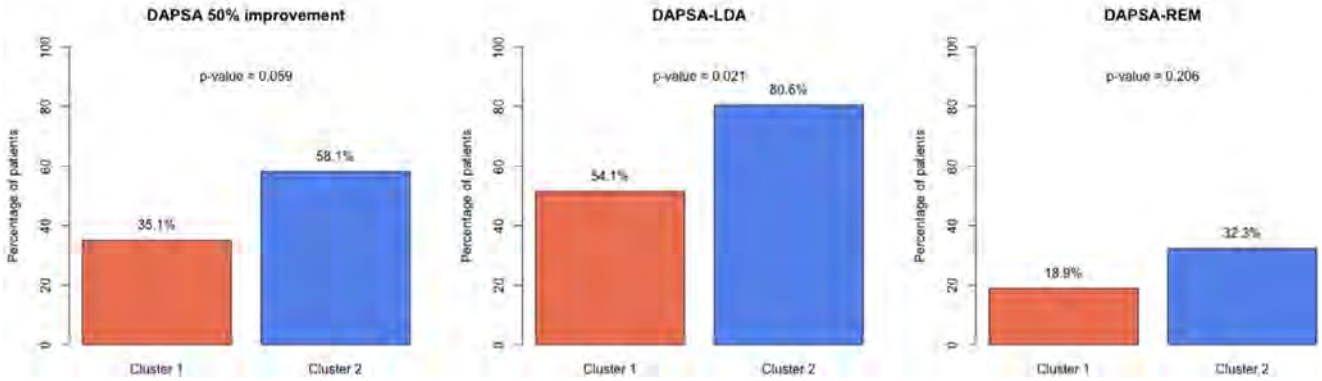
Background/Purpose: Previous studies have identified subgroups of patients with psoriatic arthritis (PsA) based on the severity of the disease [1,2]. However, no analysis to date has evaluated hidden pattern of PsA according to the peripheral manifestations and their influence on the response to TNF inhibitors (TNFi). The objectives of this study were: a) to identify

Table 1. Baseline characteristics of patients with Psoriatic Arthritis prior to initiation of biologic therapy, stratified by clusters.

Characteristics	Baseline characteristics. N = 68	Cluster 1 N = 37	Cluster 2 N = 31	p-value
Sex, male	38 (55.8)	20 (54.1%)	18 (58.1%)	0.931
Age in years, mean (SD)	49.0 (10.8)	51.1 (10.8)	46.4 (10.8)	0.075
Disease duration, mean (SD)	7.4 (5.7)	7.3 (4.8)	7.5 (6.8)	0.912
Current or former smoking	11 (16.17%)	5 (31.3%)	6 (35.3%)	0.100
Tender joints, mean (SD)	5.7 (4.4)	6.0 (4.8)	5.4 (3.9)	0.628
Swollen joints, mean (SD)	3.3 (3.9)	3.0 (3.6)	3.7 (4.2)	0.497
Nail involvement	23 (33.8%)	9 (56.3%)	14 (82.4%)	0.141
Current or past psoriasis	52 (75%)	24 (64.9%)	28 (90.3%)	0.029
Current or past arthritis	66 (97.1%)	35 (94.6%)	31 (100%)	0.553
Current or past dactylitis	31 (45.6%)	0 (0%)	31 (100%)	<0.001
Current or past enthesitis	17 (25%)	9 (24.3%)	8 (25.8%)	1.000
Baseline DAPSA score, mean (SD)	24.7 (9.1)	25.9 (8.6)	23.2 (9.6)	0.228
Baseline CRP (mg/dL), mean (SD)	15.5 (27.1)	21.4 (34.9)	8.5 (9.0)	0.049
Current or past corticosteroid use	40 (58.8%)	26 (70.3%)	14 (46.7%)	0.088
Current or past csDMARDs use	48 (70.6%)	32 (86.5%)	26 (83.9%)	1.000
Arterial Hypertension	11 (16.17%)	7 (21.9%)	4 (16.0%)	0.739
Diabetes Mellitus	5 (7.35%)	4 (12.5%)	1 (4.0%)	0.372
Dyslipidemia	7 (10.29)	7 (23.3%)	0 (0%)	0.015
Obesity	17 (25%)	9 (34.6%)	8 (38.1%)	1.000

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Comparison of treatment response to TNF inhibitors between clusters after 6 months.



clusters of PsA patients based on the presence of peripheral manifestations and psoriasis at the time of TNFi initiation, and b) to compare the effectiveness of the first TNFi across these clusters after 6 months of follow-up.

Methods: An observational, retrospective study was conducted in PsA patients naïve to TNFi. An unsupervised cluster analysis using the k-means technique was performed based on key peripheral features of PsA (arthritis, enthesitis, and dactylitis) and the presence of psoriasis. The response to TNFi treatment at 6 months (defined as ≥50% improvement in DAPSA) as well as achievement of DAPSA-LDA (DAPSA ≤ 14) and DAPSA-REM (DAPSA ≤ 4), were compared between clusters using the chi-square test.

Results: A total of 68 patients were included, 55.8% of whom were male, with a mean age of 50 years (SD 16.7) and a mean disease duration of 7.2 years. Two clusters were identified after the k-means analysis. Phenotypically, Cluster 1 (n=37) had a significantly lower prevalence of dactylitis (0% vs. 100%, p< 0.001) and psoriasis (64.9% vs. 90.3%, p=0.029) compared to cluster 2 (n=31) (Table 1). Other clinical variables at baseline, including mean swollen joint count (3.0 vs. 3.7, p=0.497) and tender joint count (6.0 vs. 5.4, p=0.628), were similar between clusters. However, CRP levels were significantly higher in Cluster 2 (21.4 vs. 8.5, p=0.049). No significant differences were found on the prevalence of concomitant csDMARDS (86.5% vs. 83.9%).

After 6 months of TNFi treatment (Figure 1), the percentage of responders (defined as a ≥50% improvement in DAPSA) was numerically higher in Cluster 2 compared to Cluster 1, approaching statistical significance (35.1% vs. 58.1%, p=0.059). The proportion of patients achieving DAPSA-LDA was significantly greater in Cluster 2 (54.1% vs. 80.6%, p=0.021), while no significant difference was observed in DAPSA-REM rates between clusters.

Conclusion: Our findings suggest the presence of two distinct clinical phenotypes, primarily defined by the presence of dactylitis and psoriasis. Patients belonging to this phenotype had a higher likelihood of achieving low disease activity after 6 months of TNFi treatment. These results suggest that baseline phenotypic features may help predict treatment response.

Disclosure: R. Granados: None; **J. Martín Salazar**: None; **M. Puche-Larrubia**: None; **P. Ortiz Buitrago**: None; **M. López-Montilla**: None; **J. Calvo**: None; **R. Ortega-Castro**: None; **M. Romero-Gómez**: None; **A. Escudero-Contreras**: None; **N. Barbarroja**: None; **C. López Medina**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0584

Difficult-to-Manage Axial Spondyloarthritis According to ASAS Criteria in Reuma-Check Cohort: Frequency, Predictive Factors, and Treatment Patterns.

Rodrigo García Salinas[1], Nataly Mejia[2], Santiago Ruta[3] and Sebastian Magri[4], [1]Hospital Italiano La Plata, La Plata, Argentina, [2]Hospital Italiano de La Plata, La Plata, Argentina, [3]Hospital San Martin de La Plata, La Plata, Argentina, [4]Hospital Italiano La Plata, Melchor Romero, Argentina

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose:

The concept of difficult-to-Manage axial spondyloarthritis (axSpA D2M), recently introduced by ASAS, describes patients who fail ≥2 lines of b-tsDMARDs treatment and remain active (amog others). Refractory patients are defined as those with D2M and objective signs of inflammation. This study aimed to estimate the frequency of D2M in the Argentinian Reuma-Check axSpA cohort, describe treatment trends, and analyze baseline characteristics associated with D2M during follow-up.

Methods: This prospective observational study (2017–2024) included axSpA patients aged ≥18 years. The Reuma-Check program conducted structured assessments, including blood tests (HLA-B27), sacroiliac X-rays, MRI (ASAS protocol), and enthesis ultrasound. Data collected included demographics, educational levels, back pain characteristics, diagnostic delay, NSAID response, VAS pain scores, morning stiffness, BASDAI, BASFI, MASES, and HAQ (figure 1). D2M was defined as the lack of response to ≥2 biological therapies with active disease. Descriptive statistics, comparative analyses, and logistic regression were performed to identify associated factors.

Results: A total of 129 axSpA patients were included, with a follow-up of 12 months (IQR: 3–36). The frequency of D2M was 8.53% (n=11; 95% CI: 4.83%-14.62%). The average time on the first biologic was 19 months (SD: 16) and the prevalence of use was 50%, 21 months (SD: 19) on the second before D2M definition. Among first-line therapies 30% failure: 8% failed TNFi, and 20% IL17, regardin second-line faiuler: 85% failed TNFi, 10% IL17, and 5% JAKi (figure1). Only four patients met criteria for refractory disease, two showing elevated CRP and two active MRI findings. Baseline variables associated with D2M included BASFI (4.16 ± 2.54 vs. 2.87 ± 2.15; p=0.04; 95% CI: 0.03–2.54), BASDAI (5.11 ± 2.87 vs. 3.54 ± 2.42; p=0.01; 95% CI: 0.32–2.82), and ASDAS (3.72 ± 1.45 vs. 2.84 ± 1.16; p=0.009; 95% CI: 0.23–1.53). Significant categorical variables included smoking (OR=6.347; 95% CI: 1.256–32.084; p=0.012), psoriasis (OR=3.771; 95% CI: 1.069–13.305; p=0.029), sacroiliac joint maneuvers (OR=3.71; 95% CI: 1.030–13.417; p=0.043), peripheral X-rays (OR=5; 95% CI: 1.3–6.487; p=0.01), and articular ultrasound (OR=10.65; 95% CI: 1.42–80.09; p=0.022). Multivariate analysis identified articular ultrasound as the only significant predictor (OR=10.651; 95% CI: 1.416–80.094). Among D2M patients, six received JAKi, three IL17, and two TNFi as third-line therapies.

Conclusion: The Reuma-Check cohort revealed a low prevalence of axSpA D2M. Clinical and imaging features, particularly articular ultrasound and disease activity scores (BASFI, BASDAI, ASDAS), were predictive of D2M. These findings underscore the importance of advanced diagnostic tools and a multidimensional approach to optimizing the management of this complex population

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of D2M vs non-D2M axSpA

Variable	D2M (n 11)	No-D2M (n 118)	p-value	RR (95% CI)
Male	18%	51%	0.05	0.35 (0.11–1.10)
Years of Education	14.3 ± 2.7	13.4 ± 3.1	0.3	
Age at Diagnosis	41 ± 13.5	41 ± 12	0.9	
Smoking	**80%**	**39%**	**0.01**	**2.05 (1.17–3.57)**
Inflammatory Back Pain (IBP)	91%	84%	0.5	1.08 (0.57–2.06)
NSAID Good Response	64%	65%	0.8	0.97 (0.54–1.73)
Anterior Chest Pain	90 %	80%	0.4	1.13 (0.63–2.03)
Presence Enthesitis	40 %	34%	0.6	1.17 (0.58–2.37)
Presence Arthritis	36%	21%	0.1	1.75 (0.75–4.10)
Uveitis	9%	6%	0.7	1.49 (0.18–12.38)
Inflammatory Bowel Disease (IBD)	0%	8%	0.3	0.00 (0.00–3.57)
Psoriasis	**54%**	**24%**	**0.02**	**2.26 (1.10–4.62)**
SpA Family History	81.8%	72%	0.4	1.14 (0.68–1.91)
HLA-B27 +	60%	46%	0.6	1.29 (0.68–2.44)
Erythrocyte Sedimentation Rate (ESR)	17.1 ± 8.7	19.5 ± 16.4	0.4	
C-Reactive Protein (CRP)	**1.8 ± 2**	**5.6 ± 11.3**	**0.004**	
Elevated CRP (>5 mg/L)	73%	62%	0.4	
Structural Damage on X-ray	**54%**	**23%**	**0.01**	**2.31 (1.21–4.42)**
MRI Sacroiliac Lesions (any)	90%	85%	0.6	1.06 (0.78–1.45)
Ultrasound Enthesitis	50%	65%	0.3	0.77 (0.36–1.63)
Pain (0-10 VAS)	6.4± 1.36	6.8 ± 1.7	0.4	
Night Pain (0-10 VAS)	6.3 ± 2.36	5.3 ± 2.4	0.2	
Morning Stiffness (min)	43 ± 19.54	34.6 ± 27.8	0.3	
BASDAI Score (0-10)	**6 ± 1.6**	**4.5 ± 1.7**	**0.04**	
ASDAS Score (0-10)	**4 ± 1**	**3.1 ± 1.2**	**0.03**	
BASFI Score (0-10)	**5 ± 0.6**	**4.6 ± 1.4**	**0.04**	
HAQ Score (0-3)	0.8 ± 0.4	0.7 ± 0.3	0.5	
Diagnostic Delay (months)	80 ± 56.1	73.7 ± 84.3	0.7	
Bone Marrow Edema (MRI)	70%	59%	0.5	1.18 (0.85–1.64)
Fat Lesions (MRI)	33%	50%	0.8	0.67 (0.23–1.95)
Erosions (MRI)	37%	52%	0.5	0.72 (0.27–1.89)
Sclerosis (MRI)	44%	80%	0.08	0.55 (0.19–1.56)
Bone Bridges (MRI)	10%	9%	0.3	1.09 (0.91–1.30)
Chronic MRI Changes	72%	67%	0.6	1.08 (0.66–1.76)
Ultrasound Joint Changes	**75%**	**20%**	**0.0001**	**3.75 (2.35–5.98)**
TJC	2.8 ± 2.44	1.8 ± 2.5	0.204	
SJC	1.5 ± 1.86	0.6 ± 1.5	0.042	

Values reported as mean (SD) or n (%), as appropriate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

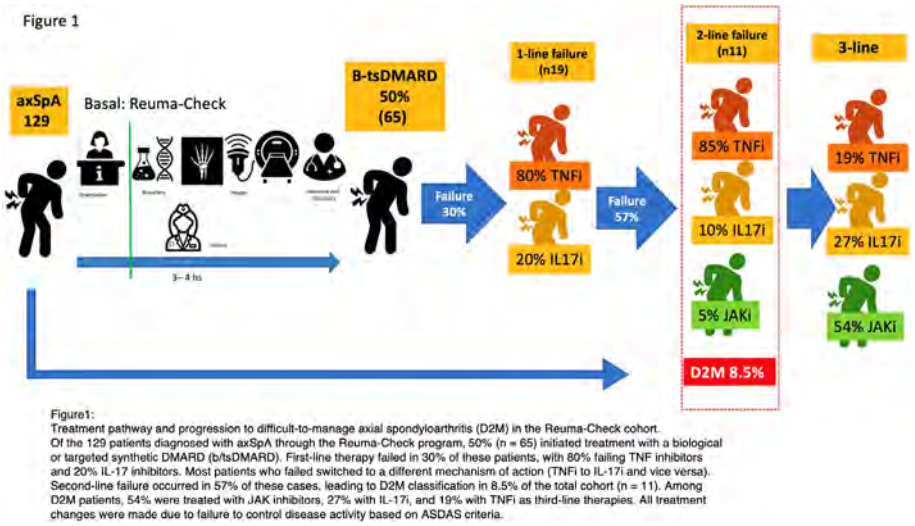


Figure1:
Treatment pathway and progression to difficult-to-manage axial spondyloarthritis (D2M) in the Reuma-Check cohort. Of the 129 patients diagnosed with axSpA through the Reuma-Check program, 50% (n = 65) initiated treatment with a biological or targeted synthetic DMARD (b/tsDMARD). First-line therapy failed in 30% of these patients, with 80% failing TNF inhibitors and 20% IL-17 inhibitors. Most patients who failed switched to a different mechanism of action (TNFi to IL-17i and vice versa). Second-line failure occurred in 57% of these cases, leading to D2M classification in 8.5% of the total cohort (n = 11). Among D2M patients, 54% were treated with JAK inhibitors, 27% with IL-17i, and 19% with TNFi as third-line therapies. All treatment changes were made due to failure to control disease activity based on ASDAS criteria.

Disclosure: R. García Salinas: AbbVie/Abbott, 2, 5, 6, Adium, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Raffo, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **N. Mejia**: None; **S. Ruta**: None; **S. Magri**: None.

Abstract Number: 0585

Fungal Infections, Including *Candida*, in Patients With Active Axial Spondyloarthritis Treated With Secukinumab: A Pooled Analysis of 10 Phase 3 Trials

Shikha Singla[1], Linda Grinnell-Merrick[2], Weibin Bao[3], Artem Zharkov[4] and Abhijeet Danve[5], [1]Medical College of Wisconsin, Milwaukee, WI, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]Novartis Pharmaceuticals Corporation, Hanover, NJ, [4]Novartis Pharma AG, Basel, Switzerland, [5]Section of Rheumatology, Department of Medicine, Yale School of Medicine, New Haven, CT

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic disease characterized by inflammatory low back pain and is often accompanied by inflammation of the peripheral joints and entheses. Patients receiving treatment with an IL-17 inhibitor, such as secukinumab (SEC), reported higher incidence of *Candida* and other fungal infections. The objective of this post hoc analysis is to describe the incidence, severity, seriousness, and type of fungal infections, including *Candida*, among patients with active axSpA treated with SEC.

Methods: This post hoc analysis included patients with active axSpA, including radiographic and non-radiographic disease, from a pooled population of 10 phase 3 clinical trials who received SEC 150 mg or placebo (PBO). Following the PBO-controlled period, patients randomized to PBO were switched to SEC 150 mg, while patients randomized to SEC 150 mg at baseline continued the same dose or were uptitrated to SEC 300 mg through the entire treatment period. Baseline demographic and clinical characteristics are reported in patients with or without ≥1 fungal infection adverse event during the entire treatment period. Incidence of fungal infections, including *Candida*, are reported for the PBO-controlled period and through

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Fungal Infections, Including *Candida*, During the PBO-Controlled Period in Patients With AxSpA Receiving Secukinumab

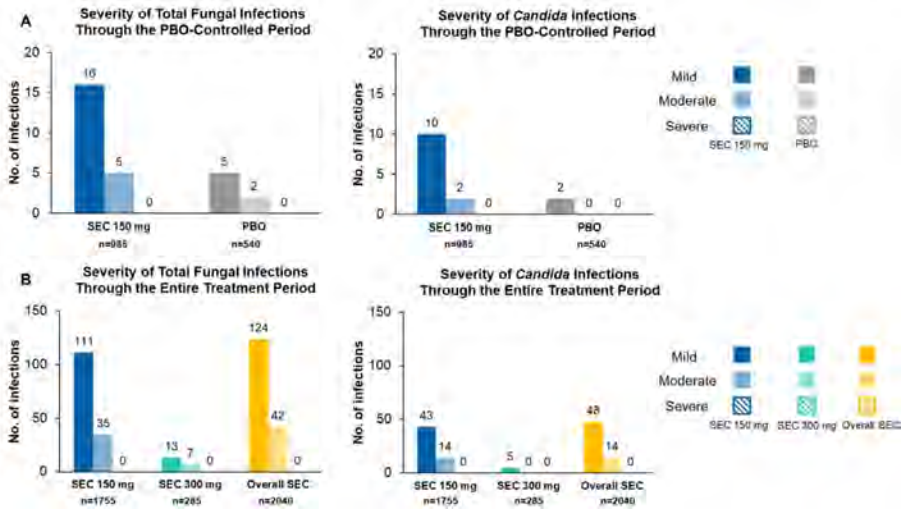
Infection type, EAIR (95% CI)[a,b]	SEC 150 mg (n=985)	PBO (n=540)
Total fungal infections	5.51 (3.26-8.70)	3.39 (1.24-7.38)
Candida infections	3.05 (1.46-5.60)	0.56 (0.01-3.13)
Oral candidiasis	1.52 (0.49-3.54)	0.56 (0.01-3.13)
Vulvovaginal candidiasis	1.22 (0.33-3.11)	0.56 (0.01-3.13)
Oesophageal candidiasis	0.30 (0.01-1.69)	0.00 (0.00-2.07)
Fungal infections (NEC)[c]	1.21 (0.33-3.11)	2.25 (0.61-5.77)
Fungal foot infection	0.61 (0.07-2.19)	0.56 (0.01-3.13)
Onychomycosis	0.30 (0.01-1.69)	1.13 (0.14-4.07)
Vulvovaginal mycotic infection	0.30 (0.01-1.69)	0.56 (0.01-3.13)
Tinea infections	1.22 (0.33-3.11)	0.56 (0.01-3.13
Tinea pedis	1.22 (0.33-3.11)	0.00 (0.00-2.07)
Tinea versicolour	0.00 (0.00-1.12)	0.56 (0.01-3.13

EAIR, exposure adjusted incidence rate per 100 patient-years; MedDRA, Medical Dictionary of Regulatory Activities; NEC, not elsewhere classifiable; PBO, placebo; SEC, secukinumab. a MedDRA preferred term. b A patient with multiple occurrences of an infection while receiving 1 treatment was counted only once in the infection category for that treatment. c NEC denotes infections that were not specifically classified into any of the MedDRA preferred terms.

the entire treatment period. Characteristics of infections including the specific types (defined by MedDRA preferred term), severity grades, resolution, and infections resulting in treatment discontinuation are reported through the entire treatment period.

Results: Overall, 2040 and 540 patients with active axSpA receiving SEC or PBO, respectively, were included. A total of 124 (6.1%) patients receiving SEC reported ≥1 fungal infection through the entire treatment period, and most (55.6%) were male. Male patients comprised 66.7% of the entire study population and the mean age was 41.3 years. During the PBO-controlled period, the incidence of total fungal infections were infrequent in each treatment group (exposure adjusted incidence rate [EAIR] per 100 patient-years [95% CI], SEC 150 mg: 5.51 [3.26-8.70], PBO: 3.39 [1.24-7.38], **Table 1**). EAIRs of *Candida* infections were also infrequent in patients receiving either SEC 150 mg: 3.05 (1.46-5.60) or PBO: 0.56 (0.01-3.13). Through the entire treatment period, the rates of total fungal infections (SEC 150 mg: 3.70 [3.01-4.50]; SEC 300 mg: 2.9 [1.73-4.76]) and *Candida* infections (SEC 150 mg: 1.30 [0.91-1.79]); SEC 300 mg: 0.68 [0.19-1.74]) did not increase. All fungal infections, including *Candida*, in patients receiving any dose of SEC through the entire treatment period were mild or moderate; no serious infections were reported (**Figure 1**). The vast majority (86.7% of total fungal infections

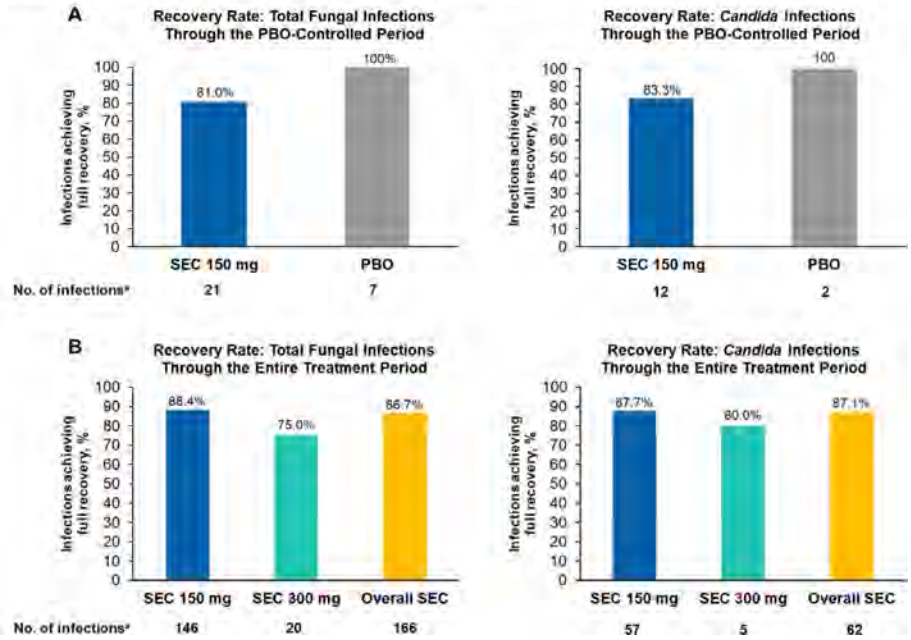
Figure 1. Severity of Total Fungal and *Candida* Infections Through (**A**) the PBO-Controlled Period and (**B**) the Entire Treatment Period[a]



PBO, placebo; SEC, secukinumab. a Infections are reported as the number of infections per treatment arm.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Recovery Rates of Total Fungal and *Candida* Infections Through (**A**) the PBO-Controlled Period and (**B**) the Entire Treatment Period



PBO, placebo; SEC, secukinumab. a Total number of infections through the indicated time.

and 87.1% of *Candida* infections) were fully resolved before the end of the treatment period (**Figure 2**), and 5 (3.0%) of infections resulted in treatment discontinuation.

Conclusion: Fungal infections, including *Candida*, were infrequent with incidence rates not increasing throughout the entire treatment period. Fungal infections during treatment with SEC were mild or moderate and most infections were fully resolved before the end of treatment, allowing almost all patients to continue treatment.

Disclosure: S. Singla: AbbVie/Abbott, 2, Eli Lilly, 5, Janssen, 2, 6, Prometheus Biosciences, 5, UCB, 2; **L. Grinnell-Merrick**: Novartis, 3, 11; **W. Bao**: Novartis, 3, 11; **A. Zharkov**: Novartis, 3, 11; **A. Danve**: AbbVie, 2, Amgen, 2, Eli Lilly, 5, Janssen, 2, Novartis, 2, 5.

Abstract Number: 0586

Immune Checkpoint agonists: A New horizon for treatment of psoriatic arthritis

Siba Raychaudhuri[1], Christine Abria[2] and Smriti K Raychaudhuri[3], [1]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [2]Sacramento VA Medical Center, Mather, CA, [3]Sacramento VA Medical Center, Davis, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Check point inhibitor PD-1 (programmed death protein 1) is upregulated during T lymphocyte activation and is important for limiting the duration of activation. Thus, maintain self-tolerance. Insufficient PD-1 signaling can

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

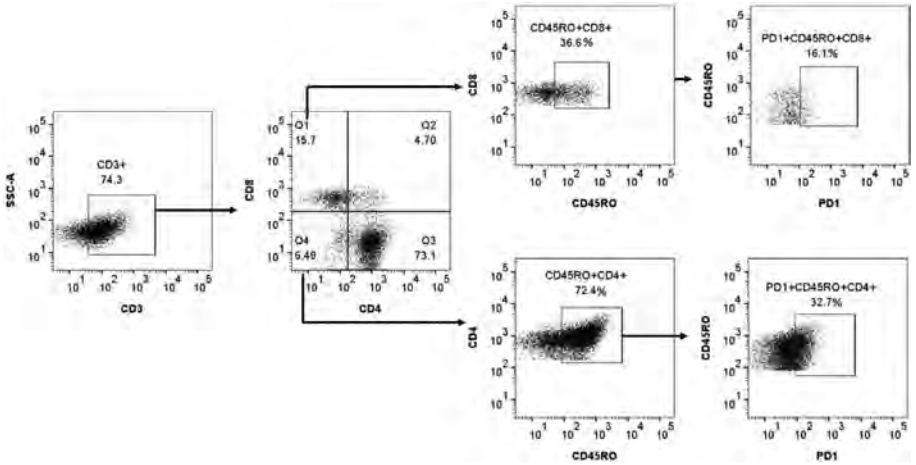


Figure 1. In flow cytometric Hi-D FACS study it was observed that a high number of psoriatic arthritis synovial CD4+/CD8+ Effector Memory T cells expressed Check point inhibitor PD-1 (programmed death protein 1). First activated live lymphomononuclear cells were gated and then effector memory [CD4+/CD8+CD11a+CD45RO+] T (TEM) cells were characterized.

lead to dysregulated T cell response. The functional significance of PD-1 and its ligands PD-L1/L2 is not studied in psoriatic arthritis (PsA). Our objectives were to (i) investigate the expression of PD-1 in PsA synovium (ii) determine its functional significance (iii) explore mechanistic of checkpoint agonists (Recombinant Human PD-L1/B7-H1; R&D system) as a novel therapy for T cells mediated autoimmune diseases.

Methods: Mononuclear cells from peripheral blood (PBMC) and synovial fluid (SFMC) of age/sex matched PsA patients (n=10), and RA patients (positive control, n=10) were isolated. Isolated $CD3^+$ T cells (1x 10^6/ml) were activated with CD3/CD28 antibody (5μg each/ml) for 3 days in the presence/absence of recombinant PD-L1 (1μg/mL).

Hi-D FACS studies were done : (1) to identify PD-1 in activated effector memory [CD4+/CD8+CD11a+CD45RO+] T (TEM) cells in PsA and RA SFMC; (2) to determine the anti-proliferative effect of recombinant PD-L1 on the SFMCs TEM cells by CFSE dilution test; (3) to determine the effect of recombinant PD-L1 agonist on the expression of IL-17A, IL-17F, IL-22 on SFMC TEM cells. Studies were performed using a FACSfusion Aria flow cytometer and data were analyzed using FlowJo software (Treestar, Ashland, OR). Western blot assays were done on lysates of the cultured CD3+T cells with recombinant PD-L1 in PsA and RA PBMC to determine effect on T cell signaling proteins (stat3/p-stat3, RORγt).

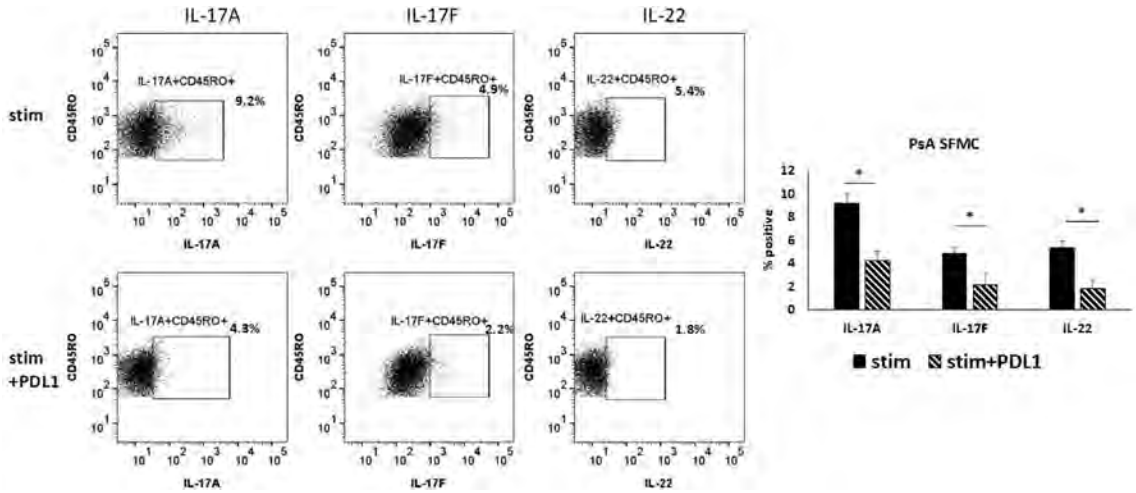


Figure 2. Hi-D FACS study to determine the effect of recombinant PD-L1 agonist on the key pathologic Th17 cytokines (IL-17A, IL-17F, IL-22) which drives the pannus formation in psoriatic arthritis (PsA). Expression of IL-17A, IL-17F, and IL-22 in CD4+CD45RO+ T (TEM) cells were significantly reduced when CD3/CD28 stimulated PsA synovial fluid mononuclear cells were treated with recombinant human PD-L1 (1μg/mL).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

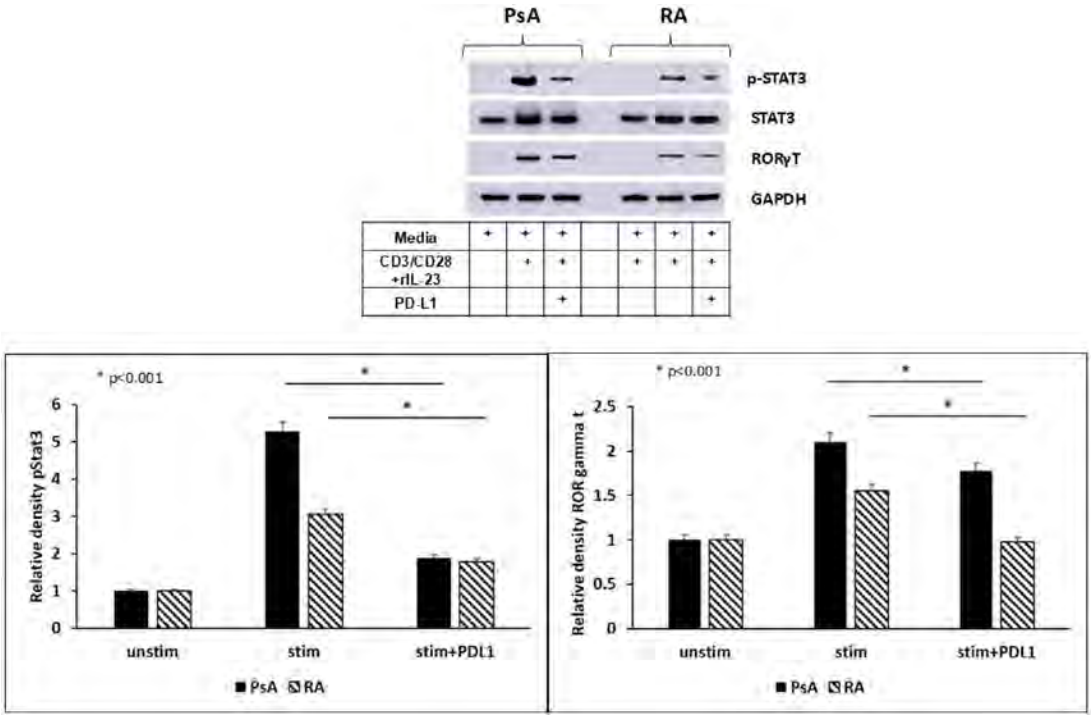


Figure 3. PD-1 activation in T cells regulates Th17 cell function by inhibiting IL-23 induced STAT3/ RORγt activation. Western blot assays were done on lysates of the cultured CD3+T cells. PBMC T cells from psoriatic arthritis (PsA) and rheumatoid arthritis (RA) were stimulated with anti-human CD3 (1μg/mL) and CD28 (1μg/mL) and rIL-23 (40ng/mL) in presence/absence of recombinant human PD-L1 agonist (1μg/mL). AS expected rIL-23 induced phosphorylation of STAT3 and upregulated RORγt expression. PD-L1 agonist treated PsA PBMC and RA PBMC CD3+ T cells had significant decreased expression of phospho-STAT3 compared to untreated CD3+ T cells ($p<0.001$). Similar effect was seen on the expression of RORγt.

Results: High PD-1 expression (Fig 1) was observed in CD4+ (43.3%±12.6) and CD8+ (20.5%±6.5) activated TEM cells of PsA PBMC/SFMC and RA PBMC/SFMC. CFSE dilution assay showed proliferation of CD3/CD28 antibody stimulated memory CD4+ SFMC of PsA reduced significantly from 72.2%±2.2 to 30.1%±3.13 when treated with recombinant PD-L1 ($p< 0.001$). Similarly in RA SFMC with recombinant PD-L1, CD4+ TEM cell proliferation significantly reduced from 53.3% ±2.6 to 26.2%±2.7 ($p< 0.001$).

In CD3/CD28 stimulated PsA SFMC, Hi-D FACS analysis showed expression of IL-17A (9.2+0.8%), IL-17F (4.9+0.5%), and IL-22 (5.3+0.5%) in CD4+CD45RO+ T (TEM) cells were significantly reduced when treated with recombinant PD-L1 (4.3+0.8%, 4.9+0.5%, and 5.3+0.5%, respectively, $p< 0.001$). (Fig 2)

Findings from western blot assays showed PD-L1 agonist treated PsA PBMC and RA PBMC activated CD3+ T cells had decreased expression of phospho-STAT3 compared to PD-L1 agonist untreated CD3+ T cells by 5-fold and 3-fold decrease, respectively ($p< 0.001$, Fig 3). Similar results were also seen in the expression of RORγt, the signaling proteins induced by rIL-23. (Fig 3)

Conclusion: Here we identified significance of PD-1 in PsA: (i) PD-$1^{+}T_{EM}$ cells in SFMC of PsA are functional and regulates Th17 cell function through STAT3/ RORγt; (ii) recombinant human PD-L1 agonist significantly inhibited SFMC TEM cell proliferation and Th17 cell cytokine production (IL-17A, IL-17F, IL-22). Agonistic immune checkpoint-based therapy is likely to offer new avenues for treatment of psoriatic disease.

Disclosure: S. Raychaudhuri: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **C. Abria**: None; **S. Raychaudhuri**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0587

Regulatory Role of IL17 F in the Pannus Formation of Psoriatic Arthritis: A Comparative Study with IL-17A

Siba Raychaudhuri[1], Christine Abria[2] and Smriti K Raychaudhuri[3], [1]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [2]Sacramento VA Medical Center, Mather, CA, [3]Sacramento VA Medical Center, Davis, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: IL-17A and IL-17F are the key inflammatory mediators in the IL-17 cytokine family (IL-17A to IL-17F). IL-17A is the widely recognized inflammatory cytokine in this family. IL-17F has drawn increasing attention for its functional similarity with IL-17A and its clinical efficacy in psoriatic arthritis (PsA). Like IL-17A, IL-17F utilizes IL-17RA/RC receptor. Limited studies are available on IL-17F in human diseases. The objective of this study was to evaluate the significance of IL-17F in the pathognomonic 'pannus' formation in PsA and to compare that with the contributing role of IL-17A.

Methods: Here we determined functional role IL-17F on Synovial fibroblasts (FLS) proliferation and on induction of inflammatory cytokines/endopeptidase (IL-6, IL-8, MMP3) related with pannus formation.

A. FLS isolated from PsA (n=5) were cultured with rIL-17F (100 ng/ml) for 5 days. For proliferation assay MTT/CFSE dilution assays were done. To determine the effect of IL-17F on the production of relevant cytokines/chemokines the PsA-FLS culture supernatants were evaluated for IL-6, IL-8, and MMP3 by specific ELISA kits. Similar experiments were done with rIL-17A (100 ng/ml), rIL-22 (100 ng/ml), TNF-α (20ng/mL). Concentrations of rIL-17 A/F, rIL-22, TNF-α were selected by doing dose curves.

B. As IL-17F and IL-17A shares ~50% homology, we evaluated additive or synergistic effect of these cytokine combinations on FLS proliferation and cytokine/chemokine production in PsA-FLS.

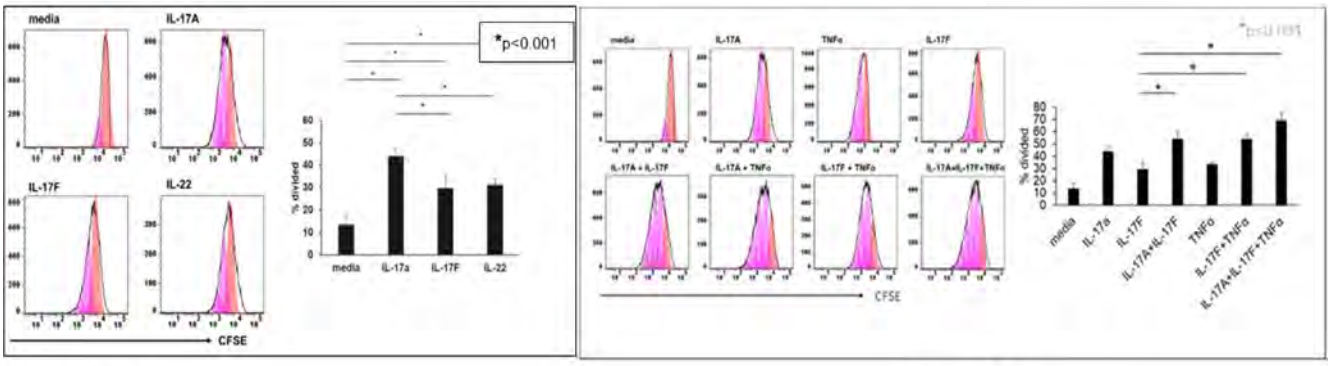


Figure 1 A **Figure 1 B**

Figure 1. Comparative effect of IL-17A and IL-17F and their synergism on proliferation of synovial cells (FLS) of psoriatic arthritis (PsA). All experiments were done in triplicate. Fig 1 A. Effect of IL-17F on Fibroblast proliferation. Representative histograms showing proliferation of PsA FLS cells stimulated with rIL-17A, rIL-17F, and rIL-22 on left. Bar diagram on right shows significant increase of proliferation of PsA FLS with rIL-17A compared to rIL-17F or rIL-22 ($p<0.001$). All experiments were done in triplicate. Fig 1B. Synergistic effect of IL-17F with IL-17A and/or with TNF-α on PSA FLS proliferation. On left side representative histograms showing proliferation of PsA FLS cells stimulated with rIL-17F, rIL-17A and TNF-α. Bar diagram on right showing the significant synergistic effect of IL-17F with IL-17A and with TNF-α on PsA FLS proliferation ($p<0.001$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

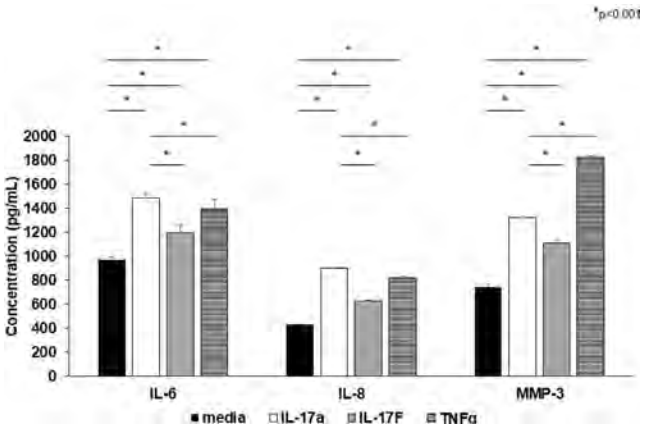


Figure 2. Effect of rIL-17F on IL-6, IL-8, and MMP-3 Expression. Bar diagrams of the average concentration (pg/mL) of cytokines in cell culture supernatant of PsA FLS treated with rIL-17A, rIL-17F or TNF-α. Compared to rIL-17F upregulation of IL-6, IL-8 and MMP3 were significantly higher with rIL-17 A ($p<0.001$) All experiments were done in triplicate.

C. By Flow cytometric studies of T cells derived from PsA synovial fluid (SF) (n=10) we identified the expression of IL-17A and IL-17F in the effector memory T (TEM) cells.

Results: In MTT assay we observed rIL-17F induced significant proliferation in PsA FLS (OD: 1.49±0.05) compared to unstimulated (OD: 0.19±0.04; $p< 0.001$). Treatment with rIL-17A (OD: 1.85±0.07) induced significantly more proliferation than rIL-17F and rIL-22 (1.49±0.05; $p< 0.05$, 1.48±0.02; $p< 0.001$, respectively). However, compared to rIL-17A alone (OD:1.85±0.07) stimulation with rIL-17A+rIL-17F induced significantly more proliferation in PsA FLS (OD: 2.05±0.09; $p< 0.001$). Furthermore, PsA FLS treated with TNF-α+rIL-17A+rIL-17F had highest proliferation (OD 1.85±0.07). In CFSE proliferation assay the results were similar (Fig 1).

PsA FLS stimulated with rIL-17A, rIL-17F and TNF-α produced significantly more IL-6, IL-8 and MMP3 compared to media ($p< 0.001$). However, compared to IL-17F upregulation of IL-6, IL-8 and MMP3 were significantly higher with IL-17 A ($p< 0.001$) as shown in Fig 2.

In the SF of PsA patients the level of IL-17A was higher than IL-17F (Fig 3). In SF derived T cells with Hi-D FACS studies we identified (i) CD4+ TEM cells secreted IL-17A and IL-17F (ii) IL-17A+ TEM cells were more than IL-17F (Fig 3B, $p< 0.001$).

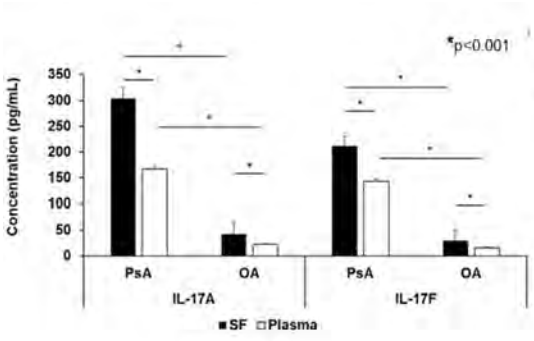


Figure 3 A

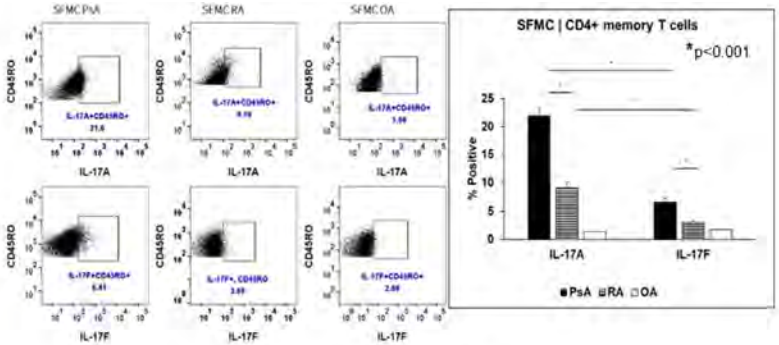


Figure 3 B

Figure 3. Source of IL-17A & IL-17F: Both in the synovial fluid (SF) of psoriatic arthritis (PsA) and at single cell level of effector memory CD4+ T cells IL7A is the predominant cytokine compared to IL-17F. Fig 3A. Bar diagrams demonstrating average concentration (pg/mL) of IL-17A and IL-17F in synovial fluid and plasma of PsA and osteoarthritis (OA) patients. IL-17A levels were significantly higher than IL-17F ($p<0.001$). All experiments were done in triplicate Fig 3B. Expression of IL-17A is significantly higher compared to IL-17F in activated CD4+ T memory T cells in synovial fluid T cells of psoriatic arthritis patients. A representative flow plot showing expression of IL-17A and IL-17F in CD4+ memory T cells. Bar diagram showing significantly higher numbers of IL-17A+ CD4+ memory T cells compared to IL-17F ($p<0.001$) in PsA and RA in synovial fluid derived T cells. All experiments were done in triplicate.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: IL-17A is more in the PsA synovium and functionally more potent than IL-17F in respect to its regulatory role on pannus formation. That explains the success of anti-IL-17A mab therapy in PsA. There is moderate level of synergism with IL-17A and IL-17F in respect to FLS proliferation and upregulations of FLS secreted inflammatory cytokines. This substantiates the combined role of IL-17A/F in the pathogenesis of PsA.

Disclosure: S. Raychaudhuri: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **C. Abria**: None; **S. Raychaudhuri**: None.

Abstract Number: 0588

The effect of biological and targeted synthetic DMARDs on peripheral manifestations in axial spondyloarthritis: a systematic literature review

Casper Webers[1], AUGUSTA ORTOLAN[2], Elena Nikiphorou[3], Alexandre Sepriano[4], Louise Falzon[5], Clementina López Medina[6], Dafne capelusnik[7], Désirée Van Der Heijde[8], Anna Molto[9] and **Sofia Ramiro**[10], [1]Maastricht University Medical Centre, Maastricht, Netherlands, [2]Policlinico Universitario Agostino Gemelli IRCSS, Rome, Italy, [3]King's College London, London, United Kingdom, [4]Department of Rheumatology, Leiden University Medical Centre, Portela Loures, Portugal, [5]Sheffield Centre for Health and Related Research, University of Sheffield, Sheffield, United Kingdom, [6]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [7]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [8]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [9]Assistance Publique Hôpitauxde Paris, Paris, France, [10]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: In axial spondyloarthritis (axSpA), peripheral musculoskeletal manifestations (peripheral arthritis, enthesitis, dactylitis) are common and contribute to the burden of disease. Our objective was to evaluate the evidence on the efficacy of biological and targeted synthetic therapies (bDMARDs/tsDMARDs) on peripheral musculoskeletal manifestations in axSpA.

Methods: Systematic literature review (SLR) of controlled trials that assessed the effect of bDMARDs/tsDMARDs compared to any active treatment or placebo on peripheral arthritis, enthesitis or dactylitis in adult axSpA patients (PROSPERO CRD42024532666). Studies were identified using previous SLRs on bDMARD/tsDMARD efficacy for the 2016/2022 updates of the ASAS-EULAR axSpA management recommendations (≤2021)[1-3] and an updated search (2022 – March 2024). Standardised mean differences (SMDs; < 0.5 small, 0.5-0.8 moderate, >0.8 large effect; negative SMDs favour intervention) were calculated for change from baseline, and complete resolution of each peripheral manifestation was assessed. If SMDs could not be calculated, post-intervention outcome values were considered instead.

Results: In total, 50 studies were included. Most investigated bDMARDs, especially TNF inhibitors (n=24 [48%]) and IL-17 inhibitors (n=13 [26%]), while few focused on tsDMARDs (n=6 [12%]). Studies often compared active treatment to placebo (n=35 [70%]), although several included a head-to-head comparison (n=6 [13%], usually biosimilar versus originator comparison). Some studies (n=4 [8%]) focused on tapering or complete withdrawal of bDMARDs. Risk of bias was often low (n=33 [66%]).

Of the 50 included studies, 37 (74%) reported results on peripheral arthritis, 46 (92%) on enthesitis and only 1 (2%) on dactylitis. Effects on peripheral arthritis were small for both bDMARDs and tsDMARDs (n=16 studies), with most SMDs ranging from -0.5 to 0 (Table). Of note, only few studies reported results in the subgroup with peripheral arthritis at baseline, showing

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Efficacy of bDMARDs/tsDMARDs on peripheral manifestations* in axSpA trials

Study	Intervention	Peripheral arthritis Instrument	SMD**	Enthesitis Instrument	SMD**
Comparator = placebo, population = patients with enthesitis or peripheral arthritis at baseline					
ACHILLES	Secukinumab	-	-	Heel pain	-0.11
				Heel enthesopathy (phys)	-0.27
				Heel enthesopathy (pt)	-0.11
Baeten 2018	Risankizumab	SJC¥	-0.33 / -0.30 / -0.10‡	MASES	-0.32 / 0.23 / 0.09‡
		TJC¥	-0.47 / -0.46 / -0.62‡		
BE AGILE	Bimekizumab	-	-	MASES#	-0.08
BE MOBILE 1	Bimekizumab	-	-	MASES	-0.38
BE MOBILE 2	Bimekizumab	-	-	MASES	-0.21
Deodhar 2020	Tofacitinib	SJC44	-0.23	MASES	-0.22
HEEL trial	Etanercept	-	-	MASES	-0.43
				Heel enthesopathy (pt)	-1.18
				Heel pain	-0.98
TORTUGA	Filgotinib	SJC44	0.05	-	-
		TJC44	-0.50		
Comparator = placebo, population = all (with/without enthesitis or peripheral arthritis at baseline)					
AILAS	Netakimab	-	-	MASES	0.13 / -0.46 / 0.00‡
COAST-V/W	Ixekizumab	BASDAI Q3#	-0.34	BASDAI Q4#	-0.47
COAST-X	Ixekizumab	BASDAI Q3#	-0.23	BASDAI Q4#	-0.22
EMBARK	Etanercept	SJC44	-0.29	MASES	-0.23
		TJC44	0.00		
GO-AHEAD	Golimumab	SJC¥	-0.14	MASES	-0.27
		TJC¥	-0.22		
GO-RAISE	Golimumab	-	-	MASES	-0.11
				UCSF index	-0.21
Huang 2013	Adalimumab	SJC44	-0.14	MASES	-0.20
		TJC46	-0.19		
INFAST-1	Infliximab†	SJC66	-0.30	-	-
		TJC68	-0.07		
Peters 2023	Tildrakizumab	SJC44	0.14	MASES	0.05
		TJC46	-0.26		
SELECT-AXIS1	Upadacitinib	SJC66	-0.13	-	-
		TJC68	-0.29		
		BASDAI Q3	-0.29		
van der Heijde 2016	Tofacitinib	SJC44	0.07	-	-
Wei 2021	Brodalumab	SJC44	-0.06	MASES	-0.04
Tapering study (comparator = continuation), population = all (with/without enthesitis or peripheral arthritis at baseline)					
C-OPTIMISE	Stop/taper certolizumab	SJC44	0.00 / 0.00§	MASES	-0.30 / 0.00§
		TJC44	0.14 / 0.26§		
Head-to-head (comparator = originator), population = all (with/without enthesitis or peripheral arthritis at baseline)					
Su 2020 BioDrugs	Adalimumab biosimilar	SJC46#	0.10	MASES	0.11

For studies that investigated multiple dosing schemes, results are shown for the registered dosage (if approved for axSpA, otherwise all investigated doses are shown). *For dactylitis, no SMDs could be calculated due to lack of data. **Negative SMDs favour intervention over comparator. #Study also included other instruments to assess enthesitis or peripheral arthritis, but without sufficient data to calculate SMD. ¥Number of joints considered not reported. †With naproxen. ‡For dose/frequency arms: 18/90/180mg (Baeten 2018), 40/80/120mg (AILAS). §For stopping and tapering arms, respectively. Phys = physician, pt = patient, SJC = swollen joint count, TJC = tender joint count.

slightly higher effects. Complete resolution of peripheral arthritis in those affected at baseline (n=2 studies, both on bimekizumab) occurred in 58-64% for bimekizumab and 36-42% for placebo. Similar to peripheral arthritis, SMDs indicated mainly small to moderate effects on enthesitis for both bDMARDs and tsDMARDs (n=19 studies, Table). Complete resolution of enthesitis (n=5 studies) occurred in 34-52% of patients for various bDMARDs and 14-33% for placebo. Results were similar in studies for which no SMD could be calculated. Finally, for dactylitis, the only available study was a TNF inhibitor tapering study. Dactylitis counts were similar in both study arms (median of 0 in both), although most patients did not have active dactylitis at baseline.

Conclusion: In axSpA, bDMARDs and tsDMARDs have small to moderate effects on peripheral arthritis and enthesitis. For dactylitis, efficacy data for these drugs are very scarce in axSpA. Most studies do not report results in the population of interest (those affected at baseline), possibly resulting in an underestimation of intervention effects.

References

1. Sepriano et al. RMD Open 2017.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2. Webers et al. ARD 2023.
3. Ortolan et al. ARD 2023.

Disclosure: C. Webers: Novartis, 6; **A. ORTOLAN**: AbbVie/Abbott, 6, AstraZeneca, 6, Eli Lilly, 6, GlaxoSmithKlein(-GSK), 6, Janssen, 6, Novartis, 6; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6; **A. Sepriano**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, UCB, 2, 6; **L. Falzon**: None; **C. López Medina**: None; **D. capelusnik**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 0589

Comparing Efficacy of Upadacitinib in Male and Female Patients with axSpA: Results from the SELECT-AXIS 1 and 2 Trials

Sofia Ramiro[1], Anna Molto[2], Elena Nikiphorou[3], Marcelo Pinheiro[4], Jamie Urbanik[5], Tianming Gao[6], Shirley Chen[7], Jayne Stigler[8], Jessica A. Walsh[9] and Lihi Eder[10], [1]Leiden University Medical Center, Bunde, Netherlands, [2]Assistance Publique Hôpitauxde Paris, Paris, France, [3]King's College London, London, United Kingdom, [4]UNIFESP/ EPM, São Paulo, São Paulo, Brazil, [5]AbbVie, Grayslake, IL, [6]AbbVie, North Chicago, IL, [7]AbbVie, Somerset, NJ, [8]AbbVie, Round Lake, IL, [9]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [10]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

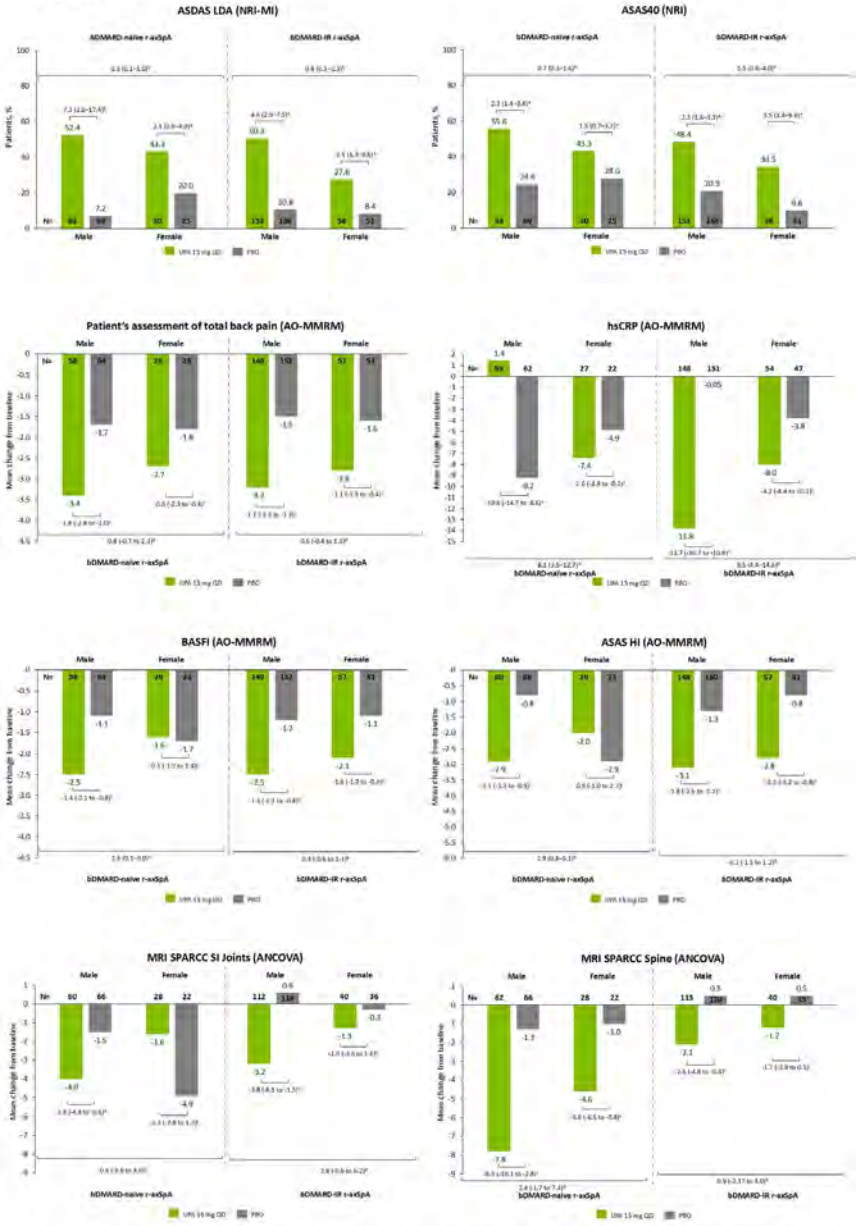
Background/Purpose: Evidence suggests that the treatment effectiveness of TNFis and IL-17is is higher in male (M) vs female (F) patients (pts) with axSpA.[1,2] Data comparing the efficacy of JAKis in M and F pts with axSpA are limited. This post hoc analysis of data from 2 phase 3 clinical trials evaluated differences in efficacy between M and F pts with axSpA who were treated with upadacitinib (UPA), an oral JAKi.

Methods: Data were from SELECT-AXIS 1 (NCT03178487; included pts with r-axSpA [historically referred to as AS] naïve to bDMARDs [bDMARD-naïve]) and SELECT-AXIS 2 (NCT04169373; 2 substudies: [1] pts with r-axSpA with an intolerance or inadequate response to bDMARD therapy [bDMARD-IR], [2] pts with nr-axSpA, which included 33% bDMARD-IR pts).[3–5] Pts were randomized to UPA 15 mg once daily (UPA15) or placebo (PBO) for 14 (bDMARD-naïve and bDMARD-IR) or 52 (nr-axSpA) weeks (W). In this post hoc analysis, efficacy endpoints were assessed through W14 in all pt populations, and through W52 in the nr-axSpA population. Response rates, stratified by sex (M vs F), were calculated using non-responder imputation (NRI) or NRI with multiple imputation for binary endpoints, and as observed with mixed-effect model for repeated measures for continuous endpoints. Analysis of covariance model was used for mean change from baseline in MRI SPARCC score (SI joints and spine). Efficacy of UPA15 vs PBO was assessed by relative risk (RR) (binary outcomes) or mean between-group differences (continuous outcomes) within each sex (M and F), and the effect of UPA vs PBO in M and F was assessed by the RR ratio (RRR) (binary outcomes) or difference between groups in means (continuous outcomes). Information on the interpretation of RRR and difference between groups in means can be found in the figures.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 920 pts were included, of whom 460 (283/177 M/F) received UPA15 and 460 (290/170 M/F) received PBO. Baseline characteristics were generally similar between sexes, except for greater hsCRP, HLA-B27, and MRI scores in M vs F at baseline. Higher efficacy was seen with UPA vs PBO in both sexes for most endpoints (Figures). At W14, although M generally had numerically better outcomes, results were mostly consistent between M and F, as reflected by RRR or mean difference between differences showing minor differences between both sexes. A trend for higher efficacy outcomes among M vs

Figure 1. Efficacy outcomes stratified by sex in the bDMARD-naïve r-axSpA and bDMARD-IR r-axSpA populations at W14

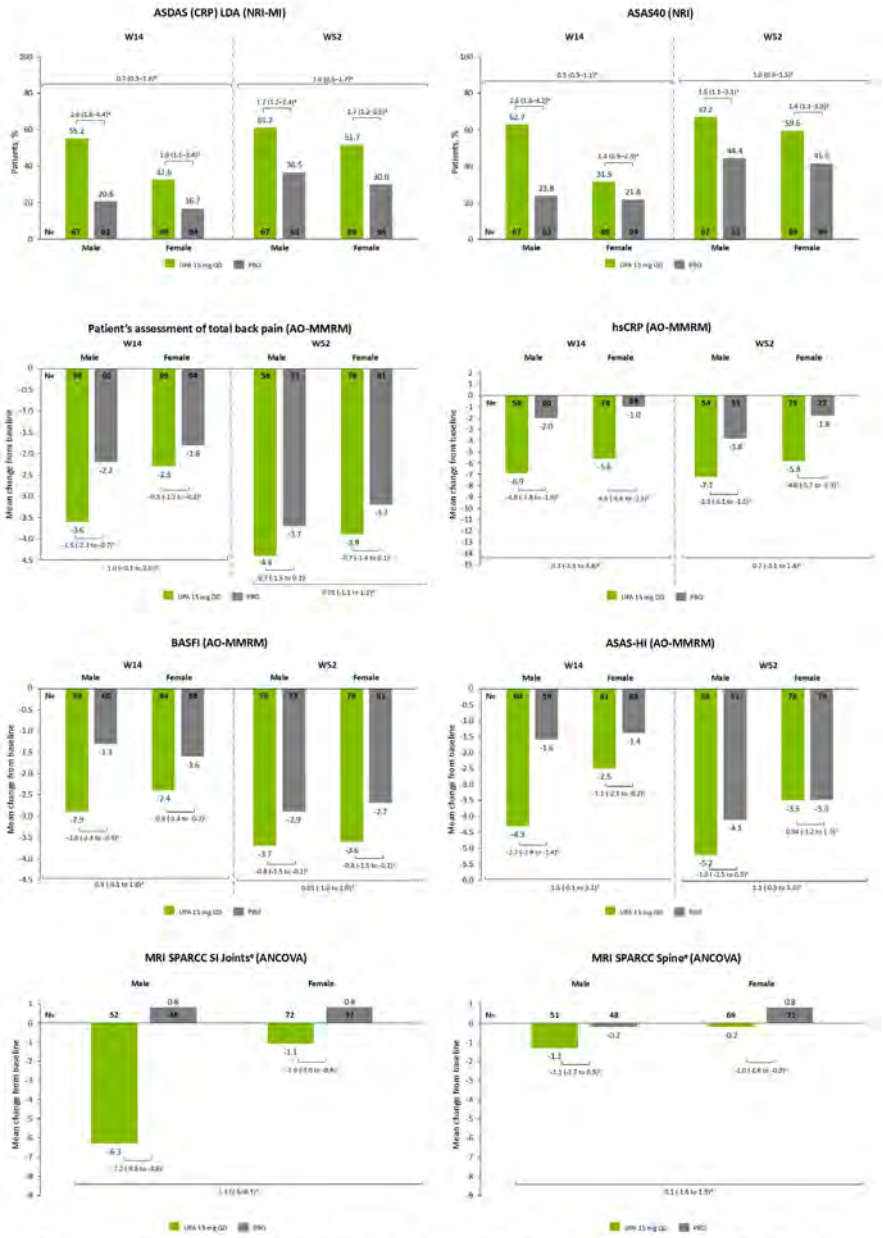


Response rates for binary endpoints were calculated using non-responder imputation (NRI) or NRI with multiple imputation (SELECT-AXIS 2 study only, where missing data due to COVID-19 was imputed).
For continuous endpoints, an AO-MMRM was applied.
For change from baseline in MRI SPARCC score (SI joints and spine), the analysis of covariance model was used.
For binary endpoints, an RR above 1 indicated better outcomes with UPA vs PBO. For all continuous endpoints a between-group difference lower than 0 indicated better outcomes with UPA vs PBO.
For binary endpoints, an RRR above 1 indicated better outcomes with females vs males, while an RRR below 1 indicated worse outcomes with females vs males. For all continuous endpoints, a between treatment group difference above 0 indicated worse outcomes with females vs males, while a between treatment group difference below 0 indicated better outcomes with females vs males.
[a]RR (95% CI) UPA vs PBO. [b]RRR (95% CI) male vs female. [c]Between-group difference (95% CI) UPA vs PBO. [d]Between treatment group difference (95% CI) male vs female.
AO, as observed; bDMARD, biologic DMARD; bDMARD-IR, intolerance or inadequate response to bDMARD therapy; bDMARD-naive, naive to bDMARDs; CI, confidence interval; Hi, health index; MMRM, mixed-effect model for repeated measures; NRI-MI, non-responder imputation with multiple imputation; PBO, placebo; QD, once daily; r-axSpA, radiographic axSpA; RR, relative risk; RRR, RR ratio; SPARCC, SpondyloArthritis Research Consortium of Canada; UPA, upadacitinib; W, Week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

F pts was most apparent among the bDMARD-naïve r-axSpA population, which had the smallest number of F pts (311/109, M/F). In 3 instances (ASAS40 and ASAS HI in bDMARD-IR r-axSpA, and MRI SPARCC SI joints in bDMARD-naïve r-axSpA), F had numerically better outcomes vs M, based on the RRR or mean difference between differences (Figure 1). In nr-axSpA, there was no strong evidence of differences between M vs F pts at W52 (Figure 2).

Figure 2. Efficacy outcomes stratified by sex in the nr-axSpA population at W14 and W52



Response rates for binary endpoints were calculated using non-responder imputation (NRI) or NRI with multiple imputation (SELECT-AXIS 2 study only, where missing data due to COVID-19 was imputed).
For continuous endpoints, an AO-MMRM was applied.
For change from baseline in MRI SPARCC score (SI joints and spine), the ANCOVA model was used.
For binary endpoints, an RR above 1 indicated better outcomes with UPA vs PBO. For all continuous endpoints, a between-group difference lower than 0 indicated better outcomes with UPA vs PBO.
For binary endpoints, an RRR above 1 indicated better outcomes with females vs males, while an RRR below 1 indicated worse outcomes with females vs males. For all continuous endpoints, a between treatment group difference above 0 indicated worse outcomes with females vs males, while a between treatment group difference below 0 indicated better outcomes with females vs males.
[a]RR (95% CI) UPA vs PBO. [b]RRR (95% CI) male vs female. [c]Between-group difference (95% CI) UPA vs PBO. [d]Between treatment group difference (95% CI) male vs female. *Only W14 data available.
ANCOVA, analysis of covariance; AO, as observed; CI, confidence interval; HI, health index; MMRM, mixed-effect model for repeated measures; nr-axSpA, non-radiographic axSpA; NRI, non-responder imputation; NRI-MI, NRI with multiple imputation; PBO, placebo; QD, once daily; RR, relative risk; RRR, RR ratio; SPARCC, SpondyloArthritis Research Consortium of Canada; UPA, upadacitinib; W, Week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: UPA generally demonstrated better efficacy vs PBO in both sexes and across all axSpA populations. Efficacy in M vs F pts was generally comparable.

References

1. Hellamand P, et al. *RMD Open*. 2023;9:e003325.
2. van der Horst-Bruinsma IE, et al. *Adv Ther*. 2022;39:2806–19.
3. Deodhar A, et al. *Lancet*. 2022;400:369–79.
4. van der Heijde D, et al. *Ann Rheum Dis*. 2022;81:1515–23.
5. van der Heijde D, et al. *Lancet*. 2019;394:2108–17.

Disclosure: S. Ramiro: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6; **M. Pinheiro**: AbbVie/Abbott, 2, Johnson & Johnson, 2, UCB, 2; **J. Urbanik**: AbbVie, 3, 11; **T. Gao**: AbbVie, 3, 11; **S. Chen**: AbbVie, 3, 12, provided statistical analysis support that was funded by AbbVie, Tigermed-BDM Inc, 3; **J. Stigler**: AbbVie, 3, 11; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5.

Abstract Number: 0590

Effect of Deucravacitinib Treatment on Disease Activity–Associated Plasma Biomarkers in Patients With Active Psoriatic Arthritis: Results From 2 Phase 3 Studies

Vinod Chandran[1], Oliver FitzGerald[2], Philip J. Mease[3], Lihi Eder[4], Jose Scher[5], Christopher Ritchlin[6], Dafna D. Gladman[7], Walter P Maksymowych[8], Coryandar Gilvary[9], Aditi Basu Bal[9], Eleni Vritzali[10] and Jinqi Liu[9], [1]Division of Rheumatology, Departments of Medicine and Laboratory Medicine and Pathobiology, University of Toronto, and Gladman Krembil Psoriatic Arthritis Research Program, Krembil Research Institute, University Health Network, Toronto, Canada, [2]UCD, Dublin 6, Dublin, Ireland, [3]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [4]University of Toronto, Toronto, ON, Canada, [5]New York University School of Medicine, New York, NY, [6]University of Rochester Medical Center, Canandaigua, NY, [7]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [8]Department of Medicine, University of Alberta, Edmonton, AB, Canada, [9]Bristol Myers Squibb, Princeton, NJ, [10]Bristol Myers Squibb, Boudry, Switzerland

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

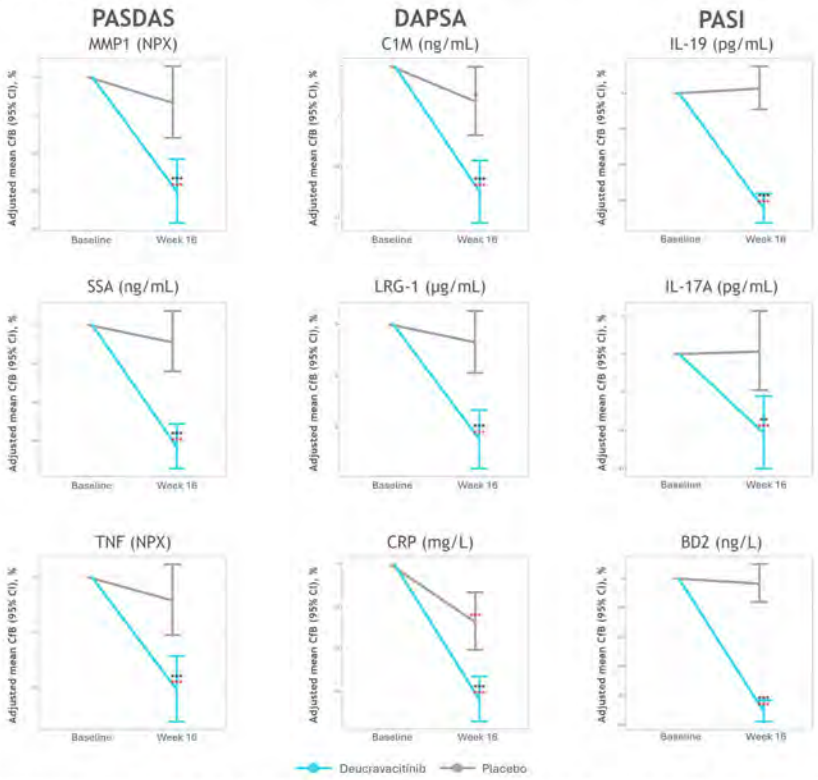
Background/Purpose: Understanding how treatments affect disease-relevant biomarker expression is essential for advancing targeted therapies. Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, has demonstrated superior efficacy in the placebo (PBO)-controlled phase 3 POETYK PsA-1 (NCT04908202) and PsA-2 (NCT04908189) studies. This pooled post hoc analysis of the POETYK PsA studies aimed to identify biomarkers reflecting clinically relevant factors potentially associated with poor prognosis in PsA and to evaluate associations among these biomarkers, deucravacitinib treatment, and clinical responses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Spearman correlations between 48 PsA and immune response–related biomarkers and PsA disease activity (PASDAS, DAPSA, PASI) at baseline (BL) and W16 were performed. Pharmacodynamic effects of deucravacitinib on biomarkers were analyzed using a mixed effects model to show covariate-adjusted change from BL for disease activity and Patient Global Assessment of Pain (Pain). Logistic regression was used to assess the relationship between BL biomarkers (eg, CRP, neutrophil-to-lymphocyte ratio [NLR]) and ACR 20 response, minimal disease activity (MDA) response, and modified Sharp-van der Heijde (mSvdH) total score (radiographic progression [defined as change of mSvdH > 0]; evaluated in POETYK PsA-1 only); covariates included BL BMI and prior MTX use. mSvdH nonprogression was evaluated using a stratified Cochran-Mantel-Haenszel test with BL csDMARD use as the stratification factor.

Results: Deucravacitinib significantly reduced disease activity–associated biomarkers, including those impacting skin (eg, IL-19, IL-17A, BD2) and joint (eg, CRP, C1M, LRG-1, MMP1, SAA, TNF) manifestations vs PBO (**Figure 1**). Patients treated with deucravacitinib were more likely to achieve ACR 20 and MDA response vs PBO at W16 in those with high (≥ median) BL NLR, IL-19, IL-17A, CRP, BD2, and SAA (**Figure 2A,C**). Response rates for ACR 20 and MDA were higher with deucravacitinib vs PBO at W16, with significant differences observed in patients with high (≥ median) BL IL-19, IL-17A, and BD2 for ACR 20 (**Figure 2B**) and high BL NLR (≥ 2.81) or high BD2 levels (≥ 7185 ng/L) for MDA (**Figure 2D**). Deucravacitinib reduced pain-associated biomarkers (eg, CRP, C1M, MMP3, TNF, ICAM-1) vs PBO at W16. Given the clinical relevance of CRP, additional analyses in patients with high BL CRP (≥ 3 mg/L) showed that deucravacitinib significantly reduced Pain score vs PBO as early as W4 ($P < 0.01$) with sustained reduction at W16 ($P < 0.001$), provided a greater reduction in mSvdH total score (PBO corrected) vs those with normal BL CRP, and led to reduced radiographic progression vs PBO at W16 (21.1% vs 30.6%; $P < 0.05$).

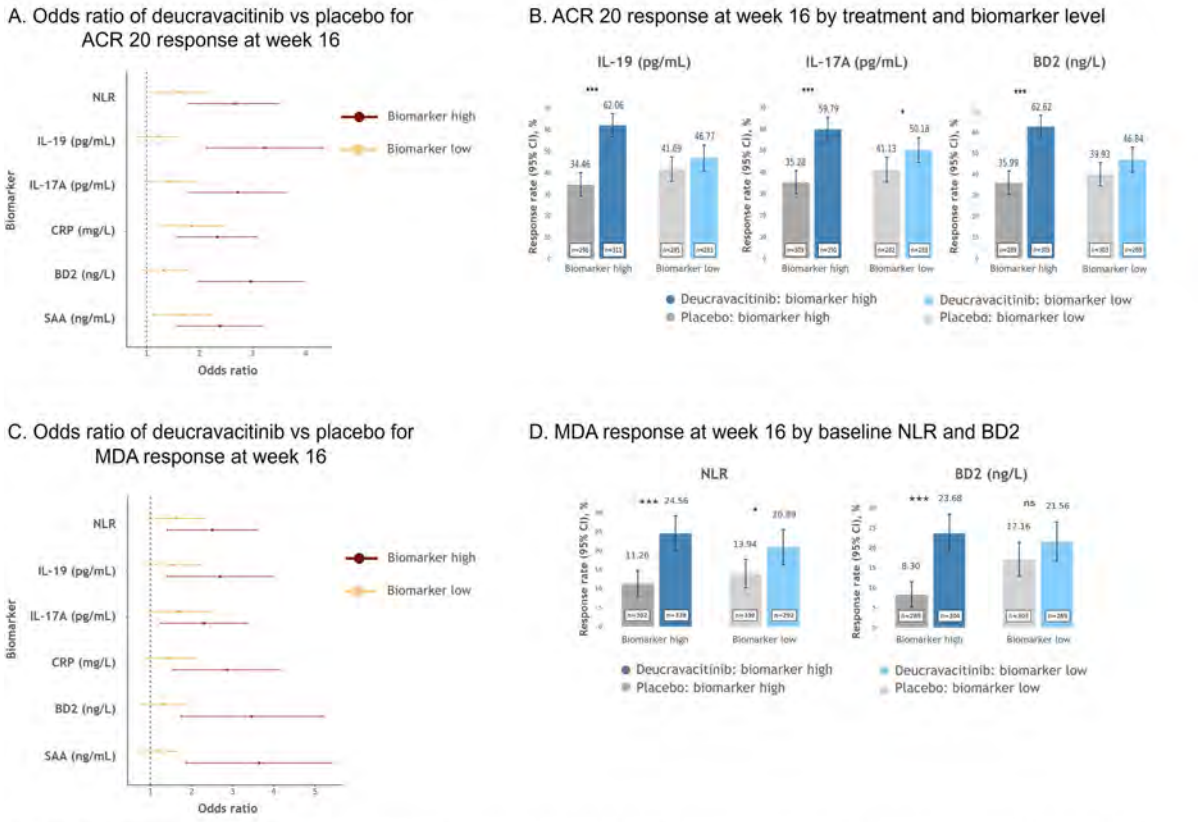
Figure 1. Changes in expression of disease-relevant biomarkers with deucravacitinib vs placebo at W16



Representative biomarkers are shown. *** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$. Red asterisks indicate a significant CfB within a treatment group. Black asterisks indicate a significant difference between deucravacitinib and placebo. Covariates included BL PASI score, BL DAS28-CRP score, and prior MTX use. CfB was used as the repeated measures; fixed effects included BL value, visit, arm, visit-by-arm interaction, and randomization stratification factors. NPX is the Olink unit of protein expression level in a $\log_2$ scale.
BD2, beta-defensin 2; BL, baseline; C1M, MMP-mediated type I collagen degradation; CfB, change from baseline; DAPSA, Disease Activity in Psoriatic Arthritis; LRG-1, leucine rich alpha-2-glycoprotein 1; NPX, Normalized Protein eXpression; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; SSA, serum amyloid A; W16, week 16.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Biomarkers associated with response to deucravacitinib at W16



*** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$. Logistic regression was used to assess the relationship between treatment response and BL biomarkers; data were dichotomized based on median cutoffs of biomarker expression levels (high vs low).
ACR 20, American College of Rheumatology 20% improvement in response; BD2, beta-defensin 2; BL, baseline; MDA, minimal disease activity; NLR, neutrophil-to-lymphocyte ratio; ns, not significant; SSA, serum amyloid A; W16, week 16.

Conclusion: Deucravacitinib significantly reduced PsA disease–associated biomarkers in patients with elevated BL biomarkers (eg, CRP, NLR), which may be indicative of severe disease and poor prognosis, and improved efficacy outcomes for multiple disease domains, including radiographic progression. These data provide biological evidence for deucravacitinib as a potential new oral PsA therapy that may benefit patients with severe and difficult-to-treat disease.

Disclosure: V. Chandran: AbbVie, 1, 2, AstraZeneca, 12, Spousal employment, Bristol Myers Squibb, 1, 2, Eli Lilly, 1, 2, 5, Fresenius Kabi, 1, 2, Johnson & Johnson, 1, 2, 5, Novartis, 1, 2, UCB, 1, 2; **O. FitzGerald**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **W. Maksymowych**: AbbVie, 2, 5, 6, 12, Educational grants, Bristol-Myers Squibb(BMS), 2, 5, 6, CARE Arthritis, 12, Chief Medical Officer, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, educational grants, Pfizer, 2, 5, 6, 12, educational grants, UCB Pharma, 2, 5, 6; **C. Gilvary**: Bristol-Myers Squibb(BMS), 3, 11; **A. Bal**: Bristol-Myers Squibb(BMS), 3, 11; **E. Vritzali**: Bristol Myers Squibb, 3, 11; **J. Liu**: Bristol-Myers Squibb (BMS), 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0591

An Interim Analysis of Health-related Quality of Life Outcomes from an International Multicentre Observational Study in Patients with Psoriatic Arthritis Initiating Bimekizumab in Real-world Clinical Practice

Xenofon Baraliakos[1], Uta Kiltz[1], Kurt de Vlam[2], Adeline Ruyssen-Witrand[3], Felipe Julio Ramirez Garcia[4], Jessica A. Walsh[5], Denis Poddubnyy[6], David Nicholls[7], Marga Oortgiesen[8], Francesca Maria Ester Castagna[9], Marie-Alix Bonny[10], Hervé Besson[11], Jérémy Lambert[12], Rajan Bajracharya[13], Patrik Öhagen[14] and William Tillett[15], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]Department of Rheumatology, UZ Leuven, Leuven, Belgium, [3]CHU of Toulouse - Pierre-Paul Riquet Hospital (Inflammation, Infection, Immunology and Locomotor Center - Rheumatology Service, Toulouse, France, [4]Rheumatology Department, Hospital Clinic and IDIBAPS of Barcelona, Barcelona, Spain, [5]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [6]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [7]Clinical Trials Unit, University of the Sunshine Coast, Queensland, Australia, [8]UCB, Raleigh, NC, [9]UCB SpA, Milano, Italy, [10]UCB, Brussels, Belgium, [11]UCB, Breda, Netherlands, [12]UCB, Colombes, France, [13]UCB, Slough, England, United Kingdom, [14]UCB, Stockholm, Sweden, [15]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: PsA is a chronic inflammatory disease with a significant burden on patients' (pts) health-related quality of life (HRQoL).[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated sustained efficacy to 2 years in clinical trials of pts with PsA.[2–3] BKZ has been approved for treatment of PsA in Europe since June 2023, and the US since September 2024.[4,5] SPEAK is the first prospective, observational study in routine clinical practice in Europe evaluating HRQoL and clinical outcomes with BKZ in pts with active PsA or axial spondyloarthritis (axSpA). We report interim data from SPEAK, describing characteristics of pts with PsA at BKZ treatment initiation and HRQoL to 24 weeks (wks) in a real-world setting.

Table. Baseline characteristics of PsA patients in the SPEAK study

	Previous b/tsDMARD exposure			
Characteristic, mean (SD) unless otherwise stated	b/tsDMARD naïve N=80	1 b/tsDMARD N=89	≥2 b/tsDMARDs N=207	Total N=376
Age, years	51.6 (12.1)	50.8 (11.8)	53.2 (10.6)	52.3 (11.2)
Sex, male, *n* (%)	39 (48.4)	43 (48.3)	74 (35.7)	156 (41.5)
BMI	29.3 (6.5)	30.9 (6.4)	29.5 (6.2)	29.8 (6.3)
Time since diagnosis, years	4.7 (6.0)	7.2 (8.0)	11.6 (9.2)	9.1 (8.8)
History of IBD, n (%)	0 (0)	1 (1.1)	4 (1.9)	5 (1.3)
TJC	10.5 (8.3)	10.2 (10.1)	13.1 (12.3)	11.9 (11.2)
SJC	5.0 (4.9)	6.7 (8.0)	5.4 (6.6)	5.7 (6.7)
CRP, mg/L, median (min–max)	3.6 (0.0–46.0)	3.3 (0.0–49.8)	3.6 (0.0–112.0)	3.6 (0.0–112.0)
PsAID-12 total score	5.0 (1.9)	5.3 (2.2)	5.5 (2.1)	5.4 (2.1)
HAQ-DI score	1.0 (0.6)	1.2 (0.8)	1.4 (0.7)	1.3 (0.7)
PGADA score	57.0 (19.3)	57.6 (23.3)	61.1 (21.3)	59.4 (21.4)
SF-36 PCS score	37.3 (8.1)	36.4 (9.4)	34.3 (9.3)	35.6 (9.2)

Safety analysis set (includes all patients enrolled into the study). BMI: body mass index; b/tsDMARD: biologic/targeted synthetic disease-modifying antirheumatic drugs; CRP: C-reactive protein; HAQ-DI: Health Assessment Questionnaire Disability Index; PGADA: Patient Global Assessment of Disease Activity; PsA: psoriatic arthritis; PsAID-12: 12-item PsA Impact of Disease; SD: standard deviation; SJC: swollen joint count; SF-36 PCS: Short Form 36-Item Health Survey Physical Component Summary; TJC: tender joint count; VAS: Visual Analog Scale.

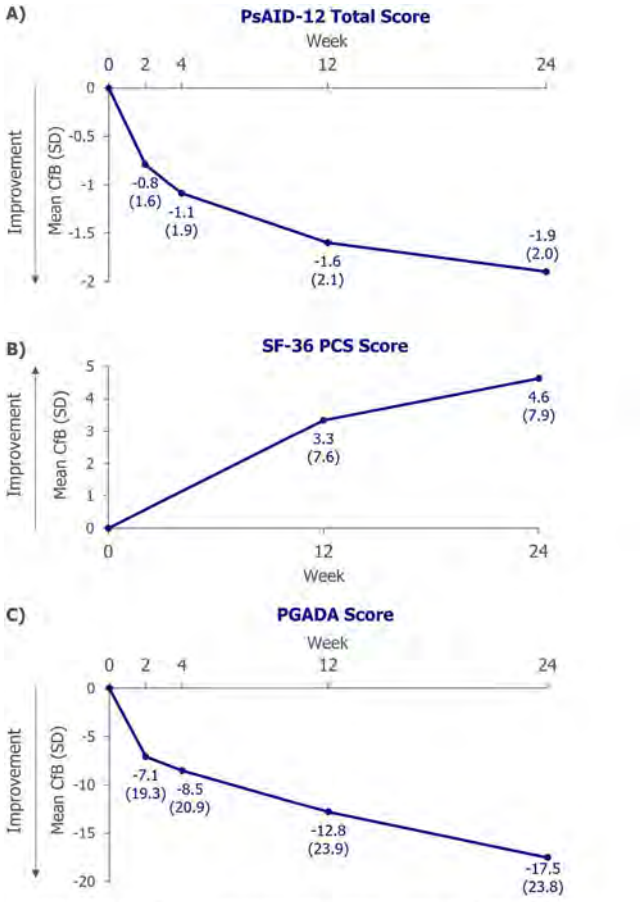
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: SPEAK is an ongoing 52-wk, multi-country, observational study in Belgium, Czechia, France, Germany, Greece, Spain, and the United Kingdom. This planned interim analysis reports data to April 2, 2025 (~50% enrolment). Adult pts with active PsA or axSpA who initiated BKZ in routine clinical practice could be included if receiving treatment per label (subcutaneous BKZ 160 mg every 4 wks). We report PsA Impact of Disease 12-Item Questionnaire total score (PsAID-12; 0–10), Short Form 36-item Health Survey Physical Component Summary (SF-36 PCS, norm-based T-scores with mean [SD]: 50 [10] in the US general population), and Pt Global Assessment of Disease Activity score (PGADA; 0–100) for pts with PsA to 24 wks. Other clinical outcomes were collected but not available for the data cut. Baseline (BL) characteristics and adverse events are also reported.

Results: By April 2025, BL characteristics were available for 376 pts with PsA (**Table**). Overall, 80 were biologic/targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) naïve, 89 had 1 previous b/tsDMARD and 207 had ≥2 previous b/tsDMARDs.

Improvements in PsAID-12 total score were observed to 24 wks, with mean (SD) CfB at Wk 24 of –1.9 (2.0). SF-36 PCS scores improved to Wk 24 (mean [SD] CfB: +4.6 [7.9]), as did PGADA scores (Mean [SD] CfB: –17.5 [23.8]); **Figure**; BL values in **Table**).

TEAEs were reported in 61.4% pts; in 34.8% they were deemed drug-related. One pt reported uveitis (0.3%). 43 pts reported *Candida* infections (11.4%), including 29 with oral candidiasis (7.7%; 3.5% led to BKZ discontinuation). There were no cases of IBD or suicidal ideation/behavior.



Full analysis set. b/tsDMARD: biologic/targeted synthetic disease-modifying antirheumatic drugs; CfB: change from baseline; PGADA: Patient Global Assessment of Disease Activity; PsA: psoriatic arthritis; PsAID-12: 12-item PsA Impact of Disease; SD: standard deviation; SF-36 PCS: Short Form 36-Item Health Survey Physical Component Summary; VAS: Visual Analog Scale.

Figure. CfB in PsAID-12, SF-36 PCS and PGADA scores to week 24 (OC)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this first report of HRQoL outcomes in an observational setting of BKZ-treated pts with PsA in routine clinical practice, BKZ treatment led to improvements in pt-reported outcomes at 24 wks, with changes observed as early as Wk 2, demonstrating rapid HRQoL improvements. The real-world findings complement data from phase 3 trials, for both HRQoL and safety.

References: 1. Coates LC. CME Rheum 2017;17:65–70; **2**. McInnes IB. Lancet 2023;401:25–37; **3**. Merola JF. Lancet 2023;401:38–48; **4**. EMA. Bimekizumab Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/bimzelx-epar-product-information_en.pdf; **5**. FDA. 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761151s009lbl.pdf.

Disclosure: X. Baraliakos: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **K. de Vlam**: AbbVie, 2, 6, Alphasigma, 2, 6, Amgen, 2, 6, BMS, 2, 6, Galapagos, 2, 6, J&J, 2, 6, Lilly, 2, 6, MoonLake, 2, Novartis, 2, 6, Roche, 2, Sandoz, 2, UCB, 6; **A. Ruyssen-Witrand**: None; **F. Ramirez Garcia**: AbbVie, 2, 6, Eli Lilly, 6, Johnson and Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, UCB, 2, 6; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **D. Nicholls**: AbbVie, 1, 5, 6, AstraZeneca, 1, 6, BMS, 5, Eli Lilly, 5, Gilead, 5, Incannex, 5, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Servatus, 5, Sun Pharma, 5, UCB, 1, 5, 6; **M. Oortgiesen**: UCB, 3, 11; **F. Castagna**: UCB, 3, 11; **M. Bonny**: UCB, 3, 11; **H. Besson**: UCB, 3, 11; **J. Lambert**: UCB, 3, 11; **R. Bajracharya**: UCB, 3, 11; **P. Öhagen**: UCB, 3, 11; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ono Pharma, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0592

An Interim Analysis of Health-related Quality of Life Outcomes from an International Multicentre Observational Study in Patients with Axial Spondyloarthritis Initiating Bimekizumab in Real-world Clinical Practice

Xenofon Baraliakos[1], Uta Kiltz[1], Kurt de Vlam[2], Adeline Ruyssen-Witrand[3], Julio Ramírez Garcia[4], Jessica A. Walsh[5], Denis Poddubnyy[6], David Nicholls[7], Marga Oortgiesen[8], Francesca Maria Ester Castagna[9], Marie-Alix Bonny[10], Hervé Besson[11], Rajan Bajracharya[12], Patrik Öhagen[13], Christine de La Loge[10] and William Tillett[14], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]Department of Rheumatology, UZ Leuven, Leuven, Belgium, [3]CHU of Toulouse - Pierre-Paul Riquet Hospital (Inflammation, Infection, Immunology and Locomotor Center - Rheumatology Service, Toulouse, France, [4]Rheumatology Department, Hospital Clinic and IDIBAPS of Barcelona, Barcelona, Spain, [5]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [6]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [7]Clinical Trials Unit, University of the Sunshine Coast, Queensland, Australia, [8]UCB, Raleigh, NC, [9]UCB SpA, Milano, Italy, [10]UCB, Brussels, Belgium, [11]UCB, Breda, Netherlands, [12]UCB, Slough, England, United Kingdom,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[13]UCB, Stockholm, Sweden, [14]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0554–0592) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease with a significant burden on patients' (pts) health-related quality of life (HRQoL).[1] Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated sustained efficacy to 2 years in clinical trials of pts with non-radiographic [nr-] and radiographic [r-]axSpA.[2] BKZ has been approved for treatment of axSpA in Europe since June 2023, and the US since September 2024.[3,4] SPEAK is the first prospective, observational study in routine clinical practice in Europe evaluating HRQoL and clinical outcomes with BKZ in pts with active axSpA and PsA. We report interim data from SPEAK, describing characteristics of pts with axSpA at BKZ treatment initiation and HRQoL to 24 weeks (wks) in a real-world setting.

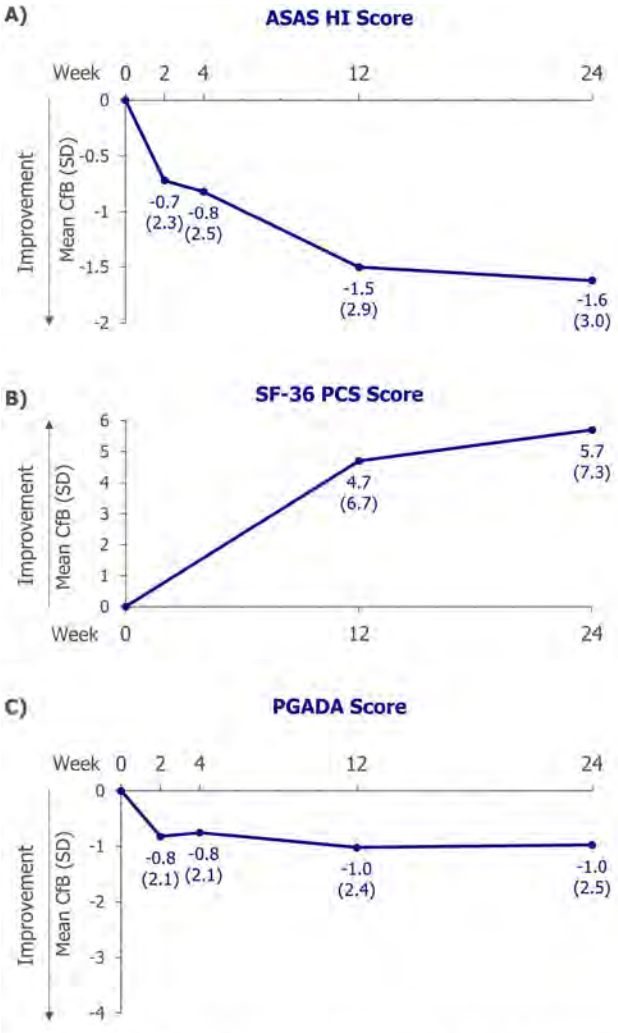
Methods: SPEAK is an ongoing 52-wk, multi-country, observational study in Belgium, Czechia, France, Germany, Greece, Spain, and the United Kingdom. Adult pts with active axSpA or PsA who initiated BKZ in routine clinical practice could be included if receiving treatment per label (subcutaneous 160 mg every 4 wks). This planned interim analysis reports data to April 2, 2025 (~50% enrolment). We report Assessment of SpondyloArthritis international Society Health Index (ASAS HI; 0–17), Short Form 36-item Health Survey Physical Component Summary (SF-36 PCS, norm-based T-score with mean

Table. Baseline characteristics of patients with axSpA in the SPEAK study

	Previous b/tsDMARD exposure			
Characteristic (mean [SD] unless otherwise stated)	**b/tsDMARD naïve n=38**	**1 b/tsDMARD n=56**	**≥2 b/tsDMARDs n=103**	**Total N=197**
Age, years	38.8 (10.7)	46.6 (13.0)	47.4 (12.4)	45.5 (12.7)
Sex, male, n (%)	20 (52.6)	27 (48.2)	45 (43.7)	92 (46.7)
BMI	28.6 (5.9)	28.8 (8.9)	27.8 (6.0)	28.2 (6.9)
nr-axSpA, n (%)	18 (23.1)	23 (29.5)	37 (47.4)	78 (39.6)
r-axSpA, n (%)	20 (16.8)	33 (27.7)	66 (55.5)	119 (60.4)
Time since first symptoms, years	9.1 (7.5)	13.1 (10.6)	16.1 (11.9)	13.9 (11.1)
Time since diagnosis, years	3.7 (5.6)	7.6 (8.8)	11.0 (9.6)	8.6 (9.1)
History of uveitis, n (%)	3 (7.9)	12 (21.4)	16 (15.5)	31 (15.7)
History of IBD, n (%)	0 (0)	0 (0)	3 (2.9)	3 (1.5)
CRP, mg/L, median (min-max)	5.3 (0.3–62.0)	4.0 (0.5–93.0)	3.9 (0.0–90.0)	4.0 (0.0–93.0)
ASAS HI score	7.7 (3.5)	8.8 (3.9)	9.6 (3.7)	9.0 (3.8)
SF-36 PCS score	37.5 (7.1)	35.7 (6.6)	33.7 (7.3)	35.1 (7.2)
PGADA score	5.4 (1.8)	5.9 (2.0)	6.3 (1.9)	6.0 (1.9)
ASDAS	3.2 (1.0)	3.0 (0.9)	3.2 (0.8)	3.1 (0.9)
BASDAI total score	5.5 (1.9)	5.7 (1.7)	6.0 (1.8)	5.8 (1.8)

Safety analysis set (includes all patients enrolled into the study). PGADA in this study was assessed using a 0-100 Visual Analog Scale (VAS). Data presented here is the rescaled score used to derive the ASDAS and which ranges from 0 to 10; ASAS HI: Assessment of SpondyloArthritis international Society Health Index; ASDAS: Axial Spondyloarthritis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; b/tsDMARD: biologic/targeted synthetic disease-modifying antirheumatic drugs; BMI: body mass index; CRP: c-reactive protein; IBD: inflammatory bowel disease; nr-axSpA: non-radiographic axSpA; PGADA: Patient Global Assessment of Disease Activity; r-axSpA: radiographic axSpA; SD: standard deviation; SF-36 PCS: Short Form 36-item Health Survey Physical Component Summary; VAS: visual analog scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Full analysis set. PGADA in this study was assessed using a 0–100 Visual Analog Scale (VAS): data presented here is the rescaled score used to derive the ASDAS and which ranges from 0 to 10. ASAS HI: Assessment of SpondyloArthritis international Society Health Index; axSpA: axial spondyloarthritis; b/tsDMARD: biologic/targeted synthetic disease-modifying antirheumatic drugs; CfB: change from baseline; nr-axSpA: non-radiographic axSpA; OC: observed case; PGADA: Patient Global Assessment of Disease Activity; r-axSpA: radiographic axSpA: SD: standard deviation; SF-36 PCS: Short Form 36-Item Health Survey Physical Component Summary; VAS: visual analog scale.

Figure. Change from baseline in ASAS HI, SF-36 PCS and PGADA scores to Week 24 (OC)

[SD]: 50 [10] in the US general population) and Pt Global Assessment of Disease Activity score (PGADA; 0–10) for pts with axSpA to 24 wks. Other clinical outcomes were collected but not available for data cut. Baseline (BL) characteristics and adverse events are also reported.

Results: By April 2025, BL characteristics were available for 197 pts with axSpA (nr-axSpA: 78, r-axSpA: 119; **Table**). Overall, 38 were biologic/targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) naïve, 56 had 1 previous b/tsDMARD and 103 had ≥2 previous b/tsDMARDs.

Improvements in ASAS HI score were observed to 24 wks, with mean (SD) CfB at Wk 24 of –1.6 (3.0). SF-36 PCS scores improved to Wk 24 (mean [SD] CfB: +5.7 [7.3]), as did PGADA scores (mean [SD] CfB: –1.0 [2.5]; **Figure**; BL values in **Table**).

TEAEs were reported in 62.9% of pts; in 33.0% they were deemed drug-related. Three cases of uveitis were reported by 2 pts (1.5%), 15 Candida infections (7.6%), including 12 oral candidiasis (6.1%, 3.0% led to BKZ discontinuation), 1 case of IBD (0.5%) and no suicidal ideation and behavior.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this first report of HRQoL outcomes in an observational setting for BKZ-treated pts with axSpA in routine clinical practice, BKZ treatment led improved pt-reported outcomes at 24 wks, with changes observed as early as Wk 2, demonstrating rapid HRQoL improvements. The real-world findings complement data from phase 3 trials, for both HRQoL and safety.

References: 1. Strand V. J Clin Rheumatol 2017;23:383–91; **2**. Baraliakos X. Rheumatology 2025;keaf009; **3**. EMA. 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/bimzelx-epar-product-information_en.pdf; **4**. FDA. 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761151s009lbl.pdf.

Disclosure: X. Baraliakos: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **K. de Vlam**: AbbVie, 2, 6, Alphasigma, 2, 6, Amgen, 2, 6, BMS, 2, 6, Galapagos, 2, 6, J&J, 2, 6, Lilly, 2, 6, MoonLake, 2, Novartis, 2, 6, Roche, 2, Sandoz, 2, UCB, 6; **A. Ruyssen-Witrand**: None; **J. Ramírez Garcia**: AbbVie, 2, 6, Eli Lilly, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, UCB, 2, 6; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **D. Nicholls**: AbbVie, 1, 5, 6, AstraZeneca, 1, 6, BMS, 5, Eli Lilly, 5, Gilead, 5, Incannex, 5, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Servatus, 5, Sun Pharma, 5, UCB, 1, 5, 6; **M. Oortgiesen**: UCB, 3, 11; **F. Castagna**: UCB, 3, 11; **M. Bonny**: UCB, 3, 11; **H. Besson**: UCB, 3, 11; **R. Bajracharya**: UCB, 3, 11; **P. Öhagen**: UCB, 3, 11; **C. de La Loge**: UCB, 2; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ono Pharma, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0593

Genetic Risk Profiles Predict Clinical Heterogeneity in Systemic Lupus Erythematosus

Nina Oparina[1], Sarah Reid[1], Ahmne Sayadi[1], Maija-Leena Eloranta[1], Martina Frodlund[2], Karoline Lerang[3], Andreas Jönsen[4], Øyvind Molberg[3], Solbritt Rantapää-Dahlqvist[5], Anna Rudin[6], Chrisopher Sjöwall[7], Anders Bengtsson[8], Lars Rönnblom[1] and **Dag Leonard**[1], [1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [2]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Linkoping, Sweden, [3]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [4]Department of Clinical Sciences, Lund University, Lund, Sweden, [5]Department of Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden, [6]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy of University of Gothenburg, Gothenburg, Sweden, [7]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden, [8]Department of Clinical Sciences, Lund University, Lund, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with diverse clinical manifestations. Genetic predisposition contributes significantly to its pathogenesis, and higher genetic load is linked to more severe disease[1]. This study aims to elucidate the role of genetic variation in shaping the clinical heterogeneity observed in SLE.

Methods: Scandinavian SLE patients meeting the 1997 ACR criteria were genotyped using Illumina's Global Screening Array, with clinical data extracted from medical records. Participants were randomly assigned to a discovery (n=884) and a test (n=524) cohort. A weighted SLE polygenic risk score (SLE-PRS) was calculated using 138 established non-HLA SLE risk single nucleotide variants (SNVs) (GWAS-significant in European populations). Subphenotype-specific PRSs were constructed in the discovery cohort, by analysis of 4,088 SNVs previously associated with immune or inflammatory diseases. Validation in the test cohort was conducted using logistic regression comparing the top quartile to the remainder, adjusting for sex and age, with model performance evaluated via ROC curve analysis. Disease and pathway enrichment analyses were conducted using FUMA[2] and Metascape[3].

Results: The SLE-PRS was associated with nephritis (OR=1.4, $p=1.1\times10^{-5}$, AUC=0.60) and photosensitivity (OR=1.1, $p=3.6\times10^{-3}$, AUC=0.57), but not with other ACR-97 manifestations. Excluding SNVs not associated with specific SLE subphenotypes enhanced the predictive accuracy of the SLE-PRS, with improved performance for nephritis (OR=1.6, $p=4.4\times10^{-6}$, AUC=0.61) and serositis (OR=1.3, p=0.02, AUC=0.56).

We next developed subphenotype-specific PRSs, each comprising an average of 34 SNVs. Of the total 307 SNVs, 26 were shared across multiple PRSs, with the largest overlap observed in the immunological disorder-PRS (9 shared SNVs). The nephritis-PRS contained the largest fraction of known SLE loci (23%). Several PRSs demonstrated predictive ability, including the malar rash-PRS (OR=1.3, $p=7.1\times10^{-5}$, AUC 0.66), nephritis-PRS (OR=1.4, $p=4.6\times10^{-12}$, AUC 0.70), and neurological disorder-PRS (OR=1.1, p=0.02, AUC 0.60).

Enrichment analysis of SNV annotated genes showed significant association between multiple sclerosis and all PRSs, with the strongest association for neurological disease ($p=1.17\times10^{-11}$). Functional enrichment analysis showed strong association between photosensitivity and the Nuclear factor of activated T-cells (NFAT) pathway ($p=7.8\times10^{-12}$) and hematological manifestations with interleukine-27 signaling ($p=2.5\times10^{-6}$).

Conclusion: The results demonstrate that subphenotype-specific PRSs are selectively associated with distinct clinical manifestations of SLE, and that inclusion of non-SLE risk SNVs can enhance predictive power. The limited overlap of contributing SNVs across PRSs underscores the genetic heterogeneity of SLE. Functional enrichment analyses further reveal distinct biological pathways underlying different disease features, pointing to potential targets for personalized therapeutic strategies.

References:

1. Reid S. et al. Ann Rheum Dis. (2019).
2. Watanabe K. et al. Nat. Commun. (2017).
3. Zhou Y. et al. Nat. Commun. (2019).

Disclosure: N. Oparina: None; **S. Reid**: None; **A. Sayadi**: None; **M. Eloranta**: None; **M. Frodlund**: None; **K. Lerang**: None; **A. Jönsen**: None; **Ø. Molberg**: None; **S. Rantapää-Dahlqvist**: None; **A. Rudin**: None; **C. Sjöwall**: Bristol-Myers Squibb(BMS), 3; **A. Bengtsson**: None; **L. Rönnblom**: AstraZeneca, 6, Biogen, 2; **D. Leonard**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0594

Patients with SLE Have an Increased Bisphenol A Methylation Score Linked to SLE Risk Genes and Immune Response Pathways

Holme Vestin[1], Nina Oparina[1], Maija-Leena Eloranta[1], Martina Frodlund[2], Iva Gunnarsson[3], Chrisopher Sjöwall[2], Elisabet Svenungsson[4], Lars Rönnblom[1], Juliana Imgenberg-Kreuz[1] and **Dag Leonard**[1], [1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [2]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden, [3]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, [4]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The pathogenesis of SLE involves genetic, environmental and epigenetic factors (1). Increased levels of Bisphenol A (BPA) have been observed in the urine of patients with SLE (2). Since altered immune responses and DNA methylation changes have been observed following BPA treatment in vitro (3, 4), we aimed to investigate if a BPA methylation score associate with SLE and whether it can be linked to SLE risk genes and gene expression changes in immune signalling pathways.

Methods: Potential BPA sensitivity of 198 genes for SLE genetic loci (GWAS catalogue, $p \leq 5x10^{-8}$, reported in ≥2 studies) was tested using gene-chemical interactions data from the Comparative Toxicogenomics Database (CTD).

Swedish patients with SLE fulfilling ≥ 4 ACR-82 criteria (n=548) and healthy controls (n=587) from a discovery and replication cohort were included. DNA methylation levels were investigated by the Illumina HM450k array. CpG sites reported as differentially methylated in blood in ≥2 of 7 BPA exposure studies and verified in DepMap (n=19 loci) were selected for calculation of a BPA_{All} score based on all 19 CpG sites and a BPA_{SLE} score based on three of the sites collocated with GWAS SLE risk loci. Interferon (IFN) regulation status was determined using the database Interferome. Clinical data were collected from patient charts.

BPA treatment effects were checked using GEO2R-recalculated publicly available gene expression data from four BPA-treated cell lines; Ishikawa, HepG2, Y79 and MCF7. Functional enrichment was estimated using PANTHER pathways.

Results: For 152 (77%) of the 198 SLE risk genes, BPA was among the top ten gene-interacting chemicals in CTD. BPA was the top interacting compound for 50 (25%) of the genes.

Patients with SLE had significantly higher BPA_{SLE} score compared with controls in the discovery (OR 1.34, $p=4.6x10^{-13}$), replication (OR 1.28, $p=1.1x10^{-5}$), and meta-analysis (OR 1.32, $p=3.3x10^{-17}$). Higher BPA_{All} score associated with SLE in the discovery (OR 1.05, $p=2.3x10^{-3}$) but not in the replication cohort with a significant difference in the meta-analysis (OR 1.05, $p=7.0x10^{-4}$). In the combined cohort, both scores associated with prednisolone treatment ($p< 0.001$) and the BPA_{SLE} score associated with serositis (p=0.019) and anti-RNP antibodies (p=0.027).

BPA-induced gene expression changes common for ≥2 of four cell lines showed enrichment of B cell activation, MAP kinase cascade and IFN-γ (type II IFN) signaling pathways. Out of the 29 genes annotated to the BPA-sensitive sites, 20 (69%) were reported as type II IFN-regulated in Interferome and 10 (34%) were reported as differentially expressed in at least one of the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

four cell lines, of which *MAP3K9* exhibited the most significant change (logFC 1.17, p=2.1x10^{-17}). One of the genes annotated to a an SLE-collocated BPA-sensitive CpG site, *MICB*, was differentially expressed.

Conclusion: This is the first study to suggest an association between BPA exposure and epigenetic changes in SLE, possibly altering expression of genes involved in immune response pathways such as IFN-γ and MAPK signalling.

References

1. Tsokos GC. Nat. Immunol. 2024
2. Wang Y, et al. Ecotoxicol. Environ. Saf. 2024
3. Panchanathan R, et al. Mol Cell Endocrinol. 2015
4. Besaratinia A. Int J Mol Sci. 2023

Disclosure: H. Vestin: None; **N. Oparina**: None; **M. Eloranta**: None; **M. Frodlund**: None; **I. Gunnarsson**: None; **C. Sjöwall**: Bristol-Myers Squibb(BMS), 3; **E. Svenungsson**: AstraZeneca, 11, Pfizer, 11; **L. Rönnblom**: AstraZeneca, 6, Biogen, 2; **J. Imgenberg-Kreuz**: None; **D. Leonard**: None.

Abstract Number: 0595

Sustained Remission In SLE Is Infrequent On Standard Of Care: A Decade Of Insights From The Asia Pacific Lupus Collaboration

Rangi Kandane-Rathnayake[1], Yi-Hsing Chen[2], Alberta Hoi[3], Vera Golder[4], Worawit Louthrenoo[5], Jiacai Cho[6], Aisha Lateef[7], Laniyati Hamijoyo[8], Shue Fen Luo[9], Yeong-Jian Jan Wu[10], Chiu Wai Shirley Chan[11], Leonid Zamora[12], Yasuhiro Katsumata[13], Sargunan Sockalingam[14], Zhanguo Li[15], Haihong Yao[15], BMDB Basnayake[16], Yih Jia Poh[17], Yanjie Hao[18], Zhuoli Zhang[19], Madelynn Chan[20], Jun Kikuchi[21], Yuko Kaneko[22], Tsutomu Takeuchi[23], Shereen Oon[24], Kristine Ng[25], Sang-Cheol Bae[26], Cherica Tee[27], Michael Tee[27], Nicola Tugnet[28], Sean O'Neill[29], Geraldine Hassett[30], Fiona Goldblatt[31], Naoaki Ohkubo[32], Yusuke Miyazaki[32], Mark Sapsford[33], Yoshiya Tanaka[34], Sandra Navarra[35], Chak Sing Lau[36], Mandana Nikpour[37] and **Eric Morand**[38], [1]Center for Inflammatory Diseases, Monash University, Clayton, Victoria, Australia, [2]Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Taichung, Taiwan, Taichung, Taiwan (Republic of China), [3]Centre for Inflammatory Diseases, Monash University and Department of Rheumatology, Monash Health, Clayton, Victoria, Australia, [4]Monash University, Clayton, Australia, [5]Chiang Mai University Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai, Thailand, Chiang Mai, Thailand, [6]National University Hospital, Rheumatology Division, Department of Medicine, Singapore, Singapore, Singapore, Singapore, [7]Woodlands Health, Singapore, Singapore, [8]Padjadjaran University/Hasan Sadikin General Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Bandung, Indonesia, Badung, Indonesia, [9]Chang Gung Memorial Hospital, Chang Gung University, Department of Rheumatology, Allergy and Immunology, Taipei, Taiwan, Taoyuan, Taiwan (Republic of China), [10]Chang Gung Memorial Hospital, Chang Gung University, Taoyuan City, Taiwan (Republic of China), [11]Division of Rheumatology and Clinial Immunology, Department of Medicine, the University of Hong Kong, Hong Kong, Hong Kong, China, [12]University of Santo Tomas Hospital, Manila, Philippines, [13]Tokyo Women's Medical University, Tokyo, Japan, [14]University of Malaya Medical Center, Kuala Lumpur, Malaysia, [15]Peking University People's Hospital, Beijing, China (People's Republic), [16]National Hospital Kandy, Kandy, Sri Lanka, [17]Singapore General Hospital, Singapore, Singapore, [18]St Vincent's Hospital Melbourne, Fitzroy, Australia, [19]Peking University First Hospital, Beijing, Beijing, China (People's Republic), [20]Tan Tock Seng Hospital, Singapore, Singapore, [21]Keio University, Tokyo, Japan, [22]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [23]Saitama Medical University and Keio University, Tokyo, Japan, [24]St Vincent's Hospital Melbourne, Melbourne, Victoria, Australia, [25]Health New Zealand Waitemata, Te Whatu Ora, Auckland, New Zealand, [26]Hanyang University Medical Center, Seoul, South Korea, [27]University of the Philippines, Manila, Philippines, [28]Health New Zealand Auckland, Te Whatu Ora (Auckland District Health Board), Auckland, New Zealand, [29]The University of Sydney, Sydney, Australia, [30]Liverpool Hospital, NSW, Liverpool, Australia, [31]Flinders Medical Centre, Bedford park, Australia, [32]University of Occupational and Environmental Health, Kitakyushu, Japan, [33]Health New Zealand Counties Manukau, Te Whatu Ora (Middlemore Hospital), Auckland, New Zealand, [34]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [35]University of Santo Tomas, Manila, Philippines, [36]The University of Hong Kong, Hong Kong, Hong Kong, [37]University of Sydney School of Public Health and Department

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of Rheumatology, Royal Prince Alfred Hospital, Sydney, Victoria, Australia, [38]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Treat-to-target (T2T) states in SLE, such as the Lupus Low Disease Activity State (LLDAS) and remission (REM) as defined by the Definitions of Remission in SLE (DORIS), are now reflected in treatment guidelines. However, while sustained attainment of these states is reported in response to CD19 CAR-T treatment, limited long-term data exist quantifying the frequency of sustained attainment of these states on standard of care.

Methods: We examined the cumulative and sustained (continuous) attainment of LLDAS, REM, and steroid-free remission (REM-0) utilising the Asia Pacific Lupus Collaboration (APLC) patient cohort. Data were collected from 25 sites across 13 countries between 1st January 2013 and 31st December 2023 using standardised templates. LLDAS was defined as Golder *et al*., 2019 (1) (SLEDAI≤4, no new activity, PGA ≤1, prednisolone (PNL) ≤7.5 mg/d, antimalarials (AM) and immunosuppressants (IS) allowed). REM was defined as Vollenhoven et al, 2021 (2) (clinical SLEDAI=0, PGA < 0.5, PNL≤5 mg/d, AM/ IS allowed), while REM-0 was defined as clinical SLEDAI=0, PGA < 0.5, PNL=0 mg/d, AM/ IS allowed. We examined these outcomes in all patients, and in patients who at enrolment were not at target (i.e. not in LLDAS).

Table 1 — Patient characteristics

	All patients n=5,053	Non-LLDAS at enrolment n=2,517
	Median [IQR] or n (%)	
Study duration (years)	3.1 [2.0, 7.0]	3.2 [2.0, 7.1]
Age at APLC enrolment (years)	40 [30, 50]	37 [29, 48]
SLE duration at enrolment (years)	8.0 [3.0, 15]	7.0 [2.0, 14]
Females	4604 (91.4%)	2290 (91.3%)
Glucocorticoids (GC) at least once (ever)	4352 (86.1%)	2371 (94.2%)
TAM-GC (mg/day)	5.0 [2.0, 8.4]	7.5 [4.7, 10.6]
Cumulative GC (g)	5.4 [1.4, 12.3]	8.5 [3.8, 16.3]
Anti-malarials (AM) -ever	4281 (84.7%)	2098 (83.4%)
Immunosuppressants (IS) -ever	3656 (72.4%)	2069 (82.2%)
TAM-SLEDAI-2K (AMS)	2.7 [1.1, 4.4]	3.9 [2.2, 5.5]
TAM-PGA	0.3 [0.1, 0.6]	0.5 [0.3, 0.9]
Mild/moderate/severe flare ever	3023 (59.8%)	1773 (70.4%)
Annual flare rate	0.3 [0.0, 0.7]	0.5 [0.0, 1.0]
Organ damage present (SDI>0) at enrolment	1846 (42.6%)	968 (43.5%)
Damage accrual (ΔSDI>0)	1111 (25.6%)	643 (28.9%)
Deceased patients	139 (2.8%)	87 (3.5%)
LLDAS-ever	4131 (82.2%)	1655 (65.8%)
%T in LLDAS	48.2 [13.0, 74.1]	22.2 [0, 50]
LLDAS-50	2442 (48.3%)	639 (25.4%)
12m sustained LLDAS	1916 (37.9%)	600 (23.8%)
REM-ever	3507 (69.9%)	1281 (51.1%)
%T in REM	29.2 [0.0, 66.8]	2.8 [0.0, 35.8]
REM-50	1866 (36.9%)	411 (16.3%)
12m sustained REM	1704 (33.7%)	480 (19.1%)
REM-0-ever	1554 (31.0%)	451 (18.0%)
%T in REM-0	0 [0, 12.2]	0 [0, 0]
REM-0-50	684 (13.5%)	106 (4.2%)
12m sustained REM-0	682 (13.5%)	140 (5.6%)

IQR = interquartile range; TAM = time adjusted mean; %T = cumulative percent-time, LLDAS/REM-50 = ≥50% in LLDAS/REM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

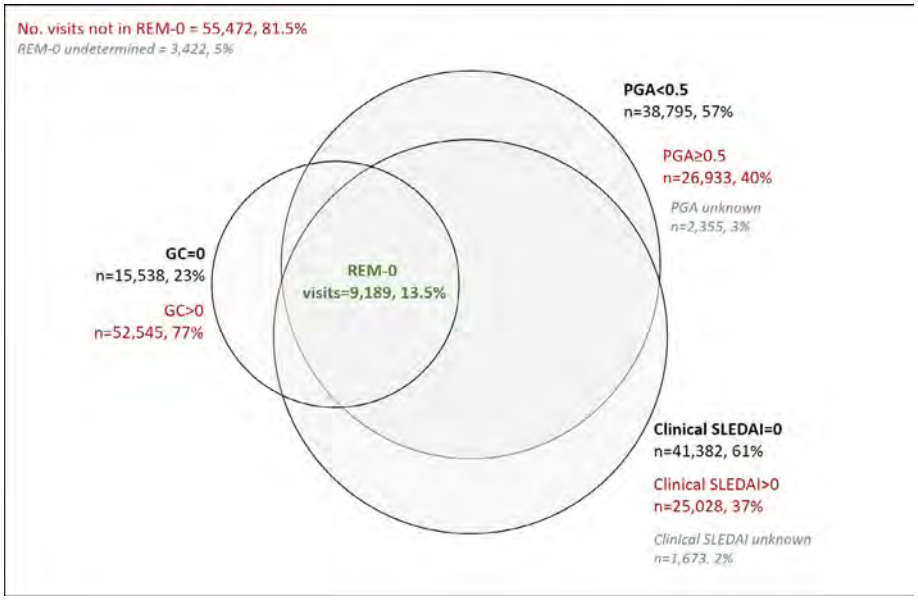


Figure 1: Patient visits fulfilling REM-0

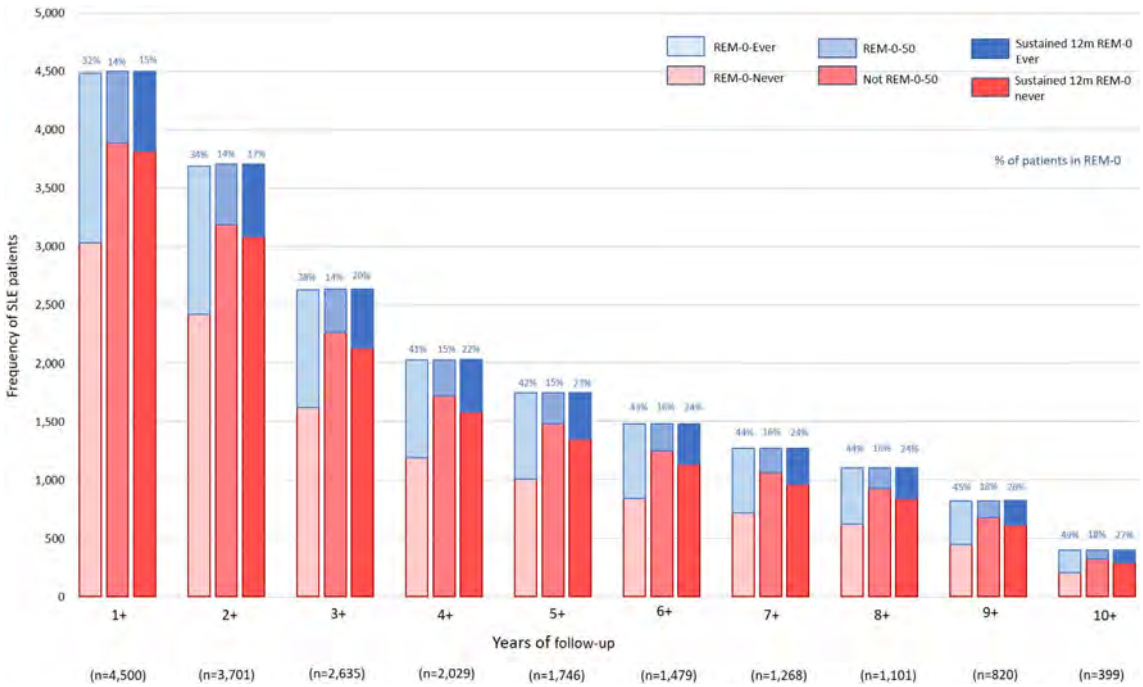


Figure 2 – Attainment of steroid-free remission (REM-0) overtime

Results: A total of 68,083 visits from 5,053 patients with ≥2 visits were evaluated. About 82% of patients attained LLDAS; ~70% attained REM, and 31% attained REM-0 at least once during the observation period. Accordingly, LLDAS was achieved in 48% of visits (n= 31,706); REM in 37% of visits (n= 31,706), and REM-0 in 13.5% of visits (9,189) (Figure 1). Cumulative and sustained attainment of these T2T states were low, especially sustained REM-0 (~14%) (Table 1). Although the proportion of patients attaining sustained REM-0 gradually increased over time, the majority of patients never achieved this state (Figure 2). Overall, patients who attained sustained REM0 were older, had a longer study duration, and had used more AM (88% vs. 84% of sustained REM0-never patients, p=0.015).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We further examined the attainment of these T2T states in 2,517 patients who were not at target (i.e. not in LLDAS) at enrolment (51% of the cohort). These patients were younger and had shorter SLE disease duration than those in LLDAS at enrolment. Fewer of these patients attained T2T states; only 18% achieved REM-0 at least once, and < 6% achieved 12 months sustained REM-0 (Table 1).

Conclusion: Sustained attainment of steroid-free remission was infrequent in SLE patients receiving standard of care.

References

1. Golder V, Kandane-Rathnayake R, Huq M, Nim H, Louthrenoo W, Luo SF, et al. Lupus low disease activity state as a treatment endpoint for systemic lupus erythematosus: a prospective validation study. The Lancet Rheumatology. 2019;1(2):e95–e102.
2. van Vollenhoven RF, Bertsias G, Doria A, Isenberg D, Morand E, Petri MA, et al. 2021 DORIS definition of remission in SLE: final recommendations from an international task force. Lupus Sci Med. 2021;8(1).

Disclosure: R. Kandane-Rathnayake: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKline (GSK), 5, Novartis, 5; **Y. Chen**: Abbvie, 12, 2, 6, Agnitio Science Technology, 2, 6, Astellas, 12, 2, 6, AstraZeneca, 12, 2, 6, Biogen, 12, BMS, 12, 2, 6, Boehringer-Ingelheim, 12, Celldex, 12, CSL Behring, 2, 6, Eisai, 2, 6, Gilead, 12, 2, 6, GSK, 12, 2, 6, Guigai, 12, 2, 6, Inova Diagnostics, 2, 5, Johnson & Johnson, 12, 2, 6, Lilly, 2, 6, Medigen Vaccine Biologics, 12, MSD, 12, 2, 6, Novartis, 2, 6, Pfizer, 12, 2, 6, Roche, 12, Sanofi, 12, 2, 6, Taichung Veterans General Hospital, 12, Taiwan Department of Health, 12, Taiwan Ministry of Science and Technology, 12, Thermo Fisher, 2, 6, UCB, 12, 2, 6, United Biopharma, 2, 6; **A. Hoi**: AstraZeneca, 1, 5, 12, contract research, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, GlaxoSmithKline (GSK), 1, Johnson & Johnson, 1, Merck/MSD, 12, contract research, UCB, 5; **V. Golder**: None; **W. Louthrenoo**: None; **J. Cho**: None; **A. Lateef**: None; **L. Hamijoyo**: None; **S. Luo**: None; **Y. Wu**: None; **C. Chan**: None; **L. Zamora**: None; **Y. Katsumata**: None; **S. Sockalingam**: None; **Z. Li**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5; **H. Yao**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd, 5; **B. Basnayake**: None; **Y. Jia Poh**: None; **Y. Hao**: None; **Z. Zhang**: AbbVie/Abbott, 1, 6, Amgen, 6, BMS, 1, Eisai, 5, 6, Eli Lilly, 6, GSK, 6, Novartis, 6, Rongchang Pharmaceutials, 6, Xiansheng Pharmaceutials, 6; **M. Chan**: None; **J. Kikuchi**: None; **Y. Kaneko**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Chugai, 5, 6; **T. Takeuchi**: AbbVie, 2, 6, Astellas Pharma, 6, AstraZeneca, 6, Chugai Pharmaceutical, 6, Eisai, 6, Eli Lilly, 2, 6, Gilead Sciences, 2, 6, Janssen, 6, Mitsubishi Tanabe Pharma, 2, 6, Pfizer, 6, Taisho Pharmaceutical, 2, 6; **S. Oon**: None; **K. Ng**: None; **S. Bae**: None; **C. Tee**: None; **M. Tee**: None; **N. Tugnet**: None; **S. O'Neill**: None; **G. Hassett**: None; **F. Goldblatt**: None; **N. Ohkubo**: None; **Y. Miyazaki**: None; **M. Sapsford**: None; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **S. Navarra**: Astellas, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Biogen, 2, 12, Independent Data Monitoring Committee, Viatris (Idorsia), 2, 6; **C. Lau**: None; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer Ingelheim, 2, 5, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0596

Effect of Gender and Follow-up Time in Damage Accrual: Data from a Latin America Lupus Cohort

Diana Fernandez[1], Rosana Quintana[2], Karen Roberts[3], Romina Nieto[2], Marina Scolnik[4], Carmen Funes Soaje[5], CINTIA OTADUY[6], Veronica Saurit[7], Valeria Arturi[8], GUILLERMO ARIEL BERBOTTO[9], Maria Constanza Bertolaccini[10], Mario Eduardo Kerzberg[11], Maria de los Angeles Gargiulo[12], Cecilia Pisoni[13], Ana Carolina Ralle[14], Joaquín Martinez Serventi[15], Ana Silva[16], ODIRLEI MONTICIELO[17], Henrique Mariz[18], Laíssa Cristina Alves Alvino[19], Eduardo Borba[20], Emily Figueiredo Neves Yuki[21], Edgard Torres dos Reis-Neto[22], Iris Guerra Herrera[23], Milena Mimica[24], Gustavo Aroca-Martínez[25], Antonio Iglesias-Gamarra[26], Carlos Alberto Cañas[27], Gerardo Quintana-Lopez[28], Carlos Toro-Gutierrez[29], Mario Moreno Alvarez[30], Olga-Lidia Vera-Lastra[31], Margarita Portela Hernández[32], Hilda Fragoso-Loyo[33], Luis H Silveira[34], Yelitza Gonzalez Bello[35], Carlos Abud-Mendoza[36], Jorge Antonio Esquivel Valerio[37], Marcelo Barrios[38], Lourdes Carolina Vázquez[39], Magaly Alva Linares[40], Manuel Ugarte-Gil[41], Armando Calvo[42], Roberto Muñoz-Louis[43], Ana Carina Pizzarossa[44], Gonzalo Silveira[45], Federico Zazzetti[46], Ashley Orillion[47], Urbano Sbarigia[48], Guillermo Pons-Estel[2], Graciela Alarcón[49] and Bernardo Pons-Estel[50], [1]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina, Rosario, Argentina, [2]Centro Regional de Enfermedades Autoinmunes y Reumáticas, GO-CREAR, Rosario, Argentina, Rosario, Argentina, [3]Consultora externa de GLADEL, Rosario, Argentina, Rosario, Argentina, [4]Hospital Italiano de Buenos Aires, Argentina, Buenos Aires, Argentina, [5]Hospital Italiano de Córdoba, Córdoba, Argentina, Cordoba, Argentina, [6]Servicio de Reumatología Hospital Córdoba y Sanatorio Allende, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Córdoba, Argentina, Córdoba, Argentina, [7]Hospital Privado Universitario de Cordoba, Córdoba, Argentina, CCórdoba, Argentina, [8]Hospital San Martin de La Plata, La Plata, Argentina, La Plata, Argentina, [9]Sanatorio Británico, Rosario, Argentina, ROSARIO, Argentina, [10]Hospital Ángel C. Padilla, Tucumán, Argentina, Tucumán, Argentina, [11]Hospital J.M Ramos Mejía, Buenos Aires, Argentina, CABA, Argentina, [12]Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires; Buenos Aires, Argentina, Buenos Aires, Argentina, [13]CEMIC Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno", Buenos Aires, Argentina, Ciudad Autonoma Buenos Aires, Argentina, [14]Hospital Señor del Milagro Salta, Salta, Argentina, Salta, Argentina, [15]Hospital General de Agudos Dr. Juan A. Fernández, Buenos Aires, Argentina, Buenos Aires, Argentina, [16]Hospital das Clinicas da Universidade Federal de Goias, Goiania, Brazil, Goiania, Brazil, [17]Hospital de Clínicas de Porto Alegre, Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil, PORTO ALEGRE, Rio Grande do Sul, Brazil, [18]Universidad Federal de Pernambuco, Pernambuco, Brazil, Pernambuco, Brazil, [19]Hospital Universitário Pedro Ernesto - Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, Rio de Janeiro, Brazil, [20]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [21]Faculdade de Medicina da USP, São Paulo, São Paulo, Brazil, [22]Universidad Federal São Paulo, São Paulo, Brazil, São Paulo, Brazil, [23]Hospital del Salvador Santiago de Chile, Santiago, Chile, Santiago, Chile, [24]Facultad de Medicina y Ciencia, Universidad San Sebastián, Santiago, Chile, Santiago, Chile, [25]Clínica de la Costa y Universidad Simón Bolívar, Barranquilla, Colombia, barranquilla, Colombia, [26]Universidad Nacional de Colombia, Barranquilla, Colombia, [27]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia, Cali, Colombia, [28]Facultad de Medicina, Universidad Nacional de Colombia; Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogotá, Colombia, [29]Pontificia Universidad Javeriana de Cali, Cali, Colombia, Cali, Colombia, [30]Universidad de Especialidades Espíritu Santo, Guayaquil, Ecuador, Guayaquil, Ecuador, [31]División de Investigación en Salud, Hospital de Especialidades Dr. Antonio Fraga Mouret, CMN La Raza, IMSS, CDMX, Mexico, Mexico City, Mexico, [32]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico, Mexico City, Mexico, [33]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico, [34]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [35]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, Guadalajara, Mexico, [36]Facultad de Medicina de la Universidad Autónoma de San Luis Potosí y Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí, Mexico, San Luis Potosi, Mexico, [37]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [38]Hospital de Clínicas II, Uruguay, Uruguay, Uruguay, [39]Facultad de Ciencias Médicas. Universidad Nacional de Asunción-Paraguay, Paraguay, Asunción, Paraguay, [40]HOSPITAL EDGARDO REBAGLIATI MARTINS, San Borja, Peru, [41]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [42]Hospital Nacional Cayetano Heredia Universidad Peruana Cayetano Heredia, Lima, Peru, Jesús María, Peru, [43]Hospital Docente Padre Billini, Santo Domingo, Distrito Nacional, Dominican Republic, [44]Clínica Médica C, Hospital de Clínicas, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [45]Facultad de Medicina - Universidad de la República, Montevideo, Uruguay, Montevideo, Uruguay, [46]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [47]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [48]Johnson & Johnson, Beerse, Belgium, [49]University of Alabama at Birmingham, Oakland, CA, [50]El Grupo Oroño - Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Previous studies have shown that male gender is an independent predictor of organ damage in patients with systemic lupus erythematosus (SLE), particularly in the early stages of their disease.[1,2] In the previous GLADEL cohort, male patients had a higher SLICC/ACR Damage Index (SDI) than their female counterparts, although this difference was not statistically significant.[3] This study assessed organ damage, as measured by the SDI, as a function of gender in the GLADEL 2.0 cohort.

Methods: A total of 43 centers from 10 Latin American countries enrolled patients 18 years of age or older who met the 1982/1997 ACR and/or 2012 SLICC classification criteria. Descriptive analyses were conducted. An interaction analysis between gender and time was performed using a mixed-effects model in R. SDI was the dependent variable, while gender (between-subjects) and time (within-subjects) were the independent variables. A random intercept per participant was included to account for within-subject variability.

Logistic regression modeling was used to examine the factors associated with changes in the SDI from baseline to the end of follow-up. A significance level of 5% was applied to all analyses and R version 4.4.0 software was used.

Results: Of the 1081 patients enrolled in the GLADEL 2.0 cohort, 385 patients matched by gender were considered. Of these, 190 completed at least four annual visits and were included in these analyses. Seventy percent of patients were women and 30% were men (Table 1). No statistically significant differences in organ damage, as measured by the SDI, were

Table 1. Sociodemographic and clinical characteristics of patients with SLE by gender

	Male (N=113)	Female (N=272)	*p*-value	Total (N=385)
Age at diagnosis, Median [Q1, Q3]	27.6 [22.6, 37.6]	26.2 [20.0, 35.1]	0.129	26.5 [20.9, 35.5]
Ethnicity, n (%)			0.204	
Afro-Latin Americans	6 (5.4)	26 (9.6)		32 (8.4)
Indigenous	2 (1.8)	1 (0.4)		3 (0.8)
Mestizos	82 (73.2)	178 (65.7)		260 (67.9)
White	22 (19.6)	65 (24.0)		87 (22.7)
Others	0 (0)	1 (0.4)		1 (0.3)
Socioeconomic status, n (%)			0.287	
High	3 (2.7)	6 (2.3)		9 (2.4)
Low	10 (9.0)	28 (10.7)		38 (10.2)
Middle	49 (44.1)	94 (35.9)		143 (38.3)
Upper middle	21 (18.9)	40 (15.3)		61 (16.4)
Lower middle	28 (25.2)	94 (35.9)		122 (32.7)
Missing	2 (1.8)	10 (3.7)		12 (3.1)
Medical coverage, n (%)			0.154	
Partial coverage	20 (18.0)	33 (12.3)		53 (14.0)
Without coverage	29 (26.1)	93 (34.7)		122 (32.2)
Total coverage	62 (55.9)	142 (53.0)		204 (53.8)
Missing	2 (1.8)	4 (1.5)		6 (1.6)
SLICC_BASAL, Median [Q1, Q3]	0 [0, 1.00]	0 [0, 1.00]	0.56	0 [0, 1.00]
Disease duration, Median [Q1, Q3] in years	2.35 [0.192, 8.92]	2.91 [0.562, 9.82]	0.286	2.70 [0.452, 9.50]
Use of glucocorticoids at baseline, n (%)	64 (97.0)	158 (95.8)	1.000	222 (96.1)
Use of antimalarial at baseline visit, n (%)	64 (56.6)	162 (59.5)	1.000	226 (58.7)
Type of lupus, n (%)			0.838	
1= Patient with SLE, no history of lupus nephritis.	31 (27.4)	82 (30.1)		113 (29.4)
2= Patient with SLE, with prevalent inactive lupus nephritis.	21 (18.6)	55 (20.2)		76 (19.7)
3= Patient with SLE, with active prevalent lupus nephritis.	28 (24.8)	67 (24.6)		95 (24.7)
4= Patient with SLE, with incident (active) lupus nephritis.	33 (29.2)	68 (25.0)		101 (26.2)

found between male and female patients (p=0.563). This trend remained consistent throughout the follow-up period, with no significant interactions observed (p=0.90). Damage accumulation over time increased significantly in both sexes (Figure 1A). The affected SDI domain frequency was examined both at baseline and during follow-up (Figure 1B). In general, males had a higher occurrence of ocular and cutaneous, and a moderate increase in malignant involvement compared to females, whereas females had a higher frequency of gastrointestinal, gonadal failure, pulmonary, peripheral vascular and musculoskeletal involvement. After adjusting for sociodemographic and clinical/immunologic characteristics, multivariate analysis revealed that disease duration (odds ratio [OR]: 1.05; 95% CI: 1.0-1.1) and disease activity, as measured by the SLEDAI-2K (OR: 1.05; 95% CI: 1.0-1.1), were associated with a higher likelihood of an increase in SDI.

Conclusion: Although male gender was not associated with an increased risk of damage accumulation, the proportion of patients with an increased SDI was higher in males than in females. Organ damage during follow-up increased significantly in both sexes. As patients in this cohort continue to be closely monitored, the impact of gender on damage accumulation may become more evident.

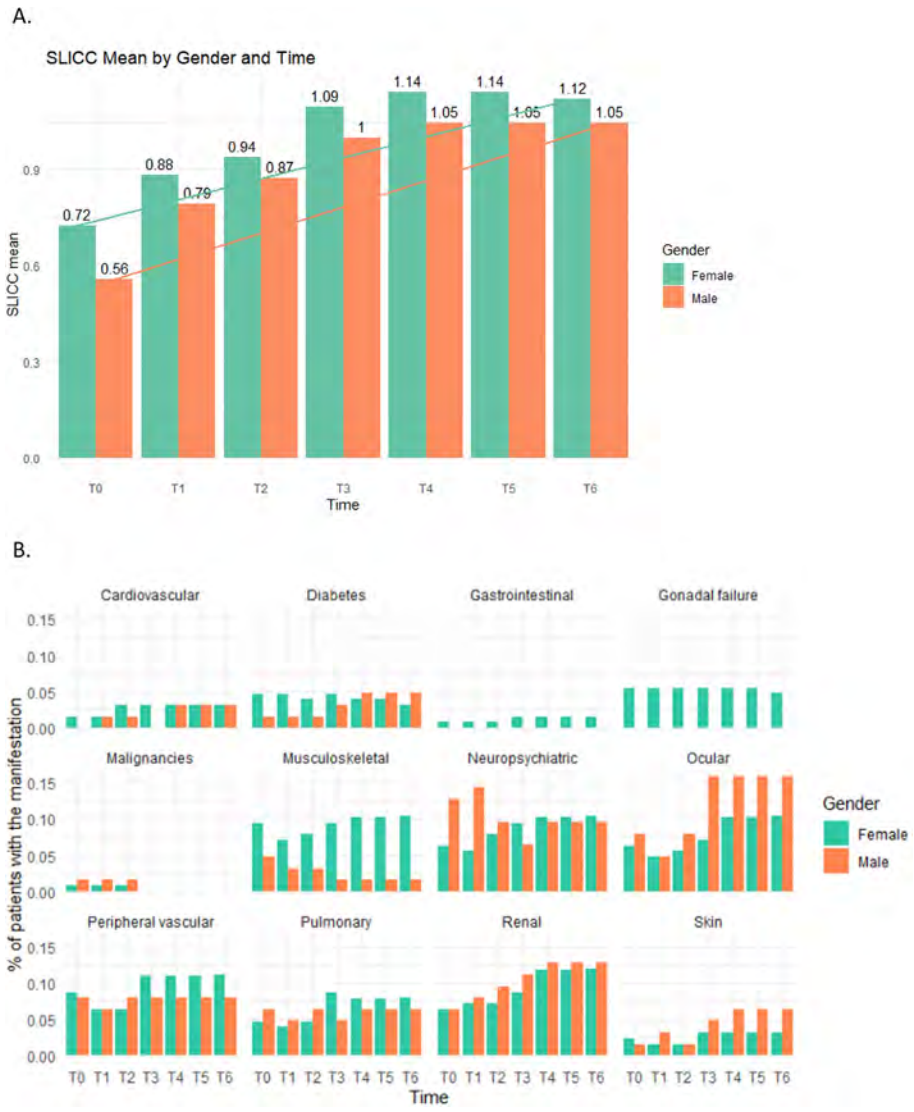


Figure 1. (A) Mean SLICC/ACR score and (B) frequency of manifestations by SDI area by gender and follow-up time

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References:

1. Bruce IN, et al. *Ann Rheum Dis*. 2015;74:1706-13.
2. Andrade RM, et al. *Arthritis Rheum*. 2007;56:622-30.
3. García MA, et al. *Lupus*. 2005;14;938-046.

Disclosure: D. Fernandez: None; **R. Quintana**: None; **K. Roberts**: None; **R. Nieto**: None; **M. Scolnik**: AstraZeneca, 2, 5, 6, GSK, 1, 5, 6, Janssen, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6; **C. Funes Soaje**: None; **C. OTADUY**: None; **V. Saurit**: None; **V. Arturi**: None; **G. BERBOTTO**: None; **M. Bertolaccini**: None; **M. Kerzberg**: None; **M. Gargiulo**: None; **C. Pisoni**: None; **A. Ralle**: None; **J. Serventi**: None; **A. Silva**: AstraZeneca, 6, GSK, 6; **O. MONTICIELO**: None; **H. Mariz**: None; **L. Alves Alvino**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. Figueiredo Neves Yuki**: GlaxoSmithKlein(GSK), 5; **E. Torres dos Reis-Neto**: None; **I. Guerra Herrera**: None; **M. Mimica**: None; **G. Aroca-Martínez**: None; **A. Iglesias-Gamarra**: None; **C. Cañas**: None; **G. Quintana-Lopez**: None; **C. Toro-Gutierrez**: None; **M. Moreno Alvarez**: None; **O. Vera-Lastra**: None; **M. Portela Hernández**: None; **H. Fragoso-Loyo**: None; **L. Silveira**: None; **Y. Gonzalez Bello**: None; **C. Abud-Mendoza**: None; **J. Esquivel Valerio**: None; **M. Barrios**: None; **L. Vázquez**: None; **M. Alva Linares**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **A. Calvo**: None; **R. Muñoz-Louis**: None; **A. Pizzarossa**: None; **G. Silveira**: None; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **U. Sbarigia**: Johnson and Johnson, 11; **G. Pons-Estel**: AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen, 1, 6; **G. Alarcón**: None; **B. Pons-Estel**: AstraZeneca, 5, 6, GlaxoSmithKlein (GSK), 5, 6, Janssen, 5, 6, Novartis, 6, Roche, 5.

Abstract Number: 0597

Low 25-hydroxyvitamin D Levels are Associated with Higher Mortality and More Cardiovascular Events in Systemic Lupus Erythematosus

Theerada Assawasaksakul[1], Andrea Fava[2], Daniel Goldman[3], Laurence Magder[4] and **Michelle Petri**[3], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Timonium, MD, [4]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: No studies have directly examined the link between 25-hydroxyvitamin D [25(OH)D] and cardiovascular outcomes in SLE. This study aimed to assess this association, hypothesizing that low 25(OH)D levels correlate with increased mortality and cardiovascular event risk in SLE.

Methods: Our longitudinal cohort measured 25(OH)D levels at quarterly clinic visits from 2009 onwards. Patients were categorized based on their first measured, mean, and most recent 25(OH)D levels (the last two measures reflecting supplementation). The "most recent 25(OH)D" was defined as the 25(OH)D level measured at the most recent past visit. The first prospective analysis examined monthly follow-up data, categorizing by 25(OH)D levels and assessing cardiovascular events (CVE) or mortality using pooled logistic regression. For the analysis using mean 25(OH)D levels, the mean 25(OH) vitamin D in previous visits was the mean 25(OH)D level from all visits prior to that month. The second lifetime

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Rates of Cardiovascular events (Myocardial Infarction, Stroke, Angina, or Bypass), by Demographic variables and 25(OH)D levels

Variable	Value	Person-Years of follow-up	Number of Events	Rate (per 1000)
All		11302	67	5.9
First 25(OH)D in Cohort	<20	2785	24	8.6
	20-29	2665	18	6.8
	30-39	3011	8	2.7
	40-49	1778	15	8.4
	50+	1064	2	1.9
Mean 25(OH)D in last year	<20	588	5	8.5
	20-29	1526	10	6.6
	30-39	2800	19	6.8
	40-49	2579	14	5.4
	50+	2941	16	5.4
Most recent past 25(OH)D	<20	626	5	8.0
	20-29	1562	8	5.1
	30-39	2577	18	7.0
	40-49	2348	12	5.1
	50+	3243	20	6.2

[1]Adjusted for age, sex, race, and body mass index

analysis evaluated the association between initial 25(OH)D levels and a patient's lifetime cardiovascular event history, adjusting for confounders with a Cox Proportional Hazards model. This approach included events that might occur before cohort entry.

Results: The study analyzed a cohort of 1,792 SLE patients, primarily female (92%), White (48%), and African American (40%), with a mean age of 42 years. In the prospective analysis, cardiovascular events (CVE; defined as stroke, myocardial infarction (MI), and angina/bypass) were assessed over 11,302 person-years of follow-up, with 67 events recorded. Patients with 25(OH)D levels below 20 ng/mL had the highest mortality and CVE rates (Table 1). Only initial 25(OH)D levels were significantly associated with mortality and cardiovascular risk, while mean and recent levels were not (Table 2). Compared to patients with levels of 30-39 ng/mL, those with levels below 20 ng/mL had: higher mortality risk (HR: 2.05, 95% CI: 1.19–

Table 2: Prospective Analysis of 25(OH)D Levels and Mortality, Combined Cardiovascular Events, Stroke Alone and Myocardial Infarction Alone.

25(OH)D (ng/mL)	Initial 25(OH)D				Mean 25(OH)D in last year				Most recent past 25(OH)D			
		95% CI				95% CI				95% CI		
	Rate Ratio[1]	Lower	Upper	P-value[1]	Rate Ratio[1]	Lower	Upper	P-value[1]	Rate Ratio[1]	Lower	Upper	P-value[1]
Mortality												
<20	2.05	1.19	3.54	0.0095	2.01	0.86	4.72	0.1089	1.67	0.67	4.18	0.2735
20-29	1.01	0.53	1.94	0.9760	1.95	1.08	3.54	0.0273	2.21	1.23	3.99	0.0084
30-39	1 (ref)				1 (ref)				1 (ref)			
40-49	1.01	0.52	1.96	0.9761	0.92	0.53	1.61	0.7821	0.99	0.55	1.79	0.9810
50+	1.20	0.58	2.49	0.6232	0.57	0.32	1.02	0.0566	0.70	0.40	1.24	0.2184
Stroke, Myocardial infarction, or Angina/Bypass												
<20	2.98	1.30	6.85	0.0100	1.40	0.51	3.80	0.5126	1.24	0.46	3.41	0.6696
20-29	2.62	1.13	6.06	0.0247	1.01	0.47	2.19	0.9747	0.76	0.33	1.77	0.5292
30-39	1 (ref)				1 (ref)				1 (ref)			
40-49	3.49	1.47	8.27	0.0045	0.77	0.39	1.55	0.4713	0.72	0.35	1.51	0.3900
50+	0.82	0.17	3.89	0.8045	0.76	0.39	1.50	0.4313	0.87	0.46	1.66	0.6774
Stroke												
<20	3.53	1.13	11.0	0.0302	0.73	0.16	3.26	0.6787	0.76	0.17	3.43	0.7158
20-29	2.39	0.73	7.82	0.1478	0.68	0.24	1.89	0.4561	0.87	0.32	2.32	0.7746
30-39	1 (ref)				1 (ref)				1 (ref)			
40-49	5.24	1.68	16.3	0.0042	0.51	0.21	1.28	0.1537	0.62	0.24	1.58	0.3176
50+	None				0.64	0.28	1.48	0.2987	0.70	0.31	1.61	0.4011
Myocardial infarction												
<20	1.90	0.57	6.33	0.2979	3.59	0.94	13.7	0.0625	3.65	0.89	15.0	0.0720
20-29	1.82	0.53	6.27	0.3436	1.05	0.25	4.44	0.9424	0.78	0.14	4.27	0.7731
30-39	1 (ref)				1 (ref)				1 (ref)			
40-49	1.44	0.32	6.45	0.6370	1.63	0.52	5.18	0.4033	1.78	0.50	6.32	0.3731
50+	0.91	0.10	8.23	0.9316	1.07	0.31	3.76	0.9143	1.61	0.47	5.55	0.4520

[1] Adjusted for age, race, sex, and body mass index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Lifetime Relationship Between 25(OH)D Levels Measured at the First Cohort Visit and Risk of Stroke, Myocardial Infarction, or Angina/Bypass; Stroke Alone; and Myocardial Infarction Alone

25(OH)D (ng/mL)	Adjusted Analysis[1]			
		95% CI		
	Hazard Ratio	Lower	Upper	P-value
Stroke, Myocardial Infarction, or Angina/Bypass				
<20	1.74	1.20	2.54	0.0038
20-29	1.46	0.99	2.13	0.052
30-39	1 (ref)			
40-49	1.35	0.91	2.02	0.14
50+	1.32	0.83	2.10	0.25
Stroke				
<20	1.41	0.90	2.20	0.14
20-29	1.21	0.77	1.91	0.40
30-39	1 (ref)			
40-49	1.28	0.79	2.06	0.31
50+	1.17	0.66	2.06	0.60
Myocardial Infarction				
<20	2.42	1.12	5.24	0.025
20-29	2.10	0.96	4.58	0.062
30-39	1 (ref)			
40-49	1.69	0.73	3.92	0.22
50+	3.41	1.50	7.74	0.0033

[1] Adjusted for age, race, sex, and body mass index

3.54, p = 0.0095); higher risk of CVE (HR: 1.74, 95% CI: 1.20–2.54, p = 0.0038); increased MI risk (HR: 2.42, 95% CI: 1.12–5.24, p = 0.025); but no significant association with stroke (HR: 1.41, 95% CI: 0.90–2.20, p = 0.14).

In the second (lifetime) analysis (Table 3), the analysis included more CVE than the prospective analysis (261 stroke/MI/angina; 229 stroke or MI; 176 stroke; 76 MI). A U-shaped relationship was observed, with both low (< 20 ng/mL) and high (≥50 ng/mL) 25(OH)D levels linked to an increased risk of myocardial infarction. Using mean 25(OH)D levels in the model for mortality (assuming the log-rate of mortality declines in a linear way), the slope was significant (p=0.0002). The odds ratio was 0.72 for each 10 unit increase in mean 25(OH)D level (i.e., a 28% decline in mortality per 10 unit increase in 25(OH)D levels).

Conclusion: An initial 25(OH)D level below 20 ng/mL led to a significantly increased risk of mortality and cardiovascular events (but not stroke) in SLE. The U-shaped association with MI, found in the lifetime analysis, suggests both deficient and high 25(OH)D levels increase the risk of myocardial infarction. Analysis of mean 25(OH)D levels (which represent routine supplementation) found a 28% decline in mortality per 10 unit increase in 25(OH)D levels.

Disclosure: T. Assawasaksakul: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **D. Goldman**: None; **L. Magder**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0598

Study of Long Term HCQ Safety on Cardiac Muscle Function in Patients with SLE and other Rheumatic Diseases

Jaspreet Bhatti[1], Kyu-In Lee[2], **Nirali Sanghavi**[3], Stephen Zak[4], Julia Ash[5], James Miceli[6], Kirk Sperber[4], Stephen Pan[7] and Amy Wasserman[8], [1]Westchester Medical Center, Hopewell Junction, NY, [2]Westchester Medical Center, Fort Lee, NJ, [3]Westchester Medical Center, White Plains, NY, [4]New York Medical College, Valhalla, [5]Westchester Medical center, Dobbs Ferry, NY, [6]Westchester Medical Center, Hawthorne, NY, [7]Westchester Medical Center, Valhalla, [8]New York Medical College at Westchester Medical Center, Armonk, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: HCQ induced cardiomyopathy leading to heart failure is a rare but serious potential treatment complication. Currently there are no screening guidelines for detecting HCQ related cardiotoxicity. This study aims to identify signs of cardiotoxicity, including cardiomyopathy, in patients on HCQ. Secondary objectives include identifying non-invasive modalities for detection of HCQ induced cardiac toxicity.

Methods: We conducted a cross-sectional observational study from 2023 to 2025 at an academic medical center. We included patients aged 18–75 with a confirmed diagnosis of rheumatic disease and current HCQ therapy. We excluded patients with known history of cardiomyopathy from an alternative etiology. BNP, Troponin, serum HCQ level, ECG and echocardiogram were performed. Interventricular septal thickness at end-diastole (IVSd), an established echocardiogram criterion for LVH and a reported early finding of HCQ cardiac toxicity, was documented (1). Patients with increased IVsd (>1.2cm) and/or other cardiac abnormalities were referred to cardiology for further evaluation and possible biopsy.

Baseline Characteristics			
	<5years (n=22)	5-10 years (n=23)	>10years (n=39)
Mean Age	45.55	44.74	49.08
Female	17 (77%)	22 (87%)	37 (95%)
Race			
•Caucasian	3 (14%)	4 (17%)	6 (15%)
•Black	4 (18%)	5 (22%)	10 (26%)
•Asian	0 (0%)	2 (9%)	1 (3%)
•Hispanic	15 (68%)	12 (52%)	22 (56%)
Diagnosis			
•SLE	15 (68%)	18 (78%)	34 (87%)
•SS/MCTD/UCTD	6 (27%)	1 (4%)	0 (0%)
•RA	1 (5%)	4 (17%)	0 (0%)
Comorbidities			
•CAD	0 (0%)	0 (0%)	2 (5%)
•HTN	4 (18%)	4 (17%)	11 (28%)
•DM	1 (5%)	1 (4%)	3 (8%)
Median HCQ Level	421.50	463.60	244.20
HCQ Dose			
•200	3 (14%)	6 (26%)	15 (38%)
•300	2 (9%)	2 (9%)	2 (5%)
•400	17 (77%)	15 (65%)	22 (56%)
GFR			
•<30	0 (0%)	1 (4%)	0 (0%)
•30-60	2 (9%)	1 (4%)	9 (23%)
•>60	20 (91%)	21 (91%)	30 (77%)
QTC Prolonging Medications*	2 (9%)	1 (4%)	3 (8%)

*QTC prolonging medications included: Amitriptyline, Sumatriptan, Tizanidine, Trazadone, Nortriptyline, Ranolazine, and Donepezil.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cardiac Parameter Results			
	<5years (n=22)	5-10 years (n=23)	>10years (n=39)
LVEF <40%	0 (0%)	1 (4%)	0 (0%)
BNP 100-500	2 (9%)	1 (4%)	7 (18%
BNP >500	0 (0%)	1 (4%)	2 (5%)
HS Troponin >36	0 (0%)	1 (4%)	0 (0%)
QTc Prolongation*	6 (27%)	4 (17%)	15 (38%)
IVSd >1.2	0 (0%)	2 (9%)	5 (13%)
Cardiac Biopsy Performed	0 (0%)	0 (0%)	2 (5%)
Biopsy Proven HCQ Toxicity	0 (0%)	0 (0%)	2 (5%)

ANOVA Analysis				
	<5years (n=22)	5-10 years (n=23)	>10years (n=39)	p-value
QTC	436.27	431.6	442.48	0.37
Troponin	5.58	13.48	4.27	0.36
BNP	37.31	63.65	96.18	0.42
IVSD	0.83	0.91	0.96	0.08
Chi Squared Analysis				
LVEF <40%	0 (0%)	1 (4%)	0 (0%)	0.26

Results: We evaluated 84 patients on HCQ, with baseline characteristics summarized in Table 1. Patients were divided into three groups based on treatment duration and cardiac parameters were compared (Table 2). Cardiac abnormalities of QTc > 440 ms were observed in 25 patients, IVSd > 1.2 cm in 7 patients, BNP > 100 pg/mL in 18 patients, troponin elevation in one patient, and reduced EF (< 40%) in one patient. Two patients underwent cardiac biopsy with findings consistent with HCQ toxicity. Both had MCTD diagnosis (SLE/SSc and positive anti-RNP), were on HCQ for over 10 years, had GFR < 40, QTc >450 ms; one had IVSd > 1.2 cm, and both had normal EF. ANOVA analysis did not show statistically significant differences in QTc, troponin, BNP or IVSd between the treatment duration groups. A chi-squared test assessing EF by HCQ duration also showed no significant difference ($p = 0.24$). A secondary analysis using a one-tailed t-test revealed a statistically significant difference in IVSd between patients receiving HCQ for >10 years compared to those treated for < 10 years ($p = 0.03$).

Conclusion: Our study found no statistically significant difference between the duration of HCQ use and measures of cardiac toxicity. Overall, abnormal cardiac findings were infrequent and did not correlate with HCQ exposure length. Numerically, there is a trend toward increased LVH in patients on long-term HCQ (>10 years), and a secondary analysis shows a statistically significant difference in IVSd between patients on HCQ for >10 years compared to those treated for < 10 years. However, given the small sample size in this cross-sectional study, a definitive association cannot be established. IVSd appears to be superior to EF as a noninvasive marker for potential HCQ cardiac toxicity. Similar to HCQ retinal toxicity, patients with reduced GFR and higher cumulative dose may benefit from enhanced screening.

1. Tselios K, Deeb M, Gladman DD, Harvey P, Urowitz MB. Antimalarial-induced cardiomyopathy: a systematic review of the literature. Lupus. 2018 Apr;27(4):591-599. doi: 10.1177/0961203317734922. Epub 2017 Oct 9. PMID: 28992800.

Disclosure: J. Bhatti: None; **K. Lee**: None; **N. Sanghavi**: None; **S. Zak**: None; **J. Ash**: None; **J. Miceli**: None; **K. Sperber**: None; **S. Pan**: None; **A. Wasserman**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0599

Efficacy of Statin Medications for Secondary Prevention of Atherosclerotic Cardiovascular Disease Among Patients with Systemic Lupus Erythematosus

Aakash V. Patel[1], Lingxiao Zhang[2], Emily S. Lau[3], Baijun Zhou[2], Yuqing Zhang[4], Hyon K. Choi[5] and April Jorge[6], [1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Massachusetts General Hospital, Harvard Medical School, Boston, [4]Massachusetts General Hospital, Quincy, MA, [5]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [6]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with up to a three-fold increased risk of myocardial infarction (MI) and stroke. Statins have well-established cardioprotective benefits among non-SLE patients with atherosclerotic cardiovascular disease (ASCVD), but data assessing their efficacy for the secondary prevention of ASCVD in this population are scarce.

Methods: We specified and emulated a pragmatic target trial to compare outcomes among SLE patients initiating versus not initiating a statin following their first clinical ASCVD event. We identified an SLE cohort from TriNetX, a large electronic health record (EHR) database in the United States. We included patients with SLE (≥2 ICD codes ≥30 days and ≤2 years apart) between January 2002 and August 2021 who had a first clinical ASCVD event, including acute MI, coronary artery disease requiring intervention, unstable angina, ischemic stroke, or transient ischemic attack (TIA), identified by ICD codes during an inpatient or emergency room encounter. We excluded patients treated with a statin in the year preceding the index ASCVD event or with a contraindication. We compared the treatment strategies of statin initiation within 30 days after the index event versus no statin initiation. Study follow up commenced at the date of statin initiation or a randomly assigned date within the same 30-day period for non-initiators. We employed propensity score overlap weighting to emulate randomization. Covariates included demographics, type of index ASCVD event, comorbidities, SLE disease manifestations, medications, and healthcare utilization. Efficacy outcomes included all-cause death, major adverse cardiovascular events (MACE),

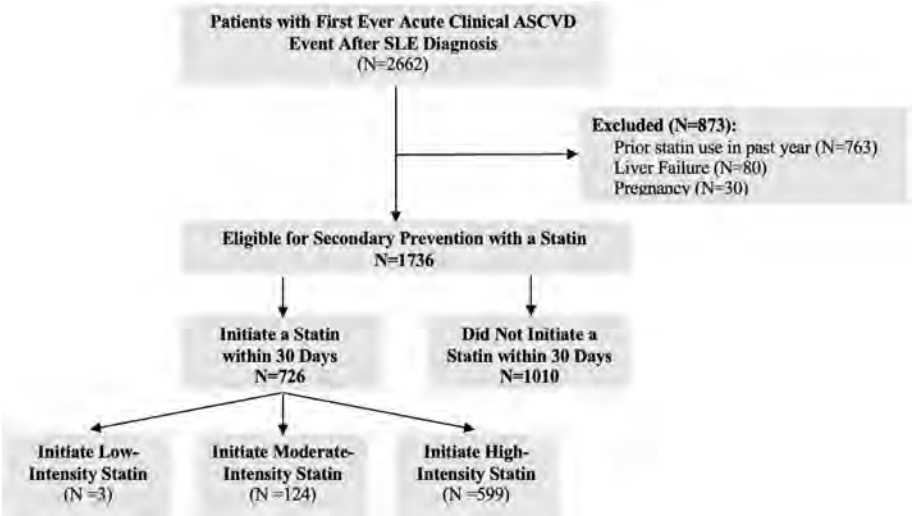


Figure 1. Consort Diagram of Entry into the Study

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Statin Initiators and Non-Initiators with Systemic Lupus Erythematosus Following an Atherosclerotic Cardiovascular Disease Event

Characteristics	Before Propensity Score Overlap Weighting			After Propensity Score Overlap Weighting		
	Statin Initiators (n=726)	Statin Non-Initiators (n=1010)	Std. Diff.	Statin Initiators	Statin Non-Initiators	Std. Diff.
Age, mean (SD)	54.8 (12.7)	49.2 (14.5)	0.4114	52.7	52.7	<0.001
Female Sex, n (%)	602 (82.9)	880 (87.1)	-0.1181	85.4	85.4	<0.001
Race and Ethnicity, n (%)			0.2396			<0.001
White	291 (40.1)	310 (30.7)		37.3	37.3	
Black	217 (29.9)	349 (34.6)		32.6	32.6	
Hispanic	61 (8.4)	110 (10.9)		8.9	8.9	
Asian	15 (2.1)	9 (0.9)		1.2	1.2	
Other	142 (19.6)	232 (23.0)		20.1	20.1	
Geographic Region, n (%)			0.3113			<0.001
Northeast	121 (16.7)	110 (10.9)		15.5	15.5	
Midwest	120 (16.5)	147 (14.6)		16.6	16.6	
West	58 (8.0)	59 (5.8)		7.1	7.1	
South	416 (57.3)	623 (61.7)		58.2	58.2	
SLE Severity Index, n (%)			0.1409			<0.001
Mild	310 (42.7)	369 (36.5)		39.5	39.5	
Moderate	70 (9.6)	90 (8.9)		9.0	9.0	
Severe	346 (47.7)	551 (54.6)		51.5	51.5	
Charlson Comorbidity Index, mean (SD)	4.0 (2.4)	3.9 (2.1)	0.0344	4.0	4.0	<0.001
Type of Acute Clinical ASCVD Event, n (%)			0.1257			<0.001
Acute MI	299 (41.2)	393 (38.9)		38.0	38.0	
CABG Procedure	13 (1.8)	18 (1.8)		1.5	1.5	
PCI Procedure	9 (1.2)	9 (0.9)		1.4	1.4	
Unstable Angina	49 (6.8)	46 (4.6)		5.3	5.3	
Acute Stroke	283 (39.0)	401 (39.7)		41.4	41.4	
Acute TIA	73 (10.1)	143 (14.2)		12.4	12.4	
SLE Medications, n (%)						
Glucocorticoid use	438 (60.3)	576 (57.0)	0.0671	62.0	62.0	<0.001
Hydroxychloroquine	328 (45.2)	339 (33.6)	0.2394	41.3	41.3	<0.001
Mycophenolate Mofetil	109 (15.0)	157 (15.5)	-0.0148	15.6	15.6	<0.001
Azathioprine	35 (4.8)	62 (6.1)	-0.0579	5.9	5.9	<0.001
Methotrexate	40 (5.5)	51 (5.0)	0.0206	6.0	6.0	<0.001
Belimumab	15 (2.1)	22 (2.2)	0.0078	1.9	1.9	<0.001
Cyclophosphamide	15 (2.1)	35 (3.5)	-0.0854	2.3	2.3	<0.001
Rituximab	14 (1.9)	24 (2.4)	-0.0309	2.2	2.2	<0.001
Tacrolimus	28 (3.9)	31 (3.1)	0.0431	3.9	3.9	<0.001
SLE Manifestations, n (%)						
Lupus Nephritis*	295 (40.6)	463 (45.8)	-0.1053	42.4	46.5	<0.001
Antiphospholipid Syndrome	127 (17.5)	167 (16.5)	0.0255	15.0	17.1	<0.001
Other Medications, n (%)						
SGLT2 Inhibitor	4 (0.6)	4 (0.4)	0.0226	0.4	0.4	<0.001
GLP-1 RA	0 (0.0)	3 (0.3)	-0.0772	0.0	0.0	<0.001
ACEi or ARB	308 (42.4)	272 (26.9)	0.3299	36.7	36.7	<0.001
Aspirin	552 (76.0)	358 (35.5)	0.8953	61.7	61.7	<0.001
Antiplatelet	216 (29.8)	68 (6.7)	0.6244	15.1	15.1	
Anticoagulation	135 (18.6)	171 (16.9)	0.0436	20.8	20.8	
Comorbidities, n (%)						
Hypertension	585 (80.6)	791 (78.3)	0.0560	80.6	83.1	<0.001
Diabetes Mellitus	660 (90.9)	879 (87.0)	0.1241	89.4	90.0	<0.001
Hyperlipidemia	374 (51.5)	367 (36.3)	0.3095	44.4	51.8	<0.001
CKD ≥ 4	98 (13.5)	203 (20.1)	-0.1772	16.4	17.5	<0.001
Obesity	224 (30.9)	283 (28.0)	0.0622	30.5	33.2	<0.001
Tobacco Use	98 (13.5)	124 (12.3)	0.0365	12.3	12.3	<0.001
Alcohol Use Disorder	13 (1.8)	24 (2.4)	-0.0410	1.9	1.9	<0.001
Healthcare Utilization						
Outpatient Encounters, median (IQR)	5.0 (1.0 – 13.0)	4.5 (1.0 – 13.0)	0.0059	5.0	5.0	<0.001
Hospital/ER Encounter, n (%)	597 (82.2)	905 (89.6)	-0.2132	86.1	86.1	<0.001
Encounter for Physical Examination, n (%)	86 (11.9)	117 (11.4)	0.0081	12.1	12.1	<0.001
Received Influenza Vaccine, n (%)	59 (8.1)	83 (8.1)	0.0039	7.7	7.7	<0.001

SLE, systemic lupus erythematosus; ASCVD, atherosclerotic cardiovascular disease; MI, myocardial infarction; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; SGLT2, sodium-glucose-cotransporter 2; GLP-1 RA, glucagon-like peptide-1 receptor agonist; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; BMI, body mass index; GFR, glomerular filtration rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ER, emergency room
*defined by ≥1 specific lupus nephritis code (ICD-10 M32.14/15) or ≥ 2 nephritis codes (ICD-9 580-586, 791.0; ICD-10 N00, N04, N05, N17, N18, R80.9)

Table 2. Outcomes Associated with Statin Initiation vs Non-Initiation Following an Atherosclerotic Cardiovascular Disease Event in Patients with Systemic Lupus Erythematosus

Outcomes	Events, n		Follow-up Time, years		Incidence Rate, per 100 person-years		Adjusted Hazard Ratio (95% CI)	P-value
	Any Statin	No Statin	Any Statin	No Statin	Any Statin	No Statin		
Per-Protocol								
Cardiovascular Outcomes								
Major Adverse Cardiovascular Event*	177	277	1.73	2.07	14.82	14.24	0.96 (0.77-1.21)	0.7412
Myocardial Infarction	32	49	1.98	2.39	2.06	2.30	0.85 (0.50-1.43)	0.5297
Ischemic Stroke	49	54	1.94	2.31	3.55	2.51	1.33 (0.83-2.13)	0.2296
Heart Failure	114	165	1.88	2.22	8.62	7.90	1.02 (0.77-1.36)	0.8810
Venous Thromboembolism	54	109	1.92	2.20	4.54	4.64	0.91 (0.62-1.34)	0.6313
Kidney Outcome								
End-Stage Kidney Disease	38	51	1.99	2.33	2.97	2.27	1.26 (0.77-2.08)	0.3560
All-Cause Death	27	72	2.05	2.44	2.15	3.55	0.55 (0.34-0.91)	0.0207
Control Outcome								
Injury/Trauma	86	144	1.82	2.13	6.89	6.79	0.97 (0.71-1.33)	0.8527
Intention-to-treat								
Cardiovascular Outcomes								
Major Adverse Cardiovascular Event*	200	323	2.45	2.60	11.51	13.10	0.84 (0.68-1.04)	0.1078
Myocardial Infarction	37	60	2.84	3.12	1.70	1.99	0.80 (0.49-1.29)	0.3499
Ischemic Stroke	55	63	2.77	3.04	2.75	2.32	1.13 (0.73-1.74)	0.5957
Heart Failure	129	195	2.66	2.85	6.76	7.09	0.90 (0.69-1.17)	0.4275
Venous Thromboembolism	60	122	2.74	2.87	3.44	4.05	0.81 (0.56-1.17)	0.2561
Kidney Outcome								
End-Stage Kidney Disease	42	62	2.83	3.05	2.26	2.01	1.10 (0.69-1.74)	0.6914
All-Cause Death	35	87	2.94	3.25	1.80	3.25	0.53 (0.34-0.82)	0.0049
Control Outcome								
Injury/Trauma	98	175	2.60	2.69	5.47	6.37	0.82 (0.61-1.09)	0.1784

*Includes myocardial infarction, ischemic stroke, heart failure hospitalization, or cardiovascular death

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and new-onset end-stage kidney disease (ESKD). We assessed the control outcome of injury/trauma. We utilized Cox regression to compare incidence rates between the two groups and employed a primary per-protocol approach, censoring patients upon deviation from their assigned treatment, and an intention-to-treat (ITT) approach as a secondary analysis.

Results: There were 1736 patients with SLE who met the inclusion/exclusion criteria (**Figure 1**). Of these, 726 patients initiated a statin, compared with 1010 non-initiators **(Table 1)**. Baseline covariates were similar across both groups following propensity sore overlap weighting (standard difference < 0.001). The mean age was 53 years; 85% were female. In the per-protocol and ITT analyses, statin users had a lower risk of all-cause death (HR 0.55 [95% CI 0.34-0.91] and 0.53 [95% CI 0.34-0.82], respectively, **Table 2)**. There was no difference in the risks of MACE (HR 0.96 [0.77-1.21], ESKD (HR 1.26 [95% CI 0.77-2.08]), or the control outcome of injury/trauma (HR 0.97 [95% CI 0.71-1.33]).

Conclusion: In this emulated target trial using a large, EHR-based cohort of patients with SLE and clinical ASCVD, we identified a lower risk of all-cause death associated with initiating a statin, although there were no significant differences in rates of MACE or ESKD. This study is limited by the possibility of residual bias and the use of administrative codes. These findings underscore the role for statin treatment in patients with SLE and ASCVD.

Disclosure: A. Patel: None; **L. Zhang**: None; **E. Lau**: Amissa Health, 1, Roche, 6, Systole Health, Inc, 1; **B. Zhou**: None; **Y. Zhang**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **A. Jorge**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 0600

Toward a Consensus-Based Definition of Difficult-to-Treat Systemic Lupus Erythematosus: A Multinational Survey of Clinicians from the MENA Region

Ahlam Almarzooqi[1], Sarah Al Qassimi[2], Nelly Ziade[3], Mohammed Omair[4], Samar Al emadi[5], FARIDA ALBALUSHI[6], Waleed Hafiz[7], Hiba Khogali[8], Saadeya Naji[9], Suzan Attar[10], Khalid Alnaqbi[11] and Rajaie Namas[12], [1]Emirates Health Services, Sharjah, United Arab Emirates, [2]Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates, [3]Department of Rheumatology, Saint-Joseph University and Hotel-Dieu de France, Beirut, Lebanon, [4]King Saud university, Riyadh, Saudi Arabia, [5]Hamad medical corporation, Doha, Qatar, [6]Royal hospital, Dubia, United Arab Emirates, [7]Umm Al-Qura university, Makkah, Makkah, Saudi Arabia, [8]Madinat Zayed Hospital , Al Dhafra hospitals, Abu Dhabi, Abu Dhabi, United Arab Emirates, [9]Salmaniya medical complex, BAHRAIN, Al Asimah, Bahrain, [10]King Abdulaziz University, Saudi Arabia, Jeddah, Saudi Arabia, [11]Sheikh Tahnoon Medical city, Al Ain, United Arab Emirates, [12]Cleveland Clinic Abu Dhabi, Detroit, MI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Difficult-to-treat systemic lupus erythematosus (D2T-SLE) presents a major challenge due to disease heterogeneity and a lack of unified classification. While the D2T concept has advanced management in other autoimmune diseases, no operational definition exists for SLE. This study aimed to define clinician-endorsed criteria for D2T-SLE across the Middle East and North Africa (MENA) region.

Methods: A cross-sectional online survey was distributed to rheumatologists and nephrologists in 12 MENA countries. Clinicians rated factors relevant to D2T-SLE, including disease persistence, treatment failure, corticosteroid use, patient-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Summary of Key Findings from the D2T-SLE Clinician Survey

Key Variable	Value
Total Respondents	141
Rheumatologists (%)	125 (88.7%)
Nephrologists (%)	10 (7.1%)
Included PROs in DTT-SLE definition	93%
Supported Organ-Specific Criteria	88%
Supported Corticosteroid Criterion	82%
Supported Overlap Syndromes Inclusion	62%
Mean QOL Importance (1–5)	3.87
Factor 1 Loading (QOL)	-0.85
Factor 2 Loading (Fatigue)	-0.32
Top Cluster Focus	PRO-heavy (Cluster 1)
Logistic: Pain -> QOL (p)	0.042
Cohen's Kappa (Steroid Inclusion)	-0.009

reported outcomes (PROs), overlapping syndromes, and psychosocial factors. Quantitative analysis included descriptive statistics, exploratory factor analysis, k-means clustering, logistic regression, and Cohen's Kappa for agreement.

Results: A total of 141 clinicians responded (89% rheumatologists). Most participants had experience in academic lupus settings, with 68% involved in research or publication and 50% in international SLE workshops. There was broad support for incorporating both clinical and PRO elements (93%), organ-specific involvement (88%), and corticosteroid dependency (82%) into a D2T-SLE definition. Top criteria included persistent moderate-to-high disease activity, failure of multiple therapies, and recurrent flares. Overlapping autoimmune syndromes—particularly APS, MAS, and Sjögren's—were identified as major complicating factors, with 62% supporting their inclusion in D2T-SLE criteria. The agreement on corticosteroid thresholds was low (κ = -0.009).

Factor analysis identified two latent domains: psychosocial burden (fatigue, psychological distress) and functional burden (pain, QOL, and activity limitation). Cluster analysis revealed three clinician phenotypes: one prioritizing PROs, another emphasizing clinical damage, and a balanced group. Logistic regression showed that fatigue ($p = 0.015$), pain ($p < 0.001$), and functional impairment ($p = 0.027$) significantly predicted prioritization of QOL. Clinicians favored including kidney and CNS involvement in the definition, based on persistent SLEDAI-2K ≥6, BILAG A/B scores, and frequent flares.

Commonly cited causes of treatment failure included primary inefficacy, secondary loss of response, toxicity, comorbidities, and non-adherence.

Conclusion: Clinicians across the MENA region strongly supported defining D2T-SLE using a composite of treatment failure, corticosteroid burden, PROs, and organ involvement. These findings align with the broader D2T paradigm seen in other autoimmune diseases and advocate for a multidimensional, consensus-based framework. This study provides the quantitative foundation for future international classification efforts.

Disclosure: A. Almarzooqi: None; **S. Al Qassimi**: None; **N. Ziade**: None; **M. Omair**: None; **S. Al emadi**: None; **F. ALBALUSHI**: None; **W. Hafiz**: None; **H. Khogali**: None; **S. Naji**: None; **S. Attar**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 5, 6, Gilead, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Hikma, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Organon, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Sandoz, 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6; **K. Alnaqbi**: None; **R. Namas**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0601

Precipitants and Long-Term Outcomes of Posterior Reversible Encephalopathy Syndrome in Systemic Lupus Erythematosus: A Multicenter Cohort Study and Systematic Review

Ali Ardekani[1], Alain Sanchez-Rodriguez[2], Mariana González-Treviño[3], Jose Meade-Aguilar[4], Maria O. Valenzuela-Almada[5], Hannah Langenfeld[1], Larry J. Prokop[4], Isabel Valenzuela Almada[6], Gabriel Figueroa-Parra[7], Nicolás Sánchez Domínguez[8], Alejandro A. Rabinstein[4], M. Hassan Murad[4], Cynthia Crowson[9] and Ali Duarte-Garcia[1], [1]Mayo Clinic, Rochester, MN, [2]ABC Medical Center, Ciudad de México, Federal District, Mexico, [3]Vanderbilt University Medical Center, Nashville, [4]Mayo Clinic, Rochester, [5]Children's National Medical Center, Washington D.C, [6]Universidad Panamericana, Ciudad de México, Federal District, Mexico, [7]Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico, [8]Clínica Alemana de Santiago, Santiago, Chile, [9]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Posterior reversible encephalopathy syndrome (PRES) is an underrecognized neuroradiologic complication of SLE, characterized by acute neurological symptoms and vasogenic edema on neuroimaging. Its precipitating factors, clinical spectrum, and long-term outcomes remain poorly defined. We sought to delineate the presentations, triggers, and prognoses of PRES in patients with SLE through a multicenter cohort study and systematic literature review (SLR).

Methods: We conducted a multicenter retrospective cohort study (August 1999–October 2024) and an SLR according to the PRISMA guidelines. Patients were included if they met the 2019 EULAR/ACR SLE classification criteria or were described as having SLE by study authors in the SLR, had confirmed PRES episodes, defined as: 1) first sudden appearance of neurologic symptoms attributed to PRES such as seizures, altered mental status, headache, visual impairment, or focal deficits; 2) radiologic evidence of vasogenic edema on CT or MRI; and 3) not better explained by alternative diagnoses.

We did a comprehensive search in multiple databases from their inception to October 1, 2024, in any language. Two reviewers independently screened and reviewed the articles. We included studies reporting cases that met the inclusion criteria used for the cohort. Extracted data included demographics and clinical characteristics at presentation, laboratory data, radiologic findings, therapeutic strategies, and clinical outcomes. For outcome analyses, we included only cases with sufficient data that met our quality criteria, adapted from the Murad et al. tool for evaluating case reports. Kaplan-Meier methods estimated time-to-event outcomes. Logistic and Cox regressions, adjusted for age and sex, identified associated factors.

Results: We analyzed 550 patients (53 cohort; 497 SLR), mean age 26.7 ± 10.2 years, 504/546 (92%) female. In the cohort, PRES was most often precipitated by hypertension in lupus nephritis 43/53 (81%), followed by hypertension without nephritis 7/53 (13%), sepsis 2/53 (4%), and immunosuppression 1/53 (2%). Also, 42/53 (79%) patients required antiseizure medications (ASMs), and among those who did, median time to ASMs discontinuation was 0.4 years (95% CI 0.1–3.9), with 78.1% off therapy by five years (Figure 1a).

Across all cases (cohort and SLR), presenting symptoms included seizures 389/490 (79%), headache 251/464 (54%), altered mental status 205/466 (44%), and visual disturbances 192/464 (41%). PRES was the initial SLE manifestation in 48/362 (13%) of cases (Table 1). Five-year PRES recurrence was 11.5% (95% CI: 2.3–19.9) (Figure 1b). Thirty- and 180-day survival rates were 96.3% and 93.7%, respectively (Figure 1c). Older age increased odds of persistent neurological deficits (OR 1.63 per 10-year increase in age, 95% CI 1.12–2.39) (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical background, PRES presentation, and treatment of included cases.

Variables	N=550 (%)
Comorbidities	
Overweight/obesity	28 /127 (22)
Dyslipidemia	34/193 (18)
Diabetes	13/194 (7)
Hypertension	156/315 (50)
Ischemic heart disease	7/175 (4)
SLE characteristics (history, or at onset)	
Mucocutaneous involvement	173/369 (47)
Arthritis	161/368 (44)
Serositis	106/367 (29)
Hematological involvement	222/380 (58)
Neurological involvement	46/358 (13)
Antiphospholipid syndrome	49/368 (13)
Obstetric complications	37/320 (12)
Diffuse alveolar hemorrhage	29/368 (8)
Lupus Nephritis*	382/461 (83)
End Stage Renal Disease (any cause)	72/319 (23)
Positive Anti-dsDNA antibodies	210/272 (77)
Positive Anti-Sm antibodies	54/129 (42)
Positive Antiphospholipid antibodies	97/243 (40)
Clinical Characteristics of PRES	
SLE duration, median (IQR), months (n=430)	37.3 (12-65)
SLEDAI at PRES event (mean ± SD) (n=265)	18.6 ± 8.0
PRES as the first manifestation of SLE	48/362 (13)
Seizures	389/490 (79)
Headache	251/464 (54)
Visual disturbances	192/464 (41)
Focal deficits	37/418 (9)
Altered mental status	205/466 (44)
High blood pressure (>140/90 mmHg)	405/479 (85)
Systolic blood pressure at PRES event, mmHg (mean ± SD) (n=379)	177.4 ± 26.4
Diastolic blood pressure at PRES event, mmHg (mean ± SD) (n=337)	108.4 ±17.6
Developed epilepsy	3/201 (1)
Admission to ICU	135/230 (59)
Mortality during hospitalization	14/470 (3)
Reported treatments during PRES events**	
Antihypertensives	287/340 (84)
Glucocorticoids	184/225 (82)
Anticonvulsants	263/398 (66)
Cyclophosphamide	99/195 (51)
Mycophenolate Mofetil	38/154 (25)
Rituximab	15/136 (11)
Azathioprine	15/156 (10)
Hydroxychloroquine	13/135 (10)
Methotrexate	0
Renal replacement therapy	84/279 (30)
Plasma exchange (PLEX)	44/275 (16)

Abbreviations: PRES, posterior reversible encephalopathy syndrome; SLE, systemic lupus erythematosus; Anti-dsDNA, anti–double-stranded DNA antibody; Anti-Sm, anti–Smith antibody; SD, standard deviation; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; ICU, intensive care unit * Biopsy-proven disease or renal involvement, including proteinuria without biopsy. **This was not unique to PRES; some cases presented with overlapping symptoms, and the medications may have been given for reasons beyond PRES.

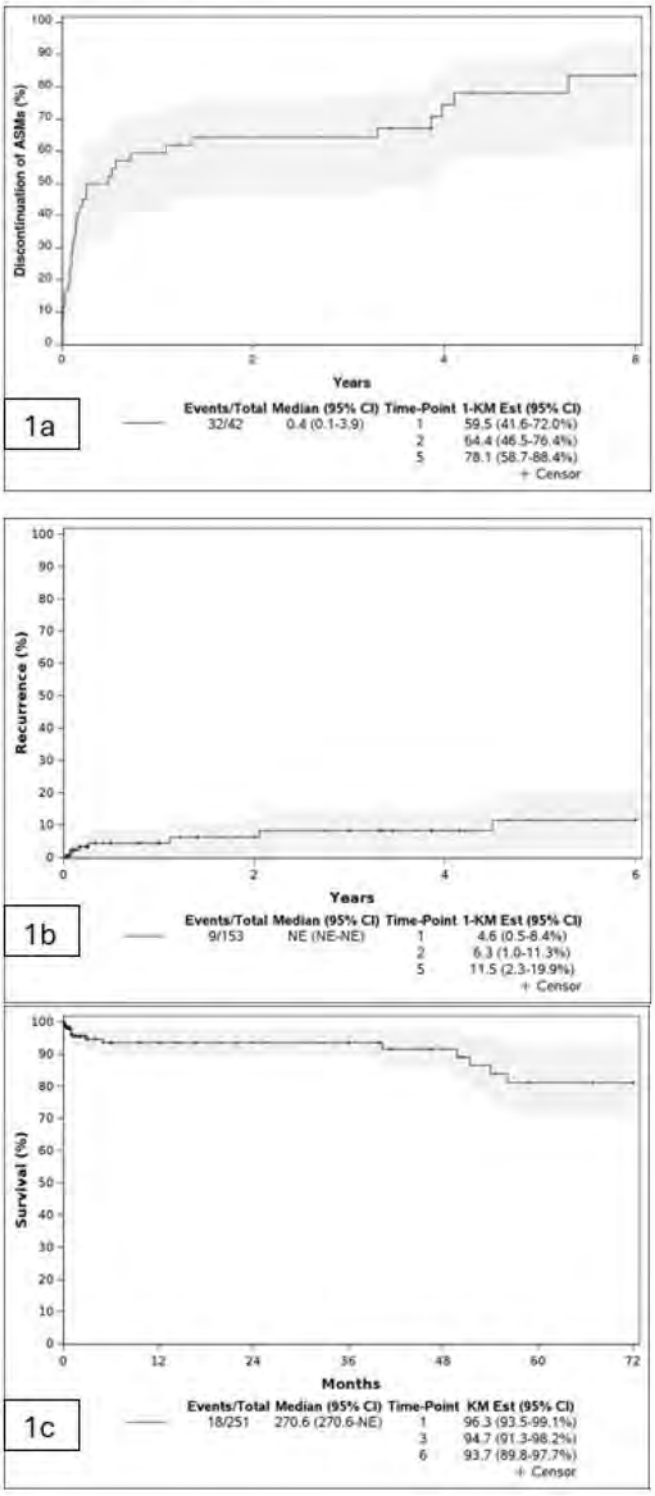
Table 2. Associations of PRES recurrence, and longstanding neurological sequelae with variables*.

Variables	Recurrence HR (95% CI)	Long standing neurological sequelae** OR (95% CI)
General Features		
Age per 10 years	0.41 (0.15, 1.15)	**1.63 (1.12, 2.39)**
Gender (Male)	1.75 (0.19, 15.93)	0.88 (0.09, 8.47)
Lupus nephritis (past or present)	0.61 (0.35, 1.07)	0.76 (0.21, 2.67)
SLEDAI at PRES event Per 2 points increase	1.00 (0.95, 1.06)	0.90 (0.79, 1.03)
Laboratory features		
Positive Anti-dsDNA antibodies	0.86 (0.51,1.46)	1.17 (0.32, 4.29)
Positive Anti-Sm antibodies	1.26 (0.72, 2.20)	1.56 (0.39, 6.20)
Positive Antiphospholipid antibodies	0.89 (0.54, 1.45)	1.29 (0.39, 4.26)
Platelets (less than 100 x 10^9/L)	0.95 (0.58, 1.55)	1.03 (0.30; 3.56)
Glomerular filtration rate (per 10-unit decrease)	0.93 (0.83, 1.03)	0.99 (0.79, 1.24)
Proteinuria >0.5g	1.70 (0.93, 3.10)	0.37 (0.07, 1.86)
Hematuria	1.14 (0.62, 2.11)	1.01 (0.21, 4.83)
Low complement	1.89 (0.96, 3.72)	1.15 (0.21, 6.25)

Abbreviations: PRES, posterior reversible encephalopathy syndrome; HR, hazard ratio; OR, odds ratio; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; Anti-dsDNA, anti–double-stranded DNA antibody; Anti-Sm, anti–Smith antibody. *Adjusted by age and sex. ** >6months Long lasting or permanent deficits occurred during acute episode, but present after stabilization of precipitating factors and discharge. For SLR as per authors description on the clinical course after discharge. If follow-up information was not available, or it was not described by the author and/or could not be inferred, it was abstracted as unknown.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1a-c. Kaplan-Meier curves for outcomes in SLE patients with PRES: (a) anti-seizure medications discontinuation; (b) recurrence of PRES; (c) overall survival.



Conclusion: In SLE, PRES most commonly follows hypertensive crises in lupus nephritis and presents with seizures and headache. While short-term prognosis is excellent, long-term deficits are influenced by age.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Ardekani: None; **A. Sanchez-Rodriguez**: None; **M. González-Treviño**: None; **J. Meade-Aguilar**: None; **M. Valenzuela-Almada**: None; **H. Langenfeld**: None; **L. Prokop**: None; **I. Valenzuela Almada**: None; **G. Figueroa-Parra**: None; **N. Sánchez Domínguez**: None; **A. Rabinstein**: Chiesi, 1; **M. Murad**: None; **C. Crowson**: None; **A. Duarte-Garcia**: None.

Abstract Number: 0602

Association of Systemic Lupus Erythematosus with Healthcare Resource Utilization and Healthcare Expenditures: Analysis of Nationally Representative Data, 2017-2022

Ami Vyas[1], Steven Cohen[2] and Christine Eisenhower[2], [1]University of Rhode Island, Kingston, RI, [2]University of Rhode Island, Kingston

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Limited information is available about the effect of systemic lupus erythematosus (SLE) on healthcare resource utilization and healthcare expenditures. The associations between SLE and healthcare resource utilization and expenditures were examined using the most recently available data.

Methods: A retrospective US population-based study was conducted using Medical Expenditure Panel Survey data for 2017-2022. Patients with SLE were those who both self-reported SLE diagnosis and who reported SLE-related medication use and/or visit to a rheumatologist in the survey year. Eight patients without SLE were matched to each SLE patient on survey year, age, and sex, to create a reference cohort. Appropriate multivariable generalized linear regression, either negative binomial regression or Poisson regression, with log link, was used to obtain an adjusted annualized event rate ratio (AAERR) for each component of healthcare resource utilization. Multivariable ordinary least square regression was conducted to examine the association between SLE and log expenditures. To avoid retransformation bias of log expenditures, the subgroup-specific smearing factor was used to account for unequal variances between the SLE and non-SLE patients.

Results: Compared to those without SLE, patients with SLE had higher adjusted rates of outpatient visits (AAERR=2.603, $p< 0.05$), office-based provider visits (AAERR=1.447, $p< 0.05$), and emergency room visits (AAERR=1.518, $p< 0.05$). However, there were no significant differences in adjusted rates of inpatient visits between those with and without SLE (AAERR=1.365, p=0.065). With regard to healthcare expenditures, those with SLE had significantly higher average annual healthcare expenditures compared to those without SLE ($18,566 vs. $9,366, $p< 0.0001$), and the findings were consistent for expenditures by each healthcare resource component. In the adjusted analyses, average annual healthcare expenditures for those with SLE were significantly higher than those without SLE ($13,664 vs. $11,781, $p< 0.05$).

Conclusion: Our study findings suggest higher healthcare resource utilization and, hence, higher healthcare expenditures among patients with SLE compared to their non-SLE counterparts.

Disclosure: A. Vyas: Merck/MSD, 5; **S. Cohen**: Merck/MSD, 5; **C. Eisenhower**: Merck/MSD, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0603

Transverse Myelitis in Systemic Lupus Erythematosus: Disease Manifestations and Clinical Outcomes from Multi-Center Data

Amir Daneshvar[1], Areeb Tiwana[2], Dana Nachawati[1], Keri Ann Pfeil[1], Elleson Harper[1], Lindsay Frumker[3], Meghan Gump[1] and Omer Pamuk[4], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]Canton Medical Education Foundation, Canton, OH, [3]University hospitals Cleveland medical center, Highland Heights, OH, [4]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1: Demographic Characteristics and Clinical Manifestations/Comorbidities of Patients With Systemic Lupus Erythematosus With and Without Transverse Myelitis Before and After Propensity Matching.

	Before matching			After propensity matching		
Variable	SLE w TM (N=1,224)	SLE wo TM (N=133,803)	p-value	SLE w TM (N=1,219)	SLE wo TM (N=1,219)	p-value
Demographics						
Age at index (Mean ± SD)	42.7 ± 16.5	46.8 ± 17.2	**<0.001**	42.8 ± 16.5	42.6 ± 17.0	0.768
Female	1,033 (84.4%)	115,989 (86.7%)	**0.019**	1,029 (84.4%)	1,037 (85.1%)	0.652
African-American	383 (31.3%)	33,131 (24.8%)	**<0.001**	382 (31.3%)	419 (34.4%)	0.111
White	525 (42.9%)	64,992 (48.6%)	**<0.001**	523 (42.9%)	491 (40.3%)	0.189
Hispanic	108 (8.8%)	12,723 (9.5%)	0.416	107 (8.8%)	85 (7.0%)	0.098
Asian	131 (10.7%)	9867 (7.4%)	**<0.001**	130 (10.7%)	138 (11.3%)	0.604
Clinical manifestations & comorbidities						
Glomerular disease	105 (8.6%)	7,897 (5.9%)	**<0.001**	103 (8.4%)	107 (8.8%)	0.773
ESRD	51 (4.2%)	4,847 (3.6%)	0.311	51 (4.2%)	46 (3.8%)	0.604
APS	77 (6.3%)	5,105 (3.8%)	**<0.001**	77 (6.3%)	62 (5.1%)	0.190
Venous emboli/ thrombosis	81 (6.6%)	5,483 (4.1%)	**<0.001**	80 (6.6%)	74 (6.1%)	0.617
Discoid lupus	99 (8.1%)	11,105 (8.3%)	0.790	98 (8.0%)	93 (7.6%)	0.706
Seizures/Epilepsy	138 (11.3%)	4,336 (3.2%)	**<0.001**	134 (11.0%)	118 (9.7%)	0.287
Psychosis	37 (3.0%)	828 (0.6%)	**<0.001**	36 (3.0%)	33 (2.7%)	0.714
Myasthenia	10 (0.8%)	10 (0.0%)	**<0.001**	10 (0.8%)	0 (0.0%)	**0.002**
Neuromyelitis optica	81 (6.6%)	99 (0.1%)	**<0.001**	81 (6.6%)	10 (0.8%)	**<0.001**
Mononeuropathies of the upper limb	40 (3.3%)	4,945 (3.7%)	0.429	40 (3.3%)	37 (3.0%)	0.728
Inflammatory arthritis	223 (18.2%)	25,521 (19.1%)	0.449	222 (18.2%)	231 (18.9%)	0.639
Pleurisy	14 (1.1%)	1,364 (1.0%)	0.666	14 (1.1%)	14 (1.1%)	1.0
Acute pericarditis	12 (1.0%)	969 (0.7%)	0.293	11 (0.9%)	12 (1.0%)	0.834
Sjogren's syndrome	118 (9.6%)	12,267 (9.2%)	0.569	118 (9.7%)	121 (9.9%)	0.838
Hemolytic anemia	54 (4.4%)	3,389 (2.5%)	**<0.001**	52 (4.3%)	57 (4.7%)	0.624
Neutropenia	47 (3.8%)	2,326 (1.7%)	**<0.001**	46 (3.8%)	42 (3.2%)	0.664
Lymphocytopenia	30 (2.5%)	1,022 (0.8%)	**<0.001**	28 (2.3%)	22 (1.8%)	0.391
Thrombocytopenia	125 (10.2%)	6,319 (4.7%)	**<0.001**	122 (10.0%)	124 (10.2%)	0.893
Tobacco use	95 (7.8%)	12,870 (9.6%)	**0.028**	95 (7.8%)	91 (7.5%)	0.760
Alcohol use	25 (2.0%)	2,295 (1.7%)	0.380	25 (2.1%)	23 (1.9%)	0.771
Type 2 Diabetes	138 (11.3%)	14,519 (10.9%)	0.635	137 (11.2%)	120 (9.8%)	0.262

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Medication Treatment and Autoantibody Profile of Patients With Systemic Lupus Erythematosus With and Without Transverse Myelitis Before and After Propensity Matching.

	Before matching			After propensity matching		
Variable	SLE w TM (N=1,224)	SLE wo TM (N=133,803)	p-value	SLE w TM (N=1,219)	SLE wo TM (N=1,219)	p-value
Medications						
Hydroxychloroquine	561 (45.8%)	57,014 (42.6%)	**0.023**	557 (45.7%)	567 (46.5%)	0.685
Glucocorticoids	824 (67.3%)	72,645 (54.3%)	**<0.001**	819 (67.2%)	825 (67.7%)	0.795
Azathioprine	101 (8.3%)	6,660 (5.0%)	**<0.001**	101 (8.3%)	102 (8.4%)	0.942
Mycophenolate mofetil	196 (16.0%)	10,853 (8.1%)	**<0.001**	193 (15.8%)	214 (17.6%)	0.254
Mycophenolic acid	41 (3.3%)	3,119 (2.3%)	**0.019**	41 (3.4%)	50 (4.1%)	0.336
Cyclophosphamide	117 (9.6%)	1,884 (1.4%)	**<0.001**	112 (9.2%)	107 (8.8%)	0.723
Methotrexate	68 (5.6%)	8,702 (6.5%)	0.180	68 (5.6%)	70 (5.7%)	0.861
Belimumab	23 (1.9%)	2,077 (1.6%)	0.358	23 (1.9%)	27 (2.2%)	0.568
Rituximab	78 (6.4%)	1,745 (1.3%)	**<0.001**	76 (6.2%)	82 (6.7%(	0.622
Autoimmune labs						
DsDNA	160 (13.1%)	14,697 (11.0%)	**0.020**	158 (13.0%)	174 (14.0%)	0.345
Ro/SSA	107 (8.7%)	7,089 (5.3%)	**<0.001**	105 (8.6%)	91 (7.5%)	0.297
La/SSB	120 (9.8%)	7,482 (5.6%)	**<0.001**	119 (9.8%)	89 (7.3%)	**0.030**
RNP	60 (4.9%)	4,710 (3.5%)	**0.009**	60 (4.9%)	62 (5.1%)	0.853
Ribosomal-P	23 (1.9%)	562 (0.4%)	**<0.001**	21 (1.7%)	23 (1.9%)	0.761
Low complement C3	228 (18.6%)	11,404 (8.5%)	**<0.001**	223 (18.3%)	188 (15.4%)	0.058
Low complement C4	140 (11.4%)	6,911 (5.2%)	**<0.001**	135 (11.1%)	125 (10.3%)	0.512

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with widespread clinical manifestations. Neuropsychiatric SLE (NPSLE), a complex and poorly understood subset of SLE, comprises of 19 conditions with high rates of morbidity and mortality. Included in the spectrum of NPSLE is transverse myelitis (TM), a neuroinflammatory disorder characterized by rapid-onset motor and sensory deficits. In this study, we aim to investigate the prevalence of TM among the general SLE population and to compare clinical characteristics and outcomes between SLE patients with and without TM.

Methods: A retrospective chart review was conducted utilizing data from the TriNetX global research network platform, a health record electronic database. A total of 135,027 patients with SLE (ICD-10: M32) were identified across 97 health care organizations, of which 1,224 patients had a diagnosis of transverse myelitis (ICD-10: G37.3 or G04.9) and 133,803 patients did not have transverse myelitis. A 1:1 propensity score matching was done using 60 demographic and clinical variables, and yielded two cohorts of 1,219 patients each. The variables studied included baseline patient demographics, clinical manifestations/comorbidities, and autoantibody profile. Outcomes analyzed included mortality, laboratory findings, and medication usage. Kaplan-Meier curve and log-rank test were used for survival analysis. Statistical significance was defined as a p-value of < 0.05.

Results: The prevalence of TM among the general SLE population was 0.91%. Analysis of the demographic data before propensity matching revealed higher rates of TM in male (p=0.019), African-American, and Asian patients (p-values < 0.001).

Clinical manifestations such as glomerular disease, thrombosis, other neurological involvement including seizures, psychosis and neuromyelitis optica (NMO), as well as various hematological lab abnormalities were more frequent in the TM group prior to matching (all p-values < 0.001). The frequencies of Ro/SSA, La/SSB, Ribosomal-P (all p-values < 0.001), RNP

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

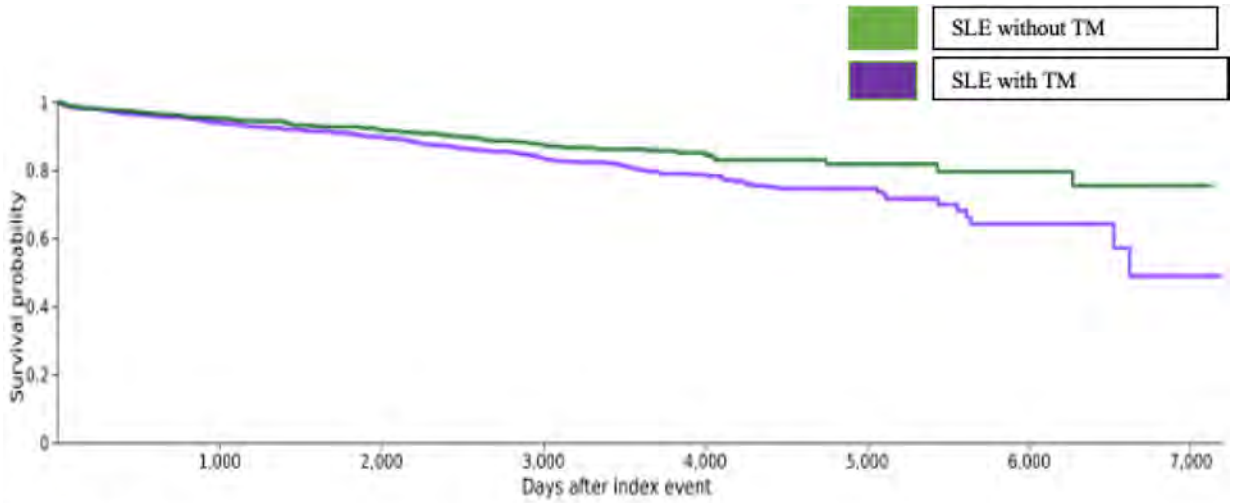


Figure 1A

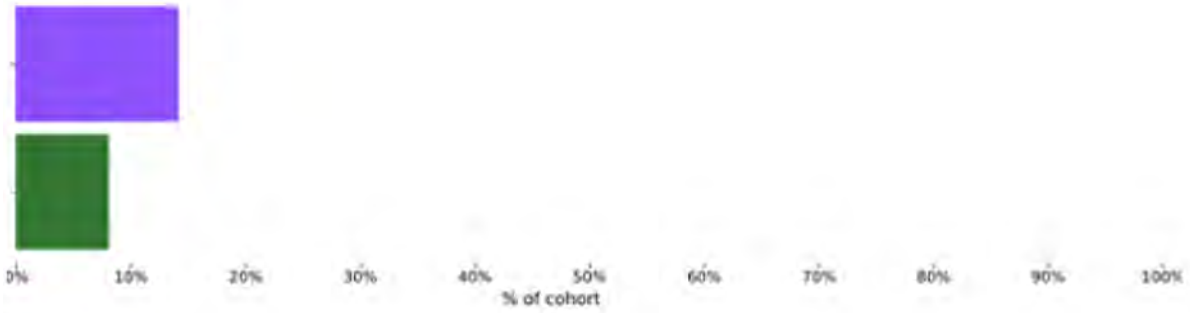


Figure 1B

Figure 1A: Survival Probability in Systemic Lupus Erythematosus With and Without Transverse Myelitis Using Kaplan-Meier Survival Analysis. Figure 1B: Mortality Rate Data in Systemic Lupus Erythematosus With and Without Transverse Myelitis.

(p=0.009), DsDNA antibodies (p=0.020), as well as low C3 and C4 complements (p< 0.001) were significantly higher in TM patients before matching (Table 1 and 2).

After propensity matching, neurological manifestations such as myasthenia (p=0.002) and NMO (p< 0.001) as well as the frequency of La/SSB antibody (p=0.030) were significantly higher in the TM SLE group (Table 1 and 2).

Kaplan-Meier survival analysis revealed that TM is a significantly poor prognostic factor in SLE patients, with lower survival probability compared to patients without TM (HR: 1.423, 95% CI:1.11-1.82). During the study period, 14.2% of patients with TM died and 8.1% of patients without TM died (RR: 1.75, 95% CI: 1.38-2.21) (Figure 1A and 1B).

Conclusion: Transverse myelitis is a rare, but significant complication of SLE and with a poor prognostic factor in SLE patients. TM was also associated with distinct antibody profiles and clinical manifestations/comorbid conditions, especially other NPSLE findings. Given the risk of profound neurological deficits, early diagnosis and treatment is of the utmost importance to help improve long-term outcomes.

Disclosure: A. Daneshvar: None; **A. Tiwana**: None; **D. Nachawati**: None; **K. Pfeil**: None; **E. Harper**: None; **L. Frumker**: None; **M. Gump**: None; **O. Pamuk**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0604

Assessment of the Metabolic Score for Insulin Resistance (METS-IR) and Its Associated Factors in Patients with Systemic Lupus Erythematosus

Antonio Aznar-Esquivel[1], Fuensanta Gómez-Bernal[1], María García-González[2], Marta Hernández Díaz[1], Juan C. Quevedo-Abeledo[3], Miguel A. González-Gay[4] and Iván Ferraz Amaro[1], [1]Servicio Canario de Salud, La Laguna, Canarias, Spain, [2]Servicio Canario de Salud, La Laguna, Spain, [3]Hospital Doctor Negrín, Las Palmas de Gran Canaria, Canarias, Spain, [4]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The Metabolic Score for Insulin Resistance (METS-IR) is a recently developed index proposed as a predictor of cardiovascular (CV) events. In this study, we calculated the METS-IR in patients with systemic lupus erythematosus (SLE), a condition associated with increased CV risk. We assessed its relationship with disease characteristics and CV comorbidities, including disease activity and damage, lipid profile, carotid atherosclerosis, and insulin resistance (IR) indices.

Methods: A total of 308 patients with SLE were enrolled. METS-IR was calculated as previously described: METS-IR = (Ln [(2 × glucose) + triglycerides] × BMI) / Ln(HDL-cholesterol). Disease activity and damage were assessed using the SLEDAI and SDI scores, respectively. Additional evaluations included a full lipid profile, IR indices via HOMA2 (Homeostatic Model Assessment), and carotid ultrasound to measure intima-media thickness and detect carotid plaques. Multivariable linear regression analysis was performed to examine associations between disease characteristics and METS-IR.

Results: METS-IR value in SLE patients was 39.6 ± 10.2. Both waist and hip circumference were significantly and positively associated with METS-IR. Among classical CV risk factors, hypertension was significantly associated with higher METS-IR values, whereas diabetes and smoking were not. No significant associations were observed between METS-IR and disease duration, SLEDAI score, LLDAS or DORIS remission indices, antinuclear antibody profile, or the use of prednisone or other therapies. The SDI damage index showed a significant association with METS-IR in univariable analysis (β = 1.0, 95% CI 0.3–2.0, p = 0.013), but this was not confirmed after adjustment. In contrast, C-reactive protein levels remained positively associated with METS-IR after adjustment for covariates (β = 0.1, 95% CI 0.05–0.2, p = 0.004). Regarding the lipid profile, METS-IR (which includes HDL and triglycerides in its formula) was not significantly associated with serum total cholesterol or LDL-cholesterol levels but showed significant associations with apolipoprotein A1 (β = -0.08, 95% CI -0.1 to -0.07, p < 0.001) and apolipoprotein B (β = 0.04, 95% CI 0.02–0.06, p < 0.001). Although METS-IR does not include insulin or glucose metabolism parameters, both insulin and C-peptide serum levels showed a significant positive association with METS-IR after adjustment. Similarly, HOMA2-IR and beta-cell function indices were also independently and positively associated with METS-IR. In contrast, the presence of carotid plaque and intima-media thickness were not related to METS-IR values. Notably, the SCORE2 CV risk calculator showed a significant positive association with METS-IR (β = 0.4, 95% CI 0.04–0.7, p = 0.030).

Conclusion: In patients with SLE, the METS-IR index is significantly associated with markers of central adiposity, insulin resistance, classical CV risk factors, inflammatory activity, and CV risk estimation, but not with disease activity, accumulated damage, or subclinical carotid atherosclerosis. These findings suggest that METS-IR reflects the metabolic and cardiovascular risk profile in SLE, independently of specific disease characteristics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Aznar-Esquivel: None; **F. Gómez-Bernal**: None; **M. García-González**: None; **M. Hernández Díaz**: None; **J. Quevedo-Abeledo**: None; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2; **I. Ferraz Amaro**: None.

Abstract Number: 0605

The Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) Predicts Worsening Self-Efficacy in the Patients from the Almenara Lupus Cohort

Anubhav Singh[1], Rocío Gamboa-Cárdenas[2], Victor Pimentel-Quiroz[3], Zoila Rodriguez-Bellido[4], Cesar Pastor-Asurza[5], Risto Perich-Campos[6], Manuel Ugarte-Gil[7] and Graciela Alarcon[8], [1]Baptist hospital of southeast Texas, Beaumont, TX, [2]Universidad Científica del Sur, Lima, Peru, [3]Universidad Científica del Sur, San Isidro, Peru, [4]Universidad Nacional Mayor de San Marcos, Lima, Peru, [5]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Pakistan, [6]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [7]Universidad Cientifica del Sur, Lima, Peru, [8]The University of Alabama at Birmingham, Oakland, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) was developed to ascertain frailty in systemic lupus erythematosus (SLE) patients. The aim of this study is to evaluate the SLICC-FI as a predictor of self-efficacy in patients from a prevalent Latin American Mestizo lupus cohort.

Methods: Patients from a single-center lupus cohort were included in these analyses. Self-efficacy was ascertained with the Patient-Reported Outcomes Measurement Information System (PROMIS) self-efficacy for managing chronic conditions. Frailty was ascertained using the SLICC-FI. Results are shown as means and standard deviations or numbers and percentages, as appropriate. Generalized estimating equations were performed, using each domain of the PROMIS self-efficacy as an outcome in the subsequent visit and the SLICC-FI (as a continuous variable) in the previous visit. Alternative analyses were also carried out including the SLICC-FI as a categorical variable (frail versus non frail). In both approaches, the multivariable models were adjusted for possible confounders (age at diagnosis, sex, socioeconomic status, ethnicity, Systemic

Table 1: The predictive value of the SLICC-FI (as a continuous variable) on PROMIS self-efficacy for managing chronic conditions in SLE patients *Adjusted for age at diagnosis, sex, ethnicity, socioeconomic status, Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K), Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI), disease duration at baseline, prednisone daily dose, antimalarial, immunosuppressive drugs use and the same domain of self-efficacy from the previous visit. **QIC - Quasi-likelihood Information Criterion value to assess model fit

PROMIS	Unadjusted		Adjusted*		QIC**
	B (SE)	*p* value	B (SE)	*p* value	
General	**-1.58 (0.37)**	**<0.001**	**-0.78 (0.31)**	**0.012**	37.288
Medication	**-0.68 (0.31)**	**0.026**	-0.42 (0.30)	0.154	54.044
Social interaction	0.03 (0.28)	0.930	-0.15 (0.23)	0.514	40.351
Symptoms	**-0.82 (0.26)**	**0.002**	-0.39 (0.21)	0.067	62.424
Emotions	-0.23 (0.31)	0.463	-0.14 (0.23)	0.539	38.770
Daily activities	**-1.91 (0.24)**	**<0.001**	**-0.55 (0.19)**	**0.004**	38.967

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: The predictive value of frailty (as a categorical variable) on PROMIS self-efficacy for managing chronic conditions in SLE patients *Adjusted for age at diagnosis, sex, ethnicity, socioeconomic status, Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K), Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI), disease duration at baseline, prednisone daily dose, antimalarial, immunosuppressive drugs use and the same domain of self-efficacy from the previous visit. **QIC - Quasi-likelihood Information Criterion value to assess model fit

PROMIS	Unadjusted		Adjusted*		QIC**
	B (SE)	*p* value	B (SE)	*p* value	
General	**-3.24 (0.88)**	**<0.001**	**-1.30 (0.60)**	**0.031**	36.766
Medication	-1.87 (0.80)	0.019	-1.19 (0.64)	0.061	54.076
Social interaction	-0.02 (0.67)	0.978	-0.32 (0.52)	0.533	40.127
Symptoms	-1.79 (0.67)	0.008	-0.92 (0.48)	0.054	62.254
Emotions	-0.85 (0.71)	0.235	-0.87 (0.53)	0.097	38.809
Daily activities	**-3.86(0.65)**	**<0.001**	**-1.18 (0.41)**	**<0.001**	38.429

Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K), SLICC/American College of Rheumatology Damage Index (SLICC/ACR or SDI), disease duration, prednisone daily dose, antimalarial and immunosuppressive drug use, and the same domain of the PROMIS self-efficacy in the previous visit). Statistical significance set at $p < 0.05$.

Results: Three-hundred and seventy SLE patients and 1561 visits were included in this study; these patients were followed for 4.9 (3.7) years; 342 (92.4%) were women and the age of diagnosis was 35.2 (13.4) years. At baseline, the disease duration was 1.01 (7.4) years, while SDI and SLICC-FI scores were 1.3 (1.5) and 0.17 (0.05), respectively. Eighty patients (21.6%) were classified as frail, 270 (73.0%) were classified as least fit, 20 (5.4%) were classified as less fit, and no patient was classified as robust. At baseline, of the PROMIS general self-efficacy was 47.3 (9.8), self-efficacy for managing emotions was 44.8 (7.5), for managing symptoms was 47.4 (7.5), for managing daily activities was 45.5 (7.2), for managing social interactions was 42.4 (7.6) and for managing medications and treatment was 43.8 (7.5). In the main analyses, after adjusting by possible confounders, the SLICC-FI scores predicted worse general self-efficacy and worse self-efficacy for managing daily activities; these data are depicted in Table 1. In the alternative analyses, the frail category, predicted worse general self-efficacy and worse self efficacy for managing daily activities, after adjustment by possible confounders; these data are depicted in Table 2.

Conclusion: The SLICC-FI predicts worse self-efficacy as assessed by the PROMIS self-efficacy for managing chronic conditions in a prevalent Latin American lupus cohort, supporting the relevance of this index in the evaluation of these patients.

Disclosure: A. Singh: None; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **Z. Rodriguez-Bellido**: None; **C. Pastor-Asurza**: None; **R. Perich-Campos**: None; **M. Ugarte-Gil**: AstraZeneca, 1, 6, Ferrer, 1, GlaxoSmithKlein(GSK), 6, Janssen, 5, technofarma, 1; **G. Alarcon**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0606

Increased Recombinant Zoster Vaccination in SLE following Public Reimbursement: Data from Two Prospective SLE Cohorts

Arielle Mendel[1], Nathalie Amiable[2], Yvan St-Pierre[3], Sasha Bernatsky[4], Ines Colmegna[5], Michaël Desjardins[6], Louis-Pierre Grenier[7], Fares Kalache[8], Christian Pineau[9], Chantal Sauvageau[10], Evelyne Vinet[4] and Paul Fortin[11], [1]McGill University Health Centre, Montreal, QC, Canada, [2]Centre de recherche du CHU de Québec – Université Laval, Quebec City, QC, Canada, [3]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [4]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [5]The Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [6]Centre Hospitalier de l'Université de Montréal (CHUM)), Montreal, QC, Canada, [7]Montreal General Hospital, Montréal, QC, Canada, [8]McGill University Health Center, Montreal, QC, Canada, [9]McGill University, Montreal, QC, Canada, [10]Institut national de santé publique du Québec, Quebec City, QC, Canada, [11]Centre ARThrite - CHU de Québec - Université Laval, Quebec, QC, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Herpes Zoster (shingles) is a common preventable adverse event in SLE. In Quebec, Canada, the Recombinant Zoster Vaccine (RZV) became free of charge for immunocompromised adults in May 2023. We evaluated RZV vaccination rates before and after this date, and examined factors associated with vaccination in SLE.

Methods: We studied participants from 2 prospective SLE cohorts who met ACR/SLICC classification criteria. Annual standardized data collection included demographics, clinical characteristics, medications, and vaccinations. Follow-up started at the first study visit after October 2017 (when RZV first became available), left-censoring person-time prior to the first study visit and excluding participants vaccinated before this date. Follow-up continued until RZV vaccination, death, end of cohort follow-up, or December 31, 2024. We compared vaccination rates before and after May 2023 (start of free vaccination), and evaluated demographic and clinical associations with vaccination using Cox proportional hazards regression.

Results: Among 647 participants, 89% were female, 65% were White, and mean age was 47.4 years (SD 16), with an SLE duration of 15 years (SD 12). Nearly half (46%) were taking an immunosuppressant, primarily mycophenolate (24%). A history of previous shingles was reported in 108/489 (22%; data from one cohort only). Over the study follow-up, 172 (27%) received at least one RZV dose (Table 1). Vaccination rates were higher May 2023-December 2024 (16 per 100 person-years; 95% CI 13-20) compared to October 2017-April 2023 (3 per 100-person years; 95% CI 2-4). In multivariable analyses, age (each year, adjusted HR 1.04; 95% CI 1.02-1.05), White race/ethnicity (aHR 1.7; 95% CI 1.2-2.5), and immunosuppressant use (aHR 2.1, 95% 1.5-3.0) were associated with receiving the RZV, while prednisone use was potentially associated (HR 1.4, 95% CI 0.9-2.2). Among those who received a first RZV dose, 76/170 (45%) received the second dose within 3 months, and 120/139 (86%) received the second within 12 months (median time between doses 84 days, IQR 64-134).

Conclusion: Despite the young age of this cohort, nearly a quarter had previous shingles, highlighting a high burden in SLE. Although a provincial policy providing the 2-dose RZV free of charge to immunocompromised adults was associated with increased vaccination rates, less than a third of patients across both cohorts have been vaccinated. Interventions should target subgroups less likely to receive the vaccine (or complete the vaccination series).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Baseline characteristics of the SLE cohort (N=647)

Characteristic	Overall (N=647)	Site 1* (n=489)	Site 2* (n=158)
Age, mean years (SD)	47.4 (16.1)	**46.5 (16.2)**	**50.3 (15.5)**
Female n (%)	576 (89)	439 (90)	137 (87)
Race/ethnicity n (%)			
White	417 (65)	**276 (56)**	**141 (89)**
Black	80 (12)	**75 (15)**	**5 (3)**
Asian	72 (11)	**71 (15)**	**1 (1)**
Indigenous	13 (2)	12 (2)	1 (1)
Hispanic	24 (4)	22 (5)	2 (1)
Other	34 (5)	**32 (7)**	**2 (1)**
Unknown	7 (1)	1 (0)	6 (4)
Post-secondary education n (%)	499 (77)	380 (77)	125 (79)
Current smoker n (%)	75 (12)	58 (12)	17 (11)
Employment n (%)			
Working	334 (52)	251 (51)	83 (52)
Retired	117 (18)	**79 (16)**	**38 (24)**
Family caregiver	43 (7)	33 (7)	10 (6)
Disability	66 (10)	54 (11)	12 (8)
Student	40 (6)	32 (7)	8 (5)
Other	40 (6)	**40 (8)**	**0 (0)**
SLE characteristics			
SLE duration, mean years (SD)	15.0 (12)	**15.0 (12)**	**12.8 (11.9)**
Years of cohort follow-up, mean (SD)	6.9 (7.5)	**8.1 (9.4)**	**1.4 (1.8)**
SLEDAI-2K ≥4, n (%)	273 (42)	**229 (47)**	**44 (28)**
SLICC Damage Index, mean (SD)	1.3 (2)	**1.4 (2)**	**0.9 (2)**
ACR criteria n (%)			
Mucocutaneous	466 (72)	**365 (75)**	**101 (64)**
Arthritis	506 (78)	383 (78)	123 (78)
Serositis	242 (37)	**201 (41)**	**41 (26)**
Renal	254 (39)	**204 (42)**	**50 (32)**
Neuropsychiatric	55 (9)	46 (9)	9 (6)
Hematologic	531 (82)	**413 (84)**	**118 (75)**
Anti-DNA +	461 (71)	**364 (74)**	**97 (61)**
Antiphospholipid +	258 (40)	187 (38)	71 (45)
Medications n (%)			
Current prednisone	91 (14)	**52 (11)**	**39 (25)**
Prednisone> 20 mg/day in prior year	67 (10)	**40 (8)**	**27 (17)**
Current antimalarial	513 (79)	379 (78)	134 (85)
Current immunosuppressant (any)	295 (46)	215 (44)	81 (51)
Methotrexate	47 (7)	**25 (5)**	**22 (14)**
Mycophenolate	156 (24)	127 (26)	29 (18)
Azathioprine	71 (11)	47 (10)	24 (15)
Tacrolimus	19 (3)	11 (2)	8 (5)
Belimumab	37 (6)	31 (6)	6 (4)
Quality of life			
SF-36 Physical Component Score, mean (SD)	42.7 (10.9)	43.3 (11)	40.3 (10)
SF-36 Mental Component Score, mean (SD)	44.7 (11.8)	45.4 (11.9)	42.1 (11)
Zoster and vaccine history n (%)			
Prior live attenuated varicella vaccine	21 (3)	20 (4)	1 (1)
Prior Zostavax (live attenuated shingles vaccine)	11 (2)	2 (0)	9 (6)
Prior herpes zoster (shingles)	-	108 (22)	-

***Bold** indicates that the 95% CI for difference in mean or proportion between sites excludes the null value

Table 2. Association of baseline characteristics with subsequent RZV vaccination during SLE cohort follow-up (N=647; 3025 person-years)

Characteristic	Hazard Ratio (95% CI)	
	Univariable	Multivariable
Age (each year)	**1.04 (1.03-1.05)**	**1.04 (1.02-1.05)**
Female sex	0.78 (0.5-1.2)	0.87 (0.5-1.4)
White race/ethnicity (vs all other)	**1.96 (1.4-2.8)**	**1.69 (1.2-2.5)**
Post-secondary education	**0.63 (0.5-0.8)**	0.91 (0.6-1.3)
Employed	**0.63 (0.5-0)**	1.09 (0.8-1.6)
Current smoker	0.7 (0.4-1.2)	-
SLE duration at cohort entry (each year)	1.01 (1.00-1.03)	-
Cohort follow-up (each year)	1.01 (0.99-1.03)	-
SLEDAI-2K ≥4	0.94 (0.7-11)	-
SLICC-DI ≥1	1.20 (0.9-1.6)	-
Baseline prednisone	1.59 (1.1-2.3)	1.42 (0.9-2.2)
Baseline immunosuppressant	1.79 (1.3-2.4)	**2.12 (1.5-3.0)**
Baseline mycophenolate	1.05 (0.8-1.5)	-
SF-36 Physical Component Score	**0.98 (0.96 0.99)**	0.99 (0.98-1.01)
SF-36 Mental Component Score	1.01 (1.0-1.03)	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Mendel: None; **N. Amiable**: None; **Y. St-Pierre**: None; **S. Bernatsky**: None; **I. Colmegna**: None; **M. Desjardins**: None; **L. Grenier**: None; **F. Kalache**: None; **C. Pineau**: None; **C. Sauvageau**: None; **E. Vinet**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1.

Abstract Number: 0607

Age at Diagnosis of SLE Has Increased in a United States Longitudinal Cohort

Daniel Goldman[1], Andrea Fava[2], Laurence Magder[3] and Michelle Petri[1], [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]Johns Hopkins University, Baltimore, MD, [3]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The demographics of our lupus cohort have shifted over the decades towards an older population. While much of the shift can be attributed to advances in patient care leading to longer survival, we have also observed an increase in the age at which patients are being diagnosed with lupus. We examined this increase in the age of diagnosis and the impact on the disease manifestation profile.

Methods: The study was based on 3060 patients from a longitudinal SLE cohort in whom the date of SLE diagnosis was known (extracted from review of medical records), and who had at least 1 cohort visit. Patients were divided into 7 cohorts based on the decade of SLE diagnosis (1960-1969, 1970-79, 1980-89, 1990-99, 2000-09, 2010-2019, ≥2020). The catchment area of the cohort has remained Baltimore city and surrounding counties.

The study incorporated all components of the 1997 ACR classification criteria for SLE (malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, pleuritis or pericarditis, proteinuria, neurologic manifestations, hematologic manifestations, immunologic manifestations) to determine if there were differences in the percent of patients presenting with a given

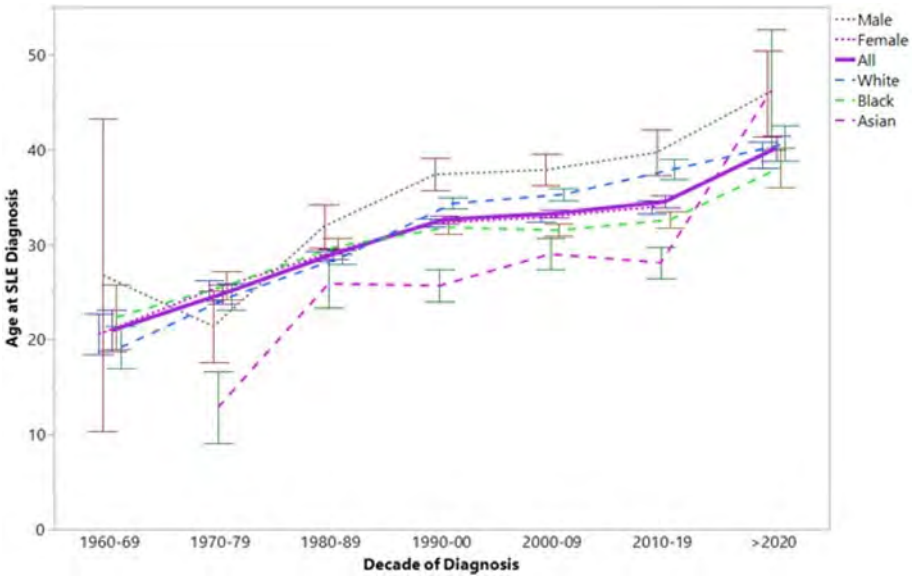


Figure 1 - Average Age of Diagnosis by Decade

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Age of Diagnosis by decade of diagnosis for demographic subgroups – mean ± SD (t-test).

	1960-69 (n=30)	1970-79 (n=117)	1980-89 (n=431)	1990-99 (n=902)	2000-09 (n=919)	2010-19 (n=513)	>2020 (n=148)
All	21.0 ± 12	24.8 ± 11	29.0 ± 11	32.7 ± 13	33.3 ± 13	34.5 ± 14	40.2 ± 16
Female	20.6 ± 11	25.1 ± 11	28.8 ± 11	**32.3 ± 13**	**32.8 ± 13**	**34.0 ± 14**	39.5 ± 16
Male	26.8 ± 23	21.4 ± 12	31.9 ± 12	**37.4 ± 14**	**37.9 ± 15**	**39.7 ± 17**	45.9 ± 18
p-value F vs M	0.4807	0.3023	0.1401	**0.0017**	**0.0012**	**0.0245**	0.1380
Whites (W)	19.1 ± 8	24.5 ± 11	28.7 ± 11	**34.3 ± 13**	**35.3 ± 14**	**38.0 ± 16**	40.6 ± 16
Blacks (B)	22.4 ± 14	25.7 ± 10	29.8 ± 11	**31.8 ± 12**	**31.5 ± 12**	**32.6 ± 13**	38.1 ± 15
East Asians (A)	---	12.8 ± 5.4	25.9 ± 8	**25.7 ± 9**	**29.0 ± 12**	**28 .0± 11**	46.3 ± 22
p-value W vs B	0.4707	0.5735	0.2862	**0.0042**	**<0.0001**	**<0.0001**	0.3933
p-value W vs A	---	0.1369	0.4301	**0.0005**	**0.0013**	**<0.0001**	0.2698
p-value B vs A	---	0.1043	0.2862	**0.0139**	0.2068	**0.0414**	0.1225

Table 2. Manifestations of SLE at Diagnosis, by Age at Diagnosis – Percent of total

Manifestation	< 30 yrs (n=1512)	30 yrs to 50 yrs (n=1189)	> = 50 yrs (n=345)	P-value Pearson	P-value Trend
Malar Rash	**43.9%**	**33.9%**	**22.3%**	**<0.0001**	**<0.0001**
Discoid Rash	11.4%	14.3%	13.7%	0.0659	0.0549
Photosensitivity	36.8%	41.4%	38.1%	0.0520	0.1368
Oral Ulcers	**30.0%**	**39.9%**	**38.2%**	**<0.0001**	**<0.0001**
Arthritis	54.3%	58.4%	58.0%	0.0854	0.0517
Pleuritis or Pericarditis	26.5%	29.1%	28.8%	0.2951	0.1790
Proteinuria	**31.6%**	**23.0%**	**23.1%**	**<0.0001**	**<0.0001**
Neurologic	5.9%	6.0%	7.3%	0.6145	0.4685
Hematologic	**44.0%**	**47.7%**	**53.1%**	**0.0060**	**0.0015**
Immunologic	**58.1%**	**67.3%**	**78.5%**	**<0.0001**	**<0.0001**
ANA positive	**76.4%**	**83.5%**	**88.8%**	**<0.0001**	**<0.0001**

manifestation at the time of SLE diagnosis (and up to 1 year after diagnosis). For analysis of lupus manifestations we used Chi-squared tests (Pearson) and exact Cochran Armitage for trend.

Results: The average age of diagnosis steadily increased over time, from 21.0 years in the 1960's to 40.2 years after 2020 (Figure 1). Similar increases were seen for Blacks, Whites and East Asians as well as females and males (Figure 1). For those diagnosed between 1990 to 2019, men were significantly older than women at diagnosis and Whites were significantly older than Blacks and East Asians at diagnosis (Table 1). Those diagnosed after 30 years of age were more likely to have oral ulcers, hematologic manifestations, immunologic manifestations and positive ANA, and less likely to have malar rash and proteinuria compared to those diagnosed before 30 years of age (Table 2). The same patterns for the ACR classification criteria were also observed at 5 years after diagnosis.

Conclusion: SLE has long been characterized as a disease with onset under 30. While diagnosis before the age of 30 years still predominates, diagnosis after the age of 30 has become more and more evident. SLE diagnosed in older adults exhibits a different profile of manifestations with less malar rash and proteinuria, but more hematologic and immunologic manifestations.

Disclosure: D. Goldman: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **L. Magder**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2.

Abstract Number: 0608

Strong Correlation Between SLEDAI and SLE-DAS in the Spanish Population: Assessment of Discordant Patients

Elena Heras Recuero[1], Antia Garcia Fernandez[2], Cristina Gomez-Moreno[3], Ivan Ferraz Amaro[4], Javier Llorca[5] and Miguel A. González-Gay[6], [1]Hospital Fundacion Jimenez Dias, Madrid, Spain, [2]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain, [3]Fundacion Jiménez Díaz School of Nursing, Madrid, Autonomous University Madrid, Madrid, Spain, [4]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [5]CIBER Epidemiología y Salud Pública (CIBERESP) and Department of Medical and Surgical Sciences, University of Cantabria, Santander, Spain, [6]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

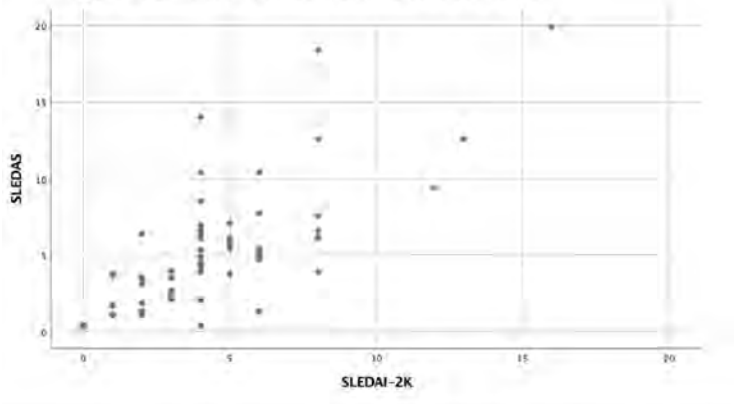
Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Assessing disease activity in systemic lupus erythematosus (SLE) is essential for effective treatment. SLEDAI-2K uses dichotomous items, while SLE-DAS incorporates both dichotomous and continuous variables. We intend to analyze the correlation between SLEDAI-2K and SLE-DAS in patients with systemic lupus erythematosus from central Spain, as well as to identify factors contributing to discordance in disease activity classification.

Methods: Retrospective assessment of 324 SLE patients followed up from 2010 to 2024 at Madrid's Fundación Jiménez Díaz Hospital (Spain). Data were collected from the patients' most recent visits and disease activity was evaluated using SLEDAI-2K and SLE-DAS, and discordant classifications between the tools were analyzed.

Figure 1. Correlation between SLEDAI-2K and SLE-DAS*.



*Strong correlation was observed between both scores (ρ = 0.970, p < 0.001), with high concordance (linearly weighted Kappa index = 0.8004, p < 0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical characteristics of 296 patients classified as having remission or low disease activity according to SLEDAI-2K, who were either concordant or discordant when assessed using SLEDAS.

	Concordant	Discordant	Low disease activity patients	*p value*
n (%)	266 (89.1)	30 (10.1)	296 (100)	
Female, n (%)	237 (89.1)	27 (90.0)	264 (89.2)	1.00
Age at diagnosis, years, mean (SD)	35.0 (19.1)	37.6 (11.4)	35.3 (18.4)	0.47
Disease duration, years, mean (SD)	16.6 (17.1)	13.0 (9.1)	16.2 (16.5)	0.25
Race, n (%)				0.35
White	160 (60.2)	15 (50.0)	175 (59.1)	
Hispanic	93 (34.5)	12 (40.0)	105 (35.5)	
Asian	11 (4.1)	3 (10.0)	14 (4.7)	
Black	2 (0.8)	0 (0)	2 (0.7)	
Hypertension, n (%)	79 (29.7)	7 (23.3)	86 (29.1)	0.47
Diabetes, n (%)	9 (3.4)	4 (13.3)	13 (4.4)	0.03
Dyslipidemia, n (%)	63 (23.7)	7 (23.3)	70 (23.7)	0.97
Smoking, n (%)	36 (13.5)	1 (3.3)	37 (12.5)	0.15
BMI, mean (SD)	24.5 (4.1)	25.0 (4.9)	24.5 (4.1)	0.51
Clinical symptoms, n (%)				
Skin	190 (71.4)	27 (90.0)	217 (73.3)	0.03
Arthritis	174 (65.4)	20 (66.7)	194 (65.5)	0.89
Hematologic	141 (53.0)	22 (73.3)	163 (55.1)	0.03
Renal	75 (28.2)	7 (23.3)	82 (27.7)	0.57
Serositis	30 (11.3)	5 (16.7)	35 (11.8)	0.39
Neurologic	3 (1.1)	1 (3.3)	4 (1.4)	0.35
Pulmonary	4 (1.5)	1 (3.3)	5 (1.7)	0.42
Cardiac	1 (0.4)	0 (0)	1 (0.3)	1.00
Antiphospholipid syndrome n (%)	23 (8.7)	6 (20.0)	29 (9.8)	0.05
SLEDAI-2K value, mean (SD)	0.8 (1.2)	3.0 (1.1)	1.0 (1.4)	<0.001
SLE-DAS value, mean (SD)	0.7 (0.5)	4.6 (1.8)	1.1 (1.4)	<0.001
SDI value 0, n (%)	197 (74.1)	17 (56.7)	214 (72.3)	0.04
SDI value, mean (SD)	0.4 (0.8)	0.8 (1.2)	0.4 (0.8)	0.01
LLDAS 2019, n (%)	263 (98.9)	21 (70.0)	105 (91.3)	<0.001
DORIS 2021, n (%)	255 (96.2)	3 (10.0)	258 (87.5)	<0.001
Antiphospholipid antibodies, n (%)	71 (26.7)	13 (43.3)	84 (28.4)	0.06
Positive Lupus anticoagulant, n (%)	53 (19.9)	9 (30.0)	62 (21.0)	0.20
Anti-dsDNA, n (%)	144 (54.1)	16 (53.3)	160 (54.1)	0.93
Anti-Smith, n (%)	49 (18.4)	7 (23.3)	56 (18.9)	0.52
Anti-U1RNP, n (%)	57 (21.4)	7 (23.3)	64 (21.6)	0.81
Anti-ribosomal P protein, n (%)	14 (5.3)	2 (6.7)	16 (5.4)	0.67
Anti-histones, n (%)	13 (4.9)	1 (3.3)	14 (4.7)	1.00
Anti-nucleosome, n (%)	21 (7.9)	2 (6.7)	23 (7.8)	1.00
Anti-Ro60, n (%)	89 (33.5)	13 (43.3)	102 (34.5)	0.28
Anti-Ro52, n (%)	63 (23.7)	8 (26.7)	71 (24.0)	0.72
Glucocorticoids, n (%)	67 (25.2)	15 (50.0)	82 (27.7)	0.004
Average dose of glucocorticoids (mg/day), mean (SD), in patients receiving glucocorticoids	3.8 (1.4)	4.4 (1.2)	3.9 (1.4)	0.11
Hydroxychloroquine, n (%)	227 (85.3)	25 (83.3)	252 (85.1)	0.77
Immunosuppressants, n (%)	82 (34.9)	13 (48.2)	95 (36.3)	0.18
Biologics, n (%)	32 (12.0)	15 (50.0)	47 (15.9)	<0.001

BMI: body mass index; DORIS: Definition of Remission in Systemic Lupus Erythematosus; LLDAS: Lupus Low Disease Activity State; SD: standard deviation; SDI: Systemic Lupus International Collaborating Clinics / American College of Rheumatology Damage Index; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K); SLE-DAS: Systemic lupus erythematosus disease activity state.

Results: The number of patients in each disease activity category was as follows: Remission (Clinical SLEDAI-2K =0, n=254 [78.4%] vs. clinical SLE-DAS =0, regardless of serology, and prednisone up to 5 mg/day, n=253 [78.3%]); Low activity (SLEDAI-2K 1-4 and prednisone dose ≤ 5 mg/day, n=42 [13.0%] vs. SLE-DAS >0 and ≤ 2.48 with prednisone dose ≤ 7.5 mg/day, n=14 [4.3%]); Mild activity (SLEDAI-2K 1-4 and prednisone dose > 5 mg/day or score 5-6, n=19 [5.9%] vs. SLE-DAS >0 and ≤ 2.48 with prednisone dose > 7.5 mg/day or score >2.48 and ≤7.64, n=46 [14.2%]); Moderate (SLEDAI-2K 7-12 n=7 [2.2%] vs. SLE-DAS >7.64 and ≤9.9 ,n=3 [0.9%]); Severe SLEDAI-2K > 12 (n=2 [0.6%] vs. SLE-DAS >9.9,n=7 [2.2%]). SLEDAI-2K and SLE-DAS showed strong correlation (ρ=0.970, p< 0.001), with high concordance (linearly weighted Kappa index=0.7715, p< 0.001). Forty-four patients were discordant in terms of disease activity categorization. Of these,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariate analysis to identify predictors of discordant evaluation of disease activity when SLEDAI-2K and SLE-DAS were applied.

	OR CI 95%	p value
Skin (ref. absence)	4.36 (1.09, 17.4)	0.04
Hematologic (ref. absence)	2.94 (1.05, 8.29)	0.04
LLDAS (ref. no use)	0.03 (0.01, 0.14)	<0.001
Lupus anticoagulant (ref. negative)	1.73 (0.62, 4.80)	0.29
Corticosteroids (ref. no)	2.06 (0.80, 5.28)	0.13
Biological therapy (ref. no)	5.98 (0.02, 1.32)	0.09

LLDAS: Lupus Low Disease Activity State; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K); SLEDAS: Systemic lupus erythematosus disease activity state.

39 were discordant at only one level of disease activity. Notably, in 37 of the 44 cases, SLE-DAS classified patients as having a higher degree of disease activity compared to SLEDAI-2K. Patients with skin and hematological manifestations were more commonly discordant in terms of disease activity.

Conclusion: SLEDAI-2K and SLE-DAS demonstrate a strong correlation and high reproducibility for assessing disease activity in the Spanish population. However, SLE-DAS offers additional information, particularly in patients with hematologic and skin involvement, enabling a more precise evaluation of disease activity in SLE patient.

Disclosure: E. Heras Recuero: None; **A. Garcia Fernandez**: None; **C. Gomez-Moreno**: None; **I. Ferraz Amaro**: None; **J. Llorca**: None; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2.

Abstract Number: 0609

Neutropenia in SLE: a Retrospective Cohort Study of Etiologies, Severity, Management, and Infection Outcomes

Eleni Papachristodoulou[1] and Vasileios Kyttaris[2], [1]Mount Auburn Hospital, Harvard Medical School, Cambridge, MA, [2]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Neutropenia is a known hematologic manifestation of SLE, yet its clinical implications remain poorly defined. We conducted a retrospective study to characterize the frequency, severity, causes, management, and infectious outcomes of neutropenia episodes in patients with SLE.

Methods: We analyzed data from patients enrolled in the Beth Israel Deaconess Medical Center Lupus Cohort (2008–2025) who met the 1997 ACR SLE classification criteria. Neutropenia episodes were defined as an absolute neutrophil count (ANC) ≤1,500/μL and categorized by severity: mild (ANC 1,000–1,500/μL), moderate (ANC 500–999/μL), or severe (ANC < 500/μL). For each episode, we collected data on demographics, timing relative to SLE diagnosis, clinical features, laboratory data, treatment, presumed etiology (SLE, medications, infections, other), and infections within 30 days.

Results: Among 150 patients with SLE (93% female, mean age 46.2 years; Table 1), 52 (35%) experienced at least one neutropenia episode, totaling 169 episodes (Table 2); 13 (25%) patients had a single episode, while 39 (75%) had recurrent episodes. Episodes occurred a median of 9 years after SLE diagnosis. Neutropenia was prolonged (>4 weeks) in 45 (27%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics of Patients with SLE	
Variable	Patients, n/N (%)
Total number of patients	150 (100%)
Female sex	140/150 (93%)
Age, mean (SD)	46.2 (12.5)
Race	
Asian	19/150 (13%)
Black	47/150 (31%)
White	72/150 (48%)
Other	11/150 (7%)
Comorbidities	
Diabetes Mellitus	21/150 (14%)
Chronic Kidney Disease	20/150 (13%)
Dialysis	2/150 (1%)
Solid Organ Transplant	3/150 (2%)
Sjögren's syndrome	6/150 (4%)
Antiphospholipid syndrome	5/150 (3%)
Outcomes	
Developed neutropenia (≥1 episode)	52/150 (35%)
• Single episode of neutropenia	13/52 (25%)
• Recurrent episodes of neutropenia	39/52 (75%)
Developed infection in the setting of neutropenia	15/52 (28.8%)
Abbreviations: standard deviation, SD.	

episodes. Median ANC was 1.26×10^3/μL; severity was mild in 134 (79%), moderate in 27 (16%), and severe in 8 (5%). Lymphopenia and hypocomplementemia were present in 61% and 57% of episodes, respectively.

Neutropenia was attributed to SLE in 138 episodes (82%), medications in 22 (13%), and as a reaction to an infection in 7 (4%); 2 episodes (1%), both in a single patient, were due to hemophagocytic lymphohistiocytosis (Table 2). Azathioprine and mycophenolate were the most commonly implicated medications, associated with 11 (6%) and 5 (3%) episodes,

Table 2. Characteristics of Neutropenia Episodes	
Variable	n/N of available data, (%)
Total neutropenia episodes	169 (100%)
Years between SLE diagnosis and neutropenia episode identification, median (IQR)	9 (4-15)
Patient age during episode (years), mean (SD)	39.08 (12.6)
Recurrent episodes	156/169 (92.3%)
Isolated episodes	13/169 (7.7%)
Episodes lasting >4 weeks	45/169 (26.6%)
ANC (cells/μL), median (IQR)	1.26 (1.03-1.40)
Concomitant lymphopenia	102/167 (61.1%)
Concomitant hypocomplementemia	79/139 (56.8%)
Severity of Neutropenia	
Mild (ANC 1.000–1.500/μL)	134/169 (79.3%)
Moderate (ANC 500–999/μL)	27/169 (16%)
Severe (ANC <500/μL)	8/169 (4.8%)
Presumed Etiology of Neutropenia	
Underlying SLE disease	138/169 (81.6%)
Immunosuppressive medications	22/169 (13.0%)
• Azathioprine	11/169 (6.5%)
• Mycophenolate mofetil or mycophenolate sodium	5/169 (2.9%)
• Methotrexate	1/169 (0.6%)
• Cyclophosphamide	1/169 (0.6%)
• Upadacitinib	1/169 (0.6%)
• Leflunomide	1/169 (0.6%)
• Dapsone	1/169 (0.6%)
• Rilonacept	1/169 (0.6%)
Infection	7/169 (4.1%)
Hemophagocytic Lymphohistiocytosis[#]	2/169 (1.2%)
Management of Neutropenia	
Escalation of immunosuppression (SLE-related neutropenia)	44/138 (31.9%)
Reduction or discontinuation of causative agent (Medication-related neutropenia)	20/22 (90.9%)
Managed with filgrastim	1/169 (0.6%)
Development of Infections	
Infection in the setting of neutropenia (per episode)*	15/169 (8.9%)
Abbreviations: absolute neutrophil count, ANC; interquartile range, IQR; standard deviation, SD. [#]Both Hemophagocytic Lymphohistiocytosis episodes occurred to the same patient *Each infection occurred in a different patient.	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Parameters of patients with neutropenia and concomitant infections

Age/Sex, comorbidities	ANC, $10^3/\mu L$	Immunosuppressive regimen at neutropenia identification; changes within last 6 months	Infection and testing	Infection Onset Relative to Neutropenia	Presumed neutropenia cause	Infection Treatment, Neutropenia Management and Outcome
37/F, DM	0.01	Corticosteroids, HCQ, MTX, Belimumab; increased MTX dose, started Belimumab	Gingivostomatitis /mucositis, throat culture negative	3 days after	Medication (MTX)	Inpatient workup for neutropenic fever for 3 days, treated with antibiotics for 8 days, full recovery. Neutropenia resolved with MTX discontinuation
47/F, None	0.42	HCQ, MNa, Belimumab; received 4 weekly doses of MTX (5 months before)	Influenza virus, PCR positive	4 days before#	Infection	Outpatient treatment with oseltamivir. Neutropenia resolved post infection.
25/F, None	0.81	Corticosteroids, HCQ, MNa, Belimumab; no changes	Periorbital cellulitis, wound and blood cultures negative	8 days after	Medication (MNa)	Hospitalized for 34 days, treated with IV antibiotics for 28 days for concern of brain abscess, full recovery. Neutropenia resolved with MNa discontinuation
25/F, None	0.94	HCQ; no changes	Coxsackie B infection, positive serologies	Same day as neutropenia	Infection	Inpatient workup for neutropenic fever for 6 days, full recovery. Neutropenia resolved post infection.
34/F, CKD	1.01	Corticosteroids, HCQ, MNa, Belimumab; missed Belimumab doses	Unclear, increased PET scan uptake in axillary & parotid glands, blood & urine cultures negative, suspected viral	Same day as neutropenia	Infection	Inpatient workup for neutropenic fever for 11 days, treated with antibiotics for 3 days, full recovery. Neutropenia resolved post infection.
55/F, None	1.03	Corticosteroids, LEF, Belimumab; missed Belimumab doses	Cervical lymphadenitis, throat culture & Strep test negative	18 days after	SLE-related	Outpatient oral antibiotics (clindamycin and azithromycin) for 10 days, full recovery. Neutropenia persisted post infection and attributed to SLE. Resumed Belimumab.
52/F, Sjogren	1.04	HCQ, Anifrolumab; restarted HCQ and Anifrolumab after break	Cystitis, *Escherichia coli*	1 day after	SLE-related	Outpatient oral Fosfomycin, full recovery. Neutropenia persisted post infection and attributed to SLE. IS unchanged
27/F, DM, CKD	1.11	Rituximab (1 year ago), HCQ, MMF; no changes	Influenza virus, PCR positive	3 days before*	Infection	Inpatient workup & treatment with oseltamivir for 6 days, full recovery. Neutropenia resolved post infection.
30/F, None	1.26	HCQ, AZA; no changes	Cystitis, *Escherichia coli*	3 days after	SLE-related	Outpatient oral Nitrofurantoin, full recovery. Neutropenia persisted post infection and attributed to SLE. IS unchanged
51/F, DM	1.30	Corticosteroids, HCQ, AZA, Belimumab; missed Belimumab doses	Pyelonephritis, *Klebsiella pneumoniae*	3 days before*	Infection	Hospitalized for 3 days, blood cultures remained negative, treated with IV antibiotics, full recovery. Neutropenia resolved post infection.
26/F, None	1.32	HCQ; no changes	Herpes Zoster, clinical diagnosis	4 days after	Infection	Outpatient valacyclovir, full recovery. Neutropenia resolved post infection.
27/F, CKD s/p kidney transplant rejection on dialysis	1.35	Corticosteroids, MNa; no changes	Cellulitis, wound ex: *Proteus spp., Staphylococcus aureus, Enterococcus faecalis, Corynebacterium spp.*	7 days before*	Infection	Hospitalized for 16 days, treated with IV antibiotics, full recovery. Neutropenia resolved post infection.
25/F, None	1.40	HCQ; no changes	Cystitis, *Proteus mirabilis*	6 days after	SLE-related	Outpatient oral Ciprofloxacin, full recovery. Neutropenia persisted post infection and attributed to SLE. IS unchanged
51/F, None	1.42	HCQ, AZA; missing AZA doses	Cystitis, culture negative	3 days after	Medication (AZA)	Outpatient oral Nitrofurantoin, full recovery. Neutropenia resolved with decreasing AZA dose
37/F, Kidney transplant	1.44	MNa; started MNa and tacrolimus after renal transplant (3 months before neutropenia)	BK Virus viremia, PCR positive	Persistent Viremia, started 3 months before*	Medication (MNa)	Outpatient management, chronic transplant rejection. On filgrastim. Neutropenia resolved with holding MNa for 2 weeks,

Abbreviations: absolute neutrophil count, ANC; Diabetes Mellitus, DM; Hydroxychloroquine, HCQ; Methotrexate, MTX; Mycophenolate sodium, MNa; Chronic Kidney Disease, CKD; Polymerase Chain Reaction, PCR; Positron Emission Tomography, PET; Mycophenolate Mofetil, Immunosuppression, IS; MMF; Leflunomide, LEF; Azathioprine, AZA.
#CBC was obtained after the onset of infection
*Bloodwork obtained at the onset of the infectious episode demonstrated normal or elevated ANC

respectively. Neutropenia was managed by escalating immunosuppression in 44 (32%) SLE-related episodes and agent reduction or discontinuation in 20 (91%) medication-related episodes. Filgrastim was used once.

Infections occurred during 15 episodes (9%), including 5 bacterial, 5 viral, and 5 of unknown etiology, each in a different patient (Table 3). No fungal infections were observed. The most frequent site was the urinary tract (n=5, 33%). Infections occurred during SLE-related (4, 27%) or medication-related (4, 27%) neutropenia in 8 episodes (53%), and preceded neutropenia in 7 (47%). Seven infections required hospitalization: 2 with medication-related neutropenia and 5 with infection-related neutropenia. All infections resolved except one case of chronic BK viremia, which preceded the neutropenia episode; no infection-related deaths occurred.

Conclusion: Neutropenia affected over one-third of patients with SLE and was frequently recurrent or prolonged. Most episodes were attributed to active SLE and a minority to medications or infections. Infections during neutropenia were infrequent, generally mild, and often preceded neutropenia, suggesting a reactive process. These findings highlight the heterogeneity of neutropenia in SLE. Clinical context should guide management, and further studies are needed to clarify the clinical significance of neutropenia in SLE and distinguish it from neutropenia in other immunocompromised states.

Disclosure: E. Papachristodoulou: None; **V. Kyttaris**: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0610

The Role of Active Nephritis, Compared to Active Non-Renal SLE, in Pregnancy Outcomes

Emma Trachman[1], Amanda Eudy[2] and Megan Clowse[3], [1]Duke University, Durham, NC, [2]Duke University, Raleigh, NC, [3]Duke University, Chapel Hill, NC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The ACR recommends against pregnancy in patients with SLE with high disease activity. These recommendations do not distinguish between the various manifestations of active SLE. While existing research highlights the poor outcomes associated with active LN during pregnancy, comparative data on pregnancy outcomes in patients with active non-renal SLE remain limited. This study aimed to evaluate pregnancy outcomes across different SLE disease manifestations. Given the pregnancy-related morbidity and mortality associated with social determinants of health in the U.S., this study also assessed and adjusted for characteristics of social disadvantage.

Table 1. Patient Demographics and SLE Activity During Pregnancy

	Overall	Inactive SLE	Non-renal Active SLE	Active LN	p-value (across all 3 groups)
	N=114	n=71	n=26	n=17	
Patient Demographics					
Maternal age at delivery	30.4 (5.2)	31.5 (5.2)	28.6 (4.5)	28.9 (5.3)	0.02
Black Race	55 (48%)	29 (41%)	12 (46%)	14 (82%)	0.007
Education Level: College (n=108)	72 (67%)	53 (77%)	13 (54%)	6 (40%)	0.009
Married/lives with partner (n=106)	82 (77%)	60 (90%)	17 (71%)	5 (33%)	<0.0001
Health Insurance: Medicaid/Medicare (n=108)	31 (29%)	11 (16%)	10 (42%)	10 (67%)	0.0001
Income <$50,000 (n=99)	39 (39%)	16 (25%)	12 (55%)	11 (85%)	<0.0001
Social disadvantage (composite of income <$50,000, Not married or living with partner, and/or Medicare/Medicaid/Uninsured) (n=104)	51 (49%)	21 (32%)	16 (70%)	14 (93%)	<0.0001
History of Lupus Nephritis	33 (29%)	9 (13%)	8 (31%)	17 (100%)	<0.0001
Positive aPL prior to or during pregnancy (n=112)	25 (22%)	14 (20%)	7 (28%)	4 (24%)	0.7
Lupus Activity Labs at Baseline					
dsDNA+	38 (33%)	14 (20%)	14 (54%)	10 (59%)	0.0004
C3/C4	26 (23%)	9 (13%)	11 (42%)	6 (35%)	0.003
SLE Activity in Pregnancy					
At initial rheumatology visit					
Type 1 PGA ≥1.5	13 (11%)	0 (0%)	5 (19%)	8 (47%)	<0.0001
At highest level in pregnancy					
Type 1 PGA ≥1.5	22 (19%)	0 (0%)	10 (38%)	12 (71%)	<0.0001
SLEPDAI +arthritis	32 (28%)	11 (15%)	17 (65%)	4 (24%)	<0.0001
SLEPDAI +rash – *vasculitis, rash, alopecia, mucosal ulcers*	41 (36%)	14 (20%)	17 (65%)	10 (59%)	<0.0001

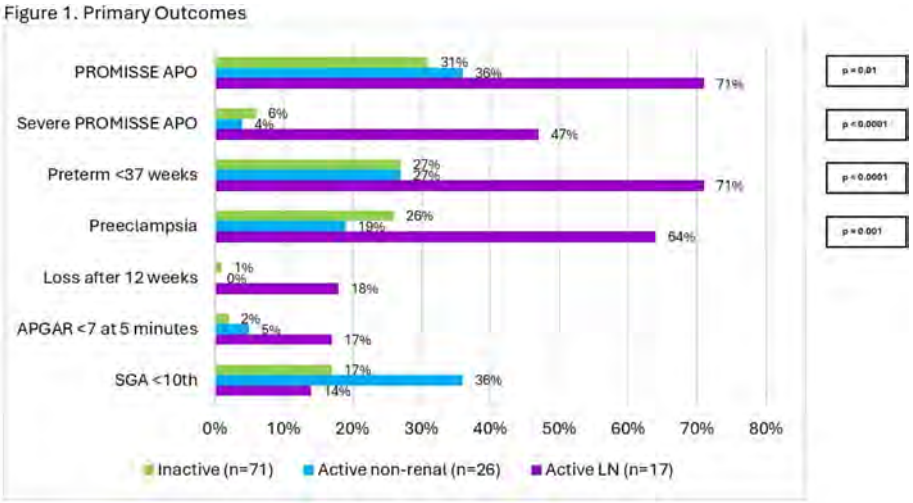
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Modeling Pregnancy Outcomes

	OR (95% CI)
Severe PROMISSE-APO	
Lupus Activity	
Inactive SLE	1.0
Active SLE, non-LN	1.12 (0.09, 13.99)
Active LN	17.81 (2.35, 135.25)
Black Race	3.47 (0.59, 20.39)
Social Disadvantage	0.59 (0.08, 4.58)
PROMISSE-APO	
Lupus Activity	
Inactive SLE	1.0
Active SLE, non-LN	1.63 (0.57, 4.66)
Active LN	3.44 (1.00, 11.83)
Black Race	1.77 (0.68, 4.59)
Social Disadvantage	1.37 (0.51, 3.69)
Preeclampsia	
Lupus Activity	
Inactive SLE	1.0
Active SLE, non-LN	1.40 (0.39, 5.11)
Active LN	5.09 (1.38, 18.71)
Black Race	2.55 (0.79, 8.21)
Social Disadvantage	1.46 (0.47, 4.59)
Preterm birth <37 weeks	
Lupus Activity	
Inactive SLE	1.0
Active SLE, non-LN	1.20 (0.34, 4.29)
Active LN	8.08 (2.05, 31.80)
Black Race	2.51 (0.91, 6.88)
Social Disadvantage	0.42 (0.13, 1.35)
Weeks gestation at delivery	β (95% CI)
Lupus Activity	
Inactive SLE	0
Active SLE, non-LN	-0.99 (-2.30, 0.32)
Active LN	-4.37 (-6.08, -2.67)
Black Race	-0.84 (-1.95, 0.26)
Social Disadvantage	1.11 (-0.10, 2.33)

Methods: We analyzed pregnancies from prospective pregnancy registries at a U.S. center. Disease activity was assessed using the Physician's Global Assessment (PGA) and the SLE Pregnancy Disease Activity Index (SLEPDAI). Patients were categorized into 3 groups: inactive SLE (PGA < 1.5 and SLEDAI < 6 throughout pregnancy, no renal activity), active non-renal SLE (PGA ≥1.5 in pregnancy or SLEDAI ≥6, no renal activity), and active LN (active nephritis during pregnancy). Primary outcomes included PROMISSE adverse pregnancy outcomes (APOs), severe APOs, small for gestational age, preterm birth, preeclampsia, loss after 12 weeks gestations, and APGAR score < 7 at 5 minutes. Race, education, marital status, income, and insurance were also studied. Logistic regression models estimated the association between disease activity group with pregnancy outcomes, adjusting for race and social disadvantage.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Results: We included 114 pregnancies, of which 71 patients had inactive SLE, 26 had active non-renal SLE, and 17 had active LN. Patient demographics and pregnancy outcomes are in Table 1. Nearly all patients were on HCQ (92%) and low dose ASA (87%). At least half of patients in both active SLE groups were also on AZA and prednisone. Half of patients in the LN group had active LN at their initial pregnancy visit.

Active LN was associated with higher rates of APOs, including preeclampsia, preterm birth with delivery 3-5 weeks earlier, and fetal loss, compared to inactive and active non-renal SLE (Fig 1). Despite similar rates of positive dsDNA and hypocomplementemia among patients with LN and those with active non-renal SLE, patients with active non-renal SLE did not experience an increase in APOs relative to the inactive SLE group. The rates of APOs, preterm birth < 37 weeks, and preeclampsia were nearly identical between these groups.

Social disadvantage was most prevalent in the active LN group (93%). In multivariate analysis (Table 2), active LN, but not race or social disadvantage, remained an independent predictor of severe APOs.

Conclusion: Active LN, but not active non-renal SLE, is a strong predictor of adverse pregnancy outcomes. While social disadvantage is associated with active LN in pregnancy, it is not an independent risk factor for adverse pregnancy outcomes. Importantly, non-renal SLE activity may not require delaying pregnancy, even in the presence of serologic activity. Our findings emphasize the need for a dual-pronged approach: prevention of pregnancy in patients with active LN and optimized management for those who conceive with active disease.

Disclosure: E. Trachman: None; **A. Eudy**: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **M. Clowse**: None.

Abstract Number: 0611

Venous Thromboembolism in Patients with Lupus Nephritis: Frequency and Risk Factors – A Cohort Study

Fadi Kharouf[1], Pankti Mehta[2], Qixuan Li[2], Dafna D. Gladman[3], Laura Whitall Garcia[4] and Zahi Touma[5], [1]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [2]Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [3]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [4]University Health Network, Toronto, ON, Canada, [5]University of Toronto, Toronto, ON, Canada

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Venous thromboembolism (VTE) is a known complication of systemic lupus erythematosus (SLE), yet there is a lack of high-quality studies specifically focused on lupus nephritis (LN). This study aimed to assess the frequency of VTE in patients with LN and identify risk factors for its development.

Methods: We included patients with biopsy-proven LN from a prospective observational cohort followed between 1970 and 2024. The primary outcome, VTE occurring after the onset of LN, was monitored longitudinally, and the time to the first event was calculated. Time-dependent univariable and multivariable cause-specific Cox proportional hazards models were used to identify factors associated with the first VTE, with death considered a competing risk.

Results: A total of 324 patients were included in the study, with a mean age of 34.2 years [IQR, 25.9, 43.0] at baseline **(Table 1)**. The cohort was predominantly female (279 patients, 86.1%) and the majority of patients identified as White (184 patients, 57%). Over a long-term follow-up period of 9.9 years [IQR: 5.0–16.4], 30 patients (9.3%) developed at least one VTE, with a median time to the first event from LN onset of 4.3 years [IQR, 0.1, 14.1] **(Figure 1)**. Most events were

Table 1. Patient characteristics at the time of LN onset (baseline).

Variable		Overall (n=324)	No VTE (n=294)	Developed VTE (n=30)
Age in years	Median [IQR]	34.2 [25.9, 43.0]	34.3 [26.3, 43.1]	32.2 [22.2, 39.7]
Sex, male	n (%)	45 (13.9)	40 (13.6)	5 (16.7)
Race	Black, n (%)	61 (18.9)	54 (18.4)	7 (23.3)
	White, n (%)	184 (57.0)	169 (57.7)	15 (50.0)
	Chinese, n (%)	40 (12.4)	36 (12.3)	4 (13.3)
	Other, n (%)	38 (11.8)	34 (11.6)	4 (13.3)
Time from SLE diagnosis in years	Median [IQR]	3.0 [0.54, 9.40]	2.8 [0.4, 9.2]	4.9 [2.0, 10.9]
Cigarette smoking	n (%)	44 (14.1)	43 (15.2)	1 (3.6)
Hypertension	n (%)	166 (51.2)	146 (49.7)	20 (66.7)
Hyperlipidemia	n (%)	238 (73.5)	215 (73.1)	23 (76.7)
Diabetes mellitus	n (%)	24 (7.4)	19 (6.5)	5 (16.7)
Creatinine, μmol/L	Median [IQR]	80.0 [64.0, 107.3]	80.0 [64.3, 111.3]	72.5 [61.3, 90.8]
eGFR, mL/min/1.73 m^2	Median [IQR]	82.2 [55.7, 106.9]	81.3 [54.2, 104.2]	94.7 [68.6, 111.9]
Serum albumin, g/L	Mean [SD]	32.5 (7.4)	32.4 (7.4)	34.2 (7.7)
Low complement	n (%)	199.0 (62.4)	184 (63.7)	15 (50.0)
Positive anti-dsDNA	n (%)	187 (57.7)	169 (57.5)	18 (60.0)
Positive aPLs	n (%)	71 (21.9)	64 (21.8)	7 (23.3)
Proteinuria, g/day	Median [IQR]	2.2 [1.0, 3.6]	2.2 [1.0, 3.6]	2.4 [1.6, 4.0]
	Mean [SD]	2.9 (2.8)	2.9 (2.8)	3.0 (2.3)
SLEDAI-2K	Median [IQR]	14.0 [10.0, 20.0]	14.0 [9.0, 20.0]	14.0 [10.0, 16.0]
SDI	Median [IQR]	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.0 [0.0, 1.8]
Biopsy class	I or II, n (%)	40 (12.3)	35 (11.9)	5 (16.7)
	III, n (%)	67 (20.7)	63 (21.4)	4 (13.3)
	IV, n (%)	103 (31.8)	91 (31.0)	12 (40.0)
	III/VI+V, n (%)	45 (13.9)	42 (14.3)	3 (10.0)
	V, n (%)	59 (18.2)	54 (18.4)	5 (16.7)
	VI, n (%)	10 (3.1)	9 (3.1)	1 (3.3)
NIH Activity Index	Median [IQR]	3.5 [1.0, 7.0]	3.0 [1.0, 7.0]	4.0 [1.5, 9.0]
NIH Chronicity Index	Median [IQR]	2.0 [0.0, 4.0]	2.0 [0.0, 4.0]	2.0 [0.0, 3.0]
Glucocorticoid use	n (%)	314 (96.9)	284 (96.6)	30 (100.0)
Use of immunosuppressives during first year	n (%)	251 (77.5)	226 (76.9)	25 (83.3)
Immunosuppressives used during the first year	MMF, n (%)	131 (40.4)	112 (38.1)	19 (63.3)
	CYC, n (%)	31 (9.6)	28 (9.5)	3 (10.0)
	AZA, n (%)	134 (41.4)	127 (43.2)	7 (23.3)
	Other*, n (%)	33 (10.2)	30 (10.2)	3 (10.0)
Antimalarial use	n (%)	186 (57.4)	166 (56.5)	20 (66.7)

VTE, venous thromboembolism; LN, lupus nephritis; SLE, systemic lupus erythematosus; IQR, interquartile range; eGFR, estimated glomerular filtration rate; dsDNA, double-stranded DNA; aPLs, antiphospholipid antibody; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SDI, Systemic Lupus International Collaboration Clinics (SLICC)/ACR Damage Index; NIH, National Institutes of Health; MMF, mycophenolate mofetil; CYC, cyclophosphamide; AZA, azathioprine
*Cyclosporine, Tacrolimus, rituximab, or Belimumab

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

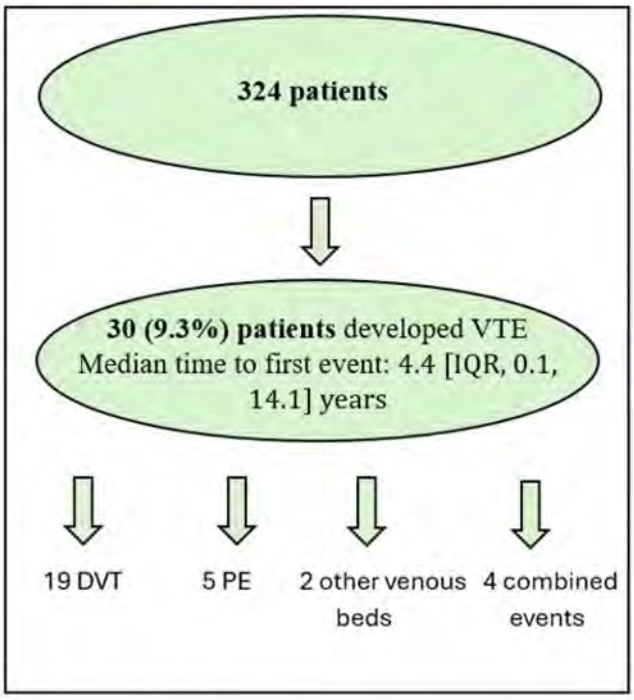


Figure 1. A flowchart depicting the frequency of venous thromboembolic events in our cohort and the involved venous beds.

DVT, deep vein thrombosis; PE, pulmonary embolism

isolated (86.7%), including 19 deep vein thromboses (DVTs, 59.4%), 5 pulmonary embolisms (PEs), and 2 events involving other venous beds.

In the multivariable model, the following factors were independently associated with the development of VTE: the SLEDAI-2K score (HR = 1.05, 95% CI: 1.01–1.10) and proteinuria level (HR = 1.26, 95% CI: 1.08–1.47) **(Table 2)**.

Conclusion: VTE can complicate the course of LN at any stage, mostly manifesting as DVT and PE. Disease activity and proteinuria are the primary risk factors for its development.

Table 2. Time-dependent univariable and multivariable cause-specific Cox proportional hazard models for factors associated with VTE in our cohort[a].

Variable		Univariable HR (95% CI)	p-value	Multivariable HR (95% CI)	p-value
Age at LN onset (1-year increase)		0.99 (0.96,1.03)	0.59		
Black vs. non-Black		1.67 (0.71,3.94)	0.24		
SLE duration (1-year increase)		1.04 (0.99,1.09)	0.16		
Number of comorbidities~ (0 as a reference)	1-2	0.91 (0.23,3.62)	0.89		
	3-4	2.27 (0.67,7.67)	0.19		
SLEDAI-2K score (1-unit increase)		1.09 (1.06,1.13)	**<0.01***	1.05 (1.01,1.10)	**0.03***
Albumin in g/L (1-unit increase)		0.89 (0.85,0.94)	**<0.01***	0.98 (0.91,1.05)	0.60
Proteinuria in g/day, (1-unit increase)		1.36 (1.21,1.52)	**<0.01***	1.26 (1.08,1.47)	**<0.01***
Membranous (including mixed) LN vs. others		0.94 (0.41,2.14)	0.88		
Positive aPLs		2.99 (1.32,6.76)	**<0.01***	1.95 (0.73,5.19)	0.18

VTE, venous thromboembolism; HR, hazard ratio; CI, confidence interval; LN, lupus nephritis; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; aPLs, antiphospholipid antibodies

~Diabetes mellitus, hypertension, hyperlipidemia, or active smoking

[a]Death was used as a competing risk

*Statistically significant ($p < 0.05$)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: F. Kharouf: None; **P. Mehta**: None; **Q. Li**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Whitall Garcia**: None; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2.

Abstract Number: 0612

Is Antimalarial Use Associated with a Reduced Risk of Lupus Nephritis in Patients with SLE? Results from an Inception Cohort-Based Study

Fadi Kharouf[1], JuanPablo Diaz Martinez[2], Pankti Mehta[3], Dafna D. Gladman[4], Laura Whitall Garcia[5] and Zahi Touma[6], [1]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [2]Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [3]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [4]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [5]University Health Network, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Antimalarials, particularly hydroxychloroquine, are a cornerstone of systemic lupus erythematosus (SLE) management, with well-established benefits including reduced disease activity, prevention of flares, and mitigation of long-term organ damage. We aimed to assess whether antimalarial use is associated with a decreased risk of developing incident lupus nephritis (LN) among patients with SLE.

Table 1: Baseline Characteristics at Clinic Entry.

Characteristic	Total (n = 674)	Never developed Proteinuria (n = 520)	Developed Proteinuria (n = 154)
Age, years (median [IQR])	33.6 [24.9–45.4]	34.4 [25.3–46.4]	30.8 [23.5–41.3]
Sex, Female (%)	598 (88.7%)	465 (89.4%)	133 (86.4%)
Race (%)			
Black	74 (11.2%)	51 (10.0%)	23 (15.1%)
Chinese	47 (7.1%)	38 (7.5%)	9 (5.9%)
White	461 (69.8%)	354 (69.7%)	107 (70.4%)
Other	78 (11.8%)	65 (12.8%)	13 (8.6%)
Disease duration, years (mean ± SD)	0.21 ± 0.27	0.22 ± 0.27	0.19 ± 0.24
Diagnosis before 2005 (%)	412 (61.1%)	306 (58.8%)	106 (68.8%)
Serum creatinine, µmol/L (median [IQR])	68.0 [58.0–80.0]	67.0 [57.0–79.0]	71.0 [60.5–80.0]
eGFR (MDRD), mL/min/1.73m² (median [IQR])	96.7 [80.9–118.8]	96.8 [81.7–118.6]	96.6 [78.9–119.1]
Low C3 (%)	232 (35.9%)	175 (34.9%)	57 (39.3%)
Low C4 (%)	180 (30.1%)	122 (25.8%)	58 (46.4%)
Anti-dsDNA positive (%)	314 (50.7%)	220 (46.4%)	94 (64.8%)
SLEDAI-2K (median [IQR])	6.0 [2.0–9.0]	6.0 [2.0–9.0]	6.0 [4.0–11.8]
SDI (median [IQR])	0.0 [0.0–0.0]	0.0 [0.0–0.0]	0.0 [0.0–0.0]
Glucocorticoid use (%)	334 (49.8%)	237 (45.8%)	97 (63.0%)
Antimalarial use (%)	294 (43.8%)	234 (45.3%)	60 (39.0%)
Chloroquine (%)	63 (21.4%)	46 (19.7%)	17 (28.3%)
Hydroxychloroquine (%)	231 (78.6%)	188 (80.3%)	43 (71.7%)
Antimalarial dose, mg/day (mean ± SD)	312.3 ± 95.5	315.7 ± 91.4	299.1 ± 110.0
Cumulative exposure, years (mean ± SD)	0.30 ± 1.22	0.34 ± 1.36	0.17 ± 0.55
Immunosuppressive use (%)	105 (15.6%)	81 (15.7%)	24 (15.6%)
Cyclophosphamide (%)	7 (6.7%)	4 (4.9%)	3 (12.5%)
Azathioprine (%)	49 (46.7%)	39 (48.1%)	10 (41.7%)
Methotrexate (%)	24 (22.9%)	17 (21.0%)	7 (29.2%)
Mycophenolate mofetil (%)	25 (23.8%)	21 (25.9%)	4 (16.7%)

IQR = Interquartile range; SD = Standard deviation; eGFR = Estimated glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; C3/C4 = Complement components 3 and 4; anti-dsDNA = Anti–double-stranded DNA antibody; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariable Cox Regression Analysis of Factors Associated with the Development of Lupus Nephritis in Patients with SLE

Variable	HR (95% CI)*	p-value
Cumulative duration of antimalarial exposure in years (1-unit increase)	0.96 (0.92–1.00)	0.08
Age in years (1-unit increase)	1.00 (0.99–1.02)	0.70
Sex (female sex as a reference)	1.57 (0.91–2.69)	0.10
Race (Black as a reference)	0.85 (0.52–1.39)	0.52
SLE disease duration in years (10-unit increase)	0.64 (0.58–0.71)	**<0.01**
Low C3	1.31 (0.85–2.01)	0.22
Low C4	0.71 (0.47–1.10)	0.12
Anti-dsDNA	1.41 (0.96–2.09)	0.08
SLEDAI-2K score (1-unit increase)	1.23 (1.19–1.26)	**<0.01**
Glucocorticoid use	1.53 (0.99–2.34)	0.053
Immunosuppressive use	1.04 (0.70–1.55)	0.84

HR = Hazard Ratio; CI = Confidence Interval; SLE = Systemic Lupus Erythematosus; C3 = Complement component 3; C4 = Complement component 4; anti-dsDNA = Anti–double-stranded DNA antibody; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000
*Adjusted for calendar time (pre-2005 vs. 2005 and onward), reflecting the introduction of mycophenolate mofetil into routine care within the cohort.

Methods: We included SLE patients from an inception cohort without prior diagnosis of LN, followed prospectively at regular intervals. The association between antimalarial exposure (measured as cumulative duration in years) and the development of LN (defined by new-onset proteinuria as per SLE Disease Activity Index 2000 [SLEDAI-2K]) was evaluated using a time-dependent univariable Cox proportional hazards model to estimate the overall effect. A time-dependent multivariable Cox regression model adjusted for clinically relevant covariates was also employed to estimate the risk of LN in the full cohort and, in a sensitivity analysis, among patients with serologically active disease. Death was treated as a competing risk.

Results: A total of 674 inception SLE patients were included, with a median baseline age of 33.6 years [IQR: 24.9, 45.4] **(Table 1)**. Over 6,961.5 patient-years of follow-up, 154 patients (22.8%) developed new-onset SLE-related proteinuria, indicating LN, yielding an incidence rate of 2.2 cases per 100 person-years. The median time to LN onset was 3.6 years [IQR: 0.9–8.8]. Cumulative antimalarial exposure was not significantly associated with reduced LN risk, in either the univariable analysis (HR: 0.98; 95% CI: 0.94–1.02, p=0.25) or the adjusted multivariable model (HR: 0.96; 95% CI: 0.92–1.00, p=0.08) **(Table 2)**. Similar results were observed in the sensitivity analysis restricted to patients who presented with serologically active disease (HR: 0.95; 95% CI: 0.89–1.01, p=0.12) **(Table 3)**. Notably, shorter SLE duration (HR: 0.64; 95% CI: 0.58–0.71 per 10-year increase) and higher SLEDAI-2K scores (HR: 1.23; 95% CI: 1.19–1.26) were significantly associated with increased risk of LN **(Table 2)**. This association persisted in patients with serologically active disease, along with glucocorticoid use **(Table 3)**, likely reflecting confounding by indication.

Table 3. Multivariable Cox Regression Analysis of Factors Associated with the Development of Lupus Nephritis in Patients presenting with serologically active disease

Variable	HR (95% CI)*	p-value
Cumulative duration of antimalarial exposure in years (1-unit increase)	0.95 (0.89–1.01)	0.12
Age in years (1-unit increase)	1.00 (0.98–1.02)	0.98
Sex (female sex as a reference)	1.43 (0.75–2.73)	0.28
Race (Black as a reference)	1.20 (0.62–2.32)	0.58
SLE disease duration in years (10-unit increase)	0.63 (0.55–0.72)	**<0.01**
Low C3	1.19 (0.69–2.04)	0.54
Low C4	0.64 (0.39–1.07)	0.09
Anti-dsDNA	1.30 (0.70–2.44)	0.41
SLEDAI-2K score (1-unit increase)	1.21 (1.17–1.26)	**<0.01**
Glucocorticoid use	2.71 (1.47–4.99)	**<0.01**
Immunosuppressive use	0.97 (0.60–1.57)	0.92

HR = Hazard Ratio; CI = Confidence Interval; SLE = Systemic Lupus Erythematosus; C3 = Complement component 3; C4 = Complement component 4; anti-dsDNA = Anti–double-stranded DNA antibody; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000
*Adjusted for calendar time (pre-2005 vs. 2005 and onward), reflecting the introduction of mycophenolate mofetil into routine care within the cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this inception cohort-based study, antimalarial use was not significantly associated with a reduced risk of incident LN. These findings should be interpreted within the context of the study's specific objective and are not intended to challenge the well-established role of antimalarials in the management of SLE or their recognized clinical benefits. Further studies with larger sample sizes are needed to confirm our results.

Disclosure: F. Kharouf: None; **J. Diaz Martinez**: None; **P. Mehta**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Whitall Garcia**: None; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2.

Abstract Number: 0613

A Baseline Kidney Biopsy Is Not Always Feasible in Incident Lupus Nephritis: Insights from an Inception Cohort

Fadi Kharouf[1], Pankti Mehta[2], Qixuan Li[3], Dafna D. Gladman[4], Zahi Touma[5] and Laura Whitall Garcia[6], [1]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [2]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [3]Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [4]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [5]University of Toronto, Toronto, ON, Canada, [6]University Health Network, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Baseline kidney biopsy is the gold standard for diagnosing incident lupus nephritis (LN). However, in certain cases, obtaining a biopsy may not be feasible due to medical, technical, or patient-specific factors, resulting in a clinical diagnosis of LN. We aimed to evaluate differences in outcomes between biopsy-confirmed and clinically diagnosed LN cases to provide guidance in scenarios where a biopsy cannot be obtained.

Methods: This retrospective study included inception SLE patients from an observational cohort (2000–2024) who developed incident LN. Patient inclusion began in 2000 to reflect treatment changes associated with the introduction of mycophenolate mofetil. The outcomes assessed were: (1) complete proteinuria recovery (CPR) (< 0.5 g/g) at one year; (2) progression to end-stage kidney disease (ESKD), defined as eGFR < 15 mL/min/1.73 m^2, dialysis, or kidney transplantation, or a sustained ≥30% eGFR decline; and (3) a composite adverse outcome, including infection, hospitalization, or death. Time-to-event outcomes were evaluated using Kaplan-Meier (KM) survival curves. Comparisons between biopsy-confirmed and clinically diagnosed LN groups were assessed using Fine-Gray subdistribution hazard models, treating death as a competing risk for the first two outcomes. The models were adjusted for proteinuria as a potential confounder, as well as for imbalanced variables known to clinically impact the outcomes.

Results: 127 patients were included: 84 (66.1%) with biopsy-confirmed LN and 43 (33.9%) with clinically diagnosed LN). Baseline characteristics are summarized in **Table 1**. Baseline differences were observed in age, proteinuria and albumin levels, SLEDAI-2K, and SLICC/ACR damage index (SDI). Outcomes are summarized in **Table 2**, and KM curves are provided in **Figures 1A-C**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics at LN onset in patients with clinically diagnosed and biopsy confirmed LN.

Variable	Overall (n=127)	Clinically Diagnosed (n=43)	Biopsy-confirmed (n=84)	p-value
Age in years, Median [IQR]	34.5 [25.6, 43.8]	28.4 [21.5, 41.6]	36.4 [27.2, 44.7]	0.09
Sex, male, n (%)	15 (11.8)	6 (14.0)	9 (10.7)	0.81
Race				
Black, n (%)	35 (28.0)	12 (28.6)	23 (27.7)	
White, n (%)	49 (39.2)	17 (40.5)	32 (38.6)	0.81
Chinese, n (%)	17 (13.6)	4 (9.5)	13 (15.7)	
Other, n (%)	24 (19.2)	9 (21.4)	15 (18.1)	
SLE duration in years, Median [IQR]	0.36 [0.15, 1.01]	0.37 [0.17, 4.41]	0.36 [0.13, 0.90]	0.20
Follow-up duration in years, Median [IQR]	7.3 [4.7, 12.0]	5.4 [2.4, 7.6])	9.4 [5.8, 12.5]	**<0.01**
Hypertension, n (%)	86 (67.7)	29 (67.4)	57 (67.9)	1.00
Hyperlipidemia, n (%)	102 (80.3)	37 (86.0)	65 (77.4)	0.35
Diabetes mellitus, n (%)	8 (6.3)	2 (4.7)	6 (7.1)	0.87
Creatinine, µmol/L, Median [IQR]	69.0 [56.5, 90.5]	67.0 [57.5, 88.5]	69.5 [56.8, 92.0]	0.58
eGFR, mL/min/1.73 m², Median [IQR]	96.5 [74.4, 121.7]	99.0 [80.0, 121.8]	95.5 [69.5, 119.7]	0.38
Serum albumin, g/L, Median [IQR]	33.0 [29.0, 37.0]	36.0 [31.0, 39.0]	33.0 [27.0, 36.0]	**0.01**
Low complement, n (%)	84 (67.2)	30 (73.2)	54 (64.3)	0.43
Positive anti-dsDNA, n (%)	91 (71.7)	33 (76.7)	58 (69.0)	0.48
Proteinuria, g/day, Mean (SD)	2.6 (2.2)	2.2 (1.7)	2.9 (2.3)	0.12
Hematuria, n (%)	74 (58.3)	21 (48.8)	53 (63.1)	0.18
SLEDAI-2K, Median [IQR]	14.0 [10.0, 18.0]	12.0 [8.0, 16.0]	16.0 [12.0, 20.0]	**<0.01**
SDI, Median [IQR]	0.0 [0.0, 1.0]	0.0 [0.0, 1.0]	0.0 [0.0, 0.0]	**0.01**
Biopsy class (n=84)				
I or II, n (%)	2 (2.4)	—	2 (2.4)	
III, n (%)	14 (16.7)	—	14 (16.7)	
III+V, n (%)	7 (8.3)	—	7 (8.3)	NA
IV, n (%)	25 (29.8)	—	25 (29.8)	
IV+V, n (%)	15 (17.9)	—	15 (17.9)	
V, n (%)	21 (25.0)	—	21 (25.0)	
NIH Activity index, Median [IQR]	5.0 [0.0, 8.0]	—	5.00 [0.0, 8.0]	NA
NIH Chronicity index, Median [IQR]	3.0 [1.0, 3.0]	—	3.0 [1.0, 3.0]	NA
Glucocorticoid use, n (%)	127 (100.0)	43 (100.0)	84 (100.0)	1.00
Glucocorticoid dose during first year, Median [IQR]*	19.2 [14.4, 26.7]	19.2 [15.5, 25.0]	19.3 [14.0, 27.9]	0.73
Use of immunosuppressives during first year, n (%)	123 (96.9)	43 (100.0)	80 (95.2)	0.36
Mycophenolate Mofetil, n (%)	97 (76.4)	37 (86.0)	60 (71.4)	0.11
Cyclophosphamide, n (%)	17 (13.4)	4 (9.3)	13 (15.5)	0.49
Azathioprine, n (%)	36 (28.3)	8 (18.6)	28 (33.3)	0.13
Other (Cyclosporine, Tacrolimus, Rituximab, Belimumab), n (%)	17 (13.4)	7 (16.3)	10 (11.9)	0.68
Antimalarial use, n (%)	97 (76.4)	36 (83.7)	61 (72.6)	0.24
ACEi or ARB use during first year, n (%)	86 (67.7)	28 (65.1)	58 (69.0)	0.80

Abbreviations: LN, lupus nephritis; SLE, systemic lupus erythematosus; IQR, interquartile range; eGFR, estimated glomerular filtration rate; dsDNA, double-stranded DNA; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SDI, SLICC/ACR Damage Index; NA, Not Applicable; NIH, National Institutes of Health; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

Statistically significant p-values are in bold (p < 0.05). Biopsy class and NIH indices only available for patients who underwent kidney biopsy.

*The 5-year cumulative glucocorticoid dose was not significantly different between patients who underwent a kidney biopsy (median 125.1 mg [IQR: 75.8, 212.5]) and those who did not (median 111.0 mg [IQR: 73.0, 148.8]; p = 0.07).

< - **CPR at 1 Year:** Achieved in 58.4% of patients, with no significant differences between groups in rate (p=0.36) and time to event (p=0.81). Adjusted models indicated comparable risk (HR 1.19, 95% CI: 0.76–1.84).

< - **ESKD or ≥30% Decline in eGFR:** Occurred in 22.4% of patients, with no significant differences between groups in rate (p=0.39), time to event (p=0.66), or risk (HR 1.11, 95% CI: 0.46–2.69).

Table 2. Outcomes of patients with clinically diagnosed and biopsy-confirmed lupus nephritis.

	Overall (n=127)	Clinically Diagnosed (n=43)	Biopsy-confirmed (n=84)	p-value
Outcomes				
Complete proteinuria recovery at 1 year, n (%)	73 (58.4)	28 (65.1)	45 (54.9)	0.36
Time to CPR, years, Median [IQR]	0.8 [0.3, 2.2]	0.9 [0.3, 1.7]	0.8 [0.5, 2.3]	0.81
ESKD or sustained[a] ≥30% decline in eGFR, n (%)	28 (22.4)	7 (16.7)	21 (25.3)	0.39
Time to ESKD or ≥30% eGFR decline, years	5.9 [2.2, 9.9]	3.4 [1.4, 7.2]	7.1 [3.9, 10.0]	0.66
Infection, hospitalization, or death, n (%)	70 (55.1)	19 (44.2)	51 (60.7)	0.11
Time to infection, hospitalization, or death, years	2.7 [0.8, 5.8]	1.6 [0.6, 4.0]	3.22 [0.8, 7.2]	0.60

Abbreviations: CPR, complete proteinuria recovery; ESKD, end-stage kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range

[a]Observed over at least two consecutive visits

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

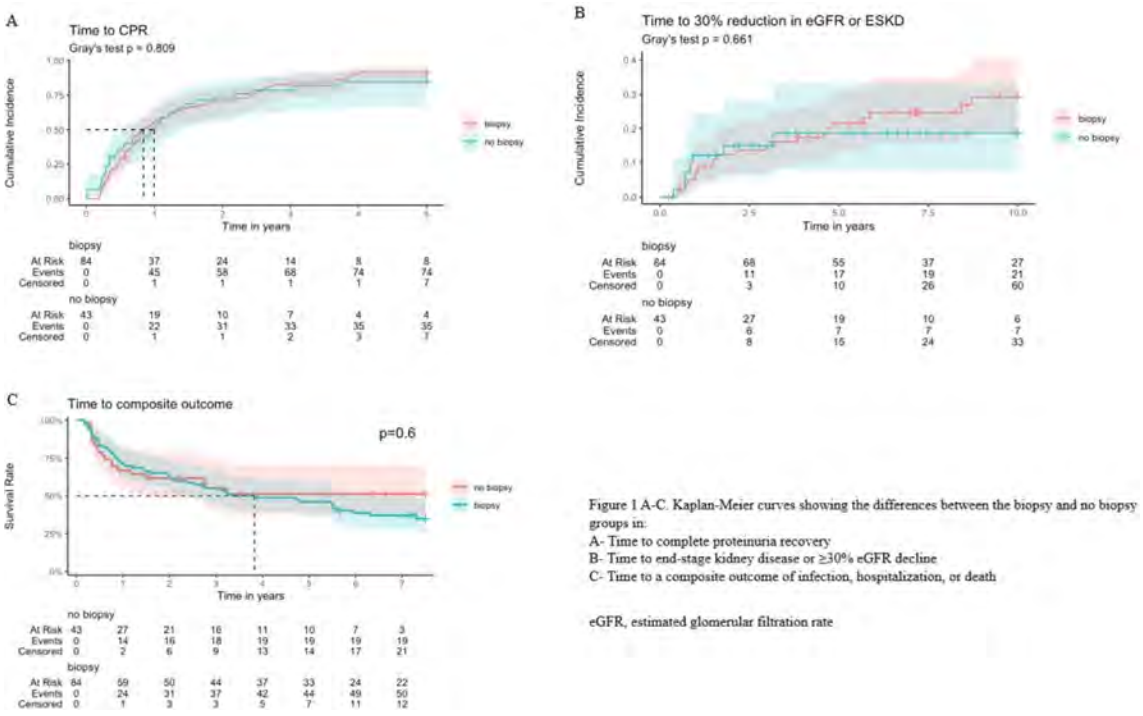


Figure 1 A-C. Kaplan-Meier curves showing the differences between the biopsy and no biopsy groups in:
A- Time to complete proteinuria recovery
B- Time to end-stage kidney disease or ≥30% eGFR decline
C- Time to a composite outcome of infection, hospitalization, or death

eGFR, estimated glomerular filtration rate

< - **Composite Outcome:** Occurred in 55.1% of the cohort, with no significant differences between groups in rate (p = 0.11), time to event (p = 0.60), or risk (HR 0.99, 95% CI: 0.56–1.74).

Conclusion: Clinically diagnosed incident LN, when treated according to standard-of-care protocols, shows comparable outcomes to biopsy-confirmed LN. While these findings may provide some reassurance, they apply specifically to cases where a baseline biopsy is not feasible and should not be interpreted as a challenge to current diagnostic standards.

Disclosure: F. Kharouf: None; **P. Mehta**: None; **Q. Li**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **L. Whitall Garcia**: None.

Abstract Number: 0614

Evaluating Cardiovascular Risk in Systemic Lupus Erythematosus: Comparing Novel Risk Scores with Carotid Ultrasound

Ileana C. Reynosa-Silva[1], Oscar Azael Garza-Flores[2], Fernanda M. Garcia-Garcia[3], Aleydis Gonzalez-Melendez[1], Iris J. Colunga-Pedraza[3], Dionicio A. Galarza-Delgado[3], Jose R Azpiri-Lopez[4], Rosa Arvizu-Rivera[5], Jesus Alberto Cardenas-de la Garza[6] and Diego Azamat Salcedo Almanza[7], [1]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [4]Cardiology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [5]Hospital Universitario \"Dr. Jose Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico, [6]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [7]Radiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease associated with an elevated risk of cardiovascular (CV) disease, largely due to chronic inflammation and its contribution to atherogenesis. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) score estimates the probability of advanced coronary artery atherosclerosis using eight factors: age, sex, cholesterol levels, smoking status, blood pressure, presence of obesity, and hyperglycemia. The PREVENT (Predicting Risk of Cardiovascular Disease Events) calculator estimates 10- and 30-year risks for atherosclerotic cardiovascular disease (ASCVD) and heart failure. Both tools are designed for younger populations, making them potentially applicable to patients with SLE, who are at risk of developing premature ASCVD. However, the utility of these new scores in this population remains underexplored. Therefore, the objective was to evaluate the correlation between carotid intima-media thickness (cIMT) and CV risk as estimated by the PDAY and PREVENT tools in patients with SLE.

Methods: A cross-sectional study was conducted including SLE patients aged ≥15 years who met the 2019 ACR/EULAR classification criteria. Patients with established cardiovascular disease, overlap syndromes, or current pregnancy were excluded. Carotid ultrasound was used to assess cIMT via B-mode ultrasonography. PDAY scores and PREVENT 10- and 30-year ASCVD risk estimates were calculated for all participants. The Kolmogorov–Smirnov test assessed data normality. Spearman's correlation coefficients (rs) were calculated to assess associations between PDAY/PREVENT scores and left/right cIMT values. A p-value ≤0.05 was considered statistically significant.

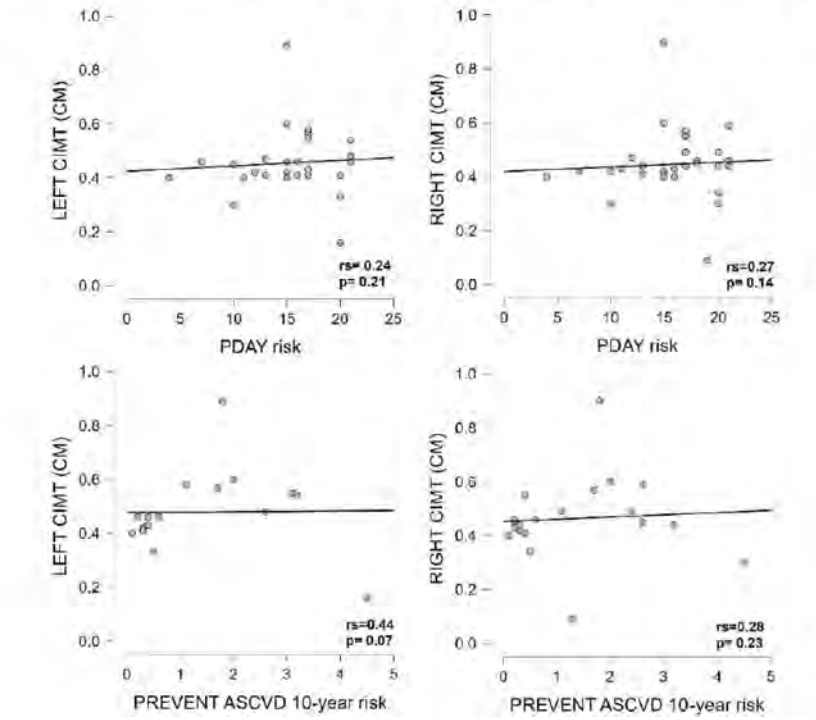
Results: Thirty-five SLE patients were included (mean age 39.6 ± 13.6 years; 94.2% female). Clinical and disease characteristics are detailed in Table 1. The mean SLEDAI score was 10.1, indicating moderate disease activity. The median PDAY score was 15. The mean 10- and 30-year ASCVD risks estimated by PREVENT were 1.4% and 6.9%, respectively. Mean

Table 1. Demographic, clinical, and disease characteristics.

	SLE patients (n=35)
Age (years), mean ± SD	39.6 ± 13.6
Women, n (%)	33 (94.2)
Disease duration (years), mean ± SD	7.6 ± 6.6
Non-HDL cholesterol (mg/dL), mean ± SD	93 ± 46.22
HDL cholesterol, (mg/dL), mean ± SD	50.2 ± 15.2
Smoking, n (%)	2.0 (5.88)
Hypertension, n (%)	12 (35.2)
Obesity, n (%)	8.0 (23.5)
HbA1c, mean ± SD	5.45 ± 0.8
HCQ, n (%)	32 (94.1)
Glucocorticoids, n (%)	25 (73.5)
SLEDAI-2K (points), mean ± SD	10.1 ± 6.8
PDAY risk, median, (IQR)	15 (10-18)
PREVENT ASCDV 10-year risk, mean ± SD	1.4 ± 1.2
PREVENT ASCVD 30-year risk, mean ± SD	6.9 ± 5.5
Left cIMT (cm), mean ± SD	0.45 ± 0.16
Right cIMT (cm), mean ± SD	0.44 ± 0.12

SD, standard deviation; IQR, interquartile range; SLE, systemic lupus erythematosus, HDL, high-density lipoprotein; HbA1c, glycated hemoglobin; HCQ, hydroxychloroquine; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; PDAY, Pathobiological Determinants of Atherosclerosis in Youth; PREVENT, Predicting Risk of Cardiovascular Disease Events; ASCVD, atherosclerotic cardiovascular disease; cIMT, carotid intima-media thickness.

Figure 1. Correlations between CV risk estimations and cIMT in SLE patients.



cIMT measurements were within normal limits: 0.45 cm (left) and 0.44 cm (right). No significant correlations were found between cIMT and either PDAY or PREVENT risk estimates (Figure 1).

Conclusion: This study found no significant association between subclinical atherosclerosis, as measured by cIMT, and cardiovascular risk predictions using the PDAY or PREVENT tools in patients with SLE. These findings highlight the limitations of conventional risk calculators in this population and support the incorporation of direct vascular imaging—such as carotid ultrasound—into routine cardiovascular risk assessment for SLE patients, given their predisposition to early, subclinical atherosclerotic CV disease.

Disclosure: I. Reynosa-Silva: None; **O. Garza-Flores**: None; **F. Garcia-Garcia**: None; **A. Gonzalez-Melendez**: None; **I. Colunga-Pedraza**: None; **D. Galarza-Delgado**: None; **J. Azpiri-Lopez**: None; **R. Arvizu-Rivera**: None; **J. Cardenas-de la Garza**: None; **D. Salcedo Almanza**: None.

Abstract Number: 0615

Systemic Lupus Erythematosus Flares in Patients with End-Stage Kidney Disease on Renal Replacement Therapy or after Transplant

Jacob Klein[1], Judith Lin[1] and Marilly Palettas[2], [1]Ohio State University Wexner Medical Center, Columbus, OH, [2]Center for Biostatistics Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: It has been observed that systemic lupus erythematosus (SLE) activity often goes into remission in patients with end-stage kidney disease (ESKD) on dialysis or after a kidney transplant, although the exact mechanism remains elusive. Greater than a quarter of these patients can experience an SLE flare, with patients on dialysis having higher flare rates compared to transplant recipients. This study aims to characterize and identify the clinical phenotypes and risk factors of patients with SLE who continue to flare on dialysis or after transplant. Furthermore, this study analyzes flare manifestations and timing of flares from initial SLE diagnosis, as well as the impact of medications, dialysis modality, and transplant on SLE activity.

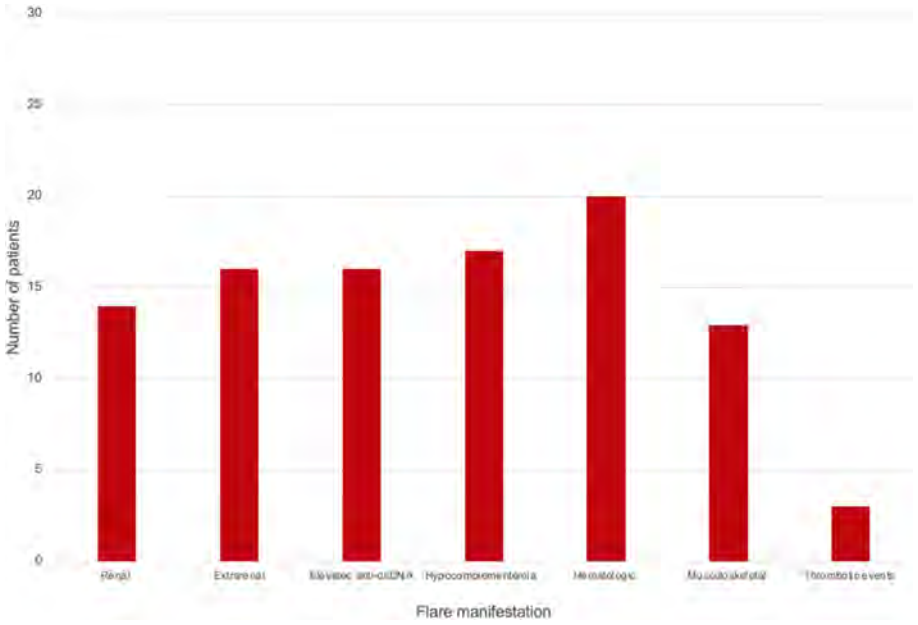
Methods: A single-center retrospective chart review was performed using the inclusion criteria of patients 18 years and older diagnosed with SLE who have ESKD on dialysis or after transplant, with records searched between 2015 and 2022. The proportion of patients who met the ACR classification criteria for SLE was 100%. SLE flare was defined as increased disease activity requiring a change in management and flare confirmation by a rheumatologist or nephrologist. For included patients, demographics, clinical phenotypes, and medical characteristics were recorded and analyzed between flare and no-flare groups.

Results: A total of 144 patients with SLE were included; there was a mean age of 48.5 years, 86.8% female, and 60.4% African American (Table 1). Lupus flare occurred in 20.8% of the study population. Flare rates were similar in patients on PD and HD, although this was not statistically significant (Table 1; p = 0.47). Of the patients who experienced a flare, 43.3% occurred within one year of dialysis initiation or after transplant. The most common flare manifestations included hematologic (66.7%), hypocomplementemia (56.7%), and kidney involvement (46.7%) (Figure 1). Mortality rates were similar in the flare group (31.6%) and no-flare group (30.0%). Lastly, patients in the flare group had lower rates of calcineurin inhibitor use (16.7%)

Characteristic	Total n = 144	Flare n = 30	No Flare n = 114	P-value
Demographic variables				
Age, mean, years	48.5	44.5	49.5	0.110[2]
Female sex, %	86.8	96.7	84.2	0.125[2]
African American race, %	60.4	83.3	54.4	0.110[2]
History of renal transplant, %	56.9	53.3	57.9	0.683[2]
Medication Use, %				
Hydroxychloroquine	54.2	53.3	54.4	0.920[2]
cDMARD (Mycophenolate, Azathioprine, Leflunomide)	56.6	56.7	56.6	0.893[2]
Prednisone maintenance	59.7	63.3	58.8	0.682[2]
Calcineurin inhibitors	27.1	16.7	29.8	0.173[2]
Other immunosuppressive medications	6.9	6.7	7.0	1.000[2]
Dialysis modality, %				0.467[2]
Never on dialysis	7.0	6.7	7.1	
Hemodialysis	75.4	83.3	73.2	
Peritoneal dialysis	17.6	10.0	19.6	
SLE diagnosis to dialysis or transplant, %				0.077[2]
1-5 years	30.7	33.3	29.9	
6-10 years	20.4	33.3	16.8	
>10 years	48.9	33.3	53.3	
Years with SLE until need for dialysis/transplant				0.253[1]
Mean (SD)	12.3 (10.14)	10.4 (9.24)	12.8 (10.36)	
Median	10.0	8.0	11.0	
Range	1, 44.0	1, 32.0	1, 44.0	
Overall mortality, %	31.3	30.0	31.6	1.000[2]

[1] ANOVA F-test p-value
[2] Fisher Exact p-value
Missing data: cDMARD, *n* = 1; dialysis modality, *n* = 2; SLE diagnosis to dialysis or transplant, *n* = 7

Demographic and clinical differences in patients with ESKD secondary to SLE on dialysis or after transplant in flare and no-flare groups



Flare manifestations in patients with ESKD secondary to SLE on dialysis or after transplant

than the no-flare group (29.8%) (Table 1; p = 0.17). The use of immunosuppression agents, including prednisone, cDMARDs, and hydroxychloroquine, was similar between the groups.

Conclusion: Greater than 20% of patients experience an SLE flare while on renal replacement therapy or after transplant. Common manifestations include hematologic abnormalities, hypocomplementemia, and kidney involvement. Only about half of the flare group had elevated anti-dsDNA or hypocomplementemia, and providers must look beyond the numbers during diagnosis. Lastly, flares frequently occur within the first year, therefore, patients should be monitored closely after dialysis initiation or transplantation.

Disclosure: J. Klein: None; **J. Lin**: None; **M. Palettas**: None.

Abstract Number: 0616

Neurofilament Light Chain Serum Levels is Associated with Neuropsychiatric Manifestations and Cognitive Dysfunction in Systemic Lupus Erythematosus Patients: A Longitudinal Study

Juliana Silvatti[1], Livia Almeida Dutra[2], Larissa Araujo Duarte[3], Andreza Salvio Lemos[3], Helena Alessi[4], Shaila Amorim Vieira[2], Gabriel D'Angelo Lacerda[2], LILIA ALVES MARIA ALVES MARIA[4], Soniza Leon Alves[3] and Cristiane Kayser[4], [1]Universidade Federal de São Paulo, SAO PAULO, Sao Paulo, Brazil, [2]Faculdade Israelita de Ciências da Saúde Albert Einstein, São Paulo, Sao Paulo, Brazil, [3]Universidade Federal do Rio de Janeiro, Rio de Janeiro, Rio de Janeiro, Brazil, [4]Universidade Federal de São Paulo, São Paulo, Sao Paulo, Brazil

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

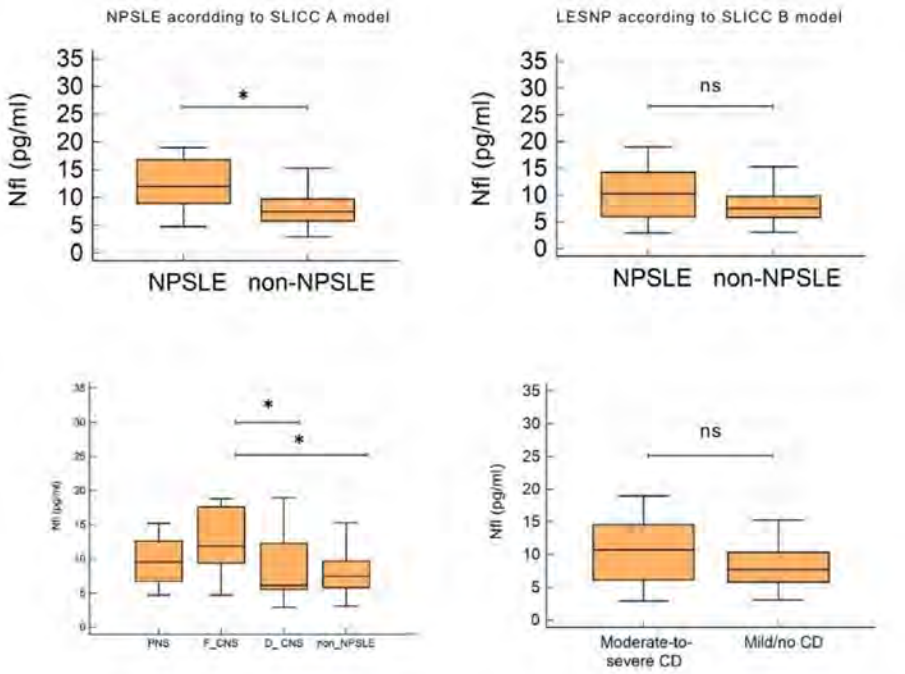
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Evaluation of NfL levels in SLE patients with and without neuropsychiatric involvement according to SLICC A and SLICC B model, according to the type of neuropsychiatric manifestation and moderate-to-severe-cognitive dysfunction



NPSLE: Neuropsychiatric systemic lupus erytematosus, PNS: Peripheral Nervous System, F_CNS: Focal Central Nervous System, D_CNS: Diffuse Central Nervous System, non-NPSLE: Systemic lupus erytematosuswithout neuropsychiatric involvement, CD: Cognitive dysfunction

Table 1. Accuracy of NfL for the identification of NPSLE according to the SLICC A and SLICC B classification models and for the detection of moderate to severe cognitive dysfunction and sensitivity and specificity for a cutoff value of NfL >10.54 pg/mL

	AUC (IC95%)	Sensitivity	Specificity
NPSLE SLICC A	0.766 (0.631 - 0.900), p =0.001	67.0%	82.2%
NPSLE SLICC B	0.631 (0.492 – 0.771), p= 0.067	51.5%	84.8%
Cognitive dysfunction	0.598 (0.431 - 0.765), p= 0.221	55.6%	75.0%

NPSLE: Neuropsychiatric systemic lupus erythematosus, AUC: Area under de curve

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Neuropsychiatric manifestations of systemic lupus erythematosus (SLE) are common and frequently represent a diagnostic challenge due to its heterogeneous manifestations. Neurofilament light chain (NfL) is a marker of axonal neuronal damage that has been investigated in neurological conditions such as multiple sclerosis, stroke, and dementia. This study aims to evaluate the serum levels of NfL in SLE patients and their association with neuropsychiatric manifestations. Secondary objectives included assessing the association of NfL levels with cognitive dysfunction (CD), and cumulative damage over a longitudinal follow-up.

Methods: A longitudinal study was conducted including 66 patients that met the SLICC/ACR 2019 criteria for SLE. NPSLE was defined according to the SLICC A and B models. Demographic and clinical data including laboratory tests, SLICC/ACR Damage Index (SDI), treatment, and presence of comorbidities were collected. Baseline serum NfL levels were measured using the Single Molecule Array (SiMoA) technique. Cognitive function was assessed through a comprehensive neuropsychological battery. After a mean follow-up of 7.46 ± 1.34 years, 48 patients were re-evaluated for disease activity, damage, and cognitive status. The best cutoff of NfL levels for the detection of NPSLE and CD was evaluated using ROC curve analysis. Univariate and multivariate analysis was used to identify risk factors associated with NPSLE and CD.

Table 2. Predictors of NPSLE and Cognitive Dysfunction in SLE Patients

	Univariate Analysis Predictors (OR [IC95%])	Multivariate Analysis Predictors (OR [IC95%])
NPSLE SLICC A	Nfl>10.54pg/ml (9.25 [2.82 - 30.29], p<0.001) Age (0.94 [0.89 - 0.99], p= 0.037) Anti-Ncs (5.60 [1.24 - 22.25], p=0.025) Renal Involvement (0.25 [0.08 - 0.75], p= 0.013) IVIG (10.46 [2.95 - 37.09], p<0,001)	Nfl>10.54pg/ml (22.94 [2.91 - 180.45], p=0.003) Age (0.90 [0.82 - 0.99] , p= 0.040) Anti-NCs (3.09 [0.38 - 25.31], p= 0.293) Renal involvement (0.25 [0.05 - 1.27], p= 0.095) IVIG (10.46 [2.95 - 37.09], p<0.001)
NPSLE SLICC B	Nfl>10.54pg/ml (5.95 [1.84 - 19.19], p=0.003) Hypertension (0.27 [0.08 - 0.82], p=0.021) Renal involvement (0.18 [0.06 - 0.53], p= 0.002) IVIG (10.46 [2.95 - 37.09], p<0.001)	Nfl>10.54pg/ml (11.28 [2.52 - 50.48], p=0.002) Hypertension (1.24 [0.23 - 6.78], p=0.805) Renal involvement (0.29 [0.07 - 1.25], p=0.290) IVIG (11.64 [2.42 - 56.11], p=0.005)
Moderate to Severe Cognitive Dysfunction	Nfl>10.54pg/ml (3.75 [1.20 - 11.68], p=0.023) NPSLE (4.40 [1.39 - 13.96], p=0.012) Diabetes Mellitus (4.68 [0.06 - 0.53], p= 0.002) IVIG (3.33 [1.06 - 10.43], p=0.039) Educational level (0.86 [0.72 - 1.03], p=0.102)	Nfl>10.54pg/ml (5.17 [1.06 - 25.10], p=0.041) NPSLE (1.74 [0.34 - 8.98, p=0.508) Diabetes Mellitus (4.80 [1.10 - 20.99], p= 0.037) IVIG (1.55 [0.35 - 6.91], p=0.560) Educational Level (0.77 [0.59 - 0.99], p=0.041)

SLE: Systemic lupus erythematosus, NPSLE: Neuropsychiatric systemic lupus erythematosus, Nfl:Neurofilament light chain, Ncs: Nucleosomo, IVIG :intravenous immunoglobulin

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The mean age of the 66 SLE patients was 38.10 ± 10.55 years. According to SLICC A model 21 patients had NPSLE and 45 had not; according to SLICC B model 33 patients had NPSLE and 33 had not. Eighteen (27,3%) patients had moderate to severe CD. Patients with NPSLE according to SLICC A had significantly higher NfL levels than non-NPSLE patients (12.90 ± 6.32 vs. 8.08 ± 3.66 pg/mL; p = 0.001). Patients with focal central nervous system (CNS) involvement exhibited higher NfL levels compared to those with diffuse CNS involvement and non-NPSLE patients (Figure 1). NfL showed good accuracy in identifying NPSLE (SLICC A) (AUC = 0.766; 95% CI: 0.631–0.900; p = 0.001) (Table 1). By multivariate analysis, NPSLE per SLICC A and SLICC B were significantly associated with NfL levels >10.54 pg/mL (OR = 22.94, 95% CI: 2.91-180.45; OR = 11.28, 95% CI: 2.52–50.48, respectively) and treatment with immunoglobulin (OR = 10.46, 95% CI: 2.95-37.09; OR = 11.64, 95% CI: 2.42-56.11, respectively). Moreover, NPSLE (SLICC A) was significantly associated with lower age (OR = 0.90, 95% CI 0.82-0.99). CD was independently associated with NfL >10.54 pg/mL (OR = 5.17; 95% CI: 1.06-25,10), diabetes mellitus (OR = 4.80; 95% CI: 1.10-20.99) and lower education level (OR=0.77; IC 95% 0.59-0.99) (Table 2). At follow-up, patients remained cognitively stable and baseline NfL levels were not predictive of worsening of CD and cumulative damage over time. The presence of anti-RNP antibodies was independently associated with mild CD at follow-up (OR = 4.46, 95% CI 1.09–18.30, p = 0.038).

Conclusion: Serum NfL is a promising biomarker for identifying NPSLE and CD in patients with SLE. Although baseline NfL did not predict cognitive decline over time, its association with NPSLE and CD supports its role in disease stratification.

Disclosure: J. Silvatti: None; **L. Almeida Dutra**: None; **L. Araujo Duarte**: None; **A. Salvio Lemos**: None; **H. Alessi**: None; **S. Amorim Vieira**: None; **G. D'Angelo Lacerda**: None; **L. ALVES MARIA**: None; **S. Leon Alves**: None; **C. Kayser**: None.

Abstract Number: 0617

Autoantibodies to Extracellular Antigens in Lupus Patients Serum Versus Controls; Predominance of Autoantibodies to Type I Interferons in Lupus Sera

Kathryn Counts[1], Dulaney Wilson[2], Leon Furchtgott[3] and Gary Gilkeson[1], [1]Medical University of South Carolina, Charleston, SC, [2]Medical University of South Carolina, Charleston, [3]SeraNova Bio, Boston, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Key features in the pathophysiology of SLE include cytokine dysregulation and autoantibody production. Traditional autoantibody testing in SLE is primarily limited to intracellular antigens best represented by the ANA and ENA. A novel technique, Rapid Extracellular Antigen Profiling (REAP), enables detection of autoantibodies to extracellular antigens in their 3D conformation via expression in a yeast library. This study investigates the presence of autoantibodies (AAbs) to over 1500 extracellular antigens, including 11 Type A IFNs in longitudinal serum samples from SLE patients and controls.

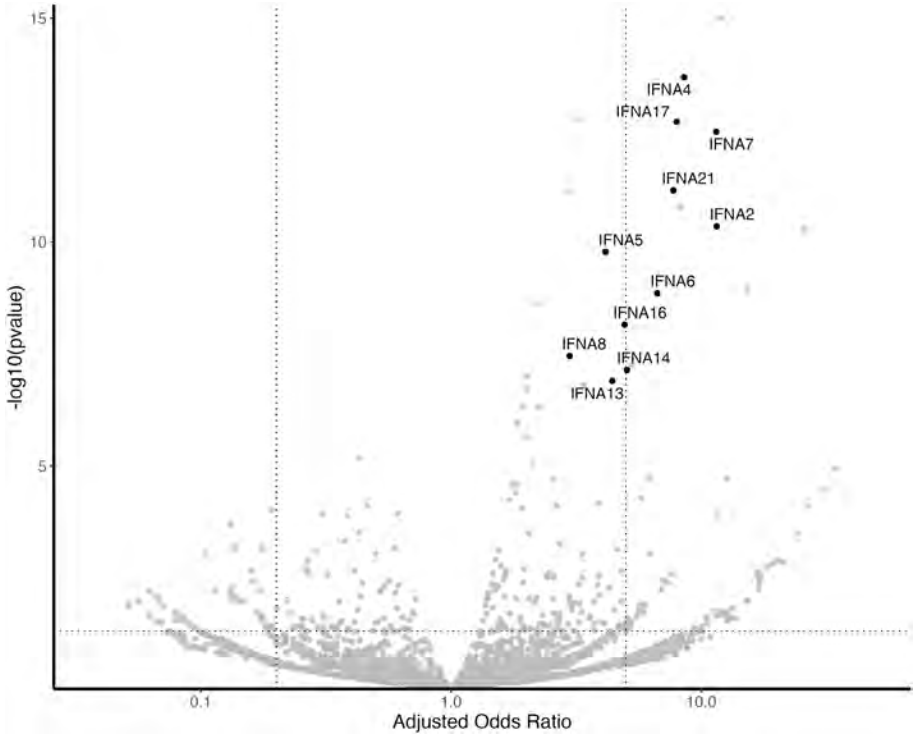
Methods: Serum Abs were quantified through the REAP assay on over 4000 individual samples from 635 SLE patients, 485 healthy controls and 186 unaffected family members. REAP score reproducibility was assessed by running samples in duplicate, with a resulting high REAP score correlation (median correlation 0.87). Results are a readout of increased

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

antibody binding to an antigen on a scale of 0-4, with higher scores indicating increased binding. Reactivity of the REAP assay was confirmed by ELISA for specific antigens.

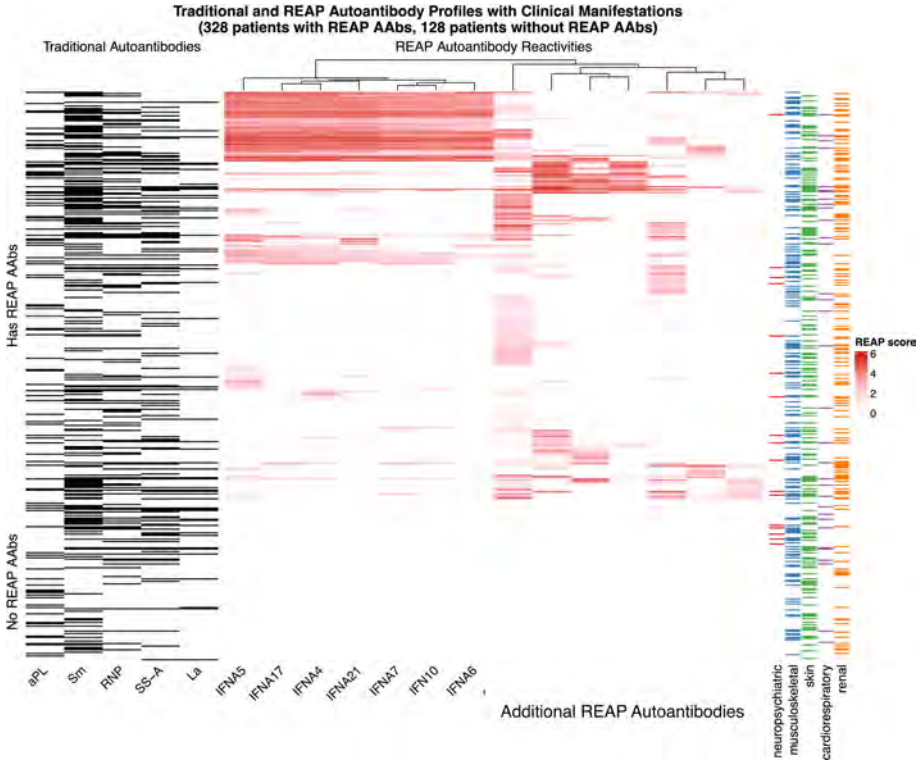
Results: Lupus patient sera had increased numbers of AAbs to extracellular antigens compared to controls. Black SLE patients had increased extracellular AAbs compared to White patients. AAbs were persistent and the number trended to increase over time in sera from SLE patients. There was correlation of AAbs in SLE patients vs first degree relatives. As shown in the volcano plot in Figure 1, there was a markedly higher prevalence of Type I IFN AAbs in SLE sera vs controls and healthy family member sera (36% vs 13%; p= $4.2x10^{-6}$). The IFN library included 11 distinct Type I IFNs. Among those with SLE who had Type I interferon reactivity, 28% exhibited reactivity to all 11 Type I IFN (Figure 2 and 3). Only 2 controls exhibited reactivity to all 11 Thpe I IFNs Inhibition assays demonstrated no cross-reactivity between the different IFN antigens, indicating that each AAb reactivity is specific to one of the 11 Type I IFN antigens. Surprisingly, presence of Type I IFN AAbs was not found to be associated with the presence of lupus nephritis nor with increased lupus disease activity as measured by SLEDAI. During 2019-2021 there was an increase in Type I IFN AAbs in control sera but not in the lupus cohort, possibly reflecting COVID vaccination or COVID infection. We are currently testing the sera and controls with or without Type I IFN AAbs for inhibitory activity against Type I IFNs and whether there is a correlation between Type I IFN inhibition with disease activity.

Conclusion: Our study demonstrates a significantly higher prevalence of autoantibodies to extracellular antigens in lupus sera compared to controls. There was a highly significant correlation of type I IFN AAbs in serum of patients with SLE compared to healthy controls. The presence of Type I IFN AAbs overall was not associated with LN or overall disease activity. Further characterization of neutralizing AAbs may yield additional insight into their disease pathogenesis. Further analysis of correlations of lupus manifestations, chronic damage and disease activity is in progress.

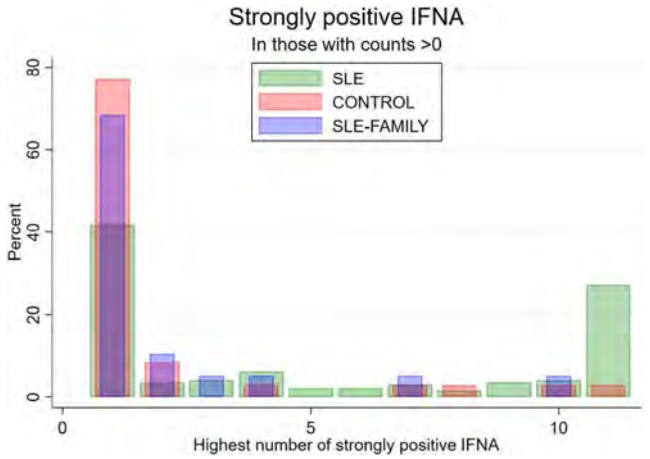


This analysis identifies AAbs associated with SLE compared to healthy controls and unaffected family members, adjusting for age, sex, race. 635 patients with SLE; 485 controls and unaffected family members. Firth (penalized) logistic regression, adjusted for age, sex, race, using baseline sample for each subject. Note significantly higher prevalence of type-I interferon AAbs in patients with SLE. Control antibodies on the left and Lupus antibodies on the right.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heat map of antibodies to extracellular antigens in with associated reactivity to intracelluar antigens targeted in lupus. Other reactivities are shown to the left along with the clinical manifestations of the patient at the time the sera was obtained. Notable are the anti-Type I IFN antibodies along with the clustering of reactivity to other extracellular antigens. Clusters of reactivity to one group of antigens is in some cases exclusive to other reactivities



Reactivity of each group to the 11 different Type I interferons noting the significantly higher prevalence of autoantibodies in the lupus cohort compared to controls or family members especially at the higher levels of number of antibodies to the Type I interferons in lupus

Disclosure: K. Counts: None; **D. Wilson**: None; **L. Furchtgott**: Seranova Bio, 3; **G. Gilkeson**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0618

Therapeutic landscape of systemic lupus erythematosus pure membranous nephropathy: a nationwide population-based study

Kevin Chevalier[1], Romain Brousse[2], alexandre karras[3], Nathalie Costedoat-Chalumeau[4], Julien Dang[5], Maxence Taillar[6], Noémie JOURDE-CHICHE[6], Charles Ronsin[7], Moglie Le Quintrec-Donnette[8], Marie Julien[9], Antoine Huart[10], Aymeric Couturier[11], Pierre Pommerolle[12], Céline Lebas[13], Antoine Coussement[14], Marion Chapal[15], Christophe Barba[16], Alexia Gauffre[17], Maxime Teisseyre[18], Johan Noble[19], Chloé Comarmond[20], Eve Vilaine[21], Jean-François Augusto[22], Aurélie Hummel[23], Evangeline Pillebout[24], Jean-Michel Halami[25], Olivier Moranne[26], Eric Daugas[27], Jean-Jacques Boffa[2] and Emmanuel Esteve[2], [1]Université Paris Cité, Montrouge, France, [2]Tenon hospital, Paris, France, [3]HEGP - assistance publique hopitaux de paris, paris, France, [4]Cochin hospital, Paris, France, [5]Bicêtre hospital, Kremlin Bicêtre, France, [6]Centre de Néphrologie et Transplantation Rénale, Hôpital de la Conception, Assistance Publique-Hôpitaux de Marseille, Marseille, France., Marseille, France, [7]Department of Nephrology and Immunology, Nantes University Hospital, Nantes, France., Nantes, France, [8]Service de Néphrologie-Soins Intensifs-Dialyse et Transplantation, Hôpital Lapeyronie, Montpellier, France., Montpellier, France, [9]Service de néphrologie, CHU de la Réunion, Saint-Denis, France., Saint-Denis, France, [10]Département de Néphrologie et Transplantation d'Organes, Axe Transplantation – Immunité – Environnement, CHU de Toulouse, France, Toulouse, France, [11]Nephrology Unit, American Hospital of Paris, Neuilly-sur-Seine, France, Neuilly-sur-seine, France, [12]Department of Nephrology, Dialysis, and Transplantation, University of Picardie Jules Verne, Amiens University Hospital, Amiens, France., Amiens, France, [13]Service de Néphrologie et Transplantation rénale, Centre Hospitalier Régional Universitaire de Lille, Lille, France., Lille, France, [14]Service de Néphrologie, CHU de Dijon, Dijon, France., Dijon, France, [15]Departement of Nephrology, Hospital of Vendée, La Roche-Sur-Yon, 85000, France., La Roche-sur-yon, France, [16]Department of Nephrology and Nutrition, Hospices Civils de Lyon, Centre Hospitalier Lyon-Sud, Pierre- Bénite, France, Lyon, France, [17]Service de néphrologie, CHU de Rouen, Rouen, France, Rouen, France, [18]Département de Néphrologie, Dialyse et Transplantation, CHU de Nice, Université Côte d'Azur, France., Nice, France, [19]Department of Nephrology, Grenoble-Alpes University Hospital, Grenoble, France., Grenoble, France, [20]Internal Medicine Department, Département Médico-Universitaire INVICTUS, Lariboisière Hospital, Assistance Publique-Hôpitaux de Paris (APHP).Nord-Université Paris-Cité, 75010 Paris, France., Paris, France, [21]Ambroise Paré hospital, Boulogne, France, [22]Service de Néphrologie-Dialyse-Transplantation, Université d'Angers, CHU Angers, Angers, France., Angers, France, [23]Department of Nephrology, Necker-Enfants Malades Hospital, APHP, Paris, France., Paris, France, [24]Nephrology Unit, Saint Louis Hospital, Paris, France., Paris, France, [25]Department of Nephrology, UMR1327 ischemia, INI-CRCT, Tours University Hospital, Tours University, Tours, France., Tours, France, [26]Service de Néphrologie, dialyse et aphérèse, CHU de Nîmes, IDESP Universite de Montpellier, France, Montpellier, France, [27]Department of Nephrology, Hospital Bichat - Claude-Bernard, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Renal involvement is a major prognostic factor in systemic lupus erythematosus. Pure lupus membranous nephropathy (PLMN, class V) represents 5–20% of lupus nephritis cases, with up to 30% progressing to end-stage kidney disease. Unlike proliferative forms, the benefit-risk profile of immunosuppressive therapy in PLMN remains poorly defined. Accordingly, real-world data from unselected patients treated with contemporary therapeutic regimens are critical to delineate response patterns, identify predictors of treatment failure, and establish clinically meaningful therapeutic targets.

Methods: We conducted a nationwide, population-based observational study between 2000 and 2020, involving 25 centers across France (IRB registration: 00012437). Patients experiencing a first flare of PLMN were classified into four treatment groups: (i) supportive care, receiving no immunosuppressive therapy; (ii) mycophenolate mofetil (MMF), treated with MMF combined with low- or high-dose corticosteroids; (iii) rituximab (RTX), treated with RTX and corticosteroids; and (iv) other treatments, receiving immunosuppressive agents excluding MMF and RTX. Renal responses were defined according to the 2024 KDIGO guidelines. Treatment failure was defined as failure to achieve complete or partial response by month 12, occurrence of a relapse, or need for a change in therapeutic class before month 12—excluding initiation of maintenance therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 – Treatments of class V LN and their efficacy

	Supportive care only (n = 53)	Immunosuppressive therapy (n = 141)	p value	MMF-based therapy (n = 54)	Rituximab-based therapy (n = 26)	Other therapies (n = 61)	p value
Prior class III or IV LN flare	7/53 (13.2)	21/141 (14.9)	0.77	7/54 (13.0)	6/26 (23.1)	8/61 (13.1)	0.45
Hydroxychloroquine – n. (%)	41/51 (80.4)	111/139 (79.9)	0.93	45/54 (83.3)	24/26 (92.3)	42/59 (71.2)	0.06
Therapeutic switch during the first 24 months – n. (%)	10/53 (18.9)	32/141 (22.7)	0.56	9/54 (16.7)	2/26 (7.7)	21/61 (34.4)	0.01
Treatment duration (months), median, (IQR)	51.3 (12.5 – 85.1)	11.9 (4.3 – 32.6)	<0.001	23.3 (7.5 – 36.3)	8.2 (0.9 – 19.4)	8.0 (3.3 – 38.1)	<0.01
Corticosteroids starting dose – g/day median (IQR)	0 (0 – 5)	35 (10 – 60)	<0.001	40 (20 – 60)	10 (0 – 60)	40 (20 – 60)	0.02
UPCr < 0.1 g/g, n (%)	12/51 (23.5)	26/137 (19.0)	0.49	6/53 (11.3)	5/26 (19.2)	15/58 (25.9)	0.15
UPCr ≥ 0.1 < 0.5 g/g, n (%)	28/51 (54.9)	46/137 (33.6)	0.01	24/53 (45.3)	6/26 (23.1)	16/58 (27.6)	0.07
UPCr ≥ 3 g/g, n (%)	11/51 (21.6)	65/137 (47.4)	0.01	23/53 (43.4)	15/26 (57.7)	27/58 (47.5)	0.48
Nephrotic syndrome – n. (%)	13/50 (26.0)	62/129 (48.1)	0.01	23/51 (45.1)	15/24 (62.5)	24/54 (44.4)	0.29
eGFR (CKD-EPI), median (IQR)	123.2 (100.0 – 130.2)	121.6 (97.7 – 135.5)	0.64	118.8 (94.7 – 136.8)	119.6 (93.9 – 134.2)	124.3 (104.4 – 135.5)	0.91
PRR at 6 months	6/47 (12.8)	24/124 (19.3)	0.31	12/50 (24.0)	8/23 (34.8)	4/51 (7.8)	**0.01**
CRR at 6 months	1/47 (2.1)	30/124 (24.2)	0.01	11/50 (22)	5/23 (21.7)	14/51 (27.4)	0.78
ORR at 6 months	7/47 (14.9)	54/124 (43.5)	<0.001	23/50 (46.0)	13/23 (56.5)	18/51 (35.3)	0.21
PRR at 12 months	9/49 (18.4)	14/131 (10.7)	0.17	7/51 (13.7)	2/25 (8.0)	5/55 (9.1)	0.66
CRR at 12 months	18/49 (36.7)	65/131 (49.6)	0.12	24/51 (47.1)	16/25 (64)	25/55 (45.4)	0.27
ORR at 12 months	27/49 (55.1)	79/131 (60.3)	0.55	31/51 (60.8)	18/25 (72)	30/55 (54.5)	0.35
Class V LN relapse – n. (%)	12/49 (24.5)	22/137 (16.1)	0.19	9/52 (17.3)	3/25 (12.0)	11/60 (18.3)	0.82
Proliferative class (III or IV) renal relapse– n. (%)	7/53 (13.2)	13/141 (9.2)	0.42	6/54 (11.1)	2/26 (7.7)	5/61 (8.2)	0.83
Extra-renal relapse up – n. (%)	12/53 (22.6)	30/141 (21.3)	0.84	11/54 (20.4)	4/26 (15.4)	15/61 (24.6)	0.62
Follow up duration – months median (IQR)	76.0 (41.1 – 117.1)	62.3 (36.1– 97.6)	0.31	80.9 (35.3– 99.4)	38.3 (27.6 – 68.1)	71.2 (45.8 – 101.6)	**0.03**

Abs: antibodies, CRR: Complete renal response, eGFR: estimated glomerular filtration rate, IQR: Interquartile range, LN: Lupus nephritis, n: Number, ORR: Overall renal response, PRR: Partial renal response, UPCR: urine protein creatinine ratio

Results: A total of 194 patients with a first flare of PLMN were analyzed. At the time of PLMN diagnosis, 53 patients (27.3%) received supportive care only, while 141 (72.7%) were treated with at least one immunosuppressive agent. Among them, 54 (38.3%) received a mycophenolate mofetil (MMF)-based regimen, 26 (18.4%) a rituximab (RTX)-based regimen, and 61 (43.2%) other types of immunosuppressive treatment (**Table 1**). Complete renal response (CRR) at 6 and 12 months was achieved in 1/47 (2.1%) and 18/49 (36.7%) patients in the supportive care group, 11/50 (22%) and 31/51 (60.8%) patients treated with MMF, 5/23 (21.7%) and 16/25 (64.0%) patients treated with RTX, and 14/51 (27.4%) and 25/55 (45.4%) patients treated with other regimens, respectively. Treatment with steroids was not associated with treatment response (p = 0.3). Patients treated by RTX had a shorter duration treatment (p< 0.01) and a lower corticosteroids exposure (p=0.02) than patients treated by other regimens (**Figure 1**). Independent risk-factors for treatment failure were the presence of anti-U1RNP antibodies (OR=2.5 [95% CI: 1.35-4.75]) and the absence of extra-renal involvement (OR=0.34 [95% CI: 0.19 – 0.73]) (**Table 2**).

Conclusion: While 22–27% of patients achieve CRR by 6 months, this proportion increased substantially without treatment modification to 45–64% at 12 months, underscoring that premature modification of therapy may be unwarranted in PLMN

Table 2 – Characteristics at baseline associated with renal outcomes in univariable and multivariable analysis.

UNIVARIABLE ANALYSIS						
Variable		**Number of patients**	**Number of treatment failure at 12 months**	**OR**	**95% CI**	**p**
Age (per 1-year increment)		180	73	0.992	0.966 – 1.019	0.548
Sex	Female	157	63	0.871	0.360 – 2.110	0.760
Origin	Afro-Caribbean ancestry	79	33	1.094	0.601 - 1.992	0.769
Previous renal flare	Yes	36	17	1.406	0.674 – 2.933	0.364
Time between lupus and PLMN diagnoses (per 1-year increment)		173	80	0.987	0.946 – 1.030	0.562
CKD-Epi (per 1 ml/min/1/73m² increment)		180	73	0.999	0.989 - 1.009	0.839
Proteinuria (per 1 g/g increment)		176	72	1.175	0.854 – 1.616	0.322
Nephrotic syndrome	Yes	61	27	1.173	0.622 - 2.211	0.621
Proteinuria < 1 g/g	Yes	35	14	0.903	0.448 – 2.030	0.803
Proteinuria ≥ 1 and ≤ 3 g/g	Yes	72	35	0.645	0.347 – 1.199	0.166
Nephrotic range proteinuria (> 3 g/g)	Yes	69	33	1.598	0.864 – 2.956	0.135
	Yes	121	40	0.389	0.205 – 0.737	**0.004**
C3 levels at diagnosis (per 1 mg/L increment)		141	57	0.688	0.257 – 1.848	0.459
Presence of anti-dsDNA	Yes	123	49	0.910	0.481 – 1.723	0.773
Presence of anti-Sm	Yes	68	29	1.149	0.623 – 2.120	0.656
Presence of anti-U1RNP	Yes	80	42	2.460	1.337 – 4.528	**0.004**
Presence of anti-SSA	Yes	66	27	1.023	0.552 – 1.896	0.941
Presence of anti-SSB	Yes	19	8	1.074	0.410 – 3.813	0.884
Dose of corticosteroids (per 1 mg increment)		180	73	0.993	0.981 – 1.006	0.287
Hydroxychloroquine prescription	Yes	143	54	0.573	0.272 – 1.206	0.142

MULTIVARIABLE ANALYSIS						
Variable		**Number of patients**	**Number of treatment failure at 12 months**	**OR**	**95% CI**	**p**
Extrarenal involvement	No	59	33	1		
	Yes	121	40	0.377	0.194 – 0.728	0.004
Presence of anti-RNP	No	100	31	1		
	Yes	80	42	2.334	1.353 – 4.747	0.004

Abs: antibodies, dsDNA: Double strain deoxyribonucleic acid, eGFR: estimated glomerular filtration rate, U1 RNP: U1 ribonucleoprotein, Sm: Smith

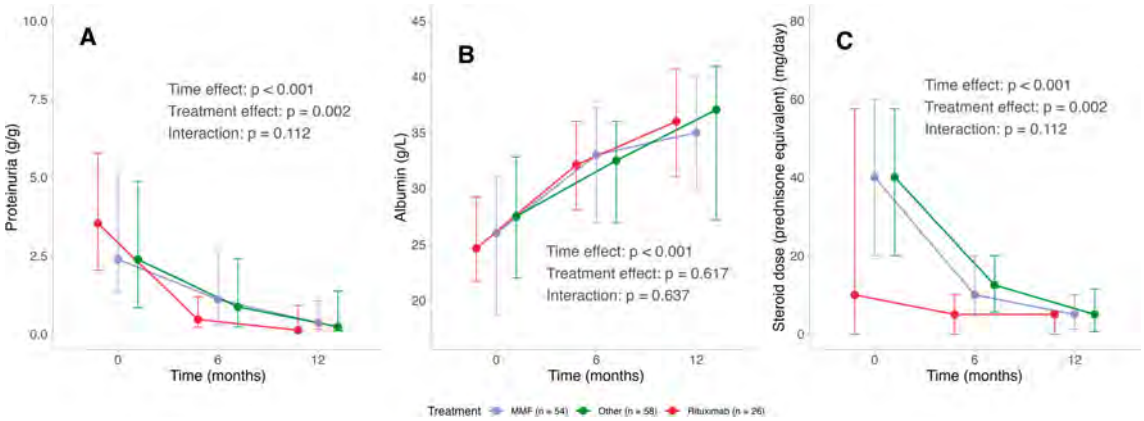


Figure 1 – Evolution of (A) proteinuria (urine protein creatinine ratio), (B) serum albumin and (C) corticosteroids dosage at month 0, 6 and 12 according to the initial immunosuppressant group of treatment.

patients. RTX was associated with a lower corticosteroid exposure and a shorter treatment duration. Anti-U1RNP was independently associated with treatment response, suggesting its potential to stratify the risk of treatment failure in PLMN patients and foster individualized follow-up.

Disclosure: K. Chevalier: None; **R. Brousse**: None; **a. karras**: None; **N. Costedoat-Chalumeau**: None; **J. Dang**: None; **M. Taillar**: None; **N. JOURDE-CHICHE**: None; **C. Ronsin**: None; **M. Le Quintrec-Donnette**: None; **M. Julien**: None; **A. Huart**: None; **A. Couturier**: None; **P. Pommerolle**: None; **C. Lebas**: None; **A. Coussement**: None; **M. Chapal**: None; **C. Barba**: None; **A. Gauffre**: None; **M. Teisseyre**: None; **J. Noble**: None; **C. Comarmond**: None; **E. Vilaine**: None; **J. Augusto**: None; **A. Hummel**: None; **E. Pillebout**: None; **J. Halami**: None; **O. Moranne**: None; **E. Daugas**: Alexion, 12, Support for Attending Meetings and Travel, Amgen, 2, AstraZeneca, 2, 6, 12, Support for Attending Meetings and Travel, CSL, 12, Support for Attending Meetings and Travel, GlaxoSmithKline, 2, 6, 12, Support for Attending Meetings and Travel, Novartis, 2, Otsuka, 2, 12, Support for Attending Meetings and Travel, Vifor, 12, Support for Attending Meetings and Travel; **J. Boffa**: None; **E. Esteve**: None.

Abstract Number: 0619

Interim Analysis of the Impact of a Recombinant Herpes Zoster Vaccine on Systemic Lupus Erythematosus: A Randomized Controlled Study on Immunogenicity, Safety and Immunosuppressor Effects

Luciana Parente Costa Seguro[1], Andrea Negrini[2], Sandra G Pasoto[3], Nadia E Aikawa[4], Ana C Medeiros-Ribeiro[3], Eduardo Borba[1], Emily Figueiredo Neves Yuki[5], Artur Sartori[2], Danieli Andrade[6], Thiago Freitas[7], Henrique Giardini[7], Clovis Artur Silva[8] and Eloisa Bonfa[1], [1]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil, Sao Paulo, Sao Paulo, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas HCFMUSP, Sao Paulo, Brazil., Sao Paulo, Sao Paulo, Brazil, [5]Faculdade de Medicina da USP, São Paulo, São Paulo, Brazil, [6]University of Sao Paulo, São Paulo, São Paulo, Brazil, [7]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [8]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: SLE patients are at increased risk of infections, including herpes zoster (HZ). Prior studies evaluating the recombinant herpes zoster vaccine (RZV) in SLE have been limited by small sample sizes and the absence of control groups. To address these gaps, we conducted a prospective, randomized controlled trial to evaluate the humoral immunogenicity, safety and impact of immunosuppressive therapies on RZV response in a large SLE cohort compared to healthy controls.

Methods: This prospective, randomized, placebo-controlled study enrolled SLE patients randomized 1:1 to receive the RZV (P1 group) or placebo (P2 group) on Day 0 (D0) and Day 42 (D42). Healthy control group (CG) received the RZV at D0 and D42. At D84, the blinding was lifted, and the placebo group (P2) received the RZV at D84 and D126. Anti-gE antibody concentrations (ELISA) were assessed before the 1st vaccine dose and 6 weeks after the 2nd dose. Disease activity was defined as new exacerbation or worsening based on SLE activity criteria: Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), Physician Global Assessment (PGA) and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI). SLE patients (P1 and P2) were blindly analyzed for disease activity, laboratory and treatment data at D0, D42 and D84. Participants were also followed through scheduled visits and telephone contact for the first 3 months to assess adverse events.

Results: A total of 301 SLE patients and 137 controls balanced for age and sex were enrolled with 266 SLE patients completing the 3-month follow-up for this interim analysis. At D84, seroconversion was significantly lower in SLE vs. CG (89.5% vs. 99.3%, p< 0.001). SLE patients also exhibited a lower geometric mean titer (GMT) of anti-gE [7.35 (95%CI 6.35 – 8.51) vs. 11.92 (95%CI 10.66 – 13.34) mUI/mL, p=0.001] and a reduced factor increase in GMT [25.13 (95%CI 20.87 – 30.27) vs. 59.15 (95%CI 47.20 – 74.12), p< 0.001] compared to CG. The overall systemic adverse events were lower in SLE compared to CG: fever (12% vs. 21%, p=0.015) and headache (26% vs. 38, p=0.010) after the 1st dose; fever (12% vs. 22%, p=0.009) and chills (12% vs. 31%, p< 0.001) after the 2nd dose. No serious adverse events were reported. Further analysis of disease activity parameters showed no significant difference in disease flare between SLE patients receiving RZV (P1) and placebo (P2) (1.9% vs. 7.0%, p=0.104), as well as similar median of SLEDAI-2K, PGA and CLASI in both groups. Among SLE patients, male sex, lower prednisone dose, previous HZ and belimumab use were associated with higher anti-gE titers after the 2nd dose (p< 0.05). Patients receiving MMF had a reduced antibody response compared to non-users, as evaluated by GMT [6.18(95%CI 4.89 – 7.70) vs. 8.51 (95%CI 7.08 – 10.23) mUI/mL, p=0.048].

Conclusion: This large, randomized study confirms RZV safety and immunogenicity in SLE, despite a reduced response versus controls. Importantly, MMF impaired vaccine response and may require strategies to enhance protection. Conversely, we provide evidence that lower glucocorticoid doses and belimumab improves vaccination antibody titers. (ClinicalTrials NCT05879419).

Disclosure: L. Costa Seguro: AstraZeneca, 6, GlaxoSmithKlein(GSK), 5, 6; **A. Negrini**: None; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **N. Aikawa**: GlaxoSmithKlein(GSK), 5; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. Figueiredo Neves Yuki**: GlaxoSmithKlein(GSK), 5; **A. Sartori**: None; **D. Andrade**: None; **T. Freitas**: None; **H. Giardini**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0620

The usefulness of neutrophil-to-lymphocyte ratio as a biomarker to predict lupus flares in patients under remission

Luis Daniel Fajardo Hermosillo and María Karina Lizbeth López Ramírez, Unidad Médica de Alta Especialidad, Hospital de Especialidades, Centro Médico Nacional de Occidente, Instituto Mexicano del Seguro Social, GUADALAJARA, Jalisco, Mexico

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Remission in Systemic Lupus Erythematosus (SLE) is described by the Definition of Remission in SLE (DORIS), but it is hardly achieved in clinical practice, while Lupus Low Disease Activity State (LLDAS) is easier achieved by a larger proportion of patients. Lupus flares negatively impact patient outcomes and survival. Only 24-hour urine protein (24hUP), anti-double-stranded DNA antibodies (anti-dsDNA) and serum complement components (C3) have been described as predictors of lupus flares [1]. Lately, the neutrophil-to-lymphocyte ratio (NLR) has emerged as potential biomarker of SLE activity and some studies have showed a correlation between NLR and lupus flares [2]. Since the lupus manifestations vary across different populations, can NLR be used as a biomarker to predict flares in the Mexican-Mestizo SLE patients under remission?

To explore the usefulness of NLR as a biomarker to predict lupus flares in patients under remission.

Methods: A retrospective cohort study including patients over 18 years of age with a diagnosis of SLE according to the SLICC 2012 criteria, who achieved LLDAS and DORIS remission for more than two years. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) was used to assess disease activity. NLR, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), SLEDAI-2k, 24hUP, anti-dsDNA, and C3 were compared between patients with and without lupus flares. Correlations between NLR and previous variables were analyzed. Receiver operating characteristic (ROC) analysis was performed to determine the best NLR cutoff value for detecting lupus flares. Test characteristics, including

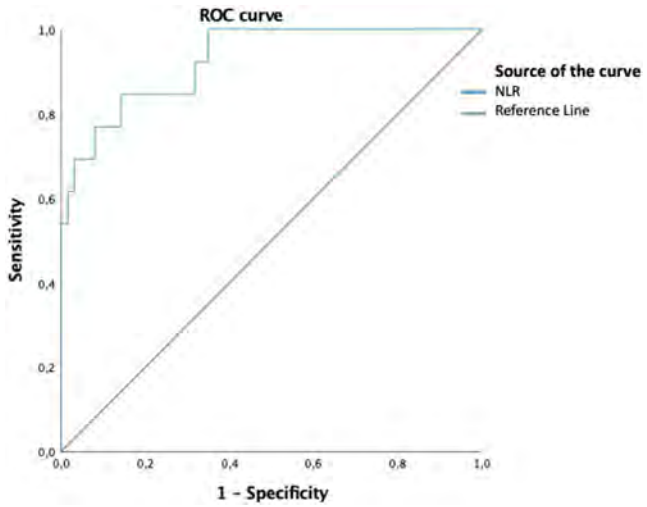


Figure 1. Receiver operating characteristic (ROC) curve analysis of neutrophil-to-lymphocyte ratio (NLR) to predict lupus flares in patients under remission. For NLR, the cut-off value was 2.59, and the area under the curve was 0.928 (95% confidence intervals: 0.856-0.997; p=<0.001), with sensitivity, specificity, and diagnostic accuracy of 84.6%, 85.7%, and 85.5% respectively.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

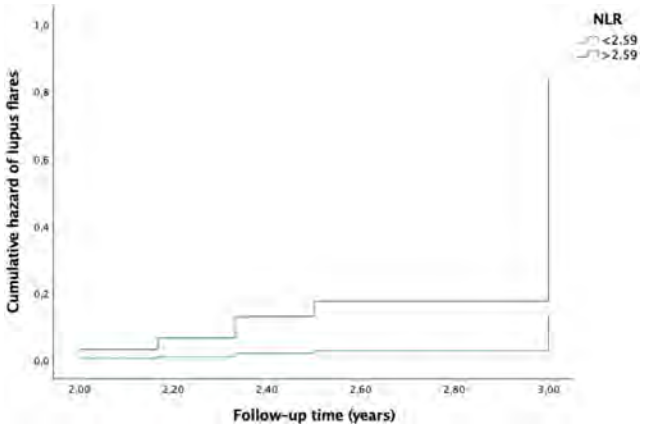


Figure 2. Multivariate Cox regression analysis using the Cox proportional hazards model was conducted to evaluate the risk of lupus flares, establishing NLR as predictive factor.

sensitivity and specificity were calculated. A Cox proportional hazards model (CHM) was conducted to evaluate lupus flares risk with NLR as a predicting factor, reporting hazard ratio (HR) and 95% confidence intervals (95% CI).

Results: Of the 250 patients with SLE, 76 (30.4%) and 40 (16%) achieved LLDAS and DORIS remission, respectively. The most common lupus manifestation was articular (64.5%), followed by cutaneous (53.9%) and renal involvement (46.1%). A total of 13 (17.1%) patients experienced lupus flares, followed for a mean of 2.7 years (SD 0.35), across 912 visits. Of these, 46.2% had renal flares and 38.5% had articular flares. Patients with lupus flares more frequently had hypocomplementemia, and higher levels of anti-dsDNA, 24hUP, and CRP compared to patients without lupus flares (p=0.001). The median (IQR) NLR was higher in lupus flares patients than in those without flares [3.57 (2.74-4.36) vs 1.71 (1.40-2.34); p=< 0.001]. NLR had a moderate correlation with SLEDAI-2K (r=0.411; p=< 0.001). The NLR cut-off value was 2.59, and the area under the curve was 0.928, with 84.6% of sensitivity and 85.7% of specificity (Figure 1). In CHM, NLR > 2.59 (HR 6.45; 95% CI, 1.10-37.1; p= 0.039) was an independent factor associated with lupus flares during the follow-up (Figure 2).

Conclusion: This study suggests that NLR can be a useful and low-cost biomarker to predict lupus flares in patients under remission. However, these observations must be confirmed in larger and prospective studies.

1. Fatemi A et al. BMC Rheumatol 2023;7(1):10.
2. Predescu OR et al. Curr Health Sci J 2024;50(3):347.

Disclosure: L. Fajardo Hermosillo: None; **M. López Ramírez**: None.

Abstract Number: 0621

Risk Factors for Pulmonary Manifestations in GLADEL 2.0, a Systemic Lupus Erythematosus Latin American Cohort

Luis Javier Cajas Santana[1], Sebastián Molina-Ríos[1], Lucia Hernández[2], Romina Nieto[3], Gricel Maita Romero[4], Nidia Noemí Merás[5], Veronica Gabriela Savio[6], Veronica Saurit[7], Valeria Arturi[8], Boris Kisluk[9], Inés Verónica Bellomio[10], Mario Eduardo Kerzberg[11], Nicolas Perez[12], Cecilia Pisoni[13], Vicente Juarez[14], Joaquín Martinez Serventi[15], Nalzio Silva[16], ODIRLEI MONTICIELO[17], Mariana Souza Pessoa de Luna[18], Laíssa Cristina Alves Alvino[19], Eduardo Borba[20], Luciana Parente Costa Seguro[20], Edgard dos Reis-Neto[21], Iris Guerra Herrera[22], Milena Mimica[23], Gustavo Aroca Martínez[24], Valentina Pérez jiménez[25], Carlos Alberto Caoas[26], Gerardo Quintana-Lopez[27], Carlos Toro-Gutierrez[28], Rafael Ignacio López Martínez[29], MIGUEL SAAVEDRA[30], Margarita Portela Hernández[31], Hilda Fragoso-Loyo[32], Luis H Silveira[33], Yelitza Gonzalez Bello[34], Carlos Abud-Mendoza[35], Jorge Antonio Esquivel Valerio[36], Patricia Langjahr[37], Astrid Paats[38], Claudia

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

S. Mora-Trujillo[39], Victor Pimentel-Quiroz[40], Carlos Bedia[41], Teresandris Polanco Mora[42], Martin Rebella[43], Alvaro Danza[44], Federico Zazzetti[45], Ashley Orillion[46], Guillermo Pons-Estel[3] and Graciela Alarcon[47], [1]Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogotá, Colombia, [2]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina, Rosario, Argentina, [3]Centro Regional de Enfermedades Autoinmunes y Reumáticas, GO-CREAR, Rosario, Argentina, Rosario, Argentina, [4]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, Buenos Aires, Argentina, [5]Hospital Italiano de Córdoba, Córdoba, Argentina;, Córdoba, Argentina, [6]Universidad Nacional de Córdoba, Córdoba, Argentina, Córdoba, Argentina, [7]Hospital Privado Universitario de Cordoba, Córdoba, Argentina, Córdoba, Argentina, [8]Hospital San Martin de La Plata, La Plata, Argentina, La Plata, Argentina, [9]Sanatorio Británico, Rosario, Argentina, Rosario, Argentina, [10]Hospital Padilla, Tucumán, Argentina, San Miguel de Tucumán, Argentina, [11]Hospital J.M Ramos Mejía, Buenos Aires, Argentina, CABA, Argentina, [12]Instituto de Investigaciones Médicas Dr. Alfredo Lanari, Buenos Aires, Argentina, [13]CEMIC Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno", Buenos Aires, Argentina, Ciudad Autonoma Buenos Aires, Argentina, [14]Hospital Señor del Milagro Salta, Salta, Argentina, Salta, Argentina, [15]Hospital General de Agudos Dr. Juan A. Fernández, Buenos Aires, Argentina, Buenos Aires, Argentina, [16]Hospital das Clinicas da Universidade Federal de Goias, Goias, Brazil, Goiânia, Brazil, [17]Hospital de Clínicas de Porto Alegre, Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil, PORTO ALEGRE, Rio Grande do Sul, Brazil, [18]Universidad Federal de Pernambuco, Recife, Brazil, Recife, Brazil, [19]Hospital Universitário Pedro Ernesto - Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, Rio de Janeiro, Brazil, [20]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [21]Escola Paulista de Medicina / Universidade federal de São Paulo (EPM / Unifesp), São Paulo, Brazil, São Paulo, Brazil, [22]Hospital del Salvador Santiago de Chile, Santiago, Chile, Santiago, Chile, [23]Facultad de Medicina y Ciencia, Universidad San Sebastián, Santiago, Chile, Santiago, Chile, [24]Universidad Simón Bolívar, Barranquilla, Colombia y Clínica de la Costa, Barranquilla, Colombia, [25]Clínica de la Costa y Universidad Simón Bolívar Barranquilla, Barranquilla, Colombia, Barranquilla, Colombia, [26]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia, Cali, Colombia, [27]Facultad de Medicina, Universidad Nacional de Colombia; Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogotá, Colombia, [28]Pontificia Universidad Javeriana de Cali, Cali, Colombia, Cali, Colombia, [29]Universidad de Especialidades Espíritu Santo, Guayaquil, Ecuador, Guayaquil, Ecuador, [30]Hospital de Especialidades Dr. Antonio Fraga Mouret, Centro Médico Nacional La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico, MEXICO, Mexico, [31]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico, Mexico City, Mexico, [32]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico, [33]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [34]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, Guadalajara, Mexico, [35]Facultad de Medicina de la Universidad Autónoma de San Luis Potosí y Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí, Mexico, San Luis Potosí, Mexico, [36]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [37]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, San Lorenzo, Paraguay, [38]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asunción, Paraguay, [39]Hospital Nacional Edgardo Rebagliati Martins-EsSalud, Lima, Peru, Lima, Peru, [40]Universidad Científica del Sur, San Isidro, Peru, [41]Hospital Nacional Cayetano Heredia, Universidad Peruana Cayetano Heredia, Lima, Peru, Lima, Peru, [42]Hospital Docente Padre Billini, Santo Domingo, Distrito Nacional, Dominican Republic, [43]Hospital de Clínicas, Facultad de Medicina, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [44]Médica Uruguaya, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, Montevideo, Uruguay, [45]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [46]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [47]The University of Alabama at Birmingham, Oakland, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a multisystemic autoimmune disease. Pleuropulmonary (PP) manifestations, including pleural effusion (PE), interstitial lung disease (ILD), pulmonary hypertension (PH), shrinking lung syndrome (SLS), and alveolar hemorrhage (AH) have been described (Medlin JL et al, Semin Arthritis Rheum 2018; Liu Y et al, Lupus 2023); however, data on the frequency and associated risk factors related to occurrence are scarce in the Latin American SLE population. A better understanding of PP manifestations in this population is crucial due to the risk of severe and irreversible damage, the direct impact on morbidity, mortality, and patient quality of life.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Risk Factors for Pulmonary Manifestations in GLADEL 2.0 Cohort Patients: Univariate and Multivariate Analysis. IQR: Interquartile range, SLEDAI: SLE Disease Activity Index, SDI: SLICC/ACR Damage Index

Variable	Total	No Complication	Complication	P value
Pleural disease (n)		791	242	
Age at diagnosis, years, median (IQR)	27.0(20.6–35.4)	27.4(20.8–36.1)	25.2(19.8–34.0)	0.023
Lupus nephritis, n (%)				0.001
None, n (%)	430 (39.7)	338 (42.7)	92 (31.5)	
Lupus nephritis, active, n (%)	425 (39.2)	285 (36.0)	140 (47.9)	
Lupus nephritis, inactive, n (%)	228 (21.1)	168 (21.2)	20 (20.5)	
SLEDAI-2K, median (IQR)	3 (0-8)	2 (0-6)	6 (2-12)	0.001
24 hours proteinuria, median (IQR)	0.4 (0.1–1.7)	0.3 (0.1–1.1)	1.3 (0.3–3.3)	0.001
Anti dsDNA, positivity, n (%)	851 (78.6)	610 (77.1)	241 (82.5)	0.005
Interstitial lung disease (n)		1045	38	
Age at diagnosis, median (IQR)	27.0 (20.6–35.4)	26.9 (20.5–35.0)	30.7 (22.5–43.0)	0.050
Duration of disease, months, median (IQR)	68.0 (19.7–145.6)	67.8 (19.3–144.8)	101.7 (40.9–166.8)	0.041
Lupus nephritis, n (%)				0.015
None, n (%)	430 (39.7)	408 (39.0)	22 (57.9)	
Active, n (%)	425 (39.2)	418 (40.0)	7 (18.4)	
Inactive, n (%)	228 (21.1)	219 (21.0)	9 (23.7)	
SDI, median (IQR)	0 (0–1)	0 (0–1)	2 (1–3)	0.001
C3 complement decrease, n (%)	830 (76.6)	807 (77.2)	23 (60.5)	0.029
C4 complement decrease, n (%)	837 (77.3)	814 (77.9)	23 (60.5)	0.017
Pulmonary hypertension		1057	26	
Duration of disease, months, median (IQR)	68 (19.7–145.6)	67.5 (19.3–141.5)	124 (64.5–242.1)	0.003
Lupus nephritis, n (%)				0.042
None, n (%)	430 (39.7)	422 (39.9)	8 (30.8)	
Active, n (%)	425 (39.2)	418 (39.5)	7 (26.9)	
Inactive, n (%)	228 (21.1)	217 (20.5)	11 (42.3)	
Serositis, n (%)	367 (33.9)	351 (33.2)	16 (61.5)	0.005
SDI, median (IQR)	0 (0–1)	0 (0–1)	2 (1–4)	0.001
Shrinking lung syndrome		1063	20	
Serositis, n (%)	367 (33.9)	355 (33.4)	12 (60)	0.017
SDI, median (IQR)	0 (0–1)	0 (0–1)	1 (1–3)	0.001
	Multivariate logistic regression			
		OR (CI 95%)		P value
Pleural disease				
Lupus nephritis, inactive		1.94 (1.03–3.64)		0.039
SLEDAI-2K		1.11 (1.07–1.14)		<0.001
Interstitial lung disease				
SDI		1.35 (1.03–1.77)		0.030
Pulmonary hypertension				
SDI		1.56 (1.30–1.93)		<0.001
Serositis		2.71 (1.12–6.55)		0.027
Shrinking lung syndrome				
Serositis		2.62 (1.01–6.80)		0.047
SDI		1.46 (1.17–1.82)		<0.001

Methods: Patients from the Latin American GLADEL 2.0 cohort who met the American College of Rheumatology/European Alliance for Rheumatology (ACR/EULAR) 2019 and/or the Systemic Lupus International Cooperating Clinics (SLICC) SLE classification criteria were included. Patients with PP manifestations (PE, ILD, PH, SLS, AH) were identified and compared to those without PP manifestations. Patients with polyautoimmunity, where the disease could have another explanation,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

were excluded. Univariate (UV) analyses were conducted to determine possible associations for each PP manifestation, using data recorded prior to the report of the PP manifestation. Subsequently, multivariate (MV) logistic regression analyses were performed, adjusting for age, gender, and other variables found to be significant in the UV analyses ($P< 0.05$).

Results: From 1,083 patients included in the GLADEL 2.0 cohort, 242 patients with PE, 38 with ILD, 26 with PH, 20 with SLS, and 9 with AH were identified. The factors associated with each manifestation, except for AH (due to small n), are summarized in Table 1. Age at diagnosis, disease duration, history of renal involvement (including both active and inactive nephritis), and the degree of organ damage, assessed with the SLICC Damage Index (SDI), were frequently associated with PP manifestations. In the MV analysis, the association between SDI and PP remained statistically significant for all complications, with odds ratios ranging from 1.35 to 1.56. Disease activity, measured by the SLE Disease Activity Index (SLEDAI-2K), was only found to be significant for PE (P=0.001). Significant associations between the presence of serositis and PH (P=0.005) and SLS (P=0.001) were found.

Conclusion: Damage, as assessed by the SDI score, was a consistent risk factor associated with PP manifestations among patients in the GLADEL 2.0 cohort; this risk factor has not been previously reported for PP in SLE. These data highlight the importance of close monitoring for PP in patients with SLE who have organ damage. Additionally, serositis significantly increased the risk of developing PH and SLS in this cohort, consistent with data reported in previous studies. Risk factors for AH could not be examined due to small case numbers.

Disclosure: L. Cajas Santana: AstraZeneca, 6, GSK, 6; **S. Molina-Ríos**: None; **L. Hernández**: None; **R. Nieto**: None; **G. Romero**: None; **N. Merás**: None; **V. Gabriela Savio**: None; **V. Saurit**: None; **V. Arturi**: None; **B. Kisluk**: None; **I. Bellomio**: None; **M. Kerzberg**: None; **N. Perez**: None; **C. Pisoni**: None; **V. Juarez**: None; **J. Serventi**: None; **N. Silva**: None; **O. MONTICIELO**: None; **M. Pessoa de Luna**: None; **L. Alves Alvino**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **L. Costa Seguro**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 5, 6; **E. dos Reis-Neto**: None; **I. Guerra Herrera**: None; **M. Mimica**: None; **G. Aroca Martínez**: None; **V. Pérez jiménez**: None; **C. Caoas**: None; **G. Quintana-Lopez**: None; **C. Toro-Gutierrez**: None; **R. López Martínez**: None; **M. SAAVEDRA**: None; **M. Portela Hernández**: None; **H. Fragoso-Loyo**: None; **L. Silveira**: None; **Y. Gonzalez Bello**: None; **C. Abud-Mendoza**: None; **J. Esquivel Valerio**: None; **P. Langjahr**: None; **A. Paats**: None; **C. Mora-Trujillo**: None; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **C. Bedia**: None; **T. Polanco Mora**: None; **M. Rebella**: None; **A. Danza**: None; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **G. Pons-Estel**: AstraZeneca, 1, 5, 6, Boehringer Ingelheim, 1, 5, 6, GSK, 1, 5, 6, Janssen, 2, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, RemeGen, 1, 5, 6, Sanofi, 1, 5, 6, Werfen Diagnostics, 1, 5, 6; **G. Alarcon**: None.

Abstract Number: 0622

Shrinking Lung Syndrome in Systemic Lupus Erythematosus: A Pooled Database Analysis of Clinical, Immunological and Therapeutic Factors Impacting Outcomes

Malvika Gupta[1] and Chander Raman[2], [1]Mayo Clinic, Rochester MN, Rochester, MN, [2]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Shrinking Lung Syndrome (SLS) is a rare pulmonary complication of systemic lupus erythematosus (SLE), characterized by unexplained dyspnea, pleuritic chest pain, loss of lung volume and a restrictive ventilatory defect without overt parenchymal or pleural disease. The pathogenesis is poorly understood. Due to its rarity and non-specific presentation, the diagnosis is often delayed. Treatment is individualized, as there are no defined guidelines for management. This study aims to identify the clinical and immunological risk factors, and therapeutic interventions impacting outcome in SLS, define prognostic indicators and inform treatment management.

Methods: We compiled a pooled database of all 49 published cases of confirmed SLS associated with SLE from the literature. We then performed a retrospective analysis describing the demographic and clinical characteristics, immunological signatures and therapeutic interventions that influenced outcomes. Fisher's exact test was used to assess the association between prognostic factors and outcomes. Odds ratio (OR) and *p*-values were computed.

Results: The median age of SLS diagnosis was 30 years (range 12-58) and females were predominantly affected (Table 1). Median time from diagnosis of SLE to SLS was 36 months (range: 0 - 240). The most common presenting symptoms were pleuritic chest pain and exertional dyspnea (Table 1). Moderate to severe pulmonary restriction (forced vital capacity % predicted [FVCpp] < 60%) was seen in 71.4% of patients. The median nadir FVCpp was 38.5% (range 14-77). Table 2 describes the therapeutic interventions. Although improvement of symptoms with immunosuppression (corticosteroids, azathioprine, hydroxychloroquine, cyclophosphamide, methotrexate, mycophenolate mofetil [MMF], and Rituximab) was observed in 92% of patients, only 61% showed functional improvement on pulmonary function tests. Relapse or progression of symptoms were noted in 12% of patients (Table 3). Despite high morbidity, mortality was low (2%). High ANA titres (>1:2560) (OR=33.0, *p*=0.027) and anti-SSA antibody positivity (OR=6.75, *p*=0.036) were associated with poor outcomes and these patients additionally required rituximab for management of disease. Anti-dsDNA positivity was associated with favorable outcomes, with patients demonstrating >100% increase in FVCpp after treatment (OR = 12.29, *p*=0.048). Anti-SSB antibody positivity (OR = 9.39, *p*=0.062) and the use of beta-agonists (OR = 10.02, *p*=0.052) were also associated with

Table 1: Baseline Demographics and Clinical Characteristics of Patients with Shrinking Lung Syndrome (SLS) in Systemic Lupus Erythematosus (SLE) (N=49)

Characteristic	Number of Patients (%)	Characteristic	Number of Patients (%)
Age (years)		**Presenting Symptoms of SLS**	
<19	7 (14.3%)	Pleuritic chest pain	49 (100%)
20-29	17 (34.7%)	Dyspnea on Exertion	48 (98%)
30-39	8 (16.3%)	Orthopnea	12 (24.5%)
40-49	10 (20.4%)	Dyspnea at Rest	4 (8.2%)
50-59	7 (14.3%)	Cough	8 (16.3%)
Gender		Fever	8 (16.3%)
Female	44 (89.8%)	**Radiological Features of SLS**	
Male	5 (10.2%)	Elevation of Diaphragm	31 (63.2%)
Race/Ethnicity		Unilateral Elevation of Diaphragm	13 (26.5%)
Asian	3 (6%)	Bilateral Elevation of Diaphragm	18 (36.7%)
Hispanic	3 (6%)	Basilar Atelectasis	24 (49%)
African American	2 (4%)	**Immunological Signatures**	
Caucasian	2 (4%)	ANA Titre <1:640	5 (10.2%)
Not Known	39	ANA Titre 1:1280-1:2560	7 (14.3%)
Age at Diagnosis of SLE (years)		ANA Titre >1:2560	4 (8.2%)
<19	12 (24.5%)	Homogenous ANA	8 (16.3%)
20-29	15 (30.6%)	Speckled ANA	6 (12.2%)
30-39	6 (12.2%)	Anti-ds-DNA	31 (63.2%)
40-49	6 (12.2%)	Low Complements	8 (16.3%)
50-59	3 (6%)	Anti-SSA	15 (30.6%)
Not Known	7	Anti-SSB	5 (10.2%)
Time between diagnosis of SLE and SLS (years)		Anti-RNP	7 (14.3%)
Immediate	6 (12.2%)	Anti-Smith	10 (20.4%)
<1	3 (6%)	Anti-Cardiolipin	10 (20.4%)
1-5	21 (42.8%)	**Nadir Forced Vital Capacity (% of predicted**	
6-10	7 (14.3%)	<45 (severe)	26 (53%)
11-15	3 (6%)	45-60 (moderately severe)	9 (18.3%)
16-20	2 (4%)	60-80 (mild)	5 (10.2%)
Not Known	7	Not Known	9
Pre-Existing Pulmonary Comorbidity	**18 (36.7%)**	**Time between Onset of Respiratory Symptoms and Initiation of Treatment for SLS (months)**	
Pulmonary Embolism	4 (8.2%)	Immediate	20 (40.8%)
Pulmonary Hypertension	2 (4%)	<1	4 (8.2%)
Asthma	3 (6%)	1-6	12 (24.5%)
Pleuritis	11 (22.4%)	>6	13 (26.5%)
No Pulmonary Comorbidities	31 (63.3%)		
Other Co-existing Autoimmune Diseases	**9 (18.4%)**		
Sjogren's Syndrome	3 (6%)		
Myositis	2 (4%)		
Scleroderma / Systemic Sclerosis	2 (4%)		
Rheumatoid Arthritis	1 (2%)		
Oligoarticular Juvenile Idiopathic Arthritis	1 (2%)		
No Other Autoimmune Disease	40 (81.6%)		

Baseline Demographics and Clinical Characteristics of Patients with Shrinking Lung Syndrome (SLS) in Systemic Lupus Erythematosus (SLE) (N=49)

Table 2: Therapeutic Interventions for Systemic Lupus Erythematosus (SLE) and Shrinking Lung Syndrome (SLS) (N=49)	
Intervention	**Number of Patients (%)**
Treatment for SLE	
Corticosteroids	33 (67.3%)
Hydroxychloroquine	23 (46.9%)
Azathioprine	11 (22.4%)
Methotrexate	8 (16.3%)
Mycophenolate Mofetil	6 (12.2%)
Cyclophosphamide	6 (12.2%)
Treatment for SLS	
Corticosteroids	44 (89.8%)
Pulse Steroid Therapy	11 (25%)
Prednisone Dose >30 mg/day	26 (66%)
Prednisone Dose <30 mg/day	4 (9.1%)
Improvement with steroids alone	8 (16.3%)
Hydroxychloroquine	8 (16.3%)
Azathioprine	16 (32.6%)
Cyclophosphamide	18 (36.7%)
Mycophenolate Mofetil	5 (10.2%)
Methotrexate	3 (6.1%)
Rituximab	9 (18.4%)
Theophylline	5 (10.2%)
Beta Agonist	5 (10.2%)
Change to SLE Regimen for Management of SLS	38 (77.5%)
Medications Added to SLE Regimen	31 (63.3%)
Doses of Medications in SLE Regimen Increased	23 (46.9%)
Other Therapeutic Interventions	
BiPAP or Non-Invasive Ventilation	5 (10.2%)
Intubation	2 (4%)

Therapeutic Interventions for Systemic Lupus Erythematosus (SLE) and Shrinking Lung Syndrome (SLS) (N=49)

Table 3: Outcomes of Patients with Shrinking Lung Syndrome in Systemic Lupus Erythematosus with Treatment (N=49)	
Outcome	**Number of Patients (%)**
Symptomatic Improvement	**45 (91.8%)**
<2 weeks	8 (16.3%)
>2 weeks, <3 months	8 (16.3%)
3-6 months	6 (12.2%)
6-12 months	3 (6.1%)
>1 year	3 (6.1%)
No Symptomatic Improvement	2 (4%)
Time to symptomatic improvement not available	17
Symptomatic outcome not available	2
Improvement in Forced Vital Capacity (% of Predicted Value)	**30 (61.2%)**
1-50% increase	11 (22.4%)
51-100% increase	8 (16.3%)
101-200% increase	3 (6.1%)
>200% increase	2 (4%)
No Improvement	9 (18.3%)
% Improvement not available	6
Data not available	10
Time to Improvement of Forced Vital Capacity (months)	
<6	6 (12.2%)
6-12	12 (24.5%)
>12	5 (10.2%)
No Improvement	9 (18.3%)
Not available	17
Radiological Findings After Treatment	
Improvement	10 (20.4%)
No Improvement	5 (10.2%)
Status on Follow-Up	
Median follow up (months)	22 (3-240)
Improved clinically and functionally	27 (55.1%)
Remained stable	14 (28.5%)
Worsened / Relapsed	6 (12.2%)
Died	1 (2%)
Not available	2

Outcomes of Patients with Shrinking Lung Syndrome in Systemic Lupus Erythematosus with Treatment (N=49)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

clinical and functional improvement. In contrast, treatment with azathioprine correlated with delayed symptomatic recovery exceeding 1 year (OR = 33.44, p=0.01), and MMF use was associated with increased need for non-invasive ventilation or intubation due to respiratory compromise (OR = 20.0, p=0.01).

Conclusion: SLS is a rare complication of SLE associated with high rates of morbidity. Specific immunologic profiles and therapeutic interventions were associated with better clinical and functional recovery, and can guide prognostication and treatment selection. These findings highlight the need for greater clinical awareness, and development of standardized treatment protocols to optimize patient outcomes.

Disclosure: M. Gupta: None; **C. Raman**: None.

Abstract Number: 0623

Cluster Analysis of Socioeconomic and Environmental Determinants Modifying Activity, Chronicity and Clinical Manifestations of Systemic Lupus Erythematosus in the GLADEL 2.0 Cohort

Marco Martinez[1], Karen Roberts[2], Rosana Quintana[3], Marina Scolnik[4], Carmen Funes Soaje[5], Paula Alba[6], Veronica Saurit[7], Mercedes Garcia[8], GUILLERMO ARIEL BERBOTTO[9], Inés Verónica Bellomio[10], Mario Eduardo Kerzberg[11], Graciela Noemi Gomez[12], Cecilia Pisoni[13], Vicente Juarez[14], Ana Malvar[15], Antonio Da Silva[16], ODIRLEI MONTICIELO[17], Henrique Mariz[18], Francinne Ribeiro[19], Eduardo Borba[20], Eloisa Bonfa[20], Edgard dos Reis-Neto[21], Iris Guerra Herrera[22], Maria Loreto Massardo[23], Gustavo Aroca-Martínez[24], Lorena Gómez Escorcia[25], Carlos Alberto Caoas[26], Gerardo Quintana-Lopez[27], Carlos Toro-Gutierrez[28], Mario Moreno Alvarez[29], MIGUEL SAAVEDRA[30], Margarita Portela Hernández[31], Hilda Fragoso-Loyo[32], Luis H Silveira[33], Ignacio García-De la Torre[34], Carlos Abud-Mendoza[35], Jorge Antonio Esquivel Valerio[36], Maria Isabel Acosta[37], Astrid Paats[38], Claudia S. Mora-Trujillo[39], Manuel Ugarte-Gil[40], Armando Calvo[41], Roberto Muñoz-Louis[42], Martin Rebella[43], Alvaro Danza[44], José Gomez-Puerta[45], Federico Zazzetti[46], Ashley Orillion[47], Guillermo Pons-Estel[3] and Ingris del Pilar Pelaez Ballestas[48], [1]HGSZ No 9, Instituto Mexicano del Seguro Social, San Luis Potosí, México, Rioverde, Mexico, [2]Instituto de Investigación, Rosario, Argentina, Wyomissing, PA, [3]Centro Regional de Enfermedades Autoinmunes y Reumáticas, GO-CREAR, Rosario, Argentina, Rosario, Argentina, [4]Hospital Italiano de Buenos Aires, Argentina, Buenos Aires, Argentina, [5]Hospital Italiano de Córdoba, Córdoba, Argentina, Cordoba, Argentina, [6]Hospital Córdoba y Sanatorio Allende, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Córdoba, Argentina, Cordoba, Argentina, [7]Hospital Privado Universitario de Cordoba, Córdoba, Argentina, Córdoba, Argentina, [8]Hospital Interzonal General de Agudos "General San Martín" de la plata, La Plata, Argentina, [9]Sanatorio Británico, Rosario, Argentina, ROSARIO, Argentina, [10]Hospital Padilla, Tucumán, Argentina, San Miguel de Tucumán, Argentina, [11]Hospital J.M Ramos Mejía, Buenos Aires, Argentina, CABA, Argentina, [12]Instituto de Investigaciones Médicas Dr. Alfredo Lanari, Don Torcuato, Argentina, [13]CEMIC Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno", Buenos Aires, Argentina, Ciudad Autonoma Buenos Aires, Argentina, [14]Hospital Señor del Milagro Salta, Salta, Argentina, Salta, Argentina, [15]Organización Médica de Investigación, Buenos Aires, Argentina, [16]Hospital das Clinicas da Universidade Federal de Goias, Goias, Brazil, Holzkirchen, Germany, [17]Hospital de Clínicas de Porto Alegre, Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil, PORTO ALEGRE, Rio Grande do Sul, Brazil, [18]Universidad Federal de Pernambuco, Pernambuco, Brazil, Pernambuco, Brazil, [19]Hospital Universitário Pedro Ernesto - Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, Rio De Janeiro, Rio de Janeiro, Brazil, [20]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [21]Escola Paulista de Medicina / Universidade federal de São Paulo (EPM / Unifesp), São Paulo, Brazil, São Paulo, Brazil, [22]Hospital del Salvador Santiago de Chile, Santiago, Chile, santiago, Chile, [23]Facultad de Medicina y Ciencia, Universidad San Sebastián, Santiago, Chile, Santiago, Chile, [24]Clínica de la Costa y Universidad Simón Bolívar, Barranquilla, Colombia, barranquilla, Colombia, [25]Clínica de la Costa y Universidad Simón Bolívar Barranquilla, Barranquilla, Colombia, Barranquilla, Colombia, [26]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia, Cali, Colombia, [27]Facultad de Medicina, Universidad Nacional de Colombia; Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogota, Colombia, [28]Pontificia Universidad Javeriana de Cali, Cali, Colombia, Cali, Colombia, [29]Universidad de Especialidades Espíritu Santo, Guayaquil, Ecuador, Guayaquil, Ecuador, [30]Hospital de Especialidades Dr. Antonio Fraga Mouret, Centro Médico Nacional La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico, MEXICO, Mexico, [31]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico, Mexico City, Mexico, [32]Instituto Nacional de Ciencias Médicas y

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico, [33]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [34]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, Guadalajara, Jalisco, Mexico, [35]Facultad de Medicina de la Universidad Autónoma de San Luis Potosí y Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí, Mexico, San Luis Potosí, Mexico, [36]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [37]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asuncion, Paraguay, [38]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asunción, Paraguay, [39]Hospital Nacional Edgardo Rebagliati Martins-EsSalud, Lima, Peru, Lima, Peru, [40]Universidad Cientifica del Sur, Lima, Peru, [41]Hospital Nacional Cayetano Heredia Universidad Peruana Cayetano Heredia, Lima, Peru, Jesus Maria, Peru, [42]Hospital Docente Padre Billini, Santo Domingo, Distrito Nacional, Dominican Republic, [43]Hospital de Clínicas, Facultad de Medicina, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [44]Médica Uruguaya, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, Montevideo, Uruguay, [45]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, [46]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [47]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [48]Hospital General de México "Dr. Eduardo Liceaga", Mexico City, Mexico, Mexico, Mexico

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with heterogeneous clinical manifestations. Evidence from high-income countries suggests that socioeconomic status (SES) and environmental factors influence SLE outcomes, yet data from Latin America remain limited. The objective of this research was to evaluate, across three levels (individual, regional, and national), whether socioeconomic and environmental factors impact the clinical presentation of SLE in the GLADEL 2.0 cohort.

Methods: We analyzed data from 1,083 patients with SLE enrolled in the GLADEL 2.0 cohort across 10 Latin American countries. All patients fulfilled the 1982/1997 American College of Rheumatology (ACR) or 2012 Systemic Lupus International Cooperating Clinics (SLICC) classification criteria. Clinical outcomes were disease activity (SLEDAI-2K), organ involvement (renal, hematologic, cutaneous, musculoskeletal), and organ damage (SLICC/ACR damage index; SDI). Variables

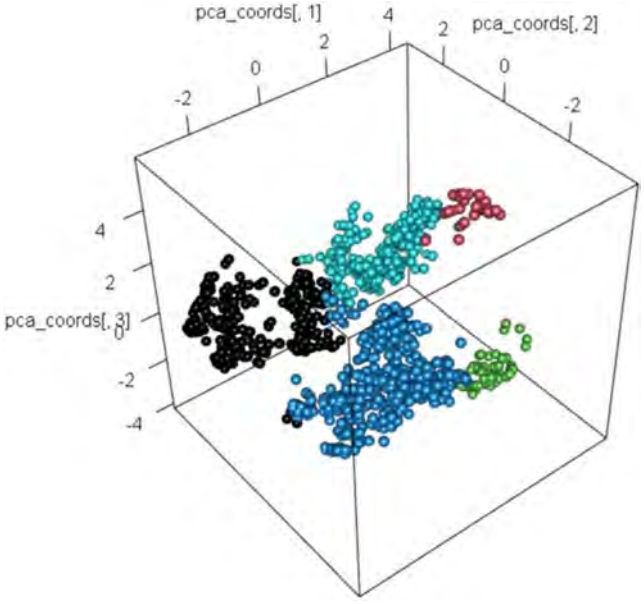


Figure. Three-dimensional representation of the first three principal components, showing the five clusters of SLE patients derived from socioeconomic and environmental variables

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

were structured into three levels: Level 1 (individual), Level 2 (state/province), and Level 3 (national). Multilevel analyses included sociodemographic variables, environmental exposure to air pollutants ($PM_{2.5}$, PM_{10}, NO_2), and contextual indicators (income, unemployment, distribution of income or wealth through the Gini index, CO_2 emissions). Statistical analysis included cluster analysis (Ward's method) and principal component analysis (PCA).

Results: Five clusters emerged based on socioeconomic and environmental determinants. Cluster two (urban, high-income, low inequality) exhibited low damage (SDI [mean ± SD] 0.66 ± 0.9) and high disease activity (SLEDAI [mean ± SD] 13.0 ± 9.2). Conversely, Cluster four (middle-low SES, high inequality, high NO_2 exposure) demonstrated high disease impact (SDI [mean ± SD] 1.06 ± 1.4) and greatest work productivity loss (36.1%). Cluster three (low-income, low pollution) presented the highest accumulated damage (mean SDI [mean ± SD] 1.73 ± 1.95). Environmental exposures varied significantly; Cluster five showed the highest CO_2 emissions and solar irradiance, while Cluster three had the lowest environmental burden. PCA showed that clinical manifestations, disease activity and chronicity were different across clusters. The figure highlights the separation of the characteristics according to the three principal components.

Conclusion: Socioeconomic and environmental factors at individual, regional, and national levels influence the cumulative clinical manifestations and patient-reported outcomes in SLE. Our findings underscore the role of social vulnerability and environmental stressors as potential modifiers of SLE phenotype in Latin America, highlighting the need for context-sensitive interventions and policies to mitigate health inequities.

Disclosure: M. Martinez: None; **K. Roberts**: None; **R. Quintana**: None; **M. Scolnik**: AstraZeneca, 2, 5, 6, GSK, 1, 5, 6, Janssen, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6; **C. Funes Soaje**: None; **P. Alba**: None; **V. Saurit**: None; **M. Garcia**: None; **G. BERBOTTO**: None; **I. Bellomio**: None; **M. Kerzberg**: None; **G. Gomez**: None; **C. Pisoni**: None; **V. Juarez**: None; **A. Malvar**: Bristol-Myers Squibb(BMS), 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Kezar, 2, Novartis, 2, Pfizer, 2; **A. Da Silva**: None; **O. MONTICIELO**: None; **H. Mariz**: None; **F. Ribeiro**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. dos Reis-Neto**: None; **I. Guerra Herrera**: None; **M. Massardo**: None; **G. Aroca-Martínez**: None; **L. Gómez Escorcia**: None; **C. Caoas**: None; **G. Quintana-Lopez**: None; **C. Toro-Gutierrez**: None; **M. Moreno Alvarez**: None; **M. SAAVEDRA**: None; **M. Portela Hernández**: None; **H. Fragoso-Loyo**: None; **L. Silveira**: None; **I. García-De la Torre**: None; **C. Abud-Mendoza**: None; **J. Esquivel Valerio**: None; **M. Acosta**: None; **A. Paats**: None; **C. Mora-Trujillo**: None; **M. Ugarte-Gil**: AstraZeneca, 1, 6, Ferrer, 1, GlaxoSmithKlein(GSK), 6, Janssen, 5, technofarma, 1; **A. Calvo**: None; **R. Muñoz-Louis**: None; **M. Rebella**: None; **A. Danza**: None; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **G. Pons-Estel**: AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen, 1, 6; **I. Pelaez Ballestas**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0624

Polygenic risk of lupus is differentially associated with individual EHR-derived classification criteria

Noah Forrest[1], Sachleen Tuteja[2], Jennifer Pacheco[3], Vesna Mitrovic[3], Rosalind Ramsey-Goldman[1], Theresa Walunas[3] and **Matthew Dapas**[1], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Northwestern University, Evanston, [3]Northwestern University Feinberg School of Medicine, Chicago

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by diverse clinical presentation, posing significant challenges in diagnosis and management. Reflecting this clinical complexity, multiple sets of classification criteria have been developed for SLE. Genetic factors contribute significantly to SLE susceptibility, with genome-wide association studies (GWAS) identifying over 130 distinct genetic loci linked to increased disease risk. Importantly, polygenic risk scores (PRSs) derived from these loci have been associated with specific clinical manifestations, including cardiovascular and renal involvement, indicating that genetic risk may drive distinct phenotypic expressions within SLE. Here, we developed an SLE PRS and evaluated its associations with electronic health record (EHR)-derived clinical phenotypes and laboratory parameters available in the Electronic Medical Records and Genomics (eMERGE) Network biobank. We further assessed the relationships between the PRS and individual Systemic Lupus International Collaborating Clinics (SLICC) classification criteria.

Methods: We modeled polygenic risk for lupus using PRS-CS on summary statistics from a large genome-wide association study consisting of 6,748 SLE cases and 11,516 controls of European ancestry and derived PRSs in European ancestry eMERGE participants. We performed a phenome-wide association study between the lupus PRS and 1,706 phecodes in Northwestern University eMERGE participants (n=1,061), adjusting for age, sex, number of encounters, and the top 3 principal components of ancestry. We then calculated correlations between the lupus PRS and the prevalences of individual SLICC criteria across all eMERGE sites (n=32,329), adjusting for the number of encounters.

Results: The PRS predicted SLE with a receiver operating characteristic area under the curve of 0.724. Within the Northwestern cohort, the PRS was significantly associated with "Lupus (localized and systemic)" ($P=1.6\times10^{-9}$) and "systemic lupus erythematosus" ($P=3.0\times10^{-9}$). Nominally associated phecodes ($P< 5.0\times10^{-3}$) included "cardiac complications" ($P=2.8\times10^{-3}$) and "impaired renal function" ($P=4.6\times10^{-3}$). PheWAS associations were significantly enriched for circulatory system ($P=9.7\times10^{-5}$) and hematopoietic ($P=3.2\times10^{-2}$) traits. Across eMERGE, the SLE PRS was significantly associated with 5/6 immunological and 3/11 clinical SLICC criteria (Acute cutaneous lupus, thrombocytopenia, and leukopenia). Of the SLICC criteria, the PRS was most strongly associated with low complement levels ($P=7.4\times10^{-31}$), with nearly twice the rate of lupus patients with low complement levels in the highest PRS decile than those in the bottom PRS decile (55% vs. 30%, respectively).

Conclusion: Our findings indicate that different clinical and immunological criteria are more or less associated with genetic SLE risk. Future studies should consider incorporating genetic risk for developing more comprehensive and accurate prediction models of SLE to inform strategies for clinical prevention, intervention, and management.

Disclosure: N. Forrest: None; **S. Tuteja**: None; **J. Pacheco**: None; **V. Mitrovic**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **T. Walunas**: None; **M. Dapas**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0625

DNA methylation patterns in systemic lupus erythematosus associated with nephritis status

Meghan Nelson[1], Mary Horton[2], Joanne Nititham[3], Jinoos Yazdany[4], Maria Dall'Era[5], Cristina Lanata[3] and Lindsey Criswell[2], [1]NIH/NIAMS/NHGRI, Bethesda, MD, [2]NIH/NHGRI, Bethesda, MD, [3]NIH/NHGRI, Bethesda, [4]UCSF, San Francisco, CA, [5]Division of Rheumatology, University of California, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Individuals with systemic lupus erythematosus (SLE) experience significant variability in clinical outcomes. Our current understanding of the causes of disease heterogeneity are limited, preventing successful risk stratification. To investigate the contribution of epigenetic variation to disease heterogeneity, we generated DNA methylation profiles for a large cohort of SLE patients and examined methylation patterns associated with presence of nephritis, given its importance to morbidity and mortality in SLE.

Methods: We studied 1,882 multi-ancestry SLE patients recruited during routine clinical care. Clinical data were collected at study enrollment and peripheral blood cell collection. Genome-wide methylation profiles were generated using Illumina's EPICv2 BeadChip which includes 937,690 CpG sites. Samples were randomly subset into discovery (n= 1505; ~80%) and validation (n= 377; ~20%) cohorts. Normalization and quality control were performed using *minfi*. Methylation sites (CpGs) with high detection p-values and cross-reactive probes were excluded. Among the discovery cohort, differentially methylated positions (DMPs) associated with nephritis were identified using limma. We used methylation beta values for coefficient interpretation, and methylation M values to determine statistical significance. Models adjusted for genetic principal components, Houseman estimated blood cell proportions, batch, age, disease duration, and sex. DMPs with FDR q< 0.05 were considered significant. Significant DMPs were then tested for their association in the validation cohort using the same models. DMPs with FDR q < 0.05 and the same direction of effect in both cohorts were considered validated.

Results: In the discovery cohort, we identified 5,783 CpGs with FDR q< 0.05. Of these, 12 CpGs had at least a 5% difference in methylation between nephritis cases and non-nephritis SLE controls. 184 CpGs had FDR q < 0.05 and the same direction of effect in the validation cohort. Of these validated CpGs, 13 had at least a 5% difference in methylation between nephritis cases and controls. Validated CpGs included CpGs in *IL1R1* (receptor for Interleukin-1), *STAB1* (a scavenger

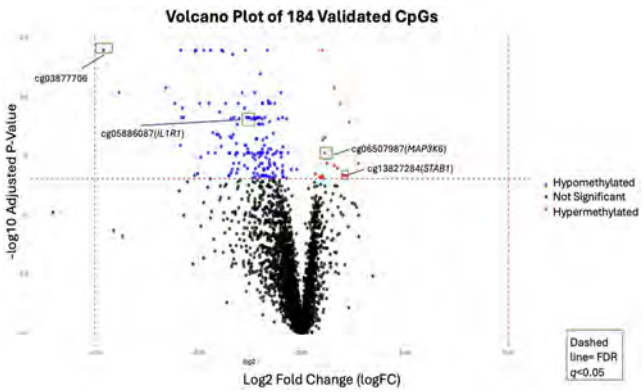


Figure 1. Volcano Plot of validated significant CpG sites.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

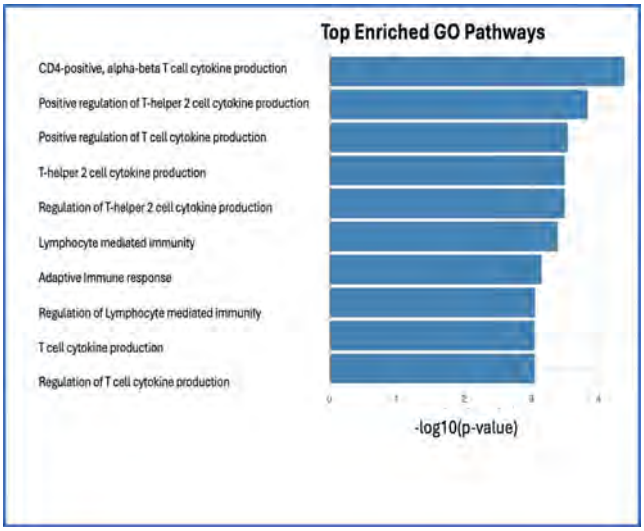


Figure 2. Gene Set Enrichment Analysis (GSEA) with Gene Ontology.

receptor expressed in macrophages and modulator of inflammation), and *TRIM62* (a tripartite motif involved in innate immunity and antiviral response). Of the validated CpG sites, the absolute change in methylation between nephritis cases and controls ranged from 0.2 to 9.5%. A majority of these were hypomethylated; 13 were located within genes, and 23 were in promoter regions. Gene set enrichment analysis revealed enrichment in T-cell production and lymphocyte mediated immunity, although adjusted p-values were not significant (Figure 2).

Conclusion: In the largest SLE multi-ancestry methylation data set to date, we identified 5,783 CpGs that were differentially methylated in SLE patients with nephritis, and we validated approximately 3% of these CpGs in a validation cohort. These results suggest that methylation patterns may provide opportunities to further subtype SLE patients for risk stratification in clinical settings.

Disclosure: M. Nelson: None; **M. Horton**: None; **J. Nititham**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **C. Lanata**: None; **L. Criswell**: None.

Abstract Number: 0626

Evaluation of Novel Anti-ATP1A1 Autoantibodies by ELISA to Predict Cardiac Neonatal Lupus (Cardiac-NL)

Nalani Sachan[1], Philip Carlucci[2], Mala Masson[3], Nicola Fraser[1], Peter Izmirly[4], Camila Hernández-Blanco[5], Robert Clancy[6], Bettina Cuneo[7], Jill Buyon[1] and STOP BLOQ Consortium, [1]NYU Grossman School of Medicine, New York, NY, [2]New York University School of Medicine, New York, NY, [3]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [4]New York University Grossman School of Medicine, New York, NY, [5]NYU Langone Health, New York, NY, [6]Columbia University, New York, NY, [7]University of Arizona College of Medicine, Tucson, AZ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

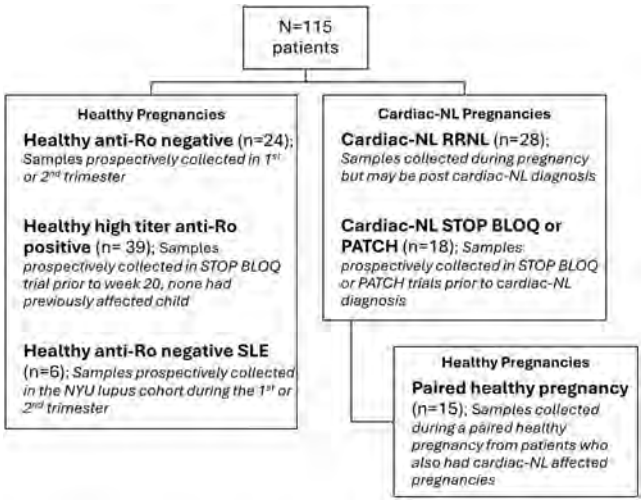
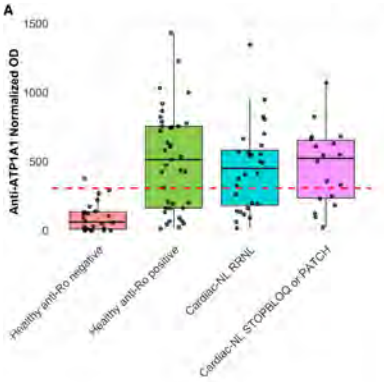


Figure 1: Flow chart describing the sources of the samples used in the study. RRNL: Research Registry for Neonatal Lupus; STOP BLOQ: Surveillance and Treatment to Prevent AV Block Likely to Occur Quickly; PATCH: Preventive Approach To Congenital Heart Block with Hydroxychloroquine

Background/Purpose: For childbearing women with SLE and other autoimmune diseases, the nearly invariant association of cardiac-NL with maternal SSA/Ro52/60kD autoantibodies supports the necessity of these reactivities in the pathogenesis. Although high titer and a history of a previously affected child further increase the risk of fetal disease, the incidence is < 20%, suggesting that another factor, be it protective or permissive, is operative. Addressing the latter, a novel antigenic target Na+/K+ ATPase subunit α1 (ATP1A1), which maintains ion balance across cell membranes, was discovered by western blot screening of fetal hearts and stem-cell derived immature cardiomyocytes, and found to be uniquely targeted only in pregnancies affected by cardiac-NL (Hamilton, ACR, 2022). To facilitate high throughput clinical assessments of this specificity, we leveraged an extensive collection of sera from high titer anti-Ro pregnancies, both affected and unaffected by cardiac-NL, to evaluate the utility of an ELISA based approach to detect anti-ATP1A1 for risk evaluation (Fig 1).

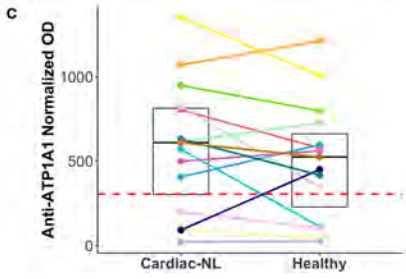
Methods: Commercially available full-length ATP1A1 was coated at a concentration of 0.2 ug/well. All sera were diluted 1:1000. The patient with the highest OD on the first plate was tested on all subsequent plates and all samples were divided

Figure 2: (A) Boxplots showing the normalized optical density (OD) values for the healthy anti-Ro negative, healthy anti-Ro positive, Research Registry for Neonatal Lupus (RRNL) cardiac-NL, and STOP BLOQ or PATCH cardiac-NL samples. The red dashed line at 305 indicates mean + 2 standard deviations above the healthy anti-Ro negative samples. (B) Table showing the percent of patients in each group above the 305 threshold and the median and interquartile range. (C) Boxplots showing the ATP1A1 levels between paired samples collected from a patient during a cardiac-NL (RRNL, PATCH, or STOP BLOQ) and a healthy pregnancy.



B

Group	Total N	Positive anti-ATP1A1 by threshold N (%)	ATP1A1 Normalized OD Median (IQR)
Healthy anti-Ro Positive	39	25 (64%)	514 (162-755)
Cardiac-NL RRNL	28	18 (64%)	450 (183-582)
Cardiac-NL STOPBLOQ or PATCH	18	12 (67%)	522 (234-654)



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

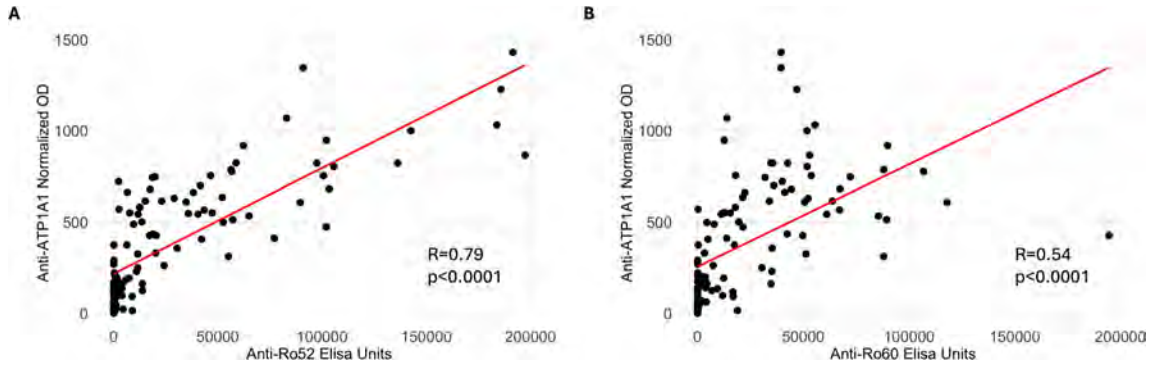


Figure 3: Correlation between Anti-ATP1A1 and Anti-Ro52 (A) or Anti-Ro60 (B). Pearson's correlation coefficient and p-value are listed on the graphs.

by this calibrator to generate a normalized OD. Positive reactivity was defined as 2SD above the mean normalized OD obtained for 24 sera from healthy anti-Ro negative first trimester pregnancies. Sources of all samples are shown in Figure 1.

Results: Of the 46 anti-Ro positive sera tested during pregnancies affected by cardiac-NL (18 in the early second trimester prior to the identification of a fetal arrhythmia), 65% were reactive with full length ATP1A1 (Fig 2A & 2B). Comparable frequencies were observed in 39 anti-Ro positive sera tested during the second trimester of cardiac healthy fetuses, specifically 64%. Similarly, on a continuous scale, ATP1A1 levels did not distinguish cardiac-NL from healthy outcomes (Fig 2A & 2B). To address whether anti-ATP1A1 may be present only during affected pregnancies, unlike anti-Ro antibodies, we evaluated 15 pairs in which one pregnancy was healthy and another affected in the same individual. There were no significant differences between ATP1A1 levels in the affected vs unaffected pregnancy (Fig 2C). One patient became seropositive in the affected pregnancy, while one other lost reactivity in the affected pregnancy (Fig 2C). ATP1A1 levels correlated with anti-Ro52 ($r=0.8$, $p < 0.0001$) and anti-Ro60 ($r=0.5$, $p< 0.0001$) titers. Consistent with this association, reactivity with ATP1A1 was not detected in any of six anti-Ro negative SLE pregnancies.

Conclusion: These data suggest that autoantibodies against full length ATP1A1, measured by ELISA, are present in the majority of anti-Ro+ pregnancies and represent a novel reactivity. However, as tested, this reactivity does not predict the development of cardiac-NL. Binding specific epitopes in the western blot could differ from our approach. The strong correlation with anti-Ro52 implicates cross-reactivity between these targets.

Disclosure: N. Sachan: None; **P. Carlucci**: None; **M. Masson**: None; **N. Fraser**: None; **P. Izmirly**: Hansoh Bio, 2; **C. Hernández-Blanco**: None; **R. Clancy**: None; **B. Cuneo**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2.

Abstract Number: 0627

Marked Decline in SLE Mortality Despite Rising Mortality in the General Population During the COVID-19 Pandemic

Omer Pamuk[1] and Ahmed Nasuhbeyoglu[2], [1]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [2]Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

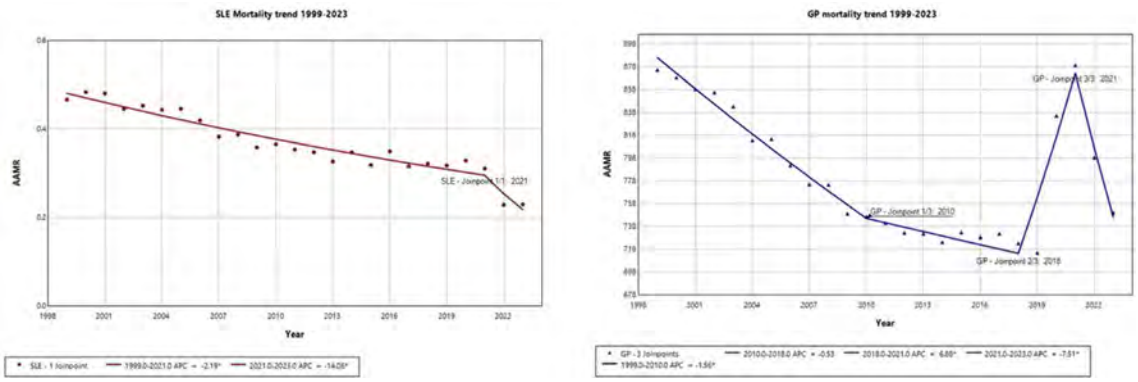


Figure 1 A. Mortality trends in SLE between 1999-2023. Figure 1B. Mortality trends in general population between 1999-2023.

Background/Purpose: Previous studies have shown a decline in systemic lupus erythematosus (SLE)-related mortality rates from 1999 to 2020. This study aimed to evaluate SLE-related mortality trends in the United States during the COVID-19 pandemic.

Methods: We analyzed SLE mortality data from 1999 to 2023 using the CDC WONDER Underlying Cause of Death database and its query system. Age-adjusted mortality rates (AAMRs) were calculated by sex, race, and ethnicity for both SLE and the general population (GP). The first cases and deaths related to COVID-19 in the U.S. were reported in 04/2020. To assess the impact of COVID-19, we focused on mortality rates from 2020 onward. Trends over the study period were assessed using the NCI's Joinpoint Regression Program to identify statistically significant changes in the slope of mortality trends and to calculate annual percentage changes (APCs).

Results: From 1999 to 2023, a total of 30,060 deaths were identified in the US with SLE listed as the underlying cause. Joinpoint trend analysis revealed one inflection point in 2021 within the SLE group. The AAMR for SLE declined between 1999-2021 (APC =–2.19; 95%CI:–2.52 to –1.51; p=0.032), followed by a more pronounced decrease from 2021 to 2023 (APC = –14.1; 95%CI:–22.5 to –3.67; p< 0.00001) (Fig 1A). In the GP, 3 joinpoints were identified (Fig 1B). Pairwise comparison testing indicated a parallel trend in AAMRs between the SLE and general population cohorts over the study period.

Among female SLE patients, trend analysis identified one joinpoint. AAMR declined modestly from 1999 to 2021 (APC =–2.03; 95%CI: –2.39 to –1.6; p=0.0024), followed by a sharp decline after 2021 (APC = –18.93; 95%CI: –25.66 to –8.59; p< 0.00001) (Fig 2A). In females in the GP, 2 joinpoints were identified (Fig 2B). In the male SLE group, no joinpoints were detected, and AAMR declined consistently across the entire study period (APC = –2.32; 95%CI: –3.02 to –1.66; p< 0.00001). In contrast, 3 joinpoints were identified in males in the GP.

Joinpoint analysis identified two inflection points in African American (AA) patients with SLE. The AAMR declined between 1999 and 2013 (APC=–3.14; 95%CI: –7.9 to –2.1; p=0.038), remained stable from 2013 to 2020 (APC= 0.28; 95%CI: –

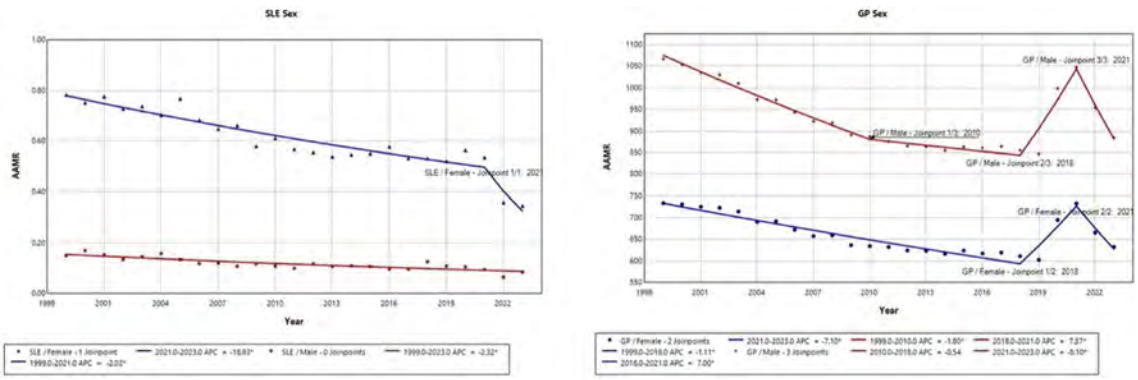


Figure 2A. Mortality trends in SLE by sex. Figure 2B. Mortality trends in general population by sex.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

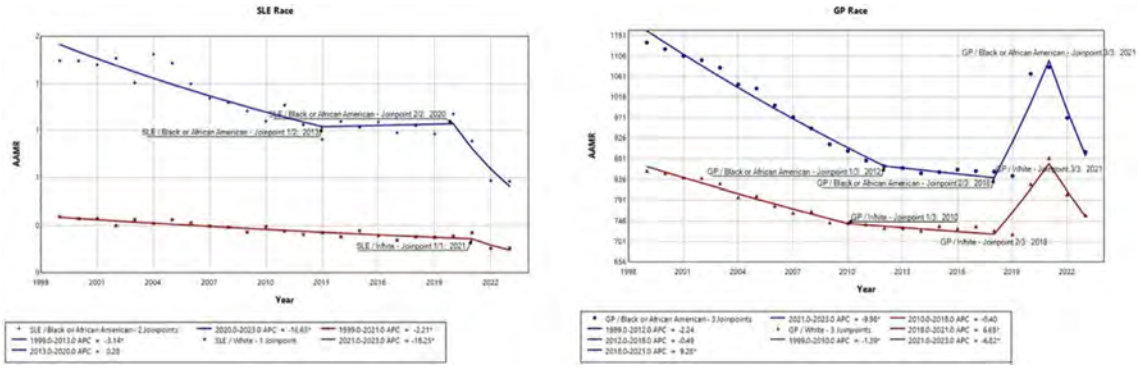


Figure 3A. Mortality trends in SLE by race Figure 3B. Mortality trends in general population by race.

2.1 to 7.3; p=0.76), and then decreased significantly after 2020 (APC=–16.6; 95%CI:–27.1 to –9.9; p< 0.00001). In the White SLE group, 1 joinpoint was identified in 2021. AAMR declined gradually until 2021 (APC = –2.2; 95%CI: –2.7 to –0.6; p=0.045), followed by a more pronounced decrease thereafter (APC=–18.2; 95%CI: –29.9 to –3.0; p=0.0004) (Fig 3A).

In the GP, both White and AA groups showed 3 joinpoints (Fig 3B). Hispanic and non-Hispanic SLE patients displayed similar patterns, with a notable joinpoint observed in 2021.

Conclusion: While overall SLE-related mortality continued to decline through 2023, a marked inflection point was observed during the COVID-19 pandemic across demographic subgroups. Notably, AA patients showed significant post-2021 improvements in mortality trends, suggesting potential impacts of healthcare access, disease management, or pandemic-related factors. Continued monitoring of these trends is essential to understand long-term outcomes and disparities in SLE mortality.

Disclosure: O. Pamuk: None; **A. Nasuhbeyoglu**: None.

Abstract Number: 0628

A user-friendly machine-learning tool for early damage prediction in patients with Systemic Lupus Erythematosus

Panagiotis Garantziotis[1], Dionysis Nikolopoulos[2], Spyridon Katechis[3], Alp Temiz[4], Danae-Mona Nöthling[1], Christina Adamichou[5], Prodromos Sidiropoulos[6], Georg Schett[7], Fanouriakis Antonis[3], Dimitrios Boumpas[8] and George Bertsias[9], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [3]National and Kapodistrian University of Athens Medical School, Athens, Greece, Athens, Greece, [4]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [5]Medical School University of Crete, Heraklion, Greece, Heraklion, Germany, [6]Department of Rheumatology, Clinical Immunology and Allergy, University Hospital of Heraklion, Heraklion, Greece, [7]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [8]Joint Rheumatology Program, University of Athens Medical School, Athens, Greece, [9]Rheumatology and Clinical Immunology, University Hospital of Heraklion and University of Crete Medical School and Foundation for Research and Technology-Hellas (FORTH), Infections and Immunity, Institute of Molecular Biology and Biotechnology, Heraklion, Greece

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Organ damage drives morbidity and mortality in systemic lupus erythematosus (SLE), yet no validated tools exist to predict early damage. We aimed to develop and validate a machine learning model using standard clinical features to forecast organ damage within five years since diagnosis.

Methods: We analyzed a discovery cohort of 914 SLE patients and an independent validation cohort of 50 SLE patients to associate clinical and immunological features with increases in the SLICC/ACR Damage Index within five years of diagnosis (physician-based). The discovery cohort was split into training (70%) and test (30%) sets. Clinically curated panels of classification and non-criteria features were used to build LASSO logistic regression models, with hyper-parameter tuning via 10-fold cross-validation. Performance was assessed by AUC, sensitivity, specificity, and accuracy. Cutoffs were selected by maximizing the F1 score or Youden's index.

Results: A LASSO logistic regression model, integrating both classification criteria and non-criteria clinical features, outperformed

existing classification criteria in predicting early organ damage, with an AUC of 0.86 (95% CI 95% CI 0.76 to 0.97) in the external validation cohort. Key damage predictors were neurologic involvement (SLICC-2012), class III/IV lupus nephritis (EULAR/ACR-2019), and myocarditis. The model achieved a specificity of 0.898 (95% CI: 0.78–0.95) as a binary classifier. When simplified into an 8 variable scoring system, a threshold of > 3 yielded an AUC of 0.86 (95% CI: 0.75–0.96).

Conclusion: We developed and validated an interpretable tool for predicting early organ damage in SLE. Pending further validation, this tool may facilitate individualized risk assessment and damage-preventative strategies including the timely use of biologic treatments.

Disclosure: P. Garantziotis: None; **D. Nikolopoulos**: None; **S. Katechis**: None; **A. Temiz**: None; **D. Nöthling**: None; **C. Adamichou**: None; **P. Sidiropoulos**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **F. Antonis**: None; **D. Boumpas**: None; **G. Bertsias**: AbbVie, 6, AstraZeneca, 2, 5, 6, Eli Lilly, 2, 6, GSK, 2, 5, 6, MSD, 5, Novartis, 2, 6, Otsuka, 6, Pfizer, 6.

Abstract Number: 0629

Characterizing Arthritis Subtypes in SLE: Prevalence, Clinical Features, and the Role of Type I Interferon Signatures

Pankti Mehta[1], Fadi Kharouf[2], Virginia Carrizo Abarza[3], Qixuan Li[4], Dafna D. Gladman[5], Zahi Touma[6] and Laura Whitall Garcia[7], [1]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [2]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [3]University of Toronto, Toronto, [4]Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada, [7]University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: We aimed to study the prevalence of subtypes of lupus arthritis and determine their association with clinical features, serology, and type I interferon signature.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic, clinical and treatment characteristics of the cohort				
	Non-deforming arthritis, 908	Rhupus, 101	Jaccoud's arthropathy, 239	p-value**
Age at diagnosis of SLE in years (median [IQR])	27.87 [20.56, 38.41]	31.42 [22.15, 40.12]	28.57 [21.60, 38.68]	0.20
Sex, female, n (%)	799 (88.1)	91 (90.1)	225 (94.1)	0.03
Disease Duration at enrollment in years (median [IQR])	1.08 [0.07, 5.80]	1.84 [0.25, 6.07]	2.37 [0.20, 8.85]	<0.01
Follow-up duration in years from enrollment (median [IQR])	10.87 [5.08, 19.49]	19.30 [11.47, 27.86]	11.99 [5.81, 23.50]	<0.01
Organ involvement ever, n (%)				
Mucocutaneous	814 (89.6)	96 (95.0)	217 (90.8)	0.21
Neurologic	316 (34.8)	48 (47.5)	94 (39.3)	0.03
Vasculitis	254 (28.0)	32 (31.7)	69 (28.9)	0.72
Renal	443 (48.8)	49 (48.5)	126 (52.7)	0.55
Serositis	170 (18.7)	19 (18.8)	52 (21.8)	0.57
Hematologic	680 (74.9)	76 (75.2)	186 (77.8)	0.64
Constitutional	296 (32.6)	42 (41.6)	87 (36.4)	0.14
Serology and other biomarkers ever, n (%)				
Anti Smith	376 (41.4)	41 (40.6)	110 (46.0)	0.41
Anti RNP	376 (41.4)	41 (40.6)	110 (46.0)	0.12
Anti Ro	513 (56.5)	71 (70.3)	135 (56.5)	0.03
Anti La	290 (31.9)	35 (34.7)	77 (32.2)	0.86
Anti-ribosomal P	77 (8.5)	10 (9.9)	26 (10.9)	0.49
Anti-dsDNA	686 (75.6)	81 (80.2)	193 (80.8)	0.17
Low C3	684 (75.3)	77 (76.2)	178 (74.5)	0.93
Low C4	444 (48.9)	40 (39.6)	110 (46.0)	0.18
Rheumatoid factor	114 (12.7)	17 (16.8)	30 (12.8)	0.5
Anti-CCP, 130 patients	10 (12.9)	5 (29.3)	3 (8.3)	0.11
High type 1 interferon signature, 318 patients	122 (55.7)	7 (26.9)	49 (67.1)	<0.01
Treatment received ever				
Glucocorticoids, n (%)	756 (85.2)	90 (89.1)	224 (94.9)	<0.01
Glucocorticoid dose, median [IQR]	10.00 [6.18, 15.00]	9.12 [6.13, 13.25]	10.00 [7.08, 12.86]	0.60
Antimalarials, n (%)	770 (86.8)	87 (86.1)	209 (88.6)	0.74
Cyclophosphamide, n (%)	75 (8.5)	12 (11.9)	13 (5.5)	0.12
Mycophenolate Mofetil, n (%)	254 (28.6)	31 (30.7)	92 (39.0)	0.01
Azathioprine, n (%)	369 (41.6)	47 (46.5)	118 (50.0)	0.06
Methotrexate, n (%)	195 (22.0)	42 (41.6)	72 (30.5)	<0.01
Rituximab, n (%)	36 (4.1)	7 (6.9)	8 (3.4)	0.31
Belimumab, n (%)	36 (4.1)	5 (5.0)	19 (8.1)	0.04
Joint surgery	73 (8.0)	30 (29.7)	32 (13.4)	<0.01
Disease Activity and Damage				
Adjusted mean SLEDAI-2K	3.82 [2.26, 5.96]	3.11 [2.09, 5.21]	3.96 [2.62, 6.08]	0.09
SDI*, median [IQR]	0.00 [0.00, 1.00]	0.87 [0.00, 1.66]	0.50 [0.00, 1.24]	<0.01

*SDI without the Musculoskeletal component at the last follow-up visit
** univariable analyses comparing non deforming, rhupus, and Jaccoud's arthropathy using chi square/ANOVA.
Abbreviations: IQR: Interquartile range, CI: Confidence Intervals, OR: Odds Ratio, SLEDAI-2K: SLE Disease Activity Index 2000, SDI: SLE damage index, SF: short form, MCS: mental component score, PCS: physical component score, CCP: cyclic citrullinated peptide

Methods: This is a retrospective analysis of a prospective SLE cohort with arthritis defined by the ACR or EULAR/ACR SLE classification criteria at presentation and SLEDAI 2K over follow-up identified from a single-center SLE database (July 1970-Aug 2024) from both inception and prevalent cohorts. Demographic, clinical, laboratory (including interferon signature), radiographic features, and treatment variables were retrieved from the database. Descriptive statistics were used to outline features across three subtypes of arthritis: ND arthritis (determined by clinical examination), arthritis with reducible

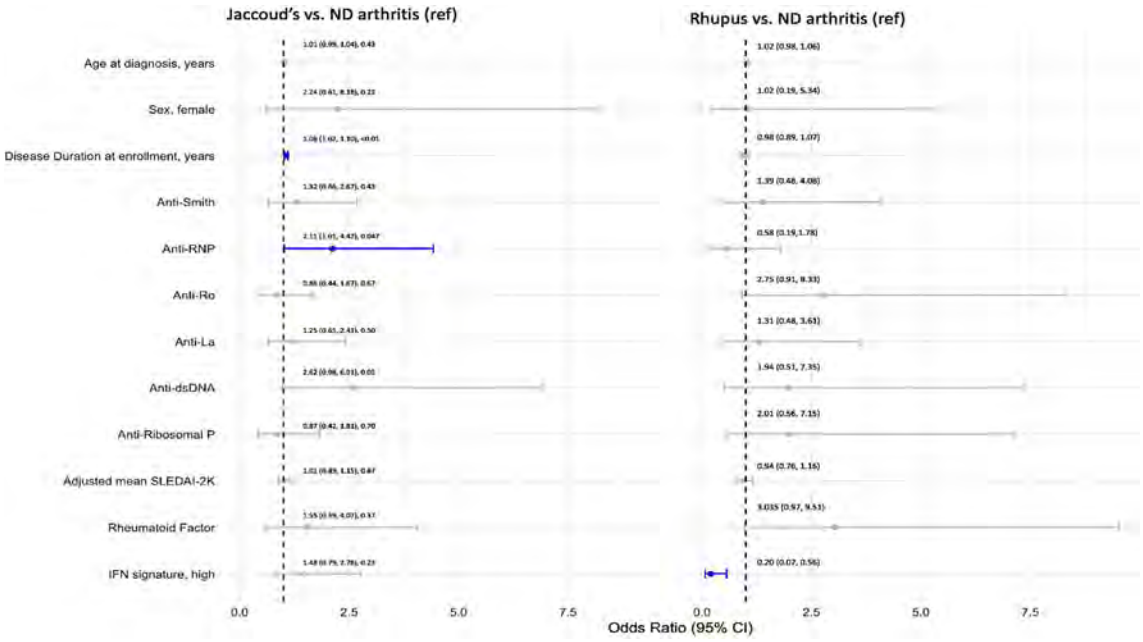


Figure 1: Multivariable logistic regression analyses to identify associations with Jaccoud's and rhupus, non-deforming arthritis being the reference. (n=318)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

deformities or Jaccoud's Arthropathy (JA), and arthritis with non-reducible deformities or rhupus. Factors associated with deforming arthritis were determined using binary logistic regression, including age, sex, disease duration, antibodies, adjusted mean SLEDAI-2K, and Type 1 IFN scores. Time to deformities and predictors were studied in the inception subgroup using fine and gray time-to-event analyses.

Results: Arthritis was observed in 1,248 of 2264 (55.12%) patients, of whom 908 (72.6%) had ND, 239 (19.2%) had JA, 101 (8.1%) had rhupus. The median age at diagnosis of SLE was comparable, though a higher proportion of females was observed in JA (p=0.03).

The distribution of organ involvement and antibodies was similar across the three subtypes, except nervous system involvement (p=0.03) and anti-Ro antibodies (p=0.04) being more frequent in rhupus. Rheumatoid factor and anti-citrullinated protein antibody positivity did not differ significantly. The proportion of patients with high interferon signature was the highest in JA, followed by ND arthritis, and lastly, rhupus (p< 0.01). Radiographs (n, 95) revealed erosive disease in 10 of 43 (23.2%) with JA, 12 of 36 (33.3%) with rhupus, and 2 of 16 (12.5%) with non-deforming arthritis. (Table 1)

In the multivariable analysis, rhupus was associated with a lower odds for a high type I IFN signature (0.20 [0.07, 0.56]) with a direction of positive association towards rheumatoid factor (3.04 [0.97, 9.51] and anti-Ro (2.75 [0.91, 8.33]) positivity when compared with ND arthritis. No associations were observed with JA when compared with ND arthritis. (Figure 1)

The time to development of deformities from enrollment was 2.07 (1.15, 7.6) years for JA and 4.64 (1, 9.78) years for rhupus within the inception cohort. Anti-RNP was predictive of JA on multivariable analysis [4.88 (1.02, 23.5)].

Conclusion: Arthritis was observed in half the cohort, with the majority being non-deforming. Among deforming arthritis, JA was more common than rhupus. JA and ND arthritis were associated with a high IFN signature score while rhupus was characterized by a low IFN signature score. This sheds light on two different mechanisms for deforming arthritis in SLE. Erosions were observed in both types of deforming arthritis blurring the line of radiologic differences historically outlined between them.

Disclosure: P. Mehta: None; **F. Kharouf**: None; **V. Carrizo Abarza**: None; **Q. Li**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **L. Whitall Garcia**: None.

Abstract Number: 0630

Development, Validation and Performance of a Patient Knowledge Assessment Tool for Assessing the Immediate and Short-term Impact of an Information Course in Systemic Lupus Erythematosus

Ranjan Gupta, Rudra Prosad Goswami and Anju Mohan, All India Institute of Medical Sciences, New Delhi, Delhi, India

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Long-term outcomes in rheumatic diseases can be improved by improving patients' knowledge, beliefs and perception about their disease. However, there is a lack of tools/instruments in Systemic Lupus Erythematosus

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table – 1 Question-wise assessment of responses before and after the information course and the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=56)			Post-Test Performance (n=39)			Statistical Significance (p<0.05)* Y/N
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	
1.	Etiology of disease	44.64	5.36	50	66.67	12.83	20.5	N
2.	Hereditary nature	44.64	10.76	44.6	64.10	15.4	20.5	N
3.	Dietary restrictions in SLE	50.00	21.4	28.6	64.10	20.5	15.4	Y
4.	Possibility of cure	55.36	14.24	30.4	69.23	12.87	17.9	Y
5.	Extra-articular manifestations	60.71	24.99	14.3	71.79	10.31	17.9	Y
6.	Possibility of pregnancy	42.86	16.04	41.1	74.36	5.14	20.5	N
7.	Breastfeeding in SLE	60.71	13.69	60.7	66.67	7.73	25.6	N
8.	Prevention of flare	67.86	3.54	28.6	87.18	5.12	7.7	N
9.	Blood tests (CBC, LFT, RFT)	7.14	78.56	14.3	41.03	56.37	2.6	N
10.	Repeat ANA test	21.43	37.47	41.1	64.10	23.1	12.8	N
11.	Reason for doing urine test	25.00	57.1	17.9	43.59	51.31	5.1	Y
12.	Identification of steroids	58.93	10.67	30.4	69.23	15.37	15.4	Y
13.	Identification of DMARDs	46.43	12.47	41.1	69.23	2.57	28.2	Y
14.	Drugs during pregnancy & breastfeeding	8.93	8.97	82.1	33.33	23.07	43.6	Y
15.	Hydroxychloroquine in pregnancy	23.21	10.69	66.1	38.46	20.54	41.0	Y
16.	Duration of treatment in SLE	76.79	1.81	21.4	92.31	0.0	7.7	N
17.	Cure by using alternative medicine	37.50	19.6	42.9	66.67	15.43	17.9	Y
18.	Steroid adverse effects 1	10.71	28.59	60.7	35.90	30.8	33.3	N
19.	Steroid adverse effects 2	48.21	5.39	46.4	69.23	7.67	23.1	Y
20.	Forgetting to take medicines	66.07	10.73	23.2	82.05	10.25	7.7	Y
21.	Onset of DMARDs action	46.43	30.37	23.2	71.79	17.91	10.3	Y
22.	Lupus Nephritis	33.93	17.87	48.2	69.23	15.37	15.4	Y
23.	Renal Biopsy	25.00	23.2	51.8	66.67	10.23	23.1	N

*change with respect to the correct responses before and after the information course (Assessed by McNemar test)

(SLE) to 1. objectively assess patients' knowledge in various domains & 2. To assess the impact of a patient education program.

The aim of the study was to develop, validate and assess the performance of a self-prepared questionnaire for assessing patients' knowledge about their disease and to use this tool to assess the impact of an information course in improving the above-mentioned elements among patients.

Methods: A self-prepared questionnaire (Hindi/English) containing 23 multiple choice or true-false type questions with single correct answer assessing patients' knowledge about SLE in 3 domains (a. etiology, disease process, signs & symptoms

Table – 2 Question-wise assessment of responses before the information course and after 4 months with the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=56)			6 months responses (n=36)			Statistical Significance (p<0.05)* Y/N
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	
1.	Etiology of disease	44.64	5.36	50	72.22	16.68	11.1	N
2.	Hereditary nature	44.64	10.76	44.6	83.33	11.07	5.6	N
3.	Dietary restrictions in SLE	50.00	21.4	28.6	77.78	11.12	11.1	N
4.	Possibility of cure	55.36	14.24	30.4	80.56	11.14	8.3	Y
5.	Extra-articular manifestations	60.71	24.99	14.3	75.00	19.4	5.6	Y
6.	Possibility of pregnancy	42.86	16.04	41.1	88.89	11.11	0	N
7.	Breastfeeding in SLE	60.71	13.69	60.7	50.00	33.3	16.7	N
8.	Prevention of flare	67.86	3.54	28.6	91.67	5.53	2.8	N
9.	Blood tests (CBC, LFT, RFT)	7.14	78.56	14.3	27.78	72.22	0.0	N
10.	Repeat ANA test	21.43	37.47	41.1	61.11	30.59	8.3	N
11.	Reason for doing urine test	25.00	57.1	17.9	38.89	61.11	0.0	N
12.	Identification of steroids	58.93	10.67	30.4	77.78	11.12	11.1	Y
13.	Identification of DMARDs	46.43	12.47	41.1	69.44	8.36	22.2	Y
14.	Drugs during pregnancy & breastfeeding	8.93	8.97	82.1	33.33	22.27	44.4	N
15.	Hydroxychloroquine in pregnancy	23.21	10.69	66.1	38.89	16.71	44.4	Y
16.	Duration of treatment in SLE	76.79	1.81	21.4	97.22	2.78	0.0	N
17.	Cure by using alternative medicine	37.50	19.6	42.9	72.22	22.18	5.6	N
18.	Steroid adverse effects 1	10.71	28.59	60.7	22.22	44.48	33.3	Y
19.	Steroid adverse effects 2	48.21	5.39	46.4	72.22	5.58	22.2	Y
20.	Forgetting to take medicines	66.07	10.73	23.2	94.44	2.76	2.8	N
21.	Onset of DMARDs action	46.43	30.37	23.2	75.00	19.4	5.6	N
22.	Lupus Nephritis	33.93	17.87	48.2	69.44	11.16	19.4	Y
23.	Renal Biopsy	25.00	23.2	51.8	58.33	22.27	19.4	N

*change with respect to the correct responses at 6 months compared to the correct responses before the information course

(Assessed by McNemar test)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

b. drug therapy & monitoring c. role of investigations in disease diagnosis and monitoring) was prepared. All questions had an item-level content validity index (I-CVI) of at least 0.9. The scale-level content validity index based on the universal agreement method (S-CVI/UA) was 0.8 for the whole questionnaire as assessed by 6 experts. All questions had an option of 'I don't know' which would prevent patients from guessing the answer from the available options. Each question was given a score of 1 if answered correctly. The questionnaire was applied 3 times: at baseline, immediately after an information course to see the immediate impact and after 6 months to see the retention of the information. Information on demographic features and socio-economic status was also collected. Frequency data were compared using McNemar test for paired nominal data & kappa statistics for ordinal data. Student's paired t-test was used for comparison of mean scores to see the impact. A p-value< 0.5 was considered significant.

Results: At baseline, the questionnaire was applied to 56 patients with SLE (F:M=54:2; median age 29(16-53) years) and the median(range) score was 10(2-19) (Table–1). Among them, 39 patients attended the information course. The option 'I don't know' was exercised 509 times (39.51%) before the information course which reduced to 169 (18.84%) times after the course and 108 (13.04%) times at 6 months.

After the information course, median score increased from 10(2-19) to 17(0-23) (p< 0.001) which was irrespective of the socio-economic classes and education status of the patients (Figure-1). A total of 13 questions recorded a higher number of correct responses as compared to baseline and this increase was significant for all 13 questions (Table–1).

Upon re-administering the questionnaire after 6 months, 36 patients out of 39 responded. The median score 16(0-23) of the questionnaire (n=36) remained significantly higher (p< 0.001) as compared to baseline score. Eight out of 23 questions achieved statistical significance (Table–2).

Conclusion: Indian patients with SLE have a poor knowledge base which can be improved by implementing short information courses. The information course was effective across the socio-economic classes and educational status and the information was retained at 6th month without any reinforcement course.

Disclosure: R. Gupta: None; **R. Goswami**: None; **A. Mohan**: None.

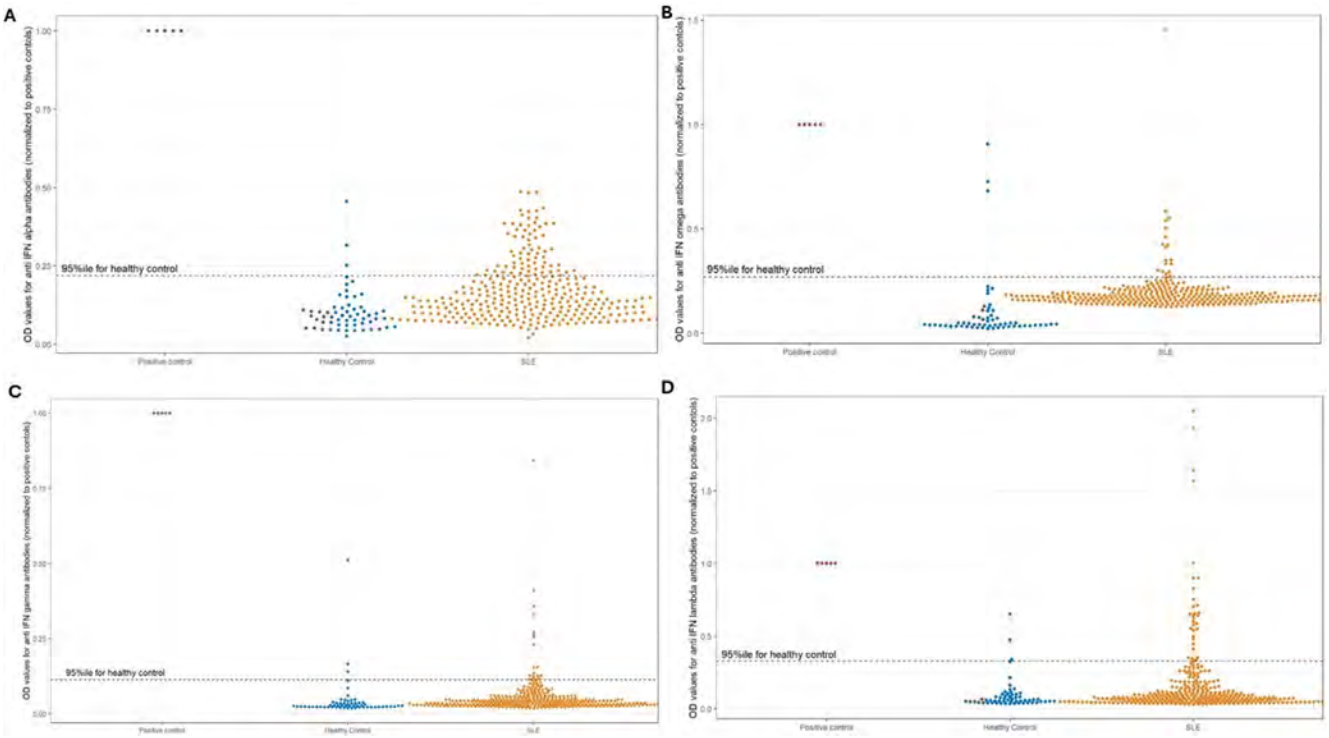
Abstract Number: 0631

Antibodies to Type I and Type III Interferons at Diagnosis Predispose to Serious Infections on Follow up in an Inception Cohort of SLE (INSPIRE) from India

Rudrarpan Chatterjee[1], Komal Singh[2], Ranjan Gupta[3], Sudhir Sinha[4] and Amita Aggarwal[5], [1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow., Lucknow, Uttar Pradesh, India, [2]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Lucknow, Uttar Pradesh, India, [3]All India Institute of Medical Sciences, New Delhi, Delhi, India, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Lucknow, India, [5]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Background/Purpose: Patients with systemic lupus erythematosus (SLE) are predisposed to infections due to immune dysregulation. Autoantibodies to cytokines can cause serious infections, including severe COVID-19, by mycobacteria or other intracellular microbes. We describe here antibodies to type I, II and III interferons (IFNα, ω, γ & λ) as a cause for infections in an inception cohort of SLE (INSPIRE) from India.

Methods: Newly diagnosed SLE (SLICC 2012 criteria) within 6 months of disease onset were enrolled in the INSPIRE cohort from 2018-2023. We developed an ELISA for antibodies to IFN α, ω, γ and λ. Baseline sera retrieved from the biobank were tested for these antibodies. Antibody titres were expressed as optical density (OD) and the 95th percentile of antibody titres in healthy-control population was used to develop cutoffs for positivity. Outcomes studied were infections in the initial 2 years of follow up. Serious infections were those that led to hospitalisation or mortality.

Results: A total of 313 patients of SLE (294 females) with a mean age 27.7±10.2 years were enrolled from 2 centres in North India. In addition, sera from 59 healthy controls were also tested for anti IFN antibodies. Antibodies to IFN-α, IFN-ω, IFN- γ and IFN-λ were present in 73 (23.3%), 18 (5.5%), 18 (5.5%) and 30 (9.6%) patients respectively. Eight patients (2.72%) had more than 1 anti-interferon antibodies. In contrast, 3 (5.08%) healthy controls had antibodies to IFN-α, IFN-ω, IFN- γ and IFN-λ each.

In the initial 2 years, there were 107 infections, of which 31 were serious infections. Bacterial including mycobacterial infections (79, 25.2%) were most common followed by viral (32, 10.2%) and fungal (15, 4.8%). Herpes zoster (25, 7.9%) was the most common infection followed by tuberculosis (11, 3.5%). No healthy control had history of serious infections.

Antibodies to IFN-α were associated with serious infections (OR 2.79, 1.29-6.04), tuberculosis (OR 3.46, 1.03-11.68), viral infections (OR 2.64, 1.23-5.68) and Herpes zoster (OR 3.1, 1.2-8.02), but not with overall infections (OR 1.3, 0.76-2.35), bacterial (OR 1.27, 0.69-2.36) or fungal (OR 1.23, 0.38-3.99) infections. Antibodies to IFN-λ were associated with serious infections (OR 2.93, 1.1-7.83) but not with any subtype of infection. Antibodies to IFN-ω and IFN-γ were not associated with any higher risk of infections.

Conclusion: Antibodies to IFN-α are the most common anti-interferon antibody in an Indian inception cohort of SLE and predispose to serious infections, especially viral infections, Herpes zoster and tuberculosis in the initial 2 years of follow-up.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Chatterjee: None; **K. Singh**: None; **R. Gupta**: None; **S. Sinha**: None; **A. Aggarwal**: None.

Abstract Number: 0632

Comparative Outcomes of GLP-1 Receptor Agonists Versus SGLT2 Inhibitors in Patients with Systemic Lupus Erythematosus and Diabetes: A Propensity-Matched Retrospective Cohort Study

Rusudan Tskitishvili[1], Abdallah Hussein[2], Roman Karagulyan[2], Shatha Shahwan[3] and Priju Varghese[2], [1]Virtua Health, Camden, NJ, [2]Virtua Health, Camden, [3]Jordan University of Science and Technology, Jordan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with a heightened risk of cardiovascular and renal complications, particularly in patients with comorbid diabetes mellitus. While both GLP-1 receptor agonists and SGLT2 inhibitors have shown cardio-renal benefits in the general diabetic population, comparative outcome data in patients with SLE remain limited.

Methods: This retrospective cohort study utilized data from the global TriNetX Collaborative Network and included adult patients (aged ≥18 years) diagnosed with both SLE and diabetes between January 1, 2015, and December 31, 2023. Patients were grouped based on exposure to either GLP-1 receptor agonists or SGLT2 inhibitors. The primary outcome was all-cause mortality, while secondary outcomes included major adverse cardiovascular events (MACE) and lupus nephritis. Propensity score matching (1:1) was used to balance baseline characteristics between groups. Risk ratios (RRs), 95% confidence intervals (CIs), and p-values were calculated for outcome comparisons after matching.

Results: After matching, 885 patients were included in each group. The mean ± SD age was 57.7 ± 12.1 years, with approximately 82% female and 39% identifying as White. Baseline characteristics were well balanced following propensity score matching. The incidence of MACE was significantly lower in the GLP-1 group (3.2%) compared to the SGLT2 group (6.0%; RR, 0.53; 95% CI, 0.337–0.827; $p = 0.0045$). Similarly, the incidence of lupus nephritis was significantly lower in the GLP-1 group (4.7%) compared to the SGLT2 group (9.8%; RR, 0.48; 95% CI, 0.338–0.689; $p < 0.0001$). All-cause mortality was slightly lower in the GLP-1 group (1.6%) versus the SGLT2 group (2.1%), but this difference did not reach statistical significance (RR, 0.74; 95% CI, 0.372–1.46; $p = 0.737$).

Conclusion: Among patients with systemic lupus erythematosus and diabetes, treatment with GLP-1 receptor agonists was associated with significantly lower rates of major adverse cardiovascular events (MACE) and lupus nephritis compared to SGLT2 inhibitors. While all-cause mortality was numerically lower in the GLP-1 group, the difference was not statistically significant. These findings suggest that GLP-1 receptor agonists may offer greater cardio-renal protection in this high-risk population and warrant further investigation in prospective clinical trials.

Disclosure: R. Tskitishvili: None; **A. Hussein**: None; **R. Karagulyan**: None; **S. Shahwan**: None; **P. Varghese**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0633

Diffuse Alveolar Hemorrhage in ANCA-Associated Vasculitis (AAV) and Systemic Lupus Erythematosus (SLE): A Comparative Analysis

Sai Shanmukha Sreeram Pannala[1], Medha Rajamanuri[2], Srikar Sama[3], Fares Saliba[4], Omar Mourad[5], Elizabeth Fagin[6], Koushik Varma Sangaraju[7], Veena Katikineni[8] and Anastasia Slobodnick[9], [1]Northwell health/Staten Island university Hospital, new york city, NY, [2]Southern Illinois University School of Medicine, Springfield, IL, [3]University of California San Francisco Fresno, Fresno, CA, [4]Staten Island University Hospital, Staten Island, NY, [5]Zucker School of Medicine at Hofstra/Northwell at Staten Island University Hospital, Staten Island, NY, [6]Staten Island University Hospital, Teaneck, NJ, [7]St. Luke's University Health Network, Bethlehem, PA, [8]Desert Orthopaedic and Rheumatologic Institute, Apple Valley, CA, [9]Northwell, Staten Island, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Diffuse alveolar hemorrhage (DAH) is a rare but severe complication in Systemic Lupus Erythematosus (SLE), occurring in up to one-third of cases at disease onset. In ANCA-associated vasculitis (AAV), the prevalence of DAH is around 25%, with high morbidity and mortality. DAH in both SLE and AAV requires prompt investigation, presenting challenges in initiating life-saving treatments. The objective of this study is to compare the in-hospital mortality in patients with DAH secondary to AAV versus DAH secondary to SLE, aiming to inform management strategies and improve clinical decision-making.

Methods: We used the National Inpatient Sample database from Jan 2020 to Dec 2022 to compare baseline characteristics and outcomes of patients with DAH due to AAV versus SLE. Both groups were analyzed for demographic factors, comorbidities, hospital-related variables, and clinical outcomes. Key outcomes included length of stay (LOS), total charges, and in-hospital mortality, with logistic regression used to assess factors associated with mortality.

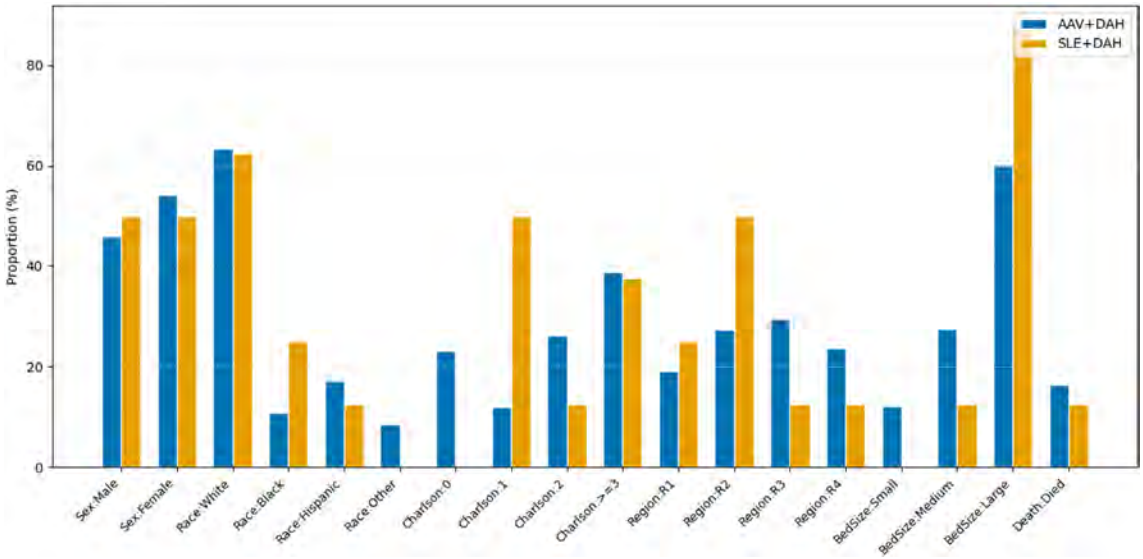


Figure 1: Baseline comparison of Diffuse Alveolar Hemorrhage (DAH) due to Systemic Lupus Erythematosus (SLE) versus ANCA-associated vasculitis (AAV).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 1,470 patients with AAV + DAH and 915 patients with SLE + DAH were identified. In the AAV + DAH group, 54.2% were female, compared to 50% in the SLE + DAH group. The mean age for AAV + DAH patients was significantly higher at 55.34 years, compared to 43.25 years in the SLE + DAH group. Racial distribution showed 63.4% of AAV + DAH patients were White, compared to 62.5% in the SLE + DAH group. AAV + DAH patients had a higher proportion of severe comorbidities (38.8%) compared to SLE + DAH (37.5%). Hospital region distribution showed SLE + DAH patients were more likely to be admitted to hospitals in the South (50%) compared to AAV + DAH (27.3%). More SLE + DAH patients were admitted to large hospitals (87.5%) compared to AAV + DAH (60.1%) (Fig 1).

The mean LOS was 16.30 days for AAV + DAH and 15.87 days for SLE + DAH, with total charges for AAV + DAH higher at $273,083 compared to $233,180 for SLE + DAH. The mortality rate for AAV + DAH was 16.4%, compared to 12.5% for SLE + DAH ($p = 0.7671$). Logistic regression showed no significant difference in mortality between the two groups. (OR 0.73, $p = 0.7680$).

Conclusion: This study highlights the similarities and differences in the clinical characteristics, comorbidities, and healthcare burden of DAH secondary to AAV versus SLE. While both groups share significant morbidity and mortality, AAV + DAH patients were older, had more severe comorbidities, and incurred higher healthcare costs compared to SLE + DAH patients. Despite these differences, there was no significant difference in in-hospital mortality between the two groups, suggesting that the severity of DAH may not differ substantially based on the underlying disease. The findings underscore the need for further research to better understand the impact of DAH in these distinct patient populations.

Disclosure: S. Pannala: None; **M. Rajamanuri**: None; **S. Sama**: None; **F. Saliba**: None; **O. Mourad**: None; **E. Fagin**: None; **K. Sangaraju**: None; **V. Katikineni**: None; **A. Slobodnick**: None.

Abstract Number: 0634

Association of Lifestyle and Integrative Health Practices with Health-related Quality of Life in Women with Systemic Lupus Erythematosus and Connective Tissue Disease

Sarah Lieber[1], Yongjay Kim[2], Lucy Masto[3], Amaya Smole[4], Neha Nagpal[1], Ranqing Lan[1], Michael Parides[1], Caroline Siegel[1], Lisa Mandl[1], Michael Lockshin[5], Medha Barbhaiya[1] and Lisa Sammaritano[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Englewood Cliffs, NJ, [3]Hospital for Special Surgery, San Francisco, CA, [4]Hospital for Special Surgery, Brooklyn, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Although available evidence supports the benefits of lifestyle interventions in SLE, the prevalence of lifestyle and integrative health behaviors and their association with health-related quality of life (HRQoL) in real world practice are not well understood. We describe the association of physical activity (PA), diet, and integrative health behaviors with HRQoL in women with SLE and other connective tissue disease (CTD) at a single tertiary care musculoskeletal center.

Methods: We included women aged 18-65 years evaluated by a Hospital for Special Surgery rheumatologist ≥2 times who enrolled in the Rheumatology Women's Reproductive Health and Wellness Cohort from 12/2022-5/2024. The current cross-sectional analysis includes women with SLE and other CTD (identified by ≥2 ICD-10 codes ≥7 days apart) who shared

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

type and frequency of PA, dietary quality, and integrative health practices and responded to questions on HRQoL reflecting 4 domains (life satisfaction, life worthwhile, happiness, anxiety, each scored on a 0-10 scale, with 0 "not at all" and 10 "completely") from the United Kingdom Office for National Statistics. We performed descriptive analyses to summarize self-reported demographic and clinical characteristics, diet, PA, and integrative health practices. Logistic regression models were built using each of the 4 HRQoL domains (dichotomized) as outcomes, with lifestyle and integrative health behaviors as independent variables. Adjusted models controlled for age, race, ethnicity, and immunosuppressive medication use.

Results: Of 255 women (mean age 46.8 ±12.1 years), 180 (71%) reported exercising ≥1-3 times per week, and 105 (41%) rated their diet as very good or excellent; 166 (65%) participants were pursuing ≥1 integrative health practice at survey completion (Table 1). In unadjusted models, participants who reported never engaging in PA were less likely to report life satisfaction (odds ratio [OR] 0.18, 95% confidence interval [CI] 0.03-0.81] and happiness (OR 0.21, 95% CI 0.04-0.90) compared to those who exercised >3x/week while participants with a poor diet had lower odds of reporting life worthwhile (OR 0.17, 95% 0.03-0.94) and higher odds of reporting anxiety (OR 6.75, 95% 1.42, 39.68) compared to those with an excellent diet

Table 1. Characteristics of 255 women with SLE and other CTD who enrolled in the Hospital for Special Surgery Women's Reproductive Health and Wellness Cohort and completed Health-Related Quality of Life Questionnaires

Variable			*N (%) or mean (SD)*
Age (years), mean (SD) (N=255)			46.8 (12.1)
Race, N (%) (N=248)	White		175 (71)
	Black or African American		39 (16)
	Asian		23 (9)
	American Indian or Alaska Native		3 (1)
	Other		20 (8)
Ethnicity, N (%) (N=254)	Hispanic or Latino		46 (18)
	Not Hispanic or Latino		208 (82)
Current immunomodulatory and immunosuppressive medications, N (%) (N=251)	Systemic steroids		79 (31)
	Antimalarials		166 (65)
	Biologics		53 (21)
	DMARDs or immunosuppressive medications		94 (37)
	JAK inhibitors		2 (1)
	Other		34 (13)
Physical exercise frequency, N (%) (N=254)	Never		15 (6)
	<Once a month		26 (10)
	<Once a week		33 (13)
	1-3 times per week		89 (35)
	>3 times per week		91 (36)
Physical exercise type, N (%) (N=239)	Walking		193 (76)
	Running, biking/spinning, elliptical, or similar cardio/aerobic		77 (30)
	Yoga, pilates, Barre, or similar program		91 (36)
	Strength training or weightlifting		86 (34)
	Other		30 (12)
Current supplement use, N (%) (N=130)			130 (51)
Self-rated diet, N (%) (N=255)	Poor		14 (5)
	Fair		45 (18)
	Good		91 (36)
	Very good		74 (29)
	Excellent		31 (12)
Current integrative health practices, N (%) (N=254)	Meditation		78 (31)
	Mindfulness		94 (37)
	Acupuncture		20 (8)
	Chiropractic care		15 (6)
	Massage		72 (28)
	Other/none of the above		120 (47)
	≥1 practice		166 (65)
Ever (current or past) integrative health practices, N (%) (N=255)	Meditation		126 (50)
	Mindfulness		126 (50)
	Acupuncture		94 (37)
	Chiropractic care		64 (25)
	Massage		148 (58)
	Other/none of the above		77 (31)
	≥1 practice		219 (86)
General wellbeing (Office of National Health Statistics-4)	Life satisfaction (N=249)	Low[a], N (%)	14 (6)
		Medium[b], N (%)	48 (19)
		High[c], N (%)	109 (44)
		Very high[d], N (%)	78 (31)
	Life worthwhile (N=247)	Low[a], N (%)	11 (4)
		Medium[b], N (%)	39 (16)
		High[c], N (%)	85 (34)
		Very high[d], N (%)	112 (45)
	Happiness (N=245)	Low[a], N (%)	15 (6)
		Medium[b], N (%)	52 (21)
		High[c], N (%)	99 (40)
		Very high[d], N (%)	79 (32)
	Anxiety (N=251)	Very low[e], N (%)	52 (21)
		Low[f], N (%)	57 (23)
		Medium[g], N (%)	38 (15)
		High[h], N (%)	104 (41)

[a] 0-4; [b] 5-6; [c] 7-8; [d] 9-10; [e] 0-1; [f] 2-3; [g] 4-5; [h] 6-10

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Logistic regression models relating lifestyle and integrative health practices to health-related quality of life (life satisfaction, life worthwhile, happiness, and anxiety) in participants with SLE and other CTD

Lifestyle or integrative health practice	Health-related quality of life			
	Life satisfaction[a]	Life worthwhile[a]	Happiness[a]	Anxiety[b]
	Unadjusted OR (95% CI)			
Physical activity level				
>3 times/week	Reference	Reference	Reference	Reference
1-3x/week	1.34 (0.62-2.96)	1.98 (0.87-4.66)	0.75 (0.35-1.59)	0.75 (0.39-1.46)
<1x/week	0.89 (0.34-2.42)	2.42 (0.8-8.59)	0.78 (0.29-2.15)	0.61 (0.24-1.50)
<1x/month	2.41 (0.67-11.82)	1.78 (0.53-7.33)	0.6 (0.2-1.87)	1.25 (0.46-3.40)
Never	0.18 (0.03-0.81)	0.29 (0.06-1.29)	0.21 (0.04-0.90)	1.44 (0.33-6.59)
Self-rated diet				
Excellent	Reference	Reference	Reference	Reference
Very good	2.19 (0.79-6.00)	0.89 (0.25-2.77)	1.81 (0.65-4.92)	1.16 (0.46-3.03)
Good	1.41 (0.52-3.71)	0.53 (0.15-1.59)	1.29 (0.47-3.40)	1.64 (0.66-4.27)
Fair	2.32 (0.66-8.52)	0.9 (0.21-3.84)	2.11 (0.63-7.18)	1.49 (0.5-4.54)
Poor	0.43 (0.08-2.09)	0.17 (0.03-0.94)	0.77 (0.16-3.64)	6.75 (1.42-39.68)
≥1 integrative health practice	0.91 (0.45-1.80)	0.88 (0.41-1.81)	1.05 (0.54-2.00)	1.47 (0.81-2.70)

[a]Dichotomized into high/very high (score 7-10) and medium/low (score 0-6) based on Office of National Health Statistics-4
[b]Dichotomized into high (score 4-10) and medium/low/very low (score 0-6) based on Office of National Health Statistics-4

Table 3. Adjusted* logistic regression models relating lifestyle and integrative health practices to health-related quality of life (life satisfaction, life worthwhile, happiness and anxiety) in participants with SLE and other CTD

Lifestyle or integrative health practice	Health-related quality of life			
	Life satisfaction[a]	Life worthwhile[a]	Happiness[a]	Anxiety[b]
	Adjusted* OR (95%)			
Physical activity level				
>3 times/week	Reference	Reference	Reference	Reference
1-3x/week	1.57 (0.69-3.63)	2.41 (1.01-6.02)	0.79 (0.36-1.73)	0.78 (0.38-1.57)
<1x/week	0.95 (0.34-2.74)	2.85 (0.88-10.89)	0.82 (0.29-2.38)	0.6 (0.22-1.56)
<1x/month	2.88 (0.75-14.86)	2.24 (0.63-9.76)	0.63 (0.21-2.06)	1.08 (0.38-3.07)
Never	0.19 (0.03-0.90)	0.34 (0.07-1.57)	0.20 (0.04-0.88)	1.40 (0.3-6.7)
Self-rated diet				
Excellent	Reference	Reference	Reference	Reference
Very good	2.19 (0.78-6.11)	0.88 (0.25-2.81)	1.81 (0.64-4.99)	1.27 (0.49-3.41)
Good	1.16 (0.42-3.14)	0.44 (0.12-1.36)	1.11 (0.40-2.99)	1.75 (0.67-4.75)
Fair	1.89 (0.52-7.23)	0.79 (0.17-3.50)	1.97 (0.57-6.91)	1.39 (0.44-4.44)
Poor	0.39 (0.07-1.91)	0.15 (0.03-0.85)	0.77 (0.16-3.68)	8.19(1.62-51.18)
≥1 integrative health practice	0.97 (0.47-1.95)	0.95 (0.44-2.00)	1.08 (0.55-2.09)	1.39 (0.75-2.59)

[a]Dichotomized into high/very high (score 7-10) and medium/low (score 0-6) based on Office of National Health Statistics-4
[b]Dichotomized into high (score 4-10) and medium/low/very low (score 0-6) based on Office of National Health Statistics-4
*Adjusted for age, race, ethnicity, and immunosuppressive medication use

(Table 2). In adjusted models, participants who reported never engaging in PA were less likely to report life satisfaction (OR 0.19, 95% CI 0.03-0.90) and happiness (OR 0.20, 95% CI 0.04-0.88) compared to those who exercised >3x/week while participants with a poor diet had lower odds of reporting life worthwhile (OR 0.15, 95% 0.03-0.85) and higher odds of reporting anxiety (OR 8.19, 95% 1.62, 51.18) compared to those with an excellent diet (Table 3); any exercise was potentially associated with life worthwhile (high/very high versus medium/low).

Conclusion: In this sample, engagement in lifestyle and integrative health behaviors was common in SLE and other CTD. Lack of PA and poor diet were generally associated with decreased HRQoL. Interventional strategies promoting PA and healthy diet may improve wellbeing in this population alongside disease-directed therapies.

Disclosure: S. Lieber: None; **Y. Kim**: None; **L. Masto**: None; **A. Smole**: None; **N. Nagpal**: None; **R. Lan**: None; **M. Parides**: None; **C. Siegel**: None; **L. Mandl**: ACP, 12, Associate Editor Annals of Internal Medicine, Wolters, 9; **M. Lockshin**: None; **M. Barbhaiya**: None; **L. Sammaritano**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0635

Comparison of the SARC-F with Objective Measures of Sarcopenia in Women with Systemic Lupus Erythematosus

Sarah Lieber[1], Neha Nagpal[1], Julia Nguyen[2], Ashley Chung[2], Dongmei Sun[1], John Carrino[3], M. Carrington Reid[4] and Lisa Mandl[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, New York, [3]Department of Radiology and Imaging, Hospital for Special Surgery, New York, NY, [4]Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1. Sociodemographic and disease characteristics and SARC-F components of adults with systemic lupus erythematosus (SLE) with high (≥4) versus low (<4) SARC-F scores

Variable N (%) or median [IQR]	Overall (N=57)	SARC-F score ≥4 (N=16)	SARC-F score <4 (N=40)	p-value
Age (years)	47.0 [36.0, 60.0]	59.5 [45.0, 62.5]	39.0 [30.8, 58.0]	0.02
Gender				
Female	57 (100.0)	16 (100.0)	40 (100.0)	
Race*				0.89
Asian	5 (8.9)	1 (6.2)	4 (10.3)	
Black or African American	19 (33.9)	7 (43.8)	12 (30.8)	
White	15 (26.8)	3 (18.8)	11 (28.2)	
Other	15 (26.8)	5 (31.2)	10 (25.6)	
Declined to state	2 (3.6)	0 (0.0)	2 (5.1)	
Ethnicity**				0.77
Hispanic or Latino	17 (30.9)	6 (37.5)	11 (28.9)	
Not Hispanic or Latino	38 (69.1)	10 (62.5)	27 (71.1)	
Disease characteristics				
SLE duration (years)	16.0 [9.0, 24.0]	17.0 [12.8, 33.3]	15.0 [8.8, 23.3]	0.21
Disease activity[a]	4.0 [0.0, 4.0]	4.0 [0, 4.0]	3.5 [0, 4.0]	0.84
Organ damage[b]	0.0 [0.0, 2.0]	2.5 [1.0, 4.0]	0 [0, 1.0]	<0.01
Current SLE medication use				
Prednisone dose (mg)	5.0 [4.8, 10.0]	5.0 [3.0, 8.0]	5 [5, 11.5]	0.22
Hydroxychloroquine	44 (77.2)	10 (62.5)	33 (82.5)	0.16
Immunosuppressive medication[c]	37 (64.9)	11 (68.8)	25 (62.5)	0.76
SARC-F components[d]				
Strength				
None	25 (43.9)	0 (0.0)	25 (62.5)	<0.01
Some	19 (33.3)	5 (31.2)	14 (35.0)	
A lot or unable	13 (22.8)	11 (68.8)	1 (2.5)	
Assistance in walking				
None	38 (67.9)	1 (6.2)	37 (92.5)	<0.01
Some	13 (23.2)	10 (62.5)	3 (7.5)	
A lot, use aids, or unable	5 (8.9)	5 (31.2)	0 (0.0)	
Rise from a chair				
None	37 (64.9)	3 (18.8)	34 (85.0)	<0.01
Some	17 (29.8)	10 (62.5)	6 (15.0)	
A lot or unable without help	3 (5.3)	3 (18.8)	0 (0.0)	
Climb stairs				
None	24 (42.1)	0 (0.0)	24 (60.0)	<0.01
Some	26 (45.6)	10 (62.5)	16 (40.0)	
A lot or unable	7 (12.3)	6 (37.5)	0 (0.0)	
Falls				
None	42 (73.7)	8 (50.0)	33 (82.5)	0.05
1-3 falls	12 (21.1)	6 (37.5)	6 (15.0)	
≥4 falls	3 (5.3)	2 (12.5)	1 (2.5)	

*1 value missing
**2 values missing
[a]Safety of Estrogens in Lupus Erythematosus National Assessment-SLE Disease Activity Index: Scores range from 0-105, with higher scores indicating greater disease activity.
[b]Systemic Lupus International Collaborating Clinics/ACR Damage Index: Scores range from 0-47, with higher scores indicating greater damage.
[c]Methotrexate; azathioprine; mycophenolate mofetil; mycophenolic acid; belimumab; cyclophosphamide; rituximab; tocilizumab; cyclosporine; tacrolimus
[d]Morley et al. J Nutr Health Aging 2012;16(7): 601-8.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Objective sarcopenia measures of adults with systemic lupus erythematosus with high (≥4) versus low (<4) SARC-F scores

Objective Sarcopenia Definition	Overall (N=56)	SARC-F score ≥4 (N=16)	SARC-F score <4 (N=40)	p-value
The Asian Working Group for Sarcopenia[a]				
Muscle strength (Handgrip strength,18kg for women)	26 (46.4)	10 (66.7)	15 (37.5)	0.07
Physical performance (6-m walk <1.0 m/s)	41 (73.2)	14 (93.3)	26 (65.0)	0.04
Appendicular skeletal muscle mass (DXA <5.4 kg/m^2 in women)	5 (8.8)	2 (12.5)	3 (7.5)	0.94
The European Working Group on Sarcopenia in Older People[b]				
Muscle strength (Handgrip strength, <16kg for women)	24 (42.9)	9 (60.0)	14 (35.0)	0.13
Physical Performance (Gait speed <0.8 m/s)	18 (32.1)	10 (66.7)	8 (20.0)	<0.01
Appendicular skeletal muscle mass (DXA <5.5 kg/m^2 in women)	5 (8.8)	2 (12.5)	3 (7.5)	0.94
The International Working Group on Sarcopenia[c]				
Physical performance (Gait speed <1 m/s)	41 (73.2)	14 (93.3)	26 (65.0)	0.04
Appendicular skeletal muscle mass (DXA ≤5.67 kg/m^2 in women)	13 (22.8)	4 (25.0)	9 (22.5)	1.00
Foundation for the National Institutes of Health Sarcopenia Project[d]				
Muscle Strength (Handgrip strength, <16 kg for women)	24 (42.9)	9 (60.0)	14 (35.0)	0.13
Appendicular lean body mass adjusted for BMI (DXA <0.512 for women)	5 (8.8)	1 (6.2)	3 (7.5)	1.00

[a]Chen et al. JAMDA 2020;21(3):300-7.
[b]Cruz-Jentoft et al. Age Ageing 2019;48(1):16-31.
[c]Fielding et al. JAMDA 2011;12(4):249-56.
[d]Studenski et al. J Gerontol A Biol Sci Med Sci 2014;69(5):547-58.

Background/Purpose: Sarcopenia, i.e., loss of skeletal muscle mass and strength, has been associated with multiple adverse health outcomes, including mortality. We have previously demonstrated associations of the SARC-F, a simple self-report screening tool for sarcopenia, with functional outcomes in adults with systemic lupus erythematosus (SLE). However, to our knowledge, whether the SARC-F is associated with objective measures of sarcopenia in patients with SLE has not been explored [1]. Accordingly, this study sought to assess the association of the SARC-F with dual energy x-ray absorptiometry (DXA)-based definitions of sarcopenia.

Table 3. Cross sectional association of SARC-F with objective sarcopenia definitions

Objective Sarcopenia Definition (N, %)	SARC-F*		p-value
	Sarcopenia (N=16)	No sarcopenia (N=40)	
The Asian Working Group for Sarcopenia			
No sarcopenia (N=53)	15 (26.79)	38 (67.86)	1.00
Sarcopenia (N=3)	1 (1.79)	2 (3.57)	
The European Working Group on Sarcopenia in Older People			
No sarcopenia (N=54)	15 (26.79)	39 (69.64)	0.49
Sarcopenia (N=2)	1 (1.79)	1 (1.79)	
The International Working Group on Sarcopenia			
No sarcopenia (N=45)	13 (23.21)	35 (62.50)	0.68
Sarcopenia (N=8)	3 (5.36)	5 (8.93)	
Foundation for the National Institutes of Health Sarcopenia Project			
No sarcopenia (N=52)	15 (26.79)	37 (66.07)	1.00
Sarcopenia (N=4)	1 (1.79)	3 (5.36)	

*1 value missing

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Women 18-70 years of age with validated SLE were enrolled in a single-center cross-sectional study. Sociodemographic characteristics, clinical features, and the SARC-F (which includes questions on strength, assistance walking, rising from a chair, climbing stairs, and falls) were self-reported or collected from the patient's electronic medical record. Disease activity and damage were provided by treating physicians. Sarcopenia was measured via DXA using 4 consensus definitions. Descriptive statistics were used to compare sociodemographic characteristics, clinical features, SLE disease severity, and objective measures of sarcopenia between participant groups. SARC-F scores were dichotomized as ≥4 (i.e., at risk for sarcopenia) versus < 4 (i.e., not at risk for sarcopenia) based on established cut points. Fisher's exact tests evaluated the relationship between the SARC-F and objective measures of sarcopenia.

Results: Of 57 participants, 16 (29%) were at risk for sarcopenia based on SARC-F score ≥4 (Table 1). Participants with SARC-F ≥4 were older (p=0.02) and had greater organ damage (p< 0.01) and slower gait speed (p< 0.01 to p=0.04) than those with SARC-F < 4 (Tables 1 and 2). Among 56 women who had DXA, there were no significant associations between the SARC-F and any of the 4 standard validated measures of objective sarcopenia (Table 3). The European Working Group on Sarcopenia in Older People definition had the highest specificity (data not shown).

Conclusion: In this exploratory study of adult women with SLE, very few participants had low muscle mass meeting DXA-based definitions of sarcopenia. In non-elderly women with SLE, DXA scores with a lower threshold for sarcopenia, without BMI adjustment (i.e., European Working Group on Sarcopenia in Older People definition), may preferentially identify those at risk for sarcopenia. Ongoing studies in larger cohorts are needed.

References:

1. Malmstrom et al. J Cachexia Sarcopenia Muscle 2016;7:28-36.

Disclosure: S. Lieber: None; **N. Nagpal**: None; **J. Nguyen**: None; **A. Chung**: None; **D. Sun**: None; **J. Carrino**: Arthritis & Rheumatology, 12, Editorial Board, Carestream, 4, Cartilage Imaging, 12, Editorial Board, Covera, 2, Image Analysis Group, 4, Image Biopsy Lab, 4, Radiology, 12, Editorial Board; **M. Reid**: None; **L. Mandl**: ACP, 12, Associate Editor Annals of Internal Medicine, Wolters, 9.

Abstract Number: 0636

AA Novel Kidney-specific Biomarker Panel Accurately Differentiates Lupus Nephritis from Diabetic Kidney Disease Through Distinct Molecular Pathways Novel Kidney-specific Biomarker Panel Accurately Differentiates Lupus Nephritis from Diabetic Kidney Disease Through Distinct Molecular Pathways

Sepehr Taghavi[1], Ines Silva[2], Jacob Vasquez[3], Vasileios Kyttaris[4], Tyler O'Malley[5] and Mike Nerenberg[6], [1]Exagen Inc, Escondido, CA, [2]Exagen, Carlsbad, CA, [3]Exagen, Inc., Vista, CA, [4]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, [5]Exagen, Vista, CA, [6]Exagen, DEL MAR, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Total (N=260)	AHV LN Matched (N=31)	LN (N=31)	AHV DKD Matched (N=99)	DKD (N=99)
Sex - n(%)					
Female	146 (56%)	26 (84%)	26 (84%)	47 (47%)	47 (47.5%)
Male	114 (44%)	5 (16%)	5 (16%)	52 (53%)	52 (52.5%)
Race - n(%)					
Black	86 (33%)	10 (32%)	10 (32%)	33 (33%)	33 (33.3%)
White	116 (45%)	11 (35%)	11 (35%)	47 (47%)	47 (47.5%)
Hispanic	41 (16%)	0 (0%)	3 (10%)	19 (19%)	19 (19.2%)
Asian	12 (5%)	6 (19%)	6 (19%)	0 (0%)	0 (0.0%)
Other	5 (2%)	4 (13%)	1 (3%)	0 (0%)	0 (0.0%)
Age					
Mean (SD)	51.4 (14.1)	34.7 (9.5)	35.0 (9.8)	56.6 (11.0)	56.6 (11.0)
Creatinie					
Mean (SD)	1.9 (2.4)	0.9 (0.2)	0.9 (0.5)	0.9 (0.2)	3.6 (3.3)
eGFR					
Mean (SD)	71.7 (35.5)	88.0 (16.6)	99.3 (30.5)	86.6 (22.7)	43.1 (32.6)

Table 1. Demographic and Clinical Characteristics of Study Cohort
Table shows sex, race, age, serum creatinine, and eGFR across five groups: lupus nephritis (LN, n=31), matched apparently healthy volunteers for LN (n=31), diabetic kidney disease (DKD, n=99), matched AHV for DKD (n=99), and the combined cohort (n=260). LN mainly affects younger females, while DKD affects older individuals with a balanced sex ratio. (Introduction)

Background/Purpose: Lupus nephritis (LN) and diabetic kidney disease (DKD) are leading causes of chronic kidney disease (CKD) that differ by age, sex, and underlying mechanisms. Both would benefit from earlier detection, but in both cases conventional markers such as serum creatinine or estimated glomerular filtration rate (eGFR) are insensitive for detection of early renal damage. We hypothesized that a panel of kidney-enriched cell type specific plasma proteins could provide earlier detection of LN and DKD and reflect disease-specific biological pathways.

Methods: Four kidney-specific biomarkers—uromodulin (UMOD), myo-inositol oxygenase (MIOX), heparanase (HPSE), and apoptosis-resistant E3 ubiquitin ligase 1 (AREL1)—were measured in plasma specimens from apparently healthy volunteers (AHV), patients with DKD, and patients with biopsy-confirmed LN. Cohorts included type 1 and type 2 diabetes CKD (combined n=99) and LN (n=31), with age and sex matched AHV controls (total n=130). Biomarker levels were quantified by ELISA. A multi-class logistic regression model was trained to classify AHV, DKD, and LN based on the four biomarkers. Performance was evaluated by area under the ROC curve (AUC) for each class (one-vs-rest), as well as confusion matrix and predicted probability distributions (Figure 1). Pathway enrichment (KEGG and Reactome) as well as protein–protein interaction (STRING) analyses were performed to interpret functional roles of the biomarkers. Data from PERL and FIND were provided by NIDDK CR, a program of the National Institute of Diabetes and Digestive and Kidney Diseases.

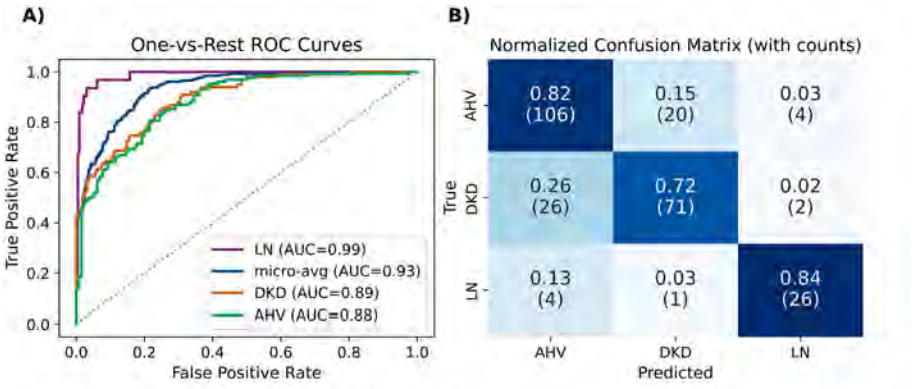


Figure 1. Multi-class Classification Performance of the Four-Biomarker Panel.
(A) One-vs-rest ROC curves illustrate the ability of a logistic regression model trained on UMOD, MIOX, HPSE, and AREL1 to distinguish among AHV, DKD, and LN groups. Class-wise AUCs demonstrate near-perfect discrimination for LN (AUC = 0.99), excellent performance for DKD (AUC = 0.89), and strong accuracy for AHV (AUC = 0.88). The micro-average AUC (AUC = 0.93), which aggregates true positives and false positives across all classes, reflects the overall model performance.
(B) Normalized confusion matrix with raw counts confirms high accuracy across all three classes. LN samples were correctly classified in 84% of cases, with minimal confusion between DKD and AHV. DKD was correctly predicted in 72% of cases, with most misclassifications being AHV. AHV samples were correctly identified 82% of the time.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

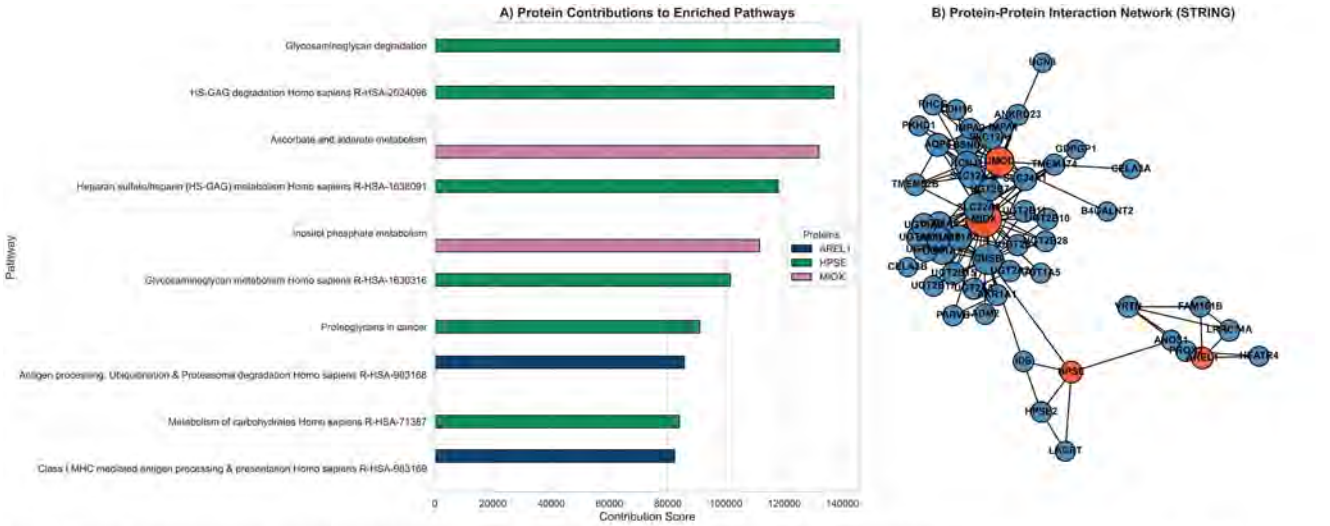


Figure 2. Distinct pathway enrichment and interaction networks for kidney biomarkers. (A) KEGG and Reactome pathway enrichment analysis for three of the biomarkers (HPSE, MIOX, AREL1) revealed unique, non-overlapping pathway associations (UMOD was not included due to absence of significant annotation in KEGG/Reactome databases). HPSE was enriched in glycosaminoglycan degradation and extracellular matrix (ECM) remodeling pathways; MIOX in inositol phosphate and ascorbate metabolism; and AREL1 in antigen processing (MHC class I-mediated) and proteasomal degradation pathways. (B) STRING protein–protein interaction (PPI) analysis showed that the biomarkers primarily clustered within distinct functional modules, with limited shared interactors between groups. UMOD and MIOX clustered with renal tubular transport proteins (including solute carriers, UDP-glucuronosyltransferases [UGTs], and aquaporin-6 [AQP6]); HPSE interacted with ECM components and lysosomal enzymes involved in glycosaminoglycan catabolism (e.g., iduronate 2-sulfatase [IDS], β-glucuronidase [GUSB]); and AREL1 associated with a protein degradation cluster, including ubiquitin pathway components (e.g., UBE2D1, UBC), consistent with its role in ubiquitin-mediated proteostasis. These distinct enrichment profiles and PPI clusters underscore each marker's distinct mechanistic role in kidney pathology, highlighting their complementary contributions to disease mechanisms.

Figure 2. Distinct pathway enrichment and interaction networks for kidney biomarkers

Results: LN patients had markedly lower UMOD and MIOX but higher HPSE and AREL1 compared to AHV and DKD ($p < 0.001$). DKD patients exhibited reduced HPSE and elevated MIOX relative to AHV. The panel yielded AUCs of 0.99 for LN, 0.89 for DKD, and 0.88 for AHV, indicating strong discriminatory performance across all three groups. Confusion matrix and probability plots confirmed minimal misclassification and clear separation between classes, underscoring the model's robustness. Notably, the biomarker panel vastly outperformed creatinine and eGFR in detecting LN. Pathway enrichment analysis linked HPSE to glycosaminoglycan metabolism (extracellular matrix remodeling), MIOX to inositol phosphate metabolism (tubular function), and AREL1 to MHC class I antigen processing and proteasomal degradation pathways (Figure 2, Panel A), consistent with its known role as an E3 ubiquitin ligase. Consistently, STRING network analysis showed UMOD and MIOX clustering in a renal tubular transport network, HPSE in an extracellular matrix network, and AREL1 in a protein degradation network, consistent with its role in ubiquitin-mediated proteostasis (Figure 2, Panel B).

Conclusion: A four-protein biomarker panel reliably detects early LN and DKD and differentiates between them, when compared to healthy states, providing both high diagnostic accuracy and insight into disease-specific mechanisms. Its strong performance—especially the near-perfect discrimination for LN (AUC = 0.99)—suggests this panel can greatly enhance early detection of lupus nephritis and diabetic kidney disease.

Disclosure: S. Taghavi: Exagen, 3; **I. Silva**: None; **J. Vasquez**: None; **V. Kyttaris**: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2; **T. O'Malley**: Exagen, 12, 3, 11; **M. Nerenberg**: Exagen, 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0637

DNA Methylation Patterns Differ Between Genetically Similar Systemic Lupus Erythematosus (SLE) Patients From Peru and the U.S.

Sundus Dwidar[1], Mary Horton[2], Meghan Nelson[3], Joanne Nititham[2], Richard Oppong[3], Frank Donovan[4], Jinoos Yazdany[5], Maria Dall'Era[6], Lisa Barcellos[7], Heinner Guio[8], Manuel Ugarte-Gil[9], Lindsey Criswell[2] and Cristina Lanata[10], [1]National Institutes of Health, Washington, [2]NIH/NHGRI, Bethesda, MD, [3]National Institutes of Health, Bethesda, MD, [4]National Institutes of Health, Bethesda, [5]UCSF, San Francisco, CA, [6]Division of Rheumatology, University of California, San Francisco, CA, [7]UC Berkeley, Berkeley, [8]Universidad de Huanuco, Lima, Peru, [9]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [10]NIH/NHGRI, Bethesda

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease that disproportionately affects individuals of Amerindian ancestry and those who self-identify as Hispanic. The term "Hispanic" encompasses diverse populations, genetic backgrounds, and environments, making it challenging to understand the drivers of disease disparities. Since DNA methylation (DNAm) is shaped by genetic and environmental factors, it may help disentangle these influences. We aim to assess whether DNAm differs between genetically similar SLE individuals living in Peru and the U.S.

Methods: We utilized whole blood genotype and methylation data from SLE cohorts in the U.S. (n=1,671) and Peru (n=74). We used principal component analysis (PCA), including genetic data from the 1000 Genomes and Peruvian Genome Project, to identify genetically similar individuals.We selected individuals within 1.75 standard deviations of the Peruvian population centroid based on the first three principal components (PCs). DNAm was profiled using the Illumina EPIC v2.0 array. After quality control and normalization, 801,370 CpG sites were retained. We linearly modeled differential methylation by country (U.S. vs. Peru) using *limma*, adjusting for age, disease duration, estimated blood cell proportions, and genetic PCs 1–3. Pathway analyses was performed using missMethyl.

Results: We identified genetically similar Peruvian (n=64) and U.S. individuals (n=86). Results showed 13,736 CpG sites differentially methylated by country at a false discovery rate (q) < 0.05 (Figure 1). Of these, 870 CpGs had an average absolute methylation difference ≥3% between the two groups. The sites with the largest differences in methylation between U.S and

Table 1. Top 10 Differentially Methylated Genes Between U.S. and Peruvian Samples, Sorted by Absolute Average Effect Size

Table 1. Top 10 Significant Genes

CpG	Gene Name	LogFC	q value (FDR)	Percent change
cg10596483	*PSCA*	-0.19	0.04	-19
cg10596483	*JRK*	-0.19	0.04	-19
cg22550084	*NMI*	-0.11	0.04	-11
cg15073853	*ISYNA1*	-0.10	0.02	-10
cg07103917	*HTATIP2*	0.08	0.03	+8
cg01358804	*TXNIP*	-0.08	0.03	-8
cg01349190	*MAP2K5*	0.08	0.007	+8
cg09000178	*CBFB*	0.08	0.04	+8
cg00593536	*NXPH2*	-0.08	0.04	-8
cg18116600	*MRPL18*	0.07	0.003	+7

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

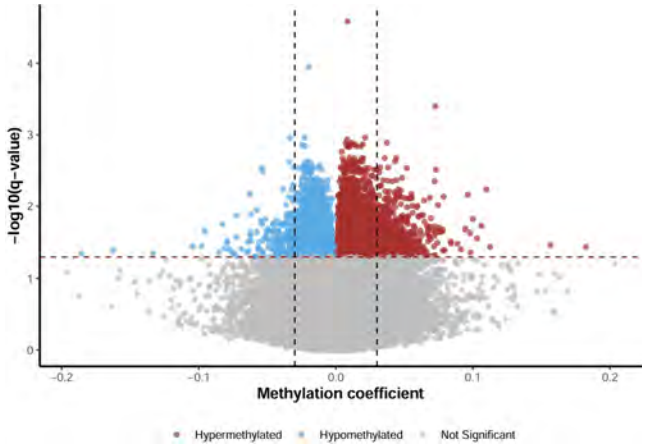


Figure 1. Volcano plot showing hypomethylated and hypermethylated CpG sites. The horizontal line marks the $-\log_{10}$(q-value) threshold of 0.05. Vertical lines indicate a log fold change cutoff of ±0.03

Peru SLE cases were located in genes involved in immune function (Table 1). In particular, a CpG site within *PSCA* had an average of 19% lower methylation in U.S. compared to Peruvian samples. This gene is linked to immune cell infiltration and may reflect cohort-specific differences in inflammatory regulation. Another CpG site within *NMI* had an average of 11% less methylation in U.S. samples. *NMI* enhances STAT-mediated transcription in response to cytokines such as IL-2 and IFN-γ, both critical to SLE pathogenesis. Additionally, a Cpg within *TXNIP* was 7% more methylated in Peruvian samples. *TXNIP* is a vitamin D–responsive gene involved in oxidative stress and immune signaling via JAK-STAT and PI3K/Akt pathways.

Conclusion: As an epigenetic mechanism shaped by genetic and environmental factors, DNAm offers insights into population-level disease variation. Our findings suggest that geographic context is associated with epigenetic variation in SLE when accounting for similar genetic ancestry. The most differentially methylated CpGs were in genes involved in immune regulation, pointing to geographically distinct immune responses potentially shaped by environmental exposures. Although the precise drivers are uncertain, these differences may reflect an interplay of social, cultural, and environmental factors. Understanding how these shape epigenetic patterns may offer new insights into SLE pathogenesis across populations.

Disclosure: S. Dwidar: None; **M. Horton**: None; **M. Nelson**: None; **J. Nititham**: None; **R. Oppong**: None; **F. Donovan**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **L. Barcellos**: None; **H. Guio**: INBIOMEDIC, 4, Universidad de Huanuco, 5; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **L. Criswell**: None; **C. Lanata**: None.

Abstract Number: 0638

Prevalence of lupus nephritis, end stage kidney disease, avascular necrosis, and mortality in systemic lupus erythematosus in the recent era

Takehiro Nakai[1], Sho Fukui[2], Yukihiko Ikeda[3], Masei Suda[4], Hiromichi Tamaki[1], mitsumasa kishimoto[5] and Masato Okada[6], [1]Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, [2]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [3]St Luke's international hospital in Japan, Tokyo, Japan, [4]Suwa Central Hospital, Nagano, Japan, [5]Kyorin University School of Medicine, Tokyo, Japan, [6]St. Luke's International Hospital, Tokyo, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease associated with an increased risk of chronic kidney disease (CKD), avascular necrosis (AVN), and mortality. Despite advancements in management, the contemporary prevalence and risk factors for these complications remain incompletely characterized. This study aimed to assess these outcomes within the context of modern SLE management.

Methods: We conducted a retrospective analysis of patients with SLE who received follow-up care at a tertiary referral center between April 2006 and February 2023. The prevalence and risk factors for lupus nephritis, progression to CKD stage 4 or 5, AVN, and all-cause mortality were evaluated using hazard ratios.

Results: Among 484 patients, lupus nephritis was observed in 26.2%, AVN in 4.8%, and CKD stage 4 or 5 in 2.9%, while the overall mortality rate was 2.5%. Lupus nephritis was more prevalent in patients diagnosed before age 20, whereas CKD progression and mortality were significantly higher in those with later-onset SLE. Hydroxychloroquine use was protective against CKD progression (HR 0.19, 95% CI 0.05–0.69, p = 0.012) and mortality (HR 0.14, 95% CI 0.031–0.66, p = 0.013). Methylprednisolone pulse therapy was associated with an increased risk of AVN (HR 6.10, 95% CI 2.42–15.35, p < 0.001).

Conclusion: Compared to historical cohorts, the prevalence of CKD stage 4 or 5, AVN, and mortality has declined in this cohort. Hydroxychloroquine improves outcomes by reducing CKD progression and mortality, while caution is warranted with methylprednisolone pulse therapy due to its association with AVN.

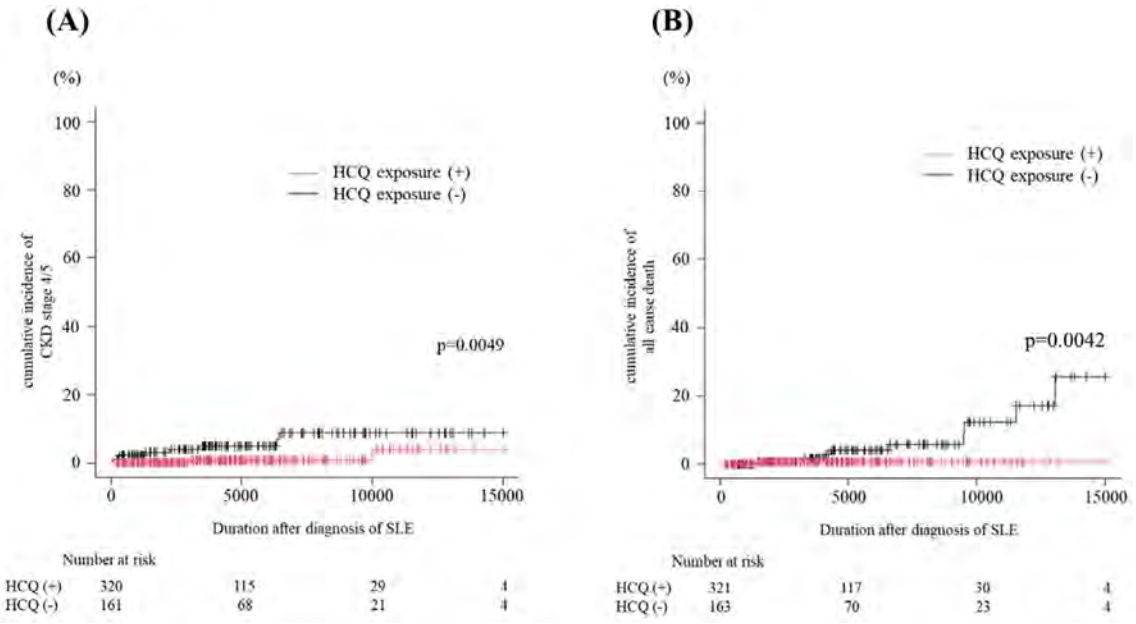


Figure 1 Hydroxychloroquine prescription and its impact on cumulative incidence of CKD stage 4 or 5 and all-cause mortality (A) Hydroxychloroquine prescription and its impact on cumulative incidence of CKD stage 4 or 5 (B) Hydroxychloroquine prescription and its impact on cumulative incidence of all-cause mortality

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Hazard ratio of incidence of CKD stage 4 or 5

	CKD stage 4/5			Univariate analysis			Multivariate analysis		
Factor	(-)	(+)	p value	HR	95% CI	p value	HR	95% CI	p value
n	469	14							
Age of onset≥40yo (%)	139 (29.6)	7 (50.0)	0.14	**4.76**	**1.47-15.36**	**0.009**	**6.48**	**1.91-22.02**	**0.0028**
Lupus nephritis (%)	120 (25.6)	6 (42.9)	0.21	2.25	0.72-7.01	0.16			
LN class III/IV (%)	81 (17.3)	4 (33.3)	0.24	2.13	0.62-7.31	0.23			
Neurological (%)	39 (8.3)	1 (7.1)	1.00	0.86	0.11-6.71	0.89			
anti-DNA Ab (%)	293 (63.8)	8 (61.5)	1.00	1.25	0.37-4.16	0.72			
anti-RNP Ab (%)	136 (34.3)	2 (18.2)	0.35	0.47	0.10-2.2	0.34			
anti-Sm (%)	110 (26.6)	3 (27.3)	1.00	1.32	0.34-5.13	0.69			
mPSL pulse therapy (%)	87 (19.7)	4 (30.8)	0.30	1.50	0.45-5.04	0.51			
HCQ exposure (%)	**317 (67.6)**	**3 (21.4)**	**0.001**	**0.19**	**0.05-0.69**	**0.012**	**0.18**	**0.048-0.66**	**0.0097**
MMF exposure (%)	108 (23.0)	4 (28.6)	0.75	1.63	0.49-5.42	0.42			
CNI exposure (%)	186 (40.9)	5 (35.7)	0.79	0.73	0.22-2.42	0.60			

Table 2: Hazard ratio of incidence of all cause death

	All cause death			Univariate analysis		
factor	(-)	(+)	p value	HR	95% CI	p value
n	472	12				
Diagnosis age≥40yo (%)	**138 (29.2)**	**8 (66.7)**	**0.009**	**11.69**	**3.05-44.78**	**<0.001**
Sex (male)	39 (8.3)	3 (25.0)	0.077	**5.77**	**1.50-22.17**	**0.011**
Lupus nephritis (%)	126 (26.7)	1 (8.3)	0.20	0.21	0.026-1.62	0.13
LN class III/IV (%)	84 (17.9)	1 (9.1)	0.70	0.38	0.048-3.03	0.36
Neurological (%)	38 (8.1)	2 (16.7)	0.26	1.72	0.37-7.94	0.49
CKD stage 4 or 5 (%)	**10 (2.1)**	**4 (33.3)**	**<0.001**	**13.75**	**3.97-47.61**	**<0.001**
anti-DNA Ab (%)	292 (63.2)	10 (90.9)	0.11	NA	NA	NA
anti-RNP Ab (%)	136 (34.3)	3 (27.3)	0.76	1.05	0.27-4.11	0.94
anti-Sm Ab (%)	113 (27.0)	0 (0.0)	0.20	NA	NA	NA
Glucocorticoid treatment (%)	372 (85.7)	11 (91.7)	1.00	0.84	0.11-6.71	0.88
mPSL pulse therapy (%)	90 (20.2)	1 (10.0)	0.70	0.33	0.041-2.63	0.29
HCQ exposure (%)	**319 (67.6)**	**2 (16.7)**	**0.001**	**0.14**	**0.031-0.66**	**0.013**

Disclosure: T. Nakai: None; **S. Fukui**: None; **Y. Ikeda**: None; **M. Suda**: None; **H. Tamaki**: AbbVie/Abbott, 6, Astellas Pharma, 6, Ayumi Pharma, 6, Chugai pharmaceutical, 6, Dai-ichi-Sankyo, 12, Personal Fees, Eisai, 12, Personal Fees, GSK, 12, Personal Fees, Illy-lily, 12, Personal Fees, Kyowa-KIrin, 6, Ono pharmaceutical, 6, Pfizer, 12, Personal Fees, Takeda Pharmaceutical, 6, Tanabe-Mitsubishi, 6; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **M. Okada**: Abbott, 6, Eli Lilly, 6, Mitsubishi Tanabe Pharma, 6, Pfizer, 6, Santen Pharmaceutical, 6.

Abstract Number: 0639

Kidney Transplantation In Lupus Nephritis. Multicenter Study Of 103 Patients

Vanesa Calvo-Río[1], Lara Sánchez Bilbao[1], Carmen Secada-Gómez[1], Paúl Hernández Velasco[2], Celia González-García[3], Enrique Morales[4], María Galindo-Izquierdo[5], Sebastián Sandoval-Moreno[6], Josefina Cortés-Hernández[7], César Antonio Egües Dubuc[8], Niccolo Viveros-Pérez[9], María Caeiro[10], Adrián Mayo-Juanatey[11], Miriam Retuerto Guerrero[12], María Camila Osorio-Sanjuan[13], Luis Sala[14] and Ricardo Blanco[1], [1]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [2]Nephrology, Hospital Universitario 12 de Octubre, Madrid. Spain, Madrid, Madrid, Spain, [3]Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Madrid, Spain, [4]Nephrology, Hospital Universitario 12 de Octubre, Madrid, Madrid, Spain, [5]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Madrid, Spain, [6]Hospital Universitario Vall D'Hebron, Barcelona, Spain, [7]Hospital Universitari Vall d'Hebron-Universitat Autónoma de Barcelona,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Barcelona, Spain, [8]Donostia University Hospital, San Sebastián, Pais Vasco, Spain, [9]Hospital Universitario Germans Trias i Pujol, Badalona, Spain, [10]Centro Hospitalario Universitario de Pontevedra, Pontevedra, Spain, [11]Hospital Universitario Doctor Peset, Valencia, Comunidad Valenciana, Spain, [12]Complejo Asistencial Universitario de León, Leon, Castilla y Leon, Spain, [13]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [14]Hospital Universitario de Torrejón, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE) affecting to 40-60% of SLE. End-stage renal disease (ESRD) occurs in up to 10-20% of LN, occasionally requiring kidney transplantation (KT) **[1]**.

In a series of LN patients who underwent KT, our aim was to assess a) clinical and histological features, b) frequency of renal graft loss, and c) SLE and LN flares.

Methods: Multicenter study of all consecutive patients who underwent KT due to LN in 10 Spanish reference University hospitals between January 1980 and December 2023. Demographic, epidemiological, clinical, analytical and histological data on SLE and LN were collected. In addition, cases of graft loss and their causes, as well as LN flares, were recorded.

Results: We include 103 (80 women, 77.7%), patients; mean age of 38.6±17.1 years. When KT was performed, the main clinical manifestations were joint (n=54; 52.4%) and mucocutaneous involvement (n=44, 42.7%). The predominant histological diagnosis of LN was class IV (n= 47, 45.6%), followed by class III (n=12; 11.6%). The main general features are summarized in **TABLE 1**.

The subtypes of renal replacement therapy (RRT) used prior to KT were: hemodialysis (n=67, 65%), peritoneal dialysis (n=17, 16.5%), combined therapy (n=9, 8.7%) The median [IQR] time from initiation of RRT to KT was 3 years [1-5].

Age (mean± D, years)	38.6±17.1
Sex	
- Male, n (%)	23 (22.3%)
- Female, n (%)	80 (77.7%)
Cardiovascular Risk Factors	
- Arterial hypertension, n (%)	73 (70.3%)
- Dyslipidemia, n (%)	33 (32%)
- Diabetes mellitus, n (%)	9 (8.7%)
Heart disease, n (%)	25 (24.3%)
Histological Diagnosis	
- Class I, n (%)	1 (0.97%)
- Class II, n (%)	9 (8.7%)
- class III, n (%)	12 (11.6%)
- Class IV, n (%)	47 (45.6%)
- Class V, n (%)	4 (3.9%)
- Class IV-V, n (%)	3 (2.9%)
- Unclassifiable LN, n (%)	3 (2.9%)
- Unknown, n (%)	24 (23.3%)
Time from RRT to Kidney Transplantation, median [IQR]	3 years [1–5]

TABLE 1. MAIN GENERAL FEATURES OF THE 103 PATIENTS UNDERWENT TO KIDNEY TRASNPLANTATION. Abbreviations: SD: Standard Deviation; LN: Lupus Nephritis; RRT: Renal Replacement Therapy; IQR: Interquartile RangeTABLE 2. KIDNEY TRANSPLANT COMPLICATIONS AND EVOLUTION

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Immediate post-transplant complications, n (%)	42 (40.8%)
Graft thrombosis, n (%)	3 (7.14%)
Bleeding, n (%)	3 (7.14%)
Obstructive uropathy, n (%)	3 (7.14%)
Infections, n (%)	3 (7.14%)
Thrombotic microangiopathy), n (%)	3 (7.14%)
Delayed graft function, n (%)	2 (4.7%)
Acute rejection, n (%)	2 (4.7%)
Renal artery stenosis, n (%)	2 (4.7%)
Hypertension, n (%)	2 (4.7%)
Acute pyelonephritis, n (%)	2 (4.7%)
Seroma, n (%)	1 (2.4%)
Acute tubular necrosis, n (%)	1 (2.4%)
Tacrolimus nephrotoxicity, n (%)	1 (2.4%)
Pelvicalyceal dilation, n (%)	1 (2.4%)
Altered liver function tests, n (%)	1 (2.4%)
Renal infarction + urinary leakage, n (%)	1 (2.4%)
Unknown	9 (21.4%)
Graft loss	31 (30.1%)
Within the first year, n (%)	9 (29%)
Between year 1 and 5, n (%)	8 (25.8%)
After 5 years, n (%)	9 (29%)
Unknown, n (%)	5 (16.2%)
Causes of graft loss	
Acute rejection, n (%)	11 (35.5%)
Chronic rejection, n (%)	8 (25.8%)
Acute and chronic rejection, n (%)	5 (16.2%)
Graft thrombosis, n (%)	4 (12.9%)
LN flare in the graft, n (%)	3 (9.7%)
Current status	
Functioning transplant, n (%)	65 (63%)
Re-transplantation, n (%)	9 (8.7%)
Hemodialysis, n (%)	12 (11.6%)
Peritoneal dialysis, n (%)	1 (0.9%)
Deceased, n (%)	14 (13.6%)
Unknown, n (%)	2 (1.9%)

TABLE 2. KIDNEY TRANSPLANT COMPLICATIONS AND EVOLUTION. Abbreviations: LN: Lupus Nephritis

The most frequently reported types of donations were brain death (n=45, 43.7%) and asystole (n=29, 28.2%).

Renal graft loss was observed in 31 (30.1%) patients. The most common causes were: acute rejection (n=11, 35.5%), chronic rejection (n=8, 25.8%), combined acute and chronic rejection (n=5, 16.2%), graft thrombosis (n=4, 12.9%) (**TABLE 2**).

In most patients, the graft remains functional (n= 65; 63%). A SLE flare was observed in 17 (13.1%) patients, with renal involvement in 6 (5.8%) cases. LN flare in the graft was the cause of organ loss in only 3 patients (9.7%).

Conclusion: Despite concerns about the recurrence of LN after KT, our results indicate that graft loss is lower in our cohort compared to other published series, and that LN recurrence in the graft is not a frequent cause of organ loss

REFERENCES

1. ZHANG L et al.: Long-term outcomes of end-stage kidney disease for patients with lupus nephritis. Kidney Int 2016; 89: 1337-45.

Disclosure: V. Calvo-Río: AstraZeneca, 6, MSD, Roche, AbbVie, Lilly, Celgene, Grünenthal, and UCB Pharma, 2, 6; **L. Sánchez Bilbao**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **C. Secada-Gómez**: None; **P. Hernández Velasco**: None; **C. González-García**: None; **E. Morales**: None; **M. Galindo-Izquierdo**: None; **S. Sandoval-Moreno**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

None; **J. Cortés-Hernández**: AstraZeneca, 6, Bristol-Myers Squibb (BMS), 1, GlaxoSmithKline (GSK), 6, Novartis, 1, 5, 6; **C. Egües Dubuc**: None; **N. Viveros-Pérez**: None; **M. Caeiro**: None; **A. Mayo-Juanatey**: None; **M. Retuerto Guerrero**: None; **M. Osorio-Sanjuan**: None; **L. Sala**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0640

Impact of Clinically Important Improvements in Patient-Reported Outcomes on Disease Activity in Patients With Systemic Lupus Erythematosus Treated With Upadacitinib or Placebo: Results From the Phase 2 SLEek Study

Vibeke Strand[1], Zahi Touma[2], Anca Askanase[3], Christopher Saffore[4], Denise Kruzikas[5], Karim Masri[5], Siran Fang[5], Yi Peng[6], Patti Katz[7] and Marta Mosca[8], [1]Stanford University School of Medicine, Palo Alto CA, Portola Valley, CA, [2]University of Toronto, Toronto, ON, Canada, [3]Columbia University Medical Center, New York, NY, [4]AbbVie Inc., waukegan, IL, [5]AbbVie Inc., North Chicago, IL, [6]AbbVie Inc., Maple Grove, MN, [7]UCSF, San Rafael, CA, [8]University of Pisa, Pisa, Pisa, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0593–0640) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

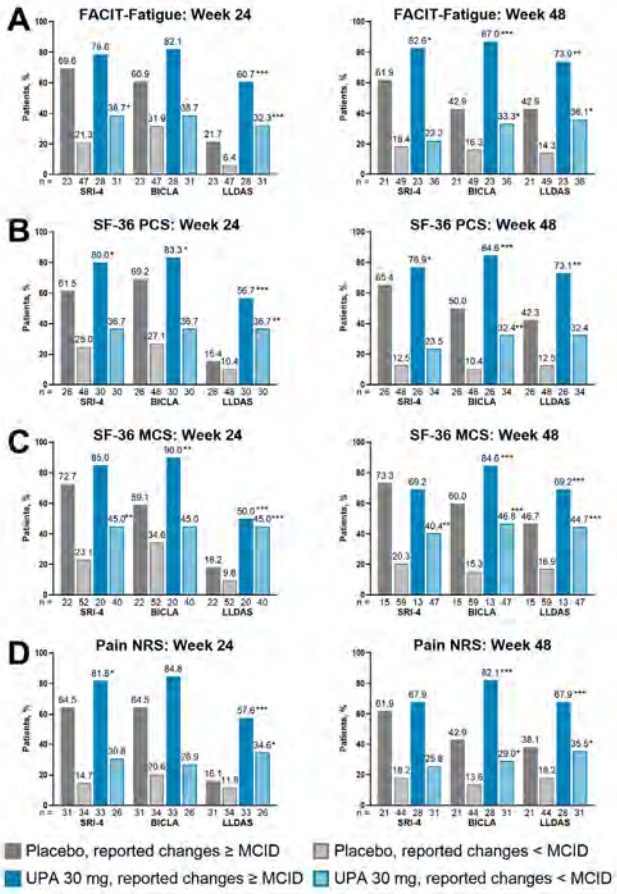
Background/Purpose: This analysis evaluated associations between clinically important improvements in patient-reported outcomes (PROs) and reduced disease activity from the phase 2 SLEek trial evaluating upadacitinib (UPA) vs placebo (PBO) in patients with systemic lupus erythematosus (SLE).

Methods: Data are reported for patients in SLEek who received UPA 30 mg monotherapy or PBO for 48 weeks. Assessments included achievement of British Isles Lupus Assessment Group-Based Composite Lupus Assessment (BICLA), Systemic Lupus Erythematosus Responder Index 4 (SRI-4), and Lupus Low Disease Activity State (LLDAS) responses among patients who reported or did not report minimum clinically important differences (MCID) in PROs at weeks 24 and 48. MCIDs were defined as: ≥ 4-point increase in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (in patients with FACIT-Fatigue ≤ 48 at baseline), ≥ 2.5-point increase in 36-Item Short-Form Health Survey Physical and Mental Component Summary scores, (SF-36 PCS and MCS scores; in patients with SF-36 PCS and MCS scores ≤ 97.5 at baseline), and ≥ 1-point reduction from baseline in Patient's Assessment of Pain Numerical Rating Scale (NRS). Between-group differences and P values were estimated using Cochran-Mantel-Haenszel test, adjusted for baseline corticosteroid dose, Systemic Lupus Erythematosus Disease Activity Index 2000 score at screening, baseline interferon score, and baseline immunosuppressant use.

Results: 137 patients were included in the analysis (UPA 30 mg, n = 62; placebo, n = 75); 90% were female and most were White. Mean baseline FACIT-Fatigue, SF-36 PCS, SF-36 MCS, and Pain NRS scores were 29.3, 40.3, 42.4, and 5.3 (PBO); and 27.1, 38.2, 43.7, and 7.1 (UPA). Among patients who reported changes ≥ MCID for fatigue, physical or mental function, or pain at week 48, a higher proportion achieved SRI-4, BICLA, and LLDAS responses with UPA vs PBO ($P < .05$ for most; Figure 1). Similar trends were observed at week 24 (Figure 1). SRI-4, BICLA, and LLDAS responses at weeks 24 and 48 were lower among patients who did not report clinically meaningful improvements in PROs; however, a higher proportion of these patients achieved SRI-4, BICLA, and LLDAS responses with UPA vs PBO. Of patients who received UPA and reported changes ≥ MCID for FACIT-Fatigue at week 48, over 80% achieved SRI-4 and BICLA responses, and approximately

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Proportion of Patients Achieving SRI-4, BICLA, or LLDAS Responses With Upadacitinib vs Placebo Based on Changes in MCID for (A) FACIT-Fatigue, (B) SF-36 PCS Scores, (C) SF-36 MCS Scores, or (D) Pain NRS at Weeks 24 and 48 (NRI).



BICLA, British Isles Lupus Assessment Group-Based Composite Lupus Assessment; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; LLDAS, Lupus Low Disease Activity State; MCID, minimal clinically important differences; NRI, nonresponder imputation; Pain NRS, Patient's Assessment of Pain Numerical Rating Scale; PRO, patient-reported outcome; SF-36 MCS, 36-Item Short-Form Health Survey Mental Component Summary; SF-36 PCS, 36-Item Short-Form Health Survey Physical Component Summary; SRI-4, Systemic Lupus Erythematosus Responder Index 4; UPA, upadacitinib.
After a planned interim analysis when 50% of the patients reached week 24 or withdrew from the study, the upadacitinib 15 mg/elsubrutinib 60 mg and elsubrutinib 60 mg monotherapy treatment arms were discontinued due to lack of efficacy with no safety concerns.
*P < .05; **P < .01; ***P < .001 vs placebo.

three-quarters achieved LLDAS (Figure 1A). In patients who received UPA and reported clinically meaningful changes in SF-36 PCS or MCS scores or Pain NRS at week 48, over 80% achieved BICLA, and SRI-4 and LLDAS were achieved by approximately three-quarters of patients who reported changes ≥ MCID for SF-36 PCS scores (Figure 1B) and approximately two-thirds of patients who reported changes ≥ MCID for SF-36 MCS scores (Figure 1C) and Pain NRS (Figure 1D).

Conclusion: Patients who reported changes ≥ MCID in PROs for fatigue, physical and mental function, and pain generally demonstrated higher SRI-4, BICLA, and LLDAS responses than those who did not. These findings demonstrate the strong association of PRO improvements with disease activity improvements in SLE and highlight the potential multifaceted benefits of UPA for patients with SLE.

Disclosure: V. Strand: AbbVie/Abbott, 2, Alumis, 2, Amgen, 2, Arthrosi, 2, Artiva, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer-Ingelheim, 2, catalys, 2, contura, 2, Cullinan, 2, Fate Therapeutics, 2, Fortress Biotech, 2, genasence, 2, GlaxoSmithKlein(GSK), 2, Inmedix, 2, Lipum, 2, Longitude Capiral, 2, MED institute, 2, Novartis, 2, RAPT, 2, Royalty

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Pharma, 2, Sanofi, 2, scipher medcine corp, 2, SetPoint Medical, 2, Sobi, 2, Spherix, 2, Synact, 2, Takeda, 2, Topography, 2, Zoe, 2; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **C. Saffore**: AbbVie, 3, 11; **D. Kruzikas**: AbbVie, 3, 11; **K. Masri**: AbbVie, 3, 11; **S. Fang**: AbbVie, 3, 11; **Y. Peng**: AbbVie, 3, 11; **P. Katz**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6.

Abstract Number: 0641

Safety and efficacy of autologous CD19-CAR T-cell therapy in patients with autoimmune disease - data from the CASTLE Phase I/II basket study

Melanie Hagen[1], Andreas Wirsching[1], Fabian Müller[2], Soraya Kharboutli[3], Christina Bergmann[1], Sebastian Böltz[1], Jule Taubmann[4], Carlo Tur[1], Laura Bucci[1], Simon Völkl[3], Michael Aigner[3], Sascha Kretschmann[3], Louis Schuster[4], Koray Tascilar[4], Silvia Spoerl[3], Ingrid Vasova[3], Panagiotis Garantziotis[1], Daniel Aletaha[5], Hans-Peter Kiener[6], gerlando Natalello[7], Franco Locatelli[8], Maria Antonietta D'Agostino[9], Aline Bozec[1], Linda Hanssens[10], Dirk De Vries[10], Ricardo Grieshaber-Bouyer[11], Andreas Mackensen[12] and **Georg Schett**[13], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]University Hospital of Erlangen, Erlangen, Germany, [3]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [4]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [5]Medical University Vienna, Wien, Austria, [6]Medical University of Vienna, Vienna, Austria, Vienna, Austria, [7]Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [8]IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, [9]Catholic University of the Sacred Heart, Rome, Rome, Italy, [10]Miltenyi Biomedicine, Bergisch Gladbach, Bergisch Gladbach, Germany, [11]University Hospital Erlangen, Erlangen, Germany, [12]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) and Uniklinikum Erlangen, Erlangen, Germany, [13]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Engineered T cells expressing a chimeric antigen receptor (CAR) binding CD19 are powerful tools to deplete B-cells, representing an attractive therapy for severe autoimmune diseases, such as systemic lupus erythematosus (SLE), idiopathic inflammatory myositis (IIM) and systemic sclerosis (SSc). Case reports and case series have supported the feasibility of CAR T-cell therapy in SLE, IIM and SSc showing preliminary safety and efficacy (1-3). Clinical data from phase I/II studies investigating the potential of CAR T-cell therapy in autoimmune disease are underway. Their results will provide further insights in the therapeutic role of CAR T-cells in these diseases.

Methods: CASTLE is a phase I/II basket study (Miltenyi Biomedicine, EudraCT-Nr.2022-001366-35) assessing the safety (primary endpoint) and efficacy (secondary endpoint) of $1x10^6$ autologous CD19 CAR T-cells (MB-CART19.1) /kg BW after lymphodepleting chemotherapy with Fludarabin/Cyclophosphamide in patients with SLE, IIM and SSc. Previous immunosuppressants/immunomodulatory therapies were stopped at the time of lymphodepletion. 8 patients were recruited in a first safety phase, followed by additional 16 patients in the second phase. Dose limiting toxicity (DLT) and consecutive stopping rules were grade 3/4 cytokine release syndrome (CRS), grade 3/4 immune cell-associated neurotoxicity syndrome (ICANS), clinically relevant neutropenia or thrombopenia lasting >4 weeks or grade 3/4 organ toxicity within 4 weeks after IMP-infusion. Efficacy was assessed by B-cell depletion and CAR T-cell expansion. Clinical responses were defined by DORIS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

remission in SLE, ACR/EULAR Moderate or Major Response in IIM, and no progression of interstitial lung disease in SSc.

Results: In total, 28 patients were screened, 24 patients were enrolled (17 women, 7 men) with a median (IQR) age of 39 [26; 53] years. 10 patients had SLE, 9 SSc and 5 IIM with a median (IQR) number of 4 [3; 6] previous immunosuppressive treatments. 18/24 developed mild CRS (17 grade 1; 1 grade 2). No higher-grade CRS and no ICANS occurred. No clinically relevant neutropenia or thrombopenia >4 weeks were recorded. One grade 3 organ toxicity due to renal thrombotic microangiopathy in conjunction with CMV infection occured. Local immune effector cell-associated toxicity syndrome (LICATS (4)) was reported in 88% of patients with grade 1/2 in the vast majority of patients. Median (IQR) CAR T-cell expansion was 140 [82; 360] cell/microliter, median (IQR) time of CAR T-cell presence was 83 [56; 113] days. B-cells were depleted in all patients. Six-month efficacy data were available in 19/24 patients at data cut-off of May 12, 2025: All 7 SLE patients were in DORIS remission, all 8 SSc showed no disease progression and all 4 IIM patients met ACR/EULAR Moderate or Major Response. In addition, clinical responses were also observed in the residual 5 patients, in whom follow-up time was still less then 6 months. All 24 patients stopped any immunosuppressive medication.

Conclusion: The CASTLE study met its primary safety and secondary efficacy endpoint. The data confirm favorable safety and high efficacy of MB-CART19.1 in the setting of a controlled phase I/II study in patients with autoimmune disease.

Disclosure: M. Hagen: None; **A. Wirsching**: None; **F. Müller**: AbbVie/Abbott, 6, ArgoBIO, 2, AstraZeneca, 2, 6, Beigene, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CRISPR Therapeutics, 2, EcoR1, 2, Incyte, 6, Janssen, 2, 6, Kite/Gilead, 2, 5, 6, Merck/MSD, 6, Miltenyi, 2, 6, Novartis, 2, 6, Pfizer, 6, Sobi, 2, 6, Takeda, 6; **S. Kharboutli**: None; **C. Bergmann**: Kyverna Therapeutics, Inc., 5; **S. Böltz**: None; **J. Taubmann**: None; **C. Tur**: Sanofi, 2; **L. Bucci**: None; **S. Völkl**: None; **M. Aigner**: None; **S. Kretschmann**: None; **L. Schuster**: None; **K. Tascilar**: None; **S. Spoerl**: None; **I. Vasova**: None; **P. Garantziotis**: None; **D. Aletaha**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sanofi, 6; **H. Kiener**: None; **g. Natalello**: None; **F. Locatelli**: None; **M. D'Agostino**: None; **A. Bozec**: None; **L. Hanssens**: Miltenyi Biomedicine, 3; **D. De Vries**: Miltenyi Biomedicine, 3; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6; **A. Mackensen**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6.

Abstract Number: 0642

Belimumab-Based Triple Therapy in Proliferative Lupus Nephritis: Renal Outcomes and Glucocorticoid Tapering in a Real-World Multicenter Cohort

Paola Vidal Montal[1], **Javier Narváez**[2], Aina Fabregat[3], Iñigo Rúa-Figueroa[4], José María Pego-Reigosa[5], Andrea Hernández-martín[6], Clara Moriano[7], Maria Garcia-Villanueva[8], Sandra Garrote Corral[9], Sergi Heredia[10], Julia Martínez Barrio[11], Júlia Bernardez Moreno[12], Paloma Vela Casasempere[13], Beatriz Tejera Segura[14], Leyre Riancho[15], Francisco Javier Novoa[16], Vicenç Torrente-Segarra[17], Maria Piqueras García[18], Beatriz Frade Sosa[19], José Gomez-Puerta[20], Consuelo Ramos Giraldez[21], Tarek Salman Montes[22], María Galindo-Izquierdo[23], EVA GLORIA TOMERO MURIEL[24], Jaime calvo[25], Jorge Juan Fragío Gil[26], Marta De la Rubia Navarro[27], Berta Magallares[28] and Irene Altabás-González[29], [1]Bellvitge University Hospital, Barcelona, Spain, [2]Hospital Universitario de Bellvitge, Barcelona, Spain, [3]Department of Rheumatology. Hospital Universitario de Bellvitge., Barcelona, Spain, [4]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [5]Department of Rheumatology, University Hospital of Vigo, Vigo, Spain; IRIDIS Group (Investigation in Rheumatology and Immune-Diseases), Galicia Sur Health Research Institute, Vigo, Spain, [6]Hospital Universitario de Gran Canaria Dr Negrín, Las palmas, Spain, [7]Hospital León, LEON, Castilla y Leon, Spain, [8]Hospital Ramón y Cajal, Madrid, Spain, [9]Hospital Ramón y Cajal, Madrid, [10]Hospital Moisès Broggi, Barcelona, Spain, [11]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [12]Hospital de Sant Pau, Barcelona, Spain, [13]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [14]Hospital Insular de Gran Canaria, Las palmas,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Spain, [15]Hospital de Sierrallana, Torrelavega, [16]Hospital Insular de Gran Canaria, Las palmas, [17]Hospital Comarcal Alt Penedés Garraf, Vilafranca del Penedès, Spain, [18]Servicio Murciano de Salud, Murcia, Spain, [19]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [20]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, [21]Hospital Universitario Virgen de Valme, Servicio de Reumatología, Seville, Spain, [22]Hospital del Mar/Parc de Salut Mar-IMIM, Barcelona, Spain, [23]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Madrid, Spain, [24]Hospital Universitario de la Princesa, Madrid, Spain, [25]Hospital de Araba, Vitoria, Spain, [26]Hospital General Universitario, Valencia, Spain, [27]Hospital de La Fe, Valencia, [28]Hospital de Sant Pau, Bareclona, [29]Complejo Hospitalario de Vigo, Vigo, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The newly published ACR guidelines recommend initiating triple therapy for all patients with proliferative lupus nephritis (LN). While belimumab (BEL) has demonstrated efficacy in clinical trials, real-world data on its early use in combination regimens remain limited.

We aimed to evaluate the effectiveness of triple therapy including BEL plus standard of care (SoC) initiated within 6 months of LN onset in achieving renal response and glucocorticoid tapering in a real-world multicenter cohort.

Methods: Retrospective multicenter study in Spain including patients with proliferative LN (ISN/RPS class III, IV, or mixed III/IV+V) treated with BEL-based triple therapy within 6 months of diagnosis.

Results: A total of 38 patients were included (78.9% female, mean age 38±14 years); 68.4% were Caucasian and 21.1% Hispanic. A history of previous LN episodes was present in 38.5% of patients.Histological classification included class III (n=11), class IV (n=20), and mixed III/IV+V (n=7); two had thrombotic microangiopathy. Mean activity and chronicity indices were 9.4±4.0 and 2.3±1.9, respectively. All patients had a minimum follow-up of 6 months, with a median follow-up of 25 months (IQR 14.5–41).

Induction therapy included intravenous methylprednisolone in 63.2%, with a mean initial oral prednisone dose of 35.7±17.9 mg/day. Most patients (76.3%) received MMF, while 23.7% were treated with cyclophosphamide. Maintenance therapy consisted of MMF in 94.7% of cases, with only two patients (5.3%) receiving azathioprine.

CRR was achieved in 60% within 12 months; 65.7% achieved a primary response and 72.2% a partial response (Figure 1). Proteinuria decreased from 3.0±2.9 g/day at baseline to 560±466 mg/day at 12 months; eGFR remained stable, with progressive improvement from 71.3±30.3 to 78.4±23.1 mL/min/1.73m^2 at 12 months and 80.9 at 24 months (Table 1).

Table 1. Evolution of renal parameters over time

Variable	Basal	3 Months	6 Months	12 Months	24 Months
Prednisone (mg/día)	35,7 ± 17,9	12,4 ± 8,4	6,0 ± 3,2	4,0 ± 3,7 (n=30)	3,6 ± 5,0 (n=16)
Creatinine (µmol/L)	126,6 ± 120,7	106,2 ± 108,2	98,7 ± 78,8	101,8 ± 105,8 (n=29)	100,1 ± 107,4 (n=19)
eGFR (ml/min/1.73 m^2)	71,3 ± 30,3	74,6 ± 23,5	75,6 ± 23,0	78,4 ± 23,1 (n=32)	80,9 ± 19,5 (n=21)
Proteinuria (mg/24h)	3 ± 2.9	1.408 ± 1.486	904 ± 1.153	560 ± 466 (n=33)	350 ± 462 (n=19)
Anti-dsDNA (IU)	478,8 ± 526,4	148,7 ± 161,3	148,4 ± 164,2	175,3 ± 227,0 (n=28)	105,1 ± 186,7 (n=18)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

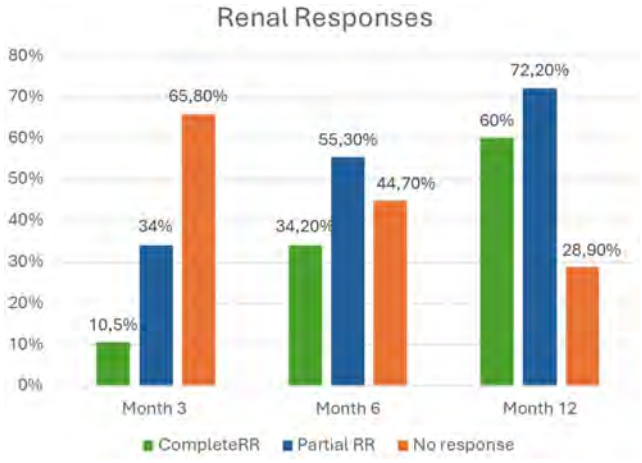


Figure 1. Evolution of Renal Response Rates

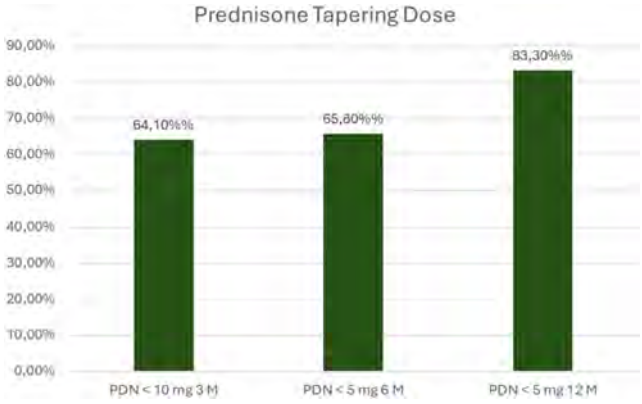


Figure 2. Proportion of Patients Achieving Glucocorticoid Tapering Targets

Regarding glucocorticoid tapering, the 2023 ACR recommendations propose a target of ≤5 mg/day of prednisone by month 6. In our cohort, 65.8% of patients achieved this goal, with a mean dose of 6.0±3.2 mg/day at 6 months. Mean prednisone dose declined from 35.7±17.9 mg/day at baseline to 4.0±3.7 mg/day at 12 months. By month 12, 83.3% of patients were receiving ≤5 mg/day (Figure 2). At 24 months, mean prednisone was 3.6±5.0 mg/day (Table 1).

Renal relapse occurred in 6 patients while on treatment with BEL (15.7%); BEL was discontinued in 2, while 4 continued BEL with intensified immunosuppression. Three patients experienced mild to moderate non-renal flares, managed with therapy adjustments (anifrolumab, methotrexate, or prednisone increase).

When comparing early initiation of BEL (< 3 months) versus delayed initiation (3–6 months post-flare), early use was associated with a significantly shorter time to achieve CRR (HR 4.7, 95% CI 1.6–13.5; p=0.04) and partial renal response (HR 2.47, 95% CI 1.1–5.8; p=0.037).

Conclusion: Initiation of triple therapy with BEL in proliferative LN was associated with robust renal responses and achievement of ACR steroid-sparing targets in most patients. Earlier treatment onset may further enhance renal outcomes

Disclosure: P. Vidal Montal: None; **J. Narváez**: None; **A. Fabregat**: None; **I. Rúa-Figueroa**: None; **J. Pego-Reigosa**: AstraZeneca, 1, 5, 6, GlaxoSmithKline (GSK), 1, 5, 6, Otsuka, 1, 6; **A. Hernández-martín**: None; **C. Moriano**: None; **M. Garcia-Villanueva**: None; **S. Garrote Corral**: None; **S. Heredia**: None; **J. Martínez Barrio**: None; **J. Bernardez**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Moreno: None; **P. Vela Casasempere**: None; **B. Tejera Segura**: None; **L. Riancho**: None; **F. Novoa**: None; **V. Torrente-Segarra**: None; **M. Piqueras García**: None; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **C. Ramos Giraldez**: None; **T. Salman Montes**: None; **M. Galindo-Izquierdo**: None; **E. TOMERO MURIEL**: None; **J. calvo**: None; **J. Fragío Gil**: Quibim, 1; **M. De la Rubia Navarro**: None; **B. Magallares**: None; **I. Altabás-González**: None.

Abstract Number: 0644

Improvement of Fatigue, Musculoskeletal Pain, and Morning Stiffness in Patients with Systemic Lupus Erythematosus Treated with Dapirolizumab Pegol: 48-Week Results from a Phase 3 Trial

Ioannis Parodis[1], Caroline Gordon[2], **Joan Merrill**[3], Matthias Schneider[4], Zahi Touma[5], Teri Jimenez[6], Thomas Morel[7], Mina Nejati[8], Christian Stach[9], Christine de La Loge[10] and Laurent arnaud[11], [1]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [2]Department of Inflammation and Ageing, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom, [3]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [4]Clinic of Rheumatology and Hiller Research Unit, Heinrich-Heine-University, Düsseldorf, Germany, [5]University of Toronto, Toronto, ON, Canada, [6]UCB, Raleigh, NC, [7]UCB, Basel, Switzerland, [8]Biogen, Cambridge, MA, [9]UCB, Monheim am Rhein, Germany, [10]UCB, Brussels, Belgium, [11]Service de rhumatologie, Hôpitaux Universitaires de Strasbourg, INSERM UMR-S 1109, Strasbourg, France, Strasbourg, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table. Baseline demographics, disease characteristics, and PRO scores

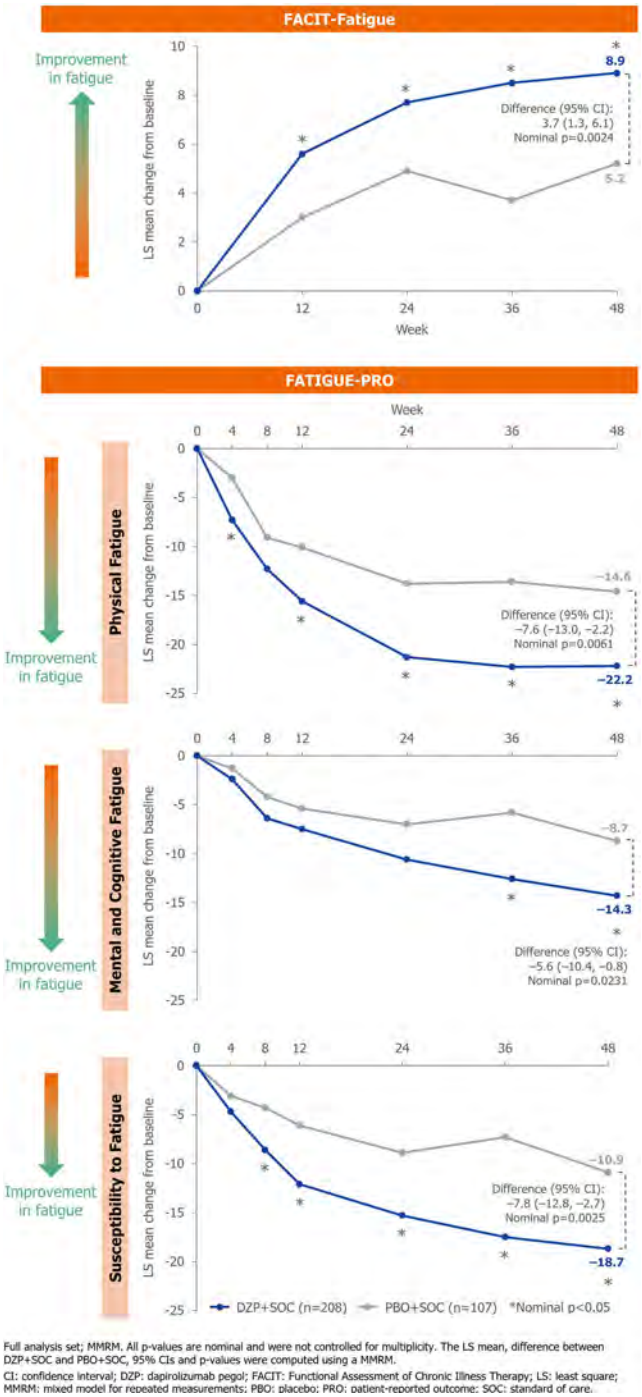
	DZP+SOC n=208	PBO+SOC n=107
Age, years, mean (SD)	43.5 (12.3)	41.5 (12.4)
Female, n (%)	193 (92.8)	100 (93.5)
Time since first diagnosis of SLE, years, mean (SD)	10.1 (7.9)	9.8 (8.5)
SLEDAI-2K, mean (SD)	10.7 (3.5)	11.2 (3.4)
SLEDAI-2K ≥10, n (%)	140 (67.3)	79 (73.8)
Concomitant systemic glucocorticoids, n (%)	171 (82.2)	87 (81.3)
Glucocorticoid dose, mg/day, mean (SD)	7.9 (5.9)	9.6 (8.1)
Glucocorticoid dose >7.5 mg/day, n (%)	105 (50.5)	51 (47.7)
FACIT-Fatigue,[a] mean (SD)	28.5 (11.2)	27.7 (10.5)
FATIGUE-PRO,[b] mean (SD)		
Physical Fatigue	49.2 (22.7)	51.4 (23.0)
Mental and Cognitive Fatigue	35.2 (23.8)	38.2 (24.1)
Susceptibility to Fatigue	49.3 (24.1)	49.7 (23.4)
LAMDA,[c] mean (SD)		
Musculoskeletal pain	56.0 (23.1)	54.1 (25.5)
Morning stiffness	54.9 (26.2)	52.7 (26.1)

Full analysis set. Baseline was defined as the last available value before the first dose of the study drug. It was generally the value at Day 1 but if there were no available data at Day 1 then the screening visit data were used. [a] FACIT-Fatigue score range: 0–52, lower scores indicate greater fatigue and an increase in score over time reflects improvement; [b] FATIGUE-PRO score range: 0–100 calculated for each of the three scales, higher scores indicate greater fatigue and a decrease in score over time reflects improvement; [c] LAMDA is a composite musculoskeletal disease activity measure; VAS range: 0–100, higher scores indicate more musculoskeletal pain or morning stiffness and a decrease in score over time reflects improvement.

DZP: dapirolizumab pegol; FACIT: Functional Assessment of Chronic Illness Therapy; LAMDA: Lupus Arthritis and Musculoskeletal Disease Activity; PBO: placebo; PRO: patient-reported outcome; SD: standard deviation; SLE: systemic lupus erythematosus; SOC: standard of care; VAS: visual analogue scale.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

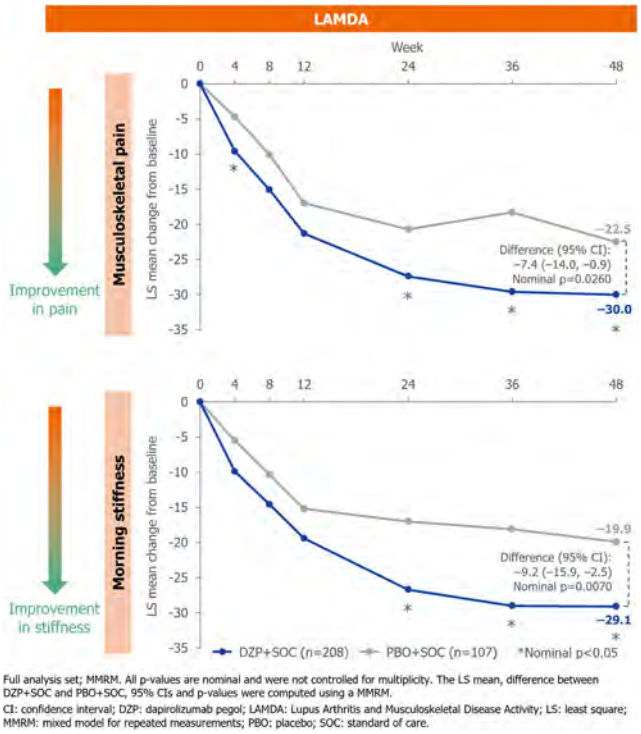
Background/Purpose: Fatigue, musculoskeletal pain, and joint stiffness are common manifestations of SLE, presenting considerable treatment challenges, particularly in addressing chronic fatigue. Dapirolizumab pegol (DZP) is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[1,2] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain. In the phase 3 PHOENYCS GO trial (NCT04294667), the primary endpoint was met; DZP plus standard of care (DZP+SOC) resulted in significantly higher rates of BILAG-based Composite Lupus Assessment (BICLA) response vs placebo (PBO)+SOC at Week (Wk) 48.[3] We report the impact of DZP on patient (pt)-reported fatigue, musculoskeletal pain, and morning stiffness in PHOENYCS GO.



Full analysis set; MMRM. All p-values are nominal and were not controlled for multiplicity. The LS mean, difference between DZP+SOC and PBO+SOC, 95% CIs and p-values were computed using a MMRM.
CI: confidence interval; DZP: dapirolizumab pegol; FACIT: Functional Assessment of Chronic Illness Therapy; LS: least square; MMRM: mixed model for repeated measurements; PBO: placebo; PRO: patient-reported outcome; SOC: standard of care.

Figure 1. LS mean change from baseline in FACIT-Fatigue and FATIGUE-PRO scores by visit

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Full analysis set; MMRM. All p-values are nominal and were not controlled for multiplicity. The LS mean, difference between DZP+SOC and PBO+SOC, 95% CIs and p-values were computed using a MMRM.
CI: confidence interval; DZP: dapirolizumab pegol; LAMDA: Lupus Arthritis and Musculoskeletal Disease Activity; LS: least square; MMRM: mixed model for repeated measurements; PBO: placebo; SOC: standard of care.

Figure 2. LS mean change from baseline in LAMDA musculoskeletal pain and morning stiffness scores by visit

Methods: PHOENYCS GO, a 48-wk, randomized, double-blind, PBO-controlled trial, included pts aged ≥16 years with moderate-to-severe, active SLE characterized by persistently active or frequently flaring/relapsing-remitting disease activity despite stable SOC medication (antimalarials, glucocorticoids and/or immunosuppressants). Pts were randomized 2:1 to intravenous DZP 24 mg/kg+SOC or PBO+SOC every 4 wks.

Fatigue was assessed using Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue and FATIGUE-PRO (which consists of three scales: Physical Fatigue, Mental and Cognitive Fatigue, and Susceptibility to Fatigue). Musculoskeletal pain and morning stiffness were evaluated using the visual analogue scales (VAS) from the Lupus Arthritis Musculoskeletal Disease Activity (LAMDA) instrument. The least square (LS) mean change from baseline is reported through Wk 48. For FACIT-Fatigue, the proportion of pts with an improvement ≥4 (minimal clinically important difference [MCID])[4] at Wk 48 is also reported.

Results: The study was completed on treatment through Wk 48 by 85.4% (182/213) of pts randomized to DZP+SOC and 79.6% (86/108) randomized to PBO+SOC. Baseline fatigue, musculoskeletal pain, and morning stiffness scores were comparable between the groups (full analysis set; DZP+SOC: n=208; PBO+SOC: n=107; **Table**).

Pts receiving DZP+SOC vs PBO+SOC demonstrated consistently larger LS mean changes from baseline to Wk 48 in FACIT-Fatigue and all three FATIGUE-PRO scores (nominal p< 0.05; **Figure 1**). A nominally significantly greater proportion of pts receiving DZP+SOC vs PBO+SOC achieved an improvement of ≥4 (MCID) in FACIT-Fatigue at Wk 48 (50.5% vs 35.5%; difference: 14.5 [95% CI: 3.0, 25.9]; nominal p=0.0131).

LS mean changes from baseline to Wk 48 in musculoskeletal pain and morning stiffness were also larger for pts receiving DZP+SOC vs PBO+SOC (nominal p< 0.05; **Figure 2**).

Conclusion: Improvements in fatigue, musculoskeletal pain, and morning stiffness were greater in pts treated with DZP +SOC vs PBO+SOC. Alongside the previously reported improvements in clinical measures of SLE disease activity,[3] these data suggest that DZP improves core pt-reported symptoms in SLE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References: 1. Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); **2**. Powlesland A. Ann Rheum Dis 2024;83 (suppl 1):261; **3**. Clowse M. Arthritis Rheumatol 2024;76 (suppl 9); **4**. Lai J. J Rheumatol 2011;38:672–9.

Disclosure: I. Parodis: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5; **C. Gordon**: Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB, 2; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **M. Schneider**: AbbVie, 2, AstraZeneca, 2, 5, 6, BMS, 2, GSK, 2, 5, 6, Novartis, 2, Otsuka, 2, Roche, 2; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **T. Jimenez**: UCB, 3, 12, Shareholder; **T. Morel**: UCB, 3, 12, Shareholder; **M. Nejati**: Biogen, 3, 12, Shareholder; **C. Stach**: UCB, 3, 12, Shareholder; **C. de La Loge**: UCB, 2; **L. arnaud**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, 6, Eli Lilly, 2, 6, Grifols, 2, 6, GSK, 2, 5, 6, Janssen, 2, 6, Kezar, 2, LFB, 2, 6, Medac, 2, 6, Merck, 2, Nordic Pharma, 2, Novartis, 2, 6, Pfizer, 2, 6, Roche-Chugaï, 2, 6, UCB, 2, 6.

Abstract Number: 0645

Achievement of Low Disease Activity and Remission in Patients with Systemic Lupus Erythematosus Treated with Dapirolizumab Pegol: 48-week Results from a Phase 3 Trial

Eric Morand[1], Lucy Carter[2], **Maria Dall'Era**[3], Michelle Petri[4], Ed Vital[5], Teri Jimenez[6], Janine Gaiha-Rohrbach[7], Bernard Lauwerys[8], Annette Nelde[9], Christian Stach[10] and Ronald van Vollenhoven[11], [1]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [3]Division of Rheumatology, University of California, San Francisco, CA, [4]Johns Hopkins University School of Medicine, Timonium, MD, [5]University of Leeds, Leeds, England, United Kingdom, [6]UCB, Raleigh, NC, [7]Biogen, Cambridge, MA, [8]Systemic and Inflammatory Rheumatic Diseases Section, Institute of Experimental and Clinical Research (IREC), UCLouvain, Brussels, Belgium, [9]Biogen, Baar, Switzerland, [10]UCB, Monheim am Rhein, Germany, [11]Department of Rheumatology, Amsterdam University Medical Centre, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Dapirolizumab pegol (DZP) is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[1,2] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain. In the phase 3 PHOENYCS GO trial (NCT04294667), the primary endpoint was met; DZP plus standard of care (DZP+SOC) resulted in significantly higher rates of BILAG-based Composite Lupus Assessment (BICLA) response vs placebo (PBO)+SOC at Week (Wk) 48.[3] Remission (based on Definition of Remission in SLE [DORIS]) and low disease activity (based on Lupus Low Disease Activity State [LLDAS]) are recommended treatment targets in SLE,[4] and achievement of both DORIS and LLDAS are associated with reduced organ damage accrual and improved outcomes in patients (pts).[5,6] We report achievement of LLDAS and DORIS in pts with SLE treated with DZP in PHOENYCS GO.

Methods: PHOENYCS GO, a 48-wk, randomized, double-blind, PBO-controlled trial, included pts aged ≥16 years with moderate-to-severe, active SLE characterized by persistently active or frequently flaring/relapsing-remitting disease activity

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

despite stable SOC medication (antimalarials, glucocorticoids and/or immunosuppressants). Pts were randomized 2:1 to intravenous DZP 24 mg/kg+SOC or PBO+SOC every 4 wks.

Achievement of LLDAS in ≥50% of visits through Wk 48, achievement of LLDAS by visit, cumulative number of visits in LLDAS through Wk 48, and achievement of DORIS[7] by visit are reported.

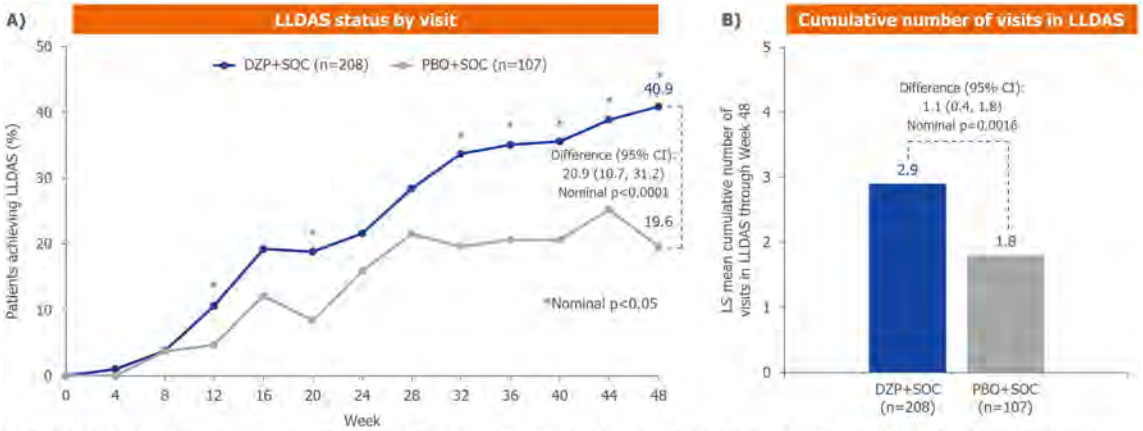
Results: The study was completed on treatment through Wk 48 by 85.4% (182/213) of pts randomized to DZP+SOC and 79.6% (86/108) randomized to PBO+SOC. Baseline characteristics were comparable between the groups (full analysis set; DZP+SOC: n=208; PBO+SOC: n=107; **Table**).

Through 48 wks, 23.6% of pts receiving DZP+SOC achieved LLDAS in ≥50% of visits vs 15.9% receiving PBO+SOC (nominal p=0.1042). At Wk 48, 40.9% of pts receiving DZP+SOC achieved LLDAS vs 19.6% receiving PBO+SOC (nominal p< 0.0001; **Figure 1**). As early as Wk 12, greater proportions of pts receiving DZP+SOC achieved LLDAS vs PBO+SOC (nominal p< 0.05). The proportion of DZP+SOC LLDAS-responders continued to rise to Wk 48, while in PBO+SOC pts, achievement of LLDAS plateaued from Wk 28. The least square mean (SE) cumulative number of visits in LLDAS through Wk 48 was greater in pts receiving DZP+SOC (2.9 [0.2]) vs PBO+SOC (1.8 [0.3]; nominal p=0.0016; **Figure 1**).

Table. Baseline demographics and disease characteristics

	DZP+SOC n=208	PBO+SOC n=107
Age, years, mean (SD)	43.5 (12.3)	41.5 (12.4)
Female, n (%)	193 (92.8)	100 (93.5)
Time since first diagnosis of SLE, years, mean (SD)	10.1 (7.9)	9.8 (8.5)
SLEDAI-2K, mean (SD)	10.7 (3.5)	11.2 (3.4)
SLEDAI-2K ≥10, n (%)	140 (67.3)	79 (73.8)
PGA, mean (SD)	58.9 (14.1)	59.7 (14.1)
Concomitant systemic glucocorticoids, n (%)	171 (82.2)	87 (81.3)
Glucocorticoid dose, mg/day, mean (SD)	7.9 (5.9)	9.6 (8.1)
Glucocorticoid dose >7.5 mg/day, n (%)	105 (50.5)	51 (47.7)

Full analysis set.
DZP: dapirolizumab pegol; PBO: placebo; PGA: Physician's Global Assessment; SD: standard deviation; SLE: systemic lupus erythematosus; SLEDAI-2K: SLE Disease Activity Index-2K; SOC: standard of care.

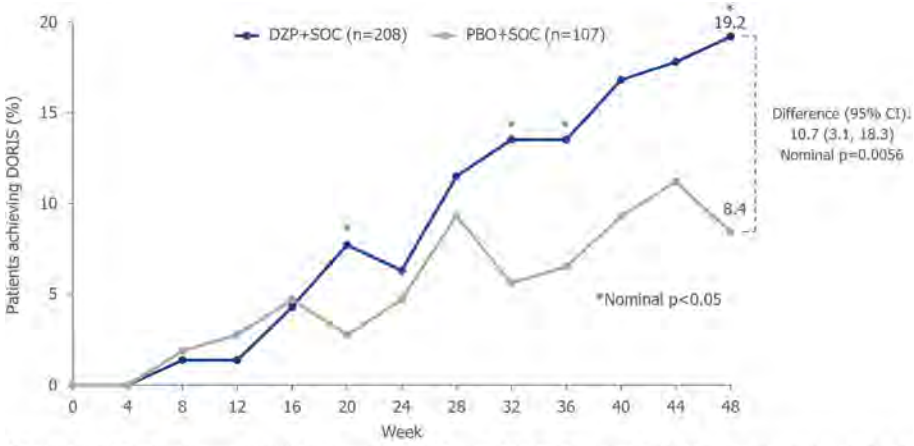


Full analysis set; NRI. All p-values are nominal and were not controlled for multiplicity. LLDAS requires all of the following criteria to be met: SLEDAI-2K score ≤4 with no activity in major organ systems (renal, CNS, cardiopulmonary, vasculitis, fever); no new and/or worsening disease activity defined as no SLEDAI-2K component documented as present that was not documented present at previous visit; PGA ≤33 mm; prednisone equivalent systemic dose ≤7.5 mg/day at >50% of the last 28 days and ≤7.5 mg/day at all days in the 7 days before a visit, at the day of the visit and at the day after the visit; stable standard maintenance doses of immunosuppressive drugs. (A) Differences in proportions between DZP+SOC and PBO+SOC, 95% CIs and p-values were estimated and tested using the CMH risk difference estimate controlling for stratification factors. (B) The LS means, difference between DZP+SOC and PBO+SOC, 95% CIs and p-values were estimated using ANCOVA including stratification factors.

ANCOVA: analysis of covariance; CI: confidence interval; CMH: Cochran-Mantel-Haenszel; CNS: central nervous system; DZP: dapirolizumab pegol; LLDAS: Low Lupus Disease Activity State; LS: least square; NRI: non-responder imputation; PBO: placebo; PGA: Physician Global Assessment; SLE: systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2K; SOC: standard of care.

Figure 1. (A) Achievement of LLDAS by visit and (B) cumulative number of visits in LLDAS through Week 48

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Full analysis set; NRI. All p-values are nominal and were not controlled for multiplicity. DORIS requires all of the following criteria to be met: clinical SLEDAI-2K score of 0 (SLEDAI-2K without serology: anti-dsDNA and C3/C4 items); PGA ≤16 mm; prednisone equivalent systemic dose ≤5 mg/day at >50% of the last 28 days and ≤5 mg/day at all days in the 7 days before a visit, at the day of the visit and at the day after the visit. Differences in proportions between DZP+SOC and PBO+SOC, 95% CIs and p-values were estimated and tested using the CMH risk difference estimate controlling for stratification factors.

Anti-dsDNA: anti-double stranded DNA; CI: confidence interval; C3: complement C3; C4: complement C4; CMH: Cochran-Mantel-Haenszel; DORIS: Definition of Remission in SLE; DZP: dapirolizumab pegol; NRI: non-responder imputation; PBO: placebo; PGA: Physician Global Assessment; SLE: systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2K; SOC: standard of care.

Figure 2. Achievement of DORIS by visit

A higher proportion of pts receiving DZP+SOC vs PBO+SOC achieved DORIS at Wk 48 (19.2% vs 8.4%; nominal p=0.0056), as well as at Wks 20, 32, and 36 (nominal p< 0.05; **Figure 2**).

Conclusion: Treatment with DZP+SOC resulted in higher rates of achievement and time in the prognostically important endpoints of LLDAS and DORIS vs PBO+SOC. These findings provide further insights into the potential benefits of treatment with DZP for pts with SLE.

References: 1. Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); **2**. Powlesland AS. Annals Rheum Dis 2024;83 (suppl 1):261; **3**. Clowse M. Arthritis Rheumatol 2024;76 (suppl 9); **4**. Parra Sánchez AR. Rheumatol Ther 2023;10:1459–77; **5**. Fanouriakis A. Ann Rheum Dis 2024;83:15–29; **6**. Tani C. Lupus Sci Med 2018;5:e000234; **7**. van Vollenhoven RF. Lupus Sci Med 2021;8:e000538.

Disclosure: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **L. Carter**: Alumis Inc., 12, Paid instructor, UCB, 2; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6; **T. Jimenez**: UCB, 3, 12, Shareholder; **J. Gaiha-Rohrbach**: Biogen, 3, 12, shareholder, may hold Biogen stock; **B. Lauwerys**: UCB, 3, 12, Shareholder; **A. Nelde**: Biogen, 3, 12, Shareholder; **C. Stach**: UCB, 3, 12, Shareholder; **R. van Vollenhoven**: AbbVie, 2, 6, Alfasigma, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 5, 6, Galapagos, 2, 5, 6, GSK, 2, 6, Janssen, 2, 6, MSD, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, 6, Roche, 5, Sanofi, 5, UCB, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0646

A-319, a CD3×CD19 T Cell Engager, for the Treatment of Refractory Systemic Lupus Erythematosus: Preliminary Evidence of Autoimmune Reset

Chunli Mei[1], Xin Guan[1], Rong Du[1], Bin Wu[2], You Song[1], Xiaoqi Chen[3], Mengjiao Li[1], Xiaojing Liu[1], Xi Cheng[1], Weiwei Wang[1], Cheng Wang[1], Huiling Mei[1], Xiaoru Duan[1], Lijuan Jiang[1], Wenlin Qiu[1], Likai Yu[1], Yuhong Liu[1], Di Wu[1], Guiqi Quan[1], Blal Chakhabi[1], Xing Zhao[4], Xuanfan Zhong[4], Shengjie Xue[4], Wuzhong Shen[4], Ying Tan[4], Guojian Yu[4], Guiyun Tu[4], Hanyang Chen[4], Amy Sun[4], Jing Liang[4], Sharon Song[4], Jason Xu[4], Xiaoqiang Yan[4], Anbing Huang[1] and **Qiubai Li**[5], [1]Union Hospital,Tongji Medical College, Huazhong University of Science and Technology, WUHAN, China (People's Republic), [2]First People's Hospital of Jingzhou, Jingzhou, China (People's Republic), [3]Zhongnan Hospital, Wuhan University, Wuhan, China (People's Republic), [4]ITabMed Co., Ltd., Shanghai, China (People's Republic), [5]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Immune reset of autoimmune disease has been proposed to be a potential benefit of T cell engagers (TCEs) and CD19 CAR T therapy. A-319, a highly potent TCE, can deplete CD19+ B cells in patients (pts) with hematological malignancies. We evaluated the safety profile of A-319 in systemic lupus erythematosus (SLE) pts and explored if A-319 has the potential to reset autoimmunity in a dose-finding clinical study.

Methods: Twelve pts were enrolled in the study with baseline characteristics shown in Table 1. In week (W) 1, pts received A-319 at 0.05μg/kg/day(D), on D1, 3 and 5 by 24hr IV infusion. In W2-4, pts received A-319 at 0.3 (cohort 1, n=6), or 0.6 (cohort 2, n=3) or 1.2μg/kg/day (cohort 3, n=3), on D1, 3 and 5 by 6hr IV infusion. Safety, pharmacokinetics (PK) and pharmacodynamics (PD) parameters including peripheral blood (PB) B cell counts, autoantibodies, and other disease-related biomarkers and efficacy are evaluated for up to 1 year. The study, approved by the local hospital IRB, was registered as NCT06400537.

Table 1. Baseline characteristics

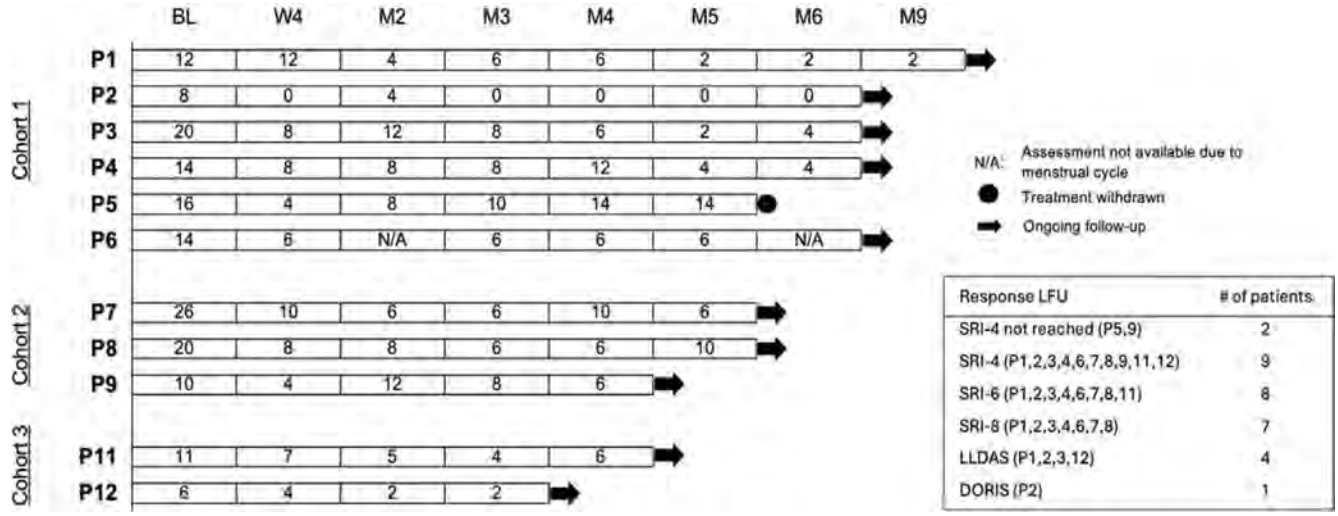
Characteristic	Total (n=12)	Characteristic	Total (n=12)
Age, years		Autoantibodies present	
Mean (SD)	35.9 (10.2)	ANA (≥ 1: 100), n (%)	12 (100)
Median (Min; Max)	38 (21; 54)	dsDNA, n (%)	7 (58)
Female sex, n (%)	12 (100)	Sm, n (%)	5 (42)
SLEDAI-2K, mean (SD)	14.1 (5.7)	SS-A, n (%)	9 (75)
Concurrent autoimmune conditions, n (%)		SS-B, n (%)	1 (8)
Systemic sclerosis	1 (8)	RNP A, n (%)	6 (50)
Rheumatoid arthritis	1 (8)	RNP 68, n (%)	3 (25)
Idiopathic inflammatory myopathy	1 (8)	Sm/RNP, n (%)	7 (58)
Disease duration, years		Ro-52, n (%)	3 (25)
Mean (SD)	9.1 (6.5)	Ribo P, n (%)	8 (67)
Median (Min; Max)	8.5 (0.5; 26)	Chromatin, n (%)	9 (75)
Organ involvement, n (%)		Scl-70, n (%)	1 (8)
Renal	11 (92)	MDA5, n (%)	1 (8)
Mucocutaneous	9 (75)	CENPB, n (%)	1 (8)
Musculoskeletal	3 (25)	SLE-related treatment history	
Cardiorespiratory	2 (17)	Glucocorticoids	12 (100)
Vascular	2 (17)	Hydroxychloroquine	12 (100)
Serosal	2 (17)	Mycophenolate	11 (92)
Hematological involvement, n (%)		Cyclophosphamide	8 (67)
Anemia	5 (42)	Methotrexate	4 (33)
Leukopenia	2 (17)	Tacrolimus	6 (50)
Thrombocytopenia	1 (8)	Telitacicept	6 (50)
Kidney function		Belimumab	4 (33)
eGFR, ml/min/1.73 m2, mean (SD)	105.0 (33.2)	Leflunomide	4 (33)
Urinary protein in 24h (mg/24 h) (Min; Max)	1848.6 (104,6585)	IVIg	2 (17)
Protein to creatinine ratio (mg protein /g creatinine)	1559.9	Cyclosporin A	2 (17)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Safety summary

Variable	Cohort 1 (n=6), n	Cohort 2 (n=3), n	Cohort 3 (n=3), n	Total (n=12), n (%)
Patients with any AE	6	3	3	12 (100)
Patients with any serious AE	0	0	0	0 (0)
AE leading to withdrawal	0	0	1	1 (8)
AE leading to dose interruption	0	0	1	1 (8)
Deaths	0	0	0	0 (0)
CRS	6	3	3	12 (100)
Grade 1	6	2	3	11 (92)
Grade 2	0	1	0	1 (8)
Grade ≥3	0	0	0	0 (0)
ICANs (any grade)	0	0	0	0 (0)
Infection (any grade)	2	0	1	3 (25)
Lymphopenia (any grade)	6	3	3	12 (100)
Anemia	5	3	2	10 (83)
Grade 1	3	1	0	4 (33)
Grade 2	2	2	0	4 (33)
Grade ≥3	0	0	2	2 (17)
Leukopenia (any grade)	1	0	2	3 (25)
Neutropenia (any grade)	1	1	0	2 (17)
Hypogammaglobulinemia	0	0	0	0 (0)

AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.



Response LFU	# of patients
SRI-4 not reached (P5,9)	2
SRI-4 (P1,2,3,4,6,7,8,9,11,12)	9
SRI-6 (P1,2,3,4,6,7,8,11)	8
SRI-8 (P1,2,3,4,6,7,8)	7
LLDAS (P1,2,3,12)	4
DORIS (P2)	1

Figure 1. Clinical response (SLEDAI-2K score)

Results: Safety summary is listed in Table 2. No Grade ≥3 cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANs), or hypogammaglobulinemia were reported. One case of Grade 2 CRS was reported and resolved within 12hr without tocilizumab. One pt (P10) in Cohort 3 withdrew on D10 due to renal complications. One pt (P5) in Cohort 1 withdrew from the study at Month(M) 5 due to disease rebound.

Dose-dependent peripheral blood B cell depletion was demonstrated. Cohort 1 achieved incomplete B cell depletion with 10±9% remaining at W4. However, B cell counts in Cohorts 2 and 3 were at 0.0 cell/uL at W4 and W2-W6, respectively. B cell recovery observed at ~W6 and M2, except for pts 9 and 11. The B cell subtype analysis and single cell sequence results demonstrated significantly different profiles at baseline, end of dosing and follow-up. Disease-related biomarker changes including autoantibody reduction (e.g., anti-ANA, dsDNA, Sm, SS-A, SS-B, ribosomal P protein, chromatin, Scl-70, Ro-52), normalization of complement levels (C3 and C4), and reduction of 24hr proteinuria, were also observed.

The preliminary efficacy (Figure 1) at the last follow-up (LFU, 9 to 3 months) visit showed reduced SLEDAI-2K scores with the achievement of SRI-4 (n=9), SRI-6 (n=8), SRI-8 (n=7), LLDAS (n=4), and DORIS (n=1). Seven pts had reductions in 24hr total urine protein (Utp) levels. Four of 7 pts with baseline Utp ≥0.5 g/24hr achieved levels < 0.5 g/24hr by M6 (3 in Cohort 1, 1 in Cohort 2). All pts reduced glucocorticoid (GC) dose below baseline levels. At the LFU, 8 pts reduced to < =7.5 mg/day,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

including 6 pts further reduced to < =5 mg/day. Disease rebound in P5 corelated with incomplete B cell depletion and auto-antibody level rebound.

Conclusion: A-319 was well tolerated and demonstrated efficacy even at a (low) dose associated with incomplete B cell depletion. These results suggest that A-319 could potentially reset autoimmunity in refractory SLE patients to achieve remission.

Disclosure: C. Mei: None; **X. Guan**: None; **R. Du**: None; **B. Wu**: None; **Y. Song**: None; **X. Chen**: None; **M. Li**: None; **X. Liu**: None; **X. Cheng**: None; **W. Wang**: None; **C. Wang**: None; **H. Mei**: None; **X. Duan**: None; **L. Jiang**: None; **W. Qiu**: None; **L. Yu**: None; **Y. Liu**: None; **D. Wu**: None; **G. Quan**: None; **B. Chakhabi**: None; **X. Zhao**: ITabMed Co., Ltd., 3; **X. Zhong**: ITabMed Co., Ltd., 3; **S. Xue**: ITabMed Co., Ltd., 3; **W. Shen**: ITabMed Co., Ltd., 3; **Y. Tan**: ITabMed Co., Ltd., 3; **G. Yu**: ITabMed Co., Ltd., 3; **G. Tu**: ITabMed Co., Ltd., 3; **H. Chen**: ITabMed Co., Ltd., 3; **A. Sun**: ITabMed Co., Ltd., 2; **J. Liang**: ITabMed Co., Ltd., 2; **S. Song**: ITabMed Co., Ltd., 2; **J. Xu**: ITabMed Co., Ltd., 2; **X. Yan**: ITabMed Co., Ltd., 4; **A. Huang**: None; **Q. Li**: None.

Abstract Number: 0647

anti-cd19 Chimeric Antigen Receptor T Cell Therapy for Refractory Systemic Lupus Erythematosus: An Open-label Pilot Study

Jinxia Zhao, Xiaoying Zhang, Xinyi Li, Hui Wei, Rui Liu, Lin Sun, Zhaohua Li, Wei Guo and **Rong Mu**, Peking University Third Hospital, Beijing, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: This pilot study aims to evaluate the preliminary efficacy and safety of autologous anti-CD19 chimeric antigen receptor T cell (CAR T) named IM19 therapy in patients with refractory systemic lupus erythematosus (SLE).

Methods: Six patients with refractory SLE (three women and three men) with a median (range) age of 37 (19 to 43) years, median (range) disease duration of 9.5 (3 to 14) years were enrolled in the study. All met the 2019 EULAR/ACR classification

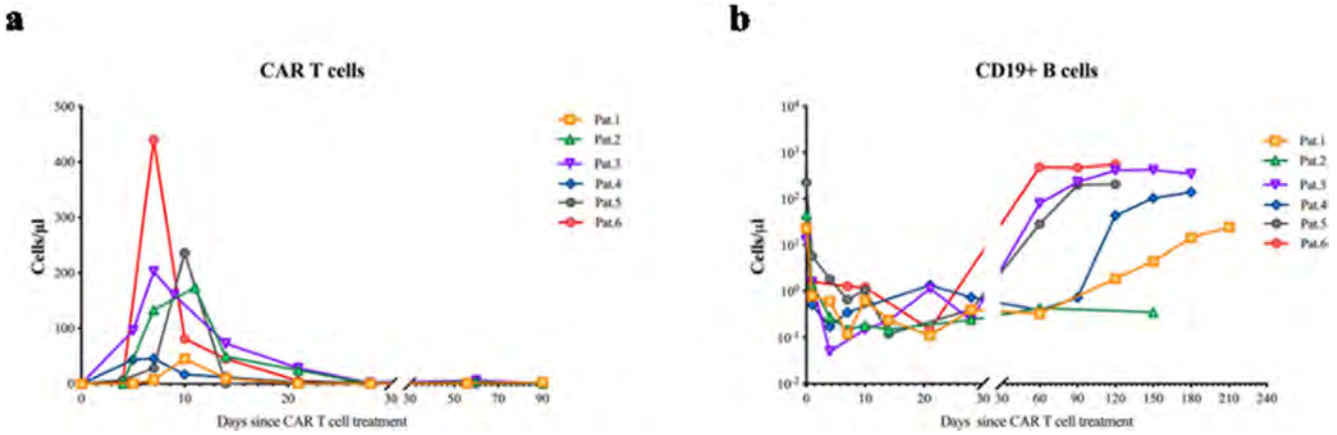


Fig.1 CAR T cell expansion in vivo and depletion of B cells. a, Circulating CAR T cell number in the six patients within the 90 days after treatment (N=6). b, Circulating B cell numbers in the six patients since treatment (N=6).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

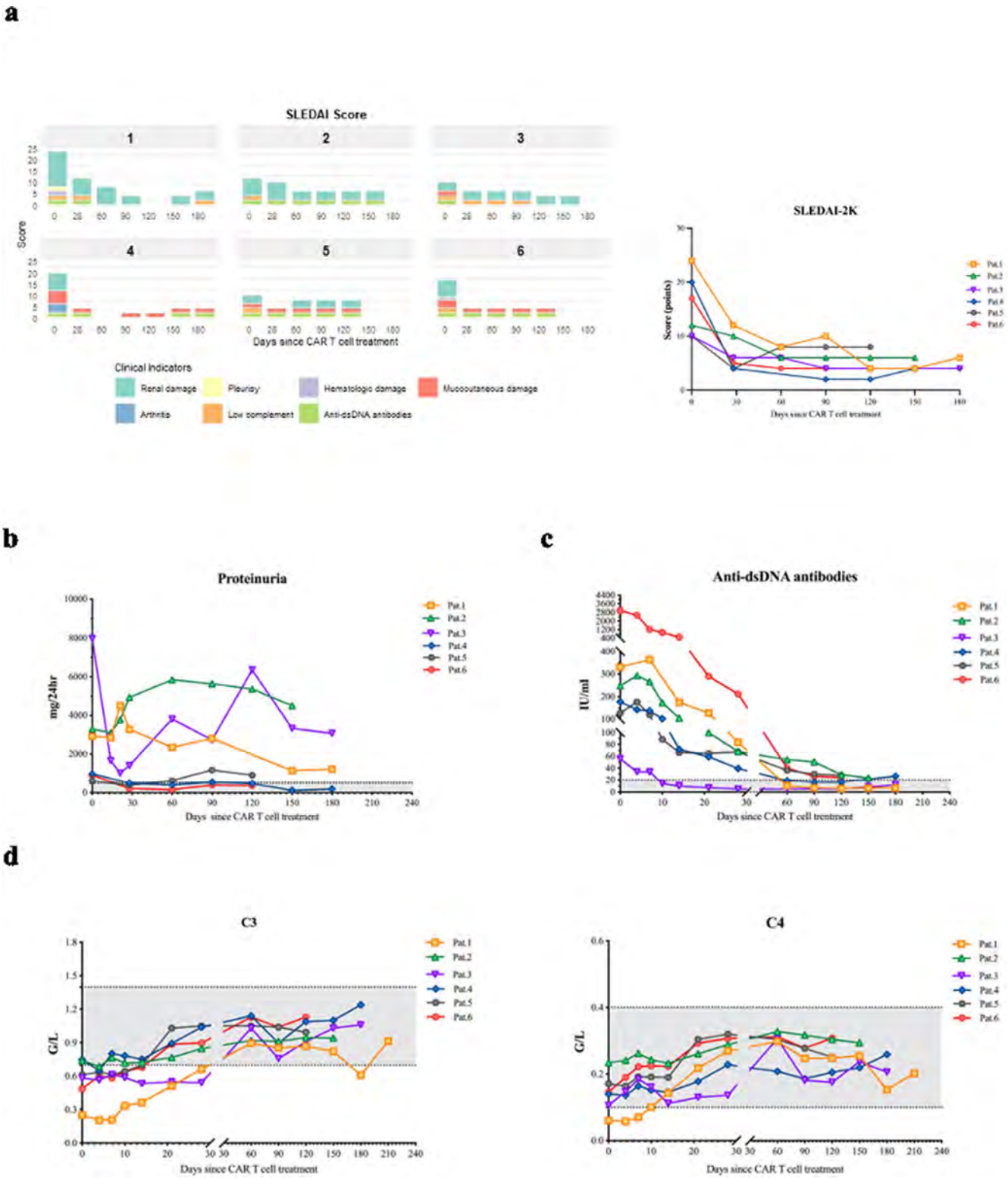


Fig.2 Effects of CAR T cell treatment on the activity of systemic lupus erythematosus. a, The change of SLEDAI-2K scores after CAR T cell administration (N=6). b, The change of proteinuria after CAR T cell administration (N=6). c, Anti-double stranded (ds) DNA antibodies assessed by radioimmunoassay after CAR T cell administration (N=6).d, The change of complement factor C3 and C4 levels after CAR T cell administration (N=6). The shaded gray areas in b through d indicate the normal range. SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index-2K.

criteria for SLE and had active disease (SLEDAI-2K≥10) with inadequate response to at least two lines of therapies including steroids, immunosuppressants and biologic agents. Autologous T cells from patients with SLE were transduced with a lentiviral anti-CD19 CAR vector, expanded and reinfused at a dose of 1×10^6 CAR T cells per kg body weight or 1×10^8 cells into

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Characteristics of 6 patients with refractory SLE at baseline

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	43	41	39	19	35	32
Sex (female/male)	F	M	F	F	M	M
Weight (kg)	68	62	83	69	73	69
Disease duration (years)	7	6	14	3	13	12
Follow-up (months)	7	4	5	5	4	4
PGA score	3	2	2	2	2	2
Disease activity SLEDAI-2K	24	12	10	20	10	17
Baseline laboratory value						
Wight blood cells (N/μl)	2.43	9.25	3.73	7.92	4.13	4.13
Hemoglobin (g/l)	74	108	112	108	121	112
Lymphocyte (N/μl)	0.78	1.89	0.4	0.91	1.23	1.13
Platelets (N/μl)	80	152	226	241	189	188
eGFR (ml/min/1.73m^2)	96.7	63.2	119.3	132.6	118.4	122.2
Autoantibodies						
ANA (titer)	1:160	1:160	1:640	1:640	1:320	1:640
Anti-dsDNA	+	+	+	+	+	+
Anti-SSA/Ro60	+	-	+	-	+	+
Anti-Ro52	-	-	+	-	+	+
Anti-SSB	-	-	+	-	-	-
Anti-RNP	+	-	-	-	-	-
Organ involvement (presence/absence)						
Mucocutaneous	-	+	-	+	-	+
Renal	+	+	+	+	+	+
Renal biopsy stage	IV	IV	V	NA	IV	NA
Serosal	+	-	-	-	-	-
Hematologic	+	-	-	-	-	+
Musculoskeletal	-	-	-	+	-	-
Treatments (yes/no)						
Glucocorticoids	+	+	+	+	+	+
Hydroxychloroquine	+	+	-	+	+	+
Cyclophosphomide	+	+	+	+	+	+
Mycophenolate	+	+	+	+	+	+
Tacrolimus	+	+	+	+	+	-
Leflunomide	-	-	+	+	-	-
Azathioprine	-	-	-	-	+	-
Belimumab	+	+	+	+	+	+
Telitacicept	-	-	-	-	+	-

ANA, antinuclear antibody; eGFR, estimated glomerular filtration rate; kg, kilogram; PGA, physician global assessment; SLE, systemic lupus erythematosus; SLEDAI-2K, systemic lupus erythematosus disease activity index-2000.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the patients after lymphodepletion with fludarabine and cyclophosphamide. Preliminary efficacy was assessed by the changes of SLEDAI-2K at 3 months after CAR T cell therapy. Safety was assessed by recording cytokine-release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) during the first 28 days. The study was registered at ClinicalTrials.gov (NCT06513429).

Results: The demographic and clinical characteristics of the patient at baseline are summarized in Table 1. The median (range) follow-up was 5.5 (4 to 7) months. The CAR T cells expanded significantly (median peak CAR+ T cells: 188.1cells/μL at median day 8.5 (range 7-11))(Fig.1 a). Complete circulating B-cell depletion (CD19+ B cells< 5 cells/μL) was achieved in 5/6 patients by day 1 post-infusion and in all patients by day 4 (Fig.1 b). The median SLEDAI-2K score demonstrated a significant reduction from 12 (range, 10 to 24) to 5.5 (range, 4 to 13) at 1 month, with a further decline to 5.0 (range, 2 to 10) by the 3-month follow up (Fig.2 a). During the observation period, complete renal remission was achieved in 2 patients, with partial remission observed in 1 patient. The remaining 3 patients exhibited persistent proteinuria with no significant improvement throughout the follow-up period (Fig.2 b). Anti-dsDNA antibodies converted to negative in 3 patients (Fig.2 c) and the complement returned to normal levels in all the patients within 2 months after CAR T cell administration (Fig.2 d). IM19 CAR T cell therapy was well tolerant with grade 1 CRS in 4 patients. No ICANS occurred in the study.

Conclusion: IM19 CAR T cell therapy demonstrated an acceptable safety profile and induced profound circulating B-cell depletion in refractory SLE, which correlated with accelerated serological normalization and clinically meaningful reductions in disease activity. Notably, the study revealed renal response in 50% of participants with refractory lupus nephritis, indicating a selective rather than universal therapeutic effect. These findings underscore the necessity of future large-scale trials with prolonged follow-up durations to evaluate the durability of therapeutic effects and safety profiles of this innovative cellular therapy.

Disclosure: J. Zhao: None; **X. Zhang**: None; **X. Li**: None; **H. Wei**: None; **R. Liu**: None; **L. Sun**: None; **Z. Li**: None; **W. Guo**: None; **R. Mu**: None.

Abstract Number: 0648

Real World Comparative Use of Anifrolumab in Systemic Lupus Erythematosus and Cutaneous Lupus Erythematosus: A Multicenter Cohort Study

Rajaie Namas[1], **Sarah Al Qassimi**[2], Rowaida Abdou[3], Jawahir Alameri[2], Reem Alblooshi[4], Fatima Abdulla[4], Muriel Ghosn[4], Amir Malik[4], Raghda Almaashari[4], Fulvio Salvo[4], Mohamed Abuzakouk[4], Atheer Al Ansari[5], Hazem Helmy Ali Rifaai[5], Ahlam Almarzooqi[6], Asia Mubashir[7], Ahmed Aldhaheri[4], Suzan Attar[8] and Mohamed Elarabi[9], [1]Cleveland Clinic Abu Dhabi, Detroit, MI, [2]Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates, [3]NMC Specialty Hospital Abu Dhabi, Abu Dhabi, United Arab Emirates, [4]Cleveland Clinic Abu Dhabi, Abu Dhabi, [5]Mediclinic, Abu Dhabi, United Arab Emirates, [6]Emirates Health Services, Sharjah, United Arab Emirates, [7]Cleveland Clinic, Abu Dhabi, Abu Dhabi, United Arab Emirates, [8]King Abdulaziz University, Saudi Arabia, Jeddah, Saudi Arabia, [9]Cleveland Clinic Abu Dhabi, Hannon, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multiorgan organ damage, and early mortality. Anifrolumab (ANI), a human monoclonal antibody targeting the type I interferon receptor, is approved for the treatment of moderate to severe SLE. However, its efficacy and safety profile for cutaneous lupus erythematosus (CLE) is limited. Our aim was to assess the efficacy and safety of ANI in subgroups of SLE and CLE.

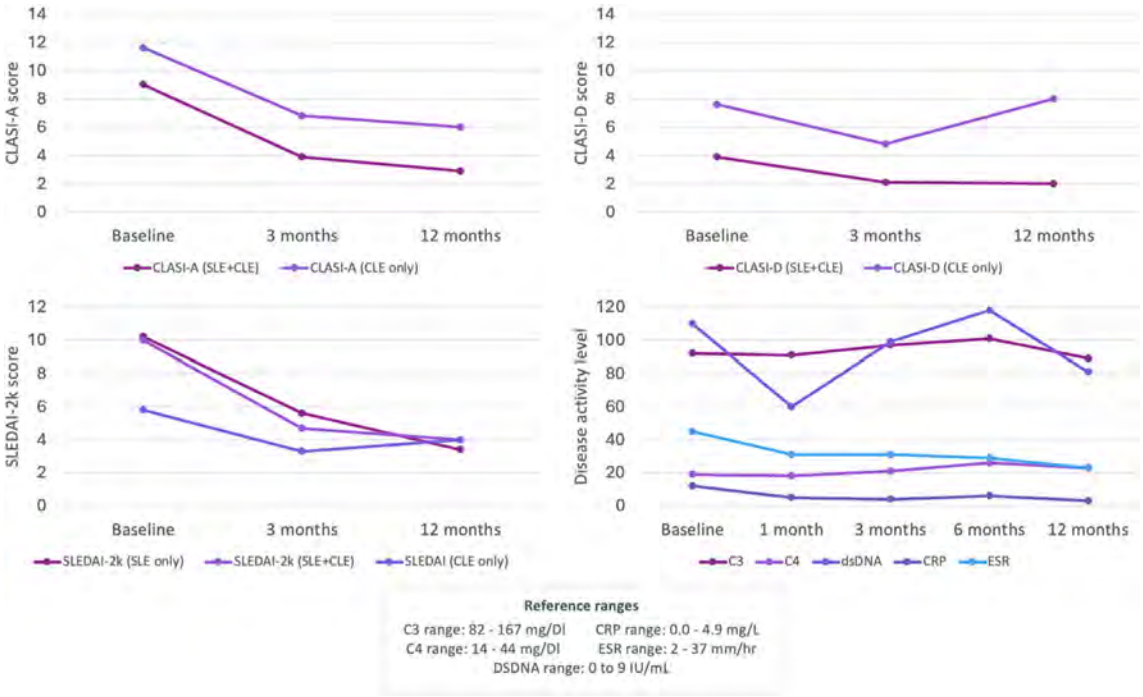
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients with SLE were identified from each hospital's electronic database between April 2015 and April 2025 in five centers after receiving IRB approval. Those aged >18 years who were receiving ANI every 4 weeks were included in the study. These patients were categorized into four subgroups: Total cohort, SLE only, SLE and CLE, and CLE (subacute and chronic) only. Data collected encompassed sociodemographic details, clinical features, SLE organ involvement, laboratory findings, previous and current medications along with their adverse effect profiles, and disease activity indices. Serial

	Total cohort (n = 63)	SLE only (n = 16)	SLE and CLE (n = 42)	CLE only (n = 5)
Ethnicity (n, %)				
Arab	*42 (66.7)*	*13 (81.3)*	*26 (61.9)*	*3 (60)*
Non-Arab	*21 (33.3)*	*3 (18.8)*	*16 (38.1)*	*2 (40)*
Gender (n, %)				
Female	*56 (88.9)*	*16 (100)*	*36 (85.7)*	*4 (80)*
Male	*7 (11.1)*	*0 (0)*	*6 (14.3)*	*1 (20)*
BMI (kg/m², mean ± SD)	25.8 ± 6.0	26.8 ± 4.9	25.7 ± 6.6	23.7 ± 1.7
Age at time of SLE diagnosis (years, mean ± SD)	31.4 ± 10.5	30.9 ± 11.6	31.8 ± 10.5	29.2 ± 8.2
Age at presentation to clinic (years, mean ± SD)	35.7 ± 10.7	36.1 ± 12.1	36.1 ± 10.4	30.4 ± 8.5
SLE/CLE disease duration (months, mean ± SD)	87.3 ± 87.8	100.3 ± 89.9	87.2 ± 91.2	45.6 ± 32.2
Completion of herpes zoster vaccination, n (%)	12 (19)	1 (6.3)	10 (2.4)	1 (20)
Comorbidities (n, %)				
Tuberculosis	*2 (3.2)*	*0 (0)*	*2 (4.8)*	*0 (0)*
Herpes zoster	*1 (1.6)*	*0 (0)*	*1 (2.4)*	*0 (0)*
Diabetes mellitus	*2 (3.2)*	*1 (6.3)*	*1 (2.4)*	*0 (0)*
Thyroid disease	*12 (19)*	*2 (12.5)*	*9 (21.4)*	*1 (20)*
Osteoporosis	*3 (4.8)*	*0 (0)*	*3 (7.1)*	*0 (0)*
Hypertension	*7 (11.1)*	*2 (12.5)*	*5 (11.9)*	*0 (0)*
Hyperlipidemia	*12 (19)*	*2 (12.5)*	*10 (23.8)*	*0 (0)*
Depression	*13 (20.6)*	*3 (18.8)*	*9 (21.4)*	*1 (20)*
Fibromyalgia	*11 (17.5)*	*3 (18.8)*	*8 (19)*	*0 (0)*
SLE organ domain involvement				
Mucocutaneous (n, %)	**47 (74.6)**	**0 (0)**	**42 (100)**	**5 (100)**
Acute cutaneous lupus	*18 (38)*	*0 (0)*	*18 (43)*	*0 (0)*
Subacute cutaneous lupus	*12 (26)*	*0 (0)*	*26 (11)*	*1 (20)*
Chronic cutaneous lupus	*22 (46.8)*	*0 (0)*	*23 (54.8)*	*4 (80)*
Musculoskeletal (n, %)	**46 (73)**	**15 (93.8)**	**32 (76.2)**	**1 (20)**
Arthritis	*35 (76.1)*	*13 (86.7)*	*22 (68.8)*	*0 (0)*
Arthralgia	*46 (100)*	*15 (100)*	*30 (93.8)*	*1 (100)*
Hematological (n, %)	**39 (61.9)**	**7 (43.8)**	**32 (76.2)**	**0 (0)**
Anemia of chronic disease	*17 (43.6)*	*3 (43.9)*	*14 (43.8)*	*0 (0)*
Leukopenia	*28 (71.8)*	*4 (57.1)*	*24 (75.0)*	*0 (0)*
Idiopathic thrombocytopenia purpura	*5 (12.8)*	*2 (28.6)*	*3 (9.4)*	*0 (0)*
Neurological (n, %)	**4 (6.3)**	**1 (6.3)**	**4 (9.5)**	**0 (0)**
Headache	*3 (75)*	*1 (100)*	*2 (50)*	*0 (0)*
Peripheral neuropathy	*3 (75)*	*0 (0)*	*3 (75)*	*0 (0)*
Respiratory (n, %)	**6 (9.5)**	**1 (6.3)**	**5 (11.9)**	**0 (0)**
Pulmonary embolism	*4 (66.7)*	*0 (0)*	*3 (60)*	*0 (0)*
Pleural effusion	*5 (83.3)*	*1 (100)*	*3 (60)*	*0 (0)*
Pleuritis	*5 (83.3)*	*1 (100)*	*4 (80)*	*0 (0)*
Cardiac (n, %)	**5 (7.9)**	**2 (12.5)**	**3 (7.1)**	**0 (0)**
Myocarditis	*1 (20)*	*0 (0)*	*1 (33.3)*	*0 (0)*
Pericardial effusion	*2 (40)*	*0 (0)*	*2 (66.7)*	*0 (0)*
Pericarditis	*2 (40)*	*1 (50)*	*1 (33.3)*	*0 (0)*
Renal (n, %)	**6 (9.5)**	**2 (12.5)**	**4 (9.5)**	**0 (0)**
Lupus nephritis III	*1 (1.6)*	*0 (0)*	*1 (2.4)*	*0 (0)*
Lupus nephritis IV	*2 (3.2)*	*0 (0)*	*2 (4.8)*	*0 (0)*
Lupus nephritis V	*2 (3.2)*	*0 (0)*	*2 (4.8)*	*0 (0)*
Unknown class	*2 (3.2)*	*1 (12.5)*	*0 (0)*	*0 (0)*
Serologies (n, %)				
IF-ANA	*58 (92.1)*	*15 (93.8)*	*40 (95.2)*	*3 (60)*
Anti-Smith	*32 (50.8)*	*6 (37.5)*	*25 (59.5)*	*1 (20)*
SSA	*35 (55.6)*	*7 (43.8)*	*26 (61.9)*	*2 (40)*
SSB	*10 (15.9)*	*4 (8.5)*	*5 (11.9)*	*1 (2.4)*
Previous therapy prior to anifrolumab (n, %)				
Prednisolone	*51 (80.9)*	*14 (87.5)*	*36 (85.7)*	*1 (20)*
Hydroxychloroquine	*60 (95.2)*	*15 (93.8)*	*41 (97.6)*	*4 (80)*
Methotrexate	*16 (24.4)*	*6 (37.5)*	*8 (19.1)*	*2 (40)*
Cyclophosphamide	*1 (1.6)*	*0 (0)*	*1 (2.4)*	*0 (0)*
Mycophenolate mofetil	*19 (30.2)*	*1 (6.3)*	*16 (38.1)*	*2 (40)*
Belimumab	*15 (23.8)*	*2 (12.5)*	*13 (30.9)*	*0 (0)*
Rituximab	*6 (9.5)*	*1 (6.25)*	*5 (11.9)*	*0 (0)*
Adverse events due to prior therapy (n, %)	**17 (26.9)**	**6 (37.5)**	**11 (26.2)**	**0 (0)**
Hair loss	*7 (41.2)*	*2 (33.3)*	*5 (45.5)*	*0 (0)*
Ocular changes	*3 (17.7)*	*1 (16.7)*	*2 (18.2)*	*0 (0)*
Elevated liver function tests	*5 (29.4)*	*1 (16.7)*	*4 (36.4)*	*0 (0)*
Gastrointestinal upset	*6 (35.3)*	*2 (33.3)*	*4 (36.4)*	*0 (0)*
Lower extremity pain	*3 (17.7)*	*1 (16.7)*	*2 (18.2)*	*0 (0)*
Steroid-induced psychosis	*1 (5.9)*	*1 (16.7)*	*0 (0)*	*0 (0)*
Steroid-induced avascular necrosis	*1 (5.9)*	*0 (0)*	*1 (9.1)*	*0 (0)*
Cytomegalovirus colitis	*1 (5.9)*	*0 (0)*	*1 (9.1)*	*0 (0)*
Rituximab-related vasculitis	*1 (5.9)*	*0 (0)*	*1 (9.1)*	*0 (0)*
Age at anifrolumab initiation (years, mean ± SD)	37.9 ± 11.0	38.3 ± 11.7	38.5 ± 10.9	32 ± 9.8
Adjunct therapy to anifrolumab (n, %)				
Prednisolone	*33 (52.4)*	*6 (37.5)*	*26 (61.9)*	*1 (20)*
Average prednisolone dose (mg, mean ± SD)	*7.7 ± 5.6*	*7.5 ± 6.7*	*7.8 ± 5.2*	*7.5*
Hydroxychloroquine	*51 (80.9)*	*11 (68.8)*	*37 (88.1)*	*3 (60)*
Azathioprine	*16 (25.4)*	*5 (31.3)*	*10 (23.8)*	*1 (20)*
Mycophenolate mofetil	*16 (25.4)*	*1 (6.3)*	*14 (33.3)*	*1 (20)*
Duration on anifrolumab (months, mean ± SD)	9.7 ± 5.7	10.2 ± 5.5	7.6 ± 5.5	9.8 ± 5.5
Adverse events post-anifrolumab (n, %)	**8 (12.7)**	**2 (12.5)**	**6 (14.3)**	**0 (0)**
Upper respiratory tract infection	*8 (100)*	*2 (100)*	*6 (100)*	*0 (0)*
Gastroenteritis	*1 (12.5)*	*0 (0)*	*0 (0)*	*0 (0)*

Demographic and characteristics of patients on anifrolumab categorized by lupus involvement.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Changes in disease activity scores and levels over a 12-month period on anifrolumab.

measurements of C3, C4, dsDNA, SLEDAI-2k, CLASI-A, and CLASI-D, as well as adverse effects related to ANI, were tracked over a 12-month period. Descriptive statistics were used for data analysis.

Results: The total cohort (n = 63) was predominantly female (88.9%) and of Arab ethnicity (66.7%) with a mean SLE disease duration of 87.3 ± 87.8 months. Mucocutaneous involvement was the most common disease manifestation (74.6%), followed by musculoskeletal (73%) and hematological (61.9%) domains. The mean age at ANI initiation was 37.9 ± 11 years and the mean duration on ANI was 9.7 ± 5.7 months. The most reported adverse event reported was upper respiratory tract infection (URTI) (12.7%), with one patient report of both URTI and gastroenteritis (**Table 1**). The SLE subgroup had the longest disease duration at 100.3 ± 89.9 months and had the highest previous use of prednisolone (87.5%) and the highest prevalence of adverse effects from prior therapy (37.5%). The SLE and CLE subgroup commonly had mucocutaneous (100%) and musculoskeletal involvement (76.2%), with a higher anti-Sm (59.5%) and SSA positivity (61.9%) compared to the SLE only group. They received immunosuppressive agents such as MMF (38.1%) and belimumab (30.9%). Mean duration on anifrolumab was 7.6 ± 5.5 months and 14.3% reported URTI as an adverse event. The CLE subgroup consisted mainly of females (80%). Organ involvement was limited to the skin, with chronic cutaneous lupus being most common (80%), followed by subacute cutaneous lupus (20%). Serologies were less frequently positive. Prior immunosuppressive use was limited. The mean age of ANI initiation was 32 ± 9.8 years and remained on ANI for 9.8 ± 5.5 months with no adverse events reported. Over the 12-month follow up, disease activity scores and laboratory investigations across all subgroups showed numerical improvement (**Figure 1**).

Conclusion: Anifrolumab demonstrated a favorable safety and tolerability profile across both SLE and CLE in a multicenter setting. These findings support the expansion of the role of ANI in CLE and highlight the need for further studies to understand its utility across the lupus spectrum.

Disclosure: R. Namas: None; **S. Al Qassimi**: None; **R. Abdou**: None; **J. Alameri**: None; **R. Alblooshi**: None; **F. Abdulla**: None; **M. Ghosn**: None; **A. Malik**: None; **R. Almaashari**: None; **F. Salvo**: None; **M. Abuzakouk**: None; **A. Al Ansari**: None; **H. Rifaai**: None; **A. Almarzooqi**: None; **A. Mubashir**: None; **A. Aldhaheri**: None; **S. Attar**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 5, 6, Gilead, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Hikma, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Organon, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Sandoz, 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6; **M. Elarabi**: None.

Abstract Number: 0649

Belimumab Real-World Effectiveness in Chinese Patients with Systemic Lupus Erythematosus: Interim Analysis of an Ambidirectional, Observational Cohort Study (RELIABLE)

Zhuoli Zhang[1], Shengyun Liu[2], Min Yang[3], Yasong Li[4], Qinghong Yu[5], Xinwang Duan[6], Qiang Shu[7], Qibing Xie[8], Yanfei Chen[9], Daming Ou[10], Lan He[11], Hongbin Li[12], Pingting Yang[13], Juan Li[14], **Terry Yan**[15], Xin He[16], Daniel Moldaver[17], Ciara O'Shea[18] and Liya Fan[16], [1]Peking University First Hospital, Beijing, Beijing, China (People's Republic), [2]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China (People's Republic), [3]Nanfang Hospital Southern Medical University, Guangzhou, China (People's Republic), [4]Zhejiang Provincial People's Hospital, Hangzhou, China (People's Republic), [5]Zhujiang Hospital of Southern Medical University, Zhujiang, China (People's Republic), [6]The Second Affiliated Hospital of Nanchang University, Nanchang, China (People's Republic), [7]Qilu Hospital of Shandong University, Jinan, China (People's Republic), [8]West China Hospital, Sichuan University, Chengdu, China (People's Republic), [9]The First Hospital of Lanzhou University, Lanzhou, China (People's Republic), [10]The First Affiliated Hospital of University of South China, Hengyang, China (People's Republic), [11]The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China (People's Republic), [12]The Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China (People's Republic), [13]The First Hospital of China Medical University, Shenyang, China (People's Republic), [14]The First Affiliated Hospital of Hainan Medical University, Haikou, China (People's Republic), [15]Medical Affairs, GSK, Shanghai, China (People's Republic), [16]VEO, GSK, Shanghai, China (People's Republic), [17]GSK, Global Real-World Evidence & Health Outcomes Research, Toronto, ON, Canada, [18]Global Medical Affairs, GSK, Dublin, Ireland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Belimumab, a B-cell modulator monoclonal antibody that selectively inhibits BLyS and reduces autoreactive B-cells that drive lupus disease activity, has consistently demonstrated improved efficacy compared with standard therapy alone, across diverse groups of adults and children with systemic lupus erythematosus (SLE). This 2-year, large, ambi-directional, observational cohort study (RELIABLE; funding: GSK214958) conducted across China aimed to assess the real-world effectiveness of belimumab.

Methods: Eligible patients were adults with SLE who were newly prescribed belimumab within 6 months and had ≥1 available assessment of all components for the Lupus Low Disease Activity State (LLDAS) within 3 months before belimumab initiation (index). Patients were followed up retrospectively (up to 6 months after index) and/or prospectively for a total maximum of 24 months. The primary outcome was proportions of patients achieving LLDAS at 12 and 24 months after index. The results for this interim analysis which was conducted after all patients completed baseline visits are reported here, focusing on LLDAS.

Results: From July 08, 2023, to September 29, 2024, 400 patients were enrolled (female, 366 [91.5%]). Mean (standard deviation [SD]) age was 31.0 (12.7) years at SLE diagnosis and 36.3 (12.5) years at index, with a mean gap of 63.7 (SD, 76.2) months (**Table 1**). At baseline, 273 (68.3%) patients had a SLICC/ACR Damage Index (SDI) of 0, 156 (39.0%) received ≤1 prior immunosuppressant, 274 (68.5%) received oral steroid ≥7.5 mg/d, 6 (1.5%) had a disease duration of < 2 years, and mean SLEDAI-2K score was 10.2 (SD, 5.9). By data cut-off (October 31, 2024), 76 (19.0%) patients completed a 12-month follow-up and 22 (5.5%) withdrew. Thirty-eight (9.5%) patients received belimumab consecutively for ≥12 months

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and Baseline Characteristics

Characteristics	Patients (N=400)
Female, n (%)	366 (91.5)
Mean (SD) age at diagnosis, years	31.0 (12.7)
Mean (SD) age at belimumab initiation, years	36.3 (12.5)
Mean (SD) time since first SLE diagnosis, months	63.7 (76.2)
SDI=0, n (%)	273 (68.3)
Disease duration <2 years, n (%)	6 (1.5)
≤1 prior immunosuppressant, n (%)	156 (39.0)
Oral concomitant steroid ≥7.5 mg/d, n (%)	274 (68.5)
Mean (SD) SLEDAI-2K score	10.2 (5.9)
Employed, n (%)	176 (44.0)
Recorded medical history, n (%)	
Lupus nephritis	151 (37.8)
Anemia	73 (18.3)
Leukopenia	22 (5.5)
Thrombocytopenia	21 (5.3)

Abbreviations: SD, standard deviation; SDI, SLICC/ACR Damage Index; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC/ACR, Systemic Lupus International Collaborating Clinics/American College of Rheumatology.

Table 2. Summary of Efficacy Results

Efficacy measure	n (%, [95% CI*])
LLDAS attainment	
Baseline (N=394)	34 (8.6, [6.1, 11.9])
Month 3 (N=269)	50 (18.6, [14.1, 23.8])
Month 6 (N=182)	66 (36.3, [29.3, 43.7])
SLEDAI-2K: a reduction of ≥4 points from baseline	
Month 3 (N=142)	138 (97.2, [92.9, 99.2])
Month 6 (N=109)	105 (96.3, [90.9, 99.0])
FACIT-F: total score >34 (i.e. no significant fatigue)	
Baseline (N=177)	129 (72.9)
Month 3 (N=270)	212 (78.5)
Month 6 (N=213)	183 (85.9)
High† anti-dsDNA antibodies	
Baseline (N=359)	233 (64.9)
Month 3 (N=244)	113 (46.3)
Month 6 (N=160)	71 (44.4)
Low† C3	
Baseline (N=375)	271 (72.3)
Month 3 (N=307)	122 (39.7)
Month 6 (N=200)	66 (33.0)
Low† C4	
Baseline (N=374)	187 (50.0)
Month 3 (N=307)	62 (20.2)
Month 6 (N=201)	24 (11.9)

Note: *95% CIs were estimated using the Clopper-Pearson method. †Based on investigator assessment. **Abbreviations**: CI, confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; LLDAS, Lupus Low Disease Activity State; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

and 249 (62.3%) had a proportion of days covered of ≥0.8. The proportion of patients achieving LLDAS progressively increased from 8.6% (34/394) at baseline (treatment initiation) to 18.6% (50/269) at Month 3 and 36.3% (66/182) at Month 6 following belimumab initiation. At Month 3, 97.2% (138/142) of patients achieved a reduction of ≥4 points in SLEDAI-2K from baseline; this trend continued at Month 6 with a proportion of 96.3% (105/109). The proportion of patients without significant fatigue, i.e., scoring >34 on the Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-F), rose from 72.9% (129/177) at baseline to 78.5% (212/270) at Month 3 and 85.9% (183/213) at Month 6. Improvements in biomarkers were observed after belimumab initiation (**Table 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The interim results of RELIABLE demonstrated that belimumab reduces disease activity, evidenced by increased rates of LLDAS attainment, along with improved biomarkers and patient-reported outcomes, within 6 months after belimumab initiation among Chinese SLE patients from real-world settings. These findings are clinically important due to the large and diverse patient population from 14 sites across China. Long-term follow-up is expected to further demonstrate enhanced clinical outcomes and improved quality of life following belimumab initiation and to enrich the clinical, real-world, and long-term evidence for belimumab in China.

Disclosure: Z. Zhang: AbbVie/Abbott, 1, 6, Amgen, 6, BMS, 1, Eisai, 5, 6, Eli Lilly, 6, GSK, 6, Novartis, 6, Rongchang Pharmaceutials, 6, Xiansheng Pharmaceutials, 6; **S. Liu**: Boehringer-Ingelheim, 2, 6, GSK, 2, 6, Roche, 2, 6; **M. Yang**: AbbVie, 6, BMS, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, GSK, 6, Johnson & Jonhson, 6, Novartis, 6, Pfizer, 6, Roche, 6; **Y. Li**: None; **Q. Yu**: AbbVie, 6, BMS, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, GSK, 6, Johnson & Johnson, 6, Novartis, 6, Pfizer, 6, Roche, 6; **X. Duan**: None; **Q. Shu**: GSK, 2; **Q. Xie**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GSK, 5, 6, Novartis, 6; **Y. Chen**: GSK, 2; **D. Ou**: AbbVie, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, GSK, 6, Novartis, 6, Pfizer, 6; **L. He**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GSK, 5, 6, Novartis, 6, Qilu Pharmaceutical, 6; **H. Li**: AbbVie, 1, 6, Boehringer-Ingelheim, 1, 6, Eli Lilly, 1, 6, GSK, 1, 6, Novartis, 1, 6, Pfizer, 1, 6; **P. Yang**: Eli Lilly, 6, GSK, 6, Novartis, 6, Pfizer, 6, Roche, 6; **J. Li**: None; **T. Yan**: GSK, 3; **X. He**: GSK, 3; **D. Moldaver**: GSK, 3, 8; **C. O'Shea**: GSK, 12, 3; **L. Fan**: GSK, 3.

Abstract Number: 0650

Obinutuzumab Demonstrates Steroid-Sparing Effects and Consistent Benefit In Patients with Lupus Nephritis When Using Multiple Primary Endpoint Definitions: A Secondary Analysis of Phase III Trial Results

Brad Rovin[1], Jay Garg[2], Richard Furie[3], Rachel Jones[4], Amit Saxena[5], Pasquale Esposito[6], Elsa Martins[7], Claire Petry[7], Nicolas Frey[7], Bongin Yoo[2], Imran Hassan[8], Thomas Schindler[7], Theodore Omachi[9], William Pendergraft[2], Mittermayer Santiago[10], Gustavo Aroca Martínez[11] and Ana Malvar[12], [1]The Ohio State University, Columbus, OH, [2]Genentech, Inc., South San Francisco, CA, [3]Division of Rheumatology, Northwell Health, Great Neck, NY, [4]Renal Medicine, Cambridge University Hospitals, Cambridge, England, United Kingdom, [5]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [6]Clinica Nefrologica, Dialisi, Trapianto, Department of Internal Medicine, University of Genoa and IRCCS Ospedale Policlinico San Martino, Genova, Italy, [7]F. Hoffmann-La Roche Ltd, Basel, Switzerland, [8]Hoffmann-La Roche Ltd, Mississauga, ON, Canada, [9]Genentech, Inc., South San Francisco, [10]Bahiana School of Medicine and Public Health and UFBA, Federal University of Bahia, and Clínica SER da Bahia, Salvador, Bahia, Brazil, [11]Universidad Simón Bolívar, Barranquilla, Colombia y Clínica de la Costa, Barranquilla, Colombia, [12]Organización Médica de Investigación, Buenos Aires, Argentina

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The Phase III REGENCY study (NCT04221477) demonstrated superiority of obinutuzumab (OBI) over placebo (PBO) in achieving complete renal response (CRR) at Week 76 when added to standard therapy (ST) of mycophenolate mofetil (MMF) plus glucocorticoids in patients with active lupus nephritis (LN).

Improvement or stabilization of kidney function and improvement of proteinuria are commonly included in the definitions of complete response in recent LN clinical studies, but there is no standardized definition of the CRR endpoint.

In these post hoc analyses, we evaluated i) the effect of OBI+ST vs PBO+ST across different renal response definitions used in recent studies, ii) the efficacy of OBI+ST vs PBO+ST on each component included in the REGENCY CRR definition, and iii) the oral prednisone intake over time between the two treatment groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: REGENCY, BLISS-LN and AURORA-1 renal response endpoint definitions were used for analysis of the REGENCY dataset at Week 76. Endpoint measure definitions are in **Table 1**. The Cochran–Mantel–Haenszel test statistic stratified by the IxRS stratification factors, region and race, was used for the two treatment comparisons. All patients met ACR criteria for SLE and had biopsy-proven active LN. As part of ST, all patients received oral prednisone (or equivalent) and followed a standardized tapering schedule to achieve a target dose of 5 mg/day (or equivalent) by study Week 24.

Results: In the OBI+ST (n=135) and PBO+ST groups (n=136), respectively, 46.4% and 33.1% of patients achieved CRR at Week 76 (adjusted difference 13.4%, 95% CI, 2.0 to 24.8%; *P*=0.0232). The proportions of patients at Week 76 achieving i) a modified BLISS-LN primary efficacy renal response were 51.8% and 39.7% (adjusted difference: 12.1%, 95% CI, 0.5 to 23.8%; *P*=0.0432); ii) a modified BLISS-LN CRR were 48.7% and 33.1% (adjusted difference: 15.7%, 95% CI, 4.3 to 27.2%; *P*=0.0084); iii) a modified AURORA-1 CRR were 48.7% and 33.8% (adjusted difference: 15.0%, 95% CI, 3.6 to 26.5%; *P*=0.0117) (**Figure 1**).

In REGENCY, the proportions of patients achieving the individual components of CRR at Week 76 were numerically higher in the OBI arm compared with the PBO arm for all three components (UPCR < 0.5 g/g: 47.4% vs 36.0%; eGFR ≥85% of baseline: 83.7% vs 75.7%; no occurrence of intercurrent events: 88.9% vs 75.0% for OBI+ST and PBO+ST, respectively). In both arms, the main reasons for not attaining CRR were a UPCR ≥0.5 or an eGFR < 85% of baseline (54.8% OBI+ST vs 65.4% PBO+ST).

The mean daily prednisone intake was consistently lower in patients in the OBI arm compared with the PBO arm from Week 24-76, although the 95% CI overlapped at some intermediate visits (**Figure 2**). The proportions of patients achieving a daily prednisone (or equivalent) dose of ≤5 mg/day were consistently higher in the OBI vs PBO arm from Week 36. This reached a 10-percentage point absolute difference from Week 64-76 (78.5% vs 68.4% for OBI+ST vs PBO+ST, respectively; adjusted difference (95% CI): 10.1% (–0.5 to 20.4), *P*=0.0589).

Conclusion: In a post hoc analysis of the REGENCY trial outcomes, OBI showed consistent benefit across various patient subgroups, utilizing multiple alternative definitions of CRR, and also exhibited steroid-sparing properties.

Table 1. Renal Response Definitions

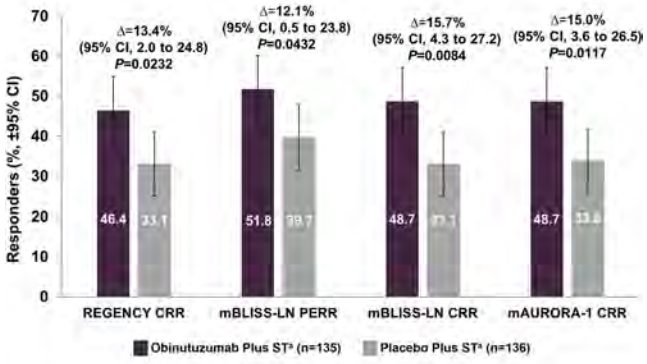
Renal Response	Definition
REGENCY CRR	• eGFR ≥85% of baseline eGFR • UPCR <0.5 • No rescue therapy, treatment failure, death or study withdrawal
Modified BLISS-LN PERR[a]	• eGFR ≥80% (no worse than 20%) of baseline eGFR or eGFR ≥60 mL/min/1.73 m² • UPCR ≤0.7 • No rescue therapy, treatment failure, death or study withdrawal
Modified BLISS-LN CRR[b]	• eGFR >90% of baseline eGFR or eGFR ≥90 mL/min/1.73 m² • UPCR <0.5 • No rescue therapy, treatment failure, death or study withdrawal
Modified AURORA-1 CRR[c]	• eGFR ≥60 mL/min/1.73 m² or no decrease from baseline in eGFR of >20% • UPCR ≤0.5 • No rescue therapy, treatment failure, death or study withdrawal • No more than 10 mg prednisone equivalent per day for 3 or more consecutive days or for 7 or more days from Week 64 through Week 76

CRR, complete renal response; eGFR, estimated glomerular filtration rate; LN, lupus nephritis; PERR, primary efficacy renal response; UPCR, urine protein-to-creatinine ratio.

[a]The original primary endpoint at Week 104 was a PERR (a UPCR of ≤0.7, an eGFR ≥20% below the value before the renal flare [preflare value] or ≥60 mL/min/1.73 m² of body surface area, and no use of rescue therapy); [b]The original major secondary endpoint at Week 104 was a CRR (a ratio of UPCR of <0.5, an eGFR that was ≥10% below the preflare value or ≥90 mL/min/1.73 m², and no use of rescue therapy); [c]The original primary endpoint at Week 52 was CRR defined as a composite of UPCR of ≤0.5 mg/mg, stable renal function (defined as eGFR ≥60 mL/min/1.73 m² or no confirmed decrease from baseline in eGFR of >20%), no administration of rescue medication and no more than 10 mg prednisone equivalent per day for 3 or more consecutive days or for 7 or more days during Weeks 44 through 52, just before the primary endpoint assessment.

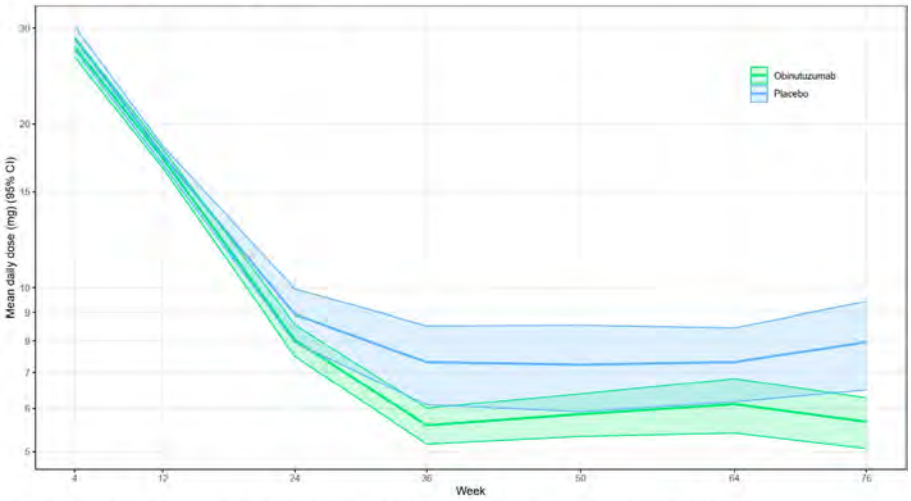
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Proportion of Patients Achieving Renal Responses at Week 76 According to Different Endpoints Across the REGENCY, AURORA-1 and BLISS-LN Studies Using REGENCY Dataset



CI, confidence interval; CRR, complete renal response; LN, lupus nephritis; m, modified; MMF, mycophenolate mofetil; PERR, primary efficacy renal response; ST, standard therapy.
[a]ST consisting of MMF plus glucocorticoids.

Figure 2: Mean Daily Dose of Prednisone for Patients Treated With Obinutuzumab or Placebo Plus Standard Therapy



Y axis is on a logarithmic scale. Solid lines represent the mean, shaded areas represent the 95% CI.
Only oral doses were considered. For each patient, the individual corticosteroid prednisone equivalent dose was computed (no dose=0 mg). The individual mean daily dose was then calculated between 2 consecutive visit weeks:
[0-4 Weeks], [4-12 Weeks], [12-14 Weeks], [24-36 Weeks], [36-50 Weeks], [50-64 Weeks], [64-76 Weeks].
Then in each treatment arm, the mean daily dose was calculated between these consecutive visit weeks. Week 4 value corresponds to the mean daily dose between actual Weeks 0 (Day 1) and 4 (Day 28); Week 12 value corresponds to the mean daily dose between actual Weeks 4 (Day 28) and 12 (Day 84) etc.

CI, confidence interval.

Disclosure: B. Rovin: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Garg**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **R. Jones**: CSL Vifor, 2, 5, F. Hoffman-La Roche Ltd, 2, 5, GlaxoSmithKline, 2, 5; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **P. Esposito**: F. Hoffmann-La Roche Ltd, 1, Sanofi, 1; **E. Martins**: F. Hoffman-La Roche Ltd, 3; **C. Petry**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **N. Frey**: F. Hoffman-La Roche Ltd, 3; **B. Yoo**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3, GlaxoSmithKlein(GSK), 12, Shareholder; **I. Hassan**: F. Hoffmann-La Roche Ltd, 3; **T. Schindler**: F. Hoffman-La

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Roche Ltd, 3, 12, Shareholder; **T. Omachi**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **M. Santiago**: None; **G. Aroca Martínez**: None; **A. Malvar**: Bristol-Myers Squibb(BMS), 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Kezar, 2, Novartis, 2, Pfizer, 2.

Abstract Number: 0651

The ERβ Agonist, OSU-ERβ-012, Suppresses Systemic, Kidney and Heart Inflammation in a Chimeric Mouse Model of Systemic Lupus Erythematosus

Braden Zeno[1], Tim Alexandrov[2], Hongyu Yuan[3], Shane Bruckner[3] and Wael Jarjour[2], [1]Ohio State University, upper arlington, OH, [2]The Ohio State University, Columbus, OH, [3]OSU, Columbus, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

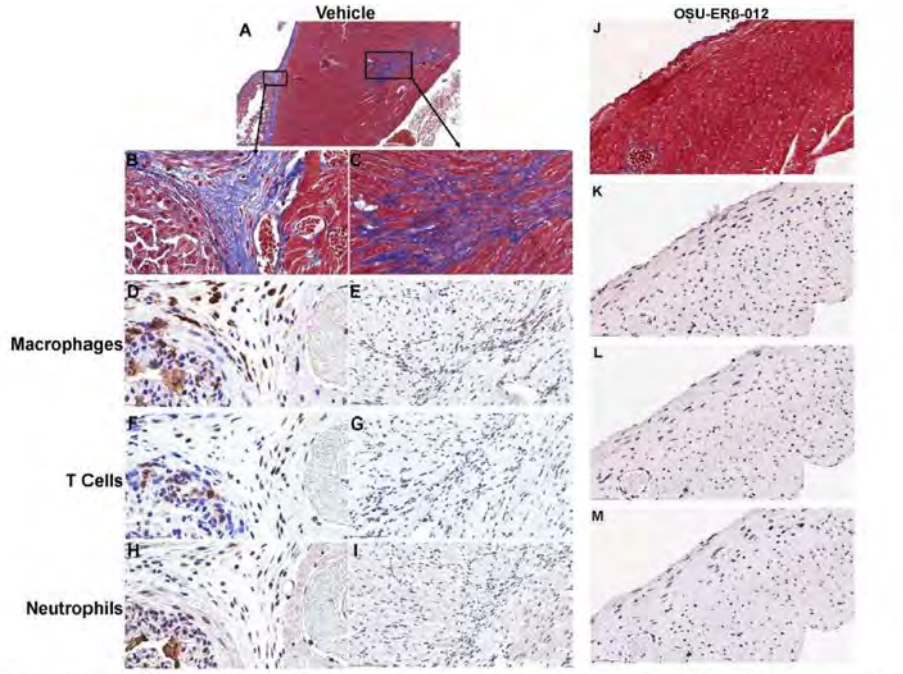
Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that causes inflammation in many of the body's tissues, including the skin, joints, lungs, kidneys and heart. This inflammation causes damage to these tissues and produces significant mortality, with most complications of the disease involving direct effects on these organs. SLE affects young women between the ages of 15 and 45 years at a 9:1 rate as compared to men. The etiology is complex and remains elusive, however the susceptibility of women during the years in which estrogen levels are at their highest suggests a significant and critical contribution to the development of SLE. Estrogens are known to have pleiotropic effects on the immune system which is mediated through either estrogen receptor α (ERα), estrogen receptor β (ERβ) or the cell surface G-protein coupled receptor GPER1. ERα has been studied extensively in this context, however ERβ and GPER1 have received much less attention. Previously, our group and others have shown that ERα carrying immune cells are mediators of proinflammatory effects of estrogen more so than cells that lack this receptor. In the pursuit of a drug that is tailored to have a favorable selective estrogenic effect, the OSU Drug Development Institute discovered a novel carborane-based selective estrogen receptor modulator (SERM), OSU-ERβ-012. This ERβ agonist exhibits potent binding of human ERβ (Ki = 2.0 nM) and functional selectivity for ERβ over ERα of at least 200-fold. The work presented herein describes the utility of OSU-ERβ-012 in treating SLE in a humanized mouse model of the disease.

Methods: PBMC isolated from patients with active SLE were adoptively transferred into NSG mice and allowed to expand in vivo for one week. The mice were divided into 3 cohorts receiving either vehicle control, prednisone or OSU-ERβ-012 via daily oral gavage for five weeks. Blood samples were taken at baseline, 3 and 5 weeks. Serum was analyzed for circulating cytokines using the MSD human V-PLEX Proinflammatory Panel. At 5 weeks, mice were euthanized, kidneys and hearts were harvested and processed for H&E, Masson's Trichrome and IHC histology. Lupus patient PBMCs were isolated and stimulated *in vitro* under various conditions and then flow cytometry was used to identify specific cell types affected by OSU-ERβ-012.

Results: OSU-ERβ-012 was as effective as prednisone in suppressing glomerular inflammation and more effective at inhibiting inflammation of the heart. More specifically, the ERβ agonist was superior to prednisone at inhibiting pericarditis, myocarditis and cardiac fibrosis. OSU-ERβ-012 demonstrated effectiveness in suppressing pro-inflammatory cytokines. The in vitro effect of OSU-ERβ-012 confirmed the suppression of IFNγ and TNFα and revealed the cell type specific effects of the drug.

Conclusion: OSU-ERβ-012 is an effective inhibitor of the SLE inflammatory process and warrants additional study as a potential therapeutic in patients with SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Lupus humanized NSG mouse hearts manifested both pericarditis and myocarditis which was inhibited by OSU-ERβ-012. **(A-I)** Representative images of a vehicle treated mouse heart section stained with Masson's Trichrome **(A)** demonstrating both pericardial and myocardial fibrosis (magnification = 5X, scale bar = 500μm). **(B, D, F & H)** Zoomed in images of the left box in **A**, detailing the pericardial fibrosis via Masson's Trichrome stain **(B)** and the presence of macrophages **(D)**, T cells **(F)** and Neutrophils **(H)** (magnification = 40X, scale bar = 50μm). **(C, E, G, I)** Zoomed in images of the right box in **A**, detailing the myocardial fibrosis via Masson's Trichrome stain **(C)** and the presence of macrophages **(E)**. T cells **(F)** and Neutrophils **(H)** were absent in the myocardial fibrotic lesion (magnification = 20X, scale bar = 100μm). **(J-M)** Representative images of OSU-ERβ-012 treated mouse heart sections. **(J)** Masson's trichrome stain showing the lack of fibrosis, **(K)** showing the lack of macrophages, **(L)** T cells and **(M)** neutrophils.

Disclosure: B. Zeno: None; **T. Alexandrov**: None; **H. Yuan**: None; **S. Bruckner**: None; **W. Jarjour**: None.

Abstract Number: 0652

Evolution and Readiness: Preparing for Cell Therapy in Lupus Trials, A LuCIN Network Evaluation

Brandon Jackson[1], Saira Sheikh[2], Roberto Caricchio[3], Taylor Irons[4], Maria Dall'Era[5], Amit Saxena[6], Alfred Kim[7], Jose Rubio[8], Sasha Bernatsky[9], David Goddard[10], Fotios Koumpouras[11], Aimee Williams[12], Maya Merrell[13], Jennifer Meriwether[14] and Stacie Bell[15], [1]Lupus Therapeutics, Miami, FL, [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]University of Massachusetts Chan Medical School, Worcester, MA, [4]Lupus Therapeutics, Houston, TX, [5]Division of Rheumatology, University of California, San Francisco, CA, [6]NYU Grossman School of Medicine, New York, NY, [7]Washington University School of Medicine, St. Louis, MO, [8]University of Alabama at Birmingham, Hoover, AL, [9]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [10]NYU Langone Grossman SOM, Brooklyn, NY, [11]Yale School of Medicine, New Haven, CT, [12]Lupus Therapeutics, Raleigh, NC, [13]Lupus Therapeutics, Charleston, SC, [14]Lupus Therapeutics, Westminster, CO, [15]Lupus Therapeutics, Lakewood, CO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus Therapeutics (LT), the clinical affiliate of the Lupus Research Alliance, oversees the premier North American Lupus Clinical Investigators Network (LuCIN). As cell therapy emerges as a potentially transformative, but operationally demanding modality in lupus trials, understanding site readiness and barriers is essential. To address the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

anticipated expansion of cell therapy trial activity, an annual network-wide survey was conducted to assess the capability and requirements necessary for sites to engage in cell therapy clinical studies.

Methods: Using an internet-based platform, an annual survey was administered between Dec 17, 2024, and Feb13, 2025; a total of 60 LuCIN sites submitted multiple team responses. The survey asked about institutional infrastructure, interdepartmental collaboration, readiness for various cell therapy modalities, and educational/training priorities.

Results: Of the 124 respondents, enthusiasm for cell therapy was high: 60% expressed a preference to participate in Phase 2 trials while 35% in Phase 1 cell therapy trials. Chimeric antigen receptor T-cell (CAR-T) was the preferred modality (75%) followed by allogenic CAR-Natural Killer cell (44%) or other allogeneic approaches (40%) **Table 1**. Most sites (≥74%) reported the presence of core inpatient infrastructure (e.g., apheresis, drug storage, certified infusion providers, SOPs, toxicity monitoring), 62% had outpatient infusion capabilities, highlighting significant network readiness and evolution to adopt cell therapy for further study in lupus. Interdepartmental collaboration was active, as 66% reported partnerships with oncology/hematology and 59% seeking training to enable further collaboration. The most common operational challenges were logistical hurdles (74%), competing clinical studies (58%), and limited shared staffing capacity (39%). Meanwhile, 48% of respondents noted there are "too many" cell therapy opportunities. Investment in cell therapy capabilities, while increasing, was uneven where 59% reported enhanced multidisciplinary collaboration, 31% on additional staff or expertise and 20% reported new infrastructure, but 31% reported no new investments. Educational gaps were present as 76% requested new patient education materials, including CAR-T, with a priority on safety monitoring (66%), recruitment and patient

Table 1: Trial Preferences and Cell Therapy Readiness Across LuCIN Sites

Table 1: Trial Preferences and Cell Therapy Readiness Across LuCIN Sites

Total Investigator and Coordinator Respondents (N=124) 60 LuCIN Centers Surveyed		%
Primary Role		
	Investigator	54
	Study Coordinator	32
	Research Director/Manager	14
What type of clinical trial would you prefer to take on in 2025? *		
	Cell Therapy Phase 1 clinical trials	35
	Cell Therapy Phase 2 clinical trials	60
What type of cell therapy studies are you currently engaged or interested in? *		
	CAR NK	44
	CAR-T	75
	Stem cells	14
	Allogeneic	40
	Autologous	31
	T-cell engagers	33
Do you partner with any colleagues from the following departments within your institution?		
	Oncology/Hematology	66
Which educational topics would your site's team members be interested in?		
	Cell therapy and partnership between rheumatologists and oncologists	59
Are the following available at your site to support cell therapy trials? *		
	Access to apheresis equipment/staff	82
	Cell processing laboratory	81
	Ability to receive and store cellular therapy drug product, e.g., liquid nitrogen shipping dewars, vapor-phase liquid nitrogen storage units	84
	Experience in administration of lymphodepleting chemotherapy	80
	Cell therapy experienced provider certified for infusion/CAR-T	80
	SOPs for cell therapy administration and management	75
	Outpatient cell infusion center or equivalent	62
	Inpatient administration of cell therapies and inpatient monitoring for potential related toxicities	77
	Access to multi-disciplinary subspecialty for management of cell therapy toxicities, i.e. access to an ICU	79
	Ability to monitor and manage cytokine release syndrome (CRS), immune effector cell associated neurotoxicity syndrome (ICANS), hematologic cytopenia's, immune-mediated adverse events	79
	On-site availability of tocilizumab (Actemra) for management of CRS	79
	Recovery support (e.g., providers for frequent follow-up, medications, care coordination)	74
*Selection of more than 1 response option were allowed		

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Barriers, Investments, and Educational Needs for Cell Therapy Trials

Table 2: Barriers, Investments, and Educational Needs for Cell Therapy Trials

Total Investigator and Coordinator Respondents (N=124) 60 LuCIN Centers Surveyed		%
What challenges persist for cell therapy trials at your site *		
	Logistical reasons	74
	Lack expertise	14
	Lack shared resources or teams (Onc/Hem) staffing	40
	Monetary	31
	Trial number limited by institution	11
	Limited capacity for enrollment by institution	24
	Competing indications	30
	Prefer later phase	22
What are some of the challenges when partnering with Pharma/CROs?		
	Too many cell therapy opportunities	48
What ways have your site/institution invested in enhancing cell therapy capabilities in the last year specifically for lupus or in rheumatology? *		
	Increased monetary support	12
	New Infrastructure	20
	Additional Staffing/expertise	31
	Enhanced multi-disciplinary collaboration	59
	None	31
What topics for educational materials do you believe would be of most benefit to help support patient education at your site?		
	New and upcoming treatments (such as CAR-T)	76
What specific educational or training areas related to cell therapy would you like offered to you? *		
	Scientific concepts	52
	Clinical protocol design and assessment	61
	Safety monitoring	66
	Investigational product preparation, storage and use	44
	Patient recruitment and education	65
Would your site prefer cell therapy educational opportunities for any of the following audiences? *		
	Providers	56
	Patients	62
	Research staff	64
	None	17
*Selection of more than 1 response option were allowed		

education (64%), clinical protocol design (61%), among others (**Table 2**). Respondents identified target audiences of research staff (64%), patients (62%), and providers (56%) for cell therapy education opportunities.

Conclusion: Understanding readiness for cell therapy in lupus is critical to build a network of capable cell-therapy trialists for lupus and beyond. Using this knowledge, strategic investment in operational planning, capacity building and tailored education efforts for staff, patients, and providers will provide the research community support for the safe, effective and scalable integration of cell therapy in lupus trials. Careful attention to resource allocation, multidisciplinary partnerships and trial prioritization will be essential to avoid saturation and sustain momentum across LuCIN sites.

Disclosure: B. Jackson: None; **S. Sheikh**: AstraZeneca, 1, Aurinia Pharmaceuticals, 5, Biogen, 1, Cabaletta Bio, 5, GlaxoSmithKlein(GSK), 1; **R. Caricchio**: Abbvie, 1, Cabaletta, 5, GlaxoSmithKlein(GSK), 1, Kyverna, 5, Novartis, 1; **T. Irons**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **A. Saxena**: AbbVie/Abbott, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, 6, Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 5, Synthekine, 1, 2, UCB, 1, 6; **A. Kim**: Abbvie, 2, AstraZeneca, 2, 5, Atara Bio, 2, Bristol Myers Squibb, 5, Cargo Therapeutics, 2, CRISPR Therapeutics, 1, 5, Exagen Diagnostics, 2, 6, Genentech/Roche, 2, GlaxoSmithKline, 2, 6, Hinge Bio, 2, Invivyd, 2, Kypha, Inc., 2, 10, Novartis, 5, Zenas BioPharma, 2; **J. Rubio**: None; **S. Bernatsky**: None; **D. Goddard**: UCB, 5; **F. Koumpouras**: AbbVie/Abbott, 5, Adicet Bio, 2, AstraZeneca, 1, 2, 5, 6, Atara Bio, 2, Bristol-Myers Squibb(BMS), 5, 12, Clinical Trial, Cabaletta Bio, 2, Gilead, 12, Clinical Trial, GlaxoSmithKlein(GSK), 2, 5, ITN, 12, Clinical Trial, LRA/LuCIN, 5, Miltenyi Bio, 2, NIH, 5, Novartis, 2, RRF, 5, UCB, 12, Clinical Trial; **A. Williams**: None; **M. Merrell**: None; **J. Meriwether**: None; **S. Bell**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0653

In Vitro Pharmacological Profile of GLPG3667 Suggests Differentiation from the TYK2 Inhibitors Deucravacitinib and Zasocitinib at Their Clinical Dose Regimens

May-Linda Lepage[1], Patrick Nolain[1], Céline Cottereaux[1], Emilie Lagoutte[1], Justine Dao[1], Adrien Cosson[1], Laetitia Furio[1], Willem Hettema[2], **Chantal Tasset**[3], Roland Blanqué[1], Isabelle Parent[1] and René Galien[1], [1]Galapagos SASU, Paris, France, [2]Galapagos B.V., Leiden, Netherlands, [3]Galapagos NV, Mechelen, Belgium

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Tyrosine kinase 2 (TYK2), a Janus kinase (JAK) family member, is attracting a lot of interest as a new target to treat patients with autoimmune and inflammatory diseases, including inflammatory bowel diseases, and several inhibitors are currently in clinical development. *In vitro* pharmacological profiling of TYK2 inhibitors has been employed to evaluate potency and selectivity; however, such data are best viewed in relation to clinical exposure levels. We compared expected levels of inhibition of TYK2-dependent and -independent pathways for deucravacitinib, zasocitinib and GLPG3667 at their respective clinical dose regimens and demonstrate that relevant differences exist between these compounds.

Methods: Potency of the TYK2 inhibitors was compared for TYK2-dependent pathways (IFNα, IL-12, IL-23), TYK2-independent pathways (IL-6, IL-2, GM-CSF) and the anti-inflammatory IL-10 pathway in *in vitro* human whole blood assays using STAT phosphorylation (flow cytometry) and cytokine release (ELISA) measures. Sigmoidal E_{max} models were fitted to the concentration–inhibition data from healthy donors to estimate IC_{50}, E_{max} and Hill slope for each assay and compound. The obtained relationships were subsequently coupled to the clinical pharmacokinetic (PK) profiles of the compounds (such as C_{avg}, C_{max} and C_t from population PK model for GLPG3667 and published PK metrics for deucravacitinib and zasocitinib) to estimate the level of inhibition of the various pathways at clinically relevant dose regimens.

Results: Human whole blood assays performed for various JAK pathways demonstrated that all TYK2 inhibitors display selectivity for TYK2 over the JAK1–3 family members, with zasocitinib being the most selective. At exposure levels associated with its clinical dose of 150 mg once daily, GLPG3667 showed inhibition of the IFNα, and IL-23 pathways, comparable to the expected inhibition for deucravacitinib at its clinical dose regimens, without a measurable impact on TYK2-independent pathways. Inhibition of the IL-12 pathway was more pronounced for GLPG3667 than for deucravacitinib. Zasocitinib showed the most sustained inhibition of TYK2-dependent pathways. GLPG3667 showed no measurable inhibition of IL-10-mediated signalling up to the highest concentration tested (~10-fold above clinical concentrations) in monocytes, $CD4^+$ T cells and $CD19^+$ B cells, while strong inhibition was observed with deucravacitinib and overall zasocitinib at concentrations corresponding to the respective clinical dose regimens.

Conclusion: At concentrations corresponding to its highest anticipated clinical dose, GLPG3667 shows selective inhibition of TYK2-mediated signalling, with a level of inhibition similar to deucravacitinib clinical dose regimens. While GLPG3667 did not show any impact on IL-10-mediated signalling, inhibition of this anti-inflammatory pathway is expected for the allosteric TYK2 inhibitors at their clinical exposure levels.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Lepage: Galapagos SASU, 3, NovAliX, 3; **P. Nolain**: Galapagos SASU, 3, Novo Nordisk, 3; **C. Cottereaux**: Galapagos SASU, 3, NovAliX, 3; **E. Lagoutte**: Calida Therapeutics, 3, Galapagos SASU, 3; **J. Dao**: Antabio, 3, Galapagos SASU, 3; **A. Cosson**: Galapagos SASU, 3, NovAliX, 3; **L. Furio**: Calida Therapeutics, 3, Galapagos SASU, 3; **W. Hettema**: Argenx, 3, Galapagos BV, 3; **C. Tasset**: Galapagos NV, 3; **R. Blanqué**: Galapagos SASU, 3, NovAliX, 3; **I. Parent**: Galapagos SASU, 3, NovAliX, 3; **R. Galien**: Galapagos SASU, 3.

Abstract Number: 0654

Obinutuzumab Shows Promise in Lupus Nephritis Regardless of Baseline Serological Markers: An Exploratory Post Hoc Analysis of a Phase II Trial

Ed Vital[1], Benni Vargas[2], Julie Rae[2], Tracey Wang[3], Jason Hackney[2], Cary Looney[4], William Pendergraft[2], Liz Lightstone[5], Brad Rovin[6], Richard Furie[7] and Harini Raghu[2], [1]University of Leeds, Leeds, England, United Kingdom, [2]Genentech, Inc., South San Francisco, CA, [3]Hoffmann-La Roche Ltd, Missssauga, ON, Canada, [4]F. Hoffmann-La Roche Ltd, Basel, Switzerland, [5]Department of Immunology and Inflammation, Faculty of Medicine, Imperial College London, London, England, United Kingdom, [6]The Ohio State University, Columbus, OH, [7]Division of Rheumatology, Northwell Health, Great Neck, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is characterized by kidney inflammation. B cells play a central role in LN pathogenesis and type I interferon (IFN-I) pathway activation amplifies inflammation. Obinutuzumab, a glycoengineered, type II CD20 antibody demonstrated efficacy in patients (pts) with LN when added to standard therapy in the Phase II NOBILITY (NCT02550652) and Phase III REGENCY (NCT04221477) trials.

This study explored the efficacy of obinutuzumab vs placebo (plus standard therapy) in various serological biomarker subgroups of pts with LN from the NOBILITY trial.

Methods: Pts received obinutuzumab or placebo at Weeks 0, 2, 24 and 26, plus standard therapy of mycophenolate mofetil (MMF) plus glucocorticoids. All pts met ACR SLE classification criteria and had biopsy-proven proliferative LN. Whole blood from participants (88/126 pts) was used for bulk RNA sequencing. Baseline IFN-I status (high [hi] vs low [lo]) was determined in samples from healthy volunteers, using previously published gene signatures from the ROSE (NCT00962832) and TULIP (NCT02446912) trials. Cut-off for IFN-I status was determined using the median +2x median absolute deviation of age- and sex-matched healthy controls. Anti-dsDNA, anti-nuclear antibodies (ANA; SSA, SSB, RNP and Sm) and complement C3/C4

Table 1. Obinutuzumab's Impact on CRR* at Week 52 in High and Low IFN-I Subgroups

	Placebo, n=43 (CRR over total)	Obinutuzumab, n=45 (CRR over total)	OR (80% CI)	*P* value
All patients	8/43 (18.6)	18/45 (40.0)	3.08 (1.64 to 5.99)	0.02133
High IFN-I gene signature	7/36 (19.4)	16/39 (41.0)	2.94 (1.49 to 6.00)	0.0395
Low IFN-I gene signature	1/7 (14.2)	2/6 (33.3)	4.00 (0.69 to 29.44)	0.3115

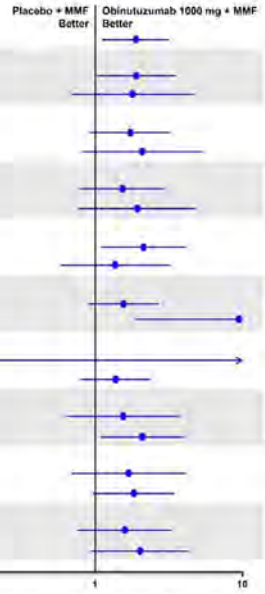
CI, confidence interval; CRR, complete renal response; HPF, high-power field; IFN, interferon; OR, odds ratio; RBC, red blood cell; ULN, upper limit of normal; UPCR, urine protein-to-creatinine ratio.

*A composite measure requiring a UPCR of <0.5, normal renal function (serum creatinine ≤ULN) without worsening of baseline serum creatinine by >15% and inactive urinary sediment (<10 RBCs/HPF without RBC casts).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. CRR at Week 52 in the Obinutuzumab and Placebo Groups Across Biomarker Subgroups of Interest in the mITT Population

Baseline risk factors	Total n	Placebo + MMF n	Placebo + MMF Responders (n)	Placebo + MMF Response (%)	Obinutuzumab 1000 mg + MMF n	Obinutuzumab 1000 mg + MMF Responders (n)	Obinutuzumab 1000 mg + MMF Response (%)	OR	80% CI
All patients	125	62	14	22.6	63	22	34.9	1.88	1.12 to 3.15
Anti-dsDNA									
Positive	88	46	10	21.7	42	14	33.3	1.90	1.02 to 3.53
Negative	37	16	4	25.0	21	8	38.1	1.79	0.69 to 4.61
C3									
Low	80	37	10	27.0	43	16	37.2	1.72	0.93 to 3.21
Normal	45	25	4	16.0	20	6	30.0	2.08	0.81 to 5.36
C4									
Low	81	44	10	22.7	37	11	29.7	1.54	0.80 to 2.97
Normal	44	18	4	22.2	26	11	42.9	1.93	0.78 to 4.78
Serologically active 1*									
Yes	75	40	9	22.5	35	13	37.1	2.12	1.10 to 4.11
No	50	22	5	22.7	28	9	32.1	1.37	0.59 to 3.19
Serologically active 2†									
Yes	111	56	13	23.2	55	17	30.9	1.55	0.89 to 2.69
No	14	6	1	16.7	8	5	62.5	9.84	1.89 to 51.24
Anti-La SSB antibodies									
Positive	16	6	0	0	10	5	50.0	≥999.99	0.00 to ≥999.99
Negative	109	56	14	25.0	53	17	32.1	1.38	0.80 to 2.37
Anti-RNA polymerase antibodies									
Positive	43	19	5	26.3	24	8	33.3	1.55	0.65 to 3.72
Negative	82	43	9	20.9	39	14	35.9	2.09	1.10 to 3.97
Smith antibodies									
Positive	40	19	5	26.3	21	8	38.1	1.69	0.70 to 4.08
Negative	85	43	9	20.9	42	14	33.3	1.83	0.97 to 3.45
Anti-Ro SSA antibodies									
Positive	58	27	8	29.6	31	12	38.7	1.58	0.76 to 3.28
Negative	67	35	6	17.1	32	10	31.2	2.01	0.95 to 4.25



There are only a few responders in the serologically active 2 and anti-La SSB-positive subgroups, thus the results from the logistic regression may not be reliable/interpretable.

Anti-dsDNA, anti-double-stranded DNA; CI, confidence interval; CRR, complete renal response; mITT, modified intention to treat; MMF, mycophenolate mofetil; OR, odds ratio.

*Defined as anti-dsDNA+ and hypocomplementemia. †Defined as anti-dsDNA+ or hypocomplementemia.

levels were assessed. Subgroup analyses were performed on baseline biomarker categories using the endpoint of Week 52 complete renal response (CRR). Odds ratios (OR) relative to placebo or MMF were estimated by logistic regression, with a significance level of α=0.2.

Results: Of 88 pts, 75 (85.2%) were categorized as IFNhi and 13 (14.8%) as IFNlo using the ROSE IFN-I gene signature. Baseline IFN-I status did not reliably predict the likelihood of achieving CRR at Week 52. At Week 52, in the IFNhi subgroup, 41% (16/39) of pts receiving obinutuzumab achieved CRR vs 19.4% (7/36) of pts receiving placebo (P< 0.2; OR [80% CI], 2.9 [1.5 to 6], **Table 1**). A statistically significant trend favoring obinutuzumab was observed in the IFNlo subgroup (33.3% [2/6] vs 14.2% (1/7); P >0.2; OR [80% CI], 3.0 [0.9 to 9.6], **Table 1**). Using the REGENCY Week 76 CRR definition and the TULIP IFN-I gene signature yielded similar results. A multivariable logistic regression analysis using treatment and baseline IFN-I status as covariates did not reveal a statistically significant association between IFN-I status and response (P=0.6221; OR [80% CI], 1.4 [0.5 to 3.64]. Across subgroups defined by baseline complement, anti-dsDNA and other autoantibodies, more CRRs were observed with obinutuzumab vs placebo, including in pts with high serological activity (**-Figure 1**). Results were generally consistent using the Week 76 REGENCY CRR definition.

Conclusion: Analyses suggest that obinutuzumab may be an effective therapy in pts with LN regardless of baseline serological biomarker status. A significant CRR benefit was observed in the IFNhi subgroup and a similar trend was seen in the IFNlo subgroup. Obinutuzumab generally demonstrated greater efficacy vs placebo across baseline serological biomarker subgroups. Whilst limited sample size restricted significance, similar ORs across subgroups suggest a consistent trend favoring obinutuzumab regardless of serological status.

Disclosure: E. Vital: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6; **B. Vargas**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech Inc., 3; **J. Rae**: F. Hoffman-La Roche Ltd,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

12, Shareholder, Genentech Inc., 3; **T. Wang**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **J. Hackney**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **C. Looney**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **L. Lightstone**: Alexion, 2, AstraZeneca, 2, F. Hoffman-La Roche Ltd, 2, GlaxoSmithKline, 2, Kezar, 2, Novartis, 2, Otsuka, 2, Pfizer, 2; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **H. Raghu**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3.

Abstract Number: 0655

Blood pressure remains elevated in patients initiating voclosporin with low baseline blood pressure: evidence from patients in routine clinical care

Eric Roberts[1], gabriela Schmajuk[2] and Jinoos Yazdany[3], [1]University of California, San Francisco, SF, CA, [2]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [3]UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Hypertension was a common adverse event in RCTs testing voclosporin, an oral calcineurin inhibitor approved in 2021 to treat lupus nephritis (LN). In these trials, increases in blood pressure (BP) were generally transitory and frequently diminished after the first 4 weeks of use. Here we characterize BP changes in real-world data.

Methods: Data came from RISE, a national registry with electronic health records from over 1100 US rheumatologists. Voclosporin use was abstracted from medication tables. All systolic and diastolic BPs from 60 days before the first order to 90 days after the last order were tabulated. Baseline BP was defined as the lowest BP before the index date (inclusive) and categorized as follows: normal < 130 mmHg AND < 80 mmHg; elevated, 130-164 mmHg OR 80-104 mmHg; and high, ≥165 mmHg OR ≥105 mmHg. Covariates included age, sex, race and ethnicity, insurance coverage, area deprivation index, BMI, smoking status, and time-varying antihypertensive drug use.

We describe patient characteristics overall and stratified by whether the patient experienced an 8 mmHg increase in systolic BP (minimum clinically important difference (MCID)) during the first year of use. We calculated the median time to a MCID within a year for both systolic and diastolic using Kaplan Meier estimates. Finally, we present mean changes in BP between baseline and the lowest BP reading in windows of 0-1, 1-2, 2-3, 3-6, 6-9, and 9-12 months after the index date.

Results: We included 287 patients: 83.6% were female, 32% were black; mean (SD) age was 41.4 (±14.1) years (Table 1). The mean systolic BP at baseline was 125.7 (±16.1)/79.2 (±10.8) (42.2% categorized as normal, 54% elevated, and 3.8% high). At baseline, 67.3% were on an antihypertensive medication.

Overall, 63.8% experienced a systolic MCID, and 49.1% a diastolic MCID. The median time to a recorded increase in systolic was 77 days (95%CI: 62-91) (Figure 1), and 134 days (95%CI: 99-198) for diastolic. The average systolic/diastolic BP change was largest in the first month for patients with normal baseline BP 13.7 (±18.6)/6.0 (±13.8), and less pronounced

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of voclosporin patients in RISE overall and stratified by experiencing an 8 mmHg increase in systolic blood pressure during the first year of use.

	Overall (N=287)		Systolic MCID				
			no (n=104)		yes (n=183)		
	N	%	N	%	N	%	p-value
Baseline blood pressure							
Systolic (mean; sd)	125.74	16.06	133.46	16.27	121.35	14.22	<0.01*
Diastolic (mean; sd)	79.22	10.83	82.55	11.14	77.33	10.2	<0.01*
Baseline hypertension category							<0.01**
Normal: <130 AND <80	121	42.16	28	23.14	93	76.86	
Elevated: 130-164 OR 80-104	155	54.01	67	43.23	88	56.77	
High: >165 OR >105	11	3.83	9	81.82	2	18.18	
Antihypertension Med use at start							0.78**
Yes	193	67.25	71	36.79	122	63.21	
No	94	32.75	33	35.11	61	64.89	
Demograhic characteristics							
Age	41.35	14.07	42.58	13.31	40.66	14.48	0.27*
Sex							0.32**
Female	240	83.62	84	35	156	65	
Male	47	16.38	20	42.55	27	57.45	
Race and Ethnicity							0.39**
Black	92	32.06	35	38.04	57	61.96	
Asian	16	5.57	5	31.25	11	68.75	
Hispanic	49	17.07	18	36.73	31	63.27	
Other/mixed	3	1.05	2	66.67	1	33.33	
Unknown	58	20.21	15	25.86	43	74.14	
White	69	24.04	29	42.03	40	57.97	
Insurance							0.67**
Private	152	52.96	57	37.5	95	62.5	
Medicaid	43	14.98	12	27.91	31	72.09	
Medicare	38	13.24	14	36.84	24	63.16	
Other	54	18.82	21	38.89	33	61.11	
ADI (n=250)	52.12	28.05	52.44	26.86	51.93	28.82	0.89*
Smoking							0.18**
Ever	43	14.98	21	48.84	22	51.16	
Never	167	58.19	57	34.13	110	65.87	
Missing	77	26.83	26	33.77	51	66.23	
BMI (n=282)	29.62	7.63	29.55	7.85	29.66	7.52	0.91*

*ANOVA
**chisquare

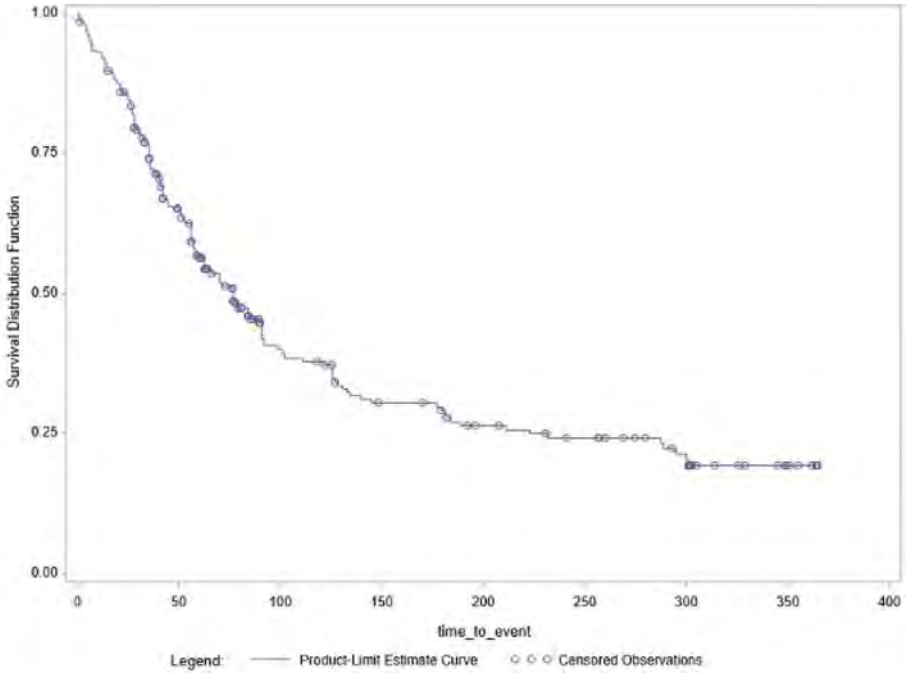


Figure 1. Kaplan Meier curve showing the time to an MCID in systolic blood pressure of 8 mmHg after initiating voclosporin.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

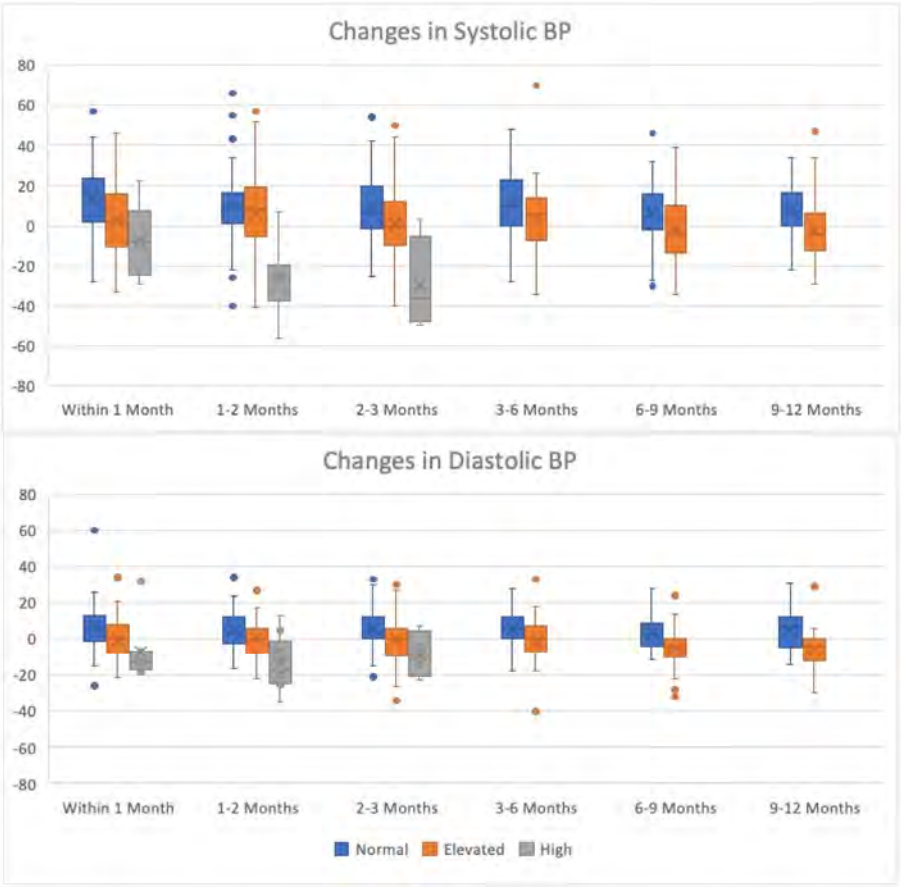


Figure 2. Box and whisker plots of mean change in systolic and diastolic blood pressure between baseline and the specified time stratified by patient's baseline hypertension category.

for those with elevated BP 2.7 (±18.8)/-0.6 (±11.2); BP decreased for those with high baseline BP -7.9 (±17.8)/-7.3 (±16.5) (Figure 2). BPs were stable over time for those with baseline normal BP whereas BPs returned to baseline levels after 6 months for patients with elevated baseline BPs. Although the sample size was small for patients with high baseline BPs we observed large decreases in BP during the first 3 months of use, likely due to the beneficial effects of voclosporin on underlying LN.

Conclusion: >50% of patients using voclosporin had a MCID in the first year of use. Increases tend to occur in the first 3 months of use and on average were larger for patients with normal baseline BPs. In contrast to findings reported from RCTs, BP increases for patients with normal baseline BPs were persistent over 12 months. Although the MCID may seem small, it has been associated with up to 20% increase in the risk of cardiovascular disease (CVD) events. The clinical significance of BP changes related to voclosporin use warrant further investigation, especially since people with LN are already at increased risk for CVD.

Disclosure: E. Roberts: None; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0656

Low-dose belimumab reduced disease flares in patients with systemic lupus erythematosus at low disease activity: a multicenter, randomized, double-blind, placebo-controlled trial

Fangfang Sun[1], Huijing Wang[1], Danting Zhang[1], Nan Shen[1], Sheng Chen[1], Tiing Li[1], Weiguo Wan[2], Shengming Dai[3] and Shuang Ye[4], [1]Renji Hospital, Shanghai, China (People's Republic), [2]Huashan Hospital, Shanghai, China (People's Republic), [3]Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China (People's Republic), [4]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: B-lymphocyte stimulator was involved in the pathogenesis of SLE. The humanized monoclonal antibody belimumab with 10mg/kg was effective for active patients. The efficacy of low-dose belimumab for prevention of disease flares in patients with SLE with low disease activity was evaluated in this randomized trial (NCT04515719).

Methods: This was a 52-week, randomized, placebo-controlled trial. Patients who have Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) scores≤6; with no A score or no more than one B score on the British Isles Lupus Assessment Group (BILAG) scale; and who are treated with prednisone ≤20mg/day at screening were enrolled and randomly assigned in a 1:1 ratio to intravenous 120mg belimumab or placebo (saline) arm on weeks 0, 2, and 4, and then every 4 weeks until 48 weeks on the basis of standard of care (SOC). The primary outcome was a composite index of severe or mild-to-moderate disease flare (SELENA-SLEDAI Flare

Table 1. Baseline characteristics of participants in two arms.

	Belimumab (n=116)	Placebo (n=115)
Age, years	35.84 (9.93)	35.50 (10.00)
Gender (%)	112 (96.6)	101 (87.8)
SLE duration, years	9.26 (12.37)	9.43 (16.01)
Laboratory results		
WBC*10^9/L	5.40 (1.74)	5.84 (1.99)
Hemoglobin, g/L	122.61 (26.44)	127.69 (15.16)
PLT*10^9/L	208.66 (78.49)	210.32 (62.89)
ALT, U/L	20.16 (15.55)	21.36 (11.65)
Creatinine, umol/L	55.94 (12.74)	61.40 (15.76)
ESR, mm/H	17.98 (13.68)	15.09 (11.13)
CRP, mg/L	2.46 (2.86)	2.98 (6.49)
anti-dsDNA, IU/ml	107.94 (132.77)	111.46 (150.37)
C3, g/L	0.81 (0.22)	0.82 (0.24)
C4, g/L	0.14 (0.08)	0.15 (0.06)
IgG, g/L	15.78 (5.48)	14.77 (5.08)
IgA, g/L	2.76 (1.29)	3.03 (1.39)
IgM, g/L	0.98 (0.83)	0.91 (0.67)
Disease activity		
PGA (0-3)	0.19 (0.21)	0.18 (0.23)
SELENA-SLEDAI score	2.71 (1.68)	2.43 (1.74)
Treatment		
Prednisone, mg/day	7.18 (4.12)	7.05 (4.65)
Hydroxychloroquine (%)	109 (94.0)	103 (89.6)
Immunosuppressants (%)	54 (46.6)	59 (51.3)
Azathioprine	7 (6.0)	4 (3.5)
Cyclosporin	2 (1.7)	5 (4.4)
Tacrolimus	5 (4.3)	4 (3.5)
Iguratimod	0 (0.0)	1 (0.9)
Leflunomide	4 (3.4)	2 (1.8)
Mycophenolate	24 (20.7)	27 (23.7)
Mycophenolate+Tacrolimus	1 (0.9)	1 (0.9)
Methotrexate	11 (9.5)	15 (13.2)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

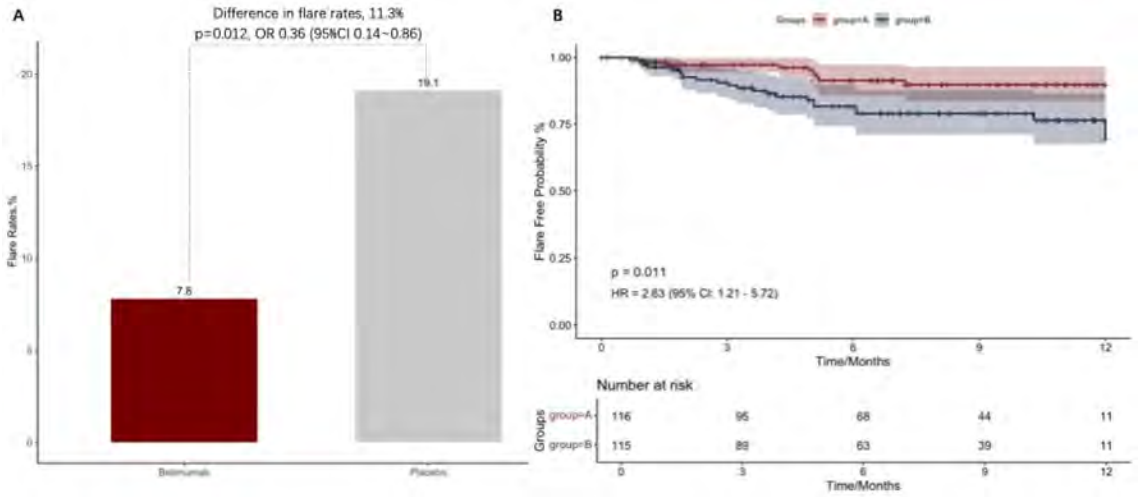


Figure 1. The difference of overall disease flares between low-dose belimumab and placebo on the basis of SOC (A). Kaplan-Meier Curves demonstrated flare-free survival of participants from two arms (B).

Index) within 52 weeks. Secondary outcomes included the percentage of severe flare, the percentage of mild-to-moderate flare, time to the first disease flare, changes in prednisone dose, SELENA-SLEDAI and safety analysis. The locked-down due to COVID-19 pandemic in Shanghai, China from April 2022 to June 2022 has greatly impacted patient recruitment and follow-up. Therefore, the trial was terminated prematurely at April 10th, 2022 when Renji Hospital, South campus was designated as a COVID-19 referral center during Shanghai locked-down.

Results: Overall, 90.5% of 116 patients receiving belimumab and 86.1% of 115 patients receiving placebo completed the study within a mean follow-up of 31.0 ± 16.1 weeks. Baseline characteristics were generally similar between treatment groups (**Table 1**). The primary endpoint was met. 7.8% (9/116) of patients receiving low-dose belimumab + SOC had disease flares within follow-up, which was significantly lower than that in patients receiving placebo + SOC, that is 19.1% (22/115) (p=0.012; difference 11.3%, OR 0.36 (95%CI 0.14∼0.86); **Figure 1A)**. Severe flares in belimumab group was only numerically lower than that in placebo group (1.7% vs 6.1%, p=0.1). Kaplan-Meier curves also demonstrated higher flare-free survival in patients receiving belimumab plus SOC (p=0.011, HR 2.63, 95% CI (1.21-5.72)) (**Figure 1B**). Glucocorticoid-sparing effects were observed in two groups (changes in prednisone from baseline to last visit, 1.64 ± 10.24 vs 0.91 ± 7.48, p=0.055). SELENA-SLEDAI was reduced by 0.62 ± 2.17 in belimumab group, however increased

Table 2. Adverse events.

	Belimumab (n=116)	Placebo (n=115)
Adverse event (n≥1)	71 (61.2%)	53 (64.3%)
Severe adverse event (n≥1)	4 (3.4%)	6 (5.2%)
Discontinuations due to adverse events	3 (2.6%)	6 (5.2%)
Infections	45 (38.8%)	41 (35.7%)
Upper respiratory infections	29 (25.0%)	25 (21.7%)
Skin infections	3 (2.6%)	3 (2.6%)
Gastroenteritis	7 (6.0%)	8 (7.0%)
Urogenital tract infection	6 (5.2%)	7 (6.1%)
Gingivitis	2 (1.7%)	1 (0.9%)
Pneumonia	3 (2.6%)	2 (1.7%)
Admission to hospital due to infections	3 (2.6%)	2 (1.7%)
Headache	3 (2.6%)	1 (0.9%)
Hypertension	2 (1.7%)	2 (1.7%)
Abdominal discomfort	3 (2.6%)	4 (3.5%)
Infusion reactions	3 (2.6%)	4 (3.5%)
Rash	10 (8.6%)	8 (7.0%)
Athralgia	6 (5.2%)	8 (7.0%)
Elevated liver enzyme	3 (2.6%)	4 (3.5%)
Leukopenia	5 (4.3%)	4 (3.5%)
Osteonecrosis	2 (1.7%)	0 (0%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

by 0.22 ± 2.82 in placebo group (p=0.004). Any adverse events were comparable between belimumab and placebo groups (61.2% vs 64.3%). Only 4 (3.4%) and 6 (5.2%) severe adverse events occurred in two groups (**Table 2**). There was no death.

Conclusion: Treatment with low-dose belimumab helped reduce disease flare risks in Chinese patients with SLE at low disease activity. Belimumab was generally well tolerated.

Disclosure: F. Sun: None; **H. Wang**: None; **D. Zhang**: None; **N. Shen**: None; **S. Chen**: None; **T. Li**: None; **W. Wan**: None; **S. Dai**: None; **S. Ye**: None.

Abstract Number: 0657

Preliminary Analysis Of Open-Label Dose-Titration Phase Of SLE Treatment With N-Acetylcysteine (SNAC) Shows Evidence For Potential Improvement Of SLEDAI, BILAG, ADHD And Fatigue Scores In Patients With Active SLE

FNU Ruchi[1], Ioana Coman[1], Bryan Blaker[1], Lucero Blaker[1], Joy Park[2], Jorge Cabezas[1], Dilip Rao[1], +Xiaojing Wang[1], Aparna Godavarthy[1], Marlene Marte Furment[3], Sandy Nasr[4], Sravani Lokineni[5], Christina Donath[4], SARA KAHLOWN[6], Damira Sereda[1], Binod Kc[1], Ilya Ivyanskiy[1], Bhavya Poudyal[7], Arthur Weinstein[8], Rosalind Ramsey-Goldman[9], Michael Weisman[10], Cynthia Aranow[11], Mariko Ishimori[10], Kyriakos Kirou[12], Jihad Ben Gabr[13], Sheetal Rayancha[14], Nancy Olsen[15], Fotios Koumpouras[16], Judith Lin[17], Stephen Faraone[1], Daniel Wallace[18], Michael McDermott[19] and Andras Perl[20], [1]SUNY Upstate Medical University, Syracuse, NY, [2]Upstate Medical University, Syracuse, NY, [3]Medical Affiliates of Cape Cod, Hyannis, MA, [4]SUNY Upstate University Hospital, Syracuse, NY, [5]Deaconess Hospital, Evansville, IN, [6]Suny upstate medical university, Camillus, NY, [7]SUNY Upstate Medical University, Cicero, NY, [8]retired from clinical practice, volunteer academic faculty, Claremont, CA, [9]Northwestern University Feinberg School of Medicine, Chicago, IL, [10]Cedars-Sinai Medical Center, LOS ANGELES, CA, [11]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [12]Hospital for Special Surgery, New York, NY, [13]Division of Rheumatology & Clinical Immunology, SUNY Upstate Medical University, Syracuse, NY, [14]SUNY Upstate Medical University, Jamesville, NY, [15]Penn State University/Milton S Hershey, Hershey, PA, [16]Yale School of Medicine, New Haven, CT, [17]Ohio State University Wexner Medical Center, Columbus, OH, [18]Cedars Sinai Medical Center, Studio City, CA, [19]University of Rochester Medical Center, Rochester, NY, [20]SUNY, Syracuse, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology with mortality still approaching 10% in 5 years. The major causes of death in SLE include infections due to the toxicity of immunosuppressant medications. Our study design has been formulated on the premise that safe and effective treatment should target key checkpoints of pathogenesis. The depletion of cysteine and reduced glutathione (GSH) underlie mitochondrial oxidative stress, activation of the mechanistic target of rapamycin (mTOR), inflammatory lineage specification and antinuclear autoantibody production in SLE. An earlier completed double-blind, placebo-controlled study provided preliminary evidence that replacement of cysteine and GSH with amino acid precursor, N-acetylcysteine (NAC), can safely reduce mTOR activation, anti-DNA antibody production, and disease activity in SLE (PMID: 22549432; PMID: 23400548).

Methods: The study is a multicenter randomized, double-blind, placebo-controlled clinical trial, using an innovative enriched enrollment randomized withdrawal (EERW) design that allows participants to use an individualized dosage of study medication, which mimics clinical practice in terms of how NAC would be administered. Eligibility criteria required clinically active

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Clinical assessment as measured by SLEDAI, BILAG, ASRS Inattention and Hyperactivity, and FAS Physical and Mental Fatigue scores. BILAG organ domain scores were converted to numerical values: A=12, B=8, C=1, D/E=0. Data are presented as mean ± standard deviation (STDEV). P values indicate comparisons between pretreatment (Month 0) and 3-month post-treatment measurements (Month 3) using a two-tailed paired t-test, corrected for multiple comparisons; differences (Δ) between Month 0 and Month 3 are also reported.

Clinical Assessment Scores	Month 0 (M0)		Month 3 (M3)		M0 vs M3	Difference (Δ)	
	Mean	STDEV	Mean	STDEV	P Value	Mean	STDEV
SLEDAI (n=68)	8.73	3.093	4.91	2.92	$1.1x10^{-11}$	3.671	3.201
BILAG (n=68)	23.808	5.099	8.750	6.027	$1.9x10^{-22}$	15.058	8.424
ADHD Inattention (n=54)	19.259	2.960	16.407	7.449	$1.5x10^{-2}$	2.851	6.645
ADHD Hyperactivity (n=54)	14.962	7.530	13.185	7.809	$1.3x10^{-2}$	1.777	4.063
Physical Fatigue (n=54)	19.259	2.960	16.092	3.972	$2.5x10^{-8}$	3.166	3.318
Mental Fatigue (n=54)	14.425	4.574	12.092	4.814	$6.2x10^{-5}$	2.333	3.518

disease with ≥6 SLE Disease Activity Index (SLEDAI) and British Isles Lupus Assessment Group (BILAG) organ domain scores ≥1 BILAG A or ≥2 BILAG B (clinicaltrials.gov NCT00775476). All participants received NAC for 3 months, titrated up to a maximally tolerated dosage between 2.4 g/day and 4.8 g/day. Subjects tolerating ≥2.4 g/day NAC have been randomized to receive either NAC or placebo at the subject's tolerated dosage for the remaining 9 months of treatment. Our preliminary analysis evaluated the BILAG and SLEDAI scores in 68 patients, and validated Fatigue Assessment (FAS) and ADHD Self-Report Scales (ASRS) (PMID: 23400548) in 54 SLE patients, before and after a 3-month open-label dose titration phase. Statistical analysis included two-tailed paired t-tests and correlations corrected for multiple comparisons using the Bonferroni correction in GraphPad software.

Results: We observed a significant reduction of SLE disease activity as measured by the reduction of SLEDAI and BILAG muco-cutaneous and musculoskeletal organ domain scores. ASRS cognition/inattention and fatigue scores also improved (Table 1). Adverse events—including headache, nausea, gastrointestinal upset, constipation, and diarrhea—were all transient and reversible. By month 3, 18 participants had withdrawn: 1 due to adverse events, 1 due to scheduling conflicts, 6 were lost to follow-up, 3 were unwilling to continue, 5 withdrew consent, and 2 experienced serious adverse events unrelated to the study drug.

Conclusion: This preliminary analysis supports the notion that NAC may serve as a safe and effective treatment for patients with SLE, but these observations could be affected by the absence of blinding in the open-label phase and regression-to-the-mean. The double-blind phase of the ongoing multicenter trial will confirm whether NAC is efficacious in treating SLE.

Disclosure: F. Ruchi: None; **I. Coman**: None; **B. Blaker**: None; **L. Blaker**: None; **J. Park**: None; **J. Cabezas**: None; **D. Rao**: None; **+X. Wang**: None; **A. Godavarthy**: None; **M. Marte Furment**: None; **S. Nasr**: None; **S. Lokineni**: None; **C. Donath**: None; **S. KAHLOWN**: None; **D. Sereda**: None; **B. Kc**: None; **I. Ivyanskiy**: None; **B. Poudyal**: None; **A. Weinstein**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **M. Weisman**: Spyre Therapeutics, 1, 2; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **M. Ishimori**: None; **K. Kirou**: AMPEL Biosolutions, 5, Bristol-Myers Squibb(BMS), 5, Novartis, 5; **J. Ben Gabr**: None; **S. Rayancha**: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5; **F. Koumpouras**: AbbVie/Abbott, 5, Adicet Bio, 2, AstraZeneca, 1, 2, 5, 6, Atara Bio, 2, Bristol-Myers Squibb(BMS), 5, 12, Clinical Trial, Cabaletta Bio, 2, Gilead, 12, Clinical Trial, GlaxoSmithKlein(GSK), 2, 5, ITN, 12, Clinical Trial, LRA/LuCIN, 5, Miltenyi Bio, 2, NIH, 5, Novartis, 2, RRF, 5, UCB, 12, Clinical Trial; **J. Lin**: None; **S. Faraone**: None; **D. Wallace**: PPD, 2; **M. McDermott**: None; **A. Perl**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0659

Human papillomavirus infection and systemic lupus erythematosus under biologic therapy: a retrospective analysis in a multicenter cohort

Ivette Casafont-Solé[1], Judit Font-Urgelles[1], Iñigo Rúa-Figueroa[2], Andrea Hernández-martín[3], Tarek Salman Montes[4], Marta De la Rubia Navarro[5], Maria Piqueras García[6], Sandra Garrote Corral[7], EVA GLORIA TOMERO MURIEL[8], Elena De la Mata Pinilla[9], Belén Álvarez Rodríguez[10], Julia Martínez Barrio[11], José Gomez-Puerta[12], Paola Vidal-Montal[13], Eleonora Penzo[14], Consuelo Ramos Giraldez[15], Francisco Javier Novoa[16], Vicenç Torrente-Segarra[17], Jorge Juan Fragío Gil[18], Leyre Riancho[19] and Irene Altabás-González[20], [1]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [2]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [3]Hospital Universitario de Gran Canaria Dr Negrín, Las palmas, Spain, [4]Hospital del Mar/Parc de Salut Mar-IMIM, Barcelona, Spain, [5]Hospital de La Fe, Valencia, [6]Servicio Murciano de Salud, Murcia, Spain, [7]Hospital Ramón y Cajal, Madrid, [8]Hospital Universitario de la Princesa, Madrid, Spain, [9]Hospital 12 de Octubre, Madrid, [10]Hospital de Áraba, áraba, Spain, [11]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [12]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, [13]Rheumatology. Hospital Universitari de Bellvitge, Barcelona, Catalonia, Spain, [14]Hospital Vall d'Hebrón, Barcelona, Spain, [15]Hospital Universitario Virgen de Valme, Servicio de Reumatología, Seville, Spain, [16]Hospital Insular de Gran Canaria, Las palmas, [17]Hospital Comarcal Alt Penedés Garraf, Vilafranca del Penedès, Spain, [18]Hospital General Universitario, Valencia, Spain, [19]Hospital de Sierrallana, Torrelavega, [20]Complejo Hospitalario de Vigo, Vigo, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Human papillomavirus (HPV) is responsible for 99.7% of cervical neoplasms and is the fourth most common cancer among women worldwide. Patients with systemic lupus erythematosus (SLE) have been shown to have a higher prevalence of HPV infection than the general population, with a greater frequency of high-risk serotypes and intraepithelial squamous lesions (SIL), particularly high-grade lesions (H-SIL). While an association has been described between immunosuppressive treatment and cyclophosphamide use, there is limited evidence on HPV progression in patients treated with biologic disease-modifying antirheumatic drugs (bDMARDs).

Our objectives were to assess the relationship between HPV infection and biologic therapy in SLE patients, as well as with factors associated with SLE disease course and HPV progression.

To determine the prevalence of HPV infection in a Spanish cohort of SLE patients receiving biologic therapy.

Methods: We conducted a retrospective, multicenter, cross-sectional study including 232 women with SLE treated with bDMARDs. Clinical, laboratory, and treatment-related variables associated with SLE and HPV infection were reviewed. Logistic regression analysis was performed to evaluate associations between HPV infection, SLE-related disease activity, and HPV progression.

Results: A total of 232 women with SLE were included, with a mean age of 46 years. HPV infection was identified in 9.9% (n=23) of patients. Among infected patients, 65.5% (n=19) had SIL (53.9% L-SIL [n=7]; 46.2% H-SIL [n=6]). Two patients (2.1%) developed cervical cancer. All patients had received at least one bDMARD (100%); 52 patients (22.41%) received two, and 3 patients (1.29%) received three different bDMARDs. Among HPV-infected patients, three had received more than one biologic agent.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

No statistically significant associations were found between HPV infection, biologic therapy, SLE disease-related variables (SLEDAI, SLICC, number of previous flares, disease duration), or risk factors for HPV progression (smoking, leukopenia).

No significant associations were observed between HPV infection and the analyzed potential risk or progression factors. The cohort included a homogeneous group of patients with high SLE activity but lacked a control group, which may limit the interpretation of associations. Additionally, socioeconomic data—potentially relevant to HPV risk—were not available.

The observed HPV prevalence (9.9%) was lower than previously reported in Spain (14.3%), potentially influencing the absence of significant associations. This may be due to low screening adherence among patients, though data were insufficient to confirm this hypothesis.

Table 1. Baseline characteristics of the cohort

	Total (n=232)
Age (years), mean (SD)	46 (13,3)
Smoking status, n (%)	62 (26,7)
Previous conventional DMARD, median (IQR)	218 (93,8)
Previous bDMARd, n (%)	55 (23,7)
SLICC, n (%)	
0	142 (62,0)
1	52 (22,7)
2	13 (5,7)
3	15 (6,6)
>3	7 (3,1)
SLEDAI, n (%)	
0-3	17 (7,4)
4-12	174 (46,0)
>12	38 (16,6)
Leukopenia, n (%)	41 (18,1)
High dsDNA, n (%)	162 (71,4)
Low C3/C4, n (%)	156 (68,4)
Flares during last year, n (%)	
0	8 (4,3)
1	97 (5,2)
2	48 (25,8)
3	18 (9,68)
4	13 (7,0)
>4	2 (1,1)

Table 2. Use of bDMARDs

bDMARDs received, n (%)	
Belimumab	232 (100)
Rituximab	46 (19,82)
Abatacept	5 (2,15)
Anti-TNF	4 (1,72)
Other bDMARDs	8 (3,45)
Nº of bDMARDs received during follow-up, n (%)	
1	
2	232 (100)
3	52 (22,41)
	3 (1,29)
bDMARDs received by patients HPV+, n (%)	
Belimumab	23 (9,9
Belimumab + Rituximab	1 (0,4)
Belimumab + Others	1 (0,4)
Belimumab + Rituximab + Abatacept	1 (0,4)

Table 3. Logistic regression analysis between HPV+ status and potential risk factors

	OR	CI 95%	p-value
Smoking status	1,73	0,57-5,23	0,329
Nº bDMARDs	0,40	0,08-1,89	0,250
SLEDAI	1,02	0,91-1,16	0,673
Nº of flares	1,15	0,74-1,78	0,537
SLICC	1,00	0,59-1,71	0,971
Disease duration	1,03	0,97-1,09	0,297
Leukopenia	1,45	0,36-5,85	0,598

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The prevalence of HPV infection in this cohort was 9.9%, with 65.5% of HPV-positive patients presenting SIL and two cases of cervical cancer (2.1%).

No significant associations were found between HPV infection, biologic therapy, SLE-related disease parameters, or HPV progression.

HPV prevalence in this cohort was lower than the general prevalence reported in Spain.

Disclosure: I. Casafont-Solé: None; **J. Font-Urgelles**: None; **I. Rúa-Figueroa**: None; **A. Hernández-martín**: None; **T. Salman Montes**: None; **M. De la Rubia Navarro**: None; **M. Piqueras García**: None; **S. Garrote Corral**: None; **E. TOMERO MURIEL**: None; **E. De la Mata Pinilla**: None; **B. Álvarez Rodríguez**: None; **J. Martínez Barrio**: None; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **P. Vidal-Montal**: None; **E. Penzo**: None; **C. Ramos Giraldez**: None; **F. Novoa**: None; **V. Torrente-Segarra**: None; **J. Fragío Gil**: Quibim, 1; **L. Riancho**: None; **I. Altabás-González**: None.

Abstract Number: 0660

Effects of Deucravacitinib on Dysregulated Autoimmune Gene Modules That Correlate With Skin Disease Severity and Treatment Response in Patients With Cutaneous Manifestations of Lupus Erythematosus: Biomarker Results From a Global, Randomized, Placebo-Controlled Phase 2 Study

J. Michelle Kahlenberg[1], Victoria Werth[2], Joerg Wenzel[3], John Schwarz[4], Jinqi Liu[4] and Brandon Johnson[4], [1]University of Michigan, Ann Arbor, MI, [2]University of Pennsylvania, Philadelphia, PA, [3]Department of Dermatology and Allergy, University Hospital of Bonn, Bonn, Germany, [4]Bristol Myers Squibb, Princeton, NJ

SESSION INFORMATION

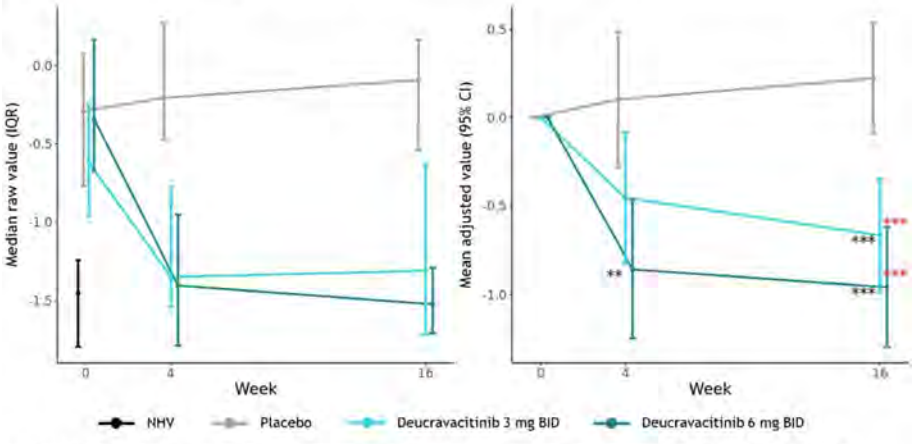
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in moderate to severe plaque psoriasis, has demonstrated significant improvements in cutaneous manifestations in the phase 2 PAISLEY SLE study (NCT03252587). TYK2, an important mediator of cytokine signaling (eg, types I and III IFNs, IL-23, and IL-12) involved in immune-specific responses, plays a role in cutaneous lupus erythematosus (CLE) pathophysiology. In the phase 2 PAISLEY CLE study (NCT04857034), the primary endpoint of Cutaneous Lupus Erythematosus Disease Area and Severity Index activity (CLASI-A) improvement was met with deucravacitinib in patients with CLE. This post hoc analysis aimed to identify dysregulated gene modules associated with CLE, evaluate the impact of deucravacitinib on these modules, and determine their predictive value for response to deucravacitinib.

Methods: Gene expression in whole blood was evaluated using a targeted PCR array (DxTerity AIP panel) in samples from patients with CLE with or without SLE treated in PAISLEY CLE (deucravacitinib 3 mg [n = 24] or 6 mg twice daily [n = 22] vs placebo [PBO; n = 24]). Selected genes were normalized and clustered into predefined modules, including IFN-5 (5-gene module associated with type I IFN transcription; *MX1, HERC5, IFIT1, RSAD2, EIF2AK2*), IFN-γ (*TRIM38, SP100, LBA1*), and inflammation (*CXCL10, LGALS3BP, APOL6, TNFSF13B*). Gene module expression (GME) in baseline (BL) samples from patients adjusted for

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure. Pharmacodynamic changes in expression of the inflammation gene module with deucravacitinib and placebo



*** $P < 0.001$; ** $P < 0.01$. Black asterisks indicate significant difference between deucravacitinib 3 mg BID or 6 mg BID vs PBO at the given time points. Red asterisks indicate significance of the overall deucravacitinib 3 mg BID or 6 mg BID curve vs the PBO curve. The inflammation gene module includes *CXCL10*, *LGALS3BP*, *APOL6*, and *TNFSF13B*.
BID, twice daily; IQR, interquartile range; NHV, normal healthy volunteer; PBO, placebo.

Table. Correlation of pharmacodynamic changes in gene modules with CLASI-A changes over time

	All patients				SLE absent			
Biomarker	Correlation direction	n	R	*P* value	Correlation direction	n	R	*P* value
Week 4								
IFN-5 module	Positive	66	0.35	0.004	Positive	38	0.40	0.013
Inflammation module	Positive	66	0.32	0.008	Positive	38	0.35	0.031
IFN-γ module	Positive	66	0.30	0.016				
Week 16								
IFN-5 module	Positive	51	0.44	0.001	Positive	29	0.52	0.004
Inflammation module	Positive	51	0.40	0.004	Positive	29	0.50	0.005
IFN-γ module	Positive	51	0.45	0.001	Positive	29	0.48	0.008

The IFN-5 gene module includes *MX1*, *HERC5*, *IFIT1*, *RSAD2*, and *EIF2AK2*. The inflammation gene module includes *CXCL10*, *LGALS3BP*, *APOL6*, and *TNFSF13B*. The IFN-γ gene module includes *TRIM38*, *SP100*, and *LBA1*.
IFN, interferon, R, correlation coefficient; SLE, systemic lupus erythematosus.

covariates and modeled by least-squares mean change was compared to GME in age- and sex-matched normal healthy volunteers (NHVs). Changes in GME with deucravacitinib vs PBO were compared using mixed model for repeat measures. Correlation analyses of clinical response with GME at BL and change from BL were performed using Spearman's rank correlation.

Results: Higher BL CLASI-A was associated with higher BL IFN-5 GME ($P = 0.0005$). There were no significant differences in BL CLASI-A or the ratio of high-to-low IFN-5 GME by SLE subgroup. IFN-5, IFN-γ, and inflammation GME were significantly elevated at BL in patients vs NHVs in both SLE subgroups ($P = 0.0001$ [IFN-γ, SLE absent]; $P < 0.0001$ [all others]). Higher BL IFN-5 and inflammation GME correlated with more severe BL CLASI-A ($P = 0.002–0.007$). Deucravacitinib significantly reduced IFN-5, IFN-γ, and inflammation GME vs PBO, normalizing to NHV levels (**Figure**); changes correlated with improved CLASI-A, and correlations strengthened over time (**Table**). BL IFN-γ GME correlated with response to deucravacitinib at W4 ($P = 0.044$) and W16 ($P = 0.009$); in patients with SLE, BL IFN-5 GME correlated with response to deucravacitinib at W4 ($P = 0.025$). Responders with a ≥ 50% reduction from baseline in CLASI-A had greater decreases in IFN-5 ($P = 0.0051$) and IFN-γ ($P = 0.0505$) GME vs nonresponders.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: IFN and inflammation gene modules were dysregulated in CLE and positively correlated with CLASI-A. Normalization of these signatures with deucravacitinib correlated with CLASI-A improvement. Results warrant further evaluation of deucravacitinib and the utility of these biomarkers in patients with cutaneous manifestations of lupus erythematosus.

Disclosure: J. Kahlenberg: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(-GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5; **V. Werth**: AbbVie/Abbott, 2, Alpine Immune Sciences, 2, Amgen, 2, 5, AnaptysBio, 2, argenx, 2, AstraZeneca, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Calyx, 2, Caribou, 2, CESAS Medical, 6, Corbus Pharmaceuticals, 5, Crisalis, 2, CSL Behring, 2, 5, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 2, 5, Immunovant, 2, Innovaderm, 2, Janssen, 2, Kyowa Kirin, 2, MAPI Trust, 9, Merck KGaA, Darmstadt, Germany, 2, N/A, 12, The University of Pennsylvania owns the copyright for the CLASI., Nektar, 2, Nuvig Pharmaceuticals, 2, Pfizer, 2, 5, Priovant, 5, Regeneron, 2, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Takeda, 2, UCB, 2, Ventus, 2, 5, Viela Bio, 2, 5, Xencor, 2; **J. Wenzel**: Actelion, 1, Almirall, 5, Array BioPharma, 12, Clinical studies, AstraZeneca, 1, 5, Bayer, 1, Biogen, 1, 12, Presentations, Bristol-Myers Squibb(BMS), 1, 5, GlaxoSmithKlein(GSK), 1, 5, 12, Clinical studies, Incyte, 1, 5, Janssen, 1, 12, Presentations, Kyowa Kirin, 12, Presentations, LEO, 12, Presentations and Clinical studies, medac, 12, Presentations, Merck/MSD, 1, 12, Clinical studies, Novartis, 6, 12, Clinical studies, Pfizer, 12, Clinical studies, Roche, 12, Clinical studies, Sanofi, 12, Presentations, Spirig, 5; **J. Schwarz**: Bristol-Myers Squibb(BMS), 3, 11; **J. Liu**: Bristol-Myers Squibb (BMS), 3, 11; **B. Johnson**: Bristol-Myers Squibb(BMS), 3, 11.

Abstract Number: 0661

Real-world Effectiveness and Usage of Voclosporin: Data from the Enlight-LN Registry

Leanna Wise[1], Laura Geraldino-Pardilla[2], Niloofar Nobakht[3], Mohammad Kamgar[3], Amber Rosales[4], Barbara McIntosh[4] and Ron Flauto[4], [1]LAGMC/Keck Medicine of USC, Los Angeles, [2]Columbia University, New York, NY, [3]University of California Los Angeles, Los Angeles, CA, [4]Aurinia Pharmaceuticals Inc., Edmonton, AB, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The 2024 American College of Rheumatology Lupus Nephritis (LN) Guideline recommends triple immunosuppressive therapy, including the option of a calcineurin inhibitor (CNI)-based regimen, for patients with active lupus nephritis (LN). Voclosporin is a second generation CNI approved for adults with active LN. During clinical trials, voclosporin, in combination with mycophenolate mofetil (MMF) and low-dose glucocorticoids, led to significant reductions in proteinuria with stable estimated glomerular filtration rate (eGFR) with up to 3 years of exposure compared to MMF and glucocorticoids alone. The Enlight-LN registry was designed to characterize the real-world effectiveness and usage patterns of voclosporin in the United States. Here we describe the initial outcomes of patients who participated in this registry.

Methods: The Enlight-LN registry enrolled patients between March 2022 and January 2025 (NCT05337124). Patients were ≥18 years with biopsy-confirmed LN who initiated or had already initiated treatment with commercial voclosporin prior to study consent. Patients received standard of care in accordance with usual clinical practice at each site. Mandatory assessments included renal parameters and blood pressure. Data were extracted from patient records approximately every 3 months. Safety data were collected via spontaneous reporting.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: As of April 4, 2025, data were available on 229 patients. Median (range) patient age was 34.0 (18-78), with 36.2% of patients ≤30 years; 83.4% were female. Most patients self-identified as White (43.2%) or Black/African American (38.0%); 35.4% were Hispanic/Latino. Median (range) time since first LN diagnosis was 1.6 (0, 26.2) years. The majority of patients had Class V disease (31.4%) or Class IV disease (20.1%).

Median (range) UPCR decreased from 2.3 (0.1-16.8) g/g at baseline (n=191) to 0.9 (0.1-18.7) g/g at month 6 (n=89). Median (range) corrected eGFR was 89.3 (6-90) mL/min/1.73 m^2 at baseline (n=222) and 82.0 (3-90) mL/min/1.73 m^2 at month 6 (n=120). Safety data collected during the registry appears to be consistent with the established safety profile of voclosporin.

Conclusion: Patients in the Enlight-LN registry reflect the larger LN population in the US, including high percentages of Black and Hispanic and/or Latino patients. The outcomes data from this initial analysis are consistent with the findings from the voclosporin clinical trials, with substantial reductions in proteinuria observed over the first few months of treatment, with no new safety signals. These real-world data support the recent updates to the ACR guidelines recommending use of triple immunosuppressive therapy first-line in patients with active LN.

Disclosure: L. Wise: AstraZeneca, 1, 6, 7, Aurinia Pharma, 5, 6, GlaxoSmithKlein(GSK), 6; **L. Geraldino-Pardilla**: Aurinia, 2, 6, Bristol-Myers Squibb(BMS), 1, 2, 6; **N. Nobakht**: Aurinia, 12,; **M. Kamgar**: Aurinia, 6; **A. Rosales**: Aurinia Pharmaceuticals Inc., 3, 11; **B. McIntosh**: Aurinia Pharmaceuticals Inc., 3, 11; **R. Flauto**: Aurinia Pharmaceuticals Inc., 3, 11.

Abstract Number: 0662

Efficacy Across Baseline Characteristic Subgroups in Patients With Systemic Lupus Erythematosus Treated With Upadacitinib: Results From SLEek, a Phase 2 Randomized

Marta Mosca[1], Karen H. Costenbader[2], Amit Saxena[3], Michelle Petri[4], Andrea Rubbert-Roth[5], Karim Masri[6], Christopher Saffore[7], Ling Cheng[8] and Joan Merrill[9], [1]University of Pisa, Pisa, Pisa, Italy, [2]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [3]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [4]Johns Hopkins University School of Medicine, Timonium, MD, [5]Division of Rheumatology and Immunology, Cantonal Hospital St Gallen, St Gallen, Switzerland, [6]AbbVie Inc., North Chicago, IL, [7]AbbVie Inc., waukegan, IL, [8]AbbVie, North, IL, [9]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical and immunological manifestations of systemic lupus erythematosus (SLE) vary widely across patients, complicating diagnosis and treatment (1,2). Upadacitinib (UPA), an oral selective JAK inhibitor, significantly reduced disease activity compared with placebo (PBO) in the phase 2 SLEek trial of adult patients with moderately to severely active SLE (3). In this analysis, we evaluate potential differences in treatment responses to UPA vs PBO associated with baseline patient characteristics.

Methods: SLEek was a phase 2, randomized, double-blind, PBO-controlled trial (NCT03978520) (3). This post hoc analysis included participants who were randomized to receive once-daily UPA 30 mg or PBO for 48 weeks. We report the proportions of trial participants in each group who met the composite measures of disease improvement, Lupus Low Disease Activity State (LLDAS) and/or British Isles Lupus Assessment Group-Based Composite Lupus Assessment (BICLA).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Participants were stratified into subgroups by sex, age, race, region, body mass index, medication use, clinical markers, and medical history. Missing data were handled with nonresponder imputation incorporating multiple imputation to handle missing data due to COVID-19. Between-group differences and 95% CIs were estimated according to the Cochran-Mantel-Haenszel test adjusted for baseline corticosteroid use (≤10 mg or >10 mg), Systemic Lupus Erythematosus Disease Activity Index 2000 score at screening (< 10 or ≥10), baseline interferon score (high, low, or not applicable), and baseline immunosuppressant use (yes or no). Analyses were exploratory, and the reported data are descriptive.

Results: A total of 137 participants (UPA 30 mg, n = 62; PBO, n = 75) were included. Most participants were White (56.2%) and female (96.4%). As previously published, at week 48, 31 participants (50.0%) treated with UPA 30 mg and 18 (24.0%) treated with PBO achieved LLDAS; 33 participants (53.2%) treated with UPA 30 mg and 19 (25.3%) treated with PBO achieved BICLA (3). A numerically higher proportion of participants in most baseline characteristic subgroups treated with UPA 30 mg vs PBO achieved LLDAS and/or BICLA (**Table**), with treatment differences (estimated by the Cochran-Mantel-Haenszel test) consistent with potential benefits of UPA 30 mg across most subgroups (**Figure**).

Conclusion: After 48 weeks of treatment, participants with SLE treated with UPA30 mg were more likely than those receiving PBO to achieve LLDAS and/or BICLA across various baseline demographics and clinical characteristics; however, the interpretation of data in this study is limited by sample size. These findings, if corroborated in further studies, may support the potential benefit of UPA in a broad spectrum of patients with SLE despite the heterogeneity of the disorder.

anti-dsDNA, anti–double-stranded DNA; BICLA, British Isles Lupus Assessment Group-Based Composite Lupus Assessment; BMI, body mass index; LLDAS, Lupus Low Disease Activity State; NA, not applicable; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000. aPercentage of responders with available data on LLDAS or BICLA.

anti-dsDNA, anti–double-stranded DNA; BICLA, British Isles Lupus Assessment Group-Based Composite Lupus Assessment; BMI, body mass index; LLDAS, Lupus Low Disease Activity State; NA, not applicable; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000. Response rate differences and 95% CIs were estimated according to the Cochran-Mantel-Haenszel test adjusted for baseline corticosteroid use (≤10 mg or >10 mg), Systemic Lupus Erythematosus Disease Activity Index 2000 score at screening (<10 or ≥10), baseline interferon score (high, low, or not applicable), and baseline immunosuppressant use (yes or no).

Disclosure: M. Mosca: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **A. Rubbert-Roth**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Boehringer, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6; **K. Masri**: AbbVie, 3, 11; **C. Saffore**: AbbVie, 3, 11; **L. Cheng**: AbbVie/Abbott, 3, 11; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0663

iPSC-Derived Off-the-Shelf anti-CD19 CAR T cells Deliver Improved Clinical Outcomes in Lupus with Reduced or No Conditioning Chemotherapy

Parastoo Fazeli[1], Jennifer Medlin[2], Andrew BitMansour[3], Debra Zack[4], Rebecca Elstrom[5], Bertha Villa[5], Lilly Wong[6], John Goulding[7], Nicholas Brookhouser[5], Trever Greene[5], Cara Bickers[5], Carol Wong[5], Beatrice Ferguson[5], Tom Lee[5], Jode Goodridge[5], Marie Hu[8], Veronika Bachanova[8], Jeffrey Miller[9], Bahram Valamehr[6], Matthew Lunning[10] and Vaneet Sandhu[5], [1]UMN, ST PAUL, MN, [2]University of Nebraska Medical Center, Omaha, NE, [3]Fate Therapeutics, Inc., San Carlos, CA, [4]Fate Therapeutics, Inc., Solana Beach, CA, [5]Fate Therapeutics, Inc., San Diego, [6]Fate Therapeutics, Inc., San Diego, CA, [7]Fate Therapeutics, San Diego, [8]University of Minnesota, Minneapolis, [9]University of Minnesota, Minneaspolis, MN, [10]University of Nebraska, Omaha

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-CD19 chimeric antigen receptor (CAR) T cell therapy shows promise in autoimmune disease. However, autologous CAR T-cell therapy is limited by prolonged pre- and post-apheresis timelines, access to authorized treatment centers, T cell product inconsistency, high costs, and production capacity to support a broad patient (pt) base. Derived from a clonal master induced pluripotent stem cell (iPSC) bank for mass production of CAR T cells for on-demand and broad utilization, FT819 is an off-the-shelf CD19-targeting CAR T cell product engineered with features designed to improve safety and efficacy via a 1XX CAR signaling domain that extends T cell effector function without exhaustion; integration of CAR transgene directly into the T cell receptor (TCR) alpha constant locus promotes uniform CAR expression and enhanced potency; and complete bi-allelic disruption of TCR expression for the prevention of graft-versus-host disease (GVHD).

Methods: A Phase 1 dose-escalation study evaluating the safety, pharmacokinetics, and anti-B-cell activity of FT819 in pts with B-cell mediated autoimmune diseases (NCT06308978) is ongoing. All pts enrolled to date have SLE (EULAR/ACR 2019 classification with at least one antibody: ANA 1:160, anti-dsDNA, or anti-smith), whose severity is defined by SLEDAI-2K $\geq$ 8 + 1 BILAG A/2 BILAG B scores. FT819 was administered as a single dose under 2 regimens (Reg): Reg A, fludarabine-free conditioning chemotherapy (CCT) with single-dose cyclophosphamide or bendamustine daily for 2 days prior to FT819; and Reg B, no CCT with continued stable dose of maintenance therapy, including mycophenolate (MMF).

Results: As of the data cutoff date, pts treated in Reg A and Reg B had follow-up ranging from 1-12 months (mo). All pts tolerated FT819 without dose-limiting toxicity. Expected cytopenias after CCT were observed in Reg A. No Grade >2 CRS, ICANS, GvHD, or death was reported.

Pts in Reg A experienced rapid and deep peripheral B cell depletion, with greater depletion observed at dose level 2 (DL; DL1 = 3.6×10^8 viable cells (VC)/dose; DL2 = 9×10^8 VC/dose). Reconstitution of the B cell compartment, predominantly naïve, was noted within 1-3 mo post-FT819. Pts from both Regimens experienced sustained improvements in SLEDAI-2K, PGA, and FACIT-fatigue scores and UPCr improved in pts with lupus nephritis (LN). Pts with LN achieved either a primary efficacy renal response or complete renal response (CRR) by last follow up.

In the first pt in Reg A, steroids were discontinued at 3 mo, Definition of Remission in SLE (DORIS) achieved at 6 and 12 mo, and CRR at 9 mo. In the first pt in Reg B (BILAG A cardiorespiratory), MMF was continued without CCT, and Low Lupus Disease Activity State was achieved at 3 mo. Additional pt outcomes of current and additional pts will be highlighted at the time of presentation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Preliminary patient data indicates a favorable safety profile, effective B cell depletion, and promising initial efficacy. These findings support the continued evaluation of FT819 in SLE as well as other B-cell mediated autoimmune diseases (ANCA-associated vasculitis, idiopathic inflammatory myositis, and systemic sclerosis) included in the FT819 protocol.

Disclosure: P. Fazeli: AbbVie/Abbott, 2, Amgen, 6, AstraZeneca, 1, Janssen, 1; **J. Medlin**: None; **A. BitMansour**: Fate Therapeutics, Inc., 3; **D. Zack**: Fate Therapeutics Inc, 7; **R. Elstrom**: Fate Therapeutics Inc, 12,, 2; **B. Villa**: Fate Therapeutics Inc, 2; **L. Wong**: Fate Therapeutics, Inc., 12,, 3; **J. Goulding**: Fate Therapeutics Inc, 12,, 3; **N. Brookhouser**: Fate Therapeutics Inc, 12,, 3; **T. Greene**: Fate Therapeutics Inc, 3; **C. Bickers**: Fate Therapeutics Inc, 12,, 3; **C. Wong**: Fate Therapeutics Inc, 3; **B. Ferguson**: Fate Therapeutics Inc, 3, Incyte Corporation, 3; **T. Lee**: Fate Therapeutics Inc, 3; **J. Goodridge**: Fate Therapeutics Inc, 3; **M. Hu**: None; **V. Bachanova**: Abvie, 1, ADC, 1, Citius, 5, Incyte, 5; **J. Miller**: Fate Therapeutics, 5, 11; **B. Valamehr**: Fate Therapeutics, 3; **M. Lunning**: AbbVie/Abbott, 2, Acrotech, 2, ADC Therapeutics, 2, AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Fate Therapeutics Inc, 2, Genentech, 2, Incyte, 2, Ipsen, 2, Kite, 2, Lyell, 2, Pfizer, 2, Recordati, 2, Veeva, 2; **V. Sandhu**: Fate Therapeutics Inc, 3.

Abstract Number: 0664

Pharmacodynamic Effects of Obinutuzumab on B cells and Serological Markers in Patients With Active Lupus Nephritis: Results From a Phase III Trial

Richard Furie[1], Ioannis Parodis[2], Rachel Jones[3], Liz Lightstone[4], Olivia Hwang[5], Amelia Au-Yeung[5], Imran Hassan[6], Huiyan Mao[6], William Pendergraft[5], Jay Garg[5], Harini Raghu[5] and Brad Rovin[7], [1]Division of Rheumatology, Northwell Health, Great Neck, NY, [2]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [3]Renal Medicine, Cambridge University Hospitals, Cambridge, England, United Kingdom, [4]Department of Immunology and Inflammation, Faculty of Medicine, Imperial College London, London, England, United Kingdom, [5]Genentech, Inc., South San Francisco, CA, [6]Hoffmann-La Roche Ltd, Mississauga, ON, Canada, [7]The Ohio State University, Columbus, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

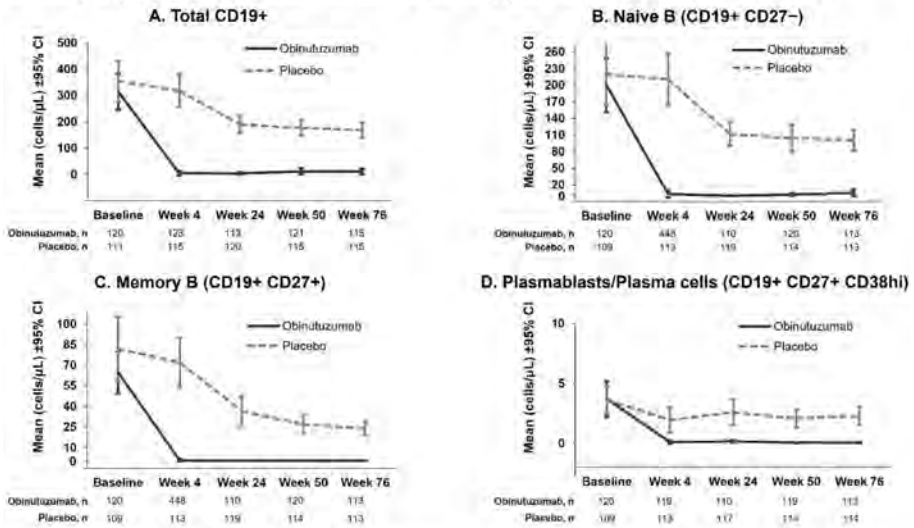
Background/Purpose: Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus, marked by kidney inflammation and damage. Obinutuzumab, a glycoengineered, type II CD20 antibody demonstrated effective B-cell depletion, reduced serum anti-double-stranded DNA (anti-dsDNA) antibodies and increased complement C3 and C4 levels in patients (pts) with LN in the Phase II NOBILITY (NCT02550652) trial. The Phase III REGENCY trial (NCT04221477) of obinutuzumab plus standard therapy in pts with active LN demonstrated a statistically significant improvement in Week 76 complete renal response and an acceptable safety profile.

Exploratory analyses of peripheral B-cell populations and serological markers were performed to confirm the pharmacodynamic effects of obinutuzumab in pts enrolled in the REGENCY trial.

Methods: Adults with active LN received placebo or obinutuzumab plus standard therapy (mycophenolate mofetil plus glucocorticoids). All pts met ACR SLE classification criteria and had biopsy-proven proliferative LN. Peripheral B cells and B-cell subsets were assessed using validated high-sensitivity flow cytometry (HSFC) assays minimal residual B-cell panel (MRB) 1.1 and BCP2.2, respectively. The lower limit of quantification (LLOQ) of CD19+ B cells by MRB1.1 is 0.441 cells/μL. Complement and anti-dsDNA antibody levels were measured by nephelometry and enzyme-linked immunosorbent assay,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Longitudinal Characterization of Total CD19+ B Cells (A), Naive B (B), Memory B (C) and Plasmablasts/Plasma Cells (D) in the Blood REGENCY Study



HSFC, high-sensitivity flow cytometry; MRB, minimal residual B-cell panel.

Table 1: Normalization of C3, C4 and Anti-dsDNA in Patients With Abnormal Baseline Values at Weeks 12 and 76 by Treatment Arm in the Phase III REGENCY Trial

Serological biomarker at baseline	Treatment arm (n = abnormal at baseline)	Normalized at Week 12, n (%)	Normalized at Week 76, n (%)
C3 <0.9g/L	Obinutuzumab (n=77) Placebo (n=76)	38 (49) 25 (33)	48 (62) 22 (29)
C4 <0.1g/L	Obinutuzumab (n=32) Placebo (n=42)	24 (75) 23 (55)	28 (88) 23 (55)
Anti-dsDNA >120 kU/L	Obinutuzumab (n=57) Placebo (n=61)	24 (42) 10 (16)	32 (56) 10 (16)

respectively. Peripheral B-cell and serum biomarker assessments were performed on samples from Weeks 0, 4, 12, 24, 50 and 76.

Results: Baseline biomarker levels were comparable between arms and no pt had B-cell levels below the LLOQ. At Week 4, mean total CD19+ B-cell levels were greatly reduced with obinutuzumab (mean cells/μL [SD]: 4.7 [45.6], –99.8 median % change from baseline) vs placebo (mean cells/μL [SD]: 317.8 [338.5], –4.2 median % change) and remained low relative to placebo at every timepoint tested through Week 76 (**Figure 1A**). Similar decreases in B-cell subsets were observed with obinutuzumab relative to placebo from Week 4-76 (**Figures 1B-D**). Obinutuzumab treatment also resulted in greater reductions in anti-dsDNA antibody levels and increases in complement C3 and C4 vs placebo. In pts with abnormal baseline serologies, higher normalization rates for C3 (43% vs 14%), C4 (70% vs 39%) and anti-dsDNA antibody levels (45% vs 11%) were observed at Week 12 for obinutuzumab vs placebo; these normalization rates were sustained or further improved through Week 76, with normalization rates of 62% vs 29% for C3, 88% vs 55% for C4 and 56% vs 16% for anti-dsDNA antibody levels at Week 76 (**Table 1**).

Conclusion: Obinutuzumab plus standard therapy induced rapid and sustained depletion of total peripheral CD19+ B cells and B-cell subsets in pts with active LN. Obinutuzumab treatment demonstrated improvements in serological markers of disease activity, increases in serum C3 and C4 levels, and reductions in anti-dsDNA antibody levels over placebo in all pts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Among pts with abnormal baseline marker values, obinutuzumab led to earlier and greater normalization rates vs placebo. These data support the hypothesis that deep B-cell depletion with obinutuzumab contributes to the improved clinical responses observed in pts with LN.

Disclosure: R. Furie: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5; **R. Jones**: CSL Vifor, 2, 5, F. Hoffman-La Roche Ltd, 2, 5, GlaxoSmithKline, 2, 5; **L. Lightstone**: Alexion, 2, AstraZeneca, 2, F. Hoffman-La Roche Ltd, 2, GlaxoSmithKline, 2, Kezar, 2, Novartis, 2, Otsuka, 2, Pfizer, 2; **O. Hwang**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **A. Au-Yeung**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **I. Hassan**: F. Hoffmann-La Roche Ltd, 3; **H. Mao**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **J. Garg**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech Inc., 3; **H. Raghu**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2.

Abstract Number: 0665

Infusion-Related Reactions (IRRs) and Hematologic Events Associated With Obinutuzumab in Lupus Nephritis: A Secondary Analysis of a Phase III Trial

Richard Furie[1], Teresa Baczkowska[2], Amit Saxena[3], Imran Hassan[4], Bongin Yoo[5], Ben Lanza[6], Himanshi Sehgal[7], Frederic Boissard[7], Jay Garg[5], Thomas Schindler[7], Elsa Martins[7], William Pendergraft[5] and Brad Rovin[8], [1]Division of Rheumatology, Northwell Health, Great Neck, NY, [2]Department of Transplantation Medicine, Nephrology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland, [3]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [4]Hoffmann-La Roche Ltd, Mississauga, ON, Canada, [5]Genentech, Inc., South San Francisco, CA, [6]Roche Products Ltd, Welwyn Garden City, United Kingdom, [7]F. Hoffmann-La Roche Ltd, Basel, Switzerland, [8]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The REGENCY (NCT04221477) trial demonstrated superior efficacy of obinutuzumab and standard therapy (OBI+ST) over placebo and ST (PBO+ST) in patients (pts) with active lupus nephritis (LN). Although an acceptable safety profile was observed, insights related to IRRs and hematologic effects of OBI are needed to guide future management. In this study, we further characterize important non-infectious adverse events including the IRR profile of OBI and describe the occurrence of neutropenia in the REGENCY trial.

Methods: Incidence, severity and attribution of IRRs and hematologic abnormalities, including drug-related neutropenia, were determined in the REGENCY trial based on investigator and NCI CTCAE v5.0 adverse event grading. Descriptive analyses were performed comparing pts receiving OBI+ST vs PBO+ST. All pts met ACR SLE classification criteria and had biopsy-proven proliferative LN.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The proportion of pts who experienced at least one IRR was higher in the OBI+ST arm vs the PBO+ST arm (21 [15.4%] vs 15 [11.4%], respectively) during the 76-week period. In the OBI+ST arm, the majority (19 [14.0%]) experienced IRRs of Grade (Gr) 1-2, which resolved following protocol guidance. Two pts (1.5%) experienced Gr 3-4 IRRs in the OBI+ST arm and both events resolved: one non-serious IRR of Gr 3 and one serious IRR of Gr 4, one leading to treatment discontinuation for this pt. No Gr 5 IRRs were observed. The most frequently reported signs and symptoms of IRRs in the OBI vs PBO arms respectively were nausea (4 [2.9%] vs 4 [3.0%]), headache (4 [2.9%] vs 3 [2.3%]) and vomiting (4 [2.9%] vs 2 [1.5%]). IRR incidence and severity was highest at first infusion, with Gr 3-4 observed only then, and decreased with additional infusions (**Table 1**).

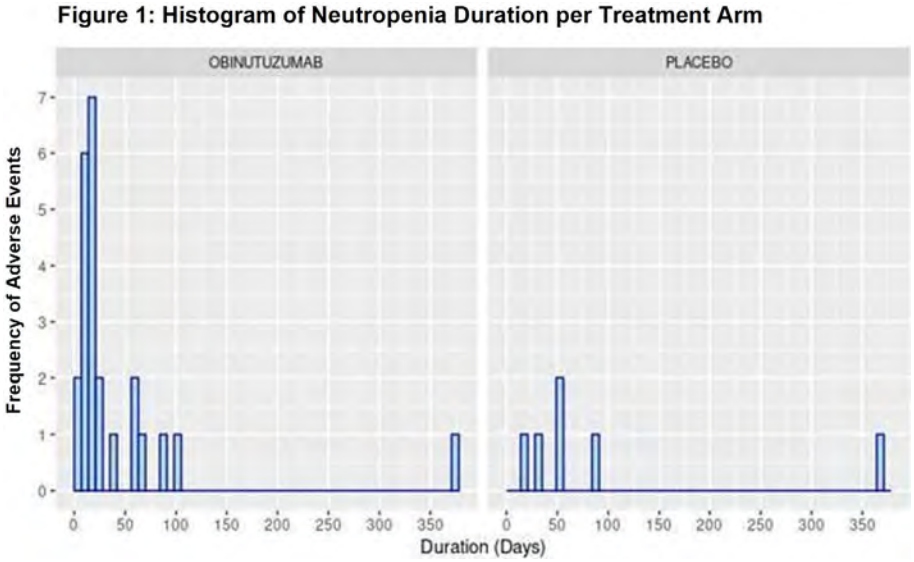
The frequencies of shifts observed from Gr 1-2 at baseline to Gr 3-4 post-baseline were notably different between the treatment arms only for neutrophils and lymphocytes. As lymphopenia is an expected pharmacologic effect of anti-CD20 therapies, this analysis focused on drug-related neutropenia. The proportion of pts who experienced at least one drug-related

Table 1: Incidence and Grade of Infusion-Related Reactions by Infusion Visits and Treatment

	Obinutuzumab (n=136)	Placebo (n=132)
Infusion 1		
Patients who had infusion, n (%)	136 (100)	132 (100)
Total patients with ≥1 IRR, n (%)	14 (10.3)	8 (6.1)
Total patients with ≥1 IRR grade 1-2, n (%)	12 (8.8)	8 (6.1)
Total patients with ≥1 IRR grade 3-5, n (%)	2 (1.5)	0
Infusion 2		
Patients who had infusion, n (%)	133 (97.8)	132 (100)
Total patients with ≥1 IRR, n (%)	5 (3.7)	4 (3)
Total patients with ≥1 IRR grade 1-2, n (%)	5 (3.7)	4 (3)
Total patients with ≥1 IRR grade 3-5, n (%)	0	0
Infusion 3		
Patients who had infusion, n (%)	128 (94.1)	124 (93.9)
Total patients with ≥1 IRR, n (%)	3 (2.2)	3 (2.3)
Total patients with ≥1 IRR grade 1-2, n (%)	3 (2.2)	3 (2.3)
Total patients with ≥1 IRR grade 3-5, n (%)	0 (0)	0 (0)
Infusion 4		
Patients who had infusion, n (%)	127 (93.4)	123 (93.2)
Total patients with ≥1 IRR, n (%)	2 (1.5)	0 (0)
Total patients with ≥1 IRR grade 1-2, n (%)	2 (1.5)	0 (0)
Total patients with ≥1 IRR grade 3-5, n (%)	0 (0)	0 (0)
Infusion 5		
Patients who had infusion, n (%)	120 (88.2)	112 (84.8)
Total patients with ≥1 IRR, n (%)	0 (0)	2 (1.5)
Total patients with ≥1 IRR grade 1-2, n (%)	0 (0)	2 (1.5)
Total patients with ≥1 IRR grade 3-5, n (%)	0 (0)	0 (0)
Infusion 6		
Patients who had infusion, n (%)	117 (86)	108 (81.8)
Total patients with ≥1 IRR, n (%)	1 (0.7)	2 (1.5)
Total patients with ≥1 IRR grade 1-2, n (%)	1 (0.7)	2 (1.5)
Total patients with ≥1 IRR grade 3-5, n (%)	0 (0)	0 (0)

Safety analyses included all patients who received any infusion of obinutuzumab or placebo, grouped according to the infusion that was actually administered. All study participants were premedicated with methylprednisolone (80 mg IV), acetaminophen (650-1000 mg) orally and diphenhydramine (50 mg orally or IV [or equivalent dose of a similar agent]) prior to each infusion of obinutuzumab or placebo.
IRR was defined as any AE occurring during or within 24 hours after IV infusion of obinutuzumab or placebo assessed by study investigators to be related to the infusion. Systemic IRRs were considered AEs of special interest.
AE, adverse event; IRR, infusion-related reaction; IV, intravenous.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



neutropenia was higher in the OBI+ST arm vs the PBO+ST arm (17 [12.5%] vs 5 [3.8%], respectively). Most cases of neutropenia were incidentally detected during routine hematology labs at scheduled study visits. Median time for resolution was 16 days (d) (min-max: 4-378 d) and 50.5 d (min-max: 21-371 d) in the OBI+ST and PBO+ST arm, respectively. Seven pts (4.1%) had Gr 3-4 drug-related neutropenia (including 1 febrile neutropenia) in the OBI+ST arm, whereas none in the PBO +ST arm had Gr 3-4 neutropenia. All drug-related neutropenia resolved with treatment by protocol guidance except for one PBO pt whose neutropenia was recovering/resolving at the clinical cutoff. No Gr 5 neutropenia was observed. Five patients received G-CSF treatment for drug-related neutropenia (4 in the OBI+ST arm vs 1 in the PBO+ST arm).

Conclusion: Although the incidence of IRRs and drug-related neutropenia was higher in pts receiving OBI+ST compared with PBO+ST, these risks remained low overall; many were Gr 1-2, self-limited, easily manageable and without consequence for most pts. These data provide insights into adverse events related to OBI.

Disclosure: R. Furie: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **T. Baczkowska**: None; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **I. Hassan**: F. Hoffmann-La Roche Ltd, 3; **B. Yoo**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3, GlaxoSmithKlein(GSK), 12, Shareholder; **B. Lanza**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **H. Sehgal**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **F. Boissard**: F. Hoffman-La Roche Ltd, 3; **J. Garg**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **T. Schindler**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **E. Martins**: F. Hoffman-La Roche Ltd, 3; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0666

Reported Adverse Events Associated With Systemic Lupus Erythematosus (SLE) Treatment: Insights From the FDA Adverse Event Reporting System (FAERS) 2023

Sarah Crisci, New York University, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with heterogeneous symptoms, complicating diagnosis and treatment. Historically, treatment included broad immunosuppressants, but real-world

Table 1: Characteristics of primary suspect reports associated with Belimumab, Anifrolumab, and all drugs, among SLE patients in 2023

	Belimumab n (%)	Anifrolumab n (%)	Total – all drugs n (%)
Total number of patients	1822	267	4707
Sex			
Male	46 (2.52%)	23 (8.61%)	319 (6.78%)
Female	862 (47.31%)	206 (77.15%)	2974 (63.18%)
Unknown/missing	914 (50.16%)	38 (14.23%)	1414 (30.04%)
Age (years)	Med: 54.00 IQR: 42.00 – 62.00	Med: 48.50 IQR: 39.46 – 56.25	Med: 45.00 IQR: 33.00 – 58.00
Age group (years)			
<20	5 (0.27%)	2 (0.75%)	74 (1.57%)
20-29	9 (0.49%)	10 (3.75%)	165 (3.51%)
30-39	37 (2.03%)	6 (2.25%)	181 (3.85%)
40-49	52 (2.85%)	19 (7.12%)	281 (5.97%)
50-59	64 (3.51%)	20 (7.49%)	280 (5.95%)
60-69	58 (3.18%)	9 (3.37%)	184 (3.91%)
70-79	19 (1.04%)	1 (0.37%)	71 (1.51%)
80+	2 (0.11%)	5 (1.87%)	12 (0.25%)
Missing	720 (86.50%)	195 (73.03%)	3459 (73.49%)
Reporter country (by continent)			
North America	1242 (68.17%)	178 (66.67%)	3181(67.58%)
Asia	219 (12.02%)	51 (19.10%)	638 (13.55%)
Europe	54 (2.96%)	38 (14.23%)	471 (10.01%)
South America	307 (16.85%)	0 (0.00%)	370 (7.86%)
Africa	0 (0.00%)	0 (0.00%)	23 (0.49%)
Oceania	0 (0.00%)	0 (0.00%)	19 (0.40%)
Missing	0 (0.00%)	0 (0.00%)	5 (0.11%)
Reporting person			
Consumer	948 (52.05%)	80 (29.96%)	1517 (32.23%)
Lawyer	0 (0.00%)	0 (0.00%)	8 (0.17%)
Physician	422 (23.16%)	138 (51.69%)	1220 (25.92%)
Pharmacist	63 (3.46%)	4 (1.50%)	106 (2.25%)
Other health professional	279 (15.31%)	45 (16.85%)	1685 (35.80%)
Missing	110 (6.04%)	0 (0.00%)	171 (3.63%)
Total number of reports	10,737	661	125,675
Adverse event type*			
Hospitalization – Initial or prolonged	4031 (31.70%)	240 (36.31%)	27692 (22.03%)
Life-threatening	291 (2.29%)	58 (8.77%)	20814 (16.56%)
Disability	188 (1.48%)	2 (0.30%)	20590 (16.38%)
Death	74 (0.58%)	14 (3.42%)	17309 (13.77%)
Congenital anomaly	20 (0.16%)	0 (0%)	1452 (1.16%)
Required intervention to prevent permanent damage	16 (0.13%)	8 (1.21%)	31 (0.02%)
Other serious (important medical event)	8097 (63.67%)	316 (47.81%)	37787 (30.07%)

*Total count of adverse event types may not equal total number of reports because reporters were able to check more than one box for adverse event type, per report

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2a: Signal strength of reports of Belimumab among SLE patients at the System Organ Class (SOC) level

SOC	Cases reporting SOC	ROR (95% CI)	chi-squared	p-value
Blood and lymphatic system disorders	83	1.24 (0.96, 1.60)	2.49	0.1149
Cardiac disorders	89	0.59 (0.47, 0.74)	20.91	<0.0001
Congenital, familial and genetic disorders	4	0.18 (0.07, 0.50)	12.72	0.0004
Ear and labyrinth disorders*	58	**2.26 (1.61, 3.17)**	22.25	<0.0001
Endocrine disorders	8	1.61 (0.68, 3.81)	0.75	0.3878
Eye disorders	115	1.78 (1.41, 2.24)	23.71	<0.0001
Gastrointestinal disorders	545	0.59 (0.53, 0.64)	125.02	<0.0001
General disorders and administration site conditions	2056	1.27 (1.20, 1.34)	68.09	<0.0001
Hepatobiliary disorders	37	0.31 (0.22, 0.44)	49.95	<0.0001
Immune system disorders	450	0.97 (0.87, 1.08)	0.25	0.6156
Infections and infestations	974	1.19 (1.10, 1.29)	19.63	<0.0001
Injury, poisoning and procedural complications	1556	1.44 (1.35, 1.53)	122.48	<0.0001
Investigations	393	0.52 (0.47, 0.58)	139.53	<0.0001
Metabolism and nutrition disorders	71	0.32 (0.25, 0.41)	88.80	<0.0001
Musculoskeletal and connective tissue disorders	643	0.47 (0.43, 0.51)	303.61	<0.0001
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	75	1.77 (1.33, 2.35)	15.00	0.0001
Nervous system disorders	592	1.15 (1.04, 1.26)	7.49	0.0062
Pregnancy, puerperium and perinatal conditions	72	0.32 (0.25, 0.41)	93.74	<0.0001
Product issues*	315	**3.48 (2.96, 4.09)**	253.85	<0.0001
Psychiatric disorders	400	1.25 (1.11, 1.40)	13.07	0.0003
Renal and urinary disorders	168	1.60 (1.32, 1.93)	23.82	<0.0001
Reproductive system and breast disorders*	35	**4.62 (2.73, 7.82)**	37.36	<0.0001
Respiratory, thoracic and mediastinal disorders*	688	**2.10 (1.90, 2.32)**	223.72	<0.0001
Skin and subcutaneous tissue disorders	474	0.57 (0.51, 0.63)	122.47	<0.0001
Social circumstances*	281	**5.27 (4.34, 6.39)**	349.73	<0.0001
Surgical and medical procedures	188	1.19 (1.00, 1.41)	3.72	0.0539
Vascular disorders	177	0.67 (0.57, 0.79)	22.22	<0.0001

ROR = Reporting Odds Ratio; CI = Confidence Interval; SOC = System Organ Class; * = positive signal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2b: Signal strength of reports of Anifrolumab among SLE patients at the System Organ Class (SOC) level

SOC	Cases reporting SOC	ROR (95% CI)	chi-squared	p-value
Blood and lymphatic system disorders	9	1.91 (0.98, 3.73)	2.92	0.0877
Cardiac disorders*	19	**2.15 (1.35, 3.41)**	9.84	0.0017
Congenital, familial and genetic disorders	0	0.00 (0.00, NA)	0.40	0.5296
Ear and labyrinth disorders	2	0.87 (0.22, 3.54)	0.00	1.0000
Endocrine disorders	2	5.59 (1.31, 23.89)	3.27	0.0706
Eye disorders	9	1.75 (0.90, 3.41)	2.08	0.1492
Gastrointestinal disorders	58	1.06 (0.81, 1.39)	0.14	0.7056
General disorders and administration site conditions	107	0.87 (0.71, 1.07)	1.67	0.1969
Hepatobiliary disorders	3	0.45 (0.14, 1.40)	1.51	0.2198
Immune system disorders	34	1.10 (0.78, 1.56)	0.20	0.6541
Infections and infestations	95	1.74 (1.40, 2.16)	24.51	<0.0001
Injury, poisoning and procedural complications	36	0.40 (0.28, 0.55)	30.57	<0.0001
Investigations	29	0.65 (0.44, 0.94)	4.97	0.0257
Metabolism and nutrition disorders	7	0.57 (0.27, 1.20)	1.87	0.1720
Musculoskeletal and connective tissue disorders	56	0.71 (0.54, 0.94)	5.63	0.0177
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2	0.58 (0.14, 2.33)	0.26	0.6134
Nervous system disorders	54	1.54 (1.16, 2.03)	8.64	0.0033
Pregnancy, puerperium and perinatal conditions	2	0.15 (0.04, 0.62)	8.35	0.0038
Product issues	4	0.39 (0.15, 1.05)	3.11	0.0778
Psychiatric disorders	21	0.90 (0.58, 1.40)	0.12	0.7249
Renal and urinary disorders*	23	**2.96 (1.93, 4.53)**	25.70	<0.0001
Reproductive system and breast disorders*	4	**4.36 (1.57, 12.06)**	6.67	0.0098
Respiratory, thoracic and mediastinal disorders	42	1.50 (1.09, 2.06)	5.98	0.0145
Skin and subcutaneous tissue disorders	57	1.18 (0.90, 1.55)	1.27	0.2592
Social circumstances	4	0.53 (0.20, 1.42)	1.23	0.2683
Surgical and medical procedures	0	0.00 (0.00, NA)	10.59	0.0011
Vascular disorders	19	1.18 (0.74, 1.87)	0.33	0.5664

ROR = Reporting Odds Ratio; CI = Confidence Interval; SOC = System Organ Class; * = positive signal

data now show significant adverse effects associated with traditional treatments. Since 2011, two biologics have been approved for SLE, but clinical trials are not always representative of real-world populations, necessitating post-marketing safety evaluation.

Methods: FDA Adverse Event Reporting System data were analyzed using a disproportionality analysis to detect risk signals for each approved biologic. Reporting odds ratios (ROR) were calculated for each system organ class (SOC) and preferred term (PT), defined by the Medical Dictionary for Regulatory Activities.

Results: In 2023, 125,675 primary suspect adverse events (AEs) were reported among individuals with SLE, including 10,737 belimumab and 661 anifrolumab cases. Belimumab AEs occurred in all 27 SOCs and were significant in five [Social circumstances (ROR 5.27, 95% CI 4.34, 6.39), Reproductive system and breast disorders (ROR: 4.62, 95% CI 2.73, 7.82), Product issues (ROR 3.48, 95% CI 2.96, 4.09), Ear and labyrinth disorders (ROR: 2.26, 95% CI 1.61, 3.17), Respiratory, thoracic and mediastinal disorders (ROR: 2.10, 95% CI 1.90, 2.32)]; and anifrolumab AEs occurred in 25 SOCs and were significant in three [Reproductive system and breast disorders (ROR: 4.36, 95% CI 1.57, 12.06), Renal and urinary disorders (ROR: 2.96, 95% CI 1.93, 4.53), Cardiac disorders (ROR: 2.15, 95% CI 1.35, 3.41)].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In total, 169 belimumab PTs and 20 anifrolumab PTs displayed significant disproportionality. The top five belimumab PTs by strength of safety signal were Product complaint (ROR 164.28, 95% CI 22.72, 1187.69), Product storage error (ROR 133.73, 95% CI 18.42, 970.81), Exposure via skin contact (ROR 127.63, 95% CI 17.56, 927.48), Wrong technique in device usage process (ROR 71.09, 95% CI 22.38, 225.82), and Product supply issue (ROR 69.77, 95% CI 9.42, 516.71); for anifrolumab these were Insurance issue (ROR 78.51, 95% CI 17.54, 351.42), Appendicitis (ROR 39.25, 95% CI 11.05, 139.39), Anaphylactic reaction (ROR 31.57, 95% CI 13.34, 74.69), Herpes zoster (ROR 23.15, 95% CI 14.23, 37.65), and Cardiac failure (ROR 19.65, 95% CI 7.12, 54.21).

Conclusion: In belimumab clinical trials, the most common SOC AEs were infections, gastrointestinal, musculoskeletal, nervous system, and skin disorders. Each of these was frequent in this study, but not disproportionately high. However, five other SOCs show significant disproportionality, indicating possible safety concerns not identified in trials.

In anifrolumab clinical trials, the most common SOC AEs were infections, general and administration site conditions, respiratory disorders, and musculoskeletal disorders. None showed disproportionately high safety signals in this study, but three additional SOCs were disproportionately high.

Despite limitations of spontaneous reporting systems, these findings highlight potential safety concerns with biologics in SLE. Further research using real-world data is needed.

Disclosure: S. Crisci: CorEvitas, part of Thermo Fisher Scientific, 3.

Abstract Number: 0667

Retrospective Chart Audit Reveals Gaps in Steroid Tapering and Use of ACR Guideline-Recommended Regimens in LN

Sawyer May[1], Lynn Price[1] and Ryan Rex[2], [1]Spherix Global Insights, Exton, PA, [2]Spherix Global Insights, Chester Springs, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In May 2025, ACR released updated recommendations for the management of LN[2]. Notably, since the previous guidelines update in 2012, the FDA has approved belimumab and voclosporin for the treatment of LN.

Methods: 1,017 moderate-to-severe (M/S) adult SLE patient records were collected in collaboration with 176 US rheumatologists via an online survey platform from January through March 2025. This analysis focuses on a subset of 226 SLE patients with biopsy-proven ISN Class III, IV, or V LN disease. These patients also had to exhibit active, new-onset, or flaring renal disease, defined as an LN diagnosis within the past five years, a flare within the past six months, or active renal involvement at their most recent rheumatology visit.

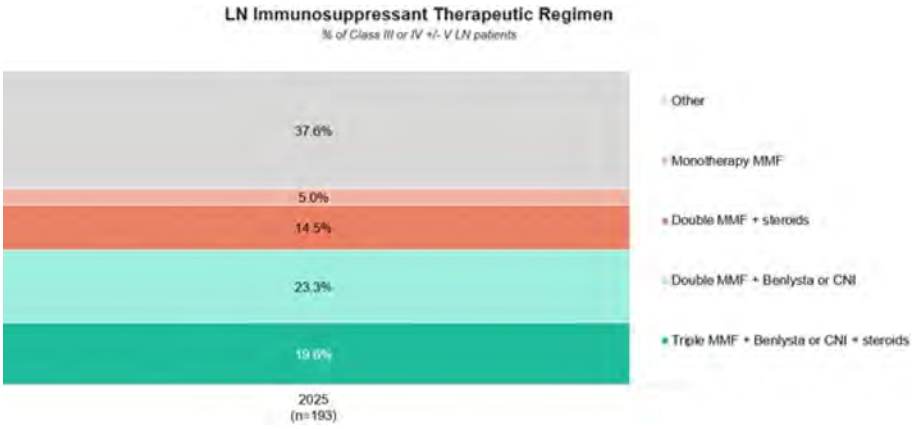
Results: ACR strongly recommends that patients with Class III, IV, or V LN be treated with hydroxychloroquine (HCQ), unless contraindicated. This retroactive chart analysis finds that 88.1% of these patients are currently prescribed HCQ.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

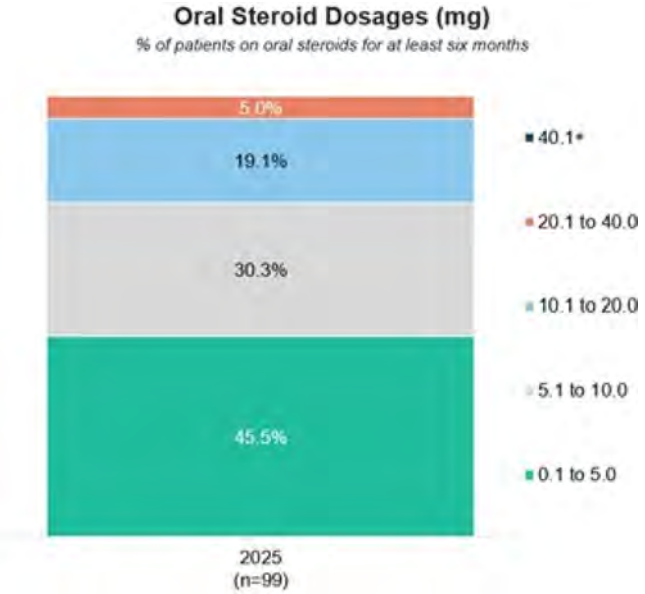
Second, ACR recommends use of RAAS-I therapy for Class III, IV, or V LN patients with any level of proteinuria in their urine. Our analysis shows that 69.3% of these patients are on RAAS-I therapy, most commonly ACE inhibitors such as lisinopril and enalapril.

Third, ACR recommends that oral steroids be tapered to at least 5mg per day within six months of initiating the treatment for Class III, IV, or V LN patients. Furthermore, daily steroid dosages should not exceed 40mg/day. Our analysis shows that 50.4% of patients are currently receiving steroid treatment, with none prescribed more than 40 mg per day. Notably, over half (54.5%) of patients who have been on oral steroids for at least six months are taking doses higher than 5mg daily. Only 51.5% of patients who are on oral steroid dosages exceeding 5mg per day are currently on a regimen consisting of belimumab or a calcineurin inhibitor (CNI), which have been demonstrated to be effective steroid-sparing agents.[3,4]

Fourth, for patients with Class III or IV ± V LN, ACR recommends a triple therapy regimen of steroids, MMF or cyclophosphamide (CYC), and either a CNI or belimumab. Among the 193 patients meeting these criteria, 19.6% are currently prescribed MMF and steroids in combination with a CNI or belimumab. Furthermore, 23.3% of patients are prescribed MMF and belimumab or a CNI without steroids.



LN Immunosuppressant Therapeutic Regimen



Oral Steroid Dosages (mg)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Currently, rheumatologists frequently prescribe HCQ and RAAS-I therapies to their LN patients, in line with the updated ACR guidelines. However, many patients remain on high-dose steroids after six months of treatment. Nearly half of those on high-dose steroids are not prescribed a CNI or belimumab, suggesting an opportunity to reduce steroid use through broader use of these drugs. Additionally, only a minority of qualified Class III or IV ± V patients are on a double therapy regimen (MMF or CYC + belimumab or a CNI ± steroids), underscoring the potential impact guideline adoption could have on the management of this disease.

Disclosure: S. May: None; **L. Price**: None; **R. Rex**: None.

Abstract Number: 0668

Glucocorticoid-Sparing Effects and Flare Suppression: Metformin Versus SGLT2 Inhibitors in Systemic Lupus Erythematosus

Takeshi Suzuki, Yoshiki Ishizaki, Takayasu Ando, Shotaro Suzuki, Keiichi Sakurai, Kumiko Tonooka, Yukiko Takakuwa, Hiroko Nagafuchi, Seido Ooka and Kimito Kawahata, St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: While both metformin (MET) and SGLT2 inhibitors (SGLT2i) have potential immunomodulatory effects in Systemic Lupus Erythematosus (SLE), their comparative efficacy in glucocorticoid (GC)-sparing remains unclear. This study aims to compare GC discontinuation and flare suppression between MET and SGLT2i in SLE patients.

Methods: This is a retrospective cohort study using TriNetX's Global collaborative network. We defined a cohort of SLE patients (ICD-10 M32) prescribed hydroxychloroquine and with anti-dsDNA antibody testing. Within this cohort, patients initiating glucocorticoid treatment (prednisolone or prednisone) were then categorized into two distinct groups for analysis: the MET group, comprising those subsequently prescribed metformin, and the SGLT2i group, comprising those subsequently prescribed a SGLT2i after glucocorticoid exposure. The primary endpoint was GC discontinuation (defined as no GC prescriptions) within a 3-12 month period following the index prescription of MET or an SGLT2i. Primary outcome sensitivity analyses focused on GC tablets ≤5 mg, with additional analyses in the glucocorticoid ≤5 mg tablet group when MET or SGLT2 inhibitors were subsequently prescribed. The secondary endpoint, assessed in patients from both groups who had discontinued GC, was GC reinitiation within a 3-month to 3-year period. The primary endpoint was compared between groups using the Chi-squared test. For the secondary endpoint, comparisons were made after propensity score matching (age, sex, race, BMI, anti-dsDNA antibody, complements, MMF, Belimumab, Anifrolumab, Diabetes mellitus, HbA1c, Heart failure, End-stage renal disease, Chronic kidney disease, unspecified) utilizing the TriNetX platform.

Results: MET was initiated in 1228 patients, with 89.5% being women, and the mean age was 56 ± 14 years. SGLT2i was initiated in 718 patients, with 82.4% being women, and the mean age was 55±17 years. The duration of SLE disease before the first prescription of MET and SGLT2i was 1827 ± 1386 and 2593 ± 1608 days, respectively. Mycophenolic acid use was 71% in the SGLT2i group and 53% in the MET group. Baseline HbA1c levels were numerically higher in the MET group (6.3 ± 1.4%) than in the SGLT2i group (5.8 ± 1.13%). Among these patients, GC was discontinued in 445 (36.2%) patients in the MET group and in 488 (68.4%) patients in the SGLT2i group. GC discontinuation was significantly more frequent in the SGLT2i group ($p < 0.001$; Odds Ratio [OR] 3.85, 95% CI 3.23-4.60). The sensitivity analyses corroborated the primary

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

results. After propensity score matching of patients who had discontinued GC, 248 patients remained in each group for the secondary endpoint analysis. In this propensity score-matched cohort, the GC reinitiation rate within 3 months to 3 years after GC discontinuation was significantly lower in the SGLT2i group (10.1%) compared to the MET group (23.0%) ($p < 0.0001$; OR 3.87, 95% CI 1.60-4.43).

Conclusion: In SLE patients treated with GC, SGLT2i use was associated with a significantly higher rate of GC discontinuation and a lower rate of subsequent GC reinitiation compared to MET. These findings suggest that SGLT2 inhibitors may offer a superior GC-sparing effect in SLE patients.

Disclosure: T. Suzuki: None; **Y. Ishizaki**: None; **T. Ando**: None; **S. Suzuki**: None; **K. Sakurai**: None; **K. Tonooka**: None; **Y. Takakuwa**: None; **H. Nagafuchi**: None; **S. Ooka**: None; **K. Kawahata**: None.

Abstract Number: 0669

Clinical and Laboratory Factors Associated With Biopsy-Confirmed Antimalarial-Induced Cardiomyopathy

Youngmin Kim[1], Norioscar Cabello[2], Robert Padera[2], Brittany Weber[3] and Karen H. Costenbader[4], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, DEDHAM, MA, [4]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is widely prescribed in rheumatology, particularly for systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Though generally safe, HCQ can cause rare but serious antimalarial-induced cardiotoxicity (AMIC). AMIC diagnosis is challenging, as cardiac biopsy with electron microscopy (EM) remains the gold standard but is invasive. This study evaluated screening practices for AMIC among HCQ users, focusing on clinical, imaging, and laboratory assessments performed prior to cardiac biopsy.

Methods: We conducted a retrospective review of patients with HCQ exposure who underwent native heart biopsy at our large academic medical center. Biopsy reports were reviewed for AMIC features (e.g., curvilinear, lamellar, myeloid bodies) or other findings. Structured EHR data were extracted for demographics, diagnoses, HCQ prescription dates, cardiac biomarkers (Troponin-I/T, NT-proBNP, CK-MB, hsCRP), and cardiac testing (EKG, echocardiogram, cardiac MRI) prior to biopsy. HCQ exposure duration was calculated from first prescription to biopsy. Abnormal biomarkers were defined by any elevated result prior to biopsy. Group comparisons used t-tests, Fisher's exact tests, ANOVA, and Tukey's HSD post-hoc tests.

Results: Among 73 HCQ users who underwent biopsy, 15 had biopsy-confirmed AMIC and 58 did not. AMIC patients more frequently had SLE (80% vs. 38%, p=0.007), while other baseline characteristics (age, sex, race, HCQ duration) did not differ significantly (**Table 1**). Mean HCQ duration before biopsy was longer in patients with AMIC on biopsy (283 vs. 205 weeks). Few patients had cardiac biomarker testing prior to biopsy, but abnormalities were more common in AMIC, including elevated troponin-T (63% vs. 35%) and CK-MB (56% vs. 32%), though not statistically significant. Cardiac MRI was also underutilized: 53% in AMIC vs. 35% in non-AMIC. Among non-AMIC patients, only 12 (21%) had EM performed as AMIC was not suspected on toluidine blue staining (**Table 2**). Most biopsies showed non-specific findings such as hypertrophy (74%), fibrosis (45%), and vacuolization (21%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, clinical, laboratory, and cardiac imaging characteristics of 73 patients with biopsy-confirmed antimalarial-induced cardiomyopathy (AMIC) and patients without AMIC (non-AMIC)

	AMIC (n = 15)	Non-AMIC (n = 58)	*p*
Demographics			
Age (mean, SD)	65.7 (13.5)	63.3 (12.0)	0.54
Females (*n*, %)	12 (80.0)	40 (69.0)	0.53
Whites (*n*, %)	12 (80.0)	45 (77.6)	1
Hydroxychloroquine Duration Prior to Biopsy (Weeks; mean, SD)	282.6 (362.6)	204.8 (300.7)	0.47
Rheumatologic Diagnosis			
Systemic Lupus Erythematosus (*n*, %)	12 (80.0)	22 (37.9)	0.007
Rheumatoid Arthritis (*n*, %)	2 (13.3)	16 (27.6)	0.33
Sarcoidosis (*n*, %)	0 (0)	6 (10.3)	0.34
Vasculitis (*n*, %)	1 (6.7)	1 (1.7)	0.37
Myositis (*n*, %)	0 (0)	3 (5.2)	1
Cardiac Biomarker Abnormalities			
Troponin-I (n, % of tested)	1/6 (16.7)	3/19 (15.8)	1.00
Troponin-T (n, % of tested)	5/8 (62.5)	7/20 (35.0)	0.23
CKMB (n, % of tested)	5/9 (55.6)	11/34 (32.4)	0.26
NT-BNP (n, % of tested)	7/9 (77.8)	15/20 (75.0)	1.00
hs-CRP (n, % of tested)	3/4 (75.0)	3/9 (33.3)	0.27
Cardiac Tests			
Electrocardiography	15 (100.0)	51 (87.9)	0.33
Echocardiography	13 (86.7)	45 (77.6)	0.72
Cardiac MRI	8 (53.3)	20 (34.5)	0.24

Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. p-values were calculated using Fisher's exact test for categorical variables and Student's t-test for continuous variables. AMIC: antimalarial-induced cardiomyopathy; HCQ: hydroxychloroquine; cBx: cardiac biopsy; SLE: systemic lupus erythematosus; CKMB: creatine kinase myocardial band; NT-BNP: N-terminal pro B-type natriuretic peptide; hs-CRP: high-sensitivity C-reactive protein.

Table 2. Features of Cardiac Biopsies in Patients Without Confirmed AMIC (n = 58)

Indications for Biopsy, Suspected Diagnoses	***n* (%)**
Cardiomyopathy	26 (44.8)
Sarcoidosis	6 (10.3)
Amyloidosis	5 (8.6)
Myocarditis	4 (6.9)
Connective Tissue Disease (SLE, EGPA)	9 (15.5)
AMIC	2 (3.4)
Autopsy	2 (3.4)
Heart Failure	4 (6.9)
H&E Biopsy Findings/Final Diagnosis	
Myocyte Vacuolization	12 (20.7)
Myocyte Hypertrophy	43 (74.1)
Interstitial Fibrosis	26 (44.8)
Ischemic Heart Disease	5 (8.6)
Amyloidosis	3 (5.2)
Sarcoidosis	2 (3.4)
Electron Microscopy	
Not performed as low suspicion AMIC	46 (79.3)
Confirmed Absence of AMIC	12 (20.7)

Conclusion: This study provides one of the largest biopsy-confirmed AMIC case series to date, comparing findings to those of patients taking HCQ who had cardiac biopsies in which AMIC was not confirmed. Few patients underwent cardiac biomarker testing or advanced imaging before biopsy, revealing missed opportunities for earlier detection. These findings underscore the need for non-invasive AMIC screening strategies to improve recognition, estimate disease burden, and enable timely intervention.

Disclosure: Y. Kim: None; **N. Cabello**: None; **R. Padera**: None; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0670

Clinical Significance of Therapeutic Drug Level Monitoring for Mycophenolate in Patients With Extra-renal Systemic Lupus Erythematosus – A Systematic Review & Meta-analysis

Zahraa Qamhieh[1], Dalia Sriwi[1], Callie Saric[2], Tripti Singh[3], Christie Bartels[4] and Shivani Garg[5], [1]University of Wisconsin, Madison, Department of Medicine, Madison, WI, [2]University of Wisconsin, Madison, School of Medicine and Public Health, Madison, WI, [3]University of Wisconsin, Madison, Department of Nephrology, Madison, WI, [4]University of Wisconsin School of Medicine and Public Health, Madison, WI, [5]University of Madison, School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0641–0670) Systemic Lupus Erythematosus – Treatment Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical response to Mycophenolic acid (MPA) is highly heterogeneous; thus, therapeutic drug monitoring (TDM) of MPA could help improve treatment efficacy. Our objective in this systematic review and meta-analysis was to examine therapeutic ranges for MPA levels that are associated with better outcomes and safety in patients with SLE, particularly those with extra-renal SLE manifestations.

Methods: We performed a comprehensive search of studies measuring an association between MPA levels and clinical SLE response. Using forest plots, we calculated pooled odds of clinical response by MPA levels. Additionally, we measured the weighted mean difference in MPA levels across clinical outcomes. Analysis was performed in all patients with SLE, then separately in patients with extra-renal SLE manifestations.

Results: Among 459 reviewed abstracts, 24 met inclusion. Summarized evidence supported maintaining MPA AUC0-12 levels within 30-60 mg h/L or MPA C12 within 1-2.5 mg/L; these levels were not associated with higher adverse events. Therapeutic MPA levels were associated with 12-fold higher odds (95% CI 5.44-27.35, $P < 0.0001$, $I2 = 41\%$) of overall clinical SLE response, and 15-fold higher odds (95% CI 4.74–46.89); $p < 0.0001$; I2=61%) of clinical response in patients with extra-renal manifestations. Additionally, MPA levels were 32 units higher (95% CIs 17.35 45.67) in overall SLE responders, and 39 units (95% CI 15.05-62.53) higher in patients with extra-renal manifestations.

Conclusion: This study highlights the clinical utility of TDM to guide precise MPA dosing to balance efficacy vs. safety in all patients with SLE, including those with extra-renal manifestations.

Disclosure: Z. Qamhieh: None; **D. Sriwi**: None; **C. Saric**: None; **T. Singh**: None; **C. Bartels**: None; **S. Garg**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0671

The Gut-Heart Axis in Systemic Sclerosis: Evidence from the GENISOS cohort

Francesca Romana Di Ciommo[1], Ashish Balar[2], Subhash Kulkarni[3], Aidan K Strother[2], Michael Hughes[4], Brian Skaug[5], Maureen Mayes[6], Shervin Assassi[7], **Ali Y Ayla**[2] and Zsuzsanna McMahan[8], [1]La Sapienza University of Rome, Rome, Italy, [2]UTHealth Houston, Houston, TX, [3]BIDMC, Boston, MA, [4]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [5]UTHealth Houston Division of Rheumatology, Houston, TX, [6]UT Health Houston Division of Rheumatology, Houston, TX, [7]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [8]UT Health Houston, Houston, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiac manifestations significantly impact the prognosis of patients with systemic sclerosis (SSc), underscoring the need for early risk stratification. While gastrointestinal (GI) symptoms are common and impair quality of life, their role as predictors of cardiac involvement remains unclear. Emerging data suggest a link between GI and cardiac manifestations, possibly through shared mechanisms like dysautonomia and immune-mediated damage to mesodermally derived neurons. This study explores whether baseline GI symptoms could serve as early indicators of future cardiac events, aiming to identify high-risk phenotypes for personalized management.

Methods: We analyzed data from 459 patients with early SSc enrolled in a prospective cohort. GI and cardiac manifestations were comprehensively evaluated both at baseline and during follow-up. GI involvement was defined as the presence of one or more of the following symptoms: dysphagia, peptic ulcer, bloating, diarrhea, malabsorption, constipation, or pseudo-obstruction. To assess whether any of these early GI symptoms could predict the later development of cardiac complications—specifically conduction abnormalities or cardiomyopathy—we applied multivariable logistic regression and Cox models, adjusting for key confounders such as age, sex, and disease duration.

Results: At baseline, GI involvement was present in 60% of patients with early systemic sclerosis. During follow-up, 26% of these patients developed cardiac complications, mainly conduction defects (24%) and less frequently cardiomyopathy (5%).

Table 1. Associations between GI manifestations and cardiac complications* in SSc patients over time: results from logistic models. Definition of GI manifestations: (a) Dysphagia, defined as pain or difficulty in swallowing or passing food; (b) Peptic ulcer, documented; (c) Bloating; (d) Diarrhea; (e) Malabsorption, confirmed by diarrhea associated with >10% weight loss or by abnormal chemical studies. Symptoms from (c) to (d) were self-reported by patients. *Cardiac complications refers to the following domains: cardiomyopathy and conduction defects. § Refers to the age at the time of the first cardiac complication (if applicable) or the maximum age reached during the study period (if no cardiac complication occurred). # Refers to disease duration from the first non-Raynaud symptom to the time of the first cardiac complication (if applicable), or to the maximum disease duration reached during the study period (if no cardiac complication occurred). Values are Odds Ratio (95% confidence interval). † Statistically significant.

Characteristic	Univariate logistic Regression: model 1	Conditional logistic adjusted for age §, sex and disease duration#: model 2	Conditional logistic including all significant variables: Model 3
Age, (years) §	0.99 (0.98-1.02)	/	1.01 (0.99-1.03)
Sex, (female)	**0.49 (0.28-0.85) †**	/	**0.46 (0.22-0.93) †**
Disease duration#	**0.78 (0.72-0.84) †**	/	**0.74 (0.67-0.81) †**
Dysphagia	**2.03 (1.23-3.36) †**	**3.68 (1.97-6.88) †**	**2.66 (1.36-5.21) †**
Peptic ulcer	**2.95 (1.48-5.87) †**	**3.08 (1.34-7.10) †**	2.22 (0.89-5.49)
Bloating	**2.42 (1.53-3.83) †**	**4.13 (2.32-7.34) †**	**3.27 (1.73-6.16) †**
Diarrhea	**1.58 (1.01-2.48) †**	**1.90 (1.10-3.27) †**	0.94(0.49-1.80)
Malabsorption	**2.63 (1.30-5.29) †**	2.09 (0.88-4.93)	0.86 (0.31-2.38)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Baseline GI predictors of cardiac complications*in patients with systemic sclerosis. Definition of GI predictors: (a) Dysphagia, defined as pain or difficulty in swallowing or passing food; (b) Bloating; (c) Diarrhea; (d) Malabsorption, confirmed by diarrhea associated with >10% weight loss or by abnormal chemical studies. Symptoms (b) and (c) were self-reported by patients. *Cardiac complications refers to cardiomyopathy and/or conduction defects. Values are Hazard Ratios (95% confidence interval). § Refers to the age at baseline. # Refers to the disease duration from the first non-Raynaud symptom at baseline. † Statistically significant.

Characteristic	Cox regression	Cox regression adjusted for age§, sex and disease duration#
Any GI	**1.45 (1.02-2.07)**	1.19 (0.79-1.78)
Upper GI	1.19 (0.84- 1.67)	1.11 (0.74-1.669
Dysphagia	1.24 (0.88-1.75)	1.14 (0.76-1.70)
Lower GI	**1.82 (1.3-2.56) †**	1.40 (0.93-2.13)
Bloating	**2.79 (1.91-4.10) †**	**2.72 (1.71 – 4.32) †**
Diarrhea	1.06 (0.69-1.64)	1.21 (0.73-2.10)
Malabsorption	**19.90 (9.89-40.06) †**	**33.56 (15.85-71.06) †**

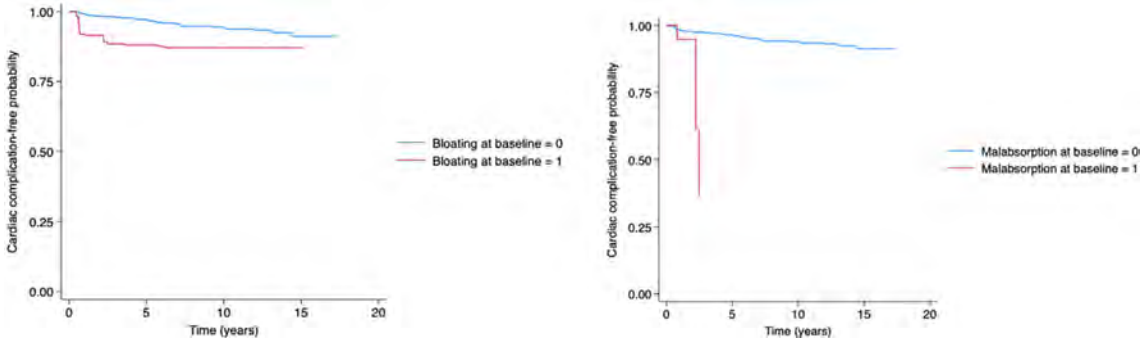


Figure 1. Kaplan-Meier analysis of time to cardiac complications* onset according to baseline bloating and malabsorption. *Cardiac complications refers to cardiomyopathy and/or conduction defects. Log-rank test: Bloating at baseline, $p < 0.001$; Malabsorption at baseline, $p < 0.001$.

A significant association was found between GI manifestations and cardiac involvement, with bloating showing the strongest association (OR 3.3, 95% CI 1.7–6.2), even after adjustment in the multivariable model (Tab.1). We then examined the strength of the association between individual GI symptoms and the two cardiac complications. Notably, upper GI symptoms like dysphagia (OR 3.3; 95% CI: 1.8–6.0) and peptic ulcers (OR 3.2; 95% CI: 1.5–7.2) were specifically associated with conduction defects, while malabsorption was strongly associated with cardiomyopathy (OR 4.6; 95% CI: 1.4–15.0). These associations remained robust even in the multivariable model. Cox regression was then applied to identify baseline GI symptoms in SSc patients that predict cardiac complications. Interestingly, malabsorption and bloating emerged as the strongest predictors of subsequent cardiac complication with malabsorption in particular conferring the highest risk, with a hazard ratio (HR) of 33.6 (95% CI: 15.8–71.1), after adjusting for potential confounders (Fig.1) (Tab.2).

Conclusion: Upper GI symptoms were selectively associated with cardiac conduction defects, suggesting that autonomic nervous system dysfunction may contribute to this relationship. In contrast, lower GI involvement—particularly malabsorption—was linked to cardiomyopathy in early SSc, pointing to a possible shared mechanism. If confirmed in other early SSc cohorts, these findings support the integration of early GI symptoms into cardiac risk stratification and highlight the importance of targeting these patient subgroups in future translational research.

Disclosure: F. Di Ciommo: None; **A. Balar**: None; **S. Kulkarni**: None; **A. Strother**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **B. Skaug**: None; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, Teneo-Four, 2; **A. Ayla**: None; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0672

Determinants of Progressive Microstomia in Systemic Sclerosis: Insights from the GENISOS Cohort with a Focus on GI Involvement

Francesca Romana Di Ciommo[1], **Ashish Balar**[2], Robert M. Anderton[2], Michael Hughes[3], Brian Skaug[4], Maureen Mayes[5], Shervin Assassi[6], Ali Y Ayla[2] and Zsuzsanna McMahan[7], [1]La Sapienza University of Rome, Rome, Italy, [2]UTHealth Houston, Houston, TX, [3]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [4]UTHealth Houston Division of Rheumatology, Houston, TX, [5]UT Health Houston Division of Rheumatology, Houston, TX, [6]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [7]UT Health Houston, Houston, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a complex autoimmune condition characterized by vascular abnormalities, immune dysregulation, and progressive fibrosis affecting both the skin and internal organs. Among its manifestations, facial and perioral involvement may lead to mouth opening reduction, known as microstomia, which negatively impacts nutrition, oral hygiene, and the tolerance of procedures like endoscopy or intubation. Despite its clinical impact, it remains unknown who will develop microstomia, and whether it is predictive of other SSc complications. This study aims to determine the evolution of microstomia over time, identify predictors of its progression, and explore its potential association with systemic manifestations of SSc.

Methods: We conducted a longitudinal analysis in the GENISOS cohort, including SSc patients with serial measurements of maximal mouth opening (MO), defined as the distance between the upper and lower lips. The percentage reduction in mouth opening was calculated from baseline to the minimum value recorded for each patient. Only patients with at least two observations separated by at least 6 months were included. Based on the distribution of MO percentage reduction values, a cut-off of 12.3% from baseline (top third of patients with the most significant MO change) was used *a priori* to define severe microstomia. Patients with a reduction >12.3% were classified as severe (group 2) and compared to those with a reduction $\leq$ 12.3% (group 1). Clinical variables, including disease duration, skin involvement, and symptoms of internal organ dysfunction (e.g., dysphagia), were compared across groups. Logistic and Cox regression models were used to identify predictors of severely reduced MO.

Table1. Longitudinal Comparison of Demographic and Clinical Characteristics in GENISOS SSc Patients With (Group 2) and Without (Group 1) Severe Reduction in Oral Aperture. MO= mouth opening;SD standard deviation; IQR = interquartile range; FVC = forced vital capacity; DLco =diffusing capacity for carbon monoxide; p p-value; GERD = gastroesophageal reflux disease; mRSS = modified Rodnan Skin Score * Age at the date of minimum oral aperture. § Disease duration from any symptom to the date of minimum oral aperture. ‡ Maximum Medsger general, GI, skin, lung, peripheral vascular, and muscle severity score of >1; Maximum Medsger cardiac and joint severity score of >1. # Value is expressed as a percentage. FVC and DLco are represented by the minimum values ever recorded. † Statistically significant.

Characteristic	Univariate logistic Regression: model 1	Conditional logistic adjusted for age §, sex and disease duration#: model 2	Conditional logistic including all significant variables: Model 3
Age, (years) §	0.99 (0.98-1.02)	/	1.01 (0.99-1.03)
Sex, (female)	**0.49 (0.28-0.85) †**	/	**0.46 (0.22-0.93) †**
Disease duration#	**0.78 (0.72-0.84) †**	/	**0.74 (0.67-0.81) †**
Dysphagia	**2.03 (1.23-3.36) †**	**3.68 (1.97-6.88) †**	**2.66 (1.36-5.21) †**
Peptic ulcer	**2.95 (1.48-5.87) †**	**3.08 (1.34-7.10) †**	2.22 (0.89-5.49)
Bloating	**2.42 (1.53-3.83) †**	**4.13 (2.32-7.34) †**	**3.27 (1.73-6.16) †**
Diarrhea	**1.58 (1.01-2.48) †**	**1.90 (1.10-3.27) †**	0.94(0.49-1.80)
Malabsorption	**2.63 (1.30-5.29) †**	2.09 (0.88-4.93)	0.86 (0.31-2.38)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Cox Regression Analysis of Risk Factors for Severe Oral Aperture Reduction in SSc Patients. Definition of Gastrointestinal manifestations: (a) Dysphagia, defined as pain or difficulty in swallowing or passing food; (b) Peptic ulcer, documented; (c) Bloating; (d) Diarrhea; (e) Malabsorption, confirmed by diarrhea associated with >10% weight loss or by abnormal chemical studies. Symptoms from (c) to (d) were self-reported by patients. *It refers to the age at baseline (years). # It refers to the disease duration from the first non-Raynaud symptom at baseline (years). §Values are Hazard ratio (95% confidence interval). † Statistically significant.

Characteristic	Cox regression	Cox regression adjusted for age§, sex and disease duration#
Any GI	**1.45 (1.02-2.07)**	1.19 (0.79-1.78)
Upper GI	1.19 (0.84- 1.67)	1.11 (0.74-1.669
Dysphagia	1.24 (0.88-1.75)	1.14 (0.76-1.70)
Lower GI	**1.82 (1.3-2.56) †**	1.40 (0.93-2.13)
Bloating	**2.79 (1.91-4.10) †**	**2.72 (1.71 - 4.32) †**
Diarrhea	1.06 (0.69-1.64)	1.21 (0.73-2.10)
Malabsorption	**19.90 (9.89-40.06) †**	**33.56 (15.85-71.06) †**

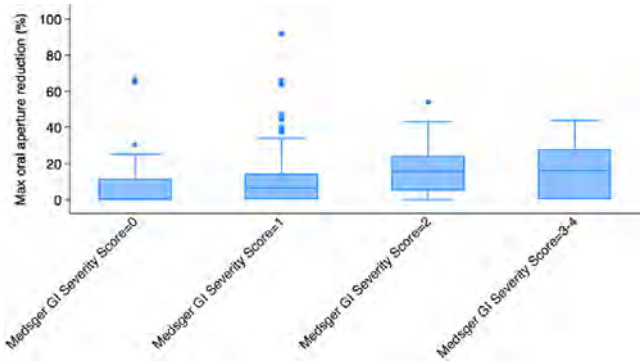


Figure 1. Distribution of maximal percent reduction in oral aperture across worsening Medsger GI Severity Scores. Score 0 (n = 52): median 0%, IQR 0–11.55 Score 1 (n = 241): median 6.25%, IQR 0–14.28 Score 2 (n = 31): median 15.55%, IQR 5–24 Score 3–4 (n = 18): median 16.1%, IQR 0–28 The p-value was calculated using the Kruskal-Wallis test to compare differences between groups. P-value < 0.001

Results: Patients with mild-to-moderate MO reduction (group 1) reached their lowest MO after a median of 0 months from baseline (IQR: 0.0-1.0), while those in the severe group (group 2) reached their lowest point after a median of 1.9 years (IQR: 0.9- 4.15). The severe group had a longer disease duration and a higher prevalence of facial telangiectasia and xerostomia. GI involvement was significantly more prevalent in group 2, with symptoms such as dysphagia, peptic ulcers, diarrhea, bloating, and malabsorption being particularly frequent (Table 1) (Figure 1). Multivariate analysis showed that longer disease duration (OR 1.2 per year; 95% CI 1.1–1.3) and GI Severity Score >1 (OR 2.7; 95% CI 1.1–6.5) were independently associated with severe reduction in MO. Cox regression confirmed that baseline GI involvement (GI Severity Score >1) predicted severe MO reduction (>12.3%) (HR 2.3; 95% CI 1.8–3.0), with baseline dysphagia (HR:1.4; 95% CI 1.2–1.7) and/or diarrhea (HR:1.8; 95% CI 1.5–2.2) being the strongest predictors (Table 2).

Conclusion: Early GI symptoms—particularly dysphagia and diarrhea—were significantly associated with severe microstomia, suggesting that microstomia may serve as an external marker of progressive internal GI involvement. These findings highlight a potential shared pathophysiological mechanism and underscore the need for further studies to validate this association and elucidate the underlying connection.

Disclosure: F. Di Ciommo: None; **A. Balar**: None; **R. Anderton**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **B. Skaug**: None; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **A. Ayla**: None; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2.

Abstract Number: 0673

Association Between Vasoactive-vasodilating Therapy and Reduced Detection of Pulmonary Arterial Hypertension in Systemic Sclerosis: Evidence from a EUSTAR Study

Nicola Farina[1], Silvia Bellando-Randone[2], SEBASTIEN SANGES[3], hilde Bjørkekjær[4], lorenzo tofani[5], Marie-Elise Truchetet[6], Vanessa Smith[7], Andra Balanescu[8], Christina Bergmann[9], Yannick Allanore[10], Philipp Klemm[11], simona Truglia[12], Luca Idolazzi[13], Christopher Denton[14], Roberta Foti[15], anna Wojteczek[16], Emmanuel Chatelus[17], Madelon Vonk[18], Serena Guiducci[19], David Launay[20], Eric Hachulla[21], Jeska de Vries-Bouwstra[22], Anna-Maria Hoffmann-Vold[23], Marco Matucci-Cerinic[24], Oliver Distler[25] and **Cosimo Bruni**[26], [1]Department of Experimental and Clinical Medicine, Scleroderma Unit, Division of Rheumatology, University of Florence, Azienda Ospedaliera Universitaria Careggi, Florence, Italy. Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Hospital, Milan, Italy, Milan, Italy, [2]University of Florence, Florence, Florence, Italy, [3]Medecine Interne CHRU Lille, Lille, France, [4]Department of Rheumatology, Hospital of Southern Norway, Kristiansand, Norway, olso, Norway, [5]Department of Statistics, Informatics and Applications, University of Florence, Florence, Italy, firenze, Italy, [6]Bordeaux University Hospital, Bordeaux, France, [7]Ghent University Hospital, Gent, Belgium, [8]UNIVERSITY OF MEDICINE AND PHARMACY CAROL DAVILA, Bucharest, Romania, [9]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [10]Université Paris Cité, Paris, France, [11]Department of Rheumatology and Clinical Immunology Center, JLU Giessen, Campus Kerckhoff, Bad Nauheim, Germany, Bad Nauheim, Germany, [12]Reumatologia, Azienda Ospedaliero-Universitaria Policlinico Umberto I, Rome, Italy, rome, Italy, [13]Section of Rheumatology, Department of Medicine, University of Verona, Verona, Italy, verona, Italy, [14]University College London, UK, London, United Kingdom, [15]Division of Rheumatology, A.O.U. Policlinico-San Marco, Catania, Italy, Catania, Italy, [16]Department of Rheumatology, Clinical Immunology, Geriatrics and Internal Medicine, Medical University of Gdańsk, University Clinical Centre, Gdańsk, Poland, Gdańsk, Poland, [17]Department of Rheumatology, University Hospital Strasbourg, France, Strasbourg, France, [18]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, [19]Department of Experimental and Clinical Medicine, Scleroderma Unit, Division of Rheumatology, University of Florence, Azienda Ospedaliera Universitaria Careggi, Florence, Italy, Pistoia, Italy, [20]Univ. Lille, Inserm, CHU Lille, Department of Internal Medicine and Clinical Immunology, Reference Center for Rare Autoimmune and Autoinflammatory diseases (CERAINOM), U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France. National Reference Center for Pulmonary Arterial Hypertension (Pulmotension), Lille, France, Lille Cedex, France, [21]University of Lille, LILLE, France, [22]Leiden University Medical Center, Leiden, Netherlands, [23]Oslo University Hospital, Oslo, Norway, [24]University San Raffaele Milano, Milano, Milan, Italy, [25]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [26]University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Vasoactive-vasodilating drugs (VVD) are the cornerstone of the treatment of pulmonary arterial hypertension (PAH), a form of precapillary pulmonary hypertension (pPH) that represents a severe complication of systemic sclerosis (SSc). VVD include the categories of endothelin receptor antagonists (ERAs), phosphodiesterase type 5 inhibitors (PDE5i) and prostanoids, which are commonly used in SSc to treat digital ulcers (DU) and Raynaud's phenomenon. As additional protective effects remain unclear, we investigated the effectiveness of VVD on the primary prevention of pPH and, specifically, of PAH.

Methods: SSc patients from the European Scleroderma Trials and Research (EUSTAR) cohort who underwent right heart catheterization (RHC) were included; postcapillary PH cases (pulmonary wedge pressure – PWP >15 mmHg) were excluded.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Data about demographics, disease features, immunosuppressive and vasoactive treatment exposure and right heart catheterization from the study population, compared between patients with and without precapillary pulmonary hypertension. ACA, anti-centromere antibody; b/csDMARDs, biologic/conventional synthetic anti-rheumatic disease modifying drugs; DLCO, diffusion lung capacity of carbon monoxide; ERA, endothelin receptor antagonists; FVC, forced vital capacity; NYHA, New York Heart Association; PH, pulmonary hypertension; PDE5i, phosphodisterase 5 inhibitors; SSc, systemic sclerosis; sPAP, systolic pulmonary arterial pressure.

	All patients (n=944)	Patients without PH (n=446)	Patients with PH (n=498)	*p-value*
Female sex	761 (81%)	350 (79%)	411 (83%)	0.116
Age (years)	61 ± 12	59 ± 13	64 ± 11	**<0.001**
Diffuse SSc	344 (36%)	185 (42%)	159 (32%)	**0.002**
Disease duration (years)	11 ± 9	10 ± 9	12 ± 9	**<0.001**
ACA positivity	438 (46%)	170 (38%)	268 (54%)	**<0.001**
Current digital ulcers	404 (43%)	206 (46%)	198 (40%)	**0.046**
Telangiectasias	706 (75%)	311 (70%)	395 (79%)	**< 0.001**
Dyspnea (NYHA class >I)	709 (75%)	303 (68%)	406 (82%)	**< 0.001**
ILD on HRCT	526 (56%)	240 (54%)	286 (57%)	0.263
Glucocorticoids ever	50 (5%)	23 (5%)	27 (5%)	0.318
csDMARD ever	245 (26%)	124 (28%)	121 (24%)	0.220
bDMARD ever	41 (4%)	22 (5%)	19 (4%)	0.400
FVC (% predicted)	86 ± 23	89 ± 22	84 ± 23	**< 0.001**
DLCO (% predicted)	54 ± 19	61 ± 18	49 ± 18	**< 0.001**
Diastolic dysfunction	240 (25%)	98 (22%)	142 (29%)	**0.021**
sPAP on Echo (mmHg)	39 ± 16	32 ± 9	46 ± 18	**< 0.001**
ERA, ever	181 (19%)	63 (14%)	118 (24%)	**< 0.001**
PDE5i, ever	111 (12%)	27 (6%)	84 (17%)	**< 0.001**
Prostanoids, ever	128 (14%)	64 (14%)	64 (13%)	0.502

Multivariable logistic regression assessed the association between exposure to VVD and detection of pPH (mPAP >20 mmHg, PVR>2 WU and PWP≤15 mmHg) and of PAH (pPH, ILD extent < 20% and FVC >70%).

Models 1 & 2 tested the exposure at the time of RHC *ever* and *ongoing* to VVD categories (ERAs, PDE5i and prostanoids), *models 3 & 4* tested the same for specific VVD molecules.

The primary outcome was the diagnosis of precapillary PH; PAH was analyzed as sensitivity analyses.

All models were adjusted for known confounders, including DLCO, age, current DU and systolic PAP on echocardiography. Interaction terms between VVDs and current DU were also tested.

Results: Among 944 eligible patients, 498 (53%) were diagnosed with pPH, of whom 367 (74%) had PAH **(Table 1)**.

For VVD classes, a statistically significant association was detected for the interaction of ERAs and current DU with the detection of pPH, in both logistic regression models 1 and 2 (**Figure 1a** and **1b**). However, this finally resulted in a non-significant association between ERAs exposure in patients with current DU and PH detection when calculating marginal effects estimates (ERAs ongoing: OR 0.435, 95% CI 0.193 - 1.064; ERAs ever: OR 0.636, 95% CI 0.349 - 1.158). Additionally, both models showed lack of effectiveness of ERAs in patients without current DU, as well as for PDE5i or prostanoids overall.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

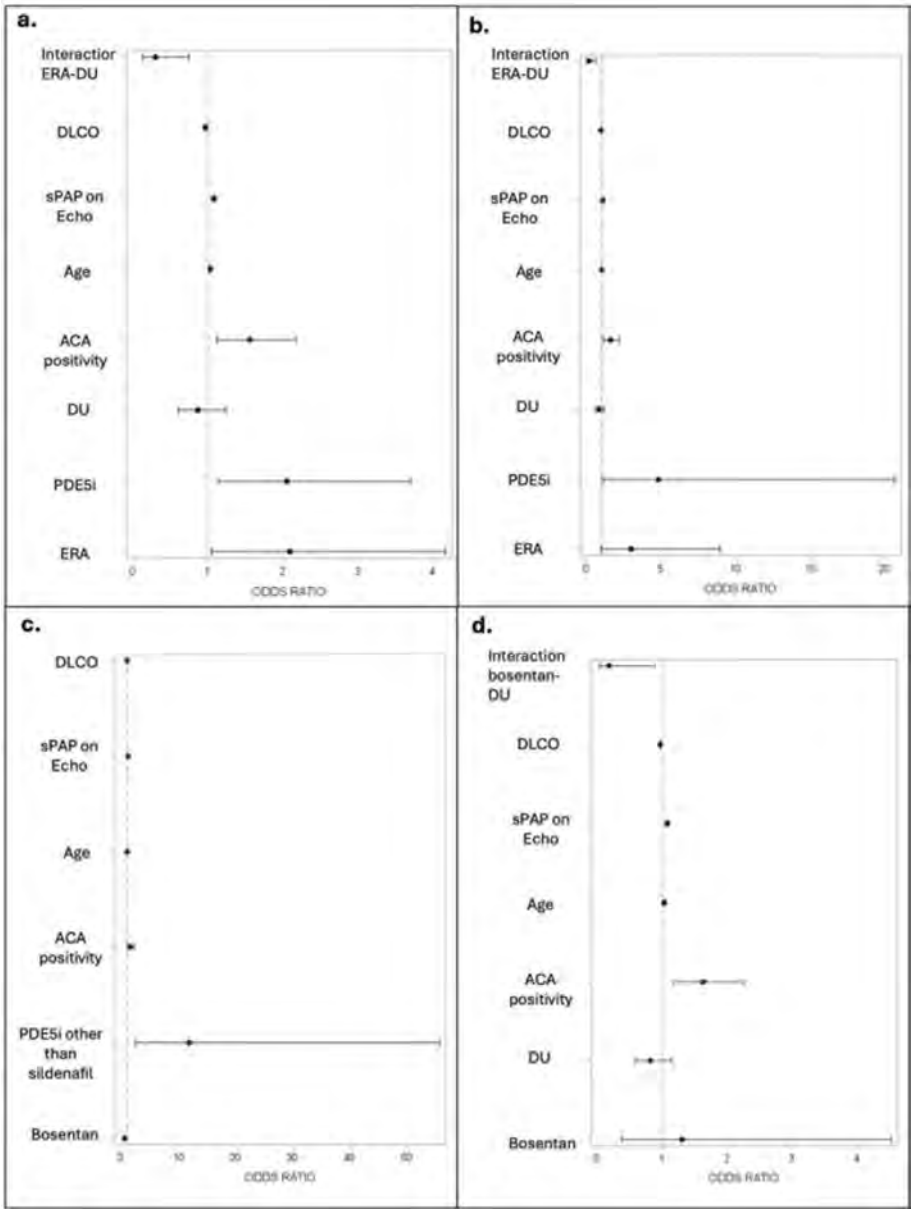


Figure 1. Forest Plots of regression Models 1 (a), 2 (b), 3 (c), and 4 (d) evaluating the association between independent variables and the detection of precapillary pulmonary hypertension. ACA, anti-centromere antibody; DLCO, diffusion lung capacity of carbon monoxide; DU, digital ulcers; ERA, endothelin receptor antagonists; PAH, pulmonary arterial hypertension; sPAP, systolic pulmonary arterial pressure; PDE5i, phosphodiesterase 5 inhibitors.

When focusing on specific VVD molecules, exposure "ever" to bosentan showed a significant protective association with precapillary PH diagnosis, independently from the presence or absence of current DU (**Figure 1c**). Finally, we noted again a statistically significant interaction between ongoing bosentan and current DU, which turned into a statistically significant marginal effects estimate (OR 0.230, 95% CI 0.081 – 0.652) indicating protective effects of this medication towards the diagnosis of precapillary PH in patients with current DU (**Figure 1d**).

The protective effects of bosentan were confirmed in all sensitivity analyses targeting PAH detection.

Conclusion: Our data show that bosentan is associated with less frequent diagnosis of PAH and precapillary PH, in particular when employed in patients with current DU at the time of RHC. Our results support further research to optimize the timing and patient selection for VVD therapy in SSc, aiming also at additional preventive effects at pulmonary level.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Farina: None; **S. Bellando-Randone**: Boehringer-Ingelheim, 2, 6; **S. SANGES**: BioCryst, 5, 12, meeting fees, Grifols, 2, Merck/MSD, 5, 6, Novartis, 2, 12, meeting fees, Sanofi-Genzyme, 12, meeting fees, Shire, 12, meeting fees, SOBI, 12, meeting fees, Takeda, 2; **h. Bjørkekjær**: Janssen, 5; **I. tofani**: None; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **A. Balanescu**: AbbVie/Abbott, 1, 6, Amgen, 2, 6, Angellini, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Ewopharma, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sobi, 2, 6, Stada, 2, 6, Theramex, 6, UCB, 2, 6; **C. Bergmann**: None; **Y. Allanore**: None; **P. Klemm**: None; **s. Truglia**: None; **L. Idolazzi**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **R. Foti**: None; **a. Wojteczek**: Boehringer Ingelheim, 6; **E. Chatelus**: None; **M. Vonk**: Boehringer-Ingelheim, 2, 6, 12, Travel grants, Janssen, 2, 6, 12, travel grants, Merck/MSD, 6; **S. Guiducci**: None; **D. Launay**: AstraZeneca, 2, 6, BioCryst, 6, 12, travel grants, CSL Behring, 2, 6, Shire, 12, travel grants, Takeda, 2, 6; **E. Hachulla**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, Pfizer, 5, Roche-Chugai, 5, Sanofi-Genzyme, 2, 5, Sobi, 5; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **M. Matucci-Cerinic**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Bruni**: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5.

Abstract Number: 0674

Quantitative Imaging in Systemic Sclerosis Patients Receiving Sodium Thiosulfate for Calcinosis Cutis

Ian Odell[1], **Crystal Cheung**[1], Megan Wu[2], Stephanie Perez[3], Agrani Dixit[4], Cassandra van Horn[3], Muhammad Hamdan[5], Baran Gunes[6], Sophia Kujawski[7], Hyojeong Lee[3], Annie Wang[3], Denise Esserman[8], Michael Zamani[9], F. Perry Wilson[3], John Onofrey[3], Xenophon Papademetris[3] and Monique Hinchcliff[10], [1]Yale University School of Medicine, New Haven, CT, [2]Yale University School of Medicine, Greenville, [3]Yale University School of Medicine, New Haven, [4]Yale School of Medicine, New Haven, CT, [5]Yale University School of Medicine, Mansfield, [6]Yale University School of Medicine, Pompton Plains, NJ, [7]The George Washington University, New Haven, CT, [8]Yale University School of Public Health, New Haven, [9]Independent Statistician, Washington D.C., [10]Yale School of Medicine, Westport, CT

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Calcinosis cutis (CC) is a disabling skin condition associated with systemic sclerosis (SSc). Although many CC treatments including sodium thiosulfate (STS) have been proposed, no clinical trials have been conducted due, in part, to a lack of validated quantitative outcome measures.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients with severe SSc-CC, enrolled in an open-label case series were treated with 25% STS was administered topically twice daily for 6-12 months or injected intradermally monthly for six months (0.1ml per injection for total of 1-2.5ml STS injected per session) to a patient-selected region-of-interest (ROI). All patients satisfied the ACR classification criteria of SSc. Three clinical coordinators independently assessed computer-assisted annotation of SSc-CC on computed

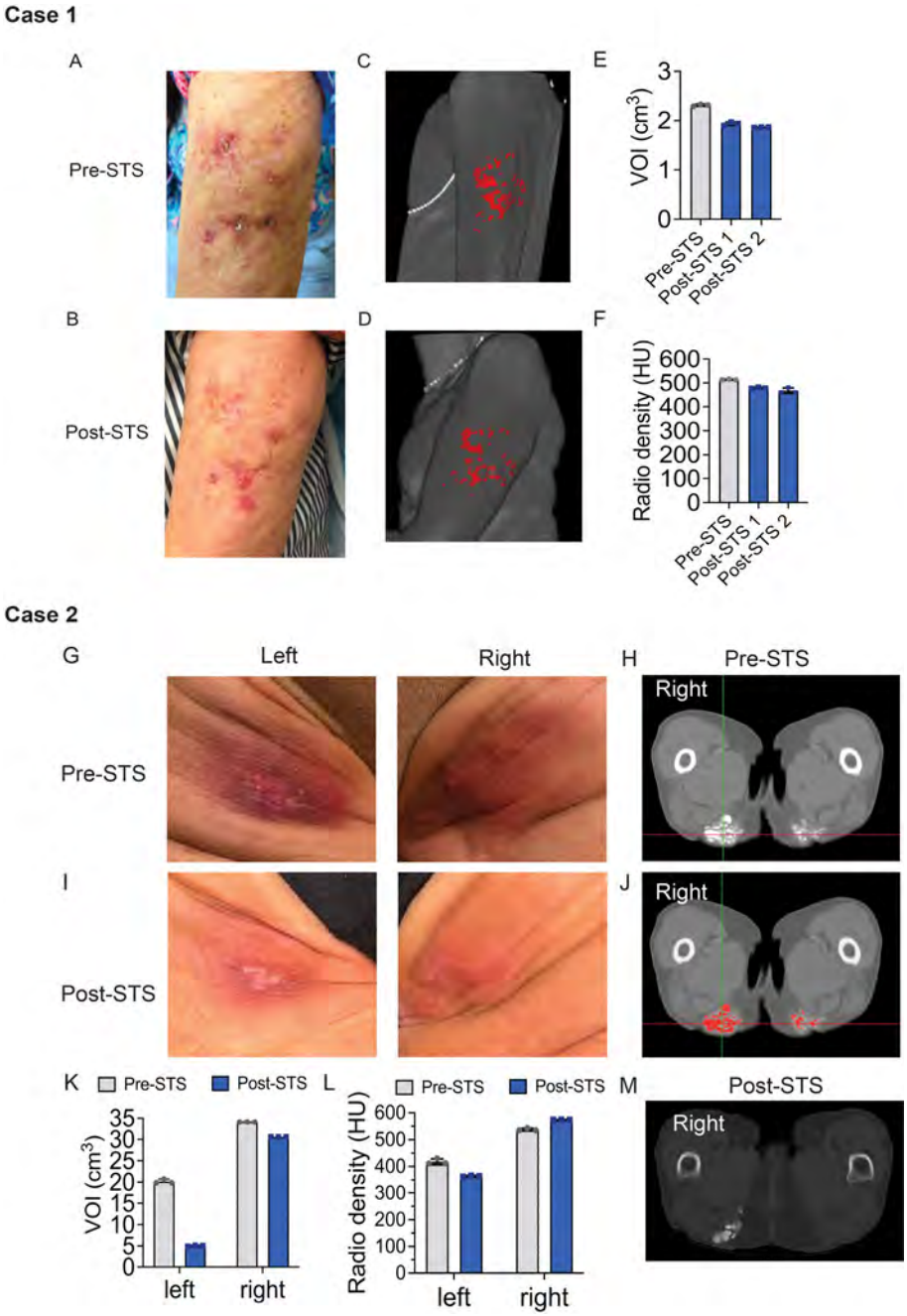


Figure 1. Intralesional sodium thiosulfate treatment of arm calcinosis cutis (CC) (Case 1) and buttock CC (Case 2). (A, B) Pre- and post-STS treatment photographs of left upper arm, respectively. (C, D) Rasterized pre- and post-STS treatment computed tomography (CT) images of CC lesions, respectively, with CC painted red. (E). Pre- and post-STS treatment CC lesional volume quantification. Post-STS treatment CT exams 1 and 2 were repeated one week apart, VOI=volume of interest. (F) Average pre- and post-treatment CC lesional radio density quantification among 3 raters. (G, I) Left and right buttock photographs of pre- and post-STS treatment, respectively. (H, J) Pre- STS treatment axial CT images without and with painting of CC lesions. (K) Pre- and post-treatment CC lesional volume quantification, VOI=volume of interest. (L) Average pre- and post-treatment CC lesional radio density quantification among 3 raters. (M) Post-treatment axial CT image without painting of CC lesions.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

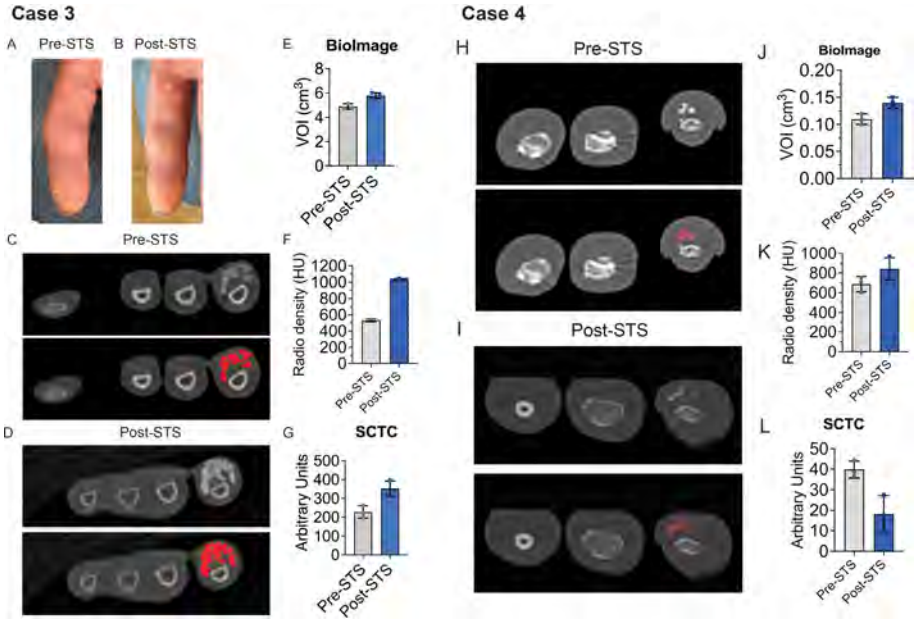


Figure 2. Intralesional (Case 3) and topical (Case 4) sodium thiosulfate treatment of finger calcinosis cutis (CC). (A, B) Pre- and post-STS treatment photographs of the right index finger, respectively. (C) Pre-STS treatment axial CT images without and with painting of CC lesions. (D) Post-treatment axial CT images without and with painting of CC lesions. (E) Average pre- and post-treatment CC lesional volume quantification among 3 raters, VOI=volume of interest. (F) Average pre- and post-treatment CC lesional radio density quantification among 3 raters. (G) Average pre- and post-treatment CC lesional SCTC scores among 3 raters. (H) Pre-STS treatment axial CT images without and with painting of CC lesions. (I) Post-treatment axial CT images without and with painting of CC lesions. (J) Average pre- and post-treatment CC lesional volume quantification among 3 raters, VOI=volume of interest. (K) Average pre- and post-treatment CC lesional radio density quantification among 3 raters. (L) Average pre- and post-treatment CC lesional SCTC scores among 3 raters.

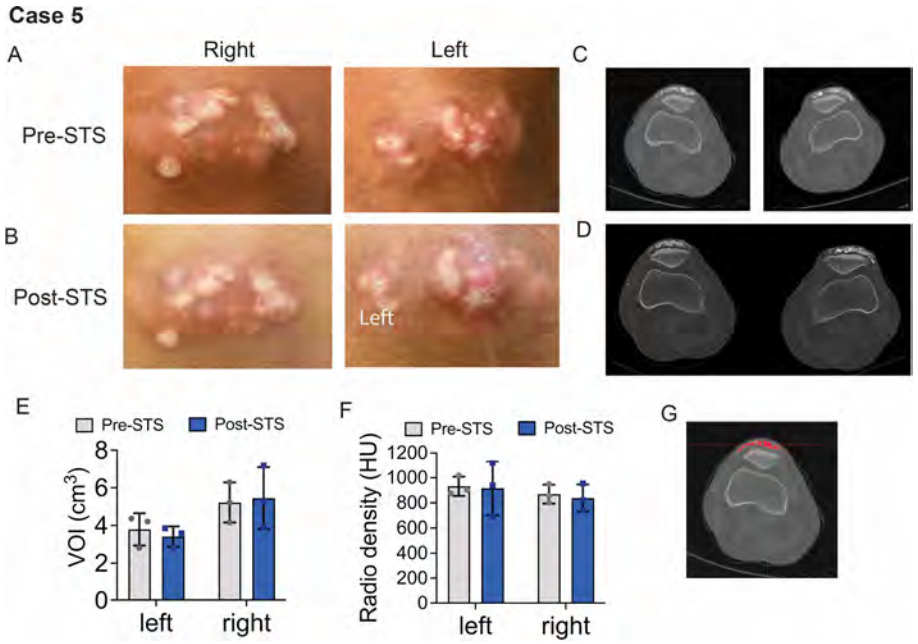


Figure 3. Topical sodium thiosulfate treatment of knee calcinosis cutis (CC). (A, B) Left and right patellae photographs of pre- and post-STS treatment, respectively. (C) Pre- STS treatment axial CT images without painting of CC lesions. (D) Post- STS treatment axial CT images of right patella without painting of CC lesions. (E) Average pre- and post-treatment CC lesional volume quantification among 3 raters, VOI=volume of interest. (F) Average pre- and post-treatment CC lesional radio density quantification among 3 raters. (G) Pre-STS treatment axial CT image with painting of CC lesion.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

tomography (CT) exams for quantitative measurement of volume changes compared to symptomatic and photographic responses during STS treatment using BioImage Suite Web software. Inter-rater agreement and test-retest reliability were determined with intraclass coefficient (ICC).

Results: Five women, with SSc-CC involving the upper arm, bilateral ischial tuberosities, hands (two patients) and bilateral patellae, received topical (n=2) or intralesional (n=3) STS. Variable changes in symptoms, digital camera imaging, and CC volume by CT imaging (28% reduction in upper arm; 75% and 10% reductions in left and right, buttock, respectively; 18% increase in left forefinger; 27% increase in right hand; and 12% reduction in left, and 4% increase in right, patellae) were observed. Inter-rater agreement was excellent with an ICC of 0.93. Volume of CC on repeated measures performed one week apart was within 3%. Annotation time ranged from < 30 minutes for arm and buttock to >four hours per case for other ROI.

Conclusion: Intradermal STS treatment was associated with symptomatic and volumetric improvement in arm and buttocks, but not finger CC. Topical STS was not associated with symptomatic or imaging CC improvement in fingers or patellae. Computer-assisted annotation and volumetric measurement of CC on CT imaging appears to be a reproducible and sensitive quantitative outcome. However, time to annotate CC close to bone was lengthy due to similar radiographic density. Computer-assisted quantification of CC on CT is a useful quantitative outcome for future clinical trials, but additional methods for automating CC annotation need to be developed.

Disclosure: I. Odell: Plythera, Inc, 10, Ventus Therapeutics, 5; **C. Cheung**: None; **M. Wu**: None; **S. Perez**: None; **A. Dixit**: None; **C. van Horn**: None; **M. Hamdan**: None; **B. Gunes**: None; **S. Kujawski**: None; **H. Lee**: None; **A. Wang**: None; **D. Esserman**: Ablative Solutions, 1, Conformal, 1, EMBLOK, 1, PhaseBio, 1, REVA Medical, 1; **M. Zamani**: None; **F. Wilson**: Amgen, 5; **J. Onofrey**: None; **X. Papademetris**: None; **M. Hinchcliff**: AbbVie/Abbott, Boehringer Ingelheim, Kadmon,, 2, 5.

Abstract Number: 0675

Neutrophil-to-Lymphocyte Ratio as a biomarker for disease onset and a predictor for mortality in Systemic Sclerosis – real-world data from a large healthcare provider in Israel.

Shiri Keret[1], Shlomit Yaari[2], gleb Slobodin[3] and **doron Rimar**[3], [1]Bnai Zion Medical Center, Atlit, Israel, [2]Maccabi Healthcare Services, HaMered 27, Tel Aviv, 68125, Israel., Tel Aviv, Israel, [3]Bnai Zion Medical Center Faculty of Medicine, Technion Israel institute of technology, Haifa, Israel

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Elevated neutrophil-to-lymphocyte ratio (NLR) in systemic sclerosis (SSc) has been demonstrated to predict worsening skin and lung involvement, and a cutoff of 2.95 was shown to be related to a decreased 5-year survival in a recent pilot study. The aim of this study was to further define a cutoff of baseline NLR that predicts poor outcome of SSc and to explore longitudinal variations of NLR with respect to disease onset in a large healthcare database.

Methods: Adult SSc patients from the Maccabi healthcare services (MHS) database,a 2.7-million-member, state-mandated, health provider in Israel, between 2003 and 2023 were included. Identification algorithm included an ICD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

9 diagnosis of "systemic sclerosis" or "scleroderma" by a rheumatologist or at hospital discharge or a diagnosis in the presence of at least one high titer autoantibody (ANA or SCL-70 or anticentromere or anti RNA POLIII).

Results: Overall, 1752 SSc patients fulfilled the inclusion criteria over the study period. In 2023 the estimated prevalence of SSc in Israel was 735 per million.

241 patients were excluded because of steroid use. Thus, baseline study cohort included 1511 patients of whom 1232 had NLR values at baseline (Table1). The mean NLR at diagnosis was 2.21±1.36, including 110 (9%) with value between 3-4 and 81 (6.5%) above 4. At diagnosis, NLR was significantly higher in men, in patients with pulmonary fibrosis (n=245, 16%), pulmonary hypertension (n=233, 15%), and with MMF treatment (n=139, 9%). In patients with a high baseline NLR >3 (n=191, NLR 4.4±2.21), NLR showed a statistically significant increase at onset when compared to values measured 1, 5, 10, and 15 years prior to diagnosis (Figure 1). Thirty six percent of these patients had specific antibodies up to 15 years before diagnosis. NLR did not change over time or with therapy over 15 years of follow-up after diagnosis (Figure 1). During 20 years of follow-up, 360 patients (20%) died. Each 1-point increase in baseline NLR was linked to higher 5- and 10-year mortality rates, as demonstrated by the Kaplan-Meier curve (figure2). The highest mortality rates were observed in NLR >4, reaching 25% at 5 years and 31% at 10 years ($p < 0.001$), (Figure 2). A Cox regression model that included covariables (age, sex, pulmonary fibrosis, pulmonary hypertension) found in patients with NLR above 4 had a hazard ratio of 2.83 (-2 log-likelihood chi-square = 277.3, $p < 0.001$) for time to death (Figure 3).

Conclusion: This extensive cohort study confirms that a high baseline NLR is predictive of 5- and 10-year mortality, with a refined threshold of NLR greater than 4. Male sex, pulmonary fibrosis and pulmonary hypertension were key risk factors for high baseline NLR and predicted mortality. Notably, elevated NLR was already present at disease onset—even when autoantibodies appeared earlier and remained persistently high for over 15 years, unaffected by treatment. NLR was not

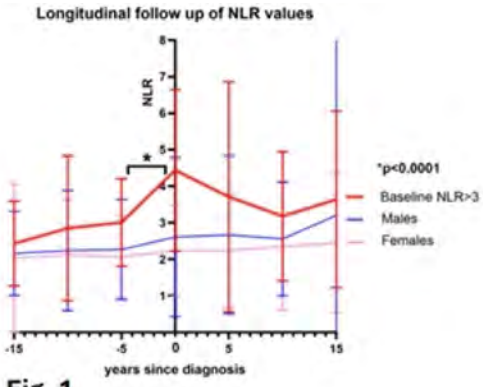


Fig. 1

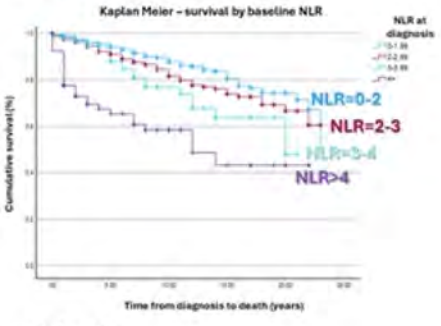


Fig. 2

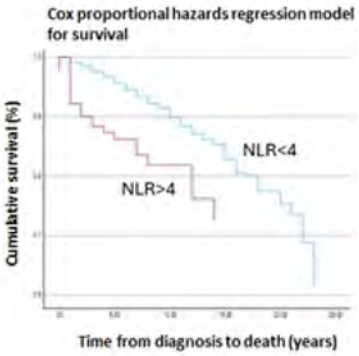


Fig. 3

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 - demographic and Clinical and characteristics

	(n=1511)	(n=1232)		
		NLR>4 (n=81)	NLR<4 (n=1151)	*P value
Sex (female)	1233(82%)	62(76.5%)	953(82.8%)	0.15
Age (years)	53.1±15.6	59.8±15.7	53.2±15	**0.001**
Baseline NLR	2.21±1.36	5.8±2.84	1.99±0.73	**0.001**
Autoantibodies				
ANA + (only)	244(16%)	13(16%)	202(17.5%)	0.73
ACA+	249(16%)	16(20%)	212(18.4%)	0.76
SCL70+	146(10%)	13(16%)	115(10%)	0.08
RNA POL III+	2(0.1%)	0(0%)	2(0.2%)	0.7
Disease manifestation/ involvement				
GERD	717(47%)	39(48%)	548(48%)	0.9
Peptic ulcer	223(15%)	12(15%)	155(13.5%)	0.7
Pulmonary fibrosis	245(16%)	25(31%)	165(14.3%)	**<0.01**
Pulmonary hypertension	233(15%)	21(25.9%)	142(12.3%)	**<0.01**
Arthritis	802 (53%)	43(53%)	606(53%)	0.9
Pericarditis	32 (2%)	4 (5%)	20(1.7%)	0.44
Malignancy	781 (52%)	42(52%)	599(52%)	0.97
Treatment				
MTX	61(4%)	2(2.5%)	36(3.1%)	0.74
Prednisone	0	0	0	
MMF	139(9%)	15(18.5%)	112(9.7%)	**0.01**
Rituximab	65(4%)	6(7.4%)	51(4.4%)	0.21
Tocilizumab	14(0.8%)	1(1.2%)	12(1%)	0.87
IVIG	34(2.2%)	1(1.2%)	19(1.7%)	0.7
Nintedanib	43(2.8%)	5(6.2%)	36(3.1%)	0.14
Iloprost	148(10%)	6(7.4%)	104(9%)	0.61
Slidenafil	151(10%)	7(8.6%)	112(9.7%)	0.74
Bosentan	1422(10%)	5(6.2%)	100(8.7%)	0.43
AHSCT	5(0.3%)	4(0.3%)	0(0%)	0.6
Lung transplantation	4(0.2%)	1(1.2%)	3(0.3%)	0.14

correlated with CRP and therefore is not a surrogate marker for inflammation. These findings support the use of NLR as a simple, accessible biomarker to identify high-risk SSc patients who may benefit from closer monitoring and more intensive therapeutic strategies.

Disclosure: S. Keret: None; **S. Yaari**: None; **g. Slobodin**: None; **d. Rimar**: None.

Abstract Number: 0676

Engineered glove for the objective assessment of hand dexterity in patients with systemic sclerosis: correlations with clinical features, nailfold videocapillaroscopy, and high frequency skin ultrasonography

Alberto Sulli[1], **Elvis Hysa**[2], Paolo Clini[3], Emanuele Gotelli[4], Tamara Vojinovic[5], Carmen Pizzorni[1], Ali Jaffal[3], Sabrina Paolino[1], Rosanna Campitiello[3], Vanessa Smith[6] and Maurizio Cutolo[3], [1]University of Genoa, Genova, Italy, [2]University of Genoa, Genoa, Italy, [3]University of Genova, Genova, Italy, [4]University of Genoa, Genoa, Liguria, Italy, [5]University of Genoa, Genova, [6]Ghent University Hospital, Gent, Belgium

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Hand disability is a major feature of systemic sclerosis (SSc), driven by skin thickening and joint contractures, with significant impact on quality of life. Its assessment remains challenging and calls for more sensitive tools than traditional clinimetric scores. The Hand Test System (HTS) engineered glove has previously provided detailed data on hand dexterity in rheumatoid arthritis [1] through three quantitative parameters: touch duration (TD), inter-tapping interval (ITI), and movement rate (MR). The primary aim was to evaluate the applicability of the HTS glove in assessing hand dexterity in SSc patients by comparing its parameters with healthy controls (HC). Secondary endpoints included the correlations between HTS parameters with patient-reported outcomes (PROMs), nailfold videocapillaroscopy (NVC) findings, and dermal thickness measured by high frequency skin ultrasonography (HFSU) at the sites assessed by the modified Rodnan skin score (mRSS).

Methods: Twenty-five patients with systemic sclerosis (SSc) and 25 healthy controls were enrolled (**Table 1**). All participants underwent assessment using the HTS glove, grip strength measurement, and the following PROMs: the Health Assessment Questionnaire for Systemic Sclerosis (SHAQ), Hand Mobility in Scleroderma (HAMIS) test, and Duruöz Hand Index (DHI).

Table 1. Clinical and demographic features of the included patients Legend. ACA; anti-centromere autoantibodies; dcSSc; diffuse cutaneus SSc, DMARDs; disease modifying anti-rheumatic drugs, lcSSc; limited cutaneous SSc, mRSS; modified Rodnan skin score, Scl-70; anti-topoisomerase I antibodies. * Patients were classified as with dcSSc if the involvement of the skin included also arms, trunk, and thighs. Vasodilating agents: Aminaftone was taken by 17/25 (68%), calcium channel blockers by 6/25 (24%), endothelin receptor antagonists by 12/25 (48%), PDE5-inhibitors by 4/25 and riociguat by 1/25 (4%). DMARDs: Mycophenolate mofetil was taken by 7/25 (28%), methotrexate by 5/25 (20%), rituximab by 2/25 (8%), hydroxychloroquine by 1/25 (4%), cyclophosphamide by 4/25 (16%), and low-dose (< or = 5 mg daily) prednisone by 6/25 (24%). Pulmonary involvement: Defined based on the presence of ILD on high-resolution computed tomography (HRCT). Gastroesophageal involvement: Defined based on manometric evidence of esophageal dysmotility. Kidney involvement: Defined based on increased renal resistive index and/or elevated serum creatinine levels. Significant p-values are reported in bold

Demographic/clinical feature	lcSSc (n = 17)	dcSSc* (n = 8)	p-value
Females (n, %)	16 (94%)	6 (75%)	0.2
Age (m ± SD, years)	67.2 ± 9.8	67.6 ± 18.8	0.97
Duration of the disease (m ± SD, years)	20.4 ± 13.6	11.0 ± 7.3	0.457
mRSS (m ± SD)	3.9 ± 2.5	13.0 ± 9.0	0.18
Patients in treatment with oral vasodilating agents (n, %)	14 (82%)	7 (88%)	0.752
Patients in treatment with aspirin (n, %)	11 (65%)	4 (50%)	0.47
Patients in treatment with DMARDs (n, %)	12 (71%)	6 (75%)	0.826
Patients in treatment with nintedanib (n, %)	5 (29%)	2 (25%)	0.82
Scl-70 positive (n, %)	6 (35%)	4 (50%)	0.47
ACA positive (n, %)	9 (53%)	0 (0%)	**0.01**
Other autoantibodies (i.e, RNA pol III, Ro52 or Pm-Scl75/100: n, %)	3 (18%)	2 (25%)	0.67
Pulmonary involvement (n, %)	10 (59%)	8 (100%)	**0.04**
Gastro-esophageal involvement (n, %)	9 (53%)	4 (50%)	0.88
Kidney involvement (n, %)	2 (12%)	2 (25%)	0.39
Previous digital ulcers (n, %)	8 (47%)	6 (75%)	0.18
Active digital ulcers (n, %)	3 (18%)	3 (38%)	0.27

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Differences of the Hand Test System (HTS) engineered glove parameters between patients with systemic sclerosis (SSc) and healthy controls (HCs) Correlations between HTS glove parameters with clinimetric, nailfold videocapillaroscopy (NVC) and high frequency skin ultrasound (HFSU) parameters in SSc patients are also reported. Legend. DHI; Duruöz Hand Index test, HAMIS; Hand Mobility in Scleroderma test, ILD; interstitial lung disease; ITI; inter-tapping interval, MR; movement rate, TD; touch duration, SHAQ; Health Assessment Questionnaire for Systemic Sclerosis. Significant p-values are reported in bold

	Mean TD (ms)	Mean ITI (ms)	Mean MR (Hz)
SSc	291±137	512±326	1,6±0,7
HCs	124±28	113±29	4,4±0,7
Statistical significance	**p < 0.0001**	**p < 0.0001**	**p < 0.0001**
Disease duration	r= 0.18, p = 0,37	r = 0.13, p= 0.50	r = 0.20, p = 0.35
DHI	r = 0.51, **p = 0.004**	r = 0.61, **p = 0.002**	r = 0.60, **p = 0.002**
HAMIS	r = 0.41, **p = 0.004**	r = 0.39, **p = 0.003**	r = 0.47, **p = 0.01**
SHAQ	r= 0.42, **p = 0.03**	r = 0,65, **p = 0.0004**	r = 0,56, **p = 0.003**
Mean grip strength test	r = -0.14, p = 0.5	r = -0.43, **p = 0.03**	r = 0.31, p = 0.13
mRSS	r = 0.41, **p = 0.04**	r = 0.4, **p = 0.03**	r = - 0.42, **p = 0.03**
Dermal thickness of the left middle finger	r = -0.24, p = 0.32	r = -0.27, p = 0.25	r = 0.21, p = 0.37
Dermal thickness of the right middle finger	r = 21, p = 0.36	r = -0.22, p = 0.34	r = 0.14, p = 0.54
Dermal thickness of the dorsum of the left hand	r = 0.65, **p = 0.001**	r = -0.17, p = 0.45	r = -0.29, p = 0.20
Dermal thickness of the dorsum of the right hand	r = 0.66, **p = 0.001**	r = 0.16, p = 0.48	r = -0.3, p = 0.19
Total dermal thickness	r = 0.45, **p = 0.04**	r = -0.06, p = 0.81	r = -0.04, p = 0.85
Mean capillary density at NVC	r = -0.03, p = 0.89	r = 0.01, p = 0.95	r = 0.02, p = 0.91
Rate of giant capillaries at NVC	r = -0.15, p = 0.46	r = 0.23, p = 0.28	r = 0.12, p = 0.58

Table 3. Subgroup analyses of glove parameters according to the clinical features and autoantibody profile Legend. See Table 1 and 2

Clinical features			
HTS glove parameters	**lcSSc**	**dcSSc**	**p-value**
TD (ms)	274.13 ± 110.07	332.8 ± 195.92	0.35
ITI (ms)	502.41 ± 331.86	536.41 ± 334.68	0.82
MR (Hz)	1.62 ± 0.66	1.51 ± 0.75	0.71
	Patients with ILD	**Patients without ILD**	
TD (ms)	296.89 ± 151.8	280.28 ± 117.07	0.80
ITI (ms)	504.7 ± 249.73	526.05 ± 508.17	0.89
MR (Hz)	1.58 ± 0.67	1.66 ± 0.78	0.80
	Patients with esophageal involvement	**Patients without esophageal involvement**	
TD (ms)	277.55 ± 118.15	309.17 ± 166.98	0.59
ITI (ms)	536.76 ± 385.66	480.39 ± 273.1	0.69
MR (Hz)	1.62 ± 0.75	1.57 ± 0.64	0.85
	Patients with active digital ulcers	**Patients with active digital ulcers**	
TD (ms)	271.8 ± 108.21	298.79 ± 151.55	0.69
ITI (ms)	455 ± 156.83	529.57 ± 375.86	0.64
MR (Hz)	1.63 ± 0.39	1.59 ± 0.77	0.92
	Patients with kidney involvement	**Patients without kidney involvement**	
TD (ms)	298.93 ± 141.31	290.67 ± 143.67	0.92
ITI (ms)	384.92 ± 141.38	536.13 ± 356.4	0.42
MR (Hz)	1.68 ± 0.76	1.58 ± 0.69	0.81
Autoantibody profile			
	ACA positive	**ACA negative**	**p-value**
TD (ms)	264.07 ± 104.97	314.5 ± 154.91	0.39
ITI (ms)	521.43 ± 449.1	527.99 ± 242.81	0.96
MR (Hz)	1.67 ± 0.74	1.47 ± 0.58	0.47
	Scl70 positive	**Scl70 negative**	
TD (ms)	255.32 ± 100.6	324.36 ± 156.77	0.23
ITI (ms)	462.03 ± 125.76	570.88 ± 413.96	0.37
MR (Hz)	1.61 ± 0.44	1.49 ± 0.76	0.67

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SSc patients met the 2013 ACR/EULAR criteria and underwent standard clinical evaluation, nailfold videocapillaroscopy (NVC)[2] and HFSU (22 MHz), used to measure dermal thickness, with a focused analysis on the middle fingers, dorsum of hands, and total dermal thickness.

Results: In SSc patients, HTS parameters significantly correlated with PROMs, worsening in parallel with poorer PROMs (-**Table 2**). Notably, both mean TD and ITI were directly correlated with the mRSS, whereas MR, as expected, was inversely correlated (Table 2). Grip strength showed a significant correlation only with mean ITI ($r = -0.43$, $p = 0.03$).

As expected, significant differences in HTS parameters were observed between SSc patients and HC (**Table 2**). SSc patients performed finger movements more slowly and less efficiently than HC, as shown by prolonged TD and ITI, and reduced MR.

When analyzing subgroups of SSc patients based on clinical features, no significant differences were detected in HTS parameters according to the different organ involvement, autoantibody profiles or NVC findings (**Tables 2-3**).

However, significant correlations were, instead, observed between the mean TD directly correlating with the increase of the HFSU-measured dermal thickness of the dorsum of the hands and with the total dermal thickness (all p-values < 0.05, **Table 2**).

Conclusion: The HTS glove can provide detailed and quantitative data on hand dexterity in SSc patients. Significant correlations with PROMs, mRSS, hand strength and with HFSU-measured dermal thickness might suggest a significant relationship between disease-related skin thickness and hand functionality. Further studies with larger cohorts are in progression to explore the HTS glove's utility in monitoring disease outcomes and therapeutic response in SSc.

References

[1] Patanè M et al. Joint Bone Spine. 2022
[2] Smith V et al. Aut Rev 2020

Disclosure: A. Sulli: None; **E. Hysa**: None; **P. Clini**: None; **E. Gotelli**: None; **T. Vojinovic**: None; **C. Pizzorni**: None; **A. Jaffal**: None; **S. Paolino**: None; **R. Campitiello**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **M. Cutolo**: None.

Abstract Number: 0677

Increased incidence of sudden cardiac death in systemic sclerosis: estimate & correlates.

Jessica Fairley[1], Elizabeth Paratz[2], Dylan Hansen[3], Susanna Proudman[4], Joanne Sahhar[5], Gene-Siew Ngian[6], Diane Apostolopoulos[6], Jennifer Walker[7], Lauren Host[8], Wendy Stevens[1], Andre La Gerche[2], Mandana Nikpour[9], **Laura Ross**[1] and The Australian Scleroderma Interest Group, [1]The University of Melbourne, Melbourne, Victoria, Australia, [2]St Vincent's Institute of Medical Research, Melbourne, Victoria, Australia, [3]St Vincent's Hospital Melbourne, Melbourne, Victoria, Australia, [4]The University of Adelaide, Adelaide, Victoria, Australia, [5]Monash Health, Melbourne, Victoria, Australia, [6]Monash University, Melbourne, Victoria, Australia, [7]Flinders University, Adelaide, Victoria, Australia, [8]Fiona Stanley Hospital, Perth, Victoria, Australia, [9]University of Sydney, School of Public Health, Faculty of Medicine and Health, Sydney, New South Wales, Australia; St Vincent's Hospital Melbourne, Department of Rheumatology, Fitzroy, Victoria, Australia, Melbourne, Victoria, Australia

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The incidence of sudden cardiac death (SCD) is suspected to be increased in systemic sclerosis (SSc). However, data describing SCD incidence in SSc are sparse and confined to small cohorts. Accordingly, this study aims to estimate SCD incidence in SSc and assess the association with disease characteristics.

Methods: Individuals from the Australian Scleroderma Cohort Study with a definable SSc subtype meeting ACR/EULAR criteria were included. International Classification of Diseases (ICD)-10 code cause of death was sourced from the Australian National Death Index. Two authors adjudicated SCD events, which were considered present when an ICD-10 code cause of death for an acute cardiovascular pathology was listed (sudden cardiac death, cardiac arrest, ventricular fibrillation/flutter, acute myocardial infarction/acute ischaemic heart disease (IHD), ventricular tachycardia, cardiac tamponade, pericardial effusion, aortic or mitral valve lesion) excluding those with major pulmonary, renal or gastrointestinal primary causes of death. Between-group comparisons (SCD vs. overall cohort) were performed using Chi-squared testing or Wilcoxon rank-sum testing as appropriate, and multivariable Cox proportional hazard modelling was used to identify associations of SCD.

Results: Among 1708 SSc patients, 32 SCD events occurred (1.9%) over 10,650 person-years' follow-up (Figure 1), equivalent to an observed incidence rate of 300 per 100,000 person-years. This rate is 3-9 times higher than published general population estimates (35-89/100,000 person-years).[1,2]

Participants who experienced SCD were more likely to have IHD (40.6% vs. 13.8%, p< 0.001) and reduced left ventricular ejection fraction (LVEF< 50%; 18.5% vs. 5.5%, p=0.004). SSc heart involvement (18.8% vs. 9.4%, p=0.074), aortic valve pathology (12.9% vs. 5.7%, p=0.089) and pulmonary hypertension (18.8% vs. 11.3%, p=0.188) were numerically more common in those with SCD, although not meeting statistical significance. While cardiovascular risk factors including

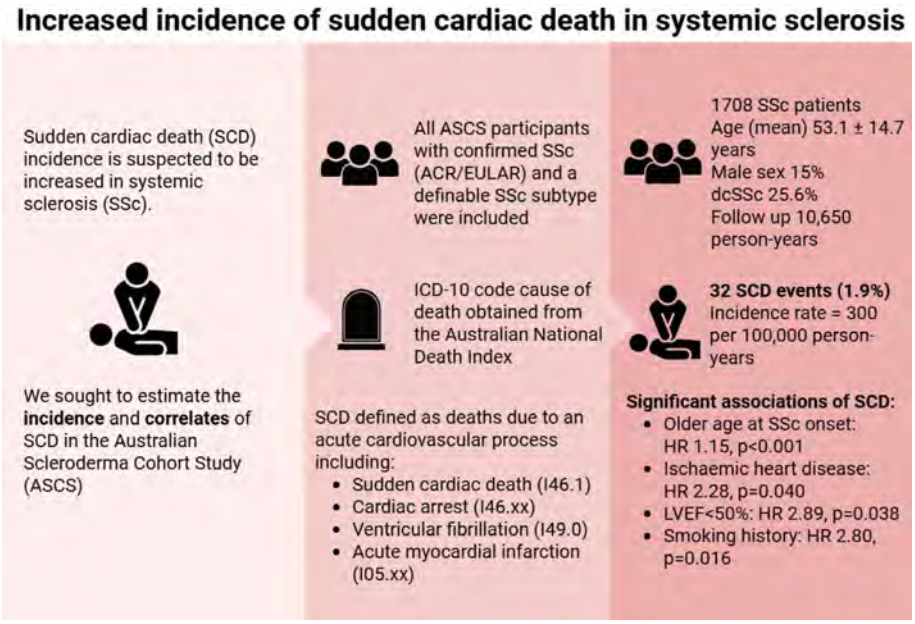


Figure 1: Graphical Abstract

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hypertension, dyslipidaemia and smoking history were not associated with SCD, these patients were numerically more likely to have two or more of these factors (60.7% vs. 47.5%, p=0.165).

Multivariable Cox hazard modelling identified that older age (hazard ratio (HR) 1.15 (95% confidence interval (CI) 1.10-1.20), p< 0.001), IHD (HR 2.28 (95%CI 1.04-5.00), p=0.040), reduced LVEF (HR 2.89 (95%CI 1.06-7.90), p=0.038) and smoking exposure (HR 2.80 (95%CI 1.21-6.49), p=0.016) were associated with SCD.

Conclusion: SCD occurred in 1.9% of a large SSc cohort, with an incidence rate of 300 per 100,000 person-years. This is significantly higher than the rate of SCD reported in the general population. Older age, IHD, reduced LVEF and smoking were key risk factors for SCD, highlighting important and potentially modifiable risk factors for SCD in SSc.

References

1. Wong CX, Brown A, Lau DH, et al. Epidemiology of Sudden Cardiac Death: Global and Regional Perspectives. *Heart Lung Circ* 2019; **28**(1): 6-14.
2. Empana JP, Lerner I, Valentin E, et al. Incidence of Sudden Cardiac Death in the European Union. *J Am Coll Cardiol* 2022; **79**(18): 1818-27

Disclosure: J. Fairley: Boehringer-Ingelheim, 6, Pfizer, 12, Support for ACR Registration 2021; **E. Paratz**: Bristol-Myers Squibb(BMS), 6, Pfizer, 12, Conference Sponsorship; **D. Hansen**: None; **S. Proudman**: Boehringer-Ingelheim, 6, Janssen, 6; **J. Sahhar**: Boehringer-Ingelheim, 6; **G. Ngian**: None; **D. Apostolopoulos**: None; **J. Walker**: Boehringer-Ingelheim, 6; **L. Host**: Abbvie, 6, Janssen, 6, The Limbic Publication, 6; **W. Stevens**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck/MSD, 2; **A. La Gerche**: None; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 2, 6; **L. Ross**: None.

Abstract Number: 0678

Targeting the plasma cell niche in systemic sclerosis: A case series about the bispecific anti-BCMAxCD3 antibody teclistamab in severe, treatment-refractory patients

Andrea-Hermina Gyorfi[1], Ayla Nadja Stuetz[2], Christina Duesing[3], Laura-Marie Lahu[4], Franca Sophie Deicher[5], Yi-Nan Li[6], Celine van Saan[5], Alexandru-Emil Matei[7], Alexander Hoelscher[5], Peter-Martin Bruch[8], Sarah Koziel[8], Manuel Roehrich[9], Mareike Cramer[10], Bernhard Homey[5], Bjoern Buehring[11], Alexander Kreuter[12], Aleksandar Radujkovic[5], Claus Peter Heußel[13], Hanns-Martin Lorenz[14], Ricardo Grieshaber-Bouyer[15], Georg Schett[16], Jörg Distler[17] and **Wolfgang Merkt**[18], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University., Düsseldorf, Germany, [2]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Nordrhein-Westfalen, Germany, [3]Klinik für Rheumatologie, Düsseldorf, Germany, [4]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Germany, [5]Uniklinik Düsseldorf, Düsseldorf, Germany, [6]University Hospital of Düsseldorf, Düsseldorf, Germany, [7]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany, [8]University Hospital Düsseldorf, Dusseldorf, Germany, [9]Universitätsmedizin Mainz, Mainz, [10]University Hospital Düsseldorf, Düsseldorf, Germany, [11]Bergisches Rheuma-Zentrum, Krankenhaus St Josef, Wuppertal, Germany, [12]HELIOS St. Elisabeth Clinic Oberhausen, University Witten-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Herdecke, Oberhausen, Germany, [13]Thoraxklinik, University of Heidelberg, Heidelberg, [14]Universitätsklinikum Heidelberg, Heidelberg, Germany, [15]University Hospital Erlangen, Erlangen, Germany, [16]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [17]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [18]University Hospital Düsseldorf, Düsseldorf, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) possesses the highest case-related mortality of all rheumatic diseases. B cell-targeting, including CD19-targeting CAR-T cells, has shown efficacy but failed to eliminate the SSc-specific anti-topoisomerase-I autoantibodies. [1-4]

Methods: We treated three high-risk cases of severe treatment-refractory diffuse cutaneous SSc (dcSSc) with the plasma cell-depleting antibody teclistamab (**Table 1**). After six cycles of teclistamab, one cycle of rituximab was administered to block recovery of autoantibody-producing cells. All patients were anti-topoisomerase-I antibody positive and have not responded sufficiently to multiple immunosuppressive therapies. Immunosuppressive and antifibrotic therapies were discontinued prior to baseline (BL). Patients were followed for more than six months.

Results: Treatment with teclistamab depleted all plasma cells in the skin. Anti-topoisomerase-I-autoantibody titers seroconverted in two patients and dropped by 83% in the third patient. This immunological response was associated with a decrease of the modified Rodnan skin score, stabilization of SSc-ILD, resolution of tendon friction rubs and decreases in the EUSTAR-AI. The effect on SSc-associated primary myocardial involvement was heterogeneous.

Table 1. Patient characteristics at baseline. Abbreviations: Scl-70 Ab, anti-topoisomerase-I (Scl70) autoantibodies; mRSS, modified Rodnan Skin Score; TFR, tendon friction rubs; ILD, interstitial lung disease; SSc-pHI, systemic sclerosis primary heart involvement

	1st patient	2nd patient	3rd patient
Age	65 years	52 years	56 years
Sex	Male	Male	Male
Disease duration	18 years	1 years	4 years
Scl-70 Ab	+	+	+
mRSS	21	22	28
TFR	+	+	+
ILD	NSIP	severe pulmonary emphysema associated with extensive smoking with bibasilar reticulations (possibly incipient ILD)	NSIP
SSc-pHI	suspected new onset	suspected	+
CRP elevation	-	+	+
Previous immunomodulatory and antifibrotic therapies			
Azathioprine	+	-	-
Hydroxychloroquine	-	+	-
Methotrexate	-	+	+
Mycophenolate	+	+	+
Cyclophosphamide	+	-	-
Tocilizumab	-	-	-
Rituximab	-	-	+
Nintedanib	-	-	+

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

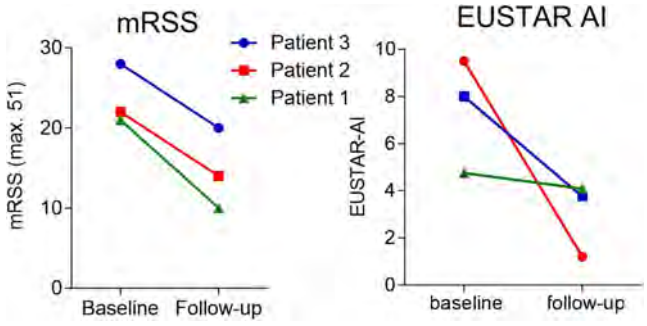


Image 1. Selected clinical outcomes (modified Rodnan skin score, mRSS; EUSTAR activity index, AI).

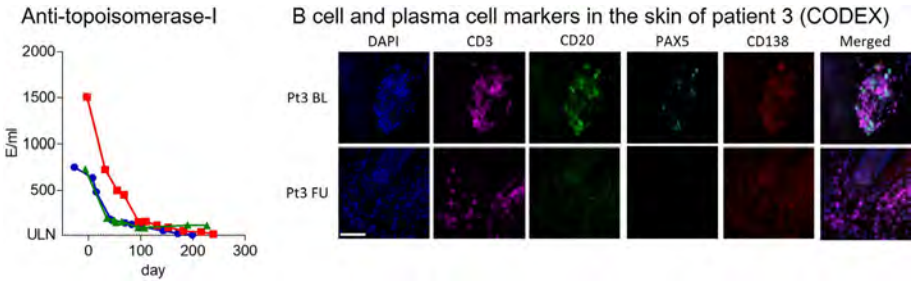


Image 2. Immunological outcomes (serological anti-topoisomerase-I titres and multi-color immunofluorescence stainings of skin biopsies from patient 3 using CODEX; DAPI stains nuclei, CD3 stains T cells and CD20, PAX5 and CD138 stain B cells and plasma cells, respectively)

Treatment with teclistamab was associated with several adverse events including cytokine release syndrome, hypogammaglobulinemia and mild infections (despite regular immunoglobulin replacement).

Conclusion: Teclistamab may offer potential as a rescue therapy for selected patients suffering from severe, treatment-refractory dcSSc, even with advanced disease.

Disclosure: A. Gyorfi: AbbVie, 6, Boehringer-Ingelheim, 6; **A. Stuetz**: None; **C. Duesing**: None; **L. Lahu**: None; **F. Deicher**: None; **Y. Li**: None; **C. van Saan**: None; **A. Matei**: None; **A. Hoelscher**: None; **P. Bruch**: None; **S. Koziel**: None; **M. Roehrich**: None; **M. Cramer**: None; **B. Homey**: None; **B. Buehring**: None; **A. Kreuter**: None; **A. Radujkovic**: None; **C. Heußel**: None; **H. Lorenz**: None; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **W. Merkt**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, Evotec, 5, Glapagos, 12, support for congress travel, Kyverna, 6, Lilly, 12, support for congress travel.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0679

Inhibition of TGFb3 in Systemic Sclerosis Patients Does Not Result in TGFb Pathway Modulation in Skin Biopsies or Circulation

Parisa Mazrooei, **Xuting Rebecca Sheng**, Xiaoyun Yang, Lyrialle Han, Samira Jamalian, Daniel Repplinger, Jingxuan He, Evelin Logis, Jeongsup Shim, Angela Hendricks, Lena Wang, Andrew Thorley and Sara Glickstein, Genentech/Roche, South San Francisco

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: There are 3 isoforms of Transforming Growth Factor Beta (TGFb), a cytokine frequently upregulated in fibrosis. Chronic targeting of TGFb1 and TGFb2 for fibrotic conditions has historically been problematic due to toxicity. Monoclonal antibodies that selectively target the TGFb3 isoform offer a potential solution, aiming to reduce fibrosis by inhibiting the TGFb pathway with a more favorable safety profile. Systemic sclerosis (SSc) is a debilitating disease where the TGFb pathway has been implicated as a disease driver. TGFb3 RNA correlated strongly with a 24-gene TGFb-responsive signature in SSc skin and also correlated with modified Rodnan skin score (Sun et al., 2024). Therefore, it was hypothesized that TGFb3 may be the main isoform involved in pathological fibrosis.

Methods: GA43360 is a Ph1b safety, tolerability, and pharmacokinetics study of SSc patients treated with 3 monthly doses of anti-TGFb3 (RO7303509). The study randomized 56 participants across three cohorts: Cohort A (75mg, n=12, and placebo, n=3), Cohort B (225mg, n=2, 360mg, n=15, and placebo, n=4), and Cohort C (1200mg, n=16, and placebo, n=4). To assess TGFb pathway modulation, we performed bulk RNAseq on patient skin biopsies collected pre- and post-anti-TGFb3 treatment and analyzed a 24-gene TGFb-responsive signature. Healthy control vendor-procured skin biopsies were also sequenced and analyzed for comparison. Indirect target engagement was assessed by measuring circulating TGFb3 protein levels in serum using the NULISA inflammation panel, and pathway modulation was evaluated by measuring serum periostin and COMP levels using immunoassays.

Results: Our drug was well tolerated at all doses, and the safety profile was acceptable. Pharmacokinetics for all doses were in agreement with model predictions and within the range of expected variability. We saw evidence of indirect target engagement through the upregulation of total TGFb3 levels in circulation post-dose with dose-dependent effects. We also observed higher levels of TGFb3 and TGFb pathway genes in SSc skin compared to healthy control skin, and elevations of periostin and COMP proteins in circulation. After 3 months of anti-TGFb3 treatment, we did not see modulation of TGFb pathway genes in the skin or circulation.

Conclusion: We demonstrated indirect target engagement but did not observe pathway modulation, suggesting that inhibition of TGFb3 alone is not sufficient for decreasing TGFb-driven pathway activation in SSc patients.

Disclosure: P. Mazrooei: Genentech, 3, 11; **X. Sheng**: Genentech, 3, 11; **X. Yang**: Genentech, 3; **L. Han**: Genentech, 3, 11; **S. Jamalian**: Genentech, 3, 11; **D. Repplinger**: Genentech, 3, 11; **J. He**: Genentech, 3, 11; **E. Logis**: Genentech, 3, 11; **J. Shim**: Genentech, 3, 11; **A. Hendricks**: Genentech, 3, 11; **L. Wang**: Genentech, 3, 11; **A. Thorley**: Genentech, 3, 11; **S. Glickstein**: Genentech, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0680

Altered Mirna Patterns of Peripheral Blood Mononuclear Cells Show Correlations with Pulmonary Manifestations of Systemic Sclerosis

Dóra Csige, Szilárd Póliska, János Rózsa, Dóra Tari, Szilvia Szamosi, **Zoltán Szekanecz**, Gabriella Szűcs and Levente Bodoki, University of Debrecen, Debrecen, Hungary

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune rheumatic and musculoskeletal disease (RMD) with a high mortality. Epigenetic factors, such as miRNAs might play an important role in the pathogenesis of SSc. In this cross-sectional study we assessed miRNA in SSc and associated miRNA expression with disease-related organ manifestations.

Methods: We investigated the miRNA profiles of 52 SSc patients (42 women and 10 men; mean age: 59.1 years (range: 33-76 years). Anticoagulated blood samples were taken from SSc patients, as well as age- and gender-matched healthy controls. Peripheral blood mononuclear cells (PBMC) were isolated on a Ficoll gradient, stored in TRIzol at -20°C until use. Total RNA was purified. Sequencing of miRNAs was performed using high-throughput, new generation (Illumina) sequencing, and an established miRNA library.

Results: Altogether 58 miRNAs showed significantly differential expression in SSc patients compared to controls. Among these miRNAs, 34 were significantly upregulated and 24 downregulated. Out of the differentially expressed miRNAs, 9 upregulated (let-7e-3p, miR-16-1-3p, miR-16-2-3p, miR-27a-5p, miR-34c-5p, miR-92a-1-5p, miR-130b-5p, miR-143-5p, miR-183-5p) and 8 downregulated miRNAs (miR-7-1-3p, miR-17-5p, miR-20a-5p, miR-30b-5p, miR-106a-5p, miR-151a-5p, miR-320b és miR-335-5p) had previously been described in the literature. Thus, the differential expression of further 41 (25 upregulated and 16 downregulated) miRNAs is a novel finding. When comparing SSc patients with (n=34) and without (n=18) interstitial lung disease (ILD)/pulmonary fibrosis, 4 miRNAs (miR-210-3p, miR-222-3p, miR-379-5p, miR-3935-5p) showed elevated, while 4 miRNAs (miR-125a-5p, miR-199b-5p, miR-941, miR-1226-3p) showed decreased expression levels in patients with SSc-ILD. Some of the differentially expressed miRNAs are associated with TGFβ signalling pathways.

Conclusion: SSc is associated with differential expression of several miRNAs. The up- or down-regulated expression of some miRNAs might be associated with SSc-ILD. Thus, miRNAs might have an important role in the molecular pathogenesis of SSc, as well as SSc-ILD and some of them might serve as therapeutic targets as well.

Disclosure: D. Csige: None; **S. Póliska**: None; **J. Rózsa**: None; **D. Tari**: None; **S. Szamosi**: None; **Z. Szekanecz**: AbbVie/Abbott, 1, 2, Bristol-Myers Squibb(BMS), 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Roche, 1, 2; **G. Szűcs**: Boehringer-Ingelheim, 1, 2; **L. Bodoki**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0681

Evaluation of Serial Cardiovascular Magnetic Resonance Monitoring and Immunosuppressive Therapy in Predicting Long-Term Outcomes in Systemic Sclerosis

Aïcha Kante[1], Sandra Mghaieth[2], bertrand Dunogue[3], Alice berezne[3], Cloé Comarmond[1], Marie-Pierre Revel[2], Guillaume Chassagnon[2], Luc Mouthon[3] and Benjamin Chaigne[3], [1]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, INSERM U942, Paris, France, [2]Radiology Department, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [3]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a connective tissue disease that can manifest as widespread skin and visceral fibrosis, potentially affecting major organs including the heart. Cardiac involvement is a major complication in SSc, often asymptomatic but associated with increased mortality. Despite recent improvement in survival and therapies, SSc remains the rheumatic disease associated with the highest morbidity and mortality. Cardiovascular magnetic resonance (CMR) is a sensitive, non-invasive tool for detecting cardiac abnormalities. However, the prognostic value of serial CMR monitoring and the effects of immunosuppressive therapy remain unclear. This study aimed to assess the prognostic significance of changes in CMR parameters for long-term cardiovascular outcomes, and to evaluate the impact of immunosuppressive treatments.

Methods: We conducted a monocentric retrospective study including consecutive SSc patients followed in the Internal Medicine department at Cochin University Hospital who underwent two CMR exams due to cardiovascular involvement. All patients met the American College of Rheumatology and European Alliance of Associations for Rheumatology 2013 classification criteria for SSc. Patients with two CMR scans performed on the same equipment between February 2009 and June 2023 were included, and parameter changes were compared using paired t-tests. The impact of treatments and CMR parameter changes on major adverse cardiovascular event (MACE) and all-cause mortality was assessed using Kaplan-Meier curves and log-rank tests.

Results: Forty-four SSc patients were included with a median [interquartile range] follow-up duration of 6.3 [3.1-9.2] years. The median interval between CMR scans was 1.5 [1.0-3.9] years. MACE occurred in 16 (33%) patients. There was no significant difference in the distribution of cardiovascular risk factors – including smoking (p=0.3), diabetes (p >0.9), and hypertension (p=0.7) – between patients who experienced MACE and patients who did not. In contrast, the prevalence of anti-Scl70 antibodies (p=0.023) and pulmonary hypertension (p=0.022) was higher among patients with MACE, although baseline functional, volumetric, and anatomical CMR parameters were not altered (**Table 1**). Right ventricle end-diastolic volume significantly decreased at the time of second CMR scan (p=0.04), contrary to maximal T1 (p=0.2), left ventricle end diastolic volume (p=0.1), left (p=0.5) and right (p=0.7) ventricular ejection fractions. Importantly, rituximab significantly decreased maximal T1 (p=0.029) (**Figure 1**), a marker of diffuse fibrosis also linked to an increased risk of all-cause death (p=0.044). Methotrexate was associated with a significant increase in left ventricular ejection fraction (p=0.032) (**Figure 1**) and a reduced risk of MACE (p=0.024).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical, biological and CMR parameters data were collected at the date of first CMR examination (baseline), and stratified by MACE status. Continuous data are presented as median (Q1, Q3) and compared using a Wilcoxon rank sum exact test. Categorical variables are presented as n (%) and compared using Fisher's exact test or Pearson's Chi-squared test as appropriate. Abbreviations: ACE: angiotensin-converting enzyme; ANA: anti-nuclear antibodies; Anti-PM/Scl: anti-polymyositis/scleroderma antibodies; CMR: cardiovascular magnetic resonance imaging; LA: left atrium; LGE: late gadolinium enhancement; LV: left ventricle; LVEDV: left ventricle end diastolic volume; LVEF: left ventricle ejection fraction; MACE: major adverse cardiovascular events; mRSS: modified Rodnan skin score; PH: pulmonary hypertension; RV: right ventricle; RVEDV: right ventricle end-diastolic volume; RVEF: right ventricle ejection fraction; SSc: systemic sclerosis. * Disease duration was determined from first non-Raynaud symptom. † Obesity was defined by a body mass index ≥ 30 kg/m2. ‡ All PH were confirmed by right heart catheterization and defined by a mean Pulmonary Arterial Pressure > 20 mmHg.

Clinical and biological characteristics	Overall SSc N=44	No MACE N=28	MACE N=16	p-value
Demographic characteristics				
Female sex	33 (75)	22 (79)	11 (69)	0.5
Age (years)	49 (42, 57)	49 (42, 57)	51 (40, 60)	0.9
Disease duration (years)*	3 (1, 10)	2 (1, 8)	6 (1, 11)	0.2
Cardiovascular risk factors				
High blood pressure	13 (30)	9 (32)	4 (25)	0.7
Dyslipidemia	7 (16)	6 (21)	1 (6.3)	0.4
Diabetes	2 (4.5)	1 (3.6)	1 (6.3)	>0.9
Obesity†	2 (4.5)	1 (3.6)	1 (6.3)	>0.9
Smoking (ever)	12 (27)	6 (21)	6 (38)	0.3
SSc clinical manifestations				
mRSS (mm)	13 (6, 21)	5 (18)	2 (13)	>0.9
Inter-incisive distance (mm)	31 (25, 40)	34 (24, 41)	30 (26, 37)	0.4
Active digital ulcers	12 (27)	5 (21)	7 (47)	0.2
Pulmonary hypertension‡	10 (23)	3 (11)	7 (44)	**0.022**
Muscle involvement	23 (53)	16 (59)	7 (44)	0.3
Interstitial lung disease	27 (61)	15 (54)	12 (75)	0.2
Lung fibrosis	18 (41)	10 (36)	8 (50)	0.4
Scleroderma renal crisis	7 (16)	4 (15)	3 (19)	>0.9
SSc antibody status				
Anti-Scl70	23 (52)	11 (39)	12 (75)	**0.023**
Anti-RNA polymerase III	2 (4.5)	2 (7.1)	0 (0)	0.5
Anticentromere	4 (9)	1 (3.6)	3 (19)	0.13
Anti-fibrillarin	23 (52)	5 (18)	1 (6.3)	0.4
Anti-PM/Scl	6 (14)	3 (11)	1 (6.3)	>0.9
ANA without specificity	7 (16)	5 (18)	2 (13)	>0.9
Immunosuppressive treatments at baseline				
Mycophenolate Mofetil	17 (39)	9 (32)	8 (50)	0.2
Cyclophosphamide	15 (34)	7 (25)	8 (50)	0.092
Rituximab	3 (7)	2 (7.1)	1 (6.3)	>0.9
Methotrexate	14 (32)	11 (39)	3 (19)	0.2
Corticosteroids	25 (57)	17 (61)	8 (50)	0.5
CMR parameters				
Maximal T1 value (ms)	1,362 (1,287, 1,459)	1,361 (1,287, 1,400)	1,482 (1,335, 1,483)	0.4
LGE	21 (48)	16 (57)	5 (31)	0.10
T2 hypersignal	4 (9.3)	3 (11)	1 (6.3)	>0.9
LA dilation	1 (2.3)	1 (3.6)	0 (0)	>0.9
Maximal T1 value (ms)	1,362 (1,287, 1,459)	1,361 (1,287, 1,400)	1,482 (1,335, 1,483)	0.4
LGE	21 (48)	16 (57)	5 (31)	0.10
T2 hypersignal	4 (9.3)	3 (11)	1 (6.3)	>0.9
LA dilation	1 (2.3)	1 (3.6)	0 (0)	>0.9
RA dilation	2 (4.5)	1 (3.6)	1 (6.3)	>0.9
LVDEV mL/m²	73.0 (61.0, 87.0)	75.0 (60.0, 87.0)	70.0 (64.0, 87.0)	0.9
LVEF (%)	57.0 (49.0, 61.0)	56.0 (48.0, 61.0)	57.0 (51.0, 63.0)	0.6
RV dilation	8 (18)	5 (18)	3 (19)	>0.9
RVEF (%)	4.0 (34.0, 44.0)	41.0 (36.0, 44.0)	38.0 (33.0, 43.0)	0.5
Pericardial effusion	25 (57)	18 (64)	7 (44)	0.2
Paradoxical septum	4 (9.3)	3 (11)	1 (6.3)	>0.9

Conclusion: Methotrexate use was associated with a decrease in MACE occurrence, highlighting a possible cardioprotective effect. Rituximab was linked to a decrease in maximal T1 value, a marker of diffuse fibrosis associated with increased mortality. These findings support the prognostic value of CMR monitoring and the potential benefit of immunosuppressive therapy in SSc-related cardiac involvement.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

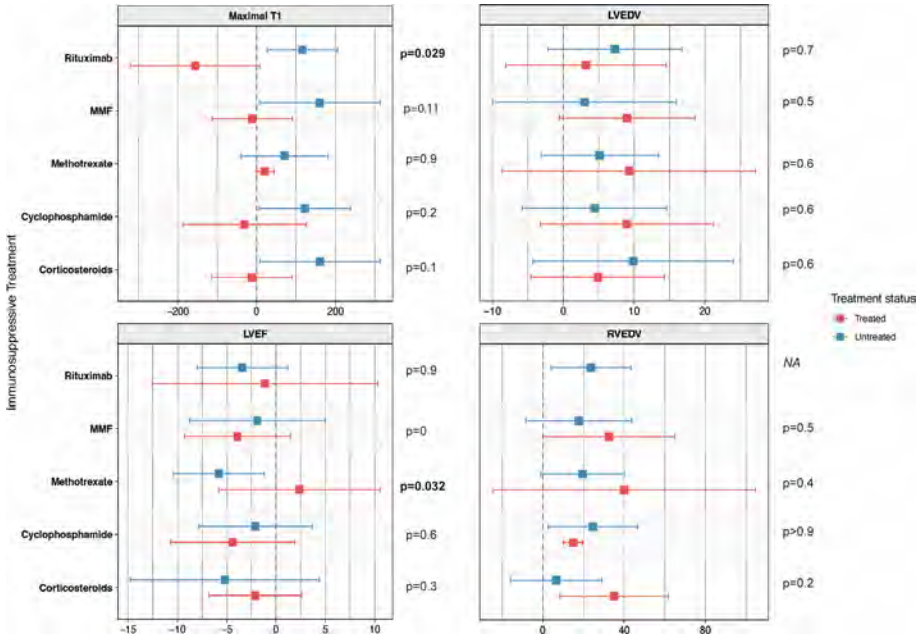


Figure 1. Forest plot representation of changes in CMR parameters stratified by immunosuppressive treatment. Mean differences in CMR measurements were compared between patients who received immunosuppressive therapies (including corticosteroids, mycophenolate mofetil, cyclophosphamide, rituximab, and methotrexate) and those who did not. Comparisons were performed using paired t-tests. Each square represents the mean difference, and the horizontal lines indicate the 95% confidence intervals. Patients treated with rituximab had a significant decrease in Maximal T1 value between 2 CMR scans. Abbreviations: CMR: cardiac magnetic resonance imaging; LVEDV: left ventricle end diastolic volume; LVEF: left ventricle ejection fraction; RVEDV: right ventricle end-diastolic volume; RVEF: right ventricle ejection fraction.

Disclosure: A. Kante: None; **S. Mghaieth**: None; **b. Dunogue**: None; **A. berezne**: None; **C. Comarmond**: Roche, 5; **M. Revel**: None; **G. Chassagnon**: None; **L. Mouthon**: None; **B. Chaigne**: None.

Abstract Number: 0682

Predictors of Severe Outcomes in Scleroderma Renal Crisis: Updated Results from a Single Center Study

Alex Luta[1], Saloni Mitchell[2] and Virginia Steen[3], [1]Hospital for Special Surgery, New York, NY, [2]Mount Sinai West and Morningside, New York, NY, [3]Georgetown University School of Medicine, Washington, DC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Scleroderma Renal Crisis (SRC) is a severe manifestation of Systemic Sclerosis (SSc) associated with elevated morbidity and mortality. We aimed to address the challenges of studying this rare condition by collecting and analyzing data to further our understanding of SRC. This research builds upon our previous work presented at ACR in 2022. We previously found that patients who did not have a diagnosis of SSc before SRC had a statistically significant higher odds of requiring hemodialysis (HD) during SRC compared to patients who had a prior diagnosis of SSc. We also found that patients with a history of hypertension (HTN) had a statistically significant higher odds of 1-year mortality compared to patients without HTN. We did not find any statistically significant increase in the odds of severe outcomes in SRC for African-American patients, patients with RNA Polymerase III antibodies, or patients with late SRC.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Selected Characteristics of 44 Scleroderma Renal Crisis Patients Seen at MedStar Georgetown University Hospital from 2008 to 2020

Variables	Number of Patients	Percentage of All Patients
Female	36	82%
African-American	20	45%
Diffuse SSc Disease	37	84%
Anti-RNA Polymerase III (+)	19	43%
Late SRC	7	16%

Legend: SSc = Systemic Sclerosis, also known as Scleroderma, Anti-RNA Polymerase III (+) = Patients who tested positive for the Anti-RNA Polymerase III antibody, SRC = Scleroderma Renal Crisis, Late SRC = Patients with at least 4 years between first SSc symptom and SRC. The mean age of patients was 51.5, and the ages of patients ranged from 27 to 88 years old.

Table 2: Associations of Potential Predictors with Hemodialysis Requirement at the Time of SRC Diagnosis

	HD Need at SRC (N=19)	No HD Need at SRC (N=24)	P-value
Sex	Male: 75%	25%	0.111
	Female: 37%	63%	
Specialist Care	Yes: 18%	82%	0.077
	No: 53%	47%	
Schistocytes at SRC	Yes: 47%	53%	0.115
	No: 0%	100%	
Hgb Nadir at SRC	7.5 (7.0, 8.0)	8.8 (7.8, 10.2)	**0.023**
Platelet Nadir at SRC	111.0 (82.0, 162.5)	219.0 (124.0, 279.0)	**0.044**
Creatinine at SRC Dx	2.60 (1.80, 3.30)	1.24 (0.90, 1.80)	**0.001**

Legend: SRC = Scleroderma Renal Crisis, HD = Hemodialysis, Dx = Diagnosis, Specialist Care = Patients under the care of a rheumatologist with Scleroderma expertise, Schistocytes = Presence of schistocytes on a peripheral blood smear at the time of Scleroderma Renal Crisis diagnosis. For continuous variables, median and interquartile range (Q1 and Q3) are reported. For categorical variables, proportions (%) are reported. Statistically significant P-values are bolded. *One patient had missing data regarding dialysis need at Scleroderma Renal Crisis Presentation.

Methods: We obtained data through chart review of 44 patients at our institution who developed SRC between 2008 and 2020. All patients met ACR/EULAR 2013 classification criteria for SSc. We evaluated predictors of HD at time of SRC and 1-year mortality post-SRC using Fisher's exact tests and Wilcoxon rank-sum tests, and we reported related p-values.

Results: Table 1 includes selected characteristics of our patients with SRC. We found that patients who required HD at time of SRC had a statistically significant elevation in creatinine and decreases in platelet count and hemoglobin, compared to patients who did not require HD (Table 2). While there were no statistically significant differences regarding HD need at time of SRC based on sex, specialist care, or presence of schistocytes on peripheral blood smear (PBS), there were trends toward statistical significance. Furthermore, we found statistically significant differences in 1-year mortality based on patient sex and age (Table 3). Male sex and older age were associated with 1-year mortality, which supports previously reported findings (1). There was not a statistically significant difference in 1-year mortality between patients on HD 6 months-post SRC and those who were not on HD 6 months-post SRC.

Conclusion: We identified statistically and clinically significant differences in SRC lab parameters between patients who required HD at SRC and those who did not. The median creatinine and hemoglobin levels differed by over one unit, and thrombocytopenia was a predictor of HD requirement at SRC. Because there were trends toward statistical significance for sex, specialist care, and presence of schistocytes regarding HD requirement, we hope to reevaluate these potential predictors on larger datasets. We found that older age and male sex were associated with elevated 1-year mortality. Combining these results with our previous findings, we have identified several predictors of severe outcomes in SRC. These findings can assist clinicians with risk-stratification of SRC patients, lay the groundwork for future research, and help mitigate severe outcomes.

Table 3: Associations of Potential Predictors with Mortality One Year after SRC Diagnosis

	Not Alive 1 year Post-SRC (N=7)	Alive 1 year Post-SRC (N=36)	P-value
Sex	Male: 50%	50%	**0.015**
	Female: 9%	91%	
Age	62.0 (56.0, 72.0)	47.5 (34.0, 62.0)	**0.029**
HD 6 Mo. Post-SRC	Yes: 29%	71%	0.197
	No: 11%	89%	

Legend: SRC = Scleroderma Renal Crisis, HD = Hemodialysis. For continuous variables, median and interquartile range (Q1 and Q3) are reported. For categorical variables, proportions (%) are reported. Statistically significant P-values are bolded. *One patient had missing data regarding 1-year mortality after Scleroderma Renal Crisis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1. Steen VD, Medsger TA Jr. Long-term outcomes of scleroderma renal crisis. Ann Intern Med. 2000 Oct 17;133(8):600-3. doi: 10.7326/0003-4819-133-8-200010170-00010. PMID: 11033587.

Disclosure: A. Luta: SurgiBox, Inc., 12,; **S. Mitchell**: None; **V. Steen**: None.

Abstract Number: 0683

Symptom-Based Clustering of Gastrointestinal Involvement in Systemic Sclerosis

Ali Ayla[1], Ernesto Calderon Martinez[2], Meng Zhang[3], Claudia Pedroza[4], Bingrui Chen[5], Ashish Balar[5], Michael Hughes[6], Silvia Bellando Randone[7], Brian Skaug[1], Maureen Mayes[8], Shervin Assassi[9] and Zsuzsanna McMahan[10], [1]UTHealth Houston Division of Rheumatology, Houston, TX, [2]UTHealth Houston, Houston, [3]UTHealth Houston Division of Rheumatology, Houston, [4]UTHealth Houston Institute for Clinical Research & Learning Health Care, Texas, TX, [5]UTHealth Houston, Houston, TX, [6]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [7]University of Florence, Florence, Italy, [8]UT Health Houston Division of Rheumatology, Houston, TX, [9]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [10]UT Health Houston, Houston, TX

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Virtually all patients with systemic sclerosis (SSc) experience gastrointestinal (GI) manifestations over the course of their disease, affecting any region from the mouth to the anorectum. Currently, there are limited risk factors predicting worse GI outcomes in patients with early SSc. In this study, we aimed to use baseline GI symptoms to better characterize the clinical heterogeneity and outcomes in SSc-related GI disease.

Methods: Patients with SSc who were enrolled in our large, well-defined prospective cohort were included in the study. All participants met the 2013 ACR/European League Against Rheumatism classification criteria and had a disease duration of less than five years from the onset of their first non-Raynaud's symptom at the time of enrollment. They were followed every six months for the first three years and annually thereafter. Hierarchical clustering was used to divide the patients according to their baseline GI symptoms and manifestations. These were dysphagia, gastroesophageal reflux disease (GERD), peptic ulcer, bloating, constipation, diarrhea, malabsorption, and pseudo-obstruction. The characteristics and the disease outcomes of the clusters were compared.

Results: A total of 450 patients were included, with a mean follow-up of 5.3 years. Three symptom-based gastrointestinal (GI) clusters were identified: Cluster 1 (upper GI predominant), Cluster 2 (lower GI predominant), and Cluster 3 (diffuse GI involvement). GERD was highly prevalent across all clusters. The majority of patients (n = 406) belonged to Cluster 1, which was characterized by dysphagia (41%) and peptic ulcer disease (5%). Cluster 2 included 30 patients and was marked by bloating, constipation, and diarrhea. Cluster 3, the most severe phenotype, comprised 14 patients, all of whom had malabsorption; 93% had diarrhea, and 86% had dysphagia. Extraintestinal features also varied between clusters. Cluster 3 had the highest proportion of male patients (43%, $P = 0.026$) and diffuse cutaneous disease (91%, $P = 0.037$). Baseline forced vital capacity (FVC%) and modified Rodnan skin score (mRSS) did not differ significantly among the three groups. Although cluster 3 had higher mortality, it did not reach significance ($P = 0.088$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of Patients with Systemic Sclerosis Stratified by GI Symptom-Based Clusters

Characteristic	Cluster 1 N = 406	Cluster 2 N = 30	Cluster 3 N = 14	p-value
Age, mean (SD)	48 (14)	47 (11)	47 (11)	0.237
Female sex, n (%)	341 (84%)	23 (77%)	8 (57%)	0.022
Race, n (%)				0.084
Asian	17 (4.2%)	0 (0%)	0 (0%)	
Black	75 (18%)	7 (23%)	3 (21%)	
Indian	1 (0.2%)	1 (3.3%)	1 (7.1%)	
White	313 (77%)	22 (73%)	10 (71%)	
Hispanic ethnicity, n (%)	106 (26%)	10 (33%)	4 (29%)	0.614
Diffuse involvement, n (%)	251 (77%)	16 (57%)	10 (91%)	0.037
Disease duration, yrs, mean (SD)	2.45 (1.51)	2.20 (1.18)	3.61 (1.17)	0.125
mRSS, mean (SD)	17 (12)	15 (10)	18 (12)	0.659
FVC%, mean (SD)	81 (20)	72 (18)	75 (11)	0.056
Anti-centromere antibody positivity, n (%)	55 (14%)	4 (14%)	0 (0%)	0.448
Anti-Scl70 antibody positivity, n (%)	76 (19%)	4 (14%)	2 (14%)	0.897
Anti-RNA polymerase III antibody positivity, n (%)	89 (23%)	4 (14%)	1 (7.1%)	0.275
Dysphagia, n (%)	165 (41%)	7 (23%)	12 (86%)	<0.001
GERD, n (%)	302 (74%)	30 (100%)	12 (86%)	<0.001
Peptic ulcer, n (%)	21 (5.2%)	0 (0%)	0 (0%)	0.559
Bloating, n (%)	21 (5.2%)	29 (97%)	6 (43%)	<0.001
Constipation, n (%)	73 (18%)	12 (40%)	1 (7.1%)	0.011
Diarrhea, n (%)	60 (15%)	11 (37%)	13 (93%)	<0.001
Pseudo-obstruction, n (%)	0 (0%)	3 (10%)	2 (14%)	<0.001
Malabsorption, n (%)	0 (0%)	2 (6.7%)	14 (100%)	<0.001

Conclusion: Patients with systemic sclerosis exhibit distinct patterns of gastrointestinal symptoms at baseline. Recognizing these symptom-based clusters may improve risk stratification, help predict clinical outcomes, and inform clinical trial design for GI disease in patients with SSc.

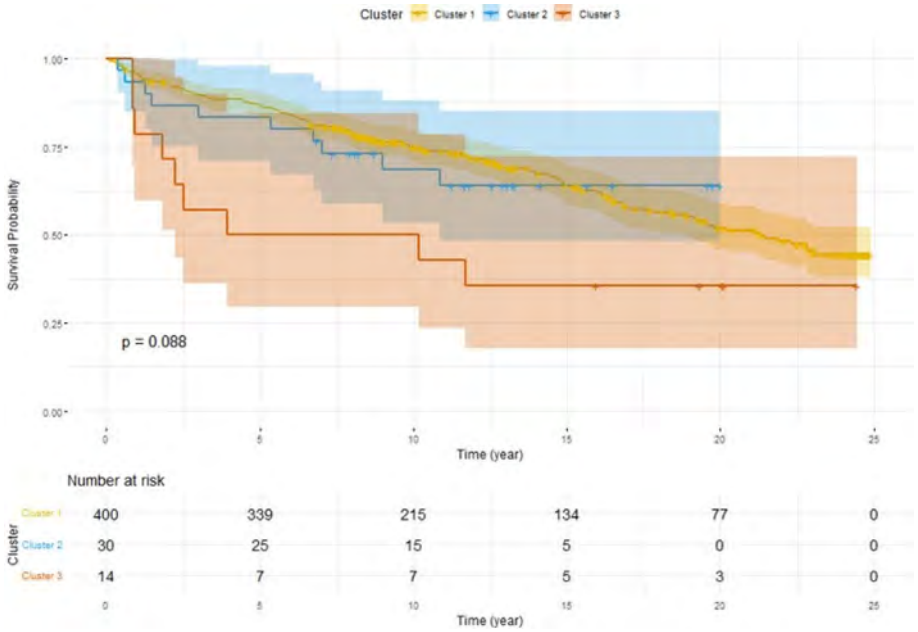


Figure 1. Survival According to the Clusters

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Ayla: None; **E. Calderon Martinez**: None; **M. Zhang**: None; **C. Pedroza**: Medicem, 5; **B. Chen**: None; **A. Balar**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **S. Bellando Randone**: Boehringer-Ingelheim, 2, 6; **B. Skaug**: None; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2.

Abstract Number: 0684

Translation to Spanish and Linguistic Validation of the Assessment of Systemic Sclerosis-associated Raynaud's Phenomenon (ASRAP)

Antonia Valenzuela[1], Adriana Miguel Alvarez[2], Patricia E. Carreira[3], Alejandra Babini[4], Diana Rocío Gil Calderón[5], John Pauling[6] and Tatiana Rodriguez-Reyna[2], [1]Pontificia Universidad Catolica de Chile, Santiago, Chile, [2]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [3]Hospital Universitario 12 de Octubre, Madrid, Spain, [4]Hospital Italiano, Córdoba, Argentina, [5]Hospital Universitario Mayor MEDERI, Universidad del Rosario, Artmedica SAS, Bogotá, Colombia, [6]North Bristol NHS Trust, Bristol, United Kingdom

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis-associated Raynaud's phenomenon (SSc-RP) significantly impacts patients' quality of life, yet validated tools to assess this condition in Spanish-speaking populations are lacking. The Assessment of Systemic Sclerosis-associated Raynaud's Phenomenon (ASRAP) is a new patient-reported outcome measure originally developed in English. This study aims to adapt the ASRAP into Spanish using a rigorous cross-cultural methodology.

Methods: We designed a prospective, qualitative, observational, and multicenter study to ensure cultural and linguistic equivalence of the ASRAP in Spanish. The adaptation process followed established international guidelines and included the following steps: (1) forward translation by two independent native Spanish-speaking healthcare professionals; (2) reconciliation to create a consensus version; (3) back-translation by a native English speaker unfamiliar with the questionnaire; (4) review of the back-translation to identify discrepancies; (5) harmonization through expert panel input involving bilingual SSc specialists from Spain and Latin America; (6) cognitive debriefing with iterative testing in 11 Spanish-speaking SSc-RP patients using semi-structured interviews and a 5-point rating scale to assess comprehension and relevance; (7) two rounds of professional proofreading; and (8) generation of the final Spanish version of the ASRAP.

Results: The four initial steps of the translation process were completed without complications. During the harmonization phase with the expert panel, some discrepancies emerged, particularly in wording choices. After discussion, the term *"Medianamente"* was replaced with *"Algo"*, and *"Episodios"* was revised to *"Ataques"* to better reflect common usage among Spanish-speaking patients with RP. The pre-final Spanish version of the ASRAP was field-tested in 11 patients with SSc-RP (6 from Chile and 5 from Mexico). The mean age was 58.5 ± 13.0 years, and 10 participants were female. The mean disease duration since RP onset was 11.3 ± 14.4 years, and 10.9 ± 13.7 years since the first non-RP symptom. Six participants (54%) had completed higher education. Overall, patients found the questionnaire clear and easy to understand. A minor revision was suggested during cognitive debriefing, specifically for item 27. Based on patient feedback, the phrase *"Un cambio en mi rutina normal ha hecho que me preocupe sobre un posible empeoramiento de mis síntomas de Raynaud"* was revised to *"Un cambio en mi rutina normal hizo que me preocupara sobre un posible empeoramiento de mis síntomas de*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Raynaud". As an initial validation step, the short-form ASRAP (ASRAP-SF, 10 items) was administered to 37 consecutive patients with SSc-RP (25 from Mexico and 12 from Chile), yielding a broad distribution of scores (mean ± SD: 50.5 ± 9.8; range: 31.32–67.07).

Conclusion: This collaborative cross-cultural adaptation process ensures that the Spanish version of the ASRAP is conceptually and culturally equivalent to the original, linguistically neutral, and relevant, clear, and comprehensible for Spanish-speaking patients with SSc-RP. Ongoing validation will further establish its utility across Spanish-speaking populations.

Disclosure: A. Valenzuela: None; **A. Miguel Alvarez**: None; **P. Carreira**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, Emmerald Health Pharmaceuticals, 2, 6, Janssen, 2, 6, Mitsubishi Tanabe, 2, 6, Novartis, 2, 6, Prometheus, 2, 6; **A. Babini**: None; **D. Gil Calderón**: None; **J. Pauling**: AstraZeneca, 2, Boehringer-Ingelheim, 2, IsoMab, 2, Janssen, 2, Permeatus Inc, 2, Sojournix Pharma, 2; **T. Rodriguez-Reyna**: None.

Abstract Number: 0685

Targeting Refractory Reflux in Systemic Sclerosis: Early Outcomes following a Novel Intervention

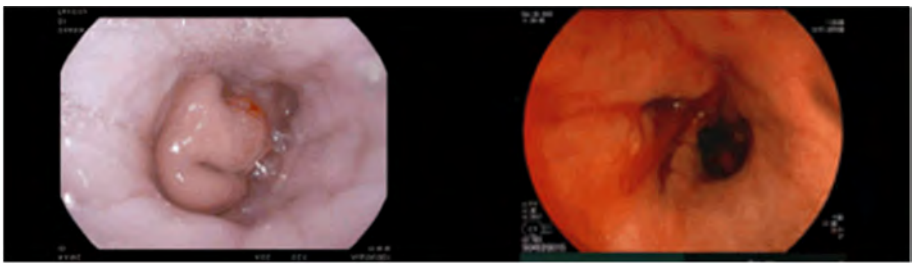
Areeka Memon[1], Monique Hinchcliff[2] and Amir Masoud[3], [1]Yale New Haven Health, New Haven, CT, [2]Yale School of Medicine, Westport, CT, [3]Hartford Healthcare, hartford

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Gastrointestinal tract (GIT) symptoms impact up to 90% of individuals with SSc. Hiatal hernia, decreased esophageal contractility, and lower esophageal sphincter tone contribute to dysphagia and gastroesophageal reflux disease (GERD) reducing quality-of-life.

Nissen fundoplication is often avoided in SSc due to risk of worsening dysphagia. Transoral incisionless fundoplication (TIF) with the EsophyX System (EndoGastric Solutions Redmond, WA, USA), in conjunction with hiatal hernia repair—termed cTIF—was employed to treat SSc patients with refractory GERD. The EsophyX System offers an alternative treatment option by enabling fasteners to be placed endoscopically at the gastroesophageal junction, resulting in partial recreation of the lower esophageal sphincter at less than or equal to 270 degrees. This approach avoids generating high distal esophageal pressures, which is important in SSc, where esophageal hypomotility increases risk of outflow obstructions and dysphagia. We present a case series highlighting effective use of cTIF for patients with SSc.



pre and post cTIF endoscopy photos revealing improvement of the gastric contents intussuscepting through the esophagus

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patent	Age	Gender	Race/Ethnicity	Date of SSc Diagnosis	Disease Subtype	mrSS	NFC finding	Antibodies	ANA titer	ANA pattern	ROS before cTIF	ROS after cTIF
1	49	female	white	1996	dcSSc/PM	8	drop out	none	1:160	homogenous	gerd, dysphagia, nausea, diarrhea	diarrhea
2	63	female	white	2013	lcSSc	7	late drop out, giant capillaries, capillary loss	scl 70	1:320	homeogenous, speckled	gerd, choking, dysphagia	some dysphagia
3	67	female	white	2000	lcSSc	2	normal	none	negative	negative	dysphagia, gerd	dysphagia, gerd
4	68	female	white	2008	lcSSc	6	not reported	none	ND	nucleolar	gerd, dysphagia, vomiting, constipation	gerd, dysphagia, vomiting, constipation
5	63	male	white	2022	lcSSc	2	abnormal	none	negative	negative	gerd	gerd
6	59	female	white	1990	lcSSc	3	not reported	centromere	1:40	nuclear, homogenous	dyphagia to solids, bloating, constipation	dyphagia to solids, bloating, constipation

baseline characteristics

Patient #	Esophagram Report	pH Study - Acid Exposure Time (severe >10, normal <4)	High Res Manometry (Chicago Classification)	Functional Luminal Imaging Probe Plethysmography	Procedure Wrap Degree
1	Normal peristaltic motion in proximal 1/3; no distinct primary wave in distal 2/3. Likely due to scleroderma.			Absent contractility	270
2	Barium tablet retained at GE junction, passed with water. Mild narrowing suspected.	12.3	Normal		270
3	Patulous thoracic esophagus; diminished stripping wave. Narrowing at GE junction; 13 mm barium tablet initially hangs then passes. Hiatal hernia present.				270
4	Frequent mid-distal tertiary contractions with ineffective peristalsis. Dysmotility.			Absent contractility	270
5	Mild dysmotility in distal third. No reflux.	7.3	Ineffective esophageal motility		240
6	Delayed transit of 13 mm barium tablet and both liquid/solid boluses through GE junction; aided by water.	10.5	Ineffective esophageal motility	Diminished contractility	270

Summary of pre-procedure esophageal function testing, including esophagram findings, pH study results (acid exposure time), high-resolution manometry (Chicago Classification), and functional luminal imaging probe (FLIP) assessment, alongside procedural wrap degree following cTIF intervention.

Methods: We retrospectively identified patients who fulfilled 2013 ACR/EULAR SSc Classification Criteria and underwent cTIF using the EsophyX System between February 2023 to March 2024. Esophagram, EGD with high-resolution manometry, 24-hour impedance testing, and functional luminal imaging probe plethysmography data were queried. At a mean (SD) post procedure follow-up of 23 (5) months, patients completed the GERD-HRQL survey, a 16-item questionnaire. Patients reported their current (post-procedure) symptoms and retrospectively assessed pre-procedure burden. Small sample sizes precluded formal statistical testing.

Results: Six patients with refractory GERD and/or dysphagia despite medical management who underwent cTIF were identified (Table 1). Esophagrams (n=6) revealed dysmotility in three, and narrowed GE junction in two, patients. Esophageal manometry (n=2) revealed ineffective esophageal motility in one patient and normal in another. pH impedance (n=2) revealed severe GERD per upright acid exposure time in both patients (Table 2). One patient had gastroesophageal intussusception that resolved post-cTIF (Figure 1).

At follow-up, one patient had died of respiratory failure, and one patient did not complete, and four completed the GERD-HRQL. The mean (SD) GERD-HRQL pre- vs. post-procedure was 62(4.39) and 19.25(16.29), respectively. Improvement in scores ranged from 30% to 90%, exceeding the minimal clinically important difference.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: cTIF appears to be a promising treatment for refractory GERD and dysphagia in SSc. No patient reported worsening dysphagia, and four patients reported overall improvement in symptoms. These outcomes suggest cTIF may safely and effectively fill a critical treatment gap for patients with refractory SSc-GERD.

Disclosure: A. Memon: None; **M. Hinchcliff**: AbbVie/Abbott, Boehringer Ingelheim, Kadmon,, 2, 5; **A. Masoud**: None.

Abstract Number: 0686

Use of a Smartphone App which Incorporates Feedback to Patients to Monitor Systemic Sclerosis-related Digital Ulcers – a Potential New Tool for Remote Clinical Monitoring

Ariane Herrick[1], Paul New[2], Graham Dinsdale[3], Andy Vail[2], Joanne Manning[3], Michael Hughes[4], Will dixon[5], Chris Taylor[5], Mark Dickinson[5] and Andrea Murray[6], [1]The University of Manchester, UK, Aberdeen, United Kingdom, [2]The University of Manchester, Manchester, United Kingdom, [3]Northern Care Alliance NHS Foundation Trust, Salford, United Kingdom, [4]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [5]The University of Manchester, Manchester, [6]University of Manchester, Salford, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To facilitate clinical trials we previously developed a smartphone app to allow 'tracking' of systemic sclerosis (SSc)-related digital ulcers (DUs) and their associated pain and disability, via capture of a combination of photographs and patient reported outcome measures [PROMS]. Members of the patient user group who informed the study felt that the app might be helpful in routine clinical care, as this could provide a means of their clinician viewing the ulcer(s), and assessing treatment response, remotely, thus reducing the need for hospital visits. Our aim was to assess the feasibility of using the app in a clinical setting, and to gauge patient opinion of its benefits, including a newly added lesion feedback function for patients.

Methods: Patients fulfilling the ACR/EULAR 2013 criteria for SSc and who had active DUs were recruited either face-to-face or remotely. Study design throughout was informed by the patient user group. Participants were assessed twice: on study entry (when they downloaded the app on to their own smartphone and were trained in its use) and at the point of DU healing. Participants were asked to image their lesions and record PROMs (including pain score) with the app twice weekly. Specifically for this study a lesion feedback function was added to the app, showing lesion size (measured from the photographs) over time (Figure 1). Feasibility was assessed by the number of patients who elected to participate, by the number of photographs and PROMS recorded via the app, by patient questionnaire feedback (Table 1), and by verbal feedback during patient user group meetings.

Results: Of the 22 patients assessed for eligibility, 10 were recruited: 9 (90%) female, median age (range) 55 (36-74) years, median disease duration (range) 11.6 (1.7-29.7) years. Nine (90%) completed the study. One patient consented for a second time (therefore 10 'DU episodes' were included). Of the 12 patients not recruited, 2 were about to have DU surgery, in 6 the DU had almost healed, and 4 were not interested. The median duration of study participation per DU episode was 39 days (range 18-140). In total, 210 images were returned, median (range) 12 (4-87) per episode from 10 DU episodes. and 101 pain scores returned out of a possible total of 144 (70%). Patient questionnaire feedback is summarised in Table 1: most patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

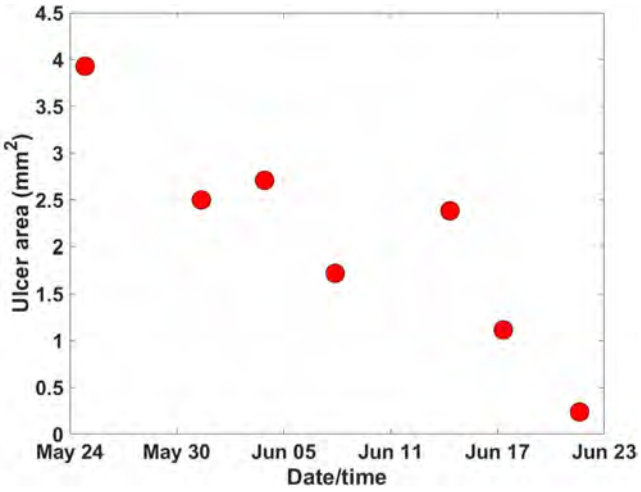


Figure 1 - Example of a lesion feedback graph sent to patients during the study. The ulcer size on the vertical axis is plotted against the date/time stamp of the image from which it was derived

Table 1 - Responses to the post-study questionnaire from the 10 'episodes' from the 9 participants who completed the study

Question [1]	Median (range)
Remembering to take photos/videos of finger ulcers (twice per week)	3 (1-6)
Taking photographs/videos at the same time on each occasion (twice per week)	3 (1-6)
Taking photographs/videos in the same place on each occasion (twice per week)	2 (1-6)
Keeping the environment and lighting the same on each occasion (twice per week)	1.5 (1-5)
Making sure the hands were in the same condition (e.g. no recent hand cream or hand washing) on each occasion(twice per week)	1 (1-4)
Overall experience of using the mobile phone to photograph/video your finger ulcer	2.5 (1-10)
Holding the phone when imaging	4 (1-9)
Pressing the button or screen to take an image	4 (1-8)
Getting a good clear image of your finger ulcer	2 (1-7)
Was it helpful to know (via app feedback) whether your ulcer was improving (getting smaller) or worsening (getting bigger) over time?[2]	1.5 (1-8)
Was it easy to understand the feedback provided via the app (was it presented in a clear and concise manner)?	2 (1-8)
Would you be keen to use the app again (to monitor the progress of any further ulcers)?[3]	1 (1-4)
How easy was it to send images/video to the research team through the SALVE app?	1 (1-3)

1. Answers on a 1-10 scale. 1 = very easy, 10 = very difficult unless otherwise stated.
2. Answers on a 1-10 scale. 1 = very helpful, 10 = not helpful
3. Answers on a 1-10 scale. 1 = very keen, 10 = not keen

found the app very easy to use, feedback was very helpful, and all were keen to use the app again. One participant required help from someone else to take the photographs, and one patient used a tripod. The patient with most difficulties reported 'cracked skin' and limited hand mobility. The 4 patients attending the final user group meeting confirmed feasibility, and made suggestions about 'next steps', including feedback on DU size being expressed as percentage change.

Conclusion: 1. Using the smartphone app was feasible for most patients despite the hand function problems of SSc.

2. Patients found the feedback function helpful in gauging 'progress' of the DU.

3. Our findings lend support to wider use of the app in routine clinical practice, thus allowing remote DU monitoring (facilitating early identification of clinical deterioration) and reducing the need for hospital attendance for many patients.

Disclosure: A. Herrick: Abbvie, 2, Boehringer-Ingelheim, 2, Janssen, 2, 6, Zura Bio, 2; **P. New**: None; **G. Dinsdale**: None; **A. Vail**: None; **J. Manning**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **W. dixon**: None; **C. Taylor**: None; **M. Dickinson**: None; **A. Murray**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0687

Distinct Cancer Risk Profiles in Patients with Systemic Sclerosis with Autoantibody Stratification

Arjun Mahajan[1], Nikki Zangenah[2], Maria Vazquez-Machado[2], Avery LaChance[3] and Jeffrey Sparks[4], [1]Harvard Medical School, Boston, [2]Brigham and Women's Hospital, Harvard Medical School, Boston, [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [4]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with systemic sclerosis (SSc) face increased cancer risk compared to the general population, yet current evidence on specific cancer patterns and their relationship to autoantibody status remains poorly characterized. We investigated cancer risk patterns in systemic sclerosis (SSc) patients and investigate associations between specific autoantibodies and cancer development.

Methods: This multi-center cohort study analyzed 5-year cancer incidences in adults with SSc versus matched controls with seborrheic keratosis using electronic medical record data from 128 healthcare organizations (from 2016-2024) in the TriNetX platform, a Health Insurance Portability and Accountability Act and General Data Protection Regulation-compliant federated research network. Patients were stratified by autoantibody status (anti-Scl-70, RNA polymerase III, anti-

Table 1. Baseline Patient Characteristics in Systemic Sclerosis and Seborrheic Keratosis Control Cohorts

	Before PSM, n (%)			After PSM, n (%)		
Characteristic	SSc (n = 73,392)	Control (n = 2,007,613)	SMD	SSc (n = 66,637)	Control (n = 66,637)	SMD
Age at index, mean (SD)	55.3 (16.6)	62.1 (13.8)	0.442	55.5 (16.5)	56.1 (16.2)	0.032
Sex						
Female	55,092 (81.3)	1,055,584 (55.0)	0.589	53,993 (81.0)	54,427 (81.7)	0.017
Male	11,099 (16.4)	770,016 (40.1)	0.546	11,066 (16.6)	10,654 (16.0)	0.017
Unknown Gender	1,580 (2.3)	94,961 (4.9)	0.140	1,578 (2.4)	1,556 (2.3)	0.002
Race						
American Indian/Alaska Native	243 (0.4)	3,430 (0.2)	0.035	240 (0.4)	252 (0.4)	0.003
Asian	3,285 (4.8)	34,383 (1.8)	0.171	3,129 (4.7)	2,950 (4.4)	0.013
Black or African American	7,545 (11.1)	52,123 (2.7)	0.336	6,994 (10.5)	7,076 (10.6)	0.004
Native Hawaiian/Pacific Islander	327 (0.5)	24,759 (1.3)	0.086	323 (0.5)	347 (0.5)	0.005
Other Race	2,439 (3.6)	46,175 (2.4)	0.070	2,400 (3.6)	2,315 (3.5)	0.007
Unknown Race	15,931 (23.5)	317,715 (16.5)	0.175	15,776 (23.7)	15,638 (23.5)	0.005
White	38,001 (56.1)	1,441,976 (75.1)	0.408	37,775 (56.7)	38,059 (57.1)	0.009
Comorbidities						
Chronic kidney disease	3,103 (4.6)	110,784 (5.8)	0.054	2,924 (4.4)	3,105 (4.7)	0.013
Diabetes mellitus	4,889 (7.2)	236,636 (12.3)	0.173	4,764 (7.1)	5,015 (7.5)	0.014
Hypertension	12,766 (18.8)	684,155 (35.6)	0.384	12,385 (18.6)	12,597 (18.9)	0.008
Nicotine dependence	2,815 (4.2)	155,084 (8.1)	0.164	2,752 (4.1)	2,895 (4.3)	0.011
Hyperlipidemia	9,678 (14.3)	746,859 (38.9)	0.580	9,570 (14.4)	9,840 (14.8)	0.011
Sjögren syndrome	2,317 (3.4)	11,736 (0.6)	0.201	1,987 (3.0)	2,387 (3.6)	0.034
Rheumatoid arthritis	3,569 (5.3)	37,384 (1.9)	0.179	3,194 (4.8)	3,578 (5.4)	0.026
Systemic lupus erythematosus	4,217 (6.2)	8,918 (0.5)	0.324	3,233 (4.9)	3,149 (4.7)	0.006

Abbreviations: PSM, propensity score matching; SMD, standardized mean difference.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Occurrence and Risk of Malignancies in Patients with Systemic Sclerosis vs. Seborrheic Keratosis Controls in a Propensity Score-Matched Analysis

Outcome	SSc Cohort Outcome Events (n=66,636)	Control Cohort Outcome Events (n= 66,636)	Hazard Ratio (95% CI)
All-Type Cancer	2,896	2,573	**1.17 (1.11, 1.23)**
Hematologic Cancers	800	498	**1.68 (1.50, 1.88)**
Hodgkin Lymphoma	36	24	1.56 (0.93, 2.62)
Non-Hodgkin Lymphoma	145	80	**1.89 (1.44, 2.49)**
Lymphoma	317	177	**1.87 (1.55, 2.24)**
Leukemia	207	153	**1.41 (1.14, 1.74)**
Myelodysplastic Syndromes	116	60	**2.03 (1.49, 2.77)**
Multiple Myeloma	151	74	**2.13 (1.61, 2.81)**
Solid Organ Cancers	2,142	1,810	**1.23 (1.16, 1.31)**
Digestive Tract Cancer	477	350	**1.43 (1.24, 1.64)**
Esophageal Cancer	69	18	**3.96 (2.36, 6.65)**
Colon Cancer	159	145	1.15 (0.92, 1.44)
Pancreatic Cancer	82	57	**1.51 (1.08, 2.11)**
Liver Cancer	107	71	**1.58 (1.17, 2.13)**
Lip, Oral Cavity, and Pharynx Cancer	123	82	**1.56 (1.18, 2.06)**
Nasopharynx Cancer	10	13	0.72 (0.31, 1.69)
Breast Cancer	577	739	**0.81 (0.73, 0.90)**
Lung Cancer	557	252	**2.32 (2.00, 2.69)**
Kidney Cancer	96	93	1.08 (0.81, 1.43)
Bladder Cancer	82	94	0.91 (0.68, 1.23)
Ovarian Cancer	74	74	1.04 (0.75, 1.44)
Cancer of Female Genital Organs	233	246	0.99 (0.83, 1.18)
Thyroid Cancer	111	107	1.08 (0.83, 1.41)
Brain Cancer	54	39	1.44 (0.96, 2.18)
Melanoma	133	438	**0.31 (0.26, 0.38)**
Negative Controls			
Varicose Veins	342	326	1.10 (0.94, 1.28)
Laceration of the Head	149	191	0.82 (0.66, 1.02)

Table 3. Occurrence and Risk of Malignancies in Patients with Systemic Sclerosis with anti-Scl-70 Antibody Positivity vs. Seborrheic Keratosis Controls in a Propensity Score-Matched Analysis

Outcome	SSc (anti-Scl-70) Events (n = 2,596)	Control Events (n=2,596)	Hazard Ratio (95% CI)
All-Type Cancer	**154**	**103**	**1.40 (1.09, 1.79)**
Hematologic Malignancies	**52**	**17**	**2.81 (1.63, 4.86)**
Hodgkin Lymphoma	≤10	≤10	6.21 (0.76, 50.47)
Non-Hodgkin Lymphoma	**14**	**≤10**	**6.30 (1.43, 27.70)**
Lymphoma	**19**	**≤10**	**3.44 (1.28, 9.20)**
Leukemia	**14**	**≤10**	**3.14 (1.03, 9.53)**
Myelodysplastic Syndromes	≤10	≤10	0.90 (0.22, 3.59)
Multiple Myeloma	**16**	**≤10**	**7.26 (1.67, 31.57)**
Solid Organ Malignancies	**111**	**75**	**1.37 (1.02, 1.83)**
Malignancy of Digestive Tract	22	18	1.12 (0.60, 2.08)
Esophageal Cancer	≤10	≤10	1.82 (0.33, 9.96)
Colon Cancer	≤10	≤10	1.20 (0.42, 3.47)
Pancreatic Cancer	≤10	≤10	2.74 (0.29, 26.30)
Liver Cancer	≤10	≤10	0.54 (0.13, 2.24)
Malignancy of Lip, Oral Cavity, and Pharynx	≤10	≤10	1.52 (0.36, 6.36)
Nasopharynx Cancer	≤10	0	–
Breast Cancer	37	33	1.01 (0.63, 1.62)
Lung Cancer	34	14	2.20 (1.18, 4.10)
Kidney Cancer	≤10	≤10	2.06 (0.63, 6.69)
Bladder Cancer	≤10	≤10	0.90 (0.26, 3.10)
Ovarian Cancer	≤10	≤10	0.31 (0.03, 2.94)
Malignancy Female Genital Organs	≤10	≤10	1.83 (0.63, 5.36)
Thyroid Cancer	≤10	≤10	2.23 (0.70, 7.12)
Brain Cancer	≤10	≤10	0.90 (0.18, 4.44)
Melanoma	**≤10**	**18**	**0.35 (0.15, 0.83)**
Negative Controls			
Varicose Veins	27	17	1.42 (0.78, 2.61)
Laceration of the Head	11	≤10	1.40 (0.54, 3.60)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

centromere) from available clinical laboratory testing. To facilitate comparative analysis, propensity score matching (1:1 using a greedy nearest neighbor algorithm) balanced cohorts on characteristics like age, sex, race and ethnicity, and comorbidities (Table 1). Primary outcomes included 5-year incidences of hematologic and solid-organ cancers, and varicose vein and trauma (laceration of the head) were selected as negative control outcomes. Hazard ratios (HRs) and their 95% confidence intervals (CIs) were calculated using Cox proportional hazards regressions.

Results: After propensity score matching, 66,637 patients were included in each cohort, with no statistically significant differences in baseline demographics and covariates between the treatment and control groups; in the SSc cohort, the mean age was 55.5 years (SD: 16.5) and 81.0% were female. SSc patients demonstrated elevated 5-year risks of any cancer compared to matched controls (HR 1.17; 95% CI 1.11–1.23) (Table 2). Hematologic cancer risk was significantly increased (HR 1.68; 95% CI 1.50–1.88), particularly for multiple myeloma (HR 2.13; 95% CI 1.61–2.81) and myelodysplastic syndromes (HR 2.03; 95% CI 1.49–2.77). For solid organ cancers (HR 1.23; 95% CI 1.16–1.31), esophageal cancer showed the highest risk (HR 3.96; 95% CI 2.36–6.65), followed by lung cancer (HR 2.32; 95% CI 2.00–2.69). Among autoantibody subgroups, anti-Scl-70 positive patients showed increased overall cancer risk (HR 1.40; 95% CI 1.09–1.79), RNA Polymerase III positive patients had higher rates of hematologic cancers (HR 2.56; 95% CI 1.19–5.54), while anti-centromere positive patients showed no increased cancer risks aside from a decreased melanoma risk (HR 0.26; 95% CI 0.10–0.69).

Conclusion: SSc patients demonstrate significantly increased risks for both hematologic and solid organ cancers, with risk profiles varying by autoantibody status. These findings suggest the need for targeted cancer screening strategies in SSc and further research to confirm the generalizability of these findings.

Disclosure: A. Mahajan: None; **N. Zangenah**: None; **M. Vazquez-Machado**: None; **A. LaChance**: Johnson & Johnson, 2, johnson and johnson, 2, Merck, 5, Pfizer, 2; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 0688

Total lung capacity is predictive of disease severity and survival in systemic sclerosis: a longitudinal analysis in 2347 patients from the French National Cohort Study

Benjamin Chaigne[1], Alexandre bense[2], Frédérique Aubourg[3], Christian AGARD[4], Yannick Allanore[5], Alice berezne[1], Gregory Pugnet[6], Eric Hachulla[7], Vincent Cottin[8], Arnaud Hot[8], bertrand Dunogue[1], Anuxcy Kanagaratnam[2], Sylvain Palat[9], Alain Lescoat[10], Sabine berthier[11], Emmanuel Chatelus[12], Sébastien Rivière[13], David Launay[14], Marie-Elise Truchetet[15], Anh-Tuan Dinh-Xuan[3], Luc Mouthon[1] and the French Systemic Sclerosis Network, [1]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [2]AP HP, Paris, France, [3]Unité exploration fonctionnelle respiratoire, Pneumology department, Cochin Hospital, APHP, PARIS, France, [4]Internal medicine, Nantes University Hospital, Nantes, France, [5]Universit Paris Cit, Paris, France, [6]CHU, Montpelliers, France, [7]CHU, Lilles, France, [8]CHU, Lyon, France, [9]Limoges, Limoges, France, [10]CHU Rennes - University Rennes, Rennes, France, [11]CHU, Dijon, France, [12]Department of Rheumatology, University Hospital Strasbourg, France, Strasbourg, France, [13]AP HP, Parsi, France, [14]Univ. Lille, Inserm, CHU Lille, Department of Internal Medicine and Clinical Immunology, Reference Center for Rare Autoimmune and Autoinflammatory diseases (CERAINOM), U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France. National Reference Center for Pulmonary Arterial Hypertension (Pulmotension), Lille, France, Lille Cedex, France, [15]Bordeaux University Hospital, Bordeaux, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

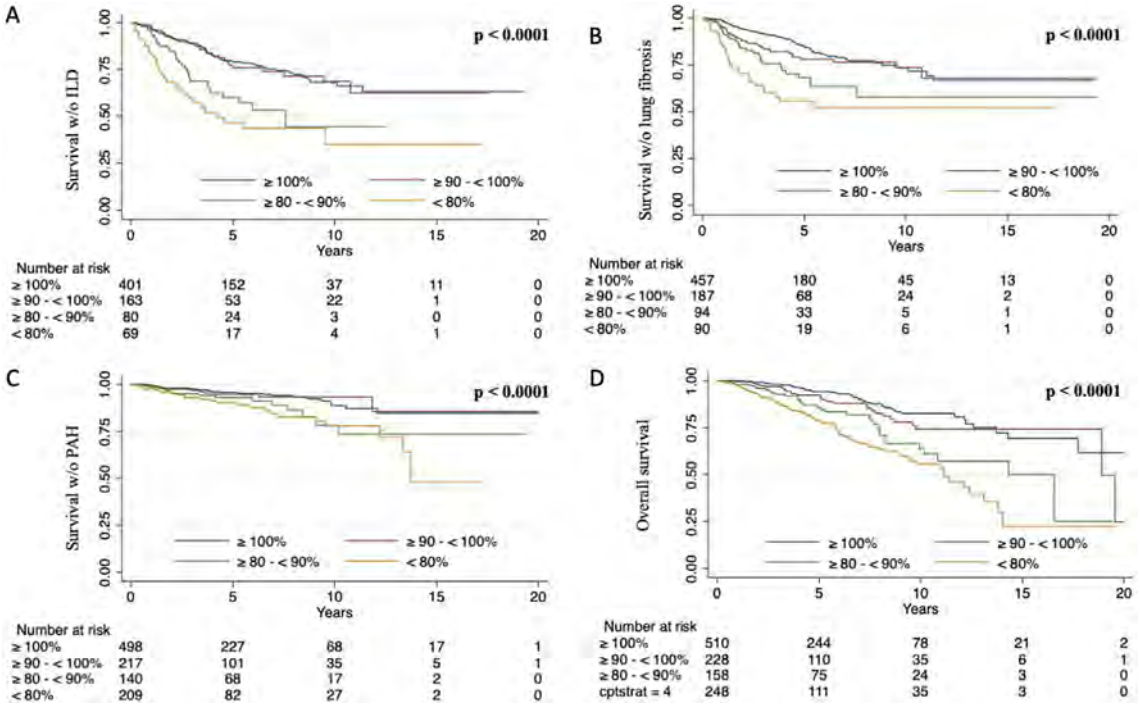


Figure 1. Overall probability of survival according to total lung capacity in patients with systemic sclerosis

Background/Purpose: Total lung capacity (TLC) is seldom assessed in the prediction of systemic sclerosis (SSc) disease severity.Herein, we utilized the French SSc national database to analyse TLC in SSc patients, examine its longitudinal trajectories, and explore its associations with organ involvement and patient survival.

Methods: We performed a retrospective multicentre study of SSc patients enrolled in the French national SSc cohort with at least one TLC assessment, described patients based on baseline TLC measurements, modelized TLC trajectories in SSc,

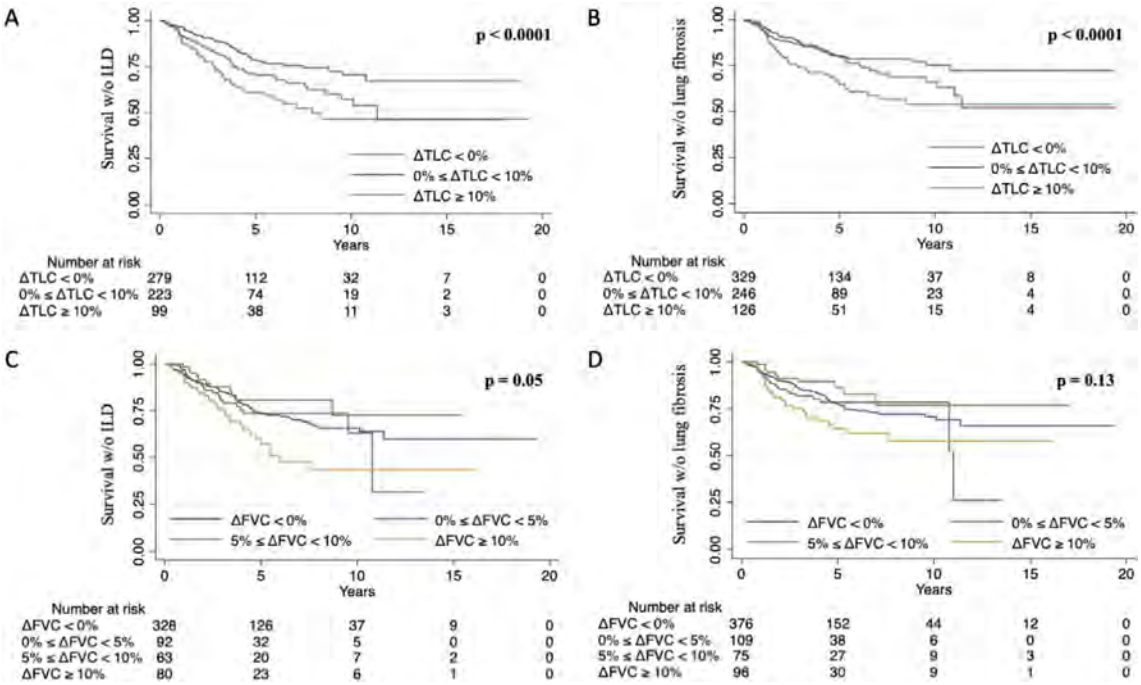


Figure 2. Overall probability of time to interstitial lung disease and lung fibrosis onset according to total lung capacity and forced vital capacity decrease in patients with systemic sclerosis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and associated TLC measures with disease prognosis. Only patients who met the 2013-American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) SSc classification criteria and had baseline TLC measure available were included in the study.

Results: Two thousand three hundred and forty-seven patients were included in the study. Median [interquartile] (IQR) age at SSc diagnosis was 52 [41-63] years. The proportion of females was 81%, and the proportion of dcSSc patients was 30%. Thirty percent, 38%, and 4% of patients were positive for ATA, anti-centromere (ACA), and anti-RNA polymerase III antibody (ARA), respectively. Thirty-nine percent and 28%, had ILD and LF, respectively.

At baseline, forty-three percent had a TLC above or equal to 100 % and 24 % had a TLC below 80%. During a median [IQR] follow-up of 4.6 [2.5-7.9] years, 190 (16%) patients died, 617 (53%) developed de novo interstitial lung disease (ILD), 499 (43%) developed de novo LF, 175 (15%) were diagnosed with PAH following right heart catheterization, and 69 (6%) developed scleroderma renal crisis (SRC). Kaplan-Meier curves showing the overall 20-year probabilities of survival and survival without ILD, LF, and PAH after SSc diagnosis according to baseline TLC showed that a lower TLC was associated with worse survival and a higher risk of ILD, LF, or PAH occurrences ($p < 0.001$) (Figure 1).

Among 2347 patients with at least one TLC measure, 988 (42%) patients had at least 2 TLC measures. Individual TLC trajectories varied among patients. Different models of TLC trajectories were assessed using latent process mixed models. The best model showed that the vast majority of SSc patients had stable TLC trajectories and clustered patients into three groups predictive of SSc survival, ILD, LF, and PAH ($p < 0.05$).

Interestingly, a 10% decrease of TLC was found to be predictive of a 5% decrease in forced vital capacity (FVC)($p < 0.0001$), a 10% decrease in DLCODLCO ($p < 0.001$), and consequently an earlier predictive marker of ILD and LF than FVC (Figure 2).

Conclusion: The present study shows that TLC measurement is associated with SSc severity and prognosis. It suggests that TLC may be an early marker of ILD and PF development, and that a 10% TLC decrease is a useful and early marker of FVC or DLCO decreases, as well as ILD or LF occurrence. Overall, our findings support the use of TLC along with FVC in monitoring and assessing ILD and LF in both clinical practice and clinical trials.

Disclosure: B. Chaigne: None; **A. bense**: None; **F. Aubourg**: None; **C. AGARD**: None; **Y. Allanore**: None; **A. berezne**: None; **G. Pugnet**: None; **E. Hachulla**: None; **V. Cottin**: None; **A. Hot**: None; **b. Dunogue**: None; **A. Kanagaratnam**: None; **S. Palat**: None; **A. Lescoat**: None; **S. berthier**: None; **E. Chatelus**: None; **S. Rivière**: None; **D. Launay**: AstraZeneca, 2, 6, BioCryst, 6, 12, travel grants, CSL Behring, 2, 6, Shire, 12, travel grants, Takeda, 2, 6; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2; **A. Dinh-Xuan**: None; **L. Mouthon**: None.

Abstract Number: 0689

Development of an Articular Activity Score in Systemic Sclerosis (ASSESS): Identifying Core Instruments for Disease Activity Assessment

Blaz Burja[1], Paco Welsing[2], Alain Lescoat[3], Andreas Eisenring[4], Anna-Maria Hoffmann-Vold[5], Claire Leroy David[6], Dinesh Khanna[7], Francesco Del Galdo[8], Michele Iudici[9], Janet Pope[10], julia Spierings[11], Madelon Vonk[12], Marie-Elise Truchetet[13], Martine Clergeau[14], Michael Hughes[15], Susan Murphy[16], Tracy Frech[17], Oliver Distler[18] and Muriel Elhai[19], [1]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Zurich, Switzerland, [2]Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, Utrecht, Netherlands, [3]CHU Rennes - University Rennes, Rennes, France, [4]Patient research partners, Zurich, Switzerland, [5]Oslo University Hospital, Oslo, Norway, [6]Patient research partners, Sos, France, [7]University of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Michigan, Ann Arbor, MI, [8]University of Leeds, Leeds, United Kingdom, [9]Division of Rheumatology, Department of Medicine, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland, Geneva, [10]University of Western Ontario, London, ON, Canada, [11]Department of Rheumatology & Clinical Immunology, University Medical Center, Ultrecht, The Netherlands, Utrecht, Netherlands, [12]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, [13]Bordeaux University Hospital, Bordeaux, France, [14]Patient research partners, Paris, France, [15]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [16]Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Michigan, [17]Vanderbilt University Medical Center, Nashville, TN, [18]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [19]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, Schlieren, Switzerland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory joint and/or tendon involvement affects up to 30% of patients with systemic sclerosis (SSc), resulting in pain, reduced joint function, and impaired patients' quality of life. The lack of standardized outcome measures for assessing articular activity in SSc hampers therapeutic development and data comparability. To bridge this gap, we aimed to develop a consensus-based composite score to assess articular activity in adult SSc, suitable for research settings and/or clinical practice.

Methods: A steering committee was convened, consisting of 12 rheumatologists, 1 epidemiologist, 1 occupational therapist, and 3 patient research partners. The development of the articular activity score followed a stepwise process (Figure 1). First, a scoping review was conducted using PubMed (January 1960 to April 2023); two reviewers (B.B. and M.E.) independently screened studies on joint/tendon involvement in SSc and extracted assessment tools. Following expert discussions, instruments demonstrating at least 70% validity and feasibility after the committee voting were further evaluated by two independent reviewers according to OMERACT (Outcome Measures in Rheumatology) guidelines. These findings were then presented to the steering committee, and a two-round online Delphi survey was used to finalize the core set.

Results: Of the 770 references initially identified, 658 were excluded based on title or abstract screening, leaving 112 articles for full-text review; ultimately, 86 studies met the inclusion criteria. From these, 46 instruments that were used in at least two studies were identified. Based on domain validity and feasibility, 9 clinical, 1 serological, 3 composite scores, and 3 patient-reported outcome measures were shortlisted for further evaluation (Table 1). Following an assessment of measurement properties according to OMERACT guidelines, the steering committee voted and excluded 10 items due to missing

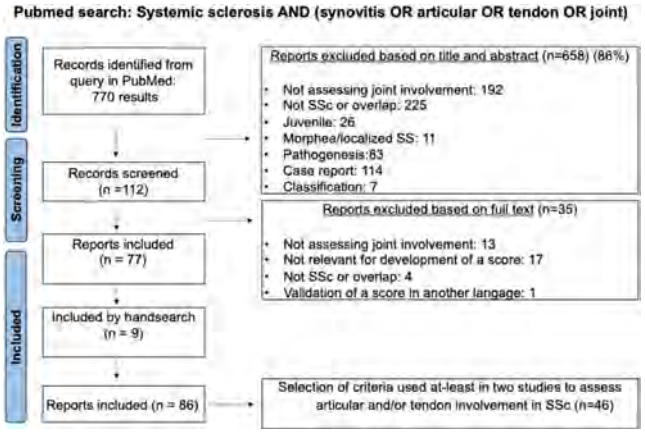


Figure 1: Scoping review search strategy.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Identified core instruments for assessing disease articular activity in SSc patients. The 28-joint count includes the wrists, metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints, elbows, shoulders, and knees. The 50-joint count builds on the 28-joint count by also including the distal interphalangeal (DIP) joints, hips, ankles, and metatarsophalangeal (MTP) joints.

Clinical	Serology	Composite score	Patient reported outcomes
○ Ritchie articular index ○ Number of tender joints (n=28, n=50) ○ Number of swollen joints (n=28, n=50) ○ Number of synovitis (n=28, n=50) ○ Presence of tendon friction rubs ○ Number of tendon frictions rubs	○ CRP	○ DAS28-ESR ○ DAS28-CRP ○ SDAI	○ Visual analogic scale for articular pain (patient) ○ Visual analogic scale for disease activity (patient) ○ Visual analogic scale for disease activity (physician)

specificity or feasibility on joint activity assessment. 6 final instruments were selected for inclusion in a composite outcome measure to assess articular activity in patients with SSc. The selected instruments covered clinical (28-joint tender/swollen joint count with the addition of distal interphalangeal joints; presence of tendon friction rubs), serologic (CRP) and patient/physician reported outcomes (VAS activity pain patient, VAS activity doctor) domains.

Conclusion: International, multi-disciplinary SSc experts and patient partners have identified 6 feasible core instruments to assess articular activity in SSc patients, covering both joint and tendon involvement. This core set provides the basis to further develop a composite score for articular involvement in SSc for use in clinical practice and clinical trials. Future steps will include performance validation within longitudinal SSc cohorts.

Disclosure: B. Burja: None; **P. Welsing**: None; **A. Lescoat**: None; **A. Eisenring**: None; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **C. Leroy David**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **M. Iudici**: None; **J. Pope**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Frese, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mallinckrodt Pharmaceuticals, 2, 5, Merck/MSD, 2, Mitsubishi Tanabe Pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2, Sanofi, 2, Teva, 2, UCB, 2, Viatris, 2; **j. Spierings**: None; **M. Vonk**: Boehringer-Ingelheim, 2, 6, 12, Travel grants, Janssen, 2, 6, 12, travel grants, Merck/MSD, 6; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2; **M. Clergeau**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **S. Murphy**: None; **T. Frech**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **M. Elhai**: AstraZeneca, 12, Congress support, Boehringer-Ingelheim, 6, FOREUM, 5, Iten Kohaut foundation, 5, Janssen, 12, Congress support, Kurt und Senta Herrmann foundation, 5, Novartis, 5, Pfizer, 5, University Zurich, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0690

Quantitative ^{18}F-FDG PET-CT of the lungs detects treatment induced changes in patients with early severe diffuse cutaneous systemic sclerosis and interstitial lung disease

Bo Broens[1], esther Nossent[1], Lilian Meijboom[1], Gerben Zwezerijnen[1], julia Spierings[2], Jeska de Vries-Bouwstra[3], Jacob M. van Laar[4], Conny van der Laken[1] and Alexandre Voskuijl[5], [1]Amsterdam UMC, Amsterdam, Netherlands, [2]Department of Rheumatology & Clinical Immunology, University Medical Center, Ultrecht, The Netherlands, Utrecht, Netherlands, [3]Leiden University Medical Center, Leiden, Netherlands, [4]UMC Utrecht, Utrecht, Netherlands, [5]Amsterdam University Medical Center, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with early severe diffuse cutaneous systemic sclerosis (dcSSc) with interstitial lung disease (ILD) have poor prognosis. New tools are needed to improve treatment stratification and monitoring. Studies with repeated positron emission tomography-computed tomography with [^{18}F]Fluorodeoxyglucose ([^{18}F]FDG PET-CT) in this specific high-risk group have not been performed and may have clinical value. In this study we aimed to (1) assess changes in [^{18}F]FDG lung uptake between baseline and follow-up after different treatment regimens (2) identify if [^{18}F]FDG lung uptake at baseline is associated with ILD progression during follow-up.

Methods: [^{18}F]FDG PET-CT scans of the lungs were performed at baseline and repeated one year after initial randomization to cyclophosphamide pulse therapy or autologous stem cell transplantation within the UPSIDE trial (NCT04464434). All [^{18}F]FDG PET-CT scans were analyzed by manual placement of 2 cm volumes of interest (VOIs) in 22 pre-defined lung areas and mean standardized uptake values (SUVs) of [^{18}F]FDG tracer uptake were corrected for the uptake in the mediastinal blood pool.

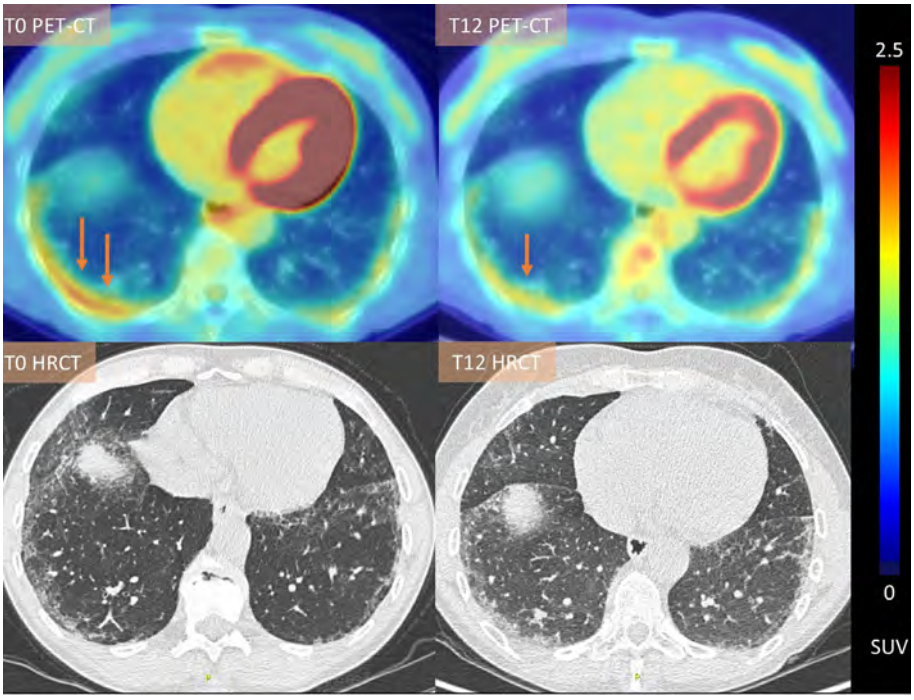


Figure 1. Visual and quantitative decrease in pulmonary [18F]FDG uptake in a patient with early severe diffuse cutaneous systemic sclerosis and interstitial lung disease with clinical improvement

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

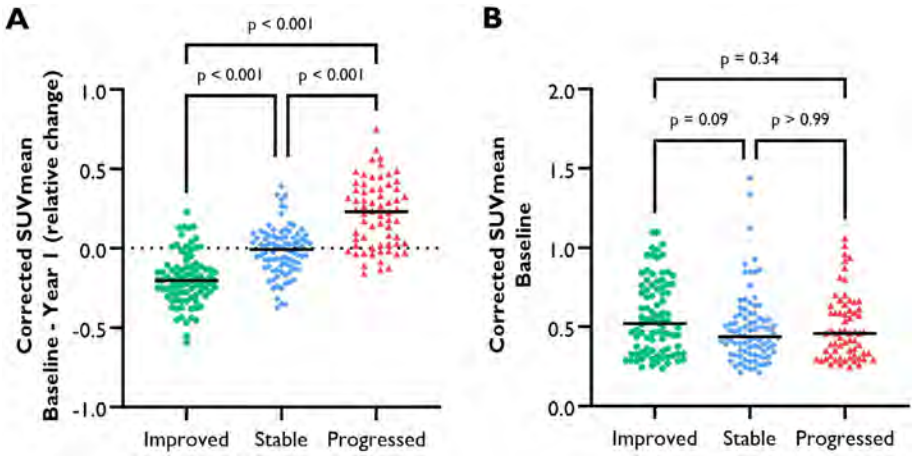


Figure 2. (Changes in) Quantitative [18F]FDG uptake between different patient groups (improved, stable or progressed interstitial lung disease)

Percentual changes after one year were calculated by the mean of all VOIs. Changes in [^{18}F]FDG lung uptake were compared to clinical assessment of ILD development. At 1 year follow-up, ILD progression was defined according to the Progressive Pulmonary Fibrosis (PPF) criteria (2 out of 3 criteria): (1) increased respiratory symptoms, (2) decreased FVC≥5% or DLCO≥10% (3) increased lung fibrosis on HRCT, while patients met criteria for ILD improvement with (2 out of 3) reversed criteria: (1) decreased respiratory symptoms, (2) increased FVC≥5% or DLCO≥10% (3) decreased lung fibrosis on HRCT. Stable ILD was defined as having neither progression nor improvement. Between group differences were analyzed using non-parametric tests.

Results: Eleven patients were included. Five patients were female, with a median age of 54 years and median disease duration of 9.5 months at baseline. Patients with ILD progression at 1 year (n=3) showed increased [^{18}F]FDG uptake (corrected SUVmean +21.7%) after 1 year, while patients with improved ILD (n=4) showed decreased [^{18}F]FDG uptake (corrected SUVmean -19.4%) over time (Figure 1 and 2A). Less evident differences were observed in patients with stable ILD (n=4; corrected SUVmean -1.5%). Finally, [^{18}F]FDG uptake at baseline did not differ between patients who did or did not progress at 1 year of follow-up (Figure 2B).

Conclusion: [^{18}F]FDG uptake in the lungs changed in line with clinical response to therapy in patients with early severe dcSSc and ILD. These results suggests that [^{18}F]FDG PET-CT has the potential to have additive value in the monitoring of SSc-ILD.

Disclosure: B. Broens: None; **e. Nossent**: None; **L. Meijboom**: None; **G. Zwezerijnen**: None; **j. Spierings**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **J. van Laar**: None; **C. van der Laken**: None; **A. Voskuijl**: None.

Abstract Number: 0691

Association of Elevated Platelets and CRP with Severe Disease and Poor Survival in Systemic Sclerosis

Brian Lee[1], Shufeng Li[1], Srijana Davuluri[2], Jennifer Lee[1] and Lorinda Chung[2], [1]Stanford University, Stanford, [2]Stanford University, Stanford, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic and Clinical Characteristics of Four CRP/Platelet-Defined Groups at Baseline and Over Two-Year Follow-Up

	Overall (n=139), n (%)	NP/NC (n=84), n (%)	NP/EC (n=33), n (%)	EP/NC (n=10), n (%)	EP/EC (n=12), n (%)	p-value
Gender						0.47
Female	124 (89.2%)	74 (88.1%)	28 (84.8%)	10 (100.0%)	12 (100.0%)	
Male	15 (10.8%)	10 (11.9%)	5 (15.2%)	0 (0.0%)	0 (0.0%)	
Race						0.94
Asian	13 (9.3%)	10 (11.9%)	2 (6.1%)	1 (10.0%)	0 (0.0%)	
Black	5 (3.6%)	4 (4.8%)	1 (3.0%)	0 (0.0%)	0 (0.0%)	
White	81 (58.3%)	49 (58.3%)	19 (57.6%)	5 (50.0%)	8 (66.7%)	
Other/Unknown	40 (28.8%)	21 (25.0%)	11 (33.3%)	4 (40.0%)	4 (33.3%)	
Ethnicity						0.25
Hispanic/Latino	25 (18.0%)	11 (13.1%)	6 (18.2%)	4 (40.0%)	4 (33.3%)	
Age at first blood draw, in years						0.11
Median	54.4	54.0	58.8	45.5	61.6	
Range	18.8-83.0	18.8-83.0	30.1-81.7	22.6-61.0	20.0-78.7	
Time from 1st non-Raynaud symptom to first blood draw, in years						0.02
Median	3.8	4.4	6.2	2.4	1.5	
Range	0.1-42.6	0.1-42.6	0.3-21.2	0.6-12.6	0.3-8.0	
Serologies						
Scl-70 positive (n=130)	29/130 (22.3%)	11/77 (14.3%)	8/31 (25.8%)	4/10 (40.0%)	6/12 (50.0%)	0.01
RNA Pol III positive (n=81)	22/81 (27.2%)	10/49 (20.4%)	5/17 (29.4%)	3/8 (37.5%)	4/7 (57.1%)	0.16
Centromere positive (n=125)	44/125 (35.2%)	30/77 (39.0%)	11/29 (37.9%)	2/10 (20.0%)	1/9 (11.1%)	0.30
Organ involvement						
Skin involvement						
Diffuse (n=139)	59/139 (42.4%)	31/84 (36.9%)	12/33 (36.4%)	5/10 (50.0%)	11/12 (91.7%)	0.002
Cardiac						
Pericarditis (n=139)	1/139 (0.7%)	1/84 (1.2%)	0/33 (0.0%)	0/10 (0.0%)	0/12 (0.0%)	1.00
Myocarditis/Cardiomyopathy (n=137)	4/137 (2.9%)	0/83 (0.0%)	1/32 (3.1%)	0/10 (0.0%)	3/12 (25.0%)	0.001
Conduction abnormalities (n=138)	14/138 (10.1%)	8/83 (9.6%)	3/33 (9.1%)	0/10 (0.0%)	3/12 (25.0%)	0.29
Pulmonary						
ILD (n=127)	64/127 (50.4%)	37/78 (47.4%)	16/27 (59.3%)	6/10 (60.0%)	5/12 (41.7%)	0.62
FVC < 70% with FEV/FVC > 80% (n=111)	19/111 (17.1%)	11/65 (16.9%)	4/25 (16.0%)	2/10 (20.0%)	2/11 (18.2%)	1.00
Pulmonary Hypertension (n=127)	25/127 (19.7%)	12/78 (15.4%)	8/28 (28.6%)	2/10 (20.0%)	3/11 (27.3%)	0.39
Renal						
Scleroderma Renal Crisis (n=139)	5/139 (3.6%)	2/84 (2.4%)	2/33 (6.1%)	0/10 (0.0%)	1/12 (8.3%)	0.41
Gastrointestinal						
GERD (n=138)	112/138 (81.2%)	66/84 (78.6%)	27/32 (84.4%)	8/10 (80.0%)	11/12 (91.7%)	0.77
Dysphagia (n=119)	60/119 (50.4%)	33/70 (47.1%)	15/27 (55.6%)	2/10 (20.0%)	10/12 (83.3%)	0.02
Malabsorption/SIBO (n=127)	21/127 (16.5%)	13/73 (17.8%)	3/33 (9.1%)	2/10 (20.0%)	3/11 (27.3%)	0.43
GAVE (n=90)	10/90 (11.1%)	3/52 (5.8%)	1/23 (4.3%)	2/7 (28.6%)	4/8 (50.0%)	0.003
Musculoskeletal						
Joint pain (n=138)	100/138 (72.5%)	60/83 (72.3%)	23/33 (69.7%)	6/10 (60.0%)	11/12 (91.7%)	0.37
Joint contracture (n=133)	45/133 (33.8%)	23/80 (28.7%)	5/31 (16.1%)	5/10 (50.0%)	12/12 (100.0%)	<0.0001
Myositis (n=135)	46/135 (34.1%)	28/82 (34.1%)	7/32 (21.9%)	4/10 (40.0%)	7/11 (63.6%)	0.09
Vascular						
Telangiectasias (n=134)	94/134 (70.1%)	55/80 (68.8%)	26/33 (78.8%)	5/9 (55.5%)	8/12 (66.7%)	0.50
Raynaud's (n=139)	134/139 (96.4%)	82/84 (97.6%)	32/33 (97.0%)	9/10 (90.0%)	11/12 (91.7%)	0.21
Digital gangrene (n=137)	11/137 (8.0%)	6/83 (7.2%)	4/32 (12.5%)	0/10 (0.0%)	1/12 (8.3%)	0.68
Digital ulcers (n=137)	58/137 (42.3%)	30/84 (35.7%)	16/31 (51.6%)	3/10 (30.0%)	9/12 (75.0%)	0.04
Calcinosis (n=126)	26/126 (22.2%)	19/77 (24.7%)	6/28 (21.4%)	1/9 (11.0%)	2/12 (16.7%)	0.86
Transplant						
Lung	2/139 (1.4%)	1/84 (1.2%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	0.64
Autologous stem cell	1/139 (0.7%)	0/84 (0.0%)	0/33 (0.0%)	0/10 (0.0%)	1/12 (8.3%)	0.16
Medications						
Immunosuppressants/modulators						
Biologics*	7/139 (5.0%)	4/84 (4.8%)	2/33 (6.1%)	0/10 (0.0%)	1/12 (8.3%)	0.83
Tofacitinib	2/139 (1.4%)	1/84 (1.2%)	0/33 (0.0%)	1/10 (10.0%)	0/12 (0.0%)	0.24
Mycophenolate/Mycophenolic acid	50/139 (36.0%)	27/84 (32.1%)	10/33 (30.3%)	5/10 (50.0%)	8/12 (66.7%)	0.09
Methotrexate PO/Methotrexate SQ	19/139 (13.7%)	7/84 (8.3%)	6/33 (18.2%)	1/10 (10.0%)	5/12 (41.7%)	0.02
Cyclophosphamide	4/139 (2.9%)	2/84 (2.4%)	1/33 (3.0%)	1/10 (10.0%)	0/12 (0.0%)	0.44
Tacrolimus	2/139 (1.4%)	1/84 (1.2%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	0.64
Azathioprine	6/139 (4.3%)	2/84 (2.4%)	2/33 (6.1%)	1/10 (10.0%)	1/12 (8.3%)	0.22
Hydroxychloroquine	52/139 (37.4%)	25/84 (29.8%)	17/33 (51.5%)	3/10 (30.0%)	7/12 (58.3%)	0.06
Sulfasalazine	2/139 (1.4%)	1/84 (1.2%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	0.64
Steroids#	33/139 (23.7%)	21/84 (25.0%)	8/33 (24.2%)	1/10 (10.0%)	3/12 (25.0%)	0.83
IVIG	6/139 (4.3%)	1/84 (1.2%)	2/33 (6.1%)	0/10 (0.0%)	3/12 (25.0%)	0.09
Antifibrotics†	3/139 (2.2%)	0/84 (0.0%)	1/33 (3.0%)	0/10 (0.0%)	2/12 (16.7%)	0.01
Vasodilators						
Calcium channel blockers‡	65/139 (46.8%)	39/84 (46.4%)	16/33 (48.5%)	5/10 (50.0%)	5/12 (41.7%)	0.99
PDE5 inhibitors^	40/139 (28.8%)	24/84 (31.0%)	9/33 (27.3%)	2/10 (20.0%)	3/12 (25.0%)	0.99
Endothelin Receptor Antagonists^	6/139 (4.3%)	2/84 (2.4%)	3/33 (9.1%)	0/10 (0.0%)	1/12 (8.3%)	0.25
Prostacyclins/PRAs^	3/139 (2.2%)	2/84 (2.4%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	1.00
Cilostazol	4/139 (2.9%)	3/84 (3.6%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	1.00
Dipyramidole	1/139 (0.7%)	0/84 (0.0%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	0.40
Pentoxyfylline	3/139 (2.2%)	2/84 (2.4%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	1.00
Terazosin	1/139 (0.7%)	0/84 (0.0%)	1/33 (3.0%)	0/10 (0.0%)	0/12 (0.0%)	0.40

Abbreviations: NP/NC: normal platelet/normal CRP, NP/EC: normal platelet/elevated CRP, EP/NP: elevated platelet/normal platelet, EP/EC: elevated platelet/elevated CRP, PDE5: phosphodiesterase type 5, PRAs: prostanoid receptor agonists.

* Biologics include Abatacept SQ, Abatacept Infusion, Certolizumab SQ, Rituximab, and Tocilizumab.

Steroids include Methylprednisolone and Prednisone.

† Antifibrotics include Nintedanib and Pirfenidone.

Background/Purpose: Elevated acute phase reactants such as platelets and C-reactive protein (CRP) have been used as inclusion criteria to enrich systemic sclerosis (SSc) clinical trials for patients with active disease. While elevated CRP levels have been associated with severe disease and worse survival, the role of platelet levels remains largely unexplored.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1A: Longitudinal Changes in Forced Vital Capacity (FVC, %) Over Time Using Mixed Models

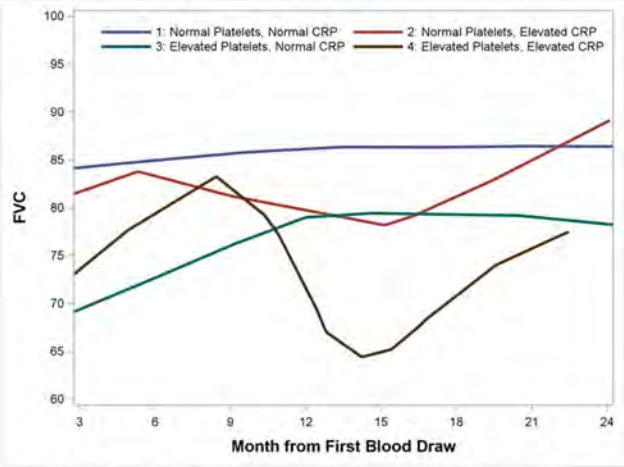


Figure 1B: Longitudinal Changes in modified Rodnan Skin Score (mRSS) Over Time Using Generalized Estimating Equation Model

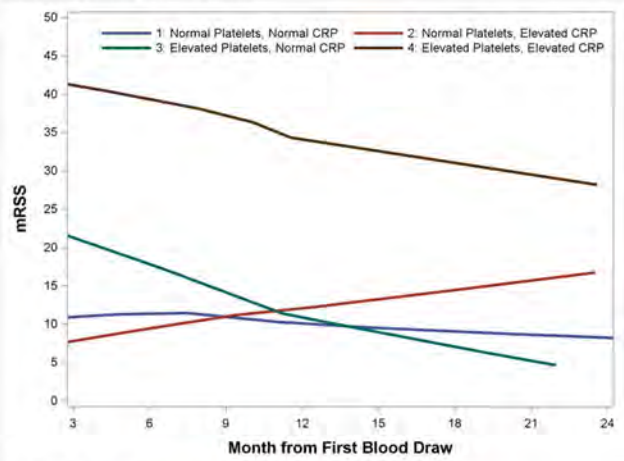
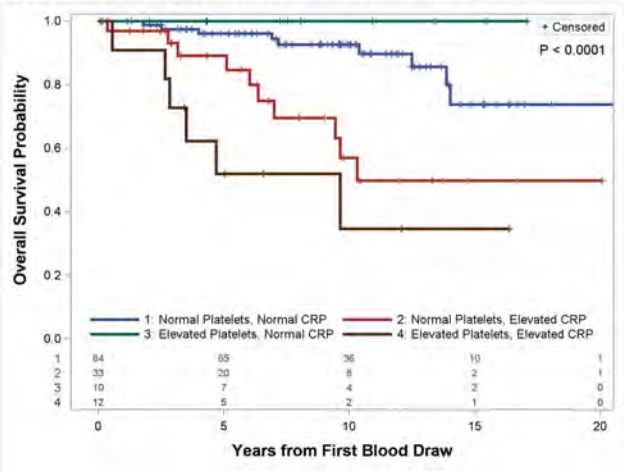


Figure 1C: Overall Survival of Patients by Four CRP/Platelet-Defined Groups



Methods: We performed a retrospective study of adult SSc patients seen at a single tertiary care center from 1996 to 2022. Based on the first available blood draw after onset of first non-Raynaud symptom, patients were categorized into four groups using cutoffs of ≥330,000/μL for elevated platelet and ≥6.0mg/L for elevated CRP: 1) normal platelet/normal CRP (NP/NC), 2) elevated platelet/normal CRP (EP/NC), 3) normal platelet/elevated CRP (NP/EC), 4) elevated platelet/elevated CRP (EP/EC). Longitudinal forced vital capacity (FVC) and modified Rodnan skin score (mRSS) were captured over two years following the initial blood draw. Survival data were collected until end of study (12/31/2024), death, or the last available

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: COX Model Comparing Overall Survival Across Different Groups

	HR (95% CI)	p-value
NP/EC vs NP/NC	3.94 (1.60 - 9.72)	0.003
EP/EC vs NP/NC	8.04 (2.84 - 22.79)	<0.0001
EP/EC vs NP/EC	2.04 (0.74 - 5.64)	0.17
Elevated CRP vs Normal CRP	5.44 (2.39 - 12.36)	<0.0001
Elevated Platelet vs Normal Platelet	1.98 (0.79 - 4.95)	0.15

Abbreviations: NP/NC: normal platelet/normal CRP, NP/EC: normal platelet/elevated CRP, EP/NP: elevated platelet/normal platelet, EP/EC: elevated platelet/elevated CRP.

clinic date. Fisher's exact test, Kruskal-Wallis Tests, mixed model, generalized estimating equation model, log-rank test of Kaplan-Meier, and Cox regression analyses were used, with $p< 0.05$ considered statistically significant.

Results: There was a total of 139 patients in the study, with 84, 33, 10, and 12 patients in the NP/NC, NP/EC, EP/NC, and EP/EC groups, respectively. The EP/EC group had the highest percentage of patients with Scl-70 positive antibody, diffuse skin involvement, myocarditis/cardiomyopathy, dysphagia, gastric antral vascular ectasia (GAVE), joint contracture, and digital ulcers compared to other groups ($p< 0.05$ for all) (Table 1). The EP/EC group had significantly higher use of methotrexate and antifibrotic agents compared to other groups ($p< 0.05$ for all). Over two years, the NP/NC group had the highest FVC baseline values and remained the most stable. In contrast, both elevated CRP groups (NP/EC and EP/EC) had a decline in FVC values during the first year followed by some improvement, with EP/EC group having the steepest drop during the first year. However, there were no statistically significant differences between the groups over time (Figure 1A). Over the same period, EP/EC group had the worst mRSS scores, which improved over time but remained significantly higher than the other three groups ($p< 0.05$ for all comparisons with the EP/EC group) (Figure 1B). Survival was lowest in the EP/EC group, with a median survival of 9.6 years compared to 21.3 years in the NP/NC group ($p< 0.0001$) (Figure 1C) and a hazard ratio (HR) of 8.04 (2.84-22.79, $p< 0.0001$) (Table 2). When comparing the EP/EC group to the NP/EC group, the HR was 2.04 (0.74-5.64, $p=0.17$) (Table 2).

Conclusion: SSc patients with elevated platelets and CRP developed more severe disease than the other groups. This subset had an eightfold increased risk of mortality compared to those with normal platelets and CRP. The combination of elevated platelets and CRP may have a greater impact on survival than CRP alone. Assessing CRP and platelet levels after symptom onset may help identify high-risk patients and guide clinical care.

Disclosure: B. Lee: None; **S. Li**: None; **S. Davuluri**: None; **J. Lee**: None; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2.

Abstract Number: 0692

A Randomised Open Label Pilot Trial Comparing Mycophenolate Mofetil with No Immunosuppression in Limited Cutaneous Systemic Sclerosis (MINIMISE-Pilot)

Christopher Denton[1], Philip Yee[2], medha kanitkar[3], Charlotte Clarke[4], Saiam Ahmed[4], Voon H. Ong[3], Francesco Del Galdo[5], John Pauling[6], Marina Anderson[7], Muditha Samaranayaka[8], Michael Hughes[9], Smita Bhat[10], Bridget Griffiths[11], MAYA BUCH[12], David D'Cruz[13], Ariane Herrick[14], Madelon Vonk[15], Nicholas Feemantle[4] and Dehbi Hakim-Moulay[4], [1]University College London, UK, London, United Kingdom, [2]Division of Medicine, Centre for Rheumatology, University College London, London, England, United Kingdom, [3]Division of Medicine, Centre for Rheumatology, University College London, London, United Kingdom, [4]University College London, London, United Kingdom, [5]University of Leeds, Leeds, United Kingdom, [6]North Bristol NHS Trust, Bristol, United Kingdom, [7]Lancaster University and NHS University Hospitals of Liverpool Group, Liverpool, United Kingdom, [8]Salford Royal Hospital, Salford, United Kingdom, [9]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [10]Ninewells Hospital Dundee, Dundee, Scotland,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

United Kingdom, [11]Ninewells Hospital Dundee, Newcastle, England, United Kingdom, [12]UNIVERSITY OF MANCHESTER, MANCHESTER, United Kingdom, [13]Kings College London, London, United Kingdom, [14]The University of Manchester, UK, Aberdeen, United Kingdom, [15]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Figure 1

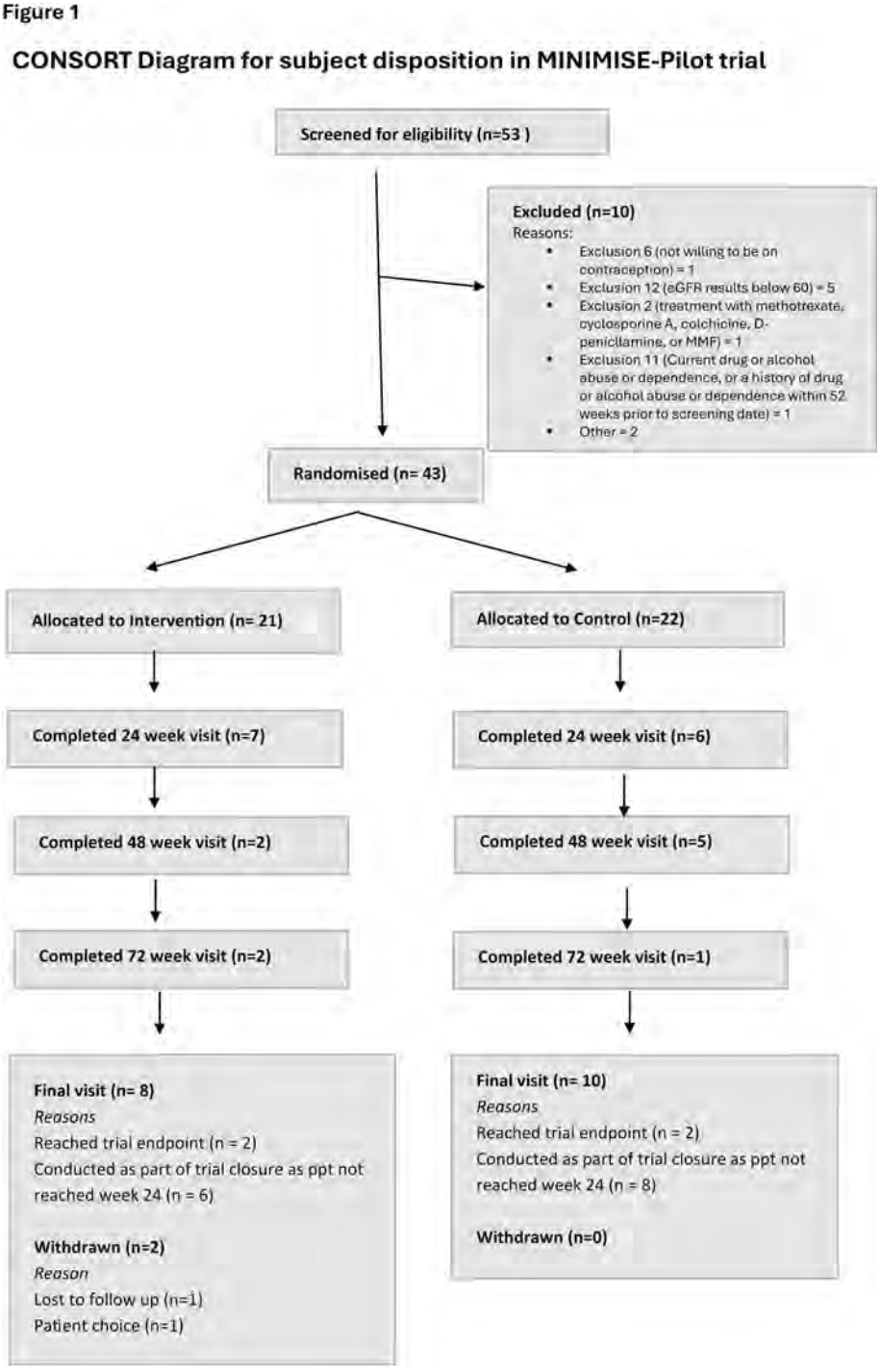


Figure 1 Subject disposition in MINIMISE-Pilot trial

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Baseline characteristics by treatment allocation

Table 1 MINIMISE-Pilot Baseline characteristics by treatment allocation

	Treatment Allocation					
	Control N = 22 (51.2%)		MMF N = 21 (48.8%)		Total N = 43 (100%)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age (years)	57.14	(10.71)	55.95	(7.51)	56.56	(9.20)
Estimated GFR (mL/min1.73sqm)	77.12	(12.02)	75.78	(12.05)	76.43	(11.87)
	Median	**(IQR)**	**Median**	**(IQR)**	**Median**	**(IQR)**
Upper limb mRSS	2.00	(3.00)	2.00	(3.00)	2.00	(4.00)
Total mRSS	2.00	(4.00)	2.00	(5.00)	2.00	(4.00)
Total PASTUL score	4.00	(4.00)	4.00	(5.00)	4.00	(5.00)
	N	**(%)**	**N**	**(%)**	**N**	**(%)**
ACA status						
Positive	17	(77.27)	14	(66.67)	31	(72.09)
Negative	5	(22.73)	7	(33.33)	12	(27.91)
Disease duration						
Up to 4 years (<4)	16	(72.73)	14	(66.67)	30	(69.77)
Four years or more (≥4)	6	(27.27)	7	(33.33)	13	(30.23)
Sex						
Female	19	(86.36)	17	(80.95)	36	(83.72)
Male	3	(13.64)	4	(19.05)	7	(16.28)

Background/Purpose: Mycophenolate mofetil (MMF) is recommended for skin in diffuse cutaneous (dc)SSc, and for lung fibrosis in SSc, but patients with limited cutaneous (lc)SSc are not routinely started on MMF at diagnosis. This may miss an opportunity to prevent or treat major complications early. MINIMISE-Pilot tested feasibility of a randomised event-driven trial of MMF in lcSSc.

Methods: We explored recruitment and feasibility of a trial evaluating impact of MMF on a novel event-driven composite endpoint. The MINIMISE endpoint measures time to clinical worsening of lcSSc determined by one of the following: progressive lung fibrosis, pulmonary hypertension, scleroderma renal crisis, heart failure, severe gut involvement, major digital vascular complications, or death. Subjects were stratified by anticentromere antibody (ACA) status.

This study prioritised remote assessment and used the novel Patient self-Assessment of Skin Thickness of Upper Limb (PASTUL) questionnaire to measure skin fibrosis. Primary outcomes were safety and feasibility. Pre-specified "go and no-go" criteria were based on patient number and event rate with agreed thresholds of success.

Results: Recruitment was challenging and a total of 53 subjects were screened and 43 randomised, 21 to the MMF arm (**-Figure 1**). Average age of participants was 57 years, with near equal distribution between the control and MMF groups. Baseline characteristics and treatment allocation are summarised in **Table 1**. Most participants were female (84%), of White British ethnicity (81%) and had positive ACA (67%). Since recruitment was below 60 participants, MINIMISE-Pilot was terminated based upon the prespecified threshold for continuation.

There were no major safety concerns. Serious Adverse Events (SAEs) occurred in 3 patients (7%). These included 2 (9%) in the control group and one (5%) in the MMF group. SAEs reported were gastrointestinal disorders (1 on MMF), injury and procedural complications (1 control), and musculoskeletal and connective tissue disorders (1 control). During the treatment

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

period no participants experienced clinical worsening endpoints. Adherence to MMF was generally high, with 19 participants (95%) being 100% adherent at Week 1, decreasing to 9 participants (64%) at Week 24.

Conclusion: This study achieved its key goal as a feasibility pilot leading to early termination of the study due to low recruitment. This precludes interpretation of effectiveness and safety of MMF in lcSSc. Whilst emerging evidence strongly supports the use of MMF to treat skin and lung fibrosis in SSc, and other studies have validated the novel composite MINIMISE endpoint of "clinical worsening in lcSSc" and PASTUL endpoint for skin, the results of MINIMSE-Pilot suggest that a randomised prospective trial across 8 active sites in UK with relatively short duration is not feasible. This is important and will inform design of future studies testing benefit of MMF in lcSSc. Our previous power calculations suggest that around 400 patients and a treatment period of 36 months would be needed for the current study design, although emerging enrichment strategies may reduce the required subject number.

Disclosure: C. Denton: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **P. Yee**: None; **m. kanitkar**: None; **C. Clarke**: None; **S. Ahmed**: None; **V. Ong**: Boehringer-Ingelheim, 6; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **J. Pauling**: AstraZeneca, 2, Boehringer-Ingelheim, 2, IsoMab, 2, Janssen, 2, Permeatus Inc, 2, Sojournix Pharma, 2; **M. Anderson**: None; **M. Samaranayaka**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **S. Bhat**: None; **B. Griffiths**: None; **M. BUCH**: Bristol-Myers Squibb(BMS), 5; **D. D'Cruz**: None; **A. Herrick**: Abbvie, 2, Boehringer-Ingelheim, 2, Janssen, 2, 6, Zura Bio, 2; **M. Vonk**: Boehringer-Ingelheim, 2, 6, 12, Travel grants, Janssen, 2, 6, 12, travel grants, Merck/MSD, 6; **N. Feemantle**: None; **D. Hakim-Moulay**: None.

Abstract Number: 0693

Impact of X Chromosome Dosage on the Development of Diffuse and Limited Systemic Sclerosis in Klinefelter, Triple X, and Turner Syndromes: A Multicenter Cohort Study

Hanieh Akbari[1], Anna-Kay Palmer[2] and Irene Tan[3], [1]Jefferson Einstein Montgomery Medical Center, Norristown, PA, [2]Jefferson Einstein Philadelphia Hospital, Department of Internal Medicine, Philadelphia, PA, [3]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Diffuse and limited systemic sclerosis (SSc) are autoimmune connective tissue diseases with a strong female predominance, suggesting a potential role for X chromosome dosage in disease susceptibility. While previous

Table 1. Demographic Characteristics of the Study Population

Demographic Information	Men, General Population	Klinefelter (47,XXY)	Women, General Population	Triple X (47,XXX)	Turner (45,XO)
Total Population	40,546,430	5,169	48,390,403	717	9,272
Mean Age (SD, range in years)	46.3 (±20.2, 18-85)	34.9 (±17.8, 18-82)	45.6 (±20.2, 18-89)	27.6 (±13.4, 18-80)	31.5 (±16.3, 18-81)
Male (%)	100%	99.79%	0%	0%	0%
Female (%)	0%	0%	100%	100%	100%
Unknown (%)	0%	0.21%	0%	0%	0%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Prevalence and Relative Risk of Diffuse and Limited Systemic Sclerosis in X Chromosome Aneuploidies

Cohort	Diffuse Systemic Sclerosis Prevalence (%)	Relative Risk (95% CI), p-value (Diffuse)	Limited Systemic Sclerosis Prevalence (%)	Relative Risk (95% CI), p-value (Limited)
Klinefelter Syndrome (47,XXY)	0.19	9.0 (5.1–15.9), p < 0.001	0.22	16.9 (9.3–28.6), p < 0.001
Triple X Syndrome (47,XXX)	0.25	5.2 (2.7–8.9), p < 0.001	0.48	14.5 (7.1–27.1), p < 0.001
Turner Syndrome (45,XO)	0.047	0.98 (0.51–1.78), p = 0.82	0.009	0.28 (0.14–0.56), p < 0.001

studies linked X chromosome aneuploidies to immune dysregulation, their specific impact on diffuse and limited SSc remains unclear. This study evaluates the relationship between Klinefelter syndrome (47, XXY), triple X syndrome (47, XXX), and Turner syndrome (45, XO) and the development of diffuse and limited systemic and limited sclerosis compared to the general population using a large-scale electronic health record database.

Methods: This multicenter, retrospective cohort study utilized TriNetX, a global federated research network comprising 141 healthcare centers. Three cohorts were analyzed: individuals with Klinefelter syndrome compared to the general male population, individuals with Turner syndrome compared to the general female population, and individuals with triple X syndrome compared to the general female population. Patients were identified using the International Classification of Diseases, Tenth Revision, Clinical Modification codes, between January 1, 2015, and January 1, 2025. The prevalence and risk of diffuse and limited SSc were assessed in each cohort. Relative risk, odds ratios, and 95 percent confidence intervals were calculated. The statistical significance was assessed using Fisher's exact test.

Results: A total of 88,951,991 patients were identified. Among individuals with Klinefelter syndrome, the prevalence of diffuse SSc prevalence was 0.19% (RR = 9.0, 95% CI: 5.1–15.9, p < 0.001), and the prevalence of limited SSc was 0.22% (RR = 16.9, 95% CI: 9.3–28.6, p < 0.001). In triple X syndrome, the prevalence of diffuse SSc was 0.25% (RR = 5.2, 95% CI: 2.7–8.9, p < 0.001), and limited SSc prevalence was 0.48% (RR = 14.5, 95% CI: 7.1–27.1, p < 0.001). In Turner syndrome, the prevalence of diffuse SSc was 0.047% (RR = 0.98, 95% CI: 0.14-0.56, p = 0.82), and limited SSc prevalence was 0.009% (RR = 0.28, 95% CI: 0.14–0.56, p < 0.001).

Conclusion: Excess X chromosome in Klinefelter syndrome and triple X syndrome is associated with significant increased risk of having diffuse and limited systemic sclerosis in a nonproportional, synergistic manner. Deficient X chromosome in Turner syndrome is associated with a lower risk of having limited systemic sclerosis but no effect on diffuse SSc when compared with the general population. These findings support the role of X chromosome dosage in susceptibility of developing systemic sclerosis and highlight the complex interplay between X chromosome dosage and immune regulation. This study underscores the need for heightened clinical awareness and targeted screening in individuals with Klinefelter and Triple X syndromes.

Disclosure: H. Akbari: None; **A. Palmer**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

Abstract Number: 0694

Treatment of Sjögren's disease by blocking FcRn: clinical and translational data from RHO, a phase 2 randomized, placebo controlled, double-blind, proof-of-concept study with efgartigimod

isabelle peene[1], Gwenny Verstappen[2], Joke Deprez[3], Frans Kroese[2], Suzanne Arends[2], Andrew Kelly[4], Lana Vandersarren[5], Edward Bowen[6], Julie Jacobs[7], Paul Meyvisch[8], Dirk Elewaut[9] and Hendrika Bootsma[10], [1]University Hospital Ghent, Ghent, Belgium, [2]University Medical Center Groningen, Groningen, Netherlands, [3]Ghent University, Ghent, Belgium, [4]Argenx, Philadelphia, PA, [5]Argenx, Boston, MA, [6]IQVIA, Stevenage, United Kingdom, [7]argenx, Ravels, Belgium, [8]argenx, Ghent, Belgium, [9]VIB Center for Inflammation Research, and Ghent University Hospital, Department of Rheumatology, Ghent, Belgium, [10]UMCG, Groningen, Netherlands

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

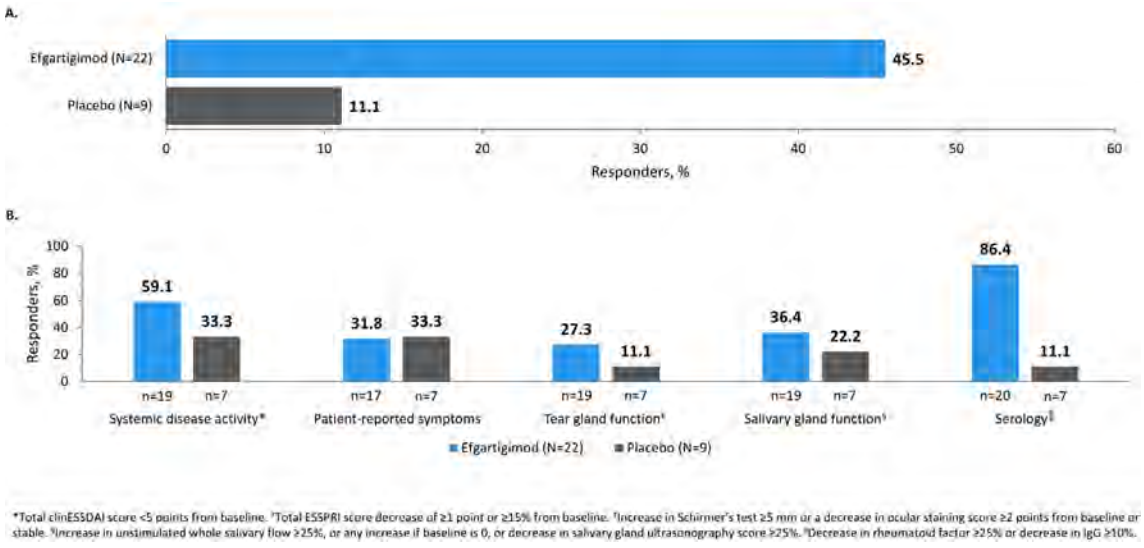
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Background/Purpose

Sjögren's disease (SjD) is a chronic, systemic autoimmune disease characterized by lymphocytic infiltration and progressive, immune-mediated dysfunction of the exocrine glands. Immunoglobulin (Ig) G autoantibodies targeting Sjögren's syndrome-related antigens (A/Ro and B/La ribonuclear complexes) and RF play a pivotal role in SjD development and are produced by B-cell activation. Current SjD therapies focus on symptom management, with limited efficacy in preventing glandular damage or suppressing systemic disease activity. Efgartigimod, an IgG1 antibody Fc fragment, selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production, albumin levels, or other parts of the immune system. By targeting disease-specific IgG autoantibodies, efgartigimod may reduce disease activity and symptoms in patients with SjD. We present the results of RHO, a phase 2, multicenter, randomized, placebo-controlled, double-blind, proof-of-concept study to explore the safety and efficacy of efgartigimod in adult participants with SjD (NCT05817669).

Methods: Anti-Ro/SSA positive patients meeting ACR/EULAR 2016 Sjogren's syndrome criteria ≤7 years before screening, with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) ≥5 and residual salivary flow, were randomly allocated (2:1) to receive weekly intravenous efgartigimod or placebo for 24 weeks. The primary endpoint was the proportion of responders to the Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS; response on ≥3 out of 5 items) at week 24. Key secondary endpoints were proportion of responders to the candidate Sjögren's Tool for Assessing Response (cSTAR), change from baseline in ESSDAI, Clinical ESSDAI (ClinESSDAI), EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI) scores, and safety.

Results: Of thirty-four patients randomized, three did not meet eligibility criteria and were removed from analyses. The study met its primary endpoint, with more responders to ≥3 of 5 CRESS items in the efgartigimod than placebo group at week 24 (45.5% [10/22] vs 11.1% [1/9]). Efgartigimod treatment resulted in a positive signal for 4 of 5 individual CRESS items compared with placebo (Figure), and an increased cSTAR response at week 24 (54.5% [12/22] participants compared with 33.3% [3/9] of placebo-treated participants). All participants showed improvements from baseline in disease activity (ESSDAI and ClinESSDAI scores), and no relevant changes in ESSPRI score. Efgartigimod rapidly reduced mean (SE) IgG



*Total clinESSDAI score <5 points from baseline. †Total ESSPRI score decrease of ≥1 point or ≥15% from baseline. ‡Increase in Schirmer's test ≥5 mm or a decrease in ocular staining score ≥2 points from baseline or stable. §Increase in unstimulated whole salivary flow ≥25%, or any increase if baseline is 0, or decrease in salivary gland ultrasonography score ≥25%. ¶Decrease in rheumatoid factor ≥25% or decrease in IgG ≥10%.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and anti-Ro52 autoantibodies by 58.3% (2.4) and 63.8% (3.9), respectively, from Week 4, and mean (SE) C1Q immune complexes by 4.0 (1.3) μg Eq/mL, and mean (SE) RF by 19.6% (4.1) compared with 6.3% (3.0) by placebo at study end. Efgartigimod was well tolerated, with no new safety signals.

Conclusion: Proof-of-concept was demonstrated using efgartigimod in patients with SjD, which was generally well tolerated. The ongoing phase 3 UNITY trial (NCT06684847) will assess efficacy and safety of efgartigimod in patients with SjD with clinESSDAI ≥6 (moderate-to-severe systemic disease activity).

Disclosure: i. peene: argenx, 2, BMS, 2; **G. Verstappen**: argenx, 2; **J. Deprez**: None; **F. Kroese**: argenx, 2; **S. Arends**: argenx, 2, BMS, 2, Novartis, 2; **A. Kelly**: argenx, 3, 11; **L. Vandersarren**: argenx, 3, 11; **E. Bowen**: IQVIA, 3; **J. Jacobs**: argenx, 3, 11; **P. Meyvisch**: argenx, 3, 11; **D. Elewaut**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6, UCB, 2, 6; **H. Bootsma**: Bristol-Myers Squibb(BMS), 2, 5, Medimmune, 2, Novartis, 2, Roche, 2, 5, Union Chimique Belge, 2.

Abstract Number: 0695

Global Longitudinal, Circumferential, and Radial Strain in Systemic Sclerosis Patients with Left Ventricular Dysfunction

Jennifer Elise Abdalla[1], Yuichiro Okushi[2], Zoran Popovic[2], Heba Wassif[2] and Soumya Chatterjee[3], [1]Cleveland Clinic, Cleveland, OH, [2]Cleveland Clinic, Cleveland, [3]Cleveland Clinic, Richmond Heights, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune rheumatologic disease characterized by fibrosis and vascular complications, which significantly impact various organs, including the heart. Cardiac involvement contributes substantially to morbidity and mortality, yet early myocardial dysfunction often remains undetected due to its asymptomatic nature. While a transthoracic echocardiogram (TTE) is the standard tool for assessing ventricular dysfunction and pulmonary hypertension, it may fail to identify early/subclinical myocardial dysfunction. Strain echocardiography, particularly global longitudinal strain (LVGLS), has emerged as a more sensitive method for detecting early cardiac impairment. However, data on radial and circumferential strain—critical components of multidimensional cardiac function—remain limited. This study evaluates the progression of strain patterns over five years and compares strain echocardiography to conventional TTE.

Methods: A retrospective analysis was conducted on SSc patients (2013 ACR criteria, Table 1) with LV diastolic and/or systolic dysfunction (LVD) who underwent at least three TTEs over the past decade. Strain values were obtained using speckle-tracking echocardiography from the most recent TTE and those from three and five years prior. To ensure consistency, strain measurements were recalculated using TomTec® technology. Patients with incomplete data were excluded. Strain data was analyzed as mean values.

Results: Left ventricular global longitudinal (LVGLS) and circumferential strain (LVGCS) are expressed as a negative percentage, with normal values defined as < -18% (LVGLS) and < -15.3% (LVGCS). Radial strain (LVGRS) is expressed as a positive percentage, with normal values ≥ 25.5%. Over five years, all three mean strain patterns showed progressive decline:

- LVGLS: -17.1 -15.6 -14.4
- LVGCS: -18.8 -16.4 -14.2
- LVGRS: 20.6 18.0 15.9

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Notably, 31-44% of patients with normal LV function on conventional TTE (LVEF ≥ 50% and normal diastolic function) exhibited abnormal LVGLS or LVGRS. In contrast, LVGCS aligned more closely with conventional TTE findings (Figure 1). Though all patients in the study were diagnosed with SSc-LVD, 46.8% showed no current LVD based on conventional TTE. This discrepancy may reflect treatment-related normalization of standard TTE parameters.

Table 1: Patient Characteristics

Table 1:

Patient Characteristics	
Baseline Characteristics	
Total patients	94
Age (years)	72.0 [60.0-79.7]
Sex	
Male	18 (19.1%)
Female	76 (80.8%)
Race	
White	77 (81.9%)
Non-white	17 (18.1%)
BMI (kg/m²)	23.5 [20.2-28.3]
Hypertension	71 (75.5%)
Diabetes	15 (15.9%)
Hyperlipidemia	66 (70.2%)
Tobacco Use	
Current	2 (2.1%)
Former	35 (37.2%)
Never	57 (60.6%)
Disease Characteristics	
Disease Duration (years)	12 [8.0-20.0]
Limited Cutaneous	69 (73.4%)
Diffuse Cutaneous	25 (26.6%)
Interstitial Lung Disease	48 (51.1%)
Pulmonary Hypertension	39 (41.5%)
Antibody	
Topoisomerase I (Scl-70)	18 (19.1%)
Centromere	36 (38.3%)
RNA Polymerase III	7 (7.4%)
PM-Scl	3 (3.2%)
Th/To	1 (1.1%)
SSA	9 (9.6%)
ANA only	20 (21.3%)
Medication Exposure	
ACE-Inhibitor	71 (75.5%)
Angiotensin Receptor Blocker	39 (41.5%)
Beta-Blocker	78 (83.0%)
Calcium-Channel Blocker	81 (86.2%)

Continuous variables are presented as Median (IQR). Categorical variables are presented as N (column %).

Figure 1:

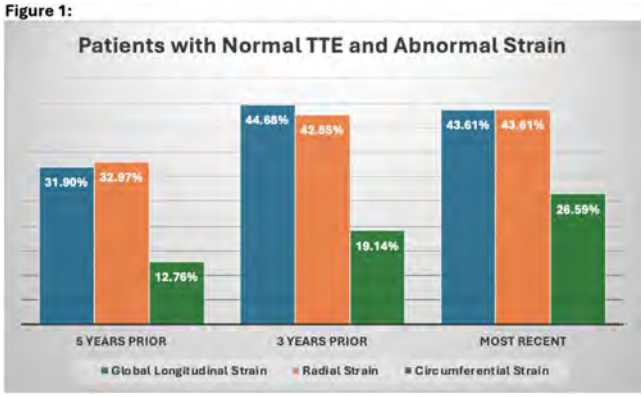


Figure 1: Patients with Normal TTE and Abnormal Strain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Global longitudinal and radial strain measurements may outperform circumferential strain in detecting early LVD in SSc patients. These findings support the potential of strain echocardiography as a valuable, routine screening tool that may enable earlier intervention and improve patient outcomes compared to conventional TTE.

Disclosure: J. Abdalla: None; **Y. Okushi**: None; **Z. Popovic**: None; **H. Wassif**: None; **S. Chatterjee**: None.

Abstract Number: 0698

A Retrospective Comparison of Transplant Outcomes with Different Induction Methods and Maintenance Prednisone in Systemic Sclerosis Patients

Lilit Grigoryan, Sumbal Wajid, Giovanni Faddoul and Swati Mehta, Albany medical center, Albany, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) or scleroderma is a rare systemic autoimmune disease with multiple organ involvement. Renal involvement in SSc remains a significant concern, with the most concerning complication being scleroderma renal crisis (SRC). Up to 20-50% of these patients still require long-term dialysis and subsequently kidney transplantation (KT). We performed a retrospective study using the United Network for Organ Sharing (UNOS) database, to compare the impact of different induction immunosuppression regimens and maintenance prednisone amongst our SSc cohort.

Table 1. Hazard ratios for graft and patient survival among systemic sclerosis patients looking at different induction therapies, and maintenance prednisone

Table 1.

	Graft Survival				Patient Survival			
	HR	p-value	95% CI		HR	p-value	95% CI	
Maintenance prednisone	1.596	0.045	1.011	2.521	1.494	0.093	0.936	2.383
Induction:								
thymo	(reference)				(reference)			
alemtuzumab	1.798	0.028	1.066	3.031	1.601	0.066	0.969	2.645
basiliximab/daclizumab	1.119	0.653	0.686	1.825	1.051	0.847	0.636	1.735
thymo+basiliximab/thymo+daclizumab	2.346	0.044	1.025	5.370	2.198	0.095	0.872	5.540
Patient age:								
<40	(reference)				(reference)			
40-59	1.724	0.132	0.848	3.506	2.370	0.029	1.090	5.153
>=60	3.766	0.001	1.758	8.068	6.239	<0.001	2.773	14.036
Donor age:								
<10	(reference)				(reference)			
10-19	0.271	0.100	0.057	1.283	0.177	0.009	0.048	0.651
20-39	0.649	0.479	0.197	2.143	0.482	0.137	0.184	1.261
40-59	0.479	0.223	0.147	1.565	0.329	0.022	0.127	0.854
>=60	0.492	0.262	0.143	1.699	0.371	0.051	0.137	1.003
Donor hypertension	1.635	0.013	1.107	2.415	1.847	0.003	1.227	2.781

* Standard errors are robust to address potential heteroskedasticity

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A retrospective analysis was conducted using UNOS database from 2000 to 2022.We had a total of 211 based on diagnostic coding consistent with scleroderma related diagnoses who underwent KT from deceased donors (DD) and live donors (LD). Cox regression analyses were conducted for patient survival and graft survival for patients with SSc. In these models, we excluded interaction terms and KDPI, while including a binary indicator for donor type (live vs. deceased) as well as induction and maintenance therapies. The patients with no induction information were excluded.

Results: There were statistically significant worse outcomes in graft survival in SSc patients receiving induction therapy with alemtuzamab, and thymo+basiliximab/thymo+daclizumab as well as with maintenance prednisone. (Table 1) There was no statistically significant difference in patient survival for both induction therapies and maintenance prednisone, amongst SSc patients. (Table 1)

Conclusion: Different induction therapies in KT are chosen for either their safety profiles or immunosuppressive effects. Alemtuzumab a relatively newer agent, has recently been studied in a retrospective review of 225 SSc patients using data from 2012-2022 which demonstrated significantly poorer graft survival outcomes. This correlates with our findings for poor graft survival among SSc patients receiving alemtuzumab induction. Like alemtuzumab a recent study looked at death-censored graft failure in individuals receiving combination therapy with thymo+basiliximab and found a statistically significant increased rate of death censored graft failure. This observation also aligns with our study.

We further found that maintenance steroid use was associated with poorer graft survival as well. One hypothesis is that steroids may contribute to SRC recurrence after KT. Although the association between steroids and increased SRC risk is well established, data on post-transplant recurrence is limited. A 2005 case study documented two SRC recurrences, with the earlier event occurring in the patient on higher steroid doses. Further research is needed to clarify this potential relationship.

Disclosure: L. Grigoryan: None; **S. Wajid**: None; **G. Faddoul**: None; **S. Mehta**: None.

Abstract Number: 0699

A Retrospective Comparison of Transplant Outcomes in Patients with and Without Systemic Sclerosis

Lilit Grigoryan, Sumbal Wajid, Giovanni Faddoul and Swati Mehta, Albany medical center, Albany, NY

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Scleroderma renal crisis (SRC) is one of the life threatening complications of systemic sclerosis (SSc). Up to 20-50% require long term dialysis and subsequently kidney transplant. We performed a retrospective study using the United Network for Organ Sharing (UNOS) database, to compare graft and patient survival in kidney transplantation (KT) patients with and without systemic sclerosis. We further investigated whether different induction immunosuppression strategies had varying outcomes in above cohort.

Methods: A retrospective analysis was conducted using UNOS database from 2000 to 2022. A total of 211 patients were chosen based on diagnostic coding consistent with scleroderma related diagnoses who underwent KT from deceased donors (DD) and live donors (LD). This cohort was then matched to non-SSc recipients using a propensity score matching.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Induction immunosuppressive regimens analyzed included alemtuzumab, basiliximab/daclizumab, and combinations of thymoglobulin with either basiliximab or daclizumab, using thymoglobulin alone as the reference group. Maintenance prednisone was also analyzed following KT. Graft and patient survival were compared between the SSc and matched non-SSc cohorts using hazard ratios (HR), both overall and stratified by induction regimen.

Results: There was a statically significant association with poorer outcomes in both graft and patient survival from both DD, and LD following KT in our SSc cohort when compared to non-SSc cohort (Table 1) (Figure 1). There was no statistically significant difference in graft and patient survival between the SSc and matched non-SSc cohorts across the various induction immunosuppression regimens along with maintenance prednisone (Table 2).

Conclusion: Using UNOS data from 211 SSc patients, we found statistically significant worse outcomes in both graft and patient survival when compared to matched controls in both DD and LD groups. Our findings align with prior UNOS-based studies which also reported lower graft survival rates in SSc transplant recipients. These poorer outcomes are likely multifactorial, potentially driven by SRC recurrence and multi-organ involvement. The use of different induction methods along with maintenance prednisone had no statistically significant difference in graft and patient outcomes when compared to our non-SSc cohort.

Table 1. Hazard ratios of graft and patient survival after kidney transplant in systemic sclerosis patients from both deceased donor (DD) and live donor (LD) groups

Table 1.

	DD: Graft Survival				DD: Patient Survival				LD: Patient Survival				LD: Graft Survival			
	HR	p-value	95% CI		HR	p-value	95% CI		HR	p-value	95% CI		HR	p-value	95% CI	
Sclerosis	1.399	0.015	1.068	1.832	1.558	0.004	1.157	2.099	1.685	0.030	1.050	2.704	1.671	0.015	1.105	2.529
Patient age:																
<40	(reference)				(reference)				(reference)				(reference)			
40-59	1.918	0.313	0.770	2.257	1.799	0.060	0.975	3.321	1.445	0.343	0.675	3.093	0.995	0.987	0.556	1.781
>=60	2.547	0.001	1.468	4.421	4.593	<0.001	2.450	8.611	4.174	0.001	1.742	9.997	1.705	0.134	0.849	3.425
Patient male	1.097	0.493	0.842	1.428	1.219	0.151	0.931	1.596	0.940	0.836	0.524	1.687	1.099	0.711	0.683	1.751
Patient white	1.256	0.063	0.987	1.599	1.393	0.010	1.084	1.790	0.870	0.733	0.455	1.843	0.887	0.676	0.505	1.558
Dialysis	1.600	0.014	1.037	2.469	1.921	0.039	1.021	2.764	1.475	0.409	0.679	2.585	1.845	0.046	1.012	3.361
Patient diabetes diagnosis	1.409	0.116	0.919	2.159	1.672	0.022	1.078	2.593	2.469	0.161	0.697	8.739	1.736	0.289	0.626	4.812
Patient BMI	0.999	0.911	0.975	1.024	0.991	0.316	0.965	1.018	0.959	0.137	0.903	1.018	0.985	0.525	0.940	1.032
KDPI	2.256	<0.001	1.471	3.462	2.143	0.001	1.344	3.419								
Induction:																
thymo	(reference)				(reference)				(reference)				(reference)			
alemtuzumab	1.011	0.954	0.688	1.486	1.169	0.323	0.788	1.712	1.943	0.060	0.973	8.882	1.398	0.310	0.732	2.668
basiliximab/daclizumab	1.087	0.551	0.827	1.429	0.983	0.908	0.740	1.307	1.983	0.751	0.663	1.769	0.855	0.551	0.510	1.431
thymo+basiliximab/thymo+daclizumab	0.999	0.997	0.561	1.780	1.136	0.556	0.649	1.988	0.976	0.982	0.106	8.943	0.390	0.405	0.043	3.566
Maintenance prednisone	1.148	0.351	0.859	1.534	1.049	0.755	0.775	1.422	1.707	0.061	0.976	2.986	1.482	0.137	0.883	2.487

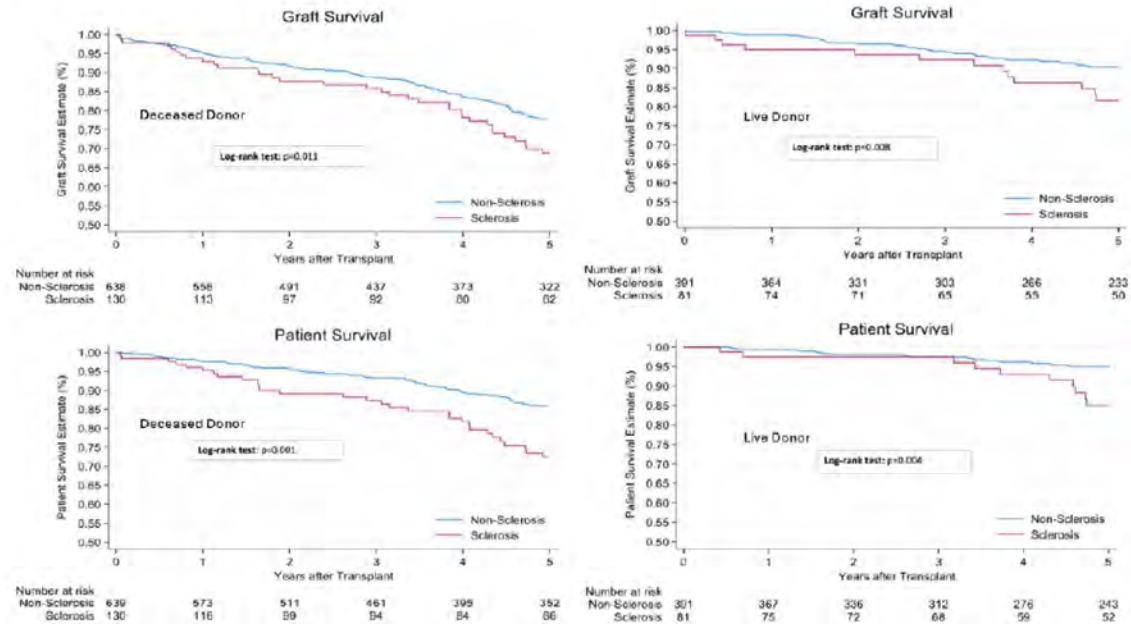
Table 2. Hazard ratios of graft and patient survival after kidney transplant in systemic sclerosis patients looking at different induction methods and maintenance prednisone

Table 2.

	DD: Graft Survival				DD: Patient Survival				LD: Graft Survival				LD: Patient Survival			
	HR	p-value	95% CI		HR	p-value	95% CI		HR	p-value	95% CI		HR	p-value	95% CI	
Sclerosis	1.079	0.798	0.603	1.931	1.078	0.797	0.606	1.920	1.381	0.587	0.431	4.429	2.494	0.198	0.620	10.030
Patient age:																
<40	(reference)				(reference)				(reference)				(reference)			
40-59	1.320	0.313	0.770	2.262	1.784	0.063	0.968	3.286	0.986	0.962	0.552	1.759	1.458	0.337	0.677	3.126
>=60	2.561	0.001	1.467	4.474	4.685	<0.001	2.485	8.835	1.700	0.140	0.840	3.443	4.207	0.002	1.721	10.281
Patient male	1.099	0.486	0.843	1.434	1.236	0.122	0.945	1.616	1.097	0.702	0.682	1.765	0.930	0.809	0.515	1.678
Patient white	1.251	0.068	0.983	1.592	1.364	0.015	1.062	1.751	0.877	0.658	0.489	1.571	0.918	0.830	0.422	1.998
Dialysis	1.608	0.033	1.038	2.489	1.521	0.038	1.024	2.257	1.842	0.043	1.018	3.334	1.344	0.385	0.689	2.622
Patient diabetes diagnosis	1.338	0.183	0.872	2.055	1.599	0.037	1.029	2.484	1.727	0.324	0.584	5.111	2.758	0.128	0.747	10.181
Patient BMI	1.001	0.967	0.977	1.025	0.993	0.614	0.966	1.020	0.985	0.534	0.940	1.033	0.958	0.142	0.905	1.014
KDPI	2.213	<0.001	1.439	3.405	2.086	0.002	1.306	3.332								
Induction:																
thymo	(reference)				(reference)				(reference)				(reference)			
alemtuzumab	0.800	0.373	0.491	1.306	0.918	0.745	0.549	1.536	1.398	0.810	0.732	2.668	2.063	0.083	0.910	4.679
basiliximab/daclizumab	1.050	0.756	0.773	1.425	0.963	0.815	0.701	1.323	0.855	0.551	0.510	1.431	1.181	0.804	0.641	2.174
thymo+basiliximab/thymo+daclizumab	0.787	0.594	0.327	1.896	1.193	0.575	0.643	2.214	0.390	0.405	0.043	3.566	1.056	0.962	0.113	9.861
Maintenance prednisone	1.096	0.607	0.773	1.553	0.941	0.738	0.659	1.343	1.462	0.137	0.883	2.487	1.834	0.077	0.937	3.593
Sclerosis * Maintenance prednisone	1.331	0.699	0.606	2.112	1.419	0.282	0.750	2.684	1.110	0.855	0.362	3.398	0.743	0.667	0.192	2.872
Sclerosis * Induction:																
Non-sclerosis * thymo	(reference)				(reference)				(reference)				(reference)			
Sclerosis * alemtuzumab	2.170	0.061	0.964	4.883	2.016	0.080	0.921	4.414	1.556	0.482	0.453	5.340	0.754	0.704	0.176	3.230
Sclerosis * basiliximab/daclizumab	1.757	0.664	0.600	2.232	1.128	0.745	0.547	2.326	1.119	0.831	0.398	3.144	0.745	0.619	0.233	2.383
Sclerosis * thymo+basiliximab/thymo+daclizumab	1.689	0.396	0.503	5.669	0.905	0.864	0.288	2.839	(no observations)				(no observations)			

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1.



Kaplan-Meier survival curves comparing graft survival and patient survival between sclerosis and non-sclerosis patients following a transplant over a 5-year period

Disclosure: L. Grigoryan: None; **S. Wajid**: None; **G. Faddoul**: None; **S. Mehta**: None.

Abstract Number: 0700

Distinct Breath Metabolomic Signature in Systemic Sclerosis Patients with Pulmonary Arterial Hypertension

Martina Iacubino[1], Lorenzo Rocco[2], Marco Vicenzi[2], Chiara Bellocchi[2], Marta Mozzo[3], adriana severino[3], Monica Caronni[3], Alessandro Santaniello[3], Gaia montanelli[3], Barbara Vigone[3], Llam Grimmett[4], Matt Kerr[4] and **Lorenzo Beretta**[5], [1]UNIMI, Milano, Milan, Italy, [2]University of Milan, Milan, Italy, [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy, [4]Owlstone Medical, Cambridge, United Kingdom, [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Milan, Italy

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a severe complication of systemic sclerosis (SSc), associated with high morbidity and mortality. Accurate and early diagnosis of SSc-PAH is essential to initiate targeted therapies that may improve outcomes by counteracting key pathophysiological mechanisms. Breathomics, the analysis of volatile organic compounds (VOCs) in exhaled breath, has emerged as a promising non-invasive tool, as VOCs reflect underlying metabolic and pathological processes. This study investigates the potential of breathomics in SSc-PAH, both for disease understanding and diagnosis.

Methods: fourteen SSc patients with a diagnosis of PAH confirmed by right heart catheterization, 28 age- and sex-matched SSc patients without PAH, and 36 matched healthy controls (HCs)were enrolled in a single-center, case-control observational study. Exhaled breath VOCs were collected using the ReCIVA® breath sampler connected to a clean air supply

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

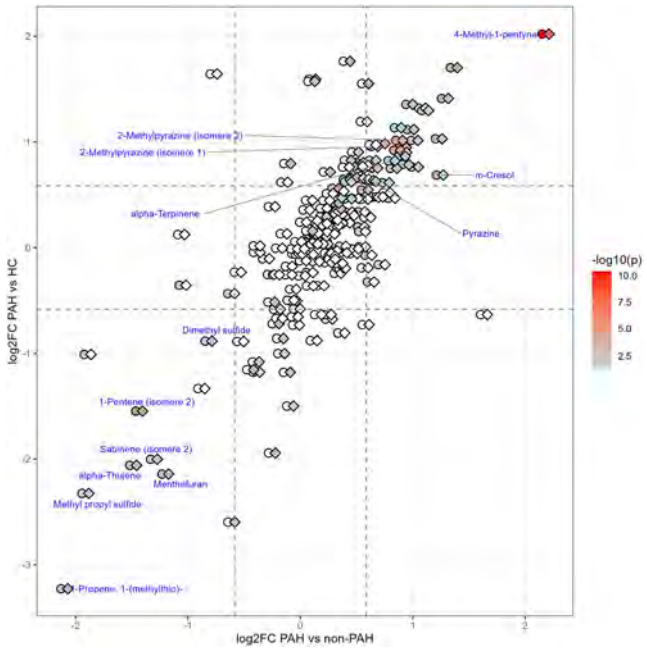


Figure 1 – Pairwise logFC comparison of SSc-PAH vs comparators

(CASPER®). Samples were trapped on sorbent tubes and analyzed by thermal desorption gas chromatography–mass spectrometry (TD-GC-MS) at Owlstone Medical. VOCs were chemically identified according to Metabolomics Standards Initiative (MSI) criteria, and blank air samples were analyzed to distinguish true breath compounds from environmental contaminants. Data were analyzed using linear regression, adjusting for relevant covariates and excluding outliers.

Results: all SSc participants were female and predominantly affected by lcSSc (n = 23, 63.4%) and mostly tested positive for ACA (n = 40, 85%). The mean age was 68 ± 9 years, with no differences between the SSc-PAH and SSc-noPAH groups. A total of 1.382 VOCs were analyzed; of these, 186 were confirmed to be genuinely present "on breath" and annotated with high confidence (MSI tier 1 or 2). Among these, 55 VOCs significantly differentiated SSc-PAH from SSc-noPAH, and 40 differentiated SSc-PAH from healthy controls. Notably, 32 VOCs distinguished SSc-PAH from both comparator groups ($p < 0.05$ and $|\text{fold change}| > 1.5$) (Figure 1). Findings of interest included: a reduction in terpenes in SSc-PAH, potentially reflecting impaired vasodilatory capacity (Figure 2); a decrease in sulfur-containing compounds, suggestive of reduced control

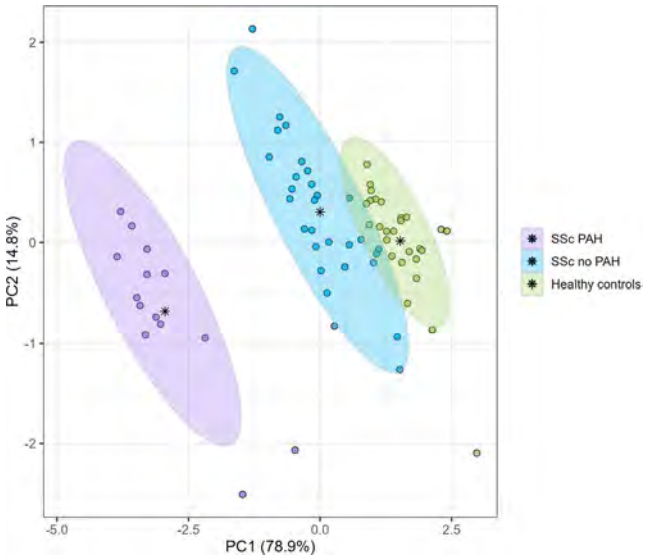


Figure 2 – Principal component analysis biplot of terpenes across study groups

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

over vasoconstriction; a reduction end-products (i.e. 1-pentene) of allyl organosulfur derivates with anti-inflammatory properties; an increase in pyrazines, possibly indicative of enhanced gut permeability; and elevated levels of the uremic toxin m-cresol, which has been associated with endothelial dysfunction.

Conclusion: breathomics revealed a distinct metabolic signature in SSc-PAH, distinguishing it from both SSc without PAH and healthy controls. The identified VOCs not only hold promise as non-invasive biomarkers for early diagnosis but also shed light on key pathogenic mechanisms of PAH, including impaired vasoregulation, increased gut permeability, and endothelial dysfunction. These findings support the role of breath analysis as a valuable tool for both clinical and mechanistic insights in SSc-PAH.

Disclosure: M. Iacubino: None; **L. Rocco**: None; **M. Vicenzi**: None; **C. Bellocchi**: None; **M. Mozzo**: None; **a. severino**: None; **M. Caronni**: None; **A. Santaniello**: None; **G. montanelli**: None; **B. Vigone**: None; **L. Grimmett**: Owlstone Medical ltd, 3; **M. Kerr**: Owlstone Medical ltd, 3; **L. Beretta**: None.

Abstract Number: 0701

Exploring Calcinosis On Hand X-Rays In Systemic Sclerosis: a Mayo Clinic Cohort

Maximiliano Diaz Menindez[1], Simran Ravindra Nimal[2], Michael Pham[2], Caroyln Harvey[3], Leroy W. Griffing[2] and Vivek Nagaraja[2], [1]Mayo Clinic School of Graduate Medical Education, Phoenix, AZ, [2]Mayo Clinic, Scottsdale, AZ, [3]Mayo Clinic, Phoenix, AZ

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Calcinosis is a vexing manifestation in patients with systemic sclerosis (SSc) with a variable prevalence among cohorts. Up to 86% of calcinosis cases are localized in the hands. This study aims to evaluate the prevalence of calcinosis on hand radiographs in a cross-sectional cohort of SSc patients at their initial evaluation and to compare clinical and laboratory features between those with and without calcinosis.

Methods: We conducted a retrospective cohort study using data from the Mayo Clinic Arizona Scleroderma Program. Only patients who underwent bilateral hand X-rays as part of baseline evaluation were included. Demographic data, clinical features, laboratory results, and treatment were collected. Descriptive statistics were stratified by calcinosis status. Categorical variables were summarized as counts and percentages, with group differences assessed using Chi-square or Fisher's exact tests. Continuous variables were reported as means with standard deviations; comparisons were made using two-sample t-tests.

Results: Of the 196 patients in our cohort who had hand x-rays, 71 (36.2%) showed evidence of calcinosis. Demographic characteristics and SSc subtypes are summarized in Table 1. Patients with calcinosis had a longer time from scleroderma diagnosis to hand X-rays (12.7 vs. 7.3 years, $p = 0.001$). Compared to those without calcinosis, patients with calcinosis had higher rates of acroosteolysis, finger ulcers, joint contractures, telangiectasias, and osteopenia (Table 2). There were no significant differences between the groups in the prevalence of Raynaud's phenomenon, ILD, pulmonary arterial hypertension, or renal involvement. Serologically, anti-Scl-70 antibodies were more common in patients without calcinosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical characteristics of sleroderma patients with and without calcinosis

	Calcinosis seen on hand x-rays			
	No (N=125)	Yes (N=71)	Total (N=196)	P-value
Age at scleroderma diagnosis				0.062[1]
Mean (SD)	49.7 (15.35)	45.3 (15.96)	48.1 (15.67)	
Gender, n (%)				0.162[2]
Female	108 (86.4%)	66 (93.0%)	174 (88.8%)	
Male	17 (13.6%)	5 (7.0%)	22 (11.2%)	
Ethnicity, n (%)				0.341[3]
Asian	3 (2.4%)	1 (1.4%)	4 (2.0%)	
Black	5 (4.0%)	0 (0.0%)	5 (2.6%)	
Caucasian	116 (92.8%)	70 (98.6%)	186 (94.9%)	
Unknown / Not Reported	1 (0.8%)	0 (0.0%)	1 (0.5%)	
BMI				0.196[1]
Mean (SD)	25.6 (5.68)	24.5 (5.46)	25.2 (5.61)	
Smoking, n (%)	18 (14.4%)	16 (22.5%)	34 (17.3%)	0.148[2]
Scleroderma type, n (%)				0.652[3]
Limited Cutaneous	68 (54.4%)	40 (56.3%)	108 (55.1%)	
Diffused cutaneous	44 (35.2%)	21 (29.5%)	65 (33.2%)	
CREST Variant	5 (4%)	6 (8.5%)	11 (5.6%)	
Sine Scleroderma	8 (6.4%)	4 (5.7%)	12 (6.1%)	
Years from scleroderma diagnosis to hand x-rays				**0.001[1]**
Mean (SD)	7.3 (10.14)	12.7 (12.59)	9.3 (11.36)	

[1]Equal variance two sample t-test; [2]Chi-Square p-value; [3]Fisher Exact p-value;

(27.2% vs. 14.1%, p = 0.034), whereas anti-centromere (49.3% vs. 34.4%, p = 0.041) and anti-SS-A 52kD antibodies (19.7% vs. 8.0%, p = 0.023) were more frequent in those with calcinosis. Medication use is detailed in Table 3.

Table 2. Associated symptoms and system involvement in scleroderma patients with and without calcinosis

	Calcinosis seen on hand x-rays			
	No (N=125)	Yes (N=71)	Total (N=196)	P-value
Acroosteolysis, n (%)	11 (8.8%)	27 (38.0%)	38 (19.4%)	**<.001[2]**
Raynaud, n (%)	119 (95.2%)	69 (97.2%)	188 (95.9%)	0.713[3]
History of finger ulcers, n (%)	30 (24.0%)	34 (47.9%)	64 (32.7%)	**<.001[2]**
History of Botox digital injections, n (%)	6 (4.8%)	11 (15.5%)	17 (8.7%)	**0.011[2]**
History of digital sympathectomy, n (%)	7 (5.6%)	10 (14.1%)	17 (8.7%)	**0.043[3]**
Digital amputations, n (%)	5 (4.0%)	4 (5.6%)	9 (4.6%)	0.725[3]
Hand swelling, n (%)	41 (32.8%)	22 (31.0%)	63 (32.1%)	0.794[2]
Hand/joint stiffness, n (%)	45 (36.0%)	23 (32.4%)	68 (34.7%)	0.610[2]
Joint contracture, n (%)	28 (22.4%)	29 (40.8%)	57 (29.1%)	**0.006[2]**
Sclerodactyly, n (%)	83 (66.4%)	53 (74.6%)	136 (69.4%)	0.229[2]
Telangiectasias, n (%)	79 (63.2%)	61 (85.9%)	140 (71.4%)	**<.001[2]**
Osteoporosis, n (%)	31 (24.8%)	24 (33.8%)	55 (28.1%)	0.178[2]
Osteopenia, n (%)	56 (44.8%)	43 (60.6%)	99 (50.5%)	**0.034[2]**
Low vitamin D, n (%)	11 (8.8%)	12 (16.9%)	23 (11.7%)	0.090[2]
Hypercalcemia, n (%)	5 (4.0%)	6 (8.5%)	11 (5.6%)	0.210[3]
Hyperparathyroidism, n (%)	5 (4.0%)	5 (7.0%)	10 (5.1%)	0.501[3]
PAH Echocardiogram, n (%)	14 (11.2%)	13 (18.3%)	27 (13.8%)	0.165[2]
No renal involvement, n (%)	122 (97.6%)	66 (93.0%)	188 (95.9%)	0.141[3]
ILD, n (%)	46 (36.8%)	30 (42.3%)	76 (38.8%)	0.451[2]
Dysphagia, n (%)	71 (56.8%)	41 (57.7%)	112 (57.1%)	0.898[2]
Myositis, n (%)	14 (11.2%)	10 (14.1%)	24 (12.2%)	0.554[2]
Arthralgias, n (%)	29 (23.2%)	19 (26.8%)	48 (24.5%)	0.577[2]

[1]Equal variance two sample t-test; [2]Chi-Square p-value; [3]Fisher Exact p-value;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Medications used in patients with and without calcinosis

	Calcinosis seen on hand x-rays			
	No (N=125)	Yes (N=71)	Total (N=196)	P-value
Biphosphonates, n (%)	10 (8.0%)	7 (9.9%)	17 (8.7%)	0.657[2]
Calcium Channel Blockers, n (%)	53 (42.4%)	34 (47.9%)	87 (44.4%)	0.457[2]
Colchicine, n (%)	2 (1.6%)	5 (7.0%)	7 (3.6%)	0.101[3]
Calcium, n (%)	21 (16.8%)	5 (7.0%)	26 (13.3%)	0.053[2]
Vitamin D, n (%)	51 (40.8%)	25 (35.2%)	76 (38.8%)	0.440[2]
Sildenafil, n (%)	10 (8.0%)	16 (22.5%)	26 (13.3%)	**0.004[2]**
Steroids, n (%)	29 (23.2%)	9 (12.7%)	38 (19.4%)	0.073[2]
Mycophenolate mofetil, n (%)	52 (41.6%)	20 (28.2%)	72 (36.7%)	0.061[2]
Methotrexate, n (%)	26 (20.8%)	11 (15.5%)	37 (18.9%)	0.361[2]
Azathioprine, n (%)	4 (3.2%)	2 (2.8%)	6 (3.1%)	>0.999[3]
Cyclophosphamide, n (%)	3 (2.4%)	0 (0.0%)	3 (1.5%)	0.555[3]
Tacrolimus, n (%)	0 (0.0%)	1 (1.4%)	1 (0.5%)	0.362[3]
Rituximab, n (%)	12 (9.6%)	3 (4.2%)	15 (7.7%)	0.174[2]
Tocilizumab, n (%)	9 (7.2%)	6 (8.5%)	15 (7.7%)	0.752[2]
Intravenous Immunoglobulin, n (%)	6 (4.8%)	2 (2.8%)	8 (4.1%)	0.713[3]
Hydrocychloroquine, n (%)	35 (28.0%)	11 (15.5%)	46 (23.5%)	**0.047[2]**

[1]Equal variance two sample t-test; [2]Chi-Square p-value; [3]Fisher Exact p-value;

Conclusion: In a single center cohort of SSc patients, calcinosis on bilateral hand X-rays was observed in over one-third (36.2%) of patients. This is a higher prevalence compared to 10% in prior literature. Calcinosis was associated with a longer time from scleroderma diagnosis to hand X-rays, suggesting it progresses over time and may explain variation in prevalence based on radiograph timing. Osteopenia was more frequent among patients with calcinosis, although calcinosis was not significantly associated with vitamin D deficiency or hyperparathyroidism. These findings are consistent with other studies where bone metabolism might be playing a role in the pathogenesis of calcinosis. Higher frequencies of anti-centromere and anti-SS-A 52kD antibodies were seen in patients with calcinosis, whereas anti-Scl-70 antibodies were more common in those without calcinosis. This highlights an opportunity to explore serologic distinctions in larger cohorts. This study highlights the high prevalence of calcinosis detected on baseline hand X-rays suggesting that imaging may serve as a valuable tool for early detection. Consistent early identification is required to better understand calcinosis before exploring targeted interventions for the future.

Disclosure: M. Diaz Menindez: None; **S. Nimal**: None; **M. Pham**: None; **C. Harvey**: None; **L. Griffing**: None; **V. Nagaraja**: None.

Abstract Number: 0702

Effectiveness of Oral Anticoagulants in Precapillary Pulmonary Hypertension Associated with Systemic Sclerosis: a EUSTAR Cohort Study.

Nicola Farina[1], Silvia Bellando-Randone[2], hilde Bjørkekjær[3], David Launay[4], Patricia E. Carreira[5], paolo airò[6], Serena Guiducci[7], Dilia Giuggioli[8], Gabriela Riemekasten[9], carmen-Pilar Simeón Aznar[10], Christina Bergmann[11], Elise Siegert[12], Ivan Castellví[13], Lesley Ann Saketkoo[14], Jeska de Vries-Bouwstra[15], Dr. Philipp Klemm[16], ulf Müller-Ladner[17], Alexandra Balbir- Gurman[18], Vanessa Smith[19], Florenzo Iannone[20], Luca Idolazzi[21], Christopher Denton[22], edoardo rosato[23], Britta Maurer[24], Yannick Allanore[25], Yoshiya Tanaka[26], elisabetta zanatta[27], Marie-Elise Truchetet[28], Masataka Kuwana[29], Mickaël MARTIN[30], Alberto Cauli[31], Kamal Solanki[32], Francesco Del Galdo[33], Ana Maria Gheorghiu[34], Branimir Anic[35], Gábor Kumánovics[36], Gonsalo Boleto[37], Kristofer Andréasson[38], Simona Rednic[39], Lorinda Chung[40], susana Oliveira[41], marius cadar[42], Francesco Paolo Cantatore[43], Carolina de Souza Müller[44], Vivien Hsu[45], Yair Levy[46], Gianluca Moroncini[47], Jörg Henes[48], Andra Balanescu[49], Ellen De Langhe[50], Carlomaurizio Montecucco[51], Petros Sfikakis[52], Michele Iudici[53], Stefan Heitmann[54], Madelon Vonk[55], Anna-Maria Hoffmann-Vold[56], Oliver Distler[57], Marco Matucci-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cen[58], Cosimo Bruni[57], [1]Department of Experimental and Clinical Medicine, Scleroderma Unit, Division of Rheumatology, University of Florence, Azienda Ospedaliera Universitaria Careggi, Florence, Italy. Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Hospital, Milan, Italy, Milan, Italy, [2]University of Florence, Florence, Florence, Italy, [3]Department of Rheumatology, Hospital of Southern Norway, Kristiansand, Norway, olso, Norway, [4]Univ. Lille, Inserm, CHU Lille, Department of Internal Medicine and Clinical Immunology, Reference Center for Rare Autoimmune and Autoinflammatory diseases (CERAINOM), U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France. National Reference Center for Pulmonary Arterial Hypertension (Pulmotension), Lille, France, Lille Cedex, France, [5]Hospital Universitario 12 de Octubre, Madrid, Spain, [6]Rheumatology and Clinical Immunology Unit, ASST Spedali Civili of Brescia, University of Brescia, Brescia, Italy, brescia, Italy, [7]Department of Experimental and Clinical Medicine, Scleroderma Unit, Division of Rheumatology, University of Florence, Azienda Ospedaliera Universitaria Careggi, Florence, Italy, Pistoia, Italy, [8]Scleroderma Unit, Rheumatology Unit, University Hospital of Modena and Reggio Emilia, Modena, Italy, Modena, Italy, [9]University Clinic Schleswit-Holstein (UKSH), Lübeck, Germany, [10]Hospital Universitario Vall d'Hebron Passeig, Department of Internal Medicine, Systemic Autoimmune Diseases Unit, Barcelona, Spain, Zaragoza, Spain, [11]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [12]Charité University Hospital, Department of Rheumatology, Berlin, Germany, Berlin, Germany, [13]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, barcelona, Spain, [14]University Medical Center - Comprehensive Pulmonary Hypertension Center and ILD Clinic Programs // New Orleans Scleroderma and Sarcoidosis Patient Care & Research Centeris, New Orleans, LA, [15]Leiden University Medical Center, Leiden, Netherlands, [16]Kerckhoff-Klinik Bad Nauheim, Berlin, Germany, [17]JLU Giessen, Campus Kerckhoff, Department of Rheumatology and Clinical Immunology Center, Bad Nauheim, Germany, Bad Nauheim, Germany, [18]Rambam Health Care Campus, Rheumatology Institute, Haifa, Israel, israel, Israel, [19]Ghent University Hospital, Gent, Belgium, [20]Rheumatology DiMePReJ, University of Bari, School of Medicine, Bari, Italy, Bari, Italy, [21]Section of Rheumatology, Department of Medicine, University of Verona, Verona, Italy, verona, Italy, [22]University College London, UK, London, United Kingdom, [23]Sapienza University of Rome, Department of Translational and Precision Medicine Azienda Ospedaliero-Universitaria Policlinico Umberto 1-Centro di riferimento regionale per la sclerosi sistemica, Rome, Italy, rome, Italy, [24]Department of Rheumatology & Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [25]Université Paris Cité, Paris, France, [26]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [27]Padova University Hospital, Rheumatology Unit, Padova, Italy, padova, Italy, [28]Bordeaux University Hospital, Bordeaux, France, [29]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [30]Poitiers University Hospital, Department of Internal Medicine, Poitiers, France, MIGNALOUX-BEAUVOIR, France, [31]Rheumatology Unit, Department of Medicine and Public Health, AOU and University of Cagliari, Cagliari, Italy, [32]Waikato Hospital, Hamilton, New Zealand, [33]University of Leeds, Leeds, United Kingdom, [34]Spitalul Clinic Dr. Ion Cantacuzino, Bucharest, Romania, [35]University of Zagreb, School of Medicine, University Hospital Center Zagreb, Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, Zagreb, Croatia, zagreb, Croatia, [36]University of Pécs, Department Of Rheumatology And Immunology, Medical Centre, Pecs, Hungary, Pecs, Hungary, [37]Local de Saúde Santa Maria, Centro Académico de Medicina de Lisboa, Rheumatology Department, Lisbon, Portugal, Paris, France, [38]Skåne University Hospital, Department of Rheumatology, Lund, Sweden, Lund, Sweden, [39]University of Medicine and Pharmacy Iuliu Hatieganu Cluj, Clinica Reumatologie, Cluj-Napoca, Romania, Cluj-Napoca, Romania, [40]Stanford University, Stanford, CA, [41]Fernando Fonseca Hospital, Department of Medicine IV, Systemic Immunomediated Diseases Unit, Amadora, Portugal, amadora, Portugal, [42]Sapienza University of Rome, Rheumatology Clinic, Rome, Italy, Rome, Italy, [43]University of Foggia, Department of Medical and Surgical Sciences, Rheumatology Unit, Foggia, Italy, foggia, Italy, [44]Hospital de Clinicas da Universidade Federal do Parana, Curitiba, Brazil, curitiba, Brazil, [45]Rutgers- RWJ Medical School, South Plainfield, NJ, [46]Meir Medical Center, Kfar-Saba, Israel, Kefar Sava, Israel, [47]Department of Internal Medicine, Marche University Hospital, Clinica Medica, Ancona, Italy, Ancona, Italy, [48]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tuebingen, Germany, [49]UNIVERSITY OF MEDICINE AND PHARMACY CAROL DAVILA, Bucharest, Romania, [50]University Hospital Leuven, Laboratory of Tissue Homeostasis and Disease, Department of Development and Regeneration, KU Leuven, Leuven, Belgium, Leuven, Belgium, [51]Università di Pavia e IRCCS Fondazione Policlinico S. Matteo, Pavia, Italy, [52]NKUA - SCHOOL OF MEDICIN, Athens, Greece, [53]Division of Rheumatology, Department of Internal Medicine Specialties, Geneva University Hospitals, Geneva, Switzerland, [54]Department of Rheumatology, Marienhospital Stuttgart, Böheimstrasse 37, D-70199 Stuttgart, Germany, [55]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, [56]Oslo University Hospital, Oslo, Norway, [57]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [58]University San Raffaele Milano, Milano, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Precapillary pulmonary hypertension (PH) in systemic sclerosis (SSc) associates with severe morbidity and mortality. The prothrombotic state observed in idiopathic pulmonary arterial hypertension (PAH) has historically supported the use of oral anticoagulants (OAC) in its management. However, the benefit of OAC in SSc-related precapillary PH remains uncertain, with studies reporting conflicting results, including possible harm. The objective of this study was to evaluate whether OAC use is associated with improved survival or reduced disease worsening in SSc patients with precapillary PH.

Methods: We conducted a cohort study using the European Scleroderma Trial and Research (EUSTAR) database to investigate the impact of OAC exposure vs. non-exposure on the prognosis of SSc patients with precapillary PH confirmed by right heart catheterization (RHC- mean PAP >20 mmHg, PVR >2 WU and PWP≤15 mmHg). Exposure to OAC was defined when lasting for at least 3 months after the RHC diagnosis.

The primary outcome was a combination of all-cause death or otherwise PH worsening, the latter defined as at least one of the following: decrease of 6MWD >15%, worsening of NYHA class, onset of right heart failure, additional PAH medication, starting i.v./s.c. prostanoids, lung transplantation, or atrial septostomy. Mortality and PH worsening were also analyzed as secondary endpoints.

Table 1. Data about demographics, disease features, treatment exposure, functional and hemodynamic parameters, and outcome variables, compared between patients who received oral anticoagulants and those who did not. Categorial and continuous variables are reported as absolute numbers (%) and mean (standard deviation), respectively. BNP, brain natriuretic peptide; CI, cardiac index; DLCO, diffusion lung capacity of carbon monoxide; HR, hazard ratio; HRCT, high resolution computed tomography; ILD; interstitial lung disease; mPAP, mean pulmonary arterial pressure; NYHA, New York Heart Association; PH, pulmonary hypertension; 6MWT, 6-minute walking test. Bold represents statistical significance with p value <0.05.

	All patients (n=644)	Patients not exposed to OAC (n=471)	Patients exposed to OAC (n=173)	*p-value*
Female sex	533 (83%)	389 (83%)	144 (83%)	0.847
Age (years)	63 ± 15	62 ± 15	65 ± 11	**0.040**
Caucasian	490 (76%)	350 (89%)	140 (99%)	**< 0.001**
Smoking ever	209 (32%)	149 (32%)	31 (19%)	**< 0.001**
Diffuse SSc	180 (28%)	158 (34%)	51 (30%)	0.487
Disease duration (years)	11 ± 9	11 ± 9	10 ± 9	0.914
ACA positivity	312 (48%)	215 (46%)	96 (56%)	**0.017**
ATA positivity	147 (23%)	109 (23%)	38 (22%)	0.759
Digital ulcers, ever	218 (34%)	162 (37%)	56 (36%)	0.861
Esophageal symptoms	465 (72%)	347 (74%)	116 (68%)	0.105
Telangiectasias	499 (78%)	353 (75%)	146 (85%)	**0.007**
Renal crisis, ever	21 (4%)	18 (4%)	3 (2%)	0.184
ILD on HRCT	400 (62%)	302 (64%)	98 (57%)	0.083
Dyspnea (NYHA class ≥III)	335 (52%)	239 (51%)	96 (55%)	0.611
Increased NTproBNP/BNP	230 (36%)	151 (32%)	79 (46%)	**0.001**
Decreased 6MWT distance	502 (78%)	369 (82%)	133 (27%)	0.950
Vasoactive therapy, ongoing at RHC	285 (44%)	219 (46%)	66 (38%)	0.120
Vasoactive therapy, ever	532 (83%)	381 (81%)	149 (86%)	**0.026**
Immunosuppressants, ever	330 (51%)	232 (50%)	98 (57%)	0.130
FVC (% predicted)	84 ± 24	84 ± 24	84 ± 21	0.380
DLCO/SB (% predicted)	43 ± 15	43 ± 15	43 ± 15	0.921
sPAP on RHC (mmHg)	55 ± 19	54 ± 18	59 ± 20	**0.011**
dPAP on RHC (mmHg)	20 ± 9	20 ± 8	22 ± 10	**0.021**
mPAP on RHC (mmHg)	34 ± 11	34 ± 11	36 ± 12	**0.007**
PVR (Wood Units)	12 ± 45	10 ± 31	18 ± 71	**0.032**
PWP (mmHg)	10 ± 3	9 ± 3	10 ± 3	0.216
Decreased CI < 2.5 L/min	225 (35%)	154 (32%)	71 (42%)	**0.040**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

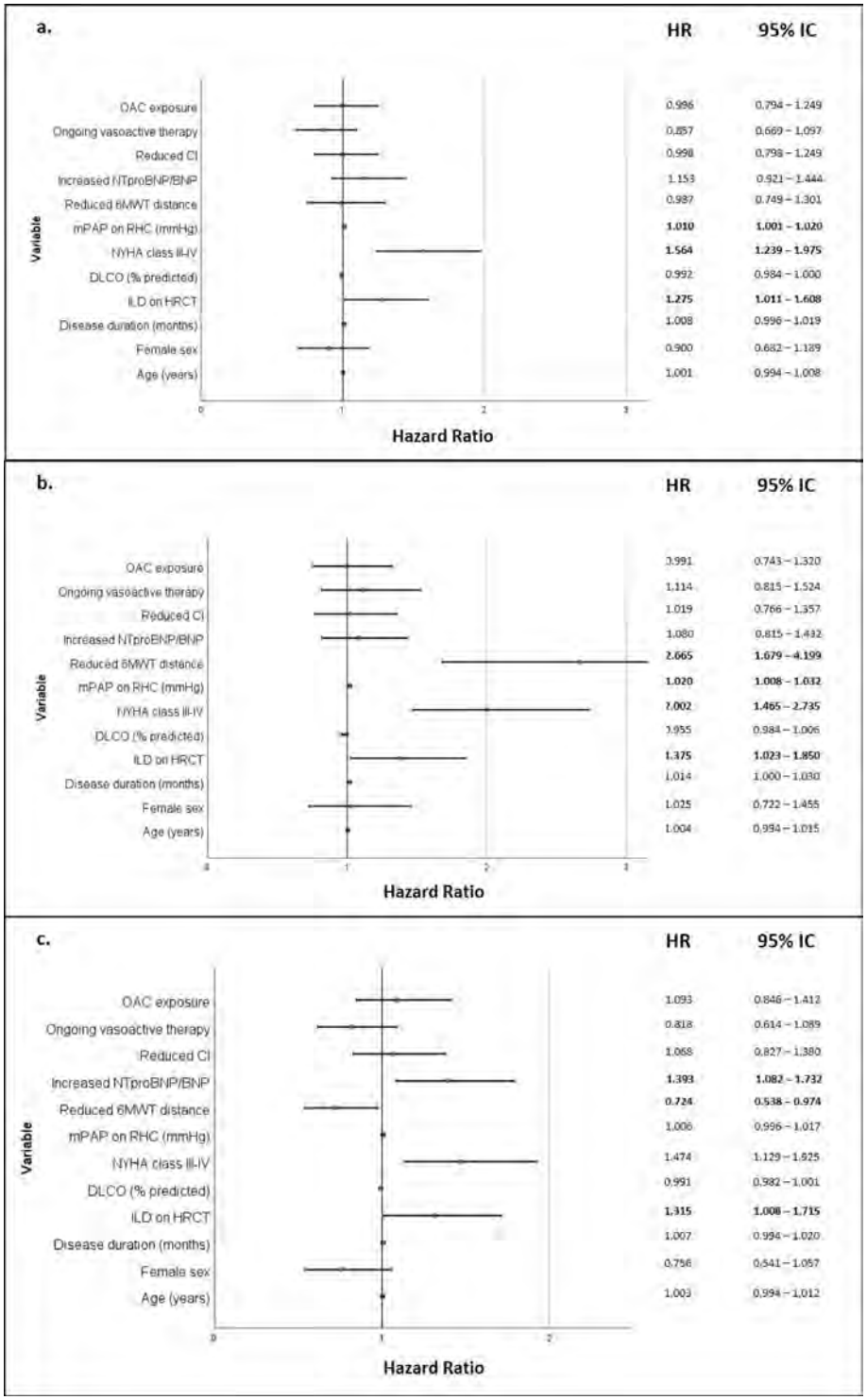


Figure 1. Forest plots of multivariable regression models testing the association between exposure to oral anticoagulants and the prognosis (panel a primary endpoint, panel b death, panel c pulmonary hypertension worsening) of patients with pulmonary arterial hypertension at right heart catheterization. BNP, brain natriuretic peptide; CI, cardiac index; DLCO, diffusion lung capacity of carbon monoxide; HR, hazard ratio; HRCT, high resolution computed tomography; ILD; interstitial lung disease; mPAP, mean pulmonary arterial pressure; NYHA, New York Heart Association; PH, pulmonary hypertension; 6MWT, 6-minute walking test. Bold represents statistical significance with p value <0.05.

Multivariable Cox regression was used to assess associations of exposure to OAC and the endpoints. Additionally, propensity score matching (PSM) was performed to balance confounding factors among OAC treated vs. untreated patients. Time to endpoints was assessed using Kaplan Mayer estimates. Covariates for both Cox regression and PSM were chosen

23265205, 2025, S9, Downloaded from https://accjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

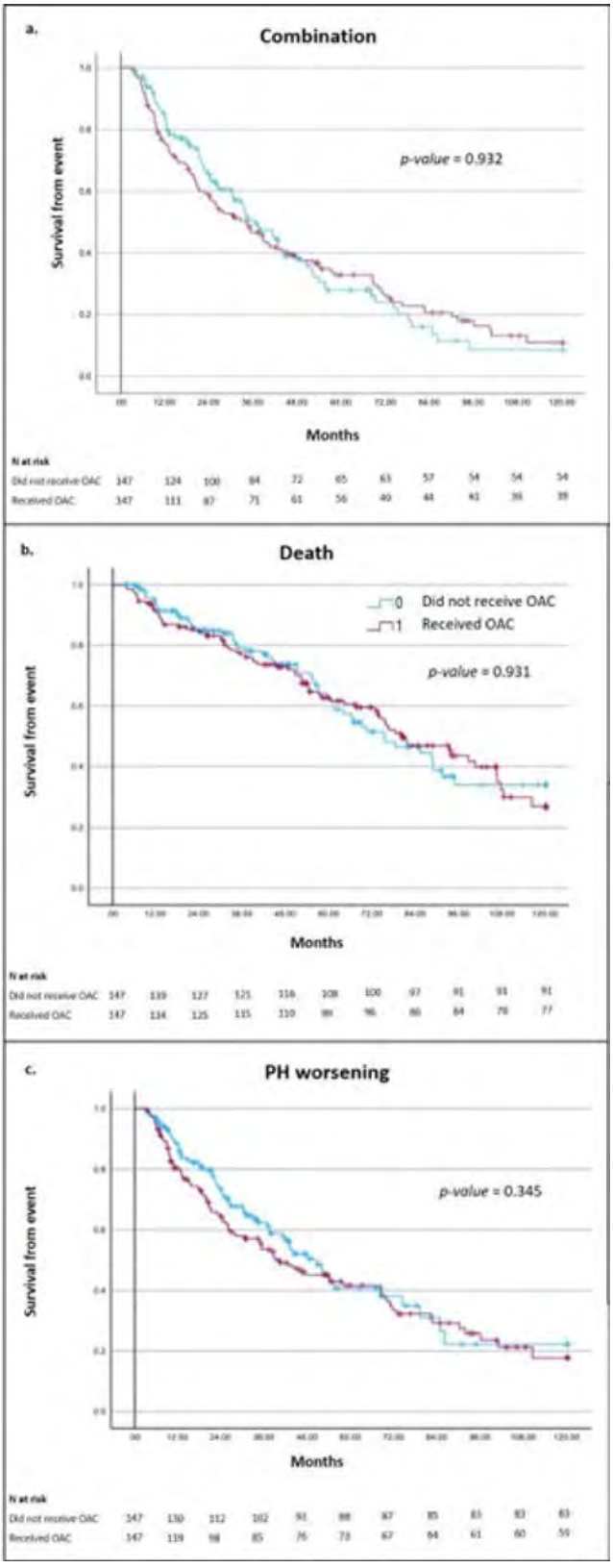


Figure 2. Survival curves for different outcome variables according to the exposure status to oral anticoagulants, in the match-control population identified using propensity score matching. NYHA:New York Heart Association; OAC, oral anticoagulants; PH, pulmonary hypertension.

based on literature support and included risk factors for worse prognosis in SSc and PH (i.e., age, sex, mPAP, reduced cardiac index, DLCO%). Missing data on the covariates were imputed using the Random Forest algorithm.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 644 eligible patients, 173 (27%) received OAC at the time of RHC or afterwards. Patients treated with OAC were older and had more severe hemodynamic parameters (**Table 1**). During a median follow-up of 4 (2-6) years, 40% of patients died and 49% experienced PH worsening. Both events were recorded more frequently in the group treated with OAC, compared to non-treated patients (46% vs 37% and 59% vs 45%, respectively). Cox regression analysis did not show any significant association between OAC exposure and the combined endpoint (HR 0.996, 95% CI 0.794–1.249), mortality (HR 0.991, 95% CI 0.743–1.320) or PH worsening (HR 1.093, 95% CI 0.846–1.412) - **Figure 1**.

PSM identified two balanced groups of 148 patients exposed and 148 not exposed to OAC. Kaplan Meier curves (**Figure 2**) confirmed the lack of association between OAC and the explored prognostic outcomes.

Conclusion: In this large multicenter cohort of SSc patients with precapillary PH, OAC therapy did not impact survival or disease worsening. These findings argue against the routine use of anticoagulation in this population and highlight the importance of individualized treatment decisions based on comorbidities and safety profile. Prospective studies are needed to identify whether specific subgroups may benefit from OAC therapy.

Disclosure: N. Farina: None; **S. Bellando-Randone**: Boehringer-Ingelheim, 2, 6; **h. Bjørkekjær**: Janssen, 5; **D. Launay**: AstraZeneca, 2, 6, BioCryst, 6, 12, travel grants, CSL Behring, 2, 6, Shire, 12, travel grants, Takeda, 2, 6; **P. Carreira**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, Emmerald Health Pharmaceuticals, 2, 6, Janssen, 2, 6, Mitsubishi Tanabe, 2, 6, Novartis, 2, 6, Prometheus, 2, 6; **p. airò**: Amgen, 12, meeting/travel support, CSL Behring, 12, meeting/travel support, Eli Lilly, 12, meeting/travel support, Janssen, 6, 12, meeting/travel support, Novartis, 6; **S. Guiducci**: None; **D. Giuggioli**: None; **G. Riemekasten**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 2, 6, Galapagos, 6, Janssen, 2, 6, Merck/MSD, 6, Novartis, 6, Roche, 6, Sanofi, 5; **c. Simeón Aznar**: Boehringer-Ingelheim, 2, 6, 12, travel grants, Janssen, 2, 6, 12, travel grants, Merck/MSD, 6; **C. Bergmann**: None; **E. Siegert**: None; **I. Castellví**: Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 6, Gebro, 6, GlaxoSmithKlein(GSK), 2, Innovarderm, 2, Janssen, 2, 6, Kern Pharma, 2, 6, Novartis, 2, Roche, 6, Sanofi-Genzyme, 6; **L. Saketkoo**: Abbvie, 6, Argenx, 1, 2, 5, aTyr Pharmaceuticals, 12,, 1, 5, Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 5, EMD Serono, 2, 5, Horizon, 5, Johnson & Johnson, 6, Kadmon, 5, Kinevant, 12,, 2, 5, Mallinckrodt, 1, 2, 5, Novartis, 1, 2, 5, Priovant, 5; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **D. Klemm**: None; **u. Müller-Ladner**: None; **A. Balbir- Gurman**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **F. Iannone**: None; **L. Idolazzi**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **e. rosato**: None; **B. Maurer**: AbbVie/Abbott, 5, Actelion, 12, Congress support, Boehringer-Ingelheim, 1, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Medtalk, 12, Congress support, Mepha, 12, Congress support, Merck/MSD, 12, Congress support, Novartis, 2, 5, 6, Otsuka, 6, Pfizer, 12, Congress support, Protogen, 5, Roche, 12, Congress support, UCB, 12, Congress support; **Y. Allanore**: None; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **e. zanatta**: None; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2; **M. Kuwana**: AbbVie, 2, Asahi Kasei Pharma, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 6, GlaxoSmithKlein(GSK), 2, Medical and Biological Laboratories, 5, 9, Mochida, 2, Novartis, 2, Ono Pharmaceuticals, 6; **M. MARTIN**: None; **A. Cauli**: None; **K. Solanki**: Apollo Hospitals Educational and Research Foundations, 12, Honorary adjunct professor; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **A. Gheorghiu**: Boehringer-Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5; **B. Anic**: None; **G. Kumánovics**: None; **G. Boleto**: Boehringer-Ingelheim, 12, support for attending meetings; **K. Andréasson**: Janssen, 6; **S. Rednic**: None; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **s. Oliveira**: None; **m. cadar**: None;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

F. Cantatore: None; **C. de Souza Müller**: None; **V. Hsu**: None; **Y. Levy**: None; **G. Moroncini**: None; **J. Henes**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, Janssen, 1, 6, Novartis, 1, 1, 6, 6, Otsuka, 1, Pfizer, 1, Roche, 1, SOBI, 1, UCB, 1, 6; **A. Balanescu**: AbbVie/Abbott, 1, 6, Amgen, 2, 6, Angellini, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Ewopharma, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sobi, 2, 6, Stada, 2, 6, Theramex, 6, UCB, 2, 6; **E. De Langhe**: None; **C. Montecucco**: None; **P. Sfikakis**: None; **M. Iudici**: Boehringer-Ingelheim, 6; **S. Heimann**: None; M. Vonk: Boehringer-Ingelheim: 2, 6, 15; Janssen, 2, 6, 15; Merck/MSD: 6; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 15, Brostol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon, 2, 6, AG, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6 Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **M. Matucci-Cerinic**: None; **Cosimo Bruni**: Beohringer Ingelheim, 2, EMDO Foundation, 5, Iten-Kohaut Foundation, 5, Scleroderma Clinical Trials Consortium (SCTC), 5, Scleroderma Research Foundation (SRF), 2.

Abstract Number: 0703

Trends and Disparities in Systemic Sclerosis-related Mortality Rates in the United States from 1999 to 2023

Nicolas Barnechea Alvarado[1], Khadija Mohib[1], Rameez Qasim[2] and Muhammad Ali[3], [1]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, [2]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [3]Dow International Medical College, Karachi, Sindh, Pakistan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

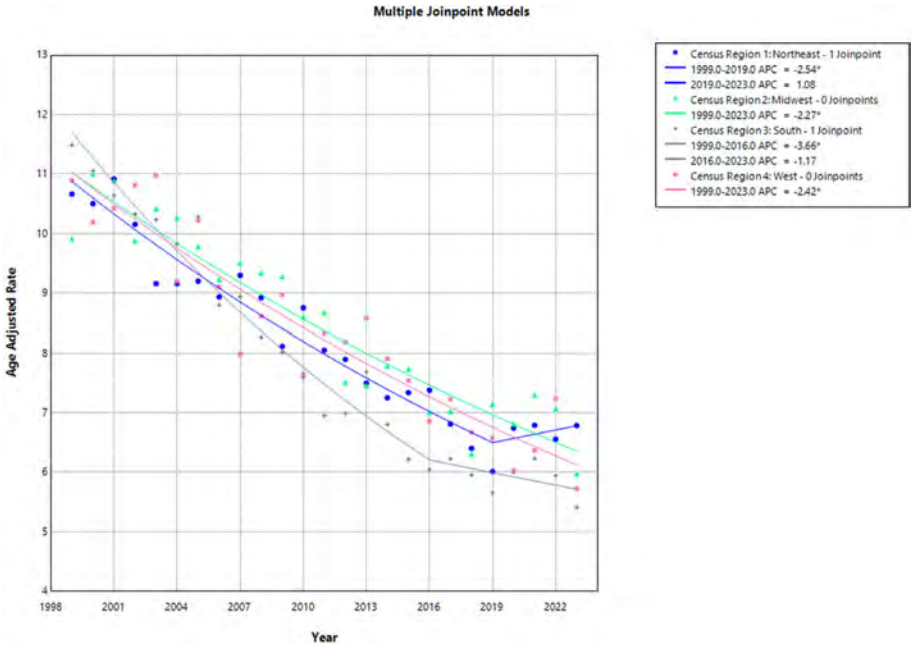
Background/Purpose: Systemic sclerosis is one of the most fatal rheumatologic diseases, with significantly higher mortality rates compared to the general population, likely due to its fibrotic nature and consequential effects on the vasculature system. Although previous observational population-based studies looked into the mortality rates of this disorder, more recent research beyond 2020 is limited, especially analyses stratified by demographic and regional distributions in the United States.

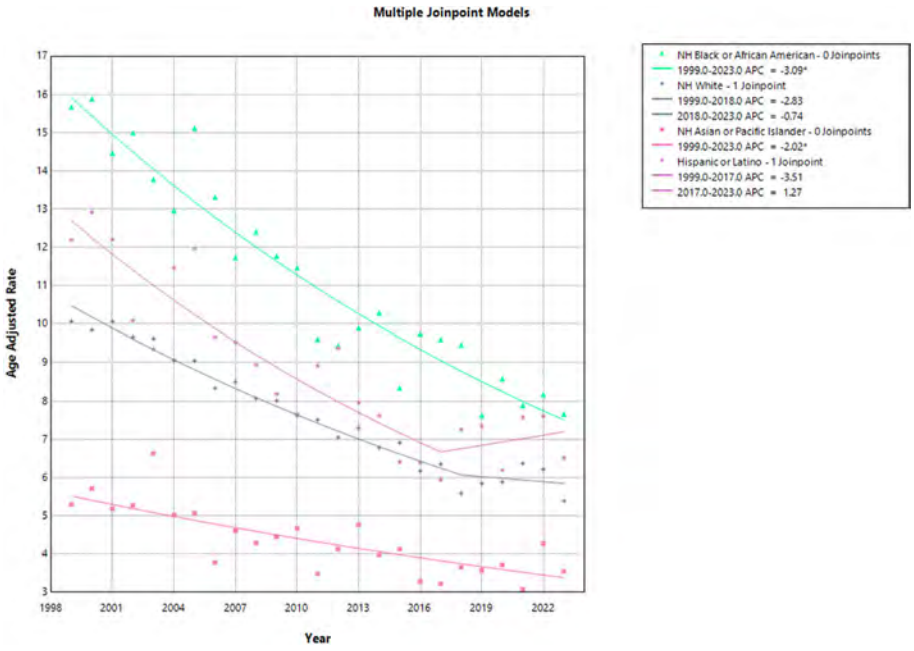
Methods: Datasets from the CDC WONDER Multiple Cause-of-Death public use records from 1999 to 2023 were used to analyze deaths in adults ≥25 years old assigning ICD-10 codes (M34 series) to systemic sclerosis by year and place of death, as well as by demographic (sex, age group, race) and regional (state, census region, rural-urban) stratifications. Age-adjusted mortality rates (AAMR) were calculated per 1,000,000 with 95% confidence intervals by standardizing crude mortality rates (CMR). Annual percent change (APC) and average annual percent change (AAPC) were evaluated using Joinpoint regression software.

Results: 44,407 deaths occurred from 1999 to 2023, mostly in medical facilities (57.3%). AAMR declined from 10.8 to 6.3 in 2018, followed by stability until 5.8 in 2023 (AAPC: -2.4; 95%CI: -2.8 to -2.2). Women had a higher average AAMR compared to men, along with a lower rate of decrease (AAPC women: -2.3; 95%CI: 2.6 to -2.0, men: -2.6; 95%CI: -3.4 to -2.1). Adults ≥65 years old had the highest average AAMR along with the lowest rate of decrease amongst the age groups

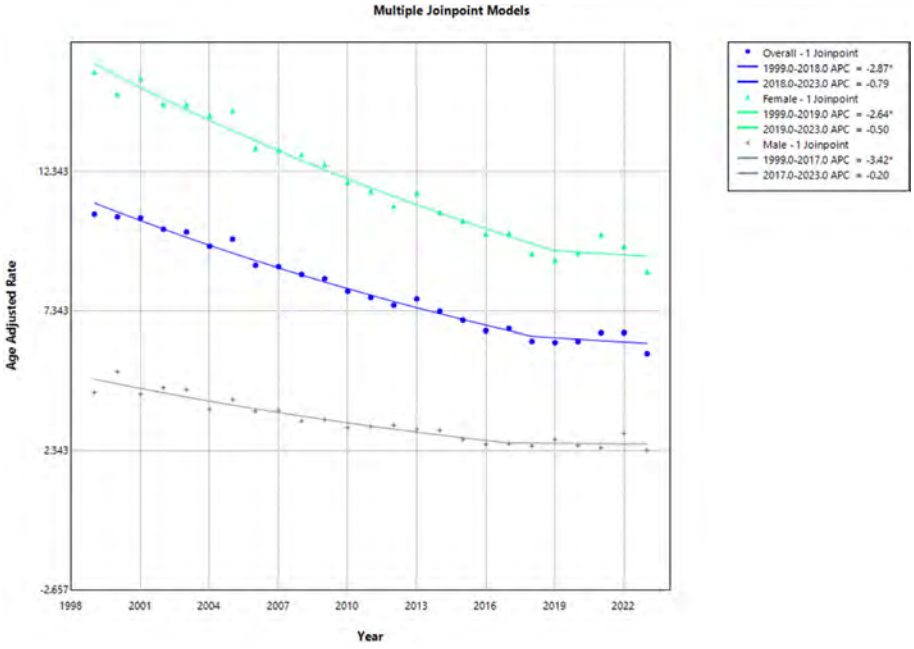
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(AAPC ≥65 years old: -2.0; 95%CI: -2.4 to -1.6, 45-65 years old: -3.3: 95%CI: -3.6 to -3.0, 25-44 years old: -3.2; 95%CI: -3.9 to -2.6). NH Black/African Americans had the highest average AAMR, but had had the highest rate of decrease (AAPC NH Black/African American: -3.1; 95%CI: -3.5 to -2.7, NH White: -2.4; 95%CI -2.9 to -2.1, NH Asian/Pacific Islander: -2.0; 95%CI: -2.7 to -1.3, Hispanic/Latino: -2.3; 95%CI -3.5 to -1.2). Regionally, the Midwest had the highest average AAMR, though the South had the highest rate of decrease (AAPC South: -2.9; 95%CI: -3.4 to -2.5, West: -2.4; 95%CI: -2.9 to -2.0, Midwest: -2.3; 95%CI: -2.6 to -2.0, Northeast: -1.9; 95%CI: -2.4 to -1.6). From 1999 to 2020, AAMR extended from 4.8 in Nevada to 13.6 in South Dakota. From 2021 to 2023, AAMR extended from 3.3 in Alabama to 9.9 in Montana. From 1999-2020, urban areas had higher average AAMR, with a higher rate of decrease (AAPC urban: -2.9; 95%CI: -3.1 to -2.7, rural: -2.5; 95%CI: -2.9 to -2.0).





23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Conclusion: Whilst systemic sclerosis-related mortality rates in adults declined from 1999 to 2023, disparities amid demographic and regional stratifications were observed; this highlights the need to select prevention and assistance programs for at-risk communities to improve survival outcomes

Disclosure: N. Barnechea Alvarado: None; **K. Mohib**: None; **R. Qasim**: None; **M. Ali**: None.

Abstract Number: 0704

Human Pharmacokinetics of Inhaled Liposomal Iloprost Support a Dosing Regimen for Treating Systemic Sclerosis- Related Digital Ulcer

Pei Kan, Ko-Chieh Chen and Shin-Shin Chuang, Pharmosa Biopharm Inc, Taipei, Taiwan (Republic of China)

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Iloprost is recommended and widely used in Europe for treating systemic sclerosis (SSc)-related Raynaud Phenomena (RP) and Digital Ulcer (DU). EULAR recommendation suggests continuous intra-venous (IV) infusion at 0.5-2.0 ng/kg/min for 6 hours daily over 5 consecutive days. Prolonged systemic exposure has been associated with improved therapeutic outcomes. [1] To enable convenient at-home treatment, an inhaled liposomal iloprost was developed. This efficacy study was designed based on human pharmacokinetics (PK) to evaluate the feasibility of such a regimen. This study investigated the PK of inhaled liposomal iloprost in healthy volunteers. The repeated-dose PK simulation is established to compare the systemic exposure of the inhaled liposomal iloprost with the existing IV iloprost regimens used in Europe.

Methods: Human PK of inhaled liposomal iloprost on healthy subjects was investigated in a single ascending dose study (NCT06429930). 8 participants administered liposomal iloprost or placebo (6:2) via a breath-actuated nebulizer for each

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cohort. Blood samples were collected over 24-hour period post-dosing and analyzed by LC-MS-MS. The PK simulation was established according to human PK data.

Results: A single dose of inhaled liposomal iloprost can prolong the detectable plasma concentration up to 12 hours. The PK parameters show a proportional increase with dose over the investigated dose range. The apparent half-life is extended to 4 hours, significantly longer than 20-30 mins reported for currently approved iloprost products. PK simulations were established based on human clinical data of iloprost administered via IV infusion and oral inhalation. The results indicate multiple inhalation doses extend the systemic exposure duration longer than 6 hours as compared with the existing IV iloprost infusion. Meanwhile, the plasma concentrations are also higher than the steady-state concentration attained via 0.5 ng/kg/min infusion.

Conclusion: Inhaled liposomal iloprost is an extended-release formulation [2] which prolongs iloprost exposure in healthy subjects as demonstrated in phase 1 clinical trial. The results support a 28-day dosing regimen for self-administration in treating patients with systemic sclerosis-related digital ulcer.

Disclosure: P. Kan: Pharmosa Biopharm Inc, 3, 4; **K. Chen**: Pharmosa Biopharm Inc, 3; **S. Chuang**: Pharmosa Biopharm Inc, 3.

Abstract Number: 0705

Multimodal Imaging Evaluation of Patients with Raynaud's Phenomenon meeting the Criteria for "Early" Systemic Sclerosis according to LeRoy versus Healthy Controls: a Prospective Cross-sectional study

Ramona Govender[1], Elvis Hysa[2], Rosanna Campitiello[3], Steven Wallaert[1], Matthias Vandycke[1], Emanuele Gotelli[3], Tessa Du Four[1], Maurizio Cutolo[4] and Vanessa Smith[5], [1]University of Ghent, Ghent, Belgium, [2]University of Genoa, Genoa, Italy, [3]University of Genoa, Genoa, Liguria, Italy, [4]University of Genova, Genova, Italy, [5]Ghent University Hospital, Gent, Belgium

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a complex autoimmune disorder. To date, no comparative multi-modal imaging data exist for precursor patients, those with Raynaud's phenomenon (RP) fulfilling the 2001 LeRoy and Medsger criteria[1] for early SSc but without clinical skin thickening, compared to healthy controls.

Methods: This prospective cross-sectional study included unselected RP patients (n=20) fulfilling LeRoy's criteria (RP plus SSc-specific antibodies, RP plus scleroderma pattern, or RP plus both) of the Ghent University (hospital) Raynaud's clinic. Age-, sex-, and BMI-matched healthy controls (HC) (n=20) were recruited for baseline comparison. Dermal thickness (DT) was measured using high-frequency ultrasound (HFUS, 18 MHz) at 17 anatomical sites, a reliable technique, as described by our previous findings[2]. Nailfold videocapillaroscopy (NVC ×200 magnification) was evaluated qualitatively and quantitatively using standardized Scleroderma Clinical Trial Consortium (SCTC)/ European Alliance of Associations for Rheumatology (EULAR) Study Group on Microcirculation in Rheumatic Diseases consensus definitions. Peripheral blood perfusion (PBP) was assessed by laser speckle contrast analysis (LASCA) in the volar aspect of both hands under standardized conditions, as described previously[3]. Exploratory statistical analysis included Student T-test, Wilcoxon, and Fischer exact tests for between-group comparisons as appropriate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

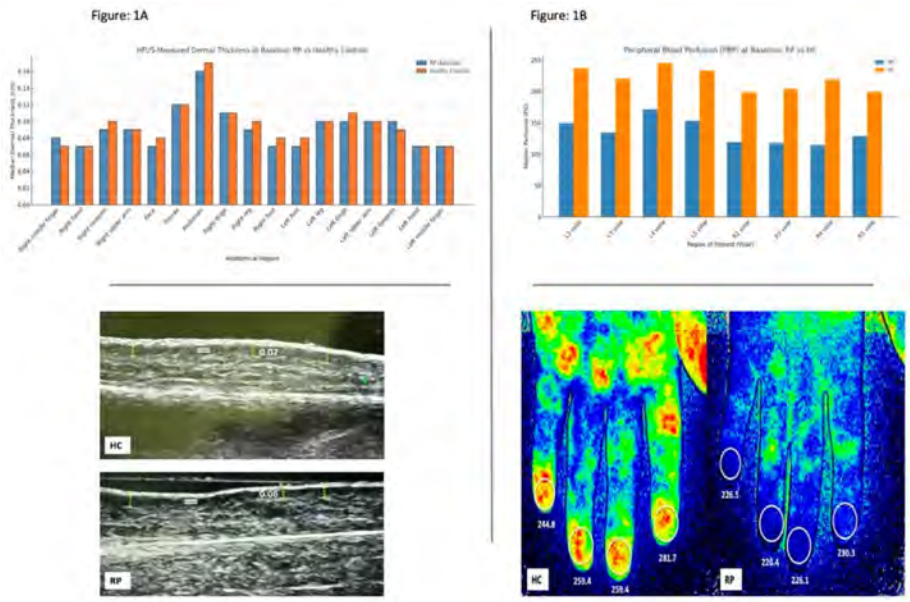
Table 1. Baseline characteristics of study population

Baseline characteristics	Raynaud's patients (n=20)	Healthy Controls (n=20)
Demographics		
Age (years), mean (SD)	46.4 (13.8)	46.8 (16.0)
Female, n (%)	17 (85.0)	17 (85.0)
Caucasian, n (%)	20 (100.0)	22 (100.0)
BMI (kg/m^2), median (IQR)	23.4 (20.0 – 28.3)	23.2 (21.6-27.2)
Smoker, n (%)	7 (35.0)	0
RP subsets		
RP + scleroderma pattern* only	9 (45.0)	
RP + SSc-specific antibody only	8 (40.0)	
RP + scleroderma pattern + SSc-specific antibody only	3 (15.0)	
Antibody status		
ANA positivity, n (%)	19 (95.0)	
SSc-specific antibody, n (%)	11 (55.0)	
Anticentromere antibody, n (%)	6 (30.0)	
Anti-topoisomerase-I antibody, n (%)	1 (5.0)	
Anti-RNA-polymerase III antibody, n (%)	3 (15.0)	
Anti-PM/Scl-75 antibody, n (%)	1 (5.0)	
Inflammatory markers		
CRP (mg/L) (normal range: 0-5), mean (SD)	1.7 (1.7)	
ESR (mm/hr) (normal range: 0-20), mean (SD)	8.3 (6.3)	
SSc-related organ involvement	0	
Peripheral vascular involvement, Active, n (%)	0	
Active digital ulcers, n (%)	0	
Active gangrene, n (%)	0	
Active pitting scars, n (%)	0	
Pulmonary involvement		
ILD, n (%)	0	
Vascular lung involvement		
PH, n (%)	0	
PAH, n (%)	0	
Skin		
mRSS, mean	0	
Puffy fingers, n (%)	2 (10.0)	
Telangiectasia, n (%)	6 (30.0)	
Scleredema, n (%)	0	
Heart		
Diastolic dysfunction (grade 1), n (%)	3 (15.0)	
LVEF < 50%, n (%)	0	
Pericardial effusion, n (%)	0	
Gastrointestinal tract		
Esophageal symptoms, n (%)	7 (35.0)	
Stomach symptoms, n (%)	0	
Intestinal symptoms, n (%)	0	
Intestinal obstruction, n (%)	0	
Malabsorption, n (%)	0	
Renal		
Creatinine level (mg/dl), mean (SD)	0.7 (0.1)	
SRC, n (%)	0	
Musculoskeletal involvement	0	
Synovitis, n (%)	0	
Muscle weakness, n (%)	0	
CK elevation, n (%)	0	
Medication		
Vasodilator therapy, n (%)	5 (25.0)	
Prostacyclin, n (%)	0	
Calcium antagonists, n (%)	5 (25.0)	
Endothelin receptor antagonists, n (%)	0	
Phosphodiesterase type 5 inhibitor	0	
Immunosuppressive therapy, n (%)	2 (10.0)	
HCQ, n (%)	2 (10.0)	
MTX, n (%)	0	
MMF, n (%)	0	
CYC, n (%)	0	
AZA, n (%)	0	
Rituximab, n (%)	0	
Autologous stem cell transplantation, n (%)	0	

n= number; SD= standard deviation; BMI= body mass index; IQR= inter-quartile range; RMDs= rheumatic musculoskeletal diseases; SSc= systemic sclerosis; RP=Raynaud's phenomenon; SDP= scleroderma pattern; Ab= antibodies; ANA= antinuclear antibody; ILD= interstitial lung disease; PH= pulmonary hypertension; PAH= pulmonary arterial hypertension; mRSS= modified Rodnan skin score; LVEF= left ventricular ejection fraction; SRC= scleroderma renal crisis; CK= creatinine kinase; HCQ= hydroxychloroquine; MTX= methotrexate; MMF= mycophenolate mofetil; CYC= cyclophosphamide; AZA= azathioprine
* Scleroderma pattern as seen on 200X magnification nailfold videocapillaroscopy, defined as per EULAR Study Group on Microcirculation in Rheumatic Diseases (EULAR SGMC/RD).

Results: RP patients showed no evidence of SSc-related organ involvement[4], except for gastro-oesophageal reflux without oesophageal dilatation on high-resolution computerised tomography (HRCT) (Table. 1). HFUS revealed no clinically meaningful differences in DT between groups (all $p > 0.05$) (Figure. 1A). LASCA showed significantly reduced volar fingertip PBP in RP patients compared to HC (all $p < 0.005$) (Figure. 1B). Baseline NVC showed significantly lower capillary density in RP

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(Fig. 1A) Bar graph of median DT (cm) measured by HFUS at 17 anatomical sites (left panel, above). Representative HFUS images of the right middle finger at baseline, illustrating DT measurements in a HC and an RP patient (left panel, below).
(Fig. 1B) Bar graph of median PBP, as measured in PU, on volar aspect of hands (right panel, above). Representative LASCA images of the left hand at baseline, illustrating PBP measurements in a HC and an RP patient (right panel, below).

Abbreviations: DT: dermal thickness; HFUS: high frequency ultrasound, RP: Raynaud's phenomenon, HC: healthy controls, BL: baseline, PBP: peripheral blood perfusion, PU: perfusion units

Figure 1. High frequency ultrasound (HFUS) and laser speckle contrast analysis (LASCA) findings in Raynaud's patients versus healthy controls at baseline

patients across all 8 fingers (all $p < 0.05$). RP patients exhibited higher frequencies of giant capillaries (5–21% vs 0%) and microhaemorrhages (32–35% vs 0–5%, $p < 0.05$), with no significant differences in abnormal shapes (Figure. 2). Early and active scleroderma patterns were observed exclusively in RP patients.

Conclusion: In RP patients meeting the LeRoy's criteria for early SSc, functional and structural microvascular abnormalities are detectable before skin or organ involvement. In line with the clinical absence of skin thickening in both the RP as well as in the HC groups, HFUS was indiscriminatory. Future longitudinal studies will be needed to determine at what point HFUS detects discriminatory changes compared to HC.

References:

1. LeRoy et al. J Rheumatol. 2001
2. Cutolo et al. Clin Exp Rheumatol. 2025
3. Willems et al. Diagnostics. 2023
4. Vanhaecke et al. Rheumatology (Oxford). 2022

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

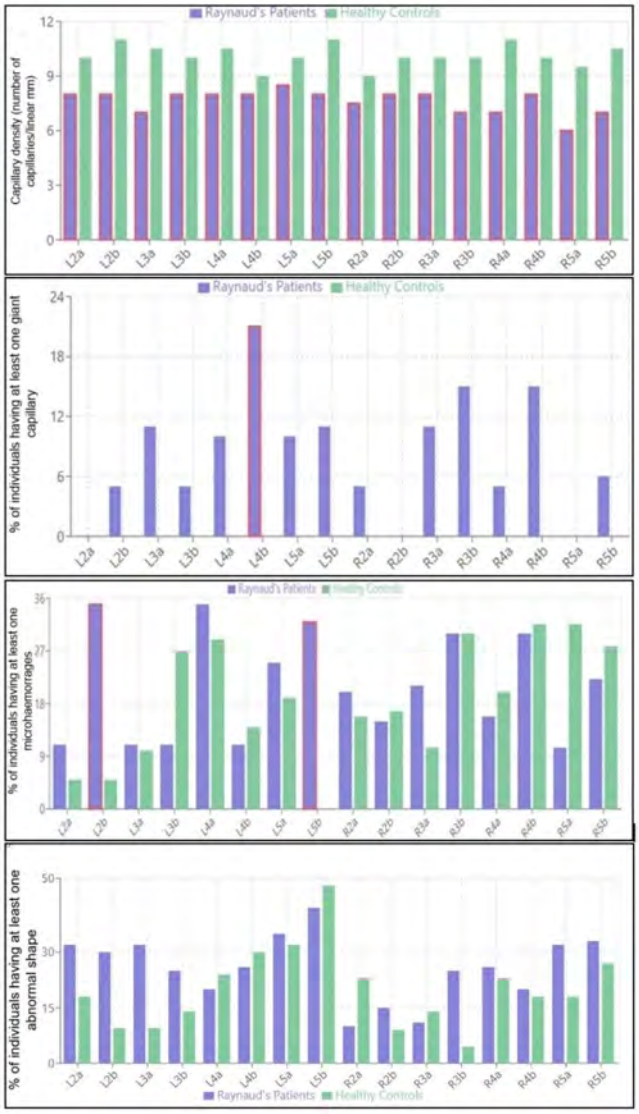


Figure 2. Multi-panel image showing nailfold videocapillaroscopy (NVC) findings in Raynaud's phenomenon (RP) patients (purple bars) vs healthy controls (green bars) at baseline. Significant p-values are graphically reported with the red outlines.

Disclosure: R. Govender: None; **E. Hysa**: None; **R. Campitiello**: None; **S. Wallaert**: None; **M. Vandycke**: None; **E. Gotelli**: None; **T. Du Four**: None; **M. Cutolo**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6.

Abstract Number: 0706

Major salivary glands Ultrasound features in a group of patients with systemic sclerosis: a multicentric study

Roberto D'Alessandro[1], Francois Zimmermann[2], sandrine jousse[3], AURORE BLEUZEN[4], Guillaume Coiffier[5], Jérôme Avouac[6], Alain Lescoat[7] and Yannick Allanore[8], [1]Rheumatology Unit, Cochin Hospital, Paris, France, Paris, France, [2]Internal medicine department, University Hospital of Rennes, Rennes, France, Rennes, France, [3]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [4]Medical Imaging, University Hospital of Tours, Tours, France, Tours, France, [5]Dinan Hospital, Dinan, France, [6]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France, [7]CHU Rennes University Hospital, Rennes, France, [8]Department of Rheumatology, Université Paris Cité UFR de Médecine, Paris, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Ultrasound (US) abnormalities of major salivary glands are frequent in systemic sclerosis (SSc) patients. However, US role is not yet fully understood, and the data available on this topic is limited.

The aim of this study is to evaluate the role of major salivary gland ultrasound (SGUS) in patients with SSc

Methods: We consecutively recruited patients with SSc who were regularly followed in two Rheumatology and Internal Medicine centers in France between 2023 and 2024.

- SGUS was performed with a 4–15 MHz and 4–12.5 MHz linear ultrasound probe, by two operators.

- The parotid and submandibular glands were bilaterally studied and scored on a 0 to 4 scale using the Jousse-Joulin (JJ) score, based on progressive bands and hypoechoic areas.

Table: Features of our Systemic sclerosis patients evaluated

Total: 123 patients		JJ ≥ 2 56 patients (45.5%)	P-value Vs group JJ < 2	FIBROSIS SCORE ≥ 2 45 patients (36.6 %)	P-value vs group FS < 2
General features					
Sex	H 13 (10.6%) F 110 (89.4%)				
Age (years old)	58.5 ± 13.2 DS 22-84	60 ± 12.4	0.252	60.1 ±12.6	0.311
Disease duration (months)	126 ± 107 DS	148 ± 122	**0.044**	157 ± 123	**0.014**
Disease form	Diffuse 33 (26.8%)	14 (42%)	0.675	14 (42%)	0.416
Sicca syndrome	88 (71.5%)	45 (51%)	0.086	34 (39%)	0.578
Schirmer o Salivary flow rate	64/84 (77%)	37 (58%)	**0.044**	20 (31%)	0.389
Minor salivary gland biopsy MSGB	73 (59.3%)				
Pathological MSGB (FS > 1)	35/72 (48,6 %)	23 (65%)	**0.032**	18 (48%)	0.430
Overlap with Sjogren syndrome	29 (23.6%)	21 (72%)	**< 0.001**	14 (48%)	0.230
Organ involvement					
Interstitial lung disease	47 (38.2%)	18 (38%)	0.205	17 (36%)	0.940
Modified Rodnan skin score	5.13 ± 5.53 DS Range 0-28	5.96 ± 5.57	0.127	5.44 ±5.22	0.422
DLCO %	71.6 ± 17.7 SD Range 28-129	71.4 ±14.6	0.371	70 ± 16.7	0.926
CVF %	95.9 ± 20.8 SD Range 5-152	96.6 ±20.6	0.744	94.6 ±16.5	0.611
Articular involvement	17 (35.4%)	9 (53%)	0.102	10 (58%)	0.489
Renal crisis	2 (1.6%)	2 (100%)	0.119	2 (100%)	0.060
Serological profile					
CENP	57 (46.7%)	31 (54%)	0.078	23 (40%)	0.458
SCL-70	36 (29.5%)	14 (39%)	0.315	12 (33%)	0.599
SSA	8 (6.5%)	7 (87,5%)	0.014	5 (62,5%)	0.116
RNA POL 3	7 (5.7%)	1 (14%)	0.084	4 (57%)	0.253
ANTI FIBRILLARINE	4 (3.3%)	2 (50%)	0.855	2 (50%)	0.571
PM-SCL	4 (3.3%)	2 (50%)	0.855	2 (50%)	0.571
FR	11 (23%)	8 (73%)	0.006	8 (73%)	0.119
Hypergammaglobulinemia	12 (25%)	6 (50%)	0.302	7 (58,3%)	0.617

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

- SGUS findings were considered pathological with a JJ score ≥ 2 in at least one gland.

- Hyperechoic bands indicating fibrosis were evaluated with a 0 to 3 scoring system based on the JJ reference atlas.

- A fibrosis score ≥ 2 in at least one gland was considered pathological.

US data was compared to clinical and biochemical data of our patients.

Results: A total of 123 patients were included: 13 men (10.6%) and 110 women (89.4%), with a mean age of 58.5 ± 13.2 years. Thirty-three (26.8%) had diffuse cutaneous SSc. Subjective sicca syndrome was present in 88 patients (71.5%), with objective sicca syndrome in 77% of cases. An overlap with Sjögren's syndrome was diagnosed in 29 patients (23.6%), all of whom had pathological minor salivary gland biopsies (MSGB).

Fifty-six patients (45.5%) had a JJ score ≥ 2, while 45 (36.6%) had a fibrosis score ≥ 2.

- The group of patients presenting with a JJ score ≥ 2, compared to the group JJ < 2, presented significatively more frequently an overlap with Sjögren's syndrome in 21 cases (72%) ($p < 0.001$) with a Pathological MSGB more frequent. Higher prevalence of Objective Sicca syndrome in 58% of cases ($p = 0.044$) along with the Presence of anti-SSA antibodies in 87.5% of cases ($p = 0.014$), and a Longer disease duration ($p = 0.044$). No association was found between a JJ score ≥ 2 and visceral disease involvement.

- On the other side, patient with a Fibrosis score ≥ 2 compared to those with a fibrosis score < 2, presented a longer disease duration ($p = 0.014$).

There was no association between either score and the disease-specific antibodies or visceral involvement, such as cutaneous, pulmonary, articular, or renal involvement.

Conclusion: Ultrasound abnormalities of major salivary glands are common in patients with SSc. A global JJ score ≥ 2 should raise suspicion of an overlapped Sjögren's syndrome. However, while fibrotic lesions are common, they do not appear to be related to the severity of the SSc phenotype.

Disclosure: R. D'Alessandro: None; **F. Zimmermann**: None; **s. jousse**: None; **A. BLEUZEN**: None; **G. Coiffier**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **J. Avouac**: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6; **A. Lescoat**: None; **Y. Allanore**: None.

Abstract Number: 0707

When Can Support Lead to Missed Clinic Appointments in Patients with Systemic Lupus Erythematosus?

Samiha Karim[1], Gaobin Bao[1], Charmayne Dunlop-Thomas[1] and S. Sam Lim[2], [1]Emory University, Atlanta, GA, [2]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Sociodemographic and Clinical Features of Systemic Lupus Erythematosus Patients

Characteristic	Category	Number (total N=222)
Age (Mean ± SD)		47.0 ± 13.5
Disease Duration (Mean ± SD)		15.3 ± 10.6
Gender (SD)	Male	24 (10.8)
	Female	198 (89.2)
Race (SD)	Asian	1 (0.5)
	Black	210 (94.6)
	White	11 (5.0)
Education (Mean ± SD)		13.5 ± 2.8
Work status (SD)	Employed	89 (41)
	Unemployed	106 (44.3
	Retired	26 (12.0)
	Student	6 (2.8)
Marital status (SD)	Not Married	168 (77.1)
	Married/Cohabiting	50 (23)
Insurance (SD)	No Insurance	55 (25.2)
	Private	34 (15.6)
	Medicare	36 (16.5)
	Medicaid	58 (26.6)
	Medicare/Medicaid	35 (16.1)
Disease activity (SLAQ)* (Mean ± SD)		14.1 ± 8.4
Organ damage (SA-BILD)+ (Mean ± SD)	Mean ± SD	4.6 ± 4.3
Organ damage severity (SD)	No damage (BILD=0)	25 (11.3)
	Mild damage (BILD=1-2)	57 (25.7)
	Severe damage (BILD≥3)	140 (63.1)

SD=standard deviation
*Systemic Lupus Activity Questionnaire (SLAQ)
+Self-administrated Brief Index of Lupus Damage (SA-BILD)

Table 2: Logistic Regression with Repeated Measures on Missed Appointments (n=597 appointments)

Factors	Category	Uni-variable		Multi-variable	
		OR (95%)	P value	OR (95%)	P value
Age at appointment	(per 5 years ↓)	**1.12 (1.03-1.21)**	**<0.01**	-	-
Age at SLE diagnosis	(Per 5 years ↓)	1.02 (0.93-1.12)	0.66	-	-
Disease duration at appointment	(Per 5 years ↓)	**1.20 (1.07-1.35)**	**<0.01**	**1.15 (1.02-1.30)**	**0.02**
Education (per 3 years)	(Per 3 years ↑)	**1.21 (1.00-1.46)**	**0.05**		
Gender (ref: female)	(female)	1.12 (0.55-2.30)	0.75		
Race (ref: White)	Black	2.39 (0.53-10.80)	0.26		
	Other	2.38 (0.54-10.60)	0.25		
Marital status (ref: Married)	Never married	1.37 (0.73-2.60)	0.33	0.98 (0.52-1.82)	0.94
	Separated	0.96 (0.41-2.23)	0.93	1.27 (0.72-2.26)	0.41
	Divorced	0.78 (0.32-1.90)	0.59	1.40 (0.71-2.77)	0.33
	Widowed	0.91 (0.25-3.34)	0.89	0.91 (0.38-2.17)	0.83
	Living with partner	1.15 (0.44-3.02)	0.77	0.82 (0.32-2.11)	0.68
Poverty	(Yes)	0.90 (0.60-1.34)	0.60	-	-
Work status (ref: Employed)	Off Workforce	0.92 (0.50-1.70)	0.79	-	-
	Unemployed	1.17 (0.73-1.87)	0.51	-	-
Insurance (ref: Private)	No Insurance	1.06 (0.58-1.92)	0.85	1.09 (0.29-4.09)	0.89
	Public (Medicare/Medicaid)	1.05 (0.61-1.83)	0.85	1.31 (0.47-3.69)	0.61
Disease activity (SLAQ score)	(per 3 points ↑)	1.06 (0.98-1.15)	0.13	1.02 (0.98-1.05)	0.36
Organ damage (BILD score)	(per 1 point ↑)	0.97 (0.92-1.03)	0.33	0.96 (0.90-1.03)	0.23
ER visit	(Yes)	1.53 (0.97-2.41)	0.07	1.20 (0.66-2.19)	0.54
Number of ER visits	(Per 1 visit ↑)	1.04 (0.95-1.15)	0.39	-	-
Hospitalization	(Yes)	**1.66 (1.01-2.72)**	**<0.05**	1.38 (0.71-2.70)	0.34
Number of Hospitalizations	(Per 1 visit ↑)	**1.16 (1.03-1.31)**	**0.02**	-	-
Number of ER visits or Hospitalizations	(Per 1 visit ↑)	1.05 (1.00-1.12)	0.07	-	-
PROMIS Depression (Tscore)	(Per 5 points ↑)	1.07 (0.96-1.18)	0.22	-	-
Perceived Stress Scale 10	(Per 4 points ↑)	1.10 (0.98-1.23)	0.09	1.11 (0.98-1.27)	0.11
PROMIS Fatigue 8a (Tscore)	(Per 5 points ↑)	1.04 (0.93-1.16)	0.50	-	-
PROMIS Emotional support (Tscore)	(Per 5 points ↑)	1.06 (0.95-1.17)	0.32	**1.14 (1.00-1.30)**	**<0.05**
PROMIS Informational support (Tscore)	(Per 5 points ↑)	1.03 (0.93-1.14)	0.58	-	-
PROMIS Instrumental support (Tscore)	(Per 5 points ↑)	0.92 (0.82-1.03)	0.16	-	-
PROMIS Physical health (Tscore)	(Per 5 points ↑)	0.96 (0.83-1.10)	0.55	0.96 (0.80-1.14)	0.62
PROMIS Mental health (Tscore)	(Per 5 points ↑)	0.95 (0.84-1.07)	0.37	-	-

PROMIS T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation of 10. Higher scores represent more of the concept measured. Values indicate the mean.
Poverty – <100% Federal poverty level
ER = emergency room
SLAQ = Systemic Lupus Activity Questionnaire
SA-BILD = Self-administrated Brief Index of Lupus Damage

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: People from underrepresented groups with SLE can face barriers to health care and management, including discrimination and a lack of resources and social and financial support. This can lead to missed appointment visits. Limited data exist on factors that contribute to appointment compliance rates. This study evaluates clinical and non-clinical factors and their association with missed appointments.

Methods: Patients with SLE in the Grady Rheumatology and Lupus Clinics from 2023-2024 who completed a Georgians Organized Against Lupus (GOAL) cohort survey within six months prior to a scheduled appointment were identified as having completed or missed their scheduled appointments. Grady Health System is the only indigent care health system in Atlanta, Georgia, whose patient population is primarily Black and of lower socioeconomic status. The GOAL cohort is a Centers For Disease Control and Prevention (CDC)-supported, population-based cohort of SLE patients followed prospectively through regular surveys with validated instruments. We assessed their demographics, socioeconomic factors, and psychosocial factors that could contribute to their appointment compliance. Univariable logistic regression analysis was conducted using a generalized estimating equation model with repeated measures for each characteristic. Multivariable analyses were then performed to explore the independent effect of important clinical and psychosocial factors.

Results: We identified 222 patients with 597 appointments, of which 447 visits (75%) were completed and 150 were missed (25%). Clinical and sociodemographic characteristics are shown in Table 1. We observed higher emotional support scores in patients who missed their Rheumatology appointment with an OR of 1.14 (1.00-1.30, p-value < 0.05). Additionally, patients who missed their appointments were younger (OR of 1.12, [1.03-1.21, p-value < 0.01]) and had less years of disease duration (OR of 1.15 [1.02-1.30], p-value 0.02).

Conclusion: Our study found an unexpected association between higher levels of emotional support and missed appointments. Some studies have suggested improved outcomes in patients with chronic disease in those with higher levels of emotional support from not only their family/friends but also their healthcare providers. Although healthcare providers can play a crucial role as a surrogate for emotional support in patients with chronic diseases by providing counseling, open communication, and resources for support groups, we hypothesize that some patients with sufficient social support may lack this additional motivation and be at higher risk for missed appointments. It is also notable that, apart from shorter disease duration, no other clinical or socioeconomic factor in our model was associated with missed appointments.

Disclosure: S. Karim: None; **G. Bao**: None; **C. Dunlop-Thomas**: None; **S. Lim**: Accordant, 2, AstraZeneca, 2, Biogen, 5, BMS, 5, Genentech, 2, Gilead, 5, GSK, 2, Novartis, 5, UCB, 5.

Abstract Number: 0708

Association of Choroidal Sub-foveal Thickness with Skin Manifestations and Serum Monocyte HDL Ratio in Patients with Systemic Sclerosis-a Case Control Study

Tejaswini Ramineni[1], Vijaya prasanna Parimi[2], Radhika M[3] and Narsimulu Gumdal[3], [1]Esic Medical College And Hospital, Sanathnagar, Hyderabad, Telangana, India, [2]ESIC Medical College and Super Specilaity Hospital, hyderabad, Telangana, India, [3]ESIC MEDICAL COLLEGE AND HOSPITAL, Hyderabad, Telangana, India

SESSION INFORMATION

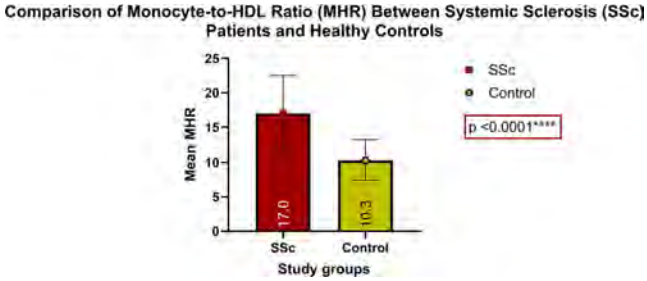
Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparison of Monocyte-to-HDL Ratio Between Systemic Sclerosis Patients and Healthy Controls

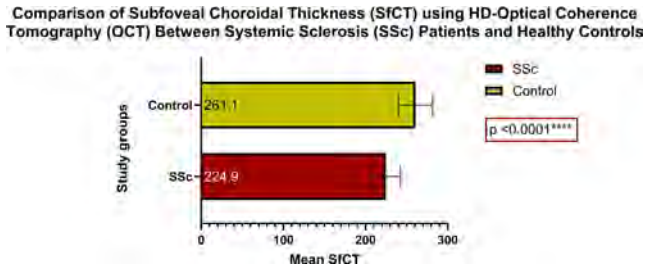
Background/Purpose: The vascular hypothesis in systemic sclerosis (SSc) posits that vasculopathy is the initial inciting event that triggers inflammation and subsequent fibrosis in the progression of the disease. The primary objective of this study was to evaluate the association of serum MHR with skin manifestations, including Raynaud's phenomenon (assessed via the Raynaud's Condition Score), digital ulcers (measured by the Digital Ulcer Score), and skin fibrosis (evaluated using the Modified Rodnan Skin Score) in patients with SSc. The secondary objectives included assessing choroidal subfoveal thickness in SSc patients and investigating the associations between choroidal thickness, MHR, and skin manifestations.

Methods: After obtaining approval from the Institutional Ethics Committee (IEC), this case-control study was conducted at ESIC Medical College and Hospital in Telangana, India. A total of 35 adult patients with systemic sclerosis and 35 age- and gender-matched healthy controls were recruited, all of whom met the inclusion criteria. Serum monocyte-to-HDL cholesterol ratio (MHR) was calculated and compared between the two groups. High-definition optical coherence tomography (HD-OCT) was used to measure choroidal subfoveal thickness, and these measurements were also compared between the groups. Correlations between serum MHR values, choroidal subfoveal thickness and skin manifestations among systemic sclerosis patients were analyzed. Statistical analysis was performed using SPSS Version 21, with significance set at $p< 0.05$.

Results: In our study, both groups consisted of 35 individuals, with 30 females in each group. The mean age was 37.6 years in systemic sclerosis patients and 38.9 years in healthy controls. The mean MHR was significantly higher in patients with systemic sclerosis compared to healthy controls ($p< 0.05$). Choroidal subfoveal thickness was significantly lower in patients than in controls ($p< 0.05$).

While MHR values showed a positive correlation with markers of peripheral microvascular involvement—such as the Raynaud's Condition Score (RCS), Digital Ulcer Score (DUS), and skin fibrosis assessed by the Modified Rodnan Skin Score (MRSS)—statistical significance was not achieved. Choroidal subfoveal thickness exhibited a negative correlation with all skin parameters asessed.

Conclusion: The findings from this study support the use of non-invasive techniques, such as high-definition optical coherence tomography (HD-OCT), for evaluating choroidal microvasculature in patients with systemic sclerosis, even at early stages of the disease. Additionally, the study suggests that the monocyte-to-HDL cholesterol ratio (MHR) may serve as a simple, cost- effective, and easily measurable serum biomarker. MHR could help identify SSc patients at higher risk for vasculopathy, including digital ulcers and more advanced skin fibrosis.



Comparison of Choroidal Sub-foveal Thickness using HD-OCT Between Systemic Sclerosis Patients and Healthy Controls

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

As an indirect marker of oxidative stress and inflammation, MHR showed a correlation with changes in choroidal microvasculature. Therefore, combining MHR with choroidal vascular evaluation provides valuable adjunctive diagnostic support for assessing overall microcirculation in patients with systemic sclerosis.

Disclosure: T. Ramineni: None; **V. Parimi**: None; **R. M**: None; **N. Gumdal**: None.

Abstract Number: 0709

Systemic Sclerosis Inducible Pluripotential Stem Cells Reprogrammed into Endothelial Cells Identify Vascular Permeability May Not Be Cytokine Driven

Tracy Frech[1], Venkateswara Gogulamudi[2], Denisse Moreno[2], Eric Austin[1], Charles Frech[3], Anna Hemnes[1], Tania Ruiz[1], Alex Shahin[1], Megha Talati[1], Colin Maguire[4] and Anthony Donato[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Salt Lake Veterans Affairs Medical Center, Salt Lake City, UT, [3]Vanderbilt University, Nashville, TN, [4]University of Utah, Salt Lake City, UT

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I

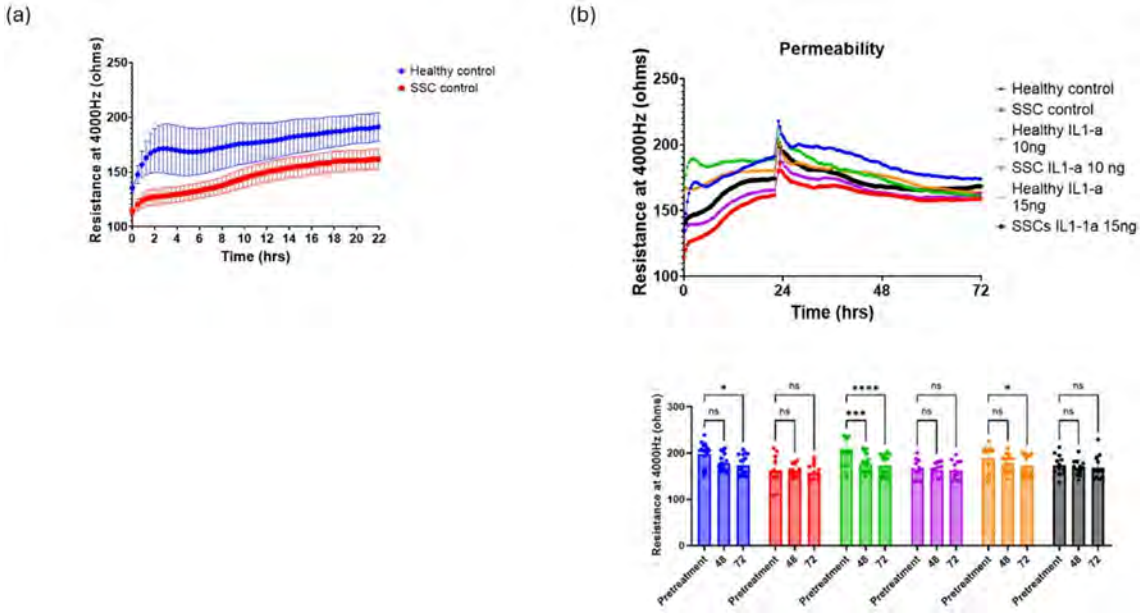
Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

SSc Patient Characteristics	Attempted reprogramming (n=22)	Successful Reprogramming (n=13)
Age (years), Mean (SD)	57 (11)	53 (8)
Sex: Female	20 (90%)	11 (85%)
Race:		
• **White**	18 (82%)	11 (85%)
• **Black**	4 (18%)	1 (7%)
• **Asian**	0	0
• **Other**	1 (4%)	1 (4%)
Disease duration (years) for non-Raynaud's (SD)	18 (16)	23 (14)
Cutaneous Subset		
• Limited	17 (77%)	11 (85%)
• Diffuse	5 (23%)	2 (15%)
ANA positive	22 (100%)	13 (100%)
Autoantibody Subset		
• Centromere	9 (41%)	8 (62%)
• RNA polymerase III	4 (18%)	2 (15%)
• Topoisomerase	1 (5%)	1 (8%)
• PM-SCL	1 (5%)	1 (8%)
Echocardiogram Features:		
• Elevated RVSP	16 (72%)	11 (84%)
• Regional wall motion abnormality	3 (3%)	1 (8%)
• LVEF < 50%	1 (4%)	0
• LV diastolic dysfunction	2 (9%)	1 (8%)
• Pericardial effusion	0	0
Immunosuppression	22 (100%)	13 (100%)
Vasodilators	22 (100%)	13 (100%)
Vasculopathy Clinical Features	22 (100%)	13 (100%)
• Digital Ulcers	6 (29%)	3 (23%)
• Gastric Antral Vascular Ectasia	1 (4%)	0
• Pulmonary Arterial Hypertension	9 (40%)	9 (69%)
• Scleroderma Renal Crisis	1 (4%)	0
• Myocardial inflammation on Cardiac MRI	1 (4%)	1 (8%)
• Abnormal Capillaroscopy		
○ Early	0	0
○ Active	14 (63%)	11 (85%)
○ Late	8 (36%)	3 (23%)
• Abnormal Sublingual Videomicroscopy Perfused Barrier Region (PBR)	22 (100%)	13 (100%)

Systemic Sclerosis Registry Patients with an Abnormal Echocardiogram Referred to the Cardio-Rheum Clinic or Pulmonary Arterial Hypertension Clinic

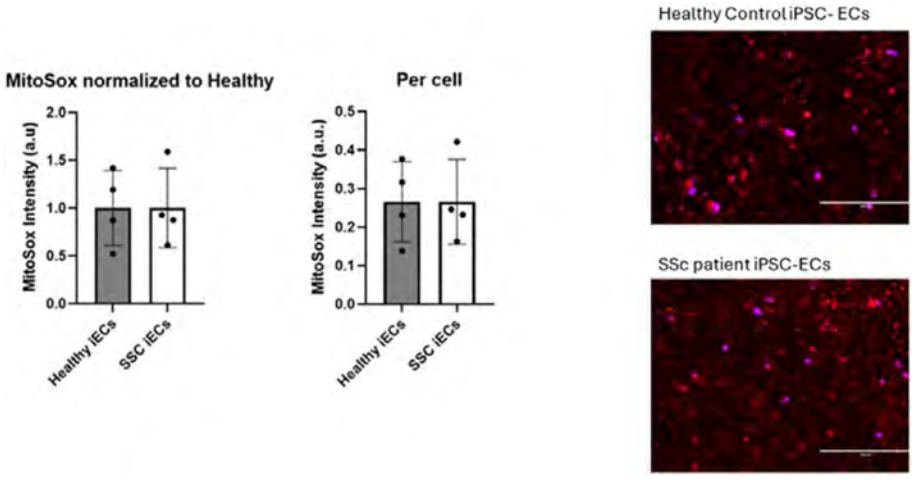
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Measure of permeability in inducible pluripotential stem cells (iPSC) generated from healthy controls (HC) and systemic sclerosis (SSC) and cultured on the electric cell-substrate impedance sensing (ECIS) platform at baseline (a) and in response to interleukin-(IL) 1 alpha 10ng and 15 ng over 72 hours (b)

Background/Purpose: Systemic sclerosis (SSc) disease models that faithfully recapitulate endothelial mediated vasculopathy are critical for testing and developing novel treatments. The generation of inducible pluripotential stem cells (IPSC) from SSc patients' serum and the ability to develop those into patient specific endothelial cells (EC) allows for vasculopathy analysis. The objective of this study was to examine iPSC-EC-barrier function at baseline and in response to an inflammatory cytokine interleukin 1 (IL-1α), which may have a cardinal role in SSc cardiopulmonary dysfunction and tissue fibrosis.

Methods: SSc patients with an abnormal echocardiogram and age-and sex matched healthy controls (HC) were consented at a two SSc Centers. Peripheral blood monocytes cells (PBMC) were collected at the time of a routine care visit and clinical features were recorded. PBMC were differentiated into iPSC-EC at the Cell Therapy and Regenerative Medicine Program (CellReGen™) at the University of Utah, which adheres to quality control metrics including specimen karyotyping. Measures of mitochondrial superoxide using MitoSox in SSc-IPSC-ECs and HC were determined by the intensity of protein expression as observed through immunofluorescence. We cultured the reprogrammed cells on electric cell-substrate impedance sensing (ECIS) to provide a platform to properly study vascular barrier function. Baseline impedance and response to IL-1α was measured.



Measures of mitochondrial superoxide in reprogrammed SSc-iPSC-EC (n=13) when compared to HC (n=9).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: IPSC-EC reprogramming was attempted in 22 SSc registry patients with abnormal echocardiograms. Thirteen of 22 individual SSc cell lines were successfully reprogrammed. The SSc clinical features are shown in Table 1. For these 13 SSc patients, 9 age- and sex-matched HC samples were selected and successfully reprogrammed. Samples that did not have PBMC isolation in less than 12 hours of collection failed to reprogram. There was no significant difference in clinical features of the SSc patients that reprogrammed successfully. Under baseline conditions, IPSC-EC from SSc patients had ~20% reduced EC resistance (enhanced endothelial permeability) compared to healthy controls over the length of the experiment (Figure 1a). The treatment effect of EC with IL-1α demonstrated that there was a significant decrease in endothelial resistance (higher permeability) response to IL-1α in the HC patients, but IL-1α had no influence on SSc endothelial resistance (Figure 1b). There were no differences in Mitosox between SSc and HC patient EC (Figure 2), suggesting the baseline permeability differences in the SSc EC were not due to mitochondrial ROS.

Conclusion: In this largest to date study of SSc-IPSC-EC, we identified increased baseline permeability in SSc compared to HC. While HC had a typical IL-α increase in permeability, SSc lacked this typical physiological response. We found that despite some alterations in EC phenotype, mitochondrial ROS were similar in SSc and HC ECs. Our data suggests that genetic or epigenetic changes were preserved in SSc patient IPSCs as a patient vascular phenotype was recapitulated in cells developed into EC. IPSC-EC generated from PBMCs hold high potential in elucidating the role of vascular endothelium in the pathogenesis of SSc.

Disclosure: T. Frech: None; **V. Gogulamudi**: None; **D. Moreno**: None; **E. Austin**: None; **C. Frech**: None; **A. Hemnes**: None; **T. Ruiz**: None; **A. Shahin**: None; **M. Talati**: None; **C. Maguire**: None; **A. Donato**: None.

Abstract Number: 0710

Vascular Events in Systemic Sclerosis Patients with Anti-Phospholipid Antibodies

Vivian Shing[1], Emily Thompson[2], Emma Terwilliger[3], Simran Ravindra Nimal[4], Alejandro Diaz Arumir Vergara[2], Michael Pham[4] and Vivek Nagaraja[4], [1]Mayo Clinic Alix School of Medicine, Scottsdale, AZ, [2]Mayo Clinic, Scottsdale, [3]Mayo Clinic Alix School of Medicine, Scottsdale, [4]Mayo Clinic, Scottsdale, AZ

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0671–0710) Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: APS is a pro-thrombotic autoimmune condition often associated with other systemic autoimmune rheumatic diseases (SARDs), most notably SLE. The link between aPL positivity and other SARDs is less understood. Specific to systemic sclerosis (SSc), the occurrence of thrombotic events is variable in aPL-positive SSc patients as per prior studies. The objective of this retrospective study is to compare the prevalence of vascular manifestations in a cohort of aPL-positive SSc patients to aPL-negative SSc patients in a North American cohort.

Methods: The electronic medical record was reviewed for eligible patients through a copyrighted data capture tool. All patients had SSc diagnosed by a rheumatologist. A total of 365 patients who were tested for at least one aPL were identified. Patients were categorized as aPL-positive patients if they had positive serologies for at least one aPL (aCL IgG/IgM, anti-beta-2-glycoprotein 1 IgG/IgM, or LA) (n=178), and as aPL-negative patients were included if they had been tested for at least one aPL and were found to be negative (n=187). Positive serologies were based on the Mayo Clinic Laboratories—at least 15 aCL or anti-beta-2-glycoprotein 1 units, or a positive LA profile interpretation. Outcomes of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	aPL Negative (N=103)	aPL Positive (N=178)
Sex assigned at birth, n (%)		
Female	90 (87.4%)	155 (87.1%)
Male	13 (12.6%)	23 (12.9%)
Ethnicity, n (%)		
Hispanic or Latino	9 (8.7%)	17 (9.6%)
American Indian or Alaskan Native	0 (0.0%)	7 (3.9%)
Asian	2 (1.9%)	2 (1.1%)
Black or African American	5 (4.9%)	9 (5.1%)
White	83 (80.6%)	141 (79.2%)
Unreported/Other	4 (4.3%)	2 (1.1%)
Age at diagnosis		
Mean (SD)	47.4 (16.08)	50.2 (16.74)
Scleroderma subtype, n (%)		
Limited Cutaneous	63 (61.2%)	114 (64.0%)
Diffuse Cutaneous	8 (7.8%)	17 (9.6%)
Sine Scleroderma	8 (7.8%)	10 (5.6%)
Unknown	10 (9.7%)	14 (7.9%)
Mixed Connective Tissue Disease	14 (13.6%)	23 (12.9%)

Baseline Characteristics of Patients in Primary Analysis

	aPL Negative (N=103)	aPL Positive (N=178)	Regression Adjusted for Age and Sex p-value
Diagnosed with Raynaud's phenomenon (Yes), n (%)	98/101 (97.0%)	172 (96.6%)	>0.9
History of digital ulcers (Yes), n (%)	46 (44.7%)	83 (46.6%)	0.5
History of digital amputations (Yes), n (%)	8 (7.8%)	25 (14.0%)	0.13
Pulmonary arterial hypertension/pulmonary hypertension (Yes), n (%)	25 (24.3%)	50 (28.1%)	0.5
History of PE/DVT (Yes), n (%)	24 (23.3%)	45 (25.3%)	0.9
Unprovoked PE/DVT (Yes), n (%)	11/24 (45.8%)	34/45 (75.6%)	0.007
History of heart failure (Yes), n (%)	20 (19.4%)	38 (21.3%)	0.9
History of renal crisis (Yes), n (%)	3 (2.9%)	7 (3.9%)	>0.90
History of Gastric Antral Vascular Ectasia (Evidence by endoscopy or biopsy)? (Yes), n (%)	3 (2.9%)	11 (6.4%)	0.2
History of ischemic stroke (Yes), n (%)	7 (6.8%)	21 (11.8%)	0.14
History of miscarriage* (Yes), n (%)	20/46 (43.5%)	30/89 (33.7%)	0.3

*patients who were not assessed for history of miscarriage were excluded

Primary Analysis of aPL Negative vs. aPL Positive Patients

interest included: history of pulmonary embolism (PE) or deep venous thrombosis (DVT), pulmonary arterial hypertension (PAH), stroke, digital ulcers, and miscarriage. In the primary analysis, vascular outcomes were compared between the aPL-positive group (n= 178) and the aPL-negative patients who had been tested for all three aPLs (n=103). In the secondary analysis, outcomes were compared between positive and negative patients for each specific aPL.

Results: In the primary analysis, there were significantly more unprovoked PE/DVTs (75.8% vs. 45.6%) in the aPL-positive group (p=0.007, Table 2). No significant differences were found in the history of digital ulcers, PAH, renal crisis, heart failure, miscarriage, or ischemic stroke. In the secondary analysis, patients testing positive for aCL IgG/IgM had significantly greater prevalence of unprovoked PE/DVTs (p=0.037). Patients positive for anti-beta-2-glycoprotein 1 IgG/IgM had significantly greater prevalence of digital amputations (p=0.013). In LA-positive patients, mean total lung capacity (TLC) as measured by PFT was decreased (p=0.006), and mean pulmonary capillary wedge pressure (PCWP) as measured by RHC was increased (p=0.022).

aPL	Outcome	N (both positive and negative patients)	Coefficient^ (adjusted for age and sex)	p-value
Anti-cardiolipin IgG/IgM	Unprovoked DVT/PE	72	3.19	0.037
Beta-2-glycoprotein 1 IgG/IgM	Digital amputation	243	3.09	0.013
	Ischemic stroke	243	2.45	0.065
Lupus anticoagulant	TLC	118	-17	0.006
	PCWP	57	4.3	0.022

^linear/median regression coefficient for continuous outcomes, odds ratio for binary outcomes

Sensitivity Analysis of Outcomes Between Positive and Negative Patients for Specific Antibodies

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In our retrospective cohort of SSc patients, those with positive aPLs had a stronger association with unprovoked PE/DVTs. Furthermore, there were suggestions of association with specific vascular events in the presence of certain aPLs: aCLs with unprovoked PE/DVTs, anti-beta-2-glycoprotein-1 with more severe Raynaud's disease manifestations, and LA with reduced TLC (pertinent to interstitial lung disease) and increased PCWP (pertinent to pulmonary hypertension). These findings need to be evaluated prospectively and in other cohorts.

Disclosure: V. Shing: None; **E. Thompson**: None; **E. Terwilliger**: None; **S. Nimal**: None; **A. Diaz Arumir Vergara**: None; **M. Pham**: None; **V. Nagaraja**: None.

Abstract Number: 0711

Analytical Performance of a Novel, Fully Automated Multiplexed Microarray Immunoassay Prototype for the Simultaneous Detection of Autoantibodies to GBM, PR3, and MPO: A Multicenter Evaluation

Natalia Swierczynska[1], Ruaridh Armour[1], Anthony Yau[1], Enn Rusi[1], Mark Hooper[1], Jason Sillitoe[2], Caroline Wilson[2], Paula Griffiths[3], Tariq El-Shanawany[3], Faye Sims[4], **Gerber Gomez**[5], Christian Fischer[5], Michael Hausmann[6] and Helen Laird[1], [1]Research & Development, AliveDx, Edinburgh, Scotland, United Kingdom, [2]North East Innovation Lab, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, England, United Kingdom, [3]Immunology Department, Laboratory Medicine, Swansea Bay University Health Board, UK. Cardiff and Vale UHB, Swansea, Wales, United Kingdom, [4]Clinical Biochemistry and Immunology Department Peterborough City Hospital, North West Anglia NHS Foundation Trust, Peterborough, England, United Kingdom, [5]Scientific & Medical Affairs, AliveDx Suisse SA, Eysins, Switzerland, [6]AliveDx Suisse SA, Eysins, Switzerland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-neutrophil cytoplasmic antibodies (ANCA), including those directed to myeloperoxidase (MPO) and proteinase 3 (PR3) as well as antibodies against anti-glomerular basement membrane (anti-GBM) are critical markers in the diagnosis of small vessel vasculitides and anti-GBM disease, respectively. While some multiplex platforms are available, conventional testing often involves sequential single-analyte assays, which may delay diagnosis and increase workload. There remains a clinical need for fully automated multiplexed assays capable of simultaneously detecting these key markers. This multicenter study evaluated the analytical performance of a novel, fully automated multiplexed microarray immunoassay prototype (MosaiQ AiPlex® VAS microarray; AliveDx, Switzerland), designed for the simultaneous detection of IgG autoantibodies to PR3, MPO, and GBM, in comparison with routine singleplex and multiplex methods.

Methods: The study was conducted at four sites in the United Kingdom, including three public reference laboratories (two located in England and one in Wales) and a sponsor's site in Scotland. Comparator methods varied by site and included fluorescence enzyme immunoassay (FEIA), addressable laser bead immunoassay (ALBIA) and chemiluminescent immunoassay (CLIA). De-identified, banked serum samples previously characterized as reactive or non-reactive for PR3, MPO or GBM antibodies were tested using the investigational microarray prototype on its proprietary automated platform. Analytical performance was assessed by calculating positive percent agreement (PPA), negative percent agreement (NPA) and overall percent agreement (OPA) both in comparison to each site's routine method and in aggregate across all sites and platforms. One site using CLIA did not have anti-GBM reactive samples available for testing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Agreement of the investigational microarray prototype with comparators

Site	Site 1 (Peterborough)			Site 2 (Newcastle)			Site 3 (Swansea)			Site 4 (Edinburgh)			All sites		
Method	FEIA			ALBIA			CLIA			ALBIA			All methods		
Measurand	anti-PR3	anti-MPO	anti-GBM	anti-PR3	anti-MPO	anti-GBM	anti-PR3	anti-MPO	anti-GBM	anti-PR3	anti-MPO	anti-GBM	anti-PR3	anti-MPO	anti-GBM
Reactive results (n)	11	15	2	32	37	5	52	40	NA	35	36	16	130	128	23
PPA (%)	90.9	93.3	100	87.5	89.2	100	82.7	77.5	NA	97.1	100	100	88.5	89.1	100
95% CI	62.3-99.5	70.2-99.7	17.8-100	71.9-95.0	75.3-95.7	56.6-100	70.3-90.6	62.5-87.7	NA	85.1-99.9	90.3-100	79.4-100	81.6-93.3	82.4-93.9	85.2-100
Non-reactive results (n)	143	143	43	92	87	57	178	190	41	107	121	96	520	541	237
NPA (%)	95.1	95.1	100	95.7	95.4	96.5	95.5	95.3	100	100	99.2	100	96.4	96.1	99.2
95% CI	90.2-97.6	90.2-97.6	91.8-100	89.4-98.3	88.7-98.2	88.1-99.4	91.4-97.7	91.2-97.5	91.4, 100	96.6-100	95.3-100	96.2-100	94.5-97.8	94.0-97.6	96.9-99.9
OPA (%)	94.8	94.9	100	93.6	93.6	96.8	92.6	92.2	100*	99.3	99.4	100	94.8	94.8	99.2

ALBIA: addressable laser bead immunoassay, CI: confidence interval, CLIA: chemiluminescent immunoassay, FEIA: fluorescent enzyme immunoassay, NA: not applicable, NPA: negative percent agreement, OPA: overall percent agreement, PPA: positive percent agreement. *Limited to NPA (due to lack of anti-GBM reactive samples)

Results: The investigational microarray prototype consistently demonstrated high NPA across all measurands and comparator methods, ranging from 95.1% (anti-PR3 and anti-MPO, FEIA) to 100% (anti-PR3 at 1 ALBIA site and anti-GBM with FEIA, CLIA and at 1 ALBIA site). Overall NPA was 96.4% for anti-PR3 (95% CI: 94.5, 97.8), 96.1% for anti-MPO (95% CI: 94.0, 97.6) and 99.2% for anti-GBM (95% CI: 96.9, 99.9).

PPA ranged from 77.5% (anti-MPO, CLIA) to 100% (anti-GBM across methods). Overall PPA across sites and methods was 88.5% for anti-PR3 (95% CI: 81.6, 93.3), 89.1% for anti-MPO (95% CI: 82.4, 93.9) and 100% for anti-GBM (95% CI: 85.2, 100).

OPA across sites and methods ranged from 94.8% to 99.2%. Detailed results are summarized in **Table 1**.

Conclusion: In this multicenter study, the investigational microarray prototype showed high concordance with routine singleplex and multiplex methods for the detection of anti-PR3, anti-MPO, and anti-GBM autoantibodies. These findings support the potential utility of the assay as a single-platform solution for streamlined, simultaneous serologic evaluation of ANCA-associated vasculitis and anti-GBM disease. Future studies incorporating clinically characterized samples will enable expanded assessment of the assay's diagnostic performance.

Disclosure: N. Swierczynska: AliveDx, 3; **R. Armour**: AliveDx, 3; **A. Yau**: AliveDx, 3; **E. Rusi**: AliveDx, 3; **M. Hooper**: AliveDx, 3; **J. Sillitoe**: None; **C. Wilson**: None; **P. Griffiths**: None; **T. El-Shanawany**: None; **F. Sims**: None; **G. Gomez**: AliveDx, 3; **C. Fischer**: AliveDx, 3; **M. Hausmann**: AliveDx, 3; **H. Laird**: AliveDx, 3.

Abstract Number: 0712

Effects of Bacterial Secretome on Nasal Epithelial Cell Gene Expression in ANCA-Associated Vasculitis

A. Nikolai von Krusenstiern[1], Eleni Bouziani[2], Sokratis Apostolidis[2], Li Hui Tan[2], Swetha Rajagopal[3], Nicholas Bolden[2], Paul J. Planet[3], Dylan Curry[3], Elliot Friedman[3], Noam A. Cohen[4] and Rennie Rhee[2], [1]Hospital of the University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Children's Hospital of Philadelphia, Philadelphia, PA, [4]University of Pennsylvania, Philadelphia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The nasal microbiome has been implicated as a contributor to relapse in ANCA-associated vasculitis (AAV). Previous research on nasal bacteria, particularly *Staphylococcus aureus*, has focused on interactions with circulating immune cells and mediators in the blood. However, alterations in the antibacterial responses of nasal epithelial cells, an understudied cell population in AAV, and their contribution to systemic relapse in AAV are still poorly understood. The aim of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

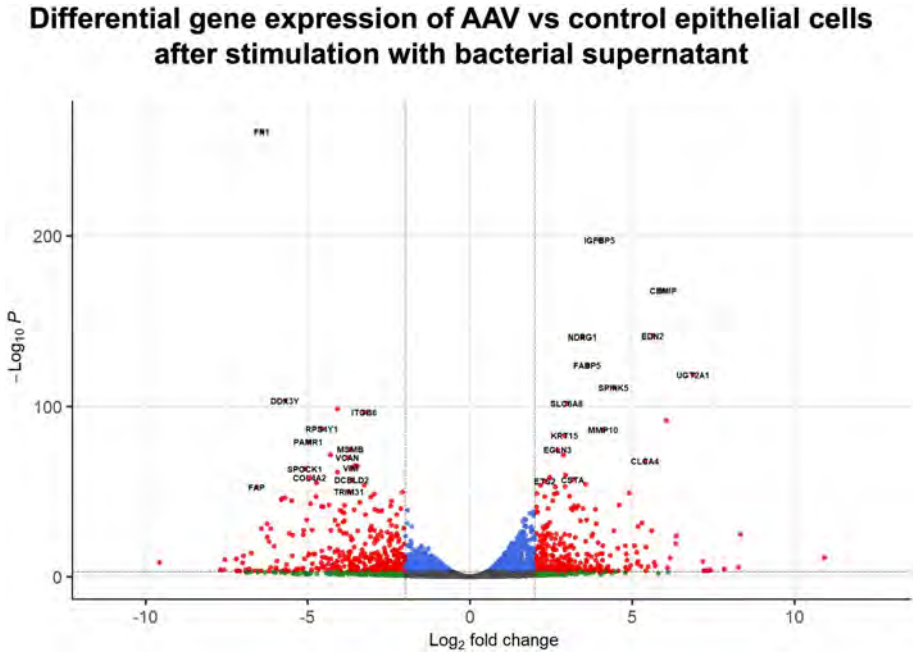


Figure 1. Transcriptional changes after bacterial challenge of primary human nasal epithelial cell cultures of ANCA-associated vasculitis vs healthy controls. Volcano plot showing log2FC on the x-axis and -log10(adjusted p-value) on y-axis. Genes meeting significance (FDR $P < 0.001$ and $|\log2FC| > 2$) are highlighted in red and labeled.

this study is to compare the effects of bacterial secreted proteins (secretome) on primary human nasal epithelial cells (HNECs) derived from patients with AAV versus healthy controls.

Methods: Primary HNECs from 3 patients with AAV and 3 healthy controls were cultured at air-liquid interface, which mimics air-facing nasal epithelium. Patients with AAV met 2022 ACR-EULAR classification criteria for granulomatosis with polyangiitis. Bacterial cell-free supernatant was obtained from a co-culture of two bacterial strains (*S. aureus* and *Corynebacterium tuberculostearicum*) isolated from a nasal swab of a patient with relapsing AAV; these two strains were selected based on a previous study of the nasal microbiome in AAV. HNECs were stimulated with the bacterial supernatants and then harvested for RNA sequencing to evaluate for differential changes in gene expression using FDR-corrected $P < 0.001$.

Results: RNA-seq of HNECs stimulated with bacterial supernatant revealed differences in transcriptional response between AAV and controls (**Figure 1**). Increased expression of genes related to angiogenesis, extracellular matrix modification, and cell cycle pathways were observed in AAV vs controls. Intracellular pathways upregulated in AAV included Wnt signaling, MAPK, and PI3K-Akt signaling, indicating a heightened activation state. Genes related to neutrophil biology were upregulated in AAV vs control including *PADI2*, *LTF*, and *CD177*. Down-regulated transcripts included pathways related to immune signaling, complement and coagulation cascade, extracellular matrix receptor interaction and adhesion, and mucin and barrier function, indicating an attenuated barrier repair and innate immune program upon bacterial challenge in AAV.

Conclusion: Nasal epithelial cell cultures derived from patients with AAV display an altered transcriptional response to bacterial secretome. Specifically, impaired host defenses, including barrier function and innate immune responses, were observed. These findings suggest antibacterial responses are significantly altered in the nasal epithelium of patients with AAV. Mechanistic studies are needed to elucidate the role of these changes in relapsing AAV, which eventually may identify novel targets for treatment or prevention of disease flares.

Disclosure: A. von Krusenstiern: None; **E. Bouziani**: None; **S. Apostolidis**: None; **L. Tan**: None; **S. Rajagopal**: None; **N. Bolden**: None; **P. Planet**: None; **D. Curry**: None; **E. Friedman**: None; **N. Cohen**: None; **R. Rhee**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0713

Differentiating Primary Anti-Neutrophil Cytoplasmic Antibody (ANCA) Associated Vasculitis from Secondary Forms

Adil Vural[1], Chao Zhang[2], Yaseen Kinanah[1], Cassandra Calabrese[3] and Adam Brown[4], [1]Cleveland Clinic, Cleveland, OH, [2]Cleveland Clinic, Cleveland Heights, OH, [3]Cleveland Clinic Foundation, Cleveland Heights, OH, [4]Cleveland Clinic, Shaker Heights, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA associated vasculitis (AAV) is a severe autoimmune disorder with substantial morbidity and mortality. Establishing the diagnosis might be challenging due to the existence of noteworthy mimickers, most notably infective endocarditis (IE) and drug-induced AAV. We aimed to identify differences in initial labs, serologies, clinical manifestations, and histopathology findings with the goal recognizing diagnostic clues that can raise suspicion for a secondary process.

Methods: A retrospective chart review was conducted on patients with glomerulonephritis (GN) secondary to IE, drug-induced AAV and primary AAV, from January 1, 2008, to January 1, 2024. Patients were filtered using SNOMED clinical terms of vasculitis and GN and any positive ANCA test. GN diagnosis was established either histologically or clinically by elevated creatinine and new onset hematuria with active urinary sediment. IE diagnosis was established by modified Duke Criteria or positive PCR on removed valve. Primary and drug induced AAV diagnosis were established by vasculitis specialist. Blood counts, and serologies were collected prior to any treatment including glucocorticoids. Statistical analysis included the use of Kruskal-Wallis test for continuous variables and Chi-square test for categorical variables.

Table 1. Summary of study population characteristics and clinical presentation.

Table 1. Summary of study population characteristics and clinical presentation.

Variable	Infective Endocarditis Related Glomerulonephritis n=42	Drug induced ANCA vasculitis n=35	Primary ANCA vasculitis n=50
Age at time of diagnosis, Median [25th;75th]	58.4 [49.0;67.2]	70.7 [62.2;75.8]	59.1 [50.0;69.4]
Sex, N (%)			
Male	33 (78.6%)	18 (51.4%)	25 (50%)
Female	9 (21.4%)	17 (48.5%)	25 (50%)
Race, N (%)			
Caucasian	42 (100%)	22 (62.8%)	45 (90%)
African American	0 (0%)	11 (31.4%)	0 (0%)
Hispanic	0 (0%)	3 (8.5%)	2 (4%)
Comorbidities, N (%)			
Hypertension	19 (45.2%)	34 (97.1%)	12 (24%)
Chronic kidney disease	14 (33.3%)	16 (45.7%)	4 (8%)
Diabetes	6 (14.3%)	8 (22.8%)	7 (14%)
Underlying cardiac valvular disease	21 (50%)	N/A	N/A
Exposure to Hydralazine, N (%)	N/A	34 (97.1%)	N/A
Microorganism, N (%)			
Bartonella	22 (52.4%)	N/A	N/A
Streptococcus mitis	3 (7.1%)	N/A	N/A
Streptococcus mutans	3 (7.1%)	N/A	N/A
Clinical presentation, N (%)			
Constitutional symptoms	18 (42.9%)	6 (17.1%)	23 (46%)
Hypoxia	4 (9.5%)	16 (45.7%)	25 (50%)
Diffuse alveolar hemorrhage	0 (0%)	6 (17.1%)	11 (22%)
Stroke	6 (14.2%)	0 (0%)	2 (4%)
Biopsy proven leukocytoclastic vasculitis	6 (14.2%)	3 (8.5 %)	9 (18%)
Rise in creatinine more than 30%	42 (100%)	35 (100%)	50 (100%)
Documented dysmorphic RBC or RBC cast	26 (61.9%)	24 (66.7%)	38 (76%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Laboratory values and serologies..

Table 2. Laboratory values and serologies.

Variable	Infective Endocarditis Related Glomerulonephritis n=42	Drug induced ANCA vasculitis n=35	Primary ANCA vasculitis n=50	p value
Complete blood count components				
Leukopenia, N (%)	18 (42.8%)	17 (48.5%)	1 (2%)	<0.001[a]
Normal leukocyte count, N (%)	19 (45.2%)	18 (51.5%)	9 (18%)	<0.001[a]
Leukocytosis, N (%)	5 (11.9%)	0 (0%)	40 (80%)	<0.001
Thrombocytopenia, N (%)	38 (90.4%)	13 (37.1%)	1 (2%)	<0.001
Normal thrombocyte count, N (%)	4 (9.6%)	21 (60%)	15 (30%)	<0.001
Thrombocytosis, N (%)	0 (0%)	1 (2.86%)	34 (68%)	<0.001[a]
Leukocyte count k/uL, Median [25th;75th]	5.4 [3.18; 8.78]	4.0 [3.35; 5.49]	13 [10.4; 15.6]	<0.001[a]
Neutrophil count k/uL, Median [25th;75th]	3.7 [2.02; 6.18]	3.07 [2.40;4.85]	10.0 [7.00;13.0]	<0.001[a]
Lymphocyte count k/uL, Median [25th;75th]	0.92 [0.50;1.34]	0.70 [0.38;0.86]	1.20 [1.00;2.00]	<0.001
Thrombocyte count k/uL, Median [25th;75th]	101 [74.2;140]	200 [123;239]	411 [266;523]	<0.001
Serology, N/available (%)				
Anti-nuclear antigen	16/41 (39%)	35/35 (100%)	11/50 (22%)	0.001[b]
Rheumatoid factor	16/25 (64%)	8/23 (34.8%)	13/35 (37.1%)	0.041[a,b,c]
Double stranded DNA	7/17 (41.2%)	23/23 (100%)	0/36 (0%)	<0.001[a]
Cryoglobulins	21/29 (72.4%)	12/25 (48%)	6/25 (24%)	0.002[a,c]
Anti-histone	1/3 (33.3%)	33/33 (100%)	N/A	<0.001[b]
ANCA, N/available (%)				
c-ANCA	23 (54.8%)	3 (8.5%)	32 (64%)	<0.001[b]
p-ANCA	11 (26.2%)	35 (100%)	21 (42%)	<0.001[b]
Proteinase-3	17 (40.5%)	12 (34.2%)	29 (58%)	0.199
Myeloperoxidase	3 (7.1%)	34 (97.1%)	21 (42%)	<0.001
Concordance between IF and antigen	17 (40.5%)	21 (60%)	47 (94%)	<0.001[a]
Complements, N (%)				
Low C3	30 (71.4%)	25 (71.4%)	3 (6%)	<0.001[a]
Low C4	21 (50%)	19 (54.2%)	8 (16%)	<0.001[a]
Either low C3 or C4	32 (76.2%)	28 (80%)	11 (22%)	<0.001[a]

p-value represents overall value between all groups. [a] p > 0.05 (IE-GN vs. drug-AAV), [b] p > 0.05 (IE-GN vs. primary AAV), [c] p > 0.05 (drug-AAV vs. primary AAV).

Results: Baseline characteristics are outlined in Table 1. There were 42 patients with IE related GN, 35 with drug-induced AAV, and 50 with primary AAV. Median age at diagnosis was 58.4, 70.7, and 59.1 years, respectively. Bartonella was the most common microorganism (52.4%) in the IE-related GN group, and almost all drug-induced AAV cases (97%) were linked to hydralazine.

Baseline labs and serologies are detailed in Table 2. Initial blood counts showed that IE-related GN and drug-induced AAV patients commonly presented with leukopenia (42.8% and 48.5%, respectively) and thrombocytopenia (90.4% and 37.1%, respectively) and seldomly presented with thrombocytosis (0% and 2.8%, respectively). Primary AAV patients frequently presented with leukocytosis (80%) and thrombocytosis (68%), and rarely with leukopenia (2%) and thrombocytopenia (2%). Median initial leukocyte, neutrophil, lymphocyte, and platelet counts were higher in primary AAV compared to other groups ($p < 0.001$). Hypocomplementemia was found in 76.2% of IE-related GN and 80% of drug-induced AAV cases, compared to 22% in primary AAV ($p < 0.001$).

Table 3. Renal biopsy findings and outcomes.

Table 3. Renal biopsy findings and outcomes.

	Infective Endocarditis Related Glomerulonephritis n=42	Drug induced ANCA vasculitis n=35	Primary ANCA vasculitis n=50	p value
Renal biopsy findings, N/available (%)				
Pauci-immune glomerulonephritis	9/20 (45%)	28/28 (100%)	45/45 (100%)	<0.001[c]
Immune complex mediated glomerulonephritis	11/20 (55%)	0/28 (0%)	0/45 (0%)	<0.001[c]
Immunofluorescence findings, N/available (%)				
Positive IgM	13/20 (65%)	7/28(25%)	0/45 (0%)	<0.001[a]
Positive C3	15/20 (75%)	10/28 (35.7%)	2/45 (4.4%)	<0.001
Positive C1q	9/20 (45%)	6/28 (21.4%)	0/45 (0%)	<0.001[b]
Positive IgA	2/20 (10%)	3/28 (10.7%)	0/45 (0%)	0.19
Positive IgG	2/20 (10%)	6/28 (21.4%)	0/45 (0%)	0.001[a,b]
Induction treatment, (N%)				
Cyclophosphamide	N/A	10 (28.5%)	15 (30%)	
Rituximab	N/A	19 (54.2%)	35 (70%)	
Plasma exchange	N/A	3 (8.5%)	7 (14%)	
Renal outcomes, N (%)				
Dialysis during the treatment course	13 (31%)	16 (45.7%)	8 (16%)	0.001[a]
Dialysis cessation at 6 months	4/13 (30.7%)	3/16 (18.7%)	6/8 (75%)	<0.001[b]
Complete renal recovery	13 (30.9%)	7 (20%)	19 (38%)	0.417
Mortality within 6 months, (N%)	8 (19%)	12 (34.2%)	1 (2%)	<0.001[b]

p-value represents overall value between all groups. [a] p > 0.05 (IE-GN vs. drug-AAV), [b] p > 0.05 (IE-GN vs. primary AAV), [c] p > 0.05 (drug-AAV vs. primary AAV).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Majority of patients underwent renal biopsy (Table 3). C3 was the most common immunofluorescence staining in IE-related GN and drug-induced AAV. Dialysis cessation at 6 months occurred in 75% of primary AAV patients, whereas 30.7% of IE related GN patients, and 18.7% of drug-induced AAV patients (p< 0.001). Six-month mortality was significantly higher in IE related GN and drug induced AAV compared to primary AAV (p< 0.001).

Conclusion: The presence of cytopenia including leukopenia and thrombocytopenia, along with low complement levels upon presentation of IE related GN and drug-induced AAV can help clinicians to discern from primary AAV. Early recognition of these mimickers is critical, as they are associated with lower rates of renal recovery and higher six-month mortality.

Disclosure: A. Vural: None; **C. Zhang**: None; **Y. Kinanah**: None; **C. Calabrese**: Eli Lilly, 2, Invivyd, 2, 6, sanofi, 2, 6; **A. Brown**: AbbVie/Abbott, 2, Amgen, 2, Sanofi, 2.

Abstract Number: 0714

Factors Associated With Depression And Anxiety In ANCA-Associated Vasculitis Patients: Data From The Almenara Vasculitis Cohort

Alvaro Oyarce-Calderon[1], Allison Figueroa-Sánchez[2], Leonor León-Yaurimucha[2], Rocío Gamboa-Cárdenas[3], Zoila Rodríguez-Bellido[4], Risto Perich-Campos[5], Graciela Alarcon[6], Manuel Ugarte-Gil[7] and Victor Pimentel-Quiroz[8], [1]Hospital Nacional Guillermo Almenara Irigoyen, San Miguel, Lima, Peru, [2]Universidad Científica del Sur, Lima, Peru, [3]Universidad Científica del Sur, Lima, Peru, [4]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, Lima, Peru, [5]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [6]The University of Alabama at Birmingham, Oakland, CA, [7]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [8]Universidad Científica del Sur, San Isidro, Peru

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Depression and anxiety symptoms have been reported in 28% of patients suffering from vasculitides. However, in patients with ANCA-associated vasculitis (AAV), their frequency and their associated factors remain to be identified at global level. The aim of this study is to determine the factors associated with depression and anxiety in AAV patients from a Latin American cohort.

Methods: Patients from a single-center Peruvian AAV cohort [the Almenara Vasculitis cohort] were included. Depression symptoms were assessed by the Patient Health Questionnaire-9 (PHQ-9) questionnaire whereas anxiety symptoms were assessed by the Generalized Anxiety Disorder-7 (GAD-7) questionnaire. For both questionnaires, the higher the score, the greater the intensity of the corresponding symptoms: GAD-7 ranges from 0 to 21 while PHQ-9 ranges from 0 to 27. Potential associated factors were sex, age, ethnicity, educational level, relationship status, employment and socioeconomic status (SES), disease activity, erythrocyte sedimentation rate level, C-reactive protein level, ANCA status, glucocorticoid use and doses, immunosuppressive (IS) use and type, diagnosis and the AAV-Patient reported outcome (PRO) questionnaire domains. Cross-sectional univariable and multivariable linear regression models were performed. The multivariable models were done using a backward selection procedure with an alpha to stay in the model of 0.05.

Results: Eighty-eight patients were included; 49 (69%) were female and their mean age at diagnosis was 61.4 (13) years. The GAD-7 and the PHQ-9 scores at baseline were 6.3 (4.3) and 7.2 (4.9), respectively. In multivariable analysis, middle SES, active disease, and the social and emotional impact domain of the AAV-PRO were negatively associated with anxious

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Factors associated with depression symptoms as assessed by the PHQ-9 questionnaire.

	Multivariable model	
Variable*	ß (SE)	*p* value
Socioeconomic status		
High	Ref.	
Middle	1.74 (1.14)	0.125
Low	2.73 (1.29)	0.033
Disease state		
Remission	Ref.	
Active	2.93 (1.16)	0.011
Relapse	3.38 (1.24)	0.007
AAV-PRO		
Organ-Specific Symptoms	0.05 (0.23)	0.025
Systemic Symptoms		
Treatment Side Effects		
Social and Emotional Impact	0.07 (0.03)	0.018
Concerns about the future		
Physical function		

*All variables were assessed at a single visit. SE=standard error.
AAV-PRO: AAV-Patient reported outcome. Ref: Reference

symptoms. On the other hand, low SES, relapsing and active disease, and organ-specific symptoms and the social and emotional impact domains of the AAV-PRO were negatively associated with depressive symptoms.

Conclusion: A middle-low SES, relapsing and active disease, and some domains from the AAV-PRO (social and emotional impact, organ-specific symptoms) were associated with higher intensity of anxiety and depression symptoms. Further studies are needed to evaluate these findings in other populations and seek better strategies to improve depression and anxiety symptoms in AAV patients.

Table 2: Factors associated with anxiety symptoms as assessed by the GAD-7 questionnaire.

	Multivariable model	
Variable*	ß (SE)	*p* value
Socioeconomic status		
High	Ref.	
Middle	2.92 (0.99)	0.003
Low	1.51 (1.12)	0.179
Disease state		
Remission	Ref.	
Active	2.74 (0.99)	0.005
Relapse	1.89 (1.08)	0.081
AAV-PRO		
Organ-Specific Symptoms		
Systemic Symptoms		
Treatment Side Effects		
Social and Emotional Impact	0.09 (0.02)	<0.001
Concerns about the future		
Physical function		

*All variables were assessed at a single visit. SE=standard error.
AAV-PRO: AAV-Patient reported outcome. Ref: Reference

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Oyarce-Calderon: None; **A. Figueroa-Sánchez**: None; **L. León-Yaurimucha**: None; **R. Gamboa-Cárdenas**: None; **Z. Rodríguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcon**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6.

Abstract Number: 0715

Supervised machine learning algorithm to identify patients with eosinophilic granulomatosis with polyangiitis in France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Identifying patients with eosinophilic granulomatosis with polyangiitis (EGPA) in claims databases such as the French National Health Data System (SNDS) is a major challenge for real-world studies. Although a specific ICD-10 diagnosis code (M301) exists, patient identification may be incomplete because i) the disease does not always require hospitalisation and ii) long-term disease (LTD) is mostly recorded under the broader code M30, which includes other vasculitis. This study aims to develop and evaluate a machine learning algorithm to identify EGPA patients in the SNDS.

Methods: Adults (>18) with a hospitalization M301 or an LTD M30/M300/M301/M302/M303/M308 in 2010-2019 were extracted from the SNDS. Among them, patients were identified as (1) EGPA with a M301 code and without any M300/M302/M303/M308/M317 code or (2) non-EGPA with a M300/M302/M303/M308 LTD or a M30 LTD with a M300/M302/M303/M308/M317 hospitalization, and without any M301 code, and were included in the labeled data used for model training and testing. Unlabeled patients were constituted of all other patients. Potential clinically relevant variables to predict EGPA diagnosis and differentiate it from other vasculitis were defined with experts and included medical visits, treatments, comorbidities and hospitalizations. Variables were pre-selected using univariate and multivariate analysis. Several supervised machine learning techniques were then implemented. For each combination, a 4-fold cross-validation method was implemented and repeated 100 times. Average metrics (accuracy, sensitivity, specificity, and precision) were calculated. As a final step, the model with the highest precision and sensitivity score was chosen among the 5 final models and the model was tested on the EGPA patients from French Vasculitis Study Group (FVSG) registry linked to the SNDS.

Results: On 8,756 individuals with a M301 hospitalization or an LTD M30/M300/M301/M302/M303/M308 in 2010-2019, 2,243 (25.6%) were labeled EGPA and 1,223 (14.0%) were labeled non-EGPA, and 5,290 were unlabeled patients.

Thirteen variables were selected and included in the supervised models, with the most significant predictive factors being glucocorticoids use, asthma and pneumologist visits. All the five supervised models resulted in good performance [metric (min-max): precision (0.79-0.82); sensitivity (0.79-0.81); specificity (0.71-0.77); accuracy (0.80-0.83)].

The model finally chosen was a random forest model which, when applied to the 5,290 unlabeled patients, identified 1,930 EGPA patients, with a precision of 0.82, a sensitivity of 0.81, a specificity of 0.75 and an accuracy of 0.83. The estimated prevalence and incidence of EGPA in France was 47.5 and 2.8 per million inhabitants, respectively, in 2019. Out of 49 incident EGPA patients from the FVSG registry, all but one (98%) were predicted as EGPA, confirming the robustness of the model.

Conclusion: This machine learning-based approach shows promising results for identifying adults with EGPA using SNDS data. The algorithm developed could serve as a valuable tool for real-world study based on comprehensive database.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: B. Terrier: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **S. Tauty**: None; **A. Salhi**: None; **F. Bugnard**: None; **S. Benard**: None; **V. Cottin**: AbbVie, 2, AstraZeneca, 2, Avalyn, 2, Boehringer Ingelheim, 2, 6, 12, Support for attending meetings and medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb/Celgene, 2, CSL (Behring/Vifor), 2, Ferrer/United Therapeutics, 2, 6, FibroGen, 12, Adjudication committee, GlaxoSmithKleine, 1, 2, Gossamer, 2, Liquidia, 2, Molecure, 1, Pliant, 2, PureTech, 2, Roche, 2, 6, Roivant, 2, Sanofi, 2, 6, 12, Support for attending meetings, Shionogi, 2; **C. Taillé**: None; **X. Puéchal**: Roche, 5.

Abstract Number: 0716

Utility of Follow-Up Cardiac Magnetic Resonance Imaging In Patients With Eosinophilic Granulomatosis With Polyangiitis

Chelsea Cheng[1], Justine Lafleur-Careau[2], Navneet Kang[1], Medha Soowamber[3] and Christian Pagnoux[3], [1]Mount Sinai Hospital, Toronto, Canada, [2]Mount Sinai Hospital, Saint-Augustin-de-Desmaures, Canada, [3]Mount Sinai Hospital, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare multisystem disorder characterized by asthma, rhinitis, peripheral blood eosinophilia, and necrotizing vasculitis of small vessels. Cardiac involvement occurs in approximately 10-30% of patients with EGPA and has been identified as a major predictor of mortality. Cardiac manifestations can be diagnosed clinically, as well as through electrocardiogram and echocardiogram. Cardiac magnetic resonance (CMRI) has higher sensitivity to detect cardiac involvement, especially late gadolinium enhancement (LGE), which can indicate myocardial inflammation and/or fibrosis. However, the exact role of CMRI at diagnosis and the utility of repeat CMRI to monitor evolution of cardiac manifestations in EGPA remain unclear. Our aim was to report on the use and findings of CMRI in our EGPA patient cohort, determine the added value of repeat CMRI, and evaluate the outcome and prognostic value of persistent LGE.

Methods: In this monocentric retrospective descriptive cohort study, we included 75 patients diagnosed with EGPA who were seen at least twice between 2015 and January 2023, of which 30 patients had undergone CMRI, with 11 patients undergoing repeat CMRI during follow-up. All patients satisfied the 2022 ACR/EULAR Classification Criteria for EGPA.

Results: 75 patients (male 56%, mean age at diagnosis 46 years, 2022 ACR/EULAR score range 6-13) seen at least twice in the clinic between 2015 and January 2023 were included. Antineutrophil cytoplasmic antibody (ANCA) was positive in 29 patients (39%), with 22 (39%) being anti-myeloperoxidase antibody (anti-MPO) positive and 4 (5%) being perinuclear ANCA (p-ANCA) positive. 17 (23%) had cardiac symptoms, such as chest pain, orthopnea, and syncope. 30 patients underwent CMRI, 9 (30%) of whom had cardiac symptoms. 11 underwent one or more repeat CMRI. All 30 patients (100%) were treated with glucocorticoids, with 13 (43%) also receiving cyclophosphamide. 11/11 patients who underwent repeat CMRI had LGE on first CMRI, 10/11 had persistent LGE on second CMRI, 4/4 had LGE on third CMRI, and 2/2 had LGE on fourth CMRI. The average time between first CMRI and second CMRI was 22 months (range 4-81 months). Of the 30 patients, 3 (10%) had cardiovascular events at follow-up, 2 of whom had atrial fibrillation (neither had LGE on their CMRIs), and 1 of whom had coronary artery disease requiring stenting (with LGE on his 4 CMRIs).

Conclusion: The role of initial and further serial CMRIs to study and monitor cardiac involvement in EGPA remains unclear. Late gadolinium enhancement most often persists despite treatment, with no major differences in adverse cardiac outcomes in this cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Cheng: None; **J. Lafleur-Careau**: None; **N. Kang**: None; **M. Soowamber**: AbbVie/Abbott, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 6; **C. Pagnoux**: AstraZeneca, 1, ChemoCentryx, 1, GlaxoSmithKlein(GSK), 1, 5, InflaRx GmbH, 1, otsuka, 1, 5, Pfizer, 1, 5, Roche, 1, 5.

Abstract Number: 0717

Circulating Bacterial sRNAs are Altered in Patients with Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis

Christopher Xavier[1], Kevin Byram[2], Carol Langford[3] and Michelle Ormseth[4], [1]Meharry Medical College, Nashville, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Cleveland Clinic, Moreland Hills, OH, [4]Vanderbilt University Medical Center, Nashville

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis (AAV) is an autoimmune disease causing small vessel inflammation. Underlying mechanisms of disease are unclear, but the human microbiota may be a contributor. One way that bacteria can affect the immune system is through small RNAs (sRNAs), which are found abundantly in human circulation. The purpose of this study is to determine if circulating bacterial sRNAs are altered in patients with AAV compared to those with and without other inflammatory autoimmune diseases.

Methods: Patients with AAV were recruited from Vanderbilt University Medical Center (VUMC) and Cleveland Clinic. Participants with other inflammatory diseases (rheumatoid arthritis [RA] and systemic lupus erythematosus [SLE], termed here as "inflammatory control") and control participants were recruited from VUMC. Total RNA was extracted from plasma from all participants and libraries were constructed for next-generation sequencing. sRNAs not aligning to the human genome with up to one mismatch were aligned to bacterial genomes in RefSeq using the TIGER pipeline. sRNA sequences and sRNA counts of bacterial taxa were compared using DESeq2 and the Benjamini-Hochberg method to adjust for multiple comparisons with false discovery rate at 5%.

Results: The study included 31 AAV, 20 inflammatory control (2 RA,18 SLE) and 4 control participants (Table 1). Examining sRNA counts of bacterial taxa, sRNAs aligning to 79 orders (which is the most specific taxonomy to which sRNAs can be assigned with confidence due to the short length and conserved sequences) were altered in AAV versus control and inflammatory control participants (Figure 1). Over half of the orders came from the phyla Pseudomonadota and Actinomycetota. Examining the sRNA sequences, 23 bacterial sRNAs were altered after multiple comparison adjustment in AAV versus control and inflammatory control participants (Figure 2). Of the 23 sequences, 21 were aligned to the phylum Pseudomonadota and all were either tRNA-derived RNAs (tDR) or ribosomal RNA-derived RNAs (rDRs). Among the altered sRNAs were 4 sRNAs with the same base sequence of GGGGCUGUAGCUCAGCUGGGA (thus having the same regulatory seed region, GGGCUGU). These sRNAs were predicted to downregulate key genes involved in T-cell activation and inflammatory processes, including ICOS/ICOSL, CTLA4, NFATC2, CASP3.

Conclusion: The plasma bacterial sRNA composition is altered in patients with AAV compared to control and inflammatory control participants, and the majority of altered sRNAs were from the phylum Pseudomonadota. Among altered bacterial sRNAs were several with a similar base sequence which was predicted to downregulate multiple genes that dappen immune responses, particularly via T cells. Thus, these sRNAs could promote autoimmune inflammation. Future mechanistic studies will be needed to confirm these findings.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Participant demographics

Table. Participant demographics			
	AAV (N=31)	Control (N=4)	Inflammatory control (N=20)
Age, years	66 [56,71]	62 [59.75,66.5]	36 [25.75,44.5]
Race, # (%) Caucasian	29 (94)	4 (100)	13 (65)
Sex, # (%) female	16 (52)	1(25)	16 (80)
Disease duration, years	2 [0.5, 4]	-	-
ESR, mm/h	10 [5, 16]	-	-
CRP, mg/l	0.4 [0.125, 0.675]	-	-
Creatinine (mg/dL)	1.22 [1.06,1.465]	-	-
eGFR (mL/min/1.73 m^2)	43 [34,56]	-	-
Corticosteroid use, # (%)	10 (48)	0 (0)	7 (41)
Trimethoprim-sulfamethoxazole (low dose) use, # (%) current	9 (43)	-	-
Methotrexate use, # (%) current	3 (14)	0 (0)	0 (0)
Azathioprine use, # (%) current	2 (10)	0 (0)	2 (12)
Rituximab use, # (%) current	13 (62)	0 (0)	0 (0)
Vascular damage index, units	1 [1, 3.25]	-	-
BVAS3, units	0 [0,1]	-	-
Anti-PR3 positive, #(%)	10 (50)	-	-
Anti-MPO positive, #(%)	6 (30)	-	-

Laboratory measurements within 30 days. Abbreviation: ESR, erythrocyte sedimentation rate; hsCRP, high-sensitivity C-reactive protein; BVAS, Birmingham Vasculitis Activity Score 3; anti-PR3= proteinase 3 antibody; anti-MPO= myeloperoxidase antibody. Data presented as median [interquartile range] or # number (%). Missing data: disease duration (10 AAV), ESR (12 AAV), CRP (13 AAV), Creatinine(12 AAV), eGFR (16 AAV), corticosteroid use (10 AAV, 3 control, 3 inflammatory control), trimethoprim-sulfamethoxazole use(10 AAV), methotrexate use (10 AAV, 3 control, 3 inflammatory), azathioprine use (10 AAV, 3 control, 3 inflammatory), rituximab use (10 AAV, 3 control, 3 inflammatory), Vascular damage index (11 AAV), BVAS (12 AAV), MPO-ANCA (11 AAV), PR3-ANCA (11 AAV)

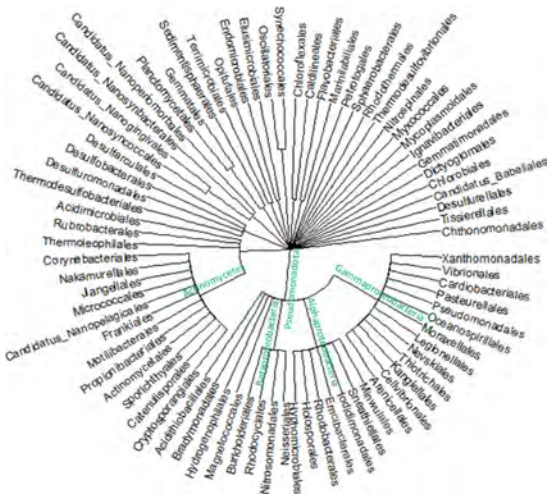


Figure 1: Cladogram representing significantly altered phylum, class, and order level taxonomy of sRNA counts. Those order-level taxa counts with significant alteration (adjusted P value <0.05) in both AAV versus control and versus inflammatory control participants were included.

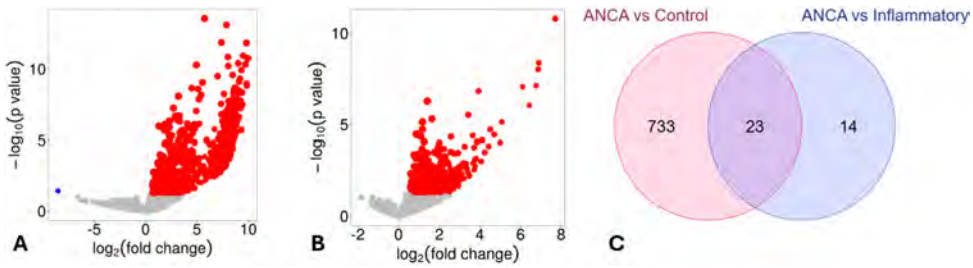


Figure 2: Volcano plots of altered plasma bacterial sRNAs in (A) AAV versus control and (B) AAV versus inflammatory control participants. Dots indicate one sRNA sequence with colored dots being those with a fold difference >1.5 and unadjusted p value <0.05. (C) Venn diagram illustrating specific and common sRNA sequences altered in AAV versus controls and versus inflammatory controls after multiple comparison adjustment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Xavier: None; **K. Byram**: None; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **M. Ormseth**: None.

Abstract Number: 0718

Incidence of Venous Thromboembolism in Patients with ANCA-Associated Vasculitides – a Nationwide Registry-Based Study from Sweden

Hanna Lindberg[1], Klytaimnistra Voudouri[1], Lars Lindhagen[1], Maria K Svensson[2], Ann Knight[1] and Johanna Dahlqvist[3], [1]Uppsala University, Uppsala, Sweden, [2]Uppsala University, Uppsala, [3]Uppsala University Hospital, Uppsala, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV) are rare yet severe autoimmune diseases. Previous studies have indicated that patients with AAV have an increased risk of venous thromboembolism (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE). However, it remains unclear whether the risk is increased equally in granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), and across both sexes. Therefore, the aim of this study was to assess the risk and timing of VTE events in men and women with GPA and MPA, respectively.

Methods: In a nationwide case-control study, all patients >18 years old with incident GPA or MPA between January 1, 2005, and December 31, 2020, where identified from the National Patient Registers (NPRs) in Sweden. For each patient, five population controls matched for sex and age were selected from the Statistics Sweden Register of Total Population. Primary outcomes were DVT and PE following av AAV diagnosis, identified in the NPRs using ICD codes. Hazard ratios (HRs) of the primary outcomes were calculated using Cox models stratified for AAV subtype and sex, with complete follow-up time or censored after one year and 90 days follow-up post AAV diagnosis, respectively.

Results: In total, 4317 patients (3159 with GPA and 1158 with MPA and 21582 population controls were included in the study. There was no significant difference in risk of VTE between patients with GPA and MPA. Both GPA and MPA were associated with a more than three-fold increased risk of DVT and PE during the entire follow-up time, compared to population controls. This risk was increased to more than 11-fold when follow-up time was censored after one year and more than 20-fold when censored after 90 days (HR (95% confidence interval); HR 21.30 (10.67-42.52)) and PE (HR 22.84 (13.04-40.02)). In sex-stratified analyses, men with GPA and MPA, respectively, exhibited a more than four-fold increased risk of DVT (HR 4.15 (3.07-5.61); 3.49 (2.01-6.06)) and PE (HR 4.68 (3.61-6.06); HR 4.01 (2.47-6.51)). Similarly, women with GPA and MPA, respectively, showed a more than three-fold increased risk of DVT (HR 3.22 (2.28-4.55); HR 4.51 (2.56-7.92)) and PE (HR 3.24 (2.43-4.31); HR 3.54 (2.30- 5.45)). Adjusting for kidney disease had only modest effects on HRs across all comparisons.

Conclusion: Both patients with GPA and MPA exhibit an increased risk of DVT and PE following diagnosis of AAV. Our study did not reveal any significant sex differences in VTE among patients with AAV. This study highlights the importance of being aware of the risk for thromboembolic events, in particular during the first year following an AAV diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Lindberg: None; **K. Voudouri**: None; **L. Lindhagen**: None; **M. K Svensson**: Amgen, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, CSL Vifor Pharma, 6, GlaxoSmithKlein(GSK), 6, NovoNordisk, 6; **A. Knight**: None; **J. Dahlqvist**: CSL Vifor, 6.

Abstract Number: 0719

A Combined Transcriptomics and Proteomics Approach to Identify Immune Signatures in ANCA-Associated Glomerulonephritis

Ivana Stojkic[1], Arnon Arazi[2], Huijuan Song[3], Pearlly Yan[3], Estela Puchulu-Campanella[3], Hubao Wang[3], Lynn Fussner[3], Brad Rovin[4], Stacy Ardoin[1] and Salem Almaani[3], [1]Nationwide Children's Hospital, Columbus, OH, [2]The Feinstein Institutes for Medical Research, Manhasset, [3]OSU, Columbus, OH, [4]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA-associated vasculitis frequently involves the kidneys causing glomerulonephritis (AAGN). Despite advances in treatment, many patients develop end-stage kidney disease. An improved understanding of the immune drivers of AAGN has the potential to improve treatment outcomes. To achieve that goal, we utilized a combined transcriptomics/compartmental proteomics approach to identify the major immune pathways driving AAGN.

Transcriptomic Cohort (23 patients)		Proteomic Cohort (10 patients)
Age at biopsy, median (IQR)	58 (41-68)	58 (41-67)
% female	57% (13/23)	40% (4/10)
% white	96% (22/23)	90% (9/10)
Newly diagnosed	91% (21/23)	100% (10/10)
ANCA ELISA*		
anti-PR3	43% (10/22)	40% (4/10)
anti-MPO	43% (10/22)	50% (5/10)
both positive	5% (1/22)	0% (0/10)
negative	5% (1/22)	10% (1/10)
ANCA IIF		
c-ANCA	52% (12/23)	50% (5/10)
p-ANCA	30% (7/23)	30% (3/10)
Negative **	17% (4/23)	20% (2/10)
Phenotype		
GPA	52% (12/23)	60% (6/10)
MPA	35% (8/23)	30% (3/10)
EGPA	13% (3/23)	10% (1/10)
Serum Creatinine, average +/- SD	3.5 +/- 2.9	3.6 +/- 2.9

* not available in one patient

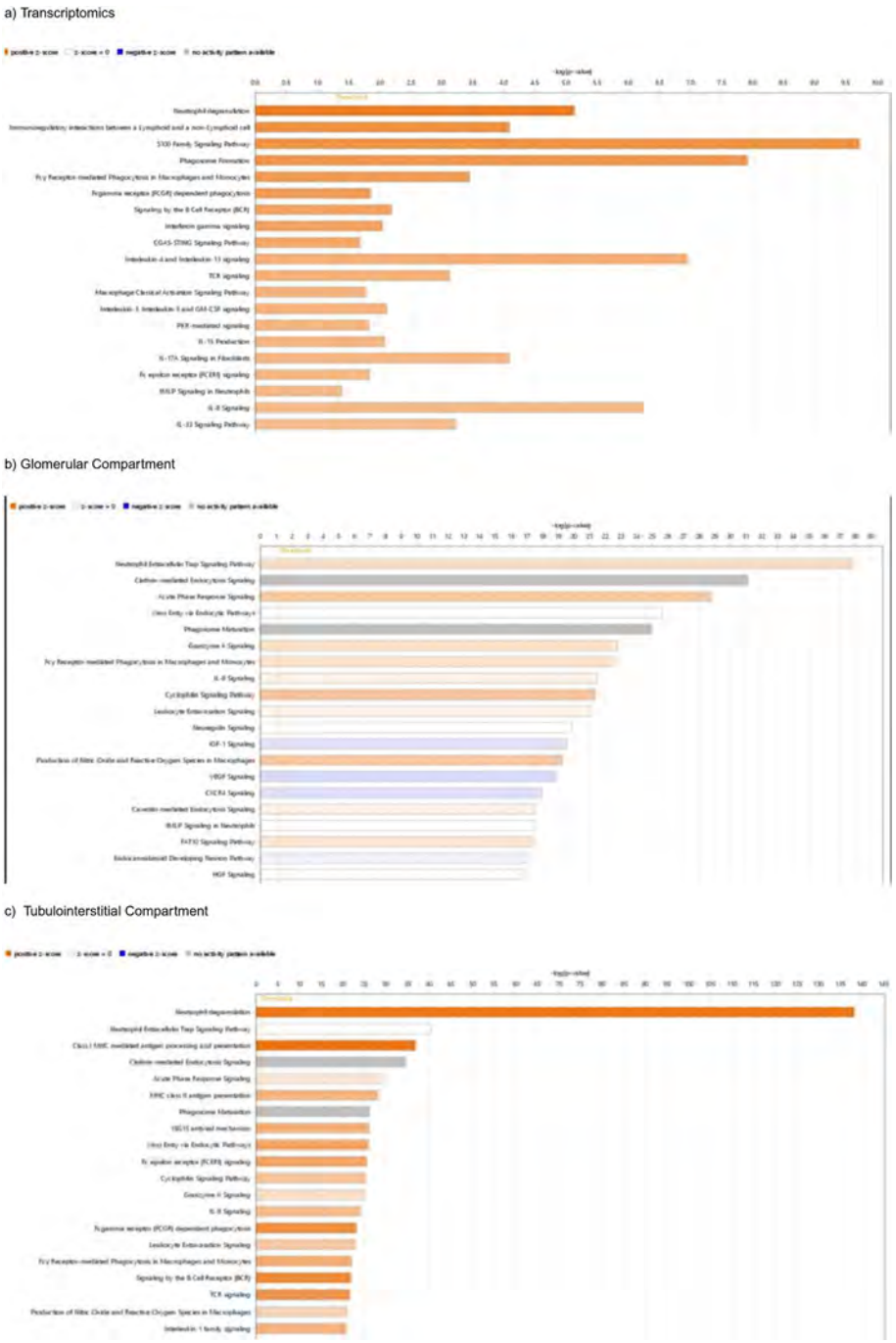
** all hed detectable ANCAs by ELISA

Abbreviations: ANCA: antineutrophil cytoplasmic antibodies

PR3: proteinase 3; MPO: myeloperoxidase; c-ANCA: cytoplasmic ANCA ; p-ANCA: perinuclear ANCA; GPA: granulomatosis with polyangiitis; MPA: Microscopic polyangiitis; EGPA: Eosinophilic granulomatosis with polyangiitis

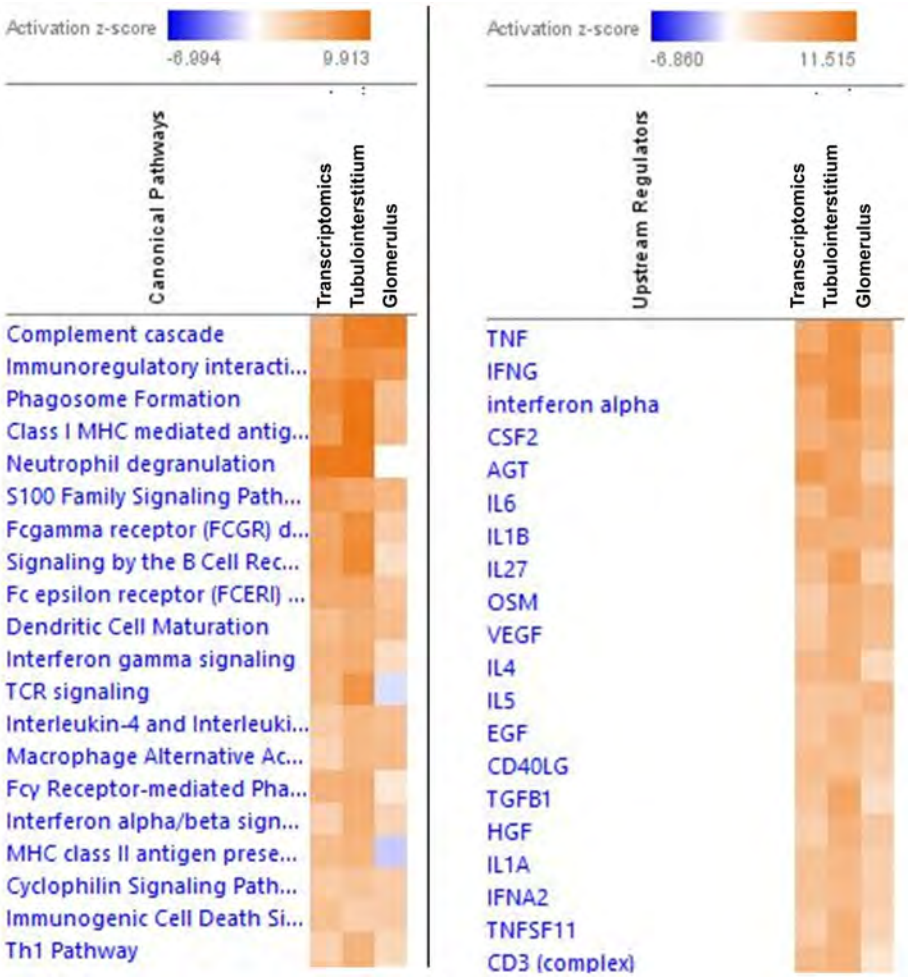
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Formalin-fixed paraffin embedded kidney biopsies of 23 patients with AAGN and 5 healthy controls (pre-implantation kidney donor biopsy) were used. For transcriptomics, RNA was extracted and bulk RNAseq was performed on all 23 AAGN biopsies and controls. Differential expression analysis was performed using the DESeq framework. For proteomics, laser capture microdissection was utilized to collect the glomerular and tubulointerstitial compartments separately using 10 AAGN biopsies and all controls. Peptides were extracted and submitted for mass-spectrometric analysis. After normalization, differential expression analysis was done using T-tests. The Benjamini-Hochberg method was used for multiple hypothesis testing correction in all experiments. Differentially abundant mRNA and peptide spectral counts were used to identify enriched immune pathways using Ingenuity pathway analysis.



Top 20 upregulated pathways of immunologic relevance in a) transcriptomic data b) glomerular proteomic data and c) tubulointerstitial proteomic data

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heatmap of identified canonical pathways and upstream regulators across transcriptomic and proteomic datasets

Results: Patient and disease characteristics of the full (transcriptomic) and proteomics cohort are described in table 1. The top enriched pathways in each of the 3 experiments (whole tissue transcriptomics, glomerular proteomics, tubulointerstitial proteomics) are depicted in Figure 1a-c. Comparison analysis using data from the 3 experiments demonstrated many shared enriched and upregulated pathways including complement, neutrophil degranulation, and FC gamma receptor signaling. PD-1/PDL1 and IL-10 signaling were downregulated across the 3 tissues studied. Upstream analysis demonstrated upregulation of TNF, INF-gamma, INF-alpha, and IL-6.

Conclusion: Analysis of biopsies from patients with AAGN demonstrated largely similar upregulated/downregulated immune pathways and upstream regulators when comparing transcriptomic and compartmental proteomics approaches. These may help inform patient stratification and therapy development.

Disclosure: I. Stojkic: None; **A. Arazi**: None; **H. Song**: None; **P. Yan**: None; **E. Puchulu-Campanella**: None; **H. Wang**: None; **L. Fussner**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **S. Ardoin**: None; **S. Almaani**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0720

Current State of Racial, Ethnic, Sex, and Geographical Diversity in ANCA-associated vasculitis and Giant Cell Arteritis Trials

Manuel Carpio Tumba[1], Aida Mohamadi[2], Diana Louden[3], Victor Pimentel-Quiroz[4], Michael Putman[5], Didem Saygin[6], Raisa Lomanto Silva[7] and Sebastian E Sattui[8], [1]University of Pittsburgh, Pittsburgh, PA, [2]Tehran University of Medical Sciences, Tehran, Iran, [3]University of Washington, Seattle, WA, [4]Universidad Científica del Sur, San Isidro, Peru, [5]The Medical College of Wisconsin, Milwaukee, WI, [6]Rush University Medical Center, Chicago, IL, [7]Massachusetts General Hospital, Boston, MA, [8]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Randomized controlled trials (RCTs) generate unbiased efficacy estimates and are required for regulatory approval. Understanding the degree to which they include racial, ethnic, sex, and geographical groups is important in understanding their generalizability and in addressing healthcare disparities. This systematic review summarizes the current state of representation in ANCA-associated vasculitis (AAV) and giant cell arteritis (GCA).

Methods: A systematic literature review using PubMed, EMBASE, CINAHL Complete, Europe PMC, ClinicalTrials.gov, and the International Clinical Trials Registry Platform was performed. All pharmacologic phase 2,3, and 4 RCTs in AAV and GCA (2010-2023) were included. This study followed the protocol of a larger systematic review (PROSPERO CRD42023457996), however all RCTs independent of age cut-offs were included in this analysis. Two authors independently reviewed the titles, abstracts, and full texts. Data extraction included demographics, year of publication, trial phase, sponsor category, and location of enrolling sites (continent, country, ZIP+4 for U.S. sites). U.S. enrollment sites were categorized at the county level using Urban-Rural Classification Scheme (small, medium, large metropolitan, and non-metropolitan) and into Medically

Table 1. Race, ethnicity, sex, and geographical location distribution of vasculitis (AAV and GCA*) RCTs (n=41).

	N (%) or median (range)
Race	
RCTs that reported race	14 (34.1%)
RCTs with ≥20% reported non-White participants	1 (2.4%)
Racial groups in all trials with reported race	
White	89.2% (0 – 79.4%)
Black	1.4% (0 – 7.1%)
Asian	3.7% (0 – 5.96%)
Ethnicity	
RCTs that reported ethnicity	10 (24.4%)
Hispanic or Latino participants in all trials	2% (0 – 7.1%)
Sex	
RCTs that reported sex	40 (97.6%)
RCTs with ≥45% female participation	26 (63.4%)
Female participants in all trials	49.9% (21.9 – 90.2%)
Geographical location of enrollment sites	
North America[a]	16 (39%)
Large metropolitan	69.8%
Medium metropolitan	19.2%
Small metropolitan	9.9%
Non-metropolitan	1.2%
Medically underserved area[c]	69.8%
Non-North America	25 (61%)
Europe	80.5%
Asia	19.5%
Australasia	36.6%

*AAV: ANCA-associated vasculitis; GCA: giant cell arteritis
[a]North America: RCTs that had at least one site in either Canada or the U.S.
[c]Based on the Health Resources and Services Administration designation of MUA lacking access to primary care services at the county level (last updated 2023).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Geographic distribution of enrolling sites for ANCA-Associated Vasculitis (Panel A) and Giant Cell Arteritis (Panel B) RCTs worldwide.

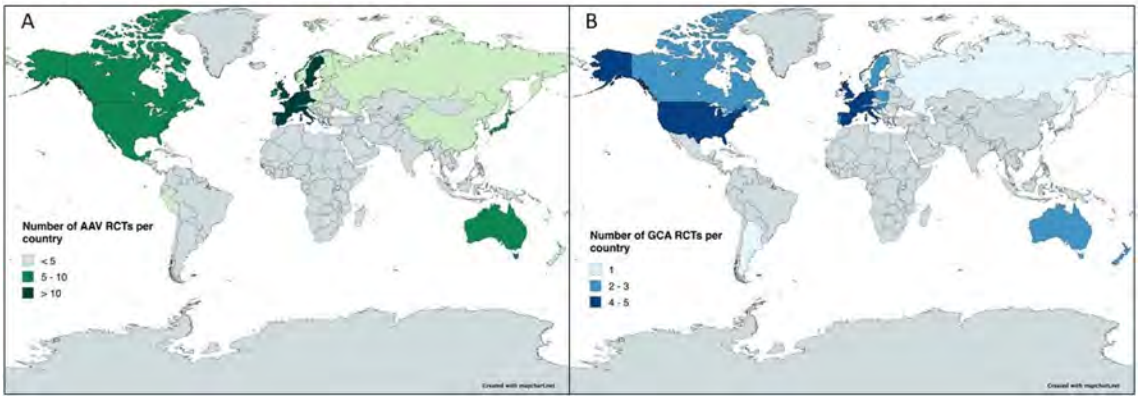
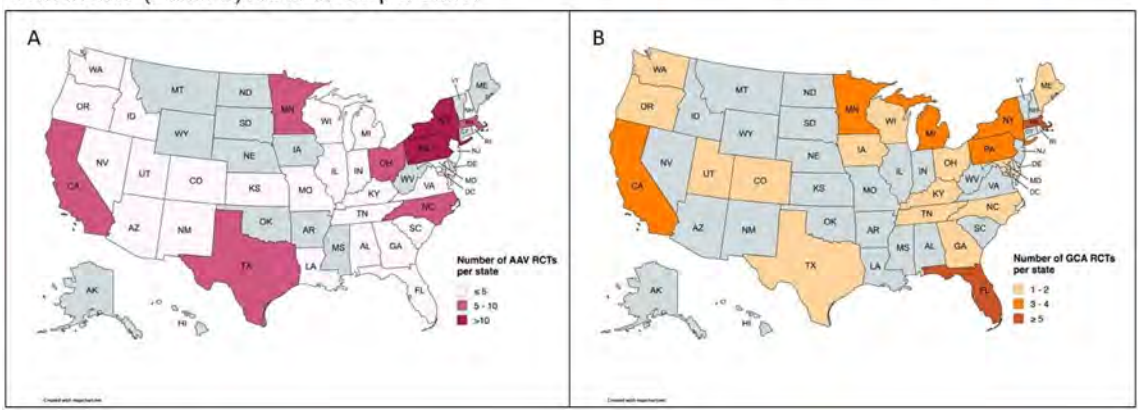


Figure 2. Geographic distribution of enrolling sites for ANCA-Associated Vasculitis (Panel A) and Giant Cell Arteritis (Panel B) RCTs in US per state.



Underserved Areas (MUA) (yes/no) according to the U.S. Department of Health & Human Services data. Diverse populations were defined as enrolling ≥20% non-White and/or ≥45% female participants based on U.S. Census Data.

Results: A total of 32 AAV RCTs (3954 participants, mean age 58.6 years) and 9 GCA RCTs (773 participants, mean age 71.7) were included. Less than 35% of trials reported race or ethnicity in their results. Among 14 trials that included data on race, the median percentage was highest for white (89.2%) followed by Asian (3.7%) and Black (1.4%) participants. Among 10 trials that included data on ethnicity, the median percentage of Hispanic or Latino participants was 2.0%. Out of 40 trials that reported data on sex, 49.9% were female. The majority of RCTs were multicentric (AAV 87.5%, GCA 88.9%). European centers participated in 78.1% of AAV and 88.9% of GCA RCTs; North American centers participated in 34.4% of AAV and 55% of GCA RCTs. No trials were conducted in Africa (**Figure 1**). A total of 172 U.S. sites participated in enrollment, of which 120 (69.8%) were located in MUAs. The majority (69.8%) of sites were situated in large metropolitan areas (**Figure 2**).

Conclusion: Enrollment in AAV and GCA RCTs has been primarily concentrated in Europe, North America, and Australasia. In the U.S., most participating sites are located in large metropolitan areas. The representation of diverse racial and ethnic groups has been notably limited across these trials. Greater efforts are needed to ensure adequate representation in AAV and GCA clinical trials.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Carpio Tumba: None; **A. Mohamadi**: None; **D. Louden**: None; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **M. Putman**: AbbVie/Abbott, 5, Amgen, 5, AstraZeneca, 2, 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5; **D. Saygin**: None; **R. Lomanto Silva**: None; **S. Sattui**: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2.

Abstract Number: 0721

Pulmonary Manifestations of Granulomatosis with Polyangiitis and Microscopic Polyangiitis

Mats Junek[1], Sara Choi[2], Stephanie Garner[3], Saara Rawn[4], David Cuthbertson[5], Curry Koening[6], Carol Langford[7], Carol McAlear[8], Paul Monach[9], Larry Moreland[10], Christian Pagnoux[11], Philip Seo[12], Ulrich Specks[13], Kenneth Warrington[13], Gerard Cox[1], Nader Khalidi[14], Peter Merkel[8] and The Vasculitis Clinical Resarch Consortium, [1]St Joseph's Healthcare Hamilton, Hamilton, ON, Canada, [2]Queen's University, Kingston, ON, Canada, [3]University of Calgary, Calgary, AB, Canada, [4]NOSM School of Medicine, Sudbury, ON, Canada, [5]University of South Florida, Tampa, [6]University of Texas Dell Medical School, Austin, TX, [7]Cleveland Clinic, Moreland Hills, OH, [8]University of Pennsylvania, Philadelphia, PA, [9]VA Boston Healthcare System, Boston, MA, [10]University of Colorado, Denver, CO, [11]Mount Sinai Hospital, Toronto, ON, Canada, [12]Johns Hopkins University, Baltimore, MD, [13]Mayo Clinic, Rochester, MN, [14]McMaster University, Hamilton, ON, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: There is limited knowledge of the epidemiology and complications of pulmonary manifestations in ANCA-associated vasculitis (AAV). This analysis focused describing the range of pulmonary disease in two forms of AAV: granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

Methods: Patients with GPA or MPA enrolled in a prospective longitudinal cohort between April 2006 and December 2023 were included. Patients satisfied a modified ACR 1990 classification criteria for GPA or the Chapel Hill Consensus Conference definition for MPA. Comprehensive data concerning diagnosis, demographics, pulmonary manifestations at onset of disease and/or follow up, and pulmonary damage were collected in a protocolized manner.

Results: Data from 1033 individuals (865 with GPA and 105 with MPA) were included for analysis, including 4511 patient-years of follow up. The mean age at diagnosis was 51.3 years and 55.0% of patients were female. Pulmonary manifestations at any time in the disease course were seen in 70.3% of individuals with AAV: 621 (71.8%) with GPA and 105 (62.5%) with MPA (Figure 1). In GPA, 63.6% had pulmonary involvement at the time of diagnosis and an additional 11.4% at follow-up. In MPA, 56% had manifestations at diagnosis and 4.8% at follow up. Among patients with GPA with pulmonary disease, nodules/cavities were most common manifestation (62.6%); among patients with MPA with pulmonary disease diffuse alveolar hemorrhage was the most common manifestation (61%). Among patients with pulmonary involvement, 285 (45.9%) of those with GPA and 45 (42.9%) of those with MPA had more than one pulmonary manifestation at the same time. 185 (17.9%) individuals had irreversible pulmonary damage, most commonly breathlessness, loss of lung function, or interstitial lung disease (Table 1).

Conclusion: Pulmonary manifestations are common in AAV, differ in frequency between GPA and MPA, and are associated with accumulation of damage. Individuals may have multiple pulmonary manifestations concurrently, suggesting multiple pathophysiologic processes. Systematic assessments of individuals with AAV for pulmonary involvement could potentially lead to earlier detection of these manifestations and reduce pulmonary damage.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

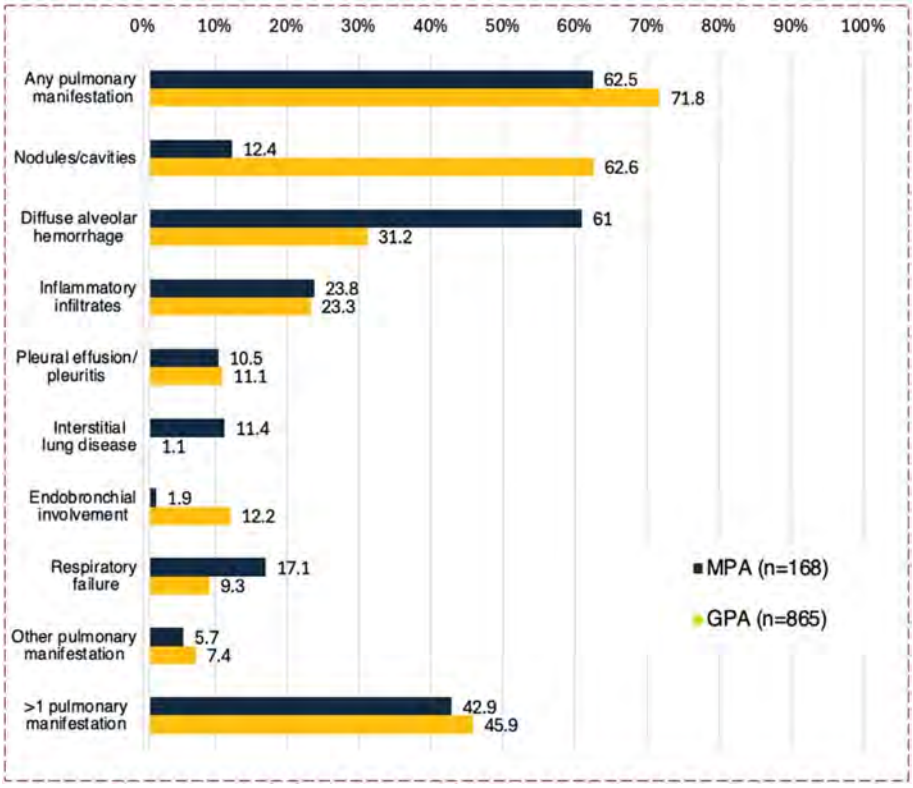


Figure 1: Frequency of pulmonary manifestations in individuals with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)

Table 1: Pulmonary damage in patients with granulomatosis with polyangiitis or microscopic polyangiitis.

	GPA n=865 (%)	MPA n=186 (%)	All n=1033 (%)
Any damage	149 (17.2)	36 (21.4)	185 (17.9)
Chronic asthma	18 (2.1)	2 (1.2)	20 (1.9)
Breathlessness	80 (9.2)	15 (8.9)	95 (9.2)
Irreversible loss of lung function	57 (6.6)	18 (10.7)	75 (7.3)
Fixed large airway obstruction	25 (2.9)	1 (0.6)	26 (2.5)
Pulmonary embolism	24 (2.8)	6 (3.6)	30 (2.9)
Need for vena cava filter	4 (0.5)	1 (0.6)	5 (0.5)
Pleural fibrosis	6 (0.7)	1 (0.6)	7 (0.7)
Interstitial lung disease	25 (2.9)	20 (11.9)	45 (4.4)
Pulmonary hypertension	8 (0.9)	2 (1.2)	10 (1)
Need for home oxygen	16 (1.8)	3 (1.8)	19 (1.8)
Other lung damage	8 (0.9)	0 (0)	8 (0.8)

GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis

Disclosure: M. Junek: AbbVie/Abbott, 1, Roche, 5; **S. Choi**: None; **S. Garner**: None; **S. Rawn**: None; **D. Cuthbertson**: None; **C. Koening**: Amgen, 1, Boehringer-Ingelheim, 1; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **C. McAlear**: None; **P. Monach**: Boehringer-Ingelheim, 2; **L. Moreland**: None; **C. Pagnoux**: AstraZeneca, 1, ChemoCentryx, 1, GlaxoSmithKlein(GSK), 1, 5, InflaRx GmbH, 1, otsuka, 1, 5, Pfizer, 1, 5, Roche, 1, 5; **P. Seo**: None; **U. Specks**: Amgen, 1, 2, 5, Argenx, 2, AstraZeneca, 1, 5, Boehringer-Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 5, CSL Vifor, 1, Genentech, 5, GlaxoSmithKlein(GSK), 5, Mayo Foundation for Education and Research, 9, Melodia Therapeutics, 2, NorthStar Medical Radioisotopes, 5, Novartis, 1, 2, 5, NS Pharma, 5, UpToDate, 9; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **G. Cox**: None; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 6, Mallinckrodt, 6, NS Pharma, 5, Otsuka, 6, Roche, 2, Sanofi, 5; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2.

Abstract Number: 0722

Estimating two-year risk of relapse in individuals with ANCA-associated vasculitis in a randomized controlled trial of plasma exchange and glucocorticoids

Mats Junek[1], Quazi Ibrahim[2], Peter Merkel[3], Eswari Vilayur[4], Ron Wald[5], Todd Fairhead[6], David Massicotte-Azarniouch[6], Louis Girard[7], Christian Pagnoux[8], Nader Khalidi[2], David Jayne[9], Michael Walsh[2] and The PEXIVAS Investigators, [1]St Joseph's Healthcare Hamilton, Hamilton, ON, Canada, [2]McMaster University, Hamilton, ON, Canada, [3]University of Pennsylvania, Philadelphia, PA, [4]John Hunter Hospital, Newcastle, New South Wales, Australia, [5]St Michael's Hospital, Toronto, ON, Canada, [6]University of Ottawa, Ottawa, ON, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]Mount Sinai Hospital, Toronto, ON, Canada, [9]University of Cambridge, Cambridge, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: People with anti-neutrophil cytoplasm antibody (ANCA) associated vasculitis (AAV) vary in their risk of a relapse of disease. Estimating an individual's risk may inform decision-making around their care.

Methods: We developed and internally validated a model to predict the risk a relapse of AAV using a cohort of patients from a randomized controlled trial with severe AAV defined as an eGFR < 50 mL/min/1.73m2 or diffuse alveolar haemorrhage. We estimated risk of relapse within two years of remission. Candidate variables to estimate risk of relapse were selected using Lasso regression in Cox proportional hazard time-to-event models. Non-parametric estimates of baseline survival at two years were used to obtain absolute estimates of risk of relapse. Frequency of variable inclusion in the model was assessed using the same procedure across 1000 bootstrap samples. We assessed model discrimination using concordance statistics, and calibration using the mean calibration slope.

Table 1: Cox proportional hazard regression model studying association between relapse within 2 years for individuals with ANCA-associated vasculitis. Overall model significance: Likelihood ratio chi-squared = 53.35, p-value < 0.001 for the final model and 69.78.

Predictor	Final Model Adjusted Hazard ratio (95% CI)
Female sex	0.61 (0.40, 0.93)
ANCA type	
MPO-ANCA (reference)	1
PR3-ANCA	1.46 (0.96, 2.24)
Non-hemorrhagic respiratory involvement	1.38 (0.90, 2.11)
Mucus membrane/eye	1.39 (0.81, 2.39)
Induction therapy	
Intravenous cyclophosphamide (reference)	1
Rituximab	0.45 (0.23, 0.85)
Oral cyclophosphamide	0.46 (0.28, 0.76)
eGFR at remission (10 mL/min/1.73m^2)	1.14 (1.06, 1.21)

MPO: myeloperoxidase; PR3: proteinase 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

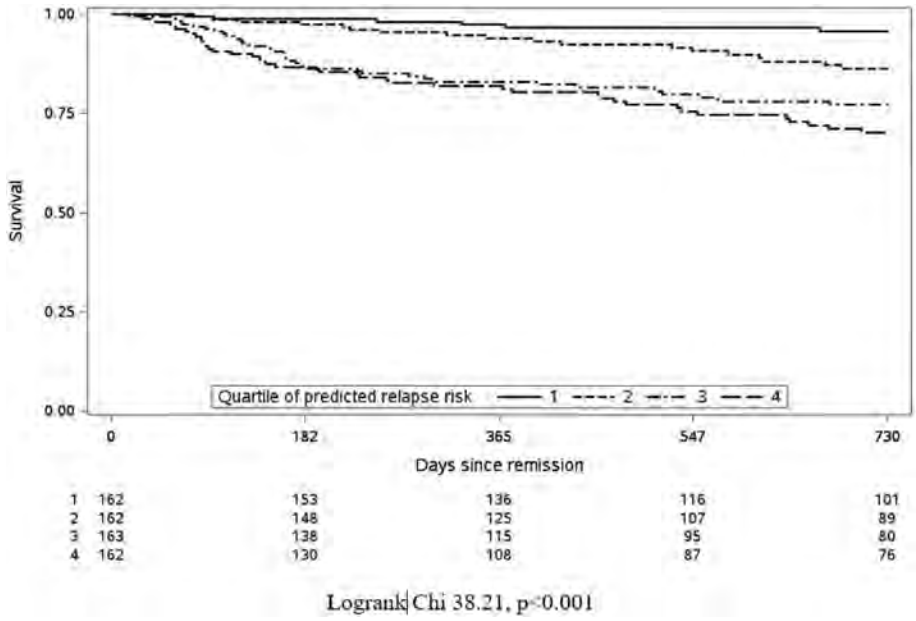


Figure 1: Kaplan Meier curve of relapse-free survival based on quartile of predicted risk of relapse as well as the risk of relapse contained within each quartile

Results: 649 participants met inclusion criteria of whom 100 relapsed within 2 years. The final model included participant sex, type of induction immunosuppression, ANCA serotype, non-hemorrhagic respiratory involvement, mucous membrane/eye involvement, and eGFR at remission (Table 1). Variables selected for inclusion in the final model were selected across 76% or more bootstraps. The optimism-corrected area under the receiver operator curve statistic was 0.71 (95% confidence interval [CI] 0.71-0.71). The mean calibration slope was 0.99 (95% CI 0.65-1.34). 18 (11.1%) of individuals at the lowest quartile of estimated risk of relapse experienced relapse and 58 (35.8%) of those at the highest quartile of estimated risk of relapse (Figure 1).

Conclusion: Our model accurately estimates the risk of relapse for individuals with AAV within two years after remission.

Disclosure: M. Junek: AbbVie/Abbott, 1, Roche, 5; **Q. Ibrahim**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **E. Vilayur**: None; **R. Wald**: None; **T. Fairhead**: None; **D. Massicotte-Azarniouch**: None; **L. Girard**: None; **C. Pagnoux**: AstraZeneca, 1, ChemoCentryx, 1, GlaxoSmithKlein(GSK), 1, 5, InflaRx GmbH, 1, otsuka, 1, 5, Pfizer, 1, 5, Roche, 1, 5; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 6, Mallinckrodt, 6, NS Pharma, 5, Otsuka, 6, Roche, 2, Sanofi, 5; **D. Jayne**: Alentis, 2, 11, Amgen, 2, 6, AstraZeneca, 1, 2, 6, Aurinia, 1, 11, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, ChemoCentryx, 2, 6, Chinook, 1, Chugai, 2, 6, CSL Vifor, 2, 6, Fate, 2, GlaxoSmithKlein(GSK), 2, 6, GSK, 1, Hansa, 1, Novartis, 1, 2, 6, Otsuka, 2, Roche, 2, 6, Takeda, 1, 2, 6; **M. Walsh**: AstraZeneca, 2, Bayer, 2, GlaxoSmithKlein(GSK), 2, Novo Nordisc, 12, Support for event adjudication committees, Otsuka, 2, Visterra, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0723

Neutrophil and Eosinophil Extracellular Traps in Eosinophilic Granulomatosis with Polyangiitis: Phenotype-based Characterization and Response to Mepolizumab

Michele Moretti[1], Francesco Ferro[2], Francesco Pisani[3], Elisa Ferrigno[3], Gaetano La Rocca[4], Federica Di Cianni[5], Rosaria Talarico[6], Marta Mosca[7], Chiara Baldini[7] and Ilaria Puxeddu[3], [1]University of Pisa, Rheumatology Unit, Pisa, Italy, [2]Clinical and Experimental Medicine Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Pisa, Italy, [3]University of Pisa, Pisa, Italy, [4]University of Pisa, Rheumatology Unit, Pisa, Pisa, Italy, [5]Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy, [6]Azienda Ospedaliero Universitaria Pisana, Pisa, Pisa, Italy, [7]University of Pisa, Pisa, Pisa, Italy

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: EGPA variably presents eosinophil (EOS)-related features and vasculitic manifestations. Recent introduction of mepolizumab (MEP) has revolutionized the treatment of EOS manifestations of EGPA. However, the efficacy of MEP also in vasculitic phenotypes suggests direct interactions between EOS and neutrophilic inflammation in EGPA. Extracellular traps formed by neutrophils (NETs) are an important innate immune response and are involved in ANCA-associated vasculitis pathogenesis. Similarly, EOS produce extracellular traps (EETs), recently detected in tissues of EGPA patients.

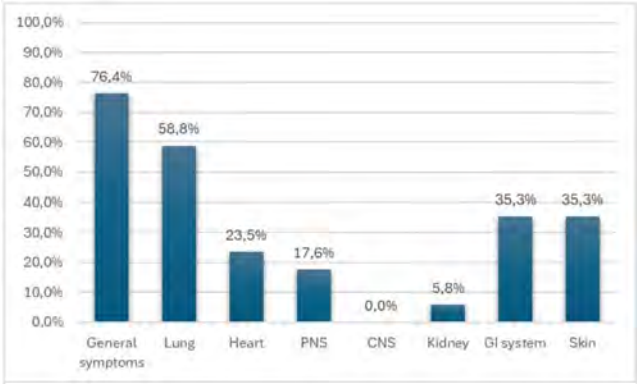


Figure 1. Distribution of patients according to organ involvement.

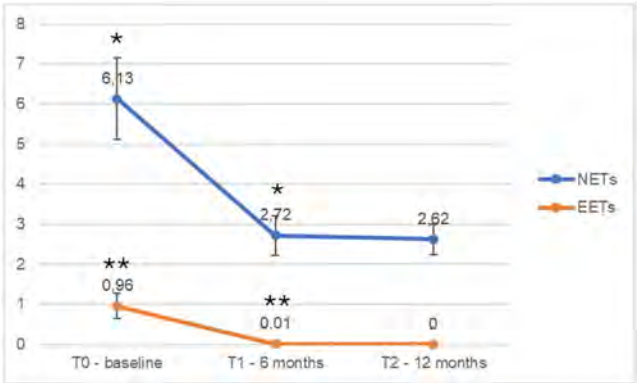


Figure 2. NETs and EETs response to mepolizumab treatment, *p=0.001, **p=0.014

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Our study aims to evaluate the efficacy of MEP in EGPA and the potential role of this treatment on NETs and EETs formation in different disease phenotypes.

Methods: Patients classified as EGPA according to MIRRA trial and/or ACR/EULAR 2022 criteria and eligible for therapy with MEP were consecutively enrolled. Clinical and routine blood chemistry data were collected before (T0) and after 6 (T1) and 12 (T2) months of treatment with MEP 300 mg/4 weeks. Oral steroid was tapered according to clinical judgement, therapy with immunosuppressants, if taken, was unchanged during the study. In parallel, we evaluated NETs and EETs on peripheral blood by immunofluorescence staining (Petretto et al., 2019). NETs and EETs were expressed as percentage of the total area of cells in the fields. Patients were stratified by disease phenotype according to the presence/absence of MPO-ANCA, asthma and nasal polyposis (CRSwNP) and organ involvement.

Results: 17 patients with EGPA and eligible for MEP were enrolled (53% female (9/17)). MPO-ANCA were detected in 29.4% of patients (5/17). 88% (15/17) were asthmatic, 60% of them had severe asthma. 53% (9/17) were atopic and 82% had CRSwNP. At T0 94% (16/17) were taking prednisone therapy (5.83±4.18 mg, average dose). Distribution of organ involvement is reported in Figure 1.

Following MEP introduction, EOS blood count reduced from T0 to T1 (p=0.036) but not from T1 to T2, while neutrophils did not vary in any period. Steroid dose was reduced to 1.04±2.59 mg at T2 (p=0.003), with 10 patients (58.8%) being steroid-free. No relapse was observed during the study.

At T0, NETs and EETs levels did not vary by ANCA status, organ involvement, EOS peak count, asthma or CRSwNP presence/severity. NETs levels were negatively correlated to total IgE titre (r=-0.52, p=0.05). EETs values are higher in atopic patients (p=0.017) regardless of steroid dose and EOS blood count.

NETs and EETs decreased at T1 (respectively p=0,001 and p=0,014) but were stable between T1 and T2 in the overall group (Figure 2). After stratification for ANCA status, NETs significantly decreased only in ANCA positive patients at T1 (p=0.01), while EETs only in ANCA negative patients at T1 (p=0,025), without any difference observed between T1 and T2. No difference was found according to asthma and CRSwNP presence.

Conclusion: In a small but representative cohort of EGPA patients, NETs and EETs vary by atopic status but not by ANCA status or organ involvement. MEP treatment, after 6 months of therapy, influences NETs and EETs formation in EGPA patients, also in relation to their ANCA profile, supporting potential utility of NETs and EETs evaluation in disease management.

Disclosure: M. Moretti: None; **F. Ferro**: None; **F. Pisani**: None; **E. Ferrigno**: None; **G. La Rocca**: None; **F. Di Cianni**: None; **R. Talarico**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **C. Baldini**: None; **I. Puxeddu**: GlaxoSmithKlein(GSK), 5.

Abstract Number: 0724

Risk of Drug Induced Liver Injury with Use of Avacopan in ANCA Vasculitis - Results from Real-World Data

Milad Heydari-Kamjani[1], Elleson Harper[2] and Haseeb Chaudhary[3], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [3]Case Western Reserve University, Westlake, OH

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic autoimmune vasculitis. Avacopan, a novel oral C5a receptor inhibitor, has emerged as an adjunct therapy for AAV. However, a notable side effect of avacopan is drug-induced liver injury (DILI). This study aims to assess the risk of DILI associated with avacopan in patients with AAV.

Methods: We conducted a retrospective cohort study using the TriNetX Research Network, a de-identified, federated electronic health record database (accessed April 16, 2025). Adult patients (≥18 years) with AAV (ICD-10: M31.3, M31.7, I77.82) and DILI (K71.0, K71.1, K71.2) were included. A 1:1 propensity score matching was performed using demographics, comorbidities, and CYP3A4 inhibitor medication exposures to balance baseline characteristics of patients on standard of care treatment with or without avacopan. Continuous and categorical variables were compared using t-tests and chi-squared tests ($\alpha = 0.05$).

Table 1: Baseline demographics and comorbidities in patients with AAV treated with or without avacopan before and after propensity score matching.

	Before Matching			After Matching		
Variables	**AAV with Avacopan (n=522)**	**AAV without Avacopan (n=28,641)**	**p-Value**	**AAV with Avacopan (n=516)**	**AAV without Avacopan (n=516)**	**p-Value**
Demographics						
Age (Mean ± SD)	56.1 ± 19.7	56.4 ± 18.5	0.716	56.2 ± 18.6	55.5 ± 19.2	0.571
Female	282 (54.0%)	15,694 (57.0%)	0.181	279 (54.1%)	263 (51.0%)	0.319
African American	41 (7.9%)	2,261 (8.3%)	0.773	41 (7.9%)	29 (5.6%)	0.137
White	364 (69.7%)	19,326 (70.1%)	0.844	360 (69.8%)	360 (69.8%)	1
Asian	20 (3.8%)	1,083 (3.9%)	0.909	20 (3.9%)	19 (3.7%)	0.87
Hispanic	60 (11.5%)	2,356 (8.5%)	0.017	58 (11.2%)	75 (14.5%)	0.114
Comorbid Conditions						
Obesity	159 (30.5%)	3290 (11.9%)	<0.001	155 (30.0%)	157 (30.4%)	0.892
Alcohol related disorders	16 (3.1%)	564 (2.0%)	0.105	16 (3.1%)	23 (4.5%)	0.253
Diabetes mellitus	146 (28.0%)	3,596 (13.0%)	<0.001	142 (27.5%)	147 (28.5%)	0.729
Nonalcoholic steatohepatitis	10 (1.9%)	108 (0.4%)	<0.001	10 (1.9%)	10 (1.9%)	1
Alcoholic Hepatic Steatosis	0 (0%)	10 (0%)	0.663	0 (0%)	0 (0%)	0.34
Metabolic syndrome	69 (13.2%)	784 (2.8%)	<0.001	66 (12.8%)	54 (10.5%)	0.244
Chronic kidney disease	136 (26.1%)	2025 (7.3%)	<0.001	131 (25.4%)	128 (24.8%)	0.829
Essential hypertension	309 (59.2%)	8,786 (31.9%)	<0.001	303 (58.7%)	318 (61.6%)	0.34
Acute viral hepatitis	10 (1.9%)	78 (0.3%)	<0.001	10 (1.9%)	10 (1.9%)	1
Chronic viral hepatitis	10 (1.9%)	251 (0.9%)	0.018	10 (1.9%)	10 (1.9%)	1

Table 2: Use of CYP3A4 inhibitors in patients with AAV treated with or without avacopan, before and after propensity score matching.

	Before Matching			After Matching		
Variables	**AAV with Avacopan (n=522)**	**AAV without Avacopan (n=28,641)**	**p-Value**	**AAV with Avacopan (n=516)**	**AAV without Avacopan (n=516)**	**p-Value**
CYP3A4 Inhibitors						
Itraconazole	10 (1.9%)	100 (0.4%)	<0.001	10 (1.9%)	10 (1.9%)	1
Ketoconazole	25 (4.8%)	568 (2.1%)	<0.001	23 (4.5%)	27 (5.2%)	0.562
Fluconazole	78 (14.9%)	1,752 (6.4%)	<0.001	75 (14.5%)	71 (13.8%)	0.721
Posaconazole	10 (1.9%)	55 (0.2%)	<0.001	10 (1.9%)	10 (1.9%)	1
Clarithromycin	15 (2.9%)	520 (1.9%)	0.102	14 (2.7%)	16 (3.1%)	0.711
Erythromycin	37 (7.1%)	793 (2.9%)	<0.001	36 (7.0%)	30 (5.8%)	0.445
Nirmatrelvir	16 (3.1%)	143 (0.5%)	<0.001	13 (2.5%)	10 (1.9%)	0.527
Ritonavir	10 (1.9%)	150 (0.5%)	<0.001	10 (1.9%)	10 (1.9%)	1
Amiodarone	20 (3.8%)	470 (1.7%)	<0.001	20 (3.9%)	16 (3.1%)	0.497
Diltiazem	22 (4.2%)	912 (3.3%)	<0.001	22 (4.3%)	25 (4.8%)	0.654
Verapamil	18 (3.4%)	546 (2.0%)	0.018	17 (3.3%)	16 (3.1%)	0.86
Cimetidine	10 (1.9%)	83 (0.3%)	<0.001	10 (1.9%)	10 (1.9%)	1
Cyclosporine	14 (2.7%)	384 (1.4%)	0.014	12 (2.3%)	11 (2.1%)	0.833

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 29,163 patients with ANCA-associated vasculitis (AAV) were identified, including 522 treated with avacopan and 28,641 who were not. Before matching, significant differences were observed between groups in several demographic and clinical characteristics. The avacopan group had higher proportions of Hispanic patients (11.5% vs. 8.5%; p = 0.017) (Table 1). Comorbid conditions such as diabetes mellitus, nonalcoholic steatohepatitis (NASH), metabolic syndrome, chronic viral hepatitis, and essential hypertension were all more common among those receiving avacopan (all p < 0.05). Additionally, avacopan group had significantly higher use CYP3A4 inhibitors including itraconazole, ketoconazole, fluconazole, posaconazole, voriconazole, nirmatrelvir, ritonavir, amiodarone, diltiazem, cimetidine, and cyclosporine (all p < 0.05) (Table 2). Following 1:1 propensity score matching, 516 patients remained in each group. No statistically significant differences were observed in age, sex, race, ethnicity, comorbidities, or medication use. The incidence of DILI was nearly identical between the two groups (2.0% vs. 1.9%), with a risk difference of 0.0% (95% CI: –0.017 to 0.017; p = 0.975). There was no significant difference in DILI-free survival between groups (log-rank p = 0.873), and the hazard ratio for time to DILI was 1.25 (95% CI: 0.078–20.07; p = 0.171).

Conclusion: In this matched cohort analysis, the incidence of DILI was low and comparable between patients treated with avacopan and those who were not. While no significant difference was observed, the limited number of events precludes definitive conclusions regarding comparative risk.

Disclosure: M. Heydari-Kamjani: None; **E. Harper**: None; **H. Chaudhary**: None.

Abstract Number: 0725

Sinonasal Symptom Profiles Associated with Disease Activity in an International Cohort of Patients with ANCA-Associated Vasculitis

Rennie Rhee[1], Christine Yeung[2], Darrin White[3], Mary Gibson[3], Jessica Nguyen[4], Cristina Burroughs[5], Jennifer Gordon[6], Noam A. Cohen[4], Jeffrey Morris[4] and Peter Merkel[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Vasculitis Patient-Powered Research Network, Philadelphia, PA, [3]2. Patient Research Partner, Vasculitis Patient-Powered Research Network, Philadelphia, [4]University of Pennsylvania, Philadelphia, [5]University of South Florida, Tampa, FL, [6]Vasculitis Foundation, Kansas City, MO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Sinus and nasal symptoms are common and associated with a higher risk of relapse in patients with ANCA-associated vasculitis (AAV). Previously, our group found that a patient questionnaire called the Sino-Nasal Outcome Test-22 (SNOT-22), a validated patient-reported outcome measure in chronic rhinosinusitis, is associated with future relapse even in patients without a prior history of sinonasal disease. A detailed understanding of sinonasal symptoms is still lacking in AAV. The aim of this analysis was to evaluate sinonasal symptom profiles associated with disease activity in patients with AAV.

Methods: Patients with a self-reported diagnosis of AAV were recruited between January and March 2025 through an international research network (Vasculitis Patient-Powered Research Network). Participants rated 26 sinonasal symptoms on a scale from 0 (no problem) to 5 (problem as bad as it can be); the 26 symptoms included the original 22 items from the SNOT-22 plus four additional items related to vasculitis. The 4 vasculitis-specific items were selected based on patient and investigator input and included: nasal crusting, blood-tinged nasal discharge/crusts, nose bleeds, and nasal pain. Total and subdomain scores of the SNOT-22 were compared using linear regression. Sinonasal symptoms associated with active

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

vasculitis versus remission were determined using LASSO-penalized logistic regression. The penalty term (λ) was chosen by 10-fold cross-validation; variables with nonzero coefficients were carried forward into a post-LASSO unpenalized model to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results: A total of 663 participants with AAV from 24 countries were included: 130 with active disease, 423 in remission, and 110 who had unknown disease status. Median age at enrollment was 63 years, median disease duration was 8 years, 91% had positive ANCA in the past, and 88% had a prior history of sinonasal disease related to vasculitis. Total and subdomain SNOT-22+ scores were all significantly higher in active vasculitis vs remission group (**Figure 1**) and remained significant

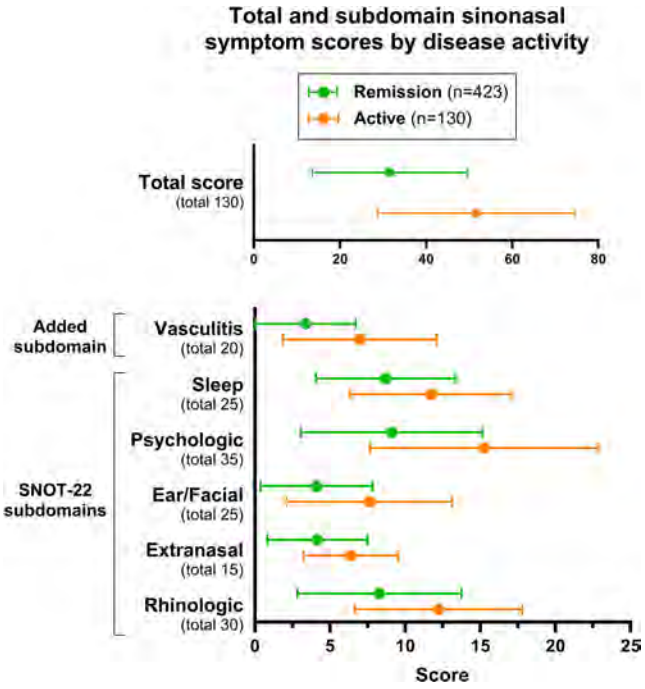


Figure 1. Comparison of Sino-Nasal Outcome Test scores by disease activity in patients with ANCA-associated vasculitis. Mean (SD) of total and subdomain scores from the SNOT-22 plus additional vasculitis-specific questions. Compared to patients with AAV in remission, patients with active disease had a greater burden of sinonasal symptoms and poorer quality of life across all domains (all $P < 0.01$).

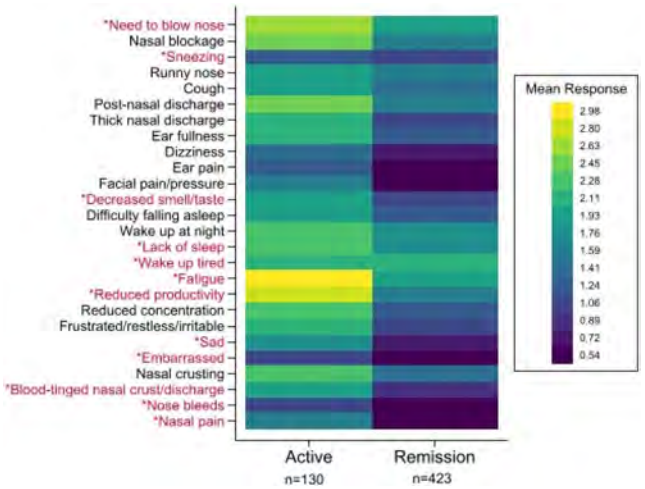


Figure 2. Mean response to individual items in the Sino-Nasal Outcome Test by disease activity in ANCA-associated vasculitis. Heatmap depicts the mean response to each item by group (active vs remission). Responses to all items except "wake up tired" were significantly higher in the active vs remission group (all $P < 0.05$). Items with asterisk and red font were retained in the final model after variable selection.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

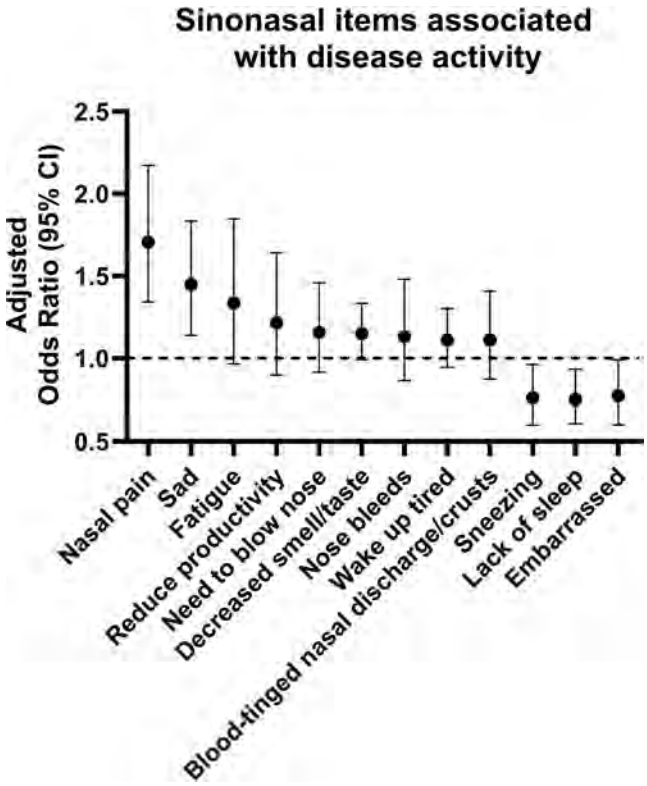


Figure 3. Odds ratio with 95% CI for association of sinonasal items with active disease in ANCA-associated vasculitis. Figure displays variables selected in post-LASSO logistic regression model. Nasal pain, feeling sad, sneezing, and lack of good night's sleep were among the items associated with disease activity in AAV in the multivariable model.

even after adjusting for age, sex, and disease duration. Both groups had higher scores compared to historical healthy control cohorts (mean score 9). Responses to 25 of 26 items were significantly higher in the active vs remission group (**Figure 2**). LASSO-based variable selection identified 12 items associated with disease activity (**Figure 3**).

Conclusion: Active AAV is associated with greater sinonasal symptom burden compared to quiescent disease although patients in remission continue to experience higher levels of symptoms compared to healthy patients. More severe nasal pain, more sadness, and less severe sneezing had the strongest association with active disease. A detailed understanding of the sinonasal symptom profile associated with active disease may improve clinical monitoring of disease activity in AAV.

Disclosure: R. Rhee: None; **C. Yeung**: None; **D. White**: None; **M. Gibson**: None; **J. Nguyen**: None; **C. Burroughs**: None; **J. Gordon**: None; **N. Cohen**: None; **J. Morris**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0726

Real-World Avacopan Use in Granulomatosis with Polyangiitis and Microscopic Polyangiitis: Insights from United States Claims Data on Outcomes and Adherence

Sebastian E Sattui[1], Elizabeth Ibiloye[2], Niranjan Kathe[3], Sam Oh[4], Virginia Noxon-Wood[5], Iman Mohammadi[5], Laura Moore-Schiltz[5] and Tingting Li[6], [1]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, [2]Amgen Inc, Thousand Oaks, CA, [3]Amgen Inc, San Diego, CA, [4]Amgen Inc, South San Francisco, CA, [5]Inovalon, Bowie, MD, [6]Washington University School of Medicine, St. Louis

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are the most common types of anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV). Treatment-related toxicities, particularly from glucocorticoid (GC) exposure, are common in patients with AAV. Avacopan is an adjunctive treatment for adults with severe active GPA/MPA that can aid in achieving and sustaining remission while reducing GC use. This study aims to describe patient characteristics, real-world treatment patterns, and outcomes among adults receiving avacopan in the United States.

Methods: This retrospective analysis included administrative claims from the Medicare Fee-for-Service (FFS) and MORE^2 Registry® databases from 10/07/2021 to 12/31/2022 (FFS) or 06/30/2023 (MORE^2). Adults with ≥1 claim for avacopan (index date: first avacopan claim), continuous enrollment for 12 months prior (baseline) and 12 months after (follow-up) index

Table 1. Characteristics among all patients treated with avacopan

Characteristics	N=167
Age, mean (SD)	54.5 (17.8)
Sex, N (%)	
Female	96 (57.5%)
Male	71 (42.5%)
Race/ethnicity, N (%)	
White	82 (49.1%)
Non-Hispanic Other	56 (33.5%)
Hispanic/Latino	29 (17.4%)
Payer, N (%)	
Medicare Fee-for-Service	51 (30.5%)
Commercial	53 (31.7%)
Medicare Advantage	12 (7.2%)
Managed Medicaid	51 (30.5%)
Geographic region, N (%)	
Northeast	40 (24.0%)
Midwest	33 (19.8%)
South	42 (25.1%)
West	52 (31.1%)
Deyo-Charlson Comorbidity Index Score, median (IQR)	2.0 (3.0)
Other comorbid conditions, N (%)	
Hypertension	117 (70.1%)
Heart disease[1]	85 (50.9%)
Type 2 diabetes	37 (22.2%)
Depression	43 (25.7%)
Osteoporosis	12 (7.2%)

IQR: interquartile range; SD: standard deviation; 1. Includes heart failure, cardiovascular disease, cardiomyopathy, myocarditis and myocardial infarction.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Treatment patterns among patients with ≥2 avacopan claims

Treatment Patterns	N=152
Index avacopan claim prescriber specialty, N (%)	
Rheumatologist	53 (34.9%)
Nephrologist	20 (13.2%)
Internal/Family Medicine[1]	48 (31.6%)
Other	19 (12.5%)
Unknown	12 (7.9%)
Avacopan treatment patterns	
PDC, median (IQR)	0.8 (0.6)
Adherence (PDC ≥ 0.8), N (%)	82 (53.9%)
Patients who discontinued avacopan[2], N (%)	58 (38.2%)
Time to discontinuation in days, median (IQR)	365.0 (222.5)

IQR: interquartile range; PDC: proportion days covered; 1. Includes physician assistants supervised by a specialist.; 2. Defined as ≥90-day gap in avacopan treatment.

Table 3. Renal and extrarenal manifestations, medication use, and relapses among patients who did not discontinue avacopan

	Baseline (N = 94)	Follow-up (N = 94)
Kidney Manifestations, N (%)		
Chronic kidney disease	46 (48.9%)	46 (48.9%)
Extrarenal Manifestations, N (%)		
Ear, nose and throat manifestations	34 (36.2%)	22 (23.4%)
Chest manifestations[1]	49 (52.1%)	38 (40.4%)
AAV Medication Use		
Any non-GC immunosuppressive therapy, N (%)	76 (80.9%)	81 (86.2%)
Rituximab treatment, N (%)	61 (64.9%)	68 (72.3%)
Any systemic GC use, N (%)	83 (88.3%)	83 (88.3%)
Relapse, N (%)		
Patients with a relapse during follow-up		13 (18.3%)

GC: glucocorticoid; GPA/MPA: granulomatosis with polyangiitis or microscopic polyangiitis; 1. Includes interstitial lung disease, respiratory failure, pleurisy and alveolar hemorrhage.

date were included. Information on demographics, comorbidity burden, including Deyo-Charlson Comorbidity Index (DCI), were collected. Among patients with ≥2 avacopan claims during follow-up, avacopan-specific treatment patterns (i.e., prescriber specialty, median proportion of days covered [PDC], and adherence) were reported. In patients who did not discontinue avacopan (discontinuation defined as ≥90-day gap in treatment) during follow-up, information on GC and other non-GC AAV treatments, percent change in in prednisone-equivalent daily dose (PEDD), and renal and extrarenal manifestations were assessed. Additionally, relapses based on an adapted claims-based algorithm: ≥1 inpatient, ≥1 ER or ≥2 outpatient claims for GPA/MPA, or ≥1 renal or extrarenal claim, each accompanied by ≥20% increase in PEDD within 30 days, were measured.

Results: A total of 167 patients were included. Mean age was 54.5 years, most were female (57.5%) and White (49.1%), with a median DCI of 2.0 (Table 1). Among patients with ≥2 claims of avacopan (n = 152), the most common specialists to initially prescribe avacopan were rheumatologists (34.9%) and nephrologists (13.2%). The median PDC was 0.8, and over half (53.9%) had a PDC ≥0.8 at 12 months (Table 2). Nearly half (48.9%) of patients persistent on avacopan treatment (n=94) had chronic kidney disease. Extrarenal manifestations observed during baseline and follow-up included ear, nose and throat, 36.2% and 23.4%, respectively, and chest, 52.1% and 40.4%, respectively (Table 3). These patients also had a median percent change in PEDD of 12.5% between 90 days pre- and 90 days post-index, and 18.3% experienced a relapse during follow-up (Table 3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Among real-world patients prescribed avacopan early after its availability in the US, demographic and disease characteristics were consistent with the known epidemiologic profile of GPA/MPA. During the 12-month follow-up, most patients showed adequate adherence and did not experience a disease relapse. A reduction in PEDD was observed among patients taking avacopan. Additional studies with longer follow-up are needed to understand the long-term outcomes of this population.

Disclosure: S. Sattui: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2; **E. Ibiloye**: Amgen, 3, 11, AstraZeneca, 3, 11; **N. Kathe**: Amgen, 3, 11; **S. Oh**: Amgen, 3, 11; **V. Noxon-Wood**: Amgen, 2; **I. Mohammadi**: None; **L. Moore-Schiltz**: Amgen, 2, Inovalon, 3; **T. Li**: Amgen, 2, Calliditas, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, Travere, 2.

Abstract Number: 0728

Incidence and Clinical Characteristics of ANCA-Associated Vasculitis: A Nationwide Study in Spain

Susana Romero-Yuste[1], Marta Domínguez-Álvaro[2], Antonio Fernndez-Nebro[3], Miquel Blasco[4], Beatriz Ventosa[5], Javier Narváez[6], Gema Fernández[7], Iñigo Rúa-Figueroa[8], Desirée Luis-Rodríguez[9], Manuel Macía[10] and RESERN/VAN collaborative group, [1]University Hospital Complex of Pontevedra, Pontevedra, Spain, [2]Sociedad Española de Reumatología, Madrid, Spain, [3]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [4]Hospital clinic Barcelona, Barcelona Spain, Spain, [5]Spanish Society of Rheumatology, Madrid, Spain, [6]Hospital Universitario de Bellvitge, Barcelona, Spain, [7]Hospital la Paz, Madrid, Madrid, Spain, [8]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [9]Hospital Universitario Nuestra Señora de Candelaria, Tenerife, Spain, [10]Hospital Universitario Nuestra Señora de Candelaria,, Tenerife, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA-associated vasculitides (AAV)—granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), and microscopic polyangiitis (MPA)are rare but severe systemic vasculitides with significant morbidity and mortality. Existing epidemiological data in Spain are limited to specific regions, hindering comprehensive national understanding.

Table 1. Clinical Characteristics of Included AAV Cases

Characteristic	Value
Total number of patients	840
Median age at diagnosis [IQR]	66 [55, 75]
Female sex (%)	53.7%
Most frequent subtype	Microscopic polyangiitis (MPA) (51.0%)
Fulfilled ACR/EULAR 2022 criteria (%)	84.0%
Renal involvement at diagnosis (%)	70.3%
Patients with biopsy performed (%)	79.7%
Histological confirmation of AAV (%)	68.4%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Cumulative and Annual Incidence of AAV (per million adults ≥18 years)

Vasculitis Subtype	Cumulative Incidence (95% CI)	Annual Incidence (95% CI)
Microscopic polyangiitis (MPA)	35.8 (32.2 – 39.6)	5.7 (5.2 – 6.3)
Granulomatosis with polyangiitis (GPA)	18.8 (16.2 – 21.5)	3.0 (2.3 – 3.5)
Eosinophilic granulomatosis with polyangiitis (EGPA)	10.0 (8.1 – 12.0)	1.6 (1.3 – 1.9)
Overall	70.3 (65.1 – 75.6)	11.3 (10.4 – 12.1)

Table 3. General information and lifestyle habits.

Category	N 840 N %
Time between onset of symptoms and diagnosis	57 (19-145)
Smoking Habit	
- Smokers	99 (11.8)
- Non-smokers	660 (78.6)
Alcohol Consumption	
- Consumers	168 (20)
- Non-consumers	534 (63.6)
Cocaine Use	
- Yes	13 (1.9)
- No	674 (98.1)
Suspected Previous Drug or Toxicity Exposure	
- Yes	21 (2.5)
- No	793 (94.4)
- Unknown	26 (3.1)
Previous Infections	
- Yes	112 (13.3)
- Not recorded	728 (86.7)
SARS-CoV-2 Infection during follow-up	
- Yes	224 (26.7)
- Not recorded	616 (73.3)
Number of SARS-CoV-2 Infections	1 [1-1]
SARS-CoV-2 Vaccination	
- Yes	591 (70.4)
- No	157 (18.7)
- Unknown	92 (11)
Number of SARS-CoV-2 Vaccine Doses	4 [3-4]

Purpose: to estimate the incidence of AAV in Spain and describe its clinical, analytical, histopathological, and prognostic features, treatment patterns, and long-term outcomes.

Methods: Retrospective, multicenter cohort study involving 32 hospitals across Spain. Patients ≥18 years with newly diagnosed AAV between January 1,2015and March 31, 2021, were included. Data were extracted from medical records and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

entered into a centralized electronic database. The follow-up period ensured a minimum follow-up of 15 months for each patient. Incidence rates were calculated based on the adult population within each center's reference area. Disease activity, organ damage, and outcomes were assessed using validated scores (BVAS, FFS, VDI).

Results: 840 patients were included (53.7% women; median age 66 years).(Table 1) After excluding patients who did not reside within the reference area of the hospital where they were treated, 695 patients were included in the incidence análisis. For the analysis of clinical characteristics, all patients were included (N = 840).MPA was the most frequent subtype (51%), followed by GPA (26.8%) and EGPA (13.7%). Most patients (84%) fulfilled the 2022 ACR/EULAR classification criteria. The cumulative incidence was 70.3 cases per million adults (95% CI: 65.1–75.6) over the study period, and the overall annual incidence was 11.3 (95% CI: 10.4–12.1) cases per million adults.

By vasculitis subtype, the annual and cumulative incidence was: MPA**:** anual 5.7 (95% CI: 5.2–6.3); cumulative: 35.8 per million(95% C: 32,2-39,6). GPA: anual 3.0 (95% CI: 2.3–3.5); cumulative: 18.8 per million (95% CI: 16,2-21,5). EGPA: anual 1.6 (95% CI: 1.3–1.9); cumulative: 10.0 per million (95% CI: 8,1-12). (Table 2). At diagnosis, 70.3% of patients had renal involvement and 64.4% were MPO-ANCA positive. The median BVAS at diagnosis was 15.0 [12.0, 20.0]. The median **Five-Factor Score (FFS)** at diagnosis was **1.0 [1.0, 2.0]**. Biopsies were performed in 79.7% of patients, with 68.4% confirming AAV-compatible histopathology. During follow-up, 35.4% experienced relapse, 42.2% achieved remission. 17.1% died; death was higher in men (p=0.006) (main causes of death were infections and active disease). Median Vasculitis Damage Index (VDI) increased from 2.0 at 6 months to 3.0 at the end of follow-up. General information and lifestyle habits are shown in table 3.

Conclusion: This is the largest AAV registry in Spain to date and the first to provide national incidence estimates. The findings confirm MPA as the predominant subtype followed by GPA and EGPA. Mortality was higher in men than in women

Disclosure: S. Romero-Yuste: AbbVie, 2, 6, AstraZeneca, 2, 6, Eli Lilly & Co., 2, 6, Galapagos, 6, UCB, 2; **M. Domínguez-Álvaro**: None; **A. Fernández-Nebro**: Argenx, 5, AstraZeneca, 2, 5, 6, Chemo, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Gebro Pharma, 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 5, Merck Serono, 5, MSD, 5, Novartis, 2, 5, 6, Takeda, 5, UCB, 5; **M. Blasco**: None; **B. Ventosa**: None; **J. Narváez**: None; **G. Fernández**: None; **I. Rúa-Figueroa**: None; **D. Luis-Rodríguez**: None; **M. Macía**: None.

Abstract Number: 0729

Anca-associated Vasculitis - Does the Type Matter?

Tamanna Vinodkumar Mohta[1] and Umeh Chukwuemeka[2], [1]Hemet Global Medical Center, Irvine, CA, [2]Hemet Global Medical Center, Hemet

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis is a heterogeneous group of rare autoimmune disorders that cause inflammation of blood vessels with various manifestations. Our study compares the differences in clinical outcomes in patients with the three main ANCA–associated vasculitis, granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparing various demographics and complications in different types of ANCA-associated vasculitis.

	Granulomatosis with polyangiitis (GPA)	Microscopic polyangiitis (MPA)	Eosinophilic granulomatosis with polyangiitis (EGPA)	All patients	P-value
Mean Age in years	61.07	63.02	60.70	61.30	
Females	53.6%	62.4%	57.2%	55.3%	<0.001
Race					
White	76.2%	59.1%	73.3%	73.4%	<0.001
Black	7.4%	11.2%	11.5%	8.4%	
Hispanics	11.4%	19.5%	7.4%	12.1%	
Asian	1.7%	4.9%	4.2%	2.5%	
Others	3.4%	5.2%	3.7%	3.7%	
Died during hospitalization	4.7%	6.1%	2.9%	4.7%	<0.001
Pulmonary hypertension	6.5%	9.7%	5.3%	6.8%	<0.001
Congestive heart failure	24.9%	31.3%	23.3%	25.6%	<0.001
Pulmonary embolism	1.9%	1.9%	2.6%	2.0%	<0.001
Acute kidney injury	30.2%	47.9%	21.2%	31.7%	<0.001
End-stage renal disease	24.2%	31.2%	3.5%	22.8%	<0.001
Ischemic stroke	1.1%	1.1%	1.2%	1.1%	0.888
Acute myocardial infarction	4.1%	5.1%	4.1%	4.3%	<0.001
Interstitial lung disease	4.6%	11.9%	4.5%	5.6%	<0.001
Proximal deep venous thrombosis	1.5%	1.7%	1.3%	1.5%	0.028

Methods: We analyzed data of patients hospitalized with a primary or secondary diagnosis of ANCA-vasculitis admitted in United States hospitals from 2017 to 2021 using the National Inpatient Sample (NIS) data. The NIS database is the largest publicly available database of patients hospitalized in the United States.

Results: There were 77,100 patients with a diagnosis of ANCA-associated vasculitis with a mean age of 61.3 years. Of this, 56965 (73.9%) had GPA, 11020 (14.3%) MPA, and 9115 (11.8%) EGPA. In the bivariate analysis, MPA patients had more kidney, heart, and lung complications and worse outcomes compared to GPA and EGPA patients. MPA patients when compared to GPA and EGPA patients were more likely to have acute kidney injury (47.9% vs. 30.2% vs. 21.2%), end-stage renal disease (31.2% vs. 24.2% vs. 3.5%), acute myocardial infarction (5.1% vs. 4.1% vs. 4.1%), congestive heart failure (31.3% vs. 24.9% vs. 23.3%), pulmonary hypertension (9.7% vs. 6.5% vs. 5.3%) and interstitial lung disease (11.9% vs. 4.6% vs. 4.5%), all with $p< 0.001$. There was no difference in the prevalence of ischemic stroke between the MPA, GPA, and EGPA ($p=0.88$).

In the multivariate analysis with GPA as the reference group, there was no difference in in-hospital all-cause mortality between GPA and MPA patients (aOR 0.98, 95% CI 0.89-1.08). However, EGPA patients had lower mortality than GPA patients (aOR 0.67, 95% CI 0.58-0.77).

Conclusion: GPA is the most common type of ANCA vasculitis in hospitalized patients in the US. Kidney involvement, interstitial lung disease, and acute myocardial infarction appear to be more common in MPA than other ANCA vasculitis. However, MPA patients did not have worse in-patient all-cause mortality than GPA patients. EGPA patients appear to have the best in-hospital prognosis.

Disclosure: T. Mohta: None; **U. Chukwuemeka**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0730

Levels of Disease Activity and Their Relationship With Health-Related Quality of Life In ANCA-Associated Vasculitis Patients: Data from the Almenara Vasculitis Cohort

Victor Pimentel-Quiroz[1], Alvaro Oyarce-Calderon[2], Allison Figueroa-Sánchez[3], Leonor León-Yaurimucha[3], Rocío Gamboa-Cárdenas[4], Zoila Rodríguez-Bellido[5], Risto Perich-Campos[6], Graciela Alarcon[7] and Manuel Ugarte-Gil[8], [1]Universidad Científica del Sur, San Isidro, Peru, [2]Hospital Nacional Guillermo Almenara Irigoyen, San Miguel, Lima, Peru, [3]Universidad Científica del Sur, Lima, Peru, [4]Universidad Científica del Sur, Lima, Peru, [5]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, Lima, Peru, [6]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [7]The University of Alabama at Birmingham, Oakland, CA, [8]Universidad Cientifica del Sur, Lima, Peru

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0711–0730) Vasculitis – ANCA-Associated Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: It is known that health-related quality of life (HRQoL) in patients with ANCA-associated vasculitis (AAV) is impaired. Categories of disease activity levels have been proposed for these patients; however, it is unknown whether these categories might impact these patients' HRQoL. Therefore, the aim of this study is to determine the relationship between HRQoL and levels of disease activity in AAV patients.

Methods: We included patients from the Almenara Vasculitis cohort who had at least one visit between December 2022 and November 2024 and had a diagnosis of either microscopic polyangiitis (MPA) or granulomatosis with polyangiitis. Sociodemographic features, disease activity measured with the Birmingham Vasculitis Activity Score version 3 score, damage measured with the Vasculitis Damage Index score, and HRQoL assessed by the AAV-PRO (Spanish version) and the Short Form 36 (SF-36), were obtained. Levels of disease activity were categorized as complete remission, clinical remission off therapy (CROffT), clinical remission on therapy (CRonT), low disease activity (LDA) and active disease; these definitions are shown in Table 1. For these analyses, complete remission, CROffT and CRonT were examined together due to the relatively small sample size for each of them individually. Unadjusted and adjusted linear regression models were performed; possible confounders included in the adjusted model were age, sex, ethnicity, education level, socioeconomic status, type of diagnosis, ANCA status, vasculitis damage index, current prednisone dose, current immunosuppressive drug.

Results: Eighty-four patients were enrolled; female sex and MPA were more frequent. In the adjusted analyses, regarding the SF-36, active disease was associated negatively with general health, role emotional and the mental component summary domains; likewise, LDA was negatively associated with role physical. Regarding the AAV-PRO, active disease was positively associated with the treatment side effects domain.

Table 1. Definitions of levels of disease activity.

	Disease activity	New features of AAV activity	ANCA status	Prednisone dose	Immunosuppressants
Complete remission	BVAS=0	No	No	No	No
CROffT	BVAS=0	No	Yes	No	No
CROnT	BVAS=0	No	Yes/No	=5mg/d	Yes
LDA	0=BVAS=3 and no activity in major organ systems	No	Yes/No	=7.5mg/d	Yes (standard maintenance dose)
Active disease	BVAS>3	Yes	Yes/No	Yes/No	Yes/No

CROffT: clinical remission off therapy. CROnT: clinical remission on therapy. LDA: low disease activity. AAV: ANCA-associated vasculitis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Unadjusted and adjusted analyses.

Table 2. Unadjusted and adjusted analyses.

		Unadjusted				Adjusted[a]			
		Active disease[b]		LDA[b]		Active disease[b]		LDA[b]	
		B (SE)	*p* value	B (SE)	*p* value	B (SE)	*p* value	B (SE)	*p* value
SF-36	PF	-7.56	0.175	13.31	0.255	0.11	0.986	14.48	0.156
	RF	**-17.64**	**0.021**	-28.59	0.074	-15.08	0.151	**-39.26**	**0.020**
	BP	**-11.39**	**0.019**	0.65	0.949	-11.73	0.087	-6.47	0.558
	GH	**-7.65**	**0.033**	-8.10	0.283	**-11.94**	**0.017**	-14.54	0.073
	VT	-5.73	0.166	-3.28	0.705	-6.81	0.214	-3.44	0.697
	SF	-6.70	0.114	-10.16	0.254	-5.35	0.368	-5.02	0.600
	RE	**-27.12**	**0.001**	15.42	0.377	**-24.57**	**0.038**	6.23	0.744
	MH	-5.28	0.171	0.80	0.921	-7.94	0.144	-2.24	0.798
	MCS	**-10.34**	**0.006**	-1.09	0.890	**-11.06**	**0.038**	-3.75	0.662
	PCS	**-9.94**	**0.008**	-5.21	0.508	-9.14	0.060	-9.94	0.203
AAV-PRO	OSS	-0.39	0.941	-4.88	0.657	4.46	0.539	-2.42	0.836
	SS	1.17	0.834	-7.58	0.518	5.19	0.496	-2.15	0.861
	TSE	**8.39**	**0.041**	-2.03	0.814	**16.62**	**0.003**	2.67	0.770
	SEI	4.47	0.329	10.94	0.254	9.47	0.123	8.39	0.396
	CF	-1.74	0.719	7.22	0.476	0.35	0.957	5.41	0.607
	PF	4.70	0.356	-11.95	0.263	6.88	0.233	-7.58	0.415

SF-36: Short form 36. PF: Physical function. RF: Role physical. BP: Bodily pain. GH: General health. VT: Vitality. SF: Social functioning. RE: Role emotional. MH: Mental health. PCS: Physical component summary. MCS: Mental component summary. AAV-PRO: ANCA-associated vasculitis patient-reported outcome. OSS: Organ-specific symptoms. SS: Systemic symptoms. TSE: Treatment side effects. SEI: Social and emotional impact. CF: Concerns about the future.

[a] Adjusted to age, sex, ethnicity, education level, socioeconomic status, type of diagnosis, ANCA status, vasculitis damage index, current prednisone dose, current immunosuppressive drug.

[b] Compared to remission (complete remission + clinical remission off therapy + clinical remission on therapy).

Conclusion: Active disease impacted in the HRQoL as assessed by the-SF36 and the AAV-PRO questionnaires, although the first one was more associated with levels of disease activity.

Disclosure: V. Pimentel-Quiroz: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **A. Oyarce-Calderon**: None; **A. Figueroa-Sánchez**: None; **L. León-Yaurimucha**: None; **R. Gamboa-Cárdenas**: None; **Z. Rodríguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcon**: None; **M. Ugarte-Gil**: AstraZeneca, 1, 6, Ferrer, 1, GlaxoSmithKlein(-GSK), 6, Janssen, 5, technofarma, 1.

Abstract Number: 0731

The Efficacy of Leflunomide in the Treatment of Giant Cell Arteritis: A Systematic Review and Meta-Analysis

Linda Zhu[1], Arielle Mendel[2], Carolyn Ross[3] and **Jean-Paul Makhzoum**[1], [1]Universite de Montreal, Montreal, Canada, [2]McGill University Health Centre, Montreal, QC, Canada, [3]University of Montreal, Longueuil, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The objective of this systematic review is to assess the effectiveness of leflunomide in the treatment of new-onset, refractory or relapsing giant cell arteritis (GCA) as a glucocorticoid (GC)-sparing agent.

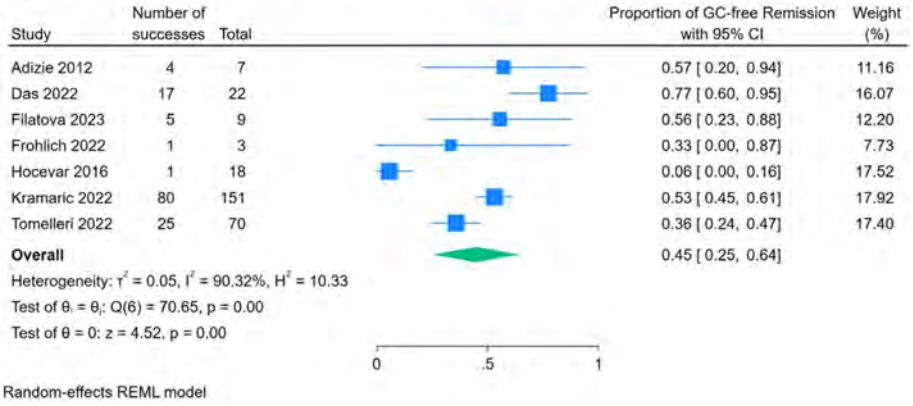
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of 358 pooled patients treated with leflunomide for giant cell arteritis

Characteristics	Patients (N=358)
Age (in years), median (IQR)	80 (73.8-77.9)
Female, n (%)	231 (69)
Disease subtype, n (%)	
New onset	233 (65)
Relapsing	83 (23)
Refractory	19 (5)
Unknown	23 (7)
Constitutional symptoms, n/N (%)	183/254 (72)
Polymyalgia rheumatica, n/N (%)	98/313 (31)
Headache, n/N (%)	159/212 (75)
Jaw claudication, n/N (%)	89/201 (44)
Visual symptoms, n/N (%)	45/206 (22)
Visual loss, n/N (%)	24/206 (12)
Stroke, n/N (%)	7/176 (4)
CRP (mg/L), median (IQR)	27 (24.1-84.3)
Radiologic findings, n/N (%)	54/92 (59)
Biopsy-proven disease, n/N (%)	32/117 (27)

All numbers are reported as *n*/group *N* (%) unless otherwise specified.
IQR: interquartile range
CRP: C-reactive protein

Figure 1: Meta-analysis of proportions for the efficacy of leflunomide to achieve GC-free remission in patients with giant cell arteritis.



Methods: A systematic review was conducted using MEDLINE, CENTRAL, EMBASE, and conference proceedings to identify studies on leflunomide in patients with GCA. We included randomized controlled trials, cohort studies, case-control studies, and case series. The primary efficacy outcome was the proportion of patients who attained GC-free remission with leflunomide assessed at any time between 6 to 12 months of therapy. GC-free remission was defined as the absence of signs or symptoms of GCA, and/or normalization of inflammatory markers, and/or radiologic response, and complete discontinuation of GC. Our secondary efficacy outcome was the proportion of patients who attained low-dose GC remission (< 5 mg of prednisone equivalent). All included studies were appraised for risk of bias. We performed a meta-analysis of proportions using a random-effects model and a restricted maximal likelihood approach. We evaluated heterogeneity with I2 and Cochran's Q test. Publication bias was assessed by producing funnel plots for each outcome.

Results: 357 studies were screened with 10 observational studies included in the final analysis. Out of the 358 patients that we pooled for analysis, 231 (69%) were females (table 1). A total of 233 (65%) patients had new-onset GCA, 83 patients had relapsing GCA (23%), and 19 patients had refractory GCA (5%). The disease subtype was not specified for 23 patients. The proportion of patients achieving GC-free remission with leflunomide was 45%, (95% CI 0.25-0.64, p< 0.001, 7 studies) (figure 1). Substantial statistical heterogeneity was present (I2=90.3%, Q=70.7, p< 0.001). Meanwhile, the pooled proportion of patients achieving low-dose GC remission was 48% (95% CI 0.27-0.69, p< 0.001, 6 studies). Funnel plots were slightly asymmetrical, which suggested the presence of publication bias as well as possible poor methodological quality in the reporting of outcomes. All the included studies were deemed to be at serious risk of bias.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The main challenge in treating GCA is achieving and maintaining remission with minimal glucocorticoids. Our study shows that leflunomide may offer potential benefits in achieving remission without GCs or with low-dose GCs; however, the results exhibited variability due to differences in sample sizes and inconsistent reporting. Leflunomide's role as a glucocorticoid-sparing agent is promising but needs further investigation into higher-quality studies. PROSPERO registration CRD42023490373.

Disclosure: L. Zhu: None; **A. Mendel**: None; **C. Ross**: None; **J. Makhzoum**: AbbVie/Abbott, 12, Investigator, AstraZeneca, 6, 12, Investigator, GlaxoSmithKlein(GSK), 6, Janssen, 12, Investigator, Novartis, 12, Investigator, Otsuka, 6, Roche, 6, Sanofi, 6.

Abstract Number: 0732

Blocking GM-CSF receptor alpha with mavrilimumab reduces production of growth factors involved in vascular remodeling in an ex-vivo model of temporal artery culture from patients with giant-cell arteritis (GCA)

marc Corbera-bellalta[1], Roser Alba-Rovira[1], Nina Visocnik[1], Farah Kamberovic[1], Ferran Araujo-Ayala[1], Georgina Espigol-Frigolé[1], Patricia Perez-Galán[1], Ken Bondensgaard[2], John Paolini[3] and **Maria Cid**[4], [1]Hospital Clínic. University of Barcelona. IDIBAPS., Barcelona, Spain, [2]Kiniksa Pharmaceuticals, Lexington, [3]Kiniksa Pharmaceuticals, LEXINGTON, MA, [4]Department of Autoimmune Diseases (member of European Reference Network RITA), Hospital Clinic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Background: Giant-cell arteritis(GCA) is a chronic inflammatory disease targeting large and medium-sized arteries. Inflammation-induced vascular remodeling leads to vascular occlusion, with ischemic complications. Myofibroblasts are key cells in this process, and they differentiate from quiescent vascular smooth muscle cells under the influx of several factors, including PDGFs produced by inflammatory cells, mainly macrophages(1).

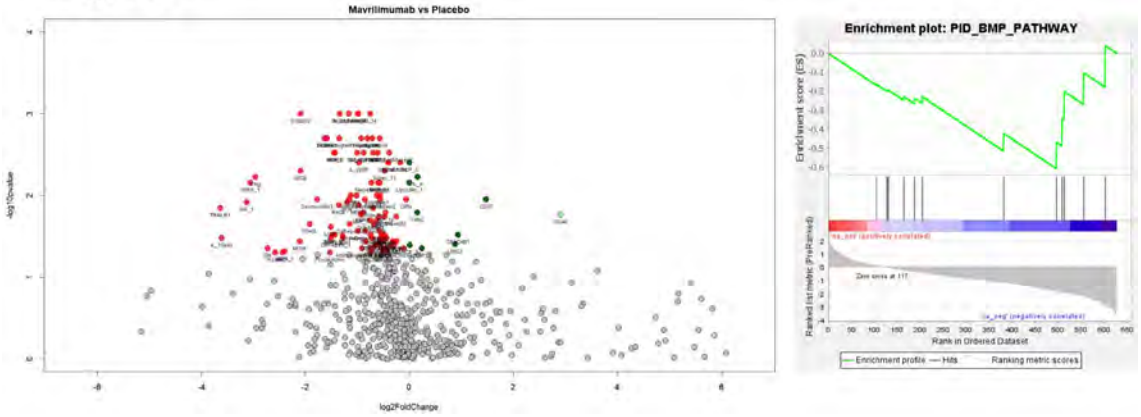
GM-CSF is a key proinflammatory cytokine with pleiotropic effects on a variety of cells. Macrophages, the predominant infiltrating cells in GCA, are among the main targets of GM-CSF. Using an ex-vivo culture of patient's arteries in 3D matrix(2), we have previously shown that intimal myofibroblasts express GM-CSF receptors and that blocking GM-CSF receptor with mavrilimumab(MAV) inhibits key pro-inflammatory pathways(3). In a phase 2 clinical trial, MAV, along with a standardized prednisone taper, was superior to placebo in reducing the risk of GCA flare and increasing the rate of sustained remission at week 26(4), indicating that MAV efficiently blocks clinically-relevant inflammatory pathways in GCA

Purpose: We aimed to investigate the impact of MAV on pathways involved in myofibroblast differentiation and vascular remodeling.

Methods: Three patients (1 placebo, 2 MAV) consented to have a second temporal artery biopsy (TAB) at the trial completion. Nineteen TAB from patients with GCA (obtained for diagnostic purposes) were cultured ex-vivo as published(2,3) and treated with placebo or MAV (20 mg/ml) for 5 days. Arteries were processed for RNA extraction, and candidate transcripts were assessed by RT-qPCR. The supernatants were processed for proteomic analysis using G-series Human cytokine array (640 proteins). Differences were analyzed by paired Wilcoxon test. GSEA, Hallmark, C2 curated gene sets, C3 motif

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1



gene sets, and C5 gene ontology gene sets were used for pathway analysis. We focused on pathways involved in myofibroblast differentiation and fibrosis.

Results: Biopsies from MAV-treated patients showed better lumen preservation than the placebo-treated. MAV significantly reduced mRNA expression of PDGFA and B. No impact was seen in other relevant growth factors, such as FGF1, FGF2 or TGFb1 at the mRNA level. Pathway analysis of the proteins released into the supernatant revealed a significant impact of MAV on proteins related to BMP pathway (figure 1). A decrease in BMP-4(p=0.004), BAMBI (p= 0.07) and XIAP(p=0.053) was detected. In addition, a significant decrease in FGF12(p=0.0018) and FGF 17(p=0.0014) was also observed. A decrease in the corresponding mRNAs was also observed.

Conclusion: MAV modulates production of molecules involved in vascular remodeling in cultured arteries from patients with GCA. Whether MAV acts directly on myofibroblasts or indirectly through impairing macrophage function is being currently investigated. Further studies are ongoing to assess the functional impact of the modulated pathways on myofibroblast biology in GCA.

Disclosure: m. Corbera-bellalta: None; **R. Alba-Rovira**: None; **N. Visocnik**: None; **F. Kamberovic**: None; **F. Araujo-Ayala**: None; **G. Espigol-Frigolé**: CSL-Vifor, 1, 6, GlaxoSmithKlein(GSK), 1, 2, 5, 6; **P. Perez-Galán**: None; **K. Bondensgaard**: Kiniksa Pharmaceuticals, 3; **J. Paolini**: Kiniksa Pharmaceuticals, 3, 11; **M. Cid**: AbbVie, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL-Vifor, 2, 6, GSK, 2, 6, Kiniksa Pharmaceuticals, 5, UpToDate, 9.

Abstract Number: 0733

Cerebrovascular Accidents in Patients with Giant Cell Arteritis: A Population-Based Retrospective Cohort Study

Saman Tanveer[1], **Pranathi Bandarupalli**[2], Vineeth Potluri[3], Fatima Tanveer[4] and Abdullah Saeed[5], [1]The University of Chicago, Chicago, IL, [2]Mercy St Vincent Medical Center, Toledo, OH, [3]Mercy Health St. Vincent Medical Center, Toledo, OH, [4]CMH Lahore Medical College and Institute of Dentistry, Lahore, Punjab, Pakistan, [5]John H. Stroger Jr. Hospital of Cook County, Chicago, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of Hospitalized Stroke Patients with and without GCA or GCA with PMR

Characteristic	Stroke without GCA or GCA with PMR (n =)	Stroke with GCA or GCA with PMR (n =)	P-value
No of Patients	4139183	4454	
Age, mean (years)	69.9 Years	76.27 years	<0.001
Female sex (%)	49.5%	67.3%	
Male Sex (%)	50.5%	32.7%	<0.001
Hypertension	84.45%	89%	<0.001
Type1/2 Diabetes	39.38%	36.03%	0.0453
Smoking	19.73%	12.57%	<0.001
Hyperlipidemia	59.65%	62.74%	<0.001
Obesity	15.07%	14.25%	<0.001
Chronic Steroid Use	0.8%	18.74%	<0.001
Peripheral Vascular Disease	9.61%	15.26%	<0.001
Intravenous thrombolysis (IVT)	8.5%	4.7%	<0.001
Mechanical Thrombectomy (MT)	4.9%	2.8%	<0.001
Mechanical Ventilation	5.8%	7.2%	<0.001

Table 2: Multivariate Regression Analysis of Outcomes Among GCA or GCA with PMR Patients Admitted With Stroke

Outcome	Adjusted OR	(95% CI)	P-value
In-Hospital Mortality	1.18	(0.83–1.50)	0.467
Length of Stay	+0.26 days	(−0.15 to +0.68)	0.022
Total Hospital Charges	+506$	-$7,319 to +$8,331	0.899
Odds of Receiving IV Thrombolysis	0.57	0.42–0.78	<0.001
Odds of Mechanical Thrombectomy	0.62	0.41–0.95	0.027
Mechanical Ventilation	0.77	0.51–1.17	0.227
PEG Tube Placement	0.99	0.67-1.48	0.98
Cerebral Edema or Herniation	0.76	0.52–1.10	0.146

Background/Purpose: To assess the characteristics, interventions, and outcomes of cerebrovascular accidents (CVAs) in people with giant cell arteritis (GCA). Strokes are uncommon in this population, however, it is uncertain whether patients with GCA are at a higher risk of stroke compared to the general population.

Methods: A retrospective cohort study was performed by analyzing the National Inpatient Sample (NIS) 2017-2022 for all patients with GCA, GCA with Polymyalgia Rheumatica (PMR), and Cerebral Infarction as primary or secondary diagnoses via ICD-10 (International Classification of Diseases 10th Revision) codes. Frequencies, demographics, and trends were determined and compared between hospitalized patients with GCA or GCA with PMR and those without GCA or GCA with PMR. STATA version 17 was used for data analysis. A p-value of ≤0.05 was considered statistically significant.

Results: Hospitalized patients with stroke who had GCA or GCA with PMR were less likely to be male (32.7% vs. 50.5%, $p < 0.001$), less likely to have history of smoking (12.57% vs 19.73%, $p < 0.001$), more likely to have concomitant hypertension (89% vs 84.45%, $p< 0.001$ or concomitant peripheral vascular disease (15.26% vs 9.61%, $p< 0.001$), less likely to undergo intravenous thrombolysis (4.7% vs 8.5%, $p < 0.001$), and less likely to undergo mechanical thrombectomy (2.8% vs 4.9%,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

p< 0.001), have a higher mortality (5.16% vs 4.65%, p=0.045) when compared to hospitalized patients with stroke who do not have GCA or GCA with PMR.

Conclusion: Hospitalized patients with stroke who had GCA or GCA with PMR were more likely to be female, older in age, have concomitant hypertension and less likely to undergo mechanical thrombectomy or intravenous thrombolysis when compared to patients with stroke without GCA or GCA with PMR. The cohort with GCA or GCA with PMR also had higher mortality when compared to the cohort without GCA or GCA with PMR.

Disclosure: S. Tanveer: None; **P. Bandarupalli**: None; **V. Potluri**: None; **F. Tanveer**: None; **A. Saeed**: None.

Abstract Number: 0734

Glucocorticoid Exposure and Comorbidity Profile in Patients with Polymyalgia Rheumatica and Giant Cell Arteritis: a multi-country cohort study

Julie Mouchet[1], Lauren Revie[2], Tim Nguyen[3], Liwei Zhao[4], **Valeria Jordan M.**[5], G S Ramakrishna[6], Linda Grinnell-Merrick[3], Atif Adam[7] and Minouk Schoemaker[8], [1]Novartis Pharma AG, Basel, Switzerland, [2]IQVIA, EMEA, London, United Kingdom, [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [4]IQVIA, Real World Solutions, Mölndal, Sweden, [5]Novartis Pharmaceuticals Corporation, Tenafly, NJ, [6]Novartis Healthcare Private Limited, Hyderabad, India, [7]IQVIA Inc, Boston, [8]IQVIA, Real World Solutions, Amsterdam, Netherlands

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are systemic inflammatory conditions that predominantly affect individuals ≥50 years of age. The conditions share overlapping clinical features[1,2] and can significantly impact patients' quality of life. The main symptoms of PMR include pain and stiffness in the shoulder, neck, and hips; and patients with GCA present with headache, scalp tenderness, jaw claudication, and visual disturbances[2]. Both conditions are associated with significant disease burden, including cardiovascular, cerebrovascular diseases, and particularly malignancies for PMR, and a detrimental effect on vision for GCA. The primary treatment is with glucocorticoids (GC); however, unmet needs exist in GC treatments, including non-response to GC, and high relapse rate[3]. Managing the side effects of long-term GC use is also challenging, with a substantial proportion of patients experiencing disease recurrence during GC dose tapering[4]. Concerns about long-term use of GC include risk of infections, osteoporosis, cardiovascular events, and metabolic conditions[1,2]. This multi-country study aims to gain insight into the proportion of patients with PMR and GCA treated with GC and the prevalence of comorbidities across three continents.

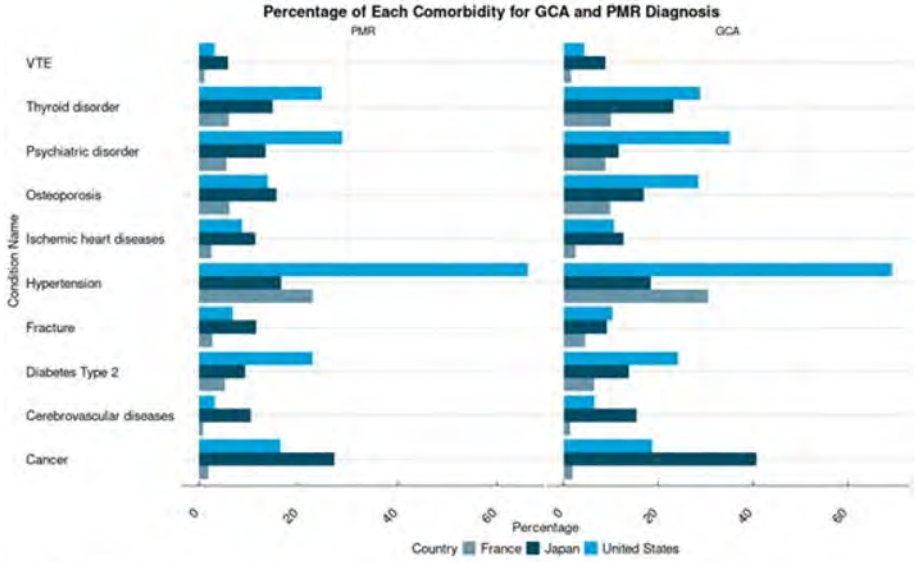
Methods: Patients with a first diagnosis (index date) of PMR or GCA aged ≥50 years during 2014-2024 and with at least 1 year of database enrollment pre-index were identified from healthcare databases including PharMetrics Plus (United States), Longitudinal Patient Database (France), and Japan Claims Plus 2. To increase the specificity of the diagnosis, at least two diagnosis codes recorded ≥7 days apart were required. The total number of patients and the distribution by age, sex, and comorbidities during the 12 months before index date were reported. The percentage of patients with at least two GC records within six months after index date was also reported.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Total number, characteristics, and percentage with at least two records of glucocorticoids (GC) in the six months following diagnosis of PMR or GCA

Database	Study period	PMR				GCA			
		N	Mean Age (years)	% Female	% treated with GC[1]	N	Mean Age (years)	% Female	% treated with GC[1]
US PharMetrics Plus	2017-2024	70,784	72.5	61.0	49.7	2,053	73.8	71.3	49.4
France LPD	2017-2024	8,920	75.2	58.2	65.8	1,693	77.1	69.5	58.9
Japan Claims Plus 2	2014 -2023	16,064	78.5	62.8	71.4	1,080	76.5	62.4	70.6

[1] Patients who had at least two records of GC within six months after the first diagnosis of PMR or GCA.
GC: Glucocorticoids; GCA: Giant cell arteritis; LPD: Longitudinal patient database; N: number of patients; PMR: Polymyalgia rheumatica.



VTE: Venous thromboembolic diseases; GCA: Giant cell arteritis; PMR: Polymyalgia rheumatica.
Figure 1. Percentage of comorbidity of interest within 12 months prior to diagnosis of GCA or PMR

Results: Overall 95,768 patients with PMR and 4,826 with GCA were included (Table 1). The mean age ranged from 72.5-78.5 years for PMR and 73.8-77.1 for GCA, and 58.2-62.8% of patients with PMR and 62.4-71.3% with GCA were female. The most common pre-index comorbidity was hypertension in France (PMR: 22.9%, GCA: 30.4%) and the US (PMR: 66.1%, GCA: 69.4%), and cancer in Japan (PMR: 27.3%, GCA: 40.7%) (Figure 1). Between 49.7-71.4% of patients with PMR and 49.4-70.6% with GCA received GC within six months after the first diagnosis.

Conclusion: Across three continents, both patients with PMR and GCA were predominantly of elderly age, with a majority being female, and exhibited a high prevalence of comorbidities. The use of GC was widespread, ranging from 49% of patients in the US to 71% in Japan. The significant burden of common comorbidities, which include diabetes, hypertension, and osteoporosis, underscores the challenges in clinical management of these two conditions. It is crucial to understand how GC are tapered in the real-life settings and to assess the associated safety burden, particularly given the comorbidity profile of these patients.

References:

1. Gazitt et al. 2020 *Curr Rheumatol Rep*
2. Mahr et al. 2021 *Front Med*.
3. Unizony et al. 2021 *Ann Rheum Dis*
4. Mainbourg et al. 2020 *Arthritis Care Res*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Mouchet: Novartis, 3, 11; **L. Revie**: IQVIA, 3; **T. Nguyen**: Novartis, 3, 11; **L. Zhao**: IQVIA, 3; **V. Jordan M.**: Novartis, 3, 12, Shareholder; **G. Ramakrishna**: Novartis, 3; **L. Grinnell-Merrick**: Novartis, 3, 11; **A. Adam**: IQVIA, 3; **M. Schoemaker**: IQVIA, 3.

Abstract Number: 0735

A Real-world Study from the Greater Paris Clinical Data Warehouse

Aïcha Kante[1], Olivier Hassanaly[2], Geoffroy Peyrac[3], David Saadoun[4], Cacoub Patrice[4], Alexis REGENT[5], Benjamin Terrier[6], Luc Mouthon[7], Arsène Mekinian[8], Karim Sacré[9], Jean-François Alexandra[10], Sébastien Abad[11], Robin Dhote[11], Cécile goujard[12], Damien Sène[13], Stéphane Mouly[14], Baptiste Hervier[15], Olivier Bory[16], Elisabeth Aslangul[16], Isabelle Mahé[16], Anne Couvelard[17], Yann Nguyen[18], Agnès Lefort[18], Sophie georgin-Lavialle[19], Olivier Steichen[19], Viet-Thi Tran[20] and Cloé Comarmond[1], [1]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, INSERM U942, Paris, France, [2]Unité de recherche clinique, AP-HP, Hôpital Saint Louis, F75010, Paris, France, Paris, France, [3]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, AP-HP, Paris, France, [4]Department of Internal Medicine and Clinical Immunology, Sorbonne Universités, AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Centre national de références Maladies Autoimmunes et systémiques rares, Centre national de références Maladies Autoinflammatoires rares et Amylose inflammatoire (CEREMAIA), INSERM, UMR S959, Immunology-Immunopathology-Immunotherapy (I3), Paris, France, Paris, France, [5]Hopital Cochin, Paris, France, [6]Cochin Hospital, Paris, France, [7]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [8]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [9]Department of Internal Medicine, Bichat University Hospital, Université Paris Cité, AP-HP, Paris, France, Paris, France, [10]Internal Medicine, Hôpital Bichat, APHP, Paris, France, [11]Service de Médecine Interne, Hôpital Avicenne, Assistance Publique-Hôpitaux de Paris (AP-HP); Université Paris 13, Sorbonne Paris Cité, Bobigny, France, Bobigny, France, [12]Université Paris Saclay, Department of Internal Medicine and Clinical Immunology, Bicêtre Hospital, APHP, UMR1184 Inserm, CEA, Le Kremlin Bicêtre, France, Kremlin Bicêtre, France, [13]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, Paris, Ile-de-France, France, [14]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, Paris, France, [15]Internal Medicine Department, Hôpital Saint-Louis, AP-HP, Université Paris Cité, Paris, France., Paris, France, [16]Department of Internal Medicine, Louis-Mourier Hospital, AP-HP, Colombes, France, Colombes, France, [17]Pathology Department, Bichat and Beaujon Hospitals, AP-HP, FHU MOSAIC, Université Paris Cité, Paris, France, Paris, France, [18]Department of Internal Medicine, Beaujon Hospital, AP-HP Nord, Université Paris Cité, Clichy, France, Clichy, France, [19]Sorbonne university, Tenon hospital, DMU3ID, CEREMAIA, ERN RITA, Paris, France, [20]Université Paris Cité and Université Sorbonne Paris Nord, Inserm, INRAe, Centre for Research in Epidemiology and Statistics (CRESS), Paris; and Centre d'Epidémiologie Clinique, Hôpital Hôtel-Dieu, AP-HP, Paris, France, Paris, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) relapses are frequent and often require therapeutic intensification in the form of glucocorticoids (GC) increase. GCA management has significantly evolved following the publication of the GiACTA trial and the subsequent approval of tocilizumab (TCZ) in 2017, allowing for faster GC tapering without relapse. In this study, we aimed to describe real-world diagnostic practices, management strategies and mortality outcome in patients with new-onset GCA from 2017 to 2024.

Methods: All patients diagnosed GCA between August 1st 2017 and May 30th 2024, were identified in the Clinical Data Warehouse of Assistance Publique–Hôpitaux de Paris using the French Medical Information System Program coding system. Stored data integrates clinical, biological and imaging data from patients hospitalized across all public hospitals in the Greater Paris area. To improve cohort accuracy, a natural language processing algorithm was applied to detect and exclude miscoded entries. Patients without a recorded prescription for GC were excluded. The study flowchart is presented in **Figure 1**. The risk of death was assessed using a multivariate Cox proportional hazards model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 843 patients were included in the study, 543 (64%) of whom were female, with a median [interquartile range] age at diagnosis of 74 [68–81] years, and median follow-up 6.4 [3.0-9.9] years (**Table 1**). The use of positron emission tomography increased from 30.4% of patients in the year 2017, to 36.5% in the year 2024. Conversely, the proportion of temporal artery biopsies declined from 47.8% in 2017, compared to 38.5% in the year 2024. At diagnosis, 772 (91.6%)

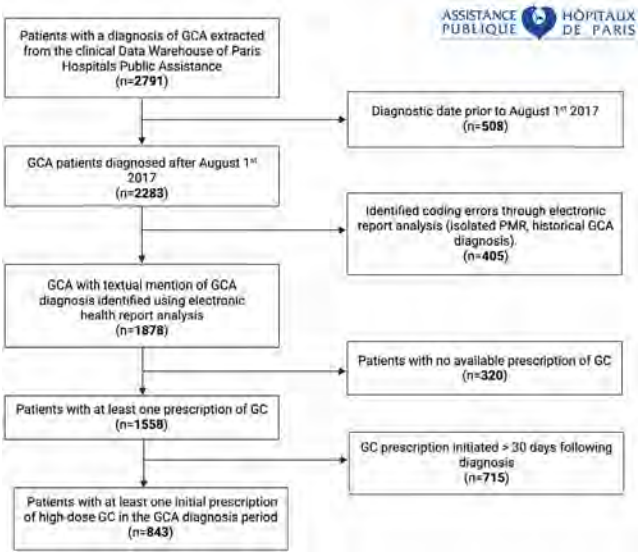


Figure 1. Study flowchart Abbreviations: GCA: giant cell arteritis; GC: glucocorticoids; PMR: polymyalgia rheumatica.

Table 1. Clinical characteristics at GCA diagnosis. Abbreviations: GCA: giant cell arteritis; CT: computed tomography; PET : positron emission tomography * Comorbidities at baseline were defined as clinical history or concomitant to GCA diagnosis.

Characteristics at baseline	**N = 843**
Demographic characteristics	
Female gender (%)	543 (64%)
Age at diagnosis (years)	74 [68 – 81]
Comorbidities at baseline*	
Stroke	73 (8.7%)
Diabetes	183 (22%)
Ischemic cardiopathy	277 (33%)
Osteoporosis	67 (7.9%)
Explorations at diagnosis	
Temporal arterial biopsy	369 (44%)
PET CT	280 (33%)
Contrast CT	263 (31%)
Treatment at diagnosis	
Aspirin	367 (44%)
Tocilizumab	71 (8.4%)
Prednisone	843 (100%)
Corticosteroid dose (mg)	40 [25 – 60]
Follow-up	
Follow-up duration (years)	6.4 [3.0 - 9.9]

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Survival analysis for risk of death among GCA patients. Results of both univariate and multivariate survival analysis for the risk of death following GCA diagnosis, using a Cox proportional hazard model. Comorbidities at baseline were defined as clinical history or concomitant to GCA diagnosis. Abbreviations: CI: confidence interval; GCA: giant cell arteritis; HR: hazard ratio

	Univariate analysis		Multivariate analysis	
	HR [95% CI]	p-value	HR [95% CI]	p-value
Male gender	1.60 [1.06 - 2.42]	**0.025**	1.43 [0.93 – 2.20]	0.1
Ischemic cardiopathy	4.43 [2.3 - 8.55]	**<0.01**	1.97 [0.99 – 3.92]	0.054
Osteoporosis at baseline	2.05 [1.16 - 3.62]	**0.014**	1.49 [0.82 – 2.71]	0.196
Cancer at baseline	2.70 [0.99 – 7.36]	0.052	-	-
Diabetes at baseline	1.64 [1.05 - 2.56]	**0.03**	1.22 [0.77 – 1.94]	0.406
Stroke at baseline	3.98 [2.46 - 6.43]	**<0.01**	2.65 [1.60 – 4.38]	**<0.01**
Aspirin at baseline	1.57 [1.04 – 2.38]	**0.031**	1.24 [0.81 – 1.88]	0.324
Tocilizumab at diagnosis	1.28 [0.64 – 2.55]	0.483	-	-
Age at diagnosis	1.10 [1.07 – 1.12]	**<0.01**	1.08 [1.05 – 1.11]	**<0.01**

received GC monotherapy while 71 (8.4%) received combined therapy with TCZ and GC. During follow-up, 400 (47.5%) GCA patients required GC intensification, including 319 (38%) at 1 year, 363 (43%) at 2 years and 380 (45%) at 3 years. The median time to first GC intensification was 1.4 [0.1–5.6] years. The median GC dose before intensification was 10 [5-20] mg/day which increased to 35 [20-50] mg/day following intensification. Overall, 91 (11%) patients died during follow-up. In a multivariate analysis (**Table 2**), older age at diagnosis (p< 0.01) and the presence of a stroke at baseline (p< 0.01) were independently associated with an increased risk of mortality.

Conclusion: In this contemporary French cohort, nearly half of patients with GCA required at least one GC intensification during the course of treatment. Stroke at baseline and older age at diagnosis were identified as independent risk factors for all-cause mortality.

Disclosure: A. Kante: None; **O. Hassanaly**: None; **G. Peyrac**: None; **D. Saadoun**: None; **C. Patrice**: None; **A. REGENT**: Novartis, 2; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **L. Mouthon**: None; **A. Mekinian**: Roche, 5; **K. Sacré**: None; **J. Alexandra**: Chugai France, 2; **S. Abad**: None; **R. Dhote**: None; **C. goujard**: None; **D. Sène**: None; **S. Mouly**: None; **B. Hervier**: None; **O. Bory**: None; **E. Aslangul**: None; **I. Mahé**: None; **A. Couvelard**: None; **Y. Nguyen**: None; **A. Lefort**: None; **S. georgin-Lavialle**: Novartis, 2, Sobi, 2; **O. Steichen**: None; **V. Tran**: None; **C. Comarmond**: Roche, 5.

Abstract Number: 0736

Effectiveness of Tocilizumab in strokes in patients with giant cell arteritis. Spanish multicenter study of clinical practice

Ana Serrano-Combarro[1], Javier Loricera[2], Clara Moriano[3], Santos Castañeda[4], Javier Narváez[5], Vicente Aldasoro Cáceres[6], Rafael B. Melero-González[7], Isabel De la Morena[8], Ivan Ferraz Amaro[9], Ricardo Blanco[10] and Tocilizumab in Giant Cell Arteritis Spanish Collaborative Group, [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [3]Hospital Len, LEON, Castilla y Leon, Spain, [4]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [5]Hospital Universitario de Bellvitge,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Barcelona, Spain, [6]Hospital Universitario de Navarra, Pamplona, Spain, [7]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [8]HOSPITAL CLINICO UNIVERSITARIO DE VALENCIA, VALENCIA, Spain, [9]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [10]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Stroke is a feared complication of giant cell arteritis (GCA). Tocilizumab (TCZ) has shown efficacy and safety in large-vessel vasculitis (LVV) including GCA. Our objective was to assess the effectiveness of TCZ in the stroke associated with GCA regarding to: i) prevent the appearance of new strokes, and ii) improve stroke if present.

	Overall (n=471)	GCA with stroke (n=7)	GCA without stroke (n=465)	P
Main demographic features				
- Age at diagnosis, years (mean±SD)	72.1±9.1	73.3±4.7	72.1±9.1	0.84
- Age at TCZ initiation, years (mean± SD)	74±9	75.9±7.9	73.5±9.0	0.71
- Sex, women/men, n (% women)	342/129 (73)	2/5 (29)	340/124 (73)	**0.019**
GCA fulfilling ACR 1990 classification criteria, n (%)	344 (73)	6 (86)	338 (73)	0.68
Time from diagnosis to TCZ initiation (months), median [IQR]	6 [2-18]	8 [2-21.5]	6 [2-18]	0.84
Biopsy-proven GCA, n (%)	201 (43)	4 (57)	197 (42)	0.99
GCA phenotypes, n (%)				
- Cranial	217 (46)	4 (57)	213 (46)	0.71
- Extracranial	80 (17)	0 (0)	80 (17)	0.61
- Mixed	174 (37)	3 (50)	171 (37)	0.71
Cardiovascular risk factors, n (%)				
- High blood pressure, n (%)	272 (58)	5 (71)	267 (57)	0.71
- Dyslipidemia, n (%)	241 (51)	6 (86)	235 (50)	0.13
- Diabetes, n (%)	81 (17)	3 (50)	78 (17)	0.12
- Previous or current smoking history, n (%)	47 (10)	3 (50)	44 (12)	**0.028**
Systemic manifestations, n (%)				
- Fever, n (%)	57 (12)	2 (33)	55 (12)	0.21
- Constitutional syndrome, n (%)	175 (37)	1 (17)	174 (37)	0.26
- PMR, n (%)	284 (60)	4 (57)	280 (60)	0.99
Cranial manifestations, n (%)				
- Visual involvement, n (%)	81 (17)	2 (29)	79 (17)	0.35
- Headache, n (%)	259 (55)	3 (50)	256 (55)	0.71
- Jaw claudication, n (%)	112 (24)	4 (67)	108 (23)	0.069
Analytical findings				
- ESR, mm/1st hour, median [IQR]	32 [12-57]	77 [44-88.5]	30 [11-54]	0.075
- CRP, mg/dL, median [IQR]	1.5 [0.5-3.4]	6.1 [1.3-7.9]	1.4 [0.4-3.4]	0.66
- Hemoglobin (g/L), mean±SD	12.6±1.5	12.2±2.0	12.6±1.5	0.85
TCZ administration schedule				
- TCZmono / TCZcombo, n (% TCZ mono)	353/118 (75)	5/2 (71)	348/116 (75)	0.99
TCZ administration route and dose				
- Intravenous (IV) 8 mg/kg/4 weeks/subcutaneous (SC) 162 mg/week (% IV)	238/233 (50)	5/2 (71)	233/231 (50)	0.45

Abbreviations: ACR: American College of Rheumatology; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; IQR: interquartile range; n: number; PMR: polymyalgia rheumatica; SD: standard deviation; TCZcombo: tocilizumab in combination with synthetic immunosuppressant (besides glucocorticoids) agents; TCZmono: tocilizumab in monotherapy (besides glucocorticoids).

TABLE. Main features of the GCA patients with and without strokes treated with tocilizumab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Observational, multicenter study of 471 patients with GCA treated with TCZ. Patients were diagnosed with GCA accordingly to: a) American College of Rheumatology (ACR) criteria, and/or b) positive biopsy of temporal artery, and/or c) the presence of imaging techniques consistent with LVV. Patients were divided into two groups: i) with, and ii) without stroke.

All patients in whom stroke was diagnosed had lesions on computed tomography (CT) and/or magnetic resonance imaging (MRI) scans that were read by a neuroradiologist and correlated clinically by a neurologist.

Results: 471 (342 females; 72.1±9.1 years) patients with GCA treated with TCZ were included. Stroke at any time (before and after TCZ) were observed in 7 (1.5%) patients. In 5 of them stroke was present at TCZ initiation. One patient had a stroke previously with complete recovery and another patient had a stroke after starting TCZ and died. Main features of GCA with and without stroke are shown in TABLE. Patients with stroke were predominantly male and were or had been smokers. At TCZ initiation 5 patients had a stroke in vertebrobasilar territory.

Only one patient suffered lacunar infarctions after TCZ initiation, while the 5 patients who had a stroke at TCZ initiation experienced progressive improvement.

Conclusion: Stroke in GCA is an infrequent manifestation of GCA and occur mainly in the vertebrobasilar territory. TCZ might prevent the appearance of new strokes and appears to aid recovery in existing ones.

Disclosure: A. Serrano-Combarro: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **C. Moriano**: None; **S. Castañeda**: None; **J. Narváez**: None; **V. Aldasoro Cáceres**: None; **R. Melero-González**: None; **I. De la Morena**: None; **I. Ferraz Amaro**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0737

Effectiveness and Safety of Janus Kinase Inhibitors in Giant Cell Arteritis. Real-World Clinical Practice Study and Literature Review

Ana Serrano-Combarro[1], Fernando Lopez Gutierrez[2], Javier Loricera[3], toluwalase Tofade[4], Diana Prieto-Peña[5], Susana Romero-Yuste[6], Eugenio de Miguel[7], Anne Riveros frutos[8], DALIFER FREITES[9], Ivan Ferraz Amaro[10], Santos Castañeda[11], Eztizen Labrador-Sanchez[12], Olga Maiz[13], Elena Becerra-Fernández[14], Javier Narváez[15], Eva Galíndez Agirregoikoa[16], Ismael González[17], Ana Urruticoechea-Arana[18], Angel Ramos Calvo[19], Patricia Moya Albarado[20], Sebastian H Unizony[21] and Ricardo Blanco[22], [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, Immunopathology Group -IDIVAL, Reumatología, Santander, Santander, Spain, [3]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [4]Massachussetts General Hospital, Boston, MA, [5]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [6]University Hospital Complex of Pontevedra, Pontevedra, Spain, [7]Hospital Universitario La Paz, Madrid, Spain, [8]Hospital Germans Trias i Pujol, Barcelona, Spain, [9]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [10]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [11]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [12]Hospital Universitario San Pedro, Laguardia, Spain, [13]Hospital Universitario de Donostia, San Sebastián, Pais Vasco, Spain, [14]Hospital Universitario de Elda, Alicante, Comunidad Valenciana, Spain, [15]Hospital Universitario de Bellvitge, Barcelona, Spain, [16]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [17]Complejo Asistencial Universitario de León, León, Castilla y Leon, Spain, [18]Hospital Son Espases, Palma de Mallorca, Islas Baleares, Spain, [19]Complejo Hospitalario de Soria, Soria, Castilla y Leon, Spain, [20]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [21]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [22]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with giant cell arteritis (GCA) can relapse despite glucocorticoids, methotrexate and tocilizumab treatment. The JAK/STAT signalling pathway is involved in the pathogenesis of GCA, and JAK inhibitors (JAKi) are a potential treatment alternative. Our Objective was to evaluate the effectiveness and safety of JAKi in GCA.

Methods: Real-world, retrospective clinical practice study of patients with GCA treated with JAKi. Outcomes assessed included clinical remission and EULAR remission (clinical remission+CRP and ESR normalization), disease relapse and safety. A literature search for other JAKi-treated GCA cases was conducted in PubMed from inception to 11/30/2024.

Results: We include 40 patients (35 females/87.5%), mean age, 72.2 years, relapsing disease 40 (100%) that received JAKi. The initial JAKi was baricitinib (n=15), tofacitinib (n=10) and upadacitinib (n=15) **(Table and Figure)**. After a mean±SD follow-up of 12.4±6.8 months, 24 (60%) achieved a maintained remission, and 16 (40%) patients discontinued the initial JAKi due to relapse (n=12, 30%) or severe adverse events (SAEs) (n=4, 10%) including elevation of liver enzymes (n=1), disseminated herpes zoster (n=1), glioblastoma multiforme (n=1), and palpitations/dyspnea (n=1). Two patients developed an urinary tract infection and one patient anemia without requiring permanent JAKi discontinuation. The 12 patients failing the initial JAKi were switched to an alternative JAKi (n=2), biologic therapy (n=8) and azathioprine (n=1). One patient discontinued JAKi therapy due to sustained remission.

The literature review identified another 37 GCA patients (26 females, mean age 71.4 years) treated with JAKi, mostly with baricitinib (n=35). Most of these patients benefited from JAKi therapy **(Table)**. With respect to relevant adverse events, one patient suffered an *Aspergillus fumigatus* infection, other patient an *Enterococcus faecalis* bacteremia, and other thrombocytopenia **(Table)**.

Conclusion: This real-world analysis suggests that JAKi could be effective and relatively safe in GCA, including patients failing to other immunosuppressive therapies.

Reference	Number of cases	Sex	Age, mean±SD	JAKi received	Previous conventional synthetic immunosuppressive drugs	Previous biologic drugs	Follow-up (months), mean±SD	Outcome	Adverse events
Herlihy et al	1	Female	75	Ruxolitinib	Methotrexate, mycophenolate mophetil	None	9	No outcome data reported	None
Prigent et al	1	Female	76	Baricitinib	Methotrexate	Tocilizumab	12	Clinical improvement	None
Sanada et al	1	Female	72	Upadacitinib	Sulfasalazine	None	7.5	Clinical improvement	None
Camellino et al	4	Female (n=4)	70.5±11.7	Baricitinib (n=4)	Methotrexate (n=2), hydroxychloroquine (n=1), sulfasalazine (n=1), cyclosporine (n=1), mycophenolate mophetil (n=1)	Tocilizumab (n=4)	21.5±13.0; (no data in 1 patient)	Clinical improvement (n=2); no clinical improvement (n=2)	None
Koster et al	15	Female (n=11), male (n=4)	72.4±7.2	Baricitinib (n=15)	Methotrexate (n=2), Cyclophosphamide (n=1)	Sirukumab (n=1)	11.3±2.3	Clinical improvement (n=13); no improvement (n=1); no outcome data reported (n=1)	Thrombocytopenia (n=1), infections not requiring antibiotics (n=8), infections requiring antibiotics (n=5), nausea (n=6), leg oedema (n=2), fatigue (n=2), diarrhoea (n=1), abdominal pain (n=1), herpes zoster (n=1)
Eriksson et al	15	Female (n=8), male (n=3)	70.2±6.0	Baricitinib / tofacitinib	Methotrexate (n=3)	Tocilizumab (n=3), infliximab (n=1)	19±10.5	Clinical improvement (n=15)	Aspergillus fumigatus infection (n=1); Enterococcus faecalis bacteriemia (n=1)
Current series	40	Female (n=35), male (n=5)	72.2±7.9	Baricitinib (n=15), tofacitinib (n=10), upadacitinib (n=15)	Methotrexate (n=25), hydroxychloroquine (n=3), leflunomide (n=1)	Tocilizumab (n=29), sarilumab (n=3), abatacept (n=8), adalimumab (n=2), ustekinumab (n=2)	12.4±6.9	Clinical improvement (n=24); no improvement (n=12)	Urinary tract infection (n=2); anemia (n=1); elevation of liver enzymes (n=1); palpitations (n=1); dyspnea (n=1), disseminated herpes zoster (n=1); glioblastoma multiforme (n=1)

TABLE. Current series and literature review of patients with GCA treated with JAKi.

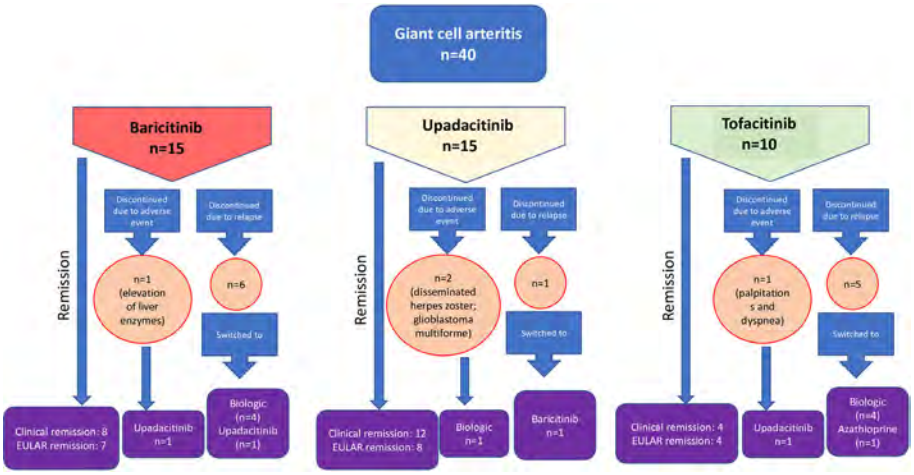


FIGURE. Flow chart of the 40 GCA patients treated with JAKi.

References

1. Calderón-Goercke M, et al. Clin Exp Rheumatol. 2023 Apr;41(4):829-836. doi: 10.55563/clinexprheumatol/oqs8u9
2. Loricera J et al. Clin Exp Rheumatol. 2014 May-Jun;32(3 Suppl 82):S79-89. Epub 2014 May 15. PMID: 24854377.
3. Prieto Peña D, et al. Clin Exp Rheumatol. 2021 Mar-Apr;39 Suppl 129(2):69-75
4. Loricera J, et al. Ther Adv Musculoskelet Dis. 2022 Jul 22;14:1759720X221113747. doi: 10.1177/1759720X221113747

Disclosure: A. Serrano-Combarro: None; **F. Lopez Gutierrez**: Roche, Galápagos, Novartis, UCB Pharma, MSD, Celgene, Astra Zeneca, Grünenthal, Janssen, Abbvie, Lilly, Pfizer, 12, support for attending meetings and/or travel; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **t. Tofade**: None; **D. Prieto-Peña**: None; **S. Romero-Yuste**: AbbVie, 2, 6, AstraZeneca, 2, 6, Eli Lilly & Co., 2, 6, Galapagos, 6, UCB, 2; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **A. Riveros frutos**: None; **D. FREITES**: None; **I. Ferraz Amaro**: None; **S. Castañeda**: None; **E. Labrador-Sanchez**: None; **O. Maiz**: None; **E. Becerra-Fernández**: None; **J. Narváez**: None; **E. Galíndez Agirregoikoa**: None; **I. González**: None; **A. Urruticoechea-Arana**: None; **A. Ramos Calvo**: None; **P. Moya Albarado**: None; **S. Unizony**: Harvard Pilgrim Healthcare, 2, IQVIA, 2, Sanofi, 2; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0738

Real World Steroid Burden, Treatment Patterns, and Rheumatologists' Perceptions on Advanced Therapy in Giant Cell Arteritis

Anisha Dua[1], Aditi Kadakia[2], Patrick Zueger[3], Simran Marwaha[4], Nathaniel Zerad[3], Arathi Setty[3], William Jones[4] and Valerie Devauchelle[5], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]AbbVie Inc, Woburn, MA, [3]AbbVie Inc, North Chicago, IL, [4]Adelphi Real World, Bollington, United Kingdom, [5]UBO, Brest, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

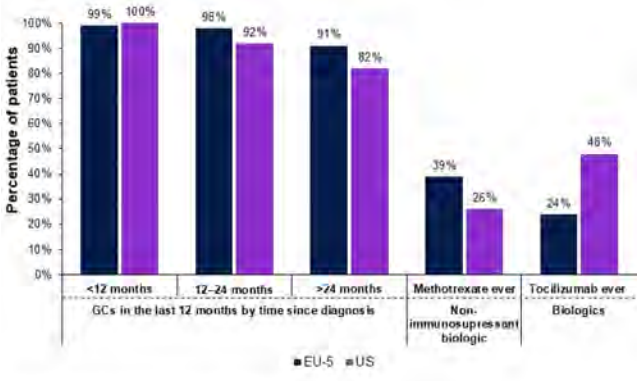
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Treatments received by patients in the EU-5 and US



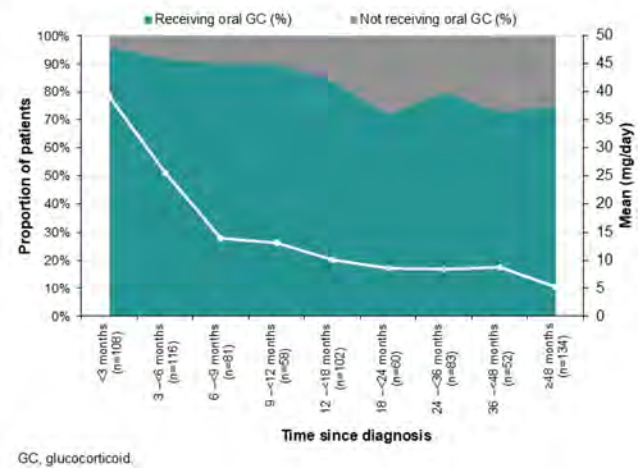
EU, Europe; GC, glucocorticoid; US, United States

Background/Purpose: Giant cell arteritis (GCA) is the most common vasculitis in patients 50 years and older. Glucocorticoids (GC) are the mainstay of treatment for GCA but can cause significant adverse events (AE). This study assessed GC burden, treatment patterns and rheumatologists' perceptions of advanced therapies (AT) for GCA.

Methods: Data were from the Adelphi Real World GCA Disease Specific Programme™, a cross-sectional, retrospective survey of rheumatologists and their adult (≥18 years) patients with GCA in France, Germany, Italy, Spain, and the United Kingdom (EU-5), and the United States (US) from 05/2024–10/2024. Rheumatologists completed patient record forms (PRF) for each patient to record demographics, treatment history and clinical characteristics. Rheumatologists were surveyed on their patient management approach and treatment perceptions. Patients for whom a PRF was completed were invited to fill in a self-assessment form.

Results: Overall, 189 rheumatologists were surveyed. Among 846 patients with GCA (EU-5: France, N=133; Germany, N=120; Italy, N=144; Spain, N=120; UK, N=129; US: N=200), 63% were female, 94% were white, mean age was 71 years and median time since diagnosis was 15.2 months. Most patients were using GCs, regardless of time since diagnosis. The next most common treatments were tocilizumab (EU-5, 24%; US, 48%) and methotrexate (EU-5, 39%; US, 26%; **Figure 1**). Median time from diagnosis to receiving tocilizumab or methotrexate was approximately 5 months. Over the last 12 months, median cumulative GC doses were 4343 mg, 5200 mg and 2196 mg for patients diagnosed < 1 year, 1–2 years, and >2 years ago, respectively. Most rheumatologists (87%) aimed to taper to low dose GCs by 12 months and 79% aimed to

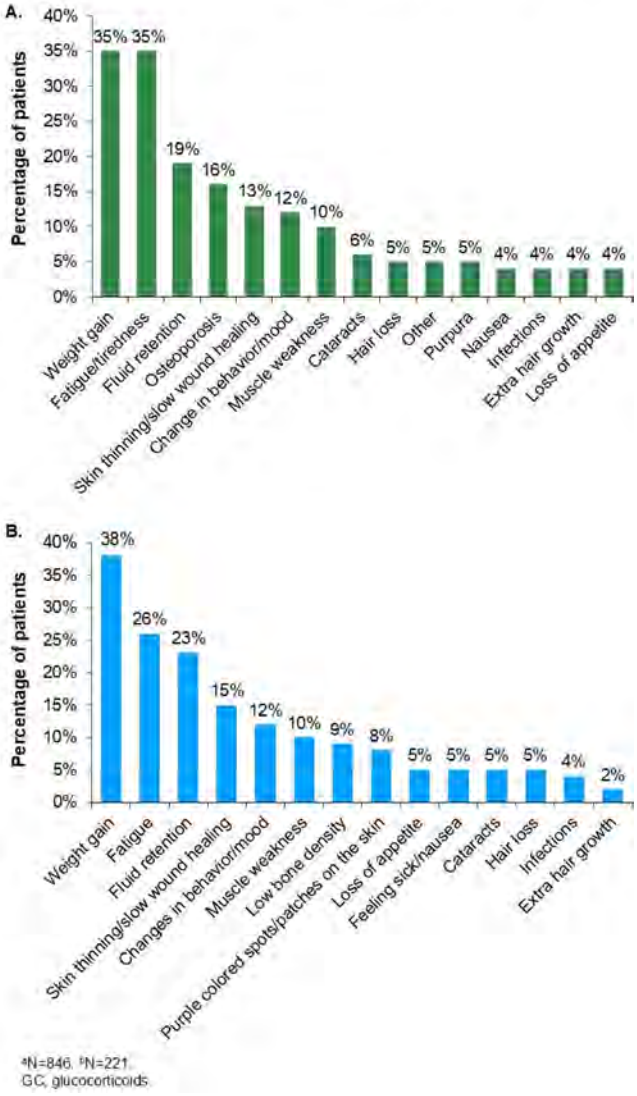
Figure 2. Oral GC received by disease duration



GC, glucocorticoid.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3. GC-related adverse events, reported by (A) rheumatologists[a] and (B) patients[b]



[a]N=846. [b]N=221.
GC, glucocorticoids

taper off GCs completely by 24 months post-diagnosis. At 24–< 36 months post-diagnosis, 80% of patients were on an average daily GC dose of 8.4 mg, and 75% were taking an average of 5.3 mg/day at ≥48 months (**Figure 2**). The number of patients experiencing ≥1 GC-related AE was higher when reported by rheumatologists (74%) compared to patients (55%; **Figure 3**). Most rheumatologists (EU-5, 90%; US, 94%) agreed that ATs should be given early in GCA treatment to improve outcomes and reduce GC toxicity. Over 90% of rheumatologists believed the following AT attributes were important: maintenance of remission; achievement of GC-free remission; reduction of high-dose/cumulative GC use; to allow GC cessation; and to be safe, tolerable, and patient-compliant. Most rheumatologists agreed that limited choices in AT administration routes are a barrier to widespread use (EU-5, 51%; US, 80%) and that convenient administration is an important attribute of ATs (EU-5, 65%; US, 84%). Most patients (75%) stated that they preferred receiving treatments orally rather than by injection or infusion.

Conclusion: Even though most rheumatologists aimed to taper patients off GCs completely by 24 months, 75% of patients were using GCs at 4 years. Both rheumatologists and patients reported several AEs associated with GC use, and rheumatologists recognize the need for early and effective steroid sparing intervention with ATs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Dua: AbbVie/Abbott, 2, Amgen, 2, 5, 12, Clinical Trials, AstraZeneca, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, 12, Clinical Trials, Rheumatology Research Foundation, 4, 5, 12, Clinical Trials, Sanofi, 2, Vasculitis Foundation, 4; **A. Kadakia**: AbbVie, 3, 11; **P. Zueger**: AbbVie, 3, 11; **S. Marwaha**: Adelphi Real World, 3; **N. Zerad**: AbbVie, 3, 11; **A. Setty**: AbbVie, 3, 11; **W. Jones**: Adelphi Real World, 3; **V. Devauchelle**: None.

Abstract Number: 0739

Tocilizumab in Giant Cell Arteritis with ischemic vs non-ischemic manifestations

Carmen Secada-Gómez[1], Javier Loricera[2], Clara Moriano[3], Santos Castañeda[4], Javier Narváez[5], Vicente Aldasoro Cáceres[6], Olga Maiz[7], Rafael B. Melero-González[8], Paloma Vela Casasempere[9], Susana Romero-Yuste[10], Jose Luis Callejas[11], Eugenio de Miguel[12], Eva Galíndez Agirregoikoa[13], Francisca Sivera[14], Ivan Ferraz Amaro[15], Julio Sánchez Martín[16] and Ricardo Blanco[1], [1]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Hospital León, LEON, Castilla y Leon, Spain, [4]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [5]Hospital Universitario de Bellvitge, Barcelona, Spain, [6]Hospital Universitario de Navarra, Pamplona, Spain, [7]Hospital Universitario de Donosti, Donostia, Spain, [8]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [9]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [10]University Hospital Complex of Pontevedra, Pontevedra, Spain, [11]Department of Internal Medicine, Hospital San Cecilio, Granada, Spain, [12]Hospital Universitario La Paz, Madrid, Spain, [13]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [14]Hospital General Universitario Elda, Elda, Spain, [15]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [16]Hospital Universitario 12 de Octubre, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

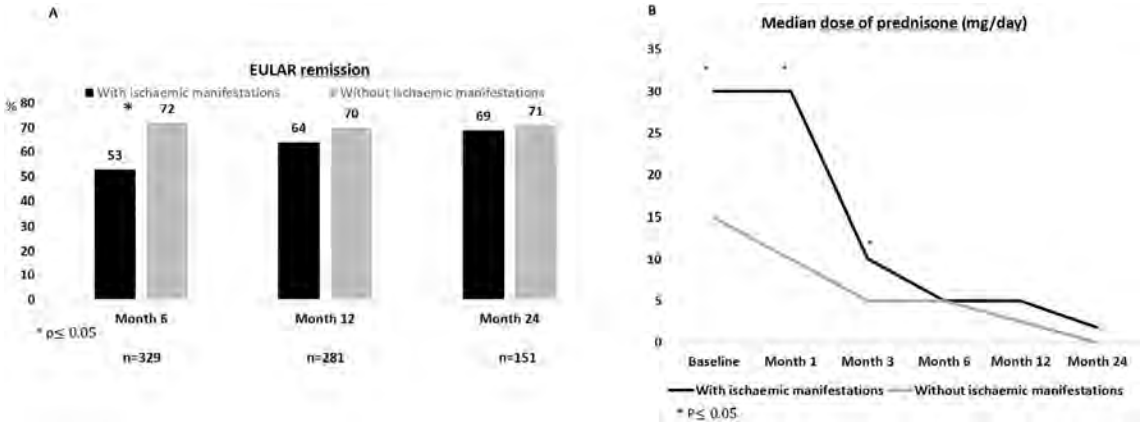
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Tocilizumab (TCZ) is the only approved biological drug in the treatment of giant cell arteritis (GCA). However, there are no comparative studies on the efficacy of TCZ in patients with GCA with ischaemic vs. non-ischaemic manifestations.

Our aim was to compare the effectiveness of TCZ in patients with GCA with ischaemic vs. non-ischaemic manifestations in clinical practice.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Multicentre observational and comparative study of 471 patients with GCA treated with TCZ. GCA was diagnosed by: i) ACR criteria, and/or ii) temporal artery biopsy, and/or iii) imaging techniques. In this case, a comparative subanalysis between patients with GCA with ischaemic manifestations (visual involvement and/or jaw claudication and/or stroke) and those with GCA with non-ischaemic manifestations was done. Remission was considered according to EULAR definitions, as the absence of signs and symptoms of GCA and the normalization of the ESR and CRP values (1).

Results: The 471 patients with GCA were divided into 2 subgroups: a) GCA with ischaemic manifestations (n=162), and b) GCA with non-ischaemic manifestations (n=309) (TABLE). Patients with ischaemic manifestations were older, met ACR1990 criteria more often, had positive temporal biopsy more frequently and the time from diagnosis to onset of TCZ was shorter. The predominant phenotype in patients with ischaemic manifestations was cranial GCA and they presented more frequently hypertension and higher mean CRP and ESR values. The mean dose of prednisone was higher in this group, while concomitant use with a conventional synthetic DMARD was more frequent in the non-ischaemic group.

No significant differences were observed between the two groups in terms of remission except within the 6 months of starting TCZ, which was higher in the non-ischaemic group (FIGURE). Glucocorticoid dose was higher in the GCA group with ischaemic manifestations during the first 3 months, but was similar in both groups thereafter.

	Overall (n=471)	GCA with ischaemic manifestations (n=162)	GCA without ischaemic manifestations (n=309)	P
Main demographic features				
- Age at diagnosis, years (mean±SD)	72.1±9.1	75.2±7.8	70.5±9.3	**<0.001**
- Age at TCZ initiation, years (mean± SD)	74±9	76.1±7.9	72.2±9.3	**<0.001**
- Sex, women/men, n (% women)	342/129 (73)	110/52 (68)	232/77 (75)	0.097
GCA fulfilling ACR 1990 classification criteria, n (%)	344 (73)	144 (89)	200 (65)	**<0.001**
Time from diagnosis to TCZ initiation (months), median [IQR]	6 [2-18]	4 [1-11.2]	8 [3-24]	**<0.001**
Biopsy-proven GCA, n (%)	201 (43)	84 (52)	117 (38)	**0.003**
GCA phenotypes, n (%)				
- Cranial	217 (46)	109 (67)	108 (35)	**<0.001**
- Extracranial	80 (17)	0 (0)	80 (26)	**<0.001**
- Mixed	174 (37)	53 (33)	121 (39)	0.17
Cardiovascular risk factors, n (%)				
- High blood pressure, n (%)	272 (58)	110 (68)	162 (52)	**0.004**
- Dyslipidemia, n (%)	241 (51)	85 (53)	156 (50)	0.98
- Diabetes, n (%)	81 (17)	35 (22)	46 (15)	0.096
- Previous or current smoking history, n (%)	47 (10)	19 (12)	28 (9)	0.41
Systemic manifestations, n (%)				
- Fever, n (%)	57 (12)	25 (15)	32 (10)	0.12
- Constitutional syndrome, n (%)	175 (37)	68 (42)	107 (35)	0.14
- PMR, n (%)	284 (60)	97 (60)	187 (60)	0.76
Cranial manifestations, n (%)				
- Visual involvement, n (%)	81 (17)	81 (50)	0 (0)	**<0.001**
- Headache, n (%)	259 (55)	127 (78)	132 (43)	**<0.001**
- Jaw claudication, n (%)	112 (24)	112 (70)	0 (0)	**<0.001**
- Cerebrovascular accident, n (%)	5 (1)	5 (3)	0 (0)	**0.005**
Analytical findings				
- ESR, mm/1st hour, median [IQR]	32 [12-57]	36 [12-69.5]	27 [11-51]	**0.023**
- CRP, mg/dL, median [IQR]	1.5 [0.5-3.4]	1.5 [0.4-4.7]	1.4 [0.4-2.9]	**0.005**
- Hemoglobin (g/L), mean±SD	12.6±1.5	12.5±1.6	12.7±1.5	0.24
TCZ administration schedule				
- TCZmono / TCZcombo, n (% TCZ mono)	353/118 (75)	135/27 (83)	218/91 (71)	**0.002**
TCZ administration route and dose				
- Intravenous (IV) 6 mg/kg/4 weeks/subcutaneous (SC) 162 mg/week (% IV)	238/233 (50)	71/91 (44)	167/142 (54)	**0.035**

Abbreviations: ACR: American College of Rheumatology; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; GCA: giant cell arteritis; IQR: interquartile range; n: number; PMR: polymyalgia rheumatica; SD: standard deviation; TCZcombo: tocilizumab in combination with synthetic

TABLE. Main features of GCA patients with and without ischaemic manifestations treated with tocilizumab.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The effectiveness of TCZ appears to be similar in patients with GCA with ischaemic and in patients with non-ischaemic manifestations, although in the latter group combined treatment was more frequent.

Disclosure: C. Secada-Gómez: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **C. Moriano**: None; **S. Castañeda**: None; **J. Narváez**: None; **V. Aldasoro Cáceres**: None; **O. Maiz**: None; **R. Melero-González**: None; **P. Vela Casasempere**: None; **S. Romero-Yuste**: AbbVie, 2, 6, AstraZeneca, 2, 6, Eli Lilly & Co., 2, 6, Galapagos, 6, UCB, 2; **J. Callejas**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **E. Galíndez Agirregoikoa**: None; **F. Sivera**: None; **I. Ferraz Amaro**: None; **J. Sánchez Martín**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0740

Intravenous versus subcutaneous administration of Tocilizumab in aortitis associated with giant cell arteritis: multicenter open-label study of 196 patients

Carmen Secada-Gómez[1], Javier Loricera[2], Adrian Martin-Gutierrez[3], Santos Castañeda[4] and Ricardo Blanco[1], [1]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Piélagos, Spain, [4]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Aortitis associated to Giant cell arteritis (GCA) (GCA-aortitis) is one of the most severe manifestation of GCA. Tocilizumab (TCZ) has demonstrated efficacy in large-vessel vasculitis (LVV) including GCA, previous pharmacokinetic studies, have shown more stable and sustained levels of tocilizumab with the subcutaneous form compared to the intravenous form. However, there are no studies comparing intravenous (IV) vs subcutaneous (SC) administration of TCZ in GCA-aortitis.

Our aim was to compare the effectiveness of TCZ in GCA-aortitis according the route of administration (IV vs SC) in a wide series of patients in a clinical world setting.

Methods: Multicentre study of 196 patients diagnosed with GCA-aortitis by imaging techniques and treated with TCZ. Patients were divided in two groups according to the route of administration of TCZ: i) IV, and ii) SC. GCA was diagnosed by 1990 ACR criteria, and/or temporal artery biopsy and/or imaging techniques. Aortitis was diagnosed mainly by ^{18}F-FDG-PET/CT. Main outcomes were EULAR remission definition (clinical remission and normalization of CRP and ESR), imaging remission (considered when vascular FDG uptake was less than liver uptake in ^{18}F-FDG PET/CT) and glucocorticoid withdrawal after TCZ initiation.

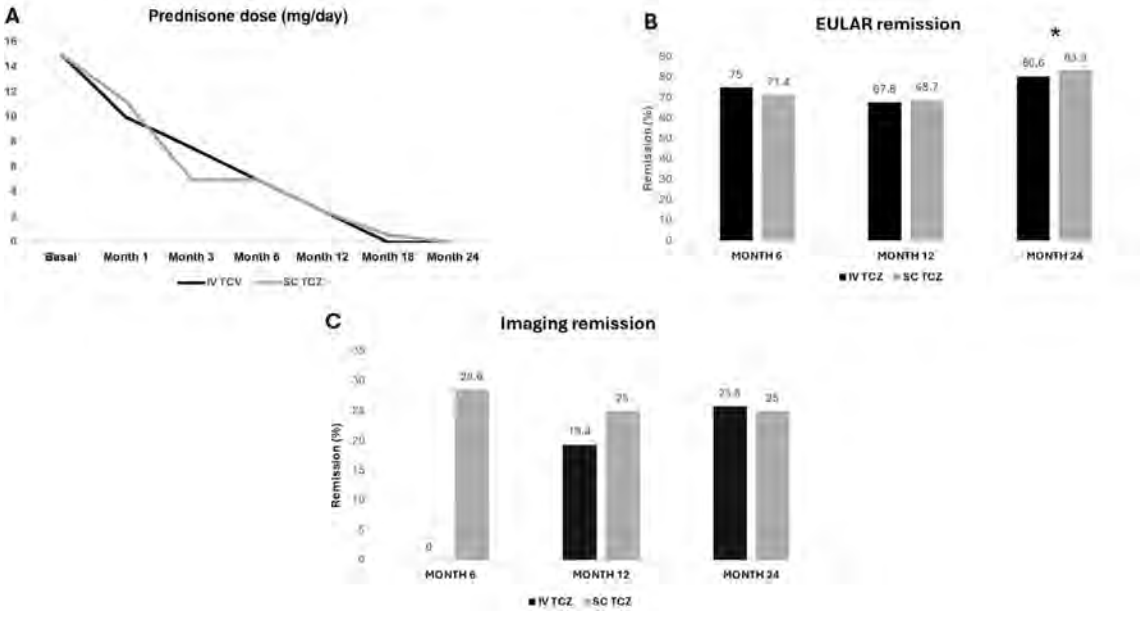
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	TCZ IV (n=110)	TZC SC (n=86)	p
Baseline characteristics at TCZ onset			
Age (years), mean±SD	70.4±9.5	69±9.3	0.34
Sex, female/male (% female)	81/29 (73.6)	67/19 (77.9)	0.49
Time from GCA diagnosis to TCZ onset (months), median [IQR]	9.5 [3 -21.3]	6 [2-17]	0.26
ACR 1990 criteria, n (%)	63 (57.3)	41 (47.7)	0.11
Phenotype, n (%)			
-*Extracranial*	34 (30.9)	36 (41.9)	
-*Mixed*	76 (69.1)	50 (58.1)	
Cardiovascular risk factors, n (%)			
-*High blood pressure*	60 (54.5)	48 (55.8)	0.85
-*Dyslipidaemia*	62 (56.4)	41 (47.7)	0.22
-*Diabetes*	20 (18.2)	14 (16.3)	0.72
-*Previous or current smoker history*	12 (10.9)	8 (9.3)	0.71
Systemic manifestations, n (%)			
-*PMR*	73 (66.4)	58 (67.4)	0.87
-*Constitutional syndrome*	48 (43.6)	39 (45.3)	0.81
-*Fever*	17 (15.5)	7 (8.1)	0.12
Ischemic manifestations, n (%)			
-*Headache*	43 (39.1)	31 (36)	0.66
-*Jaw claudication*	16 (14.5)	11 (12.8)	0.72
-*Visual impairment*	11 (10)	5 (5.8)	0.28
-*Stroke*	0	1 (1.2)	0.26
Laboratory parameters			
-*ESR, mm 1st hour , median [IQR]*	29 [14-54]	32 [14.5-55]	0.72
-*CRP, mg/dl, median [IQR]*	1 [0-3]	1 [0-3]	0.89
Prednisone dose, mg/day, median [IQR]	15 [10-30]	15 [9.25-30]	0.37
TCZ monotherapy / TCZ combined (% monotherapy)	69/41 (62.7)	67/19 (77.9)	—

Abbreviations: ACR: American College of Rheumatology, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, GCA: giant cell arteritis, IQR: interquartile range, IV: intravenous, n: number, PMR: polymyalgia rheumatica, SC: subcutaneous, SD: standard deviation, TCZ: tocilizumab.

Results: We studied 196 patients (148 women 48 men) ,mean age 69.8±9.4 years treated with TCZ were included. One hundred and ten received IV-TCZ and 86 SC-TCZ (Table). Time between diagnosis of aortitis-GCA and TCZ initiation was shorter in SC group, although without reaching statistical significance. Interestingly, no differences in acute phase reactants were observed at TCZ initiation between both groups. There were no differences between the two routes of TCZ

Figure. Evolution of main outcomes in patients with GCA- aortitis treated with TCZ. A comparison between intravenous and subcutaneous TCZ. (A) Prednisone dose (mg/day). (B), (C) EULAR and imaging remission at 6, 12 and 24 months. * p<0.05



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

administration in glucocorticoid-sparing effect after TCZ initiation. Noticeably, statistical differences in EULAR remission definition were observed after 24-month follow-up, although there were no differences in imaging remission (Figure).

Conclusion: In GCA-aortitis, SC TCZ might be more effective than IV in achieving the EULAR remission target in clinical practice conditions after 24-month follow-up.

Disclosure: C. Secada-Gómez: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **A. Martin-Gutierrez**: None; **S. Castañeda**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0741

Characteristics of African American vs. Non-African American Patients with Giant Cell Arteritis: A Retrospective Cohort Study

Dana Nachawati[1], Milad Heydari-Kamjani[2], Keri Ann Pfeil[1], Elleson Harper[1], Meghan Gump[1], Lindsay Frumker[1], Ansaam Daoud[3] and Omer Pamuk[2], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [3]Case Western Reserve University/University Hospitals, Cleveland, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: GCA is a vasculitis of large and medium-sized arteries that has been well-studied in populations of European descent; however, data on African American (AA) patients remain sparse. We aimed to assess racial differences in demographics, comorbidities, treatment, inflammatory markers, and outcomes in GCA.

Methods: We conducted a retrospective cohort study using TriNetX, a network of de-identified electronic medical records from 102 healthcare organizations. Adults with GCA (ICD-10-CM: M31.5, M31.6) from 2004–2024 were grouped as AA or non-African American (non-AA) (including White, Asian, Hispanic, and others). After 1:1 propensity score matching (33 covariates), cohorts were compared for comorbidities, treatments, inflammatory markers (CRP,ESR at 0/6/12 months), and mortality. Kaplan-Meier survival analysis and Cox regression were used for survival analysis.

Results: 6,507 AA and 40,683 non-AA patients were identified; after matching, 6,505 remained in each group. AA patients were younger at diagnosis (65.1 vs 68.9 years, $p< 0.001$) and more likely to be female (79 vs.67%, $p < 0.001$). Hypertension (HTN) and diabetes (DM) were more prevalent in AA, while PMR, anterior ischemic optic neuropathy (AION), and aortic aneurysms were more common in non-AA individuals. Prednisone, MTX, and tocilizumab were comparable between groups (Table 1).

After matching and at baseline, CRP was lower in AA than non-AA patients (25.4 vs. 32.7 mg/L, $p< 0.001$), while ESR was higher (54.5 vs. 42.6 mm/h, $p< 0.001$). Notably, AA patients continued to exhibit higher ESR and CRP levels at 6 and 12 months (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of African American cohort versus non-African American cohort

	Before Matching			After Matching		
Variable	African American (n = 6,507)	Non-African American (n=40,683)	P-Value	African American (n=6,505)	Non-African American (n=6,505)	P-Value
Demographics						
Age at Index (Mean ± SD)	65.1 ± 11.4	68.9 ± 10.8	<0.001	65.1 ± 11.4	64.9 ± 11.8	0.308
Female	5,135 (78.9%)	27,356 (67.2%)	<0.001	5,132 (78.9%)	5,107 (78.5%)	0.592
Male	1,273 (21.1%)	13,092 (32.3%)	<0.001	1,372 (21.1%)	1,396 (21.5%)	0.607
Baseline comorbidities						
Essential hypertension	4,484 (68.9%)	19,891 (48.9%)	<0.001	4,482 (68.9%)	4,445 (68.3%)	0.485
Diabetes mellitus	3937 (60.5%)	12,071 (29.7%)	<0.001	2,689 (41.3%)	2,649 (40.7%)	0.476
GCA related comorbidities						
Polymyalgia rheumatica	251 (3.9%)	3,317 (8.2%)	<0.001	251 (3.9%)	228 (3.5%)	0.284
Thoracic aortic aneurysm	65 (1.0%)	659 (1.6%)	<0.001	65 (1.0%)	45 (0.7%)	0.055
Abdominal aortic aneurysm	84 (1.3%)	705 (1.7%)	0.010	84 (1.3%)	81 (1.2%)	0.814
Osteoporosis with vertebral fracture	16 (0.2%)	203 (0.5%)	0.005	16 (0.2%)	11 (0.2%)	0.335
Right femur fracture	10 (0.2%)	30 (0.1%)	0.040	10 (0.2%)	10 (0.2%)	1
Left femur fracture	10 (0.2%)	24 (0.1%)	0.008	10 (0.2%)	10 (0.2%)	1
Blindness of both eyes	25 (0.4%)	80 (0.2%)	0.003	25 (0.4%)	19 (0.3%)	0.365
Blindness of one eye	52 (0.8%)	226 (0.6%)	0.017	52 (0.8%)	36 (0.6%)	0.087
Unspecified visual loss	340 (5.2%)	1,462 (3.6%)	<0.001	340 (5.2%)	298 (4.6%)	0.088
Amaurosis fugax	70 (1.1%)	505 (1.2%)	0.258	70 (1.1%)	58 (0.9%)	0.286
Ischemic optic neuropathy	87 (1.3%)	858 (2.1%)	<0.001	87 (1.3%)	68 (1.0%)	0.125
Central retinal artery occlusion	74 (1.1%)	321 (0.8%)	0.004	74 (1.1%)	52 (0.8%)	0.049
Medications						
Prednisone	2,659 (40.9%)	14, 765 (36.3%)	<0.001	2,658 (40.9%)	2,582 (39.7%)	0.174
Methotrexate	227 (3.5%)	1,360 (3.3%)	0.545	227 (3.5%)	193 (3.0%)	0.092
Tocilizumab	50 (0.8%)	328 (0.8%)	0.751	50 (0.8%)	43 (0.7%)	0.466
Laboratory						
C reactive protein (mg/L)	25.4 ± 42.8	34.5 ± 53.6	<0.001	25.4 ± 42.8	32.7 ± 52.7	<0.001
Erythrocyte sedimentation rate (mm/h)	54.4 ± 31.2	40.4 ± 31.2	<0.001	54.5 ± 31.2	42.6 ± 31.3	<0.001

Survival analysis revealed a statistically significant difference in mortality between the two groups (Figure 1). Mortality risk was 11.9% in AA vs. 14.3% in non-AA, a difference of –2.4% ($p < 0.001$). The risk ratio was 0.833 and the odds ratio was 0.811, suggesting a 17–19% relative risk reduction. Kaplan-Meier analysis showed higher survival probability in AA patients (50.44% vs. 36.05%; $p = 0.001$). Cox regression showed a 14.4% lower mortality hazard (hazard ratio 0.856), with the proportional hazards assumption met.

Table 2. Inflammatory marker analysis at time of diagnosis, 6 months, 12 months in African American cohort versus non-African American cohort after matching

	African American (n=6,505)	Non-African American (n=6,505)	P-value
C reactive protein (mg/L)			
Time of diagnosis	25.4 ± 42.8 (n=1,673)	32.7 ± 52.7 (n=1,745)	<0.001
6 months after diagnosis	23.8 ± 45.9 (n=1,839)	20.7 ± 42.2 (n=1,669)	<0.001
12 months after diagnosis	23.7 ± 47.2 (n=742)	15.8 ± 33.8 (n=794)	<0.001
ESR (mm/h)			
Time of diagnosis	54.5 ± 31.2 (n=1,996)	42.6 ± 31.3 (n=2,079)	<0.001
6 months after diagnosis	43.4 ± 29.8 (n=2,124)	27.9 ± 26.4 (n=2,209)	<0.001
12 months after diagnosis	41.1 ± 29.7 (n=894)	25.6 ± 24.0 (n=1,093)	<0.001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

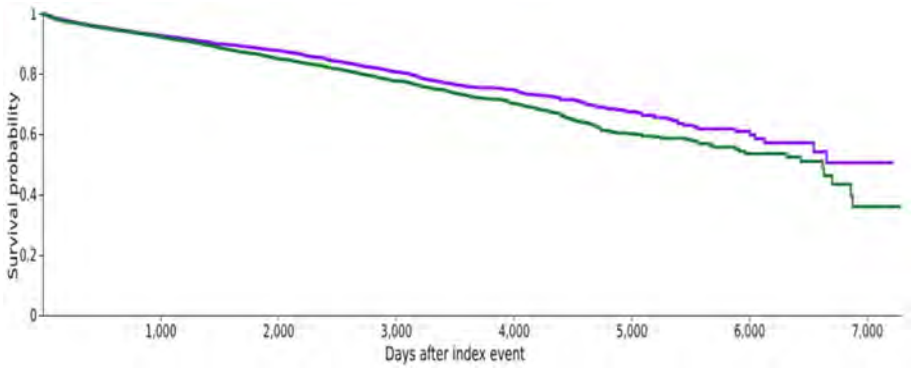


Figure 1. Kaplan-Meier Survival Analysis of Mortality in African American versus non-African American Patient's with GCA. Key: Purple = African American cohort. Green = non-African American cohort

Conclusion: In our study, AA patients with GCA were younger and more often female at diagnosis compared to non-AA patients. Comorbid HTN and DM were more common in the AA group, while PMR, AION, and aortic aneurysms were more prevalent in the non-AA group.

Despite higher inflammatory markers, AA patients had lower mortality and improved survival than other races in this matched cohort. Variations in disease phenotype, comorbidity burden, healthcare access, or other clinical and sociodemographic factors may drive these differences. Further investigation is warranted to explore potential contributors to these outcome differences.

Disclosure: D. Nachawati: None; **M. Heydari-Kamjani**: None; **K. Pfeil**: None; **E. Harper**: None; **M. Gump**: None; **L. Frumker**: None; **A. Daoud**: None; **O. Pamuk**: None.

Abstract Number: 0742

Exploring Racial Variation in the Clinical Manifestations of Giant Cell Arteritis: A Retrospective Single-Center Study

Dana Nachawati[1], Chelsea Guan[1], Amir Daneshvar[1], Ansaam Daoud[2] and Omer Pamuk[3], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]Case Western Reserve University/ University Hospitals, Cleveland, OH, [3]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a large and medium vessel vasculitis affecting older adults of Northern European descent. While GCA is well characterized in Caucasian (CA) populations, emerging data suggest possible racial differences in disease expression. This study aimed to assess racial variation in clinical and lab presentation of GCA between African American (AA) and CA patients.

Methods: We performed a retrospective chart review of patients meeting the 2022 ACR/EULAR classification criteria for GCA in the Rheumatology Department at University Hospitals. Patients were categorized as AA vs. CA. Extracted data included demographics, presenting symptoms, temporal artery biopsy (TAB) status and results, relapse, mortality, and lab parameters at diagnosis. This study was IRB approved.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Exploration of variables including baseline characteristics, presenting symptoms, rate of biopsy-proven GCA, relapse, and all cause-mortality in Caucasian versus African American patients with GCA

Variables	Caucasian with GCA (n=55)	African American with GCA (n=10)	p-value
Characteristics			
Female	40 (72.7%)	10 (100%)	0.060
Male	15 (27.3%)	0 (0%)	0.060
Age ± Standard Deviation	78.75 ± 9.16	78.6 ± 12.39	0.972
Hyperlipidemia	48 (87.3%)	7 (70%)	0.164
Hypertension	46 (83.6%)	8 (80%)	0.778
Diabetes	13 (23.6%)	5 (50%)	0.087
Smoking	19 (34.5%)	5 (50%)	0.766
Alcohol use	19 (34.5%)	4 (40%)	0.109
Presenting symptoms			
Headaches	43 (78.5%)	8 (80%)	0.898
Temporal headache	39 (70.9%)	8 (80%)	0.555
Scalp tenderness	31 (56.4%)	7 (70%)	0.421
Jaw claudication	28 (50.9%)	4 (40%)	0.526
PMR	13 (23.6%)	5 (50%)	0.087
Visual complaint	28 (50.9%)	7 (70%)	0.265
Visual loss	11 (20%)	2 (20%)	1.000
Amaurosis fugax	10 (18.2%)	2 (20%)	0.892
Diplopia	10 (18.2%)	1 (10%)	0.526
Anterior ischemic optic neuropathy (AION)	6 (10.9%)	2 (20%)	0.421
Large vessel involvement	3 (5.5%)	0 (0%)	0.450
Fever of unknown origin	3 (5.5%)	1 (10%)	0.582
Fatigue	13 (23.6%)	2 (20%)	0.802
Night sweats	8 (14.5%)	0 (0%)	0.198
Weight loss	5 (9.1%)	0 (0%)	0.321
Biopsy proven	38 (69.1%)	2 (20%)	0.003
Relapse	19 (34.5%)	5 (50%)	0.352
All-cause mortality	5 (7.7%)	0 (0%)	0.321

Chi-square (χ^2) tests evaluated associations between race and categorical variables; Two-sided t-tests assessed continuous variables.

Results: Sixty-five patients (55 CA, 10 AA) were included. In this comparative analysis, mean age at diagnosis was similar (78.75 vs. 78.6 years, *p = 0.486*). All AA patients were female vs. 72.7% CA (p = 0.060). TAB was positive in 69.1% of CA vs. 20% of AA (p=0.003). Clinical manifestations, including headache, jaw claudication, and visual symptoms, were similar across groups.

Notable lab differences were seen at diagnosis. AA patients had higher ESR (79.8 vs. 58.4 mm/h, p = 0.005), while CRP levels were marginally higher in CA patients (8.4 vs. 4.7 mg/dL, p = 0.051). Hemoglobin and platelet counts were higher in CA patients (12.9 vs. 11.4 g/dL, p = 0.042) and (336 vs. 282 x10^3//μL, p = 0.047), respectively. No significant differences were observed in white blood cell (WBC) counts, relapse, or mortality.

Table 2. Comparison of inflammatory markers and hematologic laboratory values at time of GCA diagnosis

Lab value	Caucasian with GCA	African American with GCA	p-value
ESR (mm/h)	58.36 ± 31.74	79.80 ± 16.92	0.005
CRP (mg/dL)	8.37 ± 9.83	4.68 ± 3.74	0.051
WBC (x10*3/uL)	9.84 ± 3.12	8.68 ± 4.10	0.417
Hemoglobin (g/dL)	12.9 ± 1.29	11.4 ± 1.97	0.042
Platelets (x10*3/uL)	336.2 ± 117.24	282 ± 60.70	0.047

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Although age and clinical presentation were comparable, AA patients exhibited higher ESR and more anemia, while CA patients had marginally higher CRP and more biopsy-confirmed diagnoses. These findings may reflect biologic or system-level differences influencing disease recognition or expression. Further investigation is warranted to further clarify potential racial variations in GCA presentation and diagnostic pathways.

Disclosure: D. Nachawati: None; **C. Guan**: None; **A. Daneshvar**: None; **A. Daoud**: None; **O. Pamuk**: None.

Abstract Number: 0743

Giant Cell Arteritis Relapse After Treatment with Two Months of Prednisone and 12 Months of Tocilizumab

David O'Dea[1], Guy Katz[1], Belen Arevalo Molina[1], Adam Jarvie[2], Mark Matza[1], Ana Fernandes[1], John Stone[3] and Sebastian H Unizony[4], [1]Massachusetts General Hospital, Boston, MA, [2]Emory University School of Medicine, Atlanta, GA, [3]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The optimal duration of tocilizumab (TCZ) treatment for giant cell arteritis (GCA) is unclear. Observational studies have shown that 50-60% of patients relapse after receiving TCZ for ≥12 months in combination with ≥6-10 months of glucocorticoids (GC) [1]. However, there are no data on outcomes after treatment discontinuation in patients receiving TCZ with shorter GC tapers. We investigated the relapse rate of GCA patients after treatment with 2 months of prednisone and 12 months of TCZ.

Methods: The electronic medical records of patients with GCA who completed a pilot clinical trial of TCZ in combination with a short prednisone taper (11/2018-12/2021) [1] were retrospectively reviewed. During the clinical trial, in the absence of relapse, patients weaned off prednisone within 2 months and discontinued TCZ at month 12. The primary endpoint of the

Table 1: Baseline characteristics of GCA patients in remission after treatment with 2 months of glucocorticoids and 12 months of tocilizumab

	GCA patients (N = 23)
Age*, years	75 (71, 82)
Female sex	15 (65)
White race	23 (100)
New onset disease*	10 (43.5)
Disease duration at baseline, months	14.8 (13.8, 36.4)
Biopsy-proven disease	17 (74)
Imaging-proven disease	12 (52)
Cranial signs or symptoms*	20 (87)
GCA-related visual manifestations*	9 (39)
Polymyalgia rheumatica symptoms*	14 (61)
ESR*, mm/hour	50 (23, 63)
CRP*, mg/liter	40 (12.7, 80.4)
Cumulative prednisone dose during the trial, mg	962.5 (682.5, 1610)

Values are n (%) for categorical variables and median (IQR) for continuous variables. * At the time of onset of the clinical trial. ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

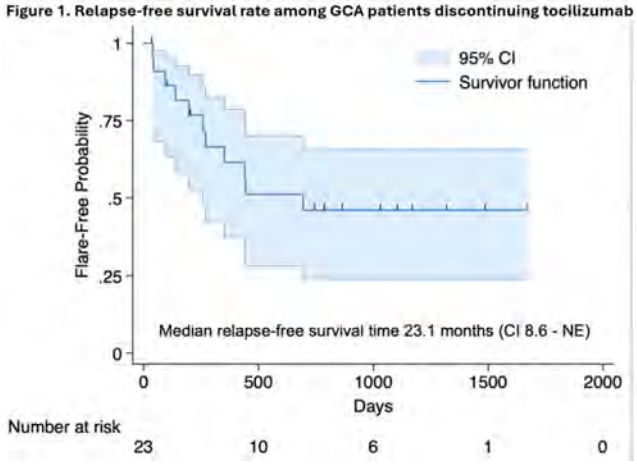
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Disease relapse and features of disease relapse after tocilizumab discontinuation

	Relapsers (N = 11)	Non-Relapsers (N = 12)	P-value
Female sex	7 (63.6)	8 (66.7)	1
Age	73 (71, 76)	78.5 (69.5, 83)	0.21
Cumulative GC dose	962.5 (717, 1610)	857.5 (735, 1124.4)	0.70
Newly diagnosed GCA at clinical trial onset	4 (36.4)	6 (50)	0.68
Disease duration at baseline, months	12.7 (15.1, 44)	13.6 (13, 19.8)	0.94
Time to relapse, months	8.6 (3.8, 13.2)	N/A	–
Clinical and laboratory manifestations at relapse			
Headache	4/11 (36.4)		
GCA-related visual manifestations	0/11 (0)		
Polymyalgia rheumatica symptoms	7/11 (63.6)		
Other*	1/11 (9.1)		
ESR, mm/hour	39 (25, 43.75)		
CRP, mg/liter	10.5 (5.6, 24.73)		
Relapse treatment			
Prednisone	10/11 (90.9)		
Initial prednisone dose, mg/day	20 (11.25, 52.5)		
Duration of prednisone taper, months	6 (6.53)		
Tocilizumab re-initiation	6/11 (54.5)		
Upadacitinib	2/11 (18.2)		

Values are n (%) for categorical variables and median (IQR) for continuous variables. Fisher's exact and Wilcoxon rank-sum tests used for univariable comparison of categorical and continuous variables, respectively. A logistic regression model including the variables tested in univariable comparisons did not show predictors independently associated with relapse. * Biopsy-proven aortitis. ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Figure 1. Relapse-free survival rate among GCA patients discontinuing tocilizumab



analysis was relapse after month 12. Relapse was defined as the recurrence of GCA signs or symptoms that required treatment, regardless of the ESR and CRP values. Time to relapse and features of relapse were assessed. Factors potentially associated with relapse were assessed in univariate analyses and multivariate logistic regression.

Results: The results of the clinical trial were published elsewhere [1]. In brief, of 30 patients receiving 12 months of TCZ and 2 months of prednisone, 23 (77.7%) maintained disease remission through month 12 and 7 (23.3%) relapsed before month 12 [1]. The 23 patients that maintained remission received a median (IQR) cumulative prednisone dose of 962.5 (682.5, 1610) mg during the trial and were followed for a median (IQR) period of 36 (22, 44) months after the trial ended. Other baseline characteristics are shown in **Table 1**. During follow-up, 11 (47.8%) patients relapsed following TCZ discontinuation (**-Table 2**). The median relapse-free survival time was 23.1 (95% CI 8.6-NE) months (**Figure 1**). At relapse, 4 (36.4%) patients had cranial symptoms and 7 (63.6%) had polymyalgia rheumatica symptoms (**Table 2**). One (9.1%) patient had biopsy-proven aortitis despite being asymptomatic. No patients reported visual symptoms at the time of relapse. The median (IQR) ESR (mm/hour) and CRP (mg/liter) values at relapse were 39 (25, 43.75) and 10.5 (5.6, 24.73), respectively. Of all relapsing patients, 10 (90.9%) received prednisone. In addition, 6 (54.5%) patients re-initiated TCZ and 2 (18.2%) patients received upadacitinib (**Table 2**). All patients regained control of their symptoms with treatment. Sex, whether

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

GCA was newly diagnosed at the onset of the clinical trial, cumulative prednisone dose in the year preceding baseline and disease duration did not predict relapse after TCZ withdrawal.

Conclusion: Nearly 50% of patients relapsed after treatment with 12 months of TCZ and 2 months of prednisone. The observed post-treatment relapse rate was similar to that reported in patients receiving TCZ in combination with longer GC tapers, suggesting that the amount and duration of GC treatment does not have a significant effect on the risk of relapse once TCZ is discontinued. Clinical trials to determine the optimal duration of TCZ treatment and assess different TCZ weaning strategies are needed.

1. Unizony et al. *Lancet Rheumatol* 2023

Disclosure: D. O'Dea: None; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **B. Arevalo Molina**: Amgen, 2; **A. Jarvie**: None; **M. Matza**: Expert Review, 12,, Novartis, 1, Summus Global Inc., 2, USSONAR, 6; **A. Fernandes**: None; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **S. Unizony**: Harvard Pilgrim Healthcare, 2, IQVIA, 2, Sanofi, 2.

Abstract Number: 0744

Age and Sex Influence on Clinical Manifestations of Giant Cell Arteritis: Results from the ARTESER Registry

Delia Fernandez-Lozano[1], Marta Domínguez-Álvaro[2], Javier Narváez[3], Noemí Garrido[4], Eugenio de Miguel[5], Paula Estrada-Alarcón[6], Iñigo Hernández-Rodríguez[7], Maite Silva-Diaz[8], Joaquín M Belzunegui[9], Clara Moriano[10], Julio Sánchez Martín[11], Itziar Calvo-Zorrilla[12], Vicente Aldasoro Cáceres[13], lydia Abasolo Alcazar[14], Javier Loricera[15], rafeal Benito-Melero[16], Maria Garcia-Villanueva[17], Fernando Sánchez-Alonso[2], Santos Castañeda[18], José L. Hernández[19], Ricardo Blanco[20] and ARTESER Project Collaborative Group, [1]Hospital Universitario y Politecnico La Fe, Valencia, Spain, [2]Sociedad Española de Reumatología, Madrid, Spain, [3]Hospital Universitario de Bellvitge, Barcelona, Spain, [4]Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, Spain, [5]Hospital Universitario La Paz, Madrid, Spain, [6]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [7]Complejo Hospitalario Universitario de Vigo, Vigo, Spain, [8]Complexo Hospitalario Universitario A Corua, A Corua, Galicia, Spain, [9]Hospital Universitario Donostia, San Sebastian, Spain, [10]Hospital Len, LEON, Castilla y Leon, Spain, [11]Hospital Universitario 12 de Octubre, Madrid, Spain, [12]Galdakao-Usansolo University Hospital, Bilbao, Spain, [13]Hospital Universitario de Navarra, Pamplona, Spain, [14]IdISSC. HCSC, Madrid, Madrid, Spain, [15]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [16]MD, barcelona, Spain, [17]Hospital Ramón y Cajal, Madrid, Spain, [18]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [19]Instituto de Investigación Marqués de Valdecilla (IDIVAL), Universidad de Cantabria, Santander, Spain, [20]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a large vessel vasculitis that predominantly affects older adults, with a higher prevalence in women. Previous studies exploring sex-related differences in clinical presentation have shown disparate results. The aim of this study was to analyze whether there are differences in the clinical presentation of GCA between men and women, stratified by age at diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Clinical manifestations between sexes according to age at diagnosis.

Clinical manifestations	<70 years				70-80 years				>80 years			
Age group	Men	Women	Total	p-Value	Men	Women	Total	p-Value	Men	Women	Total	p-Value
Recent-onset headache, n (%)	59 (64.8)	153 (73.9)	212 (71.1)	0.053	154 (79.4)	410 (84.4)	564 (82.9)	0.139	169 (79.7)	392 (81.0)	561 (80.6)	0.619
Temporal artery tenderness or decreased pulsation, n (%)	33 (36.3)	89 (43.0)	122 (40.9)	0.204	87 (44.9)	256 (52.7)	343 (50.4)	**0.032***	111 (52.4)	248 (51.2)	359 (51.6)	0.809
Visual symptoms, n (%)	30 (33.0)	45 (21.7)	75 (25.2)	**0.038***	68 (35.1)	165 (34.0)	233 (34.3)	0.797	96 (45.3)	201 (41.5)	297 (42.7)	0.319
Jaw claudication, n (%)	19 (20.9)	62 (30.0)	81 (27.2)	0.085	72 (37.1)	189 (38.9)	261 (38.4)	0.8	81 (38.2)	174 (36.0)	255 (36.6)	0.539
Hypersensitive scalp, n (%)	23 (25.3)	43 (20.8)	66 (22.2)	0.637	51 (26.3)	150 (30.9)	201 (29.6)	0.258	53 (25.0)	131 (27.1)	184 (26.4)	0.494
Facial pain, n (%)	4 (4.4)	29 (14.0)	33 (11.1)	**0.014***	27 (13.9)	71 (14.6)	98 (14.4)	0.777	24 (11.3)	58 (12.0)	82 (11.8)	0.783
Vertigo, n (%)	7 (7.7)	8 (3.9)	15 (5.0)	0.172	17 (8.8)	40 (8.2)	57 (8.4)	0.971	14 (6.6)	41 (8.5)	55 (7.9)	0.448
Ischemic and/or hemorrhagic stroke, n (%)	7 (7.7)	4 (1.9)	11 (3.7)	**0.015***	12 (6.2)	11 (2.3)	23 (3.4)	**0.013***	6 (2.8)	23 (4.8)	29 (4.2)	0.255
Dysphagia, n (%)	2 (2.2)	7 (3.4)	9 (3.0)	0.609	14 (7.2)	12 (2.5)	26 (3.8)	**0.005***	9 (4.3)	12 (2.5)	21 (3.0)	0.201
Hearing loss, n (%)	3 (3.3)	8 (3.9)	11 (3.7)	0.784	6 (3.1)	14 (2.9)	20 (2.9)	0.941	7 (3.3)	7 (1.5)	14 (2.0)	0.103
Transient ischaemic attack, n (%)	4 (4.4)	4 (1.9)	8 (2.7)	0.232	7 (3.6)	5 (1.0)	12 (1.8)	**0.024***	2 (0.9)	10 (2.1)	12 (1.7)	0.305
Polymyalgia rheumatica, n (%)	38 (41.8)	96 (46.4)	134 (45.0)	0.439	64 (33.0)	225 (46.3)	289 (42.5)	**0.003***	76 (35.9)	200 (41.3)	276 (39.7)	0.221
Claudication - lower limbs, n (%)	5 (5.5)	17 (8.2)	22 (7.4)	0.322	24 (12.4)	37 (7.6)	61 (9.0)	**0.045***	24 (11.3)	50 (10.3)	74 (10.6)	0.712
Claudication - upper limbs, n (%)	6 (6.6)	20 (9.7)	26 (8.7)	0.309	13 (6.7)	47 (9.7)	60 (8.8)	0.238	19 (9.0)	47 (9.7)	66 (9.5)	0.748
Peripheral synovitis, n (%)	3 (3.3)	12 (5.9)	15 (5.1)	0.399	9 (4.8)	25 (5.2)	34 (5.1)	0.824	15 (7.1)	22 (4.6)	37 (5.4)	0.149
Asthenia, n (%)	48 (52.8)	127 (61.4)	175 (58.7)	0.108	96 (49.5)	256 (52.7)	352 (51.8)	0.329	95 (44.8)	251 (51.9)	346 (49.7)	0.18
Anorexia, n (%)	29 (31.9)	88 (42.5)	117 (39.3)	**0.07***	78 (40.2)	160 (32.9)	238 (35.0)	0.099	73 (34.4)	180 (37.2)	253 (36.4)	0.913
Weight loss, n (%)	29 (31.9)	82 (39.6)	111 (37.3)	0.131	80 (41.2)	137 (28.2)	217 (31.9)	**0.001***	65 (30.7)	148 (30.6)	213 (30.6)	0.721
Fever/low-grade fever, n (%)	24 (26.4)	76 (36.7)	100 (33.6)	0.026	52 (26.8)	101 (20.8)	153 (22.5)	0.152	37 (17.5)	77 (15.9)	114 (16.4)	0.495

*Significant differences in bold ($p<0.05$).

Methods: ARTESER is a large Spanish multicenter epidemiological registry of GCA promoted by the Spanish Society of Rheumatology (SER*) in which 26 general hospitals participated. The recruitment period was between June 2013 and March 2019. Standardized data were included for all patients diagnosed with GCA in these centers, including demographic and clinical presentation. Age was artificially grouped into three categories (< 70, 70–80, and >80 years) to reflect the most frequent age range of presentation and to optimize the visualization of clinical patterns. This grouping also accounted for the relatively small number of patients in the youngest and oldest age groups. Differences between sexes were compared in a bivariate analysis. Statistical analysis was performed by using STATA statistical package, V.13.1 and SPSS version 21.0.

Results: A total of 1,675 patients with GCA were included in the study, of whom 1,178 were women and 497 men. Among patients younger than 70 years, men presented more frequently with visual symptoms (33.0% vs. 21.7%; p=0.038) and stroke events (7.7% vs. 1.9%; p=0.015) compared to women. In the 70-80 years group, men had a higher frequency of stroke (6.2% vs. 2.3%; p=0.013), dysphagia (7.2% vs. 2.5%; p=0.005), and transient ischaemic attacks (3.6% vs. 1.0%; p=0.024), whereas women showed a greater prevalence of polymyalgia rheumatica (46.3% vs. 33.0%; p=0.003). Weight loss was also more common among men (41.2% vs. 28.2%; p=0.001). No significant sex-based differences were observed in patients aged over 80 years. Results are shown in **Table 1**.

Conclusion: Sex-related differences in the clinical presentation of GCA were mainly observed in patients diagnosed before the age of 80. Men showed a higher frequency of cranial ischemic manifestations, such as visual symptoms and stroke, whereas women more frequently presented with polymyalgia rheumatica. These findings highlight the importance of considering both sex and age at diagnosis when assessing patients with suspected GCA.

Disclosure: D. Fernandez-Lozano: None; **M. Domínguez-Álvaro**: None; **J. Narváez**: None; **N. Garrido**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **P. Estrada-Alarcón**: None; **I. Hernández-Rodríguez**: None; **M. Silva-Diaz**: None; **J. Belzunegui**: None; **C. Moriano**: None; **J. Sánchez Martín**: None; **I. Calvo-Zorrilla**: None; **V. Aldasoro Cáceres**: None; **I. Abasolo Alcazar**: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **r. Benito-Melero**: AbbVie/Abbott, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6; **M. Garcia-Villanueva**: None; **F. Sánchez-Alonso**: None; **S. Castañeda**: None; **J. Hernández**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0745

Prevalence and Clinical Significance of Low ESR and CRP in Giant Cell Arteritis: A Population Based Study

Eugenio de Miguel, Natalia López-Juanes, Maria-Eugenia Miranda-Carus, Carlota Ureta, Chamaida Plasencia-Rodríguez and Irene Monjo Henry, Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Traditionally, elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) had been considered a hallmark of GCA and both are included in the 2022 ACR/EULAR GCA classification criteria. However, emerging evidence indicates that a subset of patients even with biopsy-proven GCA may present with normal or low ESR levels. The identification and characterization of this subgroup of patients is essential to improve diagnostic accuracy and optimize the therapeutic management of GCA. The main objective of this study was to determine the prevalence of low ESR and CRP in GCA, and to investigate whether there are differences in clinical manifestations between patients with and without elevation of these acute phase reactants.

Methods: This is a retrospective population-based analysis including consecutive unselected GCA cases from a cohort diagnosed since 2017 with basal data of ESR or CRP. All patients underwent standardized bilateral ultrasound (US) of cranial arteries (common temporal artery and branches) and extra-cranial arteries (carotid, subclavian and axillary). Subtypes were classified as cranial, extra-cranial, or mixed based on vascular involvement identified by US and/or positron emission tomography (PET-CT). Demographic and clinical variables were extracted from clinical records and diagnosis required at least six months of clinical follow-up. Constitutional syndrome included weight loss, malaise, and fever. Patients included were without treatment or with less of two weeks of oral corticosteroid therapy.

Table 1: Clinical manifestations related with ESR and CRP

ESR	Sex female	Age Mean(±SD)	Headache	PMR	AION	Stroke	Jaw claudication	Fever	Constitutional syndrome	Major relapses	Minor relapses
ESR All n=211 (%)	114 (54%)	80.0 (8.7)	131 * (62.1%)	109 ** (51.7%)	38 (18.1%)	18 * (8.5%)	43 (20.4%)	33 * (15.6%)	48 ** (22.7%)	15 (7.1%)	69 (32.7%)
ESR<50 mm/h n=	42 (49.4%)	80.2 (8.8)	44 (51.8%)	57 (67.1%)	11 (12.9%)	3 (3.5%)	13 (15.3%)	7 (8.2%)	11 (12.9%)	4 (4.7%)	27 (31.8%)
ESR≥50 mm/h	72 (57.1%)	79.8 (8.6)	87 (69.0%)	52 (41.3%)	27 (21.4%)	15 (11.9%)	30 (23.8%)	26 (20.6%)	37 (29.4%)	11 (8.7%)	42 (33.3%)
CRP	**Sex female**	**Age Mean(±SD)**	**Headache**	**PMR**	**AION**	**Stroke**	**Jaw claudication**	**Fever**	**Constitutional syndrome**	**Major relapses**	**Minor relapses**
CRP All n=213	113 (53.1%)	213 79.0 (8.3)	125 (58.7%)	115 (54.0%)	37 (18.1%)	19 (8.9%)	45* (21.1%)	33 (15.5%)	50 * (23.5%)	17 (8.0%)	75 (35.2%)
CRP<10 mg/L	12 (44.4%)	27 78.1 (7.9)	13 (48.1%)	18 (66.7%)	2 (7.4%)	1 (3.7%)	1 (3.7%)	1 (3.7%)	2 (7.4%)	0 (--%)	11 (40.7%)
CRP ≥10 mg/L	101 (54.34%)	186 79.1 (8.3)	112 (60.2%)	97 (52.2%)	35 (18.8%)	18 (9.7%)	44 (23.7%)	32 (17.2%)	48 (25.8%)	17 (9.1%)	64 (34.4%)
ESR or CRP	**Sex female**	**Age Mean(±SD)**	**Headache**	**PMR**	**AION**	**Stroke**	**Jaw claudication**	**Fever**	**Constitutional syndrome**	**Major relapses**	**Minor relapses**
ESR if CRP All n=228 (%)	121 (53.1%)	228 78.7 (8.4)	137 (60.1%)	120 (52.6%)	40 (17.5%)	19 (8.9%)	49 (21.5%)	36 (15.8%)	51 * (22.4%)	18 (7.9%)	78 (34.2%)
ESR<50 mm/h and CRP<10 mg/L	10 (37.0%)	27 78.1 (7.9)	44.4 (48.1%)	19 (70.4%)	2 (7.4%)	0 (--%)	3 (11.1%)	2 (7.4 %)	1 (3.7%)	1 (3.7%)	11 (40.7%)
ESR≥50 mm/h or CRP ≥10 mg/L	111 (55.2%)	186 79.1 (8.3)	125 (62.2%)	101 (50.2%)	38 (18.9%)	19 (9.5%)	46 (22.9%)	34 (16.9%)	50 (24.9%)	17 (8.5%)	67 (33.3%)

ESR=Erythrocyte sedimentation rate; CRP= C reactive protein; PMR= polymyalgia rheumatica; AION= arterial ischemic optic neuritis;*p<0.05; ** p<0.01

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Influence of the acute phase reactants and the vascular subtype of GCA

	Isolated cranial			Mixed cranial and large vessel			Isolated large vessel		
ESR n (%)	All	ESR <50 mm/h	ESR≥50 mm/h	All	ESR <50 mm/h	ESR≥50 mm/h	All	ESR <50 mm/h	ESR≥50 mm/h
	109 (51.6%)	36 (42.3%)	73 (57.9%)	59 (28.0%)	23 (27.1%)	36 (28.6%)	43 (20.5%)	26 (30.6%)**	17 (13.5%)
CRP n (%)	All	CRP <10 mg/l	CRP≥10 mg/l	All	CRP <10 mg/l	CRP≥10 mg/l	All	CRP <10 mg/l	CRP≥10 mg/l
	108 (50.7%)	12 (44.4%)	96 (51.6%)	62 (29.1%)	10 (37.0%)	52 (28.0%)	43 (20.2%)	5 (18.5%)	38 (20.4%)
ESR or CRP n (%)	All	ESR <50 or CRP <10*	ESR≥50 or CRP≥10*	All	ESR <50 or CRP <10*	ESR≥50 or CRP≥10*	All	ESR <50 or CRP <10*	ESR≥50 or CRP≥10*
	117 (51.3%)	9 (33.3%)	108 (53.7%)	65 (28.5%)	11 (40.7%)	54 (26.9%)	46 (20.2%)	7 (25.9%)	39 (19.4%)

ESR=Erythrocyte sedimentation rate; CRP= C reactive protein ** p<0.01

Table 3: Sensitivity of acute phase reactants for diagnosis of GCA

Acute phase reactants combination	Sensitivity (%)
ESR ≥50 mm/h	59.7
CRP ≥10 mg/L	87.3
ESR ≥50 mm/h **or** CRP ≥10 mg/L	88.2
ESR ≥50 mm/h **and** CRP ≥10 mg/L	62.7

ESR=Erythrocyte sedimentation rate; CRP= C reactive protein

Results: A total of 228 cases were included (Table 1). 85/211 GCA patients had ESR below 50 mm/h (40.3%), 27/213 (12.7%) CRP below 10mg/L and 27/228 (11.8%) CRP or ESR below these ranges. Therefore, the sensitivity of acute phase reactants as isolated value for the diagnosis of GCA in our cohort was 59.7% for patients with ESR≥ 50 mm/h, 87.3% for patients with CRP≥ 10 mg/L, and 88.2% for patients with at least one of them elevated. Headache, stroke and fever were less frequent in patients with ESR< 50 ($p< 0.05$) and in patients with constitutional syndrome ($p< 0.01$), however polymyalgia rheumatica (PMR) was more frequent with ESR< 50 ($p< 0.01$). CRP ≥10 mg/L was significantly more frequent in patients with jaw claudication and constitutional syndrome ($p< 0.05$) and the presence of at least one acute phase reactant was significantly more frequent in patients with constitutional syndrome. Regarding the vascular subtype, a statistically significant difference was observed in the large vessel subtype, which was more frequent in patients with ESR < 50 mm/h ($p< 0.01$).

Conclusion: An ESR ≥50 mm/h showed lower sensitivity for the diagnosis of GCA (57.3%) compared to CRP ≥10 mg/L (87.3%) or the combination of elevated ESR or CRP (88.2%). Patients with low ESR values had a lower prevalence of headache, stroke, fever, and constitutional symptoms, but a higher frequency of polymyalgia rheumatica and the large-vessel vasculitis subtype. Similarly, lower CRP levels were associated with fewer ischemic and systemic symptoms, with significant differences observed in the frequency of jaw claudication and constitutional syndrome.

Disclosure: E. de Miguel: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **N. López-Juanes**: None; **M. Miranda-Carus**: None; **C. Ureta**: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **I. Monjo Henry**: None.

Abstract Number: 0746

Impact of Frailty on Mortality in GCA and PMR: A Retrospective Cohort

Fatima Hassan[1], Michael Putman[2] and Sebastian E Sattui[3], [1]Medical College of Wisconsin, Menomonee Falls, WI, [2]The Medical College of Wisconsin, Milwaukee, WI, [3]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Frailty, a syndrome associated with decreased physiologic reserve, is associated with adverse outcomes. The prevalence and impact of baseline frailty on the risk of mortality in patients with incident giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) is unknown. The objective of this study was to describe the risk of mortality - stratified by frailty - among patients with GCA, PMR, and general population controls.

Methods: We conducted a retrospective cohort study using the US-based TriNetX electronic health records network. Adults ≥50 years with new-onset PMR or GCA were included if they had ≥2 ICD-9/10-CM codes, ≥1 year of prior follow-up, and a prednisone prescription within 30 days of the first code (index date). Matched general population control cohorts

Table 1: Demographic and Clinical Characteristics of Included Patients, n = 60,039

	Overall	PMR	General Population - PMR Comparators	GCA	General Population - GCA Comparators
Number of Patients	60,039	17,955	27,318	4,963	9,803
Age at Diagnosis, mean (SD)	69.5 (8.4)	71.2 (8.1)	67.3 (8.1)	71.7 (8.2)	71.5 (8.1)
Sex					
Male	20,672 (34.4%)	7,795 (43.4%)	8,656 (31.7%)	1,494 (30.1%)	2,727 (27.8%)
Female	39,367 (65.6%)	10,160 (56.6%)	18,662 (68.3%)	3,469 (69.9%)	7,076 (72.2%)
Race/Ethnicity					
White	50,032 (83.3%)	15,382 (85.7%)	23,103 (84.6%)	3,779 (76.1%)	7,768 (79.2%)
Black or African American	4,246 (7.1%)	927 (5.2%)	1,770 (6.5%)	543 (10.9%)	1,006 (10.3%)
Hispanic or Latino	1,601 (2.7%)	396 (2.2%)	694 (2.5%)	192 (3.9%)	319 (3.3%)
Asian	702 (1.2%)	168 (0.9%)	301 (1.1%)	82 (1.7%)	151 (1.5%)
Other / NA	3,458 (5.8%)	1,082 (6.0%)	1,450 (5.3%)	367 (7.4%)	559 (5.7%)
Frailty					
Non-Frail	37,117 (61.8%)	10,713 (59.7%)	17,821 (65.2%)	2,508 (50.5%)	6,075 (62.0%)
Pre-Frail	21,301 (35.5%)	6,818 (38.0%)	8,823 (32.3%)	2,205 (44.4%)	3,455 (35.2%)
Frail	1,621 (2.7%)	424 (2.4%)	674 (2.5%)	250 (5.0%)	273 (2.8%)
Charlson Comorbidity Index	0.8 (1.5)	0.9 (1.5)	0.7 (1.4)	1.2 (1.7)	0.8 (1.4)
Admissions during Prior Year, mean (SD)	0.5 (2.0)	0.5 (1.7)	0.4 (1.9)	1.1 (3.0)	0.5 (1.9)
Comorbidities at Diagnosis					
Chronic Obstructive Pulmonary Disease	10,252 (17.1%)	2,902 (16.2%)	4,584 (16.8%)	1,061 (21.4%)	1,705 (17.4%)
Obesity	7,659 (12.8%)	2,364 (13.2%)	3,401 (12.4%)	769 (15.5%)	1,125 (11.5%)
Diabetes	6,577 (11.0%)	2,226 (12.4%)	2,720 (10.0%)	662 (13.3%)	969 (9.9%)
Renal Disease	5,294 (8.8%)	1,964 (10.9%)	1,835 (6.7%)	667 (13.4%)	828 (8.4%)
Liver Disease	2,326 (3.9%)	738 (4.1%)	1,019 (3.7%)	266 (5.4%)	303 (3.1%)
Atherosclerosis	2,039 (3.4%)	628 (3.5%)	732 (2.7%)	340 (6.9%)	339 (3.5%)
Smoking	1,735 (2.9%)	442 (2.5%)	840 (3.1%)	194 (3.9%)	259 (2.6%)

Abbreviations: polymyalgia rheumatica (PMR), giant cell arteritis (GCA), standard deviation (SD), not applicable (NA)
*Control groups were matched to PMR and GCA, respectively

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Unadjusted Incidence of Mortality, n = 60,039

	Events	Follow Up Time (years)	Incidence / 1000 person years	Adjusted hazard ratio for mortality
Disease Group				
General Population (GCA)	83	9,194	9.0	Referent*
General Population (PMR)	264	25,614	10.3	Referent*
PMR	205	16,828	12.2	0.85 (0.71-1.03)
GCA	115	4,579	25.1	2.17 (1.63-2.90)
Frailty Category				
Non-Frail	188	34,920	5.4	Referent
Pre-Frail	381	19,845	19.2	2.45 (2.03-2.96)
Frail	98	1,451	67.5	5.16 (3.84-6.94)
GCA vs General Population, Stratified by Frailty Group				
General Population - Non-Frail	337	34,563	9.8	Referent*
General Population - Frail	10	245	40.7	1.27 (0.67-2.42)
GCA Non-Frail	92	4,364	21.1	1.52 (1.20-1.92)
GCA Frail	23	216	106.6	2.91 (1.82-4.66)
PMR vs General Population, Stratified by Frailty Group				
General Population - Non-Frail	304	34,203	8.9	Referent*
General Population - Frail	43	606	71.0	3.04 (2.13-4.34)
PMR Non-Frail	183	16,444	11.1	0.96 (0.79-1.15)
PMR Frail	22	384	57.3	1.86 (1.17-2.96)

*Disease groups compared to their respective general population control groups

for PMR and GCA were constructed using 1:3 nearest-neighbor matching on the following variables: sex, race/ethnicity, regional location, birth year, year of cohort entry, and year of cohort exit. The exposure of interest was frailty as measured using a validated claims-based frailty index (CFI) during the year prior to the index date. Multivariable Cox proportional cause-specific hazard ratios (aHR) and 95% confidence intervals (CI) were calculated to assess the risk of mortality.

Results: Of 60,039 included patients, 17,955 had PMR, 4,963 had GCA, and 37,121 were matched controls. Compared to matched general population controls, the risk of death was elevated among patients with GCA (aHR 2.17, 95% CI 1.63-2.90) but not PMR (aHR 0.85, 95% CI 0.71-1.03). In the overall cohort, the risk of death was increased in pre-frail (aHR 2.45, 95% CI 2.03-2.96) and frail (HR 5.16, 95% CI 3.84-6.94) patients as compared to non-frail patients. In the stratified analysis, as compared to non-frail general population controls, the risk of death was not elevated for frail general population controls (aHR 1.27, 95% CI 0.67-2.42) but elevated for non-frail patients with GCA (aHR 1.52, 95% CI 1.20-1.92) and frail patients with GCA (aHR 2.91, 95% CI 1.82-4.66). In a stratified analysis, as compared to non-frail PMR general populations controls, the risk of death was elevated for frail general population controls (aHR 3.04, 95% CI 2.13-4.34) and frail

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

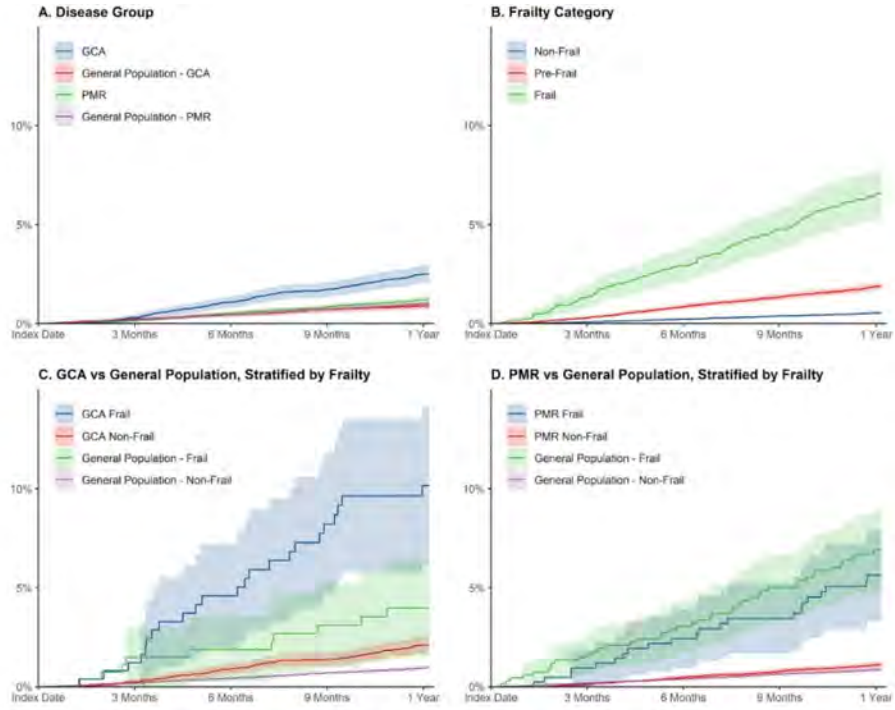


Figure 1: Cumulative incidence of mortality during the first year of therapy, stratified by (A) disease group, (B) frailty category, (C) dichotomized frailty category (frail vs. pre-frail and non-frail) among GCA and GCA controls, (D) dichotomized frailty category (frail vs. pre-frail and non-frail) among PMR and PMR controls

patients with PMR (aHR 1.86, 95% CI 1.17-2.96) but not for patients with PMR who were non-frail (aHR 0.96, 95% CI 0.79-1.15).

Conclusion: Both frailty and GCA were associated with an increased risk of mortality, but patients with PMR did not have an elevated risk of mortality unless they were also frail. Frailty in patients with GCA and PMR identifies a group of patients at risk for mortality and highlights the value of frailty assessment.

Disclosure: F. Hassan: None; **M. Putman**: AbbVie/Abbott, 5, Amgen, 5, AstraZeneca, 2, 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5; **S. Sattui**: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2.

Abstract Number: 0747

Patterns of Macrophage Polarization Induced by Serum from Patients with Giant Cell Arteritis and Takayasu's Arteritis

Irene Carrión-Barberà[1], Ryan D. Stultz[2], David Cuthbertson[3], Nader Khalidi[4], Curry Koening[5], Carol Langford[6], Carol McAlear[7], Paul Monach[8], Larry Moreland[9], Christian Pagnoux[10], Philip Seo[11], Kenneth Warrington[12], Peter Merkel[7], Christian Lood[13] and Vasculitis Clinical Research Consortium, [1]Department of Rheumatology. Hospital del Mar, Barcelona, Spain, [2]University of Washington, Division of Rheumatology, Seattle, WA, [3]University of South Florida, Tampa, [4]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Canada, [5]University of Texas Dell Medical School, Austin, TX, [6]Cleveland Clinic, Moreland Hills, OH, [7]University of Pennsylvania, Philadelphia, PA, [8]VA Boston Healthcare System, Boston, MA, [9]University of Colorado, Denver, CO, [10]Mount Sinai Hospital, University Health Network, Toronto, and Canadian Vasculitis Research Network (CanVasc), Toronto, ON, Canada, [11]Johns Hopkins University, Baltimore, MD, [12]Mayo Clinic, ROCHESTER, MN, [13]University of Washington, Division of Rheumatology, Seattle

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Macrophages play a central role in the pathogenesis of large-vessel vasculitides, including giant cell arteritis (GCA) and Takayasu's arteritis (TAK). Characterizing patterns of macrophage polarization induced by patient serum may uncover disease-specific immune signatures and therapeutic targets.

Methods: Purified monocytes from healthy donors were differentiated into macrophages (M0) using M-CSF and 10% fetal bovine serum for 4 days, followed by polarization toward M1 (IFNγ + LPS), M2a (IL-4 + IL-13), M2b (immune complexes + LPS), or M2c (IL-10 + dexamethasone) phenotypes. These in vitro-polarized macrophages served as the training dataset. Flow cytometry assessed CD40 (M1 marker), CD206 (M2a), HLA-DR (negative in M2b), and CD163 (M2c) expression. Macrophages exposed to serum from patients in remission with GCA (n=40), TAK (n=40), and healthy controls (HC, n=19) were analyzed (test samples).

Data were extracted from FlowJo™ workspaces using CytoML and flowWorkspace in R and arcsinh-transformed. A K-Nearest Neighbors (KNN) classifier (k=10) trained on M0–M2c macrophages predicted phenotypes in test samples. Uniform Manifold Approximation and Projection (UMAP) was used for visualization, using 250 cells/sample for training and test samples, and all available cells for other analysis. Group-level differences were assessed using Fisher's exact test, and per-sample differences with Mann–Whitney U tests.

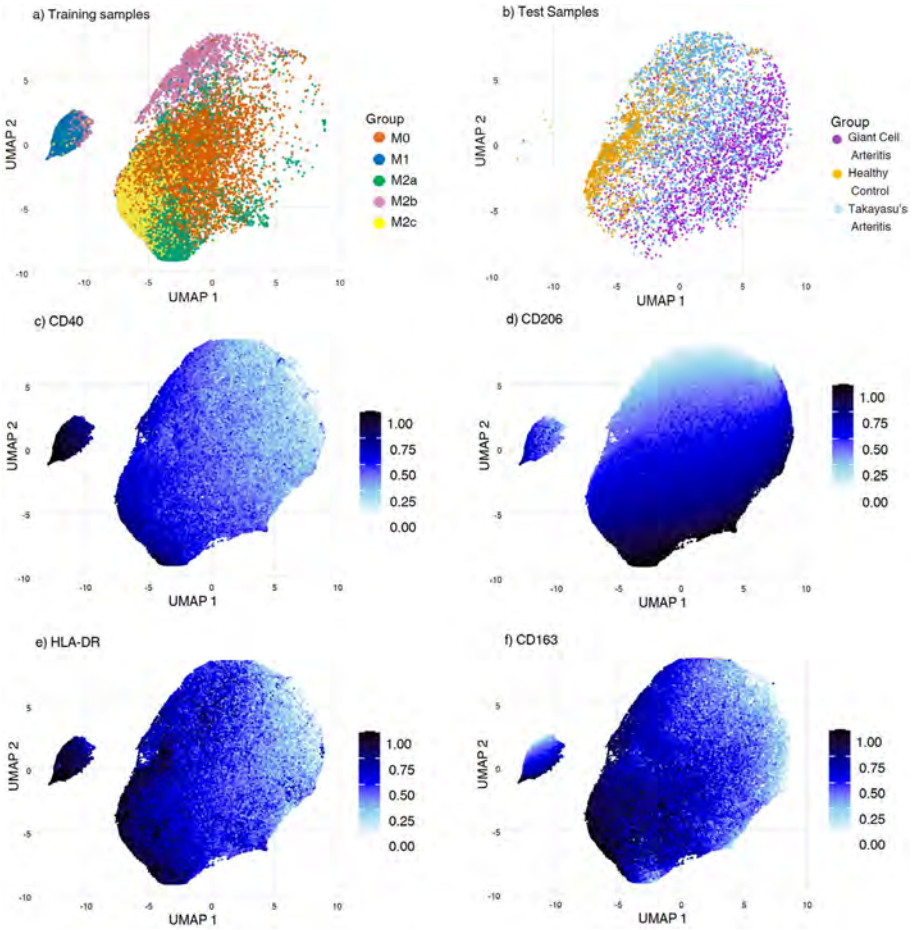


Figure 1: Uniform Manifold Approximation and Projection (UMAP) of training samples M0-M2c (a), test samples (b) and individual polarization markers (c-f).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

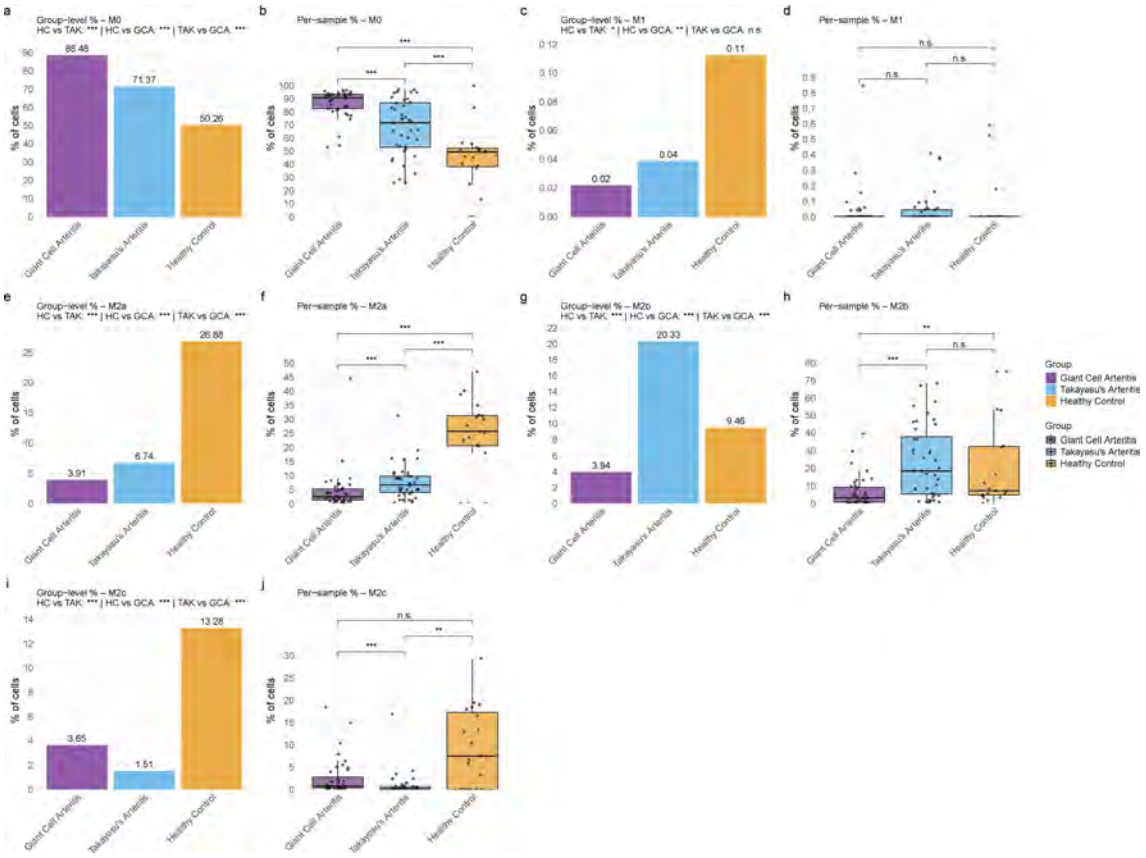


Figure 2: Percentage of each macrophage phenotype per group within all the cells of that group (a-c-e-g-i). Percentage of the median +/- inter-quartile range of each phenotype within each cell of the group (b-d-f-h-j). n.s. = non-significant; * = p-value < 0.05 – 0.01 ; ** = p-value < 0.01 – 0.001; *** = p-value < 0.001. GCA: giant cell arteritis; TAK: Takayasu's arteritis; HC: healthy control.

Results: UMAP visualization revealed distinct clustering patterns among groups. Macrophages exposed to HC serum formed a relatively compact cluster, while those exposed to serum from patients with GCA and TAK showed greater dispersion, especially TAK, indicating broader phenotypic heterogeneity (**Figure 1a-b**). Spatial distribution of individual polarization markers is shown through UMAP overlays (**Figure 1c-f**).

Quantitative analysis revealed that GCA samples retained the highest proportion of M0-like macrophages, followed by TAK, with HC showing the lowest. HC exhibited the highest proportions of M2a- and M2c-like macrophages, while TAK samples showed an increase in M2b-like macrophages. Despite tighter spatial clustering, HC macrophages polarized toward more varied phenotypes than the other groups (**Figure 2**). There were statistically significant differences among all groups, except for M1 between GCA and TAK. Although the proportion of M1 was negligible across all groups, HC showed a 6- and 4-fold increased prevalence compared to GCA and TAK, respectively.

Conclusion: Serum from patients with GCA and TAK induces distinct macrophage polarization profiles compared to HC. Serum in GCA maintains macrophages in an undifferentiated M0-like state, whereas serum in TAK promotes a modest M2b-skewed response associated with immune complex stimulation. In contrast, serum in HC predominantly favors regulatory and repair-associated macrophage phenotypes (M2a and M2c). These findings highlight macrophage phenotyping as a promising tool to uncover disease-specific immune dysregulation in large-vessel vasculitis.

Disclosure: I. Carrión-Barberà: AstraZeneca, 6, GlaxoSmithKlein(GSK), 2; **R. Stultz**: None; **D. Cuthbertson**: None; **N. Khalidi**: AbbVie/Abbott, 2, 5, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 5, GlaxoSmithKlein(GSK), 2, 6, Mallinckrodt, 2, NS Pharma, 5, Otsuka, 2, 6, Roche, 2, 6, Sanofi, 2, 5; **C. Koening**: Amgen, 1, Boehringer-Ingelheim, 1; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **C. McAlear**: None; **P. Monach**: Boehringer-Ingelheim, 2; **L. Moreland**: None; **C. Pagnoux**: amgen, 1, 2, 6, Astra zeneca, 1, 6, csl vifor, 1, 2, 6, gsk, 1, 2, 6, Novartis, 2, ns pharma, 1, otsuka, 1, 2, 5, 6, Pfizer, 2, 6; **P. Seo**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11.

Abstract Number: 0748

Does The Number Of Arteries Affected At The Disease Onset Predict Relapses Of Giant Cell Arteritis?

Iztok HOLC[1], Metka Koren Krajnc[2], Marko Gačnik[3] and Anja Lah[4], [1]University Medical Center Maribor, 2000 Maribor, Slovenia, [2]University Medical center, Maribor, Slovenia, [3]University Medical Center Maribor, Braslovče, Slovenia, [4]University Medical Center Maribor, Laporje, Slovenia

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a chronic vasculitis where relapses frequently occur. The rates of relapses of GCA have not been defined by now.

We aimed to evaluate the factors associated with relapses in our cohort.

Methods: In 58 GCA patients the diagnosis was confirmed according to history, clinical signs, laboratory tests and ultrasound examination. Ultrasound of cranial, carotid and axillar arteries was performed in all participants. We collected data cross-sectionally at first evaluation and at the second evaluation 5 years later. Predictors of relapses were identified by logistic regression analysis.

Results: 58 GCA patients were included initially (62 % women, mean age 74 years). At the end 53 patients completed the study and their data have been analyzed. 2 (3,4%) patients died, 3 (5,1%) were lost (didn't show up on controls). All patients received glucocorticoid treatment (60mg of

prednisolone, or pulse treatment if the vision was impaired), during follow up 16 (30,1%) received leflunomide (non-biologic agent as steroid sparing drug), 16 (30,1%) tocilizumab (biologic agent).

Relapses occurred in 17 (33,3%) of patients. A Mann-Whitney U value of 0.46 and t test (Welch) indicates that the relationship between the number of affected arteries and the occurrence of relapses in GCA patients is weak or negligible. There were no association with relapse occurrences and the time to diagnosis (t-test value of 0.99, Mann-Whitney 0,62). Mann-Whitney U test 0,07 result provides stronger evidence for a relationship between CRP levels and relapse, while the t-test 0,12 suggests that the mean CRP difference at the time of diagnosis is not substantial enough to be considered clinically significant.

Conclusion: GCA relapses occurred in 33,3 % of patients. Relapses were not associated with number of affected arteries, with the value of CRP at the time of diagnosis or with the time to diagnosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: I. HOLC: Roche, 6; **M. Koren Krajnc**: None; **M. Gačnik**: None; **A. Lah**: None.

Abstract Number: 0749

Prevalence and characteristics of subclinical Polymyalgia Rheumatica in patients with Giant Cell Arteritis

Javier Narváez[1], Paola Vidal-Montal[2], Martí Aguilar-Coll[3], Montserrat Roig Kim[4], Laia De Daniel Bisbe[4], Monica Cubells[5], Aina Fabregat[6], Judith Palacios-Olid[3], Pol Maymó-Paituvi[4], Carmen Moragues[3] and Joan Miquel Nolla[4], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Rheumatology. Hospital Universitari de Bellvitge, Barcelona, Catalonia, Spain, [3]Department of Rheumatology. Hospital Universitario de Bellvitge, Barcelona, Spain, [4]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [5]Hospital Universitari de Bellvitge, Barcelona, Spain, [6]Department of Rheumatology. Hospital Universitario de Bellvitge., Barcelona, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: In clinical practice, ^{18}F-FDG PET-CT often reveals findings suggestive of polymyalgia rheumatica (PMR) in patients with giant cell arteritis (GCA) who lack symptoms or signs indicative of this condition. This study aimed to analyse the prevalence, characteristics, and clinical significance of subclinical PMR in patients with apparently isolated GCA.

Methods: This was a cross-sectional, single-centre study including consecutive patients with newly diagnosed, biopsy-proven GCA and no clinical features of PMR. All underwent ^{18}F-FDG PET-CT at diagnosis. FDG uptake was assessed at anatomical sites typically involved in PMR, including shoulders, sternoclavicular joints, acromioclavicular joints, hips, ischial tuberosities, greater trochanters, symphysis pubis enthesis, and cervical/lumbar interspinous bursae. Visual grading was performed by all raters using liver uptake as reference: 0 (no uptake), 1 (lower than liver), 2 (equal to or greater than liver).

Results: PET findings suggestive of PMR were identified in 57 of 99 patients (57.6%). The distribution of involved anatomical sites is shown in Table 1.

The proportion of patients meeting PET-based diagnostic criteria was 26.5% for the Leuven score (≥16), 17% for the Leuven/Groningen score (≥8), 74.0% for the Besançon score, 56.0% for the Yamashita criterion, 54.0% for the Saint-Étienne algorithm, and 42.0% for the Heidelberg algorithm.

Compared with patients with GCA without any evidence of PMR (neither clinical nor subclinical), those with subclinical PMR showed a greater frequency of involvement of the thoracic aorta (p=0.080), abdominal aorta (p=0.001), and supra-aortic

Table 1. Comparison of ^{18}F-FDG uptake across different anatomical sites between GCA patients with subclinical PMR and those with concomitant clinical PMR.

Location	Clinical PMR N=62	Subclinical findings of PMR N=57	P
Shoulders	54 (87%)	43 (75.4%)	0.102
Sternoclavicular joints	27 (43.5%)	14 (24.5%)	0.029
Acromioclavicular joints	14 (22.5%)	9 (16%)	0.349
Cervical interspinous bursae / process	27 (43.5%)	19 (33%)	0.253
Lumbar interspinous bursae / process	41 (66%)	21 (37%)	0.001
Hips	19 (31%)	6 (10.5%)	0.004
Greater trochanter / Trochanteric bursa	57 (92%)	44 (77%)	0.051
Ischial tuberosities	36 (58%)	29 (51%)	0.496
Symphysis pubis enthesis	7 (11%)	4 (7%)	0.534
Peripheral arthritis	13 (21%)	2 (3.5%)	0.005
Diffuse reactive bone marrow uptake in axial and appendicular skeleton	17 (27%)	9 (16%)	0.151

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

trunks (p=0.012). No differences were observed at diagnosis regarding cranial manifestations, severe ischaemic complications, intensity of systemic inflammation, or long-term outcomes, including relapse rates, glucocorticoid use and the need for steroid-sparing agents, or mortality.

Compared with patients with GCA and clinical PMR (n=62; see table 1), those with subclinical PMR showed lower frequencies of involvement of the sternoclavicular joints (p=0.029), lumbar interspinous bursae (p=0.001), hips (31% vs 10.5%, p=0.004), and peripheral arthritis (p=0.005). The proportion of patients requiring tocilizumab was also significantly lower in this group (29.8% vs 50%; p=0.025).

Conclusion: Subclinical PMR findings are detected by PET-CT in nearly 58% of patients with apparently isolated GCA, supporting the concept of a GCA–PMR spectrum. A substantial proportion fulfilled PMR diagnostic criteria across different PET-based scoring systems. Subclinical PMR was associated with more frequent large-vessel involvement and a distinct anatomical distribution. Its presence does not appear to influence long-term clinical outcomes.

Disclosure: J. Narváez: None; **P. Vidal-Montal**: None; **M. Aguilar-Coll**: None; **M. Roig Kim**: None; **L. De Daniel Bisbe**: None; **M. Cubells**: None; **A. Fabregat**: None; **J. Palacios-Olid**: None; **P. Maymó-Paituvi**: None; **C. Moragues**: None; **J. Nolla**: None.

Abstract Number: 0750

Fibrinogen as a biomarker in the diagnosis of giant cell arteritis and detection of flares

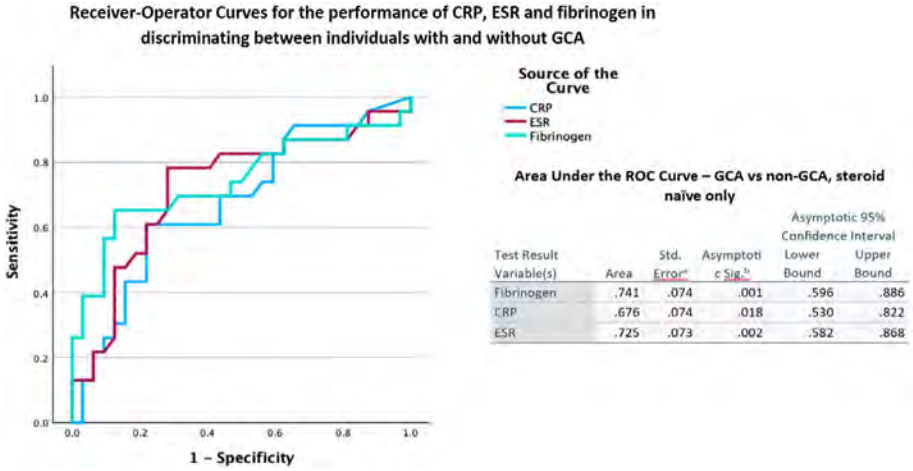
Jonathan Miller[1], Sharon Cowley[2], Patricia Harkins[3], David O'Sullivan[4], Gearoid McGeehan[5], Eamonn Molloy[6], Richard Conway[7], David Kane[8] and Geraldine mcCarthy[9], [1]St Vincent's University Hospital, Dublin, Ireland, [2]Tallaght University Hospital, Dublin, Dublin, Dublin, Ireland, [3]Trinity College Dublin, Dublin 8, Dublin, Ireland, [4]Tallaght University Hospital, Dublin, Dublin, Ireland, [5]Mater Misericordiae University Hospital, Dublin, Dublin, Ireland, [6]St Vincent's University Hospital, Dublin, Dublin, Ireland, [7]Trinity College Dublin, Dublin, Dublin, Ireland, [8]Tallaght University Hospital & Trinity College Dublin, D24, Dublin, Ireland, [9]Mater Misericordiae University Hospital, Dublin, Ireland

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is the commonest idiopathic systemic vasculitis in adults over 50 years of age. It can be associated with high morbidity. Diagnosis is typically made by clinical and laboratory assessment, supported by imaging or histopathology from a temporal artery biopsy. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are often used to help distinguish between cases and noncases, however between 4-10% of patients with active GCA have normal readings for both at the time of diagnosis. Furthermore, the sensitivity and specificity of both biomarkers are reduced following administration of glucocorticoids (GC), often given empirically to reduce the risk of visual loss. Fibrinogen has previously been studied for its role as a biomarker in polymyalgia rheumatica (PMR). Data support the usefulness of assessment of plasma fibrinogen in PMR diagnosis and management.

Methods: 65 patients with GCA or large vessel vasculitis (LVV) diagnosed between 2012 and 2024 were identified across three hospital sites in Dublin, Ireland; 42 of these were receiving GC at baseline. Data were retrospectively analysed from patients' electronic healthcare records. Blood values at baseline were identified for all, as well as during remission in 56 patients and during 22 flare episodes. The values for fibrinogen, CRP and ESR were analysed in comparison with 38 patients who attended with suspected GCA, but in whom an alternative diagnosis was made following rheumatologist

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Area Under the ROC Curve – GCA vs non-GCA, steroid naïve only

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval Lower Bound	Upper Bound
Fibrinogen	.741	.074	.001	.596	.886
CRP	.676	.074	.018	.530	.822
ESR	.725	.073	.002	.582	.868

Receiver-Operator Curves for the performance of CRP, ESR and fibrinogen in discriminating between steroid-naive individuals with and without GCA

Cutoff	Fibrinogen >4.7g/L	Fibrinogen >4.7g/L, excluding GC	ESR >54mm/hr	ESR >54mm/hr, excluding GC	CRP >42mg/L	CRP >42mg/L, excluding GC
Sensitivity	40%	62.9%	47.5%	69.7%	42.1%	63.6%
Specificity	81.5%	81.5%	65.6%	65.6%	76.3%	76.3%
Positive Predictive Value	81%	70.8%	77.6%	67.6%	79.5%	70%
Negative Predictive Value	40.7%	75.6%	33.3%	67.7%	37.7%	70.7%

Performance of fibrinogen, ESR and CRP at optimal cut-off values in diagnosis of GCA

assessment. Sensitivity and specificity were calculated for all three biomarkers, with adjustments made for whether patients were exposed to GC prior to blood collection at baseline. Receiver-Operator Curves (ROC) were generated for all three biomarkers, with an area-under-the-curve (AUC) calculated for each. The ROC were used to identify optimal cut-off values for fibrinogen, CRP and ESR.

Results: When individuals on GC at baseline were included, the mean fibrinogen level for patients with GCA was 4.64g/L, compared with 4.27g/L in individuals without GCA (p=0.198); mean ESR for patients with GCA was 52.5mm/hr compared with 44.8mm/hr (p=0.265) and mean CRP was 48.8mg/L compared with 42.4mg/L (p=0.56). When individuals on GC at baseline were excluded, the mean fibrinogen level for patients with GCA rose to 5.45g/L, compared with 4.27g/L in non-cases (p=< 0.001), mean ESR rose to 68.4mm/hr compared with 44.8mm/hr (p=0.03) and CRP to 68.8mg/L, compared with 42.4mg/L (p=0.071). In identifying flares, all three biomarkers perform comparably. Fibrinogen >4g/L had a sensitivity of 78.6% and specificity of 96%, CRP >5mg/L had a sensitivity of 95.2% and specificity of 74.5%, and ESR >20mm/hr had a sensitivity of 90% and specificity of 82%.

Conclusion: Fibrinogen may have a role in the diagnosis of GCA. The sensitivity of fibrinogen is substantially reduced by the introduction of GC prior to blood collection, as is that of CRP and ESR. Fibrinogen set at a cut-off value of 4.7g/L has comparable sensitivity and specificity for the presence of active GCA when adjusted for GC exposure, when compared with CRP and ESR. Fibrinogen may also be used in the detection of GCA flares, with lower sensitivity but greater specificity than ESR or CRP.

Disclosure: J. Miller: None; **S. Cowley**: Novartis, 5; **P. Harkins**: Johnson and Johnson, 5, 6, Novartis, 5; **D. O'Sullivan**: None; **G. McGeehan**: None; **E. Molloy**: None; **R. Conway**: AbbVie/Abbott, 1, 5, 6, Celltrion, 5, Fresenius Kabi, 6, Galapagos, 1, 6, Janssen, 5, 6, Novartis, 5, Vifor, 1; **D. Kane**: None; **G. mcCarthy**: PK Med and Avalo, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0751

Impact of Treatment with Upadacitinib on Biomarkers Identified by Proteomics in Giant Cell Arteritis

Lisa Christ[1], Shalina Taylor[2], Yilin Xu[2], Rhiya Sharma[2], Thierry Sornasse[2], Yingtao Bi[2], Heath Guay[2], Arathi Setty[3], Ana Romero[4], Peter Merkel[5], Eugenio de Miguel[6], Christian Dejaco[7] and Cornelia Weyand[8], [1]Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland., Bern, Switzerland, [2]AbbVie Inc, North Chicago, [3]AbbVie Inc, North Chicago, IL, [4]AbbVie, Barcelona, Spain, [5]University of Pennsylvania, Philadelphia, PA, [6]Hospital Universitario La Paz, Madrid, Spain, [7]Medical University of Graz, Department of Rheumatology, Graz, Austria; Department of Rheumatology, Hospital of Brunico (SABES-ASDAA), Brunico, Italy, [8]Division of Rheumatology, Department of Internal Medicine, Mayo Clinic, Rochester

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin-6 (IL-6) and interferon-gamma (IFNγ) have been identified as key drivers in the pathogenesis of giant cell arteritis (GCA), that promote disease progression. The phase 3 SELECT-GCA study showed that upadacitinib (UPA), a Janus Kinase inhibitor, was efficacious in treating GCA with a favorable benefit-risk profile compared to placebo (PBO). This study evaluated the impact of UPA on immune mediators in GCA, including IL-6 and IFNγ pathways, in the SELECT-GCA study.

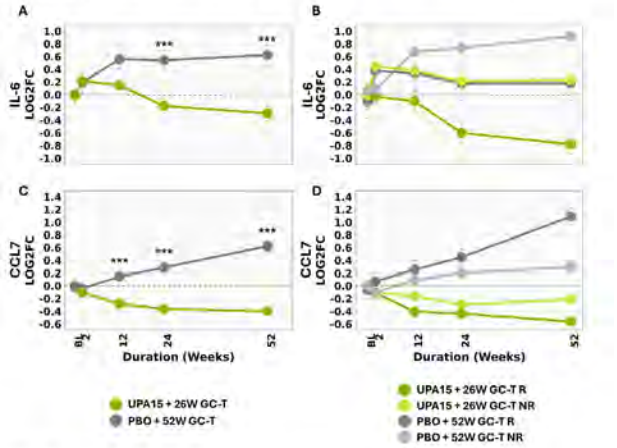
Methods: Patients from SELECT-GCA were included in this analysis, termed "Biomarker Cohort": PBO n =72/112; UPA 15 mg daily (UPA15), n =141/209. UPA15 patients underwent GC tapering over 26 weeks, while PBO patients underwent GC tapering over 52 weeks. Plasma samples were collected at baseline and weeks 2, 12, 24, and 52. A multiplexed assay platform designed for targeted detection and quantification of 45 immune related proteins was used, with significant differences identified in 30 proteins. IL-6 and IFNγ pathway proteins were assessed. A mixed model for repeated measures was used to compare biomarkers between UPA and PBO as well as to analyze treatment response and non-response. The least-square mean biomarkers between UPA and PBO were contrasted, and significant pharmacodynamic markers had a false discovery rate (FDR) ≤ 0.05.

Results: This analysis focused on proteins in the IL-6 and IFNγ pathways, core pathogenic dysregulated biomarkers in GCA. UPA significantly reduced IL-6 levels compared to PBO (Figure 1). This reduction was more pronounced in responders versus non-responders in UPA. Circulating IFNγ increased with UPA; however, IFNγ-modulated chemokines CXCL9, CXCL10, and CXCL11 decreased significantly with UPA and tended to increase with PBO (Figure 2). UPA reduced IL-18, amplifying the effect of IFNγ on CXCL9, CXCL10, and CXCL11. No significant difference was seen for these cytokines when comparing responders and non-responders to UPA. CCL7 was significantly reduced with UPA versus PBO; however, when comparing responders to non-responders with UPA, the difference was not significant by FDR. With PBO, levels of IL-6, CCL7, CXCL9, and CXCL10 progressively increased throughout the study, with no apparent reduction below baseline levels for CXCL11 and IL-18.

Conclusion: Treatment of GCA with UPA15 inhibits essential immune pathways implicated in GCA pathogenesis, including IL-6 and downstream proteins of IFNγ (CXCL9, CXCL10, CXCL11, IL-18). This reduction in activity of the IFNγ pathway is indicative of a decrease in T-helper 1 cytokines due to treatment with UPA. Although CCL7 is not considered a primary disease driver, its decrease with UPA treatment aligns with cytokines associated with disease activity. UPA's molecular effect was observed as early as week 2, suggesting rapid onset of action. While the primary focus was on IL-6 and IFNγ proteins

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

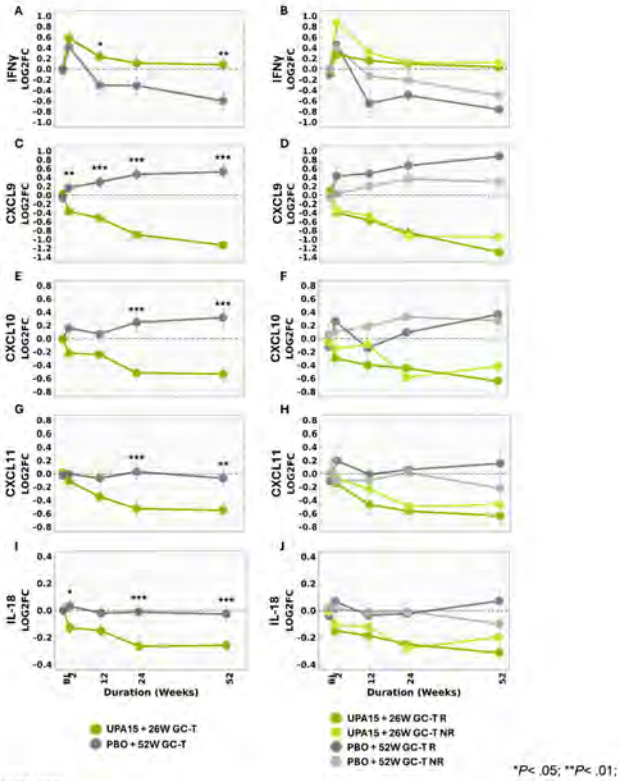
Figure 1: Levels of (A, B) Interleukin-6 and (C, D) Chemokine (C-C Motif) Ligand 7 in Patients with Giant Cell Arteritis Undergoing Upadacitinib Treatment Versus Placebo in the SELECT-Giant Cell Arteritis Trial



***P< .001

Pharmacodynamic profiles of IL-6, and CCL7 are depicted with data collected at BL and then weeks 2, 4 12, 24, and 52 comparisons between PBO and UPA treatment (A and C) as well as comparing responders (R) and non-responders (NR) (B and D). UPA 15mg treated patients completed a 26-week GC taper (T), compared to a 52-week GC taper in the PBO group. There was a significant difference observed between responders and non-responders for IL-6 (B) but not CCL7 (D) after FDR correction. The mixed model for repeated measures was employed to evaluate temporal changes in protein levels providing pharmacodynamic behavior over the study period, with an FDR of ≤ .05.

Figure 2: Impact of Treatment of Giant Cell Arteritis with Upadacitinib on the Interferon Gamma Pathway: (A, B) Interferon Gamma; (C,D) C-X-C Motif Chemokine Ligand 9; (E,F) C-X-C Motif Chemokine Ligand 10; (G,H) C-X-C Motif Chemokine Ligand 11; (I,J) Interleukin-18



*P< .05; **P< .01;

***P< .001

Pharmacodynamic profiles of IFNγ, CXCL9, CXCL10, CXCL11, and IL-18 are depicted with data collected at BL and then weeks 2, 4, 12, 24, and 52 comparisons between PBO and UPA treatment (A, C, E, G, I) as well as comparing response groups (B, D, F, H, J). UPA 15mg treated patients completed a 26-week GC taper, compared to a 52-week GC taper in the PBO group. There were no observed significant differences between treatment response groups for all proteins presented in this analysis. The mixed model for repeated measures was employed to evaluate temporal changes in protein levels providing pharmacodynamic behavior over the study period, with an FDR of ≤ .05.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

due to their roles in GCA biology, other modulated biomarkers warrant investigation to further characterize UPA's effect. UPA's clinical activity in GCA relates partly to its impact on IL-6, IFNγ pathway proteins, and CCL7, suggesting the efficacy of UPA for GCA is related to modulation of these cytokines.

Disclosure: L. Christ: Bristol-Myers Squibb(BMS), 6, Gebauer Foundation Switzerland, 5, Gilead, 5, 11, Novartis, 1, 6, 11, Pfizer, 5, Roche, 5, 11, sanofi, 12, Congress support, Swiss Foundation for Research on Muscle Diseases, 5, Vifor, 6; **S. Taylor**: AbbVie, 3, 11; **Y. Xu**: AbbVie, 3, 11; **R. Sharma**: AbbVie, 3, 11; **T. Sornasse**: AbbVie, 3, 11; **Y. Bi**: AbbVie, 3, 11; **H. Guay**: AbbVie, 3, 11; **A. Setty**: AbbVie, 3, 11; **A. Romero**: AbbVie/Abbott, 3; **P. Merkel**: AbbVie/Abbott, 2, 5, 6, Alpine, 2, 5, 6, Amgen, 2, 5, 6, ArGenx, 2, 5, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CSL Behring, 2, 5, 6, Eicos, 2, 5, 6, Electra, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, iCell, 2, 5, 6, Interius, 2, 5, 6, Kinevant, 2, 5, 6, Kyverna, 2, 5, 6, Lifordi, 2, 5, 6, Metagenomia, 2, 5, 6, Neutrolis, 2, 5, 6, Novartis Corp, 2, 5, 6, NS Pharma, 2, 5, 6, Q32, 2, 5, 6, Quell, 2, 5, 6, Regeneron, 2, 5, 6, Sanofi, 2, 5, 6, Sparrow, 2, 5, 6, Takeda, 2, 5, 6, Vistera, 2, 5, 6; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **C. Dejaco**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Sparrow, 2, 6; **C. Weyand**: AbbVie, 2, BMS Global, 2, Boehringer Ingelheim, 2, Ono Pharmaceutical, 2, Seismic Therapeutics, 2, Sparrow Pharmaceutical, 2.

Abstract Number: 0752

Characterization of patients with polymyalgia rheumatica in the ARTESER giant cell arteritis cohort

Maite Silva-Diaz[1], Marta Domínguez-Álvaro[2], Rafael B. Melero-González[3], Elisa Fernández-Fernández[4], Jesús Alejandro Valero[5], Ismael González[6], Julio Sánchez Martín[7], Javier Narváez[8], Eva Galíndez Agirregoikoa[9], Vicente Aldasoro Cáceres[10], lydia Abasolo Alcazar[11], Javier Loricera[12], Noemí Garrido[13], Santos Castañeda[14], Carlota L Iñiguez[15], Alicia Garcia[16], Clara Molina Almela[17], María Alcalde Villar[18], Antonio Juan Mas[19], Ricardo Blanco[20] and the ARTESER Project Collaborative Group, [1]Complexo Hospitalario Universitario A Corua, A Corua, Galicia, Spain, [2]Sociedad Española de Reumatología, Madrid, Spain, [3]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [4]Hospital Universitario La Paz, Madrid, Spain, [5]Hospital Universitario Donosti, Donosti, Spain, [6]Complejo Asistencial Universitario de León, León, Castilla y Leon, Spain, [7]Hospital Universitario 12 de Octubre, Madrid, Spain, [8]Hospital Universitario de Bellvitge, Barcelona, Spain, [9]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [10]Hospital Universitario de Navarra, Pamplona, Spain, [11]IdISSC. HCSC, Madrid, Madrid, Spain, [12]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [13]Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, Spain, [14]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [15]Hospital del Bierzo, Ponferrada, Castilla y Leon, Spain, [16]Rheumatologist, La Laguna, Spain, [17]Consorci Hospital General Universitari de València, Valencia, Spain, [18]Department of Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain, Madrid, Spain, [19]Hospital Universitari Son Llàtzer, Palma de Mallorca, Spain, [20]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a chronic granulomatous vasculitis affecting medium- and large-sized arteries (1). The classic symptoms are cranial symptoms, including headache, jaw claudication, scalp hyperalgesia and sometimes visual disturbances. Additionally, extracranial involvement may occur due to stenosis and aneurysms in different

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics, clinical variables and phenotypes of patients with GCA according to presence of PMR

	Total (n=1527)	Non-PMR (n=861)	PMR (n=666)	p-value
Women, n (%)	1076 (70,46)	580 (67.36)	496 (74.47)	**0.003**
Age, mean (SD)	76.95 (8.05)	77.35 (8.03)	76.45 (8.06)	0.030
Duration of symptoms (months), median (IQR)	15.74 (6.69 - 35.41)	12.20 (5.11 - 25.97)	24 (11.41 - 48)	**<0.001**
Smoker, n (%)	116 (8.04)	81 (9.98)	35 (5.55)	**0.005**
Headache, n (%)	1215 (79.72)	672 (78.14)	543 (81.78)	0.080
Temporal artery abnormalities, n (%)	744 (52.39)	417 (51.04)	327 (54.23)	0.234
Scalp hypersensitivity, n (%)	412 (30.68)	216 (28.16)	196 (34.03)	**0.021**
Mandibular claudication, n (%)	549 (37.27)	281 (33.65)	268 (42.01)	**0.001**
Visual manifestations, n (%)	541 (35.9)	362 (42.24)	179 (27.54)	**<0.001**
Stroke, n (%)	57 (3.83)	39 (4.62)	18 (2.80)	0.070
Synovitis, n (%)	82 (5.99)	15 (1.95)	67 (11.19)	**<0.001**
Constitutional syndrome, n (%) (n=1393)	928 (60.77)	470 (54.59)	458 (68.77)	**<0.001**
Asthenia, n (%)	795 (56.14)	382 (47.10)	413 (68.26)	**<0.001**
Anorexia, n (%)	559 (40.13)	284 (35.32)	275 (46.69)	**<0.001**
Weight loss, n (%)	497 (36.01)	254 (31.83)	243 (41.75)	**<0.001**
Fever, n (%)	330 (23.72)	187 (22.94)	143 (24.83)	0.416
Cranial phenotype, n (%)	412 (26.98)	209 (24.27)	203 (30.48)	**0.007**
Involvement of large vessels phenotype, n (%)	99 (6.48)	57 (6.62)	42 (6.31)	0.805
Mixed phenotype, n (%)	201 (13.16)	119 (13.82)	82 (12.31)	0.387

Table 2. Multivariate analysis

	OR	95% CI	p-value
Sex	0.986	0.768 - 1.265	0.910
Age	0.995	0.983 - 1.008	0.478
Duration of symptoms	1.002	1.001 - 1.003	**0.002**
Ex-smoker	1.172	0.740 - 1.858	0.498
Never smoker	1.346	0.882 - 2.055	0.169
Scalp hypersensitivity	1.042	0.843 - 1.288	0.702
Mandibular claudication	1.349	1.054 - 1.726	**0.017**
Vision manifestations	0.900	0.688 - 1.179	0.445
Synovitis	1.656	1.187 - 2.311	**0.003**
Constitutional syndrome	1.126	0.727 - 1.746	0.595
Asthenia	1.533	1.022 - 2.298	0.039
Anorexia	0.949	0.717 - 1.256	0.717
Weight loss	0.898	0.682 - 1.183	0.445
Cranial	1.298	0.990 - 1.701	0.059
Prednisone dose at diagnosis	0.660	0.447 - 0.975	**0.037**
Methotrexate	0.936	0.725 - 1.209	0.614
Leflunomide	0.768	0.102 - 5.769	0.797
Tocilizumab	0.811	0.480 - 1.370	0.434
Relapses	1.092	0.953 - 1.251	0.204

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

segments of the aorta, potentially leading to pulse loss and limb claudication. Polymyalgia rheumatica (PMR) is a disease characterized by pain and stiffness in the cervical region and/or the shoulder and/or pelvic girdles (2). Approximately, 50% of patients with GCA also present with PMR (3).

The aim of this study was to define the clinical, analytical and imaging characteristics, as well as the factors associated with PMR in patients with GCA.

Methods: The ARTESER study (Arteritis of the Spanish Society of Rheumatology), promoted by the Spanish Society of Rheumatology, is a longitudinal observational study based on a review of clinical records of patients diagnosed with GCA between June 1, 2013, and March 29, 2019, in 26 hospitals of the Spanish National Health System. Sociodemographic, clinical, analytical, and imaging variables at diagnosis were collected. Additionally, treatment and outcome variables were recorded at the end of follow-up.

Patients with and without PMR were compared through a bivariate analysis. To identify potential factors associated with PMR, a multivariate logistic regression model was performed. Statistical significance set at $p< 0.05$.

Results: A total of 1,527 patients with GCA were included in the analysis, of whom 43.6% presented with PMR at the time of diagnosis (Table 1).

When comparing patients with and without PMR at diagnosis, it was observed that patients with PMR had a higher proportion of women, were younger, and had a longer duration of symptoms ($p< 0.05$). Regarding comorbidities, patients with PMR showed lower rates of smoking and a higher frequency of osteoporosis. They also more frequently presented scalp hypersensitivity, jaw claudication, and constitutional syndrome ($p< 0.05$).

Regarding treatment, the initial dose of corticosteroids at diagnosis was lower in patients with PMR ($p< 0.001$).

When evaluating outcomes, patients with PMR experienced more relapses, with minor relapses being particularly more frequent in this group ($p=0.024$).

In the multivariate analysis, factors associated with PMR were longer symptom duration at diagnosis, the presence of jaw claudication, asthenia, and synovitis. Conversely, the initial dose of glucocorticoids was associated with a lower risk of PMR (Table 2).

Conclusion: Patients with GCA and PMR present a longer duration of symptoms at diagnosis, higher prevalence of osteoporosis, scalp hypersensitivity, jaw claudication, constitutional syndrome, cranial phenotype and a lower initial corticosteroid dose. Factors associated with PMR included longer symptom duration, jaw claudication, asthenia and synovitis, while the initial corticosteroid dose was associated with a lower risk of PMR.

Disclosure: M. Silva-Diaz: None; **M. Domínguez-Álvaro**: None; **R. Melero-González**: None; **E. Fernández-Fernández**: None; **J. Valero**: None; **I. González**: None; **J. Sánchez Martín**: None; **J. Narváez**: None; **E. Galíndez Agirregoikoa**: None; **V. Aldasoro Cáceres**: None; **I. Abasolo Alcazar**: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **N. Garrido**: None; **S. Castañeda**: None; **C. Iñiguez**: None; **A. Garcia**: None; **C. Molina Almela**: None; **M. Alcalde Villar**: None; **A. Mas**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0753

Incidence of Ischemic Vision Loss Among Patients with Polymyalgia Rheumatica and Giant Cell Arteritis

Mary Peng[1], Kylie Carlson[2], Sebastian E Sattui[3] and Michael Putman[4], [1]Medical College of Wisconsin, Wauwatosa, WI, [2]Medical College of Wisconsin, Milwaukee, WI, [3]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, [4]The Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Ischemic vision loss affects up to one quarter of patients with giant cell arteritis (GCA). The incidence of ischemic vision loss among patients with isolated polymyalgia rheumatica (PMR) is poorly defined. This study aimed to quantify the risk of ischemic vision loss among patients with PMR, GCA, and matched population controls.

Methods: We conducted a retrospective cohort study using the US-based TriNetX electronic health records network. Adults ≥50 years were included if they had ≥2 ICD-9/10-CM codes for GCA or PMR, ≥1 year of prior follow-up, and a prednisone prescription within 30 days of their first diagnostic code. Matched general population control cohorts for PMR and GCA were constructed using 1:3 nearest-neighbor matching on the following variables: sex, race/ethnicity, regional location, birth year, year of cohort entry, and year of cohort exit. The primary outcome was ischemic vision loss, which was defined by ICD-9/10 codes for ischemic optic neuropathy and retinal artery occlusion. Multivariable Cox proportional cause-specific adjusted hazard ratios (aHR) and 95% confidence intervals (CI) were calculated to define the risk of ischemic vision loss.

Table 1: Demographic and Clinical Characteristics of Included Patients, n = 56,899

	Overall	PMR	General Population - PMR Controls*	GCA	General Population - GCA Controls*
Number of Patients	56,899	16,001	31,113	3,054	6,731
Median Follow-Up Time	3.39 [1.4-6.2]	3.69 [1.7-6.5]	3.21 [1.1-6.0]	3.39 [1.5-6.1]	3.52 [1.5-6.3]
Age at Diagnosis, mean (SD)	70.0 (8.4)	71.1 (8.1)	69.0 (8.5)	71.3 (8.0)	71.1 (8.3)
Sex					
Male	21,797 (38.3%)	7,036 (44.0%)	11,958 (38.4%)	882 (28.9%)	1,921 (28.5%)
Female	35,102 (61.7%)	8,965 (56.0%)	19,155 (61.6%)	2,172 (71.1%)	4,810 (71.5%)
Race/Ethnicity					
White	48,288 (84.9%)	13,787 (86.2%)	26,874 (86.4%)	2,335 (76.5%)	5,292 (78.6%)
Black or African American	3293 (5.8%)	783 (4.9%)	1,559 (5.0%)	310 (10.2%)	631 (9.4%)
Hispanic or Latino	1,266 (2.2%)	322 (2.0%)	639 (2.1%)	103 (3.4%)	202 (3.0%)
Asian	588 (1.0%)	146 (0.9%)	282 (0.9%)	51 (1.7%)	109 (1.6%)
Other / NA	3,474 (6.1%)	963 (6.0%)	1,759 (5.7%)	255 (8.3%)	497 (7.4%)
Charlson Comorbidity Index	0.7 (1.4)	0.8 (1.4)	0.6 (1.3)	1.0 (1.6)	0.6 (1.3)
Admissions during Prior Year, mean (SD)	0.4 (1.7)	0.4 (1.6)	0.3 (1.7)	0.8 (2.6)	0.4 (1.7)
Comorbidities at Diagnosis					
Chronic Obstructive Pulmonary Disease	7,750 (13.6%)	2,442 (15.3%)	3,867 (12.4%)	581 (19.0%)	860 (12.8%)
Obesity	5,572 (9.8%)	1,951 (12.2%)	2,652 (8.5%)	393 (12.9%)	576 (8.6%)
Diabetes	5,207 (9.2%)	1,930 (12.1%)	2,383 (7.7%)	376 (12.3%)	518 (7.7%)
Renal Disease	4,050 (7.1%)	1,660 (10.4%)	1,634 (5.3%)	329 (10.8%)	427 (6.3%)
Liver Disease	1,687 (3.0%)	595 (3.7%)	795 (2.6%)	137 (4.5%)	160 (2.4%)
Atherosclerosis	1,480 (2.6%)	509 (3.2%)	643 (2.1%)	167 (5.5%)	161 (2.4%)
Smoking	1,286 (2.3%)	377 (2.4%)	656 (2.1%)	115 (3.8%)	138 (2.1%)

Abbreviations: polymyalgia rheumatica (PMR), giant cell arteritis (GCA), standard deviation (SD), not applicable (NA)
*Control groups were matched to PMR and GCA, respectively

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 56,899 patients, 16,001 had PMR, 3,054 had GCA, and 37,844 were matched controls. Median follow-up time was 3.4 years (interquartile range, 1.4-6.2). The incidence of ischemic vision loss over the entire follow-up period (10 years) was highest for GCA (9.2 per 1,000 person-years) followed by PMR (1.7 per 1,000 person-years), GCA controls (1.5 per 1,000 person-years), and PMR controls (1.4 per 1,000 person-years). Ischemic vision loss was increased in GCA as compared to PMR (aHR 5.36, 95% CI 4.09–7.02) and GCA as compared to matched-controls (aHR 5.69, 95% CI 3.95–8.18). No significant differences were observed for PMR as compared to matched controls (aHR 1.10, 95% CI 0.86–1.41). Sensitivity analyses over the first one year and the first 5 years of therapy supported the primary analyses.

Conclusion: In this large retrospective cohort study, patients with PMR had no increased risk of ischemic vision loss as compared to the general population or to patients with GCA. In contrast, patients with GCA were significantly more likely to suffer ischemic vision loss. These findings support the current approach of ophthalmology referral for patients with GCA and screening by symptoms alone for PMR.

Table 2: Unadjusted Incidence of Ischemic Vision Loss Among Included Patients, n = 56,899

Analysis	Events	Follow Up Time	Incidence / 1000py
Total Follow Up			
PMR	113	65,673	1.7
General Population (PMR)	158	116,755	1.4
GCA	111	12,022	9.2
General Population (GCA)	41	27,140	1.5
One Year Outcomes			
PMR	21	14,774	1.4
General Population (PMR)	32	25,581	1.3
GCA	76	2,796	27.2
General Population (GCA)	6	5,846	1.0
Five Year Outcomes			
PMR	84	28,903	2.9
General Population (PMR)	114	51,268	2.2
GCA	103	5,438	18.9
General Population (GCA)	26	11,633	2.2

Abbreviations: Polymyalgia rheumatica (PMR), Giant Cell Arteritis (GCA), person years (py)

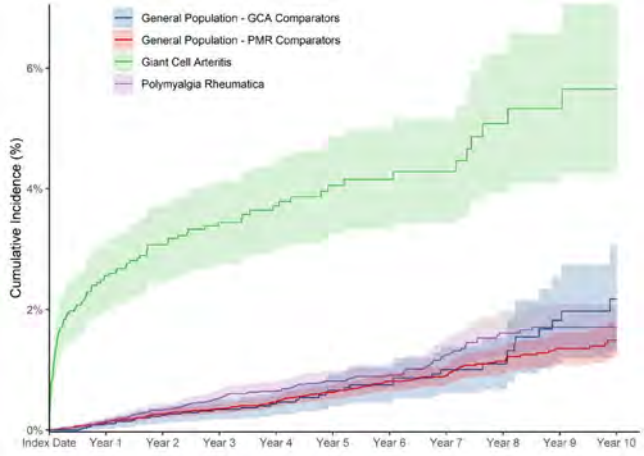


Figure 1: Cumulative incidence of ischemic vision loss among patients with GCA, PMR, and matched controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Peng: None; **K. Carlson**: None; **S. Sattui**: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2; **M. Putman**: AbbVie/Abbott, 5, Amgen, 5, AstraZeneca, 2, 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5.

Abstract Number: 0754

Is There a Seasonal Pattern in Giant Cell Arteritis? Revisiting the Evidence in a Large Monocentric Cohort of 1203 patients

Milena Bond[1], Philipp Bosch[2], Aaron Juche[3], Hans Bastian[3] and Wolfgang Schmidt[4], [1]South Tyrol Health Trust and Teaching Hospital of the Paracelsus Medical University, Brunico, Italy, [2]Medical University of Graz, Graz, Austria, [3]Rheumaklinik Berlin-Buch, Berlin, Germany, [4]Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch; Waldfriede Hospital, Rheumatology, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Table 1. Baseline characteristics of the 1149 patients included in the analysis.

Category	Result	N (%) of available data
***Total population**, n*	***1149***	
Men, *n (%)*	399 (34.7%)	1149 (100%)
Age (years), *median (range)*	72 (43–95)	1147 (99.8%)
***Clinical features**, n (%)*		
Cranial GCA*	558 (48.6%)	1149 (100%)
Large-vessel GCA*	234 (20.4%)	1149 (100%)
Cranial+large-vessel GCA*	347 (30.2%)	1149 (100%)
Isolated Aortitis*	10 (0.9%)	1149 (100%)
PMR symptoms	600 (52.7%)	1138 (99%)
Headache	740 (65.1%)	1136 (98.9%)
Jaw claudication	468 (41.4%)	1131 (98.4%)
Clinically abnormal temporal artery	562 (52.1%)	1078 (93.8%)
Ocular manifestations, overall	231 (20.1%)	1149 (100%)
Permanent vision loss	129 (11.2%)	1149 (100%)
Amaurosis fugax	55 (4.8%)	1149 (100%)
Diplopia	47 (4.1%)	1149 (100%)
Stroke	3 (0.3%)	1144 (99.6%)
***Laboratory findings at diagnosis**, median (range)*		
CRP (mg/l)	69 (0–420)	883 (76.8%)
ESR (mm/h)	77 (0–200)	851 (74.1%)
***Ultrasonographic findings**, n (%)*		
Normal	29 (2.5%)	1149 (100%)
Temporal artery halo sign	853 (74.2%)	1149 (100%)
Temporal artery stenosis	213 (18.5%)	1149 (100%)
Temporal artery occlusion	155 (13.5%)	1149 (100%)
Axillary artery involvement (at least one)	515 (44.9%)	1146 (99.7%)
***Biopsy**, n (%)*		
Biopsy performed	203 (17.7%)	1149 (100%)
Positive findings	147 (12.8%)	1149 (100%)

Legend. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis; PMR, polymyalgia rheumatica. *, vessel involvement documented at any type of imaging.

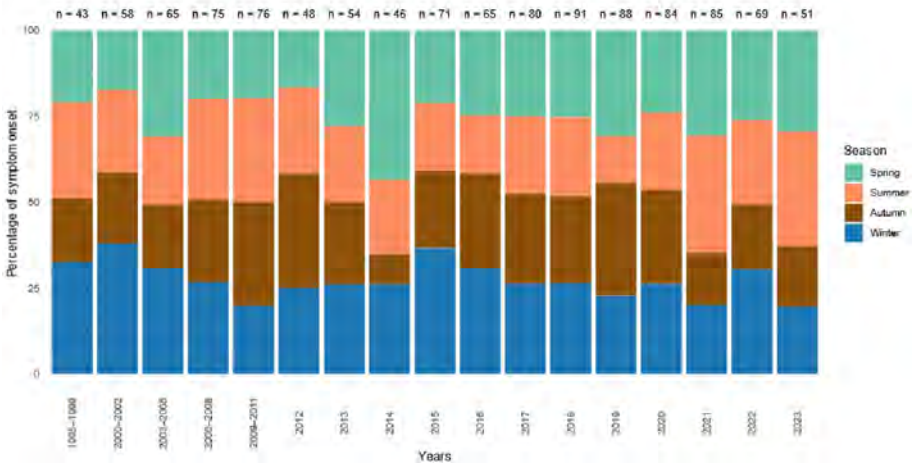
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Seasonal Distribution of Symptom Onset by Subgroup

Population	N	Spring n (%)	Summer n (%)	Autumn n (%)	Winter n (%)	P value
Main analysis	1149	292 (25.4%)	276 (24.0%)	271 (23.6%)	310 (27.0%)	0.360
Female only	750	185 (24.7%)	174 (23.2%)	171 (22.8%)	220 (29.3%)	0.196*
Male only	399	107 (26.8%)	102 (25.6%)	100 (25.1%)	90 (22.6%)	0.673*
Cranial involvement only	558	137 (24.6%)	141 (25.3%)	129 (23.1%)	151 (27.1%)	0.673*
Extracranial involvement only	234	59 (25.2%)	49 (20.9%)	56 (23.9%)	70 (29.9%)	0.555*

*Sensitivity analysis p values corrected by Bonferroni Holms correction

Figure 1. Seasonal Distribution of Symptoms Onset



Background/Purpose: Whether the disease onset in giant cell arteritis (GCA) exhibits a seasonal pattern remains unclear. Previous studies have yielded conflicting evidence: some report no seasonality, while others suggest seasonal variation, though findings are inconsistent and difficult to compare, especially due to methodological limitations, including small cohort sizes and reliance on diagnosis or biopsy dates rather than symptoms onset. We aimed to clarify whether a seasonal pattern exists by analyzing a large cohort using the date of symptom onset as the temporal reference.

Methods: Consecutive patients from a large German monocentric GCA cohort in Berlin-Buch (1994–2024) with a documented date of symptom onset were included. To ensure balanced seasonal representation, patients with symptom onset outside the period of December 1, 1994, to November 30, 2023, were excluded. Meteorological seasons were used for the analysis (spring: Mar–May; summer: Jun–Aug; autumn: Sep–Nov; winter: Dec–Feb). To assess whether symptom onsets were equally distributed across seasons (25% per season), we applied an exact multinomial test using the "ExactMultinom" package in R. Sensitivity analyses were performed for subgroups by sex and clinical phenotype (cranial vs extracranial involvement), with Bonferroni-Holm correction for multiple testing.

Results: Of 1203 patients in the full cohort, 1149 fulfilled the inclusion criteria and were included in the main analysis (population's characteristics are reported in Table 1). The overall seasonal distribution of symptom onset was: spring 292 (25.4%), summer 276 (24.0%), autumn 271 (23.6%), winter 310 (27.0%) (p = 0.36). Figure 1 illustrates the seasonal distribution of symptom onset stratified by years across the study period. Subgroup analyses revealed no overall significant seasonal variation as shown in Table 2.

Conclusion: This large, single-center cohort study using symptom onset data found no evidence of a significant seasonal pattern in the disease onset of GCA patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Bond: AbbVie/Abbott, 6; **P. Bosch**: AbbVie/Abbott, 1, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, UCB, 6; **A. Juche**: AbbVie/Abbott, Novartis, 12, participated in trials as investigator; **H. Bastian**: Alfasigma, 12, Congress and travel expenses, Celltrion, 12, Congress and travel expenses, Novartis, 5, 12, Congress and travel expenses; **W. Schmidt**: AbbVie, 1, 5, 6, Alfasigma, 6, Amgen, 6, Boehringer-Ingelheim, 1, Chugai, 6, Eli Lilly, 6, Fresenius Kabi, 1, GlaxoSmithKline, 6, Medac, 6, Novartis, 1, 5, 6, Pfizer, 6, UCB, 6.

Abstract Number: 0755

Sex Differences in Subtypes of Vascular Involvement and Clinical Manifestations in Giant Cell Arteritis

Natalia Lopez Juanes, Carlota Ureta, Irene Monjo Henry, Maria-Eugenia Miranda-Carus, Chamaida Plasencia-Rodríguez and Eugenio de Miguel, Hospital Universitario La Paz, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Recognizing gender-specific differences in diseases is critical to improve diagnostic and therapeutic strategies. Giant cell arteritis (GCA) has been traditionally considered a predominantly female disease, but this predominance may be declining with new classification criteria and advanced imaging. While gender-related differences in cranial and extra-cranial GCA phenotypes have been observed, most studies have focused mainly on clinical patterns. The objective of this study is to assess gender-specific differences in GCA clinical presentation, particularly patterns of vascular involvement, age at diagnosis and clinical manifestations.

Methods: This is a retrospective population-based study including consecutive unselected GCA cases from a cohort diagnosed since 2017. Standardized bilateral ultrasound (US) of cranial arteries (common temporal artery and branches) and extra-cranial arteries (carotid, subclavian, axillary) were performed in all patients. Subtypes were categorized as cranial, extracranial, or mixed according to the pattern of vascular involvement identified by ultrasound (US) and/or positron emission tomography-computed tomography (PET-CT). Demographic and clinical data were obtained from medical records, and a confirmed diagnosis required a minimum of six months of clinical follow-up.

Results: A total of 249 GCA cases (table 1) were analyzed (mean age 78.9±8.3 years, range 58–105), with 134 females (53.8%). Cranial involvement was present in 195/249 cases (78.3%), significantly more common in males (84.3%) than females (73.1%, p=0.03). Large vessel involvement was detected in 128/249 patients (51.4%) without significant sex differences (56.5% males vs. 47.0% females, p=0.16)

Table 1: Sex, age and subtypes of GCA.

Sex	Cases	Age (mean±SD)	Subtype of GCA		
			Isolated cranial	Mixed	Isolated large vessel
All	249	78.9±8.3	121 (48.6%)	74 (29.7%)	54 (21.7%)
Female (F)	132 (53.4%)	78.6±8.5	71 (53.0%)	27 (20.1%)	36 (26.9%)*
Male (M)	115 (46.6%)	79.4±8.1	50 (43.5%)	47 (40.9%)**	18 (15.7%)

* = p < 0.05, ** = p < 0.01 between males and females.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Clinical manifestations.

			Headache	PMR	AION	Stroke	Jaw claudication	Fever	Constitutional syndrome	Aortic syndrome	All relapses	Major relapses	Minor relapses
All			150 (60.2%)	132 (53,0%)	46 (18.5%)	22 (8.8%)	49 (19.7%)	44 (17.7%)	59 (23.9%)	11 (4.4%)	95 (38.3%)	19 (7.7%)	89 (35.9%)
F			94 (70.1%)**	68 (50.7%)	27 (20.1%)	14 (10.4%)	34 (25.4%)*	25 (18.7%)	37 (27.6%)	4 (3.0%)	55 (41.4%)	12 (9.0%)	50 (37.6%)
M			56 (48.7%)	64 (55.7%)	19 (16.5%)	8 (7.0%)	15 (13.0%)	19 (16.5%)	22 (19.1%)	7 (6.1%)	40 (34.8%)	7 (6.1%)	39 (33.9%)
Subtypes of GCA	Isolated cranial	All	87 (71.9%)	59 (48.8%)	30 (24.8%)	11 (9.1%)	31 (25.6%)	12 (9.9%)	26 (21.5%)	4 (3.3%)	44 (36.4%)	7 (5.8%)	45 (37.2%)
		F	57 (80.3%)*	33 (46.5%)	18 (25.4%)	9 (12.7%)	23 (32.4%)	7 (9.9%)	17 (23.9%)	1 (1.4%)	28 (39.4%)	5 (7.0%)	28 (39.4%)
		M	30 (60.0%)	26 (52.0%)	12 (24.0%)	2 (4.0%)	8 (16.0%)	5 (10.0%)	9 18.0%)	3 (6.0%)	16 (32.0%)	2 (4.0%)	17 (34.0%)
	Mixed	All	41 (55.4%)	37 (50.0%)	13 (17.6%)	10 (13.5%)	13 (17.6%)	15 (20.3%)	20 (27.0%)	4 (5.4%)	31 (41.9%)	6 (8.1%)	27 (36.5%)
		F	21 (77.8%)*	13 (48.1%)	6 (22.2%)	5 (18.5%)	7 (25.9%)	5 (18.5%)	10 (37.0%)	2 (7.4%)	12 (44.4%)	2 (7.4%)	10 (37.0%)
		M	20 (42.6%)	24 (51.1%)	7 (14.9%)	5 (10.6%)	6 (12.8%)	10 (21.3%)	10 (21.3%)	2 (4.3%)	19 (40.4%)	4 (8.5%)	17 (36.2%)
	Isolated large vessel	All	22 (40.7%)	36 (66.7%)	3 (5.6%)	1 (1.9%)	5 (9.3%)	15 (31.5%)	14 (25.9%)	3 (5.6%)	20 (37.7%)	6 (11.3%)	17 (32.1%)
		F	16 (44.4%)	22 (61.1%)	3 (8.3%)	0 (0%)	4 (11.1%)	11 (36.1%)	11 (30.6%)	1 (2.8%)	15 (42.9%)	5 (14.3%)	12 (34.2%)
		M	6 (33.3%)	14 (77.8%)	0 (0%)	1 (5.6%)	1 (5.6%)	4 (22.2%)	3 (16.7%)	2 (11.1%)	5 (27.8%)	1 (5.6%)	5 (27.8%)

* = $p < 0.05$, ** = $p < 0.01$ between males and females.

Analysis by subtype showed isolated cranial involvement in 121 patients (48.6%), isolated large vessel vasculitis in 54 (21.7%), and mixed patterns in 74 (29.7%). Significant sex differences were observed: mixed pattern was more frequent in males (40.9% vs. 20.1%, $p< 0.01$), while isolated large vessel vasculitis was more common in females (26.9% vs. 15.7%, $p=0.03$). Isolated cranial involvement was also more frequent in females, though not statistically significant.

No significant age differences were found between sexes (78.6±8.5 years in females vs. 79.4±8.1 in males) or within vascular subtypes. Clinical manifestations (table 2) were generally more common in women, with significant differences in headache ($p< 0.01$) and jaw claudication ($p=0.04$). Women also tended to present more relapses, though this did not reach statistical significance.

Conclusion: GCA shows only a mild female predominance (53.6%). Important sex differences exist in vascular involvement patterns: cranial involvement was more common in males, isolated large vessel vasculitis more frequent in females, and mixed patterns predominated in males ($p< 0.01$). Age at diagnosis did not differ between sexes. Women tended to present significantly more headache ($p< 0.001$) and jaw claudication ($p=0.04$). These findings highlight the need for sex-specific considerations in the diagnosis and management of GCA.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Lopez Juanes: None; **C. Ureta**: None; **I. Monjo Henry**: None; **M. Miranda-Carus**: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6.

Abstract Number: 0756

Stroke Characteristics in Giant Cell Arteritis and Takayasu Arteritis: A Multicenter Cohort Study of 108 Patients

Omar Dhrif[1], Charlotte Caudron[2], Simon Parreau[3], Eric Liozon[3], Adrien Mirouse[4], Jean-François Alexandra[5], Laurent Sailler[6], Mathieu Groh[7], Hubert De Boysson[8], Mikael Ebbo[9], Cloé Comarmond[10], Cécile Audrey Durel[11], Juliette Woessner[12], Pierre-André Jarrot[13], Kévin Didier[14], Goulabchand Radjiv[15], Cacoub Patrice[16], Bernard Bonnotte[17], David Saadoun[16] and Maxime Samson[1], [1]CHU Dijon Bourgogne, Dijon, France, [2]CENTRE HOSPITALIER UNIVERSITAIRE DE DIJON, Paris, France, [3]CHU de Limoges, Limoges, France, [4]Médecine Interne et Immunologie Clinique, Groupe Hospitalier Pitié-Salpêtrière, APHP, Paris, Paris, France, [5]Internal Medicine, Hôpital Bichat, APHP, Paris, France, [6]CHU Toulouse, Toulouse, France, [7]Hôpital Foch, Suresnes, France, [8]Internal Medicine, CHU Caean, Caen, France, [9]Internal Medicine, Marseille-APHM, hôpital La Timone, Marseille, France, [10]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, INSERM U942, Paris, France, [11]Médecine Interne, Hôpital Saint Joseph Saint Luc, Lyon, Lyon, France, [12]Médecine Interne, CH d'Avignon, Avignon, Avignon, France, [13]Médecine Interne, Hôpital de la Conception, APHM, Marseille, Marseille, France, [14]Médecine Interne, CHU Reims, Reims, Reims, France, [15]Médecine Interne, CHU Nîmes, Nîmes, Nîmes, France, [16]Department of Internal Medicine and Clinical Immunology, Sorbonne Universités, AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Centre national de références Maladies Autoimmunes et systémiques rares, Centre national de références Maladies Autoinflammatoires rares et Amylose inflammatoire (CEREMAIA), INSERM, UMR S959, Immunology-Immunopathology-Immunotherapy (I3), Paris, France, Paris, France, [17]Internal medicine and clinical immunology, Université Bourgogne Europe , CHU Dijon Bourgogne, Dijon, France

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: In giant cell arteritis (GCA) and Takayasu arteritis (TA), strokes occur in approximately 7.4% and 15.8% of cases, respectively. Although these two large-vessel vasculitides share similarities, stroke presentation may differ in terms of clinical and radiological characteristics. This study aimed to compare the epidemiological, clinical, and prognostic features of stroke in patients with GCA and TA

Methods: This was a multicenter retrospective cohort study conducted in France, including patients meeting the 2022 ACR/EULAR classification criteria for GCA and either the 2022 ACR/EULAR criteria or modified Ishikawa criteria for TA. Eligible patients had at least one stroke confirmed by imaging, occurring either at the time of or within 4 weeks of vasculitis flare.

Results: A total of 108 patients (68 with GCA and 40 with TA) were analyzed. The female-to-male ratio was 0.78 in GCA and 5.2 in TA ($p< 0.001$). The mean age at stroke onset was 76+/-9 years in GCA and 35±10 years in TA ($p< 0.001$).

At the time of stroke, cardiovascular risk factors in GCA versus TA were as follows: overweight (22.4% vs. 10.3%, p=0.174), obesity (7% vs. 2.6%, p=0.645), smoking (40.9% vs. 39.4%, p=0.885), hypertension (64.7% vs. 32.4%, RR=1.99, p=0.003), dyslipidemia (36.8% vs. 8.8%, RR=4.2, p=0.002), and diabetes (14.7% vs. 2.9%, p=0.095).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Stroke occurred at the time of vasculitis diagnosis in 95.6% of GCA cases and 81.1% of TA cases (RR=1.18, p=0.031). All strokes were ischemic. The initial clinical presentation in GCA versus TA included motor deficits (47.1% vs. 30%, p=0.207), sensory deficits (14.7% vs. 16.7%, p=0.754), ophthalmologic symptoms (39.7% vs. 34.2%, p=0.677), cerebellar syndrome (29.4% vs. 0%, p=0.001), cranial nerve involvement (19.7% vs. 0%, p=0.017), language impairment (41.2% vs. 12.5%, RR=3.3, p=0.012), and neurosensory disturbances (55.9% vs. 18.4%, RR=3.04, p< 0.001).

Strokes involved the carotid territory in 35.3% of GCA cases and in 79.5% of TA cases (RR=0.44, p< 0.001) while the vertebrobasilar territory was involved in 75% of GCA cases and 20.5% of TA cases (RR=3.7, p< 0.001). Stroke recurrence occurred in 14.7% of GCA cases and 7.5% of TA cases (p=0.364), with a median recurrence time of 6 months (IQR: 1–10 months) after the initial stroke. Vascular surgery was required in 6% of GCA cases and 41% of TA cases (RR=0.14, p< 0.001). The mean follow-up duration was 5 ± 6.1 years, with mortality rates of 14.5% in GCA and 5% in TA (p=0.194). The survival curve for both groups is presented in Figure 1.

In multivariate analysis excluding age, independent factors associated with TA diagnosis were the absence of dyslipidemia (OR=0.085, p=0.035), carotid territory involvement (OR=13.7, p=0.003), and the need for vascular surgery (OR=10.6, p=0.009).

Conclusion: Stroke presentation differs between GCA and TA. In GCA, strokes predominantly affect older individuals with cardiovascular risk factors and mainly involve the vertebrobasilar territory. While in TA, carotid involvement is more frequent and often necessitates vascular intervention. These clinical and prognostic differences are crucial for optimizing patient management

Disclosure: O. Dhrif: None; **C. Caudron**: None; **S. Parreau**: None; **E. Liozon**: None; **A. Mirouse**: None; **J. Alexandra**: Chugai France, 2; **L. Sailler**: None; **M. Groh**: None; **H. De Boysson**: AbbVie/Abbott, 1, 2, Chugai, 2, Fresenius Kabi, 1, 2, Novartis, 2; **M. Ebbo**: None; **C. Comarmond**: Roche, 5; **C. Durel**: None; **J. Woessner**: None; **P. Jarrot**: None; **K. Didier**: None; **G. Radjiv**: None; **C. Patrice**: None; **B. Bonnotte**: Boehringer-Ingelheim, 2, Chugai, 2, Novartis, 2, Vifor Pharma, 2; **D. Saadoun**: None; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2.

Abstract Number: 0757

The role of Methotrexate in the treatment of Giant Cell Arteritis: data from the ARTESER registry.

Pablo Muñoz-Martínez[1], Marta Domínguez-Álvaro[2], Lucia Otero[3], Clara Moriano[4], Julio Sánchez Martín[5], Javier Narváez[6], Eva Galíndez Agirregoikoa[7], Javier Mendizábal[8], lydia Abasolo Alcazar[9], Javier Loricera[10], Alejandro Muñoz[11], Santos Castañeda[12], rafeal Benito-Melero[13], Carmen Larena[14], Paula Estrada-Alarcón[15], Carlos Galisteo[16], Anne Riveros frutos[17], Francisco Ortiz sanjuán[18], Tarek Salman Montes[19] and Ricardo Blanco[20], [1]Hospital Universitario y Politécnico La Fe, Sagunto, Spain, [2]Sociedad Española de Reumatología, Madrid, Spain, [3]Spanish Society of Rheumatology, Madrid, Spain, [4]Hospital Leon, LEON, Castilla y Leon, Spain, [5]Hospital Universitario 12 de Octubre, Madrid, Spain, [6]Hospital Universitario de Bellvitge, Barcelona, Spain, [7]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [8]Navarra Hospital, Pamplona, Spain, [9]IdISSC. HCSC, Madrid, Madrid, Spain, [10]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [11]Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, Spain, [12]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [13]MD, barcelona, Spain, [14]Hospital Universitario Ramón y Cajal, Madrid, Madrid, Spain, [15]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [16]Hospital Parc Taulí, Sabadel, Sabadel, Spain, [17]Hospital Germans Trias i Pujol, Barcelona, Spain, [18]Hospital Universitario y Politécnico La Fe, Valencia, Comunidad Valenciana, Spain, [19]Hospital del Mar/Parc de Salut Mar-IMIM, Barcelona, Spain, [20]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is the most common large-vessel vasculitis, and its cornerstone treatment is the use of corticosteroids (CS). Various therapies have been proposed as CS-sparing agents, with methotrexate (MTX) being the only conventional synthetic drug that has received favorable recommendations in clinical practice guidelines. However, results from clinical trials and observational studies have been inconsistent. The aim of this study was to evaluate the role of MTX added to standard CS therapy in facilitating CS withdrawal in real-world clinical practice, by analyzing data from the Spanish national ARTESER registry.

Table 1. Baseline clinical and treatment characteristics at the time of GCA diagnosis, stratified by MTX use (CS monotherapy vs CS+MTX).

	CS monotherapy N=615	CS+MTX N=270	p value
Female sex, n (%)	405 (65.85%)	202 (74.81%)	**0.008**
Age at diagnosis (years), mean (SD)	77.97 (7.83)	75.72 (7.94)	**<0.001**
Symptoms duration (months), median [IQR]	1.05 [0.46 - 2.54]	1.48 [0.69 - 3.05]	**0.004**
ACR 2022 classification criteria, n (%)	575 (93.50%)	248 (91.85%)	0.378
Clinical manifestations, n (%)			
New-onset headache	487 (79.71%)	205 (76.21%)	0.244
Temporal artery tenderness or reduced pulse	315 (55.46%)	119 (47.41%)	**0.033**
Scalp tenderness	164 (31.60%)	76 (31.28%)	0.929
Jaw claudication	207 (36.06%)	90 (33.96%)	0.554
Visual symptoms	245 (40.97%)	78 (29.21%)	**0.001**
Polymyalgia rheumatica	222 (38.68%)	122 (46.04%)	**0.044**
Fever	123 (22.57%)	69 (27.38%)	0.14
Risk factors, n (%)			
Smoking status			
Current smoker	48 (8.35%)	16 (6.40%)	
Former smoker (>1 year)	124 (21.57%)	49 (19.60%)	0.461
Never smoker	403 (70.09%)	185 (74.00%)	
Treatment			
Corticosteroids			
Oral, n (%)	612 (99.51%)	270 (100.00%)	0.25
Intravenous, n (%)	145 (23.58%)	71 (26.30%)	0.386
Mean initial CS dose at diagnosis, mean (SD)	638.81 (1319.08)	507.26 (1152.04)	0.156
Cumulative CS dose, mean (SD)	7555.35 (4846.31)	8865.47 (4645.97)	**<0.001**
Methotrexate			
Initial MTX dose, n (%)			
<=10 mg/week	-	182 (67.41%)	-
>10 y <=15 mg/week	-	69 (25.56%)	-
>15 mg/week	-	19 (7.04%)	-

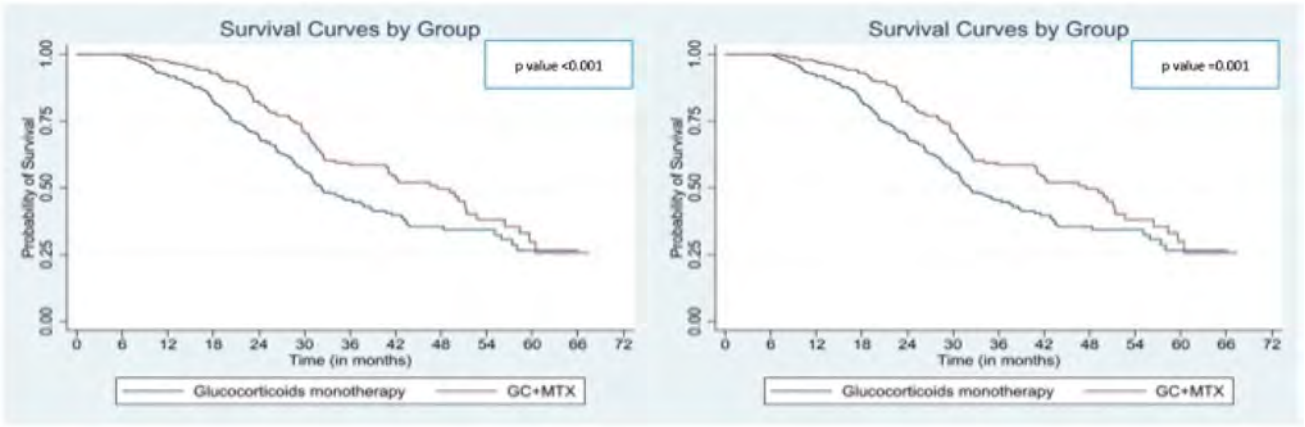


Figure 1. Kaplan-Meier survival curves: a) CS discontinuation and b) CS-free sustained remission (last 6 months).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariable Cox regression models (parsimonious models).

	Hazard Ratio (HR)	95% CI	p-value
CS discontinuation			
CS+MTX (Ref. CS monotherapy)	0.563	0.434 - 0.732	**<0.001**
Female sex (Ref. male)	0.750	0.583 - 0.963	**0.024**
Extracranial manifestation	1.387	0.916 - 2.098	0.122
Positive temporal artery biopsy	0.774	0.604 - 0.992	**0.043**
CS free-sustained remission (last 6 months)			
CS+MTX (Ref. CS monotherapy)	0.724	0.533 - 0.983	**0.039**
Female sex (Ref. male)	0.696	0.515 - 0.942	**0.019**
Smoker (Ref. never smoker)	1.581	0.955 - 2.618	0.075
Time from symptoms onset until diagnosis (months)	0.959	0.911 - 1.010	0.113
New-onset headache	0.668	0.481 - 0.926	**0.015**
Visual symptoms	0.784	0.568 - 1.083	0.140

Methods: Descriptive, observational, multicenter study of patients diagnosed with GCA undergoing treatment with corticosteroids in real-life settings. Baseline characteristics and treatments were compared between patients on CS monotherapy and those receiving concomitant MTX (CS+MTX). A survival analysis was performed using the Kaplan-Meier method, and the groups were compared using the log-rank test. Additionally, a Cox regression analysis was conducted to identify factors associated with complete CS withdrawal and CS-free sustained remission for at least 6 months.

Results: A total of 885 patients with GCA were included (615 treated with CS monotherapy and 270 with CS+MTX). Compared to those receiving CS monotherapy, patients in the CS+MTX group were younger, predominantly female, had a higher prevalence of concomitant polymyalgia rheumatica, and experienced a longer symptom duration before diagnosis (Table 1).

A higher relapse rate was observed in patients treated with CS+MTX compared to those on CS monotherapy (32.9% vs 12.5%, $p< 0.001$). Similarly, the cumulative dose of corticosteroids during follow-up was higher (8.87 g vs 7.56 g, $p< 0.001$). Time to reach doses of 5 mg, 7.5 mg, complete CS withdrawal, and CS-free remission for over 6 months was longer in the CS+MTX group.

Survival analysis revealed statistically significant differences in time to CS withdrawal ($p< 0.001$) and CS-free remission sustained for more than 6 months ($p< 0.001$) (Figure 1). No significant differences were observed between the groups in time to reach 5 or 7.5 mg of prednisone.

In the Cox regression models, the use of MTX (HR 0.563; 95% CI: 0.434–0.732; $p< 0.001$), female sex, and positive temporal artery biopsy were associated with a lower likelihood of achieving CS-free remission. Furthermore, MTX use was associated with a lower probability of achieving CS-free remission sustained for over 6 months (HR 0.724; 95% CI: 0.533–0.983; $p< 0.001$), along with female sex and headache (Table 2).

Conclusion: In the ARTESER registry, the use of MTX was not associated with a higher probability of achieving complete CS withdrawal or sustained CS-free remission compared to CS monotherapy. Additionally, patients did not show a lower cumulative dose of CS or a reduced relapse rate. Therefore, MTX use did not seem to be associated with better CS sparing outcomes in our real-life registry. Further research is needed to confirm our results and explore specific subgroups.

Disclosure: P. Muñoz-Martínez: None; **M. Domínguez-Álvaro**: None; **L. Otero**: None; **C. Moriano**: None; **J. Sánchez Martín**: None; **J. Narváez**: None; **E. Galíndez Agirregoikoa**: None; **J. Mendizábal**: None; **I. Abasolo Alcazar**: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **A. Muñoz**: None; **S. Castañeda**: None; **r. Benito-Melero**: AbbVie/Abbott, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6; **C. Larena**: None; **P. Estrada-Alarcón**: None; **C. Galisteo**: None; **A. Riveros frutos**: None; **F. Ortiz sanjuán**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

None; **T. Salman Montes**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 0758

Association Between Baseline IL-6 Levels and the Clinical Phenotype of Giant Cell Arteritis

Raquel Ugena-García[1], Clara Churtichaga Domenech[2], Judith Vidal-Ripoll[2], Francina salabert-Carreras[2], Cristina Calomarde-Gómez[1], Cristina Rocamora-Gisbert[3], Irene Peralta-García[4], Niccolo Viveros[2], Anne Riveros Frutos[3], Ivette Casafont-Solé[1] and Judit Font-Urgelles[1], [1]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [2]Hospital Germans Trias i Pujol, Barcelona, [3]Hospital Germans Trias i Pujol, Barcelona, Spain, [4]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna. Karolinska University Hospital, Medical Unit of Gastroenterology, Dermatology, Rheumatology. Theme Inflammation and Ageing, Stockholm, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is the most common form of vasculitis in patients over the age of 50. Interleukin-6 (IL-6) has been shown to play a potential role in the pathogenesis and prognosis of GCA, becoming a key therapeutic target. Moreover, some studies have suggested a potential prognostic value.

This study explores the association between baseline IL-6 concentrations and the clinical phenotype of the disease, with the aim of identifying patients who may benefit from anti–IL-6 therapies.

Methods: We conducted a cross-sectional study of a cohort of patients diagnosed with GCA between 2020 and 2024 in a tertiary care hospital. Patients were classified into two groups: those with exclusively cranial involvement (cranial GCA) and those with extracranial fluorodeoxyglucose (FDG) uptake at a PET-CT scan with or without cranial involvement (extracranial/mixed GCA).

A multiple linear regression model was used to evaluate the association between IL-6 levels and the clinical phenotype of GCA, adjusting for potential confounding and interaction variables (age, BMI, smoking status, type 2 diabetes mellitus, and prior corticosteroid therapy).

Regression coefficients (β), 95% confidence intervals (95% CI), and p-values were calculated, using a significance threshold of $p < 0.05$.

Model fit was assessed using the adjusted R-squared (adjusted R^2) and the F-test.

Results: A total of 39 patients were included. Epidemiological, clinical and diagnostic variables are detailed in Table 1. In the multiple regression analysis, no significant association was found between IL-6 levels and clinical phenotype ($p = 0.673$).

A significant negative association was observed between IL-6 levels and age ($\beta = -1.059$, 95% CI: -1.741 to -0.376, $p = 0.003$), as well as between IL-6 le levels and prior corticosteroid therapy ($\beta = -16.398$, 95% CI: -26.709 to -6.086, $p = 0.003$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient's epidemiological, clinical, and diagnostic characteristics.

	Total	Cranial GCA	Extracranial/Mixed GCA	p value
Age at diagnosis (years), *mean (SD)*	75.2 (8.0)	76.2 (6.5)	74.7 (8.8)	0.591
Female sex, *n (%)*	31 (79.5)	8 (61.5)	23 (88.5)	0.05
Headache, *n (%)*	34 (87.2)	12 (92.3)	22 (84.6)	0.498
Jaw claudication, *n (%)*	20 (51.3)	7 (53.9)	13 (50.0)	0.821
Scalp tenderness, *n (%)*	14 (35.9)	6 (46.2)	8 (30.8)	0.345
Stroke, *n (%)*	2 (5.1)	0 (0.0)	2 (7.7)	0.305
Amaurosis fugax, *n (%)*	4 (10.3)	1 (7.7)	3 (11.5)	0.709
Permanent visual loss, n (%)	10 (25.6)	4 (30.8)	14 (53.8)	0.640
Polymalgia rheumatica, *n (%)*	23 (59.0)	7 (53.8)	16 (61.5)	0.645
Constitutional symptoms, n (%)	18 (46.2)	4 (30.8)	14 (53.8)	0.173
Fever, *n (%)*	4 (10.3)	0 (0.0)	4 (15.4)	0.135
ESR (mm), *mean (SD)*	65.9 (33.8)	56.7 (41.8)	70.2 (29.3)	0.256
CPR (mg/L), *mean (SD)*	59.9 (63.4)	42.2 (64.9)	68.8 (62.0)	0.222
IL-6 (pg/mL), *mean (SD)*	15.61 (18.9)	11.54 (14.7)	17.6 (20.7)	0.349
Doppler vasculitis signs, *n (%)*	14 (35.9)	6 (46.2)	8 (30.8)	0.253
PET-CT positivity, *n (%)*	26 (66.7)	0 (0.0)	26 (100.0)	<0.001
Positive temporal artery biopsy, n (%)	15 (38.5)	4 (30.8)	11 (42.3)	0.439

A significant positive correlation was found between IL-6 and CRP ($r = 0.4546$, $p = 0.0032$) and between IL-6 and ESR ($r = 0.3754$, $p = 0.0185$).

Other clinical and diagnostic variables did not reach statistical significance.

Conclusion: In our cohort, no significant association was found between IL-6 levels and the clinical phenotype of GCA. Patients with constitutional symptoms and PMR tended to have higher IL-6 levels, which may suggest a greater inflammatory burden—an observation that should be confirmed in studies with larger sample sizes.

Notably, IL-6 levels were inversely associated with age, a finding that contrasts with current literature and may open new avenues for research.

This study reinforces the importance of further exploring the role of IL-6 to identify patients who may benefit most from targeted therapy against this molecule.

*The first two authors contributed equally to this abstract.

Disclosure: R. Ugena-García: None; **C. Churtichaga Domenech**: None; **J. Vidal-Ripoll**: None; **F. salabert-Carreras**: None; **C. Calomarde-Gómez**: None; **C. Rocamora-Gisbert**: None; **I. Peralta-García**: Johnson & Johnson, 5; **N. Viveros**: None; **A. Riveros Frutos**: None; **I. Casafont-Solé**: None; **J. Font-Urgelles**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0759

Distinct differences between giant cell arteritis diagnosed by fluorodeoxyglucose (FDG) positron emission tomography (PET) versus temporal artery biopsy-a comparative cohort study

Sehreen Mumtaz[1], Lerone Clark[2], Archit Srivastava[2], Hannah Langenfeld[3], Andrew C. Hanson[3], Cynthia Crowson[4], Andy Abril[2], Nouran Eshak[5], Megan Sullivan[6], Matthew Koster[3] and Kenneth Warrington[3], [1]Mayo Clinic Florida, Jacksonville, FL, [2]Mayo Clinic, Florida, Jacksonville, FL, [3]Mayo Clinic, Rochester, MN, [4]Mayo Clinic, Stewartvillle, MN, [5]Mayo Clinic, Arizona, Scottsdale, AZ, [6]Mayo Clinic Arizona, Scottsdale, AZ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is clinically heterogenous, and the presenting manifestations may influence diagnostic testing. The aim of this study was to evaluate the clinical manifestations of patients with GCA diagnosed by

	Overall (N=62)
Age at diagnosis, years mean (SD)	70.1 (8.9)
Male/Female	24 (39%) / 38 (61%)
Race White	60 (97%)
Weight, kg mean (SD)	72.3 (15.5)
Type of GCA	
Cranial GCA	1 (2%)
Large vessel GCA	52 (84%)
Mixed GCA	9 (15%)
Time from symptom onset to diagnosis, months median (IQR)	4.8 (1.8, 12.9)
Temporal artery biopsy positive for GCA	9/23 (39%)
Aorta histology showing vasculitis	8/29 (28%)
Meets ACR 2022 Classification criteria	44 (71%)
Death	8 (13%)
Cause of death	
Heart disease	2/8 (25%)
Pulmonary disease	2/8 (25%)
Other	1/8 (12%)
Unknown	3/8 (38%)
Length of follow up, years median (IQR)	4.5 (2.3, 8.3)
Prednisone at last follow up	29/57 (51%)
Prednisone dose at last follow-up, mg mean (SD)	13.4 (16.2)

Table 1 Demographics and clinical characteristics

	Overall N=62
Time from symptom onset to PET, months median (IQR)	5.7 (2.5, 14.9)
Patients receiving prednisone at the time of PET scan	18 (29%)
Dose of corticosteroids during PET, mg/day median (IQR)	0.0 (0.0, 10.0)
Duration on corticosteroids before PET, days median (IQR)	0 (0, 30)
Treated with corticosteroid pulses	3 (5%)
PET vessel involvement	
Thoracic aorta	55 (89%)
Abdominal aorta	36 (58%)
Innominate	4 (6%)
Carotid	27 (44%)
Vertebral	4 (6%)
Subclavian	32 (52%)
Axillary	14 (23%)
Iliac	21 (34%)
Mesenteric	3 (5%)
Femoral	18 (27%)
Polymyalgia rheumatica on PET	14 (23%)
Abnormal uptake in shoulder girdle	9 (15%)
Abnormal uptake in pelvic girdle	11 (18%)
Presence of aneurysms/ectasia	15 (24%)
Follow up PET scan	
Remission	8/31 (26%)
Improved	14/31 (45%)
Worsened	3/31 (10%)
Stable	6/31 (19%)
Time from first PET to follow up PET scan, months median (IQR)	10.1 (6.1, 27.2)
CT angiogram positive for GCA	24/37 (65%)
MR angiogram positive for GCA	14/21(67%)
Temporal artery ultrasound positive (halo sign, thickening, stenosis)	6 (10%)
Aneurysm/ectasia at last follow up	17 (27%)

Table 2: Imaging characteristics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Temporal artery biopsy positive GCA (n=286)	PET positive GCA (n=62)	P value
Age at diagnosis, years mean (SD)	75.0 (7.6)	70.1 (8.9)	**<0.001**
Male/Female	73 (26%)/213 (74%)	24 (39%)/38 (61%)	**0.036**
Race White	279 (98%)	60 (97%)	0.778
Duration of follow up, years median (IQR)	5.5 (3.1, 9.4)	4.5 (2.3, 8.3)	0.071
Time from symptom onset to diagnosis, months median (IQR)	2.1 (0.9, 4.4)	4.8 (1.8, 12.9)	**<0.001**
Polymyalgia rheumatica	125/282 (44%)	24 (39%)	0.419
Constitutional symptoms	165 (58%)	41 (66%)	0.220
Extremity claudication	12 (4%)	7 (11%)	**0.026**
Sedimentation rate, mm/Hr median (IQR)	65.0 (42.8, 93.2)	46.5 (24.2, 105.5)	0.123
C-Reactive protein, mg/Liter median (IQR)	54.7 (23.2, 100.1)	41.0 (10.0, 96.8)	0.247
Headache	187/281 (67%)	34 (55%)	0.081
Any cranial symptoms	246 (86%)	37 (60%)	**<0.001**
Temporal artery tenderness	46/280 (16%)	2 (3%)	**0.007**
Jaw claudication	149/285 (52%)	6 (10%)	**<0.001**
Abnormal temporal artery exam	50/284 (18%)	3 (5%)	**<0.011**
Decreased temporal artery pulse	42/280 (15%)	2 (3%)	**0.012**
Tongue claudication	6/285 (2%)	1 (2%)	0.803
Large artery bruit	20/282 (7%)	8 (13%)	0.130
Visual manifestations			
Transient visual loss	20/285 (7%)	7 (11%)	0.255
Permanent visual loss	16/283 (6%)	0 (0%)	0.055

P-values were calculated using Chi-Square and Kruskal-Wallis tests

Table 3: Comparison with Temporal artery biopsy cohort

fluorodeoxyglucose (FDG) positron emission tomography (PET) / computed tomography (CT), and to compare PET-positive patients with those diagnosed with temporal artery biopsy (TAB).

Methods: A retrospective cohort of patients with GCA diagnosed by (FDG) PET/CT between 01/01/1990 and 12/30/2022 was assembled. The comparator cohort included patients with GCA diagnosed with temporal artery biopsy (TAB) at the same institution. The study was approved by the local Institutional Review Board (IRB). For statistical analysis, categorical variables were expressed as number (percentage) and continuous variables were expressed as mean (standard deviation) or median (interquartile range). Comparisons between cohorts were performed using chi-square and Kruskal-Wallis tests. A two tailed p value less than 0.05 was considered significant.

Results: The PET-positive cohort included 62 patients; demographics and baseline variables are presented in Table 1. Mean age was 70.1 years (SD 8.9), with 61% (38/62) female and 97% White (60/62). 71% (44/62) of patients met the 2022 ACR Classification Criteria for GCA. 65% (24/37) patients had a positive CT angiogram, and 67% (14/21) patients had a positive magnetic resonance angiogram (Table 2). A minority of patients underwent TAB, with 39 % (9/23) positive. Aortic ectasia and/or aneurysms were present in 24% (15/62) patients at diagnosis. 23% (14/62) patients had an abnormal FDG uptake consistent with polymyalgia rheumatica.

The comparator cohort included 286 patients with TAB-positive GCA (Table 3). Compared to patients with TAB-positive GCA, the PET-positive patients were significantly younger ($p< 0.001$), more often males ($p=0.036$) and had longer time from symptom onset to GCA diagnosis ($p< 0.001$). PET positive patients had more frequent extremity claudication ($p=0.026$). Cranial manifestations were significantly less frequent among the PET-positive patients ($p< 0.001$), and none had permanent vision loss.

Conclusion: Patients with GCA diagnosed by PET scan were younger, more males and had less cranial manifestations compared to those diagnosed by TAB with a longer time to diagnosis. None of the patients diagnosed by PET had permanent vision loss. In clinical practice, distinct clinical GCA phenotypes tend to influence choice of diagnostic evaluation.

Disclosure: S. Mumtaz: None; **L. Clark**: None; **A. Srivastava**: None; **H. Langenfeld**: None; **A. Hanson**: None; **C. Crowson**: None; **A. Abril**: None; **N. Eshak**: None; **M. Sullivan**: None; **M. Koster**: Amgen, 2; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0760

The Efficacy Of Targeted Therapies In Giant Cell Arteritis: A Systematic Review and Meta-Analysis

Sema Kaymaz-Tahra[1], Cansu Arslantürk Güneysu[2], Sinem Nihal Esatoglu[3], Güllü Sandal Uzun[4], Burak Ince[5], Mete Kara[6] and Gulen Hatemi[3], [1]Bahcesehir University Faculty of Medicine Department of Internal Medicine Division of Rheumatology, Istanbul, Turkey, [2]Sakarya Training and Research Hospital, Division of Rheumatology, Sakarya, Turkey, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [4]Hacettepe University, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [5]Istanbul University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, [6]Izmir City Hospital, Division of Rheumatology, Izmir

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: To assess the sustained remission rates of the targeted therapies in 52th week in patients with giant cell arteritis (GCA).

Methods: We performed a systematic literature review in PUBMED and Scopus databases and performed a metanalysis using Revman. A total of 1085 articles were scanned. We included 60 articles for review. Retrospective studies, non-randomised prospective studies were excluded and only randomised-controlled trials (RCT) were involved. In the meta-analysis 10 RCTs were included. Two independent reviewers extracted the data. The primary outcome was sustained remission (SR) rate at the 52th week of the treatment. The SR rates for similar glucocorticoid tapering arms in the targeted therapy and placebo groups were compared.

Results: A total of 869 patients were included in the involved studies. All the studies compared the outcomes with placebo. No head-to-head comparison was performed. SR rates were significantly higher compared to placebo in the patients who received tocilizumab (tocilizumab IV RR(CI 1.90 (1.01-3.56), tocilizumab SC 1.45 (1-06-1.99)), mavrilumab (RR (CI) 1.67 (1.12-2.47)), secukinumab (RR(CI): 7.41 (1.89-29.02)) and upadacitinib 15 mg (RR (CI) 1.58 (1.14-2.17). On the contrary, the sustained remission rate was found to be similar to placebo with the study drug in studies conducted with sarilumab and sirukumab. Safety outcomes of targeted drugs were similar with placebo in all of the involved studies.

Conclusion: Tocilizumab, mavrilumab, secukinumab and upadacitinib appear to increase the rate of 52-week sustained remission rate. Sarilumab and sirukumab has not shown significant efficacy.

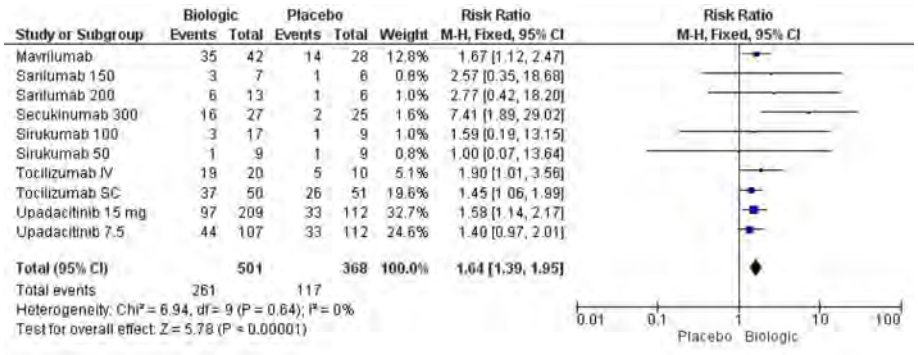


Figure 1. Meta-analysis of the effect of the targeted therapies on the sustained remission at the 52th week of treatment

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Kaymaz-Tahra: None; **C. Arslantürk Güneysu**: None; **S. Esatoglu**: None; **G. Sandal Uzun**: None; **B. Ince**: None; **M. Kara**: None; **G. Hatemi**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 2, Novartis, 6, Pfizer, 6, UCB, 6.

Abstract Number: 0762

Relapse rate, predictors of relapses and impact of introduction of interleukin-6-receptor inhibition on relapse rate in GCA- Data from the large REATS cohort from six vasculitis centers

Verena Schoenau[1], Giulia Corte[2], Koray Tascilar[3], Fabian Hartmann[2], Sebastian Ott[2], Wolfgang Schmidt[4], Andreas Krause[5], Pfeil Alexander[6], Peter Oelzner[6], Marc Schmalzing[7], Matthias Fröhlich[8], Michael Gernert[8], Jörg Henes[9], Nils Venhoff[10], Bernhard Hellmich[11], Bernhard Manger[2], Georg Schett[12] and Juergen Rech[12], [1]- Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, [2]- Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [4]Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch; Waldfriede Hospital, Rheumatology, Berlin, Germany, [5]Department of Rheumatology and Clinical Immunology, Immanuel Krankenhaus Berlin, Berlin, Germany, [6]Department of Internal Medicine III, Jena University Hospital - Friedrich Schiller University Jena, Jena, Germany, [7]Department of Medicine II, Rheumatology/ Immunology,University Hospital of Wuerzburg, Wuerzburg, Bayern, Germany, [8]University Hospital of Wuerzburg, Department of Medicine II, Rheumatology/ Immunology, Wuerzburg, Germany, [9]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tuebingen, Germany, [10]University of Freiburg, Freiburg, Germany, [11]Klinik für Innere Medizin, Rheumatologie, Pneumologie, Nephrologie und Diabetologie, Medius Kliniken, Akademisches Lehrkrankenhaus der Universität Tübingen, Kirchheim unter Teck, Germany, [12]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: The diagnosis and management of giant cell arteritis (GCA) has significantly evolved over the last decades, mainly due to advances in imaging techniques and the introduction of new treatment modalities, respectively. Herein, we addressed the relapse rate, factors influencing relapses and the effect of introduction of interleukin-6-receptor targeting on relapse rates in GCA.

Methods: The REATS (GCA- Real-Life Assessment of Treatment Efficacy and Safety in GCA Patients) observational cohort included patients with a confirmed clinical diagnosis of GCA or a GCA flare between the first of January 2013 and 31st of December 2021. Six highly experienced German vasculitis centers participated and sequentially documented the disease course and treatment of GCA patients. Using a structured chart survey, we collected data on various outcomes, i.e. symptoms, treatments, acute-phase response, relapses. We used unsupervised clustering methods to identify symptom-based disease clusters and generalized additive models to analyze glucocorticoid dose and acute-phase response over time. Time-to-relapse was analyzed using survival methods.

Results: We included 395 patients with newly diagnosed GCA or a GCA flare. Diagnosis was supported by temporal artery ultrasound (37%), 18F-FDG-PET/CT (29%), temporal artery biopsy (14%) and by MRI (5,8%). The mean C-reactive protein value at disease onset or flare was 72,1 mg/dl, indicating a highly active cohort at the start of the documentation. The median total follow-up was 22.2 (CI 11.7-40.6) months. During this follow up time 97 of the 395 patients relapsed including 15 patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

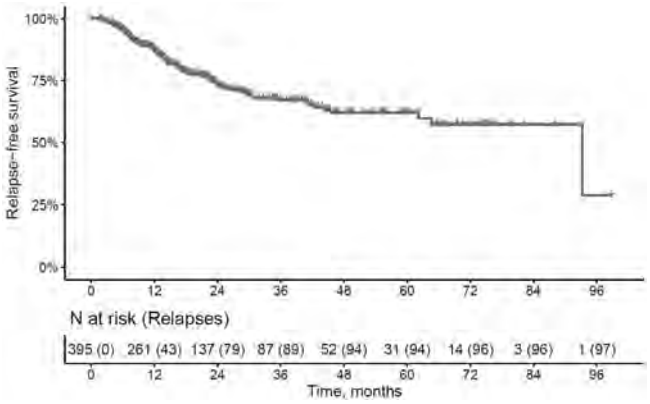


Figure 1 relapse-free survival

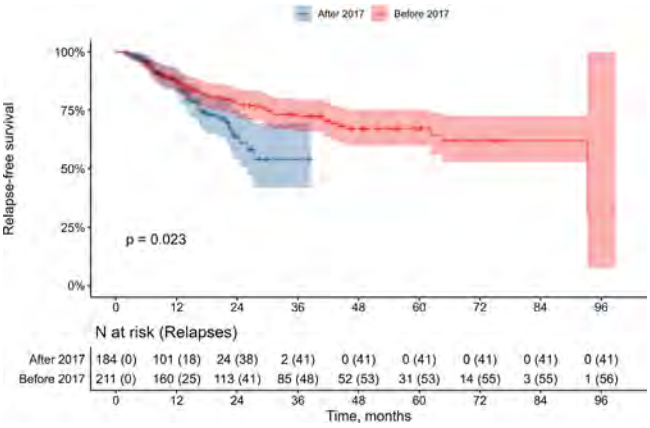


Figure 2 relapse-free survival by era

Symptom at relapse	N=97 (%)
Headache	35 (30.7)
Polymyalgia (PMR)	23 (20.2)
Fatigue	19 (16.7)
Vision impairment	13 (11.4)
Night sweats	12 (10.5)
Headache in the temporal area	12 (10.5)
Jaw pain	11 (9.6)
Morning stiffness	7 (6.1)
Weight loss	7 (6.1)
Claudication upper limb	6 (5.3)
Arthralgia	6 (5.3)
Claudication lower limb	5 (4.4)
Vision loss	3 (2.6)
Arthritis	3 (2.6)
Scalp tenderness	2 (1.8)
Fever	2 (1.8)
Swelling temporal arteries	2 (1.8)

Symptoms at relapse

who relapsed more than once (Figure 1). The median (IQR) time to first relapse was 12.5 (CI 7.1-21.8) months. Most common symptoms at relapse were headache (31%) and PMR symptoms (20%) (Table 1). Though over 90 different baseline characteristics were analysed to identify risk factors for a future relapse, no significant predictors could be identified. None of the applied treatment regimes showed any superiority in preventing disease relapses. Looking at the relapse rates before (2013-2017) and after interleukin-6-receptor targeting (2017-2021) was introduced more relapses occurred after 2017 (Figure 2).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Relapses are frequent in GCA and did not decrease with introduction of interleukin-6-receptor targeting in GCA. No risk factor for relapses could be identified, despite many different risk factors were assessed. Also, none of the treatment regimens used appear to be superior in preventing relapses. Interestingly, since the introduction of interleukin-6-receptor targeting, relapse rate increased in GCA. This finding could be based on a less stringent use of pharmacotherapies in GCA, including glucocorticoids, considering that treatment options have become larger with the introduction of interleukin-6-receptor targeting.

Disclosure: V. Schoenau: AbbVie/Abbott, 1, 6, Chugai, 5, 6, Novartis, 1, 6, Roche, 5; **G. Corte**: None; **K. Tascilar**: None; **F. Hartmann**: None; **S. Ott**: None; **W. Schmidt**: AbbVie, 1, 5, 6, Alfasigma, 6, Amgen, 6, Boehringer-Ingelheim, 1, Chugai, 6, Eli Lilly, 6, Fresenius Kabi, 1, GlaxoSmithKline, 6, Medac, 6, Novartis, 1, 5, 6, Pfizer, 6, UCB, 6; **A. Krause**: None; **P. Alexander**: None; **P. Oelzner**: None; **M. Schmalzing**: None; **M. Fröhlich**: None; **M. Gernert**: None; **J. Henes**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, Janssen, 1, 6, Novartis, 1, 1, 6, 6, Otsuka, 1, Pfizer, 1, Roche, 1, SOBI, 1, UCB, 1, 6; **N. Venhoff**: AbbVie, 1, 6, 12, Consulting fees, meeting or travel grants, expert testimony, AstraZeneca, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, 6, 12, Meeting or travel grants, Chugai, 1, 6, 12, Consulting fees, GlaxoSmithKlein(GSK), 6, Novartis, 1, 5, 6, 12, Consulting fees, meeting or travel grants, expert testimony, 12, Pending patent application on the use of secukinumab in GCA, Roche, 6, UCB, 1, 6, Vifor, 1, 6, 12, Expert testimony, Meeting or travel grants, Consulting fees; **B. Hellmich**: AbbVie, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Chugai, 2, 6, CSL Vifor, 2, 6, GlaxoSmithKlein(GSK), 2, 6, InflaRx, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Phadia, 2, 6, Roche, 2, 6; **B. Manger**: AbbVie/Abbott, 6, AstraZeneca, 1, Eli Lilly, 6, Novartis, 6, Pfizer, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **J. Rech**: AbbVie, 6, 12, Received consulting fees, Biogen, 6, 12, Received consulting fees, Bristol-Myers Squibb(BMS), 6, 12, Received consulting fees, Chugai, 6, 12, Received consulting fees, Eli Lilly, 6, 12, Received consulting fees, GlaxoSmithKlein(GSK), 6, 12, Received consulting fees, Janssen, 6, 12, Received consulting fees, MSD, 6, 12, Consulting fees, Novartis, Sobi, 1, 2, 5, 6, Roche, 6, 12, Received consulting fees, Sanofi, 6, 12, Received consulting fees, Sobi, 6, 12, Received consulting fees, UCB, 6, 12, Received consulting fees.

Abstract Number: 0763

Diagnostic Utility of Temporal Artery Biopsy in Giant Cell Arteritis: A Single Center Experience

Wendy Perdomo, Sean Welch and Timothy Wilson, Thomas Jefferson University, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is predominantly large vessel vasculitis that has a specific prediliction for vasculature of the head, eyes and jaw and if untreated can lead to permanent vision loss. The gold standard for diagnosis is a temporal artery biopsy (TABx) although only a portion of patients have a positive biopsy and the biopsy itself can be associated with additional morbidity. There is a significant need to more clearly understand the clinical features that are most specific to clinical presentation and positive biopsy as this has significant implications on treatment strategies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We completed a single center large cohort (n=138) retrospective analysis of patients who underwent a TABx based on the clinical suspision for GCA. All biopsies were done within the Thomas Jefferson University Health System between August 2023 and June 2024. After IRB approval, chart review was completed to identify a variety of patient related characteristics including demographics, clinical features on presentation, lab and imaging results. Indepdent sample t-tests and both univariate and multivariate logistic regression models were used where appropriate to characterize differences between subjects with positive and negative TABx results.

Results: The demographics and clinical features are summarized in table 1. The most common symptoms on presentation were vision changes (78%), vision loss (50%), temporal headache (50%) and scalp tenderness (23%). In 33% of patients, vision changes or vision loss was the only manifestation. The mean duration of steroid exposure prior to completion of biopsy was 3.8 days. The mean TABx length was 2.7 cm and a biopsy consistent with GCA was identified in 17/138 patients (12.1%). Of the 121 patients with a negative biopsy, 8 (6.6%) were treated for presumed GCA based on high clinical suspicion for the disease process. In simple logistic regression analysis, age ($p< 0.01$), jaw claudication ($p< 0.01$), grossly abnormal TA on exam ($p=0.04$), C-reactive protein (CRP) levels (0.04) and platelet count (0.05) were associated with increased odds of having a biopsy consistent with GCA (Table 2). In multivariate models, age, jaw claudication and platelet count remained independeltly

TABLE 1. DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF TOTAL COHORT*

n	138
Age	70.6 (10.1)
Female (%)	60%
Former/Current Smoker (%)	53%
Race/ethnicity	
White	60%
Black	32%
Hispanic	4%
Asian	2%
Prior Rheumatic Diagnosis	20%
Polymyalgia Rheumatica (PMR)	6%
Presenting symptoms	
Vision changes	78%
Vision loss	50%
Headache	50%
Scalp Tenderness	23%
Constitutional symptoms**	23%
Jaw claudication	16%
Grossly abnormal temporal artery	6%
PMR-like symptoms	5%
Chest pain	1%
Laboratory workup	
Sedimentation rate (mm/hr)	59.7 (30)
C-reactive protein (mg/L)	26.9 (50.6)
White blood cell ($x10^9$/L)	8.9 (3.4)
Hemoglobin (g/dL)	12.8 (1.9)
Platelets ($x10^9$/L)	282.3 (109.5)
Temporal Artery Biopsy length (cm)	2.7 (1.03)
Temporal Artery Ultrasound completed	14%
Abnormal***	7%
Temporal Artery Biopsy Consistent with GCA	12%

*Data is displayed as % or mean (SD)
**Constitutional symptoms included any combination of weight loss, fatigue, fevers, night sweats
***Any vessel with abnormal wall thickening as determined by radiology

TABLE 2. POSITIVE VS NEGATIVE BIOPSY LOGISTIC REGRESSION ANALYSIS

	Univariate		Multivariate*	
	Odds Ratio (CI)**	P-value	Odds Ratio (CI)**	p-value
Age	1.01 (1.04, 1.17)	<0.01	1.15 (1.06, 1.25)	<0.01
Female (%)	1.2 (0.4, 3.48)	0.73	–	–
Former/Current Smoker (%)	0.92 (0.32, 2.68)	0.89	–	–
Presenting symptoms				
Vision changes	1.95 (0.42, 9.11)	0.39	–	–
Vision loss	1.07 (0.39, 2.96)	0.90	–	–
Headache	0.82 (0.30, 2.26)	0.70	–	–
Scalp Tenderness	2.67 (0.93, 7.77)	0.07	–	–
Constitutional symptoms	2.56 (0.89, 7.37)	0.11	–	–
Jaw claudication	4.59 (1.53, 13.80)	<0.01	4.38 (1.02, 19.7)	0.05
Abnormal TA	4.97 (1.07, 23.07)	0.04	6.37 (0.79, 51.32)	0.06
PMR-like symptoms	1.20 (0.14, 10.60)	0.87	–	–
Chest pain	N/A		–	–
Laboratory workup			–	–
Sedimentation rate	1.0 (0.98, 1.02)	0.98	–	–
C-reactive protein (CRP)	1.01 (1.0, 1.02)	0.04	1.01 (0.99, 1.02)	0.15
WBC	1.05 (0.91, 1.21)	0.51	–	–
Hemoglobin	1.05 (0.81, 1.37)	0.69	–	–
Pfatelets	1.01 (1.0, 1.01)	0.05	1.01 (1.0, 1.01)	0.03
Temporal Artery Biopsy length (cm)	1.13 (0.69, 1.86)	0.63	–	–
Abnormal TA ultrasound	0.95 (0.04, 2.84)	0.33	–	–

*Multivariate logistic regression model using covariates with statistical significance ($p<0.05$) in univariate model (age, jaw claudication, grossly abnormal TA, CRP and platelet count)
** Odds ratio including 95% confidence interval

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

significantly associated with odds of having a positive biopsy. Despite this, 3/17 (18%) patients with a positive TABx had 1) normal sedimentation rate (ESR) or CRP and 2) the only clinical feature on presentation was vision changes.

Conclusion: In this large retrospective analysis, we found several clinical features (age, jaw claudication, TA enlargement, CRP levels and platelet count) associated with pathology consistent with GCA with the most specific features being age, jaw claudication and increased platelets. A small portion of patients with a positive biopsy only exhibited vision changes and at least one normal inflammatory marker (ESR or CRP). Future studies are needed to more reliably characterize the full spectrum of the presentation of GCA and thus more expansive indications for invasive diagnostic studies such as a temporal artery biopsy.

Disclosure: w. Perdomo: None; **S. Welch**: None; **T. Wilson**: None.

Abstract Number: 0764

Frequency of large vessel vasculitis in giant cell arteritis with and without adventiitis of temporal artery - Is the presence of temporal arteritis sufficient to diagnose giant cell arteritis?

Yoichiro Akiyama, Jun Nakamura, Ayako Kokuzawa, Hiroi Kusaka, Sho Tani, Fuminori Taniguchi, Kohei Morikawa, Haruka Kondo, Shotaro Yamamoto, Yasuyuki Kamata and Kojiro Sato, Jichi Medical University, Shimotsuke, Tochigi, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0731–0764) Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Takayasu arteritis (TAK) and giant cell arteritis (GCA) belong to the large vessel vasculitis group. Differences between the two diseases have been reported based on age, clinical presentation, and HLA. ACR/EULAR classification criteria for GCA have been reported, but no pathological criteria for the temporal artery (TA) have been proposed. Pathologically, inflammation of the aorta in TAK starts from the adventitia and inflammation of the temporal artery (TA) in GCA starts from the tunica media, indicating different sites of inflammation in the two diseases. Therefore, it is important to classify TAK and GCA based on pathological findings rather than distinguishing between them based on age. In this study, it was examined whether there is a difference in the presence or absence of aortitis depending on the site of inflammation of the TA (presence or absence of adventitial inflammation) in cases diagnosed with GCA.

Methods: The study included patients admitted to our hospital from 2004 to 2023, who underwent temporal artery biopsy (TAB) and contrast-enhanced thoraco-abdominal computed tomography, and were diagnosed with GCA. According to the pathology of the TAB, the patients were divided into two groups: those with (Ad+ group) and without (Ad- group) adventitial inflammation. In those two groups, clinical symptoms, laboratory findings, and the presence of aortitis were compared between the groups.

Results: Thirty-two patients were included in the study, 21 in the Ad+ group and 11 in the Ad- group. The median age in the Ad+ and Ad- groups was 73 and 69 years, respectively (p=0.010), the frequency of clinical findings were as follows: fever (52.4% vs. 36.4%, p=0.472), headache (81.0% vs. 90.9%, p=0.637), polymyalgia rheumatica (PMR) symptoms (23.8% vs. 36.4%, p=0.681), and TA symptoms (42.9% vs. 81.8%, p=0.061). Blood test findings (median values) showed no

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

significant differences in WBC (7,900 /μl vs. 7,800 /μl, p=0.984) or CRP (9.60 mg/dl vs. 9.26 mg/dl, p=0.736); however, ALP levels in Ad+ group were lower than those in the Ad- group (244 U/L vs. 446 U/L, p=0.009). The frequency of aortitis in the Ad+ group was significantly higher than in the Ad- group (81.0% vs. 27.3%, p=0.006). The initial dose of glucocorticoid (GC) tended to be higher in the Ad+ group (1.0 mg/kg vs. 0.6 mg/kg, p=0.066).

Conclusion: In this study, the Ad- group may have true GCA and the Ad+ group may have TAK; it may be important to distinguish between GCA and TAK based on TAB pathology rather than age.

Disclosure: Y. Akiyama: None; **J. Nakamura**: None; **A. Kokuzawa**: None; **H. Kusaka**: None; **S. Tani**: None; **F. Taniguchi**: None; **K. Morikawa**: None; **H. Kondo**: None; **S. Yamamoto**: None; **Y. Kamata**: None; **K. Sato**: None.

Abstract Number: 0765

Rural Access to Physical Therapy for Osteoarthritis Rehabilitation (RAPTOR): A Pilot Feasibility Study

Allyn Bove, Emma Zavacky, Hallie Zeleznik, Christopher Bise, Charity Patterson, Bambang Parmanto and G Kelley Fitzgerald, University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Individuals who live in rural areas are more likely to experience knee osteoarthritis-related disability and less likely to be referred to physical therapy for osteoarthritis. Limited access to physical therapy due to lack of licensed professionals in the area and long distances from home to the nearest clinic may exacerbate the underutilization of physical therapy among rural residents with knee osteoarthritis. Increasing uptake of telerehabilitation may mitigate these challenges, but telerehabilitation can be challenging in rural areas due to lower availability of LTE wireless coverage and broadband internet service. In this study, we aimed to evaluate feasibility and future trial design parameters for a novel hybrid in-person + telerehabilitation program (RAPTOR) for rural residents with knee osteoarthritis.

Methods: The study was a single-arm pilot feasibility study with pre-post design. Twenty rural-dwelling adults with knee osteoarthritis were eligible to participate in the RAPTOR program, consisting of up to 10 visits with a physical therapist: two visits delivered in-person and eight visits delivered using a secure, HIPAA-compliant telehealth platform. Feasibility was defined as a combination of acceptability, demand, implementation, integration, and safety. Clinical outcomes entailed a combination of patient-reported (Knee Injury and Osteoarthritis Outcome Score, or KOOS) and performance-based (OARSI-OMERACT core set of performance-based measures) functional measures. Satisfaction with telerehabilitation was assessed using the Telehealth Usability Questionnaire.

Results: RAPTOR was feasible and safe based on meeting recruitment and attendance targets and having no adverse events during the study, and participants reported high satisfaction with the telerehabilitation component of the program. Eighty-one percent (13/16) of participants who completed the RAPTOR program demonstrated clinically important improvement in patient-reported physical function, and more than half (7-10/14) demonstrated clinically important improvement on the various performance-based physical function tests.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

FIGURE 1. Study enrollment and attrition flow chart

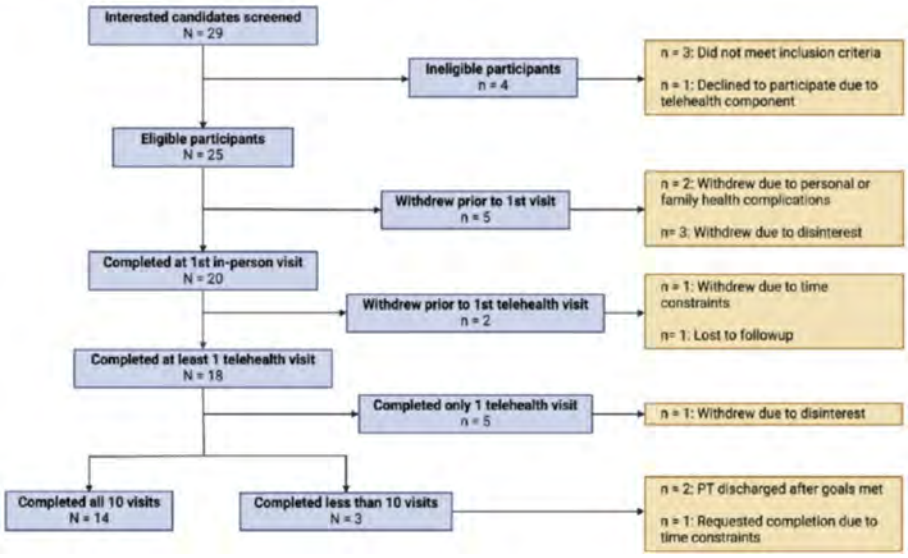


TABLE 1. Feasibility outcomes assessed in RAPTOR pilot study

Outcome(s)	How Outcome was Measured	Definition of Successful Outcome
Demand*	Recruitment progress	Recruitment target met within 1-year timeline
Implementation*, Integration*	Attendance rate	Mean visit attendance of at least 75%
Acceptability*	Post-study Telehealth Usability Questionnaire completed by participants	Average item rating of at least 5/7 on Likert scale items
Safety*	Number of study-related adverse events and/or serious adverse events	Zero study-related adverse events or serious adverse events
Clinical Outcome Change and Variability	Participant-reported outcome measures and performance-based outcome measures	Achievement of minimum clinically important difference

*denotes outcome included in the overall study definition of "feasibility"

TABLE 2. Participant-reported and performance-based outcomes

Outcome Measure	Sample Size	Baseline, mean (SD)	Follow-Up, mean (SD)	Change, mean (95% CI)
KOOS ADL subscale	13	68.2 (18.6)	81.9 (11.8)	13.7 (4.4-22.9)*
KOOS Pain subscale	14	64.3 (17.6)	75.8 (12.5)	11.5 (-0.6-23.6)
30-Second Chair Rise Test, # of rises	14	11.3 (5.0)	13.6 (5.8)	2.4 (0.2-4.6)*
Stair Climbing Test, in seconds	14	18.0 (7.2)	14.5 (6.3)	3.5 (2.2-4.7)*
Timed Up and Go, in seconds	14	9.5 (1.8)	8.0 (1.4)	1.5 (0.8-2.2)*
6-Minute Walk Test, in meters	14	388.0 (112.4)	460.3 (108.3)	72.3 (39.5-105.1)*

*indicates statistical significance of paired samples t-test.

KOOS = Knee Injury and Osteoarthritis Outcome Score; ADL = Activities of Daily Living; SD = standard deviation; 95% CI = 95% confidence interval

Conclusion: A novel hybrid in-person + telerehabilitation program was safe and feasible. A high proportion demonstrated improvements in function. Participants expressed high degrees of satisfaction with telerehabilitation and minimal barriers to using the platform, supporting the use of telerehabilitation among rural-dwelling older adults. Further testing of this hybrid approach is needed in a comparative trial.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Bove: None; **E. Zavacky**: None; **H. Zeleznik**: None; **C. Bise**: None; **C. Patterson**: None; **B. Parmanto**: None; **G. Fitzgerald**: None.

Abstract Number: 0766

Effects of Walking During the 6-Minute Walk Test on Cognition in Adults with Knee Replacement

Christine Pellegrini[1], Jongwon Lee[1], Chih-Hsiang Yang[1], Scott Jamieson[2], Clare Kennerley[1] and Sara Wilcox[1], [1]University of South Carolina, Columbia, SC, [2]The University of South Carolina, Columbia, SC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: The majority of adults with knee replacement remain physically inactive after surgery and are at high risk for Alzheimer's and related dementias (ADRD). This study investigated the acute effects of a 6-minute walk on processing speed, visuospatial memory, and visual memory in adults with a history of TKR ≤6 months ago.

Methods: Within a cross-over design, participants were randomized to either first engage in the 6-minute walk test or rest. Cognition was assessed via brief phone-based tests 3 times (baseline and after walking and resting). Symbol search, grid memory, and color shape tests from the NIH Mobile Toolbox were used to measure processing speed, visuospatial memory, and visual memory, respectively.

Results: Participants (n=52) were 77% female, 65.1 (9.1) years, 85% completed some college or higher, and were on average 94.1 (21.7) days since knee replacement. Participants walked 1126.67 (205.69) feet during 6-minute walk test. Controlling for demographics and potential learning effects, mixed-effects models revealed that 6 minutes of walking was associated with improved visuospatial memory, as indicated by shorter error distances on the grid memory test (b=-3.87, p=0.04). The walking effect was not observed for processing speed (b=178.8, p=0.45) or visual memory (b=0.01, p=0.92).

Conclusion: Although the physiological mechanisms to which exercise benefits domain-specific cognition remain unclear, the results of this study suggest that a short bout of walking may immediately improve visuospatial memory in adults with knee replacement. Healthcare providers could highlight this cognitive benefit and encourage short walking bouts in this population.

Disclosure: C. Pellegrini: None; **J. Lee**: None; **C. Yang**: None; **S. Jamieson**: None; **C. Kennerley**: None; **S. Wilcox**: None.

Abstract Number: 0767

Quality of Life in Patients with Rheumatoid Arthritis with Foot and Ankle Involvement

Egla Samantha Sanchez-Peralta[1], Andrea Cantero-Castro[2], Karina Deciderio-Pavon[3], Jesús Gilberto Espinoza-Gámez[3], Irasema Arcibar-Liceaga[3], Carolina De Leon-Carrillo[3], Angel Kevin Garza-Elizondo[1], Ryan Jared Sanchez-De la Cruz[3], Jesus Alberto Cardenas-de la Garza[4], Dionicio A. Galarza-Delgado[5], Diana E. Flores-Alvarado[1] and Jorge Alberto Elizondo-Rodriguez[2], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [2]Traumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo Leon, Mexico, [4]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [5]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Foot and ankle involvement in patients with rheumatoid arthritis is a common yet often underexplored and underrecognized manifestation. This can negatively affect patients' quality of life and functional capacity. We aimed to describe the effect of foot and ankle joint involvement on the quality of life in patients with rheumatoid arthritis.

Methods: An observational, cross-sectional study was conducted at a university hospital rheumatology and traumatology outpatient clinics. Patients >18 years with a diagnosis of rheumatoid arthritis (ACR/EULAR 2010) were included. Health-related quality of life concerning foot health was assessed using the Foot Health Status Questionnaire (FHSQ), with higher scores indicating a better result. The Foot Function Index (FFI) was used to measure the impact of the disease on foot function, higher scores indicate worse foot function. Pain was evaluated using a visual analog scale (VAS). To measure the involvement of the foot, x-rays of both feet were taken in three projections and evaluated by an unaffiliated radiologist. The modified Sharp/van der Heijde (vdH-S) was utilized to evaluate the radiological findings of the lower extremity joints, separating high and low scores with a cutoff point of 4. Descriptive analysis was performed. Mann-Whitney´s U test and Chi-Square test were applied as appropriate, with a p-value < 0.05 considered statistically significant.

Results: A total of 81 patients were included, of whom 77 (95.1%) were women, with a median age of 59 years (IQR: 51–65). At the time of evaluation, the majority of patients (n=43, 53.1%) were in remission. The most common comorbidity was obesity (n = 28, 34.6%), followed by osteoarthritis (n = 16, 19.8%). Additionally, 62.79% of participants described living a sedentary lifestyle. The mean body weight was 69.2 ± 15.5 kg, with a median BMI of 28.2 (IQR: 24–32).

Radiological findings revealed that 69 patients (85%) experienced some degree of lower extremity joint involvement. The median score of vdH-S was 4 (IQR: 2–20), with a median erosion subscale score of 2 (IQR: 0–4.5) and a median joint space narrowing subscale score of 3 (IQR: 2–16). Among patients with lower-extremity joint involvement, subluxations were

Table 1. Baseline characteristics of patients

	N= 81
Women, n (%)	77 (95.1)
Age, median (IQR)	59 (51-65)
Weight, mean ± SD	69.2 ± 15.5
BMI, median (IQR)	28.2 (24-9 – 32.6)
Disease duration, n (%)	
1-9 years	44 (54.3)
>10 years	37 (45.7)
Steroids dosage, mean ± SD	2 ± 1.9
Disease activity, n (%)	
Remission/low activity	57 (70.4)
Moderate/high activity	26 (29.7)
FHSQ, mean ± SD	40.4 ± 3.5
FFI, median (IQR)	51.1 (27.6 – 80.2)
VAS, median (IQR)	5 (4-7)
Modified vdH-S method, median (IQR)	4 (2-20)
Erosions	2 (0-4.5)
Joint space narrowing	3 (2-16)
Radiological findings, n (%)	
Osteoporosis	38 (46.9)
Luxations	63 (77.8)
Subchondral cysts	38 (46.9)
Synovitis	12 (14.8)

IQR: Interquartile range; SD: Standard Deviation; FHSQ: Foot Health Status Questionnaire; FFI: Foot Function Index; VAS: Visual Analog Scale; vdH-S: Sharp/van der Heijde.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of quality of life, functionality and radiological findings regarding foot health between low and high scores in the modified vdH-S method

	Low score (n=31)	High score (n=50)	p-value
FHSQ, mean ± SD	40.2 ± 3.6	40.4 ± 3.1	0.631
FFI, median (IQR)	39.1 (23.5-80.1)	43.2 (33.2-92.4)	0.560
VAS, median (IQR)	5 (4-8)	5 (3.7-6)	0.101
Erosions, median (IQR)	0.2 ± 0.7	7.4 ± 10	< 0.001
Space joint narrowing, median (IQR)	0.5 (0-2.2)	12 (3-20)	< 0.001
Osteoporosis	7 (22.6)	31 (62)	< 0.001
Luxations	24 (77.4)	39 (78)	0.951
Subchondral cysts	11 (35.5)	27 (54)	0.105
Synovitis	4 (12.9)	10 (20)	0.079

IQR: Interquartile range; SD: Standard Deviation; FHSQ: Foot Health Status Questionnaire; FFI: Foot Function Index; VAS: Visual Analog Scale; vdH-S: Sharp/van der Heijde.; Involvement: > 4 points on the modified vdH-S method

observed in 63 cases (77.8%), while 38 patients (46.9%) had evidence of osteoporosis and subchondral cysts, and 12 patients (14.8%) presented with synovitis. Patients with a score in vdH-S > 4 points, had a higher number of erosions and space joint narrowing compared to patients with a score < 4 points (p= < 0.001). Patients with a score of vdH-S >4 points had a significantly higher prevalence of osteoporosis (62% vs. 22.6%) than those with a score < 4 points (p= < 0.001). Regarding the quality of life and foot functionality, there was no differences in the involvement of the foot and ankle (p= 0.631, p=0.560, respectively).

Conclusion: Most patients (85%) had radiologic findings in the lower extremity joints, with subluxations in 77.8% and osteoporosis and subchondral cysts in 46.9%. There was no significant difference between quality of life and foot functionality in patients with foot and ankle joint involvement compared to those without.

Disclosure: E. Sanchez-Peralta: None; **A. Cantero-Castro**: None; **K. Deciderio-Pavon**: None; **J. Espinoza-Gámez**: None; **I. Arcibar-Liceaga**: None; **C. De Leon-Carrillo**: None; **A. Garza-Elizondo**: None; **R. Sanchez-De la Cruz**: None; **J. Cardenas-de la Garza**: None; **D. Galarza-Delgado**: None; **D. Flores-Alvarado**: None; **J. Elizondo-Rodriguez**: None.

Abstract Number: 0768

Veteran Rehabilitation, Physical Therapy Care Delivery, and Outcomes after Total Knee Arthroplasty

Nina Carson[1], Jeremy Graber[2], Shane O'Malley[3], Dennis Hanse[4], Amy Peters[5], Jennifer Stevens-Lapsley[6] and Michael Bade[6], [1]University of Colorado Anschutz Medical Campus, Aurora, CO, [2]University of Colorado Anschutz Medical Campus & the VA Denver-Seattle Center of Innovation, Aurora, CO, [3]Eastern Colorado Health Care System, Aurora, CO, [4]Eastern Colorado Health Care System & University of Colorado Anschutz Medical Campus, Aurora, CO, [5]Eastern Colorado Health Care System and University of Colorado Anschutz Medical Campus, Aurora, CO, [6]University of Colorado Anschutz Medical Campus & Eastern Colorado Health Care System, Aurora, CO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster

Session Type: Poster Session A

Session Time: 10:30AM–12:30PM

Background/Purpose: Compared to the general population, Veterans have higher prevalence of knee osteoarthritis, comorbidities, activities of daily living limitations, and healthcare utilization following total knee arthroplasty (TKA). Despite these limitations, there is a significant gap in knowledge regarding how physical therapy care is delivered and what factors influence recovery for Veterans. To address this gap, we examined Veteran outcomes and physical therapy care delivery after TKA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We recruited 86 Veterans [74 male, age 68±8 (mean ± standard deviation), body mass index 31±4.5, Charlson Comorbidity Index 1±1] who attended rehabilitation following TKA for ≥1 session in two Veterans Integrated Service Networks. We collected preoperative outcomes for knee range of motion, the timed up and go test, and the Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS JR). The KOOS JR was collected postoperatively at 90-days (primary outcome) and at 180-days. Physical therapy care outcomes were collected from the electronic medical record from April 2022 to April 2025 including time to physical therapy evaluation, duration of care, and number of visits.

Paired t-tests were performed to assess changes in KOOS JR scores from preoperative values at 90-day and 180-day. Pearson correlation coefficients were calculated on the relationship between the 90-day KOOS JR scores and preoperative characteristics (KOOS JR scores, the timed up and go test, knee flexion, knee extension) as well as time to outpatient evaluation, number of visits, and duration of care.

Results: Prior to surgery the Veterans were recorded to have 115 ± 11^{0} of knee flexion, 11.5±4 seconds on the timed up and go test, and a KOOS JR interval score of 49.9±13. On average, 90-day KOOS JR scores were 18.6±2.0 points higher than preoperative scores (95% Confidence Interval 14.8, 22.9, $p< .001$). On average, the 180-day KOOS JR scores were 26.9±3.4 points higher than preoperative scores (95% CI 20.0, 33.8, $p< .001$) and 8.1±2.0 points higher than the 90-day KOOS JR scores (95% CI 3.9, 12.4, $p< .001$). Number of visits (11±6 visits, $r= -0.26$, $p< 0.001$) and time to outpatient evaluation from (15±14 days, $r = -0.25$, $p< 0.001$) were negatively correlated with 90-day KOOS JR scores. Preoperative KOOS JR scores ($r = 0.26$, $p< .001$) and preoperative knee flexion ($r = 0.16$, $p< .001$) were positively correlated with 90-day KOOS JR scores.

Conclusion: Despite the significant change in scores following TKA, on average these Veterans did not meet the threshold associated with meaningful change in physical function on the 90-day KOOS JR (≥ 27). The negative correlation between the number of visits and time to outpatient evaluation may result from these Veterans having poor recovery, increasing the need for additional services such as home health rehabilitation, sub-acute rehabilitation, or skilled nursing facility stays prior to outpatient physical therapy. Veterans with worse preoperative KOOS JR scores and reduced knee flexion may benefit from enhanced postoperative care. Additionally, factors related to postoperative care pathways should be explored to improve outcomes.

Disclosure: N. Carson: None; **J. Graber**: None; **S. O'Malley**: None; **D. Hanse**: None; **A. Peters**: None; **J. Stevens-Lapsley**: None; **M. Bade**: None.

Abstract Number: 0769

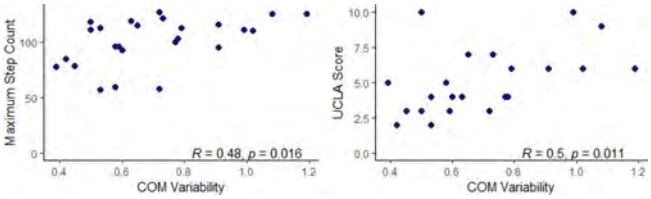
Increased Gait Variability at Preferred Walking Speeds is Associated with Increased Physical Activity Measures in People with Knee Osteoarthritis

Ogundoyin Ogundiran, Steven Garcia, Joy Itodo, Oiza Peters and Kharma Foucher, UNIVERSITY OF ILLINOIS, CHICAGO, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: People with knee osteoarthritis (OA) often exhibit reduced physical activity levels and increased fall risk. Gait variability, specifically center of mass (COM) variability is a measure of balance and stability; characteristics that may

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



be impaired with OA. Higher COM variability has been linked to better adaptability to environmental perturbations. It is plausible that more physically active people with OA will exhibit more typical levels of gait variability compared to less active individuals. The association between gait variability and physical activity measures in individuals with knee OA, nonetheless, remains unclear. The purpose of this study was to evaluate the associations between physical activity and COM variability during walking in people with knee OA. We hypothesized that greater amounts of physical activity will be associated with greater amounts of COM variability in people with knee OA.

Methods: We studied 25 people with knee OA (57 ± 8 years: 9 M, 16 W) using 3D gait analysis and physical activity monitoring. Physical activity was assessed through self-reported UCLA scores, and a wrist-worn Actigraph accelerometer. Using the UCLA Scale, Participants rated themselves from 1 (inactive) to 10 (highly active). Steps per day were calculated through Actigraph software. Participants walked on an instrumented treadmill collecting kinetic data at 1200 Hz, synced to an 8-camera system set up collecting kinematic data at 120 Hz. A full-body modified Helen Hayes marker set was used for biomechanical analysis. Gait variability was quantified using the coefficient of variation of the vertical COM trajectory displacement, over ten consecutive steps. We used Pearson's correlation to test for associations between COM variability and activity measures.

Results: Aligned with our hypotheses, higher COM was associated with higher levels of activity in both the self-reported (R=.500, p=.011) and objective activity measures (R=.476, p=.016). This suggests individuals with more physical activity may retain more robust gait patterns, evidenced by the association to higher COM variability. No significant association found between COM variability and intensity measures such as total MVPA (R=-1.92, p=.358) or percentage in MVPA (R=-.200, p=.337), indicating that global activity levels may be more relevant than intensity.

Conclusion: People with knee OA face a lack of physical activity due to multifactorial influences. Our previous work has indicated that kinesiophobia can be a potential explanatory factor of physical inactivity in the population. Center of mass variability may also provide insight into the physical inactivity people with knee OA face. Increased gait variability has been linked to improved efficiency in responding to environmental perturbations. It known that individuals with knee OA have a greater fall prevalence, balance/stability deficits, and lower amounts of physical activity. Findings from this study illustrated a positive correlation between increased amounts of physical activity, and gait variability. This study illustrates how better understanding gait variability can provide insight into novel physical activity and fall interventions trainings for this population.

Disclosure: O. Ogundiran: None; **S. Garcia**: None; **J. Itodo**: None; **O. Peters**: None; **K. Foucher**: None.

Abstract Number: 0770

Interrelationships of Depression, Pain, and Gait Mechanics and their Associations with Physical Activity Levels Among People with Knee Osteoarthritis

Oiza Peters, Steven Garcia, Joy Itodo, Ogundoyin Ogundiran and kharma Foucher, UNIVERSITY OF ILLINOIS, CHICAGO, Chicago, IL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Depression is associated with low physical activity (PA) levels in people with knee osteoarthritis (KOA)[1]. Pain contributes to both depression and PA levels in people with knee OA[1,2] but can also influence gait biomechanics which may, in turn, adversely impact PA. Understanding how depression, pain, gait biomechanics, and PA are interrelated in KOA could guide more effective interventions. This study, therefore, investigated the relationships among these factors. We focused on joint powers as a relevant aspect of gait biomechanics because they are directly related to force absorption and generation during motion and may be directly related to the ability to be physically active. We hypothesized that (i) depression, pain, and affected limb hip, knee, and ankle joint powers are all associated with PA, and (ii) that more depression and pain are associated with lower joint powers.

Methods: We evaluated 34 people with knee OA (20 Women, 56±8 years, 34.7±7.1 kg/m^2) walking at self-selected speeds on an instrumented split-belt treadmill, using standard motion capture methods. We calculated sagittal plane peak positive joint powers of the hip, knee, and ankle during terminal stance. Participants reported their PA levels using the UCLA activity scale which ranges from 1 (“wholly inactive”) to 10 (“regularly participate in impact sports”). Participants also completed the KOOS pain subscale, where 100 indicates the absence of pain and the PROMIS Depression Computerized Adapted Test, (US average = T score of 50, higher scores indicate more depression). We used Spearman correlations to quantify the associations among variables.

Results: Surveys indicated that, on average, participants were moderately active (UCLA 5±2), reported an average level of depression symptoms (T score 50±11) and reported moderate pain (KOOS Pain 54.0±22.6). UCLA scores were significantly correlated with pain, depression, and all joint powers (Table 1). More depression and pain were associated with lower PA levels but, surprisingly, depression and pain were not correlated with each other. Finally, more pain was associated with lower joint powers but there were no associations with depression.

These findings support our hypothesis that depression, pain, and joint powers are associated with PA levels in KOA. Pain may lower PA levels directly as well as indirectly through its influence on joint mechanics. Hip and ankle powers had moderate to strong associations with PA indicating the need to include a multi-joint rehabilitative strategy to preserve power

Table 1. Spearman correlation coefficients and p values quantifying associations among PA levels, joint powers, pain, and depression in people with knee OA. Greater joint powers, less pain, and less depression are associated with higher levels of PA. Shading highlights statistically significant correlations.

	Peak ankle power	Peak knee power	Peak hip power	Pain	Depression
UCLA	**0.675**	**0.576**	**0.348**	**0.600**	**-0.389**
	<0.001	**<0.001**	**0.043**	**<0.001**	**0.023**
Peak ankle power		**0.790**	**0.588**	**0.541**	-0.174
		<0.001	**<0.001**	**<0.001**	0.325
Peak knee power			**0.689**	**0.407**	-0.216
			<0.001	**0.017**	0.219
Peak hip power				0.207	-0.113
				0.240	0.526
Pain				1.000	-0.276
					0.114
Depression					

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

generation along the entire kinetic chain, rather than the knee only. Further, the association of PA levels with depression amplifies its independent importance. Multi-factored interventions that include depression management may be helpful to improve PA in this population.

Conclusion: There is an interplay of psychosocial and structural factors that influence PA in people with knee OA. Effective clinical intervention should include a well-defined holistic approach.

Disclosure: O. Peters: None; **S. Garcia**: None; **J. Itodo**: None; **O. Ogundiran**: None; **k. Foucher**: None.

Abstract Number: 0771

Radiographic Knee Osteoarthritis and Corticosteroid Injection Use: The Moderating Role of Physical Activity

Sydney Liles[1], Jennifer Copson[2], Daniel K. White[1] and Jason Jakiela[3], [1]University of Delaware, Newark, DE, [2]University of Delaware, Wilmington, DE, [3]Winston-Salem State University, Winston-Salem, NC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (0765–0771) Orthopedics, Low Back Pain, & Rehabilitation Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Knee osteoarthritis (OA) is a chronic disease with no current cure and a leading cause of disability among adults. Treatment for knee OA focuses on symptom management, with physical activity (PA) and Corticosteroid (CS) injections being strongly recommended. However, increased utilization of CS injections may increase the risk of total joint replacement, and those with higher Kellgren-Lawrence (KL) grades have been shown to have higher odds of receiving a CS injection. Further, it is unknown if PA mitigates the use of CS injections for those with worse radiographic evidence of knee OA. The purpose of this study was to determine if PA modifies the relationship between radiographic OA (ROA) presence and utilization of CS injections during a 5-year follow-up period in adults with or at high risk for knee OA.

Methods: We performed a secondary analysis of Osteoarthritis Initiative (OAI) data. Our exposure was ROA presence (KL grade ≥ 2 vs < 2), at the 48-month visit (analytic baseline, BL). Our outcome was receiving a CS injection assessed using the question "In the past 6 months, have you received a CS injection?" from BL to the 108-month follow-up visit. We excluded participants who answered yes to the CS injection question at BL. PA, measured using an Actigraph GT1M at BL, was examined as an effect measure modifier between ROA presence and CS injection, and 6000 steps/day was used to stratify the sample. We produced Kaplan-Meier survival curves for cumulative incidence of not receiving a CS injection and used Cox proportional hazards regression to calculate discrete-time hazard ratios (HR) adjusted for confounders.

Results: 1763 participants (mean age = 65.0 years old, 55% female, mean BMI =28.5 kg/m^2) were included in the overall analytic sample. 204 participants received at least one CS injection over 5 years of follow-up. For participants with ≥ 6000 steps/day, survival probability was 82% for those with ROA and 92% for those without ROA (Figure 1a). Those with ROA had 223% increased hazard of receiving a CS injection compared to those without ROA (adjusted HR [95% CI] = 3.23 [2.05, 5.08]) (Table 1). For participants with < 6000 steps/day, survival probability was 67% for those with ROA and 91% for those without ROA (Figure 1b). Those with ROA had a similar hazard of CS injection whether they walked < 6000 steps/day (3.45 [1.73, 6.89]) or ≥ 6000 steps/day (3.05 [1.66, 5.61]) (Table 2). The interaction term for ROA presence and steps/day was not significant (p = 0.68).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Kaplan-Meier survival curves for not receiving a CS injection, for total sample and by ROA exposure group, in those who walked ≥ 6000 and < 6000 steps/day at baseline.

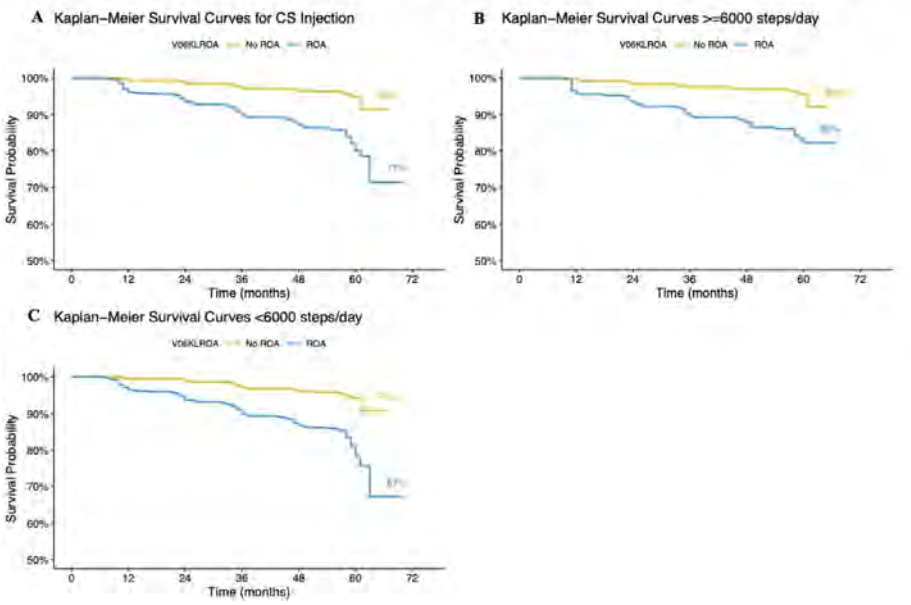


Table 1: Hazard ratios and 95% confidence intervals for ROA and KL Grade exposure groups for receiving a CS injection

	CS Injection n/N (%)	HR [95% CI] (unadjusted)	HR [95% CI] (adjusted)
ROA			
No ROA (< 2)	33/703(4.7%)	1.0 [REF]	1.0 [REF]
ROA (≥ 2)	171/1060(16.1%)	**3.82 [2.63, 5.54]**	**3.23 [2.05, 5.08]**

Note: models were adjusted for age, sex, BMI, race, education, comorbidity, function measured by the Knee Osteoarthritis Outcome Score (KOOS), baseline steps/day, and pain

Table 2: Hazard ratios and 95% confidence intervals for receiving a CS injection, ROA and KL Grade exposure groups, stratified by steps/day at baseline.

	CS Injection n/N (%)	HR [95% CI] (unadjusted)	HR [95% CI] (adjusted)	Interaction *P*
ROA				
≥ 6000 steps/day				
No ROA (< 2)	15 / 348(4.3%)	1.0 [REF]	1.0 [REF]	
ROA (≥ 2)	68 / 441 (15.4%)	**3.97 [2.27, 6.94]**	**3.05 [1.66, 5.61]**	0.68
< 6000 steps/day				
No ROA (< 2)	18 / 355 (5.1%)	1.0 [REF]	1.0 [REF]	
ROA (≥ 2)	103 / 619(16.6%)	**3.60 [2.18, 5.93]**	**3.45 [1.73, 6.89]**	

Note: models were adjusted for age, sex, BMI, race, education, comorbidity, function measured by the Knee Osteoarthritis Outcome Score (KOOS), and pain

Conclusion: Physical activity does not seem to modify the relationship between ROA presence and CS injection utilization. However, for people with ROA, those who were more active had a slightly attenuated risk of receiving a CS injection than those who were less active as those with ROA who were more active had an 82% chance of not receiving a CS injection compared to a 67% chance for those who were less active over a 5-year period.

Disclosure: S. Liles: None; **J. Copson**: None; **D. White**: None; **J. Jakiela**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0772

Redefining When to Biopsy the Kidney in Patients with SLE

Michelle Petri[1], Andrea Fava[2], Mohamed Atta[3], Avi Rosenberg[3], Sanchit Sanyal[3], Peter Izmirly[4], Erin Carter[5], Mala Masson[6], Michael Belmont[7], Jennifer Barnas[8], Jennifer Anolik[9], Brad Rovin[10], Jill Buyon[4] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM), [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Baltimore, MD, [4]NYU Grossman School of Medicine, New York, NY, [5]New York University Grossman School of Medicine, New York, NY, [6]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [7]NYU Langone Health, New York, NY, [8]University of Rochester, Rochester, NY, [9]University of Rochester Medical Center, Rochester, NY, [10]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Plenary I (0772–0776)

Session Type: Plenary Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Current ACR, EULAR and KDIGO guidelines recommend kidney biopsy in SLE patients with urine protein to creatinine (UPCR) ratio of $\geq$ 0.50 g/g. However, SLE patients who undergo kidney biopsy at lower levels of UPCR are frequently found to have proliferative lupus nephritis (Wang S, et al. Clin J Am Soc Nephrol. 2022;17:1150-1158). As part of the Accelerated Medicines Partnership we investigated first onset of UPCR 0.250-0.499 g/g.

Methods: SLE patients with no history of LN and UPCR of 0.250 to 0.499 g/g PLUS another predictor of lupus nephritis (LN) including non-White race, serologies (low C3, low C4, or anti-dsDNA). or active urine sediment, were enrolled. Kidney biopsies were done at the site institution and reported as ISN Class I-VI with NIH Activity and Chronicity Index, if LN.

Results: Twenty-eight patients were enrolled: 24 (86%) females, 6 (21%) Hispanic, and 13 (46%) African-American, 7 (25%) White, 2 (7%) Asian and 6 (21%) Other race. Twenty-five (89%) were anti-dsDNA positive, 20 (71%) had low C3 and 19 (68%) had low C4 at enrollment. All had GFR >60, no immunosuppression and prednisone < 10mg/day. Seven patients were taking ACEi/ARBs, two SGLT2 inhibitors (both were no LN on subsequent biopsy) and 23 hydroxychloroquine. Twenty had LN: two Class I; five Class II; six Class III; and seven Class V. Eight did not have LN (Table 3): 6 (75%) had a history of positive anti-dsDNA; 3 (38%) had a history of low C3; and 3 (38%) had a history of low C4. Table 1 shows the NIH Activity

Table 1. Characteristics of lupus nephritis patients and biopsies

	N=28	Class I (N=2)	Class II (N=5)	Class III (N=6)	Class V (N=7)	Non-Lupus (N=8)
Kidney Histology						
Median Activity Index (Q1-Q3)	0 (0-2.25)	0	0	4 (3-4)	0 (0-.25)	N/A
Median Chronicity Index (Q1-Q3)	0 (0-2)	0	1 (1-2)	0.5 (0-1.5)	2.5 (0-3.5)	N/A
Laboratory Results						
Median UPCR (Q1-Q3)	.38 (.31-.42)	0.439 (.39-.48)	0.43 (.27-.45)	.39 (.35-.47)	.34 (.30-.42)	.328 (.27-.38)
Median Serum Creatinine (Q1-Q3)	.7 (.64-.90)	.79 (.7-.83)	.64 (.6-.9)	.74 (.65-.93)	.71 (.60-1.07)	.83 (.68-.89)
Median GFR (Q1-Q3)	97.1 (81.6-115.7)	97.3 (91.3-103.2)	110.8 (76.9-125.4)	102.2 (97.8-118.5)	86.5 (75.2-116.4)	87 (72.6-115.8)
Serologies						
Positive DsDNA n (%)	22 (79)	2 (100)	3 (60)	6 (100)	6 (86)	5 (63)
Low Complement n (%)	14 (50)	0 (0)	2 (40)	5 (83)	4 (57)	2 (25)
SLEDAI Score Median (Q1-Q3)	7 (2.5-10)	5.5 (3-8)	8 (2-11)	9.5 (6.5-10.5)	7.5 (4.25-12.25)	5 (0-6)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of inclusion criteria between those with lupus nephritis vs those without lupus nephritis

Criteria	LN pos (n=19)	Not LN (n=8)	P-value
Age at Biopsy (yrs)	42.0 ± 15.1	52.1 ± 18.7	0.1976
Race (Black/Other)	16 (80%)	5 (63%)	0.3715
History of anti-dsDNA positive	19 (95%)	6 (75%)	0.1880
History of low C4	**16 (80%)**	**3 (38%)**	**0.0296**
History of low C3	**17 (85%)**	**3 (38%)**	**0.0223**
History of low Complement (C3 or C4)	**18 (90%)**	**4 (50%)**	**0.0384**
Anti-dsDNA positive at visit	17 (85%)	5 (63%)	0.3107
C4 low at first AMP visit	11 (55%)	2 (25%)	0.2218
C3 low at first AMP visit	10 (50%)	1 (13%)	0.0987
Complement low (C3 or C4) at first AMP visit	12 (60%)	2 (25%)	0.2087

Table 3. Histology of non-lupus nephritis biopsies

Histology	UPCR (g/g)	Serum Creatinine	GFR	Low C3	Low C4	DsDNA
Glomerulomegaly, segmental foot process effacement, swollen endothelial cells, ?TMA	0.293	0.68	92.4	Normal	Normal	Positive
Arteriosclerosis (mild-moderate), thin GBM disease	0.38	0.86	81.6	Normal	Normal	Negative
Histologically unremarkable, rare TRI, 20-25% foot process effacement	0.30	0.51	130.9	Normal	Normal	Positive
Glomerulosclerosis (50%), unquantifiable IFTA, arteriosclerosis (severe), 20-30% foot process effacement	0.411	0.79	73.2	Normal	Low	Positive
Arteriosclerosis (mild), 25% foot process effacement	0.358	0.86	72.4	Normal	Normal	Negative
Global Glomerulosclerosis (38%) and mild IFTA, mild mesangial matrix and cells increased, 20% foot process effacement	0.38	1.1	54.1	Normal	Normal	Negative
Arteriosclerosis (mild-moderate), early diabetic glomerulopathy (thick GBM, increase mesangial matrix), 20-25% foot process effacement	0.265	0.9	92.5	Low	Low	Positive
IgA nephropathy	0.26	0.69	123.6	Normal	Normal	Positive

and Chronicity Indices, UPCR and serologies by ISN Class. There were no biopsy complications. Patients with LN were more likely to have had a history of low C3 (p=0.0223) or low C4 (p=0.0296) prior to enrollment (Table 2).

In longitudinal follow up, two Class II, two Class III and three Class V have progressed to greater than 0.5 g/g of UPCR (in spite of treatment of Class III and Class V).

Conclusion: The 0.50 g/g UPCR cut-off for kidney biopsy in LN guidelines is arbitrary, omitting an opportunity to identify early LN before accrual of kidney damage. Earlier biopsy of LN, as defined by the AMP algorithm (UPCR between 0.250 and 0.499 g/g PLUS another LN predictor), found LN in 69%, with 61% initiating mycophenolate (6 Class III and 5 Class V) and 17% already showing some degree of chronicity. History of low C3 or C4 was the most important component of the AMP algorithm. The AMP early LN algorithm identified a high incidence of patients with consequential pathology and strongly support an adjustment to the UPCR cutoff for kidney biopsy in LN guidelines.

Disclosure: M. Petri: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **M. Atta**: GSK, 1, Novartis, 5; **A. Rosenberg**: None; **S. Sanyal**: None; **P. Izmirly**: Hansoh Bio, 2; **E. Carter**: None; **M. Masson**: None; **M. Belmont**: None; **J. Barnas**: None; **J. Anolik**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2.

Abstract Number: 0773

Clinical Significance of Anti-MDA5 Epitope Antibodies as Prognostic Indicators for Interstitial Lung Disease With or Without Dermatomyositis

Tsuneo Sasai[1], Ran Nakashima[2], Motohiro Nonaka[3], Norimichi Nomura[4], Atsubumi Ogawa[1], Yasuhiro Nohda[1], Mirei Shirakashi[2], Ryosuke Hiwa[1], Hideaki Tsuji[1], Hajime Yoshifuji[2], Shogo Matsuda[5], Masao Katsushima[6], Michinori Ishitoku[7], Yusuke Yoshida[7], Yasuyuki Todoroki[8], Satoshi Kubo[9], Tomohiro Handa[10], Hiromi Tomioka[11], Ryo Tachikawa[12], Keisuke Tomii[12], Kiminobu Tanizawa[13], Toru Arai[14], Takuya Kotani[15], Motomu Hashimoto[16], Shintaro Hirata[7], Yoshiya Tanaka[17], Tsuneyo Mimori[18] and Akio Morinobu[19], [1]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [2]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [3]Department of Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [4]Department of Cell Biology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [5]Department of Internal Medicine IV, Division of Rheumatology, Osaka Medical and Pharmaceutical University, Osaka, Japan, [6]Department of Clinical Immunology, Osaka Metropolitan Graduate School of Medicine, Osaka, Japan, [7]Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, [8]Department of Molecular Targeted Therapies, University of Occupational and Environmental Health, Kitakyushu, Japan, [9]Department of Molecular Targeted Therapies (DMTT), University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [10]Department of Advanced Medicine for Respiratory Failure and Graduate School of Medicine, Kyoto University, Kyoto, Japan, [11]Department of Respiratory Medicine, Kobe City Medical Center West Hospital, Kobe, Japan, [12]Department of Respiratory Medicine, Kobe City Medical Center General Hospital, Kobe, Japan, [13]Respiratory Medicine, National Hospital Organization Kyoto Medical Center, Kyoto, Japan, [14]Clinical Research Center, NHO Kinki-Chuo Chest Medical Center, Sakai, Japan, [15]Division of Rheumatology, Department of Internal Medicine IV, Osaka Medical and Pharmaceutical University, Osaka, Japan, [16]Osaka Metropolitan University, Osaka, Japan, [17]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [18]Takeda Clinic for Rheumatic Diseases, Kyoto, Japan, [19]Kyoto University, Kyoto, Kyoto, Japan

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Plenary I (0772–0776)

Session Type: Plenary Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Melanoma differentiation-associated gene 5 (MDA5) is a cytoplasmic RNA sensor and activates the innate immune response. Autoantibodies against MDA5 are associated with rapidly progressive interstitial lung disease (ILD) in dermatomyositis (DM). Moreover, MDA5 protein expression is upregulated in the lungs of patients with MDA5-positive-ILD and idiopathic pulmonary fibrosis. We hypothesized that specific antibody reactivity against certain MDA5 epitope peptides correlates with severe ILD phenotypes and could serve as biomarkers not only in anti-MDA5-positive DM-ILD but also in idiopathic interstitial pneumonias (IIPs).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

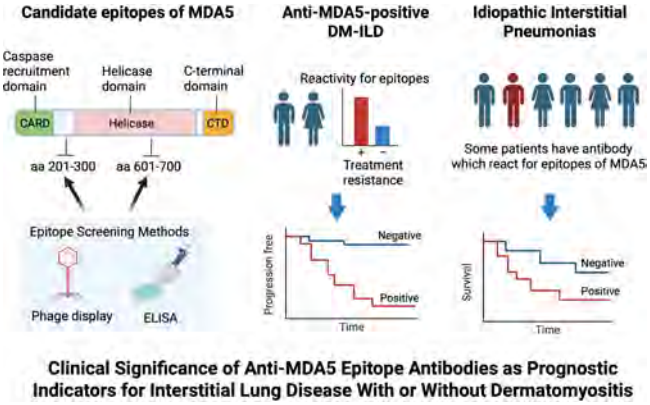


Figure 1. Graphical abstract

Methods: We screened sera from patients with anti-MDA5-positive DM-ILD to identify epitopes using T7 phage display and ELISA with recombinant MDA5 fragments. Two candidate regions, MDA5 (amino acids 201–300) and MDA5 (amino acids 601–700), were identified (Figure 1). We retrospectively analyzed 30 anti-MDA5-positive DM-ILD patients treated with unified therapy (discovery cohort) and validated findings in 54 patients from a multicenter cohort (validation cohort). Resistance to initial triple therapy (glucocorticoid, calcineurin inhibitor, cyclophosphamide) was defined as the need for additional therapy or death within 6 months. Moreover, we examined 288 IIP patients for reactivity to MDA5 (201-300 and 601-700) and assessed their clinical significance in predicting survival outcomes.

Results: In the discovery cohort, high reactivity to MDA5 (201-300) and MDA5 (601-700) was significantly associated with resistance to initial therapy. ROC analysis showed strong predictive ability (sensitivity and specificity were 88% and 71% in MDA5 (201-300), and 63% and 93% in MDA5 (601-700), respectively). In the validation cohort, MDA5 (201-300) positivity was significantly associated with lower 6-month progression-free survival (43% vs. 74%, $p < 0.05$, Figure 2). Reactivity to MDA5 (601-700) trended toward poorer outcomes but was not statistically significant. Among IIP patients, MDA5 (201-300) and MDA5 (601-700) positivity were significantly more frequent in non-survivors. Patients positive for MDA5 (201-300) or MDA5 (601-700) had lower 5-year survival rates (34% vs. 66%, $p < 0.01$; 42% vs. 67%, $p < 0.01$, respectively, Figure 3).

Conclusion: We identified two MDA5 epitope regions—MDA5 (201-300) and MDA5 (601-700)—that are strongly associated with treatment resistance and poor prognosis in anti-MDA5-positive DM-ILD. Furthermore, reactivity to these epitopes also predicted poor outcomes in IIPs. Epitope-specific reactivity may reflect underlying pathogenic mechanisms and serve as novel biomarkers for risk stratification and treatment decision-making in ILD with or without obvious autoimmune disease background.

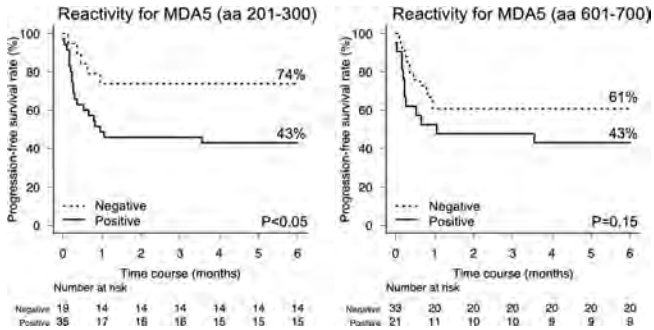


Figure 2. Progression free survival rates of anti-MDA5-positive DM-ILD

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

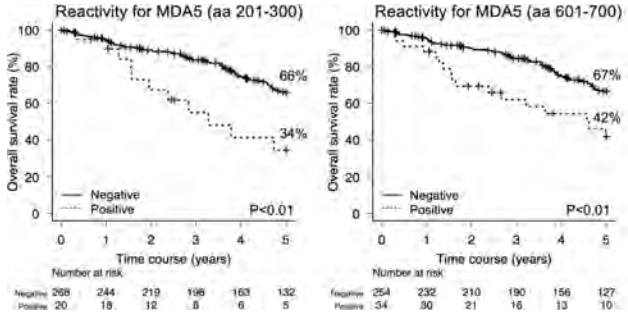


Figure 3. Overall survival rates of idiopathic interstitial pneumonias

Disclosure: T. Sasai: None; **R. Nakashima**: None; **M. Nonaka**: None; **N. Nomura**: None; **A. Ogawa**: None; **Y. Nohda**: None; **M. Shirakashi**: None; **R. Hiwa**: None; **H. Tsuji**: None; **H. Yoshifuji**: AbbVie/Abbott, 6, Chugai, 6, Janssen, 6; **S. Matsuda**: None; **M. Katsushima**: None; **M. Ishitoku**: None; **Y. Yoshida**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Daiichi-Sankyo, 6, Eisai, 6, GlaxoSmithKlein(GSK), 6; **Y. Todoroki**: None; **S. Kubo**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6; **T. Handa**: FUJIFILM Corporation, 5, Teijin Pharma Co., Ltd, 5; **H. Tomioka**: Nippon Boehringer Ingelheim Co., Ltd., 6; **R. Tachikawa**: None; **K. Tomii**: Boehringer-Ingelheim, 6; **K. Tanizawa**: FUJIFILM Corporation, 5; **T. Arai**: AstraZeneca, 6, Boehringer-Ingelheim, 6, Sekisui Medical, 5, 6, Shionogi, 6, Sysmex, 5; **T. Kotani**: None; **M. Hashimoto**: None; **S. Hirata**: AbbVie/Abbott, 6, Asahi-Kasei Pharma, 5, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 5, 6, Daiichi-Sankyo, 6, Eisai, 1, 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKlein(-GSK), 6, Janssen, 6, Nihon-Shinyaku, 6, Novartis, 6, Otsuka Pharmaceutical, 5, 6, Pfizer, 6, Sandoz, 6, Taisho, 5, 6, Tanabe-Mitsubishi, 6, UCB, 6; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **T. Mimori**: None; **A. Morinobu**: None.

Abstract Number: 0774

Longitudinal peripheral blood multi-omic profiling in at-risk individuals uncovers immune signatures and predictive models for future rheumatoid arthritis conversion

Jun Inamo[1], Aleksandra Bylinska[2], Miles Smith[2], Lauren Vanderlinden[3], Christian Wright[4], Tayte Stephens[5], Marie Feser[6], Christopher Striebich[7], James O'Dell[8], Jeffrey Sparks[9], John Davis[10], Jonathan Graf[11], Maureen McMahon[12], Elizabeth Solow[13], Lindsy Forbess[14], Athan Tiliakos[15], David Fox[16], Maria I. Danila[17], Diane Lewis. Horowitz[18], Jonathan Kay[19], Judith James[2], V. Michael Holers[20], Kevin Deane[21], Joel Guthridge[2] and Fan Zhang[22], [1]University of Colorado School of Medicine, Aurora, CO, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]University of Colorado Anschutz Medical Campus, Monument, CO, [4]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [5]University of Oklahoma Health Science Center, Oklahoma City, OK, [6]University of Colorado Anschutz Medical Campus, Aurora, CO, [7]University of Colorado, Aurora, CO, [8]University of Nebraska Medical Center, Omaha, NE, [9]Brigham and Women's Hospital, Boston, MA, [10]Mayo Clinic, Rochester, MN, [11]UCSF, San Francisco, CA, [12]UCLA David Geffen School of Medicine, Los Angeles, CA, [13]UT Southwestern Medical Center, Dallas, TX, [14]Cedars-Sinai Medical Center, Los Angeles, CA, [15]Emory University, Roswell, GA, [16]University of Michigan, Dexter, MI, [17]University of Alabama at Birmingham, Birmingham, [18]Northwell Health, New Hyde Park, [19]UMass Chan Medical School, Worcester, MA, [20]University of Colorado Anschutz Medical Campus, Aurora, [21]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [22]The University of Colorado, Aurora, CO

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Plenary I (0772–0776)
Session Type: Plenary Session
Session Time: 9:30AM–11:00AM

Background/Purpose: Seropositive rheumatoid arthritis (RA) has an at-risk stage identifiable by elevations of antibodies to cyclic citrullinated peptide (CCP). Identifying the immunologic factors that distinguish CCP(+) at-risk individuals who progress to RA (Converters) from those who do not (Nonconverters) is crucial to develop strategies for prediction and prevention of clinical RA.

Methods: We used longitudinal data from CCP3(+) individuals in the StopRA trial (NCT02603146) that found hydroxychloroquine (HCQ) was not effective in preventing clinical RA. We used single-cell multi-omics on peripheral blood mononuclear cells from pre-RA/baseline and incident RA-like synovitis timepoints in Converters and at baseline and follow-up in Nonconverters (**Fig 1A-C**). For T cell analysis, we integrated CITE-seq and mass cytometry (CyTOF) data to identify shared T cell clusters, confirming concordant expression patterns across technologies (**Fig 1D-E**). We also developed a composite predictive model for clinical RA (**Fig 1F**).

Results: 47 Converters and 53 Nonconverters underwent CyTOF analyses, and 24 Converters and 12 Nonconverters iCITE-seq/scASAP-seq. At baseline (V0), T peripheral helper (Tph) cells (T-14) were significantly elevated in Converters vs Nonconverters; Converters also had expanded *GZMK+XCL1+CD57+* CD8+ T cells (**Fig 2A-B**). Differential gene expression analysis also showed that at baseline Converters had upregulation of cytotoxic genes (e.g., *GZMB*) in CD8+ T cells, Th2-associated genes (e.g., *CCR4*) and *TNF* in CD4+ T cells, among others, indicating broad dysregulation of inflammatory and cytotoxic pathways (**Fig 2C-D**). Single-cell chromatin accessibility profiling showed that specific chromatin regions were accessible at baseline in Converters, particularly in immune regulatory loci (**Fig 2E-F**). Notably, the *PTPN22* locus exhibited enhanced chromatin accessibility in NK cells at baseline in Converters (**Fig 2G-I**). In longitudinal analyses, TCR analysis showed expanded clones dominated by Tph cells and *GZMB*+ and *GZMK*+ CD8+ T cells in Converters at baseline and at synovitis onset (V1) (**Fig 2J-M**).

A predictive model using baseline Tph frequency, CCP3 levels, and rheumatoid factor (RF) distinguished Converters from Nonconverters with an AUC of 0.771 (**Fig 3A**). A decision tree model further identified those with CCP3 ≥108 units and Tph ≥2.45% of CD3+ T cells had the highest risk for conversion (**Fig 3B**). Kaplan-Meier demonstrated that, at baseline, Converters in the top 20% for Tph or CCP3 levels had a significantly shorter time to RA onset compared to the bottom 20% (**Fig 3C-D**).

Conclusion: Alterations in cellular subsets, gene expression, chromatin accessibility and clonal expansion are present in at-risk individuals with CCP3 elevations who develop synovitis. These findings inform potential targets for preventive interventions in clinical trials as well as prediction models to identify CCP3(+) individuals at highest risk for developing clinical RA. Notably, while HCQ did not show clinical effect, future studies will evaluate HCQ effect on cells and other biomarkers.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

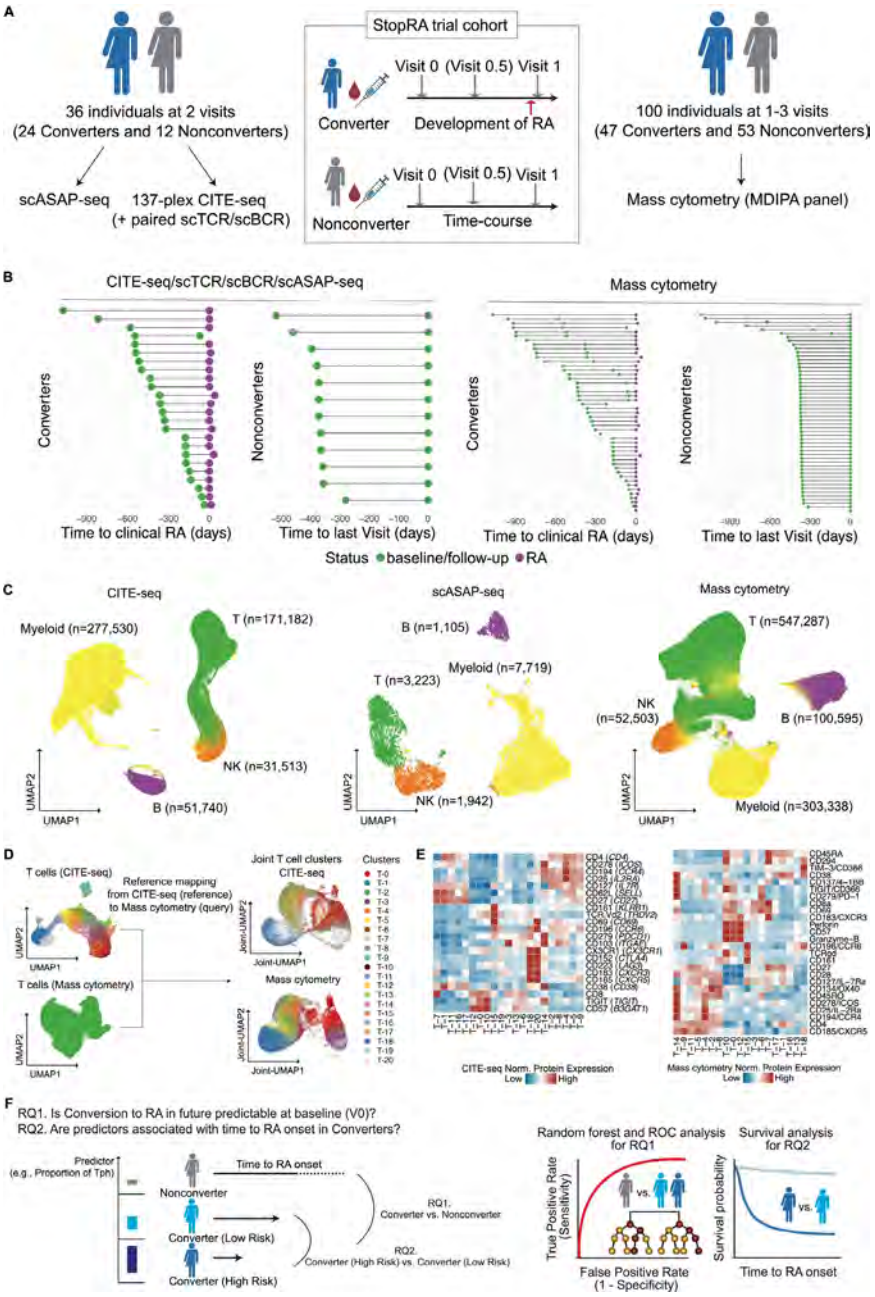


Fig.1: Study design for longitudinal single-cell omic data collection from RA-Converters and Nonconverters. A, The study cohort was selected from 144 individuals with anti-CCP3 levels ≥2 times the upper limit of normal who were enrolled and followed longitudinally in the StopRA trial that evaluated the efficacy of hydroxychloroquine (HCQ) in a placebo-controlled fashion to prevent clinical RA. A subset of 36 individuals (24 Converters and 12 Non-Converters) was profiled using single-cell ASAP-seq and 137-plex CITE-seq, including paired single-cell TCR and BCR sequencing. Another subset of 100 individuals (47 Converters and 53 Non-Converters) was analyzed with mass cytometry (MDIPA panel) across 1–3 visits. B, Time points of sample collection per individual. The time to clinical RA diagnosis (day 0) is shown for Converters, and a follow-up visit is indicated for Nonconverters. Data are presented separately for individuals analyzed by CITE-seq/scTCR-seq/scBCR-seq/scASAP-seq (left) and those analyzed by mass cytometry (right). Colored points represent visit status: baseline/follow-up (green) or post-RA (purple). C, Broad immune cell-type identification presented in the UMAP, showing major immune cell types identified across CITE-seq, scASAP-seq, and mass cytometry datasets. D, Strategy to integrate CITE-seq and mass cytometry data for T cell analysis. UMAP projection of integrative T cell subclusters projected into a shared embedding space using overlapping measured 33 proteins with CITE-seq data as reference and mass cytometry as query. Clusters in CITE-seq and joint-space are color-coded and labeled consistently across modalities. E, Normalized protein expression in joint T cell subclusters from CITE-seq (left) and mass cytometry data (right). F, Schematic of the predictive modeling approach. Two research questions were addressed: (RQ1) distinguishing Converters from Nonconverters at baseline (V0) and (RQ2) predicting time to RA onset among Converters. Predictors such as Tph proportions were incorporated into random forest model to prioritize them. Note: CyTOF analyses included study participants who received HCQ or placebo, while CITE-seq and ASAP-seq only included participants who received placebo.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

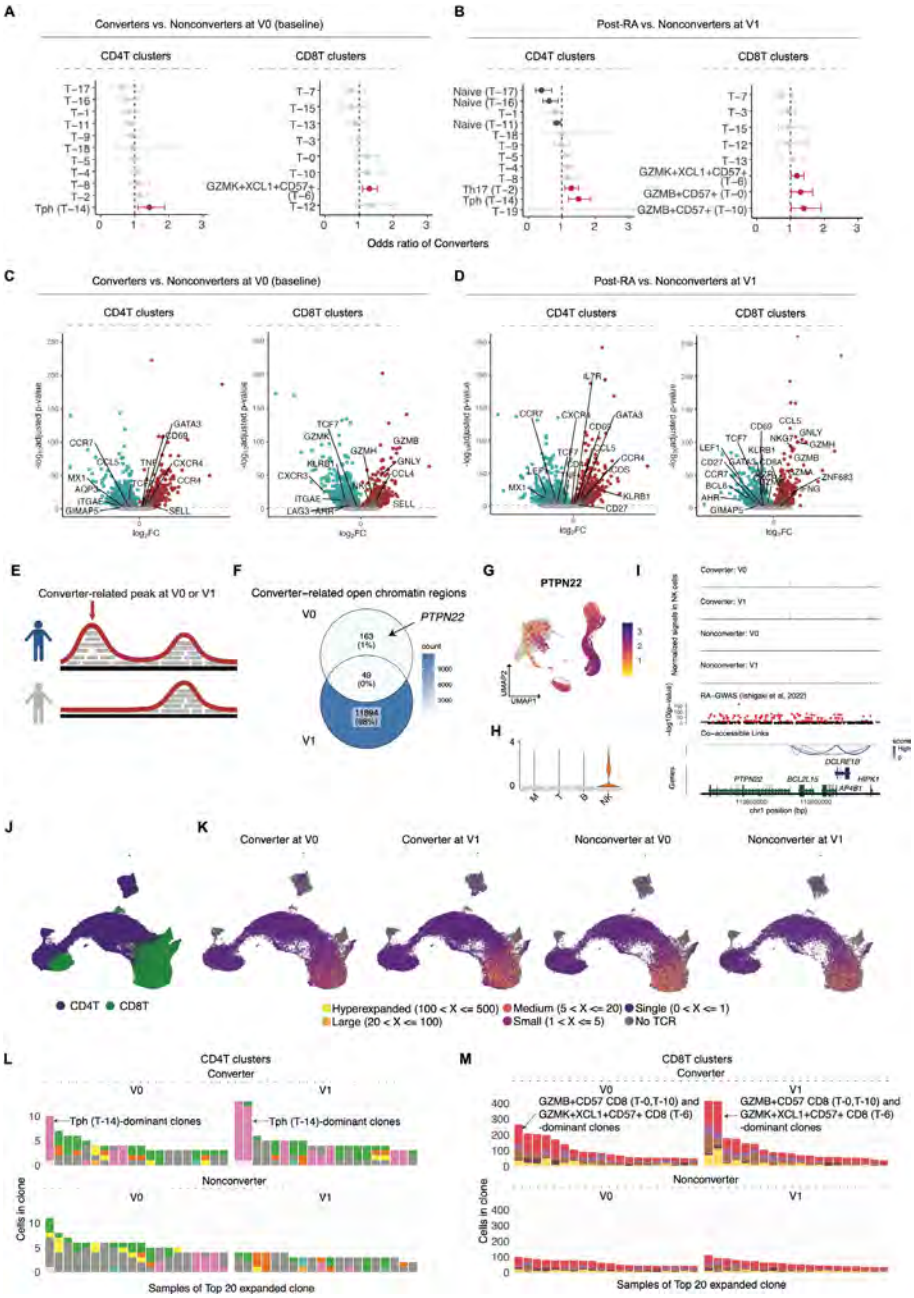


Fig. 2: T cell subcluster analysis by integrating single-cell datasets from CITE-seq, mass cytometry, scASAP-seq, and TCR. A, B, Generalized linear mixed model (GLMM) analysis comparing RA Converters and Nonconverters at each visit point. The odds ratio and 95% confidence intervals (CIs) for each T cell subcluster are shown separately for CD4+ T cells (left) and CD8+ T cells (right). Differences in datasets (CITE-seq or CyTOF), age, gender, batch, individual, and HCQ were corrected by including them as covariates. A, Comparison at baseline (V0). B, Comparison after RA onset (V1). C, D, Differentially expressed genes in CD4+ and CD8+ T cells between Converters and Nonconverters at baseline (V0) and post-RA (V1) stages. T-cell marker genes are annotated. E, Graphical representation of the Converter-related peak analysis. Open chromatin regions associated with RA conversion were identified by comparing chromatin accessibility between Converters and Nonconverters at baseline (V0) and post-RA (V1) stages. F, Venn diagram illustrating the number of significant peaks identified at V0 and V1 (adjusted p-value < 0.05). G, UMAP plot showing the expression of PTPN22, a Converter-associated locus, identified at V0 using CITE-seq data. H, Violin plot showing the PTPN22 mostly expressed by NK cells. I, Illustration of a Converter-associated open chromatin region within the PTPN22 locus. J, UMAP projection of T cells in CITE-seq data colored by CD4T (purple) and CD8T cells (green). K, Clonal expansion of TCR repertoires across visit points. L, M, The composition of the top 20 expanded T cell clones is shown for CD4+ T cells and CD8+ T cells at V0 and V1. The dominant Tph (T-14) clones are highlighted in Converters and Nonconverters.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

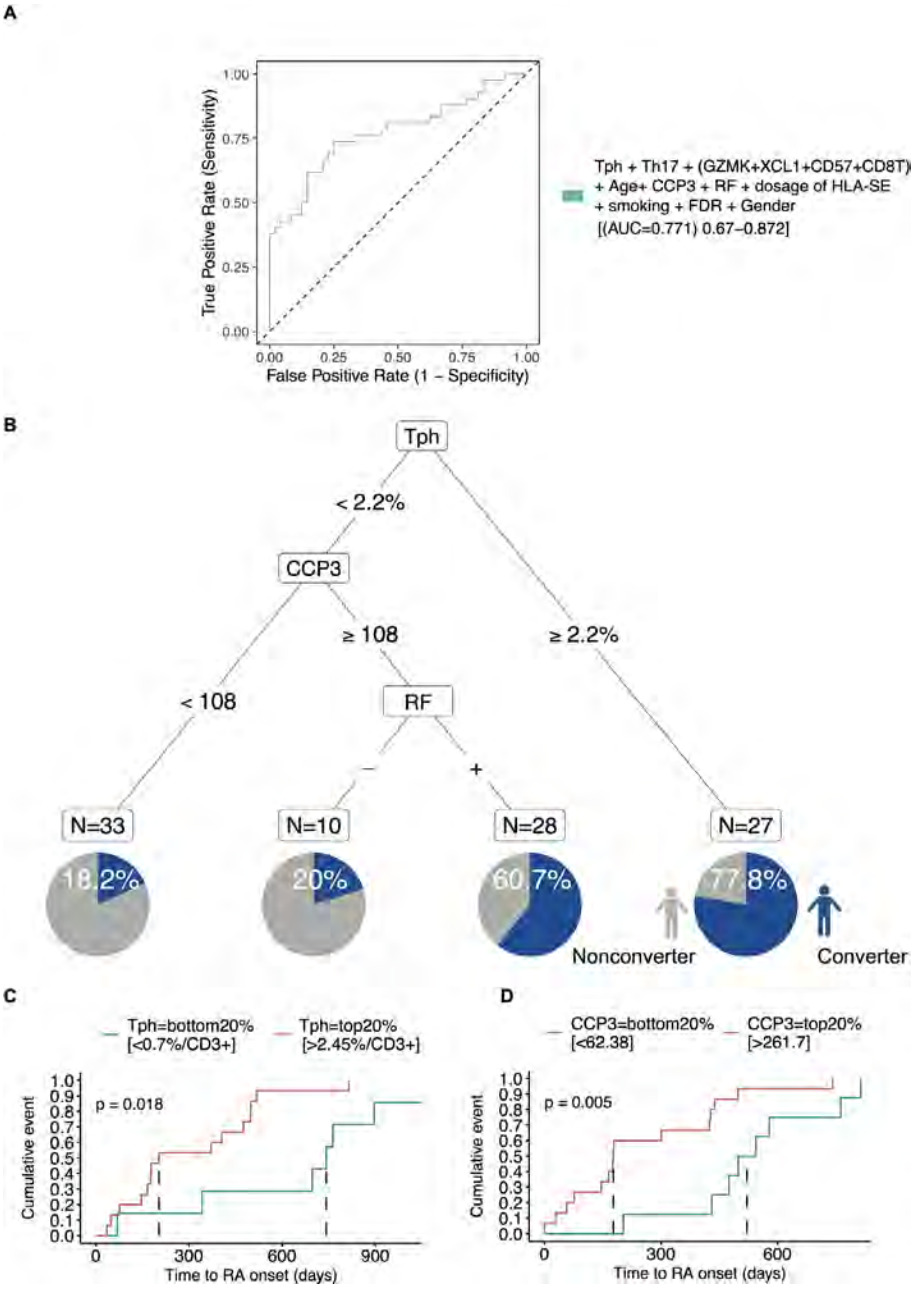


Fig. 3: Predictive modeling for RA conversion. A, ROC analysis of a composite predictive model incorporating multiple predictors using samples available CyTOF or CITE-seq data (47 Converters and 53 Nonconverters). For cell type frequencies such as Tph cells, values from CITE-seq were prioritized. For samples lacking CITE-seq data, cell type frequencies predicted via integration— as described in Figures 1—were used instead. B, Decision tree model for RA conversion. A classification tree showing hierarchical decision rules based on CCP3 levels, Tph cells (T-14), and RF status to predict RA conversion risk. Pie charts at terminal nodes indicate the proportion of Converters (blue) and Nonconverters (gray). C-D, Survival analysis of RA conversion stratified by Tph and CCP3 levels. Kaplan-Meier curves showing time to RA onset based on (C) top and bottom 20% of Tph proportions and (D) top and bottom 20% of CCP3 levels. Statistical significance was assessed using log-rank tests.

Disclosure: J. Inamo: None; **A. Bylinska**: None; **M. Smith**: None; **L. Vanderlinden**: None; **C. Wright**: None; **T. Stephens**: None; **M. Feser**: None; **C. Striebich**: None; **J. O'Dell**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **J. Graf**: None; **M. McMahon**: Artiva, 2, AstraZeneca, 2, 6, Aurinia, 6, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(-GSK), 1, 5, 6, Novartis, 5, Roche, 1; **E. Solow**: None; **L. Forbess**: Novartis, 5; **A. Tiliakos**: None; **D. Fox**: None; **M. I. Danila**: None; **D. Lewis. Horowitz**: None; **J. Kay**: Biogen, 5, Celltrion, Inc., 2, Gate Bioscience, 2, Immunitas Therapeutics, 2, Immunovant, Inc., 2, Istesso, Ltd, 2, Kolon TissueGeje, Inc, 1, Organon, LLC, 2, Sana Biotechnology, Inc.,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Santa Ana Bio, Inc., 2, Spyre Therapeutics, 2, Wolters Kluwer NV, 9; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **V. Holers**: Q32 Bio, 12, 2; **K. Deane**: Inova Diagnostics, 1; **J. Guthridge**: None; **F. Zhang**: None.

Abstract Number: 0775

Increased Circulating Microbial Small RNA tDR-1 is Associated with Decreased Progression to Future Clinical Rheumatoid Arthritis In High Risk Individuals and Reduces In Vitro Type 1 Interferon Response Gene Expression

Anastasiia Phothisane[1], Tulsi Joishy[2], Carolina Ramirez-Becerra[1], Zuofei Wang[2], Qiong Wu[3], Jennifer Seifert[4], Marie Feser[5], Jill Norris[6], Kristen Demoruelle[7], LauraKay Moss[5], Kevin Deane[8], V. Michael Holers[9] and **Michelle Ormseth**[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, [3]University of Virginia, Charlottesville, VA, [4]University of Colorado and Oklahoma Medical Research Foundation, Aurora, CO, [5]University of Colorado Anschutz Medical Campus, Aurora, CO, [6]Colorado School of Public Health, Denver, CO, [7]University of Colorado Anschutz Medical Campus, Golden, CO, [8]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [9]University of Colorado Anschutz Medical Campus, Aurora

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Plenary I (0772–0776)
Session Type: Plenary Session
Session Time: 9:30AM–11:00AM

Background/Purpose: Microbial small RNAs (sRNAs) can regulate human genes, often with anti-inflammatory effects. We previously showed that an increased plasma concentration of a tRNA-derived RNA (tDR-1), produced by multiple bacteria from the phylum Proteobacteria, was associated with lower RA disease activity, particularly fewer tender joints, in 2 independent cohorts, and better treatment response to multiple disease modifying antirheumatic drugs. The purpose of this study was to determine if tDR-1 is a biomarker associated with decreased future development of clinical RA among individuals at-risk for the disease and exhibits *in vitro* anti-inflammatory effects which may affect RA development.

Methods: Archived longitudinal plasma and clinical data from participants from the Studies of the Etiology of Rheumatoid Arthritis cohort were used for this study. Microbial tDR-1 was measured in plasma by quantitative PCR by investigators blinded to clinical details. Human THP-1 monocyte-derived macrophages were treated with tDR-1, scramble control or

Table. Participant demographics

	Control (n= 123)	CCP3+, no RA (n=35)	CCP3+, pre-RA (n=25)
Age, years	46 ± 16	48 ± 15	51 ± 12
Race/ethnicity, # non-Hispanic White	92 (77)	28 (82)	18 (72)
Gender, # Female	85 (69)	26 (74)	15 (60)
BMI, kg/m2	26 ± 5.8	26.9 ± 5.3	27.8 ± 5.3
First degree relative with RA, #	9 (7)	19 (54)	9 (36)
Shared epitope, # positive	53 (45)	11 (31)	18 (72)
Smoker, # ever	28 (23)	13 (39)	14 (56)
RF IgA, # positive	0 (0)	3 (9)	4 (16)
RF IgG, # positive	0 (0)	6 (17)	7 (28)
RF IgM, # positive	0 (0)	6 (17)	7 (28)
Anti-CCP2, # positive	0 (0)	3 (9)	16 (64)
Anti-CCP3, # positive	0 (0)	35 (100)	25 (100)
Anti-CCP3.1, # positive	0 (0)	27 (77)	24 (96)

Data presented as number (percent) for categorical variables and mean ± standard deviation for continuous variables. CCP3+, pre-RA = anti-CCP3+ participants who later developed RA. CCP3+, no RA = anti-CCP3 positive participants who did not develop RA. Missing data: Age for 1 control. Race/ethnicity for 4 control, 1 CCP3+ no RA. BMI for 2 control, 3 CCP3+ no RA, 2 CCP3+ pre-RA. Shared epitope for 4 control. Ever smoker status for 3 control, 2 CCP3+ no RA. CCP2 status for 16 control.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

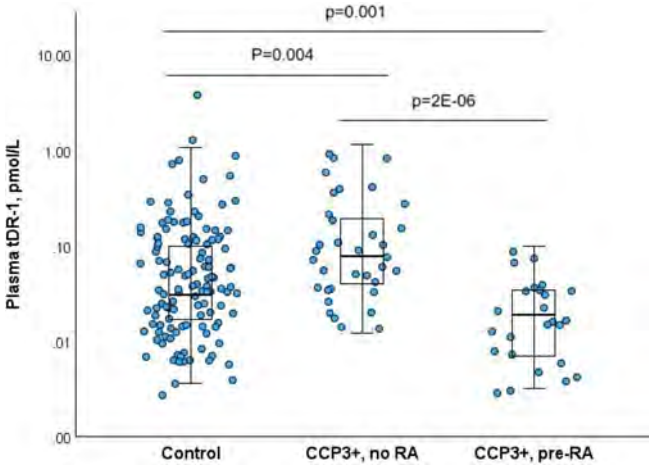


Figure 1. Plasma tDR-1 concentration in seronegative controls, CCP3+ participants who did not develop future RA (CCP3+, no RA), and CCP3+ participants who later developed RA (CCP3+, pre-RA). The Y axis is presented in log-scale. Comparison by Mann-Whitney U test.

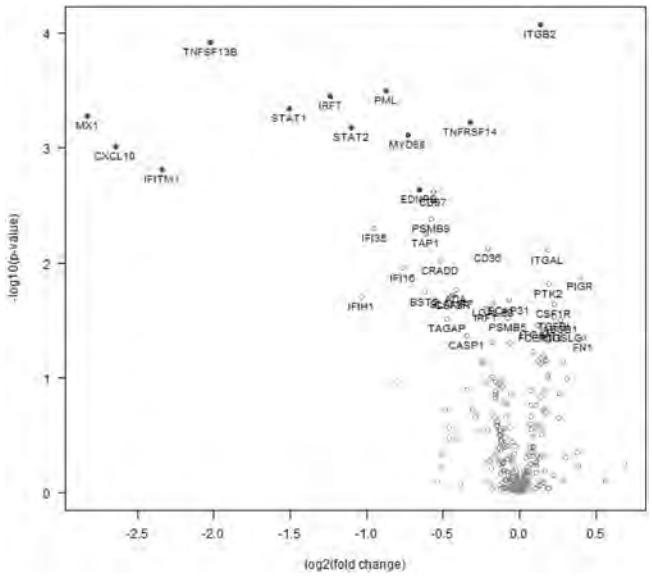


Figure 2. Change in gene expression in human THP-1 monocyte derived macrophages after treatment with tDR-1 versus scramble control. The majority of significantly downregulated genes are interferon response genes.

transfection reagent alone in triplicate. After 24 hours, gene expression was assessed by the Nanostring Immunology panel. Pathway analysis was performed using Ingenuity Pathway Analysis.

Results: The study included 60 participants at-risk for development of RA with anti-CCP3 antibody positivity (CCP3+) without synovitis at baseline and 123 seronegative control participants. Among the CCP3+ participants, 25 later developed clinical RA (defined by meeting 2010 classification criteria or presence of inflammatory arthritis) and 35 did not (**Table**). Microbial tDR-1 was 7.7-fold (p=2E-06) (**Figure 1**) enriched at baseline among CCP3+ participants who did not develop RA versus those who did, and remained independently associated with decreased RA development after adjustment for the presence or absence of any other autoantibody (including CCP2, CCP3.1, RF IgA, RF IgM, or RF IgG), shared epitope, and ever smoker status (p=0.006). Among CCP3+ at-risk participants, plasma tDR-1 concentration had an area under the receiver operating characteristic curve of 0.856 (95% CI 0.768, 0.951) for prediction of not developing RA (p=1.2E-14). Compared to scramble control, tDR-1 significantly downregulated many interferon response genes including *MX1* (**Figure 2**), and pathway analysis identified interferon signaling as most downregulated by tDR-1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Enrichment of circulating microbial tDR-1 is independently associated with decreased development of future RA among those at high risk for disease. Its ability to reduce interferon response genes, which are typically elevated in early RA, suggests a potential mechanism by which the microbiome could affect the development of RA via sRNAs.

Disclosure: A. Phothisane: None; **T. Joishy**: None; **C. Ramirez-Becerra**: None; **Z. Wang**: None; **Q. Wu**: None; **J. Seifert**: None; **M. Feser**: None; **J. Norris**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5; **L. Moss**: None; **K. Deane**: Inova Diagnostics, 1; **V. Holers**: Q32 Bio, 12, 2; **M. Ormseth**: None.

Abstract Number: 0776

Efficacy and Safety of Upadacitinib in Giant Cell Arteritis: 2-Year Results From the Re-Randomized, Double-Blind SELECT-GCA Phase 3 Trial

Wolfgang Schmidt[1], Arathi Setty[2], Christian Dejaco[3], Andrea Rubbert-Roth[4], Maria Cid[5], Tomonori Ishii[6], Avani D. Joshi[2], Nathaniel Zerad[2], Aditi Kadakia[7], Shaofei Zhao[2], Weihan Zhao[2], Ivan Lagunes[2], Charles Phillips[8], Daniel Blockmans[9] and Peter Merkel[10], [1]Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch; Waldfriede Hospital, Rheumatology, Berlin, Germany, [2]AbbVie Inc, North Chicago, IL, [3]Medical University of Graz, Department of Rheumatology, Graz, Austria; Department of Rheumatology, Hospital of Brunico (SABES-ASDAA), Brunico, Italy, [4]Division of Rheumatology and Immunology, Cantonal Hospital St Gallen, St Gallen, Switzerland, [5]Department of Autoimmune Diseases (member of European Reference Network RITA), Hospital Clinic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain, [6]Division of Hematology and Rheumatology, Tohoku Medical and Pharmaceutical University, Sendai, Japan, [7]AbbVie Inc, Woburn, MA, [8]AbbVie Inc, Princeton, NJ, [9]Department of General Internal Medicine, University Hospitals Leuven; Department of Microbiology, Immunology, and Transplantation, KU Leuven, Leuven, Belgium, [10]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

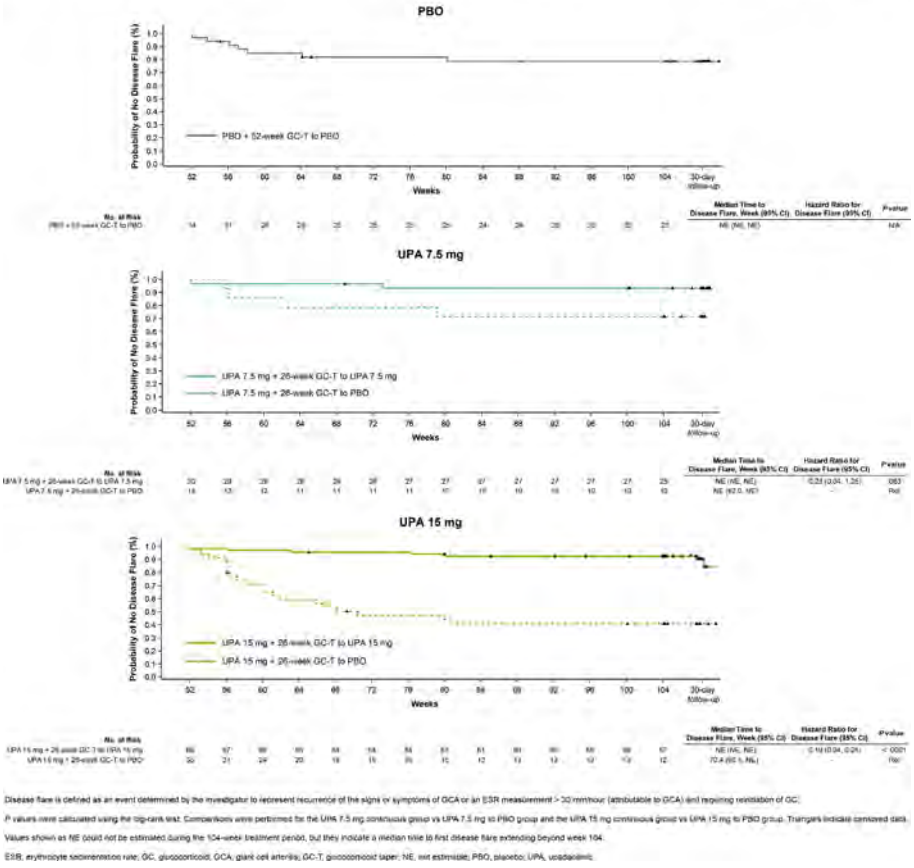
Session Date: Sunday, October 26, 2025
Session Title: Plenary I (0772–0776)
Session Type: Plenary Session
Session Time: 9:30AM–11:00AM

Background/Purpose: In the SELECT-GCA phase 3 trial, treatment of patients with GCA with upadacitinib 15 mg (UPA15) demonstrated superior rates of disease remission, fewer disease flares, and reduced glucocorticoid (GC) use compared with placebo (PBO).[1] The current study analyzed the 2-year outcomes in this trial.

Methods: SELECT-GCA included a 52-week randomized, PBO-controlled period 1 and a 52-week randomized, blinded extension period 2. Patients aged ≥ 50 years with a diagnosis of active GCA were randomized (2:1:1) to UPA15 or UPA 7.5 mg (UPA7.5) once daily with a 26-week GC taper or PBO with a 52-week GC taper. Period 2 involved patients in remission (absence of the signs or symptoms of GCA and adherence to the protocol-defined GC taper) for ≥ 24 consecutive weeks before the week 52 visit. Patients originally randomized to UPA7.5 or UPA15 were re-randomized (2:1) to continue the same dose of UPA or to switch to PBO in period 2. Patients originally randomized to PBO continued PBO. Efficacy outcomes were evaluated through week 104 and included remission (defined in period 2 as the absence of the signs or symptoms of GCA and no GC use for GCA), disease flare-related endpoints, and cumulative GC exposure. The safety analysis included all patients who received ≥ 1 dose of study drug in period 1 and continued the same treatment in period 2. Exposure-adjusted treatment-emergent adverse events (TEAEs) are reported through 2 years in this population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan-Meier Curves for Time to First Disease Flare for Patients Who Achieved ≥ 24 Consecutive Weeks of Remission in Period 1 and Entered Period 2



Disease flare is defined as an event determined by the investigator to represent recurrence of the signs or symptoms of GCA or an ESR measurement > 30 mm/hour (attributable to GCA) and requiring reinitiation of GC.

P values were calculated using the log-rank test. Comparisons were performed for the UPA 7.5 mg continuous group vs UPA 7.5 mg to PBO group and the UPA 15 mg continuous group vs UPA 15 mg to PBO group. Triangles indicate censored data.

Values shown as NE could not be estimated during the 104-week treatment period, but they indicate a median time to first disease flare extending beyond week 104.

ESR, erythrocyte sedimentation rate; GC, glucocorticoid; GCA, giant cell arteritis; GC-T, glucocorticoid taper; NE, not estimable; PBO, placebo; UPA, upadacitinib.

Results: Of 428 patients randomized and treated in period 1, 181 (42%) achieved ≥ 24 consecutive weeks of sustained remission in period 1 and entered period 2 (PBO continuous, n = 34; UPA7.5 continuous, n = 30; UPA7.5 to PBO, n = 14; UPA15 continuous, n = 68; UPA15 to PBO, n = 35). Most (91%) of these patients completed the study, with 82% remaining on study drug. From week 52 through week 104, 68.6% of patients on continuous UPA15 maintained remission vs 28.6% who switched from UPA15 to PBO (**Table 1**). Patients on continuous UPA15 showed a 90% reduction in risk of disease flare from week 52 through week 104 compared with those who switched from UPA15 to PBO (**Figure 1**). The continuous UPA15 group also showed greater improvements across most other endpoints (**Table 1**), including those related to disease flare and cumulative GC exposure.

Safety was generally similar for UPA and PBO groups among patients who continued the same treatment in period 2 (**-Table 2**). Rates of serious TEAEs were lower for both UPA doses than PBO. Compared to PBO, UPA15 showed lower rates of serious infections but higher rates of herpes zoster and elevated creatine kinase. One venous thromboembolism event occurred with UPA15 in a patient with multiple risk factors and none in the other treatment groups. No major adverse cardiovascular events or deaths occurred in period 2 in any treatment group.

Conclusion: For patients with GCA receiving UPA15, continued use of UPA in those who were in remission for ≥ 24 weeks during period 1, rather than switching to placebo, was associated with maintenance of remission and an approximately 1-gram reduction in the cumulative use of GCs in period 2. In this population (mean age: 71 yrs), no new clinically significant safety risks were identified with use of UPA for 2 years.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Efficacy Results for Patients Who Achieved ≥ 24 Consecutive Weeks of Remission in Period 1 and Entered Period 2 in the SELECT-GCA Trial[a,b]

Endpoints	PBO + 52-week GC-T to PBO (N = 34)	UPA 7.5 mg + 26-week GC-T to UPA 7.5 mg (N = 30)	UPA 7.5 mg + 26-week GC-T to PBO (N = 14)	Response rate difference: UPA 7.5 mg continuous vs UPA 7.5 mg to PBO	UPA 15 mg + 26-week GC-T to UPA 15 mg (N = 68)	UPA 15 mg + 26-week GC-T to PBO (N = 35)	Response rate difference: UPA 15 mg continuous vs UPA 15 mg to PBO
Maintenance of remission from week 52 through week 104—no. (% [95% CI])	20 (58.8) [42.3, 75.4]	21 (70.2) [53.8, 86.7]	7 (48.3) [21.5, 75.2]	21.9 [-9.0, 52.9] P = .165	47 (68.6) [57.5, 79.8]	10 (28.6) [13.6, 43.5]	40.3 [22.1, 58.6] P < .0001***
Cumulative GC exposure—median, mg [95% CI][c]							
Baseline through week 104	2882.0 [2417.0, 3172.0]	1150.0 [830.0, 1905.0]	1615.0 [1012.5, 2562.5]	P = .214	1528.0 [1150.0, 1615.0]	2204.2 [1230.0, 3896.3]	P = .001***
Week 52 through week 104	0 [0, 5.0]	0 [0, 0]	25.0 [0, 947.5]	P = .020*	0 [0, 0]	1048.0 [50.0, 2718.0]	P < .0001***
Time to first disease flare from week 52 through week 104—median, weeks [95% CI][d]	NE [NE, NE]	NE [NE, NE]	NE [62.0, NE]	P = .063	NE [NE, NE]	70.4 [60.1, NE]	P < .0001***
Experienced at least 1 disease flare from week 52 through week 104—% [95% CI]	21.3 [10.8, 39.6]	6.8 [1.7, 24.5]	28.6 [11.8, 59.4]	0.22 [0.04, 1.32] P = .099	15.5 [6.4, 34.9]	59.1 [43.2, 75.6]	0.12 [0.05, 0.31] P < .0001***
Complete remission at week 104—no. (% [95% CI])[e]	24 (70.6) [55.3, 85.9]	20 (65.1) [47.7, 82.5]	7 (47.6) [20.6, 74.6]	17.6 [-13.9, 49.1] P = .273	50 (73.1) [62.5, 83.7]	10 (28.6) [13.6, 43.5]	45.1 [27.9, 62.3] P < .0001***
Number of disease flares per patient per year— no. [95% CI]	0.3 [0.1, 0.6]	0.1 [0, 0.4]	0.3 [0.1, 0.8]	0.3 [0.1, 1.8] P = .206	0.1 [0.1, 0.3]	0.7 [0.5, 1.0]	0.2 [0.1, 0.4] P < .0001***
Change in SF-36 PCS from week 52 through week 104—LS mean [95% CI][f]	-2.30 [-4.86, 0.36]	-0.38 [-2.99, 2.23]	2.05 [-2.34, 6.44]	-2.42 [-7.50, 2.65] P = .346	0.52 [-1.29, 2.33]	-3.65 [-7.32, 0.02]	4.17 [0.23, 8.11] P = .038*
Change in FACIT-Fatigue from week 52 through week 104—LS mean [95% CI][g]	0.7 [-2.09, 3.45]	-1.1 [-3.85, 1.57]	1.8 [-2.99, 6.12]	-2.7 [-7.97, 2.56] P = .311	0.3 [-1.56, 2.20]	-1.6 [-5.42, 2.18]	1.9 [-2.13, 6.02] P = .347
TSQM global satisfaction score at week 104 —LS mean [95% CI][g]	71.5 [64.2, 78.7]	80.0 [72.9, 87.1]	73.0 [61.1, 84.9]	7.01 [-6.7, 20.8] P = .315	79.3 [74.4, 84.2]	64.9 [55.1, 74.8]	14.4 [3.7, 25.0] P = .008**

[a]At baseline, 428 patients (N = 112; PBO; N = 107; UPA 7.5 mg; N = 209; UPA 15 mg) were originally randomized and treated in the SELECT-GCA trial. This table reports efficacy outcomes for the 181 patients who achieved remission for ≥ 24 consecutive weeks in period 1 and entered period 2.

[b]Data are reported as percentage for categorical endpoints, LS mean for continuous endpoints (except for cumulative GC exposure), and median for cumulative GC exposure. The proportion of patients maintaining remission from week 52 through week 104 and the proportion of patients in complete remission at week 104 were evaluated by nonresponder imputation using multiple imputation. *$P \leq .05$; **$P \leq .01$; ***$P \leq .001$.

[c]PBO + 52-week GC-T to PBO, n = 31; UPA 7.5 mg + 26-week GC-T to UPA 7.5 mg, n = 29; UPA 7.5 mg + 26-week GC-T, n = 12; UPA 15 mg + 26-week GC-T to UPA 15 mg, n = 64; UPA 15 mg + 26-week GC-T to PBO, n = 31.

[d]Values shown as NE could not be estimated during the 104-week treatment period, but they indicate a median time to first disease flare extending beyond week 104.

[e]Complete remission was defined as follows: (1) absence of the signs and symptoms of GCA; (2) normalization of ESR (to < 30 mm/hour), although if ESR > 30 mm/hour and the elevation was not attributable to GCA, this criterion could still be met; (3) normalization of hsCRP (to < 1 mg/dL); and (4) no GC use for GCA.

[f]PBO + 52-week GC-T to PBO, n = 25; UPA 7.5 mg + 26-week GC-T to UPA 7.5 mg, n = 25; UPA 7.5 mg + 26-week GC-T, n = 9; UPA 15 mg + 26-week GC-T to UPA 15 mg, n = 57; UPA 15 mg + 26-week GC-T to PBO, n = 14.

ESR, erythrocyte sedimentation rate; GC, glucocorticoid; GCA, giant cell arteritis; GC-T, glucocorticoid taper; hsCRP, high-sensitivity C-reactive protein; LS, least-squares; NE, not estimable; PBO, placebo; PCS, physical component score; TSQM, Treatment Satisfaction Questionnaire for Medication; UPA, upadacitinib.

Table 3. Exposure-Adjusted Rates of Treatment-Emergent Adverse Events Through 2 Years in the SELECT-GCA Trial[a, b]

Variable—Events (E/100 PY)	PBO + 52-week GC-T to PBO (N = 43; PY = 82.5)	UPA 7.5 mg + 26-week GC-T to UPA 7.5 mg (N = 39; PY = 79.3)	UPA 15 mg + 26-week GC-T to UPA 15 mg (N = 92; PY = 184.1)
Overall TEAEs			
Any AE	438 (530.9)	305 (384.6)	938 (509.6)
Serious AE	21 (25.5)	16 (20.2)	32 (17.4)
AE leading to study drug discontinuation	4 (4.8)	2 (2.5)	9 (4.9)
Death	0	0	0
TEAEs of special interest			
Serious infection	6 (7.3)	3 (3.8)	5 (2.7)
Opportunistic infection[c]	1 (1.2)	0	1 (0.5)
Herpes zoster	2 (2.4)	4 (5.0)	8 (4.3)
Malignancy excluding NMSC[d]	0	2 (2.5)	2 (1.1)
NMSC	4 (4.8)	1 (1.3)	6 (3.3)
VTE (adjudicated)[e]	0	0	1 (0.5)
MACE (adjudicated)[f]	0	0	0
Gastrointestinal perforation	0	0	0
Renal dysfunction	1 (1.2)	0	0
Hepatic disorder	3 (3.6)	1 (1.3)	7 (3.8)
Anemia	4 (4.8)	4 (5.0)	12 (6.5)
Lymphopenia	0	0	1 (0.5)
Creatine kinase elevation	0	0	8 (4.3)
Retinal detachment	4 (4.8)	2 (2.5)	9 (4.9)
Bone fracture	3 (3.6)	1 (1.3)	2 (1.1)

[a]Safety results are not from the overall SELECT-GCA population but include all adverse events through 2 years (ie, both period 1 and 2) for patients originally randomized to PBO, UPA 7.5 mg, or UPA 15 mg and who received continuous treatment thereafter. All events are reported as TEAEs, which are defined as any adverse event with an onset date or worsening in severity date after initiation of study drug and no more than 30 days after the last dose of study drug in the trial.

[b]No TEAEs of active tuberculosis, lymphoma, or neutropenia, were reported in any treatment group through the end of the study.

[c]Excludes herpes zoster.

[d]UPA 7.5 mg: 1 lung adenocarcinoma and 1 papillary thyroid cancer; UPA 15 mg: 1 lentigo maligna and 1 prostate cancer.

[e]Includes pulmonary embolism and deep vein thrombosis.

[f]Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.

AE, adverse event; E, event; GC-T, glucocorticoid taper; TEAE, treatment-emergent adverse event; NMSC, nonmelanoma skin cancer; PBO, placebo; PY, patient-years; UPA, upadacitinib.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

1. Blockmans D, et al. *NEJM*. 2025.

Disclosure: W. Schmidt: AbbVie, 1, 5, 6, Alfasigma, 6, Amgen, 6, Boehringer-Ingelheim, 1, Chugai, 6, Eli Lilly, 6, Fresenius Kabi, 1, GlaxoSmithKline, 6, Medac, 6, Novartis, 1, 5, 6, Pfizer, 6, UCB, 6; **A. Setty**: AbbVie, 3, 11; **C. Dejaco**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Sparrow, 2, 6; **A. Rubbert-Roth**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Boehringer, 2, 6, Chugai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6; **M. Cid**: AbbVie, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL-Vifor, 2, 6, GSK, 2, 6, Kiniksa Pharmaceuticals, 5, UpToDate, 9; **T. Ishii**: AbbVie, 2, Asahi Kasei Pharma, 2, Astellas, 2, Ayumi Pharmaceutical, 2, BMS, 2, Chugai Pharmaceutical, 2, Daiichi-Sankyo, 2, Eisai, 2, Janssen, 2, Mitsubishi Tanabe, 2, Ono Pharmaceutical, 2, Pfizer, 2, Sanofi, 2; **A. Joshi**: AbbVie, 3, 11; **N. Zerad**: AbbVie, 3, 11; **A. Kadakia**: AbbVie, 3, 11; **S. Zhao**: AbbVie, 3, 11; **W. Zhao**: AbbVie, 3, 11; **I. Lagunes**: AbbVie, 3, 11; **C. Phillips**: AbbVie, 3, 11; **D. Blockmans**: AbbVie, 2, AstraZeneca, 2, GSK, 2, Roche, 2, 5; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2.

Abstract Number: 0777

Development of a Disease Activity Index for the Assessment of VEXAS Syndrome (VEXAS-DAI)

Kevin Byram[1], Herman Mann[2], Danielle Hammond[3], Sinisa Savic[4], Yohei Kirino[5], Carmelo Gurnari[6], Mael Heiblig[7], Thibault Comont[8], Arsène Mekinian[9], Mrinal Patnaik[10], Lachelle D. Weeks[11], Gary Ho[12], Onima Chowdhury[13], Adam Al-Hakim[14], Scott Goldberg[15], Marcela ferrada[16], Sophie georgin-Lavialle[17], Peter Grayson[18], Emma Groarke[19], Bhavisha Patel[20], Megan Sullivan[21], Sarah A. Buckley[22], Bryan G. harder[22], Sandra Goble[22], Matthew Koster[10] and David Beck[23], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Institute of Rheumatology, Praha 2, Czech Republic, [3]The University of Texas MD Anderson Cancer Center, Houston, TX, [4]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [5]Yokohama City University Graduate School of Medicine, Yokohama, Japan, [6]Department of Biomedicine and Prevention, University of Rome Tor Vergata and Translational Hematology and Oncology Research Department, Taussig Cancer Center, Cleveland Clinic, Clevland, OH, Rome, Italy, [7]Lyon-Sud Hospital, Hospices Civils de Lyon, Paris and Université Claude Bernard, Lyon, France, [8]Centre Hospitalier Universitaire Toulouse Institut Universitaire du Cancer Toulouse Oncopole, Toulouse, France, [9]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [10]Mayo Clinic, Rochester, MN, [11]Dana Farber Cancer Institute, Boston, MA, [12]New York University Grossman School of Medicine, VA New York Harbor Health Care System, Brooklyn, NY, [13]Oxford University Hospitals' NHS Foundation Trust and Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, United Kingdom, [14]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [15]New York University Grossman School of Medicine, Brooklyn, NY, [16]University of Maryland, Bethesda, MD, [17]Sorbonne university, Tenon hospital, DMU3ID, CEREMAIA, ERN RITA, Paris, France, [18]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD, [19]National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Bethesda, MD, [20]National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Beltsville, MD, [21]Mayo Clinic Arizona, Scottsdale, AZ, [22]Sobi Inc., Waltham, MA, [23]Center for Human Genetics and Genomics, NYU Grossman School of Medicine. Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine. Department of Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, New York, NY, USA, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases (0777–0782)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. VEXAS-DAI domains		
Domain	Items	Max Score
Inflammatory-type rash	2	4
Chondritis	3	3
Periorbital involvement	1	2
Ophthalmologic involvement	5	4
Joint involvement	1	2
Pulmonary involvement	3	4
Cardiovascular involvement	3	4
Genitourinary involvement	1	3
Neurological involvement	5	4
Oral/gastrointestinal involvement	3	4
Renal involvement	1	4
New thrombosis / thromboembolism	1	0
Constitutional symptoms	2	2
Total	30 scored items	40

Background/Purpose: VEXAS syndrome is a recently described severe disease characterized by a complex overlap of inflammatory and hematologic features. Due to the severity and refractory nature of inflammation in VEXAS patients, establishing effective treatment strategies is challenging, particularly in the absence of validated tools to assess disease activity. Standardized disease activity indices (DAIs) are crucial for patient care and advancing clinical research in inflammatory disorders. To date, the only proposed – though not validated – DAI for VEXAS is the VEXASCAF, which evaluates disease activity based on the presence or absence of 11 equally weighted manifestations (Kirino Y, et al. *Rheumatology (Oxford)*. 2024 Sep 28). While the VEXASCAF represents an important first step, it has limitations: it may not capture less commonly involved organ systems or be sufficiently sensitive to changes in disease severity. A more comprehensive and sensitive DAI could aid in clinical research and improve patient care.

Methods: Manifestations of VEXAS syndrome were previously identified by systematic literature review and expert feedback. The VEXAS-DAI was developed based on an expert advisory committee using modified Delphi methodology until consensus was reached (defined as ≥75% concurrence). All items were graded based on adapted Common Terminology Criteria for Adverse Events (CTCAE) criteria. Scoring was developed based on Physician Global Assessment of inflammation on 158 test cases. The final instrument was developed based on input from 24 VEXAS expert physicians worldwide.

Results: Consensus on the novel VEXAS-DAI was achieved after 4 rounds of interactive revisions. Scoring is based on severity of symptoms at the time of examination. The VEXAS-DAI includes 12 scored domains, each with a specified number of items **(Table 1)**: inflammatory-type rash (2), chondritis (3), ophthalmologic involvement (5), periorbital involvement (1), joint (1), pulmonary (3), cardiovascular (3), genitourinary (1), neurologic (5), oral and gastrointestinal (3), renal (1), and constitutional symptoms (present or absent). Additionally, a thrombosis and thromboembolism domain is included but remains unscored. Scores range from 0 to 40.

Conclusion: The VEXAS-DAI is designed to measure active inflammation in patients with VEXAS syndrome. Work is ongoing to validate this instrument in the context of a clinical trial.

This abstract has been accepted for publication by the European Alliance of Associations for Rheumatology (EULAR). The definitive copyedited version is available online at: www.ard.eular.org.

Disclosure: K. Byram: None; **H. Mann**: AbbVie, 6, Eli Lilly, 6, Novartis, 6, Sobi, 2, 6, UCB, 6; **D. Hammond**: None; **S. Savic**: BioCryst, 2, Celldex, 2, CSL Behring, 2, 5, KalVista, 2, 6, Novartis, 2, 5, 6, Pharming, 2, 6, Phavaris, 2, Sobi, 2, Takeda, 2, 6; **Y. Kirino**: Amgen, 6, Novartis, 2, 6, Sobi, 2; **C. Gurnari**: Alexion, 5, Genesis Therapeutics, 2; **M. Heiblig**: AbbVie, 2, Astellas, 2, Blueprint, 2, BMS/Celgebe, 2, Jazz Pharmaceuticals, 2, Servier, 2; **T. Comont**: AbbVie, 6, Amgen, 6, BMS, 2, 6, CSL Behring, 6, Griffols, 6, Novartis, 2, 5, 6; **A. Mekinian**: Roche, 5; **M. Patnaik**: AstraZeneca, 1, epigenetix, 5, Kura Oncology, 5, Polaris, 5, Sobi, 1, Solu therapeutics, 5, stem line pharmaceuticals, 5;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

L. Weeks: AbbVie, 2, Sobi, 2, Vertex, 2; **G. Ho**: Aclaris Therapeutics, 2, Scilex Holding, 2; **O. Chowdhury**: Jazz Pharmaceuticals, 6, Novartis, 6; **A. Al-Hakim**: None; **S. Goldberg**: None; **M. ferrada**: UpToDate, 9; **S. georgin-Lavialle**: Novartis, 2, Sobi, 2; **P. Grayson**: None; **E. Groarke**: None; **B. Patel**: None; **M. Sullivan**: None; **S. Buckley**: Sobi, Inc., 3; **B. harder**: Sobi, Inc., 3; **S. Goble**: Sobi, Inc., 3; **M. Koster**: Amgen, 2; **D. Beck**: Alexion, 2, Genesis Therapeutics, 2, GSK, 2, Novartis, 2, Sobi, 2.

Abstract Number: 0778

Clinical significance of non-infectious increased procalcitonin in Still's disease: A predictor of macrophage activation syndrome

Erdem Bektas[1], Burcu Ceren Uludogan[2], Büşra Fırlatan Yazgan[3], Ozgur Can Kilinc[4], Beste Acar[4], Oguzhan Omer Kizilkaya[4], Aysenur Yilmaz[5], Busra Yuce[6], serdal Ugurlu[7], Umut Kalyoncu[3], Timucin Kasifoglu[2] and Cemal Bes[8], [1]Istanbul University, Institute of Graduate Studies in Health Sciences, Immunology, Istanbul, Turkey, [2]Division of Rheumatology, Department of Internal Medicine, Eskisehir Osmangazi University, Eskisehir, Turkey, [3]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [4]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [5]Department of Rheumatology, Basaksehir Cam and Sakura City Hospital, University of Health Sciences, Istanbul, Turkey, [6]Department of Internal Medicine, Basaksehir Cam and Sakura City Hospital, University of Health Sciences, Istanbul, Turkey, [7]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [8]University of Health Sciences, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases (0777–0782)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Still's disease (SD) is a autoinflammatory disease (AID) characterized by a wide range of clinical manifestations and can exhibit life-threatening macrophage activation syndrome (MAS). Procalcitonin (PCT), a potential biomarker in SD, may be increased even in the absence of infection. The nature of PCT in AIDs remains unclear. We aimed to reveal the relationship between non-infectious increased PCT and the clinical features of SD.

Methods: In this retrospective study, patients with available PCT data at the time of diagnosis and fulfilling the Yamaguchi criteria were enrolled, as well as age- and sex-matched healthy individuals. Patients with any suspicious or documented infection at the time of diagnosis and/or during the active disease course and other factors that increase PCT, such as impaired renal function, were excluded from the study. Patients were classified into two groups based on the cut-off value of PCT, which was 0.5 ng/dl. Findings during the active disease, treatment, and laboratory parameters were evaluated.

Results: This study was conducted with 110 patients. PCT levels in SD, SD without MAS, and SD with MAS were significantly higher compared with healthy control (0.04 [0.03-0.04] ng/ml) (all three p< 0.001). PCT levels in SD with MAS were also significantly higher than SD without MAS (p=0.002) (Figure 1). Seventy-five (68%) patients were in the PCT < 0.5 group, and 35 (32%) patients were in the PCT ≥0.5 group. Patients' characteristics are shown in Table 1. Pleuritis and MAS were more frequent in the PCT ≥0.5 group (p=0.004, p=0.001, respectively). mPouchet score was significantly higher in the PCT ≥0.5 group (p=0.017). The requirement for bDMARD, especially anakinra, was higher in the PCT ≥0.5 group (p=0.051, p=0.008, respectively). Laboratory parameters of the patients are presented in Table 2. Platelet count was lower; thus, thrombocytopenia was higher in the PCT ≥0.5 group (p=0.008, p=0.011, respectively). AST and LDH levels were significantly higher in the PCT ≥0.5 group (p=0.006, p< 0.001, respectively). CRP and ferritin levels were significantly higher in the PCT ≥0.5 group, whereas albumin was lower (p=0.013, p< 0.001, and p=0.002, respectively). There was a positive correlation between PCT levels and AST, LDH, CRP, and ferritin levels (r=0.339, p< 0.001; r=0.584, p< 0.001; r=0.288, p<

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

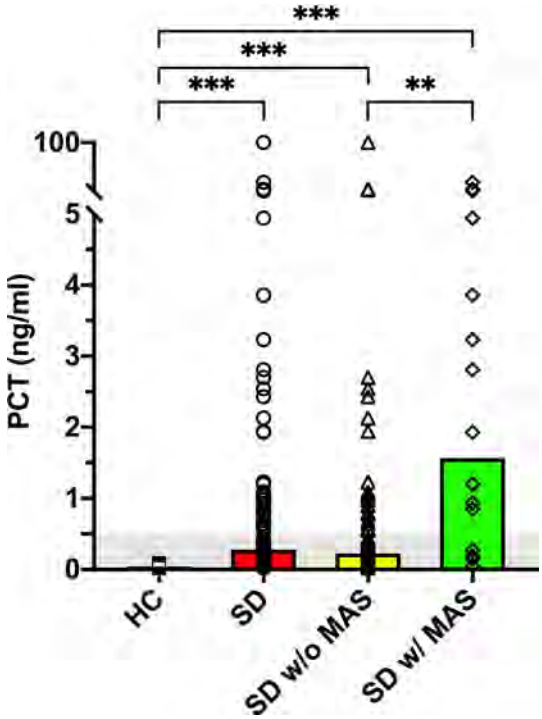


Figure 1. Procalcitonin (PCT) levels of patients with Still's disease (SD) (n=110), SD without macrophage activation syndrome (MAS) (n=94), and SD with MAS (n=16) at the time of diagnosis and healthy control (HC) (n=50). Bars show the median value. Mann-Whitney U; ** p<0.01, *** p<0.001.

0.01; and r=0.499, $p< 0.001$, respectively). In univariate logistic regression analysis, the risk for development of MAS was up to 6.4-fold in the PCT ≥0.5 group (crude OR 6.4 [CI 95% 2.0-20.4], p=0.002), while up to 4.3-fold in multivariate logistic regression analysis (adjusted OR 4.3 [CI 95% 1.1-16.8], p=0.038). Normalization of PCT levels occurred in all patients after immunosuppressive treatment.

Table 1. Demographic, clinical, and treatment characteristics of patients.

	All patients (n=110)	PCT<0.5 (n=75)	PCT≥0.5 (n=35)	p-value
Sex, male, n (%)	44 (40)	26 (34.7)	18 (51.4)	0.095‡
Age at diagnosis, y, med (IQR)	36 (27-49)	39 (27-52)	32 (25-49)	0.207¢
Follow-up period, m, med (IQR)	25 (6-63)	30 (9-65)	9 (3-60)	0.068¢
Clinical features, n (%)				
Fever	106 (96.4)	71 (94.7)	35 (100)	0.305†
Typical rash	85 (77.3)	58 (77.3)	27 (77.1)	0.982‡
Pharyngitis	65 (59.1)	46 (61.3)	19 (54.3)	0.484‡
Lymphadenopathy	48 (43.6)	29 (38.7)	19 (54.3)	0.124‡
Arthralgia	90 (81.8)	63 (84)	27 (77.1)	0.385‡
Arthritis	56 (50.9)	37 (49.3)	19 (54.3)	0.628‡
Myalgia	70 (63.6)	45 (60)	25 (71.4)	0.246‡
Splenomegaly	18 (16.4)	12 (16)	6 (17.1)	0.880‡
Hepatomegaly	26 (23.6)	16 (21.3)	10 (28.6)	0.405‡
Pleuritis	11 (10)	3 (4)	8 (22.9)	**0.004**‡
Pericarditis	11 (10)	9 (12)	2 (5.7)	0.497†
Abdominal pain	14 (12.7)	10 (13.3)	4 (11.4)	1.000†
MAS	16 (14.5)	5 (6.7)	11 (31.4)	**0.001**‡
DIC	3 (2.7)	1 (1.3)	2 (5.7)	0.237†
DAH	2 (1.8)	1 (1.3)	1 (2.9)	0.537†
Aseptic meningitis	1 (0.9)	0 (0)	1 (2.9)	0.318†
mPouchet score, med (IQR)	6 (5-7)	6 (5-7)	7 (6-8)	**0.017**¢
Treatment, n (%)				
Pulse MPRD	49 (44.5)	29 (38.7)	20 (57.1)	0.069‡
Corticosteroid	109 (99.1)	74 (98.7)	35 (100)	1.000†
csDMARD	78 (70.9)	57 (76)	21 (60)	0.085‡
bDMARD	45 (40.9)	26 (34.7)	19 (54.3)	0.051‡
Anakinra	40 (26.4)	21 (28)	19 (54.3)	**0.008**‡
IVIG	6 (5.5)	3 (4)	3 (8.6)	0.380†

†Fisher's Exact, ‡Chi-Square, and ¢Mann-Whitney U. Abbreviations: bDMARD, biologic disease modifying anti-rheumatic drug; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; DAH, diffuse alveolar hemorrhage; DIC, disseminated intravascular coagulation; IQR, interquartile range; IVIG, intravenous immunoglobulin; m, months; MAS, macrophage activation syndrome; med, median; MPRD, methylprednisolone; n, number of patients; y, years.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Laboratory parameters of patients at the time of diagnosis.

	All patients (n=110)	PCT<0.5 (n=75)	PCT≥0.5 (n=35)	*p*-value
Creatinine, med (IQR)	0.63 (0.51-0.75)	0.64 (0.48-0.73)	0.61 (0.52-0.83)	0.369¢
Hemoglobin, mean ± SD	10.42 ± 1.82	10.87 ± 1.83	10.6 ±1.83	0.483¥
Anemia, n (%)	85 (77.3)	57 (76)	28 (80)	0.641‡
Platelet, $\times10^3/\mu L$, med (IQR)	338 (243-434)	352 (272-446)	281 (157-385)	**0.008**¢
Thrombocytosis, n (%)	20 (18.2)	16 (21.3)	4 (11.4)	0.210‡
Thrombocytopenia, n (%)	10 (9.1)	3 (4)	7 (20)	**0.011**†
Leukocytosis (≥80% PMNL), n (%)	82 (74.5)	57 (76)	25 (71.4)	0.608‡
WBC, $\times10^3/\mu L$, med (IQR)	14.6 (9.89-19.43)	14.9 (10.10-19.82)	14.1 (9.1-17.48)	0.653¢
Neutrophil, $\times10^3/\mu L$, med (IQR)	11.9 (7.77-16.92)	11.9 (7.4-17.01)	11.9 (8.06-16.2)	0.852¢
Lymphocyte, $\times10^3/\mu L$, med (IQR)	1.41 (1.07-1.92)	1.5 (1.22-2.13)	1.12 (0.8-1.5)	**<0.001**¢
Monocyte, $\times10^3/\mu L$, med (IQR)	0.6 (0.4-0.78)	0.6 (0.4-0.80)	0.5 (0.33-0.7)	0.064¢
Abnormal LFT, n (%)	100 (90.9)	66 (88)	34 (97.1)	0.165†
ALT, U/L, med (IQR)	33 (17-66)	30 (15-71)	34 (19-61)	0.714¢
ALT>ULN, n (%)	44 (40)	30 (40)	14 (40)	1.000‡
AST, U/L, med (IQR)	35 (24-71)	33 (22-53)	51 (28-111)	**0.006**¢
AST>ULN, n (%)	49 (44.5)	27 (36)	22 (62.9)	**0.008**†
LDH, U/L, med (IQR)	383 (302-602)	331 (275-528)	501 (360-913)	**<0.001**¢
LDH>ULN, n (%)	94 (85.5)	61 (81.3)	33 (94.3)	0.073‡
Albumin, mg/dL, mean ± SD	3.36 ± 0.56	3.47 ± 0.55	3.12 ± 0.49	**0.002**¥
Hypoalbuminemia, n (%)	59 (53.6)	34 (45.3)	25 (71.4)	**0.011**‡
CRP, mg/L, med (IQR)	128 (65-217)	118 (65-189)	187 (88-313)	**0.013**¢
ESR, mm/h, med (IQR)	68 (44-83)	70 (48-83)	60 (35-81)	0.218¢
PCT, ng/mL, med (IQR)	0.27 (0.12-0.86)	0.17 (0.09-0.28)	1.93 (0.9-4.94)	**<0.001**¢
Ferritin, ng/mL, med (IQR)	3296 (858-8561)	2000 (657-5500)	8485 (2121-31524)	**<0.001**¢
Ferritin>3000 ng/mL, n (%)	56 (50.9)	30 (40)	26 (74.3)	**0.001**†

†Fisher's Exact, ‡Chi-Square, ¢Mann-Whitney U, and ¥Student's-t test. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; LDH, lactate dehydrogenase; LFT, liver function tests; med, median; n, number of patients; PCT, procalcitonin; PMNL, polymorphonuclear leukocytes; SD, standard deviation; ULN, upper limit of normal; WBC, white blood cell.

Conclusion: According to the results of this preliminary study, the high risk of developing MAS and the requirement of bDMARD are indicative of a high inflammatory response in patients with increased PCT. Our results provide evidence that high PCT in SD is a potential independent predictor of MAS. PCT may be a convincible marker in AIDs like other well-known inflammatory parameters. Further studies are warranted to confirm the study findings in larger cohorts and to explain the mechanism of PCT elevation in AIDs.

Disclosure: E. Bektas: None; **B. Uludogan**: None; **B. Fırlatan Yazgan**: None; **O. Kilinc**: None; **B. Acar**: None; **O. Kizilkaya**: None; **A. Yilmaz**: None; **B. Yuce**: None; **s. Ugurlu**: None; **U. Kalyoncu**: None; **T. Kasifoglu**: None; **C. Bes**: None.

Abstract Number: 0779

Interim Results of a Randomized Placebo Controlled Study of IL-1 Inhibitor Goflikicept in Patients With Familial Mediterranean Fever

Olga Uhanova[1], **Serdal Ugurlu**[2], Mikhail Kostik[3], Tamara Sarkisyan[4], Anna Yeghiazaryan[4], Lidiya Lysenko[5], Vilen Rameev[5], Omer Karadag[6], Valentina Vardanyan[7], Veli Yazisiz[8], Tatiana Sotnikova[9], Vyacheslav Podsvirov[1], Alina Egorova[10], Daria Bukhanova[10], Sergey Grishin[10], Tolga Tuncel[11], Mikhail Samsonov[10] and Ahmet Gul[12], [1]Terafarm LLC, Stavropol, Russia, [2]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [3]Saint-Petersburg State Pediatric Medical University, Saint Petersburg, Russia, [4]Center of Medical Genetics and Primary Health Care LTD, Yerevan, Armenia, [5]Sechenov's 1st State Moscow Medical University, Moscow, Russia, [6]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, [7]Ecosense Diagnostic Center, Yerevan, Armenia, [8]Akdeniz University, Faculty of Medicine, Antalya, Turkey, [9]State Budgetary Institution of Healthcare of Moscow Multispeciality Hospital named after S.P. Botkin of the Moscow City and Sechenov University, Moscow, Russia, [10]R-Pharm JSC, Moscow, Russia, [11]TRpharm, Istanbul, Turkey, [12]Istanbul University, Istanbul Faculty of Medicine, Division of Rheumatology, Istanbul, Istanbul, Turkey

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases (0777–0782)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Goflikicept (GFC; RPH-104) is a novel fusion protein inhibiting interleukin-1 (IL-1). This study aimed to investigate its efficacy and safety in IL-1β-driven monogenic autoinflammatory disorder of Familial Mediterranean Fever (FMF).

Methods: Adult patients with FMF who were resistant or intolerant to colchicine and had ongoing attacks were randomized in the international, multicenter phase 2 double-blinded study to receive GFC subcutaneously in a dose of 160 mg (day 0), 80 mg (day 7), 80 mg (day 14), and 80 mg every 2 weeks (q2w) thereafter or matching injections of placebo for 16 weeks. Marker attack was defined as the combination of Physician Global Assessment (PGA) ≥2 and CRP >10 mg/l. If the marker FMF attack was not resolved or a recurrent attack occurred, the patients were unblinded, and those on placebo switched to GFC. The primary endpoint was a proportion of patients with complete treatment response (marker attack resolution and development of no new attacks).

Results: In total, 28 patients were randomized. Of them, 24 patients completed the study per protocol, 4 patients discontinued treatment prematurely, and 3 of them were in the GFC arm: 1 due to prohibited treatment; 1 due to lack of efficacy; 1 due to an adverse event (AE). The complete response was achieved in 9 (64.3%) patients in the GFC arm and in 1 (7.1%) patient in the placebo arm (p=0.004). No recurrent attack occurred after switching from placebo to GFC in 12 of 13 patients (92%). Minimal or no disease activity (PGA < 2) and CRP decrease ≤10 mg/l were achieved in the majority of patients in the GFC arm but not in the placebo arm (*Fig. 1, Fig. 2*). At least one AE was reported in 11 (78.6%) patients in the GFC arm, in 3 (21.4%) patients in the placebo arm, and in 8 (61.5%) patients who were switched from placebo to GFC. The majority of AEs were mild to moderate in severity. In one patient (switched from placebo to GFC), there was a serious AE of inflammation during the safety follow-up period. In one of the GFC arm patients, diarrhea led to premature treatment discontinuation. GFC treatment was safe and overall well tolerated. Safety profile of GFC was consistent with other IL-1 inhibitors; no new safety signals were reported.

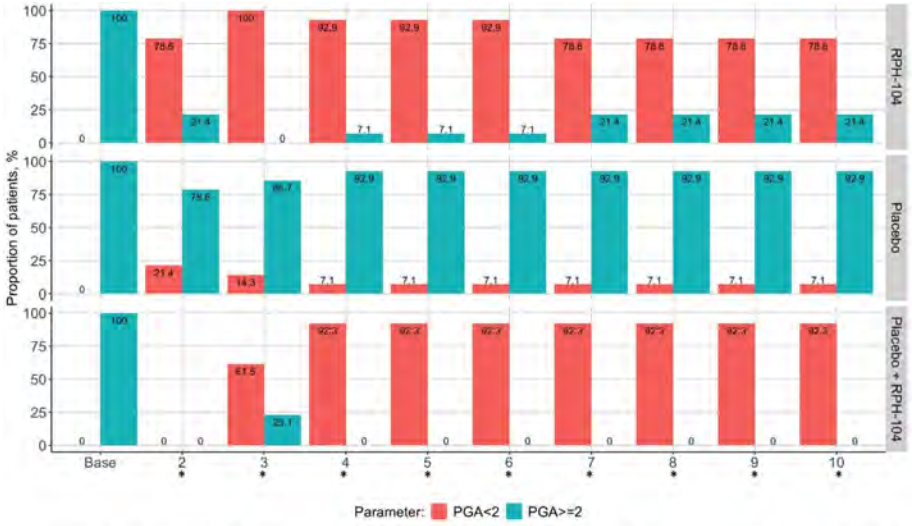


Figure 1. Proportion of subjects with minimal disease activity/ inactive disease (PGA score < 2) during the treatment period

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

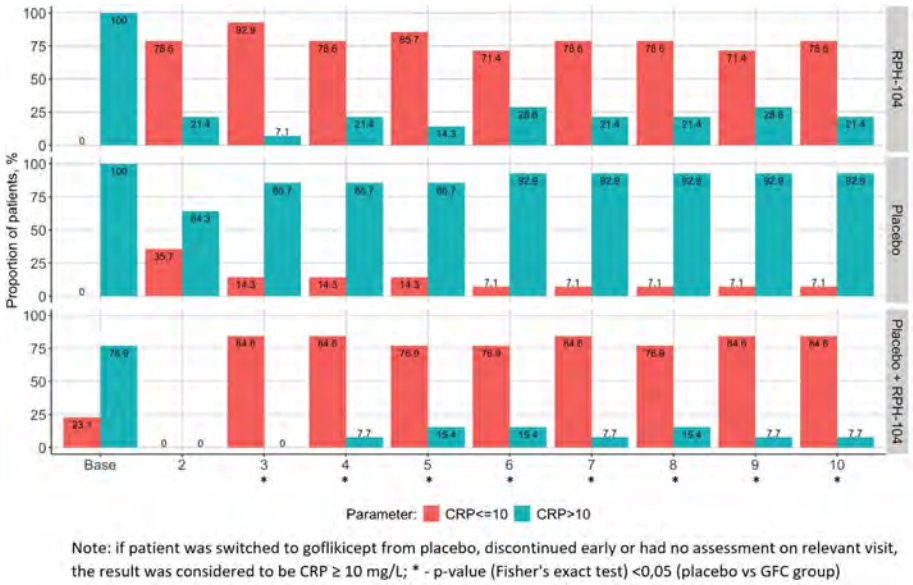


Figure 2. Proportion of subjects with CRP ≤ 10 mg/L during the treatment period

Conclusion: GFC provided a significant improvement in the disease activity of colchicine-refractory/intolerant FMF patients compared to placebo, and its safety profile was similar to other IL-1 inhibitors.

Disclosure: O. Uhanova: None; **s. Ugurlu**: None; **M. Kostik**: None; **T. Sarkisyan**: R-Pharm JSC, 5; **A. Yeghiazaryan**: R-Pharm JSC, 5; **L. Lysenko**: None; **V. Rameev**: None; **O. Karadag**: None; **V. Vardanyan**: None; **V. Yazisiz**: None; **T. Sotnikova**: None; **V. Podsvirov**: None; **A. Egorova**: R-Pharm, JSC, 3; **D. Bukhanova**: R-Pharm, JSC, 3; **S. Grishin**: R-Pharm JSC, 3; **T. Tuncel**: TRpharm, 3; **M. Samsonov**: R-Pharm, JSC, 3; **A. Gul**: None.

Abstract Number: 0780

Baseline Pharmacodynamic Markers and Response to Emapalumab in Children and Adults with Macrophage Activation Syndrome (MAS) in Still's Disease: Results from a Pooled Analysis of Two Prospective Trials

Edward Behrens[1], Sebastiaan Vastert[2], Jordi anton[3], Pierre Quartier[4], Bruno Fautrel[5], Paul Brogan[6], Melissa Elder[7], Francesca Minoia[8], Pavla Dolezalova[9], Robert Biesen[10], Masaki Shimizu[11], Uwe Ullmann[12], Adnan Mahmood[13], Andrew Danquah[12], Elena Burillo[12], Marco Petrimpol[12], Steve Mallett[14], Brian Jamieson[15], Alexiei GROM[16] and Fabrizio De Benedetti[17], [1]CHOP, West Chester, PA, [2]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [3]Hospital Sant Joan de Deu. Universitat de Barcelona, Barcelona, Spain, [4]Hôpital Necker-Enfants Malades, Paris, France, [5]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [6]Great Ormond Street Hospital for Children NHS Foundation Trust and University College London Great Ormond Street Institute of Child Health, London, United Kingdom, [7]College of Medicine and Division of Pediatric Allergy, Immunology, and Rheumatology, Department of Pediatrics, University of Florida, GAINESVILLE, FL, [8]Pediatric Immuno-Rheumatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [9]Paediatric Rheumatology and Autoinflammatory Diseases Unit, General University Hospital, Prague, Czech Republic, [10]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [11]Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, [12]Sobi, Basel, Switzerland, [13]Sobi, Stockholm, Sweden, [14]Sobi, Stock, Sweden, [15]Sobi Inc., Morrisville, NC, [16]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [17]Bambino Gesu Children's Hospital, Rome, Rome, Italy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases (0777–0782)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: MAS is a life-threatening complication of Still's disease, characterized by IFNg-driven macrophage activation and systemic hyperinflammation. Chemokine C-X-C motif ligand 9 (CXCL9) is released in response to IFNg and can be used as a marker of IFNg activity. Emapalumab binds free and receptor-bound IFNg, providing rapid and targeted neutralization of IFNg. Emapalumab achieved rapid control of MAS in a pooled patient population from two open-label, single-arm interventional studies (NI-0501-06 [NCT03311854] and NI-0501-14 [EMERALD; NCT05001737]). Changes in key PD markers in this population were evaluated according to achievement of response and time to response.

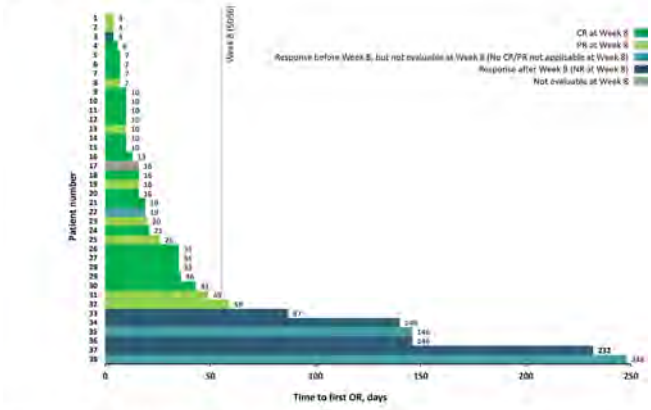
Methods: Patients with MAS in Still's disease who had an inadequate response to high-dose glucocorticoids (GCs), or investigator-assessed rapid worsening of clinical condition and/or laboratory parameters, were treated with emapalumab for 4 weeks: a 6 mg/kg loading dose, followed by 3 mg/kg every 3 days from days 4–16, then 3 mg/kg twice weekly until Day 28 (or longer if insufficient clinical response). The primary efficacy endpoint was complete response (CR) at Week 8, defined as resolution of clinical signs according to investigator assessment (visual analog scale [VAS] ≤1/10 cm) and normalization of 7 MAS-related laboratory parameters. Overall response (OR) was defined as a CR or partial response (PR; VAS < 4 cm and normalization of ≥3 abnormal baseline laboratory parameters included in the composite primary endpoint).

Results: 39 patients were enrolled (31 [79.5%] females; median age, 12 years [range, 9 months–64 years]). At Week 8, 21/39 (53.8%) patients treated with emapalumab achieved a CR (95% confidence interval, 37.2–69.9%) and 29/38 patients (76.3%) had an OR at Week 8.

The median time to first OR was 16 days with 32/39 patients achieving an OR before Week 8 and 6 patients had their first response after Week 8. (**Figure 1**). Once an OR was reached, response was generally maintained through Week 8 and most patients were able to reach CR (**Figure 2**).

Patients with CR (n=20) or PR (n=9) at Week 8 had higher geometric mean levels of CXCL9 (CR, 3206 ng/mL; PR, 2371 ng/mL), ferritin (CR, 8186 µg/mL; PR, 8452 µg/mL) and soluble CD25 (sCD25; CR, 5654 ng/mL; PR, 7436 ng/mL) at baseline versus Week 8 non-responders (n=5) (CXCL9, 291 ng/mL; ferritin, 2633 µg/mL; sCD25, 1531 ng/mL).

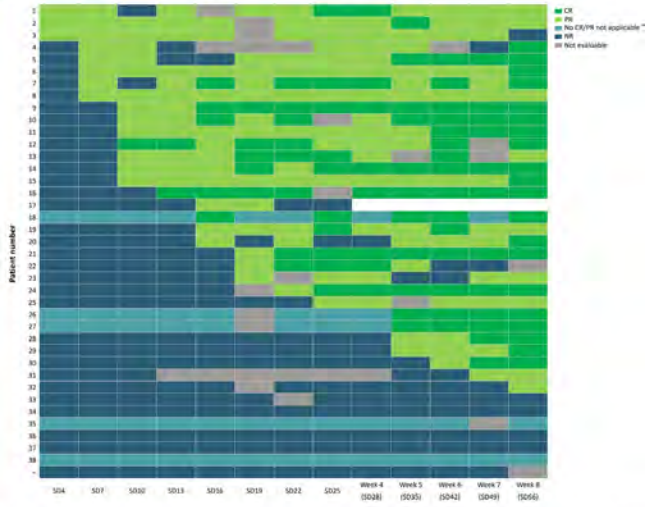
Figure 1. Time to first OR (n=38)



Patient #3 lost PR at Week 8, Patient #17 died before Week 8. CR, complete response; NR, no response; OR, overall response; PR, partial response.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Heatmap of patient-level response to emapalumab in patients with MAS in Still's disease with an inadequate response to glucocorticoids through Week 8



*A PR was not applicable for patients who could not meet the definition of a PR because <3 abnormalities in laboratory parameters were present at baseline. Patient #17 died before Week 8. 84.6% of patients received concomitant biologics alone or in combination, mainly anti-IL-1 (66.6%) and Cyclosporin A (43.6%). CR, complete response; PR, partial response, SD, study day.

All patients had rapid and sustained CXCL9 and ferritin declines over time: at Week 8, CXCL9 and ferritin median percentage reductions from baseline were -99% and -92% in patients with CR or PR, respectively. NR had similar declines in CXCL9 (n=2; -86%) and ferritin (n=5; -89%) at Week 8, though sCD25 remained relatively unchanged vs baseline (n=2; +21%).

Conclusion: Half of the patients with MAS secondary to Still's disease with an inadequate response to high-dose GCs treated with emapalumab achieved a first OR within 16 days and most patients having a sustained treatment effect reaching a CR at Week 8. Emapalumab treatment rapidly reduced key PD markers, including CXCL9 and ferritin, aligning with IFNγ's role in MAS and emapalumab's mechanism of action.

Disclosure: E. Behrens: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **J. anton**: Sobi, 1, 5, 6; **P. Quartier**: AbbVie, 2, 6, Chugai-Roche, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 1, 2, Sobi, 2, 6; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **P. Brogan**: Sobi, 6; **M. Elder**: None; **F. Minoia**: Novartis, 2, 6, Sobi, 2, 6; **P. Dolezalova**: Medac, 6, Novartis, 6, Pfizer, 6, Sobi, 6; **R. Biesen**: None; **M. Shimizu**: Medical and Biological Laboratories Co. Ltd, 5; **U. Ullmann**: Sobi, 2; **A. Mahmood**: Sobi, 2; **A. Danquah**: Sobi, 3; **E. Burillo**: Sobi, 3; **M. Petrimpol**: Sobi, 3; **S. Mallett**: Sobi, 2; **B. Jamieson**: Sobi Inc, 3; **A. GROM**: National Institutes of Health, 5, Novartis, 2, 5, sJIA Foundation, 5, Sobi, 2, 5, Up-To-Date, 9; **F. De Benedetti**: AbbVie, 2, 5, Apollo, 2, 5, Elixiron, 2, 5, Kiniksa, 2, 5, Novartis, 2, 5, Sanofi, 2, 5, Sobi, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0781

Comprehensive mass cytometry analyses of disease-related cells in adult-onset Still's disease

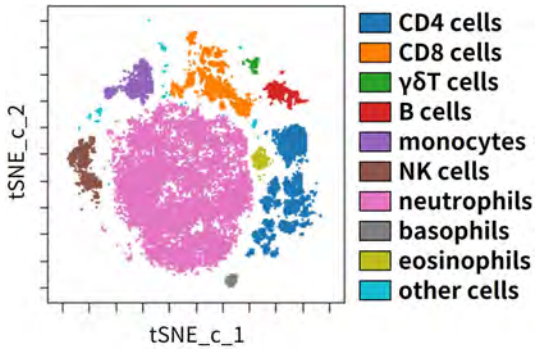
Hiroto Yoshida[1], Mayu Magi[1], Hiroya Tamai[2], Kotaro Matsumoto[2], Keiko Yoshimoto[2], Tetsuhiro Soeda[1] and Yuko Kaneko[2], [1]Chugai Pharmaceutical Co., Ltd. Product Research Dept., Yokohama, Kanagawa, Japan, [2]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases (0777–0782)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Adult-onset Still's Disease (AOSD) is a rare autoinflammatory disorder characterized by high fever, rash, and arthritis. Although overactivation of macrophages, an increase in specific neutrophils, disruption of Th17/Treg cell balance, and decreased NK cell function have been reported in the pathogenesis of AOSD, the detailed roles and interactions of these immune cells in various aspects of the disease pathogenesis remain unclear. This study aimed to identify disease-related cell populations through comprehensive immunophenotyping analysis by mass cytometry.

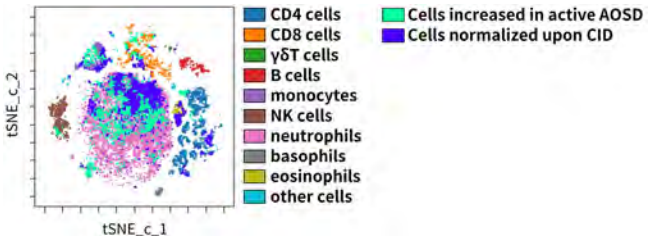
Methods: Mass cytometry of peripheral whole blood was performed using 50 samples from patients with AOSD (six untreated active and forty-four in clinically inactive disease [CID]) and 21 control samples from healthy subjects (HC). Whole blood was stained with Maxpar Direct Immune Profiling Assay from Standard BioTools which contains antibodies of 30 markers and measured by Helios. The data was analyzed in Cytobank from Beckman Coulter. Dimensionality reduction and clustering analysis was performed using tSNE-CUDA and FlowSOM.

Results: The proportions of B cells, NK cells, and gamma delta T cells were significantly decreased in the active AOSD group compared to the HC group. These changes in cell subset proportions were persistent even after achieving CID. For more detailed analysis, we used FlowSOM clustering to divide those cells into 400 clusters. In the active AOSD group, the proportions of 66 clusters were significantly higher compared with the HC group. Among the increased cell clusters, 21 clusters were not different between the CID and HC groups, including CD4 cells, CD8 cells, monocytes, neutrophils, and eosinophils. Based on the expression patterns, the monocytes were characterized as intermediate monocytes with upregulated CD11c and HLA-DR and downregulated CD38. The CD4 cells exhibited features of effector memory cells, characterized by upregulation of CXCR3, CCR4, CD28, CD38, and HLA-DR, along with downregulation of CD27 and CD127. Similarly, the CD8 cells were also classified as effector memory cells, showing upregulation of CXCR3, CD27, CD28, CD38, and HLA-DR, and downregulation of CD57 and CD127.

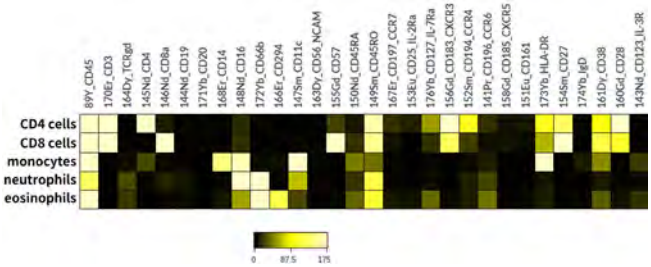


Dimensionality reduction by tSNE-CUDA in mass cytometry data of peripheral blood cells

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Cell subsets increased in untreated active AOSD and normalized upon CID



Heatmap of marker expression in cell subsets normalized upon CID

Conclusion: Comprehensive and detailed mass cytometry analysis of peripheral blood cells from patients with AOSD identified characteristic intermediate monocytes and effector memory T cells were increased in the active phase and normalized after achieving CID. Those cell subsets may play an important role in the pathogenesis of AOSD and can be a new therapeutic target.

Disclosure: H. Yoshida: Chugai Pharmaceutical Co., Ltd., 3; **M. Magi**: Chugai Pharmaceutical Co., Ltd., 3; **H. Tamai**: None; **K. Matsumoto**: None; **K. Yoshimoto**: None; **T. Soeda**: Chugai Pharmaceutical Co., Ltd., 3; **Y. Kaneko**: AbbVie, 2, 5, 6, Asahi Kasei, 2, 5, 6, Astellas Pharma, 6, AstraZeneca, 6, Ayumi, 5, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb, 2, 6, Chugai Pharmaceutical, 5, 6, Daiichi Sankyo, 6, Eisai, 5, 6, Eli Lilly, 2, 6, Gilead Sciences, 2, 5, 6, Glaxo SmithKline, 6, Janssen, 6, Mitsubishi Tanabe Pharma, 5, 6, Novartis, 6, Pfizer, 2, 6, Sanofi, 6, Taisho Pharmaceutical, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0782

Expansion of T bet Age-Associated B Cells Is Associated with Clinical Complications in Stills Disease

Krisztian Csomos[1], Boglarka Ujhazi[1], Mariana Correia Marques[2], Emily Rosenbaum[1] and Michael Ombrello[3], [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, Bethesda, MD, [2]Translational Genetics and Genomics Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), North Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases I: Focus on Auto-Inflammatory Diseases (0777–0782)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Still's disease is a rare and severe autoinflammatory disorder characterized by daily spiking fevers, arthritis, an evanescent rash, and prominent systemic features, including lymphadenopathy, hepatosplenomegaly, serositis, and systemic inflammation mediated primarily by IL-1, IL-6, and IL-18. Still's disease can lead to severe and often fatal

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

complications, such as Still's disease-associated lung disease (Still's-LD). Still's-LD is a chronic and severe pulmonary disorder, particularly observed in patients treated with modern biologic therapies. It is characterized by interstitial lung disease (ILD), pulmonary alveolar proteinosis (PAP), pulmonary arterial hypertension, and chronic respiratory failure. Although extensive innate immune dysregulation, T cell activation, and an IFN--driven inflammatory milieu have been implicated in the pathogenesis of Still's-LD, the immunopathologic basis of the disease remains poorly understood. CD21low T-bet+ atypical or Age-Associated B cells (ABCs) are known to expand under conditions of chronic antigen exposure and inflammation, such as chronic infections (e.g., malaria, HIV) and autoimmune diseases (e.g., systemic lupus erythematosus and rheumatoid arthritis). We aimed to investigate the potential role of ABCs in Still's disease and related clinical complications.

Methods: Single-cell RNA sequencing (scRNA-seq) data of peripheral blood mononuclear cells (PBMCs) of Still's disease patients (n = 21) and healthy individuals (n = 5) were studied in silico to assess B cell composition and characterize ABCs. In parallel, 36-color spectral flow cytometry immunophenotyping was performed on a separate cohort of Still's disease patients (n = 61) and healthy individuals (n = 27) to further evaluate B cell subset distribution, class-switching, activation status, and ABC phenotype.

Results: scRNA-seq analysis revealed an expansion of ABCs in Still's disease patients compared to healthy controls (7.46 +/- 5.58% vs. 3.69 +/- 1.3%), that was more prominent in active vs inactive patients (8.19 +/- 6.09% vs. 5.13 +/- 2.72%). Notably, ABCs were more abundant in patients with Still's disease-associated lung disease (Still's-LD) than in those with active or inactive Still's disease without pulmonary involvement (9.86 +/- 8.45% vs. 5.54 +/- 2.82%). Flow cytometry analysis revealed widespread B cell activation, confirmed the expansion of ABCs across the patient cohort ($p = 0.0049$), and identified a significant correlation between ABC frequency and the presence of lung disease ($p = 0.0066$).

Conclusion: These findings suggest that ABC expansion is associated with Still's disease and correlates with both disease severity and the presence of lung complications. This previously unrecognized association implicates ABCs in the pathogenesis of Still's-LD and indicates that their abundance may serve as a potential biomarker for disease progression and clinical status.

Disclosure: K. Csomos: None; **B. Ujhazi**: None; **M. Correia Marques**: None; **E. Rosenbaum**: None; **M. Ombrello**: None.

Abstract Number: 0784

Physical Activity and Exercise Therapy Reduce the Transition from Acute to Chronic Low Back Pain in the Community

Katlin Harker[1], Rebecca Fillipo[2] and Adam Goode[2], [1]Durham VA, Durham, [2]Duke University, Durham

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation (0783–0788)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Physical activity (PA) and exercise therapy are guideline-supported interventions for chronic LBP, but their influence on the transition from acute to chronic LBP is unclear. This study aimed to determine if baseline self-reported exercise therapy or sufficient PA during the acute LBP phase would prevent a transition to chronic LBP at 3 or 6 months.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Interventions used at baseline and transition to chronic low back pain at 3 and 6 months

	3-months		OR	aOR	6-months		OR	aOR
Chronic LBP	Yes (n=38)	No (n=80)			Yes (n=31)	No (n=80)		
NSAIDS	30 (79.0%)	62 (77.5%)	1.06 (0.55, 2.02)	1.12 (0.58, 2.16)	23 (74.2%)	62 (77.5%)	0.84 (0.43, 1.73)	0.90 (0.48, 1.76)
Muscle Relaxers	7 (18.4%)	13 (16.3%)	1.12 (0.57, 2.15)	1.09 (0.57, 2.10)	5 (16.1%)	12 (15.0%)	1.09 (0.35, 3.40)	1.14 (0.36, 3.59)
Opioids	2 (5.3%)	6 (7.5%)	0.77 (0.22, 2.61)	0.65 (0.18, 2.34)	2 (6.5%)	6 (7.5%)	0.85 (0.16, 4.56)	0.81 (0.15, 4.35)
Injections	3 (7.9%)	2 (2.5%)	1.94 (0.90, 4.17)	1.58 (0.70, 3.57)	2 (6.5%)	2 (2.5%)	2.68 (0.56, 20.0)	2.61 (0.54, 20.2)
Exercise Therapy	9 (23.7%)	36 (45.0%)	**0.51 (0.27, 0.99)**	**0.45 (0.25, 0.92)**	9 (29.0%)	33 (45.8%)	0.64 (0.33, 1.27)	0.57 (0.28, 1.16)
Manipulation or Chiropractic	4 (10.5%)	17 (21.3%)	0.54 (0.22, 1.47)	0.55 (0.22, 1.39)	6 (19.4%)	14 (17.5%)	1.13 (0.39, 3.27)	1.23 (0.42, 3.70)
CBT	2 (5.3%)	3 (3.8%)	1.39 (0.57, 4.38)	1.48 (0.52, 4.18)	1 (3.2%)	3 (3.8%)	0.84 (0.09, 8.25)	0.69 (0.09, 9.06)

OR=odds ratio
aOR= adjusted odds ratio, adjusted for age, sex, race, and comorbidities
NSAIDS= non-steroidal anti-inflammatory drugs
CBT= cognitive behavioral therapy

Methods: Participants were recruited from Durham and Kannapolis, NC communities from February to November 2022 and followed at 3 and 6 months. Participants were nonpregnant adults aged 18+ with acute LBP (< 4 weeks before screening and ≥30 days without LBP before acute onset) without systemic inflammatory or autoimmune conditions, non-skin cancer, lumbar spine surgery, low back trauma, congenital/acquired spinal defects. Baseline PA was measured via the Exercise Vital Signs (EVS) tool and dichotomized into sufficiently active (≥150 minutes of moderate to vigorous PA) versus not. Baseline interventions were captured as yes/no from the NIH LBP Task Force Measure. Comorbidities were measured with the Charlson Comorbidity Index. Chronic LBP was defined as pain most/every day over the past 3 months, and high impact chronic LBP as pain limiting daily work or activities most/every day. Descriptive statistics (counts, proportions, means ± SD), t-tests, or Fisher's exact tests were used for comparisons across groups. Multiple binary logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI) adjusted for age, sex, ethnicity, race, and comorbidities.

Results: We enrolled 131 participants with a transition from acute to chronic LBP of 32.2% (38/118) at 3 months and 27.9% (31/111) at 6 months. Most were female sex at birth (58.8%) with a mean age of 56.9 (SD= 13.8; range 19 to 81 years). 22.9% identified as Black/African American and 67.9% as White; 6.1% reported Hispanic ethnicity. At baseline, 39% (n=51) reported exercise therapy and 33% (n=42) were sufficiently active. These groups differed significantly (p=0.03).

Mean baseline EVS was 125.1 minutes (limits 9, 750; median 90.0). Those who transitioned to chronic LBP had a lower mean EVS (96.9 min; range 0, 350; median 85) than those who did not (139.6 min; range 0, 750; median 100), p=0.09. Participants insufficiently active at baseline (n=6, 75% vs n=0, 0.0%, exact p< 0.001) and with lower mean exercise time (37.5 ± 29.9 SD vs 122.9 ± 21.6 SD; p=0.04) were more likely to transition to high impact chronic LBP at 6 months; no differences were found at 3 months. Participants using exercise therapy were 49% less likely to transition to chronic LBP (OR=0.51, 95% CI 0.27, 0.99), and the effect strengthened when adjusted for age, sex, race, and comorbidities (0.48, 95% CI 0.25, 0.92). No other intervention showed a significant association (see table).

Conclusion: This longitudinal study is the first to examine PA and exercise therapy in the transition from acute to chronic LBP in the community. Findings suggest strong clinical utility for exercise therapy in risk reduction of chronic LBP at 3 months, and PA may help prevent high impact chronic LBP at 6 months.

Disclosure: K. Harker: None; **R. Fillipo**: None; **A. Goode**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0785

It Takes a Community: Exploring the Importance of Community-Level Social Determinants of Health in Total Knee Arthroplasty Outcomes

Chloe Heiting[1], Yiyuan Wu[2], Susan Goodman[3], Peter Sculco[4], Fei Wang[2], Rich Caruana[5], Peter Cram[6], Said Ibrahim[7] and Bella Mehta[8], [1]Northwell Health, New Hyde Park, NY, [2]Weill Cornell Medicine, New York, NY, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [4]Hospital for Special Surgery, New York, NY, [5]Microsoft, Redmond, WA, [6]University of Maryland School of Medicine, Baltimore, MD, [7]Thomas Jefferson University, Philadelphia, PA, [8]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation (0783–0788)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Despite changing trends and increased utilization of total knee arthroplasty (TKA) in the United States,[1] there are still prominent racial and ethnic disparities in utilization and outcomes. This highlights the importance of exploring the social determinants of health (SDOH) that may play a role in disparities in TKA outcomes, especially as postoperative complications are of paramount concern in patient and provider consideration of TKA. We aimed to utilize prediction modeling to elucidate the relationship between adverse total knee arthroplasty outcomes – including 90-day readmission, 90-day mortality, 1-year revision, and length of stay (LOS) – and multiple community-level SDOH.

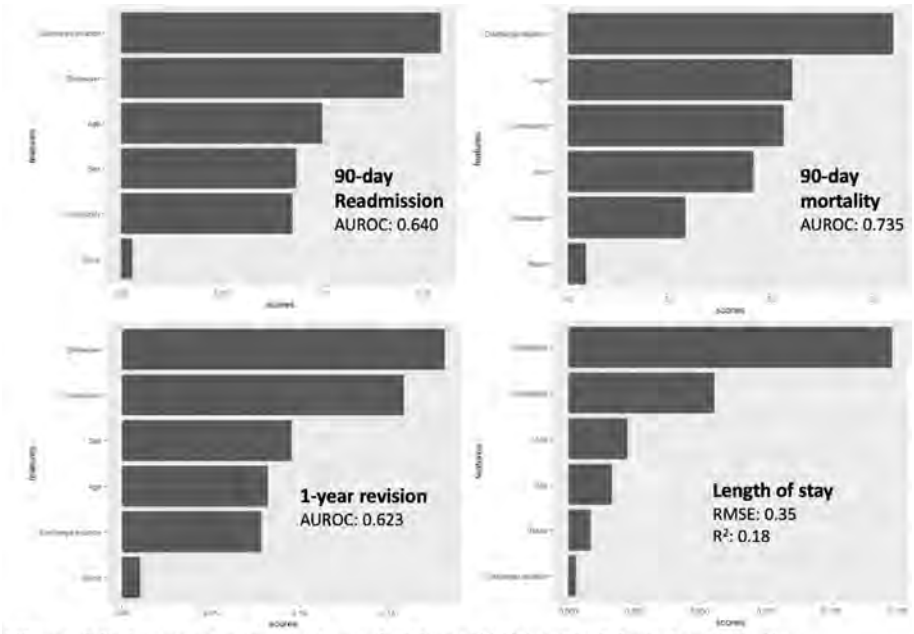
Methods: Patients who underwent TKA between 2012-2018 were identified from the Pennsylvania Health Care Cost Containment Council Database by ICD codes. Census-tract level community factors were extracted from the US census via geocoding. These SDOH variables included internet access, percent of unpaid family worker, with computer access, percent with no computer access, percent of having high school and above education, percent of having college and above education, national walking index, median income, living alone, total foreign born and percent of speak other language than English. This retrospective cohort study used explainable boosting machine (EBM), a modern form of generalized additive model (GAM), to predict 90-day readmission, 90-day mortality, and 1-year revision, and LOS. Area under the receiver operating curve (AUROC) and root mean squared error (RMSE) were used as evaluation metrics. Models were trained and tested using random train and test split and cross validation techniques to reduce overfitting and ensure robustness.

Table 1. Patient-level characteristics by outcome

Variable	90-day readmission			90-day mortality			Revision		
	No (n=198896)	Yes (n=16518)	p-value	No (n=214917)	Yes (n=497)	p-value	No (n=213694)	Yes (n=1720)	p-value
Age	66.0 [60.0, 73.0]	69.0 [62.0, 77.0]	***	66.0 [60.0, 73.0]	75.0 [66.0, 81.0]	***	66.0 [60.0, 73.0]	64.0 [56.0, 71.0]	***
Sex			***			***			***
Female	124001 (62.3%)	9764 (59.1%)		133522 (62.1%)	243 (48.9%)		132817 (62.2%)	948 (55.1%)	
Male	74895 (37.7%)	6754 (40.9%)		81395 (37.9%)	254 (51.1%)		80877 (37.8%)	772 (44.9%)	
Race			***			*			**
White	179605 (90.4%)	14608 (88.5%)		193777 (90.3%)	436 (87.7%)		192695 (90.3%)	1518 (88.5%)	
Other	19060 (9.59%)	1893 (11.5%)		20892 (9.73%)	61 (12.3%)		20756 (9.72%)	197 (11.5%)	
Length of stay	2.00 [2.00, 3.00]	3.00 [2.00, 3.00]	***	2.00 [2.00, 3.00]	3.00 [2.00, 4.00]	***	2 [2.00, 3.00]	3.00 [2.00, 3.00]	***
Elixhauser comorbidity index	0.00 [0.00, 2.00]	1.00 [0.00, 3.00]	***	0.00 [0.00, 2.00]	1.00 [0.00, 3.00]	***	0.00 [0.00, 2.00]	1.00 [0.00, 3.00]	***

Categorical variables N (%). Continuous variables median [IQR].
*p-value < 0.05. ** p-value < 0.01. *** p-value < 0.001. p-value calculated with Chi-squared test, Fisher's exact test, and Wilcoxon rank sum test. p-values compare groups with and without the outcome for each variable.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



* "Community" is the aggregate mean absolute score for % householder living alone, % foreign born, % speaking language other than English, % with computer access, % with internet access, national walkability index, % not in labor force without insurance, % above high school, % above college, % with unpaid family workers, and median household income. These variables were extracted from American Community Survey or calculated by the National Walkability Index software from patient zip code.

Figure 1. Variable importance plots in the prediction of total knee arthroplasty outcomes*

Results: We identified 215,414 patients undergoing TKA between 2012-2018 (Table 1). Model predictive performance was highest for mortality (AUROC=0.74), and was moderate for readmission (AUROC=0.64), revision (AUROC=0.62), and LOS (RMSE=0.35, R^2=0.2) (Figure 1). Community factors were among the top five predictors of mortality, revision, and LOS.

For readmission, the top 3 predictors were discharge location, comorbidities, and age (mean absolute scores = 0.16, 0.14, 0.10, respectively). For mortality, they were discharge location, community factors, and age (mean absolute scores = 0.31, 0.21, 0.21, respectively). The top 3 predictors of revision were comorbidities, community factors, gender (mean absolute scores = 0.18, 0.16, 0.09, respectively). Lastly, the top predictors for LOS were comorbidities, community factors, and age (mean absolute scores = 0.12, 0.05, 0.02, respectively).

Conclusion: In the prediction of 90-day readmission, 90-day mortality, 1-year revision, and LOS after TKA, community factors were more important than race in each of our examined models. This study provides additional nuance to the racial disparities within TKA outcomes and may suggest that community-level factors should also be considered and addressed to improve adverse TKA outcomes.

1. Ravi B et al. The changing demographics of total joint arthroplasty recipients in the United States and Ontario from 2001 to 2007. PMID:23218428

Disclosure: C. Heiting: None; **Y. Wu**: None; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2; **P. Sculco**: BetterPT, 8, Enovis, 2, 9, HS2, LLC, 8, HSS ASC Development Network, LLC, 8, Intellijoint Surgical, Inc, 8, Joint Effort Administrative Services Organization, 8, Osgenic, 1, 8, Parvizi Surgical Innovation, LLC, 8, Zimmer Biomet, 2, 5, 9; **F. Wang**: None; **R. Caruana**: None; **P. Cram**: None; **S. Ibrahim**: None; **B. Mehta**: Amgen, 1, Horizon, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0786

A Machine Learning Approach to Understand Age as a Risk Factor for Complications After Total Hip Arthroplasty

Chloe Heiting[1], Yiyuan Wu[2], Susan Goodman[3], Peter Sculco[4], Fei Wang[2], Rich Caruana[5], Peter Cram[6], Said Ibrahim[7] and Bella Mehta[8], [1]Northwell Health, New Hyde Park, NY, [2]Weill Cornell Medicine, New York, NY, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [4]Hospital for Special Surgery, New York, NY, [5]Microsoft, Redmond, WA, [6]University of Maryland School of Medicine, Baltimore, MD, [7]Thomas Jefferson University, Philadelphia, PA, [8]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation (0783–0788)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Utilization of total hip arthroplasty (THA) has grown rapidly in the United States and worldwide. Postoperative complications and patient risk is of great consideration by patients and clinicians. The risk associated with patient-level factors such as age has traditionally been examined using regression models, yet these models lack nuance necessary for detailed risk quantification. We aimed to examine the effect of age as a risk factor for adverse THA outcome through the application of modern machine learning algorithms.

Methods: Patients undergoing THA from 2012-2018 were identified from the Pennsylvania Cost Containment Database using ICD codes and included in the analysis. Patient-level covariates (demographics, discharge location, admission source, insurance, comorbidities) were extracted. Age was examined as a risk factor for the binary outcomes 90-day readmission, 90-day mortality, and 1-year revision as well as the continuous outcome length of stay (LOS) using an explainable boosting machine (EBM). EBMs are a form of generalized additive models characterized by high accuracy and full interpretability, mitigating effects for collinearity and allowing for automatic interaction detection. The predictive performance of the EBM model was described by area under the receiver operating curve (AUROC) for binary outcomes and root mean square error (RMSE) for continuous outcomes. The marginal relationship of age on adverse outcomes was characterized by partial dependency plots.

Results: We analyzed a cohort of 105,336 patients. The median age was 65.0 years, and most patients were White (90.1%), Medicare-insured (51.6%), and discharged home or to health home care (78.1%) (Table 1). The incidence of 90-day readmission was 8.00%, 90-day mortality was 0.29%, and 1-year revision was 1.54%. The EBM prediction model

Table 1. Patient level characteristics by outcome

Variable	Cohort	90-day readmission			90-day mortality			Revision		
	N=105336	No (n=96914)	Yes (n=8422)	p-value	No (n=105027)	Yes (n=309)	p-value	No (n=103719)	Yes (n=1617)	p-value
Age	65.0 [58.0, 73.0]	65.0 [58.0, 73.0]	69.0 [60.0, 77.0]	***	65.0 [58.0, 73.0]	77.0 [67.0, 84.0]	***	65.0 [58.0, 73.0]	65.0 [58.0, 74.0]	
Sex				*						***
Female	56977 (54.1%)	52330 (54.0%)	4647 (55.2%)		56826 (54.1%)	151 (48.9%)		56046 (54.0%)	931 (57.6%)	
Male	48359 (45.9%)	44584 (46.0%)	3775 (44.8%)		48201 (45.9%)	158 (51.1%)		47673 (46.0%)	686 (42.4%)	
Race				***						
White	95158 (90.3%)	87619 (90.4%)	7539 (89.5%)		94874 (90.3%)	284 (91.9%)		93695 (90.3%)	1463 (90.5%)	
Other	10096 (9.58%)	9218 (9.51%)	878 (10.43%)		10071 (9.58%)	25 (8.10%)		9943 (9.59%)	153 (9.46%)	
Length of stay	2.00 [1.00, 3.00]	2.00 [1.00, 3.00]	3.00 [2.00, 3.00]	***	2.00 [1.00, 3.00]	3.00 [2.00, 4.00]	***	2 [1.00, 3.00]	2.00 [2.00, 3.00]	***
Elixhauser comorbidity index	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]	1.00 [0.00, 3.00]	***	0.00 [0.00, 2.00]	1.00 [0.00, 3.00]	***	0.00 [0.00, 2.00]	1.00 [0.00, 3.00]	***

Categorical variables N (%). Continuous variables median [IQR].
*p-value < 0.05. ** p-value < 0.01. *** p-value < 0.001. p-value calculated with Chi-squared test, Fisher's exact test, and Wilcoxon rank sum test. p-values compare groups with and without the outcome for each variable.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

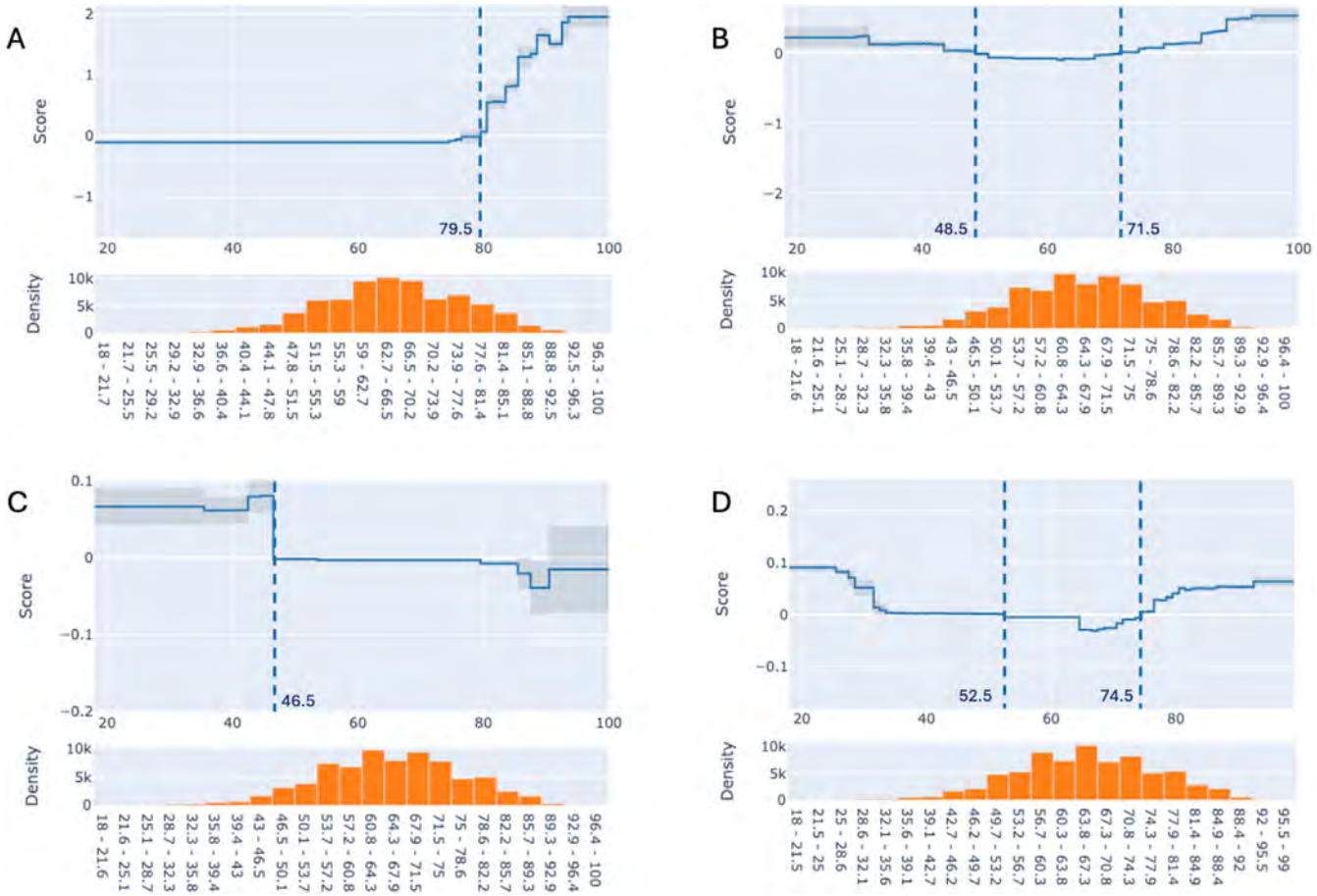


Figure 1. Partial dependency plots illustrating the marginal effect of age (years) on (A) 90-day mortality, (B) 90-day readmission, (C) 1-year revision, and (D) length of stay from the supervised explainable boosting machine models. Y-axis score in log scale. Vertical lines demonstrate where risk score is equal to 0, and show the average contribution of age to risk.

yielded highest prediction for mortality (AUROC=0.80), followed by readmission (0.68), revision (AUROC=0.60), and LOS (RMSE=0.41, R^2=0.19). Of the examined patient-level demographics and covariates, age was identified as one of the most important factors in the prediction of each adverse outcome. 90-day mortality risk increased at 79.5 years, and again dramatically at 80.5 years. Conversely, risk of revision decreased at the age of 46.5 years, whereas risk of readmission decreased at 48.5 years but increased at 71.5 years. LOS risk decreased at 52.5 years and increased at 74.5 years (Figure 1).

Conclusion: Despite decreased rates of postoperative complications in THA, age remains a prominent risk factor for consideration in clinical decision making. Modern machine learning analysis demonstrated that the relationship between age and adverse THA outcomes is nonlinear, and risk for each outcome changes drastically at different ages. This finding provides a deeper and more nuanced model compared to logistic regression, which traditionally describe fixed changes in risk with age. This study can support personalized decision-making for patients and physicians in THA.

Disclosure: C. Heiting: None; **Y. Wu**: None; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2; **P. Sculco**: BetterPT, 8, Enovis, 2, 9, HS2, LLC, 8, HSS ASC Development Network, LLC, 8, Intellijoint Surgical, Inc, 8, Joint Effort Administrative Services Organization, 8, Osgenic, 1, 8, Parvizi Surgical Innovation, LLC, 8, Zimmer Biomet, 2, 5, 9; **F. Wang**: None; **R. Caruana**: None; **P. Cram**: None; **S. Ibrahim**: None; **B. Mehta**: Amgen, 1, Horizon, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0787

The Cost-effectiveness of Physical Therapy for Patients with Meniscal Tear and Osteoarthritis

Samantha Chin[1], **Sasha Aronson**[1], Jamie Collins[1], Faith Selzer[1], Ying Heidi Yang[1], Leslie Bisson[2], Antonia Chen[3], Morgan Jones[4], Clare Norton[1], Karen Smith[1], Kurt Spindler[5], Jeffrey Katz[6] and Elena Losina[7], [1]Brigham and Women's Hospital, Boston, MA, [2]University of Buffalo, Buffalo, [3]Brigham and Women's Hospital, Newton, MA, [4]Mass General Brigham, Boston, [5]Cleveland Clinic, Cleveland, [6]Brigham and Women's Hospital, Brookline, MA, [7]BWH, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation (0783–0788)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Based on several RCTs comparing outcomes of arthroscopic partial meniscectomy (APM) to non-operative management in persons with meniscal tears and OA, physical therapy (PT) is now considered the first line treatment. The TeMPO (Treatment of Meniscal Tears in Patients with Osteoarthritis) trial established that an in-clinic PT program with home exercise component led to a small incremental pain reduction at 6 and 12 months compared to home exercise alone. We sought to determine the cost-effectiveness of PT with home exercise compared to home exercise alone using data from the TeMPO trial.

Methods: We used the Osteoarthritis Policy (OAPol) Model, a widely published and validated microsimulation of knee OA, to compare two strategies: 1) home-based exercise (HE) vs. 2) Physical Therapy focused on strengthening (PT) plus HE. The 5-year outcomes included quality-adjusted life expectancy and costs. Patients in both strategies could subsequently transition to APM, corticosteroid injections, opioids, total knee replacement (TKR), and revision TKR, if the initial treatment did not lead to meaningful pain relief. We modeled pain trajectories at baseline, 3, 6, and 12 months based on strategy-specific data from TeMPO (HE: 47, 29, 28 and 24 vs. PT: 45, 26, 22, 20 points, on a scale 0-100, 0 being no pain). We also derived APM, 1-year TKR, and opioid utilization from the overall TeMPO cohort, due to negligible observed difference across arms (11% had APM, 1% had TKR, 2% used opioids). We derived 5-year TKR utilization from the non-operative arm in the MeTeOR trial, which followed patients with meniscal tear and concomitant OA over 5 years (TKR use $\sim$ 4% over 5 years). The cost of the home exercise regimen included analgesic medications, home exercise guides and materials ($213). In addition to these costs, the cost of the PT regimen included exercise bands, pamphlets, reminder texts, and evaluation and treatment visits ($1,540).

We conducted the analysis for a cohort with mean age 59, KOOS pain 46 (0-100, 100 worst), and mean BMI 30 kg/m^2. We calculated incremental cost-effectiveness ratios (ICERs) as the difference in lifetime costs (2024 USD) divided by the difference in quality-adjusted life years (QALYs) between two strategies. We used a health care perspective and discounted clinical benefits and costs at 3% annually. We conducted sensitivity analyses to determine how uncertainty in input parameters might affect our findings.

Table 1. Clinical benefits, costs, and incremental cost-effectiveness ratios for PT compared to home exercise in patients with knee OA and meniscal tear

Strategy	QALYS	Cost	ICER ($/QALY)
Home exercise	3.290	$38,994	
Home exercise + PT	3.315	$40,330	$53,800

PT = physical therapy, OA = knee osteoarthritis, QALY = Quality Adjusted Life Year, ICER = Incremental Cost-Effectiveness Ratio. ICERs rounded to the nearest 100.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Adding PT increased the 5-year quality-adjusted life expectancy by 0.03 QALYs at the additional cost of $1,300/person, resulting in an estimated ICER for PT of $53,800/QALY (Table 1). The two parameters with the largest effect on the ICER were the difference in pain efficacy between the two regimens and the starting pain of the cohort. When the difference in pain efficacy decreased by 50%, the ICER for PT increased to $142,500/QALY. If starting pain would be reduced by about 25%, the ICER would increase to $72,700/QALY.

Conclusion: Despite relatively small incremental clinical benefits, physical therapy with the home exercise component could be a cost-effective strategy at any cost-effectiveness threshold exceeding $53,800/QALY.

Disclosure: S. Chin: None; **S. Aronson**: None; **J. Collins**: None; **F. Selzer**: None; **Y. Yang**: None; **L. Bisson**: None; **A. Chen**: AAHKS, 4, Avanos, 2, BICMD, 2, Convatec, 2, Ethicon, 2, Heraeus, 2, Hyalex, 11, IlluminOss, 11, IrriMax, 2, Journal of Bone and Joint Surgery, 1, Osteal Therapeutics, 2, 11, Peptilogics, 2, Regeneron, 2, Solenic, 2, 11, Sonoran, 11, Stryker, 2, 9, Taylor & Francis Group, 9, TrialSpark, 2; **M. Jones**: Grunenthal, 1, Pacira, 5; **C. Norton**: AstraZeneca, 12, Merck/MSD, 12,; **K. Smith**: None; **K. Spindler**: Flexion Therapeutics, 2, NFL, 2, Novo Pedics, 2, 12, Honoraria, PRO-T, 9, Summit Surgical, 12, Education Payments; **J. Katz**: Biosplice, 5; **E. Losina**: None.

Abstract Number: 0788

Spatiotemporal Gait Differences Between Fallers and Non-Fallers in People with Knee Osteoarthritis

Joy Itodo, Steven Garcia, Oiza Peters, Ogundoyin Ogundiran and Kharma Foucher, UNIVERSITY OF ILLINOIS, CHICAGO, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation (0783–0788)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: People with knee osteoarthritis (OA) have higher fall rates than their age-matched peers. Studies in another at-risk group, healthy older adults, have linked fall risk to shorter step lengths, narrower stride width, and slower walking speed. These spatiotemporal gait characteristics are also affected by knee OA, but it remains unclear whether they differ between those with a history of falls and those without. Therefore, we tested the hypothesis that spatiotemporal gait characteristics would differ between fallers and non-fallers with knee OA. We also investigated the potential influence of pain catastrophizing and physical activity as representative psychological and behavioral variables that may either influence or be influenced by a history of falls.

Table 1. Spatiotemporal gait characteristics during level treadmill walking at self-selected speeds for fallers (N = 12) and nonfallers (N = 24) with knee OA.

	Fallers	NonFallers	p value	Effect size (Cohen's d)
Walking Speed (m/s)	0.591 ± 0.206	0.512 ± 0.174	0.236	0.427
Step Length (m/height in m)	0.238 ± 0.074	0.193 ± 0.049	**0.039***	0.760
Step Width (m/height in m)	0.092 ± 0.025	0.114 ± 0.027	**0.025***	0.831
Cadence (steps/min)	99.397 ± 15.518	90.227 ± 11.448	**0.052***	0.711
Double Limb Support Time	0.486 ± 0.134	0.571 ± 0.132	0.079	0.639

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

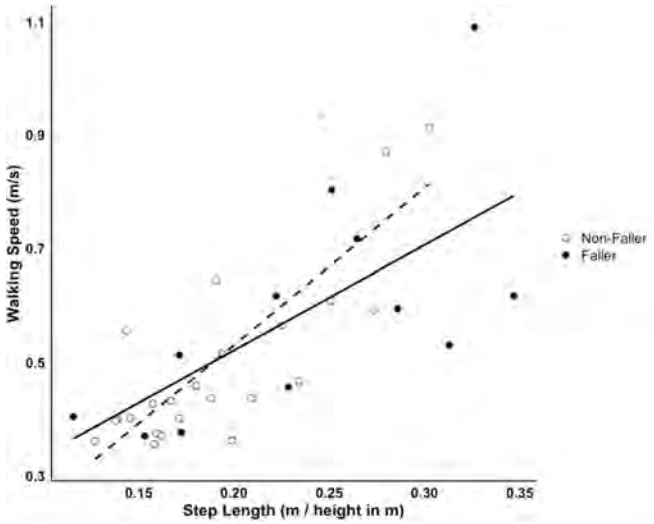


Figure 1: Association between normalized step length and walking among fallers and non-fallers with knee osteoarthritis.

Methods: We categorized 22 women and 14 men with knee OA (age 57 ± 9 years) into fallers and non-fallers based on the question: "Have you experienced a fall in the past 12 months?" Gait data were collected during walking trials on an instrumented split-belt treadmill at each participant's preferred speed. Spatiotemporal variables included walking speed, step length and step width normalized to height, cadence, and double limb support time. Surveys were completed prior to testing, and we used the KOOS pain sub-score, the Pain Catastrophizing Scale, and the UCLA activity score for this analysis. We used independent T-Tests to compare variables between fallers and non-fallers, and linear regression, controlling body mass, for further analyses.

Results: Twelve participants (33%) were classified as fallers. Although walking speeds were similar between the groups (Table 1), fallers walked with significantly shorter steps and higher cadences than non-fallers. Fallers also had significantly narrower step widths. A regression model in which walking speed was the independent variable and step length, cadence, fall status, and fall interaction terms were the dependent variables, showed that the association between step length and speed differed by fall status. Additional models demonstrated that higher UCLA scores were associated with longer step lengths ($p=0.054$) and faster walking speeds ($p = 0.005$), and lower double limb support times ($p < 0.000$). Higher pain catastrophizing was associated with lower cadence in fallers ($p = 0.052$).

Conclusion: Gait patterns differ between fallers and non-fallers with knee OA, with fallers taking shorter, narrower, and more frequent steps, despite similar speeds. While this strategy may help maintain pace, it may come at the cost of balance and stability. Narrower step width is especially concerning as it reduces the base of support during walking. Psychological and behavioral factors had a complex relationship with fall history. For example, higher physical activity levels were associated with both more favorable and less stable gait attributes. Taken together, these results suggest that addressing modifiable psychological and behavioral factors in conjunction with gait biomechanics may be important for improving function and reducing fall risk in this population.

Disclosure: J. Itodo: None; **S. Garcia**: None; **O. Peters**: None; **O. Ogundiran**: None; **K. Foucher**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0789

Short Form 36 (SF-36) Health Survey Questionnaire in Health-Related Quality of Life Assessment in Patients with Inflammatory Myopathies

Almurtada Razok[1], Jasmin Taylor[2], Ethan Ritz[3], Kristin Wipfler[4], Kaleb Michaud[5] and Didem Saygin[6], [1]John H Stroger Jr Hospital of Cook County, Chicago, IL, [2]Rush Medical College, Chicago, IL, [3]Rush Research Informatics Core, Rush University Medical Center, Chicago, IL, [4]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [5]University of Nebraska Medical Center, Omaha, NE, [6]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (0789–0794)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Patients with idiopathic inflammatory myopathies (IIM) experience significant impairment in their health-related quality of life (QoL); however, there are currently no validated measures to assess QoL in these patients. This study aims to examine the measurement properties of short form (SF)-36 in QoL assessment of adults with IIM.

Methods: FORWARD is a U.S.-based databank collecting biannual patient-reported data on rheumatic diseases, including sociodemographics, health-care utilization and forms related to patients' symptoms and experiences including patient global disease activity (visual analog scale [VAS]), pain (VAS), fatigue (VAS), physical functioning (Health Assessment Questionnaire [HAQ-II]), health satisfaction and quality of life (SF-36). SF-36 produces physical (PCS) and mental (MCS) component scores, ranging 0-100 with higher scores indicating a better QoL. Floor and ceiling effects were calculated based on the proportion of patients who have the lowest and the highest possible SF-36 score, respectively. Discriminant validity was assessed by comparing the median subgroups of patients using t test. Construct validity was assessed by Pearson correlation between the SF-36 and other relevant outcome variables based on a priori hypotheses. Adequate validity was defined as ≥70% agreement between the results and a priori hypotheses. Responsiveness was assessed using linear mixed models to examine the relationship between change in SF-36 and other outcome variables over time.

Results: A total of 168 patients with IIM were included (77.3% female, 78.5% White), with an average (± standard deviation [SD]) age of 54.3 (±13.8). No floor or ceiling effect was observed for SF-36 PCS and MCS. SF-36 PCS was significantly different between median groups with low vs high physical functioning, disease activity, fatigue and pain, while MCS was significantly different between patients with and without depression and anxiety, and low vs high fatigue and pain levels (Table 1). Over 90% of a priori hypotheses for construct validity were met (Table 2). SF-36 PCS and MCS had moderate to strong correlations with pain, fatigue, physical function, disease activity, and health satisfaction. Longitudinal changes in SF-36 were significantly associated with changes in in pain, fatigue, patient global disease activity, and physical functioning (Table 3).

Table 1. Discriminant validity assessment with comparison of SF-36 PCS and MCS across median groups of patients with IIM.

Groups	SF-36 PCS		Groups	SF-36 MCS	
	Mean (SD)	p value		Mean (SD)	p value
HAQ-II <1	44.4 (8.9)	<0.0001	Depression	36.8 (11.3)	<0.0001
HAQ-II ≥1	29.2 (7.5)		No depression	51.3 (9.7)	
Patient global <3.5	43.1 (9.9)	<0.0001	Anxiety	36.1 (11.1)	<0.0001
Patient global ≥3.5	30.2 (8.3)		No anxiety	50.2 (10.4)	
Fatigue <4.5	42.8 (9.9)	<0.0001	Fatigue <5	52.0 (9.7)	<0.0001
Fatigue ≥4.5	29.9 (7.9)		Fatigue ≥5	42.2 (12.2)	
Pain <2.5	42.5 (10.4)	<0.0001	Pain <5	52.0 (9.3)	<0.0001
Pain ≥2.5	31.9 (9.3)		Pain ≥5	43.4 (12.3)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Construct validity assessment with a priori and observed correlations between SF-36 PCS and MCS and other outcome variables.

Variables	SF-36 PCS			SF-36 MCS		
	A priori hypotheses	r	Met?	A priori hypotheses	r	Met?
Symptom duration	Weak	-0.05	Yes	Weak	0.11	Yes
Age	Weak	0.12	Yes	Weak	0.21	Yes
Body mass index	Weak	-0.25	Yes	Weak	-0.01	Yes
Education level	Weak	0.17	Yes	Weak	0.21	Yes
Annual income	Weak	0.24	Yes	Weak	0.28	Yes
Pain level	Moderate	-0.56	Yes	Moderate	-0.43	Yes
Fatigue level	Moderate	-0.66	Yes	Moderate	-0.49	Yes
Patient global disease activity	Moderate	-0.66	Yes	Moderate	-0.43	Yes
HAQ-II	Strong	-0.79	Yes	Moderate	-0.30	Yes
Rheumatic disease comorbidity index	Moderate	-0.27	No	Moderate	-0.27	No
Health satisfaction	Moderate	0.66	Yes	Moderate	0.42	Yes

Table 3. Linear mixed models examining the relationship between longitudinal change in SF-36 PCS and MCS and other outcome variables after controlling for age, sex, and obesity.

Variables	SF36 PCS		SF36 MCS	
	β [CI]	*p value*	β [CI]	*p value*
Pain level	-1.68 [(-1.88) - (-1.47)]	<0.0001	-0.64 [(-0.91) - (-0.36)]	<0.0001
Fatigue level	-1.31 [(-1.51) - (-1.11]	<0.0001	-1.29 [(-1.54) - (-1.04)]	<0.0001
Patient global disease activity	-1.22 [(-1.42) - (-1.02)]	<0.0001	-1.01 [(-1.26) - (-0.76)]	<0.0001
HAQ-II	-8.16 [(-8.93) - (-7.39)]	<0.0001	-2.50 [(-3.61) - (-1.38)]	<0.0001

HAQ-II, Health Assessment Questionnaire

Conclusion: SF-36 had no significant floor or ceiling effect and demonstrated adequate validity and responsiveness in patients with IIM. These results support using SF-36 for health-related QoL assessment in patients with IIM.

Disclosure: A. Razok: None; **J. Taylor**: None; **E. Ritz**: None; **K. Wipfler**: None; **K. Michaud**: None; **D. Saygin**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0790

Diabetes Risk in Psoriasis Patients Treated with Biologic Disease-Modifying Antirheumatic Drugs: Target Trial Emulation Using Nationwide Data

Arjun Mahajan[1], David Bates[2], Vinod Nambudiri[3], Avery LaChance[2], Jeffrey Sparks[4] and Evan Piette[3], [1]Harvard Medical School, Boston, [2]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [3]Brigham and Women's Hospital, Harvard Medical School, Boston, [4]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (0789–0794)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Psoriasis is a chronic inflammatory skin disease associated with increased risk of metabolic complications, such as diabetes mellitus. However, the impact of specific biologic DMARD therapies on these metabolic outcomes remains poorly understood. Importantly, understanding how psoriatic treatments affect metabolic outcomes may guide therapeutic choices; thus, this study evaluates the risks of diabetes and kidney disease across biologic DMARD therapies.

Methods: Utilizing data from 128 healthcare organizations in the TriNetX network (2016-2024), we conducted an emulated trial to evaluate diabetes-related disease incidence among psoriasis patients (n=20,120) treated with interleukin-23 (IL-23i), interleukin-17A (IL-17Ai), or tumor necrosis factor-alpha (TNFi) inhibitors. To emulate randomization, we applied 1:1 propensity score matching using a greedy nearest neighbor algorithm to balance cohorts on demographics, comorbidities,

Table 1. Baseline Patient Characteristics in IL-23i vs TNFi Psoriasis Cohorts

Characteristic	Before PSM, n (%)			After PSM, n (%)		
	IL-23i (n=6,489)	TNFi (n=20,120)	SMD	IL-23i (n=6,457)	TNFi (n=6,457)	SMD
Age at index, mean (SD)	49.4 (15.9)	48.1 (16.1)	0.082	49.4 (15.9)	49.0 (15.8)	0.025
Sex						
Female	3,177 (49.0)	9,722 (48.6)	0.008	3,156 (48.9)	3,231 (50.0)	0.023
Male	3,170 (48.9)	9,752 (48.7)	0.003	3,160 (48.9)	3,093 (47.9)	0.021
Unknown	142 (2.2)	549 (2.7)	0.036	141 (2.2)	133 (2.1)	0.009
Race						
Asian	295 (4.5)	543 (2.7)	0.098	285 (4.4)	291 (4.5)	0.005
American Indian or Alaska Native	23 (0.4)	67 (0.3)	0.003	23 (0.4)	22 (0.3)	0.003
Black or African American	368 (5.7)	1,000 (5.0)	0.030	366 (5.7)	353 (5.5)	0.009
Native Hawaiian or Other Pacific Islander	18 (0.3)	81 (0.4)	0.022	17 (0.3)	24 (0.4)	0.019
Other Race	254 (3.9)	761 (3.8)	0.006	254 (3.9)	262 (4.1)	0.006
Unknown Race	858 (13.2)	2,672 (13.3)	0.004	855 (13.2)	904 (14.0)	0.022
White	4,673 (72.0)	14,899 (74.4)	0.054	4,657 (72.1)	4,601 (71.3)	0.019
Diagnoses						
Hypertension	1,910 (29.4)	4,976 (24.9)	0.103	1,890 (29.3)	1,852 (28.7)	0.013
Hyperlipidemia	2,023 (31.2)	4,485 (22.4)	0.199	1,994 (30.9)	1,959 (30.3)	0.012
Smoking (nicotine dependence)	622 (9.6)	1,309 (6.5)	0.112	612 (9.5)	560 (8.7)	0.028
Overweight and obesity	1,544 (23.8)	3,196 (16.0)	0.197	1,521 (23.6)	1,515 (23.5)	0.002
Neoplasms	2,058 (31.7)	3,746 (18.7)	0.303	2,026 (31.4)	1,997 (30.9)	0.010
Metabolic Steatotic Liver Disease (MASLD)	401 (6.2)	940 (4.7)	0.066	395 (6.1)	384 (5.9)	0.007
Systemic lupus erythematosus (SLE)	30 (0.5)	126 (0.6)	0.023	30 (0.5)	27 (0.4)	0.007
Crohn's disease	60 (0.9)	424 (2.1)	0.098	60 (0.9)	44 (0.7)	0.028
Ulcerative colitis	69 (1.1)	286 (1.4)	0.033	69 (1.1)	66 (1.0)	0.005
Rheumatoid arthritis	82 (1.3)	1,002 (5.0)	0.216	82 (1.3)	72 (1.1)	0.014
Celiac disease	39 (0.6)	83 (0.4)	0.026	37 (0.6)	44 (0.7)	0.014
Alcohol abuse	180 (2.8)	536 (2.7)	0.006	179 (2.8)	168 (2.6)	0.011
Medications						
Metformin	695 (10.7)	1,380 (6.9)	0.135	680 (10.5)	654 (10.1)	0.013
Lipid modifying agents	1,605 (24.7)	3,402 (17.0)	0.191	1,581 (24.5)	1,575 (24.4)	0.002
SGLT2 inhibitors	181 (2.8)	231 (1.2)	0.118	170 (2.6)	159 (2.5)	0.011
GLP-1 agonists	453 (7.0%)	409 (2.0%)	0.234	341 (5.3%)	316 (4.9%)	0.018
Laboratory Values						
eGFR, mean (SD)	84.4 (24.2)	85.6 (25.8)	0.046	84.4 (24.1)	84.8 (25.4)	0.013
eGFR 60-90 mL/min/1.73m²	2,646 (40.8)	6,823 (34.1)	0.139	2,624 (40.6)	2,632 (40.8)	0.003
eGFR ≥90 mL/min/1.73m²	2,434 (37.5)	6,528 (32.6)	0.103	2,413 (37.4)	2,425 (37.6)	0.004
HbA1c, mean (SD)	6.1 (1.5)	6.2 (1.7)	0.082	6.1 (1.5)	6.0 (1.5)	0.021
HbA1c <5.70%	1,498 (23.1)	2,491 (12.4)	0.281	1,467 (22.7)	1,437 (22.3)	0.011
HbA1c 5.70-6.40%	1,018 (15.7)	1,804 (9.0)	0.204	997 (15.4)	977 (15.1)	0.009

*Abbreviations: PSM, propensity score matching; SMD, standardized mean difference.
**One representative trial shown for illustrative purposes; all trial cohorts matched on identical covariates

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Occurrence and Risk of Diabetes and Diabetic Complications in Psoriasis Patients Treated with Interleukin-23 Inhibitors vs. TNF Inhibitors, TNF-alpha Inhibitors vs. Interleukin-17A Inhibitors, and Interleukin-23 Inhibitors vs. Interleukin-17A Inhibitors

	IL-23i vs. TNFi trial			TNFi vs. IL-17Ai trial			IL-23i vs. IL-17Ai trial		
Outcome	IL-23i Cohort Outcome Count (n=6,457)	TNFi Cohort Outcome Count (n=6,457)	HR (95% CI)	TNFi Cohort Outcome Count (n=6,425)	IL-17Ai Cohort Outcome Count (n=6,425)	HR (95% CI)	IL-23i Cohort Outcome Count (n=5,417)	IL-17i Cohort Outcome Count (n=5,417)	HR (95% CI)
Type 2 Diabetes	148	270	**0.91 (0.75, 0.99)**	305	232	**1.16 (1.01, 1.22)**	133	208	0.83 (0.66, 1.03)
Diabetic Nephropathy	26	65	**0.71 (0.48, 0.98)**	55	36	**1.20 (1.02, 1.44)**	23	32	0.97 (0.57, 1.67)
Chronic Kidney Disease (Any Stage)	86	214	**0.70 (0.60, 0.97)**	205	162	**1.05 (1.01, 1.12)**	76	143	0.83 (0.65, 1.07)
Stage 3-5 Chronic Kidney Disease	72	180	**0.750 (0.58, 0.98)**	165	128	**1.08 (1.01, 1.16)**	63	114	0.74 (0.54, 1.01)
Negative Controls									
Varicose veins	47	84	0.93 (0.64, 1.34)	68	62	0.87 (0.62, 1.23)	39	51	1.04 (0.69, 1.59)
Laceration of the head	18	23	1.72 (0.91, 3.28)	21	14	1.05 (0.53, 2.07)	18	15	1.72 (0.91, 3.28)

laboratory data, and medication use (Table 1). Primary outcomes included new-onset type 2 diabetes, diabetic nephropathy, chronic kidney disease (CKD), and stage 3–5 CKD. Varicose vein and head laceration diagnoses served as negative control outcomes. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox proportional hazards models.

Results: In an emulated trial of IL-23i versus TNFi treatment (n=6,457 matched pairs), IL-23i treatment was associated with lower risks of diabetes (HR 0.91; 95% CI 0.75–0.99), diabetic nephropathy (HR 0.71; 95% CI 0.48–0.98), and stage 3–5 CKD (HR 0.75; 95% CI 0.58–0.98) (Table 2). In the TNFi versus IL-17Ai emulated trial (n=6,425 pairs), TNFi-treated patients had a higher risk of diabetes (HR 1.16; 95% CI 1.01–1.22) and associated kidney disease outcomes. No significant differences were observed between IL-23i and IL-17Ai treatment. Compared to systemic therapy naïve (STN) patients (n=6,489 pairs), IL-23i treatment was associated with reduced risks of diabetes (HR 0.89; 95% CI 0.80–0.98), diabetic nephropathy (HR 0.78; 95% CI 0.60–0.97), and stage 3–5 CKD (HR 0.76; 95% CI 0.62–0.92) (Table 3); IL-17Ai treatment showed similarly protective effects for diabetes (HR 0.90; 95% CI 0.83–0.98), diabetic nephropathy (HR 0.74; 95% CI 0.57–0.96), and stage 3–5 CKD (HR 0.88; 95% CI 0.75–0.99) risk (n=6,402 pairs). TNFi treatment showed no significant differences compared to STN patients. No differences were observed in negative control outcomes across comparisons.

Table 3. Risk and Occurrence of Diabetes and Diabetic Complications in Biologic-Treated vs. Systemic Therapy-Naïve Psoriasis Patients

	IL-23i vs Systemic Therapy Naïve (STN)			IL-17i vs Systemic Therapy Naïve (STN)			TNFi vs Systemic Therapy Naïve (STN)		
Outcome	IL23i Cohort Outcome Count (n=6,489)	STN Cohort Outcome Count (n=6,489)	HR (95% CI)	IL-17i Cohort Outcome Count (n=6,402)	STN Cohort Outcome Count (n=6,402)	HR (95% CI)	TNFi Cohort Outcome Count (n=20,005)	STN Cohort Outcome Count (n=20,005)	HR (95% CI)
Type 2 Diabetes	145	250	**0.89 (0.80, 0.98)**	230	278	**0.90 (0.83, 0.98)**	823	843	0.97 (0.88, 1.07)
Diabetic Nephropathy	27	70	**0.78 (0.60, 0.97)**	37	72	**0.74 (0.57, 0.96)**	172	181	0.96 (0.78, 1.18)
Chronic Kidney Disease (Any Stage)	88	218	**0.73 (0.60, 0.89)**	168	232	**0.89 (0.78, 0.99)**	573	633	0.91 (0.82, 1.02)
Stage 3-5 Chronic Kidney Disease	73	180	**0.76 (0.62, 0.92)**	130	178	**0.88 (0.75, 0.99)**	463	469	0.99 (0.88, 1.13)
Negative Controls									
Varicose veins	47	90	0.96 (0.66, 1.38)	62	97	0.85 (0.62, 1.17)	218	253	0.82 (0.69, 1.09)
Laceration of the head	18	23	1.38 (0.73, 2.61)	14	31	0.62 (0.33, 1.17)	72	87	0.84 (0.61, 1.15)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: These emulated target trials suggest that IL-17Ai and IL-23i therapies are associated with lower risks of incident type 2 diabetes and kidney disease compared to TNFi or systemic therapy naïve approaches. These findings may support the consideration of metabolic outcomes in biologic DMARD treatment selection for psoriasis patients.

Disclosure: A. Mahajan: None; **D. Bates**: None; **V. Nambudiri**: None; **A. LaChance**: Johnson & Johnson, 2, johnson and johnson, 2, Merck, 5, Pfizer, 2; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **E. Piette**: None.

Abstract Number: 0791

Disagreements in Disease Activity Measures in an Evaluation of SLE Outcome Measures in Telemedicine

Leila Khalili[1], Cynthia Aranow[2], Mimi Kim[3], Diane Kamen[4], Cristina Arriens[5], Alberto Nordmann-Gomes[6], Maya Souvignier[6], Wei Tang[7], Stephen Suh[8], Maria Dall'Era[9], Meghan mackay[10] and Anca Askanase[1], [1]Columbia University Medical Center, New York, NY, [2]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [3]Albert Einstein College of Medicine, Bronx, NY, [4]Medical University of South Carolina, Johns Island, SC, [5]Oklahoma Medical Research Foundation, Oklahoma City, OK, [6]Columbia University Irving Medical Center, New York, NY, [7]Westchester Medical Center, Valhalla, NY, [8]Columbia University Irving Medical Center, New York City, NY, [9]Division of Rheumatology, University of California, San Francisco, CA, [10]Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (0789–0794)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: We previously described the top-line results of our study and the high correlations between virtual SLE disease activity measures (DAM) and those obtained during face-to-face (F2F) visits. Here we describe the more granular data on disagreements between telemedicine (TM) and F2F DAM across 2 visits in order to better understand the reasons for these discrepancies and improve TM assessments of SLE activity.

Methods: This was an observational, longitudinal study of SLE patients from 4 academic lupus centers serving diverse populations supported by a grant from the US DoD. Each study participant was evaluated at a baseline and follow-up visit as dictated by usual care. Virtual physical exam guidelines were established and relied upon clinician-directed patient self-examination. At each visit, participants were evaluated by the same provider via a videoconference-based TM and then a F2F encounter. SLE DAM were completed after the TM and the F2F encounters. Disagreements in DAM domains between the encounters were noted and verified with the evaluator, as were changes in treatment plan. Tandem provider and patient feedback tools for encounters probed satisfaction, comfort, and problematic evaluation.

Results: 163 racially and ethnically diverse participants were enrolled and completed the first visit, 145 completed the follow-up visit as previously described (Table 1). Briefly, while intraclass correlation coefficients (ICC) showed high correlation between TM and F2F (0.877-0.998), paired T-tests showed differences for SLEDAI (mean difference -0.19 +/-1.33, p=0.011) and CLASI activity (mean differences -0.18 +/-0.76, $p < 0.001$); the main drivers were difficulty with virtual arthritis and rash evaluations. For the 145 baseline/follow-up pair visits, there were 63 disagreements across all DA instruments: 25 musculoskeletal (10 overestimating [OE], 15 underestimating [UE] DA), 25 mucocutaneous (7 OE, 18 UE), 3 cardiorespiratory [3 UE], 3 vasculitis [3 UE], 6 constitutional [3 OE/3 UE], 1 ophthalmologic [1 UE] (Fig. 1). These resulted in inconsistencies in SLEDAI 38 (pleurisy-1, arthritis-14, ulcers-5, rash-9, alopecia-6, vasculitis-3) and BILAG 36 (constitutional-6, mucocutaneous-14, musculoskeletal-14, cardiorespiratory-1, ophthalmologic-1). Sometimes, arthritis not recorded on the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographic and clinical characteristics of the participants.

	Participants (N=163)
Sex	
Female, n (%)	141 (86)
Male, n (%)	22 (14)
Age, median years (IQR)	40 (31-49)
Race	
White, n (%)	65 (40)
Black, n (%)	64 (39)
Asian, n (%)	21 (13)
Other, n (%)	13 (8)
Ethnicity	
Hispanic, n (%)	40 (25)
Not Hispanic, n (%)	123 (75)
Site	
CUMC, n (%)	58 (36)
MUSC, n (%)	44 (27)
FIMR, n (%)	31 (19)
OMRF, n (%)	30 (18)
SLE disease duration, median years (IQR)	17 (11-23)
SLE disease activity	
Asymptomatic, n (%)	33 (20)
Mild/Moderate, n (%)	111 (68)
Severe, n (%)	19 (12)
SLEDAI, median (IQR)	4 (2-8)
Number of ACR criteria, median (IQR)	6 (5-8)

Abbreviations: IQR, Interquartile range; CUMC, Columbia University Medical Center; MUSC, Medical University of South Carolina; FIMR, Feinstein Institutes for Medical Research; OMRF, Oklahoma Medical Research Foundation; SLE, Systemic Lupus Erythematosus; SLEDAI, SLE Disease Activity Index; ACR, American College of Rheumatology.

virtual SLEDAI, upon F2F evaluation swollen and tender joints were elicited by the clinician and resulted in SLEDAI scoring of arthritis, but arthralgia/mild arthritis was recorded on the BILAG. Following the F2F visit 52.9% clinicians were highly confident that their virtual DA assessment was accurate, 41.0% confident/moderately confident, 4.4% minimally confident, and 1.7% not confident at all.

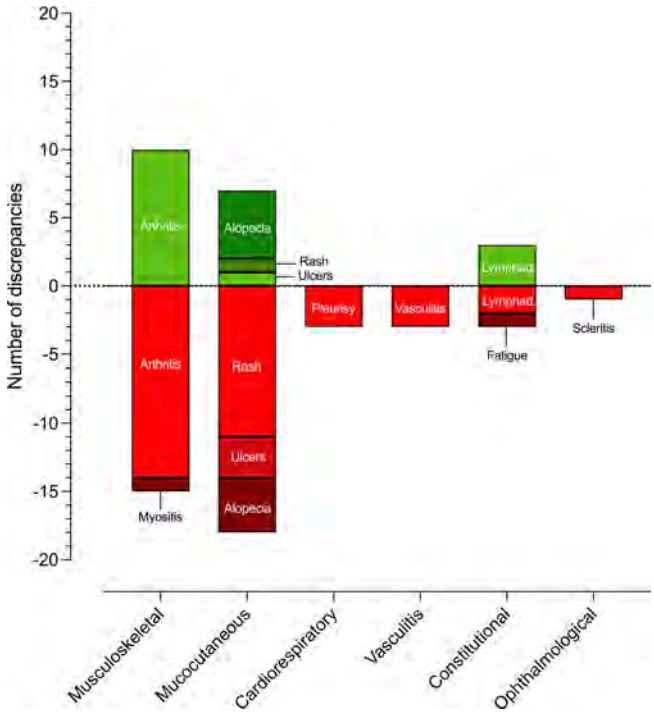


Figure 1. Discrepancies in disease activity scores between telemedicine and face-to-face visits.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: These data discuss lack of agreement for the mucocutaneous and arthritis findings, despite high overall correlations between virtual and F2F DA. TM tended to slightly underestimate DA. These data emphasize the need to further refine virtual DA assessments to provide improved agreement between TM and F2F evaluations and allow for increased adoption of telemedicine in SLE clinical care and clinical trials.

Disclosure: L. Khalili: None; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **M. Kim**: None; **D. Kamen**: None; **C. Arriens**: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **A. Nordmann-Gomes**: None; **M. Souvignier**: None; **W. Tang**: None; **S. Suh**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **M. mackay**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5.

Abstract Number: 0792

Real-World Assessment of Glucocorticoid-Induced Skin Toxicity in Individuals with Rheumatic Diseases

Tania Chiha[1], Jiaqi Wang[2], Isha Jha[3], Grace McMahon[3], John Stone[4] and Naomi Patel[3], [1]Mount Auburn Hospital, Boston, MA, [2]Massachusetts General Hospital, BOston, [3]Massachusetts General Hospital, Boston, MA, [4]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (0789–0794)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Glucocorticoids (GC) are used to treat various inflammatory and autoimmune diseases, though despite widespread use, real-world data on skin-specific GC toxicity are limited. To better characterize the burden of GC-related skin adverse effects, we prospectively evaluated GC-related skin toxicity over 6 months in a rheumatology clinic setting.

Methods: We obtained data from the Longitudinal Glucocorticoid Toxicity (LONG-TOX) prospective cohort, which enrolls adults with rheumatic diseases receiving or initiating GC therapy (≥3 month expected duration) at a large academic hospital. The domains of the Glucocorticoid Toxicity Index (GTI) were used to assess the GT-SNAPSHOT, a comprehensive baseline assessment of GC toxicity, at baseline, and the GTI at 6 months. GC exposure was tracked using patient diaries and electronic health records. GTI-defined skin toxicities (acneiform rash, easy bruising, hirsutism, atrophy/striae, and erosions/tears/ulcerations) were assessed by a study team member at both visits. We used the GTI Skin Toxicity domain to evaluate changes in GC-related skin toxicity and examined factors associated with baseline skin toxicity and worsening in skin toxicity (i.e., new and/or worsened skin manifestation) over 6 months using univariable logistic regression.

Results: Of 90 enrolled individuals, 74 completed 6-month follow-up. The mean (SD) age was 60.0 (16.6) years, 62.2% were female, median prednisone-equivalent GC dose was 30.0 mg daily, and most (64.4%) were receiving concomitant immunomodulatory therapy (**Table 1**). Those with skin toxicity at baseline had higher median GT-SNAPSHOT scores (195 vs. 141, $p< 0.01$) and significantly more neuropsychiatric (90.7% vs. 61.1%, $p< 0.01$) and infection-related toxicity (20.4% vs. 0.0%, $p< 0.01$) than those without baseline skin toxicity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographics and Clinical Characteristics of Individuals With and Without Glucocorticoid-Related Skin Toxicity

	All Individuals (N=90)	Skin Toxicity (N=54)	No Skin Toxicity (N=36)	p-value (comparing skin toxicity to no skin toxicity)
Age, years, mean (SD)	60.0 (16.6)	55.7 (16.8)	66.5 (14.1)	<0.01
Female, n (%)	56 (62.2)	37 (68.5)	19 (52.8)	0.13
Race, n (%)				0.09
White	81 (90.0)	48 (88.9)	33 (91.7)	
Black	6 (6.7)	4 (7.4)	2 (5.5)	
Asian	2 (2.2)	1 (1.8)	1 (2.8)	
More than one race	1 (1.1)	1 (1.8)	0 (0.0)	
Hispanic ethnicity, n (%)	3 (3.3)	2 (3.7)	1 (2.8)	0.16
BMI, mean (SD)	28.4 (5.8)	28.2 (5.6)	28.7 (6.1)	0.66
Rheumatic disease diagnosis or category, n (%)				<0.01
PMR/GCA	37 (41.1)	16 (29.6)	21 (58.3)	
ANCA-associated vasculitis	9 (10.0)	3 (5.5)	6 (16.7)	
Myositis	6 (6.7)	2 (3.7)	4 (11.1)	
Other rheumatic disease*	38 (42.2)	33 (61.1)	5 (13.9)	
Disease activity, n (%)				0.24
Remission	17 (18.9)	12 (22.2)	5 (13.9)	
Mild	29 (32.2)	13 (24.1)	16 (44.4)	
Moderate	32 (35.6)	21 (38.9)	11 (30.6)	
Severe	12 (13.3)	8 (14.8)	4 (11.1)	
Current glucocorticoid dose, prednisone-equivalent mg, median (IQR)	30.0 (20.0, 50.0)	30.0 (20.0, 50.0)	30.0 (15.0, 50.0)	0.84
Immunomodulatory therapy, n (%)	58 (64.4)	40 (74.1)	18 (50.0)	0.02
GT-SNAPSHOT Score*, median (IQR)	165.0 (122.0, 251.0)	195.0 (143.0, 271.0)	141.0 (95.0, 217.0)	<0.01
GT-SNAPSHOT Domains with Score > 0				
BMI domain score, n (%)	51 (56.7)	30 (55.6)	21 (58.3)	0.79
BP domain score, n (%)	74 (82.2)	43 (79.6)	31 (86.1)	0.43
Glucose Tolerance, n (%)	74 (82.2)	42 (77.8)	32 (88.9)	0.18
Lipid Metabolism, n (%)	83 (92.2)	48 (88.9)	35 (97.2)	0.15
Myopathy, n (%)	42 (46.7)	28 (51.9)	14 (38.9)	0.23
Bone, n (%)	23 (25.6)	12 (22.2)	11 (30.6)	0.37
Infection, n (%)	11 (12.2)	11 (20.4)	0 (0.0)	<0.01
Neuropsychiatric, n (%)	71 (78.9)	49 (90.7)	22 (61.1)	<0.01
Ocular, n (%)	16 (17.8)	7 (13.0)	9 (25.0)	0.14

*Adrenal and gastrointestinal domains not presented in due to no involvement in this cohort. Skin toxicity domain is not presented as it was utilized in the definition of exposure groups.

At baseline, 61.1% had at least one GTI skin toxicity manifestation, with the most common including easy bruising (34.5%), followed by atrophy/striae (22.2%) and acneiform rash (15.5%) (**Table 2**). At 6 months, 62.2% had at least one GTI skin toxicity manifestation, with the most common including easy bruising (37.9%), followed by acneiform rash (21.7%) and atrophy/striae (16.3%).

Table 2. Glucocorticoid Toxicity Index Skin Toxicity Manifestations at Baseline (Enrollment) and 6 Months

	Baseline, n (%) (N=90)	6-months, n (%) (N=74)	P-value
Any skin toxicity	55 (61.1)	46 (62.2)	0.68
Acneiform rash			0.77
None	76 (84.4)	58 (78.4)	
Mild	11 (12.2)	13 (17.6)	
Moderate	3 (3.3)	3 (4.1)	
Major	0 (0.0)	0 (0.0)	
Severe	0 (0.0)	0 (0.0)	
Easy bruising			0.43
None	59 (65.6)	46 (62.2)	
Mild	14 (15.6)	13 (17.6)	
Moderate	17 (18.9)	15 (20.3)	
Hirsutism			0.45
None	75 (83.3)	59 (79.7)	
Mild	14 (15.6)	11 (14.9)	
Moderate	1 (1.1)	4 (5.4)	
Atrophy/striae			<0.01
None	70 (77.8)	62 (83.8)	
Mild	10 (11.1)	6 (8.1)	
Moderate	10 (11.1)	5 (6.8)	
Major	0 (0.0)	1 (1.4)	
Erosion/tear/ulceration			0.80
None	79 (87.8)	69 (93.2)	
Mild	8 (8.9)	3 (4.1)	
Moderate	3 (3.3)	2 (2.7)	
Major	0 (0.0)	0 (0.0)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Factors Associated with Worsening in Glucocorticoid-Related Skin Toxicity over 6 Months

	Any Worsening in Skin Toxicity (N=42)	No Worsening in Skin Toxicity (N=32)	P-value
Age, years, mean (SD)	58.3 (15.8)	61.7 (15.8)	0.36
Female, n (%)	24 (57.1)	22 (68.8)	0.31
Race, n (%)			
White	39 (92.9)	28 (87.5)	
Black	3 (7.1)	2 (6.3)	0.31
Asian	0 (0.0)	2 (6.3)	
More than one race	0 (0.0)	0 (0.0)	
Hispanic ethnicity, n (%)	2 (4.8)	1 (3.1)	1.00
BMI, mean (SD)	29.6 (5.6)	29.3 (6.8)	0.90
Baseline disease activity, n (%)			
Remission	18 (42.9)	20 (62.5)	
Mild	11 (26.2)	10 (31.3)	0.048
Moderate	10 (23.8)	1 (3.1)	
Severe	3 (7.1)	1 (3.1)	
Cumulative 6-month GC exposure, prednisone-equivalent mg, median (IQR)	2167.00 (1196.5, 3940.0)	2013.50 (1183.5, 2831.0)	0.27
Current GC dose among those still on GCs, prednisone-equivalent mg, median (IQR)	5.0 (0.0, 10.0)	3.0 (0.0, 5.5)	0.11
Baseline concomitant immunomodulatory therapy, n (%)	32 (76.2)	25 (78.1)	0.84
GTI CWS, median (IQR)	58.5 (28.0, 116.0)	30.5 (5.5, 55.0)	<0.01
GTI Domain CWS > 0			
Body mass index score, n (%)	16 (38.10)	6 (18.75)	0.07
Glucose tolerance, n (%)	4 (9.52)	6 (18.75)	
Blood pressure, n (%)	11 (26.19)	12 (37.50)	0.30
Lipid metabolism, n (%)	9 (21.43)	3 (21.43)	0.21
Glucocorticoid Myopathy, n (%)	10 (23.81)	2 (6.25)	0.04
Skin, n (%)	18 (42.86)	0 (0.0)	<0.01
Neuropsychiatric, n (%)	18 (42.86)	6 (18.75)	0.03
Infection, n (%)	3 (7.14)	2 (6.25)	1.00

GC, glucocorticoid; GTI CWS, Glucocorticoid Toxicity Index Cumulative Worsening Score

Over 6 months, those with worsening skin toxicity (56.8%) had higher overall GTI Cumulative Worsening Scores (median 58.5 vs. 30.5, p< 0.01), higher baseline disease activity (42.9% in remission vs 62.5%, p=0.048), and numerically higher cumulative GC exposure (2167 vs. 2014 prednisone-equivalent mg, p=0.27) compared to those without worsening skin toxicity **(Table 3)**. There were no differences in sex, body mass index, race, or baseline immunomodulatory therapy between groups. Those with worsening skin toxicity had more worsening in the Neuropsychiatric (42.9% vs. 18.8%, p=0.03) and Myopathy (23.8% vs. 6.3%, p=0.04) domains.

Conclusion: Skin-related adverse effects are common with GC use and highlight the need for routine assessment in long-term GC users. Neuropsychiatric GC toxicity was more common in individuals with skin toxicity. Routine assessment of the skin manifestations of the GTI may enhance detection and guide interventions to mitigate morbidity associated with GC treatment.

Disclosure: T. Chiha: None; **J. Wang**: None; **I. Jha**: None; **G. McMahon**: None; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **N. Patel**: Amgen, 5.

Abstract Number: 0793

The weight of the past: how trauma and resilience shape medication adherence in SLE

Kai Sun[1], Sofia Pozsonyiova[1], Amanda Eudy[2], Megan Clowse[3], Rebecca Sadun[1], Mithu Maheswaranathan[4], Jayanth Doss[5], Nathaniel Harris[6], Lisa Criscione-Schreiber[4], Connor Drake[4], Tamara Somers[7], Ralph Snyderman[8] and Jennifer Rogers[4], [1]Duke University, Durham, NC, [2]Duke University, Raleigh, NC, [3]Duke University, Chapel Hill, NC, [4]Duke University School of Medicine, Durham, [5]Division of Rheumatology and Immunology, Duke University Department of Medicine, Durham, NC, [6]Duke University Medical Center, Durham, NC, [7]Duke University School of Medicine, Durham, NC, [8]Duke Center for Personalized Health Care, Durham, NC

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (0789–0794)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Summary of Baseline Characteristics by Medication Adherence Status*

	Total (N=238)	Adherent (N=127)	Nonadherent (N=111)	P-Value
Age, Median (Q1-3)	42 (33-52)	45 (35-55)	39 (32-49)	0.003[1]
Female sex, n (%)	219 (92%)	117 (92%)	102 (92%)	0.9[2]
Race, n (%)				< 0.001[3]
White	86 (36%)	60 (47%)	26 (23.4%)	
Black	135 (57%)	61 (48%)	74 (66.7%)	
Asian	6 (3%)	3 (2%)	3 (2.7%)	
Other	11 (5%)	3 (2%)	8 (7.2%)	
Hispanic ethnicity, n (%)	14 (6%)	3 (2%)	11 (9.9%)	0.02[3]
PGA, Median (Q1-3)	0.25 (0-1)	0.25 (0-0.75)	0.25 (0-1.25)	0.2[4]
Active Lupus Nephritis, n (%)	24 (10%)	11 (9%)	13 (11.7%)	0.4[2]
Symptom Severity Score, Median (Q1-3)	5 (2-7)	4 (2-7)	6 (3-8)	0.03[1]
Areas of Widespread Pain, Median (Q1-3)	3 (0-6)	2 (0-6)	3 (1-6)	0.3[1]
Total Fibromyalgia Severity Score, Median (Q1-3)	8 (3-13)	7 (3-12)	9 (5-13)	0.1[1]
Trauma, n (%)				< 0.001[2]
No trauma	39 (16%)	24 (19%)	15 (14%)	
Non-abusive trauma	101 (42%)	65 (51%)	36 (32%)	
Abusive trauma	98 (41%)	38 (30%)	60 (54%)	
Resilience, n (%)				0.9[3]
High resilience	3 (1%)	2 (2%)	1 (1%)	
Low resilience	82 (35%)	45 (35%)	37 (33%)	
Normal resilience	153 (64%)	80 (63%)	73 (66%)	

Statistical Tests used include: 1. Wilcoxon rank-sum test, 2. Pearson's Chi-squared test, 3. Fisher's Exact Test for Count Data, as appropriate

* *Adherence was assessed using the DOSE-Nonadherence-SLE survey via three Likert-scale items on missed, skipped, or not taking medication (1 = Never to 5 = Always). Patients were classified as adherent if all responses were "Never"; others were nonadherent. See Methods for full criteria.*

Background/Purpose: Medication adherence in SLE is suboptimal and contributes to increased disease activity, organ damage, and mortality. Trauma exposure is common among those with SLE and may undermine adherence behaviors by disrupting patients' sense of stability and future orientation. As a result, trauma-exposed patients may be more likely to focus on immediate needs over long-term planning, reducing the effectiveness of adherence messaging centered on future outcomes such as flare prevention or organ preservation. Resilience—the capacity to adapt to adversity—may buffer these effects. However, the relationship between trauma, resilience, and medication adherence in SLE remains underexplored.

Methods: We conducted a cross-sectional study of patients with SLE (2012 SLICC or 2019 ACR/EULAR criteria) enrolled in an academic lupus registry. The *extent of* and *reasons for* nonadherence were measured by the DOSE-Nonadherence-SLE. Patients also completed the polysymptomatic distress (PSD) scale, the Brief Resilience Scale, and the Trauma History Screen. Rheumatologists assessed SLE activity using the Physician's Global Assessment (PGA). Trauma exposure history

Table 2: Association between Trauma and Medication Nonadherence

	Model 1: Unadjusted RR (95% CI)	Model 2: Covariate Adjusted RR (95% CI)
Trauma Category		
No Trauma	(Ref)	(Ref)
Non-abusive Trauma	0.93 (0.58,1.49)	0.95 (0.59,1.52)
Abusive Trauma	1.59 (1.04,2.44)	1.58 (1.04,2.42)
Hispanic Ethnicity		
Non-Hispanic	--	(Ref)
Hispanic	--	1.57(1.08,2.26)
Race		
White	--	(Ref)
Black	--	1.77 (1.25,2.51)
Asian	--	1.71 (0.62,4.68)
Other	--	1.81 (1.04,3.15)

Note: RR = Relative Risk; CI = Confidence Interval; Ref = Reference Category

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Reasons for nonadherence based on the DOSE-Nonadherence-SLE by trauma history.

I missed my lupus pills because…	Total (N=111)	No trauma (N=15)	Non-abusive trauma (N=36)	Abusive trauma (N=60)	P-Value
Access barriers					
I could not fill in time	27 (29%)	8 (62%)	7 (25%)	12 (24%)	0.02[2]
It cost too much	11 (12%)	3 (21%)	2 (7%)	6 (12%)	0.4[1]
Logistic barriers					
I forgot or was busy	69 (71%)	10 (77%)	20 (69%)	39 (71%)	0.9[2]
I do not have a regular schedule	30 (32%)	3 (23%)	9 (32%)	18 (33%)	0.8[2]
I needed to take them with food but could not eat at that time	26 (28%)	1 (8%)	9 (33%)	16 (30%)	0.2[2]
I was too tired	17 (19%)	2 (15%)	2 (7%)	13 (27%)	0.1[1]
I take too many pills	13 (14%)	1 (8%)	1 (4%)	11 (21%)	0.09[1]
Medication instructors were too hard to follow	2 (2%)	0 (0%)	1 (4%)	1 (2%)	1.0[1]
I had a hard time swallowing them	5 (6%)	0 (0%)	1 (4%)	4 (8%)	0.7[1]
I was too stiff	5 (6%)	0 (0%)	1 (4%)	4 (8%)	0.7[1]
I had no one to help me	2 (2%)	0 (0.0%)	1 (4%)	1 (2%)	1.0[1]
Motivational barriers					
I am tired of taking medicines every day	20 (23%)	2 (15%)	1 (4%)	17 (35%)	0.004[1]
I don't feel any difference	17 (19%)	1 (8%)	4 (14%)	12 (25%)	0.4[1]
It caused side effects	16 (17%)	0 (0%)	5 (17%)	11 (21%)	0.2[1]
I feel that nothing will get better even if I take them	14 (16%)	1 (8%)	0 (0%)	13 (26%)	0.003[1]
I felt too sick	14 (16%)	0 (0%)	2 (7%)	12 (25%)	0.03[1]
I felt well	13 (14%)	2 (15%)	3 (11%)	8 (16%)	0.8[1]
I was worried about possible side effects	11 (12%)	1 (8%)	3 (11%)	7 (14%)	1.0[1]
I felt so bad, thought medicine was not working	8 (9%)	1 (8%)	1 (4%)	6 (12%)	0.6[1]
I felt too depressed	8 (9%)	0 (0%)	1 (4%)	7 (15%)	0.2[1]
I do not understand why need to take them	4 (4%)	0 (0%)	1 (4%)	3 (6%)	1.0[1]
I was worried it would affect fertility in the future	2 (2%)	0 (0%)	0 (0%)	2 (4%)	0.7[1]
My family or friend said not to	1 (1%)	0 (0%)	0 (0%)	1 (2%)	1.0[1]
I heard someone had a bad experience	1 (1%)	0 (0%)	0 (0%)	1 (2%)	1.0[1]

Statistical Tests used include: 1. Fisher's Exact Test for Count Data, 2. Pearson's Chi-Squared Test, as appropriate.

was categorized into abusive (physical, sexual, and emotional trauma as an adult or child), non-abusive, or no trauma. We used Fisher's exact test, Chi-squared test, and Wilcoxon rank sum test for group comparisons and multivariable regression models to examine the association between trauma exposure and medication nonadherence, including an interaction term for resilience.

Results: Among 238 patients (median age 42, 92% female, 36% White, 57% Black, 6% Hispanic), 111 (47%) reported non-adherence, 98 (41%) reported abusive trauma, and 101 (42%) reported non-abusive trauma. Nonadherent patients were more likely to be younger, identify as Black or Other race or Hispanic ethnicity, have higher symptom severity scores, and report a history of abusive trauma (Table 1).

In adjusted models, abusive trauma was associated with 58% higher risk of nonadherence compared to no trauma (Table 2). Black and Other race and Hispanic ethnicity also remained significantly associated with nonadherence. Resilience moderated the relationship between trauma and medication nonadherence (p=0.02); patients with abusive trauma as well as low resilience had the highest risk of nonadherence.

Nonadherent patients with abusive trauma, compared to those with non-abusive trauma or no trauma, more frequently reported missing SLE medications because "I am tired of taking medicines every day," "I feel that nothing will get better even if I take them," and "I felt too sick." They were less likely to report "I could not fill the medicines on time." (Table 3)

Conclusion: Abusive trauma was common and independently associated with greater risk of medication nonadherence in SLE, and resilience was a protective moderator. Patients with abusive trauma tended to endorse motivational barriers to adherence but were less likely to endorse difficulty filling medicines on time. These findings underscore the importance of trauma-informed, resilience-enhancing approaches to improve medication adherence for trauma-exposed patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Sun: Aurinia, 2; **S. Pozsonyiova**: None; **A. Eudy**: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **M. Clowse**: None; **R. Sadun**: The Expert Institute, 12,; **M. Maheswaranathan**: AstraZeneca, 2, UCB, 2; **J. Doss**: None; **N. Harris**: None; **L. Criscione-Schreiber**: UCB, 5; **C. Drake**: ZealCare, 12, 10; **T. Somers**: None; **R. Snyderman**: DNAnexus, 4, Heartland Whole Health Institute, 4, iRhythm Technologies, 4, OrthoTheapeutics, Inc., 1, ZealCare, 4; **J. Rogers**: AstraZeneca, 1, 1, Aurinia, 2, 5, Exagen, 5, Immunovant, 2, 5.

Abstract Number: 0794

Using Artificial Intelligence to Analyze Multilingual Qualitative Data in Lupus Pregnancy Research: A Proof of Concept with Large Language Models

Romina Boers[1], Grace Terry[2] and **Bella Mehta**[3], [1]Weil Cornell Medicine, New York, [2]Weil Cornell Medicine, Ne wYork, [3]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (0789–0794)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Women with systemic lupus erythematosus (SLE), particularly those of childbearing age, face heightened risks during pregnancy, including disease flares, adverse maternal-fetal outcomes, and emotional stress. Understanding how these women perceive pregnancy is essential for delivering personalized and empathetic care. While qualitative research is ideal for capturing such patient perspectives, analyzing interview data analyzing interview data is labor-intensive and often exclude non-English speakers. To evaluate the use of large language models (LLMs) in translating, analyzing, and summarizing qualitative interviews on pregnancy experiences in women with SLE, and to quantitatively compare LLM-generated themes with those identified by human researchers.

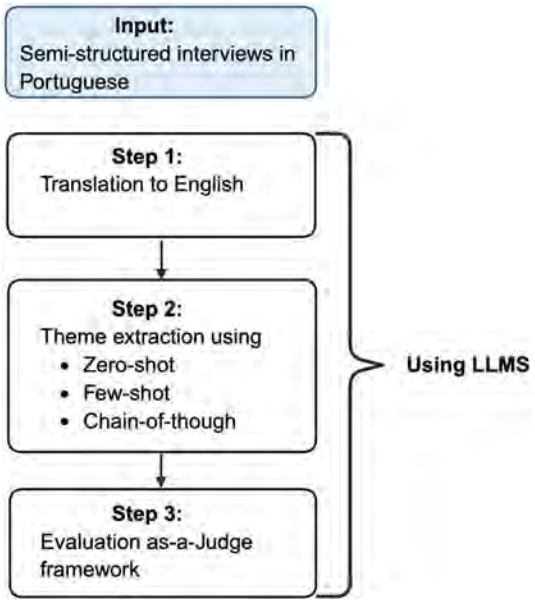


Figure 1. Workflow for LLM-Assisted Multilingual Qualitative Analysis in Lupus Pregnancy Research

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Reference Study Results	Our Results
1. Unplanned pregnancy and nonuse of contraception • family planning • reasons for pregnancy • partner's personal fulfillment • miracles-religiosity	3. Pregnancy as a Source of Hope and Transformation
2. Feeling healthy despite doctor's warning of disease worsening because of pregnancy • Doctor's opinion • Self-image • Self-perception • Willingness to engage in self-care • Treatment control	1. Diagnostic Challenges and Uncertainty 6. Everyday Struggles and Adaptation 7. Personal Growth and Acceptance
3. Joy couple with fear of the future and pregnancy • Fear of pregnancy complications • Afraid of not being able to take care of the child • Pregnancy losses • Neonatal losses • Death • Job loss • Loss of autonomy • Loss of decision-making power	2. Emotional Impact and Psychological Burden 4. Fear of Harm to the Baby and Maternal Responsibility
4. Self-perception and straight perception • Perception of the significant people • Perception of the woman herself	5. Importance of Social and Medical Support

Table 1. Comparison of themes from the reference qualitative study with themes generated by ChatGPT 4.0. The left column shows human-derived themes from Rodrigues et al. (2020), while the right column presents corresponding LLM-derived themes. This alignment confirms that use of LLM can identify relevant themes from qualitative semi-structured interviews.

Methods: We used semi-structured interviews originally conducted in Portuguese by Rodrigues et al.(1) with 26 women with SLE to explore their prenatal care experiences. Transcripts were translated into English using LLMs, and three types of prompting—zero-shot, few-shot, and chain-of-thought—were tested across four state-of-the-art LLMs (GPT o3-mini-high, Claude 3.7 Sonnet, Gemini 2.0 Flash and DeepSeek R1) to generate key themes and supporting quotes. (Figure 1) Each output was evaluated using an LLM-as-a-judge framework on five dimensions/ metrics: theme accuracy, theme coverage, semantic similarity, factual consistency, and coherence, using the published reference themes as ground truth.

Results: LLM-derived themes included: (1) diagnostic uncertainty, (2) emotional and psychological burden, (3) pregnancy as a source of hope, (4) fear of harming the baby, (5) importance of support systems, (6) everyday adaptations, and (7) personal growth. These themes aligned well with those from the original qualitative study. (Table 1) Few-shot prompting with GPT-4 yielded the highest overall performance across all five evaluation metrics - with strong theme accuracy (7.5/10), coverage (7.0/10), and coherence (9.0/10). (Table 2) .

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Performance scores Across Prompting methods

Prompt Type	Model	Theme Accuracy	Theme Coverage	Semantic Similarity	Factual Consistency	Coherence
Zero-Shot	GPT-4	6.5	5.0	0.65	7.0	8.5
	Claude	5.0	4.0	0.50	5.5	7.0
	Gemini	6.0	5.5	0.60	6.5	7.5
	DeepSeek	5.5	4.5	0.55	6.0	8.0
Few-Shot	GPT-4	7.5	7.0	0.75	8.0	9.0
	Claude	7.0	7.5	0.75	8.0	9.0
	Gemini	6.5	4.0	0.60	6.0	8.0
	DeepSeek	6.5	6.5	0.65	7.0	8.5
Chain-of-Thought	GPT-4	6.5	6.0	0.65	7.0	8.0
	Claude	7.0	6.5	0.70	7.5	8.5
	Gemini	6.0	5.5	0.60	6.5	7.5
	DeepSeek	6.5	6.5	0.65	7.0	8.0

Conclusion: LLMs show strong potential for supporting qualitative research in rheumatology by facilitating multilingual data processing, theme extraction, and instrument development. This approach can significantly reduce the labor required for traditional qualitative analysis while preserving depth and rigor, especially in studies addressing sensitive and complex experiences such as lupus pregnancy. Lastly, these methods help amplify the voices of patients who are often underrepresented in research due to language barriers, making this a valuable tool for promoting equity.

Reference

1) Larissa Rodrigues, Vera Lucia Pereira Alves, Maria Margarida Fialho Sim-Simc, Fernanda Garanhani Surita. Perceptions of women with systemic lupus erythematosus undergoing high-risk prenatal care: A qualitative study, Midwifery,Volume 87, 2020, 102715,https://doi.org/10.1016/j.midw.2020.102715.

Disclosure: R. Boers: None; **G. Terry**: None; **B. Mehta**: Amgen, 1, Horizon, 1.

Abstract Number: 0795

Molecular Stratification of Rheumatoid Arthritis Patients by Multi-Omics Integration Reveals Disease Status and Predictors of Therapeutic Response

Ismael Sanchez-Pareja[1], Daniel Toro[2], Carlos Pérez Sánchez[3], Laura muñoz-Barrera[1], Tomás Cerdó[1], Elena Moreno-Caño[4], Sagrario Corrales[1], Lydia Formanti Alonso[5], Rafaela Ortega-Castro[6], Jerusalén Calvo[5], Lourdes Ladehesa[7], Concepción Aranda-Valera[5], M Carmen Abalos-Aguilera[8], Christian Merlo-Ruiz[8], MARIA ANGELES AGUIRRE ZAMORANO[1], Marta Alarcon-Riquelme[9], Alejandro Escudero Contreras[5] and Chary López pedrera[10], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [2]GENYO / Karolinska Institutet, Granada / Stockholm, Spain, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [4]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Córdoba, Spain, [5]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [6]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [7]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [8]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [9]Fundacion Progreso y Salud, Andalusian Government, Granada, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis (0795–0800)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: To characterize molecular profiles of RA patients through multi-omics integration and evaluate their associations with disease status and therapeutic response to csDMARDs, TNF inhibitors (TNFi), and JAK inhibitors (JAKi).

Methods: Transcriptomic profiling was performed on PBMCs from established RA patients (n=206; 177 starting TNFi or JAKi), early RA (n=53; 30 initiating csDMARDs), and healthy donors (HD, n=42) using RNA-seq (Illumina). Serum levels of 92 inflammatory proteins were measured via Proximity Extension Assay (Olink). Therapeutic responses were assessed at six months according to EULAR criteria. Multivariate and machine learning approaches identified molecular subgroups and predictive biomarkers.

Results: Unsupervised clustering of PBMC transcriptomes identified three patient groups with distinct gene module involving innate and adaptive immune responses, inflammation, and cellular metabolism, most notably in cluster 1 (CL1) (Figure 1A).

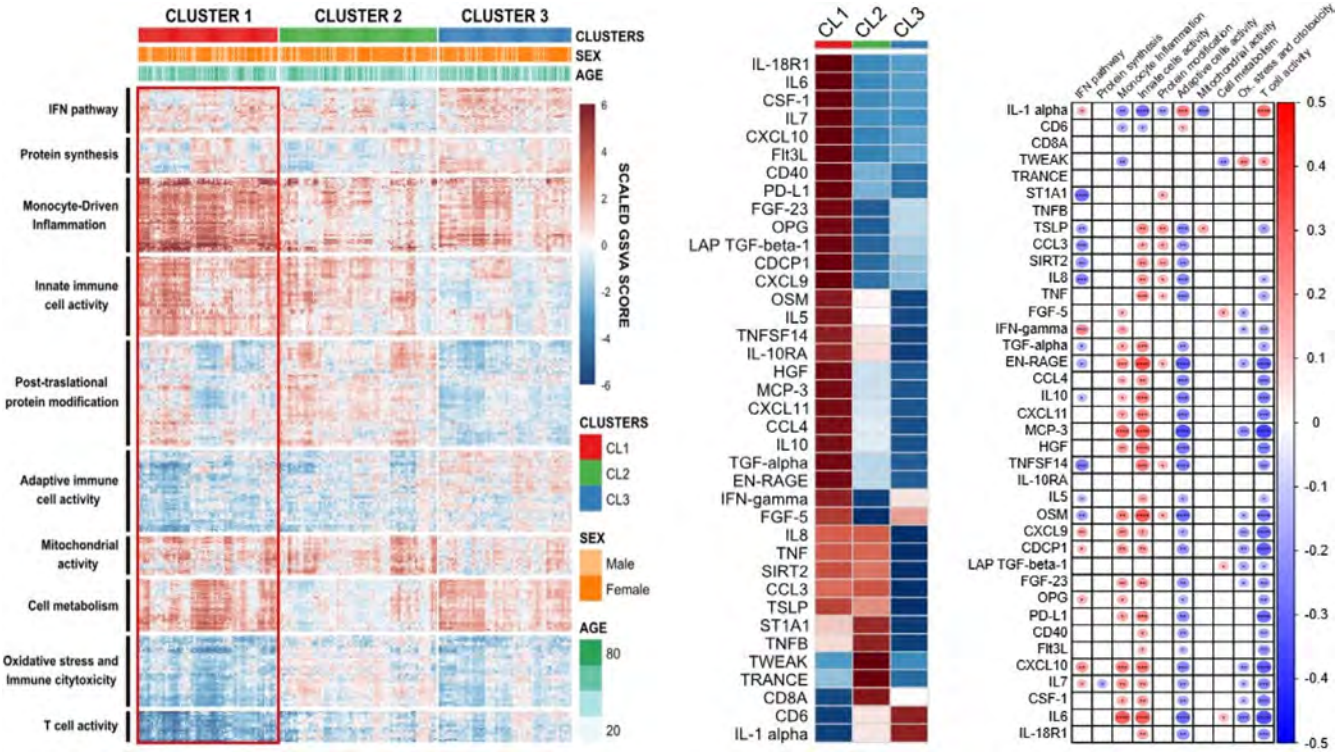


Figure 1. (A) Unsupervised clustering of PBMC transcriptomes with functional annotation of associated gene modules. (B) Differential expression profile of circulating inflammatory proteins across patient subgroups. (C) Correlation between altered inflammatory proteins and PBMC transcriptomic modules.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Circulating proteomic profiles supported these findings; 38 proteins were differentially expressed, highlighting a strong inflammatory signature in CL1 (Figure 1B & 1C).

These molecular features correlated significantly with disease activity (DAS28, SDAI), autoantibodies, and cardiovascular risk, with CL1 patients exhibiting higher activity, autoantibody titres, and systemic inflammation.

Established RA showed a greater number of differentially expressed genes and proteins compared to early RA, indicating increasing immune complexity.

Stronger correlations between molecular alterations and clinical outcomes in established RA underscored progressive molecular deregulation.

Machine learning models achieved an AUC over 0.8 in predicting response, featuring specific transcriptomic signatures: i) csDMARDs: high metabolic gene expression and low oxidative stress genes; ii) TNFi: high inflammatory and low cytotoxicity gene expression. Iii) JAKi: elevated interferon-related and decreased mitochondrial gene expression.

Clinically applicable predictive models, combining proteomic and clinical data demonstrated high accuracy: i) csDMARDs: five dysregulated inflammatory proteins, elevated monocyte count, and high SDAI; ii) TNFi: nine proteins and high disease activity scores; iii) JAKi: four proteins, high lymphocyte count, and tender joint count. Baseline inflammatory burden predicts response to csDMARDs and TNFi, while lymphocytic activity is more predictive for JAKi response.

Conclusion: Molecular profiles allow stratification of RA patients based on disease stage and clinical features. Progression involves increased molecular complexity, and treatment responses correlate with specific pre-treatment signatures. These findings highlight the potential of integrative omics to inform personalized therapy in RA.

Acknowledgments:

Supported by EU/EFPIA IMI-JU 3TR, ISCIII (PI24/00959, CD21/00187, RICOR-24/0007/0019), co-financed by European Union, and MINECO (RYC2021-033828-I/PID2022-141500OA-I00).

Disclosure: I. Sanchez-Pareja: None; **D. Toro**: None; **C. Pérez Sánchez**: None; **L. muñoz-Barrera**: None; **T. Cerdó**: None; **E. Moreno-Caño**: None; **S. Corrales**: None; **L. Formanti Alonso**: None; **R. Ortega-Castro**: None; **J. Calvo**: None; **L. Ladehesa**: None; **C. Aranda-Valera**: None; **M. Abalos-Aguilera**: None; **C. Merlo-Ruiz**: None; **M. AGUIRRE ZAMORANO**: None; **M. Alarcon-Riquelme**: None; **A. Escudero Contreras**: None; **C. López pedrera**: None.

Abstract Number: 0796

Deciphering Synovial Fluid Immune Dysregulation in Rheumatoid Arthritis through Cytokine Profiling and Single-Cell Transcriptomics

Manon LESTURGIE-TALAREK[1], Francesco Carbone[2], Virginie Gonzalez[3], Adrien Schvartz[2], Sophie Hecquet[4], Fiona Oudart[5], Marion Thomas[6], Roberto D'Alessandro[7], Yannick Allanore[8], Mickael Menager[2] and Jérôme AVOUAC[9], [1]Paris University, Paris, France, [2]Institut Imagine, Paris, [3]INSERMU1016, Paris, France, [4]Cochin Hospital, Paris, France, [5]APHP - Cochin hospital, Paris, France, [6]APHP, Paris, France, [7]Cochin Hospital, Paris, [8]Université Paris Cité, Paris, France, [9]Rheumatology department, Cochin hospital, Paris, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis (0795–0800)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Rheumatoid arthritis (RA) is driven by complex inflammatory pathways involving immune cell infiltration into synovial tissue and fluid. Synovial fluid (SF) provides direct insight into local disease mechanisms. Few studies have applied multiplex or single-cell transcriptomic technologies to dissect its cytokine and cellular composition.

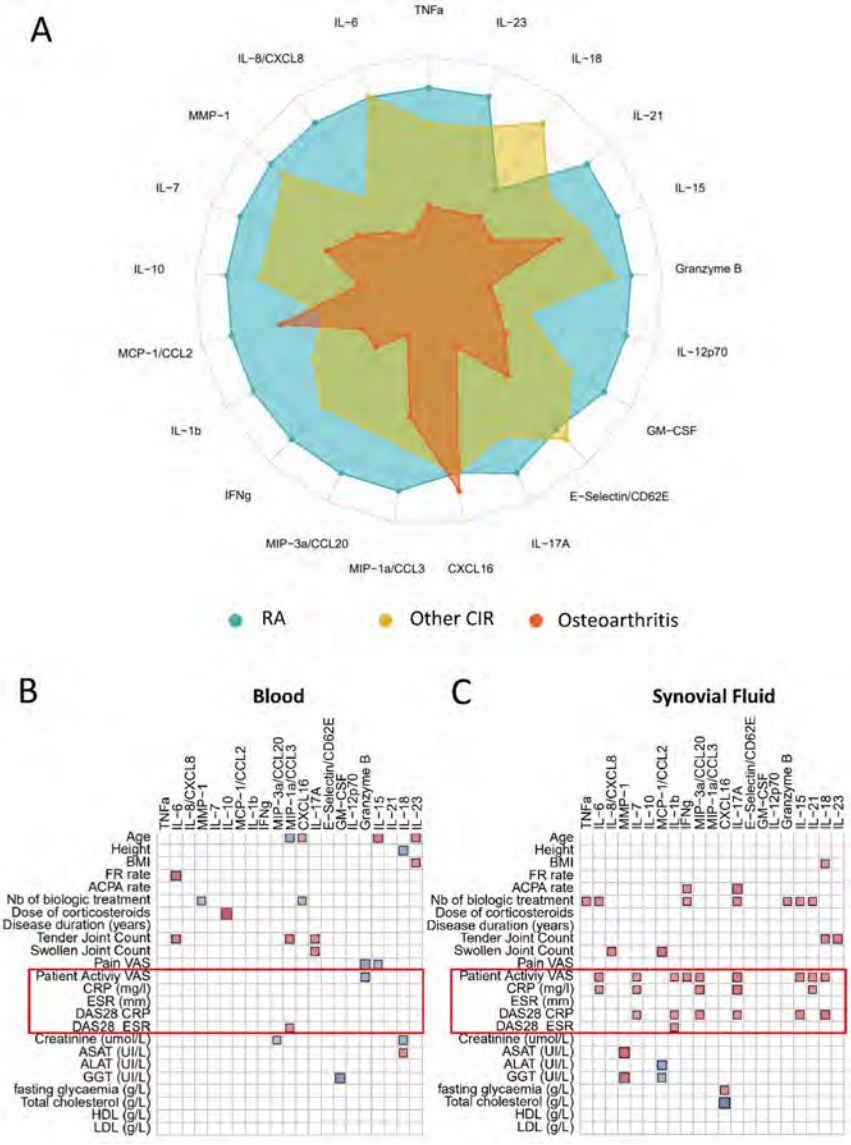


Figure1. Cytokine profiles and correlations with clinical and biological parameters in RA. (A) Radar plot illustrating the relative concentrations of 21 cytokines in synovial fluid (SF) from rheumatoid arthritis (RA, blue), other chronic inflammatory rheumatic diseases (CIR, yellow), and osteoarthritis (OA, orange). Each axis represents a specific cytokine, with values normalized to highlight differences between disease groups. (B) Correlation matrix (corrplot) between cytokines measured in blood and various clinical and biological parameters in RA patients. (C) Correlation matrix (corrplot) between cytokines measured in blood and various clinical and biological parameters in RA patients. Only significant Spearman correlation coefficients are represented by the intensity of the colour and the size of the square. Red: positive correlation. Blue: negative correlation. The boxed area highlights strong correlations between cytokines and markers of clinical disease activity, including CRP, DAS28-CRP, and patient-reported pain (VAS). ACPA: Anti-citrullinated protein antibodies. CRP: C-reactive protein. DAS28: Disease Activity Score in 28 joints. ESR: Erythrocyte sedimentation rate. VAS: Visual Analog Scale. TNF-α: Tumor Necrosis Factor-alpha. IL: Interleukin. CXCL/CCL: Chemokines.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The objective was to (1) characterize the cytokine profile of SF in RA vs other chronic inflammatory rheumatic diseases (CIRD) and osteoarthritis (OA); (2) compare SF and serum cytokines in RA; (3) explore the single-cell transcriptomic signature of RA SF mononuclear cells (SFMCs) vs. peripheral blood mononuclear cells (PBMCs).

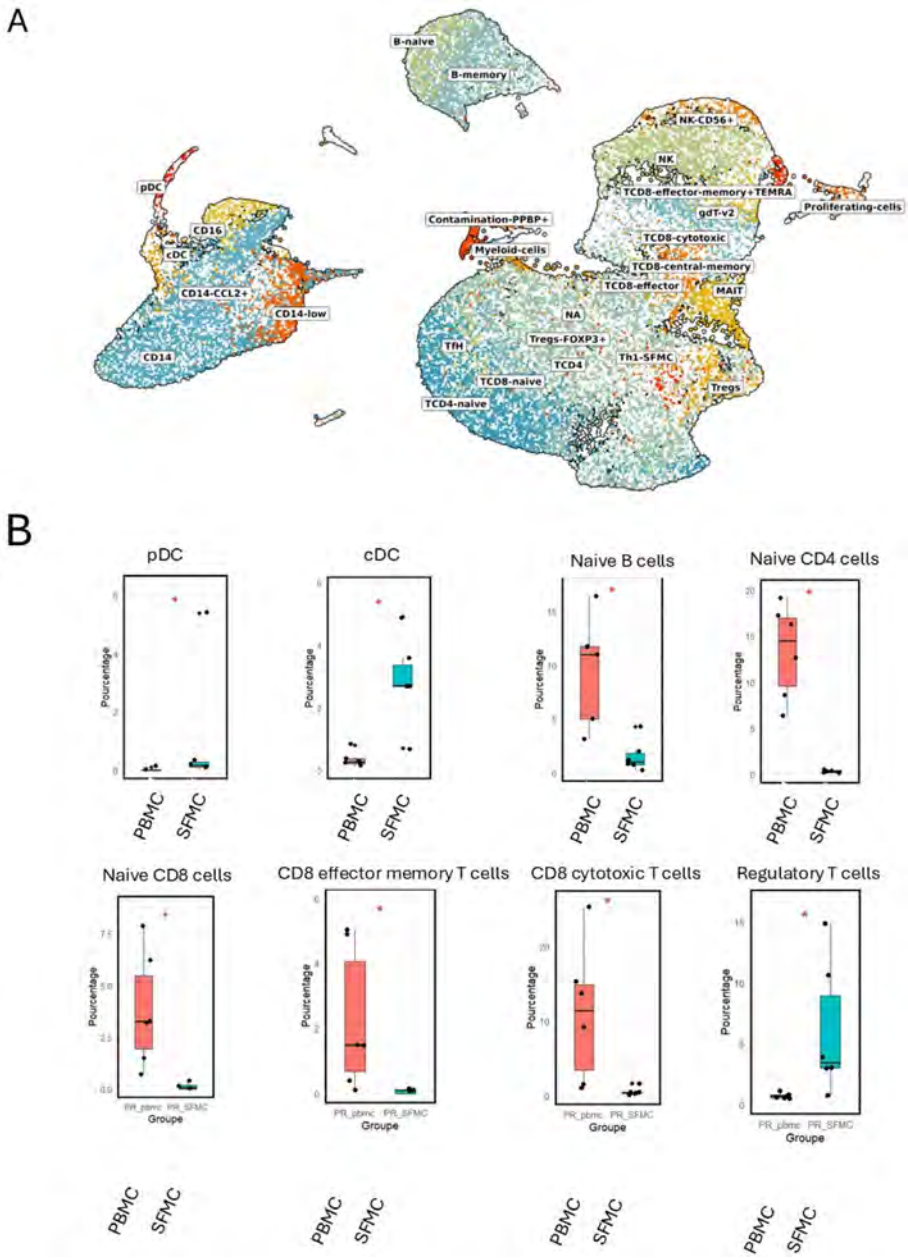


Figure 2. Immune cell composition in peripheral blood and synovial fluid of rheumatoid arthritis patients (A) Uniform Manifold Approximation and Projection (UMAP) visualization of immune cell populations from peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) of patients with rheumatoid arthritis. Distinct cell populations are annotated based on marker expression, including dendritic cells (pDC, cDC), B cells (naive, memory), T cells (CD4-naive, CD8-naive, CD8-effector, CD8-cytotoxic, regulatory T cells, Tregs), MAIT cells, and others. (B) Boxplots showing the proportions of specific immune cell subsets in PBMCs versus SFMCs. Cell subsets analyzed include pDC, cDC, naive B cells, naive CD4 T cells, naive CD8 T cells, CD8 effector memory T cells, CD8 cytotoxic T cells, and regulatory T cells. Significant differences between PBMCs and SFMCs are indicated by an asterisk (*). PBMCs: Peripheral blood mononuclear cells. SFMCs: Synovial fluid mononuclear cells. pDC: Plasmacytoid dendritic cells. cDC: Conventional dendritic cells. Tregs: Regulatory T cells. MAIT: Mucosal-associated invariant T cells. UMAP: Uniform Manifold Approximation and Projection

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: SF samples from 115 patients (45 RA, 48 CIRD, 22 OA) were analyzed using Luminex (21 cytokines including TNF-α, IL-1β, IL-6, IL-17, GM-CSF, IL-23, and CCL20). Paired serum samples were available for 29 RA patients. scRNA-seq was performed on freshly isolated SFMCs and PBMCs from six RA patients using 10X Chromium and CellRanger pipelines. Unsupervised clustering and differential expression analyses were used to define cellular subpopulations and compare their distribution.

Results: RA SF showed significantly higher levels of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-17, Granzyme B, CCL20) than OA (Fig.1A). IL-8, CCL2, and CCL3 were also elevated compared to CIRD. In RA, cytokines were consistently higher in SF than in serum and strongly correlated with CRP and DAS28-CRP, while no significant correlations were observed in serum (Fig. 1B). Heatmap analysis identified two distinct cytokine profiles in RA SF: one characterized by high cytokine secretion and elevated leukocyte count and CRP, and another with lower or moderate cytokine levels, reflecting heterogeneity in local inflammatory responses among RA patients.

scRNA-seq identified 27 immune cell clusters: 7 myeloid, 20 lymphoid (Fig. 2A). SFMCs were enriched in conventional (FC = 3.5) and plasmacytoid dendritic cells (FC = 5.5), and depleted in naïve B and T cell subsets, including CD4+ and CD8+ T cells (Fig. 2B). A distinct CD4+ T cell subset expressing PD-1, IL-17, Granzyme A, and IFN-γ was identified in SFMCs, indicating a pro-inflammatory phenotype. Regulatory T cells were enriched, while cytotoxic and effector memory CD8+ T cells were reduced (Fig. 2B).

Conclusion: RA SF exhibits a compartmentalized immune response characterized by cytokine enrichment and effector cell activation. Elevated levels of CCL20, CCL2, CCL3, and CCL8 may support dendritic cell and effector T cell recruitment into the joint. Despite this chemotactic environment, naïve T cells were markedly depleted, suggesting selective homing or local maturation. Increased IL-17 and Granzyme B at both protein and transcript levels were consistent with the presence of an inflammatory CD4+ T cell cluster co-expressing IL17A, GZMA, and PRF1. These findings reveal a coordinated inflammatory network in RA synovium, linking chemokine-mediated recruitment to local T cell activation, and highlight potential therapeutic targets identified through integrated cytokine and single-cell analysis.

Disclosure: M. LESTURGIE-TALAREK: None; **F. Carbone**: None; **V. Gonzalez**: None; **A. Schvartz**: None; **S. Hecquet**: None; **F. Oudart**: None; **M. Thomas**: None; **R. D'Alessandro**: None; **Y. Allanore**: None; **M. Menager**: None; **J. AVOUAC**: None.

Abstract Number: 0797

Spatial transcriptomics identifies density-sensing fibroblasts in synovial lining

Sonia Presti[1], Kseniia Anufrieva[2], Ce Gao[3], Sean Prell[2], Philip Blazar[2], Jeffrey Lange[2], Morgan Jones[2], Mihir Wechalekar[4], Michael Brenner[2], Ilya Korsunsky[5], **Shideh Kazerounian**[2] and Kevin Wei[6], [1]Standford University, Stanford, [2]Mass General Brigham, Boston, [3]Division of Rheumatology, Inflammation and Immunity, DOM, BWH; Harvard Medical School, Boston, MA, [4]Flinders Medical Centre, Adelaide, Australia, [5]Division of Rheumatology, Inflammation and Immunity, DOM, BWH; Division of Genetics, DOM, BWH; Harvard Medical School, Boston, MA, [6]Brigham and Women's Hospital at Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis (0795–0800)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The synovial lining is crucial for joint homeostasis, forming a barrier and producing lubricants through specialized fibroblasts. These fibroblasts differ from sublining fibroblasts, which are involved in inflammation and matrix remodeling. While vascular Notch signaling helps define vascular fibroblast positional identity (Wei et al. 2020), the factors shaping synovial lining fibroblast identity are unclear. Using spatial transcriptomics on synovial biopsies from RA patients in remission, we identify a density-dependent mechanism regulating lining fibroblast identity and suggest CREB5, SOX5, and FOXO1 as key transcriptional regulators.

Methods: Synovial tissue and synovial fibroblast micromasses were processed using the Xenium In Situ Gene Expression protocol (10X Genomics, CG000582 Rev D) with a custom 400-gene panel (Bhamidipati et al. 2025). For bulk RNA-seq and qRT-PCR, synovial fibroblasts were seeded at densities of 75–600 cells/mm^2 in 96-well plates for 3 days. For siRNA knockdown, cells were transfected with siRNA at 200K/well in 6-well plates and then re-seeded at varying densities.

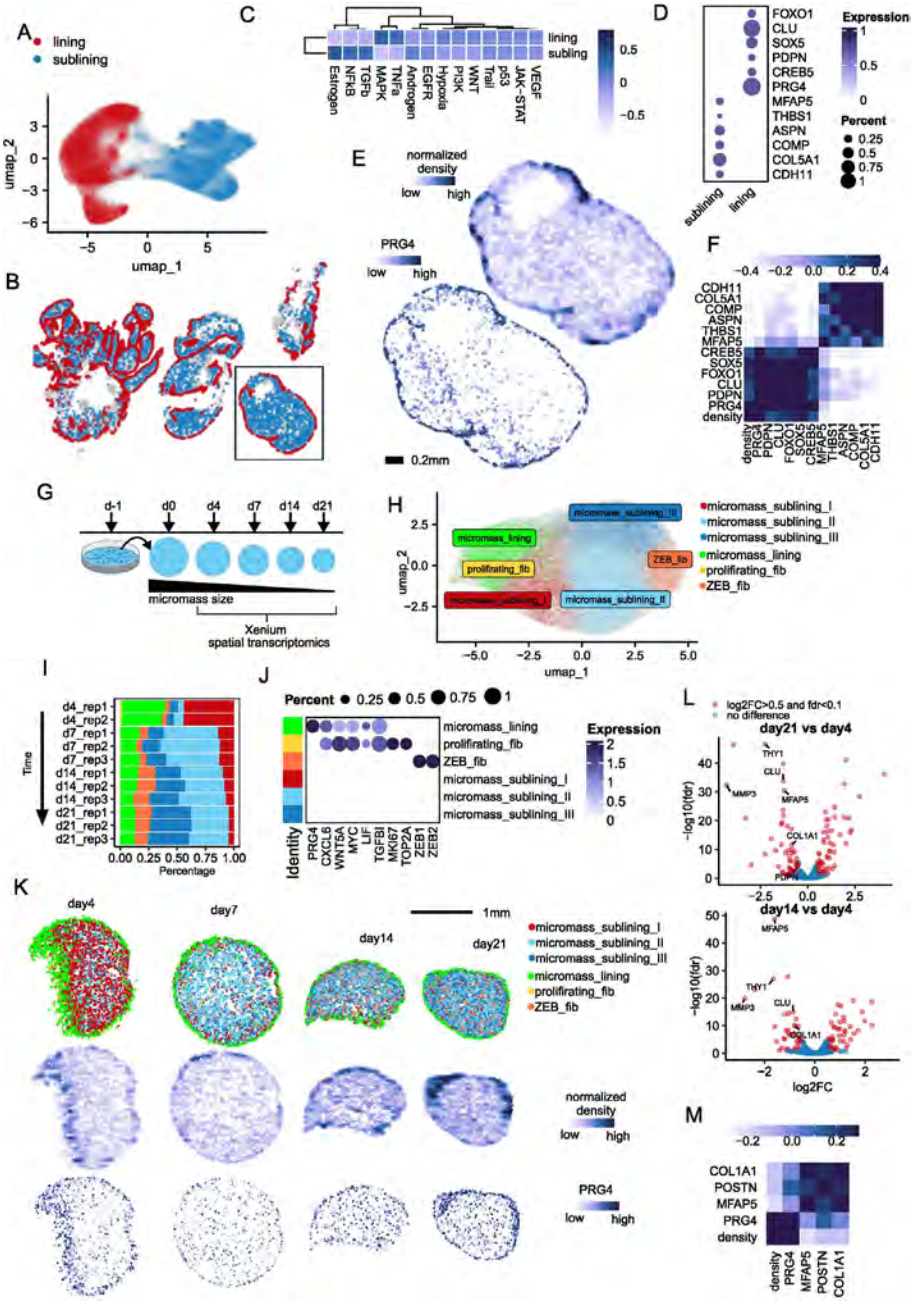


Figure 1. Characterization of fibroblast populations in RA synovial tissue and synovial fibroblast micromass culture system

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

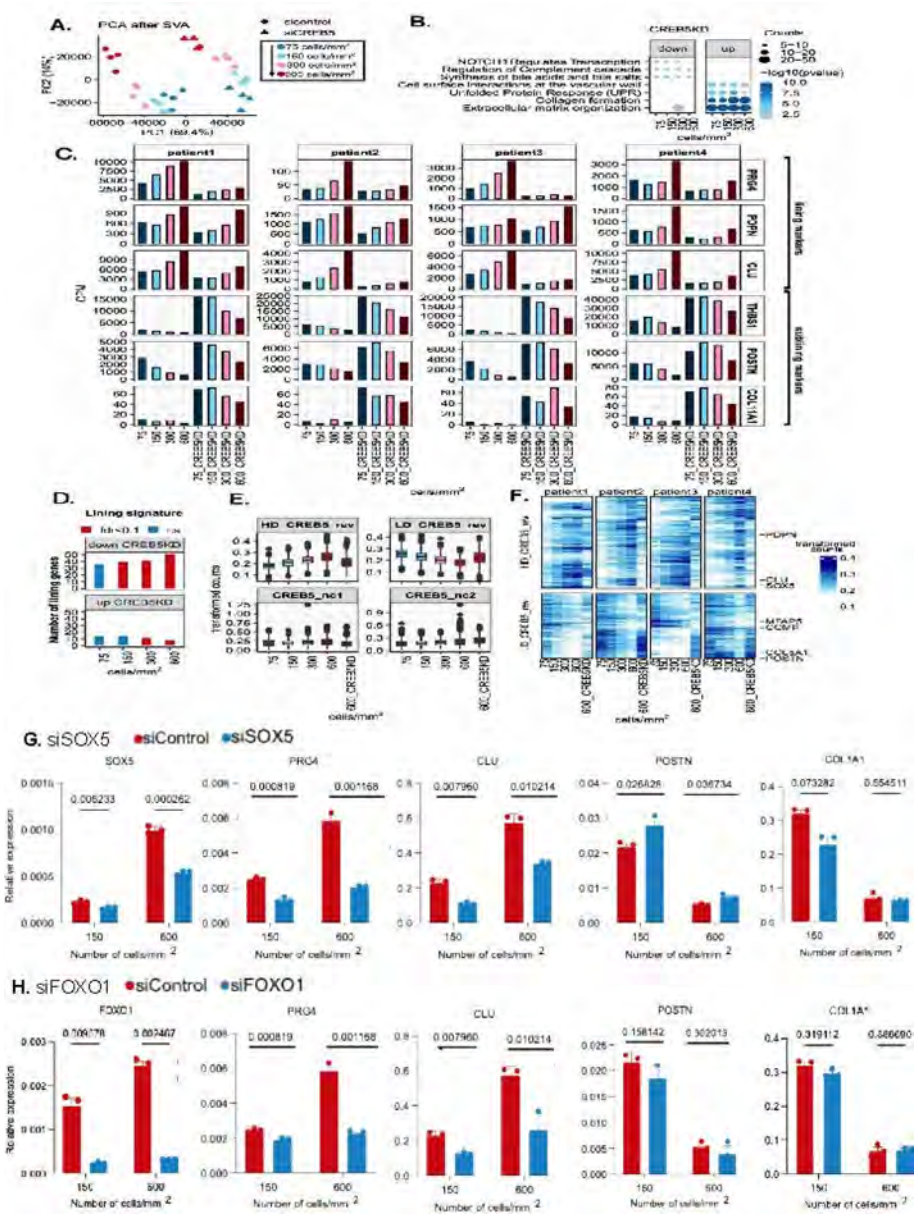


Figure 2. Bulk RNA-seq analysis of CREB5 KD (A-F) and qRT-PCR analysis of SOX5 and FOXO1 KD in synovial fibroblasts

Results: Spatial transcriptomics identified two fibroblast clusters in synovial tissue from RA patients in clinical remission: lining fibroblasts in dense, peripheral regions and sublining fibroblasts in less dense, central areas. A similar spatial organization was observed in synovial fibroblast micromass cultures maintained for 21 days. Extended culture led to increased accumulation of sublining fibroblasts in the central region, while lining fibroblasts remained localized to the periphery. Among the genes enriched in high-density regions of synovial tissue and fibroblast micromass cultures were the transcription factors CREB5, SOX5, and FOXO1, which exhibited spatial distribution patterns similar to canonical lining markers (PRG4, CLU, PDPN). These factors emerged as key candidates for regulating fibroblast identity. *In vitro* knockdown of CREB5 significantly reduced lining marker expression and increased sublining markers in a density-dependent manner. Similarly, knockdown of SOX5 and FOXO1 decreased lining marker expression without significantly affecting sublining marker levels.

Conclusion: In summary, our findings identify a density-responsive subset of lining fibroblasts defined by elevated CREB5, SOX5, and FOXO1 expression. We propose that increased cell density may activate as-yet-unidentified upstream signaling pathways that modulate the expression and/or activity of CREB5, FOXO1, and SOX5. Acting individually or synergistically,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

these transcription factors appear to mediate a cell density–dependent phenotypic transition from sublining to lining fibroblast states, thereby contributing to fibroblast identity.

Disclosure: S. Presti: None; **K. Anufrieva**: None; **C. Gao**: None; **S. Prell**: None; **P. Blazar**: Endo Pharmaceuticals, 2; **J. Lange**: Cambridge Scholars Publishing, 9, OnPoint Knee, 1, 9, Smith and Nephew, 2; **M. Jones**: Grunenthal, 1, Pacira, 5; **M. Wechalekar**: GlaxoSmithKlein(GSK), 5, Janssen, 5; **M. Brenner**: None; **I. Korsunsky**: Mestag Therapeutics, 2; **S. Kazerounian**: None; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2.

Abstract Number: 0798

Inhibition of Wnt Signaling Attenuates Inflammatory Arthritis Severity

Alisa Mueller[1], Angela Zou[2], Lucy-Jayne Marsh[3], Samuel Kemble[3], Saba Nayar[3], Gerald Watts[4], Cassandra Murphy[5], Emily Taylor[3], Triin Major[3], David Gardner[6], Christopher Buckley[7], Kevin Wei[8], Soumya Raychaudhuri[5], ilya Korsunsky[5], Andrew Filer[9], Adam Croft[10] and Michael Brenner[11], [1]Stanford University and VA Palo Alto Health Care System, Stanford, CA, [2]Harvard Medical School, Boston, MA, [3]University of Birmingham, Birmingham, United Kingdom, [4]Harvard Medical School, Brookline, MA, [5]Brigham and Women's Hospital, Boston, MA, [6]University of Birmingham, Havelock North, New Zealand, [7]University of Oxford, Oxford, United Kingdom, [8]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [9]The University of Birmingham, Birmingham, United Kingdom, [10]University of Birmingham, Hagley, Stourbridge, United Kingdom, [11]Brigham and Women's Hospital, Harvard Medical School, Newton, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis (0795–0800)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Fibroblasts are critical in promoting pathogenic synovial inflammation and bone erosion in rheumatoid arthritis (RA). Moreover, recent studies have pointed to their potential contribution to treatment-refractory disease, highlighting the value of targeting these cells therapeutically. Our prior work identified Wnt signaling as a novel mechanism

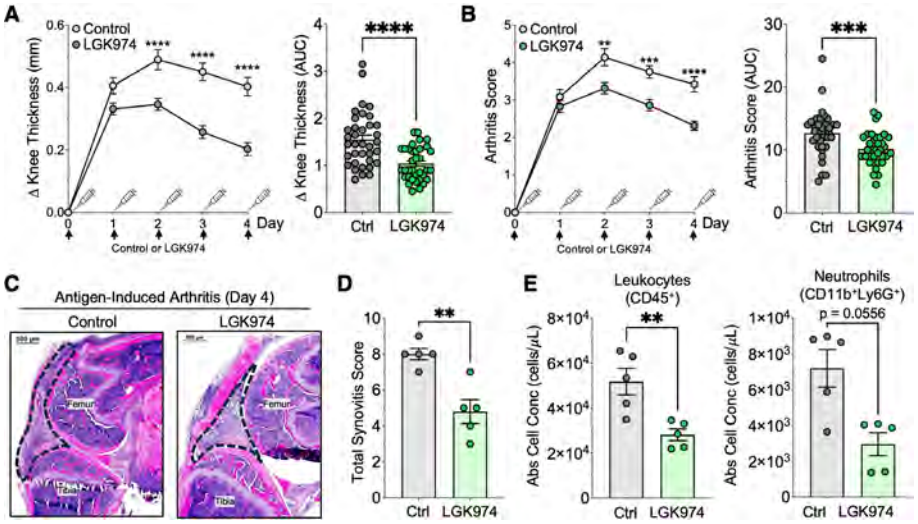


Figure 1: Inhibition of Wnt signaling reduces arthritis severity and leukocyte infiltration in a mouse model of inflammatory arthritis. (A-B) Plots and AUC calculations for knee thickness measurements (A) and clinical arthritis scores (B) at the time points indicated from mice that underwent antigen-induced arthritis (AIA) and have been treated with the Wnt signaling inhibitor LGK974 (n=35) or a vehicle control (n=36). (C-D) Representative H&E images (C) and histology synovitis scores (D) from knee joints taken from AIA mice treated with LGK975 (n=5) or control (n=5). Dotted lines indicate outline of synovial infiltrate. (E) Flow cytometry data showing absolute numbers of leukocytes and neutrophils derived from knee synovial tissue of AIA mice treated with LGK974 (n=5) or control (n=5).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

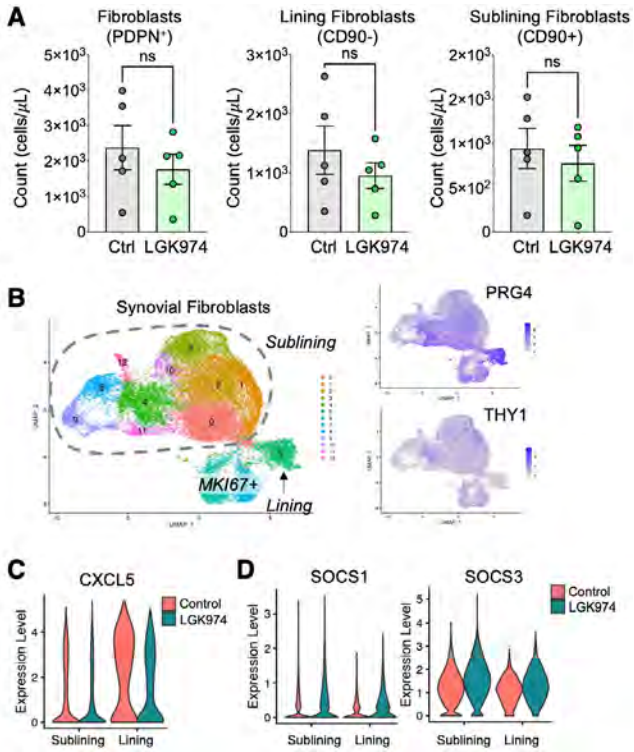


Figure 2: Wnt pathway blockade decreases the inflammatory potentiation of synovial fibroblasts during arthritis. (A) Flow cytometry showing absolute numbers of fibroblast populations in AIA mice treated with LGK974 (n=5) or vehicle control (n=5). (B) UMAP showing 34,728 fibroblasts from AIA mice treated with LGK974 (n=3) or vehicle control (n=3). PRG4+ lining, THY1+ sublining, and MKI67+ proliferative fibroblast subpopulations are depicted. (C-D) Violin plots showing expression of the chemokine CXCL5 (C) and immune regulators SOCS1 and SOCS3 (D) in sublining and lining fibroblasts from single-cell RNA sequencing of synovial tissue from AIA mice treated with LGK974 (n=3) or control (n=3).

driving stromal inflammation. In response to non-canonical Wnt activation, human synovial fibroblasts markedly increase production of inflammatory cytokines and chemokines *in vitro*. Further, we found that Wnt activation increases inflammatory arthritis severity and duration *in vivo* in a mouse model. Our analyses of human disease show that fibroblast Wnt activation signatures are increased in RA synovium and across other inflammatory conditions. Here, we investigate the therapeutic potential of Wnt pathway blockade and demonstrate that inhibiting Wnt signaling reduces arthritis severity and synovial inflammation in a mouse model of inflammatory arthritis.

Methods: C57Bl/6 mice underwent antigen-induced arthritis (AIA) by subcutaneous administration of methylated BSA (mBSA) at day -21 followed by intraarticular knee injection of mBSA at day 0. Mice were given daily intraperitoneal injections of the Wnt signaling inhibitor LGK974 or a vehicle control on days 0-4. Knee thickness and clinical scores were assessed. Synovial tissue was collected at day 4 and processed for H&E, flow cytometry analysis, cell sorting and single-cell RNA sequencing.

Results: To investigate whether the abrogation of Wnt signaling would reduce the severity of inflammatory arthritis, we utilized the AIA model and treated mice with LGK974, a pharmacologic inhibitor of Wnt ligand secretion. Mice treated with LGK974 exhibited a marked decrease in knee swelling (Fig 1A) and clinical arthritis scores (Fig 1B) compared to vehicle controls. Histologic analyses of knee joints collected at day 4 revealed decreased lining hyperplasia and leukocyte infiltration (Fig 1C-D). Moreover, flow cytometry analyses of cells isolated from synovial tissue showed decreased absolute numbers of leukocytes and a trend towards reduced neutrophil counts (Fig 1E). While total numbers of fibroblasts did not significantly differ in synovial tissue from LGK974- and control-treated mice (Fig 2A), both lining and sublining fibroblasts (Fig 2B) exhibited changes in transcriptomic phenotype. Specifically, synovial fibroblasts from LGK974-treated mice showed decreased expression of CXCL5, a chemokine that participates in neutrophil recruitment in RA and that is increased upon Wnt administration (Fig 2C). They also upregulated SOCS1 and SOCS3, inhibitors of JAK signaling (Fig 2D). These results suggest that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

blocking Wnt signaling dampens synovial fibroblast inflammatory activation during arthritis and, in turn, their ability to recruit and activate infiltrating leukocytes.

Conclusion: Collectively, our findings demonstrate the utility of Wnt pathway inhibition in reducing inflammatory arthritis severity. This work identifies a novel fibroblast-targeted therapeutic avenue for RA with a compelling potential value for patients whose disease is recalcitrant to conventional treatment modalities.

Disclosure: A. Mueller: None; **A. Zou**: None; **L. Marsh**: None; **S. Kemble**: None; **S. Nayar**: None; **G. Watts**: None; **C. Murphy**: None; **E. Taylor**: None; **T. Major**: None; **D. Gardner**: None; **C. Buckley**: Bristol-Myers Squibb(BMS), 5, Mestag, 11; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **S. Raychaudhuri**: Bonito, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Mestag, 1, 8, Nimbus, 2, Pfizer, 1, Sonoma, 1, 8, Visterra, 6; **i. Korsunsky**: Mestag therapeutics, 2; **A. Filer**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 2, 5, Synact, 5; **A. Croft**: None; **M. Brenner**: AbbVie/Abbott, 2, Johnson & Johnson, 5, Mestag Therapeutics, 2, 8, Moderna, 2, Ono Pharma, 5, Simcere, 2.

Abstract Number: 0799

Citrullination of neutrophil serine proteases enhances proteolytic activity, stability and autoantigenicity in Rheumatoid Arthritis

Mario Navarrete Lagos, Ramiza Zaman, Jun Kim, Jeba Atkia Maisha, Hani El-Gabalawy and **Liam O'Neil**, University of Manitoba, Winnipeg, MB, Canada

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis (0795–0800)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: In Rheumatoid Arthritis (RA), autoantibodies develop against endogenous proteins containing the amino acid citrulline, which results from a post-translational modification of arginine catalyzed by a family of peptidyl arginine deiminase (PAD) enzymes. Although citrullination is a ubiquitous physiological process, its impact on the structure and function of specific proteins is not well understood. Neutrophils contain 2 isoforms of PAD (2/4) and readily form citrullinated RA antigens during neutrophil extracellular trap (NETs) formation. However, the effects of citrullination on neutrophil protease activity have not been studied. We hypothesized that citrullination influences the activity of neutrophil serine proteases, namely Neutrophil Elastase (NE), Proteinase-3 (PR3) and Cathepsin G (CTG), which in turn may contribute to the pathogenesis of RA.

Methods: The activity of proteases and various biospecimens were analyzed using fluorogenic substrate after citrullination with PAD2/4 (confirmed by a cit-specific probe). Active protease sites were labelled and visualized using a probe (TAMRA-FP). Degradation of aggrecan, a proteoglycan found in cartilage, was determined. Cultured fibroblast-like synoviocytes (FLS) were treated with cit-PR3. IL-6/TNF and ACPA targeting cit-proteases were measured with ELISA.

Results: Using both recombinant proteases and neutrophil supernatant, proteolytic activity of NE, PR3 and CTG increased markedly after citrullination with PAD2, and to a lesser extent, PAD4 (Fig1A). For example, the activity of PAD2 cit-PR3 increased by 13-fold compared to native PR3. PAD2 also lead to enhanced stability of proteases, with detectable activity after 72 hours *in-vitro*, and evidence of protection from autoproteolysis (Fig1B-D) and exogenous proteases (trypsin, Fig

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

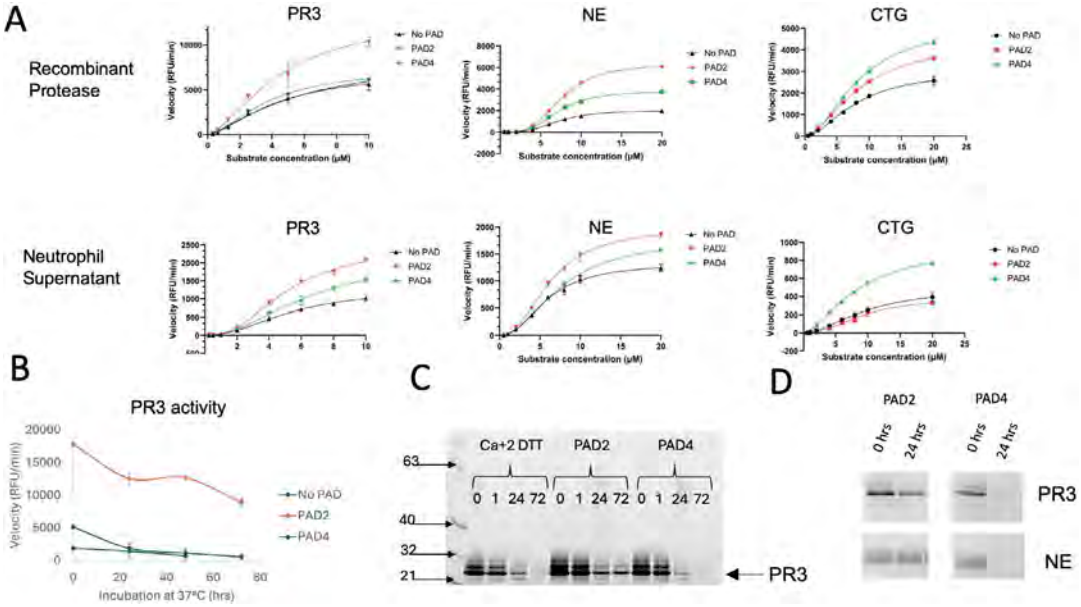


Figure 1: PAD2-citrullination enhances neutrophil serine protease activity and stability. (A) The effect of PAD2 and PAD4 on recombinant serine protease activity (upper) and neutrophil supernatant protease activity (lower) measured with a fluorogenic substrate (increasing concentrations x-axis) and enzyme velocity. (B) Proteinase-3 activity after citrullination with PAD2 (orange) and PAD4 (green) up to 72 hours in-vitro. Only PAD2 citrullinated PR3 had detectable activity at 48 and 72h. (C) Protein staining (sypro-ruby) or citrullinated PR3 by PAD2 or PAD4 compared to buffer (Ca/DTT), measured every 24 hours, revealing protection of autoproteolysis mediated by PAD2 citrullination. (D) A 24-h analysis comparing PAD2/4 citrullination in neutrophil elastase (NE) and PR3. PR3: Proteinase 3, NE: Neutrophil Elastase, CTG: Cathepsin G, DTT: Dithiothreitol (reducing agent).

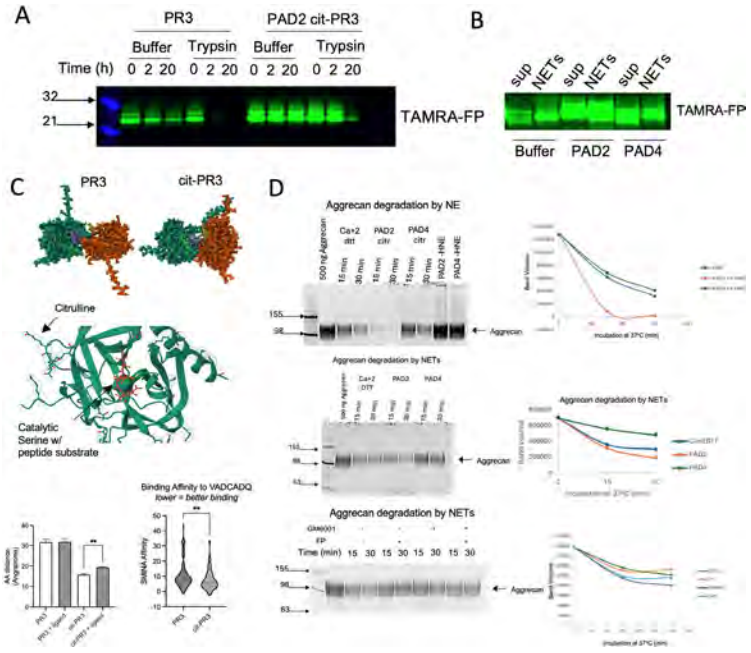


Figure 2: Citrullination induces a conformational change in neutrophil serine proteases which opens new catalytic sites to enhance activity, allowing for the degradation of aggrecan a proteoglycan in cartilage. (A) PAD2 citrullination of PR3 reveals new catalytic sites as evidenced by increased signal from a specific serine protease probe called TAMRA-FP. PR3 is protected from degradation by Trypsin, a common serine protease. (B) Evidence of new catalytic sites in neutrophil supernatants and NETs using TAMRA-FP in PAD2/PAD4 treated samples. (C) In-silico models of multimeric (dimer) proteinase-3 (upper structures) and a peptide ligand (VADCADQ, purple) which increases the distance between the 2 active sites in citrullinated PR3 but not native PR3 (lower left bar graph). Monomeric model (lower structure) revealing the peptide ligand (orange), citrulline (ball-stick) and the active serine (green sphere). SMINA affinity measure using a docking algorithm reveals a higher binding energy between the peptide substrate and cit-PR3 (lower right violin plot, $P<0.01$). (D) Degradation of aggrecan and cartilage proteoglycan by recombinant NE (upper), NETs (middle) and NETs treated with an aggrecanase (matrix metalloproteinase) inhibitors called GM6001 or a biotinylated form of the FP probe which inhibits protease function (lower).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

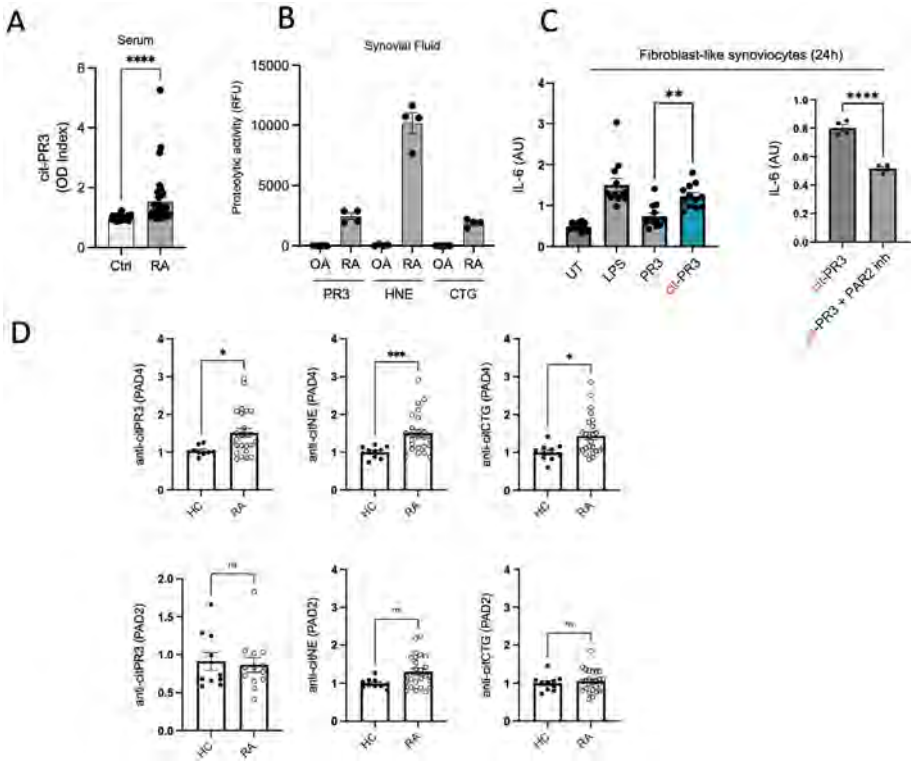


Figure 3: Proteases in RA serum, synovial fluid which serve as autoantigens. (A) Serum citrullinated proteinase-3 is higher in RA compared to controls (P<0.0001) (B) Detection of PR3, NE, and CTG in RA synovial fluid compared to OA. (C) Treatment of fibroblast-like synoviocytes (FLS) with PR3 and cit-PR3 (PAD2) leads to increased IL-6 production, which is reduced with pre-treatment with a protease activated receptor (PAR2) inhibitor. (D) Autoantibodies targeting various citrullinated neutrophil proteases via PAD4 (upper) or PAD2 (lower) (* P<0.05, ** P <0.01, *** P<0.001).

2A) in PR3 and NE. In the recombinant proteases, supernatant, and NETs, PAD2 citrullination enhanced the allosteric capacity of the protease multimers by opening new catalytic sites (Fig2A/B). This is suggestive of a conformational change induced by PAD which was confirmed by *in-silico* modelling (Fig2C). Models also suggested a higher binding energy between cit-PR3 and a peptide substrate. Aggrecan degradation was enhanced by PAD2-citrullination of NE and NETs. Using MMP and serine protease inhibitors, we found that degradation by NETs was undertaken by serine proteases, rather than aggrecanases (Fig2D). Serum cit-PR3 levels were elevated in RA than controls, and synovial fluid PR3, NE, and CTG activity were higher in RA compared to OA. FLS treated with cit-PR3 significantly increased the release of IL-6/TNF, and this was mediated by a protease activity receptor, PAR2 (Fig3C). Autoantibodies to PAD4 cit-proteases, but not PAD2, were higher in RA than controls (Fig3D).

Conclusion: PAD citrullination results in a gain of function for neutrophil serine proteases through conformational changes that result in enhanced proteolytic activity and stability. Although this process may provide a biological advantage for host defense, in the context of RA, this leads to degradation of cartilage components, inflammation and autoantibody formation.

Disclosure: M. Navarrete Lagos: None; **R. Zaman**: None; **J. Kim**: None; **J. Maisha**: None; **H. El-Gabalawy**: None; **L. O'Neil**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0800

Microbiota-Derived Indole Promotes Collagen-Induced Arthritis Type-17 Immunity through Intestinal Dendritic Cell Cytokine Production

Jing Li[1], Sucai Liu[2], Brenda Seymour[3], Brendan Allen[2], Le Yiphyo[2], Cassandra Levens[1] and Kristine Kuhn[4], [1]Rheumatology, Aurora, CO, [2]University of Colorado School of Medicine, Aurora, CO, [3]University of Colorado School of Medicine, Denver, CO, [4]2022 - 2023 / Adult/ University of Colorado, Aurora, CO

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Etiology and Pathogenesis (0795–0800)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: One of the most substantial impacts of microbe-host interactions at the intestinal mucosa is the development of type 17 immunity. A Th17 signature has been observed in pre-clinical RA, suggesting that type 17 immunity may play a role in the initiation of pre-clinical autoimmunity. Yet, the mechanistic connection between RA-associated bacteria and Th17 immunity remains a knowledge gap. Our prior work in the collagen-induced arthritis (CIA) model of inflammatory arthritis connected microbial dysbiosis with the catabolism of dietary tryptophan to indole, which was necessary for disease

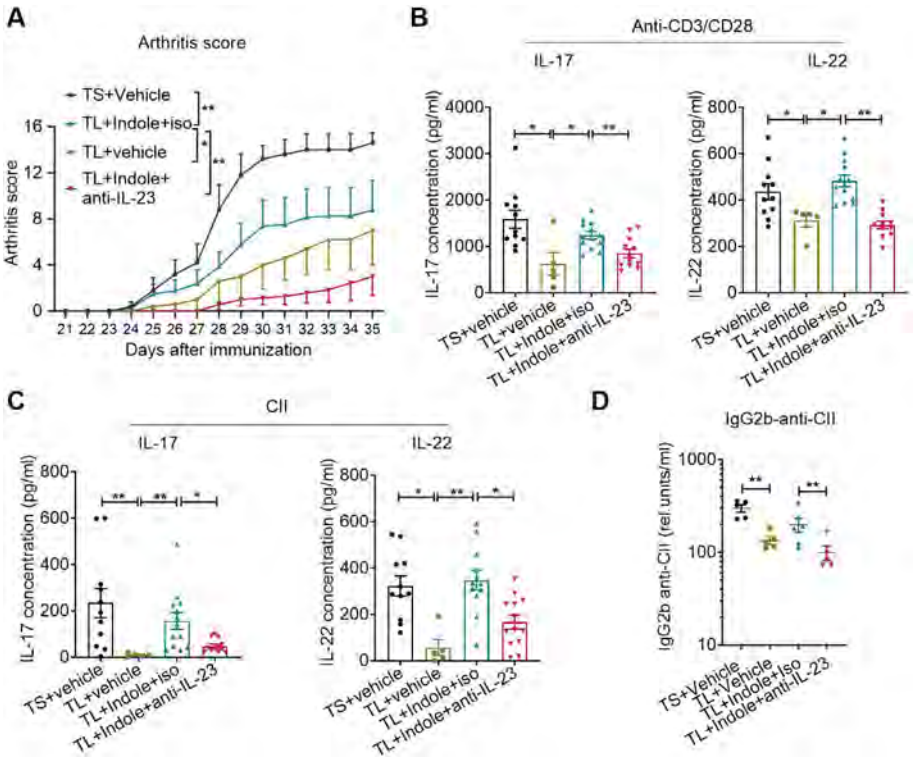


Figure 1. IL-23 neutralization suppresses indole-induced Th17 responses and autoantibodies. CIA was induced in 6–8-week-old male DBA/1 mice maintained on a tryptophan-low (TL) diet, followed by oral gavage of indole (200 µl of 10 mM, every other day). Mice were immunized intradermally on days 0 and 21 with type II bovine collagen (CII) emulsified in complete Freund's adjuvant (CFA). In addition, mice received intraperitoneal injections of either an isotype control antibody or anti–IL-23 neutralizing antibody (100 µg/mouse) once weekly on days 0, 7, 14, and 21. (A) Neutralization of IL-23 significantly reduced arthritis scores in indole-treated CIA mice compared to isotype control. (B) Ex vivo stimulation of splenocytes with anti-CD3/CD28 antibodies or (C) CII showed reduced production of IL-17 and IL-22 in the anti-IL-23 group, as measured by ELISA. (D) Serum levels of CII-specific IgG2b antibodies were also decreased in the anti–IL-23–treated group compared to controls. Data were expressed as mean ± SEM. Statistical significance was determined by two-way ANOVA with Tukey's multiple comparisons test (A), or Mann-Whitney test (B-D). *P < 0.05, **P < 0.01, ns: non-significant.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

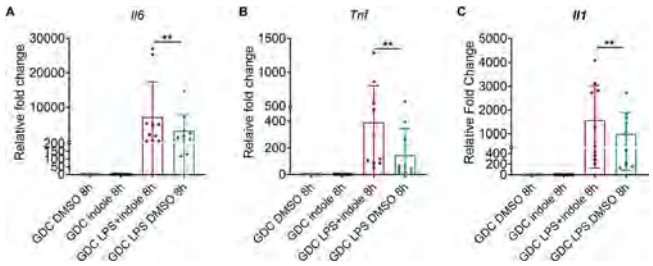


Figure 2. Indole enhances LPS-induced Th17-inducing cytokine expression in human GDCs. $CD14^+$ monocytes were isolated from peripheral blood mononuclear cells obtained from 10 healthy donors (5 male, 5 female). Cells were cultured in RPMI medium supplemented with 20 ng/ml recombinant human GM-CSF and IL-4 to generate GDCs. On day 3, retinoic acid (100 nM) was added to the culture. On day 5, GDCs were harvested and stimulated with the indicated stimuli for 8 hours. RNA was then extracted, and gene expression was analyzed by qPCR. Results showed that indole significantly enhanced the LPS-induced expression of IL-6, IL-1, and TNF in human GDCs. Data were expressed as mean ± SEM. Statistical significance was determined by Wilcoxon test (A-C). **P < 0.01.

via Th17 immunity and pathogenic autoantibody development. In this study, we aimed to examine the mechanism by which indole stimulates Th17 immunity.

Methods: Indole-CIA was induced in male 6-8-week old DBA/1 mice fed a tryptophan-low diet with every-other-day indole gavage (200μl of 10mM) and injected intradermally on days 0 and 21 with type II bovine (CII) emulsified in complete Freund's adjuvant. Mice also received intraperitoneal injections of 100μg/mouse either isotype control or anti-IL-23 neutralizing antibody once weekly at days 0, 7, 14, and 21 of CIA. Arthritis severity, immune cells, cytokines, and anti-CII antibodies were evaluated by flow cytometry and ELISA. Murine bone marrow–derived dendritic cells (BMDCs) and human gut-like dendritic cells (GDCs) from peripheral blood mononuclear cells were stimulated in vitro with 1μg/ml dose LPS plus 1μl DMSO or LPS plus 1 mM indole for 8-24 hours. The expression of cytokines was measured by qPCR. Signaling pathways were interrogated by RNA sequencing and immunoblot.

Results: IL-23 neutralization, compared to control antibody, significantly reduced the severity of indole-CIA, diminished Th17 cell and DC frequencies, and decreased CII autoantibodies (Fig 1). Upon ex vivo stimulation of splenocytes with CII or anti-CD3/CD28 antibodies, the anti-IL-23 treatment group exhibited significantly lower production of IL-17 and IL-22 compared to the control group (Fig 1). DCs produced Th17-differentiating cytokines at days 7-14 of indole-CIA. In vitro, qPCR analysis showed that indole significantly amplified LPS-induced expression of IL-23, IL-6, IL-1β, and TNF-α in both BMDCs and human GDCs (Fig 2). RNA sequencing of indole-stimulated GDCs followed by immunoblot analysis suggested that indole signaled through non-canonical pathways of aryl hydrocarbon receptor (AhR).

Conclusion: These findings suggest that microbiota-derived indole promotes CIA via priming of intestinal DCs to produce Th17-differentiating cytokines. Non-canonical signaling through AhR results in increased DC production of cytokines that are likely to induce Th17 cells. Blockade of Th17 cell differentiation by IL-23 neutralizing antibody resulted in significantly reduced disease through reduced Th17 cells producing IL-17 and IL-22. Reduction in IL-22 is likely the cause for reduced CII antibodies, although this has yet to be formally tested. Altogether, our data mechanistically connect microbial dysbiosis to the development of inflammatory arthritis, demonstrating one mechanism by which altered microbial ecology can lead to RA.

Disclosure: J. Jing Li: None; **S. Liu**: None; **B. Seymour**: None; **B. Allen**: None; **L. Yiphyo**: None; **C. Levens**: None; **K. Kuhn**: Solarea, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0801

Achieving Sustained Lupus Low Disease Activity State and Remission with Ianalumab (VAY736) in Patients with Systemic Lupus Erythematosus: A Post Hoc Analysis from a Phase II Study

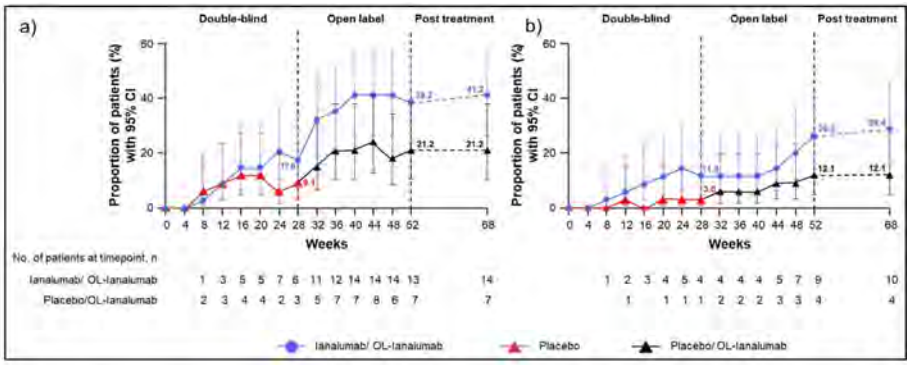
Eric Morand[1], Corine Gaillez[2], Stephen Oliver[3], Swati Ghanshani[4], Marilia Pozzobon[5], Weibin Bao[6] and **Ed Vital**[7], [1]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [2]Novartis Pharma AG, Basel, Switzerland, Croissy Sur Seine, France, [3]Novartis Pharma AG, Basel, Switzerland, [4]Novartis Healthcare Private Limited, Hyderabad, India, Hyderabad, India, [5]Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland, [6]Novartis Pharmaceuticals Corporation, Hanover, NJ, [7]University of Leeds, Leeds, England, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment I (0801–0806)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Ianalumab, a fully human monoclonal antibody against the B cell–activating factor receptor (BAFF-R), has a dual mechanism of action of B cell depletion through antibody-dependent cellular cytotoxicity and BAFF-R blockade. A treat-to-target approach, targeting Definition of Remission in SLE (DORIS) and Lupus Low Disease Activity State (LLDAS), has demonstrated potential in reducing organ damage progression and improving quality of life.[1] Here, we investigated the 52-week impact of ianalumab on attainment of LLDAS, DORIS, and glucocorticoid (GC) taper in patients with active SLE enrolled in a phase IIa study (NCT03656562).

Methods: Patients with SLE were randomized 1:1 to subcutaneous ianalumab 300 mg or placebo every 4 weeks (W). The study included two treatment periods consisting of a double-blind period with a comparison between ianalumab and placebo for 28W followed by a 24W open-label (OL) period with continued ianalumab 300 mg in the active arm (ianalumab/OL-ianalumab) and switch from placebo to ianalumab 300 mg (placebo/OL-ianalumab). Following 52W treatment, patients entered a post-treatment (PT) period up to W68. Patients on stable GC were required to undergo GC tapering from W4 to W16 and remain on the dose achieved through Week 28. Endpoints evaluated include: proportion of patients achieving LLDAS, DORIS, and tapered GC ≤5 mg at each visit; time-to-first LLDAS; cumulative time (defined as 20%/50% of time) spent in LLDAS and DORIS during the placebo-controlled period (28W) and the overall 52W treatment period; and

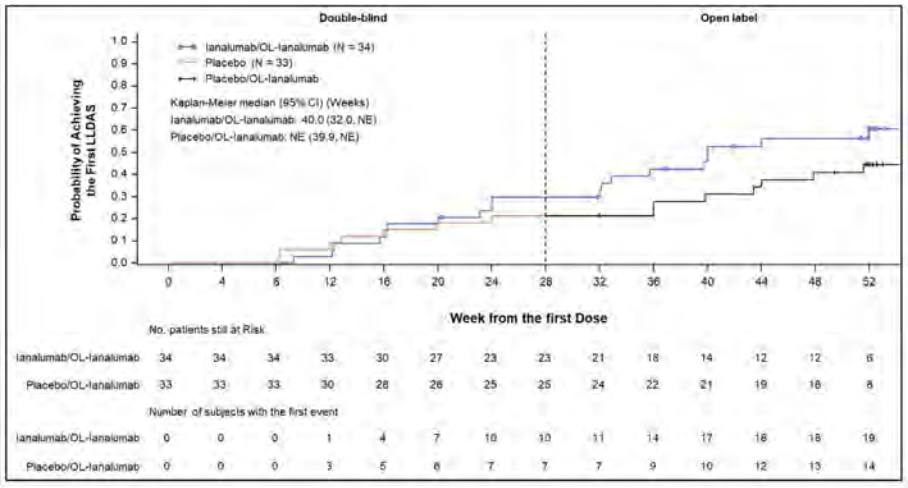


CI, confidence interval; DORIS, Definitions of Remission in Systemic Lupus Erythematosus; LLDAS, Lupus Low Disease Activity State; OL, open-label.
CIs were calculated using the Wilson score method with continuity correction.

Intermittent missing values are imputed by the worse of the two adjacent values only when both are observed and treated as non-responders otherwise.

Fig. 1. Proportion of patients who achieved a) LLDAS and b) DORIS by treatment and visit over the 52-week treatment period

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CI, confidence interval; LLDAS, Lupus Low Disease Activity State; NE, not estimable; OL, open-label. Patients who did not achieve LLDAS were censored at the end of the treatment.

Fig. 2: Time to first LLDAS over the 52-week treatment period

cumulative time with GC taper (≤5 mg and ≤ baseline dose). All efficacy outcomes are summarized descriptively. Time-to-event endpoints were assessed using Kaplan-Meier analysis.

Results: This analysis included 67 patients: 34 in ianalumab/OL-ianalumab and 33 in placebo/OL-ianalumab. Although LLDAS/DORIS attainment increased after switching, at W52, more patients in the ianalumab/OL-ianalumab group had achieved LLDAS and DORIS (38.2% and 26.5%) than those in placebo/OL-ianalumab (21.2% and 12.1%); this trend was maintained in the PT period (ianalumab/OL-ianalumab: 41.2% and 29.4%; placebo/OL-ianalumab: 21.2% and 12.1%; **Fig. 1a,1b**). Median time to first LLDAS was 40W in the ianalumab/OL-ianalumab group (**Fig. 2**). At W52, more patients in ianalumab/OL-ianalumab (85.3%) achieved GC taper than in placebo/OL-ianalumab (72.7%). During the 52W treatment period, cumulative time spent on LLDAS, DORIS, and tapered GC ≤5 mg was higher in ianalumab/OL-ianalumab than in placebo/OL-ianalumab (**Table 1**).

Table 1: Cumulative time spent on LLDAS, DORIS, and tapered GC ≤5 mg during the 28-week double-blind period and during the 52-week study period

	28-Week double-blind period		52-Week study period (double-blind + open-label)	
Assessment*	Ianalumab (N=34)	Placebo (N=33)	Ianalumab/OL-ianalumab (N=34)	Placebo/OL-ianalumab (N=33)
Time spent on LLDAS				
Cumulative time spent (days), mean (SD)	20.1 (37.0)	14.0 (33.4)	88.9 (102.9)	46.4 (86.0)
Percentage of patients who had ≥20% time spent, n (%)	7 (20.6)	4 (12.1)	14 (41.2)	6 (18.2)
Percentage of patients who had ≥50% time spent, n (%)	3 (8.8)	2 (6.1)	8 (23.5)	4 (12.1)
Time on DORIS remission				
Cumulative time spent (days), mean (SD)	13.7 (36.1)	2.8 (12.2)	44.6 (84.0)	14.9 (41.2)
Percentage of patients who had ≥20% time spent, n (%)	5 (14.7)	1 (3.0)	7 (20.6)	3 (9.1)
Percentage of patients who had ≥50% time spent, n (%)	1 (2.9)	0	3 (8.8)	0
Time with GC ≤5 mg and less than baseline level (whichever is lower)				
Cumulative time spent (days), mean (SD)	91.1 (74.7)	82.9 (85.3)	201.8 (138.2)	168.9 (159.3)
Percentage of patients who had ≥20% time spent, n (%)	22 (64.7)	18 (54.5)	25 (73.5)	19 (57.6)
Percentage of patients who had ≥50% time spent, n (%)	18 (52.9)	14 (42.4)	19 (55.9)	16 (48.5)

DORIS, Definitions of Remission in Systemic Lupus Erythematosus, GC, glucocorticoids; LLDAS, Lupus Low Disease Activity State; N, total number of patients; n, number of patients who spent time on the given assessment; SD, standard deviation.

*The patients on stable GC regimen were required to undergo guided GC tapering from Week 4 until Week 16 and remain on lowered GC dose achieved at Week 16 through Week 28.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: A 52W week of ianalumab treatment was associated with more time in LLDAS and DORIS, as well as higher attainment of GC taper goals compared to 28W placebo followed by 24W ianalumab exposure. This suggests that earlier ianalumab exposure led to cumulative clinical benefit in patients with SLE. Larger studies are required to confirm these findings.

Reference

1. Parra Sánchez AR et al. *Rheumatol Ther* 2023;10:1459-77.

Disclosure: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **C. Gaillez**: Novartis, 3; **S. Oliver**: Novartis, 3, 11; **S. Ghanshani**: Novartis, 3, 11; **M. Pozzobon**: Novartis, 3; **W. Bao**: Novartis, 3, 11; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6.

Abstract Number: 0802

Remission from cutaneous manifestations of lupus with enpatoran, a first-in-class oral small molecule toll-like receptor 7/8 inhibitor: pooled post-hoc exploratory analysis from a randomized placebo-controlled Phase II study

Eric Morand[1], Victoria Werth[2], Richard Furie[3], Sanjeev Roy[4], Ruth Fernandez Ruiz[5], Summer Goodson[6], Hans Gühring[7], Flavie Moreau[6] and David Pearson[8], [1]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [2]University of Pennsylvania, Philadelphia, PA, [3]Division of Rheumatology, Northwell Health, Great Neck, NY, [4]Ares Trading SA, an affiliate of Merck KGaA, Darmstadt, Germany, Eysins, Switzerland, [5]EMD Serono, Billerica, PA, [6]EMD Serono, Billerica, MA, [7]The healthcare business of Merck KGaA, Darmstadt, Germany, [8]Department of Dermatology, University of Minnesota, Minneapolis, MN

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment I (0801–0806)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Cutaneous manifestations of lupus are highly prevalent and have a significant impact on patients' physical and mental health and wellbeing; however, no targeted therapy is available. Toll-like receptor (TLR) 7/8 signaling has a role in regulating interferon (IFN) induction; elevated type I IFN gene transcripts in lupus skin lesions highlight the importance of the IFN signaling pathway in disease pathogenesis. Enpatoran is a first-in-class oral small molecule TLR 7/8 inhibitor. In a Phase II randomized double-blind placebo-controlled dose-finding parallel adaptive basket study (WILLOW [NCT05162586]), enpatoran improved Cutaneous Lupus Disease Area and Severity Index-Activity (CLASI-A) scores from baseline (BL) and increased CLASI-50 and CLASI-70 response rates in patients with CLASI-A ≥8 SLE and CLE (Cohort A).[1] Enpatoran also improved attainment of BICLA response with glucocorticoid taper vs placebo in patients with moderate-to-severe active SLE (Cohort B), despite no statistically significant dose response in this cohort.[2] Here we report an exploratory post-hoc analysis of pooled data for all patients from Cohort A and Cohort B who had active cutaneous manifestations (CLASI-A ≥8 at BL).

Methods: The WILLOW study design and patient enrollment criteria are summarized in Table 1. Cutaneous outcomes assessed at Week 16 and 24 were predefined secondary/exploratory endpoints in WILLOW and included: CLASI-50 and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. WILLOW Phase II study design summary

	Cohort A	Cohort B
Enrollment criteria	• CLE only (active SCLE and/or DLE with CLASI-A ≥8) or • SLE with active cutaneous manifestations (CLASI-A ≥8) and mild or no extra mucocutaneous disease activity (no BILAG A and no BILAG ≥2B)	• SLE (fulfilling ≥4 ACR[a] and/or SLICC and/or EULAR/ACR 2019 classification criteria), moderate-to-high disease activity (BILAG 2004 ≥1A/2B) despite standard of care, and hybrid SELENA-SLEDAI ≥6 and/or CLASI-A ≥8
Randomization	• 100 patients randomized 1:1:1:1 to SoC plus placebo or enpatoran 25 mg, 50 mg, or 100 mg BID	• **Part 1:** 60 patients randomized 1:2 to SoC plus placebo or enpatoran 100 mg BID • **Part 2:** 294 patients randomized 1:1:1:1 to SoC plus placebo or enpatoran 25 mg, 50 mg, or 100 mg BID
Duration	• 24 weeks	• **Part 1:** 24 weeks • **Part 2:** 24 weeks
Primary endpoint	• Percent change from BL in CLASI-A at Week 16	• BICLA response at Week 24

[a]≥80% of patients in Cohort B met ≥4 ACR classification criteria for SLE.
ACR, American College of Rheumatology; BID, twice daily; BL, baseline; CLASI-A, Cutaneous Lupus Disease Area and Severity Index Activity; CLE, cutaneous lupus erythematosus; DLE, discoid lupus erythematosus; EULAR, European League Against Rheumatism; SCLE, subacute cutaneous lupus erythematosus; SLICC, Systemic Lupus International Collaborating Clinics.

CLASI-70 response rates, achievement of remission defined as Cutaneous Lupus Activity Investigator's Global Assessment (CLA-IGA) score 0 or 1, CLASI-A 0–1 or CLASI-A 0–3, and change from BL in Physician Global Assessment (PGA) of cutaneous lupus disease activity.

Results: Baseline demographics and disease characteristics remained balanced across treatment groups in the pooled dataset; 262 patients were analyzed for efficacy in the pooled data (Table 2). Table 3 summarizes the findings for skin outcomes. Of patients receiving enpatoran, up to 71.2% and 78.8% achieved CLASI-50 at Weeks 16 and 24, respectively, vs 37.3% of patients receiving placebo at these timepoints. CLASI-70 responses at Weeks 16 and 24 were achieved by up to 46.3% and 57.1% of patients receiving enpatoran, vs 14.9% and 25.4% who received placebo. A higher proportion

Table 2. Baseline patient demographics and baseline disease characteristics: Pooled data from Cohort A FAS (N=100) and patients with CLASI-A ≥8 at baseline in Cohort B (n=162/353 in the FAS).

	Placebo (N=67)	Enpatoran 25 mg BID (N=52)	Enpatoran 50 mg BID (N=63)	Enpatoran 100 mg BID (N=80)	Total (N=262)
Patient demographics					
Age, mean years (SD)	45 (11.4)	42 (11.5)	42 (13.8)	44 (12.8)	43 (12.5)
Female sex, *n* (%)	60 (89.6)	45 (86.5)	54 (85.7)	69 (86.3)	228 (87.0)
Race, n (%)					
White	25 (37.3)	22 (42.3)	29 (46.0)	38 (47.5)	114 (43.5)
Asian	22 (32.8)	16 (30.8)	21 (33.3)	22 (27.5)	81 (30.9)
Black or African American	5 (7.5)	2 (3.8)	5 (7.9)	2 (2.5)	14 (5.3)
American Indian or Alaska Native	15 (22.4)	10 (19.2)	7 (11.1)	16 (20.0)	48 (18.3)
Hispanic or Latino ethnicity, n (%)	27 (40.3)	21 (40.4)	25 (39.7)	34 (42.5)	107 (40.8)
Disease and treatment characteristics					
Diagnosis, *n* (%)					
SLE, n (%)	53 (79.1)	38 (73.1)	48 (76.2)	65 (81.3)	204 (77.9)
CLE only, n (%)	14 (20.9)	14 (26.9)	15 (23.8)	15 (18.8)	58 (22.1)
CLASI-A total score, mean (SD)	12 (4.9)	13 (6.3)	14 (7.0)	13 (5.7)	13 (6.0)
CLASI-A severity (total score), n (%)					
Mild (0–9)	23 (34.3)	20 (38.5)	17 (27.0)	27 (33.8)	87 (33.2)
Moderate (10–20)	37 (55.2)	26 (50.0)	39 (61.9)	43 (53.8)	145 (55.3)
Severe (21–70)	7 (10.4)	6 (11.5)	7 (11.1)	10 (12.5)	30 (11.5)
CLA-IGA 0 or 1, n (%)	1 (1.9)	0	0	0	0
PGA CLE disease activity score, mean (SD)	57.9 (16.1)	58.7 (15.6)	56.6 (16.7)	58.8 (17.6)	-
Concomitant therapy, n (%)					
Immunosuppressants[a]	30 (44.8)	27 (51.9)	32 (50.8)	41 (51.3)	130 (49.6)
Antimalarials	53 (79.1)	38 (73.1)	46 (73.0)	66 (82.5)	203 (77.5)
Systemic glucocorticoids	48 (71.6)	38 (73.1)	50 (79.4)	58 (72.5)	194 (74.0)
Topical glucocorticoids	3 (4.5)	2 (3.8)	2 (3.2)	1 (1.3)	8 (3.1)

[a]Excluding antimalarials. BID, twice daily; CLA-IGA, Cutaneous Lupus Activity Investigator's Global Assessment; CLASI-A, Cutaneous Lupus Disease Area and Severity Index Activity; CLE, cutaneous lupus erythematosus; FAS, full analysis set; PGA, Physician Global Assessment; SD, standard deviation; SLE, systemic lupus erythematosus.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Efficacy of enpatoran in reducing cutaneous disease activity: Pooled data for Cohort A FAS (N=100) and patients with CLASI-A ≥8 at BL in Cohort B (n=162/353 in the FAS).

	Placebo BID (N=67)	Enpatoran 25 mg BID (N=52)	Enpatoran 50 mg BID (N=63)	Enpatoran 100 mg BID (N=80)
CLASI-50 response, n (%)[a]				
Week 16	25 (37.3)	37 (71.2)	41 (65.1)	56 (70.0)
Week 24	25 (37.3)	37 (71.2)	48 (76.2)	63 (78.8)
CLASI-70 response, n (%)[b]				
Week 16	10 (14.9)	22 (42.3)	27 (42.9)	37 (46.3)
Week 24	17 (25.4)	28 (53.8)	36 (57.1)	45 (56.3)
Attainment of remission based on CLA-IGA score 0–1, n (%)				
Week 16	13 (19.7)	18 (34.6)	24 (38.1)	38 (52.8)
Odds ratio (95% CI)[c,d]		2.26 (0.97, 5.23)	2.63 (1.18, 5.85)	5.25 (2.41, 11.44)
One-sided p-value[c]		0.0288	0.0086	<0.0001
Difference in response rate (95% CI)[c,e]		15.60 (-0.59, 31.86)	19.65 (3.81, 34.91)	35.38 (19.41, 49.59)
Week 24	21 (31.3)	24 (46.2)	31 (49.2)	48 (63.2)
Odds ratio (95% CI)[c,d]		1.98 (0.92, 4.27)	2.13 (1.03, 4.42)	3.86 (1.89, 7.87)
One-sided p-value[c]		0.0412	0.0212	0.0001
Difference in response rate (95% CI)[c,e]		14.75 (-3.16, 32.05)	17.69 (0.52, 33.93)	30.85 (14.42, 45.58)
Attainment of remission based on CLASI-A total score 0–1, n (%)				
Week 16	4 (6.0)	11 (21.2)	12 (19.0)	17 (21.3)
Week 24	11 (16.4)	14 (26.9)	19 (30.2)	23 (28.8)
Attainment of remission based on CLASI-A total score 0–3, n (%)				
Week 16	11 (16.4)	22 (42.3)	27 (42.9)	38 (47.5)
Week 24	18 (26.9)	27 (51.9)	35 (55.6)	45 (56.3)
Change from BL in PGA of cutaneous lupus disease activity, mean (SD)				
Week 16	-20.1 (20.5)	-33.6 (22.0)	-32.6 (23.9)	-38.1 (22.4)
Week 24	-22.3 (21.0)	-38.2 (21.3)	-37.4 (22.3)	-42.4 (23.2)

[a]CLASI-50 response defined as ≥50% improvement from BL in CLASI-A total score; [b]CLASI-70 response defined as ≥70% improvement from BL in CLASI-A total score; [c]Based on a logistic model with treatment group, region and Cohort as independent variables. There was no adjustment for multiplicity and all p-values are nominal; [d]95% CI computed using the Wald method; [e]Crude difference of response rate expressed as a percentage with 95% CI computed using non-stratified Miettinen-Nurminen method.
BID, twice daily; BL, baseline; CI, confidence interval; CLA-IGA, Cutaneous Lupus Activity Investigator's Global Assessment; CLASI-A, Cutaneous Lupus Disease Area and Severity Index Activity; FAS, full analysis set; PGA, Physician Global Assessment; SD, standard deviation.

of patients in each enpatoran dose group attained remission based on CLA-IGA score 0–1 (nominal p< 0.025 enpatoran 50 mg and 100 mg vs placebo). A higher proportion of patients with remission based on CLASI-A total score with enpatoran was also observed, with up to 30.2%/56.3% achieving CLASI-A 0–1/0–3 (compared with 16.4%/26.9% for placebo) by Week 24. At Week 16 and 24, mean change from BL in PGA of cutaneous lupus disease activity numerically improved across enpatoran doses vs placebo (Table 2).

Conclusion: Patients receiving enpatoran achieved higher rates of CLASI-50/70 response, CLA-IGA and CLASI-A remission vs placebo. Findings support further investigation of enpatoran efficacy and safety in patients with lupus and active cutaneous manifestations.

References:

1. Pearson DR, et al. Presented at LUPUS 2025. Abstract O010.
2. Morand EF, et al. Presented at EULAR 2025. Abstract LB0004.

Disclosure: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **V. Werth**: AbbVie/Abbott, 2, Alpine Immune Sciences, 2, Amgen, 2, 5, AnaptysBio, 2, argenx, 2, AstraZeneca, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Calyx, 2, Caribou, 2, CESAS Medical, 6, Corbus Pharmaceuticals, 5, Crisalis, 2, CSL Behring, 2, 5, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 2, 5, Immunovant, 2, Innovaderm, 2, Janssen, 2, Kyowa Kirin, 2, MAPI Trust, 9, Merck KGaA, Darmstadt, Germany, 2, N/A, 12, The University of Pennsylvania owns the copyright for the CLASI., Nektar, 2, Nuvig Pharmaceuticals, 2, Pfizer, 2, 5, Priovant, 5, Regeneron, 2, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Takeda, 2, UCB, 2, Ventus, 2, 5, Viela Bio, 2, 5, Xencor, 2; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **S. Roy**: Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany, 3; **R. Fernandez Ruiz**: EMD Serono, Billerica, MA, US, 3; **S. Goodson**: EMD Serono, Billerica, MA, US, 3; **H. Gühring**: Merck KGaA, Darmstadt, Germany, 3; **F. Moreau**: EMD Serono, Billerica, MA, US, 3; **D. Pearson**: Biogen Inc, 2, Daiichi Sankyo

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Inc, 5, EMD Serono, Billerica, MA, US, 5, Merck KGaA, Darmstadt, Germany, 2, Pfizer Inc, 2, Priovant Therapeautics, 5.

Abstract Number: 0803

Improved Efficacy and Safety Outcomes in Patients with SLE Treated with Belimumab (BEL) Versus Immunosuppressants (IS), in Addition to Antimalarials (AM) and Glucocorticoids (GC): A Post Hoc Summary of Five Phase 3 Trials

Mariele Gatto[1], Karen H. Costenbader[2], Andreas Schwarting[3], Julia Harris[4], Ciara O'Shea[5], Roger A. Levy[6] and Andrea Doria[7], [1]Academic Rheumatology Centre, Department of Clinical and Biological Sciences, University of Turin, Mauriziano Hospital, Turin, Italy, [2]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [3]Johannes Gutenberg University Mainz, University Medical Centre, Mainz, Germany, [4]GSK, Biostatistics, London, United Kingdom, [5]Global Medical Affairs, GSK, Dublin, Ireland, [6]GSK, Specialty Care, Global Medical Affairs, Collegeville, PA, [7]University of Padova, Padova, Italy

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment I (0801–0806)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Chronic GC and IS use increases damage accrual and mortality. The 2023 EULAR SLE recommendations support initiation of biologics such as BEL, a human IgG1λ monoclonal antibody that selectively binds to soluble B-lymphocyte stimulator (BLyS) with proven efficacy in SLE, without prior IS failure in AM- and GC-non-responders. Real-world evidence has shown benefits of initiating BEL without prior IS treatment. This study assessed the efficacy and safety of initiating BEL relative to being on IS at baseline of clinical trials (combined with AM and GC) in patients with SLE.

Methods: This post hoc summary pooled Week 52 data from five Phase 3 trials (BLISS-52: NCT00424476; BLISS-76: NCT00410384; North East Asia: NCT01345253; BLISS-SC: NCT01484496; EMBRACE: NCT01632241) with similar study designs and eligibility criteria, where adults with active SLE were randomized to receive BEL or placebo (PBO) in addition to AM and GC, with or without IS. This summary grouped patients by baseline treatment into an IS cohort (PBO and IS, defined as pre-treatment) and a BEL cohort (BEL 10 mg/kg intravenous or 200 mg subcutaneous and no IS); all patients received AM and GC. Efficacy endpoints were: proportion of patients with SLE Responder Index-4 (SRI-4) response through 52 weeks, time to first SELENA-SLEDAI Flare Index (SFI) flare over 52 weeks, and cumulative and mean GC dose change between baseline and Week 52. AEs and SAEs, inclusive of Phase 2 (NCT00071487) data, and baseline demographic and outcome data were summarized descriptively for the BEL and IS cohorts.

Results: Baseline demographics and clinical characteristics were similar between BEL (N=552) and IS cohorts (N=358) (**-Table 1**). Patients had mean (SD) SDI of 0.3 (0.73) and 0.5 (1.03), and median (IQR) duration of SLE of 3.9 [1.2–7.4] and 4.2 [1.6–8.8] years in the BEL and IS cohorts.

More patients were SRI-4 responders in the BEL vs IS cohort at most time points (Week 52 difference: 22%) (**Figure 1A**). In the BEL cohort, numerically fewer patients experienced any SFI flare (BEL: 59% vs IS: 81%), and had longer median [IQR] time to first on-study flare (any severity) (BEL: 85.0 [44.0–168.0] vs IS: 69.0 [32.0–134.0] days). The BEL cohort had a numerically lower cumulative baseline GC dose (× 365 days) vs IS cohort (mean [SD]: 4729 [3268.2] vs 5340 [3613.8] mg), and cumulative dose through Week 52 (mean [SD]: 4536 [3092.1] vs 5679 [5361.2] mg); mean (SD) cumulative GC change from baseline: −192 (2510.8) mg (BEL cohort), and 339 (4725.5) mg (IS cohort) (**Figure 1B**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographics and clinical characteristics. *Duration defined as: (screening date/treatment start date – SLE diagnosis date + 1)/365.25; †no data for one patient; ‡comprising intravenous, intramuscular, subcutaneous and oral GC; §defined as <90 mg/dl; ¶defined as <10 mg/dl for BLISS-SC, BLISS-North East Asia and EMBRACE, and <16 mg/dl for BLISS-52 and BLISS-76; **defined as 0.61 ng/ml for BLISS-SC and North East Asia, 0.02048 ng/ml for EMBRACE, and 0.50 ng/ml for BLISS-52 and BLISS-76. BILAG, British Isles Lupus Assessment Group; BMI, body mass index; C3/C4, complement component C3 and C4; dsDNA, double-stranded DNA; LOQ, limit of quantification; NSAIDs, nonsteroidal anti-inflammatory drugs; PGA, physician global assessment; SDI, The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index; SELENA, Safety of Estrogens in Lupus Erythematosus National Assessment; SLEDAI, SLE Disease Activity Index.

	BEL (No IS + AM + GC) N=552	IS (PBO + AM + GC) N=358
Age (years), mean (SD)	36 (11.5)	34 (10.9)
Sex (female), n (%)	524 (95)	334 (93)
Ethnicity, n (%)		
Hispanic or Latino	166 (30)	121 (34)
Not Hispanic or Latino	386 (70)	237 (66)
Race, n (%)		
Asian	194 (35)	144 (40)
White	185 (34)	93 (26)
Black African ancestry	108 (20)	82 (23)
Native Alaskan/American Indian	65 (12)	39 (11)
Multiracial	4 (1)	5 (1)
Region, n (%)		
Asia	190 (34)	141 (39)
Central/South America/Mexico	157 (28)	103 (29)
US/Canada	83 (15)	78 (22)
Europe/Israel/Australia/New Zealand/South Africa	122 (22)	36 (10)
BMI (kg/m²), n; mean (SD)	531; 25 (5.7)	341; 25 (5.9)
SLE disease duration (years)*, median (IQR)	3.9 (1.2–7.4)†	4.2 (1.6–8.8)
BILAG organ domain involvement, n (%)		
At least 1A or 2B	350 (63)	206 (58)
At least 1A	92 (17)	53 (15)
At least 1B	481 (87)	307 (86)
No A or B	42 (8)	39 (11)
SELENA-SLEDAI score, mean (SD)	10 (3.4)	10 (3.7)
≤9, n (%)	234 (42)	154 (43)
≥10, n (%)	318 (58)	204 (57)
PGA, n	550	357
Mean (SD)	1.5 (0.45)	1.5 (0.50)
SDI, mean (SD)	0.3 (0.73)	0.5 (1.03)
SLE medication at baseline (any use), n (%)		
IS	0	358 (100)
AM	552 (100)	358 (100)
GC‡	552 (100)	358 (100)
Aspirin	73 (13)	65 (18)
NSAIDs	81 (15)	67 (19)
Complement C3 (mg/dl), mean (SD)	93 (31.2)	90 (31.0)
Complement C4 (mg/dl), mean (SD)	16 (9.8)	17 (10.1)
Low C3¶ and/or low C4¶, n (%)	323 (59)	222 (62)
Low C3/C4 (at least one) and anti-dsDNA ≥30 IU/ml, n (%)	289 (52)	198 (55)
BLyS (ng/ml; above LOQ), n (%)**	463 (85)	305 (87)
Mean (SD)	1.5 (2.06)	2.0 (4.20)

Fewer patients experienced AEs and SAEs in the BEL (N=588) versus IS (N=395) cohort (AEs: 79% vs 90%; SAEs: 11% vs 20%), with one death reported in the BEL cohort (due to pneumonia; unrelated to treatment). Most common AEs by system organ class (BEL vs IS) were infections and infestations (53% vs 64%), gastrointestinal disorders (23% vs 31%), and musculoskeletal and connective tissue disorders (21% vs 35%).

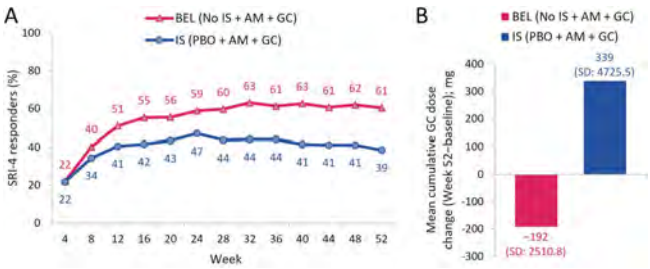


Figure 1. SRI-4* responders through Week 52 (A) and cumulative mean change in GC dose from baseline to Week 52 (B). *SRI-4 response was defined as a ≥4-point reduction in SELENA-SLEDAI score from baseline, no new BILAG A organ domain score or 2 new BILAG B scores compared with baseline, and no worsening (increase <0.3) in PGA score versus baseline.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In line with 2023 SLE EULAR recommendations for earlier biologic use in the treatment paradigm, this post hoc summary adds clinical data supporting the benefits of initiating BEL in patients not receiving IS, in those not well controlled with AM and GC.

Funding: GSK

Original presentation: EULAR 2025

Disclosure: M. Gatto: AstraZeneca, 6, Boehringer Ingelheim, 6, GSK, 5, 6; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **A. Schwarting**: AbbVie, 5, AstraZeneca, 5, Galapagos, 5, GSK, 5, 6, Vifor, 5; **J. Harris**: GSK, 12, 3; **C. O'Shea**: GSK, 12, 3; **R. Levy**: GSK, 3, 8; **A. Doria**: AbbVie, 6, AstraZeneca, 2, 6, Biogen, 2, 6, BMS, 2, 6, GSK, 2, 6, MSD, 2, Otsuka, 2, 6.

Abstract Number: 0804

Comparative Risk of All-Cause Mortality with Belimumab versus Oral Immunosuppressant Use in Patients with Non-Renal Systemic Lupus Erythematosus

Grace Haeun Lee[1], Sara Barmettler[2], Lingxiao Zhang[3] and April Jorge[2], [1]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital, Boston

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment I (0801–0806)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Belimumab is a monoclonal antibody targeting B-lymphocyte stimulator (BLyS) used in the treatment of active systemic lupus erythematosus (SLE). Our objective was to investigate the comparative risk of all-cause

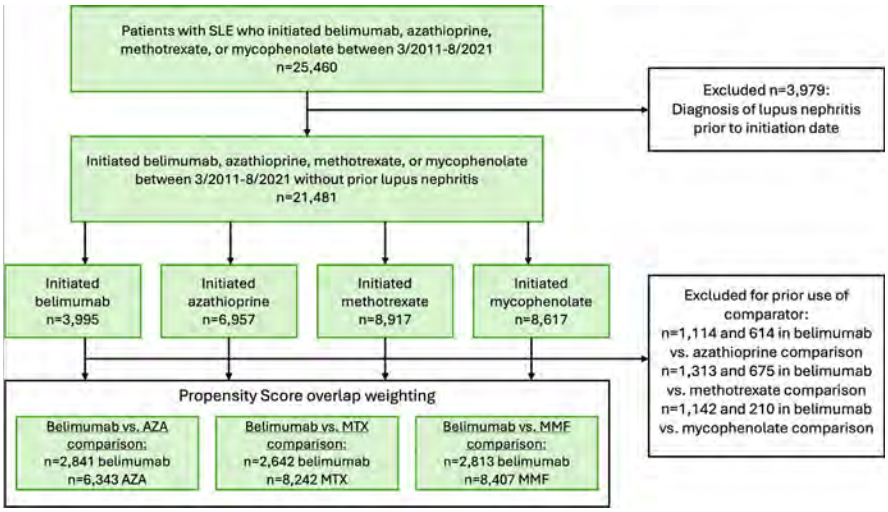


Figure 1. Flow of Patients into the Study

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Belimumab and Azathioprine Initiators with Non-Renal Systemic Lupus Erythematosus

	Before overlap weighting			After overlap weighting		
	Belimumab (n=2841)	Azathioprine (n=6343)	Std. Diff.	Belimumab	Azathioprine	Std. Diff.
Age, years, mean (SD)	44.6 (13.1)	44.8 (15.6)	0.0126	44.7	44.7	<0.001
Female, n (%)	2700 (95.0)	5820 (91.8)	0.1324	94.3	94.3	<0.001
Race/Ethnicity, n (%)			0.3034			<0.001
White	1673 (58.9)	2880 (45.4)		54.0	54.0	
Black	695 (24.5)	2128 (33.5)		27.6	27.6	
Asian	55 (1.9)	143 (2.3)		2.1	2.1	
Hispanic	204 (7.2)	675 (10.6)		8.5	8.5	
Other	214 (7.5)	517 (8.2)		7.8	7.8	
Geographic Region, n (%)			0.4224			<0.001
East	974 (34.3)	1116 (17.6)		26.1	26.1	
Midwest	322 (11.3)	1144 (18)		13.8	13.8	
South	1084 (38.2)	3142 (49.5)		43.2	43.2	
West	461 (16.2)	941 (14.8)		16.9	16.9	
Treatment initiation year, median	2018	2016	0.5439	2017	2017	
CKD stage ≥3, n (%)	355 (12.5)	999 (15.7)	0.0935	13.0	13.0	<0.001
Charlson Comorbidity Index, mean (SD)	0.88 (0.86)	0.99 (1.05)	0.1142	0.91	0.91	<0.001
SLE Severity Index, n (%)			0.1580			<0.001
Mild	1163 (40.9)	2784 (43.9)		43.4	43.4	
Moderate	1333 (46.9)	2527 (39.8)		43.4	43.4	
Severe	345 (12.1)	1032 (16.3)		13.2	13.2	
Medication Use, n (%)						
Glucocorticoids	1639 (57.7)	3463 (54.6)	0.0624	56.1	56.1	<0.001
Hydroxychloroquine	1511 (53.2)	2842 (44.8)	0.1682	48.9	48.9	<0.001
Methotrexate	595 (20.9)	641 (10.1)	0.3027	15.7	15.7	<0.001
Mycophenolate	437 (15.4)	570 (9)	0.1965	12.8	12.8	<0.001
Other oral immunosuppressant	266 (9.4)	343 (5.4)	0.1517	7.5	7.5	<0.001
Rituximab	53 (1.9)	98 (1.5)	0.0248	1.8	1.8	<0.001
Cyclophosphamide	17 (0.6)	62 (1.0)	0.0429	0.7	0.7	<0.001
Healthcare Utilization						
Outpatient visits, median (IQR)	3 (5)	3 (7)	0.0408	3	3	<0.001
ER/Inpatient visits, n (%)	520 (18.3)	1659 (26.2)	0.1897	21.0	21.0	<0.001
Prior hospitalized infection, n (%)	43 (1.5)	200 (3.2)	0.1088	1.9	1.9	<0.001

Covariates assessed within the six months prior to the index date. Non-renal lupus defined by meeting SLE definition (≥2 SLE ICD codes ≥2 months and ≤2 years apart) and not meeting lupus nephritis definition (defined by ≥1 LN code (ICD-10 M32.14) or ≥2 nephritis codes (e.g., ICD-9 580-586, 791.0 or ICD-10 N00, N04-5, N17-18, R80.9) prior to the index date.
MTX, methotrexate. CKD, chronic kidney disease, defined by ≥1 ICD codes or GFR <60 on ≥2 occasions. ER, emergency room. SLE Severity Index is adapted from Garris algorithm for administrative data, based on ICD codes and not including medication dosing. Other oral immunosuppressant use includes leflunomide, sulfasalazine, cyclosporine, tacrolimus, abatacept, tocilizumab, TNF inhibitors, IL17 inhibitors, IL12/23 inhibitors, and JAK inhibitors

mortality with belimumab use versus oral immunosuppressants (azathioprine, methotrexate or mycophenolate) for the treatment of non-renal SLE.

Methods: We performed a target trial emulation study of adult patients with SLE (defined as ≥2 ICD codes ≥2 months and ≤2 years apart) but without lupus nephritis who initiated belimumab, azathioprine, methotrexate, or mycophenolate using

Table 2. Comparative Risk of All-Cause Mortality with Belimumab versus Oral Immunosuppressant use in Non-Renal Systemic Lupus Erythematosus

Treatment arms	Number of Events	Cumulative Incidence (%)	Adherence-Adjusted Hazard Ratio (95% CI)
Per-protocol analysis			
Belimumab vs Azathioprine			
Azathioprine	113	3.35	1.00 (ref)
Belimumab	17	1.58	0.45 (0.26-0.80)
Belimumab vs Methotrexate			
Methotrexate	81	2.14	1.00 (ref)
Belimumab	15	1.46	0.66 (0.36-1.21)
Belimumab vs Mycophenolate			
Mycophenolate	187	3.35	1.00 (ref)
Belimumab	18	1.58	0.46 (0.27-0.79)
Intention-to-treat analysis			
Belimumab vs Azathioprine			
Azathioprine	182	4.05	1.00 (ref)
Belimumab	23	1.62	0.40 (0.25-0.63)
Belimumab vs Methotrexate			
Methotrexate	147	2.87	1.00 (ref)
Belimumab	24	1.76	0.61 (0.38-0.96)
Belimumab vs Mycophenolate			
Mycophenolate	293	3.96	1.00 (ref)
Belimumab	27	1.90	0.47 (0.31-0.73)

Patients are followed until the earliest of the event, death, 5-years follow-up, or the end of the study period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

observational data from a U.S. multi-center electronic health record database (TriNetX) between 2011-2021. We evaluated the comparative risk of all-cause mortality with belimumab versus each of three oral immunosuppressants (azathioprine, methotrexate, or mycophenolate) for the treatment of SLE. In each comparison, we excluded patients who had previously used belimumab or the comparator oral immunosuppressant. Patients were followed until the earliest of the event (death), 5-year follow-up, or the end of the study period. We estimated the cumulative incidence and hazard ratios (HRs) of all-cause mortality comparing belimumab to each oral immunosuppressant. Propensity score overlap weighting was used to balance baseline covariates (including age, sex, race/ethnicity, geographic region, year of initiation, use of concomitant SLE medications [other oral immunosuppressants, glucocorticoids, hydroxychloroquine, rituximab, cyclophosphamide], Charlson comorbidity index, SLE severity index, chronic kidney disease, healthcare utilization, and prior infection history). In a primary per-protocol analysis, we adjusted for adherence to treatment strategy using inverse probability of treatment weighting.

Results: We identified 21,481 patients with non-renal SLE who met eligibility criteria (Figure 1). In these three hypothetical target trials, we compared 1) initiators of belimumab (n=2841) and azathioprine (n=6343), 2) initiators of belimumab (n=2642) and methotrexate (n=8242), and 3) initiators of belimumab (n=2813) and mycophenolate (n=8407). After propensity score overlap weighting, all covariates were balanced in each comparison group, with mean age 45 years and 94% females (Table 1). In the per-protocol analysis, belimumab was associated with a lower risk of all-cause mortality compared to azathioprine (HR 0.45 [95% CI 0.26-0.8]) and mycophenolate (HR 0.46 [95% CI 0.27–0.79]) (Table 2). In the intention-to-treat analysis, belimumab was associated with a lower risk of all-cause mortality compared to all three oral immunosuppressants: belimumab vs. azathioprine (HR 0.40 [95% CI 0.25-0.63]), belimumab vs. methotrexate (HR 0.61 [95% CI 0.38-0.96]), and belimumab vs. mycophenolate (HR 0.47 [95% CI 0.31–0.73]).

Conclusion: Belimumab use was associated with reduced all-cause mortality compared with oral immunosuppressants in this large cohort of patients using rigorous propensity score overlap weighting to emulate a target trial. These findings suggest that targeted immunomodulatory therapy with BLyS inhibitors in SLE has favorable outcomes.

Disclosure: G. Lee: Bristol-Myers Squibb(BMS), 12, Travel to Investigator Meeting; **S. Barmettler**: Bristol-Myers Squibb(BMS), 5, Csl behring, 2, Octapharma, 2, Pharming, 5; **L. Zhang**: None; **A. Jorge**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 0805

Safety and Efficacy of Hydroxychloroquine According to Weight-based Dose: Results of a Global Systematic Review and Meta-analysis

Jacquelyn Nestor[1], Zahraa Qamhieh[2], Shivani Garg[3] and April Jorge[1], [1]Massachusetts General Hospital, Boston, MA, [2]University of Wisconsin, Madison, Department of Medicine, Madison, WI, [3]University of Madison, School of Medicine and Public Health, Madison, WI

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment I (0801–0806)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is a foundational therapy in systemic lupus erythematosus (SLE) treatment, as it prolongs disease-free and damage-free survival. However, the optimal dose is debated due to dose-related risks for toxicity, and the efficacy of lower dosing (≤5 mg/kg/day) needs to be further elucidated. Therefore, we designed a systematic review and meta-analysis to assess the impact of HCQ dose on risks of HCQ-related toxicities and adverse SLE outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

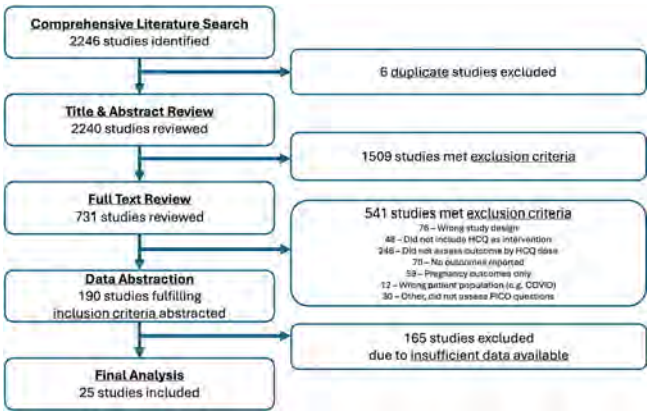


Figure 1. Literature Review and Included Studies

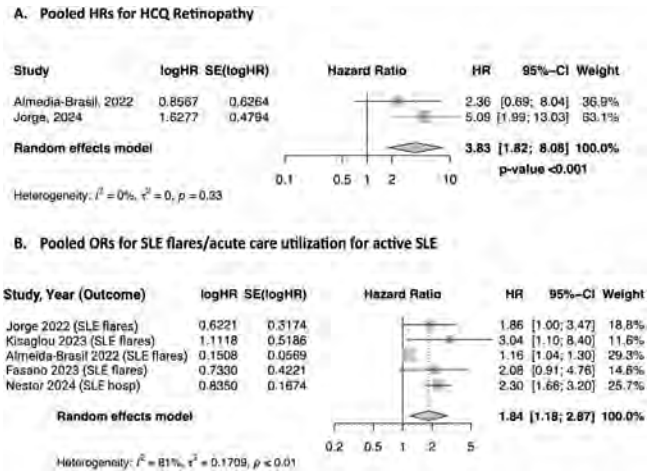
Methods: A comprehensive search was performed using MeSH headings and keywords (e.g., lupus, SLE, hydroxychloroquine, toxicity, flares, death or mortality, etc.) in Medline, Embase, CINAHL and Web of Science. We included observational and interventional studies associations between HCQ dose and: i) toxicity (cardiac or eye); ii) poor SLE outcomes defined as SLE flares, acute care utilization for active SLE, disease activity, death, cardiovascular disease, kidney failure, or thrombotic events in subjects with SLE. Risk of bias was assessed using standard tools for all studies. We examined pooled hazard ratios (HR) of HCQ retinopathy (primary outcome) and pooled odds ratios (OR) of toxicity when time-to-event data was not available (secondary outcome) in high vs. low HCQ dose groups (>5 vs. ≤5 mg/kg/day) using a random effects model.

Table 1. Included Studies Addressing the Association of Hydroxychloroquine Dose and Clinical Effectiveness, Safety

Author, Year (Ref)	Study Design	Study Population	HCQ Dose Cutoff	Outcomes Reported	Bias Assessment
Abdelbaky et al., 2021	Cross-sectional	N=18; Age 31.24±7.41 y; F=90%	N/A	HCQ retinopathy- assessed by FAF	NOS: Good
Ahn et al., 2017	Retrospective case series	N=99 SLE; Age= 42.4±11.6; F=91.9%	N/A	HCQ retinopathy- assessed by OCT or FAF with corresponding VF changes	NOS: Good
Akhlaghi et al., 2021	Cross-sectional	N=61 (40 SLE, 21 RA); Age 46.9±11.62; F=93.4%	N/A	HCQ retinopathy- assessed by mfERG	NOS: Good
Almeida-Brasil et al., 2022 (Nov)	Prospective cohort	N=1460; Age= 34.7 (SD 12.3); F=87%; White=51.7%; Black=17%; Asian=16%; Other=14.3%	5 mg/kg	HCQ retinopathy- assessed by retinal damage recorded on the SLICC Damage Index and attributed to HCQ per treating physician	NOS: Good
Almeida-Brasil et al., 2022 (Mar)	Prospective cohort	N=1460; Age= 34.7 (SD 12.3); F=89%; White=51.7%; Black=17%; Asian=16%	5 mg/kg	SLE flare- assessed by increase of ≥4 on SLEDAI-2K	NOS: Good
Balbi et al., 2022	Prospective cohort	N=60; Age 16.6±3.13; F=80%; Non-Caucasian=41.7%	N/A	SLE flare- assessed by increase of ≥3 in SLEDAI-2K and/or increase in steroid dose or more intensive immunosuppression	NOS: Good
Fasano et al., 2023	Prospective cohort	N=66; Age= 42.01±11.2; F=95%; Caucasian=100%	5 mg/kg	SLE flare- assessed by SLEDAI-2K	NOS: Good
Garg et al., 2024	Prospective cohort	N=181; Age=47±16; F=92%; Non-white or Hispanic=33%	5 mg/kg	Lupus-related acute care visits (ER visits/hospitalizations)	NOS: Good
Garg et al., 2023	Prospective cohort	N=158; Age=46±16; F=92%; White=68%; Black=16%; Asian=8%; Hispanic=9%	N/A	SLE flare- assessed by 3-point increase in SLEDAI with clinical symptoms requiring therapy change	NOS: Good
Hsu et al., 2017	Prospective cohort	N=8397; Age= 35.7 (16); F=88.2%	200 mg	Cardiovascular outcomes-ACS, Ischemic Stroke, PE, DVT, composite	NOS: Good
Jimenez et al., 2023	Retrospective cohort	N=254; Age=30.6y; F=90%; AA=45%, Hispanic=49%, White= 6%	5 mg/kg; 400mg	Cardiac toxicity assessed as arrhythmias, heart failure, or cardiac death	NOS: Good
Jin et al., 2021	Retrospective cohort	N=2446; Age=30.1y; F=93.8%	400 mg	Mortality	NOS: Good
Jorge et al., 2022	Case cross-over	N=342; Age= 43 (SD 14.7); F=88%	5 mg/kg	SLE flare-assessed by revised SELENA-SLEDAI flare index	NOS: Good
Jorge et al., 2024	Retrospective cohort	N=1604; Age=46.0 (SD 13.9); F=89.7%; White: 39%, Hispanic: 20%, Asian: 19%, Black: 16.0%	5 mg/kg	HCQ retinopathy- assessed on masked review of screening OCT exams by expert ophthalmologist and adjudicated by a second expert	NOS: Good
Kao et al., 2022	Retrospective observational	N=92; Age=42.9 (37.8-52.6)	N/A	HCQ retinopathy- assessed by ≥2 typical abnormal findings on OCT, VF, FAF, mfERG and confirmed by two ophthalmologists	NOS: Fair
Kisaoglu et al., 2024	Retrospective observational	N=124; Age=12.6±3.7; F=79.8%	5 mg/kg	SLE flare- assessed as SLEDAI ≥ 4	NOS: Good
Lenfant et al., 2020	Case-control study	N=23; Age= 52 (41-59); F= 96%	N/A	HCQ retinopathy- assessed by ≥2 typical abnormal findings on OCT, VF, FAF, mfERG	NOS: Good
Lo et al., 2021 (May)	Retrospective case control	N=193; Age= 50.4 (17.9) cases vs 49.1 (17.4) controls; F=81%	400 mg	Cardiac toxicity- assessed as arrhythmias	NOS: Good
Lo et al., 2021 (April)	Retrospective cohort	N= 579; Age= 55.1 (SD 13); F=80%	400 mg	Cardiac toxicity- assessed as arrhythmias	NOS: Good
Melles et al., 2023	Retrospective cohort	N=606; Age=47.5 (SD 14); F=90.1%; White=29.5%; Hispanic=19.8%; Asian=22.3%; Black=20.5%	5 mg/kg	HCQ retinopathy- assessed on masked review of screening OCT exams by an expert ophthalmologist and adjudicated by a second expert	NOS: Good
Nestor et al., 2024	Retrospective Case-crossover	N=122; Age= 36.5 (SD 14.3); F=91.8%; White=41.8%; Black=31.1%; Asian=9%	5 mg/kg; 400 mg	Hospitalizations for active SLE	NOS: Good
Shaharir et al., 2014	Case-control	N=150; Age=35.6±10.5; F=80%; Asian=100%	6 mg/kg	Damage progression per the SLICC Damage Index (SDI) ≥ 1	NOS: Good
Vazquez-Otero et al., 2020	Retrospective observational	N=60; Age=43.8 (SD 15.1); F=100%	5 mg/kg	Disease activity per SLEDAI; Damage accrual per SDI; ER visits and hospitalizations for SLE	NOS: Good
Wakiya et al., 2020	Retrospective observational	N=77; Age= 40.3±12.4 in usual dose group vs 46.1±9.3 in low HCQ dose group; F=72%	N/A	Disease activity per mean SLEDAI	NOS: Good
Xie et al., 2023	Prospective observational	N=489; Age= 44.18 (SD 15.39); F=86.3%; Asian=100%	200 vs 400 mg	Disease activity per mean SLEDAI	NOS: Good

FAF, fundus autofluorescence; OCT, optical coherence tomography; VF, visual fields; mfERG, multifocal electroretinography

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plots for A) pooled HRs for HCQ retinopathy, B) pooled ORs for SLE flares/acute care utilization for active SLE

Additionally, we calculated the pooled odds of SLE flares/acute care utilization for active SLE by low vs. high HCQ dose groups. Heterogeneity was assessed using I^2.

Results: Among 2246 manually reviewed studies, 190 met initial inclusion. Of these, 25 studies compared HCQ-related toxicities or poor SLE outcome by weight-based HCQ dose and were included in the meta-analysis (Figure 1). Eight studies assessed the outcome of HCQ retinopathy in SLE patients, of which two assessed HRs by weight-based dose. Among eight studies assessing outcomes of SLE flares/acute care utilization, five had available data for inclusion in pooled HRs for the 5 mg/kg weight-based dosing threshold (Table 1). The pooled HR for HCQ retinopathy associated with >5 vs ≤5 mg/kg dosing was 3.83 (95% CI 1.82-8.08), Fig. 2). At the same time, the pooled HR of SLE flare/acute care utilization for active SLE associated with ≤5 vs >5 mg/kg dosing was 1.84 (95% CI 1.18-2.87). Other outcomes of interest were each assessed by fewer than two studies that compared the 5 mg/kg weight-based dosing threshold.

Conclusion: In this systematic review and meta-analysis of HCQ dose and SLE outcomes, we found that higher HCQ dosing >5 mg/kg is associated with over three times higher risk of HCQ retinopathy but nearly two times lower risk of SLE flare/acute care utilization for active SLE. These findings indicate the need for clinicians and patients to weigh the potential harms versus benefits when determining the optimal dose of HCQ in SLE treatment.

Disclosure: J. Nestor: None; **Z. Qamhieh**: None; **S. Garg**: None; **A. Jorge**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 0806

Comparative Risk of Infection-Related Complications in Systemic Lupus Erythematosus Patients Treated with Anifrolumab versus Belimumab: A Target Trial Emulation

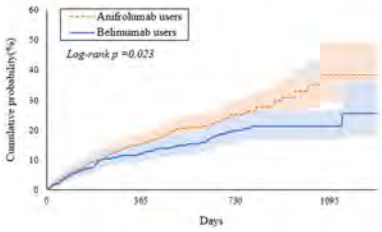
Teng-Chieh Hsu[1], An-Ping Huo[2], Pei-Lun Liao[2], Pui-Ying Leong[2] and James Wei[3], [1]Wuri Lin Shin Hospital, Taichung, Taiwan (Republic of China), [2]Chung Shan Medical University Hospital, Taichung, Taiwan (Republic of China), [3]Chung Shan Medical University Hospital, Taichung, Taichung, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment I (0801–0806)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Kaplan-Meier curves of cumulative probability (%) of Infection, comparing Anifrolumab group and Belimumab groups.



Supplementary Table 2. Hazard ratio and 95% CIs for the risk of various Infection

	Patients in cohort	Patients with outcome	Hazard ratio* (95% CI)
Herpes Zoster			
Anifrolumab user	481	12	**3.944(1.111, 13.996)**
Belimumab user	481	10	reference
Influenza			
Anifrolumab user	481	<10	1.719(0.576, 5.133)
Belimumab user	481	<10	reference
Pneumonia			
Anifrolumab user	481	24	1.624(0.840, 3.139)
Belimumab user	481	14	reference
TB			
Anifrolumab user	481	<10	0.951(0.059, 15.210)
Belimumab user	481	<10	reference
Sepsis			
Anifrolumab user	481	15	2.017(0.822, 4.949)
Belimumab user	481	10	reference
UTI			
Anifrolumab user	481	39	1.135(0.714, 1.805)
Belimumab user	481	33	reference
COVID-19			
Anifrolumab user	481	48	**1.663(1.042, 2.653)**
Belimumab user	481	28	reference

*Hazard ratio for outcomes among Anifrolumab users group compared to Belimumab users group subjects (after propensity score matching).
*95% CI, 95% confidence interval.
*propensity score matching include Age at index, Sex, Ethnicity, Race, BMI, Medical utilization, Socioeconomic, Lifestyle, and Comorbidities.
* If the patients count is 1–10 or less, the results indicate a count of 10.

Background/Purpose: Anifrolumab and belimumab are biologic agents approved for systemic lupus erythematosus (SLE), yet their comparative safety profiles, particularly regarding infection risks, remain inadequately characterized in real-world settings.

Methods: We conducted a retrospective cohort study using data from the TriNetX research network. Patients diagnosed with SLE between January 1, 2000, and June 30, 2024, with at least two diagnoses were included. We identified new users of anifrolumab or belimumab between August 1, 2021, and June 30, 2024, excluding patients with infection before the index date, patients hospitalized within 6 months before the index date, and patients who died before the index date. Propensity score matching was employed to control for confounding factors. Cox proportional hazards models were used to estimate

Table 3. Hazard ratio and 95% CIs for the risk of Second outcome

	Patients in cohort	Patients with outcome	Hazard ratio* (95% CI)
Mortality			
Anifrolumab user	481	10	1.081(0.417, 2.804)
Belimumab user	481	10	reference
Hospital Inpatient Services			
Anifrolumab user	481	74	1.273(0.900, 1.802)
Belimumab user	481	56	reference

*Hazard ratio for outcomes among Anifrolumab group compared to Belimumab group subjects (after propensity score matching).
95% CI, 95% confidence interval.
*propensity score matching include Age at index, Sex, Ethnicity, Race, BMI, Medical utilization, Socioeconomic, Lifestyle, Comorbidities and Medication.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hazard ratios (HR) and 95% confidence intervals (CI), and Kaplan-Meier analysis was used to assess cumulative infection probabilities. The primary outcome was infection occurrence (including herpes zoster, influenza, pneumonia, tuberculosis, sepsis, urinary tract infection, and COVID-19), while secondary outcomes included mortality and hospital inpatient services utilization.

Results: After applying exclusion criteria and propensity score matching, the final analytic cohort included 481 patients in each treatment group. After matching, anifrolumab users showed a significantly higher risk of infection compared to belimumab users (HR 1.40, 95% CI: 1.05-1.88), with 3-year cumulative infection rates of 38.3% and 21.3%, respectively. Analysis of specific infections revealed significantly increased risks of herpes zoster (HR 3.944, 95% CI: 1.111-13.996) and COVID-19 (HR 1.663, 95% CI: 1.042-2.653) associated with anifrolumab use. Subgroup analysis showed significantly higher infection risk in White patients receiving anifrolumab (HR 1.64, 95% CI: 1.09-2.48). Time-dependent analysis suggested that certain infection risks, such as herpes zoster, may develop or intensify with longer treatment duration. No significant differences in mortality or hospital inpatient services utilization were observed between the treatment groups.

Conclusion: Anifrolumab use in SLE is associated with a higher risk of specific infections, particularly herpes zoster and COVID-19, compared to belimumab, especially with prolonged exposure. These findings underscore the need for vigilant infection monitoring, region-specific preventive strategies, and further research to optimize biologic therapy safety across diverse populations.

Disclosure: T. Hsu: None; **A. Huo**: None; **P. Liao**: None; **P. Leong**: None; **J. Wei**: None.

Abstract Number: 0807

Deciphering Synovitis in Systemic Sclerosis

Celina Geiss[1], Miranda Houtman[1], Camino Calvo Cebrian[1], Raphael Micheroli[2], Melpomeni Toitou[1], Yannis Djeffal[3], Alexandra Khmelevskaya[1], Mojca Frank-Bertoncelj[1], Sam Edalat[1], Thomas Rauer[4], Kristina Bürki[5], Chantal Pauli[6], Michael Bonelli[7], Thomas Karonitsch[8], Oliver Distler[9], Caroline Ospelt[1] and Muriel Elhai[10], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Zurich, Switzerland, [2]University Hospital Zurich, Zurich, Switzerland, [3]INSERM, IMRB, Université Paris Est Créteil, Paris, France, [4]3Department of Traumatology, University Hospital Zurich, University of Zurich, Zurich, Zurich, Switzerland, [5]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [6]Institute for Pathology and Molecular Pathology, University Hospital Zurich, University of Zurich, Zurich, Zurich, Switzerland, [7]Department of Medicine III, Division of Rheumatology, Medical University Vienna, Vienna, Wien, Austria, [8]Department of Medicine III, Division of Rheumatology, Medical University Vienna, Vienna, Austria, [9]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [10]University Hospital zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (0807–0812)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Synovitis is a common manifestation of systemic sclerosis (SSc), driving disability and predicting disease progression and mortality. Current immunosuppressive strategies, largely extrapolated from rheumatoid arthritis (RA), offer limited efficacy. A deeper understanding of the pathomechanisms underlying SSc synovitis is therefore needed to enable the development of more effective, targeted therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

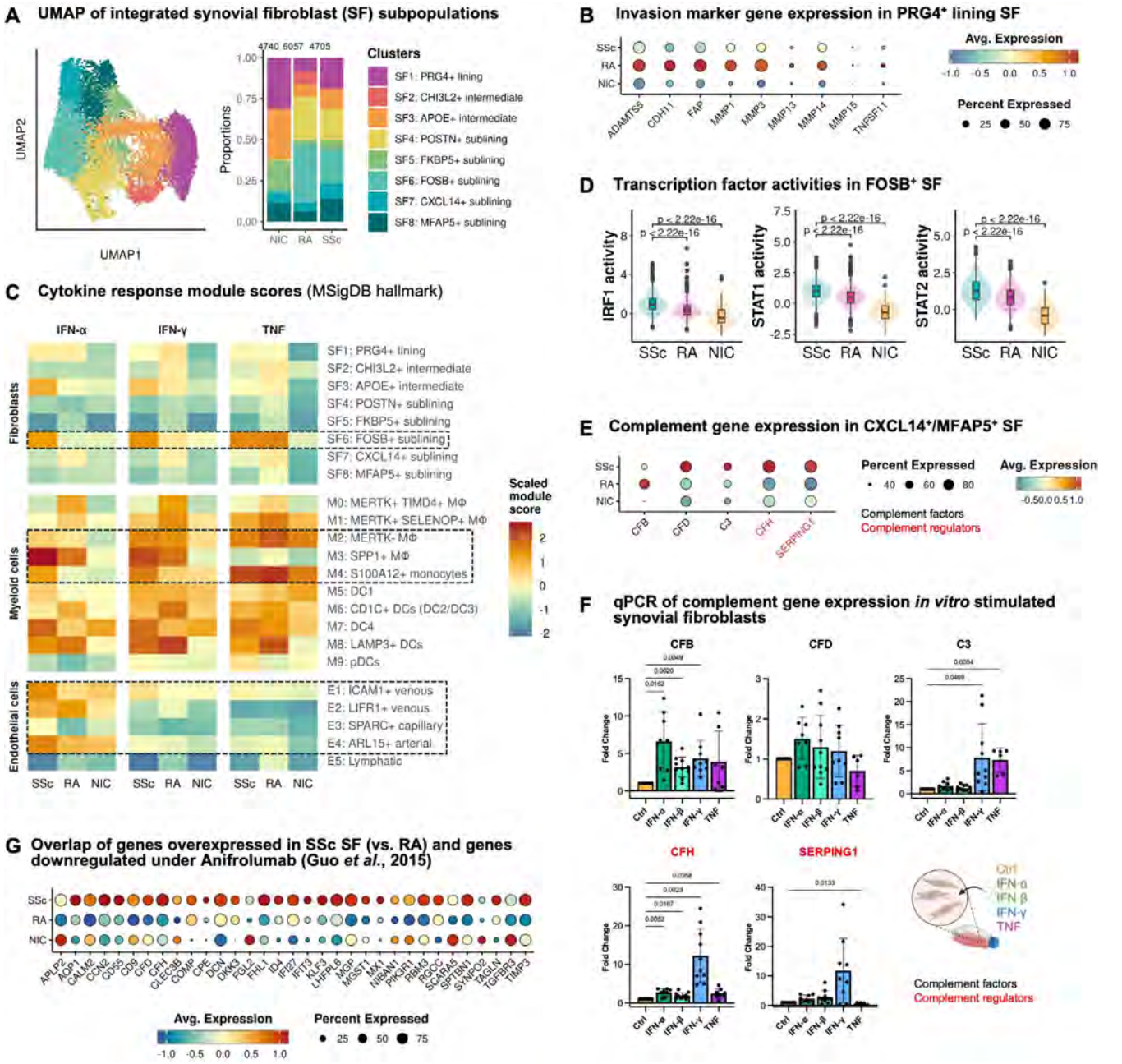


Figure 1. Overview of main results.

Methods: Synovial tissue from 11 SSc patients (91% limited cutaneous SSc, excluding overlap syndromes), 7 RA patients (all anti-CCP and RF positive), and 6 non-inflammatory controls (NIC) underwent histological classification. For single-cell RNA sequencing (scRNA-seq), synovium from 6 SSc, 6 RA, and 6 NIC samples was dissociated, yielding 78,128 cells (SSc: 21,248; RA: 32,062; NIC: 24,818) across nine cell types. Data were analysed using Seurat (v4.3) and integrated using Harmony and STACAS for subpopulation annotation. Bioinformatic analyses included differential expression analysis (MAST), pathway over-representation analysis (ORA), gene module scoring (MSigDB hallmark), and transcription factor activity inference (decoupleR). *In vitro* qPCR validation was performed on synovial fibroblasts (SF) stimulated with TNF, interferon (IFN)-α, IFN-β, and IFN-γ.

Results: Histology revealed a pauci-immune pathotype in 10/11 SSc synovial biopsies, with significantly lower Krenn scores (p=0.01) and less acute inflammation compared to RA (p< 0.01).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

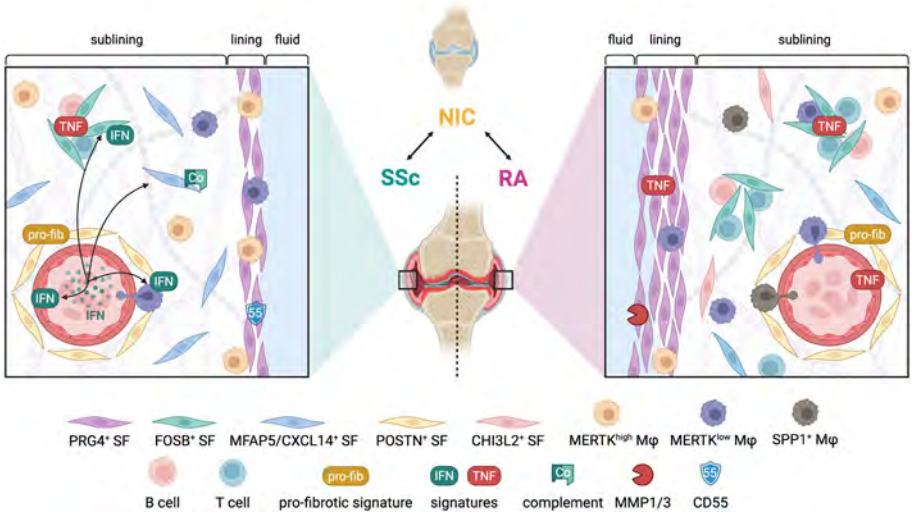


Figure 2. Graphical abstract of proposed mechanism of SSc synovitis and RA compared to non-inflammatory controls (NIC). Created with BioRender.

Given the stromal predominance in SSc, we focused our analysis on SF (n= 15'502, Fig. 1A) and observed a lower expression of invasion-associated genes in PRG4$^+$ lining SF (Fig. 1B), which may explain the lower frequency of radiographic erosions in SSc patients compared to RA (36% vs. 50%).

Across all SF, we identified a prominent IFN-α and IFN-γ signature in SSc (both FDR< 0.05, ORA) relative to RA, where TNF response was the dominant signal (FDR< 0.001, ORA). IFN-associated genes (Fig. 1C), JAK/STAT signalling, and IFN-related transcription factors (Fig. 1D) were specifically enriched in FOSB$^+$ SF in SSc. Moreover, we observed a complex expression pattern of alternative complement genes and regulators in SSc, particularly in MFAP5$^+$/CXCL14$^+$ SF (Fig. 1E), which was recapitulated following stimulation of SFs with IFN *in vitro* (Fig. 1F).

Genes specifically overexpressed in SSc SF, including canonical IFN-stimulated genes and complement-related targets, overlapped largely with transcripts previously shown to be downregulated in the skin of SSc patients after Anifrolumab treatment (Fig. 1G), indicating therapeutic potential.

Notably, a canonical IFN signature (Fig. 1C), marked by genes such as IRF1, MX1, IFI27, STAT1, and STAT2, was also evident across other synovial cell types in SSc compared to RA and NIC, including endothelial cells and infiltrating MERTK$^-$/SPP1$^+$ macrophages and S100A12$^+$ monocytes.

Conclusion: Our findings provide the first in-depth characterisation of SSc synovitis, revealing a pauci-immune, less-invasive phenotype marked by a dominant IFN signature across SF, macrophages, monocytes and endothelial cells (Fig. 2). This tissue-wide IFN response supports IFN blockade as a promising therapeutic strategy for SSc synovitis.

Disclosure: C. Geiss: None; **M. Houtman**: None; **C. Calvo Cebrian**: None; **R. Micheroli**: None; **M. Toitou**: None; **Y. Djeffal**: None; **A. Khmelevskaya**: None; **M. Frank-Bertoncelj**: None; **S. Edalat**: None; **T. Rauer**: None; **K. Bürki**: None; **C. Pauli**: None; **M. Bonelli**: None; **T. Karonitsch**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Ospelt**: None; **M. Elhai**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Astrazeneca, 12, congress support, Boehringer Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5, Iten Kohaut foundation, 5, Janssen, 12, congress support, Kurt und Senta Herrmann foundation, 5, Novartis Foundation for Bio-Medical Research, 5, pfizer, 5, University Zurich, 5.

Abstract Number: 0808

Spatial Transcriptomics Show Fibroblast LIF Receptor Drives Fibrosis in Systemic Sclerosis

Mari Kamiya[1], Hung Nguyen[1], Miles Tran[2], Ce Gao[3], Sergio Poli[1], Yunju Jeong[4], Louis Merriam[5], Jinjun Shi[6], Rachel Knipe[7], Katharine Black[8], Lida Hariri[9], Carol Feghali-Bostwick[10], Rodney Infante[11], Janelle Pugashetti[12], Justin Oldham[12], Ilya Korsunsky[13], Kevin Wei[14] and Edy Kim[1], [1]Division of Pulmonary and Critical Care Medicine, Department of Medicine (DOM), Brigham and Women's Hospital (BWH); Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Division of Rheumatology, Inflammation and Immunity, DOM, BWH; Harvard Medical School, Boston, MA, [4]Division of Pulmonary and Critical Care Medicine, Department of Medicine (DOM), Brigham and Women's Hospital (BWH), Harvard Medical School, Boston, MA, United States; Department of Food and Nutrition, College of Human Ecology, Kyung Hee University, Seoul, Republic of Korea, [5]Division of Pulmonary and Critical Care Medicine, Department of Medicine (DOM), Brigham and Women's Hospital (BWH), Boston, MA, [6]Center for Nanomedicine and Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital (BWH); Harvard Medical School, Boston, MA, [7]Division of Pulmonary and Critical Care Medicine, DOM, Massachusetts General Hospital; Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital; Harvard Medical School, Boston, MA, [8]Division of Pulmonary and Critical Care Medicine, DOM, Massachusetts General Hospital; Harvard Medical School, Boston, MA, [9]Department of Pathology, Massachusetts General Hospital; Division of Pulmonary and Critical Care Medicine, DOM, Massachusetts General Hospital; Harvard Medical School, Boston, MA, [10]Medical University of South Carolina, Charleston, SC, [11]Center for Human Nutrition, Dept. of Molecular Genetics, DOM, University of Texas Southwestern, Dallas, TX, [12]Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, [13]Division of Rheumatology, Inflammation and Immunity, DOM, BWH; Division of Genetics, DOM, BWH; Harvard Medical School, Boston, MA, [14]Brigham and Women's Hospital at Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (0807–0812)

Session Type: Abstract Session

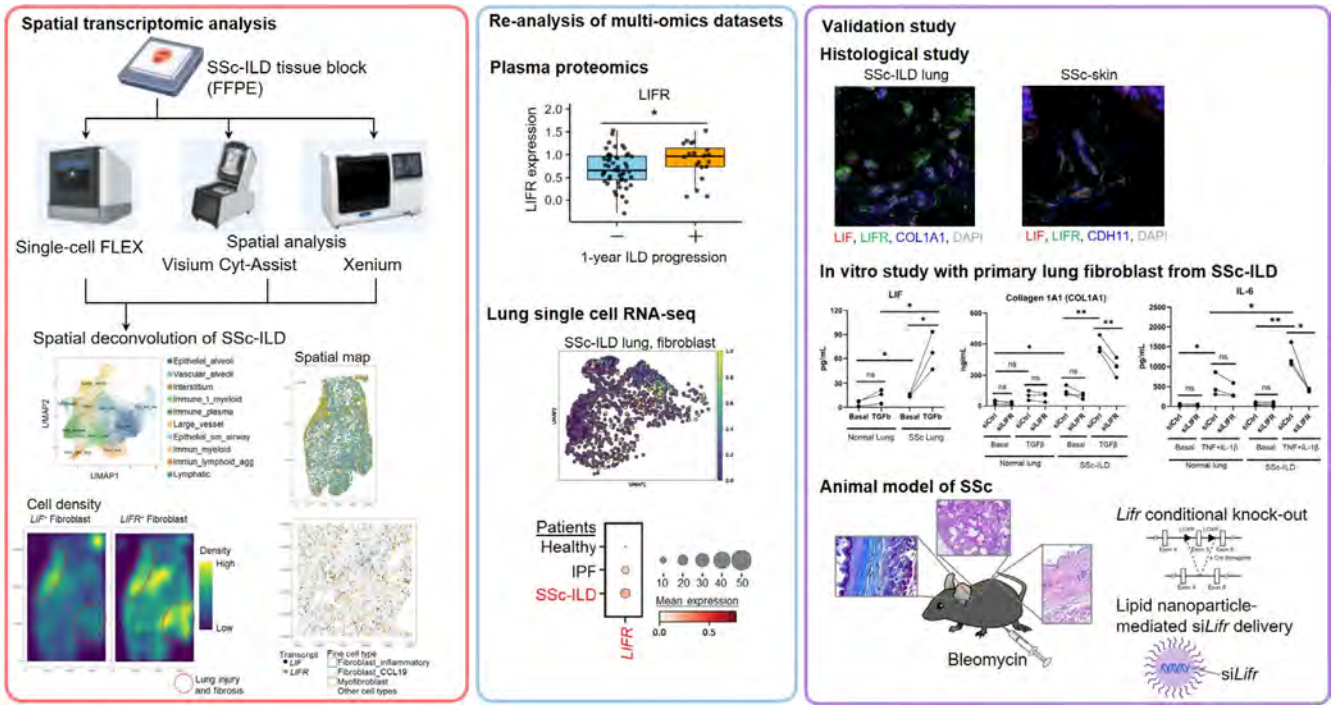
Session Time: 1:00PM–2:30PM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune, fibroinflammatory disease of skin and visceral organs. Current SSc therapies have limited efficacy for progressive fibrosis. Our prior work showed that LIF receptor (LIFR, a member of the IL-6 receptor superfamily) and its ligand LIF were expressed by synovial fibroblasts in rheumatoid arthritis and amplified pathogenic inflammation. We hypothesized that the fibroblast LIF/LIFR axis also drives fibrotic pathobiology in SSc.

Methods: We applied three 10x Genomics platforms (single-cell, Visium CytAssist spatial, and Xenium spatial transcriptomics (curated genes)) and immunofluorescence staining (IF) to explanted lung and skin biopsies from patients with SSc interstitial lung disease(ILD). We examined a published, plasma proteomic dataset of SSc-ILD patients with longitudinal follow-up. Primary lung fibroblast cell lines from control and SSc-ILD lung tissue were used for in vitro studies. Our experimental model of murine SSc (lung, skin, esophageal fibrosis) used intraperitoneal bleomycin (2x/week for 4 weeks). For testing LIFR in vivo, we compared fibroblast-specific *Lifr*-deficient mice (*Pdgfra*-CreERT2$^{+/-}$ *Lifr* $^{flox/flox}$ and *Col1a2*-CreERT$^{+/-}$ *Lifr* $^{flox/flox}$ mice) to *Lifr*$^{+/+}$ sibling controls. To therapeutically silence *Lifr*, we administered lipid nanoparticles (LNP) with si*Lifr* payload i.v. from day 7-28 after bleomycin initiation and assessed tissue at day 33.

Results: Xenium spatial analysis of SSc-ILD lungs (N=4) found *LIFR*$^{+}$ *and LIF*$^{+}$ fibroblasts enriched in inflammatory, interstitial spatial niches in regions of lung injury and fibrosis. The *LIF*$^{+}$*LIFR*$^{+}$ spatial niches were colocalized with myofibroblast-enriched spatial niches. Using IF, we validated the enrichment of LIF^{+}LIFR^{+} fibroblasts in "leading edge" regions of fibrosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Spatial transcriptomic analysis, re-analysis of multi-omics datasets, and validation studies using immunofluorescence staining, in vitro assays, and animal model revealed fibroblast LIFR as an amplifier of organ fibrosis and inflammation in SSc.

in both SSc-ILD lung (N=12) and SSc skin (N=6) tissue. Plasma LIFR level was higher in SSc-ILD patients with progressive fibrosis compared to stable disease (N=72).

We moved to in vitro and in vivo studies to understand the function of LIFR. SSc-ILD lung fibroblasts had increased constitutive expression of *LIF* in vitro; stimulation with TGFβ further increased LIF expression in SSc, but not in control fibroblasts. Silencing *LIFR* with siRNA suppressed collagen expression in SSc-ILD lung fibroblasts following in vitro profibrotic stimuli (IL-4, IL-13, or TGFβ). LIFR also drove increased expression of IL-6 and IL-8 in SSc-ILD lung fibroblasts following stimulation with IL-1β and TNFα. In the murine model of SSc, mice with fibroblast-specific *Lifr* deletion had reduced lung,skin, and esophageal fibrosis compared to $Lifr^{+/+}$ control. Therapeutic intervention with LNP-si*Lifr* reduced lung and skin fibrosis in a murine model of SSc.

Conclusion: A LIF/LIFR autocrine circuit drives both inflammatory and fibrogenic programs in SSc skin and lung fibroblasts. Targeting LIFR in a murine model of SSc reduced organ fibrosis. LIFR is a candidate therapeutic target for SSc.

Disclosure: M. Kamiya: None; **H. Nguyen**: None; **M. Tran**: None; **C. Gao**: None; **S. Poli**: None; **Y. Jeong**: None; **L. Merriam**: None; **J. Shi**: None; **R. Knipe**: None; **K. Black**: None; **L. Hariri**: None; **C. Feghali-Bostwick**: None; **R. Infante**: None; **J. Pugashetti**: None; **J. Oldham**: None; **I. Korsunsky**: Mestag Therapeutics, 2; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **E. Kim**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0809

Human blood vessel organoids as a model of vasculopathy in systemic sclerosis

Yanhua Xiao[1], Xuezhi Hong[1], Langxian Zhi[1], Yi-Nan Li[2], Martin Regensburger[3], Franz Marxreiter[4], Boris Görg[5], Sarah Koziel[6], Andrea-Hermina Györfi[7], Tim Filla[8], Peter-Martin Bruch[6], Philipp Tripal[9], James Adjaye[10], Sascha Dietrich[11], Jürgen Winkler[4], Jörg Distler[12] and **Alexandru-Emil Matei**[13], [1]Medical Faculty of Heinrich Heine University, Dusseldorf, Germany, [2]University Hospital of Dösseldorf, Dösseldorf, Germany, [3]Department of Stem Cell Biology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Erlangen, Germany, Erlangen, Germany, [4]Department of Molecular Neurology, FAU Erlangen-Nürnberg, Erlangen, Germany, Erlangen, Germany, [5]Heinrich-Heine University, Dusseldorf, Germany, [6]University Hospital Düsseldorf, Dusseldorf, Germany, [7]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [8]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [9]University Hospital Erlangen, FAU Erlangen-Nürnberg, Erlangen, [10]Institute for Stem Cell Research and Regenerative Medicine, University Hospital Düsseldorf, Moorenstrasse 5, D-40225 Duesseldorf, Germany, Dusseldorf, Germany, [11]Heinrich Heine University Duesseldorf, University Hospital Duesseldorf, Duesseldorf, Germany, [12]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [13]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany

SESSION INFORMATION

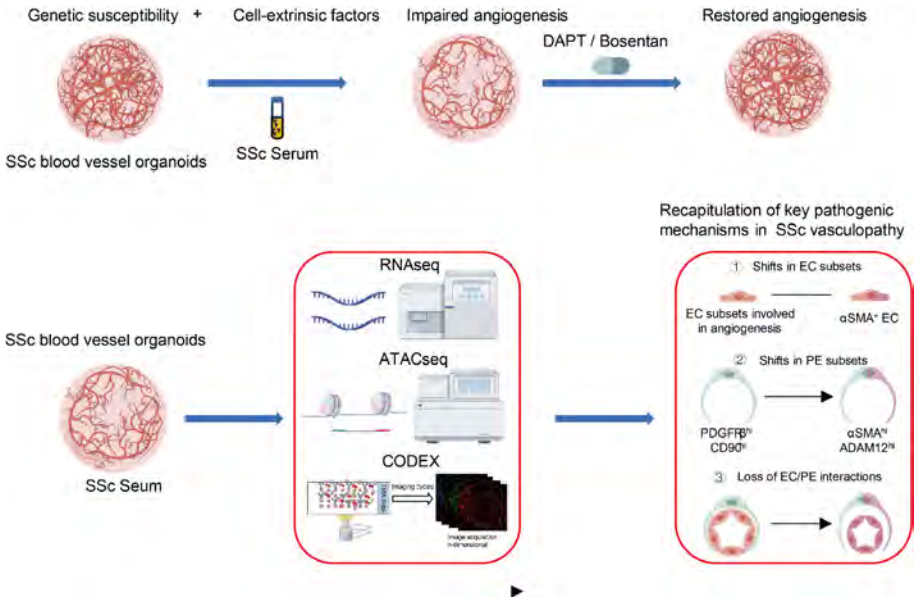
Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (0807–0812)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: While several pathogenic processes involved in vasculopathy in systemic sclerosis (SSc) have been described[1-3], the mechanisms that underlie the SSc microvasculopathy remain incompletely understood. Human models of sufficient complexity to recapitulate the key disease-relevant cell types and their interactions are currently lacking. Thus, the preclinical testing of novel therapeutic approaches for SSc microvasculopathy remains challenging.



SSc blood vessel organoids reveal mechanisms of vasculopathy and responses to targeted therapy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Our study aimed to evaluate whether blood vessel organoids (BVOs) could be employed as a novel, multicellular tissue-like three-dimensional model for studying SSc vasculopathy in vitro.

Methods: BVOs were differentiated from iPSCs of SSc patients (SSc-BVOs) and healthy individuals (healthy-BVOs) and treated with serum from healthy donors or SSc patients with active digital ulcers (SSc_aDU). Angiogenesis parameters, including vessel density, vessel length, and number of junctions, were quantified using AngioTool. Transcriptomic changes and chromatin accessibility were assessed by RNA-seq and ATAC-seq, respectively. Co-detection by indexing (CODEX), a spatial proteomics technique, was employed for cell phenotyping, evaluation of functional markers and of cell-cell interactions. The endothelin receptor antagonist bosentan (BST) and the γ-secretase inhibitor DAPT were tested for their effects in preventing angiogenesis defects in BVOs.

Results: SSc-BVOs, but not healthy-BVOs demonstrated angiogenic defects, with decreased vessel density, vessel length and number of junctions, when exposed to SSc_aDU serum.

Exposure of SSc-BVOs to SSc_aDU serum triggers concerted changes at epigenetic, mRNA and protein levels to induce upregulation of endothelial-to-mesenchymal transition (EndMT)-related pathways and proteins, such as αSMA, SNAIL1, TWIST1 and collagen synthesis, and downregulation of markers and pathways related to an endothelial cells (ECs) phenotype, such as CD31, VWF or tight junctions.

CODEX analysis demonstrated that BVOs recapitulate ECs and pericyte populations in SSc, along with their disease-specific changes in frequencies. Two αSMA^+ ECs subsets were upregulated in SSc BVOs exposed to SSc_aDU serum, as previously shown in SSc[4]. The $Tie2^+$ ECs lost interactions with pericytes, whereas the two αSMA^+ ECs were spatially avoiding pericytes in SSc-BVOs exposed to SSc_aDU serum, recapitulating the impaired ECs-pericytes interactions previously described in SSc[5].

Treatment with BST and DAPT prevented the angiogenesis defects induced by SSc_aDU serum in SSc-BVOs.

Conclusion: This study demonstrates that SSc-BVOs recapitulate key features of SSc vasculopathy, including impaired angiogenesis and enhanced EndMT, increases in pathologic ECs populations, as well as loss of ECs -pericytes interactions when exposed to SSc_aDU serum. This study further validates SSc-BVOs as a human model system for drug testing and employs this system to demostrate that γ-secretase inhibition is a potential therapeutic approach in SSc microvasculopathy.

Disclosure: Y. Xiao: None; **X. Hong**: None; **L. Zhi**: None; **Y. Li**: None; **M. Regensburger**: None; **F. Marxreiter**: None; **B. Görg**: None; **S. Koziel**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **T. Filla**: None; **P. Bruch**: None; **P. Tripal**: None; **J. Adjaye**: None; **S. Dietrich**: None; **J. Winkler**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **A. Matei**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0810

Spatial Transcriptomic-based Phenotyping of the Fibroblast Niches in Systemic Sclerosis-associated Primary Heart Involvement

Alexandru Micu[1], Alexandru-Emil Matei[2], Yi-Nan Li[3], Ann-Christin Pecher[4], Tim Filla[5], Jörg Henes[6], Markus Eckstein[7], Karin Klingel[8], Jörg Distler[9] and Andrea-Hermina Györfi[10], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Germany, [2]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany, [3]University Hospital of Dösseldorf, Dösseldorf, Germany, [4]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tübingen, Germany, [5]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [6]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tuebingen, Germany, [7]Institute of Pathology and Comprehensive Cancer Center EMN, Friedrich-Alexander- Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [8]Cardiopathology, Institute for Pathology, Eberhard-Karls-Universität Tübingen, Tübingen, Germany, [9]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [10]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (0807–0812)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

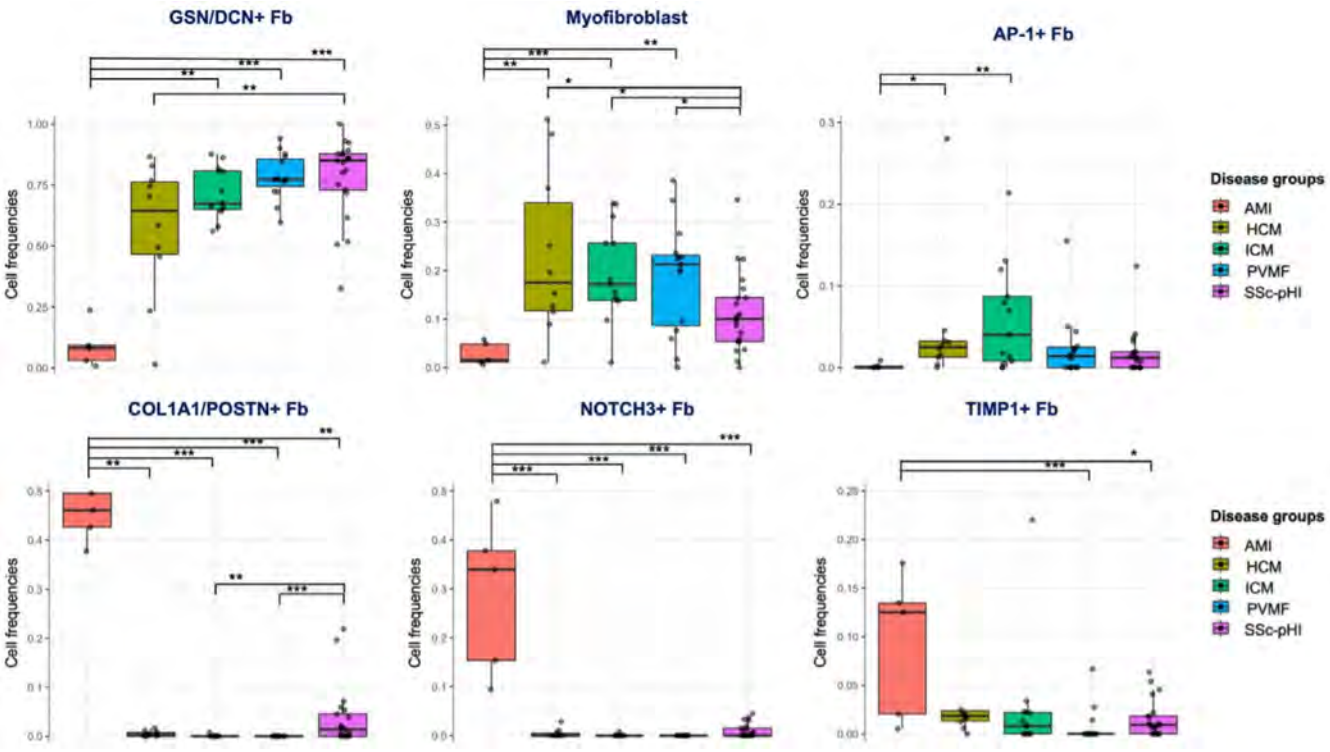


Figure 1. Distribution of fibroblast populations across diseases. Statistical significance was assessed using the Kruskal-Wallis test followed by Dunn's post hoc test with Holm adjustment. * – p-value <0.05, ** – p-value <0.01, *** – p-value <0.001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

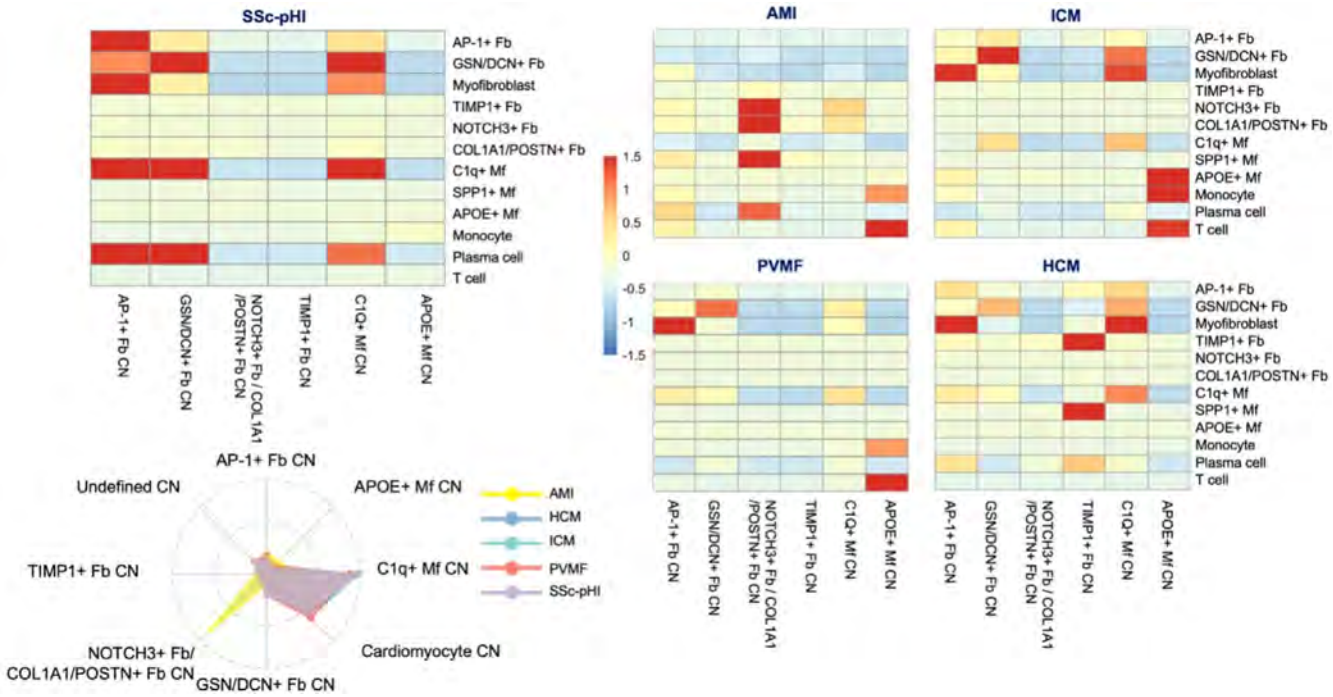


Figure 2. Cellular niche composition and frequencies across diseases.

Background/Purpose: Systemic sclerosis (SSc)-associated primary heart involvement (SSc-pHI) is one of the leading causes of mortality in SSc, yet its underlying cellular and molecular pathomechanisms are poorly understood (1, 2). We aimed to characterize the fibroblast (Fb) subpopulations, their niches and associated cellular networks in SSc-pHI and compare them to those present in other myocardial diseases which associate chronic (postviral myocardial fibrosis (PVMF), hypertrophic cardiomyopathy (HCM), and ischemic cardiomyopathy (ICM)), or acute (acute myocardial infarction (AMI)) fibrotic remodeling using cyclic-in-situ-hybridization.

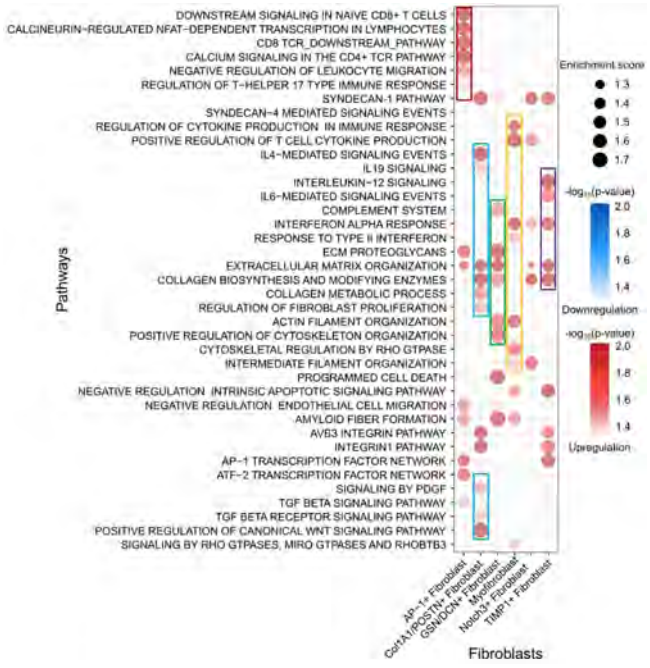


Figure 3. Functional analysis of fibroblast populations.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We employed the CosMx SMI platform to analyze FFPE myocardial biopsies from 15 SSc-pHI, 10 PVMF, 5 HCM, 5 ICM and 3 AMI patients, examining two 1.8mm^2 regions per sample. Gene expression profiling used the Human Universal Cell Characterization RNA Core Panel (950 genes), supplemented with 19 Fb subset markers (3). Data analysis was performed as described previously (4).

Results: We identified 11672 Fb. Spatially informed clustering revealed six Fb populations: GSN/DCN$^+$, AP1$^+$, TIMP1$^+$, COL1A1/POSTN$^+$, NOTCH3$^+$, and myofibroblasts. GSN/DCN$^+$ Fb and myofibroblasts were significantly enriched in SSc-pHI and other forms of chronic compared to acute fibrotic remodeling, while TIMP1$^+$, COL1A1/POSTN$^+$, and NOTCH3$^+$ Fb were significantly upregulated in acute compared to chronic conditions (Figure 1). GSN/DCN$^+$ Fb and AP1$^+$ Fb CNs were enriched and colocalized in the perivascular and the subendocardial areas in chronic conditions, while the NOTCH3$^+$ Fb/COL1A1/POSTN$^+$ Fb CN was enriched in the periinfarct zone in AMI. Furthermore, we observed significant disease-specific changes in the composition of the Fb niches (Figure 2). Functional analyses revealed distinct functions of the Fb populations while spatial interaction analyses showed profound differences in their signaling network in SSc-pHI compared to both other forms of chronic fibrotic remodeling and AMI (Figure 3).

Conclusion: We demonstrate significant alterations in the cellular composition of fibroblasts in SSc-pHI, with altered cellular interactions and signaling in their local niches, compared with other myocardial diseases with acute or chronic fibrotic remodeling. Furthermore, we identified functionally distinct fibroblast populations and uncovered subsets with disease-specific topologies. Our findings provide new insights into the pathophysiology of fibrotic myocardial remodeling and offer potential therapeutic targets.

Disclosure: A. Micu: None; **A. Matei**: None; **Y. Li**: None; **A. Pecher**: AstraZeneca, 6, Boehringer-Ingelheim, 1, 6, GlaxoSmithKlein(GSK), 6, UCB, 6; **T. Filla**: None; **J. Henes**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, Janssen, 1, 6, Novartis, 1, 1, 6, 6, Otsuka, 1, Pfizer, 1, Roche, 1, SOBI, 1, UCB, 1, 6; **M. Eckstein**: None; **K. Klingel**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6.

Abstract Number: 0811

SSc Skin Cell Atlas: a Scalable Web Portal for scRNA-Seq Analysis

Helen Jarnagin[1], Zhiyun Gong[1], Rachael Bogle[2], Alex Tsoi[2], Rezvan Parvizi[3], Madeline Morrisson[4], Dinesh Khanna[5], Johann Gudjonsson[5] and **Michael Whitfield**[6], [1]Dartmouth College, Lebanon, NH, [2]University of Michigan, Holland, OH, [3]Dartmouth, lebanon, NH, [4]Geisel School of Medicine at Dartmouth College, Hanover, NH, [5]University of Michigan, Ann Arbor, MI, [6]Geisel School of Medicine, Lebanon, NH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (0807–0812)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Despite the recent popularity and utility of modern high-resolution sequencing technologies, leveraging publicly available single-cell studies remains hampered by the need for substantial computational power and expertise. In this study, we assembled and integrated publicly available single-cell datasets from diffuse cutaneous systemic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Dataset features included in SSc Skin Cell Atlas Database.

GEO ID	Dataset Name	Original Publication	Individual Object?	Integrated Object?	Total Cell Number	Number of SSc Samples	Number of HC Samples
GSE195452	Gur	Gur et al., 2022; doi: 10.1016/j.cell.2022.09.011	Y	N	14586	93	53
GSE138669	Tabib	Tabib et al., 2021; 10.1038/s41467-021-24607-6	Y	Y	21230	10	12
GSE249279	Ma	Ma et al., 2023; https://doi.org/10.1038/s41467-023-44645-6	Y	Y	34915	11	26
GSE209635	Khanna	Khanna et al., 2022; https://doi.org/10.1172/jci.insight.159566	Y	Y	73926	30	0
GSE173706	Ma-HCs	Ma et al., 2023; https://doi.org/10.1038/s41467-023-39020-4	N	Y	2890	0	8
GSE147424	He-HCs	He et al., 2020; 10.1016/j.jaci.2020.01.042	N	Y	40336	0	3
This Study	Integrated Object	N/A	N/A	Y	172295	80	27

sclerosis (dcSSc) skin and control samples. The processed data, accessible through a web application, enables users to access and perform single-cell analyses without prior coding expertise or high-performance computing resources.

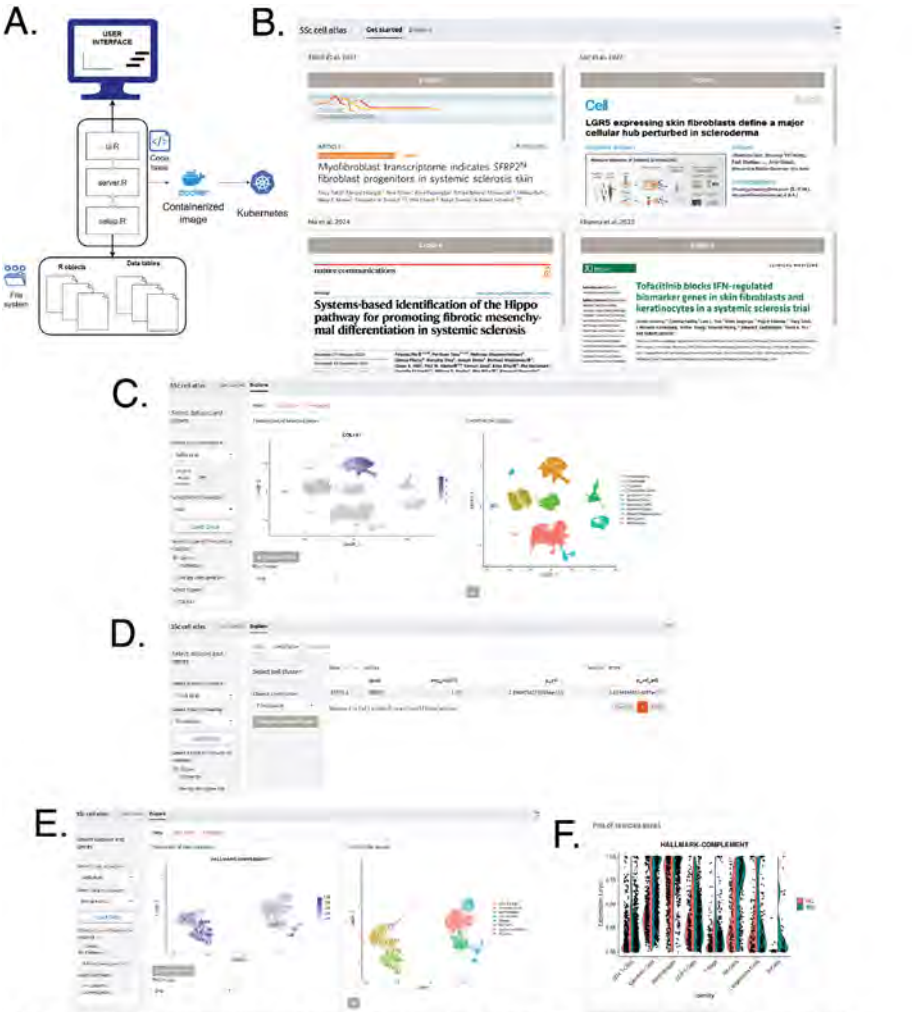


Figure 1. Web-based application for gene expression and gene set enrichment analysis of multiple single-cell datasets. **A)** Web-application development diagram for storing, accessing, and probing single-cell data. **B)** User-accessible tool for gene expression analysis on whole-skin of major single-cell skin datasets. **C)** Gene expression reveals the canonical marker expression of COL1A1, a fibroblast marker, in complete-skin objects from the Tabib et al. 2021 dataset. **D)** Individual gene differential expression, and differential expression results for SFRP4 Fibroblast 9 subcluster. **E)** Gene set expression results show Hallmark Complement Pathway enrichment in macrophage subclusters. **F)** Violin plot shows higher complement gene set enrichment in SSc macrophages compared to HC.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Single-cell counts and metadata were downloaded from the GEO repositories for each dataset (**Table 1**); each was then processed and normalized independently using Seurat. Cell typing was performed, hierarchically and then sub-clustered for detailed analysis (differential expression, CAMML, and SingleR). Gene set enrichment was performed on each dataset and cell subpopulation (VAM). Differential expression and gene set enrichment comparisons were performed using the Wilcoxon Rank Sum test. A cohort of these datasets were processed using uniform genome alignment and counts generation (CellRanger 9.0.0, GRCh38) to generate a novel integrated dataset for disease-based comparisons at a single-cell level.

Results: We standardized and reprocessed all publicly available single-cell datasets analyzing dcSSc skin biopsies. These data were optimized for efficient loading into a user-friendly web interface for gene expression and pathway querying (**Fig. 1a-c**). From individual objects, we successfully recapitulated the findings presented in the original primary research articles, such as the enrichment of SFRP4 in specific fibroblast subpopulations (Wilcoxon Rank Sum Test, p.adjust = 3.9e-151) (**Fig 1d**). This tool also enables gene set enrichment tests in specific cell subtypes that were not previously presented in the original manuscripts, such as the enrichment of the complement system in SSc macrophages (Wilcoxon Rank Sum Test, p.-adjust 1.95e-203) (**Fig. 1e-f**). Finally, we generated a fully integrated single-cell dataset across multiple studies as a novel source for comparing SSc skin samples.

Conclusion: The SSc Skin Single Cell Atlas is a user-friendly web application for rapid and detailed analysis of publicly available datasets. This tool enables users to easily ask questions regarding gene and gene set differential expression without the need to download, process, and analyze the data locally. Furthermore, given the heterogeneous nature of SSc, accessing a large cohort of patients for single-cell comparison is paramount to better understand cellular dynamics that drive SSc fibrosis. This novel study integrates publicly available datasets from multiple research reports to provide a more comprehensive understanding of SSc skin fibrosis.

Disclosure: H. Jarnagin: None; **Z. Gong**: None; **R. Bogle**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **R. Parvizi**: None; **M. Morrisson**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **J. Gudjonsson**: None; **M. Whitfield**: Boehringer Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 2, Celdara Medical LLC, 2, 5, 10, 12, Scientific Founder.

Abstract Number: 0812

anti-cd206 CAR T Cell Immunotherapy Mitigates Dermal Pathology in Systemic Sclerosis

Chanhyuk Park[1], Helen Jarnagin[2], Asmaa Mohamed[3], Noelle Kosarek[4], Owen Wilkins[1], Fred Kolling[1], Yina Huang[1], Michael Whitfield[5] and Patricia Pioli[1], [1]Geisel School of Medicine at Dartmouth, Lebanon, NH, [2]Dartmouth College, Lebanon, NH, [3]Geisel School of Medicine at Dartmouth, Charlottesville, VA, [4]Dartmouth Geisel School of Medicine, Lebanon, NH, [5]Geisel School of Medicine, Lebanon, NH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (0807–0812)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Systemic sclerosis (SSc) is a progressive, chronic multi-system disorder of unknown etiology that is characterized by immune dysfunction, fibrosis, and loss of dermal white adipose tissue (DWAT), which is an early event in SSc that precedes the onset of skin fibrosis. Despite advances in disease management, the overall prognosis for SSc

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

remains significantly worse than for other rheumatic diseases. While cooperative interactions between macrophages (MØs) and fibroblasts have been implicated in disease pathogenesis, no therapies that specifically target pathological MØs are in current clinical use for SSc.

Methods: Because our prior studies demonstrate a critical role for CD206^{high} MØs in SSc pathology, we developed a novel therapeutic approach to eliminate these cells using chimeric antigen receptor (CAR) T cells. CAR T cell efficacy was tested in the bleomycin (BLM) mouse model of SSc. BLM was delivered via osmotic pump, and a single dose of anti-CD206 or control CAR T cells was administered systemically via tail vein injection 7 days post-initiation of BLM to assess effects on established dermal pathology. Skin tissues were fixed and paraffin-embedded for single cell RNA-seq (scRNA-seq) and spatial transcriptomic analyses, and for quantification of adipose and dermal thickness by H&E. An *in vitro* co-culture model system was developed to assess the mechanisms by which CD206^{high} MØs mediate SSc pathology, and antibody blockade studies were performed to identify the MØ-derived soluble mediators that contribute to skin disease pathogenesis.

Results: We now show that CAR T cell-mediated elimination of CD206^{high} MØs to BLM mice resulted in restoration of DWAT to levels observed in mice not treated with BLM. Notably, administration of control CAR T cells failed to rescue DWAT loss. scRNA-seq and spatial transcriptomics analyses demonstrated anti-CD206 CAR T treatment increases mature adipocyte populations and alters representation of extracellular matrix (ECM)-secreting fibroblast and inflammatory myeloid subsets. In vitro modeling demonstrated that CD206^{high} MØs redirect lineage commitment of adipocyte stem cells (ADSCs) from adipocytes toward fibroblasts in a mechanism dependent, at least in part, on IL-6 receptor engagement.

Conclusion: Our new findings demonstrate that anti-CD206 CAR T cell therapy significantly attenuates dermal pathology in SSc through restoration of DWAT, implicating a novel function for MØs in the regulation of early fibrotic disease. *In vitro* mechanistic studies are supportive of a model in which CD206^{high} macrophages provide signals mediated by IL-6 that alter ADSC commitment from adipogenic to fibrogenic. Activated fibroblasts then secrete excessive extracellular matrix (ECM), culminating in fibrotic disease. Collectively, our results suggest MØ-targeted therapies may be effective in ameliorating SSc.

Disclosure: C. Park: None; **H. Jarnagin**: None; **A. Mohamed**: None; **N. Kosarek**: None; **O. Wilkins**: None; **F. Kolling**: None; **Y. Huang**: None; **M. Whitfield**: Boehringer Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 2, Celdara Medical LLC, 2, 5, 10, 12, Scientific Founder; **P. Pioli**: None.

Abstract Number: 0813

Impact of Tirzepatide on Musculoskeletal Pain and High-Risk Analgesic Use Among Non-Diabetic Patients with Overweight or Obesity: A Propensity Score-Matched, Active Comparator, New User Study

Gregory Challener[1], Kevin Sheng-Kai Ma[2], Natalie McCormick[3], Minna Kohler[4], Janeth Yinh[3], Chio Yokose[5], Sharan Rai[6], Florence Porterfield[7], Fatima Stanford[8], Dong Wook Kim[9], April Jorge[3] and Hyon K. Choi[10], [1]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, [2]Center for Global Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States, Philadelphia, PA, [3]Massachusetts General Hospital, Boston, MA, [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [5]Massachusetts General Hospital, Waltham, MA, [6]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [7]Division of Endocrinology, Massachusetts General Hospital, Boston, [8]Neuroendocrine Unit, Pediatric Endocrinology, Massachusetts General Hospital, Boston, [9]Division of Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital, Boston, [10]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Pain in Rheumatic Disease Including Fibromyalgia (0813–0818)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Tirzepatide is a dual GIP/GLP-1 receptor co-agonist approved for weight loss in patients with obesity or body mass index (BMI) > 27 kg/m^2 with comorbidities. GLP-1-based therapies may ease osteoarthritis symptoms indirectly via weight loss and directly through anti-inflammatory effects [1-3]. The STEP 9 trial demonstrated improvement in knee pain and function as well as reduced NSAID use in patients with obesity and knee osteoarthritis treated with semaglutide [4]. Tirzepatide differs from semaglutide in its dual agonism and greater weight loss [5]. No studies have examined musculoskeletal pain or analgesic use with tirzepatide. This study evaluated whether patients treated with tirzepatide had reduced joint pain and analgesic use than those receiving phentermine, the most prescribed anti-obesity medication in the U.S.

Methods: We conducted a cohort study using the TriNetX Research network, a large network of U.S. electronic health records and claims data. ICD-10 codes identified non-diabetic patients with BMI > 27 kg/m^2. Using an intention-to-treat approach, we analyzed the overall rate of musculoskeletal pain encounters and risky analgesic use, as well as cardiovascular endpoints following initiation of tirzepatide or phentermine, excluding patients with prior history of the outcomes of interest. Outcomes were defined as > 1 encounter with applicable ICD-10 code occurring one day or more after treatment initiation. Nausea served as a positive control outcome. Propensity score matching adjusted for > 400 factors including demographics, comorbidities, medications, and baseline BMI; key covariates are included in Table 1. Kaplan-Meier and Cox models estimated the risk of the outcomes of interest.

Table 1. Baseline Characteristics 0f Patients Receiving Tirzepatide versus Phentermine, after 1:1 Propensity-Score Matching

	Tirzepatide (n = 27,930)	Phentermine (n = 27,930)	Std diff.*
Age at index, mean (SD)	45.9 (12.9)	45.6 (13.1)	0.024
Male	16.7%	16.1%	0.016
Female	73.7%	74.3%	0.012
Unknown gender	9.6%	9.6%	0.001
Comorbidities			
Hypertension	40.0%	38.7%	0.026
Chronic kidney disease	2.8%	2.5%	0.007
Ischemic heart disease	5.4%	5.0%	0.021
Heart failure	2.0%	1.8%	0.015
Liver disease	11.9%	11.5%	0.013
Cerebrovascular disease	3.0%	2.8%	0.011
Nicotine dependence	13.1%	13.2%	0.002
Alcohol-related disorders	3.0%	2.8%	0.010
Osteoarthritis	24.8%	24.2%	0.016
Knee osteoarthritis	12.7%	12.6%	0.004
Knee pain	25.0%	24.9%	0.002
Low back pain	27.2%	26.9%	0.006
Medications			
Beta blockers	26.9%	26.2%	0.014
ACE inhibitors	14.3%	13.8%	0.014
NSAIDs	62.1%	62.1%	0.001
Opioid analgesics	58.4%	58.3%	0.003
Measures			
BMI, mean (SD)	37.9 (6.5)	37.8 (6.5)	0.026
A1c, mean (SD)	5.6 (1.2)	5.6 (1.3)	0.004

* Std diff. (standardized mean difference) <0.1 indicates negligible difference between groups. Baseline characteristics were defined as occurring any time up to one day prior to the index event.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Outcomes Among Patients Receiving Tirzepatide versus Phentermine

Pain/analgesic outcomes	Unmatched, HR (95% CI)	Matched, HR (95% CI)
Joint pain	1.00 (0.95, 1.05)	0.91 (0.84, 0.99)
Low back pain	0.84 (0.79, 0.89)	0.89 (0.80, 0.98)
Hip pain	1.08 (1.00, 1.16)	0.88 (0.78, 0.999)
Knee pain	0.93 (0.88, 0.995)	0.84 (0.76, 0.93)
NSAID script	0.84 (0.81, 0.89)	0.88 (0.81, 0.95)
Opioid analgesics	0.82 (0.78, 0.86)	0.86 (0.79, 0.93)
Other outcomes		
Mortality	0.74 (0.54, 1.02)	0.48 (0.28, 0.80)
Major adverse cardiac events	1.29 (1.11, 1.51)	0.77 (0.61, 0.99)
Nausea	1.33 (1.25, 1.41)	1.22 (1.10, 1.35)
Achieved normal BMI	3.24 (3.01, 3.50)	3.02 (2.61, 3.49)

Note: Phentermine serves as the reference group. Abbreviations: HR, hazard ratio; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug

Results: A total of 62,722 patients started on tirzepatide and 119,020 patients started on phentermine were included. After 1:1 matching, 27,930 patients per group had balanced baseline characteristics (**Table 1**). Mean follow-up was 276 days among patients on tirzepatide and 318 days among patients on phentermine. Tirzepatide users were more likely to achieve normal BMI (HR 3.02; 95% CI: 2.61, 3.49) with lower risk of joint pain (HR 0.91; 95% CI: 0.84, 0.99), especially knee pain (HR 0.84; 95% CI: 0.76, 0.93), and lower risk of NSAID (HR 0.88; 95% CI: 0.81, 0.95) and opioid prescriptions (HR 0.86; 95% CI: 0.79, 0.93) (**Table 2**). Risk of nausea was increased among tirzepatide users (HR 1.22; 95% CI: 1.10, 1.35), while risks of mortality and overall major adverse cardiac events (acute myocardial infarction, cerebral infarction, and/or mortality) were reduced (respectively, HR 0.48 with 95% CI of 0.28, 0.80; and HR 0.77 with 95% CI of 0.61, 0.99).

Conclusion: This large population-based study of non-diabetic patients with overweight or obesity demonstrates improvement in musculoskeletal pain requiring clinical care, reduced risky analgesic use, and better cardiovascular outcomes, among those receiving tirzepatide compared to phentermine. These findings support tirzepatide's role in reducing musculoskeletal pain and the need for NSAID and opioid medications in this population.

References

1. PMID: 35091584

2. PMID: 39476345

3. PMID: 35280931

4. PMID: 39476339

5. PMID: 38976257

Disclosure: G. Challener: None; **K. Sheng-Kai Ma**: None; **N. McCormick**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **J. Yinh**: Janssen, 2, Springer, 9; **C. Yokose**: None; **S. Rai**: None; **F. Porterfield**: None; **F. Stanford**: None; **D. Kim**: None; **A. Jorge**: Bristol-Myers Squibb(BMS), 5; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0814

Pain Patterns in a Multicenter Randomized Trial of Early RA – Link Between Initially Sustained Joint Inflammation and Subsequent Non-inflammatory Pain Outcomes

Annie Brink[1], Johan Karlsson Wallman[2], Jon T Einarsson[1], Meliha Kapetanovic[1], Elisabeth Mogard[1], Elisabet Lindqvist[1], Carmen Roseman[1], Kristina Lend[3], Merete Hetland[4], Mikkel Ostergaard[5], Kim Horslev-Petersen[6], Dan Nordstrom[7], Tuulikki Sokka-isler[8], Bjorn Gudbjornsson[9], Gerður María Gröndal[9], Marte Heiberg[10], Espen Haavardsholm[10], Michael Nurmohamed[11], Anna Rudin[12], Ronald van Vollenhoven[13], Till Uhlig[10], Jon Lampa[14] and **Tor Olofsson**[2], [1]Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden, [2]Lund University, Skane University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Skane Lan, Sweden, [3]Department of Rheumatology and Amsterdam Rheumatology Center, Amsterdam University Medical Centers, Amsterdam; Department of Medicine, Rheumatology Unit, Center for Molecular Medicine (CMM), Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, [4]Copenhagen Center for Arthritis Research (COPECARE) and DANBIO, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; Department of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark, [5]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark, [6]Danish Hospital for Rheumatic Diseases, University Hospital of Southern Denmark, Sønderborg; Department of Regional Health Research, University of Southern Denmark, Odense, Denmark, [7]Division of Rheumatology, Helsinki University Hospital, Helsinki, Finland, [8]Department of Medicine and University of Eastern Finland, Jyväskylä Central Hospital, Juväskylä, Finland, [9]Landspitali University Hospital; Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [10]Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [11]Amsterdam Rheumatology and Immunology Center, Reade; Department of Rheumatology and Amsterdam Rheumatology Center, Amsterdam University Medical Centers, Amsterdam, Netherlands, [12]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy of University of Gothenburg, Gothenburg, Sweden, [13]Department of Rheumatology, Amsterdam University Medical Centre, Amsterdam, Netherlands, [14]Department of Medicine, Rheumatology Unit, Center for Molecular Medicine (CMM), Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Pain in Rheumatic Disease Including Fibromyalgia (0813–0818)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Emerging data indicate an uncoupling between pain and inflammation during the RA disease course, and comorbid fibromyalgia – thought to stem from central pain sensitization – is displayed in up to 25% of patients. It has been hypothesized that sensitization could be induced by a period of insufficiently treated inflammation, although this remains to be explored. The current study thus aimed to 1) investigate the dynamics of persistent pain with and without inflammatory control after RA onset; and 2) examine if cumulative inflammation during the first 6 months is linked to subsequent non-inflammatory pain.

Methods: NORD-STAR is an investigator-initiated, open-label trial of early (<24 months symptom duration) RA patients randomized to methotrexate combined with (a) other csDMARDs/corticosteroids or steroids alone, (b) certolizumab pegol, (c) abatacept, or (d) tocilizumab. Here, the latter group was omitted to allow for CRP analysis, and patients were analyzed irrespective of randomized therapy. Assessment was performed at 0, 4, 8, 12, 16, 24, 32, 40 and 48 weeks (w) including *unacceptable pain* (>40 mm [0-100] on a Visual Analogue Scale [VAS]), and *refractory pain* (unacceptable pain despite inflammation control: VAS pain >40 mm + CRP< 10 mg/L + swollen joint count [SJC; of 66] ≤1)[1]. Differences in pain outcomes between EULAR response groups were analyzed by Chi-2/Fisher's exact test. Associations between cumulative inflammatory load (area-under-the-curve [AUC] from 0-24w for CRP/SJC) and unacceptable/refractory pain at 48w, as well as 48w *fibromyalgic RA* (by the published definition tender joint count [TJC]-SJC ≥7 [of 68/66][2]), were respectively estimated by logistic regression, adjusted for age, sex, ACPA positivity and BMI.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

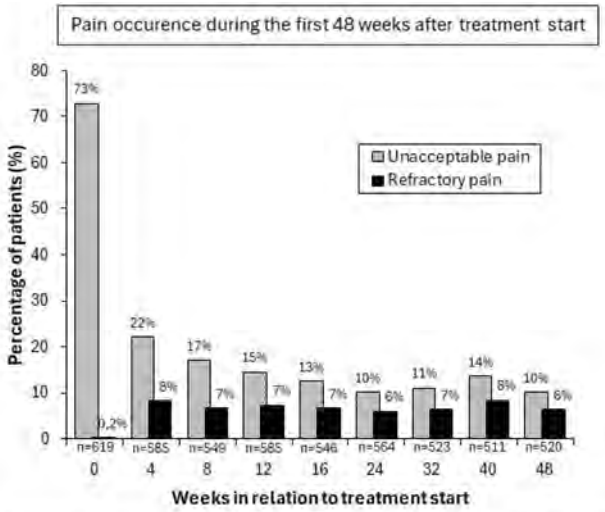


Figure 1. Occurence of unacceptable and refractory pain during the first 48 weeks after treatment start in patients with early RA. Numbers below bars indicate number of patients with complete data for all pain outcomes at the respective time-points. Unacceptable pain: VAS pain>40 mm (0–100); refractory pain: VAS pain>40 + CRP <10 + SJC ≤1 (of 66), SJC, swollen joint count (of 66); TJC, tender joint count (of 68); VAS, visual analogue scale.

Results: Included RA patients (n=624) were 69% women, 82% ACPA positive and with mean age/symptom duration of 55/0.6 years. At baseline, 73% reported unacceptable pain, declining to 10% after 48w, whereas the fraction with refractory pain was 0% (baseline) and 6% (48w). Refractory pain constituted 62% of all remaining unacceptable pain at 48w (Figure 1). Further, unacceptable pain at 12w was strongly linked to EULAR 12w response (7% in good responders versus 67% in non-responders; p< 0.001), while for refractory pain the relationship was weaker (6% versus 17%, p=0.074), with refractory pain accounting for 88% of remaining unacceptable pain in good responders (Figure 2). AUC for SJC (0-24w) was positively

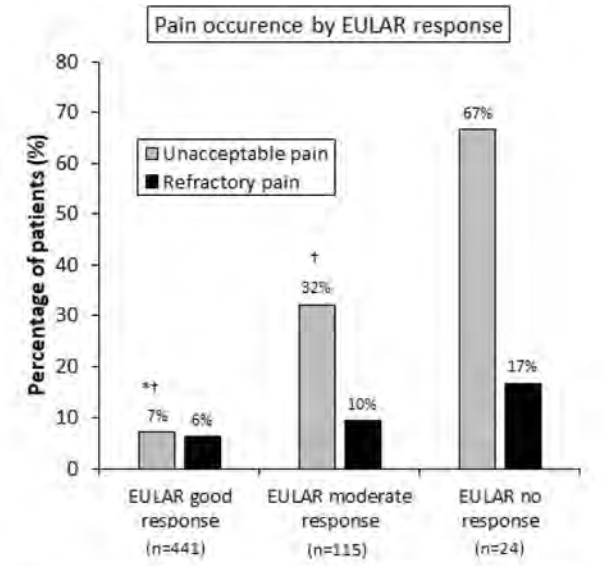


Figure 2. Pain occurence at 12 weeks in relation to EULAR 12-week response in patients with complete data for all pain outcomes both at baseline and at the 12-week follow-up. Unacceptable pain: VAS pain >40 mm (0–100); refractory pain: VAS pain >40 + CRP <10 + SJC ≤1 (of 66). Group comparisons by chi-square test and Fisher's exact test, as appropriate. *p<0.05 versus EULAR moderate response. † p<0.05 versus EULAR no response. SJC, swollen joint count (of 66); VAS, visual analogue

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Associations between cumulative inflammatory load from baseline to week 24 and pain outcomes at week 48 in early RA patients from the NORD-STAR trial.

	Unacceptable pain		Refractory pain		Fibromyalgic RA	
	OR	P value	OR	P value	OR	P value
AUC for SJC (per AUC-unit increase)						
Univariate	1.007	0.009	1.006	0.106	1.006	0.033
*Adjusted**	1.008	0.007	1.006	0.083	1.007	0.018
AUC for CRP (per AUC-unit increase)						
Univariate	1.000	0.557	1.000	0.820	0.99	0.548
*Adjusted**	1.000	0.570	1.000	0.740	0.99	0.496

Unacceptable pain=VAS pain>40 mm (0-100). Refractory pain=VAS pain>40 mm + CRP<10 mg/L + SJC <=1 (of 66). Fibromyalgic RA=TJC-SJC >=7. AUC denotes the period from baseline to week 24 with AUC units computed for (a) SJC (y; 0-66) multiplied by number of weeks (x; 0-24) with a maximum value of 66*24=1584; and (b) CRP (y; CRP-value) multiplied by weeks (x; 0-24); in both cases adopting the trapezoid method. Results from logistic regression. *Adjustment for sex, age, ACPA status and BMI. AUC, area-under-the-curve; OR, odds ratio; SJC, swollen joint count (of 66); TJC, tender joint count (of 68); VAS, visual analogue scale.

associated with 48w unacceptable pain (p=0.007) and fibromyalgic RA (p=0.018) in adjusted analysis, with a trend also for refractory pain (p=0.083). AUC for CRP (0-24w) was not associated with the pain outcomes (Table 1).

Conclusion: A relevant proportion of early, aggressively treated RA patients have persistent unacceptable pain after 1 year, with pain indicative of a non-inflammatory mechanism accounting for over 60% of this pain load. Our findings also suggest that a prolonged inflammatory period could entail more future non-inflammatory pain, underscoring the importance of rapid and sustained inflammation resolution.

1. Olofsson et al. *Arthritis Care Res* 2021;73:1312-21
2. Pollard et al. *Rheumatology* 2010;49:924-28
Jon Lampa and Tor Olofsson contributed equally

Disclosure: A. Brink: None; **J. Karlsson Wallman**: AbbVie/Abbott, 5, Amgen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5; **J. Einarsson**: None; **M. Kapetanovic**: GlaxoSmithKlein(GSK), 6, UCB, 6; **E. Mogard**: AbbVie/Abbott, 6; **E. Lindqvist**: None; **C. Roseman**: None; **K. Lend**: None; **M. Hetland**: AbbVie/Abbott, 1, 5, Alfasigma, 5, Eli Lilly, 5, Novartis, 6, Pfizer, 5, 6, Sandoz, 5, 6, UCB, 5, 6; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6; **K. Horslev-Petersen**: None; **D. Nordstrom**: Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Merck/MSD, 2, 5, Pfizer, 2, UCB, 2; **T. Sokka-isler**: None; **B. Gudbjornsson**: None; **G. Gröndal**: None; **M. Heiberg**: None; **E. Haavardsholm**: None; **M. Nurmohamed**: None; **A. Rudin**: None; **R. van Vollenhoven**: AbbVie, 2, 6, Alfasigma, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 5, 6, Galapagos, 2, 5, 6, GSK, 2, 6, Janssen, 2, 6, MSD, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, 6, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **T. Uhlig**: None; **J. Lampa**: None; **T. Olofsson**: None.

Abstract Number: 0815

Neuropathic-like Pain Characteristics Predict Worse Pain Outcomes in Early Rheumatoid Arthritis: a Prospective Cohort Study with Embedded Neuroimaging Evaluation

Eoin Kelleher[1], Amanda Wall[1], Isabelle Brennan[2], Robert Murphy[1], Antonella Delmis[1], John Davis[3], Vishvarani Wanigasekera[4], Irene Tracey[1] and **Anushka Irani**[5], [1]University of Oxford, Oxford, United Kingdom, [2]University of Cambridge, Cambridge, United Kingdom, [3]Mayo Clinic, Rochester, MN, [4]University of Oxford, Oxford, [5]Mayo Clinic, Jacksonville, FL

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Pain in Rheumatic Disease Including Fibromyalgia (0813–0818)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Despite effective control of inflammation in rheumatoid arthritis (RA), persistent and severe pain remains a clinical challenge. Dysregulated pain processing in the central nervous system ("central sensitization") may underlie this disconnect. The PainDETECT questionnaire, originally developed to identify neuropathic pain, may capture features of central sensitization. We hypothesised that neuropathic-like pain at diagnosis predicts worse pain prognosis in early RA, independent of inflammation. We also explored associated brain activation patterns using functional neuroimaging.

Methods: In this prospective cohort study, adults with newly diagnosed RA in Oxfordshire completed the PainDETECT questionnaire at baseline. The primary outcome, bodily pain, was measured using the SF-36 Bodily Pain Subscale (BPS) at baseline, 3, 6, and 12 months. Inflammatory markers (CRP) were monitored longitudinally. Linear mixed-effects models examined associations between PainDETECT and BPS and CRP over time. A subset of 27 participants underwent task-based fMRI, assessing brain responses to evoked pressure pain.

Results: Among 158 participants (mean age 58.4 years; 35% male), higher baseline PainDETECT scores were associated with significantly worse bodily pain throughout follow-up (adjusted β= -0.43; 95%CI: -0.84 to -0.02; P=0.043), independent of socio-demographics, lifestyle, comorbidities, depression, and anxiety. No association was found between PainDETECT and CRP. On neuroimaging,

higher PainDETECT scores correlated with increased activation in the left insula, dorsal anterior cingulate cortex (dACC), and left amygdala during evoked wrist pain.

Conclusion: Neuropathic-like pain at diagnosis predicts a worse pain prognosis in early RA, independently of inflammation. Early identification may support more targeted and effective pain management.

Schematic of the task-based functional MRI (tfMRI) protocol. Participants received alternating blocks of pressure pain (50 N) and light touch stimuli to the left wrist (typically affected in RA) and the left index finger nailbed (control site), during two 10-minute

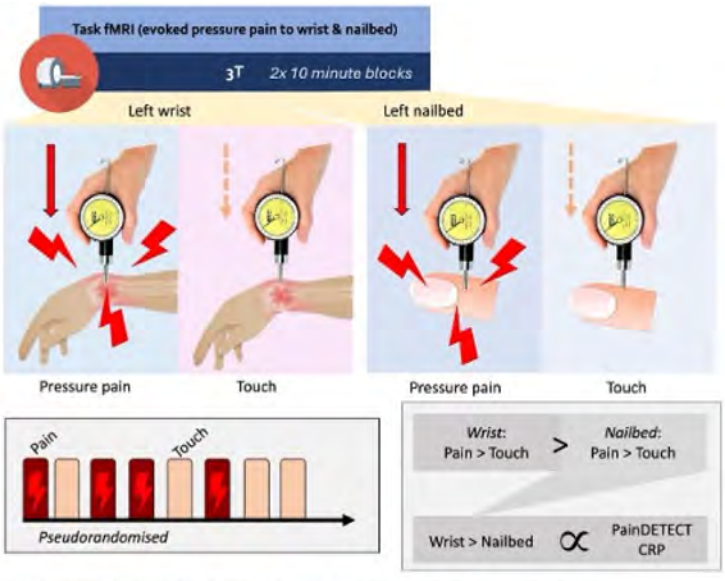


Figure 1. Task-based fMRI protocol for evoked pressure pain at RA-affected and control sites.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

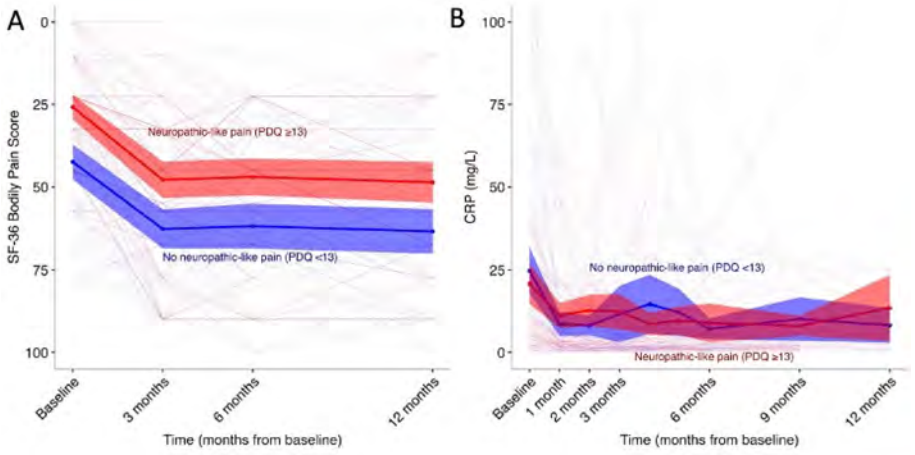


Figure 2. Higher baseline PainDETECT scores predict worse pain severity, but not inflammation, in early rheumatoid arthritis.

scan sessions on a 3T MRI scanner. Stimuli were applied manually using an MR-compatible algometer in a pseudorandomised order, guided by auditory cues. First-level contrasts modelled pain > touch at each site. Second-level contrasts compared wrist > nailbed activation, and group-level analyses examined associations with PainDETECT across the whole brain.

Lines represent individual raw patient trajectories of bodily pain (A) and C-reactive protein (CRP, B) over time, with mean values in bold. Shaded areas indicate 95% confidence intervals. Participants (N = 158, 91 scoring ≥13) were followed for one year. Neuropathic-like pain measured using the PainDETECT questionnaire (cutoff: ≥13 indicates probable neuropathic

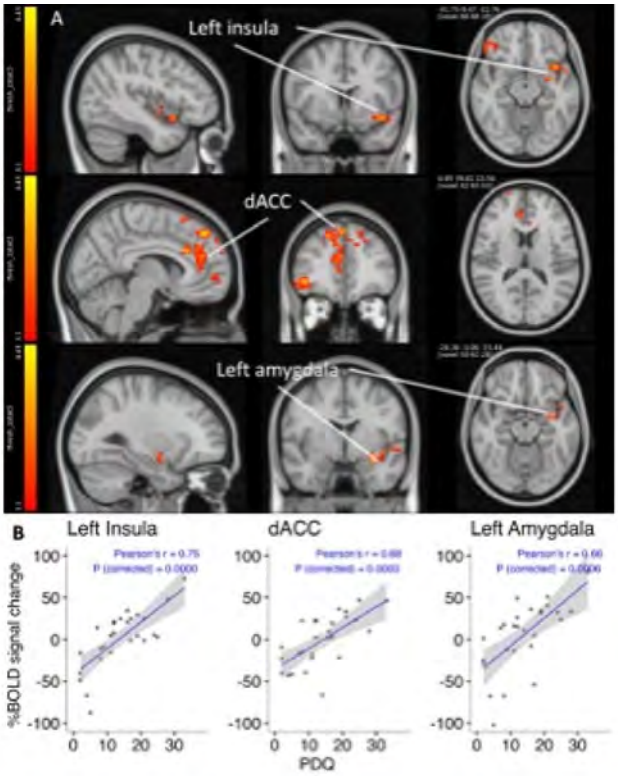


Figure 5. Neuronal activity correlates with neuropathic-like pain in early rheumatoid arthritis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pain). Note higher values of SF36-BPS indicate more severe bodily pain. CRP values were taken from linked healthcare records during follow-up, and were grouped into average CRP in each time period.

Higher PainDETECT (PDQ) scores are associated with greater activity in the left Insula, dorsal anterior cingulate cortex (dACC), and left amygdala after whole brain correction. Whole brain group-level activation maps for painful vs. non-painful stimulation of the left wrist vs. left nailbed contrast with PainDETECT scores. Maps are overlaid on a standard MNI152 T1-weighted brain template and thresholded at Z > 3.1. Higher PainDETECT scores at baseline are associated with significantly greater neuronal response in the left insula, dACC, and left amygdala. The y-axes show the induced effects of painful stimulation to the left wrist as a percentage BOLD signal change, defined as X = (Xpain (wrist) – Xno pain (wrist)) - (Xpain (nailbed) – Xno pain (nailbed)). Shaded areas represent the 95% confidence interval. Pearson correlation coefficients (r) are reported. N=27 participants who underwent neuroimaging.

Disclosure: E. Kelleher: None; **A. Wall**: None; **I. Brennan**: None; **R. Murphy**: None; **A. Delmis**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **V. Wanigasekera**: None; **I. Tracey**: None; **A. Irani**: None.

Abstract Number: 0816

Persistent Pain Despite Inflammatory Control in RA: A Pooled Analysis of 7 RCTs

Andreas Kerschbaumer[1], Marlene Steiner[2], William H. Robinson[3], Josef Smolen[4] and Daniel Aletaha[5], [1]Stanford University / Medical University of Vienna, Stanford, CA, [2]Medical University of Vienna, Vienna, Wien, Austria, [3]Stanford University, Palo Alto, CA, [4]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria, Vienna, Austria, [5]Medical University Vienna, Wien, Austria

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Pain in Rheumatic Disease Including Fibromyalgia (0813–0818)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Joint swelling and tenderness are clinical hallmarks of rheumatoid arthritis (RA) and central to disease assessment. Regardless of treatment type, stringent remission based on the ACR/EULAR index (SDAI, CDAI) and Boolean definitions is associated with a reduction in joint damage and an increase in physical function. Using the patient global assessment in defining remission may hinder achieving it, as some patients experience high pain despite resolved inflammation, potentially not benefitting from immune-directed therapies. To date, it is unclear how many patients in randomized controlled trials (RCTs) reach an inflammation-free state but continue to report high pain levels.

Here, we analysed patients achieving inflammatory control while still reporting high pain levels at endpoints in RA RCTs and compared their characteristics at baseline and longitudinally to those with inflammatory control without residual pain.

Methods: We analyzed data from 2,640 patients receiving biologic DMARDs across 7 RCTs. Patients achieving inflammatory control (CRP≤0.5 mg/dL & SJC66=0) at trial endpoint (24 weeks) were divided by pain levels: low (≤5/10 VAS) vs high (>5/10 VAS). We then compared demographics and outcomes of these groups at baseline (disease activity, PROs, CRP, ESR and radiographic damage). Between-group comparisons used t-tests or Mann-Whitney U tests. We also assessed longitudinal differences between the groups using longitudinal linear mixed models.

Results: Of 2,405 patients with 24-week data, 305 (13%) achieved inflammatory control. Only 15 (< 1% of all; 5% of those with resolved inflammation) showed persistently elevated pain levels despite control of inflammation (Figure 1). These patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

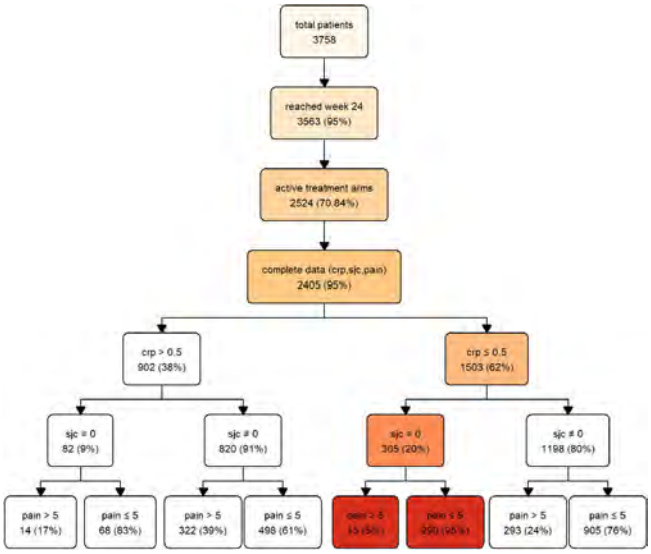


Figure 1: Flow chart of patient selection for analysis of pain discordance in RA.

showed a trend toward older age (52.8±11.1 vs 47.6±12.4) and a higher subjective disease burden at baseline (Figure 2) in TJC68 (31.8±16 vs 24.3±12.8), HAQ-DI (1.6±0.5 vs 1.2±0.6) and PGA (6.7±1.8 vs 5.1±2.2). Notably, objective measures including CRP (2.1±5.2 vs 1.9±2.2), ESR (30.5±23.4 vs 37.1±20.4), SJC66 (14.0±10.7 vs 14.5±8.6) and EGA (5.6±1.9 vs 5.6±1.7) and composite measures (CDAI, DAS28) were nearly identical between groups. However, erosion scores were twice as high in the high-pain group (19.0±23.4 vs 9.7±15.2) suggesting a higher disease burden. Longitudinal analyses (Figure 3) revealed persistent and significant differences in TJC68, pain, PGA, EGA HAQ-DI as well as composite measures (CDAI, SDAI, DAS28-ESR). Results using a lower cut-off for pain (≤3/10cm VAS) were confirmatory (data not shown).

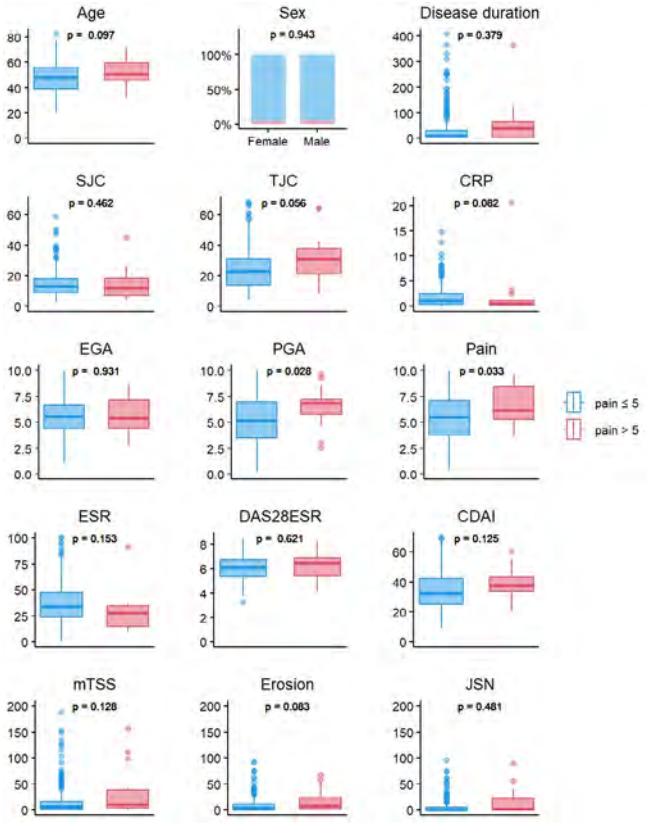


Figure 2: Comparison of baseline disease activity measures between patients who have achieved complete inflammatory control with high (>5; n=15) versus low (≤5; n=290) pain at week 24. Box plots show median (horizontal line), interquartile range (box), and range (whiskers). Dots represent outliers.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

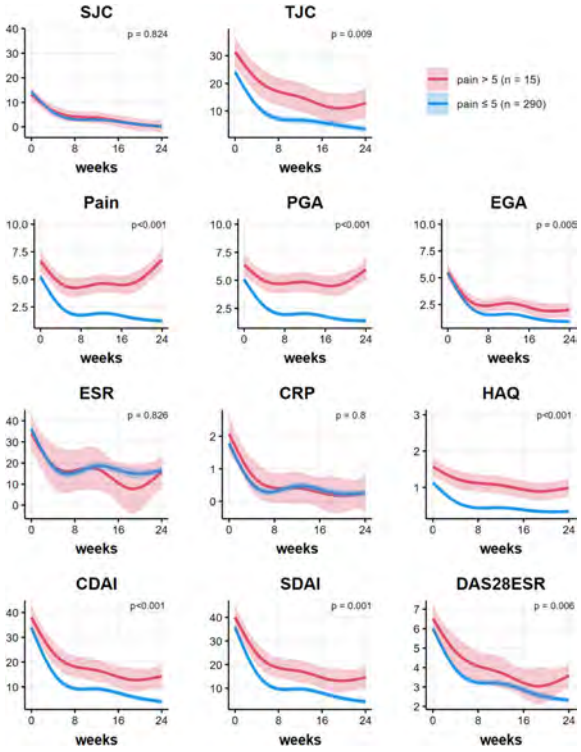


Figure 3: Longitudinal analyses of disease activity measures between patients who have achieved complete inflammatory control with high (>5; n=15) versus low (≤5; n=290) pain at Week 24. The mean linear mixed model estimates of different disease activity parameters over time are graphed.

Conclusion: In this pooled analysis of 7 RCTs, < 1% of patients treated across 7 RCTs experienced high pain levels despite complete inflammatory control revealing that such discrepancy is very rare. Patients with persistent pain had higher subjective disease burden as well as radiographic damage at baseline, suggesting that persistent pain may be attributed to structural damage and/or potential central pain sensitization, rather than inflammation.

Disclosure: A. Kerschbaumer: AbbVie/Abbott, 2, Boehringer-Ingelheim, 12, Travel, Eli Lilly, 12, Travel, Janssen, 2, 6, Pfizer, 6, Stada, 6, UCB, 2, 6, 12, Travel; **M. Steiner**: None; **W. Robinson**: None; **J. Smolen**: AbbVie/Abbott, 5, 6, Ananda, 6, AstraZeneca, 5, 6, Astro, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Celltrion, 6, Chugai-Roche, 6, Galapagos, 5, 6, Immunovant, 6, Janssen, 6, Lilly, 5, 6, Pfizer, 6, R-Pharma, 6, Samsung, 6, Sandoz, 6, Sanofi, 6; **D. Aletaha**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sanofi, 6.

Abstract Number: 0817

More than 40% of Older Adults with Rheumatic Diseases Are Prescribed Opioid Medications

Christine Anastasiou[1], Eric Roberts[2], gabriela Schmajuk[3] and Jinoos Yazdany[4], [1]Stanford University, Pleasanton, CA, [2]University of California, San Francisco, SF, CA, [3]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [4]UCSF, San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Pain in Rheumatic Disease Including Fibromyalgia (0813–0818)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with rheumatic diseases commonly experience acute or chronic pain that may lead to both short- and long-term opioid use. Many patients do not experience benefit in function or pain from increasing opioid dosages to ≥50 morphine milligram equivalents (MME)/day but do have increased risks, including dependence or overdose as the dose is increased. We used national data from the Rheumatology Informatics System for Effectiveness (RISE) registry linked to Medicare claims to quantify the prevalence and risk factors of receiving opioids including high dose prescriptions (Rx's) among older adults with rheumatic conditions associated with pain.

Methods: Adults ≥65 years old with ≥2 visits to a RISE practice in 2021, continuous Medicare enrollment (Parts A, B, & D) in 2021, and at least one rheumatic diagnosis of RA, OA, axSpA, SLE, PsA, PMR, SS, SSc, or gout were included. Patients with ≥2 ICD-10 codes for cancer were excluded. Outcomes were evaluated in Medicare claims and included: (1) any opioid dispensation, (2) chronic Rx (≥90 days), (3) max 90-day average morphine equivalent dose (MED), (4) and the MED for each claim was calculated and dichotomized into Rx's for ≥50 MME per day or less. Prescriber specialty (rheumatologist (rheum),

Table 1

Patient Demographics and Clinical Characteristics

	Total (N=43,825)		No (N=35,903)		Yes (N=7,922)		
	No.	col %	No.	row %	No.	row %	SMD
Primary rheumatic diagnosis							0.12365
Rheumatoid Arthritis	20,933	47.8	17,101	81.69	3,832	18.31	
Osteoarthritis	14,426	32.9	11,768	81.57	2,658	18.43	
Systemic Lupus Erythematosus	2,003	4.6	1,654	82.58	349	17.42	
Polymyalgia Rheumatica	1,960	4.5	1,731	88.32	229	11.68	
Psoriatic Arthritis	1,799	4.1	1,472	81.82	327	18.18	
Gout	1,023	2.3	854	83.48	169	16.52	
Axial Spondyloarthritis	1,010	2.3	760	75.25	250	24.75	
Systemic Sclerosis	461	1.1	395	85.68	66	14.32	
Sjögren's Syndrome	210	0.5	168	80	42	20	
Demographics							
Age (mean;sd)	75.9	6.4	76	6.5	75.2	6.3	0.12774
Sex							0.11477
Female	33,972	77.5	27,530	81.04	6,442	18.96	
Male	9,852	22.5	8,372	84.98	1,480	15.02	
Unknown	1	0	1	100	0	0	
Race-ethnicity							0.12436
American Indian/Alaska Native	69	0.2	47	68.12	22	31.88	
Asian/Pacific Islander	626	1.4	578	92.33	48	7.67	
Black	2,274	5.2	1,806	79.42	468	20.58	
Hispanic	1,333	3	1,115	83.65	218	16.35	
Non-Hispanic white	38,424	87.7	31,405	81.73	7,019	18.27	
Other	250	0.6	214	85.6	36	14.4	
Unknown	808	1.8	706	87.38	102	12.62	
Missing	41	0.1	32	78.05	9	21.95	
Area Deprivation Index							0.28155
First Quartile (lowest deprivation)	9,480	21.6	8,341	87.99	1,139	12.01	
Second	9,850	22.5	8,267	83.93	1,583	16.07	
Third	10,405	23.7	8,392	80.65	2,013	19.35	
Fourth (highest deprivation)	11,267	25.7	8,636	76.65	2,631	23.35	
Missing	2,823	6.4	2,267	80.3	556	19.7	
Clinical Comorbidities							
Fibromyalgia							0.39915
No	39,047	89.1	32,906	84.27	6,141	15.73	
Yes	4,778	10.9	2,997	62.72	1,781	37.28	
Mood disorder							0.26007
No	37,068	84.6	31,019	83.68	6,049	16.32	
Yes	6,757	15.4	4,884	72.28	1,873	27.72	
Anxiety disorder							0.24201
No	37,713	86.1	31,479	83.47	6,234	16.53	
Yes	6,112	13.9	4,424	72.38	1,688	27.62	
Charlson Comobidity index (score)							0.24695
0	4,080	9.3	3,492	85.59	588	14.41	
1	12,171	27.8	10,465	85.98	1,706	14.02	
2-3	15,952	36.4	13,046	81.78	2,906	18.22	
4+	11,622	26.5	8,900	76.58	2,722	23.42	
Geography							
Census Division							0.17223
East North Central	4,599	10.5	3,795	82.52	804	17.48	
East South Central	6,525	14.9	5,063	77.59	1,462	22.41	
Mid-Atlantic	4,195	9.6	3,620	86.29	575	13.71	
Mountain	1,596	3.6	1,305	81.77	291	18.23	
New England	368	0.8	313	85.05	55	14.95	
Pacific	4,009	9.1	3,412	85.11	597	14.89	
South Atlantic	15,783	36	12,983	82.26	2,800	17.74	
West North Central	2,259	5.2	1,821	80.61	438	19.39	
West South Central	4,358	9.9	3,473	79.69	885	20.31	
Missing	133	0.3	118	88.72	15	11.28	
Rural-Urban Commuting Area							0.10469
Urban	35,985	82.1	29,734	82.63	6,251	17.37	
Large	4,538	10.4	3,565	78.56	973	21.44	
Small	3,046	7	2,420	79.45	626	20.55	
Unknown	256	0.6	184	71.88	72	28.13	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2

Opioid Claims by Provider Type and Stratified by Rx Dose ≥50 MME/Day

	Total (N=112,791)		Claim >= 50 MME: No (N=93,869)		Claim >= 50 MME: Yes (N=18,922)		
	No.	col %	No.	row %	No.	row %	SMD
Provider type							0.17661
Rheumatologist	34229	30.35	29390	85.86	4839	14.14	
Non-Rheumatology Physician	53138	47.11	43311	81.51	9827	18.49	
Rheumatology affiliated NP or PA	7844	6.95	6877	87.67	967	12.33	
Non-Rheumatology affiliated NP or PA	13141	11.65	10563	80.38	2578	19.62	
Missing	4439	3.94	3728	83.98	711	16.02	

Footnote: MME: morphine milligram equivalents NP: Nurse Practitioner PA: Physician Assistant

Table 3

Odds of Chronic Opioid Use Among Patients with Rheumatic Disease

n = 43825

Variable	Unadjusted Bivariable Model		Fully Adjusted Model	
Primary Rheumatic Diagnosis				
Rheumatoid Arthritis	ref	ref	ref	ref
Osteoarthritis	1.01	(0.83 - 1.22)	1.07	(0.95 - 1.22)
Systemic Lupus Erythematosus	0.94	(0.82 - 1.09)	0.77***	(0.67 - 0.88)
Polymyalgia Rheumatica	0.59***	(0.50 - 0.70)	0.63***	(0.53 - 0.74)
Psoriatic Arthritis	0.99	(0.87 - 1.13)	1.03	(0.89 - 1.18)
Gout	0.68	(0.74 - 1.06)	0.98	(0.81 - 1.18)
Axial Spondyloarthritis	1.47***	(1.16 - 1.85)	1.51***	(1.25 - 1.82)
Systemic Sclerosis	0.75**	(0.57 - 0.98)	0.71**	(0.54 - 0.95)
Sjögren's Syndrome	1.12	(0.72 - 1.74)	0.94	(0.60 - 1.47)
Demographics				
Age (mean;sd)	0.98***	(0.97 - 0.99)	0.98***	(0.98 - 0.99)
Sex				
Female	ref	ref	ref	ref
Male	0.76***	(0.70 - 0.81)	0.90***	(0.83 - 0.97)
Area Deprivation Index				
First Quartile (lowest dep)	ref	ref	ref	ref
Second	1.40***	(1.21 - 1.63)	1.32***	(1.18 - 1.47)
Third	1.76***	(1.48 - 2.09)	1.57***	(1.39 - 1.77)
Fourth (highest deprivation)	2.23***	(1.87 - 2.66)	1.93***	(1.72 - 2.16)
Missing	1.80***	(1.50 - 2.16)	1.52***	(1.33 - 1.73)
Clinical Comorbidities				
Fibromyalgia (no is reference)	3.18***	(2.85 - 3.56)	2.64***	(2.38 - 2.94)
Mood disorder (no is reference)	1.97***	(1.82 - 2.12)	1.41***	(1.31 - 1.52)
Anxiety disorder (no is reference)	1.93***	(1.78 - 2.09)	1.45***	(1.34 - 1.56)
Charlson Comobidity index (score)				
0	ref	ref	ref	ref
1	0.97	(0.80 - 1.17)	1.04	(0.91 - 1.17)
3	1.32***	(1.11 - 1.58)	1.39***	(1.24 - 1.56)
4+	1.82***	(1.51 - 2.19)	1.85***	(1.63 - 2.09)

Footnote:
A patient was designated to have chronic opioid use if they had greater than or equal to 90 days' supply of opiates in 2021
Generalized estimating equations were used to adjust for patients nested within practices.
We present bivariable models as well as a fully adjusted model
Covariates included in the model but not shown in table: Race-ethnicity, Census division, Rural-Urban Commuting Area

The data presented here was supported by the American College of Rheumatology's RISE Registry.
However, the views expressed represent those of the author(s) and do not necessary represent the views of the American College of Rheumatology. Funding for this project was provided by the Rheumatology Research Foundation.

non-rheum physician, rheum affiliated physician assistant (PA)/nurse practitioner (NP) and non-rheum affiliated PA/NP) was determined by linking to National Provider Identifiers (NPIs). We modeled chronic opioid use as a dichotomous outcome using logit linear models using generalized estimating equations to adjust for patients nested within practices.

Results: Among 43,825 patients (mean age 75.9±6.4, 77.5% female, 87.7% non-Hispanic white), 18,991 (43.3%) filled ≥1 opioid Rx (112,791 total claims). Hydrocodone (19.6%), tramadol (19.1%), and oxycodone (12.1%) were the most common opioid Rx's. Chronic opioid Rx's were written in 7,922 patients (18.1%) and the mean maximum 90-day dose was 17.1 mg MED. A quarter of patients receiving opioids (23.8%) had Rx's written only by rheum providers, 13.4% received Rx's from a mix of rheum and non-rheum providers, and 5.4% were missing the specialty of the provider. Most Rx's for ≥50 MME per day were prescribed by non-rheum affiliated NPs/PAs and non-Rheum physicians (Table 2). In the adjusted model, patients with axSpA had more than 50% higher odds of chronic opioid Rx's compared to those with RA (OR 1.51; 95% CI 1.25-1.82) (Table 3). The odds of chronic opioid Rx increased incrementally with worsening patient socioeconomic deprivation; and fibromyalgia, mood disorders, anxiety disorders and higher comorbidity index were all significantly associated with chronic opioid Rx (Table 3).

Conclusion: In this national sample of older adults with rheumatic diseases, 43% received at least one opioid Rx; patients with axSpA were the most likely to receive an opioid Rx. Among patients receiving opioids, high dose Rx ≥50 MME/day were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

commonly written by both rheum and non-rheum providers. Further research is needed to identify safer pain therapies for these older adults and to develop targeted interventions that reduce potentially inappropriate opioid prescribing.

Disclosure: C. Anastasiou: Priovant, 12, VALOR Study. Served as Co-PI at UCSF Site.; **E. Roberts**: None; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2.

Abstract Number: 0818

Risk of Cardiovascular Events is Higher in Pregabalin Users Versus Duloxetine: A Cohort Study Among Veterans with Chronic Musculoskeletal Pain

Sachalee Campbell[1], Laura Daniel[2], Puran Nepa[2], Otis Wilson[3], Alyson L. Dickson[3], Katherine Murray[3], William D. Dupont[3], Adriana Hung[3], Wayne A. Ray[3], Michael Stein[4] and Cecilia P. Chung[2], [1]University of Miami, Miami, FL, [2]University of Miami, Research Service, Miami VA Healthcare System, Miami, FL, [3]Vanderbilt University Medical Center, Vanderbilt, TN, [4]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Pain in Rheumatic Disease Including Fibromyalgia (0813–0818)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Pregabalin and duloxetine are among the most prescribed non-opioid medications for patients with chronic pain. Pregabalin may raise the risk for heart failure, and duloxetine increases heart rate and blood pressure; however, little is known about their comparative cardiovascular safety. This study aimed to compare cardiovascular outcomes between new users of pregabalin and duloxetine in US Veterans with chronic musculoskeletal conditions.

Methods: This was a retrospective cohort study of US Veterans, ages 18-89 years, with chronic non-cancer musculoskeletal pain who were new users of pregabalin or duloxetine between 2014 and 2021. We excluded Veterans who were in long-term care or hospice, hospitalized for a month or more, and afflicted with serious illnesses in the year before their first prescription. The primary outcome was a major adverse cardiovascular event (MACE) – a composite of acute myocardial infarction, stroke, congestive heart failure, or cardiac death. For mortality causes, we used data from the National Death Index. For cardiac events, we used Veterans Affairs (VA) data and linked Medicare data. We created a propensity score using 153 covariates from ICD codes based on literature review and past studies and used it to adjust for confounding with inverse probability of treatment weighting (IPTW). Cox proportional hazard regression model was used to analyze outcomes over time.

Results: This study included 26,684 new users of pregabalin and 152,808 new users of duloxetine. The cohort was predominantly male (83%) and of reported White race (70%). The median age was 56 years old for both medications

Table: Rates of cardiovascular outcomes in new users of pregabalin vs duloxetine

	Pregabalin		Duloxetine		Hazard Ratio (95% CI)			
Model	N events	Rate/ 1000 yrs	N events	Rate/ 1000 yrs	Unadjusted		Adjusted	
MACE*	340	18.91	1458	11.84	1.61	(1.43, 1.81)	1.23	(1.08, 1.40)
Congestive heart failure	141	7.81	525	4.25	1.85	(1.53, 2.23)	1.40	(1.15, 1.72)
Acute myocardial infarction	77	4.26	235	1.90	2.26	(1.75, 2.93)	1.74	(1.31, 2.31)
Stroke	35	1.93	215	1.74	1.12	(0.78, 1.60)	0.82	(0.56, 1.19)
Cardiac Death	126	6.93	609	4.91	1.42	(1.18, 1.73)	1.11	(0.88, 1.39)

*MACE is a composite of acute myocardial infarction, stroke, congestive heart failure, and cardiac death

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(IQR:44-67 for pregabalin, 42-67 for duloxetine). Prior to IPTW, rates of neuropathic pain, diabetes, and hypertension were higher among users of pregabalin, whereas rates of stress and anxiety were higher in users of duloxetine. Following IPTW, all covariates were balanced, indicated by standardized differences of less than one percent. During the study period, there were 1,798 MACE events. Follow-up time was 17,978 patient-years for pregabalin users and 123,134 patient-years for duloxetine users. The rate of MACE was higher for pregabalin users when compared to duloxetine users [unadjusted HR: 1.61 (CI: 1.43, 1.81), adjusted HR: 1.23 (CI: 1.08, 1.40)]. These differences were explained by higher rates of congestive heart failure and acute myocardial infarction among pregabalin users compared to duloxetine users.

Conclusion: In this retrospective cohort study of US Veterans ages 18-89 with chronic non-cancer musculoskeletal pain, new users of pregabalin had an increased risk of heart failure and acute myocardial infarction compared to new users of duloxetine.

Disclosure: S. Campbell: None; **L. Daniel**: None; **P. Nepa**: None; **O. Wilson**: None; **A. Dickson**: None; **K. Murray**: None; **W. Dupont**: None; **A. Hung**: None; **W. Ray**: None; **M. Stein**: None; **C. Chung**: None.

Abstract Number: 0819

Subcellular resolution spatial transcriptomics reveals immune-stromal crosstalk within the synovium of patients with juvenile idiopathic arthritis

Jun Inamo[1], Roselyn Fierkens[2], Michael Clay[2], Clara Lin[3], Kari Hayes[2], Nathan Rogers[4], Heather Leach[2] and Kentaro Yomogida[2], [1]University of Colorado School of Medicine, Aurora, CO, [2]University of Colorado, Aurora, CO, [3]Children's Hospital Colorado, Aurora, CO, [4]Children's Hospital Colorado, Aurora, CO

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Pediatric Rheumatology – Basic Science (0819–0824)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic pediatric rheumatic disease, yet the spatial immune architecture of inflamed synovium remains poorly characterized. Prior studies in adult rheumatoid arthritis (RA) have revealed spatial niches of immune–stromal interactions that correlate with treatment response. However, whether similar pathogenic circuits exist in JIA is unknown. We aimed to map cellular ecosystems in the JIA joint using high-resolution spatial transcriptomics and to identify microanatomical features associated with inflammation and disease-relevant cell–cell interactions.

Methods: Synovial tissue biopsies were obtained from 9 children with oligoarticular or RF-negative polyarticular JIA (Fig. 1A). Subcellular-resolution spatial transcriptomic profiling was performed using the 10x Genomics Xenium Prime 5K platform, capturing >430,000 cells across all samples. Data were processed using a custom pipeline enabling cell-type annotation, spatial neighborhood enrichment, and ligand–receptor colocalization analysis.

Results: We identified diverse immune and stromal cell populations, including pro-inflammatory macrophages, THY1+-NOTCH3+ sublining fibroblasts, and cytotoxic T cells (Fig. 1B-H). Covarying neighborhood analysis revealed sublining fibroblasts and endothelial cells were enriched in JIA synovium with systemic high-inflammatory state (Fig. 1I-J). A newly developed R package, named Spatial Neighborhood Analysis (SNA) (Fig. 2A), revealed cell-cell spatial interaction in JIA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

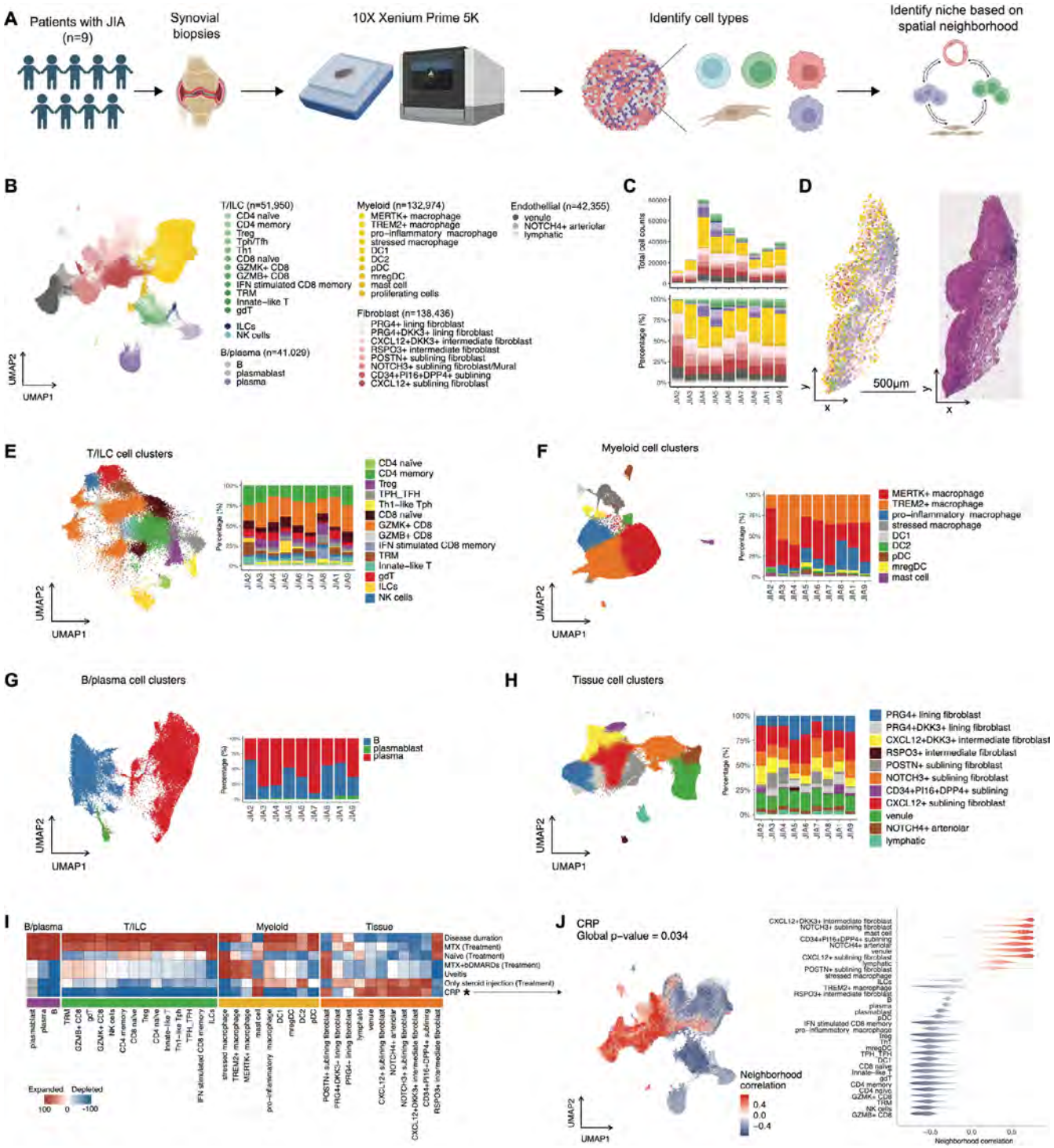


Fig.1: Spatial transcriptomic profiling of synovial tissue in JIA patients. A, Synovial biopsy samples were collected from nine patients diagnosed with JIA. Subcellular resolution spatial transcriptomic data was acquired from FFPE biopsy samples using the 10X Xenium Prime 5K platform. Cell types within synovial tissues were identified, and spatial neighborhoods were characterized based on spatial proximity analysis. B, Identified major immune and tissue-associated cellular compartments in synovium, including T cells, B cells, myeloid cells, and stromal tissue cells (endothelial and fibroblast subsets). Within each broad cell type, fine-scale cell subpopulations were annotated. C, Composition of cell-types across samples. D, Representative example of the FFPE histological slide of synovial biopsy sample and spatial mapping of identified cell clusters. Colors are corresponding with panel B. E-H, Identified fine-scaled cell clusters on UMAP (left) and composition across samples (right) for T cells (E), Myeloid cells (F), B/plasma cells (G), and stromal tissue cells (H). I, Heatmap of covarying neighborhood analysis (CNA) associations of specific cell states with each clinical variable. All testing was adjusted for age and sex. Colours represent the percentage of cell neighbourhoods from each cell state with positive phenotype correlations from white to red (expanded) or blue (depleted). Clinical variables associated globally (permutation p-value < 0.05) are annotated by asterisk (*). J, CNA for CRP association with cell states. Cells in UMAP are colored for expansion (red) or depletion (blue).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

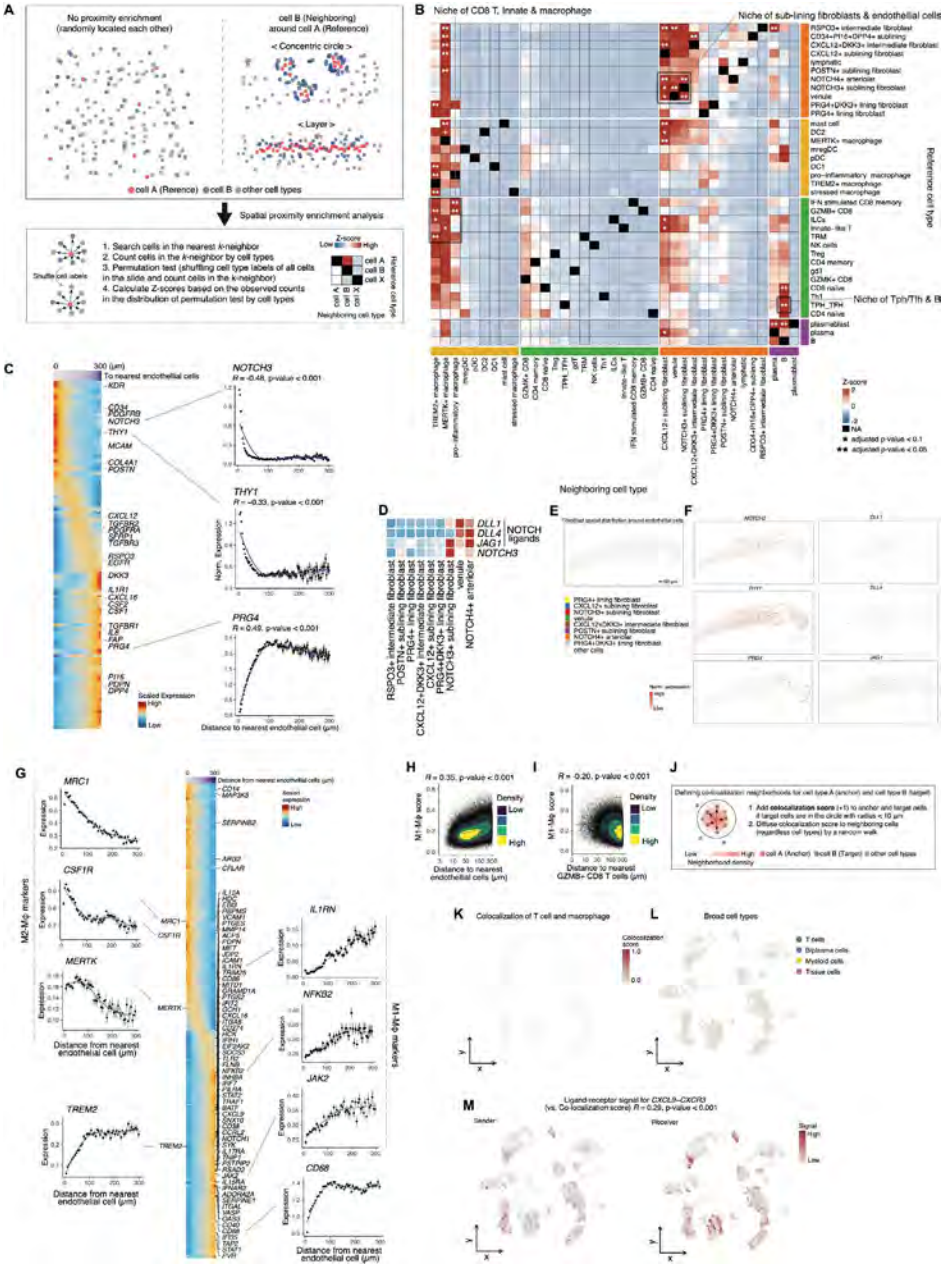


Fig.2: Spatial neighborhood enrichment and niche characterization in JIA synovium. A, Schematic description of the spatial neighborhood enrichment analysis pipeline. The procedure includes identifying nearest neighbors, quantifying neighborhood cell-type composition, performing permutation tests by shuffling cell-type labels, and calculating enrichment Z-scores. B, Spatial neighborhood enrichment in JIA synovium. Statistical significance is indicated as * (adjusted p-value < 0.1 by Benjamini-Hochberg method) and ** (adjusted p-value < 0.05). The highlighted black square indicates the niche of sub-lining fibroblasts and endothelial cells. C, Heatmap displaying the relationship between distances to nearest endothelial cells (purple bar above, 0–300 μm) and fibroblast gene expression. Rows represent fibroblast-associated genes, and columns represent individual cells. Fibroblast marker genes are labeled. Line plots depicting binned distance to nearest endothelial cells (x-axis) and normalized gene expression (y-axis) of representative fibroblast genes. Correlation coefficients and p-values indicate statistical significance. D, Heatmap of gene expressions related to Notch signaling pathway components across different cell types. E, Representative spatial coordinates of a identified niche of sub-lining fibroblasts and endothelial cells, matching pathological images. Cells are colored according to their cluster assignments. F. Spatial expression patterns of fibroblast-related and Notch signaling-related genes within the identified niche location. G, Scaled gene expression of selected M2-like (left) and M1-like (right) macrophage markers plotted as a function of distance from the nearest endothelial cell. Center heatmap shows scaled expression of macrophage-related genes in individual cells ordered by proximity to endothelial cells (0–300 μm), with representative M2- and M1-associated genes annotated. H–I, Correlation between M1-like macrophage module scores and distance to endothelial cells (H) or GZMB+ CD8 T cells (I). Each dot represents a cell. Spearman's correlation coefficient and p-values are shown. J, Schematic illustrating spatial colocalization scoring between anchor cells and target cells within a 10 μm radius. K, Spatial heatmap of colocalization scores between T cells and macrophages. L, Spatial map of broad cell type annotation including T cells, myeloid cells, B/plasma cells, and tissue cells. M, Spatial ligand–receptor analysis results for CXCL9–CXCR3, which exhibited the strongest correlation with macrophage–T cell co-localization scores.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

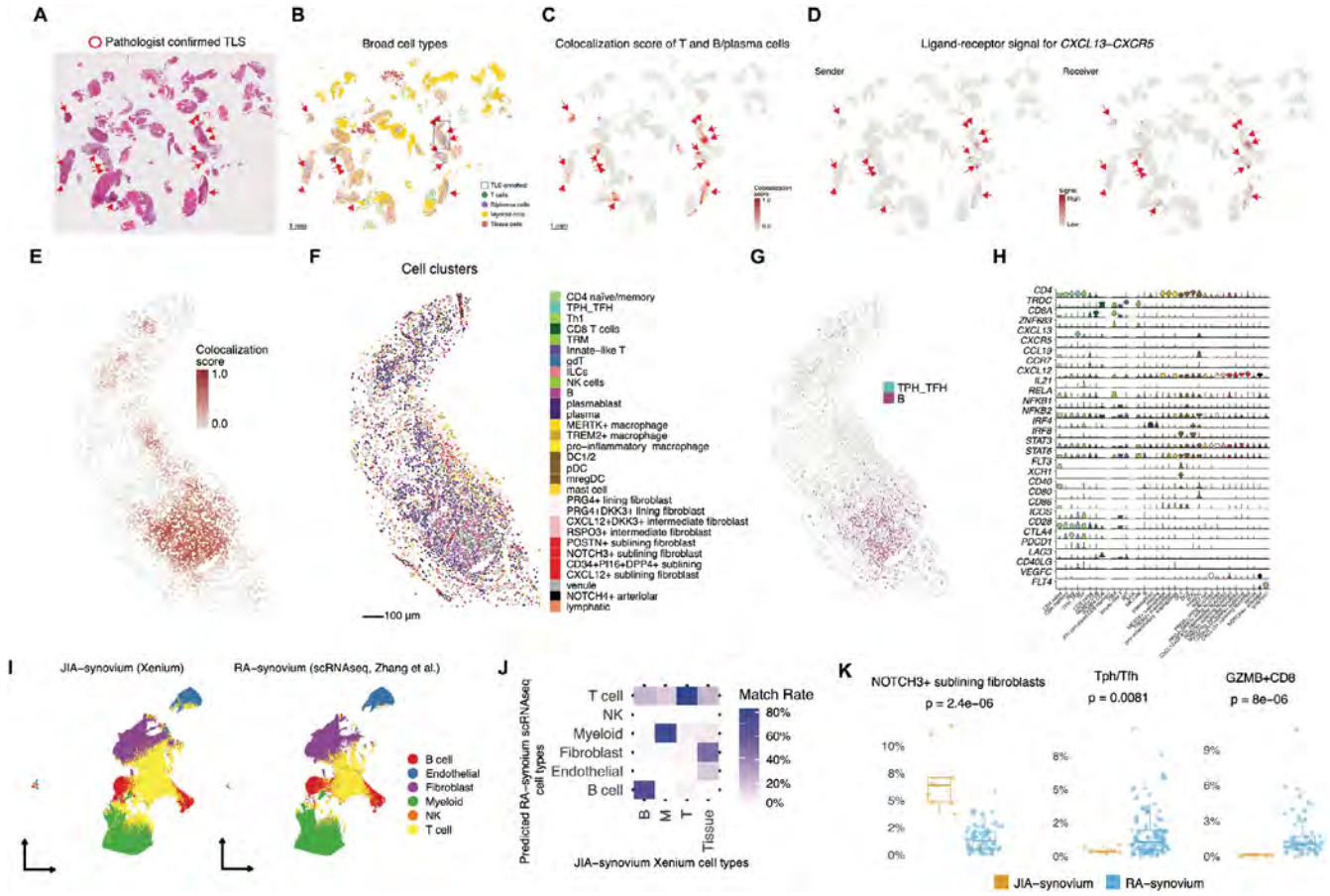


Fig.3: Identification and characterization of tertiary lymphoid structures (TLS) using T and B cell colocalization scores in JIA synovium and comparative analysis of JIA and RA synovium. A, Images of synovial tissue, illustrating representative TLS as identified by a blinded pathologist. B, Spatial distribution of broad-scale T and B cell colocalization scores. Scale bar, 1 mm. The highlighted black square indicates the TLS-enriched region. C, Colocalization scores for T and B cells. D, Spatial ligand–receptor interactions specifically involving CXCL13-CXCR5. E, Zoomed-in visualization of the area with the highest TLS density highlighted in panel B, colored by T and B cell colocalization score. F-G, Same region as in panel E, displayed according to fine-scale cell cluster assignments. H, Violin plots showing the expression levels of key TLS-related genes across different cell clusters identified within the TLS. I, Cell-type level label transfer results, where RA synovium scRNA-seq (Zhang et al.) was used as the reference and JIA synovium Xenium data as the query. RA-derived annotations were transferred to individual JIA cells using a k-nearest neighbors (kNN) approach in the integrated latent space. J, Match rate between transferred RA scRNA-seq cell types and original Xenium-based annotations in JIA synovium. Matrix shows percentage overlap between each transferred and original broad cell type. K, Box plots showing the proportion of cell clusters across individual samples, stratified by condition (JIA vs RA synovium). P-values were calculated using Wilcoxon rank-sum tests.

synovium (Fig. 2B), including fibroblast–endothelial niches with enriched NOTCH3 signaling, paralleling RA pathology (Fig. 2C-F). Analysis focusing on macrophages showed that pro-inflammatory macrophages were enriched in regions distal from vasculature but proximal to GZMB+CD8+ T cells (Fig. 2G-I), with colocalization scores strongly implicating the CXCL9–CXCR3 axis in macrophage–T cell crosstalk (Fig. 2J-M). The SNA framework also automatically captured tertiary lymphoid structures (TLS) in JIA synovium (Fig. 3A), with dense B and T cell colocalization and CXCL13-CXCR5 signalling (Fig. 3B-H), suggesting active germinal centre-like activity. Moreover, integration with public RA-synovium single-cell data revealed enrichment of NOTCH3+ fibroblasts in JIA, whereas Tph/Tfh and GZMB+ CD8 T cells were more abundant in RA (Fig. 3I-K).

Conclusion: Subcellular spatial transcriptomics uncovers conserved and disease-specific immune–stromal architectures in JIA synovium. Vascular-fibroblast niches and macrophage–T cell crosstalk may be key drivers of inflammation. The presence of TLS and unique myeloid–stromal features in JIA highlight potential biomarkers and therapeutic targets distinct from adult RA. These findings offer new insight into pediatric synovial immunopathology and pave the way for precision therapies in childhood arthritis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Inamo: None; **R. Fierkens**: None; **M. Clay**: None; **C. Lin**: None; **K. Hayes**: None; **N. Rogers**: None; **H. Leach**: None; **K. Yomogida**: None.

Abstract Number: 0820

Novel Autoantibodies Predictive of Atherosclerosis Progression and Statin Response in Juvenile-Onset Systemic Lupus Erythematosus

Junjie Peng[1], Pierre Donnes[1], Thomas McDonnell[1], Laura Schanberg[2], Stacy Ardoin[3], Laura Lewandowski[4], George Robinson[1], Elizabeth C Jury[1], **Coziana Ciurtin**[1] and APPLE trial investigators and Childhood Rheumatology Research Alliance (CARRA), [1]University College London, London, United Kingdom, [2]Duke University Medical Center, DURHAM, NC, [3]Nationwide Children's Hospital, Columbus, OH, [4]NIAMS, NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Pediatric Rheumatology – Basic Science (0819–0824)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Table 1 Demographic/clinical table of the APPLE trial sub-cohort (N=94) in the autoantibody profiling study. Abbreviations: BMI – Body mass index; SLEDAI – Systemic Lupus Erythematosus Disease Activity Index; SLICC/ACR-DI – Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index; dsDNA antibody – Anti-double-stranded DNA antibody; C3, C4 – complement fractions C3, C4; HDL – high-density lipoprotein; LDL – low-density lipoprotein.

Table 1. Characteristics of the APPLE trial sub-cohort (N=94) used for the biomarker discovery analyses

	Placebo high CVD-risk (N=26)	Placebo low CVD-risk (N=19)	Statin high CVD-risk (N=17)	Statin intermediate CVD-risk (N=19)	Statin low CVD-risk (N=13)
Number	26	19	17	19	13
Sex, no. (%) female	20 (76.9)	16 (84.2)	12 (70.6)	16 (84.2)	9 (69.2)
Puberty at baseline N(%) post-puberty	18 (69.3)	13 (68.4)	12 (70.6)	10 (52.6)	9 (69.2)
Age, mean (SD) years	15.73 (2.37)	15.04 (2.15)	14.58 (2.54)	15.01 (2.84)	16.38 (2.02)
White Race N (%)	14 (53.8)	12 (63.2)	6 (35.3)	6 (31.6)	5 (38.5)
Black Race N (%)	6 (23.1)	4 (21.1)	5 (29.4)	4 (21.1)	4 (30.8)
Asian Race N (%)	2 (7.7)	1 (5.3)	0 (0.0)	3 (15.8)	2 (15.4)
Other Race N (%)	4 (15.4)	2 (10.5)	6 (35.3)	6 (31.6)	2 (15.4)
BMI, mean (SD) kg/m^2	26.47 (6.91)	23.58 (6.25)	21.76 (3.93)	23.94 (5.47)	25.54 (4.10)
Duration of SLE, mean (SD) months	34.31 (38.08)	26.58 (23.60)	26.71 (20.94)	29.58 (27.07)	28.31 (41.35)
SLEDAI, mean (SD)	4.62 (4.22)	3.32 (4.16)	6.82 (6.41)	4.37 (3.67)	5.92 (4.41)
SLICC, mean (SD)	0.62 (0.98)	0.21 (0.63)	0.24 (0.56)	0.42 (0.69)	0.62 (0.96)
History of hypertension, no. (%)	15 (57.7)	6 (31.6)	4 (23.5)	7 (36.8)	5 (38.5)
dsDNA antibody positive, no. (%)	19 (73.1)	16 (84.2)	13 (76.5)	15 (78.9)	12 (92.3)
Creatinine clearance, mean (SD) $ml/minute/m^2$	136.76 (30.09)	132.87 (32.34)	159.48 (51.36)	144.55 (22.02)	136.78 (30.41)
C3, mean (SD) mg/dl	113.54 (26.59)	100.07 (26.04)	89.16 (26.72)	103.60 (32.96)	104.31 (22.17)
C4, mean (SD) mg/dl	19.21 (8.07)	15.71 (7.39)	12.04 (5.33)	14.89 (7.15)	16.35 (6.14)
Lipid levels, mean (SD) mg/dl					
Total cholesterol	157.56 (29.40)	129.26 (20.32)	167.35 (47.78)	157.47 (48.98)	151.31 (35.84)
HDL cholesterol	48.24 (14.46)	42.63 (10.66)	41.18 (9.09)	45.63 (12.40)	47.85 (11.80)
LDL cholesterol	82.88 (26.01)	62.32 (17.57)	103.88 (39.43)	89.68 (34.21)	84.31 (26.25)
Triglycerides	132.20 (83.26)	122.26 (59.98)	111.12 (56.46)	110.79 (70.75)	96.15 (54.24)
Lipoprotein A	16.48 (19.31)	7.05 (7.86)	37.00 (34.91)	24.37 (34.28)	28.77 (32.46)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

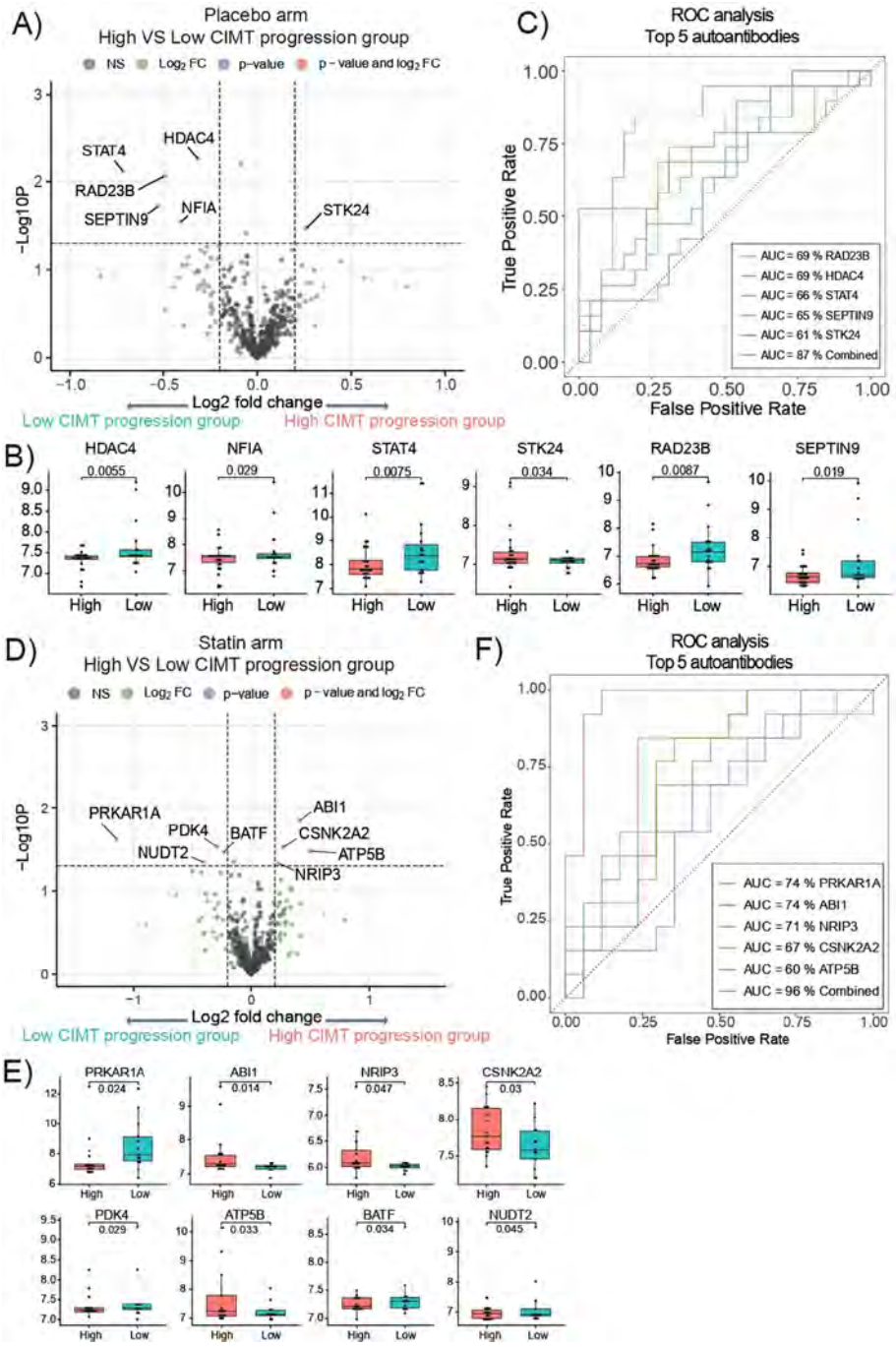


Figure 1: Juvenile-onset systemic lupus erythematosus (JSLE) patient stratification by ΔCIMT at baseline versus 36 months and autoantibody profiling in the placebo and statin arms of the APPLE trial. A, D. Volcano plot displaying fold change of all autoantibodies and Log10 p values comparing high and low CIMT progression groups - placebo and statin arm ($p<0.05$; log2(fold change)>0.2). B, E. Box and whisker plots showing the significant autoantibody levels of the high vs. low CIMT progression groups - placebo and statin arms. Empirical Bayes moderated t-test. C, F. Individual and combined ROC analysis for discriminating high vs. low CIMT progression groups in both in the placebo and statin arms of the APPLE trial using the top performing autoantibodies (individual AUC > 60%). Legend: Autoantibodies defining the atherosclerosis progression signature: RAD23B - RAD23 homolog B, HDAC4 - Histone Deacetylase 4; STAT4 - Signal Transducer and Activator of Transcription 4; STK24 - Serine/Threonine kinase 24; Autoantibodies defining the statin response signature: PRKAR1A - cAMP-dependent protein kinase type I-alpha regulatory subunit; ABI1- Abelson interactor 1; NRIP3 - Nuclear receptor interacting protein 3; CSNK2A2 - Casein kinase II subunit alpha; PDK4 - Pyruvate Dehydrogenase kinase isozyme 4; ATP5B - ATP synthase subunit beta; BATF -Basic leucine zipper transcription factor ATF-like; NUDT2 - Nudix Hydrolase 2. CIMT- carotid intima media thickness

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

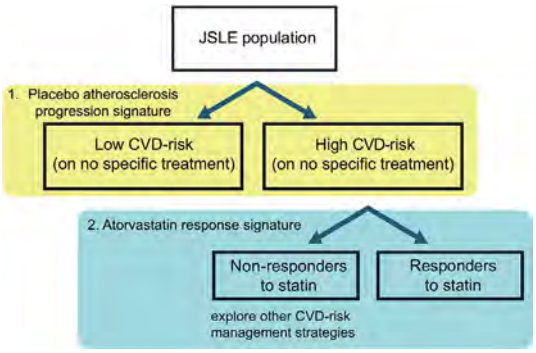


Figure 2: Algorithm for potential use of the novel autoantibody signatures in clinical practice for stratification of JSLE patient population based on CVD-risk and prediction of response to statin treatment.

Background/Purpose: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality in juvenile-onset systemic lupus erythematosus (JSLE). There is an urgent need to identify biomarkers that can predict atherosclerosis progression and therapeutic responses, enabling personalised CVD-risk management in JSLE. This study aimed to investigate whether novel autoantibody signatures can predict atherosclerosis progression and atorvastatin response in children and young people with JSLE.

Methods: We conducted a biomarker discovery study using baseline serum samples from a sub-cohort of the APPLE trial (Atherosclerosis Prevention in Paediatric Lupus Erythematosus), a multi-centre, randomised, double-blind, placebo-controlled clinical trial of atorvastatin versus placebo (1:1) to prevent atherosclerosis progression in JSLE, conducted across 21 sites in North America. Unsupervised cluster analysis based on carotid intima media thickness (CIMT) progression over 36 months was used to identify groups with high and low atherosclerosis progression within each treatment arm. Baseline differential autoantibody expression was assessed using Empirical Bayes moderated t-tests. Predictive performance was evaluated using logistic regression and ROC analysis.

Results: Ninety-four JSLE patients (mean [SD] age 15.3 [2.4] years; 78% female), with matched baseline serum samples and complete longitudinal CIMT measurements over 36 months, were included (45 randomized to the placebo and 49 to the atorvastatin arm) (**Table 1**).

A total of 579 autoantibodies were identified as true signals in the 94 baseline serum samples analysed. In the placebo arm, six autoantibodies (STK24, RAD23B, HDAC4, STAT4, SEPTIN9 and NFIA) were significantly associated with high versus low CIMT progression over 36 months in the placebo arm, achieving a combined area under the curve (AUC) of 87% (**Figure 1A-C**). In the atorvastatin arm, a distinct autoantibody profile was identified, which predicted response to statin treatment. Eight autoantibodies (ABI1, ATP5B, CSNK2A2, NRIP3, PRKAR1A, PDK4, BATF and NUDT2) were significantly associated with CIMT progression despite atorvastatin therapy, achieving an exceptional combined AUC of 96% (**Figure 1D-F**). Enriched pathway analysis of the autoantibodies that differentiated responders vs. non-responders to atorvastatin revealed lipid-independent mechanisms, such as accumulation of vascular smooth muscle cells within neointima (CSNK2A2) or vascular calcification and regulation of cell proliferation/apoptosis (PDK4).

Based on the predictive models generated from these distinct autoantibody profiles in both the placebo and atorvastatin arms, a two-step stratification strategy was proposed to enable precision risk assessment and guide treatment decisions for CVD-risk management in JSLE **(Figure 2)**.

Conclusion: In this biomarker discovery cohort study, novel autoantibody signatures were identified as the first JSLE-specific serum markers for atherosclerosis progression and prediction of statin response (currently under patent protection). These findings support the potential application of autoantibody profiling for precision medicine approaches for CVD-risk management in JSLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Peng: None; **P. Donnes**: None; **T. McDonnell**: None; **L. Schanberg**: Bristol-Myers Squibb(BMS), 5, Sanofi, 12, DSMB, UCB, 12, DSMB; **S. Ardoin**: None; **L. Lewandowski**: None; **G. Robinson**: None; **E. C Jury**: None; **C. Ciurtin**: None.

Abstract Number: 0821

Flipping The Switch – Classical Complement Activation closely linked to IFN-signalling in Stills Disease

Freya Huijsmans[1], Alejandra Bodelón de Frutos[1], Lyanne Sijbers[1], Susanne Benseler[2], Joost Swart[3], Rae Yeung[4], Sebastiaan Vastert[5] and Jorg van Loosdregt[1], [1]Pediatric Rheumatology & Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Utrecht, Utrecht, Netherlands, [2]Cumming School of Medicine, Department of Pediatrics, University of Calgary, Calgary, AB, Canada, [3]Wilhelmina Children's Hospital / UMC Utrecht, Utrecht, Utrecht, Netherlands, [4]The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada, [5]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Pediatric Rheumatology – Basic Science (0819–0824)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Stills disease (SD) is an autoinflammatory syndrome characterized by severe innate immune dysregulation. The complement system, an essential component of innate immunity, can drive inflammatory cascades through the classical, lectin or alternative pathway. Although complement activation has been implicated in various inflammatory disorders, its involvement in SD remains largely undefined. Elucidating the role of complement in SD may provide valuable insights into disease mechanisms and uncover novel therapeutic targets.

Methods: To determine whether the complement pathway is activated in SD patients, we conducted transcriptomic analysis, proteomic measurements, and in vitro stimulation assays. RNA was extracted from whole blood of SD (active n=27, inactive n=26) and active non-systemic juvenile idiopathic arthritis (JIA) patients (n=538). Gene expression of classical complement components C1QB, C1QC and IFN-regulated genes (IFN-score) was quantified by NanoString. Additionally, RNA sequencing was conducted on sorted monocytes from SD patients (active n=7, inactive n=7). Inflammatory mediators (IL-18, CXCL9, CXCL10) and complement activation products (C1q, C3a, C5a) were quantified using Luminex and ELISA. Classical complement activity was evaluated in sera of SD (active n=32, inactive n=66) and non-systemic JIA patients (active n=12, inactive n=12). To explore potential mechanisms underlying complement activation, in vitro experiments were conducted to assess which inflammatory stimuli could induce C1q production in monocytes.

Results: RNA expression of classical complement protein C1q is upregulated in both whole blood and isolated CD14+ monocytes from active SD patients compared to those with inactive disease (NanoString: C1QB 43 vs. 11, $p< 0.01$; C1QC 24 vs. 6, $p< 0.01$; Monocytes: C1QB log2FC 3.6, $p< 0.01$; C1QC log2FC 3.9, $p< 0.01$) and to active non-systemic JIA patients (C1QB 43 vs 15, $p< 0.01$; C1QC 24 vs 8, $p< 0.01$). Moreover, whole blood C1QB and C1QC expression levels positively correlate with the IFN-score ($r=0.34$, $p=0.01$), plasma levels of IL18 ($r=0.5$, $p< 0.01$) and IFN related chemokines CXCL9 ($r=0.4$, $p< 0.01$) and CXCL10 ($r=0.6$, $p< 0.01$) in SD. Protein analysis revealed elevated levels of C1q, C3a, and C5a, as well as enhanced classical complement activity in active SD compared to inactive SD (94% vs 74%, $p< 0.01$) and active non-systemic JIA patients (94% vs 81%, $p=0.02$). Furthermore, in vitro stimulation of healthy control monocytes with IFNγ robustly and specifically induces C1q mRNA expression. Flow cytometry analysis confirmed that IFNγ stimulation promotes the emergence of a distinct monocyte subset characterized by high C1q expression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our findings indicate activation of the classical complement pathway in SD, closely linked with IFN-signalling. Obtaining a better understanding of the role of the complement system, particularly the role of C1q-high monocytes, may open novel avenues for personalized therapeutic approaches in SD.

Disclosure: F. Huijsmans: None; **A. Bodelón de Frutos**: None; **L. Sijbers**: None; **S. Benseler**: None; **J. Swart**: None; **R. Yeung**: AstraZeneca, 5, SOBI, 6; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **J. van Loosdregt**: None.

Abstract Number: 0822

Clinical and Mechanistic Insight of Circulating Calprotectin and NXP2 autoantibodies in Juvenile Dermatomyositis

Kavya Sugur[1], Elizabeth Sloan[2], Emily Chong[3], Sophia Matossian[3], Katarina Kmetova[4], Alyssa Rosek[5], Christine Goudsmit[6], Celine C. Berthier[6], Pei-Suen Tsou[3], Yu (Ray) Zuo[3] and Jessica Turnier[7], [1]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Ann Arbor, MI, [2]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [3]University of Michigan, Ann arbor, MI, [4]Division of Rheumatology, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor, MI, [5]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, [6]University of Michigan, Ann Arbor, [7]University of Michigan, Saline, MI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Pediatric Rheumatology – Basic Science (0819–0824)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Most children with juvenile dermatomyositis (**JDM**) have chronic disease despite multi-drug immunosuppression, highlighting the need for targeted therapies. Neutrophil extracellular traps (**NETs**) are key in autoimmunity, but their role in JDM is unclear. This study examined neutrophil activation and NET formation, focusing on calprotectin as a candidate biomarker and mediator of tissue damage.

Methods: Plasma calprotectin was measured in JDM patients (n=51) and healthy controls (n=10). Sixteen endothelial cell analytes were assessed in 48 JDM patients. Proteomic profiling of six treatment-naïve samples was done using the Olink 3072 panel. Ex vivo and in vitro assays tested JDM plasma and recombinant calprotectin on muscle cell injury. Anti-NXP2 antibodies from treatment-naïve patients were evaluated for their ability to induce NETs by SYTOX Green-based assay.

Results: Circulating calprotectin levels were significantly elevated in JDM patients compared to healthy controls ($p < 0.0001$). Calprotectin strongly correlated with absolute neutrophil counts ($r = 0.63$, $p < 0.0001$), consistent with its origin from activated neutrophils and its link to NET formation. Notably, higher calprotectin levels were also associated with established biomarkers of muscle injury, including creatine phosphokinase ($r = 0.34$, $p = 0.036$), aldolase ($r = 0.40$, $p = 0.013$), and lactate dehydrogenase ($r = 0.37$, $p = 0.023$). Clinically, elevated calprotectin reflected reduced muscle strength, as assessed

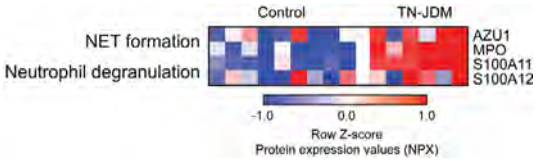


Figure 1. Upregulation of neutrophil activation and NET formation protein expression signature in JDM. Heatmap displaying individual-level Z-score Normalized Protein Expression (NPX) values of select neutrophil-specific proteins in treatment-naïve (TN) JDM plasma (n = 6) compared to healthy controls (n = 9). These proteins were also significantly associated with global disease activity, highlighting a neutrophil-driven inflammatory signature at the time of JDM diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

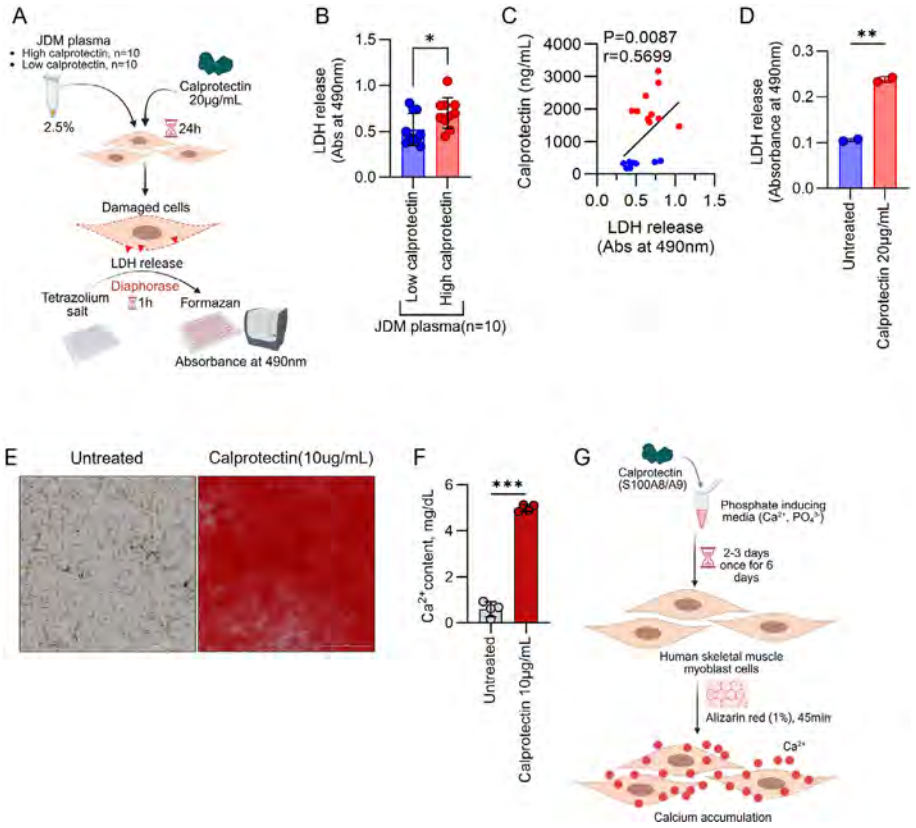


Figure 2. Impact of elevated calprotectin—both from high-calprotectin JDM samples and recombinant protein—on cytotoxicity and calcification in human skeletal muscle myoblasts (HSMMs). (A) Schematic of the skeletal muscle cell cytotoxicity assay. (B) Cytotoxicity of HSMMs was assessed via LDH release after 24-hour treatment with 2.5% plasma from JDM subjects with high (n=10) or low (n=10) circulating calprotectin. (C) Correlation between plasma calprotectin levels and LDH release in JDM samples. (D) LDH release from HSMMs following treatment with recombinant calprotectin (20μg/mL). (E) Alizarin Red staining of HSMMs treated with recombinant calprotectin (10 μg/mL) in calcification medium (PI) for 6 days, with media refreshed every 2–3 days. (F) Calcium content was quantified in parallel wells; calcium deposits were dissolved with 1N HCl for 3 hours at 4°C and measured using the QuantiChrom Calcium Assay Kit. (G) Schematic of intracellular calcium accumulation assay. *Statistical significance: *P < 0.05; **P < 0.01; ***P < 0.001.

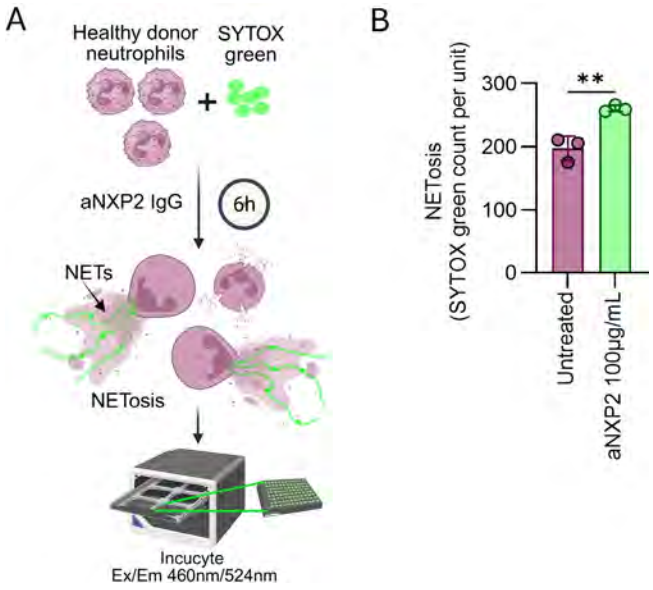


Figure 3. The JDM-specific autoantibody anti-NXP2 IgG induces NETosis in healthy donor neutrophils. (A) Schematic of the SYTOX Green-based NETosis assay. (B) Healthy donor neutrophils were treated with anti-NXP2 IgG (100 μg/mL) for 6 hours in the presence of SYTOX Green, which labels extracellular DNA released during NETosis. *Significance: **P < 0.01.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

by lower Manual Muscle Testing-8 scores (r = –0.44, p = 0.007), and higher Physician's Global Activity Assessment scores (r = 0.36, p = 0.023), underscoring its potential as a biomarker of disease activity. Furthermore, calprotectin levels showed strong correlations with multiple soluble EC analytes—including Ang-2, Tie2, Gal-9, and sTNFR-II—suggesting a role in endothelial activation or injury. Plasma proteomic expression profiling in TN JDM patients also revealed significant upregulation of multiple neutrophil activation proteins (AZU1, MPO, S100A11, S100A12) (**Fig. 1**). Mechanistic studies demonstrated that calprotectin-rich JDM plasma induced marked cytotoxicity and microcalcification in cultured human skeletal muscle cells (**Fig. 2 A-G**). These effects were recapitulated by recombinant calprotectin, confirming a direct pathogenic role. Additionally, anti-NXP2 antibodies purified from JDM plasma robustly induced NET formation when incubated with neutrophils from healthy donors, implicating this JDM-specific autoantibody in neutrophil activation and NETosis (**Fig. 3 A-B**). Ongoing experiments aim to assess the potential direct pathogenic effects of anti-NXP2 on endothelial cells and muscle tissue.

Conclusion: Calprotectin is a mechanism-informed biomarker in JDM that reflects neutrophil activation and correlates with muscle disease activity, endothelial dysfunction, and muscle damage. Anti-NXP2 autoantibodies trigger NETosis, linking adaptive immunity to neutrophil-driven pathology. These findings reveal a novel pathogenic axis at the intersection of innate and adaptive immunity with vascular health, suggesting new targets for biomarker-guided therapy.

Disclosure: K. Sugur: None; **E. Sloan**: None; **E. Chong**: None; **S. Matossian**: None; **K. Kmetova**: None; **A. Rosek**: None; **C. Goudsmit**: None; **C. C. Berthier**: None; **P. Tsou**: None; **Y. Zuo**: None; **J. Turnier**: Cabaletta Bio, 2.

Abstract Number: 0823

Longitudinal model of paired peripheral blood CITE-seq and skin scRNA-seq data in juvenile systemic sclerosis (jSSc) patients following autologous stem cell transplant (ASCT) reveals reduced expression of SSc marker genes

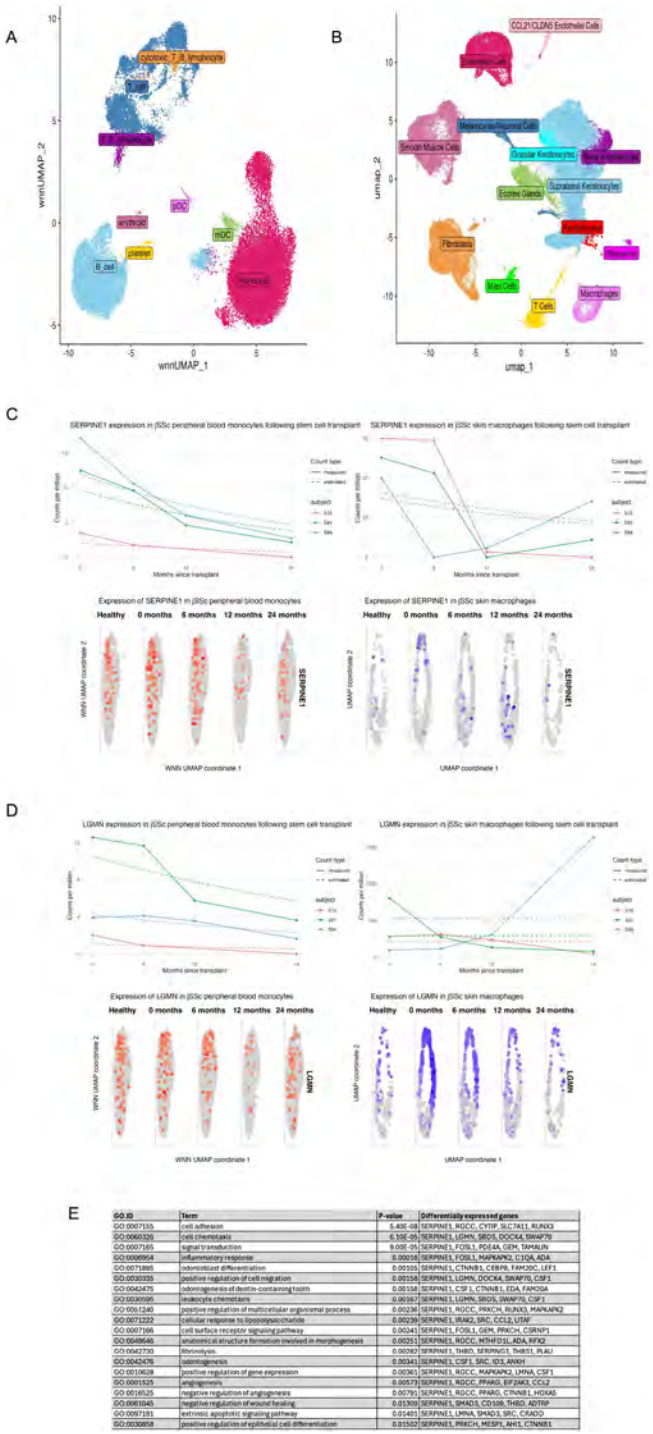
Julia Elrod[1], Theresa hutchins[2], Anwesha Sanyal[2], Paul Szabolcs[2], Paulina Horvei[2], Jon Li[2], F. William Townes[1] and Kathryn Torok[2], [1]Carnegie Mellon, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Pediatric Rheumatology – Basic Science (0819–0824)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Juvenile systemic sclerosis (jSSc) is a rare, life-threatening autoimmune disease characterized by fibrosis and immune dysregulation. Autologous stem cell transplant (ASCT) is an emerging treatment aimed at resetting immune homeostasis. Here, we present the first integrated longitudinal single-cell analysis of paired peripheral blood and skin samples in jSSc patients undergoing ASCT, using Cellular Indexing of Transcriptomes and Epitopes by sequencing (CITE-seq) in context with skin single-cell RNA sequencing (scRNA seq) data.

Methods: Peripheral blood mononuclear cell (PBMC) and skin samples were collected from three jSSc patients pre-ASCT and at 6, 12, and 24 months post-ASCT. Samples were multiplexed per patient including the different timepoints. PBMC and skin samples underwent CITE-seq and scRNA-seq respectively. Data were processed using CellRanger, Seurat, SoupX, DSB, Harmony, and RPCA. PBMCs were clustered using a shared RNA and protein weighted nearest neighbors (WNN) graph (Figure 1A), skin cells were clustered using a standard Seurat pipeline (Figure 1B), and cell types were annotated. RNA counts were subsetted by tissue and cell type and then pseudobulked to aggregate expression across cells

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



GO.ID	Term	P-value	Differentially expressed genes
GO:0007155	cell adhesion	5.40E-08	SERPINE1, RGCC, CYTIP, SLC7A11, RUNX3
GO:0060326	cell chemotaxis	6.15E-05	SERPINE1, LGMN, SRGN, DOCK4, SWAP70
GO:0007165	signal transduction	9.00E-05	SERPINE1, FOSL1, PDE4A, GEM, TAMALIN
GO:0006954	inflammatory response	0.00058	SERPINE1, FOSL1, MAPKAPK2, C1QA, ADA
GO:0071895	odontoblast differentiation	0.00105	SERPINE1, CTNNB1, CEBPB, FAM20C, LEF1
GO:0030335	positive regulation of cell migration	0.00158	SERPINE1, LGMN, DOCK4, SWAP70, CSF1
GO:0042475	odontogenesis of dentin-containing tooth	0.00158	SERPINE1, CSF1, CTNNB1, EDA, FAM20A
GO:0030595	leukocyte chemotaxis	0.00367	SERPINE1, LGMN, SRGN, SWAP70, CSF1
GO:0061240	positive regulation of multicellular organismal process	0.00236	SERPINE1, RGCC, PRKCH, RUNX3, MAPKAPK2
GO:0071222	cellular response to lipopolysaccharide	0.00239	SERPINE1, IRAK2, SRC, CCL2, UTRF
GO:0007166	cell surface receptor signaling pathway	0.00241	SERPINE1, FOSL1, GEM, PRKCH, CSRNP1
GO:0048646	anatomical structure formation involved in morphogenesis	0.00251	SERPINE1, RGCC, MTHFD1L, ADA, RFX2
GO:0042730	fibrinolysis	0.00260	SERPINE1, THBD, SERPING1, THBS1, PLAU
GO:0042476	odontogenesis	0.00341	SERPINE1, CSF1, SRC, IDS, ANXA1
GO:0010628	positive regulation of gene expression	0.00361	SERPINE1, RGCC, MAPKAPK2, LMNA, CSF1
GO:0001525	angiogenesis	0.00573	SERPINE1, RGCC, PPARG, EIF2AK3, CCL2
GO:0016525	negative regulation of angiogenesis	0.00791	SERPINE1, RGCC, PPARG, CTNNB1, HDAC6
GO:0061045	negative regulation of wound healing	0.01309	SERPINE1, SMAD3, CD109, THBD, ADTRP
GO:0097191	extrinsic apoptotic signaling pathway	0.01401	SERPINE1, LMNA, SMAD3, SRC, CRADD
GO:0030858	positive regulation of epithelial cell differentiation	0.01502	SERPINE1, PRKCH, MESP1, AHR, CTNNB1

Figure 1. Longitudinal transcriptomic changes in paired peripheral blood and skin of juvenile systemic sclerosis (jSSc) patients following autologous stem cell transplant (ASCT) Legend: A. Weighted nearest neighbor (WNN) UMAP of peripheral blood CITE-seq data from all time points, annotated by major immune cell type. B. UMAP of skin scRNA-seq data, annotated by major stromal and immune cell populations. C. SERPINE1 expression trajectories over time in peripheral blood monocytes (left) and skin macrophages (right). Top panels show log-linear longitudinal model fits for each patient, while bottom panels display SERPINE1 feature plots at each time point, including healthy controls and post-ASCT time points. D. Longitudinal expression and feature plots for LGMN, a fibrosis-associated gene, in peripheral blood monocytes and skin macrophages, using the same layout as panel C. E. Gene ontology (GO) enrichment analysis of genes downregulated following ASCT, highlighting biological processes such as cell adhesion, monocyte chemotaxis, fibrinolysis, and cell differentiation. These results highlight dynamic and coordinated downregulation of profibrotic and inflammatory gene programs in skin and blood compartments post-ASCT, with SERPINE1 and LGMN among the top differentially expressed genes associated with disease resolution.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

per gene, patient, and time point. A negative binomial GLM was fit using glmGamPoi, with time post-ASCT as the primary variable, adjusting for patient and library size. Differential gene expression was assessed using quasi-likelihood ratio tests.

Results: Monocytes (PBMC) and macrophages (skin) demonstrated the most robust transcriptomic changes over time. In PBMCs, the top differentially expressed gene was *SERPINE1* (Plasminogen Activator Inhibitor-1), a known SSc biomarker (LFC -3.48, $p = 7.86\times10^{-6}$). Figure 1C shows longitudinal model fits of *SERPINE1* in peripheral blood monocytes and skin macrophages, as well as expression feature plots across time points. Expression of *LGMN*, another fibrosis-associated gene, followed a similar trajectory (Figure 1D). Gene set enrichment analysis (GSEA) of gene expression downregulated post-ASCT identified pathways related to cell adhesion, monocyte chemotaxis, fibrinolysis, and cell differentiation (Figure 1E). Notably, *RGCC*, *LGMN*, and *FOSL1*, previously implicated in fibrotic and immune processes, were significantly downregulated in both PBMC and skin. These findings align with prior studies implicating macrophage-fibroblast crosstalk in adult SSc pathology.

Conclusion: Our integrated single-cell analysis reveals that ASCT results in significant reduction of fibrotic and inflammatory gene signatures in both blood and skin of jSSc patients. The longitudinal decrease in *SERPINE1* and other SSc-associated genes supports ASCT's role in molecular disease reversal. These transcriptomic findings, combined with parallel clinical improvement, underscore the therapeutic potential of immune reset strategies in modifying disease trajectory in jSSc.

Disclosure: J. Elrod: None; **T. hutchins**: None; **A. Sanyal**: None; **P. Szabolcs**: None; **P. Horvei**: None; **J. Li**: None; **F. Townes**: None; **K. Torok**: None.

Abstract Number: 0824

Characterizing Immune Responses in Abatacept-treated Patients with Limited Juvenile Idiopathic Arthritis

Lwiza AitDowd[1], Ekaterina Murzin[2], Alexandra Pommier[3], Ki Pui Lam[4], Claudia Harris[5], Melanie Kohlheim[6], Grant Schulert[7], Marc Sudman[8], Eveline Wu[9], Laura Schanberg[10], Peter Nigrovic[11], James Lederer[12], Lauren Henderson[13] and CARRA Registry Investigators, [1]Boston Children's Hospital, Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Harvard Medical School, Boston, MA, [4]Division of Immunology, Boston Childrens Hospital, Harvard Medical School, Boston, MA, [5]Division of Immunology, Boston Childrens Hospital, Boston, MA, [6]CARRA, Granville, OH, [7]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]Cincinnati Children's Hospital Medical Center, Cincinnati, [9]UNC Chapel Hill, Chapel Hill, NC, [10]Duke University Medical Center, DURHAM, NC, [11]Boston Children's Hospital, Brookline, MA, [12]Brigham and Women's Hospital, Millis, MA, [13]Boston Children's Hospital, Watertown, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Pediatric Rheumatology – Basic Science (0819–0824)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Our ability to tailor treatments to individual patients with JIA remains limited. To identify candidate biomarkers that may be associated with treatment response, we characterized circulating lymphocytes in patients treated with abatacept in the Improving Outcomes in Limited JIA (LIMIT-JIA) study.

Methods: LIMIT-JIA is a multicenter trial conducted within the Childhood Arthritis and Rheumatology Research Alliance (CARRA) comparing abatacept treatment for 24 weeks to usual care in patients with limited arthritis (< 5 joints at disease onset). Study subjects were diagnosed within 6 months, had no history of uveitis, and were DMARD naïve. Blood samples were collected from 12 different CARRA sites at baseline (before treatment) and at 6 months and shipped to the CARRA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

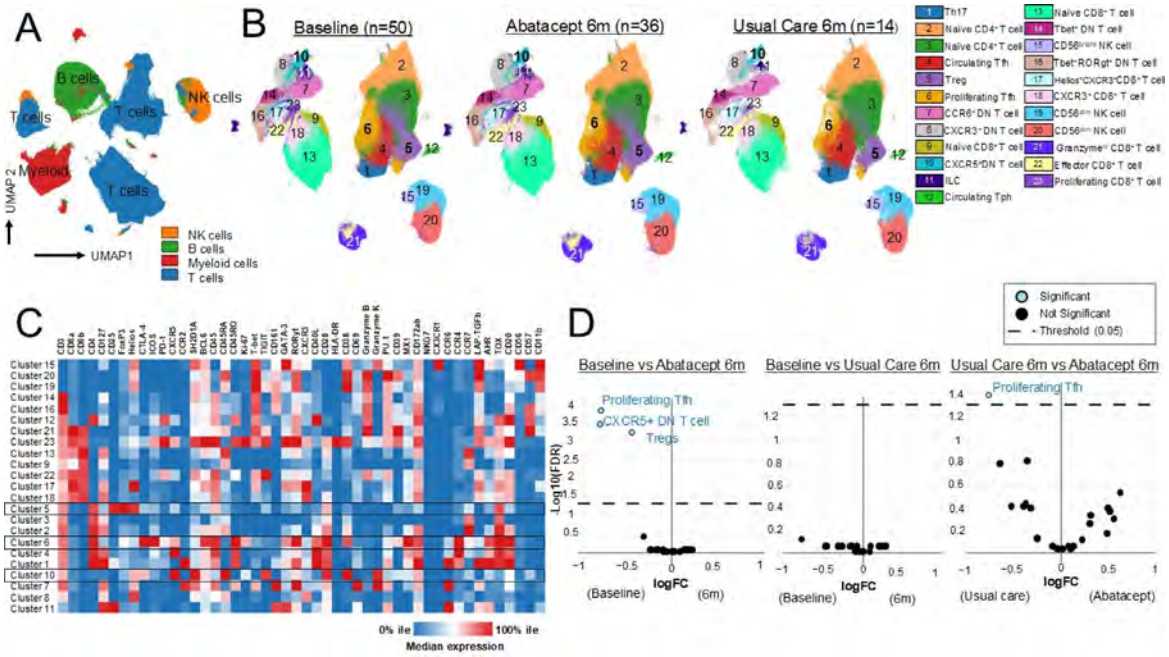


Figure 1: Abatacept treatment modulates circulating T cell subsets in patients with limited JIA. A) UMAPs generated from mass cytometry data of the 48-marker panel used to immunophenotype T and NK cells. Samples were from JIA patients at baseline (n=50) and those treated with abatacept (n=36) or usual care (n=14) at 6 months. B) UMAPs generated after filtering for T and NK cells and unsupervised clustering. C) Heatmap showing the median expression of a given marker in each cluster. D) Volcano plots showing differential abundance of the clusters in the given study groups. JIA, juvenile idiopathic arthritis; UMAPs, uniform manifold approximation and projections; mo, months; Treg, regulatory T; Tfh, T follicular helper; Tph, T peripheral helper; DN T, double negative T

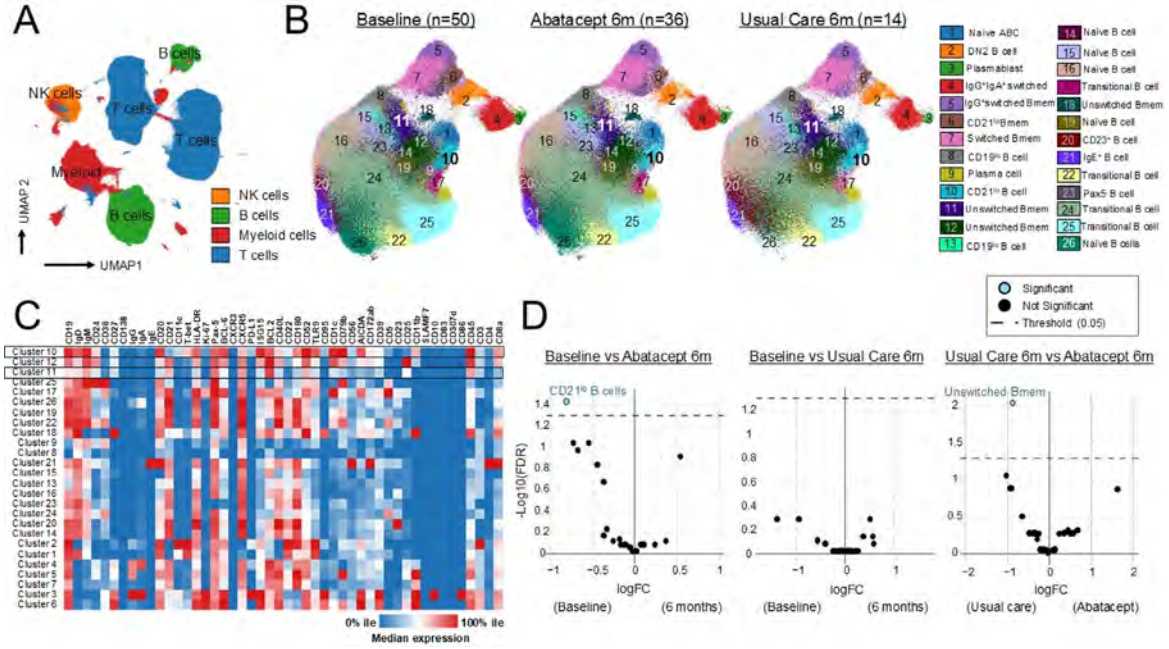


Figure 2: Abatacept treatment decreases circulating CD21lo B cells in patients with limited JIA. A) UMAPs generated from mass cytometry data of the 48-marker panel used to immunophenotype B cells. Samples were from JIA patients at baseline (n=50) and those treated with abatacept (n=36) or usual care (n=14) at 6 months. B) UMAPs generated after filtering for B cells and unsupervised clustering. C) Heatmap showing the median expression of a given marker in each cluster. D) Volcano plots showing differential abundance of the clusters in the given study group. JIA, juvenile idiopathic arthritis; UMAPs, uniform manifold approximation and projections; mo, months; ABC, age-/autoimmune-associated B cells; DN, double negative; Bmem, memory B cell

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Biobank for cryopreservation. Peripheral blood mononuclear cells (PBMCs) were then thawed, stained with antibodies from 2 panels to characterize T/B/NK cells (48 markers/panel), barcoded for mass cytometry, and acquired on a CyTOF XT instrument. Samples were processed in 5 batches with each batch containing samples from multiple study groups/time points. After compensation and debarcoding, CyCombine corrected and integrated the results from the batches. OMIQ software was used for unsupervised clustering with FlowSOM and results were visualized with a uniform manifold approximation and projections (UMAP) and heatmaps. EdgeR in OMIQ was used for statistical analysis.

Results: Patients in the abatacept (n=36) and usual care (n=14) arms provided paired samples at baseline and 6 months. T, B, NK, and myeloid cells were identified with data from each panel (Fig 1A, 2A). After gating on $CD3^+$ or $CD56^+$ cells, 23 clusters of T/NK cells were identified (Fig 1B-C). Three clusters were significantly more abundant in patients at baseline compared to those treated with abatacept at 6 months. These clusters contained cells with features of regulatory T (Treg) (cluster 5), T follicular helper (Tfh) (cluster 6), and double negative (DN) T cells (cluster 10) (Fig 1C-D). There was no difference in cluster distribution in patients at baseline vs. those receiving usual care at 6 months (Fig 1D). When comparing patients at 6 months, T cells were more frequent in the Tfh cell cluster in the usual care vs. abatacept groups (Fig 1D). Clustering on $CD20^+CD19^+$cells revealed 26 different B cell populations (Fig 2B). Cluster 10 contained $CD21^{lo}$ B cells with features of age-/autoimmune-associated B cells (ABCs) and was overrepresented in patients at baseline compared to those treated with abatacept at 6 months. There was no difference in B cell cluster abundance in patients at baseline vs. usual care at 6 months. Cluster 11, containing unswitched memory B cells, was enriched in usual care vs. abatacept at 6 months.

Conclusion: Abatacept treatment in JIA patients with limited arthritis modulated the frequency of circulating Treg, Tfh, DN T, and $CD21^{lo}$B cells. These results suggest that interactions between B cell helper T cells and $CD21^{lo}$B cells are important in the pathogenesis of this form of arthritis and may be regulated by T cell costimulatory inhibition. Further studies are needed to determine if these lymphocyte populations can predict and track treatment response in JIA patients.

Disclosure: L. AitDowd: None; **E. Murzin**: None; **A. Pommier**: None; **K. Lam**: None; **C. Harris**: None; **M. Kohlheim**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **M. Sudman**: None; **E. Wu**: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **L. Schanberg**: Bristol-Myers Squibb(BMS), 5, Sanofi, 12, DSMB, UCB, 12, DSMB; **P. Nigrovic**: Alkermes, 2, Apollo, 2, Bristol-Myers Squibb(BMS), 5, Century, 2, Edelweiss Therapeutics, 11, Merck, 2, Monte Rosa, 2, Novartis, 2, Pfizer, 2, 5; **J. Lederer**: None; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2.

Abstract Number: 0825

Rheum2Learn: A Randomized Trial of Virtual vs Text-Based Rheumatology Modules

Sonam Kiwalkar[1], Julianna Desmarais[2], Ellen Snyder[3], Lisa Schroeder[4], Marissa Meissner[5], Noelle A. Rolle[6], Sarah Donohue[7], Brittany Bettendorf[8], Ira Khanna[9], Karen Kruzer[10], Nkechi Emejuaiwe[11], Ibtissam Gad[12], David Leverenz[13], Michael George[14], Ashima Makol[15], Floranne Ernste[15] and Jilie Blaszczak[16], [1]The Vancouver Clinic, Portland, OR, [2]Oregon Health and Sciences University, Portland, OR, [3]UNC Rheumatology, Chapel Hill, NC, [4]Geisinger, Danville, PA, [5]Geisinger Medical Center, Danville, PA, [6]Medical College of Georgia at Augusta University, Evans, GA, [7]University of Wisconsin, Madison, WI, [8]University of Iowa, Iowa City, IA, [9]Mount Sinai Hospital, New York, NY, [10]Assistant Professor- University of Rochester, Victor, NY, [11]Cincinnati VA Medical Center, Cincinnati, OH, [12]University of Michigan, Plymouth, MI, [13]Duke University, Durham, NC, [14]University of Pennsylvania, Philadelphia, PA, [15]Mayo Clinic, Rochester, MN, [16]University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Professional Education (0825–0830)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

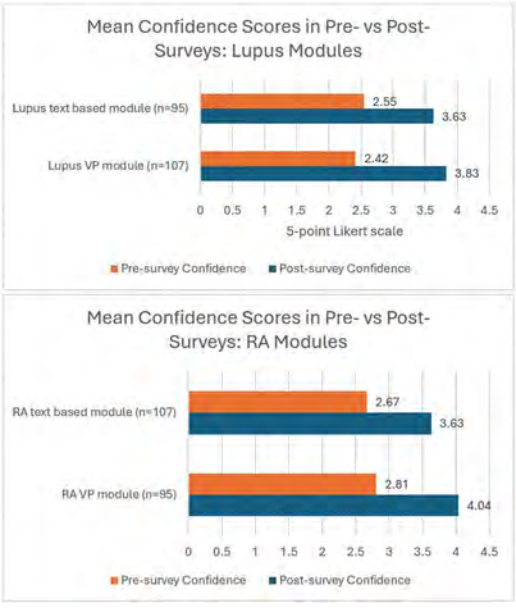
Table 1 Comparison of Pre- and Post-Test Scores for VP and Text-Based Modules in lupus and RA

Condition	Timepoint	Group A Mean (SD)	Group B Mean (SD)	p-value
Lupus	Pre-test	35.6% (10.47)	36.7% (11.43)	
	Post-test	47.5% (6.33)	46.3% (6.02)	
	Difference (Post - Pre)	+11.9% (8.01)	+9.6% (8.5)	**0.05**
RA	Pre-test	40.4% (7.88)	40.1% (7.79)	
	Post-test	45.7% (6.60)	47.8% (5.51)	
	Difference (Post - Pre)	+5.3% (7.81)	+7.7% (7.21)	**0.02**

Background/Purpose: Internal medicine (IM) residents often receive limited rheumatology training, contributing to low confidence in managing rheumatologic conditions and suboptimal performance on standardized examinations. Virtual patient (VP) modules—interactive, multimedia cases simulating real-life scenarios—offer a promising alternative by promoting clinical reasoning and learner engagement. Rooted in cognitive load and multimedia theories, VP modules may offer advantages over traditional text-based learning, which often lacks interactivity and real-world complexity. While prior research has demonstrated the effectiveness of VPs compared to no intervention, evidence comparing VPs to text-based modules in graduate medical education, particularly in rheumatology, remains limited.

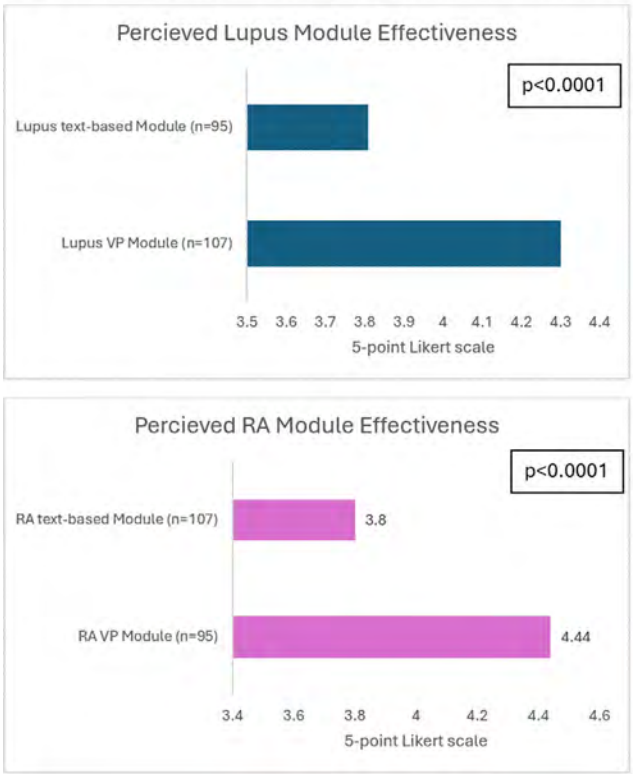
Methods: In a multi-site, randomized crossover study, 202 IM residents from 16 U.S. residency programs were randomized into two groups: Group A completed a VP module on systemic lupus erythematosus (SLE) and a text-based module on rheumatoid arthritis (RA), while Group B completed a VP module on RA and a text-based module on SLE. Clinical reasoning was assessed via 10-item multiple-choice pre- and post-tests. Self-reported confidence was measured using 5-point Likert-scale items. Learner perceptions were evaluated through a pre-validated survey and open-ended questions. Student's t-tests compared change in pre- and post-test scores, self-rated confidence, and perceived module effectiveness. These abstract reports interim results from data collected between Feb'24 and Jan'25.

Figure 1 Comparison of Mean Confidence Scores in Pre- and Post-Surveys for Lupus and RA Modules



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig. 2 Residents' perceptions of VP compared to text-based modules



Likert scale: 1 = strongly disagree, 2 = Disagree, 3 = Neither agree or disagree, 4 = Agree, 5 = strongly Agree.

Results: Interim analysis indicates that both module types improved knowledge. However, VP modules led to greater gains in post-test scores compared to text-based modules in both RA and SLE; differences were statistically significant in SLE ($p = 0.05$) and in RA ($p = 0.02$) modules. (Table 1). Compared to pre-survey confidence, residents who completed VP modules reported significantly higher post-survey confidence in diagnosing, evaluating, and managing both SLE and RA ($p < 0.0001$; Figure 1). They also rated VP modules as significantly more effective in reinforcing diagnostic reasoning and clinical decision-making skills ($p < 0.0001$; Figure 2). Open-ended feedback reflected a strong learner preference for VP modules, describing them as more engaging and realistic. Key benefits included interactive dialogue, clinical decision-making prompts, and visual content. Some residents described the VP format as lengthy or repetitive, while others appreciated its alignment with real-world reasoning.

Conclusion: Preliminary findings suggest that VP modules led to greater knowledge and confidence gains compared to text-based modules and VPs were preferred by learners. These findings support integrating VP-based learning into rheumatology education, especially in settings with limited faculty or clinical exposure as they offer a scalable, engaging approach to preparing IM residents for real-world rheumatologic care. Although long-term retention and sustained confidence were not assessed, future studies will be important to determine their lasting impact.

Data are presented as mean percent correct (standard deviation). P-values based on unpaired t-tests comparing Group A and Group B at each timepoint. Difference reflects the absolute change from pre- to post-test scores. *Group A - VP module on lupus (highlighted in grey) and text-based module on rheumatoid arthritis; Group B - text-based module on lupus and VP module on rheumatoid arthritis (highlighted in grey).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Kiwalkar: None; **J. Desmarais**: None; **E. Snyder**: None; **L. Schroeder**: None; **M. Meissner**: None; **N. Rolle**: None; **S. Donohue**: None; **B. Bettendorf**: None; **I. Khanna**: None; **K. Kruzer**: None; **N. Emejuaiwe**: None; **I. Gad**: None; **D. Leverenz**: Pfizer, 5, Sanofi, 2, UCB, 2; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **F. Ernste**: Priovant Therapeutics, 5; **J. Blaszczak**: None.

Abstract Number: 0826

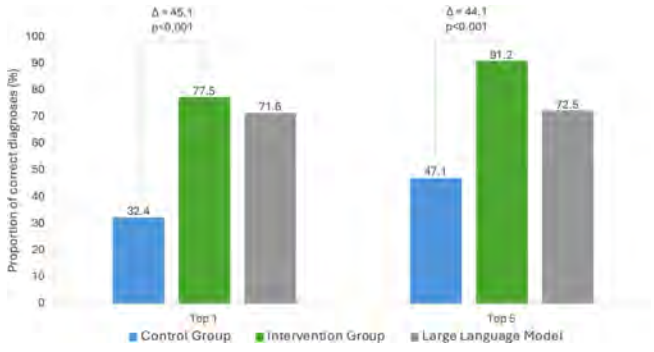
Impact of Large Language Models on Diagnostic Reasoning of Medical Students in Rheumatology: A Randomized Trial

Anna Roemer[1], Nadine Schlicker[2], Anna Kernder[3], Benedikt Albe[1], Juliana Hack[4], Martin Hirsch[5], Sebastian Kuhn[1] and **Johannes Knitza**[6], [1]Institute for Digital Medicine, University Hospital of Giessen and Marburg, Philipps University Marburg, Marburg, Germany, [2]Institute for Artificial Intelligence in Medicine, University Hospital Giessen and Marburg, Marburg, Germany, [3]Department of Rheumatology, Rheumazentrum Ruhrgebiet, Herne, Germany, [4]Center for Orthopaedics and Trauma Surgery, University Hospital Giessen and Marburg, Marburg, Germany, [5]Institute for Artificial Intelligence in Medicine, University Hospital Giessen and Marburg, Philipps University Marburg, Marburg, Germany, [6]Institute for Digital Medicine, University Hospital Gießen-Marburg, Philipps University, Marburg, Germany

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Professional Education (0825–0830)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

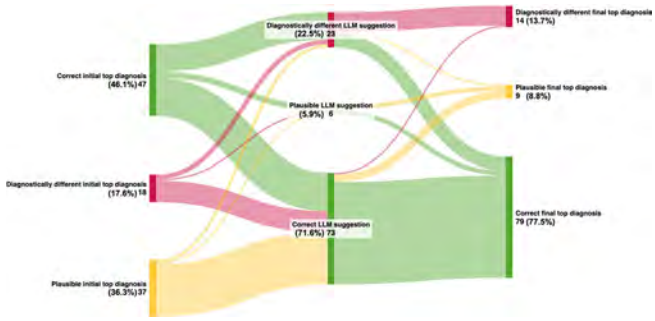
Background/Purpose: Although not certified as medical devices, Large Language Models (LLMs) such as ChatGPT-4 provide rapid support in diagnostic reasoning and may facilitate scalable upskilling of healthcare professionals and laypersons alike. This trial evaluated the impact of LLM assistance on the diagnostic reasoning of medical students solving rheumatology case vignettes.

Methods: In this RCT (NCT06748170), 68 medical students were allocated between January 7 and March 30, 2025, to either an intervention group (IG), with access to ChatGPT-4o, alongside conventional diagnostic resources, or a control group (CG), with access to conventional resources only. Participants in the IG first generated diagnostic suggestions using conventional resources and then revised their suggestions after consulting the LLM. All participants completed 3 rheumatology case vignettes—GPA , RA and SLE—originally published in the ACR's online learning center. Each vignette required a top diagnosis, and optionally up to five diagnostic suggestions in total. The suggested diagnoses were independently and blindly reviewed by two board-certified rheumatologists. Diagnostic accuracy was additionally scored by awarding two points for correct diagnoses and one point for plausible alternatives, generating a cumulative diagnostic score. Time to case completion and diagnostic confidence (0–10) were also recorded.



Proportion of correct diagnoses ranked first or within the top five suggestions

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Distribution of top diagnosis categories in the intervention group across study phases

Results: The mean (SD) age was 24.8 (2.6) years; 62% (42/68) of participants were female. Prior use of LLMs was reported by 96% (65/68) of students. Interrater agreement was substantial (Cohen's κ = 0.79). Students in the IG identified the correct top diagnosis significantly more often than those in the CG (77.5%, mean 2.3/3 [SD 0.8] vs. 32.4%, mean 1.0/3 [SD 0.8]; independent t-test = 7.3, $P < 0.001$) and were also more likely to include a correct diagnosis among their top five suggestions (91.2%, mean 2.7/3 [SD 0.5] vs. 47.1%, mean 1.4/3 [SD 0.7]; independent t-test = 8.5, $P < 0.001$), see **Figure 1**. The standalone performance of the LLM exceeded that of students using conventional resources, listing the correct diagnosis first in 71.6% of cases and within the top five in 72.5%. Median diagnostic scores per case were 4 (IQR, 3–5) in the IG, 2 (IQR, 1–3) in the CG, and 5 (IQR, 3.3–6) for the LLM. Median time to case completion was 498 seconds (IQR, 371–609) in the IG and 253 seconds (IQR, 175–395) in the CG. LLM use significantly increased the proportion of correct top diagnoses in the IG, from 46.1% (mean 1.4/3 [SD 0.7]) to 77.5% (mean 2.3/3 [SD 0.8]); paired t-test = 7.1, P < 0.001, see **Figure 2**. Diagnostic confidence in the IG also increased significantly following LLM use (mean 5.2/10 [SD 1.5] to 7.0/10 [SD 1.3]; paired t-test = –9.4, P < 0.001). Among IG participants, 97% (33/34) reported they would use the LLM again for diagnostic support, and 91% (31/34) found it easy to use.

Conclusion: To our knowledge, this is the first RCT to evaluate the diagnostic assistive potential of LLMs in rheumatology. Providing medical students with access to an LLM significantly improved diagnostic accuracy compared to conventional resources alone. Further research is warranted to determine how LLMs can be implemented to safely empower healthcare professionals as well as patients.

Disclosure: A. Roemer: None; **N. Schlicker**: None; **A. Kernder**: None; **B. Albe**: None; **J. Hack**: None; **M. Hirsch**: None; **S. Kuhn**: None; **J. Knitza**: GAIA, 2, Vila Health, 12, 2.

Abstract Number: 0827

Utilization of American College of Rheumatology Vaccination Guidelines in Clinic: A Needs Assessment in an Internal Medicine Residency Program

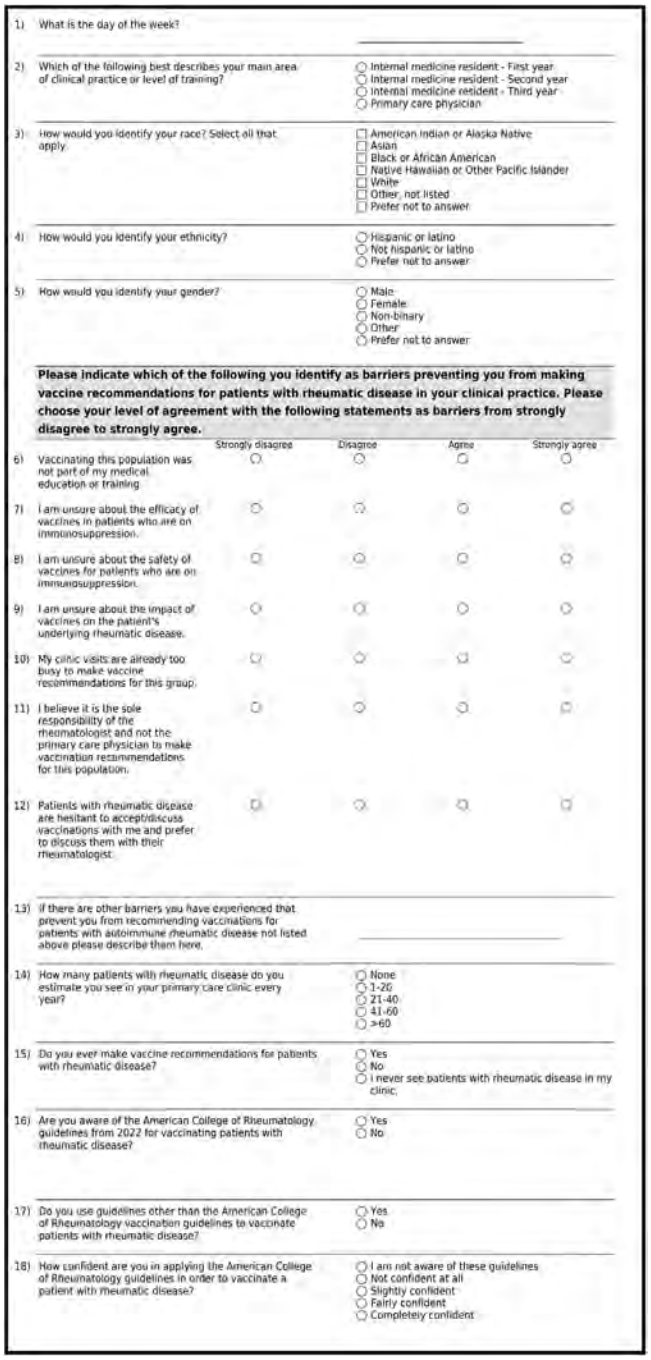
Julia Levy[1], Genna Braverman[1], Kirana Gudi[2] and Juliet Aizer[1], [1]Hospital for Special Surgery, New York, NY, [2]Weill Cornell, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Professional Education (0825–0830)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Despite increased risks of infection in patients with systemic autoimmune rheumatic disease (SARD), vaccination rates for this population are suboptimal. In 2023 the American College of Rheumatology (ACR) published guidelines on the use of vaccinations in patients with rheumatic and musculoskeletal diseases. Internists play a central

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



1) What is the day of the week? _____

2) Which of the following best describes your main area of clinical practice or level of training?
- ○ Internal medicine resident - First year
- ○ Internal medicine resident - Second year
- ○ Internal medicine resident - Third year
- ○ Primary care physician

3) How would you identify your race? Select all that apply.
- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ White
- ☐ Other, not listed
- ☐ Prefer not to answer

4) How would you identify your ethnicity?
- ○ Hispanic or latino
- ○ Not hispanic or latino
- ○ Prefer not to answer

5) How would you identify your gender?
- ○ Male
- ○ Female
- ○ Non-binary
- ○ Other
- ○ Prefer not to answer

Please indicate which of the following you identify as barriers preventing you from making vaccine recommendations for patients with rheumatic disease in your clinical practice. Please choose your level of agreement with the following statements as barriers from strongly disagree to strongly agree.

	Strongly disagree	Disagree	Agree	Strongly agree
6) Vaccinating this population was not part of my medical education or training	○	○	○	○
7) I am unsure about the efficacy of vaccines in patients who are on immunosuppression.	○	○	○	○
8) I am unsure about the safety of vaccines for patients who are on immunosuppression.	○	○	○	○
9) I am unsure about the impact of vaccines on the patient's underlying rheumatic disease.	○	○	○	○
10) My clinic visits are already too busy to make vaccine recommendations for this group.	○	○	○	○
11) I believe it is the sole responsibility of the rheumatologist and not the primary care physician to make vaccination recommendations for this population.	○	○	○	○
12) Patients with rheumatic disease are hesitant to accept/discuss vaccinations with me and prefer to discuss them with their rheumatologist	○	○	○	○

13) If there are other barriers you have experienced that prevent you from recommending vaccinations for patients with autoimmune rheumatic disease not listed above please describe them here. _____

14) How many patients with rheumatic disease do you estimate you see in your primary care clinic every year?
- ○ None
- ○ 1-20
- ○ 21-40
- ○ 41-60
- ○ >60

15) Do you ever make vaccine recommendations for patients with rheumatic disease?
- ○ Yes
- ○ No
- ○ I never see patients with rheumatic disease in my clinic.

16) Are you aware of the American College of Rheumatology guidelines from 2022 for vaccinating patients with rheumatic disease?
- ○ Yes
- ○ No

17) Do you use guidelines other than the American College of Rheumatology vaccination guidelines to vaccinate patients with rheumatic disease?
- ○ Yes
- ○ No

18) How confident are you in applying the American College of Rheumatology guidelines in order to vaccinate a patient with rheumatic disease?
- ○ I am not aware of these guidelines
- ○ Not confident at all
- ○ Slightly confident
- ○ Fairly confident
- ○ Completely confident

Figure 1. Needs assessment survey distributed to IM residents and faculty

role in engaging patients in shared decision-making on vaccination, yet the degree of guideline awareness and guideline-concordant practice among internal medicine (IM) trainees is unknown. We performed a needs assessment in an IM residency clinic to inform future educational interventions related to ACR vaccination guideline implementation.

Methods: We reviewed the literature on uptake of ACR vaccination guidelines in IM residency clinic, and barriers to vaccination. Based on barriers described in the literature for vaccinating patients with SARD, we designed an 18-item questionnaire (Figure 1) inquiring about attitudes toward vaccinating patients with SARD, ACR vaccination guideline awareness and barriers to implementation, as well as demographics. The questionnaire was distributed electronically via REDCap to all IM residents and faculty involved in outpatient clinic precepting in a large academic center between 12/2024 – 5/2025. Survey

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Barriers to providing vaccinations in IM residency clinic among residents and attendings.

Barrier	Number of Residents Who Agree (n=11)	Percent of Attendings Who Agree (n=13)
Responsibility of the rheumatologist	1 (9%)	1 (8%)
Clinic is too busy	5 (45%)	2 (15%)
Not part of education	8 (73%)	5 (38%)
Patient prefers conversation with rheumatologist	4 (36%)	6 (54%)
Aware of ACR guidelines (percent aware)	3 (27%)	3 (23%)

results were analyzed using descriptive statistics and differences between residents and faculty were examined with the Fisher exact test. The study was deemed exempt by the local Institutional Review Board.

Results: Survey responses were received from 13 out of 35 faculty (37%) and 11 out of 131 residents (8%). Among participants, 79% of faculty compared with 45% of residents reported they felt confident about their knowledge of vaccine efficacy, safety, and impact on disease (p=0.0035). Only 9% of residents and 8% of faculty felt that rheumatologists should be the sole provider of vaccinations for patients with SARD (Table 1). Only 45% of residents and 15% of faculty felt their clinic was too busy to provide vaccines for this population. A total of 73% of residents and 38% of faculty reported they did not receive training in this topic in their medical education. Only 27% of residents and 23% of faculty were aware of the ACR vaccination guidelines. Among residents, 64% reported making vaccination recommendations for this population in their clinic compared with 92% of faculty.

Conclusion: A majority of IM residents and precepting faculty participating in this single-center needs assessment reported making vaccine recommendations in clinic for their patients with SARD, and most respondents felt that vaccine guidance was a shared responsibility between rheumatologists and internists. However, over 70% were unaware of the ACR vaccination guidelines. A potential limitation of this study is the low response rate. These data help inform educational interventions to improve ACR vaccination guideline implementation by IM residents in this setting.

Disclosure: J. Levy: None; **G. Braverman**: None; **K. Gudi**: None; **J. Aizer**: None.

Abstract Number: 0828

Two Common AI Models Create Poor Rheumatology Board Style Questions

Catherine Deffendall[1], Narender Annapureddy[2], Kevin Byram[2], Erin Chew[2] and Tyler Reese[3], [1]Vanderbilt University, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Vanderbilt University Medical Center, Madison, TN

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Professional Education (0825–0830)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Rheumatology fellows frequently prepare for board examinations using case-based, multiple-choice questions. However, there are few resources with enough questions to prepare and those currently available can be costly. In this pilot study, we aim to evaluate if artificial intelligence (AI) generated questions are suitable for use.

Methods: We provided 5 identical prompts to the free versions of both Gemini and ChatGPT[1,2]. Each prompt requested one board style question using an uploaded PDF of ACR guidelines including glucocorticoid induced osteoporosis, vaccination, interstitial lung disease, rheumatoid arthritis and perioperative management. The following is an example of one such

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Average model performance of 5 questions evaluated by 3 Rheumatology Attendings

Question	Combined	Gemini	ChatGPT	p value
On a scale of 1-10 what is your overall rating of this question? (1-10)	5.5	5.72	5.28	0.94
Using Likert scale (1-5), mean				
• Is the question factually correct?	3.53	3.72	3.34	0.76
• Is there enough information provided in the question stem to answer the question?	4	3.92	4.08	1.0
• Is there redundant information in the question stem that could be eliminated? (reverse coded)	4.43	4.6	4.26	0.40
• Are all of the answers approximately the same length?	4.34	4.4	4.28	0.76
• Are the questions clinically relevant?	4.59	4.62	4.56	0.76
• Are the questions easy to understand?	4.5	4.68	4.32	0.21
• Do the wrong answer choices represent commonly mistaken choices in clinical practice?	3.87	3.86	3.88	0.92
• Is the question grammatically correct?	4.65	4.68	4.62	0.76
Is the question negatively worded? (Yes, the question is negatively worded or No, the question is positively worded)	100% No	100% No	100% No	
Compared to the similar question developed using a different model, which question do you prefer?	• 2 questions favored Gemini • 2 questions favored Chatgpt • 2 questions had no agreement*	—	—	

*One participant wrote in "Neither"

prompt, "Using the 2023 American College of Rheumatology clinical practice guidelines for Interstitial Lung Disease create one rheumatology board style question using reasonable alternatives as detractors". AI generated questions were arranged in two separate forms labeled Form 1 (Gemini) and Form 2 (ChatGPT) to blind the reviewer to which AI model created it. Ten rating metrics covering both accuracy and technical aspects of question writing were developed by an experienced question writer. Rating metrics included answer choices on a 5-point likert scale (ranging from strongly disagree to strongly agree) for 8 questions, yes/no choices for if the question was negatively worded, a 10-point scale for overall acceptability of the question and whether the Gemini or ChatGPT question was preferred. Three of the authors, who are board-certified rheumatologists engaged in medical education, independently rated questions on paper surveys. For each of the AI generated questions, the average rating metric of all three interviewers was calculated. This question average was used to calculate overall averages for each AI model. Assuming nonparametric data, Mann Whitney U was used to compare averages between models.

Results: Gemini and ChatGPT created 5 questions each with 4-5 answer choices per question. Attending rheumatologists rated these questions lowest on whether or not the question was factually correct (Combined 3.53 vs Gemini 3.72 vs ChatGPT 3.34) and if the wrong answer choices represented commonly mistaken choices in clinical practice (Combined 3.87 vs Gemini 3.86 vs ChatGPT 3.88). Technical aspects of question writing were the highest rated including if the question was negatively worded (100% No), and if the question was grammatically correct (Combined 4.65 vs Gemini 4.68 vs ChatGPT 4.62). The overall score out of 10 was low for both models (Combined 5.5 vs Gemini 5.72 vs open AI 5.28).

Conclusion: While both AI platforms created 10 grammatically correct board style questions and were rated highly on technical aspects of question writing, rheumatology attendings rated them poorly for correctness, relevant detractors and overall score. Learners should take caution when using AI to study by reviewing the original text or having experts assess questions for accuracy and validity. Improvements could be made with refining prompts and iterative modifications to the questions, however, that was not pursued in the current study.

Disclosure: C. Deffendall: None; **N. Annapureddy**: AstraZeneca, 1, GlaxoSmithKlein(GSK), 2; **K. Byram**: None; **E. Chew**: None; **T. Reese**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0829

Multi-Center Use of an Online Case-Based Simulation to Evaluate Medical Trainee Use of Diagnostic Imaging and Lab Tests to Correctly Diagnose MSK Complaints

James McCarthey[1], Kyla Driest[2], erin frank[1], Allayne Stephans[1], Stacey Tarvin[3] and Angela Robinson[4], [1]Rainbow Babies and Children's Hospital, Cleveland, OH, [2]Nationwide Children's Hospital, Columbus, OH, [3]Riley Hospital for Children at Indiana University, Indianapolis, IN, [4]Cleveland Clinic Foundation, Cleveland, OH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Professional Education (0825–0830)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Our goal is to teach medical trainees high value care concepts and musculoskeletal (MSK) disease states and then implement online case-based simulations to evaluate trainee utilization of laboratory tests and imaging to make diagnoses.

Methods: We recruited pediatric trainees from 4 institutions to participate in this simulation. Learners listened to a lecture on either pediatric MSK complaints or high value care. Participants were then asked to complete an online simulation that presented six vignettes of pediatric MSK complaints and prompted them to select diagnostic tests. The presented cases included rheumatic fever, Lyme arthritis, transient synovitis, Osgood-Schlatter's Disease, juvenile ankylosing spondylitis, and benign nocturnal limb pains of childhood. We analyzed trainee ability to identify the correct diagnosis from the available clinical information compared to pattern of diagnostic evaluation. In addition, we analyzed how exposure to high value care principles affected their likelihood of ordering diagnostic tests. We conducted an exploratory analysis using Student's t-test for comparison of groups, with p-values less than 0.05 judged as statistically significant.

Results: Within the study, 160 trainees started and completed the first case, 90 completed all cases, and 87 completed all cases and the post-simulation survey. 32 received a lecture on high value care (HVC) and 55 received a lecture on pediatric MSK complaints. 41% of trainees selected the correct diagnosis in the rheumatic fever vignette, 47% in the Lyme arthritis vignette, 77% in transient synovitis, 95% in Osgood-Schlatter's disease, 69% in juvenile ankylosing spondylitis, and 92%

Table. Rate of ANA ordering and reaching correct diagnosis and ANA ordering rate between HVC and MSK lecture exposure

Case	ANA ordered (n, %)	ANA ordered and correct dx	ANA not ordered and correct dx	P-value	ANA ordered with HVC* lecture	ANA ordered with MSK** lecture	P-value
1. Rheumatic fever	69/160 (43%)	39%	42%	P = 0.74	21%	51%	p <0.01
2. Lyme disease	20/134 (15%)	60%	45%	P = 0.21	4%	22%	p <0.01
3. Transient Synovitis	8/118 (7%)	63%	78%	P = 0.31	3%	7%	p = 0.14
4. Osgood Schlatter's	7/102 (7%)	71%	97%	P <0.01	1%	9%	p < 0.01
5. Juvenile Ankylosing spondylitis	46/93 (49%)	61%	77%	p = 0.10	10%	59%	p < 0.01
6. Nocturnal growing pains	5/90 (6%)	60%	94%	p < 0.01	2%	5%	p = 0.24

Table 1. Data of ordered ANA with correct diagnosis and ordering of ANA with exposure to HVC vs MSK simulation exposure. p<0.05 is statistically significant *: High Value Care **: Musculoskeletal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

in growing pains. Among the six cases, antinuclear antibody (ANA) levels were ordered 6 to 49% of the time per vignette (see Table). Ordering an ANA level was associated with a decreased likelihood of selecting the correct diagnosis in Osgood-Schlatter's disease (71 versus 97%, $p < 0.01$) and growing pains (60 versus 94%, $p < 0.01$). For each of the six cases results from ANA ordering was not associated with increases in selecting the correct diagnosis. In all six cases, trainees were less likely to request ANA levels if they were exposed to an HVC lecture prior to simulation, and this was statistically significant in 4 out of 6 vignettes.

Conclusion: Overall, trainees tended to order ANA more frequently in cases with higher diagnostic uncertainty and lower likelihood of selecting the correct diagnosis. Despite this, ordering an ANA had no significant difference on the trainee reaching the correct diagnosis. For the Osgood Schlatter's and growing pains vignettes, there was a higher ratio of correct trainees who did not order an ANA, suggesting that ANA was only ordered if the trainee was uncertain. For test ordering, exposure to lectures on MSK pain in children was associated with increased lab and imaging orders, but exposure to HVC concepts was associated with decreases in testing. In summary, this research is important to share as it provides valuable insights for bettering diagnostic practices among trainees, which ultimately could lead to improved healthcare outcomes for children with MSK disease.

Disclosure: J. McCarthey: None; **K. Driest**: None; **e. frank**: None; **A. Stephans**: None; **S. Tarvin**: AbbVie/Abbott, 5, American Academy of Pediatrics, 12, Editor, Amgen, 5, Childhood Arthritis Rheumatology Research Alliance, 5, Roche, 5, UCB, 5; **A. Robinson**: None.

Abstract Number: 0830

Rheum2Listen: Leveraging Podcasts to Teach Rheumatology to Internal Medical Residents

Nikita Ivanov[1], Beeta Shasti-Nazem[2], Moriah Gottman[1] and Sonam Kiwalkar[3], [1]Legacy Emanuel Internal Medicine Residency Program, Portland, OR, [2]Legacy Salmon Creek Internal Medicine Residency Program, Vancouver, WA, [3]The Vancouver Clinic, Portland, OR

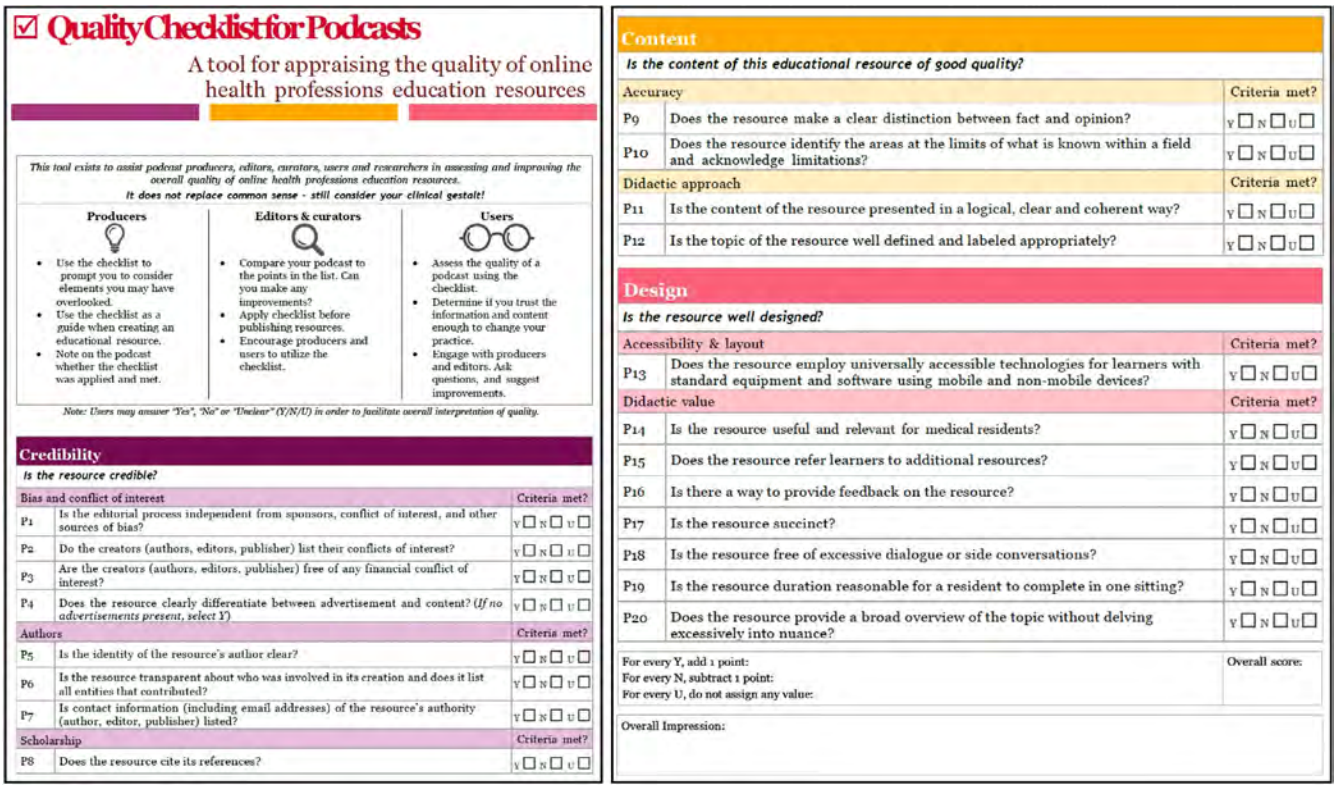
SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Professional Education (0825–0830)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Podcasts are an increasingly popular tool in medical education, shown to match or exceed traditional lectures in short term retention and learner satisfaction. Despite abundant high-quality rheumatology content, no structured podcast-based curriculum exists for internal medicine (IM) residents. This shortfall is noteworthy as rheumatology consistently emerges as one of the weakest areas of knowledge among IM residents. While podcasts are a flexible and engaging learning tool, passive listening alone may limit deeper understanding and long-term retention of key concepts. To address this, we developed a structured rheumatology curriculum that combines high-quality podcasts with active learning worksheets. This dual approach aims to foster greater engagement and enhance durable retention of rheumatology concepts among IM residents.

Methods: Curriculum development was guided by Kern's Six-Step Approach (**Figure 1)**. A targeted literature review conducted by one IM resident and one rheumatologist identified key rheumatology topics for IM residents based on four criteria: poor performance on standardized exams, low self-reported confidence among trainees, perceived importance by rheumatologists, and frequency of rheumatology consultations. These high-yield topics were queried in *Listen Notes*, a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Curriculum development guided by Kern's Six-Step Approach.



☑ Quality Checklist for Podcasts

A tool for appraising the quality of online health professions education resources

This tool exists to assist podcast producers, editors, curators, users and researchers in assessing and improving the overall quality of online health professions education resources.
It does not replace common sense - still consider your clinical gestalt!

Producers
- Use the checklist to prompt you to consider elements you may have overlooked.
- Use the checklist as a guide when creating an educational resource.
- Note on the podcast whether the checklist was applied and met.

Editors & curators
- Compare your podcast to the points in the list. Can you make any improvements?
- Apply checklist before publishing resources.
- Encourage producers and users to utilize the checklist.

Users
- Assess the quality of a podcast using the checklist.
- Determine if you trust the information and content enough to change your practice.
- Engage with producers and editors. Ask questions, and suggest improvements.

Note: Users may answer "Yes", "No" or "Unclear" (Y/N/U) in order to facilitate overall interpretation of quality.

Credibility

Is the resource credible?

	Bias and conflict of interest	Criteria met?
P1	Is the editorial process independent from sponsors, conflict of interest, and other sources of bias?	Y☐ N☐ U☐
P2	Do the creators (authors, editors, publisher) list their conflicts of interest?	Y☐ N☐ U☐
P3	Are the creators (authors, editors, publisher) free of any financial conflict of interest?	Y☐ N☐ U☐
P4	Does the resource clearly differentiate between advertisement and content? (*If no advertisements present, select Y*)	Y☐ N☐ U☐
	Authors	**Criteria met?**
P5	Is the identity of the resource's author clear?	Y☐ N☐ U☐
P6	Is the resource transparent about who was involved in its creation and does it list all entities that contributed?	Y☐ N☐ U☐
P7	Is contact information (including email addresses) of the resource's authority (author, editor, publisher) listed?	Y☐ N☐ U☐
	Scholarship	**Criteria met?**
P8	Does the resource cite its references?	Y☐ N☐ U☐

Content

Is the content of this educational resource of good quality?

	Accuracy	Criteria met?
P9	Does the resource make a clear distinction between fact and opinion?	Y☐ N☐ U☐
P10	Does the resource identify the areas at the limits of what is known within a field and acknowledge limitations?	Y☐ N☐ U☐
	Didactic approach	**Criteria met?**
P11	Is the content of the resource presented in a logical, clear and coherent way?	Y☐ N☐ U☐
P12	Is the topic of the resource well defined and labeled appropriately?	Y☐ N☐ U☐

Design

Is the resource well designed?

	Accessibility & layout	Criteria met?
P13	Does the resource employ universally accessible technologies for learners with standard equipment and software using mobile and non-mobile devices?	Y☐ N☐ U☐
	Didactic value	**Criteria met?**
P14	Is the resource useful and relevant for medical residents?	Y☐ N☐ U☐
P15	Does the resource refer learners to additional resources?	Y☐ N☐ U☐
P16	Is there a way to provide feedback on the resource?	Y☐ N☐ U☐
P17	Is the resource succinct?	Y☐ N☐ U☐
P18	Is the resource free of excessive dialogue or side conversations?	Y☐ N☐ U☐
P19	Is the resource duration reasonable for a resident to complete in one sitting?	Y☐ N☐ U☐
P20	Does the resource provide a broad overview of the topic without delving excessively into nuance?	Y☐ N☐ U☐

For every Y, add 1 point:
For every N, subtract 1 point:
For every U, do not assign any value:

Overall score:

Overall Impression:

Figure 2. "The Quality Checklist for Health Professions Blogs and Podcasts." Modified from Colmers et al., The Winnower, 2015, 2: e144720.08769.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

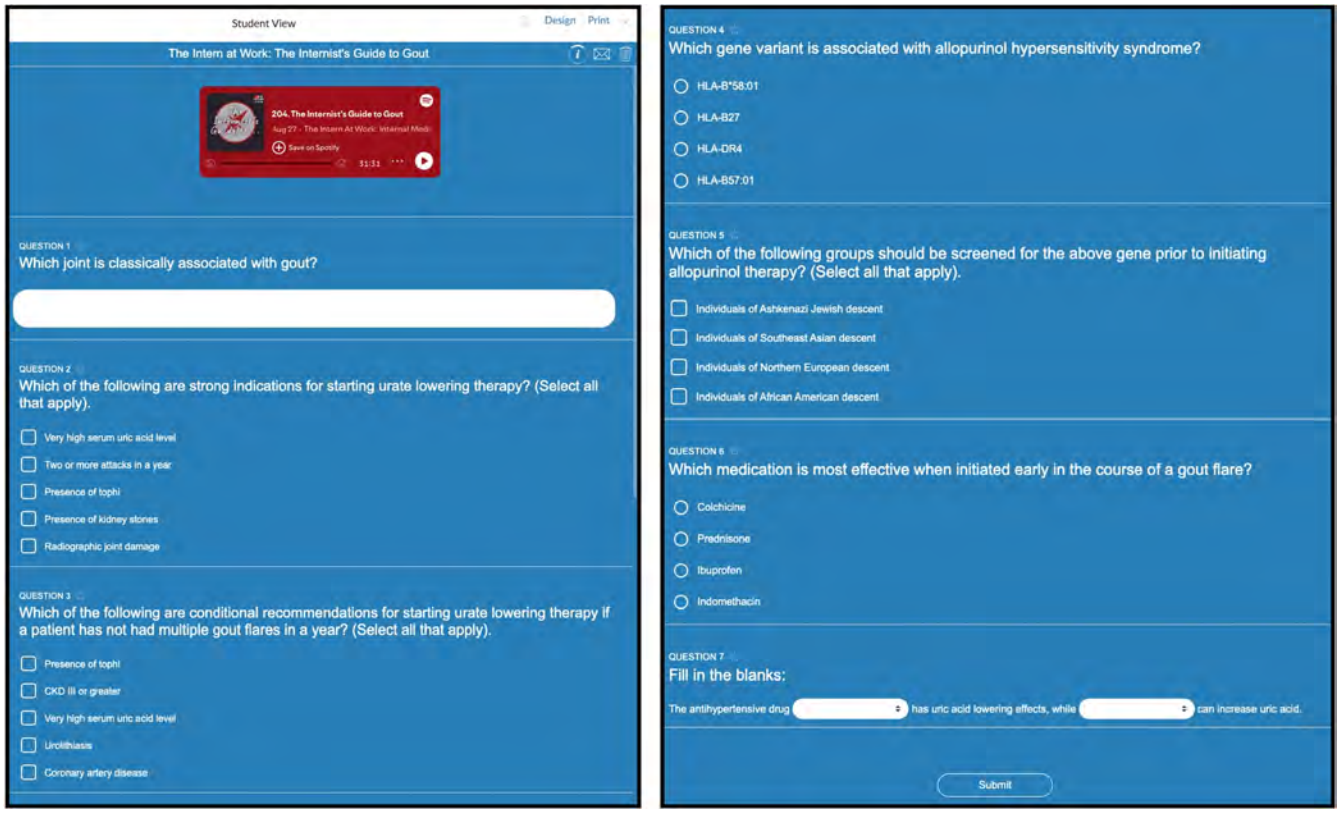


Figure 3. Example of an online quiz with embedded podcast episode.

comprehensive podcast database. Podcasts affiliated with an academic institution and targeting a generalist physician audience were prioritized. Additional episodes were identified through manual screening of titles and show notes from reputable independent podcasts. Three IM residents independently assessed each episode using a modified, validated rubric "The Quality Checklist for Health Professions Blogs and Podcasts," evaluating quality, accuracy, and educational relevance with a scoring system (**Figure 2**). Top episodes were selected based on average scores, score variability, succinctness, and alignment with the target audience. Using backward design, an accompanying online worksheet was developed to encourage active learning. This incorporated multiple-choice, short-answer, and fill-in-the-blank questions (**Figure 3**).

Results: Nine core topics were included in the final curriculum: gout, osteoarthritis, rheumatoid arthritis, spondyloarthritis, lupus, fibromyalgia, vasculitis, rheumatologic lab interpretation, and approach to joint pain. From an initial pool of 25 to 300 episodes per topic, 30 underwent evaluation using the rubric **(Figure 2)** and 12 were selected for inclusion in the study.

Conclusion: A structured, podcast-based rheumatology curriculum has been developed for IM residents, integrating high-quality curated episodes with active learning worksheets. This dual approach is designed to increase engagement and promote long-term retention of core rheumatology concepts. The curriculum is currently being piloted with IM residents, with plans for future refinement and expansion to other institutions.

Disclosure: N. Ivanov: None; **B. Shasti-Nazem**: None; **M. Gottman**: None; **S. Kiwalkar**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0831

Altered Expression of cd11c and HLA-DR on Monocyte Subsets in Individuals at Risk of Rheumatoid and Psoriatic Arthritis

Klára Prajzlerová[1], Olga Kryštůfková[2], Hana Hulejová[1], Nora Růžičková[2], Petra Hánová[1], Jiri Vencovsky[3], Ladislav Šenolt[2], Jiří Štolfa[2] and Mária Filková[2], [1]Institute of Rheumatology, Prague, Czech Republic, [2]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [3]Institute of Rheumatology, Praha 8, Czech Republic

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction) (0831–0836)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Preclinical phases of rheumatoid arthritis (RA), including therapeutic interventions, have been extensively studied. There is a growing focus on individuals at risk for psoriatic arthritis (PsA). We previously observed changes in monocyte subsets in the peripheral blood of individuals at risk for RA. CD11c and HLA-DR reflects monocyte activation and both are involved in inflammatory autoimmune disease mechanisms. The objective of this study was to evaluate their expression on subsets of monocytes in individuals at risk of RA and PsA.

Methods: The study included 284 individuals at risk of RA (having arthralgia with either ACPA positivity and/or meeting EULAR criteria for clinically suspect arthralgia), 37 individuals at risk of PsA (identified via PEST questionnaire and considered at risk based on psoriasis severity) and 57 ACPA-negative healthy controls (HC). All at-risk individuals had no arthritis on the examination of 66 joints at baseline. Peripheral blood samples were analyzed by flow cytometry. Monocytes were categorized into classical (CD14++CD16–), intermediate (CD14++CD16+/++), or nonclassical (CD14–/+CD16++) subsets. The membrane expression of CD11c and HLA-DR was quantified in each subset as median fluorescence intensity. Data were analyzed using the Mann-Whitney test and Kruskal-Wallis test with Dunn's post-hoc test.

Results: Of the 284 individuals at risk of RA, 52 developed clinical arthritis (progressors) within a median of 9 months of follow-up and after 30.5 months of symptoms duration. Of the remaining individuals without arthritis, the 217 with a symptoms duration longer than 12 months were classified as non-progressors. Among the 37 individuals at risk of PsA (PSA-risk), only 1 progressed to PsA within 7 months of follow-up and after 44 months of symptom duration. There were no significant differences in CD11c or HLA-DR expression between RA progressors and non-progressors in any of the monocyte subsets. However, compared to PsA-risk and HC, individuals at risk of RA (RA-risk) had significantly lower expression of CD11c in all monocyte subsets, regardless of progression to arthritis or ACPA status. PsA-risk individuals showed a trend to higher CD11c expression on classical and nonclassical monocytes compared to HC. Conversely, HLA-DR expression on these monocyte subsets was significantly higher in RA-risk compared to PsA-risk individuals, with a trend towards higher expression on intermediate monocytes. HLA-DR expression was lower in all monocyte subsets in PsA-risk individuals compared to HC.

Conclusion: Individuals at risk of RA exhibit lower expression of the pro-inflammatory integrin CD11c and higher expression of major histocompatibility complex HLA-DR in monocytes compared to individuals at risk of PsA. These findings suggest distinct immune activation mechanisms in RA and PsA, with elevated CD11c expression in PsA-risk individuals potentially reflecting ongoing innate inflammatory responses in the skin, while increased HLA-DR expression in RA-risk individuals may indicate adaptive immune responses involved in RA pathogenesis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Acknowledgements: NU22-05-00226, MHCR-023728, SVV-260638

Disclosure: K. Prajzlerová: None; **O. Kryštůfková**: None; **H. Hulejová**: None; **N. Růžičková**: None; **P. Hánová**: None; **J. Vencovsky**: None; **L. Šenolt**: None; **J. Štolfa**: None; **M. Filková**: None.

Abstract Number: 0832

Elevated serum peptidylarginine deiminase 4 (PAD4) levels in anti-CCP antibody positive at-risk individuals with arthralgia who progress to rheumatoid arthritis.

Sana Sharrack[1], Xia Yu[2], Arun Jayaraman[3], Laurence Duquenne[4], Andrea Di Matteo[5], Kate Harnden[5], Lucy Thornton[5], Helen Jayne-Sugden[5], Jacqueline Nam[6], Adam Smith[5], Mia Collins[7], Rachel Sparks[3], Fanyi Jiang[8], Kyriakos Konstantinidis[9], Jessica Neisen[10], Greet De Baets[10], David Close[11], Chris chamberlain[10], Adam Platt[12], Paul Emery[13], Josie Meade[2] and Kulveer Mankia[13], [1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, Sheffield, United Kingdom, [2]Division of Oral Biology, School of Dentistry, University of Leeds, Leeds, United Kingdom, Leeds, United Kingdom, [3]AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology (R&I), BioPharmaceuticals R&D, Gaithersburg, Maryland, United States of America, Gaithersburg, Maryland, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, United Kingdom, Leeds, United Kingdom, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, Leeds, United Kingdom, [6]Leeds Teaching Hospitals NHS Trust, Leeds, England, United Kingdom, [7]AstraZeneca, Gothenburg, Sweden, [8]AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology (R&I), BioPharmaceuticals R&D, Gothenburg, Sweden, Gothenburg, Sweden, [9]AstraZeneca, R&I Projects, Research and Early Development, Respiratory and Immunology (R&I), BioPharmaceuticals R&D, Cambridge, United Kingdom, Cambridge, United Kingdom, [10]AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology (R&I), BioPharmaceuticals R&D, Cambridge, United Kingdom, Cambridge, United Kingdom, [11]AstraZeneca, Royston, United Kingdom, [12]AstraZeneca, Translational Science and Experimental Medicine, Research and Early Development, Respiratory and Immunology (R&I), BioPharmaceuticals R&D, Cambridge, United Kingdom, Melbourn, Royston, United Kingdom, [13]University of Leeds, Leeds, England, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction) (0831–0836)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Anti-Cyclic Citrullinated Peptide (anti-CCP) antibodies are one of the strongest risk factors for the development of rheumatoid arthritis (RA). Anti-CCP antibodies are generated against citrullinated proteins, which arise when peptidylarginine deiminases (PADs) make post-translational modifications to proteins by the deamination of arginine residues to citrulline. PAD2 and PAD4 isomer expression is associated with RA and serum anti-PAD4 antibodies are strongly associated with anti-CCP antibody positivity and aggressive disease phenotype. However, the specific role of serum PAD4 in anti-CCP antibody positive (CCP+) at-risk individuals who do not have synovitis, and its relationship with arthritis development, is unclear.

Our objectives were to (i) investigate baseline serum PAD2/4 levels in CCP+ at-risk individuals with musculoskeletal symptoms but no synovitis, compared with CCP+ early RA patients and healthy controls and (ii) to investigate the relationship between serum PAD2/4 levels and future arthritis development.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 – Comparison of demographic, clinical and biomarker data between the three patient groups. aANOVA test b Fisher's Exact Test c t-test d Wilcoxon rank sum test. Definitions: EMS: Early morning stiffness; CCP titre: 2nd generation anti-Cyclic Citrullinated Peptide antibody titre; PAD2: peptidylarginine deiminase 2; PAD4: peptidylarginine deiminase 4; F: Female; M: Male.

Variable	Healthy controls, n=44	CCP +ve at-risk, n=79 (includes CCP+ at-risk non-progressors (n=29) and CCP+ at-risk future progressors (n=50))	Early RA, n=34	p values, statistically significant values in bold.
Age (mean, SD)	47.18 ± 13.6, 4 individuals unknown [43.0-51.3]	50.71 ± 15.4 [47.3-54.2]	53.53 ± 15.8 [48.00-59.00]	Healthy control vs CCP +ve at-risk: 0.425[a] CCP +ve at-risk vs Early RA: 0.631[a] Healthy control vs Early RA: 0.156[a]
Sex (F)	24 (54.5%) (4 unknown)	51 (64.6%)	24 (70.6%)	0.051[b]
Smoking status (never, ever smoker)	ever smoker: 19; never: 18; unknown: 7	ever smoker: 52; never: 23; unknown: 4	ever smoker: 21; never: 11; unknown: 2	0.100[b]
Anti-CCP level	N/A	273.56 ± 59.3	235.75 ± 108	0.062[c]
EMS duration (mins)	N/A	98.4 ± 136	80.1 ± 80.1	0.494[d]
PAD2 level (mean (ng/mL), SD)	3.97 ± 6.13	6.82 ± 14.6 CCP+ at-risk future non-progressor: 4.47 ± 8.49 CCP+ at-risk future progressor: 8.18 ± 17.1	10.9 ± 33.6	Healthy control vs CCP +ve at-risk: 0.614[d] CCP +ve at-risk vs Early RA: 0.330[d] Healthy control vs Early RA: 0.528[d]
PAD4 level (mean (ng/mL), SD)	13.3 ± 18.1	31.7 ± 49.2 CCP+ at-risk future non-progressor: 13.3 ± 14.3 CCP+ at-risk future progressor: 42.4 ± 58.4	46.5 ± 69.9	Healthy control vs CCP +ve at-risk: 0.084[d] CCP +ve at-risk vs Early RA: 0.243[d] **Healthy control vs Early RA: 0.00922[d]**

Methods: Stored serum samples were selected from the Leeds CCP study. We selected: (i) CCP+ at-risk individuals with high anti-CCP antibody levels (>100 U/ml) and Early Morning Stiffness (EMS) lasting ≥30 minutes (n=79) (ii) early, treatment-naïve RA patients (n=34) and (iii) asymptomatic healthy controls (n=44). Follow-up data was collated for all CCP + at-risk individuals to determine future arthritis progression status. PAD2/4 levels were assayed via Enzyme-linked Immunosorbent Assay (ELISA), performed in triplicate, following manufacturer's instructions, Cayman Chemicals PAD2 (Item No. 501450) and PAD4 (Item No. 501460). All results were analysed using R (version 4.3.1).

Results: All groups were balanced for age, sex and smoking status (Table 1). Anti-CCP antibody levels and duration of EMS were similar for CCP+ at-risk individuals and early RA patients (Table 1). PAD4 but not PAD2 levels were higher in early RA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

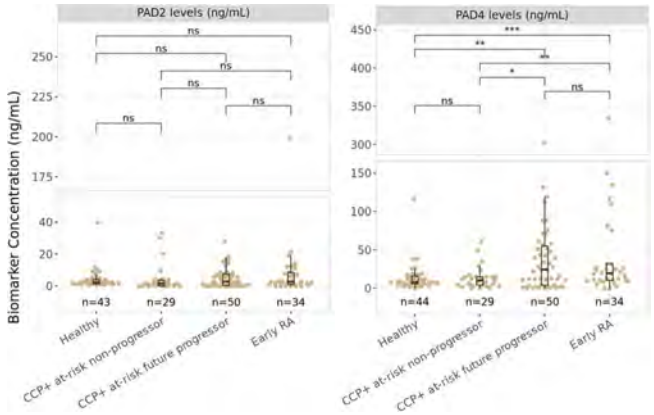


Figure 1 – PAD2 and PAD4 levels according to patient group. Plot completed via Wilcoxon rank sum test with no additional covariate adjustments. Definitions: ns: no statistical significance; * statistical significance at p<0.05; **: statistical significance at p<0.01; ***: statistical significance at p<0.001.

patients compared with healthy controls (p=0.00922). There was no statistically significant difference in PAD4 levels between CCP+ at-risk individuals and healthy controls (p=0.084). However, when CCP+ at-risk individuals were separated according to future arthritis progression status, a significant increase in PAD4 levels in future progressors (n=50) compared to both future non-progressors (n=29) (p=0.022) and healthy controls (p=0.01) was observed (Figure 1). PAD4 levels were similar in healthy controls and future non-progressors (p=0.888) as well as in future progressors and early RA patients (p=0.975). There was no statistically significant difference in PAD2 levels between any of the groups.

Conclusion: These data suggest serum PAD4 levels are increased in CCP+ at-risk individuals who progress to RA compared with CCP+ future non-progressors and healthy controls. Serum PAD4 levels are also similar in Pre-RA and RA. PAD4 levels may therefore have utility in predicting arthritis development and PAD4 may also be a potential therapeutic target for arthritis prevention in those at high risk.

Disclosure: S. Sharrack: None; **X. Yu**: None; **A. Jayaraman**: AstraZeneca, 3; **L. Duquenne**: None; **A. Di Matteo**: None; **K. Harnden**: None; **L. Thornton**: None; **H. Jayne-Sugden**: None; **J. Nam**: None; **A. Smith**: None; **M. Collins**: AstraZeneca, 3; **R. Sparks**: AstraZeneca, 3; **F. Jiang**: AstraZeneca, 3; **K. Konstantinidis**: AstraZeneca, 3; **J. Neisen**: AstraZeneca, 3; **G. De Baets**: AstraZeneca, 3; **D. Close**: AstraZeneca, 3; **C. chamberlain**: AstraZeneca, 3, 12, Chris Chamberlain has been a full time employee of Roche, UCB and Merck KGaA in addition to AZ.; **A. Platt**: AstraZeneca, 3; **P. Emery**: Abbvie, 1, Activa, 1, Anaptysbio, 1, Astra-Zeneca, 1, BMS, 1, Boehringer Ingelheim, 1, Galapagos, 1, Gedeon Richter, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, Novartis, 1; **J. Meade**: None; **K. Mankia**: AbbVie, 2, 6, ALLin Bio, 2, 6, AstraZeneca, 2, 5, 6, Bristol-Myers Squibb(BMS), 5, Deepcure, 2, 5, 6, Galapagos, 2, 5, Gilead, 5, Lilly, 2, 5, 6, Serac Healthcare, 2, 5, 6, UCB, 2, 6, Zura Bio, 2, 6.

Abstract Number: 0833

Sputum Anti-CCP-IgA and NET-Associated Proteins Predict Risk and Timing of the Transition From Systemic Autoimmunity to Classified RA

Timothy Wilson[1], Claudia Lugo[2], Marie Feser[3], Mark Gillespie[4], Troy Torgerson[5], Gary Firestein[6], V. Michael Holers[7], Kevin Deane[8] and Kristen Demoruelle[9], [1]Thomas Jefferson University, Philadelphia, PA, [2]University of Colorado, Denver, CO, [3]University of Colorado Anschutz Medical Campus, Aurora, CO, [4]Allen Institute for Immunology, Seattle, WA, [5]Allen Institute for Immunology, Enumclaw, WA, [6]University of California, San Diego, San Diego, CA, [7]University of Colorado Anschutz Medical Campus, Aurora, [8]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [9]University of Colorado Anschutz Medical Campus, Golden, CO

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction) (0831–0836)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: The presence of serum anti-CCP-IgG antibodies can predict the future development of clinically evident RA. Neutrophil extracellular trap (NET) formation can be a source of extracellular citrullinated (cit) proteins that can be antigenic targets of anti-CCP. Our group previously reported increased NET formation of sputum neutrophils from the lungs of individuals with RA and at-risk for RA that correlated with sputum anti-CCP levels. The objective of this study was to evaluate the relationship between sputum anti-CCP, sputum NET-associated proteins, and the risk and timing of transitions from an 'at-risk' state of systemic autoimmunity to clinical RA.

Methods: We included 98 individuals who were serum anti-CCP-IgG(+) (CCP3, Werfen), without examination evidence of inflammatory arthritis (IA) at baseline, had at least one follow-up visit with a joint examination, and had a baseline induced sputum sample. Nineteen individuals (19.4%) met 2010 ACR/EULAR classification criteria for RA (Classified RA) and 71 (72.4%) did not develop RA after at least 12 months of follow-up. There were 8 individuals who developed unclassifiable IA and were excluded from this analysis. Baseline sputum cell-free supernatant was tested by ELISA for anti-CCP-IgG (CCP3) and anti-CCP-IgA (CCP3.1 plate with research modification to detect IgA only). In a subset with adequate sample remaining, sputum supernatant was tested by immunoassays for NET-associated proteins, including calprotectin (Werfen), extracellular DNA (exDNA, Invitrogen), extracellular neutrophil elastase (exNE, Invitrogen), nucleosomes (Nu.Q H3.1, Volition) and cit-nucleosomes (Nu.Q H3R8Cit, Volition).

Results: Baseline sputum anti-CCP levels were higher in individuals who later transitioned to Classified RA compared to those who did not develop RA (anti-CCP-IgA, p< 0.001; anti-CCP-IgG, p=0.003, Table 1, Figure 1A-B). Sputum nucleosome and cit-nucleosome levels were also higher in individuals who transitioned to RA (Table 1, Figure 1C-D), but were not independently associated after adjusting for sputum anti-CCP-IgA level. Within individuals who transitioned to RA, sputum calprotectin and exNE levels correlated with time to RA onset (Figure 2A-B), with lower levels in those who developed

Table 1. Baseline clinical features, serologic biomarkers and sputum biomarkers associated with developing Classified RA in serum anti-CCP-IgG positive individuals

	Did not develop RA (N=71)	Developed Classified RA (N=19)	p-value
Clinical Features			
Age, in years	62 (46-70)	57 (44-65)	0.360
Female	53 (74.6)	15 (78.9)	1.000
Ever smoker	23 (32.4)	4 (21.1)	0.453
Chronic lung disease	5 (7.0)	3 (15.8)	0.360
Serologic Biomarkers			
≥ 1 shared epitope allele[1]	30 (44.8)	12 (63.2)	0.157
Serum anti-CCP-IgG level, in ELISA units	43.1 (28.2-85.1)	163.3 (48.3-870.4)	**<0.001**
Serum RF-IgM or RF-IgA+	20 (28.2)	13 (68.4)	**0.001**
Plasma calprotectin, in ug/mL	1.0 (0.8-1.6)	1.4 (0.9-1.7)	0.110
Sputum Biomarkers[2]			
Sputum anti-CCP-IgA level	21.6 (15.6-34.9)	52.9 (26.3-172.4)	**<0.001**[3]
Sputum anti-CCP-IgG level	18.0 (18.0-18.0)	18.0 (18.0-95.8)	**0.003**
Sputum calprotectin, in ug/mL[4]	47.2 (21.0-93.4)	44.5 (28.4-127.3)	0.477
Sputum exDNA[4]	1,543.8 (604.3-3,069.9)	1,778.7 (696.9-4,184.3)	0.620
Sputum exNE[4]	1,461.9 (835.2-3,150.4)	3,335.9 (788.9-7,529.9)	0.125
Sputum nucleosomes, in ng/mL[5]	157.2 (0.0-574.8)	530.5 (185.6-3,626.5)	**0.023**
Sputum citrullinated nucleosomes, in ng/mL[5]	43.1 (12.8-72.7)	106.4 (34.4-770.6)	**0.046**

All values are median (IQR) or N (%)

1. SE testing was available for all 19 who developed RA and 67 of 71 who did not develop RA.
2. All met the definition for adequate sputum sample (i.e. <80% squamous epithelial cells on cell differential)
3. Sputum anti-CCP-IgA level remained significantly associated with development of RA after adjusting for serum anti-CCP level and serum RF positivity (p=0.006)
4. Sputum calprotectin, exDNA and exNE levels were available in 17 who developed RA and 66 who did not develop RA
5. Sputum nucleosome levels were available in 14 who developed RA and 64 who did not develop RA. sputum cit-nucleosomes levels were available in 12 who developed RA and 63 who did not develop RA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

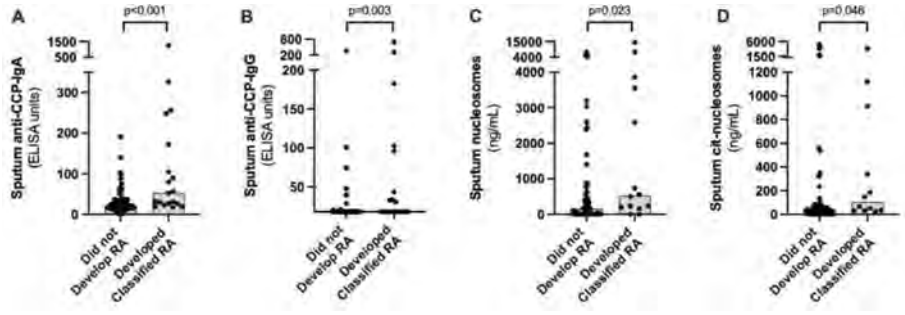


Figure 1. Sputum anti-CCP and nucleosome levels in individuals at-risk for RA. The figure depicts baseline sputum anti-CCP-IgA (Panel A), sputum anti-CCP-IgG, (Panel B), sputum nucleosome (Panel C) and sputum citrullinated nucleosome (cit-nucleosome, Panel D) in serum anti-CCP-IgG positive individuals who did vs. did not develop Classified RA during follow-up. P-values calculated by Wilcoxon rank sum test.

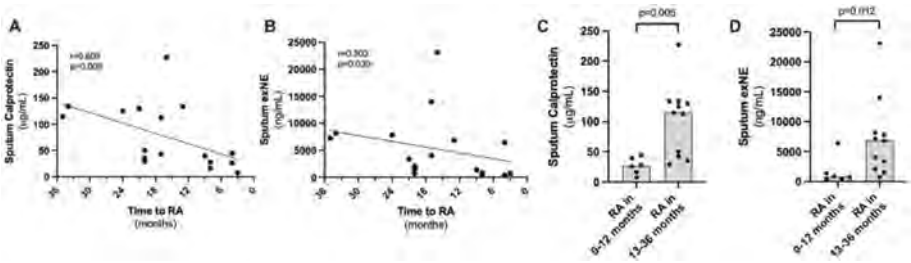


Figure 2. Sputum calprotectin and extracellular neutrophil elastase (exNE) levels associated with timing of RA onset. In serum anti-CCP-IgG positive individuals who developed Classified RA within 36 months of follow-up, the figure depicts correlations between time to RA onset (in months from baseline visit) and baseline sputum calprotectin (Panels A) or sputum exNE (Panels B). P-values by Spearman's correlation. Baseline sputum calprotectin (Panel C) and sputum exNE (Panel D) levels are compared between individuals who developed Classified RA in 0-12 months vs. 13-36 months after baseline sputum. P-values calculated by Wilcoxon rank sum test.

RA within 12 months (Figure 2C-D). Sputum anti-CCP-IgA, exDNA, nucleosome, and cit-nucleosome and plasma calprotectin levels did not correlate with time to RA onset (p >0.05).

Conclusion: We found that anti-CCP and NET-associated nucleosomes in the sputum are increased in serum anti-CCP3+ individuals who transitioned to Classified RA. Sputum NET-associated proteins calprotectin and exNE correlated with time to RA onset, though surprisingly were lower in the 12 months preceding RA onset. These data support an important role of lung immunobiology and NETosis in transitions from systemic autoimmunity to RA and identify sputum biomarkers that can enhance prediction and timing of RA. Longitudinal studies are needed to determine whether decreasing sputum calprotectin and exNE levels result from enhanced local clearance and whether this process plays a role in imminent RA onset.

Disclosure: T. Wilson: None; **C. Lugo**: None; **M. Feser**: None; **M. Gillespie**: Novo Nordisk, 11, Omeros, 11; **T. Torgerson**: Eli Lilly, 2, Pharming Healthcare, 2, Takeda, 2; **G. Firestein**: Eli Lilly, 5; **V. Holers**: Q32 Bio, 12, 2; **K. Deane**: Inova Diagnostics, 1; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0834

Heterogeneity in the Association of Genetic Risk for Rheumatoid Arthritis and Resultant Rheumatoid Arthritis Phenotypes

Thomas Riley[1], Austin Wheeler[2], Bryant England[2], Grant Cannon[3], Brian Sauer[4], Gary Kunkel[5], Katherine Wysham[6], Beth Wallace[7], Paul Monach[8], Andreas Reimold[9], Gail Kerr[10], Isaac Smith[11], John Richards[12], Iris Lee[13], Geoffrey Thiele[2], Rui Xiao[1], Scott Damrauer[14], Michael Levin[14], Michael George[1], Ted Mikuls[2] and Joshua Baker[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Utah and Salt Lake City VA, Salt Lake City, UT, [4]Salt Lake City VA/University of Utah, Salt Lake City, UT, [5]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [6]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [7]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [8]VA Boston Healthcare System, Boston, MA, [9]Dallas VA Medical Center, Dallas, TX, [10]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [11]Duke University Hospital, Durham, NC, [12]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [13]Washington University in St Louis, Saint Louis, MO, [14]University of Pennsylvania / Corporal Michael J. Crescenz VAMC, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction) (0831–0836)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: The impact of genetic risk factors on rheumatoid arthritis (RA) phenotype is incompletely understood. Comparing individual genetic variants associated with RA susceptibility to a polygenic score (PGS), we hypothesized that higher genetic risk for RA would correlate with more severe disease.

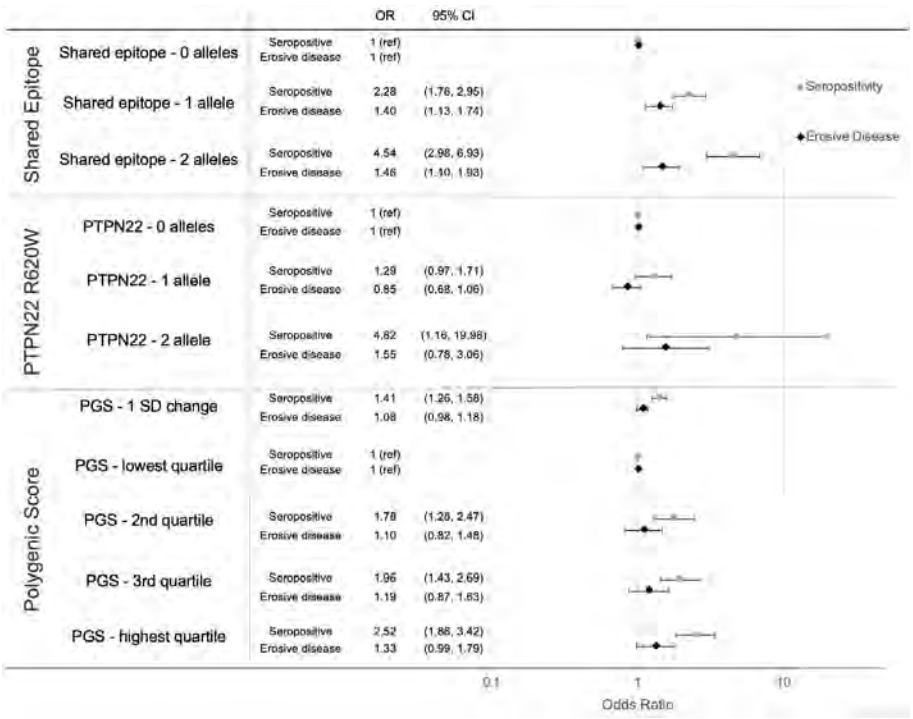


Figure 1. Effect of HLA-DRB1 SE, PTPN22 R620W, and non-HLA PGS on seropositivity and erosive disease at VARA enrollment. Effect determined by linear regression in a genotype model, adjusted for age, sex, and top 5 PCs of population structure. All genetic models demonstrated increased odds for seropositivity, whereas only SE was significantly associated with erosive disease. Abbreviations: PGS – polygenic score SE – shared epitope PC – principal components OR – odds ratio CI – confidence interval

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

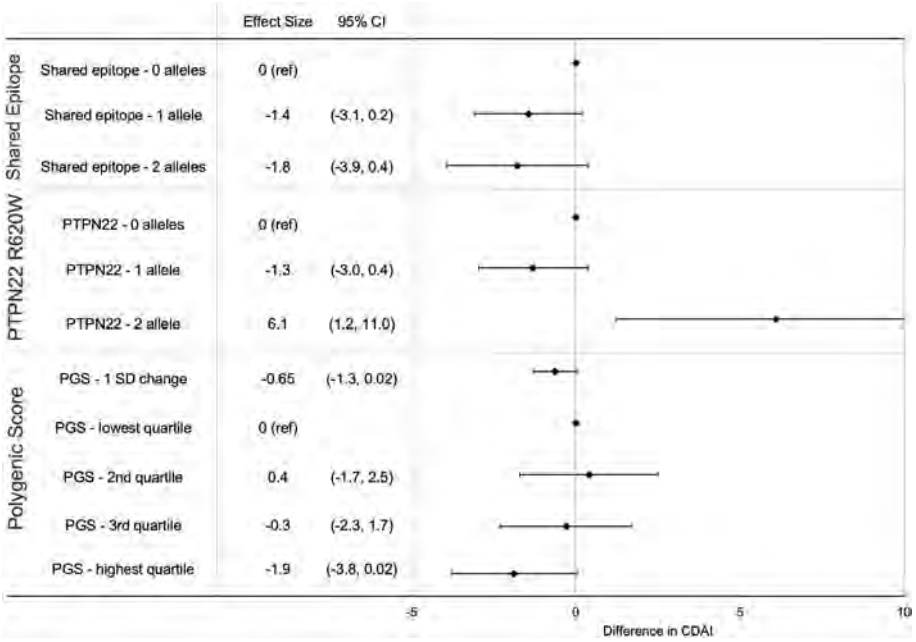


Figure 2. Effect of SE, PTPN22 R620W, and non-HLA PGS on CDAI at enrollment. Participants with 2 copies of PTPN22 demonstrated a higher CDAI (p = 0.014). A trend toward a negative association with CDAI is observed for 1 standard deviation change of PGS (p = 0.057) and in those at the highest quartile of risk by PGS) (p = 0.053). Effect at enrollment determined by linear regression in a genotype model, adjusted for age, sex, and top 5 PCs of population structure. Abbreviations: CDAI – clinical disease activity index PGS – polygenic score SE – shared epitope PC – principal components CI – confidence interval

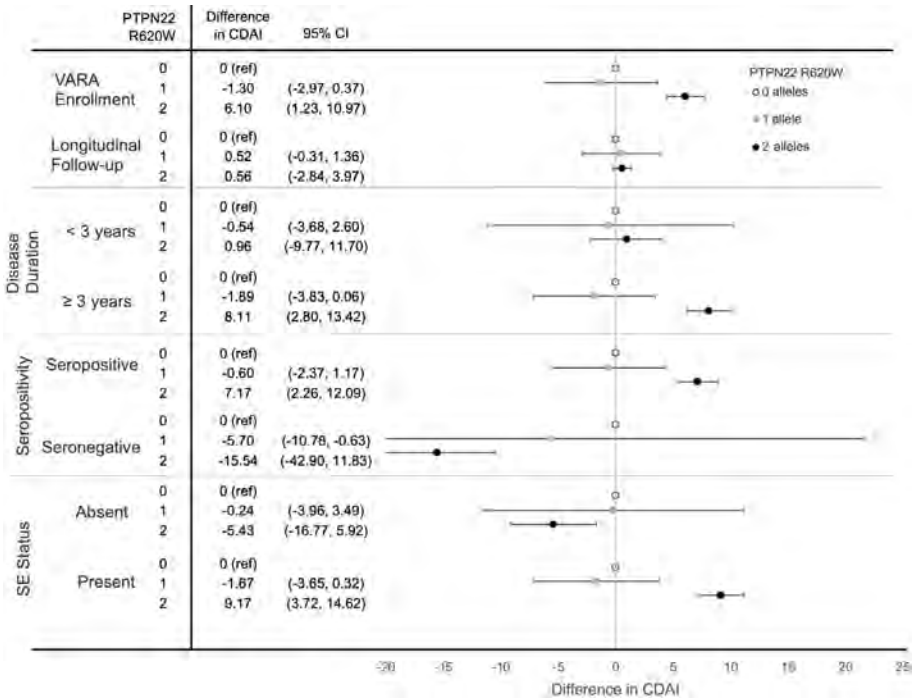


Figure 3. Subgroup Analysis for PTPN22 R620W and CDAI. Subgroup analysis performed by stratification in linear regression in a genotype model, adjusted for age, sex, and top 5 PCs of population structure. Longitudinal disease activity was analyzed using generalized estimating equations adjusting for these same factors as well as enrollment CDAI. Participants with 2 copies of PTPN22 demonstrated a higher CDAI at enrollment, but not in longitudinal disease activity corrected for the enrollment CDAI. This effect was predominant in those with seropositive RA, those with 1 or 2 shared epitope HLA alleles, and with disease duration ≥ 3 years. There was not a significant effect of genotype in early disease. Those with 1 PTPN22 R620W allele with seronegative RA had significantly lower disease activity, and a trend toward lower disease activity in those who were seronegative or without shared epitope with 2 PTPN22 R620W alleles, though this was not statistically significant. Abbreviations: CDAI – clinical disease activity index VARA – Veterans Affairs Rheumatoid Arthritis Registry SE – shared epitope PC – principal components

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We genotyped participants from the Veterans Affairs RA (VARA) registry, a prospective multicenter RA cohort. We evaluated the association between an existing non-HLA PGS (PGS Catalog PGS002745) and RA disease activity measured by the clinical disease activity index (CDAI), using linear regression adjusted for sex, age, and genetic background. We applied similar linear models to evaluate the association between individual genetic risk factors *PTPN22* R620W or *HLA*-DRB1 shared epitope (SE) and disease activity scores. We tested the association with these genetic risk factors and binary outcomes (RF or anti-CCP seropositivity, erosive disease) at enrollment using logistic regression adjusted for the same covariates. To understand the potential for gene-phenotype interactions, we tested for an interaction of genetic exposure with a) disease duration and b) seropositivity (RF or anti-CCP). We also tested for interaction of SE with *PTPN22* R620W and PGS.

Results: Among 2597 VARA participants, 50 (2%) were homozygous for *PTPN22* R620W, and 1603 (62%) had a PGS >50th percentile compared to the 1000 Genomes reference population. *PTPN22*, SE, and the PGS were strongly associated with seropositivity (PGS OR= 1.41, 95% CI 1.26-1.58, p< 0.001, **Fig. 1**). Those with 2 *PTPN22* alleles had higher disease activity (CDAI β 6.10, 95% CI 1.23-10.97, p=0.014); no difference was observed for those with one *PTPN22* allele, SE, or by PGS (**Fig. 2**).

Higher genetic risk appeared more strongly associated with disease severity in those with longer disease duration at enrollment. The association between 2 copies of *PTPN22* and higher disease activity was only observed in those with >3 years disease duration (**Fig. 3**). The association between 2 *PTPN22* alleles and higher disease activity was also primarily observed among seropositive patients (**Fig. 3**).The association between presence of 2 *PTPN22* alleles and higher disease activity was stronger in the presence of SE (CDAI: effect with SE 9.39, 95% CI 3.75-15.0, p interaction 0.01, **Fig. 3**). No interactions were observed between seropositivity or SE and the PGS.

The presence of SE was associated with erosive disease at study enrollment [1 allele: OR 1.40, 95% CI 1.13-1.74, p = 0.002; 2 allele OR 1.46, 95% CI 1.10-1.93, p = 0.009]; higher PGS and *PTPN22* were not (**Fig. 1**). A higher PGS was associated with higher odds of erosive disease in those with >3 years duration (1 SD change OR 1.12, 95% CI 1.01-1.26, p = 0.035), but not among those with shorter disease duration.

Conclusion: Genetic risk factors for RA demonstrate heterogeneous associations with resultant disease phenotypes among RA patients. Genetic effects were most significant after the early RA period and among those who were seropositive. Individual genetic variants and pathway-specific genetic risk may be more informative than the genome-wide genetic risk for RA in understanding phenotype and disease activity in RA.

Disclosure: T. Riley: None; **A. Wheeler**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **G. Cannon**: None; **B. Sauer**: None; **G. Kunkel**: None; **K. Wysham**: None; **B. Wallace**: None; **P. Monach**: Boehringer-Ingelheim, 2; **A. Reimold**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **I. Smith**: None; **J. Richards**: None; **I. Lee**: None; **G. Thiele**: None; **R. Xiao**: None; **S. Damrauer**: Amgen, 12, Non-financial research support, Novo Nordisk, 12, Non-financial research support, US Department of Veterans Affairs, 10; **M. Levin**: None; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **J. Baker**: Amgen, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0835

IgG Glycome In Early Rheumatoid Arthritis Differs From Matched Controls and Links Less Lean Mass to an Early Aging Phenotype

Sidra Hashmi[1], Brian Andonian[2], Mary Ahern[3], William Bennett[4], Alyssa Sudnick[5], Johanna Johnson[5], Sridevi Krishnan[3] and Kim Huffman[5], [1]Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, USA, Morrisville, NC, [2]Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, USA, morrisville, [3]University of Arizona, ARIZONA, [4]Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, USA, DURHAM, NC, [5]Duke Molecular Physiology Institute, Duke University School of Medicine, Durham, NC, USA, Durham

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction) (0831–0836)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Glycosylation is a post-translational enzymatic process important for protein function. Glycosylation patterns range from anti-inflammatory to inflammatory, and have been used to derive a measure of biologic age, the Glycan age (GlycAge). In patients with rheumatoid arthritis (RA), the immunoglobulin G (IgG) glycome is characterized by decreased galactosylation, possibly reflecting RA immune dysfunction. Our goals were to identify 1) alterations in the IgG glycome in patients with early RA (symptom duration < 6 months), 2) changes in glycome following a supervised lifestyle modification

Table 1: Clinical, physiologic, and glycome characteristics in patients with early RA and age-, sex-, and BMI-matched controls

Variables	Healthy Control (n=10) Mean (SD)	Early RA (n=10) Mean (SD)
Age (y)	53.2 (12.3)	53.6 (12.9)
Lean mass (%)	61.8 (7.7)	60.9 (10.0)
Absolute cardiorespiratory fitness at peak exercise (L/min)	2.22 (0.57)	1.98 (0.68)
Relative cardiorespiratory fitness at peak exercise (mL/kg/min)	27.69 (5.86)	24.29 (6.32)
BMI (kg/m^2)	27.7 (4.7)	28.1 (4.2)
Sex, female n (%)	7 (70%)	7 (70%)
Sex, male n (%)	3 (30%)	3 (30%)
Race, n (%) American Indian or Alaska Native Black or African American White	 1 (10%) 1 (10%) 8 (80%)	 0 (0%) 2 (20%) 8 (80%)
Glycan age	**42.1 (25.2518) ***	**60.2 (19.5437) ***
IgG-G0	22.0 (8.7)	27.3 (8.6)
IgG-G1	36.6 (3.6)	37.6 (2.4)
IgG-G2	19.9 (6.0)	15.4 (4.4)
IgG-G	56.4 (6.7)	53 (6.1)
IgG-S0	78.4 (3.5)	80.3 (3.3)
IgG-S1	17.3 (3.0)	15.1 (2.7)
IgG-S2	4.3 (0.6)	4.5 (0.8)
IgG-S	21.6 (3.5)	19.7 (3.3)
IgG-F	95.4 (0.9)	95.3 (1.1)
RF positive, n (%)	N/A	9 (90%)
Anti-CCP antibody positive, n (%)	N/A	8 (80%)
RF or anti-CCP positive, n (%)	N/A	10 (100%)
RA disease duration (months)	N/A	3.7 (1.1)
RA disease activity (DAS-28)	N/A	4.3 (1.7)
Prednisone use, n (%)	0/10 (0%)	7/10 (70%)
csDMARD use, n (%)	0/10 (0%)	10/10 (100%)
ESR (mm/hour)	**15.3 (13.0) ***	**32.4 (19.6) ***
SBAS-on-the-job physical activity	1.9 (0.6)	1.7 (0.7)
SBAS-leisure-time physical activity	2.6 (0.5)	2.5 (0.7)
PROMIS-Physical function (T-score)	**55.4 (6.4) ***	**39.6 (8.1) ***
PROMIS-Physical health (T-score)	**56.2 (6.9) ***	**44.6 (8.2) ***
PROMIS-Mental health (T-score)	54.5 (5.7)	50.2 (9.3)
PROMIS-Pain intensity (T-score)	**34.2 (4.7) ***	**45.7 (8.0) ***
PROMIS-Life satisfaction (T-score)	57.5 (7.8)	53.7 (9.9)
PROMIS-Fatigue (T-score)	45.0 (7.4)	49.4 (11.1)
Hand dominance, right (%)	10 (100%)	8 (80%)
Grip strength, right hand (kg)	**30.0 (7.1) ***	**23.2 (6.8) ***
Grip strength, left hand (kg)	30.9 (11.8)	25.4 (5.1)
Isometric knee extension average torque (Nm)	145.2 (48.3)	135.3 (48.1)
Peak rVO_2 (mL/kg/min)	27.7 (5.9)	24.3 (6.3)

all values are reported as mean (SD) unless noted otherwise
= p<0.05

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Percent change in clinical, physiologic, and glycome factors following SWET/lifestyle counseling interventions

Variables	N	Mean	Std Dev	Median	Minimum	Maximum	p-value
Glycan age	20	1.73	7.87	0	-10.96	31.25	0.34
IgG-G0	20	1.51	4.70	1.30	-5.61	16.52	0.17
IgG-G1	20	-0.05	1.54	-0.22	-3.10	2.32	0.88
IgG-G2	20	-0.99	5.52	-1.19	-10.48	13.58	0.43
IgG-G	20	-0.35	1.80	-0.40	-4.25	2.46	0.39
IgG-S0	20	0.21	1.20	0.02	-1.75	2.84	0.43
IgG-S1	20	-0.87	4.62	-0.26	-12.58	7.25	0.41
IgG-S2	20	-1.11	11.61	0.69	-24.44	32.78	0.67
IgG-S	20	-1.01	5.43	0.12	-15.40	6.92	0.42
IgG-F	20	-0.002	0.36	-0.07	-0.87	0.66	0.98
IgG-F0	20	-0.17	6.42	1.61	-14.34	13.68	0.91
IgG-B	20	0.37	3.62	0.83	-10.33	7.77	0.65
IgG-B0	20	-0.108	0.85	-0.25	-1.59	2.68	0.58
Lean mass	20	0.48	2.91	0.28	-4.46	5.52	0.47
Percent Lean mass	20	4.66	4.53	3.49	-2.64	15.18	0.0002
Fat mass	20	**-9.05**	**7.36**	**-8.16**	**-22.82**	**3.45**	**<.0001**
Percent Fat mass	20	**-5.41**	**5.01**	**-4.61**	**-16.11**	**4.06**	**0.0001**
BMI	20	**-4.135**	**3.55**		**-10.93**	**2.5**	**<.0001**
Absolute Cardiorespiratory fitness	19	3.10	9.70	3.51	-20.29	20.33	0.18
Relative Cardiorespiratory fitness	**19**	**7.73**	**11.09**	**5.98**	**-13.07**	**34.75**	**0.007**
Forearm k-score	18	12.21	37.05	1.50	-35.18	100.35	0.18
Gastrocnemius k-score	11	23.07	39.36	21.88	-44.32	81.03	0.08
Grip left average	19	24.90	67.03	8.70	-25	285.71	0.12
Grip right average	19	7.63	31.12	-2.44	-37.04	90	0.30
High sensitivity CRP	20	42.66	188.23	-12.10	-81.36	775	0.32
ESR	20	30.28	75.13	15.83	-62.5	266.67	0.09
Swollen joint count	**20**	**-36.55**	**60.53**	**-50**	**-100**	**100**	**0.01**
Tender joint count	19	-13.18	69.63	0	-100	200	0.42

**all values in Table 2 are reported as percent change*

in older RA patients with overweight/obesity, and 3) associations between RA glycome and clinical and physiologic parameters.

Methods: IgG glycome was analyzed using ultra-high-performance liquid chromatography (GENOS) and plasma samples from two recent studies: 1) MusculRA: early RA (n=10) versus age-, sex- and BMI-matched healthy controls (n=10); and 2) SWET-RA: older, established RA with overweight/obesity (n=20), randomized to 16 weeks of remotely supervised weight loss and exercise training or lifestyle counseling. Group differences and post-intervention changes were evaluated using t-tests and Wilcoxon tests, depending on data normality. Participants with RA from MusculRA and SWET-RA studies were combined (n=29; one participant completed both studies) to analyze associations between glycome with clinical and physiological parameters using linear regression, controlling for age and sex. Relationships between parameter changes following SWET-RA study lifestyle intervention (n=20) were assessed using Spearman's correlations.

Results: As compared to age-matched controls (mean age=53.2 years), early RA (mean age=53.6 years) had a GlycAge corresponding to 18.1±22.6 years older (p=0.03) (Table 1). Early RA GlycAge was not significantly different from older, established RA (mean age=66.65 years; p=0.32). RA GlycAge was negatively associated with cardiorespiratory fitness (VO_2 peak, mL/kg/min; beta=-1.66, p=0.005) and lean mass (kg; beta=-1.77, p=0.004). Baseline IgG digalactosylated glycan (IgG-G2) was positively associated with log lean mass (beta=17.9, p=0.008) and right hand grip strength (beta=0.16, p=0.04), and negatively associated with log CRP (beta=-1.05, p=0.02) and ESR (beta=-0.06, p=0.02). While diet and exercise lifestyle intervention did not significantly alter overall RA GlycAge (mean GlycAge percent change=1.7±7.9, p=0.34; Table 2), reductions in GlycAge associated with increases in lean mass (Spearman rho=-0.46, p=0.04).

Conclusion: Changes in the RA glycome occur early in the RA disease process, leading to almost two decades of biological aging via GlycAge. Our findings suggest the IgG glycome and GlycAge may be useful as biomarkers for RA diagnosis and

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

longitudinal monitoring. Lifestyle interventions targeting improvements in cardiorespiratory fitness and muscle health may positively impact the glycome and biological aging linked to RA.

Disclosure: S. Hashmi: None; **B. Andonian**: None; **M. Ahern**: None; **W. Bennett**: None; **A. Sudnick**: None; **J. Johnson**: None; **S. Krishnan**: None; **K. Huffman**: None.

Abstract Number: 0836

Growth Differentiation Factor-15 Predicts Frailty and Death in Rheumatoid Arthritis

Katherine Wysham[1], Hannah Brubeck[2], Aaron Baraff[2], Christian Lood[3], Punyasha Roul[4], Bryant England[5], Beth Wallace[6], Grant Cannon[7], Gary Kunkel[8], Ted Mikuls[5], Patti Katz[9], Dolores Shoback[10], Jose Garcia[11], Ariela Orkaby[12], Joshua Baker[13] and Tate Johnson[5], [1]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [2]VA Puget Sound Health Care System, Seattle, WA, [3]University of Washington, Seattle, WA, [4]UNMC, Omaha, NE, [5]University of Nebraska Medical Center, Omaha, NE, [6]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [7]University of Utah and Salt Lake City VA, Salt Lake City, UT, [8]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [9]UCSF, San Rafael, CA, [10]San Francisco VA Medical Center & University of California San Francisco, San Francisco, CA, [11]VA Puget Sound Health Care System, VA GRECC, and University of Washington, Seattle, WA, [12]VA Boston Healthcare System & Division of Aging, Brigham and Women's Hospital, Harvard Medical School & VA Geriatrics Research Education and Clinical Center, Boston, MA, [13]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes II: Look What You Made Me Do (Prediction) (0831–0836)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: RA is associated with premature aging and frailty. Growth differentiation factor-15 (GDF-15) is a biomarker that increases in response to cellular stress and inflammation and is associated with cachexia, frailty, and death in the general population. A recent trial of an anti-GDF-15 antibody demonstrated improved weight gain and lower cachexia symptoms in participants with cancer[1]. GDF-15 is elevated in RA compared to controls and is associated with disease activity. We aimed to evaluate the association of GDF-15 with frailty and death in a national RA cohort.

Methods: Participants from the Veterans Affairs Rheumatoid Arthritis (VARA) Registry, a multicenter prospective RA cohort, enrolled between 1/2003 through 12/2022 with baseline GDF-15 levels were included. Frailty was measured at baseline and annually throughout observation using the VA Frailty Index (VA-FI), a validated deficit accumulation score based on >6000 diagnostic codes. Participants were categorized as frail using the established VA-FI cutoff of >0.2. Vital status was assessed using the National Death Index. Serum GDF-15 was measured on biobanked baseline samples using the MesoScale platform and divided into quartiles for analysis. Multiple imputation with chained equations addressed missing data. Multivariable logistic regression evaluated the cross-sectional association between GDF-15 quartile and frailty. Multivariable Cox modeling also evaluated the association between GDF-15 quartile and incident frailty or death, in those not frail at baseline. Both models controlled for age, sex, race, BMI, disease duration, DAS28ESR, CCP positivity, prednisone use, csDMARD use, b/tsDMARD use and Rheumatic Disease Comorbidity Index (RDCI).

Results: In total, 2,866 participants were included in the cross-sectional analysis (mean age of 64.6±11.1, 88% male, 76% White and 29% frail) (Table 1). Compared to the lowest quartile, those in the highest quartile of GDF-15 were older (70.9±9.2 vs. 56.3±11.5 years), more frequently male (95% vs. 74%), White (80% vs 68%), had longer disease duration (12.7±12.0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline patient demographics and clinical characteristics, stratified by GDF-15 quartile (N=2866).

	Q1 N=717 (25%)	Q2 N=716 (25%)	Q3 N=716 (25%)	Q4 N=717 (25%)
Frail	102 (14%)	163 (23%)	235 (33%)	329 (46%)
Age	56.3 ± 11.5	63.2 ± 8.3	67.8 ± 8.8	70.9 ± 9.2
Age Categories				
<55	288 (40%)	108 (15%)	54 (8%)	32 (5%)
55-64	277 (39%)	313 (44%)	219 (31%)	165 (23%)
65-74	120 (17%)	250 (35%)	295 (41%)	277 (39%)
75+	32 (5%)	45 (6%)	148 (21%)	243 (34%)
Male	527 (74%)	642 (90%)	664 (93%)	678 (95%)
Race				
Black	156 (22%)	99 (14%)	91 (13%)	67 (9%)
White	487 (68%)	559 (78%)	573 (80%)	571 (80%)
Other[1]	22 (3%)	10 (1%)	13 (2%)	12 (2%)
BMI Category				
<18.5	7 (1%)	6 (1%)	11 (2%)	8 (1%)
18.5-24.9	131 (18%)	155 (22%)	169 (24%)	223 (31%)
25.0-29.9	276 (39%)	271 (38%)	258 (36%)	223 (31%)
30.0-34.9	168 (23%)	160 (22%)	161 (23%)	148 (21%)
35-39.9	68 (10%)	61 (9%)	55 (8%)	46 (6%)
≥40	28 (4%)	36 (5%)	26 (4%)	24 (3%)
DAS28ESR	3.7 ± 1.6	3.6 ± 1.6	3.8 ± 1.6	4.0 ± 1.5
Disease duration	9.6 ± 10.0	10.4 ± 10.5	12.4 ± 12.2	12.7 ± 12.0
RDCI	2.6 ±1.9	3.3 ± 2.0	3.8 ± 1.9	4.1 ± 1.8
Anti-CCP Positive	553 (77%)	544 (76%)	540 (75%)	556 (78%)
Prednisone use	222 (31%)	258 (36%)	217 (30%)	243 (34%)
csDMARD use	531 (74%)	538 (75%)	563 (79%)	575 (80%)
b/tsDMARD use	226 (32%)	226 (32%)	194 (27%)	182 (25%)

Values are reported as mean (SD) or n (%)
[1]Other: Included American Indian or Alaskan Native, Asian, Native Hawaiian or Other Pacific Islander as well as missing.
Abbreviations: BMI: Body Mass Index; DAS28-ESR: Disease Activity Score in 28 joints with Erythrocyte Sedimentation Rate; RDCI: Rheumatic Disease Comorbidity Index; anti-CCP: Cyclic Citrullinated Peptide antibody; RF: Rheumatoid Factor; csDMARD: conventional synthetic Disease-Modifying Antirheumatic Drug; b/tsDMARD: biologic/targeted synthetic Disease-Modifying Antirheumatic Drug.

vs. 9.6±10.0), and had more comorbidities (RDCI 4.1±1.8 vs. 2.6±1.9). Compared to the lowest quartile, the 3rd quartile of GDF-15 was associated with 1.5 times the odds of frailty (aOR 1.50 [95%CI 1.1-2.1], p=0.016) and the highest quartile was associated with 2.2 times the odds of frailty (aOR 2.18 [95%CI 1.57-3.04], p< 0.001) (Figure 1). The incident frailty subcohort was comprised of 2,448 participants (mean age 62.7±11.2), of whom 61% (N=1,493) became frail (N=1130) or died (N=363) over 13,631 person-years of observation. Compared to the lowest quartile, the highest quartile of GDF15 was associated with a 2.6-fold increase in the risk of incident frailty or death (aHR: 2.59, 95%CI 1.68-3.98, p< 0.001) (Figure 2).

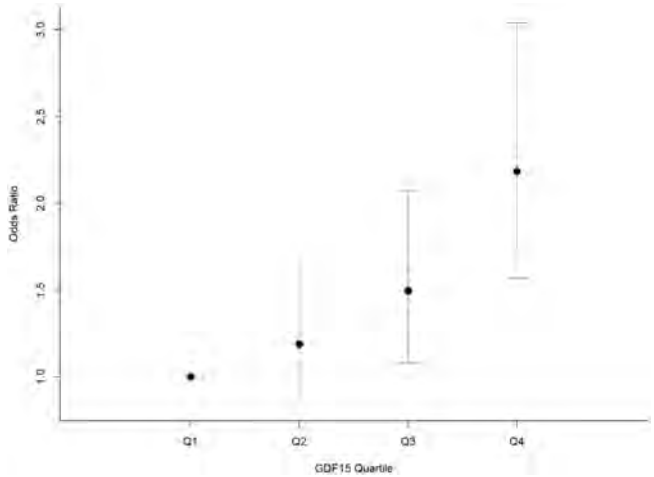


Figure 1. Adjusted logistic regression models evaluating the cross-sectional association between baseline GDF-15 quartiles and frailty at baseline. Models were adjusted for baseline age category, sex, race, BMI category, RDCI, disease duration, DAS28ESR, anti-CCP positivity, prednisone use, csDMARD use, and b/tsDMARD use. Trend analysis p<0.0001.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

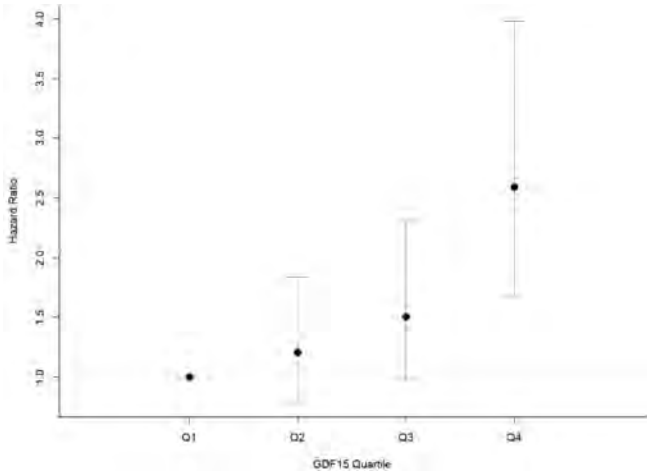


Figure 2. Adjusted Cox models evaluating the longitudinal association between baseline GDF-15 quartiles and incident frailty or death (N=1,493). Models were adjusted for baseline age category, sex, race, BMI category, RDCI, disease duration, DAS28ESR, anti-CCP positivity, prednisone use, csDMARD use, and b/tsDMARD use. Trend analysis p<0.0001.

Conclusion: Elevated GDF-15 was associated with baseline frailty and predicted incident frailty or death in a large RA cohort, independent of important demographic and disease characteristics. Further work is needed to evaluate the effect of GDF-15 on frailty onset to determine its relevance as a therapeutic target in at-risk individuals with RA.

1. Groarke et al. NEJM 2024

Disclosure: K. Wysham: None; **H. Brubeck**: None; **A. Baraff**: None; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11; **P. Roul**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **B. Wallace**: None; **G. Cannon**: None; **G. Kunkel**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **P. Katz**: None; **D. Shoback**: None; **J. Garcia**: Aveo Oncology, 2, Catalym, 2, Pfizer, 5; **A. Orkaby**: None; **J. Baker**: Amgen, 5; **T. Johnson**: None.

Abstract Number: 0837

Risk of New Proteinuria in Next Ten Years in SLE

Michelle Petri[1], Ilayda Demirayak[2], Andrea Fava[3], Daniel Goldman[1] and Laurence Magder[4], [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]Istanbul University, Istanbul, Turkey, [3]Johns Hopkins University, Baltimore, MD, [4]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis (0837–0842)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: The current 2024 ACR Lupus Nephritis guidelines recommend checking the urine protein to creatinine ratio (UPCR) every 6-12 months. Early recognition of lupus nephritis (LN), though, would lead to earlier introduction of treatment and better outcomes. A risk formula to project a patient's risk of incident proteinuria within 10 years of SLE diagnosis would allow more frequent UPCR checks in the highest risk population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Association between various manifestations in the first year after SLE diagnosis and eventual incidence proteinuria

Variable	Comparison	Hazard Ratio (95% CI)	P-value
Age of SLE diagnosis	30-44 vs <30	0.62 (0.48, 0.80)	0.0002
	45-59 vs <30	0.51 (0.32, 0.80)	0.0032
	60+ vs ,30	0.95 (0.35, 2.59)	0.9266
Race	Black vs. White	1.98 (1.58, 2.49)	<.0001
	Other vs. White	3.40 (2.42, 4.76)	<.0001
Sex	Male vs. Female	1.54 (1.09, 2.19)	0.0155
Anticardiolipin	Present vs. Absent	0.84 (0.58, 1.21)	0.3382
Anti-dsDNA	Present vs. Absent	1.91 (1.53, 2.38)	<.0001
Low C3	Present vs. Absent	1.85 (1.43, 2.39)	<.0001
Low C4	Present vs. Absent	2.08 (1.62, 2.68)	<.0001
Anti-Sm	Present vs. Absent	3.51(2.83, 4.35)	<.0001
Anti-RNP	Present vs. Absent	2.65 (2.15, 3.28)	<.0001
Anti-Ro	Present vs. Absent	1.62 (1.31, 2.00)	<.0001
Anti-La	Present vs. Absent	1.35 (1.02, 1.79)	0.0343
Lupus anticoagulant	Present vs. Absent	0.58 (0.32, 1.06)	0.0774
Coombs	Present vs. Absent	1.13 (0.75, 1.70)	0.5453
Anemia	Present vs. Absent	1.47 (1.16, 1.87)	0.0017
Hemolytic Anemia	Present vs. Absent	1.33 (0.78, 2.28)	0.2921
Hematuria	Present vs. Absent	1.60 (0.93, 2.73)	0.0869
Leukopenia	Present vs. Absent	1.12 (0.87, 1.43)	0.3954
Lymphopenia	Present vs. Absent	1.16 (0.87, 1.55)	0.3008
Thrombocytopenia	Present vs. Absent	0.80 (0.54, 1.18)	0.2565
Lymphadenopathy	Present vs. Absent	1.22 (0.93, 1.61)	0.1554
Abn. Liver Function	Present vs. Absent	1.06 (0.73, 1.56)	0.7468
Discoid Rash	Present vs. Absent	0.89 (0.65, 1.21)	0.4481
Malar Rash	Present vs. Absent	1.03 (0.83, 1.27)	0.7794
Photosensitivity	Present vs. Absent	0.68 (0.54, 0.84)	0.0005
Oral Ulcers	Present vs. Absent	0.75 (0.59, 0.96)	0.0196
Alopecia	Present vs. Absent	1.18 (0.95, 1.48)	0.1412
Arthritis	Present vs. Absent	1.13 (0.91, 1.40)	0.2652
Pericarditis	Present vs. Absent	1.12 (0.78, 1.61)	0.5344
Pleuritis	Present vs. Absent	0.92 (0.71, 1.21)	0.5640
Seizures	Present vs. Absent	0.80 (0.47, 1.37)	0.4134
Psychosis	Present vs. Absent	1.15 (0.37, 3.60)	0.8045
Sjogrens Syndrome	Present vs. Absent	0.76 (0.48, 1.19)	0.2258
Elevated ESR	Present vs. Absent	1.11 (0.85, 1.44)	0.4401

Table 2. Multivariable model to predict incident proteinuria

Variable	Comparison	Rate Ratio (95% CI)	P-value
Anti-Sm	Present vs. Absent	2.25 (1.72, 2.95)	<0.0001
Race	Black vs. White	1.57 (1.24, 2.00)	0.0002
	Other vs. White	2.32 (1.64, 3.27)	<0.0001
Anti-dsDNA	Present vs. Absent	1.51 (1.18, 1.92)	0.0009
Anti-RNP	Present vs. Absent	1.53 (1.18, 2.00)	0.0016
Low C4	Present vs. Absent	1.45 (1.10, 1.90)	0.0086
Sex	Male vs. Female	1.56 (1.09, 2.22)	0.014

Methods: The analysis is based on 1,418 members of the Hopkins Lupus Cohort who had been followed for longer than one year since SLE diagnosis. Subjects who developed proteinuria before or in the year of SLE diagnosis were excluded. A multivariate equation to predict the risk of incident proteinuria was developed using a forward-stepwise approach, considering each of the univariate associates in turn, and adding the variable that led to the greatest reduction in Akaike's Information Criterion (AIC).

Results: Univariate associates of incident (new) proteinuria after 1 year from SLE diagnosis are shown in Table 1. Table 2 shows the multivariate predictors of incident proteinuria. Major risk factors included non-Caucasian race and anti-Sm. Moderate risk factors included male sex, anti-RNP, anti-dsDNA, and low C4 at the time of SLE diagnosis. Based on this model

Table 3. Risk of incident proteinuria within 10 years of SLE diagnosis as a function of the number of risk factors (Each row in Table 2 counts as 1 risk factor except Anti-Sm and "Other" race which count as 2 risk factors)

Number of Risk Factors	10-year risk
0	2.6%
1	3.9%
2	5.8%
3	8.5%
4	12.5%
5	18.1%
6	25.9%
7	36.2%
8	49.1%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

we estimated the 10-year risk as a function of the number of risk factors a patient has (Table 3). A person with no risk factors has only a 2.6% chance of developing proteinuria in 10 years, whereas a person with all 8 risk factors has a 49% chance.

Conclusion: We built a risk score for proteinuria in the next 10 years that would allow clinicians to identify a high risk subset of SLE patients to target for more frequent measurement of urine protein to creatinine AND to consider earlier renal biopsy at even low levels of proteinuria. The risk factors include well accepted demographic variables (non-Caucasian race, male sex) and serologic tests that are easily available (low C4, anti-Sm, anti-RNP and anti-dsDNA).

Disclosure: M. Petri: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **I. Demirayak**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **D. Goldman**: None; **L. Magder**: None.

Abstract Number: 0838

Complete Renal Response and Long-Term, Progression-Free Survival in Adult Patients With Lupus Nephritis: A Retrospective Cohort Study in the United States

Lisa Lindsay[1], Shu Wang[2], Huong Trinh[1], Yunru Huang[1], William Pendergraft[1] and **Brad Rovin**[3], [1]Genentech, Inc., South San Francisco, CA, [2]Genesis Research LLC, Hoboken, NJ, [3]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis (0837–0842)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Complete renal response (CRR) and flare prevention, as early markers of long-term kidney survival, are important outcomes in lupus nephritis (LN) clinical trials.

Methods: This US-based retrospective cohort study (January 1, 2000 to October 15, 2024) used deidentified patient-level electronic health records from a national network of healthcare organizations (118 million patients) to assess time to initial CRR, LN flare, estimated glomerular filtration rate (eGFR) slope and unfavorable kidney outcomes. Patients were ≥18 years old with newly diagnosed LN (index), had baseline urine protein-to-creatinine ratio (UPCR) and eGFR within 90 days of index plus an additional UPCR and eGFR >90 days post index. Patients were required to have a baseline UPCR of ≥0.5 g/g. Patients with pre-existing end-stage kidney disease (ESKD), dialysis or kidney transplant were excluded. CRR was defined as UPCR < 0.5 g/g and eGFR ≥85% of baseline and no pre-CRR ESKD, dialysis or kidney transplant. LN flare was defined as eGFR decrease of >20%, increase in UPCR of >1 g/g if UPCR < 0.2 g/g or >2.0 g/g if UPCR ≥0.2 g/g or doubling if UPCR >1 g/g compared with baseline or receipt of intravenous methylprednisolone ≥100 mg within 14 days of a LN/systemic lupus erythematosus (SLE) diagnostic code. Unfavorable kidney outcomes included doubling of serum

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Description of Study Population Overall and According to Unfavorable Kidney Outcomes During Follow-up

	Lupus Nephritis													
	Overall	Any Unfavorable Kidney Outcome[a]		Doubling of Serum Creatinine		New-Onset CKD Stage 3b or 4[b]		New-Onset ESKD		New-Onset Dialysis		New-Onset Kidney Transplant		Death	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
n (%)	3279 (100)	1206 (37)	2073 (63)	962 (29)	2317 (71)	415 (13)	2864 (87)	555 (17)	2724 (83)	345 (11)	2934 (89)	201 (6)	3078 (94)	256 (8)	3023 (92)
Follow-up, mean (SD), months	72 (52)	57 (54)	83 (49)	89 (54)	66 (49)	97 (56)	69 (50)	94 (53)	69 (50)	96 (52)	69 (51)	125 (55)	69 (50)	71 (51)	72 (52)
Index year															
2000-2010	358 (11)	201 (17)	157 (8)	162 (17)	196 (9)	81 (20)	277 (10)	106 (19)	252 (9)	58 (17)	300 (10)	59 (29)	299 (10)	60 (23)	298 (10)
2011-2020	2139 (65)	852 (71)	1287 (62)	683 (71)	1456 (63)	286 (69)	1853 (65)	392 (71)	1747 (64)	253 (73)	1886 (64)	135 (67)	2004 (65)	179 (70)	1960 (65)
2021-2024	782 (24)	153 (13)	629 (30)	117 (12)	665 (29)	48 (12)	734 (26)	57 (10)	725 (27)	34 (10)	748 (26)	7 (4)	775 (25)	17 (7)	765 (25)
Age at index, mean (SD), years	37 (15)	39 (16)	37 (14)	37 (14)	38 (15)	34 (13)	38 (15)	38 (16)	37 (14)	35 (14)	38 (15)	34 (13)	38 (15)	46 (18)	37 (14)
Female, n (%)	2712 (83)	977 (81)	1735 (84)	788 (82)	1924 (83)	351 (85)	2361 (82)	438 (79)	2274 (84)	280 (81)	2432 (83)	156 (78)	2556 (83)	196 (77)	2516 (83)
Race, n (%)															
Asian	259 (8)	64 (5)	195 (9)	52 (5)	198 (9)	20 (5)	239 (8)	24 (4)	226 (8)	17 (5)	233 (8)	14 (7)	238 (8)	8 (2)	244 (8)
Black/AA	1128 (34)	463 (38)	665 (32)	378 (39)	750 (32)	176 (42)	952 (33)	228 (41)	900 (33)	184 (53)	944 (32)	78 (39)	1050 (34)	101 (40)	1027 (34)
White	1116 (34)	380 (32)	736 (36)	286 (30)	830 (36)	104 (25)	1012 (35)	169 (30)	948 (35)	81 (26)	1035 (35)	63 (31)	1053 (34)	82 (36)	1034 (34)
Other/unknown	785 (24)	299 (25)	486 (25)	246 (26)	539 (23)	115 (28)	670 (23)	135 (24)	650 (24)	53 (15)	732 (25)	46 (23)	739 (24)	57 (22)	728 (24)
mCCI, mean (SD)[c]	0.9 (1.5)	1.0 (1.7)	0.7 (1.4)	1.0 (1.6)	0.8 (1.4)	0.7 (1.4)	0.9 (1.5)	0.9 (1.5)	0.8 (1.5)	0.8 (1.4)	0.9 (1.5)	0.6 (1.3)	0.9 (1.5)	1.6 (2.2)	0.8 (1.4)
Renal biopsy, index ±6 months[d]	1620 (49)	505 (42)	1115 (54)	395 (41)	1225 (53)	171 (41)	1449 (51)	210 (38)	1410 (52)	148 (43)	1472 (50)	73 (36)	1547 (50)	100 (39)	1520 (50)
UPCR, g/g[e]															
≥0.5 to 1.0	700 (21)	211 (18)	489 (24)	154 (16)	546 (24)	78 (19)	622 (22)	81 (15)	619 (23)	36 (10)	664 (23)	24 (12)	676 (22)	48 (19)	652 (22)
>1 to <2	835 (26)	293 (24)	542 (26)	239 (25)	596 (26)	100 (24)	735 (26)	135 (24)	700 (26)	79 (23)	756 (26)	44 (22)	791 (26)	64 (25)	771 (26)
2 to <3	446 (14)	176 (15)	270 (13)	142 (15)	304 (13)	57 (14)	389 (14)	76 (14)	370 (14)	53 (15)	393 (13)	27 (13)	419 (14)	34 (13)	412 (14)
≥3	1298 (40)	526 (44)	772 (37)	427 (44)	871 (38)	180 (43)	1118 (39)	263 (47)	1035 (38)	177 (51)	1121 (38)	106 (53)	1192 (39)	110 (43)	1188 (39)
eGFR, mL/min/1.73 m^2[e]															
<30	297 (9)	189 (16)	108 (5)	130 (14)	167 (7)	2(1)	295 (10)	120 (23)	171 (6)	96 (28)	201 (7)	52 (26)	245 (9)	53 (21)	244 (8)
30-44	402 (12)	163 (14)	239 (12)	129 (13)	273 (12)	0 (0)	402 (14)	105 (19)	297 (11)	67 (19)	335 (11)	34 (17)	368 (12)	42 (16)	360 (12)
45-59	381 (12)	170 (14)	211 (10)	127 (13)	254 (11)	64 (15)	317 (11)	88 (16)	293 (11)	42 (12)	339 (12)	32 (16)	349 (11)	38 (15)	343 (11)
60-89	729 (22)	261 (22)	468 (23)	186 (19)	543 (23)	143 (35)	586 (21)	100 (18)	629 (23)	56 (16)	673 (23)	30 (15)	699 (23)	64 (25)	665 (22)
90+	1470 (45)	423 (35)	1047 (51)	390 (41)	1080 (47)	206 (50)	1264 (44)	136 (25)	1334 (49)	84 (24)	1386 (47)	53 (26)	1417 (46)	59 (23)	1411 (47)
Serum creatinine, mean (SD), mg/dL[e]	1.2 (0.7)	1.3 (0.8)	1.1 (0.6)	1.3 (0.8)	1.1 (0.6)	0.9 (0.4)	1.2 (0.7)	1.5 (0.8)	1.1 (0.6)	1.7 (1.0)	1.1 (0.6)	1.7 (1.0)	1.1 (0.6)	1.5 (0.8)	1.1 (0.7)
Complete renal remission, n (%) (ever post-index)	1736 (53)	393 (33)	1343 (65)	297 (31)	1439 (62)	136 (33)	1600 (56)	116 (21)	1620 (60)	53 (15)	1683 (57)	33 (16)	1703 (55)	81 (32)	1655 (55)
Flare, n (%) (ever post-index)	2153 (66)	1102 (91)	1051 (51)	923 (96)	1230 (53)	408 (98)	1745 (61)	528 (95)	1625 (60)	318 (92)	1835 (63)	181 (90)	1972 (64)	210 (82)	1943 (64)
Baseline medication (index to index +90 days)															
Antimalarial	1798 (55)	634 (53)	1164 (56)	522 (54)	1276 (55)	231 (56)	1567 (55)	274 (49)	1524 (56)	174 (50)	1624 (55)	81 (40)	1717 (56)	122 (48)	1676 (55)
Systemic glucocorticoid	2459 (75)	891 (74)	1568 (76)	718 (75)	1741 (75)	318 (77)	2141 (75)	385 (69)	2074 (76)	241 (70)	2218 (76)	127 (63)	2332 (76)	186 (73)	2273 (75)
IS	2245 (68)	778 (65)	1467 (71)	626 (65)	1617 (70)	276 (67)	1969 (69)	326 (59)	1919 (70)	211 (61)	2034 (69)	113 (56)	2132 (69)	154 (60)	2091 (69)
MMF/MPA	1779 (54)	621 (51)	1158 (56)	509 (53)	1270 (55)	223 (54)	1556 (54)	270 (49)	1509 (55)	170 (49)	1609 (55)	86 (43)	1693 (55)	126 (49)	1654 (55)
MTX	40 (1)	13 (1)	27 (1)	9 (1)	32 (1)	7 (2)	33 (1)	2 (0)	38 (1)	--	40 (1)	2 (1)	38 (1)	3 (1)	37 (1)
AZA	228 (7)	78 (7)	150 (7)	68 (7)	160 (7)	29 (7)	199 (7)	31 (6)	197 (7)	24 (7)	204 (7)	12 (6)	216 (7)	14 (6)	214 (7)
CYC	386 (12)	157 (13)	229 (11)	128 (13)	258 (11)	45 (11)	341 (12)	66 (12)	320 (12)	44 (13)	342 (12)	28 (14)	358 (12)	31 (12)	355 (12)
CNI	205 (6)	66 (6)	137 (7)	50 (5)	155 (7)	22 (5)	183 (6)	20 (4)	185 (7)	15 (4)	190 (7)	12 (6)	193 (6)	13 (5)	192 (6)
BEL	117 (4)	23 (2)	94 (5)	18 (2)	99 (4)	11 (3)	106 (4)	10 (2)	107 (4)	8 (2)	109 (4)	1 (1)	116 (4)	4 (2)	113 (4)
RTX	135 (4)	48 (4)	87 (4)	42 (4)	93 (4)	10 (2)	125 (4)	18 (3)	117 (4)	12 (4)	123 (4)	5 (3)	130 (4)	4 (2)	131 (4)
Time to post-index immunosuppressant use, mean (SD), months	5 (14)	7 (17)	4 (12)	7 (19)	4 (11)	7 (18)	5 (13)	9 (22)	4 (12)	8 (22)	5 (13)	12 (27)	4 (13)	5 (12)	5 (14)

AA, African American; AZA, azathioprine; BEL, belimumab; CKD, chronic kidney disease; CNI, calcineurin inhibitor; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; IS, immunosuppressant; mCCI, modified Charlson Comorbidity Index; MTX, methotrexate; MMF/MPA, mycophenolate mofetil/mycophenolic acid; RTX, rituximab; UPCR, urine protein-to-creatinine ratio.

*P<0.05 based on Pearson χ^2 test; Fisher exact test; Wilcoxon rank sum test.

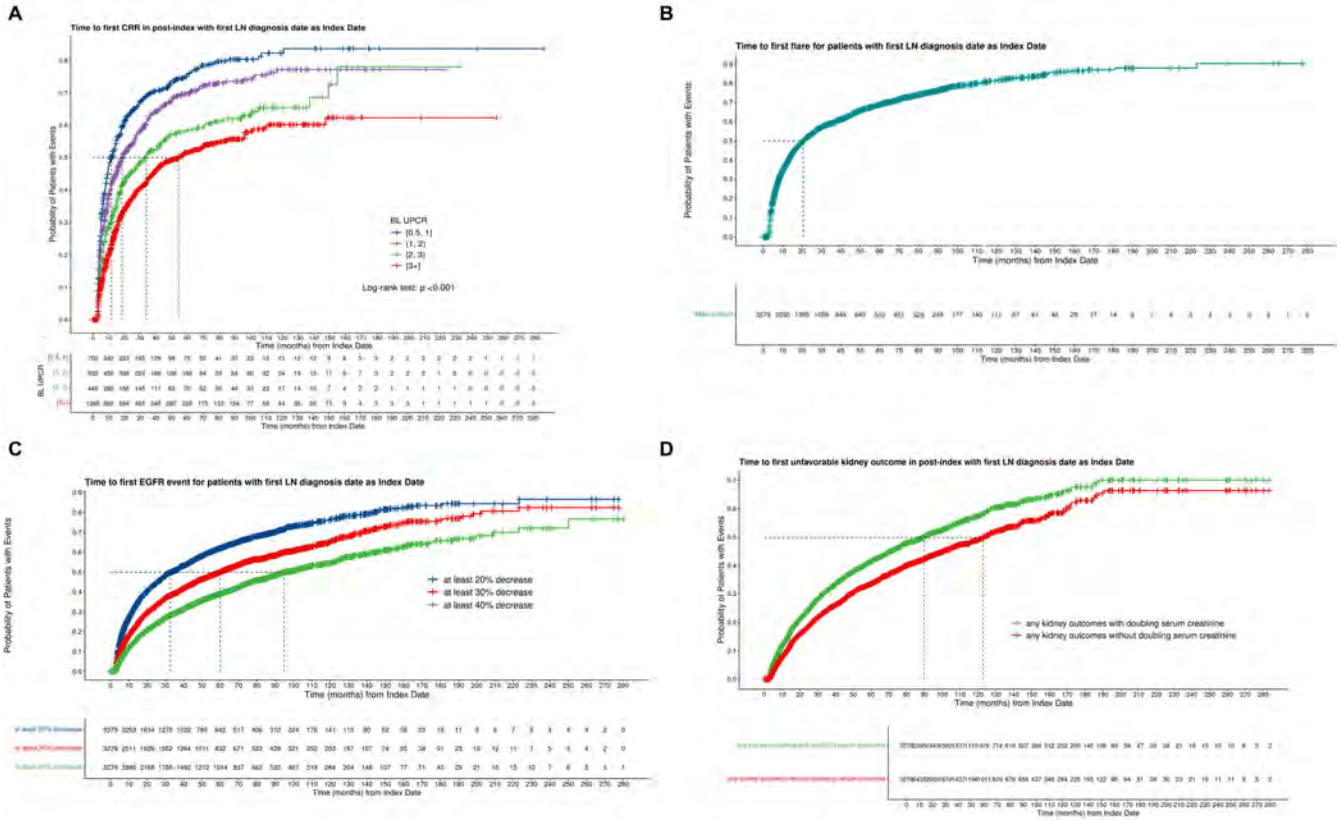
[a]Any unfavorable kidney outcome including doubling of serum creatinine; [b]CKD stage 3b/4 allowed at study entry; new onset indicates such patients did not have diagnosis or eGFR values indicative of CKD 3b/4 at index (anytime pre-index through 90 days post index); [c]mCCI; connective tissues and renal categories excluded; [d]Observed in electronic health records but may exclude biopsy procedures performed outside the participating healthcare network; [e]Within ±90 days of index (LN diagnosis).

creatinine, new-onset chronic kidney disease (CKD) Stage 3b/4, ESKD, dialysis, transplant and death. Week 52, 76 and 104 sub-cohorts included patients with follow-up data and ≥1 UPCR and eGFR during the post-index Week 52, 76 and 104 (±90 days) periods.

Results: Of 3279 patients, unfavorable kidney outcomes occurred in 37% and were more frequent in the following patients: older, longer disease duration, Black, greater comorbidities and poor baseline renal function Mean time in months (mo) from pre-index SLE diagnosis to index was 23 (SD 40). Baseline kidney biopsy (index ±6 mo) occurred in 49% of patients and more frequently in those diagnosed after 2021, with higher baseline UPCR, subsequent CRR and less frequent unfavorable kidney outcomes (P< 0.001). Immunosuppressant (IS) use (index +90 days) was 68%; mean time post-index to IS use, mo (SD) was: 5 (14); and a longer time to IS treatment was associated with poor outcomes (Table 1). Mean time from index to event, mo (SD) was: doubling of serum creatinine, 35 (33); CKD Stage 3b/4, 38 (37); ESKD, 42 (37); dialysis, 46 (38); transplant, 65 (44) and death, 61 (46).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Time to Initial CRR According to Baseline UPCR (A), Time to Initial Flare (B), Time to eGFR Decline by 20%, 30% and 40% (C), Time to Unfavorable Kidney Outcome (D)



Flare defined as: eGFR decrease >20% compared with baseline eGFR value; or increase in UPCR >1 g/g if UPCR <0.2 g/g or UPCR >2.0 g/g if UPCR ≥0.2 or doubling if UPCR >1 g/g compared with baseline values or receipt of intravenous methylprednisolone ≥100 mg with a SLE/LN diagnostic code (ICD-9 710* or 580-583 excluding 581.2, 582.2, 583.2, 583.6 and 583.7 or ICD-10 M32*) occurring ±14 days of the injection.
BL, baseline; CRR, complete renal response, eGFR, estimated glomerular filtration rate; LN, lupus nephritis; SLE, systemic lupus erythematosus; UPCR, urine protein-to-creatinine ratio.

Table 2. Unfavorable Kidney Outcome and Lupus Nephritis Flares According to CRR Status at Weeks 52, 76 and 104

	Week 52 Sub-Cohort				Week 76 Sub-Cohort				Week 104 Sub-Cohort			
	Overall	CRR+	CRR-	*P* value[a]	Overall	CRR +	CRR -	*P* value[a]	Overall	CRR+	CRR-	*P* value[a]
n (%)	**2009**	**726**	**1283**		**1712**	**655**	**1057**		**1488**	**571**	**917**	
Any unfavorable kidney outcome	**666 (33)**	141 (19)	525 (41)	<0.001	544 (32)	115 (18)	429 (41)	<0.001	478 (32)	96 (17)	382 (42)	<0.001
Unfavorable kidney outcome (excluding doubling of serum creatinine)	**519 (26)**	103 (14)	416 (32)	<0.001	424 (25)	89 (14)	353 (32)	<0.001	383 (26)	66 (12)	317 (35)	<0.001
Doubling of serum creatinine	**524 (26)**	110 (15)	414 (32)	<0.001	424 (25)	85 (13)	339 (32)	<0.001	360 (24)	69 (12)	291 (32)	<0.001
New-onset CKD stage 3b/4	**174 (9)**	41 (6)	133 (10)	<0.001	137 (8)	33 (5)	104 (10)	<0.001	126 (9)	23 (4)	103 (11)	<0.001
New-onset ESKD	**268 (13)**	45 (6)	233 (17)	<0.001	212 (12)	42 (6)	170 (16)	<0.001	186 (13)	28 (5)	158 (17)	<0.001
New-onset dialysis	**183 (9)**	21 (3)	162 (13)	<0.001	150 (9)	19 (3)	131 (12)	<0.001	125 (8)	13 (2)	112 (12)	<0.001
New-onset transplant	**125 (6)**	20 (3)	105 (8)	<0.001	100 (6)	13 (2)	87 (8)	<0.001	89 (6)	11 (2)	78 (9)	<0.001
Death	**142 (7)**	31 (4)	111 (9)	<0.001	121 (7)	28 (4)	93 (9)	<0.001	110 (7)	26 (5)	84 (9)	<0.001
LN flare	**1228 (61)**	382 (53)	846 (66)	<0.001	1027 (60)	338 (52)	689 (65)	<0.001	886 (59)	285 (50)	601 (66)	<0.001

Analyses were restricted to patients with follow-up data until the end of each time period of interest (eg, post-index Week 52 ±90 days, post-index Week 76 ± 90 days, and post-index Week 104 ±90 days) ***and*** who had ≥1 UPCR and eGFR during the specified time window. Unfavorable kidney outcomes and LN flares were identified that occurred after the end of the Week 52, 76 and 104 time periods, eg, post-week 52+12 weeks (eg, 90 days), post-week 76+12 weeks and post-week 104+12 weeks.
CKD, chronic kidney disease; CRR, complete renal response; ESKD, end-stage kidney disease; LN, lupus nephritis.
[a]*P* value based on Log rank test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

CRR was achieved in 53% of patients; mean time to initial CRR, mo (SD) was 16 (19) and varied by baseline UPCR (**-Figure 1a**). CRR at Week 52, 76 and 104 was 36%, 38% and 38% respectively. **Figure 1b** shows median time to initial flare. **Figure 1c** shows time to event according to 20, 30 and 40% eGFR decline. **Figure 1d** shows time to unfavorable kidney outcome.

Patients who achieved CRR were significantly less likely to experience an unfavorable kidney outcome or flare (**Table 2**).

Conclusion: Achieving CRR significantly reduced future severe kidney outcomes; however, a minority of patients who achieved CRR at Week 52, 76 or 104 had disease progression. Patients with high baseline UPCR had delayed CRR and those with longer time to initial IS treatment had worse long-term outcomes.

Disclosure: L. Lindsay: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **S. Wang**: Genesis Research LLC, 3; **H. Trinh**: Genentech, Inc., 3, Roche, 12, Shareholder; **Y. Huang**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2.

Abstract Number: 0839

Precision Liquid Biopsy for Lupus Nephritis: cfDNA Methylation and Fragmentomic Signatures Enable Non-Invasive Diagnosis and Dynamic Disease Tracking

Qiuyu Jing[1], Qiang Li[2], Chiu Wai Shirley Chan[3], Weixin Chen[4], Fung Yu Nick choi[4], **Iris Tang**[5], Chak Sing Lau[6], Heidi Ling[6], Jason Wong[7] and Philip Li[2], [1]Center for Oncology & Immunology, Hong Kong, Hong Kong, [2]Department of Medicine, The University of Hong Kong, Hong Kong, Hong Kong, [3]Division of Rheumatology and Clinial Immunology, Department of Medicine, the University of Hong Kong, Hong Kong, Hong Kong, China, [4]School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong, [5]Department of Medicine, LKS Faculty of Medicine, University of Hong Kong, Hong Kong, Hong Kong, [6]The University of Hong Kong, Hong Kong, Hong Kong, [7]School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hing Kong, Hong Kong

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis (0837–0842)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Lupus nephritis (LN), a severe complication of systemic lupus erythematosus (SLE), lacks reliable non-invasive biomarkers for early detection and monitoring. This study investigates plasma cell-free DNA (cfDNA) methylation and fragmentation signatures as potential LN biomarkers.

Methods: We performed whole-genome methylation profiling of plasma cfDNA from distinct cohorts: SLE patients with biopsy-proven LN (active: n=10 and inremission: n=7), SLE patients without LN (>10 years post-diagnosis, n=13), and healthy controls (n=10). Two novel methylation-based deconvolution methods were developed to quantify kidney-derived cfDNA and compared to classical non-negative least square (NNLS)algorithms. Fragmentation patterns were analyzed using cfDNA size profiles to differentiate active LN from remission.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

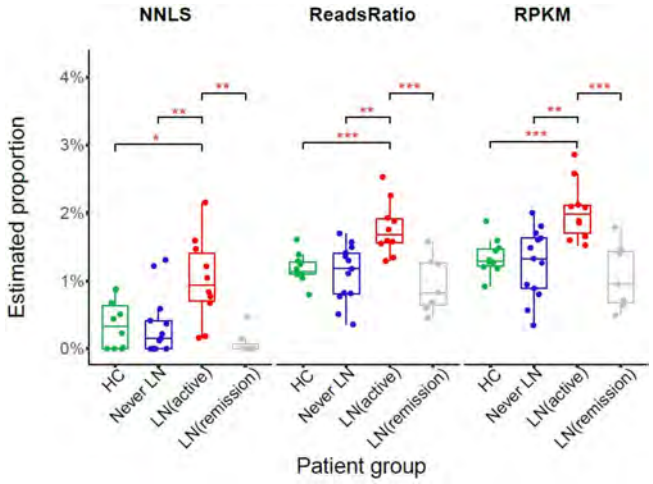


Figure 1. Kidney-derived cfDNA levels measured by three deconvolution methods are significantly elevated in active LN patients. *p < 0.05, **p < 0.01, ***p < 0.001.

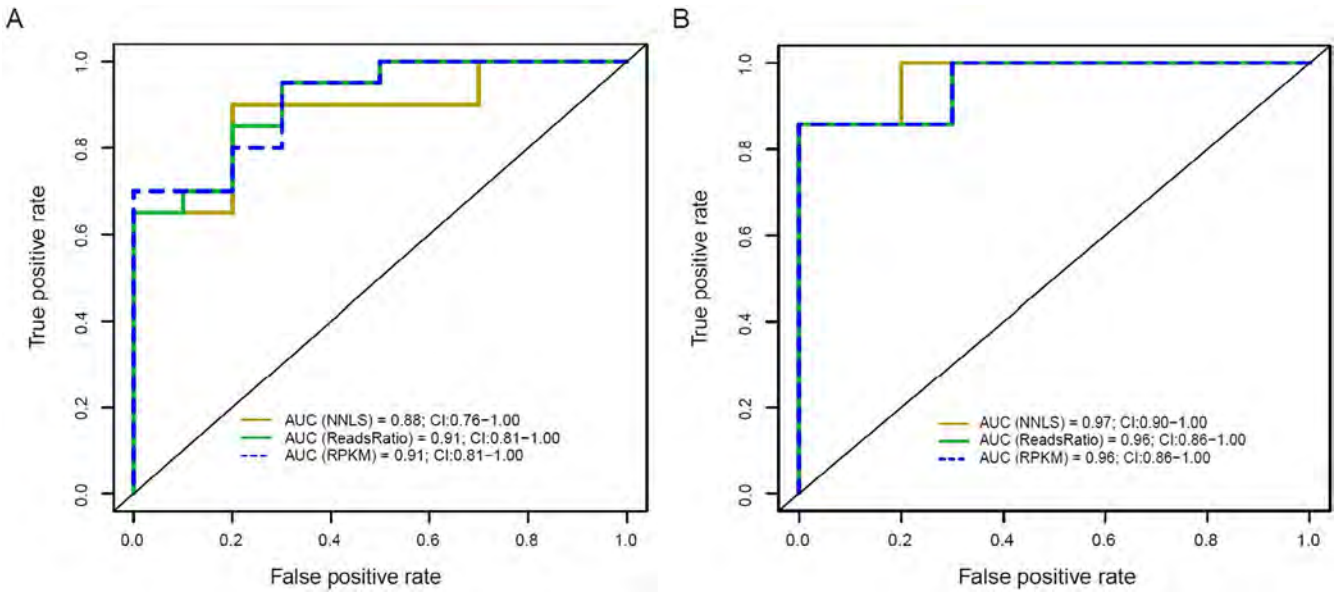


Figure 2. Receiver operating characteristic (ROC) curves of kidney-derived cfDNA levels profiled by NNLS, ReadsRatio and RPKM deconvolution algorithms distinguishing SLE patients with active LN from all other SLE patients (A) and SLE patients with active LN from those with LN in remission (B).

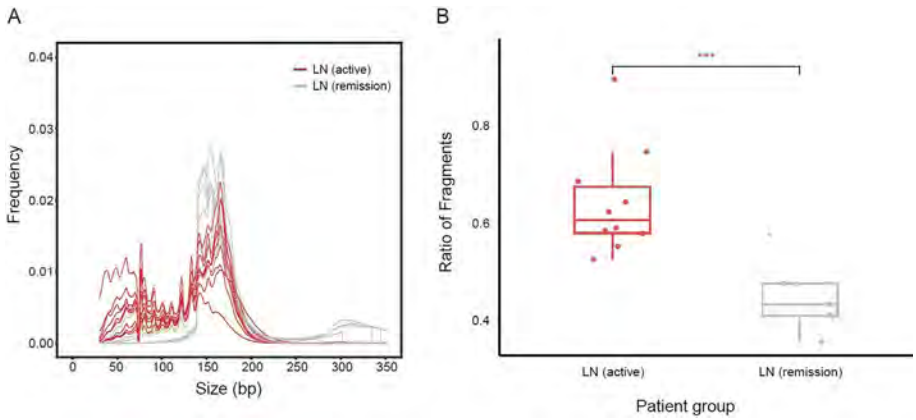


Figure 3. cfDNA fragmentation pattern for identification of active LN patients (red) and inactive LN patients (Grey). Plasma cfDNA fragments of 30-157bp are enriched in active LN patients compared to inactive LN patients. ***p < 0.001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Our novel deconvolution methods outperformed NNLS in detecting low-abundance cell types. Active LN patients exhibited significantly elevated kidney-derived cfDNA levels compared to remission, never-LN SLE, and healthy cohorts ($p< 0.05$ for all) (Figure 1). The reads ratio-based method achieved high diagnostic accuracy for active LN (AUC=0.91) (Figure 2). All three methods strongly correlated kidney-derived cfDNA levels with LN disease activity. Active LN patients also exhibited increased short cfDNA fragments (30–157 bp) compared to remission ($p< 0.001$) (Figure 3). Combining NNLS-derived kidney cfDNA levels with short fragment proportions enabled exceptional discrimination between active and remission LN (AUC=1).

Conclusion: Kidney-derived cfDNA levels and short fragment proportions are robust biomarkers for distinguishing active LN from remission and never-LN SLE. These findings underscore the clinical potential of cfDNA methylation and fragmentation profiling as a non-invasive tool for LN diagnosis, monitoring, and personalized treatment strategies.

Disclosure: Q. Jing: None; **Q. Li**: None; **C. Chan**: None; **W. Chen**: None; **F. choi**: None; **I. Tang**: None; **C. Lau**: None; **H. Ling**: None; **J. Wong**: None; **P. Li**: None.

Abstract Number: 0840

Shared and Distinct Urinary Proteomic Signatures of Lupus Nephritis and Other Glomerular Diseases

Alessandra Ida Celia[1], Daksh Saksena[2], CHEN-YU LEE[3], Carla Guthridge[4], Wade DeJager[5], Rufei Lu[4], Judith James[4], Jill Buyon[6], Michelle Petri[7], Joel Guthridge[4], Brad Rovin[8], **Andrea Fava**[3] and the Accelerating Medicines Partnership in RA/SLE and Autoimmune and Immune-Mediated Disease Program, [1]Sapienza University of Rome, Rome, Italy, [2]Johns Hopkins University, Baltimore, [3]Johns Hopkins University, Baltimore, MD, [4]Oklahoma Medical Research Foundation, Oklahoma City, OK, [5]Oklahoma Medical Research Foundation, Oklahoma City, [6]NYU Grossman School of Medicine, New York, NY, [7]Johns Hopkins University School of Medicine, Timonium, MD, [8]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis (0837–0842)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Urine collects the byproducts of kidney biology and has emerged as a valuable, noninvasive source of molecular information that reflects intrarenal pathology. In lupus nephritis (LN), multiple urinary signatures have been identified that associate with histologic activity, immune cell infiltration, and response to therapy. However, many of these biomarkers are not disease-specific and may also be elevated in other glomerular conditions. Comparing urinary proteomic profiles across inflammatory and non-inflammatory kidney diseases may uncover shared mechanisms of injury, while also revealing LN-specific signatures that could aid in diagnosis, monitoring, and therapeutic targeting.

Methods: Urine samples from patients with glomerular diseases including LN (ISN classes I–V), ANCA-associated glomerulonephritis, IgA nephropathy (IgAN), membranous nephropathy (MGN), and focal segmental glomerulosclerosis (FSGS) were collected near the time of biopsy and after screening for healthy controls (HC). Proteomic profiles were quantified using the Olink Explore HT platform (5,400 proteins). Here, we report findings for six candidate biomarkers previously linked to LN histological activity and progression: CD163, IL-16, Galectin 1 (LGALS1), Tenascin C (TNC), BAFF (TNFSF13B), and C9.

Results: We analyzed urine samples from 383 patients, including 234 with LN (21 Class I/II, 81 Class III ± V, 70 Class IV ± V, and 62 Class V), 17 with ANCA, 30 with IgAN, 30 with MGN, 30 with FSGS, and 31 healthy controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

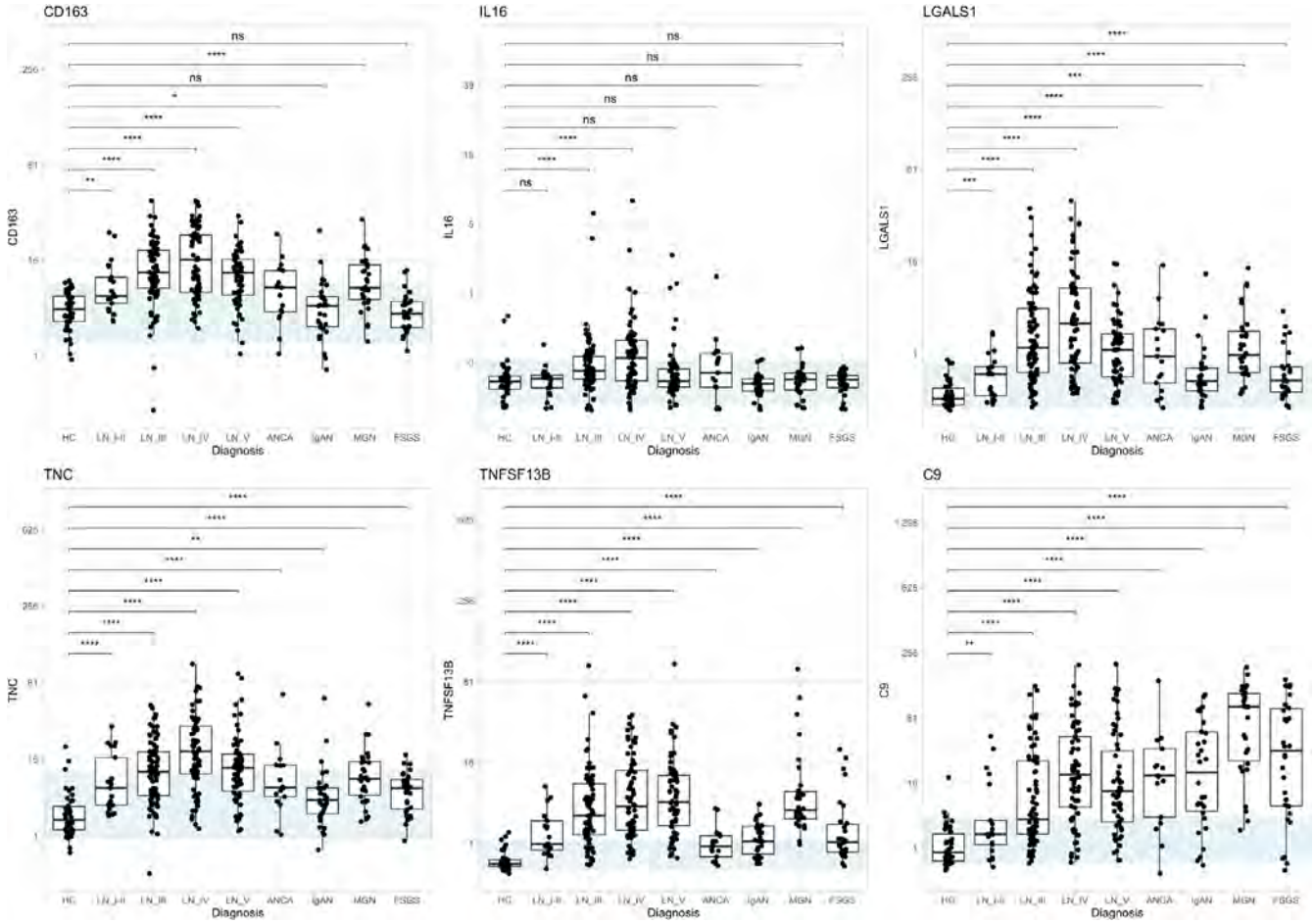


Figure 1. Urinary expression of inflammation- and fibrosis-associated proteins across glomerular diseases. Boxplots show normalized protein expression (NPX) of six urinary biomarkers—CD163, IL-16, Galectin-1 (LGALS1), Tenascin-C (TNC), BAFF (TNFSF13B), and C9—in healthy controls (HC) and patients with lupus nephritis (LN I–V), ANCA-associated vasculitis (ANCA), IgA nephropathy (IgAN), membranous nephropathy (MGN), or focal segmental glomerulosclerosis (FSGS). Each box depicts the median and interquartile range. The light-blue band marks the 5th–95th percentile range of HC values. Wilcoxon rank-sum tests comparing each disease group to HC are shown above each panel (ns, not significant; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$).

IL-16, previously linked to histologically active LN, was elevated in Class III/IV LN and in a subset of ANCA patients. CD163 was elevated in proliferative LN, in a subset of ANCA, and unexpectedly in MGN, but remained low in most IgAN cases . Galectin-1 was broadly elevated across glomerular diseases, but class II LN, IgAN and FSGS had relatively lower levels. TNFSF13B (BAFF) was increased in all conditions, but it was relatively higher in Class III, IV, and V LN, and in MGN, suggesting a stronger role in B cell–driven pathology in these conditions. C9 was elevated across all disease groups, indicating widespread complement activation. Tenascin C was highest in Class IV LN but also elevated in other LN classes and the other glomerular diseases, consistent with activation of prorepair and profibrotic pathways. Complement activation was enriched in all conditions.

Conclusion: Urinary biomarkers reveal both shared and disease-specific molecular pathways across glomerular diseases. The presence of common inflammatory and profibrotic signals—such as complement activation, macrophage involvement, and B cell–driven responses—highlights overlapping mechanisms of injury. At the same time, distinct expression patterns suggest unique pathogenic processes. These findings offer mechanistic insight into glomerular inflammation and fibrosis and, importantly, raise the potential for repurposing targeted therapies across traditionally distinct kidney diseases. Ongoing analysis of the full urinary proteome (~5,400 proteins) is expected to further expand our understanding of disease mechanisms and therapeutic opportunities.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Celia: None; **D. Saksena**: None; **C. LEE**: None; **C. Guthridge**: None; **W. DeJager**: None; **R. Lu**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. Guthridge**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2.

Abstract Number: 0841

Comparing the Impact of GLP-1 Agonists and SGLT-2 Inhibitors on Outcomes in Lupus Nephritis: A Retrospective Cohort Study

Kinga Grzybowski[1] and Irene Tan[2], [1]Jefferson Einstein Montgomery Hospital, Maspeth, NY, [2]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis (0837–0842)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Lupus Nephritis (LN) is one of the most serious complications of SLE (Systemic Lupus Erythematosus) characterized by an attack of the kidneys by the immune system which typically develops within 5 years of the initial diagnosis of SLE. It is suspected that up to 60% of those with SLE develop kidney-related complictions. Some complications of Lupus Nephritis include kidney failure requiring dialysis or transplantation, among other cardiovascular complications. Many medications exist for the management of some of the comorbidities associated with LN patients, but not much is known on the benefits on the condition itself. An observational, retrospective cohort study was designed which

Table 1: Complications and Outcomes in Patients with LN on SGLT2 inhibitors versus GLP-1 agonists

Outcomes[a,b]	LN on SGLT2	LN on GLP-1	RR (95% CI)	P-value
Dialysis (n,%)	36 (5.8%)	36 (6.26%)	0.926 (0.592-1.449)	0.7362
ESRD (n,%)	37 (6.38%	31 (5.91%)	1.08 (0.68-1.715)	0.7431
CKD (n,%)	75 (43.35%)	73 (28.4%)	1.526 (1.179-1.976)	0.0014
Renal Transplant (n,%)	<10 (1.59%)	12 (2.1%)	0.759 (0.331-1.744)	0.5146
Mortality (n,%)	48 (6.96%)	24 (3.48%)	2 (1.239-3.227)	0.0037
Acute MI (n,%)	37 (6.3%)	18 (2.8%)	2.248 (1.294-3.904)	0.0030
Stroke (n,%)	21 (3.541%)	13 (2.0%)	1.754 (0.886-3.472)	0.1018
Heart Failure (n,%)	39 (10%)	40 (7.1%)	1.421 (0.932-2.166)	0.1013

Abbreviations: Acute MI: Acute Myocardial Infarction, CKD: Chronic Kidney Disease, ESRD: End-Stage Renal Disease, GLP-1: glucagon-like peptide-1 agonists, LN: Lupus Nephritis, RR: Relative Risk, SGLT 2: sodium-glucose cotransporter-2 inhibitors, 95% CI: 95% Confidence Interval ; a- Propensity matched cohorts based on baseline demographics, comorbidities, and medication use. ; b- All patients with outcomes that occurred prior to the time window were excluded from our cohorts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

aimed to evaluate the effect of GLP-1 (glucagon-like peptide-1) agonists compared to SGLT2 (sodium-glucose cotransporter-2) inhibitors on the outcomes in patients with Lupus Nephritis using the TriNetX database which included electronic healthcare records from over 142 global collaborative healthcare organizations.

Methods: The study utilized patients 18 years or older with a diagnosis of LN (Lupus Nephritis) using the International Classification of Diseases, Tenth Revision (ICD-10) codes. Two different cohorts were created: the first cohort consisted of patient with LN who were on SGLT2 inhibitors, and the second cohort consisted of patients with LN who were on GLP-1 agonists. The index event in study was defined as the initial diagnosis of LN, later followed by three years of exposure to either SGLT-2 inhibitors or GLP-1 agonists. Propensity matching was used for the age at index, gender, race/ethnicity, comorbidities (hypertension, obesity, diabetes, tobacco use), and medications (DMARDS, steroids, biologics, statins, aspirin).

Results: A total of 1,375 patients with LN on SGLT2 inhibitors, and 1,034 patients with LN on GLP-1 agonists were reviewed. Before propensity matching was performed, patients on SGLT2 inhibitors were older (mean age of 51.9 vs. 48.2), consisted of more females (1,043 vs. 884), had more patients with hypertension (1,170 vs. 837), and consisted of mostly Black/African American patients when compared to the GLP-1 agonist group which consisted of mostly White patients. After propensity matching, 1,021patients were excluded, and a total of 694 patients remained in each group. Results showed that the group of patients with LN who were on GLP-1 agonists had reduced progression of chronic kidney disease (RR: 1.526, 95% CI: 1.179-1.976, p= 0.0014), decreased mortality (RR: 2, 95% CI: 1.239-3.227, p=0.0037), and a decreased risk of acute myocardial infarctions (RR: 2.248, 95% CI: 1.294-3.904, p=0.0030).

Conclusion: The findings suggest that patients with Lupus Nephritis taking GLP-1 receptor agonists have a reduced risk of mortality, acute myocardial infarctions, and a decreased progression of CKD compared to patients taking SGLT-2 inhibitors. Further research should be conducted with larger groups, and with longer follow up time to confirm and possibly explain any potential explanations or contributing factors.

Disclosure: K. Grzybowski: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

Abstract Number: 0842

Association of Urinary Biomarkers with Histological Features in Diagnostic and Per-protocol Repeat Kidney Biopsies in Lupus Nephritis

Andrea Fava[1], CHEN-YU LEE[1], Carla Guthridge[2], Dionysis Nikolopoulos[3], Julius Lindblom[4], Farah Tamirou[5], Michelle Petri[6], Joel Guthridge[2], Frederic Houssiau[7] and Ioannis Parodis[8], [1]Johns Hopkins University, Baltimore, MD, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [4]Karolinska Institutet, Stockholm, Sweden, [5]Cliniques universitaires Saint-Luc, Brussels, Belgium, [6]Johns Hopkins University School of Medicine, Timonium, MD, [7]CUSL, BRUSSELS, Belgium, [8]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes I: Advances in Nephritis (0837–0842)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Persistent intrarenal inflammation despite immunosuppression drives kidney damage and functional decline in lupus nephritis (LN). Yet, current guidelines do not recommend repeat biopsy to assess treatment response, relying instead on proteinuria, which does not reflect histological activity in >50% of cases. Urinary biomarkers are emerging

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient demographics and histological features at baseline and one-year repeat biopsy. (A) Demographic and (B) clinical characteristics including ISN/RPS class, NIH Activity and Chronicity indices, urine protein-to-creatinine ratio (UPCR), and estimated glomerular filtration rate (eGFR) at baseline (T0) and one-year follow-up (T1). *Paired biopsies at 1 year were available for 18 patients: one biopsy was unsuccessful, and one patient declined repeat biopsy.

A

	Total (N=20)
Sex - n(%)	
Female	19 (95.0%)
Male	1 (5.0%)
Race - n(%)	
African	6 (30.0%)
Asian	2 (10.0%)
Caucasian	12 (60.0%)
Age	
Mean (SD)	34.4 (9.62)

B

	T0 (N=20)	T1 (N=20)
Nephritis Class - n(%)		
II	0 (0%)	3 (15.0%)
III	3 (15.0%)	4 (20.0%)
III+/-V	5 (25.0%)	5 (25.0%)
IV	3 (15.0%)	0 (0%)
IV+/-V	7 (35.0%)	1 (5.0%)
V	2 (10.0%)	5 (25.0%)
NA*	0 (0%)	2 (10.0%)
Activity		
Median [Min, Max]	6.00 [0, 14.0]	0.500 [0, 7.00]
Chronicity		
Median [Min, Max]	2.00 [0, 5.00]	2.00 [0, 8.00]
Urine Protein/Creatinine		
Median [Min, Max]	1.65 [0.600, 6.80]	0.295 [0, 6.95]
eGFR CKD-EPI		
Mean (SD)	80.7 (33.0)	88.7 (29.7)

*NA: Non-available

as a promising alternative to assess histological activity and predict long-term renal outcomes. We evaluated candidate biomarkers previously linked to histological activity and risk of renal function loss in LN patients undergoing per-protocol repeat kidney biopsies one year after treatment initiation.

Methods: Twenty LN patients enrolled in Belgium and Sweden underwenta diagnostic and a per-protocol kidney biopsy one year after diagnosis. Treatment was discretionary. Urine samples were collected at time of diagnosis and one-year repeat biopsy, and profiled using Olink Explore HT (5416 proteins). Four candidate biomarkers were selected based on prior associations with histological activity (IL16, soluble CD163), renal function loss (Tenascin C), or B cell activity (BAFF).

Results: At baseline, 18/20 (90%) had ISN/RPS class III or IV +/- V LN and 2/20 (10%) pure class V (**Table 1**). Paired biopsies at one year were available for 18 patients (16 proliferative): one biopsy was unsuccessful, and one patient declined repeat biopsy. After one year of treatment, only 6/16 (37%) patients transitioned from proliferative to non-proliferative

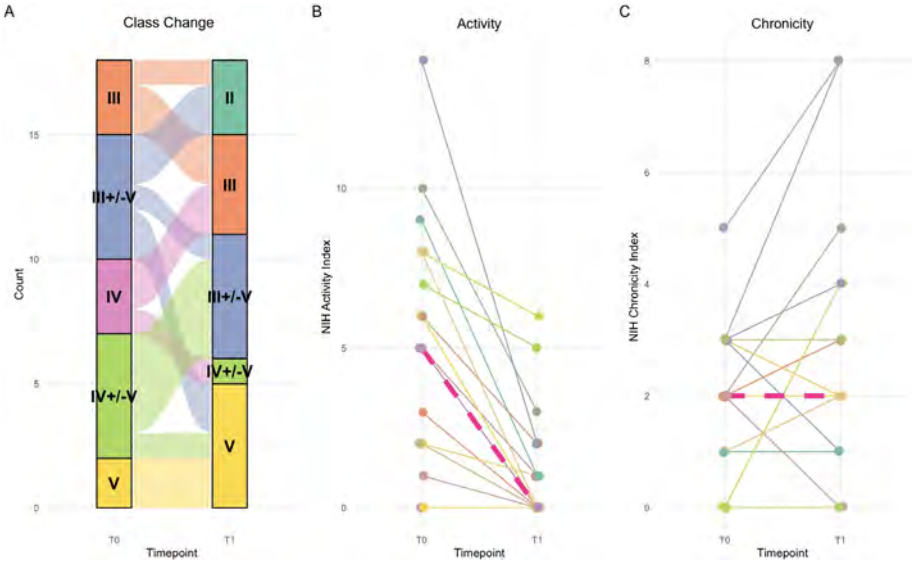


Figure 1. Transition of lupus nephritis (LN) class and histologic indices from baseline to one-year repeat biopsy. (A) Alluvial plot shows individual transitions in ISN/RPS class from T0 to T1, highlighting class change from proliferative to non-proliferative LN. (B) Individual paired trajectories of NIH activity index, showing reduction at T1 for all patients with Activity Index >0 at baseline. (C) Chronicity index at T0 and T1. The medians of the NIH Activity and Chronicity Indices at T0 and T1 are shown by the pink dashed line. Only patients with paired biopsies included (n=18)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

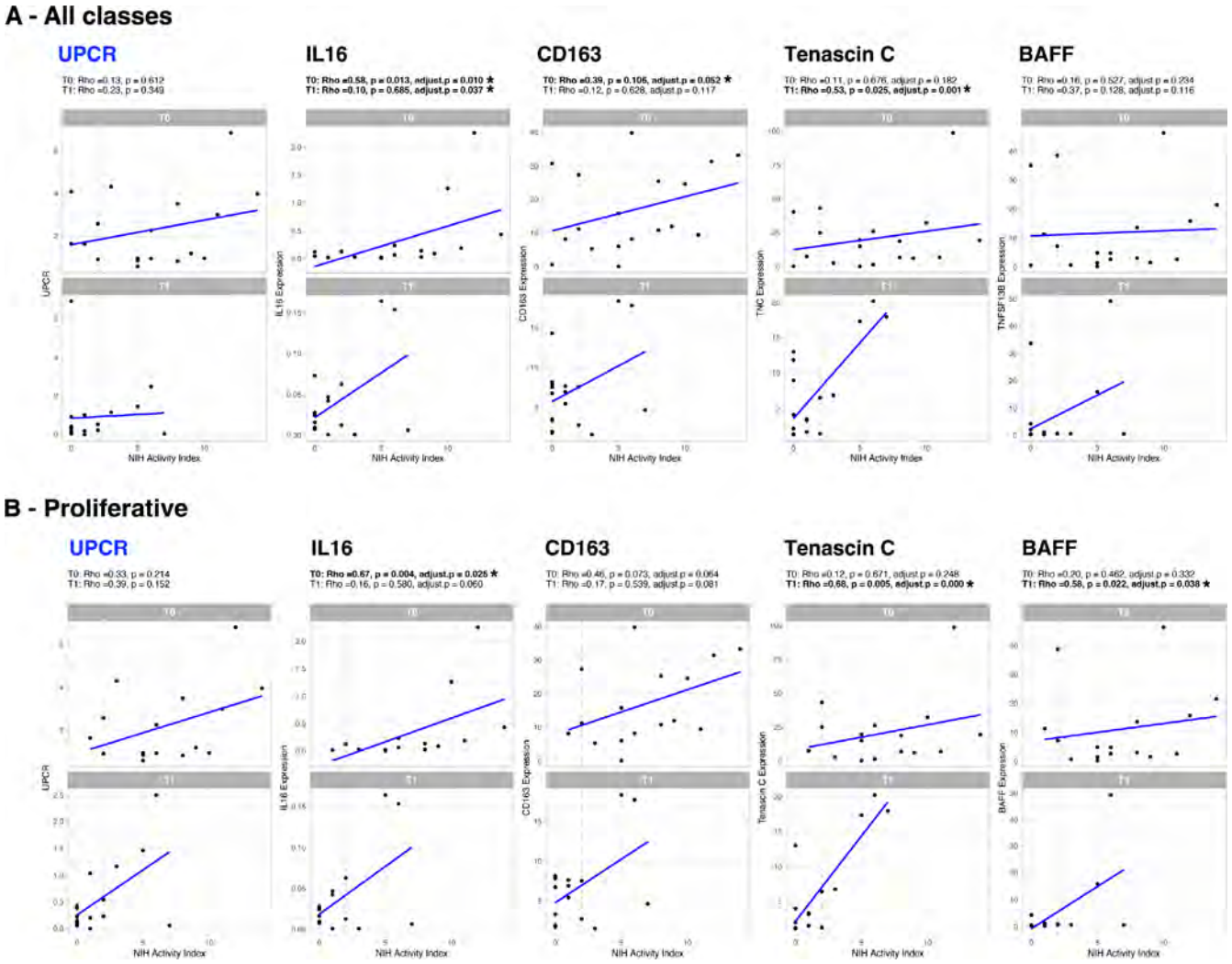


Figure 2. Correlation between urinary biomarkers and histologic activity at baseline (T0) and follow-up (T1). (A) All patients. (B) Subset with proliferative lupus nephritis. Proteins are expressed as normalized protein expression (NPX) and normalized by plate-controls. Correlation with NIH Activity Index was assessed using Spearman's rank correlation. P.adjust indicates the p value after adjusting for urine creatinine (linear model). For BAFF, most of the variability contributing to the correlation was in the lower range and not well visualized on the scale shown; the scale was kept unchanged for consistency across plots. UPCR: urine protein-to-creatinine ratio.

classes, but the NIH Activity Index declined in all proliferative LN patients (**Figure 1**). Although the NIH Chronicity Index increased in several patients, the median value remained unchanged because of improved scores in a subset. At one year, 10/16 (62%) patients still had persistent proliferative LN but only 6/16 (37%) had an activity index $\geq$2.

Proteinuria did not correlate with histological activity at baseline or at one year (**Figure 2**). At baseline, urinary IL-16 and sCD163 correlated with histological activity, especially in proliferative LN, but these associations diminished at follow-up. In contrast, urinary Tenascin C (a marker of myofibroblast activation) and BAFF were associated with histological activity at one year .

Conclusion: Urinary IL16 and sCD163 correlated with histological activity at diagnosis, whereas Tenascin C and BAFF associated with histological activity at one year, suggesting a potential temporal shift in dominant inflammatory pathways—from macrophage-driven inflammation to stromal activation and B cell persistence. Notably, urinary sCD163 at one year has been shown to predict future renal function loss but it was not correlated with one-year histological activity, highlighting a disconnect between histological and urinary predictors of outcome. This underscores the value of urinary biomarkers as complementary tools that may capture molecular activity missed by biopsy. Given the limited sample

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

size, these findings require validation in larger cohorts. Together, these results support urinary biomarkers as a noninvasive strategy to complement histologic and clinical assessment, offering insight into disease activity not always reflected by traditional measures.

Disclosure: A. Fava: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **C. LEE**: None; **C. Guthridge**: None; **D. Nikolopoulos**: None; **J. Lindblom**: None; **F. Tamirou**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. Guthridge**: None; **F. Houssiau**: Roche-Genentech, 5; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5.

Abstract Number: 0843

Efficacy and Safety of BMS-986353, a CD19-Directed Chimeric Antigen Receptor T Cell Therapy Manufactured Using a Next-Generation Process: Updated Data From a Phase 1 Trial in Patients With Systemic Sclerosis

Dinesh Khanna[1], David Korman[2], Elana Bernstein[3], Neil Kramer[4], Vikas Majithia[5], Philip J. Mease[6], Georg Schett[7], Jacques Azzi[8], Richard Nash[9], Ran Reshef[3], Mohammad Cherry[10], Ernesto Ayala[5], Matthew Schwede[11], Monalisa Ghosh[12], Fabian Müller[13], Alisha Desai[14], San-San Ou[15], Sharmila Das[14], Jerill Thorpe[16], Melissa Harnois[14], Alexis Melton[16], Ashley Koegel[16] and Margrit Wiesendanger[8], [1]University of Michigan, Ann Arbor, MI, [2]Mountain Rheumatology, Denver, CO, [3]Columbia University Irving Medical Center, New York, NY, [4]Overlook Medical Center; Atlantic Medical Group, Atlantic Health System, Summit, NJ, [5]Mayo Clinic Hospital, Jacksonville, FL, [6]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [7]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [8]Icahn School of Medicine at Mount Sinai, New York, NY, [9]Health One Cares, Denver, CO, [10]Atlantic Health System, Morristown, NJ, [11]Swedish Cancer Institute, Seattle, WA, [12]C. S. Mott Children's Hospital University of Michigan Health, Ann Arbor, MI, [13]University Hospital of Erlangen, Erlangen, Germany, [14]Bristol Myers Squibb, Princeton, NJ, [15]Bristol Myers Squibb, Seattle, WA, [16]Bristol Myers Squibb, Princeton

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical I (0843–0848)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: BMS-986353 (CC-97540) is an investigational CD19-directed T-cell therapy expressing the chimeric antigen receptor (CAR) used in globally-approved lisocabtagene maraleucel; it is manufactured via the NEX-T™ process to shorten manufacturing time and optimize phenotypic attributes. Early data from Breakfree-1 trial (NCT05869955) in severe, refractory autoimmune diseases (ADs) showed promising efficacy and manageable safety with BMS-986353.[1] Here, we report updated data on BMS-986353 in the SSc cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. CRS and ICANS by DL. a: Multiple events occurring within 7 days from each other are considered as 1 episode. CRS, cytokine release syndrome; DL, dose level; ICANS, immune effector cell-associated neurotoxicity syndrome.

CRS and ICANS by DL

	DL1 (n = 8)		DL2 (n = 1)	
	CRS	ICANS	CRS	ICANS
Maximum grade, n (%)				
Grade 1	3 (37.5)	1 (12.5)	0	0
Grade 2	1 (12.5)	0	0	0
Grade 3–5	0	0	0	0
Median onset (range), days	7.5 (3–10)	10.0	–	–
Median duration[a] (range), days	2.0 (2–2)	3.0	–	–
Treatments, n (%)			–	–
Tocilizumab	2 (25.0)	0	–	–
Dexamethasone	0	1 (12.5)	–	–

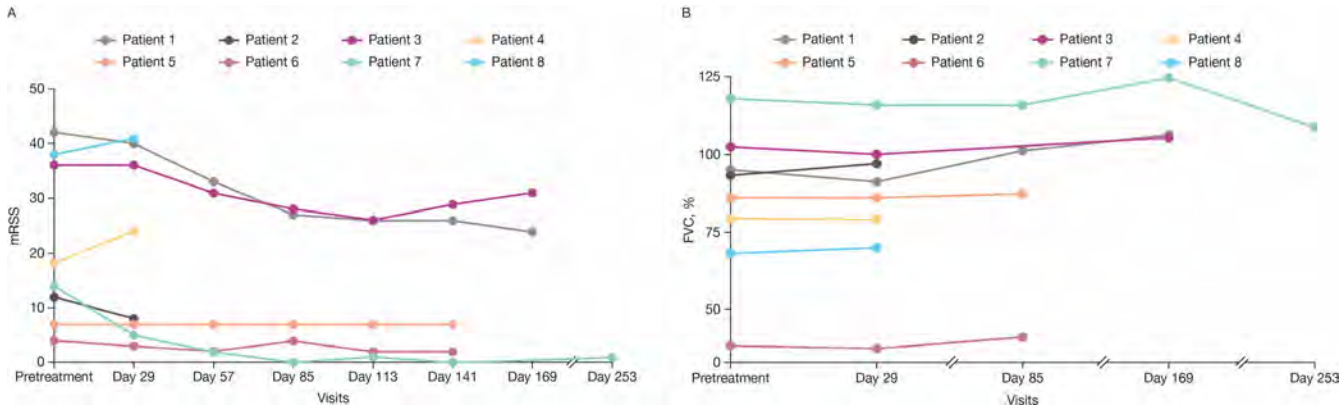


Figure 1. (A) mRSS and (B) FVC in pts with SSc ≥ 1 month post-BMS-986353 at DL1 and DL2. FVC, forced vital capacity; mRSS, modified Rodnan skin score.

Methods: This phase 1 study assesses safety and efficacy in patients (pts) with severe, refractory ADs, including recently progressing diffuse SSc or limited SSc with interstitial lung disease (ILD) and inadequate response to ≥ 1 immunosuppressant. All SSc-directed therapies were discontinued before BMS-986353 infusion. Pts received a single infusion of BMS-

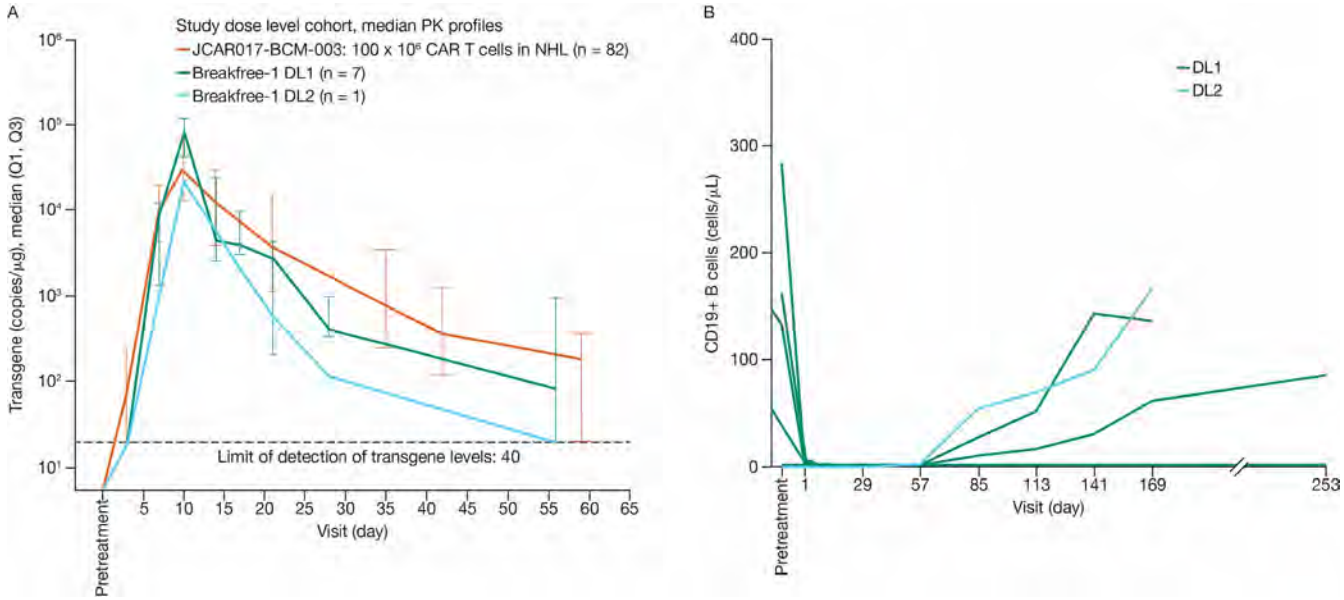


Figure 2. (A) Pharmacokinetic profile compared with lisocabtagene maraleucel and (B) B cell depletion. NHL, non-Hodgkin lymphoma; PK, pharmacokinetic; Q, quartile.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

986353 at 10×10^6 (dose level [DL] 1) or 25×10^6 (DL2) CAR+ T cells after lymphodepletion. Primary endpoint was safety.

Results: As of April 7, 2025, 14 pts with SSc were enrolled; 9 pts received BMS-986353 (DL1, n = 8; DL2, n = 1), with a median follow-up of 115.5 days (range 42–295) for DL1 and 168 days for DL2. Median age: 54.5 years for DL1, 41 years for DL2. Prior therapies: median 2 (range 1–5) for DL1 and 3 for DL2. At baseline, DL1 pts had a median modified Rodnan skin score (mRSS) of 18.0 and Physician's Global Assessment (PGA) score of 7.0; scores for the DL2 pt were 7.0 and 4.0, respectively. ILD was present in 6 pts. Eight pts were efficacy evaluable (7 DL1, 1 DL2).

All inflammatory AEs (iAE) reported were low grade. In DL1, 50.0% of pts had cytokine release syndrome (CRS; 3 grade 1, 1 grade 2) with a median duration of 2.0 days; 1 pt had grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS) that resolved in 3 days (**Table**). There were 4 transient, self-resolving grade ≥ 3 hematologic TEAEs in DL1 pts; none in DL2. There were no prolonged grade ≥ 3 cytopenias, dose-limiting toxicities, or treatment-related infections.

In DL1, median increase from baseline in absolute forced vital capacity in all patients was 3.0% on day 85 (n = 3) and 7.0% at day 169 (n = 3). In DL1, median reduction in mRSS across all pts with diffuse cutaneous SSc regardless of baseline mRSS was 14.0 points at day 85 (n = 3) and 11.5 at day 169 (n = 2) (**Figure 1**). Median reduction in PGA from baseline was 3.0 points on day 85 (DL1 n = 4; DL2 n = 1) and 4.5 on day 169 (DL1 n = 2). Improvement from baseline in revised Composite Response Index in Systemic Sclerosis was achieved in 3/3 pts at day 85 and day 169. All pts had robust CAR T cell expansion and achieved complete peripheral B-cell depletion (**Figure 2**).

Conclusion: BMS-986353 showed an acceptable safety profile and preliminary meaningful improvement in skin thickening and lung function in pts with severe, refractory SSc. iAEs were grade 1/2 and resolved quickly. Updated safety, efficacy, and translational data will be presented.

Reference: 1. Schett G, et al. *Arthritis Rheumatol* 2024;76(suppl 9):1753.

Medical writing: Joaquin Jaramillo, MD (Caudex, an IPG Health company), funded by Bristol Myers Squibb.

Disclosure: D. Khanna: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **D. Korman**: None; **E. Bernstein**: AstraZeneca, 5, aTYR, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **N. Kramer**: Amgen, 11, AstraZeneca, 5, 6, Becton Dickinson, 11, Bristol-Myers Squibb(BMS), 2, 5, GlaxoSmithKlein(GSK), 5, 6, Immunic, 11, Johnson & Johnson, 11, Pfizer, 11, Protagonist Therapeutics, 11, Stryker, 11, UpToDate, 12, author; **V. Majithia**: None; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **J. Azzi**: None; **R. Nash**: None; **R. Reshef**: AbbVie/Abbott, 5, Allogene, 2, Atara, 5, Autolus, 2, Bayer, 12, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, CareDx, 5, Genentech, 5, Gilead, 2, 5, Immatics, 5, Incyte, 2, 5, Johnson & Johnson, 5, Orca, 2, Precision, 5, Quell, 2, Sanofi, 5, Synthekine, 5, Takeda, 5, TCR2, 5, TScan, 2, 5; **M. Cherry**: Bristol-Myers Squibb(BMS), 6; **E. Ayala**: None; **M. Schwede**: AbbVie/Abbott, 2; **M. Ghosh**: None; **F. Müller**: AbbVie/Abbott, 6, ArgoBIO, 2, AstraZeneca, 2, 6, Beigene, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CRISPR Therapeutics, 2, EcoR1, 2, Incyte, 6, Janssen, 2, 6, Kite/Gilead, 2, 5, 6, Merck/MSD, 6, Miltenyi, 2, 6, Novartis, 2, 6, Pfizer, 6, Sobi, 2, 6, Takeda, 6; **A. Desai**: Bristol-Myers Squibb(BMS), 3; **S. Ou**: Bristol-Myers Squibb(BMS), 3; **S. Das**: Bristol-Myers Squibb(BMS), 3, 11, Deciphera Pharmaceuticals, 2; **J. Thorpe**: Bristol-Myers Squibb(BMS), 3; **M. Harnois**: Bristol-Myers Squibb(BMS), 3, 11; **A. Melton**: Bristol Myers Squibb, 3; **A. Koegel**: Bristol-Myers Squibb(BMS), 3, 11; **M. Wiesendanger**: Bristol-Myers Squibb(BMS), 1, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0844

Machine Learning Model Incorporating Baseline and Early Follow-up Clinical Data Predicts 52-Week Cutaneous Outcomes in Systemic Sclerosis

Kimberly Lakin[1], John Spivack[1], Jessica Gordon[1], Dana Orange[2] and Robert Spiera[3], [1]Hospital for Special Surgery, New York, NY, [2]Rockefeller University, New York, [3]Scleroderma, Vasculitis, and Myositis Center, Hospital for Special Surgery, Weill Cornell Medical College, New York, NY

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical I (0843–0848)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: As treatment options for diffuse cutaneous systemic sclerosis (dcSSc) expand, the need for data-driven, efficient approaches to therapeutic switching is becoming more urgent. Additionally, clinical trials may choose to add early exit strategies for patients highly unlikely to improve so that other treatment options can be explored. The purpose

Table 1. Characteristics of individuals with diffuse systemic sclerosis, by 52-week cutaneous improvement

Feature	Non-improver (n=126)	Improver (n=235)	p-value
Age	51 (43, 57)	52 (41, 61)	0.73
Male sex	31 (25%)	57 (24%)	1.00
Disease duration (months)	30.8 (19.1, 44.1)	29.35 (14.9, 44.1)*	0.66
Race			0.58
White	87 (69%)	163 (69%)	
Black or African American	7 (6%)	11 (5%)	
Asian	24 (19%)	50 (21%)	
Other	8 (6%)	11 (5%)	
Autoantibody profile			
RNA polymerase III positive	45 (36%)	101 (43%)	0.22
Scl-70 positive	63 (50%)	96 (41%)	0.097
Centromere positive	9 (7%)	8 (3%)	0.12
Digital ulceration, present	51 (41%)	90 (38%)	0.65
Renal crisis, history	0 (0%)	1 (0.4%)	1.00
Pulmonary			
Interstitial lung disease (chest CT)	62 (52%)	109 (47%)	0.50
%-predicted FVC, baseline	79 (67, 91) (n=122)	81 (70, 92) (n=233)	0.35
%-predicted FVC, 14 weeks	81 (67, 91) (n=115)	82 (69, 93) (n=233)	0.13
%-predicted FVC, 26 weeks	79 (67, 90) (n=108)	80.87 (68, 92) (n=225)	0.15
Laboratory			
Elevated acute phase reactant*	52 (42%)	101 (43%)	0.91
Elevated creatine phosphokinase	23 (18%)	38 (17%)	0.77
Albumin, g/L	43 (40, 45)	43 (41, 45) (n=233)	0.45
Neutrophil-to-lymphocyte ratio	3.4 (2.4, 4.8)	3.1 (2.2, 4.3) (n=229)	0.26
Treatment†			
Methotrexate	25 (20%)	34 (15%)	0.23
Mycophenolate mofetil	53 (42%)	138 (59%)	**0.003**
Immunosuppression, any	90 (71.4%)	202 (86%)	**0.001**
Modified Rodnan Skin Score (mRSS)			
Maximum mRSS prior to baseline	21 (17, 29) (n=114)	23 (18, 31) (n=210)	0.13
mRSS, baseline	20.5 (16, 25)	21 (17, 28)	0.075
mRSS, 14 weeks	18 (13, 26) (n=119)	17 (12, 22) (n=234)	**0.025**
mRSS, 26 weeks	18 (13, 25) (n=110)	15 (11, 20) (n=226)	**<0.001**
Physician Global Assessment (PhGA)			
PhGA, baseline	5 (5, 6)	5 (4, 7)	0.43
PhGA, 14 weeks	5 (4, 6) (n=119)	4 (3, 5) (n=234)	**<0.001**
PhGA, 26 weeks	5 (3, 6) (n=110)	4 (3, 5) (n=225)	**<0.001**
Patient Reported Outcomes			
PGA, baseline	5 (4, 7)	5 (3, 6)	0.073
PGA, 14 weeks	5 (3, 7) (n=118)	5 (3, 6) (n=233)	0.053
PGA, 26 weeks	5 (3, 6) (n=109)	4 (2, 6) (n=225)	0.10
HAQ, baseline	1.125 (0.375, 1.625)	1.125 (0.375, 1.75)	0.57
HAQ, 14 weeks	1.125 (0.5, 1.625) (n=126)	1 (0.375, 1.625)	0.78
HAQ, 26 weeks	1.125 (.5, 1.75)	1 (.25, 1.625)	0.20
5D Itch, baseline	11 (9, 14)	12 (9, 15)	0.61
5D Itch, 14 weeks	11 (8, 14) (n=118)	10 (8, 13) (n=233)	0.24
5D Itch, 26 weeks	11 (8, 15) (n=109)	10 (8, 12) (n=225)	**0.012**
SSPRO (total), baseline	46.8 (30.6, 66.7)	47.2 (30.6, 64.8)	0.84
SSPRO (total), 14 weeks	41.2 (22.2, 65.7) (n=118)	35.2 (20.4, 57.4) (n=233)	0.13
SSPRO (total), 26 weeks	36.1 (18.5, 65.7407) (n=109)	30.6 (15.7, 53.7) (n=225)	**0.028**

Categorical variables presented as n (%) and compared using Fisher's exact; continuous variables presented as median (interquartile range) and compared using Wilcoxon rank-sum. *One participant's disease duration was beyond that allowed in the trial and equal to the Raynaud's duration; therefore, treated as missing. †Treatment represents exposure during the 52-week period. ‡Represents elevated erythrocyte sedimentation rate, c-reactive protein, or complement. PGA=patient global assessment; HAQ=Health Assessment Questionnaire; SSPRO= Scleroderma Skin Patient Reported Outcome

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

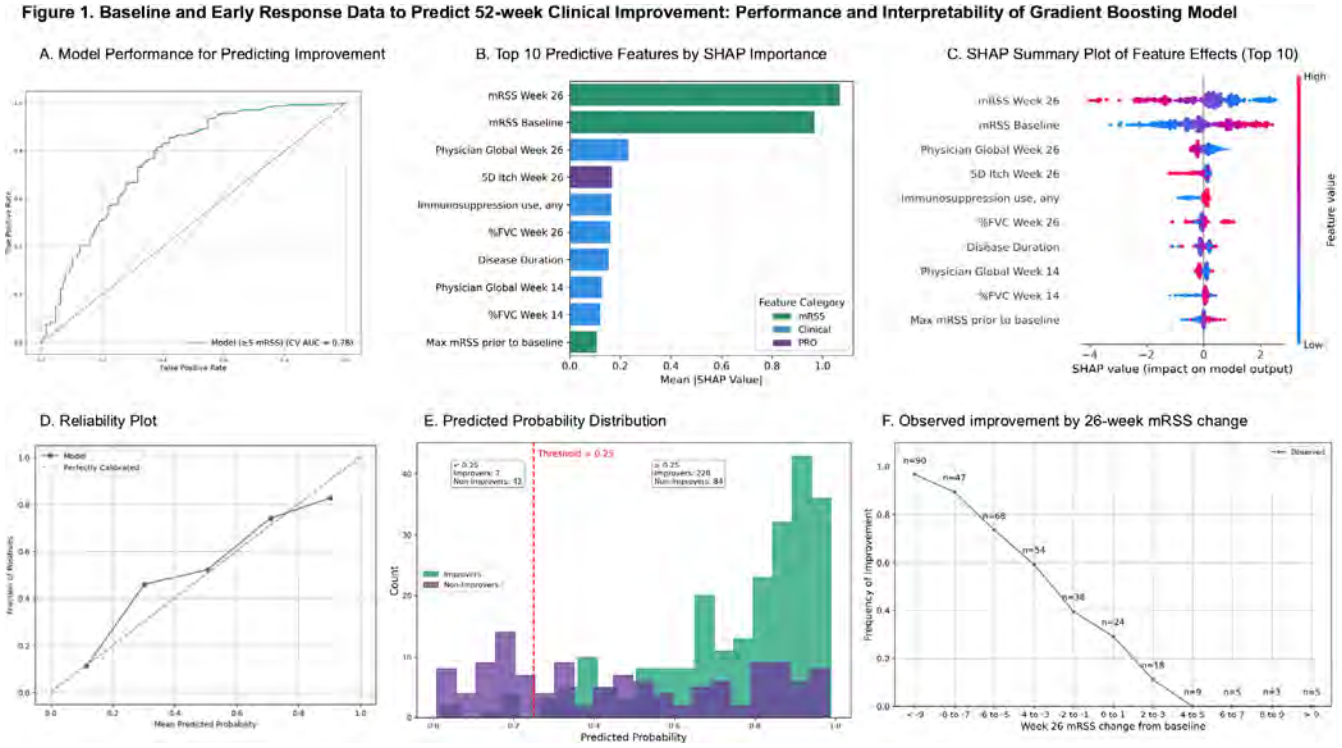


Figure 1. Baseline and early response data to predict 52-week clinical improvement among individuals with diffuse cutaneous systemic sclerosis: Performance and interpretability of gradient boosting model. A. Receiver Operating Characteristic Curve for machine learning model to predict 52-week clinical improvement (at least 5-point modified Rodnan skin score (mRSS) improvement at week 52) with cross-validated area under the curve (AUC) of 0.78. B. Top 10 features ranked by mean SHAP importance. (C) SHAP summary plot illustrates individual feature effects on model predictions. Each dot represents a single patient; red represents high values; blue represents low values. Positive SHAP values contribute to higher probability of clinical improvement, while negative SHAP values contribute to lower probability. D. Reliability plot indicating good agreement between predicted and observed outcomes. E. Histogram of predicted probabilities for 52-week improvers and non-improvers with threshold of 0.25 shown. F. Frequency of 52-week improvement according to baseline to 26-week mRSS change.

of this study is to develop a model for predicting 52-week cutaneous improvement in dcSSc using clinical data collected at baseline, 14, and 26 weeks.

Methods: Clinical data were analyzed from 361 individuals enrolled in RESOLVE-1 (Lenabasum Phase III trial). Cutaneous improvement was defined as ≥5-point decrease in modified Rodnan skin score (mRSS) from baseline to 52 weeks. Characteristics were compared between improvers and non-improvers using Fisher's exact or Wilcoxon rank-sum, as appropriate. A gradient boosting, supervised machine learning model was developed for predicting improvement. 43 candidate predictors were selected by expert opinion and included baseline, 14-, and 26-week data. Model discrimination for classifying improvement status was assessed using area under the receiver operating characteristic curve (AUROC) with five-fold cross-validation. To enhance interpretability, the Shapley Additive exPlanations (SHAP) method was used to visualize the magnitude and directionality of features' individual impact on predictions. A reliability plot was generated to compare predictions to observed outcomes. Observed 52-week improvement was plotted by baseline to 26-week mRSS change.

Results: Of 361 patients with dcSSc, 235 (65%) improved. Immunosuppression (any) and mycophenolate mofetil use were more common among improvers vs. non-improvers **(Table 1)**. By 26-weeks, 52-week improvers had lower physician global ($p< 0.001$), 5D-Itch ($p=0.012$), and Scleroderma Skin Patient Reported Outcome (total score) ($p=0.028$) vs. non-improvers. By both week 14 and 26, 52-week improvers had significantly lower mRSS vs. non-improvers (17 vs. 18, $p=0.025$; 15 vs. 18, $p< 0.001$).

The model accurately predicted 52-week cutaneous improvement with a cross-validated AUROC of 0.78 (**Fig. 1A)** and good reliability (**Fig. 1D**). The top 10 predictive features by mean SHAP value are shown in **Fig. 1B**, with mRSS at week

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

26 and baseline as the two most important features. Higher week-26 mRSS contributed to lower improvement prediction, whereas higher baseline mRSS contributed to higher improvement prediction **(Fig. 1C)**. Predicted probabilities for improvers and non-improvers are shown in **Fig. 1E**. Applying a probability threshold of 0.25 identifies improvers with a sensitivity of 97% (i.e., only 3% of improvers below 0.25 threshold at 26 weeks) and a negative predictive value of 0.86 (i.e., of those predicted to be non-improvers, 86% did not improve). 52-week improvement was uncommon among those who had not experienced any mRSS decline by week 26 (**Fig. 1F**).

Conclusion: Improvement in mRSS at 52 weeks can be reliably predicted using baseline and early follow-up data, identifying those unlikely to improve on current therapy. This model may inform personalized clinical decision making as well as adaptive trial designs with early exit strategies for those highly unlikely to improve.

Disclosure: K. Lakin: None; **J. Spivack**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **D. Orange**: None; **R. Spiera**: Abbvie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Certa, 2, Chemocentryx, 2, 5, Corbus, 5, Cytori, 2, 5, Galderma, 2, GlaxoSmithKlein(GSK), 2, 5, Horizon, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Regeneron, 2, Roche-Genentech, 2, 5, Sanofi, 2, Vera Therapeutic, 2.

Abstract Number: 0845

Machine Learning–Based Skin Transcriptome Classifier (v2.0) Links SSc Molecular Subtypes to Disease Severity and Progression

Zhiyun Gong[1], Rezvan Parvizi[2], Helen Jarnagin[1], Haobin Chen[3], Madeline Morrisson[4], Tammara Wood[5], Monique Hinchcliff[6], Dinesh Khanna[7] and Michael Whitfield[8], [1]Dartmouth College, Lebanon, NH, [2]Dartmouth, lebanon, NH, [3]Dartmouth Collge, Lebanon, NH, [4]Geisel School of Medicine at Dartmouth College, Hanover, NH, [5]Dartmouth, Hanover, NH, [6]Yale School of Medicine, Westport, CT, [7]University of Michigan, Ann Arbor, MI, [8]Geisel School of Medicine, Lebanon, NH

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical I (0843–0848)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Systemic Sclerosis (SSc) is a clinically and molecularly heterogeneous autoimmune disease. We identified five intrinsic molecular subtypes in SSc by applying semi-supervised machine learning methods to multiple transcriptomic cohorts. A supervised single-sample classifier was developed for subtype predictions. Here, this predictive classifier is validated in multiple independent datasets and is used to comprehensively assess the association between molecular heterogeneity of SSc and key clinical features, extending our previous SSc subtyping research.

Methods: We trained a stacked-ensemble model for intrinsic subtype prediction using GSVA enrichment scores in an integrated discovery cohort of 137 SSc and 37 Healthy participants (GSE9285, GSE32413, and GSE59787). Base learners were binary one-vs-all logistic regression models whose predicted probabilities were then combined by a Random Forest meta-learner. This model was applied to external DNA microarray and RNA-seq cohorts for assessment and validation. We tested associations between predicted subtypes and clinical features, such as FVC, DLCO, MRSS, ILD-risk, and autoantibody status. Discrete variables were compared with Odds Ratios (OR) test; continuous variables were tested using Wilcoxon rank-sum tests.

Results: We identified 5 intrinsic molecular subtypes of SSc through semi-supervised clustering and comparison to original publications. We identified an inflammatory-fibroproliferative group and an intermediate group between inflammatory and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

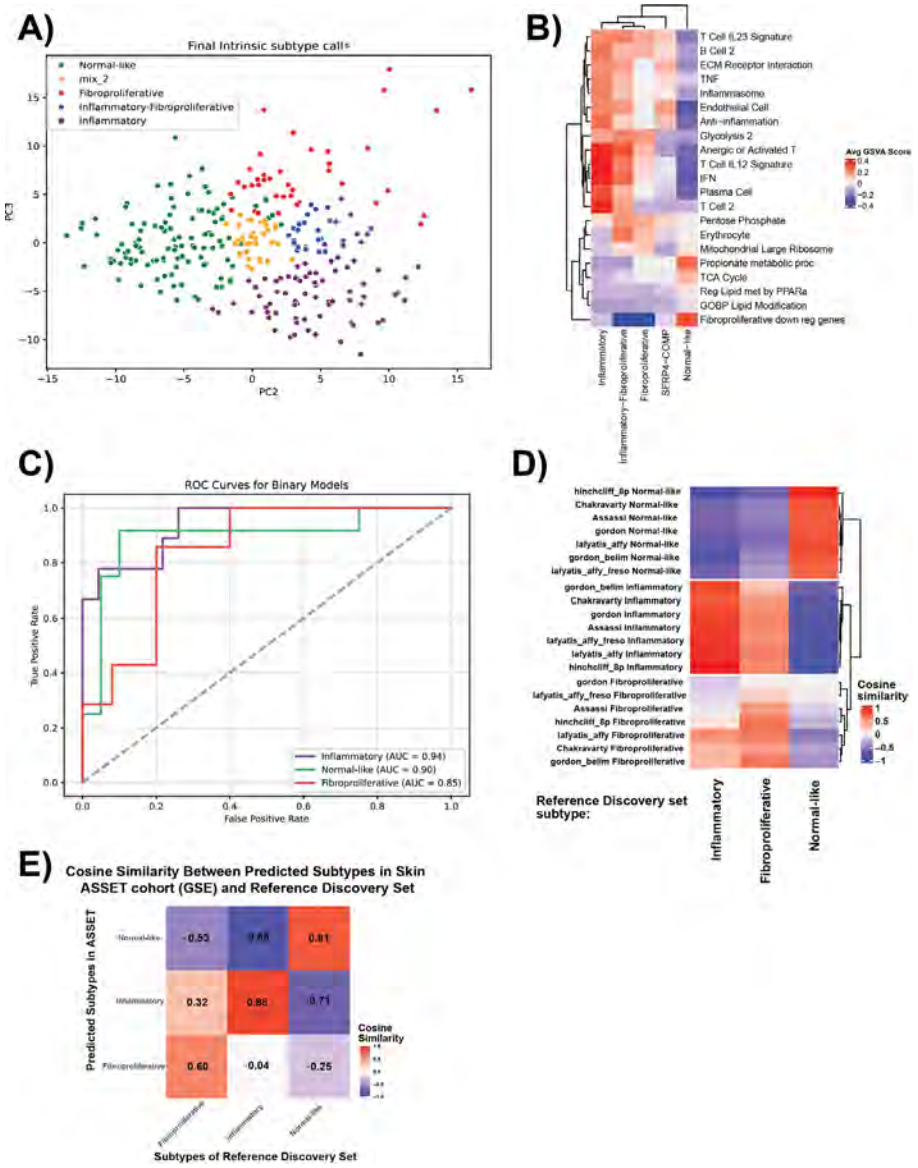


Figure 1. Identification and prediction of SSc intrinsic subtypes using semi-supervised and supervised machine learning approaches. (A) Semi-supervised constrained k-means clustering in the integrated discovery cohort (MPH, n = 174) defines five intrinsic subtypes and refines the "mixed" group into "inflammatory-fibroproliferative" and "intermediate" (between normal-like and inflammatory) subtypes. Principal component analysis (PCA) of all discovery samples colored by the final three broad subtype calls (inflammatory, normal-like, fibroproliferative) demonstrates clear separation. (B) Heatmap showing the up- and down-regulated pathways for the identified subtype. (C) Receiver operating characteristic (ROC) curves for one-vs-rest classifiers on a 20% hold-out set yield AUROC = 0.94 (inflammatory), 0.90 (normal-like), and 0.85 (fibroproliferative). (D) Concordance of predicted subtypes in independent validation cohorts (DNA microarray) versus discovery labels, shown as confusion matrices and similarity metrics. (E) Concordance of predicted subtypes in ASSET RNA-seq cohort versus discovery reference samples.

normal-like, which may represent a transitional subtype (Fig. 1A). Gene sets were identified that were most predictive for each subtype (Fig. 1B). We used the three broad subtype labels for classification due to small sample numbers. The best models showed AUROC of 0.94, 0.90, and 0.85 for inflammatory, normal-like, and fibroproliferative subtypes, respectively (Fig. 1C). The final, three-class model is able to predict SSc subtypes in independent DNA microarray and RNA-seq cohorts with strong concordance to the discovery set (Fig. 1D-E).

Inflammatory patients were enriched for dcSSc ($p < 0.001$), had shorter disease duration ($p < 0.001$), and the highest MRSS ($p < 0.001$), exhibited increased ILD risk ($p< 0.01$) with reduced FVC/DLCO ($p < 0.01$), and were most likely to have RNA-polymerase III autoantibodies ($p < 0.01$)(Fig. 2). In contrast, Normal-like patients were enriched for lcSSc (OR ≈3.0, p<

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

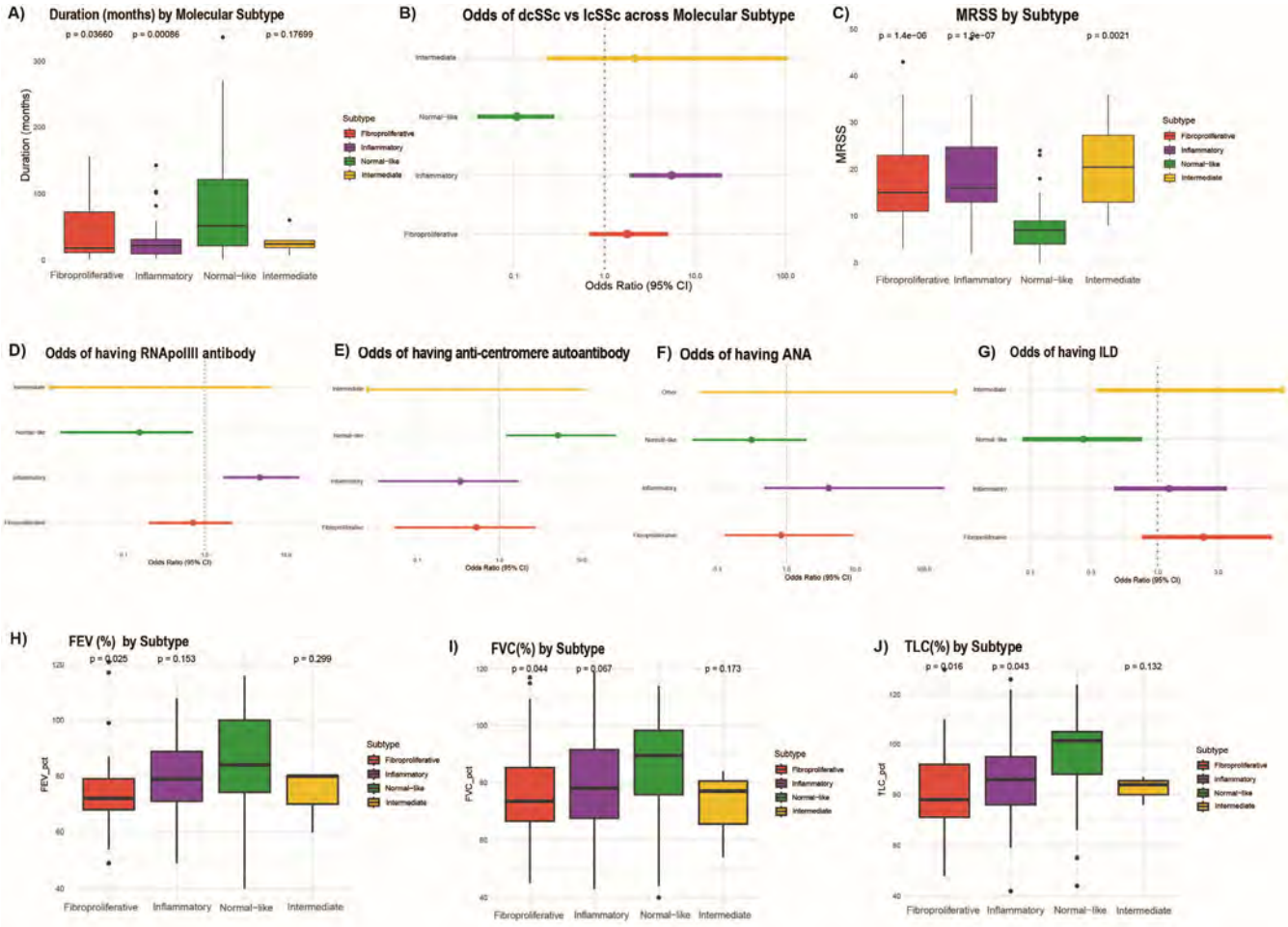


Figure 2. Clinical feature associations of intrinsic SSc molecular subtypes in MPH discovery set. (A) Disease duration (months) by subtype, shown as boxplots with Wilcoxon rank-sum p-values above each pairwise comparison. (B) Forest plot of odds ratios (95% CI) for diffuse cutaneous versus limited cutaneous SSc (dcSSc vs. lcSSc) for each subtype, relative to Normal-like (dashed vertical line at OR=1). (C) Modified Rodnan skin score (MRSS) by subtype, with p-values from Wilcoxon tests. (D–G) Forest plots of odds ratios (95% CI) for serologic and pulmonary categorical features: (D) RNA-polymerase III autoantibody, (E) anti-centromere autoantibody, (F) ANA positivity, and (G) interstitial lung disease (ILD) presence. (H–J) Pulmonary function measures (% predicted) by subtype—(H) FEV_1, (I) FVC, and (J) total lung capacity (TLC)—shown as boxplots with Wilcoxon test p-values. Subtype colors are fibroproliferative (red), inflammatory (purple), normal-like (green), and intermediate (yellow).

0.001), late-stage disease ($p < 0.01$), longer disease duration ($p < 0.001$), lowest MRSS ($p < 0.001$), showed reduced ILD risk ($p < 0.01$) and preserved lung function ($p < 0.01$), and were most likely to carry ACA ($p < 0.01$)(Fig. 2). An intermediate MRSS and pulmonary impairment were observed in Fibroproliferative patients ($p < 0.05$). These subtype-clinical patterns were largely recapitulated in 4 additional, independent cohorts (Hinchcliff 8 plex, PRESS, GENISOS, ASSET) (Fig. 3).

Conclusion: Our second-generation classifier robustly predicts intrinsic SSc subtypes across studies and platforms. Each subtype shows consistent, biologically meaningful associations with disease phenotypes, severity, and autoantibody profiles.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

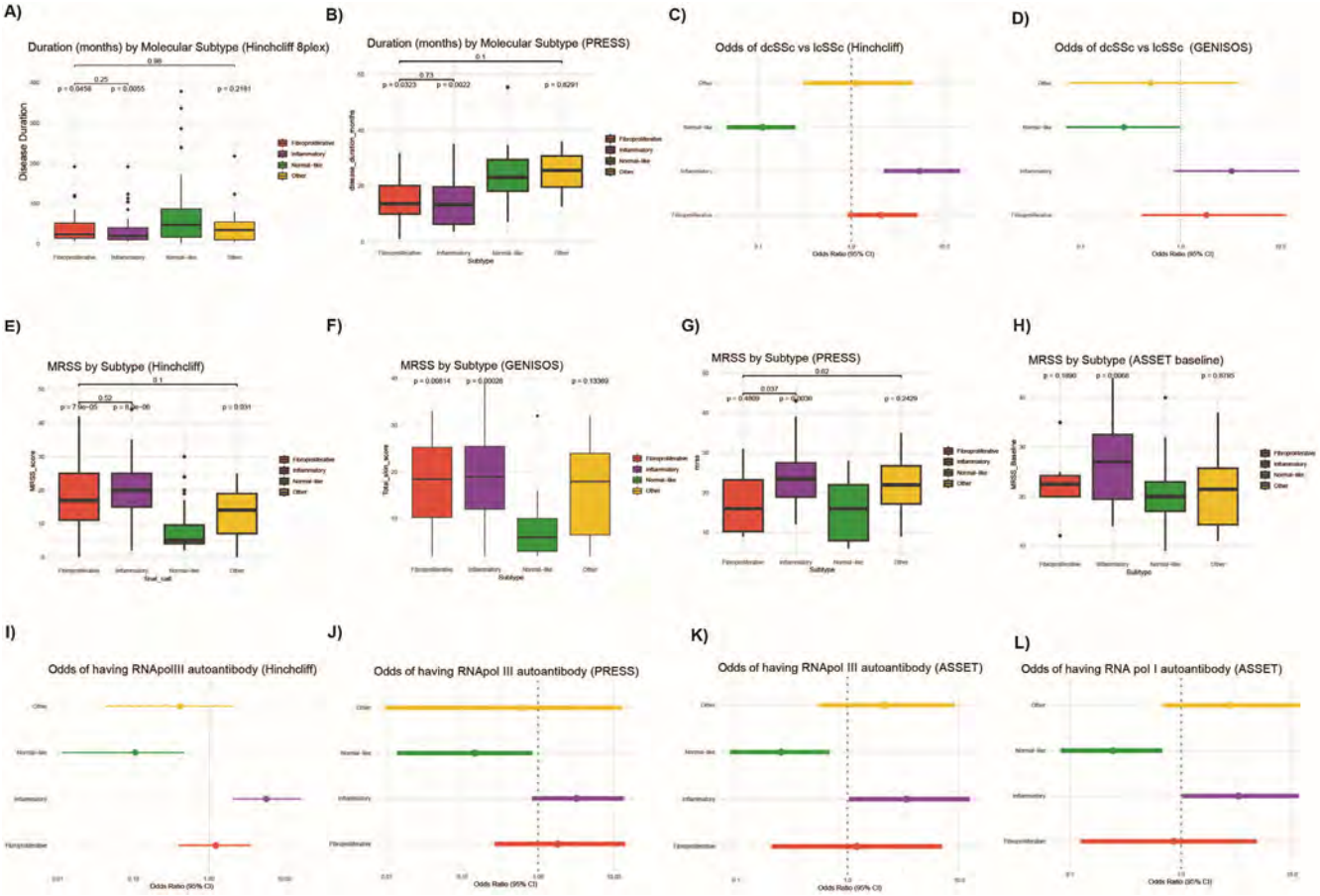


Figure 3. Validation of subtype–clinical associations in independent cohorts. (A–B) Disease duration (months) by molecular subtype in the Hinchliff microarray (A) and PRESS RNA-seq cohort (B), shown as boxplots with Wilcoxon rank-sum p-values. (C–D) Forest plots of odds ratios (95% CI) for diffuse versus limited cutaneous SSc (dcSSc vs lcSSc) by subtype in Hinchliff (C) and GENISOS (D), relative to Normal-like (dashed line at OR = 1). (E–H) MRSS by subtype in Hinchliff (E), GENISOS (F), PRESS (G), and ASSET baseline (H), with p-values from Wilcoxon tests. (I–K) Odds ratios (95% CI) for RNA-polymerase III autoantibody positivity by subtype in Hinchliff (I), PRESS (J), and ASSET (K). (L) Odds ratio (95% CI) for RNA-polymerase I autoantibody positivity by subtype in ASSET. Subtype color key: fibroproliferative (red), inflammatory (purple), normal-like (green), intermediate/other (yellow).

Disclosure: Z. Gong: None; **R. Parvizi**: None; **H. Jarnagin**: None; **H. Chen**: None; **M. Morrisson**: None; **T. Wood**: None; **M. Hinchcliff**: AbbVie/Abbott, Boehringer Ingelheim, Kadmon, 2, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **M. Whitfield**: Boehringer Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 2, Celdara Medical LLC, 2, 5, 10, 12, Scientific Founder.

Abstract Number: 0846

A Longitudinal Transcriptomic Study of Mycophenolate Mofetil in Systemic Sclerosis Skin with Clinical and Molecular Stratification

Rezvan Parvizi[1], Zhiyun Gong[2], Natania Field[3], Helen Jarnagin[2], Dillon Popovich[2], Monica Yang[4], Kathleen Aren[5], Mary Carns[6], Isaac Goldberg[7], Lorinda Chung[8], Vivien Goh[9], Zsuzsanna McMahan[10], Tammara Wood[11], Dinesh Khanna[12], Monique Hinchcliff[13] and **Michael Whitfield**[14], [1]Dartmouth, lebanon, NH, [2]Dartmouth College, Lebanon, NH, [3]Northwestern Memorial Hospital, Chicago, IL, [4]UCSF, San Francisco, CA, [5]Northwestern University Division of Rheumatology, Chicago, IL, [6]Northwestern University, Chicago, IL, [7]Wayne State University, Detroit, [8]Stanford University, Stanford, CA, [9]Northwestern, Chicago, [10]UT Health Houston, Houston, TX, [11]Dartmouth, Hanover, NH, [12]University of Michigan, Ann Arbor, MI, [13]Yale School of Medicine, Westport, CT, [14]Geisel School of Medicine, Lebanon, NH

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Sunday, October 26, 2025
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical I (0843–0848)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Mycophenolate Mofetil (MMF) is the most commonly prescribed immunosuppressive treatment for patients diagnosed with diffuse cutaneous systemic sclerosis (dcSSc). Here, we analyzed skin gene expression data for the largest longitudinal scleroderma cohort treated with MMF. By applying intrinsic molecular subtype classification to these skin gene expression data, we evaluated longitudinal changes in skin and other clinical outcomes during treatment, demonstrating an association between SSc molecular intrinsic subtypes and disease course during MMF treatment.

Methods: We analyzed longitudinal gene expression of 761 skin biopsies from a cohort of 201 scleroderma patients (based on ACR/EULAR 2013 criteria) with clinically active disease (in the treating physician's opinion) and 57 healthy participants. Biopsies were obtained from lesional and non-lesional skin at baseline and at 6, 12, 24, and 36 months after start of MMF treatment initiation (Fig 1A). Clinical metadata including age, sex, ethnicity, autoantibodies, disease duration/stage, and

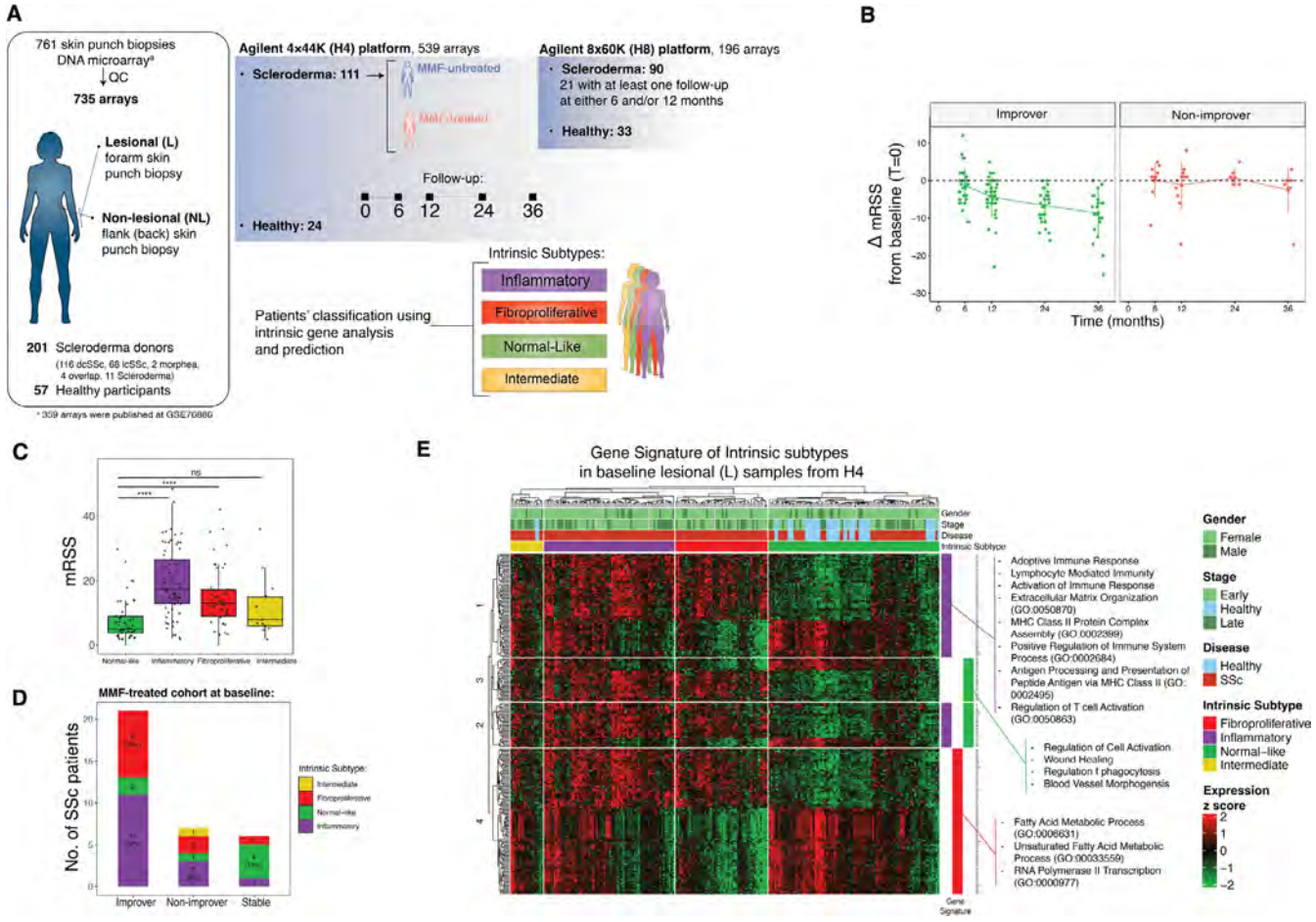


Figure 1. A) The schematic of the skin punch biopsy gene expression data set from lesional (forearm) and non-lesional (flank) of scleroderma and healthy donors that were processed in two DNA microarray platforms: Agilent 4x44K (H4) and Agilent 8x60K (H8). Intrinsic subtypes – inflammatory, fibroproliferative, normal-like and intermediate – were predicted for each skin sample. B) Change in mRSS from baseline for improvers in green and non-improvers in red. C) The mRSS levels for each intrinsic subtype for all patients at baseline. D) Distribution of subtypes for improvers, non-improvers, and stable patients who were treated with MMF. E) Heatmap showing intrinsic subtype gene signatures in baseline lesional skin samples from H4. The color bar on the right indicates gene expression levels associated with each intrinsic subtype signature. Representative Gene Ontology biological pathways enriched in each signature are shown next to the heatmap. dcSSc, diffuse cutaneous systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis; MMF, Mycophenolate Mofetil; mRSS, modified Rodnan skin score.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

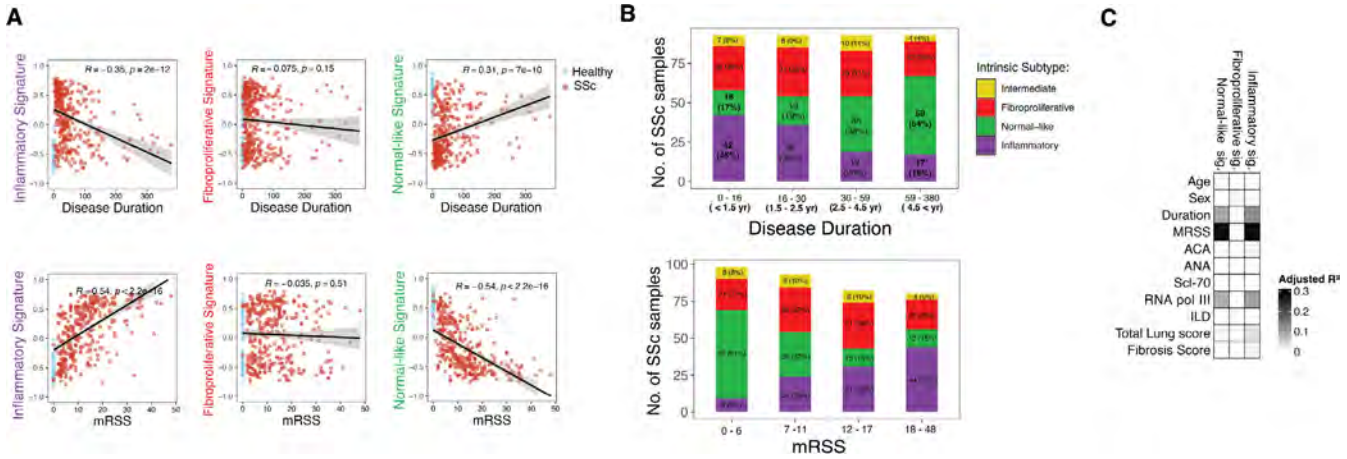


Figure 2. A) The scatter plots and Pearson correlations of the inflammatory, fibroproliferative, and normal-like signatures over disease duration and mRSS for all SSc (red) and healthy (blue) samples. R-squared and p-values of Pearson correlations are depicted in the graph. (Disease duration was identified as the time of the biopsy to the onset of the disease, which was marked as first non-Raynaud's symptom.) B) Distribution of SSc intrinsic subtypes across disease duration and mRSS. Both disease duration and mRSS values were categorized into four bins. The plot shows the number of patients in each subtype within these bins. C) Heatmap showing significant association between the intrinsic gene signatures and the clinical characteristics and manifestations.

modified Rodnan skin score (mRSS) were obtained. The intrinsic subtype of each sample was predicted using a machine learning classifier, distinct gene signatures were identified, and subtype enrichment was calculated.

Results: We identified improvers and non-improvers during MMF using 12-month mRSS post-treatment (Fig 1B). The inflammatory subtype had the highest mean mRSS, followed by the fibroproliferative and normal-like subtypes (Fig 1C). Within the MMF-treated cohort, most improvers (11 out of 21 improvers; 52%) were inflammatory. The majority of patients classified as non-improvers or stable were predicted to be normal-like (Fig 1D). The inflammatory subtype gene signature was enriched for immune cell activation pathways, whereas normal-like and fibroproliferative signatures were characterized by fatty acid metabolism, cell cycle, and other metabolic pathways (Fig 1E). The inflammatory enrichment scores correlate with markers of disease severity; negatively with disease duration and positively with mRSS, whereas the normal-like signature shows the opposite pattern (Fig. 2A). Early-stage patients (< 1.5 years after disease onset) were shown to have a 46% likelihood of being classified as inflammatory, whereas patients with disease duration > 4.5 years had a 54% likelihood of being classified as normal-like. Patients with high mRSS were more likely to be classified as inflammatory (55%), while those with low mRSS were more likely classified as normal-like (Fig 2B). Lastly, the association between subtype and the clinical manifestations showed that both inflammatory and normal-like signatures were associated with disease phenotypes (Fig 2C). The fibroproliferative subtype remained stable over the course of disease progression in this cohort.

Conclusion: These analyses suggest a link between disease severity and the intrinsic molecular subtype signatures. Inflammatory patients were more active, had higher mRSS, and showed more improvement during MMF. These data suggest that the inflammatory and normal-like subtypes represent opposite phenotypic states and disease activity.

Disclosure: R. Parvizi: None; **Z. Gong**: None; **N. Field**: None; **H. Jarnagin**: None; **D. Popovich**: None; **M. Yang**: None; **K. Aren**: None; **M. Carns**: None; **I. Goldberg**: None; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **V. Goh**: None; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **T. Wood**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **M. Hinchcliff**: AbbVie/Abbott, Boehringer Ingelheim, Kadmon, 2, 5; **M. Whitfield**: Boehringer Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 2, Celdara Medical LLC, 2, 5, 10, 12, Scientific Founder.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0847

Interferon Score Effectively Stratifies for Time to Clinically Significant Event Accrual in Systemic Sclerosis Independently of Cutaneous Subset

Stefano Di Donato[1], Rebecca Ross[2], Marco Minerba[3], Vishal Kakkar[4], Enrico De Lorenzis[5], Philip Yee[6], Christopher Denton[7] and Francesco Del Galdo[4], [1]University of Leeds, Canosa Sannita, Chieti, Italy, [2]Medicine and Health, University of Leeds, Leeds, United Kingdom, [3]Campus Bio-Medico University of Rome, Taranto, Taranto, Italy, [4]University of Leeds, Leeds, United Kingdom, [5]Catholic University of the Sacred Heart, Roma, Rome, Italy, [6]UCL, London, United Kingdom, [7]University College London, UK, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical I (0843–0848)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Systemic Sclerosis (SSc) is a heterogeneous autoimmune disease characterized by vascular damage, immune dysregulation, and fibrosis. It is typically classified into limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) subsets, each associated with distinct clinical complications. dcSSc is generally linked to more severe organ involvement and higher mortality, and given the higher disease activity is the cutaneous subset most targetetd in clinical trials. Two independent studies have recently demonstrated the value of serum IFN score activity in stratifying patients for severe outcome (1,2). This study aims to evaluate the prognostic value of serum Type I IFN activity in a "basket" observational cohort of lcSSc and dcSSc patients, tested against a time to clinically significant event endpoint.

Methods: A retrospective, longitudinal cohort of patients fulfilling the 2013 ACR/EULAR SSc classification criteria was identified within the STRIKE national, multicentre observational cohort. The combined morbi-mortality endpoint from the MINIMISE trial was used as the clinical outcome in a time-to-event analysis starting from the time of serum analysis. The IFN score was calculated as previously described, derived from the serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 (Myriad RBM). Patients were characterized according to the EUSTAR MEDS dataset. Time to endpoint was analysed using Kaplan-Meier curves, Log-rank test, and Cox Proportional Hazard regression models.

Table 1. Demographic and clinical features of patients in the analysis by LeRoy disease subset.

Characteristic	Overall N = 221[1]	dcSSc N = 72[1]	lcSSc N = 149[1]	p-value[2]	q-value[3]
Age	57 (16)	54 (9)	60 (16)	<0.001	<0.001
Sex				<0.001	<0.001
Female	193 (87%)	50 (69%)	143 (96%)		
Male	28 (13%)	22 (31%)	6 (4.0%)		
Anti Centromere	106 (48%)	6 (8.3%)	100 (67%)	<0.001	<0.001
Anti Topoisomerase I	53 (24%)	41 (57%)	12 (8.1%)	<0.001	<0.001
Anti Ro52	41 (19%)	6 (8.5%)	35 (23%)	0.007	0.010
Disease duration (months)	73 (120)	50 (96)	96 (122)	0.006	0.009
mRSS	4.5 (6.5)	9.6 (8.8)	2.1 (2.6)	<0.001	<0.001
FVC	102 (23)	87 (22)	109 (20)	<0.001	<0.001
DLCO	83 (16)	55 (14)	87 (15)	<0.001	<0.001
Event type					
HEART INVOLVEMENT	10 (4.6%)	4 (5.6%)	6 (4.0%)		
GI EVENT	5 (2.3%)	1 (1.4%)	4 (2.7%)		
MORTALITY	10 (5.4%)	3 (4.2%)	9 (6.0%)		
PAH	17 (7.7%)	4 (5.6%)	13 (8.7%)		
PROGRESSION OF ILD	20 (11.0%)	18 (24%)	6 (4.0%)		
RENAL CRISIS	1 (0.5%)	0 (0%)	1 (0.7%)		
SEVERE DIGITAL VASCULOPATHY	6 (2.8%)	3 (4.2%)	3 (2.0%)		
SKIN (mRSS)	12 (5.4%)	7 (9.7%)	5 (3.4%)		
ILD	79 (36%)	43 (60%)	36 (24%)	<0.001	<0.001
DUs history	99 (45%)	41 (57%)	58 (39%)	0.012	0.014
PAH	13 (5.9%)	4 (5.6%)	9 (6.0%)	>0.9	>0.9
IFN score	5.45 (0.49)	5.44 (0.58)	5.45 (0.46)	0.8	0.9
Median follow up (months)	88 (52)	73 (55)	92 (52)	<0.001	0.001
Event				<0.001	0.001
No	134 (61%)	32 (44%)	102 (68%)		
Yes	87 (39%)	40 (56%)	47 (32%)		
IFN score group				>0.9	>0.9
Low	121 (55%)	39 (54%)	82 (55%)		
High	100 (45%)	33 (46%)	67 (45%)		

[1] Median (IQR); n (%); Mean (SD)
[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test
[3] False discovery rate correction for multiple testing

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

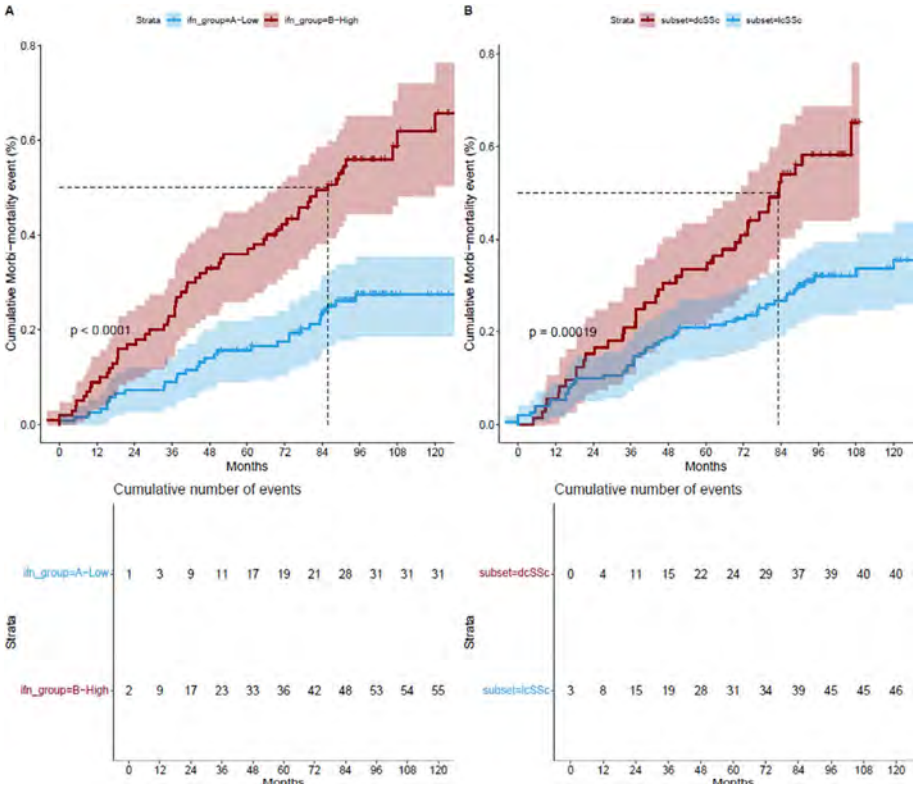


Figure 1. Kaplan-Meier curves for cumulative morbi-mortality events in SSc patients. A: Cumulative incidence of morbi-mortality events stratified by IFN score, with patients classified as IFN-low (blue) and IFN-high (red). B: Cumulative incidence of morbi-mortality events stratified by LeRoy subset, with patients classified as limited cutaneous SSc (blue) and diffuse cutaneous SSc (red).

Multivariable Cox regression models were adjusted for prognostic factors identified in univariate analyses, including age, sex, disease duration, Leroy subset, interstitial lung disease, modified Rodnan skin score (mRSS), digital ulcers (DU), and Pulmonary Arterial Hypertension (PAH).

Results: 221 SSc patients (67% lcSSc and 33% dcSSc) were included in the analysis (87% female, mean [SD] age 57 [16] years). Median (IQR) disease duration was 6 (10) years. 100 (45%) patients had a "high" IFN score (above 2 standard deviations from the Healthy Control [HC] mean), while 121 (55%) were classified as "low" IFN. Kaplan-Meier time to event analysis indicated a significantly lower event-free survival in IFN "high" compared to "low" patients ($p< 0.001$), as well as in diffuse SSc patients compared to limited SSc ($p< 0.001$). Multivariable Cox proportional hazard models confirmed that a high IFN score was associated with a Hazard Ratio (HR) of 2.57 (95% C.I. 1.64 – 4.03, $p< 0.001$) compared to IFN low, independent of subset. When used as a continuous variable, the IFN score maintained an HR of 1.60 (95% C.I. 1.18 - 2.16, $p=0.002$). Importantly, no significant interaction was detected between IFN score and disease subset ($p=0.42$) in the multivariable model including IFN score, indicating that the prognostic value of IFN score is independent of the cutaneous subset of SSc.

Conclusion: Serum assessment of Type I IFN activity is a valuable prognostic and stratification tool in SSc, providing enrichment for progressive disease independently of cutaneous subset. This approach supports the use of IFN score as a universal biomarker for risk stratification in clinical practice and trial design.

Disclosure: S. Di Donato: None; **R. Ross**: None; **M. Minerba**: None; **V. Kakkar**: None; **E. De Lorenzis**: None; **P. Yee**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5.

Abstract Number: 0848

Spatial Frequency Domain Imaging (SFDI) for Skin Assessment in Systemic Sclerosis: Insights from Histology and Clinical Correlates

Hung Vo[1], Aarohi Mehendale[2], Martin Azzam[3], Fatima-Ezzahrae El Adili[4], Rutvi Patel[3], Marcin TROJANOWSKI[3], Michael York[5], Eugene Kissin[6], Jeffrey Browning[7], Jag Bhawan[3], Darren Roblyer[5] and Andreea Bujor[5], [1]Boston Medical Center, Peabody, MA, [2]Department of Biomedical Engineering, Boston University, Boston, MA, [3]Boston University School of Medicine, Boston, MA, [4]Boston University School of Medicine, Revere, MA, [5]Boston University, Boston, MA, [6]Boston University, Newton, MA, [7]Boston University School of Medicine, Cambridge, MA

SESSION INFORMATION

Session Date: Sunday, October 26, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical I (0843–0848)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Assessing skin involvement in systemic sclerosis (SSc) is complex, with no single method capturing all pathological changes. The modified Rodnan Skin Score (mRSS) is subjective, requires experienced assessors, and has notable inter-observer variability. Our initial studies showed that Spatial Frequency Domain Imaging (SFDI), an objective,

B

	SSc	Control
Total	37	18
Sex, n (%)		
Female	23 (62%)	11 (61%)
Male	14 (38%)	7 (39%)
Disease type, n (%)		
LcSSc	5 (14%)	
DcSSc	32 (86%)	
Race (n, %)		
Black	11 (30%)	4 (22%)
White	22 (59%)	13 (72%)
Asian	2 (5%)	1 (6%)
Other	2 (5%)	0 (0%)
Mean Age ± SD (yrs)	52.2 ± 10.1	51.3 ± 9.4

C

Characteristic	Control N = 18[1]	SSC N = 37[1]	p-value[2,3]
Superficial Perivascular Lymphocytic Infiltrate (0-3)	1 (0, 1)	1 (0, 1)	0.9
Pigment Incontinence			0.091
No	17 (94%)	26 (70%)	
Yes	1 (5.6%)	11 (30%)	
Loss of Epidermal Papillae			0.6
No	10 (56%)	24 (67%)	
Yes	8 (44%)	12 (33%)	
Dermal Fibrosis			0.028*
No	17 (94%)	23 (62%)	
Yes	1 (5.6%)	14 (38%)	
Loss of Adnexa			0.091
No	17 (94%)	26 (70%)	
Yes	1 (5.6%)	11 (30%)	
Eccrine Gland Entrapment			0.057
No	18 (100%)	28 (76%)	
Yes	0 (0%)	9 (24%)	
Epidermal Thickness (μm)	52 (45, 70)	64 (50, 71)	0.2
Dermal Thickness (mm)	1.29 (1.08, 2.17)	1.64 (1.36, 2.26)	0.4
Collagen Score (H&E)*			0.005**
0	14 (82%)	7 (21%)	
0.5	1 (5.9%)	7 (21%)	
1	1 (5.9%)	5 (15%)	
1.5	0 (0%)	2 (5.9%)	
2	0 (0%)	6 (18%)	
2.5	0 (0%)	2 (5.9%)	
3	1 (5.9%)	5 (15%)	
ASMA**			0.035*
0	18 (100%)	26 (70%)	
1	0 (0%)	8 (22%)	
2	0 (0%)	3 (8.1%)	
Trichrome Staining***	2.8M (2.0M–5.0M)	5.8M (2.5M–14.2M)	0.001**

[1]Median (Q1, Q3); n (%)
[2]Wilcoxon rank sum test; Pearson's Chi-squared test; Welch Two Sample t-test
[3]*p<0.05; **p<0.01; ***p<0.001

Figure 1. Overview of study design, cohort demographics, and histologic features. (A) Diagram depicting the SFDI technology and clinical assessments. (B) Demographic and clinical summary of enrolled patients. (C) Histology assessments in systemic sclerosis (SSc) and healthy controls. Collagen score was based on visual grading (0–3) of overall collagen fiber thickening on H&E-stained sections. ASMA – Alpha smooth muscle actin. ASMA score was assessed using a 0–3 visual analog scale (VAS), excluding adnexal and vascular structures. Trichrome staining was quantified via ImageJ color deconvolution (M = millions). Data are shown as median (Q1, Q3) or n (%). p<0.05, p<0.01, p<0.001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Correlation between optical SFDI biomarkers and clinical/histologic measures of skin involvement. Spearman correlation coefficients (r_s) and p-values are shown for reduced scattering (μs′), absorption (Rd), and mRSS with respect to clinical assessments (ultrasound, durometry) and histologic markers (collagen score, ASMA, trichrome). Collagen score was graded 0–3 based on dermal fiber thickening using the method developed by Dr. Jeff Browning at BUMC. ASMA was quantified on a 0–3 VAS scale based on α-SMA–positive fibroblasts, excluding adnexal/vascular structures. Trichrome intensity was quantified using ImageJ with color deconvolution. p<0.05 considered significant.

	Clinical						*Histology*			
	Ultrasound		Durometry		Collagen Score		ASMA		Trichrome	
	r_s	p	r_s	p	r_s	p	r_s	p	r_s	p
R_d	-0.52	0.004	-0.41	0.046	-0.39	0.012	-0.52	<0.001	-0.42	0.005
μs′	-0.43	0.024	-0.36	0.040	-0.43	0.006	-0.48	<0.001	-0.53	<0.001
mRSS	0.45	0.022	0.60	0.001	0.58	<0.001	0.47	0.003	0.60	<0.001

noninvasive optical imaging modality, correlates with mRSS and has higher inter-rater reliability. However, the specific aspects of skin pathology measured by this technique remain unclear, as does its ability to track longitudinal changes. In this study, we systematically compare SFDI to mRSS, histology (gold-standard), ultrasound (for thickness), and durometry (for stiffness), and evaluate its longitudinal changes against changes in mRSS.

Methods: SSc patients and controls where enrolled under an IRB approved protocol. SFDI parameters (μ_s' and R_d at 0.2 mm^{-1} and 851 nm) were recorded at six sites: fingers, hands, and forearms. High-frequency ultrasound, durometry, and skin biopsies were done at the dorsal forearm. Two dermatopathologists evaluated histological sections for dermal thickness, alpha smooth muscle actin(ASMA)-positive fibroblast scoring, and other features. Collagen fiber score and trichrome quantification via ImageJ were also assessed. All measurements were performed blinded to clinical data. SFDI values were analyzed and compared across mRSS-defined groups using linear mixed models; clinical and histologic measurements were compared using one-way ANOVA with post-hoc Tukey tests, and correlations were assessed by Spearman's method.

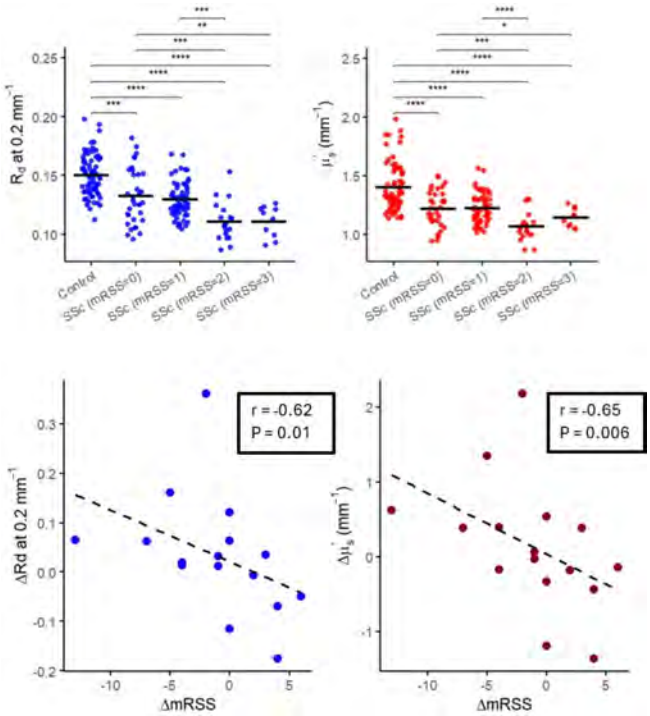


Figure 2. (A) Baseline diffuse reflectance (Rd, left) and reduced scattering coefficient (μs′, right) significantly decreased with increasing modified Rodnan skin score (mRSS), with notable differences observed even between controls and patients with clinically uninvolved skin (mRSS = 0). Each dot represents an individual skin site (forearm, hand, or finger); black bars denote group medians. Asterisks indicate statistical significance based on Tukey's post hoc test. (B) Longitudinal changes in Rd and μs′ were inversely correlated with changes in mRSS (ΔmRSS), indicating that optical properties increase in parallel with clinical improvement. Spearman correlation coefficients and p-values are shown.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 37 SSc patients and 18 controls who had skin biopsies along with SFDI measurements were included in the study. Longitudinal measurements were taken in 16 patients. Histology showed similar dermal and epidermal thickness between groups, while SSc patients had more dermal fibrosis, pigment incontinence, higher collagen and ASMA scores (Figure 1). SFDI parameters (μ_s' and R_d) showed significant correlations with histology - including trichrome, ASMA, and collagen fiber scores - that closely matched those of mRSS. For clinical measures, SFDI correlated with ultrasound to a similar degree as mRSS, but did not perform as well as mRSS for durometry, though associations remained significant (Table 1). Additionally, SFDI measurements were significantly lower in SSc patients with mRSS = 0 compared to controls and declined further with increasing mRSS. Analysis of longitudinal changes revealed a strong correlation between changes in SFDI (ΔR_d and $\Delta \mu_s'$) and changes in mRSS (ΔmRSS) in Figure 2.

Conclusion: Our study shows that SFDI parameters exhibit face, content, and criterion validity comparable to mRSS when benchmarked against skin biopsy and other clinical metrics, supporting its use as a noninvasive, objective tool. SFDI also tracks longitudinal skin changes in SSc patients, making it versatile for monitoring disease progression and treatment response. Given its objectivity and minimal training requirements, SFDI is promising as a practical clinical tool, but further validation in longitudinal and multicenter studies is needed.

Disclosure: H. Vo: None; **A. Mehendale**: None; **M. Azzam**: None; **F. El Adili**: None; **R. Patel**: None; **M. TROJANOWSKI**: None; **M. York**: None; **E. Kissin**: None; **J. Browning**: None; **J. Bhawan**: None; **D. Roblyer**: None; **A. Bujor**: None.

Abstract Number: 0849

Mortality and Major Adverse Cardiac Events (MACE) with GLP-1 Receptor Agonists in Psoriatic Arthritis

Nanuka Tsibadze[1], Irakli Tskhakaia[1] and Irene Tan[2], [1]Jefferson Health - Einstein, Philadelphia, PA, [2]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Plenary II (0849–0854)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Glucagon-like-peptide-1 receptor agonists (GLP-1 RAs) are the novel drug class that has gained widespread attention for its cardiovascular, renal and weight loss benefits in patients with type 2 diabetes mellitus. Available evidence has illustrated that weight loss, through surgical or behavioral modification, is associated with improvements in disease activity in patients with obesity and RA, PsA, or psoriasis.

Methods: This is a nationwide, retrospective study. We used the global, multicenter research network (TrinetX) database from 83 large healthcare organizations across multiple countries. We included patients older than 18 years old with a diagnosis of psoriatic arthritis, for the last 10 years (between January 2015 and December 2024), using the International Classification of Disease-10 codes. We compared psoriatic arthritis patients on GLP-1 RAs (Semaglutide, Liraglutide, Exenatide, Lixisenatide), with psoriatic arthritis patients not on GLP-1 RAs. We used 1:1 propensity score matching that accounted for demographics variables, diagnoses, and medication use. Index event was defined as simultaneous appearance of psoriatic arthritis and GLP-1 RA use in patients' charts. Outcome of interest was the incidence of major adverse cardiovascular effects and overall mortality. Patients displaying these outcomes before the index event were excluded from the analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Patient Characteristics of Study Groups, before and after Propensity Score Matching

Characteristics	GLP-1 RA Group (N=4,104)	No GLPs-1 RA Group (N=86,432)	p-value	GLP-1 RA Group (N=3,303)	No GLP-1 RA Group (N=3,303)	p-value
	Before Propensity Matching			After Propensity Score Matching		
Demographics						
Age, mean ±SD	55.4±11.5	52.6±15.1	<0.001	55.2±11.6	55.3±13.7	0.916
Female, %	69.3	55.4	<0.001	68.4	69.7	0.264
Male, %	27.1	40.3	<0.001	27.8	26.7	0.320
White, %	80.9	73.5	<0.001	80.8	81.9	0.243
Black, %	4.5	3.0	<0.001	4.5	4.3	0.632
Asian, %	2.7	4.1	<0.001	2.8	2.9	0.824
Unknown Race, %	8.5	15.7	<0.001	8.9	8.0	0.215
Diagnoses						
Endocrine Diseases, %	94.9	37.3	<0.001	93.7	95.2	0.006
Cardiovascular Diseases, %	80.2	32.1	<0.001	77.3	78.5	0.236
Overweight/ Obesity, %	72.0	12.2	<0.001	67.3	68.6	0.246
Diabetes, %	61.2	9.0	<0.001	54.7	54.1	0.621
AKI and CKD, %	17.8	3.9	<0.001	16.1	16.3	0.841
Medications						
Cardiovascular, %	90.6	37.6	<0.001	88.5	88.6	0.817
Insulin, %	35.7	4.4	<0.001	30.8	30.4	0.728
Methotrexate, %	33.4	10.9	<0.001	28.1	28.3	0.848
Sulfasalazine, %	10.1	3.1	<0.001	8.7	8.7	0.896

Table 1. Baseline Patient Characteristics of Study Groups, before and after Propensity Score Matching (Ctd.)

Leflunomide, %	8.7	1.8	< 0.001	6.5	6.9	0.491
HCQ, %	9.5	4.0	<0.001	8.8	9.6	0.251
Cyclosporine, %	5.0	1.5	<0.001	3.9	4.3	0.457
Etanercept, %	16.0	3.7	<0.001	12.5	11.7	0.290
Adalimumab, %	27.5	6.0	<0.001	22.2	22.1	0.929
Golimumab, %	3.6	0.5	<0.001	2.5	2.2	0.418
Certolizumab, %	3.2	0.5	<0.001	2.1	2.4	0.562
Ustekinumab, %	9.6	1.4	<0.001	5.8	6.1	0.640
Secukinumab, %	13.6	1.4	<0.001	8.3	7.6	0.339
Ixekizumab, %	7.9	0.8	<0.001	4.7	4.4	0.556
Brodalumab, %	0.3	0.0	<0.001	0.3	0.3	1
Bimekizumab, %	0.2	0.0	<0.001	0.3	0.3	1
Guselkumab, %	4.5	0.4	<0.001	2.5	2.7	0.698
Risankizumab, %	0.2	0.0	<0.001	2.3	2.0	0.447
Tofacitinib, %	4.1	0.5	<0.001	2.9	2.7	0.604
Baricitinib, %	0.2	0.0	<0.001	0.3	0.3	1
Upadacitinib, %	1.7	0.2	<0.001	1.2	1.3	0.912
Apremilast, %	15.7	2.3	<0.001	11.4	10.6	0.307
Ibuprofen, %	37.7	12.8	<0.001	34.9	35.3	0.718
Naproxen, %	23.5	8.4	<0.001	22.0	22.2	0.859
Diclofenac, %	33.5	8.8	<0.001	29.5	29.6	0.936
Celecoxib, %	20.5	5.5	<0.001	18.4	18.0	0.655

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Risk of major adverse cardiac events in psoriatic arthritis patients on GLP-1 RA therapy, versus not on GLP-1 RA therapy

Outcome	Groups	Overall Risk, %	Risk Ratio	Overall Risk, %	Risk Ratio
	Before Propensity Score Matching			After Propensity Score Matching	
Ischemic Heart Diseases	GLP-1 RAs	9.7 (290/2,983)	1.189 (1.063-1.330) *p* value 0.003	9.0 (238/2,656)	0.715 (0.610-0.838) *p* value 0.000
	No GLP-1 RAs	8.2 (5,929/72,518)		12.5 (320/2,554)	
Cerebrovascular Diseases	GLP-1 RAs	4.5 (157/3,451)	0.951 (0.814-1.112) *p* value 0.531	4.7 (143/3,019)	0.605 (0.494-0.740) *p* value 0.000
	No GLP-1 RAs	4.8 (3,628/75,870)		7.8 (232/2,963)	
Acute myocardial infarction	GLP-1 RAs	2.5 (91/3,593)	1.239 (1.006-1.526) *p* value 0.044	2.3 (72/3,145)	0.578 (0.434-0.769) *p* value 0.000
	No GLP-1 RAs	2.0 (1,587/77,621)		4.0 (124/3,130)	
Cerebral infarction	GLP-1 RAs	1.8 (67/3,648)	0.973 (0.763-1.240) *p* value 0.823	1.8 (58/3,191)	*0.633 (0.457-0.876)* *p* value 0.005
	No GLP-1 RAs	1.9 (1,467/77,690)		2.9 (91/3.168)	
Heart Failure	GLP-1 RAs	11.9 (451/3,791)	1.848 (1.688-2.023) *p* value <0.000	10.5 (348/3,303)	0.703 (0.618-0.799) *p* value 0.000
	No GLP-1 RAs	6.4 (5,071/78,772)		15.0 (495/3,303)	
Death	GLP-1 RAs	1.6 (59/3,778)	0.518 (0.401-0.670) *p* value <0.000	1.4 (47/3,291)	0.307 (0.222-0.425) *p* value 0.000
	No GLP-1 RAs	3.0 (2,371/78,674)		4.6 (153/3,292)	

The exposure for the outcome was any time after the diagnosis of psoriatic arthritis during the time window. Risk ratios with 95% confidence intervals were calculated for each outcome. A two-sided p-value less than 0.05 was considered statistically significant.

Results: We identified 4,104 psoriatic arthritis patients taking GLP-1 receptor agonists (GLP-1 RAs) and 86,432 psoriatic arthritis patients not taking GLP-1 RAs. At baseline, the mean age at diagnosis was 55.4 ± 11.5 years for those on GLP-1 RAs and 52.6 ± 15.1 years for those not on GLP-1 RAs. Female patients were more prevalent in GLP-1 RA group, on the contrary male patients were predominant in no GLP-1 RAs. White patients made up the largest racial group in both subgroups (80.9% for GLP-1 RA users and 73.5% for non-users). After propensity score matching, patients on GLP-1 RAs showed lower risk of developing major cardiovascular adverse events and had reduced mortality compared to those not using GLP-1 RAs (Table 2).

Conclusion: Psoriatic arthritis patients receiving GLP-1 receptor agonists have lower risk of developing major adverse cardiac events, and have reduced mortality compared to psoriatic arthritis patients not taking GLP-1 receptor agonists. GLP-1 receptor agonists may be a promising adjunct in the management of patients with inflammatory arthritis, who have comorbidities including obesity and/or type 2 diabetes mellitus. Further research is warranted to better understand the mechanisms underlying these outcomes and to confirm the long-term benefits of GLP-1 RAs.

Disclosure: N. Tsibadze: None; **I. Tskhakaia**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0850

Single-cell RNA-seq analysis of synovial CD4$^+$ T cells identifies a novel biomarker and therapeutic target in human rheumatoid arthritis

Akinori Murakami[1], Rinko Akamine[1], Koichi Murata[1], Kohei Nishitani[1], Hiromu Ito[2], Ryu Watanabe[3], Takayuki Fujii[1], Takeshi Iwasaki[1], Yuki Masuo[4], Osamu Iri[1], Shinichiro Nakamura[1], Shinichi Kuriyama[1], Yugo Morita[1], Yasuhiro Murakawa[5], Chikashi Terao[6], Yukinori Okada[7], Motomu Hashimoto[3], Shuichi Matsuda[1], Hideki Ueno[1] and Hiroyuki Yoshitomi[1], [1]Kyoto University, Kyoto, Japan, [2]Kyoto University / Kurashiki Central Hospital, Kyoto, Japan, [3]Osaka Metropolitan University, Osaka, Japan, [4]Graduate school of medicine, Kyoto University, Kyoto, Japan, [5]Kyoto University / RIKEN, Kyoto, Japan, [6]RIKEN, Tokyo, Japan, [7]The University of Tokyo / Osaka University / RIKEN, Tokyo, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Plenary II (0849–0854)

Session Type: Plenary Session

Session Time: 8:00AM–9:30AM

Background/Purpose: CD4$^+$ T cells play a central role in the pathogenesis of human rheumatoid arthritis (RA). However, therapies targeting CD4$^+$ T cell-derived humoral factors, including IL-17, have shown limited clinical efficacy. This suggests that the key CD4$^+$ T cell subsets and associated effector molecules driving synovial inflammation in RA remain incompletely understood. To address this, we performed a comprehensive single-cell transcriptomic analysis of synovial CD4$^+$ T cells from RA patients.

Methods: Single-cell RNA sequencing (scRNA-seq) was performed on CD4$^+$ T cells in the synovial tissue and synovial fluid of 11 seropositive RA patients (all female, mean age 65.6 years, mean DAS28-ESR 4.21). The function of an inflammatory factor identified in the analysis was assessed through in vitro experiments including CRISPR-Cas9. Serum levels of this factor were investigated in 30 control participants and 30 RA patients.

Results: scRNA-seq identified CD4$^+$ T cell clusters, including PD-1$^+$CXCL13$^+$ peripheral helper T (Tph), regulatory T (Treg), cytotoxic T, and Th17 cells. The frequency of Tph cells showed a significant correlation with disease activity, whereas the frequency of Treg and Th17 cells did not. We further identified a humoral factor, pathogenic helper inflammatory factor (PHIF, tentative gene name), with whose expression correlated with disease severity. PHIF was specifically expressed by human CD4$^+$ T cells, predominantly within Tph cells. In vitro experiments showed that PHIF promoted CXCL13 production in Tph cells. In addition, PHIF activated NF-κB signaling in monocytes and induced gene signatures associated with pathogenic macrophages from RA synovial tissue, including CXCL10 and CXCL9. Consistently, CRISPR/Cas9-knockout of PHIF in patient-derived synovial Tph cells suppressed the activation of CXCL10 and IFN signature in co-cultured monocytes (Figure 1). Notably, serum PHIF protein levels significantly correlated with RA disease severity and effectively discriminated RA patients, comparable to established biomarkers such as anti-citrullinated antibodies (Figure 2).

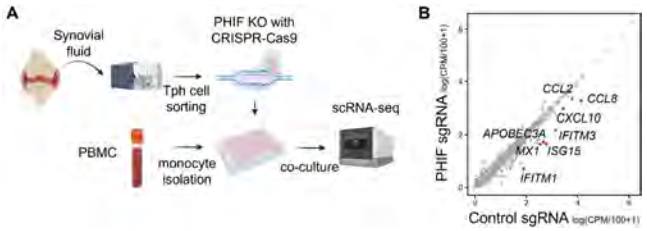


Figure 1. Effects of PHIF knockout in Tph cells on monocyte gene expression. (A) Tph cells sorted from synovial CD4+ T cells were treated with PHIF knockout using CRISPR-Cas9 and were co-cultured with PBMC monocytes, followed by scRNA-seq analysis. (B) A scatter plot comparing RNA expression of control sgRNA and PHIF sgRNA in co-cultured monocytes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

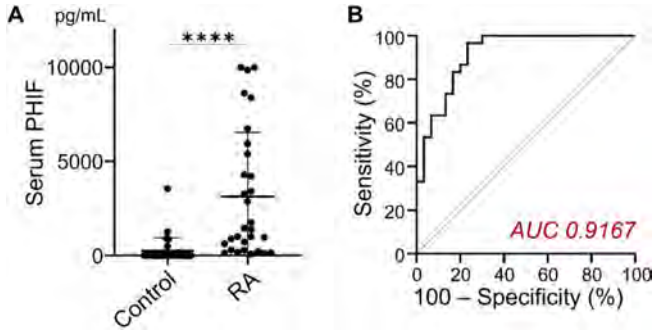


Figure 2. Clinical assessment of PHIF in RA. (A) Blood PHIF protein levels between control (n = 30) and RA (n = 30). (B) ROC curve of blood PHIF levels for RA determination with the AUC value. The means ± SD are shown in (A). ****p < 0.0001; Mann-Whitney U tests (A). ROC, receiver operating characteristic; AUC, area under the curve.

Conclusion: These findings highlight the substantial involvement of PHIF in RA pathogenesis, emphasizing how human Tph cells exert pleiotropic regulation of local immune responses via PHIF in addition to promoting antibody production via CXCL13. Thus, PHIF can be a potential biomarker and therapeutic target for RA.

Disclosure: A. Murakami: None; **R. Akamine**: None; **K. Murata**: None; **K. Nishitani**: None; **H. Ito**: None; **R. Watanabe**: None; **T. Fujii**: None; **T. Iwasaki**: None; **Y. Masuo**: None; **O. Iri**: None; **S. Nakamura**: None; **S. Kuriyama**: None; **Y. Morita**: None; **Y. Murakawa**: None; **C. Terao**: None; **Y. Okada**: None; **M. Hashimoto**: None; **S. Matsuda**: None; **H. Ueno**: None; **H. Yoshitomi**: None.

Abstract Number: 0851

Urinary Tenascin C Predicts Kidney Function Loss in Lupus Nephritis

CHEN-YU LEE[1], Sepehr Taghavi[2], Shangzhu Zhang[3], Roopa Madhu[4], Jasmine Shwetar[5], Tyler O'Malley[6], Daniel Goldman[7], Peter Izmirly[8], H Michael Belmont[9], Richard Furie[10], Noa Schwartz[11], Chaim Putterman[12], Jennifer Barnas[13], Jennifer Anolik[14], Sarah French[15], Maria Dall'Era[16], Judith James[17], Joel Guthridge[17], Jacob Vasquez[18], Mike Nerenberg[19], Andrew Concoff[20], Christine Schleif[21], Kevin Wei[22], Thomas Eisenhaure[23], Nir Hacohen[23], Rachael Bogle[24], Johann Gudjonsson[25], Lam Tsoi[25], Brad Rovin[26], Jill Buyon[27], Michelle Petri[7], **Andrea Fava**[1] and the Accelerating Medicines Partnership in RA/SLE, [1]Johns Hopkins University, Baltimore, MD, [2]Exagen Inc, Escondido, CA, [3]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China (People's Republic), [4]Brigham and Women's Hospital, Brookline, MA, [5]New York School of Medicine, Ann Arbor, MI, [6]Exagen, Vista, CA, [7]Johns Hopkins University School of Medicine, Timonium, MD, [8]New York University Grossman School of Medicine, New York, NY, [9]NYU School of Medicine, New York, NY, [10]Division of Rheumatology, Northwell Health, Great Neck, NY, [11]Division of Rheumatology, Department of Medicine, Montefiore Medical Center, New York, NY, [12]Albert Einstein College of Medicine, Safed, Israel, [13]University of Rochester, Rochester, NY, [14]University of Rochester Medical Center, Rochester, NY, [15]UCSF, Mill Valley, CA, [16]Division of Rheumatology, University of California, San Francisco, CA, [17]Oklahoma Medical Research Foundation, Oklahoma City, OK, [18]Exagen, Inc., Vista, CA, [19]Exagen, DEL MAR, CA, [20]Specialty Networks/United Rheumatology, a Cardinal Health Company, N/A, [21]Exagen, Carlsbad, CA, [22]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [23]Broad Institute, Cambridge, MA, [24]University of Michigan, Holland, OH, [25]University of Michigan, Ann Arbor, MI, [26]The Ohio State University, Columbus, OH, [27]NYU Grossman School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Plenary II (0849–0854)

Session Type: Plenary Session

Session Time: 8:00AM–9:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

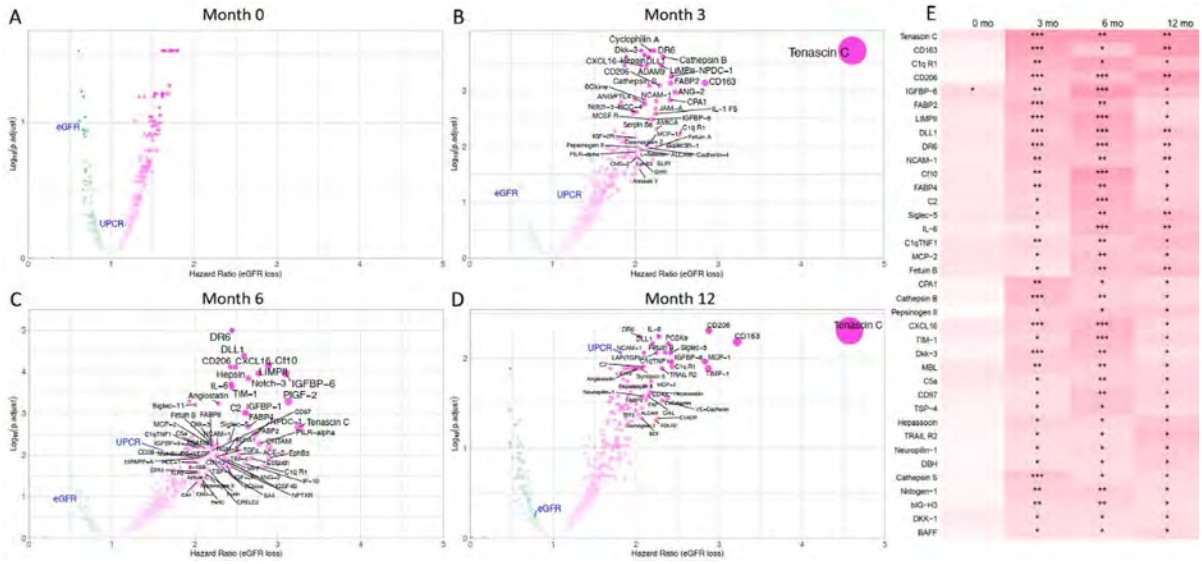


Figure 1. Proteomics signatures of increased risk of eGFR loss over time. Cox regression results at month 0, 3, 6, 12 (A-D). Only proteins with a significant hazard ratio greater than 2 are labeled on the four volcano plots. eGFR and UPCR are labeled in blue. (E) Heatmap summarizing urinary proteins significantly associated with eGFR loss from month 3 onward. Color intensity indicates the hazard ratio (HR) for eGFR loss, with white representing HR = 1 and deeper red shades indicating higher HR values. *: adjusted $p < 0.05$; **: adjusted $p < 0.01$; ***: adjusted $p < 0.001$. eGFR: estimated Glomerular Filtration Rate; UPCR: urine protein-to-creatinine ratio.

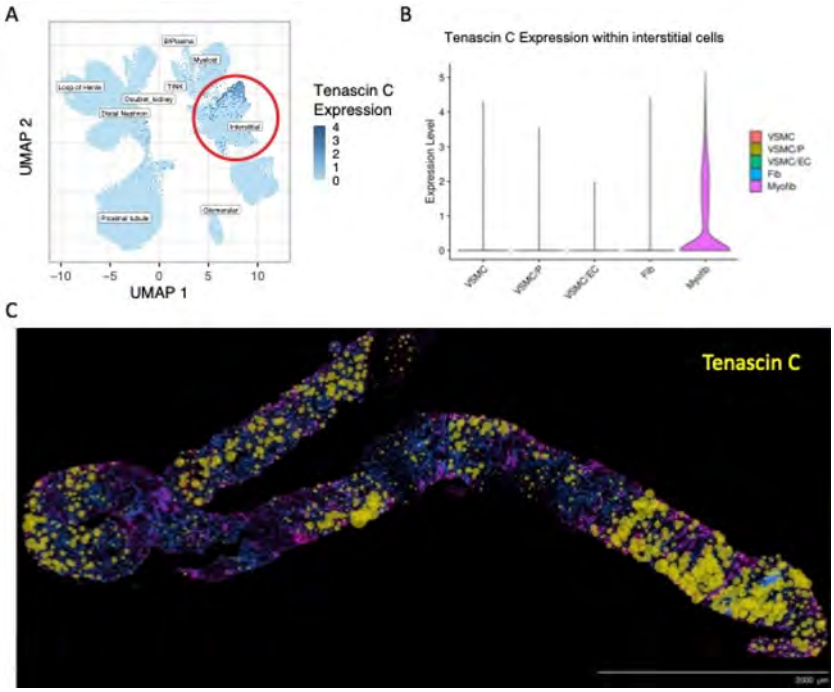


Figure 2. Tenascin C is broadly expressed in LN by myofibroblasts. (A) UMAP projection of ~ 500k cells from 16 kidney biopsies profiled using Xenium and scFFPE RNA sequencing from the AMPAIM cohort. Each cluster is labeled by its inferred cell type, and cells are colored by log-normalized expression of Tenascin C (TNC). The interstitial stromal cluster is highlighted in the red circle. (B) Violin plots of TNC expression across interstitial subpopulations): vascular smooth muscle cells (VSMC, n=3,854), VSMC/pericytes (VSMC/P, n=5,458), VSMC/endothelial cells (VSMC/EC, n=2,933), fibroblasts (Fib, n=3,584), and myofibroblasts (Myofib, n=1,220). Myofibroblasts show the highest TNC levels, indicating this cell type as the primary source. Data generated from the AMP RA/SLE cohort (n=200) using 10X Genomics scRNA-seq technology on disaggregated kidney biopsies. (C) Spatial transcriptomic map (10× Xenium) of a representative LN kidney section: yellow circles mark TNC transcript density, demonstrating broad expression within interstitial regions (scale bar = 2000 μm).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

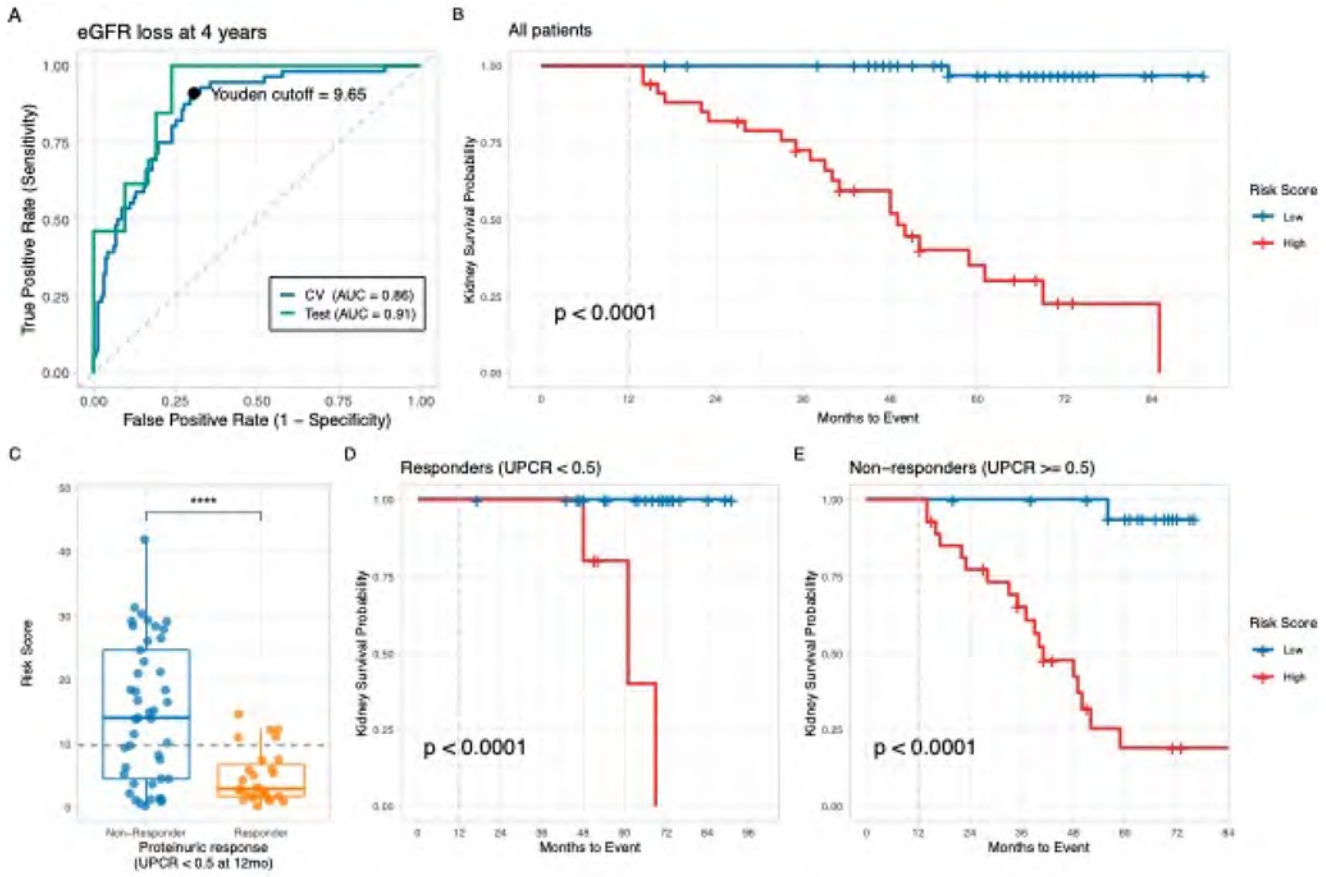


Figure 3. Urinary proteomics-based risk score predicts renal function loss and stratifies patients by treatment response. (A) Time-dependent ROC curve at 48 months demonstrates predictive performance of the risk score, with an optimal Youden cutoff of 9.65 separating high- and low-risk groups for eGFR decline. An 80:20 data split was used for model development, with 80% of patients in the training set and 20% held out for independent testing. Cross-validation within the training set optimized model hyperparameters. All follow-up visits were used to train the model to predict future eGFR loss. To prevent data leakage and overfitting, patients were split at the subject level, ensuring that all visits from a given patient remained in either the training or test set. (B) Kaplan-Meier kidney survival analysis for all patients, stratified by risk score at month 12. Patients with scores ≥9.65 were classified as high risk; those <9.65 as low risk. (C) Distribution of risk scores by treatment response at month 12. (D-E) Kidney survival stratified by risk score among proteinuric responders (D, UPCR < 0.5) and non-responders (E, UPCR ≥ 0.5).

Background/Purpose: Kidney survival is the ultimate treatment goal in lupus nephritis (LN), but long-term predictors remain understudied due to the need for extensive follow up. Proteinuria at one year is used to establish treatment response, but it is inadequate: repeat biopsy studies showed persistent intrarenal activity in ~50% of proteinuric responders with up to 30% progressing to renal insufficiency. Our objective was to identify urinary biomarkers that predict kidney function loss.

Methods: We followed 170 LN patients from the Accelerating Medicines Partnership (AMP) cohort up to 7.8 years (median 4.9). Treatment was discretionary. Estimated Glomerular Filtration Rate (eGFR) loss was defined as a sustained ≥40% decline in eGFR from baseline or development of end-stage kidney disease. We quantified 1200 biomarkers (RayBiotech) in urine samples collected at time of kidney biopsy and month 3, 6, and 12 in LN. Time-to-event models were used to evaluate associations between urinary protein levels and risk of future eGFR loss. Kidney single-cell RNA-seq and spatial transcriptomics (Xenium) were used to identify the renal cellular source of biomarkers. A Random Survival Forest model was trained to predict eGFR loss at any time after baseline and validated on a 20% hold-out test set.

Results: During follow-up, 53/170 (31%) patients developed eGFR loss. At month 3, Tenascin C emerged as the strongest predictor of eGFR loss (HR 4.6) and remained elevated through month 12 (Figure 1). Several inflammatory and fibrosis-associated markers (i.e., CD163, CD206, FABP4, IL6, IGFBP-6) were persistently associated with increased risk. Single-cell and spatial transcriptomics localized Tenascin C expression to interstitial myofibroblasts in LN kidneys, suggesting a

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pathologic role in progressive fibrosis (Figure 2). To maximize clinical applicability, we developed a urinary protein-based classifier to predict future eGFR loss at any time point after baseline. The model (11-proteins, including tenascin C) achieved excellent predictive performance (AUC = 0.91 at 48 months) stratifying patients into high- and low-risk groups (Figure 3A). For example, at month 12, the risk score was significantly associated with eGFR preservation ($p < 0.001$, Figure 3B), and revealed heterogeneity within proteinuric response groups: some responders (UPCR < 0.5) had high risk scores, while some non-responders had low scores (Figure 3C). The classifier accurately predicted eGFR loss in both groups underscoring the limitations of proteinuria and the added utility of biomarker-based risk prediction (Figure 3D-E).

Conclusion: Urinary Tenascin C, a marker of myofibroblast activation, emerged as a robust predictor of kidney function loss in LN. Elevated CD163 and CD206 levels in high-risk patients point to ongoing M2 macrophage–driven profibrotic signaling and incomplete resolution of intrarenal inflammation, even among proteinuric responders. A proteomics-based risk score outperformed proteinuria, accurately stratifying high-risk individuals regardless of response. These findings offer mechanistic insight and support early biomarker-guided strategies to personalize treatment, refine clinical trials, and prevent irreversible kidney damage.

Disclosure: C. LEE: None; **S. Taghavi**: Exagen, 3; **S. Zhang**: None; **R. Madhu**: None; **J. Shwetar**: None; **T. O'Malley**: Exagen, 12, 3, 11; **D. Goldman**: None; **P. Izmirly**: Hansoh Bio, 2; **H. Belmont**: None; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **N. Schwartz**: None; **C. Putterman**: Cullinan, 1, Progentec, 1; **J. Barnas**: None; **J. Anolik**: None; **S. French**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Guthridge**: None; **J. Vasquez**: None; **M. Nerenberg**: Exagen, 3, 11; **A. Concoff**: Exagen Inc., 3; **C. Schleif**: Exagen, 3; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **T. Eisenhaure**: None; **N. Hacohen**: None; **R. Bogle**: None; **J. Gudjonsson**: None; **L. Tsoi**: Galderma, 5, Janssen, 5; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0852

LEVI-04 Significantly Reduces Bone Marrow Lesions and Symptoms in Knee Osteoarthritis: Results from a Phase II RCT

Simon Westbrook[1], Ali Guermazi[2] and Philip Conaghan[3], [1]Levicept Ltd, Sandwich, United Kingdom, [2]Boston University, West Roxbury, MA, [3]University of Leeds, Leeds, United Kingdom

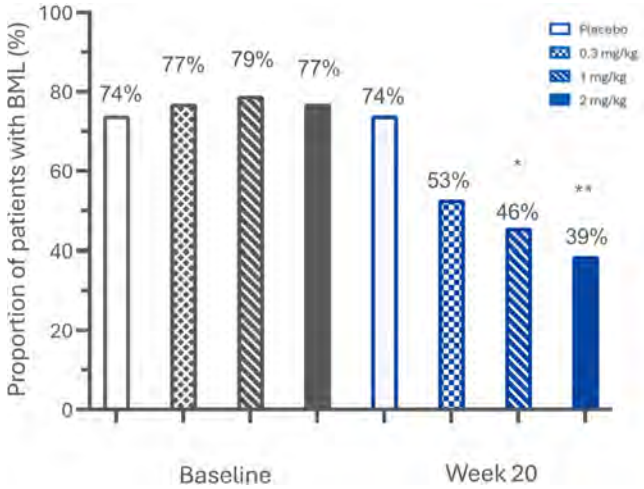
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Plenary II (0849–0854)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Bone marrow lesions (BMLs), detectable on MRI as areas of ill-defined high signal intensity on fluid-sensitive sequences, are a common feature of osteoarthritis (OA), representing areas of increased bone turnover, oedema, and fibrosis. BMLs are prevalent in ~80% of symptomatic knee OA patients, correlate with radiographic severity (Kellgren-Lawrence [KL] grade) and fluctuate with knee pain. LEVI-04, a first-in-class p75NTR-Fc fusion protein demonstrated significant and clinically meaningful improvements versus placebo for WOMAC pain, function and stiffness, patient global assessment (PGA) and pain on movement (StEPP).[1] LEVI-04 was well tolerated, with no increased incidence of joint pathologies compared to placebo.[1]

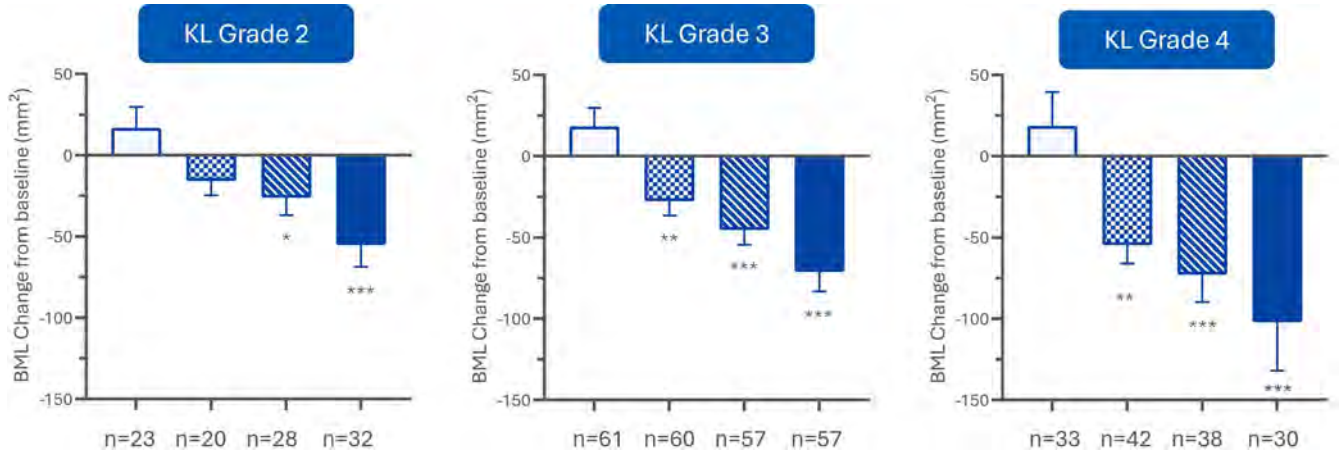
This analysis investigated LEVI-04's effects on BMLs and the relationship with OA symptoms.

Methods: 518 participants with symptomatic knee OA (WOMAC pain ≥ 4/10, KL grade ≥ 2) were enrolled in a Phase II multicentre randomized double-blinded placebo-controlled trial. Participants received placebo or LEVI-04 (0.3, 1, or 2 mg/kg) every 4 weeks through week 16. BML area (mm^2) was measured in a blinded fashion from coronal proton density-weighted fat-suppressed (PD-FS) sequences (slice thickness 3 mm, TE/TR 35/3000 ms) of the target knee at baseline and week 20. For each participant, BML area was determined as the largest area within the MRI sequence of ill-defined high signal intensity of the subchondral bone marrow, and without presence of a fracture line. The perimeter of each BML was highlighted and the area measured electronically using IAG Dynamika™ Software. For BML presence, participants were categorized as



Proportion of participants with bone marrow lesions at baseline and week 20. *P<0.05; **P<0.01 vs placebo at 20 weeks

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Change from baseline in bone marrow lesion area (mm2) in placebo or LEVI-04 0.3, 1 or 2 mg/kg groups at week 20. *P<0.05, **P<0.01; ***P<0.001 vs placebo

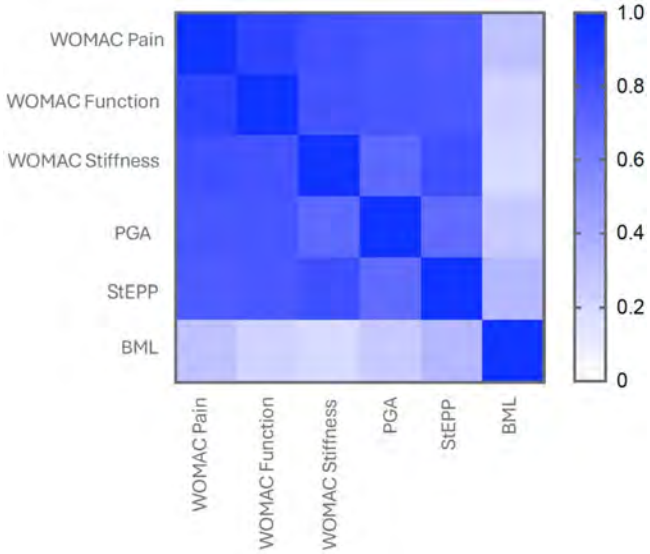


FIGURE 3: Spearman's Rho correlations between change from baseline in BML area and OA symptoms.

BML positive if ≥1 lesion was identified in the target knee. Presence and change from baseline in BML area were assessed in response to LEVI-04. Spearman's Rho correlation was used to assess the relationship between changes in BML area and changes in clinical outcomes.

Results: Presence of BMLs at baseline was similar across LEVI-04 and placebo groups (74-79%). At week 20, there was a significant, dose-dependent reduction in the proportion of participants with BMLs (figure 1) and in mean BML area from baseline (0.3 mg/kg p< 0.01; 1 mg/kg and 2 mg/kg p< 0.001) compared to placebo. A greater absolute reduction in BML area was seen in patients with higher baseline KL grades (figure 2). Comparison between change from baseline in BML area and clinical symptoms for all LEVI-04 groups showed modest yet statistically significant positive correlations (p< 0.001) for WOMAC pain (Rho=0.21), function (Rho=0.22) and stiffness (Rho=0.19), PGA (Rho=0.20), and StEPP (Rho=0.25) (figure 3).

Conclusion: A significant, dose-dependent reduction in BML presence and area across all KL grades was observed for LEVI-04 compared with placebo. Changes in BML area significantly correlated with changes in patient-reported symptoms. LEVI-04 supplements endogenous soluble p75NTR, which is present in the extracellular matrix of OA tissue including BMLs. These findings suggest that LEVI-04 holds promise as a therapy to provide contemporaneous modification of structure (BMLs) and symptoms of OA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Reference: 1. Conaghan P, et al. Arthritis Rheumatol. 2024;76 (suppl 9)

Disclosure: S. Westbrook: Levicept Ltd, 3; **A. Guermazi**: 4Moving, 2, BICL, LLC, 8, Coval, 2, Formation Bio, 2, ICM, 2, Levicept, 2, Medipost, 2, Novartis, 2, Pacira, 2, Paradigm, 2, Peptinov, 3, Scarcell, 2, TissueGene, 2; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6.

Abstract Number: 0853

Olink Proteomics Identifies Macrophage Pro-inflammatory Proteins in Maternal Sera Predictive of Fetal Atrioventricular Block Independent of Maternal Health Status

Philip Carlucci[1], Mala Masson[2], Colin Phoon[3], Ashley Roman[3], Peter Izmirly[4], Amit Saxena[5], Michael Belmont[6], Christina Penfield[3], Young Mi Lee[3], Julie Nusbaum[6], Andrew Rubenstein[3], Nalani Sachan[3], Joel Guthridge[7], Judith James[7], Elena Sinkovskaya[8], Alfred Abuhamad[8], Gary Satou[9], Whitnee Hogan[10], Anita Moon-Grady[11], Lisa Howley[12], Mary Donofrio[13], Stephanie Levasseur[14], Miwa Geiger[15], Sonal Owens[16], Kristopher Cumbermack[17], Jyothi Matta[18], Gary Joffe[19], Christopher Lindblade[20], Caitlin Haxel[21], Katherine Kohari[22], Joshua Copel[22], James Strainic[23], Tam Doan[24], Conisha Holloman[24], Stacy Killen[25], Theresa Tacy[26], Michelle Kaplinski[26], Nicola Fraser[3], Kelly Ruggles[27], Bettina Cuneo[28], Jill Buyon[3] and Robert Clancy[14], [1]New York University School of Medicine, New York, NY, [2]NYU Langone Medical Center-Division of Rheumatology, New York, NY, [3]NYU Grossman School of Medicine, New York, NY, [4]New York University Grossman School of Medicine, New York, NY, [5]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [6]NYU Langone Health, New York, NY, [7]Oklahoma Medical Research Foundation, Oklahoma City, OK, [8]Eastern Virginia Medical School, Norfolk, VA, [9]University of California Los Angeles, Los Angeles, CA, [10]University of Utah, Salt Lake City, UT, [11]University of California San Francisco, San Francisco, CA, [12]Midwest Fetal Care Center, Children's Minnesota/Allina Health, Minneapolis, MN, [13]Children's National Hospital, Washington, DC, [14]Columbia University, New York, NY, [15]Mount Sinai School of Medicine, New York, NY, [16]University of Michigan, Ann Arbo, MI, [17]University of Kentucky, Lexington, KY, [18]University of Louisville, Louisville, KY, [19]Perinatal Associates of New Mexico, Albuquerque, NM, [20]Phoenix Children's Hospital, Phoenix, AZ, [21]University of Vermont Children's Hospital, Burlington, VT, [22]Yale University, New Haven, CT, [23]UH Rainbow Babies, Cleveland, OH, [24]Baylor College of Medicine, Houston, TX, [25]Vanderbilt University, Nashville, TN, [26]Stanford University, Stanford, CA, [27]NYU Grossman School of Medicine, Brooklyn, NY, [28]University of Arizona College of Medicine, Tucson, AZ

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Plenary II (0849–0854)

Session Type: Plenary Session

Session Time: 8:00AM–9:30AM

Background/Purpose: Fetal atrioventricular block (fAVB) is presumed dependent on the transplacental passage of SSA/Ro52/60kD autoantibodies that bind to apoptotic fetal cardiomyocytes, triggering macrophage activation and cardiac fibrosis. While anti-Ro is necessary for fAVB, titers alone are insufficient for prediction which challenges preconception counseling, surveillance, and trial design. Thus, identification of additional permissive factors for injury would yield greater understanding of pathogenesis and more precise biomarkers of significant clinical utility. The biobanks generated from the STOP BLOQ and PATCH trials represent a rare opportunity to evaluate sera collected during pregnancy but prior to fAVB occurrence. Accordingly, this study leveraged these samples and Olink proteomics to identify additional predictive serum proteins for fAVB in high titer anti-Ro pregnant subjects.

Methods: Sera from 12 fAVB affected pregnancies were matched to 13 high titer anti-Ro exposed healthy pregnancies. To eliminate factors conferring a change in serum proteins and/or fAVB risk, samples were matched on race/ethnicity, maternal rheumatologic diagnosis, anti-Ro52 and 60 titers (ELISA in our research lab), and hydroxychloroquine dose. All samples were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Clinical characteristics of fAVB and Anti-Ro+ non fAVB pregnancies. Data are represented as median (IQR) or N (%). fAVB: fetal atrioventricular block, SLE: Systemic Lupus Erythematosus, SjD: Sjögren's Disease, UAS: Undifferentiated Autoimmune Syndrome

Clinical Characteristic	Anti-Ro+ fAVB N=12	Anti-Ro+ non-fAVB Healthy N=13
Age	28 (28-32)	34 (32-36)
Race		
Asian	1 (8.3%)	1 (7.6%)
Black	1 (8.3%)	1 (7.6%)
White	10 (83.3%)	11 (84.6%)
Ethnicity		
Hispanic	1 (8.3%)	0 (0%)
Non-Hispanic	11 (91.6%)	13 (100%)
Previous Child With fAVB	0 (0%)	0 (0%)
Maternal Diagnosis		
Asymptomatic/UAS	6 (50.0%)	5 (38.5%)
SLE	1 (8.3%)	1 (7.6%)
SjD	4 (33.3%)	7 (53.8%)
SjD/SLE	1 (8.3%)	0 (0%)
Any dose Hydroxychloroquine	11 (91.6%)	13 (100%)
400 mg Hydroxychloroquine	6 (50.0%)	7 (53.8%)
Ro52 titer (ELISA Units/mL)	12621 (10136-20732)	18536 (8975-20420)
Ro60 titer (ELISA Units/mL)	32772 (14536-37775)	31890 (18005-42395)

collected prospectively between weeks 10-19 during enrollment in STOP BLOQ or PATCH and, for affected pregnancies, before the development of fAVB. Samples from five anti-Ro negative healthy pregnant women were also tested. Serum proteins (>5400) were assessed by the Olink Explore HT assay. Principal component analysis (PCA) was performed and a t-test was

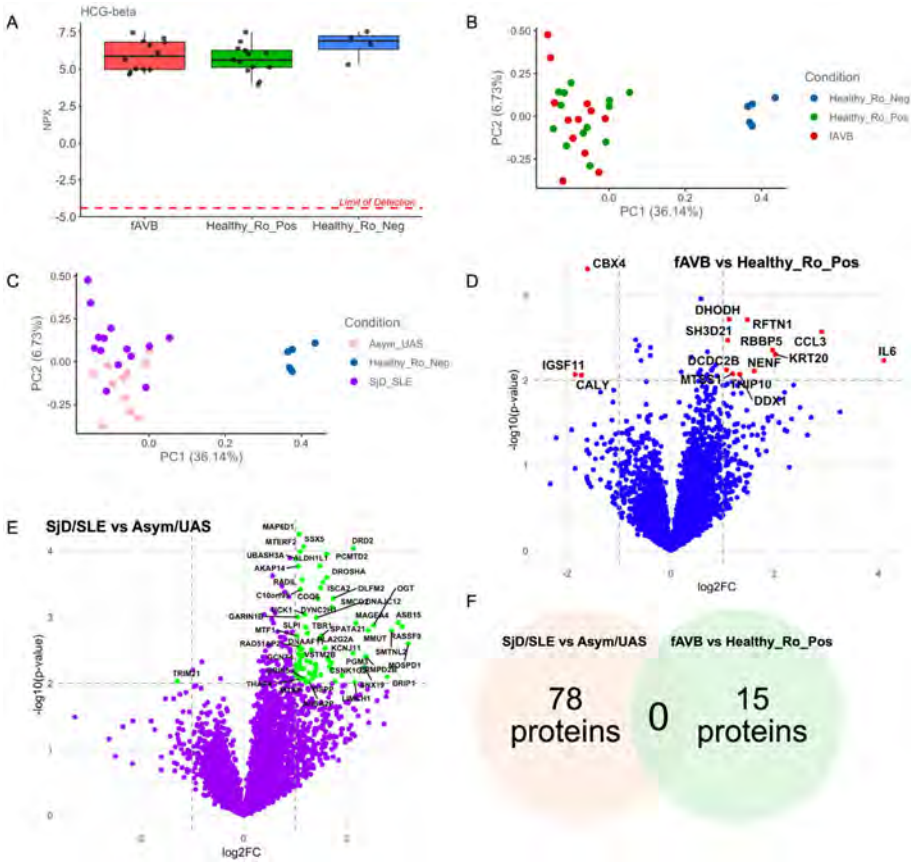


Figure 1: A) Boxplots showing the levels of HCG-beta detected among the fAVB, anti-Ro+ healthy, and anti-Ro- healthy pregnancies. Note that one healthy anti-Ro negative control is not represented due to a QC failure for the HCG-beta assay. The horizontal red dashed line represents the technical lower limit of detection for HCG-beta provided by Olink. B) PCA visualization of the fAVB, anti-Ro+ healthy, and anti-Ro- healthy pregnancies. C) PCA visualization of the Asym/UAS, SjD/SLE, and anti-Ro- healthy pregnancies. D) Volcano plot showing the 15 differentially abundant proteins between fAVB and anti-Ro+ healthy subjects. E) Volcano plot showing the 78 differentially abundant proteins between SjD/SLE and Asym/UAS subjects. F) Venn diagram showing that none of the 78 differentially abundant proteins between SjD/SLE and Asym/UAS subjects overlap with the 15 differentially abundant proteins between fAVB and anti-Ro+ healthy subjects.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

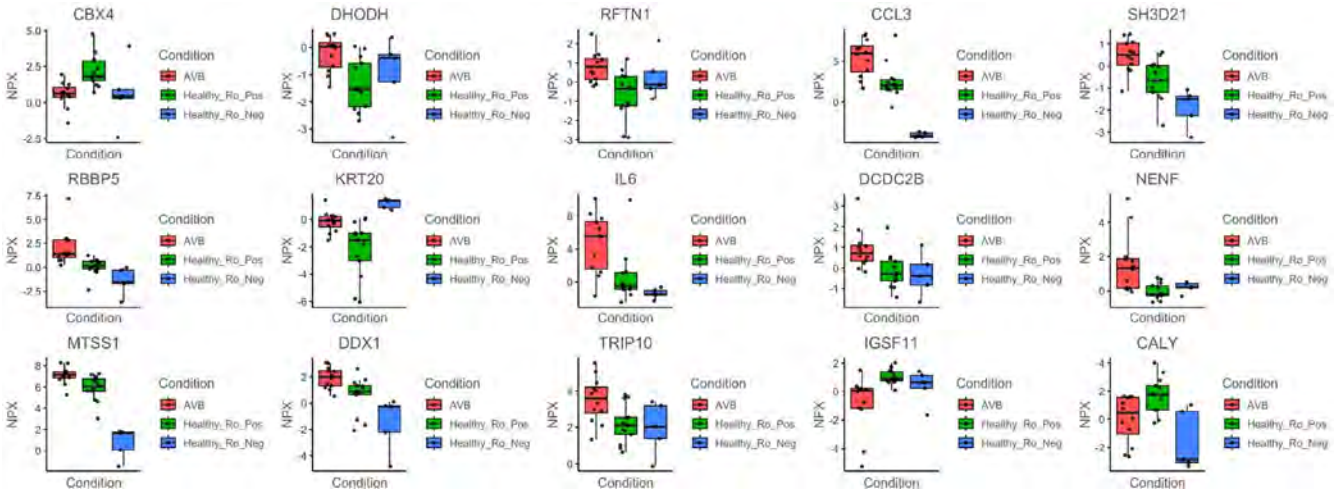


Figure 2: Boxplots showing the levels of the 15 significantly different proteins with p<0.01 and log2FC < -1 or > 1 between fAVB and anti-Ro+ healthy subjects.

employed to compare fAVB to anti-Ro exposed healthy pregnancies. Candidate proteins had a p< 0.01 and log2FC |1|.

Results: The 12 fAVB pregnancies and 13 anti-Ro+ non-fAVB pregnancies were well matched on clinical variables (Table 1). As a validation, high levels of HCG-beta were detected (Fig 1A). The PCA effectively distinguished anti-Ro+ from anti-Ro- pregnancies and asymptomatic or undifferentiated autoimmune syndrome (Asym/UAS) from SjD/SLE, but did not separate fAVB from non-fAVB cases (Fig 1B & 1C). While 78 proteins separated Asym/UAS from SjD/SLE, there were 15 other differentially abundant proteins between fAVB vs anti-Ro+ non-fAVB pregnancies (Fig 1D & 2). That these 15 proteins did not differ between UAS and SjD/SLE pregnancies supports prior observations that maternal diagnosis does not influence fAVB risk (Fig 1E & 1F). Two macrophage related proteins, IL6 (log2FC = 4.1) and CCL3 (log2FC = 3.9), showed the greatest difference between fAVB and non-fAVB subjects (Fig 2), and were highly correlated (r=0.84, p< 0.0001). Neither were correlated with either anti-Ro52 or 60 levels.

Conclusion: This high-throughput evaluation of prospective samples collected early in pregnancy provides insights into novel proteins that predict the development of fAVB in anti-Ro exposed pregnancies. Given the low molecular weight of these novel pro-inflammatory candidates, passive transport across the placenta supports an additional maternal contribution (not related to maternal disease status which was separated by other proteins) to the pathogenesis by amplifying anti Ro-mediated fetal cardiac injury.

Disclosure: P. Carlucci: None; **M. Masson**: None; **C. Phoon**: None; **A. Roman**: None; **P. Izmirly**: Hansoh Bio, 2; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **M. Belmont**: None; **C. Penfield**: None; **Y. Lee**: None; **J. Nusbaum**: None; **A. Rubenstein**: None; **N. Sachan**: None; **J. Guthridge**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **E. Sinkovskaya**: None; **A. Abuhamad**: None; **G. Satou**: None; **W. Hogan**: None; **A. Moon-Grady**: None; **L. Howley**: GE Healthcare, 2; **M. Donofrio**: None; **S. Levasseur**: None; **M. Geiger**: Brightheart, 2; **S. Owens**: None; **K. Cumbermack**: None; **J. Matta**: None; **G. Joffe**: None; **C. Lindblade**: None; **C. Haxel**: None; **K. Kohari**: Myriad, 5, Natera, 5; **J. Copel**: Janssen, 1, 2; **J. Strainic**: None; **T. Doan**: None; **C. Holloman**: None; **S. Killen**: None; **T. Tacy**: None; **M. Kaplinski**: None; **N. Fraser**: None; **K. Ruggles**: None; **B. Cuneo**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **R. Clancy**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0854

The Assessments in Spondyloarthritis International Society (ASAS) and Spondyloarthritis Research and Treatment Network (SPARTAN) Revised Classification Criteria for Axial Spondyloarthritis: Development and Validation in the Classification of Axial SpA Inception Cohort Study

Walter P. Maksymowych[1], Désirée van der Heijde[2], Liron Caplan[3], Robert Landewé[4], Lianne S. Gensler[5], Pedro Machado[6], Alexandre Sepriano[7], Floris A. van Gaalen[2], Miranda van Lunteren[2], Ben Vandermeer[8], Servet Akar[9], Sibel Aydin[10], Xenofon Barliakos[11], Wilson bautista molano[12], Stephanie Bernard[13], RUBEN BURGOS-VARGAS[14], John Carrino[15], Alberto Cauli[16], Jonathan Chan[17], Abhijeet Danve[18], Torsten Diekhoff[19], Maxime Dougados[20], iris Eshed[21], Warren Fong[22], Rodrigo García Salinas[23], Hildrun Haibel[24], Nigil Haroon[25], Kay-Geert Hermann[26], Lennart Jans[27], Anne Jurik[28], Uta Kiltz[29], Tae-Jong Kim[30], Robert G. W. Lambert[31], Clementina López Medina[32], Ennio Lubrano[33], Marina Magrey[34], Vikas Majithia[35], Helena Marzo-Ortega[36], Philip J. Mease[37], Victoria Navarro-Compan[38], John O'Neill[39], Mikkel Ostergaard[40], Salih Ozgocmen[41], Susanne Pedersen[42], Fernando Pimentel-Santos[43], Denis Poddubnyy[44], Fabian Proft[45], Sofia Ramiro[46], Monique Reijnierse[47], John Reveille[48], Ruxandra Elena Schiotis[49], Hasan Tahir[50], Michael Tuite[51], Filip Van den Bosch[52], Runshen Wang[53], Ulrich Weber[54], James Cheng-Chung[55], Joachim Sieper[56], Atul Deodhar[57], and Martin Rudwaleit[58], [1]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [3]Medicine Service, Rocky Mountain Regional VAMC, Aurora, CO, [4]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [5]Department of Medicine/ Rheumatology, University of California, San Francisco, San Francisco, CA, [6]Department of Rheumatology, University College London, and Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS Trust, Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [7]Department of Rheumatology, Leiden University Medical Centre, Portela Loures, Portugal, [8]Department of Medicine, University of Alberta, Edmonton, AB, Canada, [9]Department of Medicine, Izmir Katip Celebi University School of Medicine, Izmir, Turkey, [10]Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [11]Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany, [12]University Hospital Fundacion Santa Fe de Bogota, Bogota, Colombia, [13]Department of Radiology, Brooke Army Medical Center, Fort Sam Houston, TX, [14]Department of Rheumatology, Hospital General de Mexico, Faculty of Medicine, Universidad Nacional Autonoma de Mexico, Ciudad de México, Mexico, [15]Department of Radiology and Imaging, Hospital for Special Surgery, New York, NY, [16]Rheumatology Unit, Department of Medicine and Public Health, AOU and University of Cagliari, Cagliari, Italy, [17]Department of Medicine, University of British Columbia, Vancouver, BC, Canada, [18]Section of Rheumatology, Department of Medicine, Yale School of Medicine, New Haven, CT, [19]Department of Radiology, Immanuel Clinic Ruedersdorf, Brandenburg Medical School, Ruedersdorf, Germany, [20]Department of Medicine, Hopital Cochin, Universite de Paris, Paris, France, [21]Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer affiliated with School of Medicine, Tel Aviv University, Tel Aviv, Israel, [22]Department of Medicine, Singapore General Hospital, Singapore, Singapore, [23]Hospital Italiano La Plata, La Plata, Argentina, [24]Charite- University Medicine Berlin Campus Benjamin Franklin, Berlin, Germany, [25]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada, [26]Department of Radiology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [27]Department of Radiology, Ghent University Hospital, Ghent, Belgium, [28]Department of Radiology, Aarhus University Hospital, Aarhus, Denmark, [29]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [30]Department of Medicine, Chonnam National University Hospital, Seoul, Republic of Korea, [31]University of Alberta, Department of Radiology & Diagnostic Imaging, Edmonton, AB, Canada, [32]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [33]Department of Medicine, Università deglia Studi del Molise, CAMPOBASSO, Italy, [34]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH, [35]Mayo Clinic Hospital, Jacksonville, FL, [36]NIHR Leeds Biomedical Research Centre, The Leeds Teaching Hospitals NHS Trust and Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom, [37]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [38]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [39]Department of Radiology, McMaster University, Hamilton, ON, Canada, [40]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark, [41]Department of Rheumatology, Istinye University/Faculty of Medicine, Istanbul, Turkey, [42]Department of Medicine, Rigshopital, University of Copenhagen, Copenhagen, Denmark, [43]NOVA Medical School, Universidade NOVA e Lisboa, Lisboa, Portugal, [44]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [45]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [46]Leiden University Medical Center, Bunde, Netherlands, [47]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [48]Department of Medicine, University of Texas Medical Center, Houston, TX, [49]Clinical Hospital of Infectious Diseases, Rheumatology Department, Cluj-Napoca, Romania, [50]Department of Medicine, Royal Free NHS Foundation Trust, London, United Kingdom, [51]Department of Radiology, University of Wisconsin School of Medicine and Public Health, Madison, WI [52]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [53]Division of Rheumatology, Columbia University Irving Medical Center and Garden State Rheumatology Consultants, Union, NJ, [54]Medical Centre of Zenit, Department of Rheumatology, Schaffhausen, Switzerland, [55]Department of Medicine, Chung Shan Medical University Hospital, Taichung, Taiwan (Republic of China), [56]Department of Medicine, Charité – Universitätsmedizin Berlin, Berlin, Germany [57]Division of Arthritis and Rheumatic Diseases, Oregon Health & Sciences University, Portland, OR, [58]Bielefeld University, Medical School and University Medical Centre OWL, Klinikum Bielefeld, Department of Rheumatology, Bielefeld, Germany.

Figure 1. ASAS-SPARTAN revised classification criteria for axial spondyloarthritis in A. Tree, and B. Table, formats.

A.

Patients with a diagnosis of axial spondyloarthritis (mimics excluded)
Plus
History of chronic back pain (≥3 months) and age of onset <45 years

MRI indicative of axSpA in the sacroiliac joints* plus ≥3 additional points
OR
Radiographic Sacroiliitis** plus ≥4 additional points

OR

HLA-B27
plus ≥7 additional points

SpA Feature	Points
HLA-B27◇	4
Inflammatory back pain+	3
Peripheral arthritis	1
Inflammatory bowel disease	1
Acute anterior uveitis	1
Heel enthesitis (current, heel)	1
Elevated CRP (>5mg/L)	1
Psoriasis	1

Cut-off ≥11 points is required to classify a patient with axial spondyloarthritis

*MRI indicative of axSpA in the sacroiliac joints by global evaluation of all MRI sequences depicting active and structural lesions. **According to the modified New York criteria
◇HLA-B27 does not count twice
+Ascertained by clinician global assessment

B.

Patients with a diagnosis of axial spondyloarthritis (mimics excluded)
Plus
History of chronic back pain (≥3 months) and age of onset <45 years

SpA Feature	Points
MRI indicative of axSpA in the sacroiliac joints*	8
OR	
Radiographic sacroiliitis**	7
HLA-B27	4
Inflammatory back pain+	3
Peripheral arthritis	1
Inflammatory bowel disease	1
Acute anterior uveitis	1
Heel enthesitis	1
Elevated CRP	1
Psoriasis	1

Cut-off ≥11 points is required to classify a patient with axial spondyloarthritis

*MRI indicative of axSpA in the sacroiliac joints by global evaluation of all MRI sequences depicting active and structural lesions.
**According to modified New York criteria
+Ascertained by clinician global assessment

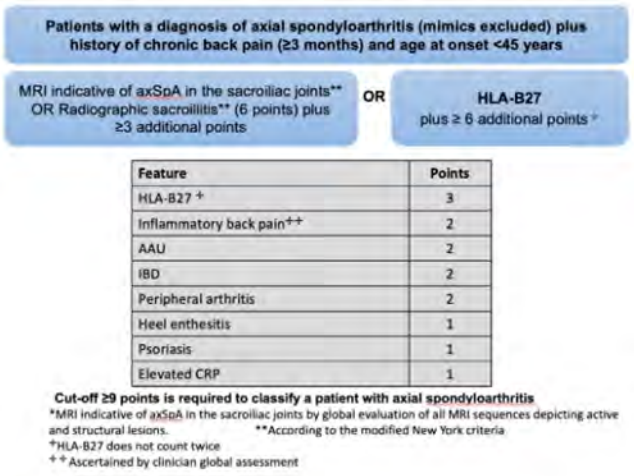
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Plenary II (0849–0854)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Figure 2. Rejected alternative proposal for axial spondyloarthritis classification criteria in A. Tree, and B. Table, formats.

A.



Feature	Points
HLA-B27 +	3
Inflammatory back pain++	2
AAU	2
IBD	2
Peripheral arthritis	2
Heel enthesitis	1
Psoriasis	1
Elevated CRP	1

Cut-off ≥9 points is required to classify a patient with axial spondyloarthritis
*MRI indicative of axSpA in the sacroiliac joints by global evaluation of all MRI sequences depicting active and structural lesions. **According to the modified New York criteria
+HLA-B27 does not count twice
++ Ascertained by clinician global assessment

B.

Feature	Points
MRI indicative of axSpA in the sacroiliac joints* OR Radiographic sacroiliitis**	6 6
HLA-B27 +	3
Inflammatory back pain++	2
AAU	2
IBD	2
Peripheral arthritis	2
Heel enthesitis	1
Psoriasis	1
Elevated CRP	1

Cut-off ≥9 points is required to classify a patient with axial spondyloarthritis
No classification if both imaging and HLA-B27 are negative
*MRI indicative of axSpA in the sacroiliac joints by global evaluation of all MRI sequences depicting active and structural lesions.
**According to the modified New York criteria
++ Ascertained by clinician global assessment

Table. Sensitivity and specificity of A. ASAS-SPARTAN revised classification criteria, and B. Rejected proposal, for final rheumatologist diagnosis of axial spondyloarthritis

A.

Source of Imaging Data	Testing Database (n=508)		Validation database (n=507)	
	Sensitivity	Specificity	Sensitivity	Specificity
Central readers (2 out 3)*	56.6	98.5	63.1	98.7
Central reader 1**	60.6	95.5	61.5	97.1
Central reader 2**	57.7	94.6	65.6	96.5
Local reader	78.9	89.2	**79.5**	**90.4**

*Adjudicated central reader data ** individual primary central reader

B.

Source of Imaging Data	Testing database (n=508)		Validation database (n=507)	
	Sensitivity	Specificity	Sensitivity	Specificity
Central readers (2 out 3)*	56.0	97.9	62.1	97.1
Central reader 1**	60.0	94.9	60.0	95.2
Central reader 2**	56.6	95.2	65.1	94.9
Local reader	72.6	89.5	**76.9**	**90.7**

*Adjudicated central reader data ** individual primary central reader

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The 2009 ASAS classification criteria had sensitivity (Sn) of 83% and specificity (Sp) of 84% for a rheumatologist diagnosis of axial spondyloarthritis (axSpA). Given the high prevalence of back pain, greater specificity would be desirable. The global Classification in Axial Spondyloarthritis Inception Cohort (CLASSIC) study was established as a combined initiative of ASAS and SPARTAN to validate the performance of the 2009 criteria according to prespecified Sn/Sp targets of ≥75%/≥90%.

Methods: CLASSIC recruited consecutive patients referred to a rheumatologist with current undiagnosed back pain of ≥3 months duration with onset ≤45 years of age. Diagnostic evaluations for axSpA were performed at 5 stages: Stage 5 provided all diagnostic information including centralized imaging review by two primary readers and an adjudicator, and served as reference standard. The cohort data were randomly divided into testing and validation datasets (50:50). The testing dataset was used to develop candidate criteria, while the validation dataset evaluated whether criteria achieved the Sn/Sp targets, using the stage 5 global diagnosis as the reference standard. Regression techniques (least absolute shrinkage and selection operator (LASSO), multivariable logistic regression (MLR)) were used to identify which SpA variables were independently associated with stage 5 diagnosis and for estimating the strength of this association according to LASSO coefficients. Final selection of SpA variables and their weighting was determined by expert consensus and the final proposal was selected by a vote of the combined ASAS and SPARTAN membership.

Results: CLASSIC included 1015 patients from 61 centers in 27 countries of whom 370 (36.5%) were diagnosed with axSpA per stage 5 global. The 2009 ASAS classification criteria did not meet the prespecified targets (Sn 82.4%, Sp 77.1%)[1], indicating the need for revised criteria. MRI of the SIJ indicative of axSpA by global assessment of both active and structural lesions had the highest independent association with stage 5 diagnosis of axSpA followed by radiographic sacroiliitis. Selected clinical variables were HLA-B27, inflammatory back pain, inflammatory bowel disease, acute anterior uveitis, heel enthesitis, and dactylitis. Expert consensus led to the inclusion of psoriasis and replacement of dactylitis by elevated CRP. Two high-performing proposals in the testing dataset achieved the Sn/Sp targets in the validation dataset (Figures 1 and 2). The final proposal selected by the ASAS-SPARTAN vote (158 vs 151, 9 abstained) assigned weights for the selected SpA variables based on LASSO coefficients and achieved Sn of 79.5% and Sp of 90.4% in the validation dataset (Table).

Conclusion: The ASAS-SPARTAN revised classification criteria for axSpA achieved prespecified performance targets of ≥75% sensitivity and ≥90% specificity, emphasizing the central role of imaging and incorporating a more focused set of clinical variables compared to the 2009 ASAS criteria.

1. Maksymowych et al. Arthritis Rheumatol 2024;76 (suppl 9):0820

Disclosure: W. Maksymowych: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **D. van der Heijde**: AbbVie/Abbott, 2, Alfasigma, 2, ArgenX, 2, Bristol-Myers Squibb(BMS), 2, Eli-Lilly, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 4, Janssen, 2, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; **L. Caplan**: None; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **L. Gensler**: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **P. Machado**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **A. Sepriano**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, UCB, 2, 6; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **M. van Lunteren**: None; **B. Vandermeer**: None; **S. Akar**: None; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **X. Barliakos**: Abbvie, 1, 2, 5, Advanz, 1, 2, Alexion, 1, 2, Alfasigma, 1, 2, Amgen, 1, 2, Astra Zeneca, 1, 2, Bristol-Myers Squibb(BMS), 1, 2, Celltrion, 1, 2, 5, Cesas, 1, 2, Clarivate, 1, 2, Eli-Lilly, 1, 2, Galapagos, 1, 2, Janssen, 5, Johnson and Johnspn, 1, 2, Moonlake, 1, 2, 5, Novartis, 1, 2, 5, Peervoice, 1, 2, Pfizer,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1, 2, Roche, 1, 2, Sandoz, 1, 2, Springer, 1, 2, Stada, 1, 2, Takeda, 1, 2, UCB Pharma, 1, 2, Zuellig, 1, 2; **W. bautista molano**: None; **S. Bernard**: None; **R. BURGOS-VARGAS**: None; **J. Carrino**: Arthritis & Rheumatology, 12, Editorial Board, Carestream, 4, Cartilage Imaging, 12, Editorial Board, Covera, 2, Image Analysis Group, 4, Image Biopsy Lab, 4, Radiology, 12, Editorial Board; **A. Cauli**: None; **J. Chan**: Abbvie, 2, 6, Celltrion, 2, 6, Eli-Lilly, 2, 6, Fresenius, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Organon, 2, 6, UCB Pharma, 2, 6; **A. Danve**: AbbVie, 2, Amgen, 2, Eli Lilly, 5, Janssen, 2, Novartis, 2, 5; **T. Diekhoff**: Abbvie, 1, 6, Berlin Flame, 1, 6, Bracco, 2, 6, Canon MS, 2, 6, Eli-Lilly, 1, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, UCB Pharma, 1, 2, 6; **M. Dougados**: None; **i. Eshed**: None; **W. Fong**: None; **R. García Salinas**: AbbVie/Abbott, 2, 5, 6, Adium, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Raffo, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **H. Haibel**: Abbvie, 2, 6, Alfasigma, 5, GlaxoSmithKlein(GSK), 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, Sobi, 5, 6, UCB Pharma, 2, 5, 6; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2; **K. Hermann**: None; **L. Jans**: Abbvie, 6, Alfasigma, 6, Eli-Lilly, 6, Janssen, 6, Novartis, 6, UCB Pharma, 6; **A. Jurik**: None; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **T. Kim**: None; **R. Lambert**: AbbVie, 2, CARE Arthritis and Image Analysis Group, 2; **C. López Medina**: None; **E. Lubrano**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GlaxoSmithKlein, 6, Johnson & Johnson, 6, Novartis, 6, UCB, 6; **M. Magrey**: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **V. Majithia**: None; **H. Marzo-Ortega**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 6, UCB, 2, 5, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **J. O'Neill**: None; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6; **S. Ozgocmen**: None; **S. Pedersen**: None; **F. Pimentel-Santos**: None; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **F. Proft**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Hexal, 2, 6, Janssen, 2, 6, Medscape, 2, 6, MoonLake Pharma, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 5, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **M. Reijnierse**: None; **J. Reveille**: Surf Therapeutics, 5; **R. Schiotis**: None; H. Tahir: Abbvie, 2, 6, Eli-Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, UCB Pharma 2, 6; **M. Tuite**: GE Health Care, 2; **F. Van den Bosch**: Abbvie, 2, 6, Alfasigma, 2, Amgen, 2, 6, Eli Lilley, 2, Galapagos, 2, Grey Wolf Therapeutics, 2, Janssen, 2, 6, Merck, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **R. Wang**: None; U. Weber: Eli-Lilly, 6, Novartis, 6; **J. Wei**: None; J. Sieper: Abbvie, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6; UCB Pharma, 2, 6; **A. Deodhar**: BMS, 2, 6, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, Moonlake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. Rudwaleit**: AbbVie, 2, Boehringer Ingelheim, 2, Janssen, 2, 6, Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2.

Abstract Number: 0855

Certolizumab Pegol to Prevent Adverse Pregnancy Outcomes in Patients with Antiphospholipid Syndrome and Lupus Anticoagulant (IMPACT): Results from Ongoing Recruitment of a Prospective, Single-Arm, Open-Label, Phase 2 Trial

Jane Salmon[1], Mimi Kim[2], Marta Guerra[1], Joseph Worden[3], Carl Laskin[4], Maria DeSancho[5], Inna Landres[5], Jason S. Knight[6], Haley Slosberg[1], Margaret Minett[1] and Ware Branch[7], [1]Hospital for Special Surgery, New York, NY, [2]Albert Einstein College of Medicine, Bronx, NY, [3]University of Utah School of Medicine, Salt Lake City, [4]University of Toronto,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Toronto, ON, Canada, [5]Weill Cornell Medicine, New York, [6]University of Michigan, Ann Arbor, MI, [7]University of Utah Health Sciences Center, Salt Lake City, UT

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Antiphospholipid Syndrome (0855–0860)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: The IMPACT trial (NCT03152058) showed that certolizumab appears effective in preventing placenta-mediated adverse pregnancy outcome (APO) in high-risk antiphospholipid syndrome (APS) patients. We have continued recruitment to this trial and herein summarize our findings.

Methods: We assessed treatment with certolizumab in pregnant patients with APS and LA, administered gestational weeks 8 through 28, in addition to standard treatment with low molecular weight heparin and low dose aspirin. The primary APO was a composite of fetal death >10 weeks' gestation or preeclampsia with severe features or placental insufficiency requiring delivery < 34 weeks' gestation. The target sample size for the IMPACT trial was 45 with expected APO rate of 20% with certolizumab versus 40%, the assumed APO rate under the null hypothesis which was considered to be conservative by the study team given the observed APO rate of 44% among IMPACT-eligible patients (ie, with APS and LA) in the PROMISSE Study (N=61). Published results of the IMPACT Trial (Branch et al., Ann Rheum Dis, ePub ahead of print 2025) include data for 45 completed pregnancies. Ongoing recruitment has enrolled 5 additional patients.

Table 1: Demographic and Clinical Characteristics of IMPACT Patients	Modified Intention-to-Treat (N=50)
Age, years, median (range)	32 (20–40)
Body mass index, kg/m^2, median (range)	25.7 (18.7–44.9)
<25, N (%)	23 (46)
25–30, N (%)	15 (30)
>30, N (%)	12 (24)
Ethnicity	
Hispanic/Latina, N (%)	10 (20)
Race	
White, N (%)	39 (78)
Asian, N (%)	4 (8)
Black, N (%)	1 (2)
>1 Race, N (%)	2 (4)
Other/Not Reported, N (%)	4 (8)
Lupus anticoagulant (LA), N (%)	50 (100)
Anticardiolipin (aCL) and LA, N (%)	28 (56)
IgG positive[4]	26 (52)
IgM only positive[4]	2 (4)
Anti-beta-2 glycoprotein-1 (aB2GP1) and LA, N (%)	25 (50)
IgG positive[4]	23 (46)
IgM only positive[4]	2 (4)
aCL or aB2GP1 and LA, N (%)	34 (68)
IgG positive	31 (62)
IgM only positive	3 (6)
aCL and aB2GP1 and LA positive, N (%)	19 (38)
IgG positive	18 (36)
IgM only positive	1 (2)
LA positive only, N (%)	16 (32)
Systemic lupus erythematosus, N (%)	8 (16)
With renal involvement, N (%)	1 (2)
History of thrombotic features of APS, N (%)	34[2] (68)
Venous thromboembolism, N (%)	29 (58)
Arterial thromboembolism, N (%)	6 (12)
Stroke, N (%)	4 (8)
Other,[3] N (%)	2 (4)
History of obstetric features of APS, N (%)	43 (86)
History of thrombotic and obstetric features of APS, N (%)	27 (54)
History of immune thrombocytopenia, N (%)	5 (10)
Medications at enrollment	
Low molecular weight heparin, N (%)	50 (100)
Thromboprophylactic, N (%)	23 (46)
Therapeutic, N (%)	27 (54)
Low dose aspirin, N (%)	50 (100)
Hydroxychloroquine, N (%)	31 (62)
Azathioprine, N (%)	2 (4)
Prednisone,[4] N (%)	1 (2)
Other,[5] N (%)	2 (4)

[1] Defined as > 40 standard units in most recent assay result
[2] One patient had a history of both arterial and venous thrombosis
[3] Includes 2 patients with amaurosis fugax
[4] Prednisone <10 mg daily
[5] Includes 1 patient on tacrolimus and 1 patient on labetalol and nifedipine

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Obstetric History of IMPACT Modified Intention-to-Treat Patients (N=50)			
Individual Patients (N=47)[1]			
Gravidity excluding study pregnancy, median (range)	2 (1-9)		
History of ≥3 consecutive early losses (<10 weeks' gestation)[2], N (%)	3 (6)		
History of fetal death(s) ≥ 10 weeks' gestation, N (%)	35 (74)		
History of preeclampsia or placental insufficiency requiring delivery <34 weeks' gestation, N (%)	35 (74)		
History of a prior IMPACT adverse pregnancy outcome[3], N (%)	41 (87)		
History of live birth surviving to hospital discharge, N (%)	17 (36)		
Prior Pregnancy Outcomes			
	All prior pregnancies	LDA and LMWH[4] treated prior pregnancies	LDA, LMWH[4] and HCQ treated prior pregnancies
Total Pregnancies, N	118[5]	53[6]	16[7]
Pregnancies beyond 10 weeks' gestation, N	74	36	12
Fetal death > 10 weeks gestation, N (% of pregnancies beyond 10 weeks' gestation)	48 (65)	20 (56)	8 (67)
Preeclampsia or placental insufficiency requiring delivery <34 weeks' gestation, N (% of pregnancies beyond 10 weeks' gestation)	43 (58)	23 (64)	9 (75)
IMPACT adverse pregnancy outcome[3], N (% of pregnancies beyond 10 weeks' gestation)	56 (76)	26 (72)	9 (75)
Live birth surviving to hospital discharge, N (% of pregnancies beyond 10 weeks' gestation)	22 (30)	13 (36)	3 (25)

[1] Three patients had no prior pregnancies
[2] In 2 of the 3 patients, thus was the only obstetric criterion for APS
[3] Otherwise unexplained fetal death and/or preeclampsia or placental insufficiency requiring delivery <34 weeks
[4] Defined as low dose aspirin and heparin agent started in 1st trimester of pregnancy
[5] Total number of pregnancies among 47 modified intention-to-treat patients with prior pregnancies
[6] Total number of pregnancies among 26 patients treated with LDA and LMWH
[7] Total number of pregnancies among 8 patients treated with LDA, LMWH and HCQ, 4 of whom had SLE

Table 3: IMPACT Outcomes	Modified Intention-to-Treat
Primary Outcome	**N = 50**
Otherwise Unexplained Fetal Death ≥10 Weeks' Gestation	3
Preeclampsia or Placental Insufficiency Requiring Delivery <34 Weeks' Gestation	7
Composite primary outcome N (%)	9[1] (18.0)
Infant survival	**N = 50**
Live births	47 (94)
Live births surviving to hospital discharge	47 (94)
Non-obstetric Secondary Outcomes	**N = 50**
Maternal thrombosis N(%)	1 (2)
Known adverse reaction to certolizumab	0
Obstetric Secondary Outcomes	**N = 47**[2]
Gestational age at delivery	
With primary outcome, median (range)	31 (27-33)
Without primary outcome, median (range)	37 (32-39)
Preterm live births (<37 weeks' gestation)	
With primary outcome, N (%)	6 (13)
Without primary outcome, N (%)	15 (32)[3]
Preeclampsia or placental insufficiency not requiring delivery <34 weeks' gestation, N (%)	3 (6)[4]
Small-for-for gestational age birthweight (<10th percentile)	
With primary outcome, N (%)	3 (6)
Without primary outcome, N (%)	6 (13)
Neonatal death due to preterm birth for preeclampsia or placental insufficiency, N (%)	0

[1] One participant met both outcomes: intrauterine fetal death at 21 weeks and preeclampsia with severe features
[2] Obstetric secondary outcomes are only applicable to live births
[3] Includes 1 case each of preterm labor at 32 weeks' gestation; maternal pulmonary hypertension at 35 weeks' gestation, flare of polychondritis at 35 weeks' gestation, and suspected fetal growth restriction at 36 weeks' gestation; 2 cases of preterm premature rupture of the membranes, 3 cases of fetal growth restriction (2 at 34 weeks' and 1 at 36 weeks' gestation), 2 cases of cholestasis of pregnancy at 36 weeks' gestation; and 4 cases of patient-physician shared-decision elective preterm delivery at 35 or 36 weeks' gestation.
[4] Diagnosed with fetal growth restriction/placental insufficiency and were delivered of small-for-gestational age infants in the absence of preeclampsia.

Results: In the now completed IMPACT Trial, the pre-determined criteria for efficacy of certolizumab were met. The primary APO rate in the original trial was 20% (9/45 in the modified intention-to-treat population) compared to 40% in historic controls from the PROMISSE Study. With ongoing recruitment, 57 patients have now been enrolled and 56 patients have completed their participation in the trial. Of those enrolled with a prior pregnancy, 87% had a history of an IMPACT primary APO. Baseline characteristics are included in Table 1. Outcomes of prior pregnancies in IMPACT participants are included in Table 2: of 39 previous pregnancies treated with LMWH and LDA that progressed beyond 10 weeks' gestation 27, (69%) resulted in an IMPACT APO, and only 15 (38%) were liveborn and survived to hospital discharge. Excluding 6 patients that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

had a pregnancy loss < 10 weeks' gestation or fetal loss due to genetic abnormalities, outcomes from the certolizumab-treated pregnancy of 50 modified intention-to-treat participants are described below (Table 3). Nine had a primary APO (18.0%; 95% CI: 8.6% - 31.4%), meeting the predetermined criteria for efficacy of certolizumab and significantly lower rates than in historical controls. There were 47 (94%) liveborn infants and all survived to hospital discharge. Median gestational age at delivery was 37 weeks for patients without the primary outcome and 31 weeks for those with the primary outcome. Three patients delivered prematurely (after 34 but before 37 weeks' gestation) because of placental insufficiency and thus met a secondary outcome. In the trial, there were no serious infections, no substantial increases in antiphospholipid antibodies or other autoantibody levels, and no new cases or severe flares of lupus.

Conclusion: Results of our ongoing enrollment indicate that certolizumab appears effective in preventing placenta-mediated adverse outcomes in high-risk APS patients.

Disclosure: J. Salmon: UCB, 1, 5; **M. Kim**: None; **M. Guerra**: None; **J. Worden**: None; **C. Laskin**: None; **M. DeSancho**: None; **I. Landres**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **H. Slosberg**: None; **M. Minett**: None; **W. Branch**: UCB, 5.

Abstract Number: 0856

Integrated Single-Cell and Spatial Transcriptomics Reveal Vascular and Immune Pathogenesis in APS Nephropathy

Shuyi Yu[1], Haoyu Pan[1], Jinyi Qian[1], Xiaohan Wei[2], Yuying Fan[1], Zhixia Yang[1], Shiyan Gu[1], Jianzhou Wu[1], Cenyi Wang[1], Tiancheng Zhou[1] and Hui Shi[3], [1]Department of Rheumatology and Immunology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [2]Shanghai JiaoTong University, Shanghai, China (People's Republic), [3]Shanghai Jiaotong University Affiliated Ruijin Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Antiphospholipid Syndrome (0855–0860)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: To elucidate the molecular and cellular mechanisms underlying antiphospholipid antibody (aPL) nephropathy using integrated single-cell and spatial transcriptomic (SP) profiling of kidney tissues.

Methods: Renal biopsy specimens from five patients diagnosed with chronic aPL nephropathy were analyzed. Single-cell RNA sequencing (scRNA-seq) was performed on three samples using the Singleron platform. SP was conducted on two samples using the 10x Genomics Visium platform. Control kidney datasets from three healthy donors were curated from GEO datasets generated using the same platform (GSE171458 and GSE171314). Data processing included dimensionality reduction, unsupervised clustering, differential expressed genes (DEGs) analysis, pathway enrichment, correlation analysis, subclustering analysis.

Results: We profiled 34,253 kidney cells from aPL nephropathy patients (n=3) and healthy controls (n=3). Integration of single-cell clustering data with SP profiles revealed three cell populations within the pathognomonic vascular lesion regions: endothelial cells (ECs), stromal cells (Stroma) and mononuclear phagocytes (MNPs). To molecularly characterize these populations,DEGs analysis was conducted, identifying upregulation of mesenchymal cell markers, CCN2, SOX18, JUN and JUNB, in ECs. ECs from aPL nephropathy samples exhibited marked inflammatory pathway activation, suggesting an inflammatory vascular microenvironment. In parallel, ECs and Stroma showed enrichment of fibrotic and proliferative

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

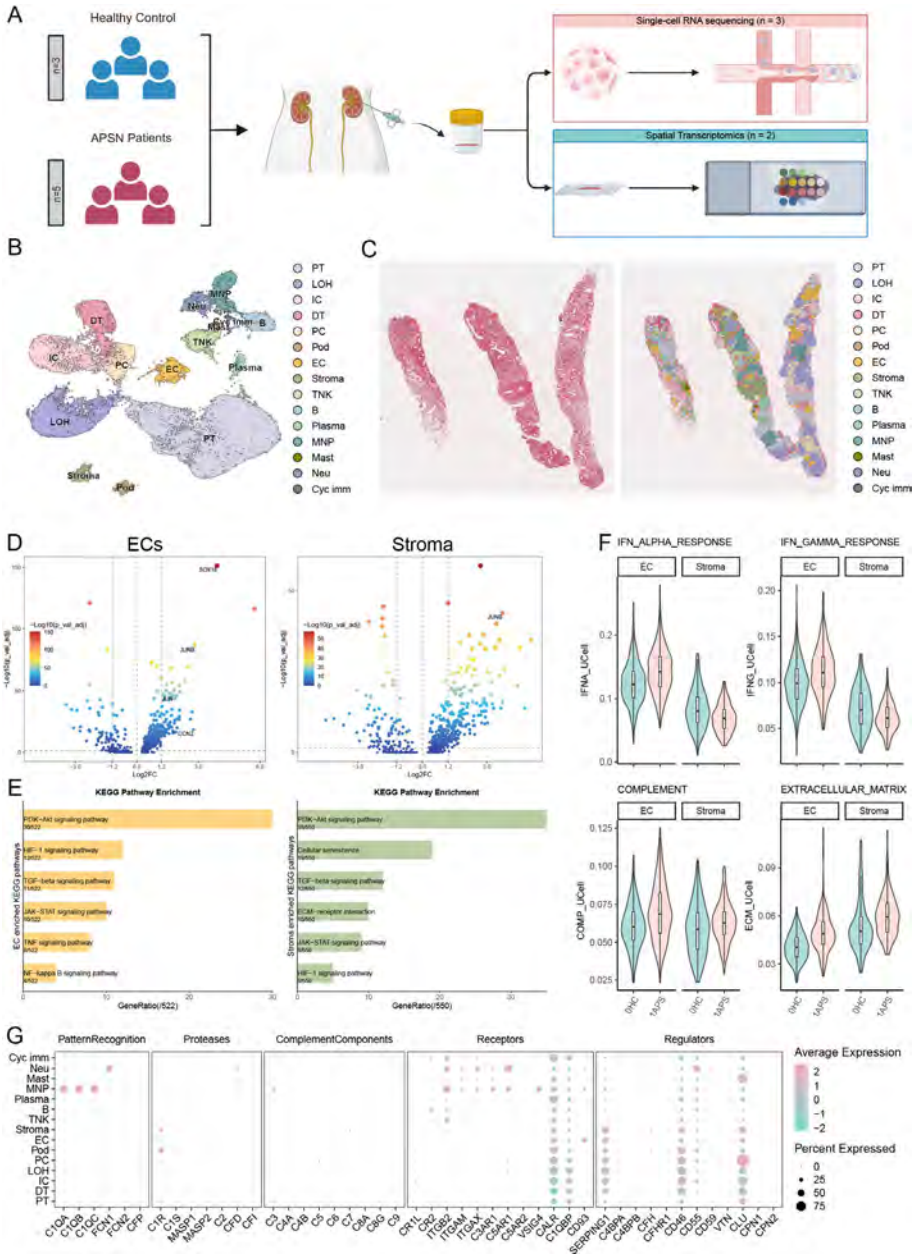


Figure 1. Integrated single-cell and spatial transcriptomic analysis reveals distinct cellular signatures of endothelial and Stroma in aPL nephropathy. (A) Schematic overview of the experimental design for the study. Kidney biopsy sample from aPL nephropathy (APSN) patients underwent single-cell RNA sequencing (scRNA-seq) (n = 3) and spatial transcriptomics profiling (n = 2). scRNA-seq datasets from 3 healthy controls(HCs) were obtained from GEO database (GSE171458 and GSE171314). (B) UMAP of 34,253 cells in an integrated human kidney scRNA-seq data generated in this study. Annotated cell types are indicated on the plot. (C) Spatial location of identified cell types using Visium. Left, haematoxylin and eosin (H&E)-stained tissue. Right, Celltrek cell-type imputations of the Visium spatial data annotations showing the location of different cell types in the kidney biopsy sample of APSN patient. (D) Volcano plot of DEGs in both ECs(left) and Stroma(right) of APSN patients compared with HCs. (E) Enriched KEGG enrichment analysis utilizing intersect DEGs in both ECs(left) and Stroma(right) of HC and APSN patients. (F) Violin plot showing estimated IFNA scores (top left), IFNG scores (top right), complement scores (bottom left) and ECM scores (bottom right) in ECs and stromal cell clusters calculated by UCELL. (G) Dot plot illustrating the expression pattern of all complement genes in various cell types annotated in the single cell transcriptome data. PT, proximal tubule cells; LOH, Loop of Henle cells; IC, intercalated cells; DT, distal tubule cells; PC, principal cells; Pod, podocytes; EC, endothelial cells; Stroma, stromal cells; TNK, T and NK cells; B, B cells; Plasma, plasma cells; MNP, mononuclear phagocytes; Mast, mast cells; Neu, neutrophils; Cyc imm, cycling immune cells.

pathways along with upregulation of complement and coagulation cascades, and ECM score, indicating the potential activation of endothelial-to- mesenchymal transition (EndoMT) in ECs. Further complement gene analysis identified MNPs as the primary renal complement source **(Figure 1)**.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

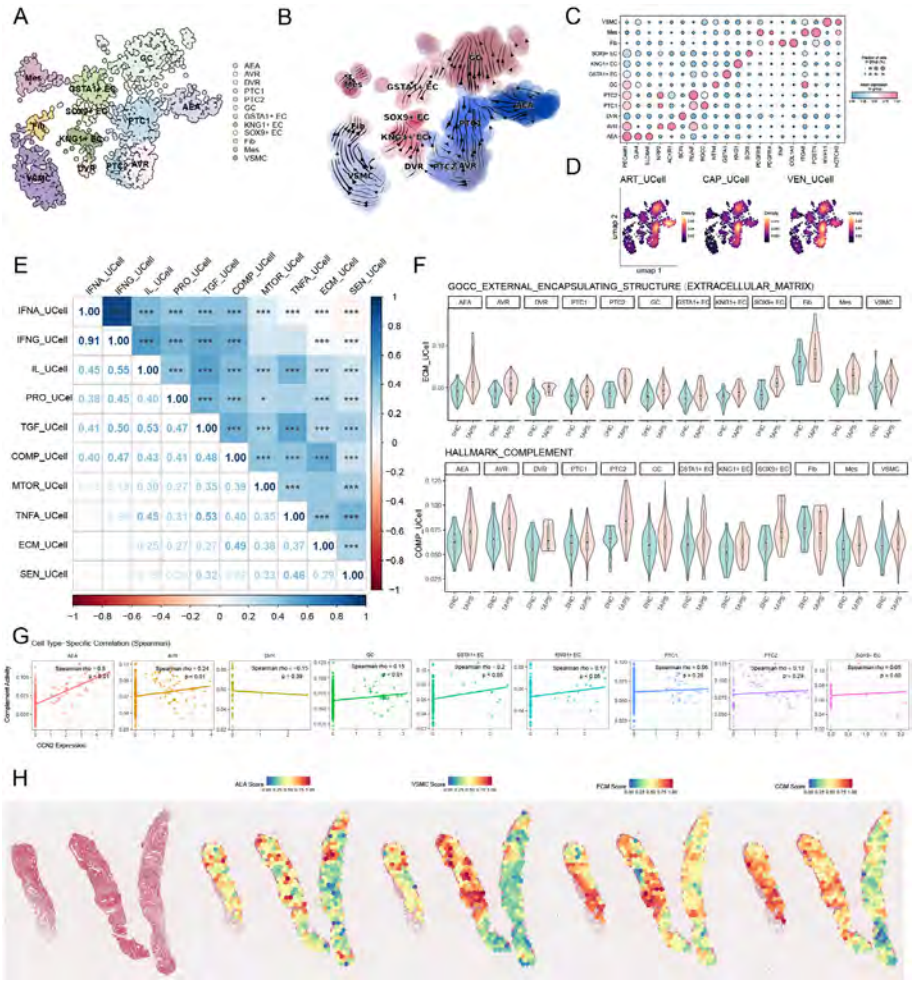


Figure 2. Complement Pathway Activation in Endothelial Subtypes Associates with Endothelial-Mesenchymal Transition (A)UMAP projection of 2,027 endothelial and stromal cells showing twelve transcriptionally distinct subclusters. (B) UMAP visualizing the predicted ECs and Stroma lineage trajectory using scvelo. (C) Dot plot displaying average expression (color) and proportion of cells (size) for representative marker genes across endothelial and stromal subclusters. (D) UMAP depicting the estimated gene set signatures of arteries (left), capillaries (middle), and veins (right) calculated using UCELL. (E) Correlation plot between each geneset score calculated by UCELL. (F)Violin plot showing estimated ECM scores (top) and complement scores (bottom) in ECs and stromal cell subclusters calculated by UCELL. (G) Correlation between CCN2 expression and complement scores (bottom) geneset scores from each endothelial subcluster. (H) AEA and VSMC, ECM and complement gene-expression score in the SP datasets using Visium. H&E sections shown on the left of the figure show individual tissue histology of our Visium sections. AEA, afferent/ efferent arteriole; AVR, ascending vasa recta; DVR, descending vasa recta; GC, glomerular capillary; PTC1, peritubular capillary type 1; PTC2, peritubular capillary type 2; Mes, mesangial cell; Fib, fibroblast; VSMC, vascular smooth muscle cell.

Subclustering of ECs and Stroma identified 12 distinct subtypes. Pathway scoring indicated dominant complement activation and significantly elevated ECM scores in afferent/ efferent arteriole (AEA), SOX9^{+} ECs and peritubular capillary type 2 (PTC2). Complement-ECM correlation (r=0.49, p< 0.001) and CCN2-complement linkage in AEA (r=0.5, p< 0.01) highlighted complement-driven ECM pathology. Spatial validation confirmed lesion-associated ECs as AEA subtypes **(Figure 2)**.

Conclusion: This study presents an integrated single-cell and SP atlas of aPL nephropathy and uncovers a pathogenic cascade involving endothelial inflammation, MNP-derived complement activation, and ECM organization. Our findings support a model of complement associated EndoMT, offering mechanistic insights and potential therapeutic targets for aPL nephropathy.

Disclosure: S. Yu: None; **H. Pan**: None; **J. Qian**: None; **X. Wei**: None; **Y. Fan**: None; **Z. Yang**: None; **S. Gu**: None; **J. Wu**: None; **C. Wang**: None; **T. Zhou**: None; **H. Shi**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0857

CD14-dependent MAP kinase signaling is required for pathogenic neutrophil extracellular trap formation in APS

Thalia Newman[1], NaveenKumar Somanathapura[1], Chao Liu[2], Srilakshmi Yalavarthi[1], Pooja Kapoor[1], Ajay Tambralli[1], Jacqueline Madison[1], Yu (Ray) Zuo[1] and Jason S. Knight[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Superior Charter Twp, MI

SESSION INFORMATION

Session Date: Monday, October 27, 2025

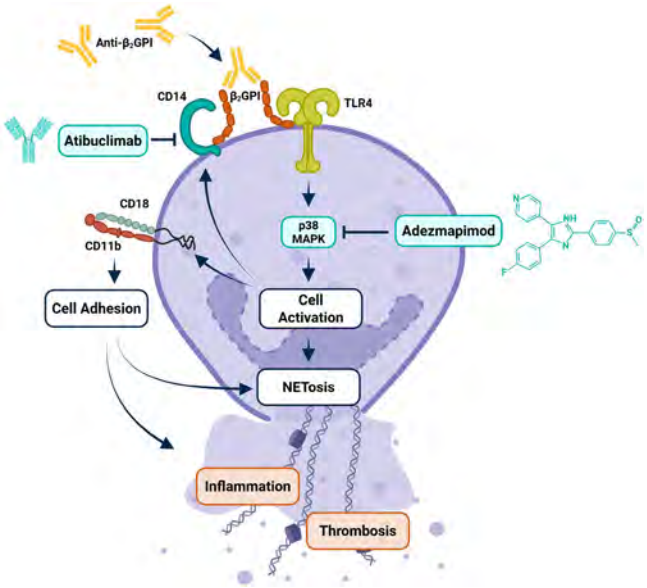
Session Title: Abstracts: Antiphospholipid Syndrome (0855–0860)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Antibodies targeting beta-2-glycoprotein I (**anti-β_2GPI**) promote inflammation and thrombosis in antiphospholipid syndrome (**APS**). It has been shown that anti-β_2GPI activate neutrophils through Toll-like receptor 4 (**TLR4**) to promote the release of pathogenic neutrophil extracellular traps (**NETs**), which promote a thrombo-inflammatory milieu. It is also known that APS patient neutrophils upregulate TLR4-associated genes, including those encoding CD14 and p38 MAP kinase (**MAPK**). Here, we sought to elucidate the potential role of CD14-dependent MAPK signaling in the neutrophil response to anti-β_2GPI.

Methods: For patient profiling, peripheral blood was collected from healthy donors (n=9) or primary APS patients (n=9, meeting the 2023 ACR/EULAR Criteria), and neutrophil expression of CD14 and activation markers was assessed by flow cytometry. For mechanistic studies, affinity-purified anti-β_2GPI IgG (10 μg/mL) was added to isolated primary human neutrophils or whole blood for 1-5 hours (depending on the assay) in the presence or absence of the CD14 blocking antibody atibuclimab (10 μg/mL). CD14 and activation marker expression was assessed by flow cytometry. NETs were visualized by immunofluorescence microscopy, and p38 phosphorylation was quantified by immunoblotting. Lastly, C57BL/6J mice were



Schematic illustration of the proposed roles for CD14 and p38 MAPK in pathogenic anti-β_2GPI antibody-mediated neutrophil activation and NETosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pretreated with the p38 inhibitor adezmapimod (25 mg/kg) or an appropriate vehicle control 1 hour prior to inducing thrombosis in the inferior vena cava. At the time of thrombosis induction, mice also received APS or control IgG (500 μg). Thrombi were collected and weighed 24 hours after surgery.

Results: Neutrophil surface CD14 showed a positive association with the activation markers CD11b and CD18 in APS patients (R^2=0.7318, p=0.0033 and R^2=0.4702, p=0.0415) but not in healthy controls (R^2=0.2448, p=0.1757 and R^2=0.2237, p=0.1985). Furthermore, healthy neutrophils treated with anti-β_2GPI displayed increased surface CD14 expression (1.7-fold change, p=0.0078). Given the association between CD14 and APS-associated neutrophil activity, we asked whether CD14 blockade with atibuclimab could mitigate the effects of anti-β_2GPI on neutrophils. Indeed, atibuclimab attenuated anti-β_2GPI-induced neutrophil CD11b expression (0.7-fold change, p=0.0319), p38 phosphorylation (0.5-fold change), and NET formation. Having seen that p38 phosphorylation downstream of anti-β_2GPI was CD14 dependent, we assessed whether p38 inhibition with adezmapimod could modulate APS-associated thrombosis in vivo. In mice, APS IgG potentiated thrombus weight (mean 5.5 mg vs 2.6 mg, p=0.002), which was significantly attenuated with adezmapimod treatment (mean 2.1 mg vs 5.5 mg, p=0.0004).

Conclusion: Neutrophil CD14 appears to be required for the p38 MAPK-mediated neutrophil activation and NETosis reliably triggered by anti-β_2GPI in APS. This work identifies neutrophil surface CD14 and downstream p38 MAPK signaling as novel therapeutic targets with the potential to restrain not only thrombosis, but also the upstream inflammation that underlies APS.

Disclosure: T. Newman: None; **N. Somanathapura**: None; **C. Liu**: None; **S. Yalavarthi**: None; **P. Kapoor**: None; **A. Tambralli**: None; **J. Madison**: None; **Y. Zuo**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

Abstract Number: 0858

IgA Anti-β2GPI Antibodies Drive Proatherogenic Myeloid Activation and Vascular Dysfunction in APS

Kavya Sugur[1], Chao Liu[2], Emily Chong[3], Srilakshmi Yalavarthi[4], Katarina Kmetova[5], Wenying Liang[6], Emily Becker[6], Gavin Poppei[6], Cyrus Sarosh[7], NaveenKumar Somanathapura[3], Ajay Tambralli[3], Jason S. Knight[3] and Yu (Ray) Zuo[3], [1]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Ann Arbor, MI, [2]University of Michigan, Superior Charter Twp, MI, [3]University of Michigan, Ann arbor, MI, [4]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, [5]Division of Rheumatology, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor, MI, [6]University of Michigan, Ann arbor, [7]University of Michigan, Temperance, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Antiphospholipid Syndrome (0855–0860)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Cardiovascular disease is a major cause of morbidity and mortality in antiphospholipid syndrome **(APS)**, with rates of accelerated atherosclerosis comparable to those seen in diabetes. Although the proatherogenic (and other) effects of IgG antiphospholipid antibodies (**aPL**) have been widely studied, emerging evidence suggests that IgA aPL—particularly IgA anti-β2-glycoprotein I (**aβ2GPI**)—may also contribute significantly to atherogenesis. For example, a population-based study demonstrated a fourfold increased risk of future atherosclerotic cardiovascular events among individuals with IgA aPL but no established autoimmune condition. In the same study, IgA aPL were associated with reduced cholesterol efflux capacity (**CEC**), a critical anti-atherosclerotic function of HDL. However, the mechanisms by which IgA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

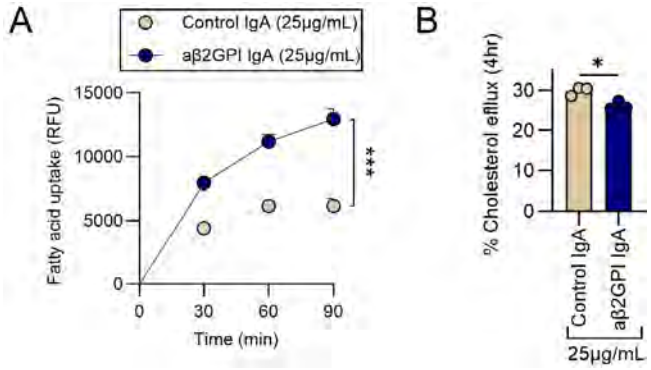


Figure 1: aβ2GPI IgA enhances fatty acid uptake in macrophages and impairs their cholesterol efflux capacity. (A) Macrophage fatty acid uptake was evaluated in real-time after 4hrs pre-treatment with 25 µg/mL of either control IgA or aβ2GPI IgA for 90 minutes. Fluorescent fatty acid analogs were used to assess intracellular uptake. (B) Comparison of % Cholesterol efflux at 4 hours after treatment with 25µg/mL of control or aβ2GPI IgA. Significance, *p<0.05, and ***p<0.001.

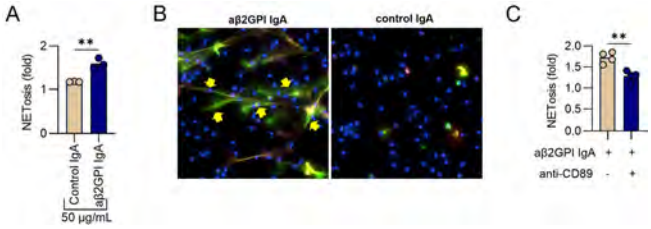


Figure 2: aβ2GPI IgA induces NETosis in neutrophils from healthy donors. (A) Donor neutrophils were treated with aβ2GPI IgA (50 µg/mL) or control IgA (50 µg/mL). NETosis was quantified by SYTOX Green assay. (B) Neutrophils treated with IgA by microscopy (green=neutrophil elastase; red=myeloperoxidase; and blue=DNA; arrows indicate netting neutrophils). (C) Treatment with anti-CD89. Significance, **p<0.01.

aβ2GPI might promote vascular dysfunction and frank atherosclerosis remain poorly defined. Here, we aimed to investigate the role of IgA aβ2GPI in promoting atherosclerosis through effects on myeloid cells, HDL function, and vascular integrity.

Methods: Total IgA was purified from IgA aβ2GPI-positive patients (**aβ2GPI IgA**) and assessed in various *in vitro* and *in vivo* systems. Myeloid cell functional assays assessed CEC, fatty acid uptake, foam cell formation, and NETosis. Aortic endothelial function was tested in mice treated with either aβ2GPI IgA or control IgA. Vascular reactivity was measured by wire myography, and plasma HDL function was evaluated using a CEC assay.

Results: Compared with control IgA, treatment of macrophages with aβ2GPI IgA significantly enhanced fatty acid uptake and promoted foam cell formation—hallmarks of early atherogenesis. aβ2GPI IgA also impaired cholesterol efflux capacity, a critical anti-atherosclerotic function of HDL (**Fig. 1**). Furthermore, aβ2GPI IgA triggered robust NETosis by healthy primary neutrophils, an effect that was markedly reduced by blockade of the IgA receptor CD89 (**Fig. 2**). *In vivo*, mice treated with aβ2GPI IgA exhibited widespread vascular dysfunction. Wire myography demonstrated impaired acetylcholine-mediated relaxation of phenylephrine-contracted aortic rings (i.e., endothelium-dependent relaxation), consistent with endothelial impairment (**Fig. 3A-B**). Plasma from the same mice demonstrated significantly reduced cholesterol efflux capacity compared to controls, suggestive of HDL dysfunction (**Fig. 3C**). Collectively, these findings support a mechanistic model in which aβ2GPI IgA promotes proatherosclerotic vascular injury via three interrelated pathways: (1) induction of lipid-laden, pro-atherogenic macrophages; (2) CD89-dependent NETosis; and (3) systemic impairment of HDL function and endothelial responsiveness.

Conclusion: By driving foam cell formation, inducing CD89-mediated NETosis, and impairing HDL function and endothelial responsiveness, aβ2GPI IgA may have a role as a key mediator of atherogenesis in APS. Targeting IgA-driven mechanisms may offer new therapeutic avenues to mitigate cardiovascular risk in affected patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

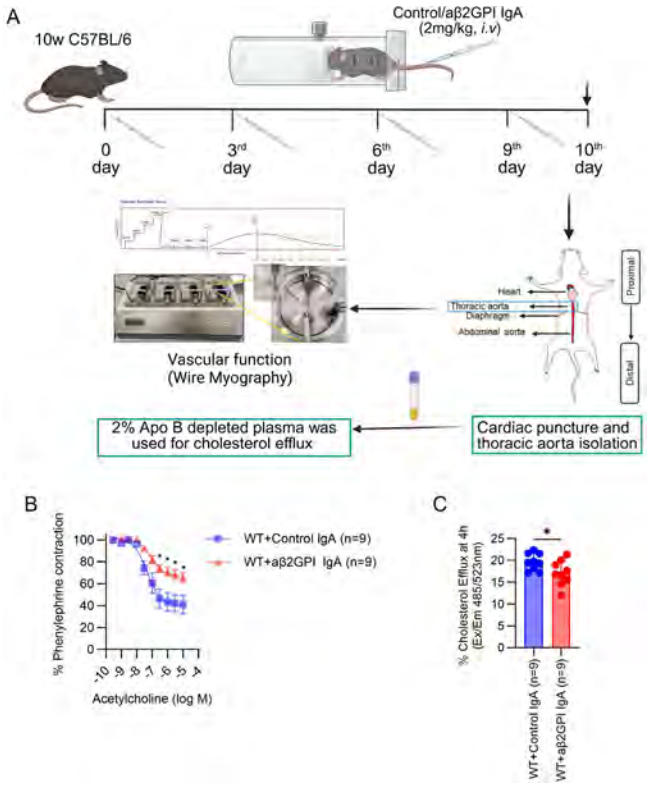


Figure 3: aβ2GPI IgA impairs global vascular function and promotes a proatherogenic vascular environment in a mouse model. (A) Schematic overview of the mouse model used to assess vascular dysfunction. (B) Ten-week-old mice were injected intravenously with control or aβ2GPI IgA (2mg/kg body weight) every three days over a 9-day period. On day 10, aortas were harvested, and vascular function was assessed via wire myography, measuring endothelium-dependent relaxation of aortic rings in response to acetylcholine. (C) Cholesterol efflux capacity was assessed in a macrophage cell line using 2% ApoB-depleted mouse plasma. *Significance: *$p < 0.05$.

Disclosure: K. Sugur: None; **C. Liu**: None; **E. Chong**: None; **S. Yalavarthi**: None; **K. Kmetova**: None; **W. Liang**: None; **E. Becker**: None; **G. Poppei**: None; **C. Sarosh**: None; **N. Somanathapura**: None; **A. Tambralli**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **Y. Zuo**: None.

Abstract Number: 0859

Trophoblast Dysfunction and Placental Alterations in a Mouse Model of Antiphospholipid Syndrome: The Potential Role of Neutrophil Extracellular Traps

Bruna Mazetto Fonseca[1], Srilakshmi Yalavarthi[2], Katarina Kmetova[2], NaveenKumar Somanathapura[3], Cyrus Sarosh[4], Kavya Sugur[5], Wenying Liang[6], Yu (Ray) Zuo[3], Richard W. Lieberman[6] and Jason S. Knight[3], [1]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, [3]University of Michigan, Ann arbor, MI, [4]University of Michigan, Temperance, MI, [5]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Ann Arbor, MI, [6]University of Michigan, Ann arbor

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Antiphospholipid Syndrome (0855–0860)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Neutrophil extracellular traps (**NETs**) are webs of chromatin and proteases (e.g., neutrophil elastase) that have been implicated in antiphospholipid syndrome (**APS**)-associated thrombosis; however, their contribution to the placental dysfunction inherent to APS remains underexplored. Here, we aimed to investigate the impact of antiphospholipid antibodies (**aPL**) and downstream NET formation on implantation, placental health, and fetal viability in mice.

Methods: Wild-type (WT) mice were injected with 2 mg of IgG pooled from either healthy donors or APS patients on gestational days 0, 3, 6, 9, and 12; placental resorptions were assessed on day 15. *Pad4*-deficient mice, which are known to have reduced NET formation, were evaluated in parallel. Circulating myeloperoxidase (MPO)-DNA complexes were quantified as markers of NETs, and plasma PlGF-2 as a measure of placenta-associated angiogenesis. Placental histopathology was assessed using a semiquantitative scoring system evaluating six parameters—vasculopathy, thrombosis, inflammation, fibrin deposition, villous ischemia, and hemorrhage—each graded from 0 (normal) to 3 (severe). Placental expression of citrullinated-histone H3 was analyzed by immunoblotting. In vitro experiments were performed with HTR-8/SVneo trophoblasts.

Results: Among APS IgG-treated WT mice, 29.6% with a vaginal plug (indicating copulation) had a false pregnancy, compared with 16.0% in the control IgG group. None of the *Pad4*$^{-/-}$ mice treated with APS IgG had a false pregnancy. Mean fetal resorption rates were significantly higher in APS IgG-treated WT mice (15.8% for n=16 mice) compared with control IgG-treated WT mice (5.8% for n=19 mice, p=0.0096). APS IgG-treated *Pad4*$^{-/-}$ mice had an average of 3.6% resorptions (n=10 mice, p=0.0079 compared with APS WT mice). Plasma MPO-DNA complexes were significantly higher in APS WT mice compared with both controls (mean 1.8-fold, p=0.0061) and APS *Pad4*$^{-/-}$ mice (1.9-fold, p=0.0135). In contrast, plasma PlGF-1 levels were reduced by approximately 2-fold in APS WT mice compared with controls (p=0.0100); the APS *Pad4*$^{-/-}$ mice did not differ from controls. Inflammation was the most prominent feature in non-resorbed APS WT placentas (mean score=2.7 versus 1.0 in controls), followed by vasculopathy and hemorrhage; the inflammatory infiltrate was predominantly neutrophilic. Notably, resorbed APS WT placentas had dramatically increased citrullinated-histone H3 expression (a marker of NETs), which was absent in resorbed control placentas. Finally, in vitro, trophoblast proliferation was impaired after 48 hours of exposure to purified NETs (1 μg/mL) compared with vehicle-treated cells (p = 0.0323). The neutrophil elastase inhibitor GW311616A restored proliferation to baseline levels, suggesting a role for elastase's enzyme activity in NET-mediated trophoblast dysfunction.

Conclusion: These findings suggest that APS IgG may contribute to fetal loss and placental alterations by triggering increased NET formation. Significant protection in NET-deficient *Pad4*$^{-/-}$ mice suggests that NET inhibition is an approach worth exploring to improve pregnancy outcomes in the APS clinic.

Disclosure: B. Mazetto Fonseca: None; **S. Yalavarthi**: None; **K. Kmetova**: None; **N. Somanathapura**: None; **C. Sarosh**: None; **K. Sugur**: None; **W. Liang**: None; **Y. Zuo**: None; **R. Lieberman**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2.

Abstract Number: 0860

Activated Protein C Resistance and Protein C Antibodies in the Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Clinical Database and Repository

Maria Efthymiou[1], Ibrahim Tohidi-Esfahani[2], Veronica Venturelli[1], Maria Tektonidou[3], Vittorio Pengo[4], Diana Parades-Ruiz[5], Ware Branch[6], Maria Gerosa[7], Cecilia Nalli[8], Esther Rodriguez Almaraz[9], Michelle Petri[10], Ricard Cervera[11], Olga Amengual[12], Danieli Andrade[13], Rohan Willis[14], Maria Laura Bertolaccini[15], Doruk Erkan[16], Hannah Cohen[17] and AntiphosPholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION), [1]University College London, London, United Kingdom, [2]University of Sydney, Syndey, Australia, Sydney, Australia, [3]National and Kapodistrian University of Athens, Athens, Greece, [4]Padova University Hospital, Padova, Italy, [5]Biobizkaia Health Research Institute, Barakaldo, Spain, Barakaldo, Spain, [6]University of Utah Health Sciences Center, Salt Lake City, UT,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[7]University of Milan, Milano, Italy, [8]ASST SPEDALI CIVILI DI BRESCIA, Brescia, Italy, [9]Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Spain, [10]Johns Hopkins University School of Medicine, Timonium, MD, [11]Hospital Clinic Barcelona, Barcelona, Spain, [12]Hokkaido University Graduate School of Medicine, Sapporo, Japan, Sapporo, Japan, [13]University of Sao Paulo, So Paulo, So Paulo, Brazil, [14]University of Texas Medical Branch, Galveston, TX, [15]King's College London, London, United Kingdom, [16]Hospital for Special Surgery, New York, NY, [17]University College London Hospitals NHS Foundation Trust, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

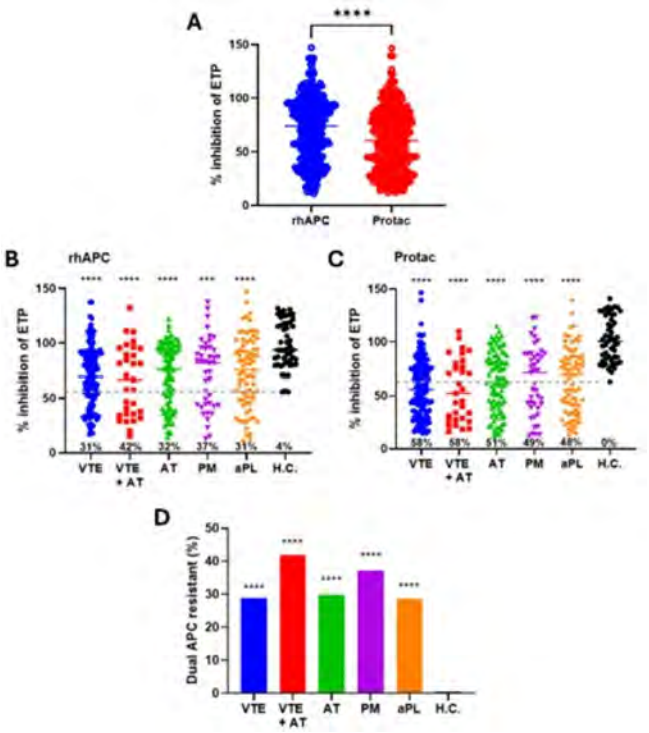
Session Title: Abstracts: Antiphospholipid Syndrome (0855–0860)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Dysregulation in the protein C anticoagulant pathway, more specifically acquired resistance to activated protein C (APCr) and antibodies against protein C (anti-PC), has been proposed as a potential contributing mechanism in the pathophysiology of antiphospholipid syndrome (APS). However, prevalence, clinical significance, and predictive value have not been established.To determine the prevalence of APCr and anti-PC, their associations with antiphospholipid antibody (aPL) profiles and clinical phenotypes, and their predictive value for new thrombotic events.

Methods: Patients with aPL with/without APS classification were identified from the prospective APS ACTION registry (n=283) and University College London Hospital database (n=87). Fifty-one healthy controls were also included. Patients (n=370) were subcategorised by clinical phenotype: aPL only (n=77), pregnancy morbidity (PM) only (n=43), venous thromboembolism (VTE) (+/-PM) (n=132), arterial thrombosis (AT) (+/-PM) (n=87), or VTE+AT (+/-PM) (n=31). Based on baseline samples of different subgroups, APCr was determined using thrombin generation with recombinant human APC (rhAPC)



Activated protein C (APC) resistance in the different aPL cohorts. Thrombin generation was measured using platelet-poor plasma (PPP)in patients with aPL (n=370) with or without antiphospholipid syndrome (APS) and healthy controls (H.C., n=51); A: Paired comparison of % inhibition of ETP by rhAPC and Protac in the patient cohort (n=370). Patients were subcategorised into clinical manifestations of venous thromboembolism (VTE, n=132), arterial thromboembolism (AT, n=87), VTE + AT (n=31), pregnancy morbidity (PM, n=43), carriers of aPL (aPL, n=77) and compared to H.C. (n=51) with rhAPC (B) and Protac (C). Grey dotted lines (56% for rhAPC, 63% for Protac) indicate cut-offs established in HC. (56% for rhAPC, 63% for Protac) are considered APC resistant, with percentages shown. The proportion of each clinical subcategory that were resistant to both rhAPC and Protac are shown (D), compared to H.C. ***p<0.001, ****p<0.0001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

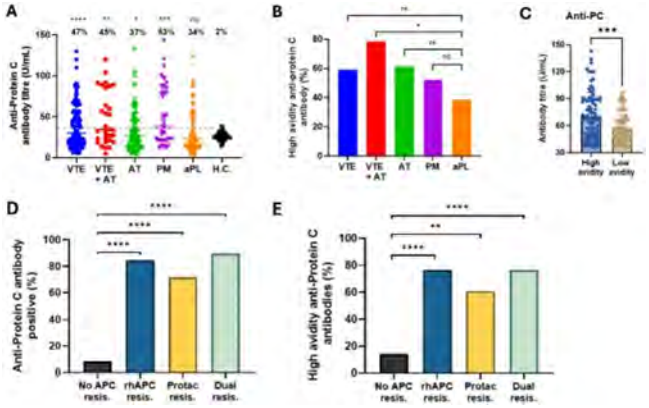


Figure 2. APC resistance and anti-protein C antibodies. Citrated plasma from APS patients with VTE, n=132, ATE, n=87, VTE + ATE (n=31), PM, n=43, aPL only, n=77 and H.C., n=51 were diluted 1:25 and run on an in-house protein C ELISA to detect anti-protein C (anti-PC) antibodies. Antibody titres of subjects in each group are shown, compared to H.C. (A): Values on or above the grey dotted line (36U/mL) are considered positive for anti-PC antibody, with percentage of each group positive for antibody shown. The proportion of the antibodies detected (VTE n=61, VTE + AT n=14, AT n=31, PM n=23, aPL n=26) that were high avidity were compared to the aPL only cohort. (B): The antibody titres of all high avidity (n=88) and low avidity (n=66) anti-PC were compared. (C): High avidity anti-PC were significantly at higher titres compared to low avidity anti-PC. (D) The proportion of patients with no APC resistance (n=167), recombinant human APC (rhAPC) resistance (n=122), Protac resistance (n=196) and resistance to both rhAPC and Protac (n=115) with anti-protein C antibodies. (E): The proportion of anti-protein C antibodies that were high avidity in each of the APC resistance groups. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, ns – not significant, resis. – resistance

or Protac (for endogenous protein C activation). Anti-PC and avidity were detected by in-house ELISA. In a subgroup analysis, based on prospective APS ACTION data, the incidence of new thrombotic events was compared in patients with and without APCr and anti-PC.

Results: All patient subgroups had markedly greater APCr than healthy controls (p< 0.001), most prominent in 'higher risk' patients, i.e., those with VTE+AT or triple aPL-positivity (Figure 1). Forty-two percent (156/370) of patients were positive for anti-PC with the highest prevalence in the PM, VTE and VTE+AT cohorts: 53%, 47%, and 45%, respectively, and lowest prevalence in aPL only patients (34%) (Figure 2A). The VTE+AT group had significantly higher prevalence of high avidity anti-PC (79%) compared to aPL only patients (38%) (p< 0.05, Figure 2B). Most patients with APCr (69.5% [141/370]) had detectable anti-PC. There was a strong association between presence of APCr and anti-PC (Figure 2D) especially in the VTE+AT and the triple aPL positive patient groups. During the follow-up (median 8.3 years) of APS ACTION patients, 25/283 (8.8%) patients had new thrombosis; there was no difference in the number of new thrombotic events in patients with or without APCr or anti-PC (p=0.60). Non-anticoagulated patients with APCr had a higher number of new thrombotic events compared to those without APCr, although this did not reach statistical significance (HR 4.5, 95% CI 0.8-25.9, p=0.14).

Conclusion: Acquired resistance to activated protein C is highly prevalent in persistently aPL-positive patients with the highest prevalence in 'higher risk' APS patients. The lack of an association with thrombosis in these patients may reflect the effectiveness of anticoagulation. The association between greater APCr and thrombosis in non-anticoagulated patients merits exploration as to whether this may provide a basis to guide consideration of initiation of prophylactic antithrombotic treatment in this subset of patients.

Disclosure: M. Efthymiou: None; **I. Tohidi-Esfahani**: None; **V. Venturelli**: None; **M. Tektonidou**: None; **V. Pengo**: None; **D. Parades-Ruiz**: None; **W. Branch**: UCB, 5; **M. Gerosa**: None; **C. Nalli**: None; **E. Rodriguez Almaraz**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **R. Cervera**: None; **O. Amengual**: None; **D. Andrade**: None; **R. Willis**: None; **M. Bertolaccini**: None; **D. Erkan**: Chugai, 5, GlaxoSmithKlein(GSK), 1, 5, 6, Merida Biosciences, 2, NIH, 5, Roche, 1, Roivant Sciences, 2, Star Therapeutics, 1, Up-To-Date, 9; **H. Cohen**: GlaxoSmithKlein(GSK), 6, Roche, 2, Roivant, 2.

Abstract Number: 0861

Identification of Anti-HDGFL1 as a Novel Autoantibody in Seronegative Idiopathic Inflammatory Myopathies

Xueting Yuan[1], Menghua Cai[2], Lu Gao[2], Chen Yu[3], Jia Shi[4], Yinghui Li[2], jiuliang Zhao[1], Dong Xu[5], Chaojun Hu[1], Mengtao Li[6], Xiaofeng Zeng[7], jianmin Zhang[2] and Qian Wang[6], [1]Peking Union Medical College Hospital (CAMS), Beijing, China (People's Republic), [2]Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing, China (People's Republic), [3]Peking Union Medical College Hospital, Dong Cheng Qu, Beijing, China (People's Republic), [4]University of Washington, Seattle, WA, [5]Peking Union Medical College Hospital, Dong Cheng District, China (People's Republic), [6]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [7]Peking Union Medical College Hospital Department of Rheumatology and Clinical Immunology, Beijing, Beijing, China (People's Republic)

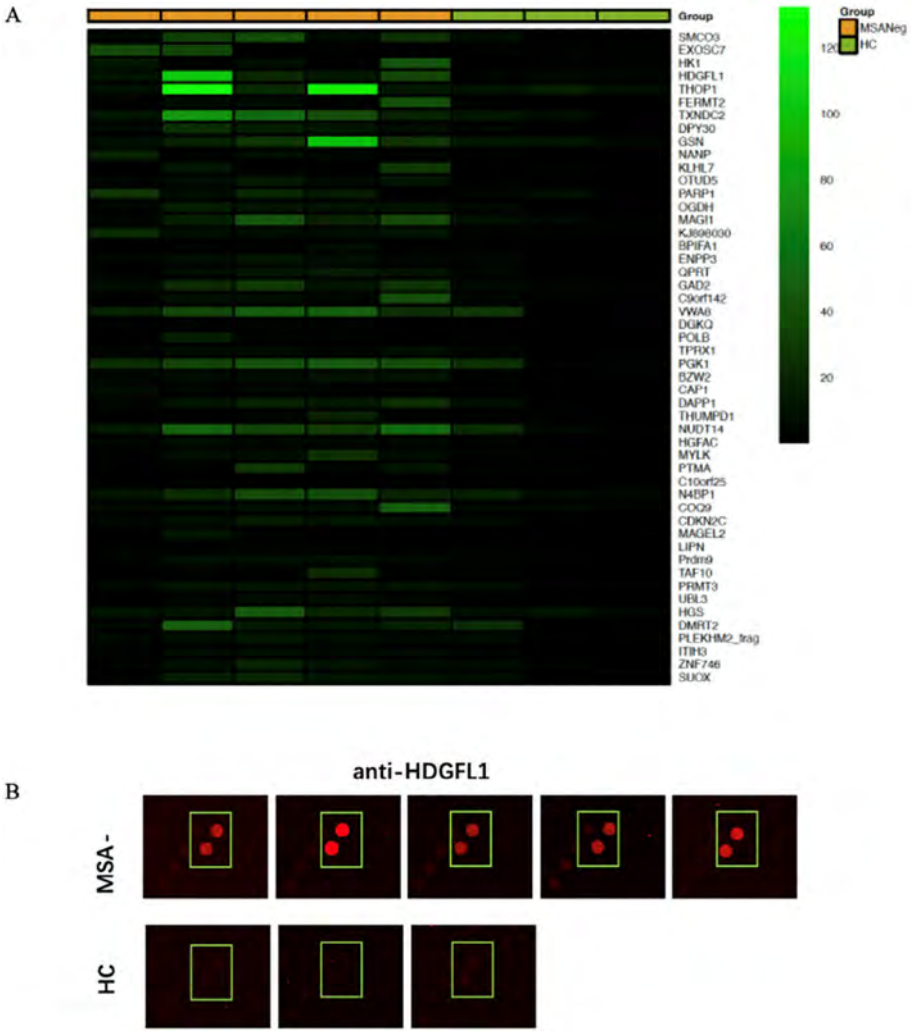


Figure 1 Discovery of HDGFL1 as an autoantigen candidate. (A) Comparative signal intensity profiles of top 50 candidate autoantigens between MSA-negative patients and healthy controls (HC) in the discovery phase. Proteins are ranked by descending fold change (FC) relative to HC. Gene symbols used to refer to protein products. (B) Representative fluorescence images of HDGFL1 autoantigens identified from the sera of MSA-negative IIM and HC on HuProt protein microarrays.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

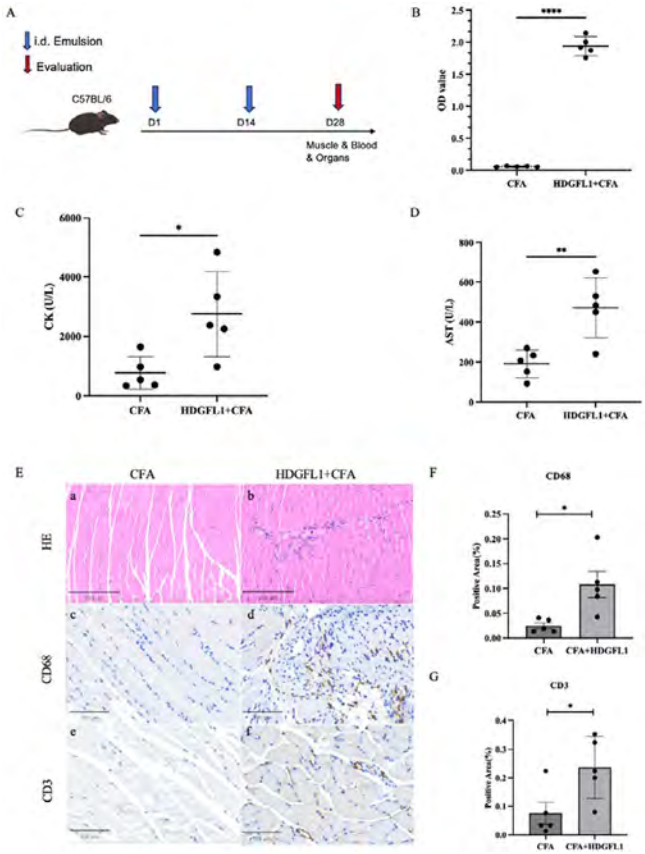


Figure 2 Immune response to HDGFL1. (A) Schematic representation of the immunization protocol. C57BL/6 mice received intradermal injections of complete Freund's adjuvant emulsions with or without HDGFL1 protein at the dorsal region, followed by booster immunization at day 14 and final evaluation at day 28. (B) Serum levels of HDGFL1-specific autoantibodies detected by ELISA in immunized vs adjuvant-only control groups. (C-D) Comparative serum analysis of muscle damage biomarkers: creatine kinase (CK, C) and aspartate aminotransferase (AST, D) levels between experimental groups. (E) Representative histopathological features (H&E staining, upper panel a-b) and immune cell infiltration patterns (IHC analysis, lower panel c-f) in muscle tissues (100× magnification). (F-G) Quantitative comparison of $CD68^+$ macrophage infiltration (F) and $CD3^+$ T lymphocyte infiltration (G) in muscle tissues between groups. Data presented as percentage of positive staining area.

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research (0861–0866)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Myositis-specific autoantibodies (MSAs) play a crucial role in diagnosing and classifying idiopathic inflammatory myopathies (IIMs). However, approximately 30% of seronegative IIM patients may be unrecognized or misdiagnosed due to the absence of reliable biomarkers. This study aims to identify potential autoantibodies in seronegative IIM.

Methods: We enrolled 42 seronegative IIM patients, 149 MSA-positive IIM cases, 83 healthy controls (HCs), and 83 autoimmune disease controls (DCs). Initial high-throughput autoantibody screening was performed using the HuProt^{TM} human proteome microarray in a discovery cohort. Subsequently, candidate antigens were expressed, purified, and validated via western blotting in an expanded cohort. An autoantigen-induced murine model was then utilized to explore immunological properties.

Results: Through systematic screening and validation, anti-hepatoma-derived growth factor-like protein 1(HDGFL1) was identified as a novel autoantibody, detected in 33% (14/42) of seronegative IIM patients but absent in HCs (0/83, $P< 0.0001$). Within the seronegative IIM group, anti-HDGFL1 antibody-positive patients demonstrated significantly higher frequencies of rash (71.4% vs 25.0%, $P=0.004$) and arthritis (28.6% vs 3.6%, $P=0.035$) compared to anti-HDGFL1 antibody-negative patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

HDGFL1-immunized mice developed specific autoantibodies, alongside elevated levels of serum creatine kinase and aspartate aminotransferase compared to the control group. Histopathological examination revealed pronounced inflammatory cell infiltration in skeletal muscle, characterized by increased CD3+ T cells and CD68+ macrophages. Flow cytometric analysis indicated enhanced splenic T cell proliferation in the HDGFL1-immunized group compared to controls.

Conclusion: Anti-HDGFL1 autoantibody was identified as a novel biomarker for the diagnosis of seronegative IIM, offering new insights into immunopathogenesis.

Disclosure: X. Yuan: None; **M. Cai**: None; **L. Gao**: None; **C. Yu**: None; **J. Shi**: None; **Y. Li**: None; **j. Zhao**: None; **D. Xu**: None; **C. Hu**: None; **M. Li**: None; **X. Zeng**: None; **j. Zhang**: None; **Q. Wang**: None.

Abstract Number: 0862

In immune-mediated necrotising myopathy, anti-HMGCR antibodies inhibit HMGCR activity, leading to the sarcoplasmic accumulation of lipid droplets and myofibres necrosis

Margherita Giannini[1], Giulia Quiring[2], Mustapha Oulad-Abdelghani[3], Béatrice Lannes[1], Yves Allenbach[4], Olivier Benveniste[5], Olivier Boyer[6], Aleksandra Nadaj Pakleza[1], Bernard Geny[7] and Alain Meyer[8], [1]Strasbourg University Hospital, Strasbourg, France, [2]University of Strasbourg, Strasbourg, France, [3]IGBMC, Strasbourg, France, [4]SORBONNE UNIVERSITE, Paris, France, [5]Sorbonne Uniersite, Hopital de la Pitie-Salpetriere, Paris, France, [6]University of Rouen, Rouen, France, [7]UR 3072, Centre de Recherche en Biomédecine, Université de Strasbourg, Strasbourg; FranceExplorations fonctionnelles musculaires, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg;, Strasbourg, Alsace, France, [8]Service de Rhumatologie, Centre de référence des maladies auto-immunes rares (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, Explorations fonctionnelles musculaires, Service de physiologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, UR 3072, Centre de Recherche en Biomédecine, Université de Strasbourg, Strasbourg; France, Strasbourg, Alsace, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research (0861–0866)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: The aim of this study was to investigate whether in immune-mediated necrotising myopathy (IMNM), anti-HMGCR antibodies interfere with HMGCR activity and have a myopathic effect.

Methods: To obtain polyclonal anti-HMGCR autoantibodies, the 6 peptides identified as the epitopes of anti-HMGCR antibodies were used to immunise a white New Zealand rabbit. Antibodies from a non-immunised animal served as control. Plasma of anti-HMGCR (n=5) and anti-SRP (n=2) IMNM patients were obtained from plasmapheresis eluates. Rabbit and human anti-HMGCR antibodies were purified by affinity chromatography. Inhibition of HMGCR was measured *in vitro* by spectrophotometry in the presence of different concentrations of autoantibodies. Pravastatin was used as a negative control. Human autoantibodies were electroporated into human myotubes: creatine-kinase levels (CK) were measured in the supernatant, and hematoxylin/eosin (H&E) as well as oil red-O stainings were performed.

Thirty-four patients with inflammatory myopathies (IM) according to the EULAR/ACR 2017 criteria, not taking immunomodulators or statins, were included (anti-HMGCR: n=10; other IM: n=24) as well as 3 patients without neuromuscular diseases (no NMD). Histological sections of deltoid muscle taken at the time of diagnosis were immunostained with an anti-human IgG antibody. Oil red-O staining was used to study the accumulation of lipid droplets, quantified (extension score 0-4) by two myopathologists blinded to the diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

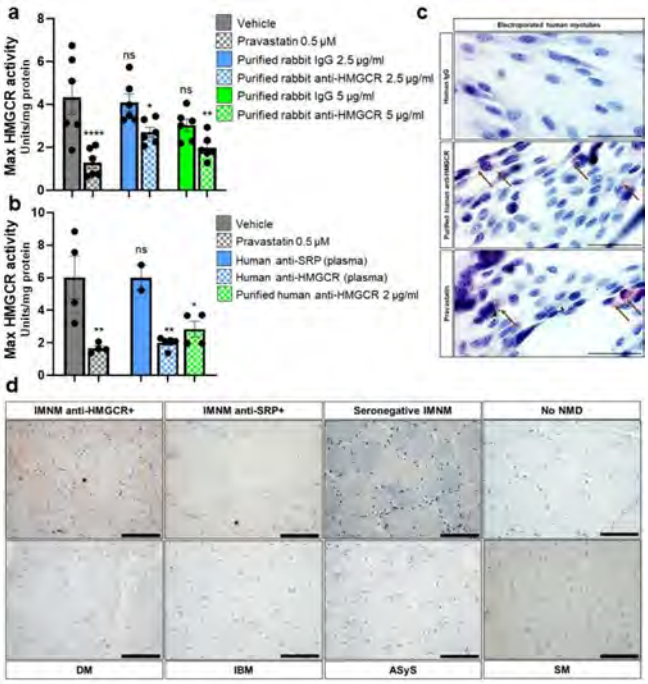


Figure 1. Anti-hydroxy-3-methylglutaryl CoA reductase (HMGCR) antibodies inhibit HMGCR activity leading to lipid droplet accumulation in myofibres. a) Maximum (max) *in vitro* HMGCR activity in the presence of rabbit purified polyclonal anti-HMGCR, control antibodies and pravastatin. *: p= 0.04, **: p=0.002, ****: p= 0.0001, ns: not significant (vs. vehicle). b) Maximum *in vitro* HMGCR activity in the presence of plasma and purified autoantibodies from anti-HMGCR immune-mediated necrotising myopathy (IMNM) patients, plasma from anti-SRP IMNM patients and pravastatin. *: p<0.05, **: p<0.01, ns: not significant (vs. vehicle). c) Representative images of oil red-O staining performed 4 days after electroporation of human myotubes exposed to purified human anti-HMGCR antibodies or human control antibodies or pravastatin. Scale bar: 50 µm. Brown arrows point to lipid droplets. d) Representative images of oil red-O-stained deltoid muscle cryosections of untreated patients with inflammatory myopathies (IM). * indicates fibres with lipid droplet accumulation (one example per image). Scale bar: 50 µm. e) Oil red-O staining score in deltoid muscle cryosections of patients with IM. Each dot represents a patient. Scores are expressed as mean ± standard error of the mean. ***: p=0.0001 compared to anti-HMGCR IMNM. #: p=0.0001, ns: not significant compared to non-NMD patients.

Results: To test whether anti-HMGCR antibodies inhibit the function of their target, HMGCR enzymatic activity was assessed *in vitro* in the presence of anti-HMGCR, control antibodies and pravastatin. A dose-dependent inhibition of HMGCR activity was observed in the presence of anti-HMGCR (Figure 1a). Rabbit anti-HMGCR 5 µg/ml and human anti-HMGCR 2 µg/ml had similar effects to that of pravastatin 0.5 µM (Figure 1a, 1b). IgG from the non-immunised rabbit and plasma from anti-SRP patients did not affect HMGCR activity (Figure 1a, 1b).

To test whether anti-HMGCR internalisation in myofibres exerts a myopathic effect, human myotubes were electroporated with human purified anti-HMGCR, control IgG or pravastatin. Antibody presence in the cytoplasm 4 days after electroporation was confirmed. CK levels were 2.4-fold higher in the supernatant of myotubes electroporated with anti-HMGCR compared to those electroporated with control IgG (p=0.0001). H&E staining showed necrotic myotubes after electroporation with purified anti-HMGCR and pravastatin, but not with control IgG. Oil red-O staining revealed a lipid droplet accumulation in myotubes electroporated with purified anti-HMGCR and pravastatin, but not with control IgG (Figure 1c). Lipid droplet accumulation score was 10-fold higher in anti-HMGCR IMNM patients compared to other IM and no NMD (3.2 ± 0.6 vs. 0.3 ± 0.5; vs. 0.3 ± 0.6, respectively, p=0.0001) and a score ≥ 2 was a hallmark of anti-HMGCR IMNM (Figure 1d, 1e).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Together, these data demonstrate that anti-HMGCR antibodies inhibit HMGCR activity, leading to the sarcoplasmic accumulation of lipid droplets and myofibres necrosis. These findings could have implications for both the diagnosis and treatment of IMNM.

Disclosure: M. Giannini: None; **G. Quiring**: None; **M. Oulad-Abdelghani**: None; **B. Lannes**: None; **Y. Allenbach**: None; **O. Benveniste**: None; **O. Boyer**: None; **A. Nadaj Pakleza**: None; **B. Geny**: None; **A. Meyer**: None.

Abstract Number: 0863

Myeloid Dendritic Cell Subsets Characterize Muscle of Inclusion Body Myositis Patients and Correlate with KLRG1+ and TBX21+ CD8+ T cells

Raphael Kirou[1], Iago Pinal-Fernandez[1], Maria Casal-Dominguez[1], Katherine Pak[1], Chiseko Ikenaga[2], Christopher Nelke[3], Stefania Dell'orso[1], Faiza Naz[1], Shamima Islam[1], Gustavo Gutierrez-Cruz[1], Werner Stenzel[4], Albert Selva-O'Callaghan[5], José Milisenda[6] and Andrew Mammen[7], [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]The University of Tokyo, Tokyo, Japan, [3]Heinrich Heine University of Düsseldorf, Düsseldorf, Germany, [4]Charite University, Berlin, Germany, [5]Hospital Universitari Vall d'Hebron, Barcelona, Spain, [6]Hospital Clinic de Barcelona, Barcelona, Spain, [7]NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research (0861–0866)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

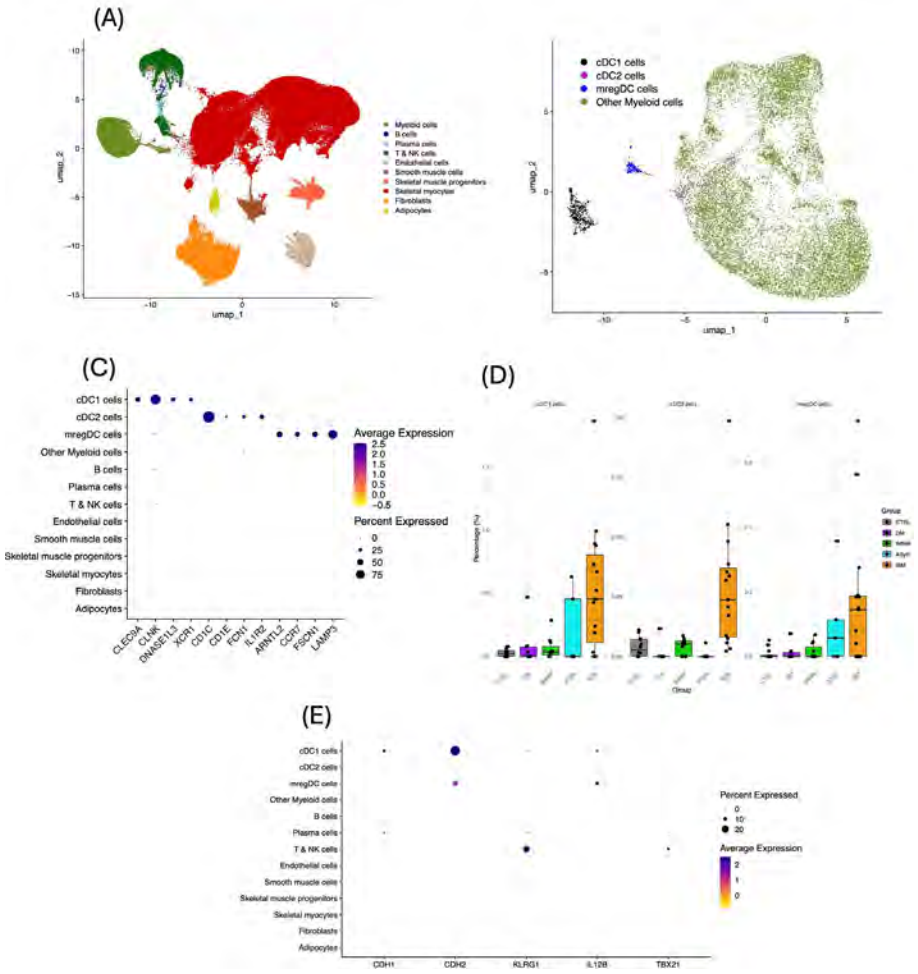
Background/Purpose: Although inclusion body myositis (IBM) is an inflammatory myopathy, there are no effective immunomodulating agents, underlying the need for better understanding of its pathogenesis. Previous studies have implicated KLRG1+ TBX21+ CD8+ T cells as drivers of IFNG-mediated inflammation in IBM. Based on previous reports, we hypothesize that myeloid dendritic cells (mDCs) may activate these CD8+ T cells. Here, we sought to identify and characterize mDC subsets in IBM muscle and examine their correlation with transcriptomic markers of disease activity.

Table 1. Patient composition of datasets used in snRNA-seq and RNA-seq analyses. Datasets B, C, and E were publicly available datasets, derived from Wischnewski et al. *Nature Aging* 2024, Nelke et al. *Acta Neuropathol* 2023, and Ikenaga et al. *Ann Neurol* 2022 respectively.

Assay	Dataset	IBM	Other Inflammatory Myopathy (OIM)	CTRL	Total
snRNA-seq	A	4	21 • 9 Dermatomyositis (DM): 4 anti-Mi2, 2 anti-NXP2, 3 anti-TIF1γ • 7 Immune-mediated necrotizing myopathy (IMNM): 4 anti-HMGCR, 3 anti-SRP • 5 Anti-synthetase syndrome (ASyS): 5 anti-Jo1	2	27
	B	8	4 • 4 Immune-mediated necrotizing myopathy (IMNM): 4 anti-SRP	7	19
	C	3	0	3	6
	Total	**15**	**25**	**12**	**52**
RNA-seq	D	53	199 • 82 Dermatomyositis (DM): 22 anti-Mi2, 11 anti-MDA5, 21 anti-NXP2, 28 anti-TiF1γ • 80 Immune-mediated necrotizing myopathy (IMNM): 60 anti-HMGCR, 20 anti-SRP • 37 Anti-synthetase syndrome (ASyS): 37 anti-Jo1	37	289
	E	43	0	9	52
	Total	**96**	**199**	**46**	**341**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. snRNA-seq Analysis. (A) UMAP clustering of all cells, (B) UMAP clustering of myeloid cells, (C) Representative specific markers of mDC subsets in snRNA-seq data, (D) Relative Proportions of mDC subsets among all cells by group, (E) Expression of *KLRG1* and its ligands (*CDH1*, *CDH2*) and *TBX21* and its activating cytokine, *IL12B*, in each cluster in IBM samples.



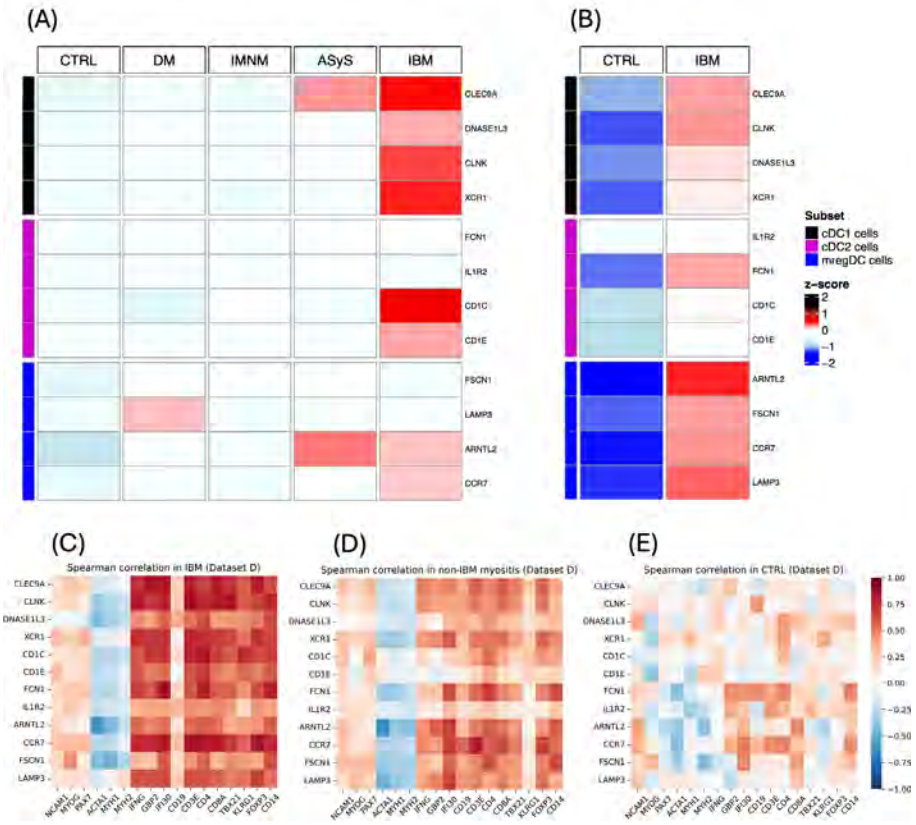
Methods: We analyzed skeletal muscle single nuclei RNA-seq (snRNA-seq) data from three datasets (A-C), including 15 IBM patients, 25 other inflammatory myopathy (OIM) patients, and 12 control (CTRL) patients (Table 1). We also analyzed skeletal muscle bulk RNA-seq data from two datasets (D-E), including 96 IBM patients, 199 OIM patients, and 46 CTRL patients (Table 1).

snRNA-seq data from Datasets A-C was merged and analyzed using Seurat/4.4.0 within R/4.4.1. Data underwent quality control, normalization, integration, UMAP generation, cluster identification to identify mDC subsets, and cluster-specific gene identification (adjusted $p < 0.001$ versus all cells and myeloid cells, $p < 0.05$ versus each cell cluster). RNA-seq data was analyzed separately using R/4.4.1 and Python/3.9.6. Counts underwent normalization using trimmed means of M values. Normalized counts were used to generate heatmaps of median mDC marker expression by myositis group and Spearman correlation heatmaps of mDC markers with transcriptomic markers of disease activity.

Results: Clustering of snRNA-seq data revealed ten main clusters. Unsupervised subclustering of the myeloid cells revealed two distinct mDC subsets: type 1 conventional dendritic (cDC1) cells and mature immunoregulatory dendritic (mregDC) cells. A third mDC subset, type 2 conventional dendritic (cDC2) cells, was identified by manually selecting cells from the main monocyte cluster expressing the cDC2 marker *CD1C* and lacking expression of the specific monocyte marker *C5AR1*. All three mDC subsets expressed subset-specific markers and were relatively increased as a proportion of total cells in IBM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. RNA-seq Analysis. (A-B) Median expression heatmaps of mDC-specific genes by group in Dataset D (A) and E (B); (C-E) Correlation heatmaps of mDC-specific genes versus transcriptomic markers of disease activity in IBM samples (C), OIM samples (D), and CTRL samples (E) from Dataset D. Markers of disease activity shown include markers of muscle regeneration (*NCAM1*, *MYOG*, *PAX7*), mature muscle (*ACTA1*, *MYH1*, *MYH2*), the IFNG pathway (*IFNG*, *GBP2*, *IFI30*), B cells (*CD19*), T cells (*CD3E*, *CD4*, *CD8A*, *TBX21*, *KLRG1*, *FOXP3*), and macrophages (*CD14*).



patients compared to other groups. Notably, cDC1 cells exhibited the highest average expression of the two ligands of KLRG1, *CDH1* and *CDH2*, while both cDC1 and mregDC cells specifically expressed the fate-specifying cytokine subunit for TBX21+ T cells, *IL12B* (Figure 1).

In the RNA-seq data, expression of specific mDC markers for all three subsets appeared higher in IBM samples compared to non-IBM samples across both datasets. In addition, all three subsets appeared strongly correlated with markers of the IFNG pathway and T cell subsets, including *KLRG1* and *TBX21*, in IBM samples to a greater degree than in OIM and CTRL samples (Figure 2).

Conclusion: Three mDC subsets are increased in IBM muscle compared to OIM and CTRL muscle. Markers of these subsets correlate with markers of the IFNG pathway and T cell subsets. We propose that cDC1 cells activate IFN-γ-secreting KLRG1+ TBX21+ CD8+ T cells via specific expression of the ligands of KLRG1, *CDH1* and *CDH2*, and *IL12B*.

Disclosure: R. Kirou: None; **I. Pinal-Fernandez**: None; **M. Casal-Dominguez**: None; **K. Pak**: None; **C. Ikenaga**: None; **C. Nelke**: None; **S. Dell'orso**: None; **F. Naz**: None; **S. Islam**: None; **G. Gutierrez-Cruz**: None; **W. Stenzel**: None; **A. Selva-O'Callaghan**: None; **J. Milisenda**: None; **A. Mammen**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0864

Immunophenotyping Reveals Upregulated IL-9R on Circulating T and B Cells in Dermatomyositis

Danica Lee[1], Daniel Reay[2], Timothy Oriss[2], Didem Saygin[3], Dana Ascherman[4] and Daniella Schwartz[4], [1]University of Pittsburgh School of Medicine, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, [3]Rush University Medical Center, Chicago, IL, [4]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research (0861–0866)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM), or myositis, comprise a group of autoimmune diseases with significant morbidity, yet the pathogenesis of myositis remains incompletely understood. In addition to inflammatory muscle disease, myositis can cause lung, vascular, and skin disease. A previous analysis of subjects with myositis revealed significant elevation of serum IL-9 (p=0.001) relative to healthy volunteers (**Saygin et al., 2024**). Therefore, we questioned whether IL-9 might *directly* promote disease pathology by modulating myocyte or immune cell function. We hypothesized that Th9 cells (IL-9$^+$ secreting CD4$^+$ T cells) infiltrate inflamed muscle tissue to promote inflammatory cell recruitment and autoantibody formation in IIM.

Methods: To determine potential cellular targets of high serum IL-9 in myositis, we first re-analyzed GSE220915 and GSE221091, two publicly available RNA-seq datasets on myositis patient muscle biopsies and dermatomyositis (DM) patient sorted immune cells, respectively. We quantified IL-9 receptor (IL-9R) mRNA levels as well as expression of *SPI1*, the master transcription factor of the Th9 cell lineage. Next, we cultured peripheral blood mononuclear cells (PBMCs) from pre-treatment DM patients and sex and age-matched healthy controls *in vitro*. Spectral flow cytometry was used to quantify IL-9R expression on B cells, T cells, and monocytes.

Results: In DM patients, immunomodulatory treatment, including oral prednisolone, methotrexate, azathioprine, and cyclophosphamide, reduced expression of *SPI1* in CD4$^+$ T cells (**Figure 1A**, GSE221091). *IL9R* was expressed in patient muscle biopsy tissue from many subtypes of IIM (**Figure 1B**, GSE220915). In sorted PBMCs, *IL9R* mRNA levels were higher in B and T cells from myositis patients compared to monocytes (**Figure 1C**, GSE221091). Furthermore, not only was *IL9R* mRNA increased, but IL-9R surface protein expression was significantly increased on circulating B cells, memory T cells, and CD4$^+$ T cells in DM patients compared to healthy controls (**Figure 2**).

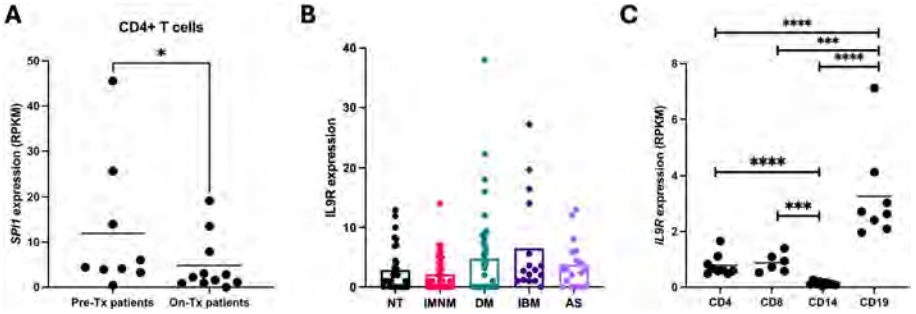


Figure 1. (A) SPI1 expression (RPKM, reads per kilobase per million mapped reads), a marker of Th9 identity, was higher in CD4+ T cells from pre-treatment (Pre-Tx) myositis patients compared to myositis patients currently on medication (On-Tx). (B) IL-9R was expressed in muscle tissue from myositis patients. NT=normal tissue, IMNM=immune-mediated necrotizing myopathy, DM=dermatomyositis, IBM=inclusion-body myositis, AS=anti-synthetase syndrome. (C) IL-9R expression (RPKM) was highest in peripheral blood B cells from myositis patients. *p<0.05, ***p<0.001, ****p<0.0001, Kolmogorov-Smirnov test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

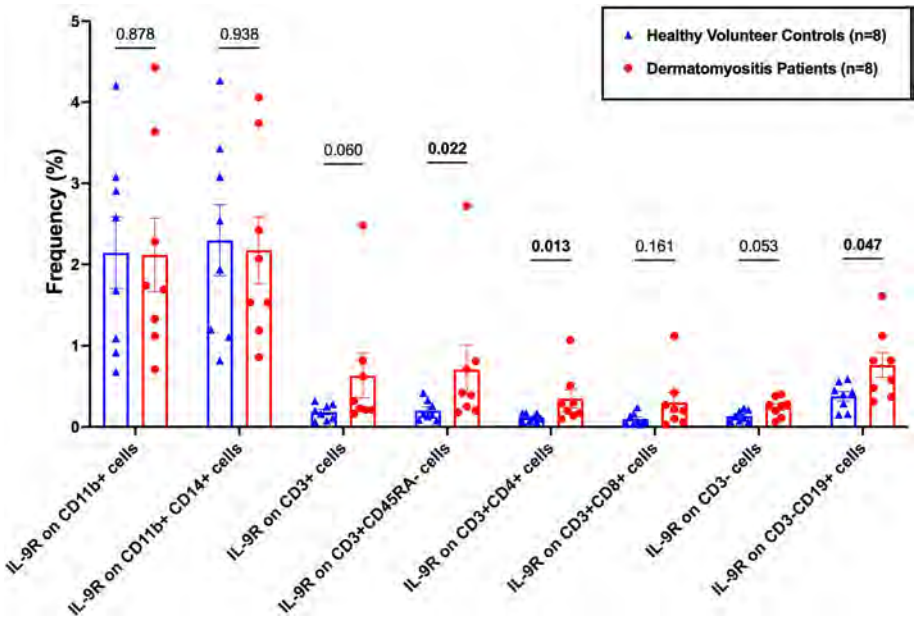


Figure 2. Frequency of IL-9R expression on unstimulated monocytes, B cells, and T cells. p<0.05, Mann-Whitney.

Conclusion: Treatment with immunomodulators reduces *SPI1* expression in CD4+ T cells, suggesting involvement of the Th9/IL-9 axis in IIM. DM is also characterized by increased IL-9R surface expression on circulating T and B cells and within inflamed muscle, suggesting they may be key cellular targets of IL-9 signaling in myositis pathogenesis. Future studies will profile human muscle samples (biopsy/RNAscope and scRNA-seq) for Th9 cells and IL-9R-expressing populations.

References: Saygin D, Biswas PS, Nouraie SM, Ren D, Moghadam-Kia S, McGeachy MJ, Oddis CV, Dzanko S, Ascherman DP, Aggarwal R. Serum cytokine profiles of adults with idiopathic inflammatory myopathies. Clin Exp Rheumatol. 2024 Feb;42(2):229-236. doi: 10.55563/clinexprheumatol/ipgoev. Epub 2024 Jan 5. PMID: 38179816.

Disclosure: D. Lee: None; **D. Reay**: None; **T. Oriss**: None; **D. Saygin**: None; **D. Ascherman**: None; **D. Schwartz**: Eli Lilly, 5, Jeffrey Modell Foundation, 5, National Institutes of Health, 5, Samuel and Emma Winters Foundation, 5, Sobi, 1, 5.

Abstract Number: 0865

Spatial Transcriptomic Analysis of Calcinosis Cutis in Dermatomyositis Uncovers Disease-Associated Pathways Involving IL-6, Tissue Remodeling, and Osteopontin

Cassie Parks[1], York Wang[1], Lisa Christopher-Stine[2], Jemima Albayda[2], Joel Sunshine[3], Shira Ziegler[1] and Chris Mecoli[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Baltimore

SESSION INFORMATION

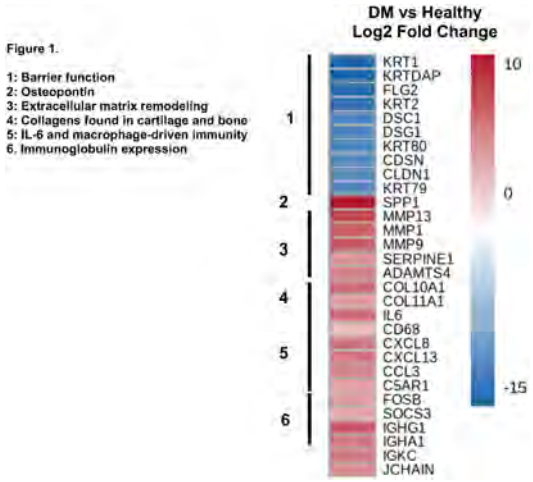
Session Date: Monday, October 27, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research (0861–0866)

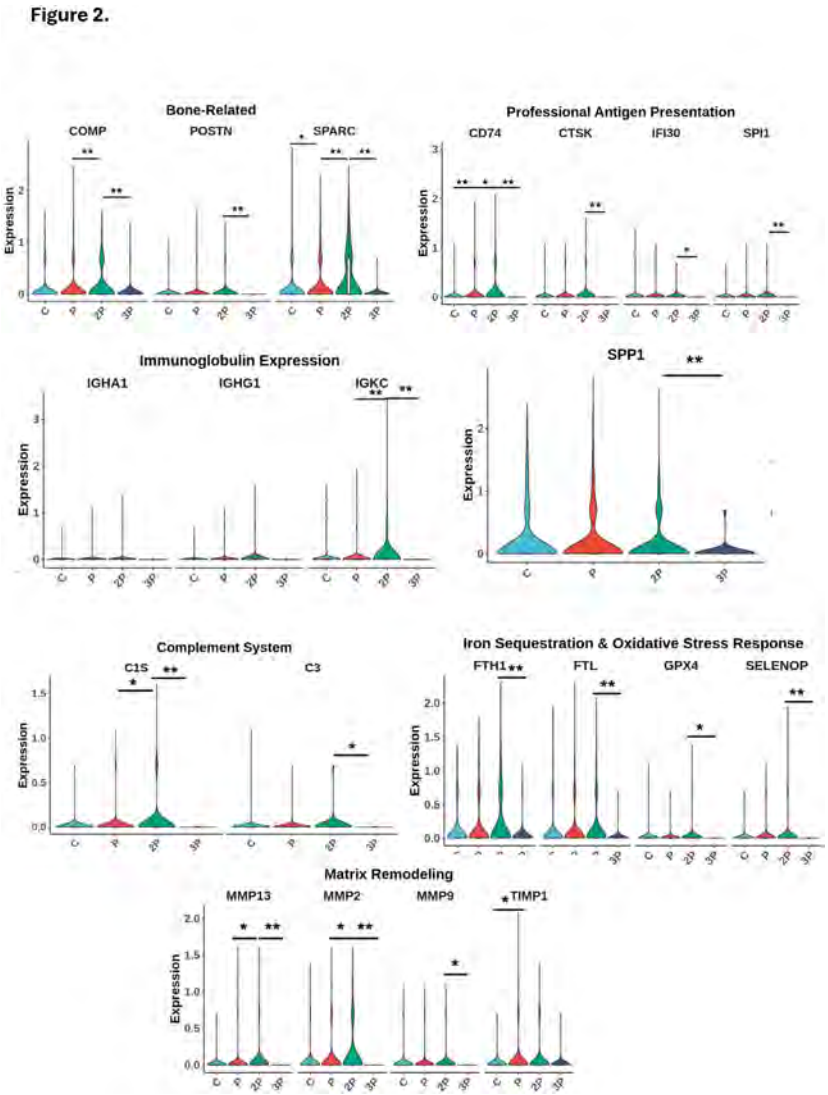
Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heatmap showing gene expression fold changes between DM-associated calcinosis and healthy skin samples from pseudobulk analysis of Visium spatial transcriptomic data. Genes selected are the top most significantly differentially expressed (all adjusted p-value <0.001).



Violin plots showing gene expression patterns across tissue regions at varying distances from calcinosis deposits in DM samples. C = calcinosis, P = perilesional (<50um from calcinosis), 2P = secondary perilesional (50-100um from calcinosis), 3P = tertiary perilesional (100-150um from calcinosis). * = adjusted p-value < 0.05, ** = adjusted p-value < 0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Calcinosis cutis affects up to 20% of adults with dermatomyositis (DM), causing significant morbidity including recurrent infections, incapacitating pain, and functional impairment. Current management focuses on surgical excision despite the risk of recurrence. To better understand and treat this devastating complication, we must first better understand its pathogenesis, including gene expression profiles and relevant cell types.

Methods: We performed Visium 10X spatial transcriptomics on four calcinosis samples from adult DM patients meeting 2017 ACR/EULAR criteria (positive for anti-MDA5, PM-Scl, Ro, and Jo-1) and three healthy adult control skin biopsies. All DM samples contained active calcinosis defined as new or evolving lesions. Data preprocessing was conducted using cellranger, with downstream analysis conducted in R using the Seurat v5.0.0 package. Pseudo-bulk analysis was conducted using the DESeq2 v. 1.44.0 package, and all other differential expression was conducted using the default FindMarkers command. Spatial annotations were conducted in Loupe Browser 8 by one observer (CP).

Results: Pseudo-bulk analysis (Fig. 1) identified a distinct inflammatory signature with elevated *IL6* RNA expression and upregulation of macrophage markers (*CD68*, *MSR1*) and chemokine *CCL3*. We observed increased transcription of RNA encoding immunoglobulins (*IGKC*, *IGHG1*, *IGHA1*, *JCHAIN*). Extracellular matrix dysregulation was evidenced by decreased keratin expression, elevated *MMPs 1/9/13*, and elevated cartilage/bone-specific collagens. Osteopontin (*SPP1*), which resorbs pathological calcification, was robustly elevated in lesional samples.

UMAP analysis revealed minimal overlap between DM and healthy control samples, prompting us to adopt a spatial-first approach. In the DM samples, spatial transcriptomic spots were categorized based on their distance from the calcinosis lesion into four groups: < 50 μm (C), 50–100 μm (P), 100–150 μm (2P), and 150–200 μm (3P). Differential expression analysis across these groups showed that *SPP1* expression was highest near the calcinosis, while professional antigen-presenting cell (APC) markers, immunoglobulin genes, and complement genes were most enriched 100–150 μm from the lesion. Additionally, a complex interplay of matrix remodeling genes, including *MMPs* and their regulators (*TIMPs*), was observed at varying distances from the calcinosis (Fig. 2).

Conclusion: This study provides the first detailed spatial molecular map of calcinosis in DM, suggesting a complex pathogenic cascade involving macrophage-driven inflammation, enhanced local antibody production, and increased osteopontin expression. Further validation is planned to refine our interpretation and explore cell types and signals driving disease pathogenesis.

Disclosure: C. Parks: None; **Y. Wang**: None; **L. Christopher-Stine**: Amgen, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Octapharma, 1, 5, Pfizer, 5, Priovant, 1; **J. Albayda**: None; **J. Sunshine**: None; **S. Ziegler**: None; **C. Mecoli**: None.

Abstract Number: 0866

Immunoglobulin from sera of patients with myositis can passively enter cultured human endothelial cells

Travis Kinder[1], maria Casal-Dominguez[1], Iago Pinal Fernandez[2], Andrew Mammen[3] and **Sandra Ogbonnaya-Whittlesey**[4], [1]National Institutes of Health, Bethesda, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [3]NIH, Bethesda, MD, [4]NIH/NIAMS, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science II: Basic & Translational Research (0861–0866)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Most patients with inflammatory myopathies have autoantibodies to intracellular proteins. We previously showed that immunoglobulin colocalizes with its cognate autoantigen in muscle biopsies from myositis patients. Transcriptomic analyses of muscle biopsy specimens revealed that each myositis autoantibody is associated with a unique transcriptomic profile.

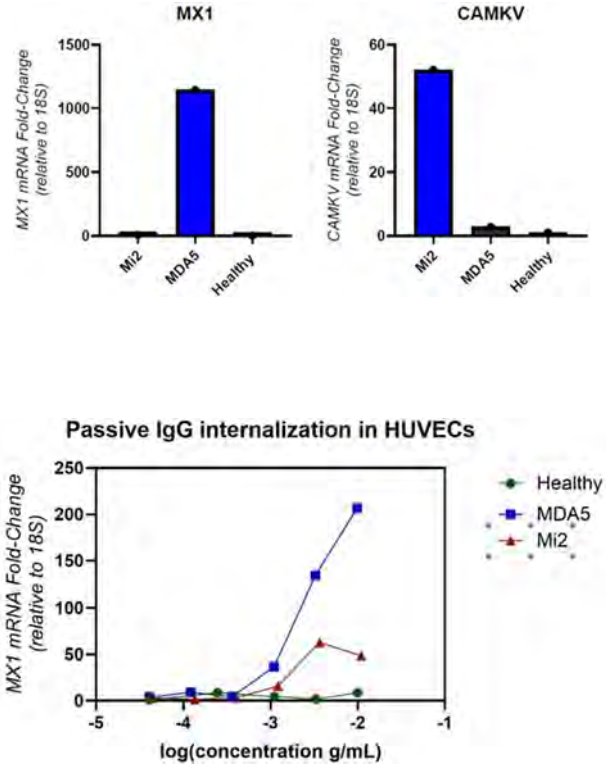
We confirmed that these effects are antibody-mediated by using electroporation to internalize antibodies from patients into cultured muscle cells. Cultured muscle cells with internalized immunoglobulin from anti-MDA5+ and anti-Mi2+ patients expressed the same genes (e.g., Mx1 and CAMKV, respectively) as seen in the muscle tissue.

The aims of the current study were to: (i) determine if electroporation of myositis-associated antibodies into human endothelial cells has similar transcriptomic profile as seen in muscle and (ii) to determine if immunoglobulin could passively enter cultured endothelial cells without electroporation.

Methods: Electroporation of purified antibody from Healthy controls, MDA5+, and Mi2 + sera was performed in HUVECS. The cells were incubated for 24hrs at 37 degrees Celsius following electroporation in appropriate growth media. The RNA was extracted from the HUVECs and RNA to CT was performed for comparative, quantitative PCR using Mx1 and CAMKV as probes and an18S as an internal loading control to assess gene expression.

For passive antibody uptake experiments, HUVECs were cultured for 24 hours in growth media with purified healthy control, Mi2 +, and MDA5 + immunoglobin at 6 different concentrations (1:3 titration). RNA was the extracted using RNEAsy kits. Taqman RNA to CT kit was used to perform comparative, quantitative PCR to measure MX1 gene expression relative to an 18S loading control.

Results: Electroporation of MDA5 antibody increased resulted in increased relative MX1 expression as measured by PCR and electroporation of Mi2 antibodies resulted in relatively increased CAMKV compared to MDA5 and Healthy controls, respectively (Figure 1).



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Purified concentrated, MDA5 IgG that was passively introduced via a 24-hour incubation resulted in significantly increased relative Mx1 expression compared to healthy control IgG or Mi2 IgG (Figure 2).

Conclusion: These results suggest that autoantibodies are able to enter the cultured endothelial cells both with electroporation and passively, without electroporation. The higher relative MX1 expression with internalization of purified immunoglobulin from MDA5 and Mi2 compared to healthy controls suggests that the antibodies themselves may be contributing to pathogenesis and that endothelial cells may be contributing to disease pathogenesis in some types of idiopathic inflammatory myositis. Additional work is ongoing to elucidate the mechanism for the antibodies passively entering the cells and reaching the antigenic target.

Disclosure: T. Kinder: None; **m. Casal-Dominguez**: None; **I. Pinal Fernandez**: None; **A. Mammen**: None; **S. Ogbonnaya-Whittlesey**: None.

Abstract Number: 0867

NLRP3 Inflammasome Impairs Fracture Repair in Rheumatoid Arthritis through RhoA/Rac1-IL1β Axis-Mediated Suppression of Osteoblast Differentiation

Wen Sun and Hua Wang, Nanjing Medical University, Nanjing, China (People's Republic)

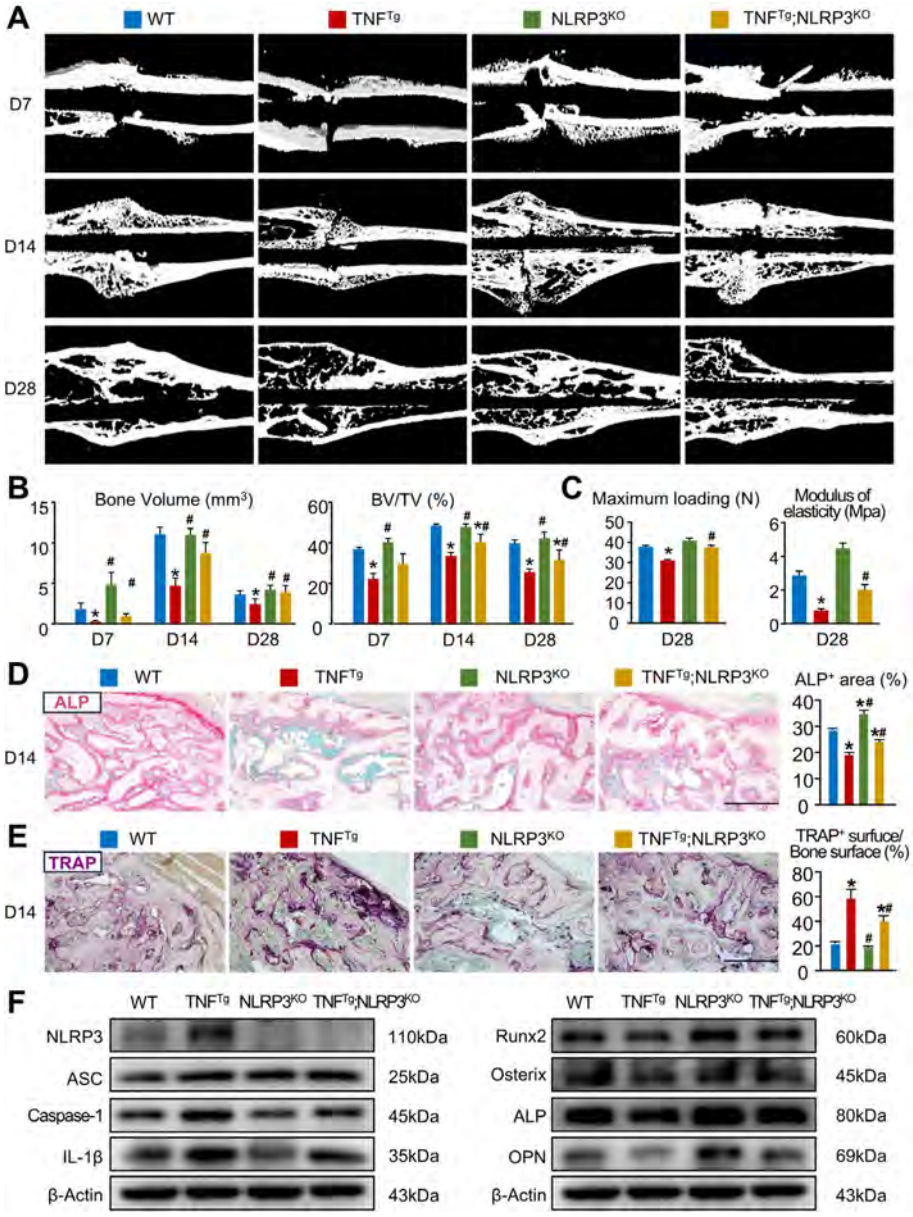
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Animal Models (0867–0872)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Rheumatoid arthritis (RA) is often characterized by bone loss and fragility fractures and is a frequent comorbidity. The NLRP3 inflammasome, a key mediator of inflammation, drives inflammatory processes that fundamentally accompany the pathogenesis of RA. However, the role of NLRP3 inflammasome in RA fracture healing remains unclear.

Methods: For in vivo analyses, we established tibial fractures in two murine RA models: TNF-transgenic (TNF^{Tg}) mice and collagen-induced arthritis (CIA). To address the contribution of NLRP3 inflammasome to fracture repair in RA, we generated TNF^{Tg};$NLRP3^{KO}$ mice by deleting the NLRP3 gene in TNF^{Tg} mice. The effects of TNFα overexpression on osteogenic differentiation were assessed using mesenchymal progenitor cells (MPCs) with or without MCC950, a potent and specific inhibitor of the NLRP3 inflammasome. The role of MCC950 in RA fracture repair was investigated using CIA mice.

Results: TNF^{Tg} mice exhibited delayed fracture healing, characterized by decreased callus bone volume and reduced bone mechanical strength. The NLRP3 inflammasome was excessively activated in TNF^{Tg} mice, leading to elevated expression of NLRP3, IL-1β, and Caspase-1. Moreover, NLRP3 deficiency in TNF^{Tg} mice significantly mitigated the delayed fracture healing (Fig. 1). Mechanistically, TNFα overexpression suppressed osteogenic differentiation of MPCs through NLRP3 inflammasome activation. This process involves RhoA/Rac1-dependent NF-κB signaling that triggers inflammasome assembly, ultimately leading to IL-1β secretion. Notably, MCC950 administration significantly attenuated these pathological effects. Lastly, in vivo MCC950 treatment rescued the delayed fracture healing by reducing NLRP3 inflammasome activation and promoting bone formation in CIA mice (Fig. 2).

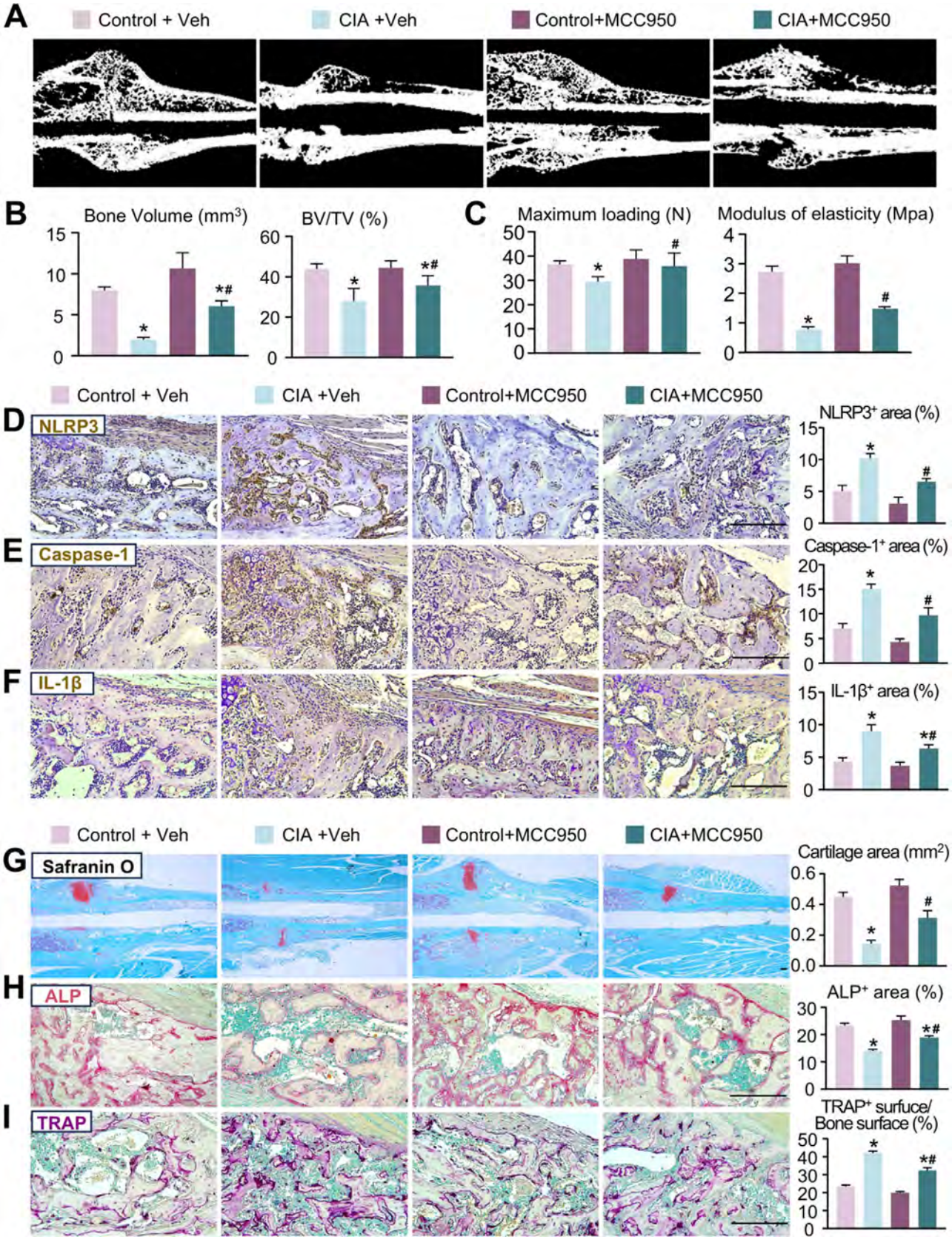
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



NLRP3 deficiency improves delayed fracture healing in TNFTg RA mice

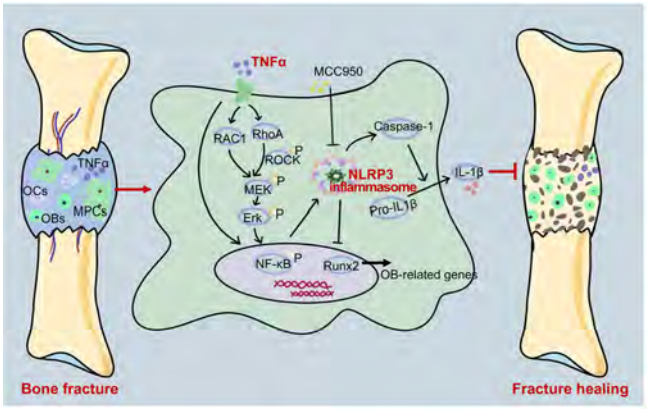
Conclusion: This study provides novel insights into the mechanisms underlying delayed fracture healing in RA and highlights the potential therapeutic benefits of targeting the NLRP3 inflammasome (Fig. 3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



MCC950 treatment alleviated the delayed fracture healing in CIA mice

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Schematic representation of the NLRP3 inflammasome delaying fracture healing in RA mice through RhoA/Rac1–IL-1β-mediated osteoblast differentiation

Disclosure: W. Sun: None; **H. Wang**: None.

Abstract Number: 0869

PD-1 inhibitor unleashes pathogenic CD8+ T cells and induce arthritis in collagen-primed mice

Clement Adedeji[1], Muhammad Hamdan[1], Hong-Jai Park[2], Kelsey Wang[1] and **Sang Kim**[3], [1]Yale University, New Haven, [2]Yale University, New Haven, CT, [3]Yale University, Branford, CT

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Animal Models (0867–0872)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Background/Purpose: Immune checkpoint inhibitors (ICIs) are associated with immune-related adverse events, including inflammatory arthritis (ICI-arthritis). The pathophysiology of ICI-arthritis, particularly the role of T cells, remains unclear due to the lack of preclinical murine models.

Methods: We immunized 8-12-week-old C57BL/6 mice with type II chicken collagen (CII) Two to three weeks later, we administered a PD-1 inhibitor and measured arthritis scores until the mice were euthanized. Inflamed joints (knees) and CII-draining lymph nodes (dLNs) were harvested for immunologic and histological analyses.

Methods: We immunized 8-12-week-old C57BL/6 mice with type II chicken collagen (CII) Two to three weeks later, we administered a PD-1 inhibitor and measured arthritis scores until the mice were euthanized. Inflamed joints (knees) and CII-draining lymph nodes (dLNs) were harvested for immunologic and histological analyses.

Results: Mice primed with CII but without PD-1 inhibitors (CII_No PD-1i) or mice that did not receive CII but were given PD-1 inhibitors (No CII_PD-1i) did not develop arthritis. In contrast, CII-primed mice began developing arthritis 4-5 days after the initiation of PD-1 inhibitors, recapitulating human PD-1i-induced arthritis. The severity of arthritis at euthanasia was comparable between mice with PD-1i arthritis and conventional collagen-induced arthritis (CIA) mice. Histological analysis of the knee joints showed inflammation and joint destruction in CII_PD-1i mice. The numbers of $CD45^+$ immune cells were increased in the joint and draining lymph nodes (dLN) in CII_PD-1i mice compared to the CII_No PD-1i and No CII_PD-1i groups. Notably, $CD8^+$ T cells were expanded in the inflamed joints and dLNs of CII_PD-1i mice. Furthermore, these

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

$CD8^+$ T cells produced inflammatory cytokines including IFNγ and TNFα in response to CII. Levels of pathogenic CII-specific antibodies in CII_PD-1i mice were lower than in CIA, suggesting that the pathogenesis of PD-1i arthritis differs from that of rheumatoid arthritis.

Conclusion: CII-primed mice developed *de novo* arthritis following PD-1 inhibition, suggesting that these mice can serve as a murine model of PD-1i arthritis. Of note $IFNg^+$ $TNFa^+$ $CD8^+$ T cells are expanded in these mice, indicating that PD-1 inhibitor unleashes pathogenic $CD8^+$ T cells in CII-primed mice.

Disclosure: C. Adedeji: None; **M. Hamdan**: None; **H. Park**: None; **K. Wang**: None; **S. Kim**: None.

Abstract Number: 0870

Same Model, Different Results: Vendor and Microbiome Influence Reproducibility in Collagen Induced Arthritis

Brenda Seymour[1], Brendan Allen[2] and Kristine Kuhn[3], [1]University of Colorado School of Medicine, Denver, CO, [2]University of Colorado School of Medicine, Aurora, CO, [3]2022 - 2023 / Adult/ University of Colorado, Aurora, CO

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Animal Models (0867–0872)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Although collagen-induced arthritis (CIA) in mice is a useful tool for studying inflammatory arthritis, it is a highly variable model with inconsistent disease severity and penetrance across studies. Previous studies have shown that CIA severity and penetrance vary by mouse strain, sex, and source of type II collagen. Furthermore, we and others have shown that CIA development is microbiome-dependent. Despite these findings, the extent to which distinct microbiome compositions affect CIA outcomes has not been well studied. As such, microbiome variation between mouse vendors, housing facilities, and even over time has the potential to negatively impact the reproducibility of CIA studies. We therefore performed a head-to-head comparison of CIA in DBA/1 mice obtained from three different vendors and compared CIA outcomes to microbiome composition.

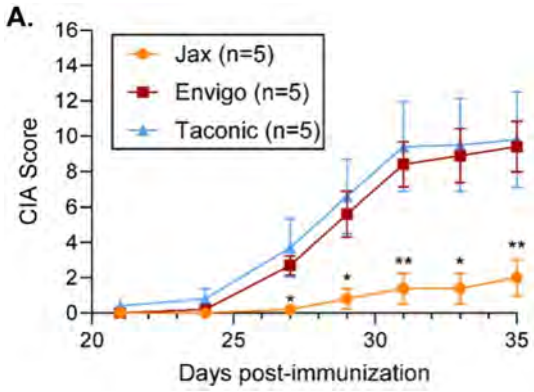


Figure 1. CIA was induced in 7-week old male DBA/1 mice from Envigo, Jax, and Taconic. Arthritis severity was scored every other day starting at day 21. Data shown are represented as mean (symbol) ± SEM (error bars). Two-way ANOVA with Tukey correction for multiple comparisons were performed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

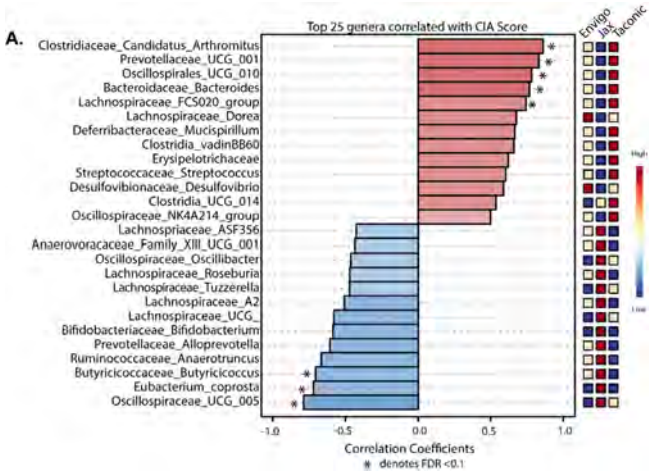


Figure 2. Fecal microbiome on CIA day 35 was assessed by 16S rRNA sequencing. The top 25 genera that correlate (spearman rank) with CIA severity were plotted. Bars represent correlation coefficient, with darker shading representing increased absolute value of the correlation efficient. * denotes FDR < 0.1.

Methods: 7-week-old male DBA/1 mice were purchased from The Jackson Laboratory (Jax), Envigo, or Taconic. Mice from the three vendors simultaneously were injected intradermally at the base of the tail with 200μg bovine CII (Elastin) emulsified in 50μl complete Freund's adjuvant (CFA, Sigma) on days 0 and 21. Disease severity was assessed every other day starting at day 21. Serum and fecal pellets were collected weekly throughout the experiment. Serum cytokines and autoantibodies were measured by ELISA; 16S rRNA sequencing was performed by the CU Anschutz Mucosal Immunobiology Core.

Results: CIA severity was significantly higher in Envigo and Taconic mice compared to Jax mice (Figure 1). While Taconic and Envigo mice had nearly identical mean CIA severity scores, there was a higher degree of score variability within the Taconic mice. Despite significant differences in CIA severity between the Jax, Envigo, and Taconic groups, there were no significant differences in total CII-IgG levels at day 28, nor CII-IgG isotypes (IgG1, IgG2a, IgG2b). We also observed significant differences in microbiome alpha and beta diversity between the three groups. Finally, we identified 7 genera that significantly correlated with CIA score (Figure 2). *Candidatus arthromitus* (also known as segmented filamentous bacteria) had the strongest positive correlation with CIA severity, while butyrate-producing *Butyricoccaceae* had a significant negative correlation with CIA severity.

Conclusion: Our findings reveal that the vendor source of mice significantly impacts CIA severity, independent of systemic autoantibody and cytokine levels. Several bacterial taxa (e.g. *Candidatus arthromitus, Butyrococcaceae)* may play a key role in disease severity differences. This highlights a critical but often overlooked source of variability that may contribute to irreproducibility across preclinical arthritis studies. Moving forward, intentional selection of mouse source—and consideration of microbiota as a key experimental variable—will be essential for enhancing the reproducibility of the CIA model.

Disclosure: B. Seymour: None; **B. Allen**: None; **K. Kuhn**: Solarea, 2.

Abstract Number: 0871

The gut microbiome shapes MTX pharmacology and is linked to treatment outcomes

Vanya Sofia Villa Soto[1], Diego Orellana[2], Erin Reilly[3], Chloe Heath[2], Alexandra Degraeve[2], Mohana Mukherjee[2], darren Dumlao[2], Rebecca Blank[4], steven Yu[2], Noah Perlmutter[2], Judith Ashouri[2], Jose Scher[5], andrew Patterson[3], Peter Turnbaugh[2] and **Renuka Nayak**[6], [1]University of California, San Francisco, San Francics, CA, [2]University of California, San Francisco, San Francisco, CA, [3]Pennsylvania State University, University Park, PA, [4]NYU Langone Health, New York, NY,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[5]New York University School of Medicine, New York, NY, [6]University of California, San Francisco (UCSF), San Francisco, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Animal Models (0867–0872)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Despite advances in targeted therapeutics, methotrexate (MTX) remains the first-line therapy in the treatment of rheumatoid arthritis (RA) and other inflammatory arthritides. However, more than 50% of patients do not achieve clinically adequate improvement on MTX alone. For decades, investigators have sought to identify determinants of MTX response, and while multiple factors have been implicated (e.g., genetics, environment), the molecular mechanisms underpinning MTX response are incompletely understood. We sought to investigate the extent to which the human gut microbiome contributes to variation in MTX response. We previously showed that among RA patients, the gut microbiome is associated with MTX efficacy. Further, we found microbial communities from RA patients variably depleted MTX *ex vivo*, and that depletion was negatively associated with future MTX efficacy. We also identified multiple representative human gut bacterial strains that directly deplete MTX *in vitro*. Given these clinical associations and supportive *ex vivo* and *in vitro* findings, here we quantify the extent to which the human gut microbiome contributes to MTX pharmacokinetics (PK) *in vivo* and whether this is linked to treatment outcomes in autoimmunity.

Methods: Germ-free mice were variably colonized with human or murine microbiota. We quantified levels of MTX and its metabolites in circulation and stool using LC-MS over an 8- to 24-hour time course. We used stable isotope labeling to identify novel MTX metabolites. We harvested strains from RA patients to test their MTX metabolism abilities *in vitro*. We used specific-pathogen-free (SPF) SKG mice reared in different facilities to test the impact of the gut microbiota on MTX pharmacology and clinical arthritis scores.

Results: MTX PK profiles significantly differed between germ-free and colonized mice *in vivo*. Further, germ-free mice colonized with different patient microbiota significantly differed in MTX plasma profiles. We harvested over 300 bacterial strains from RA patients representing 46 unique species; of these, 12 (26%) metabolized MTX *in vitro*. Stable isotope labeling studies revealed 3 novel MTX metabolites, and one of these novel metabolites was found to be the major product of microbial metabolism. Finally, studying SPF SKG mice reared at two different facilities with differing microbiota, we found that clinical response to MTX differed by facility, that co-housing reduced this difference, and that germ-free mice colonized with these different mouse microbiotas showed significantly different MTX PK profiles, suggesting that microbial MTX metabolism is linked to treatment outcomes *in vivo*.

Conclusion: We provide evidence that the human gut microbiome causally contributes to MTX pharmacology *in vivo* through known and novel mechanisms and raise the possibility that microbial metabolism can be modulated to impact MTX pharmacology and treatment outcomes in patients. These results are a first step towards understanding and manipulating the human gut microbiome in the treatment of autoimmunity and the advancement of precision medicine for millions of patients globally taking MTX for autoimmunity.

Disclosure: V. Villa Soto: None; **D. Orellana**: None; **E. Reilly**: None; **C. Heath**: None; **A. Degraeve**: None; **M. Mukherjee**: None; **d. Dumlao**: None; **R. Blank**: None; **s. Yu**: None; **N. Perlmutter**: None; **J. Ashouri**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **a. Patterson**: None; **P. Turnbaugh**: None; **R. Nayak**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0872

Silencing of Schnurri-3 protects from TNF-induced bone loss and is accompanied by upregulation of type I Interferon-Stimulated Genes (ISGs) in osteoblasts.

Priyanka Kushwaha[1], Albert Tai[2], Catherine Manning[3], Yeon Suk Yang[4], Jae-Hyuck Shim[4] and Ellen M. Gravallese[5], [1]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Boston, MA, [2]Department of Immunology, Tufts University School of Medicine, Boston, MA, [3]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [4]2Department of Medicine/Division of Rheumatology, University of Massachusetts Chan Medical School, Worcester, MA, [5]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Animal Models (0867–0872)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Schnurri-3 (SHN3) is an adaptor protein and a negative regulator of osteoblast (OB) function. Its inhibition prevents bone loss and joint erosion in models of rheumatoid arthritis (RA). TNF enhances osteoclast differentiation while suppressing OB function, promoting bone loss. Previously we reported that TNF induces SHN3 transcription via p65/p50 binding at promoter position +10, while also promoting p65 binding to 2 other sites in the SHN3 promoter. However, the contribution of SHN3 to the regulation of OB differentiation under the influence of TNF is not known.

Methods: Mice were generated with constitutively active (CA) NF-κB signaling in OB lineage cells. IKK-2-CA$^{fl/fl}$ and IKK-2-CA$^{fl/fl}$;Shn3$^{fl/fl}$ mice were crossed with *Prx1-Cre* transgenic mice. This breeding strategy produced two genotypes: IKK-2-CA^{Prx1_Cre} mice, (CA-IKK in OB lineage cells), and Shn3$^{fl/fl}$;IKK-2-CA^{Prx1_Cre} mice (CA IKK in OB lineage-cells with deletion

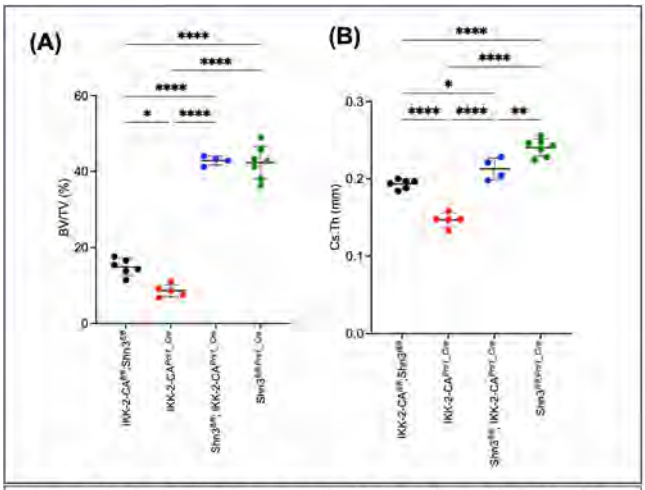


Figure 1: Deletion of Shn3 protects against NF-κB pathway-induced bone loss. MicroCT analysis was performed on 8-week-old mice as follows: IKK-2-CA$^{fl/fl}$;Shn3$^{fl/fl}$ (control) and *Prx-1^{Cre}* transgenic mice were used to generate: IKK-2-CA^{Prx1_Cre} (CA-IKK specifically in OB lineage cells),Shn3$^{fl/fl}$;IKK-2-CA^{Prx1_Cre} (CA-IKK-2 in OB lineage-cells with deletion of SHN3), and Shn3$^{fl/fl;Prx1_Cre}$ (OB lineage-cells with deletion of SHN3). Relative quantification of the femur bone parameters by microCT: **(A)** BV/TV (bone volume/tissue volume of trabecular bone), **(B)** Cs.Th (cortical bone thickness). Data are presented as mean ± SD; **P < 0.01, ***P < 0.001, ****P < 0.0001 (one-way ANOVA between groups). (n=4-6 mice).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

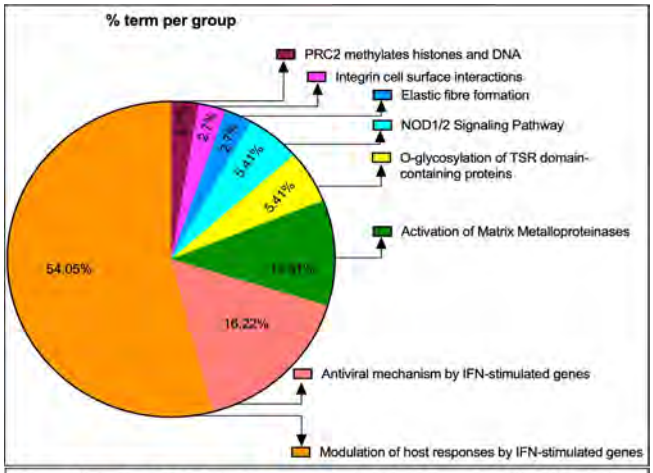


Figure 2: A ClueGO pie chart showing enriched pathways in Shn3KO+TNF vs. WT+TNF. (TNF-treated_p≤0.01)

of SHN3). Shn3$^{fl/fl;Prx1_Cre}$ served as a positive control known to promote OB formation. To determine the impact of SHN3 on OB differentiation during TNF-mediated inflammation, BMSCs from Shn3WT and Shn3KO (globally deficient) mice were differentiated into OBs and treated with TNF (2 ng/mL) from days 4-18. Alkaline phosphatase staining was performed to assess OB differentiation, and RNA was harvested for bulk RNA sequencing. Data analysis was conducted using Qlucore Omics Explorer. Functional enrichment of differentially expressed genes (DEGs) in KO+TNF vs. WT+TNF cells was performed using ClueGO in Cytoscape, and selected genes were validated by qRT-PCR.

Results: Mice with constitutive activation of NF-κB in OB-lineage cells (IKK-2-CA^{Prx1_Cre}) had reduced femoral and cortical bone volume compared with control IKK-2-CA$^{fl/fl}$;Shn3$^{fl/fl}$ mice. Shn3 deletion in OB-lineage cells (Shn3$^{fl/fl}$;IKK-2-CA^{Prx1_Cre}) rescued this loss, and demonstrated bone mass similar to Shn3$^{fl/fl;Prx1_Cre}$ mice (Fig.1). *In vitro*, SHN3 deletion reversed TNF-induced suppression of OB differentiation, indicating that SHN3 deficiency mitigates TNF-driven suppression of OB function. RNA-seq analysis identified 211 significantly DEGs (p ≤ 0.01) between TNF-treated BMSCs from WT/KO groups. Reactome

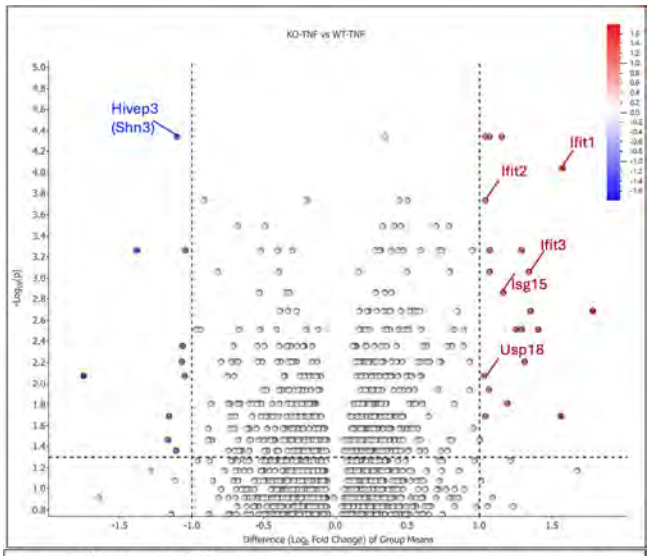


Figure 3: Volcano plot of RNA-seq analysis of differentially expressed genes using the mRNAs isolated from the WT and KO TNF treated groups with significance (p≤0.01).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and GSEA analysis showed enrichment of type I IFN pathways in KO+TNF (Fig. 2). Notably, ISGs including *Isg15*, *Usp18*, and *Ifit1/2/3* were also upregulated in KO+TNF compared with WT+TNF (Fig. 3), validated by qRT-PCR.

Conclusion: Shn3 silencing in OB-lineage cells prevents NF-κB-driven bone loss and promotes bone formation under inflammatory conditions, establishing SHN3 as an important effector of NF-κB signaling in bone. *In vitro*, Shn3 deletion restores OB differentiation in the presence of TNF and significantly increases the expression of ISGs, suggesting that SHN3 negatively regulates type I IFN responses in OBs during chronic inflammation. These findings compliment a report in non-inflammatory conditions showing that OB function is modulated by type I IFN and ISGs expression[1]. Together, our data highlight a novel axis in osteoimmunology in which SHN3 mediates TNF-induced inhibition of OB function, potentially through modulation of type I IFN signaling.

Reference: *1.doi: 10.7554/eLife.59659*.

Disclosure: P. Kushwaha: None; **A. Tai**: None; **C. Manning**: None; **Y. Yang**: AiTHEA Therapeutics, 12, Samsung Bioepis, 2, Samsung Biologics, 2; **J. Shim**: AiTHEA Therapeutics, 12, Samsung Bioepis, 2, Samsung Biologics, 2; **E. Gravallese**: Beam Therapeutics, 11, CRISPR Therapeutics, 11, Editas Medicine, 11, Elsevier, 9, Ginkgo Bioworks, 11, Intellia Therapeutics, 11, New England Journal of Medicine, 1, UpToDate, 9.

Abstract Number: 0873

Sex Differences in Proteomic Profiles and the Impact of Deucravacitinib Treatment in Patients with Active Psoriatic Arthritis: A Pooled Phase 3 Analysis

Lihi Eder[1], Shangzhong Li[2], Philip J. Mease[3], Christopher Ritchlin[4], Walter P Maksymowych[5], Hendrik Schulze-Koops[6], Josef Smolen[7], Oliver FitzGerald[8], Vinod Chandran[9], Chun Wu[10] and Jinqi Liu[2], [1]University of Toronto, Toronto, ON, Canada, [2]Bristol Myers Squibb, Princeton, NJ, [3]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [4]University of Rochester Medical Center, Canandaigua, NY, [5]Department of Medicine, University of Alberta, Edmonton, AB, Canada, [6]LMU Hospital, Division for Rheumatology and Clinical Immunology, Munich, Bayern, Germany, [7]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria, Vienna, Austria, [8]UCD, Dublin 6, Dublin, Ireland, [9]Division of Rheumatology, Departments of Medicine and Laboratory Medicine and Pathobiology, University of Toronto, and Gladman Krembil Psoriatic Arthritis Research Program, Krembil Research Institute, University Health Network, Toronto, Canada, [10]Bristol Myers Squibb, Princeton

SESSION INFORMATION

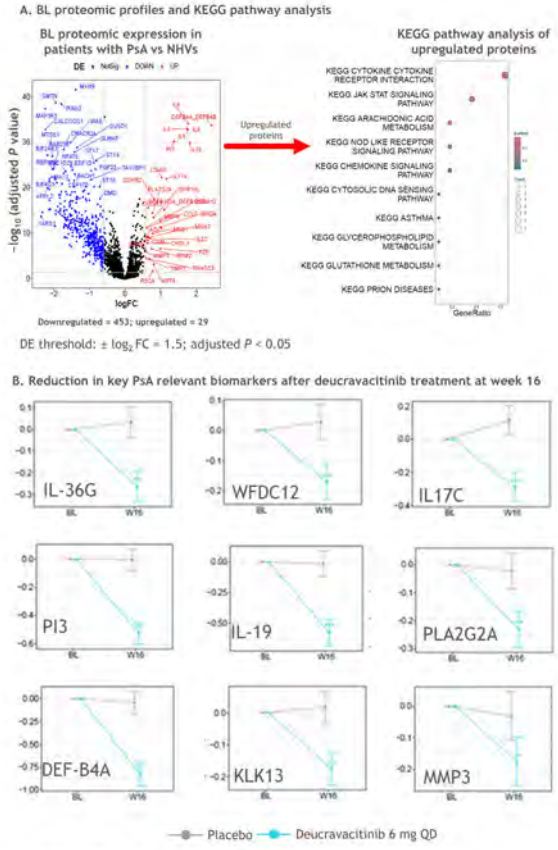
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Therapies (0873–0878)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: PsA affects male and female patients equally; however, variations in manifestations and treatment response exist between sexes. Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor. This post hoc pooled analysis of 2 randomized, placebo (PBO)–controlled, phase 3, pivotal studies (POETYK PsA-1 [NCT04908202] and POETYK PsA-2 [NCT04908189]) assessed proteomic profiles in patients with PsA by sex to identify relevant biological pathways and evaluate the effect of deucravacitinib on disease activity–related proteomic scores.

Methods: Proteomic profiling of plasma samples from POETYK PsA-1 and PsA-2 was conducted using Olink 3072, a multiplex assay that includes ≈ 3000 proteins, and harmonized using 24 bridging samples. Differential expression (DE) analysis was conducted using DREAM. Significant DE proteins were identified for all patients vs demographically matched normal

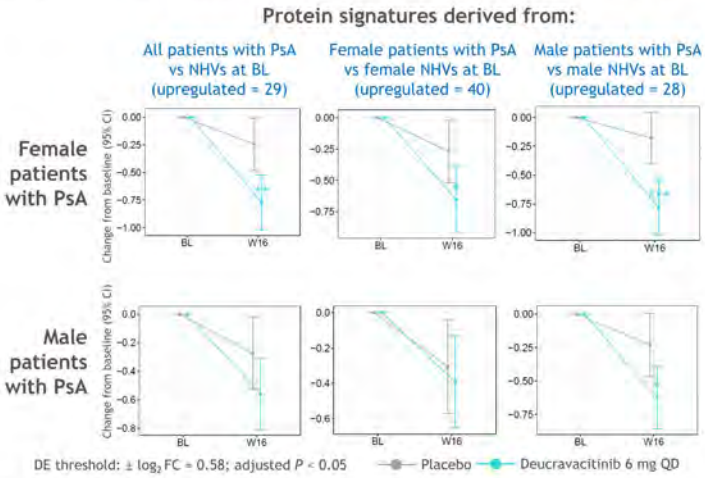
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. (A) Distinct BL proteomic profiles in patients with PsA vs NHVs and (B) pharmacodynamic changes in PsA-relevant biomarkers after deucravacitinib treatment at week 16



***P < 0.001; **P < 0.01.
BL, baseline; DE, differential expression; DEFB4A, defensin beta 4A; FC, fold change; IL, interleukin; KEGG, Kyoto Encyclopedia of Genes and Genomes; KLK13, kallikrein -13; MMP3, matrix metalloproteinase 3; NHV, normal healthy volunteer; PBO, placebo; PI3, phosphoinositide 3-kinase; PLA2G2A, phospholipase A2; QD, once daily; W, week; WFDC, WAP four-disulfide core domain protein 2.

Figure 2. Pharmacodynamic changes in protein signatures after deucravacitinib treatment at week 16 derived from all patients with PsA vs NHVs at BL, female patients with PsA vs female NHVs at BL, and male patients with PsA vs male NHVs at BL



*** P < 0.001; ** P < 0.01; * P < 0.05.
BL, baseline; DE, differential expression; FC, fold change; NHV, normal healthy volunteer; QD, once daily; W, week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

healthy volunteers (NHVs; fold change [FC] = 1.5; adj $P < 0.05$). The FC threshold was 1.23 (adj $P < 0.05$) for male vs female patient comparisons. Enriched pathways were identified using clusterProfiler based on DE proteins. Disease state protein signatures were derived from baseline DE proteins in all patients vs all NHVs, female patients vs female NHVs, and male patients vs male NHVs. Disease activity protein signatures were independently derived by selecting proteins with > 0.3 repeated measure correlations with clinical endpoints. Protein signature scores were calculated using z score normalization to standardize expression across samples. The geometric mean of the z scores for constituent proteins was calculated to obtain the final signature score via the Gene Set Variation Analysis package.

Results: DE proteins were seen in patients with PsA (n = 1222) vs NHVs (n = 121) in a KEGG pathway analysis (**Figure 1A**). Upregulated proteins (eg, PI3, IL-17, IL-19, beta-defensin, MMP3) were reduced with deucravacitinib vs PBO (**Figure 1B**). Overall, 133 and 177 unique proteins were identified in male and female patients, respectively, vs sex-matched NHVs. Female patients had greater enrichment in neuroactive ligand receptor interaction and hormone metabolism pathways vs male patients. Regardless of whether disease state protein signature scores were derived from all patients, female patients, or male patients, deucravacitinib reduced these scores vs PBO in female and male patients at W16 (**Figure 2**). Deucravacitinib also significantly reduced protein signature scores associated with PsA-relevant disease activity vs PBO in male and female patients.

Conclusion: DE was identified in patients with PsA vs NHVs. Deucravacitinib reduced upregulated proteins in all patients. Unique proteomic profiles were identified in male vs female patients with PsA. Deucravacitinib reduced disease state signature scores in the overall population, male patients, and female patients, which is consistent with improved clinical efficacy in the overall population and by sex. Deucravacitinib also reduced disease activity signature scores in male and female patients. Findings provide insight into sex-specific PsA disease biology and may help personalize disease management.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **S. Li**: Bristol Myers Squibb, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **W. Maksymowych**: AbbVie, 2, 5, 6, 12, Educational grants, Bristol-Myers Squibb(BMS), 2, 5, 6, CARE Arthritis, 12, Chief Medical Officer, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, educational grants, Pfizer, 2, 5, 6, 12, educational grants, UCB Pharma, 2, 5, 6; **H. Schulze-Koops**: AbbVie, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Amgen, 12, Research support and principal investigator (clinical trials funds to institution), Biogen Idec, 12, Research support and principal investigator (clinical trials funds to institution), Boehringer Ingelheim, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Bristol Myers Squibb, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Eli Lilly, 6, 12, Research support and principal investigator (clinical trials funds to institution), Galapagos, 2, GSK, 12, Research support and principal investigator (clinical trials funds to institution), Janssen, 6, Janssen-Cilag, 12, Research support and principal investigator (clinical trials funds to institution), Merck Sharp & Dohme, 6, 12, Research support and principal investigator (clinical trials funds to institution), Novartis, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Pfizer, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Roche, 12, Research support and principal investigator (clinical trials funds to institution), Sandoz-Hexal, 6, 12, Research support and principal investigator (clinical trials funds to institution), Sanofi, 6, 12, Research support and principal investigator (clinical trials funds to institution), UCB, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution); **J. Smolen**: AbbVie/Abbott, 5, 6, Ananda, 6, AstraZeneca, 5, 6, Astro, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Celltrion, 6, Chugai-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Roche, 6, Galapagos, 5, 6, Immunovant, 6, Janssen, 6, Lilly, 5, 6, Pfizer, 6, R-Pharma, 6, Samsung, 6, Sandoz, 6, Sanofi, 6; **O. FitzGerald**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Janssen, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5; **V. Chandran**: AbbVie, 1, 2, AstraZeneca, 12, Spousal employment, Bristol Myers Squibb, 1, 2, Eli Lilly, 1, 2, 5, Fresenius Kabi, 1, 2, Johnson & Johnson, 1, 2, 5, Novartis, 1, 2, UCB, 1, 2; **C. Wu**: Bristol Myers Squibb, 3, 11; **J. Liu**: Bristol-Myers Squibb (BMS), 3, 11.

Abstract Number: 0874

Impact of Deucravacitinib on Disease Activity in Patients With Psoriatic Arthritis (PsA): Results From the Pivotal Phase 3 PsA Studies

Atul Deodhar[1], Ricardo Blanco[2], Arthur Kavanaugh[3], Alice Gottlieb[4], Laura Coates[5], Christopher Ritchlin[6], Alan Kivitz[7], Xiaofeng Zeng[8], Akimichi Morita[9], Diamant Thaçi[10], Stefan Varga[11], Kexuan Li[11], Ying-Ming Jou[12], Eleni Vritzali[13] and Philip J. Mease[14], [1]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [2]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [3]University of California, San Diego, School of Medicine, San Diego, CA, [4]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX, [5]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [6]University of Rochester Medical Center, Canandaigua, NY, [7]Altoona Center for Clinical Research, Duncansville, PA, [8]Department of Rheumatology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Beijing, China (People's Republic), [9]Department of Geriatric and Environmental Dermatology, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan, [10]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany, [11]Bristol Myers Squibb, Princeton, NJ, [12]Bristol Myers Squibb, Princeton, [13]Bristol Myers Squibb, Boudry, Switzerland, [14]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Therapies (0873–0878)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

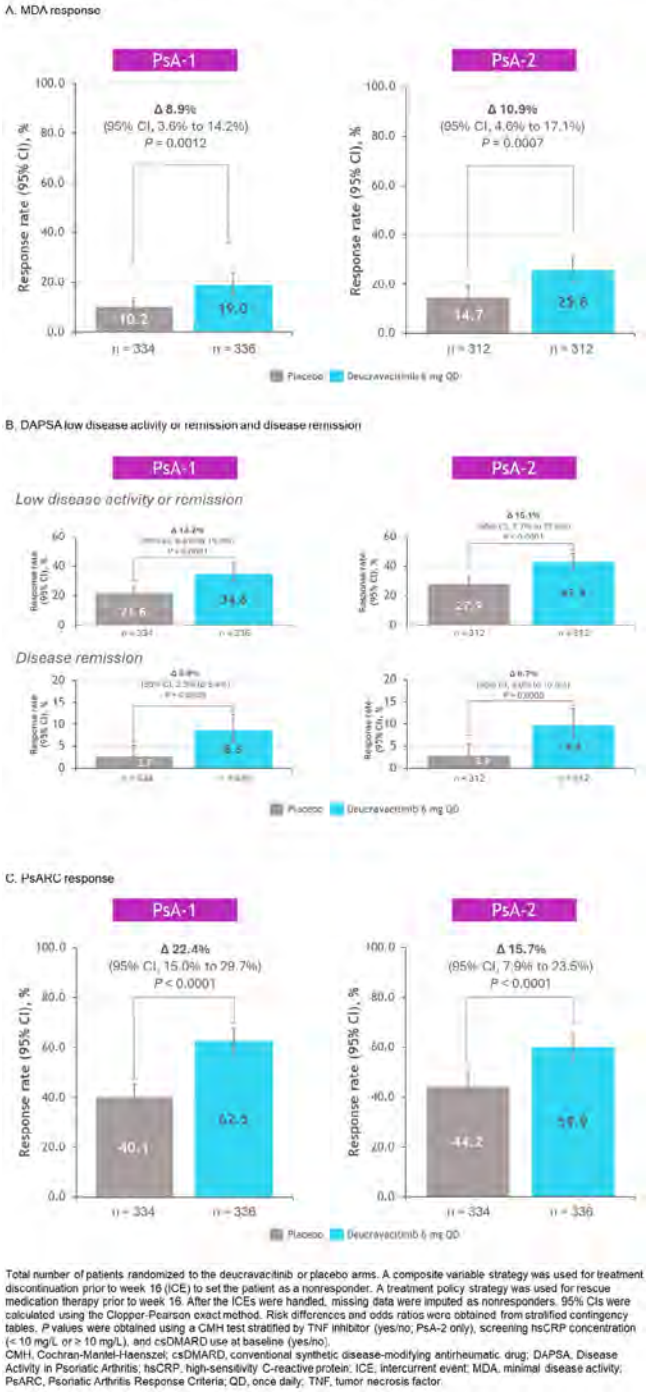
Background/Purpose: The first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor deucravacitinib has an established clinical profile in moderate to severe plaque psoriasis with over 5 years of long-term data[1] and is approved in multiple countries for this indication. Deucravacitinib showed superior efficacy vs placebo (PBO) at W16 across multiple endpoints in patients (pts) with active PsA in the global, randomized, double-blind, PBO-controlled phase 3 POETYK PsA-1 (NCT04908202) and PsA-2 (NCT04908189) studies, with no new safety signals.[2,3] Composite efficacy measures provide a comprehensive assessment of disease activity and response to treatment across several disease domains. We report deucravacitinib efficacy based on composite measures of disease activity in pts from the POETYK PsA studies.

Methods: Pts in the POETYK PsA-1 and PsA-2 studies were randomized to deucravacitinib 6 mg once daily or PBO for 16 weeks (in PsA-2, a group received apremilast as a safety reference arm). This analysis included pts treated with deucravacitinib or PBO to W16. Composite measures of disease activity, including minimal disease activity (MDA), Disease Activity in Psoriatic Arthritis (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), modified Composite Psoriatic Disease Activity Index (mCPDAI), and Psoriatic Arthritis Response Criteria (PsARC), were analyzed using nonresponder imputation for missing binary data and control-based pattern imputation for missing continuous data.

Results: At W16, a significantly higher proportion of pts treated with deucravacitinib vs PBO achieved MDA response (PsA-1, $P = 0.0012$; PsA-2, $P = 0.0007$), DAPSA low disease activity or remission (PsA-1, $P = 0.0001$; PsA-2, $P <$

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Achievement of (A) MDA response, (B) DAPSA low disease activity or remission and disease remission, and (C) PsARC response at week 16 in patients treated in the POETYK PsA-1 and PsA-2 studies



Total number of patients randomized to the deucravacitinib or placebo arms. A composite variable strategy was used for treatment discontinuation prior to week 16 (ICE) to set the patient as a nonresponder. A treatment policy strategy was used for rescue medication therapy prior to week 16. After the ICEs were handled, missing data were imputed as nonresponders. 95% CIs were calculated using the Clopper-Pearson exact method. Risk differences and odds ratios were obtained from stratified contingency tables. *P* values were obtained using a CMH test stratified by TNF inhibitor (yes/no; PsA-2 only), screening hsCRP concentration (< 10 mg/L or ≥ 10 mg/L), and csDMARD use at baseline (yes/no).
CMH, Cochran-Mantel-Haenszel; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAPSA, Disease Activity in Psoriatic Arthritis; hsCRP, high-sensitivity C-reactive protein; ICE, intercurrent event; MDA, minimal disease activity; PsARC, Psoriatic Arthritis Response Criteria; QD, once daily; TNF, tumor necrosis factor.

0.0001), DAPSA disease remission (PsA-1, $P = 0.0009$; PsA-2, $P = 0.0005$), and PsARC response (PsA-1, $P < 0.0001$; PsA-2, $P < 0.0001$; **Figure 1**). Decrease from baseline in PASDAS and mCPDAI at W16 was significantly greater in pts treated with deucravacitinib vs PBO (PASDAS: PsA-1, $P < 0.0001$; PsA-2, $P < 0.0001$; mCPDAI: PsA-1, $P < 0.0001$; PsA-2, $P < 0.0001$; **Figure 2**). Efficacy was consistently higher with deucravacitinib vs PBO in male and female pts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

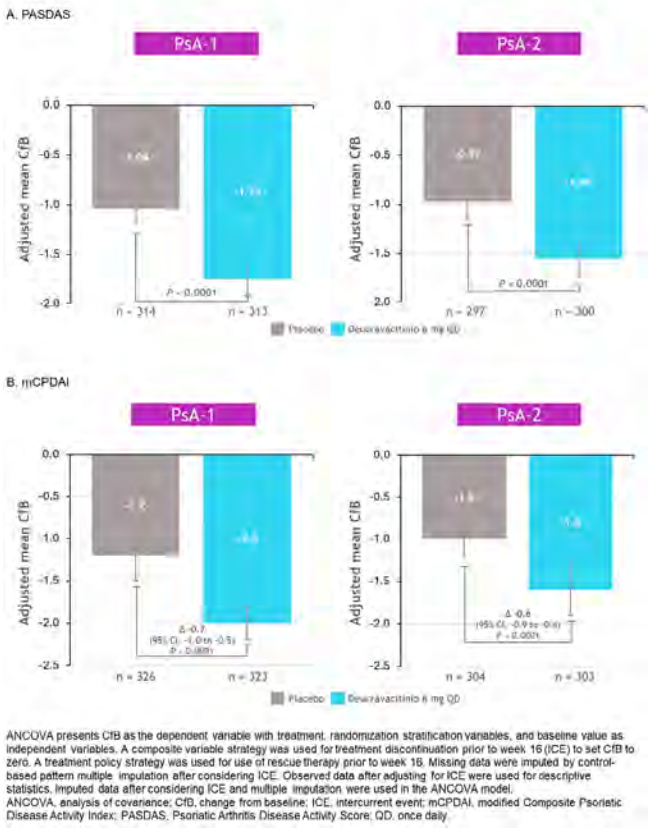


Figure 2. Change from baseline in (A) PASDAS and (B) mCPDAI at week 16 in patients treated in the POETYK PsA-1 and PsA-2 studies

ANCOVA presents CfB as the dependent variable with treatment, randomization stratification variables, and baseline value as independent variables. A composite variable strategy was used for treatment discontinuation prior to week 16 (ICE) to set CfB to zero. A treatment policy strategy was used for use of rescue therapy prior to week 16. Missing data were imputed by control-based pattern multiple imputation after considering ICE. Observed data after adjusting for ICE were used for descriptive statistics. Imputed data after considering ICE and multiple imputation were used in the ANCOVA model.
ANCOVA, analysis of covariance; CfB, change from baseline; ICE, intercurrent event; mCPDAI, modified Composite Psoriatic Disease Activity Index; PASDAS, Psoriatic Arthritis Disease Activity Score; QD, once daily.

Conclusion: In these analyses of the pivotal POETYK PsA-1 and PsA-2 phase 3 studies, deucravacitinib substantially reduced disease activity vs PBO at W16 in several composite measures of disease activity, and a significantly higher proportion of pts reached optimal control of disease activity, which aligns with the results from the primary analyses.[2,3] Given that remission and low disease activity are primary goals of PsA treatment, deucravacitinib may be an efficacious treatment choice for pts with active PsA.

References

1. Armstrong AW, et al. *J of Skin*. 2025;9:s532.
2. Mease PJ, et al. Presented at the 2025 American Academy of Dermatology Annual Meeting; March 7-11, 2025; Orlando, FL. Abstract 66894.
3. Bristol Myers Squibb. News Release. Accessed April 21, 2025. https://news.bms.com/news/details/2024/Bristol-Myers-Squibb-Announces-Positive-Topline-Results-from-Two-Pivotal-Phase-3-Trials-Evaluating-Sotyktu-deucravacitinib-in-Adults-with-Psoriatic-Arthritis/default.aspx.

Disclosure: A. Deodhar: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2; **A. Gottlieb**: Amgen, 1, 2, 6, Avalo Therapeutics, 5, Bristol Myers Squibb, 5, Eli Lilly, 1, 2, 6, Highlights Therapeutics, 1, 2, 6, MoonLake, 5, Novartis, 1, 2, 6, Sanofi, 1, 2, 6, Sun Pharma, 1, 2, 6, Takeda, 1, 2,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Teva, 1, 2, 6, UCB, 1, 2, 5, 6, Xbiotech, 1, 2, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **A. Kivitz**: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2; **X. Zeng**: None; **A. Morita**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Kyowa Kirin, 2, 5, 6, LEO Pharma, 2, 5, 6, Maruho, 2, 5, 6, Sun Pharma Japan, 2, 5, 6, Taiho Pharmaceutical, 2, 5, 6, Torii Pharmaceutical, 2, 5, 6, UCB Japan, 2, 5, 6, Ushio, 2, 5, 6; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol Myers Squibb, 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly and Company, 1, 2, 12, Investigator, Fresenius-Kabi, 2, 5, Galderma, 1, 2, 12, Investigator, Johnson & Johnson, 1, 2, 12, Investigator, Kyowa Kirin, 1, 2, 12, Investigator, L'Oreal, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, New Bridge, 1, 2, 12, Investigator, Novartis, 1, 2, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Sun-Pharma, 1, 2, 5, Target-RWE, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator, Vichy, 1, 2, 12, Investigator; **S. Varga**: Bristol Myers Squibb, 3, 11; **K. Li**: Bristol-Myers Squibb(BMS), 3, 11; **Y. Jou**: Bristol Myers Squibb, 3, 11; **E. Vritzali**: Bristol Myers Squibb, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6.

Abstract Number: 0875

Efficacy and Safety of Icotrokinra, a Novel Targeted Oral Peptide (IL-23R-Inhibitor), in Adolescents With Moderate-to-Severe Plaque Psoriasis: Subgroup Analyses From a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study (ICONIC-LEAD)

Lawrence Eichenfield[1], Ricardo Galimberti[2], Adelaide Hebert[3], Wen-Hui Wang[4], Jennifer Soung[5], Nina Magnolo[6], John Browning[7], Angela Moore[8], Mark Lebwohl[9], Dagmar Wilsmann-Theis[10], **Joseph F Merola**[11], Georgios Kokolakis[12], Dariusch Mortazawi[13], Parbeer Grewal[14], Megan Miller[15], Joseph Cafone[16], Shu Li[17], Gigi Jiang[17], Fabio Nunes[17], Cynthia DeKlotz[18] and Amy Paller[19], [1]University of California, San Diego School of Medicine, La Jolla, CA, USA, La Jolla, CA, [2]Hosp Italiano de Buenos Aires, Buenos Aires, Argentina, Buenos Aires, Argentina, [3]University of Texas Medical School-Houston, Bellaire, TX, USA, Bellaire, TX, [4]Peking University Third Hospital, Haidian District, Beijing, China, Beijing, China (People's Republic), [5]Southern California Dermatology, Inc, Santa Ana, CA, USA, Santa Ana, [6]University Hospital Muenster, Muenster, Germany, Muenster, Germany, [7]Methodist Children's Hospital, San Antonio, TX, USA, San Antonio, TX, [8]Baylor University Medical Center, Dallas, TX, USA, Dallas, TX, [9]Icahn School of Medicine at Mount Sinai, New York, NY, [10]University Hospital Bonn, Center for Skin Diseases, Bonn, Germany, Bonn, Germany, [11]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [12]Charité-Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [13]Clinical Research Center, Remscheid, Germany, Remscheid, Germany, [14]University of Alberta, Edmonton, Alberta, Canada, Edmonton, AB, Canada, [15]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, CA, [16]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, CA, [17]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [18]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, [19]Northwestern University Feinberg School of Medicine, Chicago, IL, USA, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Therapies (0873–0878)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Baseline Demographics, Disease Characteristics, and Previous Treatment Among Adolescents With Moderate-to-Severe Psoriasis

	Placebo (n=22)	Icotrokinra (n=44)	Total (N=66)
Demographics			
Age, years	15.0 (1.5)	15.0 (1.8)	15.0 (1.7)
Sex, Female	64%	52%	56%
Race, Asian/Black/White	23/0/77%	23/4/70%	23/3/73%
Weight, kg	66.4 (23.4)	75.5 (20.9)	72.5 (22.0)
BMI, kg/m^2	24.4 (7.9)	26.0 (7.1)	25.5 (7.4)
Disease Characteristics			
Psoriasis disease duration, years	5.8 (3.4)	4.9 (4.0)	5.2 (3.8)
IGA score			
Severe (4)	18%	30%	26%
Moderate (3)	82%	70%	74%
PASI score (0-72)	18.6 (4.0)	19.8 (8.2)	19.4 (7.1)
BSA (%)	27.1 (14.0)	26.1 (15.6)	26.4 (15.0)
Previous Psoriasis Treatment			
Systemic[a]	50%	52%	52%
Conventional nonbiologic systemic[b]	32%	36%	35%
Biologics[c]	41%	14%	23%
Phototherapy (PUVA or UVB)	14%	23%	20%
Novel nonbiologic systemic[d]	0	2%	2%

Data shown are mean (SD) or %. [a]Includes conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [b]Includes PUVA, methotrexate, cyclosporine, acitretin, azathioprine, and fumarate. [c]Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, and certolizumab pegol. [d]Includes apremilast, deucravacitinib, and tofacitinib. BMI=body mass index; BSA=body surface area; IGA=Investigator's Global Assessment; PASI=Psoriasis Area and Severity Index; PUVA=psoralen plus ultraviolet A; SD=standard deviation; UVB=ultraviolet B.

Background/Purpose: Icotrokinra (ICO), a novel targeted oral peptide, binds the interleukin (IL)-23 receptor to inhibit IL-23 signaling. ICONIC-LEAD (NCT06095115) is the first Phase 3 study in moderate-to-severe psoriasis to assess the efficacy and safety of a systemic therapy simultaneously in adolescents and adults.

Methods: In ICONIC-LEAD, adolescents (12 to < 18 years) with moderate-to-severe psoriasis (body surface area [BSA] ≥10%, Psoriasis Area and Severity Index [PASI] ≥12, Investigator's Global Assessment [IGA] ≥3) and body weight ≥40 kg were randomized 2:1 to once-daily ICO 200 mg or placebo through Week 16. Placebo patients transitioned to ICO after Week 16. Overall ICONIC-LEAD co-primary endpoints, IGA 0/1 response (IGA score=cleared [0] or minimal [1] and ≥2-grade improvement) and PASI 90 response at Week 16, were assessed in adolescents, as were the efficacy and safety through Week 24.

Results: Adolescents comprised 9.6% (66/684) of the ICONIC-LEAD population. The mean age was 15 years and the mean psoriasis disease duration was 5.2 years (**Table**). Higher proportions of adolescents receiving ICO vs placebo achieved clear/almost clear skin at Week 16 (IGA 0/1: 84.1% vs 27.3%; PASI 90: 70.5% vs 13.6%; nominal p< 0.001). At Week

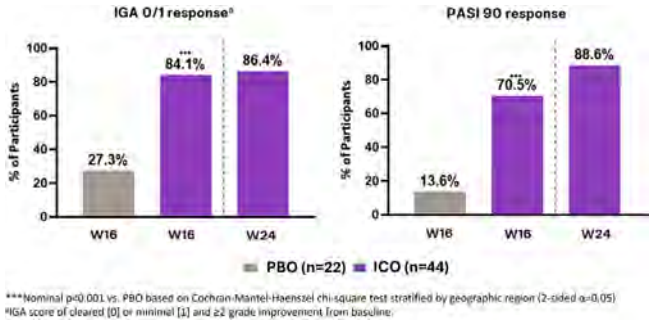


Figure. IGA 0/1 and PASI 90 Response at W16 and W24

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

24, rates of clear/almost clear skin with ICO were 86.4% (IGA 0/1) and 88.6% (PASI 90; **Figure**). Response patterns were consistent for IGA 0 and PASI 100. At Week 16, 50% of ICO and 73% of placebo adolescents had ≥1 adverse event; no safety signals emerged through Week 24.

Conclusion: In adolescents with moderate-to-severe psoriasis, higher proportions of ICO vs placebo participants achieved clear/almost clear skin at Week 16, with unprecedented response rates at Week 24 and a favorable adverse event profile.

Disclosure: L. Eichenfield: AbbVie, 2, 12, Investigator, Almirall, 2, Amgen, 2, 12, Investigator, Apogee, 2, Arcutis, 2, 12, Investigator, Attovia, 2, Bausch, 12, Investigator, Bristol Myers Squibb, 2, Castle Biosciences, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 12, Investigator, Forte, 2, Galderma, 2, 12, Investigator, Incyte, 2, 12, Investigator, Janssen, 2, LEO Pharma, 2, Novartis, 2, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, Sanofi-Genzyme, 12, Investigator, Seanergy, 2, UCB, 2, Verrica, 2; **R. Galimberti**: Amgen, 12, Investigator, Biogen, 12, Investigator, Bristol Myers Squibb, 12, Investigator, Eli Lilly, 12, Investigator, GlaxoSmithKline, 12, Investigator, Janssen, 12, Investigator, Merck Sharp & Dohme, 12, Investigator, Novartis, 12, Investigator, Pfizer, 12, Investigator, Sanofi, 12, Investigator; **A. Hebert**: AbbVie, 5, Almirall, 6, Apogee, 6, Arcutis, 5, 6, Castle Biosciences, 6, Dermavant, 5, 6, Eli Lilly, 5, GlaxoSmithKline, 12, DSMB, Incyte, 6, Janssen, 5, 6, OrthoDermatologics, 12, DSMB, Pfizer, 5, 6, Sanofi-Regeneron, 12, DSMB, Takeda, 5, UTHealth McGovern Medical School-Houston, 3, Verrica, 6; **W. Wang**: AbbVie, 2, 6, 12, Investigator, Amgen, 2, 6, 12, Investigator, Arcutis, 2, 6, 12, Investigator, Eli Lilly, 2, 6, 12, Investigator, Janssen, 2, 6, 12, Investigator, LEO Pharma, 2, 6, 12, Investigator, National Psoriasis Foundation, 2, 6, 12, Investigator, Novartis, 2, 6, 12, Investigator, Pfizer, 2, 6, 12, Investigator, Regeneron, 2, 6, 12, Investigator, Sanofi, 2, 6, 12, Investigator, UCB, 2, 6, 12, Investigator; **J. Soung**: AbbVie, 5, 12, Personal fees, Dermavant, 5, Eli Lilly, 12, Non-financial support (manuscript preparation during the conduct of the study), Kyowa Kirin, 5, LEO Pharma, 5, 12, Personal fees, Pfizer, 5, 12, Personal fees, Regeneron, 5, Sanofi, 5, 12, Personal fees; **N. Magnolo**: AbbVie, 1, 2, 6, Almirall, 1, 2, 6, Boehringer Ingelheim, 1, 2, 6, Bristol Myers Squibb, 1, 2, 6, Dr. Wolff, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, La Roche-Posay, 1, 2, 6, LEO Pharma, 1, 2, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 6, Sanofi, 1, 2, 6, UCB, 1, 2, 6; **J. Browning**: AbbVie, 12, Investigator, Amgen, 12, Investigator, Arcutis, 12, Investigator, Dermata, 12, Investigator, Dermavant, 2, 12, Investigator, Eli Lilly, 12, Investigator, Galderma, 6, Incyte, 12, Investigator, Janssen, 12, Investigator, Krystal, 6, Pfizer, 6, 12, Investigator, Quoin, 12, Investigator, Regeneron, 6, 12, Investigator, Sanofi, 6, 12, Investigator, Takeda, 12, Investigator, UCB, 12, Investigator, Verrica, 6; **A. Moore**: AbbVie, 5, 6, Acelyrin, 5, 6, Arcutis, 5, 6, Bristol Myers Squibb, 5, 6, Dermavant, 5, 6, Eli Lilly, 5, 6, Galderma, 5, 6, Incyte, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Sanofi, 5, 6, Takeda, 5, 6, UCB, 5, 6; **M. Lebwohl**: AbbVie, 5, Almirall, 2, AltruBio Inc, 2, Apogee Therapeutics, 2, Arcutis Biotherapeutics, 2, 5, AstraZeneca, 2, Atomwise, 2, Avotres, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, Cara Therapeutics, 5, Castle Biosciences, 2, Celltrion Biosciences, 2, Clexio Biosciences, 5, CorEvitas, 2, Dermavant, 2, 5, Dermsquared, 2, Eli Lilly, 5, Evommune, Inc, 2, Facilitation of International Dermatology Education, 2, Forte Biosciences, 12, Facilitation of International Dermatology Education, Galderma, 12, Facilitation of International Dermatology Education, Genentech, 12, Facilitation of International Dermatology Education, Incyte, 5, 12, Facilitation of International Dermatology Education, Inozyme, 5, Janssen, 5, LEO Pharma, 12, Facilitation of International Dermatology Education, Meiji Seika Pharma, 12, Facilitation of International Dermatology Education, Mindera, 12, Facilitation of International Dermatology Education, Mirium Pharmaceuticals, 2, Mount Sinai, 3, Pfizer, 5, 12, Facilitation of International Dermatology Education, Sanofi-Regeneron, 5, 12, Facilitation of International Dermatology Education, Seanergy, 12, Facilitation of International Dermatology Education, Strata, 12, Facilitation of International Dermatology Education, Takeda, 12, Facilitation of International Dermatology Education, Trevi Therapeutics, 12, Facilitation of International Dermatology Education, UCB, 5, Verrica Pharmaceuticals, 2; **D. Wilsmann-Theis**: AbbVie, 1, 6, 12, Investigator, Almirall, 1, 6, 12, Investigator, Amgen, 1, 6, 12, Investigator, Biogen, 1, 6, 12, Investigator, Boehringer Ingelheim, 1, 6, 12, Investigator, Bristol Myers Squibb, 1, 6, 12, Investigator, Celgene, 1, 6, 12, Investigator, Eli Lilly, 1, 6, 12, Investigator, GlaxoSmithKline, 1, 6, 12, Investigator, Hexal, 1, 6, 12, Investigator, Incyte, 1, 6, 12, Investigator, Janssen-Cilag, 1, 6, 12, Investigator, LEO Pharma, 1, 6, 12, Investigator, Medac, 1, 6, 12, Investigator, Merck Sharp & Dohme, 1, 6, 12, Investigator, MoonLake

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Immunotherapeutics, 1, 6, 12, Investigator, Novartis, 1, 6, 12, Investigator, Pfizer, 1, 6, 12, Investigator, UCB, 1, 6, 12, Investigator; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **G. Kokolakis**: Abbott, 1, 6, AbbVie, 1, 6, Actelion Pharmaceuticals, 1, 6, Amgen, 1, 6, Basilea Pharmaceutica, 1, 6, Bayer, 1, 6, Biogen IDEC, 1, 6, Boehringer Ingelheim, 1, 6, Bristol Myers Squibb, 1, 6, Celgene, 1, 6, Eli Lilly, 1, 6, Hexal, 1, 6, Janssen Cilag, 1, 6, LEO Pharma, 1, 6, Merck Sharp & Dohme, 1, 6, Mylan, 1, 6, Novartis, 1, 6, Parexel, 1, 6, Pfizer, 1, 6, Sanofi-Aventis, 1, 6, Takeda, 1, 6, UCB, 1, 6; **D. Mortazawi**: AbbVie, 1, 2, 6, 12, Investigator, Almirall, 1, 2, 6, 12, Investigator, Alumis, 1, 2, 6, 12, Investigator, Amgen, 1, 2, 6, 12, Investigator, Bristol Myers Squibb, 1, 2, 6, 12, Investigator, CVderm UKE, 1, 2, 6, 12, Investigator, Eli Lilly, 1, 2, 6, 12, Investigator, Forschungsdock CRO GmbH, 1, 2, 6, 12, Investigator, Johnson & Johnson, 1, 2, 6, 12, Investigator, LEO Pharma, 1, 2, 6, 12, Investigator, Moberg Pharma, 1, 2, 6, 12, Investigator, Novartis, 1, 2, 6, 12, Investigator, Pfizer, 1, 2, 6, 12, Investigator, Sanofi-Aventis, 1, 2, 6, 12, Investigator, UCB, 1, 2, 6, 12, Investigator, Viatris, 1, 2, 6, 12, Investigator; **P. Grewal**: AbbVie, 1, 2, 6, 12, Investigator, Amgen, 1, 2, 6, 12, Investigator, Anacor, 1, 2, 6, 12, Investigator, Apogee Therapeutics, 1, 2, 6, 12, Investigator, Arcutis, 1, 2, 6, Arena Pharmaceuticals, 12, Investigator, Aspen Pharmaceuticals, 1, 2, 6, Avillion, 12, Investigator, Bausch Health, 1, 2, 6, 12, Investigator, Biogen, 12, Investigator, Boehringer Ingelheim, 1, 2, 6, 12, Investigator, Bristol Myers Squibb, 1, 2, 6, 12, Investigator, Celgene, 1, 2, 6, 12, Investigator, Celltrion, 1, 2, 6, Cipher, 1, 2, 6, CorEvitas, 12, Investigator, Dermavant, 12, Investigator, Eli Lilly, 1, 2, 6, 12, Investigator, Galderma, 1, 2, 6, 12, Investigator, GlaxoSmithKline, 1, 2, 6, Incyte, 1, 2, 6, Innovaderm, 1, 2, 6, 12, Investigator, JAMP Pharma, 1, 2, 6, Johnson & Johnson/Janssen, 1, 2, 6, 12, Investigator, LEO Pharma, 1, 2, 6, 12, Investigator, Med Plan, 1, 2, 6, Meiji Seika Pharma, 12, Investigator, MoonLake Immunotherapeutics, 12, Investigator, Novartis, 1, 2, 6, 12, Investigator, Pfizer, 1, 2, 6, 12, Investigator, Regeneron, 1, 2, 6, 12, Investigator, Sandoz, 1, 2, 6, 12, Investigator, Sanofi-Aventis/Genzyme, 1, 2, 6, 12, Investigator, Sun Pharmaceuticals, 1, 2, 6, Takeda, 1, 2, 6, 12, Investigator, UCB, 1, 2, 6, 12, Investigator, Vitae, 12, Investigator; **M. Miller**: Johnson & Johnson, 3, 11; **J. Cafone**: Johnson & Johnson, 3, 11; **S. Li**: Johnson & Johnson, 3, 11; **G. Jiang**: Johnson & Johnson, 3, 11; **F. Nunes**: Johnson & Johnson, 3, 11; **C. DeKlotz**: Johnson & Johnson, 3, 11; **A. Paller**: AbbVie, 2, 12, Investigator and DSMB, Abeona, 2, 12, DSMB, Apogee, 2, Applied Pharma Research, 12, Investigator, Arcutis, 2, Aslan, 2, BioCryst, 2, Biomendics, 12, Investigator, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 12, Investigator, Galderma, 12, DSMB, Incyte, 2, 12, Investigator, Janssen, 12, Investigator, Johnson & Johnson, 2, Krystal, 2, 12, Investigator, LEO Pharma, 2, Mitsubishi Tanabe, 2, Nektar, 2, Primus, 2, Procter and Gamble, 2, Regeneron, 2, 12, Investigator, Sanofi, 2, Seanergy, 2, Timber, 12, Investigator, TWI Biotech, 2, UCB, 2, 12, Investigator.

Abstract Number: 0876

Effect of QX002N on Clinical and Radiographic Outcomes in Ankylosing Spondylitis: Results from a Phase III Randomized, Double-blind, Placebo-Controlled Study

Xiaofeng Zeng[1], Shangzhu Zhang[2], SHENGYUN LIU[3], Fengju Li[4], xuebin wang[5], LINGYUN SUN[6], Hongwei Du[7], Guixiu Shi[8], yanling li[9], hongwei zhang[10], Liyun Zhang[11], Jian Wu[12], mingxuan zhou[13], zhanqing gu[14], yi zhao[15], min fang[16], **Qingyi Song**[17] and ting wang[17], [1]Department of Rheumatology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Beijing, China (People's Republic), [2]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China (People's Republic), [3]The First Affiliated Hospital Of Zhengzhou University, zhengzhou, China (People's Republic), [4]Puyang Olifield General Hospital, puyang, Henan, China (People's Republic), [5]Binzhou Medical University Hospital, binzhou, Shandong, China (People's Republic), [6]Nanjing Drum Tower Hospital, NANJING, China (People's Republic), [7]Jinhua Municipal Central Hospital, Jinhua, China (People's Republic), [8]The First Affiliated Hospital of Xiamen University, xiamen, Fujian, China (People's Republic), [9]Hospital of Traditional Chinese Medicine of Zhongshan, 中山, Guangdong, China (People's Republic), [10]The First People's Hospital of Foshan, foshan, Guangdong, China (People's Republic), [11]Shanxi Bethune Hosptial, Taiyuan, China (People's Republic), [12]The First

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Affiliated Hospital of soochow University, Suzhou, China (People's Republic), [13]The Second Affiliated Hospital of Fujian Medical University, quanzhou, Fujian, China (People's Republic), [14]The First Hospital of Hebei Medical University, shijiazhuang, Hebei, China (People's Republic), [15]Xuanwu Hospital, Capital Medical University, beijing, Beijing, China (People's Republic), [16]Qyuns Therapeutics Co., Ltd., Shanghai, Shanghai, China (People's Republic), [17]Qyuns Therapeutics CO., Ltd., Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Therapies (0873–0878)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: QX002N is a novel high-affinity monoclonal antibody (mAb) that selectively targets IL-17A.

In the phase II clinical study, QX002N was well tolerated and rapidly reduced symptoms and signs of active radiographic axial spondyloarthritis (r-axSpA) compared with placebo.

We conducted the phase III pivotal study to confirm the efficacy and safety of QX002N in r-axSpA patients. A pre-planned primary analysis was performed after all patients completed week 16. Here, we report the primary analysis results of the study. Results of exploratory radiographic endpoints at 16 weeks are also presented, which are measured by the Spondyloarthritis Research Consortium of Canada (SPARCC) Magnetic Resonance Imaging (MRI) index, an objective and quantifiable variable to assess the post-treatment inflammation changes of the Sacroiliac Joints (SIJ) and the spine.

Methods: This is a multicenter, phase III, randomized, double-blind, placebo-controlled, parallel-group study. Adults with active r-axSpA were randomized 1:1 to receive 160 mg subcutaneous QX002N every 4 weeks (Q4W) or placebo. At week 16, all patients received 160mg QX002N Q4W through week 52. The primary endpoint was the proportion of participants reaching the standard of the Assessment in SpondylArthritis International Society (ASAS) 40 at week 16. The key secondary endpoint was the proportion of participants achieving ASAS20 at week 16. The exploratory endpoints included changes from baseline in SIJ and spinal SPARCC Scores at Week 16 in patients with evaluable MRI at baseline and week 16(MRI completers).

Results: A total of 641 r-axSpA patients were randomized to receive 160mg QX002N Q4W (n=322) and placebo (n = 319). Baseline characteristics were similar between treatment groups (Table 1).

Statistically significant improvements in disease activity, function, quality of life, spinal and SIJ MRI–evident inflammation were observed after 16 weeks of QX002N treatment versus placebo (Figure 1). At week 16, significantly higher proportions of QX002N patients (40.4%; P<0.0001) had achieved an ASAS40 response versus the placebo group (18.9%) (Figure 1A). Similarly, ASAS20 response rate (65.2% vs 41.3%) and other secondary endpoints all favoured QX002N versus placebo at

Table 1. Baseline characteristics.

Characteristics	QX002N N=322	PBO N=319
Age, years	33.2 (8.66)	34.2 (8.30)
Male, n (%)	260 (80.7%)	276 (86.5%)
BMI , kg/m2	24.63 (4.085)	24.73 (4.209)
Age at diagnosis	24.92 (7.446)	24.49 (7.272)
Disease duration (AS)	8.28 (6.357)	9.66 (7.405)
Prior anti-TNF therapy	66 (20.5%)	65 (20.4%)
SIJ SPARCC score¶	18.2 (16.59)	14.8 (15.76)
Spine SPARCC score¶	19.7 (19.43)	19.3 (22.13)

¶ Data were available for the magnetic resonance imaging (MRI) subclean population only. (N = 98 for the placebo group, N = 100 for the QX002N group).
Continuous parameters are presented as mean (+/-SD) unless otherwise noted. Categorical variables are presented as n(%).
Abbreviations: PBO, Placebo; BMI, Body mass index; AS , Ankylosing spondylitis; TNF, Tumor Necrosis Factor; SIJ, Sacroiliac joint; SPARCC, the Spondyloarthritis Research Consortium of Canada.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

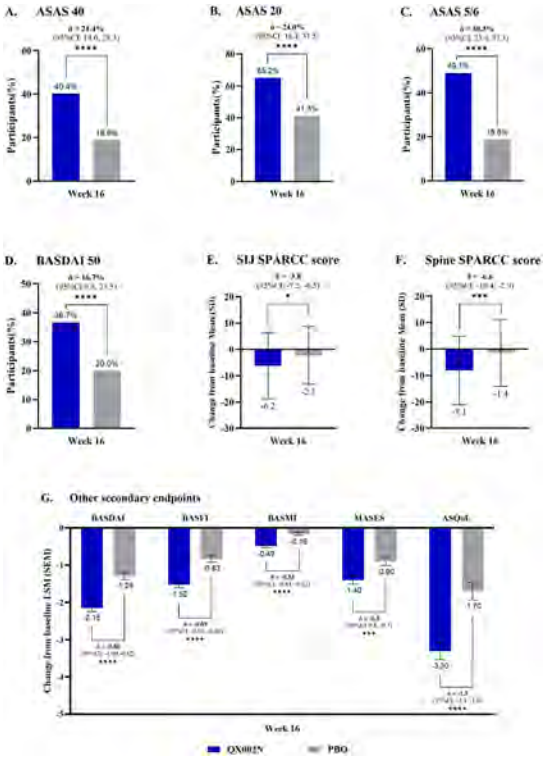


Figure 1. Efficacy outcomes. SPARCC SIJ and spine scores reported for only patients in MRI sub-study. MRI SPARCC SIJ and spine inflammation scores range from 0 to 72 and from 0 to 108, separately. Lower scores indicate less SIJ/spinal inflammation and negative changes represent improvements. Abbreviations: *: p value ≤0.05; ***: p value ≤0.001; ****: p value ≤0.0001; 95%CI: 95% confidence intervals; δ: difference between treatment groups; AS, ankylosing spondylitis; ASAS: Assessment of Spondylarthritis international Society; ASAS40: ASAS 40% response; ASAS20: ASAS 20% response; ASAS5/6: ASAS 5/6 response; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; SIJ: Sacroiliac joint; SPARCC: the Spondyloarthritis Research Consortium of Canada; BASFI: Bath Ankylosing Spondylitis Function Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; MASES: the Maastricht Ankylosing Spondylitis Enthesitis Score; ASQoL, Ankylosing Spondylitis Quality of Life; SD: standard deviation; LSM: Least Squares Means; SEM: Standard Error of the Mean.

Table 2. Safety profile.

	QX002N N=322	PBO N=319
Exposure, days	113.5 (5,74)	111.4 (11.59)
TEAE	244 (75.8%)	227 (71.2%)
CTCAE Grade 1	126 (39.1%)	126 (39.5%)
CTCAE Grade 2	101 (31.4%)	91 (28.5%)
CTCAE Grade ≥ 3	17 (5.3%)	10 (3.1%)
Discontinuation due to AE	4 (1.2%)	3 (0.9%)
SAE	7 (2.2%)	3 (0.9%)
Death	0	0
AESI	10 (3.1%)	4 (1.3%)
Infections	9 (2.8%)	4 (1.2%)
Upper respiratory tract infection	3 (0.9%)	2 (0.6%)
Infectious pneumonia	1 (0.3%)	1 (0.3%)
Cystitis	1 (0.3%)	0
Tonsillitis	1 (0.3%)	0
Febrile infection	1 (0.3%)	0
Pelvic infection	1 (0.3%)	0
Bacterial tonsillitis	1 (0.3%)	0
Bacterial pneumonia	1 (0.3%)	0
Influenza-like illness	0	1 (0.3%)
Inflammatory Bowel Disease	0	2 (0.6%)
Crohn's disease	0	1 (0.3%)
Ulcerative colitis	0	1 (0.3%)
Grade 3 or 4 neutropenia	3 (0.9%)	0
MACE	0	1 (0.3%)
Acute myocardial infarction	0	1 (0.3%)
Hepatic events	0	0
Malignance	0	0

Abbreviation: PBO, Placebo; TEAE: Treatment-emergent adverse events ; CTCAE: Common Terminology Criteria for Adverse Events; AE: Adverse Events ; SAE: Serious Adverse Events; AESI: Adverse Events of Special Interest; MACE: Major Adverse Cerebrocardiovascular events.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

week 16 (Figure 1B-D,G). For the MRI sub-study, 30.9% (198/641) and 30.6% (196/641) of the patients had SPARCC SIJ and spine assessments respectively. Rapid reduction from baseline to Week 16 in mean SPARCC SIJ score (QX002N:–6.2 , PBO: –2.3 ; P=0.0262; Figure 1E) and mean SPARCC spine score (QX002N: –8.1, PBO: –1.4; P=0.0005; Figure 1F) were observed.

The overall incidence of Treatment-emergent adverse events (75.8% vs. 71.2%) were comparable in patients receiving QX002N and placebo. Serious adverse events were reported in 2.2% and 0.9% of patients in the QX002N and placebo groups, respectively. The majority of TEAEs were categorized as CTCAE (Version 5.0) Grade 1 or 2 (Table 2).

Conclusion: QX002N provided significant improvements in the symptoms and signs, as well as marked reduction in inflammation of the spinal and SIJ as measured by MRI in r-axSpA patients, when compared to placebo at week 16. The safety of QX002N was tolerable.

Disclosure: X. Zeng: None; **S. Zhang**: None; **S. LIU**: None; **F. Li**: None; **x. wang**: None; **L. SUN**: None; **H. Du**: None; **G. Shi**: None; **y. li**: None; **h. zhang**: None; **L. Zhang**: None; **J. Wu**: None; **m. zhou**: None; **z. gu**: None; **y. zhao**: None; **m. fang**: Qyuns Therapeutics Co., Ltd., 3; **Q. Song**: Qyuns Therapeutics Co., Ltd., 3; **t. wang**: Qyuns Therapeutics Co., Ltd., 3.

Abstract Number: 0877

Therapeutic Approach in Patients with Arthralgia at Risk of Progression to Psoriatic Arthritis.

Rodrigo García Salinas[1], Gisel Reyes-Jara[2], Felicia Almada[3], Juan Arguello[2] and Sebastian Magri[4], [1]Hospital Italiano La Plata, La Plata, Argentina, [2]Hospital Italiano de La Plata, La Plata, Argentina, [3]Hospital Italiano de La Plata, La Plara, Argentina, [4]Hospital Italiano La Plata, Melchor Romero, Argentina

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Therapies (0873–0878)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: The transition from psoriasis (Pso) to psoriatic arthritis (PsA) presents an opportunity for early intervention and preventive strategies in high-risk patients with arthralgia. Objectives: To estimate the frequency of treatment initiation in patients with arthralgia at risk of progression to PsA (ARP-PsA), compare characteristics between treated and untreated groups, and analyze progression to PsA after one year.

Methods: A prospective cohort study included patients >18 years with arthralgia and no prior PsA diagnosis. Baseline assessments included laboratory tests, radiography, ultrasound, and clinical evaluation (reuma-check). Data on demographics, joint count, global VAS, HAQ, Pso, and family history (FH) were collected. ARP-PsA was defined as arthralgia + Pso and/or FH. Treatment initiation with NSAIDs and/or DMARDs was evaluated, as well as progression to PsA after one year, based on our previous published research (1). High-risk factors (Pso >15 years, Pso + FH, ultrasound synovitis/enthesopathy) were assessed. Statistical tests included, descriptive analisis, chi-squared, Fisher's exact, Student's t-test, and Mann-Whitney.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of ARP-PsA Patients Based on Treatment Initiation

Characteristic	Treated (n=52)	Untreated (n=67)	p
Female (%)	72	73	0.9
Age (SD)	49 (14)	48 (15)	0.8
Comorbidities (%)	60	65	0.5
Years of education (SD)	14 (3)	13 (2)	0.6
Psoriasis (%)	60	24	0.001
Smoking (%)	35	40	0.5
Symptoms <1 year (%)	35	31	0.7
Painful joints (SD)	3 (2.5)	3 (2.2)	0.7
VAS patient (mm, SD)	55 (22)	51 (20)	0.3
CRP+ (%)	21	26	0.6
HAQ (0-3, SD)	0.5 (0.4)	1.9 (9)	0.2
Erosions on X-ray (%)	13	7	0.6
Joint space narrowing (%)	22	24	0.8
Tenosynovitis on US (%)	4	13	0.09
Synovitis on US (%)	10	10	0.98
Power Doppler on US (%)	4	3	0.8
Enthesitis US (%)	23	16	0.4
Diagnostic delay (months, SD)	30 (45)	24 (24)	0.3

Results: Of 1419 patients with arthralgia, 8.4% (n=119) met ARP-PsA criteria. Among them, 41% initiated treatment: NSAIDs in 22%, DMARDs in 21% (56% methotrexate), and corticosteroids in 4%. Treated patients more frequently had psoriasis (60% vs. 24%, p=0.001), while other demographic, clinical, imaging, and laboratory variables showed no significant differences (Table 1). At one-year follow-up, 29% (n=34) progressed from arthralgia to clinically classified PsA, and 62% of them had received treatment (35% NSAIDs, 26% DMARDs) (Figure 1). Among those meeting at least one high-risk criterion (36% of ARP-PsA), 65% were treated.

Conclusion: In ARP-PsA patients, 41% initiated treatment, with psoriasis being the key differentiating factor. Of those progressing to PsA, 62% were under treatment, highlighting the importance of early therapeutic intervention, particularly in patients with high-risk features.

Figure 1: Reumacheck circuit

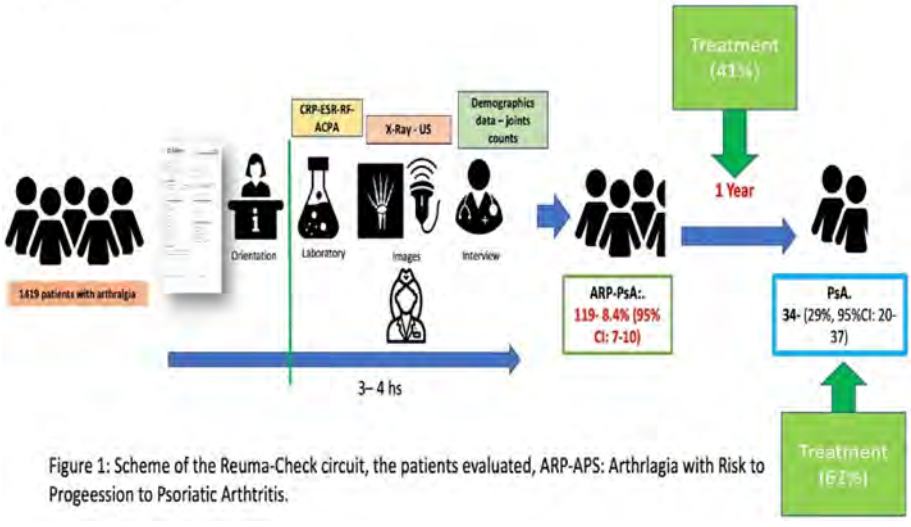


Figure 1: Scheme of the Reuma-Check circuit, the patients evaluated, ARP-APS: Arthrlagia with Risk to Progeession to Psoriatic Arthtritis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Bibliography

(1) Rodrigo GS, Sebastian M, Jonatan M, Rosario J, Ronald P, Santiago R, Xenofon B. Arthralgia with risk of progression to psoriatic arthritis: role of clinical assessments and ultrasound as prognostic factors. Rheumatology (Oxford). 2024 Oct 15: keae562. doi: 10.1093/rheumatology/keae562. Epub ahead of print. PMID: 39404885.

Disclosure: R. García Salinas: AbbVie/Abbott, 2, 5, 6, Adium, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Raffo, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **G. Reyes-Jara**: None; **F. Almada**: None; **J. Arguello**: None; **S. Magri**: None.

Abstract Number: 0878

Effects of IL-17A Inhibition on Entheseal Osteoblast and Fibroblast Dynamics in Psoriatic Arthritis: Insights from the EBIO Biopsy Study

Maria Gabriella Raimondo[1], Hashem Mohammadian[2], Simon Rauber[3], Stefano Alivernini[4], Filippo Fagni[5], Giulia Corte[6], Koray Tascilar[7], Alina Mihaela Ramming[8], Juergen Rech[2], Maria Antonietta D´Agostino[9], Georg Schett[2], Milena Pachowsky[8], Arnd Kleyer[10] and **Andreas Ramming**[11], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [3]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Bayern, Germany, [4]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [5]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Bayern, Germany, [6]- Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [7]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [8]Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [9]4Division of Rheumatology - Fondazione Policlinico Universitario A. Gemelli IRCCS - Università Cattolica del Sacro Cuore, Rome, Italy, [10]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [11]Department of Internal Medicine 3, Rheumatology & Immunology, Friedrich-Alexander-University (FAU) & Universitätsklinikum Erlangen, Erlangen, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Therapies (0873–0878)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Enthesitis is an early event in the course of psoriatic arthritis (PsA) and a hallmark feature of the disease. Currently, much of the understanding of enthesitis relies on clinical assessment and imaging techniques such as MRI and ultrasound, which complicates detailed molecular analysis due to the difficulty in acquiring high-quality entheseal tissues. Previous pre-clinical studies and surgical data indicate that interleukin-17 (IL-17) plays a pivotal role in the pathogenesis of enthesitis, supported by the efficacy of IL-17 blockers in clinical settings. However, molecular insights on how IL-17 blockade affects enthesitis in humans remain limited. This study aims to investigate the immune and non-immune compartments in active enthesitis of PsA patients and their alterations following IL-17A inhibition.

Methods: We performed minimally invasive ultrasound-guided biopsies of the lateral epicondyle on ten biologic-naïve PsA patients with active elbow enthesitis before and after six months of treatment with secukinumab. One patient did not undergo the second biopsy. Tissue samples underwent conventional histological staining, second harmonic generation (SHG) for morphological assessment, Hyperion imaging mass cytometry (IMC) for protein expression, scRNAseq and GeoMx spatial transcriptomic technology for RNA expression analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Eleven patients with active psoriatic arthritis (PsA) and lateral epicondyle enthesitis were screened, resulting in ten enrollments, where 40% were female. The mean Disease Activity in Psoriatic Arthritis (DAPSA) score at screening was 22.8 ± 12.6, indicating moderate disease activity, with an average of 9.6 ± 6.8 tender joints and a SPARCC entheseal score of 4.30 ± 2.75. Nine patients had previously failed conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs). Following treatment with secukinumab, PD signals significantly decreased six months later (P = 0.0156), and notable improvements were observed in DAPSA (11.8 ± 10.5; P = 0.0078) and SPARCC scores (1.4 ± 2.5; P = 0.0039). Adverse events were mild and managed well. Total IL-17A+ cell counts decreased substantially, contributing to the therapeutic response as assessed by Imaging mass cytometry. Spatial transcriptomics highlighted a significant shift towards DKK3 and CD200 positive fibroblasts following IL-17A inhibition, indicating a transition to a pro-resolving phenotype in the entheseal tissue. Furthermore, pathways related to osteoblast differentiation were significantly reduced upon treatment with secukinumab, indicating a decreased transcriptional activity associated with osteoblasts post-treatment.

Conclusion: Here we show a full picture of cellular changes in the microarchitecture of inflamed entheses upon anti-IL-17A treatment. Resolving entheseal inflammation is not only associated with reduction of IL-17-producing cells but also with DKK3/CD200+ fibroblast / ILC2 activation and osteoblast control.

Disclosure: M. Raimondo: UCB, 6; **H. Mohammadian**: None; **S. Rauber**: None; **S. Alivernini**: None; **F. Fagni**: None; **G. Corte**: None; **K. Tascilar**: None; **A. Ramming**: None; **J. Rech**: AbbVie, 6, 12, Received consulting fees, Biogen, 6, 12, Received consulting fees, Bristol-Myers Squibb(BMS), 6, 12, Received consulting fees, Chugai, 6, 12, Received consulting fees, Eli Lilly, 6, 12, Received consulting fees, GlaxoSmithKlein(GSK), 6, 12, Received consulting fees, Janssen, 6, 12, Received consulting fees, MSD, 6, 12, Consulting fees, Novartis, Sobi, 1, 2, 5, 6, Roche, 6, 12, Received consulting fees, Sanofi, 6, 12, Received consulting fees, Sobi, 6, 12, Received consulting fees, UCB, 6, 12, Received consulting fees; **M. D´Agostino**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **M. Pachowsky**: None; **A. Kleyer**: AbbVie/Abbott, 1, 6, Alfasigma, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, 6, Gilead, 1, Janssen, 1, 6, Novartis, 1, 6, UCB, 1, 6; **A. Ramming**: Boehringer-Ingelheim, 2, Johnson & Johnson, 2, MoonLake Immunotherapeutics AG, 2, 5, Novartis Pharma GmbH, 2, UCB, 2.

Abstract Number: 0879

Trajectories and risk factors of interstitial lung disease in limited cutaneous systemic sclerosis from the EUSTAR cohort

Antonio Tonutti[1], Francesca Motta[1], Silvia Bellando Randone[2], Nicoletta Del Papa[3], Elisabetta Zanatta[4], Marie-Elise Truchetet[5], Christina Bergmann[6], Gábor Kumánovics[7], Monique Hinchcliff[8], Yasser El Miedany[9], Britta Maurer[10], Marie Vanthuyne[11], Lijun Zhang[12], Nune Manukyan[13], Carlo Selmi[14], Maria De Santis[1] and EUSTAR Study Group, [1]Humanitas University, Pieve Emanuele, Italy, [2]University of Florence, Florence, Italy, [3]ASST Pini CTO, Milano, Milan, Italy, [4]University of Padua, Padova, Italy, [5]University of Bordeaux, Bordeaux, France, [6]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [7]University of Pecs, Pecs, Hungary, [8]Yale School of Medicine, Westport, CT, [9]Egyptian Society for Microcirculation in Rheumatic Diseases, Cairo, Egypt, [10]Department of Rheumatology & Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [11]Université Catholique de Louvain, Bruxelles, Belgium, [12]The University of Hong Kong-Shenzhen Hospital, Shenzhen, China (People's Republic), [13]Mikaelyan Institute Of Surgery, Yerevan, Armenia, [14]Humanitas University, Milan, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical II (0879–0884)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Interstitial lung disease (ILD) is traditionally associated with the diffuse subset of systemic sclerosis (dcSSc) but may be observed in limited SSc (lcSSc), with features not clearly defined, but antiScl-70. This study aims to characterize risk factors and prognosis of lcSSc-ILD within the EUSTAR cohort.

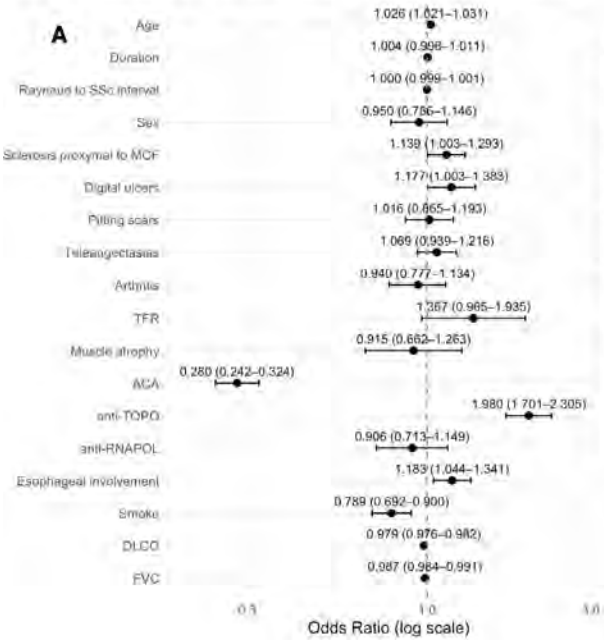
Methods: We performed the CP175 retrospective study including patients in EUSTAR up to February 2025 and arrayed according to skin subset and presence/absence of ILD at chest HRCT at enrollment (baseline). Disease features were analyzed for risk factors and survival of lcSSc patients with: (i) ILD at baseline (multivariable logistic regression), (ii) incident ILD during follow-up (Cox proportional hazards models), and (iii) progressive ILD (Hoffmann-Vold, 2021).

Results: Baseline HRCT was available in 5953/8153 (73%) lcSSc cases (vs 3248/3974 [81%] dcSSc; $p < 0.001$), more frequently with coexisting anti-Scl70 (OR 1.5, CI 1.3–1.8), lower FVC and DLCO (OR 0.99 both), but less frequently with serum ACA (OR 0.7, CI 0.6–0.8).

At baseline (Fig 1A), 36% (2127/5953) lcSSc patients had ILD, in association with older age (OR 1.03, CI 1.02–1.03), digital ulcers (OR 1.18, CI 1.00–1.38), skin thickening proximal to metacarpophalangeal (MCP) joints (OR 1.14, CI 1.01–1.29), esophageal involvement (OR 1.18, CI 1.04–1.34), anti-Scl70 (OR 1.98, CI 1.7–2.3), lower FVC (OR 0.99, CI 0.98–0.99) and lower DLCO (OR 0.98, CI 0.97–0.98). Serum ACA were protective (OR 0.28, CI 0.24–0.32), also in anti-Scl70+ or anti-RNAPOL+ lcSSc (OR 0.3, CI 0.2–0.4). Among ACA+ lcSSc cases, skin fibrosis proximal to MCP (OR 1.3, CI 1.03–1.6) and concurrent anti-Scl70 (OR 2.4, CI 1.7–3.4) were risk factors for ILD. Among anti-Scl70+ lcSSc patients, digital ulcers increased ILD risk (OR 1.5, CI 1.1–2.0). In lcSSc, ILD extension >20% (19% vs 31%) and honeycombing (14% vs 22%) were less frequent with ACA, honeycombing more with anti-Scl70 (23% vs 16%) (Fig 1B).

Among 3826 lcSSc cases without ILD at baseline, 443 developed it during follow-up (incidence rate 6% person-years) and the incidence was highest with anti-Scl70 (14% person-years) and lowest with ACA (4% person-years). Incident ILD was independently associated with age (HR 1.03, CI 1.02–1.04), male sex (HR 1.4, CI 1.1–1.9), anti-Scl70 (HR 1.7, CI 1.3–2.1), lower FVC and DLCO (HR 0.99 for both); telangiectasias (HR 0.6, CI 0.5–0.8) and ACA (HR 0.4, CI 0.4–0.6) were protective (Fig 2).

Figure 1. (A) Risk factors for ILD at baseline in lcSSc. (B) Radiological and functional features of patients with lcSSc and ILD at baseline, according to the autoantibody status.



B

Variable	ACA+	ACA-	p (ACA)	Scl70+	Scl70	p (Scl70)
ILD > 20% at HRCT	36/193 (18.7%)	125/405 (30.9%)	.002	80/264 (30.3%)	86/339 (25.4%)	0.210
Ground glass opacity	241/494 (48.8%)	691/1103 (62.6%)	<.001	478/742 (64.4%)	484/901 (53.7%)	<.001
Honeycombing	45/320 (14.1%)	164/731 (22.4%)	0.002	116/499 (23.2%)	96/586 (16.4%)	0.006
Reticular pattern	177/298 (59.4%)	428/658 (65.0%)	0.108	300/459 (65.4%)	321/521 (61.6%)	0.251
Traction bronchiectasis	22/60 (36.7%)	86/138 (62.3%)	0.002	78/133 (58.6%)	32/74 (43.2%)	0.047
DLCO (%predicted)	63 [50–76] [n=447]	61 [47–75] [n=1064]	0.077	62 [48–77] [n=708]	62 [48–74] [n=833]	0.168
FVC (%predicted)	97.8 (22.8) [n=1628]	85.6 (21.4) [n=1628]	<.001	86 [72–99] [n=757]	92 [75–109] [n=903]	<.001
TLC (%predicted)	96 [84–107] [n=351]	84 [70–99] [n=800]	<.001	86 [71–97] [n=533]	92 [74–104] [n=638]	<.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. (A) 10-year incidence of ILD in patients with lcSSc vs dcSSc. (B) Incidence of ILD in lcSSc according to autoantibodies (CTPneg if all ACA, Scl70, and RNAPOL neg); p-value of Log-rank test. (C) Risk factors for incident ILD.

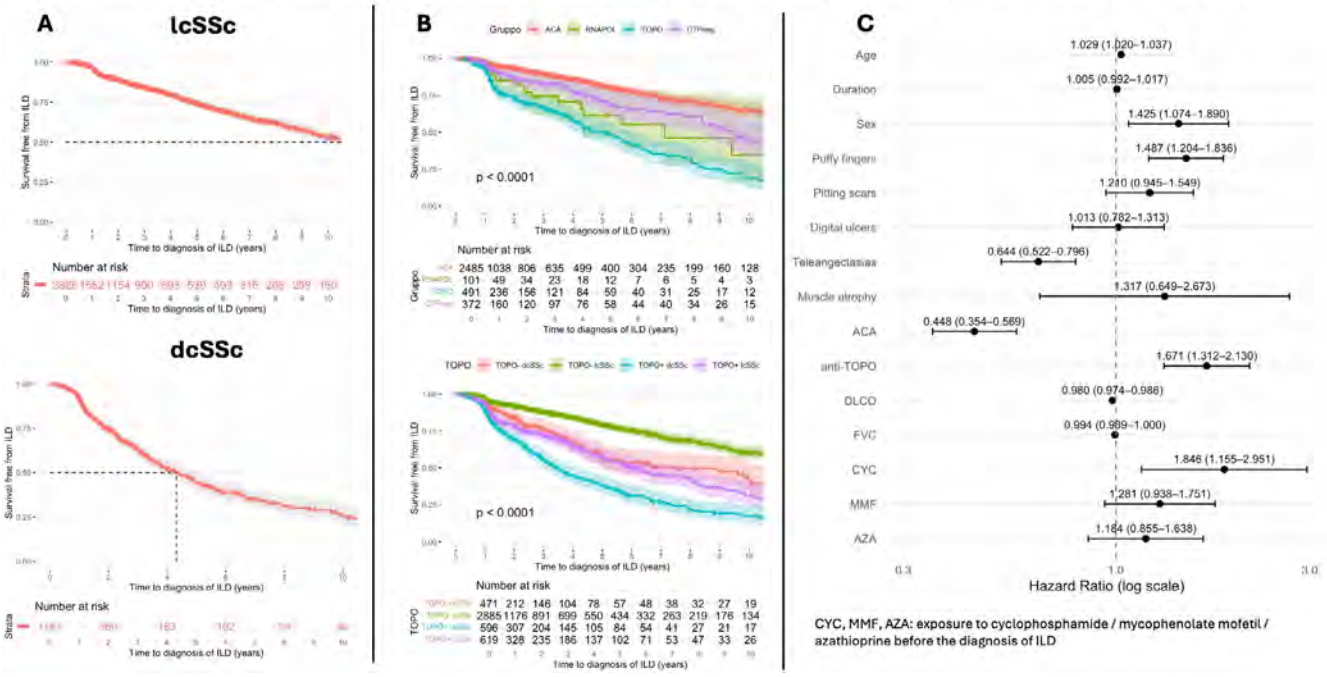
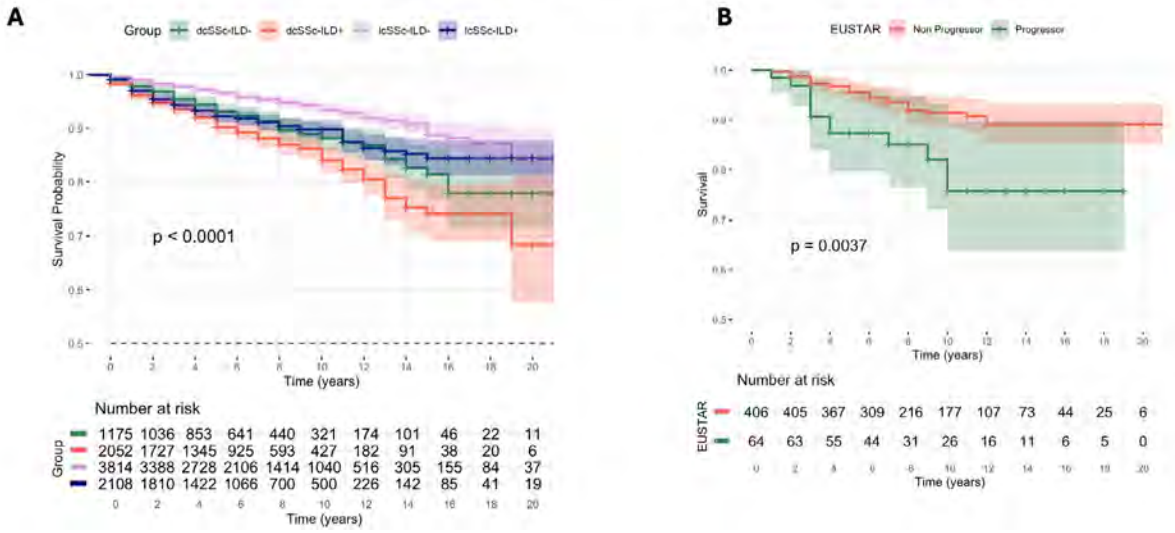


Figure 3. (A) Survival of patients with SSc depending on skin subset and presence of ILD. (B) Survival of patients with lcSSc and ILD, depending on progression vs. non-progression of pulmonary disease, according to the EUSTAR definition (Hoffmann-Vold AM, Ann Rheum Dis, 2021). P-values of Log-rank test are reported.



Of 472 ILD patients with available follow-up data, 64 (14%) met the criteria for ILD progression within the first year. ILD significantly reduced survival in lcSSc, though to a lesser extent than in dcSSc. Patients with progressive ILD had significantly worse survival compared to non-progressors (Fig 3).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: ILD is found in 36% of lcSSc patients, with a 6% person-years subsequent incidence rate. ILD in lcSSc carries a poor prognosis and may progress over time. Peculiar risk factors can aid stratify patient risk, and early identification is crucial for establishing proper treatment. This study supports the inclusion of patients with lcSSc-ILD in therapeutic trials and underscores the need for risk-adapted ILD monitoring protocols and multidisciplinary care in this subgroup.

Disclosure: A. Tonutti: None; **F. Motta**: None; **S. Bellando Randone**: Boehringer-Ingelheim, 2, 6; **N. Del Papa**: None; **E. Zanatta**: None; **M. Truchetet**: None; **C. Bergmann**: Kyverna Therapeutics, Inc., 5; **G. Kumánovics**: None; **M. Hinchcliff**: AbbVie/Abbott, Boehringer Ingelheim, Kadmon, 2, 5; **Y. El Miedany**: None; **B. Maurer**: AbbVie/Abbott, 5, Actelion, 12, Congress support, Boehringer-Ingelheim, 1, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Medtalk, 12, Congress support, Mepha, 12, Congress support, Merck/MSD, 12, Congress support, Novartis, 2, 5, 6, Otsuka, 6, Pfizer, 12, Congress support, Protogen, 5, Roche, 12, Congress support, UCB, 12, Congress support; **M. Vanthuyne**: None; **L. Zhang**: None; **N. Manukyan**: None; **C. Selmi**: AbbVie, 2, 5, 6, Alfa-Wassermann, 2, 6, Amgen, 2, 5, 6, Biogen, 2, 6, Eli Lilly, 2, 6, EUSA, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 5, SOBI, 2, 6; **M. De Santis**: Boehringer-Ingelheim, 2, 6.

Abstract Number: 0880

Detecting Interstitial Lung Disease and Identifying Extensive Disease on Chest Computed Tomography in Patients with Systemic Sclerosis: Cut-Offs for Lung Texture Analysis and its Prognostic Implications

Nicholas landini[1], lisa Jungblut[2], cecilia strappa[3], Christian Blüthgen[2], Rucsandra Dobrota[4], Muriel Elhai[5], Carina Mihai[6], Sinziana Muraru-Carbune[2], Martina Orlandi[7], mariaelena Occhipinti[8], Khadija El-Aoufy[9], Gemma Lepri[10], valeria panebianco[11], anna rita larici[3], Anna-Maria Hoffmann-Vold[12], Cosimo Nardi[13], Serena Guiducci[14], Silvia Bellando-Randone[15], Marco Matucci-Cerinic[16], Thomas Frauenfelder[2], Oliver Distler[17] and **Cosimo Bruni**[18], [1]Department of Radiological Sciences, Oncology and Pathology, "Sapienza" University, Policlinico Umberto I, Rome, Italy. Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Rueil Malmaison, France, [2]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, zurich, Switzerland, [3]Advanced Radiology Center, Department of Diagnostic Imaging and Oncological Radiotherapy, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy, rome, Italy, [4]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [5]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, Schlieren, Switzerland, [6]University Hospital Zurich, University of Zurich, Zurich, Switzerland, [7]Rheumatology Unit, Department of Medical and Surgical Sciences for Children and Adults, University Hospital of Modena and Reggio Emilia School of Medicine, Italy., modena, Italy, [8]Division of Radiology, Fondazione Toscana Gabriele Monasterio, Pisa, Italy., pisa, Italy, [9]Department of Health Science, University of Florence, Florence, Italy., firenze, Italy, [10]Department of Experimental and Clinical Medicine, University of Florence, Division of Rheumatology Scleroderma Unit, AOU Careggi Hospital, Florence, Italy., Florence, Italy, [11]Department of Radiological Sciences, Oncology and Pathology, "Sapienza" University, Policlinico Umberto I, Rome, Italy., Rome, Italy, [12]Oslo University Hospital, Oslo, Norway, [13]Department of Experimental and Clinical Biomedical Sciences, Radiodiagnostic Unit n. 2, University of Florence - Azienda Ospedaliero-Universitaria Careggi, Florence, Italy, Florence, Italy, [14]Department of Experimental and Clinical Medicine, Scleroderma Unit, Division of Rheumatology, University of Florence, Azienda Ospedaliera Universitaria Careggi, Florence, Italy, Pistoia, Italy, [15]University of Florence, Florence, Florence, Italy, [16]University San Raffaele Milano, Milano, Milan, Italy, [17]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [18]University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical II (0879–0884)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Description of the study population, stratified into derivation and validation cohorts. ACA: anticentromere antibodies; ARA: anti-RNA polymerase 3 antibodies; ATA: anti-topoisomerase I antibodies; ATA: DLCO: diffusion capacity of the lung for carbon oxide; FVC: forced vital capacity; ILD: interstitial lung disease; IQR: interquartile range; PH: pulmonary hypertension; SD: standard deviation.

Parameters	ALL (n=664)	Derivation cohort (n=433)	Validation cohort (n=231)
Age [years, mean ± SD]	55 ± 14	55 ± 14	56 ± 14
Disease duration [years, median (IQR)]	6 (2-10)	5 (2-9)	7 (2-10)
Female sex [n (%)]	552 (83)	353 (81)	119 (86)
Smoking [ever, n (%)]	174 (26)	114 (26)	59 (25)
Diffuse skin subset [n (%)]	185 (28)	115 (27)	71 (31)
ACA [n (%)]	291 (43)	186 (43)	105 (45)
ATA [n (%)]	199 (30)	131 (30)	68 (29)
ARA [n (%)]	56 (8)	40 (9)	16 (7)
Digital ulcers [ever, n (%)]	181 (27)	123 (28)	58 (25)
Arthritis [ever, n (%)]	100 (15)	65 (15)	35 (15)
PH [ever, n (%)]	56 (8)	35 (8)	21 (9)
FVC% [mean ± SD]	96 ± 19	96 ± 19	95 ± 19
DLCO/SB% [mean ± SD]	72 ± 20	71 ± 20	73 ± 20
NYHA functional class > 2 [n (%)]	43 (6)	28 (6)	15 (6)
ILD on HRCT [n (%)]	313 (47)	207 (48)	106 (46)
Extensive ILD on HRCT [n (% of ILD+)]	33%	38%	25%
Total ILD on LTA Imbio Caliper [%, median (IQR)]	1.33 (0.48-6.56)	1.60 (0.50-7.17)	1.03 (0.46-5.08)

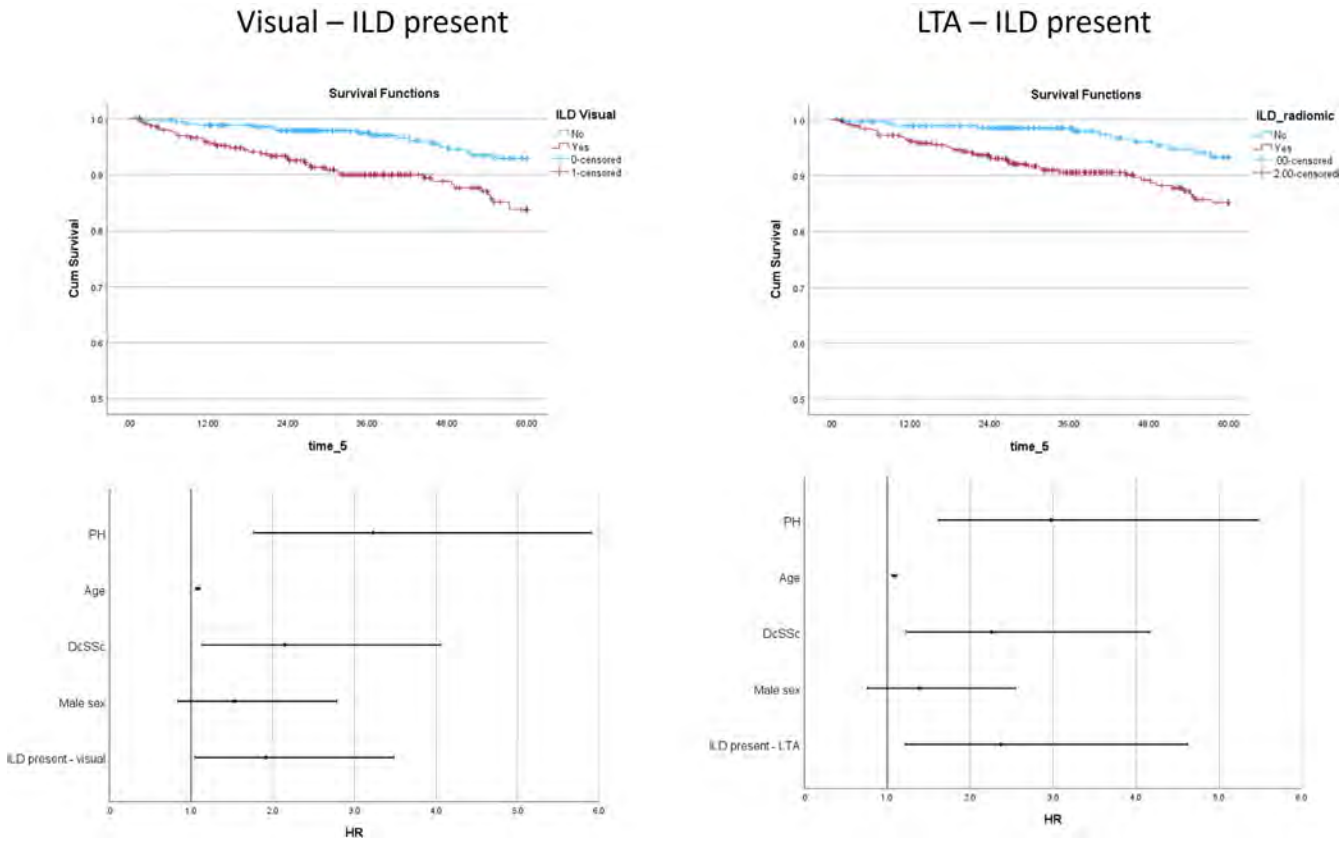


Figure 1. Prediction of mortality for interstitial lung disease identified through visual assessment vs. lung texture analysis. ILD: interstitial lung disease; HR: hazard ratio; LTA: lung texture analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

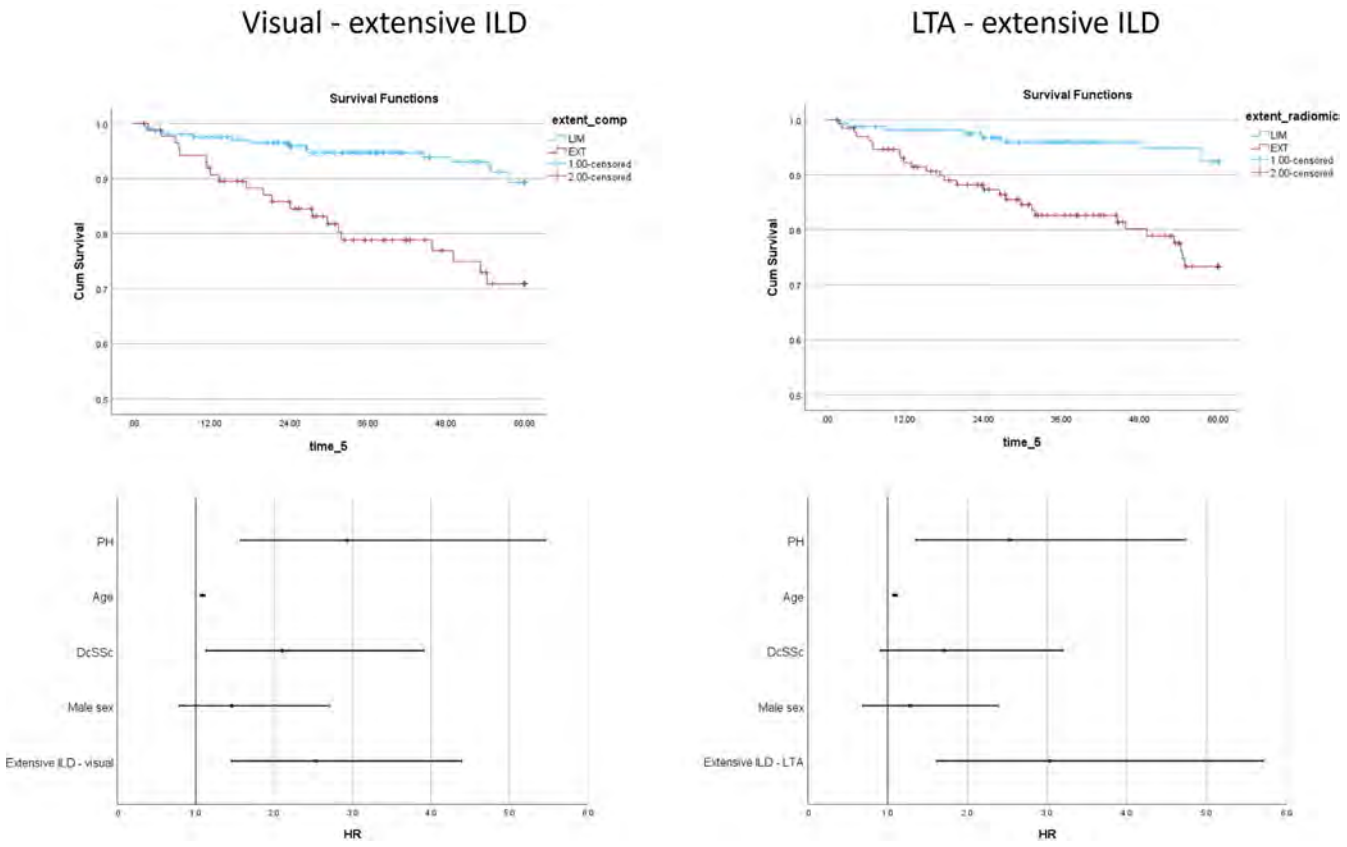


Figure 2. Prediction of mortality for extensive (EXT) versus limited (LIM) interstitial lung disease (ILD) identified through visual assessment vs. lung texture analysis (LTA). EXT: extensive disease; ILD: interstitial lung disease; HR: hazard ratio; LIM: limited disease; LTA: lung texture analysis; PH: pulmonary hypertension.

Background/Purpose: Interstitial lung disease (ILD) is a leading cause of death in patients with systemic sclerosis (SSc), especially in case of extensive disease detected on computed tomography (CT). Automated post-processing analysis software can compute the extent of ILD through lung texture analysis (LTA) of CT images. However, its use in clinical practice is limited by the lack of standardized thresholds.

The aim of our study was to identify and validate optimal thresholds of ILD extent quantified through LTA to detect the presence of ILD and to define extensive ILD in SSc patients.

Methods: SSc patients visiting two SSc referral center between 2005-2021, who underwent chest CT, were included. Technically suitable images (non-contrast, axial inspiratory acquisition, slice thickness and spacing ≤2 mm) were analyzed through LTA (Imbio), quantifying the percentage of lung volume occupied by total ILD (sum of ground glass, reticulation and honeycombing). Two radiologists blinded to the LTA data independently reviewed the CT scans to visually identify the presence of ILD and extensive ILD. The latter was defined as ILD involvement >20% of lung parenchyma or forced vital capacity < 70% predicted in case of indeterminate extent (Goh 2008). Disagreements were resolved by consensus, otherwise through a third reviewer. Patients were randomly split into derivation and validation cohorts using a 2:1 ratio. Receiver operating characteristic (ROC) curves with area under the curve (AUC) were computed to identify the optimal ILD extent threshold for detecting presence of ILD and, in patients with ILD, for identifying extensive disease, using the visual evaluation as the reference standard. Kaplan Meier curves and Cox regression analysis were performed to determine the impact of ILD and extensive disease on both visual and LTA assessments on mortality up to 5 years, the second adjusted for known mortality risk factors (age, sex, diffuse skin subset and pulmonary hypertension).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 664/1118 (58%) SSc patients were eligible for the study (Table 1). Visual analysis identified ILD in 313 (47%) cases, 103 (33%) showing extensive ILD. In the derivation cohort (433 patients, 206 ILD, 38% extensive), ROC analysis identified the optimal total ILD extent threshold for ILD detection at 1% (AUC 0.83) and at 7% for extensive ILD (AUC 0.84). In the validation cohort (231 subjects, 104 ILD, 25% extensive), these thresholds achieved 78% sensitivity / 71% specificity for ILD detection, and 81% sensitivity / 70% specificity for extensive ILD identification. Over median 5 years follow-up, 84 (13%) patients died [37 (12%) in the ILD group]. After adjustment for confounders, both ILD presence (Fig. 1) and extensive disease (Fig. 2) were independent risk factors for mortality, with comparable results by visual and LTA assessments.

Conclusion: Cutoffs for total ILD extent by LTA to detect ILD presence and identify extensive disease were derived and validated, with comparable performance to visual evaluation on negative prognostic impact. Our results lay the foundation for expanding the use of LTA post-processing in SSc-ILD towards automated diagnosis and prognostic stratification.

Disclosure: N. Iandini: None; **I. Jungblut**: None; **c. strappa**: None; **C. Blüthgen**: Promedical Foundation, 5, Swiss society of radiology, 5; **R. Dobrota**: Actelion, 5, 6, Amgen, 6, Boehringer-Ingelheim, 6, Iten-Kohaut, 5, Otsuka, 6, Pfizer, 5, Walter und Gertrud Siegenthaler Fellowship, 5; **M. Elhai**: AstraZeneca, 12, Congress support, Boehringer-Ingelheim, 6, FOREUM, 5, Iten Kohaut foundation, 5, Janssen, 12, Congress support, Kurt und Senta Herrmann foundation, 5, Novartis, 5, Pfizer, 5, University Zurich, 5; **C. Mihai**: Boehringer Ingelheim, 2, 12, congress support, Janssen, 2, MED Talks Switzerland, 6, Medbase, 6, MedTrix, 6, Mepha, 6, Novartis, 6, PlayToKnow, 6; **S. Muraru-Carbune**: AstraZeneca, 12, Congress support; **M. Orlandi**: None; **m. Occhipinti**: None; **K. El-Aoufy**: None; **G. Lepri**: None; **v. panebianco**: None; **a. larici**: None; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **C. Nardi**: None; **S. Guiducci**: None; **S. Bellando-Randone**: Boehringer-Ingelheim, 2, 6; **M. Matucci-Cerinic**: None; **T. Frauenfelder**: AstraZeneca, 2, Bayer, 6, Siemens, 6; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Bruni**: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5.

Abstract Number: 0881

Circulating Monocytes with High Interferon Signature as Precursors to Osteopontin Expressing Lung Macrophages in Patients with Systemic Sclerosis and Progressive Interstitial Lung Disease

Shu-Ju Lin[1], Kimberly Taylor[2], Shen Yang[3], Qinwei Chen[4], Shehani Alexander[1], Ye Cao[5], Takanori Sasaki[5], Deepak Rao[5], Nunzio Bottini[6], Francesco Boin[3] and Richard Ainsworth[4], [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]UC San Francisco, San Francisco, CA, [3]Cedars-Sinai Medical Center, Beverly Hills, CA, [4]Cedars Sinai Medical Center, Los Angeles, CA, [5]Brigham and Women's Hospital, Boston, MA, [6]Cedars Sinai Medical Center, Beverly Hills, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical II (0879–0884)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

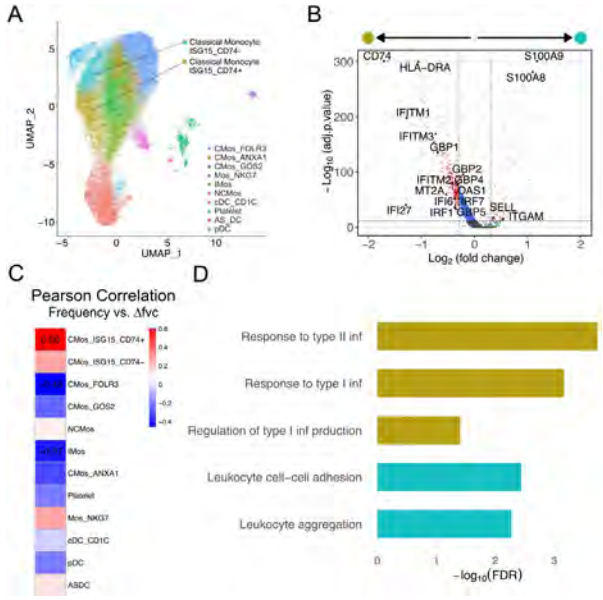


Fig. 1. A. UMAP of myeloid cells showing subclustering of monocyte cluster with type I IFN signature. B. Volcano plot of subcluster markers. C. Correlation of cluster frequencies with change in %fvc from baseline for SSc-ILD patients. D. Pathways for classical monocyte ISG15 subclusters.

Background/Purpose: Circulating monocytes with pro-inflammatory and pro-fibrotic phenotype have been implicated in SSc-ILD pathogenesis, but their potential trajectory to mature cell lineage macrophages driving organ-specific damage is not well defined.Evidence suggests that osteopontin expressing macrophages likely contribute to fibrotic mechanisms in SSc-ILD. We sought to characterize specific myeloid subpopulations associated with SSc-ILD progression and establish potential precursor relationships with lung macrophages.

Methods: Single-cell RNA-seq (scRNA-seq) was performed on peripheral blood obtained from 60 SSc patients meeting 2013 ACR/EULAR criteria. Unsupervised clustering identified two subpopulations of monocytes with type I interferon signatures. Differential expression and subtype correlation analyses against %change in forced vital capacity (FVC, liter) per year from baseline were conducted in subjects with SSc-ILD (n=40). Transcription factor (TF) analysis was conducted for progressive (>10% decrease in FVC) and non-progressive SSc-ILD patients. Reprocessed publicly available scRNA-seq data from SSc-ILD lungs were used to perform trajectory analysis.

Results: Clustering and annotation of myeloid cells identified 11 myeloid cell types and two subclusters ($CD74^+$ and $CD74^-$) of an "ISG15-hi" monocyte population expressing high levels of interferon (IFN)-inducible markers (Fig.1A). The $CD74^+$ subpopulation showed further enrichment for genes involved in "*Response to type I IFN signaling*" (FDR = 6.82×10^{-4}) whilst the $CD74^-$ subpopulation upregulated genes involved in "*Leukocyte cell-to-cell adhesion*" (FDR = 3.61×10^{-3}) (Fig.1B,D). Correlation analysis of cell type proportions against FVC %-change for SSc-ILD patients (Fig.1C) revealed a Pearson correlation

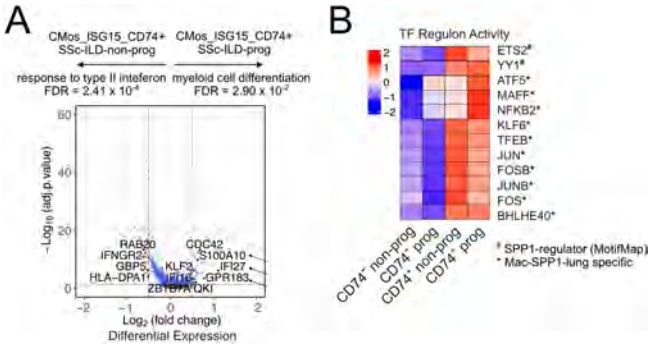


Fig. 2. A. Volcano plot for differential expression of progressive vs non-progressive SSc-ILD in CD74+ subpopulation. B. SCENIC TF analysis of subclusters split by disease progression.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

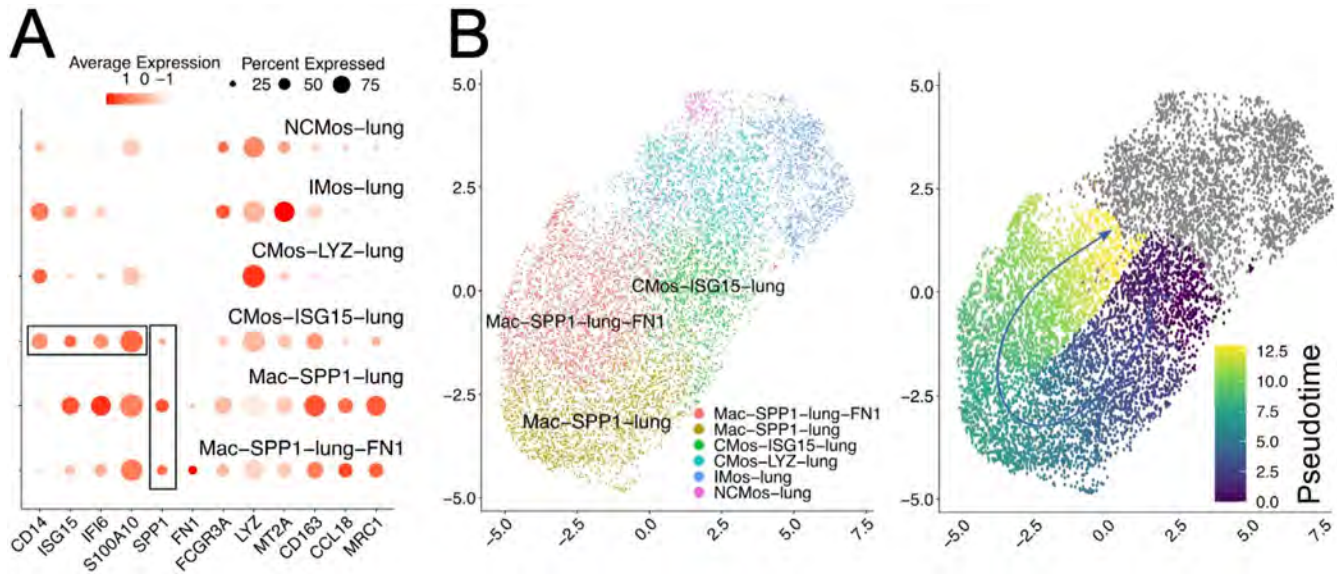


Fig. 3. A. DotPlot for markers of lung monocytes and osteopontin expressing macrophages. B. UMAP of clusters and trajectory analysis. Ref 1: Ann Rheum Dis. 2019 Aug 12;78(10):1379_1387

of 0.60 ($p=1.9x10^{-4}$) in the $CD74^+$ "ISG15-hi" monocyte population. In the $CD74^+$ subpopulation, progressive SSc-ILD patients upregulated genes involved in "*Myeloid differentiation*" (FDR = 2.90×10^{-2}) (Fig.2A) and further showed increased activity for TFs previously reported as specific regulators in osteopontin expressing lung macrophages (Mac-SPP1-lung) from SSc-ILD patients including ATF5 and MAFF (Fig.2B). A reanalysis of SSc-ILD lung scRNA-seq data identified a population of "ISG15-hi" classical monocytes CMos-ISG15-lung and the previously reported Mac-SPP1-lung (Fig.3A). Trajectory analysis predicted a differentiation trajectory from CMos-ISG15-lung to Mac-SPP1-lung (Fig. 3B).

Conclusion: We identified a novel $CD74^+$ subcluster within ISG15-high circulating monocytes, marked by strong type I IFN-inducible gene expression and significantly negatively associated with progressive SSc-ILD. This population may serve as a precursor to pro-fibrotic, osteopontin-expressing lung macrophages, suggesting a pathogenic role in SSc-ILD.

Disclosure: S. Lin: None; **K. Taylor**: None; **S. Yang**: None; **Q. Chen**: None; **S. Alexander**: None; **Y. Cao**: None; **T. Sasaki**: None; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFi-Bio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2; **N. Bottini**: Merck/MSD, 2; **F. Boin**: Adicet Bio, 2, Boehringer Ingelheim, 1, Janssen Pharmaceuticals, 6; **R. Ainsworth**: None.

Abstract Number: 0882

Serum KL-6 as a Predictive Biomarker for Interstitial Lung Disease Progression and Mortality in Systemic Sclerosis: A Prospective Cohort Study

Cristiana Sieiro[1], Jose Ordas Martínez[2], Sara Calleja Antolín[2], Juan Garcia Herrero[2], Javier De la Calle[2], Miriam Retuerto[2], Laura Sierra[2], Elena Bollo de Miguel[2] and Elvira Díez Álvarez[2], [1]Univrsity of Manchester, Manchester, United Kingdom, [2]Complejo Asistencial Universitario de León, León, Spain

SESSION INFORMATION

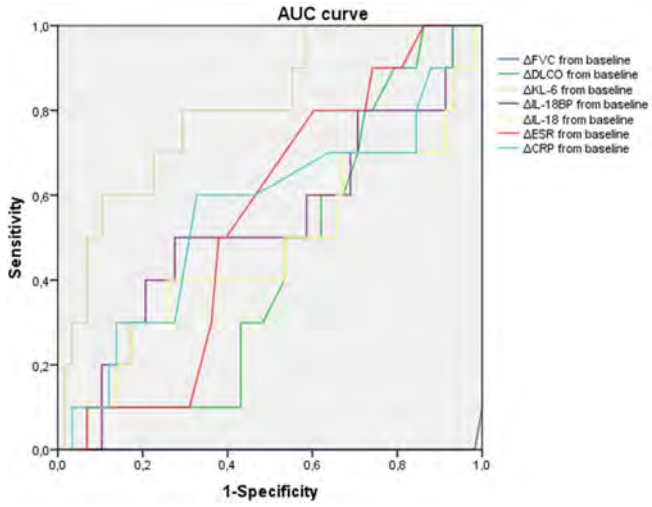
Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical II (0879–0884)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparison of the receiver operating characteristic curve of blood markers for predicting progressive ILD in patients with SSc; ROC curves: %FVC relative change from baseline; %DLCO relative change from baseline; KL-6 relative change from baseline; IL-18BP relative change from baseline; IL-18 relative change from baseline; ESR relative change from baseline; CRP relative change from baseline, AUC area under the curve.

Background/Purpose: Interstitial lung disease (ILD) is a leading cause of morbidity and mortality in systemic sclerosis (SSc). Early detection and continuous monitoring of ILD are critical for timely intervention and improved clinical outcomes. In recent years, serum biomarkers have gained recognition as potential non-invasive tools for evaluating ILD onset, progression, and prognosis. However, their clinical utility in SSc-ILD remains incompletely understood. This study aimed to evaluate the prognostic value of serum biomarkers—KL-6, IL-18, and IL-18 binding protein (IL-18BP)—for assessing ILD progression and mortality in SSc patients.

Methods: This prospective cohort study followed 74 SSc patients for 24 months. Patients were stratified based on the presence or absence of ILD using high-resolution computed tomography (HRCT). Clinical assessments, pulmonary function tests (PFTs), and serum biomarker levels (KL-6, IL-18, and IL-18BP) were measured. ILD progression was defined by changes in forced vital capacity (FVC). Relationships between biomarkers, lung function, and ILD severity were analyzed using Pearson's correlation. Receiver operating characteristic (ROC) curves determined optimal biomarker thresholds, while logistic regression identified predictors of ILD progression and mortality, accounting for potential confounders.

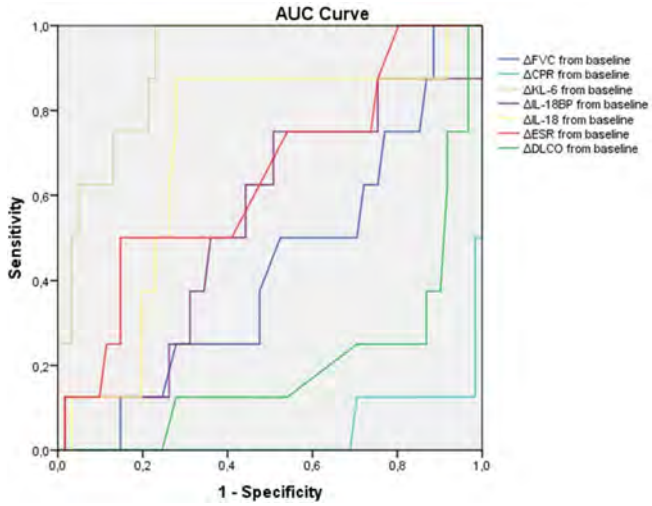


Fig 2. Comparison of the receiver operating characteristic curve of blood markers for predicting mortality in patients with SSc; ROC curves: %FVC relative change from baseline; %DLCO relative change from baseline; KL-6 relative change from baseline; IL-18BP relative change from baseline; IL-18 relative change from baseline; ESR relative change from baseline; CRP relative change from baseline, AUC area under the curve.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variable	Unadjusted analysis			Multivariable adjusted analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	5.32	1.32-7.56	0.58	-	-	-
Male sex	0.98	0.45-2.34	0.12	-	-	-
Anti-Scl70	2.24	2.05-5.15	**0.04**	1.98	1.04-3.24	**0.03**
Immunosuppressive treatment	0.21	0.14-0.87	**0.002**	0.27	0.16-0.92	**0.004**
GCs treatment	0.87	0.57-1.53	0.43	0.98	0.82-1.75	0.52
ΔFVC from baseline	1.72	1.42-3.43	**0.02**	1.32	1.02-3.12	0.13
ΔDLCO from baseline	2.14	1.52-4.21	**0.04**	1.98	1.12-3.72	**0.03**
ΔKL-6 from baseline	3.45	1.98-5.45	**0.002**	3.21	1.78-4.89	**0.03**
ΔIL-18 from baseline	0.51	0.27-1.45	0.45	0.95	0.36-1.31	0.56
ΔIL-18BP from baseline	1.45	0.98-2.56	0.64	1.04	0.56-2.32	0.62
ΔCRP from baseline	1.52	1.24-3.45	**0.02**	1.32	1.13-3.24	**0.04**
ΔESR from baseline	0.89	0.45-2.44	0.45	0.95	0.52-2.94	0.62

Logistic regression analysis for progressive ILD in SSc. FVC forced vital capacity, DLco difusing capacity of the lung for carbon monoxide, KL-6 Krebs von den Lungen-6, CRP C-reactive protein, ESR erythrocyte sedimentation rate, Δ changes from baseline

Results: Among the 74 patients, 38% had ILD at baseline, increasing to 54% over two years. The proportion of patients with lung involvement ≥20% rose from 26% to 43%. Serum KL-6 proved to be a strong biomarker for progressive ILD, with an annual increase of +14.18 serving as the threshold (AUC: 0.803, P = 0.002, sensitivity: 80%, specificity: 64%). For mortality, an annual KL-6 increase of +71.17 showed the highest predictive accuracy (AUC: 0.91, 95% CI: 0.84–0.99, P < 0.0001, sensitivity: 75%, specificity: 85%). DLCO decline (ΔDLCO) also emerged as a mortality predictor, with a -17% annual decrease as the critical threshold (AUC: 0.20, P = 0.006). ΔKL-6 (OR: 3.21, 95% CI: 1.78–4.89, P = 0.03), ΔDLCO (OR: 1.98, 95% CI: 1.12–3.72, P = 0.03), ΔCRP (OR: 1.32, 95% CI: 1.13–3.24, P = 0.04), and anti-Scl70 antibodies (OR: 1.98, 95% CI: 1.04–3.24, P = 0.03) were independent predictors of progressive ILD, while ΔIL-18, ΔIL-18BP and ΔESR exhibited limited predictive utility. Multivariate analysis confirmed that immunosuppressive therapy was protective against ILD progression (OR: 0.27, 95% CI: 0.16–0.92, P = 0.004).

Conclusion: Serum KL-6 is a reliable biomarker for predicting ILD progression and mortality in systemic sclerosis, with well-defined thresholds showing high sensitivity and specificity. ΔDLCO and anti-Scl70 antibodies were also independent predictors of ILD progression, while immunosuppressive therapy demonstrated a protective effect. These findings highlight the potential of KL-6 for non-invasive monitoring and risk stratification in SSc-ILD.

Disclosure: c. Sieiro: None; **J. Ordas Martínez**: None; **S. Calleja Antolín**: None; **J. Garcia Herrero**: None; **J. De la Calle**: None; **M. Retuerto**: None; **L. Sierra**: None; **E. Bollo de Miguel**: None; **E. Díez Álvarez**: None.

Abstract Number: 0883

Predictive Significance of Serum Proteins for the Course of Systemic Sclerosis-Related Interstitial Lung Disease in the Multicenter CONQUER Cohort

Ali Ayla[1], Chenyue Huang[2], Claudia Pedroza[3], Meng Zhang[4], John VanBuren[5], Flavia Castelino[6], Lorinda Chung[7], Luke Evnin[8], Tracy Frech[9], Jessica Gordon[10], Faye Hant[11], Laura Hummers[12], Dinesh Khanna[13], Kimberly Lakin[10], Dorota Lebiedz-Odrobina[5], Yiming Luo[14], Ashima Makol[15], Maureen Mayes[16], Zsuzsanna McMahan[17], Jerry Molitor[18], Duncan Moore[19], Carrie Richardson[20], Nora Sandorfi[21], Ami Shah[12], Ankoor Shah[22], Victoria Shanmugam[23], Brian Skaug[1], Virginia Steen[24], Elizabeth Volkmann[25], Carleigh Zahn[13], Wenjin J Zheng[2], Elana Bernstein[14] and Shervin Assassi[26], [1]UTHealth Houston Division of Rheumatology, Houston, TX, [2]UTHealth Houston, Houston, [3]UTHealth Houston Institute for Clinical Research & Learning Health Care, Texas, TX, [4]UTHealth Houston Division of Rheumatology, Houston, [5]University of Utah, Salt Lake City, UT, [6]Massachusetts General Hospital, Boston, MA, [7]Stanford University, Stanford, CA, [8]Scleroderma Research Foundation, Brisbane, CA, [9]Vanderbilt University Medical Center, Nashville, TN, [10]Hospital for

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Special Surgery, New York, NY, [11]Medical University of South Carolina, Charleston, SC, [12]Johns Hopkins Rheumatology, Baltimore, MD, [13]University of Michigan, Ann Arbor, MI, [14]Columbia University, New York, NY, [15]Mayo Clinic, Rochester, MN, [16]UT Health Houston Division of Rheumatology, Houston, TX, [17]UT Health Houston, Houston, TX, [18]University of Minnesota, Minneapolis, MN, [19]Northwestern Memorial Hospital, Chicago, IL, [20]Northwestern University, Chicago, IL, [21]University of Pennsylvania, Philadelphia, PA, [22]Duke University, Durham, NC, [23]National Institutes of Health, Great Falls, VA, [24]Georgetown University School of Medicine, Washington, DC, [25]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA, [26]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical II (0879–0884)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: The course of interstitial lung disease (ILD) in systemic sclerosis (SSc) is highly variable and difficult to predict using clinical variables alone. Therefore, there is a need for reliable biomarkers to improve prognostication. The Scleroderma Lung Study (SLS) II showed that Krebs von den Lungen 6 (KL-6), CCL18, IFNγ-inducible 10-kDa protein (IP-10), and monokine induced by IFNγ (MIG) were significant predictors of ILD progression. In this study, we aimed to validate these findings and build a multivariable model to predict the course of ILD in SSc based on longitudinal data in a US-based multicenter observational cohort.

Methods: Patients with SSc enrolled in the CONQUER cohort were included in this analysis. Enrollment in CONQUER required fulfillment of the 2013 ACR/European League Against Rheumatism classification criteria and disease duration of less than five years from the onset of the first non-Raynaud's symptom. For the current study, we included only those patients who had interstitial lung disease (ILD) confirmed by high-resolution computed tomography (HRCT) and who were treated with mycophenolate mofetil (MMF) between the baseline and 12-month visits. The study visits were scheduled every 6 months. Blood samples were collected at baseline. Sixty-two proteins were measured as part of a multiplex assay. We used linear mixed-effects models to evaluate the predictive significance of individual cytokines for ILD progression. Follow-up FVC% was the outcome, with baseline cytokine levels, MMF treatment status, baseline FVC%, and time as fixed effects. Random intercepts and slopes accounted for between-patient variability in baseline FVC% and its change over time. A Bayesian regularized linear mixed-effects model was used to develop a prediction model that included clinical variables and serum protein levels.

Results: A total of 122 patients were included, of whom 100 (82%) were female, with a median age of 52 years and a mean disease duration of 2.7 years. Higher baseline levels of IP-10 (b = 0.0020, P = 0.013) and MIG (b = 0.0007, P = 0.023) were associated with higher FVC% over time, indicating a better ILD course. In contrast, higher KL-6 levels (b = –0.0020, P =

Table 1. Baseline demographic and clinical characteristics of study participants

Variables	n = 122
Female sex, n (%)	100 (82)
Age at the baseline visit, median (IQR)	52 (40, 62)
Race, n (%)	
White	100 (82)
African American	14 (11)
Asian	5 (4)
Others	3 (2)
Hispanic ethnicity, n (%)	15 (12)
Diffuse cutaneous involvement, n (%)	77 (63)
Disease duration, median (IQR)	2.7 (1.5, 4.0)
Anti-centromere antibody positive, n (%)	6 (5)
Anti-topoisomerase I antibody positive, n (%)	46 (38)
Anti-RNA polymerase III antibody positive, n (%)	25 (20)
mRSS, median (IQR)	12 (5, 19)
FVC% predicted, median (IQR)	77 (65, 89)
DLCO% predicted, median (IQR)	70 (51, 85)
On mycophenolate at the baseline visit, n (%)	97 (80)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Predictive significance of the proteins identified by the SLS II for the FVC% course

Protein	Point estimate	95% CI	P
KL-6	-0.0020	-0.0040, -0.0004	0.015
CCL18	0.0120	-0.0050, 0.0289	0.170
IP-10	0.0020	0.0004, 0.0030	0.013
MIG	0.0007	0.0001, 0.0010	0.023

Model adjusted for baseline mycophenolate mofetil use, baseline FVC%, and time.

Table 3. A Bayesian regularized linear mixed-effects model to predict FVC% course

Variable	Estimate	Estimated Error	95% Confidence Interval
Intercept	77.44	0.77	75.91, 78.92
Baseline FVC%	14.03	0.89	12.31, 15.77
α2-macroglobulin	-1.39	1.01	-3.47, 0.08
Anti-centromere antibody positivity	1.23	1.03	-0.13, 3.45
Serum amyloid P component	-0.61	0.74	-2.46, 0.30
CCL18	0.48	0.65	-0.31, 2.13
Monokine induced by IFNγ (MIG)	0.45	0.68	-0.39, 2.24
Diffuse involvement	0.44	0.63	-0.36, 2.08
Time	-0.37	0.30	-1.01, 0.08
Apolipoprotein	0.36	0.56	-0.37, 1.81
IFNγ-inducible 10-kDa protein (IP-10)	0.33	0.60	-0.49, 1.92
Myeloperoxidase	0.29	0.63	-0.52, 2.05
VCAM-1	0.29	0.59	-0.55, 1.89
Eotaxin-1	-0.27	0.49	-1.56, 0.42
KL-6	-0.25	0.47	-1.49, 0.44

0.015) predicted lower FVC% over time. CCL18 was not significantly associated with the FVC% trajectory. In the exploratory analysis, α2-macroglobulin (α2M, b = -3.29, P < 0.001) and serum amyloid P component (SAP, b = -0.49, P = 0.007) also showed predictive significance. In the multivariable Bayesian model, baseline FVC% had the highest estimate among clinical variables (β = 14.03), while α2-macroglobulin had the highest among protein predictors (β = –1.39). The R2 of the model, including clinical predictors and a selected number of serum proteins, was 0.765.

Conclusion: This study confirmed the predictive significance of IP-10, MIG, and KL-6 for the course of SSc-ILD and identified α2M and SAP as potential biomarkers. We also built a multivariable model including clinical and protein variables to predict the SSc-ILD course.

Disclosure: A. Ayla: None; **C. Huang**: None; **C. Pedroza**: Medicem, 5; **M. Zhang**: None; **J. VanBuren**: None; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **L. Evnin**: None; **T. Frech**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **F. Hant**: None; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(-GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **K. Lakin**: None; **D. Lebiedz-Odrobina**: None; **Y. Luo**: None; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **J. Molitor**: None; **D. Moore**: AstraZeneca, 5; **C. Richardson**: Cabaletta Bio, 2; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 2, Janssen, 2, Novartis, 1; **A. Shah**: None; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **V. Shanmugam**: ; **B. Skaug**: None; **V. Steen**: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **C. Zahn**: None; **W. Zheng**: None; **E. Bernstein**: AstraZeneca, 5, aTyr, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2.

Abstract Number: 0884

Risk Score for Early Mortality to stratify for Intensive SSc Therapy

Ann-Christin Pecher[1], Boubaya Marouane[2], Oliver Distler[3], Vanessa Smith[4], Jeska de Vries-Bouwstra[5], Radim Bečvář[6], Gianluca Moroncini[7], David Launay[8], Yannick Allanore[9], Maria De Santis[10], Kamal Solanki[11], Carlomaurizio Montecucco[12], Luca Idolazzi[13], Nihal Fathi[14], Przemyslaw Kotyla[15], Muriel Elhai[16], Jörg Henes[17] and EUropean Scleroderma Trials And Research group (EUSTAR), [1]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tübingen, Germany, [2]Unit of Clinical Research, Paris Seine Saint Denis University, Bobigny, France, Paris, France, [3]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [4]Ghent University Hospital, Gent, Belgium, [5]Leiden University Medical Center, Leiden, Netherlands, [6]Department of Internal Medicine, Charles University, Prague, Czech Republic, [7]Department of Internal Medicine, Marche University Hospital, Clinica Medica, Ancona, Italy, Ancona, Italy, [8]Univ. Lille, Inserm, CHU Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, Lille, France; CHU Lille, Département de Médecine interne et Immunologie Clinique, Centre de Référence des Maladies Auto-immunes Systémiques Rares du Nord et Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille France, Lille, France, [9]Department of Rheumatology, Université Paris Cité UFR de Médecine, Paris, France, [10]Humanitas University, Pieve Emanuele, Italy, [11]Waikato Hospital, Hamilton, New Zealand, [12]Department of Internal Medicine and Therapeutics, Università di Pavia, Pavia, Italy, Pavia, Italy, [13]Rheumatology Section, Department of Medicine, University of Verona, Verona, Italy, Verona, Italy, [14]Department of Rheumatology, Rehabilitation & physical medicine, Assiut University Hospital, Assiut, Egypt, Assiut, Egypt, [15]Department of Internal Medicine, Rheumatology and Clinical Immunology, Medical University of Silesia, Katowice, Poland, [16]University Hospital zurich, Zrich, Switzerland, [17]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tuebingen, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical II (0879–0884)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Systemic sclerosis (SSc) is a rare disease that often leads to severe complications and premature mortality. Recent advancements in the field have led to the emergence of more intensive therapy strategies for refractory or severe SSc patients, including haematopoietic stem cell transplantation (HSCT) and chimeric antigen receptor T-cell (CAR T-cell) therapy. Nevertheless, these therapeutic interventions are associated with considerable risks, including treatment-related mortality (TRM). In order to identify patients who may benefit from such therapies, a reliable mortality risk score is required to allow us to identify patients for whom a high mortality risk justifies the considerable TRM.

Methods: With RESIST (**R**isk score for **E**arly mortality to stratify for **I**ntensive **S**Sc Therapy) we aimed to develop a simple risk score to predict early mortality (< 5 years) in SSc patients eligible for intensive therapies using the EUSTAR cohort. Patients deemed unsuitable for intensive therapies were defined as patients over the age of 65 years, with a history of renal crisis, LVEF < 40%, DLCO < 40%, or FVC < 45% [1]. Only patients with at-least one follow-up visit were included.

The overall survival was estimated by the Kaplan-Meier method. We compared SSc patients who had succumbed during the initial five-year period with those who had survived until the 5th year. Covariates were selected according to expert opinion, univariable models, and evidence from the literature. A multivariable Cox model with adaptive LASSO variable selection

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics

Baseline	n=4526
Sex (Male)	3813 (84%)
Age	48.8±11
BMI	24.8±6
Ethnicity	
White	3786 (93%)
Asian	154 (4%)
Black	47 (1%)
Other	97 (2%)
Extent of skin involvement	
dcSSc	1298 (36%)
lcSSc	1829 (51%)
sine scleroderma	462 (13%)
Antibody	
ACA	1675 (45%)
none	201 (5%)
RNA Pol III	264 (7%)
Scl70	1619 (43%)
Raynaud present	3471 (98%)
Worsening of finger vascularization*	728 (22%)
Worsening of skin*	578 (17%)
Upper GI involvement	2726 (61%)
Lower GI involvement	951 (21%)
Arterial Hypertension	665 (15%)
Worsening cardiopulmonary involvement*	366 (9%)
Palpitations	797 (17%)
Dyspnea	161 (5%)
DUC	1010 (37%)
mRSS	8.4±8.5
Scleroderma pattern	2585 (88%)
Synovitis	504 (11%)
Contractures	877 (20%)
Tendon friction rubs	260 (6%)
Muscle weakness	626 (14%)
Muscle atrophy	188 (4%)
CK elevation	296 (9%)
LV ejection fraction	62.6±5.6
Diastolic function abnormal	699 (16%)
PAH	279 (8%)
ILD confirmed by HRCT	894 (34%)
DLCO -SB%predicted	74.6±17.6
FVC%predicted	97.6±19.3

*within the last month

Table 2: Multivariate analysis. The simplified score was utilised to differentiate patients into distinct categories: high (>22), intermediate (1-22), and low (0).

Parameter	HR [95% CI]	p	simplified score
Male	1.41 [0.96-2.08]	0.072	3
dcSSc	1.56 [0.95-2.54]	0.070	4
Age >55 years	1.91 [1.35-2.69]	0.0002	6
CRP elevated	1.96 [1.31-2.93]	0.001	7
DUC (current/previous)	1.6 [1.02-2.5]	0.039	5
mRSS >14	1.81 [1.12-2.93]	0.014	6
LVEF<60%	1.67 [1.16-2.4]	0.005	5
DLCO<60%	2.17 [1.52-3.09]	<0.0001	8

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

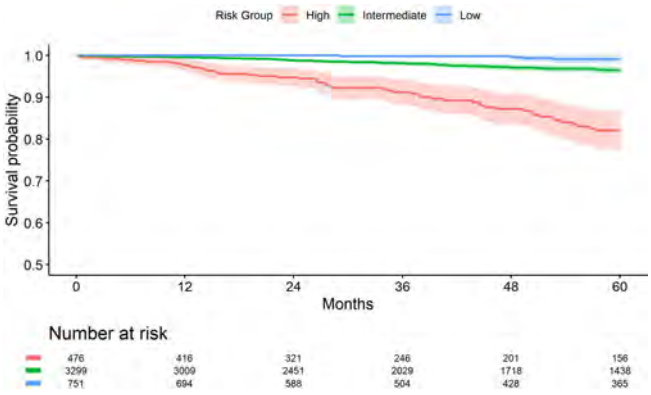


Figure 1: Overall survival according to simplified score. The 5-year survival rate was 99% (95% CI: 98–100) for low-risk patients, 96% (95% CI: 95–97) for intermediate-risk patients, and 82% (95% CI: 78–87) for high-risk patients.

was developed using 20 imputed datasets. Model performance was assessed via C-index, AUC at 3 and 5 years, and calibration. Internal validation by bootstrapping corrected for optimism using the calibration slope

Results: From 22,059 patients who were included in the EUSTAR data base, a total of 4,526 patients were included following the application of exclusion criteria. 3797/4172 met the ACR/EULAR criteria for SSc (354 missing data) Median follow-up was 53 months (95%CI: 51-55 months). The 5-year survival rate was 98% [95%CI: 97.6-98.5]. Baseline characteristics are presented in Table 1.

The RESIST score included the following eight characteristics: male sex, dcSSc, age >55 years, elevated CRP, digital ulcers (current or previous), mRSS >14, LVEF < 60% and DLCO-SB < 60% (Table 2) The AUC was 0.80 and 0.79, respectively for the 3 and 5-year mortality. As demonstrated in Figure 1, the three-cut-off system (low: 0; intermediate: 1-22; high risk: >22 points) enables an effective stratification of patients into different risk categories.

Conclusion: This future mortality risk score has the potential to serve as a valuable tool to stratify patients who could benefit from intensive (cellular) therapies in SSc patients with an acceptable benefit-risk profile. The identification of high-risk patients by clinicians is of paramount importance, as it enables the optimization of treatment plans and the improvement of overall survival.

Disclosure: A. Pecher: AstraZeneca, 6, Boehringer-Ingelheim, 1, 6, GlaxoSmithKlein(GSK), 6, UCB, 6; **B. Marouane**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Inovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **R. Bečvář**: None; **G. Moroncini**: None; **D. Launay**: AstraZeneca, 2, Biocryst Pharmaceuticals, 2, CSL Behring, 2, 5, Octapharma AG, 5, Takeda, 2; **Y. Allanore**: None; **M. De Santis**: Boehringer-Ingelheim, 2, 6; **K. Solanki**: Apollo Hospitals Educational and Research Foundations, 12, Honorary adjunct professor; **C. Montecucco**: None; **L. Idolazzi**: None; **N. Fathi**: None; **P. Kotyla**: None; **M. Elhai**: Astrazeneca, 12, congress support, Boehringer Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5, Iten Kohaut foundation, 5, Janssen, 12, congress support, Kurt und Senta Herrmann foundation, 5, Novartis Foundation for Bio-Medical Research, 5, pfizer, 5, University Zurich, 5; **J. Henes**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, Janssen, 1, 6, Novartis, 1, 1, 6, 6, Otsuka, 1, Pfizer, 1, Roche, 1, SOBI, 1, UCB, 1, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0885

MAIT cell-mediated immune modulation in lupus: antigen-driven expansion as a protective strategy

Grace Crossland[1], Iennard Ostendorf[2], Vianey Chavez[1], Lindsay Mendyka[1], Deepak Rao[3] and Sladjana Skopelja-Gardner[1], [1]Dartmouth College, Lebanon, NH, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0885–0890)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a leading cause of death for young women, and over 75% of SLE patients experience skin manifestations – cutaneous LE (CLE). Mechanisms of CLE pathogenesis are still unknown, so treatments rely on broad immunosuppression. Mucosal-associated invariant T cells (MAITs) are innate-like T cells that respond to microbial-derived antigens and have tissue repair capacity but are decreased in SLE. Here, we present new findings supporting a protective role for MAITs in SLE/CLE.

Methods: SLE and healthy PBMCs were analyzed by spectral cytometry (Dartmouth) and CytOF (Brigham, 145 SLE, 40 healthy). In 12-24 week old female MRL/lpr mice, spontaneous skin lesions (score >10) or systemic SLE (proteinuria) were treated with topical or systemic MAIT antigen (5OPRU, 1mM). 8-week-old female B6 and MAIT-deficient (*Mr1-/-*) mice were treated with imiquimod (TLR7 agonist) to induce SLE-like skin disease. MAIT profiling and expansion in non-lesional skin were conducted in 8-week-old female mice: MRL/lpr, B6, and *Mr1-/-*. Immune responses were assessed by flow cytometry; MAITs were identified by 5OPRU-loaded MR1 tetramer.

Results: MAIT cells were reduced in the circulation of SLE patients and had an activated/exhausted phenotype (CD25hiCD38hiCD69hi and CD107loCXCR3loCCR5lo), compared to healthy MAITs. In SLE-like skin of MRL/lpr mice, MAIT cells were reduced and more activated (> %$CD69^+PD1^+$), compared to controls (B6, MpJ). Topical administration of MAIT antigen (5OPRU) completely and durably resolved active CLE-like skin lesions. In contrast, skin lesions in mice treated with vehicle or 5OPRU + anti-MR1 Ig (blocks MAIT interaction with 5OPRU) never healed and continued to flare after treatment cessation. In the TLR7 agonist model of SLE, MAIT-deficient skin (*Mr1-/-*) had significantly increased expression of inflammatory (Ifng, Gzmb, Csf1) and interferon-stimulated genes, compared to the skin of imiquimod-treated B6 mice. MAIT expansion with 5OPRU (∼5-10-fold) in SLE-like non-lesional skin stimulated proliferation and expansion of regulatory T cell (Treg) and suppressed inflammatory and cytotoxic gene expression (Gzmb, Ifng, il6, Tnf). In SLE mice with marked proteinuria, systemic delivery of 5OPRU halted the rise in serum inflammatory cytokines (CXCL1, GCSF, IL2, IFNg) and stimulated systemic expansion of T_{reg}, including in the skin. The 5OPRU-mediated Treg expansion was MAIT-dependent, as no increase in Treg was seen in 5OPRU-treated *Mr1-/-* mice. MAIT expansion was captured in the skin after just 2 doses of 5OPRU and was accompanied by increases in monocyte-derived dendritic cells (moDCs) and Langerhans cells (LCs), in a MAIT-dependent fashion.

Conclusion: Topical and systemic expansion of MAITs reduces tissue and systemic inflammation, and overall disease burden in MRL/lpr mice. Their protective role in SLE is further supported by a second SLE model, where MAIT deficiency leads to heightened inflammatory and interferon responses. These effects may be mediated via MAIT-dependent expansion of Treg. MoDCs and LCs are identified as candidate antigen-presenting cells involved in MAIT activation and downstream Treg induction.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Crossland: None; **I. Ostendorf**: None; **V. Chavez**: None; **L. Mendyka**: None; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2; **S. Skopelja-Gardner**: None.

Abstract Number: 0886

A First-in-class Biologic Selectively Targeting hla-b27-reactive T Cells in Ankylosing Spondylitis

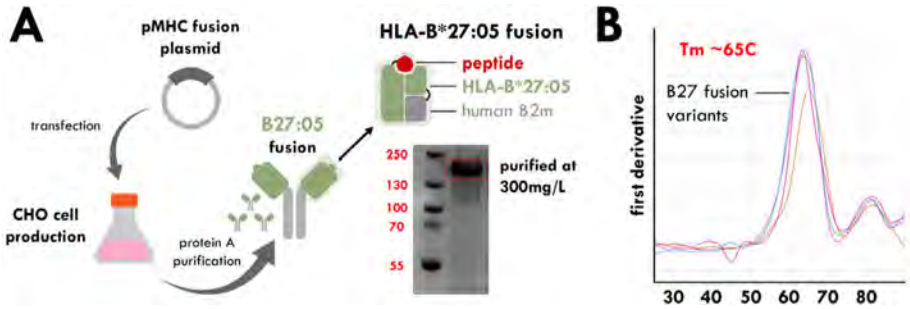
Patrick Holec, Megan Reitars, Nishant Singh and Isabelle Larsen, Fletcher Biosciences, Cambridge, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0885–0890)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Ankylosing spondylitis (AS), a chronic autoimmune disease strongly associated with HLA-B27:05, is currently managed with therapies that broadly suppress inflammation instead of targeting disease-driving immune cells. This limitation highlights the potential of emerging selective T cell depletion strategies such as those using anti-TRBV9 antibodies, which have recently demonstrated clinical promise. Here, we present a novel therapeutic approach utilizing engineered peptide–MHC (pMHC) fusion proteins designed to selectively deplete HLA-B27-restricted, autoreactive T cells in AS. These pMHC fusion molecules are optimized for stability and TCR affinity, offering a new avenue for antigen-specific immune modulation.

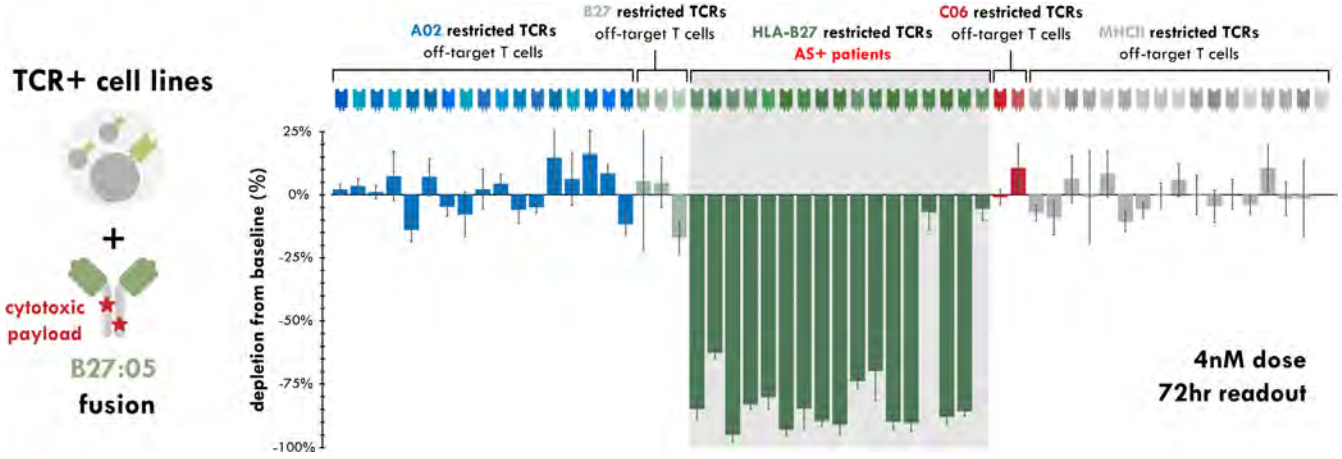
Methods: We engineered B27:05 fusion proteins presenting cross-reactive peptides identified from AS+ patient synovial TCRs. Using high-throughput protein screening, we identified mutations that enhance the stability of HLA-B27:05 and globally enhanced engagement of disease-associated T cells . Candidate pMHC fusion molecule were conjugated to select payloads to enable targeted cell killing. Selective T cell depletion was tested using T cell lines transduced with one of 50+ AS-associated or control TCRs. Additional evaluation was performed in vitro on patient PBMCs to evaluate drug efficacy and toxicity.

Results: Lead pMHC-Fc candidates demonstrated high expression (≥100 mg/L), thermal stability (Tm ≥ 60°C), and strong binding to ≥70% of patient-derived TCRs. MMAE-conjugated pMHC-Fc constructs selectively eliminated >80% of AS-specific T cell lines with low off-target toxicity. In primary human cells, pMHC-Fc-MMAE treatment resulted in dose-dependent depletion of CD8+ T cells based on antigen-reactivity, displaying no notable toxicity beyond on-target autoreactive T cells.

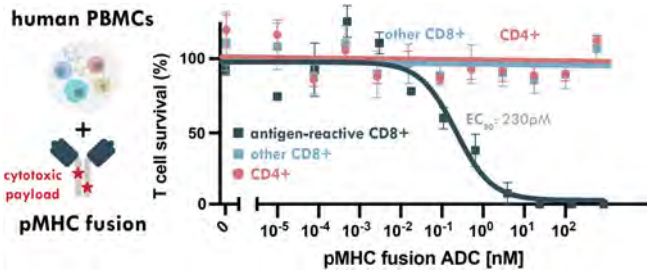


Production and biophysical characterization of B27:05 fusion proteins: (A) Schematic of the production pipeline: pMHC fusion constructs encoding HLA-B*27:05, beta-2-microglobulin, and a disease-relevant peptide are transfected into CHO cells, and purified via Protein A affinity chromatography, yielding expression levels of ~300 mg/L. (B) Thermal shift assay of purified B27:05 fusion proteins demonstrates high thermal stability, with melting temperatures (Tm) averaging 65°C across variants.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Specific depletion of AS-relevant T cells using B27:05 drug conjugates: A cytotoxic payload conjugated B27:05 was evaluated across a panel of 50+ TCR+ cell lines expressing either AS-relevant TCRs (green) or non-AS-related off-target TCRs restricted to A02 (blue), B27 (light green), C06 (red), or MHC class II alleles (gray). Following 72-hour treatment at 4 nM, selective depletion of HLA-B27-restricted TCR clones from AS+ patients was observed, with minimal off-target cytotoxicity across unrelated clones.



Selective cytotoxicity of pMHC fusion in primary human PBMCs: Treatment of antigen-specific PBMC cultures with pMHC-drug conjugate demonstrated potent depletion of antigen-reactive T-cells (EC50 = 230 pM) while sparing other T cell populations. This validates the ex vivo selectivity and potency of the pMHC fusion platform in physiologically relevant immune cell mixtures.

Conclusion: We demonstrate the first functional application of soluble, engineered HLA-B27:05 fusion molecules to selectively deplete autoreactive T cells in AS. This precision platform addresses a critical unmet need by targeting the root cause of inflammation without broad immunosuppression. These findings support the advancement of pMHC-based biologics as a novel, disease-modifying therapeutic class for AS and other HLA-associated autoimmune diseases.

Disclosure: P. Holec: Fletcher Biosciences, 3, 4, 8, 10; **M. Reitars**: Fletcher Biosciences, 3, 11; **N. Singh**: Fletcher Biosciences, 3, 4, 8, 10; **I. Larsen**: Fletcher Biosciences, 3.

Abstract Number: 0887

Dynamics of cytotoxic and regulatory CD8 T cells underlies outcome in ICI-myotoxicity

Runci Wang[1], Chunyan Xiang[2], Adrien Procureur[3], Julian Sanchez-Dal Cin[3], Qing Wang[4], Xinyue Lian[5], Michelle Rosenzwajg[3], Yves Allenbach[6], Deepak Rao[7], Qiong Fu[8], Nan Shen[9], Joe-Elie Salem[3] and Shuang Ye[10], [1]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [2]Shanghai Institute of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University (SJTUSM), shanghai, China (People's Republic), [3]Sorbonne Université, Paris, France, [4]Zhongshan Hospital, Shanghai, China (People's Republic), [5]Renji Hospital, Shanghai, China (People's Republic), [6]SORBONNE UNIVERSITE, Paris, France, [7]Brigham and Women's Hospital, Boston, MA, [8]Renji Hospital, Shanghai, Shanghai, China, [9]Shanghai Jiang Tong

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University School of Medicine, Shanghai, China (People's Republic), [10]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0885–0890)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Immune checkpoint inhibitor (ICI) therapies for cancer can induce immune-related adverse events (irAEs) involving musculoskeletal (MSK) systems. ICI myotoxicity (ICI-M) can present as a triad of fulminant myocarditis, myositis and myasthenia gravis-like syndrome, calling for rapid recognition and precise therapeutic assessment. Abatacept shown promise as a treatment option for high-grade ICI-M [1]. Previously we identified a clonal CD38^{hi} cytotoxic CD8 T cell population specifically expanded in ICI-arthritis, indicating an irAE specific T cell response in ICI-MSK systems [2]. Regulatory CD8 T cells expressing KIR have been reported in autoimmunity and cancer patients[3]. Whether these T populations can help clinical recognition and therapeutic response assessment in high-grade ICI-M calls for further investigation.

Methods: We performed immunophenotyping, single-cell transcriptomic analysis and TCR analysis of T cells from blood and muscle tissue in a multi-center cohort of ICI-M patients (n=16). Blood of ICI-A (n=7), ICI-without irAE (ICI, n=9), and cancer-without ICI therapy (non-ICI, n=6) were used as control.

Results: scRNA-seq identified 11 distinct T cell clusters in ICI-M and ICI-A (Fig 1a-b). Transcriptomic features of the top four effector memory clusters, C1 GZMB+ GZMH+ GNLY+ cytotoxic CD8 T cells, C3/6 GZMK+KLRB+/HLADR+ cytotoxic CD8 T cells, and C4 KIR+ CD8 T cells, each showing unique cytotoxic characteristics (Fig 1c). C3/6 were identified as CD38hi-like

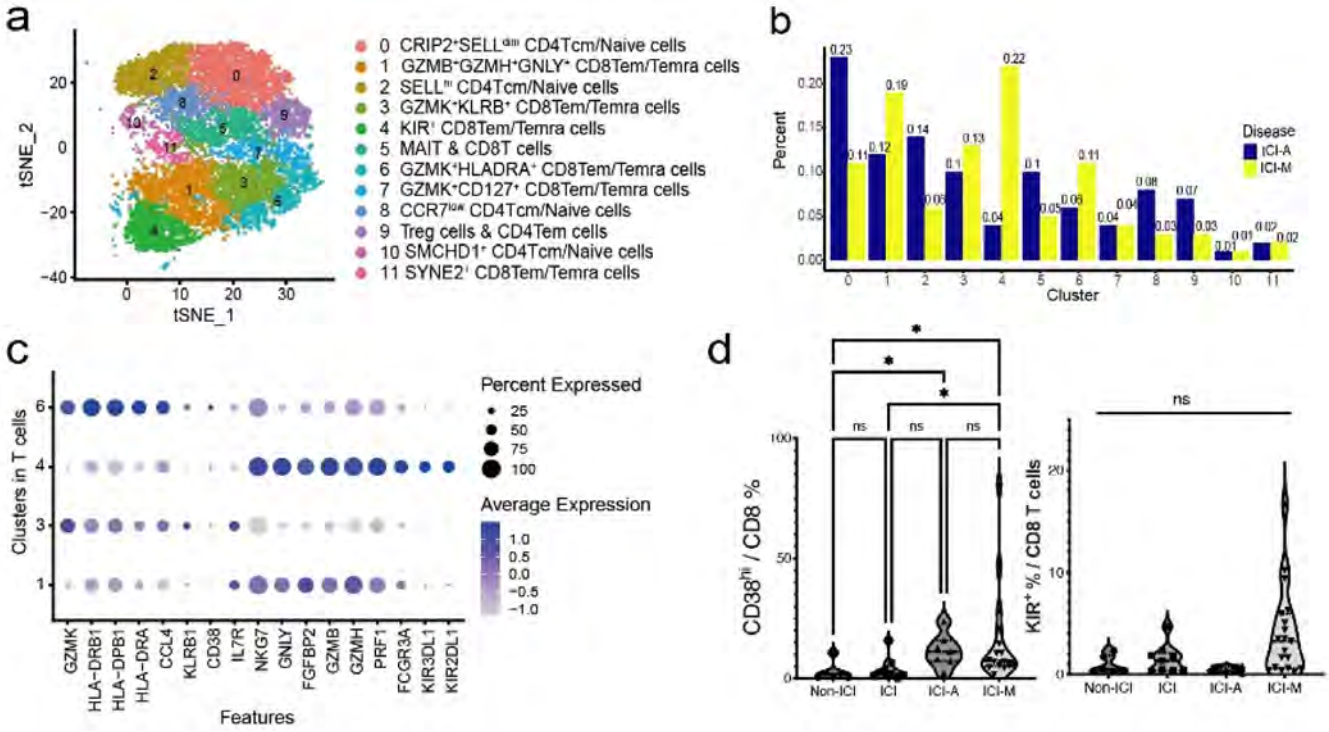


Figure 1. Transcriptomic features of ICI-M peripheral blood. scRNA-seq identified distinct T cell clusters (a) in ICI-M and ICI-A (b). Top four effector memory clusters showed distinct transcriptomic features (c). Frequency of CD38hi-like C3/6 and KIR+ C4 in ICI-M (d). Krustal-Wallis test. ns, not significant. *, p<0.05.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

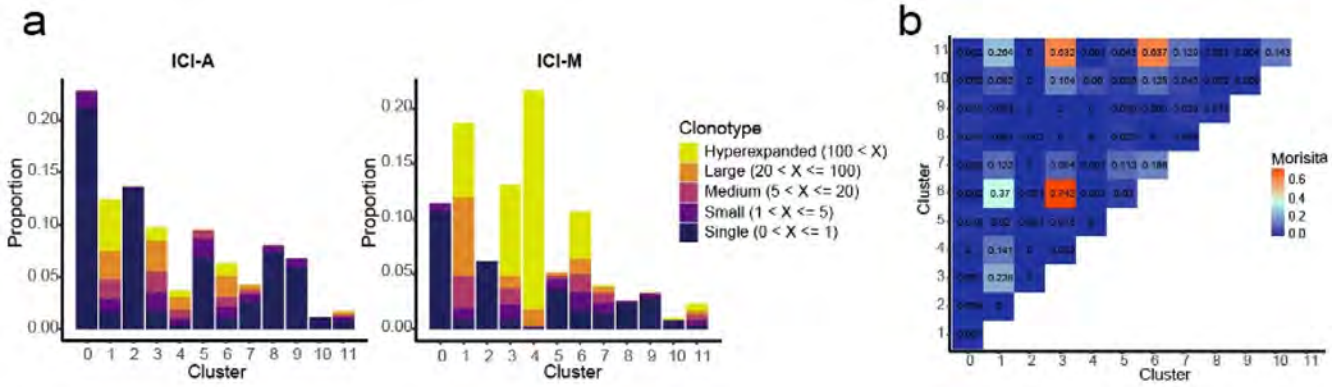


Figure 2. scRNA-seq TCR analysis showed clonality of ICI-M circulating T cells clusters (a) and their similarity represented with Morisita index (b).

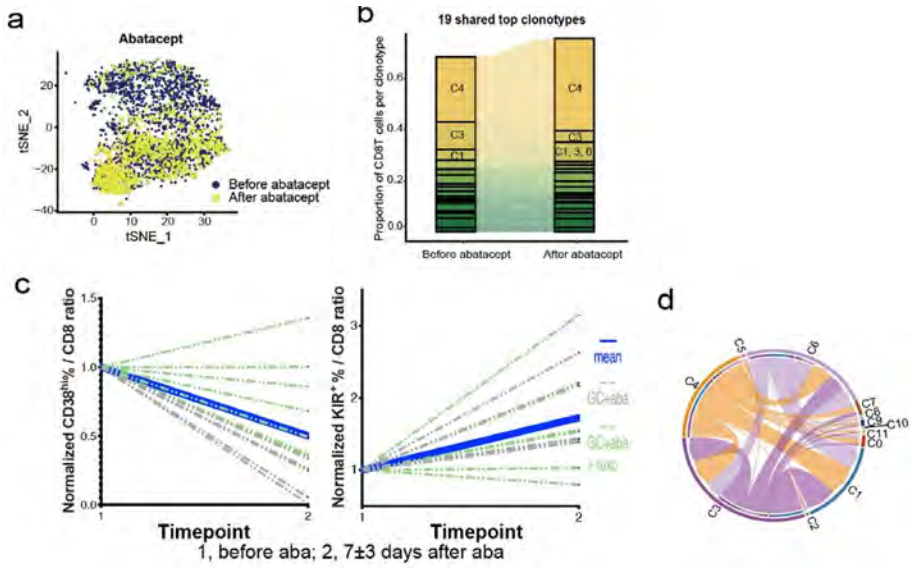


Figure 3. Therapeutic response to abatacept. tSNE plot showing abatacept altered the composition and clonality (a-b) of CD8 T cells in ICI-M. Flow cytometry analysis showed fold change of circulating CD38hi and KIR+ CD8 T cells in ICI-M before and after abatacept (c). Chord plot showing the inferred communication among T cell clusters. The edge width represents the communication probability. (d).

cells using a gene signature we previously identified [2]. Multi-color flow cytometry showed that circulating C3/6 and C4 are expanded in ICI-M (Fig 1d). C3/6 were also identified in muscle tissue of ICI-M patients.

TCR repertoire analyses revealed more prominent clonal expansion of cytotoxic CD8 Tem cells in ICI-M over ICI-A, particularly $CD38^{hi}$-like CD8 T cells (C3+C6) and KIR+ CD8 T cells (C4) (Fig 2a). C3/C6 shared clonality that's different from C4 (Fig 2b).

A tailored dosing of abatacept in addition to corticosteroids +/- ruxolitinib was applied based on the degree of CD80 blockade and successfully rescued clinically fulminant ICI-M in our multi-center cohort. The abatacept regimen altered the composition and clonality of CD8 T cells (Fig 3a-c). Using cellchat algorism, possible interactions were identified among KIR+ CD8 T cells (C4) and CD38like CD8 T (C3+C6) (Fig 3 c).

Conclusion: The dynamic of $CD38^{hi}$ CD8 T cells and KIR^{+} CD8 T cells effectively identified ICI-M patients and supported their therapeutic assessment during abatacept. Analyzing these populations may provide personalized treatment strategy for life-threatening irAEs.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Wang: None; **C. Xiang**: None; **A. Procureur**: None; **J. Sanchez-Dal Cin**: None; **Q. Wang**: None; **X. Lian**: None; **M. Rosenzwajg**: None; **Y. Allenbach**: None; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2; **Q. Fu**: None; **N. Shen**: None; **J. Salem**: None; **S. Ye**: None.

Abstract Number: 0888

TargetScan Platform Identifies Targets of CD8+ T cells in Ankylosing Spondylitis and Birdshot Uveitis

Adam S. Weinheimer[1], Olivia Pryor[2], Catalina Burbano[3], Tyler Heath[3], Livio Dukaj[3], Shoshana M.K. Bloom[3], Jackson Lirette[3], Rachel Lent[3], Prachi Dhanania[3], Nicole A. Ladd[3], Ryan Kritzer[3], Hana Husic[3], Shobitha Jillella[3], Alexander Cristofaro[2], Chandan K. Pavuluri[3], Jenna LaBelle[3], Laurie Barefoot[3], Shrikanta Chattopadhyay[3], Andrew P. Ferretti[3] and Cagan Gurer[3], [1]TScan Therapeutics, Boston, MA, [2]TScan Therapeutics, Waltham, [3]TScan Therapeutics, Waltham, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0885–0890)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Antigen-specific therapies offer a promising approach to selectively modulating autoimmune responses without broad immunosuppression. Strong associations with specific Class I HLA alleles in ankylosing spondylitis (AS) with a linkage to HLA-B*27:05 (Odds ratio of 62) and birdshot uveitis (BU) with a linkage to HLA-A*29:02 (Odds ratio of 157) suggest a role for $CD8^+$ T cells, yet the causative autoantigens remain unknown. TScan's proprietary TargetScan platform offers an unbiased high-throughput method to identify the natural targets of disease-relevant T cell receptors and aid in the development of antigen specific tolerizing modalities.

Methods: We isolated $CD8^+$ T cells from synovial fluid of patients with AS and aqueous humor or vitreous humor from patients with BU. Single-cell TCR sequencing identified 42 unique paired α/β TCR sequences from the ankylosing spondylitis samples and 113 clonotypes from the BU samples. These TCRs, along with 14 previously published TCRs from AS patients, were gene synthesized and screened using the TargetScan platform against a comprehensive cell library representing the full human proteome presented naturally by cells engineered to express the disease associated HLA allele (HLA-B*27:05 for AS, HLA-A*29:02 for BU). Screening revealed multiple putative autoantigen targets which were subsequently evaluated for disease relevance.

Results: Using this approach, we identified over 10 putative Class I–restricted T cell targets for AS and two for BU. These targets were validated through orthogonal assays, including functional T cell activation, and exhibited expression patterns consistent with disease-relevant tissues. Minimal epitopes for each target were mapped to define the core sequences required for TCR recognition. Their identification provides new insight into the antigenic drivers of these conditions and highlights potential avenues for the development of antigen-specific therapeutics.

Conclusion: TScan's discovery platform enables the identification of novel Class I-restricted autoantigens in autoimmune diseases where no targets were previously known, filling a critical gap in the understanding of T cell-driven pathology. This technology provides a foundation for the development of antigen-specific therapeutics, including tolerogenic approaches aimed at restoring immune homeostasis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Weinheimer: TScan Therapeutics, 3, 11; **O. Pryor**: TScan Therapeutics, 3, 11; **C. Burbano**: TScan Therapeutics, 3, 11; **T. Heath**: TScan Therapeutics, 3, 11; **L. Dukaj**: TScan Therapeutics, 3, 11; **S. Bloom**: TScan Therapeutics, 3, 11; **J. Lirette**: TScan Therapeutics, 3, 11; **R. Lent**: TScan Therapeutics, 3, 11; **P. Dhanania**: TScan Therapeutics, 3, 11; **N. Ladd**: TScan Therapeutics, 3, 11; **R. Kritzer**: TScan Therapeutics, 3, 11; **H. Husic**: TScan Therapeutics, 3, 11; **S. Jillella**: TScan Therapeutics, 3, 11; **A. Cristofaro**: TScan Therapeutics, 3, 11; **C. Pavuluri**: TScan Therapeutics, 3, 11; **J. LaBelle**: TScan Therapeutics, 3, 11; **L. Barefoot**: TScan Therapeutics, 3, 11; **S. Chattopadhyay**: TScan Therapeutics, 3, 11; **A. Ferretti**: TScan Therapeutics, 3, 11; **C. Gurer**: TScan Therapeutics, 3, 11.

Abstract Number: 0889

Potentially pathogenic memory CD4 T cells with a B cell helper phenotype expand in ACPA+ individuals during progression to rheumatoid arthritis

Ziyuan He[1], Marla Glass[1], Pravina Venkatesan[2], Alexandra Ferrannini[3], Marie Feser[4], Christy Bennett[1], David Boyle[5], Kristen Demoruelle[6], Kristine Kuhn[7], Fan Zhang[8], Thomas Bumol[9], Ananda Goldrath[3], Peter Skene[3], V. Michael Holers[10], Xiaojun Li[1], Adam Savage[1], Gary Firestein[11], Kevin Deane[12], Troy Torgerson[13] and Mark Gillespie[1], [1]Allen Institute for Immunology, Seattle, WA, [2]Allen Insitute, Seattle, WA, [3]Allen Institute for Immunology, Seattle, [4]University of Colorado Anschutz Medical Campus, Aurora, CO, [5]UCSD, La Jolla, CA, [6]University of Colorado Anschutz Medical Campus, Golden, CO, [7]2022 - 2023 / Adult/ University of Colorado, Aurora, CO, [8]The University of Colorado, Aurora, CO, [9]Allen Institute for Immunology, San Diego, CA, [10]University of Colorado, Denver, CO, [11]University of California, San Diego, San Diego, CA, [12]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [13]Allen Institute for Immunology, Enumclaw, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0885–0890)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Prior to the onset of clinically apparent inflammatory arthritis (IA)/synovitis (clinical RA), ACPA+ 'at-risk' individuals (ARI) show alterations in the abundance of effector T cell subsets in the peripheral circulation. However, it remains unclear which T cell subsets define the progression to clinical RA. A population of central memory CD4 T cells expanded over time as ACPA+ ARI progressed to clinical RA (termed 'converters'). In this study, we investigated the molecular phenotype of this expanding memory T cell population in converters.

Methods: We conducted a longitudinal analysis of peripheral blood mononuclear cell (PBMC) transcriptomes obtained by scRNA-seq. We performed linear mixed effects longitudinal modeling on samples from ACPA+ participants over a period of 2 years prior to the onset of clinical RA (n=13 converters; n=61 samples; mean 4.7 samples per converter; Table 1). These

Table 1: Summary of converter information

Variable	Baseline Visit (n = 13)	IA Onset (n = 13)	*P* value[1]
Age at sample collection, mean years (SD)	45 (14)	47 (14)	<0.01
Sex: Female, n (%)	13 (100%)	-	-
Ethnicity: Non-Hispanic origin, n (%)	12 (92%)	-	-
Race: White, n (%)	9 (69%)	-	-
BMI, mean kg/m2 (SD)	27 (6)	28 (8)	0.07
Met ACR/EULAR 2010 criteria, n (%)	-	10 (77%)	-
C-reactive protein, median mg/L (IQR)	3.3 (0.8-8.4)	2.9 (1.2-4.1)	1.00
Erythrocyte sedimentation rate, median mm/h (IQR)	12 (10-23)	13 (9-21)	0.67
Shared epitope present, n (%)[2]	5 (38%)	-	-
Serum ACPA, median (IQR)	133 (79-1557)	231 (51-1242)	0.29
Serum RF IgM, median (IQR)	16 (0.3-30)	16 (3.8-50)	0.11
Serum RF IgA, median (IQR)	0.3 (0.3-5.2)	1.7 (0.3-4.1)	0.94

[1]*P* values were calculated using the paired Wilcoxon rank-sum test for continuous variables. *P* values were calculated using the Fisher exact test for discrete variables.
[2]Shared epitope present at any *HLA-DRB1* **01:01, *01:02, *04:01, *04:04, *04:05, *04:08, *04:09, *04:10, *04:13, *10:00* alleles.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

samples were from a prospective longitudinal cohort study of ACPA+ individuals without baseline IA/synovitis. Cell-cell communication analyses to infer ligand-receptor interactions and downstream gene expression changes were performed using Liana and NicheNet.

Results: A memory CD4 T cell population that expanded almost 2-fold over time from baseline to conversion (FDR< 0.05) expressed PD1, ICOS, CXCR5 and KLRB1 transcripts, exhibited a transcriptionally activated state (P< 0.05) and were enriched for a published transcriptional signature of Tfh/Tph cells from RA synovial tissue (P< 0.01; Zhang 2019 Nature Immunol). Using an independent trimodal single cell validation dataset (Thomson 2023 Nature Immunol), we identified a CD4 memory population that expressed a similar PD1+ ICOS+ CXCR5+ KLRB1+ transcriptional signature. Notably, this population had the highest surface protein expression of PD-1 and ICOS, along with high expression of KLRB1 protein. We inferred key receptor-ligand communication between two lymphocyte populations that expanded as converters progressed to clinical RA: (1) the memory CD4 T cell population; and (2) CD27- TBX21+ atypical B cells. Potential receptor-ligand complexes included CD40LG-CD40, CD86-CD28, and SEMA4D-CD72, and was supported by downstream changes in gene expression following receptor-ligand interactions reported in both these populations.

Conclusion: These results suggest the increased population of central memory CD4 T cells in the peripheral blood of converters approaching transition to clinical RA is associated with changes in activated T cells with a B cell helper phenotype. This memory population could be similar to Tph cells found to be clonally expanded in RA synovium, but also shares features of Th17 cells, suggesting they could produce pro-inflammatory mediators that participate in disease pathogenesis. These findings are supported by inferred bidirectional signaling between these memory CD4 T cells and atypical B cells during progression to clinical RA. Our findings provide key insights into adaptive immune mechanisms that contribute to the progression from an at-risk state to clinical RA, and may suggest targets for early preventive intervention or biomarkers for RA prevention trials.

Disclosure: Z. He: None; **M. Glass**: None; **P. Venkatesan**: None; **A. Ferrannini**: None; **M. Feser**: None; **C. Bennett**: Adaptive Biotechnologies, 11, Eli Lilly, 5; **D. Boyle**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5; **K. Kuhn**: Solarea, 2; **F. Zhang**: None; **T. Bumol**: Tentarix Biotherapeutics, 4; **A. Goldrath**: Arsenal Bio, 1, Foundery Innovations, 1; **P. Skene**: None; **V. Holers**: None; **X. Li**: Eli Lilly, 5; **A. Savage**: None; **G. Firestein**: Eli Lilly, 5; **K. Deane**: Inova Diagnostics, 1; **T. Torgerson**: Eli Lilly, 2, Pharming Healthcare, 2, Takeda, 2; **M. Gillespie**: Novo Nordisk, 11, Omeros, 11.

Abstract Number: 0890

Granzyme K+ CD8 T cells colocalize with myeloid cells and activate them through several pathways

Julia Nicole Zeid[1], Kaitlyn Arce[2], Nanxi Guo[1], Kartik Bhamidipati[3], Kevin Wei[4], Larry Moreland[5], Fan Zhang[6] and **Anna Helena Jonsson**[2], [1]University of Colorado School of Medicine, Aurora, [2]University of Colorado School of Medicine, Aurora, CO, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [5]University of Colorado, Denver, CO, [6]The University of Colorado, Aurora, CO

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0885–0890)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

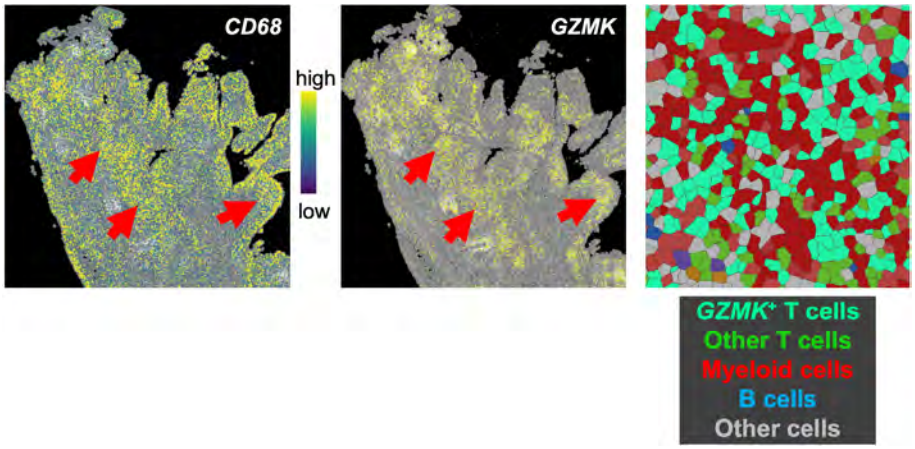


Figure 1. GZMK+ CD8A+ cells are located near myeloid cells in the sublining of RA synovial tissue. FFPE RA synovial tissue was submitted for spatial transcriptomic analysis on the Xenium platform. The panels on the left show density gradients of transcripts encoding CD68 (myeloid marker) and GZMK, respectively, superimposed on the tissue. Red arrows point to areas enriched in both CD68 and GZMK. The panel on the right shows a close-up view with cells shaded by cluster, showing intermingling of GZMK+ T cells (teal) and myeloid cells (red).

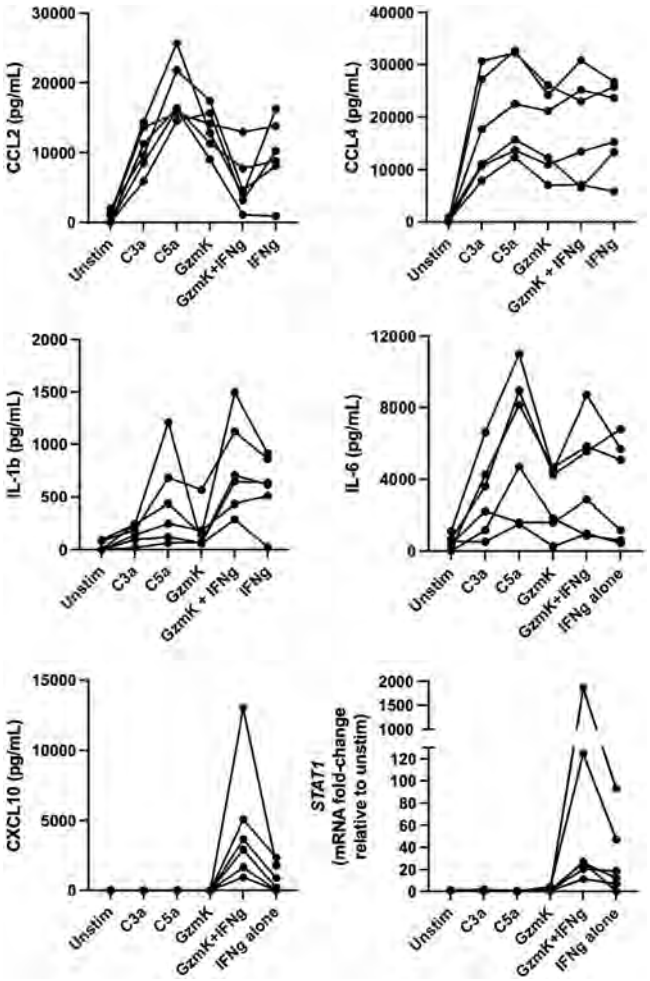


Figure 2. GZMK directly stimulates blood monocytes and also amplifies the effects of IFNγ. Human CD14+ monocytes were isolated from blood and stimulated with recombinant or serum-purified GZMK, IFNγ, C3a, or C5a, or a combination of GZMK and IFNγ for 24 hours. The supernatants were collected for analysis by ELISA, while the cells were lysed for analysis by quantitative RT-PCR. The lines connect samples from the same blood donor (N=6).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Granzyme K (GZMK)-expressing CD8 T cells have recently been detected in tissues from an increasing number of autoimmune conditions, but their role in disease pathogenesis is unclear. We have identified and characterized these cells in rheumatoid arthritis (RA), where they represent up to 30% of cells in inflamed synovium (joint lining) and express a gene program different from granzyme B (GZMB)$^+$ cytotoxic CD8 T cells. We recently showed that *Gzmk* knock-out mice exhibit a milder course antigen-induced arthritis, a mouse model of inflammatory arthritis, compared to wild-type mice, supporting a direct role for GZMK in the pathogenesis of inflammatory arthritis such as RA. GZMK$^+$ CD8 T cells have many potential effector functions. Resting GZMK$^+$ CD8 T cells continuously release GzmK, even in the absence of stimulation. They can also release cytokines such as IFNγ upon T-cell receptor (TCR)- or cytokine-mediated stimulation. Lastly, GzmK can initiate complement cascades, generating anaphylatoxins C3a and C5a. Our goal with this project is to localize GZMK$^+$ CD8 T cells in RA synovial tissue and characterize their molecular interactions with neighboring cells.

Methods: Spatial transcriptomic data were collected from three samples of human synovial tissue from patients with RA using a custom 377-probe panel on the Xenium platform (10x Genomics). For *in vitro* experiments, CD14$^+$ myeloid cells isolated from human peripheral blood mononuclear cells by magnetic-activated cell sorting and stimulated with recombinant or serum-purified GZMK, IFNγ, C3a, and/or C5a, for 24 hours and then analyzed by ELISA or RT-PCR.

Results: In spatial transcriptomic and immunofluorescence microscopy data, GZMK$^+$ CD8 T cells were preferentially located among myeloid cells in perivascular areas of the sublining in human RA synovial tissue (Figure 1). To investigate and compare molecular interactions between GZMK$^+$ CD8 T cells and myeloid cells, we stimulated CD14$^+$ blood monocytes *in vitro* with soluble factors produced by GZMK$^+$ CD8 T cells directly (GZMK, IFNγ) or via activation of complement cascades (C3a, C5a). We paid special attention to chemokines CCL2, CCL4, CXCL9, and CXCL10 since both monocytes and GZMK$^+$ CD8 T cells express the cognate receptors for these chemokines, CCR2, CCR5, and CXCR3. We found that recombinant GZMK induced monocytes to produce CCL2, CCL4, and IL-6 (Figure 2). GZMK did not induce CXCL9, CXCL10, or STAT1 on its own, but it amplified the ability of IFNγ to induce these classic interferon signature markers. The combination of GZMK and IFNγ also had modestly augmented effects on IL-1β and IL-6, while they dampened CCL2 production. C5a displayed more potent effects than C3a in terms of CCL2, CCL4, IL-1β, and IL-6 production.

Conclusion: GZMK$^+$ CD8 T cells localize near myeloid cells in the sublining of inflamed RA synovium. GZMK can directly induce monocytes to secrete CCL2, CCL4, and IL-6, and it can act together with IFNγ or through complement cascades to induce IL-1β and interferon signature genes. Together, these molecular interactions form a strong positive feedback loop, recruiting and activating additional GZMK$^+$ CD8 T cells and blood monocytes in inflamed RA synovium.

Disclosure: J. Zeid: None; **K. Arce**: None; **N. Guo**: None; **K. Bhamidipati**: None; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **L. Moreland**: None; **F. Zhang**: None; **A. Jonsson**: Arpelos Biosciences, 2, Ono Pharmaceuticals, 5, Pfizer, 6.

Abstract Number: 0891

MEthotrexate versus TOcilizumab for treatment of Giant cell Arteritis (METOGiA trial): a multicenter, randomized, controlled trial.

Maxime Samson[1], Abderrahmane Bourredjem[2], Rodérau Outh[3], Vincent Grobost[4], François Lifermann[5], Guillaume DIREZ[6], Emmanuel Ribeiro[7], Eric Oziol[8], Valerie Devauchelle[9], Mikael Ebbo[10], Nicolas Limal[11], Romain Paule[12], Boris Bienvenu[13], Antoine Poulet[13], Sébastien Miranda[14], Ygal Benhamou[14], Thomas Quemeneur[15], Claire Dingremont[16], Andre Ramon[17], Bernard Simorre[8], Quitterie Reynaud[18], Christian AGARD[19], Olivier Espitia[20], Arsène Mekinian[21], Jean-François Alexandra[22], Emilie Berthoux[23], Laurent Perard[23], Antoine Baudet[24], Rafik Mesbah[25], David Lacôte-Delarbre[26], Julien Stievenart[27], Marc André[27], Jean Sébastien Allain[28], Rolland Jaussaud[29], Julie Magnant[30], Amélie Servettaz[31], Hubert De Boysson[32], Marc Ruivard[4], Benjamin Terrier[33], Alexis REGENT[34], Amélie Cransac[35], Isabelle Fournel[36],

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Hervé Devilliers[36], Bernard Bonnotte[37] and French study group for large vessel vasculitides (GEFA), [1]CHU Dijon Bourgogne, Dijon, France, [2]Centre d'Investigation Clinique, CHU Dijon, Dijon, France ; INSERM, CIC 1432, Module Epidémiologie Clinique, Dijon, France, [3]Department of Internal Medicine, Centre Hospitalier de Perpignan, Perpignan, France., Clermont-Ferrand, France, [4]Internal medicine, CHU Clermont Ferrand Estaing, Clermont Ferrand, France, [5]Internal Medicine, CH de Dax, Dax, France, [6]Rheumatology, CH Le Mans, Le Mans, France, [7]Internal medicine and clinical immunology, CHU Bordeaux, Hôpital Saint-André, Bordeaux, France, [8]Internal Medicine, CH Bézier, Bézier, France, [9]UBO, Brest, France, [10]Internal Medicine, Marseille-APHM, hôpital La Timone, Marseille, France, [11]Internal Medicine, CHU Henri Mondor, Créteil, France, [12]Hospital Foch, Service de medicine interne, Suresnes, Paris, Suresnes, France, [13]Internal Medicine, Hôpital Saint Joseph, Marseille, France, [14]Internal Medicine, CHU Rouen, Rouen, France, [15]Nephrology and Internal Medicine, CH Valenciennes, Valenciennes, France, [16]Internal Medicine, Groupement hospitalier Tarbes-Lourdes, Tarbes, France, [17]Rheumatology, Université Bourgogne Europe, CHU Dijon Bourgogne, Dijon, France, [18]Internal medicine and vascular diseases, Hospices Civils de Lyon, Lyon, France, [19]Internal medicine, Nantes University Hospital, Nantes, France, [20]CHU de Nantes, Nantes, France, [21]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [22]Internal Medicine, Hôpital Bichat, APHP, Paris, France, [23]Internal Medicine, Saint Luc Saint Joseph Hospital, Lyon, France, [24]Internal Medicine, CH Annecy, Annecy, France, [25]Nephrology, CH Boulogne sur Mer, Boulogne sur Mer, France, [26]Internal Medicine, Hôpital d'instruction des armées Saint Anne, Toulon, France, [27]Internal Medicine, CHU Clermont Ferrand Gabriel Montpied, Clermont Ferrand, France, [28]Internal Medicine and Clinical Immunology, CH Saint Malo, Saint Malo, France, [29]Internal Medicine and Clinical Immunology, CHU Nancy, Nancy, France, [30]Internal Medicine, CHU Tours, Tours, France, [31]Internal Medicine, CHU Reims, Reims, France, [32]Internal Medicine, CHU Caean, Caen, France, [33]Cochin Hospital, Paris, France, [34]Hopital Cochin, Paris, France, [35]Pharmacy, CHU Dijon Bourgogne, Dijon, France, [36]Centre d'Investigation Clinique, CHU Dijon, Dijon, France ; INSERM, CIC 1432, Module Epidémiologie Clinique, Dijon, France, [37]Internal medicine and clinical immunology, Université Bourgogne Europe , CHU Dijon Bourgogne, Dijon, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside (0891–0896)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: This trial aimed to compare the efficacy and safety of methotrexate (MTX) vs. tocilizumab (TCZ), in combination with glucocorticoid (GC), in patients with giant cell arteritis (GCA).

Methods: METOGiA is an open label randomized controlled multicenter trial, with a non-inferiority design. Results from the first 78-week period are reported here, in which patients received either TCZ 162 mg/week subcutaneously (SC) or MTX 0.3 mg/Kg/week SC (without exceeding 20 mg/week) during 52 weeks in combination with a GC taper regimen (42 weeks for new onset GCA, 36 weeks for relapsing GCA). Eligible patients were aged ≥50 years, diagnosed with new-onset or relapsing GCA and had active GCA within 6 weeks before randomization. The primary endpoint was collected at week 78 (W78) and was the percentage of patients alive, without relapse after initial remission or deviation from the GC taper regimen from inclusion to W78. Secondary endpoints included the percentage of patients alive, without relapse after initial remission or

Table 1: exploratory results for secondary endpoints

	TCZ n=110	MTX n=108	Difference with 95% confidence interval*	superiority p-value**
Alive without relapse after initial remission or deviation from the GC taper regimen from inclusion to W52	77 (70%)	58 (54%)	16% [4%, 29%]	0.01
Alive without relapse from inclusion to W52	91 (83%)	72 (67%)	16% [5%, 27%]	0.006
Alive without relapse from inclusion to W78	63 (58%)	54 (50%)	8% [-5%, 21%]	0.25
Remission without prednisone at W52	88 (81%)	62 (60%)	21% [9%, 33%]	0.0007
Remission without prednisone at W78	54 (50%)	59 (58%)	-7% [-21%, 6%]*1	0.28
Remission with prednisone ≤ 5 mg/day at W52	94 (88%)	75 (74%)	14% [3%, 24%]	0.01
Remission with prednisone ≤ 5 mg/day at W78	59 (55%)	69 (68%)	-13% [-26%, 1%]*2	0.06
Cumulative dose of prednisone at W52 (mg, mean ± SD)	3168±909	3301±1266	-135 [-429, 160]	0.37
Cumulative dose of prednisone at W78 (mg, mean ± SD)	3595±1168	3723±1875	-228 [-646, 190]	0.28

*Dunnett & Gent method for percentages (significant MTX non-inferiority: *1with every margin > 1%, *2with every margin > 6%) and Satterthwaite method for means difference.
**Chi-2 or Student t-test

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

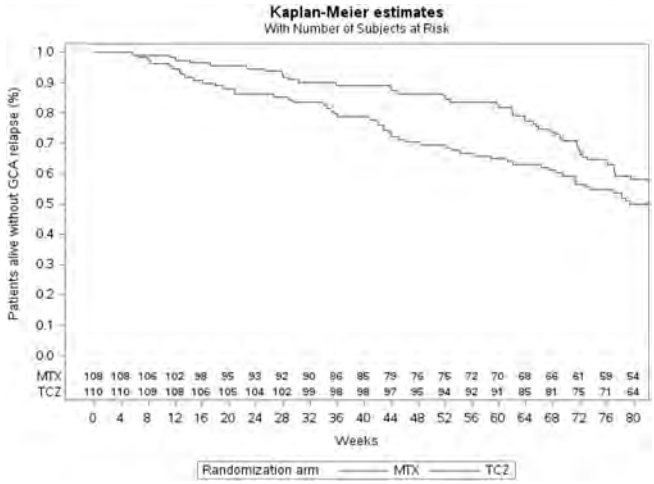


Figure 1: Relapse free survival (Kaplan-Meier estimates with number of subjects at risk)

deviation from the GC taper regimen from inclusion to W52; the percentages of patients in remission without prednisone or with prednisone ≤5mg/day at W52 and W78; the cumulative dose of prednisone at W52 and W78; and adverse events. Remission was defined as the absence of symptoms attributable to GCA and CRP≤10 mg/L. Relapse was defined as the recurrence of symptoms attributable to active GCA, whatever the value of CRP. Relapses were confirmed by an adjudication committee composed of 3 experts not participating to the study and blinded to the assigned study arm, CRP, ESR, fibrinogen and FBS values.

Results: A total of 230 patients were randomized in 39 French centers, among them 9 withdraw their consent and 3 were lost of follow up before reaching W78. Finally, 218 patients (TCZ, n=110; MTX, n=108) were analyzed in the intention-to-treat (ITT) population. GCA characteristics were balanced between groups, with 74% and 26% of patients having new-onset and relapsing GCA (TCZ: 77% and 23%; MTX: 71% and 29%), respectively. At W78, the primary endpoint was reached in 37% of MTX *vs*. 46% of TCZ patients, resulting in a 9% difference (95% CI: [-4%, 22%]), which did not meet the predefined non-inferiority margin of 20%. Thus, in the ITT population, MTX was not non-inferior to TCZ (P=0.054). However, TCZ was not superior to MTX at W78 (P=0.16). Results for secondary endpoints are detailed in **Table 1**. Relapse-free survival curves are depicted in **Figure 1**. By W78, 15 MTX-related SAEs occurred in 14 patients (8 infections, including 5 Pneumocystis infections, one of which was fatal) and 13 TCZ-related SAEs occurred in 11 patients (6 neutropenia, 3 infections). Seven deaths were reported at W78 (TCZ, n=1; MTX, n=6).

Conclusion: In the ITT population, MTX was not non-inferior to TCZ regarding the primary endpoint at W78, but was non-inferior for the remission rate with or without low-dose prednisone. At W52, results suggest that TCZ is more effective than MTX in maintaining remission and preventing relapse. These results must be confirmed by the per-protocol analysis (ongoing).

ClinicalTrials.gov identifier: NCT03892785

Disclosure: M. Samson: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2; **A. Bourredjem**: None; **R. Outh**: None; **V. Grobost**: None; **F. Lifermann**: None; **G. DIREZ**: None; **E. Ribeiro**: None; **E. Oziol**: None; **V. Devauchelle**: None; **M. Ebbo**: None; **N. Limal**: None; **R. Paule**: None; **B. Bienvenu**: None; **A. Poulet**: None; **S. Miranda**: None; **Y. Benhamou**: None; **T. Quemeneur**: Roche, 5; **C. Dingremont**: None; **A. Ramon**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, chugai, 2, Novartis, 2, 5; **B. Simorre**: None; **Q. Reynaud**: None; **C. AGARD**: None; **O. Espitia**: Novartis, 2; **A. Mekinian**: Roche, 5; **J. Alexandra**: Chugai France, 2; **E. Berthoux**: None; **L. Perard**: None; **A. Baudet**: None; **R. Mesbah**: None; **D. Lacôte-Delarbre**: None; **J. Stievenart**: None; **M. André**: None; **J. Allain**: None; **R. Jaussaud**: None; **J. Magnant**: None; **A. Servettaz**: None; **H. De Boysson**: AbbVie/Abbott, 1, 2, Chugai, 2, Fresenius Kabi, 1, 2, Novartis, 2;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

M. Ruivard: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **A. REGENT**: Novartis, 2; **A. Cransac**: None; **I. Fournel**: None; **H. Devilliers**: None; **B. Bonnotte**: Boehringer-Ingelheim, 2, Chugai, 2, Novartis, 2, Vifor Pharma, 2.

Abstract Number: 0892

Relapse and Immune Dysregulation in Giant Cell Arteritis Are Linked to Mosaic Loss of the Y Chromosome

Simon M. Petzinna, Sophie-Marie Kirch, Maike S. Adamson, De Xi, Claus-Jürgen Bauer, Lena Kreis, Pantelis Karakostas, Rayk Behrendt, Sebastian Zimmer, Raul N. Jamin and Valentin S. Schäfer, University Hospital Bonn, Bonn, Nordrhein-Westfalen, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside (0891–0896)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Mosaic loss of the Y chromosome (mLOY) is the most common acquired somatic mutation. Epidemiological studies have linked mLOY to malignancies, as well as cardiovascular and chronic kidney disease. Mechanistically, mLOY leads to the loss of epigenetic regulators on the Y chromosome, resulting in proinflammatory and profibrotic signaling. This evidence suggest a broader role for mLOY in age-related immune dysregulation and inflammation. In this context, giant cell arteritis (GCA) is a compelling candidate for further investigation, as it exclusively affects individuals over 50. This study is the first to assess the prevalence, clinical impact and pathophysiological consequences of mLOY in GCA.

Methods: Male patients with a diagnosis of GCA were enrolled. Demographic, clinical and imaging data were collected. Blood samples were obtained at the time of inclusion. Extraction and quantification of DNA was performed. Extent of mLOY was assessed using a digital droplet PCR with a SNP-based assay targeting a 6 bp difference between the AMELX and AMELY genes. The extent of mLoY was calculated as 1 – [AMELY]/[AMELX]. Cytokine concentration in the blood serum of GCA patient were assessed using the LEGENDplex™ Human Inflammation Panel 1.

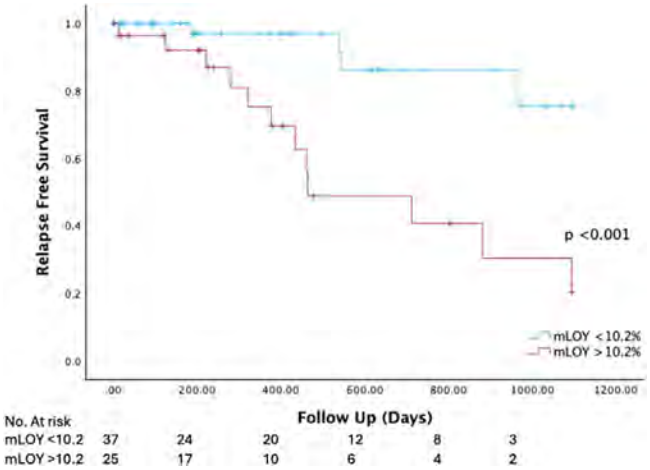


Figure 1: Survival Analysis for Predicting Relapse in Patients with Giant Cell Arteritis Figure 1 depicts the relationship between mLOY burden and relapse risk in GCA patients. Kaplan-Meier survival analysis demonstrates that patients with mLOY >10.2% had a significantly higher relapse risk ($p < 0.001$, univariate log-rank test) and a shorter median relapse-free survival (647 days [95% CI: 468–827]) compared to those with mLOY <10.2% (992 days [95% CI: 898–1,087]; $p < 0.001$). Abbreviations: GCA = giant cell arteritis, mLOY = mosaic loss of Y chromosome, No. = number.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

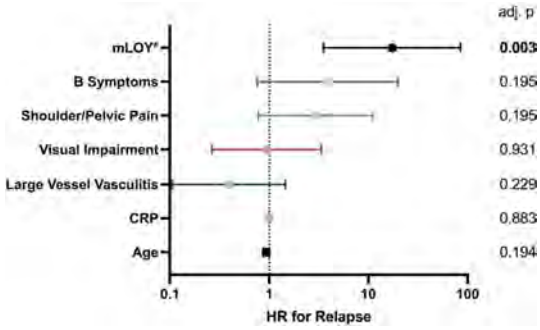


Figure 2: Cox Regression Analysis for Risk Factors Associated with Relapse in Giant Cell Arteritis This figure presents a Forest Plot summarizing the Cox regression analysis of relapse risk in patients with GCA, adjusting for factors potentially associated with relapse risk. The model included seven variables: age, mLOY burden > 10.2 %, CRP levels, visual impairment, constitutional symptoms (fever, night sweats, weight loss), large vessel vasculitis (LVV), and shoulder or pelvic pain. Abbreviations: Constit. Symptoms = constitutional sympttoms, HR = hazard ratio, mLOY = mosaic

Results: A total of 74 male patients with GCA (mean age 76.6 ± 10.7 years) were enrolled. At time of inclusion, 25.7% (19/74) exhibited active disease. During a mean follow-up of 599 ± 607 days, 24.3% (18/74) experienced at least one relapse, with a median time to relapse of 361 days (95% CI: 56.2–1470). The median mLOY burden was 17.8% (±23.7%). Receiver operating characteristic (ROC) analysis and Youden's index identified an optimal mLOY threshold of 10.2% for relapse prediction (AUC: 0.706, p = 0.006) with 39.2% (29/74) exceeding this threshold. Within three years, 43.1% of patients with mLOY >10.2% relapsed compared to 8.7% with mLOY < 10.2% (p < 0.001, Kaplan–Meier log-rank test). Median relapse-free survival was 647 days (95% CI: 468–827) for mLOY >10.2%, versus 992 days (95% CI: 898–1,087) for mLOY < 10.2%. In multivariable Cox regression adjusted for age and clinical covariates, mLOY >10.2% emerged as the only independent predictor of relapse (HR: 17.4; 95% CI: 3.5–86.0; p = 0.003). Multiplex cytokine analysis revealed a significant association between mLOY burden an IL-6 levels (p = 0.045, r = 0.24) in the overall cohort. Among patients in remission (n = 45), those with mLOY >10.2% had significantly higher IL-6 levels than those with lower mLOY (p = 0.010). In patients in remission receiving tocilizumab (n = 32), mLOY burden was associated with both IL-6 (p = 0.002, r = 0.54) and IL-17A (p = 0.026, r = 0.40).

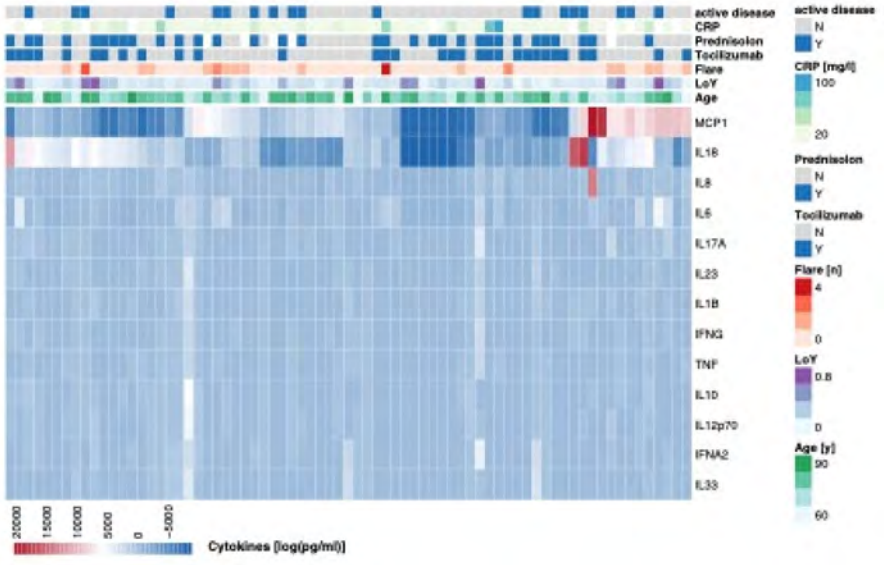


Figure 3: Inflammatory Cytokine Profile, Mosaic Loss of the Y Chromosome, and Clinical Parameters in Patients with Giant Cell Arteritis. Figure 3 depicts inflammatory cytokines measured by LegendPlex shown as heatmap. Clinical parameters are depicted above columns. In the overall cohort, mLOY as a continuous variable was positively associated with IL6 (p = 0.045). * = p<0.05 indicates statistical significance, Abbreviations: CRP= C-reactive protein, DA = disease activity, GCA = giant cell arteritis, IL = interleukin, Predn. = prednisolone, TCZ = tocilizumab, mg = milligram, mLoY = mosaic loss of the Y chromosome, N=no, Y=yes, y = years.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This is the first study to identify mLOY as a strong and independent predictor of relapse in male GCA patients, with a threshold of 10.2% mLOY burden associated with significantly reduced relapse-free survival. Elevated mLOY levels correlated with proinflammatory signaling, including increased IL-6 and IL-17A expression, particularly in patients receiving tocilizumab. Our findings suggest that mLOY may play an active role in the immunopathogenesis of GCA and serve as a prognostic biomarker to stratify patients at high risk of relapse.

Disclosure: S. Petzinna: None; **S. Kirch**: None; **M. Adamson**: None; **D. Xi**: None; **C. Bauer**: None; **L. Kreis**: None; **P. Karakostas**: None; **R. Behrendt**: None; **S. Zimmer**: None; **R. Jamin**: None; **V. Schäfer**: None.

Abstract Number: 0893

Transcriptomic insights into GCA compared to clinically diverse controls: Inflammation, Aging, Therapeutic Targets and the role of SPP1 in the temporal artery

Ingrid Lindquist[1], Alisha Eskew[2], Dongsoek Choi[3], David Wilson[4], Diva Salomao[5], Hillary Stiefel[4], Daniel Albert[4], Kiana Vakil-Gilani[6], Daniela Ghetie[7], James Rosenbaum[8] and Marcia Friedman[9], [1]Portland VA Medical Center, Portland, OR, [2]OHSU, Portland, OR, [3]OHSU, Portland, [4]Casey Eye Institute OHSU, Portland, OR, [5]Mayo Clinic, Rochester, MN, [6]PeaceHealth, Portland, OR, [7]OHSU, Lake Oswego, OR, [8]Legacy Devers Eye Institute, Portland, OR, [9]Immpact Bio, Beaverton, OR

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside (0891–0896)

Session Type: Abstract Session

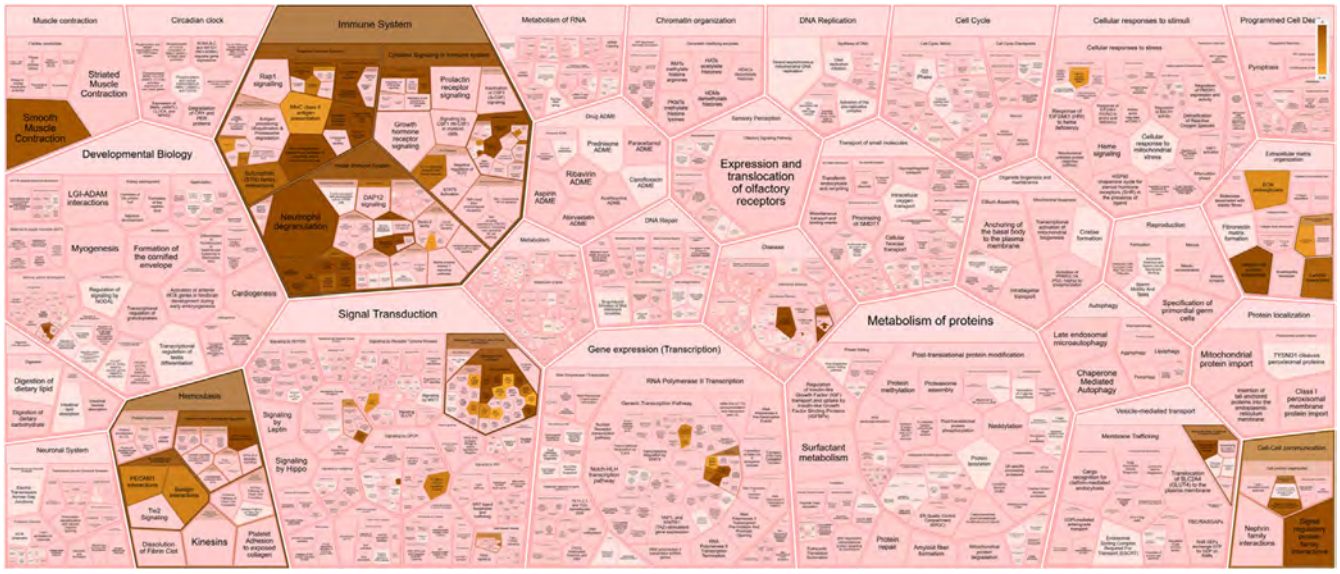
Session Time: 10:00AM–11:30AM

Background/Purpose: Giant cell arteritis (GCA) is the most common vasculitis in people over 50 years old and is a clinical diagnosis bolstered by non-specific inflammatory markers and variable pathologic findings on temporal artery biopsy (TAB). Patients with diseases that mimic GCA may undergo TAB during their workup, including those with atherosclerosis, infection, other autoimmune diseases, or simply older people with a new headache. Here we focus on the transcriptional differences in biopsy-positive GCA cases from clinically diverse controls at the level of the temporal artery.

Methods: We collected 46 TABs that were obtained during clinical care from 16 biopsy-positive GCA cases and 30 controls - polymyalgia rheumatica (3), rheumatoid arthritis (1), relapsing polychondritis (1), and granulomatosis with polyangiitis (2), infections (2), atherosclerosis (5), or an older person with new headache (16). Tissue was sequenced in bulk with RNAseq and analyzed for differential gene expression with edgeR with batch-effect correction with RUVseq and controlled for sex and age. Subsequent pathway enrichment was performed with Reactome and results were explored with data from the Human Aging Genomic Resource (HAGR) and the drug-gene interaction database (DGIdb).

Results: We found 2,279 genes to be significantly differentially expressed (DE) in biopsy-positive GCA cases compared to controls. Fifty-three pathways were enriched with an adjusted p-value < 0.05 (Fig. 1) and belonged largely to cytokine signaling (interleukin, interferon), neutrophil degranulation, cell-cell interaction (antigen presentation, integrin pathways, Fc receptor mediated signaling), and vascular activity (cell surface interactions at the vascular wall and hemostasis). Next, we found that 201 of our DE genes (8.8%) have been implicated in aging processes (HAGR). Among these is the secreted phosphoprotein 1 (*SPP1*) gene, also known as *osteopontin*, which had the largest expression fold change in cases vs controls (logFC: 6.23) in our data. *SPP1* is expressed in several immune cells, including macrophages, and is an important mediator of immune cell recruitment, migration and adhesion, macrophage activation and polarization, stimulation of inflammatory

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Fifty-three (53) pathways are significantly enriched with an false discovery rate (FDR) p-value <0.05 and belong largely to cytokine signaling (interleukin, interferon), neutrophil degranulation, cell-cell interaction (antigen presentation, integrin pathways, Fc receptor mediated signaling), and vascular activity (cell surface interactions at the vascular wall and hemostasis). Darker color corresponds with greater statistical significance (lower FDR p-value). Analysis and rendering performed at Reactome.org.

cytokines and tissue fibrosis. *SPP1* activates pathways of IL-6, IL-17, Jak/Stat, IFNγ, NFkB/ERK and granulomatous inflammation. In 2017, Prieto reported high *osteopontin* serum levels in GCA and suggested it as disease activity biomarker that is not suppressed by tocilizumab. Last, we found 705 of our genes linked to 5,824 established drugs in DGIdb, 1,564 of which are approved for use. Seventeen of these drugs were highly linked to our data (connected to 20+ genes). Fifteen drugs directly link to *SPP1*.

Conclusion: Our study recapitulates the roles of inflammation, aging and immune dysregulation in the pathophysiology of GCA that notably remain significant even with clinically diverse controls. We highlight several likely pathologic roles of *SPP1* in GCA, a gene which has not yet featured prominently in the field of GCA but may well be a key disease activity biomarker and therapeutic target. Finally, our data have provided a rich source of candidate drugs currently on the market that may effectively treat GCA.

Disclosure: I. Lindquist: None; **A. Eskew**: None; **D. Choi**: None; **D. Wilson**: None; **D. Salomao**: None; **H. Stiefel**: None; **D. Albert**: None; **K. Vakil-Gilani**: None; **D. Ghetie**: Amgen, 2, Revolo Biotherapeutics, 2; **J. Rosenbaum**: None; **M. Friedman**: alpine immune sciences, 3, lyell immunopharma, 3.

Abstract Number: 0894

Altered B Cell Subpopulations in Giant Cell Arteritis

Maria-Eugenia Miranda-Carus[1], Beatriz Nieto-Carvalhal[2], Irene Monjo Henry[1], Sara García-Carazo[3] and Eugenio de Miguel[1], [1]Hospital Universitario La Paz, Madrid, Spain, [2]Hospital Universitario La Paz, Mdrid, [3]Hospital La Paz, Madrid

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside (0891–0896)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Giant cell arteritis (GCA), a large-vessel granulomatous vasculitis, has been considered as a T cell-dependent condition. Interestingly, tertiary lymphoid structures, B cell and plasma cell infiltrates have been observed in the inflamed GCA arteries, together with an altered B cell homeostasis. This suggests that B cells can also play a role in GCA pathogenesis. Therefore, our objective was to examine the frequencies of circulating B cell subpopulations in the peripheral blood of patients with newly diagnosed GCA (nGCA).

Methods: Prospective non-interventional study on consecutive patients referred to our ultrasound (US) GCA fast track clinic, in whom newly diagnosed GCA (nGCA) was clinically confirmed (2022 ACR/EULAR criteria) over a period of 36 months. Peripheral blood was drawn immediately upon initial diagnosis and after obtaining written informed consent. For each patient, an age and gender-matched healthy control (HC) was also studied. PBMCs isolated by Ficoll- Hypaque were stained with antibodies to CD19, CD20, CD27, CD24 and CD38, and examined by flow cytometry. Patients were treated with standard therapy according to the updated 2018 EULAR recommendations.

Results: As compared with HC (n=88), nGCA patients (n=88) demonstrated significantly decreased numbers of circulating CD19+ B cells. These B cells demonstrated an altered subpopulation profile, with augmented proportions of CD19+-CD27-IgD+ naïve, CD19+CD27- IgD- double negative and CD19+CD27+CD20-CD38hi plasmablasts; at the same time, the proportions of CD19+CD27+IgD+ unswitched memory and CD19+CD27+IgD- switched memory B cells were significantly decreased whereas the proportion of circulating CD19+CD24hiCD38hi transitional B cells was not different to that observed in HC. All of these B cell population frequencies were comparable among the nGCA subgroups [cranial, large vessel or mixed (cranial + large vessel)], and in patients with or without associated polymyalgia rheumatica. Fourty-four nGCA patients donated blood for a second time, 6 months after treatment initiation. At that time, a rise in the circulating total B cell numbers, above that observed at baseline, was detected. In parallel, significant reductions in the proportions of circulating naïve B, transitional B cells and plasmablasts were apparent, together with an increase of CD27+ unswitched and switched memory B cells. Among the 46 patients who could be followed-up for 12 months, 19 experienced a relapse. Strikingly, the baseline numbers of circulating total CD19+ B cells had been significantly lower in patients who did not relapse as compared with those who relapsed; moreover, when examining separately the time-course evolution of these two groups, it was evident that only patients who did not experience a relapse demonstrated a rise of their CD19+ B cell numbers, whereas these numbers did not vary in those who relapsed.

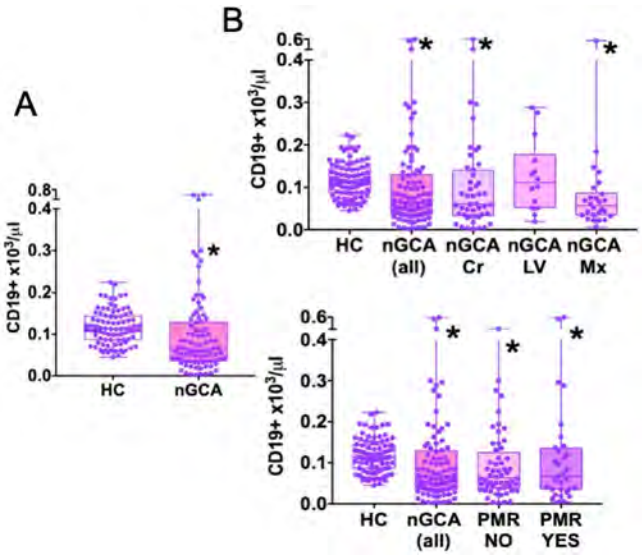


Figure 1. Absolute numbers of circulating CD19+ B cells in nGCA patients and HC.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

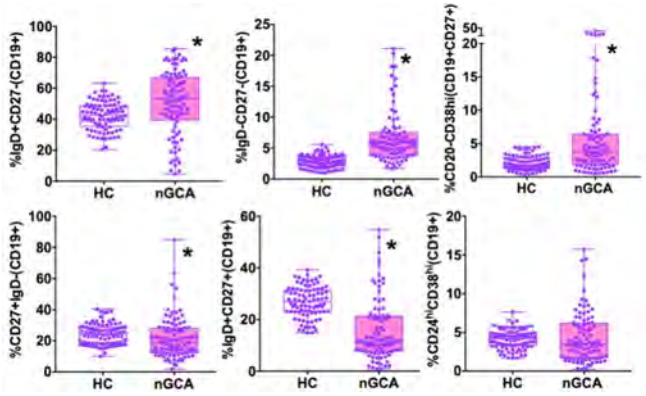


Figure 2. Frequency of circulating B cell subpopulations in nGCA patients and HC

Conclusion: Patients with nGCA demonstrate a profoundly altered B cell profile at baseline that dynamically varies along the course of the disease. This points to the implication of B cells in GCA pathogenesis and may contribute to the design of personalized therapeutic strategies.

Disclosure: M. Miranda-Carus: None; **B. Nieto-Carvalhal**: None; **I. Monjo Henry**: None; **S. García-Carazo**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6.

Abstract Number: 0895

Impact of Glucocorticoid Tapering in Giant Cell Arteritis: Analysis From the SELECT-GCA Trial

FRANK BUTTGEREIT[1], Kevin Winthrop[2], Leonard Calabrese[3], Ivan Lagunes[4], Aditi Kadakia[5], Ana Romero[6], Shaofei Zhao[4], Weihan Zhao[4], Arathi Setty[4] and Jeffrey Curtis[7], [1]Charité University Medicine Berlin, Berlin, Berlin, Germany, [2]Oregon Health & Science University, Portland, OR, [3]Cleveland Clinic, Cleveland, OH, [4]Abbvie Inc, North Chicago, IL, [5]AbbVie Inc, Woburn, MA, [6]AbbVie, Barcelona, Spain, [7]University of Alabama at Birmingham, Birmingham

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside (0891–0896)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

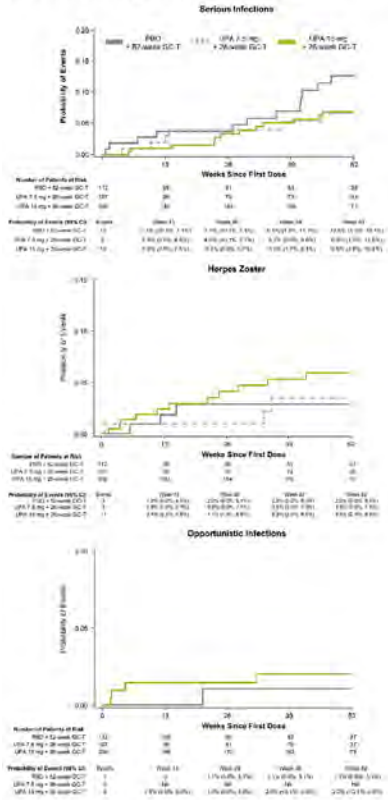
Background/Purpose: This study assessed the occurrence of adverse events of serious infections, herpes zoster, and opportunistic infection during concomitant treatment with GCs and after GC tapering in patients with GCA receiving UPA or PBO in the SELECT-GCA trial.

Methods: Patients in this analysis from SELECT-GCA[1] were diagnosed with new-onset or relapsing GCA, had previous exposure to ≥40 mg prednisone (or equivalent) daily, and were on a baseline prednisone dose of ≥20 mg daily. Kaplan-Meier method was used to analyze adverse events through week 52, presented as time to first event (patients with no events were censored at the end of the study period). Event rates were calculated for data from patients with ≥1 event of the same type.

Results: Baseline characteristics of the treatment groups were similar.[1] Baseline GC doses for UPA were: 20 mg (30%, n=95); 30 mg (22%, n=70); 40 mg (29%, n=91); 50 mg (10%, n=32); 60 mg (9%, n=28). Baseline GC doses were similarly distributed for PBO: 20 mg (27%, n=30); 30 mg (26%, n=29); 40 mg (28%, n=31); 50 mg (14%, n=16); 60 mg (5%, n=6).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Time to First Event of Serious Infections, Herpes Zoster, and Opportunistic Infections During Glucocorticoid Taper



GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.
No opportunistic infection events were reported in the UPA 7.5 mg group.
[a]Excludes herpes zoster.

Table 1. Treatment-Emergent Serious Infections Through Week 52 by Time Period and Starting Dose of Glucocorticoid Taper[a,b]

n (%) [Subgroup N]	PBO + 52-wk GCT N = 112	UPA 7.5 mg + 26-wk GC-T N = 107	UPA 15 mg + 26-wk GC-T N = 209
Overall	12 (10.7) [112]	6 (5.6) [107]	12 (5.7) [209]
20 mg	1 (0.9) [30]	2 (1.9) [33]	1 (0.5) [62]
30 mg	3 (2.7) [29]	2 (1.9) [22]	5 (2.4) [48]
40 mg	4 (3.6) [31]	1 (0.9) [31]	2 (1.0) [60]
50 mg	2 (1.8) [16]	1 (0.9) [13]	2 (1.0) [19]
60 mg	2 (1.8) [6]	0 [8]	2 (1.0) [20]
≤ Week 26	4 (3.6) [112]	4 (3.7) [107]	6 (2.9) [209]
20 mg	0 [30]	2 (1.9) [33]	0 [62]
30 mg	1 (0.9) [29]	1 (0.9) [22]	3 (1.4) [48]
40 mg	2 (1.8) [31]	1 (0.9) [31]	0 [60]
50 mg	0 [16]	0 [13]	1 (0.5) [19]
60 mg	1 (0.9) [6]	0 [8]	2 (1.0) [20]
> Week 26	8 (7.1) [112]	2 (1.9) [107]	7 (3.3) [209]
20 mg	1 (0.9) [30]	0 [33]	1 (0.5) [62]
30 mg	2 (1.8) [29]	1 (0.9) [22]	3 (1.4) [48]
40 mg	2 (1.8) [31]	0 [31]	2 (1.0) 60]
50 mg	2 (1.8) [16]	1 (0.9) [13]	1 (0.5) [19]
60 mg	1 (0.9) [6]	0 [8]	0 [20]

GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.

[a]Treatment-emergent events were defined as any adverse events with an onset date that is on or after the first dose of study drug, and no more than 30 days after the last dose of study drug.

[b]Patients were counted once in each row, regardless of the number of events they may have experienced.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rates of serious infections were lower with both doses of UPA than PBO through week 52 (UPA7.5, 7.9 [95% CI: 3.2, 16.3]; UPA15, 7.9 [4.3, 13.2]; PBO 12.7 [6.6, 22.2] events per 100 patient-years [E/100 PY]). Herpes zoster, a known risk for JAK inhibitors including UPA, had higher rates with UPA15 vs PBO (7.3 [95% CI: 3.9, 12.5] E/100 PY vs 4.2 [1.2, 10.9] E/100 PY) or UPA7.5 (4.5 [1.2, 11.6] E/100 PY). Rates of opportunistic infections were low in all groups, although numerically higher in the UPA15 group compared to PBO (2.2 [95% CI: 0.6, 5.8] E/100 PY vs 1.1 [0, 5.9] E/100 PY); no opportunistic infections were reported for UPA7.5.

In UPA-treated patients, rates of serious infections were comparable across during the GC-taper period (difference ≤ week 26 for UPA – PBO: 0.3 [95% CI: -5.8, 6.4] and -0.3 [-5.4, 4.8] E/100 PY for UPA7.5 and UPA15. Rates of serious infections were lower in the post-taper period with UPA7.5 or UPA15 relative to PBO (treatment difference from > week 26 to week 52: UPA7.5, -5.1 [95% CI: -12.1, 1.9] and UPA15, -4.6 [-11.1, 2.0] E/100 PY). Rates of herpes zoster were similar in UPA-treated patients during the GC taper (treatment difference for UPA – PBO: UPA7.5, -3.1 [95% CI: -7.8, 1.6] and UPA15, 1.4 [-4.0, 6.8] E/100 PY) and post-GC taper (treatment difference: 3.4 [95% CI: -0.4, 7.2] and 1.7 [-0.2, 3.6] E/100 PY). Of the 4 opportunistic infections in UPA15, 3 events occurred during the GC taper and 1 occurred post-taper.

Conclusion: The rate of serious infection through 52 weeks was lower in patients treated with UPA combined with a 26-week GC taper versus PBO with a 52-week GC taper, with rates lower with UPA relative to PBO after tapering GCs in the UPA groups. The decrease in serious infection rates during the GC-free phase suggests GC use may contribute to the risk of serious infections. GC tapering did not appear to affect the occurrence of HZ in the UPA groups. These results support the use of UPA15 with a standardized approach to GC tapering to reduce GC burden in older populations with an elevated infection risk.

References:

1. Blockmans D, et al. *N Engl J Med*. 2025 Apr 2. doi: 10.1056/NEJMoa2413449.

Disclosure: F. BUTTGEREIT: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6; **K. Winthrop**: AbbVie/Abbott, 2, AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly and Company, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Moderna, 2, Novartis, 2, Pfizer, 2, 5, Regeneron, 2, Roche, 2, Sanofi, 2, Union Chimique Belge, 2; **L. Calabrese**: AbbVie, 2, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, Fate Therapeutics, 2, Galvani, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, 6, Mymee, 2, Open Evidence, 2, PPD, 2, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6; **I. Lagunes**: AbbVie, 3, 11; **A. Kadakia**: AbbVie, 3, 11; **A. Romero**: AbbVie/Abbott, 3; **S. Zhao**: AbbVie, 3, 11; **W. Zhao**: AbbVie, 3, 11; **A. Setty**: AbbVie, 3, 11; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, Janssen, 5, Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi/Regeneron, 2, 5, UCB, 2, 5.

Abstract Number: 0896

Does complement product C5a and its receptor C5a receptor 1 play a role in giant-cell arteritis?

marc Corbera-bellalta[1], Nuria Farran-Centelles[2], Nina Visocnik[1], Sergio Prieto-Gonzalez[3], Jose hernandez-rodriguez[4], javier Marco-hernandez[5], Georgina Espigol-Frigolé[1] and **Maria Cid**[6], [1]Hospital Clínic. University of Barcelona. IDIBAPS., Barcelona, Spain, [2]Autoimmune diseases, Barcelona, Spain, [3]Hospital Clinic, Barcelona, Catalonia, Spain, [4]Hospital Clinic. University of Barcelona. IDIBAPS, Barcelona, Catalonia, Spain, [5]Hospital Clinic.University of Barcelona. IDIBAPS, Barcelona, Catalonia, Spain, [6]Department of Autoimmune Diseases (member of European Reference Network RITA),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Hospital Clinic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

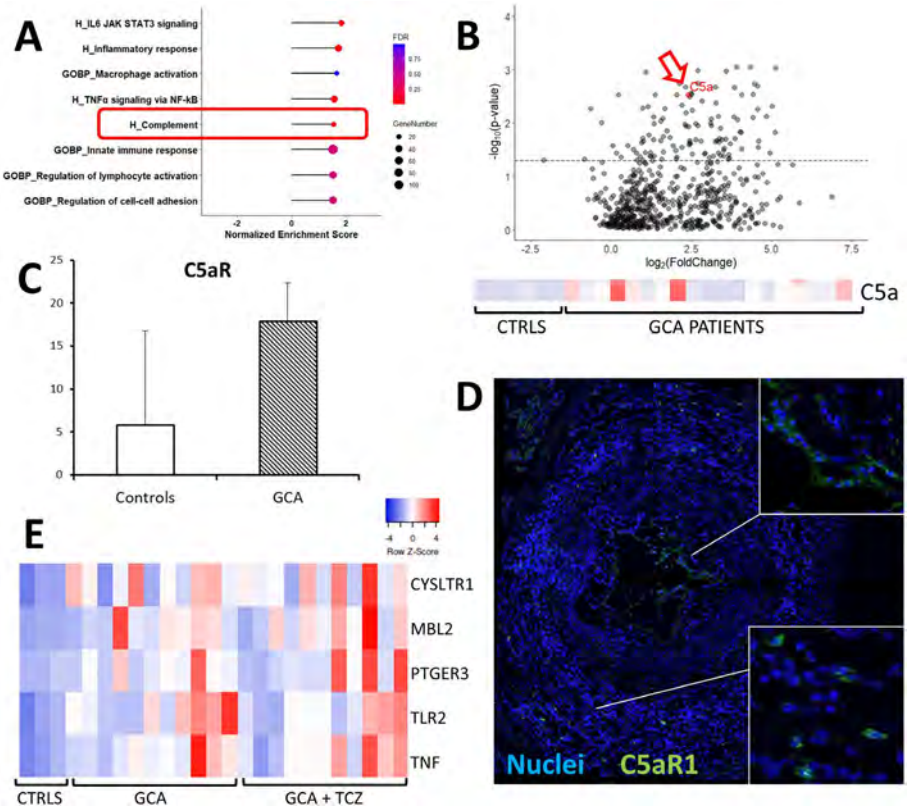
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA From Bench to Bedside (0891–0896)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Patients with giant-cell arteritis (GCA) are in an unmet need for reduction of GC exposure because of the high incidence of GC-related side effects in the elderly. Blocking C5a receptor 1 (C5aR1) with avacopan has allowed extreme minimization of GC exposure in ANCA-associated vasculitis. The complement system has not been investigated in GCA.

Aims: 1) to perform a transcriptomic analysis of cultured temporal artery biopsies from patients with GCA and controls 2) to perform a proteomic analysis of the supernatants of cultured arteries 3) to explore the expression in tissue of the C5aR1 4) to interrogate the transcriptomic data searching for transcripts regulated by C5aR1 signaling and the impact of blocking IL-6 receptor with tocilizumab (TCZ) on their expression.

Methods: Nanostring nCounter Human Inflammation Panel was applied to RNA extracted from ex-vivo cultured arteries (from 11 patients with GCA and 3 controls) with or without exposure to TCZ. Protein array (Ray-Biotech, 640 proteins) was applied to the corresponding supernatants. RT-PCR of C5aR1 was performed in frozen arteries from 10 patients with GCA and 10 controls and in cultured myofibroblasts alone or exposed to PBMCs. C5aR1 protein expression was explored by immunofluorescence. nCounter barcode counts were processed with nSolver 4.0 software. Normalized data were analyzed using R-Studio 4.0.3



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Transcriptomic analysis revealed up-regulation of complement pathways in arterial samples from patients with GCA (fig 1A). C5a was present in the supernatants of cultured GCA arteries and virtually absent in control arteries (fig1B). C5aR1 was overexpressed in temporal arteries from patients with GCA compared to controls (fig1C) and was expressed by inflammatory cells, endothelial cells and scattered vascular smooth muscle cells (fig1D).

Primary myofibroblasts derived from temporal arteries expressed C5aR1 when co-cultured with PBMCs. We interrogated the nanostring results in search for transcripts regulated by AP-1 (in the signalling cascade driven by C5aR1) but not regulated by transcription factors in the classical IL-6,IFNγ or GM-CSF cytokine signaling, based on ENCODE transcription factor targets dataset. 13 genes explored in the Human Inflammation panel had potential binding sites for AP-1 complex but not for STAT3, STAT1, STAT5 or SPI1). Of those, CYSLTR, MBL2, PTGER3, TLR2 and TNF transcripts were increased in samples from patients with GCA compared to controls and, in our experimental conditions, were not down-regulated by TCZ (fig1E)

Conclusion: Complement pathways are activated in GCA and C5a is present in the supernatant of cultured GCA arteries, indicating local processing of complement molecules. C5aR1 is expressed in GCA-involved arteries by inflammatory and stromal cells, suggesting a role in vascular remodeling. Transcripts regulated by C5aR1 (but not regulated by other cytokines present in GCA) were overexpressed in GCA and are not modulated by TCZ. Our findings suggest that blocking C5aR1 may contribute to abrogate inflammatory pathways in GCA. Exploring the transcriptomic and functional impact of C5aR1 inhibitor avacopan on cultured temporal arteries is in progress.

Disclosure: m. Corbera-bellalta: None; **N. Farran-Centelles**: None; **N. Visocnik**: None; **S. Prieto-Gonzalez**: None; **J. hernandez-rodriguez**: None; **j. Marco-hernandez**: None; **G. Espigol-Frigolé**: CSL-Vifor, 1, 6, GlaxoSmithKlein(GSK), 1, 2, 5, 6; **M. Cid**: AbbVie, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL-Vifor, 2, 6, GSK, 2, 6, Kiniksa Pharmaceuticals, 5, UpToDate, 9.

Abstract Number: 0897

APECED Disease Reorganizes the B Cell Compartment Toward Alternatively Activated Subsets

william Galbavy, Hyunjin Kim, Brian Klotz, Marine Malbec, Carley Tasker, Eva Conde, Andrea Vecchione, Seblewongel Asrat, Benjamin Daniel, Weikeat Lim, **Andre Limnander** and Jamie Orengo, Regeneron, Tarrytown, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune PolyEndocrinopathy Candidiasis Ectodermal Dystrophy (APECED) is a rare syndrome of multi-organ autoimmunity driven by the presence of self-reactive T cells and autoantibodies caused by mutations in the gene Autoimmune regulator (Aire). Compared to the well-defined role of Aire in establishing and maintaining T cell central tolerance by helping medullary thymic epithelial cells eliminate self-reactive T cells, less is known about how Aire deficiency in APECED impacts B cells and causes a breakdown in peripheral B cell tolerance.

Methods: We performed single-cell sequencing analyses, flow cytometry, and autoantibody profiling of PBMCs and serum of 10 APECED patients and 10 controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We found robust changes in the B cell compartment of APECED patients relative to that of healthy donors, with a substantially lower percentage of naïve B cells and significant increases in antigen-experienced B cell phenotypes. Among these changes seen by scRNAseq compositional analysis were increases in Memory B cells (TACI+ CD27+), and Atypical B cells (CD21lo CD11c+ Tbet+). Serum autoantibody profiling with an array of ~23,000 proteins uncovered >200 APECED associated IgG autoantibody varieties, including to type I IFN, IL17, key enzymes including the cytochrome P450 family, neurotransmitter associated proteins, and others. The Atypical B cell subset in patients was found to be especially correlated to levels of IgG autoantibodies, and had a molecular signature enriched in antigen presentation and B cell activation genes.

Conclusion: These results demonstrate that the B cell compartment is altered in APECED patients relative to healthy controls, with a marked increase in multiple activated B cell subsets that may contribute to autoantibody production and disease manifestations.

Disclosure: w. Galbavy: Regeneron, 3, 11; **H. Kim**: Regeneron, 3, 11; **B. Klotz**: Regeneron, 3, 11; **M. Malbec**: Regeneron, 3, 11; **C. Tasker**: Regeneron, 3, 11; **E. Conde**: Regeneron, 3, 11; **A. Vecchione**: Regeneron, 3, 11; **S. Asrat**: Regeneron, 3, 11; **B. Daniel**: Regeneron, 3, 11; **W. Lim**: Regeneron, 3, 11; **A. Limnander**: Regeneron, 3, 11; **J. Orengo**: Regeneron, 3, 3, 11, 11.

Abstract Number: 0898

Distinct B Cell and Plasma Cell Immunosuppression Strategies Eliminate Antigen-Specific Cells of the B Lineage

Carley Tasker[1], Nicholas Giovannone[2], Nyanza Rothman[2], Sofia Caruso[2], Julia Provino[2], Laura Johnsen[2], Johanna Napetschnig[2], Jamie Orengo[1], Christos Kyratsous[2], Andre Limnander[1], Katherine Cygnar[2] and Andrew Baik[2], [1]Regeneron, Tarrytown, NY, [2]Regeneron Pharmaceuticals, Tarrytown

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Development of effective targeting strategies to eliminate sources of antibody production presents utility in the treatment of autoimmune diseases driven by pathogenic autoantibodies. Furthermore, targeting antibody producing cells has potential benefit in settings where a pre-existing antibody response might hinder delivery of a therapeutic agent. To test the impact of B-lineage targeting approaches on a specific antigen-specific antibody response, we utilized an adeno-associated viral (AAV) model of *in vivo* gene transfer. Adeno-associated viral (AAV) vectors have emerged as safe and effective vehicles for *in vivo* gene transfer, yet, the full potential of AAV gene therapies has so far been limited by the either pre-existing or the development of host neutralizing antibodies (nAbs) against AAV capsid. Strategies to overcome anti-drug antibody responses have the potential to vastly expand the utility and accessibility of therapies limited by preexisting nAbs, in addition to potential for use in autoimmune diseases driven by pathogenic antibodies.

Methods: We tested if anti-AAV antibodies could be eliminated *in vivo* by plasma cell depletion with Linvoseltamab, a fully-human T cell-bridging bispecific antibody targeting B cell maturation antigen and CD3 (BCMAxCD3), either alone or in combination with B cell depletion (to eliminate additional sources of anti-AAV Abs) and/or therapeutic FcRn blockade (to accelerate serum IgG clearance). To model a scenario of strong pre-existing AAV immunity, we first treated dual CD3-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and BCMA-humanized mice with AAV8 to induce high-titer anti-AAV Abs. Ten weeks later, we administered weekly doses of BCMAxCD3, anti-CD19/20 antibodies, and/or an FcRn blocking therapeutic and monitored anti-AAV IgG titers for five weeks.

Results: Mice treated with both BCMAxCD3 and FcRn blocker showed rapid anti-AAV IgG titer reductions to naïve or near-naive levels, and mice additionally treated with anti-CD19/20 antibodies universally exhibited undetectable titers after five weeks of treatment. Whereas treatment with BCMAxCD3, anti-CD19/20, or FcRn blocker alone elicited only minor titer reductions. Strikingly, upon administration of a second distinct AAV8 vector, 3/6 mice receiving BCMAxCD3 + FcRn blocker and 6/6 mice receiving all three agents achieved re-transduction at levels equivalent to seronegative control mice.

Conclusion: Collectively, these results suggest plasma cell depletion with BCMAxCD3 (+ FcRn blockade) can successfully target sources of antibody production and thereby eliminating a preexisting antigen-specific antibody response. Efficacy was further improved when combined with B cell depletion. Findings from this study provides insight into optimal strategies for durably eliminating an antigen-specific antibody response.

Disclosure: C. Tasker: Regeneron, 3, 11; **N. Giovannone**: Regeneron, 3, 11; **N. Rothman**: Regeneron, 3, 11; **S. Caruso**: Regeneron, 3, 11; **J. Provino**: Regeneron, 3, 11; **L. Johnsen**: Regeneron, 3, 11; **J. Napetschnig**: Regeneron, 3, 11; **J. Orengo**: Regeneron, 3, 3, 11, 11; **C. Kyratsous**: Regeneron, 3, 11; **A. Limnander**: Regeneron, 3, 11; **K. Cygnar**: Regeneron, 3, 11; **A. Baik**: Regeneron, 3, 11.

Abstract Number: 0899

Altered B Cell Subsets Shared in Immune Checkpoint Inhibitor Associated Sicca Syndrome and Sjogren's Disease

Caroline Atlas[1], Balakrishnan Kamaraj[1], Omid Jamshidi[1], Adam Mor[1], Yevgeniya Gartshteyn[2], Teja Kapoor[3] and Robert Winchester[1], [1]Columbia University, New York, NY, [2]Columbia University Medical Center, Glen Rock, NJ, [3]Columbia University Irving Medical Center, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sicca symptoms may develop in the setting of immune checkpoint inhibitor (ICI) therapy and are clinically indistinguishable from those encountered in Sjogren's disease (SjD). B cells are known to play a role in the pathogenesis of SjD and ICI adverse events. We characterized peripheral B cell subsets in patients with these conditions to uncover potential mechanisms of immune dysregulation.

Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from 6 patients (1 healthy control, 1 patient with ICI-sicca syndrome, 4 patients with SjD) and analyzed by flow cytometry. We defined CD19 B-cell subsets on the basis of IgD, CD27, CD24 and CD38. Cells were gated as naïve (further subdivided into Transitional 1, 2, and 3), Unswitched/marginal-zone-like, Class-switched/Plasmablasts and Double Negative.

Results: In the differentiated mature B cell compartment (CD27+ IgD–), CD38 ^{hi} Plasmablasts and Class-Switched Memory B cells were decreased in all patients as compared to the control (14.4%±5.7 in SjD vs 8.4% in ICI sicca syndrome vs 40.4% in the control) (Figure 1)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

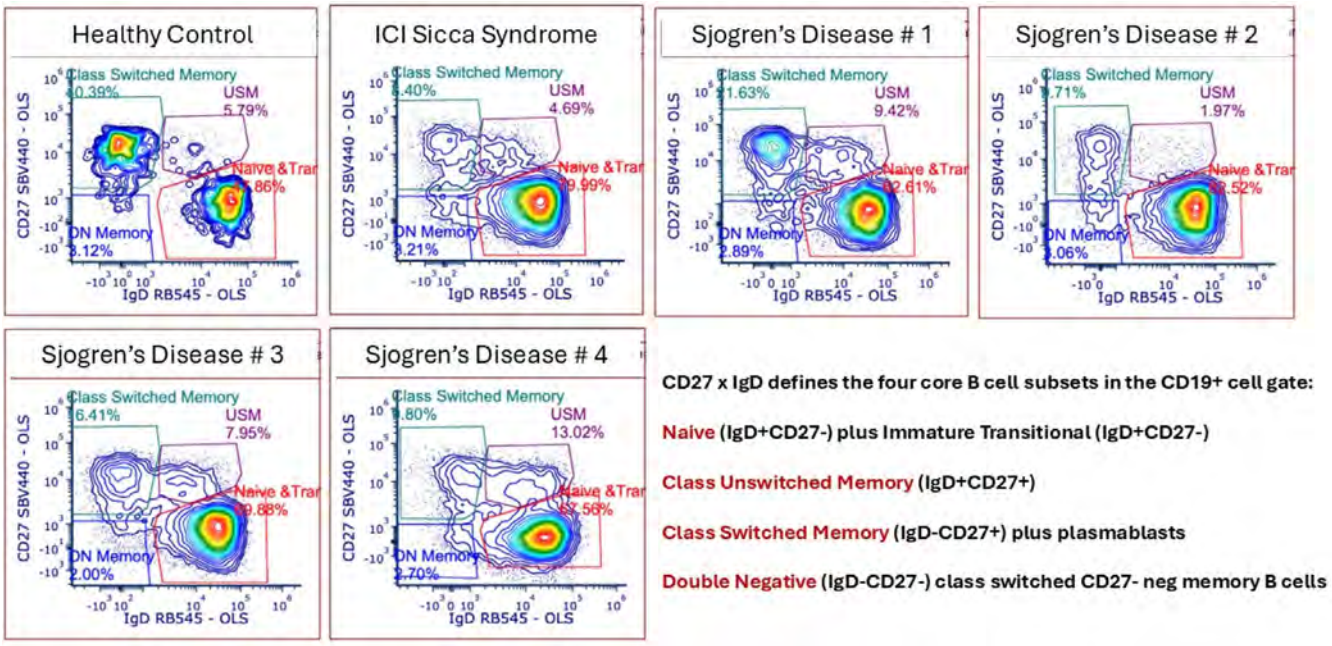


Figure 1

In the naive compartment (CD 27- IgD+), the more mature of the naive B cells (Transitional 3 subset, defined as CD 24-CD38-) were similarly decreased in disease as compared to the control (77.3%± 6.7 in SjD vs 86.0% in ICI sicca syndrome vs 95.7% in control). Conversely the less mature naive B cells (Transitional 1(CD24+CD38+) and Transitional 2 (CD24+CD38–)) were increased in disease relative to the control (Figure 2).

Additionally, the Activated Naïve B cell population was elevated in both diseases, suggesting increased peripheral activation.

In contrast, the percentage of Unswitched Memory (Marginal Zone) B cells and Double Negative Memory B cells were similar between the three groups.

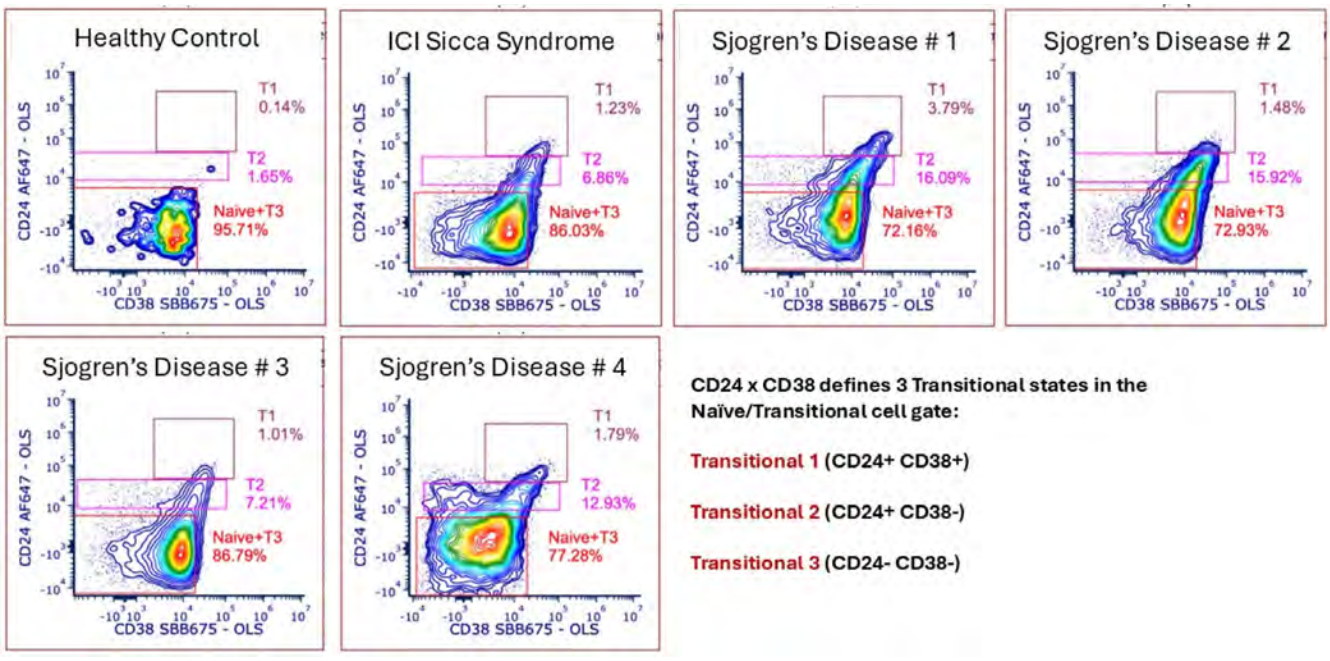


Figure 2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In SjD and ICI-sicca syndrome there is an increase in the proportion of the less mature transitional 1 and transitional 2 B cells, with a simultaneous decrease in the proportion of transitional 3 B cells as well as the mature Class Switched memory and Plasmablast subsets. This may suggest a defect in B cell development in disease. The similar findings seen in SjD and ICI-sicca syndrome may suggest a shared pathogenesis between the two conditions.

Disclosure: C. Atlas: None; **B. Kamaraj**: None; **O. Jamshidi**: None; **A. Mor**: None; **Y. Gartshteyn**: None; **T. Kapoor**: None; **R. Winchester**: None.

Abstract Number: 0901

Data-Driven Metabolomics Identifies Diagnostic Signatures and Patient Subgroups in Systemic Autoimmune Disorders

Chary López pedrera[1], Antonio Perez-Campoamor[2], Gema Dolores García-Delgado[3], Beatriz Vellón-García[4], Adrián Llamas Urbano[5], Laura Romero Zurita[6], Pedro Ortiz Buitrago[7], Christian Merlo[8], Maria del carmen abalos-aguilera[8], Nuria Barbarroja[9], Verónica Bolón-Canedo[10], MARIA ANGELES AGUIRRE ZAMORANO[11], Rafaela Ortega-Castro[12], Jerusalén Calvo[13], Lourdes Ladehesa[14], Marta Alarcon-Riquelme[15], Alejandro Escudero-contreras[8] and Carlos Pérez Sánchez[16], [1]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [2]STARTQUAKE S.L., Gijón, Spain/Research Center on Information and Communication Technologies (CITIC), University of A Coruña, A Coruña, Spain, Gijón, Spain, [3]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain/Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Cordoba, Cordoba, Spain., Cordoba, Spain, [4]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain/Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Córdoba, Córdoba, Spain, Cordoba, Spain, [5]Cobiomic Bioscience SL. EBT University of Cordoba/IMIBIC, Cordoba, Spain., Cordoba, Spain, [6]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Rheumatology service/Department of Medical and Surgical Sciences, Cordoba, Spain, Córdoba, Spain, [7]Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), Cordoba, Andalucia, Spain, [8]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain, Cordoba, Spain, [9]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [10]Research Center on Information and Communication Technologies (CITIC), University of A Coruña, A Coruña, Spain, A coruña, Spain, [11]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [12]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [13]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [14]IMIBIC-Reina Sofia Hospital-University of Cordoba, Cordoba, Spain, Cordoba, Spain, [15]Fundacion Progreso y Salud, Andalusian Government, Granada, Spain, [16]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: This study aims to characterize the metabolomic fingerprint of several systemic autoimmune diseases (SADs) and apply machine learning (ML) techniques to identify disease-specific biomarkers and improve patient diagnosis and stratification.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A total of 716 individuals from the PRECISESADS study, were analyzed, including 272 with rheumatoid arthritis (RA), 183 with systemic lupus erythematosus (SLE), 148 with primary antiphospholipid syndrome (PAPS), 70 with systemic sclerosis (SSc), and 43 healthy donors (HDs). Serum metabolomic profiles were assessed using nuclear magnetic resonance (Nightingale), alongside extensive clinical and analytical data. A combination of ML approaches, including unsupervised patient stratification, and a supervised Logistic Regression using 5-Fold Cross Validation was used to identify potential diagnostic signatures. Correlation analyses explored associations between metabolic alterations and clinical features.

Results: Several metabolites (metabs) were differentially expressed in each disease compared to HDs, with the most alterations in SSc (99 metabs) and APS (68 metabs), followed by SLE (30 metabs) and RA (17 metabs). Notably, some cardiovascular-related metabolites (e.g., histidine, albumin, L-LDL-C, L-LDL-CE) were simultaneously altered across all diseases, while each also exhibited unique metabolic change. ML generated disease-specific diagnostic signatures with AUCs above 0.8 in all cases.

Unsupervised clustering analysis of the entire cohort identified three patient clusters (C1, C2, C3), with each disease represented across all clusters in varying proportions. C1 showed significant differences compared to C3 in both clinical features and metabolomic profiles, while C2 represented an intermediate group. Patients in C1 had increased cardiovascular risk markers compared with C3, while C2 represented an intermediate group.

In APS, C1 was linked to higher thrombotic risk (aGAPSS), arterial events, and metabolic comorbidities, while C2 showed more venous thrombosis and pregnancy complications. In SLE, C1 had more cardiovascular risk factors, lupus nephritis, and anti-dsDNA positivity than C3. In RA, C1 showed higher rates of obesity, diabetes, and atherosclerosis, whereas C3 had greater disease activity and autoantibody positivity. In SSc, C1 was associated with dyslipidemia, lung fibrosis, and anti-U1-RNP, while C3 had more skin involvement and anti-centromere positivity.

Conclusion: Distinct metabolomic profiles were identified with shared and disease-specific alterations across systemic autoimmune diseases. ML revealed accurate diagnostic signatures and uncovered patient subgroups with unique clinical and metabolomic features, highlighting shared pathogenic mechanisms and disease-specific features and supporting the potential for personalized therapies targeting metabolic pathways.

Supported by CPS: RYC2021-033828-I; PID2022-141500OA-I00; DIN2022-012766 Minister of Science, Innovation and Universities co-financed by the European Union; and CLP: (PI24/00959, CD21/00187 and RICOR-24/0007/0019), co-financed by European Union. EU/EFPIA-IMI-PRECISESADS (n° 115565)

Disclosure: C. López pedrera: None; **A. Perez-Campoamor**: None; **G. García-Delgado**: None; **B. Vellón-García**: None; **A. Llamas Urbano**: None; **L. Romero Zurita**: None; **P. Ortiz Buitrago**: None; **C. Merlo**: None; **M. abalos-aguilera**: None; **N. Barbarroja**: None; **V. Bolón-Canedo**: None; **M. AGUIRRE ZAMORANO**: None; **R. Ortega-Castro**: None; **J. Calvo**: None; **L. Ladehesa**: None; **M. Alarcon-Riquelme**: None; **A. Escudero-contreras**: None; **C. Pérez Sánchez**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0902

A Novel Approach to Study ANA+ B Cells in Lupus Integrating Flow Cytometry with Single-cell Culture

Deisy Muriel Velez arteaga[1], Yemil Atisha Fregoso[2], Hasret Gunduz[3] and Betty Diamond[4], [1]The Elmezzi School of Molecular Medicine, New Rochelle, NY, [2]The Feinstein Institute, Long Island, NY, [3]The Feinstein Institute, Long Island, [4]The Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Studying antinuclear antibody (ANA) producing B cells at the single-cell level offers critical insights into their fine specificity and functional characteristics. However, conventional techniques including bulk B cell cultures, ELI-Spot assays, and single-cell sequencing present several limitations. To overcome some of these limitations, we developed an integrated platform that combines flow cytometric detection of ANA$^+$ B cells with an optimized single-B cell culture system (Nojima).

Methods: We employed a flow cytometry assay using biotinylated nuclear extracts to detect ANA reactive B cells, followed by single cell sorting and culture in the presence of feeder cells expressing CD40L and adding BAFF, IL-2, IL-21 (Figure 1).

Results: This approach enabled the isolation and in vitro expansion of ANA-producing B cells coming from patients with SLE and healthy donors from naïve, marginal zone and memory B cell subsets. Following 26 days of culture, a high proportion of wells produced significant immunoglobulin levels: 82% of naïve, 67% of marginal zone, and 57% of IgG$^+$ memory B cell cultures exceeded 1 μg/mL. ANA reactivity in culture supernatants was confirmed by HEp-2 cell staining (shown in figure

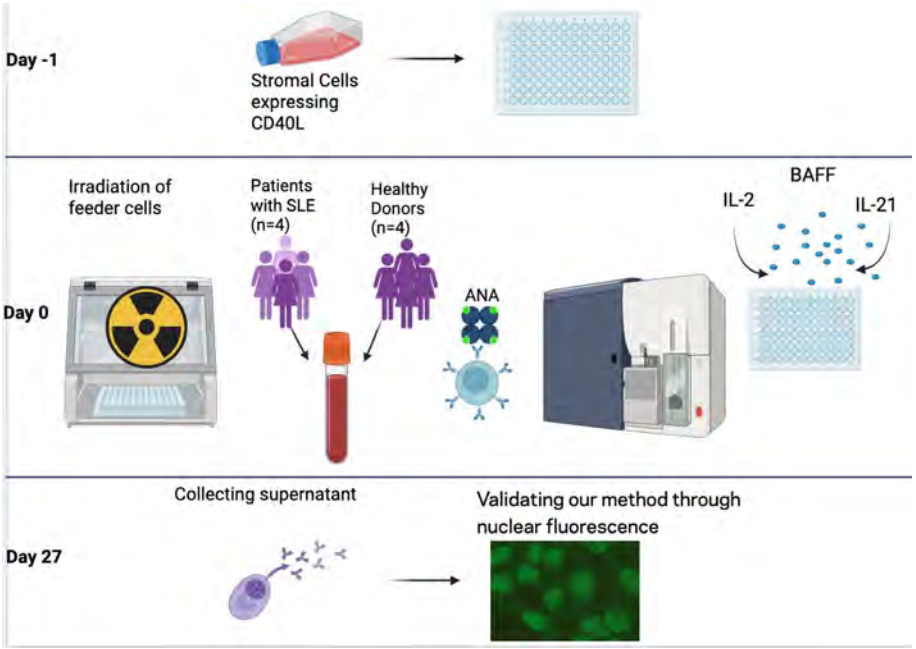


Figure 1: Experimental approach. Seeding the feeder cells until they reach 70% confluence. Irradiating the tissue culture plates with the feeder cells and then sort the cells directly into the tissue plate. Add cytokines and change media replacing cytokines every 3 days. End the culture by day 26, estimate the immunoglobulin production on the supernatant by ELISA. Finally validate the method by testing the supernatants in Hep2 cells.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Percentage of wells producing immunoglobulin by day 26 in 96-well single-cell cultures of B cell subsets from ANA-negative and ANA-positive donors using two seeding methods. Values represent the proportion of wells (out of total plated) that produced detectable IgM (for naïve and marginal zone B cells) or IgG (for memory B cells) above 1 and 10ug/mL threshold. Comparisons are shown for manually seeded versus index plate-sorted cells, grouped by ANA status.

B Cell Type	ANA Status	Percentage of wells producing >1μg/mL	Percentage of wells producing>10μg/mL
Naïve	ANA−	81%	75%
	ANA+	83%	71%
Marginal Zone B cells	ANA−	68%	53%
	ANA+	65%	56%
Memory (IgG)	ANA−	56%	53%
	ANA+	57%	41%

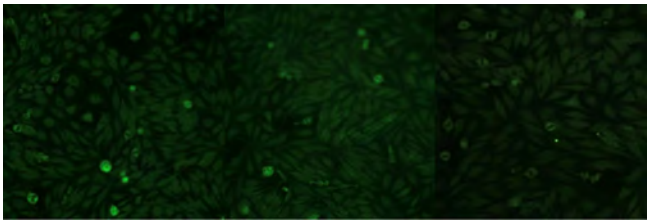


Figure 2. Hep 2 Staining in ANA sorted cells from a patient with SLE showing different nuclear patterns.

2), yielding a sensitivity of 95% and specificity of 68%, validating the functional identity of the expanded B cells. Studying previously sorted ANA+ cells significantly increases the efficiency of the assay. In order to study the immunoglobulin form 100 ANA^{+} cells would ordinarily require screening 2,857 B cells (assuming ANA prevalence of 5%), whereas our approach reduces this to just 150 cells.

Conclusion: This method provides a robust platform for isolating and expanding ANA-producing B cells, enabling the production of autoantibodies for further study. The approach has potential applications in elucidating SLE pathogenesis.

Disclosure: D. Velez arteaga: None; **Y. Atisha Fregoso**: None; **H. Gunduz**: None; **B. Diamond**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0903

Ianalumab's dual mode of action: targeting B cells through enhanced B cell depletion and blockade of B cell-activating factor receptor signaling

Catherine Wioland[1], Corinne Vedrine[2], Caroline Walter[1], Fanny Marque[2], Thomas Dannequin[2], Melanie Cecci[1], David Buffet[1], Cindy Schmid[1], Elena Degl'Innocenti[1], Gautier Robert[1], Grazyna Wieczorek[1], David Schubert[1], Catriona Paape[1] and **Isabelle Isnardi**[3], [1]Novartis Pharma AG, Basel, Switzerland, [2]Novartis Pharma AG, Basel, Basel-Stadt, Switzerland, [3]Novartis, Gueberschwihr, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: B cells are key players in the pathogenesis of Sjögren's disease (SjD) and other systemic autoimmune diseases, supporting B cell depletion as an attractive therapeutic strategy in these patients. However, survival signals mediated by high levels of B cell-activating factor (BAFF) may interfere with B cell depletion, as well as drive disease flares. Ianalumab, an investigational afucosylated monoclonal Ab targeting BAFF-receptor (BAFF-R), has been shown to deplete B cells through enhanced antibody-dependent cellular cytotoxicity (ADCC) with concurrent blockade of BAFF:BAFF-R mediated signals [1]. Here, we extensively characterize the properties of ianalumab on B cells *in vitro*, as well as its ability to deplete circulating and tissue B cells in C57/B6 mice and in the spontaneous non-obese diabetic (NOD) mouse model of SjD.

Methods: *In vitro* B cell killing was assessed using isolated NK cells and B cells from healthy volunteers (HVs) and patients with SjD or SLE. *In vitro* blockade of BAFF stimulation was evaluated through Western blots of Nuclear Factor Kappa B Subunit 2 (NF-*k*B2) intact and cleaved forms, B cell proliferation measured by thymidine incorporation, and quantification of IgG secretion. The efficacy of B cell depletion following administration of ianalumab in C57/B6 and NOD mice was investigated using flow cytometry and/or histology in blood and relevant organs.

Results: In an ADCC assay co-culturing purified NK cells with B cells from HVs, ianalumab showed a 44-fold increased potency compared to rituximab (**Fig. 1A**). This increased potency was also observed when NK cells from patients with SjD and SLE were tested (**Fig. 1B**). Additionally, ianalumab effectively prevented BAFF from binding to BAFF-R expressing cells. This blockade of BAFF-R on human B cells correlated with effective inhibition of BAFF-induced cleavage of NF-κB2, proliferation and IgG production. Notably, ianalumab was able to inhibit B cell proliferation with the same potency, when induced by a BAFF trimer or 60-mer (**Fig. 2**). *In vivo*, ianalumab induced a significant reduction of B cell subpopulations in blood and lymphoid organs of B6 mice. Ianalumab was also able to prevent B cell infiltration in the salivary glands of NOD

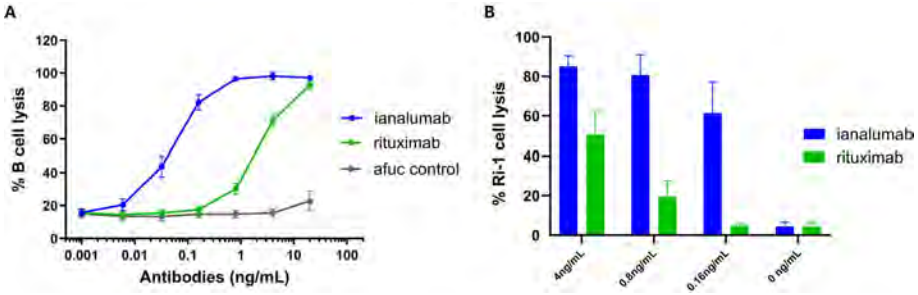


Figure 1. Ianalumab shows superior potency to rituximab in ADCC. A. B cells and NKs from HVs (N=7 donors) where cocultured in the presence of ianalumab, rituximab or an irrelevant afucosylated antibody, and B cell lysis was evaluated after 60 min. B. NK cells from patients with SjD (N=3 donors) were cocultured with RI-1 cells in the presence of ianalumab or rituximab and Ri-1 cell lysis was evaluated after 60 min.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

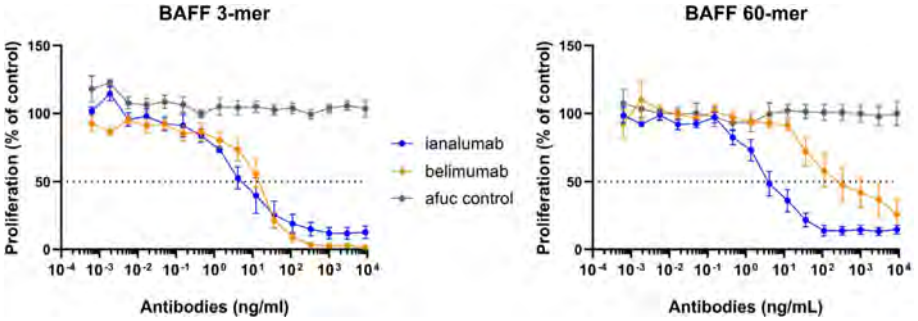


Figure 2. Ianalumab inhibits proliferation of human B cells from HVs (N=7 donors) stimulated by BAFF in combination with anti-IgM. Purified B cells were stimulated with BAFF 3-mer or BAFF 60-mer, in the presence of anti-IgM. Cell proliferation was measured by 3H-thymidine incorporation.

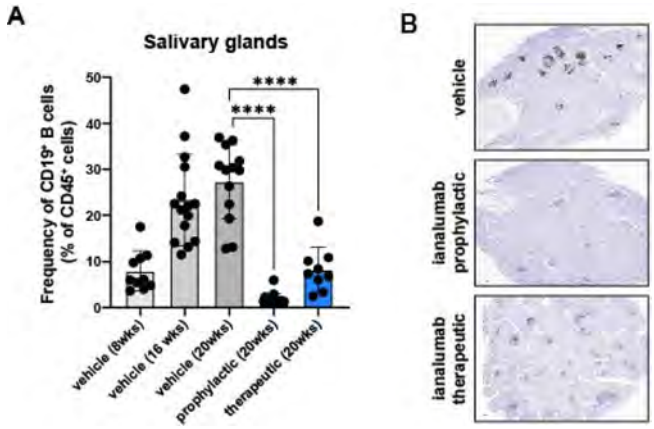


Figure 3. Ianalumab reduces infiltration of B cells in spleen and salivary glands of NOD SjD mice. A. Proportion of CD19+ cells analysed at 20 weeks in salivary glands using flow cytometry. B. CD45R+ B cells analysed on paraffin sections of submandibular salivary glands.

mice when given prophylactically and to decrease B cells infiltrating the salivary glands therapeutically, showing its ability to reduce B cells in the target organs of mice suffering from systemic autoimmunity (**Fig. 3**).

Conclusion: Ianalumab, through its dual mechanism of action, addresses limitations of first-generation B cell targeting therapies for auto-immune diseases by providing more potent B cell depletion and additional BAFF-R blockade on remaining B cells. Accordingly, patients with SLE (NCT03656562) or SjD (NCT02962895) treated with ianalumab for up to 52 weeks showed sustained reduction in disease activity in phase 2 trials [2,3]. Ongoing phase 3 studies in SjD, SLE and LN will provide further evidence on the efficacy and safety of ianalumab in larger patient populations.

References:

1. McWilliams EM, et al. Blood Adv. 2019;3:447-60
2. Shen N, et al. [abstract]. Arthritis Rheumatol. 2023;75 (suppl 9).
3. Bowman SJ, et al. Lancet. 2022;399:161-71.

Disclosure: C. Wioland: Novartis, 3, 12, Shareholder; **C. Vedrine**: Novartis, 3, 12, Shareholder; **C. Walter**: Novartis, 3, 12, Shareholder; **F. Marque**: Novartis, 3, 12, Shareholder; **T. Dannequin**: Novartis, 3, 12, Shareholder; **M. Cecci**: Novartis, 3, 12, Shareholder; **D. Buffet**: Novartis, 3, 12, Shareholder; **C. Schmid**: Novartis, 3, 12, Shareholder; **E. Degl'Innocenti**: Novartis, 3, 12, Shareholder; **G. Robert**: Novartis, 3, 12, Shareholder; **G. Wieczorek**: Novartis, 3, 12, Shareholder; **D. Schubert**: Novartis, 3, 12, Shareholder; **C. Paape**: Novartis, 3, 12, Shareholder; **I. Isnardi**: Novartis, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0904

SLAMF7 Drives Plasma Cell Differentiation in Rheumatoid Arthritis Synovium.

Jabea Ekabe[1], Ken Yasaka[2], Ruoqiao Wang[3], Nida Pellett[4], Javier Rangel-Moreno[2], Juilee Thakar[3], Jennifer Anolik[4] and Accelerating Medicines Partnership: RA/SLE Network (AMP RA/SLE), [1]University of Rochester, Brighton, NY, [2]University of Rochester, Rochester, NY, [3]University of Rochester, Rochester NY, [4]University of Rochester Medical center, Rochester, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: B cells contribute to rheumatoid arthritis (RA) pathogenesis through antibody-dependent and -independent mechanisms. Thus, identifying regulators of B cell fate in RA is essential for developing targeted therapies. SLAMF7, a transmembrane protein in the SLAM family, is known for promoting monocyte pro-inflammatory responses. Although plasma cells and some B cells express SLAMF7, its influence on B cell function and differentiation in RA remains unclear. We hypothesized that SLAMF7 regulates B cell differentiation into plasma cells (PCs) and contributes to RA progression via modulation of autoantibody-dependent and independent functions.

Methods: We analyzed single-cell transcriptomic and surface protein expression (CITE-seq) data from paired blood and synovia of RA patients (n = 61) from the Accelerating Medicines Partnership RA/SLE cohort. SLAMF7 surface protein expression was validated by flow cytometry in peripheral blood mononuclear cells (PBMCs, n = 12) and synovial fluid mononuclear cells (SFMCs, n = 7). Immunohistochemistry was performed on RA synovial tissue to localize SLAMF7 expression in $CD20^+$B cells and $CD138^+$PCs. Purified total B cells were differentiated into age-associated B cells (ABCs) using ABC polarizing conditions, then further differentiated into PCs in the presence or absence of recombinant human SLAMF7 protein (n = 3). The effect of SLAMF7 on B cell proliferation was assessed using CFSE dye dilution assays (n = 3). Data analysis was conducted using Seurat v5, Flowjo, and GraphPad Prism.

Results: SLAMF7 gene expression was significantly increased in synovial compared to blood B cells ($p < 0.05$) and greater than 80% of PCs expressed SLAMF7. Age-associated B cells (ABC) and activated B cell clusters upregulated SLAMF7 in RA synovium. $SLAMF7^+$ B cells exhibit higher plasma cell gene score compared to $SLAMF7^-$ B cells, indicating a positive correlation between SLAMF7 expression and plasma cell differentiation. Flow cytometry confirmed higher SLAMF7 surface expression in synovial B cells versus blood B cells (17.25% vs. 4.67%, $p < 0.05$). $SLAMF7^+$B cells in synovial fluid were significantly enriched in double negative (DN, 46.9% vs. 1.91%) and memory B cell populations (30.4% vs. 8.27%, $p < 0.05$). Among DN subsets, DN2 ($IgD^-CD27^-CD11c^+$

$CXCR5^-$, 54.25%) and DN3 ($IgD^-CD27^-CD11c^-CXCR5^-$, 41.7%) B cells were the predominant $SLAMF7^+$ DN populations. SLAMF7 expression in DN2 cells was significantly higher in synovium compared to blood (54.25% vs. 16.7%, $p < 0.05$). Immunohistochemistry confirmed $SLAMF7^+$expression by synovial $CD20^+$B cells and $CD138^+$PCs. Functionally, *in vitro* stimulation with recombinant SLAMF7 significantly suppressed B cell proliferation ($p < 0.05$), while enhancing plasma cell differentiation, as determined by increased expression of CD38 and CD27.

Conclusion: Our results demonstrate significant SLAMF7 upregulation in RA synovial B cells and implicate SLAMF7 as a functional regulator of B cell functions. SLAMF7 promotes plasma cell differentiation but also inhibits B cell proliferation, suggesting dual roles in modulating B cells within inflamed joints.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Ekabe: None; **K. Yasaka**: None; **R. Wang**: None; **N. Pellett**: None; **J. Rangel-Moreno**: None; **J. Thakar**: None; **J. Anolik**: None.

Abstract Number: 0906

Preclinical Characterization of IBI3034, an TACI and BCMA Chimeric Fc Fusion Protein, that Potently Modulates B Lymphocytes and Serum Immunoglobulin for the Treatment of B cell Related Autoimmune Disease

Yao Xiong, Shuaixiang Zhou, Zhimin Zhang, Bin Li, Zhihao Ming, Yuyu Wu, Liu Li, Chang Li, Fenggen Fu, Zhihai Wu, Shun Wang, Guogang Yuan, Yuling Song, **Jinyang Li**, Huizhong Xiong and Bingliang Chen, Innovent Biologics (Suzhou) Co., Ltd., Suzhou, Jiangsu, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Dysregulated B-cell activation plays a pivotal role in the pathogenesis of various autoimmune diseases. B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) are essential cytokines that support B-cell survival and differentiation. Elevated levels of these cytokines are associated with autoimmune conditions such as Systemic Lupus Erythematosus (SLE), IgA nephropathy (IgAN), and Rheumatoid Arthritis (RA). Therapeutic agents targeting these cytokines, including the anti-BAFF antibody Belimumab, anti-APRIL antibody Sibeprenlimab, and the BAFF/APRIL dual inhibitor Telitacicept, have demonstrated significant clinic efficacy, particularly in SLE and IgAN. These findings highlight the therapeutic potential of targeting BAFF and APRIL. However, the limitations associated with single-target therapies or unbalanced inhibition of these cytokines underscore the need for innovative approaches in drug development. Here we described IBI3034, a novel chimeric fusion protein, currently at the Investigational New Drug (IND) stage, designed to address these challenges in B-cell-related autoimmune diseases.

Methods: Variants chimeric constructs combining TACI and BCMA fused with Fc were designed and generated for screening. IBI3034 was selected based on its protein developability, dual binding affinity to BAFF and APRIL and *in vitro* inhibitory effects on B cells. The *in vitro* activity comparison of IBI3034 and related benchmarks were evaluated head-to-head via reporter cell lines and BAFF and APRIL induced proliferation of human B cells derived from human peripheral blood mononuclear cells (PBMCs). Then *in vivo* efficacy of IBI3034 and related benchmarks were evaluated by analyzing B-cell depletion in the spleen and serum immunoglobulin levels in BAFF-induced mouse models, KLH mouse models, and cynomolgus monkeys. Additionally, the therapeutic potential of IBI3034 was assessed in mouse models of SLE and RA.

Results: IBI3034 demonstrated potent and balanced binding ability to BAFF and APRIL at nanomolar level, effectively inhibiting the proliferation of human B cells induced by a BAFF/APRIL mixture with an IC50 of 7.7 nm. In vivo studies revealed significant depletion of various B-cell subpopulations, including marginal zone B cells, germinal center B cells, and plasma cells, accompanied by reduced serum immunoglobulin levels in BAFF-induced and KLH mouse models. Notably, a single dose of IBI3034 markedly suppressed peripheral antibody-secreting cells and immunoglobulin production up to day 35 in cynomolgus monkeys. Furthermore, IBI3034 significantly reduced proteinuria levels with extended survival in a lupus mouse model and ameliorated arthritis inflammation in an RA mouse model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: IBI3034, a novel TACI/BCMA chimeric Fc fusion protein, exhibits potent and prolonged effects on B-cell and plasma cell depletion and immunoglobulin suppression through balanced dual inhibition of BAFF and APRIL. This innovative therapeutic approach holds promise for providing deeper clinical benefits and more convenient dosing intervals for patients with B-cell-mediated autoimmune diseases.

Disclosure: Y. Xiong: Innovent Biologics (Suzhou) Co., Ltd., 3; **S. Zhou**: Innovent Biologics (Suzhou) Co., Ltd., 3; **Z. Zhang**: Innovent Biologics (Suzhou) Co., Ltd., 3; **B. Li**: Innovent Biologics (Suzhou) Co., Ltd., 3; **Z. Ming**: Innovent Biologics (Suzhou) Co., Ltd., 3; **Y. Wu**: Innovent Biologics (Suzhou) Co., Ltd., 3; **L. Li**: Innovent Biologics (Suzhou) Co., Ltd., 3; **C. Li**: Innovent Biologics (Suzhou) Co., Ltd., 3; **F. Fu**: Innovent Biologics (Suzhou) Co., Ltd., 3; **Z. Wu**: Innovent Biologics (Suzhou) Co., Ltd., 3; **S. Wang**: Innovent Biologics (Suzhou) Co., Ltd., 3; **G. Yuan**: Innovent Biologics (Suzhou) Co., Ltd., 3; **Y. Song**: Innovent Biologics (Suzhou) Co., Ltd., 3; **J. Li**: Innovent Biologics (Suzhou) Co., Ltd., 3; **H. Xiong**: Innovent Biologics (Suzhou) Co., Ltd., 3; **B. Chen**: Innovent Biologics (Suzhou) Co., Ltd., 3.

Abstract Number: 0907

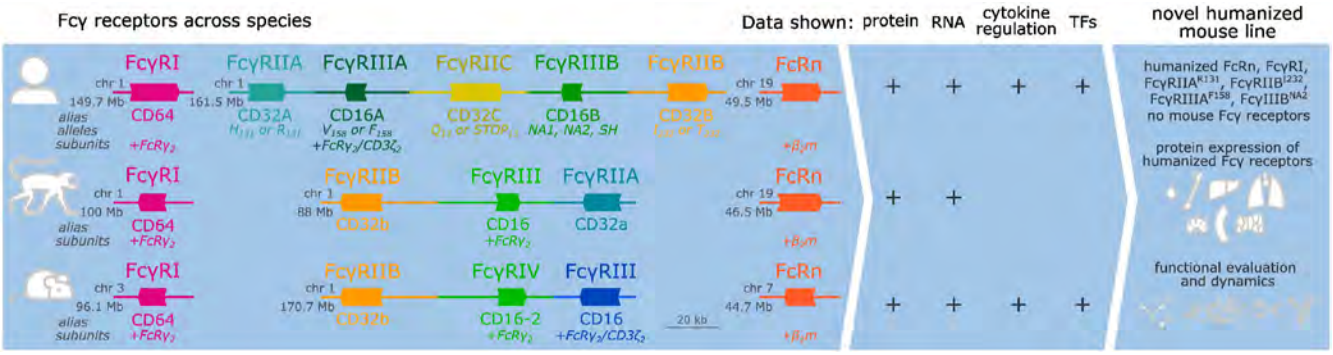
Cross-Species Cellular Mapping and Humanization of Fcγ Receptors to Advance Antibody Modeling

Karel Van Damme[1], Dorine Sichien[2], Katrien Van der Borght[3], Sofie Van Gassen[3], Elisabeth De Leeuw[3], Victor Bosteels[4], Joseph Jorssen[5], Seppe De Winter[6], Alan Korman[7], Fabio Benigni[8], Davide Corti[8], Ariane Morel[9], Eric Vivier[9], Hamida Hammad[3], Dirk Elewaut[10], Fabiane Sonego[11], Kader Thiam[11], Sofie Voet[2], bianca Balbino[12] and Bart Lambrecht[3], [1]Ghent University, Ghent, [2]argenx, Ghent, Belgium, [3]Ghent University, Ghent, Belgium, [4]The Francis Crick Institute, London, United Kingdom, [5]Liège Université, Liege, Belgium, [6]KU Leuven, Leuven, Belgium, [7]Vir Biotechnology, San Francisco, [8]Vir Biotechnology, Bellinzona, Switzerland, [9]Innate Pharma, Marseille, France, [10]VIB Center for Inflammation Research, and Ghent University Hospital, Department of Rheumatology, Ghent, Belgium, [11]genOway, Lyon, France, [12]argenx, Gent, Belgium

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fc receptors mediate the effector functions of antibodies by linking adaptive and innate immunity. Immunoglobulin G (IgG), the most abundant antibody in circulation and widely used in clinical therapeutics, interacts with a range of Fc gamma (Fcγ) receptors expressed in a cell type–specific manner. However, a systematic understanding of Fcγ receptor and neonatal Fc receptor (FcRn) expression across species and immune subsets is incomplete, limiting translational insights from preclinical models. This study aimed to create a comprehensive atlas of Fcγ receptor and FcRn



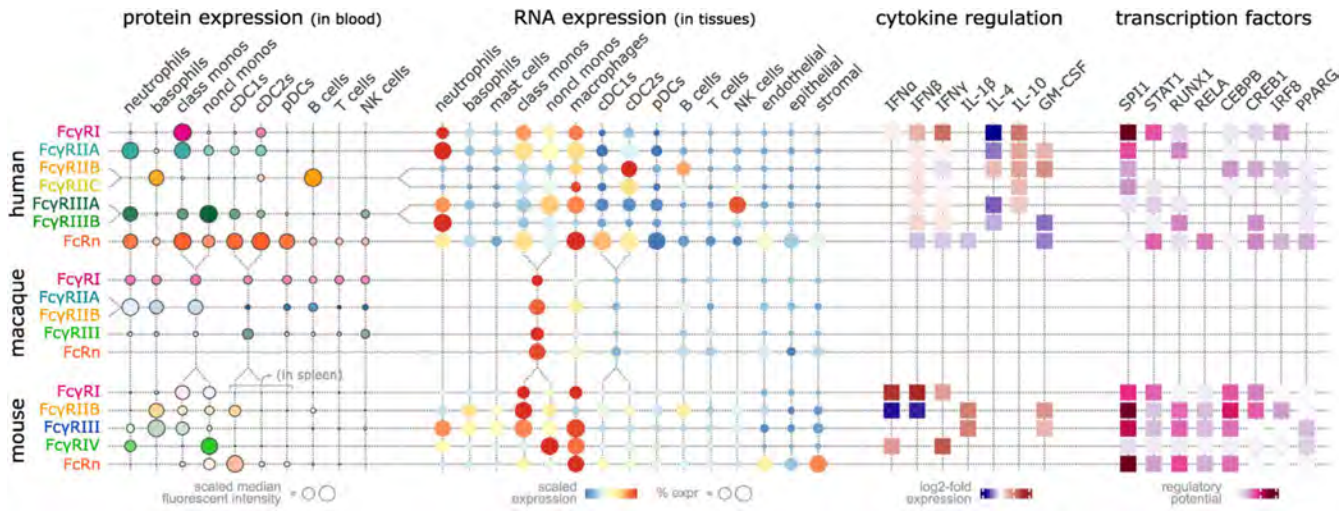
Fcγ receptors across species, their genomic mapping, and the characterization of a novel mouse model with humanized Fcγ receptors.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Protein expression profiles of Fcγ receptors in humans, macaques, mice and humanized mice.

expression across species and identify regulatory factors governing their expression. In parallel, we sought to address species-specific limitations by developing a humanized mouse model for improved antibody evaluation.

Methods: We profiled Fcγ receptor and FcRn expression in humans, cynomolgus macaques, and mice using multimodal approaches including flow cytometry, single-cell RNA sequencing, and integration of chromatin accessibility and transcriptional regulatory data. Gene regulatory networks were inferred using NicheNet, SCENIC+, ChIP-seq, and perturbation experiments to predict transcription factor (TF) influences. To overcome limitations of current preclinical models, we engineered knock-in mice in which five key human Fcγ receptors as well as FcRn are expressed under control of their endogenous human promoters.



Fcγ receptors protein and RNA expression, with upstream cytokines and gene regulatory factors across species.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Our cross-species comparison revealed marked differences in Fcγ receptor diversity, abundance, and cell type–specific expression, with especially poor conservation in myeloid and granulocyte subsets. Regulatory network analysis uncovered distinct TF programs controlling Fcγ receptor expression across species. The novel humanized FcγR/FcRn mouse model demonstrated physiologic expression of human Fcγ receptors in the appropriate immune and non-immune subsets. Functional validation showed that these receptors mediate canonical Fc-dependent processes, including antibody-dependent cellular cytotoxicity, antigen presentation, anaphylaxis, and antibody pharmacokinetics. Cytokine stimulation further revealed plasticity in receptor expression, mirroring human immune dynamics.

Conclusion: This study provides a reference atlas of Fcγ receptor and FcRn biology across species and introduces a novel, functionally validated humanized mouse model. Together, these resources will aid mechanistic studies and improve the preclinical assessment of antibody-based therapeutics.

Disclosure: K. Van Damme: None; **D. Sichien**: argenx, 3; **K. Van der Borght**: None; **S. Van Gassen**: None; **E. De Leeuw**: None; **V. Bosteels**: None; **J. Jorssen**: None; **S. De Winter**: None; **A. Korman**: Vir Biotechnology, 3, 11; **F. Benigni**: Vir Biotechnology, 3, 11; **D. Corti**: Vir Biotechnology, 3, 11; **A. Morel**: Innate Pharma, 3; **E. Vivier**: Innate Pharma, 3; **H. Hammad**: None; **D. Elewaut**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6, UCB, 2, 6; **F. Sonego**: genOway, 3, 11; **K. Thiam**: genOway, 3, 11; **S. Voet**: argenx, 3; **b. Balbino**: argenx, 3; **B. Lambrecht**: argenx, 11.

Abstract Number: 0908

E-602 (Efgitasialase alfa) Enhances Memory B Cell Depletion and Reduces Profibrotic Macrophages *via* Desialylation in Autoimmune Disease

Hrishikesh Mehta[1], Vijayashree Mysore[1], Chih-Hsing Chou[1], Lizhi Cao[1], Rui Liu[2], Tianrui Fan[2], Jijun Yuan[2], James Broderick[1] and **Li Peng**[1], [1]Palleon Pharmaceuticals, Waltham, MA, [2]Shanghai Henlius Biotech, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Abnormal cell surface glycosylation has been observed in various autoimmune diseases, including systemic lupus erythematosus (SLE) and membranous nephropathy. Among these glycan modifications, sialoglycans function as immune-inhibitory molecules that pathogenic cells, such as cancer cells and pathogenic immune cells, exploit to evade immune surveillance. Elevated levels of surface sialoglycans have been detected on memory B cells and other pathogenic immune subsets in autoimmune conditions, contributing to their resistance to immune-mediated clearance and conventional therapies. Clinical studies have linked poor depletion of $CD27^+$ memory B cells to suboptimal treatment outcomes. This study investigates E-602, an engineered human sialidase, as a novel therapeutic approach to enzymatically remove sialoglycans from the surface of pathogenic immune cells.

Methods: We assessed the effect of E-602-mediated desialylation in ADCP and CDC assays using Raji cells or human primary B cells from healthy donor PBMCs in the presence of anti-CD20 or anti-CD19 antibodies. We then evaluated its impact on depleting CD27+ memory B cells using PBMCs from SLE patients. In vivo efficacy was tested in a lymphoma mouse model, an MRL/lpr SLE mouse model, and non-human primates. We also investigated whether E-602 reduces profibrotic M2-like macrophages in chronically inflamed tissues using tumors as a surrogate in mouse tumor models.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: E-602 enhanced ADCP and CDC across multiple anti-CD20 and anti-CD19 B cell-targeting antibodies. It improved anti-CD20-mediated depletion of CD27+ memory B cells by ~50% from SLE patients, which express high levels of sialoglycans and are typically resistant to depletion using anti-CD20 antibodies alone. In lymphoma and MRL/lpr SLE mouse models, E-602 enhanced anti-CD20-mediated B cell depletion. In non-human primates, E-602 improved B-cell depletion in lymph nodes, which are often resistant to B-cell depletion compared to peripheral blood. Additionally, E-602 reduced profibrotic M2-like macrophages by ~ 90% compared to the vehicle control in the tumor microenvironment, which serves as a surrogate for chronic inflammatory tissue.

Conclusion: E-602 offers a novel therapeutic strategy through enzymatic desialylation of pathogenic immune cells to enhance their depletion and restore immune balance. Its dual MoA targets two key pathogenic subpopulations: memory B cells, which drive autoantibody production and contribute to disease relapses, and M2-like macrophages, which promote fibrosis and organ damage. This combination could potentially improve tissue level B cell depletion and reduce pro-fibrotic macrophage induced tissue damage. Based on a favorable safety and tolerability profile demonstrated in the completed Phase 1 GLIMMER-01 trial in oncology patients, E-602 represents a scientifically novel, safe, and broadly applicable add-on to existing B-cell-targeting antibody therapies in a wide range of patients with autoimmune diseases.

Disclosure: H. Mehta: Palleon Pharmaceuticals, 3; **V. Mysore**: Palleon Pharmaceuticals, 3; **C. Chou**: Palleon Pharmaceuticals, 3; **L. Cao**: Palleon Pharmaceuticals, 3; **R. Liu**: Shanghai Henlius Biotech, 3; **T. Fan**: Shanghai Henlius Biotech, 3; **J. Yuan**: Shanghai Henlius Biotech, 3; **J. Broderick**: Palleon Pharmaceuticals, 3; **L. Peng**: Palleon Pharmaceuticals, 3.

Abstract Number: 0909

Loss of MicroRNA29 expression in B cells and skin microbiota synergize to promote atopic dermatitis in mice.

Marcus Hines[1], Timothy Borbet[2] and Sergei Koralov[2], [1]New York University Grossman School of Medicine, New York, NY, [2]NYU Langone Medical Center, New York

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The microRNA(miR)29 family is encoded by two separate loci, the miR29ab1 and miR29b2c alleles. We have previously shown that the microRNA(miR)29 family regulates the survival and function of peripheral B cells by analyzing mice with miR29-deficient B cells (B29KO). Furthermore, these B29KO mice develop itching and skin inflammation akin to atopic dermatitis, with a 50% mortality rate. Our investigations using B29KO mice revealed a novel target transcript, Il4ra. This gene encodes the cytokine IL-4 which is an important signaling molecule for immune cell activation and differentiation. In B cells, IL-4 regulates class switch recombination to IgE and affinity maturation in germinal center reactions. We hypothesized that the miR29 family regulates the IL4 signaling cascade in B cells, conferring a susceptibility for developing atopic dermatitis.

Methods: miR-29ab1$^{fl/fl}$ mice (obtained from Dr. Mark Ansel's lab) and miR-29b2c$^{-/-}$ mice (obtained from Dr. Jining Lu's Lab) were bred with mb1-cre animals from Jax Labs and maintained on a C57BL/6J background. Littermates without full deletion of miR-29 family of miRNAs were used as controls. We employed flow cytometry, histology, ex vivo stimulation cultures, single-cell RNA sequencing, and statistical analysis software (GraphPad) to analyze data.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We found B29KO B cells have higher expression of Il4ra by both qPCR and single-cell sequencing. Differential gene analysis and pathway enrichment show B29KO mice exhibit heightened IL4 signaling, reduced activation, and negative regulation of cytokine production relative to littermate controls. Ex vivo studies using B cells from B29KO mice revealed an increase in IgE class switching compared with wild-type B cells - a finding recapitulated in B29KO mice that have higher serum IgE titers. When treated with a neutralizing anti-IL4Ra antibody, the phenotype of B29KO mice are rescued from mortality. Interestingly, we found that skin swabs from phenotypic B29KO mice transferred the phenotype to healthy B29KO mice but not littermate controls. Donor and recipient mice were found to be colonized with Staphylococcus aureus and xylosus.

Conclusion: Our data suggest that regulation of Il4ra by miR-29 impacts B cells responsiveness to IL-4 signaling and, as a result, the susceptibility to atopic dermatitis in mice via genetic susceptibility and microbial triggers.

Disclosure: M. Hines: None; **T. Borbet**: None; **S. Koralov**: None.

Abstract Number: 0910

Development of Four Distinct Human IgG4-Producing Mouse Models Recapitulating IgG4-Related Disease

MIN GANG KIM[1], JINA YEO[2], HEA RIM KANG[3], JAE HYUN MOON[3], Seon Uk Kim[4], SeoYoon Ban[5], MI HYEON KIM[6], Eun Young Lee[7] and Seoul National University College of Medicine, [1]Seoul National University College of Medicine, Seoul, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Republic of Korea, [3]Seoul National University College of Medicine, Jongno-gu, Seoul, Republic of Korea, [4]Seoul National University, Jongno-gu, Seoul, Republic of Korea, [5]Department of Cancer biology, Graduate School of College of Medicine, Seoul National University, Korea, Seoul, Republic of Korea, [6]Hallym university dongtan sacred heart hospital, Seocho-gu, Seoul, Republic of Korea, [7]Seoul National University College of Medicine, Seoul, South Korea

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4RD) is an immune-mediated fibroinflammatory condition characterized by multi-organ involvement, elevated serum IgG4, and IgG4-positive plasma cell infiltrates that form tumor-like lesions and fibrosis. However, conventional mice lack the IgG4 subclass, precluding in vivo modeling of IgG4RD. We aimed to develop humanized mouse models that produce human IgG4 and replicate key features of IgG4RD.

Methods: I established four distinct human IgG4-producing xenograft models using NSG (NOD-scid IL2rγ^{null}) and NSG-hIL6 (human IL-6 transgenic NSG) immunodeficient mice as hosts. The models included the following:

1. NSG mice injected with human peripheral blood mononuclear cells (PBMCs).

2. NSG-hIL6 mice, after sublethal irradiation, engrafted with human CD34^{+} hematopoietic stem cells via intrahepatic injection.

3. NSG-hIL6 mice intravenously injected with Epstein–Barr virus (EBV)-immortalized B cells derived from IgG4RD patients.

4. NSG mice injected with a luciferase-tagged, human IgG4-secreting K562 cell line.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In all models, human IgG4 in mouse serum was measured by ELISA. Spleen, kidney, and salivary gland tissues were analyzed by histology and immunohistochemistry for $IgG4^+$ cell infiltration, inflammation, and tumefactive lesions.

Results: All four models produced human IgG4 in circulation at significantly elevated levels relative to controls (a hallmark of IgG4RD), confirming engraftment. Histopathology of the spleen, kidney, and salivary glands showed dense $IgG4^+$ lymphoplasmacytic infiltration with associated inflammation, tissue hypertrophy, and pseudotumor-like lesions, closely mirroring human IgG4RD pathology with fibroinflammatory tissue remodeling. Notable differences among the models were observed. The EBV-immortalized B cell model exhibited the highest serum IgG4 concentrations and the most extensive $IgG4^+$ cell infiltration. The luciferase-expressing K562 model enabled bioluminescent tracking of IgG4-secreting cells, visualizing their migration and organ colonization. Finally, the $CD34^+$ HSC model allowed observation of IgG4 class switching, a fundamental process in IgG4RD.

Conclusion: I developed four complementary humanized mouse models that recapitulate key features of IgG4RD. These *in vivo* models are valuable tools for investigating IgG4RD pathogenesis and testing new therapies. Each model has unique advantages: the PBMC model provides a straightforward platform for inducing IgG4 production; the $CD34^+$ HSC model allows analysis of IgG4 class switching; the EBV-B cell model yields high serum IgG4 levels with severe multi-organ involvement; and the IgG4-secreting K562 model enables longitudinal bioluminescent tracking of IgG4-producing cells. Together, these models form a comprehensive platform for in-depth mechanistic studies and the development of new therapies for IgG4RD.

Disclosure: M. KIM: None; **J. YEO**: None; **H. KANG**: None; **J. MOON**: None; **S. Kim**: None; **S. Ban**: None; **M. KIM**: None; **E. Lee**: IMbiologics, 1, Samsung Bioepis, 5.

Abstract Number: 0911

A Novel Fcrn × Albumin Bispecific Antibody Demonstrates Extended Half-life And deep Igg Reduction in Preclinical Mouse Models

Hang Su[1], Lulu Li[1], Zenglin Pei[1], Barry Duplantis[2], Yuhao Wang[2], Yi Li[1] and **Quan Yu**[1], [1]Ailux, Shanghai, China (People's Republic), [2]Ailux, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and Sjögren's syndrome are characterized by elevated levels of pathogenic autoantibodies that drive inflammation. The neonatal Fc receptor (FcRn) prolongs the half-life of IgG by mediating its recycling, and FcRn blockade has emerged as a promising strategy to reduce pathogenic autoantibodies. However, the inhibition of IgG recycling also leads to a shortened half-life of FcRn blockers, necessitating frequent dosing. Here, we report a novel bispecific antibody, based on an effector-silent human IgG1 backbone, that targets both human FcRn (hFcRn) and human serum albumin (HSA). The optimized bispecific design enables potent FcRn inhibition while leveraging albumin binding to prolong half-life without compromising pharmacologic activity.

Methods: Parental anti-FcRn IgG and anti-HSA VHH were generated through epitope-focusing antibody discovery and NGS-powered phage display screening, followed by bispecific format optimization and affinity tuning. Binding properties and FcRn-blocking activity were evaluated in vitro using biochemical and cell-based assays. In vivo functional and pharmacokinetic studies were performed in hFcRn/HSA/$Rag1^{-/-}$ transgenic mice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The bispecific antibody demonstrated sub-nanomolar binding affinity to hFcRn, cross-reactivity with cynomolgus FcRn, and potent inhibition of IgG-FcRn interaction. Structural modeling and in vitro experiments confirmed that HSA binding to hFcRn was maintained in the presence of anti-FcRn or HSA antibody. A single intravenous dose of the bispecific antibody in transgenic mice led to rapid and profound clearance of exogenous administrated circulating human IgG. The bispecific antibody exhibited a prolonged serum half-life compared to the parental anti-FcRn antibody and other FcRn blockers, and did not meaningfully affect circulating HSA levels.

Conclusion: The rationally designed FcRn × HSA bispecific antibody effectively blocks FcRn-mediated IgG recycling while achieving extended systemic exposure and a favorable preclinical safety profile. These findings support its potential as a long-acting therapeutic candidate for the treatment of autoantibody-driven diseases with reduced dosing frequency.

Disclosure: H. Su: None; **L. Li**: None; **Z. Pei**: None; **B. Duplantis**: None; **Y. Wang**: None; **Y. Li**: None; **Q. Yu**: None.

Abstract Number: 0912

CD11c$^+$CD21$^-$ Autoimmune-Associated B Cells Derived from Double-Negative IgD$^-$CD27$^-$ Subsets Exhibit Enhanced IFNLR1 Expression in Systemic Lupus Erythematosus

Roukaya Yaakoub, Diana Alzamareh, Alexander Bae William and Jennifer Barnas, university of rochester, rochester, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune-associated B cells (ABCs) are increasingly recognized for their role in the pathogenesis of systemic lupus erythematosus (SLE), yet their developmental origins and specific functions remain unclear. Interferon-lambda (IFN-λ), a type III interferon implicated in SLE, may have distinct effects from the well-established pathogenic role of interferon-alpha (IFN-α), still its contribution remains incompletely understood. Prior studies suggest that ABCs—characterized by a CD11c$^+$CD21$^-$ phenotype—are most prevalent within the double-negative (DN) B-cell subset, which also shows heightened responsiveness to IFN-λ. We hypothesize that CD11c$^+$CD21$^-$ ABCs, predominantly arising from the DN IgD$^-$CD27$^-$ B-cell subset, exhibit enhanced responsiveness to IFN-λ, contributing to their pathogenic role SLE through upregulated IFNLR1 expression.

Methods: To investigate the development and function of ABCs, peripheral blood mononuclear cells (PBMCs) were isolated from patients with SLE (n = 18). Flow cytometry was employed to quantify CD11c$^+$CD21$^-$ ABCs across four B-cell subsets: naïve, switched memory (SM), unswitched memory (USM), and DN. IFNLR1 expression was later assessed within these subsets (n = 3).

To explore the intrinsic differentiation potential of ABCs, *in vitro* stimulation assays were performed using sorted-purified naïve, SM, USM, and DN B cells from healthy donors (HDs) (n = 3). Cells were cultured under ABC-inducing conditions, including B-cell receptor stimulation, R848 (TLR7/8 agonist), IFN-γ, IL-21, and BAFF. Following culture, the induction of CD11c$^+$CD21$^-$ ABCs and IFNLR1 expression were analyzed by flow cytometry.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Flow cytometric analysis of PBMCs from SLE patients (n = 18) revealed that CD11c$^+$CD21$^-$ ABCs were most enriched within DN B-cell subset. Their frequency was significantly higher relative to total CD19$^+$ B cells compared to other subsets. The mean frequencies of ABCs were 6.46% in DN, 2.59% in USM, 1.37% in naïve, and 0.29% in SM B cells (**$p < 0.02$**).

In vitro differentiation assays using sorted B-cell subsets from HDs (n = 3) demonstrated that DN and SM B cells exhibited the highest propensity to differentiate into ABCs under stimulatory conditions. The mean frequencies of induced ABCs were 46.2% for DN, 32.4% for SM, 13.4 for naïve and 4.3 for USM B cells.

Assessment of IFNLR1 expression showed significantly elevated levels on CD11c$^+$CD21$^-$ ABCs within the DN subset in SLE patients (**$p < 0.02$**). *In vitro*, ABCs derived from DN B cells exhibited a 6.3-fold increase in IFNLR1 expression under ABC-inducing conditions, compared to 2.5-fold, 1.6-fold, and 1.6-fold increases in ABCs derived from SM, naïve, and USM B cells, respectively.

Conclusion: These findings identify the DN B-cell subset as a key origin of CD11c$^+$CD21$^-$ autoimmune-associated B cells in SLE and highlight their enhanced capacity for IFNLR1 expression. The preferential differentiation of DN B cells into ABCs, coupled with their heightened responsiveness to IFN-λ, driven by increased IFNLR1 expression, suggests a distinct IFN-λ–mediated pathway in B-cell–driven autoimmunity. This IFN-λ–IFNLR1 axis may represent a novel therapeutic target for modulating B-cell–driven autoimmunity in SLE.

Disclosure: R. Yaakoub: None; **D. Alzamareh**: None; **A. William**: None; **J. Barnas**: None.

Abstract Number: 0913

Potent and Selective Oral IRF5 Degrader, KT-579, Demonstrates *In Vitro* and *In Vivo* Activity Comparable or Superior to Approved or Clinically Active Agents in Human Cellular Assays and Lupus Efficacy Models

Veronica Campbell[1], Yi Zhang[1], Virginia Massa[1], Jordan Leedberg[1], Erik Corcoran[1], Emily Lurier[1], Ryan Camire[2], Chris Carroll[1], Chris Ho[1], Dapeng Chen[1], Bradley Enerson[1], Revonda Mehovic[1], Ziyan Zhao[1], Lincoln Howarth[1], Susanne Breitkopf[1], Sarah Martinez[1], Melissa Ford[1], Xue Fei[1], Murugappan Sathappa[1], Juliet Williams[3], Matthew Weiss[3], Arsalan Shabbir[3] and Nello Mainolfi[4], [1]Kymera Therapeutics, Watertown, MA 02472, [2]Kymera Therapeutics, Watertown, MA 02472, MA, [3]Kymera Therapeutics, Watertown, [4]Kymera Therapeutics, Watertown, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IRF5 is a transcription factor and regulator of immune responses activated downstream of pattern recognition receptors, in particular endosomal toll-like receptors (TLR), TLR7, TLR8 and TLR9. IRF5 regulates pro-inflammatory cytokines (TNFα, IL-6, IL-12, IL-23), autoantibody production and Type I IFN, and is selectively expressed and activated in specific cell types such as dendritic cells, monocytes, macrophages, and B cells. Human genetic and functional studies have linked IRF5 in the pathogenesis of multiple autoimmune diseases, including SLE, RA, and Sjögren's, and *Irf5*-deficient mice are protected from lupus onset and severity. In SLE, endosomal TLRs recognize nuclear self-antigens, triggering IRF5 activation and driving the breakdown of immune tolerance via a cascade involving B cell activation, autoantibody and pro-inflammatory cytokine production. Despite its strong mechanistic and genetic validation, IRF5 has historically

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

remained undrugged likely due to its activation complexity and multiple functional isoforms. IRF5 is well suited for targeted protein degradation. KT-579, an oral IRF5 degrader, has demonstrated potent and selective activity in preclinical studies, offering a novel approach to modulating this key driver of immunity.

Methods: Peripheral blood mononuclear cells (PBMCs) derived from healthy or SLE donors were cultured with KT-579 in the presence or absence of TLR7, TLR8 or TLR9, to evaluate KT-579 selectivity, potency and functional activity. Oral IRF5 degrader was tested in mouse models of acute TLR7 or TLR9 activation, and MRL.lpr and NZBW1 lupus models.

Results: KT-579 was selective for IRF5 in the detectable proteome, including other IRF family proteins. KT-579 demonstrated sub nanomolar potencies across relevant cell types tested, and inhibited pro-inflammatory cytokines, Type I IFN production and response, and IgG levels downstream of TLR7, TLR8 or TLR9 induction in healthy or SLE PBMC assays. *In vivo*, KT-579 led to dose-dependent inhibition of both TLR7 or TLR9 induced TNFα, IL-6 and IL-12, unlike a TLR7/8 inhibitor. In the MRL.lpr lupus model, KT-579 doses achieving >85% degradation led to significant reduction of proteinuria and 100% survival. In the long term NZBW1 spontaneous lupus model, daily oral doses achieving >80% IRF5 degradation resulted in sustained reduction of proteinuria, circulating ANA and total kidney lesions. In both lupus models, IRF5 degradation was well tolerated, and IRF5 degrader activity was superior to approved or clinically active drugs. KT-579 achieved deep depletion (≥90%) across multiple species with low oral doses, and did not show adverse effects at concentrations up to 200-fold the projected human efficacious levels in preclinical safety studies.

Conclusion: We report here the first potent, selective, oral IRF5 degrader development candidate, KT-579, which depletes IRF5 in human primary cells, SLE patient derived cells, and lupus disease models, demonstrating superior activity to existing standards of care agents. These findings position KT-579 as a novel, first-in-class, oral therapeutic agent with the potential to transform the treatment landscape of lupus and multiple autoimmune diseases driven by IRF5 dysregulation.

Disclosure: V. Campbell: Kymera Therapeutics, 3; **Y. Zhang**: Kymera Therapeutics, 3; **V. Massa**: Kymera Therapeutics, 3; **J. Leedberg**: Kymera Therapeutics, 3; **E. Corcoran**: Kymera Therapeutics, 3; **E. Lurier**: Kymera Therapeutics, 3; **R. Camire**: Kymera Therapeutics, 3; **C. Carroll**: Kymera Therapeutics, 3; **C. Ho**: Kymera Therapeutics, 3; **D. Chen**: Kymera Therapeutics, 3; **B. Enerson**: Kymera Therapeutics, 3; **R. Mehovic**: Kymera Therapeutics, 3; **Z. Zhao**: Kymera Therapeutics, 3; **L. Howarth**: Kymera Therapeutics, 3; **S. Breitkopf**: Kymera Therapeutics, 3; **S. Martinez**: Kymera Therapeutics, 3; **M. Ford**: Kymera Therapeutics, 3; **X. Fei**: Kymera Therapeutics, 3; **M. Sathappa**: Kymera Therapeutics, 3; **J. Williams**: Kymera Therapeutics, 3; **M. Weiss**: Kymera Therapeutics, 3; **A. Shabbir**: Kymera Therapeutics, 3; **N. Mainolfi**: Kymera Therapeutics, 3.

Abstract Number: 0914

Preclinical Expansion of Autoreactive Naive B cells Drives RA onset in ACPA+ individuals

Xiaohao Wu[1], Mengrui Zhang[2], Orr Sharpe[3], V. Michael Holers[4], Jane Buckner[5], Gary Firestein[5], Eddie James[6], Kevin Deane[7] and William H. Robinson[8], [1]Stanford Uniersity, Stanford, [2]Stanford University, Stanford, CA, [3]Stanford University, Stanford, [4]University of Colorado Anschutz Medical Campus, Aurora, [5]Benaroya Research Institute, Seattle, [6]Benaroya Research Institute, Benaroya Research Institute, [7]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [8]Stanford University, Palo Alto, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The cellular and molecular mechanisms underlying the progression from anti-citrullinated protein antibody (ACPA) positivity to clinical rheumatoid arthritis (RA) remain poorly understood. Defining these early immunologic events is essential for identifying predictive biomarkers and developing preventive strategies.

Methods: We conducted longitudinal single-cell profiling of peripheral blood mononuclear cells (PBMCs) collected at two timepoints: a preclinical baseline and a follow-up approximately one year later. Participants were classified into three groups: (1) $ACPA^+$ converters who were ACPA-positive at baseline and developed clinical RA at follow-up; (2) $ACPA^+$ non-converters who did not develop clinical RA; and (3) healthy controls who were ACPA-negative and RA-free at both timepoints. B cells were isolated and analyzed using an integrated multi-modal single-cell approach, including 5′ scRNA-seq, VDJ-seq, and CITE-seq.

Results: Single-cell analysis revealed a marked preclinical expansion of $IGHM^+$ $IGHD^+$ $CXCR5^+$ $CD69^+$ activated naïve (aNAV) B cells in $ACPA^+$ converters. These aNAV cells exhibited a distinct pro-inflammatory transcriptional profile, characterized by upregulation of genes involved in immune activation, antigen presentation, impaired tolerance, and cellular stress, compared to non-converters and healthy controls. VDJ repertoire analysis revealed that within converters, IgM-expressing aNAV cells dominated the BCR landscape and exhibited elevated clonal diversity along with distinct V–J gene rearrangements across both heavy and light chains. Recombinant monoclonal antibodies derived from these IgM^+ aNAV cells demonstrated broad autoreactivity to multiple RA-associated autoantigens, including both native and citrullinated epitopes. In contrast, aNAV cells from non-converters more closely resembled those of healthy controls in their transcriptional profiles, BCR repertoires, and autoreactivity patterns.

Conclusion: These findings identify a preclinical expansion of $IGHM^+$ $IGHD^+$ $CXCR5^+$ $CD69^+$ naïve B cells in $ACPA^+$individuals who progress to RA. These cells are transcriptionally stressed, pro-inflammatory, and resistant to immune tolerance. Their BCR repertoire is enriched for diverse, autoreactive IgM antibodies with distinct V–J rearrangements. This autoreactive IgM pool may contribute to early immunologic activation and the eventual onset of rheumatoid arthritis.

Disclosure: X. Wu: None; **M. Zhang**: None; **O. Sharpe**: None; **V. Holers**: Q32 Bio, 12, 2; **J. Buckner**: None; **G. Firestein**: None; **E. James**: None; **K. Deane**: Inova Diagnostics, 1; **W. Robinson**: None.

Abstract Number: 0915

A Fusion of TACI Variant and Anti-ifnar Antibody with Greater Therapeutic Effect on Related Autoimmune Disease Models

Yuhao Qin[1], Huan Wang[1], Han Gao[1], Chongqi Zhang[1], Chengpan Wang[1], yanru fan[1], wei ye[1], yuan lin[1], Lu Su[2], Wenming Ren[1] and cheng liao[1], [1]Jiangsu Hengrui Pharmaceuticals Co., Ltd, Shanghai, China (People's Republic), [2]Jiangsu Hengrui Pharmaceuticals, Shanghai, Shanghai, China

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0897–0915) B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pathological elevation of type I interferon (IFN-I) , B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) has been robustly documented across multiple autoimmune diseases. But blocking these pathways individually only demonstrates limited efficacy with a considerable proportion of patients exhibiting inadequate therapeutic responses, which may be attributed to pathogenic heterogenicity of disease and population. IFN-I is required for B cell

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

activation and differentiation as well as other multiple immune cells, while BAFF and APRIL synergistically sustain plasma cell survival and clonal expansion. We developed a fusion protein (vTACI-aIFNAR) by covalently linking a BAFF/APRIL-neutralizing TACI variant to an IFN-I-blocking anti-IFNAR antibody. This multi-pathway blocker is designed to achieve greater therapeutic effect, thereby improving outcomes across heterogeneous patient populations.

Methods: Single-cell RNA sequencing data of PBMCs from 175 systemic lupus erythematosus (SLE) patients and 99 healthy controls were obtained from the cellxgene database and analyzed. Binding affinity was evaluated by surface plasmon resonance. The B cell proliferation, STAT-1 phosphorylation and plasma cell generation were measured in function related cellular assays. *In vivo* efficacy was evaluated using two distinct murine models: an allogeneic salivary gland protein-induced Sjögren's syndrome (SS) model and the NZBWF1/J spontaneous SLE model. Safety profiling was performed through a 4-week repeated-dose Good Laboratory Practice (GLP) toxicology study in cynomolgus monkeys.

Results: Pseudobulk RNA-seq analyses revealed elevated BAFF, APRIL, and IFN-I expression in SLE patients compared to healthy controls, with 82.3% exhibiting concurrent overexpression of IFN gene signature (IFGS) and BAFF, 40.6% of IFGS and APRIL, 37.7% of BAFF and APRIL, and 37.5% of all three factors, which indicates pathogenic heterogeneities of SLE patients. The vTACI-aIFNAR displayed robust BAFF/APRIL binding and potent suppression of B cell proliferation driven by these factors, while its IFN-I binding and STAT-1 phosphorylation inhibition were similar to that of anti-IFNAR antibody. Notably, vTACI-aIFNAR surpassed TACI-Fc and anti-IFNAR in blocking IFN-α/BAFF/APRIL-induced plasma cell generation *in vitro*. In murine SS models, the murine surrogate of vTACI-aIFNAR restored salivary flow rates in a dose-dependent manner, outperforming both TACI-Fc and anti-IFNAR antibody at equimolar doses. SLE models demonstrated marked alleviation in proteinuria, anti-dsDNA IgG/IgM level, and renal histopathology following treatment. GLP-compliant primate toxicity studies confirmed favorable tolerability with a 43× safety margin relative to projected clinical exposure.

Conclusion: Collectively, our findings demonstrate that the multi-pathway blocker, vTACI-aIFNAR, shows greater therapeutic effect with favorable tolerability profiles, implying enhanced therapeutic efficacy across diverse autoimmune patient subsets. These preclinical advantages substantiate its clinical translation potential for autoimmune disorders.

Disclosure: Y. Qin: None; **H. Wang**: None; **H. Gao**: None; **C. Zhang**: None; **C. Wang**: None; **y. fan**: None; **w. ye**: None; **y. lin**: None; **L. Su**: None; **W. Ren**: None; **c. liao**: None.

Abstract Number: 0916

UVB-Irradiated Keratinocyte Extracellular Vesicles Trigger Innate Immune Activation via Type I Interferons and STING Pathway

Ahmed Eldaboush[1], Darae Kang[2] and Victoria Werth[3], [1]Department of Dermatology, Perelman Shool of Medicine, University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Potomac, MD, [3]University of Pennsylvania, Wynnewood, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Extracellular vesicles (EVs) are cell-derived nanoparticles that mediate cell-cell communication. EVs are implicated in photosensitive autoimmune diseases like dermatomyositis (DM) and systemic lupus (SLE), where UVB radiation can trigger systemic flares. Given UVB's limited dermal penetration, we hypothesize that keratinocyte-derived EVs

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(KEVs) mediate UVB inflammation via relaying proinflammatory signals from keratinocytes (KCs) to dermal immune cells. Our prior work showed KEVs elicit inflammation in healthy control (HC) PBMCs, but specific immune cell targets remain undefined. This study identifies immune cell subsets responsive to KEVs.

Methods: HaCaT KCs were pretreated ±1 ng/mL IFN-β for 24h (to mimic DM skin), then irradiated with 0 or 75 mJ/cm^2 UVB and cultured overnight in EV-free media. KEVs were isolated by ultracentrifugation, resuspended in PBS, and incubated overnight with HC PBMCs. Cells were analyzed by flow cytometry.

Results: EVs from UVB-irradiated KCs (UVB-KEVs) significantly induced IFNβ compared to sham-KEVs in conventional dendritic cells (cDCs) [p=0.002], monocyte-derived dendritic cells (MoDCs) [p=0.039], macrophages [p=0.019], CD4$^+$ T cells [p=0.036], CD8$^+$ T cells [p=0.015], and CD19$^+$ B cells [p=0.036]. A similar trend was observed in natural killer cells (NKs) [p=0.09] and plasmacytoid dendritic cells (pDCs) [p=0.149], though not significant. Notably, only EVs from IFNβ-pretreated irradiated KCs (IFNβ-KEVs) significantly stimulated IFNβ in pDCs [p=0.015] and NKs [p=0.007].

UVB-KEVs also induced IFNγ in MoDCs [p=0.034], macrophages [p=0.005], CD8$^+$ T cells [p=0.047], and B cells [p=0.039], with non-significant increases in NKs [p=0.2], pDCs [p=0.06], and CD4$^+$ T cells [p=0.06]. However, only IFNβ-KEVs significantly induced IFNγ in pDCs [p=0.001].

UVB-KEVs increased p-NFκB in NKs [p=0.033], CD4$^+$ T cells [p=0.021], CD8$^+$ T cells [p=0.029], and B cells [p=0.031], with a trend in pDCs [p=0.052]. UVB-KEVs significantly upregulated p-STING in NKs [p=0.0008], pDCs [p=0.006], MoDCs [p=0.0009], macrophages [p=0.0008], CD4$^+$ T cells [p=0.017], CD8$^+$ T cells [p=0.019], and B cells [p=0.01], with a similar but non-significant trend in cDCs [p=0.12]. However, IFNβ-KEVs significantly increased p-STING in cDCs [p=0.03] and more than UVB-KEVs [p=0.043].

p-STING activation was highest in macrophages and MoDCs. IFNγ was highest in pDCs (only with IFNβ-KEVs); IFNβ was most induced in cDCs and pDCs (again only by IFNβ-KEVs). IFNβ-KEVs uniquely induced both IFNβ and IFNγ in pDCs. Of note, cDCs were previously found to be enriched in DM skin of antimalarial non-responders and express high IFNβ and p-STING, and blood pDCs and cDCs in DM patients secreted more IFNβ than HCs, and pDCs are enriched in DM skin, producing high IFNβ and IFNγ.

Conclusion: UVB-KEVs trigger type I IFN production and activate STING, both upregulated in DM and SLE. Responses were more prominent in innate immune cells. IFNβ-KEVs distinctively activated cDC p-STING and drove pDC IFNβ and IFNγ, both critical in DM/SLE pathogenesis. This suggests a mechanism by which UVB triggers systemic inflammation via KEVs. Ongoing studies aim to block KEV release, dissect their cargo, and mitigate their proinflammatory effects.

Disclosure: A. Eldaboush: None; **D. Kang**: None; **V. Werth**: AbbVie/Abbott, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta Bio, 2, Calyx, 2, CSL Behring, 5, Cugene, 2, Eli Lilly, 2, EMD Serona, 2, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 5, Immunovant, 2, Janssen, 2, Kwoya Kirin, 2, Merck/MSD, 2, Novartis, 2, Nuvig, 2, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, Rome Pharmaceuticals, 5, Sanofi, 2, Takeda, 2, UCB, 2, 2, Ventus, 2, Viela, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0917

Synovial Tissue Neutrophils are Associated with Disease Activity and Early Remission in Rheumatoid Arthritis

Annabelle Small[1], Vincent Wong[2], Christopher Altmann[1], Helen Weedon[3], Malcolm Smith[4], Susanna Proudman[5] and Mihir Wechalekar[6], [1]Flinders University, Bedford Park, South Australia, Australia, [2]College of Medicine and Public Health, Bedford Park, South Australia, Australia, [3]Flinders University of South Australia, Bedford Park, South Australia, Australia, [4]Flinders University, Adelaide, South Australia, Australia, [5]Royal Adelaide Hospital and University of Adelaide, Medindie, South Australia, Australia, [6]Flinders Medical Centre and Flinders University, Bedford Park, South Australia, Australia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0916–0933) Innate Immunity Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Neutrophils drive local pathology of rheumatoid arthritis (RA) in the synovial tissue (ST) through local production inflammatory mediators, cytokines, and extracellular traps. However, despite these roles, the relevance of their infiltration into the ST with regards to disease activity and response to treatment remain poorly understood. Thus, this project sought to assess the relationship between neutrophil infiltration into the early RA ST and clinical outcomes.

Methods: Arthroscopic ST samples preserved in FFPE from n=32 patients with treatment-naïve RA (< 12 months of onset, fulfilling 2010 ACR/EULAR criteria) were routinely stained with hematoxylin and eosin, and neutrophils judged by morphology by two independent observers. Six field of views (20x) from each section were manually assessed for neutrophil infiltration. Raw counts were reported for (1) marginating neutrophils in blood vessels, (2) tissue-infiltrating neutrophils, (3) combined total counts, and (4) total counts converted into a semiquantitative (SQA) score: 0=< 3 observed; 1=3-10 observed; 2=11-22 observed; 3=23-54 observed; 4=55-85 observed; 5= >85 observed. Manual scoring was validated by immunohistochemistry for CD15, and by comparison with matched bulk RNA sequencing data from the ST of the same patients which had previously been deconvoluted using CIBERSORT.

Results: Data was visualized by heatmap (Figure 1). Neutrophil infiltration measured by CIBERSORT was moderately positively correlated with DAS28CRP (r=0.1952, p=0.0145). Manual scores had a stronger positive correlation with DAS28CRP of higher significance (total: r=0.5409, p=0.0020; tissue infiltrating: r=0.4771, p=0.0077; marginating: r=0.6139, p=0.0003;

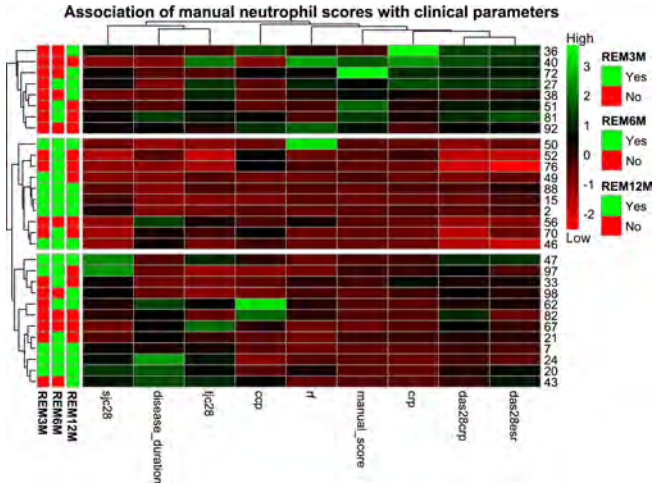


Figure 1. Heatmap of baseline characteristics and total manually determined neutrophil scores of our cohort (n=32), annotated with remission status at 3, 6, and 12 months (judged as DAS28CRP<2.4).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SQA: r=0.6444, p=0.0001). All manual scores positively correlated with CRP (total: r=0.4775, p=0.0057; tissue infiltrating: r=0.3939, p=0.0257; marginating: r=0.6135, p=0.0002; SQA: r=0.5881, p=0.0004). Margination and SQA scores were positively correlated with RF titre (p=0.0123 and 0.0302, respectively). No association between neutrophil scores were observed with disease duration, tender or swollen joint counts or CCP status or titre. Finally, patients who reached early remission (DAS28CRP< 2.4 at 3 months) had lower manual neutrophil infiltration scores at baseline than those who did not (total: p=0.0189; tissue infiltrating: p=0.0155; SQA: p=0.0102).

Conclusion: RA ST neutrophil content prior to treatment initiation was associated with baseline disease activity, CRP levels and RF titres; patients who achieved early remission had lower neutrophil counts at baseline. Together, these outcomes suggest that ST neutrophil content may prove useful as an objective, predictive measure of disease activity, and has the potential to identify patients less likely to achieve early remission.

Disclosure: A. Small: None; **V. Wong**: None; **C. Altmann**: None; **H. Weedon**: None; **M. Smith**: None; **S. Proudman**: Boehringer-Ingelheim, 5, 6, Janssen, 5, 6, Merck/MSD, 1; **M. Wechalekar**: GlaxoSmithKlein(GSK), 5, Janssen, 5.

Abstract Number: 0918

Retention of variant forms of TNFR1 in the Golgi induces stress responses and monocyte activation in systemic Juvenile Idiopathic Arthritis (sJIA)

Anthony Cruz[1], Krisztian Csomos[1], Boglarka Ujhazi[1], Hiroto Nakano[2], Marissa Krantz[3], Sophia Chou[4], Emily Rosenbaum[1], Tianmin Fu[5], Dirk Foell[6], Rae Yeung[7], Pamela Weiss[8], Faiza Naz[9], Ly-Lan Bergeron[1], Michelle Millwood[10], Carol Lake[11], Emely Verweyen[6], Grant Schulert[12], Stefania Dell'orso[9], Hao Wu[13], Zuoming Deng[14], davide Randazzo[15], Michael Ombrello[16] and INCHARGE Consortium, [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, Bethesda, MD, [2]NIAMS, NIH, Bethesda, MD, [3]University of Rochester, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, Rockville, MD, [5]Ohio State University College of Medicine, Columbus, OH, [6]University Hospital Muenster, Muenster, Germany, [7]The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada, [8]Childrens Hospital of Philadelphia, Philadelphia, PA, [9]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [10]National Institutes of Health (NIH), Bethesda, MD, [11]NIH, GAITHERSBURG, MD, [12]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [13]Harvard University, Cambridge, MA, [14]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [15]Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, [16]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), North Bethesda, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is severe and poorly understood inflammatory condition. Tumor necrosis factor receptor 1 (TNFR1) is activated by TNF and is found on most cell types. TNFR1 signaling triggers complex formation via its death domain (DD), activating proinflammatory processes through NFκB and various cell death pathways. Using a combination of genetic, *in vitro* and *ex vivo* studies, we have discovered a novel class of *TNFRSF1A* variation in children with sJIA.

Methods: We performed trio exome sequencing in a child with sJIA and targeted sequencing of *TNFRSF1A* in 525 sJIA cases. TNFR1 DD interactions were examined by modeling, Förster resonance energy transfer (FRET) and immunoprecipitation. TNFR1 variants were assayed *in vitro* for NFkB and cell death, and receptor localization was analyzed by superresolution microscopy (SRM). Patient peripheral blood mononuclear cells (PBMC) were compared to age matched control

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

PBMC using single cell RNA sequencing (scRNAseq) and SRM. Resting/LPS stimulated monocyte phenotypes, cell death and cytokine secretion were compared to age matched controls *ex vivo*.

Results: Trio exome sequencing identified a novel, *de novo* nonsense variant of *TNFRSF1A* that excludes the transmembrane domain and DD (K203X), while targeted sequencing found 2 subjects with ultra rare variants in the DD (P367S, E398K). All variants showed defective NFκB signaling and attenuated cell death *in vitro*, attributable to their impaired ability to nucleate the TNFR1 signaling complex, while SRM found reduced surface expression and enhanced Golgi localization of all 3 variants. scRNAseq of K203X PBMC revealed a paucity of classical and nonclassical monocytes. Instead, most monocytes formed a unique patient specific cluster that exhibited suppressed TNF signaling with paradoxical overactivation of NFκB signaling, resulting in a distinct inflammatory signature. Functional enrichment analysis revealed markedly reduced vesicular trafficking and autophagy related pathways, accompanied by activation of stress responses and innate immune pathways. Key regulators of Golgi and endosomal function were consistently downregulated across multiple pathways, indicating widespread disruption of Golgi homeostasis in K203X monocytes. Indeed, K203X PBMC displayed larger areas positive for a Golgi marker, indicative of fragmentation and damage. K203X monocytes also displayed a strongly M1 skewed transcriptional program, adopting a proinflammatory M1 like phenotype and producing abundant inflammatory cytokines even under steady state conditions. Finally, K203X monocytes showed downregulation of cell death related genes and demonstrated striking resistance to apoptosis upon stimulation with LPS or Fas ligand *ex vivo*, consistent with a hyperinflammatory, antiapoptotic state.

Conclusion: By investigating a novel loss of function variant of TNFR1, we identified a unique mechanism of immune dysregulation. This is characterized by dysfunctional trafficking and chronic accumulation of K203X TNFR1 in the Golgi, which leads to endosomal and autophagic failure, disruption of Golgi homeostasis, and ultimately cascading cellular stress that leads to hyperactive immune function.

Disclosure: A. Cruz: None; **K. Csomos**: None; **B. Ujhazi**: None; **H. Nakano**: None; **M. Krantz**: None; **S. Chou**: None; **E. Rosenbaum**: None; **T. Fu**: None; **D. Foell**: None; **R. Yeung**: AstraZeneca, 5, SOBI, 6; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1; **F. Naz**: None; **L. Bergeron**: None; **M. Millwood**: None; **C. Lake**: None; **E. Verweyen**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **S. Dell'orso**: None; **H. Wu**: None; **Z. Deng**: None; **d. Randazzo**: None; **M. Ombrello**: None.

Abstract Number: 0919

Proteomic Profiling of Extracellular Vesicles from Synovial Fluid of RA and OA Patients Reveals Cell-type-specific subpopulations and Disease Related Patterns

Stefanie Kurth[1], Andre Tiaden[1], Edveena Hanser[1], Simone Häner[1], Stavros Giaglis[1], Florian Geier[1], Dominik Burri[1], Katarzyna Buczak[1], Ute Heider[2], Stefan Wild[2], Yves Acklin[1], Christian Egloff[1] and **Diego Kyburz**[3], [1]University of Basel, Basel, Switzerland, [2]Miltenyi Biotec, Bergisch-Gladbach, Germany, [3]University Hospital Basel, Basel, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Extracellular vesicles (EVs) are secreted by virtually all cells and are known to carry bioactive cargo including proteins, RNA, DNA and metabolites. Analysis of the cargo of EVs derived from the synovium may provide insight into disease-specific molecular pathways of arthritis. So far, most studies characterizing EVs in disease were based on bulk analysis, neglecting the complexity of EV populations present in biofluids of patients. To investigate and characterize distinct

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

EV subpopulations in synovial fluid of patients with rheumatoid arthritis (RA) and osteoarthritis (OA) we have established an novel immunocapture separation method based on magnetic nano-sized beads targeting cell type specific markers. CD90/THY1 was selected as a synovial fibroblast marker due to the reported contribution of CD90+ to synovitis.

Methods: EVs were isolated from synovial fluid of patients with RA and OA via size exclusion chromatography (SEC) and subsequently characterized by Nano Tracking Analyzer (NTA), NanoFlow cytometry (NanoFCM) and Western Blot (WB). For separation of a CD90+ EV population prototype anti-CD90 MicroBeads (Miltenyi Biotec) were used. WB and mass-spectrometry (MS)-based proteomics were applied to analyse the EV subpopulations. The proteomic profile of separated EV subpopulations was compared with published reference single cell RNA-Seq Data from inflamed synovial tissue. Disease specific proteomic profiles of EVs from RA and OA were compared.

Results: Using our immunocapture approach we were able to separate CD90+ EVs from synovial fluid of arthritis patients. WB confirmed a CD90 enrichment, while proteomic analysis revealed a stromal cell signature in the CD90+ EV-population, in comparison to markers for infiltrated immune cells like T cells, B cells, monocytes and neutrophils enriched in the CD90- EVs. The comparison of EV populations derived from RA and OA synovial fluid showed CD90+ EVs in both diseases. Analysis of RA-derived EVs showed a prominent neutrophil and macrophage signature, while OA enriched proteins were of fibroblast, macrophage, endothelial and epithelial cell profile. Proteomic analysis revealed several proteins enriched in RA known for their involvement in inflammation (TREM1, CXCR1, CXCR2, RETN, PADI4, LOXL3, CTSZ, MPO) or in cartilage degradation (MMP8). In contrast, in OA proteins involved in cartilage degradation and bone destruction were significantly enriched (ADAM10, FMOD, GPRC5a, INPP4N, LRP1, TNXB, SPARCL1) as well as protein candidates associated with OA pathogenesis and severity (CAPG, CTSA, LTBP1, LUM, LRP1).

Conclusion: Using a novel immunocapture approach we were able to separate cell type specific subsets of EVs from synovial fluid of arthritis patients. Proteomic analysis confirmed a stromal cell pattern in CD90+ EVs and revealed enrichment of disease specific proteins in EVs derived from RA and OA synovial fluid respectively. The ability to investigate distinct cell-type specific EV subsets in synovial fluid provides insight into pathogenetic mechanisms in the synovium and may lead to the identification of biomarkers in a liquid biopsy approach.

Disclosure: S. Kurth: None; **A. Tiaden**: None; **E. Hanser**: None; **S. Häner**: None; **S. Giaglis**: None; **F. Geier**: None; **D. Burri**: None; **K. Buczak**: None; **U. Heider**: Miltenyi Biotec, 3; **S. Wild**: Miltenyi Biotec, 3; **Y. Acklin**: None; **C. Egloff**: None; **D. Kyburz**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, UCB, 6.

Abstract Number: 0920

Functional Characterization of NEMO-NDAS Causing Variants in Patients' PBMCs and in Wildtype and Mutant U937 Cells

Elizabeth Morgan[1], Bin Lin[2], Sara alehashemi[1], Adriana de Jesus[1], Keith Kauffman[3], Christopher Friend[1], Farzana Bhuyan[1], Kader Gedik[1], Kat Uss[1], Lauren Krausfeldt[4], Jason Brenchley[5], Zoran Gucev[6], Kathryn Cook[7], Vafa Mammadova[8], Gulnara Nasrullayeva[8], Mariana Correia Marques[9], Abigail Bosk[10], Brian Nolan[11], Scott Canna[12], Maude Tusseau[13], Andrea Bohrer[14], Katrin Mayer-Barber[15], Timothy Moran[16], Andrew Oler[4], Daniel Barber[3] and Raphaela Goldbach-Mansky[1], [1]Translational Autoinflammatory Diseases Section (TADS), Laboratory of Clinical Immunology and Microbiology (LCIM), NIAID, NIH, Bethesda, MD, [2]NIH, Bethesda, MD, [3]T-Lymphocyte Biology Section, Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD, [4]Bioinformatics and Computational Biosciences Branch, Office of Cyber Infrastructure and Computational Biology, NIAID, NIH, Bethesda, MD, [5]Barrier Immunity Section, Laboratory of Viral Diseases, NIAID, NIH, Bethesda, MD, [6]University Children's Hospital, Medical Faculty Skopje, Skopje, Macedonia, [7]Akron Children's Hospital, Akron, OH, [8]Azerbaijan Medical University, Baku, Azerbaijan, [9]Translational Genetics and Genomics Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [10]Children's National Hospital, Washington DC, [11]Lurie Children's Hospital, Chicago, [12]Children's Hospital of Philadelphia, Philadelphia, PA, [13]Hôpital Femme-Mère-Enfant, Bron, France, [14]Inflammation and Innate Immunity Unit, Laboratory of Clinical Immunology and Microbiology (LCIM), NIAID, NIH, Bethesda, MD, [15]Inflammation and Innate

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Immunity Unit, Laboratory of Clinical Immunology and Microbiology (LCIM), Bethesda, MD, [16]University of North Carolina School of Medicine, Chapel Hill, NC

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: NEMO-deleted 5 autoinflammatory syndrome (NEMO-NDAS) is an inflammatory disease caused by mosaic splice-site variants that lead to exon 5 skipping in *IKBKG*, encoding NEMO. Patients (pts) present with systemic inflammation, gdT-cells expansion, high serum IFNg, portal hypertension (PH) and porto-sinusoidal vascular disorders (PSVD). Here, we characterize the effect of exon 5-skipped NEMO on NFκB σιγναλινγ ιν Υ937 χελλσ, ανδ ασσεσσ ιντεστιναλ βαρριερ ανδ γυτ μιχροβιομε δψσρεγυλατιον ιν τηε πατηογενεσισ οφ ΠΗ ανδ ΠΣς∆.

Methods: U937 cells with exon 5-skipped NEMO were created by CRISPR (MUT) and compared to wildtype U937 cells (WT). NFkB signaling, cell viability, p65 nuclear translocation, NEMO/IKKb colocalization, and mRNA transcription profiling were assessed in TNF-stimulated MUT and WT U937 cells. We assessed immune activation and target killing in pts' PBMCs cocultured with WT and/or MUT U937s and quantified live U937 cells by flow cytometry. To characterize the gut-liver-axis, we analyzed intestinal fatty-acid-binding protein (I-FABP) concentrations in serum, and the stool microbiome (including virome), in NEMO-NDAS pts, inflammatory controls, and healthy household controls (HCs).

Results: Following TNF stimulation, nuclear translocation of p65 was significantly attenuated in MUT U937 cells consistent with impaired NFkB signaling. Additionally, increased susceptibility to TNF-induced cell death of MUT U937 cells was associated with a lack of upregulation of the anti-apoptotic genes *BIRC3*/cIAP2 and *CFLAR*/c-FLIP.

To test the killing potential of expanded gd T cells in pts' PBMCs, we cocultured pts' PBMCs with WT or MUT U937 cells. While viability of WT U937 cells is not affected by the pts' PBMC, mutant U937 cells are killed. When mixed WT and MUT U937s were cocultured with PBMCs, both WT and MUT U937s had decreased survival compared to PBMC-free conditions. Exploration of contributing cell types and pathomechanisms is ongoing.

Liver-gut-axis evaluation suggested that NEMO-NDAS pts have increased IFABP serum levels compared to CANDLE pts and HCs, suggestive of increased intestinal permeability and impaired gut barrier function. Microbiome studies showed increased abundance of Faecalibacterium phages and a decrease in metabolic protective markers, which is consistent with previously reported data in liver disease.

Conclusion: Exon 5-skipping in NEMO impairs NFkB signaling, sensitizes U937 cells to TNF-induced cell death, and leads to U937 cell death in cocultures with PBMCs from NEMO-NDAS pts. We hypothesize that exon 5-skipped NEMO impairs gut epithelial cell function and leads to dysbiosis and increased microbial translocation that contribute to PH and PSVD in NEMO-NDAS. Whether impaired gut barrier and dysbiosis contribute to activation and expansion of gd T cells in NEMO-NDAS is under investigation.

Disclosure: E. Morgan: None; **B. Lin**: None; **S. alehashemi**: None; **A. de Jesus**: None; **K. Kauffman**: None; **C. Friend**: None; **F. Bhuyan**: None; **K. Gedik**: None; **K. Uss**: None; **L. Krausfeldt**: None; **J. Brenchley**: None; **Z. Gucev**: None; **K. Cook**: None; **V. Mammadova**: None; **G. Nasrullayeva**: None; **M. Correia Marques**: None; **A. Bosk**: None; **B. Nolan**: None; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **M. Tusseau**: None; **A. Bohrer**: None; **K. Mayer-Barber**: None; **T. Moran**: None; **A. Oler**: None; **D. Barber**: None; **R. Goldbach-Mansky**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0921

Fibrinogen Co-Modified with Malondialdehyde-Acetaldehyde and Citrulline Promotes Pro-Inflammatory Macrophage Differentiation Through p38 and NF-κB Signaling

Hannah Johnson[1], Wenxian Zhou[2], Michael Duryee[1], Carlos Hunter[1], Geoffrey Thiele[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Medical Center, Bellevue, NE

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Citrulline (CIT) and malondialdehyde-acetaldehyde (MAA) co-adduct native proteins in RA tissues to create a dual pro-inflammatory and pro-fibrotic milieu. Our previous work demonstrated that supernatants from macrophages stimulated with CIT-MAA co-modified fibrinogen induce inflammatory, fibrotic, and invasive phenotypes in synovial and lung fibroblasts. However, the intracellular signaling pathways preceding cytokine release remain poorly defined. The aim of this study was to elucidate the inflammatory signaling pathways in macrophages following stimulation with CIT-MAA co-modified fibrinogen.

Methods: The human monocytic cell line (U-937) was differentiated into macrophages (M0 cells) using phorbol 12-myristate-13-acetate (PMA) and then stimulated with fibrinogen (FIB) that was unmodified, MAA-modified (FIB-MAA), CIT-modified (FIB-CIT), or CIT-MAA co-modified (FIB-CIT-MAA). After 1-hr of antigen stimulation, cells were lysed and protein was analyzed using Western blot analysis targeting the phosphorylated forms and total levels of p38 MAPK, NF-κB (p65), ERK1/2, STAT1, STAT3, STAT6, Akt1, Akt2, JNK, and β-actin. After 48-hrs of stimulation, supernatants were collected and analyzed by ELISA for concentrations of TNFα, IL-1β, IL-6, and MCP-1. After initial testing by Western blot, for each treatment group, there was a replicate group pre-treated with a p38 inhibitor (BIRB-796) or an NF-κB inhibitor (BAY 11-7085) for 1-hr before antigen stimulation. Statistical analysis was performed using one-way ANOVA with Tukey's multiple comparisons test.

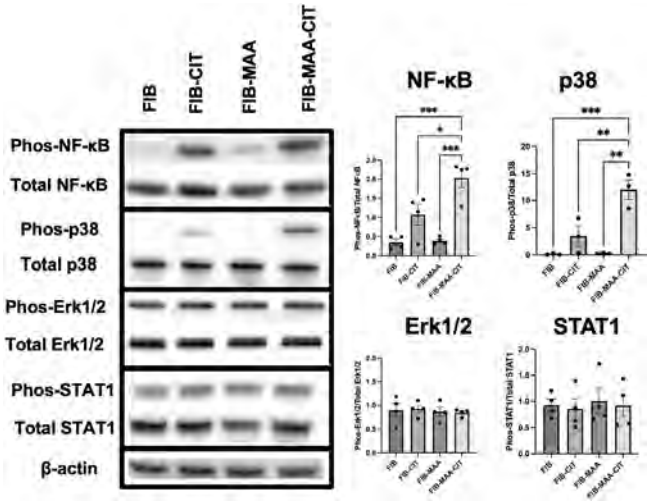


Figure 1. Intracellular Signaling Pathways Activated after Macrophage Stimulation Demonstrated by Western Blot. Macrophages were stimulated for 1-hr with fibrinogen (FIB) that was unmodified or modified with citrulline (CIT) and/or malondialdehyde-acetaldehyde (MAA) prior to measurement of intracellular signaling. Band intensity was quantified using KwikQuant Image Analyzer software. Graphs are plotted as a phosphorylated protein normalized to total protein. Note: phosphorylated Akt1, Akt2, JNK, STAT3, and STAT6 not detected (not shown); One-way ANOVA was performed and the statistical differences between groups are shown in *: * p<0.05; ** p<0.01; *** p<0.001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

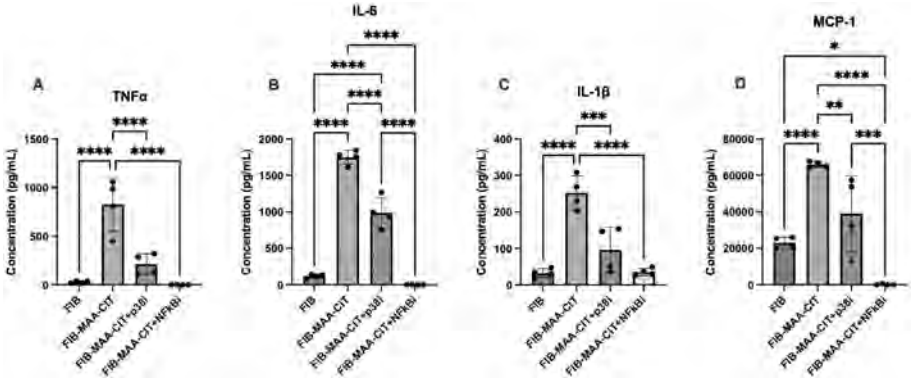


Figure 2. ELISA Demonstrating Decreased Cytokine Production in Macrophages After Inhibition of p38 or NF-κB. 48-hr cytokine concentrations in supernatants were measured for; A) TNFα, B) IL-6, C) IL-1β, and D) MCP-1. One-way ANOVA was performed and the statistical differences between groups are shown in *: * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001.

Results: Western blot demonstrated that M0 cells treated with FIB-CIT had significantly increased p38 and NF-κB phosphorylation compared to unmodified FIB, with FIB-CIT-MAA further enhancing phosphorylation of these specific signaling molecules (Fig 1). No significant changes were observed in ERK1/2 and STAT1 following stimulation with any of the antigens. Additionally, phosphorylated Akt1, Akt2, JNK, STAT3, and STAT6 were not detected. Inhibition of signaling pathways after pre-treatment with p38 MAPK and NF-κB inhibitors was validated by Western blot. ELISA revealed that FIB-CIT-MAA stimulation significantly increased secretion of TNF-α, IL-1β, IL-6, and MCP-1 compared to both unmodified FIB, FIB-MAA, and FIB-CIT. Addition of inhibitors to p38 and/or NF-κB decreased release of all 4 cytokines, but only NF-κB inhibition fully abrogated their release (Fig 2).

Conclusion: CIT-MAA co-modified fibrinogen stimulates macrophage activation via the p38 and NF-κB pathways, promoting secretion of pro-inflammatory mediators including TNF-α, IL-1β, IL-6, and MCP-1. Inhibition of these pathways attenuates inflammatory cytokine production, supporting a mechanistic link between CIT-MAA adducts and disease progression in RA. Future research will validate this finding using human monocytes and identify whether agents targeting these post-translational modifications as well as downstream signaling pathways have the potential to attenuate RA progression.

Disclosure: H. Johnson: None; **W. Zhou**: None; **M. Duryee**: None; **C. Hunter**: None; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

Abstract Number: 0922

Phenotypic and Transcriptomic Divergence in C3 Glomerular Mouse Models: Insights into Immune and Sex Correlates

Juan Liang[1] and kaiyuan zi[2], [1]Gempharmatech, Nanjing, Jiangsu, China, [2]Gempharmatech, Nanjing, Jiangsu, Jiangsu, China

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Complement component C3 plays a central role in the alternative pathway (AP) and is implicated in the pathogenesis of C3 glomerulopathy (C3G), a rare renal disease. To model human-specific complement dysregulation, we developed two humanized C3 mouse models: B6-hC3 (expressing human C3 transgene) and B6-hC3 mC3 KO (expressing human C3 transgene with knockout of mouse C3). These models were designed to induce unregulated C3 activation via the alternative pathway (AP) and recapitulate C3G-like phenotypes. Through phenotypic assessment and RNA sequencing, we sought to elucidate molecular mechanisms underlying disease development and investigate sex-associated gene expression signatures.

Methods: A human C3 transgene was introduced into B6 mouse embryos to generate B6-hC3 mice. Additionally, the endogenous mouse C3 gene in B6-hC3 mice was knocked out to generate B6-hC3 mC3 KO mice. Both B6-hC3 and B6-hC3 mC3 KO mice were evaluated longitudinally for renal dysfunction via urinalysis. RNA sequencing (RNA-seq) was performed on both B6-hC3 and B6-hC3 mC3 KO mice to identify differentially expressed genes and pathways between strains and sexes.

Results: Both B6-hC3 and B6-hC3 mC3 KO strains developed hallmark features of C3G. However, B6-hC3 mC3 KO mice exhibited more severe renal dysfunction and damage compared to B6-hC3. Notably, female B6-hC3 mC3 KO mice developed higher levels of proteinuria and exhibit diverse renal lesions compared to males, suggesting sex-specific susceptibility. RNA-seq analysis revealed strain-specific transcriptomic profiles between B6-hC3 and B6-hC3 mC3 KO strains, as well as sex-associated gene expression signatures between male and female B6-hC3 mC3 KO mice.

Conclusion: In this study, two novel humanized mouse models that recapitulate key features of human C3G were established. Phenotypic and transcriptomic analyses reveal critical differences between strains and sex, making these models valuable platforms for future mechanistic studies of C3G and for the preclinical evaluation of targeted complement-modulating therapies.

Disclosure: J. Liang: None; **k. zi**: None.

Abstract Number: 0923

Influenza Virus Infection Alters the MHC Class II Self-Immunopeptidome to Present Lupus-Associated Autoantigens

Julia Rood[1], Stephanie Suh Kyung Yoon[2], Mary Heard[1], Michael Hogan[2], Nicola Ternette[3], Edward Behrens[4] and Laurence Eisenlohr[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Dundee, Dundee, Scotland, United Kingdom, [4]CHOP, West Chester, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Viral infections and major histocompatibility complex class II (MHC II) are both implicated in the genesis of systemic lupus erythematosus (SLE), but a mechanistic understanding of how these factors promote autoimmunity is lacking. One phenomenon observed for MHC class I-restricted self-peptides – but which remains largely unexplored for MHC II – is the ability of viruses to alter processing and presentation of endogenous self-antigens. We investigated the impact of infection with influenza, a virus associated with autoantibody formation in healthy individuals and disease flares in SLE patients, on the repertoire of self-peptides presented by MHC II.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A murine antigen presenting cell (APC) line expressing C57Bl/6-derived I-Ab, BALB/c-derived I-Ed, and class II transactivator-driven antigen processing and presentation components was either infected with the mouse-adapted H1N1 influenza strain PR8 or mock-infected *in vitro*. MHC II:peptide complexes were immunoprecipitated, and peptides were fractionated by reversed-phase high-performance liquid chromatography, analyzed by nano-ultra-performance liquid chromatography-tandem mass spectrometry, and identified from a database containing the influenza and mouse proteomes.

Results: An average of 9,895 peptides were identified among influenza-infected APCs per experimental replicate. Self-peptides comprised >95% of the MHC II immunopeptidome in influenza-infected cells, concordant with published observations from other intracellular pathogens. Among these self-peptides, 24-40% were unique to infected, rather than uninfected, cells. Functional annotation clustering revealed significant enrichment of ribosomal proteins and ribonucleoproteins (RNPs) among peptides unique to infected cells. Multiple unique epitopes were identified from ribosomal P0, a known target of anti-ribosomal P antibodies in SLE patients. We also identified peptides derived from histones, other nuclear DNA-binding proteins, and complement proteins including C3, an autoantibody target in at least one-third of SLE patients. Peptides derived from complement C3 were separately identified in published MHC II immunopeptidome data from H1N1 influenza-infected human cells.

Conclusion: Active influenza infection *in vitro* substantially alters the MHC II self-immunopeptidome and is associated with presentation of SLE autoantigens. These data suggest that influenza manipulates non-classical endogenous antigen processing pathways within APCs to expose new self-epitopes capable of activating autoreactive CD4+ T cells in SLE. Future studies will investigate intracellular processing of these peptides and their presentation in murine models of SLE to elucidate the mechanistic role of viral infection in promoting autoimmunity.

Disclosure: J. Rood: None; **S. Yoon**: None; **M. Heard**: None; **M. Hogan**: None; **N. Ternette**: None; **E. Behrens**: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9; **L. Eisenlohr**: None.

Abstract Number: 0924

Human Serum Albumin Co-Modified with Malondialdehyde-Acetaldehyde and Citrulline Bind Multiple Scavenger Receptors and Alter Cellular Morphology

Lauren Klingemann[1], Michael Duryee[1], Nozima Aripova[1], Wenxian Zhou[2], Hannah Johnson[1], Breanna Butler[1], Carlos Hunter[1], Ted Mikuls[1] and Geoffrey Thiele[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Medical Center, Bellevue, NE

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Post-translational modifications (PTMs) of self-proteins are implicated in the pathogenesis of rheumatoid arthritis (RA). The PTMs, malondialdehyde-acetaldehyde (MAA), citrulline (CIT), and the co-modification of MAA and CIT have been demonstrated to be overrepresented in RA tissues in addition to exerting robust proinflammatory and profibrotic effects on macrophages and fibroblasts. Previous studies have shown that MAA and MAA-CIT protein antigens bind to scavenger receptors on macrophages. These data showed increased binding to TLR4, SRBII and SREC. However, little

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

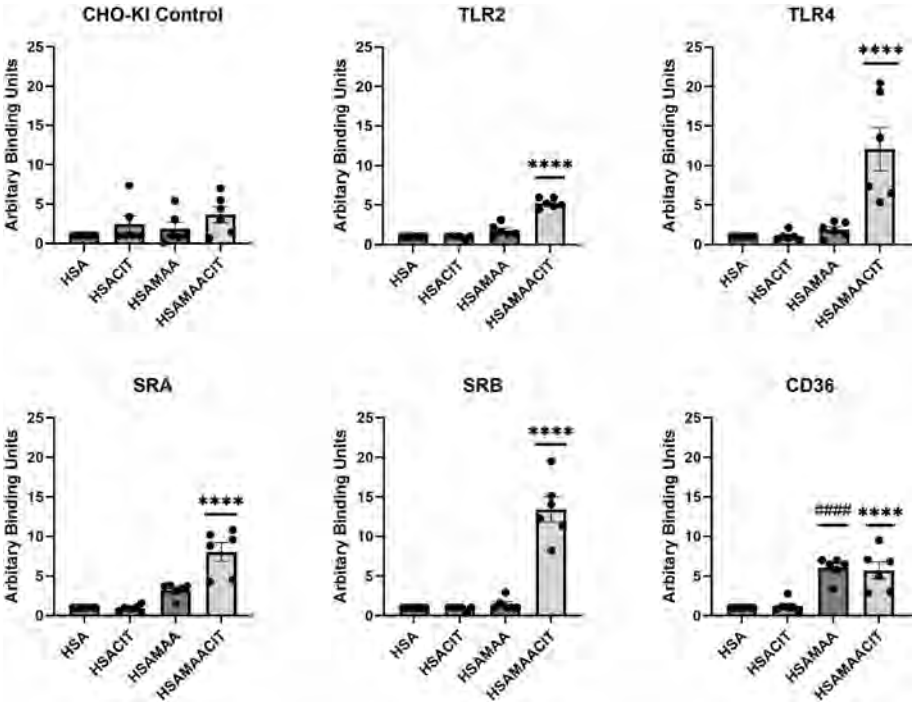


Figure 1. Arbitrary binding unit quantification following Western Blotting of post-translationally modified HSA to scavenger receptors of the different transfected CHO cells. Control CHO-K1 cells and CHO cells expressing TLR2, TLR4, SRA, SRB, and CD36 were incubated with 25 μg of HSA, HSA-CIT, HSA-MAA, or HSA-MAA-CIT for 90 minutes at 40C. Cells were washed and binding was determined by a cellular ELISA using an HRP conjugated anti-human albumin antibody that was detected using TMB substrate measuring the absorbance at 450 nm on an ELISA reader. To quantify binding, arbitrary binding units were developed by normalizing the data to native HSA. Anova was used to compare binding across treatment groups. Comparisons to native HSA shown above the bars (**** p<0.0001, ####p<0.0001). HSA-MAA-CIT demonstrated statistically significant binding to TLR2, TLR4, SRA, and SRB transfected CHO cells as compared to native HSA, HSA-CIT, and HSA-MAA. In CHO cells expressing CD36, both HSA-MAA-CIT and HSA-MAA demonstrated a statistically significant increase in binding to the scavenger receptor compared to HSA and HSA-CIT N=6 for each group.

is known as to whether MAA-CIT modified antigens bind additional receptors let alone which specific receptor(s) bind them. Therefore, it was the purpose of this study to determine which specific receptors bind MAA-CIT modified proteins, and whether this binding alters the morphology of the cells.

Methods: Chinese Hamster Ovary (CHO) cells transfected with a single scavenger receptor (SR): TLR2, TLR4, SRA, SRB and CD36 were incubated with 25 μg of Human serum albumin (HSA) modified with; CIT (HSA-CIT), MAA (HSA-MAA) or MAA-CIT (HSA-MAA-CIT) antigens for 90 minutes on ice. An in-cell ELISA was performed to determine binding capacity. Briefly, cells were washed and incubated with a horseradish peroxidase (HRP) conjugated anti-human albumin antibody

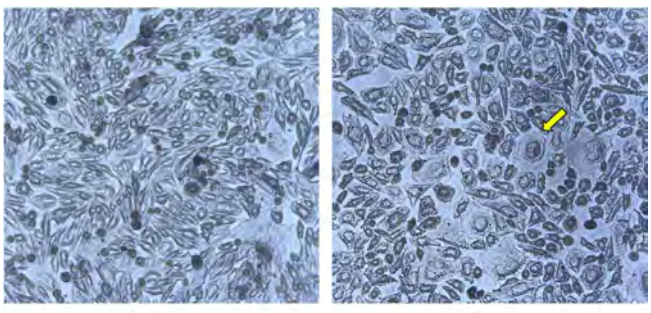


Figure 2. Representative images of CHO-K1 and CHO-TLR4 cells stimulated with HSA-MAA-CIT. Following 90 minutes of incubation with 25 μg of HSA-MAA-CIT, CHO cells transfected with TLR4 scavenger receptors demonstrate marked morphological changes compared to CHO-K1 controls. CHO-K1 control cells (left) display a spindle-shaped morphology, whereas CHO-TLR4 cells (right) show a larger polygonal morphology.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

followed by detection using TMB substrate. Reactivity was determined at 450nm and data normalized to native HSA to look for arbitrary binding units. Additionally, following exposure and incubation on ice, the cells were photographed and evaluated for morphological changes using a Nikon overhead microscope at a magnification of 20X.

Results: Binding data revealed significant increases ($p < 0.0001$) in MAA-CIT binding to TLR2, TLR4, SRA, and SRB compared to native HSA, HSA-CIT and HSA-MAA antigens (**Figure 1**). Interestingly, MAA and MAA-CIT bound equally to CD36 compared to HSA and HSA-CIT antigens suggesting MAA is the major modification resulting in binding to CD36. In other studies, the cells were imaged following incubation with MAA-CIT antigens and showed drastic morphological changes in cellular phenotype (**Figure 2)**. Changes included increased cellular size and shape compared to control CHO cells (no SR receptor) following MAA-CIT binding to TLR4 CHO cells, with similar changes being observed with the CHO cells expressing various SRs.

Conclusion: Findings from this study demonstrate that MAA-CIT modified protein binds multiple different scavenger receptors. Results confirm previous data showing that MAA-CIT co-modified antigen binds more to TLR4, and SRB receptors than TLR2 or SRA. Interestingly, MAA and MAA-CIT bind CD36 receptors at a similar compacity. While MAA-CIT binds all the receptors at similar levels, suggesting co-modification with MAA-CIT may be a better ligand than MAA or CIT alone. Further studies are warranted to investigate these receptors on human macrophages from patients with RA and how the morphological changes observed translate to effects on cellular function.

Disclosure: L. Klingemann: None; **M. Duryee**: None; **N. Aripova**: None; **W. Zhou**: None; **H. Johnson**: None; **B. Butler**: None; **C. Hunter**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **G. Thiele**: None.

Abstract Number: 0925

Pathogenic role of SPP1+ macrophages in Rheumatoid Arthritis

Megan M. Hanlon[1], Catherine Manning[1], Kevin Wei[1], Ursula Fearon[2] and Ellen M. Gravallese[3], [1]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [2]Trinity College Dublin, Dublin, Dublin, Ireland, [3]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Synovial tissue macrophages (STMs) represent a mixed population of cells contributing to the pathogenesis of rheumatoid arthritis (RA). We identified an enrichment of Secreted phosphoprotein-1 (SPP1) STMs in RA compared to healthy control (HC) synovial tissue. We show SPP1+ STMs are also enriched in individuals at risk for RA (IAR), suggesting they represent an early disease-specific myeloid subset (1). The aim of this study was to uncover the specific contributions of SPP1+ STMs to RA pathogenesis, which may provide opportunities to reinstate joint homeostasis.

Methods: Peripheral blood was obtained from HC and RA patients. CD14+ monocytes were isolated and differentiated either in the presence of M-CSF (50ng/ml) or Ca2+ (2.5 mM) for 7 days to derive Macs or SPP1-expressing-Macs (S-Macs), respectively. Inflammatory cytokine production by these cells, and their defining metabolic parameters were measured by RT-PCR, ELISA and by the Seahorse-XFE technology. Paraffin embedded synovial tissue biopsies were obtained from HC, from RA patients undergoing key-hole arthroscopy, and from seropositive IAR who have no clinical signs of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

inflammation. Spatial transcriptomics was performed using a custom Xenium 5K+ panel. Only RA patients who fulfilled the revised ACR criteria were included in this study.

Results: RA SPP1+ STMs correlate significantly with clinical inflammation and display the highest expression of glycolytic genes compared to all other STMs. RA S-Macs have increased expression of SPP1 at both the gene and protein level compared to Macs. S-Macs display increased expression of IL-6, TNF, IL-1b and IL-8 and the glycolytic genes HIF1a and HK2 compared to Macs. Importantly, this is more pronounced in cells derived from RA vs HC indicating priming in the RA periphery. RA S-Macs display decreased baseline oxidative phosphorylation and maximal respiratory capacity compared to Macs derived from HC/RA blood, while concomitantly skewing the ECAR/OCR ratio in favor of glycolysis, indicating that RA S-Macs rely heavily on glycolysis. Finally, we conducted Xenium in situ spatial profiling technology to measure RNA expression levels of 5100 genes in unique paraffin-embedded synovial tissue from HC, IAR and RA. We annotated cell clusters (including macrophages, fibroblasts, T, B cells) and identified their localization to serve as a map of the synovial cellular organization across the evolution of disease.

Conclusion: We demonstrate that SPP1+ STMs correlate with clinical inflammation in RA and are metabolically reprogrammed towards glycolysis, leading to sustained induction of pro-inflammatory responses. Xenium spatial analysis allows us to determine the cellular interactions and disease stage-specific factors that shape SPP1+ STMs in RA synovium. These cells may thus represent a potential pathway for therapeutic targeting.

(1) Hanlon, Megan M et al. "Loss of synovial tissue macrophage homeostasis precedes rheumatoid arthritis clinical onset." Sci Adv. 2024;10(39):eadj1252. doi:10.1126/sciadv.adj1252

Disclosure: M. Hanlon: Quotient, 2; **C. Manning**: None; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **U. Fearon**: Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Quotient, 2; **E. Gravallese**: Beam Therapeutics, 11, CRISPR Therapeutics, 11, Editas Medicine, 11, Elsevier, 9, Ginkgo Bioworks, 11, Intellia Therapeutics, 11, New England Journal of Medicine, 1, UpToDate, 9.

Abstract Number: 0926

Discovery and Characterization of SIM0711: a Potent and Selective IRAK4 PROTAC with Improved Efficacy and Safety

Minyun Zhou[1], Peng Gu[2], Mengyu Wang[3], Yuxi Yan[2], Li Sun[3], Yiling Chen[3], Xin Wang[3], Feng Tang[1], Shunwei Zhu[2] and Xiaofeng Zhao[4], [1]State Key Laboratory of Neurology and Oncology Drug Development, Simcere Pharmaceutical group, Nanjing, [2]State Key Laboratory of Neurology and Oncology Drug Development, Simcere Pharmaceutical Group, Shanghai, China (People's Republic), [3]State Key Laboratory of Neurology and Oncology Drug Development, Simcere Pharmaceutical Group, Nanjing, China (People's Republic), [4]State Key Laboratory of Neurology and oncolog Drug Development, Simcere Pharmaceutical Group, Nanjing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IRAK4 plays a pivotal role in the innate immune response by acting downstream of Toll-like receptors (TLRs) and the interleukin-1 receptor (IL-1R), with both kinase activity and scaffolding functions. This dual role makes it a critical target for modulating inflammatory signaling. However, traditional IRAK4 kinase inhibitors have shown limited

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

efficacy due to their inability to disrupt the scaffolding function. IRAK4-targeting PROTACs offer a more comprehensive strategy by inducing selective degradation of IRAK4 protein. Here, we report the discovery and characterization of SIM0711, a potent and selective oral IRAK4 PROTAC for the treatment of autoimmune diseases.

Methods: We developed and extensively characterized SIM0711 through a series of *in vitro* and *in vivo* studies. SIM0711 was benchmarked against KT-474 (an IRAK4 PROTAC) and PF-06650833 (a selective kinase inhibitor). IRAK4 degradation and kinetics were assessed in human immune and stromal cells. Downstream cytokine inhibition (IL-6 and/or IL-8) was measured by ELISA followed by TLR4, TLR8, TLR9, and IL-1R stimulation. *In vivo* efficacy and pharmacodynamic effects on cytokine production were evaluated in multiple mouse models of inflammation. Additionally, oral dosing studies in rodents, dogs, and non-human primates (NHPs) were conducted to characterize IRAK4 degradation, PK/PD relationships, bioavailability, and safety.

Results: In comparison to the benchmark PROTAC KT-474, SIM0711 achieved near-complete IRAK4 degradation in diverse human immune cells and stromal cell lines, with faster degradation kinetics observed in primary human monocytes. Meanwhile, SIM0711 induced more complete inhibition of IL-6 and IL-8 secretion upon TLR4, TLR7, TLR9, and IL-1R activation, outperforming both PF-06650833 and KT-474 *in vitro*. *In vivo*, SIM0711 significantly reduced inflammation and demonstrated superior efficacy over KT-474 in multiple mouse models. This enhanced efficacy correlated well with deeper IRAK4 degradation in PBMCs and near-complete suppression of pro-inflammatory cytokine release at the site of inflammation. Additionally, SIM0711 showed improved oral bioavailability, robust IRAK4 degradation (> 90%), favorable PK/PD properties and good safety profiles across rodents, dogs and NHPs. Notably, SIM0711 exhibited a more balanced tissue distribution than KT-474, with preferential accumulation only observed at the inflamed site, potentially contributing to an improved therapeutic window.

Conclusion: These findings support SIM0711 as a potential best-in-class IRAK4 PROTAC for the treatment of a range of autoimmune diseases. Its robust IRAK4 degradation, superior anti-inflammatory efficacy, and favorable pharmacological profile highlight its strong therapeutic potential. IND submission is expected by Q3 2025.

Disclosure: M. Zhou: Simcere Pharmaceutical Group, 3; **P. Gu**: Simcere Pharmaceutical Group, 3; **M. Wang**: Simcere Pharmaceutical Group, 3; **Y. Yan**: Simcere Pharmaceutical Group, 3; **L. Sun**: Simcere Pharmaceutical Group, 3; **Y. Chen**: Simcere Pharmaceutical Group, 3; **X. Wang**: Simcere Pharmaceutical Group, 3; **F. Tang**: Simcere Pharmaceutical Group, 3; **S. Zhu**: Simcere Pharmaceutical Group, 3; **X. Zhao**: Simcere Pharmaceutical Group, 3.

Abstract Number: 0927

Improved Skin Lymphatic Flow Regulates Dendritic Cells to Mediate Lymph Node Fibroblast Alterations and Immune Responses in Lupus

Mir Howlader[1] and Theresa Lu[2], [1]Weill Cornell Medical College, Brooklyn, NY, [2]Hospital for Special Surgery, NEW YORK, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Lupus is a chronic autoimmune disease with a global loss of self-tolerance. Lupus patients are photosensitive where exposure to even ambient sunlight results in skin inflammation. Lymph carries signals such as antigens and antigen-presenting cells from the skin to the lymph node. We recently demonstrated that exposure to ultraviolet radiation (UVR) causes reduced lymph flow from skin to lymph node in lupus mouse models and that improving flow reduced B and T cell responses by increasing fibroblastic reticular cell (FRC) CCL2 expression and FRC proliferation (Howlader, Ambler et al. *Journal of Clinical Investigation*, vol. 135, no. 10, 2025, e168412). How improved flow can affect the lymph node stromal compartment is not understood. Migratory dendritic cells (DCs) travel in the lymph from skin to lymph node, where they can change FRC phenotype. Reduced interferon signaling results in increased FRC CCL2 expression and increased expansion of FRCs. Here, we hypothesize that improving lymph flow allows for more migratory DCs to mediate FRC proliferation through reduced interferon signaling.

Methods: We used an inducible lupus mouse model where topical imiquimod (a TLR7 agonist) induces a lupus-like phenotype with elevated type I IFN signaling. Mice were exposed to UVR 4 days/week to study photosensitivity. We improve flow through manual lymphatic drainage (MLD), which is a light skin stretching technique that helps promote the movement of lymphatic fluid out of a swollen area. To assess the role of DCs, we generated bone marrow chimeras using zDC-DTR donors into B6 recipients, enabling selective depletion of DCs via diphtheria toxin (DT). We analyzed LN immune and stromal populations by flow cytometry and quantified interferon stimulated gene (ISG) expression by qPCR.

Results: Improving lymph flow increased the number of migratory dendritic cells in the lymph node and not Langerhans cells or resident dendritic cells. Depletion of migratory dendritic cells prior to MLD reversed the FRC proliferation, indicating that migratory DCs are required for FRC proliferation. MLD led to reduced expression of lymph node ISGs and adding interferon reverses MLD induced FRC expansion. We currently are investigating if migratory dendritic cells are required for the reduced interferon signaling.

Conclusion: Our results support a potential DC-stromal axis that plays a role in lupus photosensitivity. Imporving lymphatic flow promotes migratory DC entry into LNs, which appears to suppress IFN signaling and promote FRC proliferation. These findings highlight a lymphatic-dendritic cell-stromal axis as a potential therapeutic target to alleviate photosensitivity-associated autoimmunity.

Disclosure: M. Howlader: None; **T. Lu**: None.

Abstract Number: 0928

Radiolabelled anti-citrullinated histone antibody CIT-013 as a tool to visualize NET rich inflamed joints in a collagen induced arthritic mouse model

Annemarie Kip[1], Daphne Dorst[2], Birgitte Walgreen[2], Monique Helsen[2], Eric meldrum[1], **Renato Chirivi**[1] and Marije Koenders[2], [1]Citryll BV, Oss, Netherlands, [2]RadboudUMC, Nijmegen, Netherlands

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Neutrophil Extracellular Traps (NETs) contribute to the pathophysiology of multiple immune-mediated inflammatory diseases including Rheumatoid Arthritis (RA), and may be promising therapeutic targets. The first-in-class therapeutic anti-citrullinated histone antibody CIT-013 binds citrullinated histones H2A and H4 in NETs and has demonstrated efficacy in models of NET-mediated inflammation by inhibiting de novo NET formation and by enhancing clearance of existing NETs by Fc receptor-mediated phagocytosis (Chirivi et al 2021; van der Linden et al 2024).

In this study, we describe the use of a NET targeting antibody as an in vivo radiotracer to detect and visualize NETs in inflamed tissues.

Methods: Mice with collagen induced arthritic (CIA) mice with no, mild, moderate and established disease (n=10/group) were intravenously injected with indium-111 labeled mouse anti-citrullinated histone antibody (mACHA). Twenty-four hours after injection, whole body Single Photon Emission Computed Tomographic (SPECT) imaging was performed on selected animals. For all animals, tissue distribution of the radiotracer was quantified ex vivo by measuring gamma radiation.

Results: In CIA mice, indium-111 labeled mACHA distributes to inflamed joints and can be detected in animals with mild inflammation with increasing accumulation of the radiotracer in the fore and hind paws correlating with higher arthritis severity. Furthermore, the radiotracer enables a highly sensitive detection of inflammation in joints not apparently inflamed upon visual inspection, such as the knee.

Conclusion: mACHA can be used as a radiotracer to visualize NETs in sites of inflammation. This proof of principle imaging study enables a human whole body PET CT imaging clinical study in RA and hidradenitis suppurativa patients during 2025. This clinical study will lead to further insights in CIT-013's distribution, target engagement and mechanism of action in patients with immune mediated inflammatory diseases.

Disclosure: A. Kip: Citryll BV, 3, 5, 11; **D. Dorst**: Citryll, 12, Contract research; **B. Walgreen**: None; **M. Helsen**: None; **E. meldrum**: Citryll BV, 3, 3, 5, 11, 11; **R. Chirivi**: Citryll BV, 3, 5, 8, 10, 11; **M. Koenders**: BIRR, 7, Contura, 7, Eli Lilly, 5, Genmab, 7, Lemba Therapeutics, 7.

Abstract Number: 0929

SP2H, a Targeted Degrader of STimulator of INterferon Genes (STING), selectively inhibits STING-driven inflammation in vitro and in vivo and improves survival in Trex1$^{-/-}$ mice

Martin Jakobsen[1], Pernille Noer[2], Kristina Byskov[3], Emil Nilsson[4], Laura Ryø[5], Claus Olesen[2] and **Richard BETHELL**[6], [1]Aarhus University, Aarhus, Denmark, [2]Sulis Therapeutics, Aarhus, Denmark, [3]Notify Therapeutics, Aarhus, Denmark, [4]Sulis Therapeutics, Aarhus C, Denmark, [5]Aarhus University Hospital, Aarhus, Denmark, [6]Sulis Therapeutics, Stockholm, Sweden

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: STING plays a critical role at the intersection of innate and adaptive immunity and has been linked to the pathogenesis of SSc and SLE. While initially characterized as the adaptor protein leading to type 1 IFN induction downstream of the cytosolic DNA sensor cyclic guanosine-monophosphate adenosine-monophosphate synthase (cGAS),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

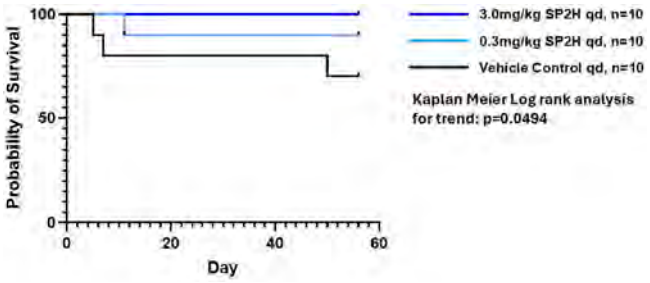


Figure 1: Kaplan Meier analysis of the survival of Trex1-/- mice treated with vehicle control, 0.3mg/kg SP2H or 3mg/kg SP2H sc qd. Each group comprised 5 male and 5 female animals. Animals were randomized by body weight, anti-dsDNA antibody titer and serum lactate dehydrogenase titer at age 5 weeks. Treatment was initiated at age 6 weeks and continued daily for 8 weeks.

STING can be activated independently of cGAS by several other mechanisms. Beyond its role in IFN induction, STING directly activates other pathways, e.g. NF-kB-driven inflammatory cytokine expression and the PERK-eIF2a arm of the unfolded protein response. We developed SP2H - a targeted STING degrader, preventing all STING driven activation mechanisms - as a new treatment strategy for SSc, SLE and other diseases characterized by excessive STING activation.

Methods: SP2H's effects on STING protein levels, and on inflammatory cytokine expression induced by STING agonists, were assessed *in vitro* using established cell lines and primary human fibroblasts. Inhibition of STING activation by single sub-cutaneous (sc) doses of SP2H *in vivo* was assessed in C57Bl6 mice following a single 1mg/kg dose of the STING agonist diABZI. Survival, serum cytokine levels and inflammatory gene expression were assessed in Trex1$^{-/-}$ mice following treatment with 0.3mg/kg and 3.0 mg/kg or vehicle control once daily (qd) sc SP2H for 56 days (n=10/group).

Results: SP2H selectively degraded STING *in vitro* with DC_{50} values of 40-100nM, and inhibited IFN-b expression induced by STING agonists with EC_{50} values of 20-100nM. When given 16h prior to diAZBI, single sc doses of SP2H (either 0.3mg/kg, 1mg/kg or 3mg/kg) resulted in a >1.2log$_{10}$ reduction in diABZI-induced serum interferon-b levels at all three doses, and dose-dependent reductions in serum CXCL10 (0.6-1.6log$_{10}$), CCL2 (1.3-2.3log$_{10}$), all $p< 0.0001$, and IL-6 (1.6-2.7log$_{10}$), all $p< 0.01$ (ANOVA). Treatment of Trex1$^{-/-}$ mice with SP2H for 8 weeks was well tolerated and improved overall survival (Kaplan-Meier analysis, log rank analysis for trend p=0.0494), with 100% survival at the higher SP2H dose as shown in Figure 1. The 3mg/kg dose of SP2H resulted in >4.5-fold lower serum levels of both CXCL10 and TNF-a (both $p< 0.0001$, ANOVA) compared to vehicle controls at the end of treatment, and significantly reduced expression of inflammatory genes (*CXCL10, TNF-a, IFN-b, CCL2, IFIT1, ISG15, IFI44, MX1*) in the heart.

Conclusion: Targeted degradation by SP2H leads to selective STING depletion and inhibition of STING-driven inflammation *in vitro* and *in vivo*. Treatment of Trex1$^{-/-}$ mice with SP2H was well-tolerated, improved survival and reduced inflammation, supporting further clinical development of SP2H as a potential treatment for diseases driven by the pathological overactivation of STING.

Disclosure: M. Jakobsen: Sulis Therapeutics, 1, 8, Unikum Therapeutics, 1, 8; **P. Noer**: Sulis Therapeutics, 3; **K. Byskov**: Notify Therapeutics, 3, Sulis Therapeutics, 3; **E. Nilsson**: Sulis Therapeutics, 3; **L. Ryø**: Sulis Therapeutics, 3; **C. Olesen**: Initiator Pharma, 12, 3, Kamino ApS, 4, 8, NMD Pharma, 12, Sulis Therapeutics, 3, 8, SynuCa ApS, 4, 8; **R. BETHELL**: GSK plc, 12, Medivir AB, 12, 10, Sulis Therapeutics, 3, 8, 10, SVF Vaccines, 4, 8, 10.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0930

Potent and Selective Oral IRF5 Degrader, KT 579, Blocks Pro-Inflammatory Cytokines and Reduces Joint Swelling in a Mouse Model of Rheumatoid Arthritis

Ryan Camire[1], Yi Zhang[2], Virginia Massa[2], Jordan Leedberg[2], Erik Corcoran[2], Emily Lurier[2], Chris Carroll[2], Chris Ho[2], Dapeng Chen[2], Bradley Enerson[2], Revonda Mehovic[2], Ziyan Zhao[2], Lincoln Howarth[2], Susanne Breitkopf[2], Sarah Martinez[2], Melissa Ford[2], Xue Fei[2], Murugappan Sathappa[2], Juliet Williams[3], Matthew Weiss[3], Arsalan Shabbir[3], Nello Mainolfi[4] and Veronica Campbell[2], [1]Kymera Therapeutics, Watertown, MA 02472, MA, [2]Kymera Therapeutics, Watertown, MA 02472, [3]Kymera Therapeutics, Watertown, [4]Kymera Therapeutics, Watertown, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0916–0933) Innate Immunity Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: IRF5, an undrugged transcription factor, is an autoimmune susceptibility gene that has been linked to RA and other autoimmune diseases including SLE, Sjögren's, and SSc. IRF5 is a regulator of immune responses activated downstream of pattern recognition receptors, like toll-like receptors (TLR). IRF5 regulates pro-inflammatory cytokines (TNFα, IL-6, IL-12, IL-23), autoantibody production and Type I IFN. IRF5 is selectively expressed and activated in specific cell types such as dendritic cells, monocytes, M1 macrophages, and B cells. RA is a chronic disease where the target tissue is synovial joints. The joints are characterized by heavy leukocyte infiltration. Inflamed synovium contains a larger number of activated macrophages and T cells in addition to B cells and dendritic cells. Studies in IRF5 deficient mice show attenuated arthritis severity in models of RA. Despite its strong mechanistic and genetic validation, IRF5 has historically remained undrugged likely due to its activation complexity and multiple functional isoforms. IRF5 is well suited for targeted protein degradation, where a single binding event drives activity. KT-579, an oral IRF5 degrader, has demonstrated potent and selective activity in preclinical in vitro myeloid assays and in vivo RA models, offering a new approach to modulating this key driver of immunity.

Methods: THP-1 monocytic cell line or peripheral blood mononuclear cells, monocytes, M1 macrophages, and dendritic cells were cultured with KT-579 in the presence or absence of TLR4, TLR7, or TLR8 stimulation and measured for pro-inflammatory cytokines including TNFα, IL-6, IL-12, IL-23, IFNy and IL-1β. KT-579 was tested in the antigen-induced arthritis (AIA) mouse model of RA and compared to the JAK inhibitor, tofacitinib.

Results: KT-579 was highly selective for IRF5 in the detectable proteome, including other IRF family proteins. In vitro, KT-579 demonstrated nanomolar inhibition of IL-1β, TNFα, IL-12, IL-23 and IFNγ, in a cell-type and stimulant-dependent manner, downstream of TLR activation. In the AIA model of RA, daily oral dosing with KT-579, achieved ~90% degradation of IRF5 and led to significant reduction in joint swelling comparable to tofacitinib. IRF5 degradation led to reduction of circulating pro-inflammatory cytokines including IL-12, IL-6 and CXCL1 and infiltrating Th1 T cells, that was differentiated from tofacitinib. In addition, KT-579 achieved deep IRF5 depletion (≥90%) across multiple species with low oral doses, and did not show adverse effects at concentrations up to 200-fold the projected human efficacious levels in preclinical safety studies.

Conclusion: We report here the first selective, potent, oral IRF5 degrader that can sufficiently deplete IRF5 and impact myeloid cell effector function by potently inhibiting pro-inflammatory cytokines found to be critical in amplifying inflammatory responses, including cytokines that promote Th1 and Th17 T cell responses, and can reduce joint swelling in a mouse model of RA. These findings support KT-579 as a novel therapeutic agent with the potential to be a first-in-class oral therapy for the treatment of RA and other autoimmune diseases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Camire: Kymera Therapeutics, 3; **Y. Zhang**: Kymera Therapeutics, 3; **V. Massa**: Kymera Therapeutics, 3; **J. Leedberg**: Kymera Therapeutics, 3; **E. Corcoran**: Kymera Therapeutics, 3; **E. Lurier**: Kymera Therapeutics, 3; **C. Carroll**: Kymera Therapeutics, 3; **C. Ho**: Kymera Therapeutics, 3; **D. Chen**: Kymera Therapeutics, 3; **B. Enerson**: Kymera Therapeutics, 3; **R. Mehovic**: Kymera Therapeutics, 3; **Z. Zhao**: Kymera Therapeutics, 3; **L. Howarth**: Kymera Therapeutics, 3; **S. Breitkopf**: Kymera Therapeutics, 3; **S. Martinez**: Kymera Therapeutics, 3; **M. Ford**: Kymera Therapeutics, 3; **X. Fei**: Kymera Therapeutics, 3; **M. Sathappa**: Kymera Therapeutics, 3; **J. Williams**: Kymera Therapeutics, 3; **M. Weiss**: Kymera Therapeutics, 3; **A. Shabbir**: Kymera Therapeutics, 3; **N. Mainolfi**: Kymera Therapeutics, 3; **V. Campbell**: Kymera Therapeutics, 3.

Abstract Number: 0931

Reduced mitophagy in salivary glands of Sjögren's disease patients is associated with mitochondrial structural damage

Salvador Campos[1], **Sergio Aguilera**[2], Juan Gutiérrez[1], Isabel Castro[3], Patricia Carvajal[3], Lorena Carvajal[1], Sergio González[4], Claudio Molina[5], María-Julieta González[6] and María-José Barrera[5], [1]Universidad San Sebastián, Santiago, Region Metropolitana, Chile, [2]Clinica Indisa, Santiago, Region Metropolitana, Chile, [3]Departamento de Tecnología Médica, Facultad de Medicina, Universidad de Chile, Santiago, Region Metropolitana, Chile, [4]Escuela de Odontología, Universidad Mayor, Santiago, Region Metropolitana, Chile, [5]Facultad de Odontología, Universidad San Sebastián, Santiago, Region Metropolitana, Chile, [6]ICBM, Facultad de Medicina, Universidad de Chile, Santiago, Region Metropolitana, Chile

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0916–0933) Innate Immunity Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Sjögren's disease (pSjD) is a systemic autoimmune disease characterized mainly by immune-mediated damage to exocrine glands. Previously, we found decreased expression of ATG5 and Beclin along with increased p62 protein levels in labial salivary glands (LSG) of SjD patients, suggesting decreased macroautophagy[1], which may contribute to the pathogenesis. On the other hand, recent evidence suggests that SjD is strongly associated with mitochondrial dysfunction, which may be related to inflammation as well as chronic fatigue, present in 70% of SjD patients. The increased presence of swollen mitochondria with membrane disorganization has been observed in salivary epithelial cells from SjD patients[2], suggesting reduced clearance by mitophagy. The aim of this study was to determine the levels of mitophagy markers in LSG from pSjD patients.

Methods: SGs from pSjD patients (n=9) and controls (n=5) were analyzed. Mitochondrial ultrastructure was observed by transmission electron microscopy (TEM). Protein levels of mitophagy markers of the PINK-Parkin-dependent pathway (pPINK, PINK, pParkin, Parkin), -independent pathway (BNIP3L) and LC3 were determined by Western blot. The localization of LC3 and mitochondrial markers was determined by immunofluorescence. In human salivary cells stimulated with pro-inflammatory cytokines, mitochondrial ultrastructure was evaluated by TEM.

Results: LSGs from pSjD patients showed increased protein levels of PINK and pPINK and decreased protein levels of p-Parkin, Parkin and BNIP3L. In addition, LC3-II was decreased. Increased PINK protein levels suggest mitochondrial damage because this protein accumulates when mitochondria lose their membrane potential; however, Parkin, pParkin, and BNIP3L are decreased, suggesting that the canonical and alternative pathways of mitophagy are reduced in LSG of SjD patients. The COXIV staining pattern by immunofluorescence showed a more fragmented mitochondrial network in SjD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients, consistent with smaller mitochondria observed by TEM. Pro-inflammatory cytokines such as IL-1β induced an increase in the presence of mitochondria altered with myelin-like figures inside.

Conclusion: In LSG samples, we identified the major markers related to mitophagy and found that PINK Parkin-dependent and -independent pathways are decreased in LSG of pSjD patients. Reduced mitophagy could explain the presence of more fragmented and damaged mitochondria. *In vitro* results show that some pro-inflammatory cytokines such as IL-1β could induce important structural changes in mitochondria, supporting the idea of a link between inflammation and mitochondrial damage. The results of this work contribute to the understanding of the altered mechanisms in pSjD and raise the idea of evaluating future innovative therapies aimed at improving mitophagy, mitochondrial morphology and function

References:

1. Rheumatology (Oxford). 2021 Apr 6;60(4):1951-1962.doi:10.1093/rheumatology/keaa670.
2. Autoimmun Rev. 2021 Aug;20(8):102867. doi: 10.1016/j.autrev.2021.102867.

Acknowledgments: Fondecyt-1241526/Fondecyt-1230852/Fondecyt-1210055.

Disclosure: S. Campos: None; **S. Aguilera**: None; **J. Gutiérrez**: None; **I. Castro**: None; **P. Carvajal**: None; **L. Carvajal**: None; **S. González**: None; **C. Molina**: None; **M. González**: None; **M. Barrera**: None.

Abstract Number: 0932

Compartment-specific NK-cell phenotypes reveal distinct maturation and activation states in inflammatory arthritis

Franca Sophie Deicher[1], Tarik Exner[2], Maren Claus[3], Schayan Yousefian[4], Lea Rodon[5], sophie leonhardt[6], Jörg Distler[7], Carsten Watzl[3], Hanns-Martin Lorenz[8], Simon Haas[4], Daniel Hübschmann[9] and **Wolfgang Merkt**[10], [1]Uniklinik Düsseldorf, Düsseldorf, Germany, [2]University Hospital Heidelberg, Heidelberg, Germany, [3]IfADo, Leibniz Institute Dortmund, Dortmund, Germany, [4]Charite, Berlin, Berlin, Germany, [5]University Hospital Heidelberg, Heidelberg, Hungary, [6]Heidelberg University, Heidelberg, Germany, [7]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [8]Universitätsklinikum Heidelberg, Heidelberg, Germany, [9]Heidelberg University, Berlin, Germany, [10]University Hospital Dösseldorf, Dösseldorf, Germany

SESSION INFORMATION

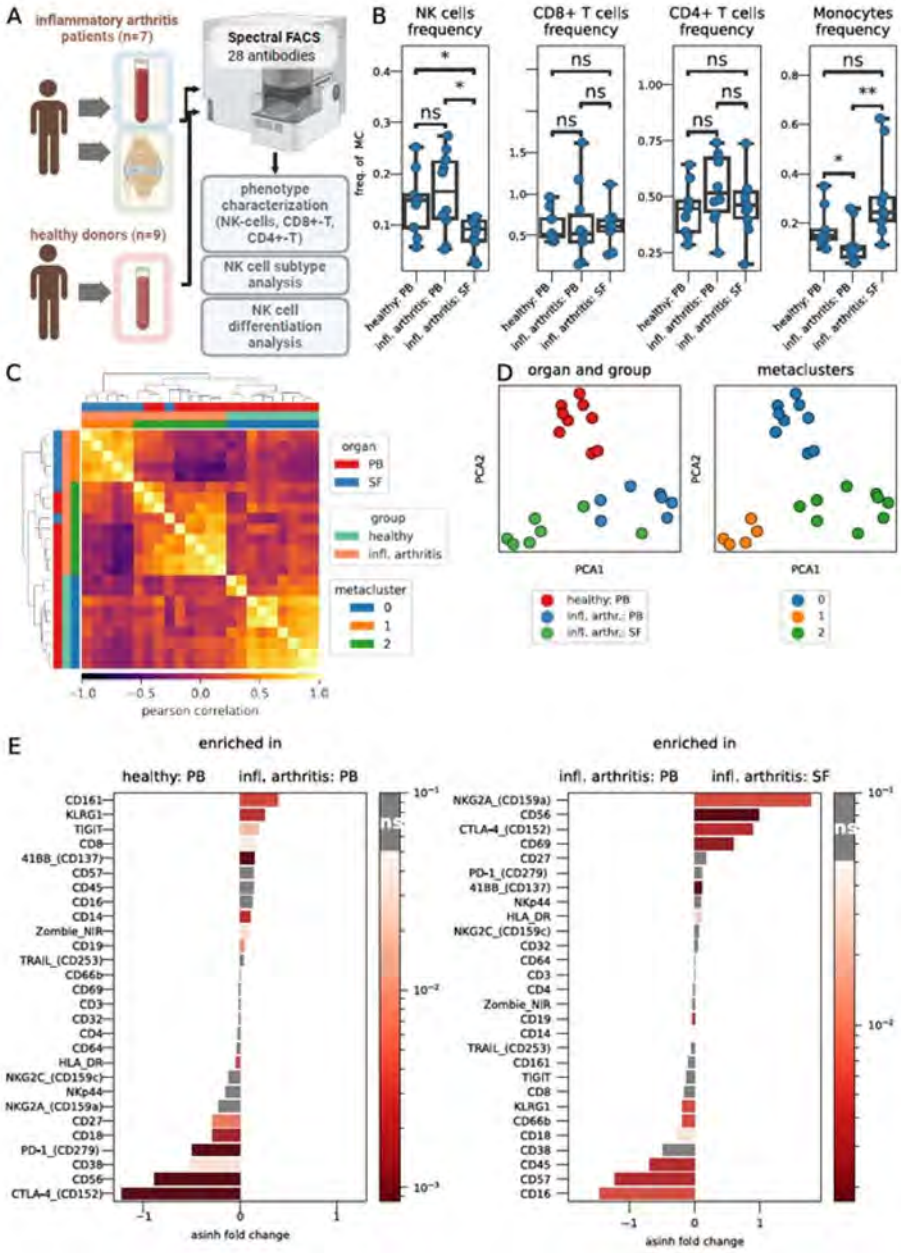
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Synovial natural killer (NK) cells contribute to inflammation in arthritis by secreting cytokines and modulating synovial fibroblast activation. The aim of this study is to describe systemic versus local inflammatory changes of NK-cell subsets as well as their physical cell-cell interactions in arthritis patients.

Methods: Spectral flow cytometry was used to compare paired peripheral blood (PB) and synovial fluid (SF) immune cells from patients with active inflammatory arthritis and healthy controls. Physical cell-cell interactions within tissues were studied by applying a recently developed cellular interaction mapping framework *Interact-omics (Vonficht et al., 2025, accepted in Nature Methods)*.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Our paired approach revealed significant local enrichment of immature and activated NK-cells in SF, characterized by elevated markers of early differentiation, immune checkpoint regulation, and tissue residency, highlighting tightly controlled immune activation at inflamed sites. Single-cell analysis confirmed heterogeneity within SF-NK-cells, suggesting multiple co-existing activation states and developmental stages. PB-NK-cells from patients differed profoundly from healthy controls, showing less immature NK-cell subsets and an enrichment of mature, pro-inflammatory subsets indicative of



NK cells display phenotypic changes in peripheral blood and synovial fluid in patients with inflammatory arthritis. A Graphical experimental design. B Cell frequencies. Frequencies of the indicated cell types were plotted as a percentage of PBMC. C Sample correlation analysis on a pseudobulk level. NK cells were correlated as described in the methods section. Hierarchical clustering revealed three subgroups which correspond to cells of different tissue and patient group (healthy and inflammatory arthritis). D Sample-wise principal component analysis. Samples were grouped by PCA and colored by tissue and patient group (left) and the metaclusters (right) as calculated in C. E Differential expression analysis. Fold-changes (x-axis, asinh_fc) were calculated as described in the Methods section. Notably, NK cells analyzed from peripheral blood show significant phenotypic differences comparing healthy controls and patients with inflammatory arthritis, including expression changes of CD161, KLRG1, PD-1 and CD56. Comparison of NK cells extracted from peripheral blood and synovial fluid show a differential phenotype with the elevation of activation markers such as NKG2A and CD69 and the corresponding downregulation of CD16 and CD57. PB: peripheral blood, SF: synovial fluid. P-values were calculated as described in the methods section where p-values above 0.05 were considered not significant (n.s.).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

systemic immune activation. Cellular interaction mapping revealed mainly NK/neutrophil interactions of patients' NK-cells, while interactions with B-cells, T-cells or monocytes were negligible.

T-cells also displayed profound local and systemic alterations. Cellular interaction mapping revealed that next to NK-cell/neutrophil interactions, interactions between B-cells with monocytes and T-cells with neutrophils characterize joint inflammation.

Conclusion: This paired high-dimensional analysis revealed systemic and local alterations in NK-cell subsets shaped by co-existing developmental stages and immune regulatory mechanisms. Cellular interaction mapping indicated that neutrophils are a main interaction partner of NK-cells in inflamed joints.

Disclosure: F. Deicher: None; **T. Exner**: None; **M. Claus**: None; **S. Yousefian**: None; **L. Rodon**: None; **s. leonhardt**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **C. Watzl**: None; **H. Lorenz**: None; **S. Haas**: None; **D. Hübschmann**: None; **W. Merkt**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, Evotec, 5, Glapagos, 12, support for congress travel, Kyverna, 6, Lilly, 12, support for congress travel.

Abstract Number: 0933

Spatial Transcriptomics Reveal Altered Immune Dynamics Regulating Placental Development In a Humanized-TLR8 Mouse Model of Spontaneous Anti-Phospholipid Antibody Induced Pregnancy Loss

Yunwei Xia[1], Paul Hoover[2], Arnon Arazi[3] and Anne Davidson[1], [1]Feinstein Institutes for Medical Research, Manhasset, NY, [2]Brigham and Women's Hospital, Boston, MA, [3]Feinstein Institutes for Medical Research, Acton, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0916–0933) Innate Immunity Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: TLR8 has been implicated in adverse outcomes of human pregnancy. We previously reported a mouse model of spontaneous aPL-induced pregnancy loss in *Sle1* mice expressing a human TLR8 transgene (Sle1.hTLR8tg). These mice experience dystocia, fetal resorptions, and placental developmental abnormalities, with both the *Sle1* and *hTLR8* loci required for the phenotype. Growth defects occur as early as embryonic day (e)8.5; bulk RNA-seq and flow cytometry revealed immune dysregulation, including decreased expression of IL15, decreased uterine (u)NK cells and increased myeloid cells as well as junctional zone thinning and placental ischemia. It is unclear how hTLR8 initiates the signaling cascade that leads to these changes in immune dynamics within Sle1.hTLR8tg placentas, or how other placental cell populations interact with uterine NK cells to regulate their recruitment and function.

Methods: To better define the spatial relationships during Sle1.hTLR8tg pregnancy, placental tissue was harvested from Sle1 and Sle1.hTLR8tg mice at e9.5 (decidualization and spiral artery remodeling occurring) and e13.5 (fully formed placenta). Spatial transcriptomics (n=2-3 per group, per timepoint) was performed using the 10x Xenium platform and a predesigned Mouse Tissue Atlas panel (379 gene targets) together with a custom panel (89 immune genes, including *hTLR8*).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

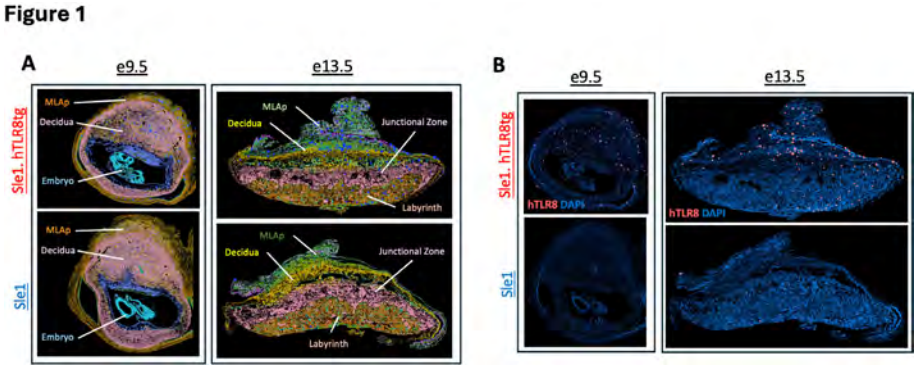


Figure 1. Spatial transcriptomics of e9.5 and e13.5 placentas in Sle1 and Sle1.hTLR8tg mice. A. K-Means Clustering at e9.5 (k=7) and at e13.5 (k=8) corresponds with distinct placental layers and cells types present during each stage of placental development. B. hTLR8 expression (red) with DAPI staining (blue) in Sle.1hTLR8 and Sle1 placentas at e9.5 (left) and e13.5 (right).

Results: K-Means clustering identified major placental regions, including decidua, junctional zone, labyrinth, and mesometrial lymphoid aggregate of pregnancy (MLAp) (**Fig.1A**). *hTLR8* was expressed only in Sle1.hTLR8tg placentas, primarily in decidua and MLAp, and in low amounts in the junctional zone and labyrinth (**Fig.1B**). *hTLR8* expression co-localized preferentially with *Itgam* (CD11b) (**Fig.2A**) but also with a small number of stromal cells. At e9.5, Sle1.hTLR8tg placentas displayed clusters of immune cells (*Cd8a, Ifng, Ncr1, Klrd1, Klrb1c, Itgam*) at the junction of the MLAp and decidua (**Fig.2B**) not observed in *Sle1* placentas and persisting through d13.5, suggesting an inflammatory/cytotoxic phenotype. An increase in placental CD8 cells was confirmed by flow cytometry. NK cell receptors (*Klrb1c, Ncr1, Klrd1*) and granzymes showed variable downregulation patterns, depending on the sub-type and placental region (**Fig.3A-B**) *Ifng* and *Cd8a* were expressed both in the MLAp and decidua (**Fig.3C**).

Conclusion: Several unique uNK cell subsets populate mouse and human placentas. The different distribution and variable downregulation of NK cell receptors and granzymes in our spatial data suggests a greater degree of uNK cell heterogeneity than previously appreciated. Future studies include understanding if these NK receptor expression patterns reflect different functions (e.g. differential granzyme production) and looking for potential correlations with human uNK subsets.

Additionally, increased expression of *Cd8a* and *Ifng* in the MLAp and their close proximity to clusters of myeloid and uNK cells suggests a pro-inflammatory environment by which myeloid cells are activated via hTLR8 and activate CD8 cells to kill target cells such as stromal and uNK cells that are required for production of key cytokines and placental growth factors.

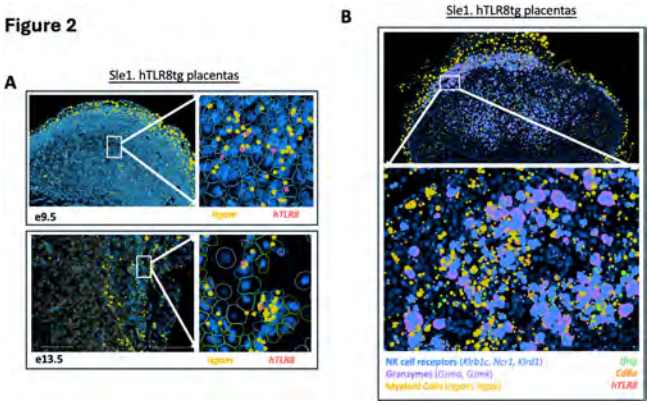


Figure 2. Co-localization of hTLR8 and immune-related genes suggests inflammatory milieu in Sle1.huTLR8tg placentas. A. Sle1.huTLR8tg placentas at e9.5 (top) and e13.5 (bottom) with inlay showing co-expression of hTLR8 (pink) with Itgam (gold-CD11b). B. Local clusters of NK cells (represented by granzyme and NK cell receptor genes), myeloid cells (represented by Itgam and Itgax), along with Ifng, Cd8a, and hTLR8 in e9.5 Sle1.huTLR8tg placenta.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3

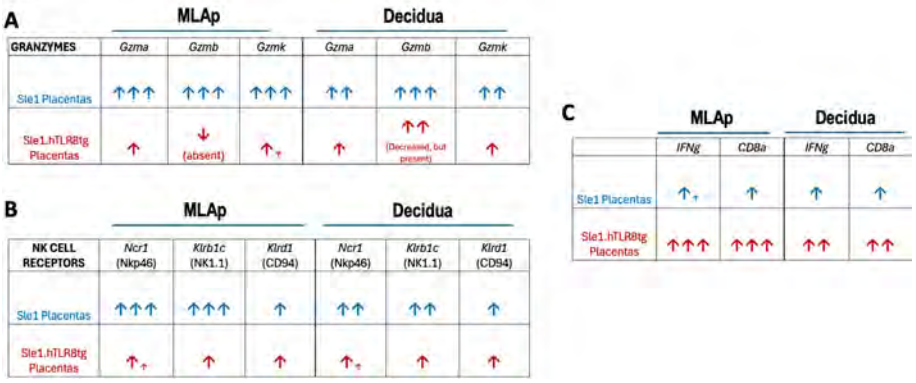


Figure 3. Immune cell-related gene expression patterns in Sle1 and Sle.1hTLR8tg placentas at e9.5. A. Granzyme genes were all downregulated in Sle1.hTLR8tg placentas compared with Sle1 placentas, but Gzmb downregulation was markedly different between the MLAp (where it was virtually absent) and the decidua (with only a modest decrease in expression). B. NK cell receptor genes were similarly downregulated in Sle1.hTLR8tg placentas, but Klrb1c showed the largest decrease whereas Klrd1 remained unchanged. Expression of Ncr1 and Klrb1c differed between the MLAp and decidua regions, suggesting a distinct composition of uNK subsets in each region. C. Ifng and Cd8a expression were both increased in Sle1.hTLR8tg placentas, particularly in the MLAp, with the large majority of Ifng co-localizing with Cd8a+/Itgam-/Itgax- cells (as opposed to cells expressing NK cell receptor genes), showing that CD8+ T cells are the main producers of IFNg at e9.5 in Sle1.hTLR8tg placentas.

Disclosure: Y. Xia: None; **P. Hoover**: None; **A. Arazi**: None; **A. Davidson**: None.

Abstract Number: 0934

The Use Of Preclinical Models To Understand Drivers Of Lupus Pathogenesis

Arielle Glatman Zaretsky[1], Carley Tasker[1], Pablo Abreu[1], Ciara Torres[2], Li-Hong Ben[1], Scott MacDonnell[1], Andre Limnander[1] and Jamie Orengo[1], [1]Regeneron, Tarrytown, NY, [2]Regeneron, Tarrytown

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic, multisystem autoimmune disease with a prevalence of 1.4-15.13/100,000 adults globally. SLE is highly heterogenous and can involve dysregulation of the adaptive and innate arms of the immune system, leading to aberrant lymphocyte activation, autoantibodies, immune complex formation, and/or organ damage. Notably, clinical benefit has been demonstrated in subsets of lupus patients. Thus, it is critical to appropriately model disease and differentiate disease drivers in relevant preclinical models, allowing better stratification of patient subsets for the development of effective therapeutics and opening the door for new target discovery.

Methods: Two mouse models of lupus-like disease were evaluated: NZB/W lupus prone mice and C9orf72-deficient mice, which display a lupus-like phenotype previously described to include elevated autoantibodies and circulating cytokines, glomerulonephropathy, splenomegaly and lymphadenopathy. Profiling of immune populations and serological readouts was performed over time using age matched female WT, NZB/W, and C9orf72 KO animals. Overexpression of IFNα via hydrodynamic DNA delivery (HDD) was used to evaluate the role of IFNα in these strains, while TACI-Ig-mediated B cell depletion was performed to determine the contribution of B cells to pathogenesis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The respective contributions of IFNa and BAFF, representing pathways with approved targeted therapeutics in SLE, were evaluated and analyzed between these strains. Systemic low dose IFNα synchronizes and significantly accelerates disease progression across NZB/W animals, while disease progression in C9orf72$^{-/-}$ mice is unaltered by overexpression of IFNα. These data suggest that lupus-like disease in NZB/W mice can be exacerbated by IFNα and thus may model patients for whom Type I IFN is a key driver of disease. Although disease in C9orf72$^{-/-}$ is unchanged by IFNα, overexpressing TACI-Ig to bind and sequester BAFF and APRIL in the C9orf72-deficient lupus model reversed lupus-associated phenotypes. TACI-Ig-mediated depletion of BAFF/APRIL in C9orf72$^{-/-}$ resulted in a decrease in B cells and a rapid reduction in anti-dsDNA antibodies. These data indicate that the C9orf72$^{-/-}$ model captures the dysregulated B cell tolerance pathways that can drive disease in some subsets of lupus patients.

Conclusion: Here we describe two models of SLE-like disease that respond differently to manipulation of key pathways targeted by existing approved therapeutics. Taken together, these data suggest that NZB/W and C9orf72$^{-/-}$ mice recapitulate distinct disease mechanisms relevant to human patients and can be used in preclinical efforts to validate therapeutic strategies for a heterogeneous SLE patient population.

Disclosure: A. Glatman Zaretsky: Regeneron, 3, 11; **C. Tasker**: Regeneron, 3, 11; **P. Abreu**: Regeneron, 3, 11; **C. Torres**: Regeneron, 3, 11; **L. Ben**: Regeneron, 3, 11; **S. MacDonnell**: Regeneron, 3, 11; **A. Limnander**: Regeneron, 3, 11; **J. Orengo**: Regeneron, 3, 3, 11, 11.

Abstract Number: 0935

Oral Antibiotic Treatment Reduces Anxiety in a Murine Model of Neuropsychiatric Manifestations of Systemic Lupus Erythematosus

Cecilia Stumpf[1], Brianna Thompson[2], Vanessa Manada De Lobos[2] and Carla Marie Cuda[3], [1]Northwestern University, Elmhurst, IL, [2]Northwestern University, Chicago, [3]Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Unclear mechanisms underlying diffuse NPSLE (anxiety, cognitive dysfunction) lead to the devastating impact of this disease on patients' health-related quality-of-life. Dysbiosis of gut microbiota is observed in patients with, and mouse models of, SLE. Fecal microbiota transfer from SLE-prone B6.*Sle1Sle2Sle3* (B6.TC) mice, as well as patients with SLE, induced production of anti-dsDNA antibodies as well as an inflammatory response in germ-free C57BL/6 (B6) mice, suggesting dysbiosis may be involved in SLE pathogenesis. We and others show that oral antibiotic treatment (OAT) have beneficial effects on systemic manifestations in SLE-prone mice. However, the impact of OAT on behavioral deficits in SLE is largely unexplored. OAT can induce anxiety and cognitive deficits in control mice, yet OAT has shown dramatically protective effects in Alzheimer's disease and multiple sclerosis models, potentially through modulating the gut-microbiota-brain-axis and altering microglial activation. As we find microglial activation in NPSLE-prone mice, we will elucidate the impact of OAT on behavioral deficits in NPSLE.

Methods: Separate cohorts of 4-week-old female B6 and B6.TC (Jackson #007228) mice were given autoclaved water plus ampicillin, neomycin sulfate, metronidazole (1 g/L), and vancomycin (0.5 g/L), supplemented with 2% sucralose or 1% sucrose 2x/wk for 5 wks with no observable weight loss. Mice underwent behavioral tasks. Perfused brains from the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

sucralose cohort were extracted after intravenous CD45 labeling to exclude remaining circulating immune cells, dural meninges were removed, and cells were analyzed by flow cytometry. Brains from the sucrose cohort were similarly processed, individual preps were hashed, and live $CD45^+$ cells were FACSorted (n=3/strain) for cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq; 10X Genomics 5' v2; analysis pending).

Results: OAT significantly reduced anxiety in B6.TC mice in the Zero maze task with no positive effect on known defects in coordination and motor learning in the Rotarod task. As expected, OAT induced mild anxiety in B6 mice in the Zeromaze task. Results were independent of the choice of sweetener. OAT did not impact systemic disease markers, including splenomegaly and lymphadenopathy. Analysis of sucralose-treated mice shows characteristic increases in total microglia, the disease-associated microglia (DAM) subset, macrophages, and extra-vascular CD4+ T cells in B6.TC mice compared to B6 mice. We did not observe the characteristic increase in extra-vascular CD8+ T cells, suggesting sucralose may impact this population in B6.TC mice. Strikingly, analysis of OAT mice shows further expansion of total microglia, DAM, and macrophages, as well as an increase in extra-vascular CD8+ T cells in B6.TC mice compared to B6 mice.

Conclusion: We find that OAT reduces anxiety in NPSLE-prone mice and further expands total microglia, DAM, and macrophage populations already elevated in disease. Future studies will identify changes in the activation status of these and other immune cell subsets in the brain by CITE-seq to interrogate potential mechanisms linking dysbiosis of gut microbiota to anxiety and other manifestations of NPSLE.

Disclosure: C. Stumpf: None; **B. Thompson**: None; **V. Manada De Lobos**: None; **C. Cuda**: None.

Abstract Number: 0936

Ultrasound-Mediated Blood–Brain Barrier Permeabilization Enables Targeted Drug Delivery in a Murine Model of Neuropsychiatric SLE

Doaa Tehawey[1], Roni Gattegno[2], Baruh Polis[1], Mike Bismuth[2], Melodie Zaknoun[1], Tali Ilovitsh[2] and **Chaim Putterman**[3], [1]Azrieli Faculty of Medicine, Safed, Israel, [2]Tel Aviv University, Tel-Aviv, Israel, [3]Albert Einstein College of Medicine, Safed, Israel

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Neuropsychiatric SLE (NPSLE) is a severe complication of SLE, characterized by CNS involvement leading to cognitive, behavioral, and neurological deficits. While monoclonal antibodies may offer therapeutic potential for the treatment of SLE, their efficacy in NPSLE is limited by the blood brain barrier (BBB), which restricts drug delivery into the CNS. We evaluated a novel method of focused ultrasound (FUS) with nanobubbles (NB) as a noninvasive strategy to transiently open the BBB and enhance CNS antibody delivery in a NPSLE model.

Methods: We utilized 12-week-old female MRL/lpr mice, an established model of NPSLE. Two separate experiments were conducted to evaluate BBB opening. Firstly, two 10 week-old female B6 mice underwent retro-orbital injection of NB (180 nm diameter, phospholipid shell, octafluoropropane gas core) followed by unilateral transcranial FUS treatment targeting the right hemisphere (NB-FUS), according to a previously established non-neurotoxic protocol from the Ilovitsh laboratory (Gattegno R et al, *J Cont Release, 369*, 506-516, 2024). FUS parameters included a center frequency of 850 kHz, peak negative pressure of 210 kPa, 4 ms pulses at a repetition frequency of 1 Hz, applied for a total duration of 1 minute.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

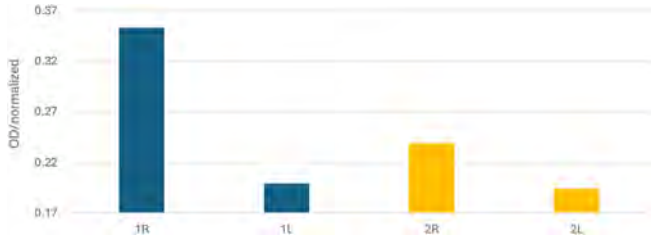


Figure 1. Brain EB concentration. Optical density reading comparison between the FUS-treated right hemispheres (R) and the untreated left hemispheres (L) within individual mice.

Immediately after FUS application, Evans blue (EB) dye was injected retro-orbitally. Mice were sacrificed, and the brain hemispheres were separated, individually homogenized, and quantitatively analyzed using ELISA to measure the EB concentration and assess differential BBB permeability between the treated and untreated sides.

In the second experiment, 6 MRL/lpr lupus-prone and 6 MRL+ control female mice at 10 weeks of age underwent the same NB-FUS protocol. In this study, BBB permeability was assessed by quantitating the fluorescence of two tracers: EB and FITC-labeled dextran (150 kDa), both injected immediately after FUS application. Brains were harvested and processed for fluorescence microscopy to evaluate the intensity of tracer uptake and its distribution in the brain parenchyma.

Results: Quantitative analysis revealed notably higher EB concentrations in the NB-FUS-treated hemispheres in both mice. The following normalized EB concentrations were observed: right hemisphere (1R: 0.353, 2R: 0.239) and left hemisphere (1L: 0.199, 2L: 0.194) (Figure 1), indicating successful spatially targeted disruption of the BBB. In the second experiment, EB penetration was macroscopically visible within the FUS targeted hemisphere in 8/12 mice. Fluorescence microscopy confirmed localized EB and FITC tracer presence in the treated hemisphere with minimal signal in the contralateral side, indicating successful BBB permeabilization. Representative mice are shown in Figure 2. No obvious differences in dye delivery were seen between the two strains. Repeating this experiment with a labeled murine antibody specific for a candidate NPSLE target is in process.

Conclusion: FUS with NB effectively and safely increases BBB permeability in a classic murine NPSLE model. These results support the potential application of this innovative method for targeted CNS delivery of peripherally administered therapeutic agents in autoimmune neuroinflammatory diseases, including NPSLE.

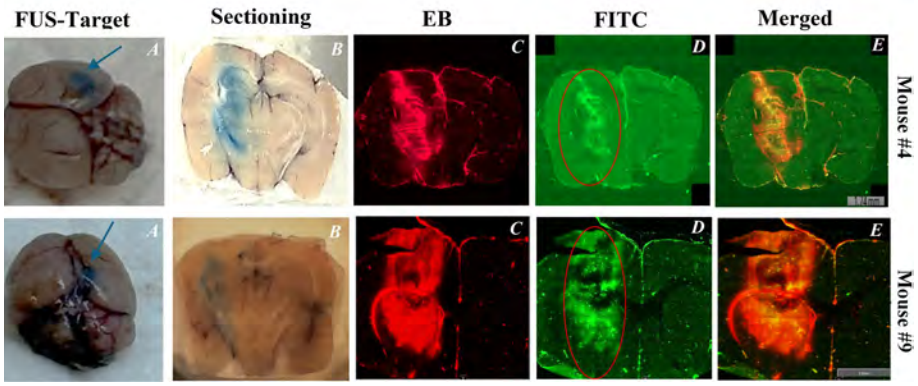


Figure 2: Focal ultrasound application following nanobubble administration locally permeabilizes the BBB and enables delivery of an antibody-sized molecule into the CNS. A. Representative image of MRL/lpr mouse brains immediately after ultrasound treatment, showing localized blue staining indicative of EB penetration into the brain parenchyma. B. A brain section during cryostat slicing, demonstrating widespread EB presence throughout the targeted ultrasound-treated region. C. Magnified (4×) image of the brain highlighting EB distribution in red fluorescence within the treated area. D. Magnified (4×) image showing FITC fluorescence in green (circled in red), indicating distribution of this additional tracer within the treated brain region. E. Merged image of C and D combining EB (red) and FITC (green) signals, demonstrating both tracers' penetration and co-localization within the ultrasound-targeted area.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: D. Tehawey: None; **R. Gattegno**: None; **B. Polis**: None; **M. Bismuth**: None; **M. Zaknoun**: None; **T. Ilovitsh**: None; **C. Putterman**: Cullinan, 1, Progentec, 1.

Abstract Number: 0937

MRL-lpr Mice Display Altered Nociception: A new model for lupus peripheral neuropathy

Melodie Zaknoun[1], Doaa Tehawey[1], Baruh Polis[1] and **Chaim Putterman**[2], [1]Azrieli Faculty of Medicine, Safed, Israel, [2]Albert Einstein College of Medicine, Safed, Israel

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

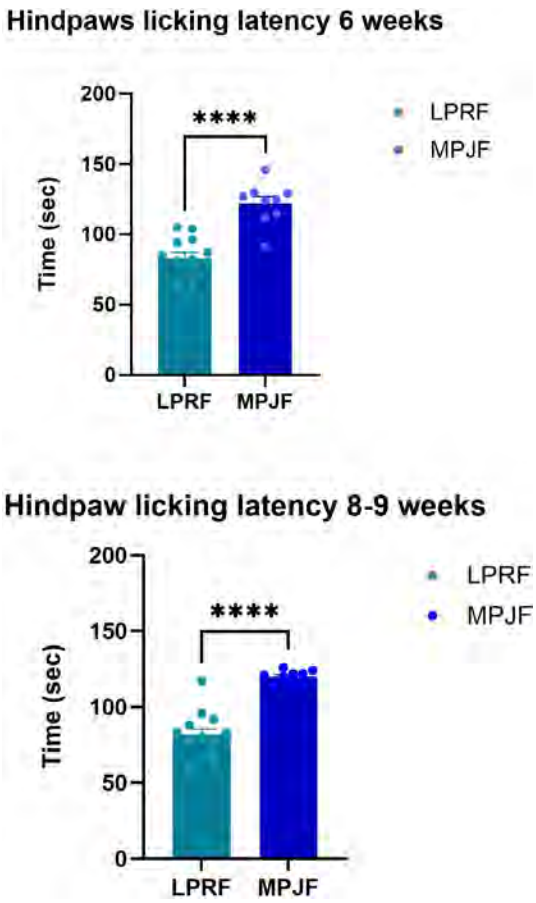


Figure 1: Top: Hindpaw licking latency at 6 weeks of age. Bottom: Hindpaw licking latency at 8-9 weeks of age. LPRF, female MRL/lpr mice; MPJF, female MRL/+ mice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

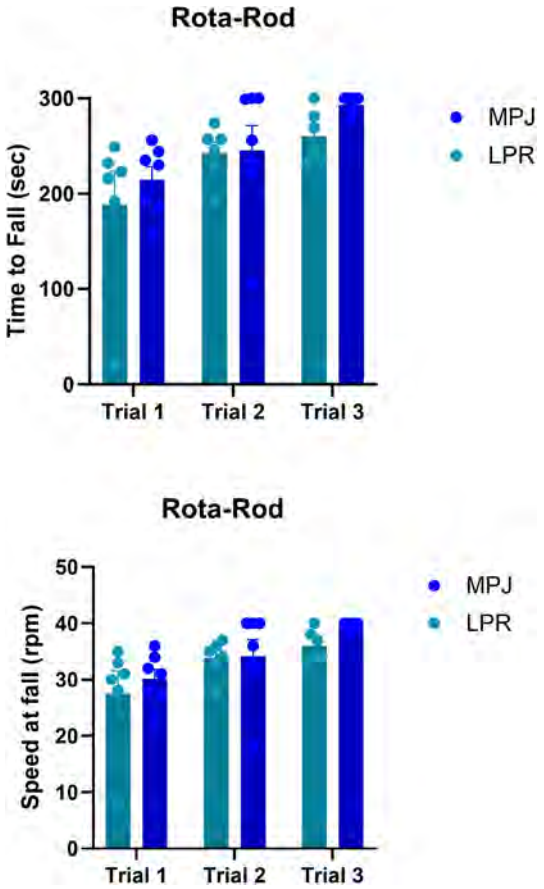


Figure 2: Top: Time in seconds until the mouse fell off the apparatus. Bottom: Speed recorded at the time of the fall. MPJ and LPR, female MRL/+ and MRL/lpr mice at 15 weeks of age, respectively.

Background/Purpose: Of the 19 ACR case definitions for NPSLE, seven involve the peripheral nervous system. MRL/lpr mice spontaneously develop anti-dsDNA antibodies, nephritis, and skin disease, as well as depressive-like behavior and cognitive abnormalities (Polis B, Autoimmunity, 57,2024). However, while peripheral neuropathy is common in human lupus (Florica B, Sem Arth Rheum, 203,2011), whether MRL/lpr mice display peripheral nervous system disease has not been carefully studied.

Methods: To better evaluate sensory function and develop an assay to easily monitor the effects of therapeutic interventions, we enhanced traditional rodent nociception testing by incrementally raising the temperature from 40 to 52°C within 180 seconds. The test focuses on paw licking, which signifies the behavioral reaction to the thermal stimulus. This careful modulation allowed us to accurately record the latency, or response time, for the animals to lick their fore- and hind paws. Female MRL/lpr, and age and sex matched congenic control MRL mice, were tested at 6, 8, and 12 weeks of age.

Rota-Rod testing was performed using Stanford's laboratory protocol. Time to fall and speed at fall were both measured for analysis. Female MRL/lpr and age and sex matched congenic control MRL mice were tested at 15 weeks of age.

A standard open field test was done where the animals were left to explore the field for 5 minutes in minimum abrasive conditions. The total time spent in the center zone and the total distance traveled by each mouse were measured. Female MRL/lpr and age and sex matched congenic control MRL mice were tested at 15 weeks of age.

Results: Nociception: We found that already at 6 weeks of age, while there is no difference in anti-dsDNA antibody levels or other characteristic clinical or serologic signs of disease activity, MRL/lpr mice exhibited a notable increase in thermal hyperalgesia, as seen by a decreased mean latency until hind paw-licking responses (withdrawal): 82.69+/-15.03 seconds (n=13)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

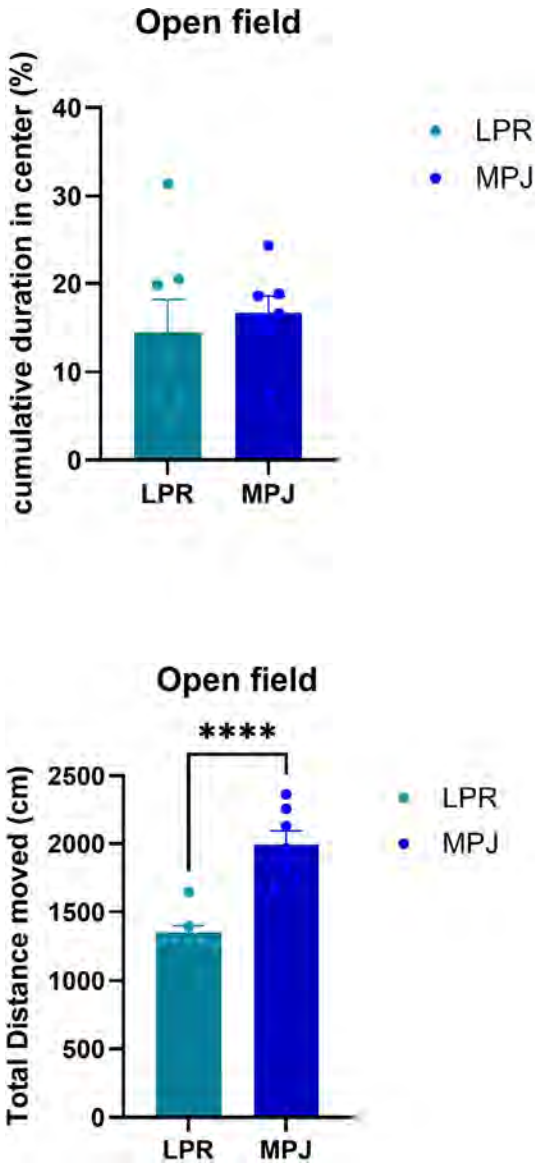


Figure 3: Bottom: Cumulative time spent in center zone shown in %. Top: Total distance traveled in cm. LPR and MPJ, female MRL/lpr and MRL/+ mice at 15 weeks of age, respectively.

compared to the control MRL strain 122+/-15.15 (n=9) (Figure 1) ($p< 0.0001$, Unpaired t-test). Similar thermal hyperalgesia responses were observed in MRL/lpr mice also at 8-9 weeks ($p< 0.0001$, Figure 1), and 12 weeks of age (data not shown). Similar testing using a cold plate approach is in process.

Rota-rod: No significant differences were observed in the time to fall/speed at fall between the MRL/lpr mice (n=6) and the MRL strain (n=7)(Figure 2), a finding not supporting a difference in proprioception between these strains.

Open Field: MRL/lpr showed a significant decrease in total distance traveled in the open field (1348+/-140.1, n=7) compared to the MRL strain (1995+/-263.3, n=7 ($p< 0.0001$, Unpaired t test), a result not supporting locomotor hyperactivity in the MRL/lpr strain. There was no significant difference observed in the cumulative time spent in the center zone (Figure 3).

Conclusion: MRL/lpr mice display significantly heightened temperature sensitivity already at 6 weeks of age, before many other disease manifestations are evident.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Altered nociception may represent an early and sensitive tool to detect peripheral neuronal involvement in this strain, and if confirmed may serve to model the involvement of the peripheral nervous system in SLE.

Disclosure: M. Zaknoun: None; **D. Tehawey**: None; **B. Polis**: None; **C. Putterman**: Cullinan, 1, Progentec, 1.

Abstract Number: 0938

Short Term Antibiotic Treatment Improves the Neurobehavioral Phenotype of MRL/lpr Mice

Melodie Zaknoun[1], Doaa Tehawey[1], Baruh Polis[1] and **Chaim Putterman**[2], [1]Azrieli Faculty of Medicine, Safed, Israel, [2]Albert Einstein College of Medicine, Safed, Israel

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Neuropsychiatric lupus (NPSLE) is a common and prognostically significant manifestation of SLE, affecting 20-40% of lupus patients. The ACR identified 19 clinical syndromes associated with NPSLE, which range from severe manifestations such as psychosis and transverse myelitis to milder involvement in the form of headaches, mood disorders, and cognitive deficits.

The gut microbiota has been implicated in the pathogenesis of autoimmune diseases, including SLE. Microbes significantly influence mammalian metabolism, the immune system, and behavior. The gut-brain axis is a communication network connecting the CNS with the gut's enteric nervous system, facilitating information exchange between the brain and digestive functions. Recent studies emphasize the gut microbiota's crucial role in this relationship.

Our goal was to examine whether modulation of the gut-brain axis using a short course of antibiotic treatment would affect the development, progression, and severity of neuropsychiatric disease in the MRL/lpr strain.

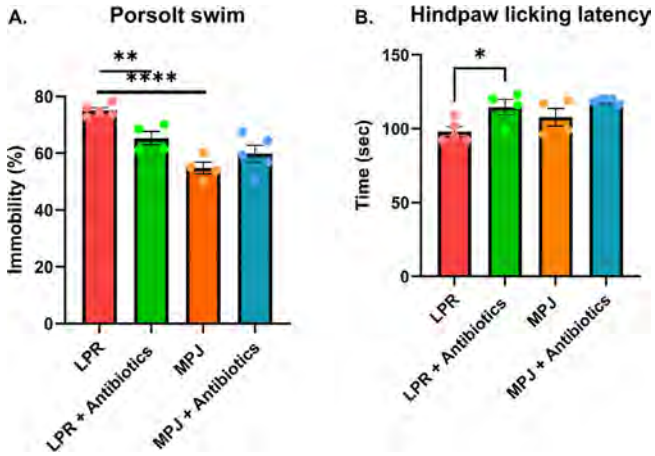


Figure 1: A. In the Porsolt swim test, the mouse is placed in a water filled cylinder for 10 minutes. Mobility time was measured, and immobility is calculated based on the ratio of time that the mice were immobile (i.e. displaying despair, or depressive-like behavior) over the total time. B. To test thermal hypersensitivity, mice are placed on a plate heated to a temperature of 40°C and increasing to 52°C within three minutes. The latency, or response time, for the mice to lick their hind paws was measured for analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

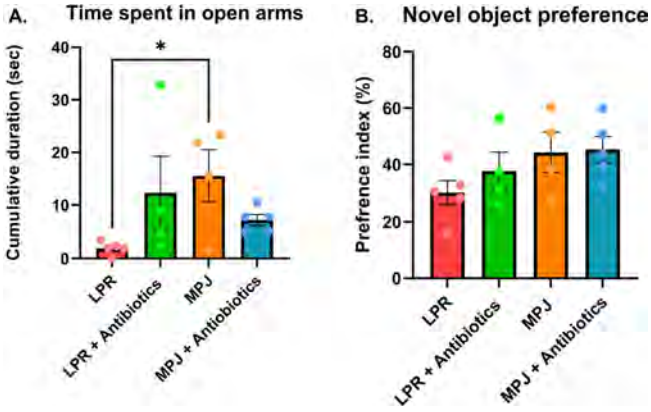


Figure 2: A. To assess for anxiety, the elevated plus maze test was employed. The maze was placed in a dark infra-red lit room and the mouse placed on the maze for 5 minutes. Time spent in open arms compared to the total time was recorded and analyzed using Ethovision software. B. In assessing memory with the novel object location test, each mouse was first placed in an arena with two similar objects for 5 minutes. After an interval of 60-90 minutes, the mouse is put in the same arena in which one of the objects was moved to a new location. The preference index (normal >50%) was calculated by dividing the time spent in the area of the newly moved object by the total time spent in both object zones.

Methods: Antibiotic Treatment: 6-week-old MRL/MpJ and MRL/lpr mice were given vancomycin 0.5 g/L in drinking water for 2 weeks, with the water being refreshed every 3 days. Control mice of these strains received regular water with no additives.

Behavioral Testing: After 2 weeks of treatment, the mice were given 4 weeks for gut microbiome recovery. Behavioral testing began at 12 weeks of age, and included standard tests for depressive-like behavior (Porsolt swim test), thermal hypersensitivity (hot plate), anxiety (elevated plus maze (EPM)), and cognition/memory (novel object location (NOL)), with rest periods of 1-3 days between the tests.

Results: Porsolt swim test: MRL/lpr showed significantly worse depressive-like (despair) behavior as shown by increased immobility in the Porsolt swim test (75.1+/-2.2 seconds) as compared to the MRL/MpJ group (65.3+/-4.7; P< 0.0001). Moreover, antibiotic-treated MRL/lpr showed significant attenuation of this phenotype (less immobility), as compared to non-treated MRL/lpr mice (Figure 1A).

Hot plate: Antibiotic treated MRL/lpr mice showed significantly increased latency until hind paw licking (114.5+/-10.7 vs 98+/-7.4 in the untreated group, p=0.029), indicating decreased thermal hypersensitivity and improved nociception. No significant change was observed in thermal hypersensitivity with antibiotic treatment in the MRL/MpJ strain (Figure 1B).

EPM: Untreated MRL/MpJ mice displayed less anxiety as compared to MRL/lpr mice, as reflected by significantly more time spent in the open arms (15.5+/- 9.9 vs 1.9+/-1.2, p=0.018). Notably, antibiotic treated MRL/lpr mice trended to less anxiety compared to the untreated MRL/lpr group (Figure 2A).

Novel Object Location: Although untreated MRL/lpr mice did appear to have the worst performance on this cognitive test of spatial memory, no significant differences were observed between the groups (Figure 2B).

Conclusion: A short term course of intestinal decontamination with oral vancomycin attenuates several key features of neuropsychiatric disease in MRL/lpr lupus mice. Studies to determine the effects on other disease features and elucidate the mechanisms of protection are in progress.

Disclosure: M. Zaknoun: None; **D. Tehawey**: None; **B. Polis**: None; **C. Putterman**: Cullinan, 1, Progentec, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0939

Exploring the Mechanism of Action and Related Biomarkers of BTK Inhibitor/Degrader in Systemic Lupus Erythematosus

Chengfeng Xue[1], Jingjing Wang[1], Mengwen Huang[1], Ting Liu[1], Panpan Wang[1], Donghai Chen[2], Xue Wang[1], Yawei Xu[1], Yajun Gong[1], Jun Yang[1], Xiaoshan Yu[1], Ke Wang[1], Yuqing Zhu[1], Kaixuan Zhu[1], Tianqi Tang[1], Wantong Qi[1], Yaqiong Pei[1], Qiyao Zhang[1], Fugang Li[2], Qingyang Gu[1] and Xiangnan Qiang[1], [1]WuXi AppTec, Shanghai, China (People's Republic), [2]WuXi ApptTec, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with diverse clinical and immunological manifestations. Bruton's tyrosine kinase (BTK) is a crucial intracellular kinase in regulating B cell development and function, and also showed pivotal impacts in numerous pathways. Small molecule inhibitors of BTK have been widely used in treating B-cell malignancies and autoimmune diseases (e.g., rheumatoid arthritis, atopic dermatitis, SLE). BTK degraders can eliminate the kinase scaffolding function and remove resistance mutations, displaying a therapeutic potential in SLE. However, the mechanism of action of BTK inhibitors/degraders in SLE is not well understood. The aim of this study is to explore the mechanism of action and identify biomarkers for BTK inhibitor/degrader by comparing cellular and protein-level changes in the mouse SLE model before and after treatment, and to predict its clinical efficacy and mechanism.

Methods: scRNA-seq and protein data from healthy donors and SLE patients, obtained from public databases, were used to narrow down the scope of biomarker research. Adoptive transfer of $CD4^{+}$T cells from BM12 spleen and lymph node to C57BL/6 mice was performed to induce the lupus-like model. Normal, vehicle, Ibrutinib (BTK inhibitor), and NX-5948 (BTK degrader) were administered daily, and the mice were sacrificed around week 2. The plasma levels of anti-double-stranded DNA (anti-dsDNA) IgM and IgG were detected by ELISA. Cell subtypes, activation, proliferation and BTK expression in splenic cells were characterized by flow cytometry. The cytokines in the plasma were analyzed by Olink technology.

Results: The BM12-induced SLE mouse model generally shares a common set of features that correlate with clinical manifestations of human SLE. Compared to normal mice, the levels of anti-dsDNA IgG and IgM increased in the model group, with an expansion of Tfh, GCB, and plasma cells. Olink analysis results indicate elevated levels of cytokines and chemokines, including TNF, IFN-γ, IL-6, CCL4, and CSF1. Both Ibrutinib and NX-5948 attenuated the BM12-induced lupus-like symptoms, including the reduction of anti-dsDNA IgM and IgG. Compared to Ibrutinib treatment, the BTK protein level in B cell, dendritic cell, monocyte and macrophage were effectively decreased in NX-5948 treatment group. Both Ibrutinib and NX-5948 treatment decreased the number of GCB, plasma cell and the expression of CD69 and CD86 in B cells. The reduction of IL-4 and IL-6 in plasma, along with the downregulation of CD25 expression on B and T cells, suggests that the use of BTK inhibitors and degraders inhibit the interaction and activation of B and T cells.

Conclusion: This study conducted a detailed comparative analysis at the cellular and protein levels among normal mice, SLE model mice, and those treated with a BTK inhibitor or degrader. Our study compared clinical data with disease model data to determine their correlation and used this model to explore the mechanisms of action of BTK inhibitors and degraders. We hope that this research approach can be applied to the study of more diseases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Xue: None; **J. Wang**: None; **M. Huang**: None; **T. Liu**: None; **P. Wang**: None; **D. Chen**: None; **X. Wang**: None; **Y. Xu**: None; **Y. Gong**: None; **J. Yang**: None; **X. Yu**: None; **K. Wang**: None; **Y. Zhu**: None; **K. Zhu**: None; **T. Tang**: None; **W. Qi**: None; **Y. Pei**: None; **Q. Zhang**: None; **F. Li**: None; **Q. Gu**: None; **X. Qiang**: None.

Abstract Number: 0940

Resident Macrophages Localize Near Fibroblasts and Drive Reprogramming in Lupus Nephritis Through Direct and Soluble Signaling

Chirag Raparia[1], Paul Hoover[2], Arnon Arazi[3], Nir Hacohen[4] and Anne Davidson[1], [1]Feinstein Institutes for Medical Research, Manhasset, NY, [2]Brigham and Women's Hospital, Boston, MA, [3]Feinstein Institutes for Medical Research, Acton, MA, [4]Broad Institute of MIT Harvard, Cambridge, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is a severe manifestation of SLE that can progress to renal fibrosis, and eventual renal failure. In LN, tubulointerstitial inflammation and macrophage infiltration are associated with a poor prognosis. Alongside macrophages, the renal fibrotic niche contains fibroblasts, and endothelial cells; however, the mechanisms of their crosstalk remain poorly understood. Using spatial transcriptomics in LN mouse models and single-cell analysis of in vitro cocultures, we reveal macrophage-driven fibroblast activation as a potential driving feature of renal fibrosis in LN.

Methods: Spatial transcriptomics in NZB/W F1 mice was performed using the 10x Genomics Xenium 389 gene platform, with markers for cell interior and boundaries and an additional gene panel customized to identify high-resolution myeloid populations. Primary NZB/W mouse embryonic fibroblasts (MEFs) were cocultured with FACS-sorted renal resident macrophages (RMs) from nephritic and pre-nephritic NZB/W mice. Cocultures were analyzed by flow cytometry and scRNA-seq. Data were processed using Seurat and Harmony, and cell-cell communication was inferred using CellChat. MEF scratch wound assays with conditioned media (CM) from cocultures were performed, followed by bulk RNA-seq and GSEA for pathway analysis.

Results: Resident macrophages are located in the interstitium and acquire a damage associated Spp1+ gene expression profile during nephritis. In nephritic mice, resident macrophages, and not infiltrating macrophages, preferentially colocalized with FAP^+ fibroblasts in renal infiltrates and peritubular spaces (Fig. 1A-B), correlating with areas of renal damage and fibrosis. In NZB/W MEF-RM cocultures, flow cytometry and scRNA-seq revealed *Spp1*+ and *Spp1*- macrophage populations and a heterogenous expansion of fibroblast populations, including *Fap*$^+$ and *Periostin*$^+$ MEFs, enriched for pro-fibrotic and inflammatory gene signatures (Fig. 2A). CellChat analysis identified signaling from $Spp1^+$ macrophages to Fap^+ MEFs via IL-1, TNF, and OSM, and GRN (Fig. 2B), facilitating a tissue remodeling phenotype. CM from nephritic cocultures induced a pro-inflammatory transcriptional program in MEFs, characterized by elevated *Cxcl1, Cxcl5, Cxcl14, and Hif1a*, confirmed by GSEA (Fig. 2C). Nephritic CM-treated MEFs experienced impaired wound closure in a scratch assay after 18 hours (Fig. 2D). In a separate study, we demonstrated that mouse and human LN resident kidney macrophages display similar transcriptional profiles and occupy comparable locations within the kidney. This similarity suggests that our findings in mouse models may also be applicable to human LN.

Conclusion: $Spp1^+$ resident macrophages in nephritic kidneys localize with and drive fibroblast activation and reprogramming through direct interaction and soluble signaling. Direct macrophage signaling via IL-1, TNF, OSM, and GRN promotes both pro-fibrotic and inflammatory fibroblasts, while indirect signaling induces a pro-inflammatory signature and impairs

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

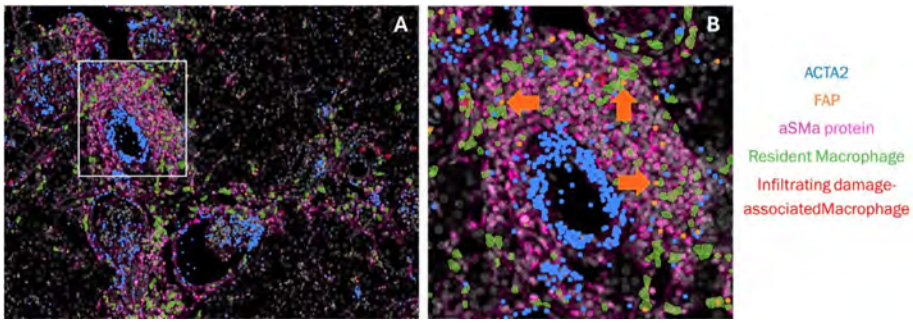


Figure 1: Spatial transcriptomic representation of a nephritic NZB/W kidney. A. An overview of a blood vessel immune infiltrate with resident macrophages labeled in green polygons and infiltrating damage-associated macrophages labeled in red. mRNA transcripts of ACTA2 and FAP are labeled with blue and orange dots, respectively. aSMA protein is depicted in pink. B. An enlarged image of the vessel infiltrate boxed in white in (A), showing resident macrophages colocalized with FAP+ ACTA2+ fibroblasts within the infiltrate.

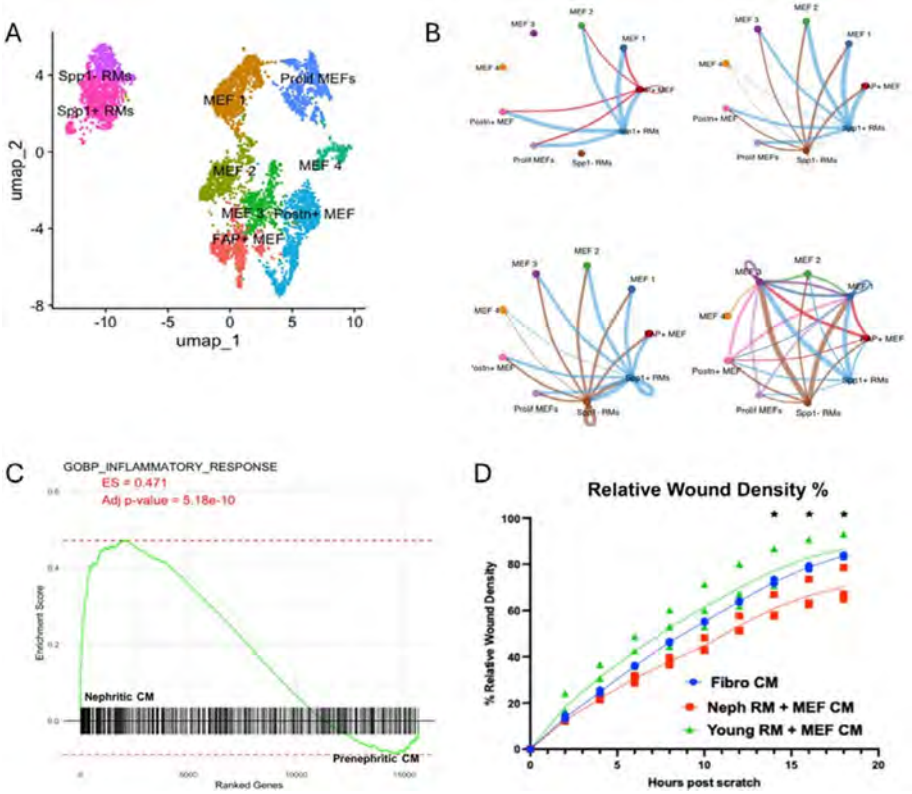


Figure 2: Direction and indirect fibroblast activation in vitro. A. UMAP of 6 MEF populations and 2 NZB/W RM populations from 48-hour direct contact coculture. N = 10, 3 nephritic mice RM-MEF cocultures, 3 pre-nephritic mice RM-MEF cocultures, 2 Time 0 MEF cultures, and 2 Time 48 cultures. B. Chord diagram of CellChat analysis of direct contact coculture of NZB/W nephritic and pre-nephritic RMs with MEFs. The thickness of each chord represents the magnitude of interaction. Blue chords originate from SPP1+ macrophages, brown from SPP1- macrophages, and red from FAP+ fibroblasts. C. GSEA plot of GOBP_Inflammatory Response pathway. Enrichment of the Inflammatory response is seen in the MEFS treated with the nephritic RM-MEF CM compared to the prenephritic (Young) RM-MEF CM. D. 18-hour scratch wound analysis of MEFs treated with conditioned media from the respective cocultures. Three biological replicates for each condition performed in duplicates. *p<0.05 between MEFs treated with prenephritic and nephritic RM-MEF coculture CM.

fibroblast wound healing. Together, these results identify potential targets to modulate renal fibrosis and improve outcomes of LN.

Disclosure: C. Raparia: None; **P. Hoover**: None; **A. Arazi**: None; **N. Hacohen**: Calico Biosciences, 5, Cytoreason, 1, 11, Danger Bio, 1, 11, Moderna, 5, Repertoire Immune Medicines, 1, 11, Takeda, 5; **A. Davidson**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0941

In Vivo PanCAR Therapy Utilizing Circular RNA for Treatment of Autoimmune Diseases

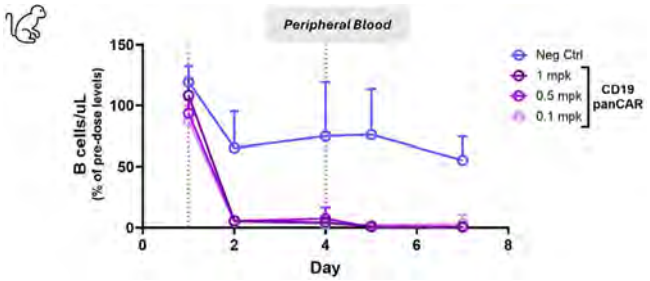
Juliet Crabtree, Thomas Lee, David Soto, Prapti Vyas, Akinola Emmanuel, Matthew Theisen, Karolina Kosakowska, Maja Sedic, Rajat Das, Muthusamy Jayaraman, Megan Hoban, Joe Bolen and **Isin Dalkilic-Liddle**, Orna Therapeutics, watertown, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Recently, traditional *ex vivo*-generated chimeric antigen receptor T (CAR-T) cell therapies have shown success in the clinic for autoimmunity indications. However, manufacturing, safety, and accessibility remain potential challenges in the *ex vivo* CAR-T approach. The prospect of an *in vivo* CAR-T cell therapy, without the need for patient cell isolation, cell culturing, and the safety risks associated with preconditioning regimens, remains a therapeutic goal. Orna Therapeutics' panCAR™ combines a synthetic, circular, coding RNA platform (oRNA®) and proprietary immunotropic lipid nanoparticle (LNP) to drive CAR expression on the surface of immune effector cells after *in vivo* administration, with a potential to provide a transient, re-dosable, and scalable immune cell therapy without the need for preconditioning lymphodepletion.

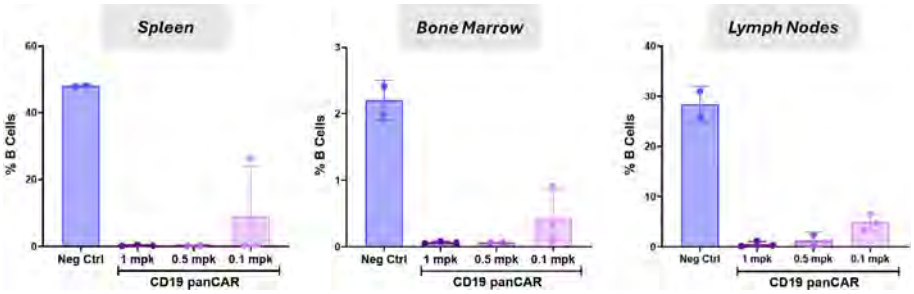
Methods: anti-CD19 panCAR™ is a non-viral platform combining anti-CD19 CAR expressing oRNA with a proprietary immunotropic LNP. Anti-CD19 panCAR was evaluated for expression in T cells and depletion of target B cells *in vitro* and *in vivo* in humanized CD34+ models upon intravenous injection. In a humanized model of lupus, anti-CD19 panCAR was dosed four times weekly, B cell levels and anti-double stranded DNA (anti-dsDNA) titers were evaluated. In cynomolgus macaques, anti-CD19 panCAR was dosed intravenously twice three days apart (Q3Dx2) at three doses levels (0.1, 0.5, and 1mpk). B cell levels were then evaluated in periphery and in lymphoid tissues by flow cytometry.

Results: With anti-CD19 panCAR oRNA-LNP, high surface expression of anti-CD19 CAR was observed in a dose-dependent manner and was maintained over 96 hours on human and NHP immune cells *in vitro*. Furthermore, CAR-mediated cytotoxicity was observed for T cells from both species, killing CD19-expressing cell lines. In the humanized mouse model, anti-CD19 CAR oRNA-LNP when administered intravenously showed significant B cell reductions in peripheral blood, spleen, and bone marrow at 24 hours (55-95%) and sustained depletion 7 days after a single dose. The functional activity of anti-CD19 panCAR can be adjusted by the dose level and dose number administered, demonstrating the tunability of the platform. *in vivo* panCAR, injected in a humanized mouse model of lupus, showed complete reduction of



CD19 panCAR completely depletes B cells in peripheral blood in NHPs: Cynomolgus macaques were dosed day 1 and day 4. CD20+ B cell levels were measured in peripheral blood by flow cytometry. Levels are normalized to average B cell levels from two pre-dose timepoints for each animal. mean+/- st dev

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CD19 panCAR robustly depletes B Cells in lymphoid tissues in NHPs. Animals were taken down 3 days post last dose and CD20+ B cell levels were measured in lymphoid tissues by flow cytometry.

B cells accompanied by anti-dsDNA titer reduction. While mice receiving rituximab exhibited reduced B cell numbers, the depletion did not correlate with reduced anti-dsDNA titers. Finally, in NHPs, our cross-reactive anti-CD19 compound showed complete (>98%) and sustained depletion of B cells in peripheral blood two weeks after the last dose and showed robust depletion in the spleen (>99%), lymph nodes (>97%), and bone marrow (>96%) three days after the last dose.

Conclusion: Our platform provides a non-viral, transient, tunable, and scalable approach without the need for preconditioning lymphodepletion that shows robust activity *in vitro* and *in vivo*. In NHPs intravenous dosing resulted in deep B cell depletion in peripheral blood and lymphoid tissues. Collectively, our pre-clinical data demonstrates the potential of Orna's *in vivo* panCAR therapy to treat B cell mediated autoimmunity.

Disclosure: J. Crabtree: Orna Therapeutics, 3; **T. Lee**: Orna Therapeutics, 3; **D. Soto**: Orna Therapeutics, 3; **P. Vyas**: Orna Therapeutics, 3; **A. Emmanuel**: None; **M. Theisen**: ORNA, 3; **K. Kosakowska**: Orna Therapeutics, 3; **M. Sedic**: Orna Therapeutics, 3; **R. Das**: Orna Therapeutics, 3; **M. Jayaraman**: Orna Therapeutics, 3, 11; **M. Hoban**: 2seventy, 12, bluebird bio, 12, 2, Orna Therapeutics, 3; **J. Bolen**: Orna Therapeutics, 3, 4, 8, 10, 11; **I. Dalkilic-Liddle**: Orna Therapeutics, 3.

Abstract Number: 0942

Sodium-Glucose Co-Transporter 2 Inhibitors Modulate Renal Injury and Autoreactive Plasma Cells in Lupus

Jennifer Nicholson[1], Maria Ossa-Echeverri[1], Arpitha Haranahalli Shivarudrappa[1], Mark Lusco[1], Maria de la Luz Garcia-Hernandez[2], John Looney[1], Jennifer Anolik[3] and Javier Rangel-Moreno[1], [1]University of Rochester, Rochester, NY, [2]University of Rochester, West Henrietta, NY, [3]University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Though immune targeted therapies have improved outcomes in lupus nephritis, a significant number of patients experience renal damage and even progression to end stage renal disease. Recently, sodium and glucose cotransporter 2 inhibitors (SGLT2i) have proven efficacious in preventing adverse renal outcomes in patients with a variety of chronic diseases. In addition to inducing shifts in cellular metabolism, SGLT2i have anti-inflammatory and antifibrotic properties. Here, we hypothesize that systemic SGLT2i-driven metabolic changes could modulate humoral autoimmunity and inflammation in lupus.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

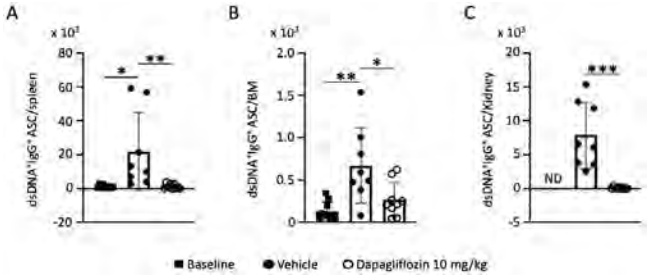


Figure 1. Dapagliflozin therapy at early stages of lupus impairs the production of splenic autoreactive antibody secreting cells (ASC) and affects their accumulation in the kidney and bone marrow (BM) of NZB/NZW female mice. 23 weeks old NZB/NZW female mice were treated with SGLT2i vs vehicle for 12 weeks. Spleen, kidney, and BM cell suspensions were used to enumerate dsDNA-specific IgG+ ASC by ELISpot. Live cells were counted by the trypan blue exclusion method to calculate the total number of autoreactive ASC per organ. A) Splenic, B) BM and C) renal dsDNA-specific IgG+ ASC were significantly reduced in NZB/NZW female mice treated with dapagliflozin. n = 8 – 10 NZB/NZW female mice/group. ND: No detected. Statistical significance was calculated with two-tailed, unpaired Student's t test in data with normal distribution or with Mann Whitney in groups with no normal distribution. *, $p < 0.05$; **, $p < 0.005$; ***, $p < 0.0005$.

Methods: 10-week-old MRL/lpr female mice were treated daily with dapagliflozin at 10 mg/kg or vehicle by gavage for 11 weeks. NZB/NZWF1 female mice were treated daily with dapagliflozin (10mg/kg) by gavage at early (23 weeks) and late disease (28 weeks) for 10-12 weeks and monitored weekly for proteinuria (n = 10 mice/experimental group). Sera was collected to measure autoantibodies, creatinine, and glucose by ELISA and colorimetric assays. Immune cells were enumerated in the spleen, bone marrow (BM), and kidneys by flow cytometry, immunofluorescence, and ELISPOT. Inflammation, fibrosis, and immune cell infiltration were assessed in kidneys by histology and quantitative PCR. Metabolite abundances were analyzed with untargeted metabolomics on kidney tissue.

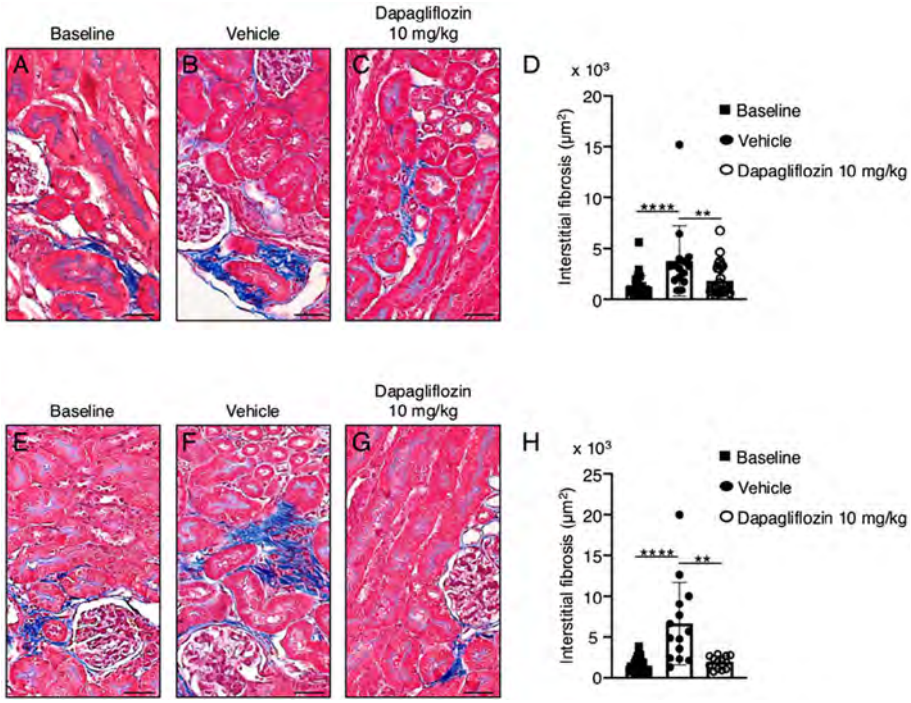


Figure 2. Dapagliflozin therapy modulates interstitial kidney fibrosis at early and advanced lupus stages in NZB/NZW female mice. 23 weeks old (early lupus) or 28 weeks old NZB/NZW female mice (advanced lupus) were treated as previously described. Kidneys were fixed in neutral buffered formalin and embedded in paraffin. Kidney sections were stained with Masson's Trichrome. Areas of interstitial fibrosis were measured with an automated tool of Zeiss microscope. A-C) Representative 200X magnification pictures of interstitial fibrosis in kidneys of NZB/NZW female mice treated with dapagliflozin at early stages of lupus. E-G) Representative 200X magnification pictures of interstitial fibrosis in kidneys of NZB/NZW female mice treated with dapagliflozin at advanced stages of lupus. Morphometric analysis of interstitial fibrosis after therapy at D) early lupus vs H) advanced lupus. Blue stain = collagen deposition. Scale bar = 20 μm. Statistical significance was calculated with two-tailed, unpaired Student's t test in data with normal distribution or with Mann Whitney in groups with no normal distribution. **, $p < 0.005$; ****, $p \leq 0.0001$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: SGLT2i therapy unexpectedly reduced autoreactive plasma cells (aPCs) in the spleen, BM, and kidney when initiated at early stages of disease in both mouse models (Figure 1 NZB/NZW). Splenic germinal centers (GCs) and generation of plasmablasts (PBs) in both spleen and BM were significantly inhibited in NZB/NZW mice treated early with dapagliflozin ($p < 0.005$ for splenic PBs, $p \leq 0.0001$ for BM PBs, compared to vehicle treated). In contrast, though SGLT2i treatment of late disease was less efficacious to target splenic GCs, aPCs were still reduced ($p < 0.05$) in the kidney of NZB/NZW mice. T regulatory cells (Tregs) were systematically increased in the axillary lymph nodes, extrafollicular areas of the spleen, and renal interstitium of SGLT2i treated MRL/lpr mice ($p < 0.005$ compared to vehicle treated). We also observed a significant enrichment in regulatory T follicular helper cells in splenic GCs of SGLT2i-treated NZB/NZW mice ($p \leq 0.0001$). Periarterial inflammation ($p < 0.005$, $p < 0.05$) and interstitial fibrosis ($p < 0.005$) were significantly ameliorated in the kidneys of MRL/lpr and NZB/NZW mice at early and late disease (Figure 2).

Conclusion: The immune modulatory and antifibrotic effects of SGLT2i in lupus prone mice support their potential as a novel treatment approach. Considering the essential role of glucose in the formation of GCs and plasma cells, our data suggests that a shift in glucose metabolism induced by SGLT2i may be the driving force behind the decrease in germinal centers, autoreactive plasma cells, and plasmablasts in MRL/lpr and NZB/NZW mice. Additional studies are underway to further define whether SGLT2i target oxidative stress in the kidney and to elucidate the systemic effects of SGLT2i on Tregs, GCs, and autoreactive PCs.

Disclosure: J. Nicholson: None; **M. Ossa-Echeverri**: None; **A. Haranahalli Shivarudrappa**: None; **M. Lusco**: None; **M. Garcia-Hernandez**: None; **J. Looney**: None; **J. Anolik**: None; **J. Rangel-Moreno**: None.

Abstract Number: 0943

Type I and Type II IFNs have both independent and overlapping effects on SLE disease severity

Haylee Cosgrove[1], Xiaoyan Gong[1], Aidan Matunis[1] and **Jeremy Tilstra**[2], [1]University of Pittsburgh, Pittsburgh, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The pathogenesis of systemic lupus erythematosus (SLE) is thought to be strongly influenced by the interferon (IFN) signaling pathway, particularly type I IFNs (IFNα/β). However, recent work suggests a significant role for type II IFN (IFNγ) and type III (IFNλ) in SLE. While anifrolumab was recently approved for the treatment of SLE, response rates were ∼16% above placebo for lupus patients in general, and for LN, complete remission rates were ∼10% over placebo, reaching under 28%. Thus, while efficacious, this suggests an opportunity to understand why these patients were not more responsive to therapy. One potential reason is that nearly 2/3 of type I IFN genes are also regulated by IFNγ, suggesting that there may be compensatory or redundant mechanisms by which IFNs regulate lupus pathogenesis.

Methods: We created two knock-out alleles, one targeting the type I IFN receptor (Ifnar1) and one targeting the type II IFN receptor (Ifngr1) on the MRL/lpr lupus-prone background. We then intercrossed these alleles to develop a cohort comprising four separate genotypes: WT, *Ifngr1*$^{-/-}$, *Ifnar*$^{-/-}$, and *Ifngr*$^{-/-}$*Ifnar1*$^{-/-}$ (DKO) mice. These cohorts were analyzed for disease pathology, including proteinuria, renal histology, autoantibodies, and immune cell activation. To corroborate our murine

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

findings, we also assessed 3 published datasets derived from human lupus nephritis patients to evaluate gene signatures for type I vs. type II IFN activation profiles.

Results: Here, we demonstrate that deficiency of *Ifnar1* has limited effects on disease endpoints in the MRL/lpr model, whereas deficiency *of Ifngr1* exhibits a dominant protective effect. However, when *Ifnar1* was deleted in concert with *Ifngr1*, we observed an additive effect. Both *Ifngr1*$^{-/-}$ and DKO MRL/lpr mice had increased survival compared to WT or *Ifnar*$^{-/-}$ mice, and this was accompanied by ameliorated lupus nephritis. Given the survival advantage of the DKO and Ifngr*1*$^{-/-}$ deficient MRL/lpr mice, we aged these mice to 27 weeks (far beyond the standard survival age of WT MRL/lpr mice). At this delayed time point, DKO mice showed improvement in glomerular disease, reduced lymphoproliferation with markedly reduced lymphadenopathy, and improved survival. When examining immune activation, we found a substantial B cell phenotype, with DKO mice exhibiting reduced age-associated B cell numbers, reduced autoantibodies, and suppressed germinal centers compared to *Ifngr1* deficiency alone. In human cohorts, we examined the unique type I and II IFN signatures and found that both were associated with the presence of lupus nephritis but, in fact, the type II IFN signature in kidney parenchymal cells is more significantly associated with the presence of lupus nephritis.

Conclusion: This data suggests that type I IFNs do, in fact, regulate disease activation in MRL/lpr mice. However, due to redundant and overlapping transcriptional regulation and the strong type II IFN signature seen in many mouse models and likely patients, blocking type I IFNs alone may not be sufficient to ameliorate disease. Furthermore, both type I and type II IFNs are responsible for regulating B cell phenotypes, which are instrumental in driving both human and murine lupus.

Disclosure: H. Cosgrove: None; **X. Gong**: None; **A. Matunis**: None; **J. Tilstra**: None.

Abstract Number: 0944

L-sepiapterin treatment reduces renal cortical gene expression associated with oxidative stress and fibrosis in NZM2410 murine lupus nephritis

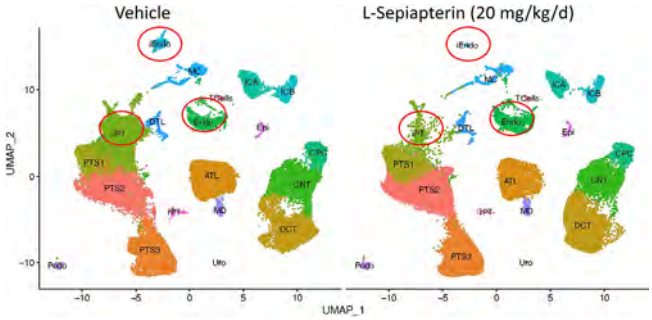
Dayvia Russell[1], Soroush Moradi[2], Suganya Subramanian[2], Silvia Vaena[2], Sandra Mungaray[2], Stanley Hoffman[2], Stefano Berto[2] and **Jim Oates**[2], [1]Ralph H. Johnson VA, Charleston, SC, [2]Medical University of South Carolina, Charleston, SC

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a disease of endothelial (EC) dysfunction. We hypothesize that much of this dysfunction stems from uncoupling of endothelial nitric oxide synthase, which leads to inflammatory and fibrotic states in endothelial cells. In the uncoupled state, eNOS produces superoxide rather than nitric oxide. Sepiapterin (PTC923) increases functional coupling of eNOS homodimers through its in vivo product, BH_4. We have reported that in a murine model of lupus nephritis (NZM2410), PTC923 improves survival and renal pathology. This study was designed to explore potential mechanisms through which this clinical effect is occurring, with a specific focus on pathways of inflammation, oxidative stress, and fibrosis.

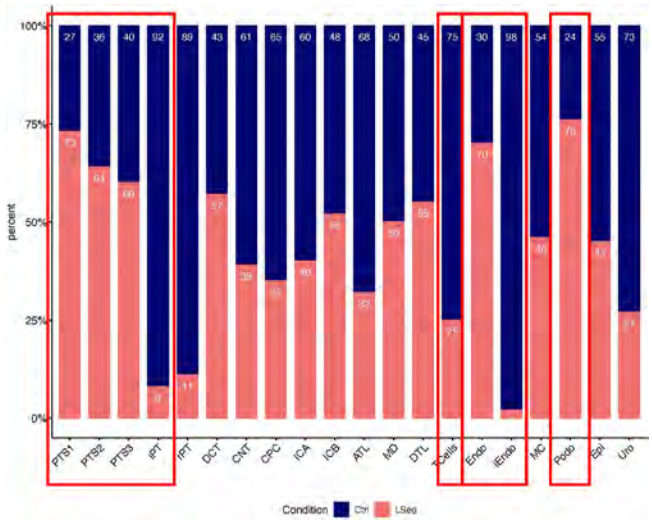
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



UMAP of cell clusters identified by single nuclear RNA sequencing of from renal cortical cells from NZM2410 mice (n=5) treated with PTC923 (L-Sepiapterin, right side) or vehicle (left side) during active nephritis (28 weeks). Circled cell clusters indicate those that are different between groups. iEndo= injured endothelial cells, Endo=endothelial cells, iPT=injured proximal tubule cells, PTS1,2,3=proximal tubule segments 1,2, or 3), rPT=re-covering proximal tubule cells, Podo=podocytes, MC=mesangial cells, MD=macula densa, etc.

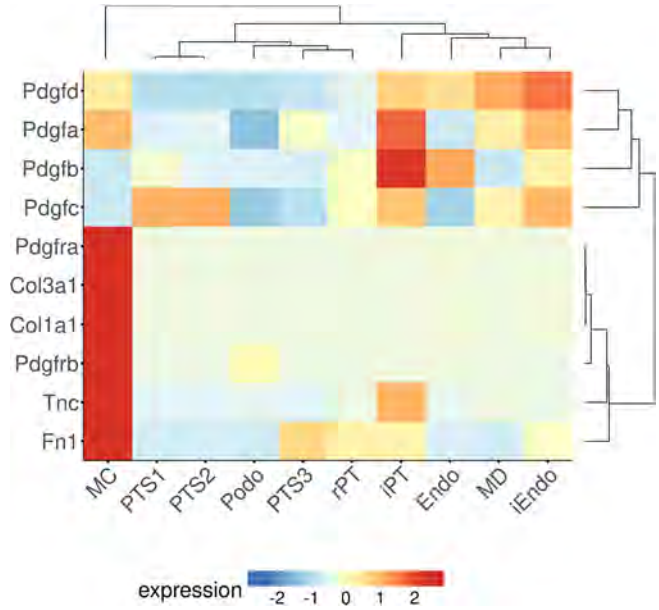
Methods: Female NZM2410 mice were aged to 22 weeks, when NZM2410 mice in our colony develop proteinuria. Mice were randomized to receive either vehicle (n=5) or 20 mg/kg/day (n=5) of PTC923 (L-sepiapterin) for 6 weeks. Mice were euthanized, and renal cortex was harvested for single nuclear RNA sequencing (snRNA-seq). Cell-specific gene markers were used to cluster cells, and differential expression of genes (DEG) was determined for each cell type. DEG with p adjusted < 0.05 and log2fold changed > 1.5 were analyzed. Pathway analysis was performed, and CellChat was used to analyze DEGs and hypothesize potential ligand-receptor interactions between cells.

Results: Endothelial cells (ECs) and proximal tubule (PT) segment 1, 2, and 3 cells were differentially increased PTC923 treatment. Inversely, injured PT cells (iPT), injured ECs (iECs), and T cells were reduced in PTC923 treated mice (Figures 1 and 2). ECs from PTC923-treated mice had increases in genes associated with nitric oxide production. Among iECs, Pdgfc and Pdgfd and among ECs, Pdgfc (associated with signaling for fibrosis) were significantly reduced in PTC923-treated mice. An analysis of redox-regulated genes revealed reductions in pathways that enrich for platelet derived growth factor binding transmembrane receptor protein phosphatase activity in PTC923-treated mice. Using CellChat, ligand-receptor interactions between injured ECs and mesangial cells are hypothesized via Pdgfd-Pdgfrb and Pdgfc-Pdgfra. In parallel, Col1a1 and Col3a1 as well as other genes associated with fibrosis were reduced with PTC923 in mesangial cells (Figure 3).



Graph indicating the percentage of cells in each cluster that are present in PTC923 (L-Sep, n=5) treated mice (salmon color) versus vehicle-treated mice (n=5, blue color). See figure 1. Additional cell types: DCT= distal convoluted tubule, CNT=connecting tubule, CPC=cortical principle cell, ICA=intercalated cell type A, ICB=intercalated cell type B, ATL=ascending thick limb or Henle, DTL=descending thick limb of Henle, Epi=parietyal epithelial cells, Uro=urothelial cells.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heatmap of differential gene expression from renal cortical cells of NZM2410 mice treated with L-Sepiapterin (PTC923) or vehicle from 22 to 28 weeks of age. Red indicates genes relatively increased in vehicle-treated mice, and blue indicates genes increased in PTC923-treated mice. Pdgf=platelet-derived growth factor, Col=collagen, Tnc=tenascin c, Fn1=fibronectin-1. iEndo= injured endothelial cells, Endo=endothelial cells, iPT=injured proximal tubule cells, PTS1,2,3=proximal tubule segments 1,2, or 3), rPT=recovering proximal tubule cells, Podo=podocytes, MC=mesangial cells, MD=macula densa, etc.

Conclusion: PTC923 therapy in the NZM2410 model of lupus nephritis reduces injured cells and genes associated with inflammation and fibrosis and increases EC expression of genes in pathways associated with ion channels and nitric oxide production. These data suggest that targeting eNOS uncoupling in ECs acts via reducing redox-regulated pathways and increasing nitric oxide production.

Disclosure: D. Russell: None; **S. Moradi**: None; **S. Subramanian**: None; **S. Vaena**: None; **S. Mungaray**: None; **S. Hoffman**: None; **S. Berto**: None; **J. Oates**: PTC Therapeutics, 12, PTC923 for this study provided by PTC Therapeutics.

Abstract Number: 0945

Nerve Injury-Induced Protein-1 (Ninj1) Deficiency Aggravates Murine Lupus Through Modulation of Macrophage Polarization

Jorge Romo-Tena[1], Luz Blanco[2], Shuichiro Nakabo[3], Victoria Hoffman[4], Norio Hanata[5], Mingzeng Zhang[2], Carmelo Carmona-Rivera[5], Eduardo Patino-Martinez[6], Dillon Claybaugh[2], Zu-Xi Yu[2] and Mariana Kaplan[5], [1]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]NIH, Bethesda, MD, [3]NIAMS, NIH, Bethesda, MD, [4]Diagnostic and Research Services Branch, Division of Veterinary Resources, Office of Research Services, National Institutes of Health, Bethesda, MD, Bethesda, [5]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, MD, [6]NIH/NIAMS, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Nerve injury-induced protein-1 (Ninj1) is an adhesion molecule that plays various roles in immune and stromal cells, including the modulation of inflammation and a critical role during cell death. Dysregulation of inflammatory pathways and cell death has been linked to the development of autoimmune diseases, such as systemic lupus erythematosus (SLE). Therefore, we hypothesized that Ninj1 may be involved in the pathogenesis of SLE.

Methods: Ninj1-deficient (*Ninj1*$^{+/-}$) and wild-type (WT) C57/B6 mice were induced to develop lupus-like autoimmunity using two induced models triggered by topical application of the Toll-like receptor 7/8 (TLR7/8) agonist imiquimod (IMQ) or by intraperitoneal injection of pristane. We assessed the mice for clinical phenotype, immune dysregulation, and organ damage.

Results: In comparison to WT mice, *Ninj1*$^{+/-}$ mice exposed to IMQ exhibited greater splenomegaly at the expense of extramedullary hematopoiesis, more severe anemia, decreased spleen lymphocyte counts, and increased spontaneous neutrophil extracellular trap (NET) formation. Although we observed no differences in autoantibody levels or proteinuria, *Ninj1*$^{+/-}$ mice developed more lupus-associated renal disease, as evidenced by increased immune complex deposition and exacerbated kidney inflammation and damage. In the pristane model, Ninj1 deficiency worsened diffuse alveolar hemorrhage and lung inflammation. Furthermore, *Ninj1*$^{+/-}$ M2 bone marrow-derived macrophages (BMDM) exposed to IMQ *in vitro* showed defective activation of the p38/Erk 1/2 mitogen-activated protein kinase (MAPK) and Akt signaling pathways, which are important in M2 macrophage polarization.

Conclusion: Preliminary, these findings suggest that Ninj1 deficiency aggravates murine lupus, at least in part, by impairing the anti-inflammatory roles of M2 macrophages. Further experimentation is needed to identify the immune system defects associated with Ninj1 deficiency, particularly in the affected tissues, and to understand their implications for autoimmune diseases.

Disclosure: J. Romo-Tena: None; **L. Blanco**: None; **S. Nakabo**: None; **V. Hoffman**: None; **N. Hanata**: None; **M. Zhang**: None; **C. Carmona-Rivera**: None; **E. Patino-Martinez**: None; **D. Claybaugh**: None; **Z. Yu**: None; **M. Kaplan**: None.

Abstract Number: 0946

A Novel Preclinical Tool for Evaluating CD20 Antibody Efficacy Based on BAFF/CD20 Dual-target Humanized Mice

Juan Liang[1] and Ting Wang[2], [1]Gempharmatech, Nanjing, Jiangsu, China, [2]GemPharmatech, Nanjing, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: CD20, a well characterized B-cell surface marker involved in B-cell activation and differentiation, plays a critical role in the pathogenesis of B-cell mediated diseases such as B-cell lymphomas, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Due to its selective expression on B-cells, CD20 is an attractive

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

target for antibody therapies targeting B-cell related diseases. Previously, we established a SLE model in transgenic mouse strains through the overexpression of human BAFF on a C57BL/6 mouse background (B6-hBAFF,T036794). To facilitate the preclinical evaluation of CD20-targeted therapeutics, we further developed a dual humanized model by crossing this mouse strain with CD20 humanized mice (BALB/c-hCD20,T057498) to obtain BAFF/CD20 dual-target humanized mice(T065937).

Methods: Serum samples from wild-type mice, hBAFF mice and hBAFF/hCD20 mice aged 8 to 27 weeks old were analyzed for anti-dsDNA autoantibodies, total IgG and IgM level via ELISA. Spleens and peripheral blood were also collected to assess B-cell populations by flow cytometry. To evaluate pharmacological response, 8-week-old hBAFF/hCD20 mice received intraperitoneal injections of ritixumab twice weekly for 20 weeks. During the administration period, serum and blood samples were collected for longitudinal assessment of immunoglobulin levels and B-cell counts.

Results: The hBAFF/hCD20 mice demonstrated a spontaneous SLE-like phenotype comparable to B6-hBAFF mice. These included elevated levels of serum IgG and IgM levels beginning at 8 weeks of age, which increased progressively as animals aged. High levels of anti-dsDNA autoantibodies, along with an increased ratio of B-cell frequency in the spleen and blood were observed, confirming an autoimmune phenotype. Following 60 days of rituximab treatment , the levels of IgM and anti-dsDNA antibodies in the serum were reduced, while the level of IgG was unchanged. By day 79, the numbers and proportions of total CD19+ B cells and plasma B cells in the peripheral blood significantly decreased, suggesting effective B-cell depletion and attenuation of the SLE phenotype.

Conclusion: We have established a novel dual humanized hBAFF/CD20 transgenic mouse model that exhibits spontaneous SLE features and enables the evaluation of CD20-targeted therapies. This model represents a powerful in vivo platform for investigating B-cell depleting agents in autoimmune disease settings.

Disclosure: J. Liang: None; **T. Wang**: None.

Abstract Number: 0947

Mechanisms of anti-NMDAR antibody-mediated neuronal pathology and mitigation by angiotensin II signaling inhibition

Kaitlin Carroll[1], Mark Mizrachi[1], Sean Simmons[2], Bahtiyar Toz[1], Czeslawa Kowal[3], Nazila Tehrani[1], Aida Zarfeshani[1], Nina Kello[1], Lara El Khoury[4], Jeffrey Wingard[1], Rachel Weissman-Tsukamoto[3], Joshua Levin[2], Bruce Volpe[3] and Betty Diamond[5], [1]Institute of Molecular Medicine, The Feinstein Institutes for Medical Research, Manhasset, NY, [2]Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, [3]Feinstein Institute of Molecular Medicine, Manhasset, NY, [4]Zucker School of Medicine at Hofstra/Northwell Health, Great Neck, NY, [5]The Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

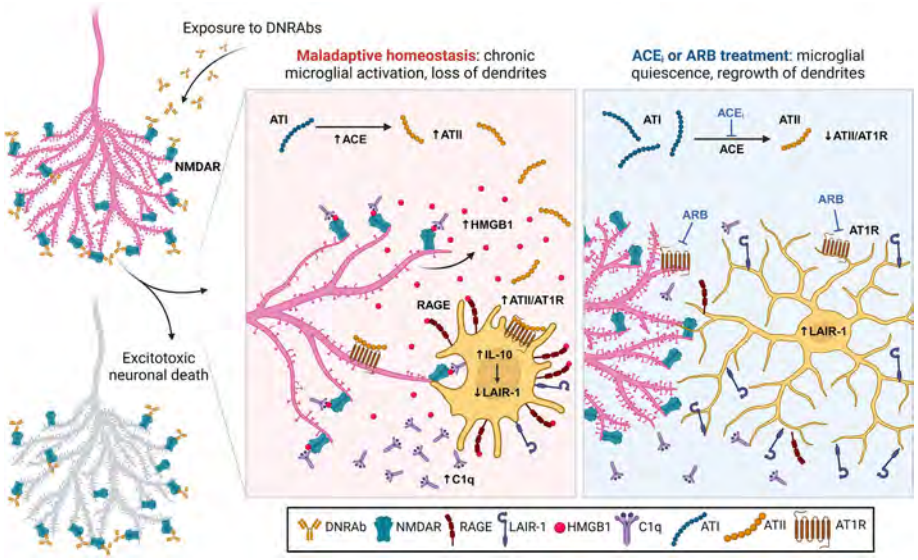
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Cognitive impairment is a frequent manifestation of neuropsychiatric systemic lupus erythematosus, present in up to 80% of patients and leading to a diminished quality of life.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Outcomes of DNRAb-mediated neuronal damage.

Methods: We used a model of lupus-like cognitive impairment that is initiated when antibodies that cross-react with DNA and excitatory neuronal receptors penetrate the hippocampus, causing immediate, self-limited, excitotoxic death of hippocampal neurons, which is then followed by a significant loss of dendritic complexity in surviving neurons and impairment in spatial memory.

Results: This injury creates a maladaptive equilibrium that is sustained in mice for at least 1 year. We identified a feedforward loop of microglial activation and microglia-dependent synapse elimination dependent on neuronal secretion of high mobility group box 1 protein (HMGB1) which binds the receptor for advanced glycation end products (RAGE) and leads to microglial secretion of C1q, upregulation of interleukin-10 with consequent downregulation of leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1), an inhibitory receptor for C1q. While we previously showed that treatment with a centrally acting angiotensin-converting enzyme inhibitor restored a healthy equilibrium, microglial quiescence and intact spatial memory, we now show that a centrally acting angiotensin receptor blocker also is effective, confirming the angiotensin pathway as a mediator of neuronal damage.

Conclusion: We have identified a mechanism by which neuroinflammation can be sustained in a feedforward process despite no intrinsic, genetically determined abnormality of neurons or microglia and no continuing external triggers for inflammation. The inhibition of angiotensin II/angiotensin receptor 1 signaling is able to half the self-sustaining inflammatory cycle by lifting the suppression of LAIR-1, which enables microglia and neurons to return to a state of quiescence and a healthy homeostasis. This has the translational implication that there needs to be a direct manipulation of the cells in the CNS to modulate or abort the inflammatory process.

Disclosure: K. Carroll: None; **M. Mizrachi**: None; **S. Simmons**: None; **B. Toz**: None; **C. Kowal**: None; **N. Tehrani**: None; **A. Zarfeshani**: None; **N. Kello**: None; **L. El Khoury**: None; **J. Wingard**: None; **R. Weissman-Tsukamoto**: None; **J. Levin**: None; **B. Volpe**: None; **B. Diamond**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0948

Presentation of Apoptotic Cell-Derived Autoantigens in Systemic Autoimmune Disease

Lance Peterson[1], Hannah KL De Cleene[2], Cheryl Lichti[2], David Bending[3] and Kodi Ravichandran[2], [1]Rheumatology and Immunology, Pediatrics, Washington University School of Medicine, St. Louis, MO, [2]Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, [3]Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, England, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus is a chronic, multisystem autoimmune disease characterized by the dysregulated clearance of dying cells, which results in the release of damage-associated molecular patterns and intracellular targets of disease-associated autoantibodies. Dendritic cells are important mediators of 'efferocytosis' (the phagocytosis of apoptotic cells) and present apoptotic cell-derived autoantigens to $CD4^+$ T cells via endocytic processing and MHC class II binding. Despite autoreactive T cells being essential to the pathogenesis and progression of diverse autoimmune diseases, there is only a nascent understanding of their autoantigen specificities. Prior studies have utilized almost exclusively model antigen systems (e.g. ovalbumin), without focus on cell death- and other inflammation-associated endogenous autoantigens.

Methods: We have developed and validated a mass spectrometry-based approach to characterize apoptotic cell-derived peptide autoantigens presented by dendritic cells (the 'efferocytic immunopeptidome'). Furthermore, we have developed a novel approach for testing T cell antigen recognition, using TCR-dependent expression of a fluorescent timer protein, that operates independently of cytokine production, proliferation or effector function. This approach will be used to define populations of autoreactive T cells during homeostasis and in multiple mouse models of lupus.

Results: Our mass spectrometry studies have identified unique subcellular pools of antigens presented in the efferocytic immunopeptidome, including those of nuclear and ribosomal origin. Through our studies on T cell autoreactivity, we identify a small population of T cells from naïve and diseased mice that are reactive against the efferocytic immunopeptidome.

Conclusion: Efferocytosis promotes the presentation of unique pools of cellular peptide antigens that represent a potential source of autoantigen and the driving of autoreactive T cell modulation of diverse immune pathology. We hypothesize that T cell autoreactivity against apoptotic cell-derived antigens will be associated with pathogenic loss of tolerance or protective regulatory responses during disease.

Disclosure: L. Peterson: None; **H. De Cleene**: None; **C. Lichti**: None; **D. Bending**: None; **K. Ravichandran**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0949

The Cancer-associated Female-biased Factor VGLL3 Drives Autoimmunity and Fibrosis

Mehrnaz Gharaee-Kermani[1], Poulami Dey[2], Vincent van Drongelen[1], Joanna Rew[1], Rachael Bogle[3], Marisa Hildebrandt[1], Benjamin Klein[1], Rezvan Moallemian[1], Monique E Verhaegen[1], Andrzej A Dlugosz[4], Lam Tsoi[1], J. Michelle Kahlenberg[1], Johann Gudjonsson[1] and Allison C Billi[1], [1]University of Michigan, Ann Arbor, MI, [2]Michigan Medicine, Ann Arbor, MI, [3]University of Michigan, Holland, OH, [4]University of Michigan, Ann Arbor

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune disease is far more common in women than men. We have determined that the skin of healthy women is primed for autoimmunity due to increased baseline epidermal expression of the transcription coregulator VGLL3. Accordingly, VGLL3 overexpression in transgenic (TG) mouse epidermis causes cutaneous and systemic murine lupus. Intriguingly, VGLL3 is also reported to act variably as an oncogene and tumor suppressor, revealing pleiotropic roles. While fibrosis is a hallmark of multiple autoimmune skin diseases, few animal models successfully recapitulate fibrosis, limiting mechanistic investigation.

Methods: Trichrome staining, immunostaining, qPCR, bulk RNA-seq, and single-cell RNA-seq (scRNA-seq) were used to analyze skin from mouse models of epidermal VGLL3 overexpression and human skin from patients with cutaneous lupus and healthy controls. Seurat, IPA, CellChat, and CellPhoneDB were used for analysis of scRNA-seq data. Human keratinocytes overexpressing VGLL3 and primary human skin fibroblasts were used for conditioned media experiments.

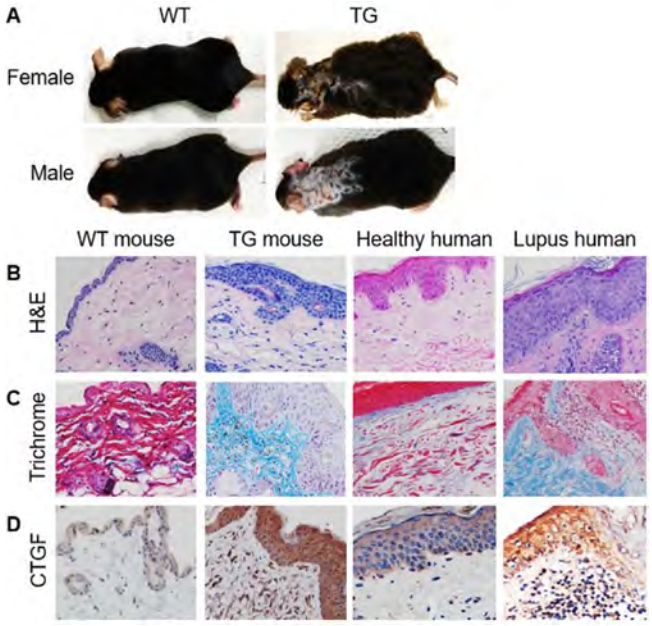


Figure 1. Epidermal VGLL3 overexpression leads to autoimmune skin fibrosis. A. Gross images of female and male transgenic (TG) and wild-type (WT) mice with epidermal overexpression of Vgll3. B. H&E staining of murine lesional TG and WT skin and human lupus patient and healthy control skin. C. Trichrome staining of murine and human skin as in (B). D. CTGF/CCN2 immunohistochemistry (IHC) of murine and human skin as in (B).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

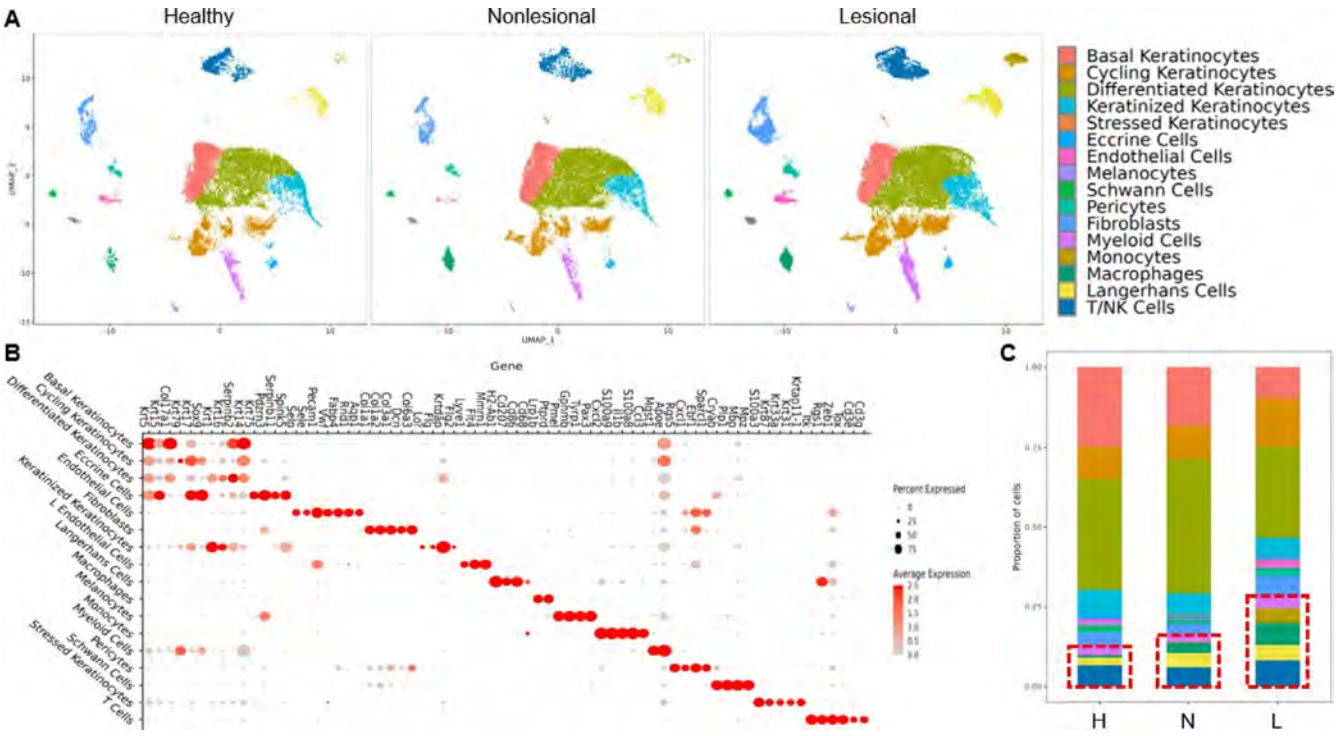


Figure 2. Single-cell RNA-sequencing (scRNA-seq) reveals immune cell expansion in skin lesions induced by epidermal VGLL3 overexpression A. Uniform Manifold Approximation and Projections (UMAPs) of all cells colored by cell type in healthy (H), nonlesional transgenic (N), and lesional transgenic (L) mouse skin. B. Dot plot of representative marker genes for each cell type. C. Histogram of all cells colored by cell type across disease states. Red boxes, immune cells.

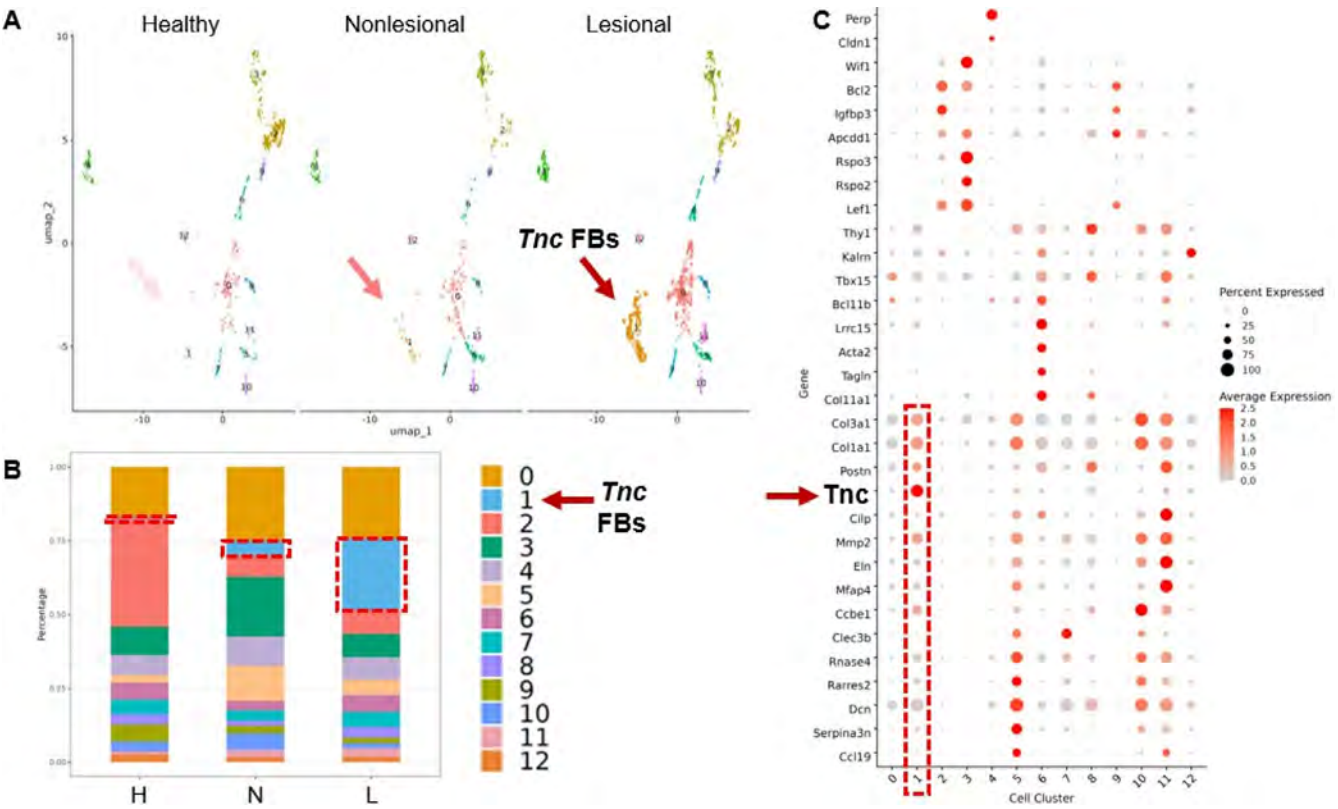


Figure 3. Fibroblast subclustering reveals emergence of Tnc-expressing fibroblasts in nonlesional and lesional transgenic mouse skin. A. Fibroblast subclustering across disease states. Red arrows indicate Tnc fibroblasts (FBs) (cells in orange). B. Histogram of fibroblast subclusters across disease states. Red boxes indicate Tnc fibroblasts (bars in light blue). C. Dot plot of representative marker genes for each cell type. Red boxes indicate Tnc fibroblasts.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We demonstrate that epidermal VGLL3 also drives autoimmune skin fibrosis. Integrating single-cell transcriptomic data from TG mice and human lupus patients, we establish a role for VGLL3-overexpressing keratinocytes in initiating autoimmune skin fibrosis through altering fibroblast transcriptional states. In pre-lesional skin, VGLL3-overexpressing keratinocytes upregulate specific cytokines including TNF and CCL20 and promote an interferon-rich environment, inducing pre-lesional fibroblasts to activate a profibrotic, proinflammatory transcriptional program implicated in fibrotic disease. Conditioned media experiments confirm a direct effect of keratinocytes on fibroblasts, increasing transcription of CCL2, a chemokine implicated in multiple fibrotic diseases. Analysis of fibroblasts reveals expansion in pre-lesional and lesional skin of a population of profibrotic fibroblasts that are shown by ligand-receptor analysis to be one of the most differentially activated cellular communicators in diseased skin. Fibroblast subclustering identifies a transgenic mouse-specific cluster of *Tnc*-positive fibroblasts, which have been shown to be crucial in the progression and maintenance of fibrotic skin diseases by promoting fibroblast activation and sustaining fibrotic responses. Analysis of human cutaneous lupus scRNA-seq data corroborates many of our murine lupus findings in human disease.

Conclusion: These results suggest that VGLL3 and keratinocytes play a dual role in early autoimmune skin fibrosis through both fibroblast reprogramming and immune cell recruitment and support the use of the *K5-Vgll3* model for investigation of autoimmune skin fibrosis.

Disclosure: M. Gharaee-Kermani: None; **P. Dey**: None; **V. van Drongelen**: None; **J. Rew**: None; **R. Bogle**: None; **M. Hildebrandt**: None; **B. Klein**: None; **R. Moallemian**: None; **M. Verhaegen**: None; **A. Dlugosz**: None; **L. Tsoi**: Galderma, 5, Janssen, 5; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5; **J. Gudjonsson**: None; **A. Billi**: None.

Abstract Number: 0950

Ep300-Catalyzed Rad50 Lactylation Compromises Genomic Stability and Drives CD4+T cells Cell Senescence in SLE

Mingyang Zhang[1], huanzi dai[2], cun lan[3] and mingyang sun[3], [1]Daping Hospital, Army Medical University, chongqing, Chongqing, China (People's Republic), [2]Daping Hospital & Research Institute of Surgery, Army Medical University, Chongqing, PR China., Chongqing, China (People's Republic), [3]Daping Hospital, Army Medical University, chongqing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Senescent $CD4^+$ T cells are increasingly implicated in systemic lupus erythematosus (SLE) pathogenesis. While metabolic reprogramming in lupus T cells enhances glycolysis and lactate accumulation, the role of lactate-induced posttranslational modifications (PTMs) in promoting T-cell senescence remains unexplored.

Methods: Peripheral blood $CD4^+$ T cells were isolated from SLE patients and healthy donors to assess lactylation levels and senescence markers (e.g., p21). A pristane-induced lupus model was established in BALB/c mice, and splenic $CD4^+$ T cells were analyzed for lactylation profiles using lactylome proteomics. Co-immunoprecipitation (Co-IP) coupled with mass spectrometry identified lactyltransferases interacting with Rad50, a DNA repair protein. To validate functional roles,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

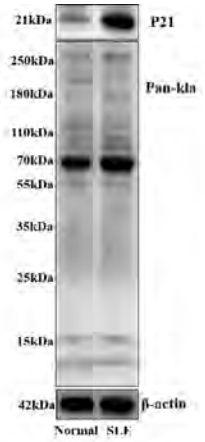


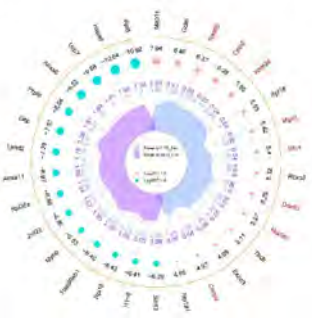
Figure 1. Lactylation levels and senescence marker p21 expression in peripheral blood $CD4^+$ T cells from healthy donors and systemic lupus erythematosus (SLE) patients.

$CD4^{cre}Ep300^{fl/fl}$ mice (with CD4+ T cell-specific EP300 deletion) were generated and subjected to pristane-induced lupus. Rad50 lactylation was quantified using site-specific antibodies, while senescence markers, serum anti-dsDNA/IgG levels, and renal histopathology were evaluated.

Results: SLE patients exhibited elevated lactylation levels in $CD4^+$ T cells compared to healthy controls, paralleled by increased p21 expression (Figure 1). Lactylome profiling identified Rad50 as the most prominently lactylated protein linked to DNA damage repair. Co-IP proteomics revealed Ep300 as the primary enzyme catalyzing Rad50 lactylation (Figure 2). In pristane-induced lupus mice, $CD4^+$ T cells displayed heightened Rad50 lactylation, amplified p21-driven senescence, elevated autoantibodies, and severe renal damage. These phenotypes were rescued in $CD4^{cre}Ep300^{fl/fl}$ mice (Figure 3).

Conclusion: EP300-mediated lactylation of Rad50 disrupts its DNA repair function, fostering genomic instability and pathogenic senescence in $CD4^+$ T cells during lupus progression. Targeting this pathway may offer a novel therapeutic avenue for SLE.

A



B

Rad50 purification

Protein	# of Pepitides	Coverage(%)
Rad50	33	49
Mre11	39	24
Nbs1	22	25
Ep300	11	10
Tcof1	4	2

Figure 2. Lactylome profiling identifies Rad50 lactylation sites, and co-immunoprecipitation (Co-IP) coupled with mass spectrometry reveals P300 as the catalytic lactyltransferase.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

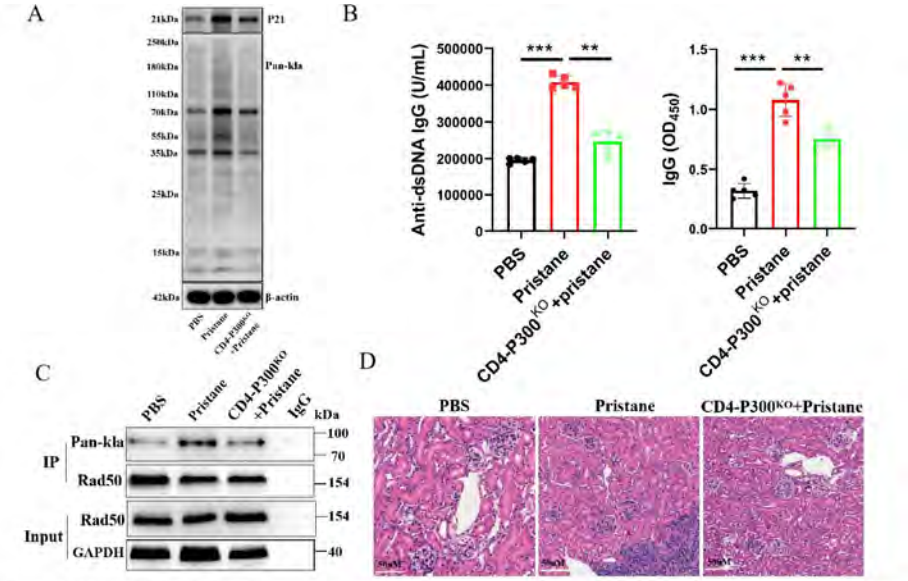


Figure 3.(A) Lactylation levels and senescence markers (p21) in CD4⁺ T cells of pristane-treated mice with or without P300 deletion.(B) Serum autoantibody levels (anti-dsDNA, IgG) measured by ELISA.(C) Rad50 lactylation quantified via co-immunoprecipitation (Co-IP).(D) Renal histopathological changes assessed by H&E staining.*P < 0.05.

Disclosure: m. zhang: None; **h. dai**: None; **c. lan**: None; **m. sun**: None.

Abstract Number: 0951

Epidermal IFNκ Increases Circulating and Cutaneous Monocytes in a C57/Bl6 Overexpression Mouse Model

Patrick O'Brien, Benjamin Klein, Deborah Colesa and J. Michelle Kahlenberg, University of Michigan, Ann Arbor, MI

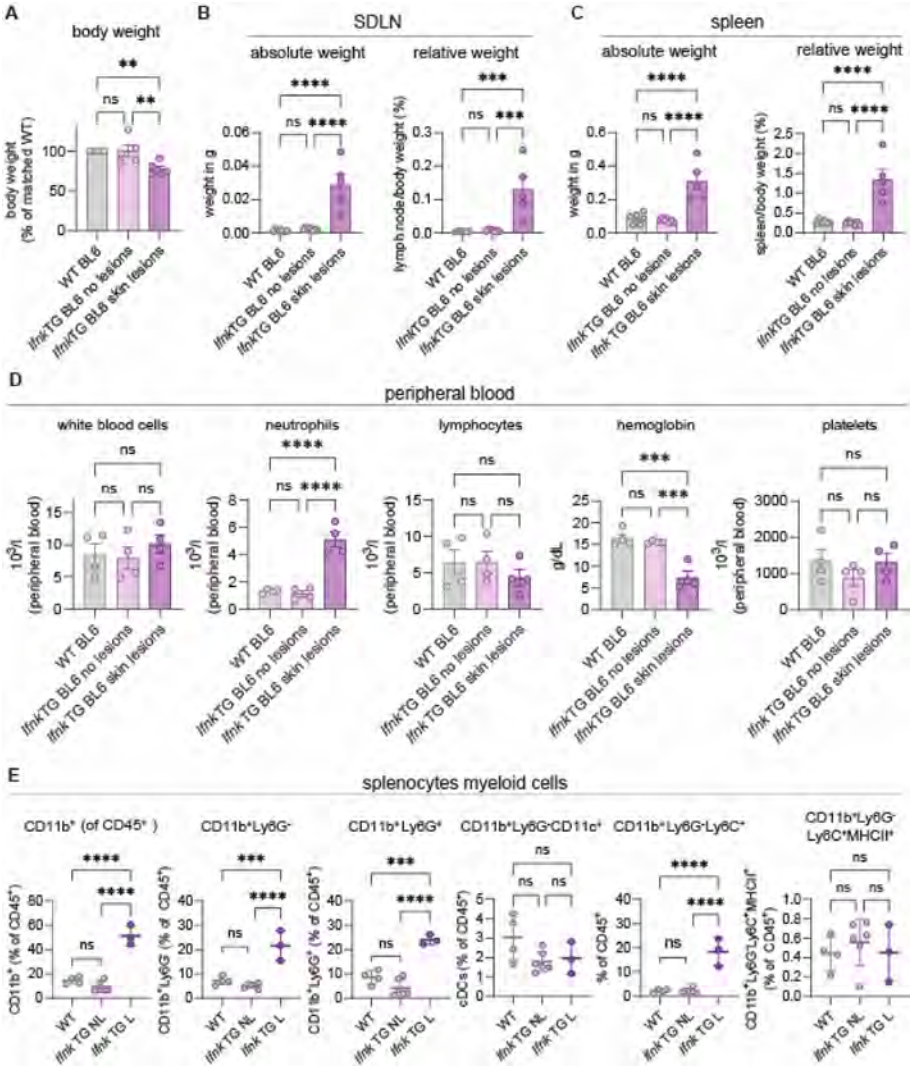
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus is a heterogeneous inflammatory autoimmune disease affecting a variety of organs, including skin manifestations such as photosensitivity and cutaneous lesions. The skin of human lupus patients is primed for disease through a variety of cellular mechanisms, including an increase in Type I interferons (IFNs) such as interferon kappa (IFNk) that activate immune cells and prime for photosensitivity. Here, we study the effects of epidermal transgenic (Tg) *Ifnk* overexpression to determine the role of skin-derived type I IFNs in driving lupus phenotypes. This experimental work utilized mice of C57/Bl6 background.

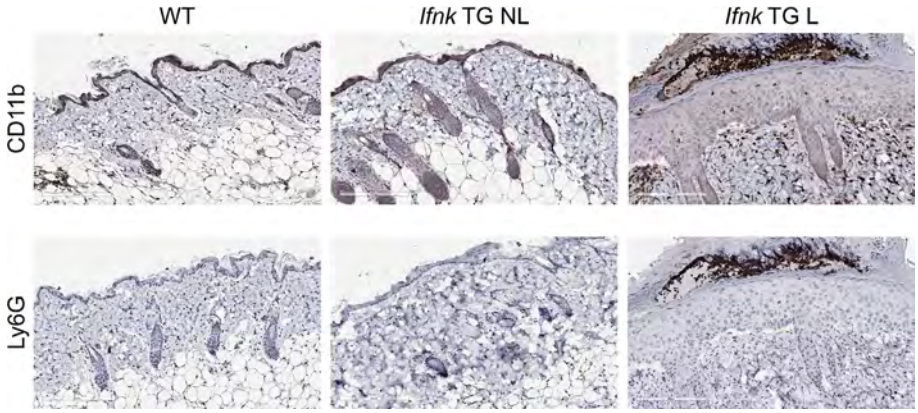
Methods: TgIFNk mice were generated utilizing the K14 promoter to direct *Ifnk* expression to the basal epidermis as previously reported. Mice were monitored for spontaneous lesions in a 12-month survival cohort. Where indicated, 3-month-old mice were exposed to 300mJ/cm^2 UVB 12 hours before euthanasia. Phenotypes of TgIFNk and wild type C57/Bl6 mice were studied via complete blood count (CBC), ELISA, flow cytometry, immunohistochemistry (IHC), immunofluorescence (IF), and quantitative real-time polymerase chain reaction (qrt-PCR) performed on blood, spleen, skin, kidney, and urine harvested at time of euthanasia. All data analysis was performed using GraphPad Prism 10, including two-way ANOVA, one-way ANOVA, or unpaired t-Test where appropriate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



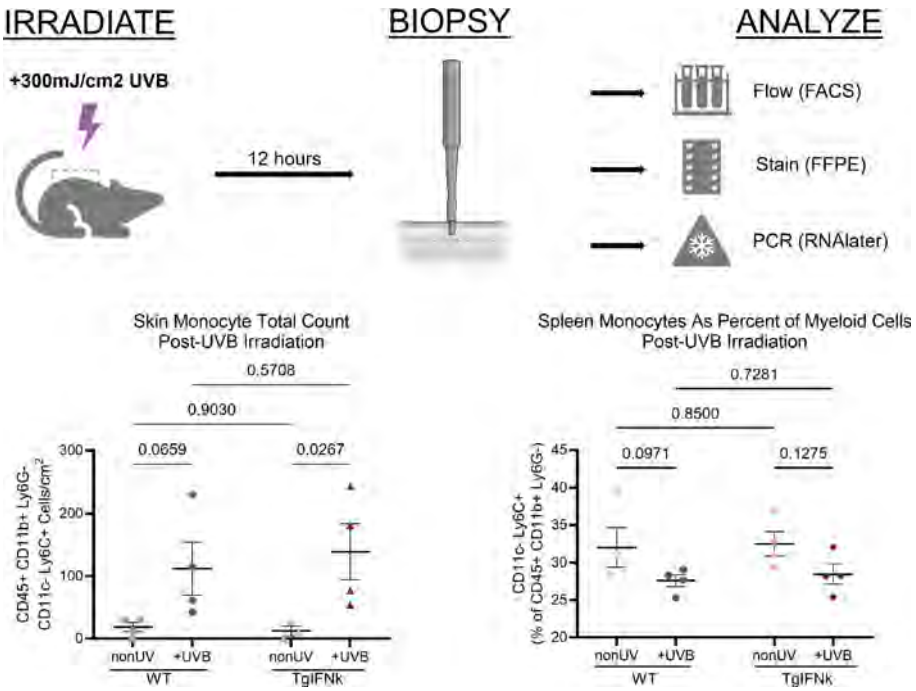
Organ weights (1A-C), Complete blood count (1D), and flow cytometry (1E) of mice generating spontaneous lesions (IfnkTG BL6 skin lesions), and age-matched sex-matched non-lesional TG or wild type (WT) controls illustrating lymphadenopathy, splenomegaly, anemia, increased circulating neutrophils, and increased circulating myeloid cells.

Results: In the C57/Bl6 background, only 4 percent of TgIFNk mice developed spontaneous skin lesions, and no mice developed proteinuria. Lesional mice demonstrated elevated circulating leukocytes compared to age-matched sex-matched non-lesional TgIFNk and WT controls. This increase was driven primarily by an expansion of neutrophils. In the skin,



Immunohistochemistry (IHC) of CD11b and Ly6G for spontaneous lesions (IfnkTG BL6 skin lesions), and age-matched sex-matched non-lesional TG or wild type (WT) controls.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



UVB experiment graphical abstract and flow cytometry results showing a reduction in monocytes in the spleen compared to an increase in monocytes in the skin.

however, immunohistochemistry revealed that skin lesions were enriched primarily in monocytes and monocyte-derived dendritic cells. Non-lesional skin showed no change in CD11b+ cells between genotypes, suggesting that increased circulating neutrophils drive enhanced recruitment of myeloid cells upon cutaneous lesion formation. WT and TgIFNk mice undergoing UVB irradiation exhibited increased monocytes in the skin, but no difference was noted between strains.

Conclusion: TgIFNk mice on the C57/Bl6 background exhibit increases in circulating inflammatory innate immune cells and aggressive myeloid-driven skin disease in a minor subset of mice. Future work seeks to further characterize the function of these innate immune cells in both spontaneous lesions and UVB-mediated disease activation.

Disclosure: P. O'Brien: None; **B. Klein**: None; **D. Colesa**: None; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5.

Abstract Number: 0952

Therapeutic Potential of PaPE-1 in Reducing TLR7-Mediated Inflammation in a Murine Model of Lupus

Rachael Werner[1], Jena Wirth[1], Gary Gilkeson[1] and Melissa Cunningham[2], [1]Medical University of South Carolina, Charleston, SC, [2]Medical University of SC, Charleston, SC

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

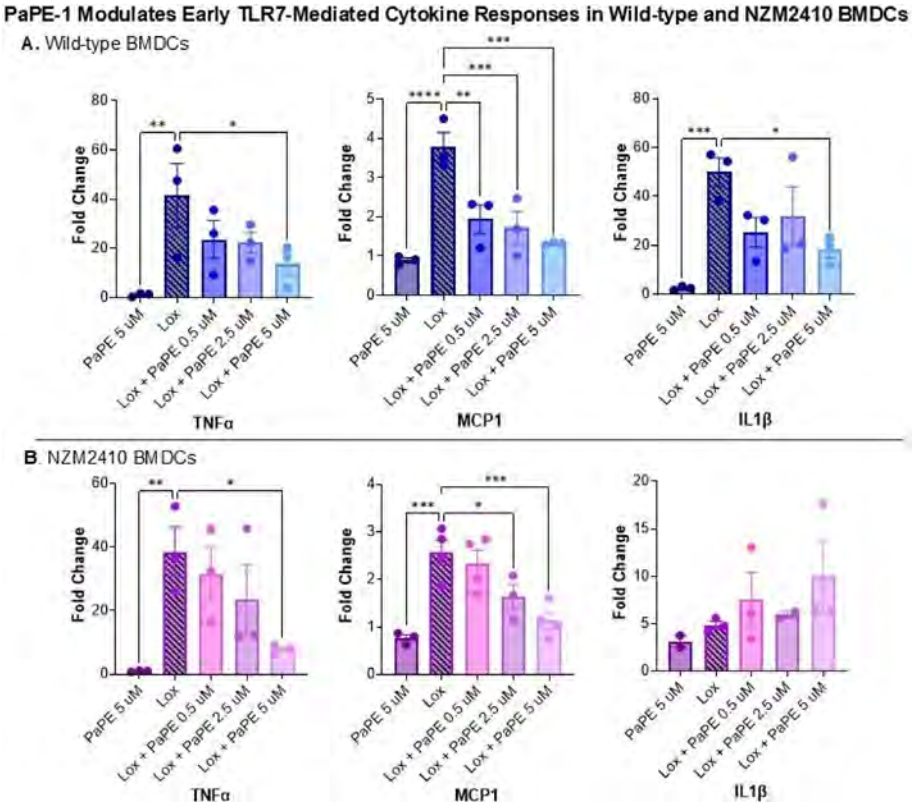


Figure 1. mRNA expression of inflammatory cytokines was measured by qPCR in BMDCs 45 minutes after TLR7 stimulation and PaPE-1 treatment. Fold change was calculated relative to housekeeping gene RPL30. Error bars represent standard error of the mean (SEM). Statistical analysis was performed using one-way ANOVA. Data represent biological replicates.*<0.05, **<0.01, ***<0.001, ****<0.0001

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that disproportionately affects women, underscoring the critical role of sex chromosomes and sex hormones—particularly estrogen—in disease pathogenesis. Estrogen signaling via estrogen receptor alpha (ERα) has been implicated in both the onset and progression of SLE; however, the therapeutic potential of selective estrogen receptor modulators (SERMs) remains underexplored.

PaPE-1, also known as "pathway preferential estrogen," is a low-affinity, non-nuclear ERα agonist that selectively activates extranuclear estrogen signaling pathways. PaPE-1 has demonstrated beneficial effects in non-reproductive tissues, including reduction of proinflammatory cytokines and enhancement of endothelial repair, while avoiding classical estrogenic actions such as cell proliferation in breast and reproductive tissues. These properties suggest that PaPE-1 could attenuate inflammation and tissue damage in lupus without increasing estrogen-related risks, making it a promising candidate for therapeutic intervention in SLE.

Methods: We utilized ex vivo bone marrow–derived dendritic cells (BMDCs) from female wild-type C57BL/6J and NZM2410 lupus-prone mice. To model lupus-relevant innate immune activation, BMDCs were stimulated with the Toll-like receptor 7 (TLR7) agonist loxoribine (Lox). Cells were cultured in charcoal-stripped, phenol red-free medium and treated with PaPE-1 or vehicle control. Inflammatory responses were assessed by mRNA expression of key cytokines at 45 minutes and 24 hours post-stimulation using quantitative PCR. All experiments included biological replicates.

Results: PaPE-1 modulated TLR7-induced proinflammatory cytokine expression in a dose-dependent manner in BMDCs from both wild-type and lupus-prone NZM2410 mice. Treatment with PaPE-1 significantly reduced MCP-1 and TNFα mRNA expression at 45 minutes post-stimulation. In wild-type BMDCs, IL-1β expression also showed a clear dose-dependent reduction. This effect was not observed in NZM2410 BMDCs, likely due to a markedly attenuated IL-1β response to TLR7 stimulation at this early timepoint (~5-fold in NZM2410 vs. ~45-fold in wild-type). These 45-minute findings are

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

shown in Figure 1. The blunted early cytokine response in NZM2410 BMDCs may reflect altered kinetics or reduced TLR7 sensitivity due to chronic immune activation. However, by 24 hours, PaPE-1 induced a dose-dependent reduction in IL-1β and IL-6 expression in NZM2410 BMDCs, suggesting altered timing of immune-regulatory effects in lupus DCs.

Conclusion: These preclinical findings support PaPE-1 as a promising therapeutic candidate for SLE. Its selective activation of non-nuclear ERα signaling and ability to attenuate TLR7-induced inflammatory responses highlight its potential to modulate pathogenic immune activation in lupus. The observed time-dependent effects underscore the importance of kinetic profiling in future studies. Further investigation is warranted to clarify PaPE-1's mechanisms of action and assess its translational relevance, including studies in human immune cells and at extended timepoints.

Disclosure: R. Werner: None; **J. Wirth**: None; **G. Gilkeson**: None; **M. Cunningham**: Allogene, 1, Aurinia, 5.

Abstract Number: 0953

NMDAR Autoantibody-Induced Neuronal Damage in the Amygdala Mediates Mood and Anxiety Disorders in a Model of Neuropsychiatric Lupus

Rachel Weissman-Tsukamoto[1], Bruce Volpe[1], Zaide Ibic[1], Kaitlin Carroll[2], An Vo[1], Czeslawa Kowal[1] and Betty Diamond[3], [1]Feinstein Institute of Molecular Medicine, Manhasset, NY, [2]Institute of Molecular Medicine, The Feinstein Institutes for Medical Research, Manhasset, NY, [3]The Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0934–0954) Systemic Lupus Erythematosus – Animal Models Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease characterized by aberrant production of autoantibodies and chronic inflammation. Up to 80% of individuals with SLE experience cognitive, emotional, or behavioral symptoms, termed Neuropsychiatric Lupus (NPSLE). NPSLE cognitive impairment and mood disorders may be mediated by autoantibodies, with specific symptoms related to the varied targets of these autoantibodies and the region of blood brain barrier (BBB) injury.

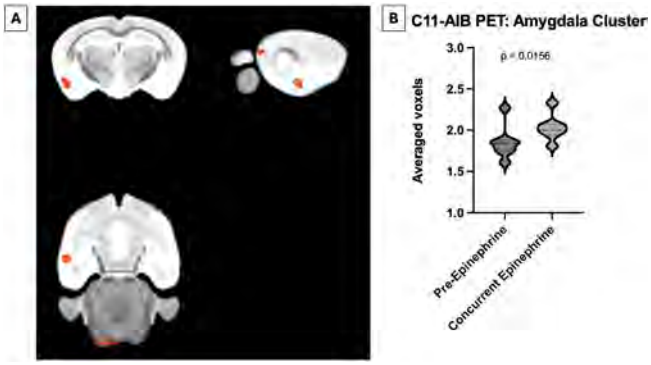


Figure 1: Epinephrine induces a specific blood brain barrier breach in the area of the amygdala in both DNRAb+ and control animals. A) Visualization of thresholded C11-AIB PET scan comparing both DNRAb+ and DNRAb- animals pre-epinephrine and post-epinephrine administration. B) Quantification of C11-AIB PET scan average of voxels in the amygdala, normalized by global mean in each mouse comparing both DNRAb+ and DNRAb- animals pre-epinephrine and post-epinephrine administration (p=0.0156, paired t test, n=8).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

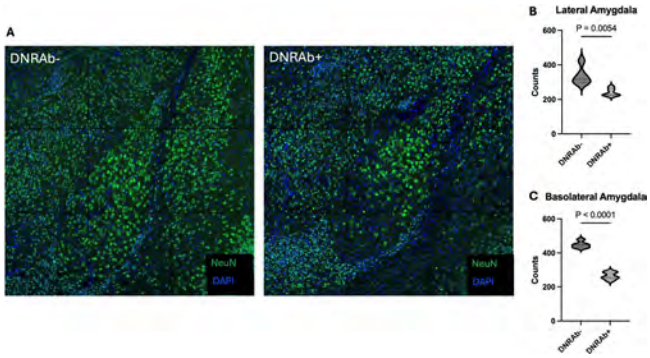


Figure 2: DNRAb+ mice demonstrate significant neuronal loss in multiple regions of the amygdala compared to control mice. A) Representative images of immunofluorescence confocal imaging of LAD and BLA of DNRAb- and DNRAb+ mice. B) Cell counts per area using unbiased stereology of the lateral amygdala nuclei in DNRAb- and DNRAb+ mice. C) Cell counts per area using unbiased stereology of the basolateral amygdala nuclei in DNRAb- and DNRAb+ mice.

We use a murine model of NPSLE induced by anti-double-stranded DNA (dsDNA) antibodies (DNRAbs), which cross-react with the excitatory neuronal N-methyl D-aspartate receptor (NMDAR) and facilitate excitotoxic neuronal death. These antibodies are present in approximately 30% of patients with SLE and at a higher rate in those with NPSLE. Prior research in our lab has shown that epinephrine administration to DNRAb+ mice leads to acute neuronal excitotoxicity in the amygdala. Investigation of the chronic phenotype in the amygdala may lead to insights into the prevalence of persistent mood and anxiety disorders experienced by patients.

Methods: Female B6H2d mice used in this study are immunized with DWEYS peptide on a polylysine backbone to produce DNRAbs or with the polylysine backbone as a control. PET studies using 11C-AIB tracer are used for BBB permeability with epinephrine administration. Unbiased stereology and immunohistochemistry are used to identify cell type morphology, protein expression, and quantify neuronal loss. Behavioral testing includes object place memory, elevated plus maze, and fear conditioning. Mann-Whitney and T-tests are used for statistical analysis between groups.

Results: In this study, we characterize the chronic effects of DNRAb antibody penetration into the brain after systemic administration of epinephrine. We show that BBB permeability due to epinephrine is selective for the amygdala using 11C-AIB PET imaging, resulting in antibody deposition into the amygdala. We observe significant neuronal loss in the basolateral and lateral nuclei of the amygdala in DNRAb+ compared to DNRAb- mice, correlating with amygdala-related behavioral findings in anxiety testing. Finally we observe an abnormal morphology and lipid oxidation suggestive of axonal degeneration in surviving neurons.

Conclusion: Interestingly, the DNRAb-mediated neuronal pathology in the amygdala, which we currently hypothesize is due to ferroptosis, differs from that in the hippocampus, which is characterized by chronic microglial-dependent synaptic elimination and loss of dendritic arborization. Further investigation will focus on circuit disruption and detailed analysis of mechanisms of chronic neuronal damage. This work expands our understanding of the neuropathological mechanisms which can underly psychiatric symptoms in NPSLE.

Disclosure: R. Weissman-Tsukamoto: None; **B. Volpe**: None; **Z. Ibic**: None; **K. Carroll**: None; **A. Vo**: None; **C. Kowal**: None; **B. Diamond**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0955

Surveying RNA methylation in scleroderma highlights roles for demethylases ALKBH5 and FTO in fibrosis

Alexander Cai[1], Alyssa Rosek[1], Neha Khanna[1], Anna Webber[1], Karly Kozicki[1], Dinesh Khanna[2] and Pei-Suen Tsou[2], [1]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [2]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Recent studies indicate that genes involved in RNA methylation may play a significant role in cellular functions, and disruptions in RNA methylation have been linked to various pathological conditions, including autoimmune diseases. However, its specific role in systemic sclerosis (SSc) remains unclear. RNA methylation influences cellular biological functions by regulating gene expression, particularly through m6A RNA methylation. This reversible process relies on "writer" methyltransferases, "eraser" demethylases, and "reader" proteins that recognize m6A marks. Given the association of m6A marks with fibrosis, we examined the expression of genes involved in m6A RNA methylation by analyzing publicly available datasets and isolated dermal fibroblasts from both healthy controls and SSc patients, further focused on RNA demethylases in SSc fibroblasts.

Methods: Data from GEO was analyzed. RNA was extracted from skin fibroblasts isolated from healthy individuals and SSc patients. Gene expression was analyzed using quantitative PCR. Knockdown or inhibition of ALKBH5 or FTO was done by siRNAs or inhibitors ALKBH5-in-3 and FB23-2. Fibrotic endpoints were examined by various assays. Statistical analyses with a P value below 0.05 were considered statistically significant.

Results: Analysis of the GEO dataset generated in whole skin biopsies revealed a distinct pattern of gene expression. While methylation writers and readers, such as *WTAP*, *METTL14*, *YTHDC1*, and *YTHDF2* were significantly downregulated, the eraser demethylases *FTO* and *ALKBH5* were notably upregulated in SSc. This upregulation correlated positively with the modified Rodnan skin score (mRSS). Follow-up quantitative PCR analyses in dermal fibroblasts from healthy controls and patients with diffuse SSc substantiated these findings. Subsequent experiments demonstrated that the knockdown of ALKBH5 or FTO in SSc fibroblasts led to a significant reduction in the expression of pro-fibrotic genes, including collagen genes and TGFβ. Moreover, applying specific inhibitors to these demethylases resulted in marked anti-fibrotic effects, reducing collagen production and fibroblast activation.

Conclusion: Our research elucidates the critical roles of RNA demethylases ALKBH5 and FTO in SSc, particularly in the context of fibrosis. The upregulation of these enzymes and their significant correlation with mRSS suggest they are key drivers in the progression of fibrosis in SSc. Functional experiments demonstrate the potential of targeting ALKBH5 and FTO to reduce pro-fibrotic gene expression and fibroblast activation, offering promising therapeutic avenues for intervention. These findings contribute substantially to our understanding of the molecular underpinnings of SSc and suggest that modulating RNA methylation could be a viable strategy to mitigate fibrosis in this challenging disease. Further research is underway to fully explore the therapeutic potential and genes and pathways involved in RNA methylation and its impact on fibrotic diseases such as SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Cai: None; **A. Rosek**: None; **N. Khanna**: None; **A. Webber**: None; **K. Kozicki**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **P. Tsou**: None.

Abstract Number: 0956

Mapping Metabolic Changes in Skin Fibrosis in Systemic Sclerosis by Spatial Proteomics

Veda Devakumar[1], Yi-Nan Li[2], Tim Filla[3], Aleix Rius Rigau[4], Andrea-Hermina Györfi[5], Bilgesu Safak Tümerdem[6], Ranjana Neelagar[7], Minrui Liang[8], Christina Bergmann[9], Georg Schett[10], Jörg Distler[11] and **Alexandru-Emil Matei**[12], [1]Heinrich Heine University, University Clinic Düsseldorf, Düsseödorf, [2]University Hospital of Dösseldorf, Dösseldorf, Germany, [3]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [4]Department of Internal Medicine 3, Rheumatology and Clinical Immunology, Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen. Deutsches Zentrum Immuntherapie (DZI), Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [5]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [6]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Nordrhein-Westfalen, Germany, [7]Heinrich Heine University Duesseldorf, University Hospital Duesseldorf, Düsseldorf, Nordrhein-Westfalen, Germany, [8]Huashan Hospital, Fudan University, Shanghai, China (People's Republic), [9]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [10]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [11]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [12]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Several tissue resident populations undergo metabolic reprogramming during tissue fibrosis as a phenotypic adaptation to their changing metabolic demands. However, these shifts in metabolic profiles in fibrotic tissues have not been previously studied at single cell level with spatial resolution. Furthermore, the spatial cellular organization within metabolic niches in fibrotic tissues was not explored until now.

Here we aimed to identify and map distinct metabolically-defined fibroblast, macrophage and endothelial cell subsets in SSc skin, characterize their cellular metabolic microenvironments, and evaluate their association with progression of skin fibrosis in SSc.

Methods: Sections from skin biopsies of nine SSc patients and seven controls were prepared. Imaging mass cytometry (IMC), a spatial proteomics technique, was employed. An IMC panel of 38 metal-labelled antibodies, of which 22 antibodies targeting key enzymes and signalling molecules in several metabolic pathways was designed and validated in human skin. Data analysis was performed as described. The glycolysis or TCA/OXPHOS scores calculated with this approach robustly correlate with the activities of the respective pathways, as determined by functional assays.

Results: We analyzed the expression of key regulators of metabolic pathways such as glycolysis, tricarboxylic acid (TCA) cycle, oxidative phosphorylation (OXPHOS), fatty acid oxidation and synthesis, aminoacid internalization, pentose

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

phosphate pathway, hypoxia, reactive oxygen species production as well as of regulators of mitochondrial dynamics, collectively termed as metabolic regulome, in SSc and control skin.

Dermal cells of SSc patients with progressive skin fibrosis had a remarkably distinct metabolic regulome compared with patients with stable skin fibrosis and to controls, with upregulation of glycolysis and TCA/OXPHOS scores.

Unbiased fibroblast clustering identified eight distinct fibroblasts subsets defined by their metabolic regulome. Of these, a subpopulation of fibroblasts with high expression of glycolysis and TCA/OXPHOS enzymes (termed Met^{hi} Fib) was upregulated in SSc patients with progressive skin fibrosis, and expressed high levels of markers of activated fibroblasts, such as αSMA and FAP.

The metabolically-defined fibroblast subsets formed niches with endothelial cells and macrophages with similar levels of metabolic pathway activities, e.g. the Met^{hi} fibroblasts were located in spatial proximity to endothelial cells and macrophages that expressed high levels of glycolysis and TCA/OXPHOS enzymes.

Conclusion: We identified distinct metabolically-defined subsets fibroblasts in SSc and control skin, with an enrichment of metabolically highly active fibroblasts in progressive skin fibrosis. This fibroblast subset expressed myofibroblast markers and formed niches with endothelial cells and macrophages with a similar metabolic profile. Thus, metabolic phenotyping of fibroblasts and their niches by IMC-based spatial proteomics might identify SSc patients at risk for progression of skin fibrosis.

Disclosure: V. Devakumar: None; **Y. Li**: None; **T. Filla**: None; **A. Rius Rigau**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **B. Tümerdem**: None; **R. Neelagar**: None; **M. Liang**: None; **C. Bergmann**: Kyverna Therapeutics, Inc., 5; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **A. Matei**: None.

Abstract Number: 0957

Multi-Omic Profiling Reveals a Monocyte-Vascular Signature Associated with the Regression of Skin Fibrosis in SSc

Astrid Hofman[1], Pietro Bearzi[2], Elena Pachera[3], Cosimo Bruni[4], Lumeng Li[2], Laura Much[5], Kristina Bürki[1], Mike Becker[6], Anna-Maria Hoffmann-Vold[7] and Oliver Distler[8], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [2]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [3]University Hospital Zurich, Zurich, Switzerland, [4]University of Zurich, Zurich, Switzerland, [5]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [6]Dept. of Rheumatology, University Hospital Zurich, Zurich, Switzerland, [7]Oslo University Hospital, Oslo, Norway, [8]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Regression of skin fibrosis is a feature of the natural history of dcSSc. The molecular mechanisms underlying this resolution remain unclear. This study aims to establish a molecular fingerprint characterizing regression of skin fibrosis in SSc patients.

Methods: All patients fulfilled the 2013 ACR/EULAR classification criteria for SSc. Regressors were defined by a 5-point decrease in the modified Rodnan's Skin Score (mRSS), and progressors by a 5-point increase at annual follow-up. Serum proteomics using the Olink High Throughput Explore panel (5,400 proteins) was performed on 44 SSc patients (25 regressors, 19 stable/progressors=non-regressors). Differentially abundant proteins (DAPs) were identified using the limma package. For single-cell RNA sequencing (scRNA-seq), peripheral blood mononuclear cells (PBMCs) were isolated from 15 SSc patients (5 each: regressor, progressor, stable) and 5 healthy controls. Single-cell libraries were prepared, and raw reads were aligned to the human genome using Cellranger 7.0. Transcriptomic data were analyzed with Seurat (v5.1.0), and differential gene expression analysis (DGEA) was performed using the MAST package, followed by Gene Set Enrichment Analysis (GSEA).

Results: Olink proteomics analysis identified 124 DAPs between skin regressors and skin non-regressors. Pathway enrichment analysis (PEA) on the DAPs revealed that MDK, THY1, JAM3, XG and VEGFB relate to cellular extravasation processes and SMOC2, RAMP2, CD160, VEGFB, HSPG2, PGF, EPHA2 to angiogenesis as top processes (Fig. 1). Seventy-three percent of these proteins are linked to monocyte extravasation.

PBMC scRNA-seq revealed 5 distinct clusters of monocytes (Fig 2A). Compositional analysis revealed a significant increase of clusters 0, 1 and 3 in the regressors compared to progressors (Fig 2B). To find whether a specific subset is involved in monocyte-vascular interactions, the expression of extravasation markers ITGAM, SELL, ICAM1, and S100A8/9 was used. These markers localized to clusters 0, 1 and 3 (Fig 2C). Additionally, chemotaxis marker CCR1 had an increased expression in clusters 0, 1, and 3, whereas CCR5 was unique to cluster 1 (Fig 2D).

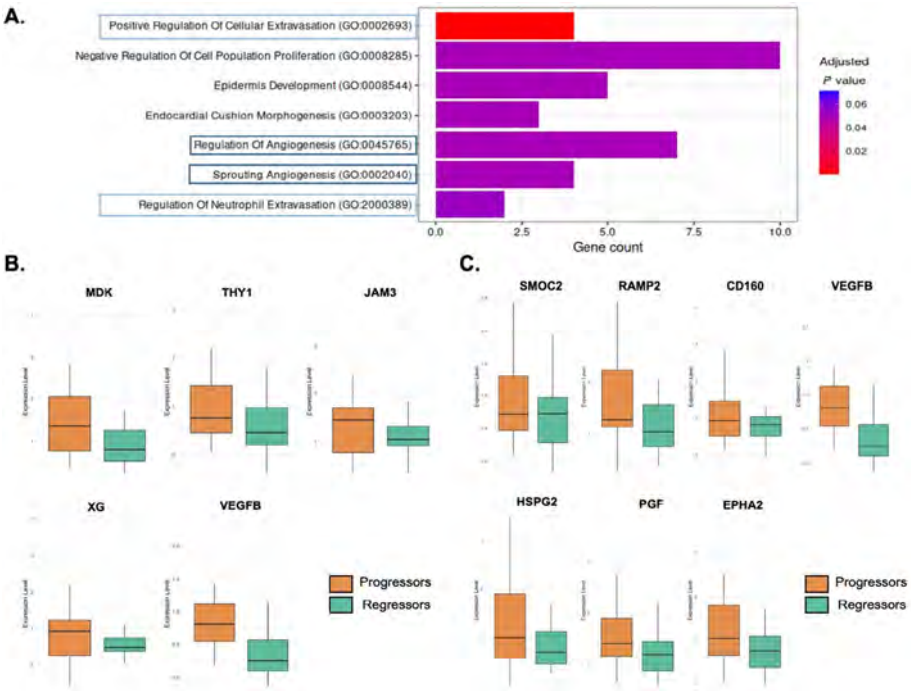


Figure 1. Serum proteomics reveals that differentially abundant proteins (DAPs) are linked to cellular extravasation and angiogenesis and downregulated in regressors. A) Enrichment analysis using GO Biological Processes of the 124 DAPS detected (Benjamini-Hochberg adjusted FDR < 0.3) shows that DAPs are linked to processes including 'Positive Regulation of Cellular Extravasation' and 'Regulation of Angiogenesis'. B) The DAPs linked to the cellular extravasation process all demonstrate a decreased expression in the regressors compared to the progressors. C) DAPs linked to the angiogenesis process show a decreased expression in the regressors compared to the progressors.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

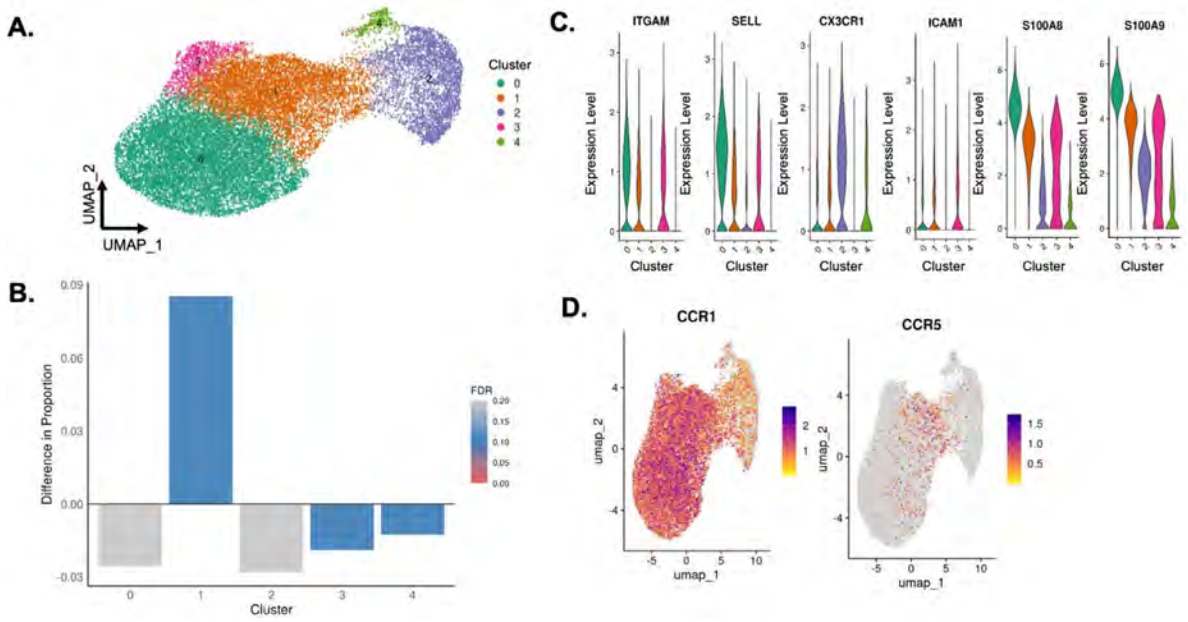


Figure 2. Monocytes in scRNA-seq display a signature related to monocyte extravasation that can be linked to cluster 1. A) UMAP of all monocytes in the PBMC scRNA-seq data revealed 5 distinct monocyte subpopulations. B) Compositional analysis shows that cluster 1 is significantly more abundant in the regressors compared to progressors (FDR = 0.11). C) Well-established markers related to cellular extravasation (ITGAM, SELL, CX3CR1, ICAM1, S100A8, S100A9) showed an increased transcript expression in cluster 1. D) CCR1, which mediates monocyte arrest showed increased expression in clusters 0, 1, and 3. CCR5, which is involved in monocyte spreading, shows a specific expression in only cluster 1.

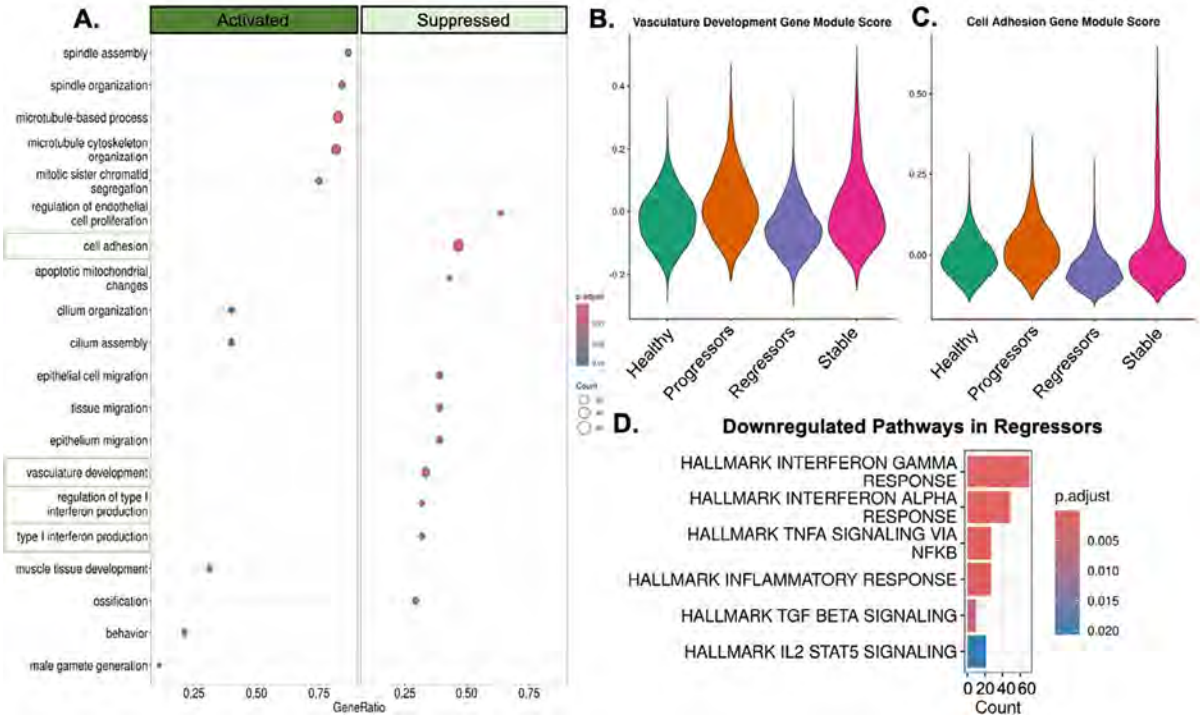


Figure 3. Characterization of Cluster 1 reveals a subpopulation of monocytes primed for extravasation. A) GSEA showed a suppression of gene sets 'regulation of endothelial cell proliferation' ad 'vasculature development' in the regressors. Similarly, gene sets 'regulation of type I interferon production' and 'type I interferon production' were also suppressed in the regressors. B) The gene module score for the vasculature development gene set was calculated using the aggregated expression of the genes in this gene set. The gene module score for 'Vasculature Development'-associated genes and 'Endothelial Cell Proliferation'-related genes D) were both found to be suppressed in the regressors compared to other patient groups. E) Pathway enrichment analysis confirmed that interferon alpha and beta (type I) response was among the top downregulated pathways in the regressors.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Further characterization of cluster 1 using GSEA revealed a suppression in the gene sets 'vasculature development' (including extravasation-related genes: ITGA5, MMP14, MMP2, MMP19, CCL2, SOCS3, HMOX1 and PPARG) and 'cell adhesion' (including extravasation-related genes: ITGA5, MMP14, MMP2, CCL2, SOCS3, SIGLEC1 and MERTK). The generated gene module scores reflect a consistent decrease in regressors compared to other patient groups (Fig 3A-C). Additionally, both PEA and GSEA on cluster 1 had a decreased expression of IFN-I genes in the regressors, which is linked to a decrease in vascular permeability (Fig 3D).

Conclusion: Our multi-omics approach identified a set of proteins linked to monocyte extravasation and a subcluster of monocytes characterized by extravasation markers. This subcluster also displayed a decreased IFN-I activity. Our data points to a reduction in monocyte extravasation to the tissue associated to the regression of skin fibrosis in SSc.

Disclosure: A. Hofman: None; **P. Bearzi**: None; **E. Pachera**: None; **C. Bruni**: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5; **L. Li**: None; **L. Much**: None; **K. Bürki**: None; **M. Becker**: Foundation for research in Rheumatology (FOREUM), 5, GSK, 6, 12, congress support, Novartis Foundation for Medical-biological Research, 5, 6, Vifor, 6, 12, congress support; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0958

Asynchronous Resolution of Inflammation and Fibrosis in a Prolonged Experimental Model Suggests Distinct Temporal Dynamics and Resolution Mechanisms in Systemic Sclerosis

Aurore Collet[1], Manel Jendoubi[2], Thomas Guerrier[2], Alexis Largy[2], Silvia Speca[2], Sylvain Dubucquoi[1] and David Launay[3], [1]Univ. Lille, Inserm, CHU Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, Lille, France ; CHU Lille, Institut d'Immunologie, Lille, France, Lille, France, [2]Univ. Lille, Inserm, CHU Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, Lille, France, Lille, France, [3]Univ. Lille, Inserm, CHU Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, Lille, France ; CHU Lille, Département de Médecine interne et Immunologie Clinique, Centre de Référence des Maladies Auto-immunes Systémiques Rares du Nord et Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille France, Lille, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is characterized by tissue fibrosis, which is defined as excessive and irreversible extracellular matrix (ECM) accumulation, leading to organ dysfunction. In SSc, ECM production is thought to be initiated by an inflammatory trigger. However, the precise kinetics of the inflammatory and fibrotic processes remain poorly

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

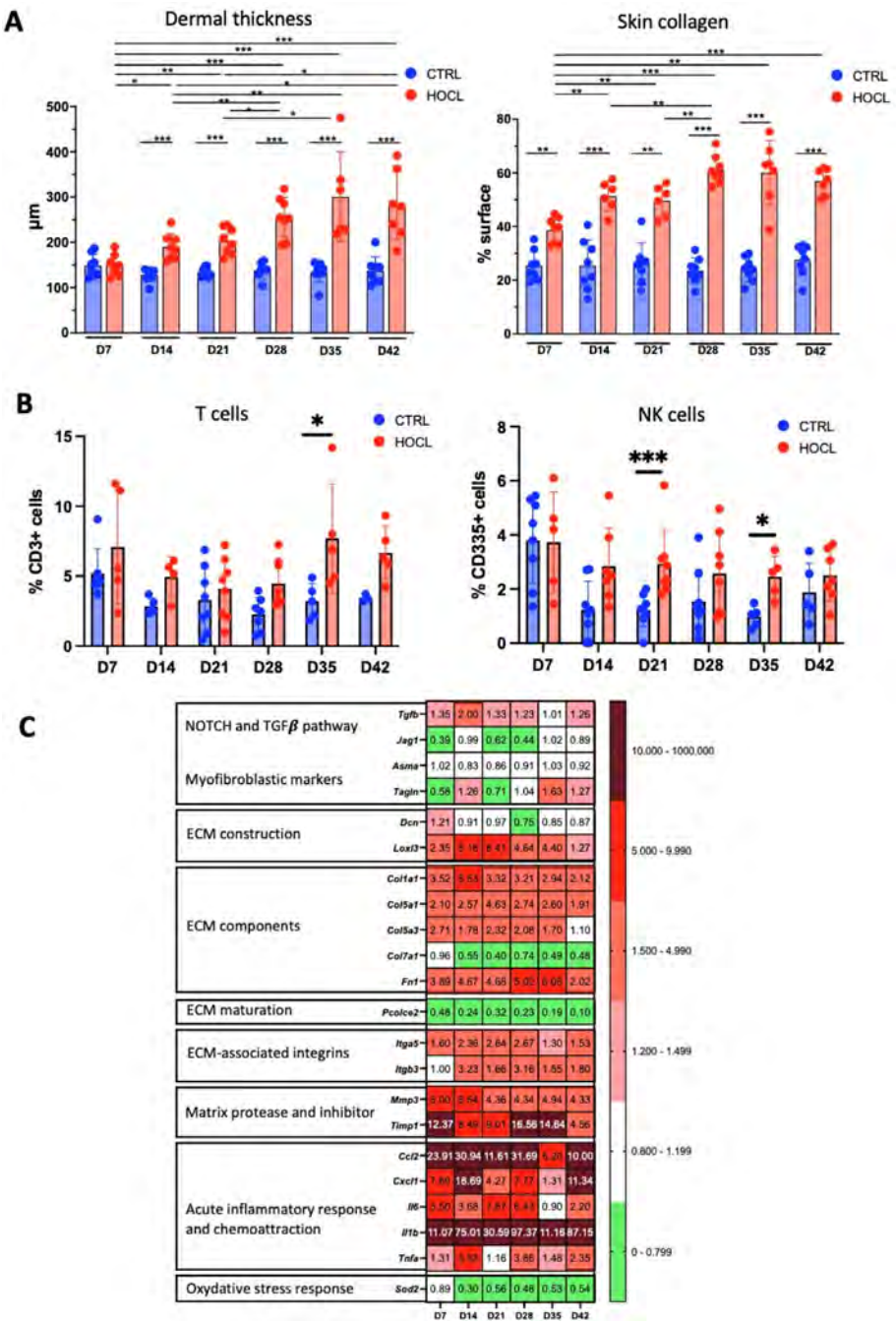


Figure 1: Kinetic evolution of skin inflammation and fibrosis in the HOCl-induced systemic sclerosis mouse model (A) Evolution of dermal thickness (in µm, on Hematoxylin-Eosin stained histological sections) and collagen content (% per section, on Picrosirius-Red stained histological sections). Results presented as mean +/- SD, N = 8 per group. (B) Evolution of T cells and NK cells percentages among skin leukocytes, measured by flow cytometry. Results presented as mean +/- SD, n = 5-8 per group. (C) Expression of genes representative of inflammatory and fibrosis processes in the skin. Heat map expressed as log2 fold change of gene expression measured by qPCR in HOCl mice, normalized on PBS mice with ***β***actin gene as internal control. N = 12 per group. * : P<0,05 ; ** : P<0,01 ; *** : P<0,001.

described. Moreover, data regarding the independence of fibrosis from the initial inflammatory stimulus are lacking. This study aims to characterize the timing and interdependence of the inflammatory and fibrosis processes using an extended experimental mouse model of SSc.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

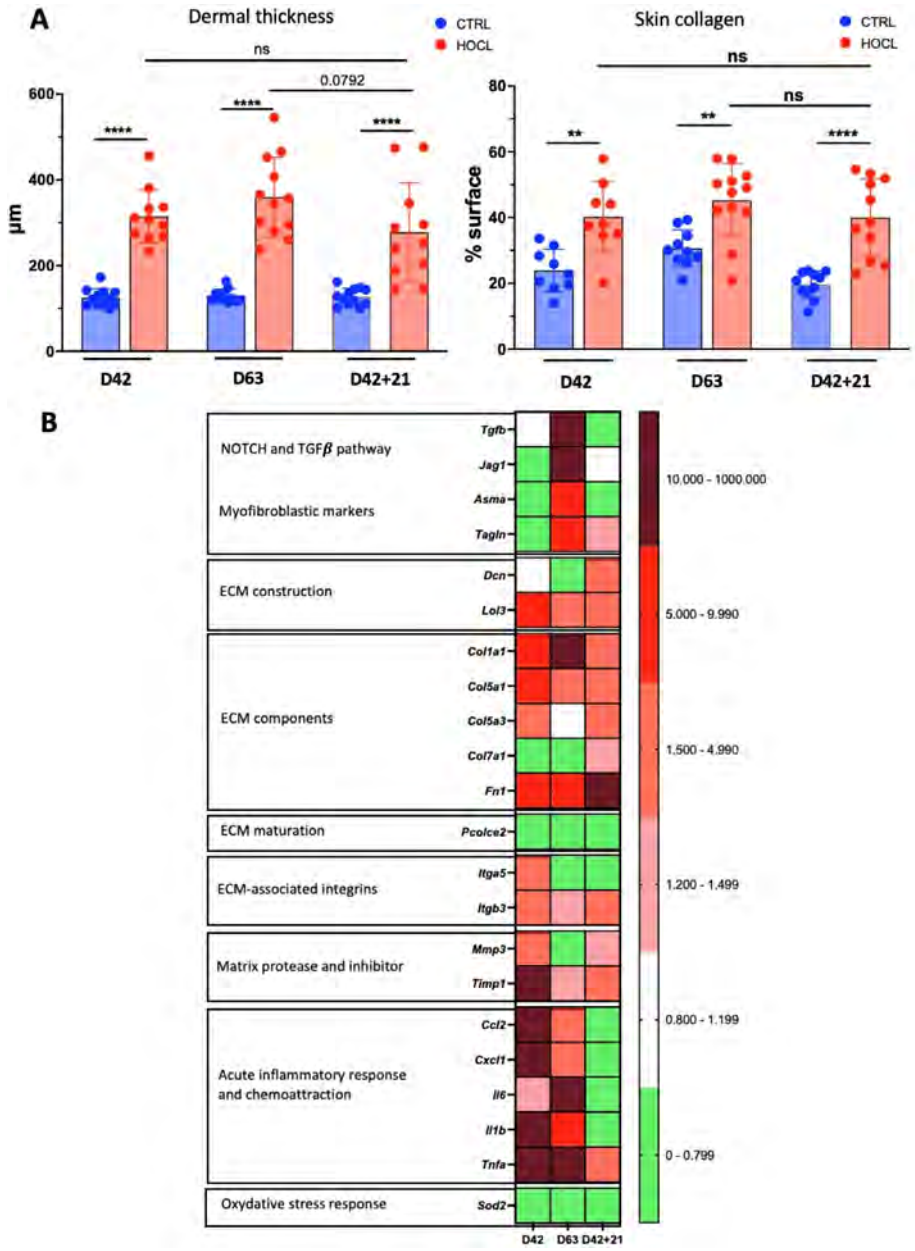


Figure 2: Evolution of skin inflammation and fibrosis after stopping the inflammatory trigger in the HOCl-induced systemic sclerosis mouse model (A) Evolution of dermal thickness (in µm, on Hematoxylin-Eosin stained histological sections) and collagen content (% per section, on Picrosirius-Red stained histological sections). Results presented as mean +/- SD, N = 12 per group. (B) Expression of genes representative of inflammatory and fibrosis processes in the skin. Heat map expressed as log2 fold change of gene expression measured by qPCR in HOCl mice, normalized on PBS mice with ***β***actin gene as internal control. N = 12 per group. ** : P<0,01 ; **** : P<0,0001.

Methods: Experimental SSc was induced by daily hypochlorous acid (HOCl) injections into the backs of mice for 9 weeks. Mice (n = 8-12 per group) were sequentially sacrificed at day (D)7, D14, D21, D28, D35, D42 and D63. Moreover, a group of mice receiving HOCl injections until D42 was sacrificed at D63 (group D42+21), to study the evolution of fibrosis after stopping HOCl injections. Skin architectural changes and ECM accumulation were assessed by histological approaches. Leukocyte count and distribution were analyzed by flow cytometry. The dynamic progression of the skin inflammatory and fibrotic functional program was assessed by RT-qPCR using a panel of 22 representative genes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Mice treated with HOCl showed early dermal thickening and collagen accumulation starting from D14 and D7, respectively, and progressing to a plateau by D28 (Figure 1A). HOCl injections impacted skin inflammatory cells in terms of number (higher number and percentage compared to control mice), localization (progressive infiltration from deep to superficial skin layers) and subset distribution (increase in NK et T cells percentages, no difference for myeloid cells or B cells, Figure 1B). Genes associated with inflammation were overexpressed in the skin from D7 to D42. Genes encoding ECM components were also upregulated starting from D7, with distinct peak expression times between type I collagen, type V collagen, and fibronectin (Figure 1C).

Three weeks after stopping HOCl injections, no decrease in dermal thickness or collagen accumulation was observed (Figure 2A). Inflammation regressed, with a significant decrease in the expression of inflammatory cytokine genes (*Ccl2, Cxcl1, Il6* and *Il1b*). A significant modification of the ECM component gene expression profile (decrease in *Col1a1* and *Col5a1* expression and increase in *Col7a1* expression) and a drop in the expression of myofibroblast differentiation genes were noted (Figure 2B).

Conclusion: Inflammatory and fibrotic parameters are closely intertwined in the HOCl model, with both processes appearing from the onset of HOCl injections. After cessation of the inflammatory trigger, progressive ECM remodeling is observed, though without a return to baseline. A better understanding of the temporal dynamics of these processes in this experimental model may elucidate inflammation and fibrosis resolution mechanisms in SSc and guide the optimal timing for evaluating anti-inflammatory and anti-fibrotic therapies, both in preclinical studies and clinical translation.

Disclosure: A. Collet: Grifols, 5; **M. Jendoubi**: None; **T. Guerrier**: None; **A. Largy**: None; **S. Speca**: None; **S. Dubucquoi**: None; **D. Launay**: AstraZeneca, 2, Biocryst Pharmaceuticals, 2, CSL Behring, 2, 5, Octapharma AG, 5, Takeda, 2.

Abstract Number: 0959

Longitudinal Multiomic Study of Skin, Peripheral Blood, and Serum: Serum Proteome Reflects the Disease Process at the End-organ Level and Predicts the Course of Modified Rodnan Skin Score

Bich Na Choi[1], Claudia Pedroza[2], Brian Skaug[3], Maureen Mayes[4] and Shervin Assassi[5], [1]UTHealth Houston Institute for Clinical Research & Learning Health Care, Houston, TX, [2]UTHealth Houston Institute for Clinical Research & Learning Health Care, Texas, TX, [3]UTHealth Houston Division of Rheumatology, Houston, TX, [4]UT Health Houston Division of Rheumatology, Houston, TX, [5]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinically useful biomarkers for systemic sclerosis (SSc) are needed. While obtaining samples from affected organs like the skin and lungs is invasive and cannot be done routinely, serum is collected for routine clinical care. Prior studies showed serum protein profiles align more with skin molecular changes than with peripheral blood cells (PBCs), though they analyzed a limited number of proteins. The current study characterizes longitudinal large-scale serum proteomic profile alongside global gene expression in PBCs and skin biopsies from SSc patients and healthy controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

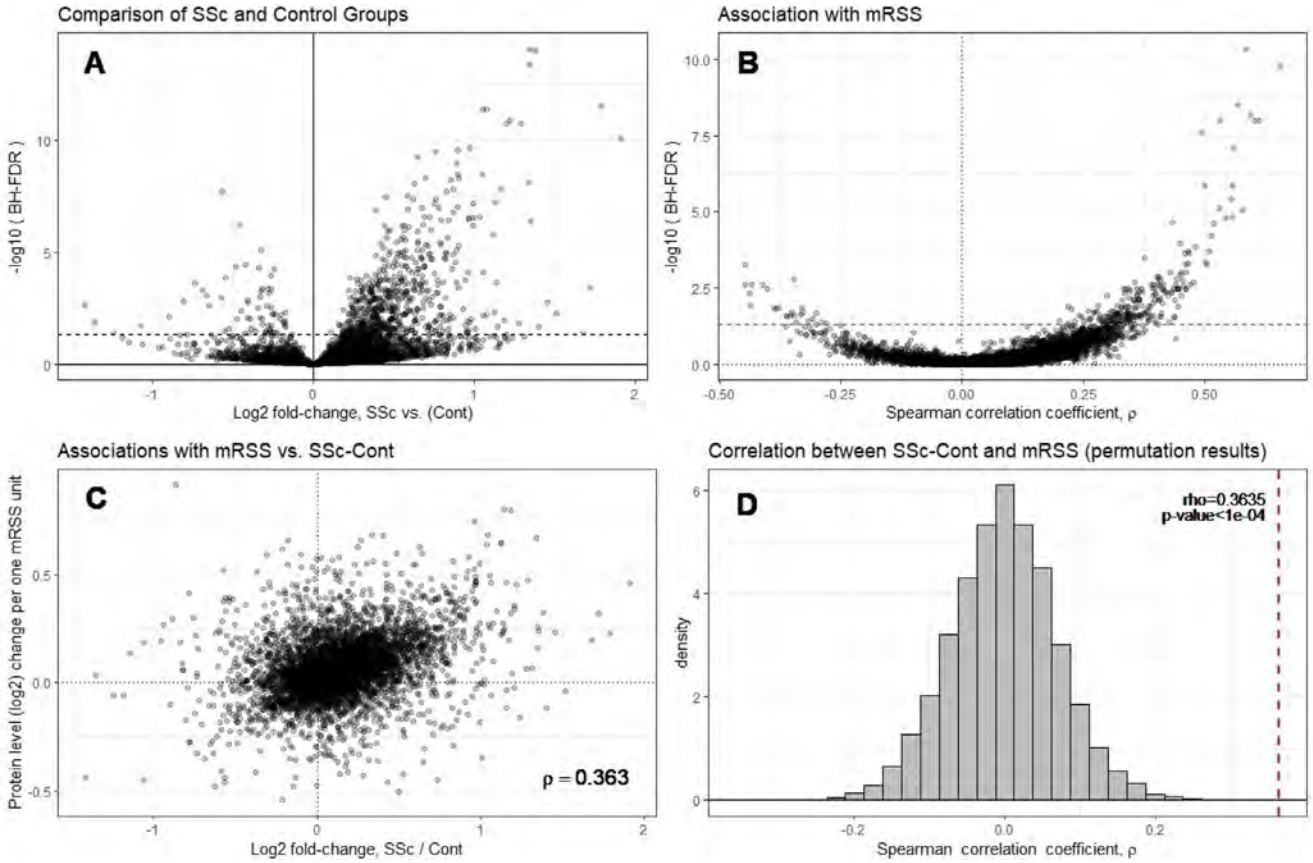


Figure 1. A) Volcano plot of differences between SSc-Controls; B) Volcano plot of the correlation between proteins and mRSS in SSc; C) Scatter plot of associations with mRSS and SSc-Controls differences; D) Permutation-based significance of correlation between differential serum protein expression (SSc vs. control) and its association with mRSS. The vertical red dashed line indicates the observed Spearman correlation coefficient based on the original sample annotation, while the histogram represents the null distribution of correlation values obtained from randomly permuted sample labels.

Methods: Three-level samples were collected from 109 SSc patients (disease duration < 6 year) and 42 matched controls. 98 SSc patients had a second sample and 47 had a third sample. 5416 serum proteins were measured using Olink Explore HT panel in serum samples. In addition, bulk global gene expression profiling was performed on concurrently collected skin and PBC RNA samples. An FDR adjusted p-value of 0.05 was considered statistically significant.

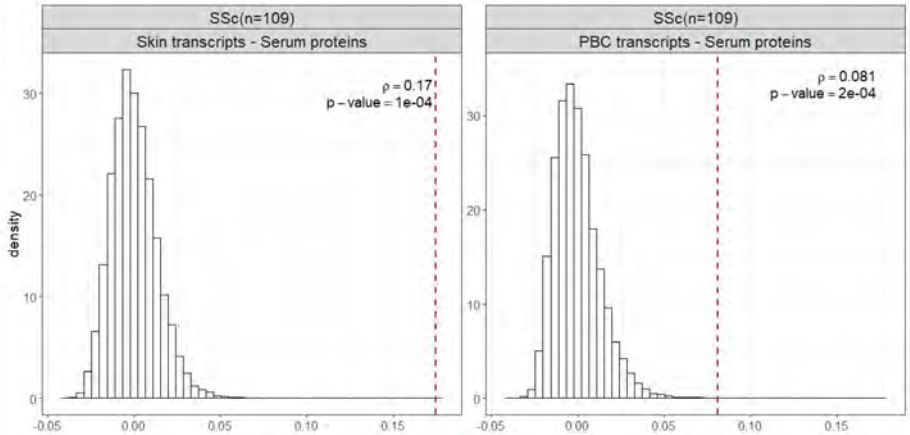


Figure 2. Concordance of between-sample similarities, measured by Spearman correlations, for pairwise comparisons of protein expression between skin and PBC. The Mantel test's observed concordance (vertical red dashed lines) was evaluated against null distributions created by random permutation of samples within each dataset.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

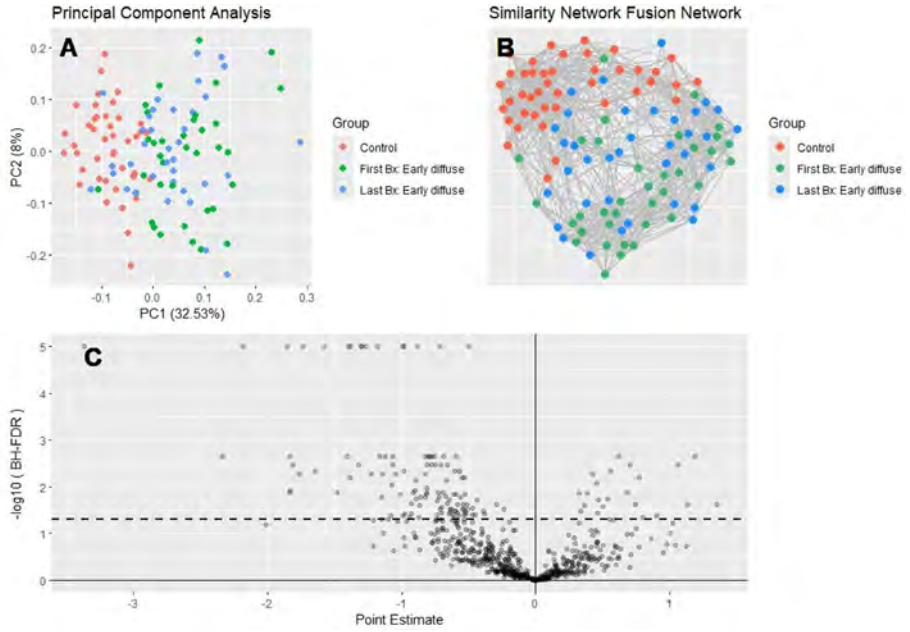


Figure 3. A) Principal component analysis (PCA) with differentially expressed serum proteins in healthy controls, first and last biopsies from early diffuse patients. B) Similarity Network Fusion (SNF) analysis of longitudinal serum protein and skin gene expression data from healthy controls and from the initial and final biopsies of early diffuse SSc patients. C) Volcano plot of serum proteins predictive of longitudinal mRSS change.

Results: The mean disease duration was 2.71 years and 61% of patients had diffuse SSc. In comparison of baseline SSc samples to controls, 697 proteins were significantly differentially expressed. Moreover, 249 proteins significantly correlated with modified Rodnan Skin Score (mRSS) (Figure 1A), of which 184 proteins were also differentially expressed in concordant direction in SSc vs control comparison (Figure 1B), indicating a significant correlation between direction of differential expression of serum proteins in SSc vs. control comparison and their association with mRSS (Figure 1C – permutation p-value < 0.0001 – Figure 1D).

The differential expression of serum proteins in SSc vs. control comparison correlated more strongly with the differential expression of corresponding transcripts in skin than in PBCs (ρ=0.17 vs ρ=0.081, Figure 2).

Similar to previously reported observations in skin, a comparison of the last to the initial serum samples in patients with early diffuse disease (n=36 – disease duration < 3 years) showed that the follow up serum samples clustered nearer to healthy controls than did initial serum samples (see the PCA analysis shown in Figure 3). Similar results were found when the skin transcriptomic and serum proteomic data were integrated using Similarity Network Fusion (SNF) analysis.

Among differentially expressed serum proteins, 141 baseline protein levels (20.1%) showed predictive significance for the rate of longitudinal change in mRSS after adjustment for disease duration and gender among patients with diffuse systemic sclerosis (Figure 3C), with 23 proteins being associated with faster increases in mRSS while 118 proteins were associated with slower increase or even a decrease in mRSS over time.

Conclusion: SSc proteomic signature reflects more closely the molecular dysregulations of skin than PBC and shows a trend towards normalization, paralleling the findings at the skin transcriptomic level. Moreover, serum proteins are associated with rate of change in mRSS over time and might aid in identifying patients with rapidly progressing skin fibrosis.

Disclosure: B. Choi: None; **C. Pedroza**: Medicem, 5; **B. Skaug**: None; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **S. Assassi**: Abb-Vie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2.

Abstract Number: 0960

Pharmaceutical Blockade of the Neonatal Fc Gamma Receptor Ameliorates Autoimmunity, Inflammation and Fibrosis in the Topoisomerase I Mouse Model of Systemic Sclerosis

Cuong Tran-Manh[1], Thuong Trinh-Minh[2], Christoph Liebel[3], Bas van der Woning[4], Piotr Zabrocki[5] and Jörg Distler[6], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Nordrhein-Westfalen, Germany, [2]Clinic for Rheumatology University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University, Dösseldorf, Germany; Hiller Research Center, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University, Dösseldorf, Nordrhein-Westfalen, Germany, [3]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [4]argenx BV, Boston, MA, [5]argenx, Ghent, Belgium, [6]University Hospital Duesseldorf and HHU, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: SSc is a rare, chronic, systemic autoimmune rheumatic disease characterized by progressive skin and internal organ fibrosis, severe vasculopathy and immune dysregulation with production of specific autoantibodies. SSc manifestations such as skin thickening, interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), and cardiac and gastrointestinal complications significantly impact patient quality of life. SSc pathophysiology is complex, but the association between autoantibodies and disease subtype, disease course, and occurrence of specific disease manifestations suggests a role in SSc pathophysiology. Moreover, several different autoantibodies have been reported that can directly

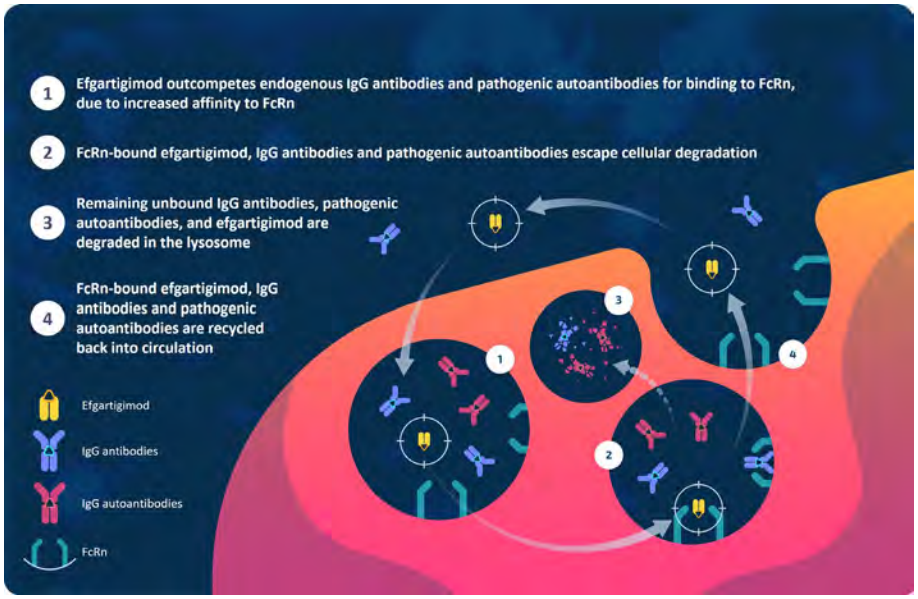


Figure 1. Mechanism of action of efgartigimod against IgG-mediated fibrosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

promote inflammation and/or fibrosis. Currently approved therapies are at best slowing down disease progression, underscoring a high medical need for novel therapies.

Methods: Efgartigimod, a human IgG1-derived Fc fragment, is engineered to block the neonatal Fc gamma receptor (FcRn), enhancing IgG degradation and reducing circulating disease-causing IgG autoantibodies (Figure 1). Efgartigimod is approved for the treatment of generalized myasthenia gravis and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). We evaluated the effects of FcRn blockade in a topoisomerase I (topo I)-induced mouse model of SSc, which recapitulates the autoimmune, inflammatory, and fibrotic features of the disease.

Results: Treatment with the murine homologue of efgartigimod (an IgG-derived Fc fragment targeting mouse FcRn) was well tolerated. Both prophylactic (treatment started before the onset of immunization) and therapeutic (treatment 2 weeks after immunization with human topo I-antigen) administration of the murine homologue of efgartigimod significantly ameliorated dermal fibrosis and interstitial lung disease as evidenced by reduced dermal thickness, Ashcroft scores, myofibroblast number, and collagen content. Notably, the antifibrotic effects were comparable to those of nintedanib. Gene expression analysis in mouse skin revealed regulatory effects of the murine homologue of efgartigimod on inflammatory/autoimmune and fibrotic signaling pathways with inhibitory effects on CCL-chemokines, interleukins, S100A4, and on transforming growth factor β and JAK/STAT signaling. In addition, treatment with the FcRn blocker improved gastrointestinal transit that was delayed in mice immunized with topo I.

Conclusion: These findings highlight that, in a murine model of SSc, FcRn blockade may have potential to simultaneously target the autoimmune, inflammatory and fibrotic features of SSc and highlight the potential of autoantibody-reducing therapies as disease-modifying approaches in this disease. Indeed, a randomized, controlled phase II trial with efgartigimod in SSc is currently ongoing.

Disclosure: C. Tran-Manh: AgenX, 6; **T. Trinh-Minh**: 4D Science GmbH, 3, ArgenX, 6; **C. Liebel**: 4D Science, 3; **B. van der Woning**: argenx, 3, 11; **P. Zabrocki**: ARGENX, 3, 10; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6.

Abstract Number: 0961

Retinoic acid-related orphan receptor-α: A novel upstream regulator of Hippo signaling and potential therapeutic target in fibrosis

Cuong Tran-Manh[1], Thuong Trinh-Minh[2], Christoph Liebel[3] and Jörg Distler[4], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Nordrhein-Westfalen, Germany, [2]Clinic for Rheumatology University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University, Dösseldorf, Germany; Hiller Research Center, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University, Dösseldorf, Nordrhein-Westfalen, Germany, [3]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [4]University Hospital Duesseldorf and HHU, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Retinoic acid-related orphan receptor-α (RORα) is a nuclear transcription factor implicated in immune regulation, circadian rhythm, and metabolism. However, its role in fibrotic diseases such as systemic sclerosis (SSc) remains undefined. Given that aberrant fibroblast activation and extracellular matrix deposition are hallmarks of fibrotic tissue remodeling, we investigated the mechanistic involvement of RORα in fibrogenesis and evaluated its therapeutic potential as a modulator of the Hippo signaling pathway.

Methods: In human samples (SSc and other fibrotic conditions) and in mouse fibrosis models, RORα expression was measured by quantitative PCR, Western blot, and immunofluorescence. RORα was silenced in cultured fibroblasts (siRNA) and in RORα-deficient mice to evaluate its function in fibrosis. The selective RORα inverse agonist SR3335 was used to pharmacologically inhibit RORα in three fibrosis models: bleomycin-induced skin and lung fibrosis, and CCl4-induced liver fibrosis. Transcriptomic profiling (RNA-Seq) identified RORα-dependent genes and signaling pathways.

Results: RORα expression was elevated in fibroblasts from various fibrotic diseases and organs, including hypertrophic scars, fibrotic skin, lungs and liver, compared to non-fibrotic controls. Increased RORα expression was also observed in murine SSc models. RORα knockdown in fibroblasts attenuated TGFβ-induced myofibroblast differentiation and collagen production. Similarly, pharmacologic inhibition of RORα with SR3335 reduced TGFβ-driven myofibroblast activation and extracellular matrix production (as indicated by decreased α-smooth muscle actin, type I collagen, and fibronectin) in human fibroblasts. In vivo, SR3335 treatment significantly ameliorated fibrosis in all three mouse models. RNA-Seq showed that RORα regulates a profibrotic gene network, including *COL1A1*, *ACTA2* (αSMA), *CTGF*, and *PAI-1*. Mechanistically, RORα modulates the Hippo signaling pathway, a key regulator of fibroblast activation. SR3335 abrogated TGFβ-induced Hippo reporter activity and prevented YAP/TAZ upregulation and nuclear translocation in fibroblasts.

Conclusion: RORα expression was upregulated in fibroblasts from fibrotic human tissues (skin, lung, and liver, including samples from SSc patients) and in fibrotic mouse models, compared to controls. RORα knockdown in fibroblasts attenuated TGFβ-induced myofibroblast differentiation and collagen production. Similarly, pharmacologic inhibition of RORα with SR3335 reduced TGFβ-driven myofibroblast activation and extracellular matrix production (as indicated by decreased α-smooth muscle actin, type I collagen, and fibronectin) in human fibroblasts. In vivo, SR3335 treatment significantly ameliorated fibrosis in all three mouse models. RNA-Seq showed that RORα regulates a profibrotic gene network, including COL1A1, ACTA2 (αSMA), CTGF, and PAI-1. Mechanistically, RORα modulates the Hippo signaling pathway, a key regulator of fibroblast activation. SR3335 abrogated TGFβ-induced Hippo reporter activity and prevented YAP/TAZ upregulation and nuclear translocation in fibroblasts.

Disclosure: C. Tran-Manh: AgenX, 6; **T. Trinh-Minh**: 4D Science GmbH, 3, ArgenX, 6; **C. Liebel**: 4D Science, 3; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6.

Abstract Number: 0962

Spatial Proteomics Analysis of the organization of tertiary lymphoid structures in Systemic Sclerosis Skin

Dennis Bleck[1], Karen Drechsel[2], Tim Filla[3], Yi-Nan Li[4], Andrea-Hermina Györfi[5], Alexandru-Emil Matei[6] and Jörg Distler[7], [1]University Hospital Dösseldorf, Department of Rheumatology, Hiller Research Center, Dösseldorf, Nordrhein-Westfalen, Germany, [2]University Hospital Düsseldorf, Department of Rheumatology, Hiller Research center, Düsseldorf, Nordrhein-Westfalen, Germany, [3]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University., Düsseldorf, Germany, [4]University Hospital of Dösseldorf, Dösseldorf, Nordrhein-Westfalen, Germany, [5]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [6]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany, [7]University Hospital Duesseldorf and HHU, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Sclerosis (SSc) is a rare autoimmune connective tissue disease and presents a significant medical challenge. It is characterized by fibrotic tissue remodeling, along with microvascular alterations and autoimmunity with the formation of specific autoantibodies. CD19- and BCMA-targeted B cell depletion therapies such as CAR-T cells or bispecific T cell engaging antibodies demonstrated profound efficacy for the treatment of SSc patients, including those who were previously unresponsive to multiple therapies. The mechanisms underlying B cell activation in target tissues of SSc patients are largely unknown. Our study focuses on characterizing immune cell infiltration and the cellular microenvironment in SSc skin, with a particular interest in the formation of tertiary lymphoid structures.

Methods: Skin punch biopsies from SSc patients were formalin-fixed, paraffin-embedded, and sectioned. Sections of 118 patients with SSc were screened by hematoxylin and eosin (H&E) histological staining for the presence of leukocyte aggregates or tertiary lymphoid structures. Ten representative samples containing tertiary lymphoid structures, six samples negative for lymphoid infiltrates and five samples derived from normal healthy skin were stained using metal isotope labeled antibodies targeting a panel of proteins of interest including markers of immune and stromal cell populations. The staining protocol was established using human tonsil sections. Imaging Mass Cytometry (IMC) was performed on the Hyperion platform (Standard BioTools) to collect data on the spatial distribution of protein targets and co-localization of cell populations within the skin tissue.

Results: Tertiary lymphoid structures were detected in 14 out of 118 skin samples (12%) (Figure 1). Large, diffuse lymphoid infiltrates were recognized in 19 Sections (16%) while 13 sections (11%) were negative for lymphoid infiltrates.

We were able to identify multiple stromal and immune cell clusters using our IMC panel with specific phenotypes of fibroblasts and endothelial cells in tertiary lymphoid structures. Immune cells were found to infiltrate defined stromal cell niches in the skin. Neighborhood analyses demonstrated context-specific interactions of leukocytes with stromal cells in these

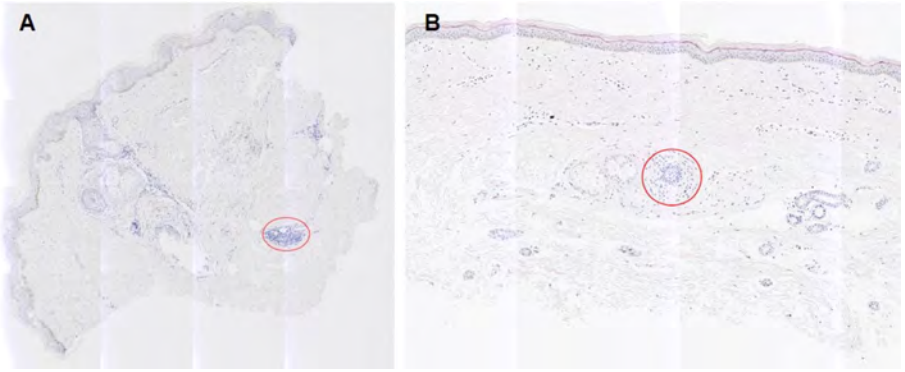


Figure 1: H&E stainings of tertiary lymphoid structures and large, diffuse lymphoid infiltrates in SSc skin sections. Exemplary images of tertiary lymphoid structures (A) and large, diffuse lymphoid infiltrates (B) in H&E stainings of SSc skin sections.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

tertiary lymphoid structures. We will further analyze the demonstrated specific cellular proximity and co-localization, with a focus on mechanisms potentially involved in immune activation and inflammation in SSc.

Conclusion: Tertiary lymphoid structures and large, diffuse lymphoid infiltrates were detected in nearly one third of the SSc samples that were screened (28%), while only 11% of samples were negative for infiltrates. Using a state-of-the-art technique such as IMC, we provide first data on the cellular composition, the topographical organization and the cellular interactions with tertiary lymphoid structures in SSc. These data may enable targeted inhibition of the formation of these structures and thereby interference with tissue resident immune responses in SSc.

Disclosure: D. Bleck: None; **K. Drechsel**: None; **T. Filla**: None; **Y. Li**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **A. Matei**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6.

Abstract Number: 0963

Increased expression of M2 pro-fibrotic markers in circulating monocytes and cultured monocyte-derived macrophages from systemic sclerosis patients with progressive interstitial lung disease (ILD)

Vanessa Smith[1], Stefano Soldano[2], Rosanna Campitiello[3], **Emanuele Gotelli**[3], Paola Montagna[4], Tamara Vojinovic[4], Sabrina Paolino[2], Carmen Pizzorni[2], Alberto Sulli[2] and Maurizio Cutolo[5], [1]Ghent University Hospital, Gent, Belgium, [2]University of Genoa, Genova, Italy, [3]University of Genoa, Genoa, Liguria, Italy, [4]University of Genoa, Genova, [5]University of Genova, Genova, Italy

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: In the complex pathogenesis of systemic sclerosis (SSc), macrophages are mainly involved in mechanism of progressive tissue fibrosis of skin and internal organs, particularly the lung[1,2]. Alternatively activated macrophages (M2) seem to drive the process through the synthesis of profibrotic molecules[3]. The presence on M2 macrophages of pro-fibrotic markers has been previously observed in ILD-SSc lung samples (i.e. presence of mixed M1/M2 cells showing TLR4)[3]. To characterize phenotype and functional M2 markers in circulating monocytes and cultured monocyte-derived macrophages (MDMs) obtained from SSc patients (pts) with progressive ILD (prog-ILD), versus non-progressive ILD (no-prog-ILD), and without ILD (no-ILD).

Methods: A total of 56 SSc pts, diagnosed according to the 2013 ACR/EULAR criteria, and 20 age-matched healthy controls (HC) were enrolled after providing informed consent. A subgroup of 37 SSc pts (10 with prog-ILD, 14 with no-prog-ILD, and 13 no-ILD; mean age 65±13 years) and 20 HC were assessed for circulating monocytes expressing M2 markers (CD204, CD163, CD206) and the M1 marker toll-like receptor-4 (TLR4) using flow cytometry. Monocyte-derived macrophages (MDMs) obtained from 29 SSc pts (13 with prog-ILD, 10 with no-prog-ILD and 6 no-ILD; mean age 64±14 years) and 5 HC were analyzed for gene expression (real-time PCR) and protein levels (Western blot) of these markers, along with Mer tyrosine kinase (MerTK) and transforming growth factor-β1 (TGF-β1) (ELISA). Statistical analyses were carried out using non-parametric tests.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Prog-ILD SSc pts showed a higher percentage of hybrid (M1/M2) circulating TLR4+CD204+CD206+CD163+-monocytes compared to no-prog-ILD and significantly higher compared to no-ILD SSc pts ($p< 0.05$). Cultured MDMs from prog-ILD SSc pts showed a gene expression and protein synthesis significantly higher for TGF- β1 ($p< 0.05$) and higher (not significant) for MerTK and CD206 compared to MDMs from no-prog-ILD SSc pts. The gene expression of TGF- β1 and TLR4, as well as the synthesis of TGF- β1, CD206, CD163, and MerTK were significantly increased in cultured MDMs from prog-ILD SSc compared to MDMs from no-ILD SSc pts (TGF- β1, TLR4 and M2 markers: $p< 0.05$; MerTK: $p< 0.01$).

Conclusion: The study shows that ILD-SSc pts are characterized by a significant increased percentage of circulating hybrid TLR4+M2 monocytes, and the related cultured MDMs express high levels of MerTK and TGF-β1 selectively in pts with prog-ILD. The detection of increased circulating TLR4+M2 monocytes and MerTK on MDMs from ILD-SSc pts is currently under investigation since might represent a potential solublebiomarker of progressive lung fibrosis.

References:

1. Volkmann ER, et al Systemic sclerosis. Lancet. 2023 Jan 28;401(10373):304-318.
2. Cutolo M, et al. Pathophysiology of systemic sclerosis: current understanding and new insights. Expert Rev Clin Immunol. 2019 Jul;15(7):753-764.
3. Gotelli E, et al. Prevalence of hybrid TLR4+M2 monocytes/macrophages in peripheral blood and lung of systemic sclerosis pts with interstitial lung disease. Front Immunol. 2024 Nov 20;15:1488867.

Disclosure: V. Smith: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **S. Soldano**: None; **R. Campitiello**: None; **E. Gotelli**: None; **P. Montagna**: None; **T. Vojinovic**: None; **S. Paolino**: None; **C. Pizzorni**: None; **A. Sulli**: None; **M. Cutolo**: None.

Abstract Number: 0964

A Single-cell Atlas Reveals Dermal Endothelial Heterogeneity and Disease-specific Pathways in Autoimmune Disorders

Haoyu Pan[1], **Jinyi Qian**[1], Shuyi Yu[1], Zhixia Yang[1], Jason S. Knight[2], Eliza Tsou[3] and Hui Shi[4], [1]Department of Rheumatology and Immunology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [2]University of Michigan, Ann Arbor, MI, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan; Ann Arbor, Michigan, USA., Ann Arbor, MI, [4]Shanghai Jiaotong University Affiliated Ruijin Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune conditions with skin involvement, including scleroderma (SSc), antiphospholipid syndrome (APS), systemic lupus erythematosus (SLE) and psoriasis (PSO), involve intricate interactions between immune cells and the vasculature, with endothelial cells (ECs) playing a critical role in disease pathogenesis. To elucidate the diverse functional roles of ECs in these conditions, we constructed a comprehensive single-cell atlas by integrating single-cell RNA sequencing (scRNA-seq) data from affected and healthy skin biopsies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

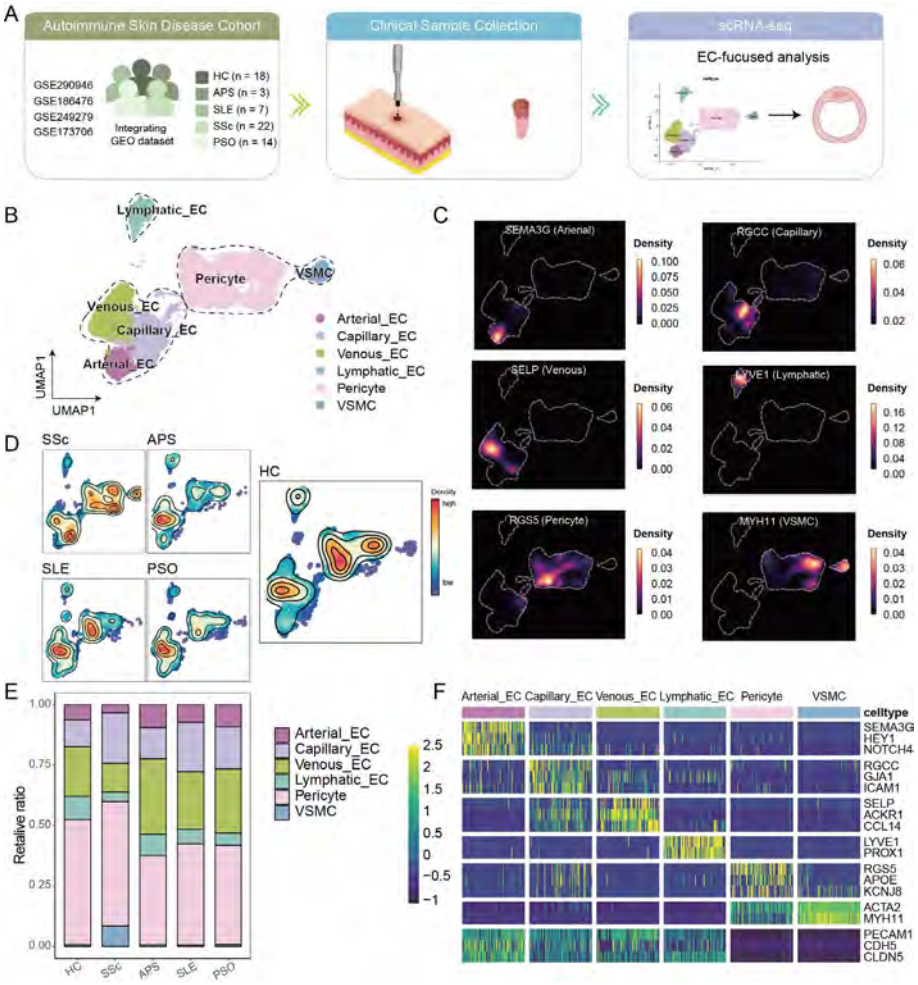


Figure 1. Cellular composition and endothelial subtypes across autoimmune skin diseases. (A) Schematic overview of the study design integrating single-cell RNA sequencing data from autoimmune skin diseases including APS, SLE, PSO, and SSc, along with healthy controls. (B) UMAP visualization of 23,410 endothelial and stromal cells from skin biopsies, annotated into arterial, venous, capillary, and lymphatic ECs, pericytes, and vascular smooth muscle cells (VSMCs). (C) Expression density of canonical markers confirming subtype identities, such as SEMA3G (arterial EC), RGCC (capillary EC), SELP (venous EC), LYVE1 (lymphatic EC), MYH11 (VSMC), and RGS5 (pericyte). (D, E) Relative abundance of vascular and stromal subtypes across disease groups. (F) Heatmap showing the averaged expression of key markers across identified cell types.

Methods: Skin biopsies from patients were analyzed using 10x Genomics scRNA-seq. Publicly available datasets from SSc (GSE249279), APS (GSE290946), SLE (GSE186476), PSO (GSE173706), and healthy controls (GSE249279 and GSE290946), generated using the same platform, were integrated **(Figure 1A)**. Skin biopsies from active skin of patients were analyzed using 10x Genomics scRNA-seq. Cell identities, gene expression profiles, and pathway activities were analyzed across endothelial and stromal populations.

Results: We profiled 23,410 endothelial and stromal cells, identifying arterial, venous, capillary, and lymphatic ECs, as well as pericytes and vascular smooth muscle cells (VSMCs) from all scRNA-seq datasets. Arterial and venous ECs were significantly reduced in SSc, while VSMCs were markedly increased. APS samples showed an expansion of arterial, capillary and venous ECs, whereas SLE and PSO exhibited cellular compositions similar to healthy controls (**Figure 1**). Pathway enrichment analysis of EC gene expression revealed both shared and disease-specific programs **(Figure 2)**. Across autoimmune conditions, common signatures relative to healthy controls included NF-κB signaling, leukocyte adhesion, and antigen presentation. APS-derived ECs were further enriched for antigen presentation, oxidized LDL response, leukocyte adhesion, and T cell activation pathways. SLE samples demonstrated prominent type I interferon responses, while SSc samples exhibited strong enrichment of intrinsic apoptotic pathways. No dominant pathway activation was observed in PSO.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

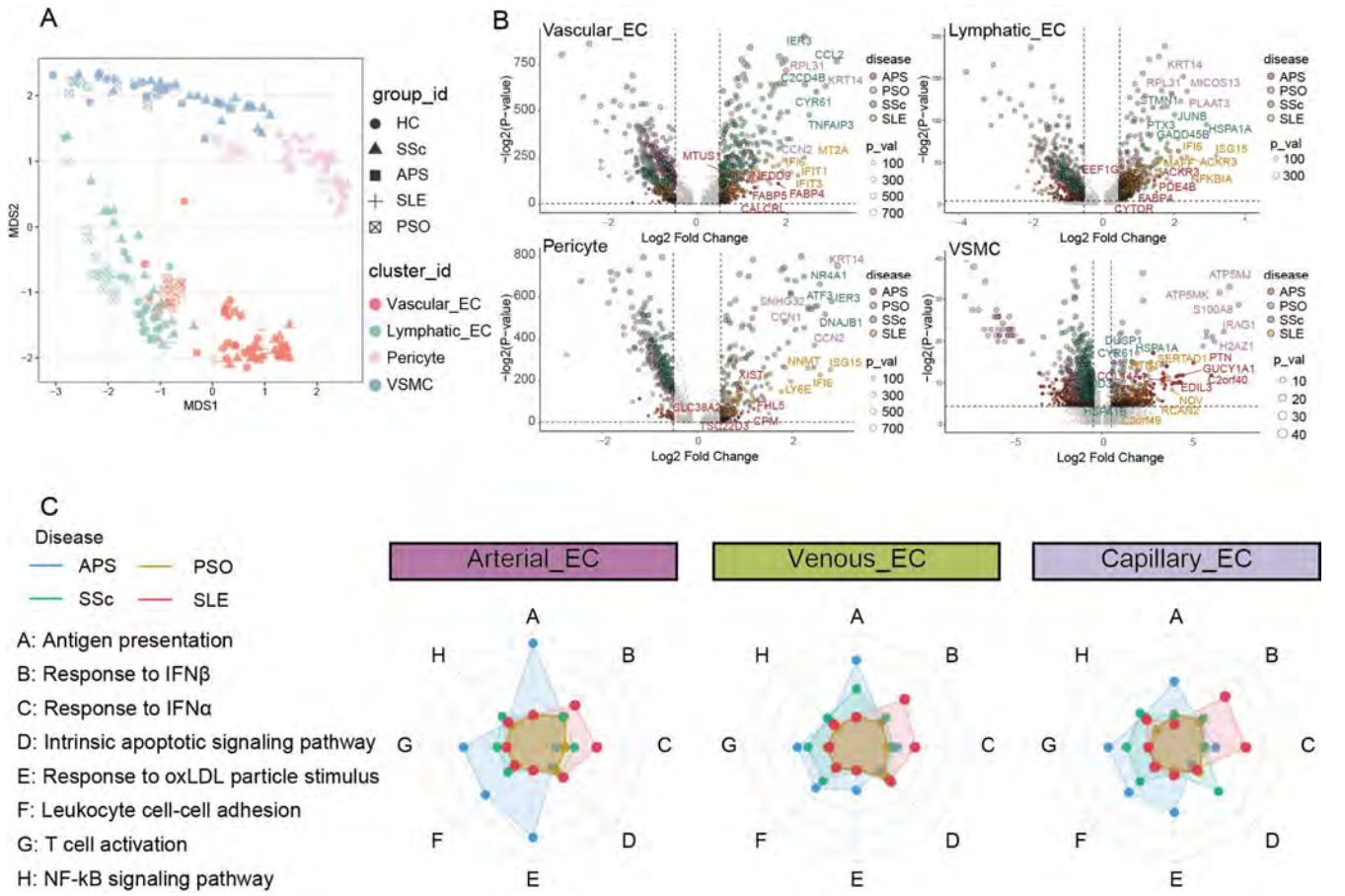


Figure 2. Transcriptional and pathway-level profiling of endothelial and stromal cells across autoimmune skin diseases. (A) Multidimensional scaling (MDS) plots of endothelial and stromal cell subsets showing global transcriptomic distribution across APS, SLE, PSO, and SSc. (B) Volcano plots showing differentially expressed genes in vascular ECs, pericytes, VSMCs, and lymphatic ECs across disease groups. (C) Radar plots depicting pathway enrichment scores of arterial, venous, and capillary ECs across eight biological processes.

Deeper subclustering of vascular ECs defined seven endothelial subtypes, including SENA3G+ arterial ECs, RGCC+ capillary ECs, TLL1^{+} venous ECs, hypoxia-associated ECs, EndoMT, cycling ECs, and a previously undefined subset IL6^{+} venous ECs (**Figure 3**). IL6^{+} and EndoMT ECs were enriched in SSc and expressed pro-inflammatory, senescence-associated, and matrix remodeling genes. SLE and PSO had elevated IL6+ EC and cycling EC populations, potentially driving immune dysregulation and vascular proliferation linked to systemic organ damage. APS was marked by abundant EndoMT+ ECs, suggesting endothelial plasticity. Senescence and EndoMT scores were highest in SSc, followed by APS and SLE, and minimal in PSO.

Conclusion: This single-cell atlas defines dermal endothelial heterogeneity across autoimmune diseases. Notably, we identified a novel IL6^{+} EC subset enriched in SSc with pro-inflammatory and senescence signatures, and revealed distinct EC programs across diseases. These findings highlight EC subtype dynamics as potential contributors to immune dysregulation and fibrotic remodeling.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

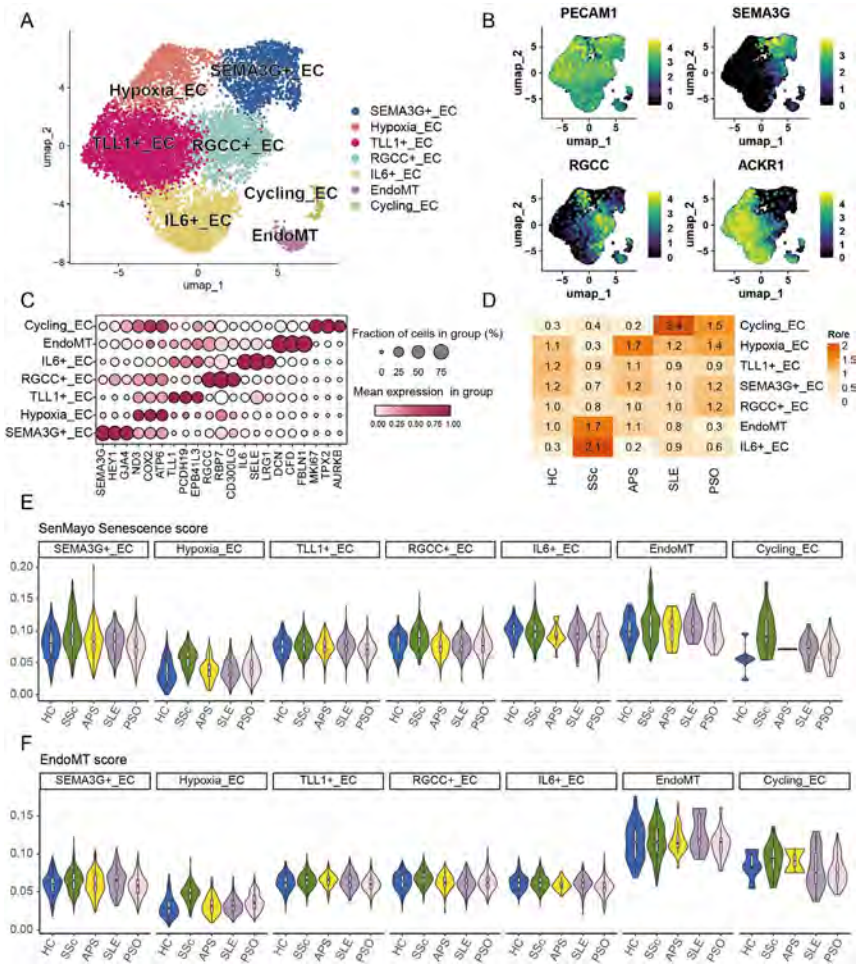


Figure 3. Endothelial subcluster identification and their distribution across autoimmune skin diseases. (A) UMAP projection of endothelial cells showing seven transcriptionally distinct subclusters: SEMA3G$^+$ ECs, RGCC$^+$ ECs, TLL1$^+$ ECs, IL6$^+$ ECs, hypoxia-associated ECs, EndoMT ECs, and cycling ECs. (B) Spatial expression of canonical endothelial and subcluster marker genes, including PECAM1, SEMA3G, RGCC, and ACKR1. (C) Dot plot displaying average expression (color) and proportion of cells (size) for representative marker genes across endothelial subclusters. (D) Disease preference (HC, SSc, APS, SLE, PSO) of each cluster estimated by the STARTRAC-dist index. Ro/e denotes the ratio of observed to expected cell number. (E) Distribution of senescence scores across endothelial subclusters and disease conditions. (F) Distribution of EndoMT scores across endothelial subclusters and disease groups.

Disclosure: H. Pan: None; **J. Qian**: None; **S. Yu**: None; **Z. Yang**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **E. Tsou**: None; **H. Shi**: None.

Abstract Number: 0965

Inhibition of Nicotinamide N-Methyltransferase Reverses Fibroblast Activation via Epigenetic and Metabolic Remodeling in Systemic Sclerosis

Kamal Saba[1], Rong Huang[2], Priyanka Verma[1], M Asif Amin[1] and John Varga[1], [1]University of Michigan, Ann Arbor, MI, [2]Purdue University, West Lafayette, IN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic sclerosis (SSc) is characterized by progressive fibrosis driven by sustained fibroblast activation and senescence. Nicotinamide N-methyltransferase (NNMT), a SAM-dependent enzyme, is upregulated in SSc and contributes to both NAD^+ depletion and methylation imbalance. This study evaluates the therapeutic impact of a novel bisubstrate NNMT inhibitor, II559, in modulating fibroblast activation and reversing metabolic-epigenetic dysfunction in SSc.

Methods: We utilized TGF-β1 to induce fibroblast activation in healthy dermal fibroblasts and evaluated basal activity in primary SSc fibroblasts. Cells were treated with 30 μM II559 for 48–72 hours. Gene and protein expression of fibrosis markers (COL1A1, α-SMA, Fibronectin), senescence markers (p16, p21), and inflammatory cytokines (IL-6, IL-8) were assessed by qPCR, Western blot, and immunofluorescence. Epigenetic status was evaluated using H3K27me3 staining. 1MNA levels were measured to assess NNMT enzymatic activity. In vivo, a bleomycin-induced mouse model of dermal fibrosis was treated with II559 (10 mg/kg, intraperitoneally) for 28 days. Hydroxyproline, NAD^+, SAM, and SAH levels were quantified in skin tissues.

Results: TGF-β1 increased NNMT, fibrotic markers, inflammatory cytokines (Fig 1A,2A,2C), and reduced H3K27me3 (Fig 2C) in healthy fibroblasts; all were reversed by II559. In SSc fibroblasts, II559 downregulated p16/p21 (Fig 1B) and ECM proteins (Fig 1A), and restored repressive H3K27me3 marks. 1MNA levels were elevated with TGF-β1 and

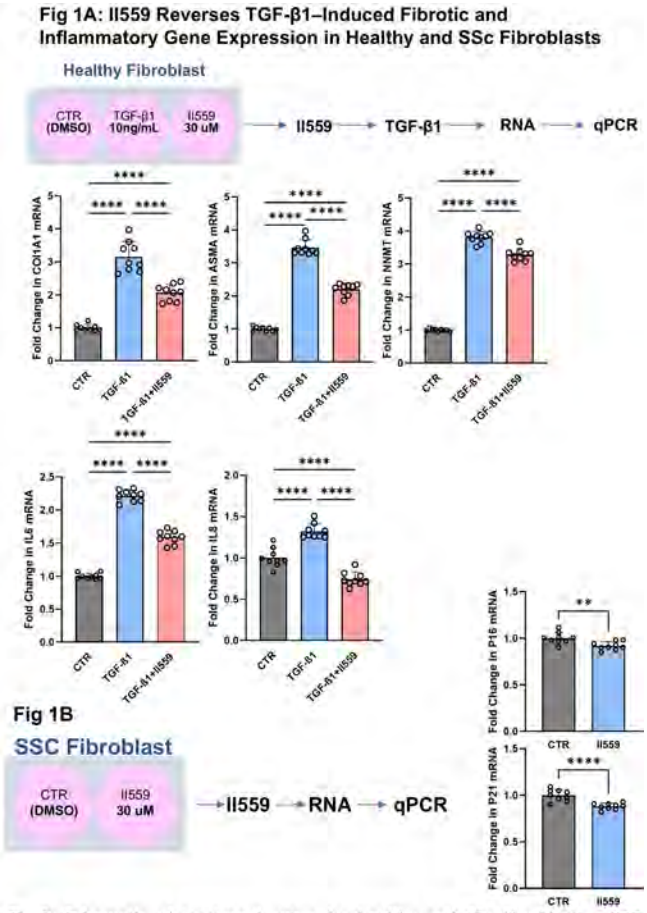


Fig 1: Schematic of treatment setup for healthy and SSc fibroblasts. qPCR showing that II559 (30 μM) attenuates TGF-β1–induced expression of COL1A1, α-SMA, IL-6, IL-8, and NNMT in healthy fibroblasts, and reduces p16 and p21 in SSc fibroblasts. Data shown as mean ± SEM.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

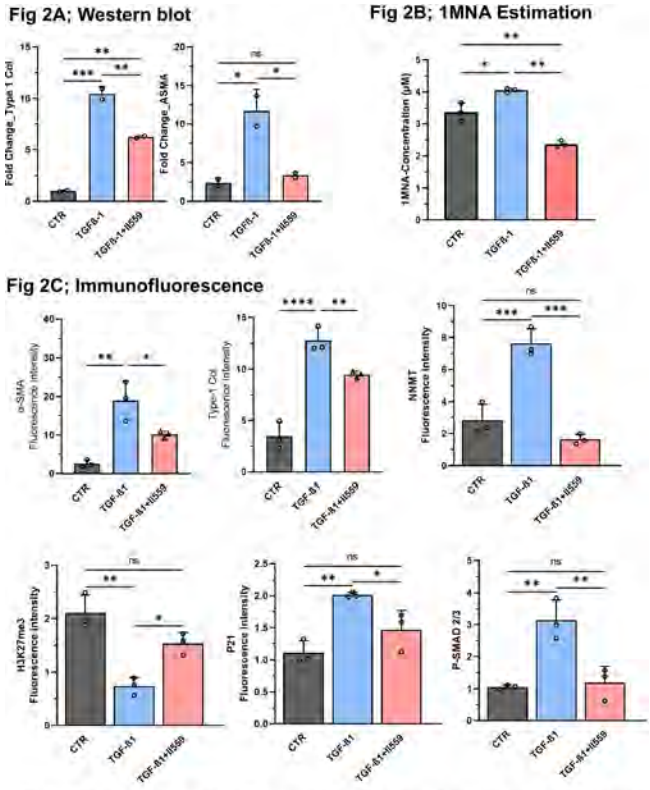


Fig 2: (A) Western blot and **(C)** Immunofluorescence showing downregulation of COL1A1, α-SMA, NNMT P21 P-SMAD2/3 in TGF-β1–treated fibroblasts upon II559 treatment. Immunofluorescence shows that TGF-β1 reduces H3K27me3, a repressive histone mark; II559 restores its levels, indicating epigenetic re-silencing of fibrotic gene programs. **(B)** II559 suppresses NNMT enzymatic activity elevated by TGF-β1. . Data shown as mean ± SEM.

suppressed with II559 (Fig 2B, 3B), confirming target engagement. In vivo, II559 reduced skin fibrosis, hydroxyproline content, and restored NAD^+ and SAM without altering SAH levels (Fig 3A), suggesting recovery of redox and methylation potential.

Conclusion: NNMT acts as a metabolic-epigenetic driver of fibrosis in SSc. II559 reverses fibroblast activation by restoring NAD^+ and histone methylation balance, suppressing pro-fibrotic and inflammatory pathways. These findings support NNMT inhibition as a promising therapeutic strategy in SSc and justify further investigation through transcriptomic and chromatin accessibility profiling.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig 3A

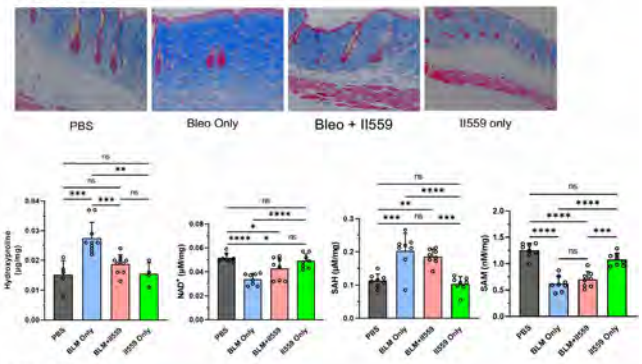


Fig 3B

Fig 3(A) Masson's trichrome staining shows increased dermal collagen in bleomycin-treated mice, which is reduced with II559 treatment. **(B)** Quantification reveals that II559 lowers hydroxyproline, restores NAD^+ and SAM levels, while SAH remains unchanged. **(C)** Summary table of molecular and metabolic markers altered in fibrosis and normalized by II559 across in vitro and in vivo models.

Disclosure: K. Saba: None; **R. Huang**: None; **P. Verma**: None; **M. Amin**: None; **J. Varga**: None.

Abstract Number: 0966

Integrated Bulk and Single Cell Analysis Confirms Differential Upregulation of the Proton Sensing Receptor GPR68 in Systemic Sclerosis Across Disease Stage and Subset

Kristina Clark[1], Xu Shiwen[2], Xue Li[2], Voon H. Ong[3] and Christopher Denton[4], [1]Kennedy Institute of Rheumatology, University of Oxford, London, United Kingdom, [2]University College London, London, United Kingdom, [3]Division of Medicine, Centre for Rheumatology, University College London, London, United Kingdom, [4]University College London, UK, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

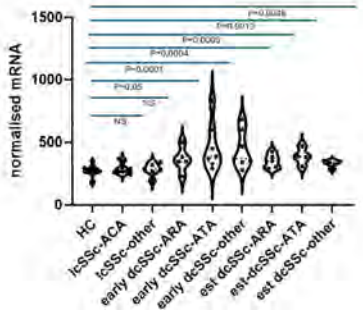
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1 GPR68 mRNA expression in whole skin



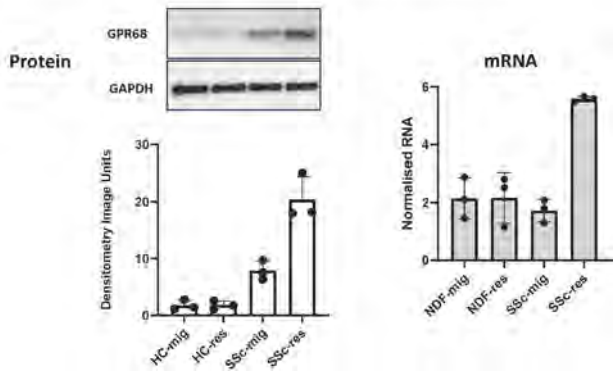
Background/Purpose: The cell surface protein GPR68 (ovarian cancer G protein-coupled receptor 1, OGR1) is a proton-sensing G-protein-coupled receptor (GPCR) that responds to extracellular acidity and regulates a variety of cellular functions. It has been associated with fibrosis and a recent phase 2 clinical trial of FT011 (asengeprast), an orally active small molecule inhibitor GPR68 suggested potential clinical benefit in diffuse cutaneous (dc) systemic sclerosis (SSc). We have explored differential expression of GPR68 in SSc skin and in pathogenic skin fibroblast subpopulations.

Methods: Normalised expression of GPR68 mRNA was explored in a well characterised cohort of SSc and control skin biopsies (n=68) comparing SSc stage, skin autoantibody and subset (ATA=anti-topoisomerase-1; ARA=anti-RNA polymerase 3; ACA=anti-centromere). Protein and RNA expression were examined in cultured SSc or control skin fibroblasts including migratory and non-migratory cells (n=3 each). Non-migratory "resident" fibroblasts have recently been characterised as a novel population strongly implicated in pathogenesis of SSc. Single cell analysis was used to further define GPR68 expression in fibroblasts and other cell types in SSc (n=12) and control (n=3) skin.

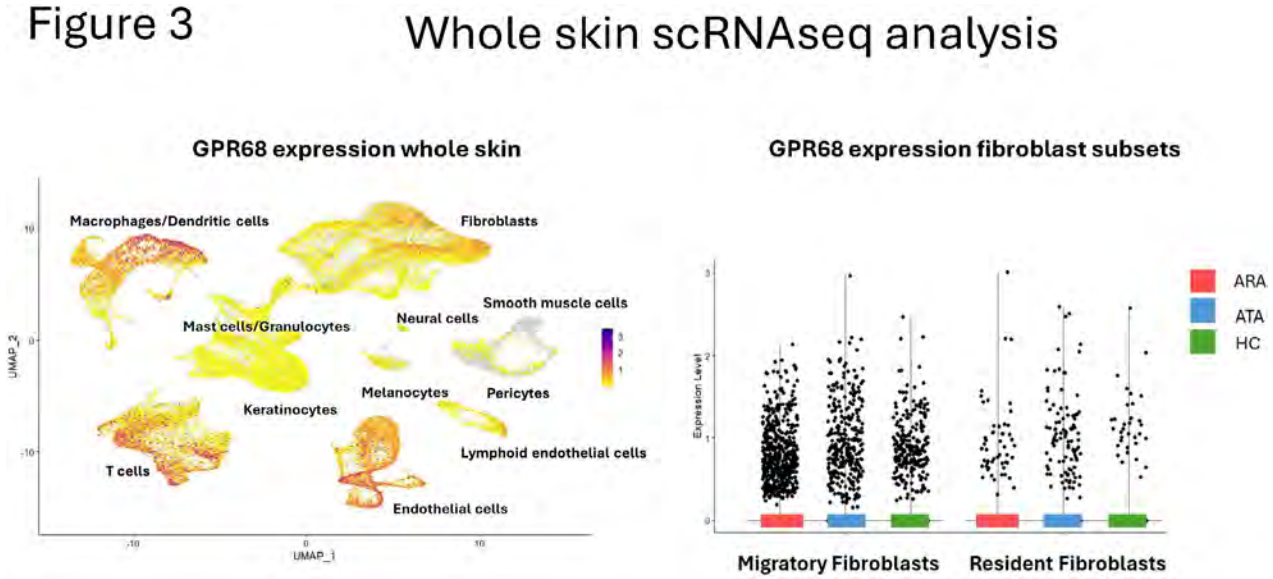
Results: There was increased expression of GPR68 RNA in skin of SSc that was most apparent in dcSSc (mean (SD) HC 268 (41) n=17; lcSSc 286 (45) n=15; dcSSc 396 (126) n=33). Further analysis suggested upregulation was greater in early (428 (153) n=19) than established (353 (53) n=14) dcSSc. ANA subgroups also showed differential elevation of GPR68 with highest levels in ATA+ dcSSc (436 (157) n=11), lower levels in ARA+ dcSSc (355 (75) n=10). Differential expression across subgroups is summarised in **Figure 1**.

GPR68 protein and mRNA were increased in cultured SSc dermal fibroblasts and highest in non-migratory cells in SSc compared with healthy control strains in bulk fibroblast culture (**Figure 2**). Single cell RNA analysis of skin confirmed expression of GPR68 in multiple relevant cell types including fibroblasts, endothelial cells, macrophages and T cells. Re-clustered fibroblast scRNAseq data suggested stage and ANA subset differences concordant with bulk RNAseq (**Figure 3**). Notably,

Figure 2 Fibroblast GPR68 Expression



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



GPR68 had greatest single cell expression in migratory fibroblasts for ARA+ and resident fibroblasts in ATA+ dcSSc skin suggesting differences across ANA subgroups.

Conclusion: We have demonstrated upregulation of GPR68 in SSc and increased expression in pathogenic fibroblast populations including the recently identified non-migratory "resident" fibroblast subpopulation that may be a key paracrine regulator of skin fibrosis. Our findings support the rationale for targeting GPR68 as a treatment for SSc fibrosis and help define the stage and subset of patients most likely to benefit from treatment.

Disclosure: k. clark: None; **X. Shiwen**: None; **X. Li**: None; **V. Ong**: Boehringer-Ingelheim, 6; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2.

Abstract Number: 0967

Single-Cell RNA Sequencing Reveals a Prominent Pro-Inflammatory Gene Signature of Dermal Fibroblasts in Pre-Stages of SSc

Lumeng Li[1], Elena Pachera[2], Rucsandra Dobrota[3], Sinziana Muraru[4], Kristina Bürki[3], Carina Mihai[5], Muriel Elhai[6], Laura Much[7], Astrid Hofman[3], Pietro Bearzi[1], Anna-Maria Hoffmann-Vold[8] and Oliver Distler[9], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [2]University Hospital Zurich, Zurich, Switzerland, [3]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [4]University of Zurich, University Hospital Zurich, Zurich, Switzerland, [5]University Hospital Zurich, University of Zurich, Zurich, Switzerland, [6]University Hospital zurich, Zurich, Switzerland, [7]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [8]Oslo University Hospital, Oslo, Norway, [9]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The poor prognosis of SSc patients demands an urgent need to prevent disease onset. Recently, we reported a global pro-inflammatory gene signature of dermal fibroblasts in pre-stages of SSc (pre-SSc). Here, we provide a detailed analysis of which fibroblast subtype and which molecular events are characteristic of this pro-inflammatory gene signature in pre-SSc.

Methods: We recruited patients with pre-SSc (n=6), established SSc (eSSc, n=7), and healthy controls (HC, n=6) (**Table 1**). Pre-SSc was defined according to the VEDOSS criteria[1]. eSSc patients met the 2013 ACR/EULAR criteria with disease duration < 5 years since their first non-Raynaud manifestation. HCs were matched for age, sex, and ethnicity. Site-matched forearm skin biopsies were collected, processed following the Chromium Next GEM protocol, and analyzed with Seurat pipeline. We refined fibroblast subclusters with functionally meaningful annotations. Over-Representation Analysis (ORA) of marker genes confirmed subcluster identities. Group-wise compositional differences were assessed (Speckle). Pairwise differential gene expression analysis was conducted (MAST, FDR < 0.05). Pathway analyses, ORA and Gene Set Enrichment Analysis (GSEA), were performed (clusterProfiler). Module scores (MS) quantified pro-inflammatory and pro-fibrotic gene expression programs.

1. Avouac, Jérôme, et al. (2011), Annals of the rheumatic diseases.

Table 1. Clinical characteristics of pre-SSc and eSSc patients, along with HCs, summarized by group. NAP: not applicable for HCs, indicating no assessment was performed in the healthy state; ILD: interstitial lung disease; HRCT: high-resolution computed tomography; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate. *Immunosuppressive therapies included mycophenolate mofetil, tocilizumab, methotrexate, prednisone, or their combinations.

Groups	Pre-SSc (n=6)	Established SSc (n=7)	Control (n=6)
Age, median (years; IQR, Q1-Q3)	48 (15, 40-55)	54 (6, 59-65)	44 (14, 37-51)
Female sex (n, %)	5 (83.3%)	4 (57.1%)	4 (66.7%)
Disease duration since first non-Raynaud symptom (years; median, IQR)	2.6 (2.8, 1.0-3.8)	2.3 (1.1, 1.7-2.8)	NAP
	Available 5/6	Available 4/7	
Modified Rodnan skin score (median, IQR, min-max)	0	1 (2, 0-13)	NAP
Digital ulcers (n, %)			
Current	0 (0.0)	1 (14.3%)	NAP
Previously	0 (0.0)	1 (14.3%)	
Never	6 (100.0%)	5 (71.4%)	
Clinical skin fibrosis of the forearm (biopsy site; n, %)			
Current	0 (0.0)	1 (14.3%)	NAP
Previously	0 (0.0)	0 (0.0)	
Never	6 (100.0%)	6 (85.7%)	
Pitting scars (n, %)	0 (0.0)	1 (14.3%)	NAP
Puffy fingers (n, %)	1 (16.7%)	3 (42.9%)	NAP
Arthritis (n, %)	0 (0.0)	1 (14.3%)	NAP
SSc pattern on nailfold capillaroscopy (n, %)	4 (66.7%)	6 (85.7%)	NAP
CRP elevation (n, %)	2 (33.3%)	0 (0.0)	NAP
ANA positive (n, %)	6 (100.0%)	6 (85.7%)	NAP
Anti-centromere positive (n, %)	5 (83.3%)	3/6 (50.0%)	NAP
Anti-Scl-70 positive (n, %)	0 (0.0)	3/6 (50.0%)	NAP
Anti-RNA Polymerase III positive (n, %)	0 (0.0)	0/5 (0.0)	NAP
ILD on HRCT (n, %)	0 (0.0)	5 (71.4%)	NAP
Current immunosuppressive therapy* (n, %)	0 (0.0)	4/7 (57.1%)	NAP

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

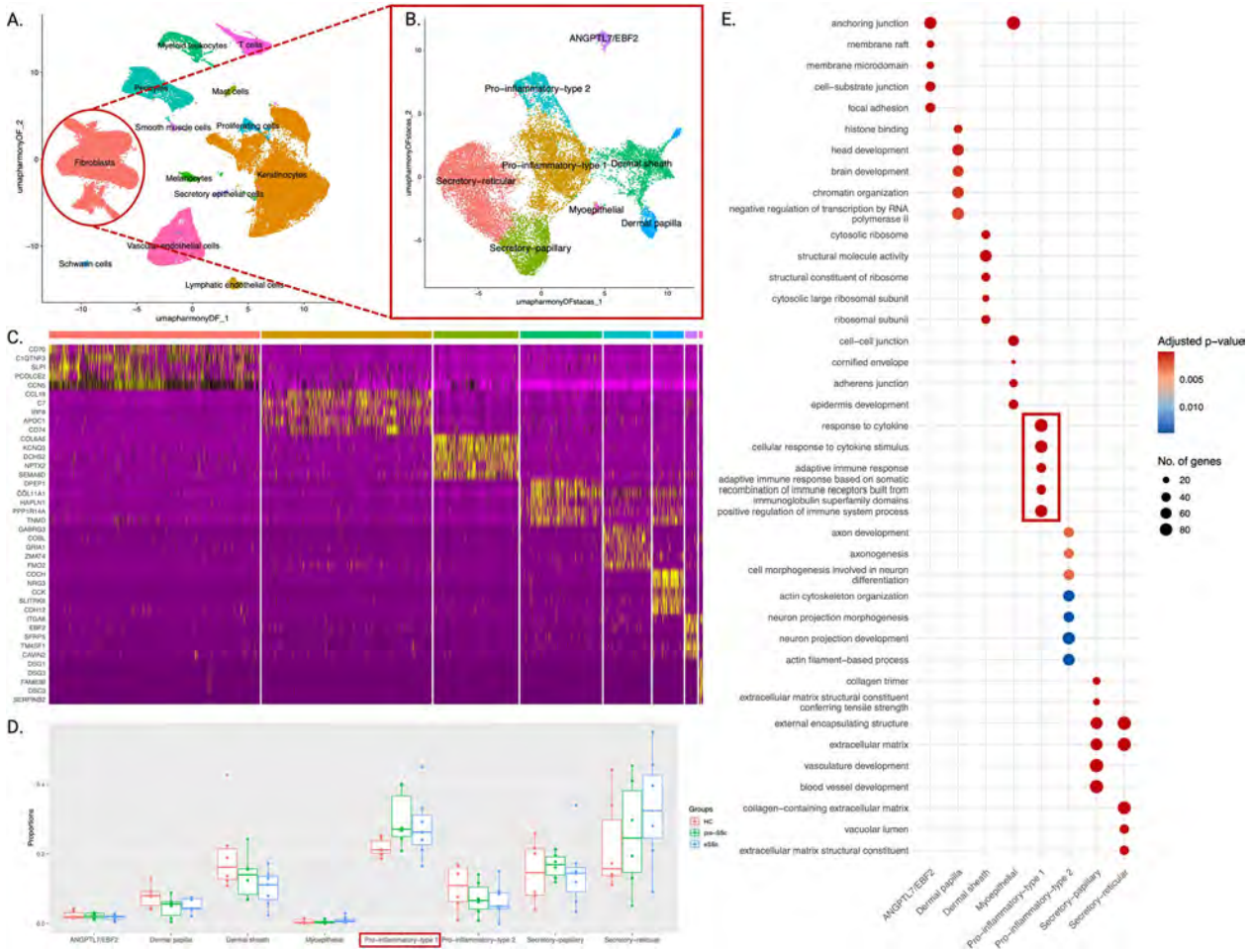


Figure 1. A) UMAP showing 13 identified dermal cell types. B) UMAP of 8 identified fibroblast subtypes. C) Heatmap of the top 5 marker genes per subtype. Color bars correspond to the fibroblast subtypes shown in (B). D) Box plot showing fibroblast subtype proportions per patient across healthy controls (HC), pre-SSc, and early SSc (eSSc) groups. A trend toward increased PF1 fibroblasts was observed in pre-SSc compared to HC (proportional ratio: 1.37; p = 0.06; FDR = 0.3) E) GO over-representation analysis reveals distinct functions for the 8 fibroblast subtypes. The top 5 significant pathways per subtype are shown, based on marker genes identified by FindAllMarkers (default settings; Benjamini–Hochberg adjusted FDR < 0.05; average log2FC > 0.5).

Results: We identified 8 subtypes of dermal fibroblasts including type 1 (PF1), and type 2 (PF2) pro-inflammatory fibroblasts (**Fig. 1A-C**). Cell compositional analysis showed an increase in PF1 fibroblasts in pre-SSc (**Fig. 1D**). ORA of top marker genes confirmed functional differences among fibroblast subtypes and indicated a specific role of PF1 in cytokine-related immune response (**Fig. 1E**). In pre-SSc vs. HC, PF1 yielded 283 significant differentially expressed genes, including *HLA-DRA*, *CD74*, *HLA-DPA1*, *HLA-DMA*, and *CCL21*, consistent with findings in the global fibroblast analysis (**Fig. 2A**). Notably, *HLA-DRA* and *HLA-DMA* were also highly upregulated in eSSc vs. HC (**Fig. 2B**). Pre-SSc PF1 showed significantly higher expression of inflammatory response-related genes compared to HC and eSSc (**Fig. 2C**). In PF1, pre-SSc showed higher expression of pro-inflammatory genes vs. HC, enriched in 17/20 top pathways linked to cytokine/chemokine signaling, leukocyte and T cell activation, and antigen presentation via MHC complexes in ORA (**Fig. 2D**), further supported by GSEA results (**Fig. 2E**). Notably, similar signatures were also observed in eSSc vs. HC in ORA (**Fig. 2F–G**). MS gradients in pre-SSc and eSSc suggest a shared inflammatory mechanism, strongest in pre-SSc and shifting toward a pro-fibrotic profile in eSSc (**Fig. 2H–I**).

Conclusion: Pre-SSc fibroblasts show marked upregulation of pro-inflammatory gene signatures, primarily driven by the type 1 subtype. These signatures peak in pre-SSc before fibrosis and persist into early fibrotic SSc, highlighting a critical window for preventive intervention. The enrichment of immune response-related pathways in pre-SSc offers key insights into early SSc pathogenesis and the potential targets for preventive therapies.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

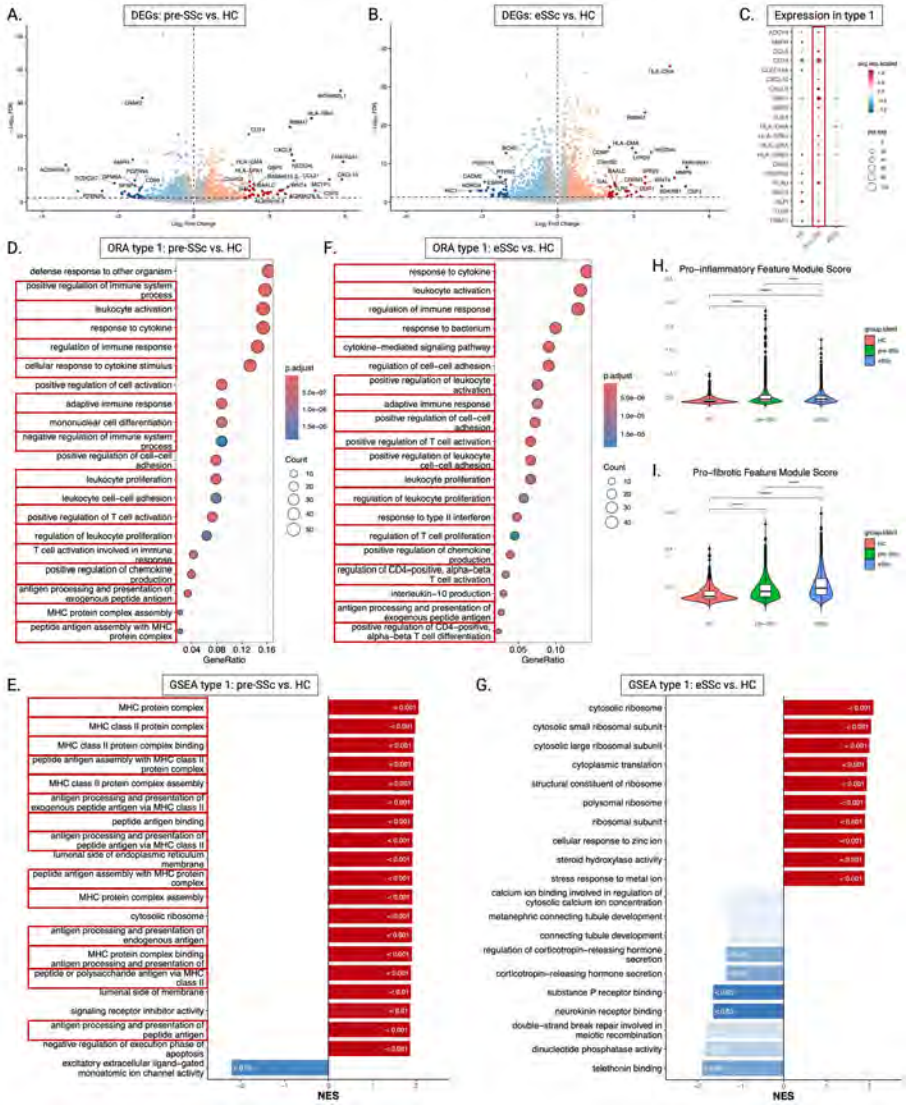


Figure 2. A) Volcano plot of differentially expressed genes (DEGs) in pre-SSc vs. healthy controls (HC), identified using the MAST model. Significant DEGs (|avg_log2FC| > 0.5; FDR < 0.05) are color-coded (blue: downregulated; orange: upregulated). Labeled genes meet stricter thresholds (|average $\log_2$FC| ≥ 2; FDR < 0.0005). B) Volcano plot of DEGs in eSSc vs. HC, as described in (A). C) Expression levels of inflammatory response-related genes in type 1 pro-inflammatory fibroblasts across HC, pre-SSc, and eSSc. Genes shown are from the intersection of significant DEGs in global fibroblasts and type 1 fibroblasts in the pre-SSc vs. HC comparison. D–E) GO-based over-representation analysis (ORA) and gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) in type 1 fibroblasts (pre-SSc vs. HC). ORA was performed using DEGs with |avg_$\log_2$FC| > 0.5 and FDR < 0.05. GSEA was based on DEGs ranked by score = avg_$\log_2$FC + (–$\log_{10}$FDR). FDR values above each NES bar indicate enrichment significance. F–G) ORA and GSEA of DEGs in type 1 fibroblasts (eSSc vs. HC), using the same thresholds and ranking method. H–I) Module scores across groups for pro-inflammatory (H) and pro-fibrotic (I) gene sets within type 1 fibroblasts. Pro-inflammatory genes include HLA-DRA, CD74, CXCL9, CXCL10, GBP1, HLA-DPA1, HLA-DRB1, PLAU, CCL21, TRAF1, GBP5, SLAMF8, CSF3, IFI30, OAS2, TLR2, IFIT2, IL4I1, CXCL11, HLA-DQA1; Pro-fibrotic genes include TNC, CTHRC1, COMP, COL4A4, CEMIP, LAMC2, WNT4, DDR1, COL4A3, IGFBP2, ADAM12, EDN1, IL23A, NOTCH4, CD37, PPARGC1A. **** indicates p < 0.0001.

Disclosure: L. Li: None; **E. Pachera**: None; **R. Dobrota**: Actelion, 5, 6, Amgen, 6, Boehringer-Ingelheim, 6, Iten-Kohaut, 5, Otsuka, 6, Pfizer, 5, Walter und Gertrud Siegenthaler Fellowship, 5; **S. Muraru**: AstraZeneca, 12, congress support; **K. Bürki**: None; **C. Mihai**: Boehringer Ingelheim, 2, 12, congress support, Janssen, 2, MED Talks Switzerland, 6, Medbase, 6, MedTrix, 6, Mepha, 6, Novartis, 6, PlayToKnow, 6; **M. Elhai**: Astrazeneca, 12, congress support, Boehringer Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5, Iten Kohaut foundation, 5, Janssen, 12, congress support, Kurt und Senta Herrmann foundation, 5, Novartis Foundation for Bio-Medical Research, 5, pfizer, 5, University Zurich, 5; **L. Much**: None; **A. Hofman**: None; **P. Bearzi**: None; **A. Hoffmann-Vold**:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0968

Mesenchymal Stromal Cells in Systemic Sclerosis are Dysfunctional and Have a Profibrotic and Senescent Phenotype

Marianela Brizio[1], Benoit Brilland[1], Maximilien Lora[2], Mathieu Mancini[1], David Langlais[1], Marie Hudson[3] and Ines Colmegna[4], [1]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, [3]McGill University, Montréal, QC, Canada, [4]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Mesenchymal stromal cells (MSCs) are non-hematopoietic multipotent cells with immunomodulatory, proangiogenic, and antifibrotic properties. MSC functions are mediated by paracrine soluble factors and small vesicles present in the MSC conditioned medium (CM). The three pathogenic axes in systemic sclerosis (SSc) are autoimmunity, vasculopathy, and fibrosis. We hypothesized that functional abnormalities of MSCs contributed to SSc pathogenesis.

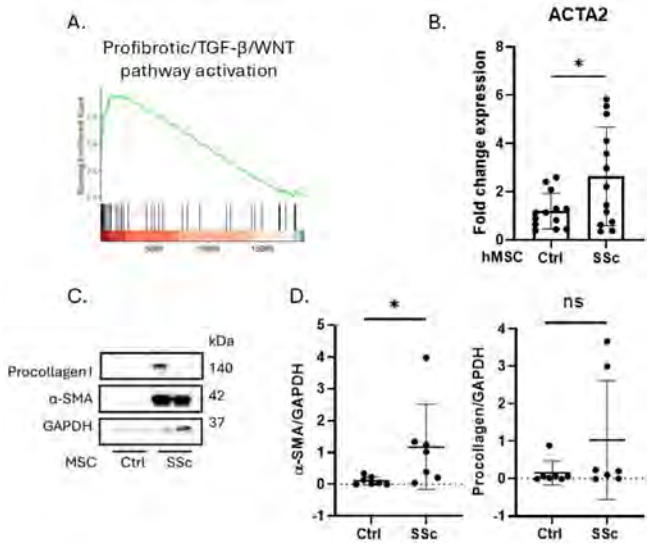


Figure 1. SSc MSCs display a myofibroblast-like phenotype A. Gene Set Enrichment Analysis (gene list: Zhu et al., 2024) B. Quantification of alpha-SMA gene expression (n=14, *p<0.05). C. Western blot representative images and quantification of alpha-SMA and procollagen protein levels(n=8, *p<0.05; ns: non-significant).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

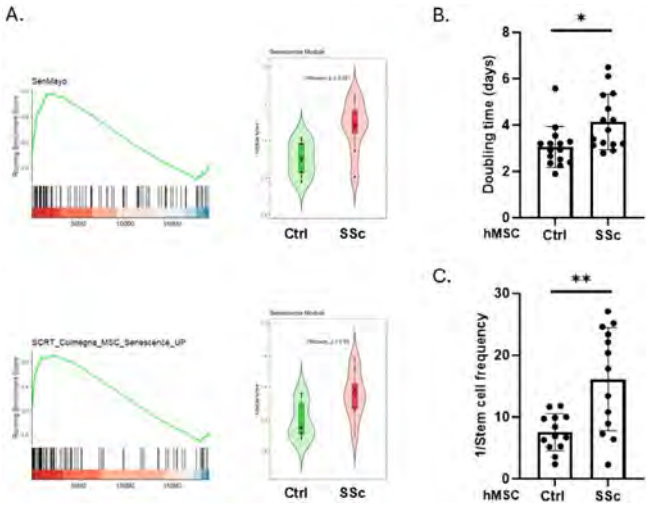


Figure 2. SSc MSCs have a senescent transcriptomic imprint underlying their reduced proliferation and clonogenic capacity A. Gene Set Enrichment Analysis plot for two gene lists (Gao et al., 2023, Psaroudis et al., 2022). B. MSCs population doubling (n=15) and C. Clonogenicity (n=15). *p<0.05 **p<0.01.

We aim to characterize the phenotype, transcriptomic signatures, and key functional properties of adipose-derived MSCs from SSc patients (SSc MSC).

Methods: MSCs were isolated from the adipose tissue associated with two 4 mm punch biopsies from the forearm of 15 SSc and 15 age- and sex-matched healthy controls (Ctrl). MSCs were characterized according to the International Society for Cell and Gene Therapy (ISCT) minimal criteria. RNA sequencing was performed on 8 SSc and 8 Ctrl MSCs. Proliferation (doubling time), stemness (fibroblast colony forming units: CFU-F), and immunopotency (flow cytometry) were assessed in vitro. MSC-CM cytokine profiling was done with the Luminex xMAP® platform.

Results: SSc and Ctrl MSC met ISCT criteria (i.e., adhered to plastic, differentiated into three lineages, and exhibited specific surface markers). Compared to Ctrl, SSc MSCs had 151 upregulated and 16 downregulated genes. Gene Set Enrichment Analysis (GSEA) documented the enrichment of proinflammatory and profibrotic pathways in MSCs recovered from SSc patients. However, SSc MSCs retain the capacity to inhibit the proliferation of activated T cells in vitro. SSc MSC depicted a myofibroblast-like phenotype, characterized by increased α–SMA gene and protein expression, and elevated levels of the profibrotic cytokine CCL2 in MSC-CM. SSc MSC had reduced proliferation and clonogenicity, and were enriched in senescence-associated gene sets.

Conclusion: SSc MSCs differ from Ctrl MSCs in their transcriptomic and functional properties. SSc MSCs have profibrotic and senescent phenotypes, which could contribute to amplify or perpetuate SSc pathogenic mechanisms. Future studies will evaluate the effect of MSC modulation on SSc severity.

Disclosure: M. Brizio: None; **B. Brilland**: None; **M. Lora**: None; **M. Mancini**: None; **D. Langlais**: None; **M. Hudson**: Astra Zeneca, 5, 6, Boehringer-Ingelheim, 5, Merck, 1, Pfizer, 5; **I. Colmegna**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0969

FOXO1 Mediated Polysialic Acid Dysregulation in Severe Systemic Sclerosis (SSc): A Novel Biomarker and Therapeutic Target?

Lamia Khan[1], Lisa Willis[2], Jan Storek[3], Desiree Redmond[4], Robert Gniadecki[4] and **Mohammed Osman**[1], [1]University of Alberta, Edmonton, AB, Canada, [2]Department of Biological Sciences, University of Alberta, Edmonton, AB, Canada, [3]University of Calgary, Calgary, AB, Canada, [4]Department of Medicine, University of Alberta, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a life-threatening autoimmune disease where fibroblasts (FB) contribute to disease severity by resisting apoptosis and driving excessive skin fibrosis. Among the limited treatment options, autologous stem cell transplantation (ASCT) is the only disease-modifying therapy, but its effects on restoring FB function remain unknown. We recently identified polysialic acid (polySia), a cancer-associated glycan, in skin sections from patients with SSc; polySia levels correlate with fibrosis and normalize post-ASCT. Additionally, severe-SSc skin has genomic instability associated with double-stranded-DNA-breaks (DSBs), which activate a transcription factor, FOXO1, to prolong FB survival. We hypothesized that the FOXO1 pathway might drive polySia expression, thereby contributing to increased cell survival and fibrosis.

Methods: We generated primary dermal fibroblast from skin biopsies of healthy controls (HC), less severe SSc (lSSc), severe fibrotic diffuse SSc (dSSc), and post-ASCT patients. DSB frequency, active (nuclear) FOXO1, and polySia levels were assessed using immunofluorescence/confocal microscopy and immunoblotting. Following FOXO1 pharmacological inhibition, we quantified polySia synthetic enzymes (ST8Sia2/4) and pro-fibrotic markers using qRT-PCR. Resistance-to-apoptosis was evaluated via TUNEL assay following inhibiting FOXO1 activity and polySia synthesis.

Results: In dSSc FB, DSBs, FOXO1 and polySia expression (ST8Sia2/4) were highest compared to lSSc and HC. Importantly, post-ASCT FB had decreased levels of these compared to dSSc. FOXO1 inhibition in dSSC resulted in increased resistance-to-apoptosis, decreased fibrotic-markers (e.g. fibronectin, CTGF) and ST8sia2/4 levels. Also, pharmacological inhibition of polySia synthesis increased resistance-to-apoptosis in dSSc FB. Suggesting that the FOXO1/polySia axis is critical for ASCT's beneficial effects in dSSc.

Conclusion: Our study identifies a novel DSB/FOXO1/polySia pathway as a key driver of severe SSc. This axis may serve as a biomarker for SSc disease progression and treatment response while providing insight into how ASCT restores fibroblast function. Targeting the FOXO1/polySia pathway could offer therapeutic potential for SSc and other fibrotic diseases.

Disclosure: L. Khan: None; **L. Willis**: None; **J. Storek**: None; **D. Redmond**: None; **R. Gniadecki**: Abbvie, 1, Boehringer Ingelheim, 6, 12, Clinical Trials, Eli Lilly, 1, Janssen, 2, 12, Clinical Trials, Kyowa Kirin, 1, Recordati, 1, Therakos, 1; **M. Osman**: AstraZeneca, 12, Clinical Trial, Boehringer Ingelheim, 1, 2, Therakos, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0970

Genomic instability in systemic sclerosis is promoted by metabolic remodelling via a FOXO1-dependent axis

Lamia Khan[1], Junqin Wang[2], Aishwarya Iyer[2], Desiree Redmond[2], Dylan Hennessey[2], Sandra O'Keefe[2], Jan Storek[3], Charmaine van Eeden[2], Robert Gniadecki[2] and **Mohammed Osman**[1], [1]University of Alberta, Edmonton, AB, Canada, [2]Department of Medicine, University of Alberta, Edmonton, AB, Canada, [3]University of Calgary, Calgary, AB, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a life-threatening autoimmune disease with limited treatment options, including autologous hematopoietic stem cell transplantation (AHSCT). We recently showed that dermal fibroblasts (DFs) in patients with diffuse cutaneous SSc (dcSSc) develop a cancer-like phenotype characterized by genomic instability and increased double-stranded DNA breaks (DSBs). However, little is known about the mechanisms promoting DF survival following the accumulation of genomic mutations and the effects of AHSCT on mutational frequency. We hypothesized that in response to reactive oxygen species (ROS), dcSSc DFs may promote a mitochondrial-dependent, resistance-to-apoptosis via the activation of the transcription factor forkhead box 1(FOXO1).

Methods: We characterized mutational frequencies and signatures in dcSSc (N =35) and AHSCT patients (N=9), using whole exome sequencing (WES) of dermal sections. We generated DFs from dcSSc, post-AHSCT (or age/sex matched health subjects). We quantified the frequency of DSBs by measuring γ-H2AX levels (immunoblot (IB)), and DSB nuclear foci (confocal microscopy). ROS and mitochondrial membrane potential were measured in DFs using flow cytometry. Changes in mitochondrial dynamics (fusion/fission, via IB), biogenesis (qRT-PCR), and morphology (confocal microscopy) were assessed. FOXO1 activation was determined by measuring nuclear (active) FOXO1, and expression of its downstream mRNA targets SOD2 and PDK4. Resistance-to-apoptosis was determined at baseline, following treatment with cyclophosphamide, a FOXO1-inhibitor, or with overexpression of constitutively active FOXO1 using TUNEL and cleaved caspase 3 levels (IB).

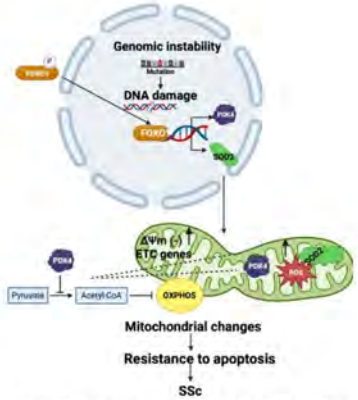


Figure 1. Overall Summary of our findings in diffuse cutaneous fibroblasts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: dcSSc patients had a reduced mutational frequency in both the dermis and in DFs compared to patients treated with AHSCT. We detected a base-excision repair signature (which is promoted by increased ROS levels) in dcSSc DFs. This was associated with an increased frequency of DSBs and ROS in dcSSc DF compared to post-AHSCT and HC. dcSSc DF had increased indicators associated with mitochondrial remodelling, mitochondrial biogenesis, and mitochondrial fusion. Importantly, FOXO1 was exclusively activated in dcSSc, but not HC or post-AHSCT DF, and its activation was required for promoting apoptosis resistance. Finally, overexpression of constitutively active FOXO1 in HC DF resulted in similar metabolic changes as seen in dcSSc and increased DF survival.

Conclusion: Our study highlights a novel mechanism whereby genotoxic stress signals in dcSSc promote cell survival via metabolic stress remodeling (Fig.1). It also provides mechanistic insights for the effects of AHSCT on the mutational landscape in dcSSc. Future studies targeting this pathway may implicate this novel mitochondrial/FOXO1 pathway as a novel therapeutic strategy in patients with dcSSc.

Disclosure: L. Khan: None; **J. Wang**: None; **A. Iyer**: None; **D. Redmond**: None; **D. Hennessey**: None; **S. O'Keefe**: None; **J. Storek**: None; **C. van Eeden**: None; **R. Gniadecki**: Abbvie, 1, Boehringer Ingelheim, 6, 12, Clinical Trials, Eli Lilly, 1, Janssen, 2, 12, Clinical Trials, Kyowa Kirin, 1, Recordati, 1, Therakos, 1; **M. Osman**: AstraZeneca, 12, Clinical Trial, Boehringer Ingelheim, 1, 2, Therakos, 1.

Abstract Number: 0971

Unraveling the role of the hippo pathway in systemic sclerosis: A focus on TEADs and VGLL3

Neha Khanna[1], Alyssa Rosek[1], Alexander Cai[1], Olesya Plazyo[2], Johann Gudjonsson[2], Dinesh Khanna[2] and Pei-Suen Tsou[2], [1]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [2]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune disorder characterized by excessive collagen production, leading to the thickening and hardening of skin and internal organs. Although its exact cause remains unknown and no cure exists, current treatments only alleviate symptoms without addressing the underlying disease mechanisms. Our research investigates the Hippo pathway, a key regulator of cell proliferation, apoptosis, and stemness. Dysregulation in this pathway within SSc results in increased YAP/TAZ transcriptional activity in fibroblasts via transcription factor binding, promoting fibrosis. Our previous work identified that the YAP inhibitor Verteporfin can reduce fibrosis. By targeting specific transcription factors and coactivators in the Hippo pathway, specifically TEADs and VGLL3, we aim to clarify its role in SSc fibrosis and develop more targeted therapies.

Methods: We examined TEAD1, TEAD2, TEAD3, TEAD4, and VGLL3 in SSc fibroblasts to assess their roles in fibrosis. Using Accell siRNA, we knocked down TEADs and VGLL3 individually in dermal fibroblasts from SSc patients. We evaluated changes in gene expression and cell functions including proliferation, migration, and contractility. Knockdown cells underwent single-cell RNA-sequencing. To induce pro-fibrotic phenotypes, healthy dermal fibroblasts were stimulated with TGF-β (10 ng/ml) for 1 or 72 hours. Statistical analysis was performed using GraphPad Prism v.10, with significance set at $p < 0.05$.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Knocking down TEADs and VGLL3 achieved over 50% gene downregulation in SSc dermal fibroblasts. Knockdown of TEAD1, TEAD3, or VGLL3 consistently reduced pro-fibrotic gene expression, whereas TEAD2 and TEAD4 did not. Protein-level confirmation by immunofluorescence showed significant decreases in alpha-smooth muscle actin, a key marker of fibroblast activation and myofibroblast differentiation, following TEAD1, TEAD3, or VGLL3 knockdown in SSc fibroblasts. VGLL3 downregulation consistently reduced cell proliferation and migration, while TEAD1 and TEAD3 downregulation impaired gel contraction. Single-cell RNA sequencing identified genes and pathways impacted by TEADs or VGLL3 knockdown. Interestingly, long-term TGF-β stimulation in healthy fibroblasts, which resulted in myofibroblast transformation in these cells, led to downregulation of TEAD1, 2, 3 and VGLL3. In contrast, transient activation of TGF-β, which resulted in increased p-SMAD2 in the nucleus, led to enhanced nuclear staining of TEAD1 or TEAD3, compared to non-treated fibroblasts.

Conclusion: TEAD1, TEAD3, and VGLL3 play crucial roles in mediating the pro-fibrotic effects of the Hippo pathway in SSc fibroblasts. These findings align with our prior research suggesting that disrupting YAP or VGLL3 binding to TEADs in the Hippo pathway could serve as a viable therapeutic strategy. Continued research will focus on the genes and pathways influenced by these transcription factors and coactivator, potentially benefiting treatment approaches for other fibrotic diseases.

Disclosure: N. Khanna: None; **A. Rosek**: None; **A. Cai**: None; **O. Plazyo**: None; **J. Gudjonsson**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **P. Tsou**: None.

Abstract Number: 0972

Prominent endothelial senescence in systemic sclerosis skin

Poulami Dey[1], William D Brodie[2], Megan N Mattichak[3], Alexander Cai[3], Qi Wu[4], Johann Gudjonsson[5], Dinesh Khanna[5], John Varga[5] and **Pei-Suen Tsou**[5], [1]Michigan Medicine, Ann Arbor, MI, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, Ann Arbor, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [4]Michigan Medicine, Ann Arbor, [5]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is characterized by extensive damage of the microvessels in multiple organs. We and others showed that endothelial cells (ECs) isolated from SSc skin biopsies show dysregulated phenotypes including impaired angiogenesis, barrier dysfunction, and spontaneous/constitutive endothelial-to-mesenchymal transition (EndoMT). Notably, these are hallmarks of EC senescence. In this study, we therefore sought to determine the presence and role of EC senescence in SSc skin fibrosis.

Methods: Dermal microvascular ECs were isolated from skin biopsies of age-matched healthy individuals and SSc patients. Cellular senescence was assessed through qPCR, immunofluorescence, β-galactosidase expression and measuring the senescence-associated secretory phenotype (SASP). To investigate EC-specific senescence at the single-cell level, we analyzed skin biopsies from 18 healthy controls and 22 patients with early diffuse SSc. Senescence and extracellular matrix (ECM) scores were constructed using specific gene lists, and receptor-ligand interactions were evaluated. P values under 0.05 were deemed statistically significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

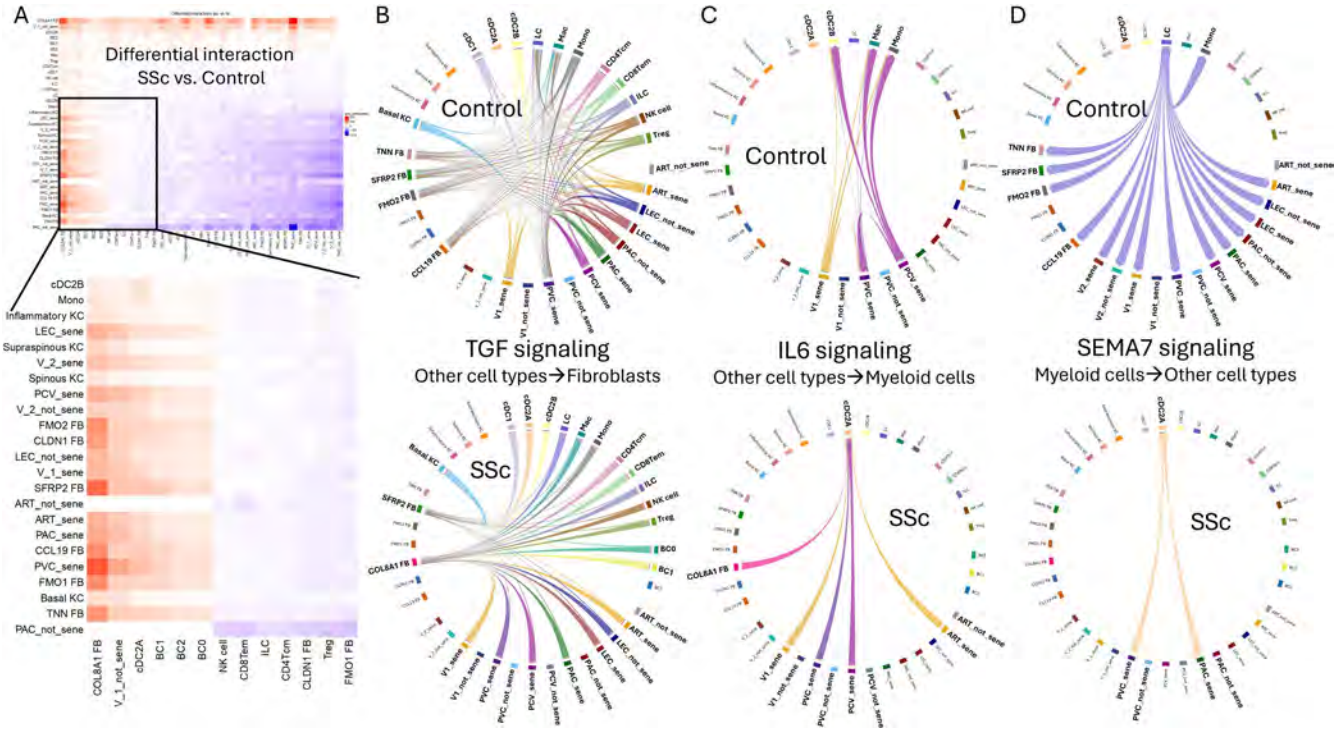


Figure 1. Bioinformatics analysis reveals that senescent SSc ECs engage in unique signaling interactions with myofibroblasts and DCs. Receptor-ligand interaction analysis, comparing SSc skin to controls, shows that senescent EC clusters have the strongest interactions with COL8A1+ myofibroblasts, cDC2A LAMP3+ DCs cells, and B cells, whereas non-senescent ECs exhibit minimal interactions (A). TGFβ signaling targeting COL8A1+ myofibroblasts in SSc skin originates predominantly from senescent ECs, among other cell types, unlike non-senescent ECs (B). In SSc skin, IL-6 signaling to LAMP3+ DCs is contributed by both COL8A1+ myofibroblasts and senescent ECs (C). Senescent PVC and PAC EC clusters interact with LAMP3+ DCs through SEMA7-integrin binding (D). ART: arterial, PAC: post-arterial capillary, PVC: pre-venular capillary, PCV: post-capillary venule, V: venule, LEC: lymphatic EC, FB: fibroblasts, KC: keratinocytes, LC: Langerhans cells, ILC: innate lymphoid cell.

Results: SSc ECs displayed increased senescence, with higher senescence markers (p16, p53, and β-galactosidase), DNA damage (γH2AX and phospho-ATM), SASP secretion (IL-6, IL-8, PAI-1, MMP1, HGF), and reduced eNOS activity, compared to age-matched healthy ECs. In SSc skin biopsies, senescence marker staining was prominently associated with small blood vessels. Single-cell RNA-seq revealed seven distinct EC clusters; one cluster, expanded in SSc biopsies, showed pronounced EndoMT traits. Most EC clusters exhibited significant senescence scores using the SenMayo gene list, independent of age. *CDKN1A*, a canonical senescence marker not included in SenMayo, was notably elevated in SSc ECs compared to controls. Cluster-specific senescence scores were highly correlated with ECM scores. Receptor-ligand analysis indicated that EC senescence in SSc was associated with signaling interactions with myofibroblasts and with dendritic cells. Dominant mediators for this cross-talk included the TGF-β, IL-6, and SEMA7 pathways (Figure 1).

Conclusion: By employing a multi-marker, stepwise approach, we identified senescent ECs in SSc skin microvasculature, confirming endothelial senescence as a key element of the disease. On-going studies are investigating the mechanistic role of senescent ECs in SSc-associated immune, vascular and fibrotic pathologies. This unusual EC phenotype may play a crucial pathogenic role in SSc and could serve as a potential target for senotherapy.

Disclosure: P. Dey: None; **W. Brodie**: None; **M. Mattichak**: None; **A. Cai**: None; **Q. Wu**: None; **J. Gudjonsson**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **J. Varga**: None; **P. Tsou**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0973

Effects of a Novel Hybrid Protein Based on S100 on Macrophage Polarization and Its Therapeutic Efficacy in a Bleomycin-Induced Systemic Sclerosis Mouse Model.

Takuya Kotani[1], Takayasu Suzuka[2], Shogo Matsuda[3] and Tohru Takeuchi[4], [1]Division of Rheumatology, Department of Internal Medicine IV, Osaka Medical and Pharmaceutical University, Osaka, Japan, [2]Division of Rheumatology, Department of Internal Medicine IV, Osaka Medical and Pharmaceutical University, Takatsuki, Japan, [3]Department of Internal Medicine IV, Division of Rheumatology, Osaka Medical and Pharmaceutical University, Osaka, Japan, [4]Department of Internal Medicine (IV), Osaka Medical and Pharmaceutical University, Takatsuki, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: S100 proteins are involved in the inflammatory responses of autoimmune diseases. We previously showed that S100 proteins regulate macrophage function via CD68. Based on this, we developed a novel human hybrid protein, human MIKO-1 (hMIKO-1), derived from the primary structure of human S100. This study aimed to investigate its effects on macrophage polarization and its therapeutic potential in a systemic sclerosis (SSc) mouse model with interstitial lung disease (ILD).

Methods: Murine macrophages were co-cultured with hMIKO-1 to evaluate its effect on macrophage polarization. In vivo, female C57BL/6 mice were injected subcutaneously with bleomycin (200 μg/mouse, every other day) to induce skin and lung lesions resembling SSc-associated ILD (SSc-ILD). Mice were divided into three groups: sham control, disease control (BLM + vehicle), and treatment (BLM + hMIKO-1). After four weeks, skin and lung tissues were collected and assessed histologically.

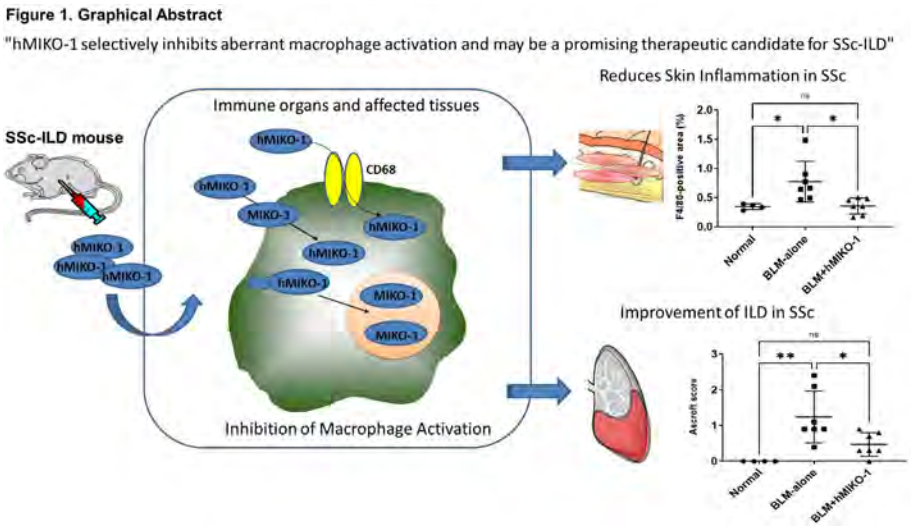


Figure 1. Graphical Abstract: Mechanism of Action and Therapeutic Effects of hMIKO-1 hMIKO-1 enters the macrophage cytoplasm via CD68-mediated uptake and endocytosis, forming complexes with β-actin and NF-κB. It subsequently binds to nuclear transport proteins and translocates into the nucleus. In THP-1 cells, hMIKO-1 significantly suppresses the mRNA expression of pro-inflammatory cytokines TNF-α and TGF-β. In systemic sclerosis (SSc) mouse models, hMIKO-1 reduces skin inflammation and improves interstitial lung disease (ILD). These findings suggest that hMIKO-1 selectively inhibits aberrant macrophage activation and may represent a promising therapeutic candidate for SSc-ILD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

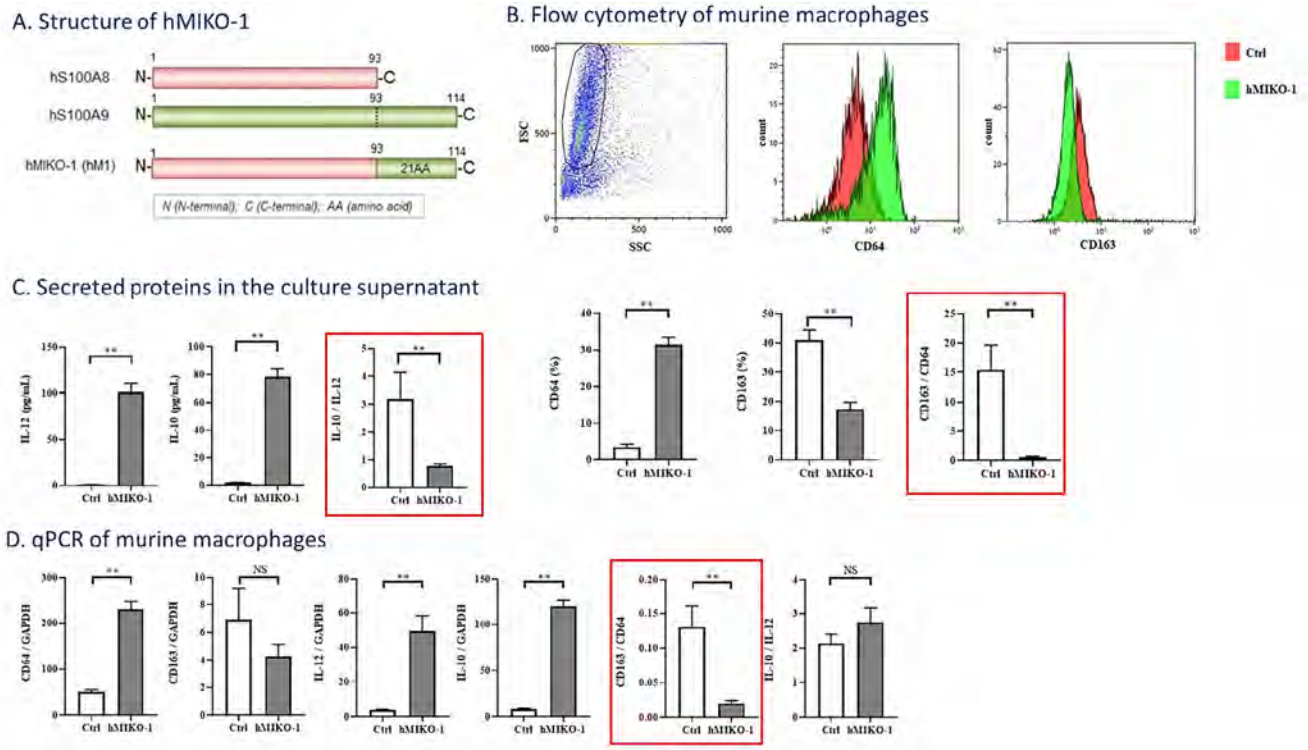


Figure 2. Inhibitory Effect of hMIKO-1 on M2 Polarization of Murine Macrophages (A) hMIKO-1 was designed based on the amino acid sequences of S100A8 and S100A9. (B–D) Co-culture with hMIKO-1 was conducted using murine peritoneal macrophages polarized toward the M2 phenotype. (B) Flow cytometry showed a significant reduction in the CD163/CD64 ratio compared to control, indicating suppression of M2 polarization. (C) The IL-10/IL-12 ratio in the culture supernatant also decreased significantly. (D) qPCR confirmed reduced CD163/CD64 expression, supporting the inhibitory effect of hMIKO-1. Ctrl: without hMIKO-1. Data are mean ± SD (n = 6). **p < 0.01; NS: not significant.

Results: hMIKO-1 significantly inhibited M2 polarization of murine macrophages in vitro. In vivo, lung fibrosis scores were significantly lower in the hMIKO-1-treated group compared to the disease control group, while no significant difference was found in skin fibrosis. F4/80-positive macrophages in both skin and lung tissues were significantly reduced in the hMIKO-1 group. Notably, hMIKO-1 accumulation differed between lungs and skin.

Conclusion: hMIKO-1 attenuated inflammation and fibrosis in the lungs of SSc-ILD model mice. Its limited effect in the skin may be due to differences in tissue accumulation. hMIKO-1 may serve as a potential targeted therapy for SSc-associated ILD.

Disclosure: T. Kotani: None; **T. Suzuka**: None; **S. Matsuda**: None; **T. Takeuchi**: None.

Abstract Number: 0974

Tissue resident macrophages derived from induced pluripotent stem cells induce tissue fibrosis in human skin equivalent models of systemic sclerosis

Xuezhi Hong[1], Yanhua Xiao[2], shihao zhu[3], Yi-Nan Li[4], Linlin Huang[3], Martin Regensburger[5], Franz Marxreiter[6], Tim Filla[7], Andrea-Hermina Györfi[8], James Adjaye[9], Jürgen Winkler[6], Florian Groeber-Becker[10], Jörg Distler[11] and Alexandru-Emil Matei[12], [1]Department of Rheumatology, University Hospital Dusseldorf, Medical Faculty of Heinrich Heine University, Dusseldorf, Germany, Dösseldorf, Germany, [2]Medical Faculty of Heinrich Heine University, Dusseldorf, Germany, [3]Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Düsseldorf, Germany,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[4]University Hospital of Dösseldorf, Dösseldorf, Germany, [5]Department of Stem Cell Biology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Erlangen, Germany, Erlangen, Germany, [6]Department of Molecular Neurology, FAU Erlangen-Nürnberg, Erlangen, Germany, Erlangen, Germany, [7]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [8]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [9]Institute for Stem Cell Research and Regenerative Medicine, University Hospital Düsseldorf, Moorenstrasse 5, D-40225 Duesseldorf, Germany, Dusseldorf, Germany, [10]Department of Ophthalmology, University Hospital Düsseldorf, 40225, Düsseldorf, Germany, Dusseldorf, Germany, [11]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [12]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Previous studies showed that monocyte-derived macrophages become pro-fibrotic in systemic sclerosis (SSc) and contribute to fibroblast activation. Macrophages are, however, a heterogeneous population. Macrophages of different ontogenies (monocyte-derived or tissue resident macrophages (TR-Macs)) can be functionally distinct in physiology and disease. However, the role of TR-Macs in the pathogenesis of SSc has not been studied thus far.

Here we aimed to evaluate the role of TR-Macs in SSc skin using induced pluripotent stem cells (iPSC)-derived macrophages and an *in vitro* human skin equivalent model.

Methods: TR-Macs were generated from SSc patients (SSc-TR-Macs) and healthy controls (healthy-TR-Macs). Functional differences were assessed using flow cytometry, phagocytosis assays, and RNA sequencing (RNA-seq). A three-dimensional human skin equivalent model was developed by co-culturing TR-Macs with fibroblasts and keratinocytes. Fluorescence staining was performed to analyze TR-Macs polarization, and single-cell RNA sequencing (scRNA-seq) was used to evaluate the subpopulations of fibroblasts and their communication with macrophages in an SSc skin equivalent in comparison to SSc skin.

Results: SSc-TR-Macs expressed higher levels of markers of M2 polarization and showed an increased phagocytic capacity compared to healthy-TR-Macs. Furthermore, SSc-TR-Macs exposed to SSc serum upregulated pro-inflammatory and pro-fibrotic pathways.

Incorporation of SSc TR-Macs in healthy human skin equivalents (containing healthy fibroblasts and keratinocytes) was sufficient to induce fibroblast-to-myofibroblast transition and excessive collagen I deposition without further stimuli. Furthermore, addition of SSc-TR-Macs in a skin equivalent formed by SSc fibroblasts greatly enhanced basal and TGFβ-induced fibroblast activation and collagen I deposition.

ScRNA-seq analysis demonstrated that SSc human skin equivalents (formed by SSc TR-Macs and SSc fibroblasts) recapitulate the composition, shifts in frequencies of fibroblast subpopulations, as well as fibroblasts-macrophages cell-cell communication networks observed in SSc skin.

Treatment with the antifibrotic drug nintedanib, as well as with the CD206-targeting peptide RP-832c (that targets M2 macrophages) effectively reduced collagen deposition in an SSc skin equivalent (containing SSc fibroblasts and SSc TR-Macs).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our study demonstrates a pro-fibrotic role of SSc TR-Macs in SSc skin. These Mac subsets are M2-like polarized and promote fibroblast to myofibroblast transition and fibrotic remodelling in an SSc skin equivalent. The SSc skin equivalent model containing TR-Macs recapitulates key fibroblast and Macs subpopulations and their cell-cell communication in SSc skin. Furthermore, not only drugs that target fibroblasts, but also drugs that specifically target macrophages demonstrate antifibrotic effects in the SSc skin equivalent containing TR-Macs. This model could be thus used for testing of antifibrotic drugs that interfere with the fibroblast-macrophage communication network in SSc.

Disclosure: X. Hong: None; **Y. Xiao**: None; **s. zhu**: None; **Y. Li**: None; **L. Huang**: None; **M. Regensburger**: None; **F. Marxreiter**: None; **T. Filla**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **J. Adjaye**: None; **J. Winkler**: None; **F. Groeber-Becker**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **A. Matei**: None.

Abstract Number: 0975

Linezolid prevents fibroblast activation and ameliorates tissue fibrosis by inhibition of mitochondrial translation

Xuezhi Hong[1], Yanhua Xiao[2], shihao zhu[3], Tim Filla[4], Andrea-Hermina Györfi[5], Yi-Nan Li[6], Meilin Xu[7], Langxian Zhi[2], Thuong Trinh-Minh[8], Clara Dees[9], Georg Schett[10], Jörg Distler[11] and Alexandru-Emil Matei[12], [1]Department of Rheumatology, University Hospital Dusseldorf, Medical Faculty of Heinrich Heine University, Dusseldorf, Germany, Dösseldorf, Germany, [2]Medical Faculty of Heinrich Heine University, Dusseldorf, Germany, [3]Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Düsseldorf, Germany, [4]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [5]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [6]University Hospital of Dösseldorf, Dösseldorf, Germany, [7]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Düsseldorf, Germany, Düsseldorf, Germany, [8]Clinic for Rheumatology University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University, Dösseldorf, Germany; Hiller Research Center, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University, Dösseldorf, Nordrhein-Westfalen, Germany, [9]Department of Internal Medicine 3, Rheumatology and Clinical Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and University Hospital Erlangen, Erlangen, Germany, Erlangen, Germany, [10]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [11]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [12]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a progressive fibrotic disease characterized by fibroblast activation and immune dysregulation, with limited therapeutic options. Mitochondrial dysfunction is increasingly implicated in fibrosis, yet the role of mitochondrial translation remains underexplored. Linezolid, a clinically approved ribosome-targeting antibiotic, inhibits mitochondrial protein synthesis. We investigated whether targeting mitochondrial translation with linezolid could mitigate fibrosis in SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We employed complementary SSc models, including TGFβ-stimulated human dermal fibroblasts, three-dimensional SSc skin equivalents (SScSE), and precision-cut skin slices (PCSS) from SSc patients. In vivo, we used a multiorgan fibrosis mouse model mimicking key features of diffuse cutaneous SSc. Mechanistic studies included immunostaining, Western blot, Seahorse analysis, and nascent mitochondrial translation assays. Transcriptomic profiling was performed on fibroblasts, SSc tissue, and TGFβ-activated macrophages.

Results: Linezolid inhibited TGFβ-induced fibroblast activation across multiple models of SSc, including cultured human dermal fibroblasts, three-dimensional SSc skin equivalents (SScSE), SSc patient-derived precision-cut skin slices (PCSS), and an inflammation-driven murine fibrosis model. Treatment reduced αSMA expression, stress fiber formation, and collagen type I deposition, indicating effective suppression of fibroblast-to-myofibroblast transition.

Transcriptomic analyses revealed that linezolid reversed profibrotic gene expression programs and downregulated key signaling pathways such as TGFβ, WNT, and JAK-STAT. In SScSE, linezolid also modulated macrophage activation profiles, suppressing pathways involved in cytoskeletal remodeling and fibroblast stimulation.

Mechanistically, linezolid impaired mitochondrial translation in fibroblasts, evidenced by reduced incorporation of nascent mitochondrial proteins and decreased MTCO1 expression. This was accompanied by diminished oxidative phosphorylation capacity and lowered NAD^+/NADH ratios, contributing to functional metabolic disruption.

Conclusion: This study identifies mitochondrial translation as a critical regulator of fibroblast activation and immune cell function in SSc. By targeting this pathway, linezolid exerts potent antifibrotic effects across human and murine models. Given its clinical availability, these findings provide strong rationale for repurposing linezolid as a novel therapeutic strategy for fibrotic disorders.

Disclosure: X. Hong: None; **Y. Xiao**: None; **s. zhu**: None; **T. Filla**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **Y. Li**: None; **M. Xu**: None; **L. Zhi**: None; **T. Trinh-Minh**: 4D Science GmbH, 3, ArgenX, 6; **C. Dees**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **A. Matei**: None.

Abstract Number: 0976

LMPTP Drives Fibrosis in Systemic Sclerosis via TGF-beta Signaling Activation

Yuan Zhan[1], Colton Sanders[2], Michael Diaz[2], Jinmin Miao[3], Arminja Kettenbach[4], Zhong-Yin Zhang[5], Paul Wolters[6], Francesco Boin[7], Stephanie Stanford[2] and Nunzio Bottini[8], [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]University of California San Diego, San Diego, CA, [3]Purdue University, West Lafayette, IN, [4]Geisel School of Medicine at Dartmouth, Lebanon, NH, [5]Purdue University, Department of Medicinal Chemistry and Molecular Pharmacology, West Lafayette, IN, [6]University of California San Francisco, San Francisco, CA, [7]Cedars-Sinai Medical Center, Beverly Hills, CA, [8]Cedars Sinai Medical Center, Beverly Hills, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

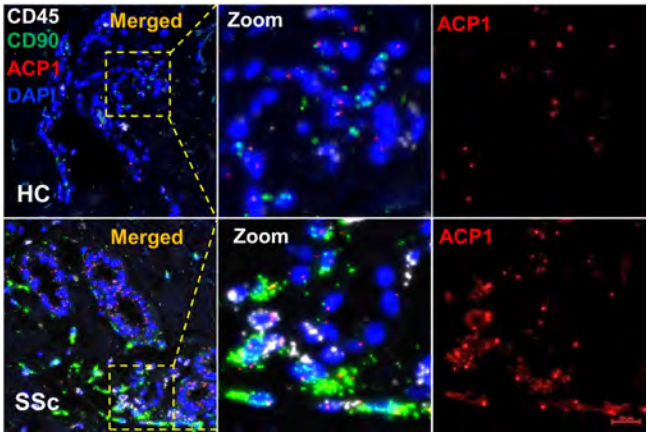


Figure 1. LMPTP expression is significantly upregulated in affected skin of SSc patients. LMPTP mRNA was quantified by RNAScope in situ hybridization using LMPTP (ACP1, red) , CD90 (fibroblast, green), CD45 (leucocytes, white) probes in both healthy (HC, n=4) and SSc patients (SSc, n=4) skin biopsies.

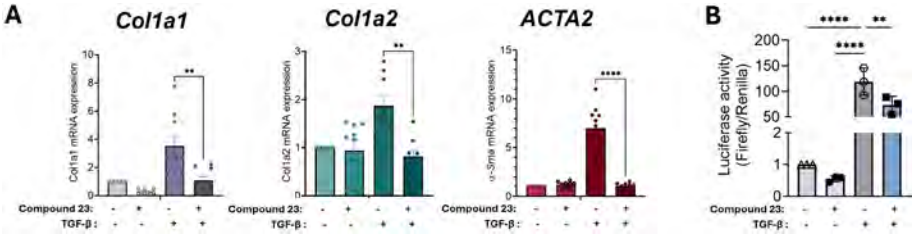


Figure 2. LMPTP inhibition reduces pro-fibrotic gene expression and dampens SMAD-dependent TGF-β signaling. A. qPCR analysis of COL1A1, COL1A2, and ACTA2 expression in human dermal fibroblasts treated with 10 μM Compound 23, stimulated with 10 ng TGF-beta1 for 24h. Error bars represent mean ± SEM normalized to control group. Statistical significance was determined using paired t test. **P < 0.01, ****P < 0.0001. B. SMAD-dependent luciferase reporter assay assessing SMAD3 transcriptional activity after 24-hour stimulation of 10 ng/mL TGF-β1 in 293T cells, with or without 10 μM Compound 23. Luciferase activity was normalized to Renilla. Error bars represent Mean ± SEM and representative at least three different experiments in triplicate. Statistical significance was assessed using One-way ANOVA test, **P < 0.01, ****P < 0.0001.

Background/Purpose: The identification of effective and safe anti-fibrotic agents is a critical unmet need in systemic sclerosis (SSc). Although fibrosis in SSc is driven by aberrant activation of pro-fibrotic signaling pathways downstream of protein kinase receptors, such as the receptor for transforming growth factor beta (TGFbeta), little is known in this condition about phosphatases, which oppose signaling by kinases. We sought to explore a potential role for the low molecular weight PTP (LMPTP) in fibrotic manifestations of SSc because the LMPTP promotes growth signaling pathways in cancer cells, is highly expressed in fibroblasts and complete knockout (KO) of the LMPTP does not induce any spontaneous phenotype.

Methods: Skin biopsies and lung explants from patients with early SSc were subjected to in situ hybridization for LMPTP. Primary dermal fibroblasts (DF) were subjected to treatment with two independent LMPTP inhibitors followed by assessment of TGFbeta signaling, immunoprecipitations, transcriptomics, proteomics and phospho-proteomics analysis. TGFbeta signaling reporter assays were performed in 293 cells. Mice were subjected to the bleomycin model of skin and lung fibrosis.

Results: We found that the LMPTP is upregulated in fibrotic skin of scleroderma patients (**Fig. 1**). An assessment of primary DF treated with small-molecule LMPTP inhibitors showed that LMPTP promotes TGFbeta signaling (**Fig. 2**). Mechanistically, LMPTP promotes early TGFbeta receptor (TGFBR) signaling through the dephosphorylation of a novel substrate. Global deletion of LMPTP in mice significantly attenuated the severity of skin and lung fibrosis in the bleomycin-induced model (**Fig. 3**). Similar results were obtained when mice were treated with an orally bioavailable LMPTP inhibitor.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

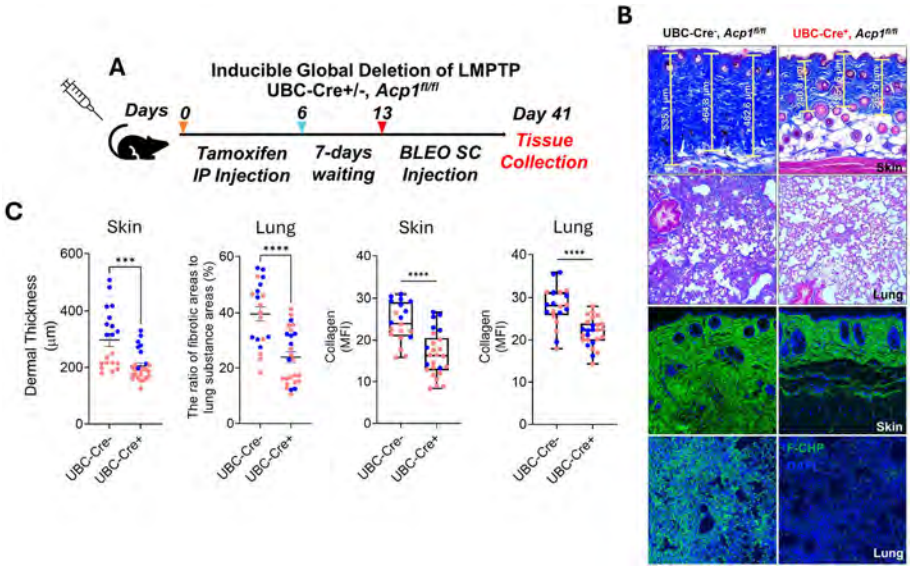


Figure 3. LMPTP promotes bleomycin-induced fibrosis in vivo. A. Schematic overview of tamoxifen-inducible ACP1 knockout mouse model and bleomycin-induced fibrosis protocol. B. Masson's trichrome and collagen-specific fluorescent staining (F-CHP) of skin and lung from wild-type and ACP1 KO mice after bleomycin treatment (Cre+, n=26; Cre–, n=20). Blue dots represent male samples and red dots represent female samples. C. Quantification of dermal thickness, collagen deposition, and fluorescence intensity in skin and lung. Data are shown as mean ± SEM. Statistical significance was determined using the Mann-Whitney test. *P < 0.05, **P < 0.01, ****P < 0.0001.

Conclusion: Taken together, these findings indicate a critical role for LMPTP in development of fibrosis through a novel mechanism of regulation of early TGFbeta signaling. As LMPTP KO mice are healthy and viable and LMPTP might be tractable for small molecule discovery, our study suggests that LMPTP inhibition is a potentially safe therapeutic strategy for preventing or treating fibrosis in scleroderma.

Disclosure: Y. Zhan: None; **C. Sanders**: None; **M. Diaz**: None; **J. Miao**: None; **A. Kettenbach**: None; **Z. Zhang**: None; **P. Wolters**: None; **F. Boin**: Adicet Bio, 2, Boehringer Ingelheim, 1, Janssen Pharmaceuticals, 6; **S. Stanford**: None; **N. Bottini**: Merck/MSD, 2.

Abstract Number: 0977

The nuclear receptor DAX1 regulates WNT/β-catenin signaling to promote fibroblast activation and skin fibrosis in systemic sclerosis

Lichong Shen[1], Xianyi Meng[2], **Yun Zhang**[3] and Joerg Distler[4], [1]3Department of Rheumatology, Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [2]Clinic for Rheumatology University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Duesseldorf, Germany, [3]University Hospital Duesseldorf, Duesseldorf, Germany, [4]Clinic for Rheumatology University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University; Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich Heine University, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0955–0977) Systemic Sclerosis & Related Disorders – Basic Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Nuclear receptors are a family of transcription factors that is commonly targeted for therapeutic intervention. Dosage-sensitive sex reversal adrenal hypoplasia congenital critical region on X chromosome gene 1, DAX1,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

also known as NR0B1, has been shown to regulate fundamental cellular processes. However, its role in fibrotic diseases has not been investigated so far. Here, we aimed to characterize the role of DAX1 in the pathogenesis of SSc.

Methods: Expression of DAX1 was analyzed by Western blot, imaging mass cytometry (IMC) and immunofluorescence. The effects of DAX1 knockdown or DAX1 antagonist BPK-29 on collagen production and myofibroblast differentiation were analyzed in cultured human fibroblasts, in bleomycin- and cGvHD-induced dermal fibrosis in mice, human 3D full-thickness skin equivalents and precision-cut human skin slices (PCSS). DAX1 signaling in TGFβ-stimulated fibroblasts was analyzed by RNASeq, co-immunoprecipitation and chromatin-immunoprecipitation.

Results: The expression of DAX1 was upregulated in SSc patients in a non-canonical TGFβ signaling dependent manner. DAX1 induced the activation of WNT/β-catenin signaling to drive fibroblast-to-myofibroblast transition. Knockout of DAX1 in murine skin by topical injection of DAX1-siRNA inhibited fibroblast-to-myofibroblast differentiation and ameliorated dermal fibrosis in two complementary mouse models of fibrosis. The selective DAX1 antagonist BPK-29 attenuated the TGFβ-induced myofibroblast activation or fibrotic tissue remodeling in cultured human dermal fibroblasts, and in three dimensional full-thickness skin equivalents. Moreover, inhibition of DAX1 ameliorated the expression of disease-relevant genes including WNT signaling in precision-cut slices of SSc skin. Mechanistically, DAX1 dimerized with E2F4 to promote WNT/β-catenin signaling via induction of *WNT4* and *WNT10B* genes in cultured fibroblasts, in murine models of fibrosis and in precision-cut skin slices of SSc patients.

Conclusion: DAX1 is upregulated in SSc in a TGFβ-dependent manner to promote fibroblast activation via WNT/β-catenin signaling. Inactivation of DAX1 normalizes WNT/β-catenin signaling, inhibits fibroblast-to-myofibroblast transition and ameliorates experimental fibrosis. Targeting of DAX1 may thus offer potential for therapeutic intervention.

Disclosure: L. Shen: None; **X. Meng**: None; **Y. Zhang**: None; **J. Distler**: AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5.

Abstract Number: 0978

IL-17A+ HLA-DR-CCR6+ regulatory T cells: Dual role in T cell suppression and synovial inflammation in arthritis.

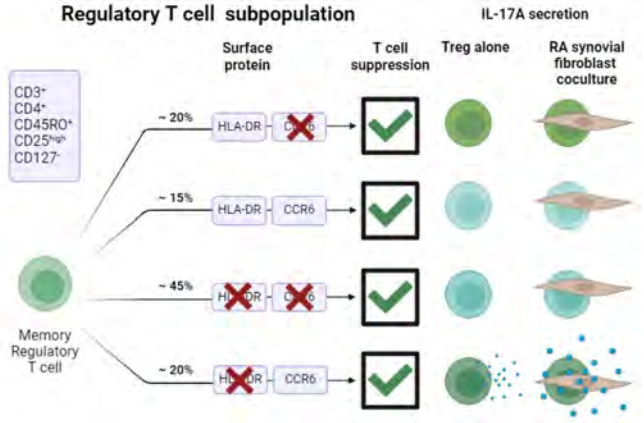
Bennie Heeswijk[1], Margot Bongenaar[1], Nadine Davelaar[1], Pascal de Jong[1], Hannah den Braanker[1], Radboud Dolhain[1] and Erik Lubberts[2], [1]Erasmus University Medical Center, Rotterdam, the Netherlands, Rotterdam, Netherlands, [2]Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Regulatory T cells (Tregs) are essential for maintaining immune tolerance and limiting excessive immune responses. However, Tregs show high levels of heterogeneity and plasticity, indicated by the production of IL-17A. In rheumatoid arthritis (RA), IL-17A intensifies synovial inflammation by activating synovial fibroblasts. We aim to characterize Treg heterogeneity in RA patients and examine their functional characteristics and role in synovial inflammation.

Methods: CITE-seq was applied to T cells from four treatment-naïve RA patients and four healthy controls. Unsupervised clustering was performed to identify Treg subpopulations. These subpopulations were verified in PBMCs from 150 RA patients and 30 healthy controls using flow cytometry. A suppression assay was conducted to evaluate the suppressive

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Schematic overview of Treg subpopulation characteristics

capacity of the sorted Treg subpopulations. In addition, the cytokine-secreting potential of sorted Treg subpopulations was investigated using ELISA, as well as the effect of interaction with RA synovial fibroblasts on cytokine secretion.

Results: CITE-seq analysis from treatment-naïve early RA patients identified Treg subpopulations based on the presence of HLA-DR and CCR6. We verified the surface expression of HLA-DR and CCR6 on Tregs in PBMCs of patients with established RA, revealing a significant decrease in HLA-DR$^-$CCR6$^+$ Treg cells in RA patients compared to healthy individuals. Significantly fewer HLA-DR$^-$CCR6$^+$ Tregs were detected specifically in RA patients with moderate and severe disease activity.

We analysed suppressive function, cytokine secretion, and fibroblast interaction to investigate the functional differences between these subpopulations. We found that all Treg subpopulations suppress proliferation of CD4$^+$ responder cells. In addition, we revealed that activated HLA-DR$^-$CCR6$^+$ Treg exclusively secreted IL-17A. Co-cultures with RA synovial fibroblasts showed that HLA-DR$^-$CCR6$^+$ Tregs induced synovial fibroblast activation, indicated by the secretion of IL-6, IL-8, and MMP-3. Interestingly, IL-17A secretion was increased upon coculturing HLA-DR$^-$CCR6$^+$ Treg and synovial fibroblast , highlighting the potential plasticity of this HLA-DR$^-$CCR6$^+$ Treg subpopulation towards a proinflammatory phenotype.

Conclusion: Regulatory T cell subsets defined by HLA-DR and CCR6 markers were identified across different stages of RA and exhibited notable functional heterogeneity. Despite maintaining suppressive capacity, some subsets, particularly HLA-DR$^-$CCR6$^+$ Tregs, displayed pro-inflammatory features, including IL-17A secretion and activation of synovial fibroblasts. These findings underscore the complexity of Treg biology in RA and suggest that HLA-DR$^-$CCR6$^+$ Tregs may paradoxically contribute to disease progression under inflammatory conditions.

Disclosure: B. Heeswijk: None; **M. Bongenaar**: None; **N. Davelaar**: None; **P. de Jong**: AbbVie/Abbott, 1, 5, 6, Eli Lilly, 5; **H. den Braanker**: None; **R. Dolhain**: Abbvie, 6, AstraZeneca, 6, Eli Lilly, 6, Galapagos, 5, Genzyme, 6, Novartis, 6, Roche, 6, UCB, 5, 6; **E. Lubberts**: None.

Abstract Number: 0979

IL-23 upregulates IFN-γ secretion in Th17.1, but not in Th17 or classical Th1 cells

Bennie van Heeswijk[1], Wida Razawy[2], Anne-Marie Mus-Otten[3], Patrick Asmawidjaja[2], Pieter Leenen[2] and Erik Lubberts[4], [1]Erasmus MC, University Medical Center Rotterdam, Hoofddorp, Netherlands, [2]Erasmus University Medical Center, Rotterdam, the Netherlands, Rotterdam, Netherlands, [3]Erasmus medical center, Rotterdam, Netherlands, [4]Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin-23 (IL-23) is a key cytokine in the pathogenesis of psoriatic diseases, as demonstrated by the clinical success of IL-23-targeted therapies. Monocytes are a primary source of IL-23, contributing to the inflammatory milieu.

IL-23 is known to drive the pathogenicity of T-helper (Th) cells with a $CCR6^+$ phenotype; however, its specific effects on distinct memory T cell subsets remain poorly defined. The $CCR6^+$ Th population is heterogeneous, comprising Th17 cells, which predominantly produce IL-17A, and Th17.1 cells, which mainly secrete interferon-gamma (IFN-γ). We aim to characterize the interactions between IL-23 and the different CCR6+ Ths, which is essential for advancing our understanding of psoriatic disease mechanisms and improving therapeutic strategies.

Methods: Human CCR6+, CCR6-, Th17, Th17.1 and classical Th1 cells were sorted from peripheral blood mononuclear cells (PBMCs). Transcription of IL-23R was determined with RT-PCR. CCR6+, CCR6-, Th17, Th17.1 and Th1 cells were stimulated with αCD3/αCD28, in the presence or absence of IL-23 for 72h before measuring cytokine secretion with ELISA. CD14+ monocytes were isolated using MACS and cocultured with Th cell populations before measuring IFN-γ secretion with ELISA.

Results: Ex vivo analysis revealed that $CCR6^+$ T-helper cells expressed significantly higher levels of IL-23R mRNA compared to $CCR6^-$ counterparts. Upon stimulation with IL-23, $CCR6^+$ Th cells secreted significantly more interferon-gamma (IFN-γ), but not interleukin-17A (IL-17A). To account for the heterogeneity within the $CCR6^+$ population, memory Th17, Th17.1, and classical $CCR6^-$ Th1 cells were further sorted and analyzed. Both Th17 and Th17.1 cells exhibited higher IL-23R expression than Th1 cells. Following IL-23 stimulation, Th17.1 cells produced significantly more IFN-γ, whereas Th17 and Th1 cells did not. IFN-γ was found to induce IL-23 production in $CD14^+$ monocytes. In co-culture experiments with monocytes, Th17.1 cells secreted significantly more IFN-γ than classical Th1 cells.

Conclusion: T-helper cell subsets exhibit distinct responses to IL-23, particularly in their ability to produce IFN-γ. Our data show that IL-23 selectively induces IFN-γ secretion in Th17.1 cells, but not in Th17 or classical Th1 cells. Additionally, IFN-γ promotes IL-23 production by monocytes, suggesting a proinflammatory feedback loop that may amplify Th17.1-mediated inflammation. When co-cultured with monocytes, Th17.1 cells produced more IFN-γ than Th1 cells,

Schematic overview of the IL-23/IFNg proinflammatory feedback loop.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

further underscoring their heightened pro-inflammatory potential. These findings highlight a unique IL-23–IFN-γ axis in Th17.1 cells that may contribute significantly to local tissue inflammation in psoriatic diseases.

Disclosure: B. van Heeswijk: None; **W. Razawy**: None; **A. Mus-Otten**: None; **P. Asmawidjaja**: None; **P. Leenen**: None; **E. Lubberts**: None.

Abstract Number: 0980

Expansion of Viral-Reactive CD8+ T cell Repertoire Stratified by Pathotype in New-onset ACPA+ Rheumatoid Arthritis

Carl Coyle[1], Wittaya Suwakulsiri[2], Lukas Andriessen[3], Megan Soon[4], Pascale Wehr[5], Sumera Qureshi[6], Christopher Altmann[7], Annabelle Small[8], Vincent Wong[9], Andrew Cope[6], Kevin Wei[10], Hendrik Nel[5], Mihir Wechalekar[11] and Ranjeny Thomas[2], [1]Kings College London, London, United Kingdom, [2]Frazer Institute, University of Queensland, Brisbane, Queensland, Australia, [3]Frazer Institute, University of Queensland, Woolloongabba, Queensland, Australia, [4]Frazer Institute, The University of Queensland, Brisbane, Australia, [5]University of Queensland, Woolloongabba, Queensland, Australia, [6]King's College London, London, United Kingdom, [7]Flinders University, Adelaide, Australia, [8]Flinders University, Bedford Park, South Australia, Australia, [9]College of Medicine and Public Health, Bedford Park, South Australia, Australia, [10]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [11]Flinders Medical Centre, Adelaide, Australia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Development of Rheumatoid Arthritis (RA) is strongly associated with specific *HLA-DRB1* genotypes and the HLA-DR antigen binding groove, the shared epitope. *HLA-B*08* also increases risk of ACPA+ RA, and large numbers of CD8+, including granzyme K (GZMK)+ tissue-resident T cells (Trm), infiltrate RA synovial tissue (ST) in active, established RA. ST from DMARD-naïve patients can be classified into lymphomyeloid (LM), diffuse myeloid (DM) or pauci-immune (PI) "pathotypes". While most T cell receptor (TCR) repertoire analysis focused on highly inflamed LM ST, TCR repertoires of DM and PI ST are poorly characterized.

Methods: We compared CD45+ antigen-presenting cells (APCs) and TCR repertoire in arthroscopic ST and paired peripheral blood (PB) from 9 recent-onset DMARD-naïve ACPA+ DM- or PI-pathotype RA patients with symptom duration up to 1 year, using single-cell(sc) RNA/TCR-sequencing (all except one *HLA-DRB1*04:01* shared-epitope+). ST biopsies from 9 ACPA+ DM and 10 PI pathotyped RA patients were imaged using spatial transcriptomic profiling (5,101 genes, 10x Genomics).

Results: scRNAseq identified PB classical and non-classical monocytes, dendritic cells (DCs). In ST, myeloid DCs and macrophages were enriched in APC and lymphocyte-activation genes. In PI pathotype PB non-classical monocytes, ST myeloid DCs and macrophages were reduced compared to DM pathotype. CD4+ T cells had limited clonal expansion. The repertoire included public non-expanded viral-reactive clonotypes. Most memory CD8+ T cells expressed *GZMB, GRZK* or both. *GZMK+GZMB+/-* CD8+ T cell clones were moderately expanded and expressed Trm markers in ST, while *GZMB+GZMK-* CD8 clones were highly-expanded in PB. Grouping of lymphocyte interactions by paratope hotspots (GLIPH) identified cytomegalovirus (CMV) and Epstein-Barr virus (EBV)-reactive TCRs, which were GZMB+ in PB, and often shared in ST as GZMK + Trm. CMV-reactive clonal expansion occurred in DM and PI pathotypes, restricted by HLA-A*02:01 and HLA-A*03:01 evenly across pathotypes. In contrast, EBV-reactive clonal expansion (*GZMK*+, HLA-B*08-restricted) was highly-enriched

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

in the PI pathotype. Xenium spatial imaging in DM and PA ST identified small numbers of infiltrating *GZMB+GZMK+/-* CD8+ T cells and rare plasma cells. Besides larger macrophage infiltrates and expanded lining fibroblasts, PI T-cell infiltrates in DM were distinguished from PI pathotype by adjacent *Clec9A+* DCs or type 1 interferon-induced *CXCL11*.

Conclusion: The data suggest strong CD8+ PB clonal expansion towards latent viruses and bystander ST infiltration in early ACPA+ RA of both pathotypes, but with *HLA-B*08*-restriction skewed to EBV-reactive Trm in PI. MHC class I genes may shape the CD8+ Trm repertoire, viral antigen presentation and ST pathology in RA.

Disclosure: C. Coyle: None; **W. Suwakulsiri**: None; **L. Andriessen**: None; **M. Soon**: None; **P. Wehr**: None; **S. Qureshi**: Bristol-Myers Squibb(BMS), 5; **C. Altmann**: None; **A. Small**: None; **V. Wong**: None; **A. Cope**: Bristol-Myers Squibb(BMS), 2, 5, 6; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **H. Nel**: None; **M. Wechalekar**: GlaxoSmithKlein(GSK), 5, Janssen, 5; **R. Thomas**: AbbVie/Abbott, 2, CSL, 2.

Abstract Number: 0981

GNTI-350: A CAR-Treg Therapy Offering Durable Immune Reset with Improved Safety for B Cell–Driven Autoimmune Diseases

Christopher Moore[1], Travis Drow[2], Peter Cook[2], Annaiz Grimm[2], Victoria DeVault-Nelson[1], Jennifer Mellen[1], Payam Zarin[1], Alaina Burgess[1], Maegan Hoover[1], Tingxi Guo[1], Brock McKinney[2], Noelle Dahl[2], Aesha Vakil[2], Brian Christin[3], Gene Uenishi[1], Tiffany Chen[1], Alberto Del Rio-Espinola[4], David Rawlings[2] and Tom Wickham[1], [1]GentiBio, Cambridge, [2]SCRI, Seattle, [3]GentiBio, Seattle, [4]GentiBio, Basel, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: CD19 CAR T therapies have demonstrated promise in systemic lupus erythematosus (SLE) by transiently depleting B cells and resetting the immune system. However, long-term remission may require sustained regulation of autoreactive immune responses, including suppression of T follicular helper (Tfh) cells that drive pathogenic B cell maturation in germinal centers (GCs). Additionally, limitations such as cytokine release syndrome (CRS), neurotoxicity, and the cost of autologous manufacturing restrict applicability of current CAR T approaches in autoimmune settings.

Methods: To overcome these limitations, we developed GNTI-350, an allogeneic CD19 CAR-engineered regulatory T cell (CAR19 EngTreg) therapy designed to achieve robust immune reset by combining the B cell depletion capacity of CAR T cells with the suppressive function of Tregs. GNTI-350 cells are generated using a proprietary platform enabling (1) stable FOXP3 expression for lineage commitment, (2) a CD19-targeted CAR for selective B cell engagement, and (3) a chemically-inducible IL-2–like signaling complex (CISC) that supports Treg function in IL-2–deficient autoimmune settings through rapamycin addition. The platform enables efficient manufacturing with high purity and scalability.

Results: In vitro, CAR19 EngTregs exhibited hallmark Treg markers (FOXP3, CD25, CTLA-4, ICOS) and drove primary B cell depletion, while maintaining low inflammatory cytokine production (IFNγ, TNFα, IL-6) compared to CAR19 T effectors. Additionally, CAR19 EngTregs suppressed T cell proliferation, blocked B cell differentiation, and reduced immunoglobulin production. In vivo studies in the SLE123 model also demonstrated short-term depletion of peripheral B cells followed by a return to baseline levels within one month, mirroring transient clinical CAR19 T effectors. However, GNTI-350 achieved sustained immunologic reset: EngTregs persisted for over 7 months, suppressed Tfh cells, reduced GC B cells, lowered

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disease-driving autoantibodies, and decreased kidney damage markers. Notably, these data demonstrate CAR19 EngTregs drive dual modulation of B and T cells, mimicking the function of follicular regulatory T cells (Tfr) that naturally restrain GC activity. In this context, GNTI-350 acted as a "super Tfr" by simultaneously suppressing Tfh cells and GC B cells—thereby disrupting the regeneration of pathogenic B cells and autoantibodies.

Conclusion: GNTI-350 is a first-in-class, allogeneic, antigen-targeted Treg therapy with the capacity to act as a potent "super Tfr," disrupting germinal center pathology by concurrently targeting B cells and Tfh cells. This dual mechanism offers a durable and safe immune reset, distinguishing GNTI-350 as a promising therapeutic candidate for B cell–driven autoimmune diseases such as SLE.

Disclosure: C. Moore: GentiBio, 3; **T. Drow**: GentiBio, 5; **P. Cook**: GentiBio, 5; **A. Grimm**: GentiBio, 5; **V. DeVault-Nelson**: GentiBio, 3; **J. Mellen**: GentiBio, 3; **P. Zarin**: GentiBio, 3; **A. Burgess**: GentiBio, 3; **M. Hoover**: GentiBio, 3; **T. Guo**: GentiBio, 3; **B. McKinney**: GentiBio, 5; **N. Dahl**: GentiBio, 5; **A. Vakil**: GentiBio, 5; **B. Christin**: GentiBio, 3; **G. Uenishi**: GentiBio, 3; **T. Chen**: GentiBio, 3; **A. Del Rio-Espinola**: GentiBio, 3; **D. Rawlings**: GentiBio, 12, 1, 5, 10; **T. Wickham**: GentiBio, 3.

Abstract Number: 0982

Impact of Immunosuppressive Therapies on Shingrix Vaccine Response in Immune-Mediated Inflammatory Diseases

Cristiana Sieiro[1], Juan García Herrero[2], Jose Ordas Martínez[3], Carolina Álvarez Castro[3], Alejandra López Robles[3], Ronald Colindres[3], Ana María Sahagún[4] and Jose María Ruiz de Morales[3], [1]Univrsity of Manchester, Manchester, United Kingdom, [2]complejo asistencial universitario de leon, León, Spain, [3]Complejo Asistencial Universitario de León, León, Spain, [4]University of Leon, León, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Herpes zoster (HZ) is a common infection, particularly in older adults and women, and can lead to complications like neuropathic pain. The risk is higher in immunosuppressed individuals. Shingrix™, a recombinant subunit vaccine, has proven effective in reducing HZ risk by stimulating robust CD4 and CD8 T-cell responses. However, data on its immunogenicity in patients with immune-mediated inflammatory diseases (IMIDs) remains limited.

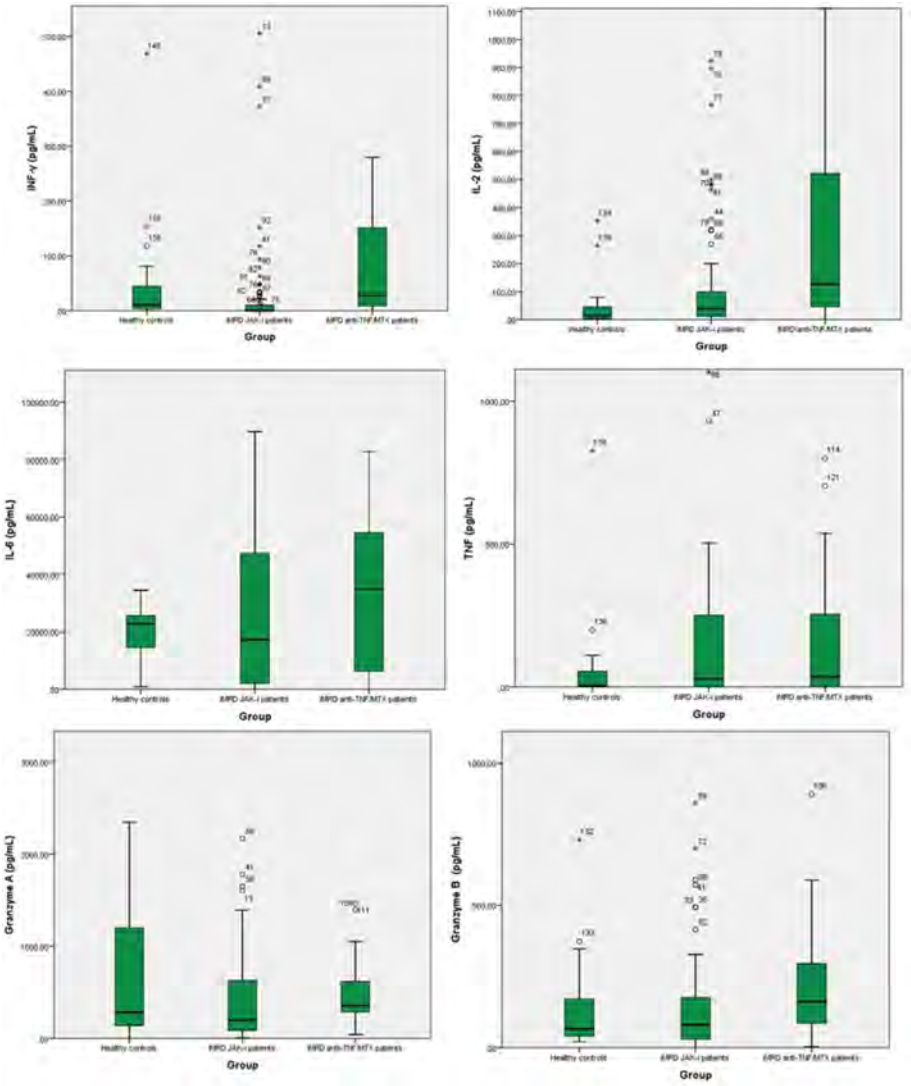
This study aimed to evaluate B-cell and T-cell immune responses to the recombinant HZ vaccine in IMID patients treated with JAK inhibitors (JAK-i), anti-TNF therapies, or methotrexate (MTX), and to identify factors associated with reduced vaccine-induced immunity.

Methods: This study investigated both humoral and cellular immune responses following a two-dose regimen of the recombinant inactivated vaccine in 131 patients with IMIDs treated with JAK inhibitors, anti-TNF therapy, or MTX. The results were compared to those of 27 healthy controls matched for age and sex. Cellular immune responses were assessed through CD4+ (Th1) and CD8+ (cytotoxic) T-cell activation, while VZV-specific IgG antibody levels were used to evaluate humoral responses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	T-CD4 response	T-CD8 response	VZV antibody concentration
Bariticinib	**β=-0.31, p=0.0002**	**β =-0.22, p=0.006**	**β=-0.18, p=0.03**
Tofacitinib	**β =-0.26, p=0.001**	β =-0.19, p=0.12	**β=-0.26, p=0.001**
Upadacitinib	**β =-0.24, p=0.002**	β =-0.16, p=0.44	β =-0.04, p=0.60
Anti-TNF/MTX	β =-0.26, p=0.06	β =-0.05, p=0.09	β =-0.34, p=0.06
Age	β =0.02, p=0.81	β =0.02, p=0.76	β =0.11, p=0.14
Gender	β =-0.03, p=0.74	β =-0.02, p=0.81	β =-0.004, p=0.96
Disease duration (years)	β =-0.07, p=0.43	β =-0.03, p=0.77	β =-0.08, p=0.37
=2 DMARDs	**β =-0.30, p=0.0002**	**β =-0.20, p=0.01**	**β =-0.28, p=0.0002**
Treatment duration with JAK-i (months)	**β =-0.30, p=0.0002**	**β =-0.20, p=0.01**	**β =-0.28, p=0.0002**
Cumulative MTX dose	**β =-0.28, p=0.002**	β =-0.1, p=0.24	**β =-0.25, p=0.002**
Cumulative GC dose	**β =-0.40, p=0.0002**	**β =-0.24, p=0.003**	**β =-0.36, p=0.0002**

Correlations between T-CD4 response, T-CD8 response, and VZV antibody concentration with JAK-I, anti-TNF/MTX, age, gender, disease duration, treatment with ≥2 DMARDs, treatment duration with JAK inhibitors, and cumulative doses of MTX and GC. Linear logistic regression coefficients (β) and p-values are presented, with significant parameters highlighted in bold.



Comparison of post-vaccination concentrations of granzyme A (2a), granzyme B (2b), TNF (2c) and IL-6 (2d) in healthy controls, IMRD JAK-I and IMRD anti-TNF/MTX patients. Higher levels of granzyme B (p=0.03), IL-6 (p=0.005) and IL-2 (p<0.0001) were observed in patients treated with anti-TNF/MTX as compared with baricitinib, tofacitinib and upadacitinib. Box-and-whiskers, 5–95 percentile, ANOVA test (3A–3D). P values are indicated above each graph.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 157 participants (mean age 58.2 years), JAK-i users had significantly lower immune responses. Seroconversion was 86% in JAK-i patients, compared to 97% in anti-TNF/MTX and 100% in controls (P = 0.03). VZV IgG titers were significantly lower in the JAK-i group (mean 1842 U/mL) versus anti-TNF/MTX and controls (both ∼3,000 U/mL, P < 0.0001). Only 28% of JAK-i patients had a full CD4+ Th1 response (vs. 74% anti-TNF/MTX, 93% controls), and CD8+ responses were similarly reduced (29% vs. 42% and 85%, respectively). Immunogenicity was negatively associated with cumulative MTX and glucocorticoid use, prior DMARDs, baricitinib and tofacitinib treatment, and longer JAK-i exposure. A positive correlation was seen between CD4+ and CD8+ responses (β = 0.36, P = 0.0002).

Conclusion: IMID patients treated with JAK inhibitors exhibit significantly reduced humoral and cellular immune responses to the HZ recombinant vaccine, suggesting lower protection against VZV reactivation. While some reduction was seen in the anti-TNF/MTX group, their immune responses remained relatively preserved. The findings underscore the impact of JAK inhibitors and cumulative immunosuppression on vaccine efficacy in this population.

Disclosure: c. Sieiro: None; **J. García Herrero**: None; **J. Ordas Martínez**: None; **C. Álvarez Castro**: None; **A. López Robles**: None; **R. Colindres**: None; **A. Sahagún**: None; **J. Ruiz de Morales**: None.

Abstract Number: 0983

Detecting Autoreactive CD4+ T Cells Relevant to Mixed Connective Tissue Disease

Grace Frechette, Thamotharampillai Dileepan, Marc Jenkins and Shawn Mahmud, University of Minnesota, Minneapolis

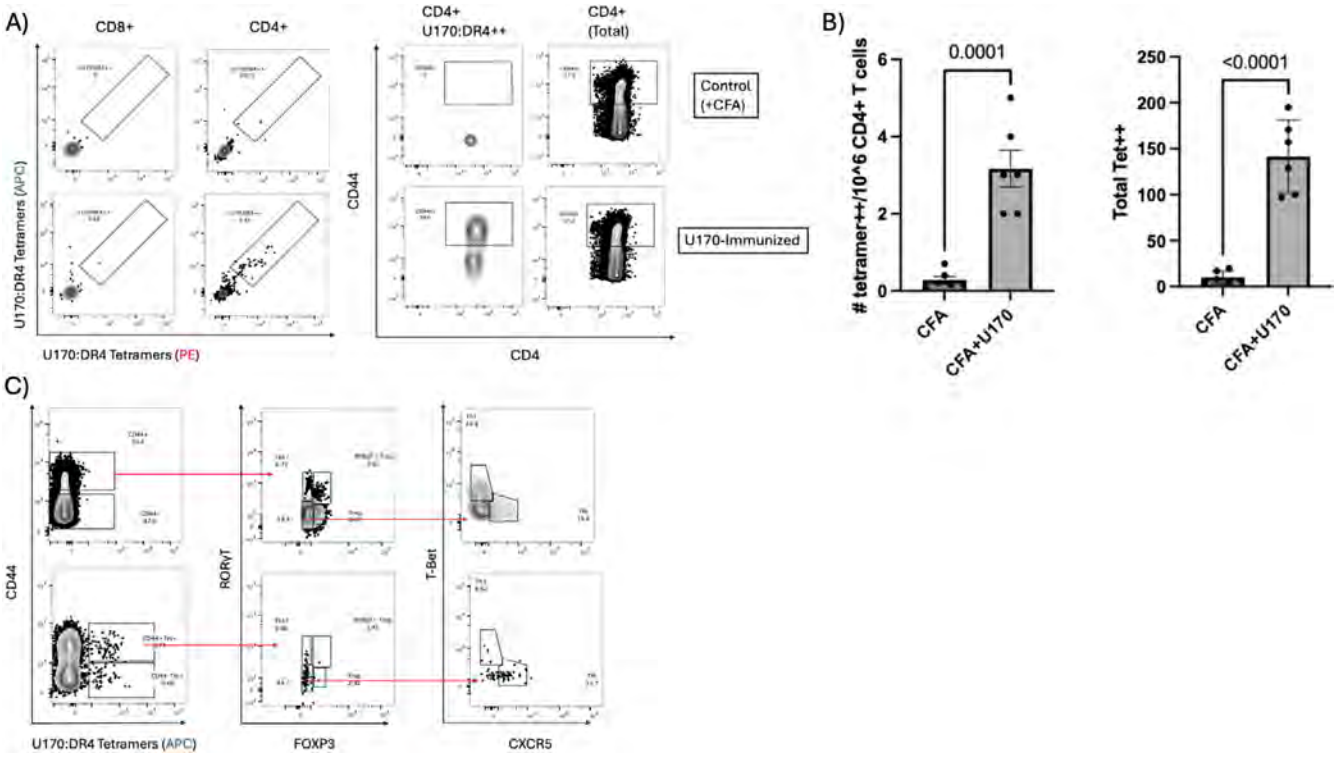
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Mixed connective tissue disease (MCTD) is a systemic autoimmune disorder marked by a U1-small nuclear ribonucleoprotein (U1-snRNP) autoantibody. The majority of U1-snRNP antibodies in MCTD target the 70 kD subunit of the protein complex (U170). How self-reactive T and B cells cooperate to drive autoantibody production in MCTD is unknown. Here, we use novel tetramers of U170 peptides bound to HLA-DRB1*0401 (U170:DR4) to detect self-reactive CD4+ T cells in a previously published mouse model of MCTD and diseased human patients. Our goals are to quantify and better characterize self-reactive CD4+ T cells in MCTD, which may eventually drive development of antigen-specific immunotherapy.

Methods: Because MCTD is linked to DR4, we use commercially available DR4 transgenic mice as previously published. We generated fluorophore-labeled DR4 tetramers with peptides bioinformatically predicted to bind DR4. We used these reagents to stain and magnetically enrich U170:DR4-specific CD4+ T cells from mice immunized with human U170 and separately from human peripheral blood mononuclear cells (PBMCs) from diseased patients. In mice, U170-specific antibodies and blood cells were quantified with a commercially available ELISA and flow cytometry, respectively.

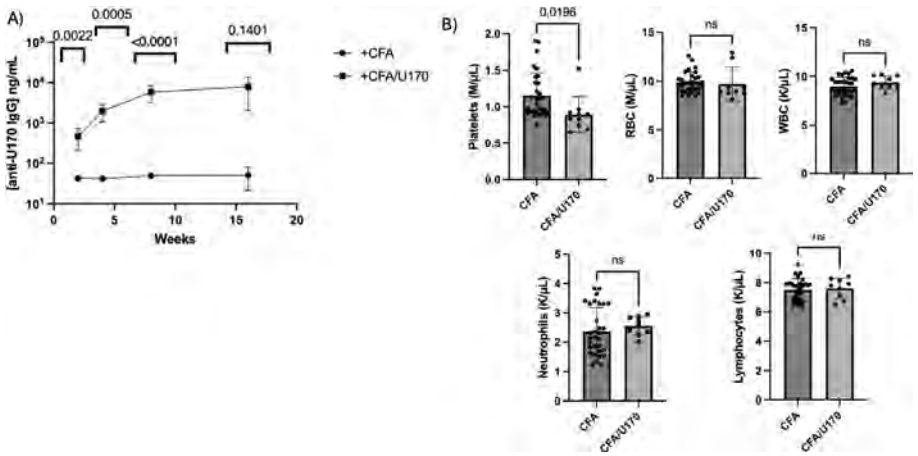
Results: Our novel U170:DR4 tetramers identified mouse CD4+ T cells expanding and upregulating CD44 and differentiating into Th1, Th17, and Tfh (Fig. 1). U170-specific antibody production in DR4 Tg mice accelerates until six weeks and plateaus (Fig. 2). Mice also develop a mild thrombocytopenia 8-10 weeks after immunization. Lastly, U170:DR4-specific tetramers detected rare CD45RA low (memory) cells in a DR4 positive MCTD patient (Fig. 3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



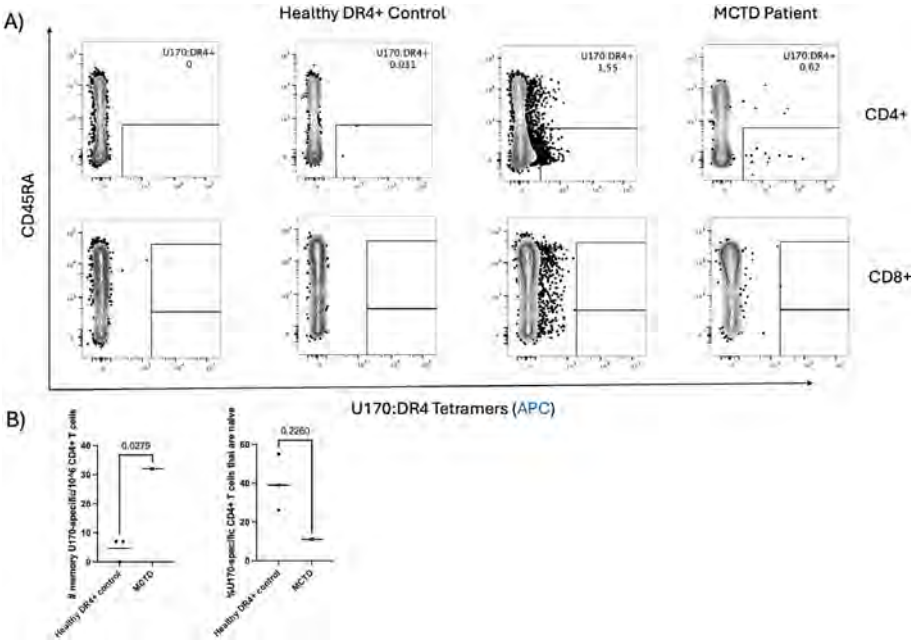
Expanding and activated mouse U170-specific CD4+ T cells primarily become Th1, Tfh, and Th17 cells in DR4-Tg mice immunized with recombinant U170 protein. DR4 Tg mice (both sexes, n=6 each group) were subcutaneously immunized with human recombinant U170 protein emulsified in CFA, and secondary lymphoid organs stained with U170:DR4 tetramers and surface markers as displayed in (a), and quantified in (b) (mean ±SEM, Mann-Whitney). (c) Analysis of phenotypes of bulk (top row) and tetramer+ cells (bottom row) with intracellular staining.

Conclusion: DR4 Tg mice produce autoantibodies in response to U170 immunization, and cognate U170-specific CD44+ T cells were detected alongside them using novel tetramers. U170-specific cells in mice were Th1, Th17, and Tfh. Mild thrombocytopenia, which is seen in MCTD, was also present at late time points in mice. Preliminary human data indicate these novel tetramers will be useful tools in longitudinal studies of humans with MCTD undergoing therapy and for development of specific treatments, such as chimeric antigen receptor (CAR) regulatory T cells.



DR4-Tg mice immunized with U170 develop U170-specific antibodies and mild thrombocytopenia. (a) DR4-Tg mice (n=14 each group at 2-8 weeks, n=5 each group at 16 weeks) were immunized with U170 protein. U170-specific antibodies were measured over time with ELISA modified to detect mouse IgG (mean ±95% CI). (b) Flow cytometry-based enumeration of platelets, red blood cells (RBC), leukocytes (WBC, neutrophils, lymphocytes) (n=9, 8-10 weeks post-immunization, mean ±SEM, Mann-Whitney).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Detection of U170-specific T cells in healthy humans and MCTD patients. PBMCs were isolated and stained with U170:DR4 tetramers and surface markers as shown in (a) and quantified in (b) (n=3 healthy control, 1 patient; mean, Mann-Whitney).

Disclosure: G. Frechette: None; **T. Dileepan**: None; **M. Jenkins**: None; **S. Mahmud**: None.

Abstract Number: 0984

Interleukin-21 as a driver of CD8 T cell tissue resident memory and pathogenesis in dermatomyositis

Heather Ren[1], havell Markus[2], Mackenzie Sennett[2], Acela Cristina Rosado[1], Matthew Helm[1], Aron Lukacher[2], Amanda Nelson[2] and Galen Foulke[1], [1]Penn State Health, Hershey, PA, [2]Penn State College of Medicine, Hershey, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis is an autoimmune disease characterized by skin and muscle pathology and can feature significant morbidity and mortality from interstitial lung disease (ILD). Dermatomyositis is traditionally considered an antibody-mediated disease driven by pathogenic CD4 T cells and B cells as there are multiple myositis specific antibodies identified in dermatomyositis. These myositis-specific antibodies can have significant differences in disease progression. CD4 T cell-derived IL-21, a cytokine best known for its stimulation of B cells during the germinal center response, may be a driver of dermatomyositis. While IL-21 likely plays a role in stimulating myositis specific antibody production, IL-21 has also been identified as a CD4 T cell-derived driver of CD8 T cell differentiation to tissue resident memory cells (T_{RM}). T_{RM} are named for their abilities to be maintained independent of the circulation in non-lymphoid tissues and rapidly release effector molecules during antigen re-encounter which we hypothesized could be an important step in the pathogenesis of dermatomyositis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We performed immunofluorescence labeling for CD4, CD8, and IL-21 on skin biopsy samples from dermatomyositis patents. We also obtained single-cell RNAseq data from the lungs of a patient with MDA5+ dermatomyositis and subsequent ILD. Using the RNAseq data, we analyzed the CD8 T cells for IL-21 receptor expression and gene expression profiles of tissue resident memory.

Results: We show that IL-21 is present in active dermatomyositis skin lesions and that IL-21 is present in areas with high CD4 T cell and CD8 T cell infiltrates. We also show with the single-cell RNAseq data that lung CD8 T cells highly express the IL-21 receptor compared to CD8 T cells from the lungs of controls. Gene set enrichment analyses showed significant enhancement in the expression of T_{RM} genes in the CD8 T cells from the dermatomyositis lung.

Conclusion: These data suggest IL-21 could be an important, understudied driver of ILD in dermatomyositis, and a potential therapeutic target. Specifically, IL-21 may act on CD8 T cells to drive differentiation into long-lived T_{RM} in the tissues of dermatomyositis, likely contributing to tissue damage and clinical pathology.

Disclosure: H. Ren: None; **h. Markus**: None; **M. Sennett**: None; **A. Rosado**: None; **M. Helm**: None; **A. Lukacher**: None; **A. Nelson**: None; **G. Foulke**: None.

Abstract Number: 0985

Lupus Skin Shapes a Distinct Inflammatory Milieu that Drives the Skewing of Treg and inflammatory T cells

Hiroshi Kato[1], Lin Zhang[1], Mehrnaz Gharaee-Kermani[2], Amy Hurst[1], Rachael Bogle[3], Alex Tsoi[3], Johann Gudjonsson[2] and J. Michelle Kahlenberg[2], [1]Michigan Medicine, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan, Holland, OH

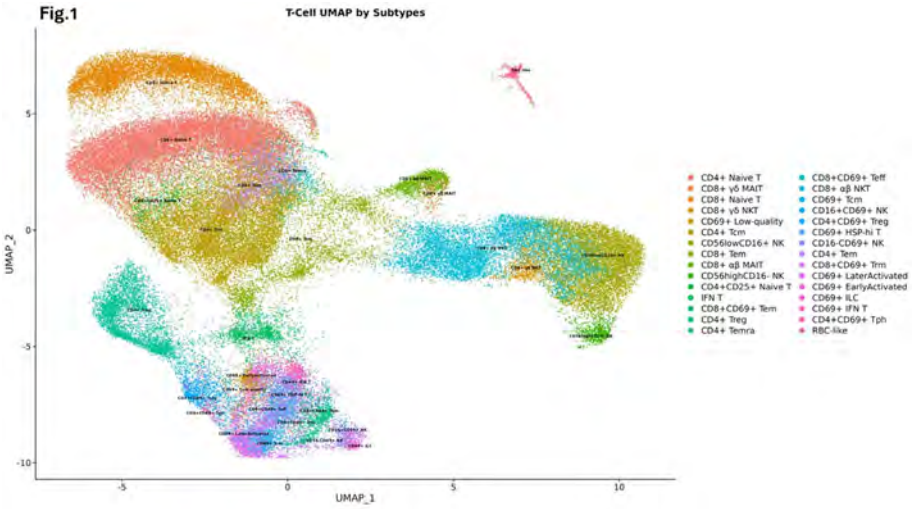
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is a frequent manifestation of systemic lupus erythematosus (SLE) and remains an important contributor to morbidity in lupus patients. Despite its clinical significance, the underlying mechanisms of CLE and its pathophysiological links to SLE are poorly understood. Importantly, new data support a critical difference between cutaneous and peripheral immune subsets in the same patient. This study aimed to elucidate the shifts in T cell and natural killer cell subsets from blood to lupus-affected skin.

Methods: We performed single-cell RNA sequencing of non-lesional and lesional skin biopsies and paired PBMCs from 17 patients with active CLE/SLE and non-lesional skin and PBMCs from 5 healthy controls via 10x Genomics pipelines. Cellular clustering and annotation were conducted using the Seurat R package by matching cluster-defining marker genes with canonical subtype signatures. To uncover key upstream regulators, we applied Ingenuity Pathway Analysis (IPA) to differentially expressed genes (DEGs). Cytokines and transcription factors with an activation z-score ≥2 or ≤–2 were considered significant regulators. Pseudotime trajectory was constructed using the R package Monocle.

Results: Visualization using uniform manifold approximation and projection (UMAP) revealed 30 distinct cell clusters (Figure 1). We identified transcription factor NONO and proinflammatory cytokines including type I interferons (IFNs), IL-1, IL-27, TNF and prolactin as primary upstream regulators of transcripts enriched in regulatory T cells (Tregs), interferon-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



UMAP plot of 92,405 cells colored by cluster

educated T (IFN-T) cells, and natural killer (NK) cells in lupus skin. These effects were observed when compared to both paired peripheral blood and healthy control skin (Figure 2), with the signaling being most pronounced in lesional as compared to non-lesional lupus skin. In contrast, the signaling of TGF-β, IL-4, MLXIPL, MYC, MYCN, SPEN, ETV3, and ETV6 was inhibited in Tregs in lupus skin compared to healthy controls. Furthermore, NONO and type I IFNs were important upstream regulators of gene expression in CD69^{lo} NK cells, while IL-1 and TGF-β were stronger regulators of gene expression in CD69^{hi} NK cells in skin. Trajectory analysis showed that circulating NK cells, IFN-T cells and Tregs upregulate CD69 whereas Tregs additionally acquire the expression of CTLA-4, GATA-3, heat shock protein, PD-1 and BATF as they infiltrate the skin.

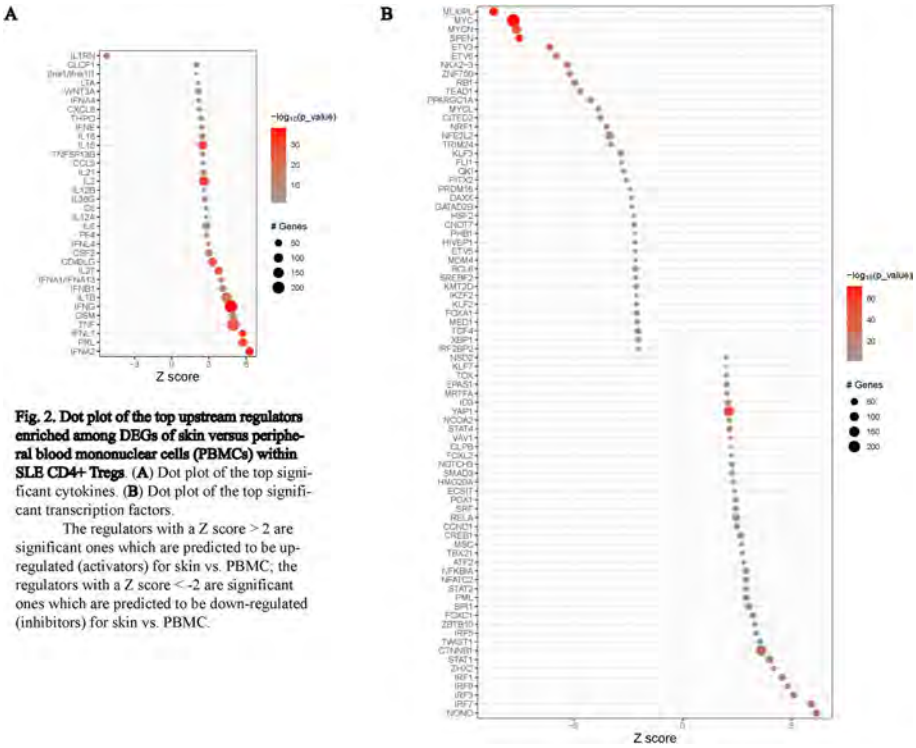


Fig. 2. Dot plot of the top upstream regulators enriched among DEGs of skin versus peripheral blood mononuclear cells (PBMCs) within SLE CD4+ Tregs. (**A**) Dot plot of the top significant cytokines. (**B**) Dot plot of the top significant transcription factors.

The regulators with a Z score > 2 are significant ones which are predicted to be up-regulated (activators) for skin vs. PBMC; the regulators with a Z score < -2 are significant ones which are predicted to be down-regulated (inhibitors) for skin vs. PBMC.

Dot plot of the top upstream regulators enriched among DEGs in Skin versus peripheral blood SLE Tregs

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our findings highlight the role of the skin in shaping an inflammatory profile in lupus Treg, IFN-T, and NK cell subsets. Treg development in lupus skin appears to shift from TGF-β- to type I IFN–mediated signaling. While NK cells, IFN-T cells and Tregs acquire activated phenotypes, Tregs additionally develop potentially exhausted phenotypes in SLE. NONO and type I IFNs contribute to the early programming of NK cells, while IL-1 drives their activation. These insights provide a deeper understanding of T cell–driven inflammation in CLE and may inform future therapeutic strategies.

Disclosure: H. Kato: None; **L. Zhang**: None; **M. Gharaee-Kermani**: None; **A. Hurst**: None; **R. Bogle**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **J. Gudjonsson**: None; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5.

Abstract Number: 0986

LBL-053, A Novel Anti-TL1A/p40 Bispecific Antibody for the Treatment of Autoimmune Disorders.

Shuijun Hu[1], Fengxia Li[1], Aixia Liu[1], Hailin Wang[1], Xiaoxiao Liu[1], Jianming Sun[1], Yurong Qin[1], Guojin Wu[1], Jing Guan[1], Hui Yuwen[1], Jordan Zhu[2], Xiaoqiang Kang[1], Xiao Huang[1] and **Hong Ling**[1], [1]Nanjing Leads Biolabs Co., Ltd., Nan Jing, China (People's Republic), [2]Nanjing Leads Biolabs Co., Ltd., Nan Jing

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory bowel disease (IBD) is a chronic, immune-mediated, inflammatory disease of the digestive tract. Several biological agents have greatly improved clinical course, remission, and complication rates in IBD patients. Ustekinumab, targeting p40 subunit, has demonstrated robust efficacy and approved for IBD. However, About 30% of patients are unresponsive to therapy , and 40% lose response over time,Therefore, more efficient therapies are needed. Recent studies showed that the Tumor necrosis factor-like cytokine 1A (TL1A) acts as a regulator of mucosal immunity and participates in immunological pathways involved in the IBD pathogenesis. Two anti-TL1A antibodies, MK-7240 and RVT-3101 have demonstrated excellent safety and effectiveness in patients with IBD. Therefore, a novel anti-TL1A/p40 bispecific antibody may hold promise in the treatment of autoimmune diseases including IBD.

Methods: An anti-TL1A monoclonal antibody was generated from mouse hybridoma and humanized by CDR grafting, then the anti-TL1A ScFv domain was fused to Ustekinumab using IgG1 Fc with LALAGA mutation. And YTE mutation was introduced to extend the half-life, creating the bispecific molecule: LBL-053. Binding affinity was assessed by Fortebio. The ligand-receptor interaction blocking capability of LBL-053 was evaluated by ELISA. The blocking efficacy of LBL-053 to TL1A and DR3 interaction was detected by reporter gene assay. The p40 and IL-12Rβ1 blocking efficacy was detected by ELISA and IFN-γ production inhibition assay .The synergistic effect of LBL-053 on TL1A and p40 was tested by IFN-γ production inhibition assay , which was conducted using $CD4^{+}$T cells cocultured with TL1A, IL-12 , IL-18 proteins and the drug. IL-23 and TL1A induced ear inflammation mouse model was used to test the in vivo efficacy of LBL-053 in which ear swelling symptoms alleviating degree was recorded. Single dose PK study was conducted in humanized FcRn mice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: LBL-053 antibody exhibited high binding affinity to human TL1A and IL-23 protein. It selectively blocked TL1A-DR3 interaction, leaving TL1A-DcR3 unaffected. The effect of LBL-053 on inhibiting TL1A-DR3 downstream signaling pathway was comparabile to RVT-3101, but better than MK-7240 and PF-07261271.LBL-053 also significantly blocked IL-23/IL-12Rβ1 interaction. The synergistic effect of LBL-053 on IFN-γ Inhibition using $CD4^+$T cells with targeting IL-23 and TL1A pathway simultaneously demonstrated greater activity than each individual monoclonal antibody, their combination and PF-07261271.The effect of LBL-053 in relieving ear swelling symptoms was better than each individual monoclonal antibody and their combination. LBL-053 exhibited excellent PK profile in humanized FcRn mice.

Conclusion: LBL-053 showed dual immunosuppressive functions, simultaneously inhibiting TL1A-DR3 and IL-23/IL-12Rβ1 signaling pathway, indicating promising clinical applications for the treatment of autoimmune diseases.

Disclosure: S. Hu: None; **F. Li**: None; **A. Liu**: None; **H. Wang**: None; **X. Liu**: None; **J. Sun**: None; **Y. Qin**: None; **G. Wu**: None; **J. Guan**: None; **H. Yuwen**: None; **J. Zhu**: None; **X. Kang**: None; **X. Huang**: None; **H. Ling**: None.

Abstract Number: 0987

S-4321, a novel dual-cell bifunctional PD-1:FcγRIIb selective agonist antibody for autoimmune disease, maintains expression of PD-1 on target cells and enhances inhibitory receptor expression on T cells *in vivo*

Julia Manasson[1], Michael Cianci[2], Minasri Borah[2], Stephanie Grebinoski[2], Joshua Vitlip[2], Stephen Lutz[2], Ishan Sharma[2], Elliott Wittenberg[2], Allison Colthart[2], Samuel Perry[2], Maria Cecilia Ramello[2], Chelsea R. Parker Harp[2], Jyothsna Visweswaraiah[2], Ryan Peckner[2], Alex Pellerin[2], Heather Vital[3], John Sundy[4], Nathan Higginson-Scott[2], Kevin L. Otipoby[2] and Daniela Cipolletta[2], [1]Seismic Therapeutic, New York, NY, [2]Seismic Therapeutic, Watertown, MA, [3]Seismic Therapeutic, Lexington, MA, [4]Seismic Therapeutic, Durham, NC

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: S-4321 is a novel antibody that agonizes the inhibitory PD-1 checkpoint receptor on T cells without competing for binding with its natural ligand, PD-L1, while selectively engaging and signaling through the inhibitory FcγRIIb on B cells/antigen presenting cells (APCs). S-4321 is expected to restore immune homeostasis in diseases such as RA, SLE, GCA, and IBD.

Methods: PD-1 expression was measured on activated T cells after culturing with S-4321 or benchmark PD-1 agonists. FcγRIIb selectivity of the S-4321 Fc domain was demonstrated via binding assays. The lack of proinflammatory activity of the S-4321 Fc domain was assessed using TNFα production from activated monocyte-derived dendritic cells or antibody-dependent cellular cytotoxicity (ADCC) of target Tregs by human NK cells. S-4321 was tested in *in vitro* Treg differentiation assays. S-4321 was assessed *in vivo* using the B6D2F1 model of GvHD and naïve mice and in cynomolgus monkeys.

Results: Treatment with S-4321 *in vivo* does not result in loss of PD-1 target expression, unlike first-generation PD-1 agonists. S-4321 enhances induced Treg (iTreg) differentiation ($p< 0.05$) *in vitro*. *In vivo*, S-4321 reduces T cell expansion and proinflammatory cytokine production ($p< 0.05$) in a murine model of GvHD and induces TIGIT expression on the surface of PD-1+ T cells in naïve mice. S-4321 demonstrates dose-proportional exposure and ∼70% bioavailability with subcutaneous dosing in cynomolgus monkeys.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In contrast to first-generation PD-1 agonists, treatment with S-4321 does not result in loss of PD-1 expression on T cells, induction of proinflammatory cytokines, or depletion of PD-1+ Tregs. S-4321 enhances TIGIT expression on PD-1+ T cells. S-4321 has the potential to restore immune homeostasis in cell-mediated autoimmune diseases and its high bioavailability will allow for convenient drug administration.

Disclosure: J. Manasson: Seismic Therapeutic, 3, 11; **M. Cianci**: Seismic Therapeutic, 3, 11; **M. Borah**: Seismic Therapeutic, 3, 11; **S. Grebinoski**: Seismic Therapeutic, 3, 11; **J. Vitlip**: Seismic Therapeutic, 3, 11; **S. Lutz**: Seismic Therapeutic, 3, 11; **I. Sharma**: Seismic Therapeutic, 3, 11; **E. Wittenberg**: Seismic Therapeutic, 3, 11; **A. Colthart**: Seismic Therapeutic, 3, 11; **S. Perry**: Seismic Therapeutic, 3, 11; **M. Ramello**: Seismic Therapeutic, 3, 11; **C. Parker Harp**: Montai, 3, Seismic Therapeutic, 3, 11; **J. Visweswaraiah**: Ampersand Biomedicines, 11, Seismic Therapeutic, 3, 11; **R. Peckner**: Seismic Therapeutic, 3, 11; **A. Pellerin**: Biogen, 12, Immediate family member has stock., Seismic Therapeutic, 3, 11; **H. Vital**: Relay Therapeutics, 11, Seismic Therapeutic, 3, 11; **J. Sundy**: Neutrolis, Inc, 4, 11, Rome Therapeutics, 2, 11, Sanofi S.A., 4, 11, Seismic Therapeutic, 3, 11, Upstream Bio, 2, 11; **N. Higginson-Scott**: ComboLink Therapeutics, 1, 11, Seismic Therapeutic, 3, 11; **K. Otipoby**: Eurofins Scientific, 12, Member of the Scientific Advisory Board, LogicBio Therapeutics, 2, Lucy Therapeutics, 2, Seismic Therapeutic, 3, 11; **D. Cipolletta**: Seismic Therapeutic, 3, 11.

Abstract Number: 0988

Distinct Effects of Inhibitory Receptor Agonism on RA Synovial CD4+ T Cell Functions

Kazuhiko Higashioka[1], John Sowerby[1], Kathryne Marks[2], Diana Pena-Nunez[1], Margaret Chang[3], Jonathan Coblyn[1], Elena Massarotti[1], Brian Jones[4], Ling-Yang Hao[4], Navin Rao[4] and Deepak Rao[2], [1]Brigham and Women's Hospital, Boston, [2]Brigham and Women's Hospital, Boston, MA, [3]Boston Children's Hospital, Boston, MA, [4]Janssen Research & Development, Spring House

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoreactive T cells play a crucial role in the autoimmune pathology of rheumatoid arthritis (RA). Activation of inhibitory receptors on T cells is a promising strategy to suppress RA immunopathology. However, the impact of various inhibitory receptors on pathogenic T cell functions in RA remains unclear. This study aimed to define the effects of three inhibitory receptors, PD-1, BTLA, and TIGIT, on activation and function of distinct synovial CD4 T cell populations.

Methods: To evaluate inhibitory receptor effects on cytokine production, we developed an artificial antigen presenting cell (APC)–T cell co-culture system delivering inhibitory signals to T cells. We used a murine fibroblast line engineered to express CD32 (Fc receptor), CD80 (a ligand for CD28) and CD58 (a ligand for CD2). We transduced PD-L2 (ligand for PD-1), HVEM (ligand for BTLA) or CD155 (ligand for TIGIT) into the APCs and assessed their impact on cytokine production by T cells or T cell subsets from RA synovial fluid or blood or tonsil. Additionally, we generated synovial organoids containing engineered fibroblast APCs co-expressing cadherin-11 and each inhibitor receptor ligand to study their functions in a 3D context.

Results: Among T cells from RA synovial tissue, PD-1, BTLA, and TIGIT were highly expressed on Tph and Tfh cells, with intermediate expression on other diverse synovial CD4 T cell populations. To functionally assess $CD4^+$ T cells from RA synovial fluid, we investigated the effects of inhibitory receptors on cytokine production by two populations: Tph cells ($PD\text{-}1^{hi}$

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

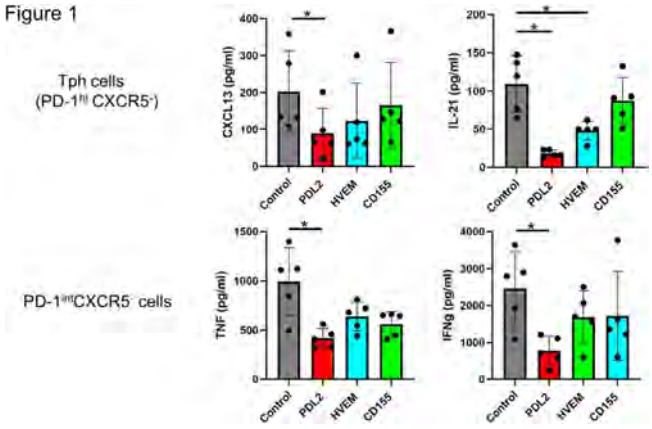


Figure 1. Effects of inhibitory receptor activation on cytokine production by synovial fluid CD4$^+$ T cells. Cytokine production by Tph cells (CXCL13 and IL-21) and PD-1intCXCR5$^-$ memory CD4+T cells (TNF and IFN-γ) from RA synovial fluid, co-cultured with APCs expressing PD-L2, HVEM, CD155, or control. Cytokine levels were measured by ELISA (n = 5 RA donors). *=P<0.05 (Tukey's multiple comparison test).

CXCR5$^-$) and PD-1^{int} CXCR5$^-$ cells. Among B cell helper cytokines produced by Tph cells, IL-21 was suppressed by PD-L2 and HVEM, while CXCL13 was suppressed by PD-L2. Analysis of inhibitory receptor function on PD-1^{int}CXCR5$^-$ cells showed that IL-2 production was suppressed by PD-L2, HVEM and CD155, while IFN-γ and TNF production were only significantly suppressed by PD-L2. In contrast, no effect of inhibitory receptors on IL-10 production was observed in PD-1^{int}CXCR5$^-$. In memory CD4$^+$ T cells from blood, PD-L2 reduced the production of TNF, CXCL13, IFN-γ, IL-21 and IL-2. HVEM suppressed TNF, IFN-γ and CXCL13, while CD155 selectively reduced CXCL13 levels. We compared these results to effects on tonsil CD4$^+$ T cell subsets, where PD-1^{hi} CXCR5^{hi} cells were identified as the primary source of CXCL13, PD-1^{int} cells showed a preference for IL-10 production, and PD-1$^{-/low}$ CXCR5$^-$ cells primarily secreted IL-2, IFN-γ and TNF. In this context, PD-L2 significantly suppressed the production of IL-2, TNF, IFN-γ and CXCL13 which was consistent with results using blood T cells. In the 3D synovial organoids, PD-L2 suppressed T cell proliferation and decreased the production of IFN-γ and TNF. In organoid containing of memory CD4$^+$ T cells, B cells and cadherin-11$^+$ APCs, PD-L2 reduced the number of T cell-B cell aggregates.

Conclusion: Our study demonstrates that the effects of inhibitory receptors on cytokine production vary across distinct CD4$^+$ T cell populations. Activation of PD-1 in particular showed strong suppressive activity in RA synovial T cells, highlighting its potential as a key modulator of pathogenic T cell responses in RA.

Disclosure: K. Higashioka: None; **J. Sowerby**: None; **K. Marks**: None; **D. Pena-Nunez**: Biogen, 3; **M. Chang**: None; **J. Coblyn**: None; **E. Massarotti**: EMD Serono, 1, Janux, 1, Xencor, 1; **B. Jones**: Janssen, 3; **L. Hao**: Janssen, 3; **N. Rao**: Janssen, 3; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2.

Abstract Number: 0989

Human MAIT cell produce IL-17 independently of IL-23 and TL1A

Kevin Hsu, Jessica Shannon, Zhiwei Fang, Anusara Daenthanasanmak, Prasad Srikakulapu, Tatiana Ort and Rafael de Queiroz Prado, AstraZeneca, Gaithersburg, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Mucosal-associated invariant T (MAIT) cells represent a specialized subset of T cells that exhibit innate-like, effector functions and have been implicated in the pathogenesis of several autoimmune disorders, including IL-17-driven diseases such as ankylosing spondylitis and hidradenitis suppurativa. MAIT cells are activated through recognition of microbial and self-metabolites presented by MR1, a non-polymorphic, MHC class I-like molecule. Upon activation, they amplify inflammation by producing pro-inflammatory cytokines (e.g., IFN-γ, TNF-α) and cytotoxic molecules such as perforin and granzyme B. Notably, MAIT cells are a potent source of IL-17A and IL-17F.

Methods: In this study, we investigated the requirement for IL-23 and TL1A, known Th17 driving cytokines, in regulating IL-17 production by MAIT cells. Using human peripheral blood mononuclear cells (PBMCs), we validated that proagent of 5-A-RU (p5-A-RU), a known MR1 ligand, specifically activates MAIT cells, as indicated by the selective upregulation of CD69 within the MAIT cell population. This activation was dependent on antigen-presenting cells (APCs), as depletion of monocytes and B cells abolished CD69 expression on MAIT cells.

Results: Furthermore, we demonstrated that p5-A-RU synergizes with IL-12 and IL-18 to drive the production of inflammatory effector molecules, including perforin, granzyme B, TNF-α, IFN-γ, and IL-17. Interestingly, IL-17A and IL-17F production was not enhanced by exogenous IL-23, nor was it reduced by the application of clinically validated neutralizing antibodies against these cytokines. In contrast, MR1 blockade completely abrogated MAIT cell activation in both PBMCs and human skin explants.

Previous work has shown that MAIT cells play a significant role in tissue repair. To explore the potential role of MAIT cells in tissue repair, we assessed the effect of conditioned media from activated MAIT cells on wound healing in vitro using primary human lung fibroblasts. No enhancement in wound repair was observed, suggesting that inflammatory MAIT cells may not contribute to tissue regeneration.

Conclusion: Collectively, our findings highlight a key role for IL-12 and IL-18 in driving IL-17A and IL-17F production by MAIT cells, independently of IL-23 and TL1A. This MR1-dependent activation pathway could represent a novel therapeutic target, particularly for IL-17-mediated autoimmune diseases such as ankylosing spondylitis and hidradenitis suppurativa.

Disclosure: K. Hsu: AstraZeneca, 3; **J. Shannon**: AstraZeneca, 3, 3; **Z. Fang**: AstraZeneca, 3; **A. Daenthanasanmak**: AstraZeneca, 3; **P. Srikakulapu**: None; **T. Ort**: AstraZeneca, 3; **R. de Queiroz Prado**: AstraZeneca, 3.

Abstract Number: 0990

An Fc-engineered Agonistic anti-pd-1 Antibody Selectively Depletes pd-1^{+} Cells and Attenuates T Cell Activation in vitro and in vivo in a Xenogeneic Graft-versus-host Disease (GvHD) Model

Laetitia Pouzol, Patrizia Murer, Nicole Egli, Laetitia Petersen, Anais Zurbach, christian Stocker, alexander Rau, andreas Katopodis and christoph huber, Anaveon, Basel, Switzerland

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: PD-1$^+$ T cells play a pivotal role in the pathogenesis of autoimmune diseases, including rheumatoid arthritis. Therapeutic antibodies targeting PD-1 with both depleting and agonistic functions have demonstrated the ability to selectively deplete T cells with high PD-1 expression, such as Tph and Tfh cells, and achieved notable clinical responses in patients with rheumatoid arthritis. However, PD-1 is expressed at varying levels across different pathogenic T cell subsets. Cells expressing low to intermediate PD-1 levels, such as cytotoxic CD8$^+$ T cell and Th1/Th17 subsets, also play pathogenic roles in autoimmunity. Therefore, therapeutic strategies capable of achieving broad depletion across this full spectrum of PD-1-expressing pathogenic T cells may offer superior benefits in treating autoimmune conditions. ANV200 is a novel, Fc-enhanced PD-1 agonistic antibody, engineered to drive robust and comprehensive depletion of PD-1-expressing pathogenic T cells.

Methods: The effects of ANV200 were assessed in human in vitro reporter cell assays and T cell activity functional assays. Then, the impact of ANV200 on circulating T cell subsets, including PD-1 expression levels, was evaluated in humanized PD-1 mice by flow cytometry. Finally, the efficacy of ANV200 was examined in a xenogeneic graft-versus-host disease (GvHD) model.

Results: ANV200 demonstrated enhanced engagement of FcγRIIIa compared to clinical benchmark antibodies while maintaining the ability to inhibit T cell receptor (TCR) signaling through PD-1 agonism. In addition, ANV200 exhibited a greater capacity to reduce human T cell activation relative to the benchmarks. In vivo, ANV200 selectively depleted PD-1$^+$ T cells without inducing a broad lymphopenia, resulting in a shift of the T cell compartment toward a more naïve state in humanized PD-1 mice. In the xenogeneic GvHD model, ANV200 effectively reduced the expansion of donor human T cells.

Conclusion: ANV200 is a novel, highly potent Fc-engineered anti-PD-1 agonistic antibody designed to deplete pathogenic T cells expressing high to low levels of PD-1. By targeting a broad spectrum of antigen-reactive T cells, ANV200 may potentially achieve deeper clinical response in autoimmune diseases.

Disclosure: l. Pouzol: Anaveon, 3; **P. Murer**: Anaveon, 3, ANAVEON AG, 3; **N. Egli**: Anaveon, 3; **L. Petersen**: Anaveon, 3; **A. Zurbach**: Anaveon, 3; **c. Stocker**: Anaveon, 3; **a. Rau**: Anaveon, 3; **a. Katopodis**: Anaveon, 3, 4, 8; **c. huber**: Anaveon, 3.

Abstract Number: 0991

MTHFD2 is a Novel Metabolic Target in Autoimmune Disease

Laura McMillan, Celia Evans, Marina Makrecka-Kuka, Niamh Richmond, Gareth Davies, Hamel Patel, Michael Herdman, Mark Whitmarsh, Alessandro Mazzacani, Peter Bunyard, Madduri Ravin Rao and Iain Kilty, Sitryx Therapeutics, Oxford, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Aberrant activation and persistence of adaptive immune responses play a central role in autoimmune pathogenesis. Where traditional immunosuppressive therapies offer a broad targeting approach, reprogramming the adaptive immune system at a metabolic level represents a novel therapeutic strategy to selectively modulate disease-driving populations. Methylenetetrahydrofolate dehydrogenase 2 (MTHFD2), a mitochondrial enzyme critical to the folate cycle is robustly expressed in inflammatory disease tissue and upregulated in activated lymphocytes, providing a unique

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

opportunity to target disease-relevant effector populations. We sought to develop MTHFD2-targeting inhibitors and to evaluate the effects of pharmacological MTHFD2 inhibition on key adaptive immune cell subsets and their therapeutic potential in models of autoimmunity.

Methods: The *in vitro* pharmacology of MTHFD2 inhibitors in specific lymphocyte subsets was tested in human primary immune cell cultures- key readouts included cell proliferation and cytokine production which were assessed using flow cytometry and HTRF. Human primary $CD4^+$ T cells were stimulated with anti-CD3 and anti-CD28 to assess impact on T helper function. Th17 polarization was performed using purified human memory $CD4^+$ T cells cultured under Th17-skewing conditions to assess effects on lineage commitment and effector cytokine production. Th1 antigen recall responses were explored in human PBMCs stimulated *ex vivo* using REVAXIS® (Diptheria, Tetanus and Poliomyelitis) antigens. B cell responses were analysed following BCR stimulation. *In vivo* efficacy was tested in a keyhole limpet hemocyanin (KLH)–induced delayed-type hypersensitivity (DTH) model and an adjuvant- induced arthritis (AIA) model in rat to assess impact of inhibition in autoimmune disease progression.

Results: MTHFD2 inhibition led to a marked reduction in the proliferation of $CD4^+$ T cells, accompanied by a decrease in Th1 and Th17 signatures, without affecting overall cell viability. During Th17 polarisation, IL-17 production was significantly diminished. Antigen recall assays showed reduced proliferation and IFNγ production upon MTHFD2 inhibition, indicating impaired memory Th1 cell function. In B cells, treatment suppressed proliferation and IgG secretion upon stimulation. *In vivo*, MTHFD2 inhibition reduced KLH-specific IgG levels and ear swelling in the DTH model. In the AIA model, treatment significantly decreased paw swelling, correlating with reduced inflammation and periosteal bone formation.

Conclusion: MTHFD2 inhibition modulates key adaptive immune pathways by targeting memory Th1/Th17 cells and B cell effector functions- suppressing pathogenic cytokine production and antibody responses central to autoimmune pathology. These findings highlight MTHFD2 as a promising metabolic checkpoint for therapeutic intervention in autoimmune disease, with dual action on both T and B cell arms of adaptive immunity.

Disclosure: L. McMillan: Sitryx Therapeutics, 3, 11; **C. Evans**: Sitryx Therapeutics, 3, 11; **M. Makrecka-Kuka**: Sitryx Therapeutics, 3, 11; **N. Richmond**: Sitryx Therapeutics, 3, 11; **G. Davies**: Sitryx Therapeutics, 3, 11; **H. Patel**: Sitryx Therapeutics, 3, 11; **M. Herdman**: Sitryx Therapeutics, 3, 11; **M. Whitmarsh**: Sitryx Therapeutics, 12, 3; **A. Mazzacani**: Sitryx Therapeutics, 12, 3; **P. Bunyard**: Sitryx Therapeutics, 3, 11; **M. Rao**: Autolus Therapeutics, 4, 11, DBV Technologies, 4, 11, OXB, 2, 4, 11, Sitryx Therapeutics, 12, 3, 4, Synact Pharma, 1, UCB Pharma, 1; **I. Kilty**: Sitryx Therapeutics, 12, 3, 4, 8, 11.

Abstract Number: 0992

FoxP3^{Lo} CD4$^+$ T cells are functionally suppressive and expanded in the immune-mediated fibrotic diseases IgG4-related disease and systemic sclerosis

Laura J. Yockey[1], Ian Doyle[2], Thomas Guy[3], Devanshi Trivedi[2], Chinmay Gadiraju[4], Federica Bonaso[5], Jesse Akaa[2], Alison Puri[6], Zachary Wallace[7], Guy Katz[8], Sydney Montesi[8], John Stone[9], Flavia Castelino[8], Shiv Pillai[10], Andrew Luster[11], Vinay S. Mahajan[12] and Cory Perugino[13], [1]MGH, Charlestown, MA, [2]Massachusetts General Hospital (MGH - Mass General) (MGB), Boston, MA, [3]Ragon Institute of MGH, MIT and Harvard/ Royal Prince Alfred Hospital Sydney, Sydney, Australia, [4]Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, [5]University of Brescia, ASST Spedali Civili of Brescia, Massachusetts General Hospital, Monza, Italy, [6]Boston University, Brookline, MA, [7]Massachusetts General Hospital, Newton, MA, [8]Massachusetts General Hospital, Boston, MA, [9]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [10]Harvard Medical School, Cambridge, MA, [11]Massachusetts General Hospital, Charlestown, MA, [12]Brigham and Women's Hospital, Boston, MA, [13]Massachusetts General Hospital, Harvard Medical School, Boston, MA

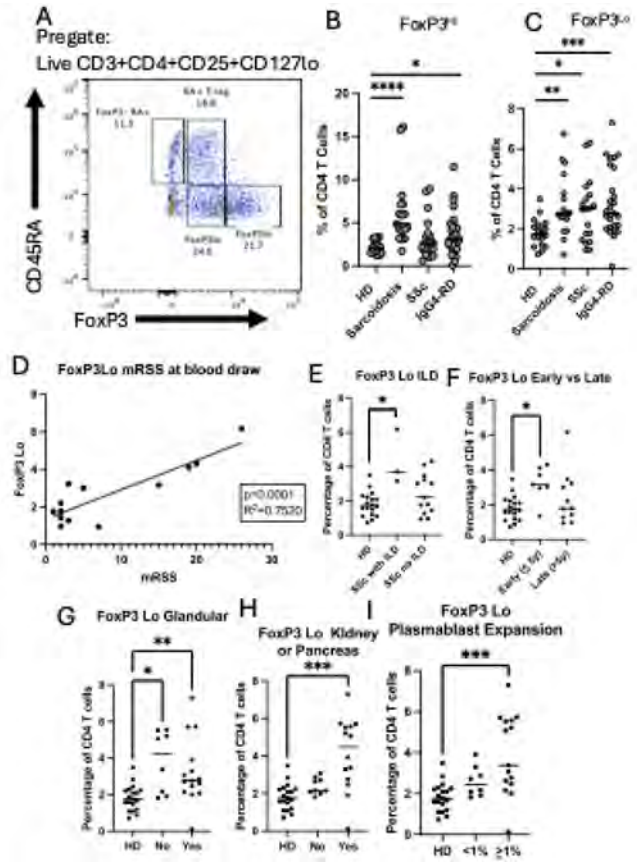
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

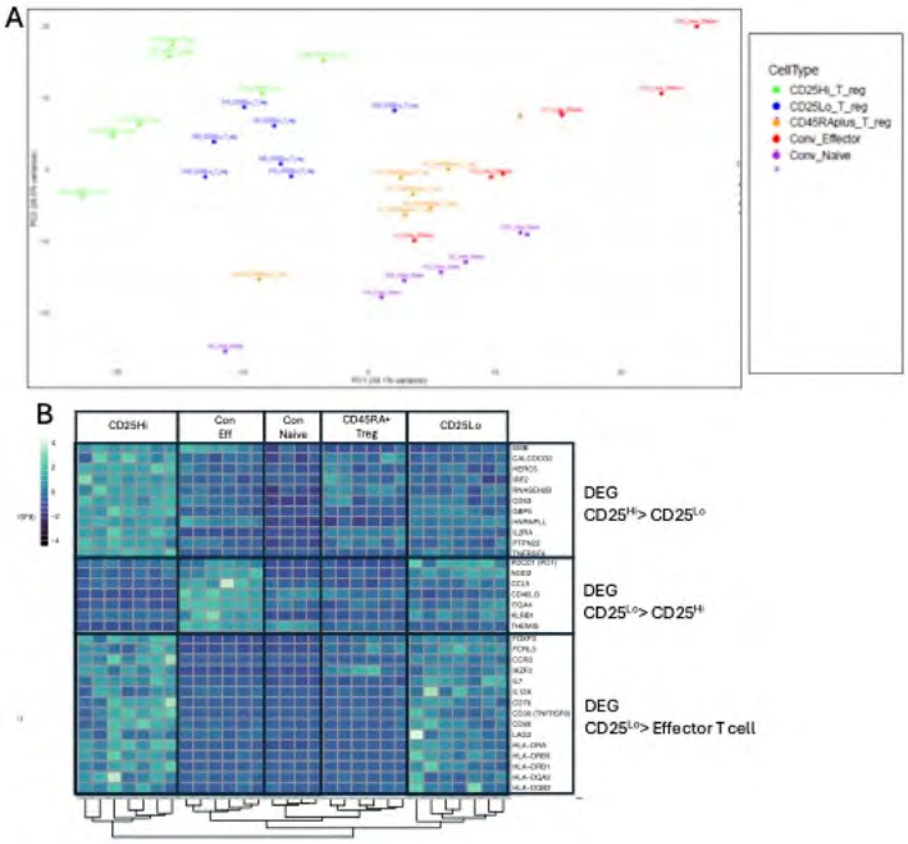
Background/Purpose: The absence of regulatory T cells (Tregs) results in multiorgan autoimmunity in the context of monogenic "Tregopathies," but their role in mediating polygenic autoimmune diseases remains less clearly defined. Antigen-experienced human T cells expressing FoxP3, a transcription factor driving regulatory function, can be divided into $FoxP3^{Lo}$ and $FoxP3^{Hi}$ subsets. $FoxP3^{Lo}$ T cells are expanded in the context of autoimmunity, but there is a paucity of data defining the function of $FoxP3^{Lo}$ T cells or their relevance to immune-mediated fibrosis. Previous studies suggest they are non-suppressive and primarily composed of activated effector T cells. We examined $FoxP3^{+}$ T cells across three different immune-mediated fibrotic diseases, systemic sclerosis (SSc), IgG4-related disease (IgG4-RD), and sarcoidosis.

Methods: We used spectral flow cytometry to examine circulating Treg subsets in PBMCs from patients with SSc (n=18, median age 55; 10 diffuse, 7 limited, 1 sine), IgG4-RD (n=27, median age 65, 15 head and neck, 10 pancreatobiliary, 2 retroperitoneal fibrosis, 6 kidney), sarcoidosis (n=17, median age 66, 7 only pulmonary, 10 extra-pulmonary involvement) and healthy donors (HD, n=17, median age 64). Bulk RNA sequencing of flow purified T cell populations was used to define



A representative flow plot of FoxP3/CD45RA subsets (pregated on live CD3+CD4+ CD25+CD127lo) are shown in (A). Graph of Treg subsets including FoxP3Hi (B, live CD3+CD4+ CD25+CD127lo CD45RA-FoxP3Hi) and FoxP3Lo (C, live CD3+CD4+ CD25+CD127lo CD45RA-FoxP3Lo). FoxP3Lo as a percentage of CD4+ T cells are graphed compared to modified Rodnan skin score (mRSS) (D). FoxP3Lo as a percentage of CD4+ T cells are graphed for SSc patients with and without ILD (E), and in early (<5 years from diagnosis)and late disease (>5 years from diagnosis) (F). FoxP3Lo as a percentage of CD4+ T cells are graphed for IgG4RD patients with and without parotid/salivary gland involvement (G), with and without kidney or pancreas involvement (H), and with and without plasmablast expansion, defined as >1% (I). For B-I: *p<0.05, **p<0.01, *** p<0.001, **** p<0.0001 by Mann-Whitney U test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



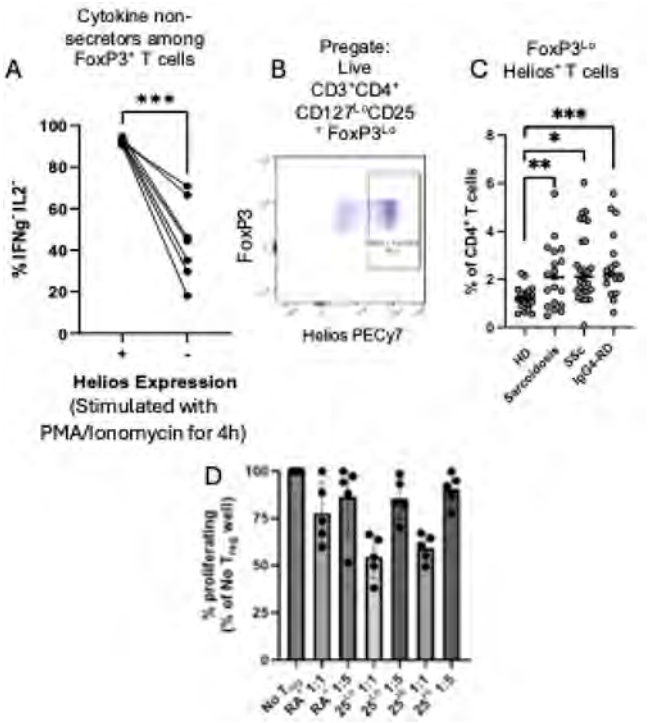
T cell subsets from 7 healthy donors were sorted using flow cytometry by gating on live CD3+CD4+ cells. For Treg subsets: CD25+CD127Lo cells were gated on CD45RA+ population (CD45RA+Treg), CD45RA-CD25Lo(CD25Lo Treg; analagous to FoxP3Lo), and CD45RA- CD25Hi (CD25HiTreg; analagous to FoxP3Hi). For conventional T cell subsets, CD127+ and CD25-cells were gated on CD45RA+CCR7+ (Conv Naïve) or CD45RA-CCR7- (Conv Effector). RNA was isolated and bulk RNA sequencing was performed from different subsets. (A) A PCA plot was used to compare populations. (B) EBSeq was used to identify genes that are differentially expressed across the cell types with a posterior probability > 0.95. Select genes related to immune function are graphed for differentially regulated (DEG) upregulated in CD25Hi compared to CD25Lo(top), upregulated in CD25Lo compared to CD25Hi (middle), and upregulated in CD25Lo compared to Effector T cells.

the transcriptional differences between Treg subsets. Purified Treg subsets were used for *in vitro* assays to measure the capacity to suppress T cell proliferation.

Results: FoxP3^{Lo} T cells were preferentially expanded in SSc and IgG4-RD (Fig 1C). FoxP3^{Lo} T cell expansion correlated with disease severity, including early disease, skin score and interstitial lung disease in SSc and internal organ involvement in IgG4-RD (Fig 1 D-H). Expression of the transcription factor Helios reliably excluded IL2 and IFNg-producing effector T cell contaminants from the FoxP3^{Lo} gate, as has been previously suggested (Fig 3A). Helios^{+} FoxP3^{Lo} T cells are also expanded in SSc and IgG4-RD, indicating that the FoxP3^{Lo} expansion is not driven by activated effector T cells (Fig 3C). FoxP3^{Lo} T cells expressed decreased levels of the suppressive protein, CTLA4, and activation marker, ICOS, relative to FoxP3^{Hi} cells, as previously reported. Transcriptionally, CD127^{Lo}CD25^{Lo} (analogous to FoxP3^{Lo}) T cells expressed decreased levels of the activation markers *TNFRSF9* (CD137), *IL2R* (CD25), *TNFRSF8* (CD30), *CD70*, and *HLA-DR*, as well as *PTPN22*, relative to CD25^{Hi} cells, suggesting a difference in TCR binding affinity or activation state between these subsets (Fig 2B). The inhibitory receptor, *PDCD1* (PD1), was uniquely upregulated in CD25^{Lo} T cells. Despite differences in activation status and expression of CTLA4, CD127^{Lo}CD25^{Lo} T cells showed an equal ability to suppress T cell proliferation *in vitro* when compared to their CD25^{Hi} counterparts (Fig 3D).

Conclusion: We show that FoxP3^{+} T cells expressing low levels of FoxP3 are legitimate regulatory T cells but have reduced expression of certain markers of activation and Treg function. FoxP3^{Lo} T cells are expanded in the immune-mediated fibrotic diseases SSc and IgG4-RD and correlate with disease severity, suggesting either a pathogenic role in the context of fibrosis or an induced regulatory response.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CD4 T cells were stimulated with PMA/Ionomycin for 4 hours and stained for intracellular FoxP3, IFNg, and IL2 (A). A representative plot of Helios gating is shown (B). (C) FoxP3Lo Helios+ T cells are pregated on Live CD3+CD4+CD127LoCD25+ and graphed as a percentage of total CD4+ T cells. (D) Conventional effector T cells were stimulated with CD3/CD28 dynabeads for 2 days then incubated at indicated ratios with FACS sorted CD45RA+ Tregs for 3 days (RA, CD3+CD4+CD127LoCD25+CD45RA+), CD25Lo Tregs (25Lo, CD3+CD4+CD127LoCD25LoCD45RA-), CD25Hi Tregs (25Hi, CD3+CD4+CD127LoCD25HiCD45RA-); proliferation as measured by Cell trace dye dilution was calculated as a percentage of the well with no Tregs. *p<0.05, **p<0.01, *** p<0.001 by Mann-Whitney U test.

Disclosure: L. Yockey: None; **I. Doyle**: None; **T. Guy**: None; **D. Trivedi**: None; **C. Gadiraju**: None; **F. Bonaso**: None; **J. Akaa**: None; **A. Puri**: None; **Z. Wallace**: Amgen, 3; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **S. Montesi**: Accendatech USA, 2, Boehringer-Ingelheim, 5, Mediar Therapeutics, 1, 2, Pliant Therapeutics, 5, Wolters Kluwer, 9; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1; **S. Pillai**: Abpro Inc, 4, BeBio, 4, Octagon Therapeutics, 4, Paratus Biosciences, 2; **A. Luster**: Human Immunology Biosciences, 2, Xilio Therapeutics, 2; **V. Mahajan**: None; **C. Perugino**: Acepodia, 2, Amgen, 1, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Zenas Biopharma, 2.

Abstract Number: 0993

NOD2 mutations mediate IL-17 predisposition in patients with Blau syndrome

Leah Huey[1], Emily Vance[2], Bryce Binstadt[3] and Ruth Napier[2], [1]Oregon Health & Science University, Denver, CO, [2]University of Colorado Anschutz, Aurora, CO, [3]University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Blau syndrome is a pediatric rheumatic disease characterized by dermatitis, arthritis, and uveitis. Blau syndrome is caused by inborn or *de novo* mutations in *NOD2*, the gene encoding the microbial sensing molecule NOD2. However, the cellular mechanism by which NOD2 causes sterile inflammation in Blau syndrome remains unknown. Recent studies have challenged the established dogma that Blau syndrome is caused by *NOD2* gain-of-function mutations to show Blau *NOD2* mutations result in a loss-of-function in NOD2 activation downstream of bacterial ligand stimulation. We previously demonstrated a novel T cell-intrinsic role for murine Nod2 in blocking pathogenic Th17/IL-17 responses and protecting against experimental autoimmune uveitis and arthritis in mice. Here we sought to determine how *NOD2* mutations in human patients with Blau syndrome alter T cell composition and function including Th17 responses.

Methods: Peripheral blood mononuclear cells (PBMCs) from patients with Blau representing 6 unique *NOD2* mutations, ages 2-64 (n=8) or controls (n=10) were analyzed before and after activation by anti-CD3 in combination with co-stimulatory agent, anti-CD28, or phorbol myristate acetate (PMA) and ionomycin (io). Cellular composition, T cell transcription factors, and cytokine expression were quantified by flow cytometry.

Results: Patients with Blau had comparable frequencies of peripheral blood CD4+ and CD8+ T cells to controls. However, these patients had a higher fraction of memory CD4+ T cells that expressed the Th17 lineage-defining transcription factor Rorgt, suggesting patients with Blau have enhanced baseline Th17 responses. Following T cell receptor (TCR)-independent stimulation (PMA/io) we found that cells from Blau patients had increased percentages of CD4+ T cells that produced IL-17A + or IL-17F+ compared to controls, yet no difference in percent of TNF+, IFNg+, or IL-2+ CD4 T cells. These data indicate that Blau patient T cells, regardless of individual *NOD2* mutations or age, have a predisposition to increased peripheral blood Th17 cells. To mimic antigen/cognate MHC-II interactions, T cells were then activated with a TCR-dependent stimulus (anti-CD3/CD28) over 5 days. On day 3 post-stimulation, PBMCs from Blau patients had increased IL-17F+, TNF+ and IL-2+ CD4 T cells with IL-17F+ CD4 T cells persistently increased through day 5 compared to controls. Cumulatively these data suggest that patients with Blau have primed Th17 immunity due to underlying *NOD2* mutations that enhance antigen-independent and -dependent T cell production of IL-17.

Conclusion: To our knowledge we are the first group to implicate T cells and Th17 immunity in Blau syndrome pathogenesis. These data provide foundational evidence for consideration of T cells and more specifically IL-17A and IL-17F as future targets for therapeutic intervention.

Disclosure: L. Huey: None; **E. Vance**: None; **B. Binstadt**: AbbVie/Abbott, 5, Amgen, 5, AstraZeneca, 5, Terremoto Biosciences, Inc., 2; **R. Napier**: None.

Abstract Number: 0994

UTAA91: An Off-the-Shelf Allogeneic CAR-Vδ1T Therapy Leveraging CD19 Nanoantibody for B-cell Depletion and PD-1 Agonist Nanoantibody for Pathogenic T-cell Elimination in Refractory Autoimmune Diseases

Licui Jiang[1], Fengtao you[1], Kunmin Yan[1], Jianan Yao[1], Hai Wu[1], Jian Wu[2], Xin Chang[2], Cheng Peng[2], Huimin Meng[1], Min Wang[3], Ping Zhang[3], Bozhen Zhang[4] and **Lin Yang**[5], [1]PersonGen BioTherapeutics(Suzhou) Co., Ltd., Suzhou, China, Suzhou, China (People's Republic), [2]The First Affiliated Hospital of Soochow University, Suzhou, China (People's Republic), [3]PersonGenAnke Cellular Therapeutics Co., Ltd.,Hefei, China, Suzhou, China (People's Republic), [4]PersonGen BioTherapeutics(Suzhou) Co., Ltd., Suzhou, China; PersonGenAnke Cellular Therapeutics Co., Ltd.,Hefei, China, Suzhou, China (People's Republic), [5]PersonGen BioTherapeutics(Suzhou) Co., Ltd., Suzhou, China; PersonGenAnke Cellular Therapeutics Co., Ltd.,Hefei, China; Cyrus Tang Medical Institute, Soochow University, Suzhou, Jiangsu, China, Suzhou, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Current therapies inadequately restore immune homeostasis due to incomplete pathogenic cell clearance and limited multi-lineage targeting. UTAA91 integrates:

1) PD-1 agonist-targeted cytotoxicity: The PD-1 nanoantibody module directs Vδ1T cells to selectively eliminate PD-1+ pathogenic T cells via their potent killing capacity: includng follicular helper T cells (Tfh), peripheral helper T cells (Tph) and effectors;

2) CD19-targeted B-cell clearance: Concurrent CD19 nanoantibody-mediated B-cell depletion disrupts T-B cell collaboration;

3) Vδ1T cells for deep tissue penetration.

Methods: Manufacturing: Vδ1T cells from donor PBMCs were enriched via MACS, engineered with CD19/PD1-CAR (Chimeric antigen receptor), and Fas-knockout via CRISPR-Cas9 to mitigate HvGR;

In vitro: PD-1+ T-cell/B-cell depletion quantified in SLE/RA/SS patient PBMCs;

In vivo: Humanized NPG mice with CD19+ tumors assessed for HvGR suppression, PD1+ T-cell clearance, tumor inhibition (flow cytometry/IVIS), and safety.

Results: The cGMP-compliant manufacturing process for UTAA91 demonstrates exceptional industrial feasibility, achieving the following critical quality attributes: Vδ1T cell purity >90%, stable CAR molecule expression rate >30%, Fas gene-specific knockout efficiency >90%, expansion capability exceeding 10,000-fold, Tnaive subset proportion >90%, and sustained high expression of NKG2D/DNAM1 and chemokine receptors, establishing a robust cellular foundation for long-term immune regulation.

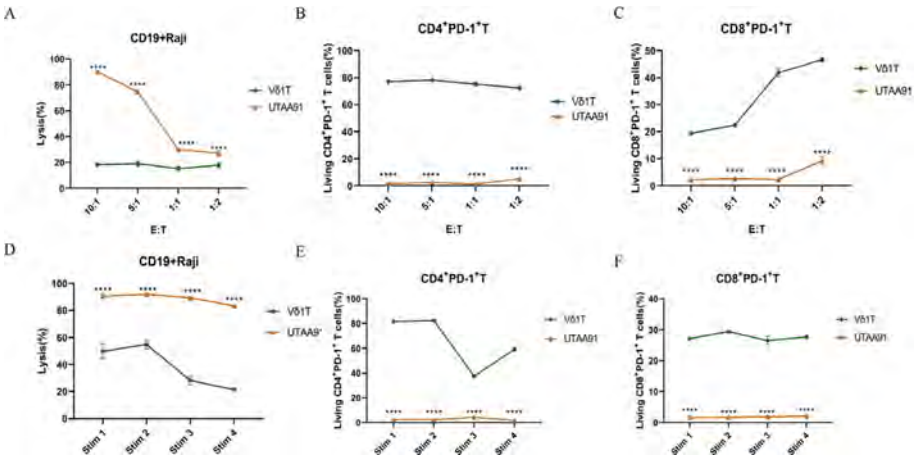


Figure 1: In vitro validation of dual-target specificity and functional persistence of UTAA91. (A) Targeted cytotoxicity of UTAA91 against $CD19^+$ Raji cells in vitro; (B) Targeted cytotoxicity of UTAA91 against $CD4^+PD1^+$ T cells in vitro; (C) Targeted cytotoxicity of UTAA91 against $CD8^+PD1^+$ T cells in vitro; (D) Persistent cytotoxicity of UTAA91 against $CD19^+$ Raji cells in vitro; (E) Persistent clearance capacity of UTAA91 against $CD4^+PD1^+$ T cells in vitro; (F) Persistent clearance capacity of UTAA91 against $CD8^+PD1^+$ T cells in vitro.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

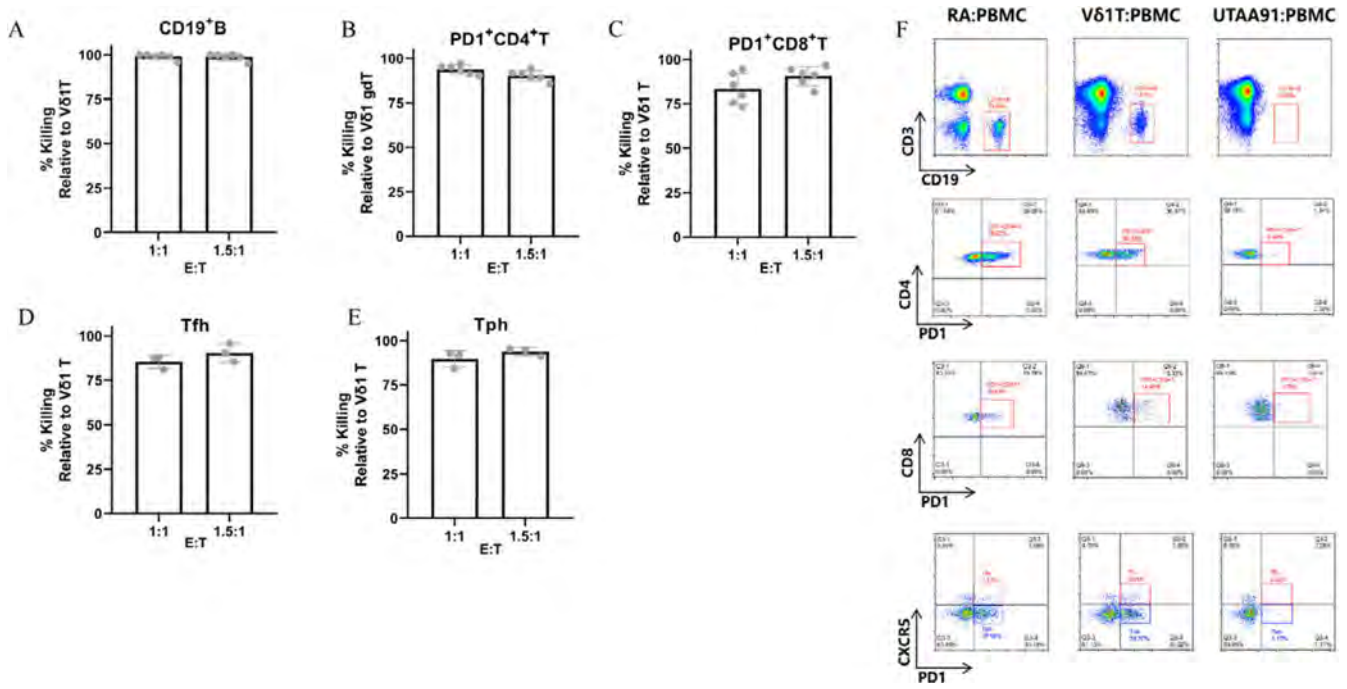


Figure 2: In vitro cytotoxicity of UTAA91 against peripheral PBMCs from autoimmune patients with various indications. (A) Clearance capacity against CD19$^+$ B cells; (B) Clearance capacity against PD1$^+$ CD4$^+$ T cells; (C) Clearance capacity against PD1$^+$ CD8$^+$ T cells; (D) Clearance capacity against Tfh cells in peripheral blood; (E) Clearance capacity against Tph cells in peripheral blood; (F) Raw flow cytometry data from one donor (RA). Notes: n=6, including patients with SLE, SSc, SS, RA, psoriasis, etc.

In vitro functional validation confirmed UTAA91's dual-targeted cytotoxicity against CD19+ and PD1+ cells, maintaining >90% specific killing efficiency through multiple rounds of antigen stimulation, which highlights its superior functional persistence. In humanized mouse models, UTAA91 effectively overcame allogeneic therapy barriers by significantly suppressing host-versus-graft reaction (HvGR), clearing peripheral PD1+ T cells, and inhibiting tumor growth, with no treatment-related toxicity observed.

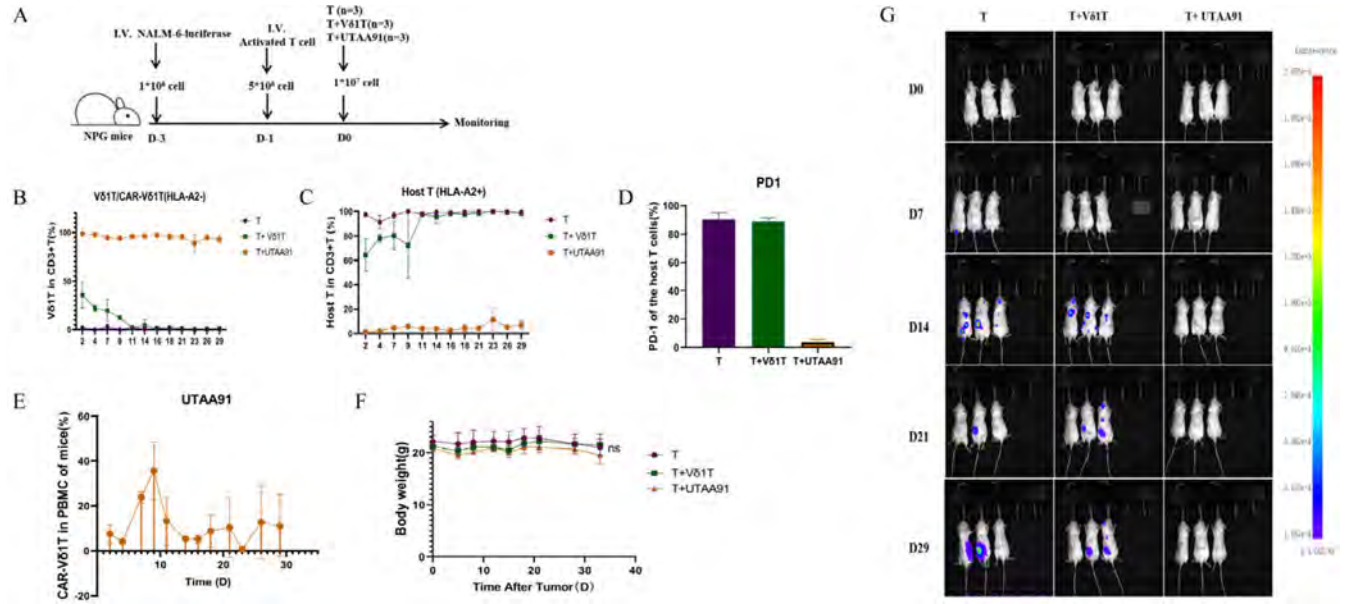


Figure 3: In vivo efficacy of UTAA91 in humanized tumor-bearing mice. (A) Preclinical in vivo experimental protocol; (B) Time-dependent monitoring of the proportion of Vδ1T/CAR-VδT cells in total CD3$^+$ T cells in peripheral blood; (C) Time-dependent monitoring of the proportion of host T cells in total CD3$^+$ T cells in peripheral blood; (D) Depletion of PD-1+ host T cell across experimental groups; (E) Pharmacokinetics of UTAA91 in peripheral blood; (F) Body weight monitoring across experimental groups; (G) Fluorescence imaging of tumor burden in mice.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Of significant translational value, UTAA91 exhibited precise and potent depletion of pathogenic cells in PBMCs derived from autoimmune disease patients (including SLE, RA, and SS), specifically eliminating CD19+ B cells and Tfh/Tph populations while selectively removing hyperactivated CD4+PD1+and CD8+PD1+T cells. Notably, functional PD1-T cell subsets were preserved post-treatment. This marks the first preclinical demonstration of UTAA91's unique capability to simultaneously target bidirectional T-B cell pathogenic pathways, offering a transformative therapeutic strategy for autoimmune diseases.

Conclusion: UTAA91, the first dual-targeting allogeneic UCAR-Vδ1T therapy, pioneers a "dual depletion" mechanism to eliminate B and Tfh/Tph cells, overcoming T-B interaction limitations and offering a groundbreaking solution for autoimmune diseases.

Disclosure: L. Jiang: None; **F. you**: None; **K. Yan**: None; **J. Yao**: None; **H. Wu**: None; **J. Wu**: None; **X. Chang**: None; **C. Peng**: None; **H. Meng**: None; **M. Wang**: None; **P. Zhang**: None; **B. Zhang**: None; **L. Yang**: None.

Abstract Number: 0995

Resident Memory T Cells Stimulate Pathogenic Activity in Fibroblast-like Synoviocytes

Madison Mangin[1], Yang Yang[2], Yusuke Miyashita[2] and Margaret Chang[2], [1]Boston Children's Hospital, St Simons Island, GA, [2]Boston Children's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by joint specific memory. We previously demonstrated that joint-specific memory is mediated by CD8+ synovial resident memory T (T_{RM}) cells that persist in arthritic joints during remission and can mediate arthritis flares. Further, we found that fibroblast-like synoviocytes (FLS) facilitate the formation of T_{RM} through IL-15 production. As cell-cell interactions can be bidirectional, we investigated the effects of T_{RM} on FLS pathogenicity.

Methods: T_{RM} were generated through two-week co-culture with FLS isolated from RA synovium in the presence of IL-15. T_{RM} development was validated by cell surface markers, gene expression profile and enhanced Bodipy free fatty acid uptake. T_{RM} were purified through multi-step magnetic nanobead sorting for CD62L-, CD25- and CD69+ cells. Purified T_{RM} cells were stimulated with anti-CD3/CD28 dynabeads for 24 hours then co-cultured with new unstimulated FLS. After 48 to 72 hours, FLS were collected and assayed for phenotypic markers of cellular activation by flow cytometry, for pathogenic gene expression by qPCR, and for protein expression by ELISA.

Results: T_{RM} generated through FLS co-culture displayed surface phenotype CD45RO+CD62L-CCR7-HLA-DR-CD25-CD69+ with variable CD103 and CD49a expression. These cells also displayed enhanced free fatty uptake and a gene expression signature consistent with T_{RM}. FLS co-cultured with purified T_{RM} upregulated surface expression of HLA-DR and ICAM-1 similar to FLS stimulated with TNF alone. T_{RM}-stimulated FLS also increased expression of inflammatory cytokines (IL-6, IL-8), chemokines (CCL5) and matrix metalloproteinases (MMP1, MMP3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: We previously showed that FLS facilitate synovial T_{RM} development. We now demonstrate that T_{RM} also promote FLS activation, stimulating the expression of inflammatory cytokines, chemokines and matrix metalloproteinases by FLS, thus contributing to arthritis pathogenesis.

Disclosure: M. Mangin: None; **Y. Yang**: None; **Y. Miyashita**: None; **M. Chang**: None.

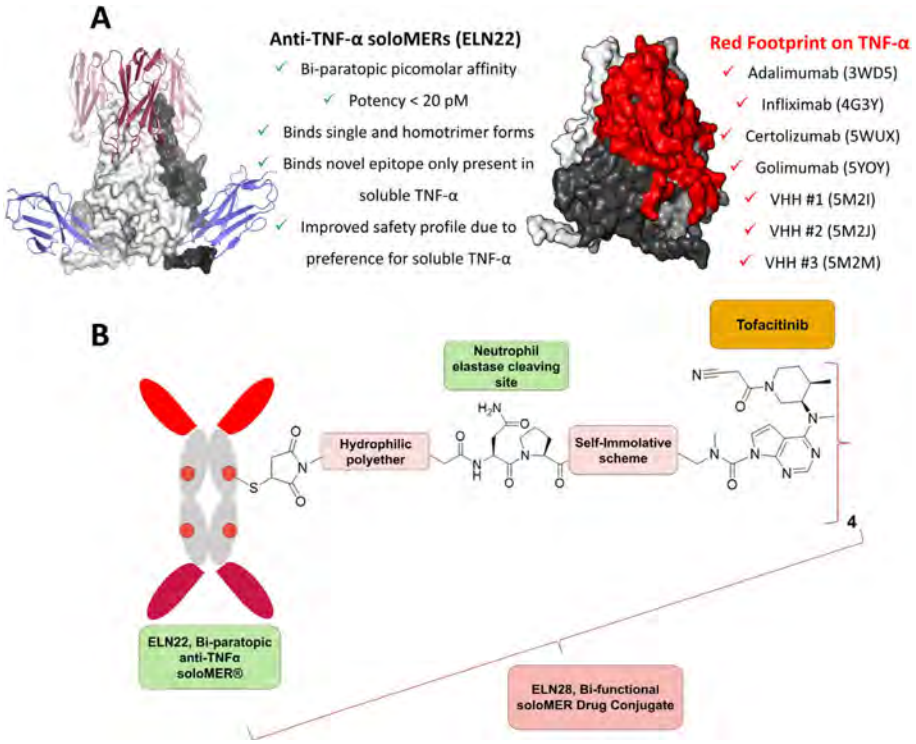
Abstract Number: 0996

Breaking Inflammatory Pathways: ELN28, a Novel Dual TNFα/JAK Inhibitor Drug Conjugate for Chronic Inflammation

Obinna Ubah, Euan Murray, Stella Priyanka, Julia Martinez Fraile, Andrew Porter, Robert Boyd and Caroline Barelle, Elasmogen Limited, Aberdeen, United Kingdom

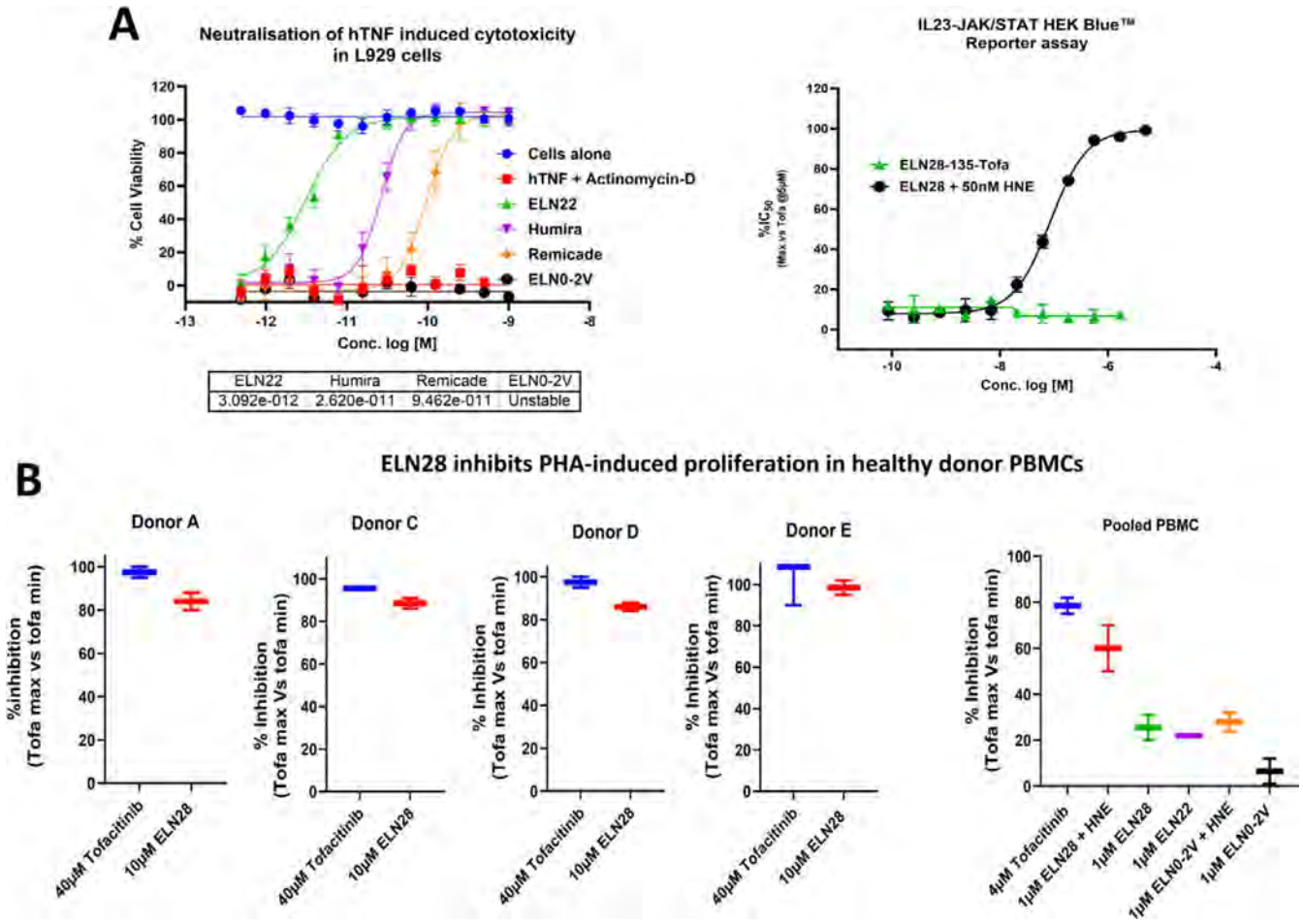
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite advances in therapies for chronic autoimmune diseases such as rheumatoid arthritis (RA), significant unmet needs persist, including therapeutic ceiling effects, adverse events, and suboptimal remission rates. We hypothesized that a rationally designed, dual-targeting molecule could enhance remission rates and reduce required dosing,



(A) X-ray structures of anti-TNF-α soloMERs expose novel TNF-α epitopes (left). On the right, crystallography data of existing anti-TNFα binding domains illustrating in red their overlapping footprint on TNF-α molecule (B) ELN28 SDC targets both soluble TNFα and Janus kinases. The overexpression of soluble TNFα in the inflamed tissues drives preferential accumulation of SDC at these sites. Tofacitinib payload is efficiently and safely released in the inflamed tissue by the action of human neutrophil elastase (HNE).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



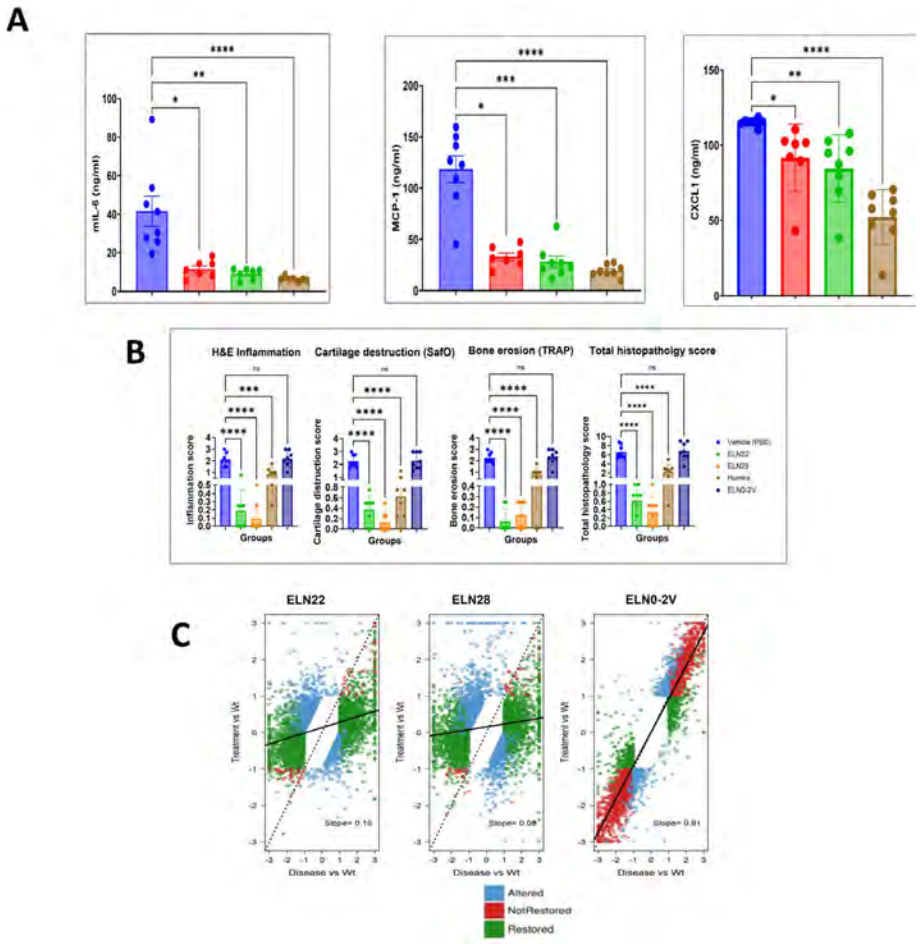
(A) Inhibition of TNF-α mediated cytotoxicity in L929 mouse fibrosarcoma cell line (left), and Anti-TNF-α independent inhibition of JAK/STAT phosphorylation signalling in human IL23-JAK/STAT HEK Blue™ Reporter cells (right). Functional Tofacitinib is released from ELN28 SDC in the presence of HNE. ELN0-2V is an isotype control soloMER (B) In the presence of HNE, ELN28 inhibited phytohemagglutinin (PHA) induced PBMC proliferation (donors A, C, D E). In a pooled PBMC sample, ELN28 +/- HNE demonstrated the additive (bifunctional) activity. ELN0-2V is an isotype control soloMER drug conjugate with a non-binding soloMER conjugated to Tofacitinib.

thereby improving the safety profile. ELN28 is a first-in-class bi-functional soloMER drug conjugate (SDC) targeting soluble TNFα and delivering the JAK inhibitor Tofacitinib directly to inflamed tissues. The payload is released in the presence of neutrophil elastase, which is enriched in inflammatory microenvironments. We evaluated ELN28's functional activity and compared it to mono-specific anti-TNFα therapies across multiple ex vivo and in vivo models of autoimmune inflammation.

Methods: Dual immunomodulatory activity of ELN28 was assessed in phytohemagglutinin (PHA)-stimulated healthy donor PBMCs. To model synovial inflammation, a 3D co-culture system was developed comprising primary RA synovial fibroblasts, endothelial cells, and monocytes (2:2:1 ratio). Organoids were treated with ELN28, followed by quantification of cytokine and chemokine production. In vivo efficacy was tested in an LPS-induced acute inflammation model (Tg1278TNFKOhTNFR1KI), where ELN28 was administered 2 hours pre-LPS exposure and cytokine levels measured after 5 hours. Chronic efficacy was evaluated in the Tg197 transgenic mouse model of polyarthritis, with biweekly ELN28 dosing over 7 weeks. Comparative treatments included Adalimumab and a mono-specific anti-TNFα soloMER (ELN22).

Results: ELN28 exhibited high-affinity (~100 pM) binding to soluble TNFα and potent neutralization in TNFα-stimulated L929 fibrosarcoma assays. Structural analysis via X-ray crystallography confirmed binding to a recessed epitope unique to soluble TNFα, enabling discrimination from membrane-bound TNFα. ELN28 inhibited PHA-induced PBMC proliferation and significantly reduced secretion of CXCL1, CXCL5, CXCL10, IL-6, and CCL2 in the RA synovial organoid model, outperforming mono-specific comparators. In vivo, ELN28 demonstrated dose-dependent, superior efficacy versus Adalimumab

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(A) ELN28 attenuates the release of proinflammatory cytokines and chemokines in an LPS induced acute inflammation human TNF-α transgenic mouse model (Tg1278TNFKohTNFR1K1). In this acute inflammation model, LPS was administered 2 h after intraperitoneal administration of test articles, and terminal blood sampling 5 h post-LPS dosing (B) Test articles were dosed at 3 mg/kg twice weekly for 7 weeks. ELN28 and ELN22 were comparable in the clinical arthritis score assessment (left panel). Histopathology analysis demonstrated superior disease control by ELN28 (C) RNAseq analysis of disease associated genes (DAGs). Two dimensional scatterplots, regression lines show deviation of the treatment profile from disease group

and ELN22 in the LPS-induced Tg1278 model. In the Tg197 chronic arthritis model, ELN28 improved histopathological outcomes—including reductions in bone erosion, cartilage destruction, and inflammatory scores—and achieved twofold superiority in normalizing disease-associated gene expression (RNA-seq) toward a wild-type baseline.

Conclusion: ELN28 is a novel bi-functional drug conjugate that combines selective TNFα neutralization with inflammation-targeted JAK inhibition. Its unique targeting of soluble TNFα and elastase-triggered delivery mechanism offer a promising strategy for overcoming limitations of current RA therapies. ELN28 demonstrated robust dual activity and disease-modifying effects in preclinical models of autoimmune inflammation. IND-enabling studies are underway to advance ELN28 toward clinical development in RA and related autoimmune diseases, including Psoriatic Arthritis, Hidradenitis Suppurativa, and IBD.

Disclosure: O. Ubah: None; **E. Murray**: None; **S. Priyanka**: None; **J. Martinez Fraile**: None; **A. Porter**: None; **R. Boyd**: None; **C. Barelle**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 0997

Identification of Novel HLA Class II–Restricted Autoantigens in Scleroderma and Ulcerative Colitis Using TargetScan

Olivia Pryor[1], Catalina Burbano[2], Nathaniel Bagge[2], Rutuja Kulkarni[2], Heather F. Jones[2], Livio Dukaj[2], Shoshana M.K. Bloom[2], Jackson Lirette[2], Rachel Lent[2], Prachi Dhanania[2], Nicole A. Ladd[2], Ryan Kritzer[2], Hana Husic[2], Shobitha Jillella[2], Candace R. Perullo[2], Jinyu Zhu[2], Teagan J. Parsons[2], Ira Jain[2], Rakshika Balasubramaniyam[2], Kenneth L. Jahan[2], Vivin Karthik[2], Alexander Cristofaro[1], Chandan K. Pavuluri[2], Jenna LaBelle[2], Laurie Barefoot[2], Shrikanta Chattopadhyay[2], Kim M. Cirelli[2], Mollie M. Jurewicz[2], Andrew P. Ferretti[2] and Cagan Gurer[2], [1]TScan Therapeutics, Waltham, [2]TScan Therapeutics, Waltham, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Selective modulation of autoimmune responses through antigen-specific therapies represents a promising direction for improving treatment specificity and safety. Genetic associations with HLA class II alleles, combined with evidence of tissue-infiltrating T cells and T cell–mediated cytokine signatures, highlight the central role of $CD4^+$ T cells in driving autoimmune pathology. However, the targets of these pathogenic T cells remain poorly defined, limiting development of antigen-specific therapies. TScan's proprietary TargetScan platform offers an unbiased, high-throughput method to identify natural targets of disease-relevant T cell receptors and support development of antigen-specific tolerizing modalities.

Methods: To identify HLA class II T cell targets for $CD4^+$ T cells, the TargetScan platform was adapted to present genetically encoded peptide libraries on ectopically expressed HLA class II molecules. We initially applied this approach to scleroderma. $CD4^+$ T cells were isolated from affected skin biopsies of patients and analyzed using 10x Genomics single-cell RNA sequencing. A total of 764 TCRs were identified, with candidates selected for screening based on pathogenic gene expression profiles and CDR3 sequence clustering shared by TCRs found in more than one patient. 61 candidate TCRs were screened for antigen recognition in the context of disease-associated Class II HLA alleles, and identified targets were assessed for disease relevance using follow-up validation assays. Similarly, we used the TargetScan platform to evaluate TCRs from inflamed colon samples derived from patients with ulcerative colitis.

Results: Screening of the candidate TCRs using the Class II TargetScan platform identified eight novel targets presented by multiple HLA Class II alleles associated with scleroderma. These reactive TCRs belonged to shared $CD3^+$ clusters found in multiple patients and were characterized by high expression of activation and tissue-homing markers, as well as genes associated with Th2 and Th17 profiles. The identified targets exhibited expression patterns consistent with disease relevance and were validated through orthogonal assays, including functional T cell activation assays. In ulcerative colitis, two novel targets were identified with expression patterns consistent with disease pathology.

Conclusion: TScan's Class II TargetScan platform enables unbiased identification of novel autoantigens in $CD4^+$ T cell–driven autoimmune diseases where antigenic drivers have remained poorly defined. These discoveries may inform the development of antigen-specific therapeutic strategies, including tolerogenic approaches aimed at restoring immune homeostasis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: O. Pryor: TScan Therapeutics, 3, 11; **C. Burbano**: TScan Therapeutics, 3, 11; **N. Bagge**: TScan Therapeutics, 3, 11; **R. Kulkarni**: TScan Therapeutics, 3, 11; **H. Jones**: TScan Therapeutics, 3, 11; **L. Dukaj**: TScan Therapeutics, 3, 11; **S. Bloom**: TScan Therapeutics, 3, 11; **J. Lirette**: TScan Therapeutics, 3, 11; **R. Lent**: TScan Therapeutics, 3, 11; **P. Dhanania**: TScan Therapeutics, 3, 11; **N. Ladd**: TScan Therapeutics, 3, 11; **R. Kritzer**: TScan Therapeutics, 3, 11; **H. Husic**: TScan Therapeutics, 3, 11; **S. Jillella**: TScan Therapeutics, 3, 11; **C. Perullo**: TScan Therapeutics, 3, 11; **J. Zhu**: TScan Therapeutics, 3, 11; **T. Parsons**: TScan Therapeutics, 3, 11; **I. Jain**: Tscan Therapeutics, 3, 11; **R. Balasubramaniyam**: Tscan Therapeutics, 3, 11; **K. Jahan**: Tscan Therapeutics, 3, 11; **V. Karthik**: Tscan Therapeutics, 3, 11; **A. Cristofaro**: TScan Therapeutics, 3, 11; **C. Pavuluri**: TScan Therapeutics, 3, 11; **J. LaBelle**: TScan Therapeutics, 3, 11; **L. Barefoot**: TScan Therapeutics, 3, 11; **S. Chattopadhyay**: TScan Therapeutics, 3, 11; **K. Cirelli**: TScan Therapeutics, 3, 11; **M. Jurewicz**: TScan Therapeutics, 3, 11; **A. Ferretti**: TScan Therapeutics, 3, 11; **C. Gurer**: TScan Therapeutics, 3, 11.

Abstract Number: 0998

Preclinical Characterization of a Novel Bi-specific Antibody Targeting IL-23p19 and IL-36R for The Treatment of Autoimmune Diseases

Qianqian Yin[1], changqing run[1], kaili liu[1], xueqin cui[1], fanpeng Meng[1], yanru fan[1], yifei yang[1], wei ye[1], Lu Su[2], yuan lin[1] and cheng liao[1], [1]Jiangsu Hengrui Pharmaceuticals Co., Ltd, Shanghai, China (People's Republic), [2]Jiangsu Hengrui Pharmaceuticals, Shanghai, Shanghai, China

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IL-23 is a pivotal cytokine driving IL-17-mediated inflammation, and its inhibition has shown efficacy in Th17-associated autoimmune diseases. However, patient heterogeneity and compensatory pathways limit therapeutic responses. The IL-36/IL-36R pathway contributes to inflammation and barrier homeostasis, with its hyperactivity related to multiple autoimmune diseases and implicated in resistance to IL-23/IL-17 inhibitors in psoriasis. Here we developed an anti-IL-23/IL-36R bispecific antibody (BsAb) to block both pathways, aiming to improve clinical outcomes across autoimmune indications.

Methods: The synergistic effect of the two pathways was validated in an intradermal dual-cytokine (IL-23 plus IL-36)-challenging murine model. The binding to targets was evaluated by Surface Plasmon Resonance (SPR) and Fluorescence-Activated Cell Sorting (FACS). The blockade of IL-23 and IL-36 signaling was separately assessed by Ba-F3 cell proliferation assay and the assay of IL-8 secretion in A431 cells. The simultaneous blockade of both pathways was assessed in a PBMC/A431 co-culturing system. *In vivo* efficacy of BsAb was evaluated in an IL-23/IL-36 co-induced murine psoriasis model. The safety profile was evaluated in a 4-week repeated-dose Good Laboratory Practice (GLP) toxicology study in cynomolgus monkeys.

Results: Intradermal dual-cytokine challenge induced exacerbated psoriasiform pathology in mice, including epidermal hyperplasia and upregulated pro-inflammatory cytokines, suggesting the synergistic effect between IL-23 and IL-36 pathways. The anti-IL-23/IL-36R BsAb demonstrated high-affinity binding to both IL-23 and IL-36R, and inhibited IL-23-dependent Ba-F3 proliferation and IL-36R-mediated inflammatory responses, with activities comparable to those of the corresponding monospecific antibodies. In the PBMC/A431 co-culture assay, the BsAb surpassed monospecific antibodies in suppressing psoriasis-related cytokines. In a murine psoriasis model induced by IL-23/IL-36 co-stimulation, the BsAb outperformed monospecific antibodies in reducing ear thickness and suppressing multiple pro-inflammatory

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cytokines and keratinocyte hyperproliferation markers. Non-human primate studies revealed no drug-related toxicity at all tested doses.

Conclusion: Our data highlight the enhanced therapeutic efficacy of the anti-IL-23/IL-36R BsAb through concurrent inhibition of two complementary signaling pathways, without compromising safety profile. This dual-targeting therapeutic shows promise for treating diverse autoimmune diseases, including psoriasis.

Disclosure: q. yin: None; **c. run**: None; **k. liu**: None; **x. cui**: None; **f. Meng**: None; **y. fan**: None; **y. yang**: None; **w. ye**: None; **L. Su**: None; **y. lin**: None; **c. liao**: None.

Abstract Number: 0999

Myositis Induced by Histidyl-Transfer tRNA Synthetase is Exacerbated by Membranopathy and Suppressed by Regulatory T Cells

Samantha Coss[1], Nicholas Young[2], Shane Bruckner[3], Braden Zeno[4], Gianni Giarrano[5], Hannah Bulgart[6], Paula Clemens[7], Jisna Paul[2], Chester V. Oddis[8], noah weisleder[9], Dana Ascherman[8] and Wael Jarjour[10], [1]Nationwide Children's Hospital, Columbus, OH, [2]Division of Rheumatology and Immunology, Department of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, OH, Columbus, OH, [3]OSU, Columbus, OH, [4]Ohio State University, upper arlington, OH, [5]Division of Rheumatology, Nationwide Children's Hospital, Columbus, OH, [6]Department of Molecular and Cellular Biochemistry, University of Kentucky College of Medicine, Lexington, KY, [7]Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, [8]University of Pittsburgh, Pittsburgh, PA, [9]University of Kentucky, Lexington, KY, [10]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune disorders targeting muscle as well as extra-muscular organs. Among the most common autoantibodies associated with IIM is anti-histidyl-tRNA synthetase (HRS; Jo-1), which defines a distinct subset of IIM. Although pathogenic mechanisms of the anti-synthetase syndrome are incompletely understood, administration of recombinant HRS in mice has been shown to recapitulate histopathological features and robust anti-HRS antibody responses that are characteristic of human disease. In this study, we used an established murine model of HRS-induced myositis to evaluate the role of membranopathy in IIM pathogenesis and to investigate the therapeutic potential of regulatory T cells (Tregs).

Methods: BALB/C-Tg(NF-κB-RE-luc)-Xen mice harboring a firefly luciferase cDNA reporter gene under the regulation of κB-responsive binding sites or synaptotagmin VII (Syt VII) knockout (KO) mice (B6.129S1-Syt7tm1Nan/J) were injected intramuscularly with a recombinant amino-terminal fragment of murine HRS (mHRS). In NF-κB-RE-luc mice, bioluminescent signals were measured longitudinally. To evaluate suppression of disease pathology, Tregs isolated from wild-type (WT) mice were co-administered with mHRS injections. At experimental endpoints, histopathology of muscle tissue was analyzed and serum was collected to measure autoantibody production. In addition, nuclear extracts of muscle tissue cells were evaluated via EMSA to measure NF-κB activation. Sarcolemmal membrane repair capacity in skeletal muscle was assessed *ex vivo* by laser injury assays.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: NF-κB-RE-luc mice stimulated with mHRS developed an acute inflammatory response consisting primarily of lymphocytes and monocytes/macrophages, which correlated with NF-κB-associated bioluminescence and enhanced nuclear NF-κB binding activity in injected muscles. Despite a reduction in NF-kB activity at later time points, histopathology of mHRS-injected muscle tissue revealed persistent endomysial inflammatory infiltrates consisting of both lymphocytes (CD4+ and CD8+ T cells) and macrophages. Similar mHRS-induced muscle tissue pathology and anti-Jo-1 autoantibody production was observed in mice with a different genetic background (C57BL/6); inflammatory pathology was further amplified in SytVII KO mice that are characterized by inherent sarcolemmal membrane instability, but was ameliorated with concurrent adoptive transfer of WT Tregs. Moreover, WT C57BL/6 mice with mHRS-induced myositis demonstrated significantly compromised cell membrane repair *ex vivo*.

Conclusion: In summary, these data indicate that the initial inflammatory response in mHRS-induced myositis is NF-κB-regulated and exacerbated by membranopathy, suggesting that aberrant exposure of intracellular antigens, including HRS, can augment autoimmune-mediated pathogenesis. However, myositis pathology is suppressed by adoptive transfer of Tregs from healthy mice. Therefore, strategies engaging the immunosuppressive capacity of Tregs and/or sarcolemmal membrane stabilization represent novel areas of future therapeutic development for the treatment of IIM.

Disclosure: S. Coss: None; **N. Young**: None; **S. Bruckner**: None; **B. Zeno**: None; **G. Giarrano**: None; **H. Bulgart**: None; **P. Clemens**: None; **J. Paul**: None; **C. V. Oddis**: None; **n. weisleder**: None; **D. Ascherman**: None; **W. Jarjour**: None.

Abstract Number: 1000

A Deep-learning Based Approach Uncovers Novel Mediators of Micro-rna Restraint of type-2 Immunity

Shaan Sekhon[1], Robin Kageyama[2], Neil Sprenkle[3], Hannah Happ[2], Eric Wigton[2], Heather Pua[3] and Mark Ansel[2], [1]University of California, San Francisco, Berkeley, [2]University of California, San Francisco, San Francisco, [3]Vanderbilt University, Nashville

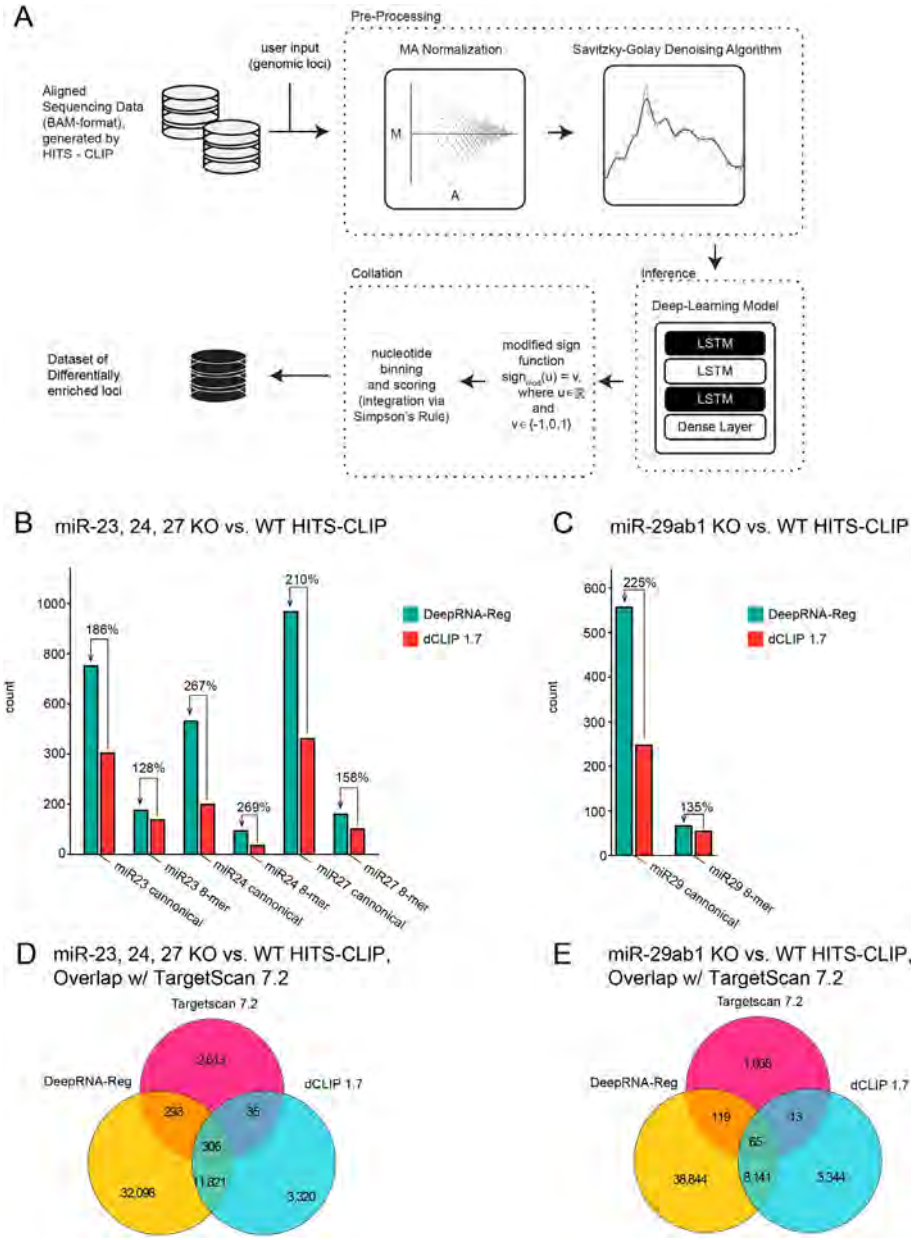
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: MicroRNAs, such as miR-24 and miR-27, co-expressed within the Mirc11 and Mirc22 clusters, orchestrate a regulatory network critical to Th2 cell differentiation and cytokine production, notably Interleukin-4 (IL-4), with emerging roles in immune dysregulation in rheumatic diseases. To probe this network, we developed DeepRNA-Reg, a deep learning-based algorithm leveraging recurrent neural networks for high-fidelity comparative analysis of high-throughput sequencing of RNA isolated by crosslinking immunoprecipitation (HITS-CLIP) datasets.

Methods: The DeepRNA-Reg algorithm utilizes deep learning to predict differentially enriched sites in paired HITS-CLIP data sets, employing a recurrent neural network to infer differential enrichment status across the transcriptome. CD4+ T cells were isolated from spleen and lymph nodes and cultured under Th2 conditions. C57BL/6 male and female age and sex matched mice between 5 to 12 weeks of age were used for all experiments. To generate "miR-23, 24, 27 KO" T cells lacking expression of all *Mirc11* cluster miRNAs (miR- 23a, miR-24-2, and miR-27a) and *Mirc22* cluster miRNAs (miR-23b, miR-24-1, and miR-27b), we intercrossed previously generated conditionally mutant Mirc22$^{tm1.1Mtm}$ mice and Mirc11$^{tm1.1Mtm}$ mice and with *Cd4-Cre* transgenic mice (*Tg(CD4-cre)1Cwi*; 4196, Taconic) to induce Cre-mediated deletion in T cells.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

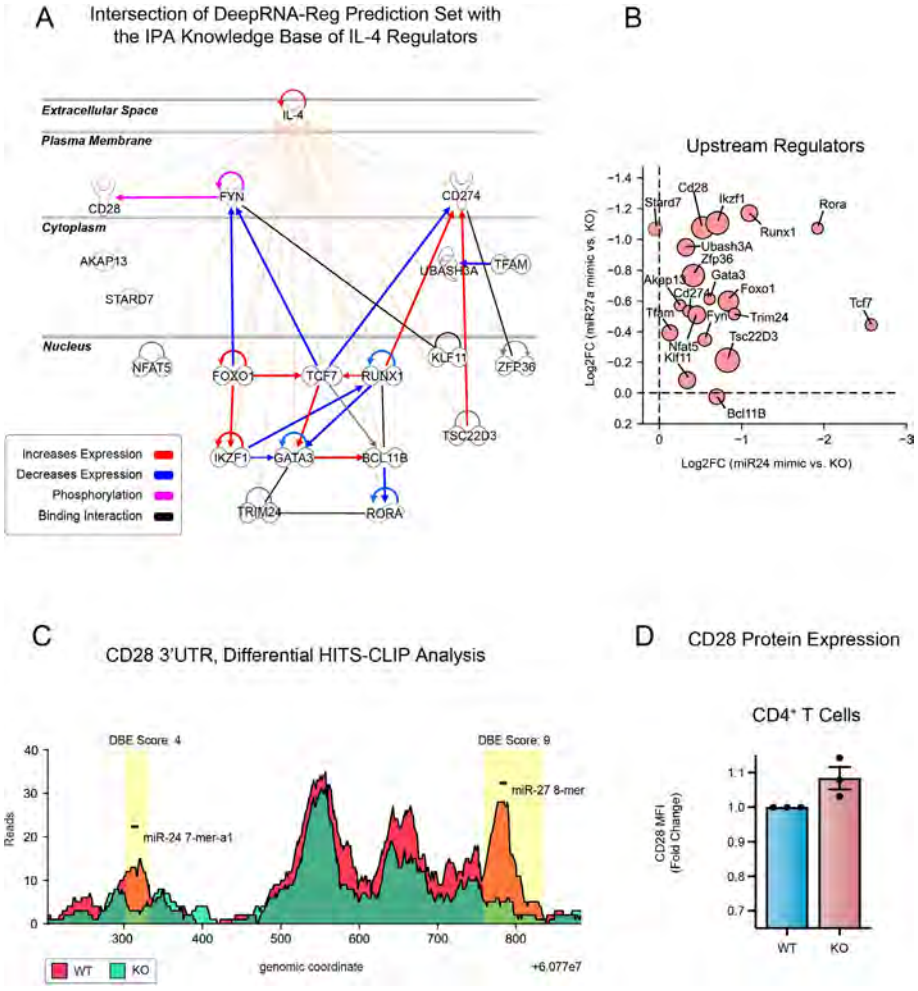


Benchmarking predicted miRNA target site capture. (A) Schematic representation of the DeepRNA-Reg algorithm. (B-C) Seed binding sequence motif abundance in the Th2 differential AHC analysis (B) and the Th17 differential AHC analysis (C) by both DeepRNA-Reg and dCLIP. (D) Venn diagram quantifying overlap events between Targetscan 7.2 predicted miRNA target sites of miR-23, 24, and 27 and the sites called to be enriched in WT Th2 cells (relative to miR-23,24,27 KO Th2 cells) by both DeepRNA-Reg and dCLIP. (E) Venn diagram quantifying overlap events between Targetscan 7.2 predicted miRNA target sites of miR-29 and the sites called to be enriched in WT Th17 cells (relative to miR-29 KO Th2 cells) by both DeepRNA-Reg and dCLIP.

Ago2 HITS- CLIP was performed using an anti-Ago2 monoclonal antibody. Lastly, differential protein expression was evaluated in CD4+ T Cells harvested from mice bearing selective microRNA cluster knock-out.

Results: This analysis of miR-24, 27 targets uncovered a suite of transcriptional regulators that are known to affect IL-4 expression, including *Gata3* and *Ikzf1* but also *Rora, Tcf7, Runx1, Bcl11b, Foxo1, Nfat5, Tsc22d3* and *Klf11*. In addition, this study uncovered the cell surface costimulatory receptor CD28 as a novel target of miR-24 and miR-27. CD28 is a key regulator of T cell activation, differentiation and cytokine production. Flow cytometric analysis of CD28 protein expression confirmed that miR-23,24,27 KO Th2 cells express a larger quantity of CD28 on their cell surface, consistent with direct targeting by miR-24 and/or miR- 27.

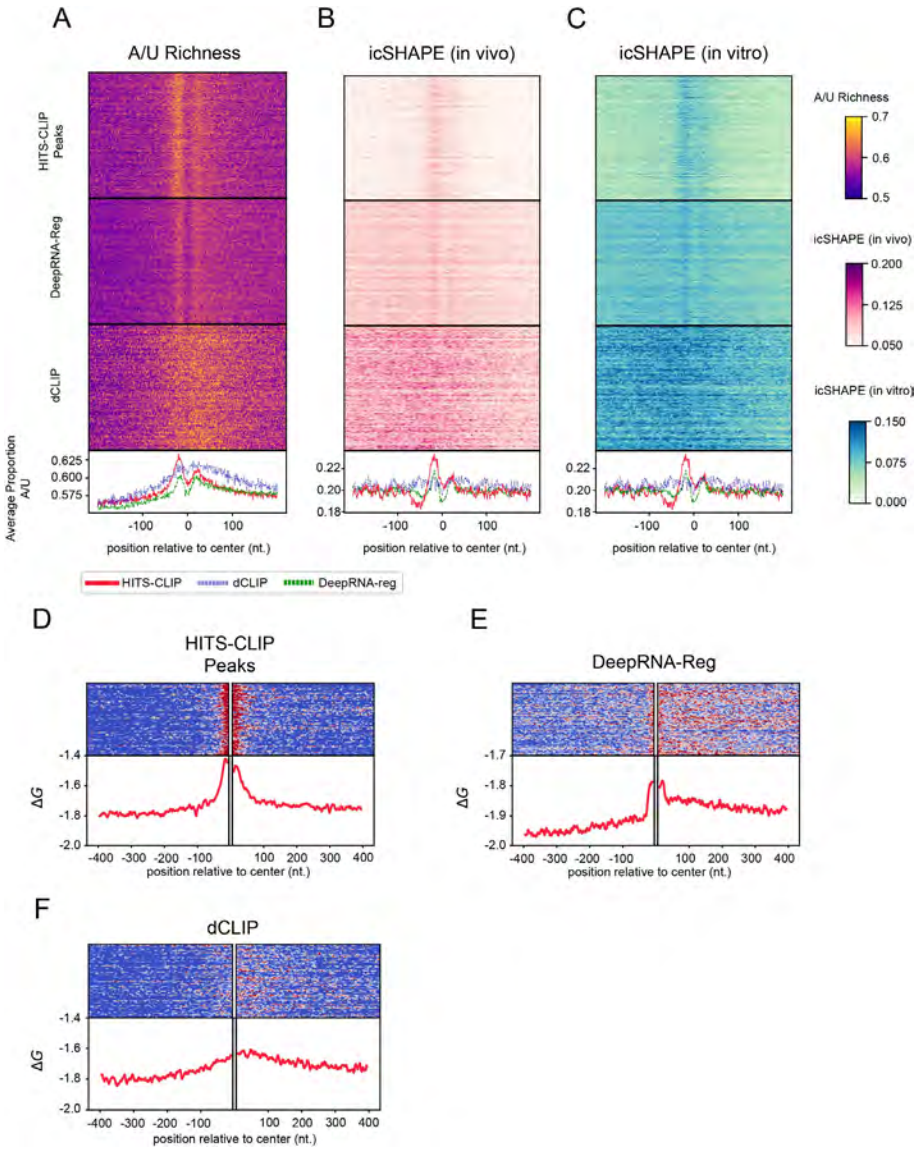
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Interrogating the Il-4 regulatory axis in the T Helper 2 Context. (A) A gene regulatory network showing the intersection of the IPA knowledge bank of known il-4 regulators and high-confidence DeepRNA-Reg predicted microRNA-24,27 targets. This high-confidence prediction set met the following conditions: a differentially enriched site with a DBE score above the median DBE score for the analysis that contains a canonical motif, with a negative response to the corresponding miRNA mimic between 15% and 85%. (B) A scatterplot of the degree of gene expression change between the miRNA mimic and control condition for microRNAs 24 and 27 on the horizontal and vertical axes, respectively. This plot represents the set of genes that lie at the intersection of the set of known upstream regulators of interluken-4 within the IPA knowledge-base and the set of high-confidence DeepRNA-Reg predictions of miR-24,27 targets. (C) A line plot representing the read depth across a section of the Cd28 3'UTR for both the WT and miR-23,24,27 KO condition HITS-CLIP experiments. Highlighted within this plot are two loci enriched in the WT condition relative to the miRNA KO condition, called and scored by DeepRNA-Reg, which overlap canonical seed sequences of miRNAs 24 and 27. (D) Flow cytometric analysis of CD28 protein expression showing that miR-23,24,27 KO Th2 cells express a larger quantity of CD28 on their cell surface, consistent with direct targeting by miR-24 and/or miR-27

Conclusion: These findings demonstrate that DeepRNA-Reg analysis of comparative Ago2 HITS-CLIP data can both confirm prior knowledge and uncover novel nodes in post-transcriptional regulatory networks. In tested data sets, DeepRNA-Reg uncovered novel mediators in the mechanism of microRNA-mediated restraint of type-2 immunity in T-Helper 2 cells, a pattern of immune response implicated in the pathophysiology.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Secondary structure of Ago2 binding sites. (A-C) Heatmaps represent a visualization of the A/U richness (A) and icSHAPE reactivity score – both in vivo (B) and in vitro (C) – for various sites of putative Ago2-miRNA binding targets. The datasets of putative Ago2-miRNA binding sites are the DeepRNA-Reg and dCLIP predicted set of miR-23,24,27 targets provided by the WT Th2 vs. miR-23,24,27 KO Th2 differential AHC analysis, and the set of all Ago2 binding sites called by the algorithm Clipper 2.0 within a dataset of HITS-CLIP performed within WT T-Helper 2 Cells. Below the heatmaps are line plots representing the average signal presented within the heatmaps, collapsed across all predicted binding sites of Ago2. (D-F) Heatmaps showing the free energy change of dimerization of a rolling 10-bp window surrounding the miRNA seed containing site and the miRNA seed containing region (a 10 bp window centered at the site center) for the set of all Ago2 binding sites called by the algorithm Clipper 2.0 within a dataset of HITS-CLIP performed within WT T-Helper 2 Cells (D), and the DeepRNA-Reg (E) and dCLIP (F) predicted set of miR-23,24,27 targets provided by the WT Th2 vs. miR-23,24,27 KO Th2 differential AHC analysis. Plots located below show the average signal across all sites presented in the heatmap.

Disclosure: S. Sekhon: None; **R. Kageyama**: None; **N. Sprenkle**: None; **H. Happ**: None; **E. Wigton**: None; **H. Pua**: None; **M. Ansel**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1001

LBL-057, a Novel ADCC Enhanced PD-1 Agonist VHH-Fc Antibody

Hongyan Shang[1], **Xiao Huang**[2], Duqing Jiang[1], Jianming Sun[2], Yurong Qin[2], Guojin Wu[2], Chengze Ni[1], Jing Guan[2], Jordan Zhu[3], Xiaoqiang Kang[2] and Hong Ling[2], [1]Nanjing Leads Biolabs Co., Ltd., nanjing, China (People's Republic), [2]Nanjing Leads Biolabs Co., Ltd., Nan Jing, China (People's Republic), [3]Nanjing Leads Biolabs Co., Ltd., Nan Jing

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Programmed cell death protein 1 (PD-1) is expressed on activated T cells and serves as a key co-inhibitory checkpoint molecule in immune regulation. Aberrant in PD-1 signaling increases human susceptibility to multiple autoimmune diseases, while insufficient PD-1 signaling can lead to dysregulated T cell responses. By targeting PD-1 regulatory mechanisms to modulate disease-driving T cells, LBL-057 aims to dampen the inflammatory cycle and restore immune balance. LBL-057 is an ADCC (antibody-dependent cellular cytotoxicity) enhanced PD-1 agonistic VHH-Fc antibody that stimulates the endogenous PD-1 inhibitory pathway, inhibits activated T cells, and reduces T cell proliferation and inflammatory cytokine secretion. In addition, the ADCC-enhanced design enables effective depletion of PD-1^+ T follicular helper cells and T effector cells, offering an attractive therapeutic approach for the treatment of PD-1^+ T cells driven autoimmune disorders such as rheumatoid arthritis (RA) and inflammatory bowel disease (IBD).

Methods: A panel of diverse VHH antibodies against PD-1 were developed via alpaca immunization and phage library screening. Candidates underwent rigorous *in vitro* evaluation, including PD-1^+ cell binding, PD-L1/PD-L2-PD-1 blockade, ADCC activity and PD-1 agonist activity. In addition, the inhibitory effect of LBL-057 on graft-versus-host disease (GvHD) was validated in a human PBMC transplantation mouse model.

Results: LBL-057 binds to PD-1 with an epitope distinct from pembrolizumab and enhances PD-1 interaction with to PD-L1/PD-L2 rather than blocking it. *In vitro* assays confirmed that LBL-057 significantly activates PD-1 pathway, suppresses PD-1^+ T-cell proliferation and activation in a dose-dependent manner. Furthermore, LBL-057 exhibits potent ADCC activity, effectively reducing PD-1^+ T cell populations. *In vivo*, LBL-057 demonstrated a better efficacy than benchmarks in inhibition of GvHD progression in mice.

Conclusion: LBL-057, a VHH-Fc antibody, specifically binds to a unique epitope on PD-1, with dual mechanisms of action. On the one hand it depletes PD-1^+ T cells with enhanced ADCC ability, on the other it enhances PD-1-PD-L1/PD-L2 interactions while activates PD-1 downstream signaling. Taken together, it potently suppresses T cell proliferation and activation *in vitro* and alleviates pathological damage in a GvHD mouse model. These findings support its therapeutic potential for PD-1^+ T cells driven autoimmune disorders.

Disclosure: H. Shang: None; **X. Huang**: None; **D. Jiang**: None; **J. Sun**: None; **Y. Qin**: None; **G. Wu**: None; **C. Ni**: None; **J. Guan**: None; **J. Zhu**: None; **X. Kang**: None; **H. Ling**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1002

ATF3 Inhibits Pulmonary Fibrosis via CD4+CD25−LAG3+ T Cells

Xiao Zhang[1], linmang Qin[2] and Yixuan Li[1], [1]The Eighth Affiliated Hospital of Sun Yat-sen University, Shenzhen, Guangdong, China (People's Republic), [2]Sun Yat-sen University, gaungzhou, Guangdong, China (People's Republic)

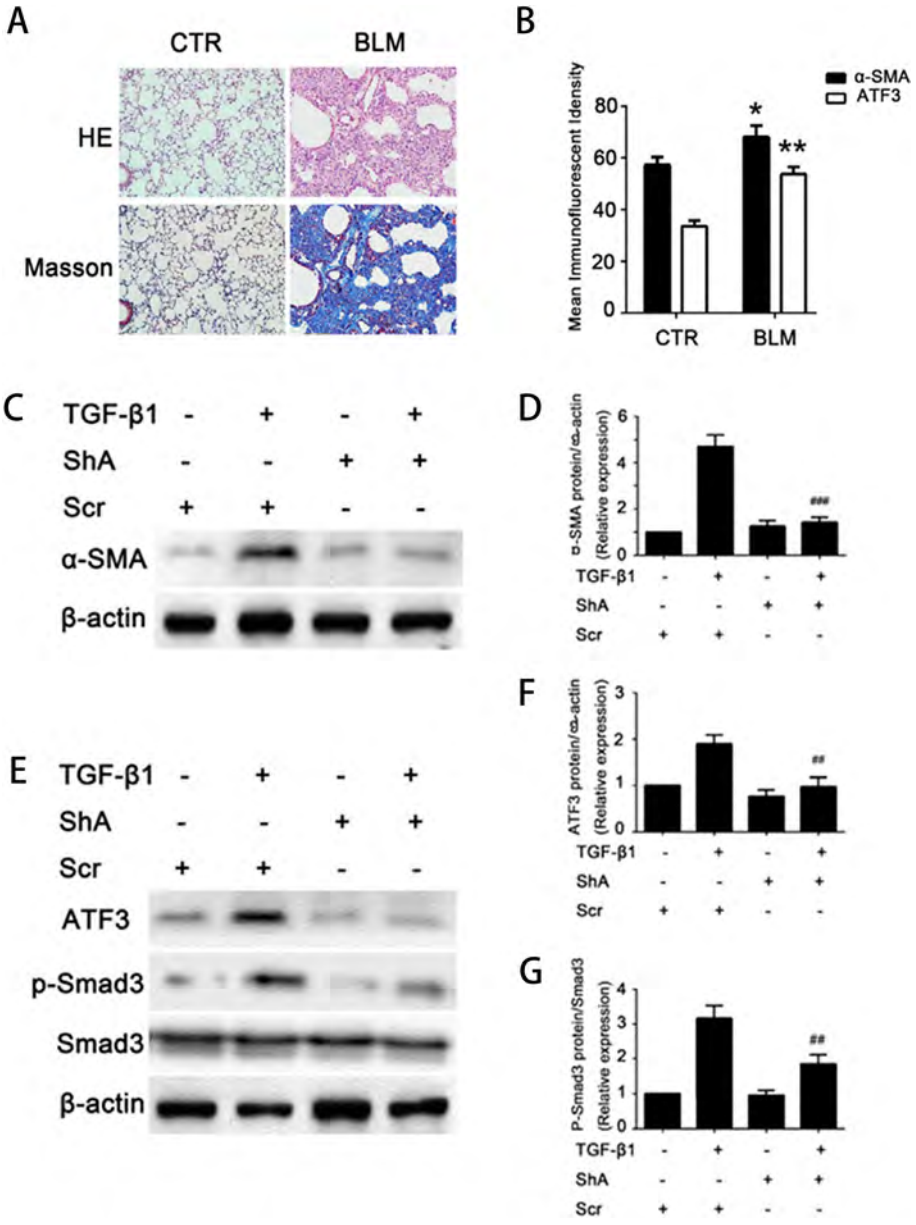
SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM



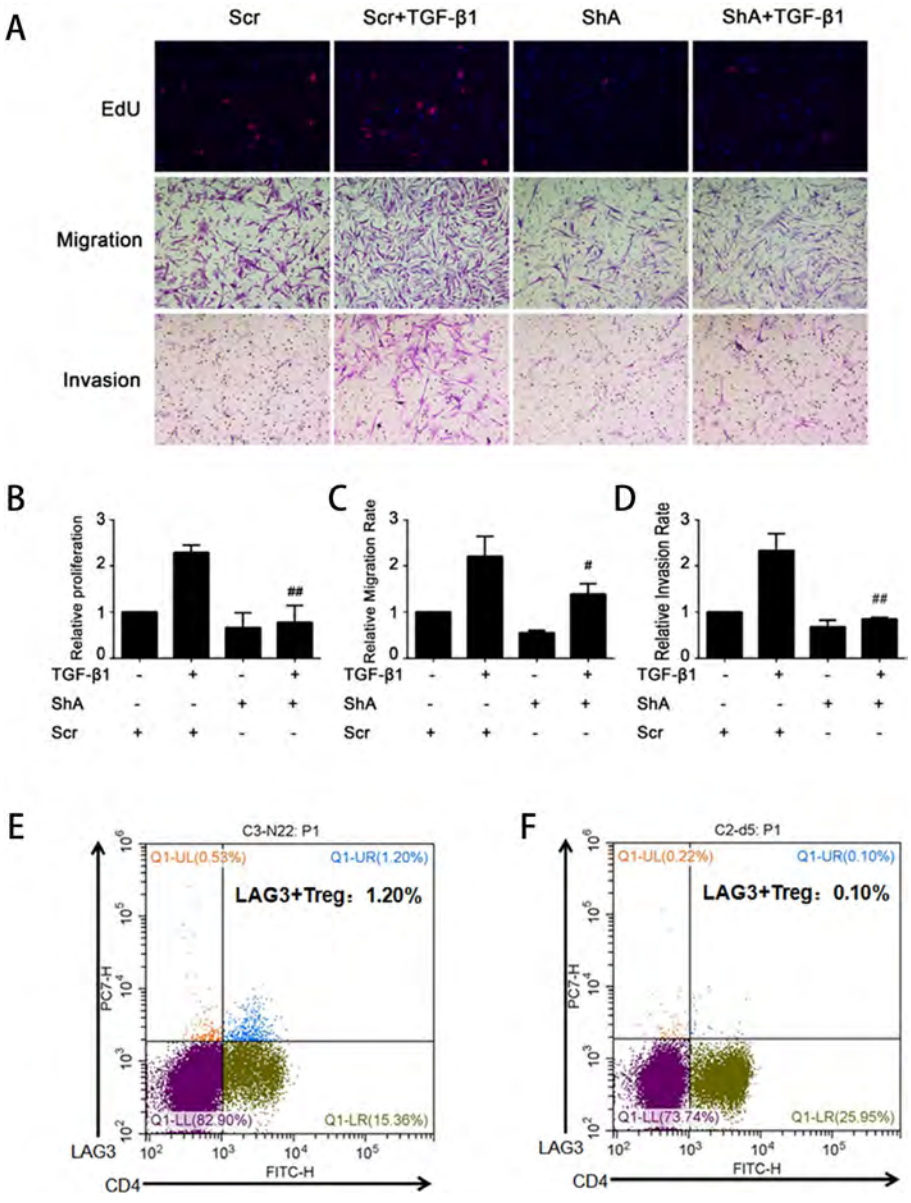
(A-B) Elevated expression of α-SMA and ATF3 in bleomycin-induced pulmonary fibrosis mouse model. (C-G) TGF-β1 induces ATF3 and Smad3 expression in human lung fibroblasts.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The rising incidence of connective tissue disease-associated interstitial lung disease (CTD-ILD) significantly worsens patient prognosis. While its pathogenesis remains unclear, immune-inflammatory dysregulation—particularly enhanced immune responses and impaired suppression—may drive chronic inflammation and fibrosis. T cells regulate fibroblast activation and collagen synthesis, interacting with other immune cells to accelerate fibrosis. Notably, reduced LAG3+ T cell populations in CTDs suggest iTreg dysfunction. Our prior studies identified elevated ATF3, a leucine zipper transcription factor, in pulmonary fibrosis. ATF3 may modulate inflammation, fibrosis, and immune responses. We hypothesize that ATF3 promotes fibrosis, and its knockdown could attenuate progression, possibly by expanding LAG3+ T cells.

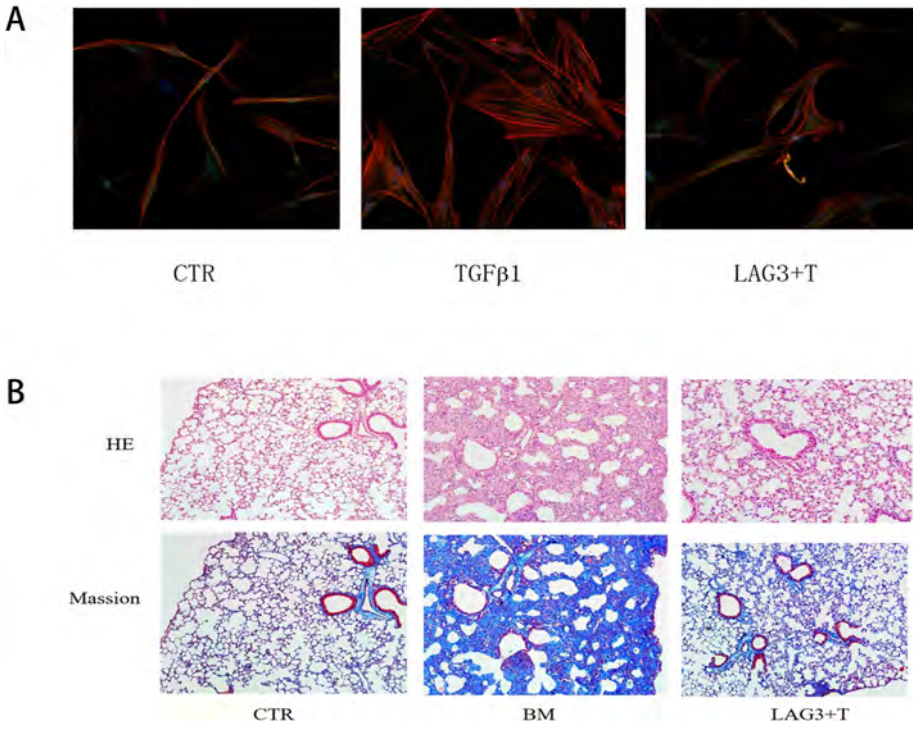
Methods: 1. Establish a bleomycin-induced pulmonary fibrosis mouse model and measure ATF3 expression levels.

2. Culture human lung fibroblasts in vitro and assess the effects of TGF-β1 induction on their proliferation, migration, and invasion capabilities.



(A-D) ATF3 knockdown suppresses TGF-β1-induced proliferation, myofibroblast differentiation, and invasion in human lung fibroblasts. (E-F) Significant reduction of CD4+CD25-LAG3+ regulatory T cells in peripheral blood of SSC-ILD patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(A) Supernatants from LAG3+ Tregs inhibit TGF-β1-induced fibroblast-to-myofibroblast transition in human lung fibroblasts (20×) (Red: F-actin; Green: α-SMA; Blue: DAPI). (B) Adoptive transfer of LAG3+ T cells ameliorates pulmonary inflammation and fibrosis in murine models.

3. Construct siATF3 knockdown/overexpression in naive CD4+ T cells and examine their regulatory effects on lung fibroblast proliferation, migration, and invasion.

4. Quantify LAG3+ T cell populations in peripheral blood of SSC-ILD patients using flow cytometry with dual-labeling techniques. Isolated LAG3+ T cells will be cultured, and their supernatants will be added to in vitro cultured human lung fibroblasts to evaluate fibrosis markers (F-actin and α-SMA).

5. Evaluate spontaneous lung inflammation, collagen deposition, and LAG3+ T cell levels in ATF3-/- mice. Additionally, adoptive transfer of LAG3+ T cells from wild-type mice will be performed to assess their impact on lung pathology in bleomycin-induced pulmonary fibrosis models.

Results: 1. ATF3 expression is upregulated in bleomycin-induced pulmonary fibrosis mice.
2. TGF-β1 induces overexpression of α-SMA, Smad, and ATF3 in human lung fibroblasts in vitro.
3. ATF3 knockdown suppresses TGF-β1-induced proliferation, activation (myofibroblast transdifferentiation), and invasion of human lung fibroblasts.
4. Peripheral blood LAG3+ T cell counts are reduced in SSC-ILD patients compared to controls.
5. Supernatants from LAG3+ T cell cultures inhibit fibrotic marker expression (blocking TGF-β1-induced fibroblast-to-myofibroblast transition).Adoptive transfer of LAG3+ T cells ameliorates lung inflammation and fibrosis in murine models.

Conclusion: ATF3 promotes proliferation, migration, and invasion of lung fibroblasts, playing a critical role in pulmonary fibrosis progression. Knockdown of ATF3 significantly attenuates fibrotic progression, suggesting its utility as a therapeutic target. Adoptive transfer of LAG3+ T cells suppresses inflammatory responses and hyperproliferation of immune cells, demonstrating their protective role in fibrosis. These findings provide A novel strategy for treating CTD-ILD by targeting the ATF3/LAG3+ T cell axis, Translational potential for developing immunomodulatory or gene-based therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: X. Zhang: None; **I. Qin**: None; **Y. Li**: None.

Abstract Number: 1003

Potent Engineering of Polyfunctional CD8+ T Cells by a Novel *In Vivo* CAR mRNA Product Candidate (CPTX2309) in a Targeted Lipid Nanoparticle (tLNP) Utilizing CellSeeker™ Technology

Yan Zhang[1], Brittany Ross[1], Aditi Upadhye[1], Diana Galvan[1], Shaun E Grosskurth[1], Yanjie Bao[1], Romina Riener[1], Annabel Wang[1], Aric Frantz[1], Gregor B Adams[1], Michael Rosenzweig[1], Ramin Farzaneh-Far[1], Priya Karmali[1], Adrian I Bot[1], Carl June[2] and Haig Aghajanian[1], [1]Capstan Therapeutics, San Diego, CA, [2]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: A major objective in autoimmunity is immune reset, requiring autoreactive B cell depletion in tissues. We designed an *in vivo* CAR product candidate (CPTX2309) utilizing a targeted lipid nanoparticle (tLNP) technology (CellSeeker™), comprising proprietary ionizable lipid-based LNP targeted to engineer CD8+ T cells from normal subjects or autoimmune disease patients, by delivering encapsulated mRNA CD19 CAR (ACR Convergence, 2024). Utilizing NHPs and a surrogate product, we defined a compact dose regimen of two infusions 72 hours apart that resulted in rapid engineering of CD8+ T cells and profound B cell depletion in peripheral blood and tissues (ASGCT, 2025). Herein, we report mechanistic data generated on human T cells *in vitro*, in support of clinical translation of CPTX2309.

Methods: CPTX2309 contains an mRNA encoding for an all human anti-human CD19 CAR, in a CD8-targeted tLNP. Transcriptomic analysis was performed on T cells upon incubating CPTX2309 with human peripheral blood mononuclear cells (PBMC). Additional analysis was performed by depletion of cell subsets from PBMC utilizing immunomagnetic beads, followed by cytotoxicity and cytokine production analysis.

Results: CPTX2309 incubation with human PBMCs *in vitro* resulted in rapid (< 24 hr) and selective engineering of CD8+ T cells to express a CD19 CAR. This resulted in rapid depletion of autologous B cells (24-72hr timeframe). The interaction with autologous B cells also resulted in activation of CAR+ CD8+ T cells, namely augmentation of cellular metabolic programs including cellular proliferation and ribosomal translational activity. Transcriptomic analysis demonstrated the activation of several immune programs known to induce immune cell effector polyfunctionality – including cytotoxicity and the type II IFN pathway. In contrast, mCherry mRNA-loaded tLNPs showed minimal effect. Depletion of CD8+ T cells but not of any other cell subset (CD4+ T cells, NK cells or myeloid cells) within the PBMC population, resulted in profound diminution of B cell depletion as well as IFNγ production in culture, demonstrating that the tLNP-engineered CD8+ CAR T cells are the primary driver of efficacy and on-target activity of CPTX2309.

Conclusion: CellSeeker™ technology affords a tunable CAR exposure without the risk of prolonged on target toxicities or genotoxicity. These novel data including transcriptomic analysis shed light on the cellular and molecular mechanism of action of CPTX2309, explaining the high engineering rate and pharmacodynamic activity afforded by this platform technology. Together with preclinical data generated in mouse and NHPs, this supports the translation of CPTX2309 to clinic.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Y. Zhang: None; **B. Ross**: None; **A. Upadhye**: None; **D. Galvan**: None; **S. Grosskurth**: None; **Y. Bao**: None; **R. Riener**: None; **A. Wang**: None; **A. Frantz**: None; **G. Adams**: None; **M. Rosenzweig**: None; **R. Farzaneh-Far**: None; **P. Karmali**: None; **A. Bot**: None; **C. June**: Capstan, 12,, 1, 10; **H. Aghajanian**: None.

Abstract Number: 1004

Single-Cell Analysis Reveals Tissue Resident Memory T Cells Heterogeneity in the Joint

Yang Yang[1], Yusuke Miyashita[2], Madison Mangin[3], Kellen Winden[1], Peter Nigrovic[2] and Margaret Chang[1], [1]Boston Children's Hospital, Boston, MA, [2]Boston Children's Hospital, Brookline, MA, [3]Boston Children's Hospital, St Simons Island, GA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint-specific memory, the phenomenon in which arthritis repeatedly flares in the same joints. We previously demonstrated that CD8 synovial resident memory T (T_{RM}) cells persist in arthritic joints and mediate joint-specific memory. There is increasing recognition of diversity among T_{RM} cells with distinct functional subsets described across tissues and diseases. Here, we evaluated the heterogeneity of CD8 T_{RM} cells within arthritic synovium in humans and mice and investigated their developmental precursors.

Methods: We evaluated the gene expression profiles of memory T cells isolated from human RA synovium through 10x single-cell RNA sequencing. As we previously demonstrated CD8 T_{RM} cells to be important for joint specific memory, we further evaluated subclusters of CD8 memory T cells from the synovium using Seurat and weighted gene co-expression network analysis packages. Cell clusters were annotated by the presence of known marker genes and comparison to published T_{RM} gene expression signatures. We further evaluated the gene expression profiles of CD8 T cells isolated from the synovium of a mouse model of arthritis of flare and remission. CD8 T cells were isolated from the synovium at several time points across the course of arthritis through acute joint inflammation and remission and sequenced by 10x single-cell RNA sequencing. Synovial T_{RM} cells were identified through transcriptomic profiles and presence in synovium during remission. Subclusters of CD8 T_{RM} cells were further refined, and trajectory of analysis and cell ancestry of these synovial CD8 T_{RM} cell clusters were computed with the Waddington Optimal Transport and Pseudotime analysis packages. We further confirmed the developmental progenitors of these T_{RM} cells using human synovial organoids.

Results: We identified diversity among CD8 memory T cells in human RA synovium, including several subclusters of cells exhibiting transcriptomic profiles consistent with T_{RM}. Gene Ontology enrichment analysis of highly expressed genes among T_{RM} subclusters reveals pathways in T cell differentiation, granzyme-mediated programmed cell death signaling, and negative regulation of T cell apoptosis, suggesting distinct functions in cytotoxicity and tissue-adaptive programming. We identified similar T_{RM} subpopulations in the synovium of murine arthritis during remission. Trajectory analysis revealed different timing in the emergence of these T_{RM} subpopulations during arthritis, further implicating distinct roles in disease.

Conclusion: Our findings reveal heterogeneity within CD8 T_{RM} cells in both murine and human synovial tissue. This diversity in function and timing of these T_{RM} subpopulations suggests different roles in arthritis pathogenesis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Y. Yang: None; **Y. Miyashita**: None; **M. Mangin**: None; **K. Winden**: None; **P. Nigrovic**: Alkermes, 2, Apollo, 2, Bristol-Myers Squibb(BMS), 5, Century, 2, Edelweiss Therapeutics, 11, Merck, 2, Monte Rosa, 2, Novartis, 2, Pfizer, 2, 5; **M. Chang**: None.

Abstract Number: 1005

CD49a Contributes to Binding and Survival of Synovial Resident Memory T cells

Yusuke Miyashita[1], Yang Yang[2], Madison Mangin[3], Maryrose Hahn[2] and Margaret Chang[2], [1]Boston Children's Hospital, Brookline, MA, [2]Boston Children's Hospital, Boston, MA, [3]Boston Children's Hospital, St Simons Island, GA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease featured with recurrent inflammation in the same joints, a characteristic termed joint-specific memory. We previously demonstrated that joint-specific memory in arthritis is mediated by resident memory T (T_{RM}) cells in the synovium. T_{RM} cells remain in the synovium of previously inflamed joints and activation of T_{RM} cells can drive recurrent arthritis flare. However, the factors that mediate the persistence of T_{RM} cells in the synovium are unclear. Here, we investigate the role of CD49a in the retention and survival of T_{RM} in synovial tissue.

Methods: We generated synovial organoids with CD8 memory T cells isolated from peripheral blood mononuclear cells, fibroblast-like synoviocytes (FLS) isolated from RA synovium, and human umbilical vein endothelial cells (HUVEC) encapsulated in Matrigel. T_{RM} cells form within the synovial organoid after 3 weeks of culture. To evaluate whether CD49a mediates binding of T_{RM} cells to FLS, isolated T_{RM} cells were incubated with isotype or CD49a neutralizing antibodies, then added to a microfluidic slide (μ-Slide I Luer) seeded with FLS. The strength of cell binding was assessed through live cell imaging of bound T_{RM} cells under increasing velocities of laminar flow. Cell survival was assessed in CD49a positive T_{RM} cells through viability dye and Annexin V staining in cells remaining within the synovial organoids and those that migrated out of the Matrigel. Cell proliferation was assessed in CD49a positive T_{RM} cells through intracellular staining for Ki67.

Results: We found that T_{RM} cells incubated with CD49a neutralizing Ab had lower binding affinity to FLS. Further, CD49a positive T_{RM} cells had less cell death compared to CD49a negative T_{RM} cells, and viability of T_{RM} cells also increased in cells remaining within the synovial organoids. Moreover, there is increased Ki67 expression in CD49a positive T_{RM} cells compared to CD49a negative T_{RM} cells at 21 days of culture.

Conclusion: We showed that CD49a contributes to binding of T_{RM} cells to FLS. Further, CD49a positive T_{RM} cells have increased viability particularly within the organoid structure and a higher proliferative capacity even after 21 days of culture, suggesting a possibility for self-renewal. Our findings implicate CD49a in the persistence and survival of T_{RM} cells in synovial tissue. Targeting T_{RM} cell anchoring could provide a novel therapeutic approach to joint-specific memory and chronic arthritis.

Disclosure: Y. Miyashita: None; **Y. Yang**: None; **M. Mangin**: None; **M. Hahn**: None; **M. Chang**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1006

Ai-guided Generation and Preclinical Evaluation of an OX40L-IL31 Bispecific Antibody

Yun Zhang, Hao Ran, Tianhong Li, Liguo Dong, Chenpeng Su, Chuan Chen, Lisha Dong, Dandan Liu, Yi Pan, Xiaoou Xu, Xiaoqian Chen, Liang Tian, Jian Peng and **Zhenping Zhu**, Helixon Therapeutics, New York

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (0978–1006) T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The itch-scratch cycle in atopic dermatitis (AD) is closely linked to skin inflammation exacerbation, which not only accelerates disease progression but also significantly impacts patients' quality of life. IL31 is a key factor in promoting itching, and antibodies targeting IL31Ra have shown promising therapeutic effect in AD patients in alleviating the disease symptoms, but with limited activity on the underlying skin inflammation and overall disease progression. In this study, we developed a bispecific antibody (bsAb), HXN-1022, that binds to and neutralizes both IL31 and OX40L, aiming to simultaneously inhibit OX40L and IL31 activities, thus providing a faster, deeper and more durable therapeutic efficacy to patients with AD and other autoimmune skin disorders.

Methods: The binding affinity of bsAb to each target was evaluated using SPR, while its interaction with membrane-bound OX40L was measured with flow cytometry. The biological activity of HXN-1022 was examined through various *in vitro* assays, including IL31R-STAT reporter assay and HaCaT cell activation assay for IL31, and OX40-NFκB-Luc reporter assay and Th2-differentiation assay for OX40L. *In vivo* efficacy was demonstrated in human PBMC-reconstituted GvHD (graft-versus-host disease) mouse model.

Results: We generated a highly potent anti-IL31 antibody through an internal AI-guided design and optimization platform. This antibody significantly inhibits IL31 biological activity, as demonstrated in the IL31R-STAT reporter assay and HaCaT cell activation assay, outperforming the benchmark antibodies Nemolizumab and NM26-2198 analogs. Using this anti-IL31 antibody and an anti-OX40L antibody as the building blocks, we engineered HXN-1022, a tetravalent bispecific antibody capable of simultaneously binding IL31 and OX40L with high affinity. HXN-1022 effectively blocks both IL31 and OX40L from interacting with and activating their respective receptors, with potency comparable to each of the parent antibodies. Moreover, HXN-1022 demonstrated a strong therapeutic efficacy in a human PBMC-reconstituted GvHD (graft-versus-host disease) mouse model. The bsAb significantly inhibited T cell proliferation, alleviated key GvHD symptoms, and prolonged the survival of the animals.

Conclusion: HXN-1022 is a first-in-class bsAb that simultaneously targets IL31 and OX40L, two major pathogenic factors associated with skin inflammation and itch. The bsAb holds great potential as a more effective therapeutic option for patients with a variety of autoimmune skin disorders.

Disclosure: Y. Zhang: None; **H. Ran**: None; **T. Li**: None; **L. Dong**: None; **C. Su**: None; **C. Chen**: None; **L. Dong**: None; **D. Liu**: None; **Y. Pan**: None; **X. Xu**: None; **X. Chen**: None; **L. Tian**: None; **J. Peng**: None; **Z. Zhu**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1007

Accelerometry-derived Activity and Sleep Patterns in the NIH All of Us Cohort: Insights and Predictive Potential for Inflammatory Arthritis

Adeep Kulkarni[1], Jose Scher[2], Rebecca Haberman[3] and Souptik Barua[1], [1]New York University Grossman School of Medicine, New York, NY, [2]New York University School of Medicine, New York, NY, [3]NYU Langone Health, New York, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with inflammatory arthritis (IA) report reduced physical activity and poor sleep, However, much remains unknown about the extent and impact of this relationship. Using accelerometry data from the NIH All of Us Research Program, we investigated (1) physical activity and sleep patterns in those with and without IA, and (2) the association of activity and sleep with risk of incident IA.

Methods: Participants who consented to share electronic health records and had at least one year of Fitbit accelerometry data in All of Us were included. IA was defined as ICD-10 codes for rheumatoid (RA) or psoriatic arthritis (PsA). Incident IA was defined as new IA diagnosis from the completion of accelerometry data up to 10 years. Daily step count, weekly moderate-vigorous physical activity (MVPA), daily sedentary time, and nightly sleep duration were assessed. Between group differences were tested using Kruskal-Wallis and Bonferroni-adjusted Dunn's tests. Associations between accelerometry metrics with incident IA were identified using Cox proportional hazards models adjusting for age, sex, and race/ethnicity.

Characteristic	All (n=24,808)	Inflammatory Arthritis (n=206)	No Arthritis (n=24,602)	p-value
Age - mean (SD)	51.86 (15.32)	58.04 (12.59)	51.81 (15.33)	<0.001
Female - n (%)	17,268 (69.6%)	168 (81.6%)	17,100 (69.5%)	<0.001
Race - n (%)				0.011
- White	19,569 (78.9%)	173 (84.0%)	19,396 (78.8%)	
- Black	1,426 (5.7%)	11 (5.3%)	1,415 (5.8%)	
- Asian	856 (3.5%)	1 (0.5%)	855 (3.5%)	
- Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Number of days - mean (SD)	319.57 (54.53)	317.15 (52.26)	319.59 (54.55)	<0.05
BMI - median (IQR)	28.31 (27.12–30.09)	29.41 (26.48–34.69)	28.30 (27.12–30.07)	<0.001
Hypertension - n (%)	8,196 (33.0%)	173 (84.0%)	8,023 (32.6%)	<0.001
Diabetes - n (%)	3,224 (13.0%)	85 (41.3%)	3,139 (12.8%)	<0.001

Cohort Characteristics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

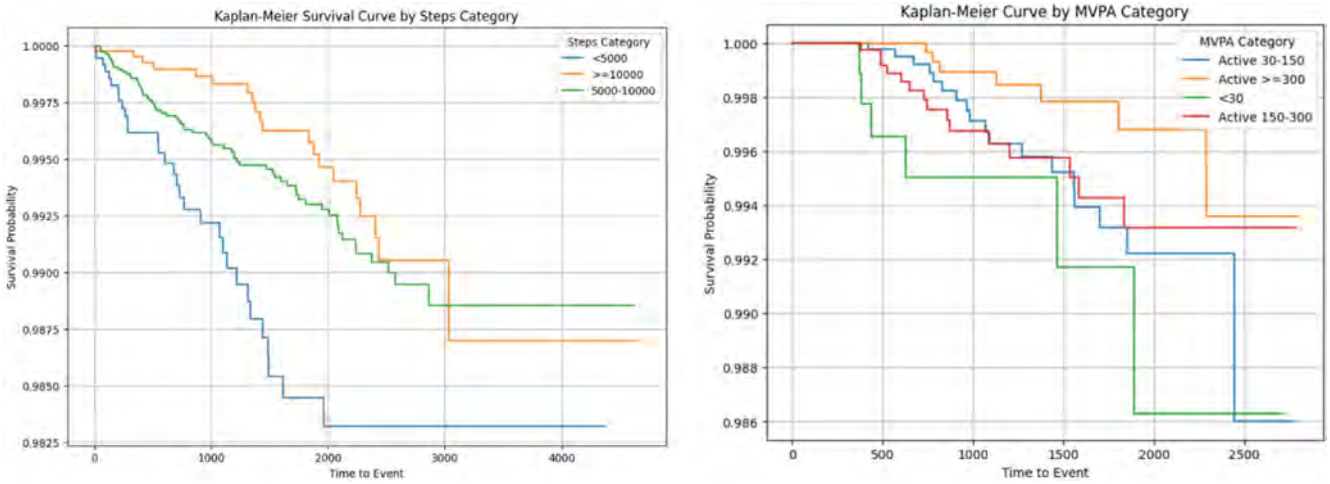
Results: 24,808 individuals were included (mean age 51.9 [15.3] years, 70% female, 79% White); 206 had IA (177 with RA and 29 with PsA). Compared to those without IA, participants with IA were older (58.0 vs 51.8 years, p< 0.001), female (81.6% vs 69.5%, p< 0.001), and had higher rates of hypertension (84.0% vs 32.6%, p< 0.001) and diabetes (41.3% vs 12.8%, p< 0.001). Participants with IA had lower median daily step counts (6,742 [5,093–9,327] vs 7,360 [5,386–9,693]; p< 0.001), lower weekly MVPA (147.0 [62.7–271.2] vs 185.3 [88.8–330.9] minutes; p< 0.001), and higher sedentary time (900.7 [759.3–981.3] vs 799.0 [704.8–961.1] minutes; p< 0.001). Sleep duration was similar between the two groups (371 [312, 418] vs 385 [332, 426] minutes; p=0.78).

125 individuals developed incident IA. Adjusting for age, sex, and race/ethnicity, each additional 1,000 steps/day was associated with an 8% lower risk of IA (HR 0.92; p=0.012). Compared to < 5,000 steps/day, 5,000–10,000 steps/day was associated with a 45% lower risk (HR 0.55; p=0.007) and >10,000 steps/day with a 57% lower risk (HR 0.43; p=0.004). MVPA showed that participants engaging in ≥300 minutes/week of MVPA had a significantly lower risk of IA (HR 0.27; p=0.022) compared to those with < 30 minutes/week. There was no significant association between incident IA and sedentary time (HR 1.00 per minute; p=0.294) or nightly sleep duration (HR 1.04 per hour; p=0.388).

Conclusion: Accelerometers provide more objective and granular measurement of physical activity and sleep compared to self-reported data. Using 1-year accelerometry data from the NIH All of Us cohort, we observed lower physical activity and higher sedentary time in those with IA. Further, higher step counts and MVPA were significantly associated with reduced 10-year risk of incident IA, highlighting the crucial role of physical activity in IA prevention. Wearable technologies may offer valuable insights into the complex interplay between activity, sleep, and arthritis, and further studies in well-phenotyped cohorts are warranted.

Variable	HR	p-value
Age (per 10 years)	1.09	0.1856
Sex (reference: Female)	0.50	0.0050
Race (reference: White)	1.41	0.1539
Ethnicity (reference: Not Hispanic)	1.15	0.7155
5000–10000 steps (reference: <5000)	0.55	0.0067
≥10000 steps (reference: <5000)	0.43	0.0040

Cox regression results showing the association between accelerometry-derived steps categorized by WHO guidelines and incident inflammatory arthritis.



Kaplan Meier Survival Probability Curves for Categorical Steps and Categorical MVPA v Incident IA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: a. Kulkarni: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **R. Haberman**: Johnson and Johnson, 1, 2, Novartis, 1, 2; **S. Barua**: None.

Abstract Number: 1008

Nationwide Historical Cohort Study on the Primary Prophylactic Effects of Colchicine in Cardiovascular Events

Hasan Satis[1], Umut Kalyoncu[2], Gizem Ayan[3], Ali Aykut Fidanci[4], Mustafa Mahir Ulgu[4], Naim Ata[4], Suayip Birinci[4], Mehmet Koçak[5] and **Ahmet Gul**[6], [1]University of Health Sciences, Abdurrahman Yurtaslan Oncology Hospital, Rheumatology, Ankara, Turkey, [2]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [3]Ankara Research and Training Hospital, Ankara, Turkey, [4]Ministry of Health, Ankara, Turkey, [5]Medipol University, Istanbul, Turkey, [6]Istanbul University, Istanbul, Turkey

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: While two trials with colchicine have demonstrated its efficacy in reducing the risk of cardiovascular events, a more recent study showed no significant impact on the composite primary outcome over three years. This study aims to evaluate the cardioprotective effects of colchicine on the incidence of myocardial infarction requiring bypass surgery or stent placement, utilizing a nationwide historical cohort.

Methods: The electronic medical registry system of Turkiye was retrospectively analyzed for the period between January 1, 2015, and December 31, 2024. Individuals aged 50 or older who regularly used colchicine (defined as being prescribed at least 3 times per year) between January 1, 2018, and December 31, 2024, were identified as the study group, which consisted mainly of patients with familial Mediterranean fever (FMF) and gout. A control group, matched 1:1 for age, gender, and history of diabetes mellitus (DM), hypertension, hyperlipidemia, and chronic renal failure, was selected. Additionally, a second set with a case-to-control ratio of 1:2 was prepared, matching participants based on geographical region. Subgroup analyses were conducted on statin users and on a third set with a 1:2 ratio, matched for a history of gout. The primary outcome was defined as the first myocardial infarction (MI) requiring bypass surgery or stent placement. The association of colchicine use with the likelihood of cardiovascular endpoint was investigated through logistic regression models.

Results: A total of 41,971 individuals who regularly used colchicine during the defined period were identified, along with a matched control group of 41,833 individuals. During the study, 5,278 participants were diagnosed with myocardial infarction (MI) requiring bypass surgery or stent placement. Multivariate logistic regression analysis showed a significantly lower rate of cardiovascular events in the colchicine group compared to the control group (OR=0.769, 95% CI: 0.724–0.816, p< 0.001). A similar analysis using a larger, geographically matched control group at a 1:2 ratio yielded comparable results (OR=0.770, 95% CI: 0.731–0.812, p< 0.001). In a subgroup analysis with a control group matched for gout, the protective effect of colchicine persisted, albeit to a lesser extent (OR=0.882, 95% CI: 0.836–0.930, p< 0.001). Interestingly, colchicine's protective effect was evident in individuals not using statins (OR=0.741, 95% CI: 0.694–0.790, p< 0.001), but no significant difference was observed among regular statin users. Additionally, there was no statistically significant difference in cardiovascular event risk between controls using statins and individuals on colchicine who were not using statins (OR=0.976, 95% CI: 0.860–1.109, p=0.0906).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This nationwide health record study represents the largest cohort of patients and controls to date, reinforcing earlier clinical trial findings by demonstrating a reduction in cardiovascular event rates associated with colchicine use. The relatively lower protective effects observed in gout patients may be linked to higher cardiovascular risks, lower colchicine dosages, and potentially greater non-compliance compared to patients with FMF.

Disclosure: H. Satis: None; **U. Kalyoncu**: None; **G. Ayan**: None; **A. Fidanci**: None; **M. Ulgu**: None; **N. Ata**: None; **S. Birinci**: None; **M. Koçak**: None; **A. Gul**: None.

Abstract Number: 1009

Pregnancy Outcomes and Comorbidities Among Individuals with Systemic Lupus Erythematosus: A Nationwide Study Using Publicly Funded Health Insurance Claims Data

Amadeia Rector[1], Sadaf Sediqi[2], Alyssa Howren[2] and Julia F Simard[3], [1]Stanford University, San Francisco, CA, [2]Stanford University, Palo Alto, CA, [3]Stanford Medicine, Stanford, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Individuals with SLE are at increased risk for pregnancy complications such as preeclampsia and preterm delivery. As SLE is commonly diagnosed and active during the childbearing years—and more individuals are pursuing pregnancy due to improved management—there is a growing need to better understand pregnancy outcomes in this population. To address this, we describe pregnancy characteristics and outcomes among individuals enrolled in Medicaid, a publicly funded health insurance program available nationwide.

Methods: Using data from Medicaid T-MSIS Analytic Files (TAF), we identified all pregnancies for patients with SLE from 2014 to 2019. SLE was defined as ≥2 ICD coded outpatient visits occurring less than 30 days apart or ≥1 ICD coded inpatient visit (ICD9: 710.0, ICD10: M32.1X, M32.8, M32.9) occurring before or during pregnancy. We described demographic factors (age, race and ethnicity, and income relative to federal poverty level) and pregnancy characteristics (parity, delivery type, complications, comorbidities occurring during and before pregnancy, and pregnancy outcomes). Additionally, we stratified the pregnancy outcomes by race.

Results: This diverse cohort consisted of 9391 pregnancies among 8201 individuals with SLE , with 2% identifying as Asian, 29% as Black, 17% as Hispanic, and 32% as white. Forty-four percent were below the federal poverty level. Most pregnancy were livebirths (93%). Approximately 16% of pregnancies were complicated by preeclampsia and 18% resulted in preterm delivery. (Table 1). When stratified by race, Black individuals had the highest prevalence of preeclampsia (19%) and preterm delivery (22%). (Table 2)

Conclusion: Pregnancies among patients with SLE had a high frequency of preeclampsia and preterm delivery compared to estimates in the general population (3-7% preeclampsia and 10% preterm). Black individuals had the highest prevalence of complications. These findings offer contemporary, national estimates of pregnancy complications and outcomes among publicly-insured individuals with SLE, highlighting variations by parity and comorbidity burden, and provide patients and providers with further data to inform pregnancy planning and risk counseling.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Demographics and clinical characteristics of pregnancies among Medicaid enrollees diagnosed with systemic lupus erythematosus, presented as n (%) unless noted otherwise

	All pregnancies (N=9391)
Demographics	
Maternal age, median (IQR), years	29 (8)
Gestational age, mean (SD), weeks	35.5 (7)
Race and ethnicity[1]	
American-Indian and Alaskan Native	141 (2)
Asian	219 (2)
Black	2738 (29)
Hawaiian/ Pacific Islander	44 (0.5)
Hispanic, any race	1572 (17)
Multiracial	34 (0.4)
White	2968 (32)
Null/Missing	1675 (18)
Income relative to federal poverty level (FPL)	
Below FPL (≤100% FPL)	4127 (44)
Low income (101 – 133% FPL)	499 (5)
Low-moderate income (134 – 150% FPL)	81 (1)
Moderate income (151 – 200% FPL)	122 (1)
Middle income (201 – 250% FPL)	32 (0.3)
High income (≥251% FPL)	19 (0.2)
Null/missing	4511 (48)
Comorbidities[2]	
Pre-Gestational Hypertension	567 (6)
Diabetes (type 1 and 2)	295 (3)
Obesity (BMI > 30 kg/m2)	1082 (12)
Lupus nephritis	1420 (15)
Pregnancy features and complications	
Multiparity	4767 (51)
Cesarean section[3]	3649 (42)
Preeclampsia/eclampsia[3]	1363 (16)
Preterm delivery (< 37 weeks)[3]	1589 (18)
Spontaneous	961 (11)
Medically indicated	558 (6)
Gestational diabetes[3]	898 (10)
Gestational hypertension[3]	58 (1)
Postpartum hemorrhage[3]	62 (1)
Pregnancy Outcomes	
Livebirth	8693 (93)
Spontaneous Abortion	304 (3)
Elective termination	110 (1)

[1]Presented as frequency of patients, [2]Collected during and before pregnancy, [3]Restricted to deliveries, IQR = interquartile range, SD = standard deviation

Table 2. Pregnancy characteristics of Medicaid enrollees diagnosed with systemic lupus erythematosus stratified by race, presented as n (%) unless otherwise noted

Characteristics	White (N=)	Black (N=)	Asian (N=)	Hispanic (N=)
Maternal age, median (IQR), years	30 (6)	29 (6)	30 (6)	29 (6)
Gestational age, mean (SD), weeks	36.1 (6.8)	35 (7.6)	34.7 (8.1)	35.7 (6.5)
Comorbidities[1]				
Pre-Gestational Hypertension	110 (4)	256 (9)	<10	81(5)
Diabetes (type 1 and 2)	72 (2)	99 (4)	<10	58 (4)
Obesity (BMI > 30 kg/m2)	324 (11)	366 (13)	13 (6)	163 (10)
Lupus nephritis	275 (9)	488 (18)	47 (22)	273 (17)
Pregnancy Complications				
Preeclampsia/eclampsia	305 (11)	474 (19)	33 (17)	233 (16)
Preterm delivery[2]	377 (14)	545 (22)	41 (21)	279 (19)
Cesarean section	1094 (60)	1089 (43)	77 (39)	630 (44)
Pregnancy outcomes				
Livebirth	2774 (94)	2509 (92)	199 (91)	1446 (92)
Spontaneous Abortion	86 (3)	93 (3)	<10	51 (3)
Elective termination	22 (1)	33 (1)	10 (5)	32 (2)

[1]Collected during and before pregnancy, [2]Restricted to deliveries, IQR = interquartile range, SD = standard deviation

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Rector: None; **S. Sediqi**: None; **A. Howren**: None; **J. Simard**: None.

Abstract Number: 1010

Confounding by Indication in Observational Studies Investigating Glucocorticoid-Associated Adverse Events in Patients with Rheumatoid Arthritis: A Systematic Literature Review

Andriko Palmowski[1], Anne Elisabeth Beenken[2], Anne Pankow[2], Judith Oldenkott[2], Henriette Käding[2], Edgar Wiebe[3], Zhivana Boyadzhieva[4], Eric L Matteson[5], Ioanna Minopoulou[6], Thorben Witte[2], David Simon[7], Arnd Kleyer[6] and FRANK BUTTGEREIT[8], [1]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [2]Charité, Berlin, Germany, [3]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Berlin, Germany, [5]Mayo Clinic College of Medicine and Science, Rochester, MN, [6]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [7]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Germany, [8]Charité University Medicine Berlin, Berlin, Berlin, Germany

Table 1. Study characteristics.

Study type	
Cohort	26 (55)
Case-control	7 (15)
Cross-sectional	13 (28)
Multiple	1 (2)
Year of publication	2018 [2012 to 2021; min: 2008; max: 2023]
Location	
North America	20 (43)
Europe	11 (23)
Asia	14 (30)
Other	2 (4)
Journal	
Ann Rheum Dis	7 (15)
Rheumatology (Oxford)	7 (15)
J Rheumatol	4 (9)
Clin Rheumatol	3 (6)
Other	26 (55)
2022 Journal Impact Factor®	4.7 [3.4 to 5.5; min: 1.6; max: 39.2]
Type of investigated adverse event	
Bone-related	16 (34)
Cardiovascular	9 (19)
Infectious	9 (19)
Multiple	5 (11)
Endocrinological	4 (9)
Mortality	2 (4)
Psychiatric	2 (4)
Ophthalmological	0 (0)
Application of investigated glucocorticoids	
Oral	25 (53)
Not specified	19 (40)
Multiple	3 (6)
Glucocorticoid-related variable	
Multiple	29 (62)
Use versus no use (dichotomous)	9 (19)
Mean daily dose	5 (11)
Cumulative dose	3 (6)
Daily dose at one specific time point	1 (2)

Numbers are n (%) or median [interquartile range; minimum; maximum].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Observational studies investigating glucocorticoids (GCs) and related adverse events (AEs) in patients with rheumatoid arthritis (RA) can suffer from bias by indication if confounders such as disease activity or systemic inflammation are not adjusted for in the statistical analyses. We assessed whether observational studies in RA which investigate the relationship between GC use and AEs regularly adjust for disease activity or systemic inflammation.

Methods: We conducted a protocolized (https://doi.org/10.17504/protocols.io.bp2l6x955lqe/v1) systematic literature review. MEDLINE was searched for observational studies published since 2008 in patients with RA that investigated the association between GCs and certain AEs. GCs had to be mentioned in the study abstract. We calculated the proportion of studies that statistically adjusted for validated disease activity scores (e.g., RAPID3) and/or systemic inflammation (e.g., serum CRP levels) and/or both (e.g., both RAPID3 and CRP or combined scores such as DAS28-CRP). Joanna Briggs Institute's critical appraisal checklists were used for quality appraisal. Analyses were further stratified by study characteristics (year of publication, study type, type of AE, critical appraisal checklist score percentages, and 2022 Journal Impact Factor®). Statistical comparisons were made with Chi-squared tests.

Results: Out of 609 initial search results, 47 observational (mostly cohort) studies were finally included (**Table 1**). Most studies had a cohort design, were from North America or Europe, and assessed oral GCs. The most commonly investigated AEs were bone-related such as bone mineral density or fractures, followed by cardiovascular and infectious AEs. Almost one third of all included studies were published in either *Annals of the Rheumatic Diseases* or *Rheumatology (Oxford)*. Most studies (57%) *neither* adjusted for validated disease activity scores *nor* markers of systemic inflammation, regardless of study

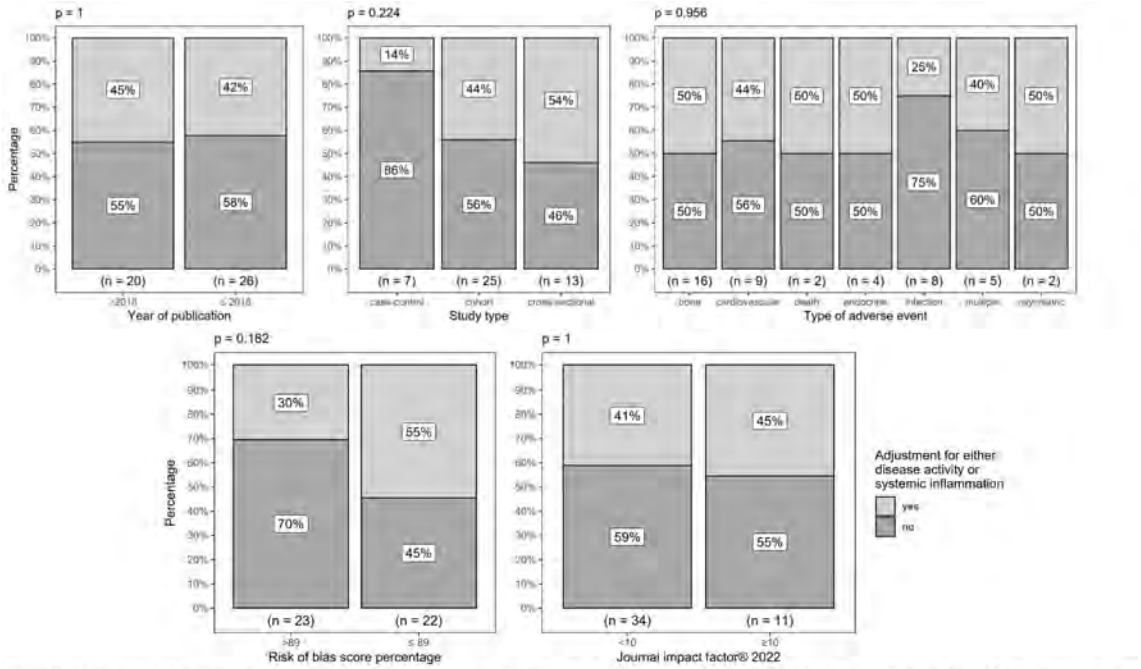


Figure 1. Proportions of studies adjusting for disease activity or systemic inflammation, stratified by year of publication, study type, type of adverse event, risk of bias score percentage and 2022 Journal Impact Factor®.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

characteristics (**Figure 1**). Even in the subsets of studies that were published in a journal with a Journal Impact Factor® of ≥10 or that had critical appraisal checklist score percentages of ≥90%, the majority of studies did not statistically adjust for disease activity or markers of inflammation.

Conclusion: Confounding by indication is likely present in most observational studies investigating the relationship between GC use and AEs. Even studies published in "high-ranking" scientific journals did not regularly adjust for disease activity or markers of systemic inflammation. Observational studies may attain relatively high quality appraisal scores according to a highly regarded, commonly used critical appraisal tool despite not accounting for the possibility of confounding by indication.

Disclosure: A. Palmowski: Novartis, 1; **A. Beenken**: None; **A. Pankow**: None; **J. Oldenkott**: None; **H. Käding**: honoraria and travel expenses from Johnson&Johnson, 12, honoraria and travel expenses from Johnson&Johnson; **E. Wiebe**: Sobi, 6; **Z. Boyadzhieva**: None; **E. Matteson**: Amgen, 4, Boehringer-Ingelheim, 2, 6, HorizonTherapeutics, 4; **I. Minopoulou**: AbbVie/Abbott, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Novartis, 6; **T. Witte**: travel cost (AbbVie, Johnson&Johnson and UCB Pharma, 12, travel cost (AbbVie, Johnson&Johnson and UCB Pharma; **D. Simon**: AbbVie, 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, Janssen-Cilag, 2, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Lilly, 2, 6, Medac, 2, 6, Novartis, 2, 6, UCB, 2, 6; **A. Kleyer**: AbbVie/Abbott, 1, 6, Alfasigma, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, 6, Gilead, 1, Janssen, 1, 6, Novartis, 1, 6, UCB, 1, 6; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

Abstract Number: 1011

Model-based Evaluation of the Potential Public Health Impact of Expanding Medicare Coverage for Weight Loss Medications for Beneficiaries with Knee Osteoarthritis and Obesity in the US.

Ethan Eickmann[1], Daniel Betensky[1], Karen Smith[1], Candace Feldman[1], Jason Kim[2], Ankur Pandya[3], Jeffrey Katz[4] and Elena Losina[5], [1]Brigham and Women's Hospital, Boston, MA, [2]Arthritis Foundation, Atlanta, GA, [3]Harvard School of Public Health, Boston, [4]Brigham and Women's Hospital, Brookline, MA, [5]BWH, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: US federal law currently does not allow Medicare Part D coverage for weight loss medications without additional indications, such as diabetes. Several glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been approved for weight loss alone. GLP-1 RAs are prohibitively expensive, and only about 1% of Medicare beneficiaries report taking GLP-1 RAs for weight loss. The substantial clinical benefits associated with GLP-1 RAs in RCTs, coupled with their high cost, have led to discussions about adding Medicare coverage for weight loss indications. We examined the potential public health impact of expanding coverage of GLP-1 RAs for weight loss among Medicare Part D beneficiaries with knee osteoarthritis (OA) and obesity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Potential public health impact of GLP-1 RA coverage by Medicare for weight loss in persons with knee OA and concomitant obesity

	Life Years	Quality-Adjusted Life Years	# of new T2DM cases	# of MACEs	# CVD-attributable deaths	# of TKRs
No coverage for GLP-1 RAs for weight loss	6,314,531	4,467,493	100,866	66,337	24,611	30,237
Maximum health benefit of Medicare coverage for GLP-1 RAs for weight loss (100% uptake)	+319,824	+341,827	-39,893	-6,745	-2,173	-6,380
Realistic health benefit of Medicare coverage for GLP-1 RAs for weight loss (20% uptake)	+93,002	+88,797	-7,577	-5,754	-2,018	-1,023

GLP-1 RAs = Glucagon-Like Peptide-1 Receptor Agonists, T2DM = Type 2 Diabetes Mellitus, MACEs = Major Adverse Cardiovascular Events, CVD = Cardiovascular Disease, TKRs = Total Knee Replacements

Methods: We used the data from OAI (the Osteoarthritis Initiative), the United States Census, NHANES (National Health and Nutrition Examination Survey) and published literature to estimate the proportion of the US population ≥65 years of age with obesity (BMI ≥30 kg/m^2) and knee OA, without type 2 diabetes mellitus (T2DM), and enrolled in Medicare Part D. Using the Osteoarthritis Policy Model (OAPol), a widely published and validated microsimulation of OA, we estimated the maximum potential clinical benefits of GLP-1 RAs coverage for weight loss among Medicare beneficiaries with knee OA and obesity as the difference in clinical outcomes with and without GLP-1 RA use. The clinical benefits included gains in life expectancy and gains in quality-adjusted life expectancy along with reductions in incident cases of MACE, T2DM, and total knee replacement (TKR). We modeled GLP-1 RA weight loss efficacy, toxicity and discontinuation rates from the SURMOUNT trials. We derived knee pain reduction using data from the STEP-9 trial, which focused on a population with knee OA. To recognize that not all eligible Medicare beneficiaries would use GLP-1 RAs for weight loss, we used data for GLP-1 RA uptake among people with GLP-1 RA insurance coverage to estimate realistic clinical benefits (~20% uptake among those who are eligible).

Results: We estimated that 591,550 Americans have obesity, symptomatic knee OA, no T2DM, and are enrolled in Medicare Part D. Cumulatively, affordable access to GLP1RA among this entire population would add 319,824 years to life expectancy (0.54/person) and 341,827 years to quality-adjusted life expectancy (0.58/person), if every eligible individual would use GLP-1 RAs. Additionally, expanded GLP-1 RA coverage could avert 39,893 cases of T2DM, 6,745 major adverse cardiovascular events (MACEs, including 2,173 CVD-attributable deaths), and 6,380 TKRs. Table 1 shows maximum and realistic health gains for scenarios of GLP-1 RA uptake.

Conclusion: Adding GLP-1 RA coverage for weight loss alone to Medicare Part D may lead to substantial health benefits in the US, increasing survival and improving quality of life, while also averting costly and morbid chronic diseases and reducing the need for TKR, even if only parts of this population would be willing to use these medications. These estimates may be useful when discussing how to balance the health benefits of expanded access to GLP-1 RAs with the potential budgetary impacts.

Disclosure: E. Eickmann: None; **D. Betensky**: None; **K. Smith**: None; **C. Feldman**: American College of Rheumatology, 2, Arthritis Foundation, 5, 12, Task Force Member, Bain Capital, 2, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 1, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2; **J. Kim**: None; **A. Pandya**: None; **J. Katz**: Biosplice, 5; **E. Losina**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1012

Racial and Gender Disparities in Gout Clinical Trials

Fizza Zulfiqar[1], Dania Kaur[2], Meaghan Bethea[3], Taylor Spencer[4], Samhitha Bitla[5], Abhinav Vyas[6] and Camelia Arsene[7], [1]Trinity Health Oakland/Wayne State University, Pontiac, MI, [2]North Alabama Medical Center, Muscle Shoals, AL, [3]Trinity Health Oakland Hopsital, Pontiac, MI, [4]Trinity Health Oaklnd Hospital, Pontiac, MI, [5]Trinity Health Oakland Hospital, Pontiac, MI, [6]Vanderbilt University, Nashvile, TN, [7]Trinity Health Oakland Hospital, Pontiac

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: To develop effective novel treatment strategies for Gout disease that cater to patients from diverse backgrounds, it is crucial that all racial groups, without exception, have equal opportunities to participate in clinical trials. This inclusivity is not just a matter of fairness, but a necessity for the advancement of medical research.

Methods: Using ClinicalTrials.gov, a web-based resource that registers all studies meeting the definition of a clinical trial according to the International Committee on Medical Journal Editors,we identified all phase 1 to phase 4 Gout disease clinical trials. We manually abstracted data on the racial distribution of enrolled participants, sex distribution, trial phase, location, and year of trial reporting. Additionally, we conducted subgroup analyses of racial distribution based on trial phase and location and evaluated trends in racial disparity within clinical trial enrollment over the years. SPSS software version 28 was used for analysis. P value of < 0.05 was considered statistically significant.

Results: We identified 78 clinical trials related to Gout, of which 91.7% were done in Europe or the United States. Most of these were phase 2 or 3 clinical trials (70.4%). The racial distribution of enrolled participants was publicly available in 44 (56.4%) clinical trials. The race distribution of enrolled subjects was reported in 33.3% of Phase 1, 60.9% in Phase 2, 48.1% in Phase 3 and 53.3% in Phase 4. The race distribution among 29,166 study participants in 78 clinical trials was: 61.3% White race (14522), 15.8 % Black race (3738), 6.1% Asians descent (1450), 9.2% Hispanics origin (2189), 2.4% American Indian/Alaskan Native (559), 0.8% Native Hawaiian/Other Pacific Islander (198), and 4.3% other races (1029). A similar race distribution trend was observed across all subgroups of clinical trials based on phase. There was a statically significant difference between trail phases regarding racial groups with $p < 0.001$. The sex distribution, as seen throughout the

			Phase				
			1.00	2.00	3.00	4.00	Total
Race	Whites	Count	45	1402	11692	971	14110
		% within Phase	64.3%	65.9%	65.7%	62.9%	65.5%
	Blacks	Count	8	282	2636	276	3202
		% within Phase	11.4%	13.3%	14.8%	17.9%	14.9%
	Asians	Count	0	206	826	74	1106
		% within Phase	0.0%	9.7%	4.6%	4.8%	5.1%
	Hispanics	Count	16	139	1730	125	2010
		% within Phase	22.9%	6.5%	9.7%	8.1%	9.3%
	American Indian/Alaskan Native	Count	1	8	538	6	553
		% within Phase	1.4%	0.4%	3.0%	0.4%	2.6%
	Native Hawaiian/Other Pacific Islander	Count	0	18	86	25	129
		% within Phase	0.0%	0.8%	0.5%	1.6%	0.6%
	Others	Count	0	71	283	67	421
		% within Phase	0.0%	3.3%	1.6%	4.3%	2.0%
Total		Count	70	2126	17791	1544	21531
		% within Phase	100.0%	100.0%	100.0%	100.0%	100.0%

Race Distribution of Participants Across Clinical Trial Stages (Stage 1 to 4)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

			Phase				
			1.00	2.00	3.00	4.00	Total
Sex	Male	Count	91	2697	17517	3594	23899
		% within Phase	72.8%	90.0%	86.8%	92.5%	87.9%
	Female	Count	34	299	2666	293	3292
		% within Phase	27.2%	10.0%	13.2%	7.5%	12.1%
Total		Count	125	2996	20183	3887	27191
		% within Phase	100.0%	100.0%	100.0%	100.0%	100.0%

Gender Distribution of Participants Across Clinical Trial Stages (Stage 1 to 4)

trials, was 87.7% in males (25572) and 12.3% in females (3594). There was a statistically significant difference between trial phases regard toregarding sex at birth with $p < 0.001$.

Conclusion: Our research revealed that only 56.4% of Gout studies reported racial distribution. The Black race was underrepresented despite a higher prevalence of Gout in this population per the literature evidence. Strategies to ensure equitable representation in Gout clinical trials are needed to address disparities and improve treatment outcomes across diverse populations.

Disclosure: F. Zulfiqar: None; **D. Kaur**: None; **M. Bethea**: None; **T. Spencer**: None; **S. Bitla**: None; **A. Vyas**: None; **C. Arsene**: None.

Abstract Number: 1013

All Roads Lead to Rheum? Modeling Scenarios of New Patients-to-pediatric Rheumatologist Ratios in Different US States

Gabriela Accetta Rojas[1], Evan Mulvihill[2], Salma Siddique[1] and Annemarie Brescia[1], [1]Nemours Children's Hospital of Delaware, Wilmington, DE, [2]Nemours/A.I.duPont Hospital for Children, Wilmington, DE

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology is among the pediatric subspecialties with the lowest workforce density in the US[1]. Initial management of most of the pediatric rheumatologic conditions relies exclusively on rheumatologist assessment. Pediatric rheumatologists might be responsible for a high patient load in some states of US.

Methods: The number of active certified pediatric rheumatologists in 2024 per state was determined by the American Board of Pediatrics (ABP)[2] and the pediatric state population < 18 years by US Census Bureau Population Estimates[3]. We estimated the number of new patients-to-pediatric rheumatologist in 1-year interval applying reported incidence rates of the main rheumatic conditions - juvenile idiopathic arthritis[4], pediatric lupus[5], juvenile dermatomyositis[6], and others[7-9] - equally to each pediatric state population under the assumption that children living in different states are at the same risk of developing a rheumatologic condition. Using Monte Carlo simulations[1,10] we then created 1,000 scenarios of varying incident cases/100,000 children at the state level in a 1-year interval ranging from the minimum to the maximum reported incidence. In a sensitivity analysis, states reported to have zero active certified pediatric rheumatologist were considered to have 0.5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

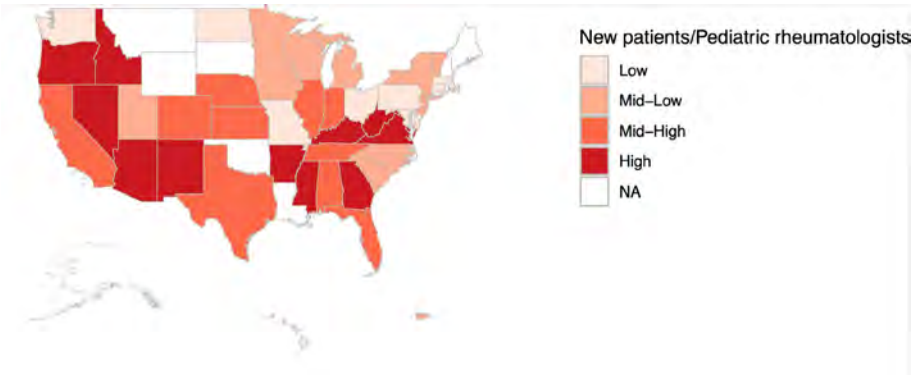


Figure 1. New patients-to-pediatric rheumatologist in each state in a scenario of lowest incidences of pediatric rheumatic conditions

Results: In the scenario of lowest incidences of all rheumatic conditions, the ratios of new patients-to-pediatric rheumatologist were categorized in quartiles, as shown in Figure 1. The states with highest ratios of new patients-to-pediatric rheumatologist were found in Arizona (189, 95%CI 176-301), Idaho (176, 95%CI 145-247), and New Mexico (165, 95%CI 143-245). States the with lowest ratio of new patients-to-pediatric rheumatologist were Delaware (24, 95%CI 14-31) and Massachusetts (26, 95%CI 18-35). In the sensitivity analysis, states with the highest ratios of new patients-to-pediatric rheumatologist were Louisiana and Oklahoma.

Conclusion: There are striking differences in the ratios of new patients-to-pediatric rheumatologist across the US. Children living in states with very high patient- to-pediatric rheumatologist might be at risk for delay in care. Further studies to examine the implications of workforce availability and pediatric access to rheumatology care are warranted.

Disclosure: G. Accetta Rojas: None; **E. Mulvihill**: None; **S. Siddique**: None; **A. Brescia**: None.

Abstract Number: 1014

Factors Associated with Fibromyalgia Diagnosis amongst People Meeting Criteria: Results from UK Biobank

Sung-A Kim, **Gary Macfarlane**, Marcus Beasley and PACFiND study group, University of Aberdeen, Aberdeen, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The diagnosis of fibromyalgia (FM) is challenging due to its reliance on patient-reported symptoms, the absence of definitive biomarkers, and numerous overlapping comorbidities. Discrepancies between diagnostic criteria and clinical practice imply the possibility of diagnostic biases, complicating timely and accurate identification. This study aimed to identify factors associated with receiving a FM diagnosis, among individuals who met 2016 criteria, and explore potential barriers to diagnosis.

Methods: Using data from UK Biobank, a total of 27 potential factors across four biopsychosocial domains were analysed for differences between diagnosed and undiagnosed individuals. Multivariate log-binomial regression was used within and across domains to evaluate prevalence ratios (PR) regarding the independent association of factors with receiving a FM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

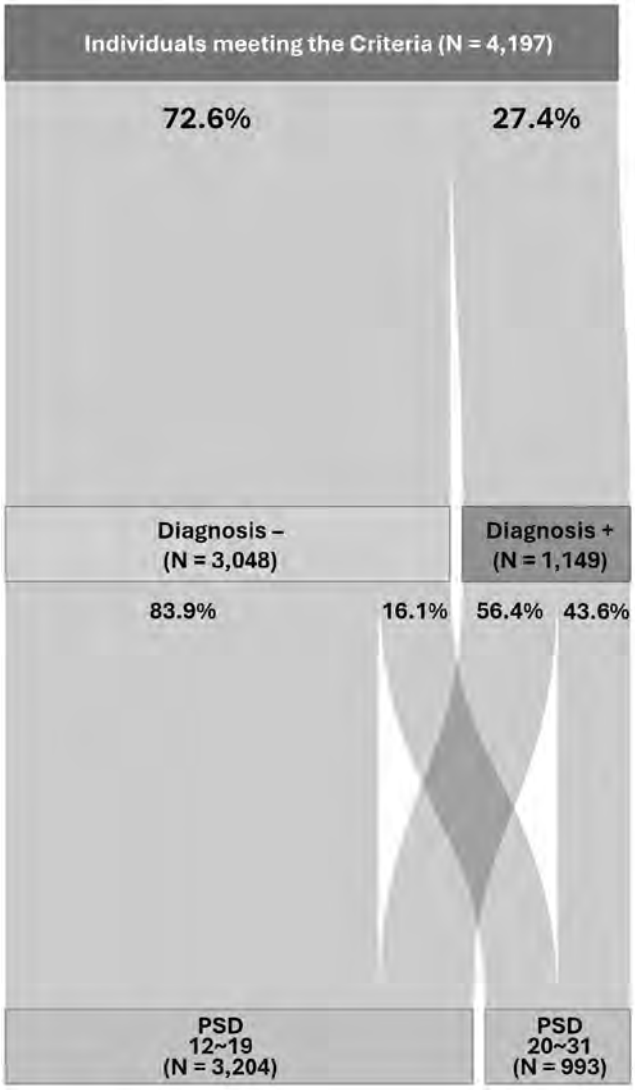


Figure 1. Diagnosis status among people meeting the 2016 fibromyalgia criteria

diagnosis. To avoid potential selection bias, we conducted a sensitivity analysis including all UK Biobank participants who completed the Experience of Pain question, regardless of whether they met the 2016 FM criteria.

Results: Among the 4,197 individuals meeting FM criteria, 72.6% reported not having received a diagnosis. We identified eight factors significantly associated with not being diagnosed: being male (fully adjusted PR 0.47, 95% confidence interval 0.41-0.56), older age (0.85, 0.75-0.96), self-reported concomitant diagnosis of neuropathy (0.91, 0.83-0.99), shorter pain duration (0.56, 0.41-0.76), lower polysymptomatic distress scores (0.56, 0.51-0.62), and less frequent fatigue (0.85, 0.76-0.96). In contrast diagnosis was more likely amongst people who also reported a diagnosis of chronic fatigue syndromes (1.65, 1.50-1.82) and complex regional pain syndrome (1.13, 1.03-1.25). The sensitivity analysis conducted on the whole population sample demonstrated results generally consistent with the main analysis.

Conclusion: Our research has identified significant disparities in the diagnosis of FM at the population-level in the UK, particularly among patients without stereotypical characteristics, with less severe symptoms, or the existence of concomitant chronic pain conditions. Understanding these diagnostic patterns can help improve alignment between criteria for identifying FM and real-world practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

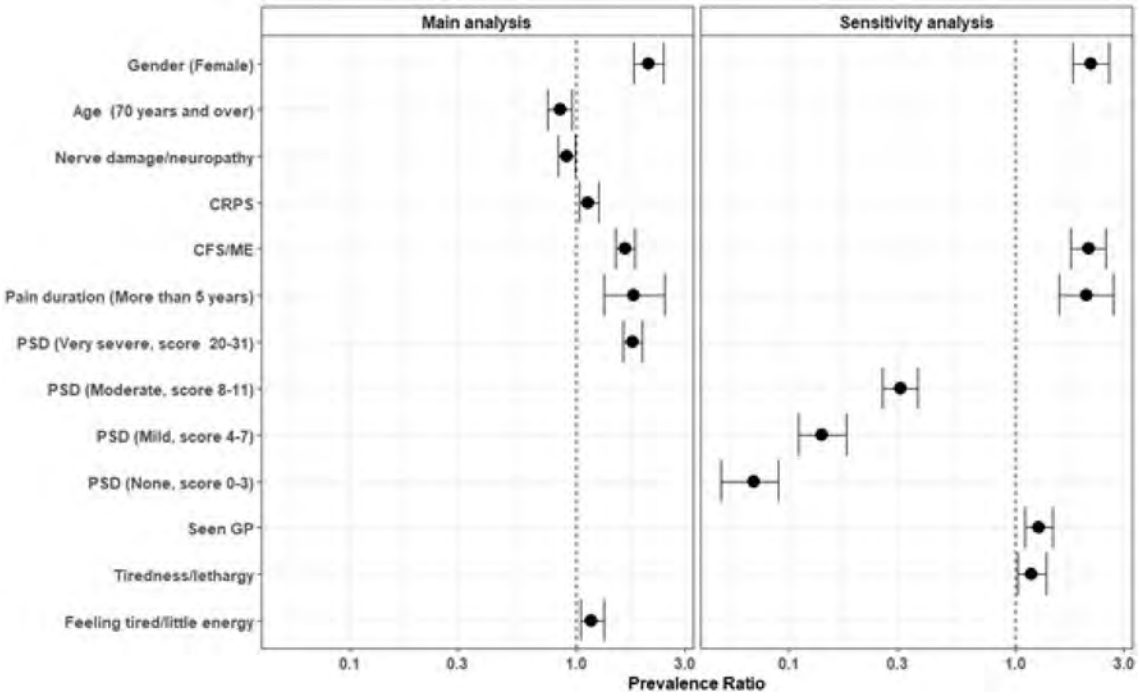


Figure 2. Factors associated with fibromyalgia diagnosis in the fully adjusted model 3

Disclosure: S. Kim: None; **G. Macfarlane**: None; **M. Beasley**: None.

Abstract Number: 1015

Refining Administrative Algorithms For Accurate Identification of Patients with Systemic Sclerosis In Trinetx Research Network

Gulsen Ozen[1], Michael O'Rorke[2], Paul Romitti[2] and Robyn Domsic[3], [1]University of Iowa, Carver College of Medicine, Division of Immunology, Coralville, IA, [2]University of Iowa College of Public Health, Department of Epidemiology, Iowa City, IA, [3]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Large data-driven medical research is invaluable in answering questions about epidemiology, genetics, therapeutics, and outcomes of rare diseases. Systemic sclerosis (SSc) is rare yet the deadliest autoimmune disease with limited treatment options available to alter the disease course. Despite the availability of large administrative datasets, there are only a few studies on SSc using these datasets, most of which define SSc cases based on one diagnostic code. Optimal use of these datasets, however, requires accurate SSc case determination, which has yet to be studied. We aimed to evaluate algorithms to identify SSc cases in an administrative dataset and to describe the performance characteristics of these algorithms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the patient cohort by confirmed SSc diagnosis by medical record review

Variables	Confirmed SSc cases (N=342)	Non-SSc cases (N=138)	P value
Age at diagnosis, mean (SD) years	52.0 (16.5)	44.1 (18.2)	<0.001
Female, %	86.8	70.1	0.001
Disease duration from diagnosis, mean (SD) years	12.5 (8.8)	-	
SSc type, %		-	
Limited cutaneous	88.3		
Diffuse cutaneous	11.7		
Autoantibody profile, %			<0.001
ANA only	20.5	30.4	
ACA	41.8	3.6	
ATA	5.6	0.7	
RNAPol3	5.8	0	
Pm-Scl	3.5	0.7	
U1RNP	4.9	6.5	
Others	8.8	2.6	
Unknown	9.1	26.1	
Overlap syndromes, %	26.6	1.5	<0.001
Organ manifestations, %			
Raynaud's	95.6	32.6	<0.001
Digital ulcers	9.7	0	<0.001
Calcinosis	12.6	0.7	<0.001
Gastrointestinal	86.3	52.1	<0.001
Interstitial lung disease	29.2	5.8	<0.001
Pulmonary hypertension	38.3	12.3	<0.001
Renal crisis	2.1	-	-
Heart failure	25.7	15.9	0.021
Cancer*, %	24.3	22.5	0.340
Mortality, %	28.6	18.1	0.017

**Excluding non-melanoma skin cancers.*

Methods: Patient records in a large, global multicenter electronic medical record dataset (TriNetX Research Network) were screened for SSc using the International Classification of Diseases, Ninth and Tenth Revisions (ICD-9 and ICD-10). The patient identifiable data were available only from one center. A medical record review was performed from a simple random sample of this cohort using a standardized data abstraction form (GO) to confirm the SSc diagnosis. All outpatient and inpatient ICD codes and dates assigned were extracted from the TriNeTx Research Network. Using data for confirmed cases, the performance of different administrative algorithms was assessed by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and receiver operator curve analyses.

Results: To date, medical records for a random sample of 480 of the 1126 patients with at least one ICD9/10 code for SSc were reviewed. Overall, 342 of the 480 (71.2%) patients were confirmed to have SSc, predominantly limited cutaneous SSc (*Table 1*). Among the tested administrative algorithms, "≥ 2 outpatient ICD9/10 codes at least 30 days apart without an alternative diagnosis code (algorithm 4)" showed the best performance with a sensitivity of 95.6%, specificity of 70.3%, PPV of 89.8%, NPV of 86.6% and area under the curve of 0.906 (*Table 2*). Although ≥1 inpatient ICD9/10 code had a high specificity (90.6%) and PPV (92.1%), its sensitivity (44.4%) and NPV (39.7%) were low. When "≥1 inpatient ICD9/10 code" was added to the algorithm 4, the performance of the algorithm did not change significantly (*Figure*). When patients with overlap syndromes were excluded, algorithm 4 still performed the best (sensitivity 96.8%, specificity 70.6%, PPV 85.9%, NPV 92.3%).

Conclusion: The administrative algorithm ("≥ 2 outpatient ICD9/10 code at least 30 days apart without an alternative diagnosis code) reliably identifies SSc cases. This algorithm can be applied to large administrative datasets to conduct clinical and epidemiologic studies with a higher validity in SSc patients. External validation of this algorithm in different datasets can further strengthen its utility.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Performance of algorithms with various diagnostic codes for SSc case identification

Algorithm	Definition	Fulfilling criteria (N)	Sensitivity (95%CI)	Specificity (95%CI)	PPV (95%CI)	NPV (95%CI)	AUC (95%CI)
1	≥1 ICD 9/10 code	480	71.2 (65.2-98.9)	-	-	28.7 (18.4-34.8)	-
2	≥2 ICD9/10 codes 30 days apart	410	96.5 (94.9-98.1)	42.0 (37.6-46.4)	80.5 (76.9-84.0)	82.8 (79.5-86.2)	0.768 (0.713-0.822)
3	≥3 ICD9/10 codes 30 days apart	373	92.5 (90.7-95.3)	60.1 (55.8-64.5)	85.3 (82.1-88.4)	77.6 (73.8-81.3)	0.831 (0.787-0.877)
4	≥2 ICD9/10 codes 30 days apart without alternative diagnostic codes*	368	95.6 (93.8-97.5)	70.3 (66.2-74.4)	89.0 (86.0-91.7)	86.6 (83.6-89.5)	0.906 (0.871-0.949)
5	≥1 inpatient ICD9/10 code	165	44.4 (40.0-49.0)	90.6 (87.9-93.2)	92.1 (89.7-94.5)	39.7 (35.3-44.1)	0.728 (0.685-0.772)
6	≥1 ICD9/10 code without alternative diagnostic codes	428	98.8 (97.9-99.8)	34.8 (30.5-39.0)	79.0 (75.3-82.6)	92.3 (89.9-94.7)	0.754 (0.697-0.812)
7	≥1 ICD9/10 code without alternative diagnostic codes OR ≥1 inpatient ICD9/10 code	384	96.2 (94.5-97.9)	60.1 (55.8-64.5)	85.7 (82.5-88.1)	86.5 (83.4-89.5)	0.858 (0.814-0.902)
8	≥2 ICD9/10 codes 30 days apart without alternative diagnostic codes* OR ≥1 inpatient ICD9/10 code	381	96.5 (94.9-98.1)	63.0 (58.7-67.4)	86.6 (83.6-89.7)	87.9 (85.0-90.8)	0.874 (0.834-0.916)

*Alternative diagnostic codes include localized scleroderma, scleromyxedema, lipodermatosclerosis, scleredema, eosinophilic fasciitis, graft versus host disease, Dupuytren's contracture, nephrogenic systemic fibrosis, diabetic chairoarthropathy

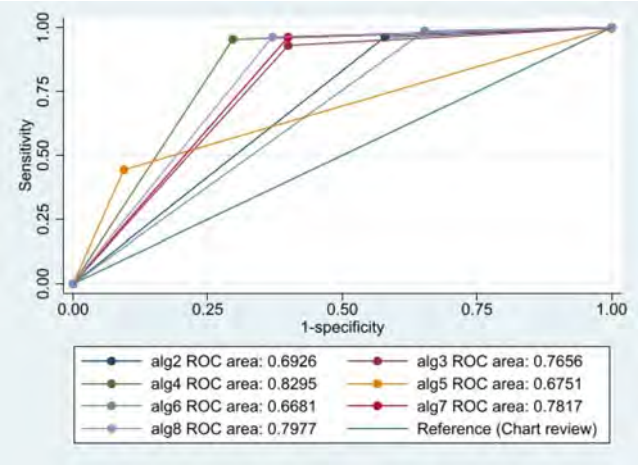


Figure. Receiver operator curves of the algorithms against the medical record review

Disclosure: G. Ozen: None; **M. O'Rorke**: None; **P. Romitti**: None; **R. Domsic**: None.

Abstract Number: 1016

Association Between Inflammatory Biomarkers and Predicted Heart Failure Risk in Rheumatoid Arthritis

Ilana Usiskin[1], Lauren rusnak[2], Katherine Zhong[3], Ying Qi[4], Nicole Yang[2], Gregory McDermott[5], Brittany Weber[6] and Katherine Liao[2], [1]Division of Rheumatology, Inflammation, and Immunity, Department of Medicine, Brigham and Women's Hospital, Boston, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Short Hills, NJ, [4]Brigham and Women's Hospital, Boston, [5]Brigham and Women's Hospital, Brookline, MA, [6]Brigham and Women's Hospital, DEDHAM, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1007–1037) Epidemiology & Public Health Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Heart failure (HF) is a major cause of morbidity and mortality in rheumatoid arthritis (RA). Prior work has suggested that higher levels of inflammation is associated with increased future risk of HF. Several inflammatory pathways are hypothesized to play a role in both RA and HF including interleukin-1-beta (IL-1b), interleukin-6 (IL-6), and soluble tumor necrosis factor-2 (sTNFR2). The Predicting Risk of Cardiovascular Disease Events (PREVENT) risk equation published in 2023 includes a validated risk estimator for predicted 10-year HF risk (PREVENT-HF). The objective of this study was to determine the cross-sectional association between inflammatory biomarkers and predicted HF risk in RA to identify potential markers of HF risk in RA.

Methods: We studied patients from the LiiRA (Lipids, Inflammation and Cardiovascular risk in RA) study, who had active RA with a plan to initiate tumor necrosis factor inhibitor (TNFi) therapy. All patients underwent measurements for high-sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), IL-1b, IL-6, sTNFR2, NT-pro-BNP, and high sensitivity cardiac troponin (hs-cTnT) at the baseline visit. We calculated the estimated risk of HF for each patient at baseline using PREVENT-HF risk equations. Spearman's correlation was calculated for each biomarker value and the PREVENT-HF score. We performed a univariable linear regression to determine the association between detectable hs-cTnT (>6ng/L) and PREVENT-HF score. Biomarkers significantly correlated with PREVENT-HF score ($p< 0.05$) in the univariable analyses were considered in a multivariable linear regression testing the association with PREVENT-HF score, adjusting for RA disease duration and disease activity (PREVENT-HF includes age and sex).

Results: We studied 73 patients, 82% female, median age 56 years (Table 1). The median RA duration at baseline was 3.6 years and median CDAI was 22 (moderate disease activity). The median PREVENT-HF 10-year estimated HF risk was 2.1% (IQR 0.7, 5.1), and 21% of the cohort had a detectable hs-cTnT. Higher levels of hsCRP, ESR, IL-6, and sTNFR2 were correlated with higher PREVENT-HF estimated HF risk, and detectable hs-cTnT was associated with higher PREVENT-HF estimated HF risk

Table 1. Baseline characteristics for LiiRA cohort (n=73)

PREVENT-HF Components	
Age [median (IQR)]	56 (45, 62)
Female (%)	82%
Current smoker	19%
SBP (mmHg)	127 (114, 147)
EGFR	96 (87, 106)
Antihypertensive medication	23%
Diabetes	4%
HbA1c	5.6 (5.3, 5.7)
Race	
Asian	4%
Black	11%
Other	7%
White	77%
PREVENT Heart Failure Score	2.1 (0.7, 5.1)
RA Factors	
RA Duration (years)	3.6 (1.2, 10.4)
Seropositive (RF or CCP)	68%
CDAI	22 (13, 33)
Inflammatory Biomarkers	
hsCRP (mg/L)	4.0 (1.8, 8.6)
ESR (mm/h)	16.0 (9.0, 36.0)
IL-6 (pg/mL)	3.7 (2.3, 8.5)
IL-1b (pg/mL)	0.2 (0.1, 0.3)
sTNFR2 (pg/mL)	2247 (1875, 2839)
Cardiac Biomarkers	
NT-proBNP (pg/mL)	59.0 (35.8, 98.4)
Detectable hs-cTnT (>6ng/L)	21%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Correlation between inflammatory and cardiac biomarkers and PREVENT-HF risk

Biomarker	Correlation coefficient	95% CI	p-value*
Inflammatory Biomarkers			
hsCRP (mg/L)	0.30	0.07, 0.52	**0.01**
ESR (mm/h)	0.29	0.02, 0.52	**0.01**
IL-6 (pg/mL)	0.23	0.00, 0.45	**0.047**
IL-1b (pg/mL)	-0.20	-0.43, 0.04	0.09
sTNFR2 (ng/mL)	0.36	0.13, 0.55	**0.002**
Cardiac Biomarkers			
NT-proBNP (pg/mL)	0.14	-0.08, 0.39	0.23
Detectable hs-cTnT (>6ng/L)	5.1**	3.3, 6.9	**<0.001**

*Bold denotes p-value <0.05
**Beta estimate for binary variable (detectable vs non-detectable hs-cTnT)

Table 3. Multivariable linear regressions for the association between cardiac and inflammatory biomarkers and PREVENT-HF risk

	Model 1*			Model 2			Model 3		
	Beta	95% CI	p-value	Beta	95% CI	p-value	Beta	95% CI	p-value
hsCRP(mg/L)	-0.01	-0.16, 0.05	0.8	-0.03	-0.09, 1.72	0.3	-0.05	-0.10, 0.01	0.10
ESR (mm/h)	0.07	0.02, 0.11	**0.003**	0.05	0.004, 0.10	**0.04**	0.07	0.03, 0.11	**0.002**
IL-6 (pg/mL)	-	-	-	0.02	-0.02, 0.07	0.30	0.01	-0.03, 0.05	0.75
sTNFR2 (ng/mL)**	-	-	-	0.13	0.03, 0.24	**0.01**	0.04	-0.05, 0.14	0.37
Detectable hs-cTnT***	-	-	-	-	-	-	4.69	2.65, 6.73	**<0.001**

*All models adjusted for RA disease activity (CDAI) and RA duration
**per every 100 unit change in sTNFR2
***>6ng/L

(Table 2). Starting with a model including inflammatory markers measured in clinic (ESR and hsCRP), sTNFR2 was associated with PREVENT-HF risk after adjustment for these inflammatory biomarkers, RA duration, and disease severity (Table 3). The addition of hs-cTnT to the model attenuated the association between sTNFR2 and estimated HF risk, and ESR maintained a significant association with estimated HF risk. Adjusting for NT-pro-BNP did not change the associations.

Conclusion: In this RA cohort with moderate disease activity, among candidate inflammatory markers, ESR and sTNFR2 were most correlated with higher PREVENT-HF risk scores. Moreover, detectable hs-cTnT was most strongly associated with higher PREVENT-HF risk scores. More studies are needed to further examine specific inflammatory pathways, e.g., TNF, and subclinical myocardial injury as potential markers of HF risk in RA.

Disclosure: I. Usiskin: None; **L. rusnak**: None; **K. Zhong**: None; **Y. Qi**: None; **N. Yang**: None; **G. McDermott**: None; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **K. Liao**: Merck/MSD, 2, UCB, 2.

Abstract Number: 1017

Effectiveness of Recombinant Zoster Vaccine in Reducing Herpes Zoster Incidence and All-Cause Mortality Among Rheumatoid Arthritis Patients: A Retrospective Cohort Study of 21,046 Individuals from TriNetX U.S. Collaborative Network

James Wei[1], Shiow-Ing Wang[2] and Ying-Li Lin[2], [1]Chung Shan Medical University Hospital, Taichung, Taichung, Taiwan (Republic of China), [2]Chung Shan Medical University Hospital; China Medical University, Taichung, Taiwan (Republic of China)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

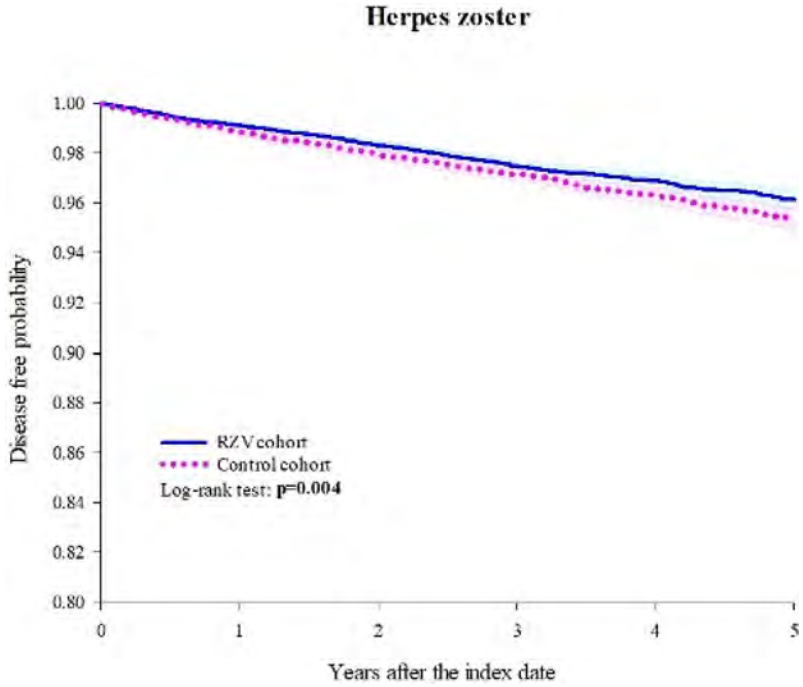
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of developing herpes zoster (HZ). This study aimed to assess the effectiveness of recombinant zoster vaccine (RZV) in reducing both the incidence of HZ and all-cause mortality among individuals with RA.

Methods: We conducted a retrospective cohort study using data from the TriNetX U.S. Collaborative Network between October 1, 2017, and March 31, 2024. The study population consisted of RA patients who received RZV (RA-RZV cohort) and those who did not (RA control cohort). Propensity score matching (PSM) was employed to balance baseline characteristics between the groups, accounting for demographics, social economic status, lifestyles, medical utilization, comorbidities, and medications. The primary outcomes were the risk of HZ and all-cause mortality. PSM-adjusted hazard ratios (HRs) were calculated using Cox proportional hazards regression models. Kaplan-Meier curves and Log-Rank tests were used to evaluate survival differences.

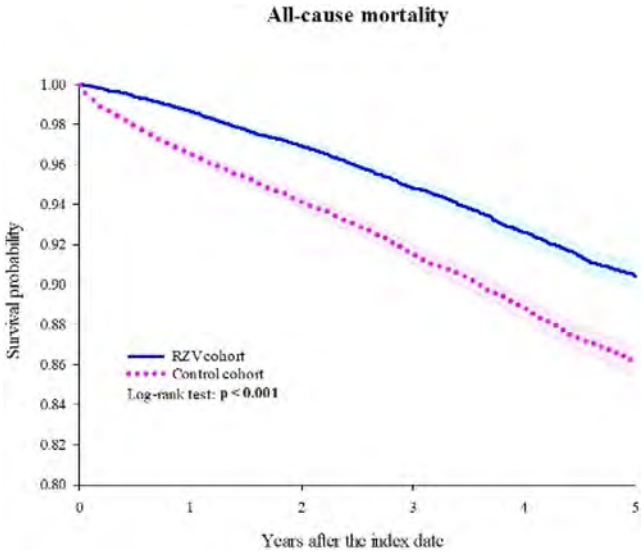
Results: After PSM, each cohort included 21,046 individuals. The RA-RZV group demonstrated significantly lower risks of HZ (HR: 0.836, 95% CI: 0.738–0.947) and all-cause mortality (HR: 0.606, 95% CI: 0.561–0.654). The HZ risk reduction was more pronounced in patients aged 50-64 years (HR: 0.731, 95% CI: 0.610–0.876), females (HR: 0.791, 95% CI: 0.684–0.915), White (HR: 0.808, 95% CI: 0.696–0.937), and Black/African American participants (HR = 0.685; 95% CI = 0.481–0.976).

Conclusion: RZV vaccination is associated with a reduced risk of HZ and mortality among RA patients aged 50 years and older. RZV vaccination should be prioritized among eligible RA patients.

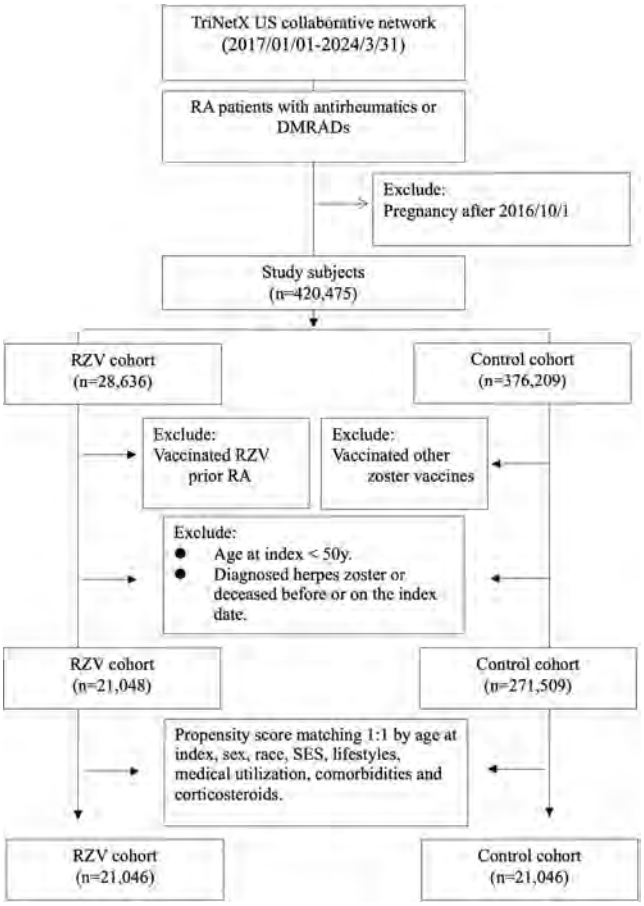


Kaplan-Meier curve of herpes zoster infection

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Kaplan-Meier curve of all-cause mortality



Study flow of patients selection

Disclosure: J. Wei: None; **S. Wang**: None; **Y. Lin**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1018

Factors Associated with Mortality in Systemic Lupus Erythematosus under a Universal Healthcare System: Results from the CAPTURED Study, a Population-Based Cohort in Catalonia, Spain

José Gomez-Puerta[1], Cristian Tebe[2], Maria Grau[3], Beatriz Frade Sosa[4], Juan Camilo Sarmiento-Monroy[5], Cristina Carbonell-Abella[6], Daniel Martinez-Laguna[7], Patricia Corzo[8], Raimon Sanmartí[9] and J. Antonio Aviña-Zubieta[10], [1]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, [2]Instituto de Investigación Germans Trias i Pujol, Badalona, Spain, [3]University of Barcelona, Barcelona, Spain, [4]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [5]Hospital Clinic Barcelona, Barcelona, Spain, [6]Medicina Familiar y Comunitaria, Centro de Salud Vía Roma, Barcelona, Spain, [7]Grup de recerca en malalties prevalents de l'Aparell locomotor en Atenció Primaria (GREMPAL), ICS, Barcelona, Spain, [8]Rheumatology Department, Hospital Clínic, Barcelona, Barcelona, Spain, [9]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [10]University of British Columbia/Arthritis Research Canada, Vancouver, BC, Canada

Table 1. General characteristics of controls and SLE

	Controls N=824,028	SLE N=10,274
Age (years) Median (IQR)	39.6 (29.4-56.7)	42.4 [32.5-55.0]
Gender (Female)	414,908 (50.3%)	8,582 (83.5%)
Age groups		
[18-29]	217,860 (26.44%)	1,923 (18.72%)
[30-39]	198,453 (24.0%)	2,597 (25.2%)
[40-49]	134,105 (16.2%)	2,313 (22.5%)
[50-59]	97,587 (11.8%)	1,651 (16.0%)
[60-69]	72,775 (8.8%)	1,044 (10.1%)
[70-79]	61,642 (7.4%)	574 (5.5%)
80 or older	41,606 (5.0%)	172 (1.6%)
Origin (Spanish)	414,772 (50.3%)	6,641 (64.6%)
Charlson score		
No comorbidities	514,085 (62.3%)	144 (1.4%)
Charlson Sc 1	211,781 (25.7%)	8,354 (81.3%)
Charlson Sc 2	75,329 (9.1%)	1,196 (11.6%)
Charlson Sc >=3	22,833 (2.7%)	580 (5.6%)
Socioeconomic status (MEDEA*)		
0R	51,456 (6.2%)	584 (5.6%)
1R	43,280 (5.2%)	482 (4.6%)
1U	176,376 (21.4%)	2,214 (21.5%
2R	91,437 (11.1%)	1,083 (10.5%)
2U	126,101 (15.3%	1 615 (15.7%)
3U	165,445 (20.0%)	2,179 (21.2%)
4U	168,649 (20.4%)	2,103 (20.4%

*MEDEA: The MEDEA index is typically stratified into 5 categories where 0 → Least deprived quintile (best socioeconomic status) 4 → Most deprived quintile (worst socioeconomic status) U=Urban, R=Rural area

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The differences in lupus-related mortality reported in population studies are partly explained by racial disparities and access to healthcare. However, population-based data from universal healthcare systems are less well known.

Our objective was to determine factors related with mortality in SLE patients in Catalonia (Spain) during the period from January 1, 2006, and December 31, 2021.

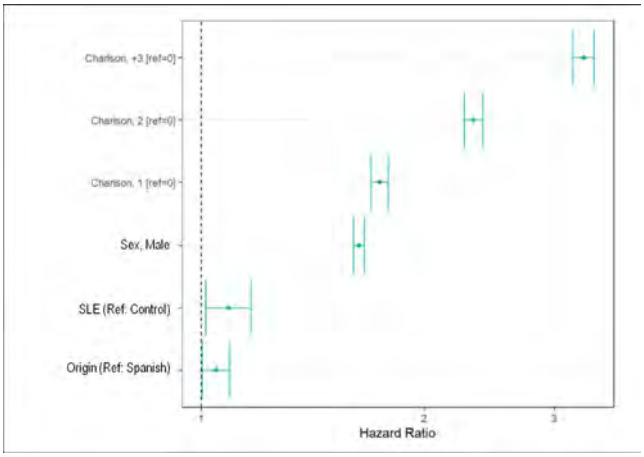
Methods: We conducted a population-based cohort study (CAPTURED study, **C**at**A**lonia e**P**idemiology s**TU**dy in **R**h**E**umatic **D**iseases) of all existing Catalonian cases who received SLE diagnosis from 2006 to 2021 by using ICD-10-CM codes from the Information System for the Development of Primary Care Research (SIDIAP). A database of primary care electronic health records that includes data from 328 primary care practices covering 5.8 million people, 75% of the Catalan population.

Patients with SLE were matched 1 with individuals from the Catalonia general population and estimate hazart ratio (HR) for mortality using a cox regression model adjusting by potential coufounding factors including sex, age, origin (Spanish vs non-Spanish), socioeconomic status (MEDEA*, Gotsens M et al. Accid Anal Prev. 2011 Sep;43(5):1802-10) and comorbidities (charlson score, CS).

Results: We identified 10,687 prevalent cases of SLE, with a mean age of 47.5 years (SD 16.3). Of these patients, 8,851 (83.4%) were female, and 6,885 (64.9%) had Spanish nationality. General characteristics are summarized in Table 1.

During the study period, we identified 1,175 deaths among SLE cases (12.5%) and 11,499 (15.6%) among 824,028 controls. Age (HR 1.05, 95% CI 1.02–1.08), male sex (HR 1.60, 95% CI 1.58–1.63), and Charlson score (CS=1 HR 1.75, 95% CI 1.70–1.80; CS=2 HR 2.38, 95% CI 2.31–2.45; CS≥3 HR 3.50, 95% CI 3.38–3.62) were associated with increased mortality risk, while patients of Spanish origin had a lower risk of death (HR 0.94, 95% CI 0.90–0.98).

After adjusting for confounding factors, patients with SLE had a slightly higher mortality rate compared to the general population (HR 1.09, 95% CI 1.01–1.17) (Figure 1).



Adjusted HR for mortality in SLE in Catalonia (Spain)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In our population-based study conducted within a universal healthcare system, we observed a slight increase in mortality among patients with SLE. Socioeconomic status did not significantly impact mortality in these patients.

Disclosure: J. Gomez-Puerta: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **C. Tebe**: None; **M. Grau**: None; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **J. Sarmiento-Monroy**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6; **C. Carbonell-Abella**: None; **D. Martinez-Laguna**: None; **P. Corzo**: GlaxoSmithKlein(GSK), 6; **R. Sanmartí**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Eli Lilly, 5, 6, Merck/MSD, 5, 6, Pfizer, 5, 6, Roche, 5, 6; **J. Aviña-Zubieta**: None.

Abstract Number: 1019

Associations Between Mental Health Diagnoses and Acute Care Use Among Individuals with Systemic Lupus Erythematosus in the All of Us Research Program

Karen H. Costenbader[1], Jeong Yee[2], Hongshu Guan[3], Emily Oakes[4], Jing Cui[3], Leah Santacroce[4], Elizabeth Karlson[4], Karestan Koenen[5], Laura Kubzansky[5] and Candace Feldman[3], [1]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [2]Sungkyunkwan University, Suwon, MA, South Korea, [3]Brigham and Women's Hospital/ Harvard Medical School, Boston, [4]Brigham and Women's Hospital, Boston, MA, [5]Harvard T.H Chan School of Public Health, Boston

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Mental health disorders, including depression, anxiety, and post-traumatic stress disorder, are prevalent among people with SLE. In other disease populations, these disorders have been associated with increased acute care use. We quantified the association between mental health conditions and recurrent acute care use (emergency department [ED] visits, hospitalizations) among patients with SLE.

Methods: We used data from the nationwide All of Us Research Program (version 8), an NIH cohort of >393,000 U.S. adults who enrolled and consented for linkage to their electronic health records. We identified those with ≥2 ICD-10 or SNOMED codes for SLE in the 2 years pre-enrollment. We assessed for mental health diagnoses in that time, identified by ≥2 ICD-10 or SNOMED codes for major depression, anxiety, or PTSD. The outcome was number of emergency department visits (only) and hospitalizations (including from emergency department) after enrollment. Incidence rates for acute care use among patients with and without mental health diagnoses were calculated. Multivariable negative binomial regression models calculated incidence rate ratios (IRRs), adjusting for age, sex, race, ethnicity, enrollment year, baseline sociodemographic factors and comorbidities.

Results: We identified 2,160 with SLE, of whom 1,333 (61.7%) had depression, anxiety, and/or PTSD (**Table 1**). Mean age overall was 49.8 (14.3) and 90.2% were female. Those with ≥1 mental health condition were more likely to be less educated, in a low-income group, to have ever smoked, and to have more comorbidities. Patients were followed for a mean 36.2 months (SD 20.9) after enrollment. Incidence rates for all acute care were much higher in those with mental health disorders (**Table 2**). In adjusted analyses (**Table 2**), we found strong associations between having mental health diagnoses and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the Patients with SLE in the All of Us Research Program (version 8) by presence of Concomitant Mental Health Diagnoses

	Without Mental Health Diagnoses (n=827)	With Mental Health Diagnoses (n=1,333)
Age, mean years (SD)	50.35 (15.42)	49.38 (13.49)
Female at birth, N (%)	727 (87.9)	1,222 (91.7)
Self-reported Race and Ethnicity[a], N (%)		
Black	226 (27.3)	368 (27.6)
Hispanic	215 (26.0)	318 (23.9)
>1 Race	32 (3.9)	65 (4.9)
White	280 (33.9)	496 (37.2)
Other/Missing	36 (4.4)	68 (5.1)
≤ High school education, N (%)	214 (25.9)	399 (29.9)
Annual household income <$35,000, N (%)	273 (33.0)	595 (44.6)
Area Deprivation Index	0.33 (0.07)	0.33 (0.06)
U.S. region of residence, N (%)		
Northeast	224 (27.1)	413 (31.0)
South	187 (22.6)	263 (19.7)
Midwest	160 (19.3)	276 (20.7)
West	256 (31.0)	381 (28.6)
Self-reported ever smoking, N (%)	233 (28.2)	487 (36.5)
Obesity[b], N (%)	298 (36.0)	658 (49.4)
Charlson comorbidity index[c], mean (SD)	1.64 (2.18)	2.56 (2.76)
Mental health diagnoses[d], N (%)		
Depression	-	1,054 (79.1)
Anxiety	-	992 (74.4)
PTSD	-	118 (8.9)
>1 one mental health diagnosis	-	738 (55.4)
Follow-up, months (mean, SD)	35.22 (20.95)	36.79 (20.80)

*Chi square tests calculated for categorical variables and t tests calculated for continuous variables
[a]Cell sizes <20 suppressed per All of Us reporting requirements. Asian category not shown here due to reporting guidelines. Race categories do not add up to 100%.
[b]Obesity: body mass index (BMI) ≥30 kg/m^2 from enrollment physical measurement data
[c]Charlson comorbidity index calculated using 16 comorbidities, excluding connective tissue disease
[d]Not mutually exclusive, >1 mental health diagnosis in 738 (55.4%)
Missing data: education level in 44 subjects, income in 527 subjects, smoking for 68 subjects, obesity in 173 subjects. Missing indicator used in models.

Table 2. Incidence Rate Ratios (per 100) for Acute Care Use for Patients with Systemic Lupus Erythematosus without Mental Health Diagnoses (MHD, n=827) compared to those with MHD (n= 1,333) in the All of Us Research Program, v.8

	n events	Follow-up Time, months (SD)	Incidence Rates (95% CI)	Incidence Rate Ratios (95% CI)
All Emergency Department Visits				
SLE without MHD	243	26.18 (20.41)	13.47 (11.83, 15.27)	1.0
SLE with MHD	584	21.64 (20.37)	24.30 (22.36, 26.35)	2.12 (1.79, 2.52)
Emergency Department Visits for SLE				
SLE without MHD	155	29.87 (20.82)	7.53 (6.39, 8.81)	
SLE with MHD	385	27.65 (21.04)	12.54 (11.32, 13.85)	2.37 (1.98, 2.84)
All Hospitalizations				
SLE without MHD	232	26.87 (20.83)	12.53 (10.97, 14.25)	1.0
SLE with MHD	534	24.74 (21.10)	19.43 (17.82, 21.15)	1.95 (1.59, 2.41)
Hospitalizations for SLE				
SLE without MHD	173	28.96 (21.07)	8.67 (7.43, 10.06)	1.0
SLE with MHD	393	27.92 (21.43)	12.67 (11.45, 13.99)	1.62 (1.34, 1.97)
All Emergency Department Visits and Hospitalizations				
SLE without MHD	351	21.78 (19.31)	23.38 (21.00, 25.96)	1.0
SLE with MHD	718	18.44 (19.75)	35.06 (32.54, 37.72)	1.92 (1.60, 2.30)
Emergency Department Visits and Hospitalizations for SLE				
SLE without MHD	250	26.00 (20.49)	13.95 (12.28, 15.79)	1.0
SLE with MHD	521	24.04 (20.95)	19.51 (17.87, 21.26)	1.80 (1.50, 2.16)

Model adjusted for age, sex, race/ethnicity, and calendar year of enrollment, annual household income, education level, smoking, obesity, and Charlson comorbidity index (calculated with 16 comorbidities, excluding connective tissue disease)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

higher rates of acute care use, both emergency department visits (adj IRR 2.12, 95%CI 1.79-2.52) and hospitalizations (adj IRR 1.95, 95%CI 1.59-2.41). This was true both for all emergency visits and hospitalizations for SLE (adj IRR 1.80, 95%CI 1.50-2.16) and for all diagnoses (adj IRR 1.92, 95% CI 1.60, 2.30).

Conclusion: In this large US-wide population of patients with SLE, mental health diagnoses were extremely prevalent and those with them had much higher rates of recurrent acute care use compared to those without these diagnoses. As patients with frequent acute care use are less likely to receive standard-of-care long-term medications and preventive care, contributing to inequities, further work is needed to develop interventions to decrease this recurrent acute care use for patients with SLE and mental health disorders.

Disclosure: K. Costenbader: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **J. Yee**: None; **H. Guan**: None; **E. Oakes**: None; **J. Cui**: None; **L. Santacroce**: None; **E. Karlson**: None; **K. Koenen**: None; **L. Kubzansky**: None; **C. Feldman**: American College of Rheumatology, 2, 12, Committee Member/Interim Chair, Arthritis Foundation, 5, 12, Task Force Member, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 2, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2.

Abstract Number: 1020

Cohort Study of European Ancestry, Geographic Region, Ambient Ultraviolet Irradiance and the Risk of Developing Polymyalgia Rheumatica among Women

Karen H. Costenbader[1], Nicole Yang[2], Emily Oakes[2], Maura Raymo[3] and Jae Kang[3], [1]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyalgia rheumatica (PMR) is one of the most common inflammatory rheumatic diseases among older women, but little is known of its etiology, and there are few established risk factors. We aimed to prospectively investigate the association between European ancestry, geographic region, ambient erythemal ultraviolet B light (UV) irradiance and PMR risk among women.

Methods: We used data from the Nurses' Health Study (NHS), an ongoing longitudinal cohort of US female registered nurses (1980-2020; aged 34-59 years in 1980). Participants provided updated information on ancestry, residential information, lifestyle factors and newly diagnosed health conditions, such as PMR, on biennial questionnaires. Two board certified rheumatologists confirmed PMR self-reported diagnoses and dates of onset with medical records. Eligible participants were women aged 50 years or older and were free of PMR. Cox proportional hazards regression models, stratified by 2-year risk period and age, were used to estimate multivariable-adjusted hazard ratios (HRs) with 95% confidence intervals (95%CIs) for ancestry, region of residence and residential erythemal ambient UV irradiance in models that simultaneously adjusted for these factors and other covariates in relation to incident PMR.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Age and age-adjusted characteristics of total person-time accrued during follow-up of 111,874 women in the Nurses' Health Study (1980-2020) by ambient erythemal UV irradiance

	Ambient Erythemal UV Irradiance based on Residence			
	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Mean ambient erythemal UV irradiance ± SD, mW/m^2	164.1± 3.3	171.5± 1.8	179± 3.5	226.3± 19.3
Mean age ± SD, years*	65.5± 9.7	66.3± 9.7	64.3± 9.4	66.7± 9.9
Smoking status: Past smoker, %	40.5	42.5	45.8	41.1
Current smoker, %	12.5	12.2	12.8	11.4
Race / ethnicity: Non-Hispanic White, %	97.2	97.3	98.2	93.1
Black, %	2.0	2.0	1.2	2.0
Asian, %	0.4	0.4	0.2	2.4
Hispanic, %	0.4	0.4	0.3	2.5
Scandinavian descent	5.6	5.3	6.1	10.0
Mean Neighborhood Socioeconomic Status Score ± SD†	-0.3± 4.4	0.3± 4.3	0.3± 4.2	-0.4± 5.3
Residential region: Northeast, %	51.8	69.3	66.7	2.5
Midwest, %	40.3	18.2	6.0	1.1
South, %	1.4	6.2	20.5	38.6
West, %	0.3	0.3	1.5	51.5
Body mass index ≥ 30 kg/m^2, %	15.3	14.6	13.2	11.2
Self-reported diabetes diagnosis, %	9.9	9.7	8.9	8.4
Self-reported hypertension diagnosis, %	49.6	49.0	48.1	46.8
Self-reported hypercholesterolemia, %	53.8	54.3	51.7	51.3
Mean alcohol intake ± SD, g/day	4.9± 8.1	5.2± 8.2	6.1± 8.9	6.5± 9.8
Mean caffeine intake ± SD, mg/day	287.2± 195.2	280.6± 189.7	292.3± 190.5	285.7± 197.2
Alternate Health Eating Index, without alcohol ± SD‡	46.3± 8.5	46.8± 8.5	47.2± 8.5	49.4± 8.9
Highest quartile of physical activity, %	23.8	24.6	25.4	27.8
Age at menopause <45 years, %	9.9	9.8	10.6	10.9
Current use of postmenopausal hormones, %	19.0	19.8	19.3	30.7

Values are means ± SD or percentages and are standardized to the age distribution of the study population.
* Value is not age-adjusted
† This score is based on the sum of the z-scores of census tract indicators based on participants' zip codes (median household income, home value, percentage with college degree, percentage of families with interest or dividends, percentage occupied housing, percentage living in poverty, percentage White).
‡ Alternate Health Eating Index without alcohol is a score (range 0-100) that measures adherence to a diet pattern based on 10 foods and nutrients most predictive of disease risk in the literature, with higher scores representing better adherence.

Results: We followed 111,874 NHS women and accrued a total follow-up of 2,990,295 person-years (**Table 1**). Among them, 129 incident PMR cases were identified, and the mean age at diagnosis was 75.6 (SD=6.5) years. In multivariable-adjusted analyses (**Table 2**), having Scandinavian ancestry, compared to other European ancestry, was associated with more than a doubling of risk (HR: 2.35; 95%CI: 1.37, 4.05). Compared to living in the Midwest region, living in the Northeastern region was associated with a higher risk (HR: 1.89; 95%CI: 1.07, 3.34), while living in the Southern or Western regions were not significantly different (p >0.58). Greater ambient erythemal UV exposure based on residence was associated with a lower risk, with every 1 mW/m^2 increase in UV being significantly associated with a 2% lower risk (p=0.0045; HR=0.98; 95%CI: 0.96, 0.99; **Figure 1**). Those in the highest versus lowest UV quartile had a 73% lower risk (HR=0.27; 95%CI: 0.10, 0.72).

Conclusion: Scandinavian ancestry and living in Northeastern US were associated with a higher risk, while greater ambient UV erythemal irradiance was associated with a lower risk of PMR, indicating the important role of genetic and environmental factors in PMR etiology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Age-adjusted and multivariable-adjusted hazard ratios (95% confidence interval) of polymyalgia rheumatica by risk factors in multivariable-adjusted Cox regression models with time-varying covariates in the Nurses' Health Study (1980-2020)

Ancestry	Other European	Non-European	Southern European	Scandinavian European
Cases	85	1	27	16
Person-years	2,225,090	86,962	476,947	201,296
Multivariable-adjusted HR (95% CI)[a] – Model 1	1 (referent)	0.33 (0.05, 2.36)	1.28 (0.83, 1.98)	2.09 (1.22, 3.57)
Multivariable-adjusted HR (95% CI)[b] – Model 2	1 (referent)	0.52 (0.07, 3.75)	1.25 (0.80, 1.93)	2.35 (1.37, 4.05)
Residential region in US	**Northeastern**	**Midwestern**	**Southern**	**Western**
Cases	81	15	16	4
Person-years	1,408,311	486,812	484,841	390,191
Multivariable-adjusted HR (95% CI)[a] – Model 1	1.96 (1.13, 3.40)	1 (referent)	0.95 (0.47, 1.92)	0.37 (0.12, 1.10)
Multivariable-adjusted HR (95% CI)[b] – Model 2	1.89 (1.07, 3.34)	1 (referent)	1.39 (0.64, 3.03)	0.95 (0.24, 3.72)

UV exposure	Ambient erythemal UV irradiance based on residence (mW/m²)						
	Quartile 1 (132-168)	Quartile 2 (169-174)	Quartile 3 (175-189)	Quartile 4 (190-281)	p_{trend}	Per 1 mW/m² increase	p-value
Cases	41	46	34	8			
Person-years	750,276	763,513	733,536	742,969			
Multivariable-adjusted HR (95% CI)[a] – Model 1	1 (referent)	1.05 (0.69, 1.61)	1.12 (0.71, 1.77)	0.24 (0.11, 0.51)		0.98 (0.96, 0.99)	
Multivariable-adjusted HR (95% CI)[b] – Model 2	1 (referent)	0.96 (0.62, 1.48)	0.95 (0.58, 1.54)	0.27 (0.10, 0.72)	.56	0.98 (0.96, 0.99)	0.0045

[a] Model 1: multivariable-adjusted analyses were stratified by age in months, period at risk.

[b] Model 2: multivariable-adjusted analyses were stratified by age in months, period at risk, and adjusted for the following covariates: pack-years of smoking (0, 1-9, 10-19, 20+), neighborhood socioeconomic status score (linear), body mass index (kg/m²: <22, 22-23, 24-25, 26-27, 28-29, 30+), self-reported history of diabetes, hypertension, cholesterol, alcohol intake (g/day), caffeine (mg/day), Alternate Healthy Eating Index (AHEI)-2010 (the overall AHEI-2010 score without alcohol intake), physical activity (Metabolic Equivalent Task-hours/week; quartiles), age at menopause (years, <45, 45-49, 50-53, 54+), postmenopausal hormone status (past use, current use) and the other variables in this table.

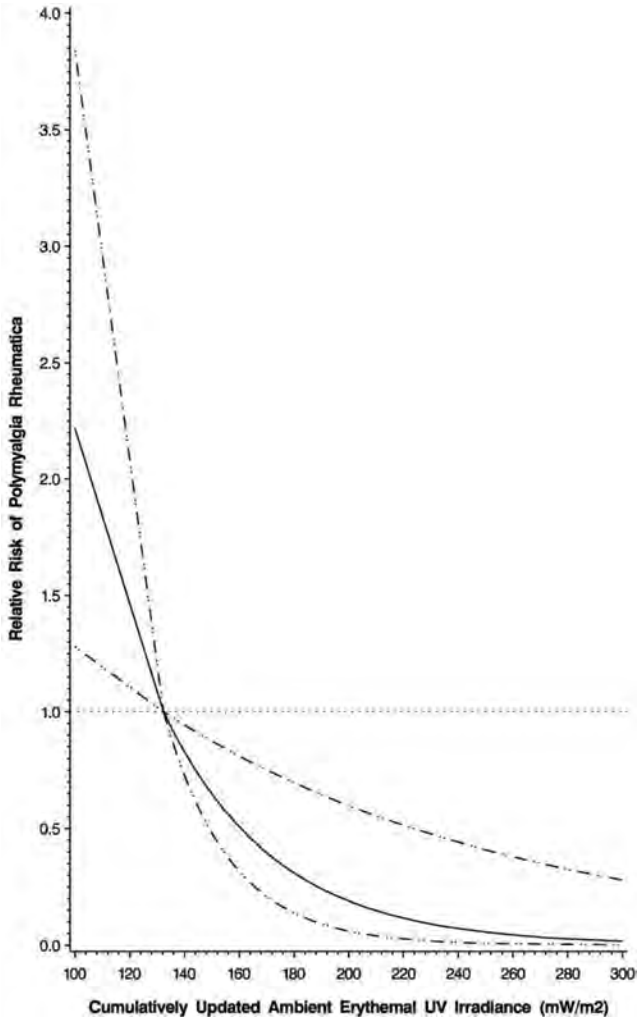


Figure 1. Spline analysis showing multivariable-adjusted hazard ratio (95% CI) for cumulatively updated ambient erythemal UV irradiance and risk of polymyalgia rheumatica among women in the Nurses' Health Study cohort

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Costenbader: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **N. Yang**: None; **E. Oakes**: None; **M. Raymo**: None; **J. Kang**: None.

Abstract Number: 1021

Recent Trends in Cannabis Use Among Individuals with Rheumatic Diseases

Kristin Wipfler[1] and Kaleb Michaud[2], [1]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [2]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cannabis use has increased substantially in the general population over the past decade, driven by changing legal landscapes and expanding public interest in its therapeutic potential. Among individuals with rheumatic and musculoskeletal diseases (RMDs), pain management remains a persistent challenge, prompting interest in alternative therapies such as cannabis. Our prior work documented a dramatic rise in cannabis use among people with RMDs between 2014 and 2019.[1] However, updated recent estimates are lacking, and the clinical landscape has evolved rapidly with changing laws and new formulations available. We aimed to describe trends in cannabis use from 2020 to 2024 among individuals with RMDs, including patterns of THC vs CBD product use, routes of administration, and reasons for use.

Table 1. Characteristics of study participants by cannabis use status.

Characteristic	Cannabis Nonusers n=3704	Cannabis Users (ever) n=2969
*Age, years, mean (SD)	69.5 (11.8)	65.2 (11.4)
*Female, %	82.4	85.1
White race, %	90.5	90.8
BMI, kg/m^2, mean (SD)	28.9 (7.3)	29.2 (7.2)
*Hx smoking cigarettes, %	41.1	51.4
*Primary Diagnosis, %		
Rheumatoid Arthritis	63.7	60.8
Osteoarthritis	14.1	16.2
Systemic Lupus Erythematosus	5.4	5.7
Fibromyalgia	4.5	6.5
Psoriatic Arthritis	2.8	3.1
Other	9.5	7.8
*Pain VAS, 0-10, mean (SD)	3.7 (2.8)	4.3 (2.8)
*Patient global VAS, 0-10, mean (SD)	3.7 (2.6)	4.0 (2.6)
HAQ-II, 0-3, mean (SD)	0.95 (0.73)	0.93 (0.68)
*Rheumatic Disease Comorbidity Index, 0-9, mean (SD)	2.0 (1.6)	2.2 (1.7)
*DMARD use, %	64.1	61.0
Non-opioid analgesic use, %	42.7	45.0
*Opioid use, %	18.7	24.1

*p<0.05; significance testing by X^2 or Student's t-tests, as appropriate

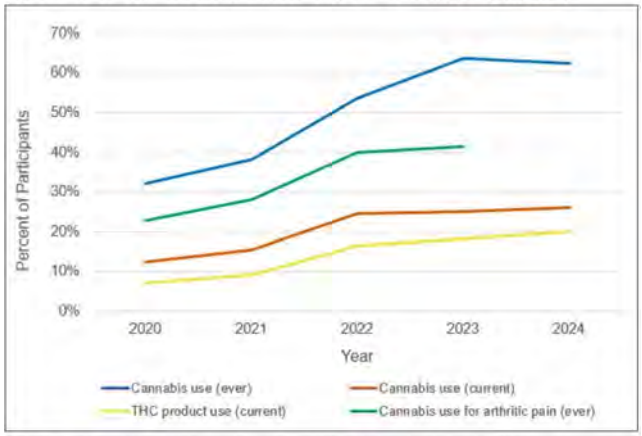
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Reasons for use and routes of administration among cannabis users (2020-2024).

	All Users n=2969	THC Product Users n=1725	CBD-Only Users n=1244
Reason for use			
Anxiety/relaxation	725 (24.4)	568 (32.9)	157 (12.6)
Arthritic pain	2024 (68.2)	990 (57.4)	1034 (83.1)
Depression	207 (7.0)	160 (9.3)	47 (3.8)
Insomnia	362 (12.2)	365 (21.2)	148 (11.9)
Recreational only	498 (16.8)	358 (20.8)	4 (0.3)
Other	234 (7.9)	124 (7.2)	110 (8.8)
Route of administration			
Smoked	891 (30.0)	882 (51.1)	9 (0.7)
Vaped	208 (7.0)	197 (11.4)	11 (0.9)
Ingested	1356 (45.7)	826 (47.9)	530 (42.6)
Topical	1181 (39.8)	510 (29.6)	671 (53.9)

Values are n (%). Participants could report multiple reasons for use and multiple routes of administration. Users are "ever" (both past and current).

Figure 1. Trends in cannabis use for the treatment of arthritis-related pain (2020-2024).



N=6673; 2020 n=4485; 2021 n=5342; 2022 n=3115; 2023 n=1728; 2024 n=1429
Reason for use data are not yet available for 2024

Methods: The study population included adults with RMDs in the FORWARD Databank who answered questions related to cannabis use between 2020 and 2024. Participants who reported use of cannabis or cannabis-derived products (hereafter "cannabis") were categorized by whether the products they used contained THC or not (CBD only) and whether their use was past or current. Descriptive statistics were calculated for characteristics of these subgroups as well as for self-reported reason(s) for cannabis use and route(s) of administration. Temporal trends for cannabis use in general, for THC-containing products, and for use related to arthritic pain were examined.

Results: A total of 6,673 participants were included in the study, 2,969 (44%) of whom reported past or current cannabis use (Table 1). Among users, 1,725 (58%) reported use of a THC-containing cannabis product, while the remainder reported use of CBD-only products (Table 2). Most cannabis users (68%) reported use of cannabis products for the purpose of treating arthritis-related pain, particularly those who reported use of CBD-only products. Ingestion and topical use were the most common routes of administration in general, although smoking was more common among users of THC-containing products. From 2020 to 2024, frequency of cannabis use in this population doubled; "ever" use increased from 32% to 62%, while current use increased from 13% to 26% (Figure 1). Each year, most current users (57-77%) were using THC-containing products.

Conclusion: Cannabis use has increased substantially among individuals with RMDs since 2020. This finding underscores the need for clinician awareness and guidance in this area, as well as the need for an understanding of any

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

therapeutic impact of cannabis use in this population. Ongoing work will explore associations between cannabis use and disease activity, physical function, and patient-reported outcomes, as well as perceived effectiveness of treatment with cannabis products and reasons for discontinuation.

1. Wipfler, K. *et al*. *Arthritis Care & Research* **74**, 2091–2099 (2022)

Disclosure: K. Wipfler: None; **K. Michaud**: None.

Abstract Number: 1022

Abuse in Rheumatic Diseases: Associations with Depression, Disability, and Psychosocial Risk Factors

Margarita Isabel Alarcon-Jarquin[1], Egla Samantha Sanchez-Peralta[2], Maria Eugenia Corral-Trujillo[3], Daniela Alejandra Salcedo-Soto[4], Judith Michelle Ramirez-Alonso[4], Ana Elena González-Rosales[5], Juan Daniel Valdez-Cruz[4], Osmel Adrián Ramirez-Uzcategui[4], Jesús Gilberto Espinoza-Gámez[6], Yessica Rubi Reyes-Yepiz1[4], Juan Pablo González-Morales[4], Virginia Pascual-Ramos[7], Dionicio A. Galarza-Delgado[8], Gabriel Figueroa-Parra[9] and Diana E. Flores-Alvarado[2], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [3]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., Monterrey, Nuevo Leon, Mexico, [4]Hospital universitario José Eleuterio González, Monterrey, Nuevo Leon, Mexico, [5]Hospital universitario José Eleuterio González, Monterrey, Mexico, [6]Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo Leon, Mexico, [7]Rheumatology Service, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, México City, Mexico, Mexico City, Distrito Federal, Mexico, [8]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [9]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Exposure to a hostile environment may negatively impact disease outcomes in patients with RD, particularly by affecting their mental health and overall quality of life. We aimed to evaluate the prevalence of abuse among patients with RD and to identify their associated factors.

Methods: We conducted a cross-sectional study at an academic rheumatology clinic, including adult patients with a clinical diagnosis of RD. A modified version of the Geriatric Mistreatment Scale was used to assess physical, psychological, neglect, economic, and sexual abuse. Psychological symptoms (DASS-21 tool), personality traits (BFI-10), functional capacity (HAQ-DI) disease activity (RAPID-3), family function (APGAR questionnaire), resilience (BRCS), and quality of life (WHOQOL-BREF) were all assessed. Patients were grouped based on reported abuse. Group comparisons were performed using X^2 and Mann–Whitney U tests. Univariable logistic regression was conducted to explore associations between abuse and clinical or psychosocial factors. Multivariable logistic regression was used to account for age, sex, education level, and marital status. $P < 0.05$ was statistically significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Sociodemographic, clinical, and psychosocial characteristics of patients with rheumatic diseases with and without abuse/mistreatment.

Variable	Abuse N=98	Non-Abuse N=152
Age, years, median (IQR)	51 (38–60)	52 (47.5–62)
Female, n (%)	93 (94.9)	139 (91.4)
Economic level, n (%)		
Very Low (<$2,670/year)	4 (4.1)	17 (11.2)
Low ($2,670 – $4,460/year)	36 (36.7)	17 (11.2)
Low-Middle ($4,460 – $5,810/year)	34 (34.7)	44 (28.9)
Middle ($5,810 – $7,160/year)	16 (16.3)	57 (37.5)
Middle-High ($7,160 – $8,530/year)	7 (7.1)	21 (13.8)
High (>$8,530/year)	1 (1)	10 (6.6)
Education, n (%)		
No education	1 (1)	5 (3.3)
Elementary	29 (29.6)	35 (23)
Secondary	24 (24.5)	55 (36.2)
High-School	19 (19.4)	37 (24.3)
College/Undergraduate	24 (24.5)	20 (13.2)
Graduate	1 (1)	--
Marital Status, n (%)		
Married, in a relationship	60 (61.2)	97 (63.8)
Single, divorced, separated, widowed	38 (38.8)	55 (36.2)
Employment, n (%)		
Formal employment	17 (17.3)	17 (11.2)
Informal employee	19 (19.4)	20 (13.2)
Homemaker	49 (50)	97 (63.8)
Retired	9 (9.2)	11 (7.2)
Student	2 (2)	6 (3.9)
Unemployed	2 (2)	1 (0.7)
Health Insurance, n (%)	27 (72.4)	123 (80.9)
Rheumatic Disease, n (%)		
Systemic Lupus Erythematosus	22 (22.4)	28 (18.4)
Rheumatoid Arthritis	43 (43.9)	81 (53.3)
Systemic Sclerosis	1 (1)	8 (5.3)
Vasculitis	3 (3.1)	2 (1.3)
Sjögren's Syndrome	8 (8.2)	12 (7.9)
Spondyloarthropathies	1 (1)	5 (3.3)
Inflammatory Myopathies	4 (4.1)	4 (2.6)
Antiphospholipid Syndrome	4 (4.1)	3 (2)
Comorbidities, n (%)		
Diabetes Mellitus	22 (22.4)	21 (13.8)
Hypertension	15 (15.3)	37 (24.3)
Hyperlipidemia	9 (9.2)	17 (11.1)
Hypothyroidism	--	1 (0.7)
Osteoporosis	3 (3.1)	8 (5.3)

Results: We included 250 patients with RD. Median age was 52 years (IQR 44–61), and 232 (92.8%) were female. Most patients had RA (124, 49.6%), followed by SLE (50, 20.0%), and SS (20, 8.0%). The prevalence of abuse/mistreatment was 39.8% (n= 98). There were no differences in age, sex, educational level, economic status, or employment status between patients with or without abuse (**Table 1**).

Patients with abuse had more functional disability (34.0%) than non-abuse patients (13.2%; p< 0.001), and fewer patients with RA and abuse were on remission according to RAPID3 (46.9% vs. 65.8%, p< 0.005). Quality of life was lower among patients with abuse in the psychological, social, and environmental domains; but not in the physical domain (**Table 2**).

In univariable logistic regression, mistreatment was associated with higher levels of depression (OR 1.10, 95% CI 1.05–1.14), anxiety (OR 1.09, 95% CI 1.05–1.13), stress (OR 1.09, 95% CI 1.06–1.13), and disability (OR 2.10, 95% CI 1.40–3.10). It was also associated with lower quality of life (psychological, social, and environmental), higher neuroticism, and reduced coping and family function (**Table 3**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical, psychological, and quality of life characteristics of patients with rheumatic diseases with and without abuse.

Variable	Abuse N=98	Non-Abuse N=152	P-value
DASS-21 (Depression), n (%)			<0.001
Normal (0–9)	59 (60.2)	131 (86.2)	
Mild (10–13)	10 (10.2)	13 (8.6)	
Moderate (14–20)	23 (23.5)	4 (2.6)	
Severe (21–27)	2 (2)	1 (0.7)	
Extremely severe (≥28)	4 (4.1)	3 (2)	
DASS-21 (Anxiety), n (%)			<0.001
Normal (0–7)	47 (48)	115 (75.7)	
Mild (8–9)	10 (10.2)	7 (4.6)	
Moderate (10–14)	15 (15.3)	19 (12.5)	
Severe (15–19)	12 (12.2)	7 (4.6)	
Extremely severe (≥20)	14 (14.3)	4 (2.6)	
DASS-21 (Stress), n (%)			<0.001
Normal (0–14)	61 (62.2)	129 (84.9)	
Mild (15–18)	10 (10.2)	13 (8.6)	
Moderate (19–25)	10 (10.2)	7 (4.6)	
Severe (26–33)	9 (9.2)	1 (0.7)	
Extremely severe (≥34)	8 (8.2)	2 (1.3)	
BIF (Personality), median (IQR)			
Extraversion	3 (2.5–3.5)	3 (2–3.5)	0.035
Agreeableness	3 (2.5-3.5)	3 (2–3.5)	0.083
Responsibility	3.5 (3-4.5)	4 (3.5-4.5)	0.149
Neuroticism	3 (2.5–4)	3.5 (3–4.5)	0.012
Openness	3 (3-4)	3.5 (3–4)	0.785
APGAR (Coping), n (%)			<0.001
Normal (7–10)	69 (70.4)	142 (93.4)	
Moderate (4–6)	20 (20.4)	6 (3.9)	
Severe (0–3)	9 (9.2)	4 (2.6)	
HAQ (Disability), n (%)			<0.001
Mild-moderate	64 (66)	132 (86.8)	
Moderate-severe	22 (22.7)	17 (11.2)	
Severe	11 (11.3)	3 (2)	
Disease Activity (RAPID3), n (%)			<0.005
Remission <1.1	46 (46.9)	100 (65.8)	
Low activity 1.1-4	16 (16.3)	21 (13.8)	
Moderate activity 4.1-8	22 (22.4)	25 (16.4)	
High activity >8	14 (14.3)	6 (3.9)	
Pain Score (0-10), median (IQR)	5 (3–6.9)	4.4 (2.5–5.5)	
WHO-QoL (Quality of Life), median (IQR)			
Physical Health	53 (35–64)	46 (32.9–50)	0.186
Psychological Health	54 (46–75)	63 (54-75)	0.014
Social Relationships	50 (42–75)	58 (50–75)	0.006
Environment	56 (41–66.7)	63 (50–75)	0.003

DASS-21: Depression Anxiety Stress Scales–21; HAQ: Health Assessment Questionnaire. WHOQOL-BREF: World Health Organization Quality of Life - Brief. BFI-10: Big Five Inventory-10.

After accounting for age, sex, education and marital status, abuse/mistreatment remained associated with higher levels of depression (aOR 1.10, 95% CI 1.05–1.15), anxiety (aOR 1.09, 95% CI 1.05–1.13), stress (aOR 1.10, 95% CI 1.06–1.13), and disability (aOR 2.10, 95% CI 1.40–3.10). In contrast, better quality of life (psychological, social, and environmental), along with lower neuroticism (aOR 0.83, 95% CI 0.72–0.96), adaptive coping (aOR 0.89, 95% CI 0.81–0.97), and stronger family support (aOR, 95% CI 0.67–0.87), were protective (**Table 3**).

Conclusion: Abuse in patients with RD is associated with greater psychological distress, disability, and disease activity, while better quality of life, coping, and family support are protective. Screening for abuse should be considered in patients care to improve outcomes.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Factors associated with abuse among patients with rheumatic diseases.

Variable	OR (95% CI)	*p*-value	aOR (95% CI)*	p-value
Age (per 1-year increase)	0.99 (0.98–1.01)	0.730	--	--
Female	1.74 (0.60–5.04)	0.310	--	--
Diagnosis (vs. RA)				
- SLE	1.39 (0.71–2.75)	0.340	--	--
- FM	1.55 (0.45–5.37)	0.490	--	--
- Other	1.39 (0.76–2.55)	0.280	--	--
Socioeconomic level	1.03 (0.61–1.73)	0.910	--	--
Social security	0.62 (0.34–1.13)	0.120	--	--
Education level	0.74 (0.44–1.23)	0.250	--	--
Marital status	0.90 (0.53–1.50)	0.680	--	--
DASS-21 Depression†	1.10 (1.05–1.14)	<0.001	1.10 (1.05–1.15)	<0.001
DASS-21 Anxiety†	1.09 (1.05–1.13)	<0.001	1.09 (1.05–1.13)	<0.001
DASS-21 Stress†	1.09 (1.06–1.13)	<0.001	1.10 (1.06–1.13)	<0.001
HAQ-DI†	2.10 (1.40–3.10)	<0.001	2.10 (1.40–3.10)	<0.001
WHOQoL-BREF Physical†	0.99 (0.97–1.01)	0.090		
WHOQoL-BREF Psychological†	0.98 (0.97–0.99)	0.020	0.98 (0.97–0.99)	0.022
WHOQOL-BREF Social Relationships†	0.98 (0.96–0.99)	0.003	0.98 (0.97–0.99)	0.001
WHOQOL-BREF Environment†	0.97 (0.96–0.99)	0.001	0.97 (0.96–0.99)	<0.001
BFI-10 Extraversion†	1.14 (0.99–1.31)	0.080	--	--
BFI-10 Agreeableness†	1.10 (0.96–1.27)	0.160	--	--
BFI-10 Conscientiousness†	0.89 (0.77–1.04)	0.140	--	--
BFI-10 Neuroticism†	0.83 (0.72–0.95)	0.007	0.83 (0.72–0.96)	0.015
BFI-10 Openness†	0.99 (0.86–1.15)	0.990	--	--
Coping†	0.88 (0.81–0.96)	0.004	0.89 (0.81–0.97)	0.008
APGAR†	0.76 (0.66–0.86)	<0.001	0.76 (0.67–0.87)	<0.001

OR: odds ratio; aOR: Adjusted odd ratio; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; FM: Fibromyalgia. DASS-21: Depression Anxiety Stress Scales–21; HAQ: Health Assessment Questionnaire. WHOQOL-BREF: World Health Organization Quality of Life - Brief. BFI-10: Big Five Inventory-10.

*Adjusted for Age, Sex, Education, and Marital Status.

†Per 1-point increase in score

Disclosure: M. Alarcon-Jarquin: None; **E. Sanchez-Peralta**: None; **M. Corral-Trujillo**: None; **D. Salcedo-Soto**: None; **J. Ramirez-Alonso**: None; **A. González-Rosales**: None; **J. Valdez-Cruz**: None; **O. Ramirez-Uzcategui**: None; **J. Espinoza-Gámez**: None; **Y. Reyes-Yepiz1**: None; **J. González-Morales**: None; **V. Pascual-Ramos**: None; **D. Galarza-Delgado**: None; **G. Figueroa-Parra**: None; **D. Flores-Alvarado**: None.

Abstract Number: 1023

Comparative Analysis of Oral Health and Dental Care in Patients With Immune-Mediated and Non-Immune-Mediated Rheumatic Diseases

Margarita Isabel Alarcon-Jarquin[1], Fernanda M. Garcia-Garcia[2], Vanessa L. Lopez-Flores[1], Aranxa Galindo-Bandt[3], Mario A. Arellano-Alvarez[3], Aleydis Gonzalez-Melendez[3], Gabriel Figueroa-Parra[3], Dionicio A. Galarza-Delgado[2] and Janett C. Riega-Torres[4], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, [4]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Oral health impairment is common in patients with immune-mediated rheumatic diseases (IMRDs) due to chronic inflammation and immune dysregulation. These complications can worsen systemic inflammation, potentially influencing disease activity and quality of life. Although previous studies have explored oral health in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Sjögren's syndrome (SS), few have compared oral health status and dental care practices between IMRDs and non-immune-mediated rheumatic diseases (NIMRDs). Understanding these differences may help optimize integrated care strategies for rheumatic patients.

Methods: We conducted a cross-sectional study including 670 patients: 569 with IMRDs and 101 with NIMRDs. Patients were consecutively enrolled from rheumatology outpatient clinics at a tertiary care center between December 2021 and May 2025, based on confirmed diagnoses according to international classification criteria. The IMRD group included patients with RA, SLE, and SS, while the NIMRD group included patients diagnosed with osteoarthritis and osteoporosis. Clinical, demographic, and treatment characteristics were recorded. A structured survey evaluated awareness of dental impact, rheumatologist advice, referral desire, dental visits, and toothbrushing habits. Primary comparisons were made between IMRDs and NIMRDs, with additional subgroup analyses comparing RA, SLE, and SS individually to the NIMRD group. Comparisons were performed using the Student's t-test and Chi-square test, with $p < 0.05$ considered statistically significant.

Results: We included 670 patients (569 IMRDs: RA n=400, SLE n=101, SS n=68; 101 NIMRDs). IMRD patients were predominantly female (93.14%) with a mean age of 50.70 ± 14.68 years. Awareness of the oral impact of rheumatic disease was higher in IMRDs vs. NIMRDs (48.85% vs. 28.71%; p< 0.001), as was rheumatologist dental advice (40.77% vs. 26.73%; p=0.008). Referral desire was high across both groups (79.96% vs. 80.19%; p=0.957).

Table 1. Clinical and treatment characteristics of patients with immune-mediated and non-immune-mediated rheumatic diseases

Variable	NIMRDs n= 101	IMRDs n = 569	RA patients n= 400	SLE patients n= 101	SS patients n= 68
Age, mean ± SD	55.21 ± 13.46	50.70 ± 14.68	53.07 ± 13.48	40.39 ± 15.67	52.04 ± 13.51
Women, n (%)	100 (99.01)	530 (93.14)	370 (92.50)	96 (95.05)	64 (94.11)
Comorbidities					
DM, n (%)	19 (18.81)	67 (11.77)	57 (14.25)	5 (4.95)	5 (7.35)
Hypertension, n (%)	26 (25.74)	148 (26.01)	113 (28.25)	22 (21.78)	13 (19.11)
Smoker, n (%)	8 (7.92)	32 (5.62)	24 (6.00)	6 (5.94)	2 (2.94)
Alcohol consumption, n (%)	9 (8.91)	48 (8.43)	28 (7.00)	10 (9.90)	10 (14.70)
Treatments					
Glucocorticoids, n (%)	6 (5.94)	166 (29.17)	114 (28.50)	36 (35.64)	16 (23.52)
DMARDs, n (%)	24 (24.24)	359 (63.76)	256 (64.48)	67 (67.67)	36 (53.73)
Methotrexate, n (%)	8 (8.08)	206 (36.59)	175 (44.08)	19 (19.19)	12 (17.91)
bDMARDs, n (%)	1 (1.01)	8 (1.42)	7 (1.76)	–	1 (1.49)

SD, Standard Deviation; NIMRDs, Non-Immune-Mediated Rheumatic Diseases; IMRDs, Immune-Mediated Rheumatic Diseases; RA, Rheumatoid Arthritis; SLE, Systemic Lupus Erythematosus; SS, Sjögren's Syndrome; DM, Diabetes Mellitus; HTN, Hypertension; DMARDs, Disease-Modifying Antirheumatic Drugs; bDMARDs, Biological DMARDs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Oral health and dental care profile of patients with immune-mediated and non-immune-mediated rheumatic diseases

Variable	NIMRDs patients n= 101	IMRDs patients n = 569	RA patients n= 400	SLE patients n= 101	SS patients n= 68	p IMRDs vs NIMRDs	p RA vs NIMRDs	p SLE vs NIMRDs	p SS vs NIMRDs
Aware of dental impact, n (%)	29 (28.71)	278 (48.85)	192 (48.00)	44 (43.56)	42 (61.76)	**< 0.001**	**< 0.001**	**0.028**	**< 0.001**
Rheumatologist dental advice	27 (26.73)	232 (40.77)	163 (40.75)	37 (36.63)	32 (47.05)	**0.008**	**0.009**	0.130	**0.007**
Patient wants dental referral, n (%)	81 (80.19)	455 (79.96)	319 (79.75)	85 (84.15)	51 (75.00)	0.957	0.920	0.462	0.423
GOHAI									
Total, mean ± SD	47.98 ± 7.95	50.20 ± 8.44	50.22 ± 8.12	51.88 ± 8.86	47.63 ± 9.12	**0.014**	**0.013**	**< 0.001**	0.739
Physical function, mean ± SD	16.44 ± 3.22	17.54 ± 4.01	17.39 ± 3.47	18.69 ± 4.76	16.76 ± 5.29	**0.009**	**0.014**	**<0.001**	0.627
Psychosocial function, mean ± SD	19.20 ± 4.10	20.32 ± 4.12	20.47 ± 4.08	20.43 ± 4.09	19.32 ± 4.30	0.105	0.058	0.151	0.670
Pain discomfort, mean ± SD	11.93 ± 2.50	12.33 ± 2.48	12.36 ± 2.44	12.75 ± 2.49	11.54 ± 1.93	0.134	0.115	**0.020**	0.332
Time since last dental visit						0.659	0.379	0.995	0.735
Within the past year, n (%)	53 (56.14)	297 (52.19)	199 (49.75)	57 (56.43)	41 (60.29)				
1-5 years ago, n (%)	24 (23.76)	151 (26.53)	114 (28.50)	22 (21.78)	15 (22.05)				
Over 5 years ago, n (%)	9 (8.91)	33 (5.80)	20 (5.00)	8 (7.92)	5 (7.35)				
Never, n (%)	15 (14.85)	88 (15.46)	67 (16.75)	14 (13.86)	7 (10.29)				
Dental visit frequency						0.142	0.061	0.381	0.495
Once a year, n (%)	20 (19.80)	71 (12.52)	44 (11.00)	12 (12.00)	15 (22.38)				
Twice or more per year, n (%)	28 (27.72)	177 (31.21)	124 (31.00)	30 (30.00)	23 (34.32)				
Never, n (%)	53 (52.47)	319 (56.26)	232 (58.00)	58 (58.00)	29 (43.28)				
Daily toothbrushing frequency						0.519	0.618	**0.027**	0.971
Once	13 (12.87)	65 (11.46)	53 (13.25)	4 (3.96)	8 (12.12)				
Twice	38 (37.62)	248 (43.73)	170 (42.50)	52 (51.48)	26 (39.39)				
Three or more	50 (49.50)	254 (44.79)	177 (44.25)	45 (44.55)	32 (48.48)				

GOHAI total scores were 50.20 ± 8.44 in IMRDs and 47.98 ± 7.95 in NIMRDs (p=0.014), with significant differences also observed in the physical function domain (17.54 ± 4.01 vs. 16.44 ± 3.22; p=0.009). No significant differences were found in psychosocial function or pain/discomfort. Subgroup analysis showed that SS patients had the lowest GOHAI total score (47.63 ± 9.12) and the lowest pain/discomfort score (11.54 ± 1.93). Dental visit frequency and toothbrushing habits showed no significant differences between groups.

Conclusion: Patients with IMRDs demonstrated greater awareness of oral health and received more dental advice than those with NIMRDs; however, significant oral health impairment persists, particularly among SS patients. These findings highlight the unmet need for integrated rheumatology-dental care to improve oral health outcomes across all rheumatic disease populations.

Disclosure: M. Alarcon-Jarquin: None; **F. Garcia-Garcia**: None; **V. Lopez-Flores**: None; **A. Galindo-Bandt**: None; **M. Arellano-Alvarez**: None; **A. Gonzalez-Melendez**: None; **G. Figueroa-Parra**: None; **D. Galarza-Delgado**: None; **J. Riega-Torres**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1024

Mortality In Progressive Pulmonary Fibrosis Associated to Autoimmune Diseases: NEREA Registry

Marta Ruiz-Valdepeñas Almansa[1], CLARA DE MIGUEL[2], DALIFER FREITES[3], Cristina Vadillo Font[4], Maria asuncion Nieto[4], Olga Sanchez Pernaute[5], fredeswinda Romero-Bueno[6], Mª Jesus Rodriguez-Nieto[7], Rosalia Laporta[8], Hilda Godoy Tundidor[9], Jesús Loarce[10], Juan A Rigual[11] and lydia Abasolo Alcazar[12], [1]HOSPITAL CLINICO SAN CARLOS, Madrid, Spain, [2]HOSPITAL CLINICO SAN CARLOS, Madrid, Madrid, Spain, [3]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [4]Hospital Clínico S Carlos, Madrid, Spain, [5]Clinica Universidad de Navarra, Madrid, Madrid, Spain, [6]University Hospital Fundación Jiménez Díaz\"\", Madrid, Spain, [7]Fundacion Jimenez Diaz (IIS-HUFJD), Madrid, Spain, [8]Hospital Puerta de Hierro Majadahonda, Madrid, Spain, [9]Hospital Universitario puerta de hierro, Madrid, Spain, [10]HOSPITAL RAMÓN Y CAJAL, MADRID, Madrid, Spain, [11]Hospital Ramón y Cajal, Madrid, Spain, [12]IdISSC. HCSC, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1007–1037) Epidemiology & Public Health Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune interstitial lung disease (ILD) may arise in various autoimmune rheumatic diseases (ARD). Some patients develop ILD with systemic symptoms and autoantibodies without fulfilling ARD criteria, as in interstitial pneumonia with autoimmune features (IPAF) and unclassifiable autoimmune ILD (ILD-UA). Autoinmune-ILD can progress to progressive pulmonary fibrosis (PPF), characterized by irreversible lung damage and high mortality. Real-world data on these patients, particularly cause-specific mortality, are still limited. This study evaluates ILD-related mortality rate over time in patients with autoimmune ILD from the onset of PPF.

Methods: A multicenter longitudinal study was conducted on patients with autoimmune origin ILD (ARD-ILD, IPAF, and ILD-UA), from Madrid, enrolled from Jun 2006 to Jun 2023 and followed up until Sept 2024. Autoimmune-ILD patients were included in a registry [pNEumology RhEumatology Autoinmune diseases (NEREA)]. Patients were required to meet progressive pulmonary fibrosis (PPF) criteria based on the ATS/ERS/JRS/ALAT Guideline. Main outcome was specific-cause mortality related to ILD. Covariables included sociodemographic, clinical, radiological, pulmonary function tests, and therapy. Time of observation comprised the period from the PPF starting until loss of follow-up, main outcome or end of study. Survival techniques were used to estimate the specific-cause mortality rate related to ILD (MR), expressed per 100 patients-year with their respective 95% confidence interval [CI].

Results: A total of 158 patients with PPF were included, of whom 62% were women (n=98). Autoimmune diseases were present in 71.5%, with rheumatoid arthritis being the most common (39.9%) followed by systemic sclerosis (12.0%). Regarding treatments at baseline, 70.9% received corticosteroids, 70.3% disease-modifying antirheumatic drugs (DMARDs) (csDMARDs: 54.4%, b/tsDMARDs: 31.7%), and 14.6% antifibrotic therapy. During follow-up, a total of 47 deaths were recorded. Of these, 37 (78.7%) were attributed to ILD-related causes, with respiratory failure being the most common (16.2%). Additional causes included cancer (n=4), sepsis(n=2), cardiovascular(n=1), neurological(n=2), and unknown(n=1). The ILD-specific mortality rate was 6.2 [4.5-8.5], with a median survival time of 7.8 years. The MR was similar between genders and higher at older ages. Regarding radiographic patterns it was higher in UIP (9.9 [7.0-14.2]) compared to NSIP (MR: 0.47 [0.06-3.4]); in diagnosis MR was higher in IPAF/UA (MR: 7.7 [4.2-13.9]), RA (MR: 9.2 [6.0-14.2]) and lower in others (scleroderma MR:1.5 [0.4-6.3]). Concerning therapy, MR was lower in those on DMARDs during the follow-up compared to those with none (MR: with 4 [2.5-6.4]; without 9.0 [5.7-14.3]).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline sociodemographic, clinical, functional, radiologic characteristics of the patients.

VARIABLES		N=158
Sociodemographic	Women, n (%).	98 (62.0)
	Mean age at ILD diagnosis ± SD, years	65.8±12.1
	Mean age at the time of PPF ± SD, years	68.1±11.8
	Smokers (active), n (%)	14 (8.9)
	BMI, median [p25-75]	26.7[24.5-30.5]
Hospital centers, n (%)	FJD	59 (37.3)
	HCSC	84 (53.2)
	HPH	8 (5.1)
	HULP	1 (0.6)
	RyC	6 (3.8)
Autoimmune diagnosis, n (%)	Rheumatic diagnosis:	113 (71.5)
	Rheumatoid arthritis	63 (39.9)
	Sjögren's disease	7 (4.4)
	Scleroderma	19 (12.0)
	Mixed connective tissue disease	5 (3.2)
	Polymyositis, dermatomyositis,	6 (3.8)
	Antisynthetase syndrome	5 (3.2)
	Overlap syndrome	2 (1.2)
	Others (Still disease, vasculitis)	6 (3.8)
	IPAF	33 (20.9)
	ILD-UA	12 (7.6)
Comorbidity, n (%)	Hypertension	70 (44.3)
	Cholesterol	54 (34.2)
	Diabetes Mellitus	14 (8.8)
	Ischemic heart disease	10 (6.3)
	Cerebrovascular disease	13 (8.2)
	Peripheral vascular disease	16 (10.2)
	Liver disease	15 (9.5)
	History of cancer	22 (13.9)
	Renal failure (dialysis)	1 (0.6)
	GER	28 (17.7)
	Sleep apnea	10 (6.3)
ILD associated (HRCT), n (%)	Emphysema (n=148)	59 (39.8)
	PHT (n=132)	19 (14.4)
PTF parameters, median [p25-75]	FVC% (n=155)	81.5 [67 – 98.0]
	DLCO% (n=144)	57 [43 – 72]
Radiographic ILD pattern (HRCT), n (%):	NSIP	45 (28.4)
	UIP	87 (55.1)
	Indeterminate UIP	6 (3.8)
	Others	20 (12.7)
Laboratory: antibodies, n (%)	ANA >1/360, (n=125)	47 [37.1]
	Anti-Ro +, (n=91)	24 (26.4)
Laboratory , median [p25-75]	ESR	26 [13-45]
Concomitant therapy, n (%)	Oxygen therapy	21 (13.3)
	Glucocorticoids	112 (70.9)
	Anti-fibrotic	23 (14.6)
	DMARDS	111 (70.3)
	csDMARDs	86 (54.4)
	b/tsDMARDs	50 (31.7)

Conclusion: This study provides real-world evidence on the clinical course and cause-specific mortality in patients with autoimmune PPF-ILD. The findings underscore the substantial mortality rate directly attributable to ILD. Moreover, the results suggest a potential survival advantage in patients receiving immunomodulatory therapy, supporting its role in the management of this patient population.

Disclosure: M. Ruiz-Valdepeñas Almansa: None; **C. DE MIGUEL**: None; **D. FREITES**: None; **C. Vadillo Font**: None; **M. Nieto**: None; **O. Sanchez Pernaute**: None; **f. Romero-Bueno**: None; **M. Rodriguez-Nieto**: None; **R. Laporta**: None; **H. Godoy Tundidor**: None; **J. Loarce**: None; **J. A Rigual**: None; **I. Abasolo Alcazar**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1025

Association Between Rural-urban Clinics and the Management of Adult Rheumatoid Arthritis in the United States

Megan Lorenz, Paxten Wahlund, Henry Elsenpeter, Abe Sahmoun and James Beal, University of North Dakota School of Medicine and Health Sciences, Grand Forks, ND

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Disease modifying anti-rheumatic drugs (DMARDs) improve symptom management and outcomes in rheumatoid arthritis (RA). While residence may influence management strategies and access to care, limited research exists on how rural vs. urban residence affects use of DMARDs and glucocorticoids. This study aimed to determine the association between rural and urban clinics and management of rheumatoid arthritis in the U.S.

Methods: We conducted a retrospective analysis of adults, 18-80 years old, rheumatoid arthritis visits utilizing the 2011-2019 National Ambulatory Medical Care Survey datasets. We compared demographic, clinical, and management factors of adult rheumatoid arthritis visits between rural and urban clinics. SPSS Complex Samples 30.0 for Windows was used to analyze the data to account for the NAMCS complex sample survey design. Chi-square and GLM means tests were performed with two-sided test and $p < .05$. This study was approved by the Institutional Review Board of the University of North Dakota.

Results: Of the estimated 35 million adult RA visits, 5.4% were in rural clinics. Rural RA visits were less likely to be female (57.9% vs 77.7%, p=.000) and more likely to occur in the Midwest (46.8% vs. 14.1%, p=.002). There was no association between rural-urban clinics and age, race, and insurance.

Rural RA patients were less likely to see a medical specialist (41.7% vs 74.7%, p=.011) and more likely to see their own primary care physician (62.8% vs 22.5%, p=.000). Rural and urban RA patients had a similar number of comorbidities (2.3 vs 2.6, p=.090). However, rural RA patients had higher rates of hypertension (43.9% vs 27.8%, p=.004) and end stage renal disease (10.4% vs 1.4%, p=.006).

Rural and urban patients received similar laboratory tests and health education. Rural RA patients were on more medications than their urban counterparts, (7.2 vs 5.3, p=.031), and had a higher rate of opioid therapy (43.1% vs. 23.2%, p=.020). However, rural and urban RA patients had similar rates of DMARD therapy (49.8% vs 51.5%, p=.841) and glucocorticoids (29.9% vs 34.0%, p=.575).

Conclusion: Rural and urban clinics had similar utilization rates of DMARD therapy and glucocorticoids in adult RA patients, despite rural RA patients being more likely to be managed by primary care physicians and urban patients by medical specialists. However, rural RA patients had higher rates of opioid therapy than their urban counterparts.

Disclosure: M. Lorenz: None; **P. Wahlund**: None; **H. Elsenpeter**: None; **A. Sahmoun**: None; **J. Beal**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1026

Seasonal Variation in Public Interest in Gout Made More Crystal-Clear: A Longitudinal Infodemiology Study Using Google Trends.

Naomi Schlesinger[1] and Ioannis Androulakis[2], [1]Spencer Fox Eccles School of Medicine, University of Utah, Salt Lake City, UT, USA, Salt Lake City, UT, [2]Rutgers University, Piscataway, NJ

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Understanding public interest in gout, as reflected by online behavior, can offer valuable insights into its perception and management. Infodemiology, which examines the distribution and determinants of information on the internet, offers insights into public health trends that are often challenging to capture through traditional epidemiological methods. This approach is especially relevant for analyzing interest patterns over time and across different regions.

Our objective was to explore whether public interest in gout, as measured by Google Trends data, shows seasonal patterns across countries, US states, and major metropolitan areas.

Methods: This study utilizes Google Trends data from January 1, 2014, to October 1, 2024, to analyze the frequency of gout-related search queries. Data were collected from 70 countries, 50 US states, and 36 major cities in the US and Canada. The analysis included both direct searches for "gout" and searches based on symptoms and covered queries in multiple languages.

The primary outcome was the seasonal variation in gout-related search queries, measured using a cosinor model to identify cyclic patterns in search behavior throughout the year. The secondary outcome assessed the influence of language-specific search terms on the seasonality of these queries.

Results: The analysis showed significant seasonal variation in gout-related search interest in 40 US states and 20 of the 70 countries analyzed, with peaks in the late spring/early summer for the Northern Hemisphere and corresponding shifts in the Southern Hemisphere (**Figures 1 and 2**). Symptom-based queries also displayed strong seasonality, aligning with

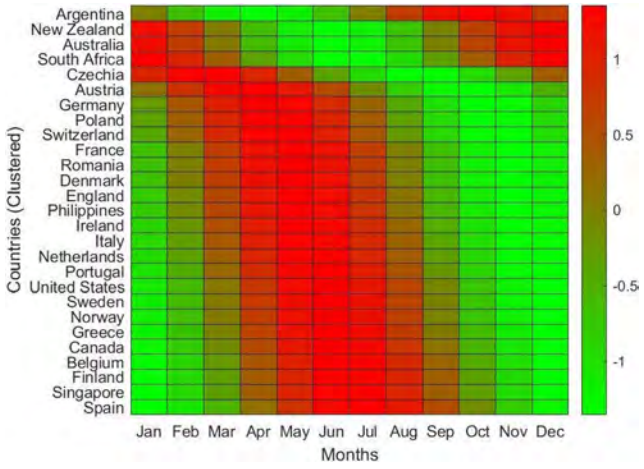


Figure 1 Frequency of query distribution using language-specific terms for "gout" across the globe. A clear separation between countries in the northern and the southern hemispheres was noted.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

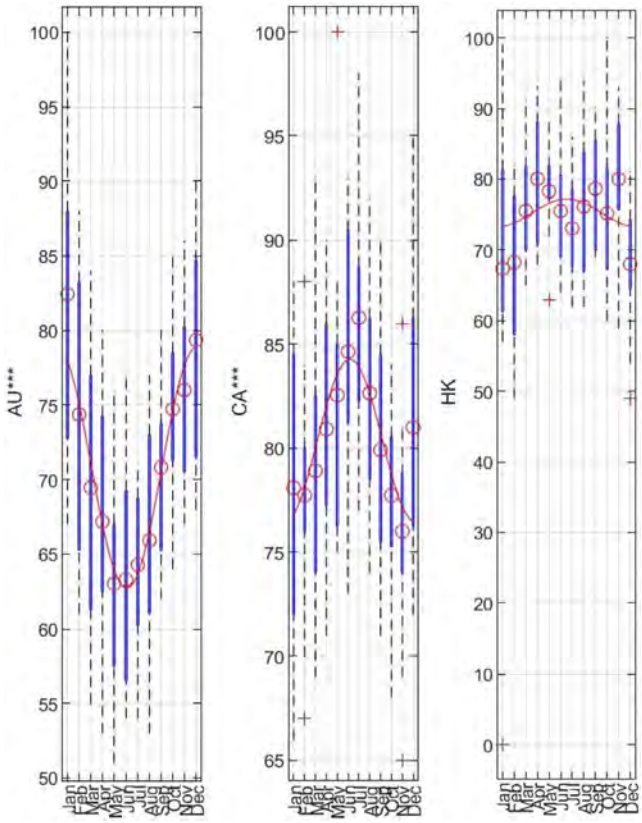


Figure 2 Typical monthly distribution of "gout" Google queries in Australia (AU), Canada (CA), and Hong Kong (HK). The presence of "***" indicates a statistically significant pattern in queries throughout the year (p_val<0.01).

known clinical patterns of gout flares. Using language-specific search terms further refined the detection of seasonal patterns, strengthening the findings.

Conclusion: Public interest in gout, as reflected by Google search behavior, follows a clear seasonal pattern, mirroring the clinical seasonality of gout flares. This study highlights the utility of infodemiology as a supplementary tool for understanding public behavior and informing health communication strategies. Accounting for linguistic nuances enhances the precision of seasonality analysis, offering valuable insights for public health initiatives to improve disease management and patient education.

Disclosure: N. Schlesinger: Amgen, 1, Arthrosi, 1, Olatec, 1, Protalix, 1, Scilex, 1, Shanton, 1, Sobi, 1; **I. Androulakis**: None.

Abstract Number: 1027

GLP-1 Receptor Agonists to Facilitate Weight Loss and Improve Disease Activity, Pain and Function in Patients With Rheumatic and Musculoskeletal Disease: Real-World Evidence From the Rheumatology Informatics System for Effectiveness (RISE) Registry

Nick McCormick[1], Jingyi Zhang[2], Emily Holladay[2], Fenglong Xie[3] and Jeffrey Curtis[4], [1]Auburn University, Auburn, AL, [2]University of Alabama at Birmingham, Birmingham, AL, [3]The University of Alabama at Birmingham, Birmingham, AL, [4]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Glucagon-like peptide-1 receptor agonists (GLP-1 RA) such as semaglutide (SEM; GLP-1) and tirzepatide (TIR; GIP/GLP-1), were initially approved for type 2 diabetes management but has seen increasing use for weight

Table 1. Baseline[a] Characteristics of New and Prevalent Users of Semaglutide[b] (SEM) or Tirzepatide[b] (TIR) for Weight Loss Treatment (WLT) in the Rheumatology Informatics System for Effectiveness (RISE) Registry (N = 60,206)

Characteristic	N (%)	SEM[b] 43,288 (71.9%)	TIR[b] 16,918 (28.1%)	Total 60,206 (100%)
Age, Mean (SD)	60,206 (100)	57.6 (12.2)	55.3 (11.7)	57.0 (12.1)
BMI at Index[c] Date, Mean (SD)	54,818 (91.1)	36.2 (7.9)	36.8 (8.1)	36.9 (7.9)
Sex, Female	60,198 (99.9)	34,370 (79.4)	14,074 (83.2)	48,444 (80.5)
Race	48,565 (80.7)			
White		27,805 (79.8)	11,230 (81.8)	39,035 (80.3)
Black		4,361 (12.5)	1,462 (10.6)	5,823 (12.0)
Other		2,670 (7.7)	1,037 (7.6)	3,707 (7.6)
Ethnicity, Hispanic	30,280 (50.3)	2,249 (10.4)	916 (10.6)	3,165 (10.5)
Region	59,471 (98.8)			
Midwest		7,949 (18.4)	2,986 (17.6)	10,935 (18.4)
Northeast		4,747 (11.0)	1,576 (9.3)	6,323 (10.6)
South		26,047 (60.2)	10,868 (64.2)	36,915 (62.1)
West		4,004 (9.2)	1,294 (7.6)	5,298 (8.9)
Index[c] Year	60,206 (100)			
Pre-2020		569 (1.3)	0 (0.0)	569 (0.9)
2020		2,906 (6.7)	129 (0.8)	3,035 (5.0)
2021		5,316 (12.3)	379 (2.2)	5,695 (9.5)
2022		9,159 (21.2)	3,267 (19.3)	12,426 (20.8)
2023		14,032 (32.4)	6,890 (40.7)	20,922 (34.8)
2024		8,479 (19.6)	6,004 (35.5)	14,483 (24.1)
Diabetes Diagnosis[d] at Baseline[a]	60,206 (100)	30,179 (69.7)	10,326 (61.0)	40,505 (67.3)
RMD Diagnosis	60,206 (100)			
Rheumatoid arthritis (RA)		8,666 (20.0)	3,795 (22.4)	12,461 (20.7)
Osteoarthritis (OA)		5,750 (13.3)	1,955 (11.6)	7,705 (12.8)
Psoriatic arthritis (PsA)		4,345 (10.0)	2,231 (13.2)	6,576 (10.9)
Sjögren's syndrome		3,022 (7.0)	1,207 (7.3)	3,022 (5.1)
Systemic Lupus Erythematosus (SLE)		1,388 (3.2)	618 (3.7)	2,006 (3.3)
Other RMD[e]		6,468 (14.9)	2,447 (14.5)	8,915 (14.8)
No definitive RMD		13,649 (31.5)	4,635 (27.4)	18,284 (30.4)
Patient Report Outcomes (PROs) at Baseline[a]				
RAPID-3 (0-30), mean (SD)	26,016 (43.2)	11.3 (6.5)	11.3 (6.5)	11.3 (6.5)
Pain (0-10), mean (SD)	20,010 (33.2)	4.6 (2.9)	4.5 (2.9)	4.6 (2.9)
MDHAQ (0-3), mean (SD)	13,920 (23.1)	0.6 (0.7)	0.6 (0.7)	0.6 (0.7)
RMD Medication Use at Baseline[a]	60,206 (100)			
Secukinumab		1,317 (3.0)	812 (4.8)	2,129 (3.5)
Ixekizumab		734 (1.7)	475 (2.8)	1,209 (2.0)
Any IL-17[f]		1,716 (4.0)	1,038 (6.1)	2,754 (4.6)
NSAID		15,006 (34.7)	6,382 (37.7)	21,388 (35.5)
Oral steroid		8,163 (18.9)	3,720 (22.0)	11,883 (19.7)
Opioid		6,801 (15.7)	2,637 (15.6)	9,438 (15.7)

RMD Diagnosis	All RISE RMD Patients 2,742,592 (100%)	SEM[g] Users N (%)	TIR[g] Users N (%)	Total WLT Users N (%)
Psoriatic arthritis (PsA)	117,965 (4.3)	5,802 (4.9)	2,459 (2.1)	7,585 (6.4)
Ankylosing spondylitis (AS)	46,189 (1.7)	1,645 (3.6)	644 (1.4)	2,289 (5.0)
Rheumatoid arthritis (RA)	390,449 (14.2)	11,316 (2.9)	4,162 (1.1)	14,326 (3.7)
Axial spondyloarthritis (AxSpA)	33,346 (1.2)	898 (2.7)	331 (1.0)	1,229 (3.7)
Systemic lupus erythematosus (SLE)	69,910 (2.5)	1,805 (2.6)	673 (1.0)	2,478 (3.5)
Other RMD[e]	835,208 (30.4)	16,095 (1.9)	4,698 (0.6)	20,793 (2.5)
No definitive RMD	1,249,703 (45.6)	9,754 (0.8)	3,463 (0.3)	13,217 (1.1)

Abbreviations: BMI, body mass index; RMD, Rheumatic and Musculoskeletal Diseases; WLT, weight loss treatment; RAPID-3, Routine Assessment of Patient Index Data 3; MDHAQ, Multi-Dimensional Health Assessment Questionnaire. a. Baseline is defined as any diagnosis, laboratory result, or medication exposure occurring on or before the index date. For new users (those with an evaluation and management [E/M] visit prior to GLP-1 initiation), the index date is the most recent E/M visit. For prevalent users (those without a prior E/M visit), the index date is the date of first GLP-1 prescription. b. Patients who use both semaglutide and tirzepatide are classified in the tirzepatide group. Among tirzepatide users, 24% also received semaglutide; among semaglutide users, 8.5% also received tirzepatide. c. For new users, the index date is the nearest prior E/M visit; for prevalent users, it is the date of first GLP-1 use (i.e., no prior E/M visit was found). d. A diagnosis (Dx) of diabetes at baseline is defined using an algorithm: presence of diabetes ICD-9 or ICD-10 codes OR antidiabetic medications (RxCUI-defined) OR hemoglobin A1c > 6.5% at any time, OR random glucose > 200 mg/dL at any time. e. Other RMD includes select inflammatory or musculoskeletal conditions not listed separately, such as fibromyalgia, ankylosing spondylitis, gout, myositis, vasculitis, psoriasis, juvenile idiopathic arthritis, and others and required 2+ diagnoses from a rheumatology provider. Patients without these diagnoses, or who only had a single diagnosis, were classified in the 'No definitive RMD' category. f. IL-17 use includes use of secukinumab, ixekizumab, or bimekizumab. Patients may have received more than one IL-17 inhibitor concurrently or sequentially. g. Patients who used both semaglutide and tirzepatide are included in both user groups. As a result, the semaglutide and tirzepatide user counts are not mutually exclusive and reflect any documented use, regardless of concurrent or sequential initiation.

Table 2. Baseline[a] Characteristics and Weight Change Among New Users of Semaglutide[b] (SEM) or Tirzepatide[b] (TIR), Stratified by Diabetes Status (N = 40,006)

Characteristic	N (%)	SEM[b] 27,535 (68.8%)		TIR[b] 12,471 (31.2%)		Total 40,006 (100%)
		Diabetes Dx[c] at Baseline[a]		Diabetes Dx[c] at Baseline[a]		
		Yes	No	Yes	No	
		16,164 (58.7)	11,371 (41.3)	7,812 (62.6)	4,659 (37.4)	
Age, Mean (SD)	40,006 (100)	60.4 (11.4)	54.9 (12.0)	57.7 (11.1)	53.1 (11.5)	57.5 (11.9)
Weight (lbs.) at Index[d] Date, Mean (SD)	34,666 (86.7)	224.6 (52.6)	224.8 (52.2)	230.1 (53.9)	226.1 (53.0)	225.0 (52.6)
% Weight (lbs.) Change[e], mean (SD)						
6 mo. ± 6 wks.	4112 (10.3)	-2.7 (6.2)	-3.3 (6.9)	-3.1 (7.6)	-4.4 (8.0)	-3.1 (6.9)
12 mo. ± 12 wks.	3,278 (8.2)	-4.3 (7.8)	-6.0 (9.2)	-5.9 (8.9)	-8.0 (11.3)	-5.3 (8.8)
18 mo. ± 18 wks.	2,254 (5.6)	-4.9 (8.9)	-6.0 (10.6)	-6.0 (16.5)	-7.0 (12.2)	-5.4 (10.8)
Sex, Female	40,006 (100)	12,242 (75.7)	9,885 (86.9)	6,285 (80.5)	4,114 (88.3)	32,526 (81.3)
RMD Diagnosis	40,006 (100)					
Rheumatoid arthritis (RA)		4,786 (29.5)	3,022 (26.6)	2,360 (30.2)	1,236 (26.5)	11,384 (28.5)
Osteoarthritis (OA)		2,303 (14.2)	1,431 (12.6)	946 (12.1)	549 (11.8)	5,229 (13.1)
Psoriatic arthritis (PsA)		2,369 (14.7)	1,451 (12.8)	1,324 (16.9)	728 (15.6)	5,872 (14.7)
Sjögren's syndrome		1,199 (7.4)	1,114 (9.8)	587 (7.5)	430 (9.2)	3,330 (8.3)
Systemic Lupus Erythematosus (SLE)		619 (3.8)	602 (5.3)	335 (4.3)	240 (5.2)	1,796 (4.5)
Other RMD[f]		2,683 (29.5)	1,673 (24.8)	1,191 (23.1)	717 15.4)	6,464 (16.2)
No definitive RMD		2,225 (13.8)	1,878 (16.5)	1,069 (13.7)	759 (16.3)	5,931 (14.8)
Patient Report Outcomes (PROs) at Baseline[a]						
RAPID-3 (0-30), mean (SD)	20,017 (50.0)	11.5 (6.6)	10.8 (6.3)	11.7 (6.6)	10.6 (6.4)	11.3 (6.5)
Pain (0-10), mean (SD)	15,809 (39.5)	4.7 (2.9)	4.5 (2.8)	4.6 (2.9)	4.2 (2.8)	4.6 (2.9)
MDHAQ (0-3), mean (SD)	11,152 (18.5)	0.6 (0.6)	0.6 (0.6)	0.6 (0.7)	0.6 (0.6)	0.6 (0.6)
RMD Medication Use at Baseline[a]	40,006 (100)					
Secukinumab		724 (4.5)	480 (4.2)	520 (6.7)	253 (5.4)	1,977 (4.9)
Ixekizumab		386 (2.4)	282 (2.5)	298 (3.8)	145 (3.1)	1,111 (2.8)
Any IL-17[g]		925 (5.7)	618 (5.4)	643 (8.2)	329 (7.1)	2,515 (6.3)
NSAID		7,171 (44.4)	5,081 (44.7)	3,550 (45.4)	2,093 (44.9)	17,895 (44.7)
Oral steroid		4,342 (26.9)	2,961 (26.0)	2,198 (28.1)	1,236 (26.5)	10,737 (26.8)
Opioid		3,715 (23.0)	1,941 (17.1)	1,679 (21.5)	685 (14.7)	8,020 (20.0)

Abbreviations: Dx, diagnosis; BMI, body mass index; mo., months; wks., weeks; lbs, pounds; RMD, Rheumatic and Musculoskeletal Diseases; RAPID-3, Routine Assessment of Patient Index Data 3; MDHAQ, Multi-Dimensional Health Assessment Questionnaire

a. Baseline is defined as any diagnosis, laboratory result, or medication exposure occurring on or before the index date. For new users (those with an evaluation and management [E/M] visit prior to GLP-1 initiation), the index date is the most recent E/M visit. b. Patients who use both semaglutide and tirzepatide are classified in the tirzepatide group. Among tirzepatide users, 24% also received semaglutide; among semaglutide users, 8.5% also received tirzepatide. c. A diagnosis of diabetes at baseline is defined using an algorithm: presence of diabetes ICD-9 or ICD-10 codes OR antidiabetic medications (RxCUI-defined) OR hemoglobin A1c > 6.5% at any time, OR random glucose > 200 mg/dL at any time. d. For new users, the index date is the nearest prior E/M visit. e. Weight and BMI change are defined as the difference between the baseline measurement (on or before the index date) and the follow-up measurement closest to the target window (6, 12, or 18 months). Follow-up ends at the last observed WLT record. Change is calculated as follow-up minus baseline. f. Other RMD includes select inflammatory or musculoskeletal conditions not listed separately, such as fibromyalgia, ankylosing spondylitis, gout, myositis, vasculitis, psoriasis, juvenile idiopathic arthritis, and others and required 2+ diagnoses from a rheumatology provider. Patients without these diagnoses, or who only had a single diagnosis, were classified in the 'No definitive RMD' category. g. IL-17 use includes use of secukinumab, ixekizumab, or bimekizumab. Patients may have received more than one IL-17 inhibitor concurrently or sequentially.

loss treatment (WLT). Given the potential for weight loss to improve disease activity, function, and patient-reported outcomes (PROs) in rheumatic and musculoskeletal diseases (RMDs), understanding GLP-1 use patterns and effects is crucial.

Methods: We conducted a retrospective analysis using Q3 2024 (1/05–9/24) data from the ACR Rheumatology Informatics System for Effectiveness (RISE) registry, among RMD patients treated with SEM or TIR. Patients were categorized as new users (with ≥1 evaluation and management [E/M] visit prior to GLP-1 initiation) or prevalent users (without a prior E/M visit). Baseline included data on or before the index date. We examined baseline characteristics, RMD diagnoses, concurrent medications, and weight changes at 6, 12, and 18 months, stratified by GLP-1 type and diabetes. GLP-1 exposure was characterized as intent-to-treat (ITT). Multivariable linear regression assessed 12-month weight loss by GLP-1 type, adjusted for baseline weight, age, sex, and diabetes.

Results: Among 60,206 RMD patients treated with SEM or TIR, 67% had diabetes and 70% used SEM. Uptake was highest among patients with RA (20.7%) and OA (12.8%), with SEM more common in both. The most rapid increase occurred in 2023, accounting for 32% of all SEM and 41% of TIR use. Patients' mean (SD) baseline BMI was 36.3 (7.9), and ~20% were on oral glucocorticoids. Across all RMD cohorts, the highest proportion of WLT use was observed in PsA patients (6.4% of all RISE PsA patients, n=117,965), followed by AS (5.0%) and RA (3.7%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Association Between GLP-1 Receptor Agonist Type and Percent Weight Loss After 12-Months in New Users

	Unadjusted			Adjusted for Demographics			Adjusted for Diabetes Diagnosis		
Characteristic	**β**	**95% CI**	**p-value**	**β**	**95% CI**	**p-value**	**β**	**95% CI**	**p-value**
GLP-1 Receptor Agonist Type									
Tirzepatide[b,c]	1.8	(1.1, 2.5)	**<0.001*** **	1.6	(0.96, 2.3)	**<0.001*** **	1.7	(0.98, 2.4)	**<0.001*** **
Baseline[a] Weight (lbs.)	0.08	(0.03, 0.14)	**0.005****	0.11	(0.05, 0.17)	**<0.001*** **	0.11	(0.05, 0.17)	**<0.001*** **
Age				-0.02	(-0.05, 0.01)	0.11	-0.01	(-0.04, 0.02)	0.5
Sex									
Male[d]				-2.1	(-2.9, -1.3)	**<0.001*** **	-2.0	(-2.8, -1.1)	**<0.001*** **
Diabetes Diagnosis[e]									
No[f]							1.5	(0.91, 2.2)	**<0.001*** **

Abbreviations: CI, confidence interval; lbs., pounds
** Significant at p ≤ .01; *** Significant at p ≤ .001
a. Baseline is defined as any diagnosis, laboratory result, or medication exposure occurring on or before the index date. For new users (those with an evaluation and management [E/M] visit prior to GLP-1 initiation), the index date is the most recent E/M visit. For prevalent users (those without a prior E/M visit), the index date is the date of first GLP-1 prescription. b. Patients who use both semaglutide and tirzepatide are classified in the tirzepatide group. Among tirzepatide users, 24% also received semaglutide; among semaglutide users, 8.5% also received tirzepatide. c. Reference group is semaglutide users. d. Reference group is female. e. A diagnosis of diabetes at baseline is defined using an algorithm: presence of diabetes ICD-9 or ICD-10 codes OR antidiabetic medications (RxCUI-defined) OR hemoglobin A1c > 6.5% at any time, OR random glucose > 200 mg/dL at any time. f. Reference group is yes.

Weight trajectories were evaluated among 40,006 new users of SEM or TIR. At baseline, PROs were similar across GLP-1 RA types, but diabetic users had greater disease burden, with higher RAPID-3 (mean 11.6 [SD 6.6] vs. 10.7 [SD 6.3]) and MDHAQ scores (mean 4.7 [SD 2.9] vs. 4.4 [SD 2.8]) than non-diabetic users. At 12 months, non-diabetic TIR users lost 8.0% (SD 11.3) of body weight, compared to 6.0% (SD 9.2) with SEM. Diabetic users showed a similar pattern, with TIR consistently outperforming SEM. Across GLP-1 RA types, non-diabetic users lost more weight than diabetic users. Weight loss plateaued after 12 months, with 1.0% weight regain in non-diabetic TIR users by 18 months. In models adjusting for baseline weight, age, sex, and diabetes, TIR users lost approximately 1.7% ($p< 0.001$) more weight at 12 months than SEM users. Patients without diabetes lost about 1.5% ($p< 0.001$) more weight than those with diabetes, regardless of GLP-1 RA type. No significant interactions were observed among models' variables.

Conclusion: In this national registry of RMD patients, SEM and TIR were increasingly used and effective weight loss treatments for individuals with and without diabetes. Across both GLP-1 RAs, non-diabetic users lost more weight than diabetic users, with TIR showing greater reductions than SEM over time. Ongoing work evaluates the impact of GLP-1 therapy on disease activity, function, and PROs in RMD populations.

Disclosure: N. McCormick: None; **J. Zhang**: None; **E. Holladay**: None; **F. Xie**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 1028

Enhanced Assessment of Psoriatic Arthritis Disease Progression Using cDAPSA plus the Contrast of Patient Reported Pain and Global Assessment versus Joint Counts

Ning Meng[1], Scott Zeger[2], John Miller[1], Uzma Haque[3], Thomas Grader-Beck[4], Laura Hummers[5], Clifton Bingham[1], Ami Shah[5], Ana-Maria Orbai[6] and Ji Soo Kim[7], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins Biostatistics, Baltimore, MD, [3]Johns Hopkins School of Medicine, Baltimore, MD, [4]Johns Hopkins, Reisterstown, MD, [5]Johns Hopkins Rheumatology, Baltimore, MD, [6]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [7]Johns Hopkins, Baltimore, MD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The clinical Disease Activity in Psoriatic Arthritis (cDAPSA) score is widely used to assess PsA disease activity and its trajectory. cDAPSA sums four measures: 2 patient-reported outcomes (PROs), pain and patient global visual analog scales, and 66 swollen/68 tender joint counts (66SJC, 68TJC) into a single score despite their different scales. It therefore may obscure clinically important patterns, especially when inflammation and symptoms are discordant. To address this, we (1) analyzed the contributions of individual cDAPSA components, (2) developed a two-score measure (cDAPSA2), and (3) evaluated its utility in predicting patient outcomes.

Methods: To perform Principal Components Analysis (PCA), we obtained cDAPSA-adjusted residuals for pain, patient global, 66SJC, and 68TJC at baseline. These residuals were generated by regressing each variable on a smooth function of cDAPSA to account for nonlinear associations; they collectively represent available information about the patient's disease state and trajectory over and above what is described by cDAPSA. PCA was then applied to the residuals to find a single measure (the dominant principal component) that explains the largest fraction of remaining variation. To assess whether this first PC can risk-stratify patients, we modeled longitudinal cDAPSA trajectories using linear mixed-effects models with a smooth function of time for each quartile of the 1st PC, adjusting for age, sex, race, BMI. We further fit a Cox proportional hazard model to study the associations between PC quartiles and time to remission (cDAPSA $\leq$ 4), adjusting for age, sex, BMI, and baseline cDAPSA.

Results: Among 752 PsA patients fulfilling the PsA CASPAR classification (median age 52.8 years; BMI 29.4 kg/m^2; follow-up 2.0 years), PCA identified what we call the PROs-Joint Contrast (PJC), that is, approximately the mean PRO scores minus the mean joint count scores. For a given cDAPSA level, PJC measures whether most of the cDAPSA is due to the PRO components or to the joint counts. PJC accounts for 49.5% of the residual variance beyond what can be described by cDAPSA itself (Table 1). All PROMIS Profile measures, enthesitis, and sex significantly differed across the PJC quartiles (Table 2).

Longitudinal analysis showed the 1st and 4th quartiles of the PJC start at the same level, higher than Q2/Q3 and that Q1 has a steeper decline while Q4 remains at higher levels over a 5-year follow-up (Figure 1). Remission rates were statistically significantly associated with PJC, (HR per 1 SD: 0.88; 95% CI: 0.77–0.99). The 4th quartile had a significantly lower remission rate than the 1st quartile (HR: 0.49; 95% CI: 0.27–0.88).

Conclusion: Based on these findings, we propose cDAPSA2 as a two-score measure combining traditional cDAPSA with PJC. For example, patients with high cDAPSA and low PJC may benefit from escalating DMARDs targeting inflammation,

Table 1. Loadings of Principal Component Analysis for Symptom Measures in Psoriatic Arthritis

	PJC	STC	PGC
Pain	0.60	-0.05	-0.70
Patient Global	0.60	-0.01	0.71
Swollen Joint Count	-0.33	0.74	-0.01
Tender Joint Count	-0.42	-0.67	0.02
Standard Deviation	1.41	1.20	0.77
Variance Explained (%)	49	36	15

* PRO: patient reported outcome; PJC: PROs and joints contrast; STC: swollen and tender contrast; PGC: pain and global contrast

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

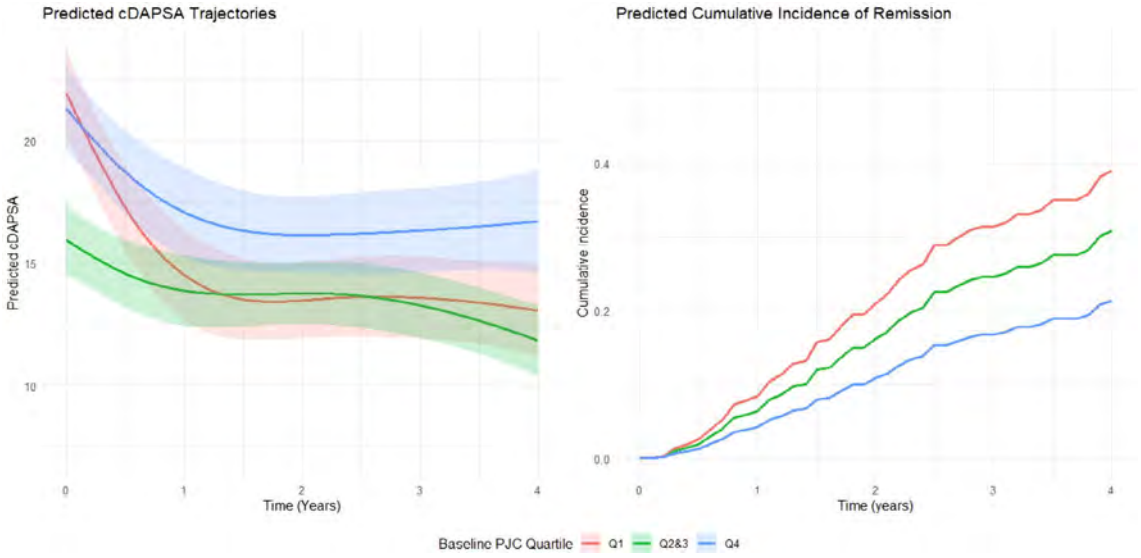
Table 2. Baseline Characteristics of patients with PsA

Patient Characteristic [Median (IQI) or Number (%)]	N	Overall	PJC quartiles				p-value
			Q1 (-5.92 to -0.80)	Q2 (-0.80 to 0.07)	Q3 (0.07 to 0.89)	Q4 (0.89 to 3.79)	
Swollen joint count at baseline, 0-66	752	2.0 (0.0, 5.0)	5.0 (3.0, 7.0)	2.0 (1.0, 4.0)	1.0 (0.0, 4.0)	1.0 (0.0, 4.0)	<0.001
Tender joint count at baseline, 0-68	752	2.0 (0.0, 8.0)	6.0 (3.0, 11.0)	2.0 (0.0, 4.0)	1.0 (0.0, 5.0)	1.0 (0.0, 7.0)	<0.001
Pain NRS Score at baseline, 0-10	752	4.0 (2.0, 7.0)	3.0 (2.0, 5.0)	3.0 (1.0, 5.0)	4.0 (2.0, 7.0)	7.0 (6.0, 8.0)	<0.001
Patient Global NRS Score at baseline, 0-10	752	5.0 (3.0, 7.0)	4.0 (2.0, 5.0)	4.0 (1.0, 5.0)	5.0 (2.0, 7.0)	8.0 (6.0, 9.0)	<0.001
cDAPSA Score, 0-154	752	13.0 (8.0, 24.0)	19.0 (12.0, 27.0)	10.0 (4.0, 18.0)	12.0 (5.0, 24.0)	17.5 (12.0, 25.5)	<0.001
BMI at baseline, kg/m²	693	29.4 (26.0, 34.5)	29.1 (25.1, 34.4)	29.7 (26.3, 33.1)	29.3 (25.6, 35.4)	29.5 (26.6, 35.7)	0.36
Sex	752						0.003
Female		445 (59%)	129 (69%)	100 (53%)	99 (53%)	117 (62%)	
Male		307 (41%)	59 (31%)	88 (47%)	89 (47%)	71 (38%)	
Race	752						0.07
Asian		35 (4.7%)	10 (5.3%)	11 (5.9%)	8 (4.3%)	6 (3.2%)	
Black		50 (6.6%)	11 (5.9%)	6 (3.2%)	12 (6.4%)	21 (11%)	
Other/Unknown		49 (6.5%)	12 (6.4%)	9 (4.8%)	10 (5.3%)	18 (9.6%)	
White		618 (82%)	155 (82%)	162 (86%)	158 (84%)	143 (76%)	
Ethnicity	752						0.005
Hispanic/Latino		33 (4.4%)	13 (6.9%)	2 (1.1%)	5 (2.7%)	13 (6.9%)	
Age at baseline, years	752	52.8 (41.7, 62.8)	54.9 (43.1, 65.9)	53.3 (41.6, 61.3)	51.7 (41.9, 61.4)	52.2 (40.0, 61.7)	0.1
Disease duration since PsA diagnosis, years	554	3.8 (1.1, 10.2)	3.3 (0.8, 10.1)	4.0 (1.1, 11.8)	4.1 (1.5, 10.5)	3.9 (1.0, 7.9)	0.72
Dactylitis (ever)	662	199 (30%)	52 (31%)	59 (35%)	47 (29%)	41 (25%)	0.32
Enthesitis (ever)	679	376 (55%)	96 (54%)	75 (45%)	101 (60%)	104 (62%)	0.01
Scalp psoriasis (ever)	752	485 (64%)	136 (72%)	116 (62%)	117 (62%)	116 (62%)	0.08
PROMIS score							
Anxiety	559	56.0 (49.0, 62.0)	54.0 (43.0, 60.0)	51.0 (46.0, 58.0)	56.0 (50.0, 62.0)	60.0 (54.0, 65.0)	<0.001
Social participation	563	48.0 (42.0, 53.0)	50.0 (44.0, 56.0)	51.0 (44.0, 60.0)	46.0 (40.0, 53.0)	44.0 (37.0, 48.0)	<0.001
Sleep disturbance	554	54.0 (46.0, 58.0)	52.0 (46.0, 57.5)	49.5 (44.0, 54.0)	54.0 (46.0, 58.0)	56.5 (52.0, 63.0)	<0.001
Physical function	552	43.0 (37.5, 48.0)	44.0 (39.0, 49.0)	46.0 (40.0, 53.0)	43.0 (36.0, 49.0)	39.0 (35.0, 44.0)	<0.001
Depression	547	50.0 (44.0, 57.0)	49.5 (41.0, 56.0)	50.0 (42.0, 53.0)	50.0 (44.0, 57.0)	55.0 (48.0, 59.0)	<0.001
Fatigue	550	57.0 (48.0, 64.0)	55.0 (48.0, 62.0)	52.0 (45.0, 61.0)	57.0 (48.0, 64.0)	61.5 (56.0, 67.0)	<0.001
Pain	553	59.0 (53.0, 64.0)	56.0 (52.0, 62.0)	56.0 (50.0, 62.0)	59.0 (53.0, 64.0)	64.0 (60.0, 67.0)	<0.001
Psoriasis location (ever, not mutually exclusive)							
Lower extremities	752	332 (44%)	88 (47%)	71 (38%)	84 (45%)	89 (47%)	0.21
Torso	752	159 (21%)	48 (26%)	42 (22%)	38 (20%)	31 (16%)	0.18
Upper extremities	752	234 (31%)	65 (35%)	60 (32%)	53 (28%)	56 (30%)	0.58
Plantar	752	57 (7.6%)	14 (7.4%)	8 (4.3%)	14 (7.4%)	21 (11%)	0.09
Palmar	752	55 (7.3%)	12 (6.4%)	9 (4.8%)	18 (9.6%)	16 (8.5%)	0.28
Intergluteal cleft/Perianal	752	106 (14%)	30 (16%)	29 (15%)	23 (12%)	24 (13%)	0.66
Abdomen	752	102 (13%)	31 (16%)	30 (16%)	19 (10%)	22 (12%)	0.19
Elbows	752	299 (40%)	74 (39%)	74 (39%)	70 (37%)	81 (43%)	0.72
Knees	752	168 (22%)	45 (24%)	37 (20%)	40 (21%)	46 (24%)	0.65
Genital	752	16 (2.1%)	2 (1.1%)	6 (3.2%)	5 (2.7%)	3 (1.6%)	0.53
Torso/Abdomen	752	34 (4.5%)	9 (4.8%)	6 (3.2%)	10 (5.3%)	9 (4.8%)	0.78
Psoriasis type (ever, not mutually exclusive)							
Plaque	752	658 (88%)	167 (89%)	164 (87%)	161 (86%)	166 (88%)	0.81
Inverse	752	152 (20%)	49 (26%)	39 (21%)	34 (18%)	30 (16%)	0.09
Guttate	752	39 (5.2%)	12 (6.4%)	13 (6.9%)	7 (3.7%)	7 (3.7%)	0.36
Pustular	752	29 (3.9%)	12 (6.4%)	1 (0.5%)	7 (3.7%)	9 (4.8%)	0.01
Erythrodermic	752	7 (0.9%)	1 (0.5%)	2 (1.1%)	1 (0.5%)	3 (1.6%)	0.84
Treatment							
TNF inhibitor	730	223 (31%)	50 (27%)	66 (36%)	61 (33%)	46 (25%)	0.08
PDE4 inhibitor	730	106 (15%)	27 (15%)	26 (14%)	23 (13%)	30 (16%)	0.78
csDMARD	730	292 (40%)	79 (43%)	71 (39%)	66 (36%)	76 (42%)	0.52
IL-12/23 inhibitor	730	62 (8.5%)	20 (11%)	12 (6.6%)	15 (8.2%)	15 (8.2%)	0.53
IL-17 inhibitor	730	181 (25%)	43 (23%)	45 (25%)	42 (23%)	51 (28%)	0.68
IL-23 inhibitor	730	62 (8.5%)	18 (9.8%)	9 (4.9%)	16 (8.7%)	19 (10%)	0.2
JAK inhibitor	730	26 (3.6%)	8 (4.4%)	5 (2.7%)	10 (5.5%)	3 (1.6%)	0.21
CTLA4 inhibitor	730	10 (1.4%)	4 (2.2%)	3 (1.6%)	2 (1.1%)	1 (0.5%)	0.67
Anti-CD20 monoclonal antibody	730	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	1 (0.5%)	0.5
TYK2 inhibitor	730	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA
IL-36Rs inhibitor	730	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA
Comorbidities, ever							
Thyroid disease	752	56 (7.4%)	16 (8.5%)	13 (6.9%)	17 (9.0%)	10 (5.3%)	0.51
Coronary artery disease	752	45 (6.0%)	11 (5.9%)	14 (7.4%)	10 (5.3%)	10 (5.3%)	0.81
Diabetes	752	74 (9.8%)	19 (10%)	20 (11%)	16 (8.5%)	19 (10%)	0.91
Osteoporosis	752	15 (2.0%)	6 (3.2%)	5 (2.7%)	3 (1.6%)	1 (0.5%)	0.24
Fatty liver disease	752	47 (6.3%)	12 (6.4%)	8 (4.3%)	11 (5.9%)	16 (8.5%)	0.43
Obesity	752	240 (32%)	54 (29%)	58 (31%)	62 (33%)	66 (35%)	0.59
Hyperlipidemia	752	90 (12%)	25 (13%)	29 (15%)	23 (12%)	13 (6.9%)	0.06
Stroke	752	9 (1.2%)	3 (1.6%)	4 (2.1%)	1 (0.5%)	1 (0.5%)	0.48
Hearing loss	752	11 (1.5%)	1 (0.5%)	3 (1.6%)	5 (2.7%)	2 (1.1%)	0.44
Vitiligo	752	5 (0.7%)	0 (0%)	0 (0%)	2 (1.1%)	3 (1.6%)	0.18
Inflammatory bowel disease	685	25 (3.6%)	4 (2.2%)	12 (7.1%)	4 (2.3%)	5 (3.0%)	0.08
Inflammatory eye disease	687	5 (0.7%)	1 (0.6%)	4 (2.3%)	7 (4.1%)	5 (3.0%)	0.15

* NRS: numeric rating scale ; BMI: body mass index; IQI: interquartile interval ** Percentage may not add up to 100% due to rounding. *** The Kruskal–Wallis test and Fisher's exact test were used to compare differences across quartiles for continuous and categorical variables, respectively, due to non-normality of the data.

while those with similar cDAPSA and high PJC may require symptom-focused management and additional diagnostics before altering DMARD therapy. cDAPSA2 captures both overall severity and underlying heterogeneity of PsA, supporting a more nuanced assessment of PsA activity and individualized treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: N. Meng: None; **S. Zeger**: None; **J. Miller**: None; **U. Haque**: None; **T. Grader-Beck**: Argenx, 5, 12, Consulting fees, Bristol-Myers Squibb(BMS), 5, 12, Consulting fees, Novartis, 5, 12, Consulting fees; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(-GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **A. Shah**: None; **A. Orbai**: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB, 2; **J. Kim**: None.

Abstract Number: 1029

Cervical cancer screening rates in Korean women of childbearing age with systemic lupus erythematosus

PIL GYU PARK[1], Jisoo Lee[2], JIN SU PARK[3], Hyunsun Lim[3], In-Woon Baek[4], Min Kyung Chung[4] and Chan Hee Lee[5], [1]National Health Insurance Service Ilsan Hospital, Seodaemun-gu, Seoul, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, Ewha Womans University College of Medicine, SEOUL, Republic of Korea, [3]National Health Insurance Service Ilsan Hospital, Goyang-si, Republic of Korea, [4]Ewha Womans University College of Medicine, Seoul, Republic of Korea, [5]Desert Regional Medical Center, Palm Springs, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cervical cancer remains a leading cause of death among women of childbearing age despite the proven efficacy of screening in reducing mortality rates. Women with systemic lupus erythematosus (SLE) are at a higher risk for cervical cancer but tend to have lower screening rates. This study aimed to assess Papanicolaou (Pap) test uptake and identify factors influencing participation in cervical cancer screening among women of childbearing age with SLE.

Methods: Women aged 20-49 with SLE and age matched controls, randomly selected at a 1:5 ratio, were identified from the 2016-2017 National Health Insurance Service-National Health Information Database (NHIS-NHID). Data from 10,981 women with SLE and 54,905 controls eligible for national cervical cancer screening in 2018-2019 were analyzed. Pap test

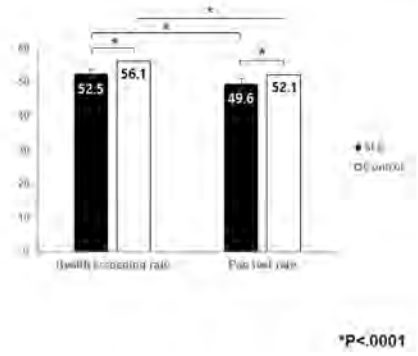
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

rates were calculated, and logistic regression was used to estimate odds ratios (ORs) for factors associated with Pap test uptake.

Results: The Pap test uptake rate was significantly lower in women with SLE compared to controls (49.6% vs. 52.1%, $P <$ .0001). Logistic regression revealed that younger age, lower income, self-employment or medical aid insurance, and rural residence were associated with reduced screening rates in both groups. The highest screening uptake occurred in the 40-44 age group for both women with SLE (OR 5.09, 95% CI 4.17-6.22) and controls (OR 4.65, 95% CI 4.26-5.07). Comorbidities increased screening uptake among controls (OR 1.18, 95% CI 1.13-1.23), but were associated with mild non-significant decrease in uptake among women with SLE (OR 0.96, 95% CI 0.87-1.04).

Conclusion: Cervical cancer screening is often underutilized by women of childbearing age with SLE, particularly those with comorbid conditions. Targeted interventions are needed to improve screening rates and address the unique challenges faced by this high-risk population.

Figure 1. NHIS health screening and cervical cancer screening participation rates in 2018-2019 among women with of childbearing age with SLE compared with the controls.



*P value < .0001 SLE, systemic lupus erythematosus; Pap, Papanicolaou.

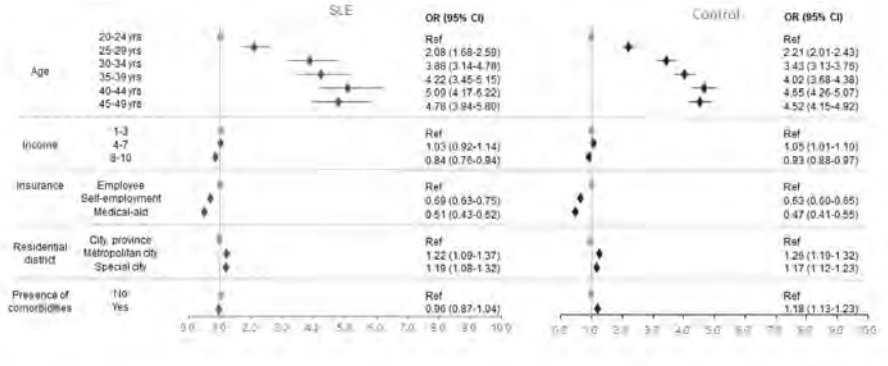


Figure 2. Factors associated with NHIS cervical cancer screening participation rates in 2018-2019 among women with of childbearing age with SLE compared with the controls

OR, odds ratio; CI, confidence interval.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	SLE			Control		
	PAP test		*P* value	PAP test		*P* value
	Yes (n=5,445)	No (n=5,536)		Yes (n=28,608)	No (n=26,297)	
Age, years			< .001			< .001
20-24	151 (2.8)	570 (10.3)		836 (2.9)	2,746 (10.4)	
25-29	407 (7.5)	724 (13.1)		2,297 (8.0)	3,354 (12.8)	
30-34	699 (12.8)	675 (12.2)		3,517 (12.7)	3337 (12.3)	
35-39	1,117 (20.5)	1017 (18.4)		5,827 (18.3)	4805 (20.4)	
40-44	1,223 (22.5)	962 (17.4)		6,314 (17.4)	4575 (22.1)	
45-49	1,884 (33.9)	1588 (28.7)		9,817 (28.4)	7480 (34.3)	
Mean ± SD	40.1 ± 7.4	37.6 ± 8.8	< .001	40.1 ± 7.5	37.5 ± 8.8	< .001
Income level†, segment			0.002			0.002
1-3	1,568 (28.8)	1,630 (29.4)		7,608 (26.6)	7,070 (26.9)	< .001
4-7	1,937 (35.6)	1,812 (32.7)		10,864 (38.0)	9,926 (36.6)	
8-10	1,804 (33.1)	1,908 (34.5)		9,390 (32.8)	8,952 (34.0)	
Medical Insurance			< .001			
Employee	4,051 (74.4)	3,650 (67.1)		21,953 (76.8)	17,954 (68.7)	< .001
Self-employed	1,140 (20.9)	1,417 (26.0)		6,325 (22.1)	7,683 (29.4)	
Medical-aid	254 (4.7)	377 (6.9)		325 (1.1)	514 (2.0)	
Residential district						
City, province	543 (22.5)	534 (26.1)	0.01	5,780 (22.0)	5,394 (18.9)	< .001
Metropolitan city	663 (26.21)	472 (23.1)		6,467 (24.6)	7,618 (26.6)	
Special city	1,239 (51.3)	1,037 (50.8)		14,050 (53.4)	15,596 (54.5)	
Comorbidities‡						
Any§	3,961 (72.8)	4,090 (73.9)	0.179	6,130 (21.4)	4,515 (17.2)	< .001
Hypertension	1,809 (33.2)	2,136 (38.6)	< .001	1,385 (4.8)	1,212 (4.6)	0.2
DM	569 (10.5)	647 (11.7)	0.039	1,401 (4.9)	1,053 (4.0)	< .001
Hyperlipidemia	3,169 (58.2)	3,203 (57.9)	0.716	4,582 (16.0)	3,231 (12.3)	< .001
Cancer	418 (7.7)	436 (7.9)	0.697	1,080 (3.8)	864 (3.3)	0.002

Differences in baseline characteristics based on cervical cancer screening participation Categorial values are provided as n (%). Variables were obtained from the 2018 National Health Insurance-National Health Information (NHIS-NHID) database. The age was determined as of January 1, 2018. *SLE and control groups were age- and sex-matched. †Income levels were determined according to the decile method (8-10 refers to the low-income group) ‡Comorbidities were identified with the diagnostic code based on the International Classification of Diseases 10th revision (ICD-10) in the NHIS-NHID database 2016-2017. SLE, systemic lupus erythematosus; DM, diabetes mellitus; Pap, Papanicolaou. § Having at least one of the comorbidities, including hypertension, DM, hyperlipidemia, cancer

Disclosure: P. PARK: None; **J. Lee**: Samsung Bioepis, 5; **J. PARK**: None; **H. Lim**: None; **I. Baek**: None; **M. Chung**: None; **C. Lee**: None.

Abstract Number: 1030

Predictors of Incident Atrial Fibrillation in Rheumatoid Arthritis Patients: A Population Based Cohort Study

Sarah Pimple[1], Alanna Chamberlain[1], Sara Achenbach[2], Cynthia Crowson[3] and Elena myasoedova[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, [3]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1007–1037) Epidemiology & Public Health Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid arthritis (RA) has been associated with an increased risk of developing atrial fibrillation (AF). However, recent data on trends in incidence of AF and risk factors associated with AF in RA from population-based cohorts are lacking. This study seeks to assess the risk of AF in patients with RA compared to the general population and identify predictors of AF in patients with RA.

Methods: Retrospective medical records review was completed to form an inception cohort of all patients with RA in 1990-2019, among residents of a geographically defined area, aged ≥18 years. The incidence date of RA was defined as the earliest date at which the patient fulfilled the 1987 or 2010 classification criteria for RA. Each patient with RA was matched on age, sex, year, and county to a randomly selected comparator without RA (using the date of RA as the index date for the matched referent without RA). Patients were followed until diagnosis of new-onset AF, death, migration, or 12/31/2023. AF was defined using a previously published electronic algorithm. Descriptive statistics and Cox models adjusted for age, sex, and calendar year of RA incidence were conducted.

Results: 3798 patients were included, with 1899 patients with RA and 1899 patients without RA (mean age 55.9 years, 68% female). RA status was not found to be a significant risk factor to predict AF (adjusted for age, sex, calendar year, smoking status, and obesity) (HR 1.10; 95% CI 0.92-1.33). Among patients with RA, significant risk factors associated with incident AF included age (HR:2.29 per 10 year increase; 95%CI:2.05-2.56), male sex (HR:1.57; 95%CI:1.22-2.03), former smoking (HR:1.35; 95%CI:1.01-1.81), current smoking (HR:2.16, 95%CI:1.51-3.09), obesity (HR:1.83, 95%CI:1.42-2.37), diabetes (HR:1.54, 95%CI:1.09-2.17), and hypertension (HR:1.60, 95%CI:1.20-2.13). Additionally, for patients with RA the following disease characteristics were associated with increased risk of AF: radiographic joint erosions or destructive changes (HR 1.36; 95% CI 1.03-1.79), rheumatoid nodules (HR 1.70; 95% CI 1.19-2.43), large joint swelling (HR 1.35; 95% CI 1.04-1.76), and severe extra-articular manifestations (HR 2.03; 95% CI 1.31-3.14).

Conclusion: While RA was not a risk factor for AF, adverse cardiovascular risk profile and RA disease severity significantly increased the risk of AF among patients with RA. Future studies will inform to what extent early recognition and management of these risk factors can help improve AF outcomes in RA.

Disclosure: S. Pimple: None; **A. Chamberlain**: None; **S. Achenbach**: None; **C. Crowson**: None; **E. myasoedova**: None.

Abstract Number: 1031

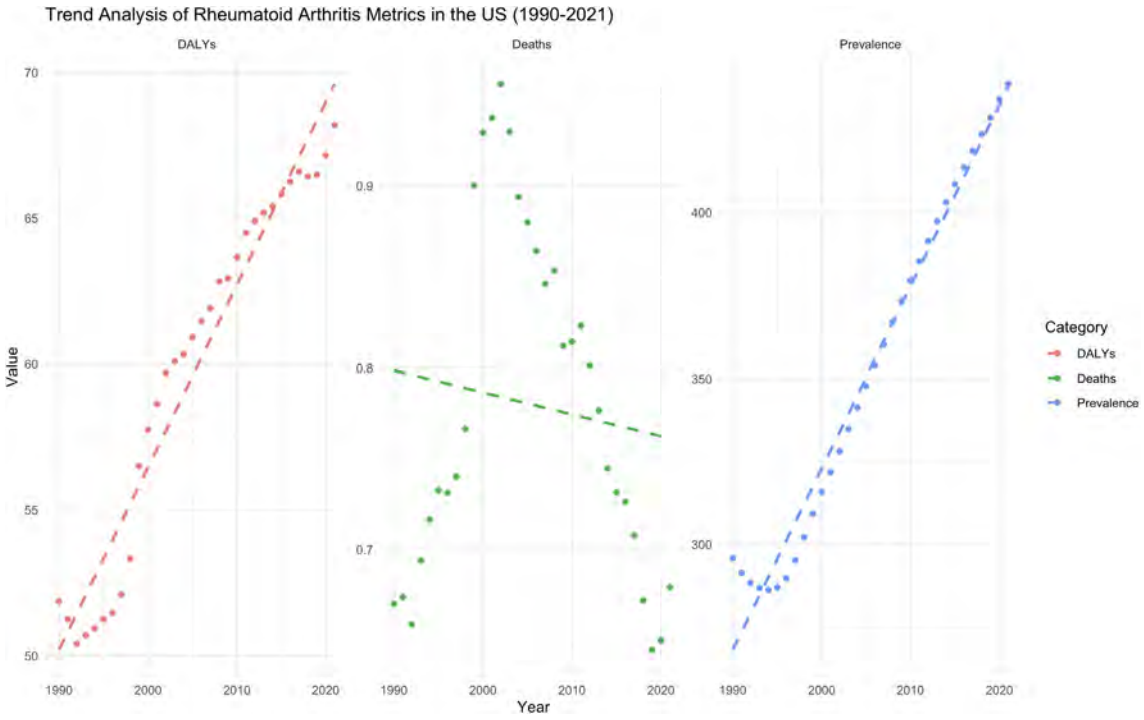
Trends and Gender Disparities in Rheumatoid Arthritis Burden in the United States: A Population-Based Time-Trend Analysis Using the Global Burden of Disease Database, 1990–2021

Satani Sharkas[1], Dina Murad[2] and Dariush Jahandideh[3], [1]Boston Medical Center - Brighton, Brighton, MA, [2]Tufts Medical Center, Boston, MA, [3]Boston Medical Center - Brighton, Boston

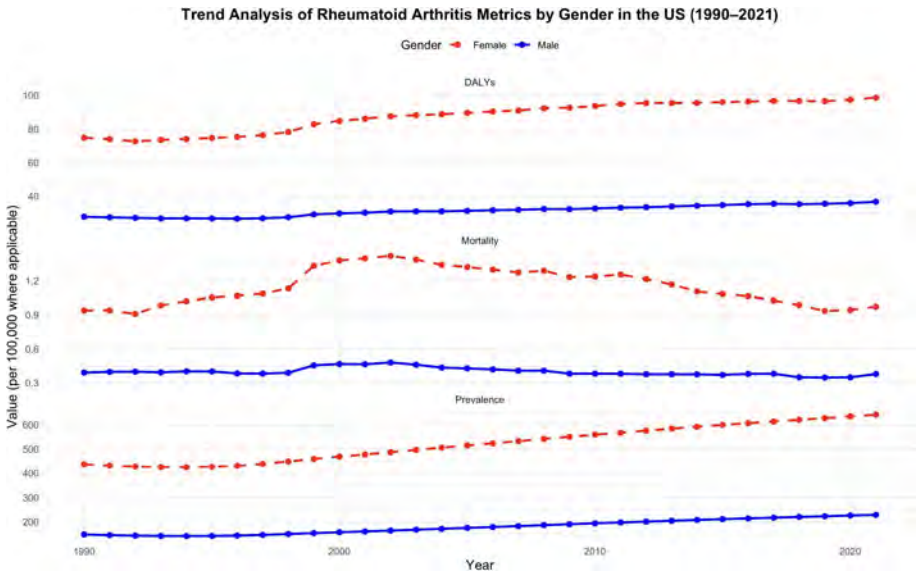
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a growing public health concern in the United States, with increasing prevalence and disease burden over recent decades. This study evaluates national time trends in RA prevalence, mortality, and Disability-Adjusted Life Years (DALYs) from 1990 to 2021, with a focus on gender-specific differences.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Temporal Trends in RA Prevalence, DALYs, and Mortality in the US (1990–2021) Line plots with scatter points showing annual values for RA prevalence (per 100,000), DALYs (per 100,000), and mortality (per 100,000) from 1990 to 2021. Each metric is displayed in a separate panel, highlighting the upward trends in prevalence and DALYs, and the stable mortality trend.



Gender Disparities in RA Prevalence, DALYs, and Mortality in the US (1990–2021) Faceted line plots with scatter points comparing RA metrics between males (blue solid lines) and females (red dashed lines) from 1990 to 2021. Panels for prevalence, DALYs, and mortality illustrate the steeper increases in prevalence and DALYs for females, alongside a slight decline in male mortality and stable female mortality.

Methods: Data were extracted from the Global Burden of Disease (GBD) 2021 database. Linear regression models were used to assess time trends in RA-related prevalence, mortality, and DALYs per 100,000 population, with the year as the independent variable. Analyses were stratified by gender, and trends were evaluated using slope estimates, 95% confidence intervals (CIs), p-values, and R-squared (R^2) values.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Nationally, RA prevalence increased significantly from 286.2 to 438.8 per 100,000 between 1990 and 2021 (slope = 5.5/year, 95% CI: 5.0–6.0, $p < 0.0001$, $R^2 = 0.98$). DALYs rose from 50.4 to 68.2 per 100,000 (slope = 0.6/year, 95% CI: 0.5–0.7, $p < 0.0001$, $R^2 = 0.94$). Mortality remained stable (0.67 to 0.68 per 100,000; slope = -0.001/year, 95% CI: -0.005 to 0.003, $p = 0.52$, $R^2 = 0.01$). Stratified analysis revealed that females bore a higher RA burden. Female prevalence rose from 436.8 to 641.5 per 100,000 (slope = 7.8/year, 95% CI: 7.4–8.2, $p < 0.0001$, $R^2 = 0.98$), compared to males (148.3 to 229.0; slope = 3.1/year, 95% CI: 2.9–3.3, $p < 0.0001$, $R^2 = 0.97$). DALYs for females increased from 74.8 to 98.6 per 100,000 (slope = 0.9/year, 95% CI: 0.8–1.0, $p < 0.0001$), while males increased from 27.8 to 36.7 (slope = 0.3/year, 95% CI: 0.3–0.4, $p < 0.0001$). Mortality declined slightly in males (0.39 to 0.38; slope = -0.002/year, $p = 0.0068$), while remaining unchanged in females (0.94 to 0.97; $p = 0.863$).

Conclusion: Rheumatoid arthritis continues to impose a rising and disproportionate burden on the U.S. population, with sharp increases in both prevalence and disability over the past three decades—particularly among women. While mortality has stabilized or modestly declined, the persistent rise in DALYs reflects significant unmet needs in disease control, long-term management, and quality of life. These findings signal a critical need for renewed public health attention and tailored intervention strategies to reduce disease burden and improve outcomes.

Disclosure: S. Sharkas: None; **D. Murad**: None; **D. Jahandideh**: None.

Abstract Number: 1032

Exploring the role of the gut microbiome in gout: Prospective analysis of dietary fiber intake and the risk of gout

Sharan Rai[1], Natalie McCormick[2], Chio Yokose[3], Robert Terkeltaub[4], Dylan Dodd[5], Lama Nazzal[6], Huilin Li[6], Qi Sun[7] and Hyon K. Choi[8], [1]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital, Waltham, MA, [4]Retired, San Diego, CA, [5]Stanford University, Palo Alto, CA, [6]NYU Langone, New York, NY, [7]Harvard T.H. Chan School of Public Health, Boston, [8]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The role of the gut microbiome has been increasingly implicated in the pathogenesis of gout. For instance, gout patients have shown depletions of bacteria that lower urate levels or produce anti-inflammatory short-chain fatty acids (SCFAs). Dietary fiber is fermented by the gut microbiota and produces beneficial microbial metabolites, including SCFAs (1). Accordingly, greater dietary fiber (particularly cereal fiber) intake is also associated with lower levels of inflammatory biomarkers (2), which may be particularly relevant to gout. Indeed, prior work has found that a pro-inflammatory diet that is low in dark leafy and yellow vegetables as well as high in refined grains is associated with a nearly two-fold increased risk of gout among women (3). Taken together, these data suggest that dietary fiber may play a role in gout prevention through the modulation of gut microbiota and corresponding inflammatory pathway. We aimed to prospectively examine whether long-term dietary fiber intake is associated with the risk of gout among women over 34 years of follow-up.

Methods: We analyzed data from 80,175 women in the Nurses' Health Study with complete dietary data who were free from gout at baseline. We used a validated food frequency questionnaire to collect repeated measures of usual intake of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Multivariable-adjusted associations between dietary fiber intake and incident gout among women in the Nurses' Health Study (1984-2018)

	Quintiles of Dietary Fiber Intake					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
Total fiber						
Median intake (g/day)	12.6	15.4	17.4	19.7	23.7	–
No. of gout cases	251	251	230	225	160	–
Person-years	442,803	443,550	444,489	442,980	444,705	–
Age-adjusted model	1.0 (Reference)	0.95 (0.79, 1.13)	0.83 (0.70, 1.00)	0.79 (0.66, 0.94)	0.53 (0.43, 0.65)	<0.001
Multivariable-adjusted model	1.0 (Reference)	1.00 (0.83, 1.20)	0.91 (0.75, 1.10)	0.91 (0.75, 1.11)	0.69 (0.56, 0.87)	0.001
Cereal fiber						
Median intake (g/day)	2.7	3.8	4.7	5.7	7.6	–
No. of gout cases	318	244	228	179	148	–
Person-years	444,526	439,570	444,511	445,688	444,232	–
Age-adjusted model	1.0 (Reference)	0.77 (0.65, 0.91)	0.71 (0.60, 0.84)	0.53 (0.44, 0.64)	0.42 (0.35, 0.52)	<0.001
Multivariable-adjusted model	1.0 (Reference)	0.81 (0.68, 0.96)	0.80 (0.67, 0.95)	0.65 (0.54, 0.79)	0.61 (0.50, 0.76)	<0.001
Fruit fiber						
Median intake (g/day)	1.6	2.7	3.7	4.8	6.7	–
No. of gout cases	237	240	268	189	183	–
Person-years	442,468	444,749	444,283	442,251	444,775	–
Age-adjusted model	1.0 (Reference)	0.96 (0.80, 1.14)	1.04 (0.87, 1.24)	0.69 (0.57, 0.84)	0.64 (0.53, 0.78)	<0.001
Multivariable-adjusted model	1.0 (Reference)	1.02 (0.84, 1.22)	1.15 (0.95, 1.38)	0.82 (0.67, 1.00)	0.81 (0.65, 1.00)	0.009
Vegetable fiber						
Median intake (g/day)	3.8	5.0	6.0	7.1	9.2	–
No. of gout cases	199	207	248	229	234	–
Person-years	441,676	443,939	445,021	444,120	443,770	–
Age-adjusted model	1.0 (Reference)	1.02 (0.84, 1.24)	1.19 (0.98, 1.43)	1.09 (0.90, 1.31)	1.09 (0.90, 1.32)	0.38
Multivariable-adjusted model	1.0 (Reference)	0.98 (0.80, 1.19)	1.14 (0.94, 1.39)	1.04 (0.85, 1.27)	1.06 (0.87, 1.30)	0.53
Legume fiber						
Median intake (g/day)	0.3	0.6	0.8	1.1	1.8	–
No. of gout cases	232	247	231	218	189	–
Person-years	442,640	449,383	441,574	439,930	445,001	–
Age-adjusted model	1.0 (Reference)	1.03 (0.86, 1.23)	0.96 (0.80, 1.15)	0.89 (0.74, 1.07)	0.76 (0.62, 0.92)	<0.001
Multivariable-adjusted model	1.0 (Reference)	1.03 (0.86, 1.23)	0.99 (0.82, 1.19)	0.95 (0.79, 1.15)	0.87 (0.72, 1.06)	0.12

All models were stratified by age and calendar time. All multivariable models were adjusted for energy intake, body mass index, hypertension status, diuretic use, physical activity, alcohol intake, postmenopausal status, postmenopausal hormone use, dairy intake, meat intake, and fish intake.

130+ food and beverage items every four years. We calculated dietary fiber intakes for all participants using the Harvard University Food Composition Database. In addition to total fiber, we calculated individual intakes of fiber sourced from cereals, fruits, vegetables, and legumes. Every two years, we collected updated data on relevant covariates as well as new confirmed cases of incident gout. We used multivariable Cox proportional hazard models to evaluate the associations between quintiles of dietary fiber intake and incident gout.

Results: We documented 1117 gout cases over 2,218,527 person-years of follow-up. At baseline, women consuming more total fiber tended to be older (Q1 vs. Q5: 49.3 vs. 53.3 years), more physically active (Q1 vs. Q5: 10.5 vs. 19.0 metabolic equivalent of task hours/week), and consume less alcohol (Q1 vs. Q5: 11.5 vs. 4.2 grams/day). After multivariable adjustment, greater intake of total dietary fiber was associated with a 31% lower risk of incident gout comparing extreme quintiles (hazard ratio [HR]=0.69 [95% confidence interval: 0.56 to 0.87]; P for trend=0.001) **(Table)**. This protective association was primarily driven by cereal fiber (from food sources such as cold cereals, dark breads [e.g., rye, pumpernickel, wheat, oatmeal, or other whole grain breads], cooked oatmeal, and added bran) (multivariable HR comparing extreme quintiles=0.61 [0.50 to 0.76]; P for trend< 0.001) and fruit fiber (multivariable HR comparing extreme quintiles=0.81 [0.65 to 1.00]; P for trend=0.009) **(Table)**.

Conclusion: Long-term dietary intake of fiber, particularly fiber sourced from cereals and fruits, is independently associated with a lower risk of incident gout among women. These findings support a role for fiber in the pathogenesis of gout, potentially by modulating the gut microbiome.

References: 1. PMID: 28208609; 2. PMID: 35357453; 3. PMID: 39866115.

Disclosure: S. Rai: None; **N. McCormick**: None; **C. Yokose**: None; **R. Terkeltaub**: Atom Bioscience, 2, BPG Bio, 2, Crystalys, 2, Novartis, 2, Shanton, 2; **D. Dodd**: None; **L. Nazzal**: None; **H. Li**: None; **Q. Sun**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1033

Rethinking ANA in Rheumatoid Arthritis: ICAP Pattern Insights from a Large-Scale Taiwanese Cohort

Tien-Ming Chan, Chang Gung Memorial Hospital, Taoyuan, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: ANA prevalence and patterns vary in RA. Using ICAP nomenclature, this study aimed to determine the prevalence of RA across different ANA patterns and the distribution of these patterns in RA patients within a large Taiwanese cohort.

Methods: This cross-sectional study used the Chang Gung Research Database (2019-2021). Patients undergoing ANA IIF testing (HEp-2 substrate, ≥1:100 positive) were included. Patients with inconsistent/mixed patterns were excluded from

Table 2. Prevalence of Rheumatoid Arthritis (RA) Across Different Pure ANA Staining Patterns Compared to ANA-negative Patients

ANA Pattern	Total	RA, n	RA Prevalence (%)	Odds Ratio	P-value
AC-0 / ANA (-)	31151	1439	4.62	-	-
AC-1	559	56	10.02	2.3	<0.001*
AC-2	629	75	11.92	2.8	<0.001*
AC-3	624	42	6.73	1.49	0.0164
AC-4	670	66	9.85	2.26	<0.001*
AC-5	1050	94	8.95	2.03	<0.001*
AC-6	38	2	5.26	1.15	0.6949
AC-7	83	6	7.23	1.61	0.2842
AC-8	194	13	6.7	1.48	0.1684
AC-9	103	2	1.94	0.41	0.3384
AC-10	93	8	8.6	1.94	0.0786
AC-11	22	3	13.64	3.26	0.0791
AC-12	31	5	16.13	3.97	0.0132
AC-13	31	5	16.13	4.13	0.0132
AC-14	7	1	14.29	3.44	0.282
AC-29	5	0	0	0	1
AC-15	9	1	11.11	2.58	0.3468
AC-16	25	1	4	0.86	1
AC-17	1	0	0	0	1
AC-18	53	3	5.66	1.24	0.7363
AC-19	100	11	11	2.55	0.0067
AC-20	42	6	14.29	3.44	0.0123
AC-21	200	16	8	1.8	0.0399
AC-22	23	3	13.04	3.1	0.0879
AC-24	7	2	28.57	8.26	0.0384
AC-25	8	0	0	0	1
AC-26	22	4	18.18	4.59	0.0172
AC-27	6	0	0	0	1
AC-28	2	0	0	0	1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

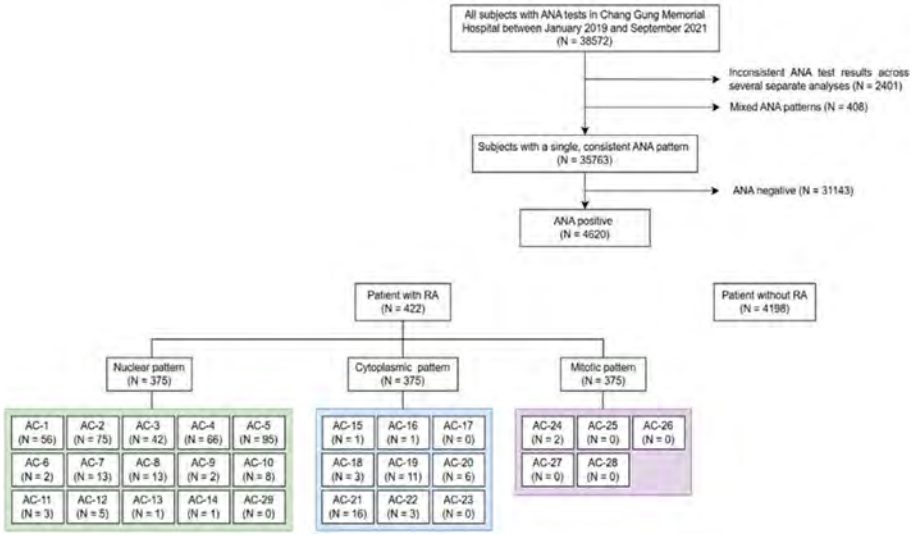
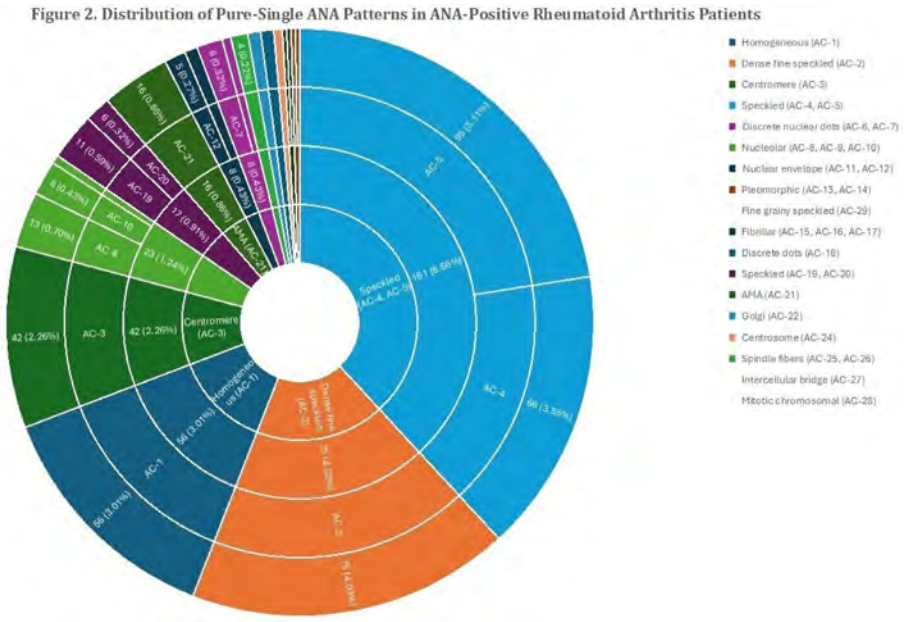


Figure 1. Flowchart illustrating the distribution of ANA patterns (AC-1 to AC-29) among rheumatoid arthritis patients tested at Chang Gung Memorial Hospital (2019–2021)



pure pattern analysis. RA diagnosis used ICD codes confirmed by rheumatologists. RA prevalence and odds ratios (ORs) were calculated for each ANA pattern (AC-1 to AC-29) versus ANA-negative (AC-0). ANA pattern/titer distributions were compared between RA and non-RA cohorts.

Results: Among 35,763 patients with single, consistent ANA patterns, 4,612 (12.9%) were ANA-positive. RA prevalence in the AC-0 group was 4.62%. Significantly higher RA prevalence occurred with AC-2 (Dense fine speckled, 11.92%, OR 2.80), AC-1 (Homogeneous, 10.02%, OR 2.30), AC-4 (Fine speckled, 9.85%, OR 2.26), and AC-5 (Coarse speckled, 8.95%, OR 2.03) patterns (all $p < 0.001$). In the RA cohort (n=1,860 with pure patterns), ANA positivity was 22.69% (vs. 12.38% in non-RA, $p < 0.0001$), with higher titers. The most frequent patterns in ANA-positive RA were Speckled (AC-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

4/AC-5, 8.66%), Dense fine speckled (AC-2, 4.03%), Homogeneous (AC-1, 3.01%), and Centromere (AC-3, 2.26%).

Conclusion: Specific ANA patterns (AC-1, AC-2, AC-4, AC-5) are significantly associated with increased RA prevalence in this Taiwanese cohort. RA patients show higher ANA positivity and titers, favoring speckled, dense fine speckled, and homogeneous patterns. Detailed ICAP pattern reporting is clinically relevant for RA assessment.

Disclosure: T. Chan: None.

Abstract Number: 1034

Healthy Dietary Patterns and Risk of Rheumatoid Arthritis: A Systematic Review and Meta-Analysis

Elena Joerns[1], Jeffrey Sparks[2], Cynthia Chelf[1], Cynthia Crowson[3], John Davis[1] and **Vanessa Kronzer**[1], [1]Mayo Clinic, Rochester, MN, [2]Brigham and Women's Hospital, Boston, MA, [3]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1007–1037) Epidemiology & Public Health Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

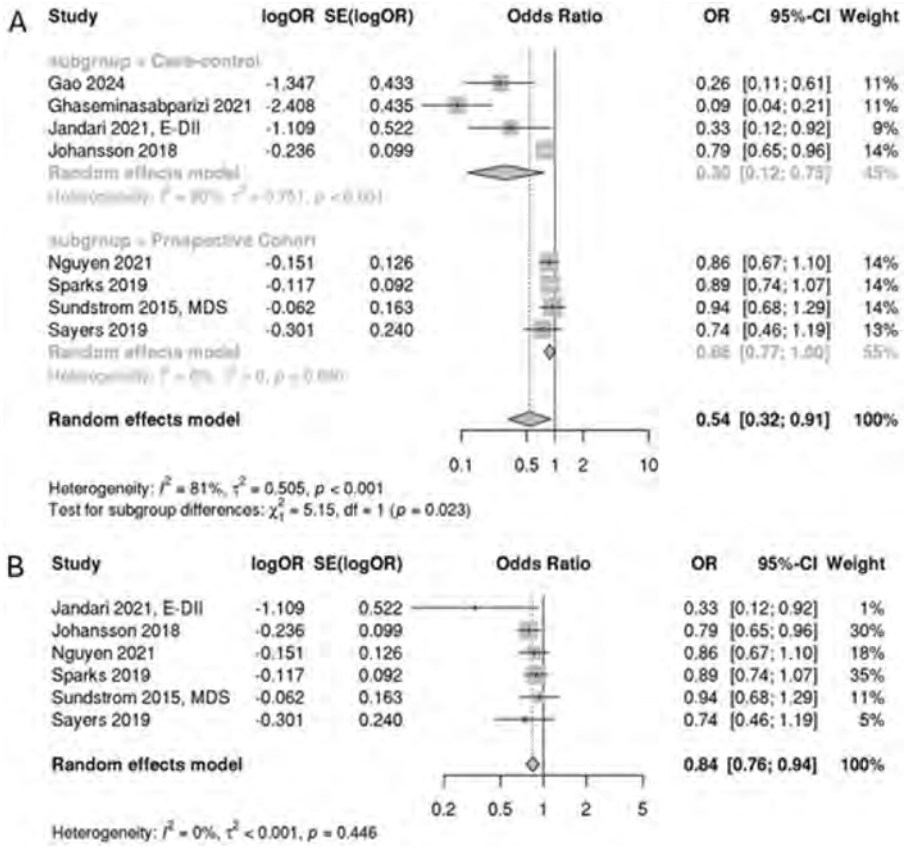


Figure 1. Association between healthy overall dietary pattern and incident RA among (A) all studies and (B) in the subset of studies with the lowest risk of bias

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

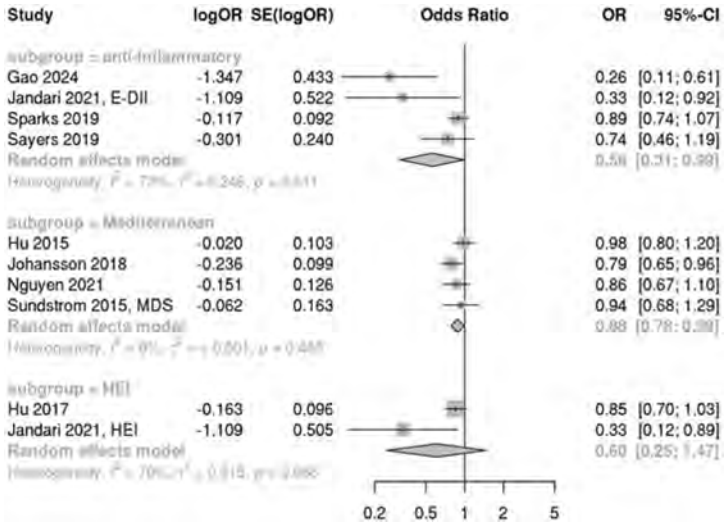


Figure 2. Association between individual healthy dietary pattern types and incident RA

Background/Purpose: Healthy dietary patterns are associated with many health benefits, including lower cardiovascular disease, mortality, and rheumatoid arthritis (RA) disease activity. Therefore, we aimed to determine the degree to which a healthy dietary pattern is associated with incident RA.

Methods: We registered this systematic review and meta-analysis in PROSPERO (CRD42025645056). Inclusion criteria were validated diet (anti-inflammatory, Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and/or healthy eating index [HEI]); validated RA definition; dietary exposure preceding RA; and randomized controlled trial, cohort, or case-control design. We searched CENTRAL, Embase, MEDLINE, Scopus, Web of Science, and grey literature as of 2/3/2025. Two reviewers independently screened each reference and abstracted all data, with agreement reported using Cohen's κ. We assessed each study's risk of bias using the Newcastle-Ottawa Scale. Meta-analyses combined adjusted odds ratios (OR) with 95% confidence interval (CI) for incident RA using random effects models. For heterogeneity, we calculated I^2 and performed subgroup analyses including only the studies with lowest risk of bias and stratifying results by dietary pattern type. We assessed certainty of evidence using GRADE.

Results: The two reviewers screened a total of 796 independent references for inclusion with almost perfect agreement (Cohen's κ 0.89, 95% CI 0.81-0.97). Ultimately, we included 12 case-control and cohort studies spanning 270,121 unique individuals in the review. Three studies were low risk of bias, 3 moderate, 3 high, and 3 very high. Among the 8 independent studies included in the meta-analysis, healthy overall dietary pattern was associated with lower risk of incident RA (OR 0.54, 95% CI 0.32-0.91, I^2=81%, **Figure 1A**). Including only the 6 studies with the lowest risk of bias was also associated with lower RA risk (OR 0.84, 95% CI 0.76-0.94, I^2=0%, **Figure1B**). Anti-inflammatory (OR 0.56, 95% CI 0.31-0.99), Mediterranean (OR 0.88, 95% CI 0.78-0.99), and HEI (OR 0.60, 95% CI 0.25-1.47) patterns all showed lower point estimates for RA (**Figure 2**). Overall level of certainty in these results was moderate due to the studies' observational nature.

Conclusion: In observational studies, healthy dietary pattern is associated with reduced risk of incident RA. Therefore, individuals at risk for RA should consider observing a healthy dietary pattern to potentially reduce their risk of disease. In addition, these findings support inclusion of healthy dietary patterns in RA guidelines.

Disclosure: E. Joerns: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **C. Chelf**: None; **C. Crowson**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **V. Kronzer**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1035

Demographic and Clinical Correlates of 30 day Re-admission or Death During Admission in Patients With Rheumatologic Conditions : A Retrospective Cohort Analysis in a Single Academic Center

Waleed Ali[1] and Deepali Sen[2], [1]Wash U/BJH, St. Louis, MO, [2]Washington University in St Louis, Chesterfield, MO

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology consults are often obtained in hospitalized patients with known or suspected rheumatologic disease. Identifying factors linked to poor short-term outcomes may improve risk stratification during hospitalization and post-discharge planning. This study aimed to characterize demographic, clinical, and social factors associated with 30-day readmission or in-hospital death in patients receiving a rheumatology consult.

Methods: We conducted a retrospective cohort study of patients hospitalized at Barnes Jewish Hospital (Saint Louis, MO) from 4/1/2024-9/30/2024 who received an inpatient rheumatology evaluation for confirmed or suspected rheumatologic conditions. Variables of age, sex, Area Deprivation Index (ADI), disabilty status were collected. Clinical data such as rheumatologic diagnosis, comorbidities (infection, CAD, hypertension) and length of stay (LOS) were collected. The primary outcomes were in-hospital mortality and 30-day all-cause readmission. Associations were assessed using chi-square tests, and independent predictors were evaluated via binary logistic regression. Statistical significance was set at $p < 0.01$ for chi-square and < 0.02 (Bonferroni-Hochberg adjusted) for regression.

Table 1: Summary of Associations with 30-Day Readmission and In-Hospital Death

Outcome	Predictor	Test	Statistic (χ^2 / OR)	95% CI	p-value
30-Day Readmission	Disability	Chi-squared	χ^2 = 11.389	—	< .001
	CAD	Chi-squared	χ^2 = 2.648	—	.104
	Disability	Logistic Regression	OR = 4.16	[1.73 – 10.02]	.001
	Male Sex	Logistic Regression	OR = 1.97	[0.87 – 4.45]	.105
In-Hospital Death	Infection	Chi-squared	χ^2 = 7.449	—	.006
	Male Sex	Chi-squared	χ^2 = 2.714	—	.099
	Length of Stay (LOS)	Logistic Regression	OR = 1.108	[1.017 – 1.208]	.020
	Age	Logistic Regression	OR = 1.059	[1.008 – 1.112]	.022
	Infection	Logistic Regression	OR = 1.197	[0.855 – 14.678]	.081
	Area Deprivation Index (ADI)	Logistic Regression	OR = 0.309	[0.083 – 1.149]	.080

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 268 rheumatology consult patients, 36 (13.4%) were readmitted within 30 days and 19 (7.1%) died during admission. Analyses showed higher readmission rates among those with disability ($\chi^2 = 11.389$, $p < .001$ [all listed are unadjusted]) and a trend with CAD ($\chi^2 = 2.648$, $p = .104$). Infections were more common among patients who died ($\chi^2 = 7.449$, $p < .006$), with a trend toward male predominance ($\chi^2 = 2.714$, $p = .099$). Logistic regression confirmed disability as the only significant predictor of readmission (OR = 4.16, $p = .001$), with male sex trending toward significance (OR = 1.97, $p = .105$). Death during admission was significantly associated with longer length of stay (OR = 1.11, $p = .020$), while age was borderline, just falling outside the corrected cut-off of $p < 0.02$ (OR = 1.06, $p = .022$). Infection (OR = 1.20, $p = .081$) and lower ADI (OR = 0.31, $p = .080$) also showed non-significant trends towards death during admission.

Conclusion: In this cohort, disability status was associated with more than a four-fold risk of 30-day readmission. Other factors such as male sex, known CAD also trended towards higher readmission risk. When looking at deaths during the index admission, LOS and age, alongside presence of infection, was more relevant. Notably, a lower ADI was linked (not significantly) with increased odds of death. This preliminary study highlights the importance of targeted post-discharge planning for patients with disabilities to reduce possible early rehospitalization alongside further research regarding comprehensive mortality risk stratification.

Disclosure: W. Ali: None; **D. Sen**: None.

Abstract Number: 1036

Factors Associated With Long-term Remission After Drug Discontinuation In IgG4-related Disease: A 3-Year Rule

Yifei Wang[1], Yuxue Nie[2], Jingna Li[3], Jialei Zhang[4], Qinhuan Luo[1], Xinli Yang[5], Jialing Jiang[1], Nianyi Zhang[6], Linyi Peng[7], Yunyun Fei[6], Jiaxin zhou[4] and Wen Zhang[8], [1]Peking Union Medical College, Beijing, China (People's Republic), [2]Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China, Dong Cheng Qu, China (People's Republic), [3]Peking Union Medical College, Dong Cheng Qu, Beijing, China, [4]Peking Union Medical College Hospital, Beijing, China (People's Republic), [5]Peking Union Medical College, Dong Cheng Qu, China (People's Republic), [6]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [7]PEKING UNION MEDICAL COLLEGE HOSPITAL, Beijing, Beijing, China, [8]Peking Union Medical College Hospital, Dong Cheng Qu, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic fibroinflammatory disorder with multi-organ involvement and elevated serum IgG4 levels. Glucocorticoids (GC) with or without immunosuppressants (IM) are the first-line treatment. GC/IM discontinuation carries a 23-41% relapse risk, but prolonged use increases infection risk, making cessation timing crucial. However, identifying patients who can achieve long-term remission remains challenging. This study aimed to investigate the characteristics of patients with and without relapse, identifying factors associated with long-term remission.

Methods: We conducted a retrospective study in China, screening 808 patients diagnosed with IgG4-RD. Eighty patients who achieved clinical remission before drug discontinuation were included in the study. Based on relapse records from the third year after drug cessation, patients were classified into no-relapse group (n = 37) and relapse group (n = 43). All patients fulfilled the 2019 ACR/EULAR classification criteria for IgG4-RD. We analyzed demographic characteristics, laboratory results, clinical symptoms, and treatment data at baseline and during follow-up.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

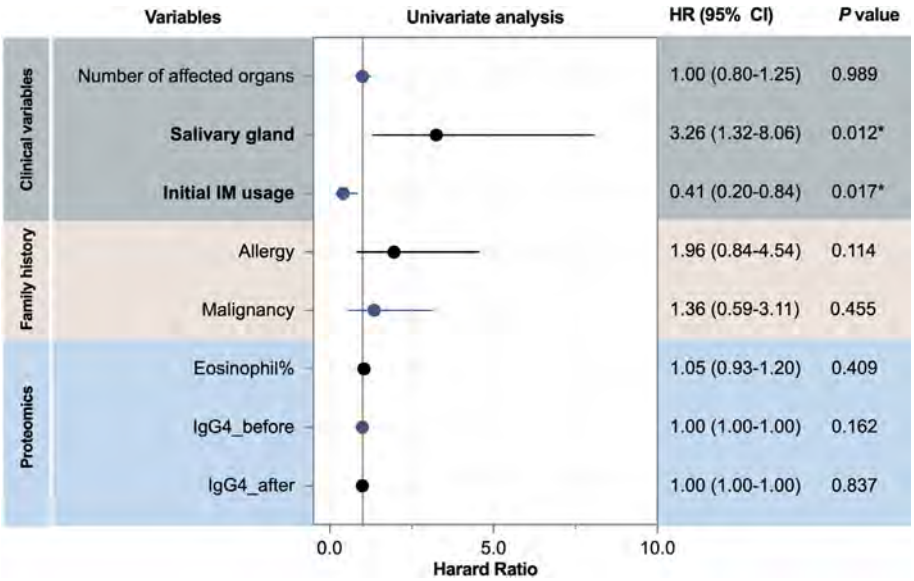


Figure 1. Hazard ratios for clinical variables in IgG4-RD relapse prediction

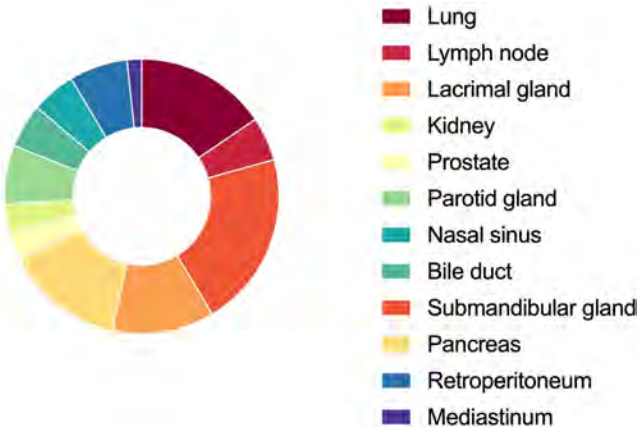


Figure 2. Distribution of relapsed organs

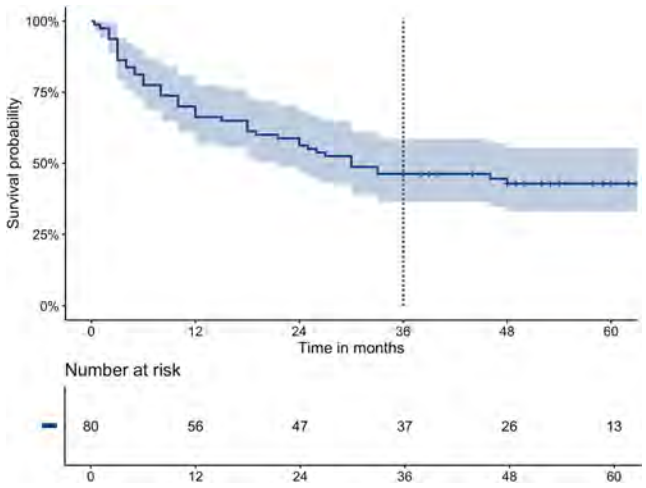


Figure 3. Kaplan-Meier curve of relapse-free survival in IgG4-RD patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Univariate analysis indicated that the no-relapse group had a lower number of affected organs (p=0.014), family history of allergy (p=0.017), and family history of malignancy (p=0.042). Laboratory findings revealed lower serum levels of eosinophils (p=0.001) and IgG4 (p=0.006) in the no-relapse group at baseline. Patients from the relapse group exhibited higher rates of submandibular (p = 0.009) and parotid glands involvement (p = 0.001).

Additionally, the relapse group had more patients without IM prescriptions (p = 0.006). Before complete medication withdrawal, the relapse group exhibited higher serum IgG4 levels (2190 g/L) than the no-relapse group (1250 g/L, p = 0.037).

Cox regression analysis identified no salivary gland involvement (HR 3.26, 95% CI: 1.32-8.06, p = 0.012) and initial IM use (HR 0.41, 95% CI: 0.20-0.84, p = 0.017) as significant protective factors (Figure 1). Figure 2 visualized the distribution of relapsed organs. Kaplan-Meier analysis revealed a biphasic relapse pattern following treatment discontinuation, characterized by a plateau after 36 months (Figure 3). These findings suggest that patients remaining relapse-free for 3 years tend to attain durable remission.

Conclusion: IgG4-RD patients without salivary gland involvement and receiving an IM prescription at baseline demonstrated a reduced likelihood of disease relapse following treatment cessation. Furthermore, patients maintaining relapse-free status for 3 years post-treatment exhibited a 94.6% probability of achieving long-term remission, suggesting this timepoint as a meaningful predictor of sustained treatment efficacy.

Disclosure: Y. Wang: None; **Y. Nie**: None; **J. Li**: None; **J. Zhang**: None; **Q. Luo**: None; **X. Yang**: None; **J. Jiang**: None; **N. Zhang**: None; **L. Peng**: None; **Y. Fei**: None; **J. zhou**: None; **W. Zhang**: None.

Abstract Number: 1037

Risk Factor Identification and Dynamic Individualized Prediction of Muscle Involvement in Systemic Sclerosis

Zixing Liu[1], Adrianne Woods[2], Julie Paik[2], Laura Hummers[2], Scott Zeger[1], Ami Shah[2] and Ji Soo Kim[3], [1]Johns Hopkins Biostatistics, Baltimore, MD, [2]Johns Hopkins Rheumatology, Baltimore, MD, [3]Johns Hopkins, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1007–1037) Epidemiology & Public Health Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Myopathy in SSc significantly increases disability, reduces quality of life, and elevates mortality risk, yet remains understudied. Most identified risk factors derive from cross-sectional studies, limiting insights into longitudinal patterns and hindering time-varying risk prediction of myopathy at the individual patient level.

Methods: We analyzed longitudinal data from a cohort of over 2,800 SSc patients in a SSc research registry, totaling approximately 24,000 visits. Among included patients, 97.6% met 1980 or 2013 ACR/EULAR classification criteria. To examine clinical risk factors for incident muscle involvement (new onset between consecutive visits), we used multivariable logistic regression models separately across three dichotomized outcomes: proximal muscle weakness (Medsger Muscle Severity Score [MSS] ≥ 1), elevated creatine phosphokinase (CPK ≥ 200 U/L), and their co-occurrence as a myopathy surrogate (MSS/CPK-defined myopathy). To support individualized risk prediction, we developed a Bayesian generalized linear mixed model for cross-validated sequential prediction, using MSS as an example outcome to showcase and validate our

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

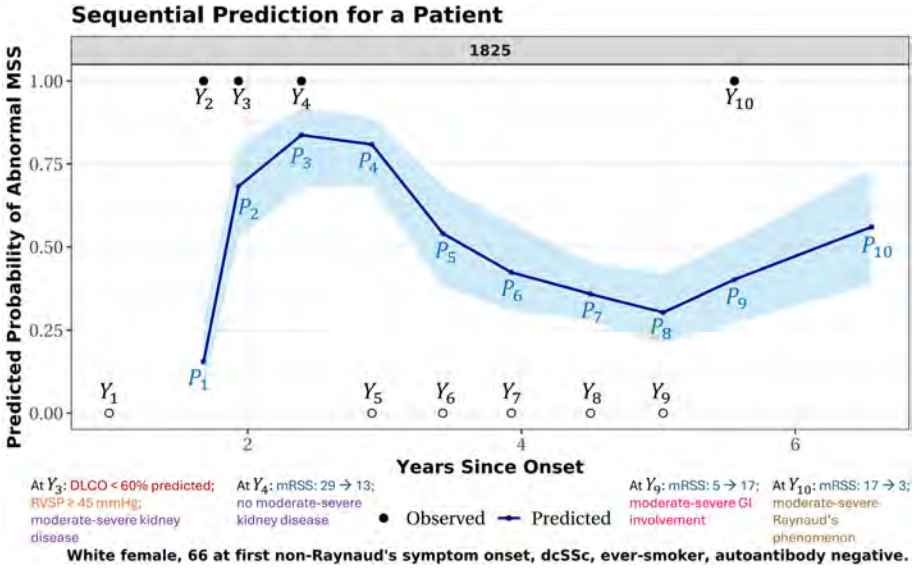


Figure 1. Predicted probability trajectory of abnormal MSS (proximal muscle weakness) for one patient. X-axis: years since the onset of first non-Raynaud's SSc symptom. Observed MSS outcomes labeled Y1-Y10: solid dots = abnormal MSS, empty circles = normal MSS. This patient initially presented with normal MSS, followed by three visits with abnormal MSS, then five consecutive visits with normal MSS, and a final visit with abnormal MSS. Predicted probabilities of abnormal MSS (P1-P10) are shown in dark blue, with 95% confidence intervals in light blue. Each prediction estimates the risk of abnormal MSS for the next visit using all available clinical information up to the current point. For example, prediction P1 estimates the risk for visit 2 (where outcome Y2 is to be observed), using only data from visit 1 (i.e., the measured outcome Y1 and associated clinical measurements). Similarly, P2 predicts the risk for visit 3 (where outcome Y3 is to be observed), using data from visits 1 and 2 (i.e., outcomes Y1-Y2 and associated clinical measurements). And P3 predicts the risk for visit 4 using earlier data from visits 1-3. This one-step-forward prediction process continues sequentially through all visits, with the final prediction, P10, estimating risk one year after the last observed visit using data from all 10 visits. Colored text annotations appear at selected visits and summarize clinical changes observed at that visit, relative to the previous one. These changes inform the next prediction (e.g., changes at visit 3, when outcome Y3 is measured, inform P3, the predicted risk for the following outcome Y4 to be observed at visit 4). DLCO: diffusing capacity for carbon monoxide (percent predicted); RVSP: right ventricular systolic pressure (≥ 45 mmHg indicates echocardiographic evidence of pulmonary hypertension); moderate-severe kidney disease: serum creatinine ≥ 1.7 mg/dL, 3-4+ proteinuria, or history of SSc renal crisis; moderate-severe GI involvement: high-dose GERD treatment, antibiotics for bacterial overgrowth, malabsorption syndrome, pseudo-obstruction, or total parenteral nutrition; moderate-severe Raynaud's phenomenon: Raynaud's with digital pitting scars, digital ulcers, or digital gangrene.

approach. The model incorporated baseline and time-varying characteristics, along with patient-specific medical history, to produce individualized risk trajectories. Cross-validation was used for efficiency and proper performance evaluation, and LASSO logistic regression model was used for variable selection.

Results: Several demographic, autoantibody, and comorbidity-related factors were associated with increased odds of incident MSS/CPK-defined myopathy. Notable predictors included diffuse subtype (OR=2.36 [1.68, 3.32]), Black race (OR=2.08 [1.49, 2.92]), anti-PM/Scl (positivity for both subunits, OR=3.42 [1.80, 6.51]), anti-Ku (OR=2.99 [1.95, 4.60]), anti-Fibrillarin (OR=1.95 [1.31, 2.91]), restrictive lung disease (ppFVC ≤ 70%) (OR=2.03 [1.46, 2.82]), tendon friction rubs (OR=1.97 [1.22, 3.17]), and moderate-severe GI involvement (OR=1.37 [1.04, 1.80]). Anti-Scl70 (OR=0.46 [0.31, 0.67]), anti-RNA polymerase III (OR=0.62 [0.41, 0.94]), and anti-U1RNP (OR=0.67 [0.46, 0.99]) were linked to lower odds of incident myopathy. Our prediction model for MSS (AUC: 0.867 [0.864, 0.869]) outperformed standard regression and random forest models, which did not capture the complete patient-specific history. With new data emerging at each visit, our method generates updated, real-time individualized predicted risk of abnormal MSS for the next visit (Figure 1).

Conclusion: This study identified key baseline and time-varying risk factors linked to SSc-associated myopathy and, to our knowledge, introduced the first longitudinal, real-time, individualized prediction model for a myopathy-related outcome (MSS). Our approach addresses unmet needs in monitoring SSc-associated myopathy by combining population-level risk

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

factors with dynamic personalized risk assessment, potentially enabling more timely interventions. This method can be easily translated to modeling other longitudinal outcomes in electronic health record data for improved risk estimation in chronic diseases.

Disclosure: Z. Liu: None; **A. Woods**: None; **J. Paik**: ArgenX, 12,, Priovant, 12,; **L. Hummers**: AbbVie/Abbott, 1, Astra-Zeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **S. Zeger**: None; **A. Shah**: None; **J. Kim**: None.

Abstract Number: 1038

Real-World Immunosuppressant Treatment Patterns in Lupus Nephritis: A Retrospective Claims Database Analysis in the United States

Anisha Patel[1], Alexandra Miller[1], Lisa Lindsay[1], Danny Sheinson[1], Zhiyu Xia[1], William Pendergraft[1] and Maria Dall'Era[2], [1]Genentech, Inc., South San Francisco, CA, [2]Division of Rheumatology, University of California, San Francisco, CA

Table 1. Baseline Characteristics of Patients Newly Diagnosed With Lupus Nephritis Between 2018-2023

Characteristics	Overall (N=2052)
Age at index, years	
Mean (SD)	44 (15)
Median (Q1, Q3)	44 (33, 54)
Female, n (%)	1684 (82)
Race/ethnicity, n (%)	
Unspecified/not linked[a]	1365 (67)
Data available and linked[b]	687 (34)
Non-Hispanic White	503 (73)
Non-Hispanic Black	87 (13)
Hispanic	63 (9)
Asian/Others	34 (5)
Payer type, n (%)	
Commercial/self-insured[c]	1922 (94)
Medicare	118 (6)
Medicaid	10 (0.5)
Others/unknown	2 (<0.1)
Region, n (%)	
East	297 (14)
Midwest	502 (24)
South	918 (45)
West	333 (16)
Unknown	2 (<0.2)
Pre-index Modified Charlson Comorbidity Index[d]	
Mean (SD)	1.3 (1.2)
Median (Q1, Q3)	1.0 (1.0, 1.0)
Pregnancy during study period, n (%)	189 (9)
SLE diagnosis in the pre-index period, n (%)	1518 (74)
Pre-index treatments used, n (%)	
Non-steroidal IST[e]	717 (35)
Systemic glucocorticoids[f]	1223 (60)
Days from index diagnosis to end of follow-up	
Mean (SD)	905 (547)
Median (Q1, Q3)	787 (443, 1,286)
Days from index diagnosis to any LN treatment initiation	
Mean (SD)	51 (150)
Median (Q1, Q3)	11 (2, 33)

AZA, azathioprine; CYC, cyclophosphamide; LN, lupus nephritis; IST, immunosuppressant; MMF, mycophenolate mofetil; Q, quartile; SD, standard deviation; SLE, Systemic lupus erythematosus.
[a]Includes those with race unknown or data not available; [b]Denotes records wherein race/ethnicity from consumer data could be linked with IQVIA PharMetrics® Plus data and was available for analysis. Race/ethnicity proportions here were calculated only for those records that could be linked; [c]Self-insured health plan is coverage offered by an employer or association; [d]Denotes Charlson Comorbidity Index after exclusion of renal disease; [e]Non-steroidal ISTs include AZA, CYC, calcineurin inhibitors (cyclosporine, tacrolimus, voclosporin), MMF, belimumab, and rituximab; [f]Includes either injection or oral glucocorticoids.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: LN is a severe manifestation of SLE requiring intensive management. We aimed to characterize real-world treatment patterns in newly diagnosed patients with LN within the United States (US), focusing on use of immunosuppressants (ISTs) and advanced therapies including belimumab and voclosporin.

Methods: This retrospective cohort study utilized US healthcare claims data from the IQVIA PharMetrics® Plus database from January 1, 2017 to December 31, 2023. Adults with LN were identified using ICD-10-CM code M32.14, requiring at least one inpatient or two outpatient claims ≥30 days apart between January 1, 2018 to June 30, 2023. The first LN diagnosis was the index date. Patients needed ≥12 months pre-index and ≥6 months post-index continuous enrollment with no prior LN diagnoses. Exclusions included claims for renal transplant, dialysis, end-stage renal disease, malignancy, HIV, hepatitis B/C, and/or tuberculosis. LN treatments (ISTs, systemic glucocorticoids, antimalarials and antihypertensives) were examined, focusing on IST treatment patterns: initiation, switching, discontinuation (≥90-day supply gap), restarting, and duration of use. First and second lines of therapy (LoT) with ISTs were descriptively assessed, along with concomitant use of other LN treatments. Transitions to the second LoT involved adding or switching ISTs in ≤30 days of the first LoT ending or a ≥90-day treatment gap with or without restarting treatment.

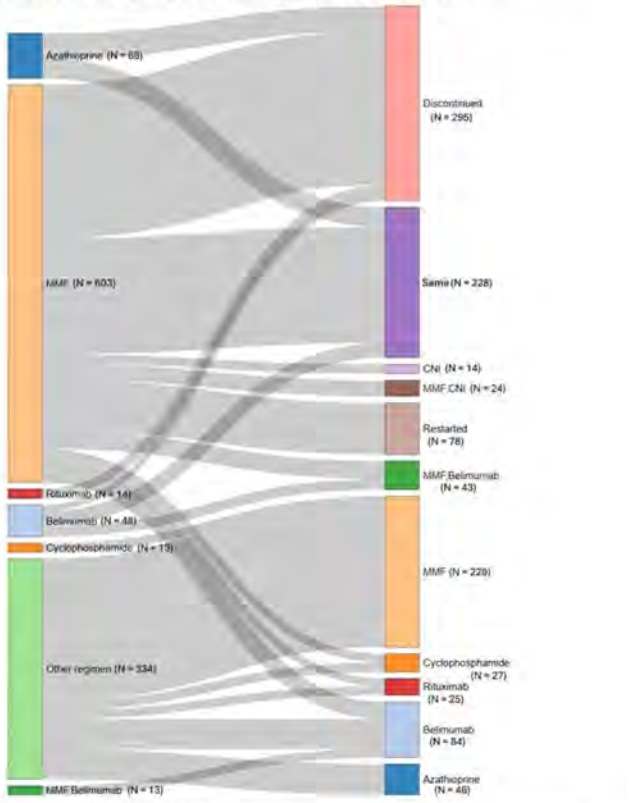
Table 2. Treatment Regimens in the First Line of Therapy by Immunosuppressants

First IST LoT[a]	Number of patients	Proportion of patients on other drug classes during first IST LoT			Days on first LoT, median (Q1, Q3)
		Glucocorticoid overall, % (injection/oral)[b,c]	Antimalarial,[d] %	Antihypertensive,[e] %	
Any IST	946	79.7 (24.1/76.1)	64.7	54.1	219 (66, 485)
MMF	620	82.7 (18.1/81.5)	69.2	60.3	257 (96, 501)
AZA	95	61.1 (16.8/57.9)	62.1	44.2	254 (48, 560)
Belimumab	59	67.8 (52.5/49.2)	61.0	42.4	322 (59, 726)
Cyclophosphamide	39	94.9 (43.6/89.7)	56.4	38.5	106 (74, 136)
MMF, belimumab	32	84.4 (21.9/84.4)	81.2	65.6	288 (104, 606)
Rituximab	27	96.3 (77.8/63.0)	22.2	22.2	43 (42, 53)
CNI	20	55.0 (20.0/55.0)	40.0	35.0	240 (98, 610)
MMF, CNI	18	55.6 (11.1/55.6)	55.6	61.1	252 (72, 432)

CNI, calcineurin inhibitors (cyclosporine, tacrolimus, voclosporin); IST, immunosuppressant; LoT, line of therapy; MMF, mycophenolate mofetil; Q, quartile.
[a]Regimens with n<10 are not shown; [b]Injection and oral steroid percentages are based on total patients in each row, not a percentage of overall steroid use; [c]Steroid injections may include pre-infusion injections or pulse therapy; [d]Antimalarial included hydroxychloroquine; [e]Antihypertensive included angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Sankey Diagram of First and Second Lines of Immunosuppressant Therapy Among Newly Diagnosed Lupus Nephritis Patients



Regimen transitions with n<10 are not shown.
Discontinued, dropped IST with a gap of ≥90 days and did not restart throughout study follow-up; Other regimen, including glucocorticoids, antimalarials, and antihypertensives, represents those who did not initiate IST in the first LoT but had it added later in the follow-up; Restarted, dropped IST with a gap of ≥90 days but reinitiated new or same IST later during study follow-up. Mean days until reinitiation ranged from 121 (CYC) to 392 days (CNI); Same: censored i.e., remained on first IST LoT throughout study follow-up.
Of the patients on MMF and belimumab as the first LoT, 41% withdrew MMF in the second LoT.
CNI, calcineurin inhibitors (cyclosporine, tacrolimus, voclosporin); LN, Lupus nephritis; LoT, line of therapy; MMF, mycophenolate mofetil.

Results: A total of 2052 newly diagnosed patients with LN were identified, with an average follow-up time of 2.5 years. The cohort was 82% female, with a mean (SD) age of 44 (15) years; 94% had private insurance, 74% had a prior SLE diagnosis and 35% had used ISTs pre-index (**Table 1**). During the post-index period, 1959 patients (95%) received any of the studied LN treatments. Of these, 946 patients (48%) received an IST as their first LoT, primarily mycophenolate mofetil (MMF, 66%), azathioprine (AZA, 10%) and/or belimumab (6%). Median treatment duration (in days) in the follow-up period varied: 257 for MMF, 254 for AZA, and 322 for belimumab. Among patients who received an IST as the first LoT, 80% were given systemic glucocorticoids (oral: 76%, injection: 24%, both: 21%), 65% antimalarials, and 54% antihypertensives (**Table 2**). By the end of their follow-up, 27% of these patients remained on their initial IST for a median of 456 days, while 19% added or switched to a second LoT with a different IST (primarily MMF, belimumab, or AZA), 16% dropped and restarted an IST after >90 days, and 37% discontinued IST treatment. Additionally, 18% (356/1959) of patients, with any LN treatment post-index, initiated non-IST treatment in the first LoT but switched to an IST during follow-up (**Figure 1**).

Conclusion: This health insurance claims-based study identified diverse treatment use in newly diagnosed patients with LN, with nearly half receiving an IST in the first LoT. Variability in treatment duration and regimens reflects dynamic patient needs and treatment practices. Understanding these patterns is essential for optimizing LN care and informing future monitoring of treatment changes following practice guideline updates and availability of newer therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Patel: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **A. Miller**: Genentech, Inc., 7; **L. Lindsay**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **D. Sheinson**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **Z. Xia**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2.

Abstract Number: 1039

CAR-T Therapy in Rheumatoid Arthritis: A Health Systems Analysis of Cost and Global Equity

Asrith Reddy Gandu[1] and Kolluri Prathyusha[2], [1]Davao medical school foundation, Hyderabad, India, [2]University of delaware, Newark, DE

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Refractory rheumatoid arthritis (RA) affects 30–40% of patients with limited therapeutic options and high disability burdens. Although CAR-T therapy has been transformative in oncology and lupus, its prohibitive cost (> $500K per patient) and limited accessibility in low- and middle-income countries (LMICs) constrain its application in RA. This systematic review evaluates CAR-T's cost-effectiveness, global equity challenges, and proposes actionable strategies for sustainable integration into rheumatology practice, aligning with ACR Convergence 2025's focus on healthcare delivery innovation.

Methods: Following PRISMA guidelines, we systematically reviewed 418 studies from PubMed and Embase (2000–2024) on CAR-T costs, access, or policy in RA/autoimmunity. Two reviewers independently screened studies using predefined inclusion/exclusion criteria. Thematic analysis categorized findings into cost-effectiveness, LMIC access barriers, and health system solutions, while study quality was assessed using AMSTAR-2.

Results: Eighteen studies met inclusion criteria (12 preclinical, 6 clinical).

In preclinical models, CD19 CAR-T cells resolved synovitis in 80% of RA mice ($p < 0.001$ vs. controls), correlating with a 90% reduction in B cells and a 3-fold increase in regulatory T cells ($p=0.002$). Early clinical trials reported 40–60% ACR50 response rates; however, 50% of patients experienced grade 1–2 cytokine release syndrome, which resolved with tocilizumab. CAR-T costs ($750K/QALY) exceed WHO-recommended thresholds (150K/QALY), with < 5% of trials including LMIC sites, while tiered pricing models in pilot programs reduced costs by 60%.

Conclusion: CAR-T therapy offers transformative potential for refractory RA but requires systemic reforms to address cost and equity challenges. Studies in oncology have demonstrated CAR-T's significant impact; adapting these cost-effectiveness models to RA supports the need for tiered pricing and LMIC-centric trials to ensure sustainable, equitable access. Implementing tiered pricing, initiating LMIC-centric trials, and developing engineered safety switches (e.g., ON/OFF CAR-T) are recommended strategies to democratize access.

Disclosure: A. Gandu: None; **K. Prathyusha**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1040

Impact of Clinical Pharmacist-Directed Patient Education on Medication Adherence and Clinical Outcomes in Patients with Inflammatory Arthritis

Cristina Hurley[1], Megha Kotha[2], Jisna Paul[3] and Jeff Barbee[4], [1]Carilion Clinic, Roanoke, VA, [2]Ohio State University, Columbus, OH, [3]Division of Rheumatology and Immunology, Department of Internal Medicine, The Ohio State University Wexner Medical Center, Columbus, OH, Columbus, OH, [4]Ohio State University Wexner Medical Center, Columbus

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1038–1054) Health Services Research Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: This study assesses the impact of a clinical pharmacist-directed intervention on medication adherence and clinical outcomes in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis receiving non-infusion disease-modifying antirheumatic drugs (DMARDs). Previous studies on patient education interventions in rheumatology have yielded mixed results due to variability in study populations and educational methods. Pharmacist-led interventions in other chronic diseases, such as hypertension and diabetes, have demonstrated improved disease management and adherence, but data on their effectiveness in inflammatory arthritis remains limited.

Methods: A prospective, controlled study was conducted from July to December 2024 at Ohio State University (OSU) Rheumatology. Fifty adult patients were enrolled and assigned to either a pharmacist-directed intervention group or a usual care control group. The intervention group received pharmacist-led education, drug toxicity monitoring, and follow-up. Surveys administered at baseline and follow-up included the Morisky Medication Adherence Scale (MMAS), the Routine

Table 1: Demographics

Variable	Treatment group N = 19[1]	Control group N = 31[1]	p-value[2]
Gender			0.8
Women	13 (68%)	20 (65%)	
Men	6 (32%)	11 (35%)	
Race			>0.9
White	16 (84%)	26 (84%)	
Non-white	3 (16%)	5 (16%)	
Current DMARD			0.4
Group 1	14 (74%)	17 (55%)	
Group 2	3 (16%)	6 (19%)	
Group 3	2 (11%)	8 (26%)	
Education	13 (68%)	21 (68%)	>0.9
Alcohol Use	7 (37%)	8 (26%)	0.4
Tobacco Use	7 (37%)	3 (9.7%)	0.030

[1]n (%)

[2]Pearson's Chi-squared test; Fisher's exact test

Table 2: Results

Variable	Treatment group N = 19[1]	Control group N = 31[1]	p-value[2]
RAPID3-Dichotomous	8 (42%)	15 (48%)	0.7
RAPID3-raw mean	5.9	7.5	0.3
Confidence question	15 (79%)	27 (87%)	0.5
MMAS	16 (84%)	28 (90%)	0.7
Infection question	15 (79%)	21 (68%)	0.4
DMARD Group			0.4
Group 1	14 (74%)	17 (55%)	
Group 2	3 (16%)	6 (19%)	
Group 3	2 (11%)	8 (26%)	
Vaccine question	14 (74%)	22 (71%)	0.8

[1]n (%); Mean

[2]Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Assessment of Patient Index Data 3 (RAPID3), and three medication knowledge questions. Statistical analyses included Pearson's chi-square test for categorical variables and Wilcoxon rank sum test for continuous variables. The primary outcome was MMAS score, with RAPID3 and medication knowledge responses as secondary outcomes.

Results: Baseline characteristics were similar between groups, except for a higher prevalence of tobacco use in the intervention group ($p = 0.03$). No significant differences were found in MMAS scores ($p = 0.84$), RAPID3 dichotomous outcomes ($p = 0.04$), or medication knowledge responses. Participants with higher education levels were more likely to report confidence in their medication knowledge. While the intervention group showed a trend toward improved disease control based on RAPID3 scores, this difference did not reach statistical significance. Correlation analysis revealed associations between gender and DMARD failure ($r = 0.37$, $p < 0.01$), race and anti-CCP positivity ($r = 0.31$, $p < 0.05$), and tobacco use with education level ($r = -0.41$, $p < 0.01$). The strongest correlation was between RF and CCP positivity ($r = 0.83$, $p < 0.001$).

Conclusion: Pharmacist-led patient education did not significantly improve medication adherence or clinical outcomes in this small cohort. However, trends in RAPID3 scores suggest a potential benefit in disease control. Confidence in medication knowledge was higher in those with greater educational attainment. Further large-scale studies are warranted to determine the impact of pharmacist-led education in inflammatory arthritis, similar to its demonstrated benefits in other chronic conditions such as hypertension and diabetes.

Disclosure: C. Hurley: None; **M. Kotha**: None; **J. Paul**: None; **J. Barbee**: None.

Abstract Number: 1041

Associated Factors and Direct Cost Analysis of Dose Reduction and Discontinuation of Biological Therapies in Rheumatoid Arthritis and Spondyloarthritis: Findings from a Colombian Cohort Within the Framework of an Integrated Management Model

Edwin Jauregui[1], Deisy Restrepo[2], Belcy Garzon[2], Alexis Atuesta[2], Nestor Correa[2], Jessica Barrera[2] and Andrea Rubio[2], [1]Riesgo de fractura S.A, Bogotá, Colombia, [2]Riesgo de fractura S.A, Bogotá, Colombia

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Dose reduction of biologic therapy (BT) in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA) has been increasingly implemented in recent years, in accordance with international and local clinical practice guidelines. This approach seeks to minimize the risk of adverse events and reduce direct healthcare costs. The objective of this study is to describe clinical characteristics and identify factors associated with dose reduction and discontinuation of BT in a cohort of RA and SpA patients managed within a comprehensive rheumatology care program at the healthcare institution Riesgo de Fractura SA – CAYRE IPS. Additionally, to evaluate direct pharmacologic treatment costs in this population.

Methods: This real-world evidence study describes a cohort of adult RA and SpA patients in sustained clinical remission—defined as DAS28 < 2.6 for RA and ASDAS < 1.3 for SpA—for at least 12 months. Patients were followed from April 2023 to October 2024. Clinical outcomes (DAS28 or ASDAS) were assessed at 6, 12, and 18 months after initiating biologic dose reduction. Per institutional policy, Rituximab and Adalimumab were used as first-line BT based on cost and biosimilar

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Sociodemographic, Clinical, and Laboratory Characteristics of Patients with Rheumatoid Arthritis and Spondyloarthritis, Stratified by Biologic Therapy Optimization Status

Characteristic	RA - Optimized (n=265)	RA - Not Optimized (n=137)	SpA - Optimized (n=74)	SpA – Not Optimized (n=72)
Age, mean (SD)	59.17 (12.13)	56.22 (13.15)	51.26 (12.95)	51.85 (13.66)
Female sex, n (%)	230 (86.8)	121 (88.3)	24 (32.4)	28 (38.9)
Disease duration, n (%)				
< 5 years	28 (10.6)	11 (8.0)	16 (21.6)	27 (37.5)
5-10 years	95 (35.8)	41 (29.9)	43 (58.1)	45 (62.5)
BMI Classification, n (%)				
Normal weight	139 (52.5)	70 (51.1)	32 (43.2)	30 (41.7)
Overweight	90 (34.0)	43 (31.4)	31 (41.9)	31 (43.1)
Obesity I	24 (9.1)	12 (8.8)	7 (9.5)	7 (9.7)
Obesity II	1 (0.4)	5 (3.6)	1 (1.4)	1 (1.4)
Obesity III	1 (0.4)	2 (1.5)	0 (0.0)	1 (1.4)
Underweight	10 (3.8)	5 (3.6)	3 (4.1)	2 (2.8)
Moderate to Severe Disability by HAQ, n (%)	19 (7.2)	13 (9.5)	--	--
Articular Involvement, n (%)				
Erosion	97 (36.6)	43 (31.4)	--	--
Peripheral arthritis	--	--	27 (36.5)	32 (44.4)
Inflammatory back pain	--	--	64 (86.5)	67 (93.1)
Sacroiliitis – Bilateral	--	--	41 (55.4)	40 (55.6)
Sacroiliitis – Unilateral	--	--	16 (21.6)	12 (16.7)
Enthesitis	--	--	13 (17.6)	14 (19.4)
Extra-Articular Manifestations, n (%)				
Uveitis	--	--	15 (20.3)	20 (27.8)
Psoriasis	--	--	1 (1.4)	3 (4.2)
Ulcerative colitis	--	--	2 (2.7)	5 (6.9)
Crohn's disease	--	--	0 (0.0)	1 (1.4)
Positive Autoantibodies, n (%)				
RF Positive	20 (7.5)	9 (6.6)	--	--
ACPAs Positive	22 (8.3)	10 (7.3)	--	--
RF + ACPAs Positive	203 (76.6)	107 (78.1)	--	--
RF + ACPAs Negative	20 (7.5)	11 (8.0)	--	--
HLA B27 Positive	--	--	40 (54.1)	46 (63.9)
NSAID Use, n (%)				
Naproxen	1 (0.4)	2 (1.5)	1 (1.4)	0 (0.0)
Ibuprofen	2 (0.8)	0 (0.0)	0 (0.0)	1 (1.4)
Diclofenac	1 (0.4)	1 (0.7)	--	--
Meloxicam	2 (0.8)	2 (1.5)	0 (0.0)	1 (1.4)
Celecoxib	1 (0.4)	0 (0.0)	1 (1.4)	6 (8.3)
Etoricoxib	7 (2.6)	4 (2.9)	15 (20.3)	24 (33.3)
csDMARD Use, n (%)				
Methotrexate	90 (34.0)	53 (38.7)	2 (2.7)	10 (13.9)
Chloroquine	1 (0.4)	1 (0.7)	--	--
Hydroxychloroquine	7 (2.6)	6 (4.4)	--	--
Leflunomide	51 (19.2)	31 (22.6)	--	--
Sulfasalazine	8 (3.0)	8 (5.8)	2 (2.7)	5 (6.9)
Combination therapy	38 (14.3)	12 (8.8)	1 (1.4)	0 (0.0)
Azathioprine	--	--	0 (0.0)	2 (2.8)
Biologic Therapy Used, n (%)				
Biologic-Naive	153 (57.7)	74 (54)	--	--
Adalimumab	16 (6.0)	33 (24.1)	35 (47.3)	45 (62.5)
Infliximab	2 (0.8)	0 (0.0)	2 (2.7)	3 (4.2)
Golimumab	9 (3.4)	10 (7.3)	13 (17.6)	10 (13.9)
Etanercept	39 (14.7)	31 (22.6)	12 (16.2)	4 (5.6)
Certolizumab	14 (5.3)	22 (16.1)	5 (6.8)	4 (5.6)
Abatacept	27 (10.2)	20 (14.6)	--	--
Rituximab	147 (55.5)	7 (5.1)	--	--
Tocilizumab	11 (4.2)	13 (9.5)	--	--
Secukinumab	--	--	7 (9.5)	6 (8.3)
Number of Prior Biologic Therapies, mean (SD)	2.59 (13.44)	5.22 (20.189	--	--
Corticosteroid Use, n (%)	110 (41.5)	56 (40.9)	--	--

Abbreviations: ACPAs= Anti-Citrullinated Protein Antibodies; BMI= Body Mass Index; csDMARD= Conventional Synthetic Disease-Modifying Antirheumatic Drug; HAQ= Health Assessment Questionnaire; RF= Rheumatoid Factor; NSAID= Non-Steroidal Anti-Inflammatory Drug; SD= Standard Deviation.

Table 2. Multivariable Logistic Regression Model for Biologic Therapy Optimization in Spondyloarthritis

	OR	CI 95%	Value *p*
Male sex	1.58	0.75 - 3.29	0.2261
HLA-B27 (+)	0.56	0.28 - 1.14	0.1118
Normal weight	1.17	0.59 - 2.34	0.6529
Disease duration (<5 years)	0.40	0.19 - 0.86	0.0192 *
Sacroiliitis (+)	1.71	0.78 - 3.79	0.1829

availability. Logistic regression was used to identify factors associated with successful dose reduction. Variables were selected based on clinical relevance and prior evidence; the most parsimonious model was applied. Limitations included small sample size and a lack of heterogeneity between groups. Drug costs were estimated using SISPRO platform by averaging unit prices, and all analyses were conducted using R software. Costs are reported in USD using an exchange rate of 1 USD = COP 4,293.00 (official Colombian rate (average), October 2024).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

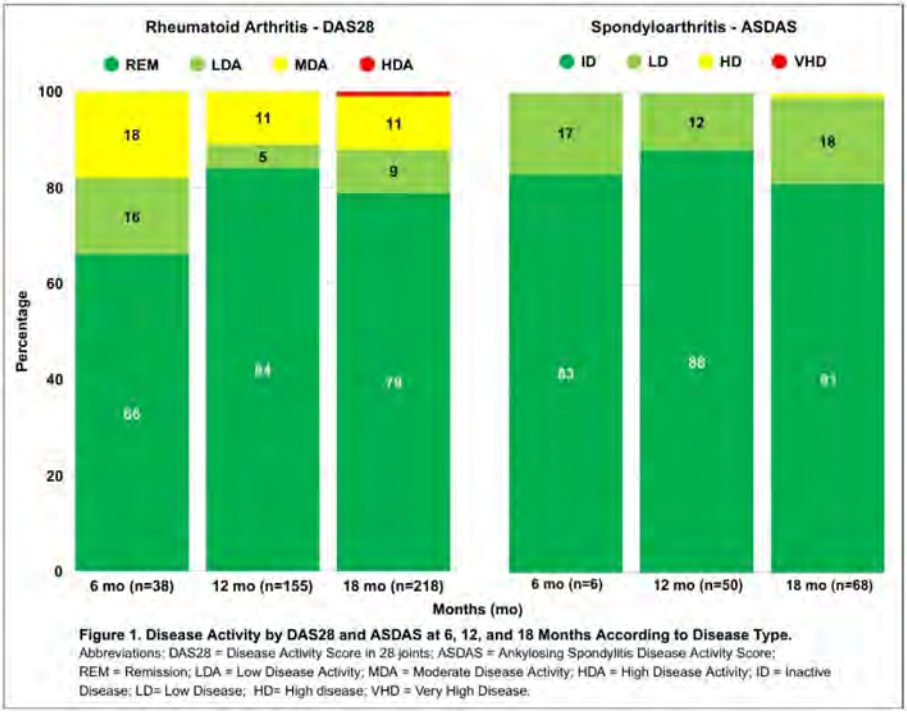


Figure 1. Disease Activity by DAS28 and ASDAS at 6, 12, and 18 Months According to Disease Type.
Abbreviations: DAS28 = Disease Activity Score in 28 joints; ASDAS = Ankylosing Spondylitis Disease Activity Score; REM = Remission; LDA = Low Disease Activity; MDA = Moderate Disease Activity; HDA = High Disease Activity; ID = Inactive Disease; LD= Low Disease; HD= High disease; VHD = Very High Disease.

Results: This cohort includes 1,456 patients with RA, of whom 402 are receiving BT, and 229 patients with SpA, of whom 146 are receiving BT. Over 18 months, BT doses were reduced in 65.9% (265) of RA patients and 50.6% (74) of SpA patients. BT was discontinued in 26 RA and 3 SpA patients. In RA, biologic dose reduction occurred in 58% of first-line and 24% of second-line therapies, with a failure rate of 17%. In SpA, reductions occurred in 65% of first-line and 24% of second-line therapies, with a 21% failure rate. Cost savings from dose reduction over 18 months were $854,874.8 for RA and $220,551.5 for SpA. Logistic regression was performed to identify variables associated with successful dose reduction. No statistically significant factors were found in RA. In SpA, shorter disease duration (< 5 years) was associated with lower odds of optimization (OR 0.40; 95% CI: 0.19–0.86; p=0.0192). HLA-B27 positivity was not significant but showed a trend toward lower odds of optimization (OR < 1, p = 0.1118).

Conclusion: This real-world study within a comprehensive care model showed that tapering or discontinuing biologic therapy in RA and SpA patients is feasible while maintaining disease control and achieving substantial cost savings, with a favorable economic impact on the healthcare system. Larger studies are needed to better identify factors associated with successful dose reduction or discontinuation of biologics.

Disclosure: E. Jauregui: AbbVie/Abbott, 6, Biopas, 6, Fresenius Kabi, 6, Novartis, 2; **D. Restrepo**: None; **B. Garzon**: None; **A. Atuesta**: None; **N. Correa**: None; **J. Barrera**: None; **A. Rubio**: None.

Abstract Number: 1042

Biosimilar adalimumab prescriptions increase before the CVS formulary change and decrease after

Eric Roberts[1], gabriela Schmajuk[2], Diana Ung[3], Mackenzie Clark[3] and Jinoos Yazdany[4], [1]University of California, San Francisco, SF, CA, [2]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [3]UCSF, San Francisco, [4]UCSF, San Francisco, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: In 2023 patent exclusivity for adalimumab expired and nine biosimilars were introduced to the U.S. market with a tenth launched in May 2024. The arrival of these biosimilars was eagerly awaited given the potential to reduce costs and improve access however uptake in the first year of availability was very low. CVS Caremark removed adalimumab from its national formulary in favor of adalimumab-adaz in April 2024. Here we assess how this decision changed the uptake of -adaz and other biosimilar adalimumab molecules in community rheumatology practices.

Methods: Data derive from RISE, a national EHR database from over 1100 US rheumatologists. We included patients age $\geq$ 18 years, with Medicare, Medicaid or private insurance, prescribed adalimumab (reference or biosimilar) in 2023 or the first 9 months of 2024 (due to data availability). Covariates include age, sex, race-ethnicity, and area deprivation index. Psoriatic

Table 1. Demographic and clinical characteristics of patients prescribed adalimumab or its biosimilars in RISE 2023-2024.

	Total (n=22,079)		No Biosimilar (n=18,593)		Ever Biosimilar (n=3,486)		
	N	%	N	%	N	%	SMD
Insurance							0.43
Medicaid	1,392	6.3	1,259	90.45	133	9.55	
Medicare	6,012	27.2	5,537	92.10	475	7.90	
Private	14,675	66.5	11,797	80.39	2,878	19.61	
Year*							1.08
2023	15,643	55.5	15,070	96.34	573	3.66	
2024 (first 9 months)	12,534	44.5	9,406	75.04	3,128	24.96	
Age							0.35
18-30	1,194	5.4	1,000	83.75	194	16.25	
31-50	6,174	28	4,997	80.94	1,177	19.06	
51-64	8,487	38.4	6,927	81.62	1,560	18.38	
>64	6,224	28.2	5,669	91.08	555	8.92	
Sex							0.11
Female	15,026	68.1	12,812	85.27	2,214	14.73	
Male	7,053	31.9	5,781	81.97	1,272	18.03	
Race-ethnicity							0.08
Black	1,520	6.9	1,284	84.47	236	15.53	
Asian	345	1.6	271	78.55	74	21.45	
Hispanic	830	3.8	701	84.46	129	15.54	
Other/mixed	169	0.8	145	85.80	24	14.20	
Unknown	4,792	21.7	4,113	85.83	679	14.17	
White	14,423	65.3	12,079	83.75	2,344	16.25	
Area Deprivation Index percentiles							0.16
25th (high SES)	4,519	20.5	3,628	80.28	891	19.72	
50th	6,364	28.8	5,344	83.97	1,020	16.03	
75th	5,723	25.9	4,898	85.58	825	14.42	
99th (low SES)	4,063	18.4	3,490	85.90	573	14.10	
Missing	1,410	6.4	1,233	87.45	177	12.55	
Diagnosis							0.05
RA	11,812	53.5	9,988	84.56	1,824	15.44	
PSA	2,204	10	1,855	84.17	349	15.83	
AS	2,824	12.8	2,330	82.51	494	17.49	
Other	5,239	23.7	4,420	84.37	819	15.63	

*Year calculation is based on receipt of biosimilar by patient in that year; all other calculations are ever receipt in 2023-2024 combined

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Count of distinct patients prescribed adalimumab or its biosimilars in RISE by year.

version	2023	2024*
adalimumab	15293	10285
adaz	43	1824
bwwd	138	624
atto	277	213
adbm	33	172
aqvh	48	131
ryvk	0	117
aacf	20	105
aaty	29	66
fkjp	8	33
afzb	0	2

*Data available through September 2024.

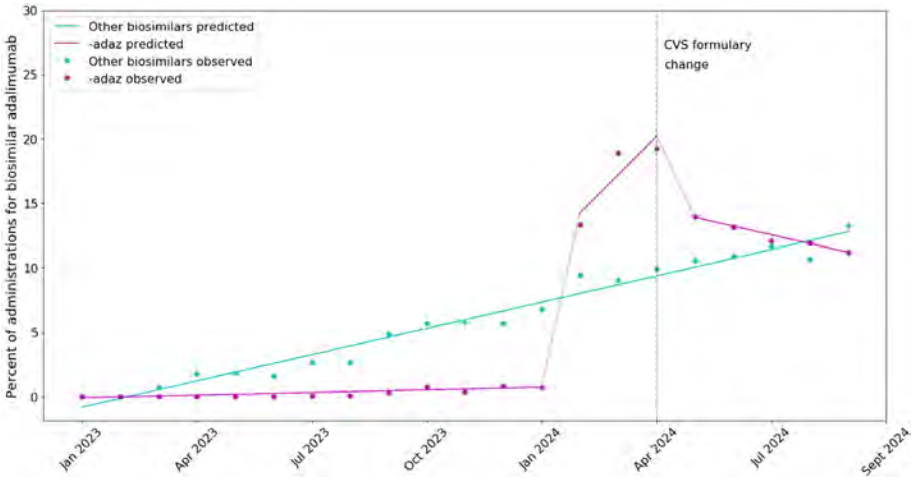


Figure 1. Interrupted time series analysis of the proportion of prescriptions dispensed that were adalimumab-adaz and linear regression of other adalimumab biosimilars by month. Each dot represents the actual proportion of prescriptions dispensed. Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

arthritis (PSA), ankylosing spondylitis (AS), or rheumatoid arthritis (RA) was defined by two ICD codes at least 30 days apart with patients assigned to one based on the clinically adjudicated hierarchy: PSA >AS >RA >other.

We tested for differences in ever use of a biosimilar between years as well as ever use in 2023/2024 combined across insurance coverage, demographics, and diagnosis using standardized mean differences. We used an interrupted time series (ITS) to model the effect of the CVS formulary change on the proportion of prescriptions (per month) for -adaz and all other biosimilars combined. Our final model is an ITS with interruptions at February 2024 and May 2024 to best characterize the observed pattern for -adaz, and a linear regression to characterize the other biosimilars (as ITS estimates suggested no discontinuity).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 22,079 patients received adalimumab or a biosimilar during our study period. In 2023 < 4% of patients received a biosimilar whereas in the first 9 months of 2024 this jumps to nearly 25% of patients (Table 1). 16.4% of patients with private insurance, 8.2% on Medicaid, and 6.5% with Medicare were ever on a biosimilar. There were only trivial differences by sex, race-ethnicity, ADI and diagnosis (Table 1). In 2024 most biosimilar prescriptions were -adaz (55.5%) followed by -bwwd (19%) (Table 2).

There were nearly no prescriptions for -adaz Jan 2023–Jan 2024 but a >13% jump in prescriptions in Feb 2024. Uptake continued to rise at the rate of nearly 3% per month through May 2024. There was a 9.3% drop from April to May with use continuing to decline thereafter at a rate of 0.7% per month (Figure 1). Prescriptions for the other biosimilars increased steadily at a rate of 0.7% per month over the study period.

Conclusion: The CVS formulary change had a dramatic effect on prescriptions. The increase started 2 months before the official date, which likely reflects proactive changes in ordering practices by clinicians and pharmacists. The large decrease immediately after the formulary change has not been reported elsewhere. This may reflect the nocebo effect, patient preference for certain reference product characteristics (e.g., citrate free formulation), or switching to a different product after the removal of manufacturer copay assistance programs.

Disclosure: E. Roberts: None; **g. Schmajuk**: None; **D. Ung**: None; **M. Clark**: None; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5.

Abstract Number: 1043

The Care Pathway and Treatment Patterns in Patients with Uncontrolled Gout: A Real-World Survey of Physicians In The United States

Gordon Lam[1], Menaka Bhor[2], James Hawthorne[2], Arinola Dada[3], Molly Edwards[4], Emily Goddard[4] and John Albert[5], [1]Arthritis & Osteoporosis Consultants of the Carolinas, Charlotte, NC, [2]Sobi Inc, Waltham, MA, [3]Overlake Arthritis and Osteoporosis Center, Bellevue, WA, [4]Adelphi Real World, Bollington, United Kingdom, [5]Rheumatic Disease Center, Glendale, WI

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Uncontrolled gout (UG) is a chronic, progressive, and systemic disease characterized by serum uric acid (sUA) >6 mg/dl and clinical manifestations such as tophi, flares and gouty arthropathy, despite the use of urate lowering therapy (ULT). Limited real-world evidence exists on the UG care pathway from diagnosis to long-term management. This study examined the care pathway and treatment patterns of patients with UG in the United States (US).

Methods: Data were extracted from the Adelphi Real World Gout Disease Specific Programme™, a cross-sectional survey, with retrospective data collection, of physicians (rheumatologists, nephrologists and primary care physicians [PCPs]) and their patients with gout in the US between August 2023 – March 2024. Physicians who participated in the study managed ≥8 patients with gout a month. UG was defined as sUA >6 mg/dl and at least one of the following: gouty arthropathy, ≥1 tophi, or ≥2 flares in the 12 months prior. Patients had to be receiving a ULT. Physicians reported patient demographics, treatment patterns, care pathway and clinical manifestations such as sUA levels, number of tophi and signs/symptoms at diagnosis, treatment initiation and data collection. All patients had a known treatment duration. Analyses were descriptive.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Overall, 88 physicians (45 rheumatologists, 22 nephrologists and 21 PCPs) reported data for 400 patients with UG. In patients who developed UG, there was a mean (standard deviation, SD) of 0.4 (1.3) years between a patients' first physician visit and gout diagnosis. At diagnosis mean (SD) patient age (n=310) was 53.0 (11.6) years, sUA level (n=330), number of tophi (n=173), and signs/symptoms (n=369) were 11.7 (4.7) mg/dL, 2.8 (2.9), and 2.7 (1.8), respectively.

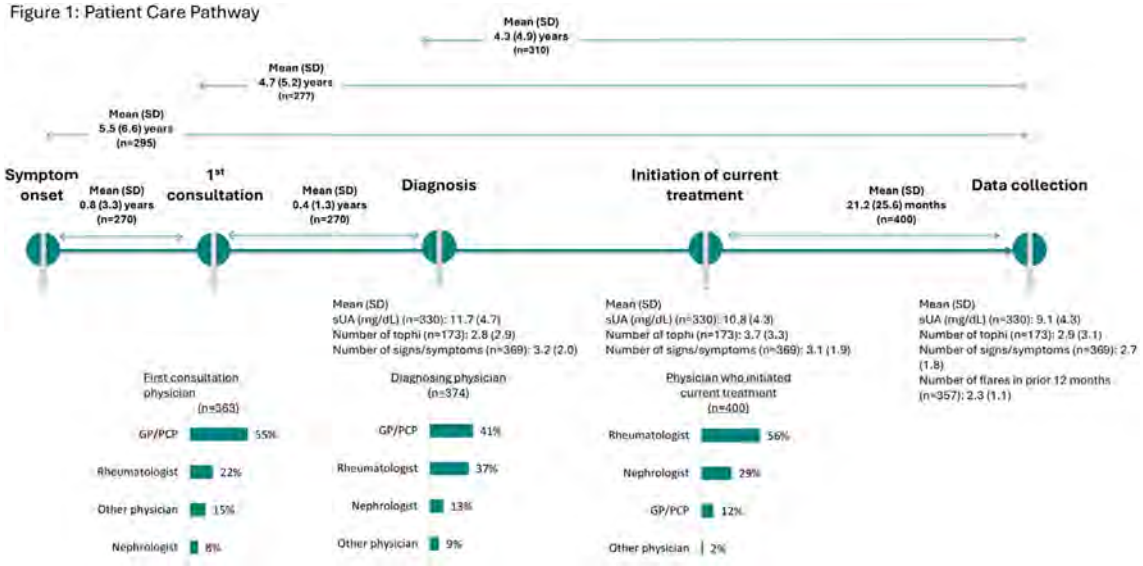
At initiation of current treatment (n=400), mean (SD) sUA level, number of tophi and signs/symptoms were 10.8 (4.3) mg/dL, 3.7 (3.3) and 3.1 (1.9), respectively. Rheumatologists prescribed the current treatment in 56% of patients, nephrologists 29% and PCPs 12%. The most common ULT was allopurinol (63%), followed by febuxostat (29%) and pegloticase (13%).

Table 1. Physician-Reported Patient Demographics At Gout Diagnosis

	Patients with uncontrolled gout (n=400)
Age at diagnosis	(n=310)
Mean (SD) years	53.0 (11.6)
Patient sex (male), n (%)	316 (79)
Race, n (%)	
White	244 (61)
Black or African American/African or Caribbean	113 (28)
South or Central American Native	11 (3)
East or Southeast Asian	10 (2)
American Indian, Indigenous American, or Alaska Native	9 (2)
South Asian (Indian subcontinent)	8 (2)
Middle Eastern or North African	7 (2)
Native Hawaiian or Pacific Islander	3 (1)
Other	3 (1)
Comorbidities present at diagnosis, n (%)	
Hypertension (≥140/90mmHg)	269 (67)
CKD	135 (34)
Obesity	129 (32)
Diabetes	119 (30)
Metabolic syndrome	118 (30)
CV disease	60 (15)
Hyperuricemia without gouty arthritis	40 (10)

CKD: chronic kidney disease. CV: cardiovascular disease. SD: standard deviation.

Figure 1: Patient Care Pathway



GP: general practitioner, PCP: Primary care physician, SD: standard deviation, sUA: serum urate acid. Other physicians include ER physician, Podiatrist, Nurse / nurse practitioner, Orthopaedic Surgeon, Other physician. Possible signs/symptoms: Cramp, Fatigue, Fever/flu like symptoms, Gouty arthropathy, defined clinically or radiographically as joint damage due to gout, High sUA (> 6mg/dL), Joint stiffness, Loss of movement/loss of mobility, Pain between flares (chronic pain), Sleep disturbance, Tender/swollen joint(s), Visible tophus(i), Warm joints, Other, None

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The most common reasons reported by physicians for choosing the current treatment were overall efficacy, long-term efficacy, and sUA reduction for 86%, 63%, and 54% of patients, respectively. However, these same characteristics were also reported by physicians as the most common areas where the treatments could perform better in 32%, 27%, 25% of patients respectively.

At data collection (n=400), after a mean (SD) of 21.2 (25.6) months on the current ULT, mean (SD) sUA level, number of tophi and signs/symptoms were 9.1 (4.3) mg/dL, 2.9 (3.1) and 2.7 (1.8), respectively. Mean (SD) number of flares (n=357) in the 12 months prior was 2.3 (1.1).

Conclusion: To our knowledge, this is the first real-world study examining the care pathway and treatment patterns of patients with UG. These data highlight that patients with UG experience extended periods of time with elevated sUA and UG clinical manifestations, despite receiving ULT for almost two years. Given that efficacy was noted as the most common reason for treatment choice and area of improvement, there is a need for optimal treatment utilization and alternative options for patients with UG.

Disclosure: G. Lam: AbbVie/Abbott, 1, 2, 6, Amgen, 2, 6, AstraZeneca, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Janssen, 1, 2, 6, Pfizer, 6, UCB, 1, 2, 6; **M. Bhor**: Sobi, 3; **J. Hawthorne**: Sobi Inc., 3; **A. Dada**: None; **M. Edwards**: AbbVie, 2, Adelphi Real World, 3; **E. Goddard**: Adelphi Real World, 3; **J. Albert**: Amgen, 1, 6.

Abstract Number: 1044

Analysis of Medicare and Medicaid Utilization and Expenditure of Newly Approved Biologics for Systemic Lupus Erythematosus Patients in the United States

Gunjan Rana[1], Mansi Mehta[1] and Joanne Cunha[2], [1]Saint Vincent Hospital, Worcester, MA, [2]BROWN MEDICINE, BROWN UNIVERSITY, Riverside, RI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine is a cornerstone in the treatment of Systemic Lupus Erythematosus (SLE), while corticosteroids and immunosuppressive agents are employed for moderate to severe disease [1]. The introduction of targeted biologic agents such as Belimumab for active SLE and lupus nephritis (LN), Anifrolumab for moderate to severe active SLE and Voclosporin for active LN, has expanded the therapeutic armamentarium. These advances, however, are accompanied by a substantial economic burden and increased utilization of biologic disease-modifying antirheumatic drugs (bDMARDs) [2].

Methods: We analyzed publicly available Medicare Part D and Medicaid data from the Centers for Medicare & Medicaid Services. We examined total spending, claims, beneficiary counts, average spending per claim, and per beneficiary for belimumab, anifrolumab, and voclosporin. Belimumab was FDA-approved in 2011, while anifrolumab and voclosporin were approved in 2021. Cost data from 2012–2021 were adjusted for inflation to 2022 dollars. Percent changes were calculated for 2012 and 2021 versus 2022. IRB oversight was not required due to the public nature of the data.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Nationwide analysis shows sharp increases in spending and utilization of these targeted therapies (Table 1). From 2012 to 2022, Medicare spending on belimumab rose by 7,047%, and Medicaid by 1,765%. Between 2021 and 2022, increases were more modest (14.83% Medicare; 19.10% Medicaid). Anifrolumab spending jumped by 932.8% in Medicare and 3,762.03% in Medicaid from 2021 to 2022, with substantial increases in claims and beneficiaries. Voclosporin spending increased by 190.45% in Medicare and 198.8% in Medicaid, with a doubling in claims and beneficiaries. Average spending per beneficiary notably rose, especially in Medicare.

Conclusion: The rapid growth in spending reflects expanded utilization of biologics (Figure 1). Although average spending per claim showed only modest changes, the substantial rise in spending per beneficiary highlights increased reliance on these newly approved therapies (Figure 2). Patients with severe SLE exhibit elevated rates of inpatient admissions and emer-

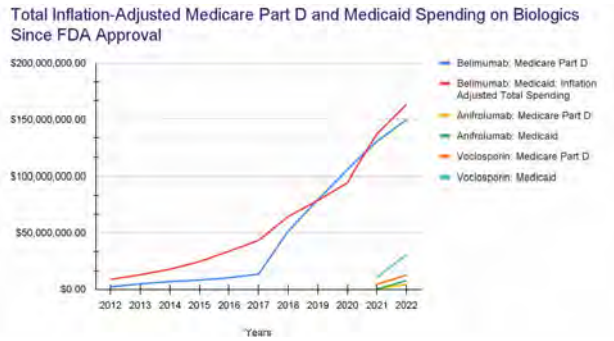


Figure 1: Total Inflation-Adjusted Medicare Part D and Medicaid Spending on Biologics Since FDA Approval

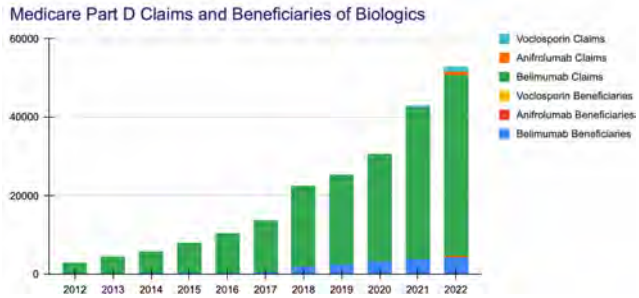


Figure 2: Medicare Part D Claims and Beneficiaries of Biologics

Table 1: Medicare Part D and Medicaid (Inflation-Adjusted) Spending on Biologics

Drug	Payer	2021 Spending	2022 Spending	Change (%)	2021 Avg Spending/Claim	2022 Avg Spending/Claim	Change (%)	2021 Avg Spending/beneficiary	2022 Avg Spending/beneficiary	Change (%)
Belimumab	Medicare Part D	$130,419,763	$149,755,010	15%	$4,453	$4,430	-1%	$34,213	$34,020	-1%
	Medicaid	$137,119,800	$163,307,664	19%	$3,565	$3,551	0%	-	-	-
Anifrolumab	Medicare Part D	$417,806	$4,315,125	933%	$5,034	$4,832	-4%	$11,292	$23,973	112%
	Medicaid	$198,214	$7,655,076	3762%	$3,887	$4,107	6%	-	-	-
Voclosporin	Medicare Part D	$4,351,893	$12,639,888	190%	$11,989	$11,286	-6%	$38,174	$55,929	47%
	Medicaid	$10,383,852	$31,026,992	199%	$11,760	$11,357	-3%	-	-	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

gency department utilization, significantly contributing to increased healthcare expenditures [3]. These findings underscore an urgent need for policy interventions aimed at regulating biologic drug pricing and improving access to effective SLE therapies, particularly for individuals insured through public programs such as Medicare and Medicaid [4].

[1] Siegel CH, Sammaritano LR. Systemic Lupus Erythematosus: A Review. JAMA 2024; 331: 1480–1491.

[2] Wu SS-J, Perry A, Tkacz J, et al. Clinical and economic characterization of mild, moderate, and severe systemic lupus erythematosus: Real-world observation across payer channels in the United States. J Manag Care Spec Pharm 2023; 29: 1010–1020.

[3] Murimi-Worstell IB, Lin DH, Kan H, et al. Healthcare utilization and costs of systemic lupus erythematosus by disease severity in the United States. J Rheumatol 2021; 48: 385–393.

[4] Pryor KP, Barbhaiya M, Costenbader KH, et al. Disparities in lupus and lupus nephritis care and outcomes among US Medicaid beneficiaries. Rheum Dis Clin North Am 2021; 47: 41–53.

Disclosure: G. Rana: None; **M. Mehta**: None; **J. Cunha**: None.

Abstract Number: 1045

Bayesian Analysis of Factors Associated with Romosozumab Adherence Among Early Adopters in Medicare Beneficiaries

Hongke Wu[1], Ye Liu[1], Tarun Arora[2] and Jeffrey Curtis[3], [1]University of Alabama at Birmingham, Birmingham, AL, [2]FASTER, Birmingham, AL, [3]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

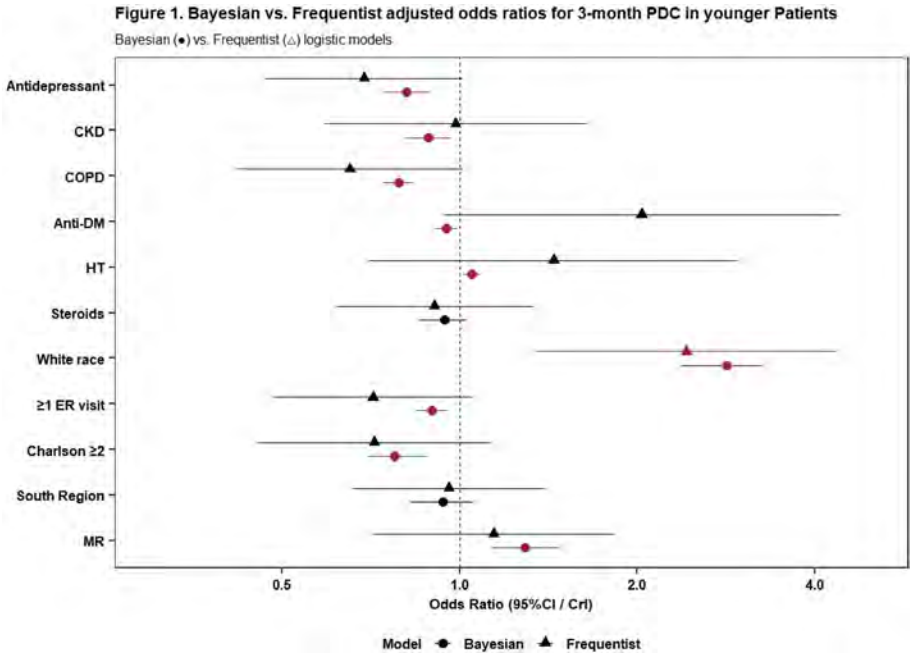
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: : Early adherence data for newly approved drugs guide clinical management, yet small cohorts hamper conventional analyses. Romosozumab (Romo), licensed April 2019 for high-risk postmenopausal osteoporosis, is an ideal example. This study is to identify determinants of Romo adherence using Bayesian logistic regression.

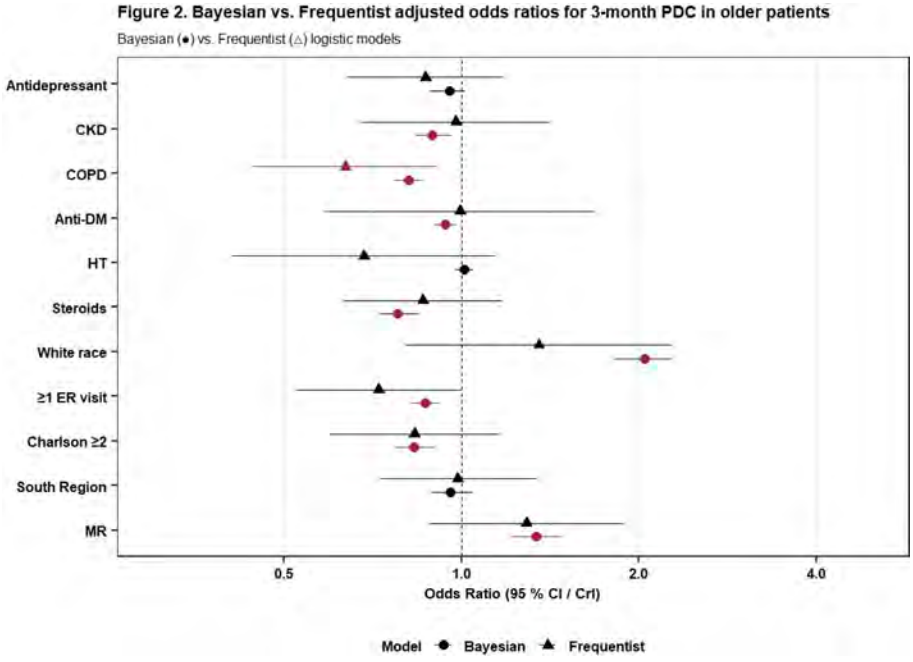
Methods: Medicare fee-for-service claims (2006–2022) were used to identify women ≥65 who began Romo in 2019 and maintained ≥4 years of continuous enrollment (≥3 baseline). Exclusion criteria include metastatic cancer, Paget's disease. A priori predictors – guided by literature and expert input – age groups (younger [≤75] vs older [>75]), race, regions, metropolitan residence (MR), Charlson Comorbidity Index (CCI), CKD, COPD, antidepressants (anti-DP), antidiabetics (anti-DM), hormone therapy (HT), steroids, and ER visits—were entered into frequentist and Bayesian logistic models. High adherence was proportional days covered (PDC) ≥80% in the first 3 months. Results are odds ratios (OR) with 95% confidence or credible intervals(CI/CrI).

Results: Among 1,777 initiators (younger: n = 752; older: n = 1,025), 77.8 % were indicated as high adherence. Frequentist analysis linked White race to higher adherence in younger women (OR 2.42, 95%CI [1.35–4.36]) and COPD to lower adherence in older women (0.64, [0.44–0.91]). Bayesian analysis revealed additional associations. In younger patients (Figure 1),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Notes: PDC: proportion of days covered; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HT: hormone therapy; ER: emergency room; MR: metropolitan region; CI: confidence interval; CrL: credit interval



Notes: PDC: proportion of days covered; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DM: diabetes mellitus; HT: hormone therapy; ER: emergency room; MR: metropolitan region; CI: confidence interval; CrL: credit interval

anti-DP (OR=0.81, 95% CrI: [0.74–0.89]), CKD (0.88 [0.81–0.97]), COPD (0.79 [0.74–0.83]), anti-DM (0.95 [0.91–0.99]), ER visits (0.90 [0.84–0.96]), and higher CCI (0.78 [0.70–0.88]) were associated with decreased adherence, while White race (2.83 [2.37–3.26]) , MR (1.29 [1.13–1.47]) and HT (1.05 [1.01–1.09]) were associated with high adherence. In older patients (Figure 2), CKD (0.89 [0.84–0.96]), COPD (0.81 [0.77–0.86]), steroids (0.78 [0.73–0.85]), and higher CCI (0.83 [0.77–0.90]) were associated with decreased adherence, while White race (2.05 [1.82–2.28]) and MR (1.34 [1.22–1.48]) were associated with high adherence.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Bayesian analysis identified additional adherence factors among early Romo adopters compared with frequentist models, including anti-DP and HT. Future research should consider Bayesian modeling when studying medication adherence, particularly when sample size may be limited.

Disclosure: H. Wu: None; **Y. Liu**: Amgen, 5; **T. Arora**: Amgen, 5; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 1046

Cannabis Knowledge, Attitudes, and Practices Among Rheumatology Providers: Implications for Clinical Care and Education

Joanna Zeiger[1], Patti Katz[2], Mary-Ann Fitzcharles[3], Stuart Kassan[4], Teresa Simon[5] and Kaleb Michaud[6], [1]Canna Research Foundation, Boulder, CO, [2]UCSF, San Rafael, CA, [3]McGill University, Montreal-West, Canada, [4]National Jewish Health, Denver, CO, [5]Physicians Research Center, LLC, Toms River, NJ, [6]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: As medical cannabis becomes increasingly integrated into clinical care, healthcare providers—particularly those managing chronic rheumatologic conditions—must navigate wide-ranging levels of knowledge, attitudes, and prescribing comfort. This international study examined how rheumatology providers' cannabis-related knowledge and attitudes influence clinical practices, including theoretical prescribing behaviors, dosing decisions, and patient communication.

Methods: Between November 14, 2023, and February 3, 2025, 281 international rheumatologists and rheumatology-affiliated clinicians completed a cross-sectional survey. A six-item cannabis knowledge score (range 0–6) was standardized and trichotomized into low (n = 36, 15.9%), average (n = 156, 69.0%), and high (n = 72, 31.9%) knowledge-level groups. Two-step cluster analysis of 11 cannabis attitudinal items yielded three profiles:

Progressive (n = 90, 39.8%)—supportive of cannabis and policy reform;

Unsure (n = 91, 40.3%)—cautious, ambivalent, and often uncertain; and

Traditional (n = 84, 37.2%)—more skeptical, concerned about harms, and less supportive of legalization. Eight clinical practice outcomes and 10 theoretical dosing practices were analyzed using chi-square.

Results: Respondents were primarily female (61.2%) and white (78.9%), with most practicing in urban (87%) and academic (68.4%) settings in the United States (47%). Compared to lower cannabis knowledge, higher knowledge levels were significantly associated with greater comfort discussing cannabis (67.5% vs. 37.0%, $p < .001$), awareness of contraindications with other medications (39.5% vs. 26.0%, $p < .05$), believe it is opioid sparing (71.9% vs. 56.2%, $p< 0.001$) and recommending CBD (47.3% vs. 36.1%, $p < 0.05$) and THC (27.4% vs. 17.8%, $P< 0.05$). A preference for 'start low and build' dosing was more common among those with high knowledge (73.3%) compared to low knowledge (47.9%, $p < .01$). Among

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Knowledge level by practice outcomes and theoretical dosing in rheumatology providers.

		Knowledge level		
Practice		Low (N=73, 27.7%)	Average N=75, 28.4%)	High (N=116, 43.9%)
		N(%)		
Comfort discussing cannabis‡	Yes	27 (37.0)	46 (61.3)	77 (67.5)
Aware of contraindications with other meds	Yes	19 (26.0)	23 (30.7)	45 (39.5)
Recommends CBD†	Yes	26 (36.1)	40 (54.8)	53 (47.3)
Recommends THC†	Yes	13 (17.8)	16 (21.3)	31 (27.4)
Prescribes opioids	Yes	23 (31.5)	25 (33.3)	38 (33.0)
Believes in opioid sparing‡	Yes	41 (56.2)	49 (65.3)	82 (71.9)
Used Cannabis‡	Yes	16 (21.9)	16 (21.3)	53 (46.1)
Asks about cannabis use	Never/rarely	29 (40.3)	16 (21.3)	36 (31.0)
	Sometimes	30 (41.7)	40 (53.3)	55 (47.4)
	Often/Always	13 (18.1)	19 (25.3)	25 (21.6)
Theoretical dosing				
Starting dose CBD	1-5 mg	4 (5.6)	9 (12.3)	24 (20.9)
	6-10 mg	3 (4.2)	4 (5.5)	6 (5.2)
	11-20 mg	0 (0.0)	2 (2.7)	3 (2.6)
	50+ mg	1 (1.4)	0 (0.0)	1 (0.9)
	Unsure	63 (88.7)	58 (79.5)	81 (70.4)
Starting dose THC*	1-5 mg	3 (4.2)	10 (13.5)	23 (20.4)
	6-10 mg	1 (1.4)	0 (0.0)	4 (3.5)
	11-20 mg	1 (1.4)	1 (1.4)	0 (0.0)
	50+ mg	0 (0.0)	0 (0.0)	0 (0.0)
	Unsure	66 (93.0)	63 (85.1)	86 (76.1)
Maximum dose THC	1-5 mg	0 (0.0)	1 (1.4)	3 (2.6)
	11-20 mg	4 (5.8)	4 (5.4)	10 (8.7)
	20-50	1 (1.4)	1 (1.4)	5 (4.3)
	50+ mg	0 (0.0)	1 (1.4)	1 (0.9)
	Unsure	64 (92.8)	67 (90.5)	96 (83.5)
Maximum dose CBD	6-10 mg	0 (0.0)	1 (1.3)	1 (0.9)
	11-20 mg	5 (7.0)	3 (4.0)	5 (4.5)
	20-50	1 (1.4)	3 (4.0)	9 (8.0)
	50+ mg	1 (1.4)	1 (1.3)	7 (6.3)
	Unsure	64 (90.1)	67 (89.3)	90 (80.4)
Times Per Day CBD	1	4 (5.6)	5 (6.8)	6 (5.2)
	2	8 (11.1)	8 (11.0)	12 (10.4)
	3	0 (0.0)	2 (2.7)	9 (7.8)
	4+	0 (0.0)	0 (0.0)	5 (4.3)
	Unsure	60 (83.3)	58 (79.5)	83 (72.2)
Times Per Day THC	0	1 (1.4)	0 (0.0)	0 (0.0)
	1	2 (2.8)	4 (5.5)	9 (7.8)
	2	4 (5.6)	5 (6.8)	7 (6.1)
	3	0 (0.0)	2 (2.7)	6 (5.2)
	4+	0 (0.0)	1 (1.4)	4 (3.5)
	Unsure	64 (90.1)	61 (83.6)	89 (77.4)
Recommend CBD only	Yes	17 (23.3)	22 (29.3)	20 (17.2)
Recommend THC only	Yes	0 (0.0)	0 (0.0)	0 (0.0)
Recommend THC and CBD	Yes	1 (1.4)	6 (8.0)	12 (10.3)
Start low and build†	Yes	35 (47.9)	47 (62.7)	85 (73.3)
Start high	Yes	0 (0.0)	0 (0.0)	0 (0.0)
Would not prescribe	Yes	36 (49.3)	44 (58.7)	58 (50.0)

*P<0.05; †P<0.01; ‡P<0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Attitudes clusters level by practice outcomes and theoretical dosing in rheumatology providers

		Attitudes Cluster		
		Progressive (N=90, 34.0%)	Unsure (N=91, 34.3%)	Traditional (N=84, 31.7%)
		N(%)		
Comfort Talking to patients	Yes	58 (64.4)	49 (54.4)	46 (55.4)
Aware of contraindications with other meds	Yes	26 (28.9)	27 (30.3)	31 (36.9)
Recommend CBD	Yes	51 (58.6)	41 (45.6)	28 (34.1)
Recommend THC*	Yes	29 (33.0)	19 (21.1)	12 (14.5)
Think cannabis is opioid sparing‡	Yes	75 (83.3)	57 (64.0)	41 (48.8)
Prescribes opioids	Yes	25 (27.8)	37 (41.1)	27 (32.1)
Ever used cannabis personally‡	Yes	44 (48.9)	25 (27.8)	19 (22.6)
How often asks patient about cannabis use	Never/Rarely	29 (32.2)	27 (30.0)	24 (28.6)
	Sometimes	42 (46.7)	48 (53.3)	37 (44.0)
	Often/Always	19 (21.1)	15 (16.7)	23 (27.4)
Starting dose CBD	1-5 mg	17 (19.3)	12 (13.5)	9 (10.7)
	6-10 mg	3 (3.4)	5 (5.6)	4 (4.8)
	11-20 mg	2 (2.3)	1 (1.1)	2 (2.4)
	50+ mg	1 (1.1)	1 (1.1)	0 (0.0)
	Unsure	65 (73.9)	70 (78.7)	69 (82.1)
Starting dose THC	1-5 mg	16 (18.2)	11 (12.6)	8 (9.5)
	6-10 mg	2 (2.3)	1 (1.1)	1 (1.2)
	11-20 mg	0 (0.0)	0 (0.0)	2 (2.4)
	50+ mg	0 (0.0)	0 (0.0)	0 (0.0)
	Unsure	70 (79.5)	75 (86.2)	73 (86.9)
Maximum dose THC	1-5 mg	3 (3.3)	0 (0.0)	1 (1.2)
	11-20 mg	7 (7.8)	4 (4.6)	6 (7.2)
	20-50	1 (1.1)	3 (3.4)	2 (2.4)
	50+ mg	2 (2.2)	0 (0.0)	0 (0.0)
	Unsure	77 (85.6)	80 (92.0)	74 (89.2)
Maximum dose CBD*	6-10 mg	1 (1.1)	2 (2.3)	0 (0.0)
	11-20 mg	3 (3.4)	4 (4.5)	6 (7.2)
	20-50	4 (4.5)	4 (4.5)	4 (4.8)
	50+ mg	8 (9.0)	0 (0.0)	0 (0.0)
	Unsure	73 (82.0)	78 (88.6)	73 (88.0)
Times Per Day CBD	1	4 (4.5)	5 (5.7)	5 (6.0)
	2	9 (10.1)	12 (13.6)	8 (9.5)
	3	6 (6.7)	3 (3.4)	1 (1.2)
	4+	3 (3.4)	0 (0.0)	1 (1.2)
	Unsure	67 (75.3)	68 (77.3)	69 (82.1)
Times Per Day THC	0	0 (0.0)	1 (1.1)	0 (0.0)
	1	3 (3.4)	4 (4.6)	8 (9.5)
	2	8 (9.0)	6 (6.9)	1 (1.2)
	3	4 (4.5)	2 (2.3)	2 (2.4)
	4+	2 (2.2)	0 (0.0)	2 (2.4)
	Unsure	72 (80.9)	74 (85.1)	71 (84.5)
Recommend CBD only	Yes	21 (23.3)	26 (28.6)	18 (21.4)
Recommend THC only	Yes	0 (0.0)	0 (0.0)	0 (0.0)
Recommend THC and CBD	Yes	7 (7.8)	5 (5.5)	7 (8.3)
Start low and build*	Yes	66 (73.3)	57 (62.6)	46 (54.8)
Start high	Yes	0 (0.0)	0 (0.0)	0 (0.0)
Would not prescribe	Yes	42 (46.7)	46 (50.5)	50 (59.5)

*P<0.05; †P<0.01; ‡P<0.001

attitudinal clusters, Progressive providers were more likely to recommend CBD (58.6%) and THC (33.0%) compared to Traditional providers (34.1% and 14.5%, respectively, $p < .05$). Progressive providers also reported higher opioid-sparing beliefs (83.3% vs. 48.8%, $p < .001$). Uncertainty regarding dosing was common across all clusters and knowledge groups, particularly regarding THC and CBD starting and maximum doses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Among rheumatology providers, both cannabis-related knowledge and attitudes significantly influence clinical perspectives and theoretical prescribing decisions. Educational efforts should address not only knowledge gaps but also attitudinal ambivalence to support informed, patient-centered cannabis care.

Disclosure: J. Zeiger: None; **P. Katz**: None; **M. Fitzcharles**: None; **S. Kassan**: None; **T. Simon**: Bristol-Myers Squibb(BMS), 2, Janssen, 2, Merck/MSD, 2; **K. Michaud**: None.

Abstract Number: 1047

Primary Care Perspectives on Giant Cell Arteritis: Diagnostic Considerations, Referral Challenges, and Opportunities for Fast-Track Pathways in the U.S.

Ellen Ann Sockman[1], **Jon Golenbiewski**[1] and Rachel Wolfe[2], [1]Wake Forest University School of Medicine, Winston-Salem, NC, [2]Wake Forest University School of Medicine, Winston-Salem

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant Cell Arteritis (GCA) is a medical emergency that can lead to irreversible vision loss without prompt recognition and treatment. Primary care providers (PCPs) often serve as the initial evaluators of suspected GCA. To date, no U.S. study has evaluated how PCPs approach GCA evaluation and management. This study aims to understand PCPs' perspectives, diagnostic and referral practices, and barriers they face in managing suspected GCA—highlighting opportunities to streamline subspecialty care and reduce risk for adverse outcomes.

Methods: A 35-question electronic survey was distributed to 350 PCPs as part of a large health system in central North Carolina. The survey explored awareness of GCA, diagnostic tools, treatment approaches, referral workflows, and perceptions of system-level challenges. Responses were analyzed descriptively.

Results: Forty-seven providers responded (13.4% response rate), including internal medicine and family medicine providers in academic (56.5%) and community (43.5%) settings. Most respondents (n=42, 89.2%) would sometimes or rarely consider GCA as a possible diagnosis. Confidence in diagnosing GCA was moderate with a mean of 6.2 (95% CI = 5.7 - 6.7) and slightly lower for management with a mean of 5.2 (95% CI = 4.6 - 5.8). Eighty percent of providers (n=38) initiate high dose glucocorticoids (≥1 mg/kg) when GCA is suspected with 58.3% (n=27) of respondents continuing until specialist evaluation. Most respondents referred to specialists for management of GCA; however, 2.1% (n=1) of PCPs manage patients independently. Over half (n=29, 63%) were unaware of biologic therapies as treatment options for GCA.

Referral pathways varied: 68.1% (n=32) referred to ophthalmology when vision loss was suspected, yet only 44.7% (n=21) involved the emergency department. Wait times to see rheumatology were frequently prolonged, with 51.1% (n=24) reporting delays greater than 4 weeks. Coordinating referrals was cited as difficult by 75.6% (n=35) of respondents, often requiring extra time and resources to have patients evaluated. Communication is rare among referring providers as only 19.1% (n=9) reported direct communication with an on-call provider. Respondents expressed strong interest (n=45, 95.7%) in a fast-track clinic or protocol to improve triage and access for suspected GCA cases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

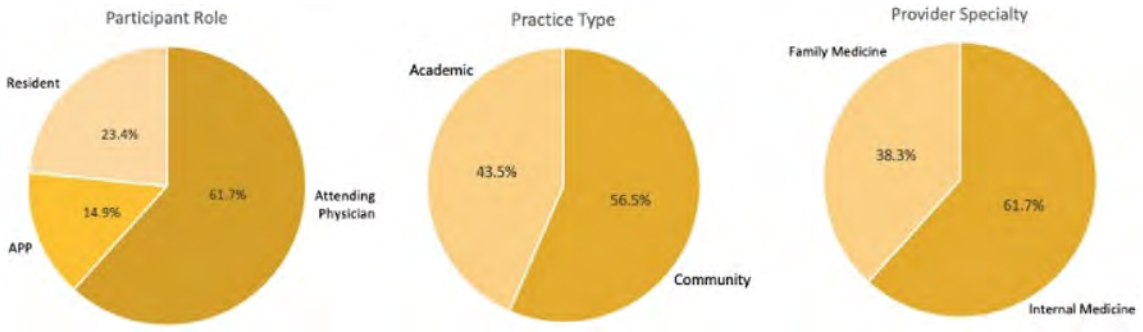


Figure 1 - Participant Demographics

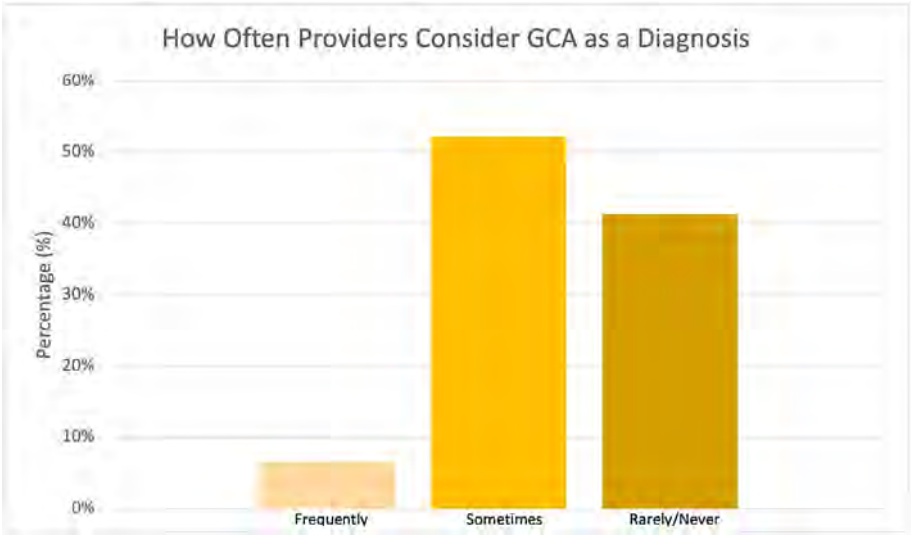


Figure 2 - Frequency Providers Consider GCA as a Diagnosis

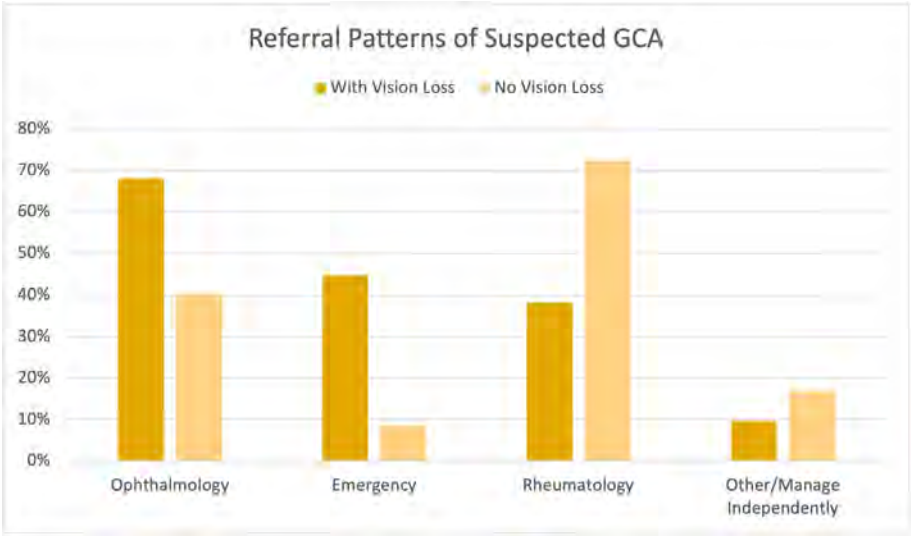


Figure 3 - Referral Patterns for Suspected GCA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This is the first U.S.-based study to explore primary care experiences in managing suspected GCA. Our study highlights that GCA remains an infrequently considered diagnosis amongst PCPs, with variability in referral patterns and steroid management, underscoring the need for education on its recognition, diagnosis, and treatment. Limited awareness regarding the use of biologic therapies in GCA and their steroid-sparing potential highlights an important educational gap. Additionally, our findings suggest that system-level interventions—such as fast-track clinics or clearer referral protocols—may support PCPs in delivering timely, coordinated care and reducing the risk of vision loss and complications of prolonged steroid use. This study was limited by a small sample size, low response rate and geographically narrow focus that may limit generalizability.

Disclosure: E. Sockman: None; **J. Golenbiewski**: None; **R. Wolfe**: None.

Abstract Number: 1048

Impact of Hydroxychloroquine Usage on QTc in Veterans with Rheumatic Musculoskeletal Disease

Malika Ibrahim[1], Samuel Good[2], Victor Tran[3], David Chetrit[4], Michael McClean[5], Myung Shin Sim[6], Hannah Kang[1], Jennifer Barton[7], Meika Fang[8], Angelo Gaffo[9], fadi Hage[10], cynthia Jackevicius[5], Michael Pillinger[11], gabriela Schmajuk[12], Jasvinder Singh[13], Alberta Warner[14], Neal Yaun[15] and John FitzGerald[16], [1]David Geffen School of Medicine at University of California, Los Angeles, Department of Medicine, Los Angeles, CA, [2]David Geffen School of Medicine at University of California, Los Angeles, Department of Medicine, Division of Rheumatology, Los Angeles, CA, [3]David Geffen School of Medicine at University of California, Los Angeles, Department of Medicine, Costa Mesa, CA, [4]Carolina Health Specialists, Myrtle Beach, SC, [5]Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, [6]West LA VA Medical Center, Los Angeles, [7]VA Portland Health Care System/OHSU, Portland, OR, [8]VA Greater Los Angeles/UCLA, Los Angeles, CA, [9]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [10]VA Birmingham health care, Birmingham, AL, [11]New York University Grossman School of Medicine, New York,, NY, [12]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [13]Baylor College of Medicine, Houston, TX, [14]VA Greater Los Angeles/UCLA, Los Angeles, [15]UCSF / SFVA, San Francisco, [16]UCLA, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is widely used for rheumatic diseases, but data on its cardiac safety, particularly QTc prolongation, remains limited. Concerns about HCQ inducing QTc prolongation, which can lead to Torsades de pointes and sudden death, arose during the COVID-19 pandemic, though extrapolating from sick patients with COVID to patients with stable RMD patients remains unclear.

Methods: We abstracted data from Veterans with RA, SLE, or Sjögren's syndrome (based on ICD-10 diagnostic codes) from 3 VA sites (Sept 2016–Mar 2022), aged 18–85 with ≥1 ECG.

Bazett-corrected QTc were abstracted. ECGs with Afib/flutter, pacing, or 300 > QTc > 600 ms were excluded. To define exposure to HCQ, windows were defined using days supplied on dispensed prescriptions (and then multiplied by 1.2 so as not to assume 100% adherence). Primary outcome was QTc > 500 ms. Secondary QTc outcomes included QTc > 400 ms and QTc mean. Multivariate models adjusted for age, gender, race/ethnicity, comorbidities, and concomitant QT-prolonging drugs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

For a subset of Veterans from the LA VA, we had HCQ blood levels and correlated with QTc (ECG obtained within 60-days of the lab value).

Variable	All (N=4,774)	SLE (N=452)	RA (N=3,243)	Sjögren's (N=1,287)
Sex				
Male, n (%)	3,981 (83.4%)	244 (54.0%)	2,801 (86.4%)	1,047 (81.4%)
Age and BMI				
Age at first ECG, mean ± SD (years)	63.7 ± 11.7	54.8 ± 14.3	64.6 ± 11.1	64.0 ± 11.4
BMI, mean ± SD (kg/m²)	29.7 ± 6.0	29.4 ± 6.4	29.6 ± 5.9	30.3 ± 6.2
HCQ Use				
HCQ user ever, n (%)	1,617 (33.9%)	285 (63.1%)	1,326 (40.9%)	185 (14.4%)
ECG count, mean ± SD	6.0 ± 9.0	6.3 ± 10.1	6.1 ± 9.2	6.0 ± 8.7
Race, n (%)				
White	3,308 (69.3%)	264 (58.4%)	2,289 (70.6%)	883 (68.6%)
Black	654 (13.7%)	102 (22.6%)	412 (12.7%)	179 (13.9%)
Asian	164 (3.4%)	25 (5.5%)	95 (2.9%)	55 (4.3%)
All Other	161 (4.4%)	27 (4.8%)	146 (4.5%)	55 (4.2%)
Null	440 (9.2%)	39 (8.6%)	301 (9.3%)	115 (8.9%)
Hispanic or Latino, n (%)	478 (10.0%)	62 (13.7%)	317 (9.8%)	126 (9.8%)
Comorbiditics, n (%)				
Hypertension	3,652 (76.5%)	308 (68.1%)	2,504 (77.2%)	994 (77.2%)
Hyperlipidemia	3,428 (71.8%)	269 (59.5%)	2,362 (72.8%)	925 (71.9%)
Heart Failure	979 (20.5%)	102 (22.6%)	677 (20.9%)	234 (18.2%)
Diabetes Mellitus	2,709 (56.7%)	241 (53.3%)	1,827 (56.3%)	765 (59.4%)
Coronary Artery Disease	369 (7.7%)	33 (7.3%)	240 (7.4%)	105 (8.2%)
CKD Stage 3 or worse	1,471 (30.8%)	147 (32.5%)	1,016 (31.3%)	386 (30.0%)
ESRD	143 (3.0%)	36 (8.0%)	84 (2.6%)	28 (2.2%)
Tobacco Use	1,692 (35.4%)	142 (31.4%)	1,212 (37.4%)	394 (30.6%)
Study Site, n (%)				
Portland	1,043 (21.8%)	49 (10.8%)	623 (19.2%)	406 (31.5%)
San Francisco	2,976 (62.3%)	305 (67.5%)	2,193 (67.6%)	617 (47.9%)
Greater Los Angeles	755 (15.8%)	98 (21.7%)	427 (13.2%)	264 (20.5%)

Baseline Characteristics (MUSE Cohort)

ECG Group	Never HCQ	HCQ Users (Ever)			
		Never on HCQ	Both (On & Off HCQ)	Not on HCQ	On HCQ
Number of ECGs	15,854	2,852		2,265	2,028
Number of Veterans	3,157	769		432	416
Mean QTc, ms (std. err.)	439 (1.2)	437 (1.6)	446 (1.8) [§§]	449 (1.8) †††	446 (1.8) †††
Proportion ECGs with QTc > 500 ms (%)	5.4 (0.1)	3.7 (0.1)	7.2 (1.1)	8.5 (1.1)	5.7 (1.1)
Proportion ECGs with QTc > 400 ms (%)	44.5 (1.8)	41.8 (2.3)	55.9 (2.6) †††	59.6 (2.7) †††	55.5 (2.7) †††

[§§] p < 0.001 for selected group vs. referent never HCQ user
[†††] p < 0.001 for selected group vs. referent never HCQ user

Adjusted QTc outcomes (MUSE Cohort)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: HCQ use was highest in Veterans with SLE (63%), followed by RA (41%) and Sjögren's (14%). Across the 3 VA sites, 4,774 Veterans had 24,549 ECGs. Of 3,157 Veterans never on HCQ, 5.4% of ECGs showed QTc >500 ms. 769 veterans were on HCQ at some time during the study period, but never on HCQ when ECG was obtained, and had the lowest proportion of QTc > 500 ms (3.7%). Veterans who were intermittently off and on HCQ at the time of ECG recordings had the highest proportion of QTc >500 (7.2% and 8.5%, respectively). While Veterans who were always on HCQ at time of ECG had similar proportion (5.7%) of QTc >500 to those Veterans never on HCQ. Differences between the proportion of QTc prolongation < 500 ms did not differ statistically across the HCQ exposure groups. Differences between the groups were statistically significant for the secondary outcomes of QTc > 400 ms and QTc mean (Refer to Table 2).

Among 35 patients with paired HCQ blood levels and ECGs, for each 100 ng/mL rise in HCQ level was linked to a 9.4 ms increase in QTc ($r = 0.50$, $p = 0.0005$). Eg. 70 kg patient taking 200 mg daily (2.9 mg/kg/day) might see a 6–12 ms QTc increase. This suggests a modest, dose-dependent QTc effect, consistent across cohorts. Of note, none of the 35 patients had a therapeutic HCQ level (suggestive of low adherence). Poor adherence was further noted in our overall cohort with a low median annual MPR of 72% yielding a median estimated dose of 2.3 mg/kg/day.

Conclusion: In this large, multi-site VA study involving patients with rheumatic diseases, HCQ use was associated with a small but statistically significant, dose-dependent QTc prolongation. Although the absolute QTc increase was small and unlikely to affect most patients, these results support targeted ECG monitoring, particularly in older or female patients, or in those receiving other QT prolonging medications or with CKD or cardiac comorbidities. These results also suggest the potential value of HCQ drug level monitoring where the detection of supratherapeutic HCQ levels should prompt ECG evaluation.

Disclosure: M. Ibrahim: None; **S. Good**: None; **V. Tran**: None; **D. Chetrit**: None; **M. McClean**: None; **M. Sim**: None; **H. Kang**: None; **J. Barton**: None; **M. Fang**: None; **A. Gaffo**: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **f. Hage**: None; **c. Jackevicius**: None; **M. Pillinger**: Amgen, Federation Bio, Fortress Biotech, Scilex, and SOBI, 2, Convergence Bio, 2; **g. Schmajuk**: None; **J. Singh**: American College of Rheumatology, 2, Atai life sciences, Kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 11, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Putnam associates, Focus forward, Navigant consu, 2, GeoVax Labs, Adaptimmune Therapeutics, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp., Aebona Pharma, 11, Intuitive Surgical Inc./Philips Electronics North America, 12, food and beverage payments, ROMTech, Atheneum, Clearview healthcare partners, Yale, Hulio, Horizon Pharmaceuticals/DINORA, ANI/Exeltis, USA Inc., Frictionless Solutions, Schipher, 2, Spherix, MedIQ, Jupiter Life Science, UBM LLC, Trio Health, Medscape, WebMD, and Practice Point communications; the National Institutes of Health, 2, Zimmer Biomet Holdings, 5; **A. Warner**: None; **N. Yaun**: None; **J. FitzGerald**: None.

Abstract Number: 1049

Provider Characteristics and Beliefs and Patient Factors Associated with Long-term Glucocorticoid Use in Patients with Rheumatoid Arthritis

Michael George[1], George Reed[2], Kevin Kane[3], Dimitrios Pappas[4] and Joel Kremer[5], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Massachusetts Chan Medical School, Worcester, MA, [3]University of Massachusetts Lowell, Lowell, MA, [4]CorEvitas, New York, NY, [5]The Corrona Research Foundation, Delray Beach, FL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1038–1054) Health Services Research Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Guidelines recommend limiting glucocorticoid (GC) use in RA, but 30% of patients continue long-term GCs. Little is known about the influence of provider attitudes and characteristics on prescribing patterns. We conducted a provider survey nested within a RA registry to identify provider factors associated with GC use.

Methods: A survey was sent to providers contributing patients to the prospective, observational, CorEvitas Rheumatoid Arthritis registry, capturing demographics, provider concerns about the safety of different medications, and a range of healthcare-related and non-healthcare related beliefs. We then identified patients with RA initiating a new biologic or Janus kinase inhibitor (JAKi) who remained on the same therapy at a 6 month follow-up visit, using the first qualifying observation per patient. Patient factors associated with GC use 6 months after treatment initiation were assessed using a mixed effects logistic regression model clustered by provider. Similar models limited to patients of the survey responders assessed whether different provider characteristics and beliefs were associated with GC prescribing 6 months after treatment initiation, adjusting for patient factors. All models were weighted for number of patients per provider.

Results: Among 256 active providers contributing patients to the registry, 92 (36%) responded to the survey and 81 had patients meeting all inclusion criteria. These 81 responders had 3966 qualifying patients, while 164 non-responders had 3219 qualifying patients. Among all 7185 patients, higher baseline disease activity, less improvement at 6 months, age

Table 1: Association between patient characteristics and provider survey response (vs. non-response) with ongoing glucocorticoid use 6 months after biologic or JAKi initiation

	N (%) or mean (SD) N = 7,185 patients	Adjusted OR (95% CI)
Patient demographics and clinical characteristics at baseline		
Female	5556 (77.6%)	0.88 (0.73-1.05)
Age, years		
≤45	982 13.7%)	Reference
46-55	1572 (21.9%)	**0.75 (0.58-0.97)**
56-65	2119 (29.6%)	**0.70 (0.54-0.90)**
66-75	1761 (24.6%)	**0.70 (0.53-0.91)**
>75	728 (10.2%)	0.94 (0.67-1.31)
Year (per 5 year increase)	Range 2002-2024	**0.83 (0.74-0.93)**
Region		
Northeast	2026 (28.3%)	Reference
Midwest	701 (9.8%)	**0.45 (0.22-0.95)**
South	2512 (35.1%)	**0.63 (0.42-0.95)**
West	1923 (26.9%)	0.77 (0.51-1.16)
Patient disease and treatment characteristics		
RA disease duration, years	Mean 9.7 (SD: 9.8)	**1.01 (1.01-1.02)**
Clinical disease activity index (CDAI) at baseline		
Remission	455 (6.4%)	**0.49 (0.35-0.68)**
Low disease activity	1468 (20.5%)	Reference
Moderate disease activity	2441 (34.1%)	0.98 (0.78-1.22)
High disease activity	2798 (39.1%)	**1.51 (1.15-1.98)**
Improvement in CDAI at 6 months, per unit change*	Mean 7.36 (SD: 13.2)	**0.98 (0.98-0.99)**
Number prior biologics/JAKi	Mean 1.3 (SD: 1.5)	**1.07 (1.01-1.14)**
DMARD initiated		
TNF inhibitor	4106 (57.3%)	Reference
Biologic other than TNF inhibitor	2236 (31.2%)	**1.40 (1.17-1.67)**
Janus kinase inhibitor	820 (11.4%)	1.03 (0.76-1.39)
Opioid use at baseline		
No	4992 (69.7%)	Reference
Yes	2170 (30.3%)	1.14 (0.98-1.34)

Adjusted odds ratio from a multivariable mixed effects logistic regression model clustering on provider, with weighting to account for the different number of patients per provider. Models also included body mass index and the Charlson comorbidity index (neither significant) and whether the treating provider responded to the survey (OR 0.68, CI 0.049-0.94). Odds ratios in bold were significant at the $p < 0.05$ level. TNF = tumor necrosis factor

* An improvement in CDAI of 1 point indicates a 1 point reduction in CDAI from baseline to 6 months

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Association between provider demographics and attitudes/beliefs with glucocorticoid prescribing 6 months after biologic or JAKi initiation in patients with rheumatoid arthritis

	Adjusted Odds Ratio [95% CI]	p-value
Provider/practice characteristics		
Provider Age		
<40	Reference	Reference
40-49	1.46 [0.67, 3.20]	0.34
50-59	0.89 [0.46, 1.71]	0.73
≥60	1.02 [0.49, 2.12]	0.96
Provider sex		
Male	Reference	Reference
Female	0.99 [0.65, 1.51]	0.44
Credentials		
Not MD	Reference	Reference
MD	1.18 [0.67, 2.09]	0.56
Practice type		
Individual Private	Reference	Reference
Group Private	0.76 [0.49, 1.17]	0.21
Other (includes academic)	1.02 [0.55, 1.89]	0.96
Accepts Medicaid	1.03 [0.64, 1.65]	0.92
Burnout score [0-12][a] *Higher score more burnout*	1.02 [0.95, 1.10]	0.54
Other attitudes/beliefs		
Shared decision score [6-36][b] *Lower score for greater shared decision making*	1.00 [0.96, 1.04]	0.99
Concern with Complementary/Alternative Medication		
Very much/somewhat	Reference	Reference
Slightly/not at all	0.78 [0.49, 1.24]	0.29
Health Professionals Beliefs about Race scale [7-35][c] *Lower score for greater belief that race is related to genetics*	1.03 [0.98, 1.08]	0.20
Politics Spectrum		
Liberal	Reference	Reference
Moderate	1.21 [0.77, 1.91]	0.40
Conservative	1.31 [0.80, 2.17]	0.29
How important is religion in your life		
Very Important	Reference	Reference
Somewhat Important	1.22 [0.68, 2.19]	0.51
Not too Important	0.86 [0.53, 1.38]	0.52
Not at all Important	0.85 [0.43, 1.68]	0.64

Analysis via individual random effects models with provider included as a random effect. All models adjusted for year, number of previous biologic/JAKi, patient sex and age, baseline clinical disease activity index (CDAI), change in CDAI, Charlson Comorbidity Index (CCI), BMI, Opioid use, Duration of disease, current DMARD, region.

[a]Burnout was based on 2 questions from the Maslach Burnout Inventory, range 0-12 with higher scores indicating higher burnout.

[b]Shared decision making was from the Alberta Shared decision-making Measurement Instrument (ASK-MI) tool, six questions with total score ranging 6 to 36 with lower scores indicating higher shared decision making. Beliefs about race were the Health Professionals

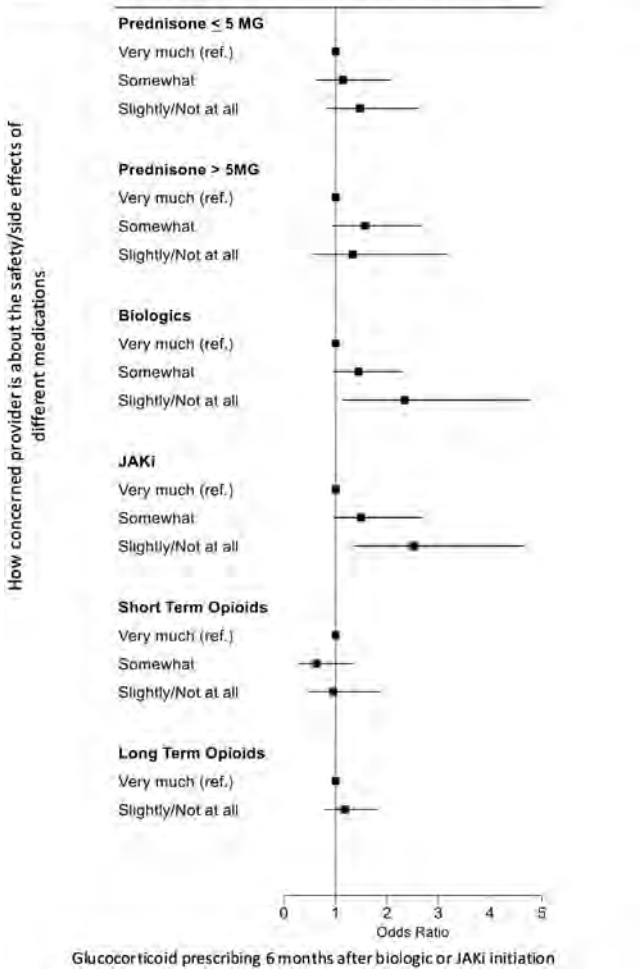
[c]Beliefs about Race (HPBR) scale - Biological domain, 7 questions with score 7 to 35 with lower scores indicating greater belief that race is a biologic factor that corresponds to genetic differences and can be useful in screening and treatment decisions.

≤45 or >75, more long-standing RA, more previous biologics/JAKi, and earlier calendar year were associated with greater GC use at 6 months (**Table 1**). Patients of survey responders were less likely to use GCs (OR 0.68, CI 0.049-0.94), and 13% of the variability in GC use was due to provider. In analyses limited to survey responders: provider demographics, burnout, and beliefs regarding shared decision making, complementary/alternative medications, race as a biologic factor in medicine, political leanings, and religiosity were not associated with GC prescribing (**Table 2**). As shown in **Figure 1**, concerns about long-term prednisone ≤5mg or >5mg or opioids were not associated with GC prescribing, but providers with less concern about biologics or JAKi were more likely to prescribe GCs at 6 months [adjusted OR 2.34 (1.15-4.76) for biologics, OR 2.52 (1.36-4.65) for JAKi for slightly/not at all vs. very much concerned].

Conclusion: While patient factors have a strong influence on GC use in RA, variability in practice patterns among providers also impacts GC use. Many provider characteristics and beliefs, and surprisingly even concerns about GCs, are not associated with GC prescribing. In contrast, providers with less concern about biologics and JAKi are more likely to prescribe GCs. These results suggest that broader attitudes towards prioritizing treatment benefits vs risks may drive GC prescribing, with important implications for provider education.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Association between provider concerns about the safety/side effects of specific medications from a provider survey and glucocorticoid prescribing 6 months after biologic or JAKi initiation among patients with RA



Disclosure: M. George: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **G. Reed**: CorEviitas, LLC, 2, Corrona Research Foundation, 2; **K. Kane**: None; **D. Pappas**: AbbVie/Abbott, 2, CorEvitas, Part of Thermofisher, 3, 11, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4, Novartis, 2, Roche, 2; **J. Kremer**: CorEvitas (part of ThermoFisher), 1, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4.

Abstract Number: 1050

Bridging the Gap: A Mixed-Methods Study to Enhance Integration of HCQ-SAFE, A Shared Decision-Making Tool for Hydroxychloroquine Use, in Routine Lupus Care

Isabella Hartel[1], Jay Patel[1], David Gazeley[2], Drake Johnson[1], Justin Levinson[1], Carmen Campbell[1], Britney Youngchild[3], Shelby Gomez[3], Amannda Weber[4], Jessica Michaud[5], Laura Dickmann[6], Sancia Ferguson[7], Betty Chewning[8], Christie Bartels[9] and **Shivani Garg**[10], [1]University of Wisconsin, School of Medicine and Public Health, Madison, Madison, WI, [2]Medical College of Wisconsin, Milwaukee, WI, [3]University of Wisconsin, School of Pharmacy, Madison, WI, [4]University of Wisconsin (UW), UW Health, Madison, WI, [5]Medical College of Wisconsin, Milwaukee, Madison, WI, [6]Medical College of Wisconsin, Milwaukee, Milwaukee, [7]University of Wisconsin School of Medicine and Public Health, Madison, Madison, WI, [8]University of Wisconsin, School of Pharmacy, Madison, [9]University of Wisconsin School of Medicine and Public Health, Madison, WI, [10]University of Madison, School of Medicine and Public Health, Madison, WI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is a key therapy for lupus (or SLE). Yet, challenged to weigh benefits vs. harms, ~80% of patients self-discontinue HCQ. Shared decision-making (SDM) tools, like HCQ-SAFE© (Garg, 2023), can support patients and clinicians in complex treatment decisions. In a clinical trial, HCQ-SAFE SDM intervention (Fig. 1A) was used by 12 clinicians during 200 visits in 8 clinics of 2 health systems. Still adoption of SDM tools can be challenging in non-research settings, particularly busy clinics and low-resource settings.

Table 1. A. Key Visits Characteristics; B. Implementation Outcome Metrics Mapped to RE-AIM

A. Visit characteristics	N (%)
Center 1	120 (60)
Center 2	80 (40)
MDs	101 (50.5)
RNs	43 (21.5)
PharmDs	56 (28)
B. Implementation Outcome Metrics Mapped to RE-AIM	**N (%) or Mean±SD**
Reach: Intervention completion rate	
Overall	100%
PharmDs	100%
RNs	100%
MDs	100%
Effectiveness: Resolution of decisional conflicts (post DCS score ≤25)	
Overall	98%
PharmDs	98%
RNs	98%
MDs	99%
Adoption: Percent intervention completion	
Overall	92%
PharmDs	100%
RNs	100%
MDs	75%
Implementation: Intervention fidelity rate (≥1 benefit, ≥1 harm, & HCQ-SAFE in preferred language/format used)	
Overall	100%
PharmDs	100%
RNs	100%
MDs	100%
Implementation: Intervention feasibility rate (1-9 Likert scale; 9=extremely feasible)	
Overall	Median 9 (9-9); Mean 8.8±0.7
PharmDs	Median 9 (9-9); Mean 8.9±0.2
RNs	Median 9 (9-9); Mean 8.9±0.3
MDs	Median 9 (8-9); Mean 8.5±0.8
Implementation: Median (IQR) time spent to complete HCQ-SAFE intervention during visit	
Overall	5 (5-7) mins
PharmDs	7 (5-10) mins
RNs	5 (5-6) mins
MDs	5 (4-6) mins
Maintenance: Average completion per month	32 per month
Maintenance: Net promoter score (% extremely/very likely - % extremely/very unlikely)	
Overall	99%
PharmDs	100%
RNs	100%
MDs	99%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Qualitative Analysis of Clinician Interviews Informed by Normalization Process Theory Domains to Deliver Strategies to Develop Practical Workflow for HCQ-SAFE Integration in Clinics

Domains	Themes	Recommended Strategies to Revise Workflow ›*(Illustrative Quotes)*
Coherence	1. Clear purpose of intervention (Why?) 2. Clear eligibility criteria (Who?) 3. Values aligned with clinic goals (Can we do this?)	**Strategy 1.** HCQ-SAFE e-tool and training should clearly states the reason to use it **Strategy 2.** Simplify eligibility criteria to all patients *"I think, all patients should see it at least once"*
Active Participation	1. Preparedness to use the intervention (How can I do it?) 2. Effectiveness of the intervention (What is the impact?) 3. Motivators or facilitators of participation (How?)	**Strategy 3.** Training should be tailored to clinician role *"The video and session [training] was good, but I think, it can be optional for MDs, but 1:1 session for staff with less experience could be helpful..."*
Collective Action	1. Compatibility with existing workflows (Easy to use?) 2. Division of labor, resources, responsibilities (Preferred user) 3. Facilitators/detractors to use 4. Strategies to circumvent challenges (What was done?)	**Strategy 4.** PharmDs or RNs should preferably complete HCQ-SAFE review in busy clinics *"RN: I liked the interaction part with patients... I would like to do more of these... It was meaningful"* *"Manager: I do not see why RNs can't do this in clinics... it only takes 5 mins..."* **Strategy 5.** Review HCQ-SAFE again during life changes (e.g., pregnancy, kidney disease), refill gaps, or resuming HCQ after self-discontinuation
Reflexive Monitoring	1. Early experiences and perception over time 2. Any adaptive improvements 3. Recommendations to ensure sustained use	**Strategy 6a.** Avoid recommending a post-HCQ-SAFE review follow up for everyone; limit follow-up to patients with concerns or refill gaps only **Strategy 6b.** Add training link to HCQ-SAFE e-tool for users to refresh training if needed **Strategy 6c.** Give patients a link to the tool in after visit summary or in patient message

We aimed to: 1) examine implementation outcome metrics mapped to the RE-AIM framework for using the HCQ-SAFE SDM intervention; 2) develop strategies based on clinician experiences using the Normalization Process Theory (NPT) to revise HCQ-SAFE implementation workflow for easier integration in clinics.

Methods: The HCQ-SAFE SDM intervention (Fig. 1A) was implemented in 200 unique visits by 6 MDs, 3 PharmDs, and 3 RNs (NCT05922722). Clinicians completed a questionnaire to report intervention details (version, topics, language), time, and rated feasibility & likelihood to use on a 1-9 Likert scale (9=best). Clinicians also participated in a cognitive interview to share experiences, barriers, & facilitators to HCQ-SAFE use.

Quantitative data from 200 questionnaires estimated RE-AIM implementation metrics. Reach: % eligible visits completing HCQ-SAFE. Effectiveness: change in decisional conflict scores (overall/by role). Adoption: % clinicians completing intervention. Implementation: Fidelity (% visits covering ≥1 benefit/harm, language) & Feasibility (median score ≥7, time ≤5 min). Maintenance: monthly completion rate & Net Promoter Score (NPS ≥80%, motivators - detractors).

Qualitative data from interviews were analyzed using a coding scheme informed by 4 NPT domains to identify strategies to refine workflows for easier integration of HCQ-SAFE in clinics.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

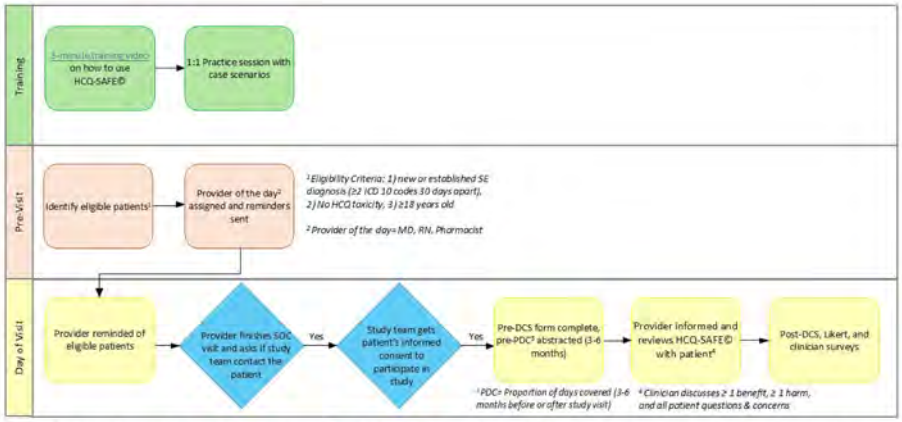


Figure 1B. An end-user-informed practical workflow for routine use of HCQ-SAFE shared decision-making intervention in clinics

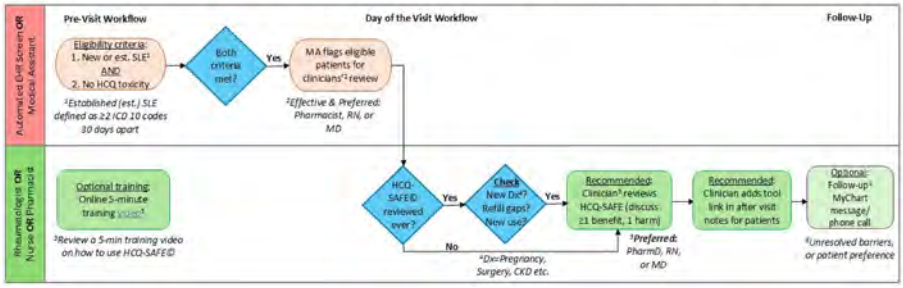


Figure 1A. Swim Lane diagram showing the study workflow used to implement the HCQ-SAFE shared decision-making intervention across 200 unique patient visits in 8 clinics of 2 health systems; Figure 1B. An end-user-informed practical workflow for routine use of HCQ-SAFE shared decision-making intervention in clinics

Results: In 200 visits, MDs (50%), PharmDs (28%), and RNs (22%) completed the HCQ-SAFE intervention (Table 1).

Data analysis showed excellent completion rates (100%) across MDs, PharmDs, RNs, with equally effective resolution of decisional conflicts regardless of clinician role (98% PharmD/RN vs. 99% MD; Table 1). Adoption was slightly lower among MDs (75%) vs. PharmDs/RNs (100%). HCQ-SAFE was rated highly feasible (median score 9, median time 5 mins) and received 100% NPS, indicating strong clinician willingness for continued use.

Content analysis of clinician experiences using NPT yielded 6 strategies for HCQ-SAFE implementation (Table 2; Fig. 1B). Key recommendations included: tailoring training by role, simplifying eligibility to include all SLE patients, using PharmDs/RNs to lead reviews. Clinicians preferred this equally effective staff-led model for easier integration and facilitate team-based care. The revised clinical workflow (Fig. 1B) gained unanimous endorsement from participating clinicians.

Conclusion: The impact of this study is 2-fold. First, it establishes HCQ-SAFE is a highly feasible and effective SDM intervention for clinical use. Second, it delivers an end-user-informed practical workflow to ensure sustainable integration in clinics to promote medication adherence via SDM.

Disclosure: I. Hartel: None; **J. Patel**: None; **D. Gazeley**: None; **D. Johnson**: None; **J. Levinson**: None; **C. Campbell**: None; **B. Youngchild**: None; **S. Gomez**: None; **A. Weber**: None; **J. Michaud**: None; **L. Dickmann**: None; **S. Ferguson**: None; **B. Chewning**: None; **C. Bartels**: None; **S. Garg**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1051

Mitigating Hydroxychloroquine (HCQ) Nonadherence by Clarifying Misbeliefs Using a Shared Decision-Making Tool (HCQ-SAFE©) Across Two Different Rheumatology Centers

Isabella Hartel[1], David Gazeley[2], Jay Patel[1], Betty Chewning[3], Shelby Gomez[4], Jessica Michaud[5], Laura Dickmann[6], Jon keevil[7], Patricia Tellez-giron[1], Christie Bartels[8] and **Shivani Garg**[9], [1]University of Wisconsin, School of Medicine and Public Health, Madison, Madison, WI, [2]Medical College of Wisconsin, Milwaukee, WI, [3]University of Wisconsin, School of Pharmacy, Madison, [4]University of Wisconsin, School of Pharmacy, Madison, WI, [5]Medical College of Wisconsin, Milwaukee, Madison, WI, [6]Medical College of Wisconsin, Milwaukee, Milwaukee, [7]N/A, Madison, [8]University of Wisconsin School of Medicine and Public Health, Madison, WI, [9]University of Madison, School of Medicine and Public Health, Madison, WI

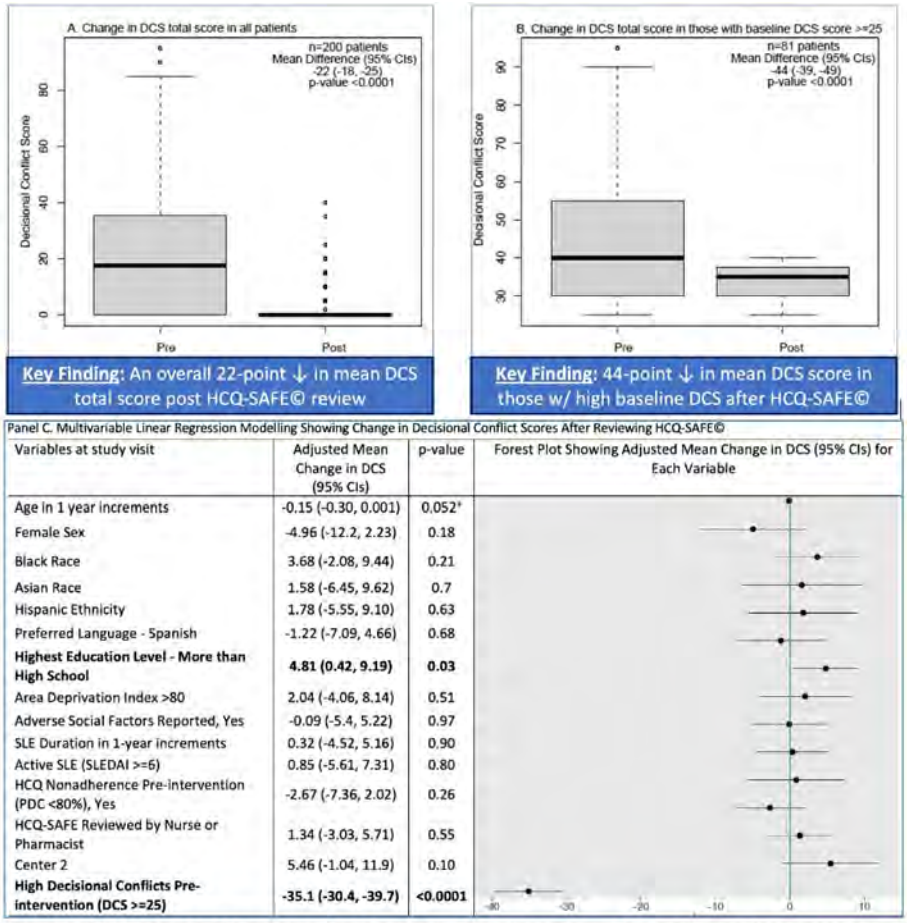
SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1038–1054) Health Services Research Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM



Panel C. Multivariable Linear Regression Modelling Showing Change in Decisional Conflict Scores After Reviewing HCQ-SAFE©

Variables at study visit	Adjusted Mean Change in DCS (95% CIs)	p-value	Forest Plot Showing Adjusted Mean Change in DCS (95% CIs) for Each Variable
Age in 1 year increments	-0.15 (-0.30, 0.001)	0.052[a]	
Female Sex	-4.96 (-12.2, 2.23)	0.18	
Black Race	3.68 (-2.08, 9.44)	0.21	
Asian Race	1.58 (-6.45, 9.62)	0.7	
Hispanic Ethnicity	1.78 (-5.55, 9.10)	0.63	
Preferred Language - Spanish	-1.22 (-7.09, 4.66)	0.68	
Highest Education Level - More than High School	**4.81 (0.42, 9.19)**	**0.03**	
Area Deprivation Index >80	2.04 (-4.06, 8.14)	0.51	
Adverse Social Factors Reported, Yes	-0.09 (-5.4, 5.22)	0.97	
SLE Duration in 1-year increments	0.32 (-4.52, 5.16)	0.90	
Active SLE (SLEDAI >=6)	0.85 (-5.61, 7.31)	0.80	
HCQ Nonadherence Pre-intervention (PDC <80%), Yes	-2.67 (-7.36, 2.02)	0.26	
HCQ-SAFE Reviewed by Nurse or Pharmacist	1.34 (-3.03, 5.71)	0.55	
Center 2	5.46 (-1.04, 11.9)	0.10	
High Decisional Conflicts Pre-intervention (DCS >=25)	**-35.1 (-30.4, -39.7)**	**<0.0001**	

Abbreviations: SLEDAI=SLE Disease Activity Index; PDC=Proportion of Days Covered (pharmacy refill information); DCS=Decisional conflict scale score. Significant p-values <0.05 shown in bold font.

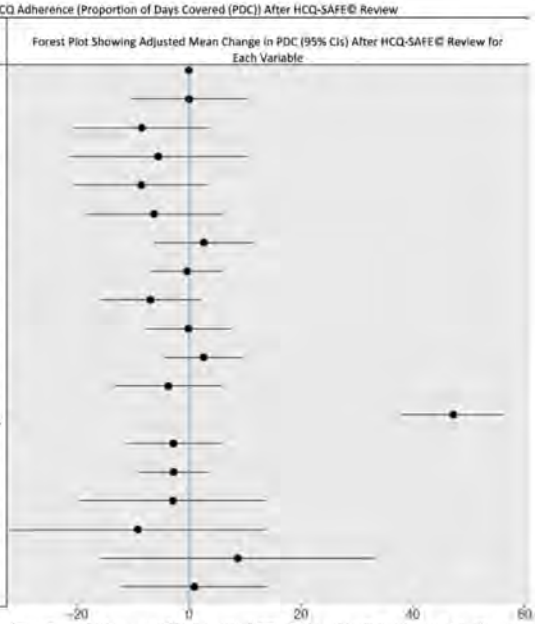
Figure 1. Panel A. Decisional conflict scale (DCS) scores pre- and post-intervention (HCQ-SAFE© review) in all patients across 8 clinics and 2 health centers (n=200); Panel B. Decisional conflict scale (DCS) scores pre- and post-HCQ-SAFE© review in patients with high DCS scores at baseline (pre-intervention) defined as DCS ≥25; Panel C. A multivariable linear regression model showing mean change in DCS after HCQ-SAFE© review.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Hydroxychloroquine (HCQ) prolongs disease-free and damage-free survival in lupus (SLE). Yet, ~80% of patients stop taking HCQ resulting in poor outcomes including early mortality. High nonadherence could be linked to complexity in treatment decisions and lack of support in decision-making. Unable to weigh benefits vs. rare harms of HCQ and align treatment goals with values, patients have greater risk aversion leading to nonadherence. Shared decision-making (SDM) tools can support patient-clinician communication, align treatment goals with values, and motivate patient

Table 1. A Multivariable Linear Regression Model Showing Change in HCQ Adherence (Proportion of Days Covered (PDC)) After HCQ-SAFE© Review

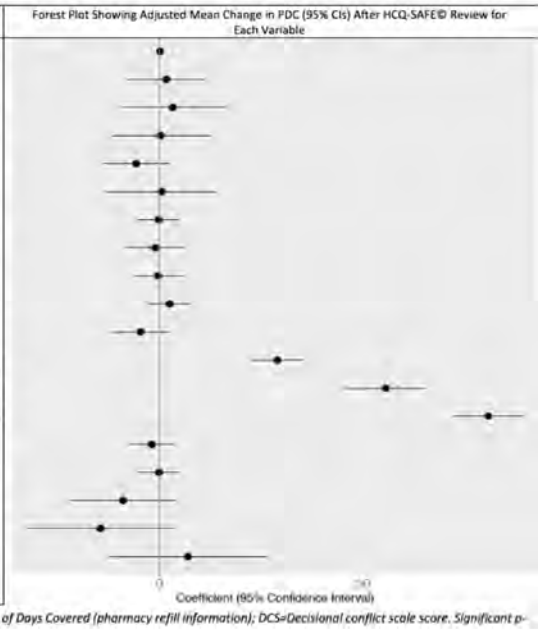
Variables at study visit	Adjusted Mean Change in PDC (95% CIs)	p-value
Age in 1-year increments	-0.03 (-0.25, 0.18)	0.78
Female Sex	0.02 (-10.4, 10.4)	0.10
Black Race	-8.49 (-20.5, 3.55)	0.17
Asian Race	-5.48 (-21.5, 10.5)	0.50
Hispanic Ethnicity	-8.55 (-20.6, 3.47)	0.16
Center 2	-6.27 (-18.4, 5.85)	0.31
Spanish (Preferred Language)	2.62 (-6.21, 11.5)	0.56
More than High School – Education Level	-0.37 (-6.8, 6.07)	0.91
State Area Deprivation Index >80th percentile	-6.91 (-15.9, 2.11)	0.13
Adverse Social Factors Reported, Yes	-0.12 (-7.77, 7.53)	0.98
SLE Duration in 1-year increments	2.59 (-4.39, 9.57)	0.47
Active SLE (SLEDAI >=6)	-3.69 (-13.1, 5.75)	0.44
HCQ Nonadherence Pre-intervention (PDC <80%), Yes	**47.2 (38.1, 56.3)**	**<0.0001**
Pre-intervention DCS >=25, Yes	-2.81 (-11.2, 5.55)	0.51
HCQ-SAFE Reviewed by Nurse or Pharmacist	-2.76 (-9.06, 3.55)	0.39
Black Race: Center 2	-2.92 (-19.6, 13.8)	0.73
Asian Race: Center 2	-9.17 (-32.1, 13.8)	0.43
Hispanic Ethnicity: Center 2	8.69 (-15.9, 33.3)	0.49
HCQ Nonadherence: Pre-intervention DCS >=25	0.945 (-12.1, 14)	0.89



Abbreviations: SLEDAI=SLE Disease Activity Index; PDC=Proportion of Days Covered (pharmacy refill information); DCS=Decisional conflict scale score. Significant p-values <0.05 shown in bold font.

Table 2. A Multivariable Linear Regression Model Showing Change in HCQ Adherence After HCQ-SAFE© Review Using pre-PDC adherence categories of 0%, <40%, 40-79%, ≥80% (Hsu et al, Rheumatology Oxford, 2018)

Variables at study visit (Pre-intervention)	Mean Change in PDC (95% CIs)	p-value
Age in 1-year increments	0.06 (-0.11, 0.24)	0.49
Black Race	1.56 (-8.05, 11.2)	0.75
Asian Race	3.25 (-9.58, 16.1)	0.62
Hispanic Ethnicity	0.25 (-11.9, 12.4)	0.97
Center 2	-5.83 (-13.9, 2.26)	0.16
Spanish (Preferred Language)	0.55 (-13.2, 14.3)	0.94
More than High School (Education Level)	-0.31 (-5.40, 4.78)	0.91
State Area Deprivation Index >80th percentile	-1.09 (-8.30, 6.12)	0.77
Adverse Social Factors, Yes	-0.45 (-6.47, 5.57)	0.88
SLE Duration >5 years	2.47 (-3.02, 7.95)	0.38
Active SLE (SLEDAI >=6)	-4.75 (-12.1, 2.61)	0.20
HCQ Adherence 40-79%, Yes	**29 (22.5, 35.5)**	**<0.0001**
HCQ Adherence 1-39%, Yes	**55.6 (45.5, 65.6)**	**<0.0001**
HCQ Adherence 0%, Yes	**80.8 (72.1, 89.6)**	**<0.0001**
Pre-intervention DCS >=25, Yes	-0.17 (-5.22, 4.89)	0.48
HCQ-SAFE Reviewed by Nurse or Pharmacist	-9.04 (-22.2, 4.1)	0.95
Black Race: Center 2	-14.5 (-32.7, 3.61)	0.18
Asian Race: Center 2	6.97 (-12.4, 26.3)	0.12
Hispanic Ethnicity: Center 2	-0.17 (-5.22, 4.89)	0.48



Abbreviations: SLEDAI=SLE Disease Activity Index; PDC=Proportion of Days Covered (pharmacy refill information); DCS=Decisional conflict scale score. Significant p-values <0.05 shown in bold font.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

participation in decision-making. Thus, we aimed to test the efficacy of an SDM tool (HCQ-SAFE©) in a) improving HCQ adherence; b) resolving decisional conflicts around HCQ in SLE.

Methods: HCQ-SAFE© (hcqsafe.medicine.wisc.edu) is a 5-domain pictorial e- and paper-tool highlighting key benefits vs. rare harms of HCQ, developed by our group in English & Spanish using a collaborative iterative process involving 30 advisors (Garg et al. 2023).

To test the efficacy of HCQ-SAFE©, we recruited 200 adults with SLE on HCQ across 8 clinics in 2 diverse health systems (NCT05922722). The primary outcome was HCQ adherence measured using proportion of days covered (PDC) 3-6 months before and after HCQ-SAFE© review; nonadherence defined as PDC < 80%. The secondary outcome was decision conflict scale (DCS) scores measured pre- and post-intervention using the low literacy 10-item DCS questionnaire (DCS scores range: 0 (best) - 100 (worst); ≥25 indicate high decisional conflicts). We used paired t-test and adjusted linear regression analyses to examine change in 1) HCQ adherence; 2) DCS scores pre- vs. post-HCQ-SAFE© review.

Results: Among 200 participants, 90% were women, 10% preferred Spanish, 54% had high decisional conflicts at baseline. SDM during visits was completed by MDs (50%), RNs (21%), and pharmacists (29%). Mean±SD time spent to review HCQ-SAFE© was 6±2 mins. Intervention completion rate was 100%.

Next, a significant increase in HCQ adherence (post-PDC) by 47% was noted after HCQ-SAFE© review compared to baseline HCQ adherence (pre-PDC) after adjusting (Table. 1). Using pre-PDC adherence categories of 0%, < 40%, 40-79%, ≥80% (Hsu et al, 2018), an increase in post-PDC adherence by 29%, 56%, and 81% was noted in 0%, < 40%, 40-79% categories vs. ≥80% category (reference) after HCQ-SAFE© review (Table 2).

After reviewing HCQ-SAFE©, a 22-point and a 44-point reduction in DCS scores was seen in all patients ($p < 0.001$; Fig 1A), and those with high DCS (≥25) at baseline (Fig. 1B), respectively. After adjusting, a 35-point reduction in DCS was noted post-intervention in patients with high DCS at baseline (Fig 1C).

In analysis stratified by language, clinician, and education level, similar significant reductions were seen in DCS scores and PDC after HCQ-SAFE© review ($p < 0.0001$, data not shown).

Conclusion: HCQ-SAFE© provides clear, concise information, reducing decisional conflicts and significantly improving adherence across SLE populations. SDM tools like HCQ-SAFE© can mitigate nonadherence due to limited health literacy, linguistic clarity, lack of decision support, potentially improving SLE outcomes.

Disclosure: I. Hartel: None; **D. Gazeley**: None; **J. Patel**: None; **B. Chewning**: None; **S. Gomez**: None; **J. Michaud**: None; **L. Dickmann**: None; **J. keevil**: None; **P. Tellez-giron**: None; **C. Bartels**: None; **S. Garg**: None.

Abstract Number: 1052

"prednisone… a Necessary Evil…" Developing an Evidence-based Benefits vs. Harms Shared Decision-making Tool (PRED-SAFE) to Support Decisions Around Chronic Prednisone Use

Isabella Hartel[1], Jay Patel[1], Justin Levinson[1], Sancia Ferguson[2], Carmen Campbell[1], Amannda Weber[3], Shelby Gomez[4], David Gazeley[5], Ali Duarte-Garcia[6], Jennifer Barton[7] and **Shivani Garg**[8], [1]University of Wisconsin, School of Medicine and Public Health, Madison, Madison, WI, [2]University of Wisconsin School of Medicine and Public Health, Madison, Madison, WI, [3]University of Wisconsin (UW), UW Health, Madison, WI, [4]University of Wisconsin, School of Pharmacy, Madison, WI, [5]Medical College of Wisconsin, Milwaukee, WI, [6]Mayo Clinic, Rochester, MN, [7]VA Portland Health Care System/OHSU, Portland, OR, [8]University of Madison, School of Medicine and Public Health, Madison, WI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Guidelines recommend limiting chronic prednisone use (>5 mg/d for >3-6 mos.) given higher risks of fractures, infections, and damage. Yet, patients struggle to stop/reduce prednisone due to its perceived rapid benefits despite long-term harms. Shared decision-making (SDM) tools can help clinicians facilitate difficult conversations and support patients in such decisions. There are no feasible SDM tools for chronic prednisone use. Thus, we developed and piloted the PRED-SAFE SDM tool to resolve decisional conflict around chronic prednisone use.

Methods: PRED-SAFE was created using a collaborative process involving a multidisciplinary panel of patients, clinicians, implementation scientists, designers, and literacy experts across 4 institutions (n=23; Fig 1). Initial prototypes were informed by AHRQ low literacy and SDM tool development guidelines, key themes about prednisone in literature and based on interviews with patients, clinicians, experts (n=23). The multidisciplinary panel reviewed the first prototype and guided an iterative process to revise subsequent prototypes until a final version was endorsed by all 23 advisors. The final PRED-SAFE SDM tool was implemented in 4 clinics during 30 visits to examine usability and feasibility. Usability was measured by patient-reported understanding of cumulative harms vs. limited benefits with chronic prednisone use and resolution of decisional conflict using SURE scale (Score >3 shows no residual decisional conflicts) post PRED-SAFE. Using a 1-9 Likert scale (9 = best) to measure users' likelihood to recommend PRED-SAFE, we estimated Net Promoter Score (NPS = %promoters (extremely/very likely) - % detractors (extremely/very unlikely)). Feasibility of tool use in clinics was assessed using clinician-reported time to review and feasibility & likelihood to use on a 1-9 Likert scale (9=best).

Results: PRED-SAFE SDM laminated tool organized data in pictograms across 6 domains: a) bone fracture, b) infections, c) organ damage, d) cardiovascular disease (CVD), e) flares, f) taper (Fig 2A-D). During visits, a patient & clinician first reviewed increased chances of fracture with chronic prednisone vs. dose ≤5mg/d, followed by higher chance of infections, organ damage, and CVD with chronic prednisone. Limited benefits of chronic prednisone included slight decline in flares with >5mg/d. Finally, steps to taper prednisone were reviewed (Fig 2A-D).

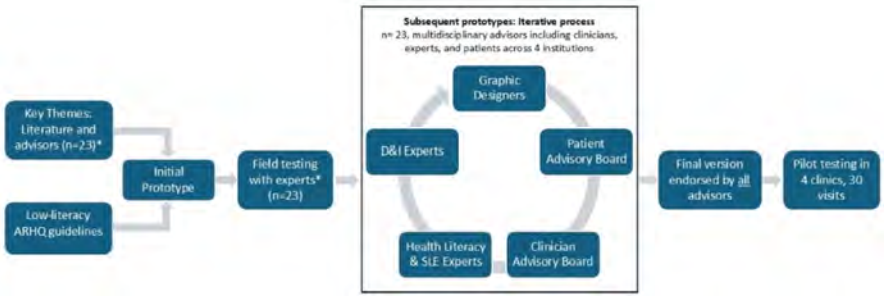


Figure 1. A Collaborative and Iterative Process to Develop PRED-SAFE, a Benefits vs. Harms Shared Decision-Making Tool Around Chronic Prednisone Use

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

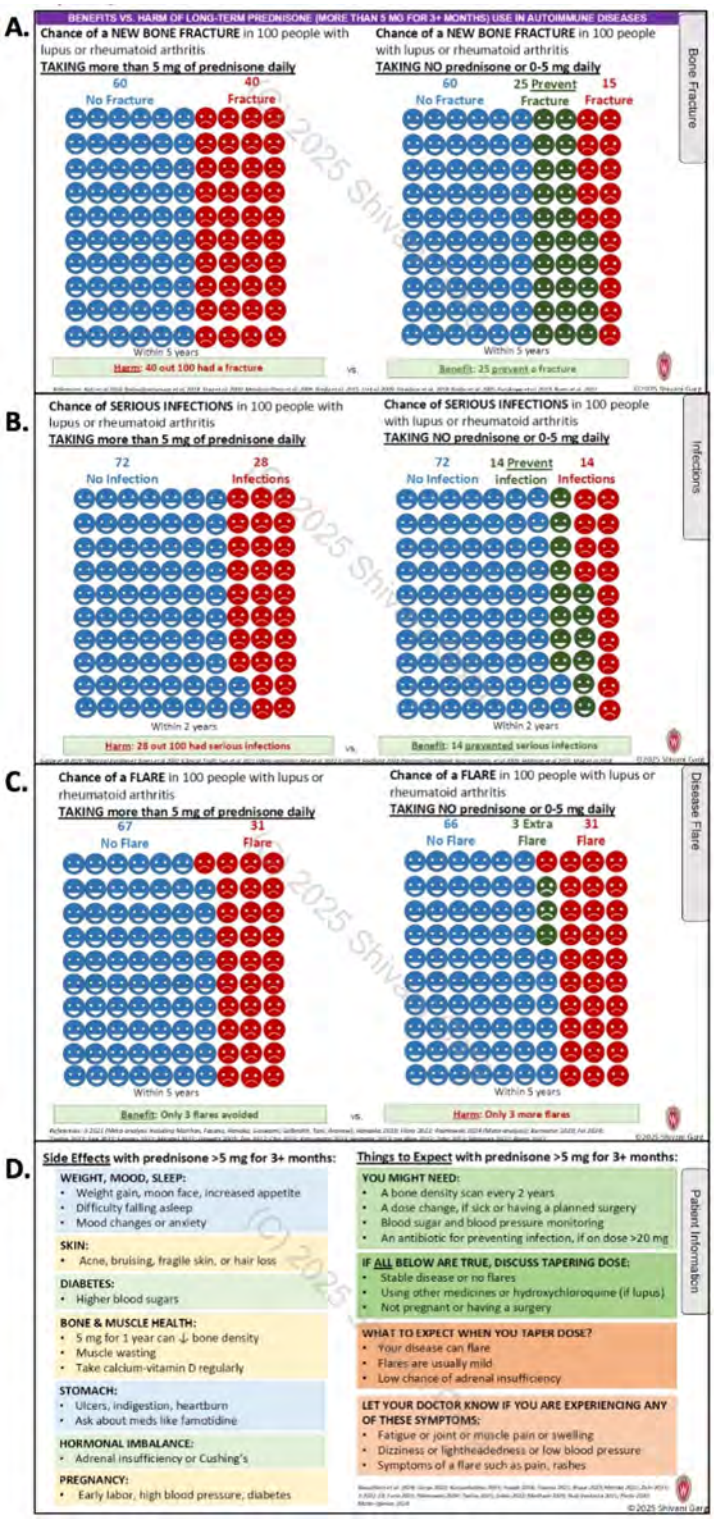


Figure 2. PRED-SAFE SDM Tool Domains Showing Harms (Panel A. Bone Fracture; Panel B. Infections) vs. Benefits (Panel C. Flares) of chronic prednisone, & patient information with a taper guide (Panel D)

PRED-SAFE was reviewed in 4 clinics by 6 clinicians across 30 visits (Table 1). All patients reported improved knowledge of prednisone's benefits vs. harms; 93% reported no residual decisional conflict post-review (Table 1). PRED-SAFE garnered high usability scores from clinicians (NPS = 100%, mean = 8.9) & patients (NPS = 73%, mean = 8). Mean time to review

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Pilot testing of PRED-SAFE, a shared decision-making tool for long-term prednisone use, n=30

Patient Characteristics	**n (%)**
Age <50 years old	15 (50)
Female	28 (93)
Black Race	2 (7)
Asian Race	3 (10)
Hispanic Ethnicity	5 (17)
English: Preferred Language	28 (93)
Spanish: Preferred Language	2 (7)
SLE	27 (90)
Rheumatoid Arthritis	6 (20)
Other autoimmune diseases	14 (47)
Long-term prednisone use, ever	21 (70)
Visit Characteristics, n (%)	
Intervention completed during visits	30 (100)
Intervention completed by:	
MDs	20 (67)
Pharmacists	6 (20)
MD Fellows and Students	4 (13)
In Clinic	30 (100)
Outcomes	
Improved Knowledge, n (%)	30 (100)
Patient likelihood to recommend to peers	NPS = 73%; 43% Extremely likely
Clinician likelihood to recommend to peers	NPS = 100%; 87% Extremely likely
Clinician reported feasibility to use	Median 9; Mean 8.67 ± 0.48 67% extremely feasible
Clinician reported ease of use	Median 9; Mean 8.80 ± 0.41 80% extremely easy
Decisional conflict scale score, mean±SD	3.93 ± 0.25 score
Residual decision conflict, n (%)	2 (7)
Time spent to review	Mean±SD = 6±2.37 mins 97% of visits ≤10 mins; 37% of visits ≤5 mins

was 6 mins; 33% of discussions were led by PharmDs/trainees. 90% of clinicians reported using PRED-SAFE was extremely/very feasible and easy for routine use (mean = 8.8; 8.7) (Table 1).

Conclusion: PRED-SAFE is a patient-centered, evidence-based, feasible, easy to use shared decision-making tool that reduces decisional conflict and encourages patient participation in decision-making around chronic prednisone use.

Disclosure: I. Hartel: None; **J. Patel**: None; **J. Levinson**: None; **S. Ferguson**: None; **C. Campbell**: None; **A. Weber**: None; **S. Gomez**: None; **D. Gazeley**: None; **A. Duarte-Garcia**: None; **J. Barton**: None; **S. Garg**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1053

Trends in Cost and Utilization of Biologic Medications for Rheumatologic Conditions: A Medicare Claims Study (2013–2022)

Taylor Koenig, Cleveland Clinic, Rocky River, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1038–1054) Health Services Research Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Biologic therapies have transformed rheumatologic disease management over the past two decades. As utilization of these high-cost medications increases and additional biologic and biosimilar therapies enter the market, understanding their financial and economic impact on the healthcare system is critical. Given rising Medicare part D drug spending, insights from longitudinal cost data can inform future policy and highlight areas for cost containment. This study leverages national Medicare Part D data from 2013 to 2022 to evaluate the cost of biologics prescribed for rheumatologic conditions with focus on the influence of market competition.

	Xeljanz		Olumiant		Rinvoq		Actemra		Kevzara		Orencia	
30-day Rx	#/year	Cost	#/year	Cost	#/year	Cost	#/year	Cost	#/year	Cost	#/year	Cost
2013	5,556	$2,640.00					2,513	$1,811.50			23,228	$2,898.84
2014	22,171	$2,872.00					7,009	$2,233.74			30,599	$3,241.78
2015	35,806	$3,277.00					11,340	$2,682.51			34,502	$3,748.96
2016	43,160	$3,992.00					14,375	$3,034.07			38,483	$4,173.32
2017	64,301	$4,435.00					17,206	$3,411.46	177	$3,552.54	39,422	$4,435.79
2018	92,577	$4,692.00	114	$2,400.00			23,863	$3,732.68	2,623	$3,624.94	41,664	$4,722.99
2019	111,371	$4,912.00	2,652	$2,456.00	199	$5,618.00	24,570	$3,662.45	6,847	$3,830.70	45,680	$4,859.90
2020	123,019	$5,037.00	3,588	$2,519.00	23,403	$5,486.00	28,020	$3,709.64	8,011	$3,951.23	49,932	$5,039.74
2021	119,471	$5,195.00	3,333	$2,635.00	48,768	$5,863.00	32,694	$3,720.86	8,188	$4,078.71	54,987	$5,202.69
2022	98,484	$5,200.00	3,240	$2,618.00	65,400	$5,935.00	39,394	$3,517.94	10,271	$4,061.33	65,669	$5,144.49

Figure 1. Annual number of and cost per 30-day prescription for selected biologics for rheumatologic indications 2013-2022. Cost is adjusted for inflation using Medical Care Consumer Price Index. As Olumiant, Rinvoq, and Kevzara entered the market during the study period, data reporting for each drug begins in the year it received FDA approval.

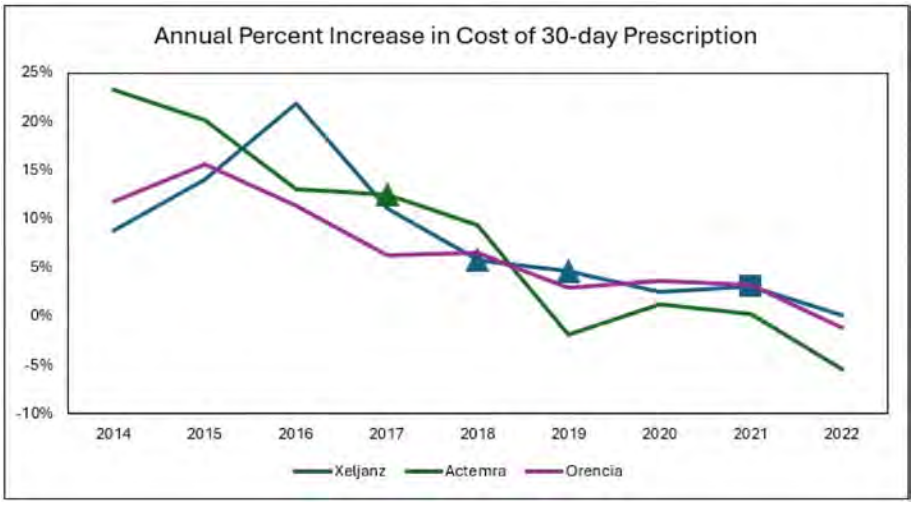


Figure 2. Comparison of the annual percent increase in cost of 30-day prescription for Xeljanz, Actemra, and Orencia 2014-2022. Triangles denote years in which a same-class drug came to market. The square denotes the year of the introduction of Xeljanz's black box warning.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

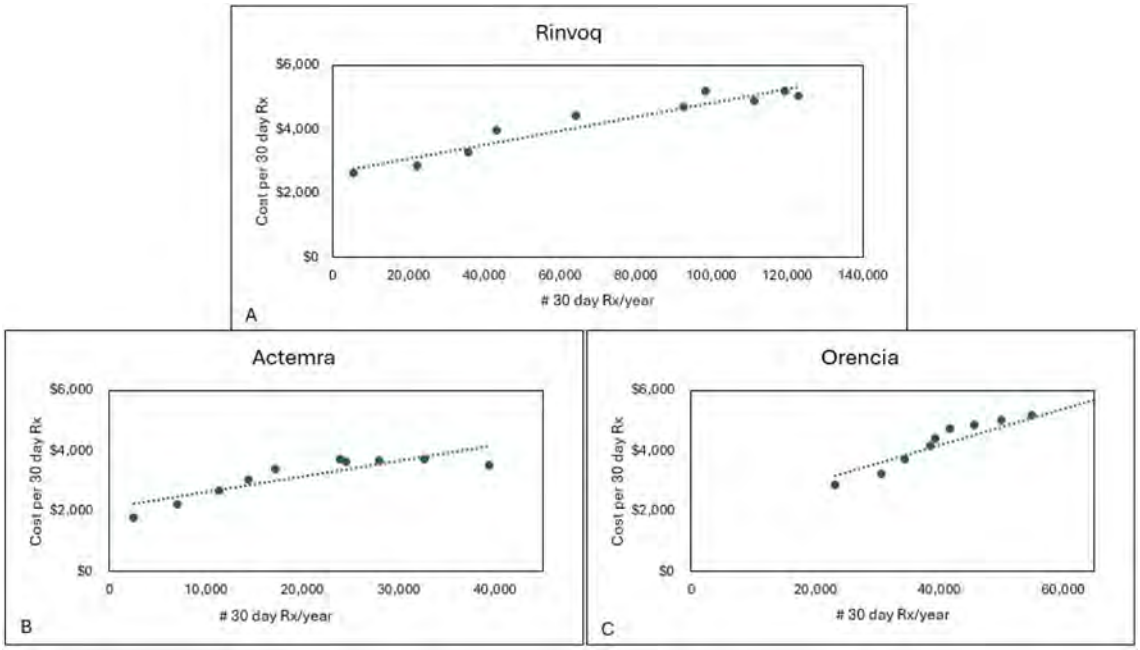


Figure 3. Correlation of annual number of 30-day prescriptions and cost per 30-day prescription for (A) Rinoq, (B) Actemra, and (C) Orencia.

Methods: This is a retrospective analysis of publicly available Medicare Part D Prescription Drug Event Data from 2013 to 2022 for Xeljanz, Olumiant, Rinvoq, Actemra, Kevzara, and Orencia. For each medication, the total number of prescribers, claims, and 30-day prescriptions as well as the total cost per year were captured. Claims attributed to non-rheumatologists were excluded. All cost values were inflation-adjusted to 2022 US dollars using the Medical Care Consumer Price Index. Trends were analyzed to evaluate changes in utilization and cost over time.

Results: The number of and cost per 30-day prescriptions increased annually, outpacing inflation, for all biologics from 2013-2022 (Figure 1). While 30-day prescription costs increased overtime, the annual percent increase declined during the study period for Xeljanz, Actemra, and Orencia (Figure 2). While additional JAK inhibitors and an IL-6 inhibitor received FDA approval and entered the market during this period, ANOVA showed no significant difference in this decline among these three drugs ($F(2, 24) = 0.094$, $p = 0.91$), including Orencia which lacks a direct market competitor. A strong correlation was also observed between drug cost (30-day prescription cost) and utilization (annual number of 30-day prescriptions) as seen in Figure 3 ($r = 0.96$ (Xeljanz), 0.76 (Olumiant), 0.82 (Rinvoq), 0.86 (Actemra), 0.96 (Kevzara), 0.91 (Orencia)).

Conclusion: This analysis demonstrates that the cost of biologics continues to increase, surpassing inflation. While the rate of increase is declining, these results suggest that market competition alone may not be a sufficient mechanism for controlling drug prices. Notably, the rate of decline in annual cost increases was similar across Xeljanz, Actemra, and Orencia—despite Orencia lacking a direct market competitor during the study period. This finding challenges the assumption that the entry of new therapies, including biosimilars, will lead to substantial price reductions. As biosimilar availability expands, their ability to generate meaningful cost savings may be more limited than anticipated. These results highlight the need for broader policy interventions and innovative reimbursement models to effectively address the growing burden of drug spending in rheumatology.

Disclosure: T. Koenig: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1054

Comedication Patterns of Romosozumab Early Adopters Among Medicare Enrollees: An Unsupervised Clustering Approach

Ye Liu[1], Hongke Wu[1], Tarun Arora[2] and Jeffrey Curtis[3], [1]University of Alabama at Birmingham, Birmingham, AL, [2]FASTER, Birmingham, AL, [3]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1038–1054) Health Services Research Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Polypharmacy is a major concern in osteoporosis (OP) management, especially in older adults. Romosozumab (romo), approved in April 2019, is a parenteral OP medicine for postmenopausal women at high fracture risk, given monthly for 12 months. We examined comedication patterns among early romo adopters and their association with treatment adherence. This study aimed to evaluate comedication patterns among early romo users.

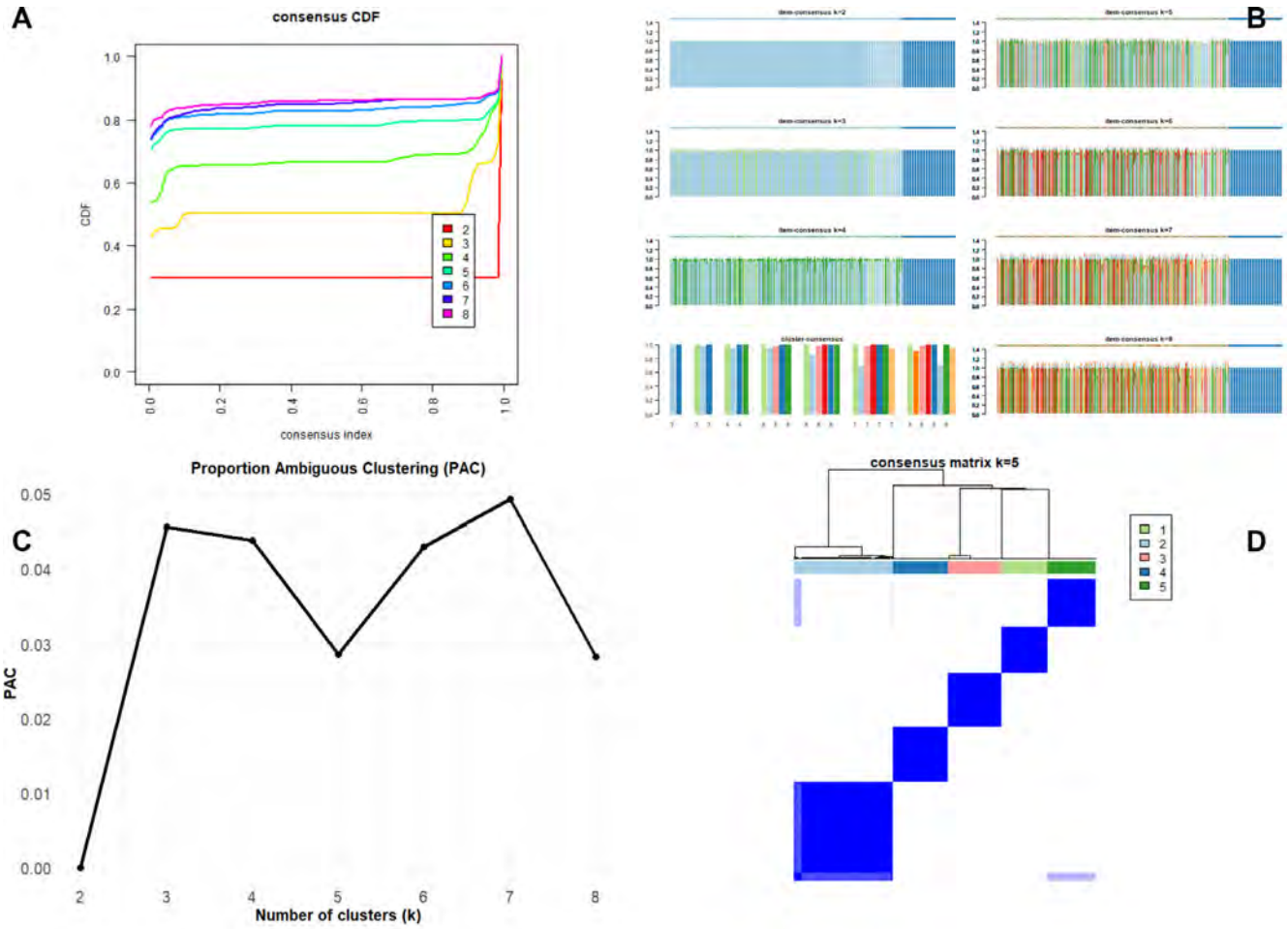


Figure 1. Diagnosis panel of consensus clustering analysis to determine optimal number of clusters (k)
A: Consensus cumulative distribution function (CDF) plot. B: item-consensus plot
C: Proportion ambiguous clustering (PAC) plot. D: Consensus matrix at optimal k = 5

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This retrospective cohort study used Medicare fee-for-service data (2006-2022) to identify female romo early adopters aged 65+ who initiated romo in 2019, with>=4 years of continuous enrollment, including 3 years pre-initiation. Those with metastatic cancer or Paget's disease were excluded.

We identified all prescription drugs covering the romo initiation day and selected 8 major medication categories for clustering: anti-hypertension (HTN), lipid-lowering, anti-diabetic, antidepressants, hypnotics, NSAIDs, opioids, and steroids. We used hierarchical agglomerative clustering to identify comedication patterns, with consensus clustering analysis to determine the optimal number of clusters.

We explored the association between comedication groups and romo discontinuation, defined as >= 60 days without injection, using a Cox proportional hazard model, adjusting for age, race, geographic region, Charlson comorbidity index (CCI), had emergency room visit, fracture history, romo billing in Part D, DXA scan, and prior OP treatment history. Patients were not considered discontinued after they completed 12 doses or 1 year of romo treatment.

Results: A total of 1,777 romo early users were included (mean age: 77.7 years; 90.9% White). Consensus clustering analysis identified 5 mutually exclusive comedication pattern groups (see Figure 1 for details):

1 (N=326). No patients used any pre-specified drugs of interest.

2 (N=275). All used anti-HTN only.

3 (N=281). All used lipid-lowering drugs, some (67%) also used anti-HTN.

4 (N=313). All used antidepressants, some also used anti-HTN (57%) and/or lipid-lowering (41%) drugs.

5 (N=582). Various drugs (>=1 of the 8 categories, not in other groups).

Patients in group 2 were the oldest (79.4 years, $p< 0.001$) and had the highest proportion from the South (47.3%, p=0.013). Group 5 had the highest CCI (4.8, $p< 0.001$) and the lowest percentage of White patients (88.5%, p=0.001). No significant differences in fracture or OP treatment history were observed. One-year overall romo discontinuation risk was 32.2% [29.1%, 35.7%]. Compared with group 1, all groups had higher discontinuation risk, with group 4 (HR=1.41 [1.14–1.76]) and group 5 (HR=1.39 [1.14–1.69]) significant after adjusting for covariables.

Conclusion: Distinct comedication patterns were identified among romo early adopters. Patients using antidepressants or multiple medication categories had a higher discontinuation risk and needed additional adherence support.

Disclosure: Y. Liu: Amgen, 5; **H. Wu**: None; **T. Arora**: Amgen, 5; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 1055

The Price of Relief: Examining the Role of Insurance in High-Cost Medication Use

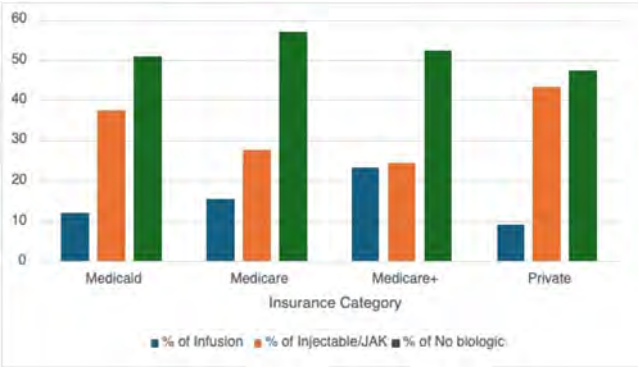
Antara Dattagupta[1], Colin Diffie[2] and Sana Cheema[2], [1]Washington University in St. Louis, St. Louis, MO, [2]Washington University in St. Louis, St. Louis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

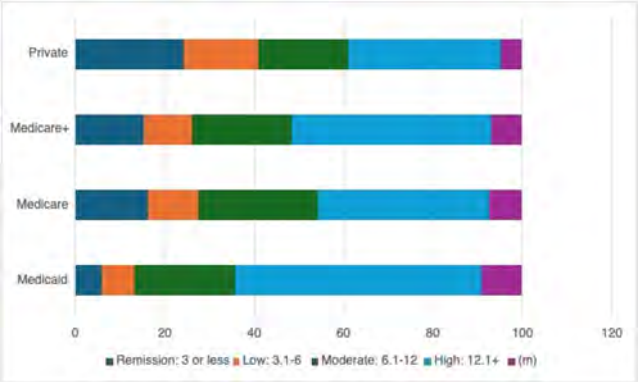
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: High-cost biologic therapies are integral to the management of rheumatoid arthritis (RA), yet access to these agents may be influenced by insurance type, particularly among publicly insured patients who may lack access to copay assistance. This study evaluated whether insurance category is associated with disparities in biologic prescribing patterns and remission outcomes among RA patients.



Graph 1: Comparing percentage of Infusion, Injectable/JAK & No Biologic use as a function of Insurance status



Graph 2: Patient reported outcome (RAPID3) scoring as a function of insurance status

Table 1: Comparing patient demographic as a function of insurance status

Table 1. Demographics as a Function of Insurance				
Insurance	**Medicaid**	**Medicare**	**Medicare+**	**Private**
Seropositivity	56.70%	65%	50.40%	59.50%
ECI	1.82 ± 6.89	3.073 ± 6.618	2.572 ± 6.243	0.196 ± 5.701
ADI	75.9 ± 18.5	62.85 ± 24.26	57.59 ± 25.13	58.57 ± 24.03
Total DMARDs	3.56 ± 2.08	3.92 ± 2.48	4.01 ± 2.75	3.6 ± 2.17
Male (%)	17.9	25	17.5	21.9
White (%)	55.2	77	76.4	77.9
Age (years)	55.2	71.4	69.9	54

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A retrospective chart review was conducted of 466 adult RA patients receiving care at a single academic medical center. Patients were stratified into four groups: private insurance, Medicaid, Medicare, and Medicare with supplemental coverage ("Medicare+"). Variables collected included current treatment regimen, route of biologic administration (infusion vs. injectable, including JAK inhibitors), radiographic erosions, seropositivity, demographics, Area Deprivation Index (ADI), Elixhauser Comorbidity Index (ECI), and patient-reported outcomes using the Routine Assessment of Patient Index Data 3 (RAPID3). Multivariable logistic regression analysis was used to assess associations between insurance type and biologic use/remission, adjusting for age, sex, race/ethnicity, and seropositivity.

Results: Biologic use was highest among privately insured patients (52.6%) compared to those with any form of government insurance (45.7%), with the lowest rates observed in Medicare patients (42.5%). Privately insured patients were also more likely to use injectable therapies compared to Medicare and Medicare+ groups (Graph 1). Remission, as assessed by RAPID3, was more common in the privately insured group, with notably lower rates among Medicaid patients (Graph 2). No significant differences were observed across insurance groups in seropositivity, prior treatment history, ECI, or ADI that could account for these disparities (Table 1).

Conclusion: Our project's findings highlight a 10% disparity in biologic prescribing and patient-reported remission between Medicare and privately insured patients with RA. Moreover, large differences were found in the RAPID3 based on insurance status. While limited by its retrospective, cross-sectional design and single-center sample, this study raises important questions about insurance-related barriers in rheumatologic care. Further research is warranted to explore systemic contributors to treatment inequities and to guide policy aimed at improving equitable access to high-cost therapies.

Disclosure: A. Dattagupta: None; **C. Diffie**: Amgen, 6; **S. Cheema**: None.

Abstract Number: 1056

High diagnostic rate of genetic testing in adult patients with autoinflammation: A Single Center Experience

Atif Towheed[1], Joshua Owens[2], Ann Parody[1] and Daniella Schwartz[3], [1]University of Pittsburgh Medical Centre, Pittsburgh, [2]UPMC Children's Hospital of Pittsburgh, Pittsburgh, [3]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Inborn errors of immunity (IEI), including autoinflammatory diseases and primary immune regulation disease (PIRD), are unfamiliar to many adult rheumatologists, leading to potential ascertainment bias and health disparities for adults with suspected IEI. While genetic testing is a cornerstone for diagnostic testing in pediatric autoinflammatory clinics, data from adult rheumatology clinics are limited. This study evaluates genetic diagnostic rates in an adult cohort with suspected IEI, including autoinflammatory diseases, at a single tertiary care center, comparing outcomes to pediatric benchmarks.

Methods: We retrospectively analyzed a cohort of 155 adult patients referred to our rheumatology immunogenetics clinic between 2022-2025 for suspected IEI, including autoinflammatory syndromes and PIRD. Patients underwent targeted array-based genetic testing (n = 68, 574 genes); somatic variant testing for *UBA1* and other genes associated with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

myelodysplastic syndrome (MDS) (n = 6, 302 genes); or whole exome sequencing (n = 2) to identify potential disease-causal or disease-contributory variants. Clinical phenotypes, inflammatory markers (CRP, ESR, SAA, ferritin, 28-gene interferon score, S100A8/9, S100A12), family pedigrees, and demographic data were correlated with genetic findings. Variants were classified per American College of Medical Genetics and Genomics guidelines.

Results: Variants of interest (pathogenic, likely pathogenic, variant of uncertain significance/VUS) were identified in 30% (24/80) of the tested patients. Of these, 24 were ACMG P/LP and 70 were VUS. Functional testing revealed a potential causal role for 24 genes and contributory for 45 genes. IEI diagnoses included familial Mediterranean fever, HA20, NAIAD, DiGeorge syndrome, Trisomy 8, and others. An additional 45 patients were found to have variants that were not disease-causal but affected management (i.e. enhanced cancer screening) due to risk for other conditions. Of the six patients tested for VEXAS, four had pathogenic *UBA1* variants, and one had clinically significant MDS-associated variants in other genes. The genetic diagnostic rate was comparable to pediatric IEI cohorts (15–35%). Approximately 60% of patients did not obtain a genetic diagnosis; this could be to variants in novel IEI-causal genes or to non-genetic etiologies.

Conclusion: This single-center study demonstrates that rheumatology immunogenetics clinics achieve similar genetic diagnostic rates (33%) in adult and pediatric cohorts, underscoring the prevalence and significance of IEI in adults. The identification of VEXAS and MDS-causal variants further highlights the clinical relevance of targeted testing in this population. These findings advocate for increased availability of adult immunogenetics clinics to enable personalized management and genetic counseling. Multicenter studies are needed to validate novel variants and address undiagnosed cases.

Disclosure: A. Towheed: None; **J. Owens**: None; **A. Parody**: None; **D. Schwartz**: Eli Lilly, 5, Jeffrey Modell Foundation, 5, National Institutes of Health, 5, Samuel and Emma Winters Foundation, 5, Sobi, 1, 5.

Abstract Number: 1057

Leveraging Social Risk Factor Screening Infrastructure in Rheumatology Clinics to Respond to Rising Rates of Tuberculosis Among Individuals Experiencing Homelessness

Rebecca Summit[1], Dylan Tierney[2], Taussia Boadi[2], Tyler Green[2], Karli Retzel[2], Virginia Bills[2], Nancy Shadick[2], Leah Santacroce[3], Sara Schoenfeld[4] and **Candace Feldman**[5], [1]Brigham & Women's Hospital, Boston, MA, [2]Brigham & Women's Hospital, Boston, [3]Brigham and Women's Hospital, Boston, MA, [4]Mass General Hospital, Boston, [5]Brigham and Women's Hospital/ Harvard Medical School, Boston

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Social risk factors, such as housing instability, influence care access and outcomes in people with rheumatic conditions. In June 2022, 9 rheumatology clinics in a multihospital medical center began to screen patients for social risk factors. In September 2024, the Massachusetts Department of Public Health issued an alert of increased tuberculosis (TB) in Boston homeless shelters. Patients with systemic rheumatic conditions have higher TB infection risk and poorer outcomes; immunosuppressive medications heighten risk. We aimed to leverage the social risk screening infrastructure to rapidly respond to TB spread among homeless individuals with rheumatic conditions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

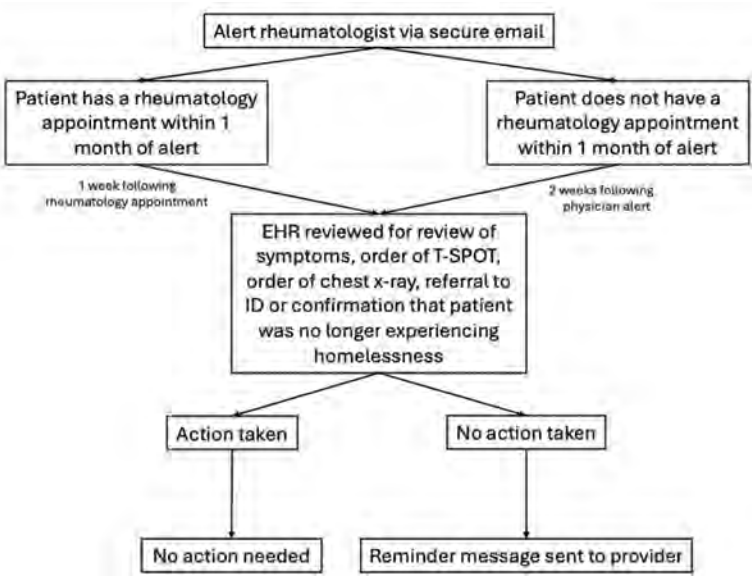
Table 1. Description of Patients Identified at High Risk for TB Exposure Receiving Immunosuppressive or Immunomodulatory Medications (N=23)	
Gender- N (%)	
Male	6 (26)
Female	17 (74)
Race- N (%)	
White	14 (61)
Patient doesn't know, not listed, unavailable	9 (39)
Ethnicity- N (%)	
Hispanic	11 (48)
Not Hispanic	12 (52)
Mean age (SD)	56 (16)
Medication – N (%)	
Abatacept	2 (9)
Anifrolumab	1 (4)
Anti-TNFs (Etanercept, Adalimumab, Certolizumab, Golimumab, Infliximab)	6 (26)
Azathioprine	1 (4)
Hydroxychloroquine	7 (30)
IL-6 inhibitors (Tocilizumab, Sarilumab)	1 (4)
Anti-IL-17s (secukinumab, ixekizumab)	3 (13)
Leflunomide	1 (4)
Methotrexate	3 (13)
Mycophenolate mofetil	3 (13)
Prednisone or Methylprednisone	6 (26)
Tacrolimus	2 (9)

Methods: Using the Research Patient Data Registry and manual electronic health record (EHR) review, we identified patients with ≥1 ICD-9/10 code for a systemic rheumatic condition receiving ≥1 immunosuppressive or immunomodulatory medication who indicated that they did not have housing, lived in a shelter, or on the street on their most recent social risk screening. The rheumatology-based social risk screening team met with infectious disease (ID) specialists to develop protocols, and we alerted rheumatologists of patients at high risk for TB with a description of their patients' risk factors, and instructions to screen for active and latent TB. We reviewed the EHR to determine provider response (Figure 1). If no action was taken, we sent a reminder. The EHR was reviewed after 2 months. Rheumatologists were surveyed for feedback.

Results: Thirty-three patients with systemic rheumatic conditions experienced housing instability. Of these, 23 (70%) patients cared for by 17 rheumatologists were prescribed ≥1 immunosuppressive or immunomodulatory medication (Table 1). After the first alert, 3 (13%) patients had documentation of TB symptom screening, one provider responded that their patient was not homeless, and one ordered an interferon-gamma release assay ("T-SPOT"). Providers for two (9%) patients prescribed hydroxychloroquine were notified in case there was a therapy escalation plan, but a reminder was not sent due to lower risk. After the second alert, 7 (30%) T-SPOT tests were ordered. One patient self-reported a negative T-SPOT. Four (17%) patients had EHR documentation of symptom review at their subsequent rheumatology appointment, and 3 (13%) patients were messaged about their TB risk. Two (9%) patients had chest imaging ordered. There were no

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1.



referrals to ID and no action taken for 4 patients. Among the 41 rheumatologists who responded to the survey, 18 (45%) received an alert for ≥1 patient. Of those, 4 (22%) found it somewhat helpful, 5 (28%) found it very helpful and 16 (89%) indicated that the alert prompted action.

Conclusion: The social risk screening infrastructure in rheumatology facilitated a rapid response to a public health concern. Rheumatologists' responses varied, possibly due to increased clinical stressors with limited support. While there were challenges reaching patients with social risk factors, actions were taken for most. Efforts are now underway to prompt yearly TB screening for patients who indicate housing instability.

Disclosure: R. Summit: None; **D. Tierney**: Compugen, 12, Stock holder, Renovaro, 12, Stock holder, Seres, 12, Stock holder, Viatris, 12, Stock holder; **T. Boadi**: None; **T. Green**: None; **K. Retzel**: None; **V. Bills**: None; **N. Shadick**: Bristol-Myers Squibb(BMS), 5, Janssen, 5; **L. Santacroce**: None; **S. Schoenfeld**: None; **C. Feldman**: American College of Rheumatology, 2, 12, Committee Member/Interim Chair, Arthritis Foundation, 5, 12, Task Force Member, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 2, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2.

Abstract Number: 1058

Prevalence of Depression Associated with Rheumatologic Medications with Labeled Warnings: Real World Evidence from a Tertiary Care Center

Cassandra Dolecki[1], Sama Hajizadeh[1], Yue Yin[2] and Adam Dore[1], [1]Allegheny Health Network, Pittsburgh, PA, [2]Allegheny Health Network, Pittsburgh

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The prevalence of depression in patients who have rheumatic diseases is high and has been shown to be associated with poorer outcomes. Additionally, certain medications for rheumatologic conditions have been associated with an increased risk of depression, depressed mood, and suicidal ideation, namely apremilast and belimumab. Patient Health Questionnaire (PHQ9) screening is a well-established tool in screening for depression at medical appointments, including those with rheumatic diseases. A score of 10 or higher is a standard cut point to diagnose depression. This study assessed PHQ9 scores for patients with psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE) on apremilast and belimumab, respectively.

Methods: The study population included patients with PsA and SLE seen within Allegheny Health Network rheumatology clinics between November 2021 through November 2024 with at least one PHQ9 score documented. Demographic and clinical variables were collected. Descriptive statistics were used to describe the patient population. PHQ9 scores for persons with PsA were compared based on apremilast usage, and scores for patients with SLE were compared based on belimumab usage. The Kruskal-Wallis test was conducted to compare the PHQ9 score amongst the two patient populations. Fisher's exact test was performed to examine the association between PHQ9 category with medications.

Results: At least one PHQ9 score was documented for 1738 patients with PsA, and 892 patients with SLE (Table 1). Of the patients with PsA, 96 (5.52%) were treated with apremilast. There was no significant difference in median PHQ9 scores between patients that were on apremilast compared to those that were not (median 0 [IQR 0-0], median 0 [IQR 0-0]; p=0.2076). In addition, when stratified by apremilast usage, there was no significant difference found in patients with PsA who had PHQ9 scores of ≤9 compared to those with a score of ≥10 (p=0.2899; Table 2).

Of the patients with SLE, 36 (4.04%) were treated with belimumab. There was no significant difference in median PHQ9 scores between those treated with belimumab compared to those that were not (median 0 [IQR 0-1.5], median 0 [IQR

Table 1. Baseline Characteristics.

Variable	Overall	PsA (n=1738)	SLE (n = 892)
Age	56.40(14.15)	57.39(13.47)	54.48(15.21)
Sex			
Female	1966(74.78%)	1150(66.17%)	816(91.58%)
Male	663(25.22%)	588(33.83%)	75(8.42%)
Race			
American Indian	5(0.19%)	1(0.06%)	4(0.45%)
Asian	19(0.72%)	11(0.63%)	8(0.90%)
Black	88(3.35%)	14(0.81%)	74(8.30%)
Native Hawaiian	2(0.08%)	2(0.12%)	0(0%)
Other	34(1.29%)	12(0.69%)	22(2.47%)
Unknown	3(0.11%)	2(0.12%)	1(0.11%)
White	2479(94.26%)	1696(97.58%)	783(87.78%)
Ethnicity			
Hispanic	34(1.29%)	15(0.86%)	19(2.13%)
Not Hispanic	2597(97.45%)	1695(97.53%)	868(97.31%)
Unknown	33(1.25%)	28(1.61%)	5(0.56%)
Medication			
Apremilast/Otezla	97(3.69%)	96(5.52%)	1(0.11%)
Belimumab/Benlysta	36(1.37%)	0(0%)	36(4.04%)
No medication	2478(94.22%)	1628(93.67%)	850(95.29%)
Other	19(0.72%)	14(0.81%)	5(0.56%)
PHQ-9 score	0(0-0)	0(0-0)	0(0-0)
PHQ-9 category			
≤9	2510(95.44%)	1670(96.09%)	840(94.17%)
>9	120(4.56%)	68(3.91%)	52(5.83%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. PHQ9 Category Comparison Among Medication Groups and Diagnoses

Disease	Variable	PHQ-score category		P value
		≤9	>9	
PsA	Medication			.2899
	Apremilast	95(5.69%)	1(1.47%)	
	No med	1561(93.47%)	67(98.53%)	
	Other	14(0.84%)	0(0%)	
SLE	Medication			.1296
	Belimumab	31(3.69%)	5(9.62%)	
	No med	803(95.71%)	47(90.38%)	
	Other	5(0.60%)	0(0%)	

0-0]; p=0.0995). And when stratified by belimumab usage, there was no significant difference in the SLE patients with PHQ9 scores of ≤9 compared to those with a score of ≥10 (p=0.1296; Table 2).

Conclusion: In this single center observational cohort, we found that PHQ9 scores were no different between patients with PsA treated with apremilast compared to those not; and no difference between patients with SLE treated with belimumab compared to those who were not. The overall positive depression screening was low in all patients. This provides real world assurance of the safety of apremilast and belimumab, but should not underscore the importance of monitoring depression in rheumatologic diseases.

Disclosure: C. Dolecki: Janssen, 6; **S. Hajizadeh**: None; **Y. Yin**: None; **A. Dore**: AbbVie/Abbott, 2, 6, Janssen, 6, Novartis, 2, UCB, 6.

Abstract Number: 1059

Assessing the Relationship Between Multidimensional Area Level Indicators and Lupus Disease Activity in Children

Chelsea Reynolds[1], Natasha Ruth[2], Paul Nietert[1], Mileka Gilbert[1], Emily Vara[1] and Joyce Chang[3], [1]Medical University of South Carolina, Charleston, SC, [2]Medical University South Carolina, Charleston, SC, [3]Boston Children's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Recent research suggests that multidimensional area-level indicators, including the Social Vulnerability Index (SVI), Area Deprivation Index (ADI) and Childhood Opportunity Index (COI), associate with childhood-onset systemic lupus erythematosus (cSLE) outcomes in primarily urban populations. However, to date, there are no studies that have assessed the utility of multidimensional area level indicators in children with cSLE living in rural areas. The goal of this study is to estimate relationships between neighborhood conditions and disease activity in children with cSLE who live in a mixed rural and urban setting. We hypothesized that patients with cSLE living in areas with higher social vulnerability and area-level deprivation have increased lupus activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We retrospectively evaluated electronic health record data for pediatric patients with cSLE across three pediatric rheumatology clinics at a single center between January 1, 2020 and December 31, 2024. We included patients with a diagnosis of cSLE before 18 years of age, a residential address within South Carolina, and excluded PO box addresses. Chart reviews were conducted to collect demographic data and addresses were linked to census tract-level indicators, including ADI, SVI and COI, ranked at state and national levels. We assessed each patient's SLEDAI-2K score at their first clinic or hospital encounter associated with a SLE diagnosis.

Results: Baseline characteristics have been established for a cohort of 85 children with cSLE. The majority of patients identified as Black 65 (79%), followed by White 11 (13%), Latino/a 6 (6%), Asian 1 (1%), and Other 1 (1%). The cohort was predominantly female (87.1%), with a mean age at diagnosis of 13.0 years (range: 6–17). The mean SLEDAI-2K at the initial encounter was 14.4 (range: 0-38). Most participants (40%) lived in areas with low state-ranked SVI scores (mean 0.42), with no significant correlation with initial SLEDAI-2K (R= 0.014). National SVI levels were higher, with most patients classified in medium-to-high (51.2%) SVI category (mean 0.69), with no significant correlation with initial disease activity (R = 0.0223). Similarly, neither state nor national ADI rank correlated with initial SLEDAI-2K (R = 0.106 and 0.0905, respectively). Most patients lived in areas with very low (35.3%) state-ranked child opportunity and very low (38.8%) nationally ranked opportunity. Again, no significant correlation was found between COI and initial disease activity (R = 0.067 and 0.050, respectively).

Conclusion: In a mixed rural and urban population, we did not observe significant associations between area-level measures of social vulnerability, area deprivation or childhood opportunity (COI) and lupus disease activity, as measured by SLEDAI-2K score at initial presentation to rheumatology care. Despite the cohort's residence in predominantly deprived and low-opportunity areas, these indicators did not appear to predict lupus severity at first presentation to care. These findings highlight limitations in the use of available area-level indicators to explain pediatric lupus outcomes in mixed rural and urban areas.

Disclosure: C. Reynolds: None; **N. Ruth**: None; **P. Nietert**: None; **M. Gilbert**: None; **E. Vara**: None; **J. Chang**: Century Therapeutics, 2.

Abstract Number: 1060

Demographic Risk Factors, Social Vulnerability Index, and Mortality in Patients with Systemic Lupus Erythematosus

Christine Kim[1], Katherine Mitchell[2], Changyong Feng[1] and Allen Anandarajah[3], [1]University of Rochester, Rochester, NY, [2]University of Rochester, Rochester, [3]University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with multi-organ involvement that is characterized by relapses and remissions. Ethnicity, socioeconomic status, gender, age, education level, and healthcare access are associated with poorer disease outcomes among patients with SLE. The social vulnerability index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Demographics

Demographics	Total Number
Sex	**405**
Female	362
Male	43
Race/Ethnicity	**392** (Frequency Missing = 13)
African American/Black	160
Asian	9
Hispanic/Latino	33
Multiple Race	8
Native American	1
White	181
Overall Social Vulnerability Index (SVI) Quartile	**404** (Frequency Missing = 1)
1st (least disadvantaged)	81
2nd	91
3rd	98
4th (most disadvantaged)	134

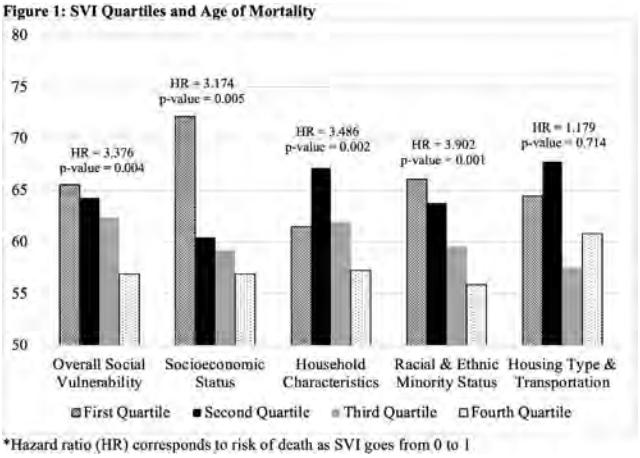
Table 2: Mortality, Patient Demographics, and Social Vulnerability Index

Characteristics	Average Age of Mortality	Number
Sex*	**61.51**	**75***
Female	61.46	60
Male	61.71	15
Race/Ethnicity*	**61.51***	**75**
African American/Black	55.72	35
Hispanic/Latino	49.45	3
Multiple Race	57.59	5
White	69.59	32
Overall Social Vulnerability Index (SVI) Quartile*	**61.51***	**75**
1st (least disadvantaged)	65.53	9
2nd	64.27	17
3rd	62.40	26
4th (most disadvantaged)	56.91	23
Socioeconomic Status Quartile*	**61.51***	**75**
1st (least disadvantaged)	72.13	15
2nd	60.47	18
3rd	59.21	23
4th (most disadvantaged)	56.91	19
Household Characteristics*	**61.51***	**75**
1st (least disadvantaged)	61.49	15
2nd	67.17	18
3rd	61.97	23
4th (most disadvantaged)	57.27	19
Racial & Ethnic Minority Status*	**61.51***	**75**
1st (least disadvantaged)	66.06	22
2nd	63.77	20
3rd	59.57	11
4th (most disadvantaged)	55.89	22
Housing Type & Transportation	**61.51**	**75**
1st (least disadvantaged)	64.44	12
2nd	67.74	17
3rd	57.52	33
4th (most disadvantaged)	60.81	13

*Indicates p-value < 0.05

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: SVI Quartiles and Age of Mortality



*Hazard ratio (HR) corresponds to risk of death as SVI goes from 0 to 1

(SVI), developed by the Centers for Disease Control and Prevention (CDC), is a measure of demographic and socioeconomic factors that adversely affect health outcomes. We aim to determine the association between SVI and mortality in our lupus cohort.

Methods: This was a single-center retrospective study of all SLE patients hospitalized at the University of Rochester Strong Memorial Hospital between July 2016 and June 2023. We analyzed the age, race and ethnicity, mortality, and SVI among all those hospitalized. SVI is measured on a percentile ranking from 0 to 1, with higher percentiles indicating more social vulnerability. Additionally, SVI is divided into 4 subcategories (socioeconomic status, household characteristics, racial & ethnic minority status, and housing type & transportation) which are also assessed on a percentile scale from 0 to 1. The SVI and the scores of the 4 subcategories were determined based on publicly available CDC data and the patient's current addresses. The ANOVA and chi-squared tests were used to assess differences in demographic risk factors and mortality. The Cox regression was used to assess the hazard ratios for SVI and its subcategories.

Results: A total of 405 patients met criteria for a diagnosis of SLE. There were 75 deaths during the specified time period (Table 1). The mean age of death for the entire cohort was 61.51 years. The mean age of death for those patients identifying as White was 69.59 years, 55.72 years for Black patients, and 49 years for Hispanic patients (p-value = 0.0019) (Table 2). Although the age of mortality was not significantly different between females and males (61.46 vs 61.71 years, p-value = 0.9583), there was a significant difference in mortality rates (16.6% in females vs 34.9% in males, p-value = 0.0035). The average age of death of patients in the first quartile of SVI was 65.53 years of age compared to 56.81 years of age for patients in the last quartile of SVI. Patients of higher social vulnerability had a significantly higher risk of death with a hazard ratio of 3.38 (p-value = 0.004) (Table 2, Figure 1). Higher percentile scores were associated with significantly higher risk of death for all subcategories of SVI, except for housing type & transportation (Table 2, Figure 1).

Conclusion: There is a significant difference in age of mortality among hospitalized SLE patients based on race. Additionally, patients with a higher social vulnerability score are at a higher risk of death. Among the four subcategories of social vulnerability, socioeconomic status, household characteristics, racial & ethnic minority status contributed to significantly increased risk of death while housing type & transportation did not. Providing additional care and developing specific interventions to overcome barriers to care may help reduce mortality among lupus patients with high SVI scores.

Disclosure: C. Kim: None; **K. Mitchell**: None; **C. Feng**: None; **A. Anandarajah**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1061

Screening for Hepatitis B in a Veterans Health Administration Subpopulation with Rheumatological Disease Prior to Initiating Immunosuppressive Therapy: a retrospective study on testing and treatment within the Black American population from the VAMC in Memphis, TN

Daniel Austin[1], Beenish Zulfiqar[2], Akhil Adla[1], Jeffrey Zuber[2] and Joshua Sullivan[3], [1]University of Tennessee Health Science Center, Memphis, TN, [2]University of Tennessee Health Science Center & Lt. Col. Luke J. Weathers, Jr. VA Medical Center, Memphis, TN, Memphis, TN, [3]Lt. Col. Luke J. Weathers, Jr. VA Medical Center, Memphis, TN, Memphis, TN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Hepatitis B virus (HBV) screening is insufficiently completed prior to initiation of immunosuppressive therapy nationwide. Various factors including alert fatigue, provider mistakes, non-compliance, and EMR faults / errors all play a role in leading to insufficient screening. HBV status is often difficult to ascertain given the indolent and asymptomatic nature of HBV progression. Immunosuppression can lead to HBV reactivation. Concerningly, the prevalence of HBV is higher in veterans than the general population at up to 1.0%, highlighting the increased importance of screening within this specific population (1). Additionally, prevalence is also higher within the Black American population as compared to others. While HBV screening rates within various Veterans Affairs Medical Centers (VAMC) facilities have been studied with regards

Patient characteristics (n=551)

Variable	n (%)
Sex, male	394 (71.5)
Age, years, Mean (SD)	60.5 (10.6)
Race/Ethnicity, black	551 (100)
Rheumatology diagnosis	
RA	350 (63.8)
SpA	67 (12.2)
SLE	50 (9.1)
Sarcoid	36 (6.6)
Uveitis	12 (2.2)
Scleritis	8 (1.5)
Sjogrens	6 (1.1)
Other	20 (3.5)
Drug class	
cDMARD	350 (63.5)
TNF	130 (23.6)
CTLA-4	16 (2.9)
JAK	15 (2.7)
IL6	13 (2.4)
IL17	9 (1.6)
PDE4	7 (1.3)
CD20	3 (0.5)
Other	8 (1.5)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2:

Screening and prescription outcomes within diagnoses

	Rheumatology diagnosis, %								
	All n=551	RA n=350	SpA n=67	SLE n=50	Sarcoid n=36	Uveitis n=12	Scleritis n=8	Sjogrens n=6	Other n=19
Drug prescribed after labs	75.8	72.6	92.5	78.0	66.7	91.7	75.0	83.3	80.0
Labs 1-180 days prior to prescription	32.7	32.0	41.8	30.0	33.3	25.0	50.0	33.3	20.0
Labs 1-30 days prior to prescription	16.9	16.0	20.9	14.0	19.4	16.7	37.5	16.7	15.0
Drug prescribed before labs	17.3	19.1	6.0	16.0	27.8	0	12.5	0	20.0
Labs 1-180 days after prescription	5.8	5.7	3.0	4.0	11.1	0	12.5	0	10.0
Labs 1-30 days after prescription	1.3	1.1	1.5	0	2.8	0	12.5	0	0
HBV core Ab+	11.3	11.7	22.4	0	2.8	0	25.0	33.3	5.0
Sent to GI	79.0	78.0	73.3	0	100	0	100	100	100
Started antiviral	50.0	56.1	40.0	0	0	0	100	0	0

Note: for Sent to GI, and Started antiviral, percentages are for patients who were HBV core Ab+

Table 3:

Screening and prescription outcomes within drug class

	Rheumatology drug class, %									
	cDMARD n=350	Non-cDMARD n=201	TNF n=130	CTLA-4 n=16	JAK n=15	IL6 n=13	IL17 n=9	PDE4 n=7	CD20 n=3	Other n=8
Drug prescribed after labs	71.6	83.1	85.4	56.3	100	69.2	55.6	71.4	100	87.5
Labs 1-180 days prior to prescription	28.4	40.3	46.9	25.0	46.7	15.4	44.4	14.3	0	25.0
Labs 1-30 days prior to prescription	14.9	20.4	23.8	0	20.0	7.7	33.3	14.3	0	25.0
Drug prescribed before labs	20.3	11.9	8.5	31.3	0	30.8	11.1	28.6	0	12.5
Labs 1-180 days after prescription	7.2	3.5	1.5	0	0	15.4	0	28.6	0	12.5
Labs 1-30 days after prescription	1.7	0.5	0	0	0	7.7	0	0	0	0
HBV core Ab+	10.0	13.4	14.6	12.5	13.3	15.4	0	14.3	0	12.5
Sent to GI	77.1	81.5	73.7	100	100	100	0	100	0	100
Started antiviral	34.3	70.4	63.2	100	100	100	0	100	0	0

Note: for Sent to GI, and Started antiviral, percentages are for patients who were HBV core Ab+

to prescribing Rituximab, which likely has the highest risk of reactivation, less research has been conducted to analyze screening rates before start of a wider array of anti-rheumatic medications, highlighting the need for further research.

Methods: A five-year retrospective study was performed reviewing HBV serologies – including HBV core Ab, surface Ag, and HBV DNA in patients who were started on immunosuppressive therapy within our rheumatology clinic at the VAMC in Memphis, TN. Using collected data from the pharmacy, patients were extracted who had previously been prescribed csDMARDs, bDMARD, and small molecules. The study period was set from 1/1/2017 to 12/31/2022. To more directly identify how well we were screening patients with a statistically higher risk of HBV infection, past or present, Black Americans within our clinic were specifically studied, with plans to study data from other races in the future as a comparison.

Results: Within our study period, 551 instances were found in which Black American patients had been prescribed medications from the list above. Out of these 551 patients, 75.9% had HBV screening labs prior to initiation of DMARD therapy. However, only 32.7% of patients had screening labs within six months of starting treatment. For those that did not have labs checked prior to start of treatment, 33.7% of these patients had labs checked within six months after starting treatment. Out of our population, 11.2% were HBV core Ab positive. Of these patients, 79% were sent to Hepatology and 50% were started on antiviral prophylaxis. No episodes of HBV reactivation leading to fulminant hepatitis or clinical deterioration / death were identified.

Conclusion: Our findings suggest a large number of patients are not being appropriately screened prior to initiation of DMARDs. While no episodes of HBV reactivation leading to fulminant hepatitis or clinical deterioration / death were identified, further correction of this lack of pre-screening is critical to ensure safety of our patients, particularly within this veteran group who inherently are at a higher risk. We plan to study data from other races to determine if there are any statistical differences between the two groups to further help us implement quality initiatives to improve outcomes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

1. Garren P, Serper M. Chronic Hepatitis B in US Veterans. Curr Hepatol Rep. 2019;18(3):310-315.

Disclosure: D. Austin: None; **B. Zulfiqar**: None; **A. Adla**: None; **J. Zuber**: None; **J. Sullivan**: None.

Abstract Number: 1062

Sex-related differences in clinical presentation and patient-reported burden in chronic back pain: Are these findings specific to axSpA? Results from the SHERPAS Cohort

Diego Benavent[1], Mar Tapia[2], Daniel Bernabeu[2], Victor Muley[2], Manuel Juárez[3], Alejandro Balsa[4], Chamaida Plasencia-Rodríguez[4] and Victoria Navarro-Compan[5], [1]Hospital Universitari de Bellvitge, Madrid, Spain, [2]HU La Paz, Madrid, Spain, [3]Rheumatology Unit, Hospital Universitario La Paz, IdiPAZ, Madrid, Spain, [4]Hospital Universitario La Paz, Madrid, Spain, [5]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1. Characteristics of patients in the SHERPAS cohort stratified by sex

Variable	Total (n=260)	Female (n=149)	Male (n=111)	p-value
Age, years	34.6 (5.6)	34.4 (5.9)	34.7 (5.1)	0.68
BMI	25.6 (4.6)	25.1 (4.8)	26.2 (4.4)	0.06
BMI categories				
Underweight	5 (2.1)	5 (3.8)	0 (0.0)	0.15
Normal weight	123 (52.8)	71 (54.2)	52 (51.0)	
Overweight	67 (28.8)	33 (25.2)	34 (33.3)	
Obesity	38 (16.3)	22 (16.8)	16 (15.7)	
HLA-B27 positive	11 (5.0)	5 (4.1)	6 (6.2)	0.67
CRP >5 mg/L	36 (15.0)	27 (19.4)	9 (8.9)	0.04
Smoking	94 (36.2)	54 (36.2)	40 (36.0)	1.00
Marital status				
Married	104 (44.6)	61 (46.2)	43 (42.6)	0.67
Other	129 (55.4)	71 (53.8)	58 (57.4)	
Other diagnosis				
Spondylolisthesis	13 (5.0)	5 (3.4)	8 (7.2)	0.39
Spondylolysis	3 (1.2)	2 (1.3)	1 (0.9)	
Disc herniation	67 (25.8)	35 (23.5)	32 (28.8)	
Disc protrusion	111 (42.7)	64 (43.0)	47 (42.3)	
Spondyloarthrosis	10 (3.8)	8 (5.4)	2 (1.8)	
No evidence of structural pathology	26 (10.0)	18 (12.1)	8 (7.2)	
Other	30 (11.5)	17 (11.4)	13 (11.7)	
MRI Lumbar findings				
No abnormalities	30 (11.7)	18 (12.2)	12 (11.0)	0.67
Structural findings	223 (87.1)	128 (87.1)	95 (87.2)	
Inflammatory findings	3 (1.2)	1 (0.7)	2 (1.8)	
MRI Sacroiliac findings				
No abnormalities	189 (73.8)	111 (75.5)	78 (71.6)	0.43
Structural signs of sacroiliitis	28 (10.9)	18 (12.2)	10 (9.2)	
Inflammatory signs of sacroiliitis	34 (13.3)	16 (10.9)	18 (16.5)	
Inflammatory and structural signs of sacroiliitis	5 (2.0)	2 (1.4)	3 (2.8)	

BMI: body mass index; CRP >5 mg/L: C-reactive protein above 5 mg/L; AxSpA: axial spondyloarthritis; MRI Lumbar: magnetic resonance imaging. Results are reported as mean (SD) or n (%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sex-related differences in axial spondyloarthritis (axSpA) have been described regarding clinical features, disease burden, and particularly patient-reported outcomes. These differences influence patient management, including diagnostic strategies and referral patterns. However, it remains unclear whether these sex-specific differences represent a distinct feature of axSpA or if similar patterns also occur in the broader population of patients with chronic back pain (CBP) without axSpA. The objective of this study is to assess sex differences in demographic and clinical features, including patient-reported disease activity and functional impairment, among young adults with CBP referred by non-rheumatology specialists.

Methods: A prospective, cross-sectional observational study was conducted between July 2021 and October 2023 as part of the "Strategy for a Hospital Early Referral in Patients with Axial Spondyloarthritis" (SHERPAS) Cohort. Adults aged 18–40 years with CBP (>3 months duration) referred for spinal magnetic resonance imaging (MRI) by non-rheumatology specialists completed detailed questionnaires capturing demographic characteristics, lifestyle factors and patient-reported outcomes (PROs), including disease activity and functional impairment measured by BASDAI and BASFI. MRI imaging of the spine and sacroiliac joints (SIJ) were performed within two weeks, as well as a consultation with the rheumatologist. Diagnoses were based on expert clinical judgment considering imaging, clinical, and laboratory data. Only patients in whom a diagnosis of axSpA had been ruled out were included. Statistical comparisons by sex were conducted using appropriate parametric or non-parametric tests.

Results: Among 260 patients, 149 (57.3%) were female, and mean age was 34.6±5.6 years. While most demographic and clinical characteristics did not differ significantly by sex (**Table 1**), marked differences were observed in PROs. Female reported significantly higher overall BASDAI (4.9±2.5 vs 3.6±2.4; p< 0.001) and higher overall BASFI (3.7±2.7 vs 2.8±2.5; p=0.004) versus males. Concerning individual BASDAI items (**Figure 1**), female reported higher scores in fatigue (5.6 ± 3.1 vs 4.1 ± 2.9; p< 0.001), spinal pain (6.5 ± 3.0 vs 5.1 ± 3.2; p=0.001), peripheral pain (3.4 ± 3.4 vs 1.9 ± 2.7; p < 0.001), and general discomfort/enthesitis (5.2 ± 3.5 vs 3.3 ± 3.1; p < 0.001) than males. Female also had higher functional impairment in BASFI items, particularly showing greater difficulty reaching an object on a shelf

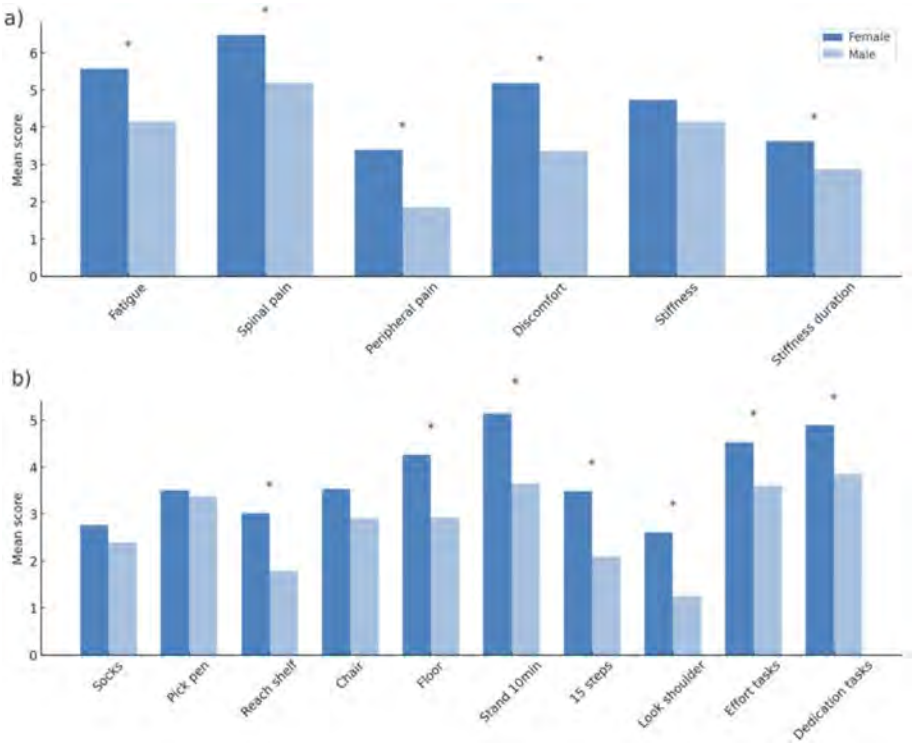


Figure 1. Items of BASDAI (a) and BASFI (b) stratified by sex

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(3.0 ± 3.4 vs 1.8 ± 2.8; p=0.002), rising from the floor (4.3 ± 3.7 vs 2.9 ± 3.3; p=0.002), standing for 10 minutes (5.1 ± 3.6 vs 3.7 ± 3.5; p=0.002), climbing 15 steps (3.5 ± 3.5 vs 2.1 ± 3.1; p=0.001) and turning the head over the shoulder (2.6 ± 3.3 vs 1.3 ± 2.4; p< 0.001).

Conclusion: Significant sex differences were observed in the clinical presentation of young adults with CBP, particularly in patient-reported disease activity and functional limitation scores. These findings suggest that sex-related disparities in disease burden are not specific to axSpA, highlighting the need for broader sex-sensitive strategies in the evaluation and management of all young patients with CBP.

Disclosure: D. Benavent: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, Pfizer, 6, Savana, 7, UCB, 2, 6; **M. Tapia**: None; **D. Bernabeu**: None; **V. Muley**: None; **M. Juárez**: Gebro Pharma, 6; **A. Balsa**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, Pfizer, 6, UCB, 6; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1063

Gender, Racial, and Geographic Trends in Mortality from Interstitial Lung Diseases Among Patients With Rheumatoid Arthritis in the U.S. Population, 1999–2020

Farheen Malik[1], Jawad Ahmed[2], Mandar Shah[1], Ritika Uttam[3] and Muhammad Fahimuddin[1], [1]Jacobi Medical Center, Bronx, NY, NY, [2]Northwest Health Porter, Valpraiso, IN, [3]Jacobi Medical Center, Bronx, NY

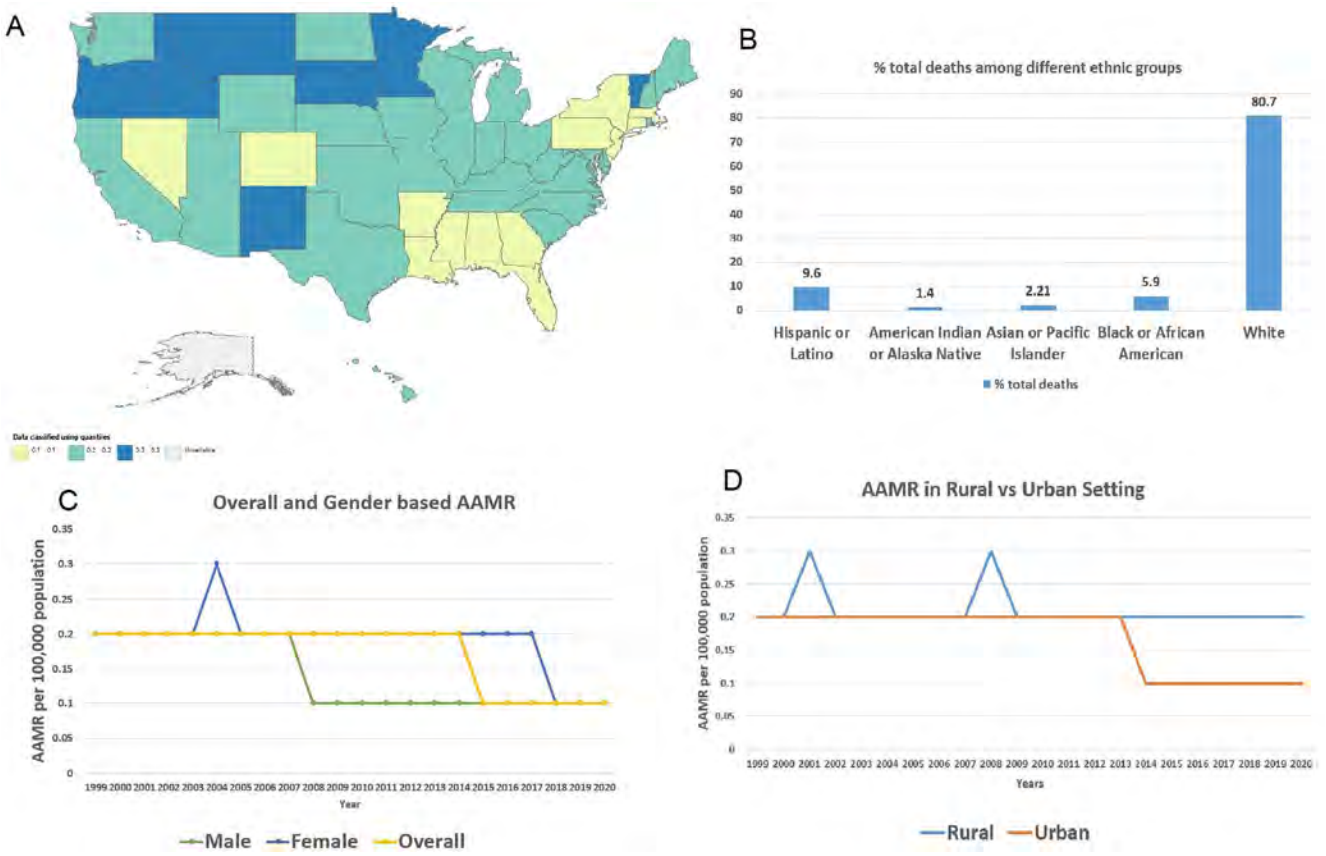
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a common autoimmune disease affecting up to 1.0% of the US population. RA is most commonly associated with synovial inflammation and articular symptoms but is also associated with extra-articular manifestations. Interstitial lung disease (ILD) is one of the most important and common pulmonary manifestations of RA and it is associated with significant morbidity and mortality. We aim to find variations in the mortality trend of ILD in RA patients.

Methods: Death certificates from the CDC Wonder Database were analyzed from 1999 to 2020 for ILD (J84.1) and RA (M05 and M06) patients. Age-adjusted mortality rates (AAMR) per 100,000 individuals, average annual percentage change (AAPC), and annual percent change (APC) with respective 95% CI were calculated and stratified for gender, racial, age, and geographic factors.

Results: A total of 10171 ILD and RA-associated deaths occurred between 1999 and 2020 with an overall AAMR of 0.2. AAMR declined from 0.2 in 1999 to 0.1 in 2020 with an AAPC of -3.08 (-4.79 to – 2.28; p< 0.01). From 1999 to 2014, a slight non-significant decrease was noted in mortality (APC -0.17), followed by a significant sharp decline from 2014 to 2017 (APC -24.09; p< 0.05)) and a gradual non-significant increase till 2020 (APC 6.70). Adults >55 years had higher AAMR

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Mortality Trends of Interstitial Lung Disease in Rheumatoid Arthritis Patients in the U.S. Population, 1999–2020. (A) By U.S. state; (B) By race/ethnicity; (C) By gender; (D) By rural vs. urban setting.

than the population < 55 years of age, and AAMR continued to increase as age increased. Females accounted for 63.5% (n=6463) of deaths and had higher AAMR of 0.2 compared to men (0.1) but had a sharp decline noted in AAMR from 2017 to 2020 (APC -24.97 [-43.01 to -2.83]). In the racial and ethnic groups, non-Hispanic (NH) Black or African American and Asian or Pacific Islanders had the lowest AAMR of 0.1 whereas the highest was observed in American Indian or Alaska Natives (0.5). White population accounted for most deaths reported (80.7%) and a significant downtrend was noted in the mortality trend from 2014 to 2020 (APC -11.99; p< 0.01). There was no difference in AAMR between Rural (0.2) and Urban (0.2) settings, but later had a falling mortality trend from 2013 to 2016 (APC -23.64 [-30.21 to -14.88], p< 0.01). The Northeast had the lowest AAMR of 0.1 whereas Midwest, South, and West had equally high AAMR of 0.2. Seven states (Idaho, Minnesota, Montana, New Mexico, Oregon, South Dakota, and Vermont) had the highest AAMR.

Conclusion: There has been a slight decrease in mortality rates from ILD in RA patients which could be due to advancements in treatment regimens. Females are more prone to developing autoimmune diseases, have higher AAMR, and therefore can contribute to a higher mortality burden. The older population was noted to have higher mortality rates. Noticeable differences were noted among different ethnic and racial groups as well as census regions and states in terms of mortality. Further research is warranted to identify the disparities noted.

Disclosure: F. Malik: None; **J. Ahmed**: None; **M. Shah**: None; **R. Uttam**: None; **M. Fahimuddin**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1064

Characterization of Juvenile Idiopathic Arthritis in Indigenous North American Children enrolled in a North American registry

Hayley M Lynch[1], Jordan E. Roberts[1] and James N. Jarvis[2] For the CARRA Registry investigators, [1]Seattle Children's Hospital/UW, Seattle, WA, [2]University of Washington Center for Indigenous Health, Seattle, WA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Several studies detail a higher prevalence and severity of juvenile idiopathic arthritis (JIA) in Indigenous North American (INA) children compared to the general population. The reasons for this pattern are likely multifactorial, but efforts to investigate them are hindered by a paucity of data available for this population. The Childhood Rheumatology and Research Alliance (CARRA) registry offers a unique opportunity to investigate JIA in INA patients from across the U.S. and Canada using prospectively collected data confirmed by pediatric rheumatologists. We sought to characterize clinical presentation, serologic profiles and treatment course of JIA in the INA children captured in the CARRA registry.

Methods: Disease-related data was extracted from the CARRA registry for all participants of INA ancestry with a physician diagnosis of JIA. Data included sex-assigned at birth, self-identified ancestry, JIA subtype, serologies, age at diagnosis, presence of uveitis, and use of biologic medication. For the purposes of this study, participants with extended oligoarthritis were counted with those with polyarticular arthritis and sorted into sero-positive and sero-negative groups accordingly. Demographic data was also collected, including zip codes of participants.

Table 1: Characteristics of INA participants enrolled in the CARRA registry. The majority of participants were female, and polyarticular, RF-negative JIA was the most common subtype. Serology data for HLA-B27, RF, and CCP status was missing for 33-46% of participants; percentages were calculated using the total with a recorded result rather than the total number of participants in the study.

Category		INA (n,%)
Total		195
	Male	44 (23%)
	Female	151 (77%)
JIA Category		
	Oligoarticular	50 (26%)
	Polyarticular, RF neg (includes extended oligo)	75 (38%)
	Polyarticular, RF pos (includes extended oligo with RF+)	20 (10%)
	ERA	18 (9%)
	Psoriatic	14 (7%)
	Systemic JIA	11 (6%)
	Undifferentiated	7 (4%)
Serologic Status		
	ANA positive	95 (48%)
	HLA-B27 positive	23 (12%)
	RF Positive	21 (13%)
	Anti-CCP Positive	20 (19%)
Uveitis		25 (13%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Incomes for INA participants in US and Canada. Median income for U.S. participants fell between $50-74,999, while that for Canadian participants fell between $75-99,999.

Income Bracket	U.S. participants	Canadian participants
<$25,000	30	5
$25-49,999	38	3
$50-74,999	19	3
$75-99,999	18	4
$100-150,000	24	7
>$150,000	11	3
Not reported/unknown	20	10

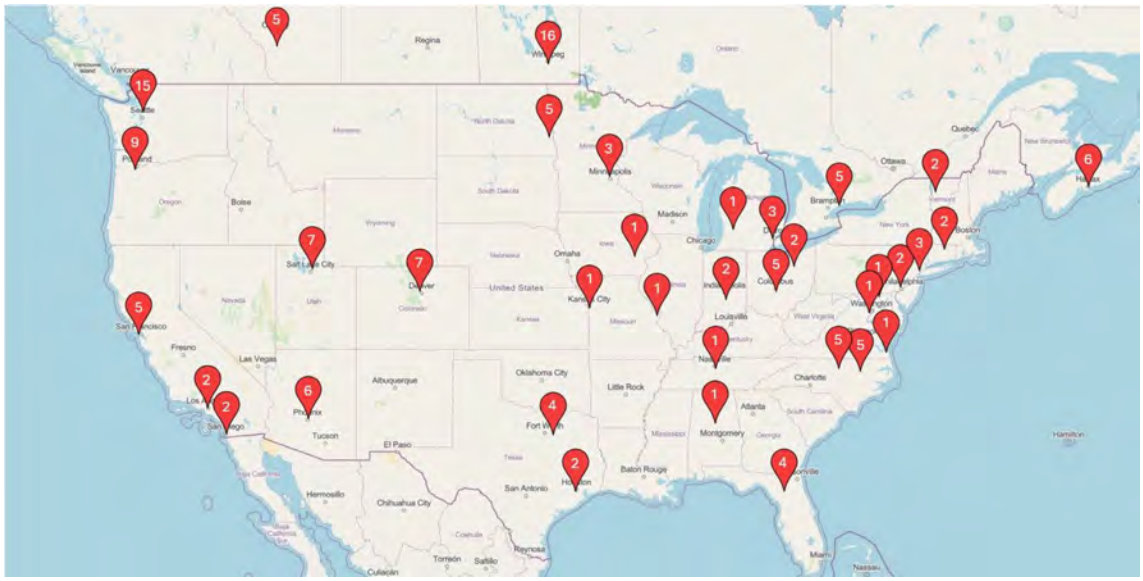


Figure 1: Map of CARRA enrollment sites with INA participants. Number of INA participants from each site indicated in the pin

Results: A total of 195 participants of INA ancestry are identified, making up approximately 1.7% of registry participants from the U.S. and Canada. Of these 195, 44 (23%) are male and 151 (77%) are female. Polyarticular, RF-negative arthritis was the most common subtype (38% of cases), followed by oligoarticular arthritis (26% of cases). 68% of INA participants received biologic therapies during their treatment. Figure 1 displays a map of enrollment centers with INA participants, and shows that only a small number of INA children were enrolled from the northern Great Plains, Canadian prairie provinces, and Alaska. The average distance traveled from home to enrollment site was 155 miles.

Conclusion: This is the first North America-wide survey of INA children with JIA using a national registry with prospectively collected data. We have characterized the disease presentation and treatment of these patients and analysis is underway to compare them with non-indigenous children in the registry. Further work is needed to evaluate the representativeness of INA children in the registry, and to identify opportunities to improve our understanding of JIA in this population.

Disclaimer: This study used data collected in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. The views expressed are the authors' and do not necessarily represent the view of CARRA

Acknowledgements: This work could not have been accomplished without the aid of the following organizations: The NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) & the Arthritis Foundation (AF). We would also like to thank all participants and hospital sites that recruited patients for the CARRA Registry.

Disclosure: H. Lynch: None; **J. Roberts**: AstraZeneca, 3, Bristol-Myers Squibb(BMS), 1; **J. Jarvis**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1065

Age of Disease Onset and Risk of Serious Infection with Anti-tnf Use in Older Adults with Rheumatoid Arthritis

Jiha Lee[1], Sofia Pedro[2] and Kaleb Michaud[3], [1]University of Michigan, Ann Arbor, MI, [2]Forward, The National Databank for Rheumatic Diseases, Wichita, KS, [3]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Older age is a recognized risk factor for serious infection (SI) associated with anti-TNF therapy in rheumatoid arthritis (RA). Among older adults with RA, one-third are diagnosed after age 60 (late-onset RA, LORA), while others are diagnosed earlier in life (young-onset RA, YORA). LORA is characterized by a more acute disease onset and higher inflammatory burden, potentially due to age-related immune dysregulation. However, it is unclear whether RA onset age independently influences infection risk associated with TNF initiation in older adults. This study examines SI risk in older adults with LORA versus YORA initiating anti-TNF therapy.

Methods: Using the FORWARD-The National Databank for Rheumatic Diseases data from 2001-2019, we studied RA patients aged ≥60 years who started anti-TNF therapy. Patients were categorized as LORA or YORA based on their age at RA diagnosis (≥60 or < 60 years) and propensity-matched on age at anti-TNF initiation, sex, race/ethnicity, Medicare coverage, comorbidities, and HAQ-disability scores. Those with other rheumatic diseases, cancer, or HIV before the first SI were excluded. Anti-TNF initiation was identified when patients not using anti-TNF at enrollment reported its use at subsequent biannual visits. SI was defined as infection requiring IV antibiotics, hospitalization, or resulting in death and was attributed to anti-TNF if it occurred during treatment or within three months of discontinuation. Patients were censored at the end of TNF treatment plus 3 months (to account for SI risk window), death, or the end of the study. Kernel propensity-matched survival analyses estimated the risk difference of SI between LORA and YORA.

Table 1: Baseline characteristics of propensity-score matched older adults with anti-TNF initiation by age of RA diagnosis

	LORA (N=1219)	YORA (N=6030)	P-value
Age at anti-TNF initiation	72.6 (5.6)	72.5 (6.3)	0.713
Female, %	74.8	74.9	0.976
Non-Hispanic White race/ethnicity, %	97.3	97.3	0.990
Medicare coverage	92.4	93.4	0.296
Educational level, years	13.1 (2.3)	13.1 (2.3)	0.621
Annual income, US$1,000	40.2 (29.2)	40.4 (28.5)	0.839
Urban community, %	26.9	26.7	0.926
RA disease duration, years	5.74 (4.5)	25.9 (13.0)	<0.001
Smoking habits			
Past	33.6	32.9	0.680
Current	10.3	7.7	0.022
RDCI (0-9)	1.8 (1.5)	1.8 (1.5)	0.438
HAQ (0-3)	1.1 (0.7)	1.2 (0.7)	0.144
Pain VAS (0-10)	4.0 (2.7)	4.1 (2.7)	0.673
Global severity VAS (0-10)	3.8 (2.5)	3.8 (2.4)	0.650
PAS (0-10)	3.89 (2.20)	3.94 (2.10)	0.785
Prior serious infections, %	4.6	7.6	0.002
Ever glucocorticoid use, %	80.7	79.4	0.404
Current glucocorticoid use, %	43.0	42.0	0.652
Long-term GC use, %	12.9	13.4	0.702
Concurrent methotrexate use, %	72.8	66.1	<0.001

Note: Each LORA patient was matched to YORA patients based on age at anti-TNF initiation, sex, race/ethnicity, Medicare coverage comorbidity burden, and HAQ disability.
*The values are presented as mean (SD) unless indicated otherwise.
Abbreviations: LORA=Late Onset Rheumatoid Arthritis, YORA=Young Onset Rheumatoid Arthritis, RDCI=Rheumatic Disease Comorbidity Index, HAQ=Health Assessment Questionnaire; VAS=Visual Analog Scale; PAS=Patient Activity Scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Adjusted HR for risk of serious infection related to anti-TNF use in older adults with LORA vs YORA

Variable	Adjusted HR	95% (CI)	
LORA	0.82	0.63	1.08
Age Group			
60-70	Reference		
70-80	1.71	1.27	2.29
≥80	1.63	1.08	2.48
Prior infections	1.95	1.13	3.40
Long-term GC use (time-varying)*	2.17	1.68	2.81
MTX use	0.95	0.73	1.24
Current smoker	0.65	0.39	1.07

LORA=late-onset RA, YORA=young-onset RA
*long-term GC use (time-varying) defined as at least 5mg/day prednisone equivalent for 90 consecutive days prior to SI

Results: 1219 LORA patients were matched to 6030 weighted YORA patients. At baseline, LORA patients had shorter RA disease duration and fewer prior infections but were more likely to be current smokers and to use concomitant MTX compared to YORA patients. All other baseline variables were well-balanced (Table 1). During follow-up, the crude incidence of SI was 34.2 per 1000 patient-years in LORA patients and 27.9 per 1000 patient-years in YORA patients. After kernel propensity matching, the risk of SI did not significantly differ between LORA and YORA (HR 0.89, 95% CI 0.60-1.34). In Cox regression analyses with GC use treated as a time-varying variable, the risk of SI increased 1.6 to 1.7-fold with older age at TNF initiation, 1.9-fold with prior infection, and 2.2-fold with recent long-term GC use (Table 2).

Conclusion: The risk of SI did not differ between LORA and YORA, indicating that age at RA onset alone does not significantly impact infection risk associated with TNF initiation in older adults. Although older age at treatment initiation was associated with increased SI risk, it should not deter anti-TNF use, as appropriate treatment can substantially improve RA outcomes. Prior infection and recent long-term GC use were also independently associated with SI risk, emphasizing the importance of minimizing GC exposure and implementing infection prevention strategies to mitigate risk and optimize outcomes in older adults initiating TNF therapy.

Disclosure: J. Lee: None; **S. Pedro**: None; **K. Michaud**: None.

Abstract Number: 1066

Assessing Disparities in Outcomes and Processes of Care for Patients with Juvenile Idiopathic Arthritis in the Pediatric Rheumatology Care and Outcomes Improvement Network

Julia Harris[1], Catherine Bingham[2], Sheetal Vora[3], Jon Burnham[4], Cagri Yildirim-Toruner[5], Tzielan Lee[6], Kerry Ferraro[7], Erik Friedrichsen[8], Katelyn Banschbach[9], Michelle Batthish[10], Danielle Fair[11], Mileka Gilbert[12], Beth Gottlieb[13], Melissa Mannion[14], Edward Oberle[15], Nancy Pan[16], Natalie Rosenwasser[17], Mary Toth[18], Jennifer Weiss[19] and Esi Morgan[17], for the Pediatric Rheumatology Care and Outcomes Improvement Network, [1]Children's Mercy Kansas City, Overland Park, KS, [2]Penn State Children's Hospital, Hershey, PA, [3]Atrium Health Levine Children's Hospital, Charlotte, NC, [4]Children's Hospital of Philadelphia, Bryn Mawr, PA, [5]Baylor College of Medicine/ Texas Children's Hospital, Houston, TX, [6]Stanford University School of Medicine, Palo Alto, CA, [7]Pediatric Rheumatology Care and Outcomes Improvement Network, Cincinnati, [8]Seattle Children's Hospital, Burien, WA, [9]cincinnati Children's hospital, Villa Hills, KY, [10]McMaster Children's Hospital, Hamilton, ON, Canada, [11]Medical College of Wisconsin/Children's Wisconsin, Wauwatosa, WI, [12]Medical University of South Carolina, Charleston, SC, [13]Cohen Children's Medical Center, Northwell Health, Lake Success, NY, [14]University of Alabama at Birmingham, Birmingham, AL, [15]Nationwide Children's Hospital, Columbus, OH, [16]Hospital for Special Surgery, New York, NY, [17]Seattle Children's Hospital, seattle, WA, [18]Nemours Foundation, Orlando, FL, [19]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) has a mission to deliver exceptional and equitable health care to children with rheumatic diseases with a current focus on patients with juvenile idiopathic arthritis (JIA). PR-COIN's registry tracks outcome, process, data quality, and balancing measures. PR-COIN assesses and addresses disparities across demographic variables by creating network SMARTIE (specific, measurable, actionable, realistic, time-bound, inclusive, equitable) aims. One aim is to increase the percent of patients with oligoarticular and polyarticular JIA who have inactive or low disease activity by the 10-joint clinical Juvenile Arthritis Disease Activity Score (cJADAS10) from 81.6% to 85% in addition to decreasing the gap between patients with commercial insurance and Medicaid from 8.8% to 5% by December 31, 2025. An additional aim is to increase the percent of patients with JIA in no pain or with mild pain intensity from 80.6% to 83% while decreasing the disparity gap between Black and White patients from 9% to 5% during this same timeframe.

Methods: A key driver diagram was created highlighting the SMARTIE aims and identifying key drivers and change ideas (Figure 1). Data from quality measures between January 2023-February 2025 were stratified by insurance type (comparing patients with commercial insurance and Medicaid) or race (comparing White and Black patients) for 2 outcome measures – inactive or low disease activity by cJADAS10 and no or mild pain – and 2 process measures – receipt of self-management support (SMS) and completion of setting a treatment target of disease activity. The differences in subgroup medians portrayed on run charts were translated to run charts of disparity gaps.

Results: Patients with JIA on commercial insurance consistently have a higher rate of inactive or low disease activity compared to patients on Medicaid (Figure 2A). The disparity gap between these populations decreased from 10% to 9% in November 2023 (Figure 2B). The percent of White and Black patients with no or mild pain have both increased slightly since January 2023

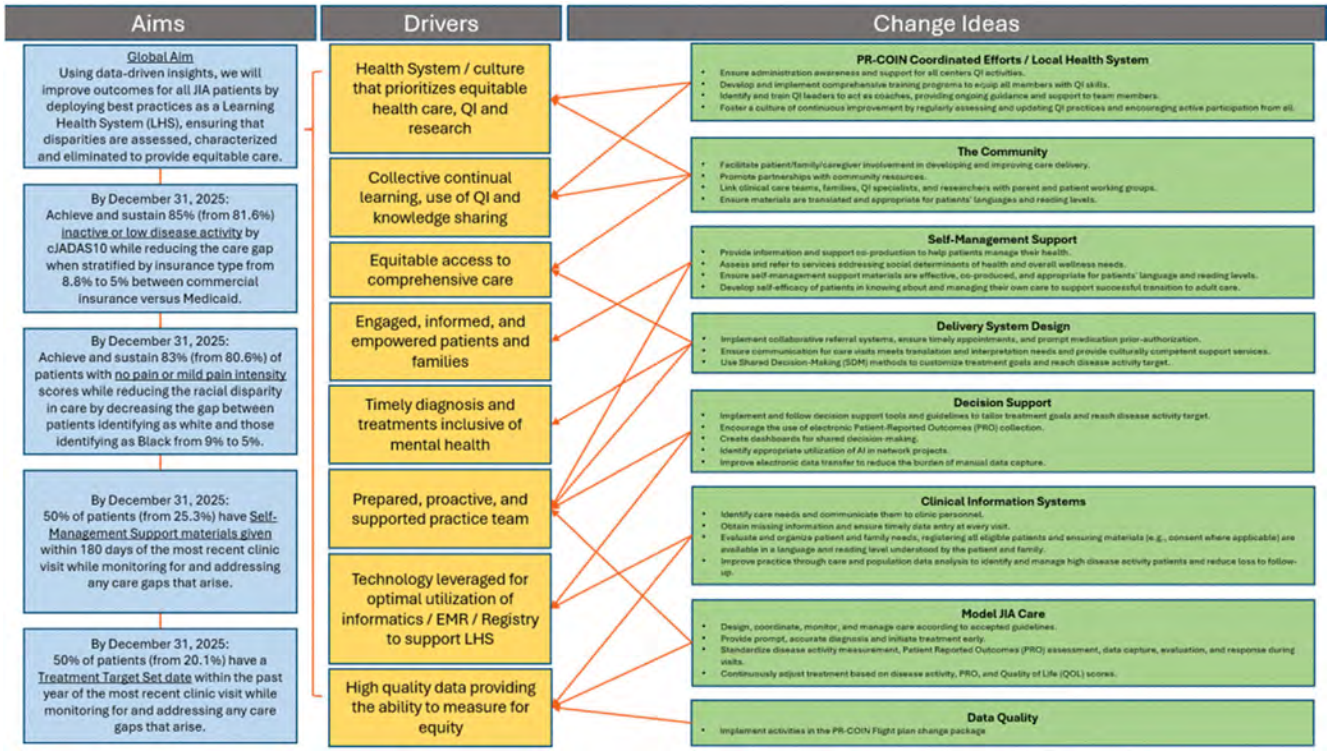


Figure 1. PR-COIN's key driver diagram.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

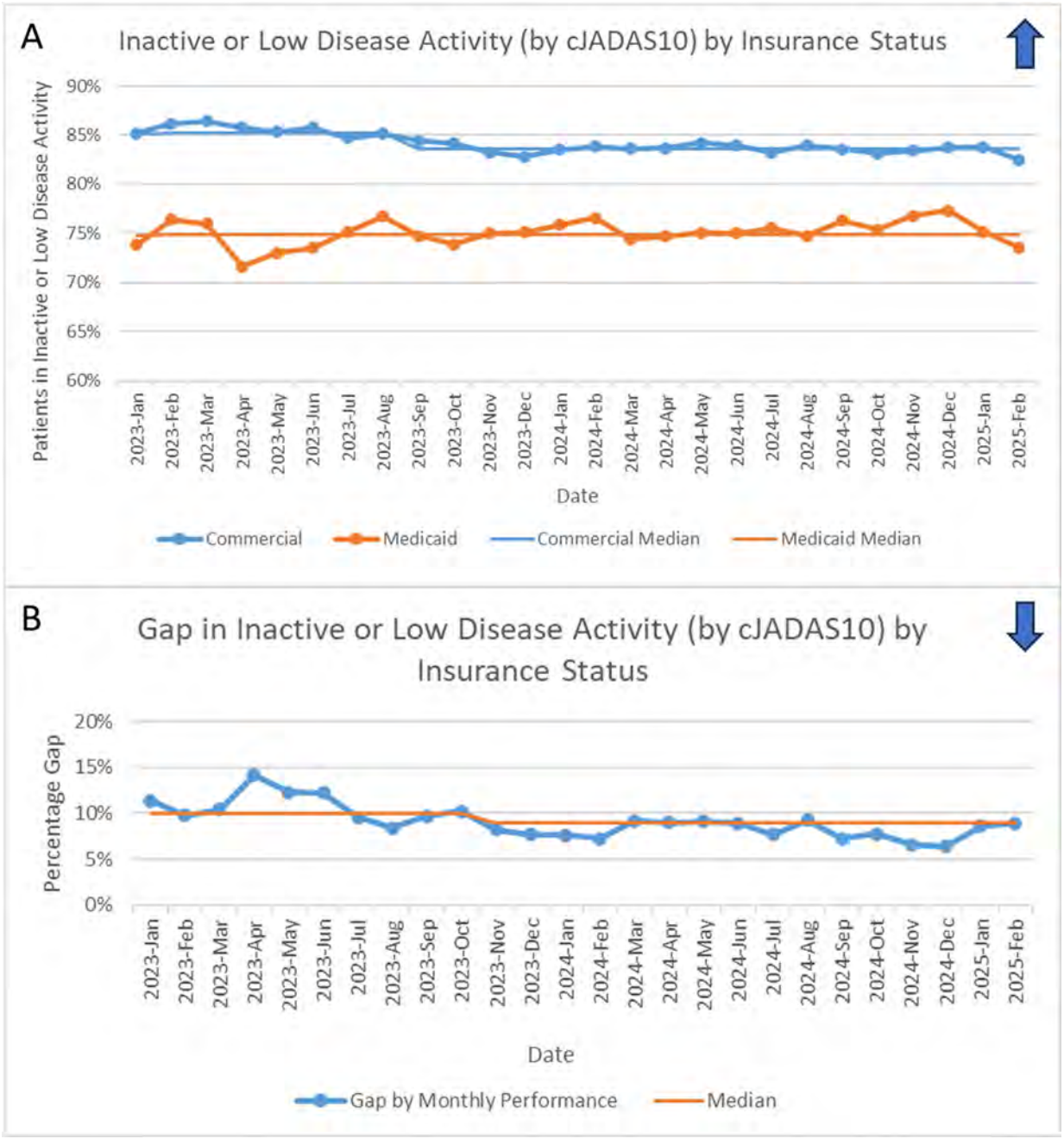


Figure 2. Run charts demonstrating inactive or low disease activity by insurance status (A) and the gap in performance by insurance status (B).

(currently 82.8% and 73.8%, respectively), although the disparity gap of 8.8% has been stable throughout this period (Figure 3). White patients are more likely to receive SMS compared to Black patients with a disparity gap of 7.7%. Patients on Medicaid were more likely to have a treatment target set than patients with commercial insurance (33.4% and 27.7%, respectively).

Conclusion: PR-COIN is striving to provide equitable health care to patients with JIA by making health equity a strategic priority, setting network aims with a health equity focus, and by assessing for differences in health outcomes related to social or demographic factors. We found a disparity by insurance type in our inactive or low disease activity measure. Disparities by race were present in pain intensity score and receipt of SMS. A focus on treatment target setting with patients on Medicaid may mitigate disparities in outcomes. PR-COIN will continue to monitor and address these disparity gaps over time to improve care for all patients with JIA. Further research into persistence of disparities is warranted.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

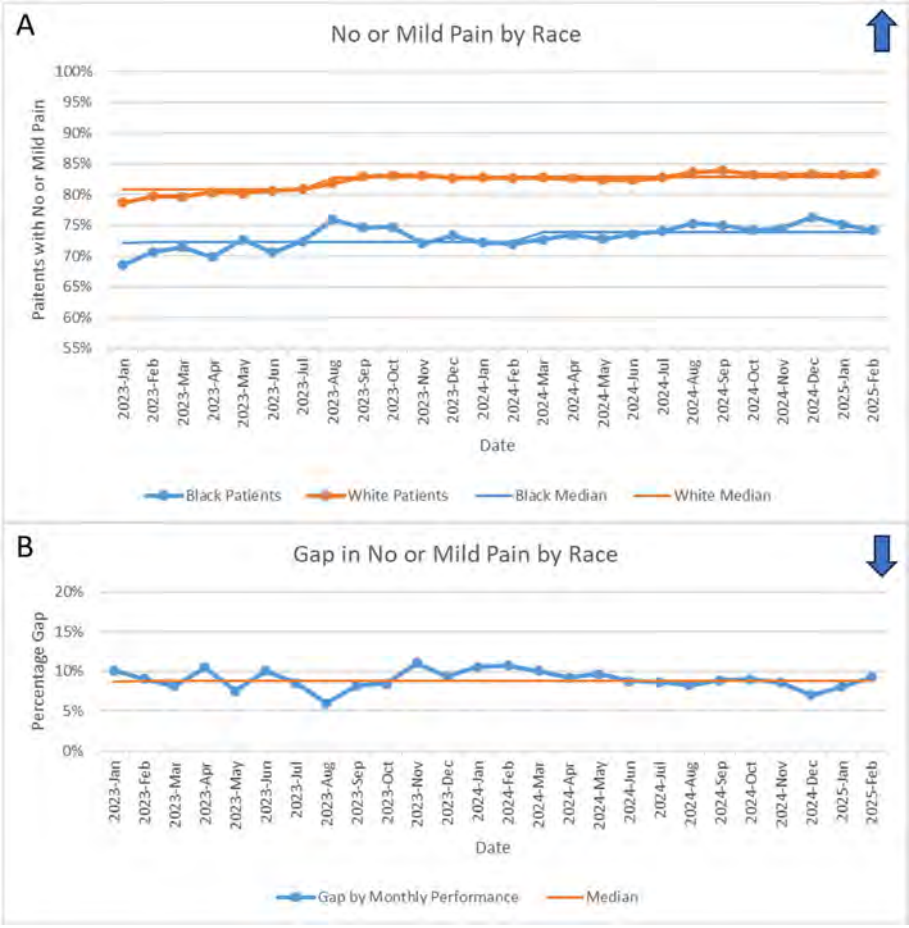


Figure 3. Run charts demonstrating no or mild pain by race (A) and the gap in performance by race (B).

Disclosure: J. Harris: None; **C. Bingham**: None; **S. Vora**: None; **J. Burnham**: Cabaletta Bio, 5; **C. Yildirim-Toruner**: None; **T. Lee**: None; **K. Ferraro**: Abby's Army, 3, 8, 12, President; **E. Friedrichsen**: None; **K. Banschbach**: None; **M. Batthish**: None; **D. Fair**: None; **M. Gilbert**: None; **B. Gottlieb**: None; **M. Mannion**: None; **E. Oberle**: Pfizer, 1; **N. Pan**: None; **N. Rosenwasser**: None; **M. Toth**: None; **J. Weiss**: None; **E. Morgan**: None.

Abstract Number: 1067

Investigating Barriers to Care through Childhood Opportunity, Social Vulnerability, Area Deprivation, and Distance to Care in Pediatric Localized Scleroderma

Karen Lin[1], Yuhan Ma[1], Simrat Morris[2] and Kristina Ciaglia[3], [1]Scottish Rite for Children, Dallas, TX, [2]UT Southwestern Medical Center and Scottish Rite for Children, Dallas, TX, [3]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Delays in diagnosis and treatment of pediatric localized scleroderma (LS) are common due to the under-recognition at initial presentation. While previous studies on pediatric rheumatic diseases have highlighted the impact race, ethnicity, and socioeconomic disparities have on access to care, there is a lack of understanding for those with LS. We examined various Census tract-level datasets and distances to care in a single-center cohort of children with LS to identify factors preventing care.

Methods: A retrospective chart review was performed for patients diagnosed with LS at a single center from January 2021 to December 2024. Those with systemic scleroderma were excluded. Census tract-level datasets for the Childhood Opportunity Index (COI), Social Vulnerability Index (SVI), and Area Deprivation Index (ADI) were utilized. Patient demographics, distance to care, and Census tract data were analyzed using standard statistical analysis.

Results: A total of 52 patients were included. Most patients were Female (63.5%) and Non-Hispanic White (65.4%) with a mean age of 13 years (Table 1). The farthest driving distance to our center was 1,796 miles, and the mean was 128 miles (Figure 1). There was a statistically significant negative correlation between distance to our center and the SVI Racial and Ethnic Minority Status Percentile Statewide and Nationwide (p=0.0002 and p=0.0012 respectively). There was also a significant difference in the mean distance to our center across the COI Overall Index Nationwide and Statewide (p=0.0314 and p=0.0335 respectively) and COI Overall Education Statewide (p=0.0312) (Table 2). There were no significant findings between race/ethnicity, gender, insurance status, or language.

Conclusion: In conclusion, patients from our center come from diverse backgrounds and travel long distances to receive care. Statistically significant associations between distance to care and Census tract-level data are prevalent. Specifically, childhood opportunity was found to be significant overall nationwide and statewide as well as education statewide. Patients who live closest to our center have higher social vulnerability. These findings are enlightening and begin to examine the burdens of healthcare our patients face outside of the office visit. Future studies are needed to determine potential interventions to improve access to care.

Table 1. Patient Demographics

Parameter	Total Number of Patients	Percentage of Patients (%)	
Sex			
Female	33	63.5	
Male	19	63.5	
Race			
White	34	65.4	
Black	8	15.4	
Asian	1	1.9	
American Indian/ Alaskan Native	2	3.9	
Other	7	13.5	
Ethnicity			
Hispanic	19	36.5	
Non-Hispanic	32	61.5	
Decline to Answer	1	1.9	
Primary Language			
English	48	92.3	
Spanish	4	7.7	
Insurance			
Private Commercial Insurance	34	65.4	
Public Government Funded	16	30.8	
Uninsured	2	3.8	
Location			
In State (Texas)	47	90.4	
Out of State	5	9.6	
Primary Diagnosis			
Localized Scleroderma	40	76.9	
Parry-Romberg or Coup de Sabre	12	23.1	
	Mean	**Median**	**Range**
Age (years)	13	13.5	5-23
Distance to Care (miles)	128.6	112	4.9-1796

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. State and Nationwide Childhood Opportunity Index Domain Levels by Diagnosis

	Statewide Comparison			Nationwide Comparison		
Childhood Opportunity Index Domains	All Patients (n= 52)	Localized Scleroderma (n= 40)	Parry Romberg or Coup de Sabre (n=12)	All Patients (n= 52)	Localized Scleroderma (n= 40)	Parry Romberg or Coup de Sabre (n=12)
Overall						
Very high	16 (30.8)	13 (32.5)	3 (25)	15 (28.8)	12 (30)	3 (25)
High	10 (19.2)	10 (25)	0 (0)	3 (5.8)	3 (7.5)	0 (0)
Moderate	10 (19.2)	6 (15)	4 (33.3)	12 (23.1)	11 (27.5)	1 (8.3)
Low	10 (19.2)	8 (20)	2 (16.7)	9 (17.3)	5 (12.5)	4 (33.3)
Very low	6 (11.5)	3 (7.5)	3 (25)	13 (25)	9 (22.5)	4 (33.3)
Education						
Very high	16 (30.8)	13 (32.5)	3 (25)	14 (26.9)	11 (27.5)	3 (25)
High	10 (19.2)	10 (25)	0 (0)	9 (17.3)	9 (22.5)	0 (0)
Moderate	12 (23.1)	7 (17.5)	5 (41.7)	9 (17.3)	7 (17.5)	2 (16.7)
Low	6 (11.5)	5 (12.5)	1 (8.3)	12 (23.1)	8 (20)	4 (33.3)
Very low	8 (15.4)	5 (12.5)	3 (25)	8 (15.4)	5 (12.5)	3 (25)
Health and Environment						
Very high	13 (25)	11 (27.5)	2 (16.7)	1 (1.9)	1 (2.5)	0 (0)
High	12 (23.1)	11 (27.5)	1 (8.3)	1 (1.9)	1 (2.5)	0 (0)
Moderate	8 (15.4)	7 (17.5)	1 (8.3)	9 (17.3)	8 (20)	1 (8.3)
Low	15 (28.8)	9 (22.5)	6 (50)	17 (32.7)	13 (32.5)	4 (33.3)
Very low	4 (7.7)	2 (5)	2 (16.7)	24 (46.2)	17 (42.5)	7 (58.3)
Social and Economic						
Very high	16 (30.8)	13 (32.5)	3 (25)	16 (30.8)	13 (32.5)	3 (25)
High	9 (17.3)	8 (20)	1 (8.3)	4 (7.7)	4 (10)	0 (0)
Moderate	10 (19.2)	7 (17.5)	3 (25)	13 (25)	10 (25)	3 (25)
Low	13 (25)	10 (25)	3 (25)	10 (19.2)	8 (20)	2 (16.7)
Very low	4 (7.7)	2 (5)	2 (16.7)	9 (17.3)	5 (12.5)	4 (33.3)

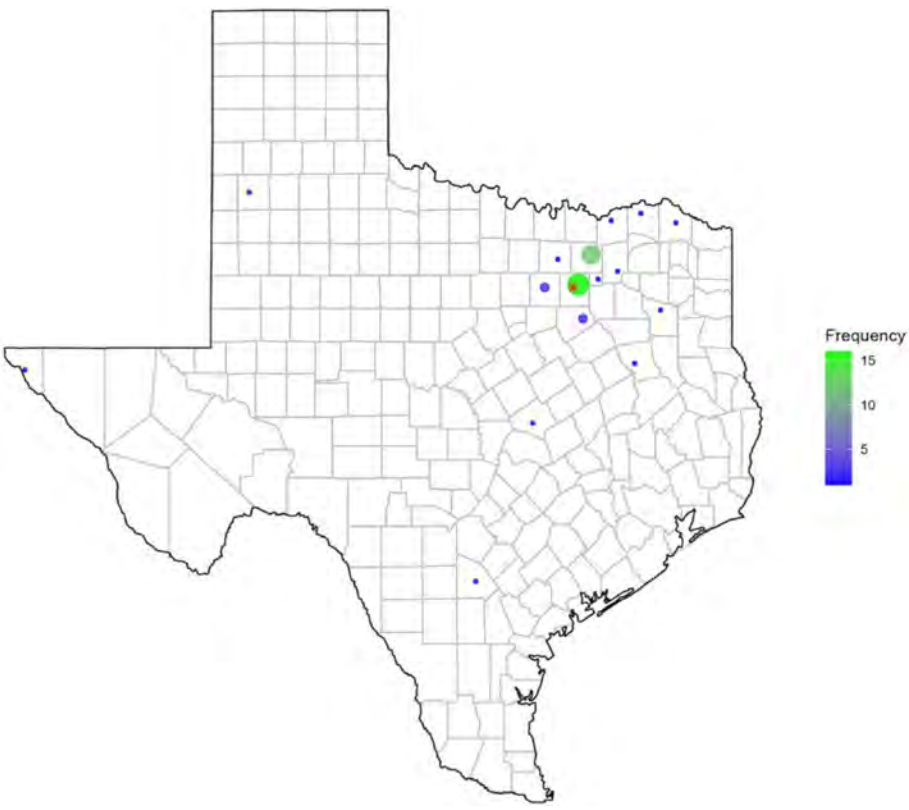


Figure 1. Geographic Distribution of Children with Localized Scleroderma in Northern Texas

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Lin: None; **Y. Ma**: None; **S. Morris**: None; **K. Ciaglia**: None.

Abstract Number: 1068

Association Between Social Determinants of Health Domains and covid-19-related Hospitalization in Individuals with Autoimmune Rheumatic Diseases: A Retrospective Analysis of National U.S. Data

Londyn Robinson[1], jerrod anzalone[2], Jasvinder Singh[3], Kaleb Michaud[2], Lesley Jackson[4], Maria I. (\"Maio\") Danila[5], Dongmei Li[6], Rena Patel[4] and Namrata Singh[7], [1]University of Washington, Seattle, WA, [2]University of Nebraska Medical Center, Omaha, NE, [3]Baylor College of Medicine, Houston, TX, [4]University of Alabama at Birmingham, Birmingham, AL, [5]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [6]University of Rochester School of Medicine and Dentistry, Rochester, NY, [7]University of Washington, Bellevue, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Although studies have been published on the baseline characteristics of patients with autoimmune rheumatic diseases (AIRDs) with COVID-19 infection, little data exists on how social determinants of health (SDoH) influence outcomes. We investigated whether specific domains of SDoH are associated with COVID-19-related hospitalizations in adults with and without AIRDs.

Methods: We conducted a retrospective cohort study using electronic health record (EHR) data from the National Clinical Cohort Collaborative (N3C) COVID Enclave. We included adults ≥18 years who tested positive for SARS-CoV-2 (PCR or antigen test or diagnostic code) between April 2020 and March 2024. We identified patients with AIRD by the presence of ≥2 ICD-10 codes for an AIRD diagnosis, recorded ≥ 30 days apart before an incident COVID-19 infection. The AIRD diagnoses we included were polymyalgia rheumatica, polymyositis, dermatomyositis, rheumatoid arthritis, systemic sclerosis, ankylosing spondylitis, psoriatic arthritis, enteropathic arthritis, reactive arthritis, Behcet's disease, ANCA-vasculitis, giant cell arteritis, polyarteritis nodosa, SLE, and Sjogren's syndrome. Only individuals with available SDoH data in N3C were included in this study and SDoH were assessed at the time of incident COVID-19 infection. SDoH were assessed across three Healthy People 2030 domains: healthcare access, economic stability, and social cohesion. The primary outcome was COVID-19-related hospitalization defined as occurring within a window from 3 days before to 14 days after diagnosis. To examine the association between specific SDoH domains and COVID-19-related hospitalization among adults with and without AIRDs, we conducted hierarchically nested logistic regression models and adjusted for covariates including age, sex, comorbidities, and vaccination status, then stratified analyses by AIRD status.

Results: There were 362,359 people with incident COVID-19 infection and available SDoH domains in N3C at the end of data collection, of whom 16,261 (4.5%) had at least one AIRD diagnosis. In unadjusted analyses, COVID-19-related hospitalization was significantly higher among AIRD patients (19%) compared to non-AIRD patients (13%, $p < 0.001$; **Table 1**).

Across both AIRD and non-AIRD groups, having SDoH issues was associated with higher odds of COVID-19-related hospitalization (**Table 2**). In adjusted models including all SDoH domains, associations were consistently stronger among the AIRD group. Having access to healthcare issues was associated with higher hospitalization risk in both groups, with a larger effect in AIRD patients (aOR 1.73, 95% CI 1.41-2.11) than in non-AIRD patients (aOR 1.55, 95% CI 1.45-1.66). Similarly, social cohesion issues (aOR 1.44 vs 1.19) and economic instability (aOR 1.20 vs 1.16) had a more pronounced association with hospitalization in the AIRD group (**Table 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of patients with and without AIRDs who had incident COVID-19 infection between April 2020 and March 2024.

	Entire Cohort N = 362,359	AIRD* N = 16,261	Non-AIRD N = 346,098
Sex			
Female	219,916 (61%)	11,889 (73%)	208,027 (60%)
Male	142,443 (39%)	4,372 (27%)	138,071 (40%)
Age at Incident COVID-19 Infection, Median (IQR)	55 (38, 69)	64 (51, 74)	55 (38, 69)
Age Group at time of COVID-19 infection			
<30	45,539 (13%)	519 (3.2%)	45,020 (13%)
30-49	102,540 (28%)	3,138 (19%)	99,402 (29%)
50-64	92,412 (26%)	4,723 (29%)	87,689 (25%)
65-74	66,267 (18%)	4,097 (25%)	62,170 (18%)
75+	55,601 (15%)	3,784 (23%)	51,817 (15%)
Race and Ethnicity			
White Non-Hispanic	252,001 (70%)	11,864 (73%)	240,137 (69%)
Black or African American Non-Hispanic	44,402 (12%)	2,083 (13%)	42,319 (12%)
Hispanic or Latino Any Race	39,009 (11%)	1,524 (9.4%)	37,485 (11%)
Other	10,296 (2.8%)	308 (1.9%)	9,988 (2.9%)
Unknown/Missing	16,651 (4.6%)	482 (3.0%)	16,169 (4.7%)
Charlson Comorbidity Index*, Median (IQR)	1 (0, 3)	2 (1, 5)	1 (0, 3)
COVID-19 Vaccination Status Before Infection			
No Documented COVID-19 Vaccine Before Infection	242,827 (67%)	9,296 (57%)	233,531 (67%)
Primary Vaccination Series Before Infection	51,419 (14%)	2,573 (16%)	48,846 (14%)
Primary and Additional Dose(s) Before Infection	68,113 (19%)	4,392 (27%)	63,721 (18%)
SDoH Domain			
Has All Three SDoH Domains Data Available	186,476 (51%)	8,189 (50%)	178,287 (52%)
Economic Stability Issue	60,788 (20%)	3,171 (23%)	57,617 (20%)
Unknown/Missing	*65,369*	*2,556*	*62,813*
Access to Healthcare Issue	14,546 (5.3%)	1,025 (8.1%)	13,521 (5.2%)
Unknown/Missing	*87,548*	*3,652*	*83,896*
Social Cohesion Issue	150,661 (57%)	7,002 (62%)	143,659 (57%)
Unknown/Missing	*98,281*	*4,900*	*93,381*
Covid-19 Related Hospitalization	49,384 (14%)	3,126 (19%)	46,258 (13%)

Autoimmune Rheumatic Diseases (AIRDs). AIRDs include polymyalgia rheumatica (PMR), polymyositis/dermatomyositis (PM/DM), rheumatoid arthritis (RA), systemic sclerosis (SSc), spondyloarthropathies (SpA) (including ankylosing spondylitis, psoriatic arthritis, enteropathic arthritis, and reactive arthritis), systemic vasculitidies (including Behcet's disease, ANCA-vasculitis, giant cell arteritis, and polyartertitis nodosa), and Sjogren's syndrome. Charlson Comorbidity Index (CCI) excludes rheumatic disease from CCI calculation.

Table 2. Odds of COVID-19-related hospitalization among Social Determinates of Health (SDoH) domains, stratified by presence of AIRD. Adjusted covariates included age, sex, comorbidities, and COVID-19 vaccination status prior to incident infection.

	AIRD Hospitalization		Non-AIRD Hospitalization	
SDoH	Unadjusted Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)	Unadjusted Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Economic Instability				
No Economic Instability Issue	Reference	Reference	Reference	Reference
Economic Instability Issue	1.15 (1.00, 1.32)	**1.20 (1.03, 1.40)**	**1.19 (1.14, 1.24)**	**1.16 (1.11, 1.21)**
Access to Healthcare				
No Access to Healthcare Issue	Reference	Reference	Reference	Reference
Access to Healthcare Issue	**2.06 (1.71, 2.46)**	**1.73 (1.41, 2.11)**	**2.25 (2.12, 2.39)**	**1.55 (1.45, 1.66)**
Social Cohesion				
No Social Cohesion Issue	Reference	Reference	Reference	Reference
Social Cohesion Issue	**1.62 (1.39, 1.90)**	**1.44 (1.23, 1.71)**	**1.28 (1.23, 1.34)**	**1.19 (1.14, 1.24)**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Having SDoH issues was independently associated with higher odds of COVID-19-related hospitalization among adults, regardless of AIRD status. These associations were stronger in those with AIRDs, highlighting how underlying social disadvantage may exacerbate vulnerability to severe outcomes in this population.

Disclosure: L. Robinson: None; **j. anzalone**: None; **J. Singh**: American College of Rheumatology, 2, Atai life sciences, Kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 11, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Putnam associates, Focus forward, Navigant consu, 2, GeoVax Labs, Adaptimmune Therapeutics, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp., Aebona Pharma, 11, Intuitive Surgical Inc./Philips Electronics North America, 12, food and beverage payments, ROMTech, Atheneum, Clearview healthcare partners, Yale, Hulio, Horizon Pharmaceuticals/DINORA, ANI/Exeltis, USA Inc., Frictionless Solutions, Schipher, 2, Spherix, MedIQ, Jupiter Life Science, UBM LLC, Trio Health, Medscape, WebMD, and Practice Point communications; the National Institutes of Health, 2, Zimmer Biomet Holdings, 5; **K. Michaud**: None; **L. Jackson**: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5; **D. Li**: None; **R. Patel**: None; **N. Singh**: None.

Abstract Number: 1069

Strengthening Rheumatology Workforce Capacity and Impact on Patient Care in Louisiana: Expanding Fellowship Training Opportunities Through Strategic Partnerships

Luke Sharrock[1], Alexandra Anderson[2], Stephen Lindsey[3] and Milena Vukelic[4], [1]Louisiana State University Health Science Center New Orleans, New Orleans, LA, [2]Louisiana State University Health Science Center New Orleans, Phoenix, AZ, [3]LSU Health Sciences Center-New Orleans, Baton Rouge, LA, [4]Rheumatology Fellowship Program Director Louisiana State University, New Orleans, LA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Louisiana, along with other states, has long experienced significant challenges in accessing specialty care, particularly in the field of rheumatology. Limited availability of trained rheumatologists leads to delayed diagnoses, suboptimal disease management, and poor patient outcomes. In response, our institution has strategically expanded rheumatology fellowship training. In addition to two ACGME-accredited fellowship spots annually, we have implemented a model to add one extra fellow when funding is available. This additional fellow is supported through contracts with rural hospitals in the United States or internationally. These hospitals provide financial support for the additional fellow and, in return, the fellow commits to return and practice in the sponsoring institution for a defined period. The prospective fellow participates in the ACGME match process. Importantly, the additional fellow is fully integrated into the accredited training program and all aspects of training meet the ACGME requirements, ensuring parity in educational quality and clinical competence. This initiative aims to address the growing shortage of rheumatology specialists, improve patient access to timely care, and enhance patient outcomes across underserved areas.

Methods: A retrospective cohort study was conducted using Slicer Dicer, a data analytics tool embedded in the Epic Electronic Health Record system. The study spanned the period from 2017 to 2025. The impact of expanding rheumatology fellowship training on patient care was measured as patient access to care: number of referrals, wait time, number of new and follow-up visits. For statistical analysis, a t-test was used.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Yearly referrals to our clinic increased 3.7-fold since 2015 (1,139 in 2015 vs. 4,218 in 2024; $p < 0.05$). We had 5 fellows during 7/2017–7/2019 and 7/2023–7/2025, with 4 fellows in between. During the academic years 2023–2025, when we had 5 fellows, our clinic saw 8,052 total patients, compared to 4,568 patients in 2019–2021 and 6,125 patients in 2021–2023 during the years with 4 fellows. In 2023–2025, we doubled the number of new patient consults seen in our clinic (2,134 patients vs. 1,072 patients in 2019–2021; $p < 0.05$). We observed a trend toward an increased number of outpatient prescriptions, corticosteroid injections, and infusions. Before 2017, the average time to the next patient appointment was 118 ± 16 days, which was significantly shortened ($p < 0.001$) during the years with 5 fellows (47 ± 13 days in 2017–2019 and 53 ± 15 days in 2023–2025). Patient demographics were similar throughout the years.

Conclusion: Our strategic collaboration serves multiple purposes: expanding the workforce by increasing the number of graduating fellows and providing immediate access to care in underserved areas. This model led to an increase in the number of consultations and follow-up appointments, reducing wait times for patients by 40%. Additionally, this initiative enhances our program's visibility and attracts mission-driven candidates. This initiative exemplifies how academic-community partnerships can produce scalable solutions to subspecialty workforce shortages.

Disclosure: L. Sharrock: None; **A. Anderson**: None; **S. Lindsey**: None; **M. Vukelic**: None.

Abstract Number: 1070

Cervical Cancer and HPV Screening in Women with Lupus vs Healthy Control Group: A Retrospective Study at a Tertiary Referral Center

Mahnoor Javed[1], Deepak Jagannath[2], Alma Aveytia Camacho[3], Alwyn Mathew[3], Konrad Harms[3], Soudabeh Daliri[3] and Myriam Guevara[4], [1]Houston Methodist, Richmond, TX, [2]Houston Methodist Hospital, Sugar Land, TX, [3]Houston Methodist, Houston, [4]Houston Methodist, Houston, TX

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Women with SLE are at an increased risk of developing cervical cancer, primarily by human papillomavirus (HPV) and immunosuppression. This elevated risk has been recognized by experts and updated guidelines recommend more frequent cervical cancer screening in women with SLE compared to the general population. This project aims to assess current cervical cancer screenings and HPV vaccination status in women with SLE compared to normal population at Houston Methodist Hospital (HMH).

Methods: We identified women aged 21-65 years who met the ACR/EULAR 2019 criteria for SLE diagnosis between 2015 and 2025 using electronic medical records, SlicerDicer software, and a retrospective chart review at HMH. Females with a history of hysterectomy or cervical cancer were excluded. A total of over 230 patients were initially identified, with 50 women confirmed through chart review. The SLE Disease Activity Index (SLEDAI) was obtained from their most recent visit. A healthy cohort of 50 women, matched by age and ethnicity, was also included. Individuals with diabetes, HIV, chronic immunosuppression, hysterectomy, cervical cancer, or tobacco use were excluded.

Results: Among the SLE group, 46% of the patients were Black, 32% were White, 16% were Hispanic, and 6% were Asian. The average age was 45, with a mean disease duration of 8 years. The mean SLEDAI score was 4, and most patients were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

on a combination of medications including Prednisone, Hydroxychloroquine, Azathioprine, Methotrexate, Mycophenolate, and Belimumab (Table 1).

Our results indicated that 6% of the SLE group had received the HPV vaccine, compared to 20% in the healthy control (HC) group. Only 74% of SLE patients had undergone cervical screening and 64% had HPV testing within the past five years. However, the HC group had 100% cervical cancer screening and 72% had HPV testing within the same timeframe (Figure 1). Furthermore, only 30% of the SLE group had an annual PAP smear and 18% had annual HPV testing (Figure 2A). Among the SLE patients, 7 abnormal PAP smears were identified, including 2 low-grade squamous intraepithelial lesions (LSIL) and 5 cases of Atypical Squamous Cells of Undetermined Significance (ASCUS), compared to just one

Category	SLE Cohort	Healthy Control (HC)
Age	Mean: 45 (SD[1] ± 12.1)	Mean: 40.7 (SD ± 10.9)
Race	White: 46%	White: 66%
	Black: 32%	Black: 14%
	Hispanic: 16%	Asian: 12%
	Asian: 6%	Native American: 2%
		Declined: 6%
Disease Duration (years)	Mean: 8.1 (SD ± 8.9)	N/A
SLEDAI	Mean: 4.1 (SD ± 4.5) Mild (1-5): 62% Moderate (6-10): 28% Severe (>10): 6%	N/A
Immunosuppression	Hydroxychloroquine: 68%	
	Prednisone: 16%	
	Mycophenolate: 14%	N/A
	Azathioprine: 14%	
	Methotrexate: 6%	
	Belimumab: 6%	
LSIL[2]	4%	0%
ASCUS[3]	10%	2%

[1]Standard Deviation

[2]Low-Grade Squamous Intraepithelial Lesion

[3]Atypical Squamous Cells of Undetermined Significance

Table 1. SLE Cohort vs Healthy Control (HC) Characteristics

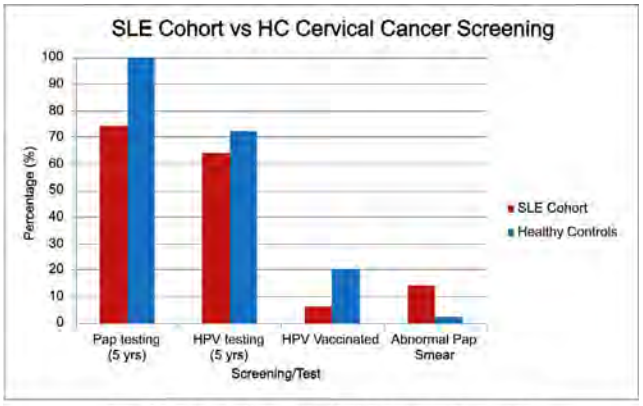


Figure 1. SLE Cohort vs Healthy Control (HC) Cervical Cancer Screening Data

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

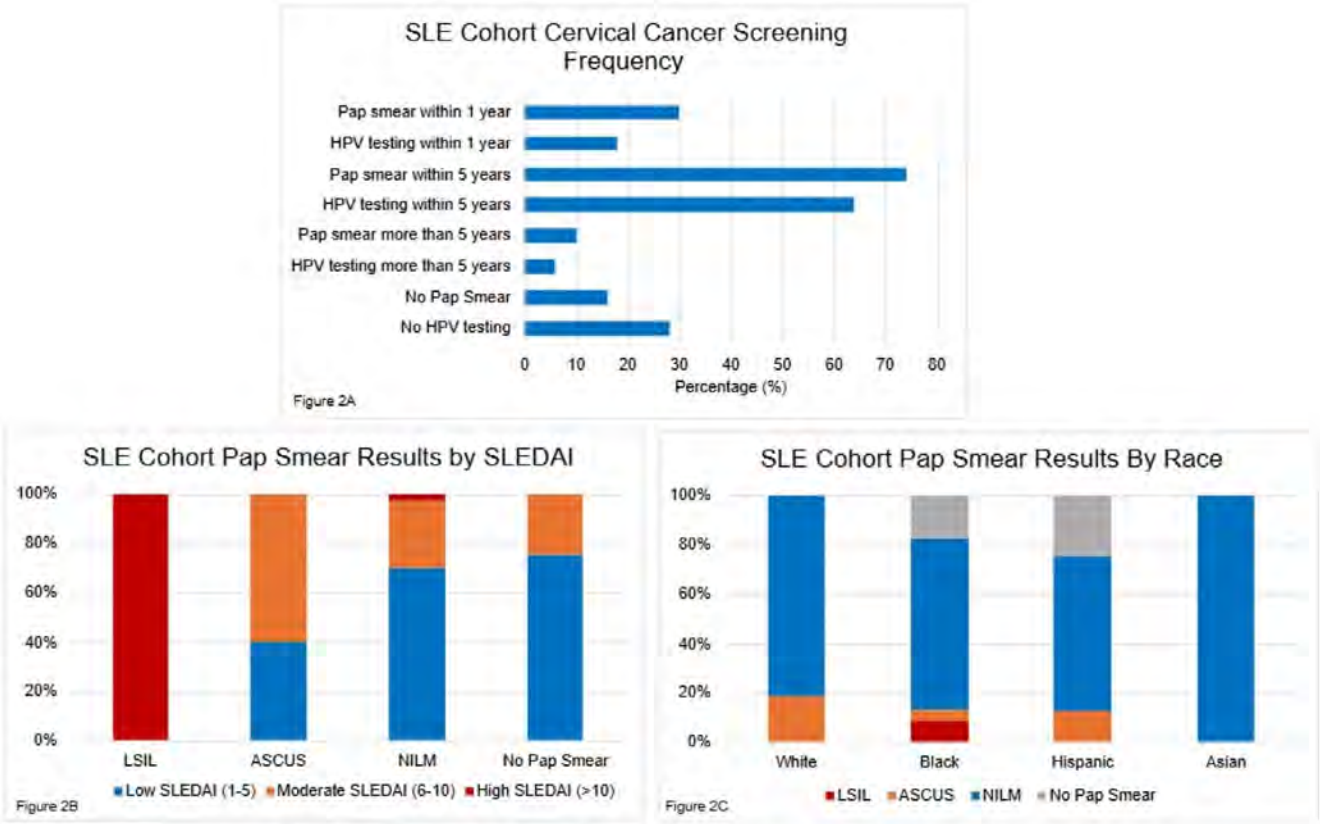


Figure 2. SLE Cohort Pap Smear Results by Frequency (2A), SLEDAI (2B) and Race (2C)

ASCUS in the HC group (Figure 2B). In the SLE group, 3% tested positive for HPV, including one patient with LSIL, while 8% of the HC group tested positive for HPV. The patients with LSIL were all Black and had notably higher SLEDAI scores (Figure 2C).

Conclusion: Our study confirms a significant gap in cervical cancer and HPV screening among women with SLE compared to healthy controls (HC). The findings underscore the importance of implementing annual screening for SLE patients. Additionally, the results suggest that a higher SLEDAI in Black patients may pose an increased risk for worse outcomes. The study also highlights the need for more HPV testing and greater education on vaccination to help prevent adverse outcomes in both groups. Collaborating with gynecologic experts could further raise awareness and improve screening practices. Larger studies are necessary to better understand the risks and long-term outcomes in this population.

Disclosure: M. Javed: None; **D. Jagannath**: None; **A. Aveytia Camacho**: None; **A. Mathew**: None; **K. Harms**: None; **S. Daliri**: None; **M. Guevara**: None.

Abstract Number: 1071

Depression and Mental Health Service Gaps in Autoimmune Disease: Insights from a Simulated BRFSS Dataset

Malay Rathod[1], Shivani Modi[2], Veera Durga Vaishnavi Kurra[3], Karan Yagnik[4] and Doantrnag Du[4], [1]Monmouth Medical Center, Ewing, NJ, [2]Jefferson Einstein Montgomery Hospital, Ewign, NJ, [3]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [4]Monmouth Medical Center, Long Branch, NJ

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

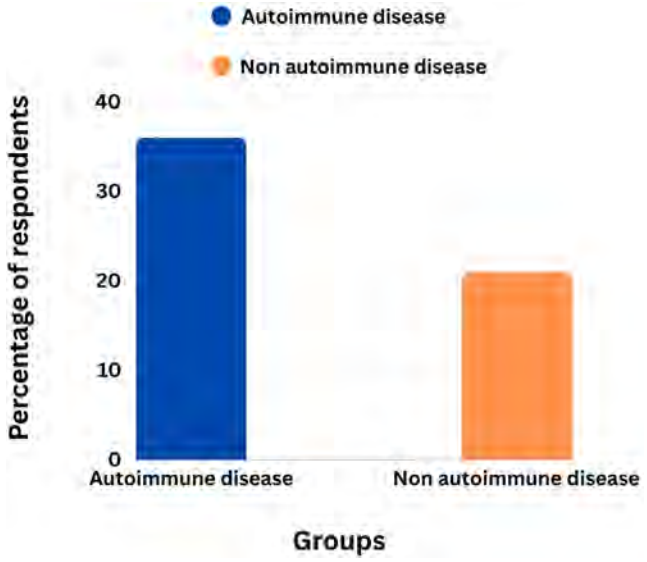
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune diseases are complex conditions that may predispose individuals to an increased mental health burden, including depression. The immune system leads to inflammation in affected organs and mediates behavioral abnormalities, including fatigue and depression-like symptoms. This study leverages data from the Behavioral Risk Factor Surveillance System (BRFSS) to evaluate the prevalence of depression and mental health service access among patients with autoimmune diseases compared to those without.

Methods: Using a simulated BRFSS dataset of 10,000 respondents, autoimmune status was defined as the presence of conditions such as rheumatoid arthritis, lupus, and psoriatic arthritis. Depression was measured using self-reported ever diagnosis (ADDEPEV2) and the number of days of poor mental health (MENTHLTH). Descriptive analyses quantified the prevalence of depression in autoimmune versus non-autoimmune groups. Bivariate analyses (chi-square tests and t-tests) were conducted to compare mental health indicators and access to services between groups. Multivariable logistic regression models, with depression as the outcome and predictors including autoimmune status, demographics (age, sex, race/ethnicity, education, income), and comorbidities, were implemented. Stratified analyses by income further evaluated disparities in mental health care.

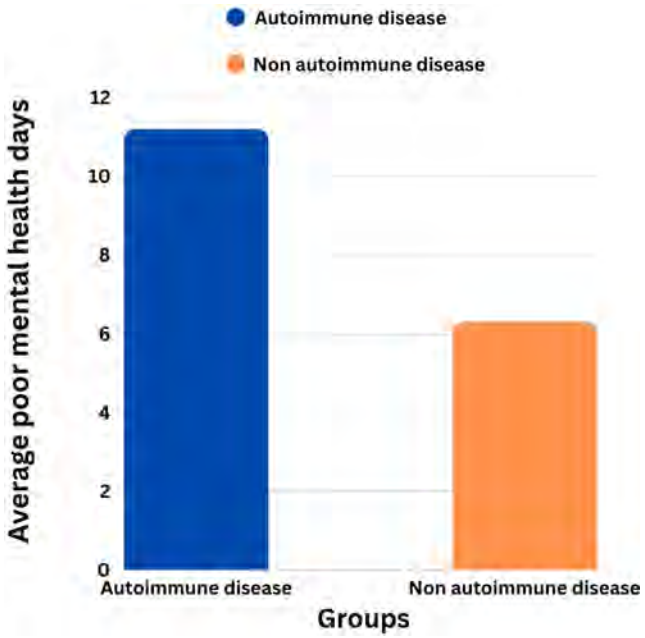
Results: Preliminary analyses indicated that 36% of respondents with autoimmune diseases self-reported depression compared to 21% among non-autoimmune respondents (χ^2 $p < 0.001$). Additionally, individuals with autoimmune conditions reported an average of 11.2 poor mental health days, significantly greater than the 6.3 days reported by non-autoimmune individuals (t-test, $p < 0.001$). Logistic regression analyses revealed that, after adjusting for demographic and comorbidity factors, the odds of reporting depression were 1.85 times higher among autoimmune patients (OR = 1.85; 95% CI: 1.60–2.15). Stratified analyses further demonstrated that lower-income autoimmune patients experienced compounded disparities; those in the lower-income bracket had an OR of 2.05 (95% CI: 1.70–2.47) compared to an OR of 1.62 (95% CI: 1.35–1.95) for their higher-income counterparts.

Conclusion: These findings suggest that individuals with autoimmune diseases have a significantly higher burden of depression and poorer mental health outcomes than those without. Moreover, the observed disparities in mental health service



A graph comparing the percentage of respondents with depression in autoimmune disease group versus non-autoimmune disease group

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A graph comparing the average poor mental health days in people with autoimmune disease versus non-autoimmune disease

access, particularly among lower-income groups, underscore the need for targeted interventions to address these inequities. Future research should continue to explore the socio-demographic determinants affecting mental health service access in this vulnerable population.

Disclosure: M. Rathod: None; **S. Modi**: None; **V. Kurra**: None; **K. Yagnik**: None; **D. Du**: None.

Abstract Number: 1072

Inclusion of Older Adults in Pharmacologic Randomized Controlled Clinical Trials of Autoimmune Rheumatic Diseases: A Systematic Review

Manuel Carpio Tumba[1], Raisa Lomanto Silva[2], Lily Sung[3], Laura C. Pedraza-Arévalo[4], Sneha Gupta[5], Jeenah Gwak[6], Aida Mohamadi[7], Diana Louden[8], Rachael Stovall[8], Namrata Singh[9], Didem Saygin[10], Sarah Lieber[11], Jiha Lee[12] and Sebastian E Sattui[13], [1]University of Pittsburgh, Pittsburgh, PA, [2]Massachusetts General Hospital, Boston, MA, [3]Stanford University Hospital & Clinics, Hayward, CA, [4]St. Barnabas Hospital, New York, NY, [5]University of Pittsburgh Medical Center McKeesport, McKeesport, PA, [6]Stanford University, Palo Alto, CA, [7]Tehran University of Medical Sciences, Tehran, Iran, [8]University of Washington, Seattle, WA, [9]University of Washington, Bellevue, WA, [10]Rush University Medical Center, Chicago, IL, [11]Hospital for Special Surgery, New York, NY, [12]University of Michigan, Ann Arbor, MI, [13]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: A growing number of older adults are living with autoimmune rheumatic diseases (AIRDs) as the global population is aging. And yet, they remain underrepresented in pharmacologic randomized clinical trials (RCTs). This has led to a gap in the evidence-base for the care of older adults with AIRDs. Understanding existing age-related inclusion practices in AIRD RCTs is essential to address this gap. This systematic review evaluates the inclusion of older adults in pharmacologic RCTs of AIRDs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a systematic review (PROSPERO CRD42023457996) using PubMed, EMBASE, CINAHL Complete, Europe PMC, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. We included completed phase II–IV pharmacologic RCTs with published results from 2010–2023. For rheumatoid arthritis (RA), the search began in 2017, as a prior review covered earlier studies.[1]

We included the following AIRDs: ANCA-associated vasculitis (AAV), axial spondyloarthritis (ax-SpA), giant cell arteritis (GCA), idiopathic inflammatory myopathies (IIM), polymyalgia rheumatica (PMR), psoriatic arthritis (PsA), reactive arthritis (ReA), RA, systemic lupus erythematosus (SLE), and systemic sclerosis (SSc). Ax-SpA, PsA, and ReA were grouped as spondyloarthritis (SpA), and GCA and PMR were analyzed together (GCA/PMR).

We included RCTs enrolling adults ≥18 years of age, except for AAV and SLE, in which a lower age threshold (≥15 years) was selected. Title/abstract screening, full-text review, and data extraction were performed independently by two reviewers. Conflicts were resolved a by a third reviewer. Mean age and standard deviation (SD) of participants by AIRD were calculated using methods developed by Palmowski et al[1] and compared to ages reported in historical observational cohorts for each AIRD.

Results: We identified 515 RCTs including 152,185 participants (Table 1). RA, SpA, and SLE accounted for 80% of RCTs and 94% of participants. Higher female representation was noted in RCTs for GCA/PMR, SLE, SSc, and IIM. Most trials were conducted in North America, Europe, and Australasia.

Age-related exclusion was common, with 56.4% of RCTs applying upper age limits, most frequently a cut-off at 70 years (Table 2). Only 33.3% of RCTs explicitly reported data on older adults. Across multiple AIRDs—including SLE, SSc, SpA, GCA/PMR, and RA—the mean participant age was lower than that observed in representative cohort studies.

Conclusion: Older adults are underrepresented in RCTs across all AIRDs. Upper age limit exclusion criteria are commonly used, restricting the inclusion of the older adult population. These findings highlight the limitations in the generalizability and applicability of RCT results to inform/guide the care of older adults. There is an urgent need to promote the inclusion

Table 1. Characteristics of included RCTs per AIRD

	AAV	GCA/PMR	IIM	RA	SLE	SpA	SSc
Number of trials included	27	10	18	172	101	141	46
Number of participants: n (median; range)	3,485 (105; 17-704)	718 (50.5; 20-250)	1,307 (49; 13-251)	72,360 (314; 5-4362)	27,179 (1,42; 9-4,003)	43387 (230; 18-1704)	3,749 (42; 12-576)
Female, sex	1,608 (46.1)	506 (70.5)	782 (59.8)	57,028 (78.8)	25,066 (92.3)	17,635 (40.6)	2,822 (75.3)
Trial phase							
II	6 (22.2)	6 (60)	12 (66.7)	35 (20.4)	44 (43.6)	26 (18.4)	23 (50)
III	13 (48.2)	4 (40)	4 (22.2)	96 (55.8)	23 (22.8)	85 (60.3)	12 (26.1)
IV	3 (11.1)	0 (0)	0 (0)	32 (18.6)	14 (13.9)	23 (16.3)	2 (4.4)
Not reported	5 (18.6)	0 (0)	2 (11.1)	9 (5.2)	20 (19.8)	7 (5.0)	9 (19.6)
Drug category studied							
Glucocorticoids	2 (6.9)	0 (0)	1 (5)	5 (2.2)	6 (5.2)	2 (1.3)	1 (2.1)
CIM	9 (31.0)	0 (0)	5 (25)	32 (13.9)	33 (28.4)	9 (5.7)	3 (6.3)
Biologic	14 (48.3)	10 (100)	7 (35)	138 (60)	41 (35.3)	111 (70.3)	11 (22.9)
Small molecule inhibitors	0 (0)	0 (0)	2 (10)	40 (17.4)	11 (9.5)	21 (13.3)	2 (4.2)
Other	4 (13.8)	0 (0)	5 (25)	15 (6.5)	25 (21.6)	15 (9.5)	31 (64.6)
Funding source							
Industry	13 (48.2)	6 (60)	11 (61.1)	144 (83.7)	66 (65.4)	121 (85.8)	25 (54.4)
Government/Federal	7 (25.9)	1 (10)	3 (16.7)	14 (8.1)	10 (9.9)	0 (0)	6 (13.0)
Other*	7 (25.9)	3 (30)	4 (22.2)	14 (7.1)	25 (24.8)	20 (14.2)	15 (32.6)
Trial start dates#							
Prior to 2010	15 (55.6)	3 (30)	3 (16.7)	18 (10.7)	30 (30)	39 (28.1)	8 (17.4)
2010-2014	8 (29.6)	2 (20)	4 (22.2)	75 (44.6)	35 (36)	41 (29.5)	13 (28.3)
2015-2019	4 (14.8)	5 (50)	11 (61.1)	71 (42.3)	33 (33)	58 (41.7)	24 (52.2)
2020-	0 (0)	0 (0)	0 (0)	4 (2.4)	1 (1)	1 (0.7)	1 (2.2)
Locations of enrollment sites, n (%)**							
Africa	0 (0)	0 (0)	0 (0)	31 (18)	17 (16.8)	14 (9.9)	0 (0)
North America	7 (25.9)	3 (30)	11 (61.1)	81 (47.1)	59 (58.4)	83 (58.9)	19 (41.3)
South/Central America	2 (7.4)	0 (0)	1 (5.6)	60 (34.9)	44 (43.6)	36 (25.5)	7 (15.2)
Asia	9 (33.3)	0 (0)	6 (33.3)	110 (64)	67 (66.3)	66 (46.8)	14 (30.4)
Europe	21 (77.8)	9 (90)	11 (61.1)	108 (62.8)	53 (52.5)	114 (80.85)	27 (58.7)
Australasia	5 (18.5)	1 (10)	2 (11.1)	37 (21.5)	13 (12.9)	39 (27.7)	5 (10.9)

Presented as n (%), unless specified otherwise.
RCT = randomized clinical trial, AIRD = Autoimmune rheumatic disease, AAV = ANCA-associated vasculitis, GCA = Giant cell arteritis, PMR = polymyalgia rheumatica, IIM = Idiopathic inflammatory myopathies, RA = rheumatoid arthritis, SLE = Systemic lupus erythematosus, SpA = Spondyloarthritis, SSc = Systemic sclerosis, CIM = conventional immunosuppressive, bDMARD = biologic disease modifying anti-rheumatic drugs, tsDMARD = targeted synthetic disease modifying anti-rheumatic drugs
#Only considered trials with reported start date
*Includes academic institutions, foundations, self-funding sources, and unspecified sources.
**Percentages are over 100% due to studies reporting multiple sites across different continents.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Mean ages and inclusion of older adults in RCTs per AIRDs

	AAV	GCA/PMR	IIM	RA	SLE	SpA	SSc
Age, mean (SD)	59.63 (14.29)	69.57 (8.73)	57.27 (13.87)	53.84 (12.84)	39.15 (12.18)	44.69 (14.44)	50.4 (12.53)
Trials with upper age exclusion criteria, n (%)	11 (40.74)	1 (10.0)	9 (50.0)	68 (39.5)	57 (56.4)	41 (29.08)	16 (34.8)
Median age for upper limit exclusion criteria, IQR	75 (75-80)	85 (85-85)	75 (75-80)	75 (70-80)	70 (65-75)	70 (65-75)	70 (65-75)
Number of trials reporting older adults, n (%)	9 (33.3)	6 (60.0)	8 (44.4)	99 (60.7)	34 (44.7)	69 (56.6)	17 (41.5)
Representative historical cohort study							
Age, mean (SD)	59.8 (15.3)	73.2 (8.1)	57 (17)	62.3 (13.9)	53.5 (15.2)	53.8 (15.2)	59.6 (13.8)
Reference	Wallace, J Rheumatol 2021	Anumolu, Semin Arthritis Rheum 2023	Kronzer, Arthritis Care Res (Hoboken) 2023	Izadi, Arthritis Care Res (Hoboken) 2022	Schmajuk, Arthritis Care Res (Hoboken) 2022	Stovall, Arthritis Care Res (Hoboken) 2025	Shah, ACR open 2019

RCT = randomized clinical trial, AIRD = autoimmune rheumatic disease, AAV = ANCA-associated vasculitis, GCA = Giant cell arteritis, PMR = polymyalgia rheumatica, IIM = Idiopathic inflammatory myopathies, RA = rheumatoid arthritis, SLE = Systemic lupus erythematosus, SpA = Spondyloarthritis, SSc = Systemic sclerosis, SD = standard deviation, IQR = interquartile range

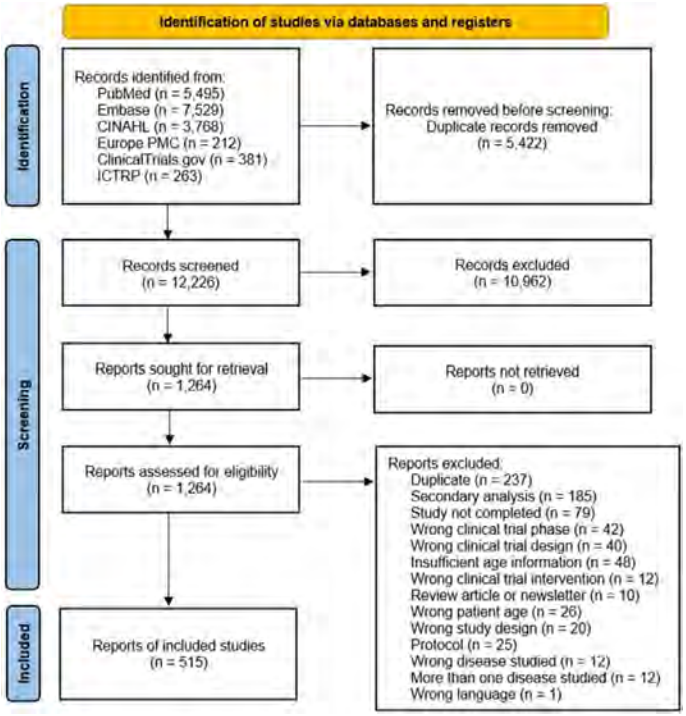


Figure 1. PRISMA flowchart for included randomized clinical trials

of older adults with AIRD in RCTs and observational studies, in line with National Institute of Health's Inclusion Across the Lifespan Policy, to improve delivery of care and outcomes in this growing population.

References

Palmoswki, et al. Semin Arthritis Rheum. 2019.

Disclosure: M. Carpio Tumba: None; **R. Lomanto Silva**: None; **L. Sung**: None; **L. Pedraza-Arévalo**: None; **S. Gupta**: None; **J. Gwak**: None; **A. Mohamadi**: None; **D. Louden**: None; **R. Stovall**: None; **N. Singh**: None; **D. Saygin**: None; **S. Lieber**: None; **J. Lee**: None; **S. Sattui**: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1073

Development of a Culturally-Tailored Storytelling Intervention to Improve COVID-19 Vaccine Uptake in Black and Latinx Patients with Autoimmune and Inflammatory Rheumatic Diseases

Maria I. (\"Maio\") Danila[1], Lesley Jackson[2], Stephanie Ford[3], Mary Wilkenson[3], Tiffany Alexander[4], Jeroan Allison[5], Candace Feldman[6], Fred Jenoure[7], Jonathan Kay[5], Stephenie Lemon[8], Kenneth Saag[9], Karen Salomon[10] and Shilpa Venkatachalam[11], [1]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, AL, [3]UAB Division of Clinical Immunology and Rheumatology, Birmingham, AL, [4]Community Investigator- AL, Birmingham, AL, [5]UMass Chan Medical School, Worcester, MA, [6]Brigham and Women's Hospital, Boston, MA, [7]Community Investigator- MA, Worcester, MA, [8]3. Division of Epidemiology, Department of Population and Quantitative Health Sciences, UMass Chan Medical School, Worcester, MA, Worcester, MA, [9]The University of Alabama at Birmingham, Birmingham, AL, [10]University of Massachusetts Medical School, Shrewsbury, MA, [11]Global Healthy Living Foundation, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Black and Latinx individuals with autoimmune and inflammatory rheumatic diseases (AIRD) face disproportionately higher risks of severe COVID-19 outcomes. Despite this elevated risk, vaccine uptake remains low in these populations. Interventions that leverage narrative communication and homophily may promote behavior change. We developed a culturally and linguistically tailored, storytelling intervention designed to support a future randomized controlled trial (RCT) of COVID-19 vaccine uptake in Black and Latinx patients with AIRD.

Methods: Intervention development was guided by a conceptual model (Figure 1) created by the study team, which included two community investigators and a representative from a patient advocacy organization. Patients with AIRD from two academic rheumatology clinics in Alabama and Massachusetts and from a patient advocacy organization were recruited as storytellers. Storytellers, selected based on congruence with anticipated background of future RCT participants, signed a media release form and were compensated for their time. Semi-structured in-person or virtual interviews elicited storytellers' experiences with COVID-19 vaccination, including barriers (e.g., access issues, safety concerns) and facilitators (e.g., trust in the healthcare system, vaccination health benefit) to vaccination. Filmed interviews were split into segments to identify key themes. Each segment was rated from 1 (lowest) to 5 (highest) for emotional authenticity, persuasiveness, content accuracy, and overall impression. The highest-rated segments discussing desired messages were compiled into a draft English-language video, which underwent structured review. A brief introduction featuring a rheumatologist was recorded to provide context for the audience. A professional videographer combined the introduction with the highest-rated storytelling segments, added titles, subtitles, and music to produce the final video. The Spanish-language footage was reviewed and edited to select storytelling segments with the same messages as those in the English-language video (Figure 2).

Results: Black (N=4) and Latinx (N=4) individuals with AIRD participated in structured ~30 minutes interviews in English or Spanish. Eight study team members reviewed and rated 165 minutes of footage in English and six Spanish-fluent study team members reviewed and rated 131 minutes of Spanish-language footage. The ~10 minutes draft English-language video was edited to ~4 minutes after the second round of review. Table 1 shows key broad themes, subthemes, and second round of review rating scores for each clip selected for the final videos. Both English and Spanish-language videos were edited to ~4 minutes (Figure 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Key overarching themes, subthemes, and rating scores for each clip represented in final storytelling video.

Broad Theme	Subthemes	Video Clips Rating Categories*				Representative Quotes
		Emotional Authenticity	Persuasiveness	Content	Overall Impression	
Infection Risk in AIRD	Ongoing concerns due to personal history of infections	4.3	4.3	4.7	4.7	"I have a lot of concerns about getting infections more easily."
	Need to stay proactive in protecting oneself	4.0	3.7	4.0	4.0	"It's like trying to fight the flu or a cold. You've got to protect yourself."
	Concern that COVID-19 could trigger RA flare	3.0	4.0	4.0	4.0	"I have my arthritis problem under control. I really would not want it to get out of whack and give me more problems."
Personal Experiences with the Updated COVID-19 Vaccine	Preventing serious health consequences	4.7	4.3	4.7	4.7	"The problems I have are already major. I decided to take all the vaccines that I needed."
	Vaccine improves safety and health outcomes	4.7	4.3	4.3	4.7	"The benefit for vaccination for people with autoimmune disease is that it keeps us safe, especially with COVID-19. I knew my risk and I knew I had a better outcome in having that vaccine."
	Vaccination is a personal health priority	4.0	3.0	2.7	3.0	"It's to protect me and keep me healthy."
	Willing to accept some risk for the potential benefit	4.7	4.7	4.7	4.7	"If there was anything that could help, I was willing to take that chance."
	Make vaccination a personal decision	4.0	4.0	3.3	3.7	"You have to think hard about what may benefit you, and then, make a decision."
Reasons to Get the Updated COVID-19 Vaccine	Stay informed—talk to providers and peers, not misinformation	4.7	4.7	4.7	4.7	"Do not rely on misinformation, social media, there's a lot of that out there. Please talk to your provider and people like me"
	New variants require updated vaccines	3.7	4.0	4.7	4.3	"I assume that as the virus mutates or changes, the newer vaccine would be adjusted, somehow, to the new virus that is prevalent in the community."
	Benefits outweigh concerns like fear or anxiety	4.0	3.0	2.7	3.0	"You may be skeptical, you be nervous. You may be scared. But in the end, you will see the benefit"
	Keep up with updated vaccines to protect yourself and loved ones	4.7	4.7	4.7	4.7	"It's very important that we continue to work on COVID. This means we have to continually get the vaccinations. As they are updated, we need to get updated with the work they are doing. Knowing that you're keeping your family safe and loved ones safe at the same time. What more can you ask for?"

Conclusion: Guided by the storytelling narrative communication theory and a structured iterative editing process, we produced two culturally tailored storytelling videos in English and Spanish that can be tested, together with patient navigation, as an approach to improve COVID-19 vaccination rates in Black and Latinx individuals with AIRD. Our robust approach to intervention development is scalable and adaptable to other preventative care interventions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

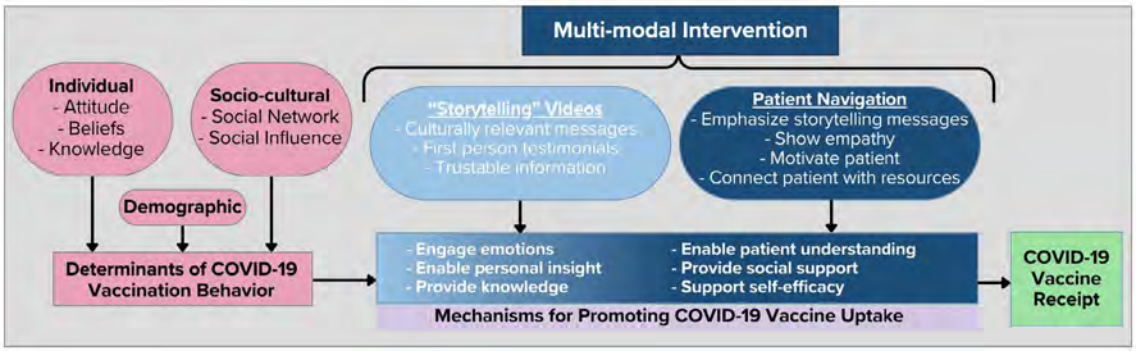


Figure 1. Conceptual Model for the Multi-modal Intervention Design.

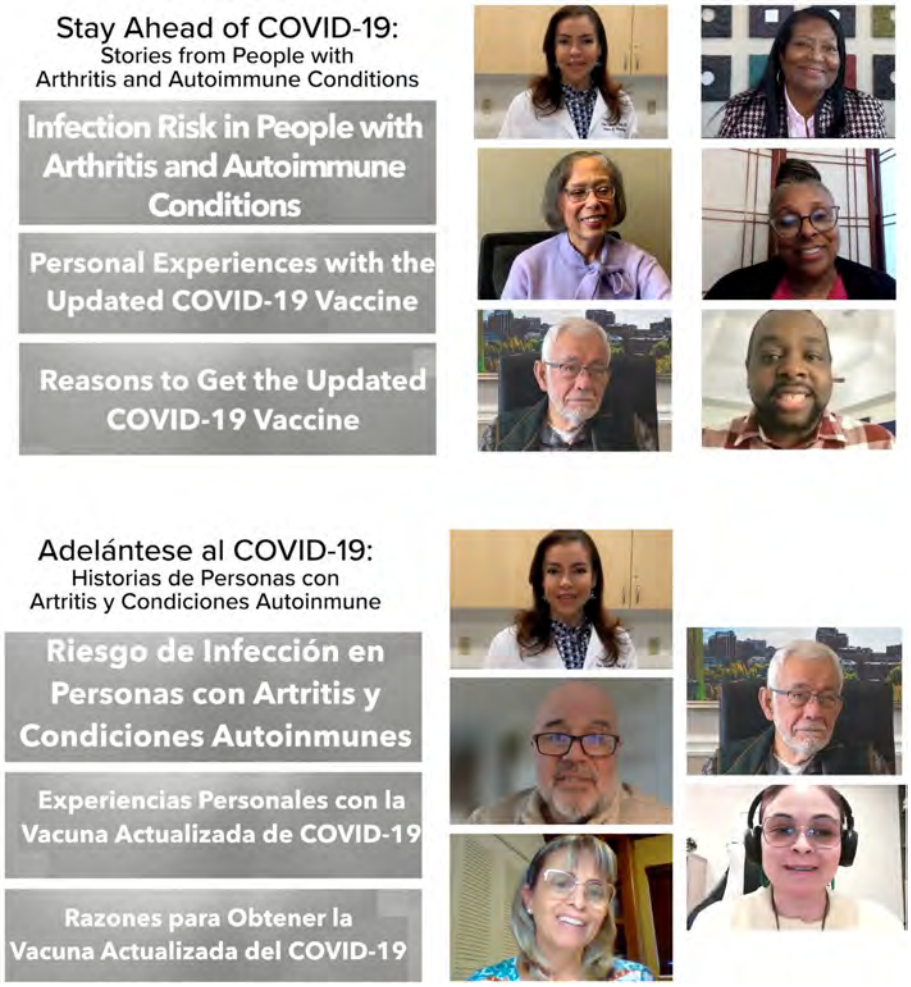


Figure 2: Storytellers and final topics chosen to promote the updated COVID vaccination in Black and Latinx patients with AIRD in English and Spanish.

Disclosure: M. Danila: Boehringer-Ingelheim, 2, Pfizer, 5; **L. Jackson**: None; **S. Ford**: None; **M. Wilkenson**: None; **T. Alexander**: None; **J. Allison**: None; **C. Feldman**: American College of Rheumatology, 2, Arthritis Foundation, 5, 12, Task Force Member, Bain Capital, 2, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 1, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2; **F. Jenoure**: None; **J. Kay**: Biogen, 5, Celltrion, Inc., 2, Gate Bioscience, 2, Immunitas Therapeutics, 2, Immunovant, Inc., 2, Istesso, Ltd, 2, Kolon TissueGeje, Inc, 1, Organon, LLC, 2, Sana Biotechnology, Inc., 2, Santa Ana Bio, Inc., 2, Spyre Therapeutics, 2, Wolters Kluwer NV, 9; **S. Lemon**: Merck/MSD, 5; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **K. Salomon**: None; **S. Venkatachalam**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1074

Racial Disparities in Cardiovascular, Ocular, and Treatment Outcomes in US Patients with Behçet's Disease: A Propensity-Matched Real-World Analysis

Michael Hamilton[1], Justin Riley Lam[2], Emmanuel Otabor[3], Laith Alomari[3], Maxim Barnett[3], Shahrzad Abdollahi[2] and Irene Tan[4], [1]Jefferson Einstein Hospital, Philadelphia, Philadelphia, PA, [2]Jefferson Einstein Hospital, Philadelphia, PA, [3]Jefferson Einstein Hospital Philadelphia, Philadelphia, PA, [4]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Racial/ethnic disparities in Behçet's disease (BD) outcomes are largely undocumented in the United States. Given known differences in disease expression across populations globally, we used a large real-world database to evaluate potential disparities in cardiovascular, ocular, and treatment outcomes between White and Black/Hispanic (B-His) patients with BD.

Methods: Using TriNetX Global Collaborative Network, we conducted a retrospective cohort study. Adults (≥18 years) with ICD-10 BD (M35.2) were assigned to a White or B-His cohort based on electronic health records (EHR) and matched 1:1 on age, sex and ten cardiometabolic comorbidities, yielding 1400 patients per group. Outcomes captured 1 day–10 years after the index BD diagnosis were- stroke, heart failure (HF), myocardial infarction (MI), venous/arterial thrombosis, uveitis, all-cause death and exposures to systemic corticosteroids, tumour-necrosis-factor (TNF) inhibitors and non-biologic immunosuppressants. Between-group differences were assessed using risk ratios (RRs) with 95% confidence intervals (CIs) and Kaplan–Meier survival analysis with log-rank tests.

Results: Groups were well balanced after matching (standardised differences < 0.03). Over the follow-up period, B-His patients experienced nearly twice the stroke incidence of White patients (3.9 % vs 1.7 %; RR 0.43, 0.26–0.69; $p = 0.001$) and a similar pattern for HF (4.6 % vs 2.5 %; RR 0.54, 0.36–0.82; $p = 0.007$). Although MI, thrombosis, seizures and death did not differ significantly, the directionality of the outcomes numerically favoured the White group. Uveitis occurred in 9.6 % of B-His and 6.4 % of White patients (RR 0.66, 0.51–0.86; $p = 0.002$). Therapeutic patterns also diverged: B-His patients were more likely to receive systemic corticosteroids (51 % vs 44 %; RR 0.86, 0.77–0.96; $p = 0.009$) and TNF inhibitors (13 % vs 10 %; RR 0.77, 0.63–0.95; $p = 0.014$), while non-biologic immunosuppressant use was similar between cohorts. Kaplan–Meier curves confirmed lower cumulative hazards for stroke, HF and uveitis in White patients (log-rank $p \leq 0.01$); survival did not differ significantly.

Conclusion: In this nationwide, propensity-matched analysis, White adults with Behçet's disease experienced significantly fewer strokes, HF events, ocular flares and immunosuppressive courses than Black/Hispanic adults, despite equivalent baseline characteristics. The data highlights racial disparities in both disease burden and treatment intensity. Further investigation into genetic susceptibility, care delivery inequities, and social determinants of health is essential to inform equitable, evidence-based management strategies for diverse BD populations.

Disclosure: M. Hamilton: None; **J. Lam**: None; **E. Otabor**: None; **L. Alomari**: None; **M. Barnett**: None; **S. Abdollahi**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1075

Racial Differences in Management and Clinical Outcomes of Giant-Cell Arteritis: A Real-World Propensity-Matched Study

Michael Hamilton[1], Justin Riley Lam[2], Emmanuel Otabor[3], Laith Alomari[3], Maxim Barnett[3], Fabian Rodriguez Quinonez[4] and Irene Tan[5], [1]Jefferson Einstein Hospital, Philadelphia, Philadelphia, PA, [2]Jefferson Einstein Hospital, Philadelphia, PA, [3]Jefferson Einstein Hospital Philadelphia, Philadelphia, PA, [4]Einstein Medical Center Philadelphia, Philadelphia, PA, [5]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Giant-cell arteritis (GCA) is usually described in people of Northern-European ancestry, and little is known about outcomes in Black and Hispanic (B-His) patients. Using a large U.S. multi-center electronic-health-record network, we compared clinical management and 1-year outcomes between White and B-His adults with GCA.

Methods: We conducted a retrospective cohort study using the TriNet-X Global Collaborative Network. Adults (≥18 years) with an ICD-10 diagnosis of GCA were assigned to a White cohort or a B-His cohort based on electronic health records; individuals with mixed race/ethnicity were excluded. One-to-one propensity-score matching on age, sex, and 12 cardiovascular or metabolic comorbidities produced two balanced groups of 8323 patients each. Outcomes recorded 1–365 days after the index date were vision loss, stroke, myocardial infarction (MI), temporal-artery biopsy, CT angiography, prednisone use, tocilizumab use, death, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Risk ratios (RRs) with 95 % confidence intervals (CIs) and Kaplan–Meier log-rank tests were used for comparisons.

Results: After matching, baseline characteristics were well balanced (standardized differences < 0.05). Inflammatory activity was greater in B-His patients, whose mean CRP (24.5 mg/L vs 21.0 mg/L; p = 0.005) and ESR (40.1 mm/h vs 27.0 mm/h; p < 0.001) exceeded those of White patients. Temporal-artery biopsy was performed more often in B-His patients (22.6 % vs 17.8 %; RR 0.79, 0.74–0.84; p < 0.001), but vision-loss and CT-angiography frequencies were low (< 0.7 % and < 0.3 %, respectively) and did not differ. Prednisone exposure was equivalent in both groups (≈58 %), yet tocilizumab was prescribed nearly twice as often to White patients (5.1 % vs 2.8 %; RR 1.82, 1.56–2.13; p < 0.001). During follow-up period, stroke occurred in 3.5 % of B-His patients and 2.6 % of White patients (RR 0.74, 95 % CI 0.62–0.89; p = 0.002), while MI rates were similar (2.0 % vs 1.9 %). All-cause mortality, however, was higher in Whites (5.0 % vs 3.2 %; RR 1.53, 1.32–1.78; p < 0.001). Survival analysis confirmed lower stroke-free survival for B-His patients and lower overall survival for Whites.

Conclusion: In this large, propensity-matched real-world cohort, Black and Hispanic adults with GCA displayed higher inflammatory markers and greater stroke risk yet were less likely to receive tocilizumab than their White counterparts. Conversely, White patients had higher 1-year mortality despite comparable comorbidity burdens. These bidirectional disparities underscore the need for earlier recognition of vascular events in B-His patients and investigation into factors driving excess mortality among White patients. Tailored diagnostic vigilance and equitable access to advanced therapies are essential to optimize outcomes across racial and ethnic groups.

Disclosure: M. Hamilton: None; **J. Lam**: None; **E. Otabor**: None; **L. Alomari**: None; **M. Barnett**: None; **F. Rodriguez Quinonez**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1076

Racial Differences in Real-World Use of Urate-Lowering and Adjunctive Therapies for Gout: A 10-Year Propensity-Matched Cohort Study

Michael Hamilton[1], Justin Riley Lam[2], Emmanuel Otabor[3], Laith Alomari[3], Maxim Barnett[3], Arthur Lau[4] and Irene Tan[5], [1]Jefferson Einstein Hospital, Philadelphia, Philadelphia, PA, [2]Jefferson Einstein Hospital, Philadelphia, PA, [3]Jefferson Einstein Hospital Philadelphia, Philadelphia, PA, [4]Jefferson Einstein Hospital, Maple Glen, PA, [5]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Although achieving target serum urate (SU) and reducing cardiovascular events are cornerstones of gout management, little is known about contemporary treatment patterns across racial and ethnic groups. We compared long-term exposure to urate-lowering therapy (ULT), acute-attack medications, procedures, SU, and major adverse cardiovascular events (MACE) between non-Hispanic White (NHW) and racial/ethnic minority (MIN) adults in routine U.S. practice.

Methods: We conducted a retrospective cohort study using TriNetX Collaborative Network. Adults ≥ 18 years with an incident gout diagnosis (ICD-10 M10) were classified as NHW or MIN (Black, Hispanic, Asian)- based on electronic health records. One-to-one propensity matching balanced age, sex, nine comorbidities, cardiometabolic drugs and BMI, yielding 359 020 patients per cohort. Outcomes captured 1–10 y post-index were initiation of allopurinol, febuxostat, pegloticase, colchicine, oral corticosteroids, NSAIDs, IL-1 inhibitors, arthrocentesis, most-recent SU, and composite MACE (myocardial infarction, heart failure, stroke). Risk ratios (RR, 95 % CI) and Kaplan–Meier log-rank tests ($\alpha = 0.05$) compared groups.

Results: Baseline characteristics were well balanced. During the follow-up period, NHW patients were modestly more likely to start allopurinol than MIN patients (29.8 % vs 28.1 %; RR 1.06, 1.05–1.07), Conversely, febuxostat initiation was nearly twice as common among MIN patients (3.8 % vs 2.1 %; RR 0.56 [0.55–0.58]; $p < 0.001$). Pegloticase use remained rare at 0.05 % in both cohorts (RR 1.13 [0.92–1.38]; $p = 0.25$).

Acute-therapy patterns differed: colchicine was prescribed to 20.1 % of MIN versus 14.3 % of NHW patients (RR 1.40 [1.38–1.42]; $p < 0.001$); NSAIDs to 32.4 % versus 30.5 % (RR 1.07 [1.06–1.08]; $p < 0.001$); and systemic corticosteroids

Table 1: Propensitiy score matching-Demographics and baseline characteristics

Variable	White (Before) (N = 905,933)	Minorities (Before) (N = 380,079)	Std Diff (Before)	White (After) (N = 359,020)	Minorities (After) (N = 359,020)	Std Diff (After)
Current Age (mean ± SD)	71.6 ± 14.3	68.1 ± 14.7	0.244	68.3 ± 15.1	68.2 ± 14.6	0.004
Age at Index	65.0 ± 14.6	61.2 ± 14.9	0.253	61.5 ± 15.3	61.4 ± 14.8	0.008
Female	237,127 (26.8%)	120,715 (33.2%)	0.140	118,599 (33.0%)	117,634 (32.8%)	0.006
Male	646,519 (73.1%)	242,787 (66.8%)	0.139	240,285 (66.9%)	241,301 (67.2%)	0.006
Hypertensive diseases	422,618 (47.8%)	185,815 (51.1%)	0.066	173,955 (48.5%)	181,798 (50.6%)	0.044
Hyperlipidemia	262,261 (29.7%)	96,212 (26.5%)	0.071	88,254 (24.6%)	95,213 (26.5%)	0.044
Type 2 diabetes	178,158 (20.2%)	94,159 (25.9%)	0.137	87,853 (24.5%)	91,196 (25.4%)	0.022
Overweight / Obesity	153,582 (17.4%)	59,738 (16.4%)	0.025	53,703 (15.0%)	58,892 (16.4%)	0.040
Neoplasms	220,823 (25.0%)	76,318 (21.0%)	0.095	71,175 (19.8%)	75,674 (21.1%)	0.031
AKI / CKD	164,297 (18.6%)	89,821 (24.7%)	0.149	82,241 (22.9%)	86,272 (24.0%)	0.026
Alcohol-related disorders	30,417 (3.4%)	13,432 (3.7%)	0.014	12,434 (3.5%)	13,192 (3.7%)	0.011
Tobacco use	18,813 (2.1%)	9,083 (2.5%)	0.025	8,281 (2.3%)	8,863 (2.5%)	0.011

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variable	White (Before)	Minorities (Before)	Std Diff (Before)	White (After)	Minorities (After)	Std Diff (After)
Diuretics	254,652 (28.8%)	117,794 (32.4%)	0.078	107,519 (29.9%)	114,435 (31.9%)	0.042
Antilipemic agents	276,465 (31.3%)	107,080 (29.5%)	0.040	96,763 (27.0%)	105,299 (29.3%)	0.053
ACE inhibitors	180,989 (20.5%)	72,668 (20.0%)	0.012	65,526 (18.3%)	71,276 (19.9%)	0.041
Other antihypertensives	118,617 (13.4%)	66,103 (18.2%)	0.131	60,061 (16.7%)	63,067 (17.6%)	0.022
Angiotensin II inhibitors	114,945 (13.0%)	63,672 (17.5%)	0.126	58,215 (16.2%)	60,924 (17.0%)	0.020
Aspirin	198,802 (22.5%)	81,558 (22.4%)	0.001	73,627 (20.5%)	79,762 (22.2%)	0.042
Niacin	18,196 (2.1%)	6,698 (1.8%)	0.016	5,601 (1.6%)	6,535 (1.8%)	0.020
Niacinamide	7,918 (0.9%)	3,198 (0.9%)	0.002	3,187 (0.9%)	3,065 (0.9%)	0.004
Cyclosporine	6,567 (0.7%)	2,884 (0.8%)	0.006	2,762 (0.8%)	2,777 (0.8%)	<0.001

Propensity score matching- Medications

Table 3- Outcomes

Outcomes After Propensity-Score Matching in Gout Cohort (NHW vs Minority)

Outcome	NHW % / Mean	MIN % / Mean	RR or Δ (95% CI)	p-value
Allopurinol initiation	29.8 %	28.1 %	1.06 (1.05–1.07)	<0.001
Febuxostat initiation	2.1 %	3.8 %	0.56 (0.55–0.58)	<0.001
Pegloticase initiation	0.05 %	0.05 %	1.00 (0.80–1.25)	0.94
Colchicine use	14.3 %	20.1 %	1.40 (1.38–1.42)	<0.001
NSAID use	30.5 %	32.4 %	1.07 (1.06–1.08)	<0.001
Systemic corticosteroid use	45.5 %	46.0 %	1.01 (1.00–1.02)	0.02
IL-1 inhibitor use	0.08 %	0.14 %	1.69 (1.43–2.03)	<0.001
Arthrocentesis	8.6 %	7.3 %	0.85 (0.83–0.87)	<0.001
Mean serum urate, mg/dL	6.39 ± 2.08	6.71 ± 2.32	+0.32	<0.001
Major adverse CV events	15.5 %	16.8 %	1.08 (1.06–1.10)	<0.001

to 46.0 % versus 45.5 % (RR 1.01 [1.00–1.02]; p = 0.001). IL-1 inhibitors, although infrequent, were used in 0.14 % of MIN versus 0.08 % of NHW patients (RR 1.69 [1.43–2.03]; p < 0.001). Arthrocentesis or joint injection occurred in 7.3 % of MIN versus 8.6 % of NHW patients (RR 0.85 [0.83–0.87]; p < 0.001).

Biochemically, mean serum urate remained higher in MIN than NHW patients (6.71 ± 2.32 vs 6.39 ± 2.08 mg/dL; p < 0.001). Clinically, major adverse cardiovascular events occurred in 16.8 % of MIN versus 15.5 % of NHW patients (RR 1.08 [1.06–1.10]; p < 0.001), and Kaplan–Meier curves showed earlier event accrual in MIN patients (log-rank p < 0.001).

Conclusion: Despite similar comorbidity profiles, minority adults with gout were less likely to initiate guideline-preferred allopurinol yet more likely to receive febuxostat and multiple acute agents, had higher residual SU, and experienced greater cardiovascular morbidity than non-Hispanic-White adults. These findings highlight treatment and outcome inequities and call for targeted dose-titration protocols, SU monitoring, and cardiovascular-risk mitigation strategies to improve gout care in underserved populations.

Disclosure: M. Hamilton: None; **J. Lam**: None; **E. Otabor**: None; **L. Alomari**: None; **M. Barnett**: None; **A. Lau**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1077

Health literacy and work status in people with inflammatory arthritis: a cluster analysis in a national cohort

Mrinalini Dey[1], Sam Norton[2], Andrew Cope[2], MAYA BUCH[3], Richard Osborne[4], James Galloway[2] and Elena Nikiphorou[2], [1]Centre for Rheumatic Diseases, King's College London, London, United Kingdom, [2]King's College London, London, United Kingdom, [3]UNIVERSITY OF MANCHESTER, MANCHESTER, United Kingdom, [4]La Trobe University, Melbourne, Victoria, Australia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Work status and employment can be impacted in people with inflammatory arthritis (IA). We aimed to assess the association between health literacy and work status in people with IA.

Methods: Adults with IA, recruited to the National Early Inflammatory Arthritis Audit (NEIAA) in the UK, were invited to complete an online survey (March to May 2024), comprising the Health Literacy Questionnaire (HLQ), Work Productivity and Activity Impairment questionnaire, and questions on demographics, employment and education.

The HLQ comprises 44 questions and nine scales which each measure an aspect of health literacy, and assess experiences of understanding, accessing and using health information.

Occupation was classified as per the International Standard Classification of Occupations (ISCO) and UK Standard Occupational Classification (SOC), which classifies by skill levels (1-4).

Responses were matched with original records within NEIAA. Agglomerative hierarchical clustering, using Ward's method, was applied. Differences in health literacy, socio-demographics and work status were compared between clusters.

Table 1: Outcomes presented by health literacy cluster. Absenteeism is defined as the percentage of time absent from work. Here, absenteeism was analysed as a binary variable, as absent ≤5% or >5% of time. Presenteeism is measured by the degree health problems affected work productivity of the last 7 days, expressed as a percentage score representing impairment due to health reasons while working; higher numbers denote greater impairment and less productivity. SD= standard deviation.

Cluster by health literacy	Highest n=90	High n=190	Moderate n=296	Low n=270	Lowest n=149
Age (Mean, SD)	63.4 (11.4)	57.1 (14.7)	57.9 (13.4)	56.9 (12.6)	53.9 (11.8)
Gender (% female)	62.2	65.8	65.6	66.0	69.8
Smoking status (%)					
Current smoker	8.9	5.3	3.7	11.5	10.7
Ex-smoker	22.2	23.7	30.4	30.0	26.2
Never smoker	53.3	45.3	44.3	39.3	42.3
Unknown	15.6	25.8	21.6	19.3	20.8
Education (%)					
No formal qualifications	6.8	8.1	7.7	12.5	9.8
GCSE, O Level, or equivalent	27.3	28.0	28.6	30.9	36.4
A Level, or equivalent	21.6	16.1	18.8	21.5	19.6
Undergraduate degree, or equivalent	26.1	25.3	26.1	20.4	19.6
Postgraduate degree, or equivalent	18.2	22.6	18.8	14.7	14.7
Work hours per week (Mean, SD)	45.7 (46)	34.4 (14.9)	34.1 (15.5)	38.8 (27.2)	36.7 (23.3)
Absent >5% of time (%)	4.7	9.0	23.4	20.0	33.8
Presenteeism (Mean, SD)	18.3 (18.9)	23.4 (23.3)	30.9 (25.3)	38.1 (26)	52.2 (27.2)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

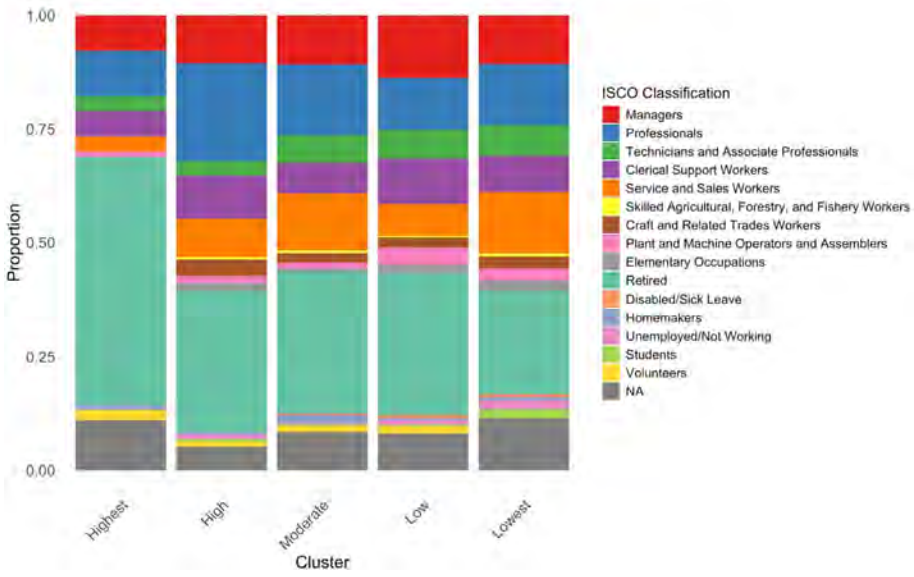


Figure 1: International Standard Classification of Occupations (ISCO) distribution by health literacy cluster

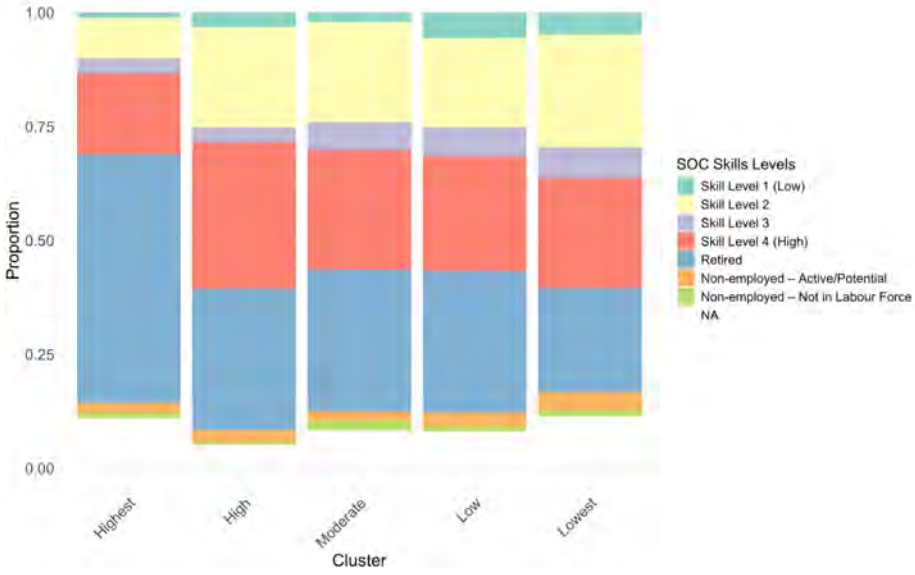


Figure 2: Standard Occupational Classification (SOC) skill levels by health literacy cluster

Results: In total, 995 patients with IA were included, with median age 59 years (IQR 50-67) and 66% female. Cluster analysis yielded five clusters according to HLQ scores (Table 1).

The "highest" health literacy cluster contained the greatest proportion of retired individuals compared to all other clusters, with the "lowest" health literacy cluster having the smallest proportion of retired individuals and greatest proportion of unemployment (Figures 2 and 3). The "highest" health literacy cluster also had lowest mean presenteeism (18.3; SD 18.9), compared to 52.2 (SD 27.2) in the cluster with lowest health literacy. The "lowest" health literacy cluster had seven-fold greater absenteeism compared to the "highest" health literacy cluster and greatest impairment in the HLQ domains: "Feeling understood and supported by healthcare providers", "Engagement with healthcare providers" and "Navigating the healthcare system".

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The greatest combined proportion of managers and professionals, and SOC Skill Level 4, was in the "high" health literacy cluster, while the greatest proportion of SOC Skill Level 1 was in the "low" health literacy cluster.

Education did not significantly vary between clusters. The lowest two health literacy clusters had the greatest proportion of people with highest educational level at GCSE or equivalent and the lowest proportion of people with a postgraduate degree or equivalent.

Conclusion: The "highest" health literacy cluster comprised largely retired individuals, compared to all other clusters. Clusters with higher HLQ scores had a greater proportion of people in high-skilled work, and lower absenteeism and presenteeism. Lower health literacy was associated with low-skilled work, and higher absenteeism and presenteeism.

Our results suggest being in work leads to increased communication, support and wellbeing of individuals with IA, important for engagement with healthcare providers. Retired individuals have very high HLQ scores, suggesting health literacy may increase with experience and engagement with health services over time.

Disclosure: M. Dey: None; **S. Norton**: None; **A. Cope**: Bristol-Myers Squibb(BMS), 2, 5, 6; **M. BUCH**: Bristol-Myers Squibb(BMS), 5; **R. Osborne**: None; **J. Galloway**: AbbVie, 2, 6, Alfasigma S.p.A., 2, Eli Lilly, 2, 6, Gilead, 2, Janssen-Cilag, 2, 5, 6, Novartis, 6, Pfizer, 2, 5, 6, Takeda, 2, UCB, 6; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

Abstract Number: 1078

Trends in Hospitalization rate with Lupus in the State of Florida: A retrospective data review from Florida Health Charts from 1992-2023

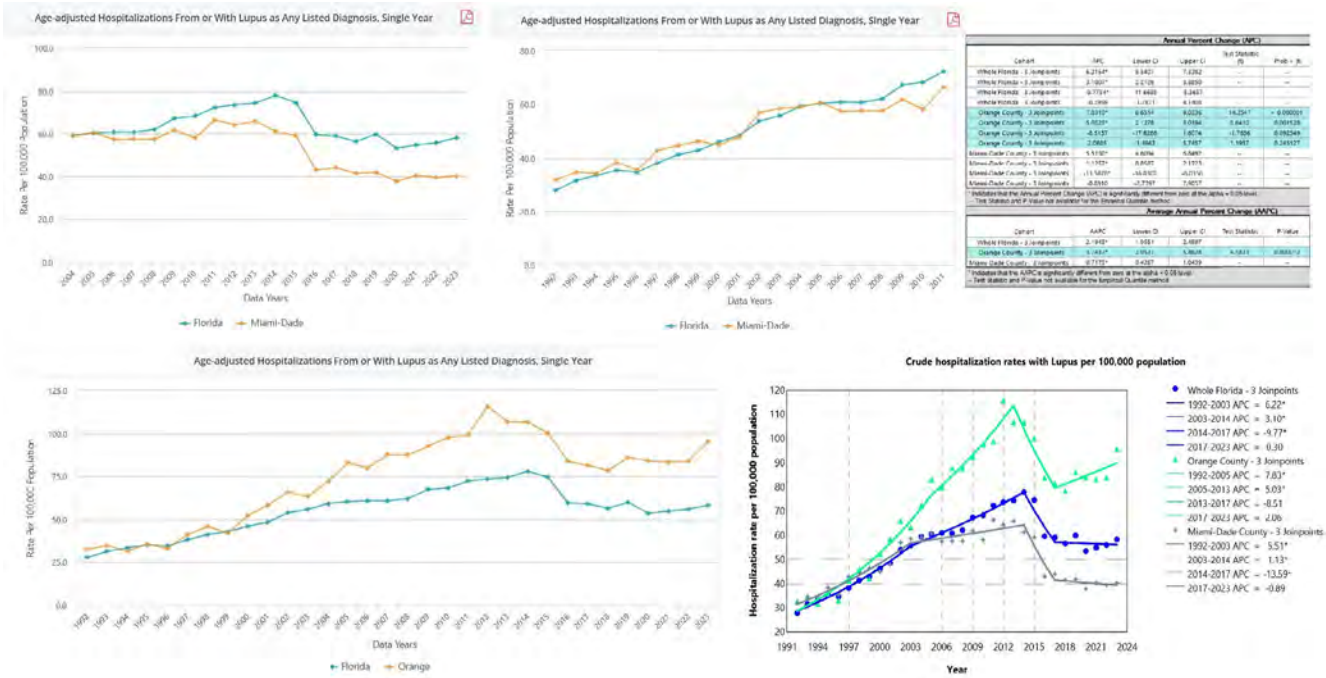
Muhammad Sohaib Asghar[1], Mohammed Akram[2], Veerkaran Banga[1], rajkaran Banga[1], Woo Joo Lee[1], Afsana Ansari Shaik[3], Syed Muhammad Muneeb Akhtar[4] and Thomas Shimshak[1], [1]AdventHealth Sebring, Sebring, FL, [2]HCA Aventura, Aventura, FL, [3]Mayo Clinic, Rochester, MN, [4]Dow University of Health Sciences, Karachi, Pakistan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

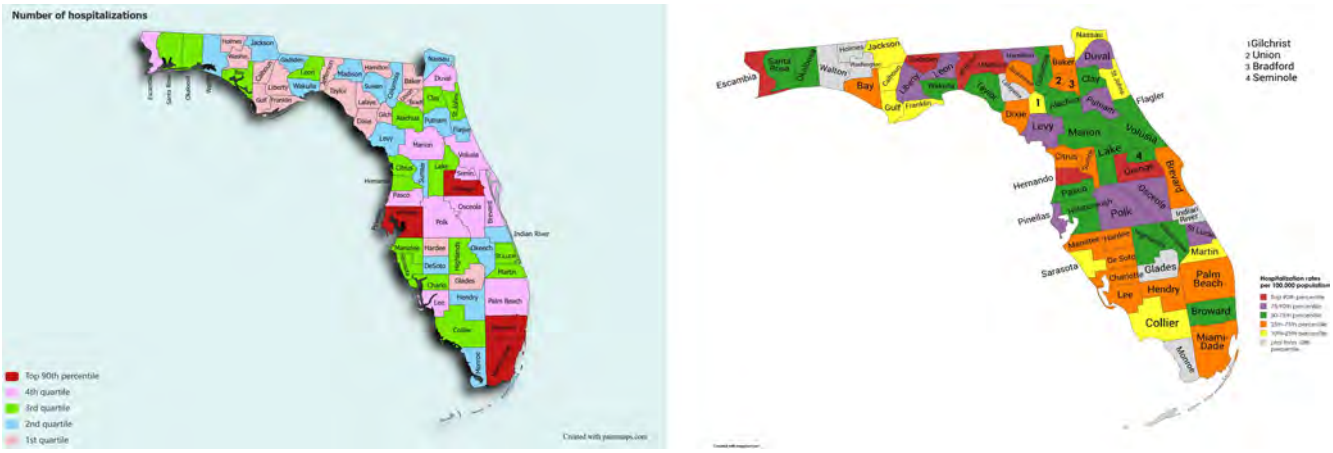
Background/Purpose: Lupus is a systemic autoimmune disease that occurs when the body's immune system attacks its own tissues and organs. This study was conducted to analyze the trends of hospitalization in patients where lupus was any listed diagnosis among the residents in the State of Florida with data from Inpatient hospitalizations, discharged from civilian, non-federal hospitals located within Florida.

Methods: Data on hospitalization rates was sourced from the Florida Department of Health's Florida CHARTS database. We included data from 1992 to 2023, utilizing hospitalization counts and rates per 100,000 population. The dataset was stratified by race (Black, White, and other categories), and ethnicity (Hispanic vs. non-Hispanic). For county-level analysis, age-adjusted hospitalization rates for lupus were compiled across the entire study period. Trends were assessed using Joinpoint regression analysis, which identified significant changes in the direction and magnitude of these trends over time. The results are expressed either as annual percent change (APC) and average annual percent change (AAPC), and their respective 95% confidence intervals (CI).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Age-adjusted hospitalization rates with lupus in Florida, including Orange County (fourth quartile) and Miami-Dade county (second quartile).

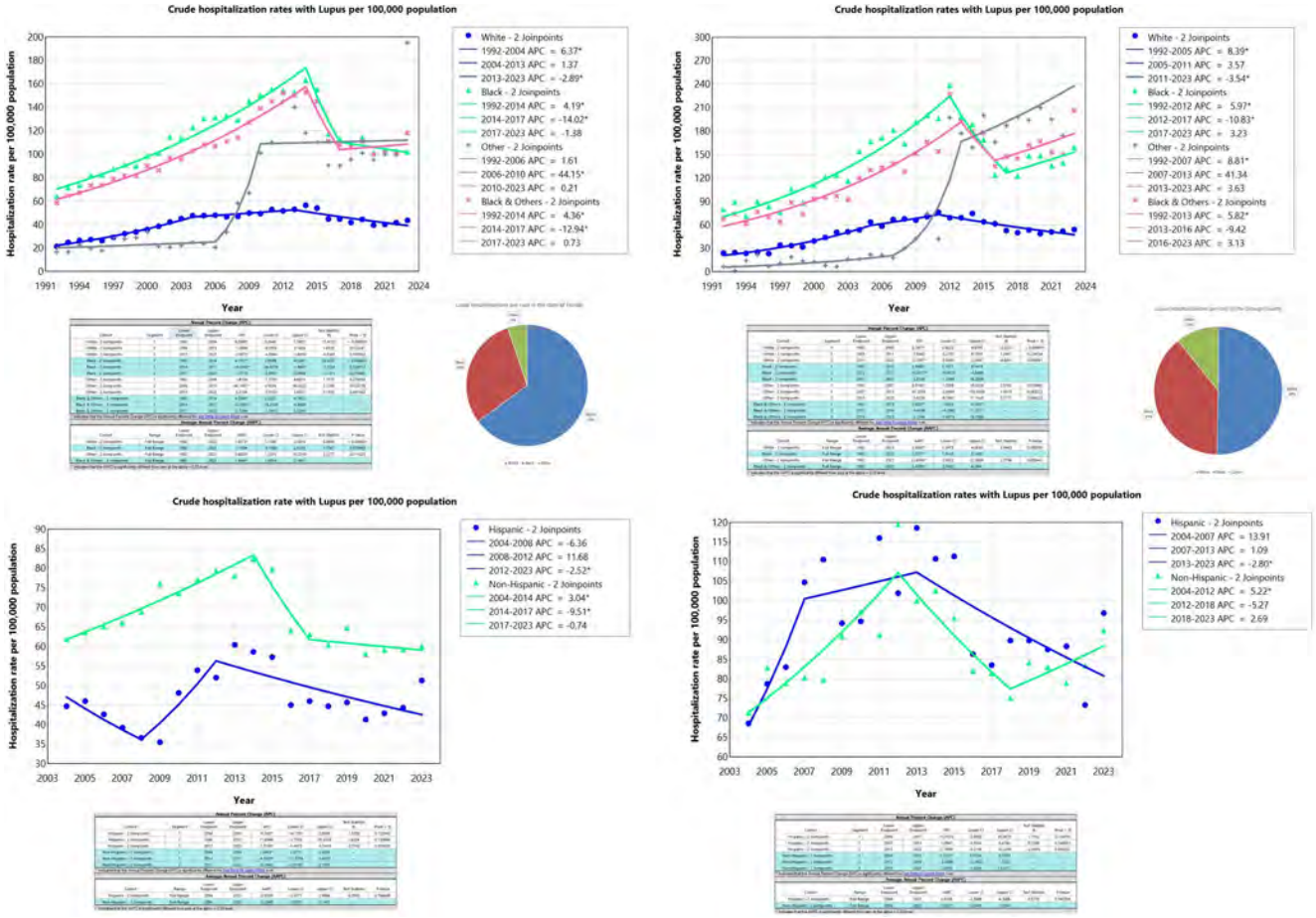


County-wise distributions of age-adjusted hospitalization count and rates in the State of Florida from 1992-2023.

Results: During 1992-2023, a total of 353,984 lupus-related hospitalizations were reported in Florida. In 2023, the age-adjusted rate per 100,000 of hospitalizations from or with lupus as any listed diagnosis in Orange County was 95.6 compared to Florida at 58.3, while the same for Miami-Dade county was 40.2 (Figure 1). Overall, from 1999-2023, the total number of hospitalizations in Orange county were 27,525 which ranked third in the State in terms of frequency, but in the highest quartile for age-adjusted hospitalization rate (Figure 2), followed by 2nd-ranked Broward county (n=33,159; third quartile) and most hospitalizations in Miami-Dade county (n=40,733; 2nd quartile). About 65% of the hospitalized patients were White, followed by 39% Black and 11% others. AAPC was found +1.86 [1.14-2.58] vs Black & others combined +1.84 [1.50-2.16], with significant p-value < 0.001 for Whites, 0.08 for Black (non-significant) and 0.01 for others (Figure 3). Data for Hispanics vs non-Hispanics were only available from 2004-2023 and showed non-significant declining trends (P=0.76).

Conclusion: Lupus can result in discomfort, lower quality of life, premature death, loss of productivity, and high medical costs from hospitalization. The State of Florida showed diverse trends in the hospitalization rates with lupus over the last three decades. By monitoring counts and rates of hospitalizations, public health professionals can take effective and timely action to prevent increases in disease and death.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Racial and ethnic disparities for lupus-related hospitalizations in Florida.

Disclosure: M. Asghar: None; **M. Akram**: None; **V. Banga**: None; **r. Banga**: None; **W. Lee**: None; **A. Shaik**: None; **S. Muneeb Akhtar**: None; **T. Shimshak**: None.

Abstract Number: 1079

Sociodemographic, Clinical, and Community-Level Deprivation Factors are Associated with Health-Related Quality of Life in Systemic Sclerosis

Sarah Smith[1], **Paula Ramos**[2], Dulaney Wilson[3], Diane Kamen[4] and Richard Silver[1], [1]Medical University of South Carolina, Charleston, SC, [2]Emory University School of Medicine, Atlanta, GA, [3]Medical University of South Carolina, Charleston, [4]Medical University of South Carolina, Johns Island, SC

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a multisystem autoimmune disease with heterogeneous manifestations and significant impairment in health-related quality of life (HRQoL). SSc outcomes are shaped by biological, clinical, socio-demographic, and psychosocial factors, with well-documented disparities by race, sex, and socioeconomic status. While clinical contributors to HRQoL are established, the role of community-level deprivation remains understudied in SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Characteristics by Systemic Sclerosis Subtype. Values are presented as number (percentage) for categorical variables and mean ± standard deviation (SD) for continuous variables. Comparisons are shown across limited cutaneous (lcSSc), diffuse cutaneous (dcSSc), and sine scleroderma subtypes. Abbreviations: ADI = Area Deprivation Index; EJI-SER = Environmental Justice Index Social-Environmental Rank; FVC = forced vital capacity; Hx = history.

Patient Characteristics	lcSSc (N=140) N(%) or Mean±SD	dcSSc (N=151) N(%) or Mean±SD	Sine (N=23) N(%) or Mean±SD	p-value
Race				**0.010**
Non-Black	99 (70.7%)	81 (53.6%)	17 (73.9%)	
Black	41 (29.3%)	70 (46.4%)	6 (26.1%)	
Gender				**0.001**
Female	123 (87.9%)	107 (70.9%)	20 (87.0%)	
Male	17 (12.1%)	44 (29.1%)	3 (13.0%)	
> High School Education				0.180
No	2 (1.6%)	5 (3.8%)	2 (8.7%)	
Yes	125 (98.4%)	126 (96.2%)	21 (91.3%)	
Insurance Status				0.340
Self-pay/uninsured	1 (0.7%)	1 (0.7%)	0 (0.0%)	
Public	35 (25.9%)	50 (36.2%)	5 (21.7%)	
Private	99 (73.3%)	87 (63.0%)	18 (78.3%)	
Employment Status				0.410
Employed	106 (77.9%)	105 (76.6%)	19 (82.6%)	
Unemployed	1 (0.7%)	2 (1.5%)	0 (0.0%)	
Disabled	16 (11.8%)	23 (16.8%)	1 (4.3%)	
Other	13 (9.6%)	7 (5.1%)	3 (13.0%)	
Community Level Indices				0.320
EJI-SER	0.402 ± 0.27	0.438 ± 0.28	0.343 ± 0.26	
ADI National Rank (out of 100)	56.7 ± 23.93	57.7 ± 23.90	48.7 ± 24.86	
ADI State Rank (out of 10)	4.8 ± 2.63	5.0 ± 2.52	4.1 ± 2.72	
Smoking Status				0.180
Never	85 (63.9%)	86 (63.2%)	8 (34.8%)	
Former	41 (30.8%)	45 (33.1%)	10 (43.5%)	
Current	7 (5.3%)	5 (3.7%)	1 (4.3%)	
Depression				0.320
No	99 (73.9%)	104 (75.4%)	14 (60.9%)	
Yes	35 (26.1%)	34 (24.6%)	9 (39.1%)	
Organ Involvement				
modified Rodnan skin score	4.4 ± 3.7	19.8 ± 12.2	0	**<0.0001**
Pulmonary Arterial Hypertension				0.74
No	90 (76.3%)	104 (80.0%)	15 (100.0%)	
Yes	28 (23.7%)	26 (20.0%)	5 (33.3%)	
Interstitial Lung Disease				0.750
No	49 (41.2%)	50 (36.8%)	7 (35.0%)	
Yes	70 (58.8%)	86 (63.2%)	13 (65.0%)	
FVC (% predicted), mean (SD)	81.1 ±17.7	73.3 ±19.5	78.2 ±20.1	**0.020**
Esophageal Stricture				**0.020**
No	62 (63.9%)	78 (78.0%)	17 (89.5%)	
Yes	35 (36.1%)	22 (22.0%)	2 (10.5%)	
Hx of Scleroderma Renal Crisis				**0.040**
No	64 (95.5%)	68 (84.0%)	10 (100.0%)	
Yes	3 (4.5%)	13 (16.0%)	0 (0.0%)	

Methods: We analyzed data from 314 adult patients with SSc who met 2013 ACR/EULAR classification criteria and were enrolled in a longitudinal observational cohort at the Medical University of South Carolina. HRQoL was measured using the SF-36 Physical (PCS) and Mental (MCS) Component Summary scores. We examined associations between HRQoL scores and sociodemographic factors, clinical characteristics, and community deprivation indices - Area Deprivation Index (ADI) and Environmental Justice Index Social-Environmental Rank (EJI-SER). ADI, evaluated at the census block level, was assessed using national percentiles and state deciles to reflect neighborhood-level disadvantage. EJI-SER, evaluated at the census tract level, captured cumulative environmental and social vulnerability. Bivariate comparisons and multivariable linear regression were used to estimate associations with PCS and MCS scores.

Results: Among 314 SSc patients (44.6% limited cutaneous, 48.1% diffuse cutaneous, 7.3% sine), significant differences by SSc subtype were observed for race, gender, modified Rodnan skin score (mRSS), forced vital capacity (FVC), esophageal stricture, and history of renal crisis (Table 1). Average PCS and MCS scores varied significantly across demographic,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

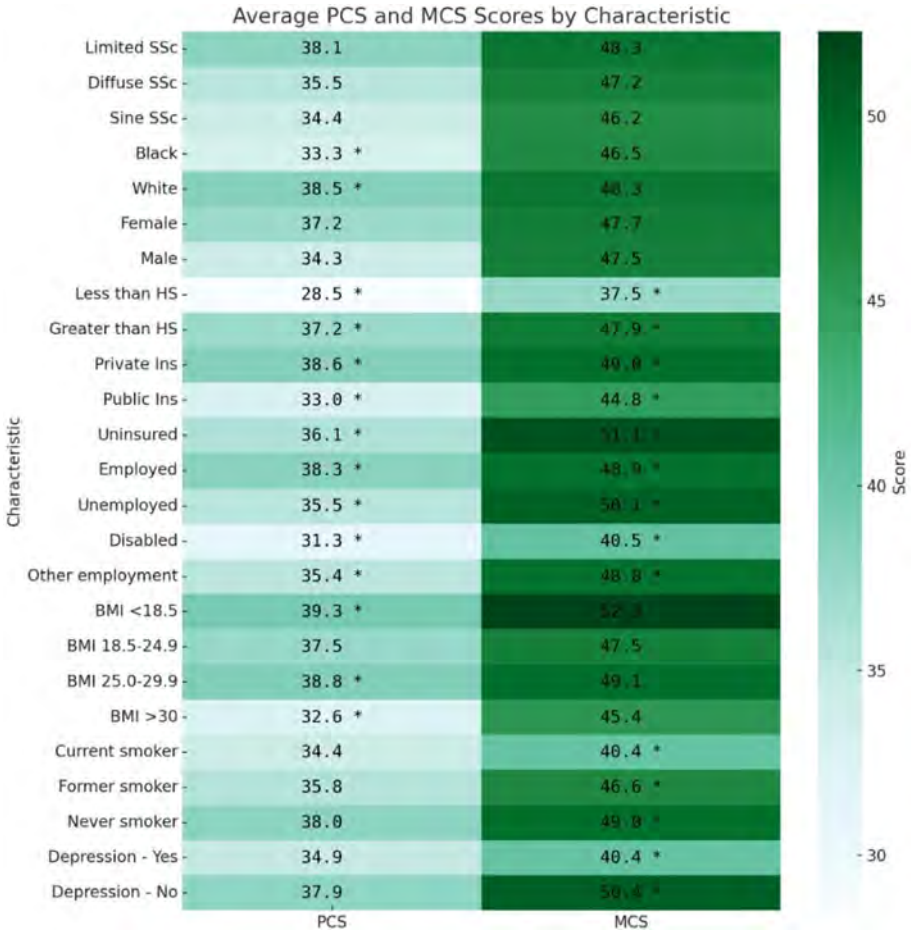


Figure 1. Heatmap of Average PCS and MCS Scores by Patient Characteristics and Social Factors. This heatmap displays mean Physical Component Summary (PCS) and Mental Component Summary (MCS) scores across demographic and socioeconomic subgroups among patients with systemic sclerosis. Darker shading indicates higher (better) average quality of life scores. An asterisk (*) indicates that the subgroup belongs to a characteristic category with a statistically significant association ($p < 0.05$) with PCS or MCS. Abbreviations: PCS = Physical Component Summary; MCS = Mental Component Summary; SSc = Systemic sclerosis; HS = High School; Ins = Insurance; BMI = Body Mass Index.

clinical, and socioeconomic factors (Figure 1). In multivariable linear regression analysis (Figure 2), lower PCS was associated with Black race (β=–4.08, p=0.002), public insurance (β=–5.65, p< 0.001), disability (β=–5.69, p=0.01), and depression (β=–5.17, p=0.001), while higher education was protective (β=8.40, p=0.02). Higher (worse) deprivation scores for ADI (state β=–1.09, p< 0.0001; and national rank β=–0.10, p=0.0002), and EJI-SER (β=–0.73, p=0.005) were associated with worse PCS. For MCS, depression (β=–0.83, p< 0.0001), current smoking (β=–6.32, p=0.01), and ADI national rank (β=–0.06, p=0.03) were significantly associated. A range of additional clinical variables, including measures of pulmonary, gastrointestinal, and renal involvement, also demonstrated associations with HRQoL scores (Figure 2).

Conclusion: Both individual- and community-level social determinants contribute meaningfully to disparities in HRQoL among patients with SSc. Consistent with prior literature, factors associated with more severe disease—such as organ involvement, Black race, lower educational attainment, public insurance, smoking, and depression—were linked to lower HRQoL. Notably, this is the first study to demonstrate that higher ADI and EJI-SER scores, reflecting neighborhood-level deprivation, are associated with worse HRQoL in SSc. These indices may offer novel tools for identifying at-risk populations and guiding equity-focused care strategies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

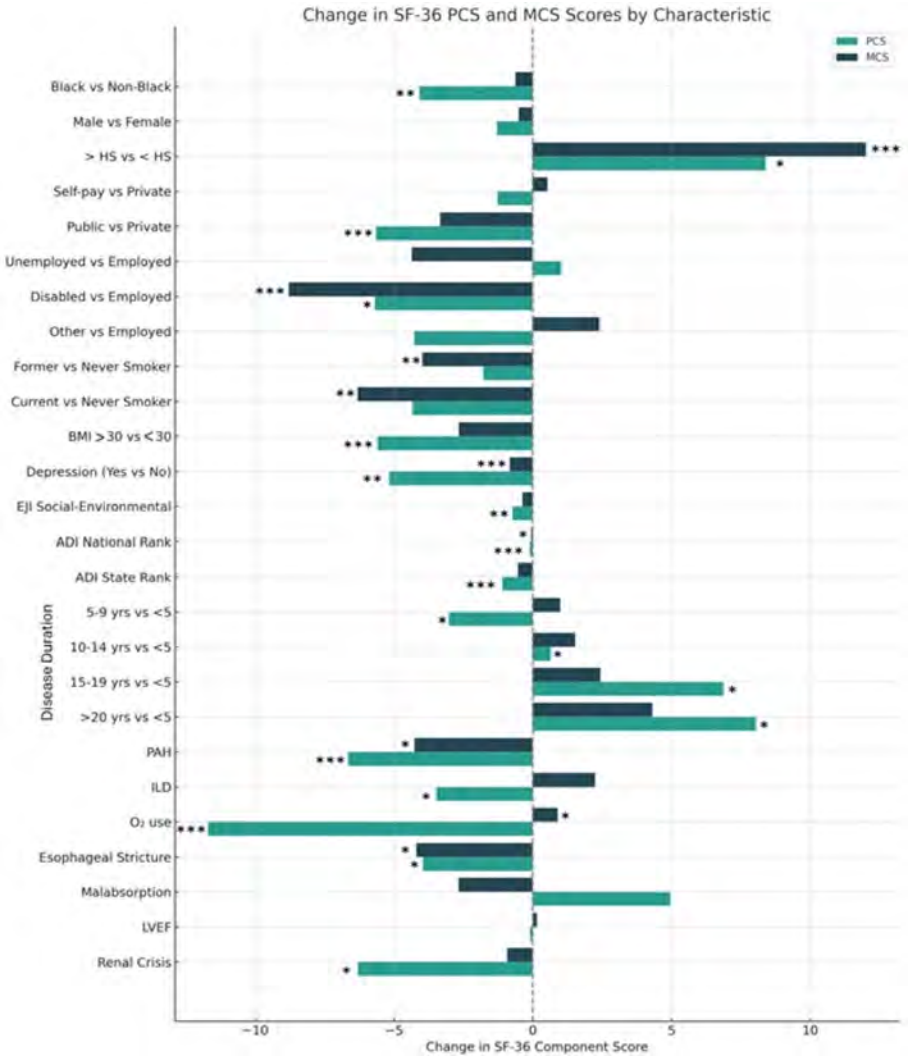


Figure 2. Estimated Changes in SF-36 Physical and Mental Component Scores by Characteristic. This figure illustrates the estimated differences in Physical Component Summary (PCS) and Mental Component Summary (MCS) scores associated with clinical, demographic, and social factors among patients with systemic sclerosis. Bars represent beta coefficients for predicted change in PCS and MCS scores from multivariable linear regression analysis. Asterisks indicate statistical significance (*p<0.05, **p<0.01, ***p<0.001). Abbreviations: PCS = Physical Component Summary; MCS = Mental Component Summary; SSc = Systemic sclerosis; EJI = Environmental Justice Index; ADI = Area Deprivation Index; LVEF = Left ventricular ejection fraction; PAH = Pulmonary arterial hypertension; ILD = Interstitial lung disease.

Disclosure: S. Smith: None; **P. Ramos**: None; **D. Wilson**: None; **D. Kamen**: None; **R. Silver**: None.

Abstract Number: 1080

Are Minority Populations Truly Vaccine Hesitant? A Provider-based Approach to RSV Vaccine Uptake Suggests Otherwise

pavana sakhamuri[1], Stephen Lindsey[2], Cathryn Leggio[3] and Ellen Mire[4], [1]LSUHSC, Dept of Rheumatology, Lafayette, LA, [2]LSUHSC, Dept of Rheumatology, NEW ORLEANS, LA, [3]University Medical center, NEW ORLEANS, LA, [4]LSUHSC, Dept of Medicine, NEW ORLEANS, LA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Respiratory Syncytial Virus (RSV) is a leading cause of hospitalization and mortality in older adults and young children, particularly those with chronic illnesses or immunocompromising conditions (IC). Patients with rheumatic diseases (RD) are at increased risk for severe RSV infection.

Three RSV vaccines (RSVPreF3, RSVPreF1, and mResvia) were approved by the FDA in May 2023 for individuals aged ≥60 with the Advisory Committee on Immunization Practices (ACIP) recommending vaccination for ≥75 and for individuals ≥60 with chronic IC, including RD and those on immunosuppressive medications. In July 2024, RSVPreF1 was approved for ages 18–59 and RSVPreF3 for ages 50–59 at high risk, with ACIP extending recommendations to these groups in April 2025.

Despite these guidelines, surveys indicate that only 16% of eligible individuals receive the RSV vaccine. Uptake is typically lowest in younger adults, minority populations, and those with lower income and educational attainment. Vaccine hesitancy in these groups is frequently cited, yet provider recommendation and patient education are well-documented factors influencing vaccine acceptance.

Table 1

Provider Questionnaire Results – Pre vs. Post Intervention

Category	Response	Pre (n=9)	Pre %	Post (n=9)	Post %
Knowledge of Guidelines	Knew FDA/CDC guidelines	2	22.2%	9	100%
Vaccination Frequency	Rarely vaccinated	7	77.7%	5	55.6%
	Often vaccinated	1	11.1%	1	11.1%
	Almost always vaccinated	1	11.1%	3	33.3%
Comfort Addressing Vaccine Hesitancy	Completely comfortable	2	22.2%	6	66.6%
	Somewhat comfortable	7	77.7%	3	33.3%
	Not at all comfortable	0	0%	0	0%
Barriers to Vaccination	Time restraints	4	44.4%	4	44.4%
	Limited understanding of who to vaccinate	1	11.1%	1	11.1%
	Limited resources (not in clinic)	4	44.4%	4	44.4%
	Patient refusal	3	33.3%	3	33.3%
	Other reasons	6	66.6%	6	66.6%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1

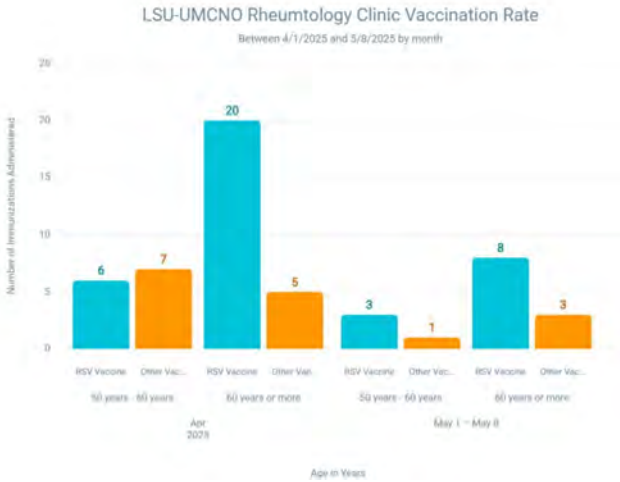
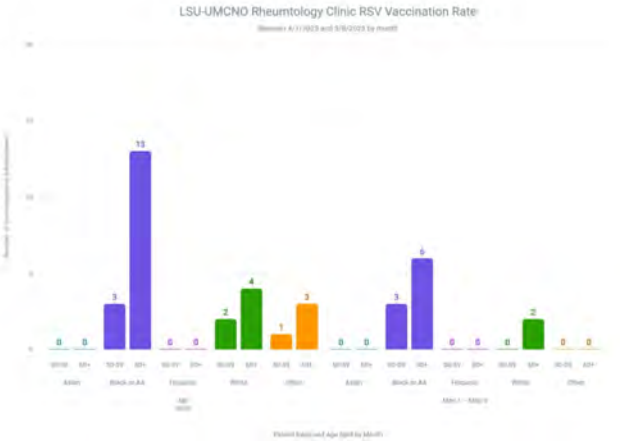


Figure 2



This study assessed RSV vaccination rates among RD patients at our clinic before and after implementing provider-focused education designed to promote in-visit patient education and vaccine administration.

Methods: We queried Epic for patients aged ≥50 with RD or immunosuppressive medication use who received an RSV vaccine at the University Medical Center New Orleans (UMCNO) LSU Safety net Rheumatology Clinic between May 1, 2023, and September 2025. In late March 2025, rheumatology faculty and fellows received an educational presentation on RSV vaccines, including pre- and post-session knowledge assessments. Beginning April 1, 2025, providers were encouraged to spend 1–2 minutes during visits educating eligible patients and recommending same-day vaccination. Key talking points included hospitalization risk, mortality, and risk to grandchildren. If patients required a steroid injection, vaccination was scheduled for a follow-up visit.

Results: Between May 1, 2023, and March 31, 2025, 381 patients aged ≥50 received vaccines at our clinic. Only one patient was vaccinated for RSV in September 2024. Post-education surveys revealed substantial knowledge improvement among providers (Table 1). UMCNO is a safety net system that cares for a majority of minority and disadvantaged people.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

From April 1 to May 8, 2025, 37 patients were vaccinated for RSV—9 aged 50–59 and 28 aged ≥60 and were of a minority population (Figure 2).

Conclusion: Approximately 70% of patients at the LSU-UMCNO Rheumatology Clinic identify as a minority groups. Following provider education and proactive in-clinic promotion, RSV vaccination rates increased markedly in a short timeframe. These results suggest that vaccine hesitancy in minority populations may be driven more by "Provider Hesitancy"—such as limited time, competing priorities, or lack of awareness—than by patient reluctance. Focused provider engagement and in-clinic vaccine availability appear to be effective strategies to improve uptake in high-risk, diverse populations.

Disclosure: p. sakhamuri: None; **S. Lindsey**: None; **C. Leggio**: None; **E. Mire**: None.

Abstract Number: 1081

Insurance, Gender, and COVID-19's Effects on Health Inequity in Rheumatoid Arthritis: A 12-Year Long Population Assessment

Ramsha Riaz[1], Lifang Zhang[2], Andrea Berger[2], Hema Srinivasan[2], Lisa Schroeder[3] and Jonida Cote[4], [1]Geisinger Medical Center, Danville, PA, [2]Geisinger Health System, Danville, PA, [3]Geisinger, Danville, PA, [4]Geisinger Health System, Wilkes-Barre, PA

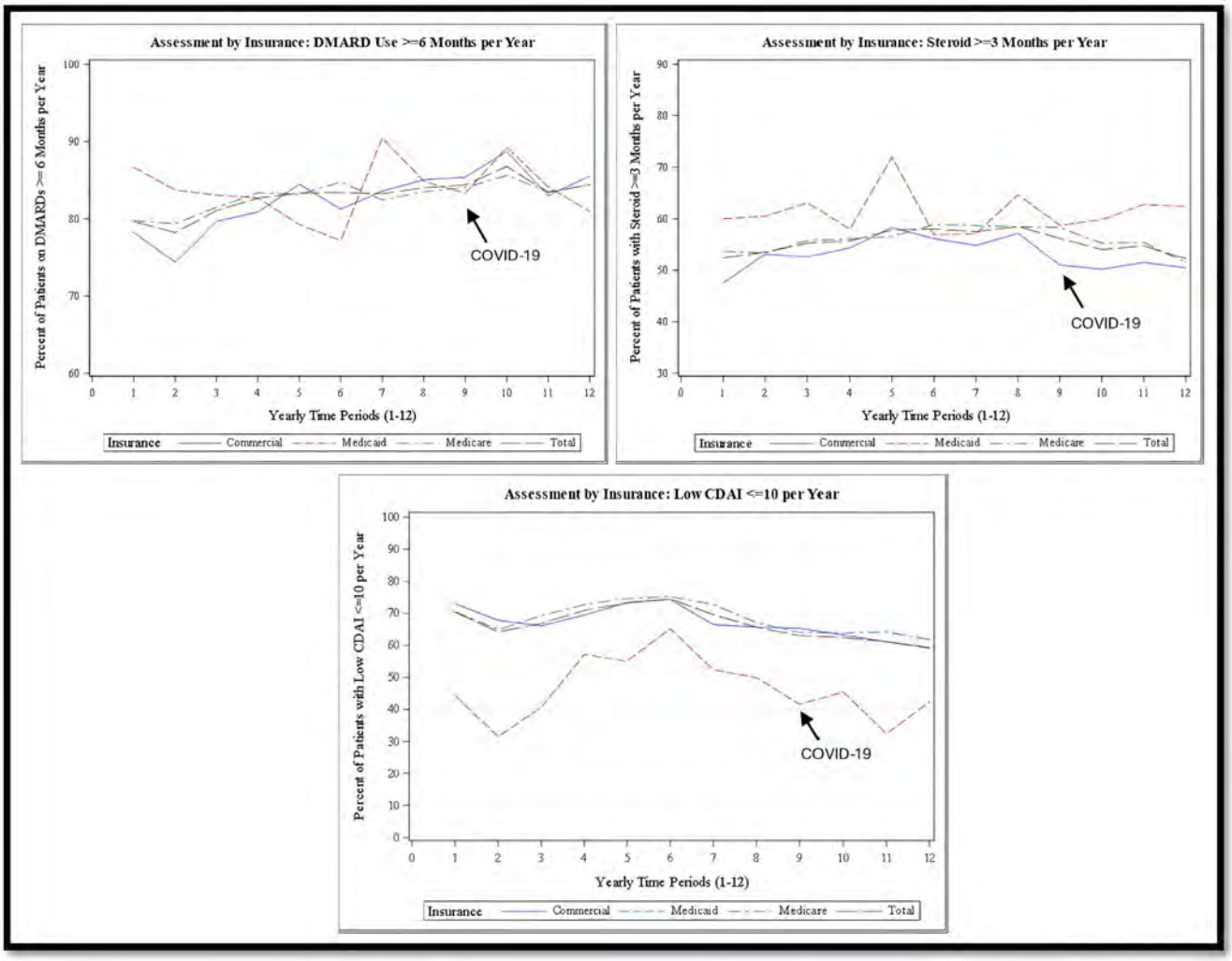


Figure 1. The Treatment Rates (DMARD ≥6 months, Steroids ≥3 months) and Disease Activity (Low CDAI ≤10) Assessment by Insurance Type

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Recognizing health care disparities in Rheumatoid Arthritis is crucial to improving outcomes. This study analyzes factors contributing to RA care inequities.

Methods: We examined RA disease activity, treatment, and vaccine rates over 12 yearly periods, 2012-2023. Eligibility criteria included RA patients ≥18 years. Low Clinical Disease Activity Index (CDAI≤10), steroid use ≥3 months, DMARD use ≥6 months, and vaccine (pneumococcal, shingles, flu) rates were compared based on insurance types and gender. Generalized estimating equations regression models were used to analyze binomial/multinomial outcomes.

Results: Population included 24,469 patients, median age 63, white 96%, women 74%, RF+ 74%, anti-cyclic citrullinated peptide (CCP+) 28%, Medicare 49%, Medicaid 5%, and Commercial insurance 22%. Insurance type didn't affect DMARD use: Commercial versus (vs) Medicare and Medicaid (Odds Ratio (OR) 0.98, 0.97, p=0.7936, p=0.8242), Medicaid vs Medicare (OR 1.01, p=0.9426) (Figure 1). More women used DMARDs than men (OR 1.22, p=0.0074) (Figure 2). Steroid use was higher with Medicaid than Medicare and Commercial patients (OR 1.25, 1.41, p=0.0128, p=0.0003) respectively (Figure 1),

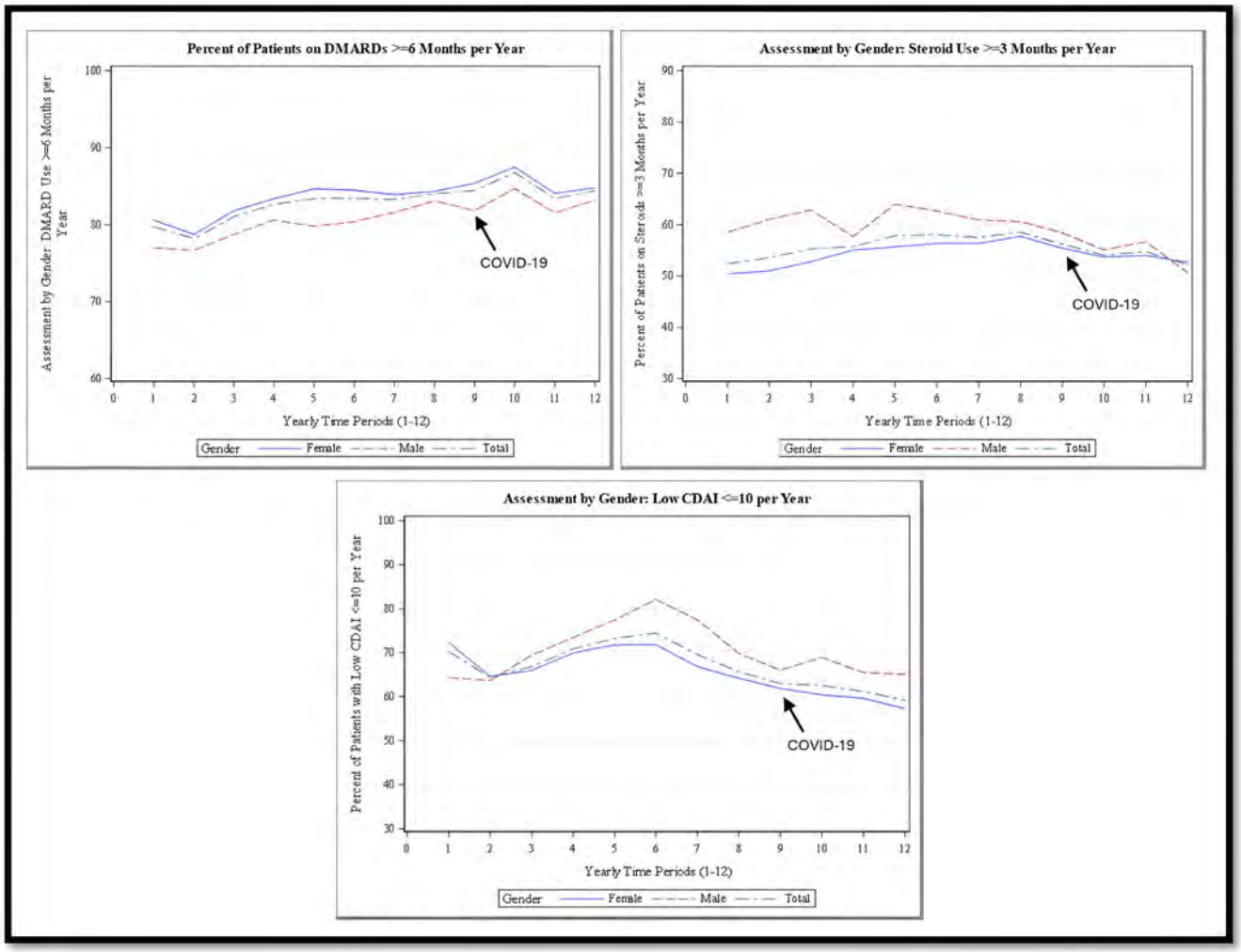


Figure 2. The Treatment Rates (DMARD ≥6 months, Prednisone ≥3 months) and Low Disease Activity (CDAI ≤10) Assessment by Gender

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

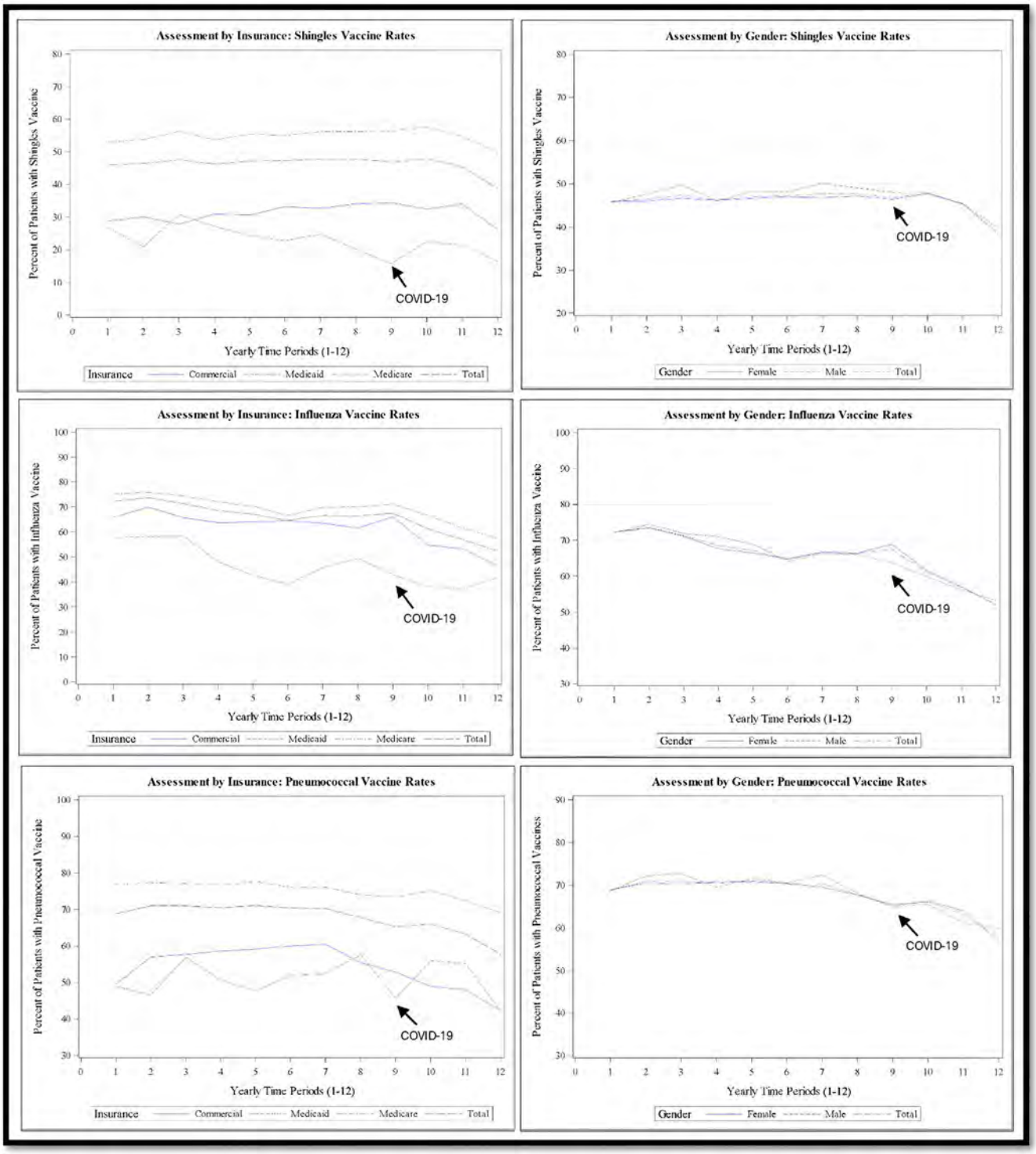


Figure 3. The Vaccine Rates (Shingles, Flu, and Pneumococcal) Assessment by Insurance types and Gender

and higher in men than women until period 9 (p=0.0002) (Figure 2). Disease control was better with Medicare and Commercial than Medicaid patients (OR 2.39, 2.22, p=0.001 respectively) but worse over time for all insurances (70.34% to 59.14%, p< 0.0001) (Figure 1). Men started with lower rates of CDAI ≤10 than women in period 1 (62% vs 71%) but achieved greater low disease activity than women in periods 2-12 (68% vs 59% p=0.046) (Figure 2). Disease activity worsened post COVID-19 pandemic for both insurance and gender in period 9 (2020) to 12 (2023) (Figures 1,2). Vaccine rates were higher with Medicare than Commercial or Medicaid (Singles OR 2.51, 3.28 p< 0.0001), (Pneumococcal OR 2.31, 2.33 p=0.0001),

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(Flu OR 1.41, 2.59 p=0.0001) (Figure 3). Pneumococcal and flu vaccine rates declined over time for all insurances (69% to 58%, 72% to 52%, p=0.0185, p=0.0001 respectively) (Figure 3). Gender didn't influence vaccine rates, but they all declined with time (p< 0.05) (Figure 3). The decline in vaccination trend was particularly worsened post COVID-19 (period 9-12) independent of insurance or gender (Figure 3). Comparing to national data, our vaccine rates were similar for flu (53-72% vs 61%) (Coca, Arth. Rheumatol.2018;70(9)) but superior for shingles (39-46% vs 19%) (Calabrese, Arth. Care Res.2020;72 (3)), and pneumococcal (58-69% vs 43%) (Alvarez, Vaccine.2024;42(3)).

Conclusion: Insurance type, gender, and COVID-19 played a substantial role in RA care delivery. Higher vaccine rates were achieved with Medicare, however, an overall declining trend, worse post COVID-19, left a considerable gap in our RA patients. Men (period 1-9) and Medicaid patients used more steroids. Men used less DMARDs, while percent at low disease activity worsened for all patients over time. This may be due to a higher capture of elevated CDAI measures (requires an in person visit) during COVID-19 (when the sickest patients were seen in person). Recognizing the drivers of RA inequities provides us with the opportunity to use a targeted approach to improving care.

Disclosure: R. Riaz: None; **L. Zhang**: None; **A. Berger**: None; **H. Srinivasan**: None; **L. Schroeder**: None; **J. Cote**: None.

Abstract Number: 1082

Lupus Patient Navigator Program for Improving Care Adherence for Minority Patients

Rashi Vora[1], Samiha Karim[2], Dulaney Wilson[3], Jasvinder Singh[4], Gary Gilkeson[1], Jim Oates[1] and Diane Kamen[5], [1]Medical University of South Carolina, Charleston, SC, [2]Emory University, Atlanta, GA, [3]Medical University of South Carolina, Charleston, [4]Baylor College of Medicine, Houston, TX, [5]Medical University of South Carolina, Johns Island, SC

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Minority patients with systemic lupus erythematosus (SLE) experience a higher disease burden and encounter more barriers to care than White patients, resulting in worse outcomes and increased healthcare utilization. A Lupus Patient Navigator Program (LPNP) has been associated with improved SLE disease activity and quality-of-life scores in minority populations. This study aims to evaluate the impact of an LPNP on adherence to medication and scheduled visits.

Methods: Self-identified minority patients with SLE aged >18 years were recruited from an academic center. Inclusion criteria included being prescribed ≥1 immunosuppressant and meeting at least one of the following: 1) ≥1 missed clinic or laboratory visit in the past 6 months, 2) nonadherence to medical therapy, or 3) newly diagnosed SLE. The LPNP was modeled after the CDC STEPS to CARE toolkit. Patients engaged with the patient navigator every 3 months over a 12-month period via phone or in-person, with real-time resource support. Patient-reported outcomes included a medication diary, with adherence defined as the ratio of pills taken to pills prescribed over the week prior to each navigator encounter. Rheumatology visit adherence (in-person or telehealth) was tracked through chart review.

Results: Twenty-five patients (96% female; 92% Black; 8% Hispanic or Latino; mean age 32 years) completed the 12-month program. Among these, 92% were high school graduates, 88% had health insurance, and 48% were unemployed or disabled (**Table 1**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline LPNP Participant Characteristics

Characteristics	LPNP Participants (N=25)
Age at enrollment (mean years ± SD)	32.2 ± 10.0
SLE age of diagnosis (mean years ± SD)	22.8 ± 10.4
Female (%)	24 (96%)
Black (%)	23 (92%)
Hispanic (%)	3 (8%)
High School Graduate (%)	23 (96%)
Commercial Insurance (%)	22 (88%)
Unemployed or Disabled (%)	12 (48%)
Taking HCQ (%)	24 (96%)
Taking glucocorticoids (%)	13 (52%)
Number of Immunosuppressants (mean ± SD)	1.7 ± 0.6

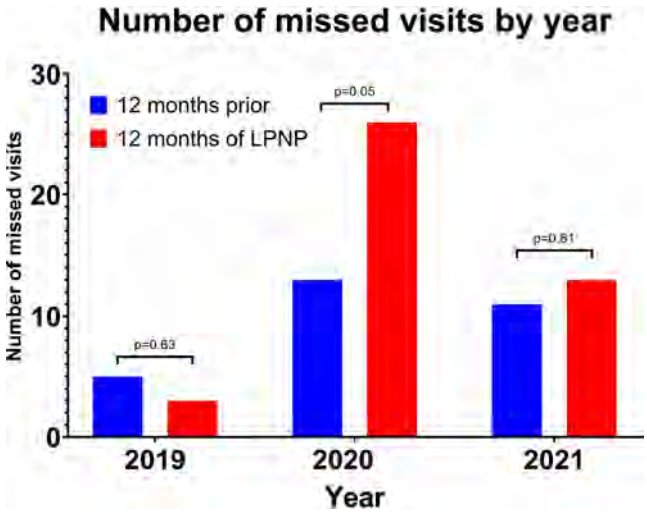


Figure 1. Number of Missed Rheumatology Visits by Year

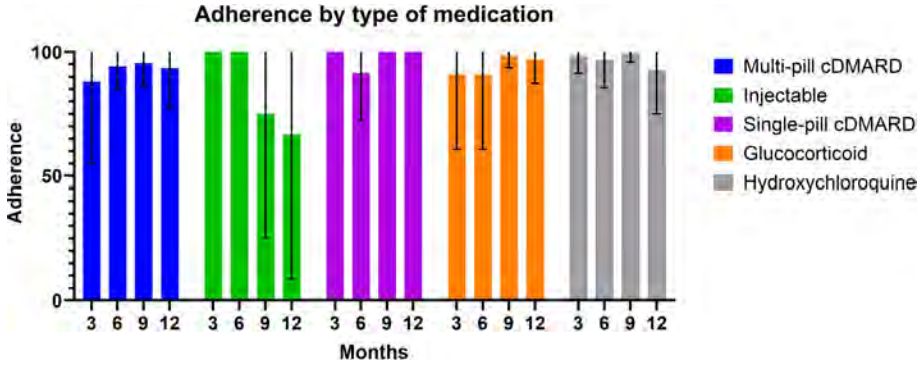


Figure 2. Adherence by Type of Medication Over 12 Months of LPNP Participation. cDMARD = conventional DMARD

There was no statistically significant difference in visit adherence when comparing the year prior to LPNP enrollment to the LPNP period (**Figure 1**), with the exception of 2020 when missed visits increased (2019 p=0.63; 2020 p=0.05; 2021 p=0.81).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

During the study period, 52% of participants reported glucocorticoid use and 96% reported hydroxychloroquine (HCQ) use, with an average of 1.7 immunosuppressive medications per patient (**Table 1**).

Medication adherence over the 12-month period (**Figure 2**) appeared to vary by medication type: adherence to injectable therapies declined, while adherence to oral agents—including DMARDs, hydroxychloroquine, and glucocorticoids—remained relatively stable.

Conclusion: The COVID-19 pandemic led to a peak in missed rheumatology visits among the high-risk patients with SLE participating in the LPNP. There appears to be mitigation of barriers with the LPNP in 2019, however missed visits increased in 2020 and 2021 despite the LPNP intervention. This may reflect a higher number of scheduled visits overall due to more frequent healthcare touchpoints introduced by the program. Tailoring navigator interventions to address the specific barriers associated with different treatment modalities—particularly injectable therapies—may enhance effectiveness. Further research is warranted to optimize navigator-based strategies and assess long-term outcomes in the context of evolving healthcare delivery challenges.

Disclosure: R. Vora: None; **S. Karim**: None; **D. Wilson**: None; **J. Singh**: American College of Rheumatology, 2, Atai life sciences, Kintara therapeutics, Intelligent Biosolutions, Acumen pharmaceutical, TPT Global Tech, Vaxart pharmaceuticals, Atyu biopharma, 11, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care options, Putnam associates, Focus forward, Navigant consu, 2, GeoVax Labs, Adaptimmune Therapeutics, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp., Aebona Pharma, 11, Intuitive Surgical Inc./Philips Electronics North America, 12, food and beverage payments, ROMTech, Atheneum, Clearview healthcare partners, Yale, Hulio, Horizon Pharmaceuticals/DINORA, ANI/Exeltis, USA Inc., Frictionless Solutions, Schipher, 2, Spherix, MedIQ, Jupiter Life Science, UBM LLC, Trio Health, Medscape, WebMD, and Practice Point communications; the National Institutes of Health, 2, Zimmer Biomet Holdings, 5; **G. Gilkeson**: None; **J. Oates**: PTC Therapeutics, 12, PTC923 for this study provided by PTC Therapeutics; **D. Kamen**: None.

Abstract Number: 1083

How Do Social Determinants of Health Differ Across Age and Disability Groups Among Adult Medicare Advantage Enrollees with Systemic Lupus Erythematosus?

Alexjandro Daviano[1], Vijay R. Nadipelli[2], Yihua Xu[1], Karen Worley[2], Shireen Haq[1], Josephine Ohioma[3], Jeffrey J. Ellis[2], Brandon T. Suehs[1] and **S. Sam Lim**[4], [1]Humana Healthcare Research, Inc., Louisville, KY, [2]GSK, Global Real-World Evidence & Health Outcomes Research, Collegeville, PA, [3]GSK, US Medical Affairs, Philadelphia, PA, [4]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Management of patients with SLE should consider social determinants of health (SDoH) and their impact on access, treatment, and patient outcomes; however, such a holistic approach is not routinely studied or adopted in clinical practice.[1] To close this knowledge gap, we assessed patient characteristics including SDoH, disease burden and clinical outcomes, and healthcare resource use (HCRU) among adult Medicare Advantage (MA) plan enrollees with SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This retrospective analysis (GSK Study 222168) used administrative claims data supplemented with patient- and community-level measures of SDoH. Humana MA enrollees 18–89 years of age (YOA) with SLE (with or without LN) and enrolled during the 2023 calendar year were included. Diagnosis of SLE was required on ≥1 medical claim during 2023 and ≥1 diagnosis prior to 2023. Measures of disease burden, medication use, and HCRU were based on claims data. Measures of social risk (e.g. low-income subsidy [LIS], dual eligibility [DE], disability) were based on enrollment file data. Community-level measures of social risk (e.g. public assistance, educational attainment) were based on publicly available data sources. Analyses were descriptive.

Results: Among 20,188 patients with SLE identified (90.3% female, 30.7% of Black race), 76.2% had a Health Equity Index and 46.3% had a DE/LIS status. Approximately half of MA enrollees were < 65 YOA (45.5%). Compared with enrollees ≥65

Table 1. Patient SDoH characteristics stratified by age and qualification for MA on the basis of disability. *Enrollees ≥65 YOA who originally qualified for MA based on disability; †a higher ADI score is indicative of high levels of area deprivation and lower score is indicative of area affluence; ‡approximately 91% of patients were matched to the AHRQ SDoH database at census tract level, and the rest were matched at zip code level. There were 72 observations with missing value on median household income, 91 on percentage of families with children that are single-parent families. The rest of the AHRQ measures had 0–5 missing values; §percentage below national median; ||percentage above national median. ADI, area deprivation index; AHRQ, Agency for Healthcare Research and Quality; CMS, Centers for Medicare and Medicaid Services; HEI, Health Equity Index; SD, standard deviation.

	<65 YOA (N=9180)	≥65 YOA (N=11,008)	≥65 YOA disability qualifiers* (n=4646)
Patient-level measures, n (%)			
DE	5012 (54.6)	2741 (24.9)	1452 (31.3)
LIS	5849 (63.7)	3445 (31.3)	1873 (40.3)
DE or LIS	5886 (64.1)	3461 (31.4)	1881 (40.5)
Disability	9023 (98.3)	4646 (42.2)	4646 (100.0)
CMS HEI (LIS, or DE, or disability)	9157 (99.7)	6226 (56.6)	4646 (100.0)
Special needs plan status	2069 (22.5)	1137 (10.3)	576 (12.4)
Chronic conditions special needs plan status	38 (0.4)	69 (0.6)	38 (0.8)
Dual special needs plan status	2031 (22.1)	1068 (9.7)	538 (11.6)
Community-level measures			
ADI score†, mean (SD)	65.5 (23.1)	60.4 (24.1)	64.6 (23.2)
ADI category, n (%)			
0–25	491 (5.3)	940 (8.5)	269 (5.8)
26–50	1734 (18.9)	2527 (23.0)	904 (19.5)
51–75	2802 (30.5)	3388 (30.8)	1439 (31.0)
76–100	3228 (35.2)	3146 (28.6)	1582 (34.1)
Missing	925 (10.1)	1007 (9.1)	452 (9.7)
AHRQ SDoH measures‡, n (%)			
Median household income§	6268 (68.6)	6934 (63.2)	3203 (69.2)
Gini Index of Income Inequality‖	4676 (51.0)	5579 (50.7)	2491 (53.6)
Households with public assistance or food stamps‖	6024 (65.6)	6559 (59.6)	3070 (66.1)
Civilian labor force that is unemployed‖	5391 (58.7)	6037 (54.9)	2719 (58.5)
Families with children that are single-parent families‖	5815 (63.5)	6359 (58.1)	2899 (62.7)
Population with less than high school education‖	5963 (65.0)	6593 (59.9)	3030 (65.2)
Limited English-speaking households‖	3998 (43.6)	5002 (45.4)	2018 (43.4)
Housing units with no vehicle‖	4848 (52.8)	5467 (49.7)	2485 (53.5)
Housing units lacking complete plumbing facilities‖	5594 (60.9)	6109 (55.5)	2823 (60.8)
Households with no internet‖	5932 (64.6)	6554 (59.5)	3027 (65.2)
Housing units with more than one occupant per room‖	4724 (51.5)	5393 (49.0)	2338 (50.3)
Households with smartphone§	5466 (59.6)	6316 (57.4)	2866 (61.7)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Patient disease and treatment characteristics, and HCRU, stratified by age and qualification for MA on the basis of disability. *Enrollees ≥65 YOA who originally qualified for MA based on disability; †PCP included family medicine, internal medicine, and general practice. ED, emergency department; PCP, primary care provider.

	<65 YOA (N=9180)	≥65 YOA (N=11,008)	≥65 YOA disability qualifiers* (n=4646)
SLE severity, n (%)			
Mild	1577 (17.2)	2381 (21.6)	858 (18.5)
Moderate	4673 (50.9)	5335 (48.5)	2230 (48.0)
Severe	2930 (31.9)	3292 (29.9)	1558 (33.5)
Deyo-Charlson Comorbidity Index, mean (SD)	2.6 (2.1)	3.0 (2.3)	3.2 (2.3)
SLE medication, n (%)			
Any medication	8250 (89.9)	9091 (82.6)	3942 (84.8)
Corticosteroids	6385 (69.6)	6324 (57.5)	2916 (62.8)
Immunosuppressants	2799 (30.5)	2147 (19.5)	980 (21.1)
NSAIDs	4460 (48.6)	3610 (32.8)	1703 (36.7)
Antimalarials	4610 (50.2)	4977 (45.2)	1999 (43.0)
Biologic use (excluding rituximab)	605 (6.6)	165 (1.5)	89 (1.9)
Rituximab	158 (1.7)	83 (0.8)	39 (0.8)
SLE-related HCRU, n (%)			
Patients with an inpatient stay	1004 (10.9)	839 (7.6)	421 (9.1)
Patients with an ED visit	1938 (21.1)	1229 (11.2)	637 (13.7)
Patients with a rheumatologist visit	3348 (36.5)	3336 (30.3)	1345 (28.9)
Patients with a nephrologist visit	659 (7.2)	551 (5.0)	255 (5.5)
Patients with a PCP† visit	4631 (50.4)	5586 (50.7)	2294 (49.4)

YOA, < 65-year-olds had elevated social risk factors, with nearly all (99.7%) having disability and DE/LIS status (**Table 1**). MA enrollees < 65 YOA also tended to reside in communities with greater social risk (lower income and educational attainment, higher unemployment, greater use of public assistance; **Table 1**). Moderate/severe SLE was more common among enrollees < 65 YOA (82.8% vs 78.4%), who also had higher treatment rates with SLE medications compared with enrollees ≥65 YOA (**Table 2**).

Disability as the original reason for MA qualification was common overall (67.7%), including 98.3% of < 65 YOA and 42.2% of ≥65 YOA enrollees (**Table 1**). Among enrollees ≥65 YOA who originally qualified for MA based on disability, social risk factors, disease severity, SLE medication use, and HCRU were generally greater than for the enrollees ≥65 YOA overall (**Table 1** and **2**).

Enrollees < 65 YOA were more likely to visit a rheumatologist (36.5% vs 30.3% of those ≥65 YOA) or a nephrologist (7.2% vs 5.0% of those ≥65 YOA) for an SLE-related visit (**Table 2**). Among the enrollees < 65 YOA who visited a rheumatologist or nephrologist, 46.1%, 70.7%, and 14.2% received immunosuppressant, antimalarial, and biologic treatment, respectively.

Conclusion: We observed substantial social risk factors among MA enrollees with SLE, with disability being the dominant reason for MA qualification. SLE severity, treatment patterns, and HCRU varied between ≥65 and < 65-year-olds. Interventions to address the unmet needs should consider the burden of SDoH and diversity of the MA SLE population. Further research is needed to identify and evaluate specific health-related unmet needs of this population, potential interventions, and impact on patient outcomes.

Funding: GSK

Reference

[1]Lim SS et al. *Arthritis Care Res* 2025 (in press)

Disclosure: A. Daviano: Humana Healthcare Research, 3; **V. Nadipelli**: GSK, 12,, 3; **Y. Xu**: Humana Healthcare Research, 12,, 3; **K. Worley**: GSK, 12,, 3; **S. Haq**: Humana Healthcare Research, 3; **J. Ohioma**: GSK, 12,, 3; **J. Ellis**: GSK, 12,, 3, 8; **B. Suehs**: Humana Healthcare Research, 12,, 3; **S. Lim**: Accordant, 2, AstraZeneca, 2, Biogen, 5, BMS, 5, Genentech, 2, Gilead, 5, GSK, 2, Novartis, 5, UCB, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1084

Access to Rheumatology Care in Patients with New Diagnosis of Polymyalgia Rheumatica: Analysis from a National Inception Cohort

Sebastian E Sattui[1], Orysya Soroka[2], Manuel Carpio Tumba[3], Emily Holladay[4], Fenglong Xie[5], Sarah Mackie[6], Jeffrey Curtis[7], Robyn Domsic[3] and Iris Navarro-Millan[8], [1]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, [2]Weill Cornell Medicine, New York, [3]University of Pittsburgh, Pittsburgh, PA, [4]University of Alabama at Birmingham, Edmond, OK, [5]The University of Alabama at Birmingham, Birmingham, AL, [6]University of Leeds, Leeds, United Kingdom, [7]University of Alabama at Birmingham, Birmingham, AL, [8]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1. Characteristics of patients with new onset Polymyalgia Rheumatica with and without a rheumatology visit during the first-year of follow-up

Characteristics	Cohort	No visit to rheumatology provider	At least one visit to a rheumatology provider
N	20,536	8,571	11,965
Age, mean (SD)	77.4 (7.3)	78.6 (7.8)	76.4 (6.9)
Sex, female	12,653 (61.6)	5,299 (61.8)	7,354 (61.5)
Race, white	18,783 (91.5)	7,870 (91.2)	10,913 (91.2)
Dual eligibility	2,019 (9.8)	1,054 (12.3)	965 (8.1)
US region			
Midwest	4,829 (23.5)	2,335 (27.2)	2,494 (20.8)
Northeast	5,673 (27.6)	2,041 (23.8)	3,632 (30.4)
South	6,517 (31.7)	2,652 (30.9)	3,865 (32.3)
West	3,510 (17.1)	1,539 (18.0)	1,971 (16.5)
other	7 (<1)	4 (<1)	3 (<1)
Social vulnerability index (SVI)*			
Q1 (least vulnerable)	5,077 (24.7)	2,173 (25.4)	2,904 (24.3)
Q2	6,177 (30.1)	2,642 (30.9)	3,535 (29.6)
Q3	6,170 (30.1)	2,451 (28.6)	3,719 (31.1)
Q4 (most vulnerable)	3,090 (15.1)	1,294 (15.1)	1,796 (15.0)
Rural urban commuting area (RUCA)			
Isolated	1,039 (5.1)	605 (7.1)	434 (3.6)
Small rural	1,145 (5.6)	658 (7.7)	487 (4.1)
Large rural	2,215 (10.8)	1,191 (13.9)	1,024 (8.6)
Urban	16,134 (78.6)	6,117 (71.4)	10,017 (83.7)
Rheumatologists per area **			
0	4,978 (24.2)	2,737 (31.9)	2,241 (18.7)
1-<10	1,160 (5.6)	463 (5.4)	697 (5.8)
10-<60	13,077 (63.7)	4,960 (57.9)	8,117 (67.8)
60+	13,21 (6.4)	411 (4.8)	910 (7.6)
Frailty, per CFI			
Not frail	6507 (31.7)	2536 (29.6%)	3971 (33.2%)
Pre-frail	11698 (57.0)	4771 (55.7%)	6927 (57.9%)
Frail^	2,331 (11.3)	1,284 (14.8%)	1,067 (8.9)
Charlson-Deyo score			
0	5,229 (25.5)	1,984 (23.1)	3,245 (27.1)
1-2	7,600 (37.0)	3,056 (35.7)	4,544 (38.0)
3-4	4,374 (21.3)	1,931 (22.5)	2,443 (20.4)
≥5	3,333 (16.2)	1,600 (18.7)	1,733 (14.5)
Initial GC dose, mg/day			
7.5-<10	906 (4.4)	350 (4.1)	556 (4.6)
10-<15	6,879 (33.5)	2,798 (32.6)	4,081 (34.1)
15-<20	6,074 (29.6)	2,230 (26.0)	3,844 (32.1)
20-30	6,677 (32.5)	3,193 (37.3)	3,484 (29.1)
Primary care visits during baseline year, mean (SD)	6.8 (8.2)	7.4 (9.2)	6.3 (7.4)

All data presented as n(%), unless specified otherwise.
*At county level. Higher SVI quartile represents higher vulnerability. ** Adult rheumatology providers per 1,000,000 adult population at county level. ^ Includes mild, moderate and severe frailty (CFI ≥0.2).
CFI = claims frailty index, GC = glucocorticoid

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with polymyalgia rheumatica (PMR) are commonly diagnosed and cared for by non-rheumatology providers (i.e., primary care). Lack of access to specialty care can impact diagnosis and treatment. The aim of this study was to describe the clinical and sociodemographic factors associated with receiving specialty care in patients with a new diagnosis of PMR.

Methods: An inception cohort of patients with a new diagnosis of PMR was created using Medicare fee-for-service claims data from 2016-2022. Patients with PMR were included if they were age ≥50 years and had: 1) ≥1 inpatient or ≥2 outpatient claims with ICD-10-CM M35.3 ≥30 days and < 365 apart, 2) a prescription for glucocorticoids (GC) 7.5–30 mg/day filled within 30 days from 1st inpatient diagnosis, or filled between 1st outpatient diagnosis to 30 days after 2nd diagnosis, with a cumulative GC use of ≥200 mg over ≥120 days of first prescription period, 3) continuous enrollment ≥1 year prior to index

Table 2. Factors associated with access to any rheumatology care during first-year of follow-up

Factors	RR (95% CI)
Age (by 5 year)	0.92 (0.91-0.93)
Dual eligibility (ref. no)	0.80 (0.77-0.84)
US region	
Midwest	0.81 (0.78-0.83)
Northeast	REF
South	0.93 (0.90-0.95)
West	0.88 (0.85-0.91)
Social vulnerability index (SVI)*	
Q1	REF
Q2	1.00 (0.97-1.03)
Q3	1.05 (1.02-1.09)
Q4	1.02 (0.98-1.06)
Rural urban commuting area (RUCA)	
Isolated	0.67 (0.63-0.72)
Small rural	0.69 (0.64-0.73)
Large rural	0.74 (0.71-0.78)
Urban	REF
Rheumatologists per area**	
0	REF
1-<10	1.33 (1.26-1.41)
10-<60	1.38 (1.33-1.43)
60+	1.53 (1.46-1.60)
Frailty	
No frailty	REF
Pre-frail	0.97 (0.95-0.99)
Frail^	0.75 (0.71-0.79)
Charlson-Deyo score	
0	REF
1-2	0.96 (0.94-0.99)
3-4	0.90 (0.87-0.93)
≥5	0.84 (0.81-0.87)
Initial GC dose category, mg/day	
7.5-<10	0.97 (0.92-1.02)
10-<15	0.94 (0.91-0.96)
15-<20	REF
20-30	0.82 (0.80-0.85)
Primary care visits at baseline (per 1 unit increase)	0.99 (0.99-0.99)

*At county level. Higher SVI quartile represents higher vulnerability. ** Adult rheumatology providers per 1,000,000 adult population at county level. ^ Includes mild, moderate and severe frailty.
GC = glucocorticoid

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Access to rheumatology in patients with PMR at 2-year follow-up (n = 16,098)*	
Rheumatology visits	N (%)
No rheumatology visits during first year	6,608 (41.0)
≥1 rheumatology visit during 2nd year follow-up	469 (7.1)
≥ 1 rheumatology visit during 1st year follow-up	9,490 (59.0)
≥1 rheumatology visit during 2nd year follow-up	6,924 (66%)
Continuous rheumatology care**	4,792 (50.5%)
* All patients with continuous enrollment in Medicare Part A, B, and D during two-year follow-up after diagnosis.	
** Continuous care defined as ≥2 rheumatology visits per year	

date (first GC prescription) with no evidence for PMR or giant cell arteritis (GCA), 4) ≥1 year of continuous enrollment after index date. Exclusion criteria applied at baseline using all available prior data included GCA or any other rheumatologic conditions, except for seronegative rheumatoid arthritis.

Sociodemographic and comorbidity data was collected at baseline. Other covariates of interest included: social vulnerability index, rural-urban commuting area, rheumatologist density per county, initial GC dose, and frailty, calculated using a validated claims-based frailty index.

The outcome of interest was care from a rheumatology provider (≥1 visit) during the first year after PMR diagnosis. Univariate Poisson regression was performed to assess factors associated with access to rheumatology. In patients with two-year follow-up, we assessed continued rheumatology visits, including ongoing rheumatology care, defined as ≥2 rheumatology visits per year during each of the 2 years after PMR diagnosis.

Results: A total of 20,536 patients with new-onset PMR were included (Table 1). During the first year of follow-up, 11,965 (58.3%) patients received care from a rheumatology provider. Of these, 3,907 (32.7%) were seen by a rheumatologist after initiation of GC treatment (i.e., inclusion in cohort), with median (IQR) time to first rheumatology visit of 57 (25, 135) days.

In univariate analysis, older age, non-northeast US region, non-urban areas, lower rheumatologist density, frailty, and higher comorbidity burden were associated with a lower likelihood of seeing rheumatology during the first year (Table 2). Patients started on GC doses either lower or higher than recommended by current guidelines were also less likely to see rheumatology during the first year. Of 16,098 patients with continuous two-year follow-up, only half who saw rheumatology during the first year remained under continuous rheumatology care (Table 3).

Conclusion: In the U.S., over half of patients newly diagnosed with PMR see a rheumatologist within the first year. However, patients at higher risk for GC toxicity (older, frail, high multimorbidity) are less likely to receive rheumatology care, highlighting the need to improve PMR referral practices.

Disclosure: S. Sattui: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2; **O. Soroka**: None; **M. Carpio Tumba**: None; **E. Holladay**: None; **F. Xie**: None; **S. Mackie**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, Fresenius Kabi, 6, Novartis, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, UCB, 6, Vifor, 6; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **R. Domsic**: None; **I. Navarro-Millan**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1085

Bridging the Gap: The Use of Patient Joint Self-Assessment in RA Treatment Response Evaluation

Sri Lakshmi Sathiyaseelan[1], Sandeep Kansurkar[2], Kavita Krishna[3] and Varsha Bhatt[4], [1]Bharati Vidyapeeth medical college and hospital, chennai, Tamil Nadu, India, [2]Bharti vidyapeeth (DTU) Medical College, Pune, Pune, Maharashtra, India, [3]Bharati Vidyapeeth University Medical College and Hospital, Pune, Maharashtra, India, [4]Department of Clinical Immunology and Rheumatology, Bharati Vidyapeeth (Deemed To Be) University Medical College,Pune, Pune, Maharashtra, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis presents with multiple joint pains and it is traditionally, examined by the clinicians. The utility of patient self-joint counts has become an increasingly important area to explore, with remote disease monitoring and telehealth taking on a larger role across rheumatology practices post the global pandemic and increasing scarcity of Rheumatologist in comparison to the increasing case load. This study was inspired from the video released by Centre for Epidemiology and Arthritis on self-assessment of joints in patients with RA to replace clinical examination.

Methods: Sixty-two consecutive patients of RA over the age of 18 who attended our out-patient department between October 2022 and December 2022 were included in this study. We prepared an instructional manual with pictorial representation in English and local language to explain the joint examination to patients. If the patient had difficulty in reading, the attendant was allowed to explain to the patient. A pilot testing was done on ten patients for clarity of understanding, and it was well accepted. Same manual was applied to study participants to maintain uniformity. They marked the tender and swollen joints and the clinical was blinded to their findings. They also scored the pain, difficulty of the questionnaire and patient global assessment score. The patient was then evaluated by an experienced Rheumatologist well versed in RA joint examination.

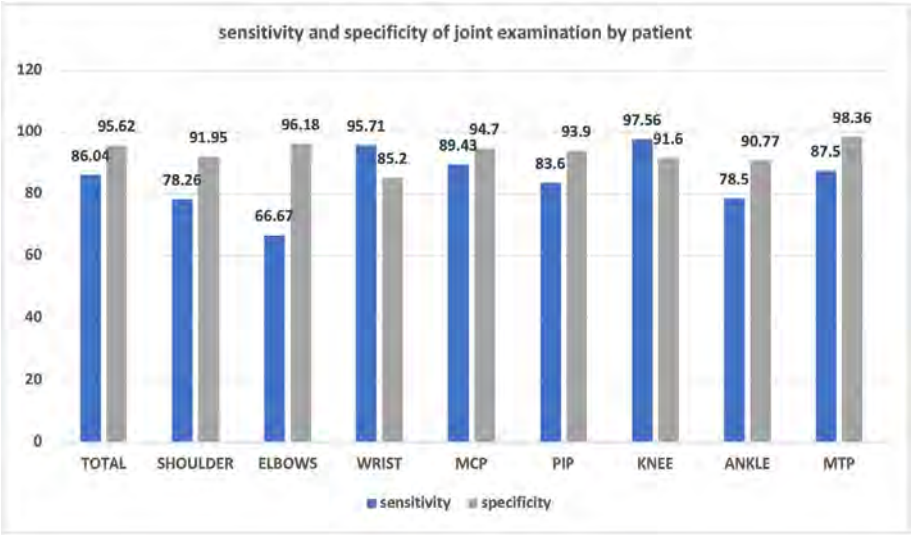


Figure 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

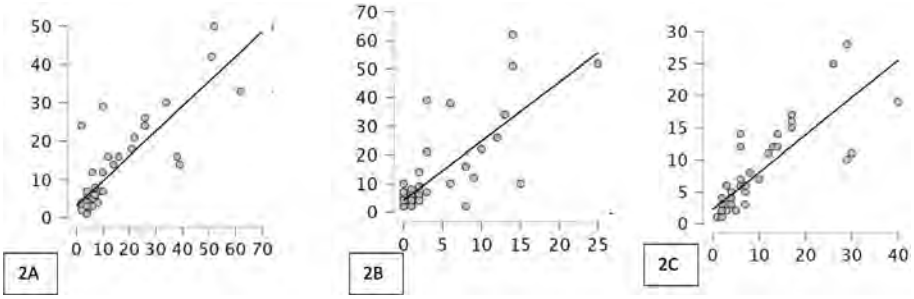


Fig 2A: correlation between total number of joints examined by patient vs clinician ; 2B: Correlation between swollen joints examined by patient vs clinician; 2C: Correlation between tender joints examined by patient vs clinician

Results: The total number of joints assessed by patients and clinicians was 3968. The number of joints with either tender or swollen as examined by clinician and patient was 559 and 499, respectively. The sensitivity of patient-reported joint counts was 86.02% (82.6–88.9%), while the specificity was 95.62% (94.8–96.3%). For swollen joints, the sensitivity was 89.2% and the specificity was 96.2%. For tender joints, the sensitivity was 85.04%, and the specificity was 93.8% (Figure 1)

Among joint categories, patient self-assessment was more accurate for proximal joints such as the shoulder (specificity 91.95%) and elbows (sp 96.18%). In contrast, distal joints like the wrist, metacarpophalangeal joints, knee, and ankle were assessed more accurately by clinicians. The CDAI was calculated as per clinician and patient tender, swollen joints were calculated individually. There was a strong correlation between CDAI (phy) and CDAI (pt) (rho-0.99).Cronbach's alpha for CDAI (patient) was 0.701.

There was a strong correlation between the total joint counts reported by physicians and patients with higher propensity for swollen joints than tender joints (rho= 0.887 and 0.827, respectively ($p < 0.001$)) Intraclass correlation coefficients (ICC) for total joints, swollen joints, and tender joints were 0.810, 0.880, and 0.770, respectively, indicating good to excellent reliability.(Figure 2A,2B,2C)

Conclusion: This study shows that with proper training, patient self-assessment of joints is a reliable alternative for online consultations, especially in remote areas. It is particularly accurate for detecting swollen joints, making it useful for remote monitoring and treatment decisions. The findings support integrating self-assessment into telemedicine to improve access and care quality.

Disclosure: S. Sathiyaseelan: None; **S. Kansurkar**: None; **K. Krishna**: None; **V. Bhatt**: None.

Abstract Number: 1086

Leveraging Natural Language Processing to Uncover Real-World Trends in Cannabis Use from Clinic Notes in Electronic Health Records

Titilola Falasinnu[1], Nathan Le[2], Yiyu Wang[2], Aishwarya Alagappan[2], Michael Weisman[3], Anushka Irani[4], Yashaar Chaichian[5] and Selen Bozkurt[6], [1]Stanford School of Medicine, Palo Alto, CA, [2]Stanford School of Medicine, Stanford, CA, [3]Cedars-Sinai Medical Center, LOS ANGELES, CA, [4]Mayo Clinic, Jacksonville, FL, [5]Stanford University, Stanford, CA, [6]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Pain management in autoimmune rheumatic diseases (ARDs) increasingly includes NSAIDs, physical therapy, and self-management. However, the role of cannabis in ARD symptom relief remains unclear. We used natural language processing (NLP) on electronic health records (EHRs) to systematically characterize cannabis use patterns, motivations, and disparities in ARD patient

	Cannabis use		
	Yes (n=1237)	No (n=3814)	Total (n=5051)
Average age (SD)	48.9 (14.7)	51.5 (15.7)	50.9 (15.5)
Sex			
Male	280 (23.7)	900 (76.3)	1180 (23.4)
Female	957 (24.7)	2914 (75.3)	3871 (76.6)
Age (years)			
18-26	95 (35.1)	176 (64.9)	271 (5.4)
27-40	270 (23.8)	866 (76.2)	1136 (22.5)
41-65	705 (26.4)	1970 (73.6)	2675 (53.0)
66+	167 (17.2)	802 (82.8)	969 (19.2)
Race			
Black	46 (36.2)	81 (63.8)	127 (2.5)
White	865 (26.5)	2395 (73.5)	3260 (64.5)
Asian	124 (14.6)	725 (85.4)	849 (16.8)
Other	153 (25.2)	453 (74.8)	606 (12.0)
Unknown	49 (23.4)	160 (76.6)	209 (4.1)
Ethnicity			
Non-Hispanic	1004 (24.1)	3160 (75.9)	4164 (82.4)
Hispanic	169 (30.1)	393 (69.9)	562 (11.1)
Unknown	64 (19.7)	261 (80.3)	325 (6.4)
Insurance			
Private	582 (23.5)	1892 (76.5)	2474 (49.0)
Public	577 (26.3)	1621 (73.7)	2198 (43.5)
Unknown	78 (20.6)	301 (79.4)	379 (7.5)
Disease			
Ankylosing spondylitis	62 (22.5)	213 (77.5)	275 (5.4)
Psoriatic arthritis	215 (27.2)	575 (72.8)	790 (15.6)
Rheumatoid arthritis	719 (24.0)	2278 (76.0)	2997 (59.3)
Sjogrens disease	239 (25.9)	684 (74.1)	923 (18.3)
Systemic sclerosis	157 (27.2)	420 (72.8)	577 (11.4)
SLE	192 (26.6)	530 (73.4)	722 (14.3)
Average charlson comorbidity index (SD)	3.3 (2.5)	2.2 (1.9)	2.5 (2.1)
Average Number of emergency department visits (SD)	5.2 (9.4)	4.1 (10.4)	4.4 (10.2)
Average Number of hospitalizations (SD)	8.7 (13.0)	6.1 (11.6)	6.8 (12.0)
Average Number of surgeries (SD)	3.9 (6.6)	2.8 (3.2)	3.1 (4.5)
Number of patients prescribed steroids	1175 (95.0)	3304 (86.6)	4479 (88.7)
Number of patients prescribed nsaids	954 (77.1)	2518 (66.0)	3472 (68.7)
Number of patients prescribed opioids	992 (80.2)	2306 (60.5)	3298 (65.3)

Characteristics of positive cannabis use patients compared to negative patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Total	Pain (%)	Nausea (%)	Sleep (%)	Anxiety (%)	Unspecified (%)	Appetite (%)
Total	990	375 (37.9)	40 (4.0)	151 (15.3)	33 (3.3)	823 (83.1)	29 (2.9)
Sex							
Male	233	77 (33.0)	4 (1.7)	27 (11.6)	8 (3.4)	201 (86.3)	7 (3.0)
Female	757	298 (39.4)	36 (4.8)	124 (16.4)	25 (3.3)	622 (82.2)	22 (2.9)
Age (years)							
18-26	67	19 (28.4)	6 (9.0)	6 (9.0)	4 (6.0)	56 (83.6)	3 (4.5)
27-40	205	69 (33.7)	10 (4.9)	33 (16.1)	4 (2.0)	184 (89.8)	5 (2.4)
41-65	578	222 (38.4)	21 (3.6)	103 (17.8)	22 (3.8)	471 (81.5)	16 (2.8)
66+	140	65 (46.4)	3 (2.1)	9 (6.4)	3 (2.1)	112 (80.0)	5 (3.6)
Race							
Black	33	18 (54.5)	2 (6.1)	9 (27.3)	4 (12.1)	29 (87.9)	3 (9.1)
White	702	270 (38.5)	27 (3.8)	108 (15.4)	22 (3.1)	584 (83.2)	19 (2.7)
Asian	88	19 (21.6)	2 (2.3)	12 (13.6)	2 (2.3)	78 (88.6)	2 (2.3)
Other	124	55 (44.4)	7 (5.6)	15 (12.1)	5 (4.0)	98 (79.0)	5 (4.0)
Unknown	43	13 (30.2)	2 (4.7)	7 (16.3)	0 (0.0)	34 (79.1)	0 (0.0)
Ethnicity							
Non-Hispanic	805	303 (37.6)	31 (3.9)	126 (15.7)	26 (3.2)	675 (83.9)	21 (2.6)
Hispanic/Latino	132	57 (43.2)	9 (6.8)	15 (11.4)	5 (3.8)	106 (80.3)	7 (5.3)
Unknown	53	15 (28.3)	0 (0.0)	10 (18.9)	2 (3.8)	42 (79.2)	1 (1.9)
Insurance							
Private	452	145 (32.1)	19 (4.2)	71 (15.7)	13 (2.9)	382 (84.5)	14 (3.1)
Public	473	210 (44.4)	16 (3.4)	68 (14.4)	19 (4.0)	388 (82.0)	12 (2.5)
Unknown	65	20 (30.8)	5 (7.7)	12 (18.5)	1 (1.5)	53 (81.5)	3 (4.6)
Disease							
AS	57	16 (28.1)	1 (1.8)	6 (10.5)	2 (3.5)	50 (87.7)	2 (3.5)
PsA	193	70 (36.3)	8 (4.1)	26 (13.5)	4 (2.1)	163 (84.5)	5 (2.6)
RA	616	251 (40.7)	21 (3.4)	82 (13.3)	24 (3.9)	510 (82.8)	11 (1.8)
SjS	201	77 (38.3)	8 (4.0)	53 (26.4)	4 (2.0)	157 (78.1)	4 (2.0)
SSc	140	44 (31.4)	11 (7.9)	20 (14.3)	5 (3.6)	126 (90.0)	13 (9.3)
SLE	73	27 (37.0)	5 (6.8)	20 (27.4)	6 (8.2)	62 (84.9)	3 (4.1)

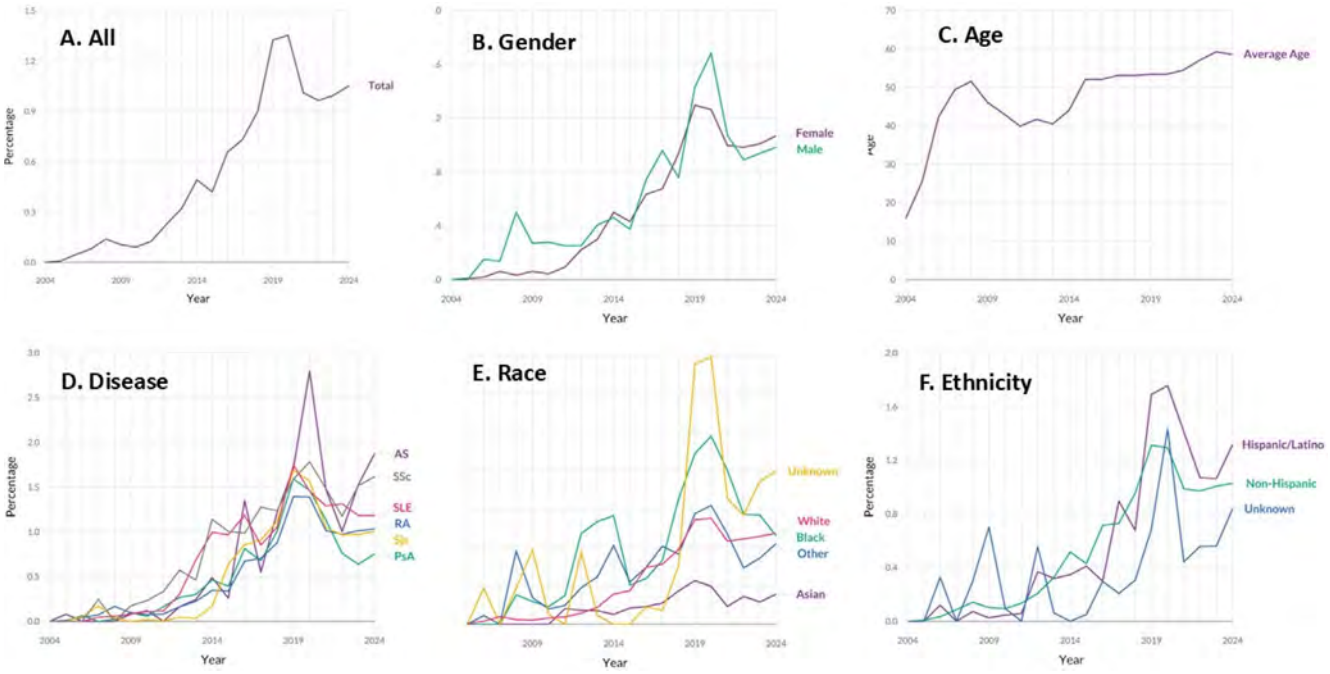
Sociodemographic and Disease-Related Distribution of Reasons for Cannabis Use Among Patients with Autoimmune Rheumatic Diseases Among Cannabis Users, 2015-2024 *These proportions add up to more than >100% because individuals can mention any or all the uses in the clinic notes

Methods: A retrospective analysis (2004–2024) included 5,051 patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjögren's syndrome (SjS), or ankylosing spondylitis (AS) from an academic health system. NLP models (ClinicalBERT) extracted cannabis documentation from 2,626,542 clinical notes, classifying cannabis use as current, past, or none and categorizing reasons as pain, sleep, anxiety, nausea, or appetite. Sociodemographic factors, comorbidities, medications, and healthcare utilization were compared between cannabis users and non-users.

Results: Clinical notes documenting current cannabis use rose from 0.1% (2017) to >1% (2024), a 900% relative increase. NLP classifiers performed well for cannabis documentation, current vs. past use (F1=0.85), and reasons for use (F1=0.86). Overall, 1,237 patients (24.5%) had current cannabis use documented. Higher usage was observed among Hispanic/Latino (30.1%) and Black (36.2%)

patients. Pain was the primary reason overall (37.9%), notably higher among Black (54.5%) and Hispanic/Latino (43.2%) patients compared with White (38.5%) and Asian patients (21.6%). Women more frequently reported using cannabis for pain (39.4%) and sleep (16.4%) compared to men (33.0%, 11.6%, respectively). Older adults (≥66 years) most likely to report

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Annual Percentage of Notes Mentioning Current Cannabis Usage by Gender, Race, Ethnicity, Mean Age, and Disease Status, 2004-2024

pain-related cannabis use (46.4%), whereas middle-aged adults (17.8%) and early middle-aged adults (16.1%) were more likely to use cannabis for sleep. Disease-specific differences showed pain-related use was highest among patients with RA (40.7%), SjS (38.3%), and SLE (37.0%), while sleep-related cannabis use was most frequently documented in patients with SLE (27.4%) and SjS (26.4%). Cannabis users had greater comorbidity burdens, more emergency visits, hospitalizations, and opioid prescriptions.

Conclusion: This study represents one of the largest and most comprehensive efforts to characterize cannabis use in ARDs using NLP and machine learning. This study demonstrates the feasibility of systematically identifying cannabis use patterns and motivations in ARD patients, highlighting opportunities for clinicians to initiate informed discussions with patients regarding cannabis as a symptom management strategy. Future research should investigate factors driving cannabis use, including specific ARD subphenotypes, disease activity and severity, treatment interactions, and the impact on overall disease management. Efforts to address disparities in medical cannabis access and rigorous studies evaluating safety and effectiveness will be essential for informing potential clinical guidance.

Disclosure: T. Falasinnu: None; **N. Le**: None; **Y. Wang**: None; **A. Alagappan**: None; **M. Weisman**: Spyre Therapeutics, 1, 2; **A. Irani**: None; **Y. Chaichian**: Lupus Therapeutics, Lupus Research Alliance, 5; **S. Bozkurt**: Flatiron Health, 2, KabaFusion, 2.

Abstract Number: 1087

Impact of Neighborhood-Level Social Vulnerability on Disease Severity, Clinical Manifestations, and Early Mortality in Systemic Lupus Erythematosus

Zoe Reed[1], Catriona Wagner[2], Xana Howard[1], Alexandre Cammarata-Mouchtouris[1], Study Team ALE06 Clinical[1], Wade DeJager[3] and Judith James[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Santa Cruz, CA, [3]Oklahoma Medical Research Foundation, Oklahoma City

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1055–1087) Healthcare Disparities in Rheumatology Posters
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with considerable clinical and molecular heterogeneity. Significant disparities exist in SLE, with minority populations experiencing higher prevalence, increased disease severity, and earlier mortality. Recent studies suggest that adverse social determinants of health may contribute to these disparities. This study evaluated the association between neighborhood-level social vulnerability, measured by the Social Vulnerability Index (SVI), and disease severity, clinical manifestations, and early mortality among female SLE patients in the Lupus Family Registry and Repository (LFRR).

Methods: The LFRR is a large, cross-sectional cohort of SLE patients and their unaffected family members. Patients met ACR 1997 classification criteria for SLE, were female, and had available residential addresses for geocoding (n=3,033). Of those patients, 1,091 were deceased prior to 2024 and included in the early mortality analysis. Disease severity was assessed using the Montgomery Lupus Severity Index (LSI; high severity defined as LSI >7). SVI percentiles (range 0-1) were categorized as high (percentile >0.50) or low (≤ 0.50) vulnerability. Early mortality was defined as death before the average age of death in the US population from 1999-2020, stratified by sex and race. Descriptive statistics and separate logistic regression models were used to evaluate associations with SVI factors, LSI, ACR criteria, and lupus nephritis (LN).

Results: Consistent with previous studies, we observed significant racial differences in disease severity, and clinical manifestations along with higher percentages of early mortality (Table 1 and Figure 1). In univariate analyses, high SVI was associated with increased odds of certain ACR criteria and LSI (Figure 1A). However, these associations were no longer statistically significant after adjusting for race (Figure 1B). Racial differences in disease severity and organ involvement persisted even after accounting for SVI (Figure 1). Patients who died early had significantly higher SVI scores for low economic and household instability factors, indicating greater social vulnerability (Figure 2). Notably, these factors remained significantly associated with early mortality following adjustment for race, sex and high LSI (Figure 2).

Table 1: Demographic and clinical characteristics

		AI/AN	Asian	Black	White	p	q
	n=3,033	n=177	n=129	n=1026	n=1460		
Race, n (%)							
AI/AN	177 (6)	-	-	-	-	-	-
Asian	129 (4)	-	-	-	-	-	-
Black	1026 (34)	-	-	-	-	-	-
NH/PI	4 (0)	-	-	-	-	-	-
White	1,460 (48)	-	-	-	-	-	-
Multiracial	22 (1)	-	-	-	-	-	-
Unknown	215 (7)	-	-	-	-	-	-
Hispanic/Latino, n (%)	377 (12)	97 (54.8)	2 (1.6)	12 (1.2)	63 (4.3)	**<0.001**	**<0.001**
Age, mean (SD)	43 (13)	41.86 (13.27)	37.86 (11.90)	42.32 (12.61)	43.94 (13.35)	**<0.001**	**<0.001**
High LSI, n (%)	1290 (43)	68 (38.4)	63 (48.8)	560 (54.6)	482 (33.0)	**<0.001**	**<0.001**
Nephritis, n (%)	814 (27)	34 (19.2)	48 (37.2)	350 (34.1)	309 (21.2)	**<0.001**	**<0.001**
	n=1,091	n=54	n=11	n=453	n=67		
Early Mortality, n (%)	885 (81)	31 (57.4)	9 (81.8)	371 (81.9)	420 (83.5)	**<0.001**	**<0.001**

AI/AN, American Indian or Alaska Native; NH/PI, Native Hawaiian or Other Pacific Islander
Chi-square or Kruskal-Wallis tests; (q) 2-stage linear step-up procedure of Benjamini, Krieger, and Yekutieli.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

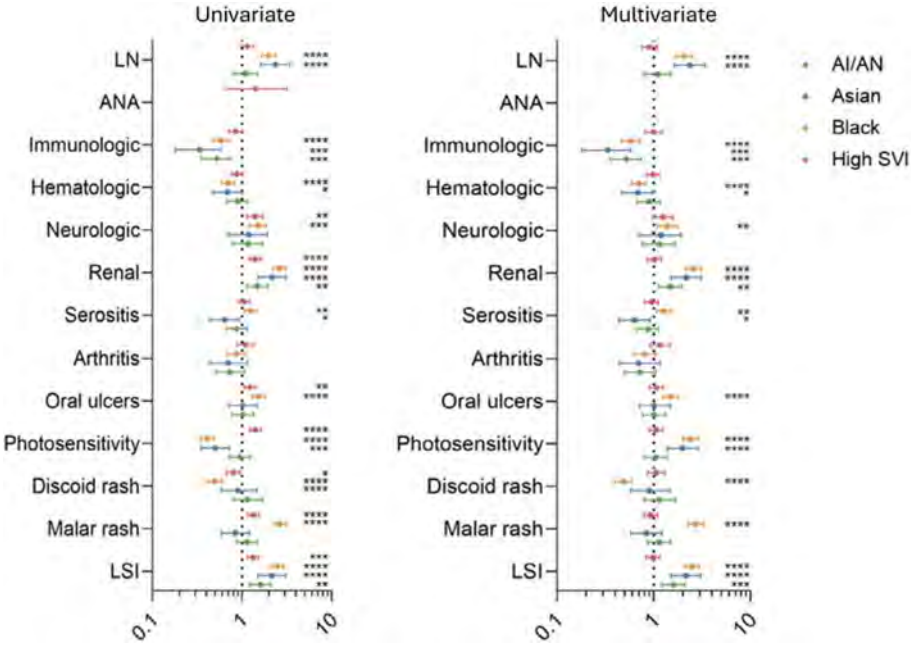


Figure 1: Associations of social vulnerability index and self-reported race with SLE disease severity and clinical manifestations. (A) Univariate and (B) multivariate logistic regression models for associations with different clinical characteristics. The multivariate model incorporates self-reported race categories and low vs high SVI.

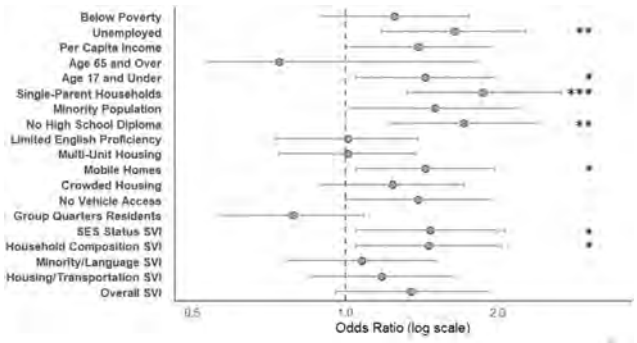


Figure 2: Associations of social vulnerability index with early mortality in SLE; multivariate logistic regression models for associations with different SVI factors. The multivariate model incorporates self-reported race categories, sex, high LSI, and low vs high SVI.

Conclusion: In the LFRR, neighborhood-level social vulnerability was not associated with SLE severity or organ involvement after accounting for race. Persistent racial disparities in SLE severity and manifestations suggest that factors beyond area-level vulnerability, including genetic, epigenetic, and individual-level environmental exposures, may play a more substantial role. Social vulnerability, particularly low economic and household instability factors, was significantly associated with early mortality.

Disclosure: Z. Reed: None; **C. Wagner**: None; **X. Howard**: None; **A. Cammarata-Mouchtouris**: None; **S. ALE06 Clinical**: None; **W. DeJager**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1088

Unsupervised characterization of immune checkpoint inhibitor induced inflammatory arthritis using cluster and latent class analysis: result from a multicenter prospective registry

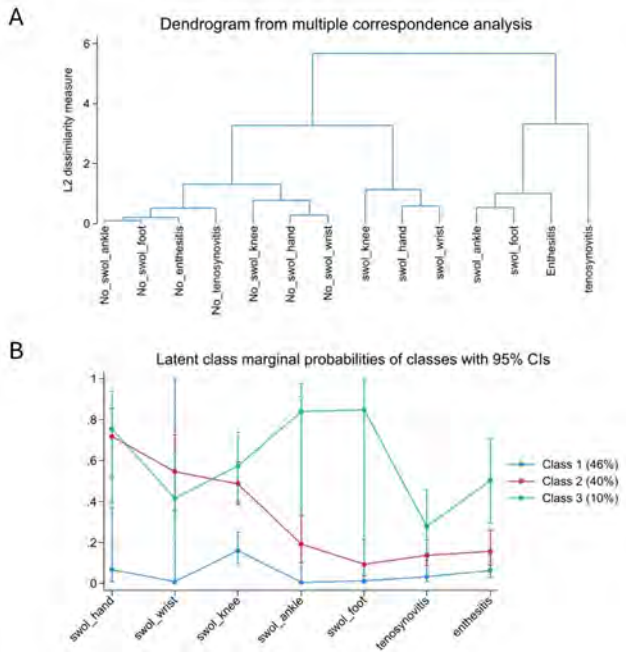
Alice Tison[1], Deanna Jannat-Khah[2], Laura Cappelli[3], Anne R. Bass[2], and the RADIOS registry consortium, [1]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [2]Hospital For Special Surgery, New York, NY, [3]Johns Hopkins School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The broad use of immune checkpoint inhibitors (ICIs) in oncology has led to the emergence of ICI-induced inflammatory arthritis (ICI-IA). The aim of this study was to define ICI-IA phenotypic patterns using unsupervised clustering and latent class analysis (LCA) and determine their association with the need for an immunosuppressive DMARD.

Methods: Data was extracted on 11/6/2024 from the Rheumatology Adverse Events Due to Immunotherapy Observational Study (RADIOS) registry regarding patients with ICI-IA or ICI-polymyalgia rheumatica (PMR) who had been prospectively recruited at nine sites around the United States. Clinical data at the date of registry enrollment was used to group patients. Clinical features involving < 10% of patients were excluded to avoid outliers. We analyzed only immunosuppressive DMARDs (methotrexate, leflunomide, biologic/targeted synthetic DMARDs). Multiple correspondence analysis (MCA) was used to group binary variables followed by a hierarchical classification on the generated coordinates using the Ward method, with Euclidean distances. An LCA was then performed to group patients. The optimal number of classes was determined according to goodness of fit. Classes were compared using descriptive statistics. Stepwise backwards multivariable logistic

Figure 1 : Results from multiple correspondence and latent class analysis in the RADIOS registry



Swol = swollen

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patients 'characteristics in the 3 LCA classes in the RADIOS registry

	RADIOS total (n=443)	RADIOS Class 1 (n=210)	RADIOS Class 2 (n=193)	RADIOS Class 3 (n=40)	p-value
N (%)					
Age, mean (SD)	63 (13)	65(13)	62 (12)	61(3)	0.1
Combination ICI (n=370)	92 (25)	37 (21)	48 (30)	7 (21)	0.17
Physician diagnosis					<0.001
ICI-IA	379 (86)	154 (74)	185 (96)	40 (100)	
ICI-PMR	64 (14)	56 (27)	8 (4.1)	0 (0)	
Maximum CTCAE grade (n=301)					0.042
1	51 (17)	31 (19)	18 (17)	2 (6.7)	
2	153 (51)	81 (50)	49 (45)	23 (77)	
3	97 (32)	51 (31)	41 (38)	5 (17)	
CDAI, median (IQR) (n=316)	13 (7.2, 21)	6.7 (3, 11)	17 (11, 23)	20 (13, 28)	<0.001
28 swollen joint count, median (IQR) (n=406)	2 (0, 6)	0 (0,0)	5 (3, 9)	7 (3.5, 11)	<0.001
28 tender joint count, median (IQR) (n=406)	1 (0, 4)	0 (0, 1)	3 (1, 6)	3 (1.5, 6)	<0.001
RF positivity (n=287)	31 (11)	9 (8.3)	16 (11)	6 (18)	0.25
Anti CCP positivity (n=263)	11 (4.2)	3 (3.3)	6 (4.3)	2 (6.1)	0.75
b/ts DMARD ever	127 (29)	45 (21)	66 (34)	16 (40)	0.004
MTX, leflunomide or b/tsDMARD ever	177 (40)	69 (33)	84 (44)	24 (60)	0.003

b/tsDMARD: biologic/targeted synthetic Disease Modifying Antirheumatic Drug, ICI-IA: immune checkpoint inhibitor mediated inflammatory arthritis, ICI-PMR: immune checkpoint inhibitor mediated polymyalgia rheumatica, LCA: Latent Class Analysis, MTX: methotrexate, RF: rheumatoid factor.

Table 2: Patients 'characteristics in the 3 LCA classes in the HSS registry

	Total (n=117)	HSS Class 1 (n=53)	HSS Class 2 (n=58)	HSS Class 3 (n=6)	p-value
N (%)					
Age, mean (SD)	68 (11)	67 (12)	67(12)	67 (7.7)	0.97
Combination ICI	29 (25)	17 (32)	9 (16)	3 (50)	0.029
Physician diagnosis					0.008
ICI-IA	96 (82)	37 (70)	53 (91)	6 (100)	
ICI-PMR	21 (18)	16 (30)	5 (9)	0 (0)	
Maximum CTCAE grade (n=110)					0.45
1	13 (12)	9 (18)	4 (7)	0 (0)	
2	71 (65)	31 (62)	35 (65)	5 (83)	
3	26 (24)	10 (20)	15 (28)	1 (17)	
CDAI, median (IQR) (n=96)	11 (5.5, 17)	7 (2, 11)	14 (7, 24)	26 (12, 34)	<0.001
28 swollen joint count, median (IQR)	2 (0, 4)	0 (0, 1)	3.5 (2, 8)	7 (2, 17)	<0.001
28 tender joint count, median (IQR)	1 (0, 2)	0 (0, 1)	2 (0, 5)	2.5 (1, 5)	<0.001
RF positivity (n=100)	14 (14.)	8 (19)	6 (12)	0 (0)	0.47
Anti CCP positivity (n=96)	16 (17)	7 (18)	9 (17)	0 (0)	0.82
b/ts DMARD ever	21 (18)	9 (17)	10 (17)	2 (33)	0.56
MTX, leflunomide or b/tsDMARD ever	38 (33)	17 (32)	18 (31)	3 (50)	0.61

b/tsDMARD: biologic/targeted synthetic Disease Modifying Antirheumatic Drug, ICI-IA: immune checkpoint inhibitor mediated inflammatory arthritis, ICI-PMR: immune checkpoint inhibitor mediated polymyalgia rheumatica, LCA: Latent Class Analysis, MTX: methotrexate, RF: rheumatoid factor.

regression (retaining variables with $p \leq 0.1$) was used to compare DMARD utilization between classes adjusted for maximum ICI-IA/PMR grade, cancer type, the use of combination ICI, recruitment institution and age. The LCA model was then validated in the HSS Registry, an independent single center prospective ICI-IA/PMR registry, and the same statistical methods were applied to compare DMARD utilization between classes.

Results: 443 patients with ICI-IA/PMR in the RADIOS registry were included in the cluster analysis. The variables included in the MCA were: swollen hand/wrist/knee/ankle/foot, tenosynovitis and enthesitis. The hierarchical classification identified 3 main groups (figure 1A) and isolated a group of variables, swollen ankle/foot, enthesitis and tenosynovitis, from the others. The LCA identified 3 classes of patients (figure 1B). Class 1 was dominated by rare swollen joints, while swollen hand, wrist and/or knee predominated in Class 2. Swollen ankle and foot reached a probability >80% in class 3, along with a high

probability of having other swollen joints. The median CDAI was higher in class 3, as was the 28 swollen joint count (Table 1). The stepwise logistic regression model showed an OR for DMARD use of 3.64 ([95%CI 1.5-9.1] p=0.006) for class 3 compared to class 1. The estimates of the LCA were applied to the validation cohort (n=117) and demonstrated greater use of DMARDs in HSS class 3 compared to class 1 and 2 (Table 2), but this was not statistically significant (OR 3.7 [95%CI 0.5-27], p=0.2), likely due to the small number of patients in class 3 (n=6).

Conclusion: In this large multicenter prospective cohort we identified 3 phenotypic patterns of ICI-IA. One group, characterized by ankle and foot joint swelling and more swollen joints in general, was more likely to require an immunosuppressive DMARD. This information could help stratify patients prognostically at their first rheumatology visit.

Disclosure: A. Tison: Celltrion Healthcare France, 12, Support for attending a congress, Galapagos, 2; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **L. Cappelli**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, 5, Sanofi, 2, Uniquity Bio, 2; **A. Bass**: None.

Abstract Number: 1089

Comparing the immunosuppressant burden in immune checkpoint inhibitor mediated inflammatory arthritis versus polymyalgia rheumatica: results from a prospective multicenter registry

Alice Tison[1], Deanna Jannat-Khah[2], Laura Cappelli[3] Anne R. Bass[2] and the RADIOS registry consortium, [1]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [2]Hospital For Special Surgery, New York, NY, [3]Johns Hopkins School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1- Clinical and laboratory features of ICI-IA and ICI-PMR at baseline RADIOS registry visit

	Total (n=443)	ICI-IA (n=379)	ICI-PMR (n=64)	p-value
N (%)				
Time from ICI initiation to ICI-IA/PMR onset (n=351), days median (IQR)	109 (31, 214)	117 (31, 214)	89.5 (36, 171)	0.25
Clinical features (n=406)				
Peripheral arthritis	265 (65)	254 (72)	11 (20)	<0.001
Swollen hand	180 (44)	173 (49)	7 (13)	
Swollen wrist	122 (30)	119 (34)	3 (5.7)	
Swollen elbow	35 (8.6)	35 (9.9)	0	
Swollen knee	145 (36)	140 (40)	5 (9.3)	
Swollen ankle	73 (18)	72 (20)	1 (1.9)	
Swollen foot	56 (14)	56 (16)	0 (0)	
No tender/swollen joints	77 (17)	49 (13)	28 (44)	<0.001
Tenosynovitis (n=390)	44 (11)	42 (12)	2 (4.3)	0.14
Dactylitis	9 (2.0)	9 (2.4)	0 (0)	0.37
Enthesitis	68 (15)	65 (17)	3 (4.7)	0.008
CDAI (n=316), median (IQR)	13 (7.2, 21)	14 (8, 22)	7.3 (4.3, 13)	0.001
Laboratory parameters				
RF or CCP positivity (N=305)	37 (12)	34 (13)	3 (7.3)	0.44
Normal CRP (n= 249)	104 (42)	90 (42)	14 (41)	0.94
Median CRP (N=252), (mg/dl) (IQR)	1.1 (.3, 3.4)	1.1 (.3, 3.6)	1.0 (.2, 2.4)	0.39

ICI-IA: immune checkpoint inhibitor mediated inflammatory arthritis, ICI-PMR: immune checkpoint inhibitor mediated polymyalgia rheumatica, RF : Rheumatoid factor

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Inflammatory arthritis (IA)- and polymyalgia rheumatica (PMR)-like syndromes occur in about 6% of patients receiving an immune checkpoint inhibitor (ICI) and can worsen quality of life. Finding the balance between immunosuppression use without affecting the tumor response is critical. Currently, ICI-IA/PMR management is not standardized and is based on expert opinion. It is unknown whether ICI-IA and ICI-PMR can be treated with the same immunosuppressive regimens. We aimed to compare the utilization of steroids and other DMARDs between these two entities.

Methods: Data were extracted from the Rheumatology Adverse Events Due to Immunotherapy Observational Study (RADIOS) registry regarding patients with ICI-IA or ICI-PMR and no preexisting IA who had been prospectively recruited into RADIOS since 2015 at nine sites around the United States. Data was downloaded on 11/6/2024. Steroids were defined as methylprednisolone and prednisone. We excluded hydrocortisone, used for adrenal replacement, and dexamethasone, used for cancer-related symptoms. Cumulative steroid utilization from the time of onset of IA was available for a subset of patients. We analyzed only immunosuppressive DMARDs, such as methotrexate, leflunomide and biologic/targeted synthetic DMARDs, because of potential impact to tumor responses from ICIs. Categorical and continuous data were compared using descriptive statistics. Kaplan Meier curves were used for survival analyses and groups were compared using a log rank test. We measured the time to a prednisone equivalent dosage i. 10 mg/day or ii. 5 mg/day starting from the first steroid dose received at or after the date of the patient's baseline visit in RADIOS. Multivariable logistic regression was used to compare DMARD utilization in ICI-IA versus ICI-PMR, adjusted for maximum grade (severity), cancer type, the use of combination ICI (anti-CTLA4 plus anti-PD1), recruitment institution and age.

Results: 443 patients were included, n=379 with ICI-IA and n=64 with ICI PMR. 49% were female, with a median age of 66 years (IQR 55,73). Anti PD-1/PDL-1 was used in 265 patients (72%) and combination ICI in 92 (25%). At baseline, 11 ICI-PMR patients (20%) had a peripheral synovitis primarily involving the hand, knee and wrist (Table 1). The median maximum steroid dose prescribed after baseline did not differ between groups (p=0.92) (Table 2). Time to reach a steroid dose of 10 or 5 mg/day from first steroid prescription after baseline was also comparable (p=0.74 and p=0.50 respectively) (Figure 1 A, B). There was no difference

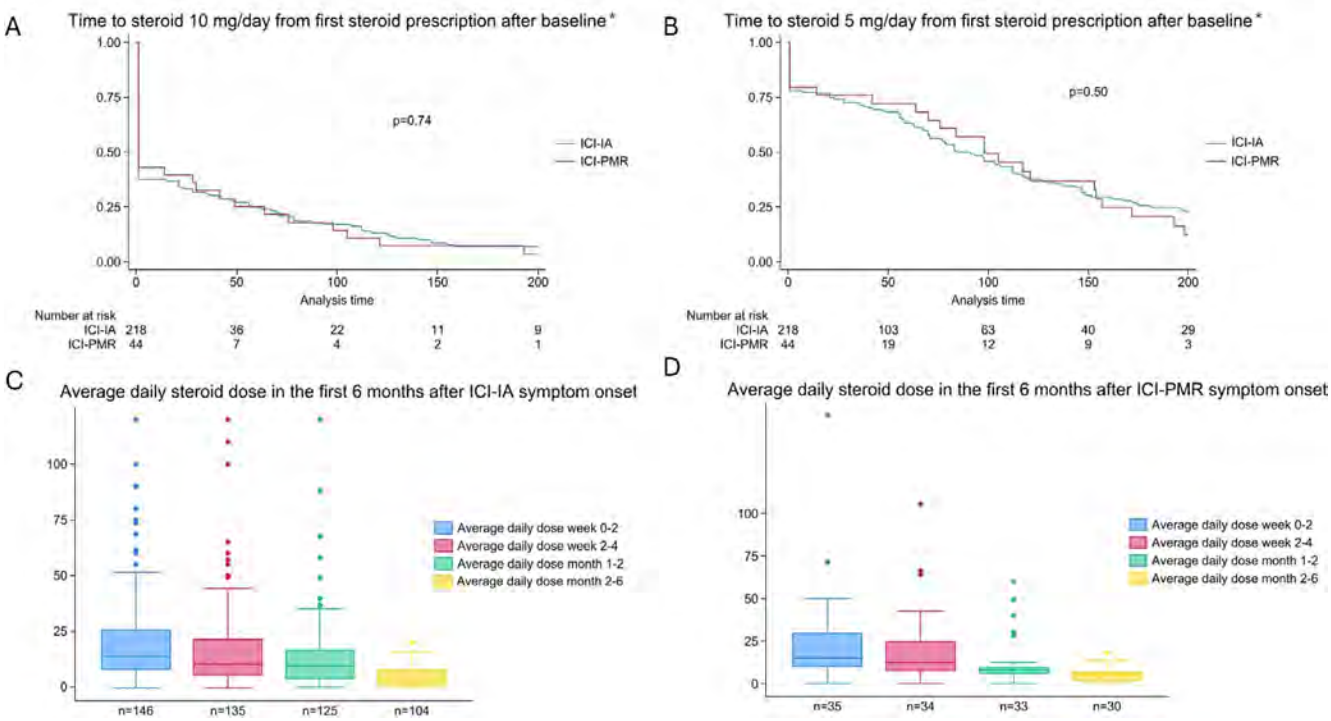
Table 2: Immunosuppressive use and ICI management in ICI-IA compared to ICI-PMR

	Total (n=443)	ICI-IA (n=379)	ICI-PMR (n=64)	p-value
N (%)				
Steroids				
No steroid ever	123 (28)	110 (29)	13 (20)	0.18
Steroid at BL	260 (59)	217 (57)	43 (67)	0.17
Maximum steroid dose after BL (n=215), median (IQR)	10 (10, 20)	10 (10, 20)	10 (10, 20)	0.92
Steroid average daily dose from onset of IA/PMR mg/d median (IQR)				
Week 0-2 (n=181)	15 (10,26)	14 (7.5,26)	15 (10,30)	0.33
Week 2-4 (n=169)	10 (6.3,23)	10 (5.0,21)	12 (7.5,25)	0.38
Month 1-2(n=158)	9.3 (4.7,16.3)	9.3 (3.5,17)	8.2 (5.6,10)	0.92
Month 2-6 (n=134)	4.0 (1.2,7.5)	3.8 (0.7,7.7)	5.0 (1.9,7.0)	0.53
DMARDs				
CsDMARD ever	187 (42)	167 (44)	20 (31)	0.057
Methotrexate	87 (20)	84 (22)	3 (4.7)	
Hydroxychloroquine	95 (21)	81 (21)	14 (22)	
Other csDMARD #	48 (11)	44 (12)	4 (6.2)	
b/tsDMARD ever	127 (29)	113 (30)	14 (22)	0.23
TNF inhibitor	78 (18)	76 (20)	2 (3.1)	
IL-6 receptor inhibitor	61 (14)	51 (14)	10 (16)	
Other b/tsDMARD ##	21 (4.7)	19 (5.0)	2 (3.1)	
MTX, leflunomide or b/ts DMARD ever	177 (40)	162 (43)	15 (23)	0.004
ICI discontinuation for irAE	111 (25)	90 (24)	21 (33)	0.16
ICI hold for irAE (n=217)	146 (67)	120 (66)	26 (74)	0.43

BL: Baseline RADIOS registry visit, b/ts DMARD: biologic/targeted synthetic Disease Modifying Antirheumatic Drug, csDMARD: conventional synthetic Disease Modifying Antirheumatic Drug, ICI-IA: immune checkpoint inhibitor mediated inflammatory arthritis, ICI-PMR: immune checkpoint inhibitor mediated polymyalgia rheumatica, irAE : immune related adverse event. # azathioprine in 2, cytoxan in 2, IVIg in 5, leflunomide in 21 (all in the ICI-IA group), mycophenolate mofetil in 4, sulfasalazine in 13, other in 7 , ## abatacept in 3 (all in the ICI-IA group), rituximab in 3 (all in the ICI-IA group), JAK inhibitor in 5 (all in the ICI-IA group), other in 10.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1 : Steroid utilization in ICI-IA and ICI-PMR



* Baseline = Baseline RADIOS registry visit

in average daily steroid dose between the two groups in the first 6 months after symptoms onset (Table 2, Figure 1 C, D). DMARDs were more prescribed to patients with ICI-IA (43%) than ICI-PMR (23%) (p=0.004). This difference remained after adjusting for confounders in a multivariable logistic regression model (OR= 3.03 [95%CI 1.10, 8.34], p=0.032).

Conclusion: Patients with ICI-IA were more likely to be treated with immunosuppressive DMARDs than patients with ICI-PMR. Treatment with steroids was comparable between the two groups. Identifying more severe phenotypes at diagnosis might help to avoid longer steroid exposure before DMARD initiation.

Disclosure: A. Tison: Celltrion Healthcare France, 12, Support for attending a congress, Galapagos, 2; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **L. Cappelli**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, 5, Sanofi, 2, Uniquity Bio, 2; **A. Bass**: None.

Abstract Number: 1090

Quantitative Immunoglobulin Screening Prior to Rituximab Initiation: A Retrospective Cohort Study

Amelia Khoo and Anokhi Saklecha, Yale University, New Haven, CT

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rituximab, a monoclonal antibody which binds to the CD20 antigen of B cells, is used in the treatment of many rheumatologic conditions. Due to its mechanism of action, which depletes B cells and reduces production of immunoglobulins, patients who receive rituximab are at significantly increased risk of developing hypogammaglobulinemia. Studies suggest that as many as 38% of patients who receive rituximab develop hypogammaglobulinemia, which in turn places them at increased risk of recurrent infection (Casulo et al., 2014). A reduced baseline level of immunoglobulins is associated with severe infections after receiving rituximab. Current literature suggests that patients should therefore be pre-screened with quantitative measurement of immunoglobulins prior to initiation of rituximab (Buch et al., 2011). In this study, we aimed to assess the prevalence of this pre-screening in a large academic health center.

Methods: We conducted a retrospective cohort study based on electronic health records in a large academic health system. Adults (≥18 years) who received their first rituximab dose between 1/1/2023 and 12/1/2024 were included. Baseline screening was defined as any recorded quantitative immunoglobulin panel drawn in the six months prior to initiation of rituximab. IVIG administration ≤ 6 months after initiation (follow-up through 1 May 2025) served as a proxy for clinically significant antibody failure. Screened and unscreened groups were compared with Fisher's exact test.

Results: Among **238** patients who started rituximab, only 115 (48.3 %) underwent guideline-recommended baseline Ig screening, leaving 123 (51.7 %) unscreened. All screened patients had normal IgA and IgM levels. Quantitative IgG levels were not available. IVIG rescue occurred in 17 patients (7.1 %) overall—11/115 (9.6 %) in the screened group and 6/123 (4.9 %) in the unscreened group (p=0.21).

Conclusion: Despite guideline recommendations, over half of patients did not receive baseline Ig screening in the 6 months before rituximab initiation. No screened patient with abnormal IgA/IgM proceeded to treatment, indicating that screening—when performed—effectively excludes overt hypogammaglobulinemia. Interestingly, however, early IVIG rescue did not differ significantly between screened and unscreened patients, calling into question the short-term protective value of current screening practice. Limitations include the absence of quantitative IgG data and single-center design. Future work includes assessing screening rates and clinical outcomes across multiple sites and launching a quality-improvement initiative using an electronic Best Practice Advisory to improve adherence.

Disclosure: A. Khoo: None; **A. Saklecha**: None.

Abstract Number: 1091

Safety Profile of ICIs in Patients with Rheumatoid Arthritis: Results from a Propensity Score-Matched Cohort Study

Betul Ibis[1], Furkan Bahar[1], Yu-Che Lee[2], Ko-Yun Chang[3], Yu Chang[4] and Cho-Han Chiang[5], [1]Mount Auburn Hospital, Harvard Medical School, Cambridge, MA, [2]University at Buffalo, Buffalo, NY, [3]National Jewish Health, Denver, CO, [4]National Cheng Kung University Hospital, Tainan, Taiwan (Republic of China), [5]Mount Auburn Hospital, Harvard Medical School, Cambridge

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Immune-related adverse events (irAEs) are a significant concern for patients receiving immune checkpoint inhibitors (ICIs), particularly those with pre-existing rheumatoid arthritis (RA). Managing ICIs in RA patients is complex due to potential immune activation leading to disease flares or new autoimmune manifestations. Although RA patients were often excluded from ICI trials, their increasing representation among cancer patients highlights the need for a better understanding of the safety and toxicity of ICIs in this population.

Methods: We conducted a propensity score-matched cohort study using the TriNetX Analytics Network database, comprising anonymized data from over 140 collaborating healthcare institutions worldwide. We compared the incidence and risk of irAEs in cancer patients with and without RA. Adult patients (age ≥18) receiving ICIs were included. The primary outcome was composite irAEs within one year of ICI initiation, while secondary outcomes were individual irAEs and all-cause mortality. Matching criteria included demographics (age, sex), metastatic disease, chemotherapy and radiation history, underlying comorbidities, ECOG performance status, and cardiovascular medication use. Risk of irAEs was assessed using Cox proportional hazards models, with hazard ratios (HR) and 95% confidence intervals (CI). P-values < 0.05 were considered significant.

Table 1. Patient baseline characteristics before and after propensity score matching

Variables	Before Matching			After Matching		
	RA Group	Non-RA Group	SMD	RA Group	Non-RA Group	SMD
Age at Index ,mean	66.2 ± 10.9	64.0 ± 13.0	0.18	66.2 ± 10.9	66.7 ± 12.0	0.05
Male	422 (43.5)	32261 (58.2)	0.3	422 (43.6)	432 (44.6)	0.02
White	730 (75.2)	35665 (64.4)	0.24	728 (75.1)	723 (74.6)	0.01
Black	67 (6.9)	4062 (7.3)	0.02	67 (6.9)	82 (8.5)	0.06
Hispanic	38 (3.9)	2380 (4.3)	0.02	38 (3.9)	38 (3.9)	0
Asian	38 (3.9)	3517 (6.3)	0.11	38 (3.9)	35 (3.6)	0.02
BMI ,mean	27.5 ± 6.7	26.7 ± 6.3	0.13	27.5 ± 6.7	27.5 ± 6.7	0
Tobacco use	73 (7.5)	3900 (7.0)	0.02	73 (7.5)	81 (8.4)	0.03
ECOG Performance Status ,mean	0.8 ± 1.3	0.8 ± 1.0	0	0.8 ± 1.3	0.7 ± 1.1	0.11
Immune-checkpoint inhibitors						
Pembrolizumab	523 (53.9)	27662 (49.9)	0.08	523 (54.0)	513 (52.9)	0.02
Nivolumab	249 (25.6)	16394 (29.6)	0.09	247 (25.5)	243 (25.1)	0.01
Avelumab	10 (1.0)	408 (0.7)	0.03	10 (1.0)	10 (1.0)	0
Ipilimumab	100 (10.3)	5419 (9.8)	0.02	99 (10.2)	97 (10.0)	0.01
Durvalumab	79 (8.1)	3491 (6.3)	0.07	79 (8.2)	85 (8.8)	0.02
Retatlimab	10 (1.0)	200 (0.4)	0.08	10 (1.0)	12 (1.2)	0.02
Tremelimumab	10 (1.0)	137 (0.2)	0.1	10 (1.0)	10 (1.0)	0
Cancer Type						
Head and Neck	41 (4.2)	3674 (6.6)	0.11	41 (4.2)	50 (5.2)	0.04
Gastrointestinal	114 (11.7)	9435 (17.0)	0.15	114 (11.8)	104 (10.7)	0.03
Respiratory	458 (47.2)	23070 (41.6)	0.11	458 (47.3)	438 (45.2)	0.04
Bone and articular cartilage	19 (2.0)	1028 (1.9)	0.01	19 (2.0)	15 (1.5)	0.03
Skin	253 (26.1)	12195 (22.0)	0.09	251 (25.9)	251 (25.9)	0
Breast	82 (8.4)	4120 (7.4)	0.04	82 (8.5)	76 (7.8)	0.02
Female Reproductive	51 (5.3)	2448 (4.4)	0.04	51 (5.3)	47 (4.9)	0.02
Male Reproductive	32 (3.3)	2203 (4.0)	0.04	32 (3.3)	33 (3.4)	0.01
Urinary	119 (12.3)	7421 (13.4)	0.03	119 (12.3)	142 (14.7)	0.07
Thyroid and other endocrine	14 (1.4)	508 (0.9)	0.05	14 (1.4)	13 (1.3)	0.01
Hematologic	43 (4.4)	2321 (4.2)	0.01	42 (4.3)	49 (5.1)	0.03
Metastatic Disease						
Lymph Nodes	312 (32.1)	15461 (27.9)	0.09	310 (32.0)	305 (31.5)	0.01
Respiratory and Digestive Organs	246 (25.3)	13703 (24.7)	0.01	245 (25.3)	234 (24.1)	0.03
Other and unspecified sites	343 (35.3)	17883 (32.3)	0.06	343 (35.4)	335 (34.6)	0.02
Underlying Comorbidities						
Hypertension	496 (51.1)	22130 (39.9)	0.23	494 (51.0)	502 (51.8)	0.02
Hyperlipidemia	297 (30.6)	12090 (21.8)	0.2	295 (30.4)	297 (30.6)	0
Type 2 Diabetes Mellitus	163 (16.8)	8124 (14.7)	0.06	162 (16.7)	164 (16.9)	0.01
Chronic obstructive pulmonary disease	207 (21.3)	7668 (13.8)	0.2	205 (21.2)	206 (21.3)	0
Chronic kidney disease	93 (9.6)	3980 (7.2)	0.09	91 (9.4)	85 (8.8)	0.02
Common Chemotherapies and Radiation Therapy						
Platinum compounds	425 (43.8)	23720 (42.8)	0.02	425 (43.9)	420 (43.3)	0.01
Taxanes	200 (20.6)	10463 (18.9)	0.04	200 (20.6)	210 (21.7)	0.03
Anthracyclines and related substances	22 (2.3)	1941 (3.5)	0.07	22 (2.3)	19 (2.0)	0.02
Cyclophosphamide	11 (1.1)	936 (1.7)	0.05	11 (1.1)	10 (1.0)	0.01
Fluorouracil	37 (3.8)	3428 (6.2)	0.11	37 (3.8)	37 (3.8)	0
Gemcitabine	46 (4.7)	2896 (5.2)	0.02	46 (4.7)	63 (6.5)	0.08
Radiation Oncology Treatment	227 (23.4)	10771 (19.4)	0.1	227 (23.4)	223 (23.0)	0.01
Medications						
Aspirin	249 (25.6)	11265 (20.3)	0.13	247 (25.5)	244 (25.2)	0.01
Clopidogrel	49 (5.0)	2404 (4.3)	0.03	49 (5.1)	45 (4.6)	0.02
Sodium-glucose co-transporter 2 (SGLT2) inhibitors	15 (1.5)	923 (1.7)	0.01	15 (1.5)	11 (1.1)	0.04
Beta Blocking Agents	387 (39.9)	17847 (32.2)	0.16	385 (39.7)	391 (40.4)	0.01
Statins	340 (35.0)	15226 (27.5)	0.16	338 (34.9)	332 (34.3)	0.01
ACE Inhibitors	202 (20.8)	9198 (16.6)	0.11	200 (20.6)	203 (20.9)	0.01
Angiotensin II Inhibitor	132 (13.6)	7280 (13.1)	0.01	132 (13.6)	137 (14.1)	0.01
Healthcare Utilization						
Outpatient Services	632 (65.1)	30354 (54.8)	0.21	630 (65.0)	650 (67.1)	0.04
Inpatient Services	273 (28.1)	12284 (22.2)	0.14	271 (28.0)	272 (28.1)	0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Mortality and risk of irAEs among patients with RA vs non-RA group

Table 2. Mortality and risk of irAEs among patients with RA vs non-RA group

Outcomes	RA Group			Non-RA Group			Hazard Ratio (95%	P-value (log rank)
	Cases with outcome	Patient Number at Risk	Incidence rates (per 1000 patient-years)	Cases with outcome	Patient Number at Risk	Incidence rates (per 1000 patient-years)		
Mortality	243	969	250.77	276	9692	284.82	0.84 (0.70, 1.00)	0.049
Composite irAE	478	969	493.29	421	969	434.46	1.12 (0.98, 1.28)	0.072
Colitis	90	969	92.87	68	969	70.17	1.28 (0.94, 1.76)	0.114
Hepatitis	25	969	25.79	34	969	35.08	0.70 (0.42, 1.18)	0.185
Pancreatitis	7	969	7.22	8	969	8.25	0.82 (0.30, 2.28)	0.714
Pneumonitis	42	969	43.34	25	969	25.79	1.61 (0.98, 2.65)	0.055
Myocarditis/Pericarditis	3	969	3.09	4	969	4.12	0.71 (0.15, 3.17)	0.653
Thyroid dysfunction	164	969	169.24	170	969	175.43	0.91 (0.74, 1.13)	0.426
Type I DM	3	969	3.09	5	969	5.15	0.55 (0.13, 2.32)	0.414
Hypophysitis	14	969	14.44	12	969	12.38	1.12 (0.51, 2.42)	0.769
Adrenal insufficiency	53	969	54.69	32	969	33.02	1.60 (1.03, 2.48)	0.033
Tubulointerstitial Nephritis	42	969	43.34	34	969	35.08	1.17 (0.75, 1.85)	0.476
Dermatitis/Rash	141	969	145.51	124	969	127.96	1.10 (0.86, 1.40)	0.415
Hematologic irAEs	48	969	49.53	50	969	51.59	0.92 (0.62, 1.37)	0.693
Neurologic irAEs	99	969	102.16	74	969	76.36	1.29 (0.95, 1.74)	0.094
Ophthalmic irAEs	4	969	4.12	2	969	2.06	1.94 (0.35, 10.59)	0.435
Other Rheumatic irAEs*	53	969	54.69	15	969	15.47	3.44 (1.94, 6.11)	<0.001
Other dermatologic irAEs	2	969	2.06	6	969	6.19	0.31 (0.06, 1.56)	0.135
*Excluding inflammatory arthritis								

Results: We included 969 RA patients and 969 non-RA patients after matching. The mean age was similar between groups (66.2 ± 10.9 years for RA vs. 66.7 ± 12.0 years for non-RA). The proportion of male patients was also comparable (43.6% in RA vs. 44.6% in non-RA). The incidence of irAEs in the RA group was not significantly different from the non-RA group (HR 1.13, 95% CI 0.99–1.29, p=0.072). Notably, the RA group exhibited a significantly lower all-cause mortality (HR 0.84, 95% CI 0.71–1.00, p=0.049). Specific irAEs with increased risk in the RA group included adrenal insufficiency (HR 1.60, p=0.033) and other rheumatic irAEs (HR 3.44, p=0.001). No significant differences were observed in the incidence of colitis, hepatitis, pancreatitis, pneumonitis, myocarditis/pericarditis, or other irAEs.

Conclusion: In this analysis, RA patients receiving ICIs demonstrated no significant difference in the incidence of composite irAEs and a lower risk of all-cause mortality compared to non-RA patients. The findings underscore the importance of close monitoring and multidisciplinary care for RA patients undergoing ICI therapy to mitigate immune toxicity while optimizing cancer outcomes.

Disclosure: B. Ibis: None; **F. Bahar**: None; **Y. Lee**: None; **K. Chang**: None; **Y. Chang**: None; **C. Chiang**: None.

Abstract Number: 1092

Prior history of arthritis and PD-1 over PD-L1 blockade predispose to immune-related adverse events in cancer patients treated with immune checkpoint inhibitors

Binod Kc[1], Aakritee Sharma Subedi[1], Salome Walsh[1], Areeba Memon[1] and Andras Perl[2], [1]SUNY Upstate Medical University, Syracuse, NY, [2]SUNY, Syracuse, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy by enhancing the immune system's ability to fight cancer. However, their use is associated with immune-related adverse events (irAEs), including rheumatologic complications such as inflammatory arthritis. This study aims to evaluate the incidence and predictors of new-onset inflammatory arthritis and other irAEs in cancer patients treated with ICIs, with a focus on the impact of PD-1 versus PD-L1 blockade and the influence of pre-existing arthritis.

Methods: This study retrospectively analyzed electronic medical records of 3,341 patients treated with ICIs at Upstate University Hospital from 2011 to 2024. It screened for rheumatic immune-related inflammatory arthritis and systemic irAEs. Statistical analysis used chi-square or Fisher's exact test with GraphPad V10 software, considering a two-tailed p-value < 0.05 as significant.

Results: Table 1 outlines characteristics of 3,341 ICI-treated patients. Pembrolizumab (51% of patients) and nivolumab were most common (17.5%). The vast majority of patients were on monotherapy (92.2%). 5.4% of patients had a pre-existing history of inflammatory arthritis.Table 2 outlines the prevalence of arthritis in ICI-treated patients. PD-1 inhibitors

Table 1: Baseline and Clinical characteristics of the patient on ICI. (N=3,341)

Characteristic	Results		
ICI Therapy			
Combined Therapy	261		
Monotherapy	3080		
Type of ICI Used and Molecular target			
PD-1			
Pembrolizumab	1698		
Nivolumab	584		
Cemiplimab	42		
PD-L1			
Atezolizumab	373		
Avelumab	31		
Durvalumab	340		
CTLA4			
Ipilimumab	11		
PD-1 and CTLA4			
Nivolumab and Ipilimumab	251		
PD-L1 and CTLA4			
Durvalumab and Tremelimumab	10		
History of Pre-existing arthritis			
Yes	180		
No	3161		
Total no of patients developed arthritis			
New Arthritis	25		
Flare of Underlying Arthritis	32		
Other irAEs		**With pre-existing arthritis**	**No pre-existing arthritis**
Myositis	12	2	10
Vasculitis	9	0	9
Sarcoidosis	3	0	3
SLE	14	2	12
Sjoca Syndrome	3	0	3
Colitis	27	10	17
Pneumonitis	48	12	36
Encephalitis	13	0	13
Hepatitis	193	20	173
Dermatitis	99	9	90
Nephritis	2	2	0
Type of cancer			
Lung Cancer	993		
Other Cancers	2348		

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table No.2 . Comparing the incidence of inflammatory arthritis among different ICIs, various cancer types in patients with a pre-existing history of arthritis versus those without

		Arthritis	No Arthritis	P value
ICI	PD-L1	10	734	<0.001
	PD-1	40	754	
	PD-L1 + CTLA4	0	10	0.5924
	PD-1 + CTLA4	7	244	
	Combined Therapy	7	254	0.2048
	Monotherapy	50	3030	
	Nivolumab	8	576	<0.001
	Pembrolizumab	32	136	
Cancer	Lung cancer	26	967	0.0081
	Other types of cancer	31	2317	
New Arthritis	Preexisting h/o of Arthritis	32	148	<0.0001
	No Preexisting h/o Arthritis	25	3136	

Table No.3: Comparing the incidence of various irAEs in patients with a pre-existing history of arthritis versus those without

Preexisting h/o of Arthritis	**Total irAEs**	**No irAEs**	
Yes	89	91	P value <0.0001
No	448	2713	
	Colitis	**No Colitis**	
Yes	10	170	P value <0.0001
No	17	3144	
	Pneumonitis	**No Pneumonitis**	
Yes	12	168	P value <0.0001
No	36	3125	
	Hepatitis	**No Hepatitis**	
Yes	20	160	P value <0.0016
No	173	2988	
	Nephritis	**No Nephritis**	
Yes	2	178	P value <0.0001
No	0	3161	
	SLE	**No SLE**	
Yes	2	178	P value <0.1395
No	12	3149	
	Dermatitis	**No Dermatitis**	
Yes	9	171	P value <0.0976
No	90	3071	
	Myositis	**No Myositis**	
Yes	2	178	P value <0.083
No	10	3151	

were associated with a higher incidence of inflammatory arthritis as compared to PD-L1 inhibitors ($p < 0.001$). Pembrolizumab was associated with a higher incidence of arthritis, affecting 19.05% of patients, compared to nivolumab, which affected 1.37% of patients ($p < 0.001$). Lung cancer patients had highest incidence of inflammatory arthritis (2.62%) compared to patients with other types of cancer (1.32%, $p = 0.0081$).Furthermore, the data shows a highly significant

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

association between a pre-existing history of arthritis and the development of inflammatory arthritis during treatment ($p < 0.0001$), with 17.8% of patients with prior arthritis developing inflammatory arthritis compared to 0.8% of those without such a history. Table 3 outlines the association between pre-existing arthritis and the development of total irAEs is highly significant ($p < 0.0001$), with 49.4 % of patients with prior arthritis developing irAEs compared to 14.2% of those without such prior history. Regarding subtypes of irAEs, conditions such as Colitis, Pneumonitis, Hepatitis, and Nephritis show highly significant associations ($p < 0.00016$), whereas other subtypes like vasculitis, sarcoidosis, sicca syndrome, encephalitis, SLE, Dermatitis, and Myositis were not statistical significance in patients with a pre-existing history of arthritis compared to those without ($p > 0.05$).

Conclusion: PD-1 inhibitors are markedly more prone to induce inflammatory arthritis than PD-L1 inhibitors. Amongst PD-1 inhibitors, pembrolizumab is associated with a higher incidence of inflammatory arthritis as compared to nivolumab. Lung cancer patients have a higher incidence of inflammatory arthritis compared to patients with other types of cancer. Moreover, prior history of arthritis overall predisposes to all types of irAEs. Prospective studies are warranted to validate these findings.

Disclosure: B. Kc: None; **A. Sharma Subedi**: None; **S. Walsh**: None; **A. Memon**: None; **A. Perl**: None.

Abstract Number: 1093

Rituximab Associated Risk for Progressive Multifocal Leukoencephalopathy Among Patients with Systemic Lupus Erythematosus: A Retrospective Cohort Study

Blake Baay[1], Lorien Nassi[2] and Zachary Most[3], [1]Scottish Rite for Children, Dallas, TX, [2]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [3]UT Southwestern, Dallas, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rituximab is one of the many immunosuppressive medications used to treat SLE that can increase a patient's risk for developing progressive multifocal leukoencephalopathy (PML), a rare but largely fatal neurologic disease. However, despite being one of the few issued with a label warning regarding its association with PML, no study has determined the specific risk rituximab poses among these other medications. We attempted to quantify this risk by retrospectively comparing the prevalence of PML in two matched cohorts of SLE patients with and without previous exposure to rituximab.

Methods: We queried the TriNetX Research Network, a large database of anonymized electronic health records, to identify patients diagnosed with SLE after January 1, 1998. Patients exposed to rituximab or diagnosed with PML prior to this date were excluded. International Classification of Disease (ICD) codes were used to identify diagnoses of SLE and PML, and RxNorm and Healthcare Common Procedure Coding System (HCPCS) codes were used to determine rituximab exposure. Patients with any previous exposure were separated from those without to create the two cohorts. After nearest neighbor propensity score matching, we used Kaplan-Meier curves and the unadjusted hazard ratio (HR) to assess the risk of PML.

Results: The network included 316,307 patients diagnosed with SLE on or after January 1, 1998, without prior orders for rituximab or diagnosis of PML. The prevalence of PML in this initial general population was 0.015%. After propensity score matching, the two cohorts each consisted of 6,452 patients, with fewer than 10 diagnosed with PML in each group. PML

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

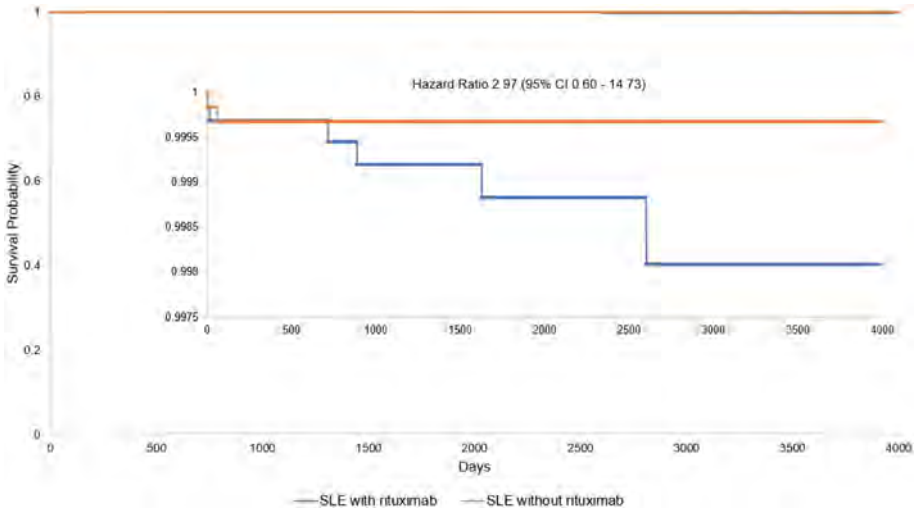


Figure 1. Kaplan-Meier curves and calculated hazard ratio of the two cohorts. The section where the curves diverge has been enlarged and overlayed onto the unaltered graph.

occurrence was higher in the rituximab exposed cohort (Figure 1), although the difference was not statistically significant by log-rank test (P = 0.16) or in the proportional hazards model (HR = 2.97, 95% CI 0.60-14.73).

Conclusion: We were unable to demonstrate a statistically significant risk of developing PML from rituximab in patients with SLE when accounting for other comorbidities and immunosuppressive medications. Even assuming the high end of the confidence interval, the number needed to harm patients given rituximab to lead to one case of PML would be high at 513 patients.

Disclosure: B. Baay: None; **L. Nassi**: None; **Z. Most**: VisualDx, 6.

Abstract Number: 1094

Changes in NK cells and TH cell phenotype in Rheumatoid Arthritis patients treated with janus kinase inhibitors: implications for adverse effects

Carmen Lasa Teja[1], Juan José Fernández-Cabero[2], Alejandra Comins-Boo[3], David San Segundo[3], Virginia Portilla González[4], Montserrat Santos-Gomez[5], José Luis Martín-Varillas[6], Marcos López-Hoyos[3] and Ricardo Blanco[7], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [2]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Cantabria, Spain, [3]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [4]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, [5]Division of Immunology, Hospital Sierrallana. Santander , Spain, Santander, Spain, [6]Rheumatology Division, Hospital de Laredo. IDIVAL, Immunopathology Group. Santander, Spain., Laredo, Spain, [7]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Janus kinase inhibitors (JAKi) are effective in rheumatoid arthritis (RA); however, concerns regarding safety, particularly the risk of infections and malignancies, have been raised. This study aimed to assess the impact of JAKi on immune cell subsets in RA patients.

Methods: This prospective study included RA patients initiating JAKi therapy (tofacitinib, baricitinib, upadacitinib, and filgotinib), diagnosed according to ACR/EULAR 2010 criteria. Control groups consisted of healthy donors and RA patients starting biological disease-modifying antirheumatic drugs (RA-bDMARDs). Peripheral blood mononuclear cells were analyzed using multiparametric flow cytometry to characterize the immunophenotype of various immune cell subsets.

Results: We analyzed 78 RA patients treated with JAKi (Baricitinib: 46.2%, Filgotinib: 24.4%, Tofacitinib: 17.9%, Upadacitinib: 11.5%), 20 RA patients treated with bDMARDs (tocilizumab: n=11, abatacept: n=9), and 20 healthy controls (Table).

RA-JAKi patients showed a significant decrease in cytotoxic NK Dim cells (vs RA-bDMARD) and NK cells expressing Nkp30 (vs RA-bDMARD and healthy controls). The proportion of effector memory (EM) $CD4^+$ T cells was higher in RA-JAKi (20.47 [14.77–30.69]) vs RA-bDMARD (12.12 [7.62–17.05]) and healthy controls (10.79 [7.16–16.25]), while central memory (CM) T cells were reduced (38.40 [29.26–45.66] vs RA-bDMARD: 48.32 [43.82–58.8] and healthy controls: 48.87 [42.07–56.52]).

Total $CD4^+$ T-helper cells were significantly increased in RA-JAKi (1.50 [0.66–3.13]) vs healthy (0.38 [0.14–1.55]) and RA-bDMARD (0.33 [0.14–1.18]) (p=0.005 and p=0.003). Th17 and $Th1^+17$ cells were reduced in RA-JAKi vs both controls (Figure 1).

The proportion of double-negative B cells differed significantly between JAKi patients and controls, with switched memory B cells elevated in RA-JAKi (20.25 [11.18–29.08] vs healthy: 12.24 [8.31–18.82], p=0.018). $CD21^-$ low B cells were higher in RA-JAKi (4.44 [3.05–7.97] vs RA-bDMARD: 3.16 [1.42–4.75], p=0.045) (Figure 2).

Table. Clinical characteristics of the patients included in the study.

	BARICITINIB n=36	FILGOTINIB n= 19	TOFACITINIB n= 14	UPADACITINIB n= 9	ABATACEPT n= 9	TOCILIZUMAB n=11	Healthy controls n=20
Age, years, mean ±SD	64.4 ± 10.4	61 ± 11.4	55.5 ± 8.6	63.1 ± 7.8	66.2 ±9	60.3 ±10.2	60 ± 4.3
Women, n (%)	28 (77.8)	18 (94.7)	14 (100)	9 (100)	5 (55.6)	8 (72.7)	17 (85)
RA duration, months, mean ±SD	178.3 ± 135.4	256 ± 307.1	166.9 ± 65.4	65.1 ± 53.9			NA
CVRF, n (%)	31 (86.1)	14 (73.7)	9 (64.3)	5 (55.6)			NA
RF / ACPA, n (%)	25 (69.4)	17 (89.5)	10 (71.4)	6 (66.7)	8 (88.9)	8 (72.7)	1 (5)
Extraarticular manifestations, n (%)	6 (16.6)	0	2 (14.3)	0			NA
Erosive, n (%)	12 (33.3)	7 (36.8)	6 (42.9)	6 (66.7)			NA
Current treatment							
Prednisone dose, mg/day, median [IQR]	2.5 [0-5]	2.5 [0-5]	2.5 [0-7.5]	5 [0-10]	5 [5-7.5]	0 [0-2]	0 [0-0]
NSAIDs, n (%)	12 (33.3)	6 (31.6)	9 (64.3)	8 (88.9)			NA
MTX, n (%)	7 (19.4)	4 (21.1)	4 (28.6)	1 (11.1)	1 (11.1)	2 (18.2)	0
Previous treatment							
MTX, n (%)	36 (100)	19 (100)	14 (100)	9 (100)	8 (88.9)	10 (90.9)	NA
Other cDMARDS, n (%)	29 (80.6)	17 (89.5)	8 (57.1)	8 (88.9)	3 (33.3)	3 (27.3)	NA
AntiTNF, n (%)	29 (80.6)	16 (84.2)	13 (92.9)	6 (66.7)	3 (33.3)	5 (45.5)	NA
Anti-IL6, n (%)	15 (41.7)	14 (73.7)	7 (50)	6 (66.7)	4 (44.4)	0	NA
cDMARDS, number, median [IQR]	2 [2-3]	3 [2-3]	1,5 [1-4]	2,5 [1,3-3.8]	1 [1-1]	1 [1-1]	NA
bDMARDS, number, median [IQR]	2 [1-3]	2 [1.3-3]	2 [1-2]	2 [0.5-3.75]	1 [1-2]	0 [0-2]	NA

CVRF: cardiovascular risk factors, **RF:** rheumatoid factor, **ACPA**: anti-citrullinated protein antibodies, **NSAIDs**: non-steroidal anti-inflammatory drugs, **MTX:** methotrexate, **bDMARD:** biologic disease modifying antirheumatic drug, **cDMARDS:** conventional disease modifying antirheumatic drug, **AntiTNF:** anti-tumour necrosis factor, **Anti-IL6:** anti-interleukin 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

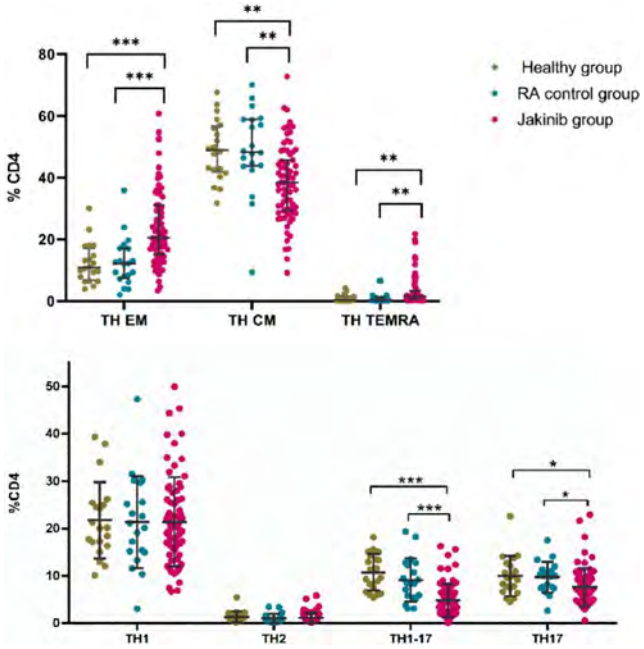


Figure 1. Differentiation status and percentage of T-Helper subsets in the three groups studied. A) Dot-plots depicting the percentage of T-helper according to their differentiation status categorized as Effector Memory T helper (TH EM, CD3+ CD4+ CD62L- CD45RA-), Central Memory T helper (TH CM, CD3+ CD4+ CD62L+ CD45RA-) and Effector memory re-expressing RA T helper cells (TH TEMRA, CD3+ CD4+ CD62L- CD45RA+) among healthy (green), rheumatoid arthritis control group (blue) and jakinib group (pink). B) Dot-plots depicting the percentage of T-helper subsets categorized as T helper 1 (TH1, CD3+ CD4+ CD45RA- CXCR3+ CCR6-), T helper 17 (TH17, CD3+ CD4+ CD45RA- CXCR3- CCR6+), T helper 1-17 (TH1-17, CD3+ CD4+ CD45RA- CXCR3+ CCR6+) and T helper 2 (TH2, CD3+ CD4+ CD45RA- CXCR3- CCR6- CD294+) among healthy (green), rheumatoid arthritis control group (blue) and jakinib group (pink).*p<0.05, **p<0.01 and ***p<0.001.

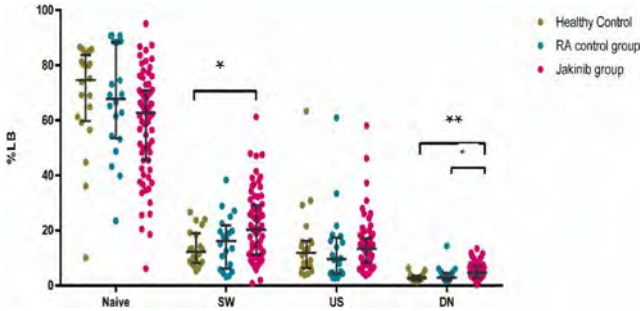


Figure 2. Differentiation status of B cells. Dot-plots depicting the percentage of B cells according to their differentiation status, categorized as Naïve (CD19+ IgD+ CD27-) Switched memory B cells (CD19+ IgD- CD27+), Unswitched memory B cells (CD19+ IgD+ CD27+) and Double negative B cells (CD19+ CD27-IgD-) among healthy (green), rheumatoid arthritis control group (blue) and jakinib group (pink).*p<0.05, **p<0.01 and ***p<0.001.

Conclusion: JAKi differentially impact innate immune cells compared to biological DMARDs. The observed reduction in cytotoxic activated NK cells and intermediate monocytes may contribute to increased susceptibility to viral infections and potential malignancies. Alterations in T and B cell subsets suggest an exhausted immune phenotype, emphasizing the need for further functional studies to fully elucidate the long-term immunomodulatory effects of JAKi.

Disclosure: C. Lasa Teja: None; **J. Fernández-Cabero**: None; **A. Comins-Boo**: None; **D. San Segundo**: None; **V. Portilla González**: None; **M. Santos-Gomez**: None; **J. Martín-Varillas**: AbbVie, Pfizer, Lilly, Celgene, Janssen, and UCB Pharma, 5; **M. López-Hoyos**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1095

Tolerance of non-TNF α treatments in patient with an inflammatory rheumatic (IRD) and autoimmune demyelinating diseases: French retrospective cases series

Dellal Azeddine[1], Jean-Guillaume Letarouilly[2], Jacques Morel[3], René-Marc Flipo[4], Valerie Devauchelle[5], richette pascal[6], Philippe Dieude[7], Hubert Marotte[8], FELTEN Renaud[9], LATOURTE Augustin[10], CHEVET Baptiste[11], HILLIQUIN Pascal[12], SORDET Christelle[9], DERNIS mmanuelle[13], WENDLING Daniel[14], Arsène Mekinian[15], Nathalie BALLANDRAUD[16], Christophe Richez[17], TOURNADRE Anne[18], salmon Jean -Hugues[19], SAILLOT Carine[20], kedra joanna[21], nahon stephane[22], LE GOFF Benoit[23], Bruno Fautrel[24], Francis BERENBAUM[25], David SAADOUN[26], PHAM Thao[16] and SELLAM JEREMIE[27], [1]GHI LE RAINCY MONTFERMEIL, Montfermeil, France, [2]Université de Lille, CHU Lille, Service de rhumatologie, Lille, France, LILLE, Nord-Pas-de-Calais, France, [3]CHU and University of Montpellier, Montpellier, France, [4]Université de Lille, CHU Lille, Service de rhumatologie, Lille, France, Lille, France, [5]UBO, Brest, France, [6]Rheumatology Department, Lariboisiere Hospital, Paris, Ile-de-France, France, [7]Service de Rhumatologie, Hôpital Bichat APHP, Paris, Paris, Ile-de-France, France, [8]INSERM 1059/University of Saint-Etienne, Saint-Etienne, France, [9]Service de Rhumatologie, Centre de référence des maladies auto-immunes rares (RESO), Hôpitaux Universitaires de Strasbourg, Strasbourg, Strasbourg, Alsace, France, [10]Rheumatology Department, Lariboisiere Hospital, Paris, France, [11]CHU BREST, brest, Bretagne, France, [12]CH SUD FRANCILIEN, PARIS, France, [13]chu caen, CAEN, Haute-Normandie, France, [14]CHU de Besançon, Besançon, Franche-Comte, France, [15]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [16]CHU MARSEILLE, marseille, Provence-Alpes-Cote d'Azur, France, [17]Bordeaux University Hospital, Bordeaux, France, [18]CHU CLERMONT, CLERMONT, Lorraine, France, [19]CHU REIMS, REIMS, Champagne-Ardenne, France, [20]CHU ORLEANS, ORLEANS, Pays de la Loire, France, [21]Pitié-Salpêtrière Hospital, Rheumatology Department, APHP, Sorbonne University,, Paris, France, [22]GHI LE RAINCY MONTFERMEIL, Montfermeil, Ile-de-France, France, [23]CHU Nantes, Nantes, France, [24]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [25]Sorbonne University/Inserm/AP-HP/4Moving Biotech, Paris, France, [26]CHU LA PITIE SALPETRIERE, PARIS, Ile-de-France, France, [27]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, F-75012 Paris, France, /Rheumatology Department, AP-HP Saint-Antoine Hospital, 184, rue du Faubourg Saint-Antoine, 75012, Paris, France., Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The use of TNFα antagonist is not recommended if the patient have a suspicion or demyelinating diseases (DD) confirmed **[1]**. There are a few cases reported that non-TNFi targeted are used in this situation **[2-3]**.

To establish the evolution of DD (stability, aggravation) in patients with a rheumatic disease receiving biological non TNFαi or synthetic therapies, in a retrospective French cohort study.

Methods: A retrospective French multicenter descriptive, national study. Reported cases followed notifications via the CRI (Club Rhumatisme Inflammatoire) newsletter.

Inclusion criteria: Patients > 18 years of age, with IRD (rheumatoid arthritis [RA], spondyloarthritis [SpPA], psoriatic arthritis [psoriatic arthritis]), treated with a non TNFi targeted therapy for more than 3 months, and presenting with demyelinating disease (MS and/or neurological manifestations suggestive of demyelinating disease), whether or not they occurred while on TNFi therapy.

Results: 51 patients received at least one non-TNF targeted therapy (33 SpA, 13 RA, 5 R Pso), with clinical, biological and therapeutic characteristics at Baseline. The mean age of diagnosis of demyelinating pathology was 37.8 years (12-76) in the SpA group, 42.7 (24-58) in the RA group and 45.8 (32-56) in the R Pso group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

51% (n=26) had at least one prior exposure to an anti-TNF before the onset of demyelinating pathology (21 SPA, 1 Rpso, 4 PR). Exposure to non-TNF treatments in the different therapeutic lines is: 40 patients to anti-IL17 with a mean duration of 25 months (2-103), 5 patients to Anti-IL6R with a mean duration of 42.2 months (21-133), 9 patients to CTLA-4Ig (Abatacept) with a mean duration of 18.6 months (3 -64), 7 patients to Jaki with a mean duration of 19.3 months (2-38), 2 patients to anti-IL23 with a mean duration of 8.5 (7-10), 12 patients to anti-CD20 with a mean duration of 18.1 months (4-118), 1 patient to apremilast (phosphodiesterase 4 (PDE4) inhibitor) with a mean duration of 29 months and 3 patients to anti-IL-12 and IL-23 with a mean duration of 31.5(14-64).

100% of patients (n=51) had stability or improvement of demyelinating pathology.

The combination in 6 patients treated with secukinumab, 1 patient with tocizulumab, and 1 patient with rituximab with a background MS treatment (interferon beta, teriflunomide, ocrelizumab, glatiramer acetate) was well tolerated.

Conclusion: The use of non-anti-TNF targeted therapies (anti-IL17, anti-IL6R, CTLA-4Ig, Jaki, anti-IL23, anti-CD20, PDE4 inhibitor, and anti-IL-12 and IL-23) in patients with RIC does not appear to worsen demyelinating disease.

Disclosure: d. azeddine: None; **J. Letarouilly**: AbbVie/Abbott, 6, Amgen, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Galapagos, 6, Janssen, 6, Nordic Pharma, 6, Novartis, 6, Pfizer, 6; **J. Morel**: AbbVie, 2, 5, 6, Biocon, 6, Biogen, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, GlaxoSmithKline, 2, 6, Lilly, 2, 6, Medac, 6, Mylan/Viatris, 6, Nordic Pharma, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche/Chugai, 6, Sanofi, 2, 6; **R. Flipo**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6; **V. Devauchelle**: None; **r. pascal**: None; **P. Dieude**: None; **H. Marotte**: None; **F. Renaud**: None; **L. Augustin**: None; **C. Baptiste**: None; **H. Pascal**: None; **S. Christelle**: None; **D. mmanuelle**: None; **W. Daniel**: None; **A. Mekinian**: Roche, 5; **N. BALLANDRAUD**: None; **C. Richez**: None; **T. Anne**: None; **s. Jean -Hugues**: None; **S. Carine**: None; **k. joanna**: None; **n. stephane**: None; **L. Benoit**: AbbVie/Abbott, 1, Amgen, 1, Bristol-Myers Squibb(BMS), 1, 5, Fresenius-Kabi, 1, Lilly, 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, 5, Roche, 1, 5, Sandoz, 5, Viatris, 1; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **F. BERENBAUM**: 4Moving Biotech, 2, 8, 10; **D. SAADOUN**: None; **P. Thao**: None; **S. JEREMIE**: None.

Abstract Number: 1096

Impact of IL-6 Receptor and JAK Inhibitors on Humoral Immunity in Inflammatory Rheumatic Diseases: An Ambispective Study.

Elisabet Perea[1], Antonio Avilés[2], Cristina RodrÍguez-Alvear[3], Paloma Vela[2], Vega Jovaní[4], Agustín Martínez[2], M.Pilar Bernabeu Gonzalvez[2], Irene Calabuig[2], Ana Lucia Jiménez-Portillo[5], Alejandra Bermúdez[2], Silvia Gomez-Sabater[2], Rocío Caño[2], Francisco Marco[5] and Mariano Andrés[6], [1]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain, Alicante, Spain, [2]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [3]Virgen de la Peña General Hospital, Fuerteventura, Spain, [4]Hospital General Universitario de Alicante, Reumatología, Alicante, Alicante, Comunidad Valenciana, Spain, [5]Immunology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [6]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Interleukin-6 (IL-6) is a proinflammatory cytokine involved in B cell differentiation and antibody production through the JAK/STAT pathway. In clinical practice, hypogammaglobulinemia (HGG) has been observed in patients with inflammatory rheumatic diseases (IRDs) treated with IL-6 receptor inhibitors (IL6Ri) (Vílchez-Oya et al., 2020), but this potential adverse effect remains insufficiently studied. We aimed to evaluate the impact of IL6Ri and Janus kinase inhibitors (JAKi) on humoral immunity through an ambispective approach.

Methods: We first conducted a retrospective chart review of adult patients with rheumatoid arthritis (RA), giant cell arteritis (GCA), or spondyloarthritis (SpA) treated with IL6Ri or JAKi. The primary endpoint was HGG (IgG < 750 mg/dL), also collecting cases of severe HGG (IgG < 450 mg/dL) and severe infections. Subsequently, we initiated a prospective observational study including patients with IRDs initiating IL6Ri or JAKi. Serum immunoglobulin levels and lymphocyte populations were assessed at baseline, 3 and 6 months. Statistical analyses included Student's t-test or Wilcoxon test for paired comparisons, and Fisher's exact test for categorical data.

Results: In the retrospective cohort (n=56) (Table 1), HGG was observed in 20 patients: 35.7% (95% CI 24–49%); 41.9% with IL6Ri (95% CI 26-59%) and 28% with JAKi (95% CI 14-48%). Among these patients, 7 had baseline HGG, three of them had prior rituximab treatment. Severe HGG occurred in 5 patients (25%), with one requiring immunoglobulin replacement. Eight cases had low IgA levels, and six had low IgM. Lymphocyte counts remained within normal limits in all cases. Five patients with HGG developed severe infections, with no associated mortality.

Table 1. Demographic and Clinical Characteristics of the Study Population.

A. Retrospective Phase (n=56).	
Age (years), mean±SD	64.8±12
Sex, n (%)	
Female	44 (78.6)
Male	12 (21.4)
Underlying disease, n (%)	
Rheumatoid arthritis	40 (71.4)
Giant cell arteritis	13 (23.2)
Spondyloarthritis	3 (5.4)
Treatment, n (%)	
Tocilizumab	25 (44.6)
Sarilumab	6 (10.7)
JAKi	25 (44.6)
Concomitant corticosteroid, n (%)	
Yes	33 (58.9)
No	23 (41.1)
Daily prednisone dose, mg/day, mean±SD	16±14
B. Prospective Phase (n=17).	
Age (years), mean±SD	58.65±12.9
Sex, n (%)	
Female	14 (82.35)
Male	3 (17.65)
Underlying disease, n (%)	
Rheumatoid arthritis	7 (41.2)
Giant cell arteritis	6 (35.3)
Spondyloarthritis	2 (11.7)
Polymyalgia rheumatica	1 (5.9)
Calcium pyrophosphate deposition disease	1 (5.9)
Treatment, n (%)	
Tocilizumab	12 (70.6)
Sarilumab	1 (5.9)
JAKi	4 (23.5)
Concomitant corticosteroid, n (%)	
Yes	11 (64.7)
No	6 (35.3)
Daily prednisone dose mg/day, mean±SD	17±9

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Distribution of Immunoglobulins at baseline, 3 and 6 months.

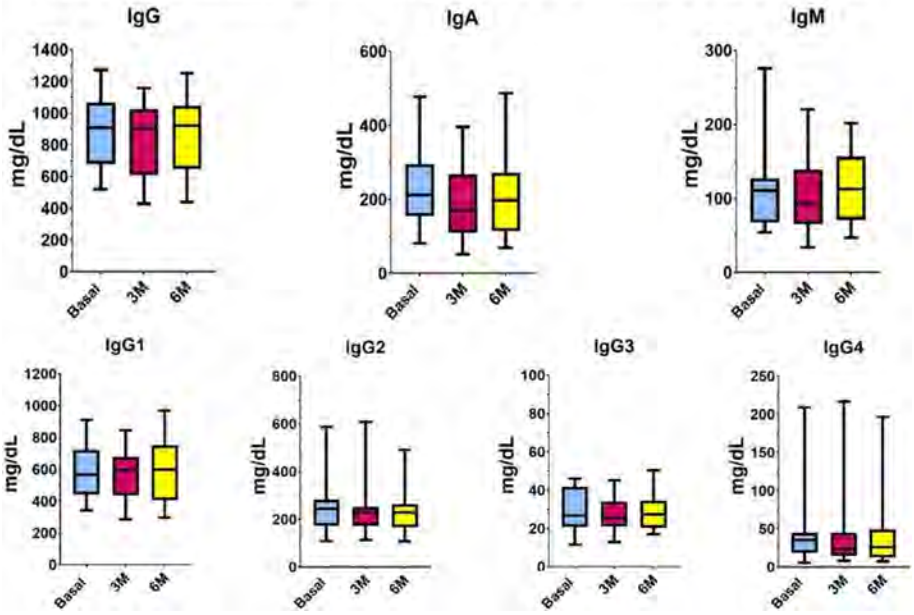
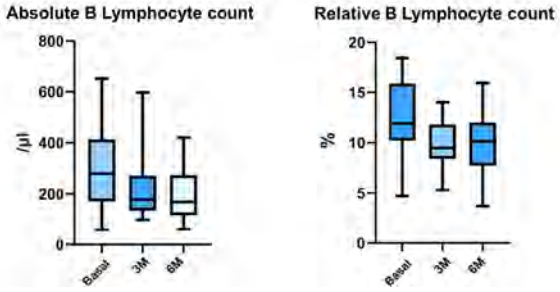


Figure 2. Distribution of B Lymphocytes at baseline, 3 and 6 months.



In the prospective cohort (n=17) (Table 1), IgG levels decreased significantly at 3 months (mean difference –50.7 mg/dL, p=0.018), primarily driven by a reduction in IgG4. However, no significant differences in IgG levels were observed at 6 months. Significant decreases in IgA and IgM levels were observed at 3 months, but only IgA persisted at 6 months (Figure 1). Four patients had baseline HGG, none had prior rituximab exposure. At 3 months, 6 patients (35.3%) had HGG (one severe), that was persistent in all cases at 6 months. Both the relative proportion and the absolute count of CD19+ B lymphocytes were reduced; however, the reduction was statistically significant only for the relative proportion at both 3 months (p=0.01) and 6 months (p=0.014) (Figure 2). No significant changes were observed in T lymphocytes.

Conclusion: Our findings suggest that HGG in patients with IRDs treated with IL6Ri or JAKi is frequent. However, the determination of immunoglobulins in these patients is not integrated into clinical practice. These therapies may impact in immunoglobulin production and B cell function. Further studies are warranted to better assess this potentially harmful association.

Disclosure: E. Perea: None; **A. Avilés**: None; **C. RodrÍguez-Alvear**: None; **P. Vela**: None; **V. Jovaní**: None; **A. Martínez**: None; **M. Bernabeu Gonzalvez**: None; **I. Calabuig**: None; **A. Jiménez-Portillo**: None; **A. Bermúdez**: None; **S. Gomez-Sabater**: None; **R. Caño**: None; **F. Marco**: None; **M. Andrés**: Grunenthal, 5, Sobi, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1097

Polymyalgia rheumatica and giant cell arteritis induced by immune checkpoint inhibitors: a systematic review and meta-analysis highlighting differences with the idiopathic forms

Elvis Hysa[1], Andrea Casabella[2], Emanuele Gotelli[3], Rosanna Campitiello[4], Carlo Genova[4], Enrica Teresa Tanda[4], Carmen Pizzorni[5], Alberto Sulli[5], Vanessa Smith[6], Marco Amedeo Cimmino[7], Sabrina Paolino[5] and Maurizio Cutolo[4], [1]University of Genoa, Genoa, Italy, [2]IRCCS Ospedale Policlinico San Martino, Genova, Italy, [3]University of Genoa, Genoa, Liguria, Italy, [4]University of Genova, Genova, Italy, [5]University of Genoa, Genova, Italy, [6]Ghent University Hospital, Gent, Belgium, [7]Rheumatology Outpatient Clinic, Villa Ravenna, Chiavari, Italy, Genova, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: An altered immune tolerance disturbed by immune checkpoint inhibitors (ICIs) may contribute to new-onset polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) in treated cancer patients. This systematic literature review (SLR) and meta-analysis synthesizes data on the characteristics of ICI-induced PMR and GCA, including pooled prevalence, demographic patterns, clinical features, and treatment-related outcomes. The aim is to present a large-scale meta-analysis offering insights into these syndromes and their potential differences from idiopathic forms.

Methods: The SLR analyzed Medline and EMBASE databases up to July 2024, comparing ICI-induced PMR and GCA to their primary forms. For studies without direct comparisons, SLRs or large observational studies provided the data on primary PMR and GCA. A meta-analysis pooled prevalence, demographics, clinical features, and treatment outcomes when sufficient data were available.

Results: From 1,237 abstracts, 46 were included, yielding 358 patients (314 with ICI-PMR and 44 with ICI-GCA).

ICI-PMR had a pooled prevalence of 0.3% [95% CI: 0.1%–1.2%] among ICI recipients. Patients were predominantly males (64% [95% CI: 54%–73%]), with a mean age of 71 years [95% CI: 68–74]. PD1/PDL1 blockers were used in 85% [95% CI: 80%–89%] of cases. Inflammatory pain in the girdles was universal (100%), however pelvic girdle involvement was explicitly reported in only 3 studies. Peripheral arthritis in ICI-PMR was present in 26% [95% CI: 9%–54%], and normal inflammatory markers were detected in 26% [95% CI: 15%–40%]. Glucocorticoids (GCs) completely improved symptoms in 83% of patients [95% CI: 66%–92%], with 13% [95% CI: 12%–34%] requiring DMARDs and 18% [95% CI: 9%–33%] experiencing relapses (Figure 1).

Two comparative studies explored differences between ICI vs primary PMR. Vermeulen et al suggested milder symptoms and better outcomes in ICI-PMR (Figure 1) while Fremont et al more frequent peripheral arthritis and higher DMARD use in the ICI group. However, the latter was a brief report with methodological limitations, warranting cautious interpretation.

ICI-GCA prevalence was 0.06% among ICI recipients. Male patients comprised 51% [95% CI: 36%–66%], with a mean age of 71 years [95% CI: 68–74]. About 50% [95% CI: 23%–77%] received anti-CTLA4 blockers (alone or with PD1 blockers), while the rest received PD1/PDL1 blockers. Clinical features included cephalic symptoms (85% [95% CI: 70%–93%]), permanent visual loss (23% [95% CI: 12%–39%]), and large-vessel involvement (62% [95% CI: 40%–80%]). High-dose GCs permitted remission in 95% [95% CI: 73%–99%], though 19% [95% CI: 7%–41%] experienced relapses and 10% [2% - 31%] required DMARDs (**Figure 1**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

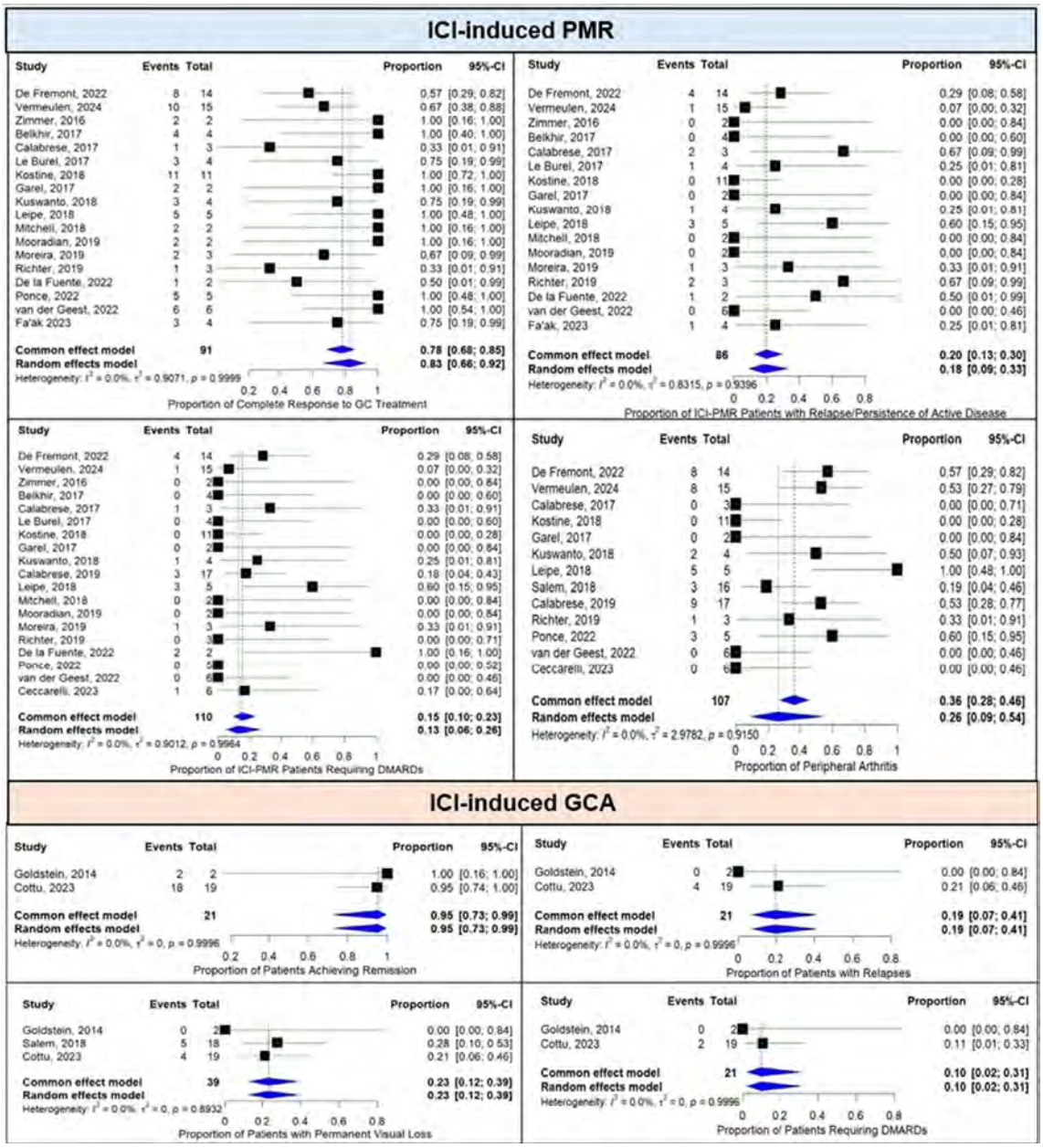


Figure 1. Forest plots related to the main outcomes and clinical features in ICI-PMR (upper panel) and ICI-GCA (lower panel)

Conclusion: ICI-induced PMR and GCA may have distinct clinical profiles than idiopathic forms, potentially with milder symptoms and better treatment responses.

Large observational data and meta-analyses on primary forms suggest higher relapse rates and prolonged GC use [1,2], yet further robust comparative studies are needed to validate whether ICI-induced syndromes truly represent a distinct and less severe clinical entity.

References

[1] Floris A et al. Clin Rheumatol. 2022
[2] Moreel L et al. Joint Bone Spine. 2023

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Hysa: None; **A. Casabella**: None; **E. Gotelli**: None; **R. Campitiello**: None; **C. Genova**: None; **E. Tanda**: None; **C. Pizzorni**: None; **A. Sulli**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **M. Cimmino**: None; **S. Paolino**: None; **M. Cutolo**: None.

Abstract Number: 1098

Tolerability of Apremilast: Gastrointestinal Side Effects Dominate While Cardiac Safety Remains Reassuring

Francisco Arias[1], Omar Hamdan[2], Asim Khanfar[3], Kristel Barturen[4] and Roa'a Alshajrawi[5], [1]University of Texas Rio Grande Valley, McAllen, TX, [2]University of Jordan, Az-Zarqa, Jordan, [3]Rochester General Hospital, Rochester, NY, [4]Universidad San Martin de Porres, McAllen, TX, [5]University of Jordan, Amman, 'Amman, Jordan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Apremilast, a PDE-4 inhibitor, is commonly indicated for patients with psoriasis as well as Behçet's disease. Although this medication is generally well tolerated, numerous adverse events have been reported, and these are among the leading causes of treatment discontinuation. This study aims to identify and describe the most common adverse effects of apremilast and to explore their relationship with underlying comorbidities, particularly cardiovascular and gastrointestinal conditions, to support more personalized and appropriate treatment selection.

Methods: The United States Food and Drug Administration Adverse Event Report System (FAERS) was searched for adverse reactions related to apremilast use. Detailed analysis of cardiac arrhythmias (Tachycardia, bradycardia, atrial fibrillation, QRS complex abnormalities, QT interval abnormalities, bundle branch block (BBB), atrioventricular blocks (AV blocks) and supraventricular tachycardia (SVT)) and gastrointestinal disorders associated with the use of apremilast were reported. Data were reported as frequencies, percentages, and as reporting odds ratios (ROR) with a 95% confidence interval (95% CI).

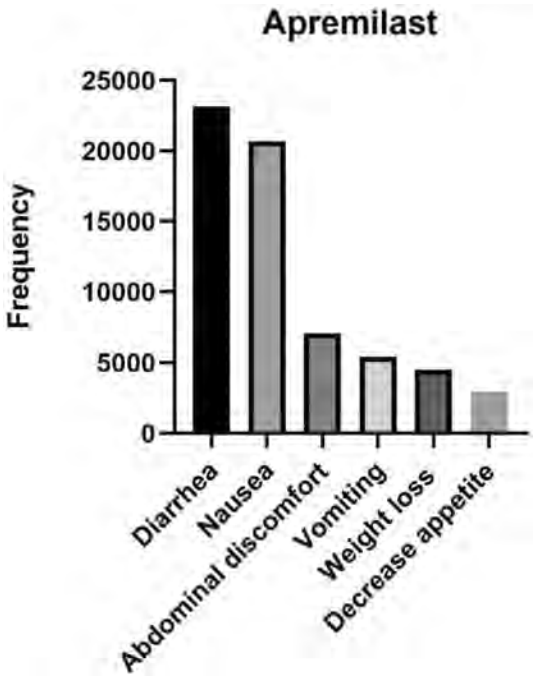
Results: We analyzed 30,179,725 adverse event reports from the FAERS database, of which 133,748 were associated with the use of apremilast. Among these, 62.91% of the cases involved females, while 4.08% had an unspecified sex. The most reported reaction group among apremilast users was gastrointestinal disorders, documented in 48,652 reports.

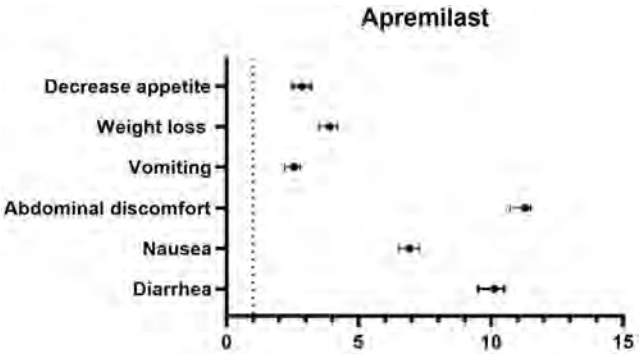
When gastrointestinal side effects were analyzed in more detail, diarrhea was the most frequently reported, occurring in 23,163 patients. Patients using apremilast had significantly higher reporting odds of diarrhea compared to users of other drugs (ROR 10.12; 95% CI: 9.98–10.27). Nausea was the second most reported gastrointestinal side effect (20,700 reports) (Figure 1), followed by abdominal discomfort (7,058 reports), with RORs of 6.91 and 11.29, respectively (Figure 2).

In contrast, when evaluating apremilast for its association with cardiac arrhythmias, none were found to have significantly increased reporting odds compared to other drug users. However, among all arrhythmias reported, the most common were tachycardia (51.6%) and atrial fibrillation (43.0%) (Table 1).

Conclusion: This FAERS analysis reveals key findings on apremilast side effects. Cardiovascular issues like tachycardia and atrial fibrillation were reported but showed no significant outcomes, reassuring for cardiac comorbidities, though careful monitoring is advised. Gastrointestinal side effects, particularly diarrhea and nausea, were the most common. Pre-existing gastrointestinal and cardiovascular comorbidities should be considered, highlighting the need for early recognition and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





Adverse reaction	Frequency	Odds Ratio	95% Confidence Interval
Tachycardia	277	0.5570	0.4950 – 0.6268
Bradycardia	11	0.03791	0.02099 – 0.06846
Atrial Fibrillation	231	0.5374	0.4722 – 0.6115
QT prolongation	1	-	-
QRS abnormalities	0	-	-
Supraventricular Tachycardia	13	0.2569	0.1491 – 0.4426
Bundle Branch Block	1	-	-
AV Block	3	0.07202	0.02322 – 0.2234

management of side effects to improve adherence. Further studies are needed to assess the impact of these adverse events on treatment discontinuation and disease control.

Disclosure: F. Arias: None; **O. Hamdan**: None; **A. Khanfar**: None; **K. Barturen**: None; **R. Alshajrawi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1099

Safety and Effectiveness of Hydroxychloroquine in the Treatment of Rheumatic Immune-Related Adverse Events

Grace Haeun Lee[1], Gregory Challener[2], Janeth Yinh[3], Jeffrey Sparks[4], Kerry L. Reynolds[5], Donald P. Lawrence[5], Meghan J. Mooradian[5], Ryan J. Sullivan[5], Hyon K. Choi[6] and Minna Kohler[7], [1]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [2]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, [3]Massachusetts General Hospital, Boston, MA, [4]Brigham and Women's Hospital, Boston, MA, [5]Massachusetts General Hospital, Boston, [6]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [7]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) has been recommended [1-3] as a steroid-sparing agent for immune checkpoint inhibitor-inflammatory arthritis (ICI-IA), preferred due to its low immunosuppressive effect. However, there is little published data on its efficacy for ICI-IA; to date, the largest study is a case series of 11 patients [4]. This study's aim was to further assess the safety and effectiveness of HCQ for treatment of rheumatic immune-related adverse events (irAEs), including ICI-IA.

Table 1: Patient characteristics

Patient Characteristics (n=40)	Number of Patients (%), Mean (SD)
Male	20 (50)
White	39 (97.5)
Age at HCQ initiation	68.6 (10.0)
Cancer Type	
Melanoma	21 (52.5)
Non-small cell lung cancer	5 (12.5)
Other*	14 (35)
Immune checkpoint inhibitor regimen	
PD-1/PD-L1 monotherapy	25 (62.5)
Dual PD-1/PD-L1 and CTLA-4 therapy	9 (22.5)
CTLA-4 monotherapy	3 (7.5)
LAG-3 (+/- other ICI)	3 (7.5)
Serology	
+RF/CCP	9 (22.5)
RF/CCP not assessed	2 (5)
+ANA	17 (42.5)
ANA not assessed	8 (20)
+SS-A/SS-B	2 (5)
SS-A/SS-B not assessed	21 (52.5)
Outcomes	
Remission or improvement to grade 1 arthritis**	17 (42.5)
Improvement, but remained ≥ grade 2 arthritis	5 (12.5)
No improvement	7 (17.5)
Unclear response or treatment course <3 months	11 (27.5)
Presentation Type	
ICI-inflammatory arthritis	34 (85)
Polymyalgia rheumatica-like	3 (7.5)
Activated crystalline arthritis	3 (7.5)
Activated osteoarthritis	1 (2.5)
Activated (pre-existing) rheumatoid arthritis	2 (5)

*Renal cell carcinoma (2), urothelial cell carcinoma (2), head and neck squamous cell carcinoma (2), Breast cancer (1), other (7)

**Includes patients requiring escalation of DMARD therapy (1) and patients who were started on HCQ as an augmenting agent (2)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Hydroxychloroquine utilization

	Mean (SD)	Median
Duration on HCQ (months)	15.5 (20.6)	7.5
Time between onset of ICI and HCQ initiation (months)	19.7 (18.7)	15
Time between discontinuation of ICI and HCQ discontinuation	14.8 (18.2)	10
DMARD Regimen	**Number of patients (%)**	
HCQ monotherapy without subsequent augmentation	25 (62.5)	
HCQ used as augmenting agent	5 (12.5)	
DMARD added onto HCQ as augmentation	9 (22.5)	
DMARD added after HCQ discontinuation	6 (15)	
HCQ Intolerance*	**Number of patients (%)**	
Patient did not tolerate HCQ	13 (32.5)	
Specific intolerance		
Gastrointestinal upset	6 (15)	
Vision change, excluding retinal toxicity	2 (5)	
Fatigue	2 (5)	
Dizziness	2 (5)	
Headache	2 (5)	
Dermatologic	1 (2.5)	
Laboratory abnormality	2 (5)	
Other	3 (7.5)	

*4 patients reported >1 AE from HCQ

Table 3: Subgroup analyses by ICI, serostatus, HCQ regimen, and arthritis type

Subgroup*	At least partial response** (%)	Remission or improvement to grade 1 arthritis (%)
ICI Type		
PD-1/PD-L1 monotherapy	15/16 (93.8)	10/16 (62.5)
Dual PD-1/PD-L1 and CTLA-4 therapy	4/7 (57.1)	4/7 (57.1)
CTLA-4 monotherapy	2/3 (66.7)	2/3 (66.7)
LAG-3 + other ICI	1/3 (33.3)	1/3 (33.3)
Serology		
RF/CCP positive	4/7 (57.1)	1/7 (14.3)
RF/CCP negative	16/20 (80.0)	14/20 (70)
ANA positive	8/12 (66.7)	7/12 (58.3)
ANA negative	10/12 (83.3)	6/12 (50)
HCQ regimen		
Monotherapy without augmentation	16/18 (88.9)	14/18 (77.8)
Arthritis Type		
ICI-IA	18/22 (81.8)	14/22 (63.6)
PMR-like	2/2 (100)	2/2 (100)
Crystalline	3/3 (100)	3/3 (100)
Activated OA	0/1 (0)	0/1 (0)

*Subjects without treatment response data were excluded from subgroup analyses

**Partial response was defined by improvement but remaining in ≥ grade 2 arthritis.

Methods: This retrospective observational study included patients at a large academic medical center who were treated with HCQ for rheumatic irAEs by rheumatologists from 2017 to 2025. Outcomes were ascertained by manual chart review. The primary outcome was arthritis control defined as grade 1 arthritis with HCQ monotherapy with grade 1 arthritis defined as at most mild pain not impacting activities of daily living [3]. HCQ and prednisone dose were recorded at the time of HCQ discontinuation or, if HCQ therapy was ongoing, at the time of data collection. Subgroup analyses were also performed.

Results: The study included 40 patients with mean age at HCQ initiation of 69 years (SD 10 years) **(Table 1)**. 25 (62.5%) patients were on anti-PD-1/PD-L1 monotherapy and 9 (22.5%) were on dual therapy with both anti-PD-1/PD-L1 and anti-CTLA-4 ICIs. Mean follow-up time was 29 months (SD 24 months) with 32 patients living at the time of chart review, 8 (25%) of whom remained on HCQ therapy. Among the 27 patients who discontinued HCQ (excluding those 5 patients who were on HCQ at time of death), 13 (48.1%) discontinued due to medication intolerance or an adverse event, 5 (18.5%) discontinued due to resolution of arthritis, and 5 (18.5%) discontinued due to inefficacy. 25 (62.5%) patients were treated with HCQ monotherapy only while 15 (37.5%) were treated with additional disease-modifying antirheumatic drug(s)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(DMARD) **(Table 2)**. 17 (42.5%) patients achieved grade 1 arthritis, noting that this includes 4 who required ongoing prednisone therapy with mean dose of 5.5 mg/day (SD 3.3 mg/day). 13 (32.5%) patients achieved grade 1 arthritis on HCQ monotherapy without concomitant prednisone dosing > 5 mg daily or subsequent escalation of DMARD therapy. Among these 13 patients, only 5 remained on ICI therapy following addition of HCQ. Seronegative patients (RF/CCP-, ANA-) had slightly higher rates of response than seropositive patients **(Table 3)**.

Conclusion: In this largest cohort to date observing patients treated with HCQ for rheumatic irAEs, we found a high rate of HCQ intolerance, in line with prior studies in SLE and RA [5, 6], noting that symptoms were often nonspecific and attributable to other treatments. While there was moderate response to HCQ therapy, many patients required escalation of DMARD therapy to achieve disease control. Most patients who achieved grade 1 arthritis after HCQ initiation had not resumed ICI therapy. These findings suggest that HCQ may be effective for a subset of patients, particularly those with mild arthritis or in cases where continuation of ICI therapy is not planned.

References:

[1] PMID: 32168068
[2] PMID: 36270461
[3] PMID: 34724392
[4] PMID: 30701346
[5] PMID: 10229401
[6] PMID: 1485814

Disclosure: G. Lee: Bristol-Myers Squibb(BMS), 12, Travel to Investigator Meeting; **G. Challener**: None; **J. Yinh**: Janssen, 2, Springer, 9; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **K. Reynolds**: Bristol-Myers Squibb(BMS), 5, Gilead, 1, Regeneron, 1, Up to Date, 2; **D. Lawrence**: None; **M. Mooradian**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 6; **R. Sullivan**: Marengo, 2, Merck/MSD, 2, 5, Novartis, 2, Pfizer, 2, Replimune, 2; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9.

Abstract Number: 1100

Associations Between Pre-existing Autoimmunity and CAR T Cell Therapy Toxicity for Cancer Treatment: A Nationwide Retrospective Cohort Study

Gregory Challener[1], Chen Wang[2], David Gritsch[2], Ilana Usiskin[3], Zandra E. Walton[1], Minna Kohler[4], Hyon K. Choi[5] and Jeffrey Sparks[6], [1]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, [2]Harvard T.H. Chan School of Public Health, Boston, [3]Division of Rheumatology, Inflammation, and Immunity, Department of Medicine, Brigham and Women's Hospital, Boston, [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [5]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [6]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients receiving chimeric antigen receptor (CAR) T cell therapy for cancer by pre-existing autoimmune disease status

	Pre-existing autoimmune disease (n=62)	Without pre-existing autoimmune disease (n=1259)
Age at admission, mean (SD)	62.3 (11.6)	60.1 (17.3)
Sex		
Male	30 (48.4%)	819 (65.1%)
Female	32 (51.6%)	440 (34.9%)
Race		
Asian or Pacific Islander	<11	58 (4.6%)
Black	<11	86 (6.8%)
Hispanic	<11	156 (12.4%)
Native American	<11	<11
Other/missing	<11	37 (2.9%)
White, n (%)	45 (72.6%)	885 (70.3%)
Comorbidities		
Hypertension	28 (45.2%)	406 (32.2%)
Hyperlipidemia	20 (32.3%)	337 (26.8%)
Ischemic heart disease	<11	92 (7.3%)
Heart failure	<11	85 (6.8%)
Type 2 diabetes	11 (17.7%)	191 (15.2%)
Chronic kidney disease	<11	160 (12.7%)
Frailty	<11	117 (9.3%)
Autoimmune disease[a]		
Rheumatologic	31 (50.0%)	
Rheumatoid arthritis	21 (33.9%)	
Systemic lupus erythematosus	<11	
Connective tissue disease	<11	
Systemic sclerosis	<11	
Systemic vasculitis	<11	
Ankylosing spondylitis	<11	
Gastrointestinal	12 (19.4%)	
Dermatologic	<11	
Endocrine	<11	
Neurologic	<11	
Underlying cancer type		
Leukemia	<11	129 (10.2%)
Non-Hodgkin lymphoma	52 (83.9%)	780 (62.0%)
Multiple myeloma	<11	297 (23.6%)
CAR T cell product		
Anti-CD19 with CD28 costimulatory domain	29 (46.8%)	466 (37.0%)
Anti-CD19 without CD28 costimulatory domain	<11	143 (11.4%)
Anti-BCMA	<11	178 (14.1%)
Unspecified, n (%)	20 (32.3%)	480 (37.1%)

Abbreviations: CAR, chimeric antigen receptor; n, number; SD, standard deviation; CD, cluster of differentiation; BCMA, B cell maturation antigen.

[a] Percentages (%) of autoimmune disease type by organ system were calculated among patients with pre-existing autoimmune disease.

Background/Purpose: Chimeric antigen receptor (CAR) T cell therapy is being investigated to treat individuals with autoimmune diseases. Data regarding the safety of CAR T cell therapy in this population is limited. We aimed to assess whether pre-existing autoimmune disease was associated with an increase in major toxicity or hospital length of stay (LOS) among patients receiving CAR T cell therapy for treatment of hematologic cancer.

Methods: This retrospective cohort study utilized nationwide United States data from the National Inpatient Sample (2021–2022) to investigate in-hospital outcomes in adult patients receiving CAR T cell therapy. The primary outcome for the study was a composite of major toxicity, defined as the occurrence of at least one of the following: cytokine release syndrome

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Hospital length of stay, toxicity, and in-hospital mortality among patients receiving chimeric antigen receptor (CAR) T cell therapy for cancer by pre-existing autoimmune disease status

	Pre-existing autoimmune disease (n=62)	Without pre-existing autoimmune disease (n=1259)
Length of stay (days), median (IQR)	14 (9–17)	14 (10–19)
Major toxicity[a], n (%)	42 (67.7%)	989 (78.6%)
CRS, all grades	34 (54.8%)	773 (61.4%)
Grade 1	20 (32.3%)	429 (34.1%)
Grade 2	11 (17.7%)	275 (21.8%)
Grade 3 or higher	<11	56 (4.4%)
ICANS, all grades	13 (21.0%)	313 (24.9%)
Grade 1	<11	62 (4.9%)
Grade 2	<11	46 (3.7%)
Grade 3 or higher	<11	84 (6.7%)
HLH	<11	17 (1.4%)
Neutropenia	23 (37.1%)	471 (37.4%)
Pneumonia	<11	40 (3.2%)
Sepsis	<11	64 (5.1%)
Intubation	<11	45 (3.6%)
Acute kidney injury	<11	185 (14.7%)
Other toxicity		
Cytopenia (includes neutropenia)	29 (46.8%)	586 (46.5%)
Lymphopenia	<11	<11
Thrombocytopenia	<11	60 (4.8%)
Anemia	<11	170 (13.5%)
Tocilizumab use, n (%)	<11	109 (8.7%)
In-hospital mortality, n (%)	<11	37 (2.9%)

Abbreviations: CAR, chimeric antigen receptor; n, number; IQR, interquartile range; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; HLH, hemophagocytic lymphohistiocytosis.

[a] Major toxicity is a composite that includes CRS, ICANS, neutropenia, HLH, pneumonia, acute kidney injury, sepsis, or intubation.

(CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), hemophagocytic lymphohistiocytosis (HLH), sepsis, pneumonia, intubation, acute kidney injury, or neutropenia. Secondary outcomes included each individual component of the primary outcome, in-hospital mortality, hospital length of stay (LOS), and tocilizumab use. Comparisons were drawn between patients with and without pre-existing autoimmune disease, identified using International Classification of Diseases, Tenth Revision (ICD-10) codes for common rheumatic, gastrointestinal, endocrine, dermatologic, and neurologic autoimmune diseases. A multivariable regression model with adjustment for age, sex, race, cancer type, and comorbidities assessed associations with hospital LOS, major toxicity, and inpatient mortality.

Results: Among 1,321 patients receiving CAR T cell therapy, 62 (4.7%) had a pre-existing autoimmune disease (**Table 1**), most commonly rheumatologic (50.0%) or gastrointestinal (19.4%). The median hospital LOS among all patients was 14 days (IQR 10-19). Patients with pre-existing autoimmune disease had a significantly shorter hospital LOS compared to patients without autoimmune disease (mean reduction of 2.1 days, 95% confidence interval [CI] 0.5, 3.6; **Tables 2 and 3**). Major toxicity was observed in 78.0% of all patients and occurred less frequently in patients with pre-existing autoimmune disease than in patients without (67.7% vs 78.6%; adjusted odds ratio 0.55, 95% CI 0.31, 0.99). Rates of CRS and ICANS were numerically lower in patients with pre-existing autoimmunity than in patients without (54.8% vs 61.4% and 21.0% vs

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

24.9%, respectively), while rates of HLH and neutropenia were similar between groups (1.6% vs 1.4% and 37.1% vs 37.4%, respectively). Tocilizumab use (11.3% among those with preexisting autoimmune disease and 8.7% among those without) and inpatient mortality (3.2% and 2.9%, respectively) were not statistically different between groups.

Conclusion: Patients with pre-existing autoimmune disease had shorter hospital stays and lower risk of major toxicity following CAR T cell therapy for cancer treatment. This nationwide study offers reassurance as to its safety in this population while providing additional data for research studies of CAR T cell therapy to treat autoimmune diseases.

Table 3. Patients with pre-existing autoimmune disease receiving chimeric antigen receptor (CAR) T cell therapy

Disclosure: G. Challener: None; **C. Wang**: None; **D. Gritsch**: None; **I. Usiskin**: None; **Z. Walton**: Bristol-Myers Squibb(BMS), 2; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 1101

Distinct Clinical Phenotypes of Immune Checkpoint Inhibitor–Associated Arthritis: Comparative Analysis of Inflammatory Arthritis, Polymyalgia Rheumatica-like, Activated Crystalline, and Activated Osteoarthritis

Heba Altarawneh[1], Gregory Challener[2], Mazen Nasrallah[3], Janeth Yinh[4], Hyon K. Choi[5] and Minna Kohler[6], [1]Mass General Hospital, Boston, MA, [2]MGH, Boston, MA, [3]MGB-Salem Hospital, Lynn, MA, [4]Massachusetts General Hospital, Boston, MA, [5]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [6]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitor (ICI)–associated arthritis has been classified into distinct phenotypes, including inflammatory arthritis (IA), polymyalgia rheumatica (PMR)-like syndrome, activated crystalline arthritis, and activated osteoarthritis (aOA). However, the boundaries between these phenotypes are often challenging to discern, and differences in their presentation, natural history and outcomes remain poorly defined[1].

Methods: We retrospectively analyzed 85 patients with ICI-associated arthritis, classified as IA (n=58), crystalline (n=9), PMR-like (n=7), and aOA (n=23), referred to rheumatology at a tertiary center (Jan 2014–Feb 2020). We compared clinical features, joint involvement, serologies, synovial fluid, treatment, symptom duration, and DMARD use. Chi-square tests were used for proportions and Kruskal-Wallis for medians.

Results: IA typically presented as polyarthritis (43%) with frequent knee (79%), PIP (43%), and MCP (41%) involvement. PMR-like cases had predominant shoulder (71%) and MCP (71%) involvement. Crystalline arthritis favored elbows (33%) and hips (33%). aOA was more often monoarthritis (26%) with a degenerative pattern (wrists 30%, PIPs 35%, DIPs 4%) (p=0.7). Inflammatory synovial fluid was most frequent in IA (31%), and rare in PMR-like (0%) and aOA (4%) (p=0.1). Peripheral involvement in both IA and PMR-like suggests classification may hinge on shoulder involvement, despite overlap with IA features.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographics, Cancer Characteristics, ICI Regimen, and Concomitant irAE

Characteristic	
Age, median (IQR), years	70 (61–75)
Sex, N (%)	
– Male	56 (66%)
– Female	29 (34%)
Cancer type, N (%)	
– Melanoma	59 (69%)
– Lung cancer	16 (19%)
– Renal cell carcinoma	4 (5%)
– Head & neck cancer	4 (5%)
– Breast cancer	2 (1%)
– Other	6 (7%)
ICI type, N (%)	
– PD1/PD-L1 monotherapy	53 (62%)
– PD1/PD-L1 + CTLA-4 combination	32 (38%)
– PD1/LAG3	1 (1%)
Concomitant irAEs, N (%)	
– Colitis/gastritis	18 (21%)
– Endocrine	12 (14%)
– Pneumonitis	12 (14%)
– Myositis	22 (26%)
– Pancreatitis	11 (13%)
– Neurological	1 (1%)
– Myocarditis/pericarditis	1 (1%)
– Renal	5 (6%)
– Ocular	2 (2%)
– Cutaneous	1 (1%)

Abbreviations: ICI = Immune Checkpoint Inhibitor; irAE = immune-related Adverse Event; IQR = Interquartile Range; N= number of patients.

Table 2: Clinical Features, Joint Distribution, Serologic Markers, and Treatment Patterns by ICI-Arthritis Phenotype

		Total (N=85)	IA (N=58)	Crystalline (N=9)	PMR-like (N=7)	AOA (N=23)	P- value*
riRAE SITC grade at onset, N (%)	**Grade 1**	63	46 (79)	4 (44)	4 (57)	15 (65)	0.2
	Grade 2	7	3(5)	1 (11)	1 (14)	4 (17)	
	Grade 3+	15	9 (16)	4 (44)	2 (29)	4 (17)	
Arthritis pattern, N (%)	**Monoarthritis**	15	11 (19)	0 (0)	0 (0)	6 (26)	0.4
	Oligoarthritis	42	22 (38)	5 (56)	4 (57)	10 (43)	
	Polyarthritis	28	25 (43)	4 (44)	3 (43)	7 (30)	
Extraarticular involvement, N (%)	**Dactylitis**	0	0 (0)	0 (0)	0 (0)	0 (0)	0.7
	Enthesitis	4	4 (7)	0 (0)	0 (0)	2 (9)	
	Tenosynovitis	38	29 (50)	4 (44)	2 (29)	8 (35)	
Joint involvement, N (%)	**Shoulders**	40	29 (50)	5 (56)	5 (71)	10 (43)	0.7
	Elbows	21	14 (24)	3 (33)	2 (29)	4 (17)	
	Wrists	24	19 (33)	0 (0)	2 (29)	7 (30)	
	MCPs	28	24 (41)	1 (11)	5 (71)	5 (22)	
	PIPs	32	25 (43)	2 (22)	3 (43)	8 (35)	
	DIPs	9	6 (10)	1 (11)	0 (0)	1 (4)	
	Hips	22	11 (19)	3 (33)	3 (43)	9 (39)	
	Knees	57	46 (79)	5 (56)	3 (43)	12 (52)	
	Ankles	28	24 (41)	3 (33)	2 (29)	5 (22)	
	MTPs	11	9 (16)	3 (33)	0 (0)	3 (13)	
	TMJ	4	3 (5)	0 (0)	1 (14)	0 (0)	
Serostatus, N (%)	**RF/CCP +**	8	6 (10)	0 (0)	0 (0)	0 (0)	0.3
	ANA +	9	4 (7)	1 (11)	0 (0)	3 (13)	
	SS-A/SS-B +	1	1 (2)	0 (0)	0 (0)	0 (0)	
Synovial fluid, N (%)	**Inflammatory fluid**	19	18 (31)	1 (11)	0 (0)	1 (4)	0.1
	Non-inflammatory fluid	17	13 (22)	3 (33)	1 (14)	7 (30)	
	Not sampled	49	27 (47)	5 (56)	6 (86)	15 (65)	
ICI management due to rIRAE, N (%)	**ICI continued**	73	43 (74)	7 (78)	3 (43)	19 (83)	0.4
	ICI held and resumed	12	7 (12)	1 (11)	1 (14)	2 (9)	
	ICI discontinued	15	8 (14)	1 (11)	3 (43)	2 (9)	
Arthritis management, N (%)	**NSAID**	54	36 (62)	8 (89)	6 (86)	15 (65)	0.9
	PO steroid	55	39 (67)	6 (67)	7 (100)	14 (61)	
	IA-CS	34	21 (36)	4 (44)	5 (71)	10 (43	
	HCQ	33	23 (40)	5 (56)	3 (43)	8 (35)	
	SSZ	28	25 (43)	2 (22)	1 (14)	3 (13)	
	MTX	10	9 (16)	1 (11)	1 (14)	0 (0)	
	IL-6i	1	1 (2)	0 (0)	0 (0)	0 (0)	
	TNFi	5	4 (7)	0 (0)	0 (0)	1 (4)	

Abbreviations: SITC=Society for Immunotherapy of Cancer, ICI = immune checkpoint inhibitor; IA = inflammatory arthritis; PMR = polymyalgia rheumatica; AOA = activated osteoarthritis; RF = rheumatoid factor; CCP = cyclic citrullinated peptide; ANA = antinuclear antibody; SSA/SSB = Sjögren's-syndrome-related antigens A and B; NSAID = non-steroidal anti-inflammatory drug; PO = oral; IA-CS= intraarticular corticosteroid; HCQ = hydroxychloroquine; SSZ = sulfasalazine; MTX = methotrexate; IL-6i = interleukin-6 inhibitor; TNFi = tumor necrosis factor inhibitor; DMARD = disease-modifying anti-rheumatic drug; irAE = immune-related adverse event.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

*P-value calculated using chi-square test.

Table 3: Symptom Duration and DMARD Exposure by ICI-Arthritis Phenotype

	Total (N=85)	IA (N=58)	Crystalline (N=9)	PMR-like (N=7)	AOA (N=23)	P- value*
Duration of symptoms, median months(IQR)	23 (5-44)	14 (6-14)	35 (26-72)	65 (63-70)	31 (21-47)	0.2
Total duration on DMARD, , median months(IQR)	24 (7-55)	33 (9-63)	13 (6-51)	12 (12-34)	20 (6-39)	0.6

*P-value calculated using Kruskal-Wallis test.

PMR-like patients had the longest symptom duration (65 months, IQR 63–70) but the shortest DMARD exposure (12 months, IQR 12–34). Crystalline (35 months, IQR 26–72) and aOA (31 months, IQR 21–47) had shorter durations but comparable DMARD use (13 months, IQR 6–51; 20 months, IQR 6–39) (p=0.2). IA had the shortest duration (14 months, IQR 6–14) but longest DMARD use (33 months, IQR 9–63) (p=0.3), reflecting higher inflammatory activity. DMARDs—methotrexate (16%), sulfasalazine (43%), hydroxychloroquine (40%), and TNFi (7%)—were used almost exclusively in IA (p=0.9). Among aOA patients, 48% had concurrent inflammatory arthritis, affecting interpretation of DMARD use. Limited DMARD use in PMR-like cases may reflect historical steroid-based treatment; however, small sample size (n=7) limits interpretation.

Conclusion: ICI-associated arthritis includes phenotypes with differing inflammatory burden, duration, and treatment. IA is more active and treated more aggressively; others persist longer but receive less therapy. Whether these differences reflect biology or treatment variation is unclear. This historical cohort had low biologic use, possibly contributing to symptom duration. Findings support phenotype-based approaches that balance arthritis and cancer therapy, but small subgroup sizes warrant further study.

Disclosure: H. Altarawneh: None; **G. Challener**: None; **M. Nasrallah**: None; **J. Yinh**: Janssen, 2, Springer, 9; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9.

Abstract Number: 1102

Checkpoint Inhibitor Inflammatory Arthritis: Single Center Case Identification and Chart Validation.

Julia Barasch[1], Nilasha Ghosh[2], Deanna Jannat-Khah[3], Kyle Ge[4], Jeffrey Curtis[5] and Anne R. Bass[3], [1]NYP- Weill Cornell, New York, [2]Hospital for Special Surgery, New York, NY, [3]Hospital For Special Surgery, New York, NY, [4]Hospital for Special Surgery, New York, [5]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: New onset inflammatory arthritis (IA) is reported in 6% of patients who receive immune checkpoint inhibitors (ICI). We previously developed an administrative claims-based algorithm to identify patients with ICI-IA.[1] In this study, we compare ICI-IA cases at a single center identified in administrative claims and those identified via manual medical record review.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of a random sample of ICI-treated patients at HSS, found to have ICI-IA or not to have ICI-IA after chart validation

	Not ICI-IA ($n = 66$) n (%)	ICI-IA, ($n = 53$) n (%)
Age, mean (SD)	69 (9)	62 (19)
Female	27 (42)	23 (43)
Medicare insurance	39 (59)	29 (55)
Doctor Type seen at HSS		
Rheumatologist MD	36 (55)	52 (98)
Orthopedist MD	21 (32)	1 (2)
Other MD	3 (5)	0 (0)
Cancer Type		
Melanoma	20 (30)	13 (25)
Bladder/ Urothelial Cancer	8 (12)	5 (9)
Renal Cell Carcinoma	7 (11)	6 (11)
Other cancer n (%)	31 (47)	29 (55)
Anti-PD1/PDL1*	55 (83)	51 (96)
Registry Patient**	11 (17)	26 (49)
Treatment for joint symptoms		
Steroids	—	46 (87)
DMARD	—	32 (60)

* Instances of treatment with anti PD1/ anti PDL1 medication as part of regimen (either as monotherapy or part of combination regimen with some patients receiving more than one PD1/PDL1 therapy)
** Enrolled in HSS or RADIOS rheumatic irAE Registry
ICI = immune checkpoint inhibitor; IA = inflammatory arthritis; HSS = Hospital for Special Surgery

Table 2: Characteristics of patients with ICI-IA identified by applying claims-based algorithm to Komodo HealthMap Database

	ICI-IA, ($n = 142$) n (%)
Age, mean (SD)	64 (11)
Female	71 (50)
Medicare insurance	68 (48)
Doctor Type seen at HSS	
Rheumatologist / Internal Medicine MD	42 (30)
Orthopedist MD	43 (30)
Other MD	57 (40)
Pembrolizumab*	74 (52)
Nivolumab*	64 (45)

* Instances of treatment with Pembrolizumab or Nivolumab medication as part of regimen (either as monotherapy or part of combination regimen with some patients receiving more than one ICI therapy)

Methods: Using an Alteryx electronic health record (EHR) screening tool, we identified patients seen at Hospital for Special Surgery (HSS) who received ICI therapy between 2016-2025. Chart adjudication was performed independently by a team of three physicians to determine whether patients had ICI-IA. We defined ICI-IA as a condition developing within 1 year of receiving ICI, in patients without a prior diagnosis of inflammatory arthritis or PMR. The diagnosis was verified by 1. MD documentation in the EHR; or 2. treatment with steroids or DMARDs for joint symptoms; or 3. imaging or joint histopathology demonstrating joint inflammation. Patients with ICI-IA treated at HSS were also identified by applying our administrative claims algorithm to the de-identified Komodo Healthmap dataset which includes patients on commercial insurance, managed and fee for service Medicare.

Results: ICI-treated patients seen at HSS (n=500) were identified and a random sample of 119 of these patients' charts were reviewed and extracted. Of these, adjudicators recognized 53/119 (45%) as having ICI-IA (44 ICI-arthritis, 2 ICI-arthralgia, 7 ICI-PMR) and 66/119 (55%) as not having ICI-IA. Patients with ICI-IA had a mean (SD) age 62 (19) years, 52 (98%) were seen by a rheumatologist, 51(96%) were enrolled in an HSS irAE registry, and 46 (87%) received oral steroids for management of joint symptoms (Table 1). Of the patients who were seen at HSS for joint-related symptoms but did not have ICI-IA, 34 (51%) of patients had OA or other non-inflammatory joint pain (such as bursitis or tendonitis) leading to presentation and others had pre-existing inflammatory arthritis. The characteristics of patients identified as having ICI-IA who were treated at HSS in the unidentified Komodo dataset is shown in Table 2. In this cohort of 142 ICI-IA patients, average

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

age (SD) was 64 (11), 71 (50%) were female, 68 (48%) were insured with Medicare, and 42 (30%) were seen by a rheumatologist or internal medicine provider.

Conclusion: Demographic characteristics and insurance of patients with ICI-IA identified through chart review and through query of the deidentified Komodo dataset were similar but fewer in Komodo were seen by a rheumatologist. In a future study using tokenization and linkage of the Komodo claims to cases identified at HSS, we will determine the positive predictive value of the ICI-IA algorithm.

[1]Bass AR et al. Rheumatology (Oxford). 2025;64(4):1637-1642

Disclosure: J. Barasch: None; **N. Ghosh**: None; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **K. Ge**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **A. Bass**: None.

Abstract Number: 1103

Validation of the Health Assessment Questionnaire Disability Index in Immune Checkpoint Inhibitor-Induced Inflammatory Arthritis

Kayla Chubbs[1], Carrie Ye[2], Shahin Jamal[3], Marie Hudson[4], Janet Pope[5], Tom Appleton[6], Sabrina Hoa[7], Alexandra Saltman[8], Megan Himmel[8], Nancy Maltez[9], Faiza Khokhar[10], Alexandra Ladouceur[11], Ines Colmegna[12], May Choi[13], Manar Elsayed[2] and Janet Roberts[1], [1]Dalhousie University, Halifax, NS, Canada, [2]University of Alberta, Edmonton, AB, Canada, [3]University of British Columbia, Vancouver, BC, Canada, [4]McGill University, Montréal, QC, Canada, [5]University of Western Ontario, London, ON, Canada, [6]Western University, London, ON, Canada, [7]University of Montreal, Brossard, QC, Canada, [8]University of Toronto, Toronto, ON, Canada, [9]Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [10]Hamilton Ontario, Hamilton, ON, Canada, [11]University of Montreal, Montreal, QC, Canada, [12]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [13]University of Calgary, Calgary, AB, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The use of immune checkpoint inhibitors (ICI) continues to increase with an expanding number of indications across varying cancer types and stages. ICIs can induce an inflammatory arthritis (ICI-IA) which can have significant impacts on patient function and quality of life. The Health Assessment Questionnaire Disability Index (HAQ-DI) is a health-related patient-reported outcome measure widely used to assess functional limitations in patients with rheumatoid arthritis. To date, use of the HAQ-DI has not been studied in patients with ICI-IA. Our objective was to evaluate the measurement properties (reliability, construct validity and responsiveness) of the HAQ-DI in patients with ICI-IA.

Methods: All patients enrolled in a multicenter prospective cohort, with a diagnosis of ICI-IA, who completed a baseline HAQ-DI at first study visit were included. Demographic, clinical and laboratory data including the HAQ-DI were extracted from the study database. Internal consistency reliability was assessed using Cronbach's alpha coefficient with values ≥ 0.7 considered acceptable. Construct validity was assessed by correlating HAQ-DI scores with other measures of disease activity including c-reactive protein (CRP), tender joint count (TJC), swollen joint count (SJC), patient global assessment of disease activity (PtGA) as well as physician global assessment of disease activity (PGA). Responsiveness was assessed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of subjects at time of baseline assessment (n=96) Legend: TJC = tender joint count; SJC = swollen joint count, PtGA = patient global assessment of disease activity, PGA = physician global assessment of disease activity, CRP = c-reactive protein, CTCAE = common terminology criteria for adverse events, HAQ-DI = health assessment questionnaire disability index

Age, years, median (range)	67 (39-84)
Sex, number (%) of subjects	
Male	48 (50)
Female	48 (50)
Ethnicity, number (%) of subjects	
White	69 (72)
Chinese	5 (5)
Black	3 (3)
Latin American	1 (1)
Arab	1 (1)
Missing	17 (18)
Cancer type, number (%) of subjects	
Melanoma	24 (25)
NSCLC	19 (20)
RCC	12 (13)
Bladder	6 (6)
Breast	7 (7)
Other	28 (29)
Stage, number (%) of subjects	
½	7 (7)
3	27 (28)
4	57 (60)
Missing	5 (5)
Metastatic disease, number (%) of subjects	
Yes	74 (77)
No	21 (22)
Missing	1 (1)
Arthritis subtype, number (%) of disease	
Polyarticular	61 (64)
Oligoarticular	24 (25)
Monoarticular	6 (6)
Axial	1 (1)
Missing	4 (4)
TJC, median (range)	6 (0, 36)
Missing	4 (4)
SJC, median (range)	2 (0, 30)
Missing	4 (4)
PtGA, median (range)	5 (0,10)
Missing	1 (1)
PGA, median (range)	5 (0,10)
Missing	12 (13%)
CRP, median (range)	7.1 (.28 – 172.7)
Missing	17 (18)
CTCAE grade, number (%) of subjects	
1	16 (17)
2	58 (60)
3	18 (19)
4	0 (0)
Missing	4 (4)
HAQ-DI score	
Standard score: median (range)	0.5 (0,3)
Alternative score: median (range)	0.375 (0,3)

by calculating the standardized response mean (SRM) and effect size (ES) in those with ≥ 3-point improvement on the PGA (defined a priori) at 3-6 month follow up.

Results: Ninety-six patients from 9 centers were included in this study. The median age of study participants was 67 years (range 39-84), 50% were female and the most common malignancies were melanoma and non-small cell lung cancer (Table 1). The most common presentation of ICI-IA was polyarticular involvement (64%) with a median TJC of 6 (range 0-36) at baseline and SJC of 2 (range 0-30). The median HAQ-DI at baseline was 0.5 (range 0, 3). The median HAQ-DI at 6 months (n=66) was 0.125 (range 0, 2.375). HAQ-DI floor and ceiling effects for the whole group were 24% and 1%, respectively. Cronbach's alpha for the 8 HAQ-DI categories ranged from 0.72-0.91 and for the 20 HAQ DI Items was 0.94 suggesting high internal consistency reliability (Table 2). The HAQ-DI had a significant positive correlation with CRP, TJC, SJC, ptGA and PGA (Table 3). Responsiveness of the HAQ-DI was moderate with an SRM =1.4 and ES = 0.3 when calculated in the 23 participants with ≥ 3-point improvement on the PGA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: HAQ-DI Score component and overall internal consistency reliability (Cronbach's alpha) component analysis at baseline (n=96)

HAQ Components	Cronbach's alpha
Dressing	0.75
Rising	0.91
Eating	0.85
Walking	0.86
Hygiene	0.75
Reach	0.72
Grip	0.80
Activity	0.88
Overall mean HAQ-DI Score	0.94

Table 3: HAQ correlations with clinical and demographic variables Legend: CRP = c-reactive protein, TJC = tender joint count, SJC = swollen joint count, PtGA = patient global assessment of disease activity, PGA = physician global assessment of disease activity

Demographic Variables	R*	p-value
Sex	-0.19	0.06
Age	-0.0024	0.98
Clinical Variables		
Stage	-0.03	0.75
Metastatic disease	-0.05	0.62
CRP	0.19	0.05
TJC	0.20	0.06
SJC	0.22	0.03
PtGA	0.40	<0.0001
PGA	0.25	0.02

*Spearman correlation coefficient used

Conclusion: In this prospective cohort study, the HAQ-DI was reliable, valid and sensitive to change in patients with ICI-IA. Future research will further explore content validity, establish the minimal clinically important difference of the HAQ-DI in ICI-IA and explore correlation of the HAQ-DI with the physical functioning components of other patient-reported outcome measures currently validated in cancer patients.

Disclosure: K. Chubbs: None; **C. Ye**: None; **S. Jamal**: AbbVie/Abbott, 1, 2, 5, Amgen, 1, Fresenius Kabi, 1, 2, 5, Merck, 1, 2, 5, Organon, 1, 5, Pfizer, 1, 2, 5, Sandoz, 1, UCB, 1, 2, 5; **M. Hudson**: Astra Zeneca, 5, 6, Boehringer-Ingelheim, 5, Merck, 1, Pfizer, 5; **J. Pope**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Frese, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mallinckrodt Pharmaceuticals, 2, 5, Merck/MSD, 2, Mitsubishi Tanabe Pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2, Sanofi, 2, Teva, 2, UCB, 2, Viatris, 2; **T. Appleton**: None; **S. Hoa**: None; **A. Saltman**: None; **M. Himmel**: None; **N. Maltez**: None; **F. Khokhar**: None; **A. Ladouceur**: None; **I. Colmegna**: None; **M. Choi**: AstraZeneca, 2, 5, 6, Celltrion, 2, MitogenDx, 2, Organon, 6, Werfen, 2; **M. Elsayed**: None; **J. Roberts**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1104

Immune Checkpoint Inhibitors and Cardiovascular Risk in Patients with Rheumatoid Arthritis and Cancer

Kevin Sheng-Kai Ma[1], Rachael Stovall[2], Jeffrey Sparks[3], You Wu[2], Richard Cheng[4], Gregory Challener[5], Hans von Eckstaedt[2], Bhavik Bansal[6], Petros Grivas[7], Steven Chen[8], Jean Liew[9] and Namrata Singh[7], [1]Center for Global Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States, Philadelphia, PA, [2]University of Washington, Seattle, WA, [3]Brigham and Women's Hospital, Boston, MA, [4]University of Washington, Seaattle, WA, [5]MGH, Boston, MA, [6]UT Southwestern Medical Centre, Dallas, TX, [7]University of Washington, BELLEVUE, WA, [8]Massachusetts General Hospital, Boston, [9]Boston University, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients (pts) with rheumatoid arthritis (RA) face a higher lifetime burden of cardiovascular disease (CVD) vs the general population with approximately 1.5-2-fold increase in heart failure, myocardial infarction and CVD mortality. Recent data suggest that immune checkpoint inhibitors (ICIs), a major anti-cancer therapy class, may also contribute to CVD risk. We conducted a comparative evaluation of CVD outcomes in pts with cancer receiving ICI-based therapy, focusing on differences between those with vs without pre-existing RA. We hypothesized that pts with pre-existing RA receiving ICI-based therapy would have a higher risk of adverse CVD events vs those without RA.

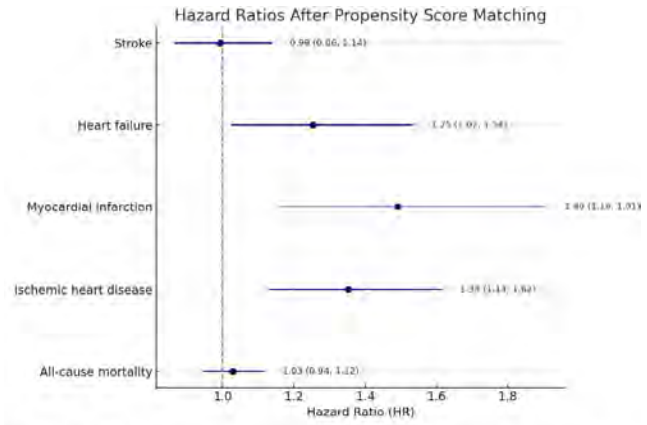
Methods: We conducted a population-based cohort study using electronic health records of pts with cancer receiving ICIs between 2011 and 2025 from 101 U.S. healthcare organizations. We identified pts with pre-existing RA using at least two diagnostic codes who were treated with anti-programmed death-1/programmed death ligand-1 (PD-1/PD-L1) and/or cytotoxic T-lymphocyte associated protein 4 (CTLA4) agents. We calculated propensity scores using covariates including demographics (age, sex, race/ethnicity), comorbidities, cancer type, metastatic status, previous and concurrent anti-cancer treatments, history of exposure to statins and systemic steroids. Pts with RA on ICI were propensity-score matched 1:1 with pts treated with ICI without RA. We used Cox proportional hazards models to assess the risk of individual outcomes of all-cause mortality, stroke, ischemic heart disease, including myocardial infarction and heart failure.

Results: We analyzed 2,270 pts with pre-existing RA treated with ICI and 2,270 propensity score-matched comparators (Table 1). Mean age was 69 years, 60% were female, 78% were White. After initiation of ICI-based therapy, over a mean follow-up of 47.6 months, pts with RA did not have a significantly higher risk of all-cause mortality (HR 1.03, 95% CI 0.94–1.12) or stroke (HR 0.99, 95% CI 0.86–1.14) vs pts without RA. However, the risk for ischemic heart disease (HR 1.35, 95% CI 1.13–1.62), specifically myocardial infarction (HR 1.49, 95% CI 1.16–1.91) and heart failure (HR 1.25, 95% CI 1.02–1.54) were higher for pts with RA vs pts without RA (**Figure 1**).

Conclusion: Among pts on ICI-based therapy, those with pre-existing RA did not have significant higher all-cause mortality or risk for stroke, but higher risk of ischemic heart disease and heart failure vs pts without RA. Our hypothesis-generating findings are consistent with the known CVD burden in pts with RA and cancer that may be possibly exacerbated by ICI. Further studies are needed to validate our data and, also, investigate prophylaxis, early diagnosis and proper management of CVD in pts with RA receiving ICI-based therapy for cancer.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	RA (n=2,270)	Non-RA (n=2,270)	SMD
Age at Index			
Mean ± SD	68.6 ± 10.2	68.9 ± 11.1	0.025
Demographics, n (%)			
Female	1,365 (60.1)	1,342 (59.1)	0.021
Male	820 (36.1)	860 (37.9)	0.037
White	1,761 (77.6)	1,764 (77.7)	0.003
Black / African American	206 (9.1)	172 (7.6)	0.054
Asian	81 (3.6)	109 (4.8)	0.062
BMI (kg/m^2)	27.3 ± 6.8	27.2 ± 6.5	0.010
Comorbidities, n (%)			
Lung cancer	1,061 (46.7)	1,088 (47.9)	0.024
Melanoma	315 (13.9)	302 (13.3)	0.017
Digestive organ cancers	382 (16.8)	369 (16.3)	0.015
Urinary tract cancers	320 (14.1)	311 (13.7)	0.011
Hypertension	1,635 (72)	1,648 (72.6)	0.013
Chronic kidney disease	506 (22.3)	483 (21.3)	0.025
Type 2 diabetes mellitus	612 (27)	586 (25.8)	0.026
Hyperlipidemia	1,299 (57.2)	1,265 (55.7)	0.03
Tobacco use	301 (13.3)	257 (11.3)	0.059
Psoriasis	128 (5.6)	122 (5.4)	0.012
Crohn's disease	24 (1.1)	22 (1)	0.009
Ulcerative colitis	31 (1.4)	25 (1.1)	0.024
Ankylosing spondylitis	30 (1.3)	34 (1.5)	0.015
Other therapy for cancer, n (%)			
Radiation therapy	795 (35)	814 (35.9)	0.017
Medications/Therapies, n (%)			
Antineoplastics, alkylating agents	98 (4.3)	98 (4.3)	<0.001
Antineoplastics, antibiotics	122 (5.4)	127 (5.6)	0.01
Antineoplastics, antimetabolites	929 (40.9)	953 (42)	0.021
Corticosteroids for systemic use	2,090 (92.1)	2,118 (93.3)	0.047
Statins	1,186 (52.2)	1,182 (52.1)	0.004



Models adjusted for demographics, comorbidities*, metastatic disease, prior cancer, and previous exposure to medical treatments

*Type 2 diabetes mellitus, hypertension, hyperlipidemia, chronic kidney disease, obesity

Figure 1. Risk of cardiovascular outcomes in persons with cancer on ICI with versus without RA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Sheng-Kai Ma: None; **R. Stovall**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **Y. Wu**: None; **R. Cheng**: None; **G. Challener**: None; **H. von Eckstaedt**: None; **B. Bansal**: None; **P. Grivas**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, Genentech, 2, Gilead, 2, Janssen, 2, Pfizer, 2; **S. Chen**: None; **J. Liew**: None; **N. Singh**: None.

Abstract Number: 1105

Association Between Pre-existing Rheumatoid Arthritis and Immune-related Adverse Events in Patients with Cancer Receiving Immune Checkpoint Inhibitors

Kevin Sheng-Kai Ma[1], You Wu[2], Rachael Stovall[2], Jean Liew[3] and Namrata Singh[4], [1]Center for Global Health, Perelman School of Medicine, Philadelphia, PA, [2]University of Washington, Seattle, WA, [3]Boston University, Boston, MA, [4]University of Washington, Bellevue, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1. Baseline characteristics of patients on immune checkpoint inhibitors with and without pre-existing rheumatoid arthritis (RA) after propensity score matching

Characteristic	RA (n=1,976)	Non-RA (n=1,976)	SMD
Age at Index			
Mean ± SD	69.0 ± 9.5	68.6 ± 10.6	0.04
Demographic, n (%)			
Female	1,091 (55.2)	1,090 (55.2)	<0.01
Male	799 (40.3)	824 (41.7)	0.03
White	1,516 (76.7)	1,507 (76.3)	0.01
Black or African American	179 (9.1)	176 (8.9)	0.01
Asian	71 (3.6)	87 (4.4)	0.04
Other or Unknown Race	145 (7.3)	139 (7.0)	0.01
Hispanic or Latino	78 (3.9)	73 (3.7)	0.01
Cancer types and comorbidities, n (%)			
Lung cancer	1,128 (57.1)	1,133 (57.3)	0.01
Melanoma	311 (15.7)	290 (14.7)	0.03
Digestive organ cancers	422 (21.4)	423 (21.4)	<0.01
Urinary tract cancers	361 (18.3)	350 (17.7)	0.01
Secondary malignancies	737 (37.3)	755 (38.2)	0.02
Hypertension	1,451 (73.4)	1,456 (73.6)	0.01
Overweight and obesity	572 (28.9)	579 (29.3)	0.01
Dyslipidemia	1,274 (64.5)	1,247 (63.1)	0.03
Type 2 diabetes mellitus	579 (29.3)	583 (29.5)	<0.01
Procedures, n (%)			
Radiation oncology treatment	713 (36.1)	740 (37.4)	0.03
Medications, n (%)			
Tumor necrosis factor alpha inhibitors	103 (5.2)	86 (4.4)	0.04
Corticosteroids for systemic use	1,791 (90.6)	1,799 (91.0)	0.01
Janus kinase inhibitors	26 (1.3)	16 (0.8)	0.05
Methotrexate	345 (17.5)	381 (19.3)	0.05
Sulfasalazine	80 (4.0)	75 (3.8)	0.01
Leflunomide	57 (2.9)	48 (2.4)	0.03

SMD: standardized mean difference; SD: standard deviation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Effect of pre-existing rheumatoid arthritis on clinical outcomes among patients with cancer receiving immune checkpoint inhibitors after propensity score matching

Outcomes	RA Events (n=1,976)	Non-RA Events (n=1,976)	HR	95% CI	P-value (log-rank)
Colitis	232	206	1.12	(0.93, 1.36)	0.22
Cutaneous irAEs	307	299	**1.18**	**(1.01, 1.39)**	**0.04**
Hepatic irAEs	244	231	1.08	(0.91, 1.30)	0.38
Pneumonitis	372	335	**1.17**	**(1.01, 1.36)**	**0.04**

CI: confidence interval; HR: hazard ratio; irAE: immune-related adverse event

Table 3. Subgroup analysis stratified by sex, after propensity score matching

Sex	Females					Males				
Outcomes	RA Events (n=1,087)	Non-RA Events (n=1,087)	HR	95% CI	P-value (log-rank)	RA Events (n=799)	Non-RA Events (n=799)	HR	95% CI	P-value (log-rank)
Colitis	145	109	**1.32**	**(1.03, 1.70)**	**0.03**	83	72	1.18	(0.86, 1.61)	0.32
Cutaneous irAEs	178	160	**1.26**	**(1.02, 1.57)**	**0.03**	116	124	1.10	(0.85, 1.41)	0.47
Hepatic irAEs	146	140	1.06	(0.84, 1.33)	0.64	96	90	1.14	(0.85, 1.52)	0.38
Pneumonitis	193	157	**1.36**	**(1.10, 1.68)**	**<0.01**	160	146	1.14	(0.91, 1.43)	0.25

CI: confidence interval; HR: hazard ratio; irAE: immune-related adverse event

Background/Purpose: Immune checkpoint inhibitors (ICIs), widely used to treat a variety of cancers, are associated with immune-related adverse events (irAEs) that are increasingly encountered in rheumatology clinics. However, it remains unclear how outcomes differ between patients with and without pre-existing rheumatoid arthritis (RA) receiving ICIs for cancer treatment. We aimed to compare irAE risk following ICI initiation between those with and without RA.

Methods: We conducted a population-based cohort study including patients receiving ICIs from 101 U.S. health care organizations between 2011 and 2025 in the U.S. We identified patients with pre-existing RA based on the presence of ≥2 ICD-10 codes before treatment with ICIs, including anti–programmed death-1/programmed death ligand-1 (PD-1/PD-L1) and cytotoxic T-lymphocyte–associated protein 4 (CTLA-4) agents. Propensity scores were calculated using demographics (age, sex, race/ethnicity), comorbidities, cancer type, metastatic status, prior cancer therapies, and previous RA treatments. Patients with RA receiving ICIs were matched 1:1 to ICI-treated patients without RA using propensity score matching. We then used Cox proportional hazards models to evaluate the risk of cutaneous, pulmonary, hepatic, and gastrointestinal irAEs among these two groups, overall and stratified by sex.

Results: We included 1,976 patients with RA and 1,976 propensity score-matched comparators (**Table 1**), with mean age 69 years, 55% female and 76% White. Lung cancer was the most common malignancy (57.1%) and 36.1% of patients with RA underwent radiation oncology treatment. After propensity score matching, those with RA had an 18% higher risk of cutaneous irAEs (aHR 1.18, 95% CI 1.01-1.39) and 17% higher risk of pneumonitis (aHR 1.17, 95% CI 1.01-1.36) versus those without RA (**Table 2**). When stratified by sex, females with RA had a higher risk than females without RA for cutaneous irAEs (aHR 1.26, 95% CI 1.02-1.57), colitis (aHR 1.32, 95% CI 1.03-1.70) and pneumonitis (aHR 1.36, 95% CI 1.10-1.68). There was no difference in the risks of these outcomes when comparing males with and without RA.

Conclusion: In this large nationwide study, those with pre-existing RA had a higher risk of cutaneous irAEs and pneumonitis. When stratifying by sex, females with RA had a higher risk of cutaneous irAEs, colitis and pneumonitis compared to females without RA while there was no difference by RA status among males. If future studies confirm these findings, these data can be used to counsel patients with RA contemplating starting an ICI as part of their cancer treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Ma: None; **Y. Wu**: None; **R. Stovall**: None; **J. Liew**: None; **N. Singh**: None.

Abstract Number: 1106

Faster Ellipsoid Zone Loss in Hydroxychloroquine Retinopathy with Tapering versus Discontinuation: A Longitudinal Optical Coherence Tomography Study from a Single Center in Taiwan

Ko-Jen Li[1], Ting-Wei Chang[2], Tso-Ting Lai[3], Jui-Hung Kao[4], TING-YUAN LAN[5], Tai-Ju Lee[6], pei-Hsinq lai[7], Shao-Yu Pai[8], Chiehyu Shen[9] and Song-Chou Hsieh[10], [1]National Taiwan University Hospital, Taipei, Taiwan, [2]National Taiwan University Hospital Hsinchu Branch, Taichung, Taiwan, [3]Naitional Taiwan University Hospital, Taipei, Taiwan (Republic of China), [4]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, Taipei, Taiwan (Republic of China), [5]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan, [6]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan (Republic of China), [7]Taipei City Hospital, Taichung, Taiwan, [8]National Taiwan University Hospital, Taichung City, Taiwan (Republic of China), [9]National Taiwan University Hospital, Taipei city, Taiwan, [10]National Taiwan Unuversity Hospital, Taipei City, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) retinopathy is a progressive, vision-threatening retinal disease. While HCQ is typically discontinued after toxicity is detected, some patients undergo tapering due to disease control needs. This study investigates whether ellipsoid zone (EZ) loss progresses more rapidly in patients who taper HCQ compared to those who discontinue it, using longitudinal optical coherence tomography (OCT) data from a Taiwanese cohort.

Methods: In the NTUH-HCQ cohort, we retrospectively included patients who were diagnosed with HCQ retinopathy by a retinologist following the onset of visual symptoms, seen at National Taiwan University Hospital between March 2017 and August 2024. The inclusion criteria required that each eye had at least 6 months of serial OCT follow-up after HCQ tapering or complete discontinuation, while patients with concurrent retinal diseases or other ocular conditions affecting the macula were excluded. Tapering was defined as the continuation of HCQ at less than 75% of the patient's long-term maintenance dose. EZ width was defined as the average distance between nasal–temporal and superior–inferior ellipsoid zone termini on OCT scans. The primary outcome was the individual rate of EZ loss (μm per year). We compared the average EZ loss rates between individuals and assessed differences across treatment and pattern subgroups.

Results: A total of 51 eyes from 26 patients were included in the analysis. Among them, 88% (23/26) were female. The median age was 55.06 years (interquartile range [IQR], 38.65–66.49), and the median duration of HCQ exposure was 11.74 years (IQR, 10.41–14.09). The median follow-up duration after HCQ retinopathy diagnosis was 2.35 years (IQR, 1.34–4.29). Pericentral-type HCQ retinopathy was observed in 15 patients (57.7%), while 12 patients (42.3%) had the parafoveal type. Following diagnosis, 15 patients (57.7%) continued HCQ on a tapered regimen, and 11 patients (42.3%) discontinued the drug entirely. Full patient characteristics are summarized in Table 1.

Figure 1 shows that the most rapid EZ loss occurred in patients with pericentral-type HCQ retinopathy who remained on a tapered regimen, averaging -600 ± 407 μm per year. In contrast, those who discontinued HCQ in the same subgroup declined significantly more slowly, at -149 ± 139 μm per year ($p < 0.001$). In the parafoveal subgroup, the corresponding rates were -162 ± 116 μm per year with taper and -124 ± 81 μm per year after discontinuation, with no significant difference between groups ($p = 0.394$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Characteristic	All, N=26	Pericentral, N=15	Parafoveal, N=11
Age, years (median (IQR))	55.06 (38.65–66.49)	47.29 (37.31–66.49)	63.52 (38.65–70.09)
Sex			
Female, n (%)	23 (88%)	13 (87%)	10 (91%)
Body measurements			
Height, cm (median(IQR))	157.70 (151.20–162.00)	160.00 (150.00–162.00)	155.60 (151.20–162.00)
Weight, kg (median(IQR))	52.08 (47.20–58.00)	52.15 (44.00–58.00)	51.50 (49.00–55.30)
BMI, kg/m^2 (median(IQR))	20.92 (19.75–22.53)	20.64 (18.36–22.10)	22.15 (20.24–23.13)
Disease			
Systemic lupus erythematosus (SLE), n (%)	9 (36%)	6 (43%)	3 (27%)
Rheumatoid arthritis (RA), n (%)	2 (8.0%)	0 (0%)	2 (18%)
Other connective tissue diseases (CTD), n (%)	14 (56%)	8 (57%)	6 (55%)
HCQ exposure			
Duration, years (median(IQR))	11.74 (10.41–14.09)	11.63 (10.92–14.61)	11.96 (10.02–14.09)
Daily dose, mg/kg/day (median(IQR))	7.48 (6.78–8.28)	7.67 (6.90–9.09)	7.27 (6.25–7.95)
Renal function			
CKD stage ≥3, n (%)	2 (7.7%)	1 (6.7%)	1 (9.1%)
eGFR, mL/min/1.73 m^2 (median(IQR))	89.00 (75.60–98.40)	94.50 (80.70–105.90)	84.40 (71.20–90.40)
HCQ regimen after diagnosis			
Tapered, n (%)	15 (58%)	10 (67%)	5 (45%)
Discontinued, n (%)	11 (42%)	5 (33%)	6 (55%)
Follow-up duration, years (median (IQR))	2.35 (1.34–4.29)	2.19 (0.94–4.29)	3.27 (1.71–4.94)

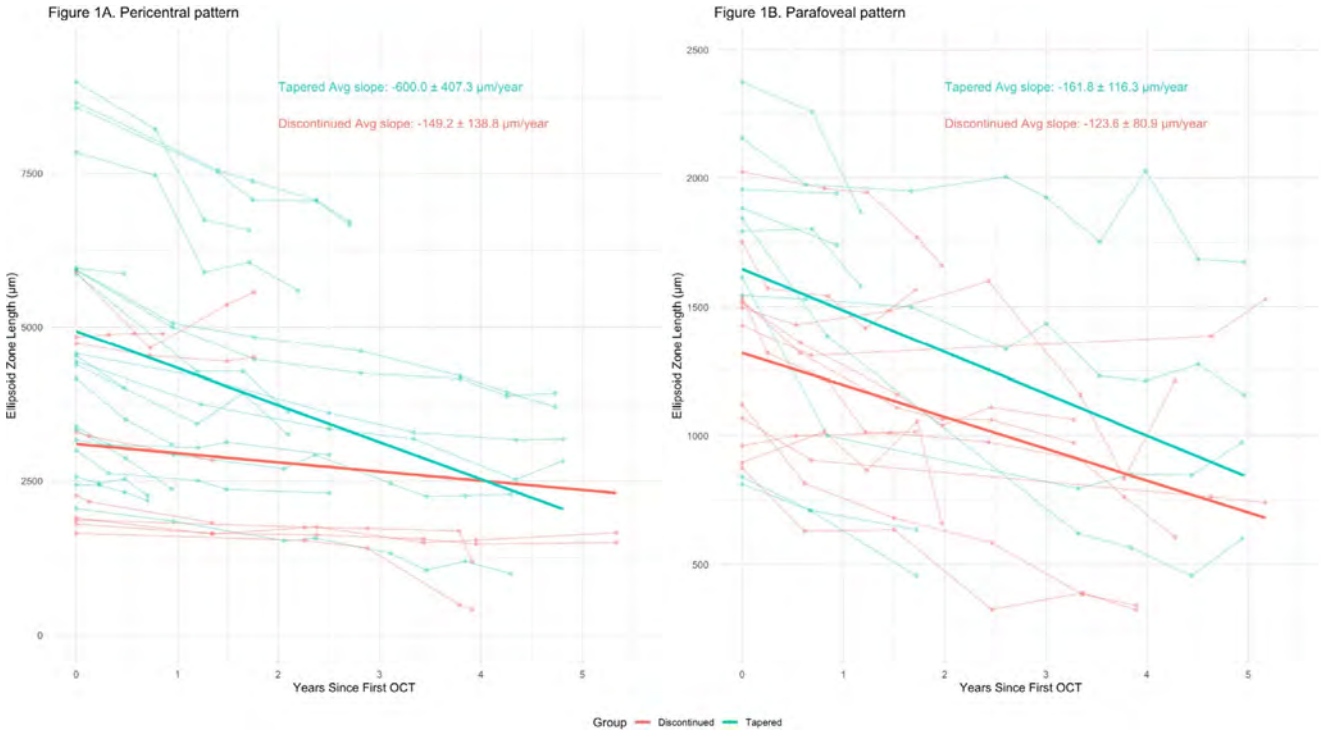


Figure 1

Conclusion: Our findings show that EZ loss progresses more rapidly in pericentral-type HCQ retinopathy patients who continued HCQ at a reduced dose than in those who discontinue it entirely, indicating heightened susceptibility of the perifoveal region to continued low-dose toxicity. These results underscore the limitations of tapering alone and support complete drug cessation once retinopathy is detected. EZ width may serve as a sensitive marker to guide management and monitor progression in clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Li: None; **T. Chang**: None; **T. Lai**: None; **J. Kao**: None; **T. LAN**: None; **T. Lee**: None; **p. lai**: None; **S. Pai**: None; **C. Shen**: None; **S. Hsieh**: None.

Abstract Number: 1107

Baseline Data on Rheumatic Immune-related Adverse Events from the Largest Prospective Multicenter US Consortium

Laura Cappelli[1], Namrata Singh[2], Noha Abdel-Wahab[3], Anne R. Bass[4], Tawnie Braaten[5], Cassandra Calabrese[6], Nilasha Ghosh[7], Tamiko Katsumoto[8], Sang Kim[9], Minna Kohler[10], Alexa Meara[11], Pankti Reid[12], Jeffrey Sparks[13], Maria Suarez-Almazor[14], Clifton Bingham[15] and Ami Shah[16], [1]Johns Hopkins School of Medicine, Baltimore, MD, [2]University of Washington, Bellevue, WA, [3]University of Texas MD Anderson Cancer Center, houston, TX, [4]Hospital for Special Surgery, New York, NY, [5]UNIVERSITY OF UTAH, Salt Lake City, UT, [6]Cleveland Clinic Foundation, Cleveland Heights, OH, [7]Hospital for Special Surgery, New York, NY, [8]Division of Immunology and Rheumatology, Stanford University, Millbrae, CA, [9]Yale University, Branford, CT, [10]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [11]The Ohio State University Wexner Medical Center, COLUMBUS, OH, [12]University of Chicago Medical Center, Chicago, IL, [13]Brigham and Women's Hospital, Boston, MA, [14]MD Anderson Cancer Center, Houston, TX, [15]Johns Hopkins University, Baltimore, MD, [16]Johns Hopkins Rheumatology, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1: Baseline characteristics of patients with rheumatic irAE in RADIOS consortium, 2015-2025 (n=671).

Characteristic	N (%) or mean (SD)
Age (years; mean, SD)	63.6 (12.7)
Sex (Female)	336 (50.1%)
Race	
- Asian	17 (2.5%)
- Black	38 (5.7%)
- Native Hawaiian/Pacific Islander	1 (0.1%)
- Other	19 (2.8%)
- White	580 (86.4%)
Ethnicity	
- Prefer not to answer	19 (2.8%)
- Hispanic	41 (6.1%)
Inflammatory Arthritis	435 (64.8%)
Arthralgia	146 (21.8%)
Polymyalgia Rheumatica (PMR)	69 (10.3%)
Other (e.g., eosinophilic fasciitis, uveitis, rash, tendinitis)	41 (6.1%)
Sicca/Sjögren's	29 (4.3%)
Myalgia	25 (3.7%)
Myositis	21 (3.1%)
Pseudogout	4 (0.6%)
Gout	4 (0.6%)
Psoriatic Arthritis	4 (0.6%)
Vasculitis	4 (0.6%)
Sarcoidosis	2 (0.3%)
Scleroderma	1 (0.1%)
Lupus	1 (0.1%)
Psoriasis	1 (0.1%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Large, multi-center efforts are needed to optimally study rheumatic immune-related adverse events (rh-irAEs) from immune checkpoint inhibitor (ICI) use. We aimed to characterize the baseline clinical features of patients enrolled in the Rheumatology Adverse Events Due to Immunotherapy Observational Studies (RADIOS) consortium and examine the severity of rh-irAE at presentation.

Methods: RADIOS is a prospective multi-institutional, national effort enrolling patients with rh-irAEs from 12 academic centers in the US. The consortium began enrolling in 2015 at the initial site and 2022 at additional sites. Patients were included if they were diagnosed by their rheumatologist as having developed a rh-irAE. Descriptive statistics were used to summarize the cohort's demographics (including age, sex, race, ethnicity), cancer characteristics, and ICI use at enrollment. We evaluated the type of rh-irAE the patient had as well as the Common Terminology Criteria for Adverse Events (CTCAE) grade of the adverse event. Among patients with ICI-induced inflammatory arthritis (ICI-IA), clinical disease activity index (CDAI) was obtained and mean (standard deviation) was calculated.

Results: As of April 1, 2025, the consortium had enrolled 671 patients with a rh-irAE with a mean age of 63.6 years (SD 12.7), of whom 336 were female (50.1%); 580 (86.4%) patients identified as White and 6% as Hispanic. ICI-IA was the most common rh-irAE (n=435, 65%) followed by arthralgia (n=146, 21.8%), PMR (n=69, 10.3%), and myalgia (n=25, 3.7%) (**Table 1**). Among the cancer types, most patients had melanoma (n=204, 30.5%), followed by non-small cell lung cancer (n=100, 14.9%); 439 patients had received PD-1 inhibitors alone as treatment; 188 patients had anti-CTLA-4/

Table 2. Cancer type, stage, and ICI exposure at baseline rheumatology visit

Characteristic	Rheum irAE Cohort (n=669), N (%)
Cancer Type	
- Melanoma	204 (30.5%)
- NSCLC	100 (14.9%)
- Renal Cell Carcinoma	86 (12.9%)
- Breast	59 (8.8%)
- Bladder	33 (4.9%)
- Endometrial	23 (3.4%)
- Other*	164 (24.5%)
Cancer Stage at Baseline	
- Stage 1	10 (1.7%)
- Stage 2	46 (7.7%)
- Stage 3	168 (28.1%)
- Stage 4	373 (62.5%)
ICI Exposure	
- Anti-PD-1	439 (65.6%)
- Anti-CTLA-4/PD-1 combination	188 (28.1%)
- Anti-PD-L1	57 (8.5%)
- Other	59 (8.8%)
- Anti-PD-1/LAG-3 combination	13 (1.9%)
- Anti-CTLA-4	3 (0.4%)
ICI Duration at Baseline (months; mean, SD)	
- Atezolizumab	10.6 (18.6)
- Avelumab	17.7 (25.9)
- Cemiplimab	10.3 (8.5)
- Durvalumab	5.0 (5.0)
- Ipilimumab alone	38.7 (63.5)
- Ipilimumab/Nivolumab	4.5 (11.0)
- Nivolumab	20.2 (15.3)
- Pembrolizumab	9.3 (9.3)
- Relatlimab/Nivolumab	4.6 (6.0)

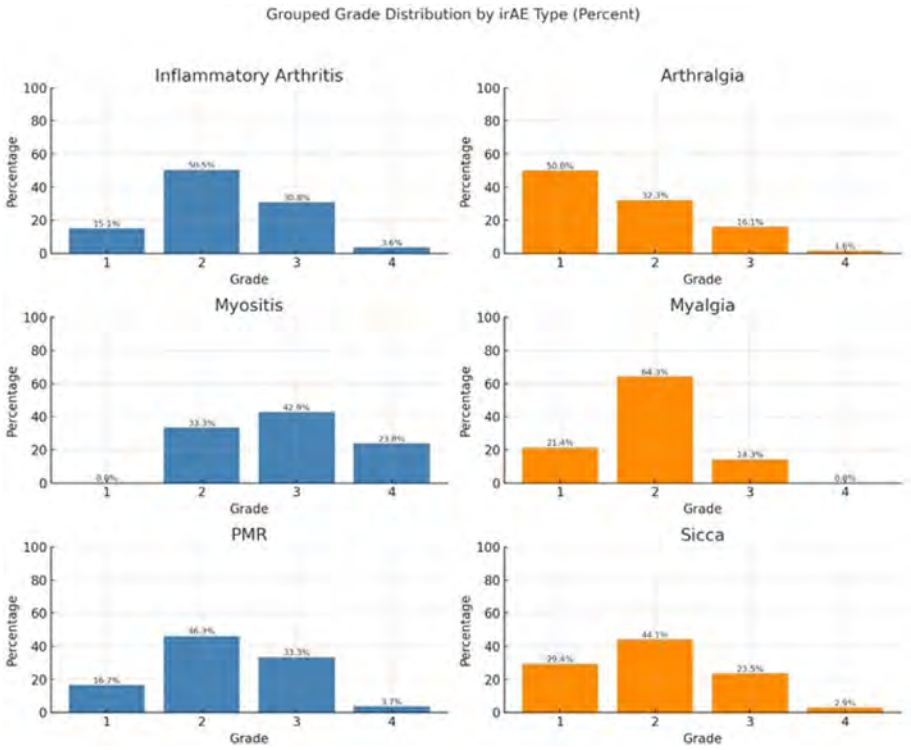


Figure 1: Common Terminology Criteria for Adverse Events (CTCAE) grade for rh-irAEs at time of enrollment to RADIOS. Grade 1 events are mild and/or self-limited, grade 2 events limit instrumental activities of daily living, grade 3 events are severe and limit self-care activities of daily living, and grade 4 events are severe, potentially life threatening, and/or require hospitalization.

PD-1 combination therapy (**Table 2**). Average duration of ICI treatment tended to be shorter in those who received combination therapies (ipilimumab/nivolumab and nivolumab/relatilmab) than in those who received anti-PD-1/PD-L1 monotherapy. Among patients with ICI-IA and baseline CDAI available (n=315), the mean score was 16.1 (SD 10.8), indicating most had moderate disease activity. Maximum CTCAE grade of rh-irAE at enrollment for each irAE type is shown in **Figure 1**. Patients with ICI-IA, PMR, and sicca syndrome most commonly had grade 2 severity while in myositis grade 3 severity was most common.

Conclusion: ICI-IA was the most common rh-irAE in RADIOS, the largest US-based prospective cohort. Melanoma and NSCLC were the most frequent tumor types, with PD-1 inhibitors being the most used class of ICI. Disease activity for ICI-IA measured by CDAI was moderate on average, and the majority of rh-irAEs were grade 2 (limiting instrumental activities of daily living), except for myositis which tended to have a more severe presentation.

Disclosure: L. Cappelli: Amgen, 2, Bristol-Myers Squibb(BMS), 2, 5, Sanofi, 2, Uniquity Bio, 2; **N. Singh**: None; **N. Abdel-Wahab**: None; **A. Bass**: None; **T. Braaten**: None; **C. Calabrese**: Eli Lilly, 2, Invivyd, 2, 6, sanofi, 2, 6; **N. Ghosh**: None; **T. Katsumoto**: Beyond Meat, 12, Unrestricted grant, Sanofi, 5; **S. Kim**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **A. Meara**: AbbVie/Abbott, 1, 2, Amgen, 1, 2, AstraZeneca, 1, 2, sanofi, 1, 2; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **M. Suarez-Almazor**: Novartis, 5, SetPoint Medical, 2, Syneos Health, 2; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **A. Shah**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1108

Baseline Features, Immunosuppression, and Immune-related Adverse Events in Patients with Pre-existing Rheumatic Disease and Cancer Requiring Immune Checkpoint Inhibitor Therapy

Laura Cappelli[1], Pankti Reid[2], Noha Abdel-Wahab[3], Anne R. Bass[4], Tawnie Braaten[5], Cassandra Calabrese[6], Nilasha Ghosh[7], Tamiko Katsumoto[8], Sang Kim[9], Minna Kohler[10], Alexa Meara[11], Namrata Singh[12], Jeffrey Sparks[13], Maria Suarez-Almazor[14], Ami Shah[15] and Clifton Bingham[16], [1]Johns Hopkins School of Medicine, Baltimore, MD, [2]University of Chicago Medical Center, Chicago, IL, [3]University of Texas MD Anderson Cancer Center, houston, TX, [4]Hospital for Special Surgery, New York, NY, [5]UNIVERSITY OF UTAH, Salt Lake City, UT, [6]Cleveland Clinic Foundation, Cleveland Heights, OH, [7]Hospital for Special Surgery, New York, NY, [8]Division of Immunology and Rheumatology, Stanford University, Millbrae, CA, [9]Yale University, Branford, CT, [10]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [11]The Ohio State University Wexner Medical Center, COLUMBUS, OH, [12]University of Washington, Bellevue, WA, [13]Brigham and Women's Hospital, Boston, MA, [14]MD Anderson Cancer Center, Houston, TX, [15]Johns Hopkins Rheumatology, Baltimore, MD, [16]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are effective therapies commonly used to treat malignancies but can cause flares or unrelated immune-related adverse events (irAEs) in patients with pre-existing rheumatic disease prior to ICI initiation (pre-ICI RD). As patients with pre-ICI RD were excluded from initial ICI studies, there is still a paucity of information about risks of ICI treatment and how to manage pre-ICI RD while patients are on ICIs.

Methods: Rheumatic Adverse Events Due to Cancer Immunotherapy Observational Studies (RADIOS) is a United States-based academic consortium of 12 sites prospectively collecting data to evaluate outcomes of patients with pre-ICI RD who receive cancer immunotherapy. Patients were included if they had pre-ICI RD and had a baseline visit with rheumatology. Descriptive statistics were calculated for the cohort's demographics (including age, sex, race, ethnicity), cancer characteristics, ICI use at enrollment, and prior treatment for autoimmune disease; clinical disease activity index (CDAI) was calculated for those with inflammatory arthritis. Data on irAE development and autoimmune disease treatment were queried for follow up visits.

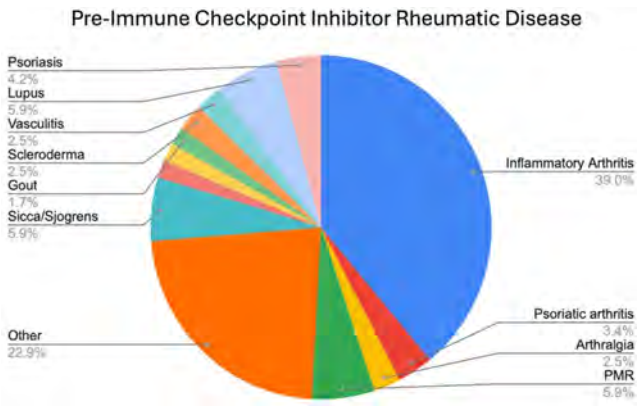


Figure 1: Frequency of Pre-Immune Checkpoint Inhibitor Rheumatic Diseases in the RADIOS Study

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

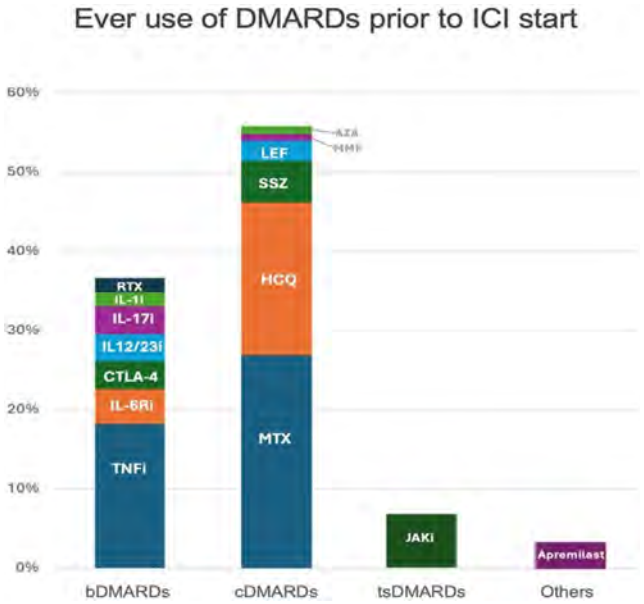


Figure 2: Ever use of disease modifying anti-rheumatic drugs (DMARDs) prior to immune checkpoint inhibitor (ICI) start

Table 1: Demographics and baseline characteristics for patients with pre-ICI Rheumatic Disease

	N (%) or Mean (SD)
Age	67.4 (10.2)
Female sex	42 (53.9%)
Cancer type	
Melanoma	23 (29.1%)
NSCLC	17 (21.5%)
Renal Cell carcinoma	5 (6.3%)
Breast	4 (5.1%)
Other	30 (38%)
Cancer stage at baseline	
1	2 (3.1%)
2	5 (10.8%)
3	21 (32.3%)
4	37 (56.9%)
ICI exposure at baseline	
CTLA-4i	0 (0%)
PD-1i	43 (54.4%)
PD-L1i	3 (3.8%)
CTLA-4i/PD-1i	10 (12.7%)
PD-1i/LAG-3i	1 (1.3%)
Other	3 (3.8%)
Not on ICI	19 (24.1%)

ICI: Immune checkpoint inhibitor; NSCLC: Non-small cell lung cancer; CTLA-4: Cytotoxic T lymphocyte associated protein inhibitor; PD-1i: Programmed cell death protein 1 inhibitor; PD-L1i: Programmed cell death protein 1 ligand inhibitor; LAG-3i: Lymphocyte activation gene 3 inhibitor

Results: As of 4/1/2025, 78 patients with pre-ICI RD were enrolled into the cohort; mean age was 67 years and 54% were female. Inflammatory arthritis was the most common diagnosis (39%) followed by systemic lupus (5.9%) and Sjogren's disease (5.9%) (Figure 1). Melanoma was the most common cancer type followed by non-small cell lung cancer. The majority of patients had stage 4 cancer, and anti-PD-1 was the most common category of ICI used (Table 1). Patients had been previously treated for their RD with a wide variety of DMARDs, most commonly TNF-inhibitors, methotrexate, and hydroxychloroquine (Figure 2). At RADIOS enrollment, 23 (29.5%) were currently on corticosteroids. For those with inflammatory arthritis and CDAI available (n=36), mean CDAI was 11.4 (SD 11.4) and most had low disease activity or remission (n=20, 55.6%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The most common non-rheumatic irAEs developed were rash and pneumonitis (n=5 for both). At follow up visits, TNF-inhibitors were the most administered biologics (n=9) followed by IL-6R inhibitors (n=7); methotrexate (n=15) and hydroxychloroquine (n=13) were the most common conventional synthetic DMARDs administered. No patients received JAK-inhibitors in follow-up.

Conclusion: By characterizing treatment patterns and outcomes in diverse rheumatic diseases, this multi-institutional, prospective research collaboration will improve knowledge regarding ICI safety for patients with rheumatic diseases who require ICI therapy for cancer.

Disclosure: L. Cappelli: Amgen, 2, Bristol-Myers Squibb(BMS), 2, 5, Sanofi, 2, Uniquity Bio, 2; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1; **N. Abdel-Wahab**: None; **A. Bass**: None; **T. Braaten**: None; **C. Calabrese**: Eli Lilly, 2, Invivyd, 2, 6, sanofi, 2, 6; **N. Ghosh**: None; **T. Katsumoto**: Beyond Meat, 12, Unrestricted grant, Sanofi, 5; **S. Kim**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **A. Meara**: AbbVie/Abbott, 1, 2, Amgen, 1, 2, AstraZeneca, 1, 2, sanofi, 1, 2; **N. Singh**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **M. Suarez-Almazor**: Novartis, 5, SetPoint Medical, 2, Syneos Health, 2; **A. Shah**: None; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9.

Abstract Number: 1109

Characteristics of SARS-CoV-2 infected Patients with Rheumatic Diseases on Rituximab: A Subanalysis of the COVID-19 Vaccine Booster in Immunocompromised Rheumatic Diseases (COVBIRD) Study

Laurianne Simard[1], Nathalie Amiable[2], Ines Colmegna[3], Anne-Sophie Julien[4], Sonia Léger-Thériault[5], Alexandra Godbout[4], Lison Fournier[6], Giuliana Alfonso[5], Josiane Bourre-Tessier[7], Marie Hudson[8], Nicolas Richard[9], Jean-Paul Makhzoum[10], Arielle Mendel[11], Sasha Bernatsky[12], Marc Dionne[6], Michael Libman[5], Gaston De Serres[6] and Paul Fortin[13], [1]Universite Laval, Quebec, QC, Canada, [2]Centre de recherche du CHU de Québec – Université Laval, Quebec City, QC, Canada, [3]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [4]Centre de recherche du CHU de Québec – Université Laval, Quebec, QC, Canada, [5]MUHC, Montreal, Canada, [6]Centre de recherche du CHU de Québec – Université Laval, Quebec, Canada, [7]Centre hospitalier de l'Universite de Montreal, Montreal, QC, Canada, [8]McGill University, Montréal, QC, Canada, [9]Hopital Maisonneuve Rosemont, Montreal, QC, Canada, [10]Universite de Montreal, Montreal, Canada, [11]McGill University Health Centre, Montréal, QC, Canada, [12]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [13]Centre ARThrite - CHU de Québec - Université Laval, Quebec, QC, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with systemic autoimmune rheumatic diseases (SARD) treated with B-cell-depleting therapies such as rituximab (RTX) have impaired humoral immune responses, increasing their susceptibility to SARS-CoV-2, including severe infections. Despite vaccination, COVID-19 remains a concern in this population. This study aimed to describe the occurrence of SARS-CoV-2 infections in RTX-treated SARD patients and to explore potential predictors of infection.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient and disease characteristics with univariable logistic regression results

	No COVID-19*	COVID-19*	Odds Ratio (95% CI)	P-value
N	96	29		
Age (years)	61.8 ± 14.0	55.2 ± 14.6	0.97 (0.94;1.00)	0.03
Sex (female)	62 (64.6)	24 (82.8)	2.63 (0.92;7.52)	0.07
Charlson Comorbidity Index	2.2 ± 1.7	1.9 ± 1.3	0.85 (0.62;1.14)	0.28
COVID-19 infection prior enrollment	50 (52.1)	18 (62.1)	1.51 (0.64;3.52)	0.35
Systemic Autoimmune Rheumatic Disease				
Rheumatoid Arthritis	34 (35.4)	11 (37.9)	Reference	0.38
ANCA-associated vasculitis	39 (40.6)	8 (27.6)	0.63 (0.23;1.7)	
Other	23 (24.0)	10 (34.5)	1.34 (0.49;3.6)	
Disease duration (years)	12.0 ± 10.7	14.3 ± 11.0	1.02 (0.98;1.06)	0.31
Rituximab treatment duration (years)	3.60 ± 3.00	4.13 ± 3.05	1.06 (0.93;1.21)	0.41
Treatment **				
Hydroxychloroquine or chloroquine	16 (16.8)	8 (27.6)	1.88 (0.71;4.99)	0.20
Methotrexate	22 (23.2)	6 (20.7)	0.87 (0.31;2.39)	0.78
Prednisone	24 (25.3)	7 (24.1)	0.94 (0.36;2.48)	0.90
Mycophenolate mofetil	13 (13.7)	3 (10.3)	0.73 (0.19;2.75)	0.64
Interval between the last dose of Rituximab and vaccination in the study (days)	167 ± 61	153 ± 41	1.00 (0.99;1.00)	0.25
Evusheld used as prophylaxis	29 (30.2)	13 (44.8)	1.88 (0.80;4.4)	0.15

*Values are presented as mean ± standard deviation or frequency (percentage by column).
**1 missing data in No COVID-19 group.

Table 2. Severe SARS-CoV-2 infections

Patient	Sex	Age	Diagnosis	Disease duration	Treatment	Number of vaccine before infection	Time since last vaccine	Time since last RTX	Evusheld prophylaxis	Anti-Spike ER[1]
1	F	60	RA	47 years	Methotrexate NSAID	4	77 days	31 days	Yes	Negative
	Day[2] 31: URTI symptoms, headache, and weakness with positive COVID test, treated with Paxlovid Day 53: Persistent symptoms with positive COVID test Day 99: Persistent URTI and fatigue with third positive COVID test Day 115: ED visit for fever, CXR with suspicion of pneumonia and SARS-CoV-2 infection sequelae, fourth positive COVID test Day 139: Clinical improvement at medical follow-up Anti-N antibodies[3] measured through the study were all negative									
2	M	62	RA	16 years	Methotrexate Sulfasalazine	5	181 days	118 days	Yes	Negative
	Day 118: URTI symptoms and positive COVID test Day 121: ED visit for cough and dyspnea, pneumonia on CT-scan, treated with inhalation therapy, antibiotics and Paxlovid Days 122-124: ED visit for increasing cough and respiratory distress, antibiotics continued and treated with Paxlovid Day 127: Negative COVID test Day 132: ED visit for bronchospasm, diagnosed with viral bronchitis Anti-N antibodies measured through the study were all negative									
3	M	72	ANCA	11 years	None	5	53 days	28 days	Yes	Negative
	Day -11: Mild SARS-CoV-2 infection with positive COVID test Day 28: Relapsing symptoms of cough and fatigue with fever and positive COVID test Days 34-36: ED visit for COVID-19 pneumonia, treated with antibiotics Day 42: Persistent fever and hospitalization for one week, treated with antibiotics and Remdesivir Anti-N antibodies measured through the study were all negative									
4	M	49	ANCA	7 years	None	5	23 days	178 days	No	Negative
	Day 178 : Respiratory symptoms, ED visit with positive COVID test, treated with Paxlovid et prednisone Anti-N antibodies measured through the study were all negative									
5	M	64	RA	13 years	Leflunomide Prednisone Sulfasalazine	5	15 days	197 days	No	Positive
	Days 197-213: Hospitalization for pulmonary embolism, COVID-19 and pseudogout Anti-N antibodies became positive after the infection									

[1]Anti-Spike ER (Evusheld-resistant) antibodies are antibodies directed against variants of the SARS-CoV-2 spike protein that are resistant to neutralization by Evusheld
[2]Days are calculated from the last RTX dose
[3]Anti-N antibodies are antibodies directed against the nucleocapsid (N) protein of SARS-CoV-2, produced in response to natural infection but not after vaccination
ANCA: ANCA-associated vasculitis
CT-scan: computed tomography scan
CXR: chest X-ray
ED: emergency department
URTI: upper respiratory tract infection
RA: rheumatoid arthritis

Methods: COVBIRD is an open-label, non-randomized, comparative trial evaluating humoral responses following at least three COVID-19 vaccinations in SARD patients treated with RTX. We conducted a subanalysis of participants who developed SARS-CoV-2 infection during the study period. Patients were grouped based on their infection status. Descriptive statistics and univariable logistic regressions were used to compare demographic and clinical characteristics between groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among the 125 RTX-treated patients, 29 (23.2%) experienced at least one SARS-CoV-2 infection, including five classified as severe. Table 1 reports on the patient demographic and diseases characteristics comparing those who developed COVID infection vs those with no infection. No significant differences were observed between groups in terms of diagnosis and treatment-related variables (see Table 1). Age was the only significantly different factor: infected individuals were younger on average (55.2 years; 95% CI, 49.7–60.8) compared to those without SARS-CoV-2 infection (61.8 years; 95% CI, 59.0–64.6); p = 0.034. We also observed a female predominance for infection, but this was not statistically significant. Table 2 summarizes the clinical presentations of the five severe cases.

Conclusion: In this cohort of immunocompromised patients treated with RTX, nearly one in four developed SARS-CoV-2 infection despite having received three to five doses of vaccines, with a subset experiencing severe disease. Baseline clinical characteristics were generally similar between infected and non-infected individuals, highlighting a broad susceptibility likely driven by both immunosuppressive therapy and underlying disease. The younger age of infected patients may reflect behavioral factors such as reduced adherence to preventive measures. These findings emphasize the elevated risk of COVID-19 in RTX-treated individuals and support the implementation of individualized, reinforced preventive strategies regardless of clinical profile.

Disclosure: L. Simard: None; **N. Amiable**: None; **I. Colmegna**: None; **A. Julien**: None; **S. Léger-Thériault**: None; **A. Godbout**: None; **L. Fournier**: None; **G. Alfonso**: None; **J. Bourre-Tessier**: None; **M. Hudson**: Astra Zeneca, 5, 6, Boehringer-Ingelheim, 5, Merck, 1, Pfizer, 5; **N. Richard**: None; **J. Makhzoum**: AbbVie/Abbott, 12, Investigator, Astra-Zeneca, 6, 12, Investigator, GlaxoSmithKlein(GSK), 6, Janssen, 12, Investigator, Novartis, 12, Investigator, Otsuka, 6, Roche, 6, Sanofi, 6; **A. Mendel**: None; **S. Bernatsky**: None; **M. Dionne**: None; **M. Libman**: None; **G. De Serres**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1.

Abstract Number: 1110

Tumor outcomes and arthritis flares in patients with pre-existing rheumatoid arthritis receiving immune checkpoint inhibitor therapy

Madalyn Walsh[1], Jeremy Zhang[2], Bashar Abuqayas[1], Sanchay Jain[3], Yosef Zakharia[4], Aleksander Lenert[5] and Jennifer Strouse[6], [1]University of Iowa Hospitals & Clinics, Iowa City, IA, [2]Rush University, Chicago, IL, [3]University of Iowa, Iowa City, IA, [4]Mayo Clinic, Rochester, MN, [5]Iowa Carver College of Medicine, Iowa City, IA, [6]University of Iowa, Iowa City

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of an increasing number of malignancies. Because patients with pre-existing autoimmune disease have been excluded from clinical trials of ICIs, there is a paucity of data regarding outcomes in patients with pre-existing rheumatoid arthritis (RA). The aim of our study was to describe rheumatologic and oncologic outcomes of patients with a pre-existing diagnosis of RA who received ICIs for treatment of their malignancy.

Methods: We conducted a cohort study of previously collected data at a single center. We used TriNetX to broadly identify patients receiving an immune checkpoint inhibitor and a disease-modifying antirheumatic drug (DMARD) from January 1st, 2010 to September 19th, 2023. Electronic medical records were abstracted to identify patients with pre-existing RA, patient demographics, laboratory investigations, type of malignancy, type of ICI administered, and flares of RA. Response

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Cohort demographics and clinical characteristics

	RA, n = 22
Age, median ± SD, y	70.4 ± 7.6
Race, white	22
Female, n (%)	12 (54.5%)
RF +, n (%)	9 (40.9%)
CCP +, n (%)	8 (36.4%)
RF or CCP +, n (%)	10 (45.5%)
Length of RA diagnosis, median ± SD, y	6 ± 3-10
History of tobacco use, n (%)	17 (77.3%)
Malignancy	
NSCLC, n (%)	7 (31.8%)
Melanoma, n (%)	3 (13.6%)
RCC, n (%)	2 (9.1%)
Other, n (%)	10 (45.5%)
First ICI administered	
Pembrolizumab, n (%)	17 (77.3%)
Nivolumab, n (%)	2 (9.1%)
Durvalumab, n (%)	3 (13.6%)
DMARDs utilized	
Hydroxychloroquine, n (%)	19 (86.4%)
Methotrexate, n (%)	18 (81.8%)
Sulfasalazine, n (%)	4 (18.2%)
TNF inhibitor, n (%)	3 (13.6%)
Other biologic, n (%)	4 (18.2%)

Table 2. Tumor outcomes and rheumatoid arthritis flare rates

	RA, n = 22
RA flare, n (%)	10 (45%)
Number of ICI cycles prior to flare, median (IQR)	1 (0)
Deceased, n (%)	15 (68.2%)
RECIST at 6 months	
Partial response, n (%)	2 (9.1%)
Complete response, n (%)	2 (9.1%)
Stable disease, n (%)	5 (22.7%)
Progressive disease, n (%)	13 (59.1%)

Evaluation Criteria in Solid Tumors (RECIST) at 6 months was performed by a radiologist to assess for malignancy progression.

Results: We identified 22 patients who had pre-existing RA and received both an ICI and a DMARD. The mean patient age was 70.4 years old and on average patients had been diagnosed with RA for 6 years. There was a history of tobacco use in 77.3% (17/22) of patients. The most common malignancy was non-small cell lung cancer in 31.8% (7/22). Pembrolizumab was the most common ICI with 77.3% (17/22) of patients receiving it. Methotrexate had been used by 81.8% (18/22) of patients, hydroxychloroquine by 86.4% (19/22), and sulfasalazine by 18.2% (4/22). Rheumatoid factor was positive in 40.1% (9/19) and anti-CCP was positive in 50% (8/16). 45% (10) of patients experienced a flare of their RA. Of the 10 patients who had an RA flare, 9 flared by 6 months following ICI initiation, and 8 after one cycle of ICI. RECIST at 6 months after ICI initiation revealed progressive disease in 59.1% (13/22), stable disease in 22.7% (5/22), partial response in 9.1% (2/22), and complete response in 9.1% (2/22).

Conclusion: Approximately half of patients with pre-existing RA treated with ICIs had flares of RA, typically after one dose of ICI administration. Eight of the ten patients who had RA flares flared within six months of ICI initiation. The average number of cycles of ICI administrations prior to flare was 2.7. The majority of patients had been treated with methotrexate and hydroxychloroquine. The rate of progressive disease at 6 months was high, though reflective of the diversity of malignancies included. It is important to be aware of a high flare rate in patients with RA who are undergoing ICI therapy. It would be prudent to increase the frequency of rheumatologic follow up in this patient population in order to quickly diagnose and treat RA flares secondary to oncologic therapy. As most patients who experience an RA flare following ICI initiation do so following the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

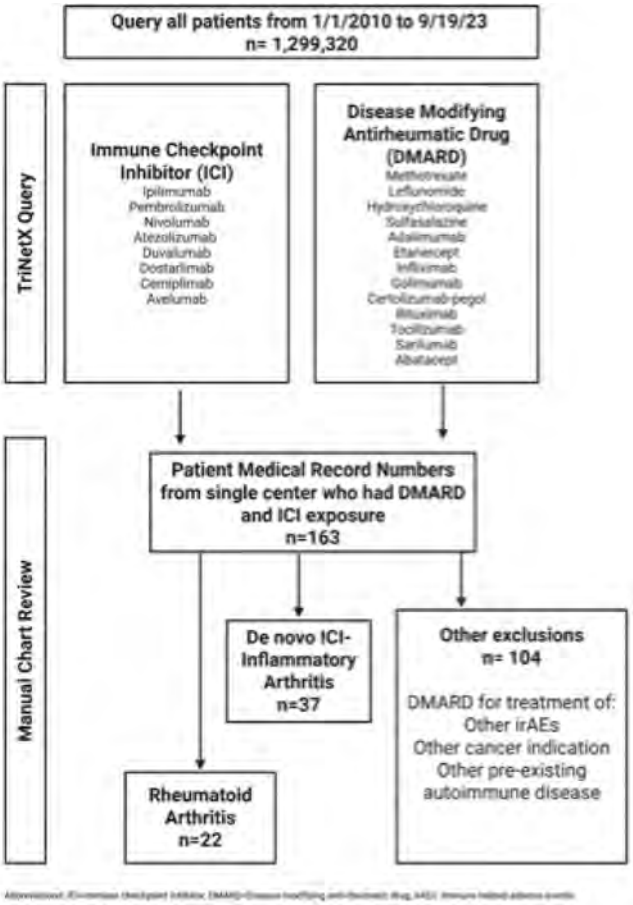


Figure 1. Flow diagram describing the stepwise approach utilized to determine patient cohort

first ICI administration, it may be useful to schedule follow up within a month of initiation. Future efforts to delineate the effects of DMARD therapy management decisions when initiating ICI therapy on both oncologic and rheumatic outcomes are planned.

Disclosure: M. Walsh: None; **J. Zhang**: None; **B. Abuqayas**: None; **S. Jain**: None; **Y. Zakharia**: None; **A. Lenert**: None; **J. Strouse**: None.

Abstract Number: 1111

Checkpoint Inhibitor Induced Myocarditis with Myositis/Myasthenia Gravis Concurrence: An Observational Study

Maja Ivanovic[1], Daming Shao[2], Andrew Wang[3], Craig Smuda[2] and Pankti Reid[1], [1]University of Chicago Medical Center, Chicago, IL, [2]University of Chicago, Chicago, IL, [3]University of Chicago Pritzker School of Medicine, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Immune checkpoint inhibitor (ICI) induced myositis is the ICI rheumatic toxicity with the greatest case mortality rate, especially when associated with myocarditis and/or myasthenia gravis (MG). Presentation, progression and treatment for ICI-myositis/myocarditis/myasthenia gravis overlap syndrome (IMOS) is poorly understood. We aim to better understand IMOS clinical presentation, evaluation and disease progression.

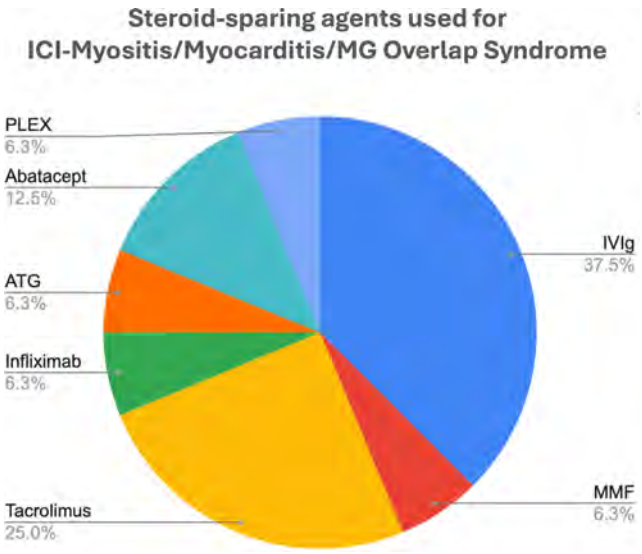


Figure 1: Most patients required therapy beyond systemic steroids. The steroid-sparing therapies ranged for the immune checkpoint inhibitor (ICI) associated Myositis/Myocarditis/Myasthenia Gravis (MG) Overlap Syndrome (IMOS) as depicted here.

Table 1: Baseline characteristics

	n (%) or Median (IQR)
Age	71.5 (67.3, 80.3)
Sex (F, %)	3 (30%)
Race, Ethnicity	
White	7 (70%)
Black	1 (10%)
Other	2 (20%)
Cancer type	
Melanoma	2 (20%)
RCC	2 (20%)
Breast	1 (10%)
Other	5 (50%)
Cancer sage	
II	4 (40%)
III	4 (40%)
IV	2 (20%)
ICI regimen	
CTLA4i + PD1i	2 (20%)
PD1i only	8 (80%)
IMOS diagnosis	
Triple M	4 (40%)
Myositis + Myocarditis	3 (30%)
Myocarditis + MG	3 (30%)
Time from ICI start to symptom or diagnosis (days)	
Patients with Myositis (n = 7)	
ICI to myositis symptoms	15 (12.8, 22.3)
ICI to myositis diagnosis	23 (19.5, 29.0)
Patients with Myocarditis (n = 10)	
ICI to myocarditis symptoms	21.5 (14.3, 30.3)
ICI to myocarditis diagnosis	28.0 (20.0, 33.0)
Patients with MG (n = 7)	
ICI to MG symptoms	30.0 (19.0, 36.5)
ICI to MG diagnosis	36.5 (31.0, 46.5)

IQR: interquartile range; F: Female; RCC: Renal cell carcinoma; ICI: Immune checkpoint inhibitor; CTLA-4i: Cytotoxic T-lymphocyte associated protein 4 inhibitor; PD1i: programmed death-ligand 1 inhibitor; Triple M: Myositis, Myocarditis and Myasthenia Gravis; MG: Myasthenia Gravis;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Clinical presentation and treatment course of IMOS

	Triple M (n = 4)	Myositis + Myocarditis (n = 3)	Myocarditis + MG (n = 3)
	n (%) or Median (IQR)	n (%) or Median (IQR)	n (%) or Median (IQR)
ICI initiation to first sx (days)	20 (14.5, 31.0)	15 (7.5, 18.0)	31 (23.0, 32.0)
ICI initiation to dx of IMOS (days)	26 (22.0, 34.0)	20 (16.0, 22.0)	34 (31.0, 40.0)
Key laboratory data			
Initial CK	3053 (1826.5, 9458.0)	3830 (2320.5, 5151.5)	1141 (857.5, 3445.5)
Peak CK	3053 (1826.5, 9458.0)	3830 (2320.5, 5151.5)	1141 (881, 3445.5)
Initial troponin	982.5 (658.0, 1626.0)	857 (662.0, 1052.0) *	921 (511.5, 1330.0) *
Peak troponin	1496.5 (969.8, 3255.8)	939 (784.5, 1093) *	1739 (1560.5, 3207.5)
AchR-Ab positive	2 (50%)	N/A	2 (67%)
AchR-Ab negative	2 (50%)	N/A	1 (33%)
Diagnoses for IMOS component			
Sequential	2 (50%)	2 (66%)	3 (100%)
Simultaneous	2 (50%)	1 (33%)	0 (0%)
Confidence of IMOS diagnosis			
Definitive	4 (100%)	0 (0%)	3 (100%)
Presumed	0 (0%)	3 (100%)	0 (0%)
ICI initiation to first steroid (days)	25 (19.0, 34.0)	19 (12.5, 23.5)	33 (29.5, 33.5)
ICI initiation to first steroid-sparing agent (days)	26 (22.0, 59.5)	27 (23.5, 30.5)	48 (39, 48.5)
Steroid-sparing agent(s) used			
Intravenous immunoglobulin	3 (75%)	0 (0%)	3 (100%)
Abatacept	1 (25%)	0 (0%)	1 (33%)
Mycophenolate mofetil	0 (0%)	1 (33%)	0 (0%)
Tacrolimus	2 (50%)	0 (0%)	2 (66%)
Infliximab	1 (25%)	0 (0%)	0 (0%)
Anti-thymocyte globulin	0 (0%)	1 (33%)	0 (0%)
Plasmapheresis	0 (0%)	0 (0%)	1 (33%)
Cancer progression at last follow up			
Yes	0 (0%)	1 (33%)	1 (33%)
No	2 (50%)	1 (33%)	0 (0%)
Unknown	2 (50%)	1 (33%)	2 (67%)
Death at last follow up			
Yes	3 (75%)	2 (67%)	3 (100%)
No	1 (25%)	1 (33%)	0 (0%)

ICI: Immune checkpoint inhibitor; CK: Creatine Kinase, AchR-Ab: Acetylcholine Receptor Binding Antibody, Triple M: Myositis, Myocarditis and Myasthenia Gravis; MG: Myasthenia Gravis; Sx: symptom, Dx: diagnosis
*Data reported excluding one patient with outside troponin using a different, non-high-sensitivity troponin assay

Methods: This is a retrospective, single center, observational study investigating patients with IMOS defined as patients with history of ICI treatment for cancer and development of some combination of ICI-myositis, myocarditis and/or MG overlap. We included adult patients with ICI therapy for cancer between 1/1/2011 and 4/1/2025. IMOS diagnosis was determined by the multidisciplinary treating team of clinicians. We examined demographics, presenting syndrome, clinical evaluation, treatment and outcomes as available in clinical annotations. Data were analyzed using descriptive statistics.

Results: Of 35 patients with either ICI-induced myositis, myocarditis or MG, 10 patients had overlap and fit definition of IMOS: four patients with ICI-myositis, myocarditis and MG (Triple M); three with myocarditis/myositis, three with myocarditis/MG (Table 1). Only three patients (30%) were diagnosed with overlap syndrome at initial diagnosis, with the other seven (70%) being diagnosed sequentially (Table 2). Initial creatine kinase (CK) was elevated in all patients (median 2507, IQR 894, 5543), even in patients without myositis. Median time to steroids after symptom onset was 4 days (IQR 3-6) and time from symptoms to steroid sparing agent was 13 days (IQR 7-15). IVIg was the most frequently used steroid-sparing agent

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(37.5%). Overall, eight patients (80%) died during the follow up period, with six deaths (60%) attributed to IMOS. The myocarditis/MG had the highest mortality at follow-up (100%) followed by Triple M (75%) and then myocarditis/myositis (67%).

Conclusion: Our findings reflect high mortality with IMOS, especially with myocarditis/MG overlap. High CK was prevalent even without myositis and 70% of patients had sequential rather than simultaneous diagnosis of the overlap syndrome. Delay in steroid sparing agent initiation may be a result of time necessary for multidisciplinary conversations and ambivalence in optimal second line therapy. Future research will require higher-powered multi-institutional study to identify the most effective and safe therapies for IMOS.

Disclosure: M. Ivanovic: None; **D. Shao**: None; **A. Wang**: None; **C. Smuda**: None; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1.

Abstract Number: 1112

Breaking Bones, Breaking Hearts: A FAERS Perspective on Osteoporosis Medications

Manush Sondhi[1], Namrata Singh[2], Julie Carkin[1] and Grant Hughes[3], [1]University of Washington, Seattle, WA, [2]University of Washington, Bellevue, WA, [3]University of Washington, Lynnwood, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The cardiovascular risks associated with osteoporosis medications remain incompletely understood. Previous studies suggest that romosozumab (ROM) is most strongly associated with major adverse cardiovascular events (MACE), while denosumab (DMB) and teriparatide (TPT) have shown associations with select cardiovascular events in some reports [1–3]. Evidence for alendronate (ALN) and zoledronic acid (ZOL) is mixed, with some studies linking ZOL to atrial fibrillation (A-fib) [4–5]. Limited data exist for risedronate (RIS) and abaloparatide (ABA), with no consistent evidence of increased cardiovascular risk [1,4]. This study aims to evaluate the association between osteoporosis treatments and MACE.

Methods: We conducted a retrospective pharmacovigilance analysis using the FDA Adverse Event Reporting System (FAERS) from 2019 to 2024. All included drugs were FDA-approved by 2019. We examined reports of MACE—including myocardial infarction (MI), stroke, A-fib, and cardiac failure (CF)—associated with ALN, RIS, ZOL, DMB, TPT, ABA, and ROM. Reports involving individuals under 18 years of age were excluded. Disproportionality signal analysis using Reporting Odds Ratios (RORs) was conducted to evaluate MACE events associated with osteoporosis medications, comparing event reporting for each drug to the overall FAERS database. When the lower limit of the 95% Confidence Interval was >1, the ROR was deemed significant.

Results: We analyzed the characteristics of MACE reported in association with each osteoporosis medication. Stroke and CF were most frequent in the 65–85 age group across most drugs, while MI and A-fib were more common in those aged 18–64. Women were more frequently affected overall, except for A-fib, where men predominated.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

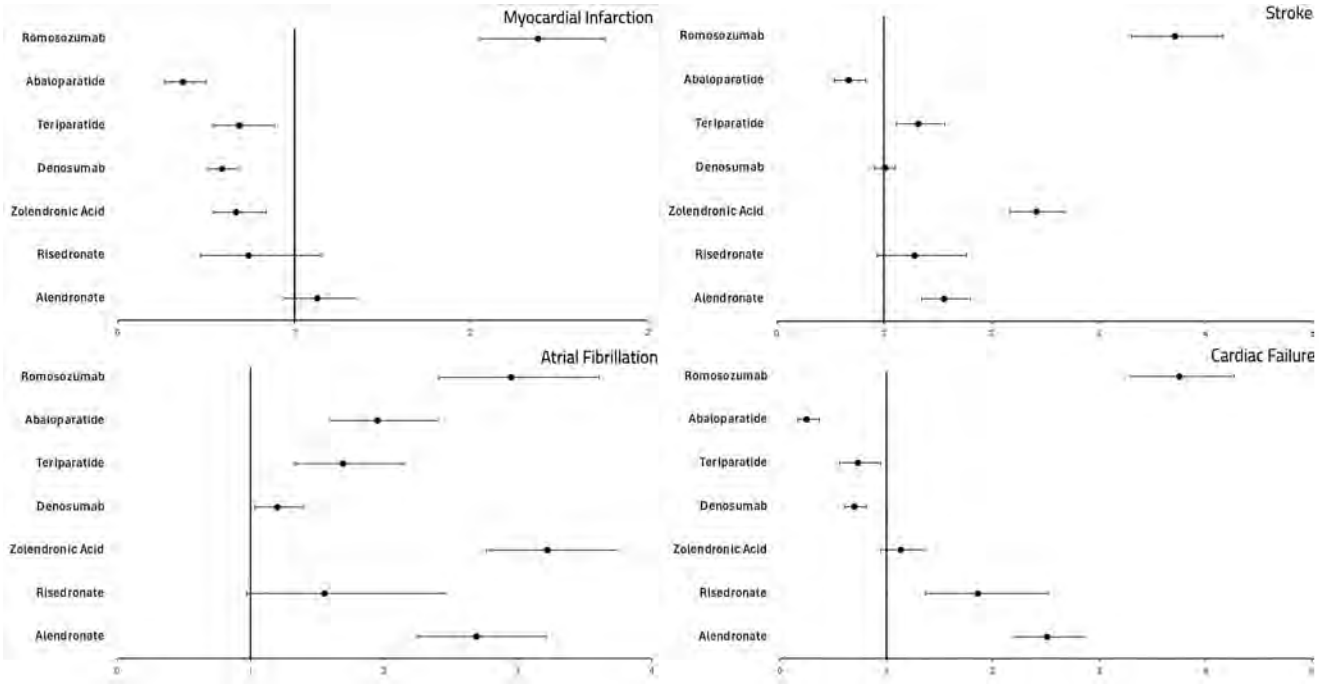
For MI, ROM had the highest ROR (2.38; 95% CI: 2.05–2.70; P < 0.0001), while DMB and ABA were linked to the lowest RORs. For stroke, ROM again showed the highest ROR (3.72), followed by ZOL (2.42). Only ABA demonstrated a negative association. For A-fib, ZOL had the highest ROR (3.22), followed by ROM and ALN; DMB showed a modest association (ROR: 1.20) relative to the other drugs. For CF, ROM had the highest ROR (3.76), followed by ALN (2.52) and RIS (1.86). ABA, TPT, and DMB were associated with the lowest RORs in this category.

Conclusion: We found that among the drugs considered, only ROM was associated with increased ROR for all MACE outcomes. In contrast, DMB and ABA demonstrated relatively low cardiovascular risk signals across most outcomes. ZOL showed notable positive associations with both stroke and A-fib, while ALN was linked to increased reporting of A-fib and CF.

Our findings suggest that a patient's individual risk for MACE should be considered when choosing osteoporosis drugs. Despite MACE risks, treating osteoporosis remains crucial, as fracture prevention significantly reduces morbidity and mortality. Limitations of our analysis include potential reporting bias, residual confounding, and its observational design, which precludes causal inference. Further prospective cohort studies and randomized clinical trials are needed to validate these associations and clarify the mechanisms of risk.

Table depicting the calculated RORs of MACE associated with the medications used for the treatment of osteoporosis.

Drugs	Myocardial Infarction	Stroke	Atrial Fibrillation	Cardiac Failure
Alendronate	1.13 (0.94-1.35)	1.56 (1.35-1.81)	2.69 (2.25-3.21)	2.51 (2.20-2.87)
Risedronate	0.74 (0.47-1.15)	1.29 (0.94-1.77)	1.55 (0.97-2.46)	1.86 (1.37-2.52)
Zoledronate	0.67 (0.54-0.84)	2.42 (2.17-2.69)	3.22 (2.76-3.74)	1.14 (0.95-1.36)
Denosumab	0.59 (0.51-0.68)	1.01 (0.91-1.11)	1.20 (1.03-1.39)	0.70 (0.61-0.81)
Teriparatide	0.69 (0.54-0.89)	1.32 (1.12-1.57)	1.69 (1.33-2.15)	0.73 (0.56-0.95)
Abaloparatide	0.37 (0.27-0.50)	0.67 (0.54-0.83)	1.95 (1.59-2.40)	0.25 (0.17-0.37)
Romosozumab	2.38 (2.05-2.76)	3.71 (3.31-4.16)	2.95 (2.41-3.61)	3.75 (3.29-4.27)



Forest plot depicting the association of MACE with the medications used for the treatment of osteoporosis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Sondhi: None; **N. Singh**: None; **J. Carkin**: None; **G. Hughes**: None.

Abstract Number: 1113

Immune checkpoint inhibitor–associated myocarditis: Incidence, risk factors, and clinical outcomes in a global real-world cohort

Qi Wang[1], Zhiting Tang[2] and Lei Deng[3], [1]Metrohealth System/Case Western Reserve University, Cleveland, OH, [2]Unity Hospital, Rochester, NY, [3]Fred Hutchinson Cancer Center, Seattle, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitor (ICI)-associated myocarditis is a rare but life-threatening immune-related adverse event (irAE), with a mortality rate of 30–50%. Most available evidence comes from case series and adverse event reporting databases, leaving its risk factors and clinical outcomes largely undefined.

Methods: We performed a retrospective investigation using the TriNetX Global Research Network. Patients were included if they had been diagnosed with solid tumors after 2016 for which ICIs are approved. We calculated myocarditis incidence among ICI users and compared myocarditis risk between ICI and non-ICI cohorts using propensity score matching (accounting for demographics, comorbidities, cancer types, and treatments). Univariate and multivariate models were applied to assess risk factors. Risks of hospitalization, ICU admission, and major adverse cardiovascular events (MACE) were compared in ICI-treated patients with and without myocarditis using propensity score matching.

Results: Among 130,234 ICI-treated patients, 643 (0.49%) developed myocarditis. Most cases (82.0%) occurred within the first year of ICI initiation. The risk of myocarditis was 27 times higher in the ICI group compared to the non-ICI group (Relative Risk [RR]=27.78, 95% CI: [17.36-44.45]).

Univariate analysis identified older age, male sex, White race, hypertension, hyperlipidemia, ischemic heart disease, diabetes, chronic kidney disease, heart failure, cardiomyopathy, urothelial cancer, melanoma, ipilimumab, nivolumab, pembrolizumab, radiation therapy, inflammatory arthritis, lupus, and systemic connective tissue disease as potential risk factors. In multivariate analysis, only age over 65 (Hazard Ratio [HR] = 1.34, 95% CI: [1.11–1.63], $p < 0.01$), hypertension (HR=1.31, 95% CI: [1.06-1.62], p=0.01), hyperlipidemia (HR=1.34, 95% CI: [1.09-1.65], $p< 0.01$), melanoma (HR=1.52, 95% CI: [1.25-1.86], $p< 0.01$), and ipilimumab (HR= 2.44, 95% CI: [1.87-3.19], $p< 0.01$) were significantly associated with myocarditis.

Patients who developed ICI-associated myocarditis had higher risks of hospitalization (RR=1.39, 95% CI: [1.28-1.52]), ICU admission (RR=2.35, 95% CI: [1.86-2.98]), myocardial infarction (RR=5.58, 95% CI: [3.73-8.34]), heart failure (RR=1.59, 95% CI: [1.38-1.85]), stroke (RR=2.94, 95% CI: [1.75-4.97]), MACE (RR=3.92, 95% CI: [2.91-5.27]), and all-cause mortality (RR=1.32, 95% CI: [1.13-1.55]) within one year compared to those who received ICIs but did not develop myocarditis.

Conclusion: ICI-associated myocarditis is a rare irAE but carries an increased risk of cardiovascular complications and death. Advanced age, hypertension, hyperlipidemia, melanoma, and ipilimumab use appear to be risk factors. Clinical vigilance is warranted to facilitate early detection and management of this potentially fatal complication.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

This abstract has been accepted for presentation at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and is scheduled to be presented in June 2025. Disclosure provided in accordance with ASCO and ACR guidelines. This abstract will not be published or presented at ACR prior to its official presentation at ASCO.

Disclosure: Q. Wang: None; **Z. Tang**: None; **L. Deng**: Bridgebio, 5, Bristol-Myers Squibb(BMS), 1, Merck, 12, Travel, Accommodations, Expenses, MJH Life Sciences, 6, 12, Travel, Accommodations, Expenses, Precisca, 6, Regeneron, 2.

Abstract Number: 1114

Multi-omics Integration Analysis of the Cross-scale Mechanism of MTX-induced T2DM Risk and the Precise Intervention Strategy of Leonurine

Mei-Feng Shi[1], Fang-Shu Zou[1], Xiao-Na Ma[1], Wei Feng[1], Yi-Fang Zhang[2], Chang-Song Lin[1], Min-Ying Liu[2] and **Qiang Xu**[1], [1]Guangzhou University of Traditional Chinese Medicine, Guangzhou, China (People's Republic), [2]The First Clinical Medical College of Guangzhou University of Chinese Medicine, Guangzhou, Guangdong, China (People's Republic)

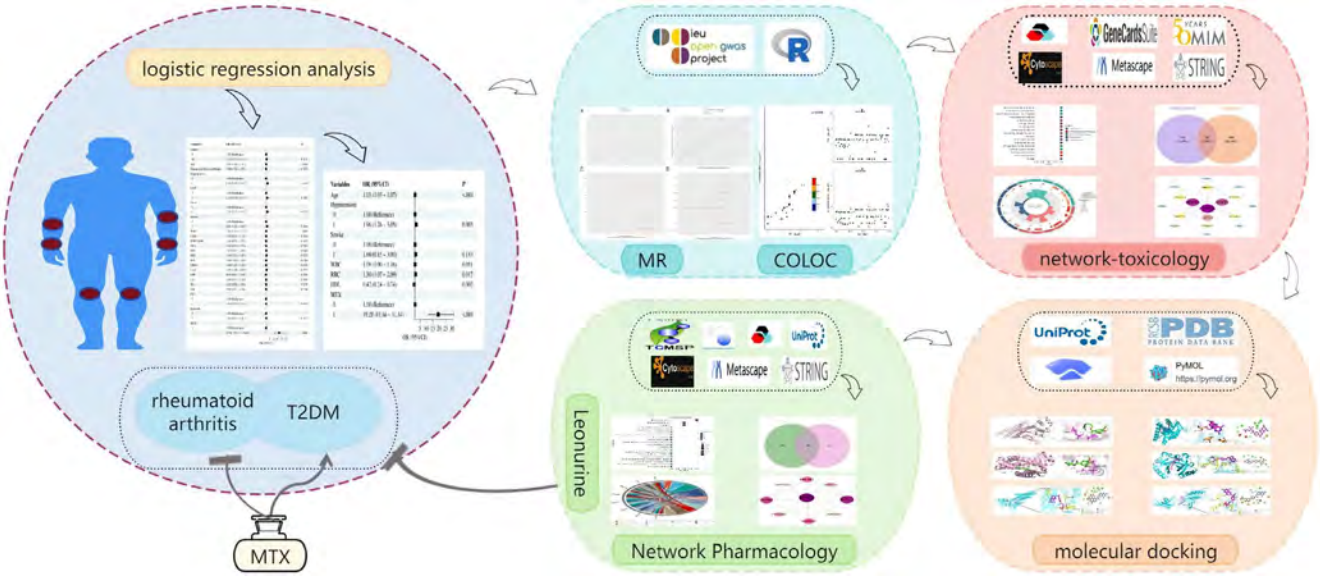
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate (MTX) is a first-line treatment for autoimmune diseases, including rheumatoid arthritis (RA). Its potential risk of inducing type 2 diabetes mellitus (T2DM) remains controversial, and the underlying mechanism is not well understood.

Methods: This study utilized a multi-omics integration approach to systematically assess the association mechanism between MTX and T2DM. Initially, a binary logistic regression model was constructed based on clinical cohort data from 1,253 RA patients, to analyze the correlation between MTX exposure and glycemic metabolism indicators. Additionally, genetic instrumental variables associated with MTX metabolism were selected using public Genome-Wide Association Study (GWAS) databases. The causal relationship was evaluated employing a two-sample Mendelian randomization (MR) framework, combined with inverse variance weighted (IVW), weighted median (WM1), MR-PRESSO, and MR-Egger regression methods, and Bayesian colocalization analysis was used to pinpoint shared genetic variations across the genome. At the molecular mechanism level, a network toxicology approach was utilized to construct an MTX-T2DM interaction network. Molecular docking validation was then performed on selected core targets to confirm their affinity. For potential intervention strategies, the network pharmacology approach was employed to predict the multi-target action network of leonurine, and molecular docking techniques were applied to evaluate the binding stability with key targets.

Results: Clinical data indicates a significant positive correlation between MTX exposure and the risk of T2DM (aOR=19.28, 95%CI:11.86-31.34). MR analysis reveals a significant positive correlation between MTX exposure and the risk of T2DM (OR: 4.50, 95% CI: 3.62-5.61, p=4.03E-31). Bayesian colocalization analysis demonstrates significant genomic colocalization between genetic variants associated with MTX drug response and T2DM risk loci, suggesting that both conditions share causal genetic drivers. Network toxicology and molecular docking elucidate that MTX disrupts fat differentiation and aggravates insulin resistance by inhibiting the PPARG ligand binding domain (docking energy -6.69 kcal/mol) and affecting lipid storage and metabolism. Notably, network pharmacology predictions, combined with molecular dynamics simulations, have confirmed that leonurine can target and activate PPARG and interfere with the Toll-like receptor signaling pathway, thereby reversing the metabolic-immune imbalance induced by MTX.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Graphical abstract

Conclusion: This study has, for the first time, constructed a four-dimensional interaction model of "drug-gene-metabolism-immunity" based on clinical data, proposed a multi-target cascading mechanism of MTX-induced T2DM, and provided interdisciplinary evidence chains for the use of leonurine as a precise intervention agent. This lays a theoretical foundation for optimizing clinical medication with MTX and strategies for the prevention and treatment of T2DM.

Disclosure: M. Shi: None; **F. Zou**: None; **X. Ma**: None; **W. Feng**: None; **Y. Zhang**: None; **C. Lin**: None; **M. Liu**: None; **Q. Xu**: None.

Abstract Number: 1115

Evaluation Of The Global Toxicity Burden In Patients Treated With Checkpoint Inhibitors Addressed For a Rheumatologic Toxicity And Its Impact On Oncological Outcomes

Juliette quelain[1], Eleonore Mourre[2], Julien Henry[1], Rakiba Belkir[3], Andrew Cope[4], Debashis Sarker[5], Yin Wu[6], Matthaios Kapiris[7], Aurelien Marabelle[8], Caroline Robert[8], Raphaele Seror[9], Xavier Mariette[10] and **Samuel Bitoun**[1], [1]APHP, PARIS, France, [2]APHP, PARIS, [3]PARIS, PARIS, France, [4]King's College London, London, United Kingdom, [5]Comprehensive Cancer Centre and Consultant Medical Oncologist at Guy's, St Thomas' and King's College Hospitals., London, United Kingdom, [6]Honorary Consultant Medical Oncologist at Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, [7]KCL, LONDON, United Kingdom, [8]IGR, PARIS, France, [9]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [10]Université Paris-Saclay, Le Kremlin Bicetre, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Approvals for immune checkpoint inhibitors (ICIs) have expanded, and triple therapy combining anti-PD-1, anti-CTLA-4, and anti-LAG3 have been evaluated with encouraging results. But they lead to increasing toxicities, called immune-related adverse events (irAEs). IrAEs have been considered one organ at a time but in reality, comprise a range of systemic inflammatory syndromes targeting multiple organs. A global toxicity score called Organ, Severity, and total Toxicity (OST) has been developed. Patients experiencing irAEs have been shown to have longer survival compared with patients without irAE. But most studies did not correctly account for the immortal time bias. The objective of this study was to quantify the OST in patients with rheumatologic irAE and determine the impact of OST on oncologic outcomes, taking into account the immortal time bias.

Methods: The inclusion criteria were ICI treatment for any cancer leading to a rheumatologic irAE. We calculated the OST score to assess the cumulative toxicity burden at 6 and 9 months after ICI initiation. The OST score was composed of 3 parameters: number of organs (O), number of ≥ CTCAE G3 irAEs (S), and the sum of all CTCAE grades (T). Patients were

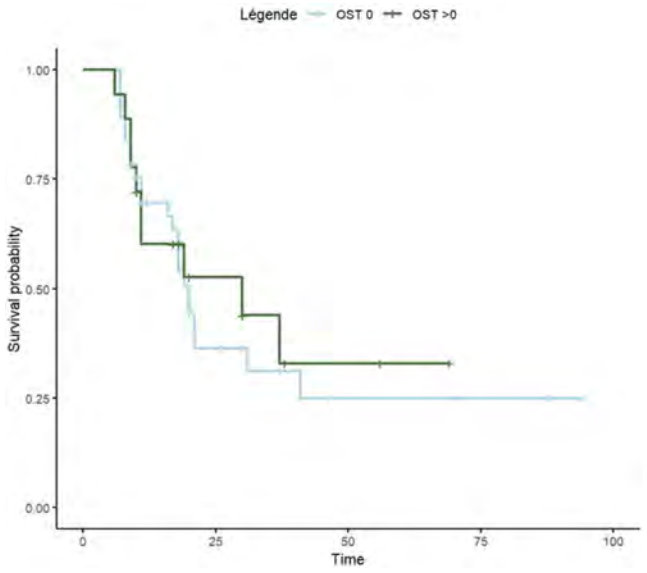
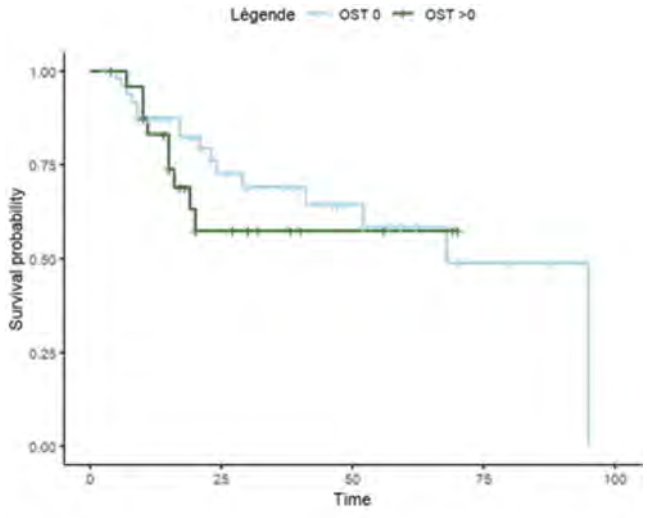


Figure 1 A Progression Free Survival (in months) depending on the cOST group calculated at 6 months from ICI initiation



OS (in months) depending on the OST category calculated at 6 months from ICI initiation

Figure 1 B Overall survival (in months) depending on the cOST group calculated at 6 months from ICI initiation

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	All patients included n=74	cOST=0 n=49	cOST>0 n=25
Age mean (SD)	65.1(11.97)	65.4(12.5)	64.3(11.07)
Charlson mean (SD)	2.56(1.68)	2.71(1.77)	2.28(1.45)
Cancer			
Melanoma n(%)	35 (47)	22(45)	13(52)
Lung Cancer n(%)	12(16)	8(16)	4(16)
Sex			
Female n(%)	25(34)	15(31)	10(40)
Stage			
III n(%)	21(28)	14(29)	7(28)
IV n(%)	52(70)	34(69)	18(72)
Clinical presentation			
PMR-like n(%)	39(53)	29(59)	10(40)
Polyarthritis n(%)	19(26)	10(20)	9(36)
Oligoarthritis n(%)	6(8)	4(8)	2(8)
Monoarthritis n(%)	6(8)	3(6)	3(12)
Treatment of the irAE			
Cumulated Steroids dosage (mg) at 6 months of ICI initiation (mean, SD)	1164(1749)	1288(2042)	915(907)

Patients characteristics according to their cOST group.

divided into low and high-toxicity groups for each O, S, and T categories: high - O≥3, S≥1, T≥4 attributing 1 point each to calculate a composite OST score (cOST). To account for immortal time bias, landmark analysis methods were used at 2 time points: 6 and 9 months. Patients were included if they had experienced rheumatologic iRAE and were alive before the time points. Kaplan Meier (univariate) analysis was performed to compare patients according to the cOST score with 2 thresholds at the landmark timepoint.

Results: Out of 109 patients 74 patients were included in the landmark analysis. They mostly presented with polymyalgia rheumatica (53%), then peripheral polyarthritis (26%). Of these patients, 49 (66%) had a cOST=0 at 6 months after the ICI initiation, whereas 25 patients (34%) had a cOST >0. In the landmark analysis starting at 6 months, there was no significant difference in progression-free survival (PFS) according to cOST (p = 0.7) Fig 1A. The median of progression-free survival was 20 months in the cOST=0 group, and 30 months in the cOST >0 group. Likewise, there was no significative difference in overall survival (OS) between patients with cOST > 0 vs cOST=0 at 6 months of ICI initiation (p = 0.4) Fig 1B. The median of overall survival was 68 months in the cOST=0 group and was not reached in the cOST > 0 group. The same analysis performed with landmark at 9 months of ICI initiation returned similar results. When using a different threshold comparing a cOST score of 0-1 with cOST score of 2-3, there was also no significant difference in PFS or OS. There was no major misbalance between cOST groups regarding factors that might influence PFS or OS (table 1). Adjusted analysis will be presented during the meeting.

Conclusion: Patients with articular irAE tend to have a mostly low global inflammatory burden when assessed with this global score that is cOST. There were no significant differences in survival (PFS and OS) in patients with high or low global burden of checkpoint inhibitors toxicity, in this cohort of patients with rheumatic irAEs.

Disclosure: J. quelain: None; **E. Mourre**: None; **J. Henry**: None; **R. Belkir**: None; **A. Cope**: Bristol-Myers Squibb(BMS), 2, 5, 6; **D. Sarker**: None; **Y. Wu**: None; **M. Kapiris**: None; **A. Marabelle**: None; **C. Robert**: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **S. Bitoun**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1116

Second-line Therapy for Immune-checkpoint Inhibitor-induced Pneumonitis

Sarah Sun[1], Cathryn Lee[2] and Pankti Reid[3], [1]University of Chicago, Chicago, IL, [2]University of Chicago, Chicago, [3]University of Chicago Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) used for cancer therapy can have varied toxicities among which pneumonitis (ICI-pneumonitis) is a rare (< 5%) but often fatal complication. There is scant data to guide second-line therapy for ICI-pneumonitis if systemic steroids are insufficient. We sought to evaluate and compare the effectiveness of key second-line immunosuppressive agents in achieving ICI-pneumonitis resolution.

Methods: For this retrospective observational study, we identified patients with ICI-pneumonitis whose symptoms were refractory or recurrent after systemic steroid treatment and who received a second line agent. We collected data regarding cancer type, ICI type, pneumonitis phenotype and grade, pulmonary comorbidities, steroid details, secondary immunosuppression and outcomes including time to pneumonitis resolution, overall survival, and progression free survival. Count data, t-tests, and chi-square tests were used when appropriate. Cox proportional hazards regression was used for survival data.

Results: Of 1156 patients with ICI-pneumonitis, 13 ICI-pneumonitis patients with second-line treatment (mean age 60.5 (SD 16.5), 8 (61.5%) males) were included in the study. 6 (46.1%) were previous or current smokers, and 9 (69.2%) had pulmonary involvement of their malignancy. 8 (61.5%) patients received chest radiation. All patients had received anti-PD1 monotherapy. Second line immunosuppressive agents included tocilizumab (6 patients), infliximab (4 patients), mycophenolate mofetil (MMF) (4 patients), and Intravenous immunoglobulin (IVIg) (2 patients). Among these, 2 were treated with tocilizumab after failing infliximab or IVIG; one received MMF after failing infliximab. Cancer progression occurred in 2 (50%) MMF, 1 (25%) infliximab, 1 (16.7%) tocilizumab, and 0% patients receiving IVIg. Pneumonitis resolution or sustained improvement occurred most frequently with tocilizumab (4 (66.7%)) compared to MMF (1 (25%), IVIg (0%), or infliximab (0%). The hazard

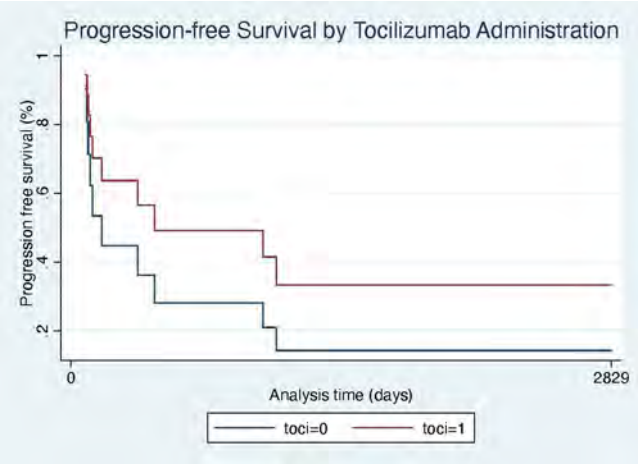


Figure 1. Progression-free survival in refractory or recurrent ICI-pneumonitis patients who received tocilizumab (toci=1, red line) compared to patients who did not receive tocilizumab (toci=0, blue line).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of the combined outcome of progression or death was lower in patients receiving tocilizumab compared to those without; however did not reach statistical significance (Figure 1; HR 0.56, 95% CI 0.16-2.01).

Conclusion: This study, while underpowered, demonstrates that tocilizumab is not associated with worse outcomes and may be associated with improved survival in patients with ICI-pneumonitis. Future studies should prospectively investigate this finding in larger cohorts.

Disclosure: S. Sun: None; **C. Lee**: None; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1.

Abstract Number: 1117

Inflammatory Arthritis after Hematopoietic Stem Cell Transplant: A Case Series and Literature Review

Scott Yeudall[1], Mark Levis[2], Jonathan Webster[2] and Laura Cappelli[3], [1]The Johns Hopkins Hospital, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]Johns Hopkins School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Hematopoietic stem cell transplant (HSCT) is a commonly employed treatment for hematologic malignancies including acute leukemias and lymphomas but can be complicated by graft-versus-host disease (GVHD), an inflammatory syndrome affecting multiple organs. While there have been case reports of post-transplant rheumatic syndromes (e.g. myositis and psoriasis), the incidence of post-HSCT inflammatory arthritis is less clear. We aimed to characterize the clinical phenotypes of patients evaluated for inflammatory arthritis after HSCT and to perform a literature review of reported cases of post-HSCT inflammatory arthritis.

Methods: We analyzed the clinical and demographic data of six patients evaluated in the Division of Rheumatology at Johns Hopkins for inflammatory arthritis with initial symptoms after HSCT for hematologic malignancy. Chart review included evaluation of the patient's hematologic malignancy treatment history, clinical arthritis phenotype, arthritis symptom severity and disease activity, serum inflammatory markers, autoantibodies, and arthritis treatment outcomes. For the literature review, the PUBMED database was queried with 24 targeted search terms including those related to inflammatory arthritis, rheumatic disease, and joint involvement combined with hematopoietic stem cell transplant and GVHD, and primary reports were reviewed to assess for common presenting clinical features, immunologic history, and response to treatment.

Results: Of the six patients evaluated in our center for concern of inflammatory arthritis presenting after HSCT, five had HSCT for treatment of acute myeloid leukemia, and three had received at least some treatment for GVHD (Table 1). Symptoms of inflammatory arthritis arose 4-72 months after HSCT (Table 1). Clinical phenotype varied in severity from mild to severe as measured by the Clinical Disease Activity Score (CDAI), and did not clearly correlate with timing of onset post-transplant, prior GVHD, or prior history of autoimmune disease (Table 2). The most frequently involved joints were PIPs, MCPs, MTPs, wrists, and ankles. A majority (5/6) of cases did not have positive serologic markers of rheumatoid arthritis (RF, anti-CCP) or other tested autoantibodies (Table 2). A variety of immunosuppressive medications were employed for treatment of arthritis symptoms, and some patients required corticosteroids for management of symptoms. Literature search identified 16 primary case reports and literature reviews of inflammatory arthritis post-HSCT. The two largest case

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Malignancy and transplant history and timing of arthritis onset after HSCT.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Malignancy History	AML (FLT3-ITD)	AML (IDH1, FLT3 mutant)	Hodgkin lymphoma, transformed to large B cell lymphoma	AML (2,16 translocation)	Testicular cancer, plasmacytoma, myeloma, therapy related AML	AML (FLT3-ITD)
Pre-HSCT Treatment(s)	Cytarabine, idarubicin, etoposide, then high-dose cytarabine	7+3 and ivosidenib	R-CHOP, rituximab, then R-ICE	7 + 3, then high-dose cytarabine	Cytarabine + daunorubicin, then HiDAc	7+3 and midastaurin, then HiDAc
Symptoms of GVHD?	No	Yes – skin, GI, mucosal	No	Yes – skin, GI, mucosal	Yes - GI	No
Time to onset of symptoms after HSCT	6 years	1 year 2 months	4 months	11 months	12 months	11 months
Prior autoimmune history?	No	No	Psoriasis	No	Graves' Disease, alopecia totalis	Hashimoto thyroiditis

Table 2. Clinical phenotype and laboratory data of patients presenting with post-HSCT inflammatory arthritis

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Clinical Phenotype						
Involved Joints	PIPs, shoulders	B/L MCPs, PIPs, MTPs, wrists L knee, ankle	B/L Shoulders, wrists, ankles, knees, PIPs,	B/L wrists, PIPs R ankle L MTP	B/L PIPs, MCPs, MTPs, ankles	B/L PIPs, MTPs, knees, wrists
Additional Manifestations	N/A	Triggering of bilateral 3rd fingers Enthesitis of Achilles, medial epicondyles, greater trochanters	Recurrent infections requiring immunoglobulin therapy Sicca symptoms (mouth, eyes)	Sicca (dry mouth)	Fluid in infrapatellar bursa	N/A
CDAI Score at Presentation	Not available	27	21.5	23	33	11.5
Laboratory Data						
Acute Phase Reactants	ESR 39	CRP 0.4 ESR 3	CRP < 0.3 ESR 8	CRP 1.0 ESR 10	CRP < 0.3 ESR 9	CRP < 0.3 ESR 21
RF	negative	negative	negative	27.9	negative	negative
ACPA	CCP negative	CCP negative	negative	negative	CCP negative	CCP negative
Other autoantibodies	ANA 1:40 speckled	ANA negative	ANA, SSB, Ro52, Ro60 negative	ANA negative	ANA negative	ANA negative

series each reported three cases. Psoriatic arthritis, seropositive rheumatoid arthritis, pseudogout, and spondylarthritis were described in case reports.

Conclusion: De novo seronegative inflammatory arthritis occurs after HSCT, characterized by variable severity of presentation and association with other symptoms of GVHD. A literature review identified a limited number of reports of inflammatory arthritis after HSCT, suggesting that continued research is needed to identify predisposing factors in the post-transplant period and advance understanding of rheumatologic complications arising from immunotherapy treatment of hematologic malignancies.

Disclosure: S. Yeudall: None; **M. Levis**: Bristol-Myers Squibb(BMS), 1, Novartis, 12,; **J. Webster**: Amgen, 2, CVS, 2, Jazz, 2, Servier, 2, Syndaxx, 2; **L. Cappelli**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, 5, Sanofi, 2, Uniquity Bio, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1118

Increased Risk of Azathioprine-Induced Leukopenia in Patients with Systemic Lupus Erythematosus: A 10-Year Retrospective Cohort Study at a Quaternary Care Hospital in Thailand

Settawut Buadee[1], Kittikorn Wilasrusmee[1], Tanakrit Kamonsumlitpon[1], Sirirat Charuvanij[2], Ekapun Karoopongse[3] and Praveena Chiowchanwisawakit[4], [1]Medical Student, Faculty of Medicine, Siriraj Hospital, Mahdol University, Bangkok, Thailand, [2]Division of Rheumatology, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, [3]Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand, [4]Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Bangkok, Thailand

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: To estimate the incidence and identify associated factors of azathioprine (AZA)-induced leukopenia.

Methods: A retrospective cohort study was conducted on 1,062 adult patients with non-malignant diseases who received azathioprine for the first time between 2014 and 2023 at Siriraj Hospital, Thailand. Inclusion criteria required patients to have a baseline complete blood count (CBC) within eight weeks before starting AZA and a follow-up CBC performed two weeks after treatment. Patients were excluded if they had an abnormal CBC, defined as a white blood cell (WBC) count < 3,000 cell/μl, a neutrophil count < 1,500 cell/μl (neutropenia), or a lymphocyte count < 1,500 cell/μl. Patients with active infections or a history of splenectomy were also excluded. Clinical and laboratory parameters were collected from a medical database during the first year of azathioprine treatment. Follow-up CBC were analyzed to identify cases of AZA-induced leukopenia, defined as a WBC count < 3,000 cell/μl and/or neutropenia. Hazard ratios for factors associated with AZA-induced hematologic abnormalities was analyzed using Cox regression.

Results: Among the cohort, SLE was the most common underlying condition, affecting 274 patients (25.80%). The overall incidence of AZA-induced leukopenia was 6.21%, with an incidence rate of 5.28 per 1,000 person-months (95% CI: 4.15–6.73).

Table 1: Incidence and incidence rates of azathioprine-induced hematologic abnormalities in the overall cohort and the SLE subgroup.

Categories of Abnormal Complete blood count	Incidence (person, percent)		Incidence rate (1000 person-month, 95% confidential interval)	
	Overall (n=1062)	SLE (n=274)	Overall (n=1062)	SLE (n=274)
AZA-induced leukopenia (WBC count < 3000 cell/μl and/or Neutrophil count < 1500 cell/μl)	66 (6.21%)	33 (12.04%)*	5.28 (4.15-6.73)	10.60 (7.54-14.91)
Leukopenia (White blood cell [WBC] count < 3000 cell/μl)	52 (4.90%)	28 (10.22%)*	4.12 (3.14-5.41)	8.88 (6.13-12.86)
Neutropenia (Neutrophil count < 1500 cell/μl)	47 (4.43%)	22 (8.03%)*	3.74 (2.81-4.97)	6.96 (4.58-10.56)
Agranulocytosis (Neutrophil count < 500 cell/μl)	9 (0.85%)	3 (1.09%)	0.71 (0.37-1.37)	0.95 (0.31-2.94)
Lymphopenia (lymphocyte count < 1500 cell/μl)	535 (50.38%)	176 (64.23%)*	64.66 (59.41-70.38)	96.89 (83.58-112.32)
Severe lymphopenia (lymphocyte count < 500 cell/μl)	14 (1.32%)	5 (1.82%)	1.69 (1.00-286)	2.75 (1.15-6.61)

*The incidence in the SLE group significantly differed from the non-SLE populations (P < 0.05) using the Chi-square test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Hazard ratios with 95% confidence intervals for factors associated with azathioprine-induced hematologic abnormalities, analyzed using Cox regression. Statistically significant associations are highlighted by color intensity based on P values. AZA-induced leukopenia was defined as a white blood cell (WBC) count <3,000 cells/μL and/or neutrophil count <1,500 cells/μL. Individual abnormalities were classified as follows: leukopenia (WBC <3,000 cells/μL), neutropenia (neutrophil count <1,500 cells/μL), and lymphopenia (lymphocyte count <1,500 cells/μL).

Factors	Hazard ratio (95% CI)			
	AZA-induced leukopenia	Leukopenia	Neutropenia	Lymphopenia
Age	0.985 (0.970-1.001)	0.981 (0.964-0.999)	0.995 (0.977-1.013)	1.003 (0.997-1.008)
Female gender	1.378 (0.737-2.567)	1.133 (0.583-2.205)	1.132 (0.563-2.276)	1.152 (0.936-1.417)
SLE patients	3.001 (1.852-4.862)	3.495 (2.026-6.029)	2.608 (1.471-4.625)	1.607 (1.342-1.925)
Other connective tissue diseases	1.332 (0.608-2.915)	1.459 (0.623-3.417)	1.338 (0.530-3.383)	1.309 (0.981-1.747)
Dose of AZA > 100 mg/day	7.033 (4.187-11.811)	9.609 (5.493-16.811)	6.719 (3.595-12.557)	1.810 (1.469-2.231)
Concurrent use of Allopurinol	13.736 (3.357-56.121)	17.007 (4.134-69.969)	6.626 (0.914-48.066)	1.080 (0.270-4.332)
Concurrent use of Cotrimoxazole	0.904 (0.363-2.250)	0.914 (0.330-2.534)	0.747 (0.232-2.405)	1.389 (1.050-1.836)
Baseline White blood cell count	0.858 (0.787-0.935)	0.808 (0.727-0.899)	0.877 (0.795-0.967)	0.954 (0.931-0.978)
Baseline Neutrophil count	0.860 (0.781-0.948)	0.826 (0.735-0.929)	0.870 (0.778-0.974)	0.994 (0.969-1.020)
Baseline lymphocyte count	0.765 (0.565-1.036)	0.559 (0.366-0.855)	0.845 (0.608-1.175)	0.485 (0.423-0.555)
Baseline eGFR less than 60mL/min/1.73m²	0.435 (0.136-1.387)	0.565 (0.176-1.819)	0.189 (0.026-1.371)	1.342 (1.022-1.762)

P <0.05 P <0.01 P <0.001 * Each color corresponds to a specific significance level.

Notably, SLE patients had a significantly higher incidence of 12.04% and an incidence rate of 10.60 per 1,000 person-months (95% CI: 7.54–14.91), $P < 0.05$ compared to non-SLE populations. Incidence and incidence rates of each lineage of WBC abnormalities with different cut point were shown in Table 1. SLE was a significant risk factor for AZA-induced leukopenia (HR = 3.001, $P < 0.001$), as well as for leukopenia, neutropenia, and lymphopenia. Other predictors included AZA dose >100 mg/day, associated with higher risk of leukopenia (HR = 9.609, $P < 0.001$) and neutropenia (HR = 6.719, $P < 0.001$). Concurrent allopurinol use conferred the highest risk for leukopenia (HR = 17.007, $P < 0.001$). Lower baseline WBC and neutrophil counts were linked to higher risk of AZA-induced leukopenia and neutropenia, as shown in Table 2. SLE remained an independent risk factor after adjusting for baseline leukocyte counts and AZA dose. Additionally, AZA-induced leukopenia incidence did not significantly differ between patients with normal pharmacogenetic profiles for Thiopurine S-methyltransferase (TPMT), Inosine triphosphate pyrophosphatase 94C >A (ITPA 94C >A), and Nudix hydrolase 15C415T (NUDT15 C415T) and those without testing.

Conclusion: Given the notably high incidence of AZA-induced leukopenia in SLE patients, regular CBC monitoring and AZA dose adjustment are essential to prevent its occurrence, even in those with normal baseline CBC at the start of treatment. Additionally, patients receiving allopurinol concurrently, an AZA dose over 100 mg/day, or those with low baseline WBC and neutrophil counts should be monitored closely. Relying solely on pharmacogenetic testing (including TPMT, ITPA, and NUDT15) may not be sufficient to prevent AZA-induced leukopenia.

Disclosure: S. Buadee: None; **K. Wilasrusmee**: None; **T. Kamonsumlitpon**: None; **S. Charuvanij**: None; **E. Karoopongse**: None; **P. Chiowchanwisawakit**: None.

Abstract Number: 1119

Microbial activation of cytotoxic CD8$^+$ T cells promotes skin immune-related adverse events in patients treated with immune checkpoint inhibitors

Shady Younis[1], Suman Acharya[1], Gayathri Swaminathan[1], Heidi Wong[1], Hannah Kim[1], Alec Eschholz[1], Subramanya Hegde[2], Andrew McKnight[3], William Robinson[4] and Lisa Zaba[1], [1]Stanford University, Stanford, CA, [2]Sanofi US, New Jersey, MA, [3]Sanofi US, Cambridge, MA, [4]Stanford University, Palo Alto, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have transformed cancer therapy, but their use is often limited by immune-related adverse events (irAEs), particularly in barrier tissues such as the skin. The mechanisms underlying cutaneous irAEs remain incompletely understood. We aimed to identify cellular and antigenic drivers of skin irAEs in ICI-treated patients

Methods: We performed single-cell RNA sequencing (scRNA-seq) and T cell receptor (TCR) sequencing on paired lesional skin biopsies and peripheral blood mononuclear cells (PBMCs) from ICI-treated cancer patients who developed cutaneous irAEs. In parallel, we conducted ex vivo stimulation of patient PBMCs with microbial antigens, followed by flow cytometry to assess T cell activation and cytokine production

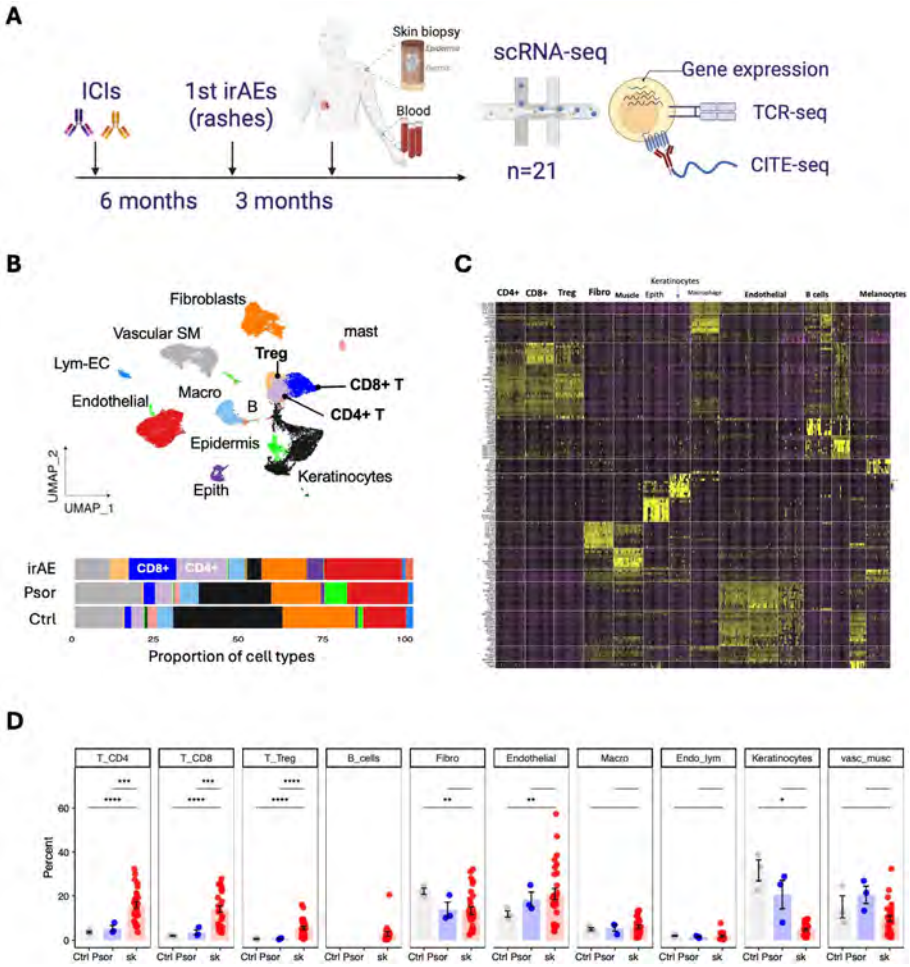


Figure 1. Single-cell analysis of skin and blood samples from patients with cutaneous irAEs following ICI therapy. (A) Schematic overview of the study design. Patients treated with immune checkpoint inhibitors (ICIs) developed immune-related adverse events (irAEs) manifesting as skin rashes. Skin biopsies and blood were collected approximately 3 months after rash onset (average 6 months post-ICI initiation) for single-cell RNA sequencing (scRNA-seq), TCR-seq, and CITE-seq. (B) UMAP embedding of skin immune and stromal cells from 28 samples, color-coded by annotated cell types. Bar plot (bottom) shows the proportion of each cell type across conditions: irAE (red), psoriasis (blue), and healthy control (gray), highlighting increased $CD4^+$ and $CD8^+$ T cell infiltration in irAE skin. (C) Heatmap of scaled gene expression across all clusters, showing top differentially expressed genes that distinguish immune, stromal, and epithelial populations. (D) Quantification of major immune and non-immune cell types across control (Ctrl), psoriasis (Psor), and irAE (sk) samples. Each dot represents an individual patient sample; statistical comparisons were performed using two-tailed t-tests. $P < 0.05$ (*), $P< 0.01$ (**), $P< 0.001$ (***), $P< 0.0001$ (****).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

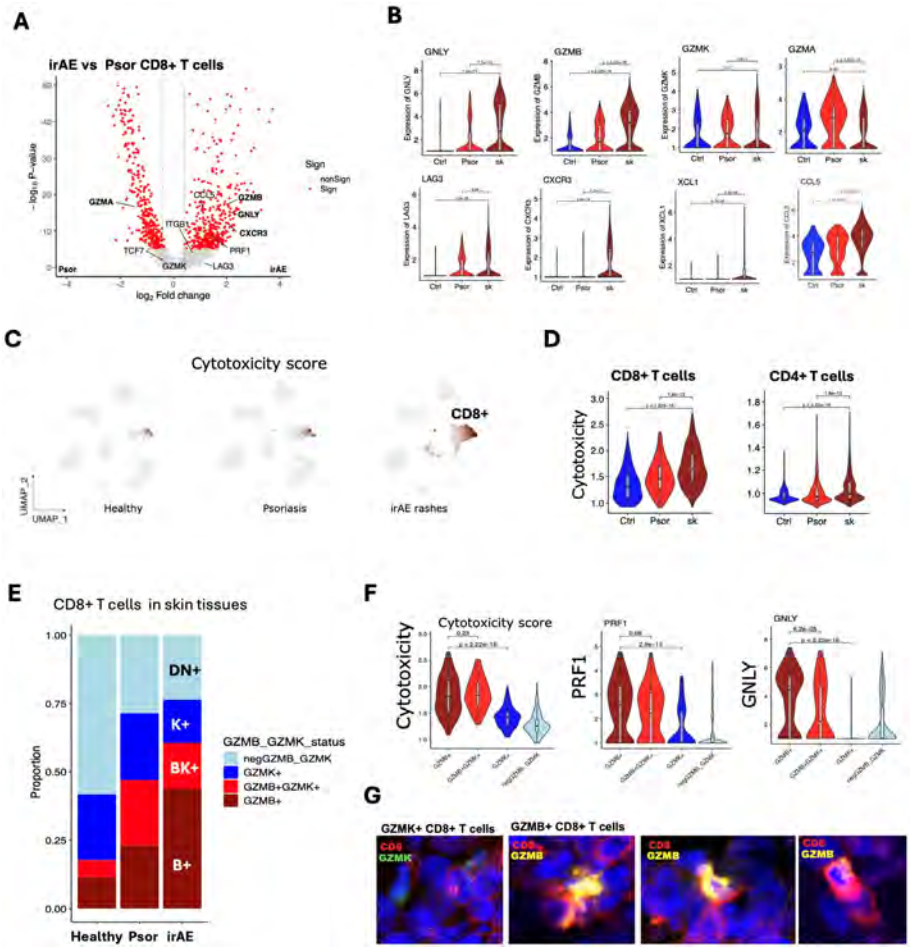


Figure 2. Cytotoxic CD8$^+$ T cells are expanded and activated in irAE skin lesions. (A) Volcano plot showing differentially expressed genes in CD8$^+$ T cells from irAE versus psoriasis skin lesions. Cytotoxic effector genes (GNLY, GZMB, PRF1) and chemokine receptors (CXCR3, XCL1, CCL5) are significantly upregulated in irAE CD8$^+$ T cells. (B) Violin plots showing expression of cytotoxic and chemotactic genes across CD8$^+$ T cells from control (Ctrl), psoriasis (Psor), and irAE (sk) samples. (C) UMAP plots depicting CD8$^+$ T cell distribution and cytotoxicity scores across healthy, psoriasis, and irAE skin tissues.

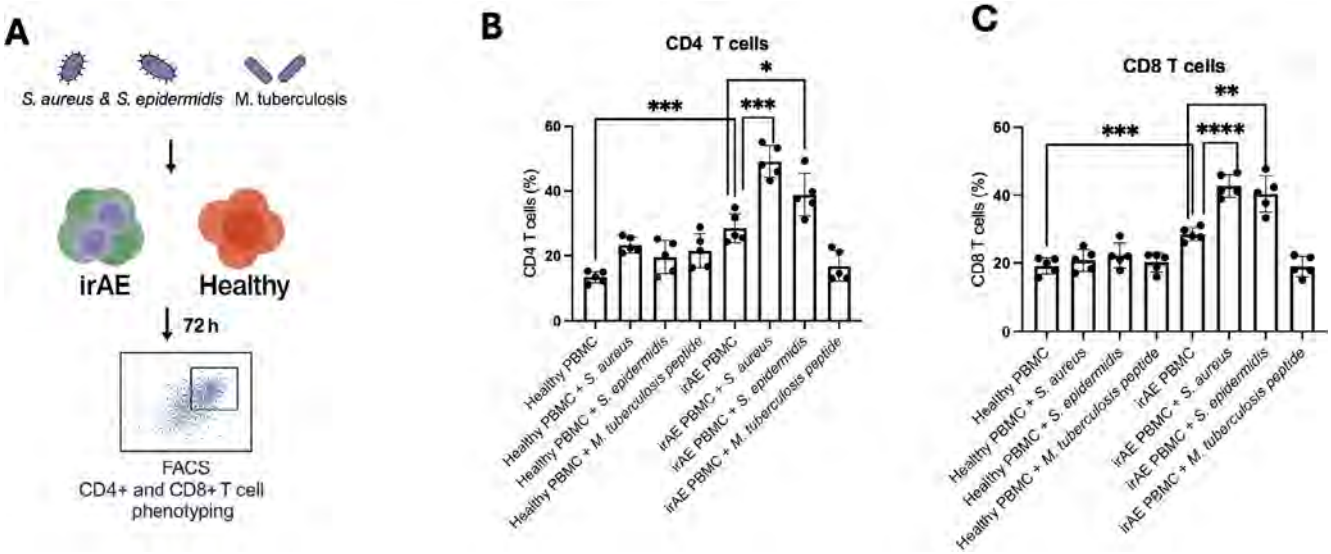


Figure 3. Bacterial stimulation induces activation of cytotoxic CD8$^+$ T cell in PBMCs from irAE patients. (A) Schematic of experimental workflow: PBMCs from irAE patients and healthy controls were stimulated ex vivo for 72 hours with S. aureus, S. epidermidis, or M. tuberculosis antigens. CD4$^+$ and CD8$^+$ T cell phenotypes were analyzed by flow cytometry (FACS). (B–C) Frequencies of CD4$^+$ T cells (B) and CD8$^+$ T cells (C) as a percentage of total lymphocytes across conditions.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Inflamed skin lesions harbored a dominant population of clonally expanded $CD8^+$ T cells expressing cytotoxic effectors including GZMB, PRF1, and IFNG, indicative of tissue-damaging potential. Notably, $CD8^+$ T cells from irAE lesions exhibited substantial expansion of the $GZMB^+$ subset accompanied by a reduction in the less cytotoxic $GZMK^+$ subset, highlighting a skew towards a more pathogenic cytotoxic phenotype. TCR clonotype tracking revealed overlap between skin-infiltrating clones and circulating $CD8^+$ T cells, suggesting antigen-driven recruitment. Computational analysis using GILPH identified shared sequence motifs between patient TCRs and known anti-pathogen TCRs. Additionally, stimulation of patient PBMCs with Staphylococcus aureus and S. epidermidis antigens led to robust activation of $GZMB^+$ $CD8^+$ T cells and enhanced IFN-γ production

Conclusion: Our study identifies microbial antigens as candidate drivers of cytotoxic and inflammatory T cell responses in cutaneous irAEs. These findings highlight the contribution of microbial-reactive $CD8^+$ T cells to irAE pathogenesis and suggest that targeting $GZMB^+$ $CD8^+$ effector functions may offer a therapeutic strategy to alleviate irAEs without compromising anti-tumor immunity

Disclosure: S. Younis: None; **S. Acharya**: None; **G. Swaminathan**: None; **H. Wong**: None; **H. Kim**: None; **A. Eschholz**: None; **S. Hegde**: None; **A. McKnight**: None; **W. Robinson**: None; **L. Zaba**: None.

Abstract Number: 1120

Synergistic Effects of IL-17F and IL-17A on Neutrophil Chemotaxis: Increased Risk of Candidiasis with Dual Blockade of IL-17A and IL17-F

Siba Raychaudhuri[1], Disha Chakraborty[2], Christine Abria[2] and Smriti K Raychaudhuri[3], [1]UC Davis, School of Medicine/VA Medical Center, Sacramento, Davis, CA, [2]Sacramento VA Medical Center, Mather, CA, [3]Sacramento VA Medical Center, Davis, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IL-17 is primarily secreted by Th17 cells. The IL-17 family has 6 related cytokines (IL-17A to IL17F); IL-17A and IL-17F, being key proinflammatory mediators. IL-17A is known for its critical role in neutrophil-mediated immune defense. Notably, dual blockade of IL-17A/F has been associated with a higher risk of candidal infections compared to IL-17A inhibition alone. The objective of this study is to investigate the reason for increased risk of candidiasis linked to dual IL-17A/F blockade. Both IL-17A and IL-17F signal through IL-17RA/IL-17RC. This shared pathway suggests a synergistic role in neutrophil-mediated innate immunity; thus, inhibiting both may increase susceptibility to infections. Here we determined synergistic effects of IL-17A/IL-17F on (i) neutrophil chemotaxis and (ii) candidal killing.

Methods: Blood was collected from psoriatic arthritis (PsA) and osteoarthritis (OA) patients (n=12/each). Neutrophils were isolated using density gradient centrifugation; 1×10*6 cells were seeded into 5 μm pore Transwell inserts (upper chamber) in a 24-well plate. In the lower chambers rIL-17A, rIL-17F, with or without anti-IL-17A/F mab antibodies were added (100 ng/ml each, ThermoScientific). After 12 hours, the inserts were removed, and neutrophil migration was quantified by measuring the number of neutrophils in the lower chamber by MTT assay (optical density (OD) at 450nm, Millipore Sigma).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

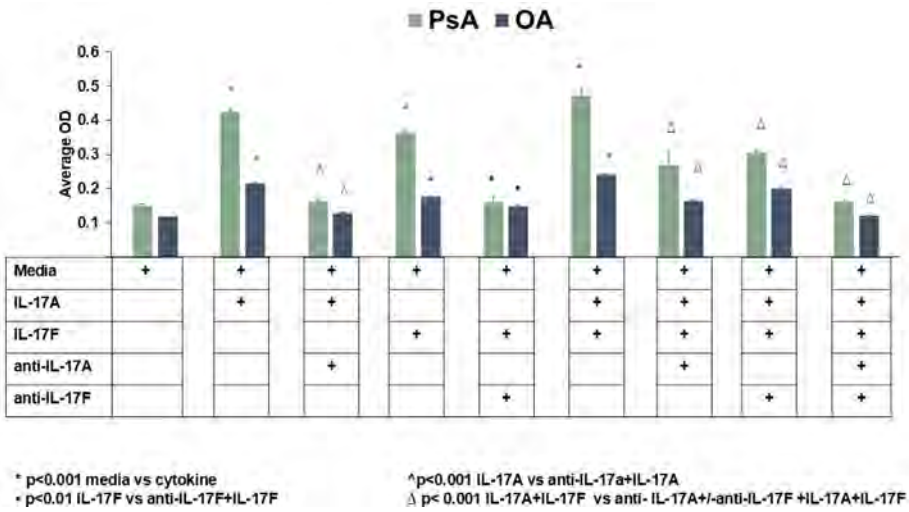


Figure 1: Comparison of neutrophil chemotaxis induced by rIL17A, rIL17F and anti rIL17A + rIL-17F. Both rIL17-A and rIL-17F induced chemotaxis of neutrophils; however combined rIL-17A + rIL-17F showed significantly higher neutrophil chemotaxis. Another intriguing observation was increased chemotaxis with rIL-17A/rIL17F on the neutrophils of psoriatic arthritis (PsA) compared to osteoarthritis (OA).

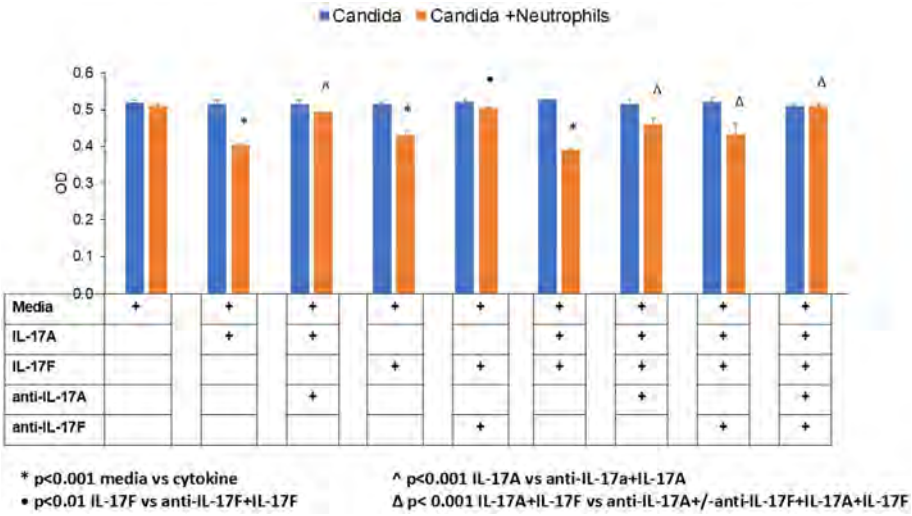


Figure 2: Reduction of candida population as a result of significant neutrophil chemotaxis induced by rIL-17A + rIL-17F. The IL-17A/ILF mabs significantly reduced neutrophil chemotaxis (Fig-1A) resulting in higher candida survival.

To assess neutrophil phagocytic killing of candida, 0.25×10*6 *Candida* with the same cytokine/antibody conditions as above were added in the lower chamber and 1×10*6 neutrophils in the upper chamber. After 12 hours, migrated neutrophils in the lower chamber were lysed with pH11 H_2O; rest of the living cells (*Candida*)were measured by MTT assay. Results are expressed in OD (Mean±SEM) of lower chamber cells.

Results: Neutrophils treated with rIL-17A (OD: 0.149±0.006), rIL-17F (OD: 0.362±0.007), and rIL-17A+rIL-17F (OD: 0.474 ±0.018) showed significantly higher chemotaxis (p< 0.001) compared to media only in PsA patients. Chemotaxis was also significantly higher with rIL-17A vs. rIL-17A+anti-IL17A mab (OD: 0.161±0.008, p< 0.001) and rIL-17F vs. rIL-17F+anti-IL-17F mab (OD: 0.160±0.019, p< 0.01). Notably, rIL-17A+rIL-17F induced greater chemotaxis compared to rIL-17A or rIL-17F (p< 0.001) and which could be effectively blocked by anti-IL17A/F (Fig-1).

rIL-17A+rIL-17F driven neutrophil chemotaxis effectively killed and significantly reduced candida population (OD: 0.363 ±0.014) compared to rIL-17A (OD: 0.410±0.005) or rIL-17F (OD: 0.435±0.25)[p< 0.004; Fig-2].

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study reports a unique innate immune function of IL-17A and IL-17F, a synergistic enhancement of neutrophil chemotaxis, which could be effectively blocked by anti-IL17A and anti-IL17F mabs (Fig-1). Furthermore, IL-17A+IL-17F significantly reduced Candida survival by inducing neutrophil chemotaxis, which was neutralized by IL-17A/IL-17F mAbs, leading to increased survival of candida (Fig-2). These findings suggest that dual IL-17A/IL-17F blockade may increase the risk of candidal infections, highlighting the need for close monitoring for mucosal and systemic candidiasis in patients with these therapies.

Disclosure: S. Raychaudhuri: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **D. Chakraborty**: None; **C. Abria**: None; **S. Raychaudhuri**: None.

Abstract Number: 1121

Latent Class Analysis Identifies Distinct Phenotypes of Multisystem Immune-Related Adverse Events Predictive of Survival After Immune Checkpoint Inhibitors

Tao Ming Sim[1], May Shuen Tang[1], Qai Ven Yap[2], Alvin Wong[1], Yiqing Huang[1] and Frank Sen Hee Tay[1], [1]National University Hospital, Singapore, Singapore, [2]National University of Singapore, Singapore

Table 1. Clustering of irAEs in various organ systems using LCA.

	Cluster 1	Cluster 2	Cluster 3	OR for cluster 2	OR for cluster 3	p-value
IrAE-1: Pulmonary No Yes	118 (100.0%) 0 (0.0%)	9 (22.5%) 31 (77.5%)	179 (97.8%) 4 (2.2%)	785.8	5.9	<0.001
IrAE-2: Hepatotoxicity No Yes	118 (100.0%) 0 (0.0%)	27 (67.5%) 13 (32.5%)	151 (82.5%) 32 (17.5%)	116.3	50.8	<0.001
IrAE-3: Cardiotoxicity No Yes	118 (100.0%) 0 (0.0%)	40 (100.0%) 0 (0.0%)	169 (92.3%) 14 (7.7%)	2.9	20.3	<0.001
IrAE-4: GI-Gastrointestinal No Yes	105 (89.0%) 13 (11.0%)	38 (95.0%) 2 (5.0%)	164 (89.6%) 19 (10.4%)	0.51	0.93	0.594
IrAE-5: GI-Endocrine No Yes	104 (88.1%) 14 (11.9%)	40 (100.0%) 0 (0.0%)	154 (84.2%) 29 (15.8%)	0.09	1.4	0.023
IrAE-6: Skin No Yes	0 (0.0%) 118 (100.0%)	24 (60.0%) 16 (40.0%)	171 (93.4%) 12 (6.6%)	0.003	0.0003	<0.001
IrAE-7: Neurological No Yes	118 (100.0%) 0 (0.0%)	40 (100.0%) 0 (0.0%)	169 (92.3%) 14 (7.7%)	2.9	20.3	<0.001
IrAE-8: Renal No Yes	118 (100.0%) 0 (0.0%)	39 (97.5%) 1 (2.5%)	181 (98.9%) 2 (1.1%)	9.0	3.3	0.222
IrAE-9: Type 1 Diabetes No Yes	118 (100.0%) 0 (0.0%)	40 (100.0%) 0 (0.0%)	182 (99.5%) 1 (0.5%)	2.9	1.9	1.000
IrAE-10: Rheumatological No Yes	118 (100.0%) 0 (0.0%)	40 (100.0%) 0 (0.0%)	152 (83.1%) 31 (16.9%)	2.9	49.0	<0.001
IrAE-11: Cytokine Release Syndrome No Yes	118 (100.0%) 0 (0.0%)	40 (100.0%) 0 (0.0%)	161 (88.0%) 22 (12.0%)	2.9	33.0	<0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

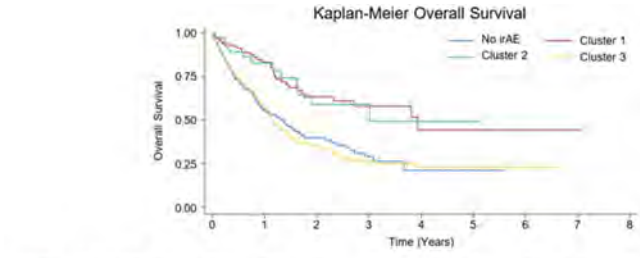
Background/Purpose: Use of immune checkpoint inhibitors (ICIs) can lead to a broad spectrum of immune-related adverse events (irAEs) affecting multiple organ systems. No clear pattern for organs and systems most likely to be affected by simultaneous toxicity has emerged in the published reports of multisystem irAEs. Understanding co-occurrence patterns and prognostic outcomes of irAEs is critical for immunotherapy management. Herein, we focused our analysis on patients from a multi-ethnic Southeast Asian cohort with the intention of identifying distinct phenotypes of irAEs associated with survival after ICIs.

Methods: In total, 870 cancer patients treated with ICIs were recruited into this prospective, multi-institution cohort study of which 341 patients had irAE(s). We used an unbiased approach to identify patients with different patterns of irAEs and to see if these clusters predict outcome. The irAE manifestations were considered as binary (yes/no) variables and used in a latent class analysis (LCA) to identify different phenotypes of multisystem irAEs. Multivariable Cox regression was performed to

Table 2. Clinical characteristics of patients with and without irAEs.

Variables		No irAE (n=526)	Cluster 1 (n=118)	Cluster 2 (n=40)	Cluster 3 (n=183)	p-value
Age at immunotherapy treatment		63.0 (55.0 - 69.0)	63.5 (57.0 - 71.0)	63.0 (54.5 - 70.0)	61.0 (52.0 - 70.0)	0.161
Gender	Female	188 (35.7%)	36 (30.5%)	11 (27.5%)	64 (35.0%)	0.557
	Male	338 (64.3%)	82 (69.5%)	29 (72.5%)	119 (65.0%)	
Ethnicity	Chinese	403 (76.6%)	96 (81.4%)	34 (85.0%)	136 (74.3%)	0.757
	Indian	24 (4.6%)	4 (3.4%)	1 (2.5%)	6 (3.3%)	
	Malay	52 (9.9%)	11 (9.3%)	3 (7.5%)	25 (13.7%)	
	Others	47 (8.9%)	7 (5.9%)	2 (5.0%)	16 (8.7%)	
PS at first dose	0	148 (41.6%)	37 (47.4%)	5 (26.3%)	49 (39.5%)	0.302
	1	167 (46.9%)	38 (48.7%)	14 (73.7%)	66 (53.2%)	
	2	33 (9.3%)	3 (3.8%)	0 (0.0%)	9 (7.3%)	
	4	7 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	5	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Concomitant Antibiotics	No	7 (43.8%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	0.089
	Yes	9 (56.3%)	5 (100.0%)	3 (75.0%)	6 (100.0%)	
Concomitant PPI	No	12 (75.0%)	2 (40.0%)	1 (25.0%)	1 (16.7%)	0.049
	Yes	4 (25.0%)	3 (60.0%)	3 (75.0%)	5 (83.3%)	
Response	Complete response	7 (1.7%)	6 (6.7%)	0 (0.0%)	1 (0.7%)	0.002
	Partial response	84 (19.9%)	31 (34.8%)	9 (27.3%)	31 (20.8%)	
	Stable disease	105 (24.9%)	17 (19.1%)	6 (18.2%)	23 (15.4%)	
	Progressive disease	189 (44.8%)	32 (36.0%)	15 (45.5%)	86 (57.7%)	
	Clinical progression	35 (8.3%)	3 (3.4%)	3 (9.1%)	7 (4.7%)	
	Mixed response	2 (0.5%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	
Concomitant Chemotherapy	No	59 (65.6%)	18 (69.2%)	10 (83.3%)	21 (65.6%)	0.656
	Yes	31 (34.4%)	8 (30.8%)	2 (16.7%)	11 (34.4%)	
BMI prior immunotherapy (kg/m²)		22.4 (20.0 - 25.8)	22.9 (19.4 - 25.1)	22.6 (20.0 - 26.2)	23.5 (20.1 - 26.4)	0.370
6 weeks platelet count (x 109/l)		284.5 (217.3 - 367.0)	277.5 (200.8 - 332.3)	314.5 (230.3 - 409.0)	287.0 (210.0 - 380.0)	0.232
Pretreatment neutrophil count (x 109/l)		4.7 (3.4 - 6.9)	4.6 (3.2 - 6.0)	4.1 (2.6 - 6.1)	4.9 (3.7 - 6.9)	0.156
Pretreatment lymphocyte count (x 109/l)		1.3 (0.9 - 1.8)	1.4 (0.9 - 1.8)	1.1 (0.8 - 1.5)	1.2 (0.9 - 1.7)	0.079
Pretreatment platelet count (x 109/l)		274.0 (210.3 - 355.8)	264.0 (206.0 - 335.0)	287.5 (230.8 - 351.5)	282.0 (205.0 - 373.0)	0.467
Pretreatment NLR		3.8 (2.5 - 6.1)	3.5 (2.1 - 5.4)	3.9 (2.7 - 5.7)	4.0 (2.6 - 6.6)	0.328
6 weeks neutrophil count (x 109/l)		4.6 (3.4 - 6.6)	4.3 (2.9 - 5.6)	4.2 (3.3 - 7.1)	5.0 (3.5 - 7.5)	0.028
6 weeks lymphocyte count (x 109/l)		1.3 (0.9 - 1.9)	1.3 (1.0 - 1.9)	1.2 (1.0 - 1.6)	1.3 (1.0 - 1.7)	0.337
6 weeks NLR		3.6 (2.2 - 6.5)	3.2 (1.7 - 5.0)	4.5 (2.4 - 6.3)	3.9 (2.3 - 7.2)	0.029
Total No. of cycles		3.0 (2.0 - 9.5)	11.0 (4.0 - 26.8)	7.0 (3.0 - 16.0)	4.5 (3.0 - 12.5)	0.003
Cumulative Exposure (Total Dose Received)		800.0 (217.5 - 2400.0)	3400.0 (1020.0 - 8850.0)	1600.0 (400.0 - 5082.5)	996.0 (400.0 - 4800.0)	0.011

Data expressed as Median (IQR) for continuous variables; n(%) for categorical variables.



No irAE	Number at risk	526	116	36	13	3	1	0	0	0
	Number of event	150	25	7	2	0	0	0	0	0
Cluster 1	Number at risk	118	55	30	16	6	2	1	1	0
	Number of event	15	12	2	2	0	0	0	0	0
Cluster 2	Number at risk	40	20	10	6	1	1	0	0	0
	Number of event	6	5	0	1	0	0	0	0	0
Cluster 3	Number at risk	183	60	31	17	9	1	1	0	0
	Number of event	62	22	7	2	0	0	0	0	0

Figure 3. Kaplan–Meier curves for OS according to the different phenotypic clusters.

determine which phenotypic cluster was associated with shorter progression-free and overall survival (OS). An odds ratio (OR) cutoff of ≥ 15.0 was used to define irAEs that drove the clustering. irAEs do not have to occur within the same timeframe to be considered as being multisystem.

Results: Three clusters were identified using LCA (Table 1). All patients in Cluster 1 (C1) (n = 118) had dermatologic (100%) irAEs. With respect to Cluster C1, Cluster 2 (C2) (n = 40) had predominant hepatic (32.5%, OR = 116.3) and pulmonary (77.5%, OR = 785.8) irAEs while Cluster 3 (C3) (n = 183) was characterized by multisystem irAEs such as cardiac (7.7%, OR = 20.3), neurologic (7.7%, OR = 20.3), cytokine release syndrome (12.0%, OR = 33.0), rheumatic (16.9%, OR = 49.0) and hepatic (17.5%, OR = 50.8) toxicities. Comparing patients without irAEs (n = 526), C1, C2 and C3, they were significantly different in terms of concomitant use of proton pump inhibitors, week 6 neutrophil count, week 6 neutrophil-to-lymphocyte ratio, number of cycles of ICI, cumulative dose of ICI and cancer treatment responses. Multivariable COX regression analysis revealed that C2 had the best OS. Compared to C2, no irAE [adjusted hazard ratio (HR) = 6.3, 95% confidence interval (CI) 2.1-18.5, $p < 0.001$], C1 (adjusted HR = 3.5, 95% CI 1.1-11.1, $p = 0.036$) and C3 (adjusted HR = 4.2, 95% CI 1.4-12.4, $p = 0.010$) were associated with shorter OS after adjusting for body mass index, performance status, primary diagnosis and number of cycles of ICI (Figure 1).

Conclusion: Our study reveals differences in patterns of clustering of irAEs. In particular, C3 tends to have toxicities in multiple organ systems and is associated with shorter OS. In addition, we found significant survival benefits for C1 and C2. This may suggest differences in terms of the interactions between the degree of immune activation, immunosuppression and treatment responses that will require further studies to elucidate.

Disclosure: T. Sim: None; **M. Tang**: None; **Q. Yap**: None; **A. Wong**: None; **Y. Huang**: None; **F. Tay**: None.

Abstract Number: 1122

A Retrospective Study of Adverse Cardiovascular Events in Patients Started on JAK Inhibitors at Two Major Health Systems in Northeast Ohio: Analysis of the 2019 JAK Inhibitors FDA Boxed Warning for Increased Risk of Serious Heart-related Problems

William Koch[1], Donald Anthony[2], Janeen Leon[2] and Nora G. Singer[2], [1]University Hospitals Parma Medical Center, Parma, OH, [2]The MetroHealth System at Case Western Reserve University School of Medicine, Cleveland, OH

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1088–1122) Immunological Complications of Medical Therapy Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Janus kinase (JAK) inhibitors are immunosuppressive medications that target the JAK-STAT signaling pathway. Tofacitinib (Xeljanz) was the first JAK inhibitor approved for the treatment of rheumatoid arthritis (RA) in November 2012. Additional JAK inhibitors such as baricitinib (Olumiant) and upadacitinib (Rinvoq) were later approved for the treatment of RA in May 2018 and August 2019, respectively. Shortly after the FDA approved tofacitinib, randomized clinical safety trials found a higher incidence of venous thromboembolic events within the first year of treatment. In 2019 the FDA released a Boxed Warning stating the increased risk of serious heart-related problems and cancers in those treated with tofacitinib. Here we compare the number of adverse cardiovascular events in those patients started on a JAK inhibitor (tofacitinib, baricitinib, upadacitinib) within two major health systems in Northeast Ohio.

Methods: SlicerDicer in EPIC at University Hospitals (Cleveland, OH) and MetroHealth (Cleveland, OH) were used to identify patients who were prescribed a JAK inhibitor (tofacitinib, baricitinib, upadacitinib) who were 18 years or older from November 2012 (first approval of tofacitinib) through May 2025. Subsequently, adverse cardiovascular event (venous thromboembolic event, stroke, ischemic heart disease, heart failure, cardiac arrest, and tachyarrhythmia) were identified using problem list and emergency department diagnosis as narrowing filters. Adverse cardiovascular events were measured from 1 week to 52 weeks after JAK inhibitor initiation.

Results: We identified 2788 patients (University Hospitals, n = 1917; MetroHealth, n = 871) treated with JAK inhibitors (tofacitinib, baricitinib, upadacitinib) of which 294 patients (University Hospitals, n = 226; MetroHealth, n = 68) were diagnosed with an adverse cardiovascular event within 1 year of treatment initiation. The majority of patients were 65 years or older (< 65 years old, n = 131; > 65 years old, n = 163), with 28% males and 72% females. The incidence of adverse cardiovascular events of those on a JAK inhibitor at University Hospitals and MetroHealth collectively was 11%. Yearly trends from November 2012 to May 2025 favored an increase in the number of adverse cardiovascular events following the 2019 FDA Boxed Warning.

Conclusion: JAK inhibitors (tofacitinib, upadacitinib and baricitinib) have been shown to be associated with increased reporting of VTE, stroke, ischemic heart disease, heart failure, cardiac arrest and tachyarrhythmia within the first year of treatment initiation. Our data from two major health systems in Northeast Ohio suggests an incidence of 11%, which is higher than commonly reported. Next steps will include adjudicating patient charts in EPIC SlicerDicer in order to validate and broaden our dataset in EPIC Cosmos. As the FDA approval for JAK inhibitors has expanded beyond inflammatory

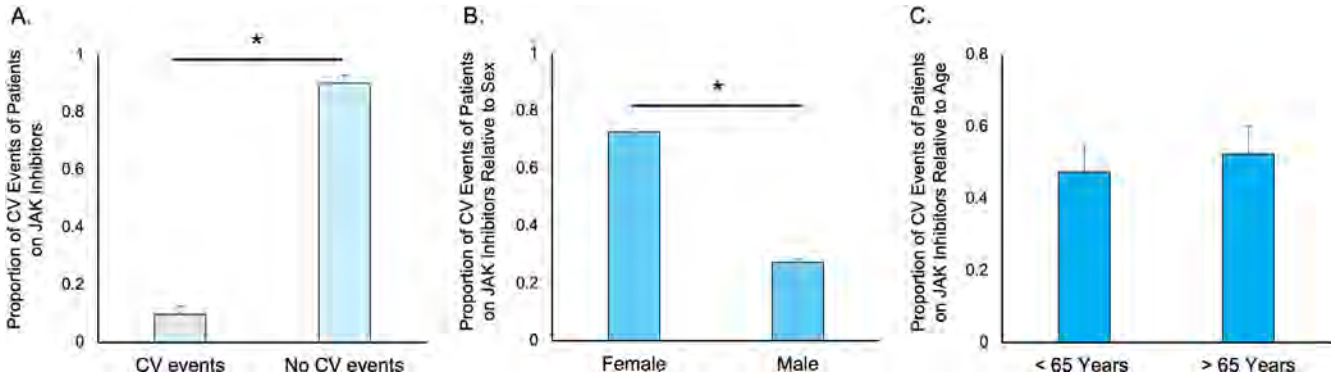


Figure 1. Proportion of adverse cardiovascular (CV) events. A) Proportion of adverse CV events of patients on JAK inhibitors, T-test, *p<0.05. B) Proportion of adverse CV events of patients on JAK inhibitors relative to sex (female vs male), T-test, *p<0.05. C) Proportion of adverse CV events of patients on JAK inhibitors relative to age (< 65 years old vs > 65 years old), no significance between age groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

conditions such as rheumatoid arthritis and psoriatic arthritis to include gastrointestinal and dermatological conditions such as ulcerative colitis and atopic dermatitis, all prescribers have an obligation to familiarize themselves with the increased risk of adverse cardiovascular events demonstrated in this population.

Disclosure: W. Koch: None; **D. Anthony**: None; **J. Leon**: None; **N. Singer**: None.

Abstract Number: 1123

Nanoencapsulated Sirolimus plus Pegadricase (NASP) Demonstrates Long Term Efficacy and Safety in Patients with Uncontrolled Gout: Results from the 24-week Double-blind Extension of the Phase 3 DISSOLVE I Study

Alan Kivitz[1], Atul Singhal[2], Anand Patel[3], Rehan Azeem[4], Ben Peace[5], Bhavisha Desai[6] and Herbert Baraf[7], [1]Altoona Center for Clinical Research, Duncansville, PA, [2]SouthWest Arthritis Research Group, Mesquite, TX, [3]Conquest Research, Winter Park, FL, USA, Winter Park, FL, [4]Global MACD, Sobi Inc., Waltham, MA, [5]Statistical Science, Sobi, Stockholm, Sweden, [6]Sobi, Glastonbury, CT, [7]The Center for Rheumatology and Bone Research, Rheumatology, Wheaton, Maryland, USA; Division of Rheumatology, The George Washington University, Washington, DC

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Uncontrolled gout (UG) occurs when serum uric acid (sUA) levels remain persistently elevated despite use of oral urate-lowering therapies and can result in progressively painful gout flares (Dalbeth *et al. Nat Rev Dis Primers* 2019). Nanoencapsulated sirolimus plus pegadricase (NASP, formerly SEL-212) is a novel investigational therapy delivered every 4 weeks as a sequential, two-component infusion consisting of targeted nanoencapsulated sirolimus and pegadricase, a pegylated uricase (**Figure 1A**). Here, we report outcomes through 48 weeks in a subset of patients (pts) in the DISSOLVE I study who received 6 doses of NASP or placebo (PBO) during the 24-week main study period.

Methods: This is a *post-hoc* analysis of the DISSOLVE I (NCT04513366) trial that randomized pts 1:1:1 to one of two doses of NASP (high-dose [HD] or low-dose [LD]) or PBO. After each study drug administration, 4 weeks of observation followed for a total of 6 treatment periods during the main study. Pts could enter a 24-week double-blind extension after the main study period (**Figure 1B**). Evaluated endpoints included reductions in sUA, gout flares, and pts meeting stopping rule criteria (Kivitz *et al. EULAR 2024*, POS0244). Safety was monitored throughout.

Results: Of the 38 pts receiving HD NASP, 37 LD NASP and 37 PBO in DISSOLVE I, 19, 16 and 25, respectively, received all 6 doses of study drug during main study period, and all (100%) entered the extension phase. At baseline, mean (standard deviation [SD]) sUA was 8.4 (1.45) mg/dL in HD NASP, 8.7 (1.08) mg/dL for LD NASP, and 8.3 (1.43) mg/dL for PBO. Immediately after the first dose, mean (SD) sUA dropped to 0.2 (0.00) mg/dL with HD and LD NASP, while remaining stable for PBO at 8.2 (1.36) mg/dL. sUA was maintained low at the end of the first treatment period (Week 4) with NASP (mean (SD) sUA: HD, 1.0 (2.5) mg/dL; LD, 0.2 (0.13) mg/dL) while remaining stable with PBO at 8.4 (1.28) mg/dL. Low sUA were maintained throughout treatment with NASP (Weeks 24: HD, 1.8 (3.29) mg/dL; LD, 1.7 (2.41) mg/dL; Week 48: HD, n=16, 2.4 (3.67) mg/dL; LD, n=12, 1.3 (2.80) mg/dL). In PBO-treated pts, sUA remained consistent at 8.6 (1.43) mg/dL and 8.1 (1.94) mg/dL at Weeks 24 and 48 (n=22), respectively. The proportion of pts with gout flares decreased with NASP treatment over the study period. During Weeks 1–4, flares occurred in 3/19 (15.8%) pts on HD NASP, 7/16 (43.8%) on LD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

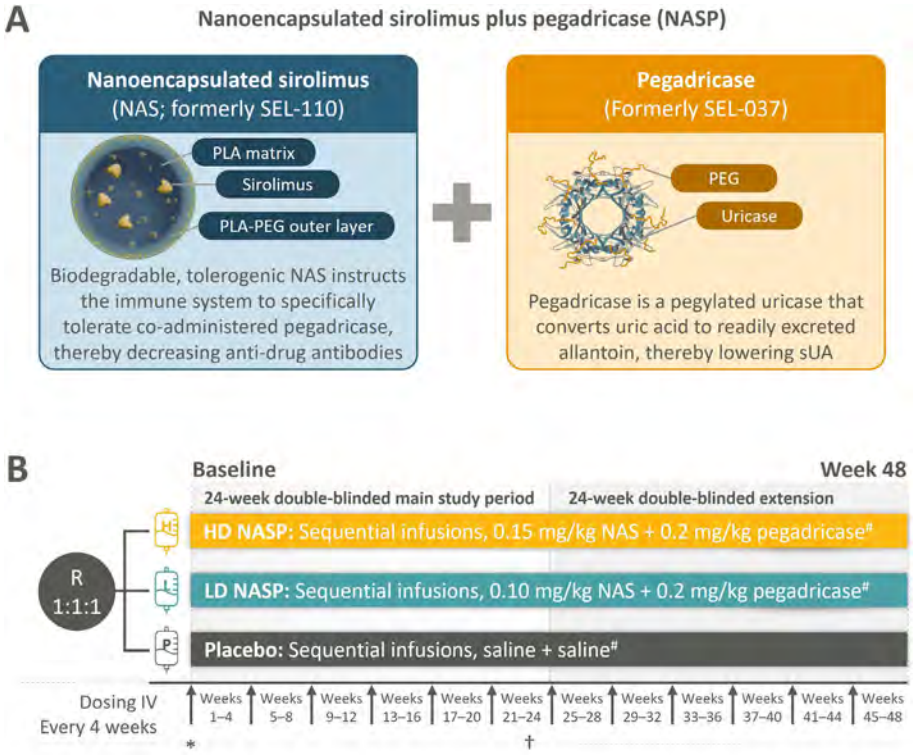


Figure 1. Schematic representation of nanoencapsulated sirolimus plus pegadricase (NASP) composition (A) and DISSOLVE I (NCT04513366) study design (B). #Treatment was discontinued if the stopping rule was met: sUA <2.0 mg/dL 1 hour after infusion of the second component of the study drug during week 1 AND either sUA >1.0 mg/dL at the end of week 3 OR sUA >6.0 mg/dL at the end of any subsequent week (i.e. week 7, 11, 15, 19, 23, 27, 31, 35, 39, or 43). Arrows at each interval indicate the timing of drug administration. *sUA measured 1 hour after completing infusion of second study drug. †Evaluation of primary endpoint, defined as the percentage of patients who achieved and maintained sUA <6 mg/dL for ≥80% of the time during Weeks 21–24. Evaluation of sUA during Weeks 21–24 for the primary endpoint was done before study drug infusion, 1 hour after completion of study drug infusion, and at the end of each week during Weeks 21–24. HD, high-dose; IV, intravenous; LD, low-dose; NAS, nanoencapsulated sirolimus; NASP, nanoencapsulated sirolimus plus pegadricase; PEG, polyethylene glycol; PLA, polylactic acid; R, randomization; sUA, serum uric acid.

NASP, and 7/25 (28.0%) on PBO. During Weeks 21–24, flares occurred in 1/19 (5.3%) pts on HD NASP, 2/16 (12.5%) on LD NASP, and remained at 7/25 (28.0%) on PBO and during Weeks 45–48, 0/16 (0%) pts on HD NASP and 1/13 (7.7%) on LD NASP experienced flares vs 5/22 (22.7%) on PBO. In the extension phase, no new safety signals were reported, and no patients experienced an infusion reaction within 1 hour. Only 1 pt (3.7%) in each NASP dose group discontinued treatment due to meeting the stopping rule criteria.

Conclusion: These data support the long-term durability of NASP as shown by sustained sUA reductions and decreased gout flares over time, with 100% on HD NASP and 92.3% on LD NASP being flare-free at the end of the extension phase. NASP was generally well tolerated with low discontinuation rates during the extension phase. Overall, NASP led to improvements in key clinical manifestations of UG.

Disclosure: A. Kivitz: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2; **A. Singhal**: AbbVie/Abbott, 5, 6, Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Fujifilm, 5, Gilead, 5, Janssen, 5, Mallinckrodt, 5, MedImmune, 5, Nichi-Iko, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Roche, 5, Sanofi, 5, UCB, 5; **A. Patel**: None; **R. Azeem**: Selecta Biosciences, 11, Sobi, 3, 12, Shareholder; **B. Peace**: Sobi, 7, Veramed, 3; **B. Desai**: Sobi, 3, 11; **H. Baraf**: Arthrosi, 2, Olatec, 2, Otsuka, 3, Pacira, 2, Selecta Biosciences, 2, Sobi, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1124

ABCG2 Variants as Genetic Risk Factors for Hyperuricemia and Gout: Focus on Pediatric and Familial Manifestations

Blanka Stiburkova[1], katerina pavelcova[2], Jana masinova[3], Pavel Jesina[4], Yu Toyoda[5] and Tappei Takada[5], [1]Institute of Rheumatology, Praha 10, Czech Republic, [2]Institute of Rheumatology, Praha 2, Czech Republic, [3]Institute of Rheumatology, Prague, Czech Republic, [4]Revmatologický ústav, Praha 2, Czech Republic, [5]The University of Tokyo Hospital, Tokyo, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Gout, a condition arising from hyperuricemia, is considered as both a metabolic disorder and an autoinflammatory disease. Genetic factors are estimated to contribute approximately 40% to serum uric acid levels. Among urate transporters, ABCG2 (ATP-binding cassette sub-family G member 2) plays a crucial role in uric acid homeostasis as an efflux machinery, being expressed in the proximal renal tubules and the intestine.

This study aimed to identify novel and functionally uncharacterized variants of the *ABCG2* gene and to determine the frequency of known pathogenic variants in patients with primary hyperuricemia and gout.

Methods: A total of **549 patients** were recruited from the RU Biobank, of whom **327 with primary gout** and **222 with primary hyperuricemia**. Individuals with secondary gout were excluded. Specific primers were designed to amplify all coding regions (15 exons; transcript ID: ENST00000650821), exon-intron boundaries, and two deep intronic variants (rs13120400 and rs7672194) of *ABCG2*. PCR amplification and Sanger sequencing were optimized and used to analyze the patient DNA (1). Identified ABCG2 variants were biochemically characterized using a mammalian cell-based expression system, followed by **urate transport assays** to assess transporter function.

Results: We detected a nonsynonymous variant p.Q141K with an allelic frequency of 0.22 (which is significantly higher than its minor allele frequency - MAF - in the European population: 0.094). This variant increases the risk of gout, while the common p.V12M variant appears to reduce the risk (MAF in patients: 0.026, MAF in European population: 0.061). We also identified one frameshift variant p.I63YfsTer54, two short deletions (p.K360del and p.F373del) and 14 rare or novel missense variants: p.M71V, p.G74D, p.M131I, p.R147W, p.T153M, p.I242T, p.R236X, p.F373C, p.T421A, p.T434M, p.S476P, p.A528T, p.S572R, and p.D620N (2,3). According to functional studies, nine of these variants lead to reduced or null transport function of ABCG2: p.M131I, p.R147W, p.T153M, p.I63YfsTer54, p.R236X, p.F373C, p.T434M, p.S476P, and p.S572R – all these variants were identified in pediatric patients with hyperuricemia and/or in patients with positive family history of hyperuricemia and gout.

Conclusion: Our findings confirm that the common **p.Q141K** variant and the majority of the identified rare ABCG2 variants negatively impact urate transport and significantly contribute to the risk of **primary hyperuricemia and gout**. Genetic screening for ***ABCG2* variants** may be valuable in clinical practice, particularly in cases of **early-onset** or **familial gout**. Early identification and treatment of hyperuricemia in genetically predisposed individuals - including pediatric or adolescent patients with asymptomatic hyperuricemia - could **delay the onset of gout** and reduce the risk of **related comorbidities**.

References: Rheumatology (Oxford). 2017 1; 56(11):1982-1992. Arthritis Res Ther. 2019 28;21(1):219. Int J Mol Sci. 2021 Feb 16;22(4):1935.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Supported by the project Institute of Rheumatology 00023728, and by the grant from the Czech Republic Ministry of Health (NU22-01-00465), and BBMRI.cz (LM2023033).

Disclosure: B. Stiburkova: None; **k. pavelcova**: None; **J. masinova**: None; **P. Jesina**: None; **Y. Toyoda**: None; **T. Takada**: None.

Abstract Number: 1125

Validation of an Allopurinol Dose Prediction Tool to Achieve Goal Serum Urate Among Patients with Gout

Brian Coburn[1], Daniel Wright[2], Jeff Newcomb[3], Mary Brophy[4], Anne Davis-Karim[5], Ryan Ferguson[4], Michael Pillinger[6], Tuhina Neogi[7], Paul Palevsky[8], Bryant England[3], James O'Dell[3], Lisa Stamp[9], Ted Mikuls[3] and Joshua Baker[10], [1]Hospital of the University of Pennsylvania, Philadelphia, PA, [2]University of Otago, Dunedin, New Zealand, [3]University of Nebraska Medical Center, Omaha, NE, [4]VA Cooperative Studies Program Coordinating Center, Boston, MA, [5]VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center, Albuquerque, NM, [6]New York University Grossman School of Medicine, New York,, NY, [7]Boston University School of Medicine, Boston, MA, [8]VA Pittsburgh Healthcare System, Pittsburgh, PA, [9]University of Otago, Christchurch, Christchurch, New Zealand, [10]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite evidence-based recommendations, allopurinol dose escalation to goal serum urate (SU) is frequently suboptimal. The EasyAllo tool was developed to facilitate pre-planned allopurinol dose escalation by predicting the allopurinol dose needed to achieve SU < 6 mg/dL >80% of the time and promote easier dose titration (Wright et al. Br J Clin Pharmacol 2024). The purpose of this study was to externally validate EasyAllo among trial participants who achieved goal SU using protocolized dose escalation.

Methods: We included participants in the STOP Gout trial who were randomized to the allopurinol arm, and limited our analyses to those without tophi at baseline who achieved goal SU < 6 mg/dL and completed week 48 of the study to ensure adequate dose escalation and SU capture. All participants fulfilled the 2015 ACR-EULAR gout classification criteria. The trial used protocolized allopurinol dose escalation if SU was ≥6 mg/dL through week 30 to a maximum of 800 mg daily. Two versions of EasyAllo exist: EasyAllo2 based on weight and creatinine clearance and EasyAllo1 which also incorporates baseline SU. We used EasyAllo2 in the primary analysis to allow for inclusion of participants taking allopurinol at enrollment whose baseline SU reflected active treatment, and secondarily explored EasyAllo1 among those not already taking allopurinol. In primary analysis, we determined the frequency with which the study dose required to achieve SU goal < 6 mg/dL between weeks 36 and 48 was at the EasyAllo2 predicted dose or lower. As a secondary aim, we assessed univariate associations between baseline characteristics and being at the EasyAllo predicted dose or lower. We also evaluated whether participants who study dose was the EasyAllo2 predicted dose at the time of first achieving SU < 6 mg/dL demonstrated superior long-term maintenance of SU < 6 mg/dL compared to participants whose study dose was less than the predicted dose.

Results: A total of 291 participants met inclusion criteria for the primary analysis (Table 1). Approximately 77% (n = 224) of participants who achieved SU goal < 6 mg/dL between weeks 36 and 48 were on the EasyAllo2 predicted dose or less. Younger age, lower kidney function, and higher SU were associated with requiring allopurinol doses higher than predicted by EasyAllo2 (Table 3). In secondary analysis using EasyAllo1, which includes baseline SU for prediction, younger age,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

higher baseline weight, and higher SU were associated with allopurinol doses higher than predicted. Considering all participants who ever achieved SU < 6 mg/dL, half (n=207, 51%) subsequently had SU that was not at goal (≥6 mg/dL). This occurred more frequently among participants on a study dose below the EasyAllo2 predicted dose relative to participants on a study dose at or above the EasyAllo2 dose prediction, though, this difference did not achieve statistical significance (55% v 45%, p = 0.06).

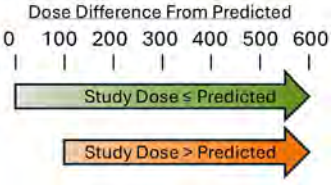
Table 1 Baseline Characteristics among Veterans Affairs Participants Randomized to Allopurinol in STOP-GOUT trial

	EasyAllo2 Cohort* (n = 291)	EasyAllo1 Cohort† (n = 181)
Age, years	63.1 (11.6)	63.7 (11.5)
Weight, kg	107.0 (23.5)	103.2 (21.7)
BMI, kg/m^2	34.1 (6.9)	33.1 (6.4)
Male	285 (98%)	178 (98%)
Race		
White	204 (70%)	134 (74%)
Black	60 (21%)	29 (16%)
Other	26 (9%)	17 (9%)
Missing	1 (<1%)	1 (1%)
CKD Stage 3	109 (38%)	61 (34%)
eGFR, mL/min/1.73 m^2	66.2 (18.8)	67.9 (18.4)
Hypertension	228 (78%)	144 (80%)
Diabetes Mellitus	103 (35%)	60 (33%)
Cardiovascular Disease	79 (27%)	41 (23%)
Serum Urate, mg/dL	8.5 (1.4)	8.8 (1.4)
Serum Urate >9.0 mg/dL	91 (31%)	71 (39%)
Duration of Gout, years	8.7 (10.2)	8.5 (9.8)
Diuretic Use	111 (43%)	65 (41%)
Baseline Allopurinol, mg/day		
None	181 (62%)	181 (100%)
50	3 (1%)	-
100	50 (17%)	-
150	3 (1%)	-
200	23 (8%)	-
300	31 (11%)	-

All values are mean (sd) or n (%). *The EasyAllo2 cohort is limited to participants without tophi at baseline who achieved goal SU <6 mg/dL and completed week 48 of the study to ensure adequate dose escalation and SU capture. †The EasyAllo1 cohort is further limited to participants not on baseline allopurinol to ensure baseline SU values do not reflect active treatment. Abbreviations: body mass index (BMI); chronic kidney disease (CKD); estimated glomerular filtration rate (eGFR)

Table 2 Final Allopurinol Study Dose versus EasyAllo2 Predicted Dose among Participants Achieving SU Goal

EasyAllo2* \ Final Study Dose	200	300	400	500	600	700	800
200	0	0	0	0	0	0	0
300	30	24	15	6	0	0	0
400	32	57	44	30	5	7	0
500	2	7	11	17	3	0	1
600	0	0	0	0	0	0	0



All doses represent mg per day of allopurinol. A total of 291 participants in the allopurinol group without baseline tophi met goal SU <6 mg/dL between weeks 36 and 48. Green represents participants in whom the final trial dose at the time of achieving SU goal <6 mg/dL was equal to (n = 85, 29%) or less than the EasyAllo2 predicted dose (n = 139, 48%). Orange represents participants whose final study dose was more than the EasyAllo2 predicted dose (n = 67, 23%). A total of 79% (n = 231) participants were on a study dose within 100 of the EasyAllo2 dose prediction. The weighted kappa, a measure of agreement where doses closer together are weighted more, was 0.27 using quadratic weighting. *EasyAllo2 dose predictions were calculated using participants baseline weight and creatinine clearance. Abbreviations: serum urate (SU)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 Baseline Characteristics Associated Study Allopurinol Dose being at the Predicted Dose or Lower among Participants Achieving SU <6 mg/dL

	EasyAllo2			EasyAllo1		
	Predicted Dose or Lower (n = 224)	Greater Than Predicted Dose (n = 67)	P value	Predicted Dose or Lower (n = 129)	Greater Than Predicted Dose (n = 52)	P value
Age, years	63.9 (11.1)	60.6 (12.9)	0.04	65.1 (10.8)	60.3 (12.1)	0.01
Weight, kg	107 (23)	106 (26)	0.73	101 (23)	109 (16)	0.02
BMI, kg/m^2	34.1 (6.7)	34.5 (7.4)	0.67	32.5 (6.8)	34.0 (5.0)	0.05
Male	220 (98%)	65 (97%)	0.54	127 (98%)	106 (99%)	0.86
Race			0.68			0.84
White	159 (71%)	45 (67%)		97 (75%)	37 (71%)	
Black	46 (21%)	14 (21%)		20 (16%)	9 (17%)	
Other	18 (9%)	8 (12%)		12 (9%)	6 (12%)	
CKD Stage 3	80 (36%)	29 (43%)	0.26	45 (35%)	16 (31%)	0.76
eGFR, mL/min/1.73 m^2	67.6 (19.2)	61.6 (17.0)	0.02	66.5 (18.9)	71.4 (16.8)	0.11
Hypertension	178 (80%)	50 (75%)	0.40	106 (82%)	38 (73%)	0.17
Diabetes Mellitus	80 (36%)	23 (34%)	0.84	48 (37%)	12 (23%)	0.07
Cardiovascular Disease	57 (25%)	22 (33%)	0.24	33 (26%)	8 (15%)	0.14
Serum Urate, mg/dL	8.3 (1.3)	9.1 (1.6)	<0.01	8.9 (1.5)	8.4 (1.2)	0.03
Serum Urate > 9.0 mg/dL	57 (25%)	34 (51%)	<0.01	57 (44%)	14 (27%)	0.03
Duration of Gout, years	8.9 (10.3)	8.2 (9.8)	0.58	8.1 (9.3)	9.5 (10.9)	0.38
Diuretic Use	82 (41%)	29 (50%)	0.25	50 (43%)	15 (36%)	0.40

All values are mean (sd) or n (%) and p-values represent testing for association between baseline participant characteristics and SU goal attainment on the predicted allopurinol dose or lower at week 30 of the study. P-values represent t-test and chi-square test for continuous and categorical variables respectively. EasyAllo2 dose predictions were calculated using participants baseline weight and creatinine clearance and EasyAllo1 calculations also use baseline SU. Abbreviations: serum urate (SU); body mass index (BMI); chronic kidney disease (CKD); estimated glomerular filtration rate (eGFR)

Conclusion: Among participants who achieved SU < 6.0 mg/dL through protocolized allopurinol dose escalation, nearly 3 out of 4 would likely have achieved SU goal at the EasyAllo2 predicted dose. These findings suggest that EasyAllo2 would perform well in this population with a small proportion requiring additional dose escalation.

Disclosure: B. Coburn: None; **D. Wright**: None; **J. Newcomb**: None; **M. Brophy**: None; **A. Davis-Karim**: None; **R. Ferguson**: None; **M. Pillinger**: Amgen, Federation Bio, Fortress Biotech, Scilex, and SOBI, 2, Convergence Bio, 2; **T. Neogi**: None; **P. Palevsky**: Chiesi Pharmaceutical, 2; **B. England**: Boehringer-Ingelheim, 2, 5; **J. O'Dell**: None; **L. Stamp**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **J. Baker**: Amgen, 5.

Abstract Number: 1126

Clinical Impact of Signs of Calcium Pyrophosphate Deposition Disease (CPPD) on Radiographs of Hands and Wrists in a Real-World Cohort of Patients with Early Rheumatoid Arthritis

Coralie Tremblay[1], Nathalie Carrier[2], Hugues Allard-Chamard[3], Javier Marrugo[4], Sophie Roux[4], Gilles Boire[5] and Ariel Masetto[4], [1]Université de Sherbrooke, Division of Rheumatology, Department of Medicine and Health Sciences, Sherbrooke, Canada, and Centre intégré universitaire de santé et de services sociaux de l'Estrie – Centre hospitalier universitaire de Sherbrooke (CIUSSS de l'Estrie – CHUS), Sherbrooke, Canada, Saint-Augustin-de-Desmaures, QC, Canada, [2]Centre integré universitaire de santé et de services sociaux de l'Estrie – Centre hospitalier universitaire de Sherbrooke (CIUSSS de l'Estrie-CHUS), Sherbrooke, Canada, [3]Université de Sherbrooke, Sherbrooke, Canada, [4]Université de Sherbrooke, Division of Rheumatology, Department of Medicine and Health Sciences, Sherbrooke, Canada, and Centre intégré universitaire de santé et de services sociaux de l'Estrie – Centre hospitalier universitaire de Sherbrooke (CIUSSS de l'Estrie – CHUS), Sherbrooke, Canada, Sherbrooke, Canada, [5]Retired, Sherbrooke, QC, Canada

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Calcium pyrophosphate deposition disease (CPPD) is a common cause of arthropathy over the age of 60. It can also manifest as a chronic polyarticular disease and may be mistaken for seronegative rheumatoid arthritis (RA). While previous retrospective cohort studies [1, 2] have explored the relationship between CPPD and RA, the potential role of specific hand joint space narrowing in the diagnosis or treatment response of CPPD has not been addressed.

We aimed to explore whether, in a cohort of patients with early non erosive RA, the presence of specific hand and wrist joint narrowing suggestive of CPPD is associated with distinct baseline features and whether it influences clinical outcomes over the first 60 months.

Methods: A retrospective analysis was conducted on RA patients from the Early Undifferentiated Polyarthritis (EUPA) cohort (1998–2023) [3].

EUPA inclusion criteria required a baseline SJC66 ≥3 and a symptom duration of one to twelve months. Patients with confirmed crystal-induced arthritis, connective tissue disease or vasculitis were excluded. For this analysis, only patients fulfilling the 1987 and/or 2010 RA classification criteria were included, while those with ≥1 erosions on hand or foot radiographs, as determined by the Sharp-van der Heijde score, were excluded.

Radiographs of hands and wrists were reviewed by two independent evaluators for the presence of at least one narrowing suggestive of CPPD such as bilateral radiocarpal, second or third metacarpophalangeal (MCP), scaphotrapeziotrapezoid (STT) joints without first carpometacarpal (CMC) involvement.

Patient characteristics were compared using descriptive statistics. Time-dependent outcomes were evaluated using generalized estimating equations (GEE) with repeated measures. Multivariable models were adjusted for baseline variables, including age, sex, BMI, smoking status, and seropositivity.

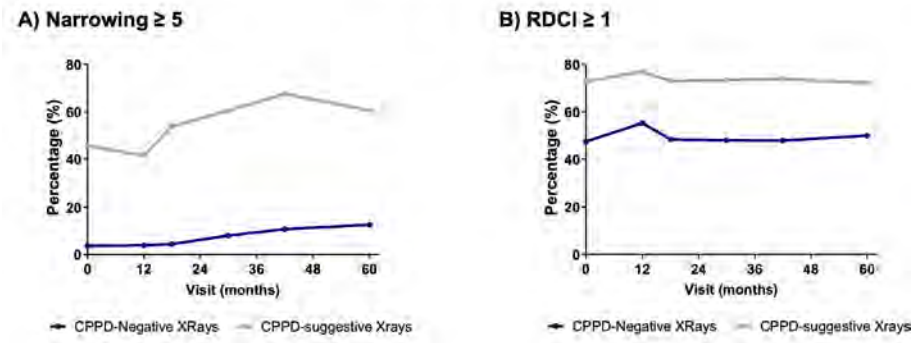
Table 1. Baseline variables of patients without (EUPA) and with (CPPD) at least one radiologic sign suggestive of CPPD

	EUPA (n=318)	CPPD (n=70)	p-value
Age	55.8 (42.4-65.4)	68.9 (60.5-73.1)	**<0.001**
Women, n (%)	216 (67.9)	41 (58.6)	0.134
BMI	26.2 (23-30.2)	26.9 (23-28.3)	0.621
Current smoker, n (%)	51 (16.8)	10 (14.7)	0.897
Race - White, n (%)	313 (98.4)	69 (100)	0.591
RDCI ≥ 1, n (%)	151 (47.5)	51 (72.9)	**<0.001**
Seropositive (RF and/or anti-CCP2), n (%)	146 (46.3)	26 (37.1)	0.161
ESR mm/h	24 (14-40)	32 (16-48)	**0.027**
CRP mg/L	9.8 (3.9-26.6)	7 (1.5-24.5)	0.370
66-Swollen joint count	12 (7-19)	12 (7-18)	0.782
≥ 1 swollen wrist, n (%)	228 (71.7)	57 (81.4)	0.095
SDAI	30.7 (20.2-46.3)	31.4 (23.4-43.7)	0.903
CDAI	29.4 (19.1-43.4)	29.2 (22.3-40.7)	0.948
M-HAQ (0-3)	0.8 (0.4-1.3)	0.9 (0.3-1.4)	0.580
Treatment Naive, n (%)	167 (52.5)	32 (45.7)	0.303
csDMARDs active, n (%)	66 (20.8)	18 (25.7)	0.362
Prednisone active, n (%)	52 (16.4)	12 (17.1)	0.872
bDMARDs active, n (%)	1 (0.3)	1 (1.4)	0.239

BMI, body mass index; RDCI, Rheumatic Disease Comorbidity Index; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; SDAI, Simplified Disease Activity index; CDAI, Clinical Disease Activity Index; M-HAQ, Modified Health Assessment Questionnaire; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; bDMARDs, biological disease-modifying antirheumatic drugs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Evolution of narrowing ≥ 5 and RDCI ≥ 1 over 60 months



RDCI, Rheumatic Disease Comorbidity Index.

Table 2. Effect of CPPD on outcomes over 60 months according to univariate and multivariate analysis

	Univariate analysis		Multivariate analysis	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Narrowing score ≥5	7.86 (5.28-11.71)	**<0.001**	5.02 (3.25-7.76)	**<0.001**
Swollen wrist	1.20 (1.00-1.43)	**0.049**	1.08 (0.88-1.32)	0.457
M-HAQ ≥ 1	1.43 (1.02-2.00)	**0.040**	1.10 (0.78-1.55)	0.579
RDCI ≥ 1	1.44 (1.21-1.70)	**0.002**	1.05 (0.89-1.23)	0.585
DMARDs active	1.12 (1.04-1.20)	**0.002**	1.14 (1.05-1.24)	**0.002**
DMARDs + Biologic	1.13 (1.06-1.21)	**<0.001**	1.17 (1.08-1.26)	**<0.001**
DMARDs + Biologic + Prednisone	1.15 (1.08-1.22)	**<0.001**	1.16 (1.08-1.25)	**<0.001**

Multivariable models were adjusted for the following baseline variables: age, sex, BMI, smoking status, and seropositivity.

Results: Among 966 EUPA patients, 388 met inclusion criteria, of which 70 (18%) exhibited at least one radiologic sign suggestive of CPPD. At baseline, CPPD+ patients were older, had higher comorbidity scores and slightly higher ESR (Table 1). The prevalence of CPPD was numerically higher among seronegative patients (20%) compared to seropositive patients (15%) (p=0.16).

Over 60 months of follow-up, CPPD+ patients were more likely to have a joint narrowing score ≥5 and a Rheumatic Disease Comorbidity Index (RDCI) ≥1 (Figure 1). They were also more likely to remain on conventional disease-modifying drug (DMARD) therapy and were more intensely treated with biologics combined with and without prednisone (Table 2). No significant differences were found in SDAI, CDAI, erosions, SJC66, TJC68, pain, or fatigue. Stratification by seropositivity yielded similar results.

Conclusion: Radiological signs of CPPD do not appear to influence RA disease trajectory, regardless of their seropositivity status. However, CPPD+ RA patients may require more intensive treatment, including biologics and prednisone. These changes in RA likely reflect a concomitant or preexisting condition rather than a distinct RA subtype. Further research is needed to enhance our understanding of this topic and its clinical implications.

Disclosure: C. Tremblay: None; **N. Carrier**: None; **H. Allard-Chamard**: AbbVie, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 1, 5, 6, GlaxoSmithKlein(GSK), 1, Janssen, 1, 5, 6, Kabi, 1, 5, 6, Novartis, 1, 6, Otsuka, 1, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Sobi, 1, 5, 6; **J. Marrugo**: None; **S. Roux**: None; **G. Boire**: Biocon, 5, Sanofi, 1; **A. Masetto**: AbbVie/Abbott, 2, AstraZeneca, 6, Johnson and Johnson, 2, Pfizer, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1127

The Pathogenetic Role of Calcium Pyrophosphate and Basic Calcium Phosphate Crystals in Osteoarthritis: Associations with Synovial Fluid Cytokines and Clinical Indices

Francesca Oliviero[1], Chiara Baggio[2], Amelia Damasco[2], Federico Zorzi[3], Mariagrazia Lorenzin[2], Giacomo Cozzi[2] and Roberta Ramonda[4], [1]Rheumatology Unit, Department od Medicine - DIMED, University of Padova, Padova, Veneto, Italy, [2]Rheumatology Unit, Department of Medicine - DIMED, University of Padova, Padova, Veneto, Italy, [3]Center for Analysis and Certification Services (CEASC), University of Padova, Padova, Veneto, Italy, [4]Rheumatology Unit-DIMED-University of Padova ITALY, Padova, Padua, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

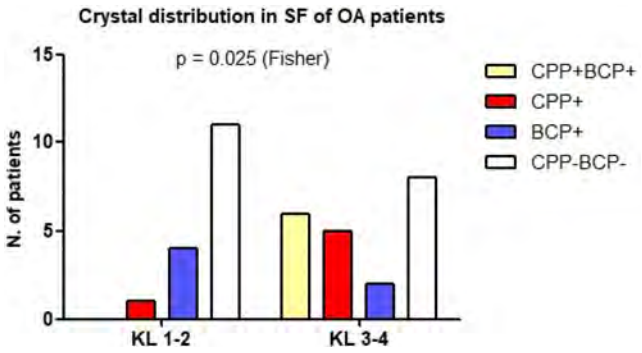
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystals are frequent features of synovial fluid (SF) in patients with osteoarthritis (OA). Although these crystals have shown pro-inflammatory properties in vitro, their pathogenetic role is not completely clear. Our previous studies demonstrated that the presence of CPP in SF is associated with a mild inflammatory status and more advanced stages of the disease (Oliviero F, 2023; Frallonardo P, 2018). With this study we aimed to investigate SF cytokines and clinical indices of disease in a cohort of OA patients with or without CPP and BCP in their SF.

Methods: SF samples were collected from 40 patients with OA attending our outpatient clinic and analyzed as part of routine procedures. Patients were asked to complete the WOMAC and Lequesne questionnaires and a VAS scale for pain. OA severity was classified according to the Kellgren and Lawrence system. Total leucocytes, differential cell count and crystal search were performed in all the samples. CPP crystals were identified by polarized light microscopy (PLM) while BCP were assessed by Environmental Scanning Electron Microscopy (ESEM) and energy-dispersive X-ray (EDX) spectra, after samples centrifugation. Discarded SFs were stored for cytokine (IL-1, IL-18, IL-8, CCL23) determinations.

Results: ESEM analysis confirmed the presence of CPP in all SF positive at the PLM (n. 14) and in no additional samples. BCP have been found in 13 specimens, 7 of which were also positive to CPP. Given the low number of BCP+ SFs, we firstly compared the CPP+ and the CPP- groups. Patients with CPP showed higher WOMAC (p=0.04) and VAS pain (0.039). Although non-significant, IL-8 and CCL23 were higher in CPP+ samples. Examining data according to ESEM results, we found a significant distribution of CPP in the group of patients with a KL=3-4 and BCP in the group KL=1-2 (p=0.025)



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(Fig.1). Patients positive for both CPP and BCP had the worse clinical indices (WOMAC and pain 0.04). The levels of CLL23, which we demonstrated to be highly induced in vitro by CPP crystals (Baggio C, 2025), are similar in the groups CPP+ and CPP+BCP+, and decrease in the group BCP+, CPP-BCP-. IL-8 was higher in the group positive to both crystals but lower in the BCP+ group.

Conclusion: This study supports the concept that calcium crystals are not mere bystanders in OA, but rather play a pathogenetic role. CCL23 emerges as a new chemokine that warrants further exploration in OA research.

Disclosure: F. Oliviero: None; **C. Baggio**: None; **A. Damasco**: None; **F. Zorzi**: None; **M. Lorenzin**: None; **G. Cozzi**: None; **R. Ramonda**: None.

Abstract Number: 1128

Association Between Leptin Levels, Body Mass Index and Health-related Quality of Life in Patients with Gout

Inna Orlova[1], Iryna Shapoval[2], Nataliia Shkolina[1], Nataliia Kuzminova[1] and Mykola Stanislavchuk[3], [1]National Pirogov Memorial Medical University, Vinnytsya, Vinnytsya, Ukraine, [2]National Pirogov Memorial Medical University, Vinnytsya (Ukraine), Vinnytsya, Ukraine, [3]National Pirogov Memorial Medical University, Vinnytsia, Vinnytsia, Ukraine

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is s a disease with a high disability rate, resulting in severe social burden and is associated with reduced health-related quality of life (HRQoL). Several studies showed that the violation of adipokine status is factor in the development and progression of crystal-induced inflammation. Therefore, assessing the association between leptin levels, body mass index (BMI) and HRQoL is very relevant. This study aimed to investigate the BMI and HRQoL patients with gout and evaluate its association with leptin levels.

Methods: 151 patients were included; 100% were men. The mean age was (mean±SD) 52.4±9.2 years. The average BMI was 31.9±3.4 kg/m2. The mean disease-specific HRQoL was evaluated using a translated and validated Ukrainian version of the Gout Impact Scale (GIS; scale 0-100); HRQoL was assessed by the SF-36 and calculated summary physical (PCS) and mental component (MCS) scores of the SF-36. Leptin in serum was determined by ELISA using the "Human Leptin ELISA Kit" (DRG, Germany). Statistical analysis was performed using MS Excel and SPSS22 software (©SPSS Inc.).

Results: The PCS of the SF-36 was 34.0±7.7, MCS was 40.0±9.2. Total GIS was 51.1±27.5. The leptin level in patients with gout ranged from 2.06 to 18.15 ng/ml (95% CI) and the mean was 6.6±4.3 ng/ml. According to the quartile distribution of serum leptin level, patients with gout were divided into 4 groups: the 1st quartile (Q1) included 36 patients (with indicator level <3.44 ng/ml), the 2nd quartile (Q2) – 37 people (from 3.44 to 5.77 ng/ml), the 3rd quartile (Q3) – 36 people (from 5.77 to 7.49 ng/ml) and the 4th quartile (Q4) – 42 people (>7.49 ng/ml). With increasing leptin levels, there was a decrease in both physical and mental health in gout patients (Fig. 1). The PHS was 22% lower in the 4th quartile than in the 1st, while the MCS was 17% lower in the 4th quartile compared to the 1st quartile. At the same time, the final indicators of the physical and mental sphere in patients in the 4th quartile were significantly different from those in patients in the 1st and 2nd quartiles. The increase in leptin content was accompanied by an increase in the impact of gout on the GIS scale. The total GIS was higher in patients in the 4th quartile and was 35.6% higher than in patients in the 1st quartile. Besides, our analysis showed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

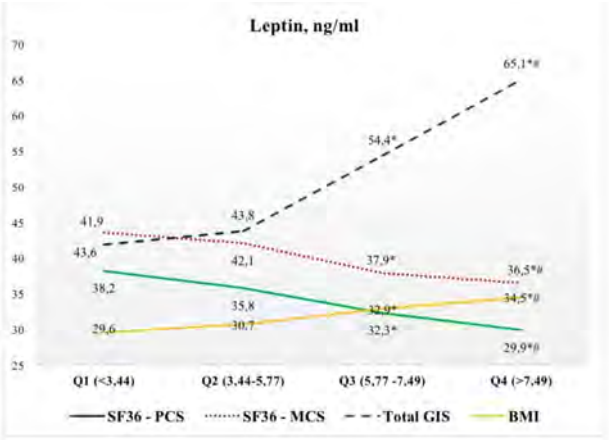


Fig.1. Characteristics of the total GIS, the total physical, mental component of the SF36 and BMI depending on the quartile distribution of leptin level. Note: * - p<0.05 relative to Q1; # - p<0.05 relative to Q2.

significant positive association between BMI and leptin level. In patients with leptin levels >7.49 ng/ml (Q4), BMI was significantly higher by 16.5% than in patients with leptin levels < 3.44 ng/ml (Q1).

Conclusion: An increased leptin level was associated with significant reductions in HRQoL in gout patients. A significant relationship is found between leptin and BMI. The results of this study support the role played by body composition and adipocytokines in HRQoL in gout patients.

Disclosure: I. Orlova: None; **I. Shapoval**: None; **N. Shkolina**: None; **N. Kuzminova**: None; **M. Stanislavchuk**: None.

Abstract Number: 1129

Effectiveness of sodium-glucose cotransporter type 2 inhibitors and urate-lowering agents in patients with gout: data from a single-center specialised clinic

Jose Doménech Serrano[1], Ivana García Loiseau[2], Cristina RodrÍguez-Alvear[3], Pablo Riesgo Sanchis[1], Oscar Moreno Pérez[1] and Mariano Andrés[1], [1]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain, [2]Miguel Hernández University, Alicante, Spain, [3]Virgen de la Peña General Hospital, Fuerteventura, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sodium-glucose cotransporter type 2 inhibitors (SGLT2I) proved substantial benefits in diabetes mellitus (DM), heart failure (HF) and kidney disease (KD). In pivotal trials, SGLT2Is reduced serum urate (SU) levels, but the evidence in patients with gout under other urate-lowering drugs (ULD) in clinical grounds is scarce. The objective is to evaluate the urate outcomes in patients with gout treated with SGLT2I and ULD in clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Retrospective, single-center observational study, enrolling patients with gout from a crystalarthritis specialised clinic. We selected those receiving combined treatment with ULD and SGLT2I, regardless of the indication. Cases with no serum urate levels available in the 6 months before andafter combined treatment or starting renal replacement therapy were excluded. The main variable of the study was SU level pre- and post-SGLT2I (mg/dL) statistically analized using Wilcoxon test as a non parametric continuous variable. As secondary variables, we measured the percentage achievement of SU target (< 6 mg/dL or < 5 mg/dL), the required allopurinol dose (mg) and pre-estimated dose according to the Easy-Allo tool (mg) [PMID 38359899].

Results: Forty-six patients were included: median age 76 years (IQR 15.25), 82.6% men, with high comorbidity (91.1% with DM, 58.7% with KD, 45.7% with HF) and 10 years (IQR 20) of gout duration. As ULD, 66.7% (n=30) of patients were treated with allopurinol, 28.9% (n=13) with febuxostat, and 4.4% (n=2) with benzbromarone. Regarding the SGLT2I, 58.7% (n=27) received dapagliflozin, 30.4% (n=14) empagliflozin, and 10.9% (n=5) canagliflozin. ULD were initially prescribed in 81.4% (n=35), while SGLT2I in the remaining 18.6% (n=8).

The target of SU < 6 mg/dL was achieved in 97.7% (95%CI 88.2-99.6%) of the patients, while 81.4% also reached < 5 mg/dL (95%CI 65.5-88.9%). The achievement of the < 5 mg/dL target was unrelated to the first prescribed medication (ULD 81.3% vs SGLT2I 87.5%, p=1.000) or the type of xanthine-oxidase inhibitor (allopurinol 79.3% vs febuxostat 91.7%, p=0.651).

The start of SGLT2I showed a median SU reduction of 0.85 mg/dL (IQR 3.02, p=0.001 for the before-after comparison) [Image 1]. The SU reduction was observed regardless of being already on ULD (median 0.80, IQR 2.90, p=0.021) or not (median 3.00, IQR 6.95, p=0.018) or of changes in diuretics use (p=0.692).

No significant differences in allopurinol dose were found pre- and post-SGLT2I use but with a trend toward a lower dosage than pre-estimated by the Easy-Allo tool [Image 2].

The use of SGLT2I showed significant reductions in fasting glucose, HbA1c, and C-reactive protein levels, increased urine glucose excretion, and no differences in urine albumin and glomerular filtration rate. We detected a significant reduction in diuretics use pre- and post- SGLT2I (60.9% vs 54.3%, p < 0.001).

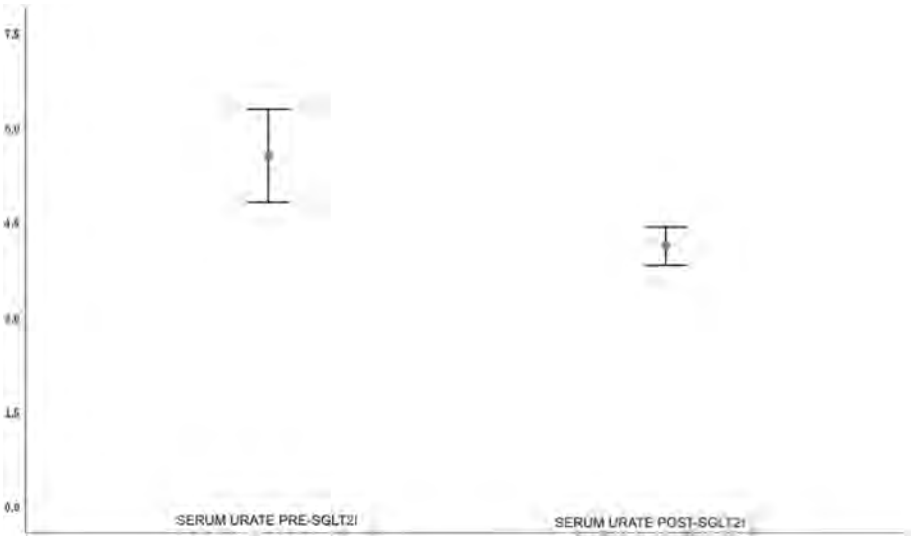


Image 1. Serum urate (SU) reduction in mg/dL after the start of SGLT2I. In brackets, 95%CIs. In the pre-SGLT2I serum urate category, the values are higher, with a mean close to 5.5 mg/dL and with regard to post-SGLT2I serum urate values these are lower, with a mean close to 4 mg/dL.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Image 2. Allopurinol dose pre-estimated and after the start of SGLT2I. Box-and-bar plot of Allopurinol dose comparison. The boxes represent the interquartile range (Q1 to Q3), the dark lines represent the median, and the brackets indicate the range of the data excluding outliers. We can observe a higher variability in the dose of allopurinol after the initiation of treatment with SGLT2I with a tendency towards the use of lower doses.

Conclusion: The combination of SGLT2I and ULD in patients with gout in clinical practice achieved significant SU level reductions and targets of SU < 6 mg/dL and < 5 mg/dL. A trend towards a lower dosage requirement of allopurinol was noted, along with a reduced use of diuretics.

These promising results require confirmation by further intervention studies.

Disclosure: J. Doménech Serrano: None; **I. García Loiseau**: None; **C. RodrÍguez-Alvear**: None; **P. Riesgo Sanchis**: None; **O. Moreno Pérez**: None; **M. Andrés**: Grunenthal, 5, Sobi, 1.

Abstract Number: 1130

Novel Anti-Obesity Medications and Serum Urate Change Among Patients with Gout and Baseline Hyperuricemia

Kiara Tan[1], Jiaqi Wang[1], Saiajay Chigurupati[2], Gregory Challener[3], Natalie McCormick[1], Sharan Rai[4], Florence Porterfield[5], Chika Anekwe[1], Dong Wook Kim[6], Fatima Stanford[7], Caroline Apovian[8], Hyon K. Choi[9] and Chio Yokose[10], [1]Massachusetts General Hospital, Boston, [2]Massachusetts General Hospital, Boston, MA, [3]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, [4]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [5]Division of Endocrinology, Massachusetts General Hospital, Boston, [6]Division of Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital, Boston, [7]Neuroendocrine Unit, Pediatric Endocrinology, Massachusetts General Hospital, Boston, [8]Brigham and Women's Hospital, Boston, [9]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [10]Massachusetts General Hospital, Waltham, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Obesity affects >50% of individuals with gout and is the most important modifiable risk factor for gout. Thus, novel anti-obesity medications (AOM, e.g., semaglutide and tirzepatide), which have revolutionized the medical management of obesity and associated cardiovascular-kidney-metabolic (CKM) comorbidities, are highly relevant for

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients with gout. Researchers have associated weight loss through bariatric surgery or lifestyle changes with reduced serum urate (SU), but no study has examined how novel AOM affects SU. We sought to determine the SU change among patients with gout and baseline hyperuricemia treated with novel AOM.

Methods: Using the Mass General Brigham electronic health record (EHR) database, we identified all patients with gout with baseline hyperuricemia (SU ≥6 mg/dL) who had SU measurements available within 3 months before and >3 months after starting a novel AOM as part of routine clinical care. We defined novel AOM as semaglutide or tirzepatide. We identified patients with gout using an algorithm with a positive predictive value of 0.9 against the 2015 ACR/EULAR gout classification criteria. A rheumatologist and a trained research team member manually reviewed all charts and adjudicated any discrepant findings by consensus. We excluded patients who had SU measured in the setting of an acute gout flare and patients who started or changed the dose of urate-lowering therapy during the study period. We calculated the weight change for all individuals using measurements available in the EHR on dates closest to the SU measurements and grouped them into three categories (< 5%, 5-10%, or >10%). We used linear general estimating equations with robust variance to evaluate the association of baseline weight and weight change (either in absolute or categorical) with serum urate.

Results: Our study included 22 patients with gout who were started on a novel AOM. The mean age was 54.6 years, and the majority were male (77.3%) (**Table 1**). Mean BMI was 39.3 kg/m^2 at baseline. The primary indication for novel AOM treatment was obesity in 11 patients and type 2 diabetes (T2DM) in 11 patients, though many of those with T2DM also had comorbid obesity. Mean treatment duration was 258 days. There were 45.5%, 31.8%, and 22.7% of patients who lost < 5%, 5-10%, and >10% body weight, respectively. There was a significant association between weight and SU change (**-Table 2**, **Figure 1**). Each kg of weight loss was associated with a 0.13 mg/dL reduction in SU, while each BMI unit reduction

Table 1. Baseline Characteristics of Patients with Gout Treated with Novel AOM

	N=22
Age, years (SD)	54.6 (12.6)
Male, n (%)	17 (77.3)
Race, n (%)	
White	19 (95.0)
Black	1 (5.0)
Asian	0
Not reported	2
Duration of AOM use, days (SD)	258.4 (120.4)
Weight, kg (SD)	116.1 (23.3)
BMI, kg/m^2 (SD)	39.3 (8.6)
T2DM, n (%)	12 (54.6)
CKD 3 or greater, n (%)	9 (40.9)
HTN, n (%)	9 (40.9)
ULT use, n (%)	17 (77.3)
Diuretic use, n (%)	5 (22.7)
SGLT2i use, n (%)	3 (13.6)

BMI, body mass index; T2DM, type 2 diabetes; CKD, chronic kidney disease; HTN, hypertension; ULT, urate-lowering therapy; SGLT2i, sodium-glucose cotransporter type 2 inhibitor

Table 2. Association Between Weight and Serum Urate Change Among Patients with Gout Treated with Novel AOM

	β Coefficient for SU Change (mg/dL)
Weight change	
Per kg	0.13 (0.08, 0.19)
Per unit BMI	0.41 (0.23, 0.59)
Weight loss category	
<5%	0 (REF)
5-10%	-0.73 (-1.76, 0.29)
>10%	-2.36 (-3.85, -0.86)
P for trend	<0.001

Adjusted for age, sex, weight loss medication, and baseline weight

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

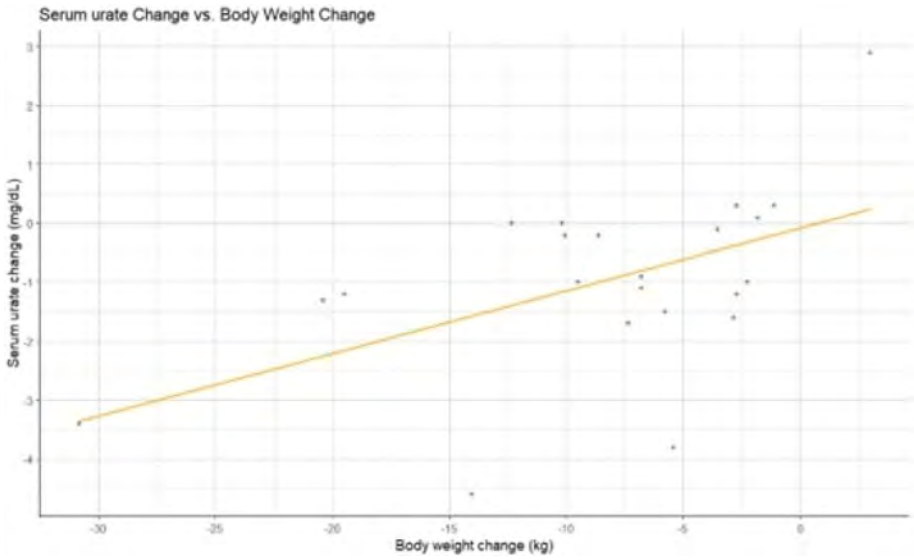


Figure 1. Body Weight Change and Serum Urate Change Among Patients with Gout and Baseline Hyperuricemia

was associated with a 0.41 mg/dL reduction in SU. Compared to those who lost < 5% of their body weight, those who lost 5-10% of their body weight had a 0.73 mg/dL greater reduction in SU, and those who lost >10% of their body weight had a 2.36 mg/dL greater reduction in SU (p for trend < 0.001) (**Table 2**).

Conclusion: In this retrospective study, novel AOM-induced weight loss was associated with a significant reduction in SU among patients with gout with baseline hyperuricemia. These results suggest that novel AOM may be a powerful multi-purpose medication for the many patients with gout and obesity and call for larger-scale studies to test this hypothesis.

Disclosure: K. Tan: None; **J. Wang**: None; **S. Chigurupati**: None; **G. Challener**: None; **N. McCormick**: None; **S. Rai**: None; **F. Porterfield**: None; **C. Anekwe**: None; **D. Kim**: None; **F. Stanford**: None; **C. Apovian**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **C. Yokose**: None.

Abstract Number: 1131

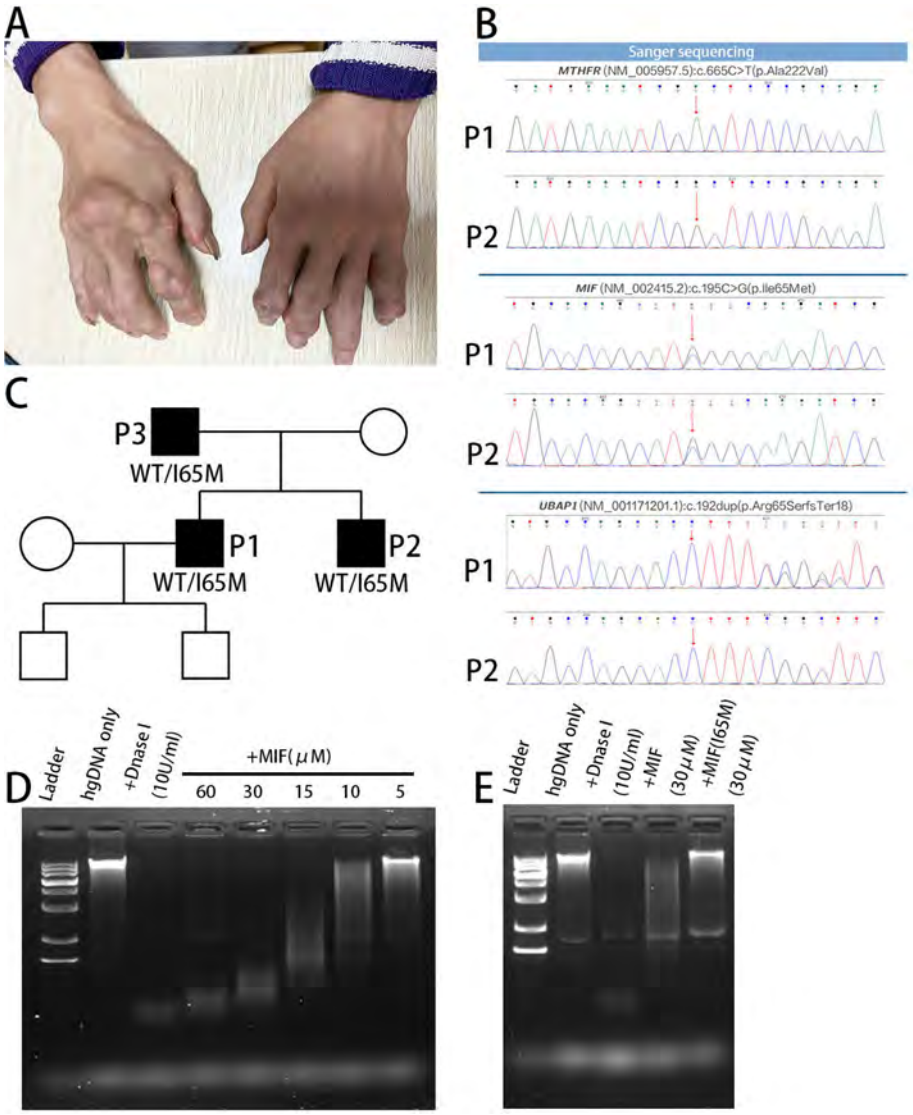
Variant Drives Tophus Formation through Dual Mechanisms: Extracellular Aggregation andvImpaired Macrophage Phagocytic Clearance

Yuqi wang[1], Lingjiang Zhu[1], Jinshuo Han[2], Junbin Qian[3], Martin Herrmann[4], Jing Xue[1] and **Lei Liu**[1], [1]The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China (People's Republic), [2]Zhejiang University, School of Medicine, Hangzhou, China (People's Republic), [3]Women's Hospital, Zhejiang University School of Medicine, Hangzhou, China (People's Republic), [4]University Hospital Erlangen, Erlangen, Germany

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: While aggregated neutrophil extracellular traps (aggNETs) constitute the primary structural component of tophi, the susceptible population for tophaceous gout remains poorly characterized. We investigated a familial case of early-onset tophaceous gout to elucidate novel mechanisms underlying tophus formation.While aggregated neutrophil

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

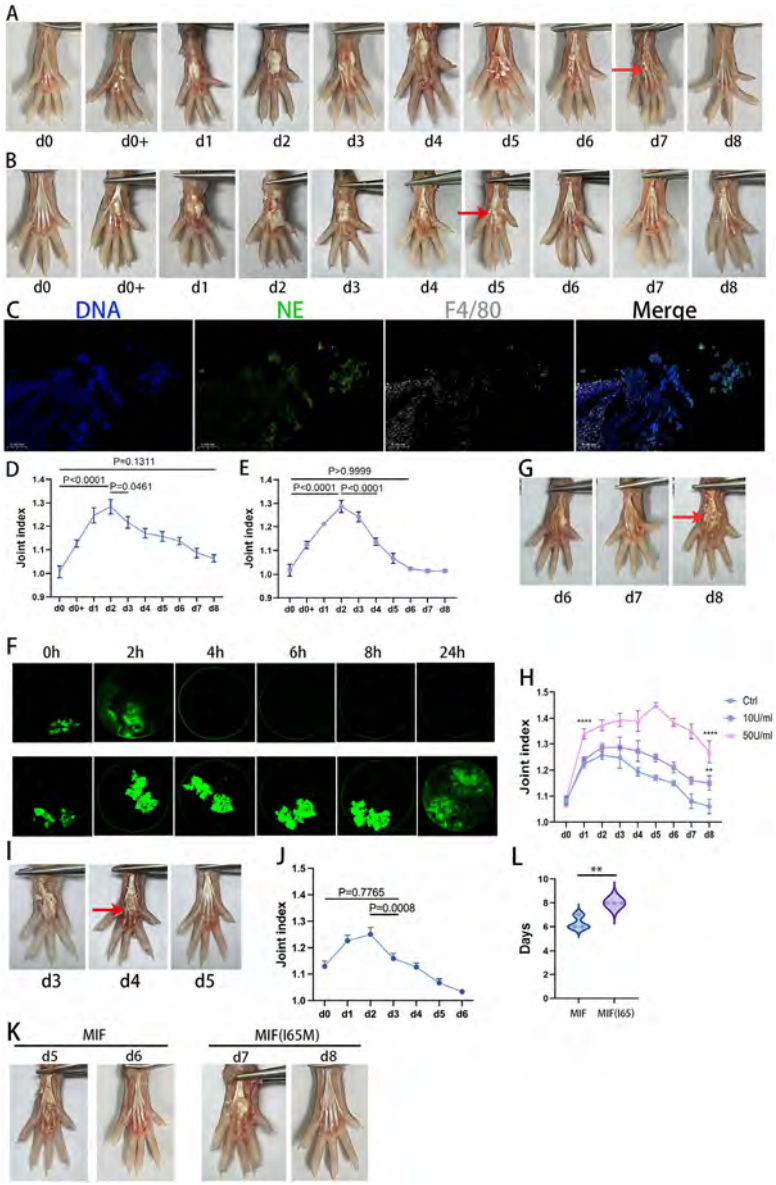


Patient with tophi, WES, and pedigree: (A) The proband P1 (index case) in this study presented with tophi covering both hands. (B) Whole-exome sequencing revealed that the proband P1, his brother P2, and father P3 (not shown) all shared a heterozygous missense mutation in MIF (NM_002415.2):c.195C>G (p.Ile65Met) in exon 2. Additionally, proband P1 carried a homozygous missense mutation in MTHFR (NM_005957.5):c.665C>T (p.Ala222Val) in exon 5 and a heterozygous frameshift mutation in UBAP1 (NM_001171201.1):c.192dup (p.-Arg65SerfsTer18) in exon 1. (C) The pedigree chart showed that the proband's father (P3) and brother (P2) were also early-onset tophaceous gout patients, with all three (P1, P2, P3) carrying the heterozygous MIF mutation, while P1 has two asymptomatic sons (aged 6 and 4). (D) In vitro pulsed-field gel electrophoresis using human genomic DNA as the substrate was performed to assess the nuclease activity of DNase-I and MIF. (E) The results demonstrate that wild-type MIF exhibits DNA-degrading activity, whereas the nuclease activity of the MIF (I65M) mutant is significantly reduced compared to the wild type.

extracellular traps (aggNETs) constitute the primary structural component of tophi, the susceptible population for tophaceous gout remains poorly characterized. We investigated a familial case of early-onset tophaceous gout to elucidate novel mechanisms underlying tophus formation.

Methods: Whole-exome sequencing was performed on a multigenerational family with early-onset tophaceous gout affecting the proband, his father, and brother. Molecular cloning generated wild-type and mutant macrophage migration inhibitory factor (MIF) expression vectors, with subsequent structural and functional characterization using three-dimensional modeling and circular dichroism spectroscopy. Tophaceous mice administered by MIF or mutant MIF vectors, *Mif* knockout mice and in vitro models assessed tophus degradation dynamics. Transwell assays with fluorescence labeling evaluated macrophage-mediated phagocytosis and intracellular processing of aggNETs.

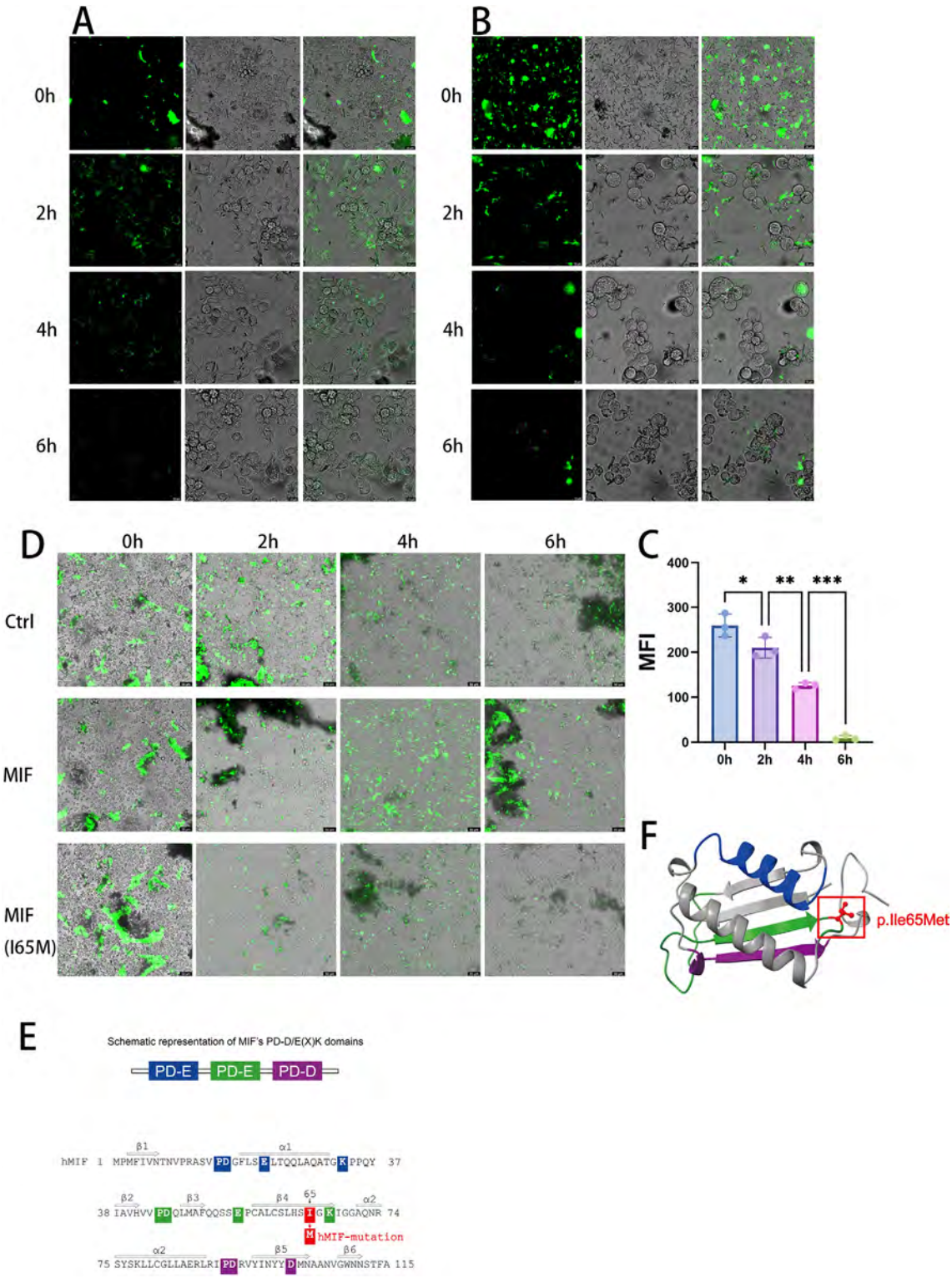
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



DNA Enzyme Intervention Promotes Tophus Resolution: (A) Classic MSU crystal-induced gouty arthritis model in mouse footpads: One footpad was injected with MSU crystals (40 μL, 25 mg/mL), while the contralateral side received an equal volume of PBS. Tophus-like material (red arrow) appeared at 8 h post-injection (d0+) and spontaneously resolved by day 8 (d8). (B) Daily footpad injection of DNase-I (20 μL, 1600 U/mL) after MSU crystal injection accelerated tophus resolution, with complete disappearance by day 6 (d6, red arrow). (C) Immunofluorescence staining of d2 tophus-like material revealed abundant NETs containing macrophages. (D) Joint swelling index in the MSU crystal-injected group returned to baseline (no statistical difference vs. d0) by day 8. (E) The DNase-I + MSU crystal group showed recovery of joint swelling index by day 6. (F) In vitro, aggNETs (formed by co-culturing neutrophils [1.2×10^7/mL] with MSU crystals [0.6 mg/10^6 cells]) were stained with Sytox (DNA). DNase-I treatment reduced aggNETs within 2 h, with near-complete dissolution at 4 h. (G, H) Uricase (10 U/mL, 50 U/mL) co-injection with MSU crystals failed to resolve tophi by day 8, with significantly higher arthritis indices vs. controls. (I, J) Combined uricase (50 U/mL) + DNase-I daily intervention achieved tophus resolution by day 5 and restored joint swelling index by day 3. (K, L) In MSU crystal-induced arthritis, MIF-treated mice showed tophus resolution at day 6.3, while MIF (I65M)-treated mice required 8 days (significantly delayed, **P<0.01, ****P<0.0001).

Results: We identified a pathogenic *MIF* variant (p.Ile65Met, hereafter referred to as I65M) segregating with disease in the affected family. Structural analysis revealed this mutation induces conformational changes in the PD-D/E(X)K domain. Functional studies demonstrated: (1) significantly reduced nuclease activity of MIF(I65M) compared to wild-type; (2) impaired tophus degradation capacity of MIF(I65M) in both murine models and in vitro systems; (3) preserved macrophage phagocytosis but defective cytoplasmic degradation of aggNETs through a lysosome-independent pathway.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



MIF Promotes Macrophage Phagocytosis of aggNETs and the Spatial Conformation of MIF (I65M): (A, C) THP-1-derived macrophages phagocytosing aggNETs. DNA (aggNETs) was stained with Sytox Green (intracellular live-cell DNA remains unstained). Over time, fluorescent signal appeared within macrophages, with gradually decreasing mean fluorescence intensity (MFI). (B) MIF-knockdown THP-1-derived macrophages exhibited significantly impaired phagocytosis of aggNETs. (D) MIF enhanced THP-1 phagocytosis of aggNETs, while MIF (I65M) showed reduced activity (peak phagocytosis at 4 h; MIF group displayed strongest intracellular green fluorescence, markedly weaker in MIF (I65M) group). (E) Schematic of human MIF's three PD-D/E(X)K domains (blue, green, purple) with amino acid sequences. Red "I→M" indicates the mutation site. (F) 3D structure of human MIF showing the mutation site (red) located in the 4th β-sheet between PD-E (blue) and PD-D (purple).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study establishes a novel pathogenesis framework for familial tophaceous gout, demonstrating how MIF mutations lead to aggNETs accumulation through impaired clearance mechanisms. Our findings identify defective aggNETs degradation as a central pathophysiological process, offering new therapeutic targets for tophaceous gout management.

Disclosure: Y. wang: None; **L. Zhu**: None; **J. Han**: None; **J. Qian**: None; **M. Herrmann**: None; **J. Xue**: None; **L. Liu**: None.

Abstract Number: 1132

DDX3X Regulates Gout Inflammation via NLRP3 Inflammasome Activation and Macrophage Pyroptosis Crosstalk

Linrui Zhong, Tianyi Lei, Quanbo Zhang and Yufeng Qing, The Affiliated Hospital of North Sichuan Medical College, Nanchong, Sichuan, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

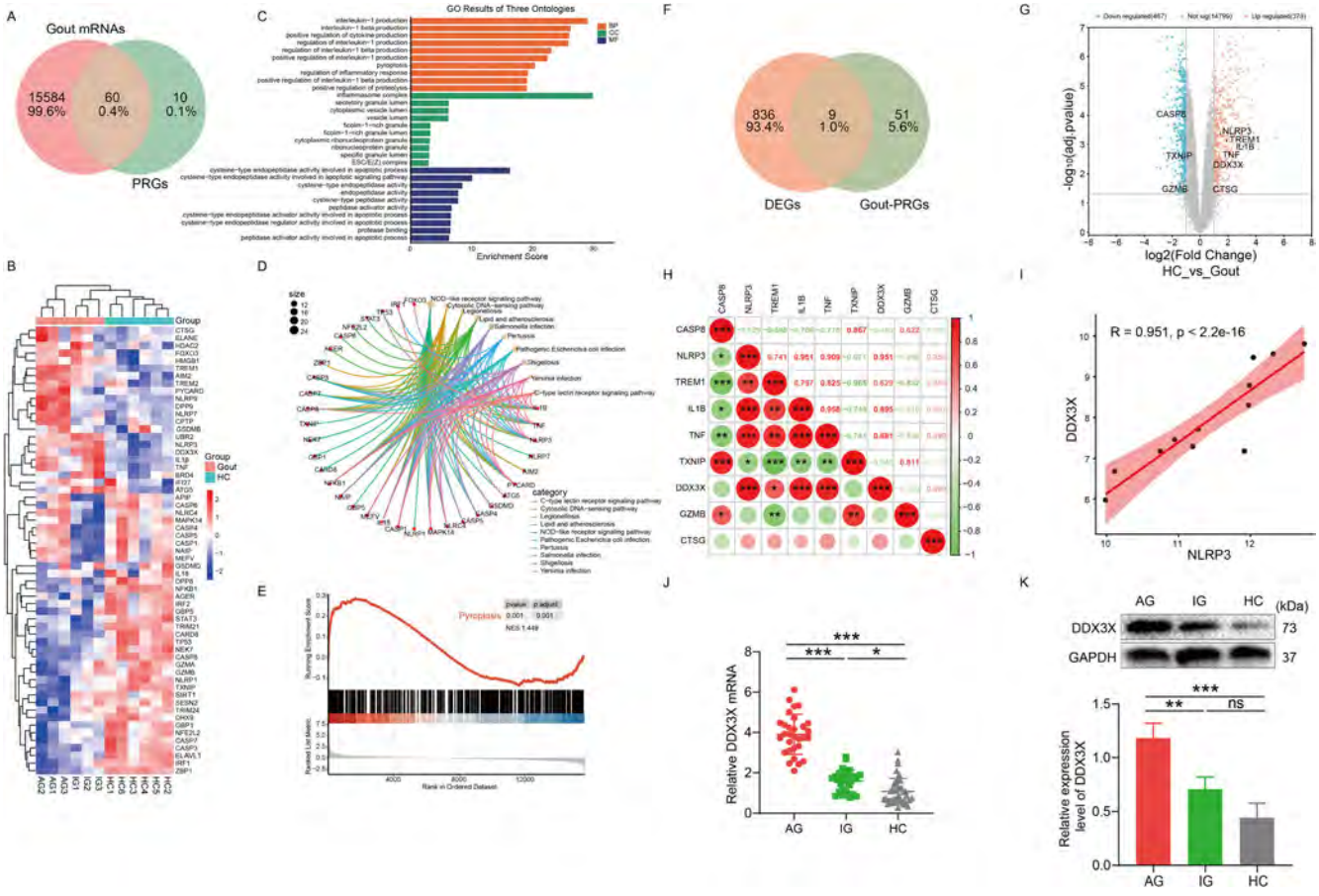


Figure1. DDX3X and pyroptosis play an important role in gout inflammation

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Pyroptosis is closely linked to acute flare-ups and spontaneous remission of gout. However, the specific mechanisms by which pyroptosis regulates gout inflammation remain unclear. This study aims to analyze the potential role of DDX3X as a hub molecule influencing pyroptosis to regulate gout inflammation.

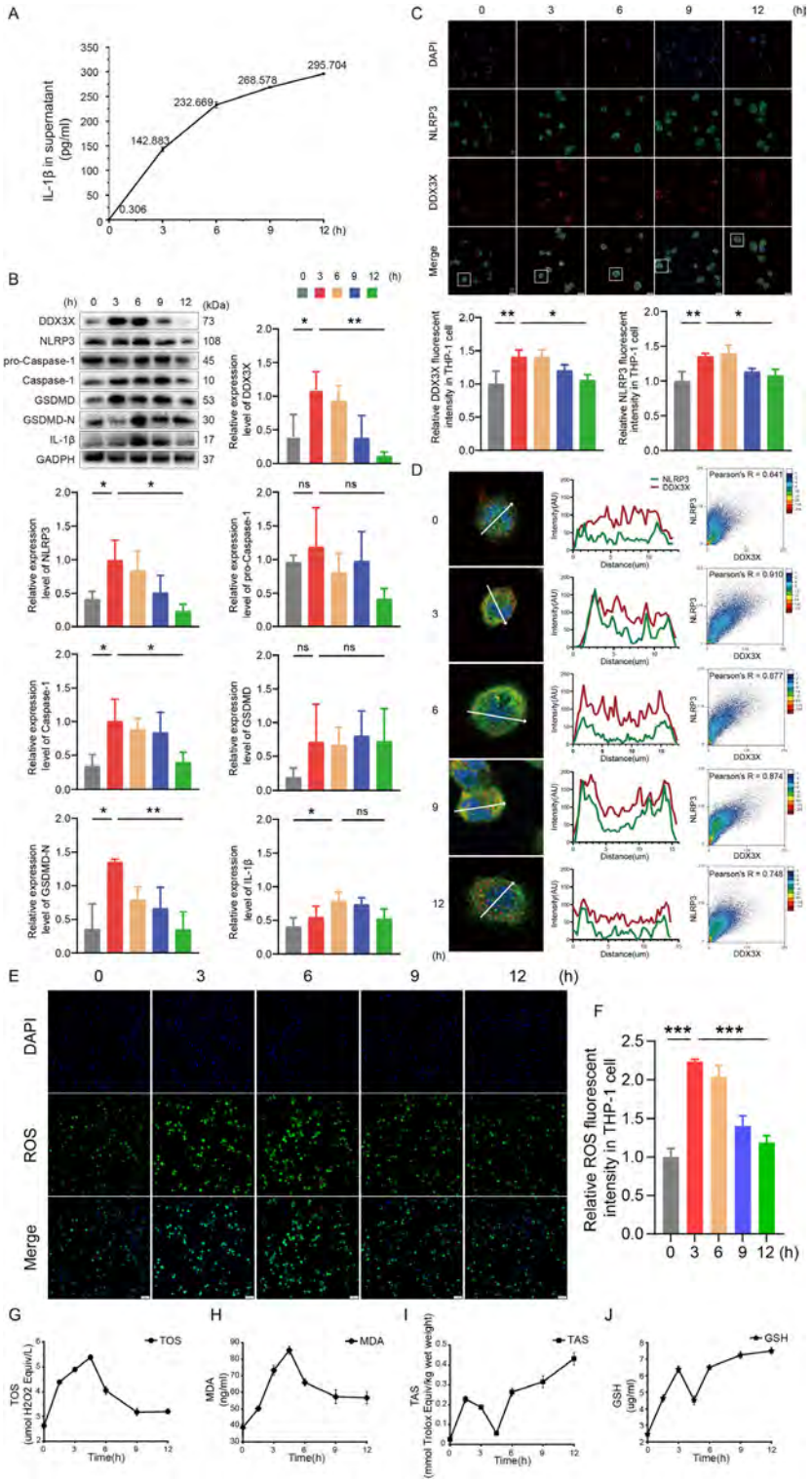


Figure2. DDX3X and pyroptosis were differentially expressed in gout and were closely related to inflammation levels and oxidative stress

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

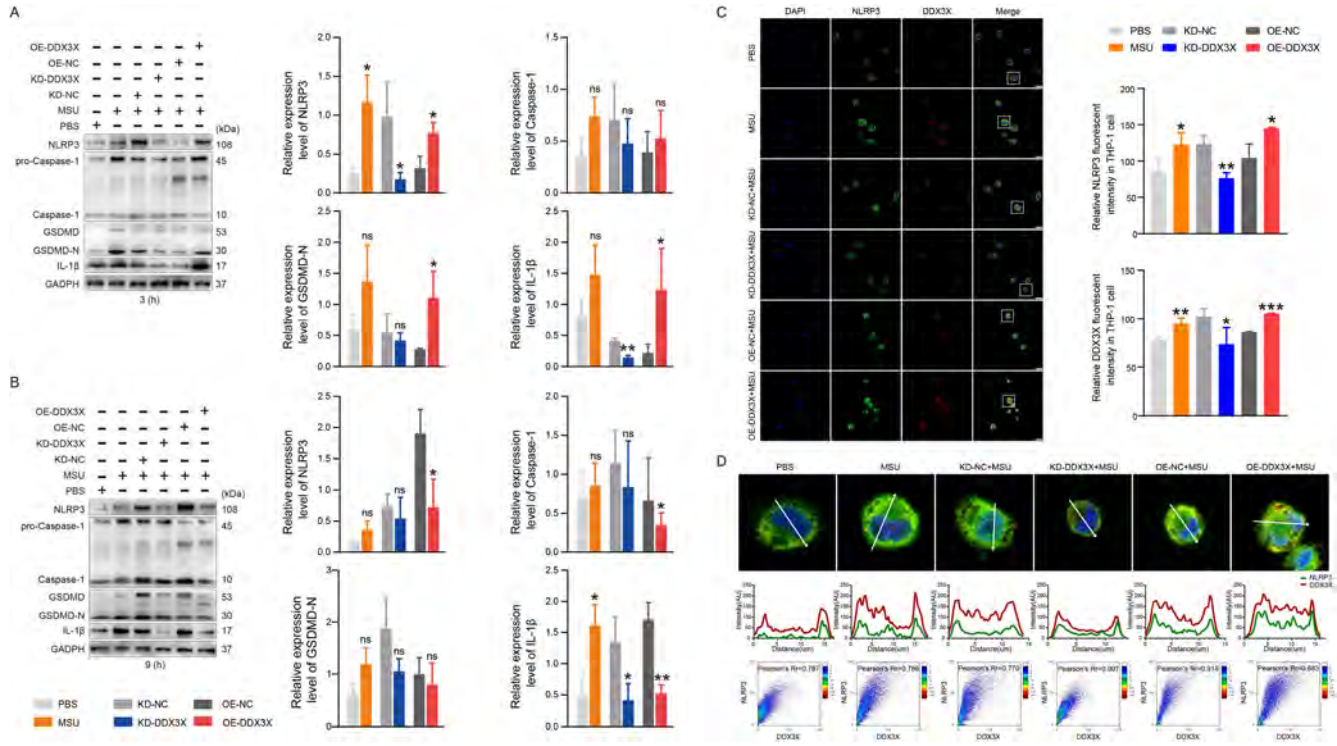


Figure2. DDX3X contributes to gout inflammation by mediating pyroptosis through modulating NLRP3 inflammasome assembly

Methods: Bioinformatics methods were used to explore whether pyroptosis is involved in regulating gout. Real-time quantitative PCR (RT-qPCR), Western blotting (WB), and immunofluorescence were employed to assess DDX3X, ROS levels, and changes in the NLRP3/Caspase-1/GSDMD pathway. The regulation of pyroptosis mediated by DDX3X under different conditions was observed.

Results: Bioinformatics analysis revealed that pyroptosis is involved in gout regulation, identifying nine (pyroptosis-related genes)PRGs with DDX3X closely related to NLRP3. DDX3X was significantly overexpressed in acute gout patients. In the time-gradient model of gout inflammatory cells, both the classical pyroptosis pathway and DDX3X showed significant nonlinear characteristics, leading to trends in IL-1β changes, with DDX3X interacting with NLRP3. After DDX3X expression intervention, pyroptosis and gout inflammation showed characteristic changes. At the 3h oxidative damage stage, DDX3X participated in activating the NLRP3 inflammasome to promote pyroptosis. At the 9h oxidative stress stage, DDX3X might respond to stress granule assembly, indirectly inhibiting pyroptosis, thereby protecting cell survival. This protective mechanism might initiate negative feedback regulation to inhibit IL-1β release.

Conclusion: DDX3X can regulate gout inflammation by activating the NLRP3 inflammasome and mediating macrophage pyroptosis. It mainly participates in early inflammation in gout and cell homeostasis maintenance in the later stages of inflammation.

Disclosure: L. Zhong: None; **T. Lei**: None; **Q. Zhang**: None; **Y. Qing**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1133

A Proteomic Analysis of Subclinical Synovial Inflammation Associated with Monosodium Urate Crystal Deposition

Mariano Andrés[1], María-Luisa Peral-Garrido[2], Samanta Ortuño[3], Rocío Caño[3], Silvia Gómez-Sabater[3], Alejandra Bermúdez[4], Teresa Lozano[5], Miguel Perdiguero[5], elena Caro-Martínez[6], Ruth Sánchez-Ortiga[5], Carolina Ruiz-García[7], Eliseo Pascual[8] and Rubén Francés[8], [1]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain, [2]Vinalopó University Hospital, Novelda, Spain, [3]Alicante Institute for Health and Biomedical Research (ISABIAL), Alicante, Spain, [4]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [5]Dr Balmis General University Hospital, Alicante, Spain, [6]HACLE San Vicente Hospital, San Vicente del Raspeig, Spain, [7]Campoamor Health Center, Alicante, Spain, [8]Miguel Hernandez University of Elche, Alicante, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Persistent subclinical inflammation from monosodium urate (MSU) crystals is present in gout and asymptomatic hyperuricemia (AH). The underlying mechanism is poorly understood. This study analyzes the articular inflammatory proteome linked to MSU crystal deposition in hyperuricemic patients without clinically active inflammation.

Methods: Observational, cross-sectional study. 100 participants with either AH (hyperuricemia as serum urate ≥7mg/dl) [n=77] or intercritical gout (2015 ACR/EULAR criteria, hyperuricemia, untreated) [n=23] underwent clinical assessment, blood testing, and lower limbs ultrasonography. In the case of effusion, synovial fluid (SF) was obtained (n=81). Samples underwent polarized microscopy for microcrystals (MSU, calcium pyrophosphate –CPP) and leukocytes (using a Neubauer chamber). The SF proteome was studied using Olink Inflammation panel in cell extracts from samples with enough volume after centrifugation (n=60). For these cases, paired serum proteome assessments were intended (n=28). Comparisons were conducted based on microcrystal deposition, identifying differential expression analysis of proteomics using Principal Component Analysis (PCA), represented by volcano plots. Also, we explored predictive models using SF features (proteome and leukocytes) to discriminate microcrystal deposition.

Results: Out of 100 participants, 81 had SF samples available for polarized microscopy; MSU and CPP crystals were detected in 5 (6.2%) and 11 samples (13.6%), respectively, while the others showed no crystals (65, 80.2%). Leukocyte

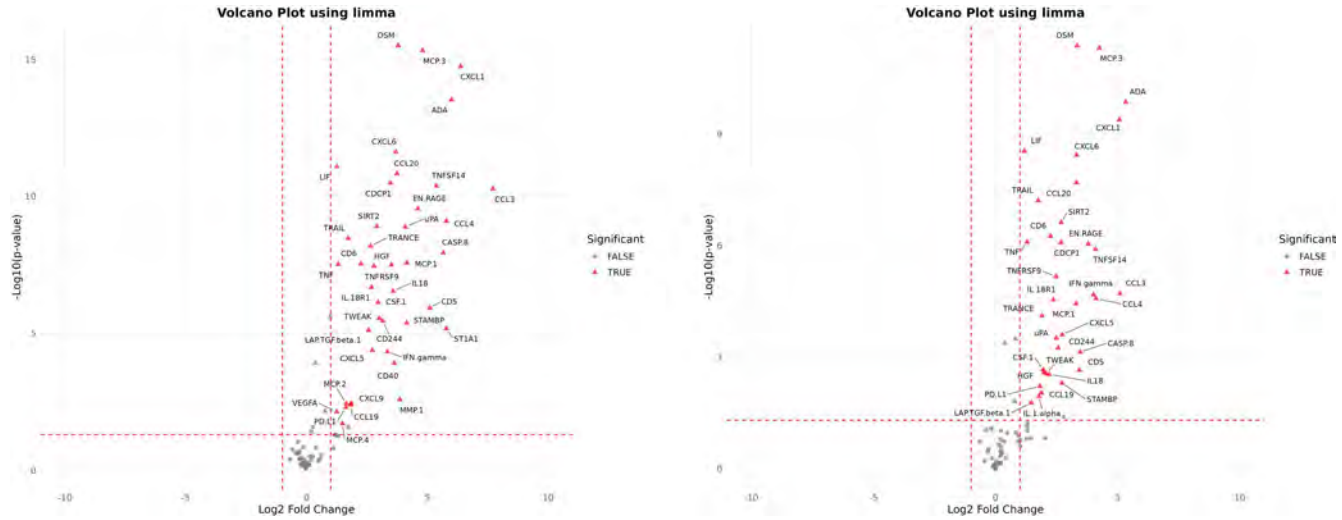


Figure 1. Volcano plot of differentially expressed proteins in SF samples (to the right favors MSU; to the left favors no crystals [left] or CPP [right]).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

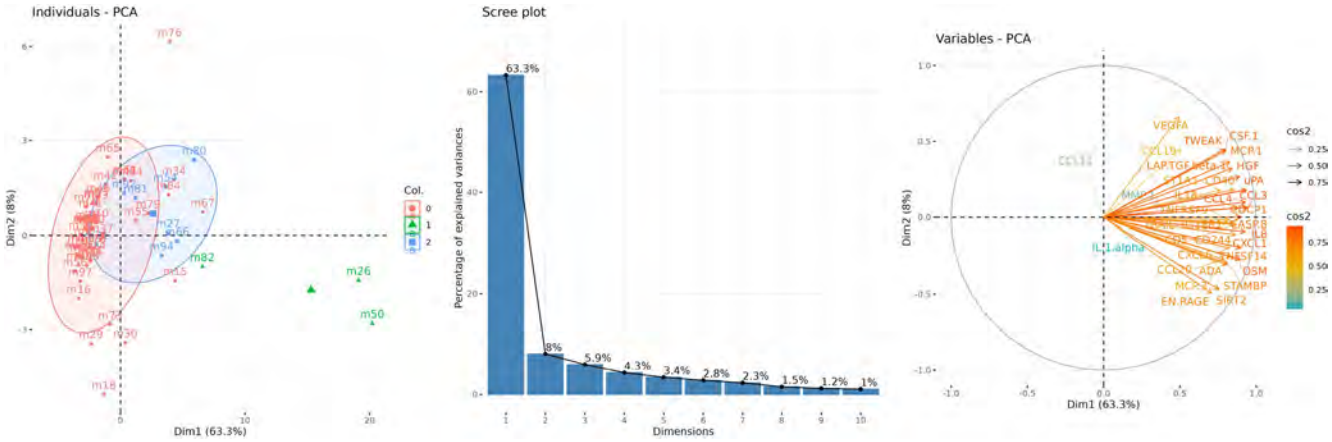


Figure 2. Left, PCA of statistically significant inflammatory proteins in synovial fluid, comparing the three patient groups, showing the distribution of patients' samples across dimensions 1 (dim1) and dim2 [red=no crystals; green=MSU; blue=CPP]. Middle, percentages of explained variances by dimensions. Right, protein distributions to dim1 and dim2 and their contribution.

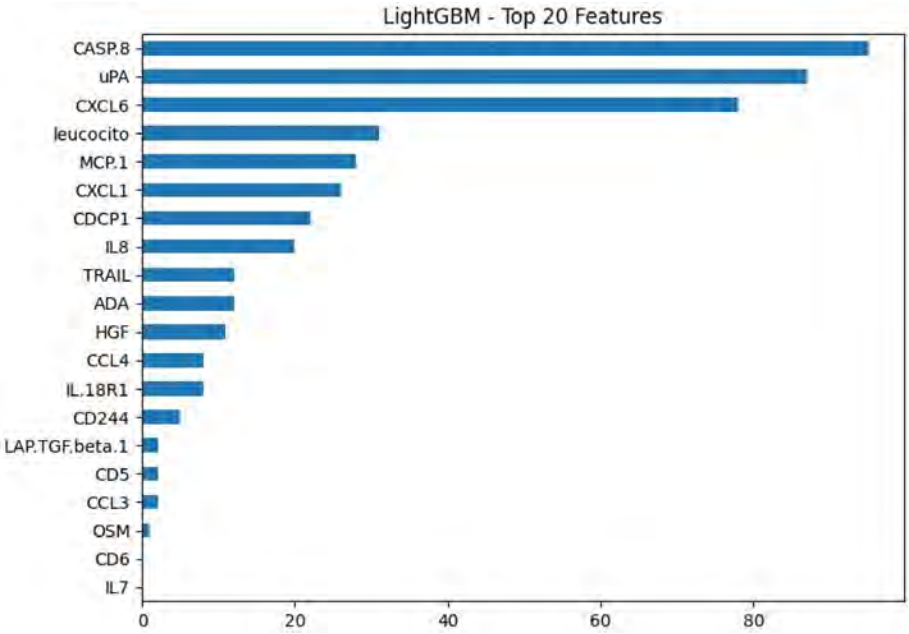


Figure 3. SF individual features and role in distinguishing the presence of microcrystals, using the lightGBM decision tree-based algorithm with KBest variable selection.

counts were significantly higher in samples with MSU (640/mm3, 245-875) compared to CPP (55/mm3, 43-203) or no crystals (40/mm3, 20-70), p< 0.001. Phagocytosis was seen in 32.4% (0-61.8%) and 8.3% (0-53.3%) of MSU and CPP samples [p=0.743]. SF leukocytes showed no correlation to serum urate, total leukocytes, or acute phase reactants.

Sixty samples underwent proteomic analysis (3 with MSU, 8 with CPP, 49 with no crystals). **Figure 1** shows the volcano plots comparing MSU versus CPP (left) and versus no crystals (right). Both comparisons yielded similar results: SF containing MSU crystals showed an increased relative expression of several inflammatory proteins. These proteins differentiated samples among the three groups (71.3% of explained variances [**Figure 2**]). Among different predictive models, lightGBM with variable selection by KBest showed the best performance (accuracy 0.83, AUC 0.8182). **Figure 3** shows the 20 features considered most relevant by the previously mentioned optimal model for prediction. Only IL-8 significantly correlated between SF and serum expression (r=+0.44, p=0.019) in paired sera [n=28].

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Subclinical inflammation associated with MSU crystal deposition involves elevated leukocyte counts and a distinctive proteomic profile, which can distinguish the presence of microcrystals. Our data also suggest that during asymptomatic stages, the subclinical inflammation appears localized and confined to the joint, the relevance of which requires further investigation.

Disclosure: M. Andrés: Grunenthal, 5, Sobi, 1; **M. Peral-Garrido**: None; **S. Ortuño**: None; **R. Caño**: None; **S. Gómez-Sabater**: None; **A. Bermúdez**: None; **T. Lozano**: None; **M. Perdiguero**: None; **e. Caro-Martínez**: None; **R. Sánchez-Ortiga**: None; **C. Ruiz-García**: None; **E. Pascual**: None; **R. Francés**: None.

Abstract Number: 1134

Efficacy and Safety of Anakinra for Acute Calcium Pyrophosphate Deposition Disease Flare: A Systematic Review and Meta-Analysis

Pannathorn Nakaphan[1], Somkiat Phutinart[2], Patavee Pajareya[2], Priabprat Jansem[3], Nattanicha Chaisrimaneepan[4], Pim Jetanalin[5] and Noppachai Siranart[2], [1]Department of Internal Medicine, Weiss Memorial Hospital, Chicago, IL, [2]Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [3]Department of Psychiatry, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand, [4]Department of Medicine, Texas Tech University Health Sciences Center, Lubbock, TX, [5]Department of Medicine, Division of Rheumatology, University of Illinois College of Medicine, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

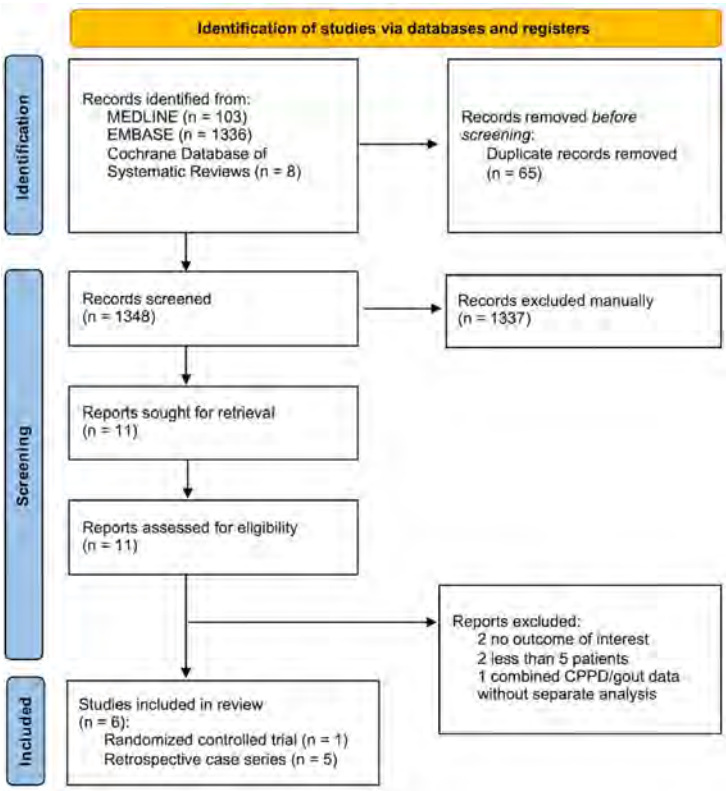


Figure 1. The PRISMA Flow Diagram

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

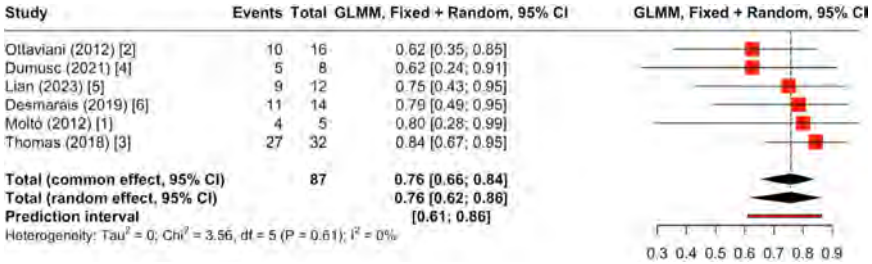


Figure 2. Subjective Physician Assessment of Clinical Responses Following Anakinra Treatment for Acute CPPD Flares. The figure depicts the proportion of patients achieving clinical responses as evaluated by physicians after treatment with Anakinra.

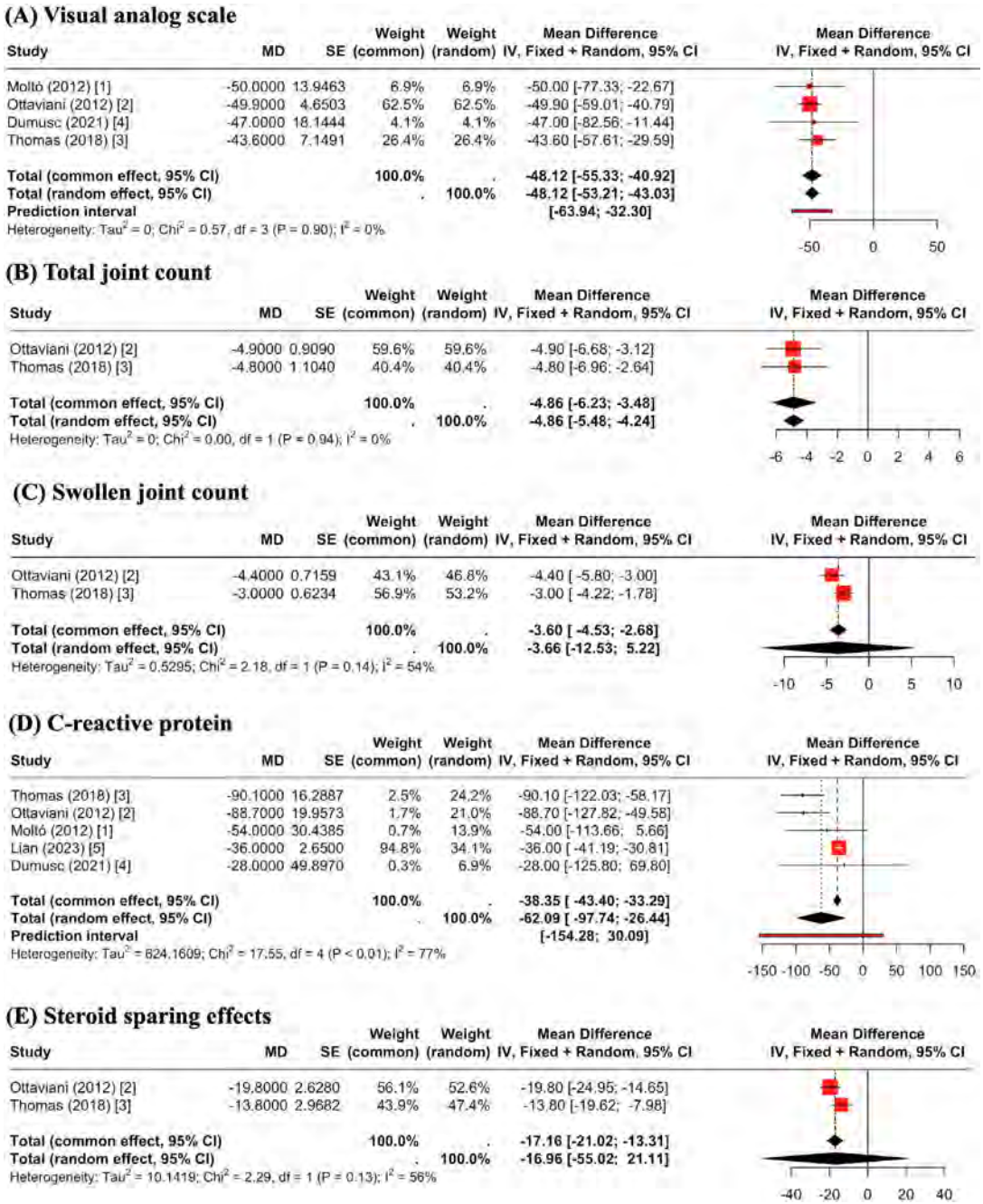


Figure 3. Mean Differences in Secondary Outcomes Following Anakinra Treatment for Acute CPPD Flares. The figure depicts the mean differences in secondary outcomes measured between baseline and post-treatment with Anakinra. Secondary outcomes include: (A) Visual analog scale, (B) Total joint count, (C) Swollen joint count, (D) C-reactive protein levels, and (E) Steroid-sparing effects.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Calcium Pyrophosphate Deposition Disease (CPPD) is a common inflammatory arthritis among older adults. Comorbidities often limit conventional treatment of acute CPPD flare. Anakinra, an interleukin-1 inhibitor, is a promising alternative. We aimed to evaluate the efficacy and safety of anakinra in acute CPPD flares.

Methods: We systematically searched studies from MEDLINE, EMBASE, and the Cochrane Database up until August 2024. The primary outcome was a positive treatment response between day 3 and day 5 after anakinra initiation. Secondary outcomes included changes in pain ratings assessed by the visual analog scales (VAS), C-reactive protein levels, tender joint counts (TJC), swollen joint counts (SJC) and corticosteroid usage.

Results: Six studies were included in our meta-analysis: five observational studies and one randomized controlled trial. A total of 84 patients were included in our analysis. Subjective physician assessments of clinical response were reported in all studies with a combined positive treatment response rate of 76% (95%CI: 61-86, I^2=0%). Our pooled analysis also showed a significant reduction of VAS scores by 48.12 mm (95% CI: 53.21 - 43.03, I^2=0%) and CRP levels by 62.09 mg/L (95% CI: 97.74-26.44, I^2=77%) from baseline. Reductions of TJC and SJC were also demonstrated, 4.86 (95% CI: 5.48 - 4.23, I^2=0%) and 3.65 (95% CI: -12.53-5.22, I^2=54%), respectively. Adverse reactions included injection site reaction, rash, bacterial pneumonitis, and neutropenia.

Conclusion: Anakinra is a promising alternative treatment for patients with acute CPPD flare as it showed desirable clinical responses and a favorable safety profile.

Disclosure: P. Nakaphan: None; **S. Phutinart**: None; **P. Pajareya**: None; **P. Jansem**: None; **N. Chaisrimaneepan**: None; **P. Jetanalin**: None; **N. Siranart**: None.

Abstract Number: 1135

A Gain-of-function 5'UTR Variant in ANKH Causes Familial CPPD with Elevated Extracellular Ppi and Citrate

Richette Pascal[1], christophe Duranton[2], Thomas Pinna[3], Manon Ricquebourg[4], LATOURTE Augustin[5], Thomas Bardin[6], Valérie Bousson[7], Hang-Korng Ea[8], Isabelle Rubera[9] and Corinne Collet[10], [1]Rheumatology Department, Lariboisiere Hospital, Paris, Ile-de-France, France, [2]CNRS-UMR 7370 - Laboratoire de Physiomedecine moléculaire, Nice, Rhone-Alpes, France, [3]INSERM U1132, PARIS, Ile-de-France, France, [4]Lariboisiere Hospital, INSERM U1132, Paris, France, [5]Rheumatology Department, Lariboisiere Hospital, Paris, France, [6]Lariboisiere Hospital, Department of Rheumatology, Paris, France, [7]Radiology Department, Lariboisiere Hospital, Paris, France, [8]INSERM U1132, Lariboisiere Hospital, Paris, France, [9]CNRS-UMR 7370 - Laboratoire de Physiomedecine moléculaire, Nice, France, [10]Reference Center for Skeletal Dysplasia, INSERM UMR 1163, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

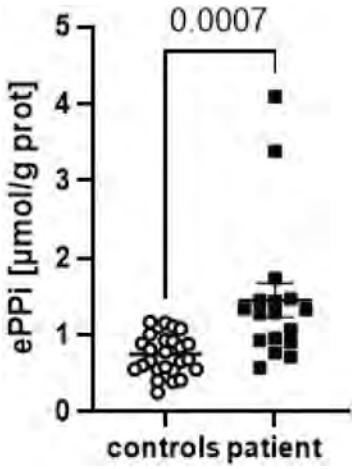
Session Time: 10:30AM–12:30PM

Background/Purpose: To identify novel pathogenic variants associated with chondrocalcinosis (CC), we systematically screened individuals with a family history of CPPD using an NGS panel. Among 26 index cases between 2016 and 2024, we identified a known mutation in the TNFRSF11B gene, a novel missense variant in the ANKH gene, and a novel mutation in the 5' untranslated region (5'UTR) of the ANKH gene, which we report here.

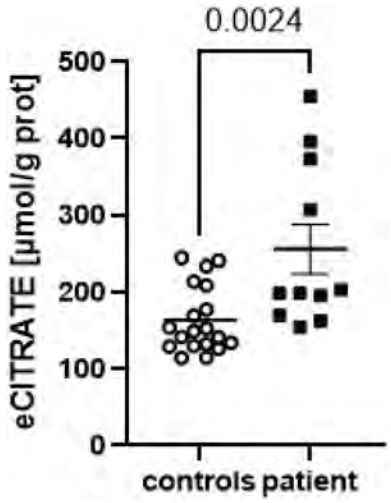
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Whole exome sequencing (WES) was performed to expand the search for pathogenic variants not detected by the targeted panel. Primary fibroblast cultures (skin biopsy) of the proband and three controls were established to assess protein levels and gene expression using Western blotting (WB), qRT-PCR, and immunocytochemistry (IC). Inorganic pyrophosphate (PPi) and ATP levels in the culture media were measured by enzymatic assay and citrate concentrations were determined by ion chromatography. Skeletal imaging of the proband was performed using a photon-counting computed tomography scanner.

Results: The proband experienced recurrent episodes of arthritis in the wrists, knees, and ankles since the age of 23. Microscopic analysis of SF confirmed the presence of CPP crystals. CT scan showed widespread calcium deposits in almost all joints without OA changes, as well as in the choroid (Figure 1). He is a member of a multiplex family in which CPPD follows a dominant mode of inheritance. Panel NGS revealed a previously unreported heterozygous variant in the 5' UTR (NM_054027.6: c.-113_-112delinsAT) introducing a novel ATG start codon in all affected individuals. WES confirmed that no other variant could explain this phenotype. This variant co-segregates with the CPPD phenotype and was further confirmed by Sanger sequencing. The plasma PPi level was elevated in the proband compared to the mean value measured in a control cohort (n=46): 2.40 μM vs. 1.61 ± 0.33 μM. In vitro, there were no differences in ANKH mRNA expression or protein expression (WB) between mutant and control fibroblasts. IC revealed both transmembrane and cytoplasmic localisation of the mutant protein. Notably, the levels of PPi and citrate in the fibroblast culture media (μmol/g protein) were significantly higher in the proband than in the controls: 1.45 vs. 0.77 for PPi ($p < 0.0007$) and 255.8 vs. 177.3 for citrate ($p = 0.0024$) (Figures 2-3). In contrast, no difference in extracellular ATP levels was observed. Treatment of fibroblasts with probenecid



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(5 mM), an ANKH inhibitor, abolished the increased citrate levels observed in the proband's fibroblast culture media. mRNA expression of IL1, IL6, MMP1, PIT1 and TNAP was unchanged in the proband's fibroblasts. In contrast, ENPP1 expression was significantly increased by approximately 8-fold ($p < 0.001$) - a finding that was further confirmed at the protein level by WB and IC.

Conclusion: We describe a novel 5'UTR variant in the ANKH gene that generates an ectopic start codon. Functional studies showed increased extracellular levels of PPi and citrate and overexpression of ENPP1 without alterations in ANKH mRNA or protein levels, supporting a gain-of-function mechanism

Disclosure: r. pascal: None; **c. Duranton**: None; **T. Pinna**: None; **M. Ricquebourg**: None; **L. Augustin**: None; **T. Bardin**: None; **V. Bousson**: None; **H. Ea**: None; **I. Rubera**: None; **C. Collet**: None.

Abstract Number: 1136

The Impact of Iron Overload and HFE Genetic Mutations on Joint Disease in Haemochromatosis: Data from the Haemochromatosis Arthropathy Inception Cohorts

Bayram Farisogullari[1], Pedro Machado[2], Stephanie Finzel[3], Graeme Carroll[4], Geraldine mcCarthy[5], John Stack[6], Simone Parisi[7], Graca Porto[8], richette pascal[9], Gyorgy Nagy[10], Marton Weidl[10], Ann Rosenthal[11], Pascal Guggenbuhl[12], Katarzyna Banaszkiewicz[13], Barbara Butzeck[14], Howard Don[15], Svenja Engelhardt[16], Jeremy Shearman[17], David Mitchell[18], Jane Barker[19], Valerie Brueton[19], Philip Coathup[19], Jacquie Dowsett[19], Marie Duncan[19], Tracey Dunleavy[19], Ian Fish[19], Allin Hoggarth[19], Mark McKinnon[19], James Minter[19], Tim Osborne[19], Marguerite Smith[19], Christine Wright[19] and **Patrick Kiely**[20], [1]University College London, London, [2]Department of Rheumatology, University College London, and Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS Trust, Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [3]Department of Rheumatology and Clinical Immunology, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, [4]Fiona Stanley Hospital, Perth, Western Australia, Australia, [5]Mater Misericordiae University Hospital, Dublin, Ireland, [6]Mater Misericordiae University Hospital, Dublin, Dublin, Ireland, [7]Ospedaliera Universitaria Città della Salute e della Scienza di Torino, Turin, Italy, [8]Centro Hospitalar Universitário de Santo António, Unidade Local de Saúde de Santo António, Porto, Portugal, [9]Rheumatology Department, Lariboisiere Hospital, Paris, Ile-de-France, France, [10]Buda Hospital of the Hospitaller Order of Saint John of God, Budapest, Hungary, [11]Department of Medicine, Division of Rheumatology, Medical College of Wisconsin, Wisconsin, [12]Rennes University

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Hospital, Rennes, France, [13]University Clinical Center in Gdańsk, Smoluchowskiego 17 Street, 80-952 Gdańsk, Poland., Gdańsk, Poland, [14]European Federation of Associations of Patients with Haemochromatosis,, Croissy-sur-Seine, France, [15]Haemochromatosis International, Barnstaple, United Kingdom, [16]University of Freiburg, Freiburg im Breisgau, Germany, [17]South Warwickshire University Foundation Trust and Warwick Medical School,, Warwick, United Kingdom, [18]Clongriffin Medical Centre, Dublin, Ireland, [19]c/o St George's University Hospitals NHS Trust, London, United Kingdom, [20]St George's University Hospitals NHS Foundation Trust, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: A EULAR task force developed classification criteria (CC) for Haemochromatosis Arthropathy (HA) using a cohort of people with the C282Y homozygous mutation and arthropathy ***with*** iron overload requiring phlebotomy (1). The CC include 8 items covering age of symptom onset, clinical and X-ray features at MCP, DIP and ankle joints, and surgery of hips or ankles. A score of ≥5/11 provides 93.3% specificity and 71.4% sensitivity for classifying HA.

Two additional cohorts were recruited, both ***without*** iron overload; 1. Arthropathy and any HFE gene mutation, and 2. Disease mimics (OA, CPPD). This study aimed to assess the role of iron overload and HFE gene mutations on joint disease expression by comparing the performance of the HA CC and its individual items across the 3 cohorts.

Methods: The HA cohorts included 373 patients from 12 centres across 10 countries. Group 1 (G1, n=154): C282Y homozygous with arthropathy and iron overload; Group 2 (G2, n=99): any HFE mutation with arthropathy and no iron overload; Group 3 (G3, n= 120): disease mimics (OA, CPPD).

We compared features of arthropathy in G1 with G2, and G2 with G3, also with G2 subgroups: C282Y homozygous and heterozygous, H63D homozygous and heterozygous, C282Y/H63D compound heterozygous, any C282Y and compound heterozygotes, any H63D and compound heterozygotes. The total CC score, prevalence of the 8 items and proportion of patients scoring ≥5/11 to fulfil CC, was compared between groups using the Chi-square/Fisher's exact tests or the independent sample T-test, as appropriate.

Results: Six of eight CC items were significantly more prevalent in G1 vs G2, and 5 of 8 items in G2 vs G3. The mean total score in G1 was 6.0, G2 4.3, $p< 0.001$ (G1 vs G2), and G3 2.7, $p< 0.001$ (G2 vs G3). The CC for HA were met in 71.4% of G1, 37.4% of G2 and 6.7% of G3 ($p< 0.001$ G1 vs G2 and G2 vs G3).

Genotype-stratified analysis of G2 revealed a consistent hierarchy in prevalence of 5 of 8 of the individual CC items, total CC score and fulfilment of the CC overall. The highest prevalence was seen in people with H63D homozygous or heterozygous mutations combined, followed by any H63D and compound heterozygotes, followed by either any C282Y and compound heterozygotes or C282Y homozygous or heterozygous mutations alone (Table 1 & 2).

Conclusion: The discriminatory features of joint disease in HA, as defined by the CC, are significantly more prevalent in patients ***with*** iron overload and the C282Y homozygous HFE mutation than in patients ***without*** iron overload and any HFE genotype, supporting the major role of iron in disease expression.

In patients without iron overload and with any HFE mutation, the discriminatory features of HA are significantly more prevalent than found in OA and CPPD disease mimics, supporting an iron-independent effect of HFE mutations on arthropathy. This appears to be most evident in patients with any H63D mutation, though subgroup numbers are low.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of EULAR HA Classification Criteria component items, total score and fulfilment of the criteria in HFE C282Y homozygous patients with iron overload (Group 1) and patients without iron overload, stratified by HFE Mutation Status (Group 2). p values refer to comparisons with Group 1, statistical significance p <0.05

	Group 1 (HA with iron overload)(n= 154)	Group 2 (HA without iron overload) (n= 99)					
Variable / score	N (%)	All patients N (%) (n= 99)	C282Y homozygous or heterozygous (n= 47)	H63D homozygous or heterozygous (n= 27)	C282Y/H63D compound heterozygous (n= 25)	Any C282Y and all compound heterozygous (n= 72)	Any H63D and all compound heterozygous (n= 52)
Joint symptom onset before 50 years of age / 2	86 (55.8)	46 (46.5) p= 0.15	22 (46.8) p= 0.28	11 (40.7) p= 0.15	13 (52) p= 0.72	35 (48.6) p= 0.31	24 (46.2) p= 0.23
Iron fist / 1	75 (48.7)	25 (25.3) p= <0.001	12 (25.5) p= 0.005	9 (33.3) p= 0.14	4 (16) p= 0.002	16 (22.2) p= <0.001	13 (25) p= 0.003
Absence of any DIP joint soft tissue swelling and bony swelling and deformity / 2	153 (99.4)	98 (99) p= 1.0	47 (100) p= 1.0	26 (96.3) p= 0.28	25 p= 1.0	72 (100) p= 1.0	51 (98.1) p= 0.44
Hip or Ankle surgery / Ankle only: 2 Hip only: 1 Ankle and Hip: 2	50 (32.5)	4 (4) p= <0.001	2 (4.2) p= <0.001	0 p= 0.002	2 (8) p= 0.04	4 (5.6) p= <0.001	2 (3.8) p= <0.001
MCP joint 2 or 3 or 4 or 5 tenderness, clinical examination / 1	70 (45.5)	29 (29.3) p= 0.01	13 (27.7) p= 0.03	10 (37) p= 0.42	6 (24) p= 0.04	19 (26.4) p= 0.006	16 (30.8) p= 0.06
Xray: any MCP joint - joint space narrowing grade 3 or surgery or subchondral cyst / 1	91 (59.1)	36 (36.4) p= <0.001	15 (31.9) p= 0.001	12 (44.4) p= 0.16	9 (36) p= 0.03	24 (33.3) p= <0.001	21 (40.4) p= 0.02
X-ray: Ankle joint - joint space narrowing grade 3 or subchondral cyst* / 1	41 (26.6)	9 (9.1) p= <0.001	3 (6.4) p= 0.003	5 (18.5) p= 0.37	1 (4) p= 0.01	4 (5.6) p= <0.001	6 (11.5) p= 0.03
X-ray: Hook osteophytes MCP joint 2 or 3 or Ankle joint* / MCP 2/3 only: 1 Ankle only: 2 MCP 2/3 and Ankle: 2	80 (51.9)	25 (25.3) p= <0.001	8 (17) p= <0.001	11 (40.7) p= 0.26	6 (24) p= 0.03	14 (19.4) p= <0.001	17 (32.8) p= 0.049
Total classification criteria score: Mean (SD)	6 (2.3)	4.3 (1.7) <0.001	4.1 (1.7) <0.001	4.7 (1.8) 0.002	4.2 (1.6) <0.001	4.1 (1.6) <0.001	4.5 (1.7) <0.001
Classification criteria met (Total score ≥5)	110 (71.4)	37 (37.4) p= <0.001	15 (31.9) p= <0.001	12 (44.4) p= 0.006	10 (40) p= 0.002	25 (34.7) p= <0.001	22 (42.3) p= <0.001

Table 2. Comparison of EULAR HA Classification Criteria Features in patients with HFE mutations with no iron overload (Group 2) and patients with disease mimics (OA, CPPD, Group 3). Group 2 stratified by HFE Mutation Status. p values refer to comparisons with Group 3, statistical significance p <0.05

	Group 3 (OA or CPPD) (n=120)	Group 2 (HA without iron overload) (n=99)					
Variable / score		All patients N (%) (n=99)	C282Y homozygous or heterozygous (n=47)	H63D homozygous or heterozygous (n=27)	C282Y/H63D compound heterozygous (n=25)	Any C282Y and all compound heterozygous (n=72)	Any H63D and all compound heterozygous (n=52)
Joint symptom onset before 50 years of age / 2	14 (11.6) **	46 (46.5) P= <0.001	22 (46.8) p= <0.001	11 (40.7) p= <0.001	13 (52) p= <0.001	35 (48.6) p= <0.001	24 (46.2) p= <0.001
Iron fist / 1	9 (7.5)	25 (25.3) p= <0.001	12 (25.5) p= 0.002	9 (33.3) p= <0.001	4 (16) p= 0.24	16 (22.2) p= 0.003	13 (25) p= 0.002
Absence of any DIP joint soft tissue swelling and bony swelling and deformity / 2	107 (89.2)	98 (99) p= 0.003	47 (100) p= 0.002	26 (96.3) p= 0.47	25 (100) p= 0.13	72 (100) p= 0.002	51 (98.1) p= 0.07
Hip or Ankle surgery / Ankle only: 2 Hip only: 1 Ankle and Hip: 2	7 (5.8)	4 (4) p= 0.76	2 (4.2) p= 0.58	0 p= 0.44	2 (8) p= 0.76	4 (5.6) p= 0.91	2 (3.8) p= 0.76
MCP joint 2 or 3 or 4 or 5 tenderness, clinical examination / 1	25 (20.8)	29 (29.3) p= 0.15	13 (27.7) p= 0.34	10 (37) p= 0.07	6 (24) p= 0.73	19 (26.4) p= 0.38	16 (30.8) p= 0.16
Xray: any MCP joint - joint space narrowing grade 3 or surgery or subchondral cyst / 1	22 (18.3)	36 (36.4) p= 0.003	15 (31.9) p= 0.06	12 (44.4) p= 0.004	9 (36) p= 0.05	24 (33.3) p= 0.02	21 (40.4) p= 0.002
X-ray: Ankle joint - joint space narrowing grade 3 or subchondral cyst* / 1	5 (4.2)	9 (9.1) p= 0.14	3 (6.4) p= 0.69	5 (18.5) p= 0.02	1 (4) p= 1.0	4 (5.6) p= 0.73	6 (11.5) p= 0.09
X-ray: Hook osteophytes MCP joint 2 or 3 or Ankle joint* / MCP 2/3 only: 1 Ankle only: 2 MCP 2/3 and Ankle: 2	10 (8.3)	25 (25.3) p= <0.001	8 (17) p= 0.12	11 (40.7) p= <0.001	6 (24) p= 0.02	14 (19.4) p= 0.04	17 (32.8) p= <0.001
Mean (SD) of the total score for the EULAR classification criteria	2.7 (1.3) **	4.3 (1.7) p= <0.001	4.1 (1.7) p= <0.001	4.7 (1.8) p= <0.001	4.2 (1.6) p= <0.001	4.1 (1.6) p= <0.001	4.5 (1.7) p= <0.001
Classification criteria met (Total score ≥5)	8 (6.7)	37 (37.4) p= <0.001	15 (31.9) p= <0.001	12 (44.4) p= <0.001	10 (40) p= <0.001	25 (34.7) p= <0.001	22 (42.3) p= <0.001

Overall, these findings increase our understanding of the interplay between HFE mutations and iron status in the pathogenesis of HA, where HFE mutations alone are associated with the phenotypic features of HA, becoming much accentuated with iron loading.

Reference:

1. Kiely et al EULAR Classification Criteria for Haemochromatosis Arthropathy. ARD 2025; POS0558

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: B. Farisogullari: None; **P. Machado**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **S. Finzel**: AbbVie/Abbott, 6, Alfasigma/Galapagos, 6, 12, meeting or travel grant, AstraZeneca, 2, Biotest, 6, 12, meeting or travel grant, Celltrion, 6, Chugai, 6, Eli Lilly, 12, meeting or travel grant, GlaxoSmithKlein(GSK), 2, 6, Johnson&Johnson, 2, 6, 12, meeting or travel grant, Novartis, 2, 6, 12, meeting or travel grant, NovoNordisk, 2, Sobi, 12, meeting or travel grant, UCB, 2, 6, 12, meeting or travel grant; **G. Carroll**: None; **G. mcCarthy**: PK Med and Avalo, 2; **J. Stack**: Janssen, 12, Support to attend meetings, UCB, 12, Support to attend meetings; **S. Parisi**: None; **G. Porto**: None; **r. pascal**: None; **G. Nagy**: None; **M. Weidl**: None; **A. Rosenthal**: None; **P. Guggenbuhl**: Amgen, 6, Eli Lilly, 5, kyowa Kirin Pharma, 5; **K. Banaszkiewicz**: None; **B. Butzeck**: None; **H. Don**: None; **S. Engelhardt**: None; **J. Shearman**: CSL Behring, 1; **D. Mitchell**: None; **J. Barker**: None; **V. Brueton**: None; **P. Coathup**: None; **J. Dowsett**: None; **M. Duncan**: None; **T. Dunleavy**: None; **I. Fish**: None; **A. Hoggarth**: None; **M. McKinnon**: None; **J. Minter**: None; **T. Osborne**: None; **M. Smith**: None; **C. Wright**: None; **P. Kiely**: Alfasigma, 6, Eli Lilly, 12, Sponsorship to attend educational meetings.

Abstract Number: 1137

Increased Risk of Cardiovascular Events and Mortality Related to Diffuse Idiopathic Skeletal Hyperostosis (DISH): A Systematic Review and Meta-Analysis

Pitchaporn Yingchoncharoen[1], Nattanicha Chaisrimaneepan[2], Miriam Paz[3], Chanokporn Puchongmart[1], Ben thiravetyan[1], Panat Yanpiset[1] and Jerapas Thongpiya[4], [1]Texas Tech Health Sciences Center, Lubbock, TX, [2]Department of Medicine, Texas Tech University Health Sciences Center, Lubbock, TX, [3]Texas Tech University Health Sciences Center, Lubbock, [4]Texas Tech University Health Sciences Center at Lubbock Program, Lubbock, TX

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Diffuse Idiopathic Skeletal Hyperostosis (DISH) is characterized by ossification and calcification of the entheses with prevalence increasing with age. It has been reported to be associated with obesity and type 2 diabetes mellitus (DM). The prevalence of hypertension and hyperlipidemia is also higher in patients with DISH. These factors are components of metabolic syndrome and the atherosclerotic cardiovascular disease (ASCVD) risk calculation score. Previously published studies on the association between DISH and the risk of cardiovascular events and mortality have yielded conflicting findings. Our study aimed to identify the potential association by pooling all available publications.

Methods: We comprehensively searched the databases of MEDLINE and EMBASE from inception to March 2025 to identify studies evaluating the association between DISH and the risk of cardiovascular events and mortality. We identified all observational studies that compared the incidence or risk of developing cardiovascular events in DISH patients compared to non-DISH patients. Pooled risk ratios (RRs) and 95% confidence intervals (CIs) were calculated using a random-effects model, DerSimonian and Laird. Publication bias was analyzed with the Egger test.

Results: A total of 426 articles were identified. Following the PRISMA guidelines for study selection, 12 studies fulfilled the inclusion criteria and were included in the meta-analysis. Stratified analyses were conducted by event types: cerebrovascular accident (CVA; 8 studies), myocardial infarction/ischemic heart disease (MI/IHD; 9 studies), congestive heart failure (CHF; 6 studies), and cardiovascular mortality (3 studies).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The pooled results of the present meta-analysis showed that DISH was associated with an increased risk of CVA (RR = 1.80, 95% CI: 1.59–2.05, $P < 0.001$; $I^2 = 0\%$) and cardiovascular mortality (RR = 1.59, 95% CI: 1.21–2.09, $P < 0.001$; $I^2 = 0\%$).

However, the associations between DISH and increased risk of MI/IHD (RR = 1.59, 95% CI: 0.92–2.74, $P = 0.09$; $I^2 = 80.86\%$) and CHF (RR = 1.07, 95% CI: 0.79–1.44, $P = 0.66$; $I^2 = 23.59\%$) were not statistically significant. Publication bias assessed using Egger's test showed no evidence of small-study effects ($P > 0.05$).

Conclusion: This analysis found that DISH is associated with a higher risk of cerebrovascular accident, but not with other cardiovascular events. Further research is needed to determine a causal relationship

Disclosure: P. Yingchoncharoen: None; **N. Chaisrimaneepan**: None; **M. Paz**: None; **C. Puchongmart**: None; **B. thiravetyan**: None; **P. Yanpiset**: None; **J. Thongpiya**: None.

Abstract Number: 1138

Efficacy of Pozdeutinurad (AR882) in Treatment Naïve and Suboptimally Treated Gouty Arthritis with Tophi

Robert Keenan[1], Puja Khanna[2], Zancong Shen[3], Sarah Morris[3], Pamela Mundell[4], Wen Wei[4], Elizabeth Polvent[5], Vijay Hingorani[6], Shunqi Yan[5] and Li-Tain Yeh[7], [1]Arthrosi Therapeutics, Raleigh, NC, [2]Division of Rheumatology, University of Michigan, Ann Arbor, MI, [3]Arthrosi therapeutics, San Diego, CA, [4]Arthrosi Therapeutics Inc, San Diego, CA, [5]Arthrosi Therapeutics, Inc., San Diego, CA, [6]Vanguard Healthsciences, Inc., San Diego, CA, [7]Arthrosi Therapeutics, Inc., Irvine, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pozdeutinurad (AR882, POZD) is a novel, selective URAT1 inhibitor currently in phase 3 clinical stage development for the treatment of gout and tophaceous gout. To date, only intravenous (IV) therapies such as pegloticase is indicated in urate-lowering (ULT) refractory patients and has demonstrated tophi dissolution by caliper measurement and Dual Energy Computer Tomography (DECT). However, IV therapy is not available or appropriate for the majority of patients given infusion costs, drug availability and potential toxicities from necessary use with concomitant immunosuppressives. POZD is an oral agent being evaluated for both urate control and dissolution of subcutaneous tophi.

This analysis explores the distinction between POZD 75 mg monotherapy or in combination with allopurinol in tophaceous gout patients who are either treatment naïve or suboptimally controlled.

Methods: The phase 2 trial recruited 42 patients with at least one subcutaneous tophus. Patients were eligible if they were either inadequately controlled on ULT with serum urate (sUA) > 6.0 mg/dL or were ULT naïve with sUA ≥ 7.0 mg/dL. After ULT washout (if applicable), patients were randomized to receive POZD 75 mg, POZD 50 mg + allopurinol, or allopurinol up to 300 mg. At 6 months all patients were able to opt into two subsequent 6-month extensions with treatment modifications. sUA, tophi measurements with calipers or urate crystal measurement using DECT were collected up to 18 months. Results for sUA response rates, complete resolution in target tophus and reduction in urate crystal volumes were analyzed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Complete resolution of at least 1 target tophus and reduction in crystal urate burden in tophaceous gout patients refractory or naïve to treatment

Endpoint	POZD 75 mg				POZD 75 mg + allopurinol			
	6-mo treatment		12-mo treatment		6-mo treatment		12-mo treatment	
	Refractory	Naïve	Refractory	Naïve	Refractory	Naïve	Refractory	Naïve
% with complete resolution of ≥1 target tophi	25% (2/8)	33% (2/6)	43% (3/7)	33% (1/3)	33% (3/9)	0 (0/2)	57% (4/7)	0 (0/2)
Mean reduction in crystal urate volume (cm^3)	-11.1	-0.3	-17.4	-0.92	-13.2	-0.31	-20.1	-0.03

Mo: month; POZD: pozdeutinurad

Results: Patients refractory to their pre-study ULT had a higher baseline sUA (9.5 to 9.8 mg/dL) than treatment naïve patients (7.6 to 8.5 mg/dL). Both populations had clinically significant and sustained sUA responses following treatment. In the 75 mg group, refractory patients had a 49% mean decrease in sUA levels, while the naïve patients achieved a 54% decrease. In the 75 mg + allopurinol group, the refractory patients had a 61% mean decrease in sUA levels, while the naïve patients achieved a 74% decrease. At 12 months, refractory patients demonstrated complete resolution of at least 1 target tophus in 43% and 57% of patients in the 75 mg group, and in 75 mg + allopurinol group, respectively. Although all ULT naïve patients had at least a partial response, only the 75 mg group had at least 1 target tophus fully resolved at 33% (**Table 1**). The refractory patients demonstrated greater reduction in their urate crystal burden compared to ULT naïve patients following 12 months treatments (-17.4 vs -0.92 cm3 for 75 mg; -20.1 vs -0.03 cm3 for 75 mg + allopurinol treatment) (**Table 1**).

Conclusion: Pozdeutinurad 75 mg monotherapy or in combination with allopurinol in tophaceous patients refractory and naïve to ULT were effective in sUA lowering, demonstrating high rates of complete resolution of target tophus and reduction in urate crystal burden. Pozdeutinurad alone or combination may provide an effective treatment option for patients with chronic tophi and inadequate response to their current treatment regimens.

Disclosure: R. Keenan: Arthrosi Therapeutics, 3; **P. Khanna**: Arthrosi, 5, Olatec, 5, Selecta Biosciences, 5, Sobi, 2; **Z. Shen**: Arthrosi Therapeutics, 3; **S. Morris**: Arthrosi Therapeutics, 3; **P. Mundell**: Arthrosi Therapeutics, 3; **W. Wei**: Arthrosi Therapeutics, 3; **E. Polvent**: Arthrosi Therapeutics, 3; **V. Hingorani**: Arthrosi Therapeutics, 2; **S. Yan**: Arthrosi Therapeutics, 3; **L. Yeh**: Arthrosi Therapeutics, 3.

Abstract Number: 1139

Synovial Counts, Cultures, and Crystals: An Analysis of 9,000 Aspirations

Sabahat Usmani[1], Gunjan Rana[2], Shivum Patel[1], Patrick Kennedy[1] and Michael Putman[3], [1]Medical College of Wisconsin, Milwaukee, [2]Saint Vincent Hospital, Worcester, MA, [3]The Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Synovial fluid analysis is an essential diagnostic tool for evaluating crystalline and infectious arthritis. Traditionally, a leukocyte count threshold of >50,000 cells/μL has been used to help identify septic arthritis while awaiting culture results. However, no large or representative studies have systematically assessed the diagnostic performance of this leukocyte cutoff or characterized leukocyte counts across different causes of inflammatory synovial fluid.

Methods: A de-identified database from Froedtert Hospital and the Medical College of Wisconsin (1.9 million patients) was queried on March 17, 2023. All patients who underwent joint aspiration with synovial fluid analysis prior to March 1, 2023 were included. Structured and unstructured text were used to identify synovial fluid leukocyte count, crystal analysis, gram stain, and culture results. Demographic data were extracted; ICD-9-CM / ICD-10-CM codes were used to identify prevalent autoimmune diseases or crystalline diseases (1 year lookback) and prosthetic joint infections (PJI) (30 days before and after synovial fluid analysis).

Results: A total of 9,054 synovial fluid analyses from 6,690 patients were identified. The average age at first aspiration was 62.3 years (standard deviation (SD) 16.1 years) and most patients were male (53.4%) and white (74.6%) (Table 1). After categorizing synovial fluid aspiration results in a hierarchical fashion, the highest leukocyte counts occurred among fluid positive for staphylococcus or streptococcus infection (65,568, SD 81892) followed by other positive cultures (41,035, SD 55,259), MSU (20,966, SD 34,186), CPPD (13,202, SD 21,132), rheumatic diseases (12,827, SD 32,234), and negative for crystals or infection (9,822, SD 31,884) (Figure 1). Joints that had an over-representation of a crystal result included the ankle (50.6% MSU), knee (48.2% negative for crystals), shoulder (63.5% CPPD), and toe/foot (69.6% MSU) (Figure 2). A conventional leukocyte count cutoff of 50,000 had a low sensitivity (0.28) and a high specificity (0.95); a higher cutoff of 100,000 had an even lower sensitivity (0.10) and a higher specificity (0.99).

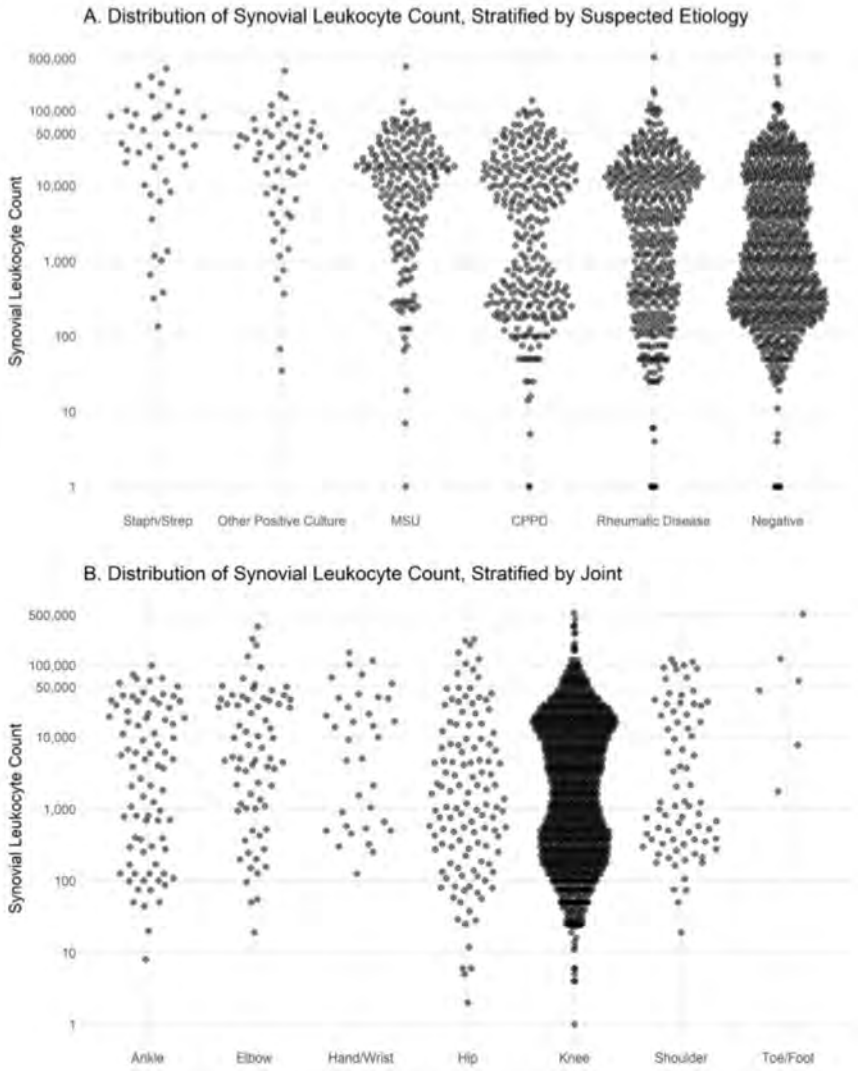
Table 1: Demographic and Clinical Characteristics of Included Patients, n = 6,687

Age at Aspiration, mean (SD)	62.3 (16.1)
Sex	-
Female	3,116 (46.6%)
Male	3,564 (53.4%)
Race/Ethnicity	-
White or Caucasian	4,983 (74.6%)
Black or African American	1,311 (19.6%)
Hispanic or Latino	200 (3.0%)
Other	116 (1.7%)
Asian	70 (1.0%)
History of Crystal Disease*	-
Gout	959 (14.3%)
CPPD	162 (2.4%)
History of Autoimmune Disease*	-
Rheumatoid Arthritis	460 (6.9%)
Inflammatory Bowel Disease	133 (2.0%)
Systemic Lupus Erythematosus	104 (1.6%)
Psoriatic Arthritis	39 (0.6%)
Systemic Sclerosis	32 (0.5%)
Sjogrens Syndrome	16 (0.2%)
Axial Spondyloarthritis	15 (0.2%)
ANCA Associated Vasculitis	11 (0.2%)
Prosthetic Infection?**	-
No	6,190 (92.5%)
Yes	500 (7.5%)

*Identified from ICD-9-CM and ICD-10-CM codes in the year prior to the index date
**Identified using any code for prosthetic infection within 30 days of the aspiration date

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Synovial Fluid Leukocyte Count, n = 6,687



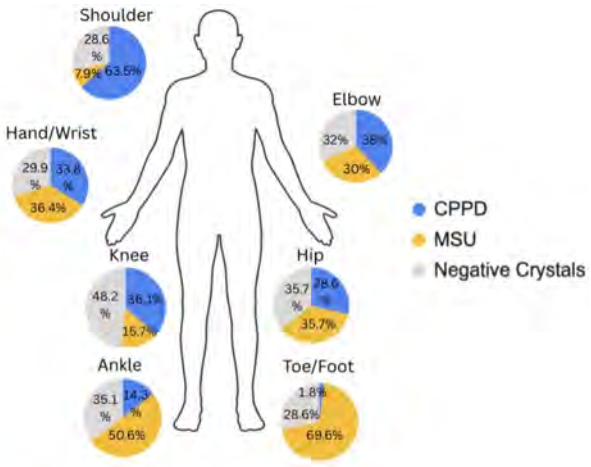


Figure 2: Distribution of Crystal Type by Synovial Fluid Joint

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Highly elevated synovial leukocyte cutoffs (>100,000) had a high specificity for septic arthritis, but even conventional cutoffs (>50,000) had a low sensitivity for "ruling out" infectious causes for inflammatory joint fluid.

Disclosure: S. Usmani: None; **G. Rana**: None; **S. Patel**: None; **P. Kennedy**: None; **M. Putman**: AbbVie/Abbott, 5, Amgen, 5, AstraZeneca, 2, 5, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5.

Abstract Number: 1140

PGG Suppresses MSU Crystal–Triggered Inflammation and Arachidonic Acid Production in PBMCs

Sadiq Umar[1], Poorna Chandra Rao Yalagala[2], Sugasini Dhavamani[2] and Sriram Ravindran[2], [1]University of Illinois at Chicago, Chicago, IL, [2]University of Illinois, Chicago, IL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is the most prevalent inflammatory arthritis globally, with rising incidence in both developed and developing regions. It is driven by monosodium urate (MSU) crystal deposition in joints and bursae of hyperuricemic individuals, triggering intense pain and inflammation. Macrophage uptake of MSU crystals activates TLR2/4 signaling, promoting NLRP3 inflammasome formation and NF-κB–mediated pro-inflammatory cytokine production. Penta-O-galloyl-β-D-glucose (PGG), a naturally occurring polyphenol, exhibits anti-inflammatory and anti-proliferative properties. This study investigated PGG's effects on MSU-induced inflammatory responses and arachidonic acid (AA) metabolism in human PBMCs.

Methods: Human PBMCs were pretreated overnight with 5 μM PGG or 1 μM colchicine, followed by stimulation with 100 μg/mL MSU for either 30 minutes or 24 hours. Cytokine levels (IL-1β, IL-18, TNF-α, IL-6, IL-8, TGFβ) were measured by qPCR and ELISA. Phosphorylated MAPKs (p38, ERK, JNK) were assessed by immunoblotting. Phagocytosis was evaluated using the Vybrant™ Phagocytosis Assay. The fatty acid composition of PBMCs lipids was analyzed by GC/ MS after conversion to methyl esters. The analysis was carried out using a Shimadzu QP2010SE GC/MS equipped with a Supelco Omegawax column (30 m × 0.25 mm × 0.25 μ).

Results: PGG significantly reduced MSU-induced expression of IL-1β, IL-18, TNF-α, IL-6, and IL-8 and increased TGFβ ($p < 0.01$; n=4), with similar trends observed at the mRNA level. PGG also inhibited phagocytosis of MSU crystals, suggesting reduced upstream TLR signaling. Immunoblotting confirmed that PGG blocked MSU-induced phosphorylation of p38, JNK, and ERK. Furthermore, PGG and colchicine treatment markedly reduced elevated arachidonic acid levels in MSU-treated macrophages.

Conclusion: PGG mitigates MSU-induced inflammation in PBMCs by suppressing cytokine production, phagocytosis, MAPK activation, and arachidonic acid accumulation. Given AA's pro-inflammatory role as a precursor to eicosanoids. These findings suggest that PGG may represent a promising therapeutic candidate for targeting crystal-induced inflammation in gout.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Umar: None; **P. Chandra Rao Yalagala**: None; **S. Dhavamani**: None; **S. Ravindran**: None.

Abstract Number: 1141

Modulation of Inflammatory Responses by Dental Pulp Stem Cell Extracellular Vesicles in Monosodium Urate-Stimulated Macrophages

Sadiq Umar[1], Kasey Leung[2] and Sriram Ravindran[2], [1]University of Illinois at Chicago, Chicago, IL, [2]University of Illinois, Chicago, IL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is the most prevalent form of inflammatory arthritis, with rising global incidence. It results from the deposition of monosodium urate (MSU) crystals in joints, leading to severe inflammation and pain in individuals with hyperuricemia. Dental pulp stem cells (DPSCs), a type of mesenchymal stem cell (MSC), release extracellular vesicles (EVs) with intrinsic anti-inflammatory properties, which are further enhanced following inflammatory stimulation. This study aimed to evaluate the anti-inflammatory effects of EVs from both untreated (naïve) and MSU-preconditioned DPSCs on MSU-activated macrophages and to identify EV-associated microRNAs (miRNAs) mediating these effects.

Methods: DPSCs were obtained from Lonza. EVs were isolated from DPSCs cultured under normal conditions or after preconditioning with MSU, and characterized by immunoblotting and nanoparticle tracking analysis (NTA). The anti-inflammatory activity of EVs was assessed in vitro using human peripheral blood mononuclear cells (PBMCs) stimulated with 100 μg/mL MSU for 24 hours, with or without treatment with naïve or MSU-preconditioned DPSC EVs. Inflammatory gene and protein expression were analyzed by qRT-PCR and ELISA. Phagocytic activity was measured using the Vybrant™ Phagocytosis Assay Kit. miRNA profiles of naïve and preconditioned EVs were determined by sequencing and bioinformatics analysis. Statistical significance was assessed using one-way ANOVA followed by Tukey's post hoc test ($P < 0.05$).

Results: EVs from both naïve and MSU-preconditioned DPSCs displayed similar physical and molecular characteristics. Both EV types significantly reduced inflammatory responses in MSU-stimulated PBMCs. Notably, MSU-preconditioned DPSC EVs showed enhanced suppression of pro-inflammatory markers (IL-1β, TNF-α, iNOS) and increased expression of anti-inflammatory markers (IL-10, ARG1, TGF-β). Phagocytosis was also significantly reduced by preconditioned EVs. miRNA sequencing revealed upregulation of anti-inflammatory miRNAs in EVs from MSU-preconditioned DPSCs compared to naïve controls.

Conclusion: MSU-preconditioned DPSC EVs exhibit enhanced anti-inflammatory activity in MSU-activated PBMCs, including suppression of phagocytosis. These effects are likely mediated by specific EV-resident miRNAs, offering a promising platform for miRNA-based EV engineering in the treatment of inflammatory diseases like gout.

Disclosure: S. Umar: None; **K. Leung**: None; **S. Ravindran**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1142

Tibial Bone Microstructure and Histomorphometry in Individuals with CPPD

Sara Tedeschi[1], Priyanka Kushwaha[2], Muneet Gill[2], Julia F. Charles[3] and Ellen M. Gravallese[4], [1]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [2]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Boston, MA, [3]Department of Orthopedic Surgery & Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: CPPD has been associated with osteopenia of the metacarpal heads and a 2x increased risk for fracture of the wrist, hip, humerus or pelvis. Inorganic pyrophosphate is a known strong inhibitor of mineralization and a

Table 1. Osteoclast surface and number per bone surface from tibial plateau specimens with CPPD and controls matched on age, sex, and race

Pair	Sample ID	Osteoclast surface/bone surface (Oc.S/BS)	Osteoclast number/bone surface (Oc.N/BS)
A	CPPD-A	0.48	0.33
	Control-A	0.26	0.14
B	CPPD-B	1.08	0.61
	Control-B	0.02	0.01

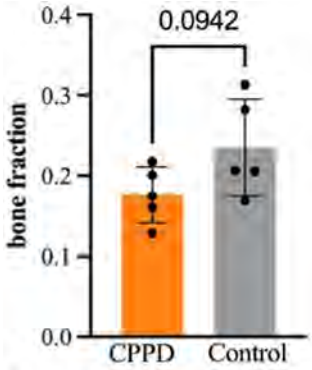


Figure 1. Tibial plateau trabecular bone volume/tissue volume (BV/TV) in 5 CPPD-control pairs matched on age, sex, and race

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

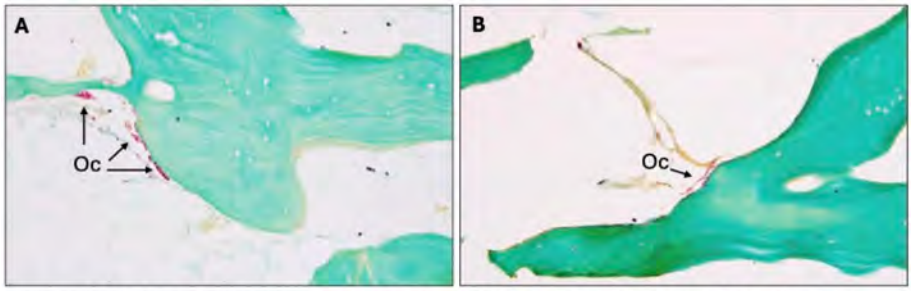


Figure 2. TRAP staining identified osteoclasts (Oc) in trabecular bone from the tibial plateau. Representative slides (20X) showing greater Oc abundance in a sample from an individual with CPPD (Panel A) than a control without CPPD matched on age, sex, and race (Panel B).

critical component of calcium pyrophosphate crystals. We conducted a pilot study testing for differences in tibial bone microstructure and histomorphometry in CPPD vs. controls.

Methods: Among patients undergoing total knee replacement surgery at a single academic medical center, we reviewed pre-operative radiographs for the presence of chondrocalcinosis in the knee, which defines the CPPD cohort. For each CPPD patient we identified one control matched on age (+/-5 years), sex, and race; controls were defined by absence of chondrocalcinosis on any joint radiograph. The tibial compartment analyzed (lateral or medial) was the same for each pair and was defined by the location of chondrocalcinosis in the CPPD patient and absence of Kellgren-Lawrence grade 4 in that compartment in both CPPD patients and controls. Microcomputed tomography (microCT) scanning was performed on formalin-fixed samples using a Scanco Medical mCT35 scanner with an isotropic voxel size of 20mm. A semi-automated contouring approach was used to exclude cortical bone and bone volume/tissue volume was calculated using software supplied by the manufacturer and a global threshold that set the bone/marrow cut-off at 398mg HA/cm^3. Following decalcification and paraffin-embedding, trabeculae in the subchondral region were traced using Osteomeasure to determine bone surface area. TRAP staining identified osteoclasts (Oc) and Safranin O staining highlighted articular cartilage. Mean Oc surface/bone surface (Oc.S/BS) and Oc number/BS (Oc.N/BS) were calculated from 3 segments per sample.

Results: We obtained samples from 5 CPPD-control pairs (4 lateral compartment pairs, 1 medial compartment pair). Mean age was 69.6 (SD 9.5) years, 2 pairs were female, and all were White. Tibial plateau BV/TV was lower in samples from individuals with CPPD than controls (p=0.09) (**Figure 1**). Histomorphometry was performed for 2 pairs; analysis of the 3 remaining pairs is ongoing. Oc.S/BS and Oc.N/BS were higher in tibial plateau subchondral trabecular bone from individuals with CPPD than controls (**Table 1, Figure 2**).

Conclusion: Tibial plateau trabecular bone had lower BV/TV and more abundant osteoclasts in knee compartments with chondrocalcinosis among patients undergoing knee replacement surgery. These preliminary findings are directionally consistent with prior cohort studies that reported a greater risk of osteopenia and fractures in CPPD, and suggest a link between localized inorganic pyrophosphate and compromised bone microstructure.

Disclosure: S. Tedeschi: Alexion, 5, Amgen, 2, Avalo Therapeutics, 2, Fresenius Kabi, 2, Kyowa Kirin, 2, Merck/MSD, 2, Novartis, 2; **P. Kushwaha**: None; **M. Gill**: None; **J. Charles**: Alexion, 2, 5, Kyowa Kirin, 2, Merck Manuals, 12, Authorship, UpToDate, 12, Authorship; **E. Gravallese**: Beam Therapeutics, 11, CRISPR Therapeutics, 11, Editas Medicine, 11, Elsevier, 9, Ginkgo Bioworks, 11, Intellia Therapeutics, 11, New England Journal of Medicine, 1, UpToDate, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1143

Gout and Renal Failure-Related Mortality Trends in USA from 1999-2020: Analysis of CDC Wonder Database

Shiamak Cooper[1], Sanjana Thimmannagari[2], Ranjini Vengilote[2] and Asim Khanfar[2], [1]Rochester General Hospital, Irondequoit, NY, [2]Rochester General Hospital, Rochester, NY

SESSION INFORMATION

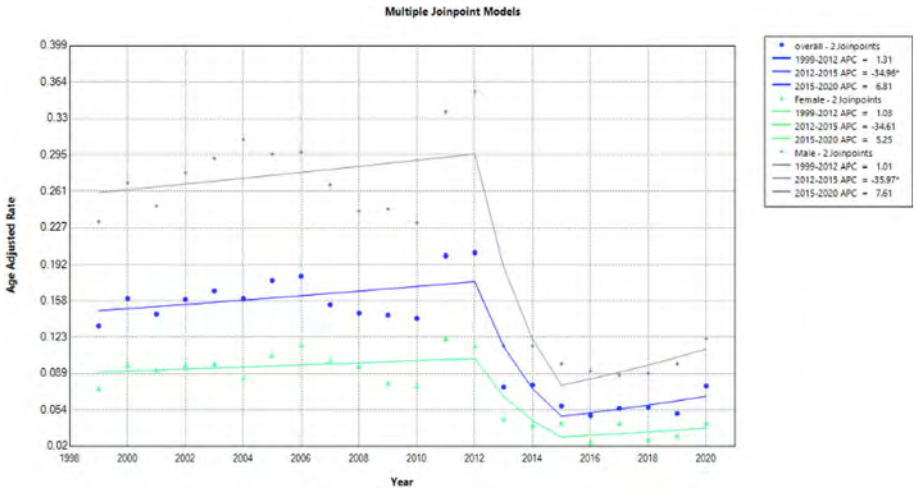
Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

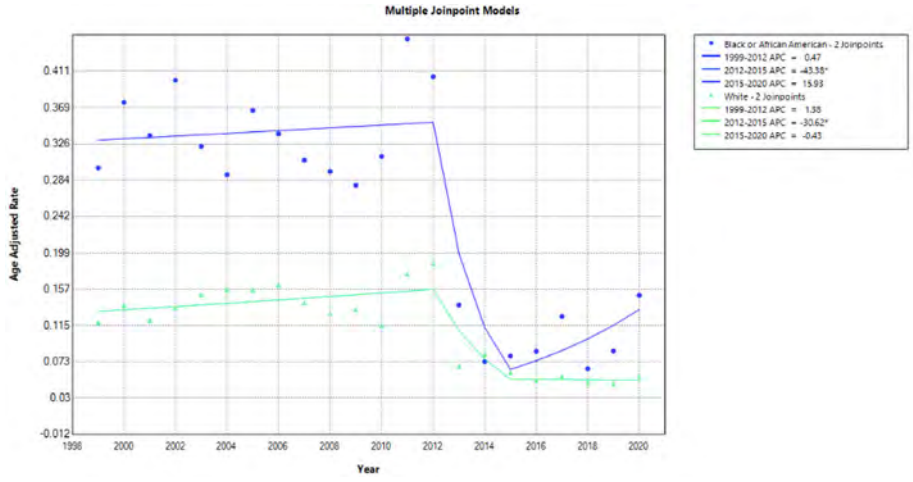
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is the most common form of inflammatory arthropathy, with a prevalence ranging from 0.1% to approximately 10% worldwide. Despite a well-established association between gout and renal disease, the real-world

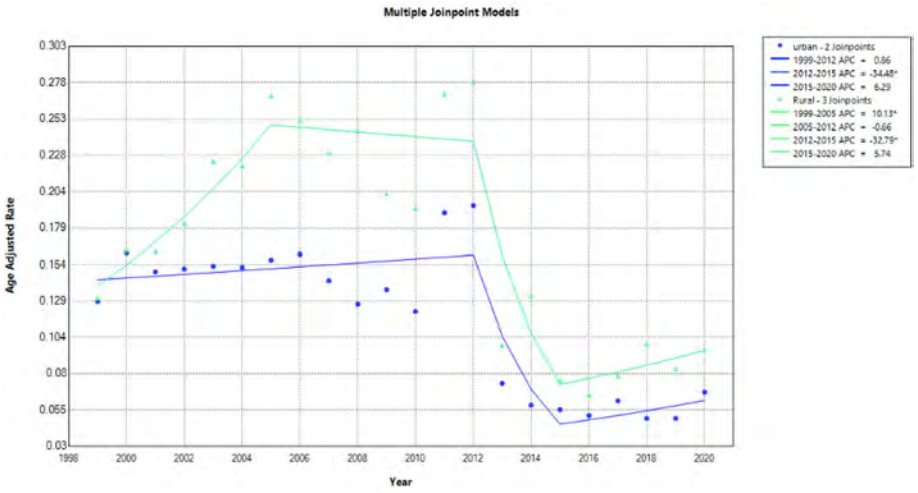


Annual Percentage Change in Gout and Renal Failure-Related Mortality by Year and Gender



Annual Percentage Change in Gout and Renal Failure-Related Mortality by Year and Race

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Annual Percentage Change in Gout and Renal Failure-Related Mortality by Year and Urban-Rural

data on the mortality rate due to renal disease or failure in patients with gout is not well established. Hence, we aim to assess the longitudinal trends in mortality rates attributed to renal disease in patients with gout. In addition, we aim to analyse for disparities in regard to race, sex, and geographical location in the United States.

Methods: Age-adjusted mortality rates (AAMR) per 100,000 individuals were obtained from the Centers of Disease Control and Prevention WONDER database from the years of 1999-2020. Joinpoint regression was applied to calculate the annual percentage change (APC) to evaluate significant differences in the change of AAMR over time.

Results: A total of 9263 deaths due to renal failure occurred in patients with Gout from 1999 to 2020. The AAMR from 1999 to 2012 insignificantly increased (APC 1.31) and sharply declined from 2012 to 2020 (APC -34.96). The same trend was reflected when stratified for females and males. The AAMR in urban areas had a trivial decline from 1999 to 2012 (APC 0.86) whereas significantly declined from 2012 to 2015 (APC -34.48). In rural areas, the AAMR initially significantly increased from 1999 to 2005 (APC 10.13), then decreased from 2005 to 2012 (APC -0.66) and subsequently significantly reduced from 2012 to 2015 (APC -32.79). The absolute AAMR for African Americans as compared to Whites were significantly different from 1999 to 2012. From 2012 to 2015, both subgroups had a statistically significant decline in AAMR, African Americans (APC -43.38 [-54.92, -21.89]) and Whites (APC -30.62 [-38.73, -3.42]). From 2015-2020, the AAMR remained fairly stable and similar in absolute numbers for both subgroups.

Conclusion: From 1999 to 2012, renal failure-related mortality in gout patients initially increased but had a significant drop from 2012 to 2015. Mortality rates reflected similarly in both sexes, females and males. Rural areas had an initial increase in mortality as compared to urban areas from 1999 to 2005. Blacks had a higher absolute mortality as compared to Whites until 2012 after which there was a sharp decline to similar rates from 2012 to 2015. These potential disparities warrant further research into quality of care delivered and phenotype of disease based on race and rural status. In addition, these findings may point towards improvement and standardization of care amongst different races and geographical areas after the introduction of the American College of Rheumatology (ACR) 2012 Gout guidelines.

Disclosure: S. Cooper: None; **S. Thimmannagari**: None; **R. Vengilote**: None; **A. Khanfar**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1144

A Quantitative Study of Renal Medulla Echogenicity in 250 Vietnames Gout Patients Shows Correlation with Poor Renal Function

Thomas Bardin[1], Quang Nguyen[2], anouk Walter-Petrich[3], Khoi Minh Tran[2], Duong Ba Pham[2], Quang Huy Nguyen[4], Chuc Van Tran[2], Day Phuoc Huynh[2], Minh Do[5], Emmanuel Letavernier[6], richette pascal[7], Matthieu Resche-Rigon[3] and Jean-Michel Correas[8], [1]Lariboisiere Hospital, Department of Rheumatology, Paris, France, [2]Vien Gut Medical centre, Ho Chi Minh City, Vietnam, [3]UMR U1342 ECSTRA team INERM, Université Paris Cité, Paris, France, [4]Vien Gut Medicfal Centre, Ho Chi Minh City, [5]University of Medicine and Pharmacy at Ho Chi Min City, Ho Chi Minh City, Vietnam, [6]Sorbonne Université and INSERM, UMR S 1155, Hôpital Tenon, Paris, France, [7]Rheumatology Department, Lariboisiere Hospital, Paris, Ile-de-France, France, [8]Department of Radiology, NeckerUniversity Hospital, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: We previously described the frequent occurrence of an hyperechogenic pattern of the renal medulla following crystal deposition in untreated Vietnamese patients with severe tophaceous gout(1), without quantifying the medulla brightness. The aim of the present study was to quantify medulla brightness and investigate correlations with gout characteristics and renal function.

Methods: This prospective monocentric study analyzed baseline data of the first 250 patients enrolled in our ongoing prospective cohort at Vien Gut (a decicated medical center for diagnosis and treatment of gout in Vietnam), that aims at describing the effect of urate-lowering drugs (ULDs) on medulla echogenicity and renal function. Inclusion criteria were: i) gout according to the ACR/EULAR criteria, ii) residency in Ho Chi Minh City, Vietnam, iii) no use of ULDs at the time of enrollment and iv) signed informed consent. All patients underwent renal ultrasonography and renal medulla echogenicity assessment by two methods: 1) a semiquantitative scale (grade 0: no medullary hyperechogenic spot; 1: few spots in 1 or 2 pyramids; 2: hyper echoic pattern involving 40-60% of most pyramids; 3: hyper echoic pattern of > 60% of pyramids), and 2) image

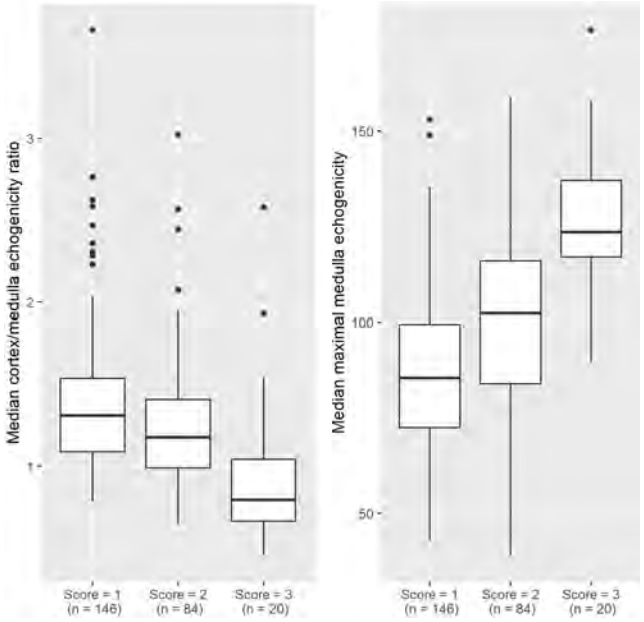


Fig 1: Boxplot of image J quantitative values according to Semi-quantitative score

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patients 'features in the whole sample and according to medulla echogenicity grades. Values are reported as No. (%) for categorical data and median [IQR] for quantitative data.BMI: Body Mass Index; CHD: Coronary Heart Disease; y: years; N°: number; SU: serum urate; UA: uric acid; FEUA: fractional excretion of uric acid; pts: patients

Features	All pts (n=250)	Grade 1 pts (n=146)	Grade 2 pts (n=84)	Grade 3 pts (n=20)	p-value univar.	p -value multivar.
Age (y)	51 [42;58.8]	48 [40.2;57.8]	52.5 [42;60]	53 [48.2;60.5]	0.055	
BMI (Kg/m2)	24.2 [22.3;26.7]	24.4 [22.6;27]	24.1 [22.2;26.6]	24.3 [21.8;26.8]	0.40	
Hypertension	53.2 %	47.3 %	57.1 %	80 %	0.011	
Type 2 Diabetes	15.2 %	14.4 %	15.5 %	20 %	0.60	
C H D	3.6 %	2.1 %	4.8 %	10 %	0.078	
Urolithiasis history	9.6 %	7.5 %	14.3 %	5 %	0.33	
Gout duration (y)	4 [3;6]	3 [1;4.8]	4 [3;6]	5 [4;8]	0.023	
N° of Clinical Tophi	5 [2;12.8]	3 [0.2;7]	11 [5;18.2]	17.5 [6;24.5]	<0.0001	<0.0001
MTP1 tophus surface	224.5 [132;460.2]	178.5 [100.5;288]	409.5 [192;633.8]	429 [180;663.8]	<0. 0001	0. 0002
SU level (micromol/l)	529 [435;599)	516.5 [411.5;588.5]	545 [470;599.5]	584 [527;607.2]	0.030	
Creatinine	85.1 [74.4;100.7]	81.2 [73.2;94.1]	88.1 [75.7;109.3]	108.8 [90.3;163.2]	<0.0001	
eGFR	96.7 [76.2;109]	101.1 [84.4;112]	95.9 [67.7;106.3]	67.9 [41.9;88.3]	<0.0001	<0.0001
Cortisol (µg/l) (normal range: 5-25)	5.5 [1;9.2]	7 [1.3;9.8]	3.4 [0.7;7.7]	1 [0.4;7]	0.001	0.004
Urine UA/ Creatinine	0.2 [0.2;0.3]	0.3 [0.2;0.3]	0.2 [0.2;0.3]	0.2 [0.2;0.3]	0.033	
Urine pH	5 [5;6]	5.5 [5;6]	5 [5;6]	5 [5;6]	0.23	
FEUA (%)	4 [3;6]	4 [3;6]	4 [3;5]	4.5 [3;5.2]	0.63	
Kidney Cysts	21.2 %	17.8 %	26.2 %	25 %	0.14	
Ultrasound features						

BMI: Body Mass Index; CHD: Coronary Heart Disease; y: years; N°: number; SU: serum urate; UA: uric acid; FEUA: fractional excretion of uric acid; pts: patients

analysis using image J software to quantify the cortex/medulla echogenicity ratio of the 2 best viewed pyramids. Clinical data were prospectively collected. Univariate proportional odds logistic regression models or linear regression models were used to compare the two methods of medulla rating and to look for correlations with patients 'features. Multivariable analysis included all statistically significant features, with model selection on the Akaike criterion (AIC).

Results: Median age and gout duration of patients (249 men) were 51 and 4 years respectively, 211 had clinical tophi, median eGFR and serum urate were 96.7 mmol/l and 529 mmol/l respectively. Medulla echogenicity was similar in both kidneys in all patients but 2, who differed by one grade; maximal grades were 0 in no patient, 1 in 146, 2 in 84, and 3 in 20 (table 1). Grades correlated negatively with corticex/medulla echogenicity ratios (p=0.0002) and positively with median maximum medulla echogenicity (p< 0.0001) (figure 1). By univariate analysis, medulla echogenicity grades correlated positively with medians of duration of gout, number of tophi, serum urate levels, and creatininemia, hypertension, MTP1 ultrasound features (double contours (graded 0 to 3) and tophus surfaces), and negatively with blood cortisol levels and eGFR; by multivariate analysis, correlations remained significant with numbers of clinical tophi, eGFR, cortisol levels, and MTP1 tophus surfaces (table 1). Median cortical/medullary echogenicity ratio correlated negatively with creatininemia.

Conclusion: The two ways of quantifying medulla echogenicity that we used provided consistent results and showed clinically meaningful correlations with patients 'features , especially renal function. Intersestingly, lower levels of cortisol were also associated, in line with the suspected effect of chronic exogenous steroid intake on tophi.

Reference

1. *Kidney Int*. 2021;*99*: 218–226.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Bardin: None; **Q. Nguyen**: None; **a. Walter-Petrich**: None; **K. Tran**: None; **D. Pham**: None; **Q. Nguyen**: None; **C. Tran**: None; **D. Huynh**: None; **M. Do**: None; **E. Letavernier**: None; **r. pascal**: None; **M. Resche-Rigon**: None; **J. Correas**: None.

Abstract Number: 1145

Numerically Reduced but MSU Crystal-Activated NK Cells Promote Osteoclastogenesis in Gout

Ki-Jeong Park[1], Young-Nan Cho[2], Hye-Mi Jin[2], Hye-Min Jeong[2], Sung-Eun Choi[3], Ji-Hyoun Kang[1], Dong-Jin Park[1], Tae-jong Kim[4], Shin-Seok Lee[5] and **Yong-Wook Park**[6], [1]Chonnam National University Hospital, Gwangju, Republic of Korea, [2]Chonnam National University Medical School, Gwangju, Republic of Korea, [3]Chonnam National University Medical School & Hospital, Gwangju, Republic of Korea, [4]Department of Rheumatology, Chonnam National University Medical School and Hospital, Gwang-Ju, South Korea, [5]Chonnam National University Medical School and Hospital, Gwangju, Republic of Korea, [6]Department of Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, South Korea

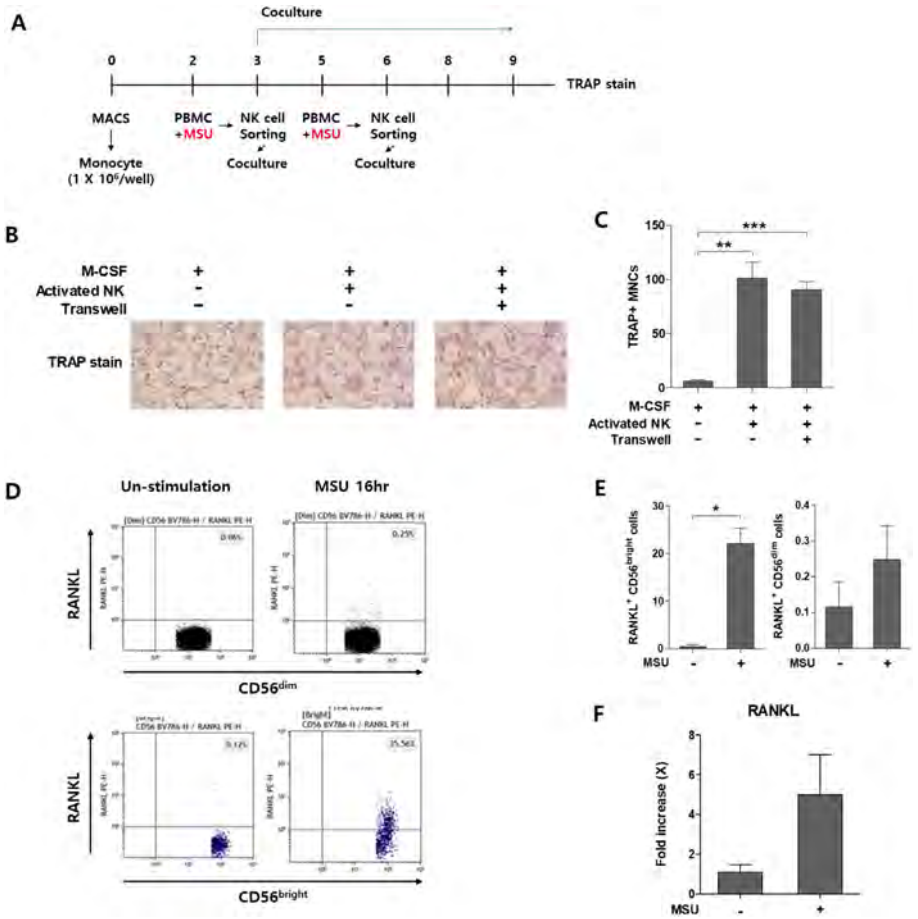
SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM



MSU-activated NK cells can induce osteoclastogenesis and express RANKL (A) Scheme of the experiment (B-C) TRAP stain of MSU-Activated NK cells (D-E) Representative gating and Frequency of RANKL in CD56dim and CD56bright NK cells with or without MSU crystal using flow cytometry (F) RANKL expression of NK cells with or without MSU crystal in RT-PCR

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Gout is an inflammatory arthritis characterized by acute attacks, tophi formation, and bone destruction triggered by inflammatory responses to monosodium urate (MSU) crystals. Natural killer (NK) cells are key effectors of the innate immune system that recognize damage-associated molecular patterns (DAMPs) to initiate and amplify inflammatory responses. While MSU crystals deposited in the synovium may act as DAMPs and potentially activate NK cells, the role of these cells in gout pathophysiology remains unclear.

Methods: Peripheral blood and synovial fluid samples were collected from patients with gout and healthy controls (HCs). Flow cytometry was performed to analyze NK cells for their activation markers (CD69, PD-1, TIM-3), apoptosis (Annexin V), and cytokine/chemokine expression (IFN-γ, TNF-α, CCR2, CCR6, CXCR3, and CXCR4). NK cells were stimulated with MSU crystals and sorted by FACS sorter, while monocytes were isolated from PBMC using MACS. To evaluate osteoclastogenesis, MSU-stimulated NK cells and monocytes were cocultured in the presence of M-CSF, followed by TRAP staining. The expression of RANKL in MSU-stimulated NK cells was assessed using both flow cytometry and RT-PCR.

Results: The frequency of NK cells was decreased in the peripheral blood of gout patients, with intercritical stage patients showing a statistically significant reduction compared to HCs. These NK cells exhibited elevated annexin V expression, indicating late-stage apoptosis. Under PMA-IM stimulation, NK cells from both gout patients and HCs produced comparable levels of IFN-γ and TNF-α. In synovial fluid, the frequency of NK cells was significantly lower than in peripheral blood, but their CD69 and annexin V expression levels were higher. Chemokine receptor expression, including CCR2, CCR6, CXCR3, and CXCR4, tend to be elevated in synovial fluid-derived NK cells. Furthermore, NK cells stimulated with MSU crystals demonstrated increased CD69 and annexin V expression, suggesting activation by MSU. Notably, MSU-activated NK cells promoted osteoclastogenesis in both direct and indirect manners, as shown in co-culture experiments with or without transwell systems. These cells also exhibited elevated RANKL expression, confirmed by both flow cytometry and RT-PCR.

Conclusion: NK cells are numerically reduced and may undergo late-stage apoptosis in the peripheral blood of gout patients. In synovial fluid, NK cells show elevated expression of activation markers and chemokine receptors despite their decreased numbers, suggesting their apoptosis or migration from peripheral tissues to the synovium. MSU crystals activate NK cells, which in turn promote osteoclastogenesis, partly through increased RANKL expression. These findings suggest that NK cells play a key role in amplifying synovial inflammation and contributing to bone destruction in gout.

Disclosure: K. Park: None; **Y. Cho**: None; **H. Jin**: None; **H. Jeong**: None; **S. Choi**: None; **J. Kang**: None; **D. Park**: None; **T. Kim**: None; **S. Lee**: None; **Y. Park**: None.

Abstract Number: 1146

Association of Walking Volume and Intensity with Incident Gout: A Population-based Cohort Study

Ziying Wu[1], Ying Hu[2], Hongyi He[3], Yuqing Zhang[4], Nicola Dalbeth[5], Junqing xie[6], Yilun Wang[7], Chao Zeng[7], Guanghua Lei[7] and Jie Wei[7], [1]Xiangya Hospital, Central South University, Chang Sha, China (People's Republic), [2]Xiangya School of Public Health Central South University, changsha, China (People's Republic), [3]Xiangya Hospital Central South University, Changsha, China (People's Republic), [4]Massachusetts General Hospital, Harvard Medical School, Boston, [5]University of Auckland, Auckland, New Zealand, [6]University of Oxford, Oxford, [7]Xiangya Hospital, Central South University, Changsha, Hunan, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1123–1146) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Association Between Total Steps and Peak 30-minute Cadence and Risk of Incident Gout

Total steps (steps/day)	Low group (<9,000)	Middle group (9,000 to 11,999)	High group (≥12,000)	*P* for trend
Participants, No.	27,493	32,884	31,689	
Incident case, No.	337	209	160	
Incidence rate, per 1000 person-years	1.79	0.91	0.72	
Follow-up time, mean, years	6.84	6.97	7	
Rate Difference (95%CI)	0.00 (reference)	-0.88 (-1.11, -0.65)	-1.07 (-1.29, -0.85)	
Hazard Ratio (95%CI)				
Crude model	1.00 (reference)	0.57 (0.48, 0.68)	0.48 (0.40, 0.58)	<.001
Model 1[a]	1.00 (reference)	0.63 (0.52, 0.75)	0.57 (0.47, 0.69)	<.001
Model 2[b]	1.00 (reference)	0.80 (0.66, 0.96)	0.85 (0.69, 1.05)	0.086
Model 3[c]	1.00 (reference)	0.82 (0.67, 1.00)	0.91 (0.71, 1.16)	0.354
Sensitivity analysis[c]				
Removing the wear time from Model 3[d]	1.00 (reference)	0.82 (0.67, 1.00)	0.91 (0.71, 1.16)	0.341
Six-month lag[e]	1.00 (reference)	0.86 (0.70, 1.05)	0.96 (0.74, 1.25)	0.674
Hospital inpatient records[f]	1.00 (reference)	0.83 (0.66, 1.03)	0.89 (0.67, 1.19)	0.366
Peak 30-minute Cadence (steps/minute)	**Low group (<70)**	**Middle group (70 to 79)**	**High group (≥80)**	***P* for trend**
Participants, No.	41,047	19,204	31,815	
Incident case, No.	389	135	182	
Incidence rate, per 1000 person-years	1.37	1.01	0.82	
Follow-up time, mean, years	6.89	6.97	6.97	
Rate Difference (95%CI)	0.00 (reference)	-0.36 (-0.58, -0.14)	-0.45 (-0.63, -0.27)	
Hazard Ratio (95%CI)				
Crude model	1.00 (reference)	0.81 (0.66, 0.98)	0.67 (0.56, 0.81)	<0.001
Model 1[a]	1.00 (reference)	0.79 (0.65, 0.97)	0.66 (0.55, 0.79)	<0.001
Model 2[b]	1.00 (reference)	0.98 (0.79, 1.20)	0.83 (0.69, 1.01)	0.066
Model 3[c]	1.00 (reference)	1.03 (0.83, 1.28)	0.88 (0.70, 1.11)	0.328
Sensitivity analysis[c]				
Removing the wear time from Model 3[d]	1.00 (reference)	1.03 (0.83, 1.28)	0.88 (0.70, 1.11)	0.319
Six-month lag[e]	1.00 (reference)	1.01 (0.81, 1.27)	0.88 (0.69, 1.12)	0.996
Hospital inpatient records[f]	1.00 (reference)	0.90 (0.70, 1.16)	0.87 (0.67, 1.14)	0.291

[a] Models were adjusted for age, sex, deprivation index, alcohol frequency, coffee intake, red meat intake, poultry intake, fish intake, and accelerometer wear time.
[b] Models were adjusted for Model 1 variables plus body mass index, serum creatinine concentration, hyperuricemia, history of hypertension, history of diabetes, diuretic usage, and nonsteroidal anti-inflammatory drug usage at baseline.
[c] For total steps, models were adjusted for Model 2 variables plus peak 30-minute cadence (and vice versa).
[d] Analyses were performed by excluding accelerometer wear time.
[e] Analyses were performed by excluding the gout cases that developed within six months after the index date.
[f] Analyses were performed by restricting case confirmation to hospital inpatient records.

Table 2. Association Between Purposeful Steps and Risk of Incident Gout

Purposeful steps (steps/day)	Low group (<5,000)	Middle group (5,000 to 7,999)	High group (≥8,000)	*P* for trend
Participants, No.	23,110	41,028	27,928	
Incident case, No.	298	272	136	
Incidence rate, per 1000 person-years	1.89	0.95	0.70	
Follow-up time, mean, years	6.83	6.97	7.00	
Rate Difference (95%CI)	0.00 (reference)	-0.94 (-1.18, -0.70)	-1.19 (-1.43, -0.95)	
Hazard Ratio (95%CI)				
Crude model	1.00 (reference)	0.57 (0.49, 0.68)	0.45 (0.36, 0.55)	<0.001
Model 1[a]	1.00 (reference)	0.60 (0.51, 0.71)	0.48 (0.39, 0.59)	<0.001
Model 2[b]	1.00 (reference)	0.78 (0.66, 0.94)	0.72 (0.58, 0.90)	0.003
Sensitivity analysis[b]				
Removing the wear time from Model 2[c]	1.00 (reference)	0.79 (0.66, 0.94)	0.72 (0.58, 0.90)	0.003
Six-month lag[d]	1.00 (reference)	0.80 (0.66, 0.96)	0.74 (0.59, 0.94)	0.010
Hospital inpatient records[e]	1.00 (reference)	0.78 (0.63, 0.95)	0.67 (0.52, 0.87)	0.002

[a] Models were adjusted for age, sex, deprivation index, alcohol frequency, coffee intake, red meat intake, poultry intake, fish intake, and accelerometer wear time.
[b] Models were adjusted for Model 1 variables plus body mass index, serum creatinine concentration, hyperuricemia, history of hypertension, history of diabetes, diuretic usage, and nonsteroidal anti-inflammatory drug usage at baseline.
[c] Analyses were performed by excluding accelerometer wear time.
[d] Analyses were performed by excluding the gout cases that developed within six months after the index date.
[e] Analyses were performed by restricting case confirmation to hospital inpatient records.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Previous studies have reported that walking is associated with a lower risk of several metabolic diseases; however, evidence of its association with gout, a metabolic condition, is lacking. We aimed to examine the relation of walking volume and intensity to the risk of incident gout.

Methods: Using data from the UK Biobank, a population-based cohort study was conducted to examine the relation of walking volume (total steps), walking intensity (peak 30-minute cadence), and their combination (purposeful steps, defined as average daily steps accumulated at a rate of exceeding 40 steps/minute) to the risk of incident gout. Participants aged 40-70 years, free of gout, and with valid accelerometer data at baseline were included. Hazard ratios (HRs) for incident gout were estimated across different walking activity metrics groups using Cox proportional hazard models, and the dose-response relationship was evaluated using restricted cubic spline regression. Three sensitivity analyses were conducted to assess the robustness of findings: (1) removing the accelerometer wear time from the multivariable adjusted model,

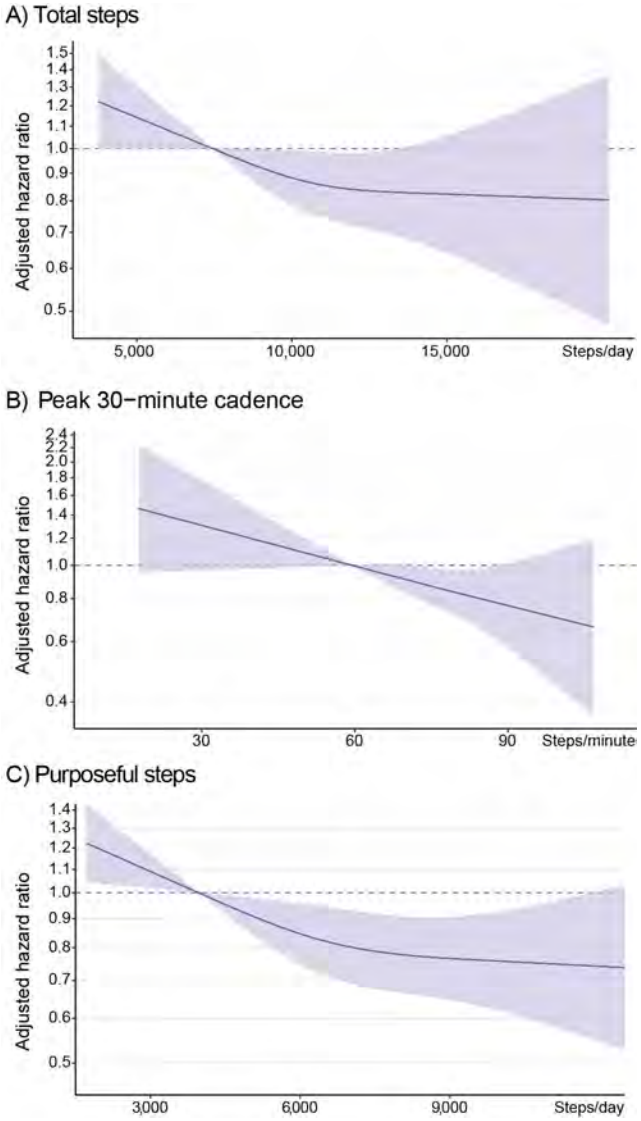


Figure 1. Associations Between Walking Activity and Incident Gout. Association between total steps (A), peak 30-minute cadence (B), and purposeful steps (C) and incident gout. Restricted cubic spline regression models fit with three knots placed at the median of three groups of categorical exposures. The y-axis is a log scale with the shaded area representing 95% confidence intervals. Hazard ratios are adjusted for age, sex, deprivation index, alcohol drinking status, coffee intake, red meat intake, poultry intake, fish intake, accelerometer wear time, body mass index, serum creatinine concentration, hyperuricemia, history of hypertension, history of diabetes, diuretic usage, and nonsteroidal anti-inflammatory drug usage at baseline. For total steps, models were further adjusted for peak 30-minute cadence (and vice versa).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(2) excluding incident gout cases within six months after the index date to mitigate potential reverse causation, and (3) restricting gout case confirmation to hospital inpatient records to minimize potential misclassification bias.

Results: Among 92,066 participants included in the current analyses, 706 developed incident gout during a mean follow-up period of 6.93 years. After adjustment for potential covariates, no significant association was observed between total steps or peak 30-minute cadence and the risk of incident gout (**Table 1**). However, compared with the low group (< 5,000 steps/day) of purposeful steps, the risk of incident gout was lower in the middle group (5,000-7,999 steps/day) and high (≥8,000 steps/day) group, with adjusted HRs and 95% confidence intervals of 0.78 (0.66–0.94) and 0.72 (0.58–0.90), respectively (P for trend =0.003) (**Table 2**). The associations remained consistent in sensitivity analyses, including when accelerometer wear time was excluded from models, those excluding incident gout cases occurring within the first six months of the index date, and those restricted to hospital-confirmed gout cases. Restricted cubic spline regression revealed significant linear inverse associations between purposeful steps and the risk of incident gout (**Figure 1**).

Conclusion: This large population-based cohort study demonstrates that higher purposeful steps, defined as the combined measure of walking volume and intensity, are associated with a lower risk of incident gout. These findings provide valuable insights for developing walking-based recommendations to prevent incident gout.

Disclosure: Z. Wu: None; **Y. Hu**: None; **H. He**: None; **Y. Zhang**: None; **N. Dalbeth**: None; **J. xie**: None; **Y. Wang**: None; **C. Zeng**: None; **G. Lei**: None; **J. Wei**: None.

Abstract Number: 1147

Renal Manifestations in VEXAS Syndrome: A Systematic Review of Clinical Features, Pathology, and Outcomes

Akhila Arya Perumangote Vasudevan[1], Vishnu Mulavini[2], Rasiya Hashim[3], Madhumitha Rondla[4] and Dileep C Unnikrishnan[5], [1]Yale University/Bridgeport Hospital, Stratford, CT, [2]Calicut Medical College, Stratford, [3]Franciscan Health Olympia & Chicago Heights, drrasiyahashim@gmail.com, IL, [4]Texas tech university health sciences center, El paso, El Paso, TX, [5]Bridgeport Hospital, Stratford, CT

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: VEXAS syndrome is a recently described, adult-onset autoinflammatory disease caused by somatic mutations in the UBA1 gene, typically affecting hematopoietic stem cells. Renal involvement was not prominently featured in early reports. The pathophysiology of VEXAS-associated kidney disease is not yet fully understood, but it is hypothesized that the UBA1-mutant myeloid clone directly infiltrates and damages renal tissue, as cytoplasmic vacuoles and UBA1-mutant cells have been identified in affected organs. Given that renal complications can lead to substantial morbidity, recognizing and characterizing kidney involvement in VEXAS is crucial.This review provides a comprehensive synthesis of the literature since VEXAS was first described, focusing on renal manifestations, biopsy findings, the frequency of kidney involvement, treatments used, and outcomes.

Methods: We searched PubMed/MEDLINE and Google Scholar for original articles with patient level data from 2020 on renal involvement in VEXAS syndrome. Key data was extracted from each report manually.The PRISMA diagram is shown below (Figure 1)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

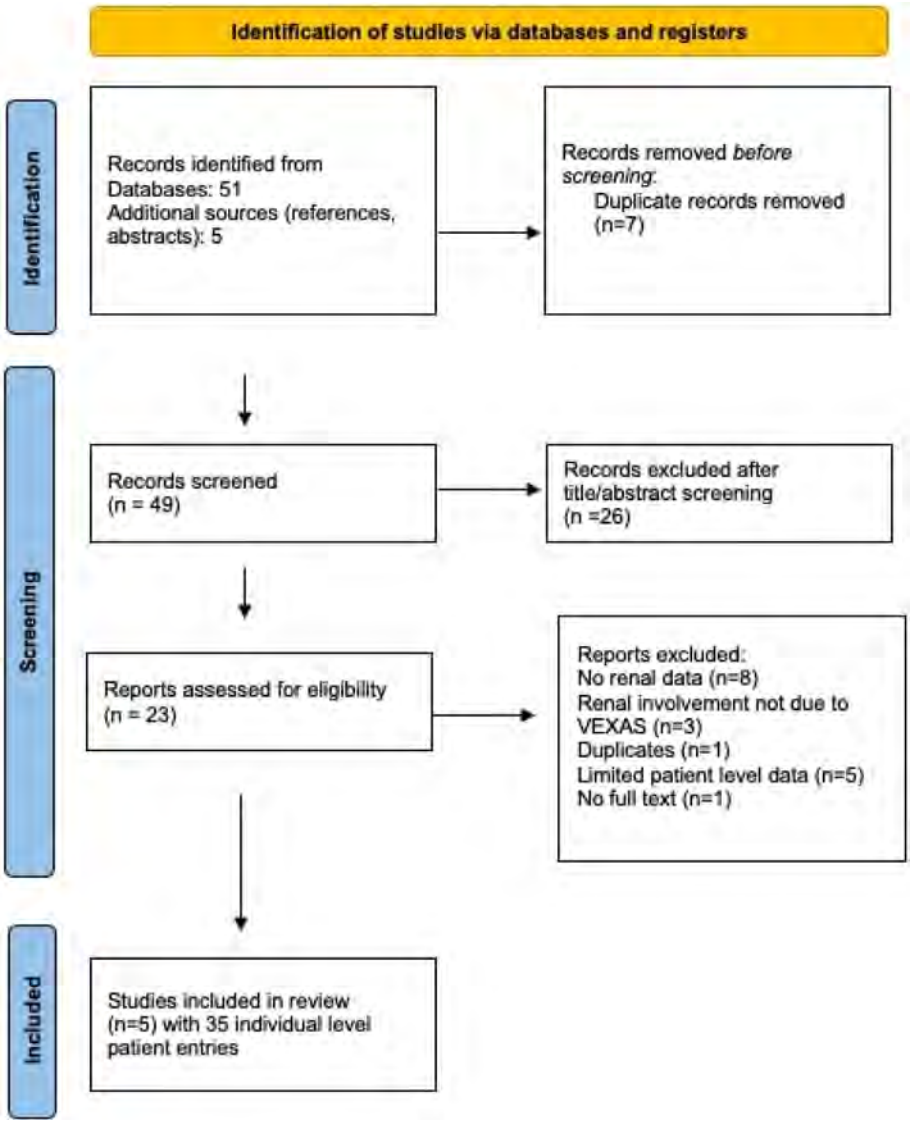


Figure 1: PRISMA diagram

Results: Kalantari et al. found AKI incidence of 6.2% at 1 year and 39% by year 10. A Dutch series showed 2 of 12 men had renal involvement; a Swiss series had 1 of 17 with AKI. In a French study, only 11 of 303 patients (3.6%) underwent biopsy. True prevalence may be higher due to avoided biopsies and empirical treatment.Patients (all male, aged 47–86) presented with CKD or abrupt AKI. Proteinuria was common; 5 of 11 French cases had nephrotic-range proteinuria. Hematuria and pyuria occurred in ∼50%. Table 1 summarises biopsy findings.The association with VEXAS flares was unclear—only 3 of 11 had flare-associated AKI. However, AKI often improved with immunosuppression. CRP elevation correlated with AKI onset in the Mayo cohort. Glucocorticoids remain first-line. In the Mayo cohort, all responded with improved kidney function and inflammation. Relapses with tapering necessitated steroid-sparing agents: cyclophosphamide, methotrexate, azathioprine, MMF. Targeted agents (tocilizumab, anakinra, JAK inhibitors) were used in refractory cases. Azacitidine may reduce inflammation by suppressing mutant clones. HSCT may induce remission; of two Mayo cases, one recovered, one had stable CKD post HSCT.AKI often improved with treatment; dialysis was rare.The role of renal disease in mortality remains unclear.

Conclusion: Kidney involvement in VEXAS can take diverse forms—most commonly interstitial nephritis and vasculitic glomerulonephritis, often parallel the activity of the systemic disease. Biopsy findings of plasma cell and neutrophil infiltration in the kidneys, along with UBA1 mutation positivity, suggest direct tissue damage by infiltrating mutant myeloid clones.The mainstay of treatment for VEXAS flares, including renal involvement, is glucocorticoids. Adjunctive therapies are frequently

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Distribution of Histopathological Lesions in VEXAS-Associated Kidney Biopsies

Table 1: Distribution of Histopathological Lesions in VEXAS-Associated Kidney Biopsies

Biopsy Category	Number of Patients
No renal biopsy available	12
Tubulointerstitial nephritis	5
Acute interstitial nephritis	3
Acute tubular necrosis, mesangial matrix expansion	2
Pauci-immune glomerulonephritis	2
Light chain cast nephropathy	1
Acute tubular injury, Tubulointerstitial nephritis	1
IgA nephropathy	1
Acute interstitial nephritis + Minimal change disease	1
Pauci-immune glomerulonephritis-Post-infectious glomerulonephritis	1
Minimal change disease (with IgA deposits)	1
Vascular and diabetic changes	1
AA amyloidosis	1
Plasma cell-rich interstitial infiltrate (MPO+, CD68+)	1
No evidence of vasculitis	1
Glomerulosclerosis, tubular injury, arteriolosclerosis	1

added. Renal prognosis following HSCT has been favorable in the two patients with AKI reported. Mortality and dialysis dependence are rarely observed.Ongoing research is needed to better understand why certain VEXAS patients develop renal involvement and to establish optimal treatment algorithms.

Disclosure: A. Perumangote Vasudevan: None; **V. Mulavini**: None; **R. Hashim**: None; **M. Rondla**: None; **D. C Unnikrishnan**: None.

Abstract Number: 1148

Interstitial Lung Disease in MCTD: A Retrospective Cohort Study at a Large Tertiary Medical Center

Alana Haussmann[1] and Elizabeth Volkmann[2], [1]University of California Los Angeles, Los Angeles, CA, [2]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Mixed connective tissue disease (MCTD) is a rare autoimmune condition defined by the presence of anti-U1-ribonucleoprotein (RNP) antibodies and clinical features of at least two other connective tissue diseases (CTDs). Pulmonary complications, including interstitial lung disease (ILD), are the leading causes of morbidity and mortality in this population. The clinical phenotype, natural history, and risk factors for ILD in MCTD remain poorly characterized. This study aims to evaluate the prevalence of MCTD and characterize clinical differences between MCTD patients with and without ILD.

Methods: We conducted a retrospective review of patients seen within the UCLA Health System between April 1, 2005, and April 1, 2025. Eligible patients had a CTD ICD-10 code of either M35.1 or M35.9, were at least 18 years of age, and had a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with MCTD with and without ILD (N=581)

	ILD (N= 120)	No ILD (N= 461)
Age, Mean (SD)	58 (±18)	48 (±17)
Age <55, N (%)	49 (41%)	292 (63%)
Age >/=55, N (%)	71(59%)	169 (37%)
Female N (%)	101(84%)	405 (88%)
BMI, Mean (SD)	26.2 (±7.13)	25.9 (±6.3)
Current Smoker, N (%)	2 (2%)	10 (2%)
Former Smoker, N (%)	22 (18%)	76 (17%)
Never Smoker, N (%)	93 (78%	357 (77%)
Smoker Status Unknown, N (%)	3 (2%)	18 (4%)
Race, N (%)		
Caucasian	45 (38%)	159 (34%)
African American/Black	26 (22%)	81 (18%)
Asian/Pacific islander	18 (15%)	73 (16%)
Native American	3 (2%)	3 (1%)
Other/Decline to Answer	28 (23%)	145 (31%)
Ethnicity, N (%)		
Hispanic	36 (30%)	75 (16%)
Non-Hispanic	84 (70%)	386 (84%)
GERD, N (%)	73 (61%)	137 (30%)
Dysphagia, N (%)	39 (33%)	63 (14%)
Pulmonary Hypertension, N (%)	47 (39%)	38 (8%)

positive anti-U1-RNP antibody. Individuals with a medical history of systemic sclerosis, rheumatoid arthritis, systemic lupus erythematosus, or inflammatory myositis were excluded. Patients with ILD were identified based on diagnosis documentation in the electronic medical record. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess differences in clinical and demographic characteristics between MCTD patients with and without ILD.

Results: A total of 581 patients with MCTD were included in the study. The majority were female (86.9%) with a mean age of 50 years (range: 18–96) (Table 1). The cohort was racially diverse, with 35.3% identifying as Caucasian, 18.4% as Black/African American, and 15.7% as Asian/Pacific Islander. ILD was present in 120 patients (20.7%). Patients with and without ILD did not differ significantly in terms of sex, body mass index (BMI), race, or smoking status. However, patients with MCTD and ILD were significantly more likely to be over the age of 55 (OR 2.50; 95% CI: 1.62–3.86), ethnically Hispanic (OR 2.21; 95% CI 1.40-3.49), report dysphagia (OR 3.03; 95% CI: 1.85–4.95), and have documented diagnoses of gastroesophageal reflux disease (GERD) (OR 3.66; 95% CI: 2.37–5.70), as well as pulmonary hypertension (PH) (OR 7.13; 95% CI: 4.24–12.10).

Conclusion: This study represents the largest evaluation of patients with MCTD and underscores the notable burden of ILD in this population. Universal screening for ILD in MCTD remains controversial. The present study sheds light on the distinguishing clinical features of patients with MCTD-ILD (e.g., older age, Hispanic, GERD, dysphagia, PH) that if present, could prompt evaluation for ILD and lead to earlier diagnosis.

Disclosure: A. Haussmann: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5.

Abstract Number: 1149

Patient Symptom State Demonstrates Validity for the Assessment of Disease Activity and Patient-reported Outcomes in Adults with SAPHO and Chronic Nonbacterial Osteomyelitis – A Longitudinal Response Profile Analysis in The SAPHO-CNO Study

Aleksander Lenert[1], Robyn Domsic[2], Jenna Thomason[3], Melanie smith[4], Petar Lenert[5], Yongdong (Dan) Zhao[6], Jonathan Templin[1], Mary Vaughan-Sarrazin[1], Daniel Solomon[7] and Polly Ferguson[8], [1]University of Iowa, Iowa City, IA, [2]University of Pittsburgh, Pittsburgh, PA, [3]University of Washington, Seattle, WA, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [5]University of Iowa Hospitals and Clinics, Iowa City, IA, [6]Seattle Children's Research

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Institute, Redmond, WA, [7]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [8]University of Iowa Carver College of Medicine, Iowa City, IA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

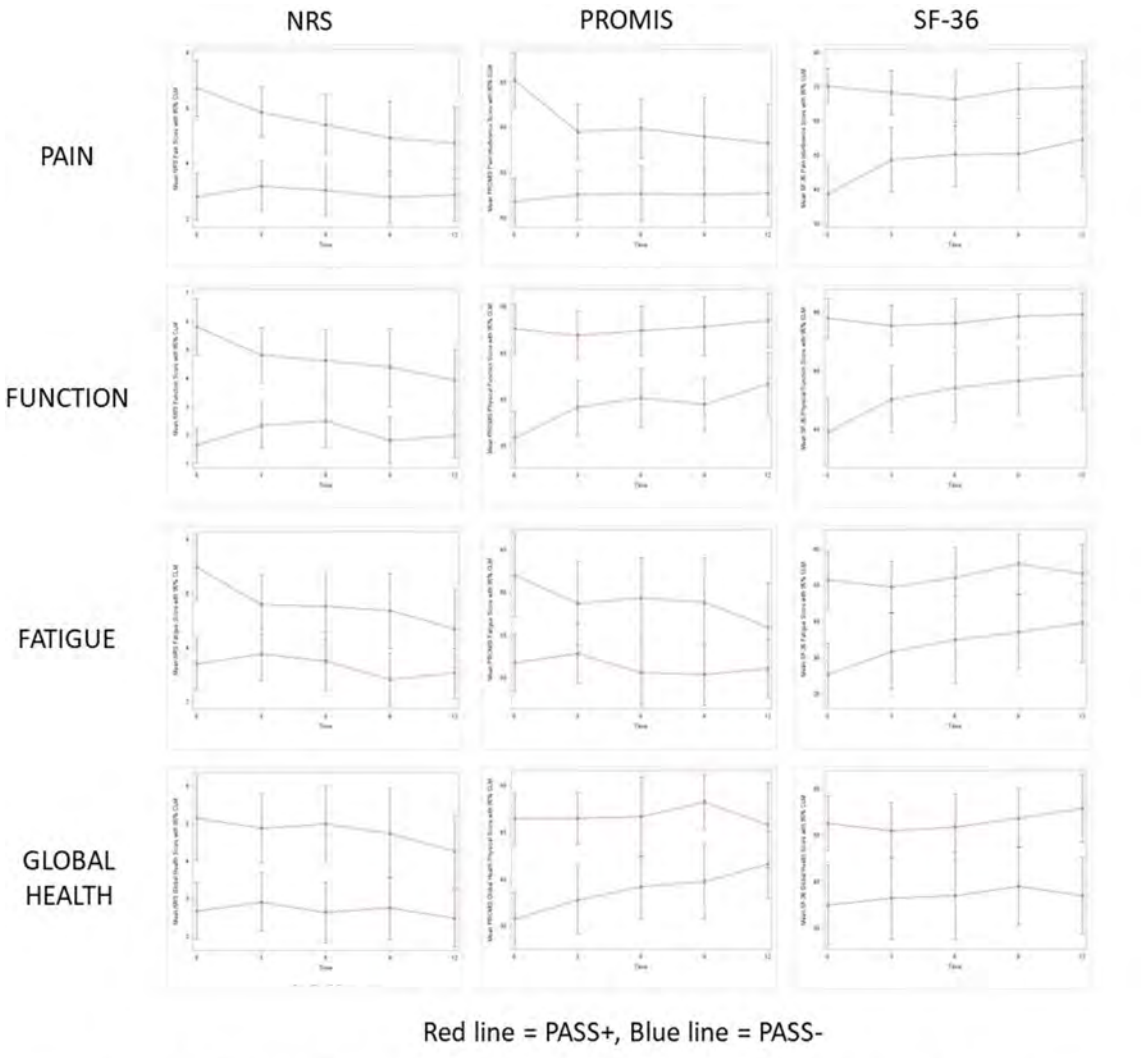
Background/Purpose: Patient symptoms are important in the assessment of disease activity. The Patient Acceptable Symptom State (PASS) is defined as the minimum symptom score beyond which patients consider themselves to be well. The PASS reflects symptom control from the patient's perspective. We analyzed between group differences for PASS+ and PASS- subjects, and we performed a longitudinal response profile analysis and assessed validity of patient-reported outcomes (PRO) for PASS in adults with SAPHO-CNO.

Table 1. Baseline demographics, clinical characteristics and patient-reported outcome measures by the patient symptom state in adults with SAPHO-CNO (n=59).

	PASS+, n=37	PASS-, n=22
Age at enrollment, mean (SD), years	35 (14)	43 (17)
Age at diagnosis, mean (SD), years	28 (15)	36 (19)
Female biological sex, count (%)	30 (81)	20 (91)
Non-Hispanic, count (%)	36 (97)	21 (95)
Race by self-report, White, count (%)	33 (89)	20 (91)
SAPHO-CNO Disease characteristics		
Disease duration, mean (SD), years	7 (6)	6 (6)
Time to diagnosis, mean (SD), years	4 (4)	8 (10)
Symptom duration, mean (SD), years	11 (6)	15 (10)
Musculoskeletal involvement, count (%)	37 (100)	22 (100)
Inflammatory arthritis (ever), count (%)	14 (38)	15 (68)
Spine involvement (ever), count (%)	12 (32)	12 (59)
Skin involvement – any, count (%)	15 (41)	9 (40)
PPP, count (%)	7 (19)	6 (27)
PsV, count (%)	7 (19)	4 (18)
Severe Acne, count (%)	3 (8)	4 (18)
HS, count (%)	1 (3)	3 (14)
Patient-reported Disease Activity by NRS		
Overall SAPHO-CNO (PATDAM), mean (SD)	2.1 (1.8)	6.2 (2.0)
MSK SAPHO-CNO, mean (SD)	2.4 (2.4)	6.3 (2.1)
Skin SAPHO-CNO*, mean (SD)	1.5 (1.8)	4.0 (2.9)
Patient-reported Outcome Measure		
PAIN		
Patient global assessment by NRS, mean (SD)	2.8 (2.5)	6.7 (2.3)
PROMIS Pain Interference, mean (SD)	51.8 (7.4)	65.3 (6.7)
SF-36 Pain, mean (SD)	70.3 (15.4)	38.8 (19.6)
PHYSICAL FUNCTION		
Patient global assessment by NRS, mean (SD)	1.7 (1.9)	5.8 (2.2)
PROMIS Physical Function, mean (SD)	47.6 (8.1)	35.9 (6.4)
SF-36 Physical Functioning, mean (SD)	78.1 (19.6)	39.3 (24.9)
FATIGUE		
Patient global assessment by NRS, mean (SD)	3.4 (2.9)	7.0 (2.7)
PROMIS Fatigue, mean (SD)	51.8 (9.9)	62.1 (11.0)
SF-36 Energy/Fatigue, mean (SD)	51.6 (23.1)	25.5 (19.5)
GLOBAL HEALTH		
Patient global assessment by NRS, mean (SD)	2.7 (2.2)	5.2 (2.5)
PROMIS Global Health – Physical score, mean (SD)	46.5 (7.9)	35.8 (6.5)
SF-36 General Health, mean (SD)	52.7 (17.6)	35.0 (19.7)

Means (standard deviation) and counts (percentage) are presented unless otherwise stated. SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis; PASS: Patient Acceptable Symptom State; PPP: Palmoplantar pustulosis; PsV: Psoriasis vulgaris; HS: Hidradenitis suppurativa; NRS: numeric rating scale, with range 0 (no pain, no limitations, no fatigue) to 10 (severe pain, severe limitations, severe fatigue); PATDAM: patient-reported disease activity overall in SAPHO-CNO by NRS, with range 0 (well controlled) to 10 (poor y controlled); MSK: Musculoskeletal; PROMIS: Patient-Reported Outcomes Measurement Information System; SF-36: 36-item Short Form survey.
*For subjects with current SAPHO-CNO related scin manifestations (n=24).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



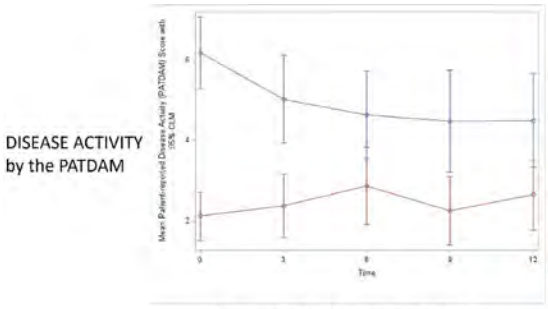
SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis; PASS: Patient Acceptable Symptom State, with red line indicating PASS+ group (reference) and blue line indicating PASS- group. NRS: numeric rating scale, with range 0 (better) to 10 (worse). PROMIS: Patient-Reported Outcomes Measurement Information System, with higher scores reflecting higher pain and fatigue, and higher function and overall health by their respective scales. SF-36: 36-item Short Form survey, with lower scores being worse (from 0) and higher scores being better (to 100).

Figure 1. Response Profile Analysis of Patient-reported Outcome Measures by the Patient Acceptable Symptom State group over 1 year of follow-up in Adults with SAPHO-CNO (n=59).

Methods: Adults (≥18 years) enrolled in the SAPHO-CNO Study, a prospective longitudinal observational study, completed the PASS question: "*Think about all the ways that your SAPHO/CNO has affected you during the last week. If you were to remain for the next few months as you were in the last week, would this be acceptable to you?*". The PASS has a binary response: acceptable (PASS+) or unacceptable (PASS-). We collected serial questionnaires on patient-reported disease activity (PATDAM) measured by the numeric rating scale (NRS, range 0-10), and PROs for pain, function, fatigue, and global health assessed by the patient NRS (range 0-10), 36-item Short Form survey (SF-36), and Patient-Reported Outcomes Measurement Information System (PROMIS) instruments.

Subject baseline characteristics were summarized as means (standard deviation) or counts (proportion) stratified by PASS. We performed a response profile analysis with longitudinal modeling to account for both the mean and the covariance of repeated measures over time. We sought to characterize changes in the mean PROs over time, and to determine whether the mean outcome differs between PASS groups. Dependent variables (responses) were PRO measures; independent

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



	Proportion of PASS+ vs. PASS- subjects over 5 timepoints	
Timepoint	PASS+ group, n=37	PASS- group, n=22
Baseline	63%	37%
3-month	68%	32%
6-month	69%	31%
9-month	71%	29%
12-month	70%	30%

SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; CNO: chronic nonbacterial osteomyelitis; PATDAM: patient-reported disease activity overall in SAPHO-CNO by numeric rating scale (NRS), with range 0 (well controlled) to 10 (poorly controlled); PASS: Patient Acceptable Symptom State, with red line indicating PASS+ group (reference) and blue line indicating PASS- group.

Figure 2. Response Profile Analysis of Patient-reported Disease Activity by the Patient Acceptable Symptom State group over 1 year of follow-up in Adults with SAPHO-CNO (n=59).

variables were time, group and time*group interaction term. Time was alternatively treated as categorical, linear, or quadratic, and model fit was evaluated by Akaike Information Criterion. All analyses were performed using SAS (v.9.4).

Results: Differences in baseline characteristics of PASS- and PASS+ subjects (n=59) are summarized in Table 1. PASS- subjects were slightly older at diagnosis, with a longer time to diagnosis and longer symptom duration. Spine involvement and skin features (PPP, acne) were more common, and mean PRO scores were higher in PASS- subjects. Mean response profiles for pain, function, and fatigue, but not global health, were significantly different between PASS groups ($p < 0.05$ for all time*group interaction terms) (Figure 1). Over time, longitudinal trajectories for all PROs remained stable in the PASS+ group, while they tended to improve in the PASS- group. Similarly, mean patient-reported disease activity (by PATDAM) was significantly different between PASS groups; it improved in PASS- subjects over time ($p< 0.05$) (Figure 2). Hence, PRO measures for pain, function and fatigue, demonstrate content validity, and PATDAM shows content and construct validity for disease activity as reflected by longitudinal changes in PASS groups.

Conclusion: The PASS identifies two distinct groups of adult SAPHO-CNO patients with differing levels of disease activity, pain, function and fatigue over time. We demonstrated the validity of PATDAM and key PROs with PASS longitudinally.

Disclosure: A. Lenert: None; **R. Domsic**: None; **J. Thomason**: None; **M. smith**: None; **P. Lenert**: None; **Y. Zhao**: american board of pediatrics, 4, Bristol-Myers Squibb(BMS), 5, UpToDate, 9; **J. Templin**: None; **M. Vaughan-Sarrazin**: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9; **P. Ferguson**: None.

Abstract Number: 1150

Impact of IL-17A on synovial fibroblast from subacromial bursae

Andre Ramon[1], Hélène Greigert[2], baptiste lamarthée[3], Corentin Richard[4], claudie Cladière[3], Noemie Klopfenstein[3], Ludovic Labattut[5], Alice Bordet[5], Sylvain Audia[6], Romain boidot[4], jean-francis Maillefert[1], Bernard Bonnotte[7] and Maxime Samson[8], [1]Rheumatology, Université Bourgogne Europe, CHU Dijon Bourgogne, Dijon, France, [2]Vascular Medicine, Université Bourgogne Europe, CHU Dijon Bourgogne, Dijon, France, [3]Marie et Louis Pasteur University, EFS, INSERM, UMR RIGHT, Besançon, France, Dijon, France, [4]Molecular Biology Unit, Georges-François Leclerc Cancer Center, UNICANCER, Dijon, France, Dijon, France, [5]Orthopedic Surgery, Université Bourgogne Europe, CHU Dijon Bourgogne, Dijon, France, [6]Internal Medicine and Clinical Immunology, Université Bourgogne Europe, CHU Dijon Bourgogne, Dijon, France, [7]Internal medicine and clinical immunology, Université Bourgogne Europe , CHU Dijon Bourgogne, Dijon, France, [8]CHU Dijon Bourgogne, Dijon, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyalgia rheumatica (PMR) is characterized by increases in serum IL-6 and the proportion of Th17 cells in circulating blood. During PMR, IL-6 may originate from circulating monocytes or from the synovial tissue itself. To clarify the role of synovial tissue, we performed experiments using synovial fibroblast (SF) cultures derived from synovial bursae, which are the affected structures in PMR. As secukinumab (SEC) is currently being evaluated in glucocorticoid-dependent PMR, we investigated, in the current study, the impact of IL-17A and SEC on SFs activation.

Methods: SFs were obtained from *ex-vivo* cultures of synovial tissue from the subacromial bursae after arthroscopy in patients with rotator cuff injury. SFs were cultivated *in vitro* with IL-17A (50 ng/mL), IFN-g (2.5 ng/mL) and/or SEC (20 µg/mL) for 24 hours. mRNA expression was analyzed by Bulk RNA sequencing and RT-PCR. The impact of IL-17A on T-cell polarization was assessed by performing co-cultures of SFs and allogenic peripheral blood mononuclear cells (PBMC) activated with anti CD3/CD28 beads. SFs were stimulated with IL-17A or IL-17A + SEC or IgG isotype control for 72 hours, then co-cultures were performed over 7 days. T-cell polarization was analyzed by flow cytometry.

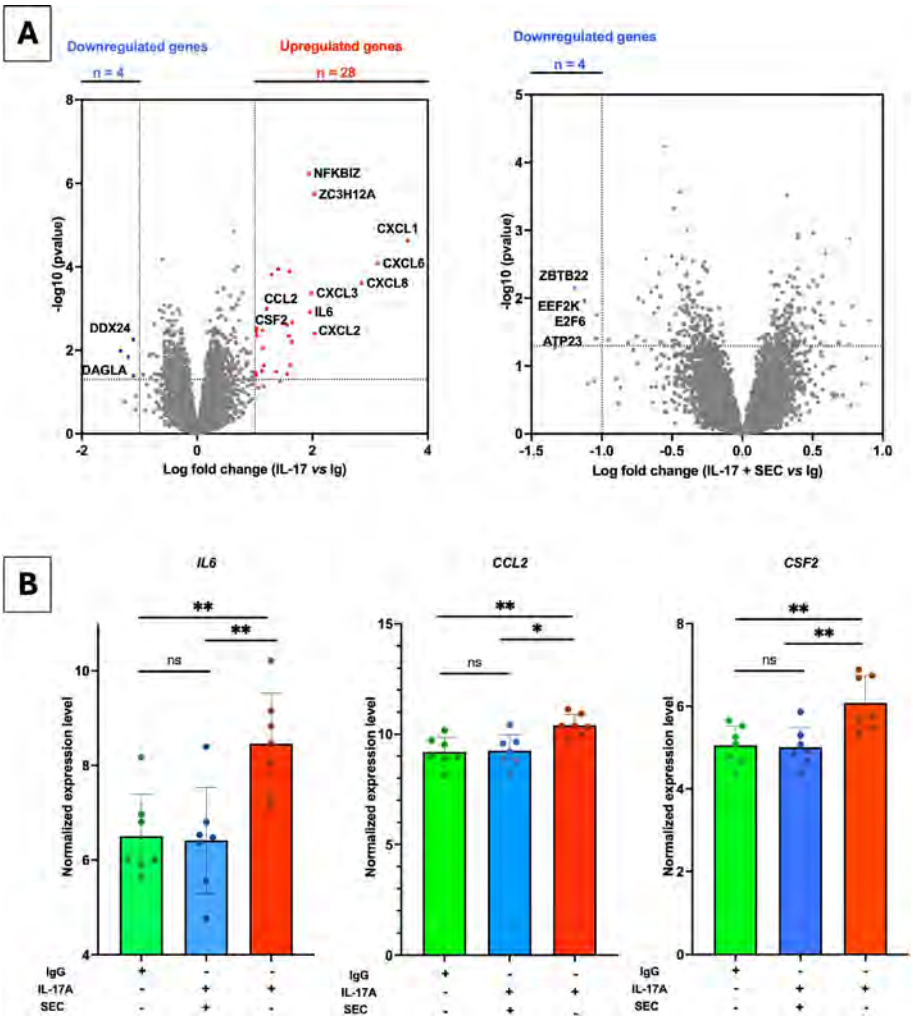


Figure 1: Bulk RNA sequencing results from IL-17A stimulated synovial fibroblasts (n = 8). (A) Volcano plot showing differential gene expression (IL-17A versus IgG; IL-17A + SEC versus IgG). (B) Barplot visualization of IL6, CSF2 and CCL2 gene expression from IL-17A, IL-17A + SEC and IgG stimulated synovial fibroblasts. Columns represent the median, the "whiskers" represent quartiles Q1 and Q3. *: $p < 0.05$, **: $p < 0.01$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

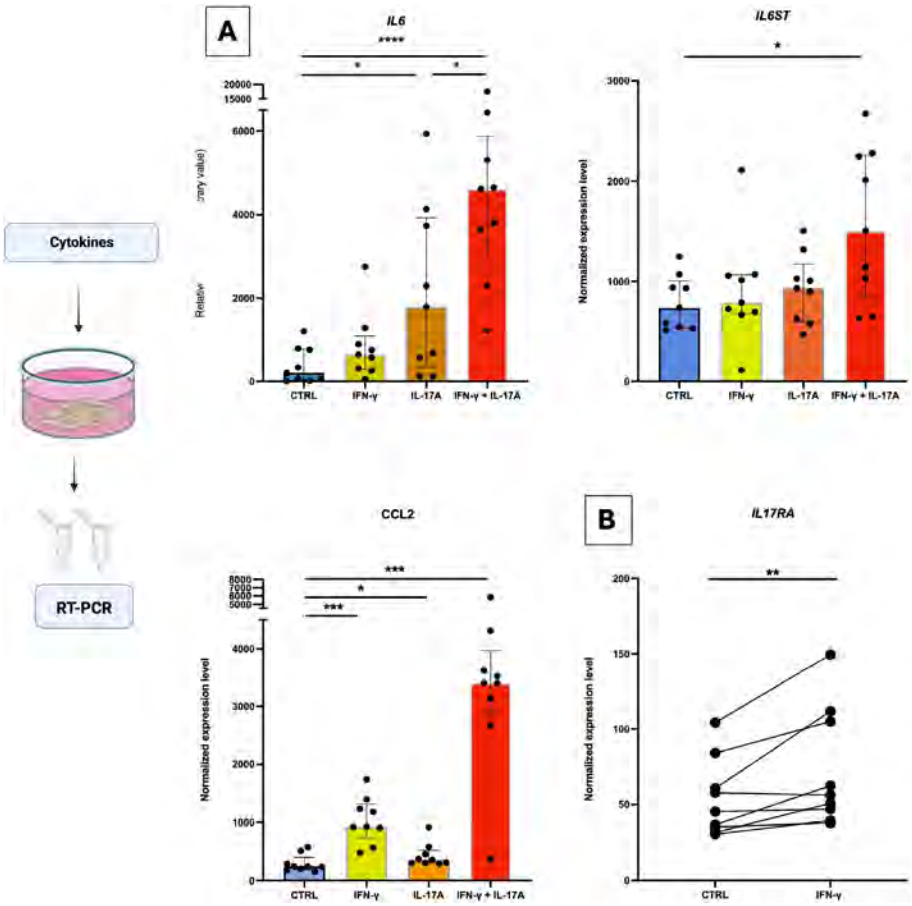


Figure 2: Level of mRNA expression of IL6, IL6ST, CCL2 and IL17RA by synovial fibroblasts after stimulation with IL-17A and/or IFN-γ (n = 9). A: Level of mRNA expression of IL6, IL6ST and CCL2 in synovial fibroblasts after stimulation with IL-17A (50 ng/mL) and/or IFN-γ (2,5 ng/mL). B: Effect of IFN-γ on mRNA expression of IL17RA by synovial fibroblasts. Columns represent the median, the "whiskers" represent quartiles Q1 and Q3. *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$, ****: $p < 0.0001$

Results: The cells obtained through synovial tissue culture exhibited a phenotype fitting with fibroblasts ($CD90^+CD105^+CD73^{int}CD34^-CD45^-$). Bulk RNA sequencing analysis showed increased levels of expression for genes associated with IL-17, PI3k-Akt and the NF-KB signaling pathway. Stimulation with IL-17A led to significant increases in 28 genes, notably *IL6*, *CSF2* (encoding for GM-CSF), and *CCL2*. The addition of SEC led to a significant decrease in these mRNAs, restoring a transcriptomic profile similar to unstimulated SF (**figure 1**). RT-PCR analyses confirmed an increase in the mRNA expression of *IL6*, *CSF2* and *CCL2* in the presence of IL-17A, while no difference was observed for *IL6ST*, *IFNGR1/2*, *IL12A*, *IL23A*, *FAP*, *IL17RA* and *IL17RC* mRNA. Co-stimulation with IL-17A and IFN-g led to a strong increase in mRNA expression of *IL6*, *IL6ST*, and *CCL2* (**figure 2A**). This synergy between IL-17A and IFN-g may be reliant on an increase in *IL17RA* mRNA expression after IFN-g stimulation (**figure 2B**). Co-cultures of SFs with allogenic PBMC were performed after 72h of SFs stimulation with either IgG isotype control, IL-17A or IL-17A+SEC. Compared to SFs pre-treated with IgG or IL-17A+SEC, SFs pre-treated with IL-17A were able to promote Th17 cell polarization without significant increases in the proportions of Th1, Tc1 or Tc17 cells (**figure 3**).

Conclusion: This work highlights the potential role of SFs in PMR via their ability to strongly express *IL6*. SFs are also sensitive to IL-17A and IFN-y, which are two key cytokines in PMR. In response to IL-17A, and with a synergistic effect with IFN-y, SFs strongly express *IL6*, leading to an increase in Th17 polarization. In addition, SFs express other markers such as *CCL2*, suggesting that they may induce the recruitment of $CCR2^+$ monocytes. Finally, SEC can restore a non-inflammatory profile in activated SF, suggesting the potential of IL-17A therapeutic target in PMR.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

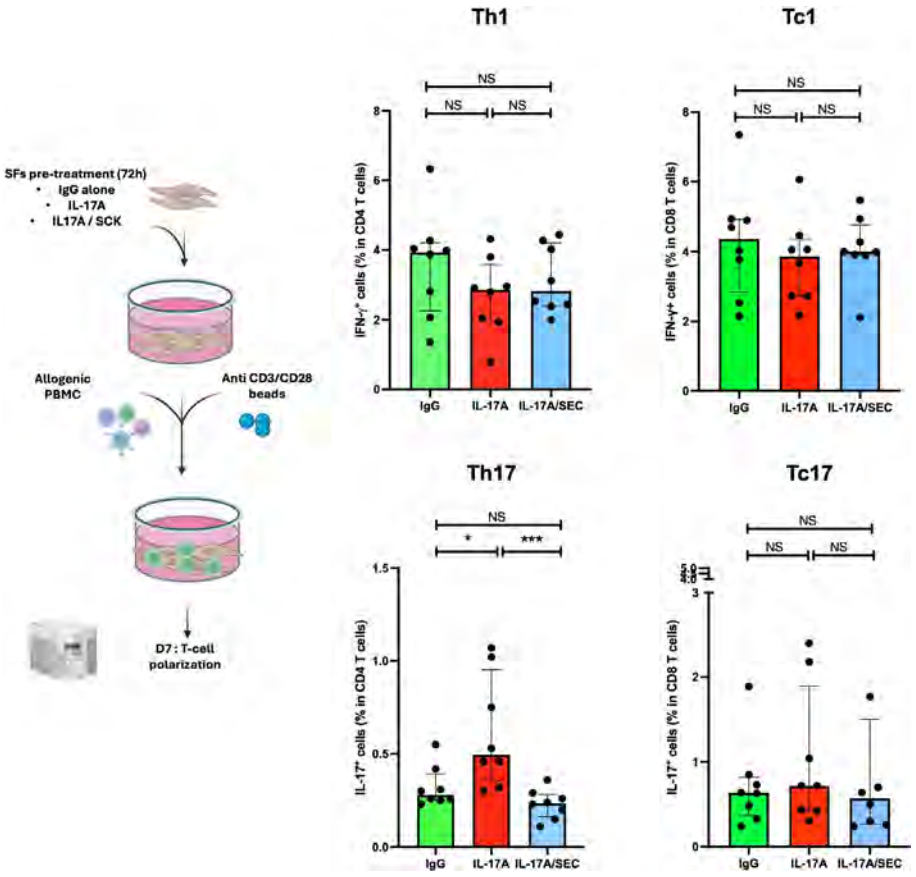


Figure 3: Study of the effect of synovial fibroblasts on T-cell polarization. Percentage of Th1 (CD4+CD8-IFN-γ+), Tc1 (CD4-CD8+ IFN-γ-), Th17 (CD4+CD8-IL-17+), and Tc17 (CD4-CD8+IL-17+) cells. Columns represent the median, the "whiskers" represent quartiles Q1 and Q3. *: $p < 0.05$, ***: $p < 0.001$. NS = not significant. SEC: secukinumab. Coculture was performed using 8 samples of synovial tissue.

Disclosure: A. Ramon: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, chugai, 2, Novartis, 2, 5; **H. Greigert**: None; **b. lamarthée**: None; **C. Richard**: None; **c. Cladière**: None; **N. Klopfenstein**: None; **L. Labattut**: None; **A. Bordet**: None; **S. Audia**: None; **R. boidot**: None; **j. Maillefert**: None; **B. Bonnotte**: Boehringer-Ingelheim, 2, Chugai, 2, Novartis, 2, Vifor Pharma, 2; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2.

Abstract Number: 1151

A Comparison of Patients with Cardiac Sarcoidosis vs. Other Systemic Manifestations of Sarcoidosis: A Retrospective Cohort Study

Chelsea Guan[1], Dana Nachawati[1], Amir Daneshvar[1], Keri Ann Pfeil[1], Elleson Harper[1], Lindsay Frumker[2], Meghan Gump[1], Vicky Nahra[3] and Omer Pamuk[4], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]University hospitals Cleveland medical center, Highland Heights, OH, [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland Heights, OH, [4]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sarcoidosis is a systemic autoimmune disease with multiorgan involvement. In this study, we analyzed the differences in characteristics in patients with sarcoid myocarditis (cardiac sarcoidosis) and sarcoidosis with other systemic manifestations (other sarcoidosis).

Methods: A retrospective cohort study was performed using TriNetX, a global federated health research network that provides access to electronic medical records across large health care organizations (HCOs). Data was used from 102 HCOs. Patients (>18 years old) were divided into two cohorts, based on the presence of cardiac sarcoidosis (ICD-10 D86.8) or other systemic manifestations of sarcoidosis. 1:1 propensity score matching was performed using 27 different baseline characteristics (Table 1 and Table 2). Kaplan-Meier survival analysis was performed to look at differences in mortality.

Results: 10,296 patients were included in the cardiac sarcoidosis cohort and 160,918 patients were included in the other sarcoidosis cohort before propensity score matching. After propensity score matching, 10,046 patients were included in each cohort.

Univariate analysis before matching showed several significant differences (Table 1 and Table 2). After propensity score matching, there was a significantly higher frequency of black or African American patients with cardiac sarcoidosis (p=0.003), where other sarcoidosis had a significantly higher frequency of white patients (p < 0.001, Table 1). Patients with cardiac sarcoidosis had a significantly increased frequency of hypertension (p=0.007), lung, cutaneous, and lymph node involvement (p< 0.001) and significantly higher frequencies of meningitis (p=0.016), iridocyclitis, arthropathy, and myositis (p< 0.001) (Table 1). The frequency of elevated ESR, CRP, and medication usage was not significantly different (Table 2).

Mortality risk was 10.1% in the cardiac sarcoidosis group vs. 15.8% in the other sarcoidosis group, resulting in a statistically significant risk difference of –5.7%, indicating a lower absolute risk of death in the myocarditis group (Figure 1A). Risk ratio was 0.64 (95% CI: 0.60–0.69) and odds ratio was 0.60 (95% CI: 0.55–0.65), suggesting a ∼40% reduction in the relative

Table 1. Baseline Characteristics of Patients with Cardiac Sarcoidosis vs. Other Sarcoidosis

Variable	Before Matching			After Matching		
	Cardiac Sarcoidosis (n = 10,296	Other Sarcoidosis (n = 160,918)	P-Value	Cardiac Sarcoidosis (n = 10,046)	Other Sarcoidosis (n = 10,046)	P-Value
Demographics						
Age at Index (Mean ± SD)	57.9 ± 12.1	54.8 ± 13.8	**<0.001**	57.9 ± 12.1	58.9 ± 13.0	**<0.001**
Female	4,263 (41.4%)	92,977 (57.8%)	**<0.001**	4,175 (41.6%)	4,203 (41.8%)	0.689
Male	5,613 (54.5%)	62,764 (39.0%)	**<0.001**	5,459 (54.3%)	5,449 (54.2%)	0.887
Black or African American	3,470 (33.7%)	53,490 (33.2%)	**<0.001**	3,356 (33.4%)	3,158 (31.4%)	**0.003**
White	5,566 (54.1%)	83,301 (51.8%)	**<0.001**	5,451 (54.3%)	5,706 (56.8%)	**<0.001**
Asian	134 (1.3%)	2,679 (1.7%	**0.005**	132 (1.3%)	122 (1.2%)	0.528
Comorbidities						
Essential hypertension	4,971 (48.3%)	42,170 (26.2%)	**<0.001**	4,797 (47.8%)	4,987 (49.6%)	**0.007**
Type 2 diabetes mellitus	2,449 (23.8%)	20,799 (12.9%)	**<0.001**	2,345 (23.3%)	2,423 (24.1%)	0.196
Ischemic heart diseases	3,312 (32.2%)	13,294 (8.3%)	**<0.001**	3,169 (31.5%)	3,268 (0.134%)	0.134
Acute pericarditis	86 (0.8%)	243 (0.2%)	**<0.001**	78 (0.8%)	79 (0.8%)	0.936
Erythema nodosum	44 (0.4%)	780 (0.5%)	0.415	41 (0.4%)	33 (0.3%)	0.351
End-stage renal disease	209 (2.0%)	1,987 (1.2%)	**<0.001**	206 (2.1%)	194 (1.9%)	0.544
Heart failure	3,946 (38.3%)	8,611 (5.4%)	**<0.001**	3,711 (36.9%)	3,745 (37.3%)	0.620
Sarcoidosis of lymph nodes	202 (2.0%)	1,865 (1.2%)	**<0.001**	194 (1.9%)	127 (1.3%)	**<0.001**
Sarcoidosis of lung with sarcoidosis of lymph nodes	458 (4.4%)	2,423 (1.5%)	**<0.001**	427 (4.3%)	147 (1.5%)	**<0.001**
Sarcoidosis of lung	2,914 (28.3%)	21,801 (13.5%)	**<0.001**	2,786 (27.7%)	1,545 (15.4%)	**<0.001**
Sarcoidosis of skin	375 (3.6%)	2,839 (1.8%)	**<0.001**	350 (3.5%)	160 (1.6%)	**<0.001**
Sarcoid meningitis	32 (0.3%)	197 (0.1%)	**<0.001**	27 (0.3%)	12 (0.1%)	**0.016**
Multiple cranial nerve palsies in sarcoidosis	13 (0.1%)	144 (0.1%)	0.232	13 (0.1%)	10 (0.1%)	0.531
Sarcoid iridocyclitis	148 (1.4%)	689 (0.4%)	**<0.001**	138 (1.4%)	33 (0.3%)	**<0.001**
Sarcoid pyelonephritis	10 (0.1%)	**62 (0.0%)**	**0.005**	10 (0.1%)	10 (0.1%)	1
Sarcoid myocarditis	10,296 (100%)	0 (0%)	**<0.001**	10,044 (100%)	0 (0%)	**<0.001**
Sarcoid arthropathy	71 (0.7%)	355 (0.2%)	**<0.001**	67 (0.7%)	23 (0.2%)	**<0.001**
Sarcoid myositis	37 (0.4%)	81 (0.1%)	**<0.001**	35 (0.3%)	10 (0.1%)	**<0.001**
Sarcoidosis, unspecified	6,480 (62.9%)	133,745 (83.1%)	**<0.001**	6,254 (62.3%)	8,154 (81.2%)	**<0.001**
Sarcoidosis of other sites	1,704 (16.6%)	6,504 (4.0%)	**<0.001**	1,609 (16.0%)	530 (5.3%)	**<0.001**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Serological Profiles and Medications Used in Patients with Cardiac Sarcoidosis vs. Other Sarcoidosis

Variable	Before Matching			After Matching		
	Cardiac Sarcoidosis (n = 10,296)	Other Sarcoidosis (n = 160,918)	P-Value	Cardiac Sarcoidosis (n = 10,046)	Other Sarcoidosis (n = 10,046)	P-Value
Laboratory values						
ESR (elevated/normal)	1,403 (13.6%)	18,177 (11.3%)	**<0.001**	1,360 (13.4%)	1,395 (13.8%)	0.473
CRP (elevated/normal)	1,410 (13.7%)	14,982 (9.3%)	**<0.001**	1,363 (13.5%)	1,275 (12.6%)	0.066
Medications						
Prednisone	4,042 (39.3%)	26,143 (16.2%)	**<0.001**	3,808 (37.9%)	3,694 (36.8%)	0.096
Methotrexate	1,174 (11.4%)	2,951 (1.8%)	**<0.001**	946 (9.4%)	897 (8.9%)	0.231
Azathioprine	328 (3.2%)	1,138 (0.7%)	**<0.001**	283 (2.8%)	274 (2.7%)	0.699
Infliximab	249 (2.4%)	394 (0.2%)	**<0.001**	181 (1.8%)	159 (1.6%)	0.229
Adalimumab	174 (1.7%)	735 (0.5%)	**<0.001**	152 (1.5%)	141 (1.4%)	0.517
Etanercept	25 (0.2%)	309 (0.2%)	0.258	24 (0.2%)	27 (0.3%)	0.675

Figure 1A

1 Mortality

Risk analysis

	Cohort	Patients in cohort	Patients with outcome	Risk
1	Sarcoid with myocarditis	10,046	1,017	0.101
2	Sarcoid all - myocarditis excluded	10,046	1,588	0.158

		95% CI	z	p
Risk Difference	-0.057	(-0.066, -0.048)	-11.992	0.000
Risk Ratio	0.640	(0.595, 0.689)	N/A	N/A
Odds Ratio	0.600	(0.552, 0.653)	N/A	N/A

Figure 1B

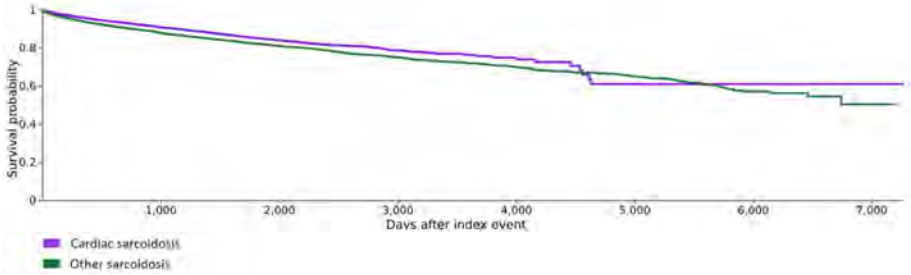


Figure 1A. Mortality Risk Analysis of Patients with Cardiac Sarcoidosis vs. Other Sarcoidosis Figure 1B. Kaplan-Meier Survival Analysis of Mortality in Patients with Cardiac Sarcoidosis vs. Other Sarcoidosis

risk or odds of mortality in the cardiac sarcoidosis group (Figure 1A). Kaplan-Meier survival analysis also showed that the survival probability at the end of study period was higher in those with myocarditis (60.99%) than those without (50.33%) (Figure 1B). The difference was statistically significant (log-rank test $\chi^2 = 33.54$, $p < 0.001$). Cox regression analysis yielded a hazard ratio of 0.79 (95% CI: 0.73–0.86, $p = 0.002$), indicating a 21% lower hazard of death over time in the myocarditis group, with the proportional hazards assumption met.

Conclusion: Black or African American race and several organ-specific sarcoidosis subtypes remained more prevalent in the cardiac sarcoidosis group after matching, suggesting that cardiac sarcoidosis may represent a distinct systemic phenotype with more frequent multiorgan involvement. Contrary to expectations, patients with sarcoid myocarditis demonstrated a lower mortality risk and better survival compared to sarcoidosis patients without myocarditis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Guan: None; **D. Nachawati**: None; **A. Daneshvar**: None; **K. Pfeil**: None; **E. Harper**: None; **L. Frumker**: None; **M. Gump**: None; **V. Nahra**: None; **O. Pamuk**: None.

Abstract Number: 1152

Cutaneous Panniculitis in Rheumatology: A Descriptive Cohort Study from a Multidisciplinary Experience

Claudia Campos-Fabre[1], Carlota Ureta-Moneva[1], Elena Sendagorta[1], Jose Rodríguez-Gago[1], Maria José Beato[1], Agustin Remesal[2], Rosa Alcobendas[1], Clara Udaondo[1], Gema Bonilla[3], Laura Nuño[4], Irene Monjo Henry[2], Carolina Tornero[5] and Chamaida Plasencia-Rodríguez[2], [1]La Paz University Hospital, Madrid, Spain, [2]Hospital Universitario La Paz, Madrid, Spain, [3]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [4]Hospital Universitario Puerta de Hierro, Madrid, Spain, [5]Hospital La Paz, Madrid, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Panniculitis refers to inflammatory disorders of subcutaneous fat that pose diagnostic challenges due to nonspecific clinical features and overlapping histopathological patterns. Although it can occur in immune-mediated diseases (IMIDs), its characterization in rheumatologic settings remains limited. This study aimed to describe the clinical, immunological, histological features and treatments of panniculitis cases jointly evaluated by Rheumatology and Dermatology.

Methods: We conducted a retrospective, observational study of patients diagnosed with panniculitis via electronic health records at Hospital Universitario La Paz between January 2022 and March 2025, during the implementation of a multidisciplinary approach involving adult and pediatric Rheumatology and Dermatology. Patients were identified using the keyword "panniculitis." Data collected included sociodemographics, diagnosis dates, histological pattern (when available), etiology, associated rheumatologic disease, clinical context (initial or subsequent manifestation), lab findings, treatments, and outcomes (remission or recurrence). Statistical analysis was performed using R v4.4.1.

Results: Of 70 patients identified, 63 with cutaneous panniculitis were included (7 pediatric). Most were women (87.3%), with a median age of 49.5 years *(Table 1)*. The leading causes were idiopathic erythema nodosum (EN: 33.3%), Behçet's disease (BD: 11.1%), systemic lupus erythematosus (SLE: 9.5%), infections (15.9%), and sarcoidosis (7.9%).

Panniculitis was the initial manifestation of an IMID in 33.3%. Among BD patients (n=7), it was the first sign in 85.7%; in SLE (n=6), it preceded diagnosis in 50%.

Histopathology was available in 27 cases, with septal panniculitis without vasculitis being most common (55.6%), associated with sarcoidosis, BD, and idiopathic EN. Lobular panniculitis without vasculitis was linked to SLE. Of 35 non-biopsied cases, 26 had idiopathic or infectious causes, likely guiding the decision to omit histology.

Panniculitis achieved remission in 73% (n=46), mainly in idiopathic EN (15) and infectious causes (10), most of whom (98%) responded to symptomatic or antimicrobial therapy. Recurrences occurred in 27% (n=17), linked to idiopathic EN (5), BD (3), SLE (2), autoinflammatory syndrome (AIS: 2), or other IMIDs (5). Of these, 82% required immunomodulatory treatment:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic,clinical, histopathological, therapeutic, and laboratory characteristics of patients with panniculitis (N = 63).

			Total (N= 63)	Behçet (N=7)	SLE (N=6)
Female sex, n/N (%)			55/63 (87.3%)	6/7 (85.7%)	6/6 (100%)
Age (years), median (IQR)			49.5 (34-62)	55 (48-60)	48(36.3–59.8)
BMI (Kg/m2), median (IQR)			25 (22–28.3)	23.4 (21.5–24.7)	24.4 (20,5–30.4)
Never smokers, n/N (%)			48/63 (70.6%)	2/7 (28.6%)	2/6 (33.3%)
Hypertension, n/N (%)			12/63 (17.4%)	1/7 (14.3%)	1/6(16.6%)
Dyslipidemia, n/N (%)			18/63 (26.1%)	2/7 (28.6%)	1/6(16.6%)
T2DM, n/N (%)			6/63 (8.7%)	2/7 (28.6%)	0 (0%)
MI/Stroke, n/N (%)			1/63 (1.5%)	0 (0%)	0 (0%)
CKD, n/N (%)			1/63 (1.5%)	0 (0%)	0 (0%)
Panniculitis as initial manifestation of IMID, n/N (%)			21/63 (33.3%)	6/7 (85.7%)	3/6 (50%)
Time to IMID diagnosis (months), median (IQR)			7 (0-29)	12 (5–22.7)	0 (0-8)
Panniculitis as progression of IMID, n/N (%)			7/63 (11.1%)	1/7 (14.2%)	3/6 (50%)
Time from IMID diagnosis to panniculitis (months), median (IQR)			20 (0-120)	48 (n=1)	86 (67-105)
Cause of panniculitis n/N (%)	Idiopathic EN		21/63 (33.3%)		
	SLE		6/63 (9.5%)		
	Behçet disease		7/63 (11.1%)		
	RA		1/63 (1.6%)		
	SpA		2/63 (3.2%)		
	JIA		1/63 (1.6%)		
	Autoinflammatory disease	Blau	1/63 (1.6%)		
		PAAND	1/63 (1.6%)		
	Sarcoidosis		5/63 (7.9%)		
	IBD	Crohn's disease	2/63 (3.2%)		
		Ulcerative colitis	2/63 (3.2%)		
	TB		3/63 (4.8%)		
	Other infections	*Streptococcus spp.*	6/63 (9.5%)		
		Staphylococcus spp.	1/63 (1.6%)		
	Neoplasia		1 (1.6%)		
	Traumatic		1 (1.6%)		
	Other		2/63 (4.8%)		
Histopathology n/N (%) (total 27)	Septal without vasculitis		15/27 (55.5%)	2/4 (50%)	
	Lobular without vasculitis		9/27 (33.3%)	2/4 (50%)	5/6 (83.3%)
	Lobular with small-vessel vasculitis		2/27 (7.4%)		1/6 (16.6%)
	Septal with large-vessel vasculitis		1/27 (3.7%)		
	Predominant cell type	Histiocytes	15/27 (6%)	4/4 (100%)	
		Lymphocytes	8/27 (32%)		5/6 (83.3%)
		Neutrophils	2/27 (8%)		1/6 (16.6%)
Maximum treatment received, n/N (%)	NSAIDs		13/63 (20.6%)	1/7 (14.3%)	0 (0%)
	Colchicine		2/63 (3.2%)	0 (0%)	0 (0%)
	ATB		6/63 (9.5%)	0 (0%)	0 (0%)
	Prednisone		28/63 (44.4%)	4/7 (57.1%)	2/6 (33.3%)
	c-DMARDs		5/63 (7.9%)	0 (0%)	3/6 (50%)
	b-DMARDs		7/63 (11.1%)	1/7 (14.3%)	1/6 (16.6%)
	Ts-DMARDs		2/63 (3.2%)	1/7 (14.3%)	0 (0%)
Panniculitis remission, n/N (%)			45/63 (72.6%)	4/7 (57.1%)	4/6 (66.6%)
Laboratory Parameters	ACE n/N (%)		6/63 (14.6%)	0 (0%)	0 (0%)
	Quantiferon n/N (%)		3/63 (6.4%)	0 (0%)	0 (0%)
	Baseline CRP, median (IQR)		5,9 (1.1-21.2)	7 (0.6–17.3)	0.5 (0.5 .1)
	Baseline ESR, median (IQR)		11 (7.2-34.8)	8 (4.6–11)	9.5 (6-16.7)
Immunological Markers n/N (%)	RF		3/63 (5.7%)	0 (0%)	0 (0%)
	ACPA		1/63 (1.6%)	0 (0%)	0 (0%)
	ANA		15/63 (23.8)	2/7 (28.6%)	3/6 (50%)
	Anti-dsDNA		0/63 (0%)	0 (0%)	0 (0%)
	aPL		4/63 (6.3%)	1/7 (14.3%)	1/6 (16.6%)
	ACA		2/63 (3.2%)	0 (0%)	2/6 (33.3%)
	Anti-Ro (SSA)		1/63 (1.6%)	0(0%)	0 (0%)
	Anti-La (SSB)		0/63 (0%)	0 (0%)	0 (0%)
	Anti-RNP		0/63 (0%)	0 (0%)	0 (0%)
	Anti-Sm		0/63 (0%)	0 (0%)	1/6 (16.6%)
	Anti-MPO		1/63 (1.6%)	0 (0%)	0 (0%)
	Anti-PR3		0/63 (0%)	0 (0%)	0 (0%)
	Anti-SCL7-0		0/63 (0%)	0 (0%)	0 (0%)
	Anti-ACA		2/63 (3.3%)	0 (0%)	2/6 (33%)
	HLA-B27		3/63 (7.3%)	0 (0%)	0 (0%)
	HLA-B51		6/63 (15%)	4/7 (57.1%)	0 (0%)

Table 1. Demographic,clinical, histopathological, therapeutic, and laboratory characteristics of patients with panniculitis (N = 63).

Data are presented as n/N (%) or median (interquartile range, IQR). ***Abbreviations:*** *EN = erythema nodosum; SLE = systemic lupus erythematosus; RA = rheumatoid arthritis; SpA = spondyloarthritis; JIA = juvenile idiopathic arthritis; AID = autoinflammatory disease; PAAND: aPyrin-Associated Autoinflammation with Neutrophilic Dermatosis; IBD = inflammatory bowel disease; TB = tuberculosis; NSAIDs = nonsteroidal anti-inflammatory drugs; ATB = antibiotics; c-DMARDs = conventional synthetic disease-modifying antirheumatic drugs; b-DMARDs = biologic DMARDs; ts-DMARDs = targeted synthetic DMARDs; ACE = angiotensin-converting enzyme; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; CKD = chronic kidney disease; T2DM = type 2 diabetes mellitus; MI = myocardial infarction; IQR = interquartile range.*

c-DMARDs (n=6) and b/s-DMARDs (n=8). All received b/s-DMARDs except one patient with juvenile idiopathic arthritis who underwent four treatment lines. Biologic and targeted therapies included TNF inhibitors (n=6), anifrolumab (n=1), anti-IL1 (n=1), anti-IL6 (n=1), anti-CD20 (n=1), and JAK inhibitors (n=2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

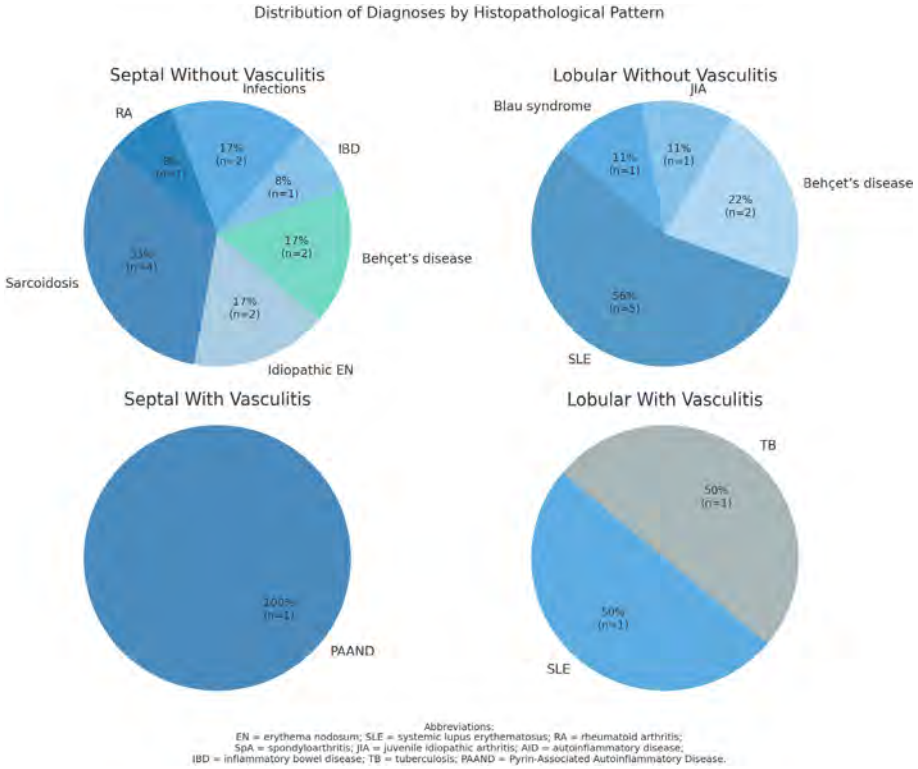


Figure 1. Distribution of diagnoses by histopathological pattern.

Conclusion: Cutaneous panniculitis may be an early or evolving feature of systemic IMIDs, particularly BD and SLE. While idiopathic and infectious cases often remit with symptomatic or antimicrobial therapy, recurrent or immune-mediated forms typically require immunosuppression, including biologics and JAK inhibitors. Multidisciplinary evaluation improves diagnostic accuracy and treatment individualization in complex cases.

Disclosure: C. Campos-Fabre: None; **C. Ureta-Moneva**: None; **E. Sendagorta**: None; **J. Rodríguez-Gago**: None; **M. Beato**: None; **A. Remesal**: None; **R. Alcobendas**: None; **C. Udaondo**: None; **G. Bonilla**: None; **L. Nuño**: None; **I. Monjo Henry**: None; **C. Tornero**: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6.

Abstract Number: 1153

New Disease Classification in the Block? A 5-year Retrospective Review on Clinical Profiles and Mortality Outcomes of Patients Presenting with Hematoinflammatory Syndromes at a University Center in Florida

Cristine Kuzhuppilly Arcilla[1], Gabriel Kirsch[2], Michael Cargill[2] and Gurjit Kaeley[3], [1]University of Florida Jacksonville, Jacksonville, FL, [2]University of Florida - Jacksonville, Jacksonville, FL, [3]UF COM-J, Ponte Vedra Beach, FL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The novel diagnosis of VEXAS in 2020 led to the proposed possibility of a new category of hematoinflammatory syndromes linking clinically overlapping hematologic and autoinflammatory diseases with multiorgan involvement, laboratory and histopathologic features, and genetic mutation in parallel to the clinical picture of VEXAS syndrome and hemophagocytosis (HLH/MAS)[1, 2]. Lack of definition and standard of care diagnostic and treatment algorithms for this subset of diagnoses pose critical complexities and challenges, given their high morbidity and mortality, hence the need for understanding these disease entities to improve patient outcomes. This study aims to review baseline disease characteristics, diagnostic and treatment approaches, and outcomes at our academic center.

Methods: This is IRB-approved retrospective analysis on all patients 18-89 years old with hematoinflammatory manifestations at University of Florida between 01/01/2020 to 03/31/2025. IDR analysis obtained 162 patients with ICD-10-specific codes for HLH/MAS/VEXAS (D76.1,.3,.2;M04.1,.2,.8,.9) for individual chart review. Inclusion criteria were determined by clinicians' discretion for diagnosis based on HLH 2004/MAS 2016 criteria, histopathology, and/or genetic tests. Subsequent data was collected and analyzed.

Results: Baseline characteristics are summarized (Table 1), with 23 patients meeting criteria for hematoinflammatory diagnosis. Mean age at diagnosis was 40 years. Mean duration of symptoms was 16.35 weeks before diagnosis. Majority were Caucasian(43%), male(57%), and younger age of < 50 years (61%). Most common underlying diagnoses are autoimmune diseases(48%), infection (30%), primarily Epstein-Barr virus (EBV), followed by hematologic etiologies (17%). Constitutional symptoms, such as fever and fatigue, and hematologic findings were present in all patients (Figure 1); gastrointestinal, lymphadenopathy, and dermatologic symptoms in 40%; 91% had at least 3 organ systems involved upon initial presentation. Diagnoses were mainly HLH (48%) and MAS (35%) with fever, elevated ferritin (mean,14,186ng/ml), and cytopenias as most common presentation. Biopsy(78%) and genetic testing (43%)revealed 7 with positive vacuoles and

Table 1. Baseline characteristics of the study population. SLE, Systemic Lupus Erythematosus; LN, Lupus Nephritis; APLS, Antiphospholipid Antibody Syndrome; AOSD, Adult Onset Still's Disease; EBV, Epstein-Barr virus; MGUS, Monoclonal Gammopathy of Undetermined Significance; ITP, Idiopathic Thrombocytopenic Purpura; DMARDs, Disease-modifying antirheumatic drugs; TNF, Tumor Necrosis Factor; HLH, Hemophagocytic lymphohistiocytosis; MAS, Macrophage activation syndrome; VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic); MDS, Myelodysplastic syndrome.

Baseline Characteristics	N-23 (%)
Age, years	Mean age at diagnosis- 40 [<50 -14 (61%); >50 -9 (39%)]
Sex	Male -13 (57%) ; Female -10 (43%)
Race	Caucasian - 10 (43%); Others [Black-7 (30%); Unknown - 6 (26%)]
Clinical presentations	Mean duration of hematoinflammatory symptoms before diagnosis- 16.35 weeks (<1 week-3; ≥1-4 weeks -7; >4 weeks -7; ≥6 months -5 (>2 years-1) Number of Organ Systems Involved -2 systems-2 (9%), >3systems- 21 (91%)
Underlying or previous diagnosis and previous treatments	Underlying or previous diagnosis Autoimmune Diseases -11 (48%) (SLE 2; SLE + LN -2; SLE + LN + APLS -1; JRA/JIA - 2; RA -1; AOSD -2; Sarcoidosis -1) Infection -7 (30%) (EBV-6, Ehrlichiosis-1) Post surgical -1 (4%) (Renal transplant) Hematologic Disease -4 (17%) (MGUS -1; ITP 1; T cell lymphoma-1, Non Hodgkin lymphoma-1) Previous Treatments None - 2 (9%) Glucocorticoids -5 (22%) Conventional DMARDs-18 (78%) (Methotrexate-6; Leflunomide-1;Sulfasalazine-2;Hydroxychloroquine-9) Biologic DMARDs -15 (65%) (Anti-TNF-6, Anakinra -3; Jakinib-2;Seculunumab -1;Abatacept -1;Rituximab -1;Belimumab-1) Others -9 (39%) (Azathioprine-3; Cyclosporine 1; Cyclophosphamide-2; Mycophenolate -2;Colchicine -1)
Diagnosis	HLH-11 (48%) MAS - 8 (35%) VEXAS -2 (9%) Autoinflammatory Syndrome -2 (9%) (Hughs-Stovin Syndrome and +BRAF genetic mutation with unknown significance)
Number of patients/ percentage based on individual parameters from HLH/MAS criteria	Fever - 23 (100%) Splenomegaly -10 (43%) Cytopenias -19 (83%) Hypertriglyceridemia - 11 (48%) Hypofibrinogenemia - 7 (30%) Hemophagocytosis in bone marrow or spleen or lymph nodes-7 (30%) Low or absent natural killer cell activity- 3 (13%) Serum Ferritin-20 (87%) Soluble IL-2 receptor -13 (57%) Genetic mutation - 0
Diagnostic evaluation completed	Genetic test- 10 (43%) Positive - 3 (2 UBA1; 1 BRAF mutations) Histopathology (bone marrow, lymph node) -18 (78%) Positive - 12 (vacuoles, hemophagocytes-7; Low grade MDS- 2; Granuloma- 3 Not done (unstable status) -2 Mean ferritin level (ng/ml) - 14,186.75 (500-2000- 1; 2000-<5000-8; >5000-10,000-4; >10000-6; >50000-100,000-1)
Treatments received upon diagnosis	Medical-23 (100%) Surgical-1 (allogenic)- with resolution of symptoms; splenectomy (1)
Outcomes	Death - 3; Home hospice-1 Mean length of stay, in days - 4.65 weeks (<1 week-3; 1-4 weeks-11; >4-8 weeks-3; >8 weeks-6)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

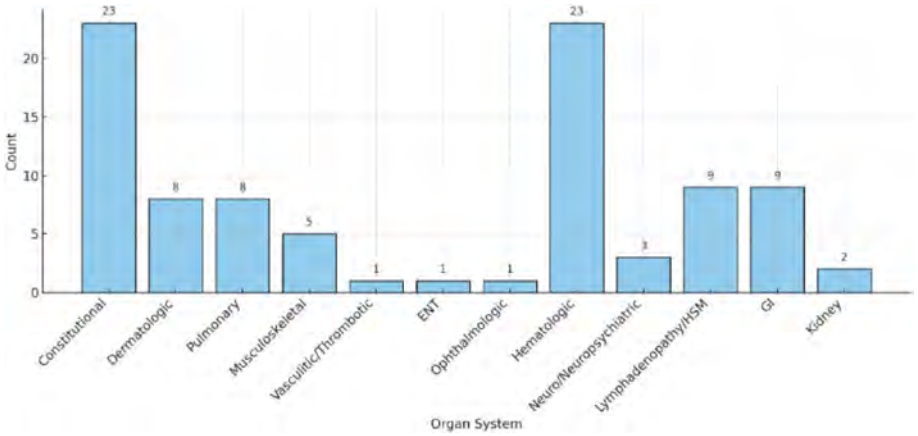


Figure 1. Frequencies of system-based organ manifestations present in our patients with hematoinflammatory syndromes.

Treatment Received Following Hematoinflammatory Diagnosis	N (%)
Glucocorticoids	23 (100%)
Anakinra	10 (43%)
Etoposide	6 (26%)
IVIg	5 (22%)
Tocilizumab	3 (13%)
Rituximab	3 (13%)
Emapalumab (anti-IFN-γ antibody)	2 (9%)
Anti-TNF	2 (9%)
Ruxolitinib	2 (9%)
Azathioprine	1 (4%)
Tacrolimus	1 (4%)
IV Cyclophosphamide	1 (4%)
PLEX	1 (4%)

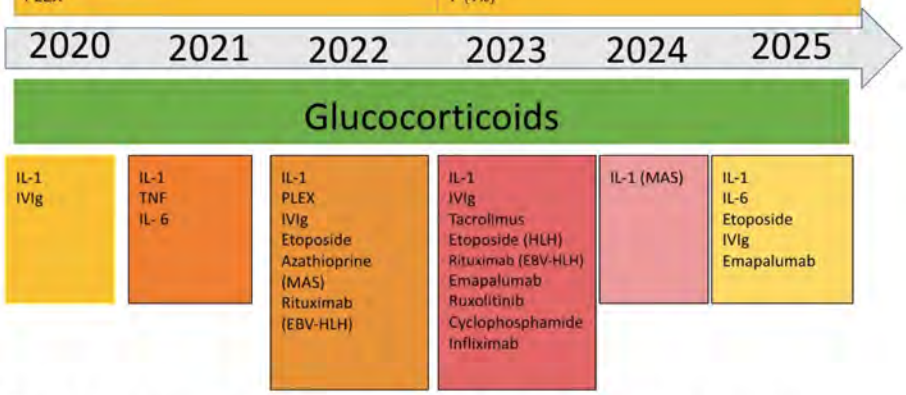


Figure 2. Treatment received with corresponding number of patients and prevailing treatment approaches over past 5 Years following hematoinflammatory diagnosis

Figure 2. Treatment received with the corresponding number of patients and prevailing treatment approaches over the past 5 Years following hematoinflammatory diagnosis.

hemophagocytes; 1 with MDS diagnosed with VEXAS after genetic confirmation, and only revealed vacuoles with repeat biopsy after 3 months. Previous treatments comprised majority with csDMARDs.Figure 2 outlines the treatments received following diagnosis-glucocorticoid (100%), Anakinra (43%), and Etoposide (26%). Mean length of stay before discharge was 4 weeks;3 patients died due to infections and hospital complications.

Conclusion: This study provides a heterogeneous presentation of hematoinflammatory syndromes at our center. Due to diagnostic complexities and multiorgan manifestations, clinicians must be cognizant of their broader definitions, familiarize with their most frequent diagnostic associations, and monitor disease indicators (e.g., serial serum ferritin levels, biopsy, etc), if with high clinical suspicion. This leads to earlier recognition and more optimal therapeutic strategies for hematoinflammatory syndromes to improve clinical outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Kuzhuppilly Arcilla: None; **G. Kirsch**: None; **M. Cargill**: None; **G. Kaeley**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Janssen, 5, Novartis, 5.

Abstract Number: 1154

Assessment of Damage Using the igg4-related Disease Damage Index

Eduardo Martin-Nares[1] and Gabriela Hernandez-Molina[2], [1]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Federal District, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic fibroinflammatory disorder affecting multiple organs, often leading to irreversible damage. Standardized tools like the IgG4-RD Damage Index (DI) are crucial for understanding disease progression and phenotype-specific characteristics, but their performance remains untested in non-Chinese populations. This study aimed to assess damage in Mexican IgG4-RD patients using the IgG4-RD DI.

Methods: We conducted a retrospective study of patients with IgG4-RD who met the 2020 Revised Comprehensive Diagnostic Criteria and/or the 2019 ACR/EULAR Classification Criteria for IgG4-RD. All patients were followed for at least one year. Damage was defined as irreversible organ dysfunction or failure caused by IgG4-RD or by procedures performed for its diagnosis or treatment and persisted for at least six months. Damage was assessed using the IgG4-RD DI at the last follow-up.

Results: We included 70 patients with a mean age of 52.1 ± 15.6 years, of whom 34 (48.6%) were male. The median duration of disease (from symptom onset to last follow-up) was 77.5 months (IQR 54–133).

At the last follow-up, organ damage was detected in 56 patients (80%) based on the IgG4-RD RI. The median DI score for the entire cohort was 1 (IQR 0–3), while for patients with damage it was 2 (IQR 1–3; range 1–9). Figure 1 shows the distribution of IgG4-RD DI scores. The most frequently affected organ-specific domains of the IgG4-RD DI were 'Pancreas' (31.4%), 'Lung' (15.7%), 'Kidney' (11.4%), 'Retroperitoneum/mediastinum' (8.6%), and 'Liver/biliary tree' (8.6%). The 'Others' domain was scored in 26 patients (37.1%), primarily due to partial or total organ resection related to IgG4-RD (22.8%), disease-related or treatment-related diabetes mellitus (15.7%), and damage in other organs (14.3%).

Patients with the head and neck-limited phenotype had lower DI scores (p=0.05). The 'Retroperitoneum/mediastinum' domain was scored more frequently in the retroperitoneal/aortic phenotype (p< 0.001), while the 'Pancreas' domain was scored more frequently in the pancreato-biliary and Mikulicz/systemic phenotypes (p=0.001). The 'Kidney' domain was more commonly scored in the retroperitoneal/aortic phenotype (p=0.01), due to obstructive nephropathy. The proliferative phenotype had more commonly damage in the 'Pancreas' domain (p=0.01), while the fibrotic phenotype in the 'Retroperitoneum/mediastinum' (p< 0.001) and 'Thyroid' domains (p=0.02). There were no significant differences in DI scores or domain involvement between men and women.

Comparing patients with and without damage (Table 1), the former group was less likely to have the head and neck-limited phenotype (20.4% vs. 56.3%, p=0.005; OR: 0.16), and more likely to have elevated IgG levels (60.9% vs. 31.3%, p=0.04; OR: 4.67).

Conclusion: Organ damage is frequent in IgG4-RD, varies by phenotype, and is most common in the pancreas. Elevated IgG levels increase damage risk, while the head and neck-limited phenotype is protective. Organ resections for diagnostic or therapeutic purposes and glucocorticoid toxicity are key contributors to cumulative damage in IgG4-RD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

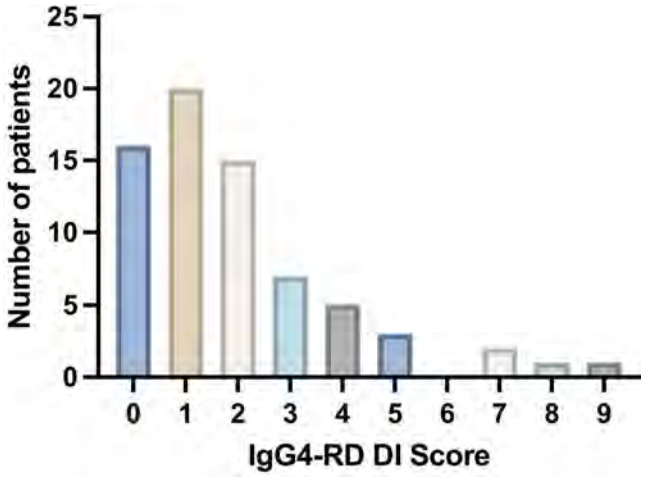


Figure 1. Distribution of the IgG4-RD DI scores

Table 1. Characteristics of patients with damage vs. no damage.

Table 1	Damage N=54	No damage N=16	p
Male, n (%)	25 (48.1)	9 (50)	0.88
Disease duration, median (IQR), months	83.5 (61.5-134.5)	62 (33-94)	0.09
Time to diagnosis, median (IQR), months	22 (5-60)	10 (5-28)	0.28
Clinical phenotype			
Pancreato-biliary, n (%)	15 (27.8)	2 (12.5)	0.21
Retroperitoneal/aortic, n (%)	6 (11.1)	1 (6.3)	0.56
Head and neck-limited, n (%)	11 (20.4)	9 (56.3)	0.005
Mikulicz/systemic, n (%)	19 (35.2)	2 (12.5)	0.08
Undefined, n (%)	3 (5.6)	2 (12.5)	0.34
Proliferative, n (%)	38 (70.4)	12 (75)	0.71
Fibrotic, n (%)	16 (29.6)	4 (25)	0.71
High IgG, n+/n (%)	28/46 (60.9)	5/16 (31.3)	0.04
High IgG4, n (%)	34 (65.4)	12 (66.7)	0.92
Low C3, n+/n (%)	13/36 (36.1)	3/16 (18.8)	0.21
Low C4, n+/n (%)	18/36 (50)	6/16 (37.5)	0.40
Remission, n (%)	37 (68.5)	11 (68.8)	0.98
Relapse, n (%)	22 (40.7)	8 (50)	0.51

Disclosure: E. Martin-Nares: None; **G. Hernandez-Molina**: None.

Abstract Number: 1155

Zasocitinib (TAK-279), an Investigational, Oral, Allosteric, Selective TYK2 Inhibitor, in Moderate-to-Severe Plaque Psoriasis: Efficacy Analysis by Baseline Characteristics from a Randomized Phase 2b Trial

Nada Elbuluk[1], Melinda J. Gooderham[2], Jessamyn Blau[3], Wenwen Zhang[3], **Ejim Mark**[3], Warren Winkelman[3] and Mark Lebwohl[4], [1]Department of Dermatology, USC Keck School of Medicine, Los Angeles, CA, [2]SKiN Centre for Dermatology, Queen's University, & Probity Medical Research, Peterborough, ON, ON, Canada, [3]Takeda Development Center Americas, Inc., Cambridge, MA, [4]Icahn School of Medicine at Mount Sinai, New York, NY

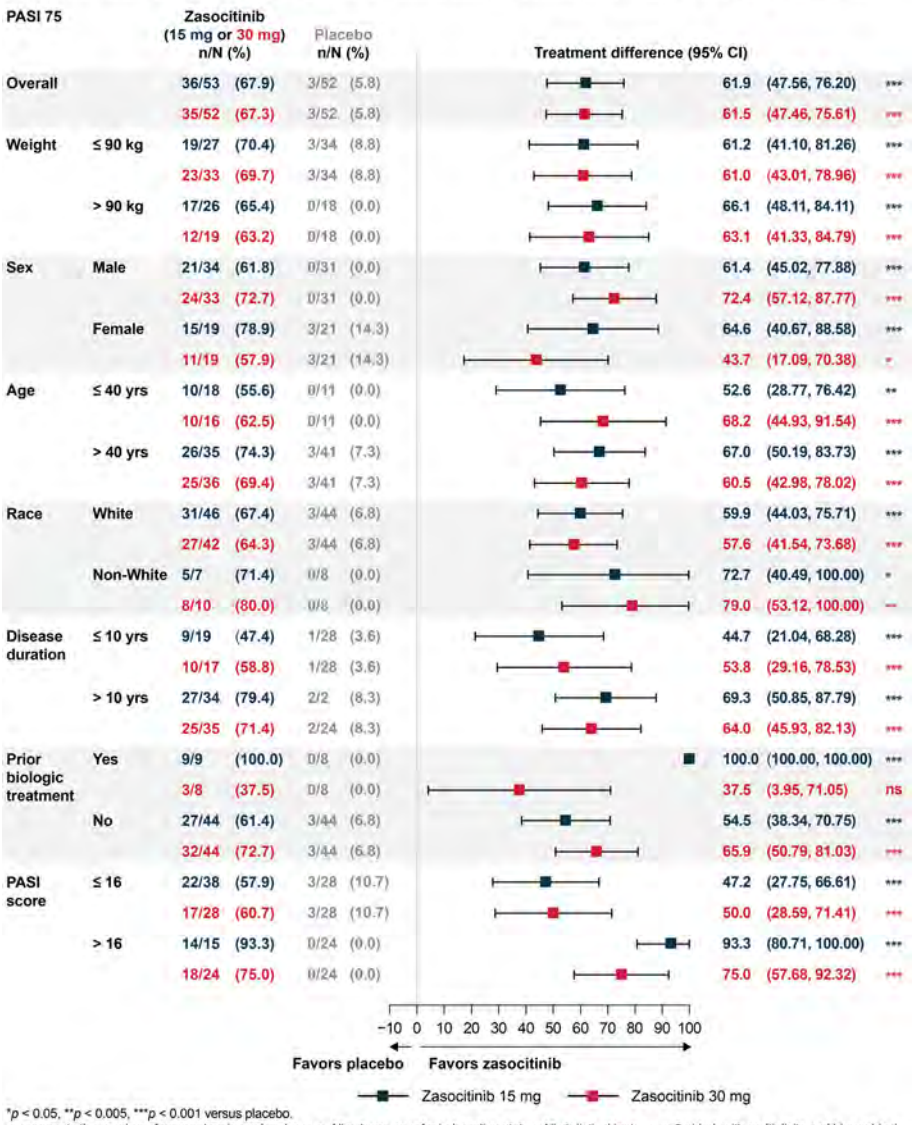
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Zasocitinib (TAK-279) is an investigational, highly selective and potent, oral, allosteric tyrosine kinase 2 (TYK2) inhibitor. In a phase 2b trial of moderate-to-severe plaque psoriasis, the primary endpoint (psoriasis area and severity index [PASI] 75 response at Week 12) was met with zasocitinib 5 mg, 15 mg and 30 mg once daily; 33% of patients receiving zasocitinib 30 mg achieved PASI 100. The objective of this *post hoc* analysis was to evaluate the influence of baseline characteristics on zasocitinib efficacy in patients with plaque psoriasis.

Figure. PASI 75 response rates were significantly greater in patients treated with zasocitinib 15 mg or 30 mg than in those receiving placebo across all subgroups except for patients receiving zasocitinib 30 mg who had prior biologic treatment.



*$p < 0.05$, **$p < 0.005$, ***$p < 0.001$ versus placebo.
n represents the number of responders in each subgroup. All subgroups refer to baseline status. All statistical tests were 2-sided, with multiplicity and hierarchical testing completed on the primary endpoint only; *p* values for all subgroup analyses are nominal. Owing to the small number of patients in some of the subgroups, data comparisons should be interpreted with caution in some instances.
CI, confidence interval; ns, not significant; PASI, Psoriasis Area and Severity Index.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This phase 2b, randomized, multicenter, double-blind, placebo (PBO)-controlled, multiple-dose study (NCT04999839) included *post hoc* analyses of Week 12 PASI 75/90/100 responses, Physician Global Assessment (PGA) scores (clear [0] or almost clear [1]) and Dermatology Life Quality Index (DLQI) scores stratified by weight, sex, age, race, disease duration, prior biologics use and baseline PASI. Treatment differences (zasocitinib versus PBO) for all subgroups except prior biologic treatment were calculated using the Mantel–Haenszel method; 95% confidence intervals and *p* values were calculated using the Wald method and Cochran–Mantel–Haenszel test (stratified for prior biologic treatment), respectively. Treatment difference estimates were unadjusted for the subgroup analysis by prior biologic treatment; *p* values were calculated using a chi-square test. For DLQI, a mixed model for repeated measures was used to calculate the least-squares mean, with treatment, visit, treatment-by-visit interaction and prior biologic treatment (not included for the subgroup analysis by prior biologic treatment) as fixed effects and baseline score as the covariate.

Results: Overall, 259 patients were included in this study. PASI 75 response rates with zasocitinib were greater than PBO regardless of **weight** (≤ 90kg: PBO, 8.8%; 15 mg, 70.4%; 30 mg, 69.7%; > 90kg: PBO, 0%; 15 mg, 65.4%; 30 mg, 63.2%, each $p < 0.001$), **sex** (male: PBO, 0%; 15 mg, 61.8%; 30 mg, 72.7%, each $p < 0.001$; female: PBO, 14.3%; 15 mg, 78.9% [$p < 0.001$]; 30 mg, 57.9% [$p < 0.005$]), **age** (≤ 40 years: PBO, 0%; 15 mg, 55.6% [$p < 0.01$]; 30 mg, 62.5% [$p < 0.001$]; > 40 years: PBO, 7.3%; 15 mg, 74.3%; 30 mg, 69.4%, each $p < 0.001$), **race** (White: PBO, 6.8%; 15 mg, 67.4%; 30 mg, 64.3%, each $p < 0.001$; non-White: PBO, 0%; 15 mg, 71.4% [$p < 0.01$]; 30 mg, 80.0% [$p < 0.005$], **disease duration** (≤ 10 years: PBO, 3.6%; 15 mg, 47.4%; 30 mg, 58.8%; > 10 years: PBO, 8.3%; 15 mg, 79.4%; 30 mg, 71.4%, each $p < 0.001$), **prior biologics use** (yes: PBO, 0%; 15 mg, 100% [$p < 0.001$]; 30 mg, 37.5% [$p = 0.055$, not significant]; no: PBO, 6.8%; 15 mg, 61.4%; 30 mg, 72.7%, each $p < 0.001$) and **baseline PASI** (≤ 16: PBO, 10.7%; 15 mg, 57.9%; 30 mg, 60.7%; > 16: PBO, 0%; 15 mg, 93.3%; 30 mg, 75.0%, each $p < 0.001$; **Figure**). PASI 90, PASI 100, PGA 0/1 and DLQI generally improved with zasocitinib treatment versus PBO in almost all subgroups.

Conclusion: Treatment with zasocitinib 15 mg or 30 mg led to greater response rates at Week 12 versus PBO in patients with moderate-to-severe plaque psoriasis, for nearly all baseline characteristics assessed. Phase 3 trials (NCT06088043 and NCT06108544) are ongoing to investigate the efficacy and safety of zasocitinib in larger patient groups.

Disclosure: N. Elbuluk: AbbVie/Abbott, 1, 2, 6, Allergan, 1, 2, 6, Avita, 1, 2, 6, Beiersdorf, 1, 2, 6, Canfield, 1, 2, 6, Dior, 1, 2, 6, Eli Lilly, 1, 2, 6, Galderma, 1, 2, 6, Incyte, 1, 2, 6, Janssen, 1, 2, 6, Kao, 1, 2, 6, La Roche Posay, 1, 2, 6, L'Oreal, 1, 2, 6, McGraw Hill, 1, 2, 6, 9, Medscape, 1, 2, 6, Pfizer, 1, 2, 5, 6, Sanofi, 1, 2, 6, Takeda, 1, 2, 6, Unilever, 1, 2, 6, VisualDx, 1, 2, 6, 11; **M. Gooderham**: AbbVie, 12,, 1, 6, Akros, 12,, 1, 6, Amgen, 12,, 1, 6, AnaptysBio, 12,, 1, 6, Apogee, 12,, 1, 6, Arcutis Biotherapeutics, 12,, 1, 6, Aristea, 12,, 1, 6, Aslan, 12,, 1, 6, Bausch Health, 12,, 1, 6, Boehringer-Ingelheim, 12,, 1, 6, Bristol-Myers Squibb(BMS), 12,, 1, 6, Celgene, 12,, 1, 6, Dermavant, 12,, 1, 6, Dermira, 12,, 1, 6, Eli Lilly, 12,, 1, 6, Galderma, 12,, 1, 6, GlaxoSmithKlein(GSK), 12,, 1, 6, Incyte, 12,, 1, 6, Inmagene, 12,, 1, 6, JAMP, 12,, 1, 6, Janssen, 12,, 1, 6, Kyowa Kirin, 12,, 1, 6, LEO Pharma, 12,, 1, 6, MedImmune, 12,, 1, 6, Meji, 12,, 1, 6, Merck, 12,, 1, 6, MoonLake Immunotherapeutics, 12,, 1, 6, Nimbus, 12,, 1, 6, Novartis, 12,, 1, 6, Pfizer, 12,, 1, 6, Regeneron, 12,, 1, 6, Roche, 12,, 1, 6, Sanofi Genzyme, 12,, 1, 6, Sun Pharma, 12,, 1, 6, Takeda, 12,, 1, 6, Tarsus Pharmaceuticals, 12,, 1, 6, UCB, 12,, 1, 6, Union Therapeutics, 12,, 1, 6, Ventyx Biosciences, 12,, 1, 6, Vyne Therapeutics, 12,, 1, 6; **J. Blau**: Takeda Development Center Americas, Inc., 3; **W. Zhang**: Takeda Development Center Americas, Inc., 3, 11; **E. Mark**: Takeda Development Center Americas, Inc., 3, 11; **W. Winkelman**: Takeda Development Center Americas, Inc., 3, 11; **M. Lebwohl**: AbbVie, 5, Almirall, 2, AltruBio Inc, 2, Apogee Therapeutics, 2, Arcutis Biotherapeutics, 2, 5, AstraZeneca, 2, Atomwise, 2, Avotres, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, Cara Therapeutics, 5, Castle Biosciences, 2, Celltrion Biosciences, 2, Clexio Biosciences, 5, CorEvitas, 2, Dermavant, 2, 5, Dermsquared, 2, Eli Lilly, 5, Evommune, Inc, 2, Facilitation of International Dermatology Education, 2, Forte Biosciences, 12, Facilitation of International Dermatology Education, Galderma, 12, Facilitation of International Dermatology Education, Genentech, 12, Facilitation of International Dermatology Education, Incyte, 5, 12, Facilitation of International Dermatology Education, Inozyme, 5, Janssen, 5, LEO Pharma, 12, Facilitation of International Dermatology Education,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Meiji Seika Pharma, 12, Facilitation of International Dermatology Education, Mindera, 12, Facilitation of International Dermatology Education, Mirium Pharmaceuticals, 2, Mount Sinai, 3, Pfizer, 5, 12, Facilitation of International Dermatology Education, Sanofi-Regeneron, 5, 12, Facilitation of International Dermatology Education, Seanergy, 12, Facilitation of International Dermatology Education, Strata, 12, Facilitation of International Dermatology Education, Takeda, 12, Facilitation of International Dermatology Education, Trevi Therapeutics, 12, Facilitation of International Dermatology Education, UCB, 5, Verrica Pharmaceuticals, 2.

Abstract Number: 1156

Incidence and Prevalence of Interstitial Pneumonia with Autoimmune Features in a Population-Based Cohort

Elena Joerns[1], Sara Achenbach[1], Cynthia Crowson[2], eva carmona[1], Robert Vassallo[3], John Joerns[1], Vanessa Kronzer[3], John Davis[3] and Elena myasoedova[3], [1]Mayo Clinic, Rochester, [2]Mayo Clinic, Stewartvillle, MN, [3]Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial pneumonia with autoimmune features (IPAF) is a type of interstitial lung disease (ILD) with features of autoimmunity, yet patients do not fulfill criteria for any defined systemic autoimmune rheumatic diseases (SARDs) (1). Classification of IPAF requires the presence of interstitial pneumonia and presence of features from at least two of three domains: serological (specific autoantibodies), clinical (signs and symptoms which may be seen in SARDs) and morphological (imaging or biopsy features within the thorax suggestive of ongoing inflammation) (1). While previously thought to be rare

Table 1: Baseline characteristics of the incident IPAF cohort *Elevated above laboratory reference level IPAF – interstitial pneumonia with autoimmune features; SD – standard deviation; UIP – usual interstitial pneumonia

Table 1: Baseline characteristics of the incident IPAF cohort

Baseline characteristic	Total (N=33) n(%)/mean [SD]
Female sex	22 (67)
Age at IPAF incidence, years	70.6 [14.8]
White race	30 (91)
Hispanic ethnicity	0 (0)
Serological domain met	28 (85)
ANA*	13 (39)
RNP	7 (21)
CCP	9 (27)
RF*	6 (18)
dsDNA	3 (9)
SSA	2 (6)
Scl-70	1 (3)
Jo-1	1 (3)
PL-7	2 (6)
OJ	1 (3)
MDA-5	1 (3)
MPO/p-ANCA	4 (12)
Clinical domain met	13 (39)
Raynaud's	13 (39)
Inflammatory arthritis	3 (9)
Morphological domain met	33 (100)
Non-UIP radiographic pattern	31 (94)
Airway involvement in non-smoker	8 (24)
Pleural or pericardial effusion	13(39)
Pulmonary hypertension	6 (18)

*Elevated above laboratory reference level

IPAF – interstitial pneumonia with autoimmune features; SD – standard deviation; UIP – usual interstitial pneumonia

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Incidence rates for IPAF *Age- and sex- adjusted to the United States White population (USW2020) IPAF - interstitial pneumonia with autoimmune features

Table 2: Incidence rates for IPAF

	Incident patients			-Incidence Rate- (per 100,000)		
Age	F	M	Tot	Female	Male	Total
18-29	0	0	0	0.0	0.0	0.0
30-39	2	0	2	1.7	0.0	0.9
40-49	1	0	1	1.1	0.0	0.5
50-59	4	1	5	3.7	1.0	2.4
60-69	3	2	5	3.8	2.9	3.3
70-79	7	4	11	14.3	9.9	12.3
80-110	5	4	9	13.9	17.2	15.2
Total*	22	11	33	3.9 (2.2-5.5)	2.5 (1.0-4.0)	3.2 (2.1-4.3)

*Age- and sex- adjusted to the United States White population (USW2020)

IPAF - interstitial pneumonia with autoimmune features

(2), a recent study revealed that 31% of ILD patients undergoing lung transplant are classified as IPAF (3). Studies of IPAF are limited by its lack of diagnostic criteria and propensity to be studied only at large tertiary referral centers. There are therefore no population-based studies of IPAF, which limits our understanding of its incidence and prevalence.

Methods: We conducted a population-based study to establish the incidence and prevalence of IPAF in a geographically defined area between 2010-2019. Prevalence was calculated on January 1st, 2020. We screened all patients with 2+ ILD codes as well as abnormal autoimmune serologies and/or 2+ codes for Raynaud's syndrome. We excluded all patients with 2+ SARD codes. We performed manual chart review and radiographic review to validate IPAF classification criteria (1) and presence of ILD. We collected data on the presence and specific features of each of the three domains included in IPAF classification: serological, clinical, and morphological (1). Date of IPAF incidence was considered the date of first ILD diagnosis. Descriptive statistics were utilized to describe the baseline characteristics of the cohort. Age- and sex-specific incidence rates were calculated using the number of incident cases as the numerator and census estimates as the denominator. Overall incidence rates were age- and/or sex-adjusted to the 2020 white population of the USA. Confidence intervals for incidence rates were obtained by assuming that the number of incident cases followed a Poisson distribution.

Results: After manual review, a total of 33 patients had confirmed incident IPAF. Table 1 describes the baseline features of those with incident IPAF. The incidence of IPAF was greater in women than in men and increased with age (Table 2). Overall, the annual sex-and age-adjusted IPAF incidence was 3.2 per 100,000 persons. On January 1, 2020, there were 30 patients with prevalent IPAF corresponding to a sex- and age-adjusted IPAF prevalence rate of 26 per 100,000 persons.

Conclusion: To our knowledge, this is the first population-based cohort study of IPAF incidence and prevalence. IPAF is a rare disease, with low prevalence and low incidence rates which are higher in women than men and increase with age. Future studies will expand on the cohort and will include study of phenotypes among IPAF patients and relationship with clinical outcomes.

References:

1. Fischer A, Antoniou KM, Brown KK, Cadranel J, Corte TJ, du Bois RM, et al. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. Eur Respir J. 2015;46(4):976-87.
2. Oldham JM, Adegunsoye A, Valenzi E, Lee C, Witt L, Chen L, et al. Characterisation of patients with interstitial pneumonia with autoimmune features. Eur Respir J. 2016;47(6):1767-75.
3. Joerns EK, De Las Casas L, Banga A, Kaza V, Torres F, Mahan L, Lawrence A TI, Mohanka M, Joerns J. Interstitial pneumonia with autoimmune features is prevalent among lung transplant recipients. European Congress of Rheumatology (submitted abstract): EULAR; 2024.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Joerns: Boehringer-Ingelheim, 1; **S. Achenbach**: None; **C. Crowson**: None; **e. carmona**: Boehringer-Ingelheim (SEPAR), 6, vitalograph, 6; **R. Vassallo**: Regeneron, 6, Rion LLC, 11, Sanofi, 2; **J. Joerns**: None; **V. Kronzer**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **E. myasoedova**: None.

Abstract Number: 1157

Safety and Tolerability of a Recombinant Zoster Vaccine in Patients with Inflammatory Rheumatic Musculoskeletal Diseases: A Prospective Longitudinal Study over 12 Months

Ella Steiner[1], Ioana Andreica[2], Stefanie Reale[3], Gianna Chierego[4], Philipp Köhler[5], Sonja Zapke[4], Benjamin Wilde[6], David Kiefer[7], Philipp Sewerin[2], Hilal Kavruk[5], Dimitra Karagkiozidou[5], Panagiotis Ermeidis[5], Barbara Guminski[5], Andreas Kribben[6], Jürgen Braun[8], Xenofon Baraliakos[9] and Uta Kiltz[9], [1]Rheumazentrum Ruhrgebiet Herne, Herne, Nordrhein-Westfalen, Germany, [2]Rheumazentrum Ruhrgebiet Herne; Ruhr-Universität Bochum, Germany, Herne, Germany, [3]Rheumazentrum Ruhrgebiet, Herne, Nordrhein-Westfalen, Germany, [4]Rheumazentrum Ruhrgebiet, Herne, Germany, [5]Rheumazentrum Ruhrgebiet Herne, Herne, Germany, [6]University Hospital, Nephrology, Essen, Essen, Germany, [7]Private practice of rheumatology, Hattingen, Germany, [8]Ruhr-University, Bochum, Germany; and Rheumatologische Versorgungszentrum (RVZ) Steglitz, Berlin, Germany, [9]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Herpes zoster (HZ) is common among older adults, with a lifetime risk of 25%. The risk is particularly increased in individuals with immunosuppression such as those with inflammatory rheumatic musculoskeletal diseases (iRMD). In this population, both the underlying disease and immunomodulatory treatments contribute to higher HZ incidence and severity. While the recombinant zoster vaccine (RZV) is recommended for immunocompromised individuals, data on its real-world safety and tolerability in patients with iRMD are still limited.

Methods: Adult patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), and giant cell arteritis (GCA) who were eligible to receive RZV were prospectively included in this ongoing study. Data on demographics, vaccination status, and iRMD diagnosis were collected at first dose visit (FDV). Disease activity and immunosuppressive treatments were assessed at FDV, second dose visit (SDV) and months 3, 6 and 12. Flares, adverse events (AEs), and zoster breakthrough cases were monitored following RZV administration at SDV and months 3, 6 and 12. AEs were categorized by system organ class (SOC) and measured per dose (%). Localized and systemic AEs, including severe AEs (SAEs) and adverse events of special interests (AESIs), were differentiated. A flare was defined as change in DAS-28 >1.2 for RA, ASDAS ≥ 0.9 for axSpA, or clinical signs/CRP ≥ 0.5 mg/dl and/or ≥30 mm for GCA. Descriptive analyses were performed.

Results: A total of 150 patients (age 22-84 years) were included, 32 (21.3%) with a history of HZ). All received RZV at FDV, and 145 (96.7%) also at SDV. Follow-up was completed by 139 (92.7%), 129 (86%), and 100 (66.7%) patients at months 3-, 6-, and 12, respectively, with 295 vaccine doses administered. At least one AE was reported by 108, 105, 30, 22 patients at months 2, 3, 6 and 12, respectively. In total,168, 169, 33 and 25 AEs occurred at those timepoints. Most frequent localized AEs were pain at the injection site (n=102; 34.6%), swelling at the injection site (n=21; 7.1%), and redness at the injection side (n=20; 6.8%). Common systemic AEs included fever (n=49; 16.6%), fatigue (n=34; 11.5%) and musculoskeletal pain (n=31; 10.5%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics

Variable*	RA (n=60)	AxSpA (n=60)	GCA (n=30)
Age	50.4 (13.0)	47.7 (10.3)	72.5 (7.8)
Sex, female, n (%)	38 (63.3)	19 (31.7)	22 (73.3)
History of zoster, n (%)	13 (21.7)	6 (10.0)	13 (43.3)
CRP, mg/dl	0.4 (0.6)	0.3 (0.6)	0.1 (0.3)
Prednisolone, mean dosage mg/dl	(n=15 (25%)) 7 (7.8)	(n=1 (1.7%) 15 (0)	(n=13 (43.3%)) 10.8 (13.8)
csDMARD, n (%)	49 (81.7)	1 (1.7)	9 (30.0)
bDMARD, n (%)	46 (76.7)	53 (88.3)	18 (60.0)
tsDMARDs, n (%)	10 (16.7)	6 (10)	0
Physician global, NRS 0-10	1.7 (1.7)	2.5 (1.6)	1.7 (2.1)
Patient global, NRS 0-10	3.6 (2.2)	3.5 (2.1)	4.2 (2.5)
Pain, NRS 0-10	3.7 (2.4)	3.5 (2.3)	3.7 (2.6)
Disease activity, composite	DAS-28: 2.6 (1.2)	ASDAS: 1.8 (1.0)	NA
Physical function	HAQ 0.7 (0.7)	BASFI 3.1 (2.7)	HAQ 1.0 (0.7)

Table 2: Adverse events over 12 months Localized adverse events are indicated in italics; systemic adverse events are presented in standard font. Shades of blue represent frequency intervals, ranging from dark to light, respectively: very common (≥ 1/10), common (≥ 1/100 to < 1/10), and uncommon (≥ 1/1,000 to < 1/100)

System Organ Class (SOC)	Adverse Events	Total vaccine doses	SDV month 2	Month 3	Month 6	Month 12	Total Cases	Rate per dose [%]
General disorders and administration site conditions								
	Injection site swelling	295	15	6	0	0	21	7.1%
	Injection site redness	295	9	11	0	0	20	6.8%
	Injection site warmth	295	0	2	0	0	2	0.7%
	Injection site pain	295	54	48	0	0	102	34.6%
	Fatigue	295	15	17	2	0	34	11.5%
	Fever/chills (Pyrexia)	295	14	34	1	0	49	16.6%
Musculoskeletal and connective tissue disorders								
	Generalized musculoskeletal pain	295	10	15	3	3	31	10.5%
	Reduced arm function	295	2	2	0	0	4	1.4%
Infections and infestations								
	Infection	295	8	5	10	5	28	9.5%
	COVID-19	295	3	1	2	1	7	2.4%
Nervous system disorders								
	Headache	295	10	9	0	0	19	6.4%
	Dizziness	295	3	2	0	0	5	1.7%
Respiratory, thoracic and mediastinal disorders								
	Dyspnea	295	0	1	1	0	2	0.7%
Gastrointestinal disorders								
	Gastrointestinal symptoms	295	1	4	0	0	5	1.7%
Blood and lymphatic system disorders								
	Leukocytopenia	295	1	0	0	0	1	0.3%
Hepatobiliary disorders								
	Elevated liver enzymes	295	1	1	0	0	2	0.7%
Neoplasms benign, malignant and unspecified								
	Malignant disease	295	1	0	1	3	5	1.7%
Other /Unclassified								
	Disease-specific complaints	295	7	6	5	5	23	7.8%
	Other	295	14	5	8	8	35	11.9%
Total	**n.a.**	**295**	**168**	**169**	**33**	**25**	**395**	**133.9%**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

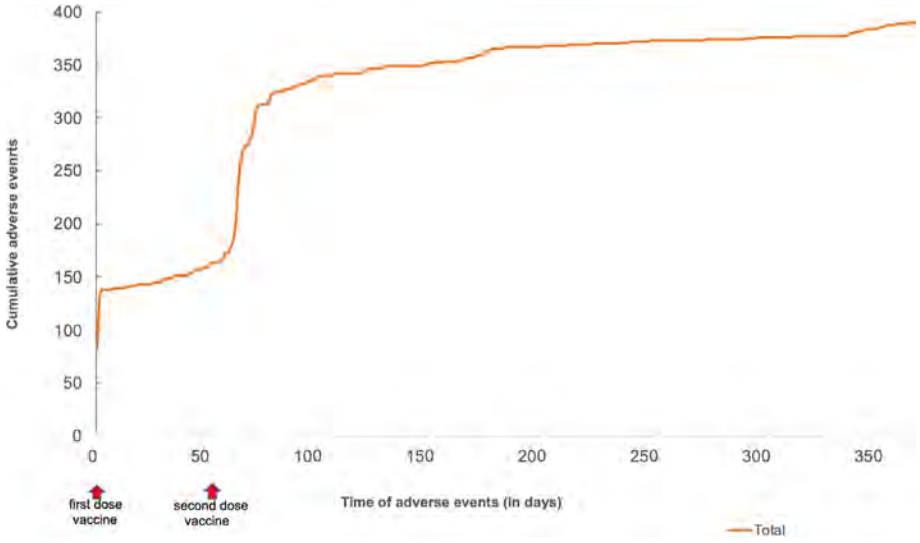


Figure 1: Cumulative adverse events over 12 months

Patients reported 29, 20, 27, and 32 flares at SDV, months 3, 6 and 12, respectively, of which 11 (7.6%), 12 (8.6%), 12 (9.3%) and 13 (13.0%) met predefined flare criteria. Twelve severe AEs (SAEs) occurred (3 flares, 6 malignancies, 3 comorbidities). No AESIs or zoster breakthrough cases were reported.

Conclusion: RZV was well tolerated in patients with iRMD. Most adverse events occurred within a few days after vaccination. Flares were infrequent, and SAEs, including malignancies were considered unrelated. No AESIs or zoster cases were reported. These findings provide reassurance for both rheumatologists and prospective vaccine recipients. They support confidence in RZV safety in this population.

Disclosure: E. Steiner: None; **I. Andreica**: Boehringer-Ingelheim, 6, Chugai, 2, 5, 12, Consulting fees, Eli Lilly, 2, 5, 6, 12, Consulting fees, Galapagos, 2, 5, 12, Consulting fees, Gilead, 2, 5, GSK, 2, 5, Janssen, 2, 5, MSD, 2, 5, 6, Novartis, 5, 12, Consulting fees, received payments for other services, Pfizer, 2, 5, Sobi, 2, 5, 6, takeda, 2, 5, UCB, 2, 6, 12, Consulting fees; **S. Reale**: None; **G. Chieregо**: None; **P. Köhler**: None; **S. Zapke**: None; **B. Wilde**: Alexion, 2, 6, AstraZeneca, 2, 6, Biotech, 2, 6, Chiesi, 2, 6, Gilead, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Hexal, 2, 6, Mirobio, 2, 6, Neovii, 2, 6, Novartis, 2, 6, Otsuka, 2, 6, Sanofi, 2, 6, TEVA, 2, 6, Vifor, 2, 6, Wyeth, 2, 6; **D. Kiefer**: AbbVie/Abbott, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, chugai, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Merck/MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **P. Sewerin**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Axiom Health, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Chugai, 2, 5, Deutscher Psoriasis-Bund, 2, 5, Eli Lilly, 2, 5, Gilead, 2, 5, Hexal, 2, 5, Janssen, 2, 5, Johnson & Johnson, 2, 5, Medical Communication, 2, Medici GmbH, 2, 5, medi-login, 2, 5, Novartis, 2, 5, Onkowissen GmbH, 2, 6, Pfizer, 2, 5, Roche, 2, 5, Sanofi-Genzyme, 2, 5, Swedish Orphan Biovitrum, 2; **H. Kavruk**: AbbVie/Abbott, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Johnson & Johnson, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Vifor, 2, 5; **D. Karagkiozidou**: None; **P. Ermeidis**: AbbVie/Abbott, 2, 5, Janssen, 2, 5, Novartis, 2, 5; **B. Guminski**: None; **A. Kribben**: None; **J. Braun**: None; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5.

Abstract Number: 1158

Clinical and Genetic Features of CTLA-4 Haploinsufficiency : A Prospective Study in China

Guishan Liu[1], Jingyuan zhang[2], jin Xu[2], JiaYuan Dai[2] and Min Shen[2], [1]Peking union medical college hospital, Beijing, Beijing, China (People's Republic), [2]Peking union medical college hospital, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

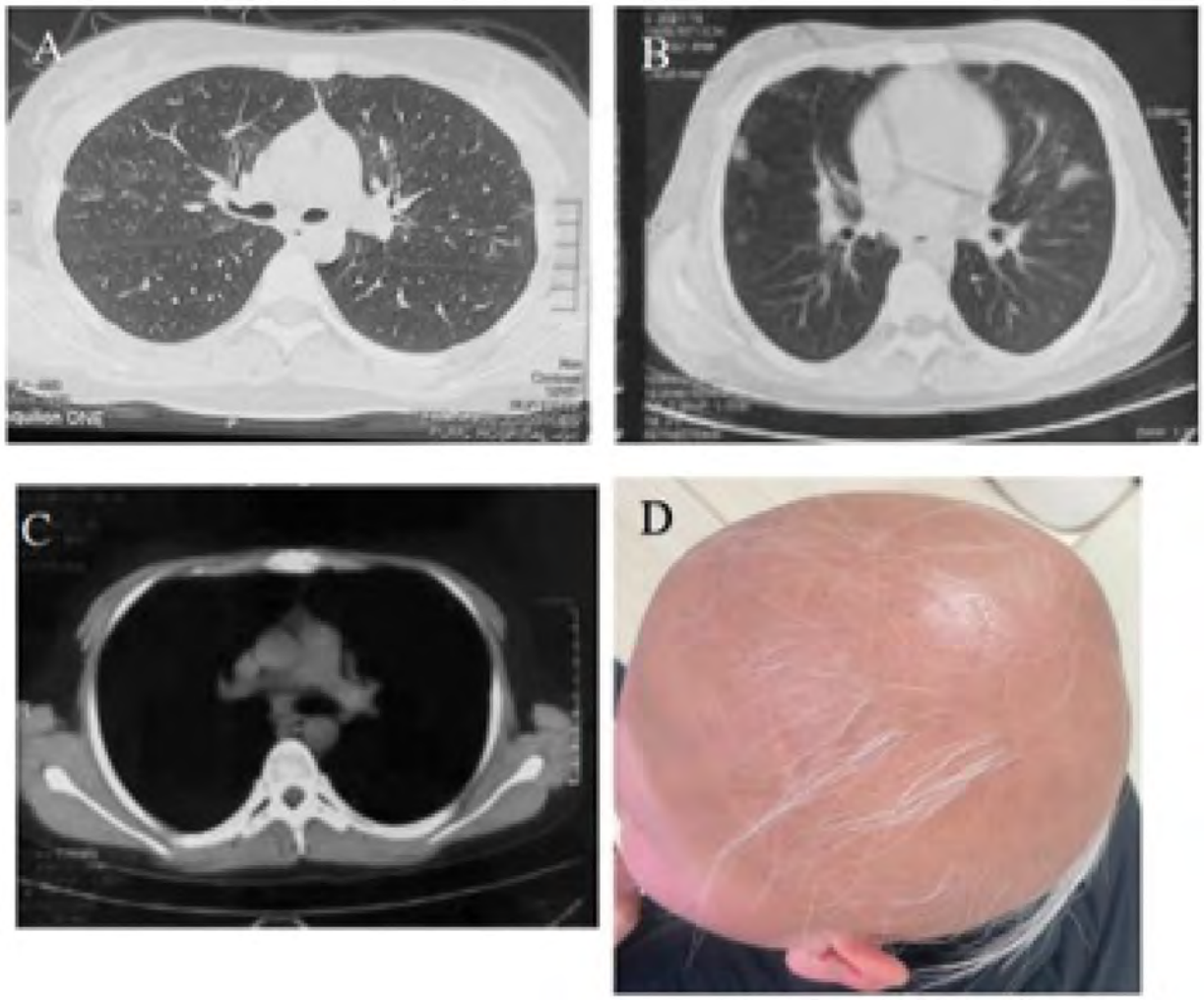


Fig1.Typical clinical manifestations of subjects with CTLA-4 deficiency. A. P1: Multiple ground-glass nodules in the lungs B. P6: Lung inflammation C. P6:Mediastinal lymphadenopathy D. P5: Complete baldness of the head and eyebrows, after treatment, the hair grows back into vellus hair

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Heterozygous loss-of-function mutations in CTLA4 cause a spectrum of immune dysregulation, characterized by hypogammaglobulinemia, autoimmune cytopenias, and lymphoproliferation, yet penetrance and expressivity remain highly variable across cohorts[1-3]

To characterize the clinical, genetic, and therapeutic features of a prospective Chinese cohort with CTLA-4 haploinsufficiency, and to compare their management outcomes with those reported in the largest international series.

Methods: Seven patients diagnosed by whole-exome sequencing underwent systematic evaluation of clinical phenotypes, laboratory parameters, imaging and histopathology, and treatment responses. Data were contrasted against the global 133-patient cohort described by Kuehn et al[1]

Results: All individuals harbored heterozygous CTLA4 variants—four missense and three truncating mutations—exhibiting classical features of immune dysregulation alongside marked phenotypic heterogeneity, even among family

Table1 : Clinical and genetic features of Chinese patients with CTLA-4h

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
CTLA4 variants	c.155G>T, p.Gly52Val	c.538C>T, p.Leu180Phe	c.347T>A, p.Ile116Asn	c.347T>A, p.Ile116Asn	c.151C>T, p.Arg51Trp	c.436G>A, p.Gly146Arg	c.151C>T, p.Arg51Trp
Variant Classification	VUS	VUS	VUS	VUS	Pathogenic	Pathogenic	Pathogenic
Gender	F	M	F	F	F	M	M
Age at Onset (years)	14	12	9	<10	10	17	38
Age at Onset of Autoimmunity	16	21	11	50	12	17	40
Hypogammaglobulinemia	-	+	+	+	-	-	-
Lymphoproliferation	-	-	+	+	-	-	-
Respiratory Manifestations	+	-	-	-	-	+	+
Autoimmune Cytopenias	+	-	+	+	+	-	-
Gastrointestinal Symptoms	-	+	+	-	+	-	+
Dermatologic Symptoms	+	-	+	-	+	-	+
Liver Involvement	-	-	-	-	-	-	-
IVIG	Effective	Effective	Effective	Effective	Effective	Effective	Effective
Abatacept	Effective	Effective	Effective	Not Used	Effective	Effective	Recommended
Steroids	Partially Effective	Not Used	Effective	Effective	Not Used	Not Used	Not Used
Sirolimus	Partially Effective	Not Used	Not Used	Not Used	Not Used	Not Used	Not Used
Other Immunosuppressants	Not Used	Not Used	Effective (Methotrexate etc.)	Effective (Cyclosporine)	Not Used	Not Used	Not Used
Outcome	Stable (monthly abatacept)	Improved, lost to follow-up	Stable (abatacept q3 weeks)	Stable on cyclosporine	Improved (hair regrowth)	Improved (residual symptoms)	Improved, follow-up ongoing

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table2:Comparison of this cohort with the largest existing cohort

Table2

Feature	Literature Cohort (n=133, global)	Our Cohort (n=7, Chinese patients)
Families / Mutation Types	54 unrelated families; 45 distinct heterozygous CTLA4 mutations (28 novel)	7 families, 7 heterozygous CTLA4 variants, all located in the extracellular domain
Clinical Penetrance	67% (90/133)	71% (7/10 tested, including 3 asymptomatic carriers)
Median Age of Onset	11 years (range <1–59 years)	14 years (range 10–16 years)
Diagnostic Delay	Several cases delayed >10 years, average not systematically reported	2–5 years
Hypogammaglobulinemia	84% (65/77)	100% (7/7)
Lymphoproliferation	73% (62/85)	86% (6/7)
Autoimmune Cytopenias	62% (55/89)	71% (5/7)
Respiratory Involvement	68% (61/90)	29% (2/7)
Gastrointestinal Involvement	59% (53/90)	57% (4/7)
Malignancy Rate	9% (11/133), predominantly EBV-associated lymphomas and gastric cancers	0% (no tumors observed over 6–12 months follow-up)
Key Immunophenotype	Reduced T, B, and NK cell counts; increased Treg percentage	Severe B and NK cell depletion; Treg proportions similar to literature
Preferred Targeted Therapy	Abatacept/belatacept, sirolimus, HSCT	Abatacept + IVIG combination. P6 also received vedolizumab
EBV-related Complications	Frequent EBV reactivation and EBV-driven lymphomas	None observed
Follow-up Outcomes	16% mortality; many HSCT recipients surviving	0% mortality; all patients clinically stable

members with identical genotypes Relative to the international cohort's median diagnostic delay exceeding 10 years, our patients reached genetic confirmation within 2–5 years, enabling earlier initiation of targeted therapy. Nearly all received abatacept (CTLA-4-Ig), achieving sustained disease stabilization and tapering of corticosteroids, complemented by IVIG to correct hypogammaglobulinemia Unlike the 9% malignancy rate observed globally—often EBV-associated—no tumors emerged during 6–12 months of follow-up, suggesting that earlier intervention may mitigate oncogenic risk. Proactive family screening identified asymptomatic carriers, underscoring the value of genetic counseling for at-risk relatives.

Conclusion: This study demonstrates that early genetic screening coupled with prompt abatacept-based immunomodulation and IVIG replacement can markedly shorten diagnostic latency, stabilize multi-system disease, and potentially reduce malignancy complications in CTLA-4 haploinsufficiency. These findings provide a model for precision-medicine approaches in diverse populations.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[1] Schwab C, Gabrysch A, Olbrich P, et al. Phenotype, penetrance, and treatment of 133 cytotoxic T-lymphocyte antigen 4–insufficient subjects[J/OL]. Journal of Allergy and Clinical Immunology, 2018, 142(6): 1932-1946. DOI: 10.1016/j.jaci.2018.02.055.

[2] Jamee M, Hosseinzadeh S, Sharifinejad N, et al. Comprehensive comparison between 222 CTLA-4 haploinsufficiency and 212 LRBA deficiency patients: a systematic review[J/OL]. Clinical and Experimental Immunology, 2021, 205(1): 28-43. DOI: 10.1111/cei.13600.

[3] Schubert D, Bode C, Kenefeck R, et al. Autosomal-dominant immune dysregulation syndrome in humans with CTLA4 mutations[J/OL]. Nature Medicine, 2014, 20(12): 1410-1416. DOI: 10.1038/nm.3746.

Disclosure: G. Liu: None; **J. zhang**: None; **j. Xu**: None; **J. Dai**: None; **M. Shen**: None.

Abstract Number: 1159

IL-18 Correlates with Pouchot Score and Inflammatory Biomarkers in Adult-Onset Still's Disease: Insights From a Repeated Measures Study

Hadeel Abdul-Rehman[1], Karen Gambina[2] and Bella Mehta[3], [1]Hospital for Special Surgery, New York, NY, [2]Columbia University Medical Center, Islip, NY, [3]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Adult-Onset Still's Disease (AOSD) is a rare systemic inflammatory disease. Interleukin-18 (IL-18) levels are significantly elevated in AOSD patients[1] and may be a promising indicator of disease activity and potential target for therapeutics. The Pouchot systemic score, used to evaluate disease activity, assigns 1 point to each: fever, rash, pleuritis, pneumonia, pericarditis, hepatomegaly, splenomegaly, lymphadenopathy, leukocytosis (>15,000/μL), sore throat, myalgia, and abdominal pain. The modified Pouchot (mPochout) score replaces splenomegaly and myalgia with arthralgia and hyperferritinemia (>3000 μg/L).

We evaluated the association between serum IL-18 levels and disease activity as measured by Pouchot scores in patients with AOSD to assess the potential of IL-18 as a biomarker.

Methods: Patients were identified by ICD-10 codes, and diagnoses were confirmed by their treating rheumatologist and via chart review by rheumatologists. Pouchot/mPouchot scores were calculated from the same day IL-18 labs were checked.

We used linear mixed-effects models to assess the association between log-transformed IL-18 levels and clinical/serologic markers of disease activity, including Pouchot/mPouchot score, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and ferritin. Patient ID was included as a random effect to account for repeated measures. Fixed effects included the independent variable of interest (e.g., Pouchot score), with IL-18 as the dependent variable. We also measured intraclass correlation coefficients (ICC).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics

Characteristic	Patient cohort (n=18)[1]	Patient visits (n=38)[2]
Demographics		
Age, mean (SD)	38.1 (15.3)	38.6 (14.8)
Sex, Female, n (%)	13 (72.2%)	24 (63.2%)
Race, White, n (%)	13 (72.2%)	28 (73.7%)
Symptoms		
Fever, n (%)	5 (27.8%)	5 (13.2%)
Rash, n (%)	5 (27.8%)	9 (23.7%)
Pleuritis, n (%)	1 (5.6%)	1 (2.6%)
Pneumonia, n (%)	0 (0%)	0 (0%)
Pericarditis, n (%)	0 (0%)	0 (0%)
Hepatomegaly, n (%)	7 (38.9%)	11 (28.9%)
Splenomegaly, n (%)	2 (11.1%)	2 (5.3%)
Lymphadenopathy, n (%)	2 (11.1%)	2 (5.3%)
Leukocytosis, n (%)	0 (0%)	0 (0%)
Sore throat, n (%)	3 (16.7%)	3 (7.9%)
Myalgia, n (%)	9 (50%)	10 (26.3%)
Abdominal pain, n (%)	4 (22.2%)	4 (10.5%)
Arthritis, n (%)	13 (72.2%)	22 (57.9%)
Hyperferritinemia, n (%)	0 (0%)	0 (0%)
Disease Activity		
Mean Pouchot score (SD)	1.5 (1.1)	1.2 (1.4)
Median Pouchot score (IQR)	1.5 (0-2.1)	1 (0-2)
Mean mPouchot score (SD)	1.9 (1.1)	1.7 (1.4)
Median mPouchot score (IQR)	2 (1-3)	1.5 (1-2)
Lab Values		
Mean ESR (SD), mm/hr	15.62 (12.2)	17.8 (16.9)
Median ESR (IQR), mm/hr	11 (5-17)	11 (5-23)
Mean CRP (SD), mg/dL	0.62 (0.83)	0.9 (1.6)
Median CRP (IQR), mg/dL	0 (0-0.96)	0 (0-1.2)
Mean Ferritin (SD), µg/L	153.6 (128.1)	196.3 (242.5)
Median Ferritin (IQR), µg/L	90 (39.8-212.6)	118.8 (48.7-240.3)
Mean IL-18 (SD), pg/mL	6446.6 (22120)	14041.8 (51295.4)
Median IL-18 (IQR), pg/mL	434 (248-1842.3)	606.5 (275.8-3122.5)

[1]Characteristics summarized by patient; symptoms are reported as present if a patient experienced them across any visit. Lab values are summarized as means of each patient's mean values across visits, or medians of each patient's median values across visits.

[2]Characterisitcs are summarized by individual visit; each visit is treated as an independent observation, and values are calculated across visits

Results: Of the Pouchot score symptoms, arthritis was the most common, followed by hepatomegaly, myalgia, rash, and fever. The mean Pouchot score, mPouchot score, and IL-18 level across all visits were 1.2, 1.7, and 14041.8 pg/mL respectively.

Pouchot scores, ESR levels, and ferritin levels showed significant positive associations with IL-18 levels: ($p< 0.01$, $p < 0.05$, $p < 0.001$). The association between mPouchot scores or CRP with IL-18 levels were not statistically significant.

ICC for the Pouchot, mPouchot, ESR, CRP, and Ferritin models ranged from 0.75-0.84 across models thus indicating 75-84% of variability in IL-18 levels was due to between-subject differences, while 16-25% was due to within-subject variability.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Results of Linear Mixed-Effects Models Assessing the Association Between Disease Activity and Inflammatory Markers with Log-Transformed IL-18 Levels

Variable	Number of patients	Number of visits	Coefficient	Standard error	p-value[1]	ICC[2]
Pouchot	18	38	0.1519	0.0534	**0.00853**	0.79
mPouchot	18	38	0.10618	0.05979	0.0866	0.75
ESR	18	37	0.010263	0.004612	**0.0355**	0.77
CRP	18	37	0.03975	0.04524	0.389	0.73
Ferritin	17	36	0.001082	0.0002265	**0.000111**	0.84

[1]Significant p-values are bolded

[2]The intraclass correlation coefficient (ICC) assesses the proportion of total variance in log-transformed IL-18 levels that can be attributed to between-subject differences

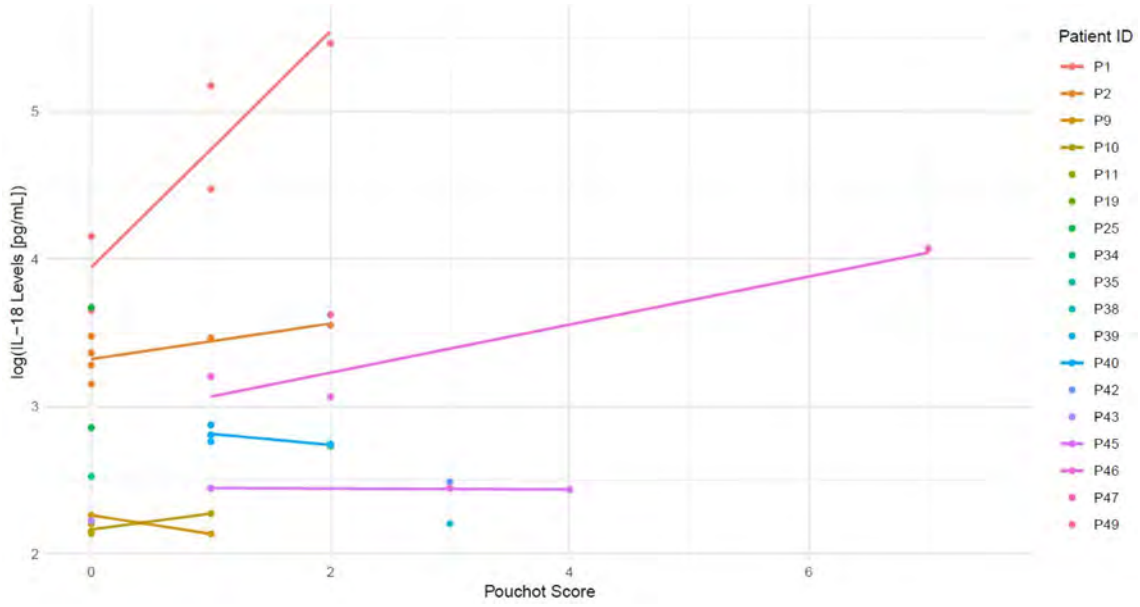


Figure 1: Log-Transformed IL-18 Levels vs Pouchot Score. Data points represent individual visits during which IL-18 levels were checked and Pouchot scores were calculated; different colors correspond to different patients. A line of best fit was constructed for patients that were tested more than once. Higher Pouchot scores indicate more severe disease activity.

Conclusion: These findings suggest the potential utility of IL-18 as a biomarker for disease monitoring in AOSD, particularly in combination with clinical activity scores such as the Pouchot score, given its strong association with disease activity markers and its stable inter-individual variability over time. Given newer potential therapeutics in AOSD, regular IL-18 and disease activity monitoring may be useful in management of these patients.

1. Colafrancesco et al. IL-18 Serum Level in Adult Onset Still's Disease: A Marker of Disease Activity. PMID: 22762008.

Disclosure: H. Abdul-Rehman: None; **K. Gambina**: None; **B. Mehta**: Amgen, 1, Horizon, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1160

Plasma Adenosine Deaminase 2 as a Potential Disease Activity Biomarker for Sarcoidosis

Jamie Lim[1], Jayanth Doss[2], Jeffrey Shen[2], Rex McCallum[2], Lisa Carnago[3], Hakim Azfar Ali[4], Ravi Karra[5], Kees Frelinger[2], Rishi Rampersad[2], Susan Kelly[2], Amanda Eudy[6], Michael Hershfield[7] and Teresa Tarrant[8], [1]Duke University School of Medicine, Durham, NC, [2]Division of Rheumatology and Immunology, Duke University Department of Medicine, Durham, NC, [3]Division of Rheumatology and Immunology, Duke University Department of Medicine, Duke University School of Nursing, Durham, NC, [4]Division of Pulmonary, Allergy, and Critical Care Medicine, Duke University Department of Medicine, Durham, NC, [5]Division of Cardiology, Duke University Department of Medicine, Durham, NC, [6]Duke University, Raleigh, NC, [7]Division of Rheumatology and Immunology, Duke University Department of Medicine, Department of Biochemistry, Duke University School of Medicine, Durham, NC, [8]Division of Rheumatology and Immunology, Duke University Department of Medicine, Durham Veterans Administration Hospital, Durham, NC

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Sarcoidosis is an inflammatory granulomatous disease of unknown etiology that can affect multiple organ systems. There is currently no standardized approach for measuring sarcoidosis disease activity. Serum tests lack sensitivity, specificity, and correlation with disease activity. Serial MRI, CT, and PET imaging can be used, but these modalities are constrained by cost and radiation exposure for the latter two.

Adenosine deaminase 2 (ADA2) is expressed by and secreted from activated monocytes and macrophages into plasma. ADA2 activity correlates with disease activity in macrophage-activated diseases such as macrophage activation syndrome and tuberculosis, but ADA2 activity in sarcoidosis is less well-characterized. Given that monocyte/macrophage activation plays an important role in sarcoidosis pathogenesis, we hypothesize that ADA2 may serve as a biomarker of disease activity, burden of disease, and treatment response.

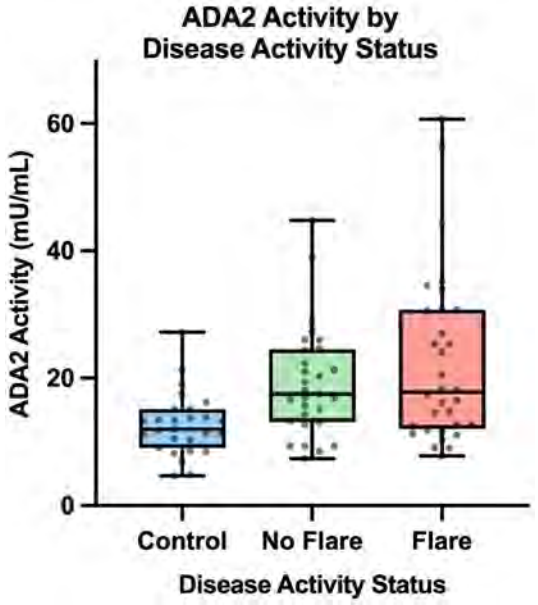


Figure 1. There was a statistically significant difference in plasma ADA2 activity between healthy controls (12.0 mU/mL (IQR 9.0-15.2), n=27), sarcoidosis patients without disease flare (17.5 mU/mL (IQR 13.3-24.4), n=29), and sarcoidosis patients with disease flare (17.8 mU/mL (IQR 12.2-30.7), n=32, p=0.001).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

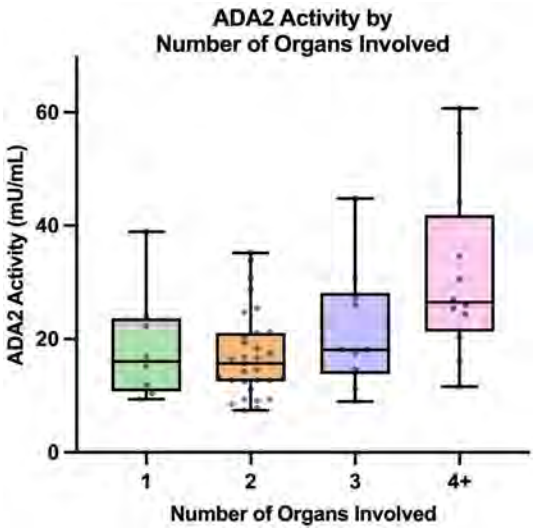


Figure 2. Plasma ADA2 activity was significantly different across groups of patients with sarcoidosis based on the number of organs involved (p=0.01). Median ADA2 activity by number of organs involved: 1 (16.1 mU/mL (IQR 11.2-23.3), n=8), 2 (15.7 mU/mL (IQR 12.5-21.1), n=31), 3 (18.1 mU/mL (IQR 14.7-27.3), n=10), 4+ (26.5 mU/mL (IQR 22.4-39.5), n=12).

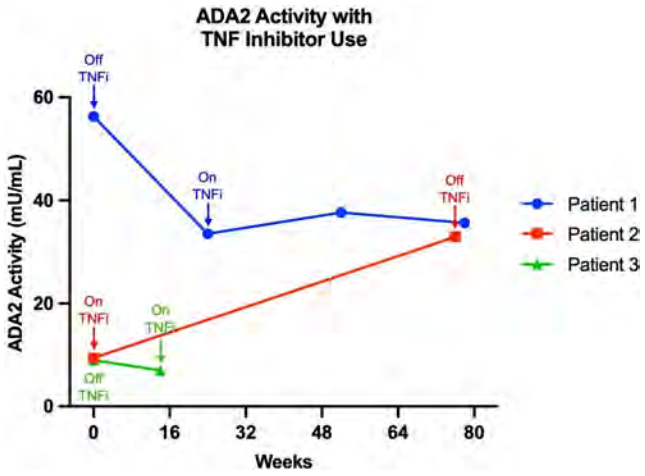


Figure 3. Plasma ADA2 activity in patients with sarcoidosis decreased following TNF inhibitor treatment.

Methods: Patients with sarcoidosis were consented for study under IRB Pro00109933. Plasma samples were collected at enrollment, and disease activity was determined by chart review. Plasma ADA2 activity was measured in the presence of the ADA1 inhibitor erythro-9-(2-hydroxy-3-nonyl)adenine (EHNA) by two independent assays of the inosine and ammonia products using high-performance liquid chromatography (HPLC) and spectrophotometry, respectively. Results of the two assays strongly correlated as measured by the Spearman correlation coefficient (R=0.98, p< 0.0001). Median ADA2 HPLC activity was compared across groups of patients using the Kruskal-Wallis test. For patients with serial ADA2 measurements, ADA2 HPLC activity following TNF inhibitor (TNFi) use was trended.

Results: Sixty-one patients with sarcoidosis were studied. There was a statistically significant difference in ADA2 activity between healthy controls, sarcoidosis patients without disease flare, and sarcoidosis patients with disease flare (Figure 1). There was a statistically significant difference in ADA2 activity across groups of patients with sarcoidosis based on the number of organs involved (Figure 2). Patients with liver, skin, and extrapulmonary lymph node involvement had statistically significantly higher ADA2 activity compared to those without (p=0.0006, p=0.0001, p=0.03, respectively), while patients with cardiac involvement had statistically significantly lower ADA2 compared to those without (p=0.02). Patients with serial

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ADA2 measurements had decreased ADA2 activity following TNFi treatment (Figure 3) that did not reach statistical significance due to small sample size.

Conclusion: Plasma ADA2 activity is elevated in patients with sarcoidosis, with differences in ADA2 observed based on the number and type of affected organs. There is a possible association between ADA2 activity and treatment response, but a larger sample size is needed to confirm these findings. These results suggest that ADA2 could serve as a plasma-based biomarker for sarcoidosis disease activity.

Disclosure: J. Lim: None; **J. Doss**: None; **J. Shen**: None; **R. McCallum**: None; **L. Carnago**: None; **H. Ali**: None; **R. Karra**: None; **K. Frelinger**: None; **R. Rampersad**: None; **S. Kelly**: None; **A. Eudy**: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **M. Hershfield**: None; **T. Tarrant**: Amgen, 5, Chiesi USA, 2, 5, Department of Justice, 12,, X4 Pharmaceuticals, 2, 5.

Abstract Number: 1161

Comparative efficacy, safety and tolerability of antifibrotic therapies across systemic autoimmune diseases

Javier Narváez[1], Orfa Barrios[2], Pol Maymó-Paituvi[3], JUAN JOSE ALEGRE SANCHO[4], Ivan Castellví[5], Vanesa Vicens Zygmunt[6], Guadalupe Bermudo[7], Laia De Daniel Bisbe[3], Martí Aguilar-Coll[8], Montserrat Roig Kim[3], Joan Miquel Nolla[3] and Maria Molina-Molina[7], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Department of Rheumatology. Hospital Nacional Arzobispo Loayza, Lima, Peru, [3]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [4]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain, [5]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, barcelona, Spain, [6]Interstitial Lung Disease Unit. Department of Pneumology. Hospital Universitario de Bellvitge, Barcelona, Spain, [7]Interstitial Lung Disease Unit. Department of Pneumology. Hospital Universitario de Bellvitge., Barcelona, Spain, [8]Department of Rheumatology. Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: To evaluate the efficacy, safety, and tolerability of the antifibrotic agents nintedanib and pirfenidone in the treatment of interstitial lung disease (ILD) associated with rheumatoid arthritis (RA), systemic sclerosis (SSc), and other systemic autoimmune diseases (SADs) fulfilling current criteria for progressive pulmonary fibrosis (PPF).

Methods: A multicentre, longitudinal retrospective observational study was conducted. Data collected included pulmonary function test (PFT) results, adverse events (AEs), tolerability, and drug retention

Results: A total of 132 patients were included (74 women): 27 with RA-ILD (20.5%), 44 with SSc-ILD (33%), and 61 with SADs-ILD (46.5%), including 24 with IPAF, 10 with antisynthetase syndrome, 9 with primary Sjögren's syndrome, 7 with ANCA-associated isolated ILD, 6 with ANCA-associated vasculitis, 3 with SLE, and 2 with sarcoidosis.

Of these, 116 (87.9%) started nintedanib and 16 (12.1%) pirfenidone. The UIP pattern was present in 47.7% (63). Eighty-five percent (112) received combination therapy with a bDMARD, a csDMARD/immunosuppressant, or both. The median post-antifibrotic follow-up was 25 months (IQR 25th–75th: 14–46).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Changes in PFTs following initiation of antifibrotic therapy

1A. Rheumatoid arthritis

Before antifibrotics				
	At time of RA-ILD diagnosis mean ± SD (IQR, 25th-75th)	**At time of initiation of initial antifibrotic medication** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* value (95% CI)**
Total sample (N=27)				
%FVC predicted	95.5 ± 14.6 (88.1 – 107.5)	85.6 ± 15 (73 – 97.1)	-8.9%	0.0001 (7.81 to 16.02)
%DLCO predicted	69.1 ± 18.8 (55.4 – 79.5)	54.3 ± 14.8 (44 – 66)	-14.8%	0.0001 (9.53 to 20.16)
After 6 months of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	**6 months post-treatment** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* value (95% CI**
Total sample (N=24)				
%FVC predicted	88.2 ± 19 (73.7 – 102.7)	89.4 ± 22.7 (74.4 – 105.5)	+1.2%	0.611 (-5.67 to 3.41)
%DLCO predicted	57.4 ± 16.6 (46.2 – 68.1)	61.3 ± 24.9 (40.5 – 79.6)	+3.9%	0.400 (-13.51 to 5.63)
After 1 year of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	**12 months post-treatment** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* value (95% CI**
Total sample (N=18)				
%FVC predicted	87.5 ± 20.7 (71.8 – 108.6)	92.2 ± 24.8 (76 – 115.8)	+4.7%	0.023 (-8.66 to 0.74)
%DLCO predicted	58.2 ± 17.9 (45.7 – 69.9)	54.4 ± 16.7 (42.7 – 67)	-3.8%	0.175 (-1.82 to -9.25)
After 2 years of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	**24 months post-treatment** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* value (95% CI**
Total sample (N=9)				
%FVC predicted	89.1 ± 19.7 (71.6 – 111.4)	97.4 ± 19.7 (84.3 – 120.1)	+7.7%	0.037 (-16.07 to 0.66)
%DLCO predicted	60.8 ± 20.3 (43.8 – 81.9)	58.6 ± 15.1 (45.5 – 73.1)	-2.2%	0.621 (-7.67 to -12.07)

1B. Systemic sclerosis.

Before antifibrotics				
	At time of SSc-ILD diagnosis mean ± SD (IQR, 25th-75th)	**At time of initiation of initial antifibrotic medication** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* value (95% CI)**
Total sample (N=44)				
%FVC predicted	80.3 ± 24.9 (58.5 – 96)	71.2 ± 20.4 (54.4 – 79.7)	-9.1%	0.002 (3.46 to 14.56)
%DLCO predicted	56 ± 18.1 (46 – 76.9)	47.9 ± 16.2 (36.2 – 55)	-7.8%	0.005 (2.27 to 11.5)
After 6 months of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	**6 months post-treatment** mean ± SD (IQR, 25th-75th)	**Delta (mean)**	***P* value (95% CI**
Total sample (N=36)				
%FVC predicted	73.3 ± 18.9 (61 – 80)	79.4 ± 22.7 (61.7 – 87.7)	+6.1%	0.005 (-1.73 to -3.03)
%DLCO predicted	48.8 ± 16.4 (37 – 55)	45.9 ± 15.4 (35.3 – 56.5)	-2.9%	0.254 (-2.71 to 9.87)

Changes in PFTs following initiation of antifibrotic therapy are summarised in Table 2. Across the entire study population, significant declines in PFTs were observed prior to antifibrotic initiation. In patients with RA-ILD, antifibrotic treatment was associated with a significant increase in %CVF at 12 months (+4.7%, p=0.023) and 24 months (+7.7%, p=0.037), while %DLCO remained stable (–3.8% and –2.2%; p=0.175 and p=0.621, respectively). In the SSc-ILD group, %CVF improved consistently (+8.7% at both 12 and 24 months; p=0.024 and p=0.018), whereas %DLCO showed a mild, non-significant decrease (–2.1% and –1.8%; p=0.560 and p=0.427).

In contrast, among patients with other SADs-ILD, %CVF remained stable at 12 months (–0.7%, p=0.665) and declined slightly at 24 months (–3.2%, p=0.103), whereas %DLCO decreased progressively (–3.7% and –5.1%; p=0.422 and p=0.025).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

After 1 year of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	12 months post-treatment mean ± SD (IQR, 25th-75th)	Delta (mean)	*P* value (95% CI
Total sample (N=33)				
%FVC predicted	71.2 ± 18.7 (59.2 – 79.7)	80.2 ± 22.7 (62 – 93.8)	+8.7%	0.024 (-14.29 to 1.10)
%DLCO predicted	48.4 ± 14.3 (39 – 57)	46.3 ± 14.8 (36 – 54.5)	-2.1%	0.560 (-6.03 to 3.33)
After 2 years of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	24 months post-treatment mean ± SD (IQR, 25th-75th)	Delta (mean)	*P* value (95% CI
Total sample (N=28)				
%FVC predicted	73.8 ± 18.1 (61 – 80)	82.5 ± 24.8 (64.2 – 102.7)	+8.7%	0.018 (-12.82 to -1.34)
%DLCO predicted	48.2 ± 15.3 (36 – 55)	46.4 ± 18.4 (32 – 55)	-1.8%	0.427 (-2.76 to 6.33)

1C. Other systemic autoimmune diseases (SADs)

Before antifibrotics				
	At time of SADs-ILD diagnosis mean ± SD (IQR, 25th-75th)	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	Delta (mean)	*P* value (95% CI)
Total sample (N=61)				
%FVC predicted	85.4 ± 16.9 (71.5 – 96.5)	80.9 ± 20.8 (68 – 93)	-4.4%	0.031 (0.42 to 8.40)
%DLCO predicted	54.5 ± 13.4 (46.5 – 63.6)	50.8 ± 14.4 (40.6 – 61.8)	-4.8%	0.026 (0.54 to 8.29)
After 6 months of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	6 months post-treatment mean ± SD (IQR, 25th-75th)	Delta (mean)	*P* value (95% CI
Total sample (N=53)				
%FVC predicted	83.8 ± 18.8 (70.7 – 92.7)	86.4 ± 23.2 (70.6 – 95.5)	+2.6%	0.046 (-6.04 to -0.05)
%DLCO predicted	52.1 ± 13.1 (41.5 – 61.4)	50.7 ± 13 (44.4 – 60)	-1.4%	0.243 (-1.01 to 3.92)
After 1 year of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	12 months post-treatment mean ± SD (IQR, 25th-75th)	Delta (mean)	*P* value (95% CI
Total sample (N=48)				
%FVC predicted	83.2 ± 18.3 (73.1 – 91.7)	82.5 ± 19.5 (69.7 – 92.5)	-0.7%	0.665 (-2.34 to 3.63)
%DLCO predicted	52.8 ± 13.1 (43 – 62)	49.1 ± 11.6 (41.3 – 58)	-3.7%	0.422 (-1.64 to 3.84)
After 2 years of treatment				
	At time of initiation of initial antifibrotic medication mean ± SD (IQR, 25th-75th)	24 months post-treatment mean ± SD (IQR, 25th-75th)	Delta (mean)	*P* value (95% CI
Total sample (N=40)				
%FVC predicted	83.3 ± 17.7 (73 – 92)	80.1 ± 17.8 (65.2 – 88)	-3.2%	0.103 (-0.68 to 7.12)
%DLCO predicted	52.5 ± 12.9 (43 – 61)	47.4 ± 14.8 (36.2 – 61)	-5.1%	0.025 (0.60 to 8.52)

%pFVC = predicted forced vital capacity; %pDLCO = predicted diffusing capacity for carbon monoxide, corrected for hemoglobin; RTX = rituximab; 6MWT= 6-minute walking test

Data on safety and tolerability are summarised in Table 2. AEs were common across all groups: 81.5% in RA-ILD, 75% in SSc-ILD, and 65.6% in SADs-ILD. Permanent dose reductions due to AEs were more frequent with nintedanib than pirfenidone.

Permanent treatment discontinuation was observed in 52.3% of SSc-ILD, 37% of RA-ILD, and 36.1% of SADs-ILD patients. Discontinuation due to AEs occurred in 31.8%, 18.5%, and 14.8%, respectively. Although these figures suggest lower tolerability in the SSc-ILD

subgroup, differences were not statistically significant in the overall comparison (p=0.100) or in pairwise analyses: p=0.276 for SSc-ILD vs RA-ILD, p=0.055 for SSc-ILD vs SADs-ILD, and p=0.754 for RA-ILD vs other SADs-ILD

Conclusion: Across the three groups, antifibrotic treatment resulted in either PFT stabilisation or a reduced rate of decline. Patients with SSc-ILD appeared to have lower tolerability, but no statistically significant differences were observed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adverse events , tolerability, and drug retention.

	Rheumatoid arthritis N=27	Systemic Sclerosis N=44	Other systemic autoimmune diseases N=61
Any adverse event	22 (81.5%)	33 (75%)	40 (65.6%)
Most frequent adverse events			
Diarrhea	17 (63%)	24 (54.5%)	28 (45.9%)
Nausea/Vomiting	9 (33%)	10 (22.7%)	11 (18%)
ALT o AST increased	7 (26%)	6 (13.6%)	8 (13.1%)
Decreased appetite/weight loss	10 (37%)	12 (27.3%)	8 (13.1%)
Asthenia	2 (7.4%)	1 (2.3%)	2 (3.3%)
Abdominal pain	3 (11%)	7 (21.2%)	5 (3.3%)
Adverse event leading to permanent dose reduction	Nintedanib: 10/25 (40%) Pirfenidone: 1/7 (14%)	Nintedanib: 17/41 (41.4%) Pirfenidone: 3/13 (23%)	Nintedanib: 25/51 (49%) Pirfenifone: 11/27 (40.7%)
Permantent treatment discontinuation	10 (37%)	23 (52.3%)	22 (36.1%)
Adverse event leading to temporal discontinuation	17 (63%)	26 (59.1%)	27 (44.2%)
Mean number of temporal discontinuation	1.38 ± 0.5, range 1-2	1.46 ± 0.9, range 1-5	1.46 ± 0.8, range 1-4
Mean number of temporal dose reductions	1.53 ± 0.5, range 1-3	1.25 ± 0.5, range 1-3	1.32 ± 0.5, range 1-3
Adverse event leading to treatment discontinuation	5 (18.5%)	14 (31.8%)	9 (14.75%)

Disclosure: J. Narváez: None; **O. Barrios**: None; **P. Maymó-Paituvi**: None; **J. ALEGRE SANCHO**: None; **I. Castellví**: Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 6, Gebro, 6, GlaxoSmithKlein(GSK), 2, Innovarderm, 2, Janssen, 2, 6, Kern Pharma, 2, 6, Novartis, 2, Roche, 6, Sanofi-Genzyme, 6; **V. Vicens Zygmunt**: None; **G. Bermudo**: None; **L. De Daniel Bisbe**: None; **M. Aguilar-Coll**: None; **M. Roig Kim**: None; **J. Nolla**: None; **M. Molina-Molina**: None.

Abstract Number: 1162

Antineutrophil Cytoplasmic Antibody-associated Isolated Interstitial Lung Disease

Javier Narváez[1], Pol Maymó-Paituvi[2], Vanesa Vicens Zygmunt[3], Guadalupe Bermudo[4], Martí Aguilar-Coll[5], Montserrat Roig Kim[2], Laia De Daniel Bisbe[2], Joan Miquel Nolla[2] and Maria Molina-Molina[4], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [3]Interstitial Lung Disease Unit. Department of Pneumology. Hospital Universitario de Bellvitge, Barcelona, Spain, [4]Interstitial Lung Disease Unit. Department of Pneumology. Hospital Universitario de Bellvitge., Barcelona, Spain, [5]Department of Rheumatology. Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: There is increasing evidence of the association between interstitial lung disease (ILD) and ANCA positivity without other manifestations of systemic vasculitis. The prognosis of these patients remains uncertain, particularly in terms of their risk of progressing to systemic vasculitis, and the appropriate treatment approach is yet to be established. Our objective was to investigate the clinical characteristics, outcomes, and response to treatment in a cohort of patients with ANCA-positivity with isolated ILD (ANCA-ILD).

Methods: Retrospective study of patients diagnosed with ANCA-ILD at a Pulmonary Interstitial Unit in a tertiary university hospital. Diagnosis was made in cases of ANCA positivity and isolated pulmonary fibrosis, with no apparent development of systemic manifestations over a minimum period of 9 months. Patients were monitored from the date of ANCA-ILD diagnosis until death or the last follow-up

Results: We identified 22 patients (15 men) with a mean age at diagnosis of 66 ± 8 years. Their main clinical features and laboratory data are summarized in Table 1. The predominant radiological pattern was usual interstitial pneumonia (UIP), observed in 59.5% of cases. This was followed by fibrosing non specific interstitial pneumonia (NSIP) in 27% of cases,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Main demographic, clinical, functional, serological and treatment-related characteristics of the entire cohort

Number of patients	22
Age (mean ± SD), years	66 ± 8
Women /Men (ratio)	7 (32%) / 15 (68%)
HCRT pattern of ILD	
Usual Interstitial pneumonia (UIP)	13 (59.5%)
Fibrosing non-specific Interstitial Pneumonia (NSIP)	6 (27%)
Combined pulmonary fibrosis and emphysema	2 (9%)
Respiratory bronchiolitis-associated ILD	1 (4.5%)
Median time from ILD diagnosis to ANCA detection, months (IQR 25 th-75 th)	9.5 (9-42.5)
ANCA subtype	
MPO	15 (68.2%)
PR3	3 (13.6%)
Both	4 (18.2%)
%pFVC at diagnosis, mean ± SD	70.4 ±16
%pDLCO at diagnosis, mean ± SD	68 ± 13
Median follow-up, months (IQR 25 th-75 th)	50 (30-70)
Maintained as ANCA-associated isolated ILD	11 (50%)
Progression to systemic vasculitis	11 (50%)
No treatment	2 (9%)
Treatment	20 (91%)
Glucocorticoids	14 (64%)
Immunosuppressants	16 (73%)
Mycophenolate	7 (32%)
Rituximab	9 (41%)

combined pulmonary fibrosis and emphysema in 9%, and respiratory bronchiolitis-associated interstitial lung disease in 4.5%. The median time from ILD diagnosis to ANCA detection spanned 9.5 months, with a range of 9 to 42.5 months. The identified ANCA subtypes were MPO in 68.2% of cases, PR3 in 13.6%, and both subtypes in 18.2%. Initial treatment involved glucocorticoids in 64% of cases and antifibrotic therapy in 59%. After a median follow-up of 54 months (IQR 25th-75th 15 – 90.5), 50% of the patients had developed clinical signs of PAM or GPA-type vasculitis after a median follow-up of 50 months post-ANCA detection (IQR 25th -75th 30-70). These patients received treatment with rituximab (73%) or MMF (27%). None of the patients died, but three developed chronic respiratory failure and became candidates for lung transplantation. Among the remaining 11 patients, who continued with a diagnosis of ANCA-associated isolated ILD and received treatment with low-dose glucocorticoids and antifibrotic therapy (72.7%), 45.5% showed pulmonary progression and required additional immunosuppressive treatment (MMF and, in one case, rituximab). Furthermore, 27.3% developed chronic respiratory failure, and there was an 18.1% mortality rate. No predictive risk factors for the progression to systemic vasculitis were identified. ANCA-MPO levels were notably higher in patients with generalized vasculitis (153±93 versus 76±48; p=0.346). Of the patients with ANCA-PR3, only 57.1% progressed to systemic vasculitis.

Conclusion: Approximately three-quarters of patients initially diagnosed with ANCA-positive isolated ILD showed pulmonary progression, and approximately half eventually developed symptoms of systemic vasculitis during the follow-up period. The use of antifibrotics and immunosuppressants seemed to slow the progression of lung disease

Disclosure: J. Narváez: None; **P. Maymó-Paituvi**: None; **V. Vicens Zygmunt**: None; **G. Bermudo**: None; **M. Aguilar-Coll**: None; **M. Roig Kim**: None; **L. De Daniel Bisbe**: None; **J. Nolla**: None; **M. Molina-Molina**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1163

Clinical and Biomarker Characteristics of Inebilizumab-Treated Participants Who Experienced an IgG4-RD Flare During the Phase 3 MITIGATE Trial

John Stone[1], Emma Culver[2], Arezou Khosroshahi[3], Wen Zhang[4], Emanuel Della Torre[5], Kazuichi Okazaki[6], Yoshiya Tanaka[7], Matthias Lohr[8], nicolas schleinitz[9], Fernando Martinez-Valle[10], Manu Nayar[11], Vinciane Rebours[12], Cory Perugino[13], Kristen Clarkson[14], Theresa Alexander[14], Xinxin Dong[14], Qian Huang[14], Sue Cheng[14] and Daniel Cimbora[14], [1]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [2]John Radcliffe Hospital; University of Oxford, Oxford, United Kingdom, [3]Emory University, Atlanta, GA, [4]Peking Union Medical College Hospital, Dong Cheng Qu, China (People's Republic), [5]IRCCS San Raffaele Scientific Institute, Milan, Italy, [6]Kansai Medical University Kori Hospital, Osaka, Japan, [7]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [8]Karolinska Institutet, Stockholm, Sweden, [9]Aix Marseille university, AP-HM, Marseille, France, [10]Vall d'Hebron Hospital, Barcelona, Spain, [11]Freeman Hospital, Newcastle upon Tyne, United Kingdom, [12]Beaujon Hospital, AP-HP, Université Paris-Cité, Clichy, France, [13]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [14]Amgen, Thousand Oaks, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-RD is a rare, chronic, fibroinflammatory disorder characterized by recurrent flares that can affect any organ and lead to permanent tissue damage. Inebilizumab (INEB) is a CD19-specific B cell depleting monoclonal antibody (mAb) approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) and recently approved for the treatment of IgG4-RD (MITIGATE trial; NCT04540497). Three doses of INEB (days 1, 15 and 183) resulted in an 87% reduction in flare risk compared to placebo-treated participants in the MITIGATE trial. The aim was to evaluate clinical and molecular characteristics of INEB-treated participants who experienced a positively adjudicated and treated IgG4-RD flare during the randomized controlled period (RCP) of the MITIGATE trial.

Methods: Disease history and clinical characteristics of INEB-treated participants (n=7) with an on-study flare were analyzed. B cell counts, IgG4 levels, and other markers were evaluated and compared to the 61 INEB-treated participants who did not flare. Temporal relationships between disease flares, INEB dosing, and changes in biomarker levels were explored.

Table 1: Baseline Disease Characteristics of Inebilizumab-treated Participants with and without On-study Flare

Baseline Characteristics	Participants with flare, N=7	Participants with no flare, N=61
Disease Duration, y, median (min, max)	2.4 (0.1, 10.0)	0.5 (0.1, 20.5)
Prior non-glucocorticoid therapy for IgG4-RD Yes, n (%)	3 (42.9)	14 (23.0)
Number of Organs affected historically, median (min, max)	5 (2, 7)	4 (2, 11)
Number of Organs affected at baseline, median (min, max)	2 (2, 5)	3 (1, 11)
Highest (Ever) IgG4 Serum Concentration (mg/dL), median (min, max)	401.2 (95.1, 2180.0)	721.0 (21.0, 34100.0)
Responder Index Score at Baseline, median (min, max)	4.0 (0, 11)	5.0 (0, 19)
ACR/EULAR Score, median (min, max)	35.0 (25, 58)	40.0 (20, 74)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Clinical Characteristics of Inebilizumab-treated Participants with On-study Flare

Participant #	Disease Duration (years)	Prior Non-glucocorticoid Therapy for IgG4-RD	Number of Organs Involved Historically	Number of Organs Involved at Baseline	Organs Involved at Baseline	Highest (ever) IgG4 Concentration (mg/dL)	Responder Index Score at Baseline	ACR/EULAR Classification Score
1	5.9	Yes	4	2	Kidney, Other Organs: Eyes (Uveitis)	767.0	0	36
2	2.4	Yes	2	2	Extra-ocular muscle, Lacrimal Glands	95.1	4	25
3	0.1	No	5	4	Lacrimal Glands, Lymph Node(s), Parotid glands, Submandibular glands	401.2	6	26
4	1.1	No	7	5	Kidney, Lymph Node(s), Pancreas, Sinus, Other Organs: prostate and spermatic cord	370.0	11	58
5	6.5	Yes	5	2	Parotid glands, Submandibular glands	2180.0	3	50
6	10.0	No	6	2	Mastoid sinus or middle ear, Other Organs: Nodulary lesions in periton	194.0	2	26
7	0.2	No	3	3	Lymph Node(s), Sinus, Submandibular glands	1570.0	6	35

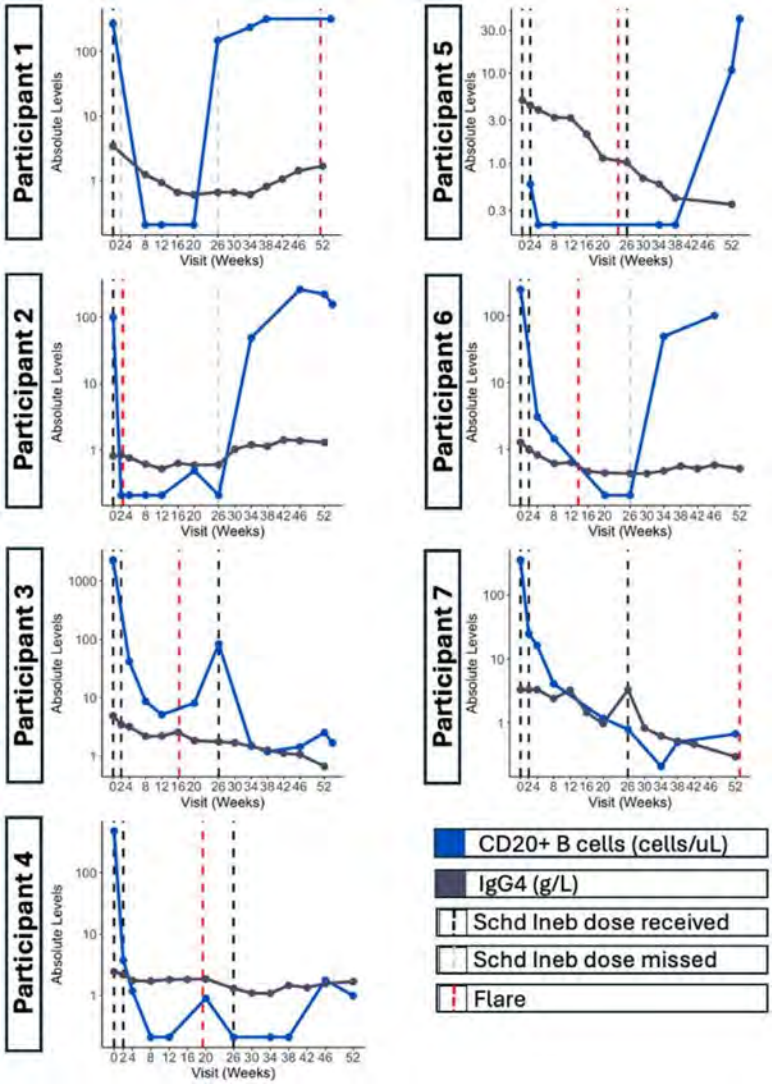


Figure 1. Relationship between B cell counts, serum IgG4 levels, inebilizumab administration, and flares in inebilizumab-treated MITIGATE participants who experienced an on-study flare (n=7). Dashed black lines represent inebilizumab dose received; dashed grey lines represent inebilizumab dose scheduled but not received; dashed red lines represent time of flare.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Overall, the baseline characteristics of the 7 INEB-treated participants who experienced a flare are generally similar to those of the 61 INEB-treated participants who did not (Table 1), with lower historic IgG4 levels, longer duration of disease, and more prevalent prior non-GC therapy noted among the INEB-treated participants who flared. Clinical characteristics of the 7 INEB-treated participants who flared show diversity in disease duration, prior non-GC therapy, organ involvement, highest historic IgG4 levels, baseline Responder Index score, and ACR/EULAR classification criteria scores at study entry (Table 2).

There is no consistent pattern in B cells, immunoglobulins, and other biomarkers among the INEB-treated participants who flared that distinguishes them from the 61 INEB-treated participants who did not flare. Analysis of the timing of biomarker changes (Figure 1) revealed no consistent pattern at the time of flare in INEB-treated participants. Of note:

- Participant 1 discontinued INEB after the first infusion (Day 1), and B cells were fully recovered at the time of flare
- Participant 2 experienced a flare 2 weeks after the first infusion, prior to development of the full pharmacodynamic effects of INEB
- Participant 3 displayed incomplete B cell depletion (>5 cells/μL) at the time of flare despite receiving all prior doses of INEB
- The remaining 4 participants experienced a flare in the setting of deep B cell depletion and reduced IgG4 levels compared to baseline

Conclusion: In this small cohort, baseline clinical and serologic characteristics did not reliably differentiate INEB-treated participants who experienced a flare (n=7) from those who did not (n=61). In INEB-treated participants, no clear patterns of biomarker changes are associated with occurrence of flare. Some participants experienced full apparent pharmacodynamic effect of INEB yet experience a flare. Two INEB-treated participants flared after discontinuing INEB or prior to development of the full pharmacodynamic effect.

Disclosure: J. Stone: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **E. Culver**: Amgen, 1, 2, Zenus, 2; **A. Khosroshahi**: Amgen, 1, 2; **W. Zhang**: None; **E. Della Torre**: Amgen, 1, 2; **K. Okazaki**: Amgen, 1; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **M. Lohr**: Amgen, 1; **n. schleinitz**: Amgen, 1, 2; **F. Martinez-Valle**: Amgen, 1; **M. Nayar**: Amgen, 1; **V. Rebours**: Amgen, 1, Viatris, 6; **C. Perugino**: Acepodia, 2, Amgen, 1, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Zenas Biopharma, 2; **K. Clarkson**: Amgen, 3, 11; **T. Alexander**: Amgen, 3, 11; **X. Dong**: Amgen, 3, 11; **Q. Huang**: Amgen, 3, 11; **S. Cheng**: Amgen, 3, 11; **D. Cimbora**: Amgen, 3, 11.

Abstract Number: 1164

Effect of TNF Inhibitors on the Postprandial Glucose Homeostasis Molecules: Amylin, Gastric Inhibitory Polypeptide, and Pancreatic Polypeptide in Rheumatic Patients

José Carlos García-Hernández[1], Iván Ferraz Amaro[2], Marta Hernández Díaz[2], Ana Isabel Rodríguez Vargas[1] and Federico Díaz González[1], [1]Hospital Universitario de Canarias, Santa Cruz De Tenerife, Canarias, Spain, [2]Servicio Canario de Salud, La Laguna, Canarias, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The effect of systemic TNF inhibition on postprandial glucose homeostasis, a parameter associated with cardiovascular health, remains unclear. This study aims to evaluate the effects of TNF inhibitors (TNFi) on hormones involved in the fine-tuning of postprandial glucose homeostasis: amylin, gastric inhibitory polypeptide (GIP), and pancreatic polypeptide (PP), in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondylarthritis (axSpA).

Figure 1

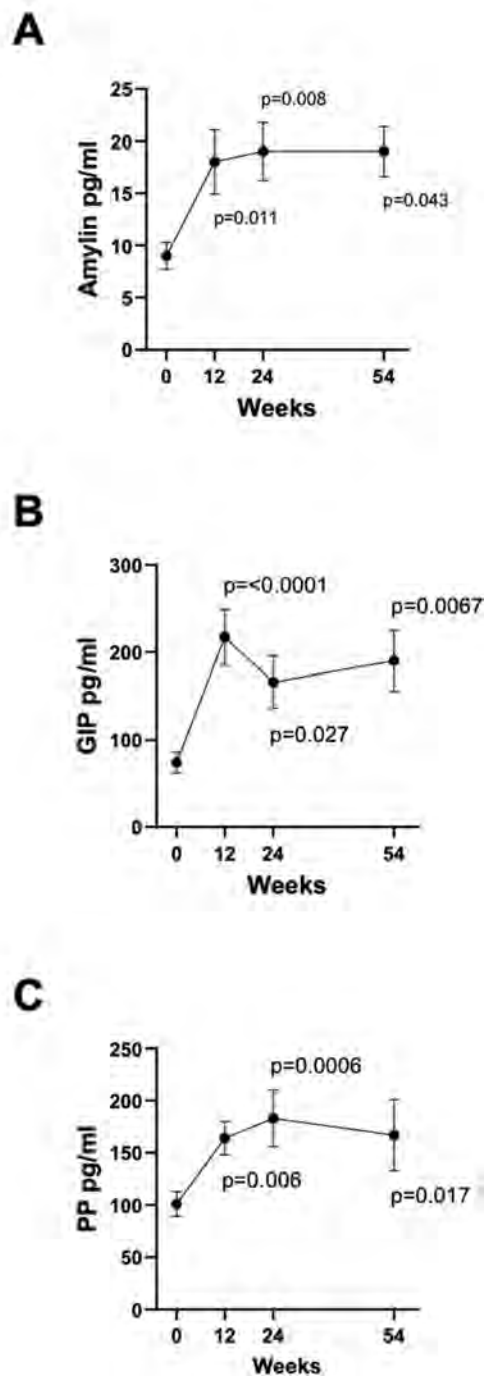


Figure 1. Dot plots showing the changes in plasma concentrations over one year of TNFi treatment in all included patients for (A) amylin, (B) GIP, and (C) pancreatic polypeptide. Data are presented as means ± SEM. p-values indicate statistically significant differences compared to baseline, as determined by mixed-effects analysis for repeated measures with Dunnett's correction for multiple comparisons.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Sixty-four non-diabetic patients (RA, n=22; PsA, n=13; axSpA, n=29) undergoing TNFi therapy were prospectively evaluated at baseline and after 12, 24, and 52 weeks. Assessments included measurements of disease activity, acute-phase reactants, fasting glucose, insulin and C-peptide levels, and insulin resistance as assessed by the updated Homeostatic Model Assessment (HOMA)-2. Serum concentrations of amylin, GIP, and PP were measured at each visit. Multivariable linear mixed-effects models were used to analyze temporal changes in these molecules of glucose metabolism homeostasis.

Results: BMI remained stable throughout the one-year follow-up period. Among patients with RA, disease activity indices, including DAS28-CRP, SDAI, and CDAI, showed significant reductions at 3, 6, and 12 months. Likewise, in patients with axSpA, there was a significant decrease in disease activity, metrological, and functional indices. Finally, in patients with PsA, a significant decrease was observed in the DAPSA index at the 6-month visit, but this improvement was not maintained at the 1-year follow-up. No significant modifications were observed in lipid-related molecules, apart from triglycerides, which showed significantly lower levels after one year of treatment compared to baseline

Serum glucose levels remained consistent with baseline levels after one year of TNFi treatment. Circulating insulin and C-peptide levels remained stable during TNFi treatment. Indices of insulin sensitivity and beta-cell function, as measured by the HOMA-2 index, remained unchanged over the one-year period of TNFi treatment. The interaction analysis showed that changes in insulin resistance indices were consistent regardless of diagnosis (RA, PsA, or AS) or type of TNFi used (adalimumab versus non-adalimumab). Despite this, amylin, GIP and PP levels increased significantly shortly after treatment initiation at week 12 and maintained this significant upregulation at 12-month follow-up (Figure). Importantly, the significance of these findings persisted after adjustment for changes in CRP during the follow-up period. No significant interactions were observed between the specific TNFi used or type of rheumatic disease and changes in amylin and GIP over time. This finding suggests that changes in these hormone levels occur independently of both the TNFi used and the underlying disease.

Conclusion: Systemic TNF inhibition is associated with sustained increases in serum levels of amylin, GIP and PP independent of systemic inflammation. This modulation of postprandial glucose-regulating hormones may contribute to the cardiovascular benefits of TNFi in patients with inflammatory disease.

Disclosure: J. García-Hernández: None; **I. Ferraz Amaro**: None; **M. Hernández Díaz**: None; **A. Rodríguez Vargas**: None; **F. Díaz González**: None.

Abstract Number: 1165

Real-World On-Label Treatment Persistence Through 24 Months in Biologic-Naïve and Biologic-Experienced Patients with Psoriatic Arthritis: Comparison of Guselkumab versus Subcutaneous Tumor Necrosis Factor Inhibitors

Philip J. Mease[1], Jessica A. Walsh[2], Timothy P. Fitzgerald[3], Soumya Chakravarty[4], Elizabeth Adamson[5], Bruno Emond[6], Carmine Rossi[7], Samuel Schwartzbein[7], Kana Yokoji[7], Yuxi Wang[7], Patrick Lefebvre[7], Dominic Pilon[7], Shikha Singla[8] and **Joseph F Merola**[9], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [3]Johnson & Johnson, Horsham, PA, USA, PA, [4]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [5]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [6]Analysis Group, Inc., Montreal, QC, Canada, QC, [7]Analysis Group, Inc., Montreal, QC, Canada, QC, Canada, [8]Medical College of Wisconsin, Milwaukee, WI, [9]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: A prior analysis found that patients (pts) with psoriatic arthritis (PsA) treated with guselkumab (GUS), an IL-23p19 subunit inhibitor, were approximately 2× more likely to remain persistent with on-label treatment up to 24 months (M) vs first-time subcutaneous (SC) TNFi users.[1] Real-world evidence comparing long-term on-label persistence between GUS and SC TNFi in biologic-naïve and biologic-experienced populations is lacking.

Methods: IQVIA PharMetrics® Plus database (1/1/2011-6/30/2023) was used to analyze treatment persistence among biologic-naïve and -experienced adults with active PsA who initiated GUS/SC TNFi (index date=first claim for GUS/SC TNFi). Analyses were performed separately for biologic-naïve (no prior pre-index biologic claims) and biologic-experienced (≥1 prior pre-index biologic claim) pts. Pts had ≥12M insurance eligibility and no claims for confounding diseases or index medications pre-index date. Baseline characteristics were summarized for the 12M pre-index period. On-label persistence was defined as continued use of index therapy without dose modification (escalation/reduction) per FDA-approved labeling. Propensity score overlap weighting was applied to balance baseline characteristics between the GUS and SC TNFi cohorts. On-label persistence over 24M was compared via weighted Kaplan-Meier (KM) curves and Cox proportional hazards model. For biologic-naïve pts, further adjustment for prior conventional synthetic (cs) and targeted synthetic (ts) disease-modifying antirheumatic drug (DMARD) use was performed.

Results: Among 3,294 pts, 361 GUS pts (49.5 years; 59.8% female) and 2,171 SC TNFi pts (48.3 years; 59.5% female) were biologic-naïve, and 443 in GUS cohort (50.8 years; 61.2% female) and 319 in SC TNFi cohort (48.5 years; 64.3% female) were biologic-experienced. Weighted baseline characteristics were balanced between cohorts, except for prior csDMARD/tsDMARD use among biologic-naïve pts. For biologic-naïve pts, the median time-to-discontinuation was 22.4M for GUS and 9.2M for SC TNFi; weighted KM on-label persistence rates at 6M/12M/18M/24M: 86.2%/73.1%/62.9%/48.9% for GUS vs 63.8%/43.8%/35.3%/28.4% for SC TNFi (all log-rank $p< 0.001$). For biologic-experienced pts, the median time-to-discontinuation was 18.4M for GUS and 7.4M for SC TNFi; weighted KM on-label persistence rates at 6M/12M/18M/24M: 76.9%/57.7%/50.6%/39.5% for GUS vs 58.1%/40.3%/31.1%/23.3% for SC TNFi (all log-rank $p< 0.001$). At 24M, GUS cohort pts were ∼2× more likely to remain persistent vs SC TNFi cohort in both biologic-naïve (HR: 2.36, 95% CI: 1.88-2.98; $p< 0.001$) and biologic-experienced pts (HR: 1.86, 95% CI: 1.46-2.37; $p< 0.001$).

Conclusion: Pts initiating GUS demonstrated statistically significantly higher on-label persistence through 24M than those initiating SC TNFi in both biologic-naïve and biologic-experienced pts with active PsA. Higher long-term on-label persistence may improve disease management outcomes, including functional status and quality of life.

Reference:

1. Mease PJ, et al. Poster. CCR-West 2024; Sept 26-29, 2024; San Diego, CA, USA.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **T. Fitzgerald**: Johnson & Johnson, 3, 11; **S. Chakravarty**: Johnson & Johnson, 3, 11; **E. Adamson**: Johnson & Johnson, 3, 11; **B. Emond**: Analysis Group, Inc., 3, 11; **C. Rossi**: Analysis Group, Inc., 3, 11; **S. Schwartzbein**: Analysis Group, Inc.,, 3, 11; **K. Yokoji**: Analysis Group, Inc., 3, 11; **Y. Wang**: Analysis Group, Inc., 3, 11; **P. Lefebvre**: Analysis Group, Inc., 3, 11; **D. Pilon**: Analysis

Group, Inc., 3, 11; **S. Singla**: AbbVie/Abbott, 2, Eli Lilly, 5, Janssen, 2, 6, Prometheus Biosciences, 5, UCB, 2; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5.

Abstract Number: 1166

Biomarkers Associated with Left Atrial Structure and Function in Individuals with Psoriasis

Julie Borchsenius[1], Maria Dons[2], Morten Sengeløv[3], Flemming Olsen[4], Caroline Espersen[4], Kristoffer Skaarup[3], Mats Lassen[4], Niklas Johansen[4], Filip Davidovski[3], Manan Pareek[4], Brittany Weber[5], Claus Zachariae[6], Lone Skov[6] and Tor Biering-Sørensen[3], [1]CTCPR / Center for translational cardiology and pragmatic research trials, Charlottenlund, Denmark, [2]Copenhagen University Hospital Gentofte, Copenhagen, Hovedstaden, Denmark, [3]Center for Translational Cardiology and Pragmatic Randomized Trials, Dep. of Cardiology, Copenhagen University Hospital - Gentofte, Copenhagen, Hovedstaden, Denmark, [4]CTCPR / Center for translational cardiology and pragmatic research trials, Copenhagen, Denmark, [5]Brigham and Women's Hospital, DEDHAM, MA, [6]Dep. of Dermatology and Allergy, Copenhagen University Hospital – Herlev & Gentofte, Copenhagen, Hovedstaden, Denmark

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

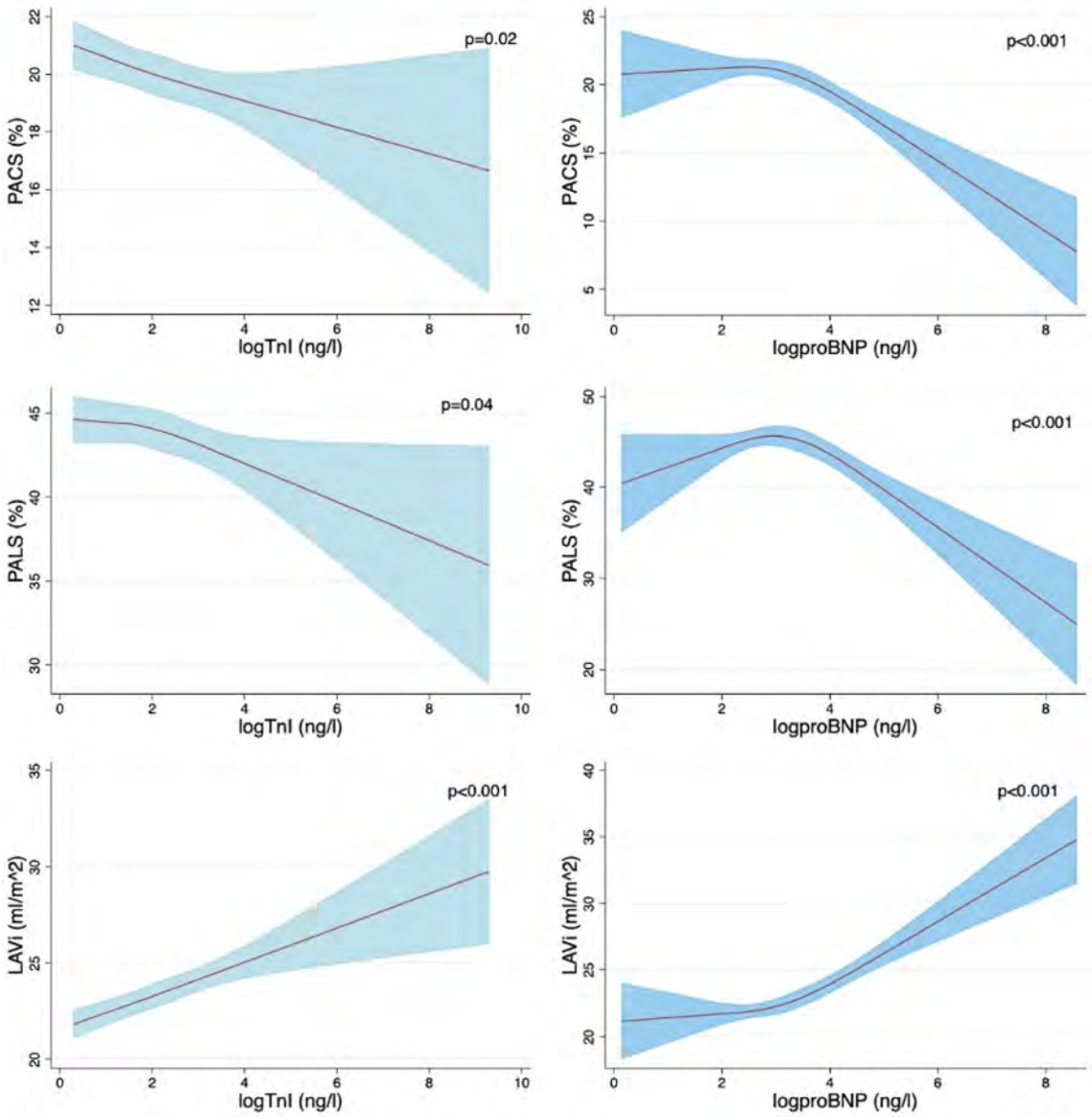
Background/Purpose: Individuals with psoriasis are at increased risk of developing heart disease. Echocardiographic parameters of impaired left atrial (LA) strain (Peak atrial contraction and longitudinal strain (PACS and PALS)) and volume index (LAVi) are associated with increased risk of heart disease. Whether cardiac and inflammatory biomarkers are associated with left atrial impairment in adults with psoriasis is unknown.

The aim of this study was to assess whether plasma levels of high-sensitivity C-reactive protein (hsCRP), high-sensitivity troponin I (hsTnI) and pro-brain natriuretic peptide (proBNP) were associated with LA structure and function in adults with psoriasis.

Methods: This was a cross-sectional analysis of a prospective cohort study of 1,010 participants with psoriasis who underwent echocardiographic examination and had blood samples analyzed from 2021-2024. Those without available measurements of hsCRP (n=27), TnI (n=5) or proBNP (n=17), LA strain (n=23) or LAVi (n=11) were excluded. The population was stratified according to hsCRP, hsTnI and proBNP tertiles, respectively. We used ANOVA, Pearson's Chi^2-test, Kruskal-Wallis test, linear regression and cubic spline models as appropriate to assess the associations between biomarkers, cardiac risk factors and measures of LA structure and function. Biomarkers were logarithmically transformed for the linear regression analyses. In multivariable analyses, models were adjusted for sex, age, package years, BMI >30, hypertension, hypercholesterolemia, diabetes mellitus, chronic kidney disease, ischemic heart disease, heart failure, atrial fibrillation and psoriasis treatment.

Results: We included 927 adults with psoriasis (mean age 54.0 years, 46.5 % women). In the entire cohort, median hsCRP was 1.1 mg/l (IQR 0.5-2.7), median hsTnI was 3.0 ng/l (IQR 1.2-6.0) and the median proBNP was 7.6 ng/l (4.2-14.3). The participants in the highest tertile groups of all three biomarkers were overall older, had more package years and a higher prevalence of hypertension. Furthermore, the highest hsCRP group >1.73 mg/l were predominantly women, had higher

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Cubic spline models analyzing the association between biomarkers and echocardiographic measures of left atrial strain and volume index.

BMI and were less physically active. The highest TnI group >5 ng/l were predominantly men, had a higher prevalence of moderate-to-severe psoriasis, and cardiovascular disease was more prevalent. The proBNP-group >11.5 ng/l had more women and a higher prevalence of cardiovascular disease.

In univariable analyses, higher levels of hsCRP were associated with lower PALS, while higher levels of TnI and proBNP were associated with lower PACS and PALS and higher LAVi. In multivariable analyses, higher levels of TnI and proBNP remained significantly associated with lower PACS and PALS and higher LAVi. (Figure)

Conclusion: In a sample of adults with psoriasis, higher levels of TnI and proBNP were associated with impaired LA structure and function. Given the known association between LA dysfunction and heart disease, these biomarkers may identify individuals with psoriasis at increased risk of cardiac disease.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Borchsenius: None; **M. Dons**: Karen Elise Jensens Foundation, 5, Lundbeck Foundation, 5; **M. Sengeløv**: None; **F. Olsen**: None; **C. Espersen**: None; **K. Skaarup**: None; **M. Lassen**: None; **N. Johansen**: None; **F. Davidovski**: None; **M. Pareek**: AstraZeneca, 1, 6, Bayer, 1, 6, Boehringer-Ingelheim, 6, Janssen, 1, 6, Novo Nordisk, 5, 6, The Danish Heart Foundation, 5; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **C. Zachariae**: None; **L. Skov**: AbbVie/Abbott, 1, 6, Almirall, 1, 5, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 6, Janssen, 1, 5, 6, Novartis, 1, Pfizer, 6, Sanofi, 1, 5, 6, stada, 1, takeda, 1, 6, UCB, 1, 5, 6; **T. Biering-Sørensen**: Amgen, 2, AstraZeneca, 5, 6, Bayer, 6, Boston Scientific, 5, CSL Seqirus, 2, GE Healtcare, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, IQVIA, 2, Novartis, 5, 6, Novo Nordisk, 2, 5, Parexel, 2, Pfizer, 5, Sanofi Pasteur, 2, 5, 6.

Abstract Number: 1167

Clinical Characteristics and Outcomes of igg4-related Disease Patients Who Chose Watchful Observation Without Treatment Intervention: A Single-center Study

Kanako Chujo[1], Hiromi Shimada[2], Shusaku Nakashima[2], Taichi Miyagi[1], Koichi Sugihara[2], Yusuke Ushio[1], Mao Mizusaki[2], Naoto Manabe[1], Mayuko Wada[2], Risa Wakiya[3], Hiroki Ozaki[4] and Hiroaki Dobashi[2], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan, [2]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa, Japan, [3]Division of Rheumatology, Departent of Internal Medicine, Toho University School of Medicine, Tokyo, Japan, [4]KKR Takamatsu Hospital, Takamatsu, Kagawa, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Treatment of IgG4-related disease (IgG4-RD) is recommended for patients with severe organ involvement or for patients with reduced quality of life even in the absence of severe organ involvement. On the other hand, some patients with no severe lesions and acceptable quality of life, especially those with asymptomatic single organ disease, can be followed up without treatment. Therefore, we aimed to investigate the clinical characteristics and outcomes of patients without therapeutic intervention at the time of IgG4-RD diagnosis in single center.

Table 1. Comparison of clinical characteristics at diagnosis between the treatment and observation groups

	Treatment group(n=54)	Observation group(n=26)	P value
Age at diagnosis (years old)#	68.5 ± 10.7	62.7 ± 8.2	< 0.01
Gender (male:female)##	38:16	13:13	0.09
Definite/probable/possible (n (%))##	28 (52.8)/7 (13.2)/18 (34.0)	14 (53.9)/5 (7.7)/18(38.5)	0.75
Laboratory findings			
IgG4 (mg/dL)#	798.7 ± 945.7	519.8 ± 706.5	0.06
IgG (mg/dL)#	2772.4 ± 1425.5	1789.4 ± 876.6	< 0.01
IgE (mg/dL)#	786.0 ± 1577.7	367.0 ± 354.2	0.74
low complement (n (%))##	21/50 (42.0)	5/19 (20.8)	0.12
CRP (mg/dL)#	1.4 ± 3.2	0.1 ± 0.1	< 0.01
sIL-2R (IU/dL)#	1233.1 ± 1013.5	968.1 ± 1612.8	< 0.01
Number of organ involvement (n)#	3.4 ± 1.5	2.4 ± 1.3	< 0.01
IgG4-RD RI#	7.7 ± 3.2	4.8 ± 2.5	< 0.01

(Values are presented as mean ± S.D. or number(%). #Wilcoxon rank sum test ##Fischer's exact test)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients with IgG4-RD diagnosed from 2005 to 2024 according to the comprehensive diagnostic criteria for IgG4-RD revised in 2020 at our institution were included in our study. Clinical characteristics including IgG4-RD Responder Index (IgG4-RD RI) and immunological laboratory findings were retrospectively collected from medical records. In the cases observed without treatment after IgG4-RD diagnosis, we investigated whether the subsequent therapeutic intervention became necessary or not. We then analyzed the predictors of the need for treatment.

Results: Of all 80 cases diagnosed with IgG4-RD, 54 cases (67.5%) were started to treat at diagnosis (treatment group), while 26 cases (32.5%) were observed without therapeutic intervention (observation group).

In the observation group, age at diagnosis was significantly younger and the levels of CRP, IgG, sIL-2R and IgG4-RD RI were lower. Serum IgG4 levels also tended to be lower compared to the treatment group (Table 1). Cases with only glandular and lymph node involvement were more common in the observation group. In contrast, patients with severe organ involvement such as retroperitoneal, renal, pancreatic, pulmonary and orbital lesions were more likely to have started treatment at the time of diagnosis (Figure 1).

Of the 26 cases in the observation group, 7 required therapeutic intervention during the observation period. New organ involvement, including the pancreas, was observed in 5 cases. There were no significant differences in clinical characteristics at the time of diagnosis between the patients with (n=7) and without (n=19) treatment intervention (Table 2). The mean

Figure 1. Organ involvement in the treatment group and observation groups

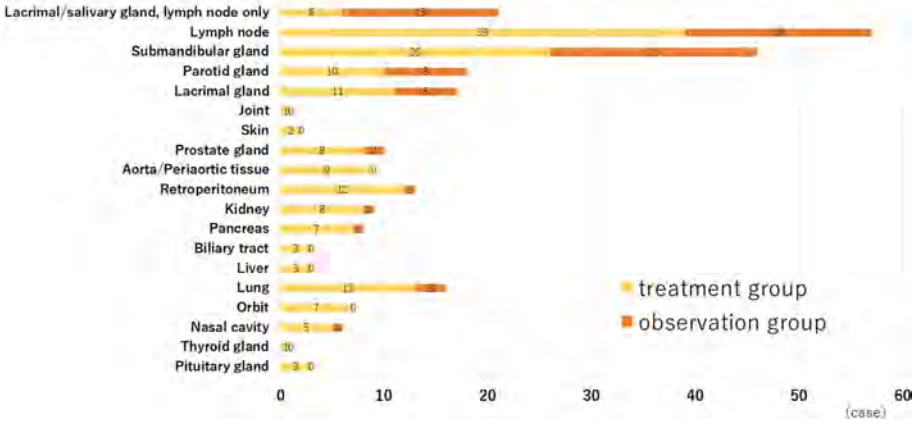


Table 2. Comparison of clinical features at diagnosis between patients with and without therapeutic intervention after observation

	Therapeutic intervention after observation(n=7)	Continuation of observation(n=19)	P value
Age at diagnosis (years old)*	60 ± 9	63.6 ± 7.9	0.31
Gender (male:female)**	4:3	9:10	1.0
Definite/probable/possible (n (%))**	4(57.1)/0 (0)/3 (42.9)	10(52.6)/ 2(10.5)/ 7(36.8)	
Laboratory findings			
IgG4 (mg/dL)*	785.4 ± 1238.3	422.0 ± 380.3	0.73
IgG (mg/dL)*	1975 ± 1247.0	1721.1 ± 728.4	0.82
IgE (mg/dL)*	501.2 ± 544.1	322.2 ± 285.7	1.00
low complement (n (%))**	2/6(33.3)	3/18(16.7)	0.57
CRP (mg/dL)*	0.1 ± 0.2	0.1 ± 0.1	0.58
sIL-2R (IU/dL)*	1287.2 ± 1275.0	861.7 ± 1737.0	0.22
Number of organ involvement (n)*	2.8 ± 1.3	2.7 ± 1.4	0.87
SUV max*	7.4 ± 3.0	9.4 ± 7.2	0.89
IgG4-RD RI*	5.1 ± 3.0	4.7 ± 2.5	0.81

(Values are presented as mean ± S.D. or number (%). #Wilcoxon rank sum test ##Fischer's exact test)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

duration from diagnosis to the initiation of therapeutic intervention was 30 ± 25 months. Among the 19 cases without treatment intervention, 13 cases (68.4%) had multiple organ involvement, such as glandular, lymph node, and pulmonary involvement.

Conclusion: In our study, some cases of IgG4-RD could be observed without treatment, even with multiple lesions. It is important to have an appropriate monitoring strategy to determine the need for therapeutic intervention in IgG4-RD.

Disclosure: K. Chujo: None; **H. Shimada**: None; **S. Nakashima**: None; **T. Miyagi**: None; **K. Sugihara**: None; **Y. Ushio**: None; **M. Mizusaki**: None; **N. Manabe**: None; **M. Wada**: None; **R. Wakiya**: None; **H. Ozaki**: None; **H. Dobashi**: None.

Abstract Number: 1168

Interstitial Lung Disease-Associated Antibody Testing and Positivity Rates in Systemic Autoimmune Rheumatic Diseases from a National Reference Laboratory

Karis Lee[1], Min Kyung Lee[2] and Stanley Naides[3], [1]Labcorp, Orlando, FL, [2]Labcorp, Durham, NC, [3]Labcorp, Dana Point, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is frequent in systemic autoimmune rheumatic diseases (SARDs) and is associated with poor prognosis. The prevalence of ILD is approximately 52% in systemic sclerosis (SSc), 41% in myositis, 23% in Sjögren's syndrome (SS), 21.4% in rheumatoid arthritis (RA), 14.5% in systemic lupus erythematosus (SLE), and 56% in overlap syndromes. While early detection of ILD is crucial, diagnostic imaging is typically limited to high-risk patients. Biomarker testing is a cost-effective method for identifying patients at increased risk of ILD. We examined testing and positivity rates of ILD-associated antibodies in patients with SARDs to assess current screening practices.

Methods: We retrospectively reviewed testing for ILD-associated antibodies (Jo-1, PL-7, PL-12, EJ, OJ, SRP, MDA-5, PM/Scl-100, Ku, and SS-A 52kD) in patients with SSc (N = 87,115), idiopathic inflammatory myopathy (IIM, N = 25,496), myositis (N = 110,645), polymyositis (PM, N = 58,619), dermato(poly)myositis (DM, N = 73,568), SS (N = 365,136), RA (N = 3,837,117), SLE (N = 956,740), and overlap syndromes (N = 104,697) from 2021 through 2024. Patients with interstitial pulmonary disease (N = 190,160) were included for reference. Diagnostic labels reflect provider-assigned ICD-10 codes at the time of testing.

Results: PL-7, PL-12, EJ, OJ, SRP, MDA-5, PM/Scl-100, Ku, and SS-A 52kD were tested in less than 1.7% of patients with SSc, SS, RA, SLE, and overlap syndromes (**Figure 1**). Testing rates for these antibodies ranged from 3.3 – 4.5% in patients with IIM, myositis, or PM, and 5.9 – 6.2% in those with DM. Among patients with SSc, PM/SCL-100 was the second most tested biomarker at 4.2%.

Jo-1 had the highest testing rate across all SARDs, with 6.7 – 9.6% of patients with SSc, IIM, myositis, PM, DM, SS, SLE, and overlap syndromes tested. Jo-1 positivity rates ranged between 0.2 – 1.4% in patients with SSc, IIM, myositis, SS, RA, SLE, and overlap syndromes (**Figure 2**). Jo-1 was positive in 7.0% of patients with PM and 2.9% of patients with DM.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

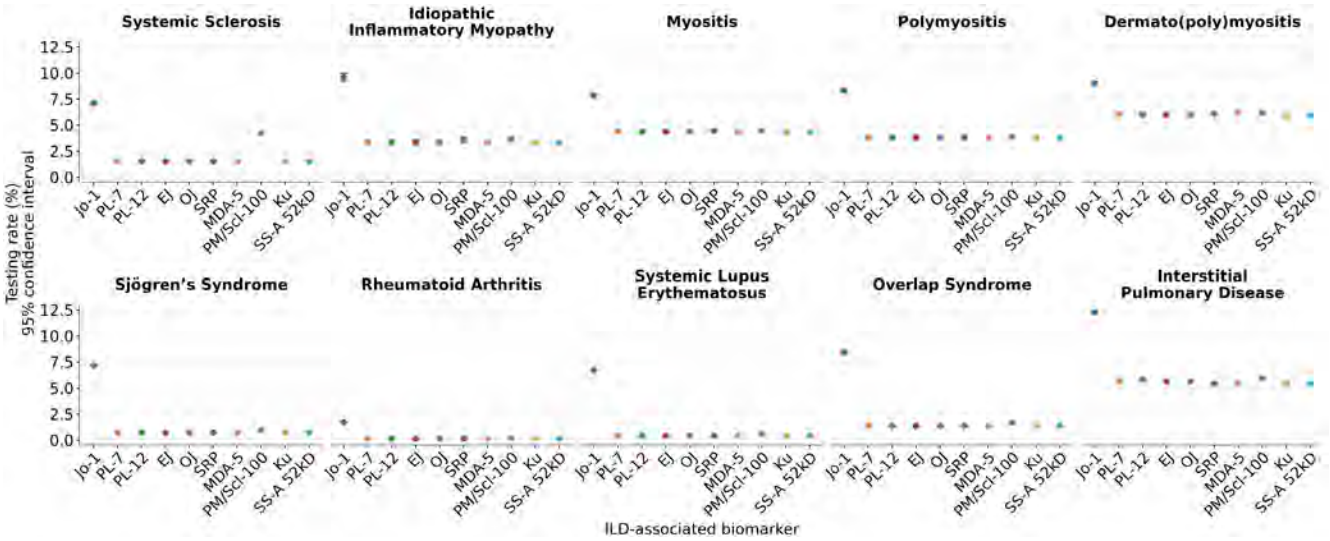


Figure 1. ILD-associated antibody testing rates

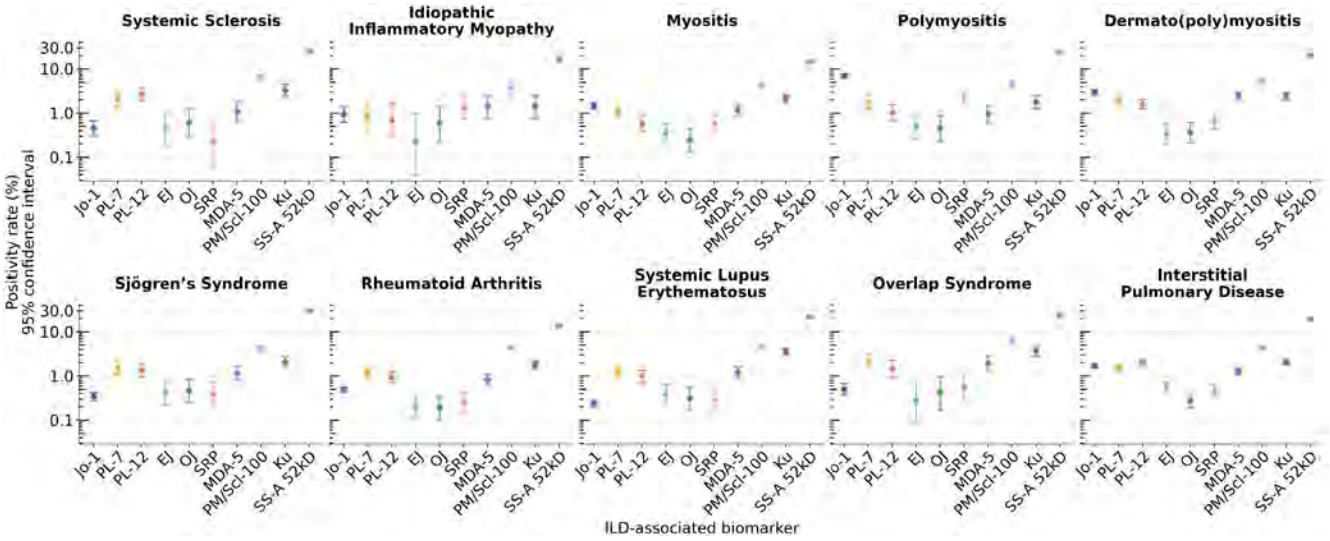


Figure 2. ILD-associated antibody positivity rates

Despite lower testing rates, positivity rates for SS-A 52kD were consistently higher than Jo-1, ranging from 13.7% in RA to 29.8% in SS. PM/Scl-100 also showed higher positivity rates than Jo-1 in all SARDs except PM, ranging from 3.7% in IIM to 6.7% in overlap syndromes. High positivity rates for Ku and PL-7 were also found in patients with SSc (3.3%, 2.1%), IIM (1.4%, 0.8%), myositis (2.2%, 1.1%), SS (2.1%, 1.5%), RA (1.8%, 1.1%), and overlap syndromes (3.8, 2.2%). MDA-5 also had high positivity rates in patients with IIM (1.4%) and in patients with DM (2.5%).

Conclusion: While Jo-1 was the most frequently tested antibody across all SARDs, positivity rates were low among patients with SSc, SS, RA, SLE, and overlap syndromes. In contrast, markers such as PL-7, Ku, and SS-A 52kD that were tested less frequently had higher positivity rates. MDA-5 had positivity rates comparable to Jo-1 among patients with IIM and DM. These findings suggest that incorporating a broader panel of ILD-associated biomarkers along with Jo-1 may facilitate early detection of ILD in patients with SARDs.

Disclosure: K. Lee: Labcorp, 3, 11; **M. Lee**: Labcorp, 3, 11; **S. Naides**: Labcorp, 3.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1169

Periodontitis in neutropenic DADA2 patients

Lorena Wilson[1], Amanda Ombrello[2], Patrycja Hoffmann[3], Cornelia Cudrici[3], Tina Romeo[4] and Daniel L. Kastner[5], [1]National Institutes of Health, Silver Spring, [2]National Institutes of Health, Rockville, MD, [3]National Insitutes of Health, Bethesda, [4]NIH, Bethesda, MD, [5]National Human Genome research Institute (NHGRI), National Institutes of Health (NIH), Bethesda

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive disease caused by pathogenic mutations in *ADA2*. Severe and refractory neutropenia is a hematologic feature in the phenotypic spectrum of DADA2. Periodontal disease is often recognized as a manifestation of severe neutropenia, but not previously highlighted in neutropenic DADA2 patients.

Methods: Retrospective review of DADA2 patients identified with known periodontal disease and severe neutropenia in the NIH DADA2 cohort. Medical records from 12/18/2005 to 12/01/2024 were reviewed.

Results: Patient 1 (R169Q/deletion in exon 7) is a 57-year-old edentulous female with a 28-year history of neutropenia (ANC = 0), fevers, cervical lymphadenopathy, splenomegaly, and splenectomy. No known history of strokes. Periodontal disease manifested by chronic tooth decay, gingivitis, severe mandibular regression, dental extractions, and poor osseointegration of dental implants. Dental imaging demonstrated severe bone loss. She was treated with cyclosporine, prednisone, and an induction dose of infliximab, followed by adalimumab, with positive treatment response and neutrophil count normalization without periodontitis recurrence.

Patient 2 (H112Q/R34W) is a 44-year-old female with a history of transient neutropenia (ANC = 0.8), Raynaud's, fevers, arthralgia, genital ulcers, livedo reticularis, splenomegaly, and recurrent skin ulcers in lower extremities. No history of strokes. Periodontal disease manifested by extensive painful oral ulcerations and mucositis which correlated with episodes of severe neutropenia. She was treated with adalimumab with resolution of neutropenia and without oral ulcers and fever recurrence.

Patient 3 (R169Q homozygous) is a 43-year-old female with a history of neutropenia (ANC = 0), Raynaud's, two episodes of central retinal artery occlusions leading to right eye blindness, fevers, headaches, arthralgia, livedo reticularis, lymphadenopathy, esophageal necrosis, and common variable immunodeficiency. Periodontal disease manifested by oral ulcers and gingivitis. She was treated with etanercept, response was not observed due to medication discontinuation after patient's decision to withdraw all medical care. Patient expired 07/2024.

Patient 4 (H112Q/R169Q) is a 26-year-old male with a history of neutropenia (ANC = 0.3), fevers, skin rashes, and splenomegaly. Periodontal disease manifested by periodontal abscess and oral ulcers. No history of strokes. He received a hematopoietic stem cell transplant with resolution of DADA2 and periodontitis.

Conclusion: This retrospective review highlights periodontitis in severe neutropenia of DADA2. We hypothesize that DADA2 neutropenia induces IL-23 and IL-17 release by resident macrophages in the gingiva, similar to leukocyte adhesion deficiency. Since the neutropenia of DADA2 is at least partially due to destruction of precursors in the bone marrow, local

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cytokine production is unabated, leading to hyperinflammation. To further understand the mechanisms, we plan to conduct careful assessments of DADA2 patients' oral history, dental exams, and when appropriate, gum biopsies.

Disclosure: L. Wilson: None; **A. Ombrello**: None; **P. Hoffmann**: None; **C. Cudrici**: None; **T. Romeo**: None; **D. Kastner**: None.

Abstract Number: 1170

A20 Haploinsufficiency (HA20): TNFAIP3 Mutation Prevalence in a Clinically Compatible Cohort

Maria Alonso de Francisco[1], Emiliano González Vioque[2], Pablo Navarro Palomo[3], Maria Machattou[4], Carlota Navarro Joven[4], Laura Ramos Ortiz de Zarate[4], Alejandro Martínez[5], Adriana Martín Bescós[4], Paula Mazo[4], María Concepción Sánchez Fernández[4], Andrea Liso Andrino[4], Maria Carmen Barbadillo Mateos[6], JESUS SANZ SANZ[7], Hildegarda Godoy Tundidor[4], Jose Campos[8], Monica Fernandez Castro[9], Blanca García Magallón[4], Olga Rusinovich[10], Laura Nuño[11], Jose Luis Andreu[12] and Carolina Merino[13], [1]H. U. Puerta de Hierro Majadahonda, Tres Cantos, Spain, [2]Hospital Puerta de Hierro Majadahonda, Madrid, Spain, [3]Hospital Universitario Puerta de Hierro Majadahonda., Majadahonda, Spain, [4]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, [5]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Afghanistan, [6]Public, Madrid, Spain, [7]SERMAS, Madrid, Spain, [8]Hospital Universitario Principe de Asturias, Madrid, Spain, [9]PUERTA DE HIERRO HOSPITAL, Madrid, Spain, [10]Puerta de Hierro Majadahonda University Hospital, Boadilla del Monte, Spain, [11]Hospital Universitario Puerta de Hierro, Madrid, Spain, [12]Hospital Universitario Puerta de Hierro, Majadahonda, Spain, [13]Rheumatology department. Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda (Madrid), Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Haploinsufficiency of A20 (HA20) is a disease at the crossroads between autoinflammation and autoimmunity, caused by heterozygous mutations in TNFAIP3, which encodes the A20 protein, a negative regulator of pro-inflammatory pathways such as NF-κB and NLRP3. Clinically, HA20 can mimic systemic lupus erythematosus, Behçet's disease, inflammatory bowel disease, familial Mediterranean fever, or PFAPA syndrome. Hallmark features include recurrent fever, bipolar aphthosis, skin and gastrointestinal inflammation. Genetic testing is required for diagnosis.

Our study aimed to assess the prevalence of relevant mutations in a cohort with clinically suggestive features, to improve diagnostic precision in daily rheumatology practice.

Methods: Fourteen patients were prospectively recruited from the Rheumatology Department at University Hospital Puerta de Hierro, meeting inclusion criteria based on current literature. Recurrent oral aphthosis before age 30 was required, along with one or more of the following: unexplained fever, genital aphthosis, arthritis/arthralgia, acneiform/pustular/erythema nodosum-like skin lesions, recurrent abdominal pain or diarrhea, or inflammatory ocular disease.

Data collected included demographics, family history, age at symptom onset, mucosal, cutaneous, articular, gastrointestinal, and ocular involvement, and fever episodes. Blood samples were analyzed for ESR, CRP, ANA, ANCA, and anti-dsDNA, and a targeted next-generation sequencing (NGS) panel for autoinflammatory genes including TNFAIP3 was performed. Treatments received were recorded, including NSAIDs, glucocorticoids, colchicine, csDMARDs, bDMARDs, and other targeted therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1, part 1. Demographics, Symptoms, Blood Analysis

Data	n (%) / median (range)
Demographics	
Female sex	12 (86%)
Onset age	17 (1-50)
Family history	9 (64%)
Symptoms	
Mucosal	14 (100%)
Oral aphthae	14 (100%)
Genital aphthae	6 (43%)
Articular	14 (100%)
Arthralgia	14 (100%)
Arthritis	6 (43%)
Abdominal	14 (100%)
Pain	14 (100%)
Diarrhoea	13 (93%)
Elevated calprotectin	2 (14%)
Skin	7 (50%)
Acne	2 (14%)
Folliculitis	4 (29%)
Pustulosis	1 (7%)
Abscesses	3 (21%)
Erythema nodosum	1 (7%)
Ocular	0 (0%)
Chest pain	2 (14%)
Recurrent fever	10 (71%)
Blood analysis	
Elevated reactants	5 (36%)
ANA positivity	5 (36%)
ANCA positivity	0 (0%)
anti-DNAds	3 (21%)

Results: Two patients (14.3%) had mutations identified via NGS: one in RIPK1 and another in PLCG2; no patient in our cohort tested positive for mutation in TNFAIP3.

Both were Caucasian women with first-degree relatives affected by autoimmune disease, but had different ages of onset (29 vs. 5 years).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1, part 2. Treatments

Data	n (%) / median (range)
Treatments	
Glucocorticoids	8 (57%)
NSAIDs	12 (86%)
Colchicine	3 (21%)
cDMARD	10 (71%)
Methotrexate	5 (36%)
Hydroxychloroquine	3 (21%)
Sulfasalazine	2 (14%)
Mycophenolate	1 (7%)
Teriflunomide	1 (7%)
bDMARD	7 (50%)
Adalimumab	6 (43%)
Golimumab	3 (21%)
Certolizumab	2 (14%)
Infliximab	2 (14%)
Etanercept	1 (7%)
Anakinra	3 (21%)
Other	4 (29%)
Tofacitinib	2 (14%)
Upadacitinib	1 (7%)
Apremilast	3 (21%)

Common symptoms included oral aphthae, arthralgia, abdominal pain, diarrhea, and fever. The RIPK1 case showed elevated fecal calprotectin and chest pain, without cutaneous or serologic abnormalities. The PLCG2 patient had acne, folliculitis, elevated acute phase reactants, and ANA positivity.

Both received treatment with NSAIDs, and colchicine in the case of the RIPK1 patient. Cohort characteristics are summarized in Table 1.

Conclusion: In our cohort, despite recruiting patients with matching criteria for HA20, we found presence of two other mutations associated with autoinflammatory syndromes, not related to our target one. This remarks the importance of genetic testing when suspecting autoinflammation, specially in patients with no defined diagnosis, as it shows the clinical overlap between different entities.

Identifying these distinct mutations could refine diagnosis and enable targeted treatment strategies by addressing underlying pathogenic mechanisms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Alonso de Francisco: None; **E. González Vioque**: None; **P. Navarro Palomo**: None; **M. Machattou**: None; **C. Navarro Joven**: None; **L. Ramos Ortiz de Zarate**: None; **A. Martínez**: None; **A. Martín Bescós**: None; **P. Mazo**: None; **M. Sánchez Fernández**: None; **A. Liso Andrino**: None; **M. Barbadillo Mateos**: None; **J. SANZ SANZ**: None; **H. Godoy Tundidor**: None; **J. Campos**: None; **M. Fernandez Castro**: None; **B. García Magallón**: None; **O. Rusinovich**: None; **L. Nuño**: None; **J. Andreu**: None; **C. Merino**: None.

Abstract Number: 1171

VEXAS Syndrome Under the Lens: A prospective analysis of temporal disease patterns, biomarker Dynamics, and therapeutic efficacy

Marta López[1], Paula Garcia Escudero[2], Berta Magallares[3], Meritxell Salles Lizarzaburu[4], Dolly Viviana Fiallo Suárez[5], Iñigo Rúa-Figueroa[6], Isla Morante Bolado[7], Elena Aurrecoechea[8], Eugenia Enriquez[9], Carolina Merino[10], Santos Castañeda[11], Irene Monjo Henry[12], César Antonio Egües Dubuc[13], Elena María Oliver García[14], Alicia Garcia[15], Judit Font-Urgelles[16], Cristina Corrales[17], Lourdes Villalobos[18], Alina-Lucica Boteanu[19], Ignacio Vázquez Gómez[20], Diego Dios[21], Clara Garcia Belando[22], Beatriz Frade Sosa[23], Delia Reina[24], Marta Ibañez[25], Irene Carrion[26], Maria Rodriguez[27], cristiana Sieiro[28], Francisco Javier Toyos[29], Alberto Mariano[30], Clara Moriano[31], Rafael B. Melero-González[32], Paloma Vela Casasempere[33], Jose Alberto Miranda[34], Giuliano Boselli[35], Jose Angel Hernandez[36], Ernesto Trallero[37], Elena Riera Alonso[38] and Jaime Calvo[39], [1]Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain, [2]H.U.Araba, Vitoria, [3]Hospital de Sant Pau, Bareclona, [4]Rheumatology Department, Althaia Xarxa Assistencial Universitària Manresa Manresa (Spain)., Manresa, Spain, [5]H.U. Doctor Negrín, Gran Canarias, [6]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [7]Rheumatology, Hospital General Sierrallana, Torrelavega, Spain., Santander, [8]H. Sierrallana, Santander, [9]Clinica Universidad de Navarra, Madrid, Spain, [10]Rheumatology department. Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda (Madrid), Madrid, Spain, [11]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [12]Hospital Universitario La Paz, Madrid, Spain, [13]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [14]H.C. U. Lozano Blesa, Zaragoza, [15]Rheumatologist, La Laguna, Spain, [16]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [17]HOSPITAL UNIVERSITARIO MARQUES DE VALDECILLA, Santander, Spain, [18]Ramon y Cajal Hospital, MADRID, Spain, [19]H.U. Ramón y Cajal, Madrid, Spain, [20]H.U. Doctor Peset, Valencia, [21]H. U de A Coruña, A Coruña, Spain, [22]H.C. U. Virgen de la arrizaca, Murcia, [23]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [24]Complex Hospitalari Moisès Broggi, Barcelona, Spain, [25]Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [26]Hospital del Mar, Barcelona, Spain, [27]H. Clínico San Carlos, Madrid, Spain, [28]Univrsity of Manchester, Manchester, United Kingdom, [29]Virgen Macarena University Hospital,, Sevilla, Spain, [30]Virgen del Rocío University Hospital, Sevilla, Spain, [31]Hospital León, LEON, Castilla y Leon, Spain, [32]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [33]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [34]C. H. U. Lucus Augusti, Lugo, Spain, [35]Rheumatology Division, Hospital Universitario Miguel Servet , Zaragoza, Spain, Zaragoza, Aragon, Spain, [36]Hospital Universitario Insular de Gran Canaria, Las Palmas de Gran CanariaHospital, Spain, [37]H. U. Vall d'Hebron, Barcelona, [38]Hospital Universitari Mùtua Terrassa, Terrassa, Spain, [39]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: VEXAS syndrome is an adult-onset autoinflammatory disorder caused by somatic mutations in *UBA1* gene, characterized by systemic inflammation and haematologic abnormalities. Evidence regarding its evolution and approach in real-world settings remains limited.

To aim of this study is to evaluate the clinical progression, inflammatory markers, and treatment response in patients with VEXAS syndrome over a 3, 6, and 12 month-period following diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline and follow-up clinical features at 3, 6, and 12 Months

Characteristic	Baseline (*n*=50)	3 months (*n*=25)	6 months (*n*=24)	12 months (*n*=19)
Fever	38 (76%)	5 (20%)	3 (12.5%)	2 (10.52%)
Weight loss	36 (72%)	2 (8%)	2 (8.33%)	3 (15.7%)
Fatigue	36 (72%)	10 (40%)	12 (50%)	8 (42%)
Night sweats	32 (64%)	2 (8%)	1 (4.16%)	1 (5.26%)
Cutaneous manifestations	44 (88%)	9 (36%)	9 (37.5%)	6 (31.5%)
Periorbital edema	13 (26%)	0 (0%)	0 (0%)	1 (5.2%)
Chondritis	24 (48%)	2 (8%)	1 (4.16%)	1 (5.2%)
Ocular manifestations	28 (56%)	2 (8%)	4 (16.6%)	1 (5.2%)
Myalgia	6 (12%)	6 (24%)	2 (8.33%)	0 (0%)
Arthralgia	9 (18%)	9 (36%)	7 (30%)	0 (0%)
Arthritis	38 (76%)	5 (20%)	8 (33.33%)	4 (21.05%)
Pulmonary involvement	19 (38%)	5 (20%)	4 (16.66%)	1 (5.26%)
Venous thrombosis	13 (26%)	2 (8%)	0 (0%)	0 (0%)
Arterial thrombosis	0 (0%)	1 (4%)	0 (0%)	0 (0%)
Neurological symptoms	2 (4%)	1 (4%)	0 (0%)	1 (5.26%)
Urological symptoms	7 (14%)	1 (4%)	1 (4.16%)	0 (0%)
Digestive involvement	3 (6%)	0 (0%)	0 (0%)	0 (0%)
Oral ulcers	1 (2%)	0 (0%)	0 (0%)	1 (5.26%)
Genital ulcers	1 (2%)	0 (0%)	1 (4.16%)	0 (0%)
Hepatomegaly	5 (10%)	0 (0%)	0 (0%)	0 (0%)
Splenomegaly	9 (18%)	2 (8%)	1 (4.16%)	3 (15.7%)
Lymphadenopathy	6 (12%)	5 (20%)	1 (4.16%)	2 (10.52%)
Hemophagocytic syndrome	0 (0%)	1 (4%)	0 (0%)	0 (0%)
Hyperferritinemic syndrome (non-MAS)	2 (4%)	0 (0%)	0 (0%)	1 (5.26%)
Cardiac involvement	3 (6%)	0 (0%)	0 (0%)	1 (5.26%)
Renal involvement	11 (22%)	7 (28%)	6 (25%)	1 (5,26%)
Anemia	47 (94%)	20 (80%)	19 (79.16%)	13 (68.42%)
Hemoglobin (g/dL)	9.8 (8.9-10.9)	9.95 (9.10–11.40)	10.60 (9.30–11.70)	9.40 (8.13–11.50)
MCV (fL)	106 (101.6-112)	105.00 (101.00–110.90)	105.15 (102.00–110.00)	104.20 (98.00–110.15)
CRP (mg/L)	20 (6.4-56.9)	30.00 (15.40–74.20)	13.00 (2.20–51.80)	12.70 (3.15–58.75)
ESR (mm/h)	74 (47.5-120)	71.50 (32.00–105.00)	51.00 (7.00–120.00)	51.00 (19.00–100.00)
Leukopenia	23 (46)	9 (37.50)	12 (54.55)	7 (43.75)
WBC count (/mm^3)	4,750 (3,325-6,708)	3,800 (2,570–7,100)	4,600 (2,700–5,700)	3,275 (2,250–5,915)
Thrombocytopenia	22 (44)	6 (25.00)	9 (40.91)	7 (41.18)
Platelet count (/mm^3)	115,000 (69,000-188,250)	71,000 (89–182,000)	82,000 (97.88–192,000)	89,500 (130–156,000)

Methods: Observational, ambispective study involving patients with a genetic diagnosis of VEXAS syndrome across rheumatology units in Spain. Follow-up data at 3, 6, and 12 months were collected, including demographic, clinical, laboratory, and treatment related variables. Response rate was defined as complete (RC) (no VEXAS symptoms, CRP ≤10mg/L, prednisone ≤10mg qd), partial (PR)(clinical remission, CRP and prednisone reduction ≥50%) or none (N) (ongoing symptoms, persistent inflammatory markers, no steroid reduction).

Results: Fifty patients (*n*=50) were identified. Follow-up data were available for 25 patients at 3 months, 24 at 6 months, and 19 at 12 months. On the one hand, VEXAS syndrome hallmark symptoms (skin lesions, constitutional syndrome, arthritis, thromboembolic disease, pulmonary and renal involvement) decreased over time ("*Table 1*"). On the other hand, inflammatory markers (CRP, ESR) and haemoglobin levels showed scarce to moderate non-significant improvement. Macrocytosis (MCV > 100 fL) remained persistently elevated ("*Figure 1*").

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

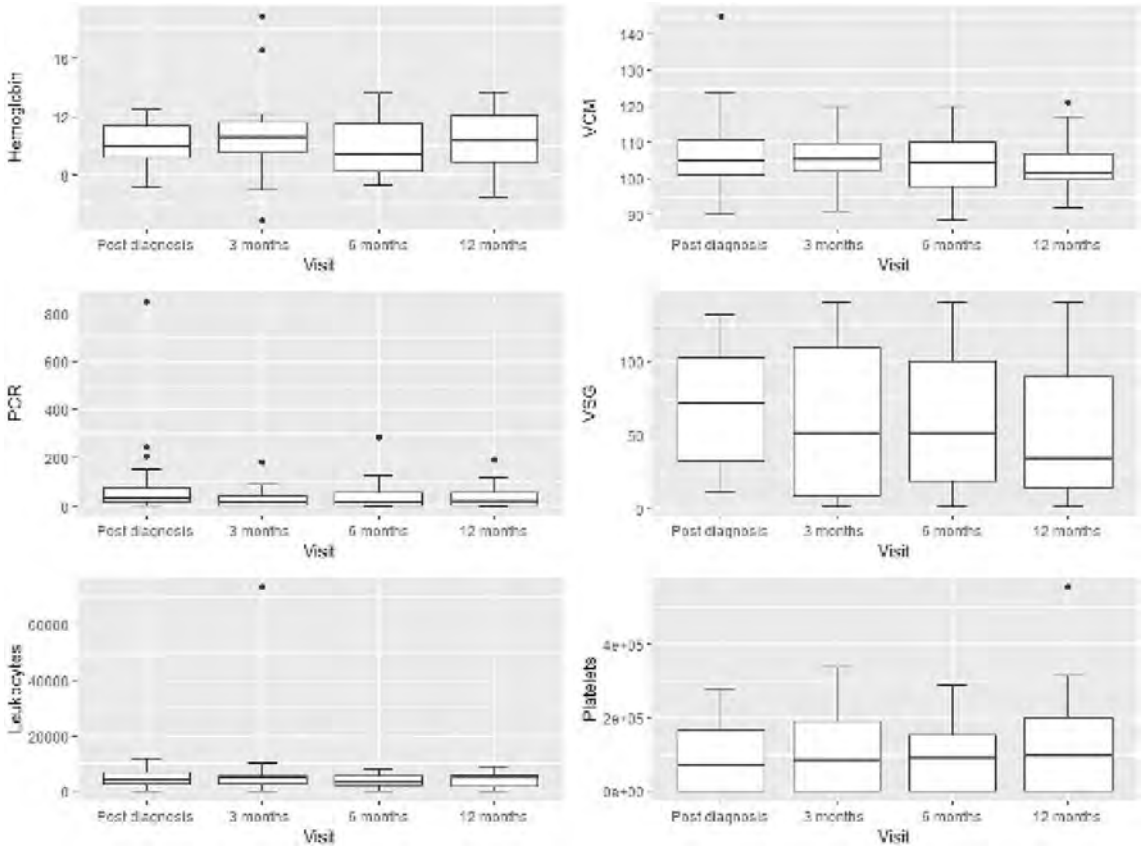


Figure 1. Longitudinal Trends in Inflammatory and Hematologic Biomarkers in Patients with VEXAS Syndrome

At the moment of diagnosis, most frequently prescribed treatments were glucocorticoids (GCs) (92%), azacitidine (28%), MTX and JAK inhibitors (24%), IL-6 inhibitors (16%), and anakinra (18%).

At 3 months, GCs remained the predominant choice of treatment (92%), though both CR and PR were estimated at 38.1%. JAK inhibitors (12%) showed 50% complete response, while IL-6 inhibitors (8%) showed 50% CP and PR response. MTX (16%) showed 75% PR. Anakinra (8%) induced only PR.

At 6 months, glucocorticoids were used in 100% of patients (31.8% CR, 50% PR). IL-6 and JAK inhibitors (both 16.16%) showed 25% CR and 75% PR. MTX (12.5%) maintained a 66.7% PR. Azacitidine (12.5%) showed limited efficacy.

At 12 months, glucocorticoids (100%) continued with 31.8% CR and 50% PR. JAK and IL-6 inhibitors (21.05% each) maintained similar response profiles. MTX (15.58%) still showed 66.7% partial response. Anakinra and azathioprine were discontinued ("*Table 2*").

Two 2 patients underwent allo-HCT, with CR in one case (50%). It has not been possible to lower GCs below 10 mg/day in 1 of the cases after 12 months (partial response 50%).

Conclusion: This multicenter, ambispective study provides real-world data on the disease course and treatment of VEXAS syndrome. GCs remain essential, but seem to lose efficacy over time. IL-6 and JAK inhibitors, especially Ruxolitinib, appear to offer sustained benefit. Despite intensive immunosuppression, inflammatory and haematologic activity persists in many patients. HSCT is a feasible option in selected cases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Longitudinal Overview of Therapies Used and Frequency at 0, 3, 6, and 12 Months

	0 month (n= 50)	3 months (n=25)	6 months (n=24)	12 months (n=19)
Glucocorticoids	46 (92%)	23 (92%)	23 (95,8%)	17 (89.47%)
Bolus glucocorticoids	1 (2%)	2 (8%)	0 (0%)	0 (0%)
Colchicine	5 (10%)	2 (8%)	0 (0%)	0 (0%)
Non-steroidal anti-inflammatory drugs (NSAIDs)	4 (8%)	3 (12%)	2 (8.3%)	2 (10.52%)
Methotrexate	12 (24%)	4 (16%)	3 (12,5%)	3 (15.58%)
Azathioprine	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Hydroxychloroquine	3 (6%)	2 (8%)	2 (8.3%)	2 (10.52%)
Cyclophosphamide	1 (2%)	1 (4%)	0 (0%)	0 (0%)
Anakinra	9 (18%)	2 (8%)	0 (0%)	0 (0%)
Canakinumab	1 (2%)	0 (0%)	0 (0%)	0 (0%)
IL6-inhibitors	8 (16%)	2 (8%)	4 (16.16%)	4 (21.05%)
TNF-inhibitors	3 (6%)	1 (4%)	1 (4.16%)	1 (5.26%)
JAK-inhibitors Ruxolitinib Tofacitinib Upadacitinib	12 (24%) 9 (75%) 2 (16.67%) 1 (8.33%)	3 (12%) 3 (100%) 0 (0%) 0 (0%)	4 (16,16%) 4 (100%) 0 (0%) 0 (0%)	4 (21.05%) 4 (100%) 0 (0%) 0 (0%)
Rituximab	3 (6%)	1 (4%	0 (0%)	0 (0%)
Mycophenolate mofetil	2 (4%)	1 (4%)	1 (4.16%)	1 (5.26%)
Cyclosporine	5 (10%)	0 (0%)	3 (12,5%)	3 (15.78%)
Dapsona	3 (6%)	0 (0%)	0 (0%)	0 (0%)
Tacrolimus	2 (4%)	0 (0%)	0 (0%)	0 (0%)
Azacitidine	14 (28%)	3 (12%)	3 (12,5%)	3 (15.78%)
Bortezomid	2 (4%)	0 (0%)	0 (0%)	0 (0%)
Allogeneic haematopoietic stem cell transplantation (HSCT)	2 (4%)	0 (0%)	0 (0%)	1 (5.26%)

Disclosure: M. López: None; **P. Garcia Escudero**: None; **B. Magallares**: None; **M. Salles Lizarzaburu**: None; **D. Fiallo Suárez**: None; **I. Rúa-Figueroa**: None; **I. Morante Bolado**: None; **E. Aurrecoechea**: None; **E. Enriquez**: None; **C. Merino**: None; **S. Castañeda**: None; **I. Monjo Henry**: None; **C. Egües Dubuc**: None; **E. Oliver García**: None; **A. Garcia**: None; **J. Font-Urgelles**: None; **C. Corrales**: None; **L. Villalobos**: None; **A. Boteanu**: GSK, 5, 6; **I. Vázquez Gómez**: None; **D. Dios**: None; **C. Garcia Belando**: None; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **D. Reina**: None; **M. Ibañez**: None; **I. Carrion**: None; **M. Rodriguez**: None; **c. Sieiro**: None; **F. Toyos**: None; **A. Mariano**: None; **C. Moriano**: None; **R. Melero-González**: None; **P. Vela Casasempere**: None; **J. Miranda**: None; **G. Boselli**: None; **J. Hernandez**: None; **E. Trallero**: None; **E. Riera Alonso**: None; **J. Calvo**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1172

A Phase II, Single-site, Open-label Study of Zanubrutinib in Patients with igg4-related Disease

Matthew Charles Baker[1], Audra Horomanski[2], Robert Fairchild[3], Yuhan Liu[3], Mariani Diaz Deluna[3], Tobias Lanz[4], Saurabh Gawde[3], Mehdi Khalighi[3], Benjamin Franc[3], Mrudula Penta[3], Nancy Pham[3] and Kip Guja[3], [1]Stanford University, Menlo Park, CA, [2]Stanford University, Palo Alto, CA, [3]Stanford University, Stanford, CA, [4]Stanford University, Stanford

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic, systemic, immune-mediated disease that is commonly treated with B cell depletion. However, due to potential risks associated with long-term B cell depletion, there is a need for alternative, non-depleting treatment options. Bruton's tyrosine kinase (BTK) plays a critical role in B cell activation and proliferation, and inhibiting BTK is efficacious in B cell driven diseases, without meaningfully reducing B cell numbers. In this phase 2 proof-of-concept study (NCT04602598), we report the efficacy and safety of zanubrutinib in patients with IgG4-RD affecting the lacrimal and/or salivary glands.

Methods: This open-label study was conducted at a single center in the United States. Eligible adult patients with symptomatic IgG4-RD affecting the submandibular and/or lacrimal glands, with prior inadequate response to glucocorticoids, and meeting the 2019 ACR/EULAR Classification Criteria for IgG4-RD, received oral zanubrutinib 80 mg twice daily for up to 24 weeks. The primary endpoint was the change from baseline in the volume of the submandibular and/or lacrimal glands on ^{18}F-fluorodeoxyglucose positron emission tomography/magnetic resonance imaging (FDG-PET/MRI) at Week 24, as determined by two board-certified radiologists blinded to scan order. Secondary endpoints included the change in metabolic activity on FDG-PET/MRI, laboratory parameters such as IgG4 serum concentration, and patient reported outcomes. The Wilcoxon signed rank exact test was used to evaluate changes on imaging.

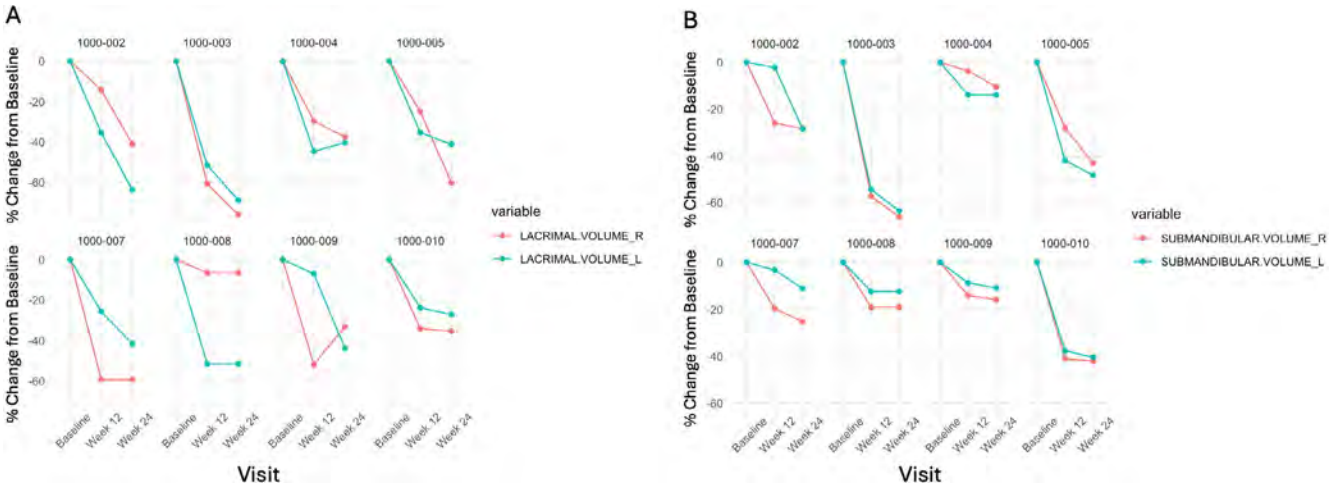


Figure 1. Individual changes in gland volume on FDG-PET/MRI. Panel A shows the percent change from Baseline to Week 12 and Week 24 in lacrimal gland volume for each subject. Panel B shows the percent change from Baseline to Week 12 and Week 24 in submandibular gland volume for each subject. Two subjects who only had Baseline data and terminated early due to adverse events were not included in this analysis. One subject terminated after Week 12 due to worsening IgG4-RD, and the Week 12 imaging data was imputed for Week 24.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

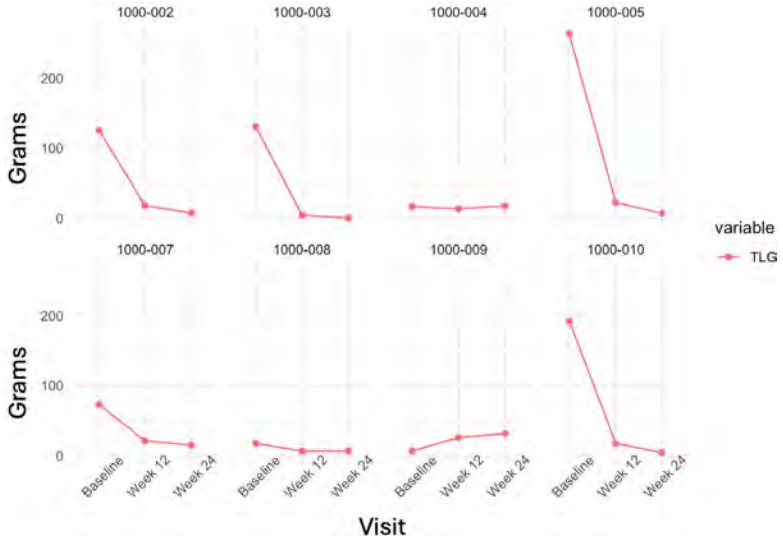


Figure 2. Individual changes in total lesion glycolysis (TLG). TLG is defined as the product of mean standard uptake value (SUVmean) and total metabolic lesion volume (tMLV) of the lacrimal glands, parotid glands, submandibular glands, and regional lymph nodes. Two subjects who only had Baseline data and terminated early due to adverse events were not included in this analysis. One subject terminated after Week 12 due to worsening IgG4-RD, and the Week 12 imaging data was imputed for Week 24.

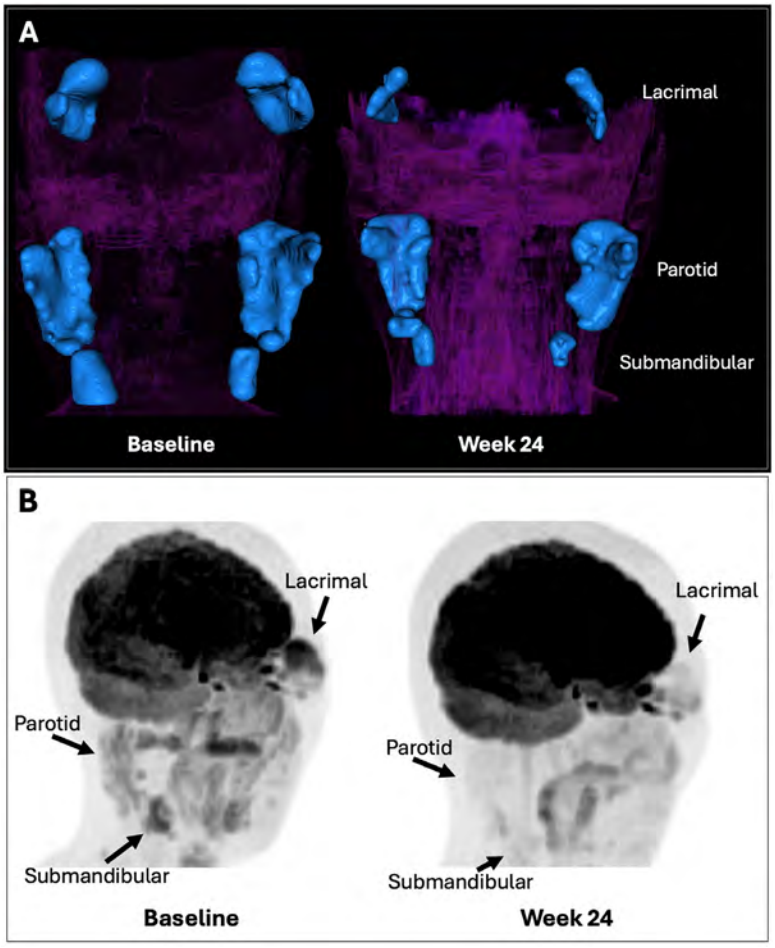


Figure 3. Change in gland volume and metabolic activity on FDG-PET/MRI. Panel A shows MRI 3D volumetric segmentation and rendering of the lacrimal, parotid, and submandibular glands at Baseline and Week 24. Panel B shows FDG-PET maximum intensity projection (MIP) images in right anterior oblique orientation (SUV scale 0-7), demonstrating hypermetabolism in all glands at Baseline, which significantly improves after treatment.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Ten patients were enrolled; most were male (70.0%), Asian (60.0%), and with a median age of 58 (range, 38-74) years. Prior treatments included prednisone (10 patients), azathioprine (2 patients), and rituximab (5 patients); for rituximab-treated patients, the mean (standard deviation [SD]) time since last dose was 2.5 years (1.5). No patients were receiving glucocorticoids or a steroid-sparing immunosuppressive treatment at the time of enrollment or during the study. The mean (SD) number of organs ever affected by IgG4-RD was 4.4 (1.4), and all patients had both lacrimal and submandibular gland disease. At Week 24, the mean (SD) percent changes from baseline were -45.4% (17.4) for lacrimal gland volume ($p < 0.001$) and -30.0% (18.6) for submandibular gland volume ($p < 0.001$) (**Figure 1**). In addition, reductions were observed in all measures of metabolic activity, including a mean (SD) change from baseline in total lesion glycolysis of -91.6 grams (98.5; $p = 0.05$) (**Figure 2**). Representative FDG-PET/MRI images are shown in **Figure 3**. The mean (SD) change in the serum IgG4 concentration over 24 weeks was -417.0 mg/dL (410). All patients had at least one treatment-emergent adverse event (TEAE), most of which were mild, and there was one serious TEAE from COVID-19.

Conclusion: Treatment with zanubrutinib alone, without the need for glucocorticoid induction or other background immunosuppression, significantly reduced both lacrimal and submandibular gland volume and metabolic activity on FDG-PET/MRI, as well as reduced serum IgG4 concentrations, with an acceptable safety profile. Given these results, zanubrutinib warrants further investigation as a treatment for IgG4-RD.

Disclosure: M. Baker: Amgen, 2, Sanofi, 2, Zenas BioPharma, 2; **A. Horomanski**: Gilead, 5, VielaBio, 5, Zenas, 5; **R. Fairchild**: None; **Y. Liu**: None; **M. Diaz Deluna**: None; **T. Lanz**: None; **S. Gawde**: None; **M. Khalighi**: None; **B. Franc**: None; **M. Penta**: None; **N. Pham**: None; **K. Guja**: None.

Abstract Number: 1173

Prevalence of Coronary Artery Involvement in IgG4-Related Disease Detected by Non-Gated Cross-Sectional Imaging

Matthew Charles Baker[1], Lauren Taylor[2], Haziq Siddiqi[2], Jison Hong[2] and Brian Pogatchnik[2], [1]Stanford University, Menlo Park, CA, [2]Stanford University, Stanford, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) classically presents with a mass or diffusely enlarged organ, but it also affects blood vessels of all sizes. Coronary artery involvement (CAI) is well described but understudied. Prior work demonstrated CAI in 13 out of 361 (4%) IgG4-RD patients, however it was limited by lack of standardized screening for the evaluation of CAI[1]. The goal of our study was to establish a conservative estimate of the true prevalence of CAI by screening IgG4-RD patients that had prior cross-sectional imaging of the chest, regardless of whether CAI was clinically suspected.

Methods: IgG4-RD patients were identified using the STAnford medicine Research data Repository by searching all adult patients seen at Stanford University between 2/28/09 and 3/1/2023 with any clinical document containing "IgG4-related disease," "IgG4-RD," or "IgG4 disease." Each chart was manually reviewed to verify the diagnosis. Cases were categorized as definite, probable, or possible IgG4-RD[2]. We included all patients with prior non-gated CT chest imaging. A radiologist with expertise in IgG4-RD and vasculitis reviewed the scans, and patients who had features concerning for possible CAI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

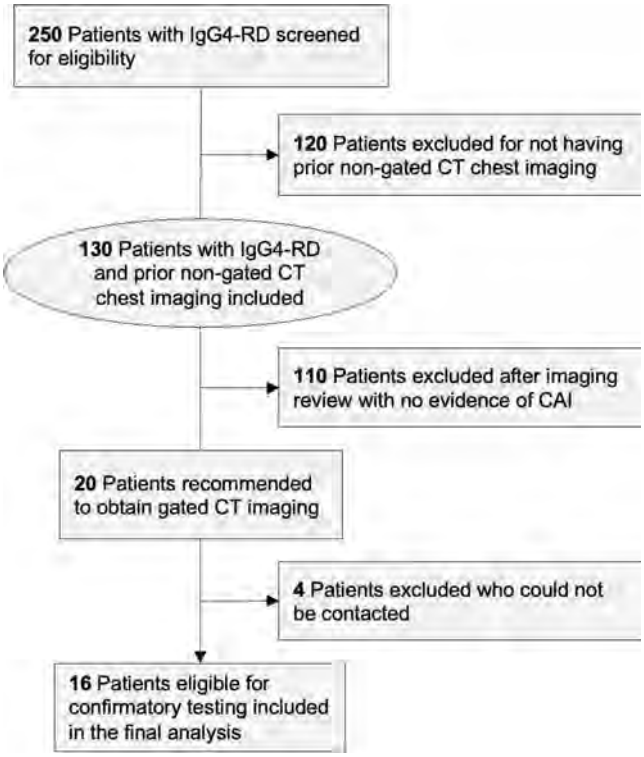


Figure 1. Cohort selection.

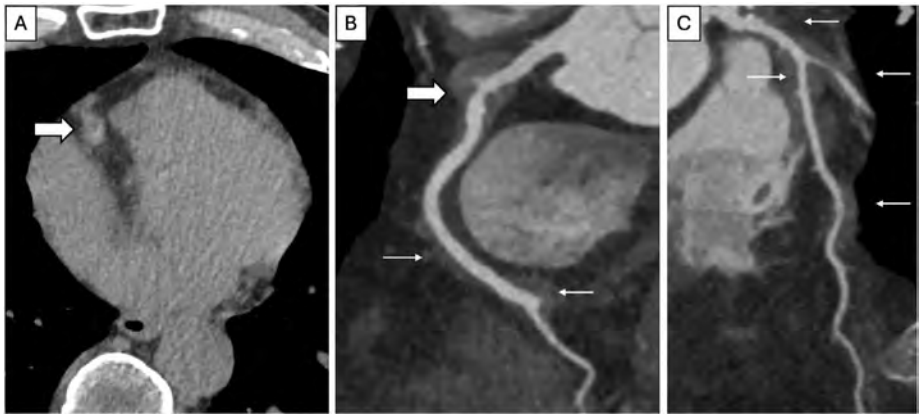


Figure 2. IgG4-RD coronary artery involvement on computed tomography. Panel A demonstrates suspected right coronary artery thickening on a non-gated chest CT without IV contrast (large arrow), which is confirmed on gated CT angiography (Panel B; large arrow). Panel C demonstrates additional sites of disease, including the left main, left anterior descending, and proximal left circumflex (small arrows), which were not clearly apparent on the initial CT.

were recommended to obtain a gated CT of the heart or chest. After reviewing the confirmatory imaging, we calculated the prevalence of CAI, as well as the positive predictive value (PPV) for detecting CAI.

Results: Of the 250 IgG4-RD patients in the full cohort, 130 patients (52.0%) had prior non-gated chest imaging (**Figure 1**). Twenty patients (15.4%) had findings concerning for possible CAI. Four of the 20 patients could not be contacted due to departure from our healthcare system or death. Of the 16 remaining patients, 3 had a negative gated CT angiography (CTA) of the chest or heart, 4 had a positive gated CTA, and 7 had prior gated CTA studies obtained after the original non-gated CT chest, which were subsequently reviewed and were positive (representative images of CAI are shown in **Figure 2**). Additionally, 2 patients had such profound results on the initial non-gated CT chest they were deemed definitely positive without the need for a confirmatory gated CTA. As **Table 1** demonstrates, patients with CAI were older (70 years

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and baseline characteristics of IgG4-RD patients.

Characteristic	Total Cohort (*n* = 130)	No CAI* (*n* = 113)	Confirmed CAI (*n* = 13)
Age, mean (SD), y	64.3 (15.8)	63.2 (16.4)	70.3 (9.0)
Sex, n (%)			
Female	62 (47.7)	58 (51.3)	3 (23.1)
Male	68 (52.3)	55 (48.7)	10 (76.9)
Race, n (%)			
White	41 (31.5)	39 (34.5)	2 (15.4)
Black	7 (5.4)	5 (4.4)	2 (15.4)
Asian	46 (35.4)	38 (33.6)	5 (38.5)
Unknown	2 (1.5)	2 (1.8)	0 (0.0)
Other	34 (26.2)	29 (25.7)	4 (30.8)
Ethnicity, n (%)			
Hispanic	28 (21.5)	25 (22.1)	2 (15.4)
Body mass index, mean (SD), kg/m^2	26.4 (5.7)	26.3 (5.8)	27.6 (5.3)
Smoking, n (%)			
Never	74 (56.9)	68 (60.2)	5 (38.5)
Former	47 (36.2)	39 (34.5)	5 (38.5)
Current	8 (6.2)	5 (4.4)	3 (23.1)
IgG4-RD duration, mean (SD), y	1.5 (2.9)	1.3 (2.8)	2.2 (3.6)
Number of organs ever affected, n (%)			
1	53 (40.8)	48 (42.5)	0 (0.0)
2	41 (31.5)	34 (30.1)	3 (23.1)
3	24 (18.5)	22 (19.5)	5 (38.5)
4	7 (5.4)	5 (4.4)	3 (23.1)
5	3 (2.3)	3 (2.7)	1 (7.7)
6	2 (1.5)	1 (0.9)	1 (7.7)
Multiorgan disease, n (%)	77 (59.2)	65 (57.5)	13 (100.0)
IgG4 concentration, mean (SD), mg/dL	535.0 (557.1)	455.8 (472.7)	973.1 (704.1)
Prior IgG4-RD treatments, n (%)			
Glucocorticoids	102 (78.5)	87 (77.0)	12 (92.3)
Rituximab	61 (46.9)	52 (46.0)	6 (46.2)
Methotrexate	16 (12.3)	13 (11.5)	3 (23.1)
Azathioprine	33 (25.4)	31 (27.4)	2 (15.4)
Mycophenolate mofetil	21 (16.2)	18 (15.9)	2 (15.4)
Leflunomide	2 (1.5)	2 (1.8)	0 (0.0)
Investigational agent**	13 (10.0)	12 (10.6)	1 (7.7)

*Based on screening or confirmatory imaging. **Investigational agents include inebilizumab, zanubrutinib, rilzabrutinib, and obexelimab. SD = standard deviation; y = year; kg = kilogram; m = meter.

vs 63 years), more likely to be male (77% vs 49%), more likely to be current smokers (23% vs 3%), more likely to have multiorgan disease (100% vs 58%), and had higher serum IgG4 concentrations (mean peak value 973 mg/dL vs 456 mg/dL). In total, 13 out of 16 patients who screened positive were confirmed to have CAI, resulting in a PPV of 81.3%. The prevalence of CAI in this cohort of patients was 13 out of 130 (10.0%).

Conclusion: By reviewing non-gated CT chest imaging to screen for IgG4-RD CAI, we observed a prevalence of CAI of 10% in our cohort. This is higher than what has been previously reported and likely represents a conservative estimate. Our results suggest that CAI is relatively common in IgG4-RD, and future studies are needed to determine which patients should be screened for CAI and whether the approach described herein has adequate sensitivity to be implemented as a screening test.

References:

Katz G, et al. Semin Arthritis Rheum. 2023;60:152184.
Baker MC, et al. J Rheumatol. 2023;50(3):408-12.

Disclosure: M. Baker: Amgen, 2, Sanofi, 2, Zenas BioPharma, 2; **L. Taylor**: None; **H. Siddiqi**: None; **J. Hong**: None; **B. Pogatchnik**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1174

High Prevalence of Autoimmunity in Rosai Dorfman Disease: A Multinational Study

Mitali Sen[1], Gordon Ruan[2], Samuel Reynolds[3], Haadi Ali[3], Xi Yang[3], Diana Morlote[1], Aishwarya Ravindran[1], Lauren Shea[1], Matthew Koster[4], Jithma Abeykoon[2], Hind Salama[5], Xin-Xin Cao[6], Asra Ahmed[3], Ronald Go[2] and Gaurav Goyal[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Mayo Clinic, Rochester, [3]University of Michigan, Michigan, [4]Mayo Clinic, Rochester, MN, [5]National Guard Health Affairs, Riyadh, Saudi Arabia, [6]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Rosai-Dorfman Disease (RDD), formerly known as sinus histiocytosis with massive lymphadenopathy, was initially thought to be inflammatory or autoimmune in nature. The discovery of MAP-ERK pathway mutations has since reclassified RDD as a histiocytic neoplasm. However, autoimmune diseases have been commonly reported, and recent consensus guidelines recognize "immune-related RDD" as a distinct subtype. Given its clinical overlap with autoimmune diseases, a deeper understanding of RDD's immunologic profile is increasingly important for rheumatologists.

Methods: We performed a retrospective chart review of histologically confirmed RDD cases from five international referral centers. Using a standardized data collection form, we gathered data on patient demographics, patterns of organ involvement, driver mutations, autoimmune serologies, and treatment outcomes of autoimmune diseases.

Results: We identified 162 patients with RDD diagnosed from Jan 2003- Jan 2025. Median age at diagnosis was 48 years (range, 7-85) with nine patients diagnosed before age 18. Cohort was 64.8% female and racial distribution was 34.6% Black, 33.3% White, and 24.7% Asian (Table 1). Multisystem involvement was noted in 53.7% of cases, with common sites including skin/subcutaneous tissue (49.4%), lymph nodes (39.5%), and bone (33.9%).

Autoimmune diseases were present in 29 patients (17.9%), among which, the most common were systemic lupus erythematosus (6, 20.7%) and rheumatoid arthritis (5, 17.2%) (Figure 1). Autoimmune disease was more frequent in multisystem vs single organ RDD (62% vs 38%, p=0.3). Mean ESR and CRP were higher in patients with autoimmune disease (37.1 mm/Hr and 53.5 mg/L) vs patients without autoimmune disease (25.5 mm/Hr and 39.4 mg/L). Autoantibodies were detected in 44 of 94 tested (46.8%), most commonly ANA in 33.3% (29/87) (Figure 2).

Tissue-based next generation sequencing was performed in 102 patients (62.9%), revealing KRAS mutation (11.7%), MEK mutations (9.3%), other mutations (16.7%) and no mutation (25.3%). No significant association was observed between mutational status and autoimmunity.

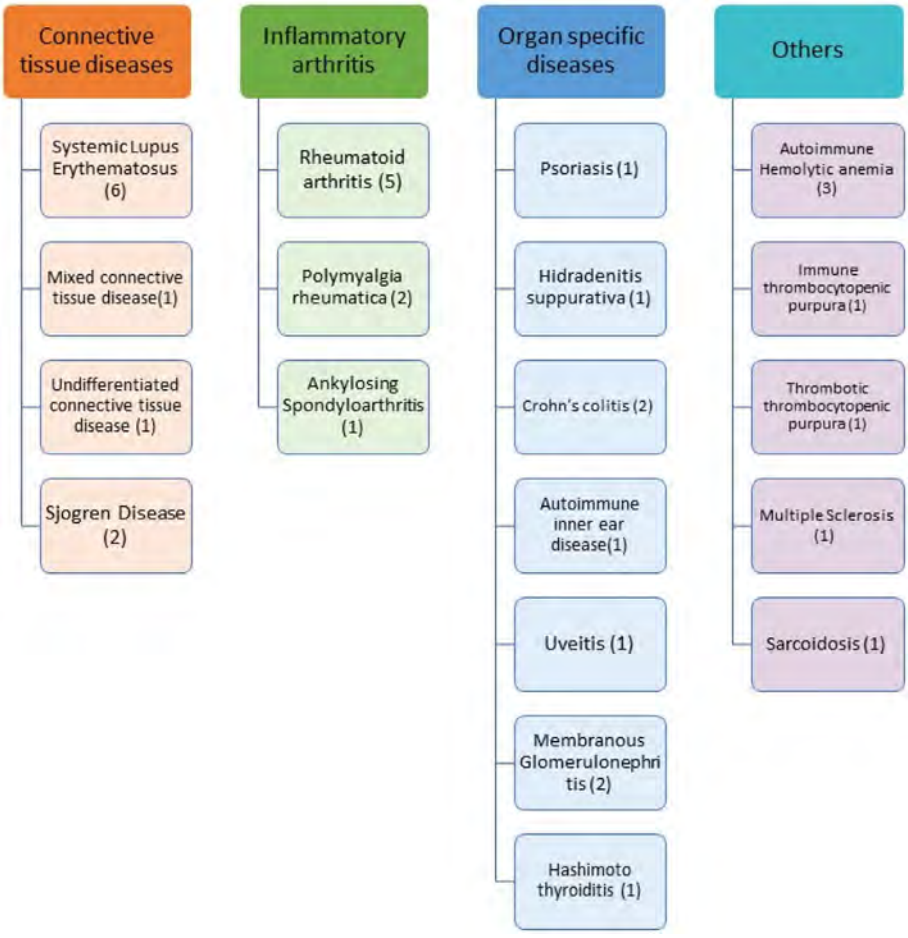
Autoimmune disease preceded RDD diagnosis in 19 cases (11.7%). Treatment data were available for 22 of 29 patients with autoimmune disease: 11 (50%) were stable off treatment, 10 (45.5%) were stable on DMARD therapy, and 1 (4.5%) had active disease despite multiple DMARDs.

Median follow-up for the entire cohort was 29.8 months (IQR 10.4–61.4). Eight deaths were reported in the cohort, none among patients with autoimmune disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

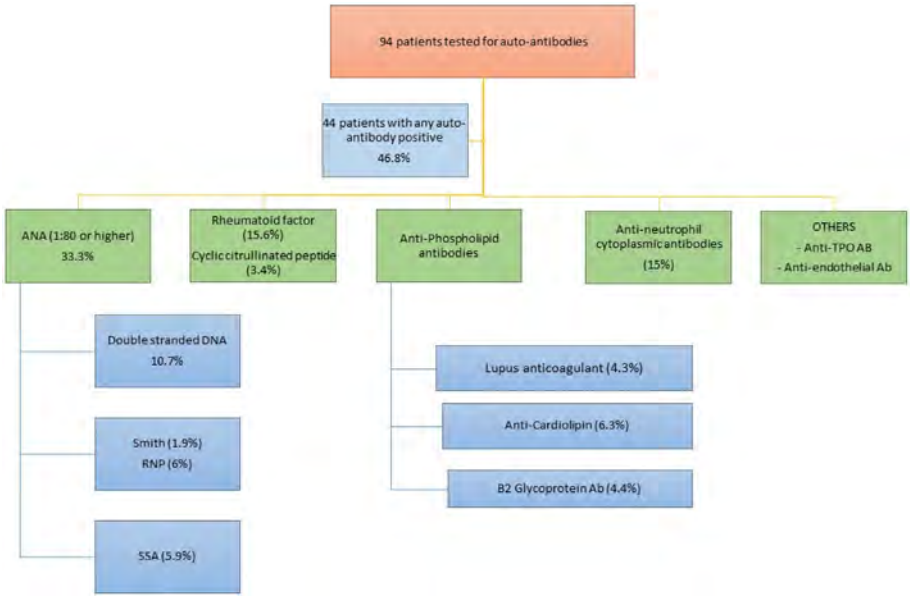
	All patients with RDD	RDD with Autoimmune disease	RDD without Autoimmune disease	P Value
No of patients (%)	162 (100%)	29 (17.9%)	133 (82.1%)	
Median Age(years)	48 (7-85)	47 (11-77)	48 (7-85)	
RACE				
Black	56 (34.6%)	13 (44.8%)	43 (32.3%)	0.19
White	54 (33.3%)	7 (24.1%)	47 (35.3%)	0.25
Asian	40 (24.7%)	4 (13.9%)	36 (27.1%)	0.16
Middle Eastern	7 (4.3%)	3 (10.3%)	4 (3%)	0.11
Other	5 (3.1%)	2 (6.9%)	3 (2.3%)	0.22
SEX				0.73
Male	57 (35.2%)	11 (37.9%)	46 (34.6%)	
Female	105 (64.8%)	18 (62.1%)	87 (65.4%)	
ORGAN INVOLVEMENT with RDD				0.32
Multisystem RDD	87 (53.7%)	18 (62.1%)	69 (51.9%)	
Single Organ RDD	75 (46.3%)	11 (37.9%)	64 (48.1%)	
INFLAMMATORY MARKERS AT DIAGNOSIS OF RDD				
Mean ESR (mm/Hour)	29.3	37.1	25.5	0.03
Mean CRP (mg/L)	20.3	53.5	39.4	0.26
DRIVER MUTATION on NEXT GEN SEQUENCING				
KRAS mutation	19 (11.7%)	4 (13.8%)	15 (11.3%)	0.23
MAP2K/MEK	15 (9.3%)	2 (6.9%)	13 (9.8%)	0.69
Other Mutation	27 (16.7%)	2 (6.9%)	25 (18.8%)	0.51
No Mutation	41 (25.3%)	4 (13.8%)	37 (27.8%)	0.76
Not tested	60 (37%)	17 (58.6%)	43 (32.3%)	0.01

Characteristics of individuals with RDD and Autoimmune disease



List of autoimmune diseases seen in patients with RDD (no of patients)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Autoantibodies in patients with RDD (% of patients positive)

Conclusion: This multi-center cohort highlights the clinical and molecular diversity of RDD. It also reveals a high prevalence of autoimmunity in RDD, both in terms of autoimmune disease (17.9 %) and positive autoantibodies (46.8 %), which is higher than general population rates of approximately 3% and 16% respectively. There was a trend toward association of autoimmune disease with multisystem RDD and with higher inflammatory markers at the time of RDD diagnosis. Overall, findings highlight the need for investigation into shared pathogenesis and potential therapeutic strategies that could target both RDD and autoimmune diseases.

Disclosure: M. Sen: None; **G. Ruan**: None; **S. Reynolds**: None; **H. Ali**: None; **X. Yang**: None; **D. Morlote**: None; **A. Ravindran**: None; **L. Shea**: None; **M. Koster**: Amgen, 2; **J. Abeykoon**: None; **H. Salama**: None; **X. Cao**: None; **A. Ahmed**: None; **R. Go**: None; **G. Goyal**: None.

Abstract Number: 1175

Secukinumab In Patients with Giant Cell Arteritis with Polymyalgia Rheumatica Symptoms: A Post Hoc Analysis of the Phase 2 TitAIN Study

Nils Venhoff[1], Wolfgang Schmidt[2], Raoul Bergner[3], Juergen Rech[4], Leonore Unger[5], Stephanie Finzel[6], Ioana Andreica[7], David Kofler[8], Stefan Weiner[9], Prof. Dr. med. Peter Lamprecht[10], Hendrik Schulze-Koops[11], Meryl Mendelson[12], Weibin Bao[13], Monica Keyport[14], Meron Maricos[15], Valeria Jordan M.[16] and Jens Thiel[17], [1]University of Freiburg, Freiburg, Germany, [2]Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch; Waldfriede Hospital, Rheumatology, Berlin, Germany, [3]Department of Internal Medicine A, Nephrology and Rheumatology, Municipal Hospital Ludwigshafen, Ludwigshafen, Germany, [4]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [5]Städtisches Klinikum Dresden, Dresden, Germany, [6]Universitätsklinikum Freiburg, Freiburg im Breisgau, Germany, [7]Rheumazentrum Ruhrgebiet Herne; Ruhr-Universität Bochum, Germany, Herne, Germany, [8]University of Cologne, Cologne, Germany, [9]Brüderkrankenhaus Trier, Trier, Germany, [10]University of Lübeck, Lübeck, Germany, [11]LMU Hospital, Division for Rheumatology and Clinical Immunology, Munich, Bayern, Germany, [12]Novartis Pharmaceuticals, Larchmont, NY, [13]Novartis Pharmaceuticals Corporation, Hanover, NJ, [14]Novartis Pharmaceuticals, Stillwater, MN, [15]Novartis, Nürnberg, Germany, [16]Novartis Pharmaceuticals Corporation, Tenafly, NJ, [17]University Hospital Freiburg, Medical University Graz, Freiburg, Germany

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: GCA and PMR are closely related, immune-mediated chronic inflammatory diseases often occurring concurrently in individuals over 50.[1,2] While glucocorticoids (GC) are the mainstay of treatment, relapses are common, and long-term use causes significant side effects, highlighting the need for GC-sparing therapies.[2]

Secukinumab (SEC), a monoclonal antibody that selectively neutralizes interleukin-17A, has shown efficacy and safety in various immune-mediated diseases.[3] In the TitAIN phase 2 study, SEC resulted in a higher sustained remission rate in patients with GCA than in placebo (PBO) at week 28, with effects lasting for 52 weeks; safety was consistent with its known safety profile.[4]

This post hoc analysis evaluated SEC vs PBO in the subgroup of GCA patients with PMR symptoms within 12 weeks prior to and/or at baseline (BL).

Methods: TitAIN was a randomized, double-blind, PBO-controlled, multicenter, phase 2 study in patients aged ≥50 years with new-onset or relapsing GCA (unequivocal cranial symptoms of GCA and/or symptoms of PMR) who were naive to biological therapy and receiving GCs at BL with a prednisolone equivalent dose of 25–60 mg/day.[4] Patients were assigned (1:1) to receive 300 mg SEC or PBO subcutaneously once a week up to week 4 and every 4 weeks thereafter. In both arms, prednisolone dose was tapered to 0 mg over a 26-week period.[4]

Results: In the TitAIN study, 27 patients received SEC and 25 received PBO; 44.4% (12/27) of patients in the SEC arm vs 32.0% (8/25) in the PBO arm had PMR symptoms and were included in this post hoc analysis.

Among patients with PMR symptoms, 58.3% (7/12) in the SEC arm vs 12.5% (1/8) in the PBO arm were in sustained GCA remission at week 52, consistent with a previous finding in the overall study population (59% vs 8%).[4]

Overall, only 3.7% (1 of 27) in the SEC arm vs 24.0% (6/25) in the PBO arm experienced PMR symptoms post BL up to week 52. In the subgroup of patients with PMR symptoms, only 8.3% (1/12) in the SEC arm had PMR symptoms post BL compared to 50.0% (4/8) in the PBO arm. Data for new-onset and relapsing GCA subgroups are presented in Table 1.

Table 1. Results at 52 weeks for the overall GCA population and the subgroup of GCA patients with PMR symptoms from the TitAIN study

	Secukinumab		Placebo	
	All patients N=27	Patients with BL PMR* N=12	All patients N=25	Patients with BL PMR* N=8
Sustained remission of GCA at week 52				
Total	16/27 (59.3%)	7/12 (58.3%)	2/25 (8.0%)	1/8 (12.5%)
New-onset GCA	15/23 (65.2%)	6/9 (66.7%)	1/19 (5.3%)	0/5 (0)
Relapsing GCA	1/4 (25.0%)	1/3 (33.3%)	1/6 (16.7%)	1/3 (33.3%)
Post-BL PMR symptoms up to week 52				
Total	1/27 (3.7%)	1/12 (8.3%)	6/25 (24.0%)	4/8 (50.0%)
New-onset GCA	1/23 (4.3%)	1/9 (11.1%)	4/19 (21.1%)	2/5 (40.0%)
Relapsing GCA	0/4 (0)	0/3 (0)	2/6 (33.3%)	2/3 (66.7%)

Data is presented as observed.
*Patients who had PMR reported within 12 weeks prior to and/or on the first day of study treatment in 1) GCA medical history eCRF, 2) Signs and symptoms eCRF at screening or BL, 3) AE summary eCRF page
AE, adverse event; BL, baseline; eCRF, electronic case report form; GCA, giant cell arteritis; PMR, polymyalgia rheumatica.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

All GCA patients with PMR symptoms had ≥1 adverse event (AE), in both arms. The most common AEs were consistent with those reported in the study population.[4] Serious AEs were reported in 8.3% of patients (n=1; facial paralysis) in the SEC arm and 37.5% (n=3; gastrointestinal pain, dizziness, and chronic obstructive pulmonary disease) in the PBO arm.

Conclusion: This post hoc analysis showed a numerical reduction in patients with PMR symptoms with SEC treatment compared to PBO. The safety profile of SEC was similar to the overall GCA study population and consistent with its known safety profile. These results support the development of SEC for PMR. A phase 3 trial (NCT05767034) is evaluating the efficacy and safety of SEC in relapsed patients with PMR.

References

1. Espígol-Frigolé G, et al. *Lancet*. 2023;402(10411):1459-72.
2. Man-Ger Sun M, et al. *Best Pract Res Clin Rheumatol*. 2022;36(4):101822.
3. COSENTYX®. Prescribing information. Novartis; 2023. Accessed on April 29, 2025. Available at: label.
4. Venhoff N, et al. *Lancet Rheumatol* 2023;5:e341-50.

Disclosure: N. Venhoff: AbbVie, 1, 6, 12, Consulting fees, meeting or travel grants, expert testimony, AstraZeneca, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, 6, 12, Meeting or travel grants, Chugai, 1, 6, 12, Consulting fees, GlaxoSmithKlein(GSK), 6, Novartis, 1, 5, 6, 12, Consulting fees, meeting or travel grants, expert testimony, 12, Pending patent application on the use of secukinumab in GCA, Roche, 6, UCB, 1, 6, Vifor, 1, 6, 12, Expert testimony, Meeting or travel grants, Consulting fees; **W. Schmidt**: AbbVie, 1, 5, 6, Alfasigma, 6, Amgen, 6, Boehringer-Ingelheim, 1, Chugai, 6, Eli Lilly, 6, Fresenius Kabi, 1, GlaxoSmithKline, 6, Medac, 6, Novartis, 1, 5, 6, Pfizer, 6, UCB, 6; **R. Bergner**: AbbVie, 1, 6, Alfasigma, 1, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eli Lilly, 6, German Rheumatology Society, 12, unpaid board member for Commission für student education, GlaxoSmithKlein(GSK), 1, 6, Janssen, 6, Merck/MSD, 6, Novartis, 1, 6, Vifor, 1, 5; **J. Rech**: AbbVie, 6, 12, Received consulting fees, Biogen, 6, 12, Received consulting fees, Bristol-Myers Squibb(BMS), 6, 12, Received consulting fees, Chugai, 6, 12, Received consulting fees, Eli Lilly, 6, 12, Received consulting fees, GlaxoSmithKlein(GSK), 6, 12, Received consulting fees, Janssen, 6, 12, Received consulting fees, MSD, 6, 12, Consulting fees, Novartis, Sobi, 1, 2, 5, 6, Roche, 6, 12, Received consulting fees, Sanofi, 6, 12, Received consulting fees, Sobi, 6, 12, Received consulting fees, UCB, 6, 12, Received consulting fees; **L. Unger**: Novartis, 12, Receives payments for speeches and seminar presentations; **S. Finzel**: AbbVie, 6, Alfasigma/Galapagos, 6, Biotest, 6, 12, Meeting or travel grants, Celltrion, 6, Chugai, 6, Eli Lilly, 12, Meeting or travel grants, Galapagos, 12, Meeting or travel grants, Johnson & Johnson, 6, 12, Consulting fees, meeting or travel grants, Novartis, 6, 12, Consulting fees, meeting or travel grants, Novo Nordisk, 12, Consulting fees, Sobi, 12, Meeting or travel grants, UCB, 6, 12, Consulting fees, meeting or travel grants; **I. Andreica**: Boehringer-Ingelheim, 6, Chugai, 2, 5, 12, Consulting fees, Eli Lilly, 2, 5, 6, 12, Consulting fees, Galapagos, 2, 5, 12, Consulting fees, Gilead, 2, 5, GSK, 2, 5, Janssen, 2, 5, MSD, 2, 5, 6, Novartis, 5, 12, Consulting fees, received payments for other services, Pfizer, 2, 5, Sobi, 2, 5, 6, takeda, 2, 5, UCB, 2, 6, 12, Consulting fees; **D. Kofler**: AbbVie, 1, UCB, 1; **S. Weiner**: AbbVie, 6, 12, Meeting or travel grants, Amgen, 6, 12, Meeting or travel grants, Arbeitskreis Nephrologie Saar-Pfalz Mosel, 12, Unpaid board member, AstraZeneca, 6, Bayer, 6, Bristol-Myers Squibb(BMS), 6, 12, Meeting or travel grants, Daiichi-Sankyo, 6, MSD, 6, Novartis, 1, 6, Otsuka, 6, 12, received meeting or travel grants, Pfizer, 6, 12, received meeting or travel grants, Roche, 6, Saarländisch-Pfälzische Internistengesellschaft, 12, Unpaid board member, UCB, 12, received meeting or travel grants; **P. Lamprecht**: AstraZeneca, 1, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Bundesministerium für Bildung und Forschung, 5, Deutsche Forschungsgemeinschaft, 5, GlaxoSmithKlein(GSK), 1, 6, Janssen, 6, John Grube Foundation, 5, Novartis, 6, UCB, 1, 6, Vifor, 1, 5, 6; **H. Schulze-Koops**: AbbVie, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Amgen, 12, Research support and principal investigator (clinical trials funds to institution), Biogen Idec, 12, Research support and principal investigator (clinical trials funds to institution), Boehringer Ingelheim, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Bristol Myers Squibb, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Eli Lilly, 6, 12, Research support and principal investigator (clinical trials funds to institution),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Galapagos, 2, GSK, 12, Research support and principal investigator (clinical trials funds to institution), Janssen, 6, Janssen-Cilag, 12, Research support and principal investigator (clinical trials funds to institution), Merck Sharp & Dohme, 6, 12, Research support and principal investigator (clinical trials funds to institution), Novartis, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Pfizer, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Roche, 12, Research support and principal investigator (clinical trials funds to institution), Sandoz-Hexal, 6, 12, Research support and principal investigator (clinical trials funds to institution), Sanofi, 6, 12, Research support and principal investigator (clinical trials funds to institution), UCB, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution); **M. Mendelson**: Novartis, 3, 12, Shareholder; **W. Bao**: Novartis, 3, 11; **M. Keyport**: Novartis, 3, 12, Shareholder; **M. Maricos**: Novartis, 3, 12, Shareholder; **V. Jordan M.**: Novartis, 3, 12, Shareholder; **J. Thiel**: AstraZeneca, 6, Bristol-Myers Squibb(BMS), 5, 6, GlaxoSmithKlein(GSK), 6, 12, Consulting fees, Janssen, 12, Consulting fees, Novartis, 1, 5, 6, 12, consulting fees, 12, Pending patent application on the use of secukinumab in GCA, Roche, 6, Vifor, 6.

Abstract Number: 1176

VISIBLE Post-Inflammatory Pigmentation Journeys: Exploring the Impact of Pigmentation

Tarek Dawamne[1], Olivia Choi, MD, PhD, FAAD[2], Alison Tran[3], Jacob Beer[4], Katelyn Rowland[2], Theodore Alkousakis[2], **Oyediran Adelakun**[2], Elizabeth Skobelev[2], Sancharitha Ramji[2], Tony Ma[5], Daphne Chan[2] and Jenna Lester[6], [1]Texas A&M School of Engineering Medicine, Houston, TX, USA, Houston, TX, [2]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [3]Lake Granbury Medical Center, Department of Dermatology, Dallas, TX, USA, Dallas, TX, [4]Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, Miami, FL, USA, Miami, FL, [5]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [6]University of California, San Francisco, CA, USA, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Post-inflammatory pigment alteration (PIPA) following resolution of psoriasis plaques is an important, neglected problem that disproportionately impacts people of color.[1-3] VISIBLE, an ongoing Phase 3b study evaluating guselkumab for moderate-to-severe psoriasis across all skin tones, is designed to collect PIPA data.

Methods: Total 211 participants were randomized (3:1) to receive guselkumab or placebo with placebo crossover to guselkumab at Weeks 16, 20, and every 8 weeks (q8w) thereafter. Through Week 48, clinician-reported Psoriasis Area Severity Index (PASI) responses and patient-reported outcomes (Skin Discoloration Impact Evaluation Questionnaire [SDIEQ], Dermatology Life Quality Index [DLQI], and Patient-Reported Outcomes Measurement Information System-29 [PROMIS-29]) were collected. Standard and cross-polarized photographs were obtained and analyzed for skin tone evenness.

Results: Mean PASI improvement was ∼95% at Week 48 for the guselkumab randomized groups. Correlation coefficients were higher for SDIEQ and DLQI versus SDIEQ and PASI at Week 48, indicating high impact of skin discoloration on quality of life (QoL). SDIEQ had moderate (r=0.4116) and weak (r=0.3204) correlations with PROMIS-29 anxiety and depression measures, respectively, whereas Week 48 PASI did not correlate with either PROMIS-29 outcome.

Conclusion: Impact of PIPA on QoL is much greater than skin clearance as measured by PASI. Awareness of patient concerns about PIPA will enable clinicians to better counsel patients starting psoriasis treatment. The study is limited by variations in photograph quality. PIPA due to psoriasis highly impacts QoL in people of color. Discussing PIPA before starting

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

treatment is imperative and its effect should be explicitly measured. While there are objective ways to quantify PIPA, further planned analyses of mechanistic changes will help identify factors predictive of PIPA outcomes.

References

1. Amico S, et al. *J Am Acad Dermatol*. 2020;83:1188-1191.
2. Kauffman BP, et al. *Am J Clin Dermatol*. 2018;19:405-423.
3. Chiu HY, et al. *J Am Acad Dermatol*. 2022;86:642-645.

Disclosure: T. Dawamne: None; **O. Choi, MD, PhD, FAAD**: Apogee Therapeutics Inc., 3, Johnson & Johnson, 11, 12, Employee of Johnson & Johnson at the time study was conducted; **A. Tran**: None; **J. Beer**: None; **K. Rowland**: Johnson & Johnson, 3, 11; **T. Alkousakis**: Johnson & Johnson, 3, 11; **O. Adelakun**: Johnson & Johnson, 3, 11; **E. Skobelev**: Johnson & Johnson, 3, 11; **S. Ramji**: Johnson & Johnson, 3, 11; **T. Ma**: Johnson & Johnson, 3, 11; **D. Chan**: Johnson & Johnson, 3, 11; **J. Lester**: Google, 2, L'Oreal, 2, Mattice biosciences, 1, OurX, 1.

Abstract Number: 1177

Pregnancy Outcomes in Women with Familial Mediterranean Fever Treated with Anakinra: A Retrospective Study

Bilgesu Ergezen[1], **Ozgur Can Kilinc**[2], Bugra Egeli[3], Oguzhan Omer Kizilkaya[2], Kerem parlar[4], Enes Azman[2], Huri ozdogan[1] and serdal Ugurlu[5], [1]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, İstanbul, Turkey, [2]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [3]Children's Hospital of Los Angeles, Los Angeles, CA, [4]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, İstanbul, Turkey, [5]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Parameter	Value
Maternal age, mean ± SD, years	31.5 ± 3.95
M694V homozygous	%72.2 (13)
Amyloidosis	%15.8 (3)
Live births	%96.2 (25)
Stillborn	%3.8 (1)
Preeclampsia	%21.7 (5)
IUGR	%18.5 (5)
Birth weight, mean ± SD, kg	2.8 ± 0.76
Birth length, mean ± SD, cm	46.5 ± 6.2 cm

Maternal and Neonatal Characteristics of the Patient Population

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Familial Mediterranean Fever (FMF) is an autoinflammatory disease mainly treated with colchicine. Anakinra, an interleukin-1 receptor antagonist, is used for colchicine-resistant cases. However, data on the safety of Anakinra during pregnancy is limited. This study aims to evaluate pregnancy outcomes of FMF patients who received at least one dose of Anakinra during pregnancy.

Methods: A retrospective single-center study was conducted to analyze clinical data and pregnancy outcomes of FMF patients who received Anakinra during pregnancy.

Results: This study included data from 27 pregnancies involving 19 mothers. The average maternal age at pregnancy was 31.5 ± 3.95 years. The most common genotype among mothers was homozygous M694V, observed in %72.2 (13/18) of cases. Amyloidosis was present in %15.8 (3/19) of mothers. In %51.9 (14/27) of the pregnancies, mothers were on Anakinra treatment prior to pregnancy, while in the remaining pregnancies Anakinra treatment was started during pregnancy.

Out of the 27 pregnancies, 26 resulted in delivery, and one is still ongoing at 15 weeks of gestation. Among the terminated pregnancies, 26 babies were born, one of whom was stillborn. The frequency of cesarean section was 80.8% (21/26), and the rate of preterm birth was 34.6% (9/26), with an average gestational age at birth of 36.6 ± 3.3 weeks. Assisted reproduction techniques were utilized in %30.4 (7/23) of the pregnancies.

The most common maternal complication during pregnancy was preeclampsia (5/23) followed by bleeding (2/23), hypertension (2/23), gestational diabetes (1/23), and cerebrovascular event (1/23).

Intrauterine growth restriction was reported in %18.5 (5/27) of the pregnancies. The rate of neonatal ICU hospitalization was %16.7 (4/24) among babies. It was reported that %34.8 (8/23) of the babies were small for gestational age. Mean weight, length, and head circumference of the babies were 2.8 ± 0.76 kg, 46.5 ± 6.2 cm, and 33.8 ± 3.8 cm, respectively. The average Apgar scores at first and fifth minutes were 7.8 ± 1.4 and 9.0 ± 1.1, respectively.

The average current age of the children is 75.3 ± 45.9 months, with a mean weight of 26.7 ± 11.4 kg and mean height of 116.4 ± 22.8 cm. Among these children, the most common chronic condition was allergic conditions (4/9), followed by growth hormone deficiency (1/9), PFAPA (1/9), torticollis (1/9), and a heart murmur (1/9).

Conclusion: Although complications such as preeclampsia and intrauterine growth restriction were observed, no lasting sequelae were reported in the children, and the majority of pregnancies resulted in live births with favorable outcomes. Anakinra appears to be safe during pregnancy, with no major teratogenic effects identified. However, long-term follow-up is warranted to fully assess potential outcomes.

Disclosure: B. Ergezen: None; **O. Kilinc**: None; **B. Egeli**: None; **O. Kizilkaya**: None; **K. parlar**: None; **E. Azman**: None; **H. ozdogan**: None; **s. Ugurlu**: None.

Abstract Number: 1178

An International Modified Delphi Study on the Evolving Role of Janus Kinase Inhibitors (JAKi) in Rheumatic and Musculoskeletal Diseases (RMDs)

Anna Barkaway[1], **Philip J. Mease**[2], Zoe Rutter-Locher[3], Robert Moots[4], Mwidimi Ndosi[5], Michael McLean[6] and International Steering Committee, [1]Pfizer UK, Tadworth, United Kingdom, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]Guys and St Thomas NHS trust, London, United Kingdom, [4]Liverpool University Hospitals, Liverpool, United Kingdom, [5]University of the West of England, Bristol, Filton, United Kingdom, [6]Pfizer, Glasgow, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Global, geographical distribution of panellists

Table 1: Statements which achieved stable consensus or stable disagreement regarding JAKi use in RMDs.

A. Current uses of JAK inhibitors
JAK inhibitors have an important role in the management of rheumatoid arthritis.
JAK inhibitors have an important role in the management of ankylosing spondylitis.
JAK inhibitors have an important role in the management of psoriatic arthritis.
JAK inhibitors may have an important role in the management of atopic dermatitis.
JAK inhibitors should be reserved for second or subsequent treatment lines.
JAK inhibitors have utility as a corticosteroid sparing agent.
When the treatment target has been achieved, patients may be maintained on JAK inhibitors.
B. Potential uses of JAK inhibitors beyond currently approved indications
JAK inhibitors have a potential role in the management of psoriasis.
Combination therapy with another targeted synthetic or biologic DMARD should only be used when there is substantial evidence on efficacy and safety from clinical trials.
Combination therapy should only be used when there is substantial evidence on efficacy and safety from clinical trials.
C. Potential uses of a specific class of JAK inhibitors: TYK2 inhibitors
TYK2 inhibitors have a potential role in the management of psoriatic arthritis.
TYK2 inhibitors have a potential role in the management of psoriasis.
D. Acquisition and access to JAK inhibitors
JAK inhibitors are currently accessible for patients who have an indication for these agents in my country.
The availability of generic JAK inhibitors may lead to their wider use.
The availability of generic JAK inhibitors may broaden the indications for which they are used.
The availability of generic versions of existing JAK inhibitors may increase their use in the early stages of conditions for which they are indicated.
The availability of generic JAK inhibitors may broaden the off-label indication for which they could be used.
JAK inhibitors should be prescribed exclusively by specialists in the condition being treated.
JAK inhibitors may be prescribed by non-specialists.
Monitoring for JAK inhibitors may be undertaken by non-specialists in the condition being treated provided there is an agreement with the specialist and agreed guidelines are followed.
Cross-disciplinary education initiatives are important to ensure effective prescribing of JAK inhibitors in people with multiple conditions who may benefit from their use

Key:

Stable Consensus
Stable disagreement

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

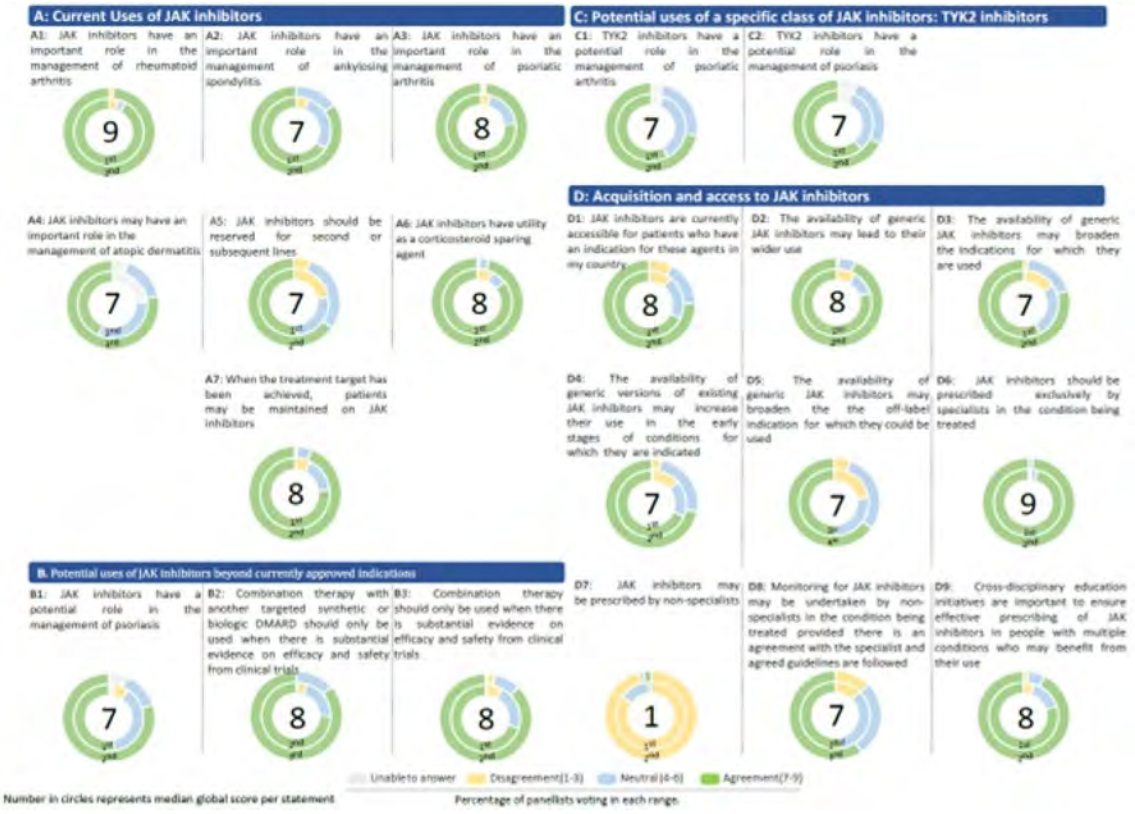


Figure 2: Detailed outcomes for statements achieving stable consensus in the overall global analysis.

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The development of advanced therapies such as JAK inhibitors (JAKi) has expanded treatment options available for patients with rheumatic and musculoskeletal diseases (RMDs). Case reports and scientific studies are increasingly demonstrating the potential scientific rationales regarding JAKi use for broader indications. Defining current and anticipated prescribing habits may help predict the future treatment paradigm and understand key evidence gaps. This study aimed to capture global discussions on the evolution of JAKi use within (1) current indications and (2) new indications where JAKi may have potential place in therapy as identified by unmet medical need, external global expert opinion and literature evidence using a modified Delphi approach.

Methods: A 4 round modified Delphi study was conducted with 178 Panellists from 23 countries worldwide. Global experts formed the academic and steering committees. Systematic and scoping reviews on published literature of JAKi use in RMDs were conducted to inform initial statements alongside committee expertise. Panellists ranked statements on a Likert scale of 1-9, provided comment on statement stringency and suggestions. Stable statement consensus or stable disagreement was considered as a median score of ≥7 or ≤3 from two consecutive rounds, respectively. Statements were presented in ≥2 rounds and wording amended based on panellist suggestions, confirmed by committees.

Results: Panellists (n=178) participated from: Americas (n=30), Europe (n=40), Eastern Mediterranean (n=35), South-East Asia (n=19), Africa (n=27), and Western Pacific (n=27) (Figure 1). Statements were grouped into the following categories: Current Uses of JAKi, Potential uses of JAKi beyond currently approved indications, Potential uses of a specific class of

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

JAKi: TYK2 inhibitors or Acquisition and access to JAKis (Figure 2/Table 1). Of the 79 statements presented, 20 reached stable consensus, and one reached stable disagreement, with >250 comments. Consistent themes included the important role of JAKi in current indications, that the availability of generic JAKi may lead to their wider use, lack of RCT data on potential new indications and accessibility. Opinion stratification across key differentiators including geography, national income and treatment practice highlighted great heterogeneity in responses, particularly in relation to cost, JAKi adoption in earlier stages of indicated conditions, and potential expansion of their use more broadly.

Conclusion: Based on available literature evidence and global expert consensus, this study highlights global consensus characterization of current uses and the evolution of JAKi use in RMDs. Clinicians were in consensus that JAKi have an important role in the management of current indications. Additionally, opinion showed availability of generic JAKi may lead to their wider use and may broaden the indications for which they are utilised.

This study was sponsored by Pfizer. Pfizer employees and academic authors designed the study, interpreted data, and wrote the abstract. Analytical and writing support was provided by Momentum data Ltd, funded by Pfizer. Some study elements previously accepted by BSR & EULAR 2025.

Disclosure: A. Barkaway: Pfizer, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **Z. Rutter-Locher**: None; **R. Moots**: Novartis, 5, Pfizer, 12, Research and medical writing support for publication; **M. Ndosi**: Pfizer, 2; **M. McLean**: Pfizer, 3.

Abstract Number: 1179

Efficacy and Safety of Ruxolitinib in Adult Patients With Refractory Connective Tissue Disease-Associated Macrophage Activation Syndrome

Jingjing Li[1], Ran Wang[1], Jie Chen[1], Antao xu[1], Yakai Fu[1], Yanwei Lin[1], Xiaodong Wang[1], Shuang Ye[2], Fang Du[1] and **Qiong Fu**[3], [1]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China (People's Republic), [2]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [3]Renji Hospital, Shanghai, Shanghai, China

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Macrophage activation syndrome (MAS) is a rare and life-threatening complication of connective tissue diseases (CTDs), with approximately 30% of cases being refractory to standard therapeutic protocols. Ruxolitinib, a Janus kinase 1/2 inhibitor, has emerged as a potential therapeutic option for refractory MAS. This study aimed to evaluate its efficacy and safety in patients with refractory CTD-associated MAS (CTD-MAS).

Methods: A meticulous chart review was conducted on 20 patients with refractory CTD-MAS who received ruxolitinib in our institution. Data from ruxolitinib-naïve CTD-MAS patients served as historical controls. Clinical and laboratory parameters, therapeutic response, and survival outcomes were analyzed. The efficacy and safety of ruxolitinib were evaluated, and survival rates were compared to historical controls.

Results: The cohort of 20 patients with refractory CTD-MAS included 17 females and 3 males, with underlying conditions comprising adult-onset Still's disease (n = 13), systemic lupus erythematosus (n = 4), and other connective tissue diseases (n = 3) (Table 1). At the initiation of ruxolitinib treatment, all patients exhibited active diseases. The survival rate was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographics and clinical characteristics of patients

Table 1. Baseline demographics and clinical characteristics of patients

	Ruxo* group (N=20)	Control group (N=21)	P Value
Age, years, median (range)	37 (18-71)	29 (18-65)	0.628
Sex, female, n (%)	17 (85)	16 (76)	0.751
Death, n (%)	1 (5)	8 (38)	0.029
Previous therapies			
High-dose intravenous glucocorticoids, n (%)	20 (100)	21 (100)	1.000
Average daily dose during week-1, mg/d prednisone-equivalent, median (range)	133 (100-267)	134 (100-625)	0.472
IVIG*, n (%)	8 (40)	5 (24)	
Etoposide, n (%)	5 (25)	8 (38)	
Tocilizumab, n (%)	3 (15)	0	
Tacrolimus, n (%)	0	1 (5)	
Ciclosporin, n (%)	4 (20)	5 (24)	
Aetiology*			
AOSD, n (%)	13(65)	17 (81)	
SLE, n (%)	4 (25)	4 (19)	
Other CTD, n (%)	3 (10)	0	
Fever, n (%)	20 (100)	21(100)	1.000
Splenomegaly, n (%)	6 (30)	12 (57)	0.080
Bone marrow hemophagocytosis, n (%)	9 (45)	9 (43)	0.890
Leucocyte count (10^9/L), median (range)	3.69 (0.58-34.03)	3.15 (0.70-31.18)	0.812
Neutrophil count (10^9/L), median (range)	1.78 (0.01-32.70)	2.30 (0.01-20.27)	0.694
Hemoglobin (g/dL), median (range)	94 (61-129)	104 (63-175)	0.274
Platelet count (10^9/L), median (range)	115 (25-359)	83 (4-188)	0.133
Aspartate aminotransferase, U/L, median (range)	72 (17-1988)	125 (28-980)	0.342
Alanine aminotransferase, U/L, median (range)	168 (10-1698)	174 (23-857)	0.944
Lactate dehydrogenase, U/L, median (range)	521 (283-10510)	794 (176-3139)	0.076
Fibrinogen, g/L, median (range)	2.00 (0.00-4.47)	1.48 (0.58-3.70)	0.123
Triglyceride concentration (mg/dL), median (range)	1.49 (0.80-17.90)	2.68 (0.85-6.35)	0.003
Ferritin, ng/mL, median (range)	5982 (712-57144)	1500 (1305-15000)	<0.001

*Ruxo: ruxolitinib; IVIG: intravenous immunoglobulin; AOSD: adult-onset Still's disease; SLE: systemic lupus erythematosus; CTD: connective tissue diseases.

significantly higher in the ruxolitinib group (19/20, 95%) than in historical controls (13/21, 62%) (P = 0.011) (Figure 1). Partial response (PR) was observed in 9 patients at the first scheduled response assessment (week 1), and the first complete remission (CR) was documented at week 2. Two additional patients progressed from PR to CR during the third week, and one patient improved from no response (NR) to PR. By week 8, 50% (10/20) and 30% (6/20) of ruxolitinib-treated patients had achieved partial and complete responses, respectively. Four patients exhibited no response to treatment, including the patient who died of complications (Figure 2). Ruxolitinib therapy led to rapid and significant clinical and laboratory parameter improvements. By week 8, the median daily glucocorticoid dose decreased from 2.7 mg/kg/day to 0.5 mg/kg/day. Cytomegalovirus infection occurred in 20% (4/20) of patients.

Conclusion: Ruxolitinib demonstrated substantial efficacy and tolerability in patients with refractory CTD-MAS, leading to significant clinical improvement and a notable reduction in glucocorticoid dependence. These findings support the potential role of ruxolitinib as a salvage therapy for refractory CTD-MAS, warranting further investigation in prospective clinical studies.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

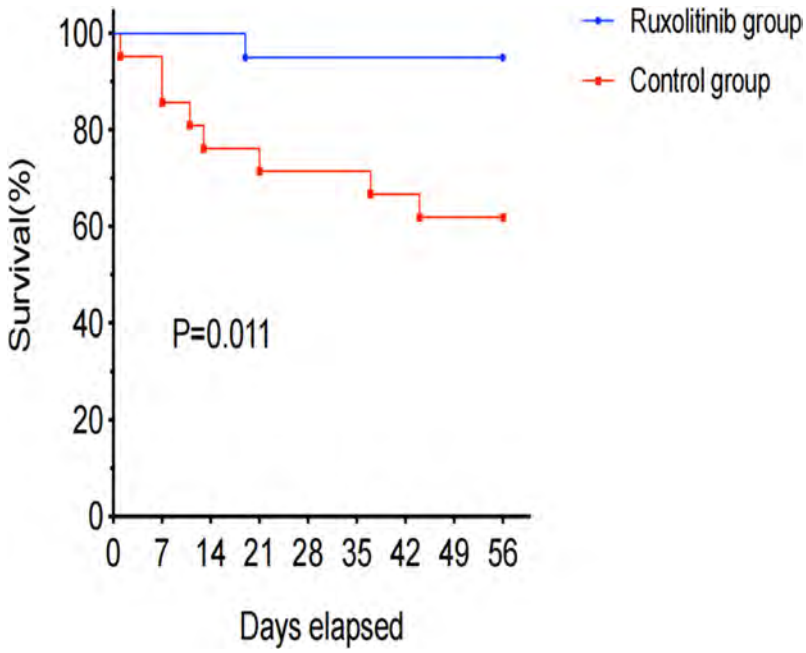


Figure 1. Survival curve of the ruxolitinib group and the historical control group.

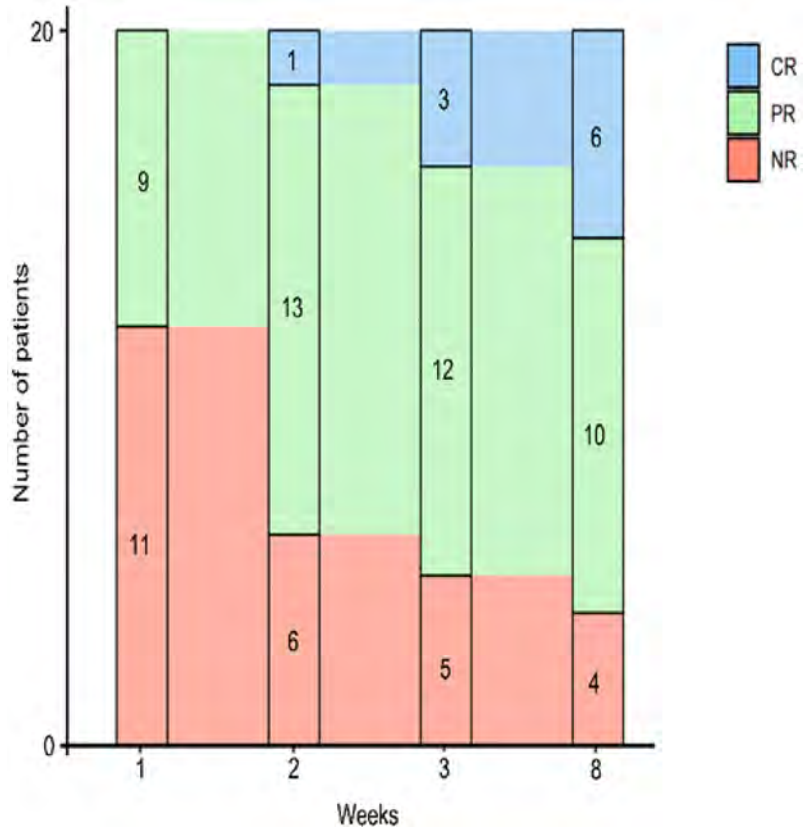


Figure 2. The response of patients with refractory CTD-MAS during the ruxolitinib treatment. *CR: complete remission; PR: partial remission; NR: no response.

Disclosure: J. Li: None; **R. Wang**: None; **J. Chen**: None; **A. xu**: None; **Y. Fu**: None; **Y. Lin**: None; **X. Wang**: None; **S. Ye**: None; **F. Du**: None; **Q. Fu**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1180

Gender-Based Clinical Differences in Behçet's Syndrome: Findings from a 24-Year Cohort in a Non-Endemic and Multiethnic Country

Rafael Bassara Macedo[1], Pedro Araujo[2], Fabio Specian[1], Carolina Ejnisman[3], Barbara Bayeh[3], Percival Degrava Sampaio Barros[3], Thiago Freitas[4], Rafael Cordeiro[5] and Henrique Giardini[4], [1]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [2]Universidade de São Paulo, Sao Paulo, São Paulo, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

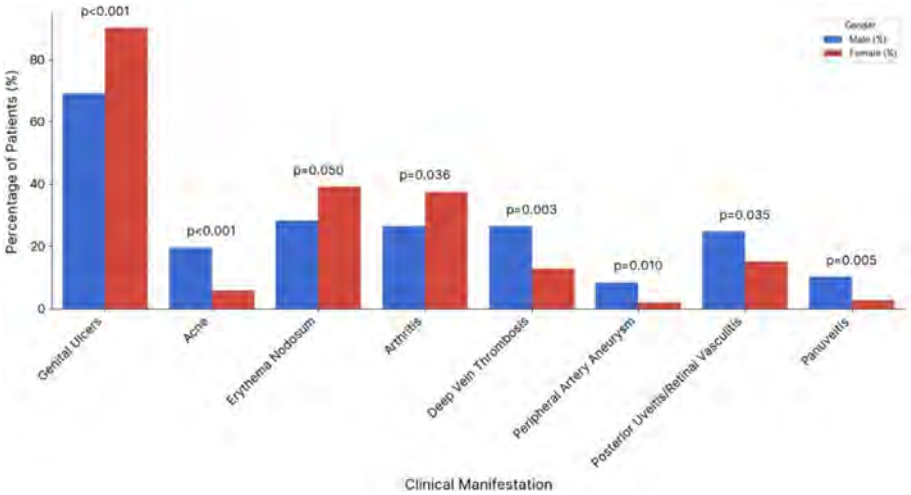
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's syndrome (BS) is a multisystemic inflammatory condition that affects both genders, although gender-related differences in disease manifestations may vary across regions. Studies report severe manifestations more commonly in men. However, gender-based differences in South America, a non-endemic region, have been less studied.

Methods: This is a retrospective analysis of a prospective, single-center, multiethnic cohort of patients with BS from January 2000 to December 2024. Patients were diagnosed according to the International Study Group and/or the International Criteria for Behçet's Syndrome. Categorical variables were analyzed using the chi-square test or Fisher's exact test, while continuous variables were compared using unpaired Student's t-test.

Results: Among 369 patients evaluated, 303 were included, of whom 117(38.6%) were male and 186(61.4%) were female. The mean age at symptom onset was 27.4±11.4 years, with males presenting at 25.9±10.4 years and females at 28.3 ±12.0 years (p=0.075). The mean age at diagnosis was 31.6±10.4 years, with no significant difference between sexes (p=0.082). The most prevalent clinical manifestations were oral ulcers (99.3%), genital ulcers (81.5%), pseudofolliculitis (51.5%) and erythema nodosum-like lesions (35%). Female patients more frequently presented genital ulcers (89.2%



Clinical Manifestations by Gender in Behçet's Syndrome

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

vs. 69.2%; $p< 0.001$), erythema nodosum-like lesions (39.2% vs. 28.2%; $p=0.050$) and arthritis (38.2% vs. 26.5%; $p=0.036$). Conversely, male patients more often exhibited acne (19.7% vs. 5.9%; $p< 0.001$), deep vein thrombosis of the limbs (26.5% vs. 12.9%; $p=0.003$), caval vein thrombosis (7.7% vs. 2.2%; $p=0.020$), peripheral artery aneurysms (8.5% vs. 2.2%; $p=0.010$), arterial occlusions (11.1% vs. 4.3%; $p=0.023$), posterior uveitis/retinal vasculitis (24.8% vs. 15.1%; $p=0.035$) and panuveitis (10.3% vs. 2.7%; $p=0.005$). Azathioprine use was more common among males (75.2% vs. 64%; $p=0.041$). Fibromyalgia was significantly more prevalent in female patients (18.3% vs. 1.7%; $p< 0.001$). No gender differences were observed regarding the use of other medications or comorbidities.

Conclusion: This is the largest cohort in South America to evaluate gender-specific features in BS. Male patients were more likely to exhibit severe manifestations, consistent with existing literature. Female patients showed a higher prevalence of mucocutaneous lesions, arthritis, and fibromyalgia. Although these manifestations are often considered benign, they can significantly affect quality of life. The higher prevalence of fibromyalgia in women may reflect the general higher incidence of this condition in females, but arthritis may also trigger central nervous system sensitization, making women more susceptible. This hypothesis requires further investigation. The higher use of azathioprine in male patients suggests the need for more aggressive immunosuppression due to the severity of their symptoms. This difference may also reflect a more conservative treatment approach for women, given the perceived milder nature of their manifestations.

Disclosure: R. Bassara Macedo: None; **P. Araujo**: None; **F. Specian**: None; **C. Ejnisman**: None; **B. Bayeh**: None; **P. Degrava Sampaio Barros**: None; **T. Freitas**: None; **R. Cordeiro**: None; **H. Giardini**: None.

Abstract Number: 1181

Clinical Relevance of Tumor Necrosis Factor Superfamily Cytokines

Robert Corty[1], Gul Karakoc[1], Ahmad Jawdat[2], Hui Yu[3], Jonathan Mosley[4], Michael Stein[1], Vivian Kawai[5] and Participants and investigators of All of Us Research Program and FinnGen study, [1]Vanderbilt University Medical Center, Nashville, TN, [2]University of Alabama at Birmingham, Birmingham, [3]University of Miami, Miami, [4]UT Southwestern Medical Center, Dallas, [5]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The tumor necrosis factor superfamily (TNFSF) includes 48 proteins involved in immune activation, inflammation, and cell death and represent an area of intense focus in current drug development efforts. However, the proteins are difficult to measure in large clinical populations, thus the clinical relevance of many of these proteins in human disease is not well characterized and the potential effects of drugs targeting them is largely unknown. The ability to associate genetically driven variability in protein levels with phenotype risk provides an opportunity to determine the potential relevance of TNFSF proteins using large populations with both genotype and clinical information available.

Methods: To define the clinical manifestations associated with TNFSF members, we examined genetic models for 38 TNFSF proteins available in the UK Biobank pQTL web portal (http://uk-ppp.gwas.eu). We estimated genetically determined levels of TNFSF proteins in participants of European ancestry in the Vanderbilt University Medical Center biobank (BioVU) and in the All of Us Research Program (AoU). We performed a phenome-wide association study (PheWAS) in each biobank to define clinical associations for TNFSF levels adjusted for sex, age, and 5 principal components; and significant associations (P-value$\leq 5x10^{-5}$) in BioVU and AoU were combined in a meta-analysis. We examined proteins with significant associations in the meta-analysis (P-value $\leq 5x10^{-5}$) using a Mendelian randomization (MR) approach. We used genetic predictors of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

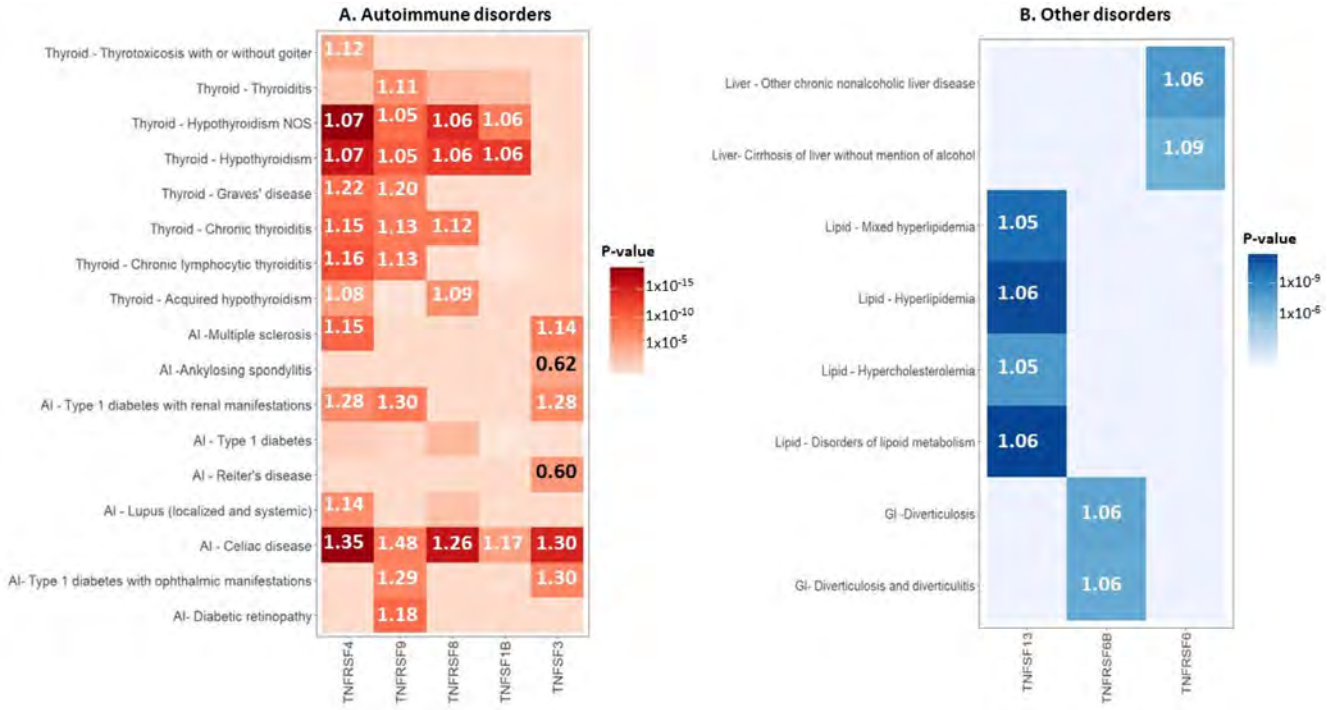


Figure 1: Heatmaps showing the association between genetically predicted levels of tumor necrosis factors super family proteins (TNFSF) with (A) Autoimmune disorders and (B) Others disorders. Darker shades represent more significant associations (P =2.2x10-19 for hypothyroidism NOS and P =1.8x10-12 for disorders of lipoid metabolism). Odds ratios (OR) for significant associations (P ≤5x10-5) are shown in each tile and OR<1 are shown in black fonts.

TNFSF proteins as instrumental variables and summary statistics for clinical diagnoses as outcome in an inverse-variance weighted regression (IVWR). We tested horizontal pleiotropy using Egger regression. A P-value< 0.05 was considered significant in the IVWR and an intercept P-value ≤0.05 suggested pleiotropy.

Results: Genetically predicted levels of twelve proteins were significantly associated with at least one clinical diagnosis in either biobank. In the meta-analysis, higher levels for TNFRSF4, TNFRS9, TNFRSF8, and TNFRSF1B increased the risk of several thyroid and autoimmune diseases including lupus; higher levels of TNFSF3 were associated with a reduced risk of both ankylosing spondylitis and Reiter's disease (**Fig. 1A**). TNFSF13 increased the risk for dyslipidemias, TNFRSF6B for diverticulosis and TNFRSF6 for non-alcoholic liver disease (**Fig. 1B**). In the IVWR analyses, TNFRSF4 (P-value =1.5x10^{-5}) and TNFRSF8 (P-value=0.02) were associated with autoimmune thyroiditis without evidence of horizontal pleiotropy (intercept P-value >0.05 for both proteins).

Conclusion: Genetic predisposition to higher levels of several TNFSF proteins is associated with increased risk of autoimmune, metabolic, hepatic, and gastrointestinal disorders and may identify potential therapeutic targets.

Disclosure: R. Corty: None; **G. Karakoc**: None; **A. Jawdat**: None; **H. Yu**: None; **J. Mosley**: None; **M. Stein**: None; **V. Kawai**: None.

Abstract Number: 1182

Cardiac Sarcoidosis in Black Patients: A Biopsy-Confirmed Cohort Study

Roshan Subedi[1], Haya Haddad[2], Rachel Barish[1], Tania Vora[1], Nana Afari-Armah[3], Ajay Kadakkal[1], Farooq Sheikh[1] and Florina Constantinescu[1], [1]Medstar Washington Hospital Center, Washington, DC, [2]Medstar Washington Hospital Center, Silver Spring, MD, [3]Medstar Washington Hospital Center, Washington

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sarcoidosis is an inflammatory disease characterized by non-necrotizing granulomatous inflammation that can affect any organ. Approximately 5% of patients with sarcoidosis develop clinically significant cardiac sarcoidosis (CS), but up to one-fourth may have clinically silent cardiac involvement. A definitive diagnosis of CS requires histologic evidence of granulomas in cardiac tissue. Due to the limited sensitivity and infrequent use of cardiac biopsies, the pursuit of a tissue diagnosis is not routinely performed. There is a paucity of data on biopsy-confirmed CS, particularly among Black patients, a population at higher risk for this disease. We aimed to characterize a cohort of Black patients with biopsy-proven CS and describe their clinical features and outcomes.

Table 1: Characteristics of the definite cardiac sarcoidosis in Black patients

Variables	Mean ± SD or number (%)
Age (in years)	58 ± 10
Age of diagnosis of sarcoidosis (in years)	51 ± 11
Age of diagnosis of CS (in years)	53 ± 11
Male	9 (53)
Hypertension	13 (76)
Hyperlipidemia	7 (41)
Smoking	8 (47)
Alcohol	10 (59)
Coronary artery disease	1 (6)
Cardiac manifestation	
Heart failure	16 (94)
Arrythmia	11 (65)
Extracardiac involvement	14 (82)
Pulmonary	10 (59)
Lymph nodes	7 (41)
LVEF in echocardiography	
< 20%	3 (18)
20-30%	9 (53)
30-40%	3 (18)
40-50%	1 (6)
50-60%	1 (6)
Atrio-ventricular block	3 (18)
Ventricular tachycardia/Ventricular fibrillation	7 (41)
Late gadolinium enhancement in cardiac MRI	6 (35)
Increased uptake in PET scan	10 (59)
Advanced therapies	
Implantable Cardioverter-Defibrillator	11 (65)
Left Ventricular Assist Device	9 (53)
Heart transplantation	7 (41)

CS: Cardiac Sarcoidosis, LVEF: Left Ventricular Ejection Fraction, MRI: Magnetic Resonance Imaging, PET: Positron Emission Tomography, SD: Standard Deviation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective study via review of electronic medical records. Patients with CS in our institution's cardiac sarcoidosis database (2014 - 2025) were identified. Black patients with biopsy-proven CS (referred to as definite CS as per the Heart Rhythm Society criteria) were included in our study. We assessed demographic, clinical presentation, diagnostic evaluation, immunosuppression, heart replacement therapies, and outcomes.

Results: Amongst 306 definite or probable CS patients, 17 Black patients had definite CS. The diagnosis was established through histopathology from endomyocardial biopsy (n = 12) or explanted heart tissue (n = 5). Demographic and clinical characteristics are summarized in Table 1. Most patients (94%) had heart failure with reduced ejection fraction, with 71% having severe left ventricular systolic dysfunction (ejection fraction < 30%). In 53% of the patients, CS was the first diagnosis of sarcoidosis. Isolated cardiac sarcoidosis was diagnosed in 18% of the patients. Almost 60% had increased multifocal uptake on PET scans at diagnosis. The median initial dose of prednisone was 40 mg (range: 20–80 mg), and the median duration of treatment was 1 year (range: 0–11 years). Mycophenolate was the most frequently used (41%) steroid-sparing agent for immunosuppression, followed by methotrexate (24%). Adalimumab and infliximab were used as second-line steroid-sparing agents (18%). Seven patients ultimately received heart transplants. Post-transplant immunosuppression typically included prednisone, mycophenolate, and tacrolimus. Over a median duration of seven years, five patients died (three of these had not received any maintenance immunosuppression), one was lost to follow-up, and the rest were clinically stable or in remission. There was no recurrence of CS in any of the patients who received heart transplantation.

Conclusion: To our knowledge, this is the largest descriptive cohort of biopsy-proven CS in Black patients. One-third of the patients in our study were diagnosed with CS after heart transplantation, which highlights the challenge in making a definitive diagnosis. Given the rarity of definite CS, multi-institutional registry study would be useful to characterize disease presentation and diagnosis.

Disclosure: R. Subedi: None; **H. Haddad**: None; **R. Barish**: AstraZeneca, 6; **T. Vora**: None; **N. Afari-Armah**: None; **A. Kadakkal**: None; **F. Sheikh**: None; **F. Constantinescu**: None.

Abstract Number: 1183

Risk of Inflammatory Bowel Disease in Psoriatic Arthritis Patients Treated with IL-17 Inhibitors

Rusudan Tskitishvili[1], Abdallah Hussein[2], Irakli Tskhakaia[3], Nanuka Tsibadze[3], Eric Osgood[2] and Humaira Khan[4], [1]Virtua Health, Camden, NJ, [2]Virtua Health, Camden, [3]Jefferson Health - Einstein, Philadelphia, PA, [4]Virtua Health, Voorhees

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic, progressive inflammatory arthritis that significantly impairs quality of life and contributes to substantial morbidity. Interleukin-17 (IL-17) plays a central role in PsA pathogenesis. Although anti–IL-17 therapies have shown clinical efficacy in PsA, clinical trials have reported cases of new-onset inflammatory bowel disease (IBD) or exacerbation of pre-existing IBD. Given these concerns, this study aimed to investigate whether treatment with IL-17 inhibitors is associated with a higher risk of IBD in a large real-world cohort of PsA patients, compared with other treatment options.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Study Groups Before and After Propensity Score Matching

Characteristics	+IL 17i (N=11,287)	- IL17i (N= 51,328)	Standardized mean difference	+IL17i (N=8,931)	-IL17i (N=8,931)	Standardized mean difference
	Before Propensity Score Matching			After Propensity Score Matching		
Age, mean ± SD	50.9 ± 12.9	54.4± 14.9	0.2531	51 ± 12.9	50.3 ± 14.3	0.0505
Female, %	58.614	55.125	0.0705	57.586	57.463	0.0025
Male, %	37.386	39.591	0.0453	38.193	39.48	0.0264
Not Hispanic or Latino %	72.6	71.514	0.0242	72.064	71.94	0.0027
White, %	75.566	76.212	0.0151	75.21	76.195	0.0230
Black or African American %	3.52	3.412	0.0059	3.493	3.426	0.0037
Asian, %	4.804	4.532	0.0129	4.759	4.277	0.0232
Unknown, %	11.778	11.675	0.0032	12.104	11.757	0.0107
Other race	3.455	2.716	0.0428	3.493	3.426	0.0037
Diagnoses						
Personal history of nicotine dependance, %	9.256	7.08	0.0795	8.51	8.241	0.0097
Overweight, Obesity, %	27.464	17.406	0.2429	25.26	23.861	0.0325
Medications						
Adalimumab, %	45.681	8.473	0.9220	38.204	40.544	0.0479
Methotrexate, %	41.866	16.877	0.5706	37.051	38.797	0.0360
Ibuprofen, %	29.857	16.535	0.3196	27.242	26.817	0.0096
Etanercept, %	25.903	6.374	0.5506	20.367	20.166	0.0050
Apremilast, %	20.296	2.91	0.5640	14.354	13.492	0.0249
Naproxen, %	20.148	11.149	0.2496	17.971	17.523	0.0117
Celecoxib, %	15.926	7.608	0.2603	14.097	13.783	0.0091
Sulfasalazine, %	12.573	5.043	0.2681	10.727	10.727	< 0.0001
Ustekinumab, %	13.432	1.604	0.4603	8.902	7.983	0.0330
Leflunomide, %	11.963	2.818	0.3550	9.103	9.081	0.0008
Infliximab, %	6.383	2.228	0.2058	5.24	5.587	0.0153
Golimumab	4.637	0.722	0.2443	3.303	2.956	0.0199
Certolizumab	4.397	0.598	0.2453	3.09	2.598	0.0296
Tofacitinib	4.582	0.524	0.2594	2.934	2.251	0.0430
Abatacept	2.919	0.481	0.1895	2.083	1.825	0.0186
Guselkumab	3.15	0.388	0.2106	2.015	1.713	0.0224
Risankizumab	1.986	0.348	0.1529	1.489	1.523	0.0028
Upadacitinib	1.081	0.179	0.1141	0.773	0.649	0.0147
Baricitinib	0.102	0.023	0.0313	0.112	0.112	<0.0001
Certolizumab	0.092	0.017	0.0324	0	0.112	0.0473

Methods: This was a retrospective observational analysis utilizing the TriNetX research network, which includes data from over 130 million patients globally. The study population consisted of 11,287 patients with psoriatic arthritis (PsA) treated with IL-17 inhibitors and 51,328 PsA patients receiving other therapies, such as other biologic DMARDs (bDMARDs), conventional synthetic DMARDs (csDMARDs), targeted synthetic DMARDs (tsDMARDs), or NSAIDs. Outcomes were evaluated

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Risks of Crohn's Disease, Ulcerative Colitis, and Other or Unspecified Noninfective Gastroenteritis and Colitis in Psoriatic Arthritis Patients With vs Without IL-17i Exposure

Outcome	Groups	Overall Risk, %	Attributable Risk, %	Overall Risk, %	Attributable Risk, %
		Before Propensity Score Matching		After Propensity Score Matching	
Crohn's disease	+ IL17i	0.708 (82/11,574)	-0.108 (-0.275 - - 0.059)	0.72 (64/8,892)	-0.276 (-0.549 - - 0.002)
	- IL17i	0.817 (542/66379)	*P*-value 0.2287	0.995 (86/8639)	*P*-value 0.0475
Ulcerative colitis	+ IL17i	0.692 (80/11,561)	-0.434 (-0.605- - 0.263)	0.721 (64/8,881)	-0.562 (-0.856 - - 0.267)
	- IL17i	1,126 (750/66,614)	*P*-value <0.0001	1,282 (112/8,734)	*P*-value 0.0002
Other and unspecified noninfective gastroenteritis and colitis	+ IL17i	5.507 (581/10,551)	-1.407(-1.885- - 0.928)	5.159 (424/8,219)	-1.617 (-2.348 - - 0.886)
	- IL17i	6.913 (4,322/62518)	*P*-value <0.0001	6.776 (538/7,940)	*P*-value <0.0001

Notes: The cohorts were matched with age, race/ethnicity, various diagnoses and medications. Discrepancies between the total number of patients before and after analysis mean that patients were excluded due to the presence of outcomes prior to the index period.

Inclusion Criteria

ICD-10 Codes

L40.5 – Artrhopathic psoriasis

RxNorm Codes for IL17 inhibitors (IL17i)

Secukinumab (1599788) **OR** Ixekizumab (1745099) **OR** Brodalumab (1872251) **OR** Bimekizumab (2668041)

Matching Criteria

ICD-10 Codes

Z87.891 - Personal history of nicotine dependence
E66 - Overweight and obesity

RxNorm Codes

6851 - Methotrexate
27169 - Leflunomide
9524 - Sulfasalazine
327361 - Adalimumab
OMOP5175190 - Certolizumab
709271 – Certolizumab pegol
214555 - Etanercept
191831- Infliximab
819300- Golimumab
847083- Ustekinumab
1928588 - Guselkumab
2166040 - Risankizumab
614391 - Abatacept
1492727 - Apremilast
135736 - Tofacitinib
2196092 - Upadacitinib
1047232 - Baricitinib
7258 - Naproxen
5640 - ibuprofen
140587 - Celecoxib

Outcomes

ICD-10 Codes

K50 – Crohn's disease
K51 – Ulcerative colitis
K52 – Other and unspecified noninfective gastroenteritis and colitis

Appendix 1. Inclusion and Exclusion Criteria, Matching Criteria and Outcomes with Corresponding ICD-10 and RxNorm Codes

both before and after propensity score matching for demographic and clinical factors. The risks of developing Crohn's disease, ulcerative colitis, and other or unspecified noninfective gastroenteritis and colitis were assessed between January 1, 2015, and April 1, 2025 (Appendix 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: After propensity score matching, 8 931 patients were included in each group. The overall cohort's mean ± SD age was 51 ± 12.9 years, with 57.586% female and the majority White (75.21%) and not Hispanic or Latino (72.064%). Matching achieved balance across cohorts ($P < 0.05$) (Table 1, Table 2). The IL-17 inhibitor–treated cohort demonstrated a slightly lower risk of developing Crohn's disease compared with the non–IL-17i cohort (Relative risk (RR) 0.723, 95% CI: 0.524 – 0.998, $p = 0.0475$). In contrast, the IL-17i group showed a significantly lower risk of developing ulcerative colitis (RR 0.562, 95% CI: 0.414– 0.763, $p < 0.01$) and other or unspecified noninfective gastroenteritis and colitis (RR 0.761, 95% CI: 0.673– 0.861, $p < 0.01$).

Conclusion: This study suggests that treatment with IL-17 inhibitors in patients with psoriatic arthritis does not appear to increase the risk of developing or exacerbating Crohn's disease. Additionally, IL-17 inhibitors may be associated with a decreased risk of developing ulcerative colitis and other unspecified noninfective gastroenteritis and colitis compared to other treatment options. Further research is warranted to better understand the mechanisms underlying these observations.

Disclosure: R. Tskitishvili: None; **A. Hussein**: None; **I. Tskhakaia**: None; **N. Tsibadze**: None; **E. Osgood**: None; **H. Khan**: None.

Abstract Number: 1184

Does Blocking IL-17 Treat Recalcitrant Uveitis? Explorative Study on the Use of Ixekizumab to Manage Patients with Uveitis

Sergio Schwartzman[1], Stephen Anesi[2], Yasmin Massoudi[2], Monica Schwartzman[3] and Peter Chang[2], [1]Weill Cornell Medical Center, New York Presbyterian Hospital, and Hospital for Special Surgery, New York, NY, [2]MERSI, Waltham, [3]Hospital for Special Surgery/New York Presbyterian Hospital-Weill Cornell Medical Center, New Rochelle, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Non-infectious uveitis can exist as a primary autoimmune disease or can be a manifestation of an underlying systemic illness. Despite the availability of new therapies, there are few medications approved for the management of uveitis. The purpose of this study was to determine the efficacy and safety of Ixekizumab, an IL-17A targeting human monoclonal antibody in patients with recalcitrant non-infectious intermediate, posterior, panuveitis, or chronic steroid-dependent anterior noninfectious uveitis.

Methods: This was a 24-week prospective, open-label, proof-of-concept exploratory study. The study was designed with two treatment arms of Ixekizumab. Both arms were treated at Week 0 with a loading dose of 160mg of Ixekizumab. Subjects in Arm 1 were then treated with biweekly dosing of 80mg SC Ixekizumab. Subjects in Arm 2 were assigned to a regimen of 80mg SC every four weeks. All subjects began an oral steroid taper starting with 60mg of prednisone alongside the loading dose at Week 0.

Primary Endpoint: A four-point composite endpoint was used to evaluate for visual acuity, control of inflammation, tapering of medication therapy and cystoid macular edema, scored .yes/no" (Suhler et. al., 2013). Control of inflammation was defined as either achieving clinical quiescence, referring to anterior chamber cells and flare of 0.5+ or less as well as vitreous haze of 0.5+ or less, or by achieving a greater than two step reduction in both AC cells and flare"

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

.Secondary Endpoints: The NEI VFQ-25 questionnaire was utilized to gain a standardized insight on each patient's subjective visual functioning throughout each timepoint of the trial, with a higher score indicating better function and lesser impact of visual impairment from uveitis on daily life. Intraocular pressure was monitored for changes, as one goal for the use of steroid-sparing immunomodulatory therapy for patients with uveitis is to avoid steroid-induced ocular hypertension

Results: The trial was closed to recruitment prematurely due to an overall lack of clinical response. Only two participants completed the entire duration of the study without being discontinued from Ixekizumab and/or without receiving additional rescue therapy. All other subjects required rescue therapy between Week 8 and Week 20. Additionally, all patients in Arm 2 assigned to a maintenance dose of Ixekizumab dosing every 4 weeks, were reassigned to Arm 1 due to inadequate clinical response to Q 4 week dosing.

Conclusion: In this study, the efficacy of Ixekizumab for the management of recalcitrant uveitis was explored. None of the nine subjects enrolled met the criteria for clinical response, and all but two patients necessitated rescue therapy and/or discontinuation of the investigational treatment. The lack of efficacy resulted in early study termination.

There are a number of potential explanations for the lack of response. The first is that IL-17A may not be the effector cytokine target in the patients studied. This population was clinically heterogeneous both in terms of the uveitis studied and underlying disease. It is possible that the dose of therapy utilized was suboptimal. Lastly, the number of patients may have been insufficient to detect a statistically benefit.

Disclosure: S. Schwartzman: AbbVie, 2, 6, Eli Lilly and Company, 2, 5, 6, Janssen, 2, 6, National Psoriasis Foundation, 12, Medical Board member, Pfizer, 6, Teijin, 2, UCB, 2, 6, UpToDate, 2; **S. Anesi**: AbbVie/Abbott, 6, ANI, 6, Eli Lilly, 5, Mallinckrodt, 2, 6; **Y. Massoudi**: Eli Lilly, 5; **M. Schwartzman**: AbbVie/Abbott, 2, Biogen, 2, Eli Lilly, 2, Janssen, 2, UCB, 2; **P. Chang**: Bristol-Myers Squibb(BMS), 2, Eli Lilly, 5.

Abstract Number: 1185

Pulmonary Arterial Hypertension in Adults with Still's Disease: Another Pulmonary Manifestation Associated with HLA-DRB1*15

Stéphane Mitrovic[1], Athénaïs Boucly[2], Maryvonnick Carmagnat[3], Laurent Savale[2], Xavier Jaïs[2], Jean-luc Taupin[3], Estibaliz Lazaro[4], Emilie Berthoux[5], nicolas schleinitz[6], Maria-Rosa Ghigna[7], kedra joanna[1], Xavier Mariette[8], Céline Roussin[9], Pierre Antoine Juge[10], Marc Humbert[2], Olivier Sitbon[2], David Montani[2] and Bruno Fautrel[11], [1]Pitié-Salpêtrière Hospital, Rheumatology Department, APHP, Sorbonne University,, Paris, France, [2]Kremlin Bicêtre Hospital, Pulmonology Department, Paris Saclay University, APHP, Le Kremlin Bicêtre, France, [3]Saint Louis Hospital, Immunology laboratory, APHP, Paris, France, [4]Internal Medicine Department, CHU Bordeaux, Bordeaux, France, [5]Saint Joseph Sain Luc Hospital, Internal Medicine Department, Lyon, Lyon, France, [6]Aix Marseille university, AP-HM, Marseille, France, [7]Marie Lannelongue Hospital, Anatomopathology department, Le Plessis-Robinson, France, [8]Université Paris-Saclay, Le Kremlin Bicetre, France, [9]Centre Hospitalier Ouest Réunion, Saint Paul, France, [10]Hopital Bichat, APHP, Paris, France, [11]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Inflammatory lung disease (ILD) in Still's disease (SD) has recently been described. Pulmonary arterial hypertension (PAH), a rare subtype of pulmonary hypertension (PH), is a potentially life-threating complication of SD. It is crucial to differentiate PAH (group 1 PH), characterized by progressive remodeling of small pulmonary arteries, from PH associated with interstitial lung disease (PH-ILD), which falls under group 3 PH and results primarily from parenchymal lung involvement and hypoxic vasoconstriction. Although in the context of SD both mechanisms, PH-ILD and PAH, may be involved, PAH has rarely been reported. This work reports a large cohort of PAH in adults with SD.

Methods: We identified 16 adult SD patients with PAH (PAH+ group, PAH was confirmed by right heart catheterization in all patients) by a call for observations from the CRIIMIDIATE network and a search of the French PH network registry. Patient characteristics and disease evolution were retrospectively compared with those of 111 SD controls without PAH (PAH-) followed in a reference center.

Results: The profile of patients in the PAH+ and PAH- groups differed (**Table**): 100% versus 69.4% female (p=0.006), 75% versus 17.1% Black (p< 0.0001), more active SD both at diagnosis and throughout the disease course, and more likely to present MAS (62.5% vs 14.4%, p< 0.0001), which was recurrent (i.e. ≥ 2 episodes) in most cases (7/10 patients), and exhibit eosinophilia during the disease course (68.7% vs 7.2%, p< 0.0001). Twelve patients in the PAH+ group presented mild radiological parenchymal features on the CT scan (interlobular septal thickening, non-specific ground-glass opacities) that could not explain PH. For the 84/127 patients with genetic typing, the HLA-DRB1*15 allele was more prevalent in

Table 1A. Characteristics of Still's disease patients with and without pulmonary arterial hypertension (PAH) 1In some patients, the disease developed in childhood (systemic juvenile idiopathic arthritis), but symptoms persisted and/or recurred in adulthood. 2The radiological parenchymal involvement was mild in the 12 patients of the PAH+ group: interlobular septal thickening in all cases, ground-glass opacities of non-specific nature in half of the cases (please see main text and figure 1 for details). The radiological parenchymal involvement was mild to moderate on the CT scan for the 3 patients of the PAH- group who had parenchymal involvement (please see supplementary tables 16 and 17 for details). Importantly, no patient in either group presented with pulmonary alveolar proteinosis and endogenous lipoid pneumonia. 3Including one patient with PAH in whom myocarditis developed in the context of major eosinophilia up to 8,000/mm3. 4Among the population with PAH, 7 patients had multiple (≥2) episodes of MAS, and 1 had a refractory episode of MAS over several months associated with uncontrolled PAH that led to death. csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs–IL, interleukin–IQR, interquartile range–JAK, Janus kinase–MAS, macrophage activation syndrome–PAH, pulmonary arterial hypertension–10N, 10 times above normal

	Still's disease with PAH (n=16)	**Still's disease without PAH (n=111)**	**p-value (PAH vs no PAH)**
Decade of Still's disease onset[1], n (%)			
Before 2010	3 (18.7)	23 (20.7)	1
≥ 2010	13 (81.3)	88 (79.3)	1
Female, n (%)	16 (100)	77 (69.4)	**0.006**
Ethnicity, n (%)			
Caucasian	3 (18.7)	64 (57.7)	**< 0.0001**
Black	12 (75.0)	19 (17.1)	
Asian	1 (6.3)	7 (6.3)	
North Africa	0 (0)	19 (17.1)	
Middle East	0 (0)	2 (1.8)	
Age at Still's disease onset[1], median (IQR)	25 (21–36)	27 (20–37)	0.982
Modified Pouchot score at Still's disease diagnosis	(data available for 15 patients)	(data available for 67 patients)	
Median [IQR]	7 [6–8]	6 [5–7]	**0.031**
Still's disease manifestations (ever during disease course), n (%)			
Fever	16 (100)	110 (99.1)	1
Rash	16 (100)	99 (89.2)	1
Arthralgia/arthritis	15 (93.7)	107 (96.4)	0.495
Odynophagia	14 (87.5)	77 (69.4)	0.233
Myalgia	13 (81.2)	47 (42.3)	**0.005**
Lymphadenopathy	16 (100)	49 (44.1)	**< 0.0001**
Hepatomegaly and/or abnormal liver tests	16 (100)	54 (48.7)	**< 0.0001**
Acute hepatitis with transaminases ≥10 N	7 (43.7)	20 (18.0)	**0.043**
Splenomegaly	11 (68.7)	15 (13.5)	**<0.0001**
Pericarditis	12 (75.0)	16 (14.4)	**<0.0001**
Pleuritis	5 (31.2)	9 (8.1)	**0.017**
Parenchymal involvement[2]	12 (75.0)	3 (2.7)	**<0.0001**
Myocarditis[3]	4 (25.0)	10 (9.0)	0.063
MAS[4]	10 (62.5)	16 (14.4)	**<0.0001**

Table 1B (table continued). Characteristics of Still's disease patients with and without pulmonary arterial hypertension (PAH) 5Eosinophilia was defined as absolute eosinophil count ≥ 700/mm3 or eosinophils ≥10% of the total white blood cell count, measured on at least two occasions (Lerman et al, Arthritis Care & Research. 2023). 6Some patients had several lines of treatment. 7Drug reactions to IL-1 and/or IL-6 inhibitors were all confirmed by a dermatologist and/or an allergologist, and included rashes atypical for SD (e.g. nonevanescent, pruritic, urticarial, a fortiori in the presence of blood eosinophilia), or acute reactions (respiratory distress, swelling or Quincke edema during or near the time of medication administration). Two patients in the HTAP+ group met the criteria for DRESS syndrome (RegiSCAR for DRESS ≥ 4) (Kardaun et al, Br J Dermatol. 2013). Local reactions at the injection site were not included in this category, as they are common with subcutaneous biotherapies. csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs–IL, interleukin–IQR, interquartile range–JAK, Janus kinase–MAS, macrophage activation syndrome–PAH, pulmonary arterial hypertension–10N, 10 times above normal

	Still's disease with PAH (n=16)	Still's disease without PAH (n=111)	p-value (PAH vs no PAH)
Eosinophilia ever during disease course, n (%)[5]	2616 [1765–3460]	937 [850–1100]	**0.002**
Maximum eosinophil count, median [IQR], /mm³			
HLA-DRB1*15-positive, n/N available (%)	8/11 (72.7)	22/73 (30.1)	**0.014**
History of treatment (ever during disease course)[6]			
Glucocorticoids, n (%)	16 (100)	108 (97.3)	1
csDMARDs, n (%)			
Methotrexate	13 (81.2)	56 (50.4)	**0.029**
Leflunomide	1 (6.2)	2 (1.8)	0.334
Sulfasalazine	1 (6.2)	1 (0.9)	0.236
Intravenous immunoglobulins	2 (12.5)	2 (1.8)	0.077
IL-1 and/or IL-6 blockade, n (%)	16 (100)	83 (74.7)	**0.021**
IL-1 inhibitor, at least one	14 (87.5)	74 (66.7)	0.145
Anakinra	14 (87.5)	71 (63.9)	0.087
Canakinumab	8 (50.0)	24 (21.6)	**0.026**
IL-6 inhibitor	8 (50.0)	45 (40.5)	0.589
TNF inhibitors, n (%)	3 (18.7)	20 (18.0)	1
Immunosuppressants, n (%)			
Ciclosporin	5 (31.2)	4 (3.6)	**0.001**
Mycophenolate mofetil	1 (6.2)	2 (1.8)	0.334
Tacrolimus	1 (6.2)	2 (1.8)	0.334
Sirolimus	0 (0)	1 (0.9)	1
Azathioprine	3 (18.7)	2 (1.8)	**0.014**
Cyclophosphamide	2 (12.5)	0 (0)	**0.014**
Etoposide	2 (12.5)	1 (0.9)	**0.041**
JAK inhibitors, n (%)	3 (18.7)	6 (5.4)	0.086
History of drug reactions to IL-1 or IL-6 inhibitors[7], n (%)	6 (37.5)	8 (7.2)	**0.002**
Deaths directly attributed to Still's disease complications, n (%)	6 (37.5)	1 (0.9)	**<0.0001**

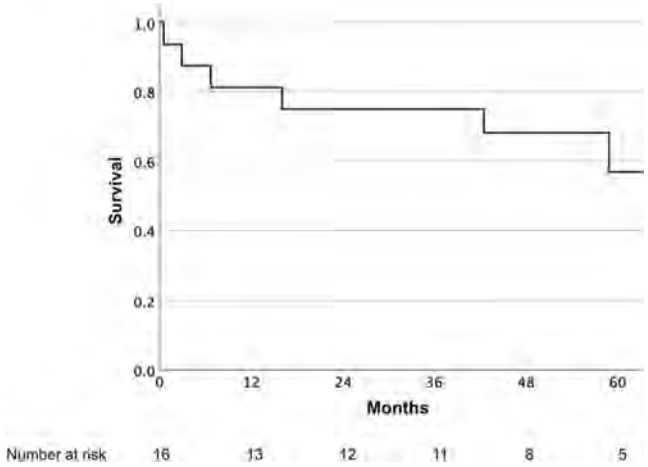


Figure. Overall survival after pulmonary arterial hypertension diagnosis in patients with Still's disease (n=16). Overall survival at 1 and 3 years was 81% and 75%, respectively.

PAH+ than PAH- patients (8/11 [72.7%] vs 22/51 [30.1%], p=0.014). The groups did not differ in treatment, except for methotrexate (81.2% vs 50.4%, p=0.029), canakinumab (50% vs 21.6%, p=0.026) or immunosuppressant agents (56.2% vs 10.8%, p< 0.0001) that were more often used in the PAH+ group, reflecting a more active underlying SD. There was higher frequency of drug reactions to interleukin 1 (IL-1) and/or IL-6 inhibitors in PAH+ than PAH- patients (37.5% vs 7.2%,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

p=0.002). Mortality was higher in PAH+ than PAH- patients (37.5% vs 0.9%, p< 0.0001), all deaths related to SD flare (**Figure)**.

Conclusion: PAH develops on the same background as other manifestations of SD-related ILD (i.e., in patients with MAS, especially when recurrent; eosinophilia; and carrying the HLA-DRB1*15 allele). Female sex and Black ethnicity seem to be risk factors. This work reinforces the association of the HLA-DRB1*15 allele with severe forms of SD and raises the question of treatment optimizations to better control both SD and its complications. The fact that PAH can be isolated in SD, i.e., it can occur in the absence of major parenchymal involvement, should encourage physicians to screen for it using echocardiography in cases of unexplained dyspnoea, before confirmation by catheterization. The existence of PAH has major therapeutic implications, since it requires the addition of vasodilating agents to targeted and non-targeted immunomodulating therapies.

Disclosure: S. Mitrovic: None; **A. Boucly**: None; **M. Carmagnat**: None; **L. Savale**: None; **X. Jaïs**: None; **J. Taupin**: None; **E. Lazaro**: None; **E. Berthoux**: None; **n. schleinitz**: Amgen, 1, 2; **M. Ghigna**: None; **k. joanna**: None; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **C. Roussin**: None; **P. Juge**: None; **M. Humbert**: None; **O. Sitbon**: None; **D. Montani**: None; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2.

Abstract Number: 1186

Increased Adoption of IL-1 Pathway Inhibition and the Steroid-sparing Paradigm Shift: Temporal Trends in Recurrent Pericarditis Treatment From the RESONANCE Patient Registry

Paul Cremer[1], Michael Garshick[2], Sushil Allen Luis[3], Ajit Raisinghani[4], Brittany Weber[5], Vidhya Parameswaran[6], Allison Curtis[6], **Sue Gibbons**[6], Allan Klein[7], John Paolini[6] and RESONANCE Study Group, [1]Cleveland Clinic, Shaker Heights, OH, [2]NYU Langone Health, Tenafly, NJ, [3]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, [4]Division of Cardiology, Department of Medicine, Sulpizio Cardiovascular Center, University of California San Diego, San Diego, CA, [5]Brigham and Women's Hospital, DEDHAM, MA, [6]Kiniksa Pharmaceuticals, LEXINGTON, MA, [7]Cleveland Clinic, Cleveland, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Recurrent pericarditis (RP) is a chronic autoinflammatory disease mediated by IL-1 that requires long-term treatment. While the 2015 European Society of Cardiology Guidelines position IL-1 pathway inhibition only after corticosteroids, complications associated with long-term steroid use underscore the importance of steroid-sparing strategies. Rilonacept, an IL-1a and IL-1b cytokine trap, is the only FDA-approved treatment for RP (available since April 2021). RESONANCE, an ongoing 5-year non-interventional US registry of patients (pts) with RP, has collected real-world data from pts cared for by cardiologists with a focus on pericardial disease, with a goal of informing contemporary RP clinical management.

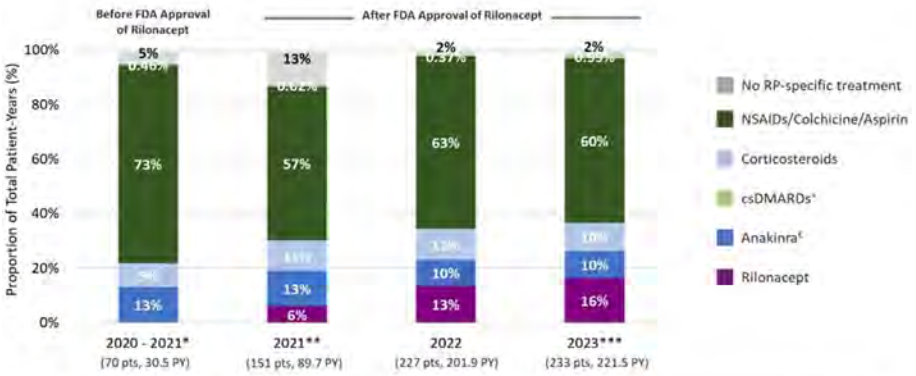
Methods: From a database cut-off (DCO) on 21 December 2023, patient demographics and disease characteristics are reported for 242 active RP pts (excluding RHAPSODY prior participants) at 20 US sites (median [Q1:Q3] 2.1 [1.5:2.6] years and 556 patient-years [PY] of observation). Complete medication class use data were available for 239 pts (total 546 PY). Proportional medication class use prior to initiating rilonacept was analyzed annually across the observation period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Mean (standard deviation) age at DCO was 50.2 (16.6) years; 58.1% were female. Median [Q1:Q3] disease duration at DCO from index pericarditis episode was 3.1 [2.2:5] years. Median [Q1:Q3] number of prior recurrences at enrollment was 3 [2:5]. Prior to rilonacept availability, NSAIDs/Colchicine/Aspirin represented the highest proportion of treatment (73% of PY); steroid use was 9% of PY, IL-1 pathway inhibition (anakinra) was 13% of PY, and conventional synthetic disease modifying antirheumatic drugs (csDMARDs) were 0.46% PY (no RP-specific treatment was 5% of PY) (**Fig 1**). In the years since rilonacept availability, proportional IL-1 pathway inhibition use has increased, from 13% of PY in 2020-21 to 26% of PY in 2023, driven by an increase in rilonacept use (6%, 13%, 16% of PY in 2021, 2022, and 2023, respectively). Over that same period, proportional NSAIDs/Colchicine/Aspirin use (57%-63% of PY) has been consistently 6-times more than proportional steroid use (10%-11% of PY). Among pts who initiated rilonacept (n=81), similar proportions transitioned from NSAIDs/Colchicine/Aspirin as from corticosteroids (**Fig 2**), a robust trend observed each year. Of those pts transitioning from corticosteroids, 1/3 had used corticosteroids for < 30 days and 1/3 for >6 months.

Conclusion: Real-world data from the RESONANCE registry reveal a temporal shift in RP management in US centers with RP-focused cardiologists, with increased proportional IL-1 pathway inhibition use since rilonacept availability in 2021. Advancing beyond 2015 guideline recommendations, IL-1 pathway inhibition is often being used as steroid-sparing treatment, i.e., after colchicine instead of chronic corticosteroids.

Figure 1. Proportion of Medication Class Use# Over Time (by patient-years)



*Prior to Rilonacept approval; **Partial year after Rilonacept commercial availability April 1, 2021 – Dec 31, 2021; ***Partial year until data cut-off of Dec 21, 2023
#Not mutually exclusive, patients could contribute patient years to multiple medication classes
+Includes azathioprine, methotrexate, hydroxychloroquine/Plaquenil, sulfasalazine
€ 22.2% of patients using anakinra went on to use rilonacept; of those, 40% used anakinra for <30 days.
Total absolute pt counts: Rilonacept (n=81); Anakinra (n=45), Corticosteroids (n=79), NSAIDs/colchicine/aspirin (n=216), csDMARDs (n=8)
csDMARDs: conventional synthetic disease modifying antirheumatic drugs; PY: patient-years; Pts: patients

Figure 2: Proportion of Prior Medication Class Use# 1 Month before initiating Rilonacept (by patient)

*Partial year after Rilonacept approval April 1, 2021 - Dec 31, 2021; **Partial year until data cut-off of Dec 21, 2023
#Patients on multiple medication classes at the same time were bucketed into one medication class by the following hierarchy: Anakinra, csDMARDs, Corticosteroids, NSAIDs/Colchicine/Aspirin, No RP-specific treatment
+Includes azathioprine, methotrexate, hydroxychloroquine/Plaquenil, sulfasalazine
¥31% of pts used corticosteroids for 30 days or less; 34% used corticosteroids for 6 months or more
€40% of pts used anakinra for 30 days or less
csDMARDs: conventional synthetic disease modifying antirheumatic drugs; Pts: patients

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Cremer: Kiniksa Pharmaceuticals, 2, 5, Sobi, 5; **M. Garshick**: Agepha, 2, Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2; **S. Luis**: Cardiol Therapeutics, 2, Kiniksa Pharmaceuticals, 2, Medtronic, 2; **A. Raisinghani**: Kiniksa Pharmaceuticals, 2; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **V. Parameswaran**: Kiniksa Pharmaceuticals, 3, 11; **A. Curtis**: Kiniksa Pharmaceuticals, 3, 11; **S. Gibbons**: Kiniksa Pharmaceuticals, 3, 11; **A. Klein**: Cardiol Therapeutics, 2, 5, Kiniksa Pharmaceuticals, 2, 5, Pfizer, 2, 5; **J. Paolini**: Kiniksa Pharmaceuticals, 3, 11.

Abstract Number: 1187

Myositis-Specific Antibody Profiles and Factors Associated With Rapidly Progressive Interstitial Lung Disease and Mortality in Antisynthetase Syndrome: A Systematic Review and Meta-Analysis

Tulaton Sodsri[1], Nattanicha Chaisrimaneepan[2], Ben Thiravetyan[3], Rabhas Boonyawairote[4], Nopavit Mohpichai[5], Nutchapon Xanthavanij[6], Natnicha Jakramonpreeya[7], Pintip Ngamjanyaporn[8] and Tananchai Petnak[8], [1]Department of Medicine, Texas Tech University Health Sciences Center, Bangkok, Thailand, [2]Department of Medicine, Texas Tech University Health Sciences Center, Lubbock, TX, [3]Department of Medicine, Texas Tech University Health Sciences Center, Lubbock, [4]University of Illinois at Chicago, Chicago, [5]Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, [6]Mount Auburn Hospital, Harvard Medical School, Cambridge, [7]Chakri Naruebodindra Medical Institute, Bangkok, Thailand, [8]Ramathibodi Hospital, Bangkok, Thailand

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The associations between various myositis-specific antibodies (MSAs), rapidly progressive interstitial lung disease (RP-ILD), and mortality in antisynthetase syndrome (ASS) have been previously reported in several studies, although limited by small sample sizes. RP-ILD has been recognized as a major risk factor for increased mortality in ASS. This study aimed to systematically assess MSAs and clinical factors associated with RP-ILD and mortality in ASS.

Methods: We conducted a systematic review and meta-analysis of cohorts identified through PubMed, MEDLINE, Embase, and Scopus. Studies enrolling individuals with ASS and evaluating risk factors for RP-ILD and mortality were included from inception to December 2024. The primary outcomes were the incidence of RP-ILD and mortality. Pooled risk ratio (RR) and 95% confidence interval (CI) were calculated using a random-effect, generic inverse variance method of DerSimonian and Laird.

Results: A total of 19 studies comprising 1,971 patients were included, with 17 studies analyzed for mortality and 5 for RP-ILD. Random-effects meta-analysis revealed that factors associated with increased mortality included age over 50 years (risk ratio [RR], 2.86; 95% confidence interval [CI], 1.50–5.43; $I^2 = 0\%$), with a mean difference (MD) of 7.74 years (95% CI, 4.15–11.34), male sex (RR, 1.44; 95% CI, 1.01–2.05; $I^2 = 0\%$), malignancy (RR, 7.59; 95% CI, 3.87–14.30; $I^2 = 0\%$), RP-ILD (RR, 4.90; 95% CI, 1.84–13.08; $I^2 = 0\%$), anti-OJ antibody positivity (RR, 3.03; 95% CI, 2.19–4.18; $I^2 = 0\%$), and anti-PL7 antibody positivity (RR, 1.65; 95% CI, 1.16–2.35; $I^2 = 0\%$). Only anti-Ro52 antibody positivity was associated with an increased risk of RP-ILD (RR, 2.75; 95% CI, 1.18–6.40; $I^2 = 38\%$), with moderate heterogeneity. RP-ILD and mortality were observed in 33.3% and 16.3% of the pooled cohort, respectively.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

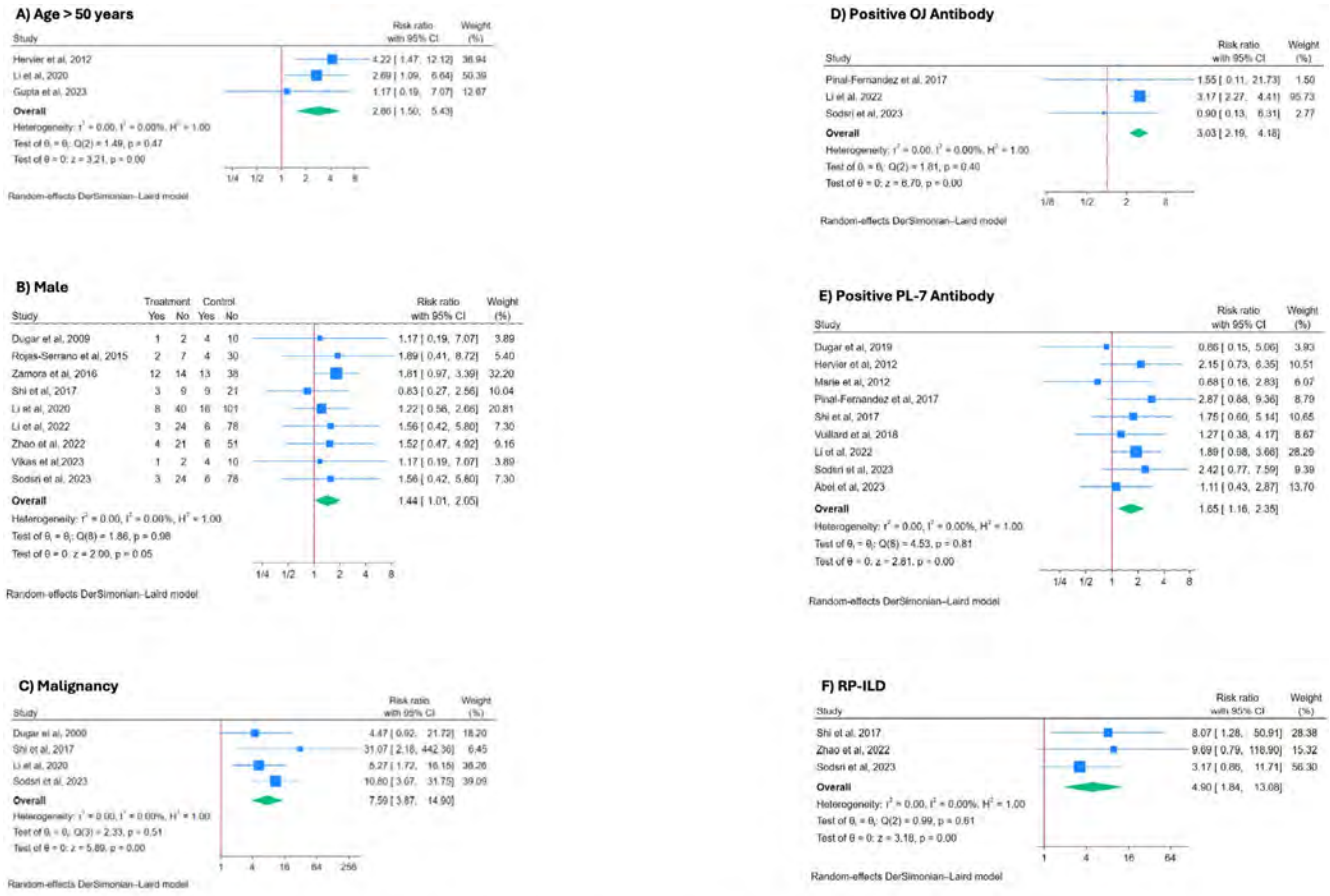


Figure 1: Forest plots of the meta-analysis of the factors affecting mortality risk

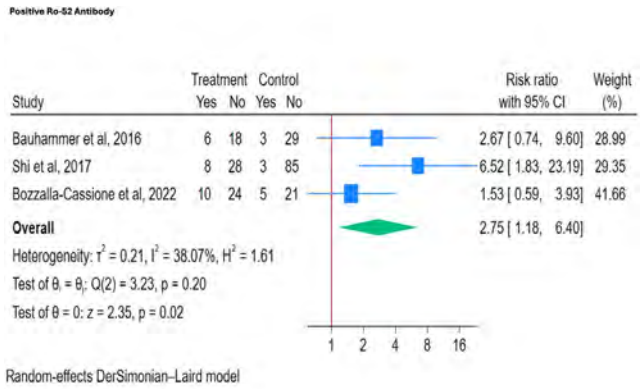


Figure 2: Forest plots of the meta-analysis of the serologies affecting RP-ILD risk

Conclusion: Anti-Ro52 antibody positivity was significantly associated with RP-ILD in ASS. Increased mortality was associated with age over 50 years, male sex, malignancy, RP-ILD, and positivity for anti-OJ and anti-PL7 antibodies. These findings highlight the potential role of MSAs in stratifying disease severity in ASS. However, given the limited number of studies and observed heterogeneity, these results should be interpreted with caution.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

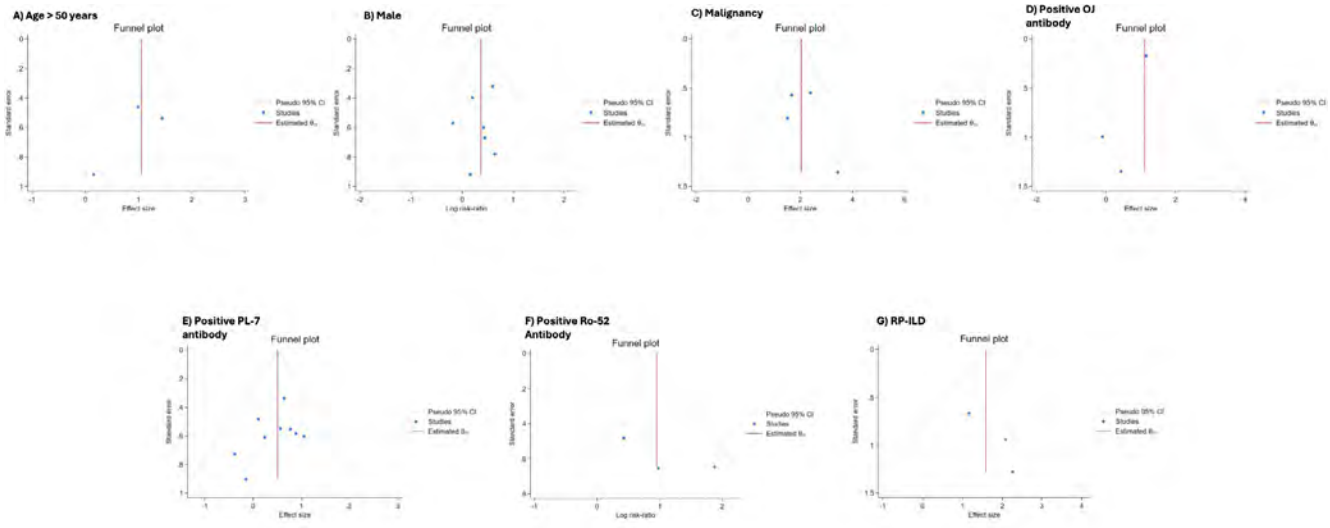


Figure 3: Funnel plots of the publication bias

Disclosure: T. Sodsri: None; **N. Chaisrimaneepan**: None; **B. Thiravetyan**: None; **R. Boonyawairote**: None; **N. Mohpichai**: None; **N. Xanthavanij**: None; **N. Jakramonpreeya**: None; **P. Ngamjanyaporn**: Boehringer-Ingelheim, 6; **T. Petnak**: None.

Abstract Number: 1188

Aortic Wall Shear Stress May Be a Protective Factor Against Development of Spinal Osteoproliferation

Sevtap Arslan Sarikaya[1], Büşra Fırlatan Yazgan[2], Ozan Sakir[3], Adalet Elcin Yildiz[4], Ustun Aydingoz[5] and **Umut Kalyoncu**[2], [1]Department of Radiology, Hacettepe University School of Medicine, Ankara, Turkey, ankara, Turkey, [2]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [3]Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, [4]Department of Radiology, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, [5]ustunaydingoz@yahoo.com, Ankara, Turkey

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Diffuse idiopathic skeletal hyperostosis (DISH) is often characterized by new bone formation along the right anterolateral spinal column, particularly in the thoracic region (1, 2). We aimed to investigate the influence of the anatomical right-sided position of the aorta on the localization of osteoproliferation in patients with DISH.

Methods: Computed tomography (CT) examinations involving the thoracic region, performed between 2014 and 2024, were re-evaluated for DISH by an experienced musculoskeletal radiologist in patients whose reports included the terms "dextrocardia," "situs inversus," or "right aortic arch." Those under 18 years of age, with inadequate imaging, or "with dextrocardia and a left aortic arch" were excluded. Patient sex and age at the time of imaging were recorded. The Resnick and Niwayama criteria were used to identify classical DISH (1), while the Kuperus criteria were applied for early-stage DISH (2).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of the 214 patients reviewed, a total of 83 patients were included in the final analysis. Imaging modalities included chest CT (n=60), cardiac CT (n=10), thoracic CT angiography (n=6), thoracoabdominal CT (n=4), and spinal CT (n=3). Of the final cohort of 83 patients 60% were male, with a mean age of 33 ± 18 years at the time of CT. Of these, 58 had dextrocardia with a right aortic arch, while 25 had levocardia with a right aortic arch. Changes consistent with DISH were observed in 8 of 83 patients (9.6%) with a right aortic arch. Early DISH findings were detected in seven of these eight patients (87.5%). All osteoproliferative changes were localized to the left side, except in one patient, where they were present on both the upper right thoracic and lower left thoracic regions. Sex distributions were similar between patients with DISH (62.5% male) and those without DISH (60% male), but the mean age at imaging was significantly higher in the DISH group (61 ± 11 years vs. 30 ± 16 years, $p< 0.001$). The age distribution of patients in the DISH group was as follows: one patient (12.5%) was under 50, two patients (25%) were between 50 and 60, four patients (50%) were between 61 and 70, and one patient (12.5%) was between 71 and 80 years of age.

Conclusion: In classic DISH patients with right-sided osteoproliferation, this localization has been shown to be more closely related to the position of the aorta rather than the heart. The inverse relationship between aortic wall stress and DISH localization may serve as a guide for future studies aimed at preventing osteoproliferation development due to repetitive mechanical stress elsewhere.

References:

1. Resnick D, Niwayama G. Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). Radiology. 1976;119(3):559-68.
2. Kuperus JS, Oudkerk SF, Foppen W, Mohamed Hoesein FA, Gielis WP, Waalwijk J, et al. Criteria for Early-Phase Diffuse Idiopathic Skeletal Hyperostosis: Development and Validation. Radiology. 2019;291(2):420-6.

Disclosure: S. Arslan Sarikaya: None; **B. Fırlatan Yazgan**: None; **O. Sakir**: None; **A. Yildiz**: None; **U. Aydingoz**: None; **U. Kalyoncu**: None.

Abstract Number: 1189

Clinical Outcomes and Response to SARS-Cov-2 Infection and Vaccination in Ianalumab-Treated Patients with Autoimmune Diseases

Valerie Devauchelle[1], Swati Ghanshani[2], CAROLE SIPS[3], Rainer Hillenbrand[3], Carol Lau[4], Wolfgang Hueber[5], Claire Bonal[3] and Stephen Oliver[6], [1]UBO, Brest, France, [2]Novartis Healthcare Private Limited, Hyderabad, India, Hyderabad, India, [3]Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland, [4]Novartis Pharmaceuticals Corporation, East Hanover, [5]Novartis Pharmaceuticals, Basel, Switzerland, [6]Novartis Pharma AG, Basel, Switzerland

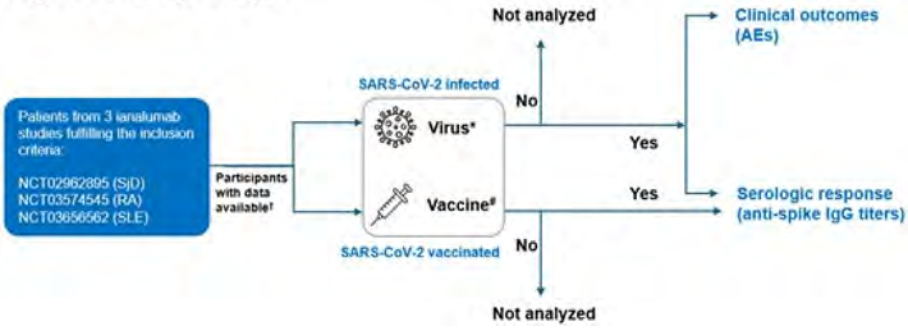
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Ianalumab, a glycoengineered IgG1 mAb directed against B cell-activating factor (BAFF)-receptor (BAFF-R), targets B cells and their functions via dual mechanism: depletion of B cells through enhanced antibody-dependent cellular cytotoxicity and blockade of BAFF:BAFF-R–mediated signals.[1]

This study evaluates the incidence rate (IR) and severity of SARS-CoV-2 infections and serological response to SARS-CoV-2 infection and vaccination in patients with Sjögren's disease (SjD), RA and SLE on ianalumab or placebo (SLE only).

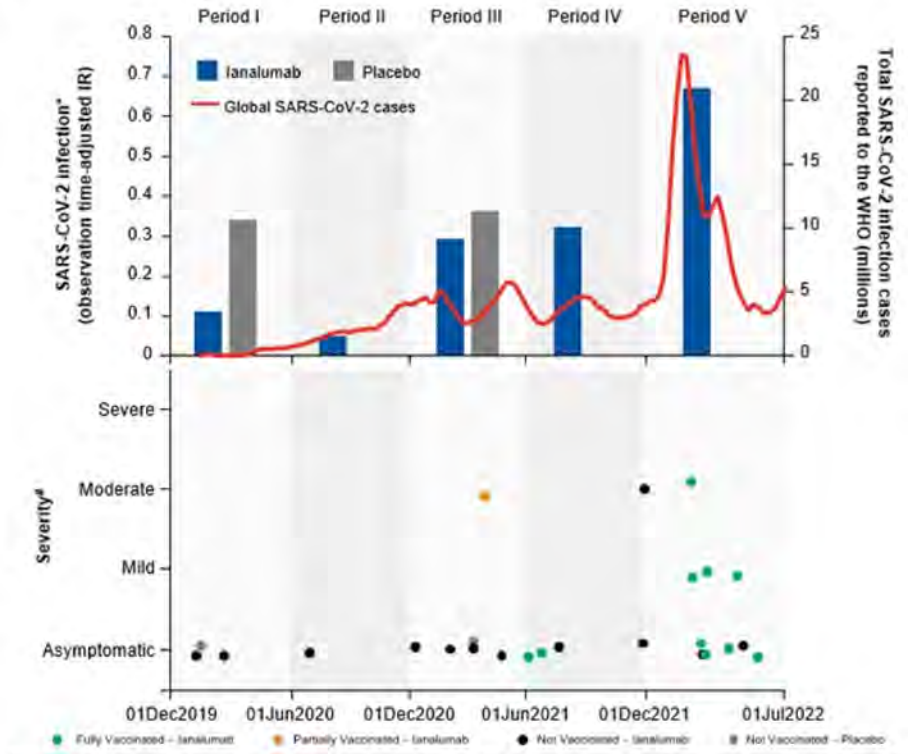
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Study design



*In patients positive for anti-nucleocapsid IgG or detectable nucleocapsid antigen or reported SARS-CoV-2–related AE; #In patients that had received SARS-CoV-2 vaccine as concomitant medicine; †anti-spike IgG, and/or anti-nucleocapsid IgG, and/or nucleocapsid antigen data. AEs, adverse events; IgG, immunoglobulin G; PD, pharmacodynamic; RA, rheumatoid arthritis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SjD, Sjogren's disease; SLE, systemic lupus erythematosus.

Figure 2. Incidence and severity of SARS-CoV-2 infection based on the study periods in patients with SjD, RA and SLE treated with ianalumab 300 mg vs. placebo



Variables (For the entire observation time: 01 Dec 2019 to 01 Jul 2022)	Ianalumab treated (N=72)	Placebo-treated (N=21)	Total (N=74)
Patient-years of exposure	84.22	9.30	93.52
Observation time-adjusted IR/100 patient-years	27	21	26

*In the placebo group, there were no patients with infection in Periods II, IV and V; #19 participants are counted under both treatment groups, treated with placebo for period 1 and ianalumab 300 mg for period 2.
IR, incidence rate; RA, rheumatoid arthritis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SjD, Sjögren's disease; SLE, systemic lupus erythematosus; WHO, World Health Organization.
Period I: December 2019–May 2020
Period II: June 2020–Nov 2020
Period III: Dec 2020–May 2021
Period IV: June 2021–November 2021
Period V: December 2021–01July 2022

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: In this retrospective analysis, patients with SjD (NCT02962895), RA (NCT03574545) and SLE (NCT03656562), who received at least one dose of ianalumab 300 mg or placebo on top of background therapies, between Dec 2019 - Jul 2022, and had anti-spike IgG, and/or anti-nucleocapsid IgG, and/or nucleocapsid antigen were included (Fig 1). Symptomatic SARS-CoV-2 infection was defined by treatment-emergent adverse events (AEs). Patients without reported SARS-CoV-2 AEs but with increased anti-nucleocapsid or nucleocapsid antigen levels were considered asymptomatic. Clinical outcomes included the incidence and severity of SARS-CoV 2–related AEs. Anti-spike IgG titers after exposure to SARS-CoV-2 antigen (virus/vaccine) were evaluated to assess the serological response (Fig 1).

Results: Overall, 123 and 28 patients who received ianalumab and placebo, respectively, were included. Of them, 74 (ianalumab: 72; placebo: 21) had anti-spike IgG, and/or anti-nucleocapsid IgG and/or nucleocapsid antigen data. The crude IRs of SARS-CoV-2 infection (not accounting for the different lengths of observation time/time at risk of SARS-CoV-2 infection) were 31.9% (23/72) and 9.5% (2/21), in the ianalumab and placebo groups, respectively.The observation time-adjusted IRs of SARS-CoV-2 infection were comparable between ianalumab and placebo groups (27 vs. 21 patients/100 patient-year). Most of the infected patients were asymptomatic in the ianalumab (17/23) and placebo (2/2) groups. Symptomatic infections in the ianalumab group (26.1%, 6/23) were mild to moderate in severity, and all patients fully recovered (Fig 2).

Among the patients who received SARS-CoV-2 vaccine during this period and had available post-vaccination anti-spike IgG titer data (ianalumab: 10; placebo: 2), all mounted a serological response. Post-vaccination, anti-spike IgG titers were slightly lower in the ianalumab group during treatment, increasing during the follow up, reaching comparable levels to the placebo group after B cell recovery.

Conclusion: This analysis suggests that ianalumab treatment did not seem to increase the risk of severe SARS-CoV-2 infection in patients with SjD, RA or SLE. Both ianalumab and placebo groups mounted a serological response to SARS-CoV-2 vaccine, which improved during the follow-up even before B-cell recovery. Limitations include small sample size, imbalance in the patient number and observation time, varying risks, geographical regions, SARS-CoV-2 variants and vaccine availability.

References:

1. World Health Organization. WHO coronavirus (COVID-19) dashboard. Available at: COVID-19 cases | WHO COVID-19 dashboard. Accessed on December 18, 2024.

Disclosure: V. Devauchelle: None; **S. Ghanshani**: Novartis, 3, 11; **C. SIPS**: Novartis, 3, 11; **R. Hillenbrand**: Novartis, 3, 11; **C. Lau**: Novartis, 3, 12, Shareholder; **W. Hueber**: Novartis, 3, 11; **C. Bonal**: Novartis, 3, 11; **S. Oliver**: Novartis, 3, 11.

Abstract Number: 1190

IgG4-related disease with comorbid autoimmune diseases: a retrospective study from a large cohort

Xinli Yang[1], Wen Zhang[2], Jiaxin zhou[3] and Yuxue Nie[4], [1]Peking Union Medical College, Dong Cheng Qu, China (People's Republic), [2]Peking Union Medical College Hospital, Dong Cheng Qu, China (People's Republic), [3]Peking Union Medical College Hospital, Beijing, China (People's Republic), [4]Department of Rheumatology, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China, Dong Cheng Qu, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1147–1190) Miscellaneous Rheumatic & Inflammatory Diseases Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aimed to explore the clinical characteristics, treatment, and prognosis of IgG4-related disease (IgG4-RD) patients with comorbid autoimmune diseases (AIDs).

Methods: A total of 879 treatment naïve IgG4-RD patients from Peking Union Medical College Hospital were retrospectively included in this study. IgG4-RD Patients with comorbid autoimmune diseases were classified into the AID-positive (AID-Pos) subgroup, while those without autoimmune diseases were classified into the AID-negative (AID-Neg) subgroup. Additionally, AIDs were classified as systemic or organ-specific. The clinical features, laboratory findings, treatment regimens, and long-term prognosis were compared among the AID-Pos and AID-Neg groups, and the characteristics of AIDs were also explored.

Results: The prevalence rate of AIDs in IgG4-RD patients was 9.67% (85/879), including 47 cases of systemic AIDs and 38 cases of organ-specific AIDs. The types of comorbid AIDs were diverse, such as vitiligo (15 patients), systemic vasculitis (12 patients), psoriasis (12 patients), Hashimoto's thyroiditis (11 patients), and rheumatoid arthritis (10 patients). Most AIDs

Table 1 Comparisons of baseline demographics and clinical features in IgG4-RD patients with or without AIDs. a Prostate involved was compared only among males, which also applied to subsequent comparisons. RI scores: Responder Index. PGA scores: Physician Global Assessment.

	AID-Pos (n=85)	AID-Neg(n=794)	P value
Sex (Male%)	46 (54.1%)	479 (60.3%)	0.267
Age of onset (years old, median [IQR])	54 [47;62]	54 [45;62]	0.864
Disease duration (months, median [IQR])	8 [3;24]	12 [4;36]	0.053
Number of organs involved (median [IQR])	3 [2;4]	3 [2;5]	**0.012**
Organ involvement, n (%)			
Pancreas	29 (34.1%)	319 (40.2%)	0.278
Biliary tract	12 (14.1%)	142 (17.9%)	0.385
Submandibular gland	33 (38.8%)	466 (58.7%)	**<0.001**
Lacrimal gland	40 (47.1%)	412 (51.9%)	0.397
Parotid gland	19 (22.4%)	151 (19.0%)	0.459
Retroperitoneum	12 (14.1%)	119 (15.0%)	0.831
Lung	17 (20.0%)	227 (28.6%)	0.093
Kidney	16 (18.8%)	109 (13.7%)	0.201
Artery	6 (7.06%)	64 (8.06%)	0.746
Mediastinum	4 (4.71%)	27 (3.40%)	0.531
Prostate[a]	5 (10.9%)	87 (18.2%)	0.214
Lymph node	29 (34.1%)	358 (45.1%)	0.053
Sinus	14 (16.5%)	203 (25.6%)	0.065
Thyroid gland	5 (5.88%)	24 (3.02%)	0.190
Liver	3 (3.53%)	11 (1.39%)	0.146
Pituitary gland	2 (2.35%)	12 (1.51%)	0.637
Skin	0 (0.00%)	22 (2.77%)	0.259
Gastrointestinal tract	4 (4.71%)	18 (2.27%)	0.155
Subtype, n (%)			0.086
Proliferative subtype	58 (68.2%)	596 (75.1%)	
Fibrotic subtype	7 (8.24%)	28 (3.53%)	
Mixed subtype	20 (23.5%)	170 (21.4%)	
RI scores, median (median [IQR])	6 [4;8]	6 [4;10]	**0.012**
PGA scores, median (median [IQR])	5 [4;6]	5.5 [4;7]	0.225
Positive AIDs family history, n (%)	11 (12.9%)	68 (8.56%)	0.180
Allergy history, n (%)	35 (43.8%)	410 (54.1%)	0.078

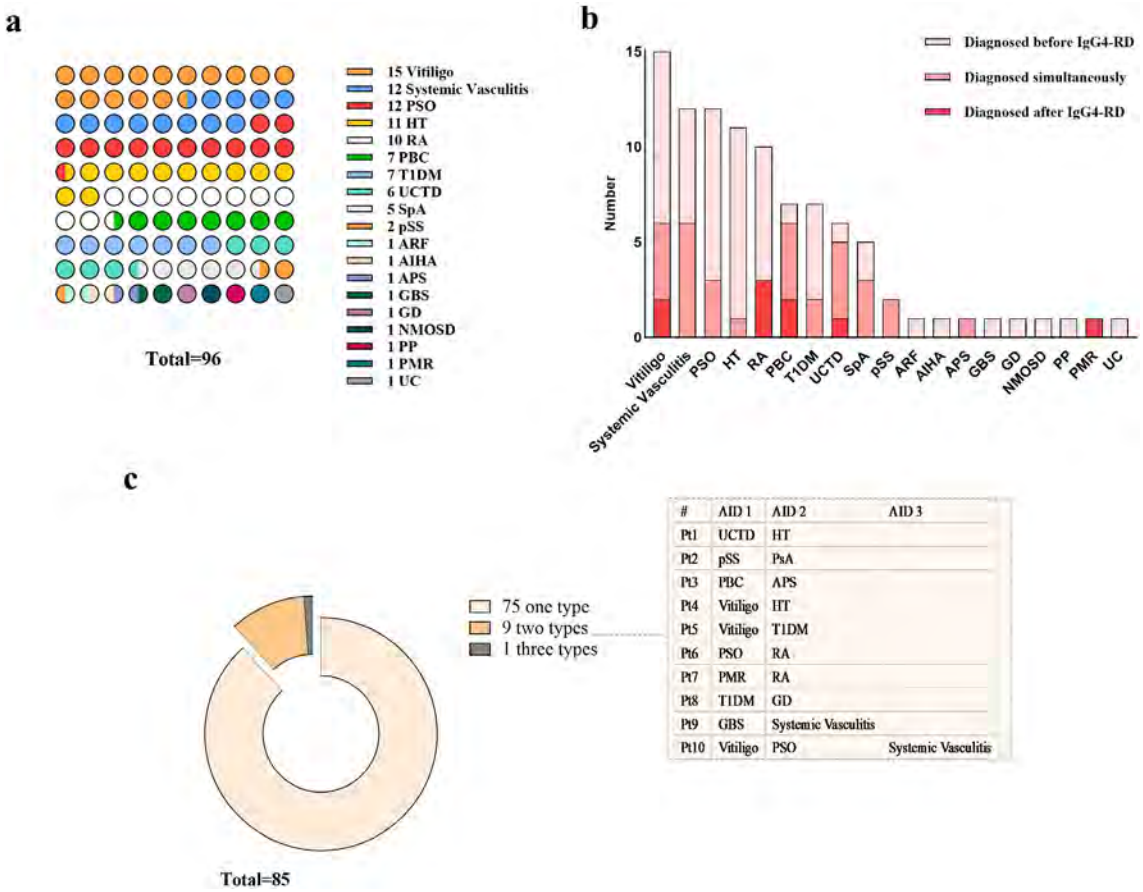


Figure 2 Types of AIDs and disease sequence. (a) The statistics of AIDs comorbid with IgG4-RD; (b) The temporal sequence of diseases between IgG4-RD and AIDs; (c) The number of AIDs each patient had. PSO: Psoriasis; HT, Hashimoto's thyroiditis; RA, Rheumatoid arthritis; PBC, Primary biliary cirrhosis; T1DM, Type 1 Diabetes Mellitus; UCTD, Undifferentiated connective tissue disease; SpA, Spondyloarthritis; pSS, Primary Sjögren's syndrome; ARF, Acute rheumatic fever; AIHA, Autoimmune hemolytic anemia; APS, Antiphospholipid syndrome; GBS, Guillain-Barré syndrome; GD, Graves' disease; NMOSD, Neuromyelitis optica spectrum disorders; PP, Palmoplantar pustulosis; PMR, Polymyalgia rheumatica; UC, Ulcerative colitis.

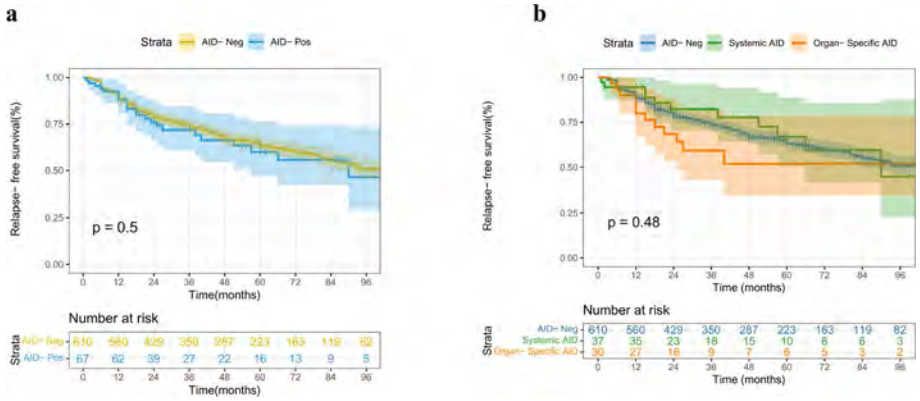


Figure 3 The prognoses of IgG4-RD patients with or without AIDs during follow-up. (a) IgG4-RD patients in AID-Pos group or AID-Neg group; (b) IgG4-RD patients in systemic AID group, Organ-Specific AID group or AID-Neg group.

occurred before or simultaneously with IgG4-RD. Among AID-Pos subgroup patients, 75 (88.2%) had only one type of AID. AID-Pos subgroup patients had lower serum IgG4 levels than AID-Neg subgroup patients (6017 [2729;13900] vs 9176 [3956;18100], p=0.004). Compared with AID-Neg subgroup patients, those with systemic AIDs had higher level of

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

erythrocyte sedimentation rate (40 [22.5; 74.] vs 18.0 [10.0;52.0] mm/hr, adjusted p < 0.001) and higher serum IgG1 level (11500 [8355;13575] vs 8700 [7215;11000] mg/L, adjusted p=0.002). There was no significant difference in treatment regimens and long-term prognosis between AID-Pos and AID-Neg subgroup patients.

Conclusion: IgG4-RD patients can complicate with other AIDs. Compared with AID-neg subgroup patients, IgG4-RD patients with comorbid AIDs have lower serum IgG4 levels, while the clinical characteristics, treatment, and prognosis were similar between two subgroups.

Disclosure: X. Yang: None; **W. Zhang**: None; **J. zhou**: None; **Y. Nie**: None.

Abstract Number: 1191

Effect of ER Stress Inhibition With 4-Phenylbutyric Acid on Disease Phenotype in a Mouse Model of Myositis

Alfredo Guzman, Elizabeth Bagley, Rita Spathis, Madison King, Kanneboyina Nagaraju and Melissa Morales, Binghamton University, Johnson City, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Dysregulation of the ER stress and interferon (IFN) pathways play a major role in the pathophysiology of autoimmune myositis. Upregulation of ER stress markers and type 1 IFN stimulated genes (an IFN 'signature') are present in myositis patients, and this IFN signature is related to disease activity. While the role of IFNα/β in myositis has been extensively studied, including clinical trials aimed at inhibiting type 1 IFN expression, the ER stress pathway—characterized by the accumulation of misfolded proteins and the activation of the unfolded protein response (UPR)—remains less explored. Therefore, we investigated the therapeutic efficacy of the ER stress inhibitor, 4-phenylbutyric acid (4PBA) in a myositis mouse model.

Methods: Myositis was induced in 21-day old female mice by removal of doxycycline from their water. Mice were randomized into 4 groups (n=10-17/group); Healthy controls (C57BL/6), myositis no treatment, myositis + 150 mg/kg 4PBA, and myositis + 300 mg/kg 4PBA. 4PBA was administered daily as a cherry syrup oral suspension at 150 mg/kg and 300 mg/kg body weight respectively for seven weeks. Treatment groups were evaluated based on survival time, body weight, muscle strength and function, and expression levels of ER stress markers CHOP, GADD34, Grp78, and Xbp1, and type 1 IFN stimulated genes (ISG) Ifit1, Irf7, Isg15, and Mx1.

Results: Untreated myositis mice had significantly reduced weight gain, muscle function and strength compared to BL/6 mice. 150 mg/kg 4PBA treatment resulted in an improvement in survival of myositis mice, with 76% surviving to the end of study compared to 59% and 63% for the untreated myositis and 300 mg/kg 4PBA treatment groups, respectively. Expression levels of the ER stress markers CHOP, GADD34, Grp78, and Xbp1, and type 1 IFN score, which were significantly elevated in untreated myositis mice, were noticeably decreased in skeletal muscle of 150 mg/kg 4PBA treated mice. However, significant increases in CHOP (p = 0.023) expression were observed in the higher dose treatment group compared to the untreated myositis group. Neither dose significantly improved muscle function.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Overall, we observed that treatment with 150 mg/kg 4PBA improved survival and showed a trend to lowering the ER stress and IFN signature, but this did not translate to functional improvement. Furthermore, 300 mg/kg did not improve any of the measures tested but instead increased the signature of selected markers. While the exact mechanisms for this dose-dependent effect are unknown, higher doses may lead to toxicity or off-target effects.

Disclosure: A. Guzman: None; **E. Bagley**: None; **R. Spathis**: None; **M. King**: None; **K. Nagaraju**: None; **M. Morales**: None.

Abstract Number: 1192

Idiopathic Inflammatory Myopathies: A Prospective Phase 4 Controlled Trial Of Recombinant Herpes Zoster Vaccine

Sandra G Pasoto[1], Thais B Gorayeb[2], **Ana Paula Luppino-Assad**[3], Nadia E Aikawa[4], Ana C Medeiros-Ribeiro[1], Leonard V Kupa[5], Bruno S Borges[6], Samuel K Shinjo[7], Fernando H De Souza[2], Renata Miossi[2], Eloisa Bonfa[8] and Clovis Artur Silva[9], [1]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, São Paulo, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, SAO PAULO, Brazil, [4]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas HCFMUSP, Sao Paulo, Brazil., Sao Paulo, Sao Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil, [6]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, [7]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, SÃO PAULO, Brazil, [8]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [9]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Although herpes zoster vaccination has been evaluated in immunocompromised populations, studies assessing vaccine immunogenicity and safety in idiopathic inflammatory myopathies (IIM) are restricted to H1N1 and SARS-CoV-2 and no data are available for the recombinant zoster vaccine (RZV). Thus, the objectives are to compare immune response of RZV in IIM patients and healthy control group (CG), and evaluate the vaccine safety profile, the influence on IIM disease activity and factors associated with vaccine responsiveness.

Methods: This prospective, randomized, placebo-controlled study included 70 immunosuppressed IIM patients (>18y) and 280 healthy controls (≥50y), all receiving two RZV doses (6 weeks apart). IIM patients were randomized 1:1 to receive vaccine (P1) or placebo (P2), with P2 subsequently vaccinated after unblinding at D84. Serum anti-glycoprotein E (anti-gE) antibody levels were measured by in-house GSK ELISA at baseline and 6 weeks post-second dose. Humoral response was defined as an anti-gE concentration ≥4-fold the pre-vaccination level. Geometric mean titers (GMTs) and Factor Increase (FI), as the ratio of post-vaccination to pre-vaccination titers were calculated. Adverse events were recorded using a standardized questionnaire. Disease activity was evaluated at baseline and 6 weeks after each RZV and placebo doses through clinical scores [Myositis Disease Activity Assessment Visual Analogue (MYOACT), Manual Muscle Test (MMT), Health Assessment Questionnaire (HAQ) and Modified Medical Research Council (mMRC) Dyspnea Scale] and serum muscle enzymes (ALT, AST, LDH, CK).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 - Humoral response rates after 12 weeks and anti-gE IgG titers before (D0) and after two doses of recombinant zoster vaccination in overall IIM patients and Control group

	Humoral response	Geometric mean titer (GMT)			Factor increase in GMT
	D84	D0	D84	p (D0 vs D84)	D0 to D84
IIM (P1 +P2), n=86	52 (78.8)	0.27 (0.2-0.4)	5.1 (3.43-7.47)	<0.001	18.5 (11.7-29.1)
CG, n=280	278 (99.3)	0.22 (0.2-0.3)	11.8 (10.9-12.8)	<0.001	53.0 (45.8-61.3)
p (IIM vs CG)	<0.001	0.269	<0.001	-	<0.001

IIM - idiopathic inflammatory myopathies; CG – control group GMT – Geometric mean titers (AU/mL); Frequencies of humoral response are presented as number (%) and they were compared using two-sided chi-square test between ARD and CG at D84. Ig-gE IgG titers and factor increase in GMT are expressed as geometric means with 95% confidence interval (95%CI). Data regarding anti-gE titers were analyzed using ANOVA with repeated measures and 2 factors [2 groups (ARD vs. CG), at 2 time points (D0 and D84)], followed by Bonferroni's multiple comparisons at neperian logarithm (ln)-transformed data. GMT and factor increase in GMT were compared using Mann-Whitney test for intergroup comparisons in ln-transformed data at pre-specified time points (D0 and D84). All analyses were two-sided. P1 – IIM patients who received the RZV on the day of randomization (D0) and after 6 weeks (D42) P2 – IIM patients who initially received placebo and were vaccinated 12 weeks after randomization, on D84 and after 6 weeks (D126)

Table 2 - Variation (delta) of disease activity parameters of patients with idiopathic inflammatory myopathies in P1 (vaccine) and P2 (placebo) groups after vaccination and placebo

	6 weeks			12 weeks		
	P1 group	P2 group	p	P1 group	P2 group	p
Delta MYOACT	0.0 (-1.2-0.2)	0.0 (-0.7-0.5)	0.477	0.0 (-1.2-2.0)	0.0 (-0.7-0.5)	0.510
Constitutional	0.0 (-5.0-5.0)	0.0 (-6.0-8.0)	0.779	0.0 (-5.0-5.0)	0.0 (-6.0-8.0)	0.556
Cutaneous	0.0 (-9.0 -10.0)	0.0 (-7.0-10.0)	0.278	0.0 (1.2 -9.0)	0.0 (-8.0 -7.7)	0.375
Skeletal	0.0 (-8.0-6.0)	0.0 (-9.0-10.0)	0.481	0.0 (-8.0--6.0)	0.0 (-8.0-5.0	0.883
Gastrointestinal	0.0 (-3.0 - 0.0)	0.0 (-8.0 -8.0)	0.700	0.0 (-3.0-7.0)	0.0 (-8.0-6.0)	0.100
Pulmonary	0.0 (-8.0-2.0)	0.0 (-8.0-7.0)	0.081	0.0 (-9.0-6.0)	0.0 (-8.0-6.0)	0.849
Cardiovascular	0.0 (0.0-0.0)	0.0 (-8.0 -8.0)	1.000	0.0 (0.0-6.0)	0.0 (-8.0-0.0)	0.166
Muscle	0.0 (0.0-9.0)	0.0 (0.0-10.0)	0.806	0.0 (9.0-6.0)	0.0 (9.0-8.0)	0.333
Delta CK	-0.5 (-628.0-14787)	1.0 (-1510-338.0)	0.311	1.0 (524.0 - 608.0)	-8.0 (-1635,0-488.0)	0.403
Delta LDH	-7.6 (-248.0-95.0)	3.0 (-59.0 119.0)	0.100	-7.0 (225.0 -79)	14.0 (-134.0-431)	0.065
Delta AST	-0.5 (-20.0-43.0)	0.0 (-65.0-11.0)	0.473	-1.0 (-21-21)	0.0 (-42-141)	0.506
Delta ALT	0.0 (-32.0-10.0)	0.0 (-33.0-9.0)	0.787	-0.5 (-25.0-16)	-1.0 (-26.0-363,0)	0.263
Delta pPGA	0.0 (-5.0-7.0)	0.0 (-6.0-8.0)	0.462	0.0 (-7.0-7.0)	0.0 (-8.0-5.0)	0.308
Delta phPGA	0.0 (-4.0-5.0)	0.0 4.0-5.0)	0.133	0.0 (-3.0-6.0)	0.0 (-4.0-5.0)	0.286
Delta HAQ	0.0 (-0.6-1.9)	0.0 (-1.1-1.8)	0.309	0.0 (-9.0-1.1)	0.0 (-6.0-1.2)	0.191
Delta MMT	0.0 (-30.0-6.0)	0.0 (-10.-6.0)	0.478	0.0 (-13-6.0)	0.0 (-18.8.0)	0.711

MYOACT-Myositis Disease Activity Assessment Visual Analogue, pPGA Patient global assessment, phPGA- Physician Global Assessment MMT-Manual Muscle Test, HAQ- Health Assessment Questionnaire, mMRC Modified Medical Research Council (mMRC) Dyspnea Scale Results are expressed in medians (interquartile range) and n (%). Continuous data were compared using Mann-Whitney test, and categorical variables with the chi-square or Fisher's exact tests, as appropriate, always as two-sided analyses. P1 – IIM patients who received the RZV on the day of randomization (D0) and after 6 weeks (D42) P2 - IIM patients who initially received placebo and were vaccinated 12 weeks after randomization, on D84 and after 6 weeks (D126)

Results: Seventy IIM patients (54 dermatomyositis, 16 antisynthetase syndrome) and 280 individuals in control group (CG) were analyzed. Groups were balanced for sex (p >0.05), although IIM were slightly younger (54 vs. 55y; p=0.022). At D84, the humoral response rate was significantly lower in IIM compared to CG (78.8% vs. 99.3%, p< 0.001%). IIM patients exhibited markedly lower post-vaccine GMT (5.1 vs 11.8 mUI/mL, p< 0.001) and factor increase (FI) (18.5 vs. 53.0, p< 0.001) (Table 1). A trend toward reduced response with mycophenolate mofetil (MMF) was observed (30.8% vs. 57.1%, p=0.069) but not confirmed in multivariate analysis. Adverse events were less frequent in IIM vs CG (71.4 vs 88.9%, p=0.001), including local (65.7 vs. 83.9%, p< 0.001) and systemic reactions (38.6 vs. 61.4%, p=0.001). Disease activity

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

metrics were comparable between groups (p >0.05), [patients VAS (p=0.308), physicians VAS (p=0,285, MMT (p=0.711), MYOACT (0,510), CPK (p=0,403) and DHL (p=0.065) (Table 2).

Conclusion: In immunosuppressed IIM patients, RZV showed good short-term immunogenicity and safety, with no disease worsening. However, reduced post-vaccination antibody titers suggest a potential risk for diminished long-term protection, highlighting the need for continued monitoring. (ClinicalTrials NCT05879419).

Disclosure: S. Pasoto: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **T. Gorayeb**: None; **A. Luppino-Assad**: GlaxoSmithKlein(GSK), 5; **N. Aikawa**: GlaxoSmithKlein(GSK), 5; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Kupa**: GlaxoSmithKlein(GSK), 5; **B. Borges**: None; **S. Shinjo**: None; **F. De Souza**: None; **R. Miossi**: None; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

Abstract Number: 1193

Lung Transplant Outcomes in Patients with Myositis- and Systemic Sclerosis-Associated Interstitial Lung Disease Compared to Idiopathic Pulmonary Fibrosis: A Multicentric Retrospective Analysis

Angela Chang[1], Navid Saleh[1], Alec Yu[1], Darya S. Jalaledin[2], Sabrina Hoa[3], Robert Levy[4], Jennifer Wilson[5], Charles Poirier[6], John Yee[1], James Choi[1], Océane Landon-Cardinal[7], Hyein Kim[8] and Kun Huang[9], [1]University of British Columbia, Vancouver, BC, Canada, [2]Université de Montréal, Saint-Lambert, QC, Canada, [3]University of Montreal, Brossard, QC, Canada, [4]University of British Columbia, Deerfield, IL, [5]UBC, Vancouver, BC, Canada, [6]University of Montreal, Montreal, QC, Canada, [7]Centre hospitalier de l'Université de Montréal, Montréal, QC, Canada, [8]The University of British Columbia, Vancouver, BC, Canada, [9]University of British Columbia, Vancouver, Surrey, BC, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a frequent complication of idiopathic inflammatory myositis (IIM) and systemic sclerosis (SSc), ranging from subclinical ILD to rapidly progressive respiratory failure. Despite advancing immunosuppressive and antifibrotic therapies, many progress to end-stage respiratory failure and may require lung transplantation. Unlike idiopathic pulmonary fibrosis (IPF), data on lung transplant outcomes for IIM and SSc patients remain limited. The aim of this study was to compare clinical characteristics and lung transplant outcomes in patients with IIM and SSc to IPF.

Methods: We retrospectively analyzed clinical data collected in patients with ILD diagnosed with IIM, SSc, and IPF who underwent bilateral lung transplant between January 1, 2014 and April 30, 2024 at the Vancouver General Hospital, and between January 1, 2012 and December 31, 2024 at the Centre hospitalier de l'Université de Montréal. All IIM and SSc patients satisfied their respective ACR classification criteria.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline patient characteristics pre-transplant.

Table 1. Baseline patient characteristics pre-transplant.

Variables*	IIM (n=18)	SSc (n=24)	IPF (n=64)	P value
Demographics				
Age at SARD diagnosis, median [IQR]	46.4 [40.0 - 51.0]	46 [38.9 – 56.4]	NA	0.52
Age at ILD Diagnosis, median [IQR]	46.4 [39.6 - 51.1]	48.5 [40.2 – 55.8]	60.5 [58 - 64]	**< 0.001** IIM-IPF: **< 0.001** SSc-IPF: **< 0.001** IIM-SSc: 0.27
Age at lung transplant, mean [IQR]	53.4 [48.2 - 58.5]	57.2 [47.7 - 62.1]	65 [62 – 68]	**< 0.001** IIM-IPF: **< 0.001** SSc-IPF: **< 0.001** IIM-SSc: 0.22
Female, n (%)	13 (72)	15 (63)	11 (17)	**< 0.001** IIM-IPF: **< 0.001** SSc-IPF: **0.002** IIM-SSc: 1.0
White, n (%)	15 (83)	16 (67)	51 (80)	0.29
Smoker, n (%)	9 (50)	9 (38)	47 (73)	**0.008** IIM-IPF: 0.25 SSc-IPF: **0.015** IIM-SSc: 1.0
BMI, median [IQR]	28.4 [21.6 -32.4]	25.1 [22.2 – 29.9]	27.6 [24 29.2]	0.55
Charleson Comorbidity index, median [IQR]	2 [1.2 - 3]	2 [1 - 3]	3 [2 - 4]	**0.005** IIM-IPF: **0.015** SSc-IPF: **0.007** IIM-SSc: 0.98
Variables at transplant				
FVC' (% of predicted), median [IQR]	49 [41 - 53.5]	48 [43 – 58]	51 [39 – 64]	0.73
DLCO (%of predicted), median [IQR]	39 [32 - 44.5]	24 [19 – 33]	31 [24 – 38]	**0.023** IIM-IPF: 0.96 SSc-IPF: **0.008** IIM-SSc: 0.058
PASP (mmHg), median [IQR]	41 [37 - 46.5]	44.5 [37.8 – 64.3]	35 [31 – 42]	**0.002** IIM-IPF: **0.03** SSc-IPF: **< 0.001** IIM-SSc: 0.63
SARD diagnosis to transplant (years), median [IQR]	2.4 [0.3 - 13.9]	6.5 [3.6 – 11.3]	NA	0.15
ILD diagnosis to transplant (years), median [IQR]	3.4[0.2 - 12.3]	6 [4 – 7.3]	3.9 [2.3 – 5.8]	**0.025** IIM-IPF: 0.88 SSc-IPF: **0.007** IIM-SSc: 0.054
Prior use of immunosuppressants, n (%)**	18 (100)	22 (92)	4 (6)	**< 0.001** IIM-IPF: 0.001 SSc-IPF: **< 0.001** IIM-SSc: 1.0
Prior use of antifibrotic, n (%)	1 (6)	1 (4)	41 (64)	**< 0.001** IIM-IPF: **< 0.001** SSc-IPF: **< 0.001** IIM-SSc: 1.0
ICU admission prior to transplant, n (%)	10 (56)	4 (17)	9 (14)	**0.001** IIM-IPF: **0.002** SSc-IPF: 1.0 IIM-SSc: 0.15
CMV mismatch Donor (+) / Recipient (-), n (%)	1 (6)	0 (0)	9 (14)	0.12
Emergent transplant, n (%)	10 (56)	5 (21)	15 (23)	**0.012** IIM-IPF: 0.054 SSc-IPF: 1.0 IIM-SSc: 0.058

* Continuous variables were analyzed using the Kruskal-Wallis test, followed by post-hoc pairwise comparisons with Dunn's test for significant results. Categorical variables were assessed using the Chi-squared test, with pairwise comparisons conducted using Fisher's Exact test and Bonferroni correction for significant results

**Does not include corticosteroids, intravenous immunoglobulin and hydroxychloroquine

Univariate analyses were performed for continuous and categorical data. Survival was assessed with Kaplan-Meier analysis, and incidence of chronic lung allograft dysfunction (CLAD) and malignancy were assessed with Poisson regression.

Results: We included 18 IIM, 24 SSc, and 64 IPF patients. Among IIM patients, 50% were anti-melanoma differentiation-associated protein 5 (MDA5) positive, 39% had anti-synthetase syndrome, and 50% had anti-Ro52. Among SSc patients, anti-Scl-70 was found in 33%, anti-centromere in 4.2%, and anti-RNA polymerase III in 4.2%. Patients with IIM and SSc were younger at the time of ILD diagnosis and lung transplantation, more likely to be female, less likely to have a smoking history, and had fewer comorbidities than IPF patients (Table 1). SSc patients had significantly lower diffusing capacity for carbon monoxide (DLCO) and longer ILD duration before transplant than IIM and IPF patients (Table 1).

Usual interstitial pneumonia (UIP) was predominant in IPF explant pathology, and nonspecific interstitial pneumonia (NSIP) was predominant in IIM and SSc (Table 2).

IIM patients had higher rates of urgent transplant, intensive care unit (ICU) admission, and prolonged post-transplant ICU/hospital stays (Table 2). At 1-year follow-up, forced vital capacity (FVC) was significantly lower in IIM and SSc patients compared to IPF. SSc patients had a significantly higher rate of non-pulmonary infections requiring hospitalization. Over long-term follow-up, all groups shared comparable post-transplant survival (Figure 1), rejection, pulmonary infection, and malignancy rates.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Short- and long-term post-lung transplant outcomes

Table 2. Short- and long-term post-transplant outcomes

Variables*	IIM (n=18)	SSc (n=24)	IPF (n=64)	P value
Dominant explant pathology				
UIP, n (%)	3 (17)	3 (13)	62 (97)	IIM-IPF: < **0.001** SSc-IPF: < **0.001** IIM-SSc: 0.91
NSIP, n (%)	5 (28)	15 (63)	0 (0)	IIM-IPF: < **0.001** SSc-IPF: < **0.001** IIM-SSc: 0.35
OP, n (%)	1 (6)	0 (0)	0 (0)	Insufficient Data
Mixed NSIP/UIP, n (%)	1 (6)	5 (21)	0 (0)	IIM-IPF: 0.14 SSc-IPF: **0.050** IIM-SSc: 1.0
Mixed NSIP/OP, n (%)	1 (6)	0 (0)	0 (0)	Insufficient Data
Diffuse alveolar damage, n (%)	5 (28)	0 (0)	0 (0)	Insufficient Data
Unclassifiable, n (%)	2 (11)	1 (4)	2 (3)	Insufficient Data
1-Year Outcomes				
Post-transplant ICU days, median [IQR]	33 [21 - 50]	7.5 [3 – 18]	4 [3 – 9]	< **0.001** IIM-IPF: < **0.001** SSc-IPF: 0.28 IIM-SSc: **0.004**
Post-transplant hospitalization days, median [IQR]	65 [34 – 112]	30.5 [19.8 - 41.5]	22 [17 – 31]	< **0.001** IIM-IPF: < **0.001** SSc-IPF: 0.18 IIM-SSc: **0.005**
Alive, n (%)**	16 (89)	19 (79)	59 (92)	0.44
FVC (% of predicted), median [IQR]	64 [52 - 86]	64 [55.3 – 71.5]	84 [67 – 99]	**0.002** IIM-IPF: **0.014** SSc-IPF: **0.002** IIM-SSc: 0.76
DLCO (%of predicted), median [IQR]	56 [41 - 62]	57 [47.5 – 63.5]	61 [45 – 75]	0.28
Acute Rejection, n (%)	6 (33)	11 (46)	31 (48)	0.51
Pneumonia requiring hospitalization, n (%)	5 (28)	11 (46)	20 (31)	0.35
Non-pulmonary infection requiring hospitalization, n (%)	6 (33)	12 (50)	14 (22)	**0.025** IIM-IPF: 1.0 SSc-IPF: **0.045** IIM-SSc: 1.0
Fungal infection requiring therapy, n (%)	2 (11)	9 (38)	22 (34)	0.11
CMV viremia requiring therapy, n (%)	6 (33)	6 (25)	13 (23)	0.70
Long-term outcomes				
Follow-up duration (years), median [IQR]	2.8 [1.8 - 5.8]	2.3 [1 – 5]	3.6 [2.1 – 6.2]	0.18
Alive at last follow-up, (%)**	13 (72)	18 (75)	42 (66)	0.95
CLAD, n (%)***	2 (11)	2 (8)	18 (28)	0.63
Post-transplant malignancy (excluding non-melanoma skin cancer), n (%)***	1 (6)	1 (4)	12 (19)	0.36

* Continuous variables were analyzed using the Kruskal-Wallis test, followed by post-hoc pairwise comparisons with Dunn's test for significant results. Categorical variables were assessed using the Chi-squared test, with pairwise comparisons conducted using Fisher's Exact test and Bonferroni correction for significant results
** Analyzed with Kaplan Meier survival analysis
*** Analyzed with Poisson incidence analysis

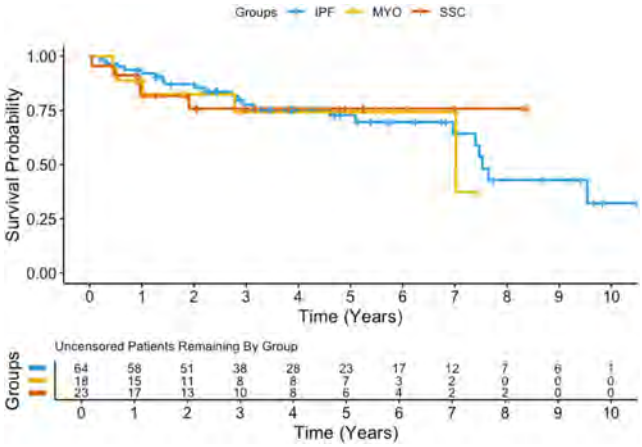


Figure 1. Kaplan Meier survival curve for IIM, SSc and IPF patients.

Conclusion: This study is the first to compare short- and long-term lung transplant outcomes from a combined cohort of IIM, SSc, and IPF patients. IIM patients required more urgent transplants and prolonged ICU stays, and SSc patients experienced higher rates of non-pulmonary infections. However, long-term post-transplant survival and complication rates were comparable across all groups. These findings suggest that lung transplantation remains a viable option for carefully selected IIM and SSc patients with advanced ILD, despite their distinct clinical challenges.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Chang: None; **N. Saleh**: None; **A. Yu**: None; **D. S. Jalaledin**: None; **S. Hoa**: None; **R. Levy**: None; **J. Wilson**: None; **C. Poirier**: None; **J. Yee**: None; **J. Choi**: None; **O. Landon-Cardinal**: None; **H. Kim**: Abbvie, 6, Boehringer Ingelheim, 6, Fresenius Kabi, 6, Johnson and Johnson, 6, Mallinckrodt, 6, Norvatis, 6, Pfizer, 6; **K. Huang**: AbbVie/Abbott, 6, Fresenius Kabi, 6, Novartis, 6, Pfizer, 5.

Abstract Number: 1194

Risk of Calcinosis with Proton Pump Inhibitor Use in Adult Dermatomyositis and Systemic Sclerosis

Antonia Valenzuela[1], Nicolás González[2], José Rojas[3], Martin Fuentes[3], Srijana Davuluri[4], Brian Lee[5], David Fiorentino[6] and Lorinda Chung[4], [1]Pontificia Universidad Catolica de Chile, Santiago, Chile, [2]Pontificia Universidad Católica de Chile, Santiago de Chile, Chile, [3]Pontificia Universidad Católica de Chile, Santiago de Chile, Chile, [4]Stanford University, Stanford, CA, [5]Stanford University, Stanford, [6]Department of Dermatology, Stanford University Medical Center, Stanford, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Calcinosis is a painful, debilitating manifestation in connective tissue diseases. Recent findings suggest a link between proton pump inhibitor (PPI) use and calcinosis in systemic sclerosis (SSc), but this association has not been studied in dermatomyositis (DM). This study aims to evaluate the relationship between PPI use and the presence of calcinosis in patients with DM and to confirm this association in SSc.

Methods: We conducted a retrospective, cross-sectional study using DM and SSc cohorts from Pontificia Universidad Católica de Chile. Adults meeting ACR/EULAR criteria for DM or SSc were included. Clinical data, PPI exposure, and presence of calcinosis was extracted from electronic medical records. PPI exposure score was calculated as described by Host et al.(1) as total duration of use in years multiplied by total daily PPI equivalent dose. Logistic regression was used to assess the association between PPI use and calcinosis, adjusting for clinical variables that were significant in univariate analysis as well as potential confounders.

Results: A total of 107 patients with SSc and 83 with DM were included. Calcinosis was present in 23 SSc patients (21.5%) and 18 DM patients (21.7%). Among SSc patients, those with calcinosis had significantly longer median disease duration from both Raynaud's phenomenon (RP) onset (12 vs. 3 years) and first non-RP symptoms (5 vs. 2.5 years), higher prevalence of digital ulcers (52.2% vs. 22.6%, p=0.0151), more frequent gastroesophageal reflux disease (GERD) symptoms (86.9% vs. 57.1%), greater PPI use (95% vs. 72.6%, p=0.02), and a markedly higher median PPI exposure score (4580 vs. 293, p< 0.0001). In DM, patients with calcinosis had a higher frequency of ulcers (27.8% vs. 1.54%, p=0.0003), but no significant differences in PPI use, although a numeric trend toward longer PPI exposure was noted (3.7 vs. 0.1 years, p=0.08). In multivariate analysis of the SSc cohort, adjusting for disease duration from first RP, longer disease duration (OR 1.11, 95% CI 1.04–1.19, p=0.0013), PPI use for 5–10 years (OR 7.41, 95% CI 1.2–45.6, p=0.03), and PPI use for more than 10 years (OR 16.4, 95% CI 2.5–107.7, p=0.0036) were significantly associated with calcinosis. In contrast, PPI use for less than 5 years was not associated with calcinosis.

Conclusion: Prolonged PPI use was significantly associated with calcinosis in patients with SSc, confirming its role as a potentially modifiable risk factor. No significant association was found in DM, although a trend toward longer PPI use in those with calcinosis warrants further study. These findings raise important questions about the long-term safety of PPI therapy in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients with calcinosis and suggest that the pathophysiology and risk factors of calcinosis may differ between SSc and DM.

References:

1. Host LV, Campochiaro C, Afonso A, Nihtyanova SI, Denton CP, Ong VH. High proton pump inhibitor exposure increases risk of calcinosis in systemic sclerosis. Rheumatology (Oxford). 2020.

Disclosure: A. Valenzuela: None; **N. González**: None; **J. Rojas**: None; **M. Fuentes**: None; **S. Davuluri**: None; **B. Lee**: None; **D. Fiorentino**: None; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2.

Abstract Number: 1195

Discordance between Immunoblot and ELISA in the detection of Jo-1 and Ro/Ro-52 Autoantibodies

Antonia Valenzuela[1], Sebastián Andrés Cerda Acevedo[2] and Francisco Vera Gutiérrez[2], [1]Pontificia Universidad Catolica de Chile, Santiago, Chile, [2]Pontificia Universidad Católica de Chile, Santiago de Chile, Chile

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoantibodies play a key role in the diagnosis, classification, and prognosis of idiopathic inflammatory myopathies (IIM). Among the most relevant are myositis-specific antibodies (MSAs), such as anti-Jo-1, and myositis-associated antibodies (MAAs), such as anti-Ro/Ro-52. Accurate serological detection using techniques such as Enzyme-Linked Immunosorbent Assay (ELISA) or immunoblot, is essential. However, in clinical practice, discordance between these methods is frequently observed. We aim to evaluate the discordance between ELISA and immunoblot in detecting Jo-1 and Ro/Ro-52 autoantibodies, and the clinical relevance of discordant results in a real-world cohort.

Methods: A retrospective, cross-sectional study was conducted on patients from a tertiary health center (Red de Salud UC Christus), who underwent testing for antinuclear antibodies (ANA), nuclear extractable antigen (ENA), and a myositis autoantibody panel within a +/-1 year interval, from March 2020 to March 2021 and had at least one clinic visit. ANA was detected using indirect immunofluorescence on HEp-2 cells, ENA by ELISA, and the myositis autoantibody panel by a 16-antigen line immunoassay/immunoblot. Demographic, clinical, and laboratory variables were collected through review of electronic medical records.

Results: A total of 112 patients met the inclusion criteria. 69 (61.6%) were female, with a mean age of 54.4 (±17.3) years. ANA was positive in 63 patients (53.4%), with the most frequent titer being 1/80 dilution, with AC-4,5 pattern (n=27, 23%). Jo-1 autoantibodies were detected exclusively by ELISA in 4 patients, exclusively by immunoblot in 5, and by both methods in 3. Ro/Ro-52 autoantibodies were positive exclusively by ELISA in 4 patients, exclusively by immunoblot in 14, and by both in 1. The discordance rate between ELISA and immunoblot was 8% for Jo-1 and 17% for Ro/Ro-52. Among the 3 patients with concordant Jo-1 positivity on both tests, all had dermatomyositis (DM)—two met definite and one met possible ACR/EULAR classification criteria. Of the 4 patients with positive Jo-1 on ELISA but negative on immunoblot, only one had DM; the remaining three had no autoimmune disease. In contrast, all patients who were Jo-1 negative on ELISA but

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Jo-1 cases	ELISA	Immunoblot	Clinical Diagnosis	Classification Criteria
1	Pos (3x)	Pos (3x)	DM	DM definite
2	Pos (1x)	Pos (1x)	DM	DM possible
3	Pos (2x)	Pos (3x)	DM	DM definite
4	Pos (1x)	Neg	DM	(-)
5	Pos (2x)	Neg	Bronchiolitis	(-)
6	Pos (1x)	Neg	2° Hypertension	(-)
7	Pos (1x)	Neg	(-)	DM probable
8	Neg	Pos (2x)	DM	DM definite
9	Neg	Pos (1x)	DM	DM definite
10	Neg	Pos (3x)	DM amyopathic	DM definite
11	Neg	Pos (3x)	ASyS	DM definite
12	Neg	Pos (1x)	ILD (ASyS?)	(-)

Ro / Ro 52 cases	ELISA	Immunoblot	Clinical Diagnosis	Classification Criteria
1	Pos (1x)	Pos (3x)	Thyroid cancer	(-)
2	Pos (2x)	Neg	Sjögren	(-)
3	Pos (2x)	Neg	ILD, Sjögren	(-)
4	Pos (2x)	Neg	ILD	(-)
5	Pos (2x)	Neg	Sjögren	(-)
6	Pos (2x)	Neg	ILD, Sjögren	(-)
7	Neg	Pos (3x)	DM	DM definite
8	Neg	Pos (3x)	ILD, Sjögren	(-)
9	Neg	Pos (3x)	DM	DM definite
10	Neg	Pos (3x)	ILD/DM	DM definite
11	Neg	Pos (2x)	ILD	(-)
12	Neg	Pos (2x)	ILD	(-)
13	Neg	Pos (2x)	ILD	(-)
14	Neg	Pos (2x)	ILD, Sjögren	(-)
15	Neg	Pos (2x)	DM	DM definite
16	Neg	Pos (2x)	PM	(-)
17	Neg	Pos (2x)	DM	(-)
18	Neg	Pos (2x)	DM amyopathic	DM definite
19	Neg	Pos (2x)	ILD, Sjögren	Sjögren
20	Neg	Pos (1x)	COP	(-)

Abbreviations
DM: Dermatomyositis
PM: Polymyositis
ILD: Interstitial Lung Disease
COP: Cryptogenic Organizig Pneumonia
IPAF: Interstitial Pneumonia with Autoimmune Features
ASyS: Antisyntetase Syndrome
Pos: Positive test
Neg: Negative test
1x: Weak Positive
2x: Moderate Positive
3x: Strong Positive

Clinical diagnoses and classification criteria according to Jo-1 and Ro/Ro-52 antibody result concordance and discordance between ELISA and immunoblot.

positive on immunoblot had confirmed autoimmune conditions (Table 1). The one patient who had Ro positivity on ELISA and Ro-52 positivity on immunoblot was ultimately diagnosed with thyroid cancer. Finally, no correlation was observed between ANA patterns (nuclear or cytoplasmic) and specific autoantibodies identified by the other methods.

Conclusion: Our findings highlight a significant rate of discordance between ELISA and immunoblot in the detection of autoantibodies, particularly for Ro/Ro-52. Notably, immunoblot-identified Jo-1 positivity alone was more consistently associated with confirmed autoimmune diagnoses than ELISA alone. These results underscore the importance of using complementary serological methods in the diagnostic workup of suspected IIM, and caution against relying solely on a single testing modality.

Disclosure: A. Valenzuela: None; **S. Cerda Acevedo**: None; **F. Vera Gutiérrez**: None.

Abstract Number: 1196

Prevalence of and Factors Associated with Chronic Opioid Use among Individuals with Inflammatory Myopathies

Anuya Natu[1], Haley Zimmerman[2], Kristin Wipfler[3], Kaleb Michaud[4], Yvonne Lee[5] and Didem Saygin[2], [1]John H. Stroger, Jr. Hospital of Cook County, Chicago, IL, [2]Rush University Medical Center, Chicago, IL, [3]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [4]University of Nebraska Medical Center, Omaha, NE, [5]Northwestern University, Chicago, IL

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1. Health-related outcomes, satisfaction, and health care utilization of FORWARD participants with IIM with and without chronic opioid use.

Characteristics	Participants without chronic opioid use (n=109)	Participants with chronic opioid use (n=43)	p value
Fatigue (0-10)	4.1 ± 3.3	5.6 ± 3.1	**0.01**
Pain (0-10)	2.8 ± 2.6	6.1 ± 2.7	**<0.001**
Patient global disease activity (0-10)	3.2 ± 2.2	4.9 ± 2.8	**<0.001**
HAQ-II (0-3)	0.9 ± 0.7	1.2 ± 0.7	**0.007**
SF-36 Physical component summary (0-100)	39.4 ± 10.9	31.2 ± 9.2	**<0.001**
SF-36 Mental component summary (0-100)	50.6 ± 10.6	45.5 ± 14.8	0.07
Health satisfaction (0-4)	2.1 ± 0.1	1.7 ± 0.2	0.06
Rheumatologist visits (>2) *	36 (39.1%)	14 (40%)	1.0
ER visits (≥1) *	16 (34%)	12 (50%)	0.2
General practitioner visits (>2) *	10 (11.8%)	7 (21.2%)	0.2

Abbreviations: HAQ-II, Health Assessment Questionnaire-II; SF-36, 36-Item Short Form Health Survey; VAS, Visual Analogue Scale
** In the last 6 months*

Table 2. Factors associated with chronic opioid use among individuals with IIM on univariable and multivariable logistic regression models.

Variables	Univariable logistic regression model		Multivariable logistic regression model	
	OR (95% CI)	p value	OR (95% CI)	p value
Age	0.99 (0.96 – 1.01)	0.4	1.01 (0.97 – 1.06)	0.5
Female (%)	1.01 (0.42 – 2.40)	1.0	1.20 (0.29 – 5.03)	0.8
Non-White race (%)	4.98 (1.85 – 13.40)	**0.001**	4.71 (0.96 – 23.25)	0.06
Ever smoker (%)	4.31 (2.01 – 9.23)	**<0.001**	4.16 (1.41 – 12.25)	**0.01**
Body mass index	1.04 (0.98 – 1.10)	1.9		
Education level (years)	0.86 (0.72 – 1.03)	0.1		
Total annual income ($)	0.99 (0.99 – 0.99)	**0.01**	0.99 (0.99 – 1.00)	0.2
Symptom duration (years)	1.03 (0.98 – 1.10)	0.2		
Dermatomyositis	0.62 (0.28 – 1.35)	0.2		
Polymyositis/IMNM	1.38 (0.66 – 2.87)	0.4		
Rheumatic Disease Comorbidity Index (0-9)	1.39 (1.12 – 1.73)	**0.003**		
Osteoarthritis	1.64 (0.68 – 3.94)	0.3		
Depression	2.34 (1.08 – 5.09)	**0.03**	1.17 (0.31 – 4.45)	0.8
Anxiety	1.27 (0.54 – 2.97)	0.6		
Hypertension	1.26 (0.62 – 2.57)	0.5		
Diabetes mellitus	1.70 (0.61 – 4.72)	0.3		
Myocardial infarction	0.82 (0.16 – 4.24)	0.8		
Cancer	0.84 (0.33 – 2.17)	0.7		
Renal disease	3.27 (1.03 – 10.38)	**0.04**	4.34 (0.79 – 23.92)	0.1
Pulmonary disease	3.78 (1.75 – 8.18)	**0.001**	3.81 (1.25 – 11.60)	**0.02**
GI disease	3.56 (1.65 – 7.68)	**0.001**	1.95 (0.66 – 5.76)	0.2
Cardiac disease	1.40 (0.59 – 3.33)	0.4		
Fibromyalgia	2.83 (1.32 – 6.04)	**0.007**	1.76 (0.53 – 5.80)	0.4

Abbreviations: GI, Gastrointestinal; IMNM, Immune-mediated necrotizing myopathy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

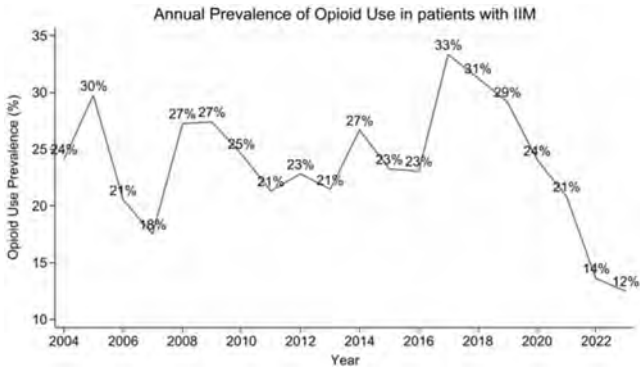


Figure 1. Annual prevalence of opioid use in individuals with IIM (2004 – 2023).

Background/Purpose: Idiopathic inflammatory myopathies (IIM) can be associated with significant pain and functional impairment. While the use of opioids has been documented in other inflammatory disorders, data regarding opioid use in patients with IIM are scarce. Given the risks of long-term opioid therapy, understanding the prevalence and predictors of chronic opioid requirements in this patient population is crucial for developing appropriate pain management strategies.

Methods: We used the FORWARD Databank - a longitudinal prospective registry of adults with rheumatic diseases in the US. Participants included in this study had a physician diagnosis of IIM and completed comprehensive semiannual questionnaires reporting sociodemographic features, pain, fatigue, physical function, disease activity, use of opioids/other medications, and health services at serial visits. Chronic opioid use was defined as documentation of opioid use in participant surveys on ≥2 consecutive study visits, amounting to a cumulative duration of opioid use of ≥ 90 days. Fischer's exact and Student's T tests were used to compare healthcare utilization, satisfaction, and outcomes between participants with and without chronic opioid use. The observation at enrollment was used for non-chronic opioid users while the first-reported opioid use observation was used for chronic opioid users. Logistic regression was used to determine variables associated with chronic opioid use. We calculated the annual prevalence and temporal trends of opioid use among participants with at least 90 days of follow-up defining use as documentation of opioid use at ≥1 visit within a given year between years of 2004-2023.

Results: Out of 210 participants with IIM, 152 (mean age ± SD, 55.4 ± 1.4, 80.5% female, and 85.8% White) with at least 90 days of follow-up were included. The participants were followed for a mean duration of 4.9 ± 0.4 years. A total of 43 participants with IIM (28.3%) were found to have chronic (90+ days) opioid use. Participants with chronic opioid use were more likely to have history of smoking, non-White race, lower annual income, and were more likely to have comorbid depression, fibromyalgia, pulmonary and gastrointestinal disorders, with a higher rheumatic disease comorbidity index. Chronic opioid use was associated with worse fatigue, pain, patient global disease activity, disability, and quality of life (Table 1). On multivariable logistic regression, history of smoking and presence of comorbid pulmonary disease were significantly associated with increased odds of chronic opioid use (Table 2). The prevalence of opioid use was relatively stable at 20% - 33% between 2004 and 2017 with a downward trend between 2017-2023 (Figure 1).

Conclusion: Approximately one in three individuals with IIM are chronic opioid users. Smoking history, comorbid pulmonary disease, and poor health-related outcomes are associated with chronic opioid use among individuals with IIM. Further studies evaluating pain mechanisms and alternate pain management strategies in IIM patients are needed.

Disclosure: A. Natu: None; **H. Zimmerman**: None; **K. Wipfler**: None; **K. Michaud**: None; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1; **D. Saygin**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1197

Genetic Profiling of Idiopathic Inflammatory Myopathies in Indian Patients Reveals Genotype-Phenotype Correlation

Bandana Jassal[1], Aishwarya Dhall[1], Mohammed Faruq[2], Danveer Bhadu[1], Uma Kumar[1] and Mehar Chand Sharma[1], [1]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, India, [2]Institute of Genomics and Integrative Biology, New Delhi, Delhi, India

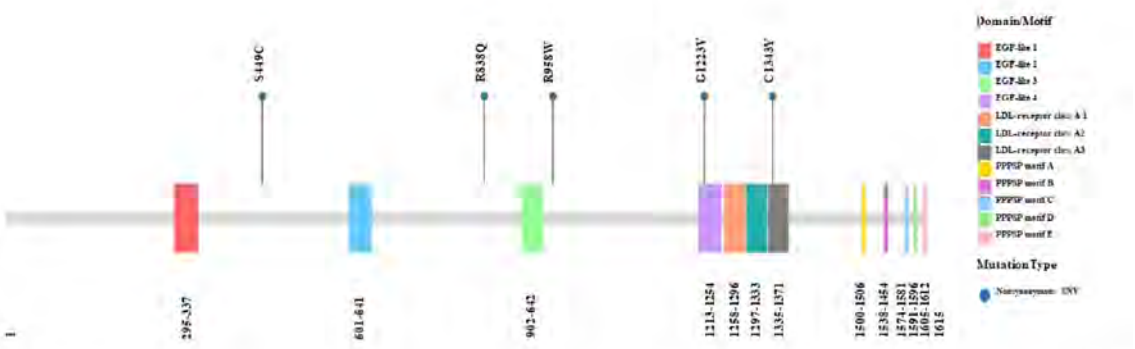
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are rare autoimmune muscle disorders with complex genetic underpinnings. Most genetic studies have focused on limited populations. This study explores genetic risk factors in Indian IIM patients, integrating clinical, serological, and histopathological features to enhance understanding of its pathogenesis.

Methods: Genomic DNA was isolated from EDTA blood and libraries were prepared using the SureSelect XT HS2 protocol and sequenced on the Illumina NextSeq 2000 (2×150 bp). Variants were prioritized based on quality, frequency, predicted impact, and pathway relevance then selected variants were validated by Sanger sequencing using custom-designed primers and standard PCR. Frequently mutated genes were assessed for phenotype associations.

Results: A total of 91 prioritized variants were identified across 86 IIM cases, with mutations present in 68.6% (59/86). Of these, 4.4% were classified as pathogenic, 14.3% as likely pathogenic, and 81.3% as variants of uncertain significance (VUS). Most were nonsynonymous SNVs (80.2%), followed by frameshift deletions (5.5%), stopgain mutations (4.4%), and others. Notably, 25.3% were novel variants. Seventeen genes harbored ≥2 variants or at least one pathogenic/likely pathogenic variant, with five genes (*CFTR, COL1A1, HBB, LRP5*, and *WDFY4*) meeting both criteria for further evaluation. Among these, *LRP5* carried five nonsynonymous SNVs across IIM subgroups. Domain mapping revealed key mutations within or

Figure 1. Mapping of *LRP5* variants identified in the IIM Cohort



Schematic representation of the *LRP5* protein (1–1615 amino acids) showing the positions of prioritized variants identified in the IIM cohort.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of characteristics of IIM Patients With and Without LRP5 Variants: This table presents a univariate comparison between idiopathic inflammatory myopathy (IIM) patients carrying prioritized LRP5 variants (n = 5) and those without such variants (n = 81). Clinical, histopathological, serological, and diagnostic variables are shown as counts with corresponding percentages. Statistical significance was assessed using Fisher's exact test. Results are expressed as p-values with corresponding odds ratios (OR) and 95% confidence intervals (CI) in parentheses.

Variables	Patient with LRP5 variant	Patient without LRP5 variant	pvalue (OR[95%CI])
n(%)	5(5.8)	81(94.2)	NA
Gender, n(%)			
Female	4(80)	47(58)	0.6442 (2.9 [0.3-27.1])
Male	1(20)	34(42)	0.6442 (0.3 [0-3.2])
Age of Onset Range, n(%)			
Age of Onset ≥ 18 years to < 45 years	1(20)	35(43.2)	0.3043 (0.3 [0-3.1])
Age of Onset < 18years	1(20)	11(13.6)	0.5375 (1.6 [0.2-15.6])
Age of Onset equal to 45 years	0(0)	4(4.9)	1 (1.9 [0.1-41.7])
Age of Onset >=45 years	3(60)	31(38.3)	0.1797 (2.4 [0.4-15.3])
Duration > 12 months	2(40)	28(34.6)	1 (1.3 [0.2-8])
Muscle Weakness, n(%)			
Proximal muscle weakness	3(60)	76(93.8)	0.0509 (0.1 [0-0.7])
Upper extremity proximal weakness	3(60)	76(93.8)	0.0509 (0.1 [0-0.7])
Lower extremity proximal weakness	3(60)	77(95.1)	0.0372 (0.1 [0-0.6])
Neck flexor greater than neck extensor weakness	1(20)	21(25.9)	1 (0.7 [0.1-6.8])
Proximal greater than distal lower extremity weakness	3(60)	69(85.2)	0.1847 (0.3 [0-1.7])
Knee extensor weakness	2(40)	38(46.9)	0.6431 (0.5 [0.1-2.9])
Clinical Features, n(%)			
Heliotrope rash	2(40)	18(22.2)	0.3295 (2.3 [0.4-15.1])
Gottron's papules	1(20)	11(13.6)	0.5375 (1.6 [0.2-15.6])
Gottron's Sign	0(0)	5(6.2)	1 (1.5 [0.1-31.9])
DM skin manifestations	2(40)	24(29.6)	0.636 (1.6 [0.2-10.1])
Dermatologic features	2(40)	30(37)	1 (1.1 [0.2-7.2])
Dysphagia or esophageal dysmotility	1(20)	30(37)	0.6497 (0.4 [0-4])
Raynaud' phenomenon	1(20)	13(16)	1 (1.3 [0.1-12.7])
Mechanic hands	0(0)	4(4.9)	1 (1.9 [0.1-41.7])
Arthritis	0(0)	13(16)	1 (0.5 [0-10.2])
Interstitial lung disease	2(40)	8(9.9)	0.1011 (6.1 [0.9-42])
Fever	2(40)	19(23.5)	0.5917 (2.2 [0.3-14])
Overlap Features	3(60)	40(49.4)	1 (1.5 [0.2-9.7])
Elevated muscle enzymes	4(80)	67(82.7)	1 (0.8 [0.1-8.1])
CK ≤3.5X normal limit	2(40)	46(56.8)	0.6362 (0.6 [0.1-4.6])
Other CTD	0(0)	9(11.1)	1 (0.8 [0-15.9])
Histopathological Features, n(%)			
Endomysial infiltration surrounding myofibre	3(60)	46(56.8)	1 (1.1 [0.2-7.2])
Perimysial and or Perivascular infiltration	2(40)	31(38.3)	1 (1.1 [0.2-6.8])
Perifascicular atrophy	2(40)	36(44.4)	1 (0.8 [0.1-5.3])
Rimmed vacuoles and or cytoplasmic protein aggregates	1(20)	18(22.2)	1 (0.9 [0.1-8.3])
Mitochondrial abnormalities	2(40)	22(27.2)	0.6156 (1.8 [0.3-11.4])
MHC I	5(100)	79(97.5)	1 (0.3 [0-6.4])
MHC II	2(40)	33(40.7)	1 (1 [0.2-6.5])
MHC I&II	2(40)	33(40.7)	1 (1 [0.2-6.5])
MAC Vessels	3(60)	55(67.9)	0.6589 (0.7 [0.1-4.5])
MAC Fibers	3(60)	44(54.3)	1 (1.3 [0.2-8])
Connective Tissue Fragmentation	1(20)	17(21)	1 (0.9 [0.1-9])
Necrosis	0(0)	13(16)	1 (0.5 [0-10.2])
Myophagocytosis	0(0)	5(6.2)	1 (1.5 [0.1-31.9])
Autoantibody Profile, n(%)			
Seronegative	1(20)	23(25.9)	1 (0.7 [0.1-6.8])
Ro52	4(80)	24(29.6)	0.0369 (9.3 [1-89.5])
PMScl75 100	1(20)	3(3.7)	0.2165 (6.5 [0.5-77.3])
SRP	0(0)	11(13.6)	1 (0.6 [0-12.5])
HMGCR	0(0)	2(2.5)	1 (4 [0.2-99.7])
Jo1	0(0)	5(6.2)	1 (1.5 [0.1-31.9])
Mi2	0(0)	16(19.8)	0.5788 (0.4 [0-7.8])
NXP2	0(0)	7(8.6)	1 (1.1 [0.1-21.4])
PL7	0(0)	6(7.4)	1 (1.2 [0.1-25.7])
MDA5	0(0)	8(9.9)	1 (0.9 [0-18.3])
PL12	1(20)	2(2.5)	0.1663 (9.9 [0.7-133.2])
TIF1γ	2(40)	2(2.5)	0.0156 (26.3 [2.7-255.9])
Ku	0(0)	1(1.2)	1 (8 [0.2-268.4])
DM specific autoantibodies	2(40)	34(42)	1 (0.9 [0.1-5.8])
IMNM specific autoantibodies	0(0)	13(16)	1 (0.5 [0-10.2])
ASS specific autoantibodies	1(20)	13(16)	1 (1.3 [0.1-12.7])
Overlap autoantibodies	4(80)	27(33.3)	0.0546 (8 [0.9-75.1])

adjacent to EGF-like and LDL-receptor domains (Figure 1). *LRP5* mutations were significantly associated with proximal lower limb weakness (p=0.0372), anti-Ro52 (p=0.0369), and anti-TIF1γ autoantibodies (p=0.0156) (Table 1), suggesting a potential genotype-phenotype correlation.

Conclusion: This study identifies key genetic variants in Indian IIM patients, highlighting *LRP5* as a potential marker linked to distinct clinical and serological features, advancing understanding of IIM pathogenesis.

Disclosure: B. Jassal: None; **A. Dhall**: None; **M. Faruq**: None; **D. Bhadu**: None; **U. Kumar**: None; **M. Sharma**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1198

Induction of stable, GC-free remission in patients with severe, therapy-refractory anti-synthetase syndrome after using the bispecific CD19xCD3 T cell engager blinatumomab

Christina Duesing[1], Ayla Nadja Stuetz[2], Andrea-Hermina Györfi[3], Laura-Marie Lahu[4], Franca Sophie Deicher[5], Gamal Chehab[6], Jutta Richter[7], Marie Celine van Saan[8], Bilgesu Safak Tümerdem[2], Alexandru-Emil Matei[9], Bjoern Buehring[10], Ricardo Grieshaber-Bouyer[11], Melanie Hagen[12], Georg Schett[13], Wolfgang Merkt[14] and Jörg Distler[15], [1]Klinik für Rheumatologie, Dösseldorf, Germany, [2]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Nordrhein-Westfalen, Germany, [3]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [4]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Germany, [5]Uniklinik Düsseldorf, Düsseldorf, Germany, [6]Policlinic of Rheumatology and Hiller Research Unit Rheumatology, Heinrich-Heine-University, Dösseldorf, Germany, [7]Clinic for Rheumatology and Hiller Research Unit, Heinrich-Heine-University Duesseldorf, Medical Faculty, Duesseldorf, Germany, Dösseldorf, Germany, [8]Department of Rheumatology, University Hospital Duesseldorf, Medical Faculty of Heinrich Heine University, Duesseldorf, [9]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany, [10]Bergisches Rheuma-Zentrum, Wuppertal, Germany, [11]University Hospital Erlangen, Erlangen, Germany, [12]Friedrich-Alexander-University Erlangen-Nuremberg, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany, [13]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [14]University Hospital Dösseldorf, Dösseldorf, Germany, [15]University Hospital Duesseldorf and HHU, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Treatment of anti-synthetase syndrome (ASyS) presents clinical challenges: myositis can lead to permanent disability and severe organ involvement is life-threatening.

Methods: We treated three patients with multidrug-resistant severe anti-Jo-1 positive ASyS with blinatumomab 143μg and added rituximab (RTX) 1000mg for maintenance therapy. Patient 1, 67-year-old female, had reoccurring myositis and new interstitial lung disease (ILD). Patient 2, 36-year-old male, suffered from progressive ILD and myocarditis. Patient 3, 47-year-old male, had debilitating myositis. All patients were unresponsive to at least three immunosuppressants including rituximab.

Results: Blinatumomab induced complete depletion of $CD19^+$ B cells in circulation and muscle tissue (Figure 2) and profound decreases in anti-Jo-1 titers. Blinatumomab induced glucocorticoid-free remission with normalization of muscle enzymes, improvement of muscle strength (Figure 1) in all patients.

Patient 1 showed an increase in CD19+ B cells and recurrence of myositis 4 months after blinatumomab. We re-started blinatumomab plus RTX and reinduced clinical remission followed by maintenance therapy with RTX (follow-up six months).

Patient 2 showed ongoing remission of myositis and improvement of ILD for six months after blinatumomab and repeated RTX.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient 3 demonstrated ongoing remission for 6 months after blinatumomab and RTX.

Adverse events: cytokine release syndrome (CRS) grade 3 (same day recovery) and respiratory infection in patient 3. No neurotoxicity occurred.

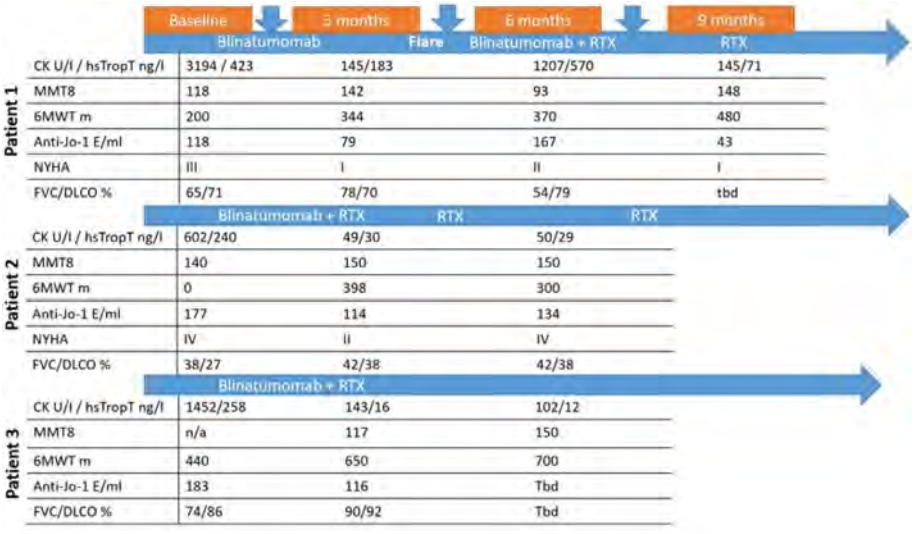


Figure 1: Clinical and serological follow-up including schedule of maintenance treatment

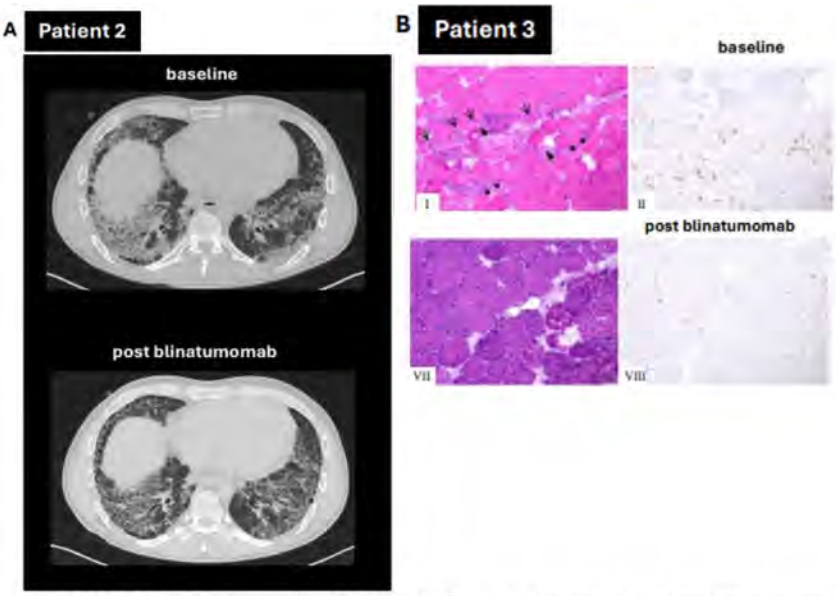


Figure 2: A: Radiologic comparison of ILD in HRCT at baseline (upper) and post blinatumomab. (lower). **B:** Histology of muscle biopsy at baseline I – II and post blinatumomab VII – VIII. **I)** H&E, magnification 200x. Perimysial and endomysial round cell infiltrates (arrows) as well as preferential perifascicular atrophy of muscle fibers (asterisk). In addition, muscle fiber necrosis (arrowhead) and regenerating muscle fibers (dots). **II)** Immunohistochemistry with anti-CD8 and slight counterstaining with hemalum, magnification 200x. Numerous CD8-positive T cells in the perimysial and endomysial infiltrate. **VII)** H&E, magnification 200x. After therapy, there are only minor signs of perifascicular atrophy. Pronounced round cell infiltrates, fiber necrosis or myophagic reactions are no longer present. **VIII)** Immunohistochemistry with anti-CD8 and slight counterstaining with hemalum, magnification 200x. Single CD8-positive T cells in the perimysial and endomysial infiltrate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This is the first report on treating patients with severe, treatment-refractory ASyS with blinatumomab. When followed by RTX, glucocorticoid-free remission remained stable for up to 10 months follow-up. Combining blinatumomab with RTX may offer potential in treatment-refractory ASyS patients.

Disclosure: C. Duesing: None; **A. Stuetz**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **L. Lahu**: None; **F. Deicher**: None; **G. Chehab**: None; **J. Richter**: None; **M. van Saan**: None; **B. Tümerdem**: None; **A. Matei**: None; **B. Buehring**: None; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6; **M. Hagen**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **W. Merkt**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, Evotec, 5, Glapagos, 12, support for congress travel, Kyverna, 6, Lilly, 12, support for congress travel; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6.

Abstract Number: 1199

Interstitial Lung Disease in Systemic Autoimmune Rheumatic Diseases (SARDs): Radiologic and Histologic Correlations

Darya S. Jalaledin[1], Aidan pye[2], Angela Chang[2], Navid Saleh[2], Saud AlHajeri[3], Beatrice Daviault[4], Arusa Shah[5], Sabrina Hoa[6], Océane Landon-Cardinal[7], Alec Yu[2], Robert Levy[8], Jennifer Wilson[9], Charles Poirier[4], James Choi[2], John Yee[2], Hyein Kim[2] and Kun Huang[10], [1]Université de Montréal, Saint-Lambert, QC, Canada, [2]University of British Columbia, VANCOUVER, BC, Canada, [3]University of British Columbia, Vancouver, Canada, [4]University of Montreal, Montreal, QC, Canada, [5]University of Montreal, Montreal, BC, Canada, [6]University of Montreal, Brossard, QC, Canada, [7]Centre hospitalier de l'Université de Montréal, Montréal, QC, Canada, [8]University of British Columbia, Deerfield, IL, [9]UBC, Vancouver, BC, Canada, [10]University of British Columbia, Vancouver, Surrey, BC, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic autoimmune rheumatic diseases (SARDs) are a major cause of interstitial lung disease (ILD), with high prevalence in inflammatory idiopathic myopathy (IIM), systemic sclerosis (SSc), and rheumatoid arthritis (RA). In clinical practice, ILD assessment relies primarily on high-resolution CT (HRCT), as surgical lung biopsy is infrequently performed in SARDs-ILD. This study aims to evaluate the correlation between radiologic patterns at diagnosis and histopathologic findings in explanted lung tissue from SARDs-ILD patients undergoing lung transplantation.

Methods: Patients with ILD secondary to IIM, SSc, or RA who underwent lung transplantation between January 1, 2014 and April 30, 2024 at Vancouver General Hospital and between January 1, 2012 and December 31, 2024 at the Centre hospitalier de l'Université de Montréal were included. Agreement between HRCT and histologic diagnoses was assessed using kappa (κ) statistics with predefined coefficient weights: complete agreement (same diagnoses, κ=1), partial agreement (overlapping terms, for example, NSIP vs. NSIP/UIP κ=0.5), or no agreement (different terms, κ=0). The HRCT-histopathology relationship was visualized using an Alluvial chart (*Flourish, UK*).

Results: The study included 70 patients (18 IIM, 24 SSc, and 28 RA) (Table 1). RA patients were older at transplant, more likely to have a smoking history, and less likely to be female compared to IIM and SSc. IIM patients were more likely to require emergency lung transplant. At initial presentation, nonspecific interstitial lung disease (NSIP) was the predominant HRCT

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pattern in IIM (55.6%) and SSc (75%) patients, while usual interstitial lung disease (UIP) was most common in RA (57.1%) (Table 2). On explant pathology, NSIP remained the primary tissue diagnosis in SSc (62.5%), followed by mixed NSIP/UIP (20.8%) and UIP (12.5%). In RA, UIP was the most frequent histopathologic pattern (50%), followed by mixed NSIP/UIP (25%) and NSIP (17.9%) (Table 2). Cohen's κ analysis with custom coefficient weight demonstrated moderate agreement between HRCT and histology for SSc (κ = 0.42, p=0.02) and RA (κ = 0.46, p=0.002). In contrast, IIM showed insignificant correlation (κ = 0.14, p=0.4), with explant pathology distributed across all six diagnostic patterns. Notably, 50% of IIM patients undergoing transplant had anti-MDA5 dermatomyositis with rapidly progressive ILD clinically, and either diffuse alveolar damage (DAD) or unclassifiable end stage fibrosis on explant.

Conclusion: This study demonstrates moderate radiologic-histologic correlation in SSc- and RA-associated ILD. However, IIM-ILD shows significant histopathologic heterogeneity that poorly correlates with HRCT patterns, particularly in anti-MDA5 positive patients who uniformly exhibited rapidly progressive ILD with diffuse alveolar damage. The major limitation of the study is that explant lungs often have extensive damage from chronic disease and infections, obscuring the original histologic pattern. Despite the limitation, these findings highlight the dynamic radiologic and histologic evolution of ILD in IIM-ILD.

Table 1. Baseline patient demographics pre-transplant.

Table 1. Baseline patient demographics pre-transplant.

Variables	IIM (n=18)	SSc (n=24)	RA (n=28)
Demographics			
Age at SARD diagnosis, median [IQR]	46.4 [40.0, 51.0]	46.0 [38.9, 56.4]	52.5 [40.6, 58.9]
Age at ILD Diagnosis, median [IQR]	46.4 [39.6, 51.1]	48.5 [40.2, 55.8]	56.0 [49.2, 60.9]
Age at lung transplant, mean [IQR]	53.4 [48.2, 58.5]	57.2 [47.7, 62.1]	62.5 [54.7, 68.2]
Female, n (%)	13 (72)	15 (63)	11 (39)
White, n (%)	15 (83)	16 (67)	26 (93)
Smoker, n (%)	9 (50)	9 (38)	21 (75)
BMI, median [IQR]	28.4 [21.6, 32.4]	25.1 [22.2, 29.9]	28.5 [25, 30]
Charlson Comorbidity index, median [IQR]	2 [1.2, 3]	2 [1, 3]	3 [2, 4]
Emergency transplant, n (%)	10 (56)	5 (21)	10 (36)

Table 2. Radiologic pattern at ILD diagnosis and histologic findings in explanted lungs.

Table 2. Radiologic pattern at ILD diagnosis and histologic findings in explanted lungs.

Variables	IIM (n=18)	SSc (n=24)	RA (n=28)
Radiographic ILD pattern			
UIP, n (%)	2 (11.1)	3 (12.5)	16 (57.1)
NSIP, n (%)	10 (55.6)	18 (75)	8 (28.6)
OP, n (%)	4 (22.2)	0 (0)	1 (0)
Mixed UIP/NSIP, n (%)	1 (5.6)	2 (8.3)	2 (7.1)
Mixed OP/NSIP, n (%)	1 (5.6)	1 (4.2)	0 (0)
Other, n (%)	0 (0)	0 (0)	1 (3.6)
Histologic ILD diagnosis			
UIP, n (%)	3 (16.7)	3 (12.5)	14 (50)
NSIP, n (%)	5 (27.8)	15 (62.5)	5 (17.9)
OP, n (%)	1 (5.6)	0 (0)	0 (0)
Mixed UIP/NSIP, n (%)	1 (5.6)	5 (20.8)	7 (25)
Mixed OP/NSIP, n (%)	1 (5.6)	0 (0)	2 (7.1)
DAD, n (%)	5 (27.8)	0 (0)	0 (0)
Other, n (%)	2 (11.1)	1 (4.2)	0 (0)
κ with custom coefficient weight, 95% CI	0.14 [-0.11, 0.39]	0.42 [0.039, 0.80]	0.46 [0.19, 0.74]
p value	0.40	0.02	0.002

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

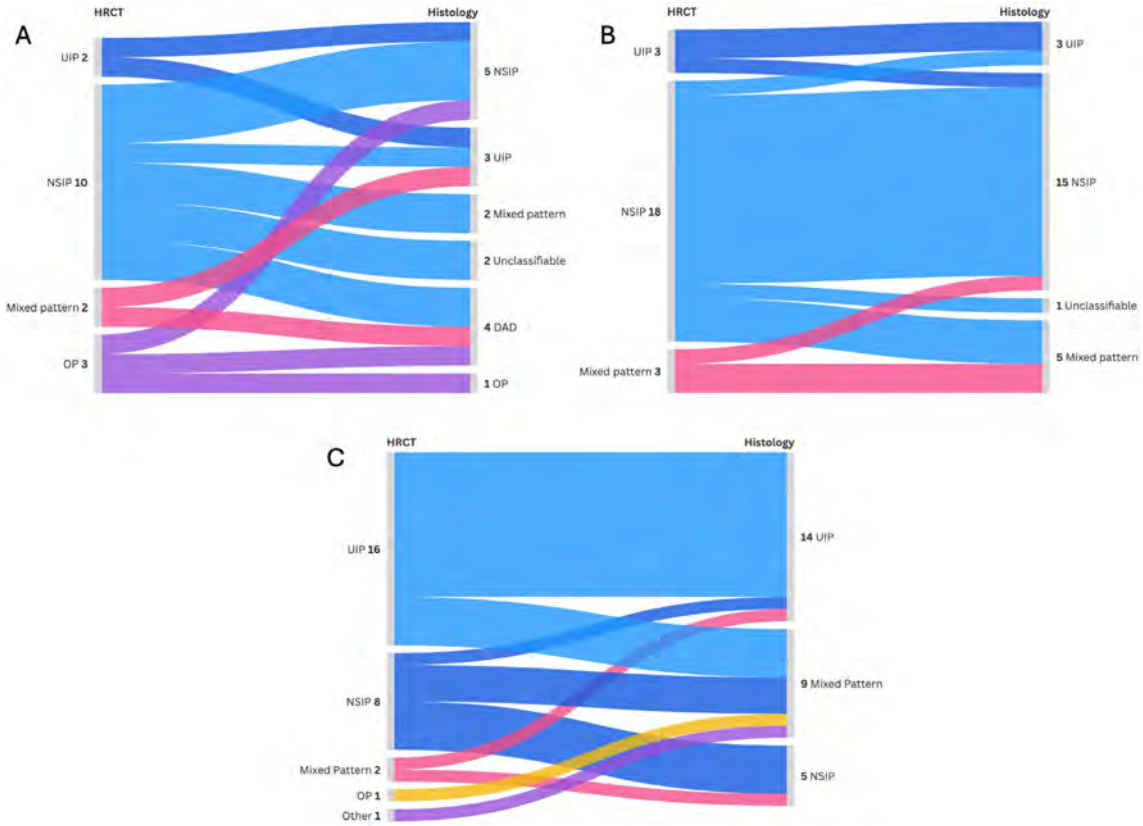


Figure 1. Alluvial chart for correlation between radiologic patterns and histopathologic findings in IIM (A), SSc (B), and RA (C).

Disclosure: D. S. Jalaledin: None; **A. pye**: None; **A. Chang**: None; **N. Saleh**: None; **S. AlHajeri**: None; **B. Daviault**: None; **A. Shah**: None; **S. Hoa**: None; **O. Landon-Cardinal**: None; **A. Yu**: None; **R. Levy**: None; **J. Wilson**: None; **C. Poirier**: None; **J. Choi**: None; **J. Yee**: None; **H. Kim**: Fresenius Kabi, 6; **K. Huang**: AbbVie/Abbott, 6, Fresenius Kabi, 6, Novartis, 6, Pfizer, 5.

Abstract Number: 1200

Mortality in Idiopathic Inflammatory Myopathy in the Toulouse cohort (MIIRTALITY)

Aurore Larrauffie[1], Chloé Bost[1], Marie Faruch[1], Claire Barrier[1], Jérémy Zordan[1], Marie Guille[1], Grégoire Prevot[1], Thomas Villeneuve[1], Morgane Mourguet[1], Laurent Alric[1], Laurent Sailler[1], Martin Michaud[1], Sébastien De Almeida Chaves[1] and **Grégory Pugnet**[2], [1]CHU Toulouse, Toulouse, France, [2]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic Inflammatory Myopathies (IIM) are a group of heterogeneous connective tissue diseases including dermatomyositis (DM), polymyositis (PM), anti-synthetase syndromes (ASS), immune-mediated necrotizing myopathies (NM), and overlap syndromes (OS). These diseases are the most severe connective tissue diseases, with a high mortality rate of 30%. These diseases represent the connective tissue disorders with the highest mortality risk compared to the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

general population, with reported standardized mortality ratios ranging from 1.56 to 7. No study has evaluated the SMRs for OS and IMNM.

The aim of this study was to evaluate the comparative mortality figure in IIM and its subgroups in a real-life setting.

Methods: A retrospective study was conducted using the MIIRTALITY cohort, including patients followed for IIM from 2010 to 2022. Patients were included if they had more than one year of follow-up or early death, were diagnosed between 2010 and 2020, and met the 2017 EULAR and/or 2019 ENMC classification criteria. They were then categorized into five subgroups: DM, PM, ASS, NM, and OS.

Crude mortality rates were calculated for the study population, and expected mortality rates were obtained from the French National Institute of Statistics and Economic Studies (INSEE). Comparative Mortality Figures (CMFs) were computed as the ratio of observed to expected deaths, adjusting for differences in age structure between the study and reference populations. CMFs were preferred over standardized mortality ratios (SMRs) due to the limited size of the IIM subgroups.

Results: A total of 225 patients were included: 83 with dermatomyositis (DM; 36.9%), 14 with polymyositis (PM; 6.2%), 55 with antisynthetase syndrome (ASS; 24.4%), 24 with immune-mediated necrotizing myopathy (IMNM; 10.7%), and 49 with overlap syndrome (OS; 21.8%). The median age at diagnosis was 59 years [IQR 46–69], with a predominance of female patients (n = 133, 59.1%). The median follow-up duration was 4 years [IQR 2–7]. An associated malignancy was identified in 29 patients (12.8%).

During follow-up, 33 patients died, corresponding to an overall mortality rate of 14.7%. The Comparative Mortality Figure (CMF) for the total IIM cohort was 3.49 (95% CI: 2.25–5.40). CMFs by subgroup were as follows: DM, 5.45 (95% CI: 3.42–8.67); PM, 24.23 (95% CI: 3.89–151.08); ASS, 1.51 (95% CI: 0.48–4.79); IMNM, 1.44 (95% CI: 0.35–5.90); and OS, 2.58 (95% CI: 1.14–5.89).

Conclusion: Patients with DM, PM, and OS demonstrated a significantly increased risk of mortality compared to the general population. No excess mortality was observed in patients with ASS or IMNM.

Disclosure: A. Larrauffie: None; **C. Bost**: None; **M. Faruch**: None; **C. Barrier**: None; **J. Zordan**: None; **M. Guille**: None; **G. Prevot**: None; **T. Villeneuve**: None; **M. Mourguet**: None; **L. Alric**: None; **L. Sailler**: None; **M. Michaud**: None; **S. De Almeida Chaves**: None; **G. Pugnet**: None.

Abstract Number: 1201

Prognostic Significance of 1-Year Pulmonary Function Changes in Myositis-Associated Interstitial Lung Disease

Shiri Keret[1], Silvia Martinez Laverde[2], **Irada Choudhuri**[2], Raisa Lomanto Silva[3], Eugenia Gkiaouraki[2], Tanya Chandra[2], Nantakarn Pongtarakulpanit[4], Shreya Sriram[2], Niladri Bhowmick[2], Vaidehi Kothari[2], Kaushik Sreerama Reddy[2], Eaman Alhassan[5], Anushka Aggarwal[6], Maha Almackenzie[7], Daniel Sullivan[2], Sara Faghihi-Kashani[8], Koichi Yamaguchi[2], Daniel Kass[2], Kevin Gibson[2], Dana Ascherman[9], Siamak Moghadam-Kia[5], Chester V. Oddis[9] and Rohit Aggarwal[10], [1]Bnai Zion Medical Center, Atlit, Israel, [2]University of Pittsburgh Medical Center, Pittsburgh, [3]Massachusetts General Hospital, Boston, MA, [4]Mahidol University, University of Pittsburgh, Bangkok, Thailand, [5]University of Pittsburgh Medical Center, Pittsburgh, PA, [6]Indraprastha Apollo Hospital, New Delhi, India, [7]Medical Cities of the Ministry of the Interior, Riyadh, Saudi Arabia, [8]UCSF, Mountain View, CA, [9]University of Pittsburgh, Pittsburgh, PA, [10]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lung involvement is the most frequent and severe extramuscular complication of Idiopathic Inflammatory Myopathy (IIM). The utility of pulmonary function test (PFT) monitoring for predicting long-term outcomes in IIM-associated interstitial lung disease (IIM-ILD) and assessing treatment efficacy in clinical trials remains unclear.

We aimed to evaluate the association between 1-year changes in PFTs and long-term outcomes, including 10-year mortality and lung transplant, in patients with IIM-ILD.

Methods: A prospective cohort of adult IIM-ILD patients was analyzed retrospectively. ILD was defined as per ATS criteria using chest HRCT, and myositis was classified according to either myositis-specific autoantibodies and/or the 2017 EULAR/ACR IIM classification criteria. Baseline was defined as the first rheumatology visit. Inclusion criteria required baseline and follow-up PFTs 6–18 months apart. Changes in forced vital capacity (FVC)% and diffusing capacity (DLCO)% were calculated as annualized values: [ΔFVC or ΔDLCO ÷ interval in months] × 12. Cox regression identified associations between PFT trends and outcomes, adjusting for age, sex, smoking, baseline FVC%, and interval from baseline to the first PFT. Kaplan-Meier analysis compared survival by FVC% trends, HRCT patterns, and IIM subsets.

Table 1. Association of One-Year FVC Change and Baseline DLCO with 10-Year Mortality and Transplant-Free Survival in IIM-ILD. Univariate Cox regression analysis showing that absolute and relative FVC declines ≥5% were significantly associated with increased mortality and adverse outcomes. Baseline DLCO was also a strong predictor of transplant-free survival.

Table 1. Univariate analysis of the association between **FVC** estimated change over a year and baseline **DLCO** and 10-year mortality or pulmonary event-free survival (all-cause death or lung transplant).

Variable	10-year Mortality				Lung-transplant or mortality			
	Number of events	Hazard Ratio	95% Confidence Interval	P value	Number of events	Hazard Ratio	95% Confidence Interval	P value
Baseline FVC% (n=149)	38	0.98	0.96-0.99	**0.016**	**39**	**0.97**	**0.96-0.99**	**0.004**
FVC **relative** change at 1 year (n=149)	38	0.99	0.98-1.01	0.18	39	0.99	0.98-1.01	0.28
FVC **relative** decline ≥ 15% (n=22)	11	2.96	1.47-5.98	**0.002**	11	2.75	1.37-5.53	**0.005**
FVC **relative** decline ≥ 12.5%, (n=29)	13	2.59	1.33-5.08	**0.005**	13	2.47	1.27-4.83	**0.008**
FVC **relative** decline ≥ 10%, (n=36)	16	2.83	1.49-5.40	**0.002**	16	2.67	1.41-5.06	**0.003**
FVC **relative** decline ≥ 7.5%, (n=41)	16	2.44	1.28-4.65	**0.007**	16	2.29	1.21-4.34	**0.011**
FVC **relative** decline ≥ 5% (n=54)	19	2.01	1.06-3.80	**0.03**	19	1.87	0.999-3.52	**0.050**
FVC **relative** decline ≥ 2.5% (n=67)	21	1.81	0.95-3.43	0.07	21	1.65	0.88-3.11	0.12
FVC **relative** decline ≤ -2.5% or any improvement (n=81)	17	0.55	0.29-1.05	0.07	18	0.61	0.32-1.14	0.12
FVC **absolute** change at 1 year (n=149)	38	0.98	0.96-1.003	0.08	39	0.98	0.96-1.003	0.096
FVC **absolute** decline ≥ 15% (n=11)	3	1.17	0.36-3.80	0.79	3	1.10	0.34-3.59	0.87
FVC **absolute** decline ≥ 12.5% (n=17)	7	2.19	0.96-4.98	0.06	7	2.05	0.91-4.66	0.09
FVC **absolute** decline ≥ 10% (n=25)	10	2.12	1.03-4.38	**0.04**	10	1.99	0.97-4.09	0.06
FVC **absolute** decline ≥ 7.5% (n=34)	14	2.45	1.27-4.75	**0.008**	14	2.32	1.20-4.47	**0.012**
FVC **absolute** decline ≥ 5% (n=45)	16	2.03	1.06-3.87	**0.03**	16	1.90	1.004-3.61	**0.048**
FVC **absolute** decline ≥ 2.5% (n=60)	20	2.01	1.06-3.80	**0.03**	20	1.84	0.98-3.46	0.057
FVC **absolute** decline ≤ -2.5% or any improvement (n=89)	18	0.49	0.26-0.94	**0.03**	19	0.54	0.29-1.02	0.057
Baseline **DLCO**% (n=136)	35	0.97	0.95-0.99	**0.001**	36	0.96	0.94-0.98	**<0.001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

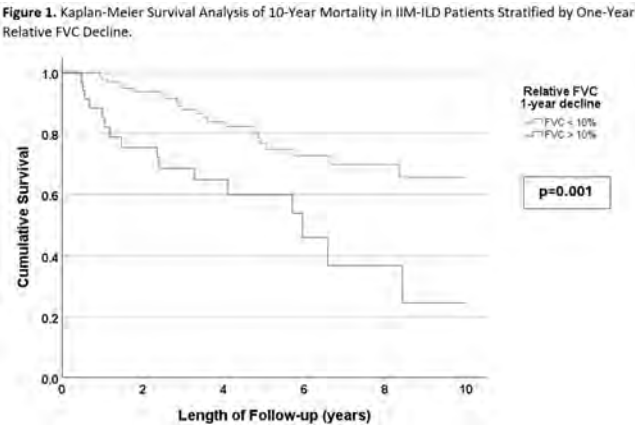


Figure 1. Kaplan-Meier Survival Curves Stratified by One-Year Relative FVC Decline in IIM-ILD. Patients with ≥10% relative FVC decline demonstrated significantly worse 10-year survival.

Results: The study included 149 patients (mean age 50.5 ± 12.9 years, 63% female, 85% White). Based on serology, ASyS was the most frequent IIM subset (73.2%), followed by dermatomyositis (10.7%) and polymyositis (8.7%). Mean baseline FVC was 67.5 ± 19.3%, and DLCO was 54.2 ± 19.4%. The HRCT ILD pattern was nonspecific interstitial pneumonia (NSIP) in 85 (57.0%) patients, usual interstitial pneumonia (UIP) in 31 (20.8%) and organizing pneumonia in 2 (1.4%). After a median follow-up of 4.4 years, 41 (27.5%) had died and 6 (4%) had undergone lung transplant.

Both absolute and relative FVC declines of ≥5% over 1 year were significantly associated with higher mortality (HR 2.03 and 2.01; [p=0.03]) and lower transplant-free survival (HR 1.90 [p=0.048] and 1.87 [p=0.050]). Relative FVC declines ≥10% or ≥15% over 1 year showed even stronger associations with mortality (HR 2.83 [p=0.002] and 2.96 [p=0.002], respectively). Conversely, stable or improved absolute FVC was linked to lower mortality (HR=0.49, p=0.04). Baseline DLCO, but not its subsequent decline, was associated with transplant-free survival (HR 0.96, p< 0.001) (**Table 1**). Multivariate analysis revealed similar results. Survival was significantly worse among patients with relative FVC decline > 5%, > 7.5%, >10%, >12.5%, and > 15% (p< 0.05) (**Figure 1**). No significant differences in survival were observed between ASyS and other IIM subsets, or UIP and other HRCT patterns.

Conclusion: FVC decline, even at a threshold as low as 5%, is a significant predictor of long-term mortality and lung transplant in IIM-ILD. However, the 10% threshold, showing stronger associations with outcomes, should be incorporated as an outcome measure in IIM-ILD clinical trials. Routine PFT monitoring from IIM-ILD provides valuable prognostic information, enabling improved risk stratification and individualized treatment planning.

Disclosure: S. Keret: None; **S. Martinez Laverde**: None; **I. Choudhuri**: None; **R. Lomanto Silva**: None; **E. Gkiaouraki**: None; **T. Chandra**: None; **N. Pongtarakulpanit**: None; **S. Sriram**: None; **N. Bhowmick**: None; **V. Kothari**: None; **K. Sreerama Reddy**: None; **E. Alhassan**: None; **A. Aggarwal**: None; **M. Almackenzie**: None; **D. Sullivan**: None; **S. Faghihi-Kashani**: None; **K. Yamaguchi**: None; **D. Kass**: None; **K. Gibson**: None; **D. Ascherman**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1202

High Prevalence of Asymptomatic Interstitial Lung Disease in Idiopathic Inflammatory Myopathies: Validation of ACR/CHEST Risk Factors in a Hong Kong Cohort

Ka Ki Yam[1], Lucas Tsz Ho Luk[1], Weng Nga Lao[2], Chiu Wai Shirley Chan[3], Dennis Tin Ho Chan[4], Billy Tin Lok Lai[5], Roy Tsz Chung Ho[6], Vivian Hoi Shan Tang[7], Ho So[8] and **Iris Tang**[9], [1]Department of Medicine & Geriatrics, Hong Kong, Hong Kong, [2]Department of Medicine & Geriatrics, Kwong Wah Hospital, Hong Kong, Hong Kong, [3]Division of Rheumatology and Clinial Immunology, Department of Medicine, the University of Hong Kong, Hong Kong, Hong Kong, China, [4]Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong, Hong Kong, [5]Department of Medicine, Tseung Kwan O Hospital, Hong Kong, Hong Kong, [6]Department of Medicine, Queen Elizabeth Hospital, Hong Kong, Hong Kong, [7]Department of Medicine, North District Hospital, Hong Kong, Hong Kong, [8]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, Hong Kong, [9]Department of Medicine, LKS Faculty of Medicine, University of Hong Kong, Hong Kong, Hong Kong

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a common and severe complication of idiopathic inflammatory myopathies (IIM), adversely impacting clinical outcomes. While the ACR/CHEST guideline recommends ILD screening in IIM patients with specific risk factors (Table 1), validation of these predictors in diverse populations remains limited. This study evaluated the utility of ACR/CHEST risk factors for ILD development in a Hong Kong IIM cohort (MyoHK).

Methods: MyoHK was a multicentre observational cohort that collected longitudinal data from IIM patients from 7 rheumatology centers in Hong Kong. IIM patients with at least 6 months of follow-up data were analyzed after excluding patients with unknown myositis-specific or myositis-associated antibodies (MSA/MAA). Data was reviewed from Jan 2024 to Feb 2025. Demographic, clinical, and serological data at IIM diagnosis were recorded. ILD was confirmed by compatible CT thorax findings or histology. The time between IIM and ILD diagnosis was determined. Multivariable regression was performed to identify the independent predictors of ILD.

Results: A total of 665 patients were analyzed and 503 (75.6%) had at least one clinical or serological risk factor for developing ILD at IIM diagnosis. More than half (53.7%) of IIM patients had ILD and 28.6% had no respiratory symptoms including cough, dyspnoea, or Velcro crackles at onset (Figure 1). There were more female patients in the IIM-ILD group (73.3% vs 63.6%, p=0.007) but there was no difference between mean age at diagnosis (55.6 ± 12.5 vs 56.7 ± 15.8, p=0.35) and median follow-up duration (73 (interquartile range: 27 – 130.5) vs 54 (27 – 131) months, p=0.651). Over 60% of ILD were diagnosed within 6 months of IIM diagnosis but ILD preceded IIM diagnosis in 62 (17.4%) patients.

Table 1. Risk factors for ILD screening in 2023 ACR/CHEST guideline [1]

Clinical Risk factors	Arthritis / Arthralgia, Ulcerative Lesions, Mechanic's hands
Serological Risk factors	Anti-synthetase (Jo-1, PL7, PL12, EJ, OJ, KS, Ha, Zo), anti-MDA5, anti-Ku, anti-Pm/Scl, anti-Ro52 antibody positivity

Reference 1: Johnson SR, Bernstein EJ, Bolster MB, et al. 2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) Guideline for the Screening and Monitoring of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases. *Arthritis Care Res (Hoboken)*. 2024;76(8):1070-1082.

Risk factors for ILD screening in 2023 ACR/CHEST guideline

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Baseline Characteristics of IIM patients

Table 2. Baseline Characteristics of IIM patients

	With ILD (n=357)	Without ILD (n=308)	p-value
Age at diagnosis, Mean ± SD	55.65 +- 12.30	56.67 +- 15.82	0.350
Female sex, n (%)	262 (73.3%)	196 (63.6%)	0.007
Clinical subtypes			
Dermatomyositis	72 (20.2%)	141 (45.8%)	<0.001
Amyopathic dermatomyositis	80 (22.4%)	38 (12.3%)	<0.001
Anti-synthetase syndrome	15 (4.2%)	63 (20.5%)	<0.001
Anti-MDA5+	100 (28.0%)	9 (2.9%)	<0.001
Anti-Jo1+	85 (23.8%)	9 (2.9%)	<0.001
Anti-PL7+	40 (11.2%)	16 (5.2%)	0.005
Anti-PL12+	20 (5.6%)	8 (2.6%)	0.054
Anti-OJ+	14 (3.9%)	5 (1.6%)	0.076
Anti-EJ+	26 (7.3%)	4 (1.3%)	<0.001
Anti-Ro52+	224 (62.7%)	89 (28.9%)	<0.001
Anti-Ku+	19 (5.3%)	21 (6.8%)	0.418
Anti-PM/Scl+	15 (4.2%)	23 (7.5%)	0.07
Dyspnea	290 (81.2%)	57 (18.5%)	<0.001
Cough	206 (57.7%)	33 (10.7%)	<0.001
Respiratory crackles	267 (74.8%)	26 (8.4%)	<0.001
Arthritis	206 (57.7%)	67 (21.8%)	<0.001
Ulcerative lesions	46 (12.9%)	5 (1.6%)	<0.001
Mechanic's hands, n	90 (25.2%)	15 (4.9%)	<0.001
Raynaud's phenomenon	64 (17.9%)	24 (7.8%)	<0.001
Fever on presentation	127 (35.6%)	34 (11.0%)	<0.001
≥1 Clinical Risk factors	259 (72.5%)	77 (25%)	<0.001
≥1 Serological risk factors	320 (89.6%)	141 (45.8%)	<0.001
Absence of risk factors	19 (5.3%)	143 (46.4%)	<0.001
Presented in absolute number (percentage) unless otherwise specified.			

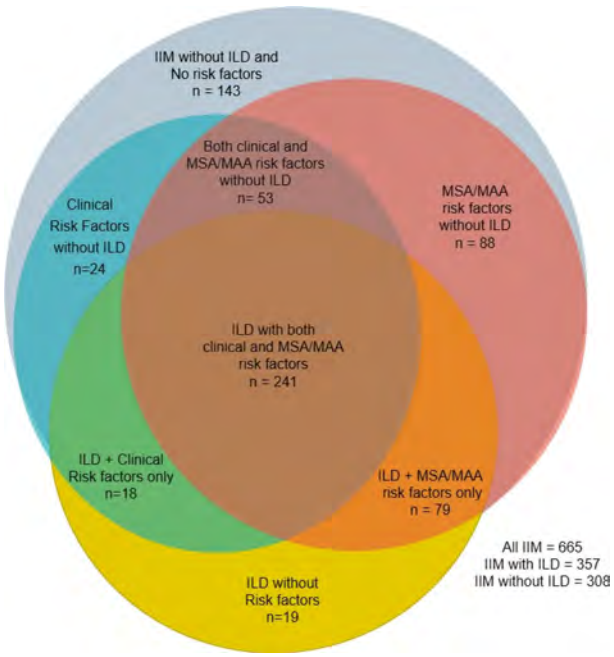


Figure 1. Distribution of clinical and serological risk factors and occurrence of ILD among IIM patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Arthritis (57.7% vs 21.8%, p< 0.001), ulcerative lesions (12.9% vs 1.6%, p< 0.001), and mechanic's hands (25.2% vs 4.9%, p< 0.001) were more common in IIM-ILD group (Table 2). Regarding MSA/MAA status, antibodies against MDA5 (28.0% vs 2.9%, p< 0.001), Jo1 (23.8% vs 2.9%), PL7 (11.2% vs 5.2%, p=0.005), EJ (7.3% vs 1.3%, p< 0.001) and Ro52 (62.7% vs 28.9%, p< 0.001) were more frequently identified among ILD patients. Independent risk factors for ILD development in line with the ACR/CHEST guideline included anti-MDA5 positivity (Odds ratio (OR):12.3, 95% CI: 4.8 - 31.0), anti-Jo1 positivity (OR: 6.8, 95% CI: 2.7 – 12.2), anti-EJ positivity (OR: 5.7, 95% CI: 1.37 – 23.6), anti-Ro52 positivity (OR: 2.8, 95% CI: 1.7 – 4.6), mechanic's hands (OR: 2.5, 95% CI: 1.1 – 5.7) and arthritis (OR: 1.8, 95%CI:1.1 – 3.2). Fever (OR: 2.27, 95% CI = 1.5 – 4.9) and Raynaud's phenomenon (OR: 2.1, 95%CI: 1.0 – 4.4) were identified as additional risk factors for ILD development. Only 5.3% of ILD patients lacked guideline-recommended risk factors.

Conclusion: The study validated the risk factors from ACR/CHEST guidelines in IIM patients in Hong Kong. However, the absence of respiratory symptoms or guideline-specified risk factors could not exclude the possibility of ILD, underscoring the need for clinical vigilance.

Disclosure: K. Yam: None; **L. Luk**: None; **W. Lao**: None; **C. Chan**: None; **D. Chan**: None; **B. Lai**: None; **R. Ho**: None; **V. Tang**: None; **H. So**: None; **I. Tang**: None.

Abstract Number: 1203

Rituximab in Treatment Refractory vs Treatment Naive Anti Signal Recognition Particle (SRP) Myositis A Case Series

Israrul Haque[1] and Parasar Ghosh[2], [1]Institute of Postgraduate Medical Education and Research(IPGMER), KOLKATA, India, [2]Dept of Clinical Immunology and Rheumatology, IPGMER & SSKM HospitalGovt of West Bengal, Kolkata, India, Kolkata, West Bengal, India

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-Signal Recognition Particle (Anti-SRP) Myositis is a form of Polymyositis. Available consensus guidelines recommend initial combination therapy of high dose corticosteroids and Methotrexate and addition of Rituximab (RTX) within 6 months of starting therapy.

Methods:

Objectives:

1. Comparison of non-rituximab vs Rituximab therapy in treatment naïve Anti-SRP Myositis patients.

2. Comparison of Rituximab in Treatment refractory vs Treatment naïve anti-SRP Myositis patients.

Methods: It is a Single centre retrospective study. Patients satisfying EULAR/ACR classification criteria for Idiopathic Inflammatory Myopathy AND anti-SRP antibody in moderate to high titer were defined as cases. Patients with concomitant presence of any other Myositis specific antibody (MSA) in moderate to high titer were excluded. Complete remission (CR) was defined as MMT increase of ≥ 20% *from baseline in Manual Muscle testing* (*MMT* —— 8) AND normalisation of CPK while

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table: 1 Comparison of Initial Rituximab vs Initial non-Rituximab Therapy for Treatment Naïve SRP Myositis Patients

Table: 1 Comparison of Initial Rituximab vs Initial non-Rituximab Therapy for Treatment Naïve SRP Myositis Patients

	Initial Rituximab therapy Group (n=5)	Initial Non-Rituximab Group (n=8)	't' value, df	P value
Mean Age (SD), years	36.40 ±11.93	36.63 ± 10.98	0.035, df=11	0.973, NS
Female sex	5/5 (100%)	4/8 (50%)	Z value= 1.900	0.057, NS
Complete remission at 6 months (%)	5/5 (100%)	3/8 (37.5%)	Z value= 2.2535	**0.024*, Significant**
Partial Remission at 6 months (%)	0	5/8 (62.5%)	Z value=-2.2535	**0.024*, Significant**
Mean disease duration in months prior to starting corticosteroid or Any Immunosuppressive Therapy (SD)	5.00 ± 2.00	4.63 ± 1.69	0.364, df=11	0.723, NS
Mean MMT-8 at baseline (SD)	90.20 ± 8.07	88.63 ± 19.48	0.170, df=11	0.868, NS
Mean MMT-8 at 6 Months (SD)	108.80 ± 14.81	106.63 ± 19.88	0.210, df=11	0.838, NS
Mean MMT-8 increase at 6 months	18.60 ± 6.84	18.13 ± 2.99	0.175, df=11	0.864, NS
Mean CPK at baseline (SD), Units/Litre (Normal 30-170)	5405.80 ± 2706.57	6123.88 ± 4726.46	-0.307, df=11	0.765, NS
Mean CPK at 6 Months (SD), Units/Litre	111.60 ± 51.51	607.00 ± 922.59	-1.180, df=11	0.263, NS
Mean Initial Prednisolone dose (SD)	58.00 ± 4.47	52.50 ± 13.89	0.846, df=11	0.415, NS
Mean Prednisolone dose at 3 Months (SD), mg/day	20.00 ± 3.06	19.69 ± 2.81	0.189, df=11	0.854, NS
Mean Prednisolone dose at 6 Months (SD), mg/day	11.50 ± 3.35	10.94 ± 2.65	0.337, df=11	0.742, NS

Table 2: Comparison of Rituximab Therapy in Treatment refractory and Treatment naive anti-SRP myositis patients.

Table 2: Comparison of Rituximab Therapy in Treatment Refractory and Treatment Naïve SRP Myositis Patients

	RTX in Treatment Refractory (N=8)	RTX in Treatment Naive (n=5)	't' value, df	P value
Complete remission (CR)at 6 Months	5/8 (62.5%)	5/5 (100%)	Z value=-1.5612	0.118, NS
Partial remission (PR) at 6 Months	3/8 (32.5%)	0	Z value=-1.5612	0.118, NS
Mean MMT-8 at baseline (SD)	95.25 ± 25.82	90.20 ± 8.07	0.4185, df=11	0.683, NS
Mean MMT-8 at 6 Months after RTX (SD)	114.38 ± 20.21	108.80 ± 14.81	0.5311, df=11	0.605, NS
Mean Change in MMT-8 from baseline at 6 months (SD)	16.13 ± 3.31	18.60 ± 6.84	0.884, df=11	0.395, NS
Mean CPK at baseline (SD), Units/liter	2617.50 ± 2507.67	5405.80 ± 2706.57	1.894, df=11	0.084, NS

partial remission was defined as ≥ 20% *increase in MMT* —— 8 but elevated CPK (>2 times of ULN). Patient with ≥ 20% worsening in MMT from highest value and/or > 3 times increase in CPK from lowest value while on standard of care therapy were defined asrefractory cases.

Results: A total of 13 patients of SRP Myositis were included. Out of 13 cases-8 cases initially received Immunosuppressants other than Rituximab (defined as initial non-rituximab therapy group) while 5 cases initially received Rituximab (defined as initial Rituximab Therapy group). In initial non-rituximab therapy group, 3 received Methotrexate, 2 received monthly Cyclophosphamide therapy for 6 months, 2 received Mycophenolate Mofetil and 1 received Azathioprine. All 8 cases relapsed after Complete or partial remission during follow-up and met the criteria of refractory disease. Refractory patients received Inj. Rituximab 1 gm two doses. In initial Rituximab therapy group cases received Rituximab 1 gm two doses and did not receive any other conventional DMARD (C-DMARDs).

Conclusion:

1. Complete remission (CR) at 6 months is higher in initial rituximab therapy group in treatment naïve anti-SRP Myositis patients. However, both groups showed similar improvement in MMT-8, reduction in CPK, and corticosteroid dose reduction at 6 months after starting therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2. RTX therapy is equally effective at 6 months in treatment refractory and treatment naïve patients in terms of improvement in MMT and reduction in CPK. Treatment-naïve patients had significantly greater corticosteroid needs throughout the treatment period.

Disclosure: i. haque: None; **P. Ghosh**: None.

Abstract Number: 1204

Validity and reliability of a new ultrasound-based semiquantitative echogenicity grading scale for myositis.

Takeshi Yoshida[1], Didem Saygin[2] and **Jemima Albayda**[3], [1]Johns Hopkins Hospital, Baltimore, MD, [2]Rush University Medical Center, Chicago, IL, [3]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The Heckmatt grading scale has been widely used as a semiquantitative assessment method for grading muscle echo intensity (EI) on ultrasound; however, this was originally developed for muscular dystrophies in the 1980s. Concerns have been raised regarding poor agreement among assessors and inadequate capture of changes seen with acute myositis. In this study, we test the reliability and construct validity of a new 4-point, semiquantitative grading scale developed for myositis, which defines increases in muscle EI relative to surrounding structures and incorporates changes in muscle architecture that occur with inflammation and damage.

Methods: Ultrasound images of deltoid, biceps brachii, and rectus femoris muscles of myositis patients and controls, obtained from 2015 to 2018 were included in this study. Two experienced raters and one less experienced rater, who had received a two-hour lecture and one training session before the assessment, independently assessed the images. We defined the Hopkins myositis grading scale as follows;

- Grade 1: *Normal - muscle EI equal to or lower than the overlying fat, with clear contrast to perimysial septation and fascia*
- Grade 2: *Mildly Abnormal - muscle EI is slightly increased, may be higher than that of overlying fat layer but lower than that of fascia, but perimysial septations remain well-defined*
- Grade 3: *Moderately Abnormal - muscle EI is high but is still less echogenic than fascia, with loss or blurring of contrast to perimysial septation*
- Grade 4: *Severely Abnormal - muscle EI is very high, equal to or nearly equal to fascia, potentially accompanied by acoustic shadows*

Construct validity was evaluated using Spearman's correlation between each grading system and muscle strength, as well as quantitative muscle EI. Interrater and intrarater reliability were evaluated using Cohen's kappa. Cohen's kappa was interpreted as substantial for 0.60-0.80 and almost perfect for 0.80-1.00.

Results: A total of 349 images from 61 myositis patients (26 inclusion body myositis (IBM) and 35 non-IBM myositis), and 222 images from 37 healthy controls were included. The Hopkins myositis grading scale demonstrated good correlations with both muscle strength and EI, ranging between rho 0.55 - 0.62, better than the Heckmatt scale (Table). In

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

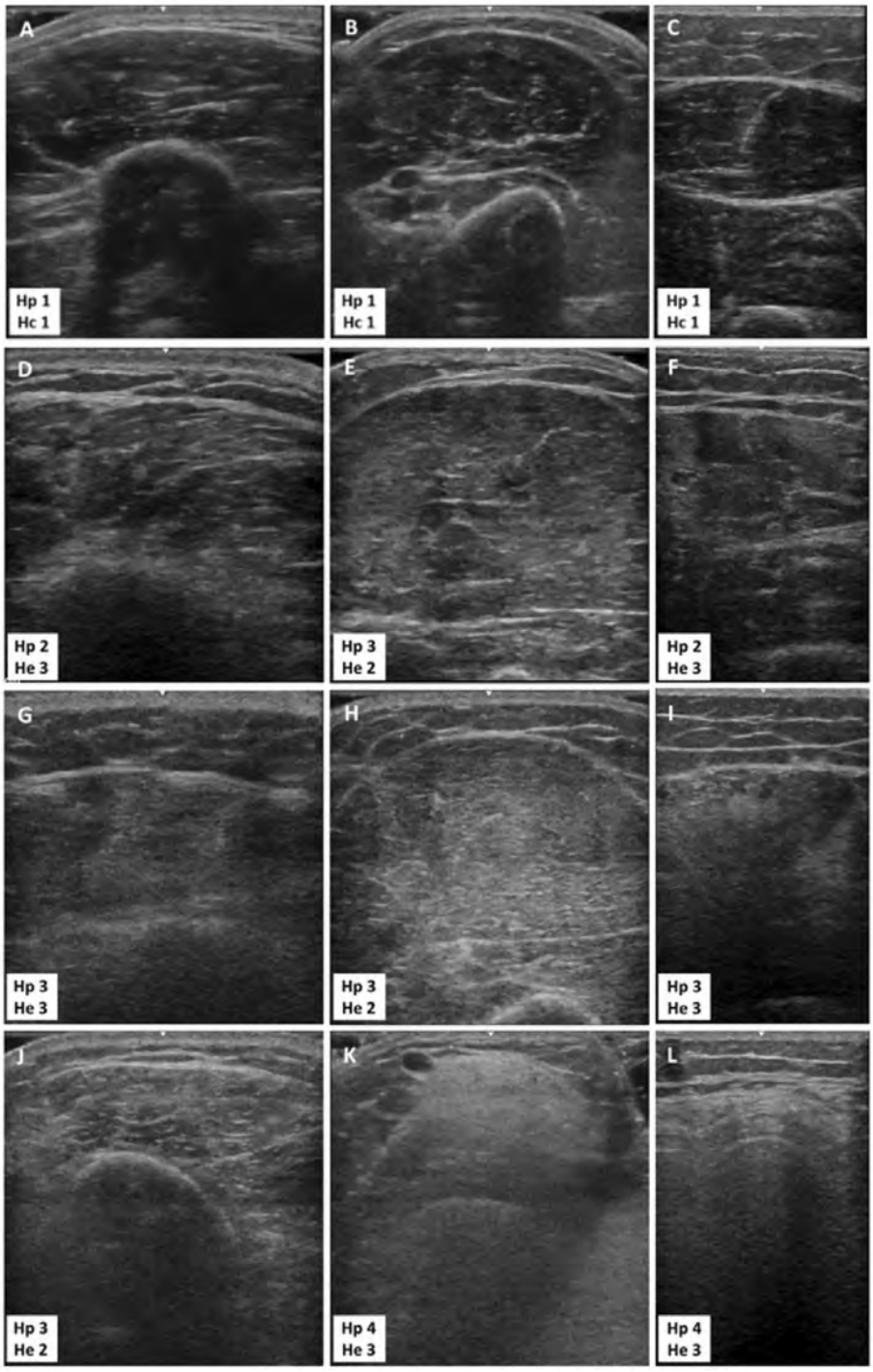


Figure 1. The Hopkins myositis grading scale in healthy controls (A-C) and myositis patients (D-F: immune mediated necrotizing myopathy, G-I: Anti-synthetase syndrome, J-L: inclusion body myositis). A, D, G, J: deltoid. B, E, H, K: biceps brachii. C, F, I, L: rectus femoris. Abbreviation: Hp: the Hopkins myositis grading scale, He: the Heckmatt grading scale.

myositis patients, interrater reliability of the Hopkins myositis grading scale demonstrated substantial agreement (Cohen's kappa 0.62 - 0.65) while the Heckmatt scale had fair agreement (Cohen's kappa 0.28 - 0.36). Similarly, intrarater reliability of the Hopkins myositis grading scale was almost perfect and better than the Heckmatt scale (0.78-0.85 vs 0.67).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Validity and reliability of the Hopkins myositis grading scale and the Heckmatt grading scale.

Subject		Assessment method	Interrater reliability, κ (% agreement)			Intrarater reliability, κ (% agreement)	
			Rater 1/2	Rater 1/3	Rater 2/3	Rater 1	Rater 2
Myositis	Total	Modified Heckmatt	0.62 (75.1)	0.643 (76.3)	0.647 (77.5)	0.846 (89.7)	0.78 (86)
		Heckmatt	0.365 (59.7)	0.358 (57.2)	0.277 (51.1)	0.67 (82.2)	0.669 (80.4)
	Non-IBM	Modified Heckmatt	0.578 (74.2)	0.621 (76.4)	0.592 (75.9)	0.839 (89.9)	0.747 (85.4)
		Heckmatt	0.324 (57.9)	0.388 (59.6)	0.251 (52.7)	0.698 (83.1)	0.575 (77.5)
	IBM	Modified Heckmatt	0.651 (76.2)	0.651 (76.2)	0.704 (79.5)	0.836 (88.9)	0.8 (86.7)
		Heckmatt	0.37 (61.5)	0.281 (53.3)	0.267 (48.4)	0.629 (82.2)	0.738 (83.3)
Healthy control		Modified Heckmatt	0.384 (73.1)	0.445 (77.4)	0.358 (76.3)	0.693 (85.1)	0.551 (82.5)
		Heckmatt	0.242 (53.2)	0.394 (63.4)	0.16 (50.5)	0.667 (79.2)	0.589 (78.9)

Subject	Assessment method	Muscle strength, ρ		QMUS, ρ	
		Rater 1	Rater 2	Rater 1	Rater 2
Total	Modified Heckmatt	-0.569	-0.551	0.626	0.559
	Heckmatt	-0.425	-0.523	0.296	0.566
Non-IBM	Modified Heckmatt	-0.540	-0.5	0.517	0.408
	Heckmatt	-0.349	-0.455	0.236	0.46
IBM	Modified Heckmatt	-0.517	-0.54	0.71	0.717
	Heckmatt	-0.498	-0.516	0.343	0.639

Conclusion: In myositis patients, the Hopkins myositis grading scale which incorporates more specific parameters to aid in assessing changes in muscle EI and architecture, showed excellent validity and reliability and showed improvements over the original Heckmatt scale. Notably, the less experienced rater demonstrated interrater reliabilities comparable to those of the experienced raters, suggesting that appropriate training can be sufficient for accurate assessment.

Disclosure: T. Yoshida: None; **D. Saygin**: None; **J. Albayda**: None.

Abstract Number: 1205

Real-time MRI for assessment of swallowing impairment in inclusion body myositis and oculopharyngeal muscular dystrophy.

Rachel Zeng[1], Anke Rietveld[2], Omar Al-Bourini[1], Rosemarie HMJM Kroon[2], Arno Olthoff[1], Matthias Weidenmüller[1], Per-Ole Carstens[1], Isabel Kommerell[1], Saskia G Schütz[1], Corinne GC Horlings[3], Johanna G Kalf[3], Bert JM de Swart[3], Baziel GM van Engelen[2], Tim Friede[1], Sabine Hofer[1], Jens Frahm[4], Ali Seif Amir Hosseini[1], **Jens Schmidt**[5] and Christiaan GJ Saris[2], [1]University Medical Center Göttingen, Göttingen, Germany, [2]Radboudumc Research Institute for Medical Innovation, Nijmegen, Netherlands, [3]Radboudumc Research Institute for Medical Innovation, Nijmegen, Germany, [4]Max Planck Institute for Multidisciplinary Sciences, Göttingen, Germany, [5]Immanuel University Hospital Rüdersdorf, Brandenburg Medical School, Rüdersdorf bei Berlin, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Swallowing dysfunction -dysphagia- is a frequent and debilitating symptom in neuromuscular disorders, leading to malnutrition, cachexia, aspiration pneumonia and death. Identification of the underlying pathophysiological mechanisms is important for diagnosis and treatment. As standard assessments have limitations, novel imaging techniques are needed. In the present study, we investigated the utility of real-time MRI and quantitative muscle ultrasound for characterizing dysphagia in two different neuromuscular disorders.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

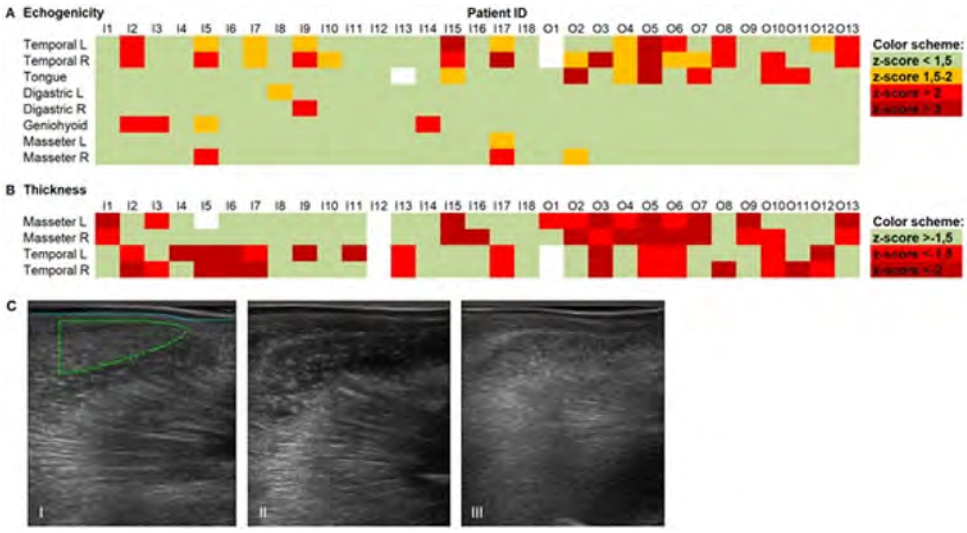


Figure 1. Quantitative muscle ultrasound (QMU) of orofacial muscles in IBM and OPMD patients. Heatmap of echogenicity (A) and muscle thickness (B) obtained by QMU. I1-I18 are individual IBM patients, O1-O13 are individuals with OPMD. Color codes represent z-scores, with echogenicity z-scores between 1.5 and 2 considered borderline abnormal, z-scores ≥ 2 considered abnormal and z-scores > 3 considered as severely abnormal. Muscle thickness z-scores -1.5 were considered abnormal. White represents missing data. (C) shows exemplary QMU findings of the tongue muscle. Echogenicity was analysed using histogram based grey-scale analysis and manually selected ROI, demarcated by the dotted green line (I), the dotted blue line delineates the border between the subcutaneous fat layer and muscle. Normal echogenicity of the tongue muscle in an IBM patient (II) and moderate signs of fibrosis and fatty infiltration in the tongue muscle of an OPMD patient (III).

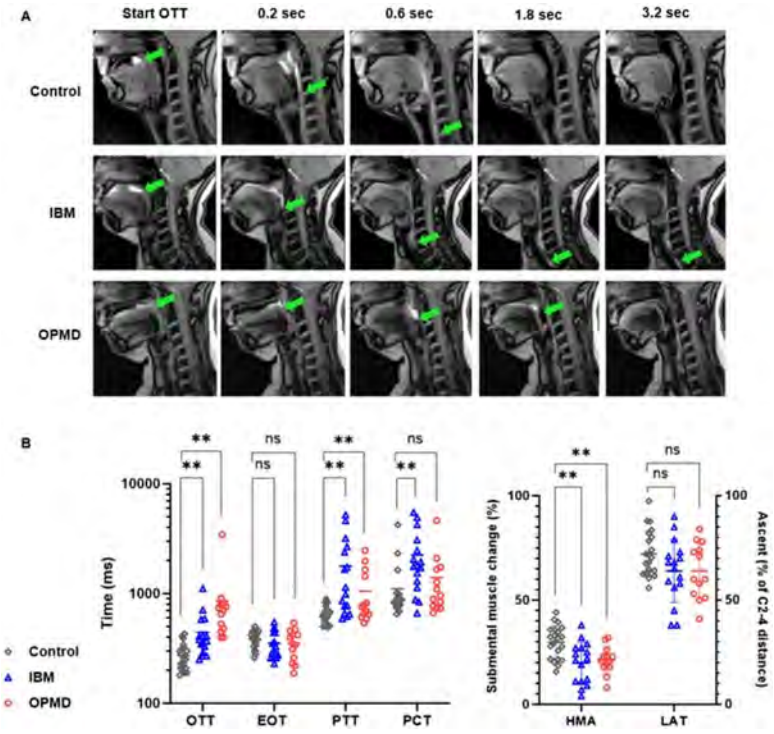


Figure 2. Real-time MRI assessment of swallowing in patients with IBM and OPMD versus control subjects. A. RT-MRI at a resolution of 40 ms with exemplary findings in a control subject (upper row), an IBM patient (middle row) and an OPMD patient (bottom row). Images were selected at start of oral transit time (OTT) and subsequently 0.2 sec, 0.6 sec, 1.8 sec and 3.2 sec. Note how swallowing one bolus of pineapple juice (bright contrast, bolus head is marked by a green arrow) is completed in the control subject at 1.8 sec, while the IBM patient shows pharyngal retention and a cricopharyngeal bar at 1.8 sec and 3.2 sec. The OPMD patient shows a prolonged oral phase of swallowing until 1.8 sec after start of OTT, while the pharyngeal phase is unaffected and swallowing is completed by 3.2 sec. These RT-MRI sequences can be viewed in movie format in Supporting Information Movies S1 and S2. B. RT-MRI shows a significantly prolonged OTT in patients with OPMD and to a lesser extent also in patients with IBM. The pharyngeal phases of swallowing (PTT and PCT) are significantly impaired in patients with IBM and in a few patients with OPMD. No differences between the cohorts were found for esophageal opening time (EOT). Hyoid-mental approximation (HMA) is significantly reduced in both diseases. No differences to controls were observed for relative laryngeal elevation (LAT). Variables were tested using t-tests and compared to a non-myopathic control group.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

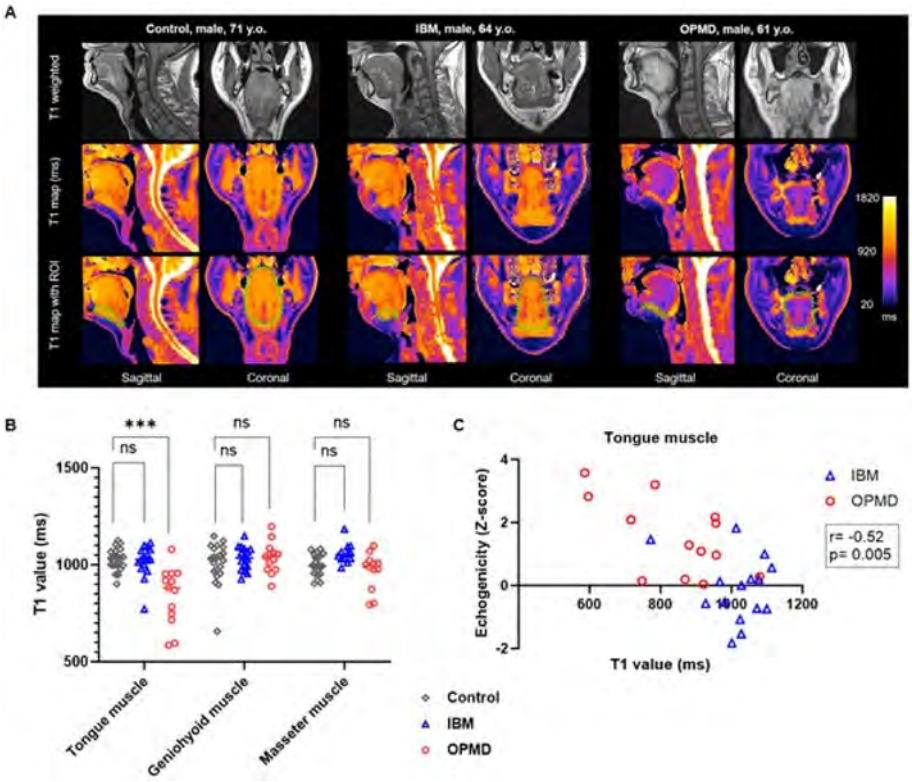


Figure 3. T1 mapping of swallowing muscles in patients with IBM and OPMD versus control subject. A. Selected T1 weighted MRI sequences (upper row) and T1 maps (middle and bottom row) obtained for head and neck region of a 71 y.o. control subject, a 64 y.o. IBM patient and a 61 y.o. OPMD patient. The bottom row outlines the manually placed regions of interest (dotted green lines) of the tongue muscles in the coronal sequences and the geniohyoid muscles in the sagittal sequences for analysis of mean T1 values. B. T1 mapping reveal significantly lower T1 values of tongue muscle in OPMD patients indicating a higher fat content. T1 values of geniohyoid muscle and masseter muscle show no significant differences between patients and controls. Variables were tested using t-test. C. The reduced T1 values of the tongue in quantitative MRI correlate significantly with increased echogenicity of the tongue on ultrasound in OPMD patients (Spearman r = -0,52; p = 0,005), both methods thereby indicating fibrosis and fatty infiltration of the tongue muscle.

Methods: This prospective cohort study included 18 patients with inclusion body myositis (IBM, 33% female, age 68.9 ± 7.7 years) and 13 with oculopharyngeal muscular dystrophy (OPMD, 62% female, age 55.9 ± 7.0 years) from two European Neuromuscular research centers (Nijmegen, NL; Göttingen, DE). Swallowing function was studied using real-time MRI (RT-MRI), FEES (flexible endoscopic evaluations of swallowing) and clinical assessments. T1-mapping and quantitative muscle ultrasound (QMUS) were used to analyze tissue properties in swallowing muscles. Outcomes were compared between the two muscle diseases. RT-MRI values were also compared to 22 age- and sex-matched non-myopathic controls.

Results: RT-MRI revealed significantly prolonged oral transit times in OPMD vs. controls (difference between means= 581.2 ms, 95% CI 225.9-936.4, p=0.002). Pharyngeal transit time was significantly prolonged in IBM vs. controls (difference between means= 1132.8 ms, 95% CI 482.2-1783, p=0.001). A cricopharyngeal bar as a well-established morphological indicator of dysphagia was identified in 80% patients with IBM compared to 53% in OPMD. Fatty degeneration of the tongue in OPMD significantly correlated between MRI-T1 values and ultrasound echogenicity (Spearman`s ρ= -0.52, p=0.005). ROC revealed excellent discrimination between diseases by combining RT-MRI, T1-mapping and QMUS (AUC= 0.95, 95% CI 0.86-1.00), while FEES and clinical assessments failed to differentiate specific patterns of dysphagia.

Conclusion: This study supports the value of novel MRI and ultrasound techniques for clinical use by identifying the pathophysiology and severity of impaired swallowing. Differentiating the phenotypes of dysphagia can aid in the diagnosis and treatment of affected patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Zeng: None; **A. Rietveld**: None; **O. Al-Bourini**: None; **R. HMJM Kroon**: None; **A. Olthoff**: None; **M. Weidenmüller**: None; **P. Carstens**: None; **I. Kommerell**: None; **S. G Schütz**: None; **C. GC Horlings**: None; **J. Kalf**: None; **B. de Swart**: None; **B. van Engelen**: None; **T. Friede**: None; **S. Hofer**: None; **J. Frahm**: None; **A. Seif Amir Hosseini**: None; **J. Schmidt**: None; **C. Saris**: None.

Abstract Number: 1206

Overexpression of lymphotoxin in autophagy-deficient mice as model for inclusion body myositis

Juliane Bremer[1], Judith Nagel[2], Jana Zschüntzsch[3], Kamil K Zajt[1], Tayfun Palaz[1], Thomas Blank[4], Aylin Ikis[1], Laura A Fischer[3], Anna SM Sensmeyer[3], Lara Wiechers[3], Josef J Reichelt[3], Kai P Hofmann[5], Monika J Wolf[6], Corinna Leuchtenberger[7], Priyanka Tripathi[1], Claudia Einer[8], Hans Zischka[2], Ulrike Rothermel[7], Anna L Eck[7], Regina Reimann[9], Veronika Kana[6], Elisabeth Rushing[6], Adriano Aguzzi[6], Marco Prinz[4], David Liebetanz[3], Francesca Odoardi[3], Chao-Chung Kuo[1], Joachim Weis[1], Florian Kraft[1], **Jens Schmidt**[10] and Mathias Heikenwälder[7], [1]University Hospital RWTH Aachen, Aachen, Germany, [2]Technical University of Munich, München, Germany, [3]University Medical Center Göttingen, Göttingen, Germany, [4]University of Freiburg, Freiburg, Germany, [5]DKFZ Heidelberg, Göttingen, Germany, [6]University Hospital Zürich, Zürich, Switzerland, [7]DKFZ Heidelberg, Heidelberg, Germany, [8]Helmholtz Munich, München, Germany, [9]University Hospital Zürich, Zürich, Germany, [10]Immanuel University Hospital Rüdersdorf, Brandenburg Medical School, Rüdersdorf bei Berlin, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Inclusion body myositis (IBM) is a progressive muscle disorder characterized by inflammation and degeneration with altered proteostasis. To better understand the interrelationship between these two features, we aimed at establishing a novel preclinical IBM model.

Methods: First, we used quantitative PCR to determine expression of pro-inflammatory chemo- and cytokines including lymphotoxin (LT)-signaling pathway components in human skeletal muscle tissue diagnosed with myositis. Based on these results we generated a mouse model that we analyzed at the histological, ultrastructural, transcriptional, biochemical, and behavioural level. Lastly, we subjected this model to anti-inflammatory treatments.

Results: After confirming and extending previous data on activation of lymphotoxin (LT)-signaling in human myositis, we generated distinct transgenic mouse lines co-expressing LTa and -b in skeletal muscle fibers. Transgenic mice displayed chronic myositis accompanied by dysregulated proteostasis, including an altered autophagolysosomal pathway. Related genes were temporarily up- and later downregulated, possibly in a compensatory fashion. Therefore, we genetically impaired autophagy in skeletal muscle cells. Autophagy impairment alone induced a pro-inflammatory transcriptional state, but no obvious cellular inflammation. However, the combination of LT-driven myositis with autophagy impairment induced the full spectrum of characteristic molecular and pathological features of IBM in skeletal muscle, including protein aggregates with typical ultrastructural morphology and mild mitochondrial pathology. Our attempts to treat the pathology by subjecting these mice to corticosteroids or anti-Thy1.2 antibodies mirrored recent treatment failures in humans, i.e., none of these treatments resulted in significant clinical improvement of motor performance or the transcriptional profile of muscle pathology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

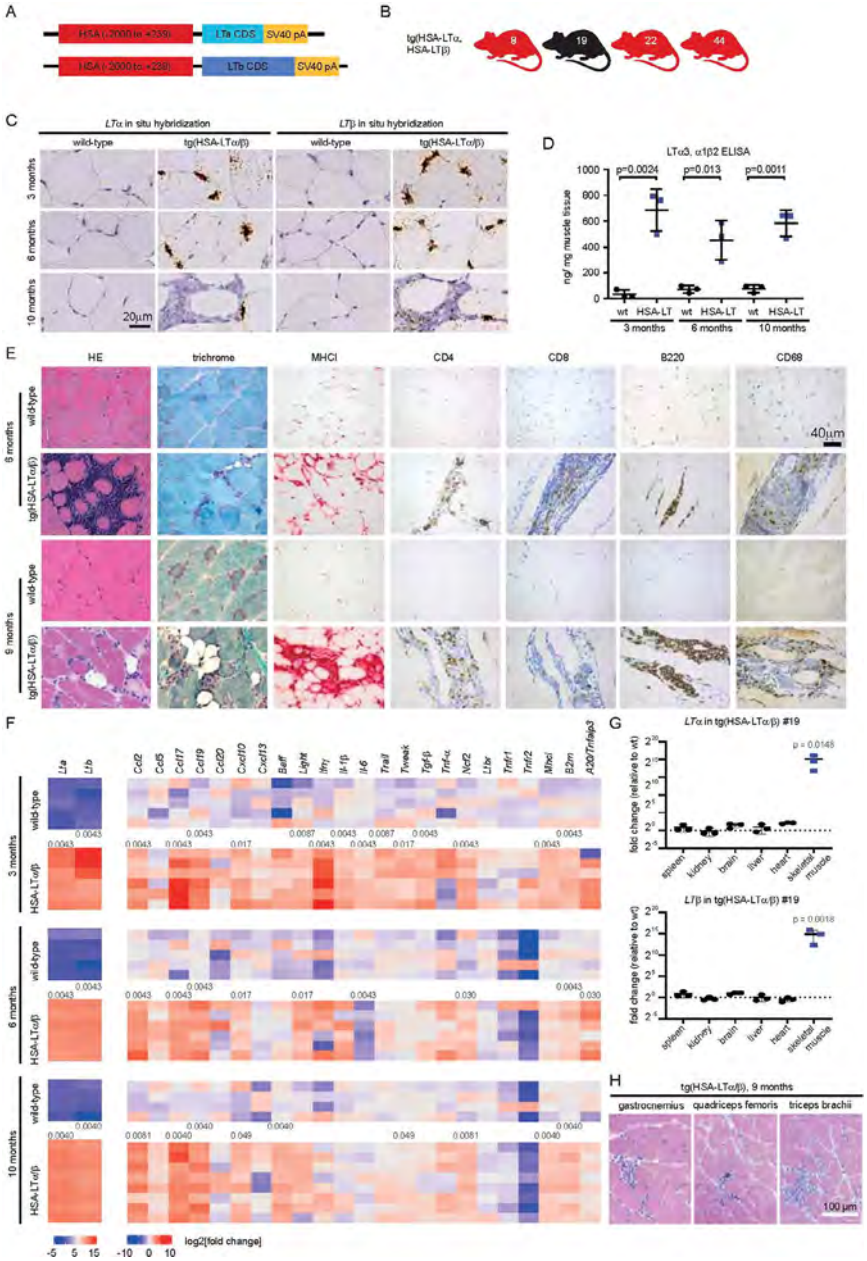


Figure 1. Generation, histology and chemo-/cytokine expression of HSA-LT/ transgenic mice. (A) Schematic drawing of the transgenic constructs of the coding sequences (CDS) of LT and LT both being cloned downstream of the human skeletal muscle actin (HSA) promoter (-2000 to +239) followed by an SV40 poly A site. (B) Four founder mice carrying both transgenes, HSA-LT and HSA-LT and transmitting them through the germline were obtained (line #8, #19, #22, #44). (C-D) LT and LT transgene expression was detected in quadriceps muscle fibers of HSA-LT/ #19 mice by RNA in situ hybridization of paraffin sections (brown signal) in the muscle fibers at 3, 6 and 10 months of age and also in inflammatory infiltrates in skeletal muscle, shown at 10 months of age (C). LT ELISA with skeletal muscle tissue homogenate from indicated time points and genotypes. Data are shown as ng LT3/LT12/LT21 protein per mg total protein. Statistical significance was tested using two-tailed Student's t-test. (E) Histologically, HSA-LT/ transgenic mice show endomysial inflammatory infiltrates and occasional muscle fiber necrosis. Especially at the age of 9 months, there is fibrosis and partial replacement by fatty tissue within the endomysium. Fiber size variation is also increased in transgenic mice (H&E and trichrome). In addition to the normal MHCI localization on endomysial capillaries seen in wild-type mice, transgenic mice display focal sarcolemmal MHCI upregulation (red signal). The inflammatory infiltrates are mostly composed of B220+ B cells and CD68+ macrophages and - to a lesser extent - of CD4+ and CD8+ T cells (brown signals). (F) Heatmap of chemo- and cytokine expression in HSA-LT/ transgenic mice determined by quantitative PCR of quadriceps femoris muscle tissue at 3, 6 and 10 months of age. P-values were determined using two-tailed Mann-Whitney tests. In case of significant differences between wild-type and transgenic mice, the p-values are displayed between the group of wild-type and transgenic line of the respective age group. (G) Quantitative PCR determining LT and LT expression in different organs of HSA-LT/ transgenic mice. P-values were determined using the ANOVA test with Šídák's multiple comparison test, significant differences compared to wild-type are displayed. (H) HE-stained sections of three different muscles from 9 months old HSA-LT/ mice.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

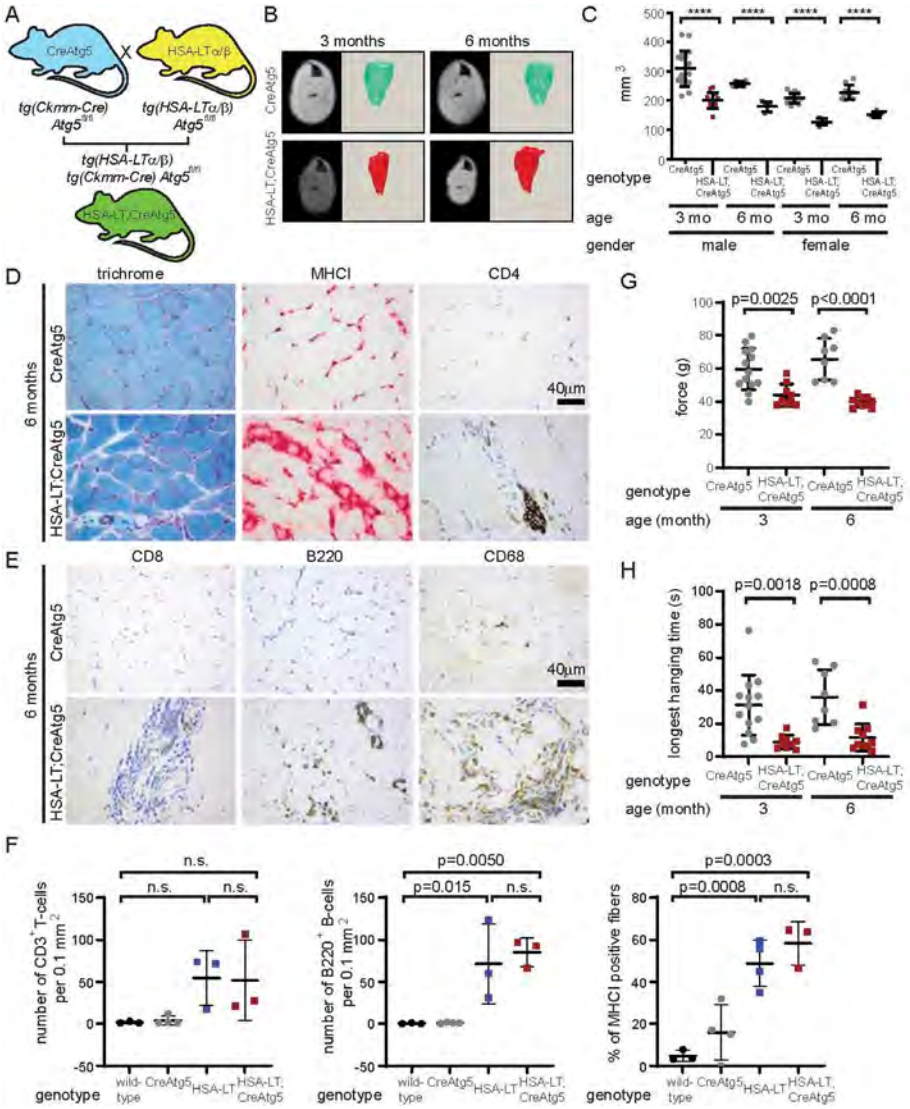


Figure 2. Behavioural and histological consequences of autophagy depletion in lymphotoxin-induced chronic myositis. (A) Breeding scheme to obtain HSA-LT/+ Ckmm-Cre+ Atg5fl/fl (HSA-LT;CreAtg5) mice. (B-C) Muscle volume was determined by magnetic resonance imaging (MRI) at 3 and 6 months of age of male and female HSA-LT;CreAtg5 compared to Ckmm-Cre+ Atg5fl/fl (CreAtg5) mice. Representative MRI (FLASH) images and 3D reconstructions of calf muscles are shown along with volumetric quantification. Muscle atrophy was observed in HSA-LT;CreAtg5 compared to CreAtg5 mice. Two-sided unpaired student's t-test was used to determine p-values. (D-F) Histological and immunohistochemical analysis for inflammatory markers revealed chronic myositis in HSA-LT;CreAtg5, but not in CreAtg5 mice, characterized by endomysial infiltrates composed of CD4+ and CD8+ T cells, B220+ B cells and CD68+ macrophages (brown signals) as previously observed in HSA-LT/ transgenic mice. Sarcolemmal upregulation of MHCI were detected in HSA-LT;CreAtg5, but MHCI was either not (1 of 4) or expressed weakly/ only on single fibers (3 of 4) in CreAtg5 mice (red signal). Quantification is shown in F. P-values were determined using the ANOVA test with Šídák's multiple comparison test. (G-H) Motor performance of CreAtg5 and HSA-LT;CreAtg5 mice was determined by the grip strength test (G) and by the hanging wire test (H). Groups were compared using the two-sided unpaired student's t-test. P-values are shown.

Conclusion: In summary, these data provide evidence that inflammation and autophagy disruption play a synergistic role in the development of IBM-like muscular pathology. Furthermore, once established, IBM-like pathology in these mice, as in human IBM patients cannot be reverted or prevented from progression by conventional means of immunosuppression. We expect that this novel mouse model will help to identify future treatment modalities for IBM.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

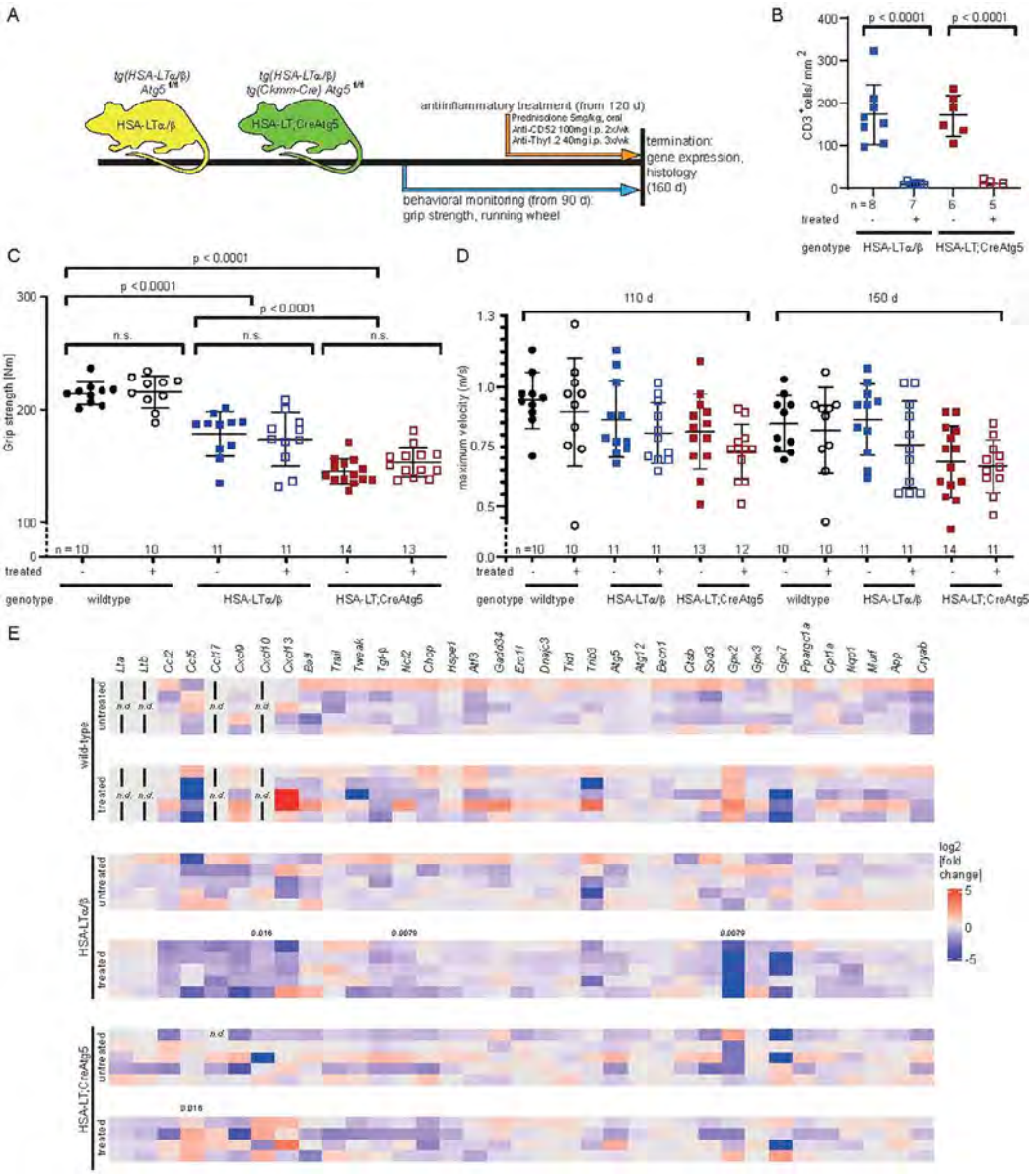


Figure 3. IBM-like myositis in mice is resistant to anti-inflammatory treatments. (A) Timeline of treatment. Density of CD3+ T cells in the liver of untreated mice and after treatment; for anti-Thy1.2 (B) and prednisolone (C) treatment. P-values were determined using two-tailed Students t-tests. Grip strength of mice at day 150. The results show genotype-dependent differences, but no treatment effect after prednisolone (D) and anti-Thy1.2 (E) treatment. (F) The heatmap shows expression examined by qPCR relative to the respective untreated controls (treated compared to untreated wild-type, HSA-LT/ and HSA-LT;CreAtg5, respectively) – here in case of prednisolone treatment. Except for a significant downregulation of Cxcl10, Ncf2 and Gpx2 following prednisolone treatment of HSA-LT/ mice compared to untreated HSA-LT/ and non-significant trends for some other genes, there was a counterintuitive upregulation of Ccl5 in treated compared to untreated HSA-LT;CreAtg5 mice, but otherwise stable gene expression. n.d. = not determined. Mann-Whitney-U test was performed as statistical test since some values were not normally distributed. P-values are only displayed in case of statistical significance between untreated and treated mice. Behavioral phenotypes and gene expression patterns following these treatments were stable (see also Supplementary figures).

Disclosure: J. Bremer: None; **J. Nagel**: None; **J. Zschüntzsch**: None; **K. Zajt**: None; **T. Palaz**: None; **T. Blank**: None; **A. Ikis**: None; **L. Fischer**: None; **A. Sensmeyer**: None; **L. Wiechers**: None; **J. Reichelt**: None; **K. Hofmann**: None; **M. Wolf**: Roche Diagnostics GmbH, 3; **C. Leuchtenberger**: None; **P. Tripathi**: None; **C. Einer**: None; **H. Zischka**: None; **U. Rothermel**: None; **A. Eck**: None; **R. Reimann**: None; **V. Kana**: None; **E. Rushing**: None; **A. Aguzzi**: None; **M. Prinz**: None; **D. Liebetanz**: None; **F. Odoardi**: None; **C. Kuo**: None; **J. Weis**: None; **F. Kraft**: None; **J. Schmidt**: None; **M. Heikenwälder**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1207

Cutaneous and Muscular Disease Trajectories in Adult Patients with Dermatomyositis

Jesus Valencia[1], Will Kelly[1], Sean Tackett[2], Amanda Finney[1], Jemima Albayda[1], Julie Paik[3], Lisa Christopher-Stine[1] and Chris Mecoli[4], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University, Baltimore, [3]Johns Hopkins Rheumatology, Baltimore, MD, [4]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is a rare autoimmune disease characterized by cutaneous manifestations and proximal muscle inflammation.[1,2] Notably, the clinical course of muscular and cutaneous disease in DM is highly variable. Some patients may exhibit predominant muscle disease while up to 20% of patients are categorized as clinically amyopathic and present with skin manifestations in the absence of muscle disease.3 However, most clinical trials require both muscle and skin involvement to be eligible.4 Our center has observed that even DM patients who are not amyopathic at presentation will often have improvement in muscle activity before skin activity, which prevents patients from being eligible for clinical trials given the lack of both muscular and skin involvement. Our study aims to characterize the clinical trajectory of muscular and cutaneous disease activity in patients with DM.

Methods: Patients with DM satisfying the ACR/EULAR 2017 classification criteria were prospectively enrolled between 2019 and 2025 at a large United States tertiary academic medical center. Patients included in this study were adult patients (≥18 years old at DM symptom onset), had clinical active disease as defined by Manual Muscle Testing-8 (MMT-8) < 142 and Cutaneous Dermatomyositis Disease Area and Severity Index-Activity (CDASI-A) >6 and at least 3 consecutive visits over 24 months (Figure 1). Demographic data, DM disease history, serologic status and treatment history were obtained through

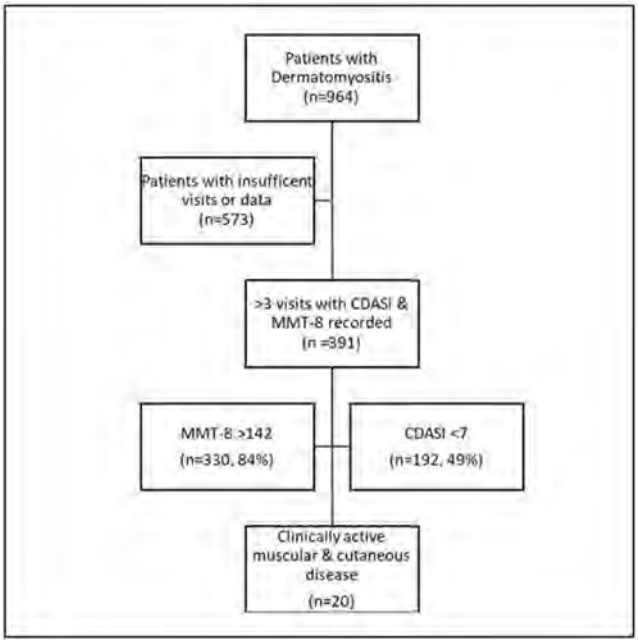


Figure 1. Of the 391 DM eligible cohort, 330 (84%) of patients did not meet muscle criteria whereas 199 (51%) met cutaneous criteria, suggesting most patients are not eligible for many clinical trials due to lack of weakness.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

prospective discrete data capture at each clinical visit. Outcomes included the percentage of patients who achieved improvement of their cutaneous and muscular disease as measured by the CDASI-A (decrease in 40%) and MMT-8 scores (near normalization of strength, ≥142).[5]

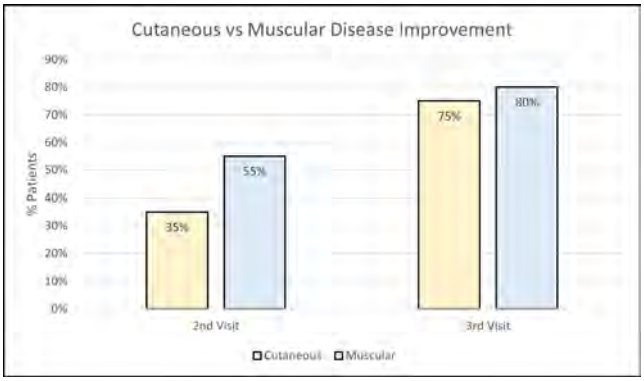


Figure 2. Cutaneous vs Muscular Disease Improvement Over Time

Table 1. Demographic and Disease Characteristics

Characteristic	Inclusion Group (n=20)	
Female sex, No. (%)	19 (95%)	
Age at DM symptom onset, mean (SD), yr	46.0 (18.0)	
Age at DM diagnosis, mean (SD), yr	46.8 (18.5)	
Age at baseline visit, mean (SD), yr	51.8 (17.9)	
Race/Ethnicity, No. (%)		
Asian	1 (5%)	
Black	4 (20%)	
Hispanic/Latino	0 (0%)	
White	15 (75%)	
CDASI-A Score Baseline, median (IQR)	9.0 (8.0-13.5)	
MMT-8 Score Baseline, median (IQR)	132 (122-137)	
Autoantibody positivity, No. (%)		
Mi-2 (line blot/ELISA)	0 (0.0%)	
NXP2 (IVTT IP)	11 (57.9%)	
MDA5 (line blot)	1 (5.6%)	
SAE1 (line blot)	0 (0.0%)	
TIF1Y (ELISA) >32	3 (30.0%)	
Medication History	**Prior Use [No. (%)]**	**Medication at Most Recent Visit [No. (%)]**
Hydroxychloroquine	4 (20%)	2 (10%)
Azathioprine	7 (35%)	0 (0%)
IVIG	4 (20%)	13 (65%)
Jak inhibitor	3 (15%)	1 (5%)
Methotrexate	15 (75%)	3 (15%)
Mycophenolate	9 (45%)	8 (40%)
Rituximab	6 (30%)	3 (15%)
Subcutaneous Ig	0 (0%)	1 (5%)
Systemic steroids (prednisone, methylprednisolone)	10 (50%)	6 (30%)
No systemic oral medications or intravenous immunoglobulin	3 (15%)	3 (15%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 20 patients with adult DM met the inclusion criteria (95% female, 75% White; mean age at DM diagnosis 47) with demographics outlined in Table 1. The baseline visit was on average five years after DM onset. Baseline median CDASI activity was 9 (IQR 8.0-13.5) and baseline median MMT-8 was 132 (IQR 122-137). From the baseline visit to the second visit (median 5 months after baseline), the median CDASI-A improved from 9 to 8 whereas the MMT-8 improved from 132 to 144. Only 7 (35%) patients experienced cutaneous improvement, whereas 11 (55%) patients experienced strength improvement. By the 3rd visit (median 10 months after baseline) median CDASI-A improved to 5 and MMT-8 improved to 146. At this time, 15 (75%) patients achieved cutaneous improvement, and 16 (80%) patients achieved muscular improvement (Figure 2). The median time to improvement for cutaneous disease was 6.5 months (IQR 5-11) whereas median time to improvement for muscular strength was 5 months (IQR 3-9.5).

Conclusion: At our U.S. tertiary academic medical center, most adult dermatomyositis (DM) patients present with relatively preserved muscle strength but more active skin disease. As a result, many are ineligible for clinical trials that require significant muscle weakness. Longitudinal data indicate that muscle symptoms often improve before skin symptoms, and the delay between disease onset and referral to a tertiary center may further hinder clinical trial recruitment.

Disclosure: J. Valencia: None; **W. Kelly**: None; **S. Tackett**: None; **A. Finney**: None; **J. Albayda**: None; **J. Paik**: ArgenX, 12,, Priovant, 12,; **L. Christopher-Stine**: Amgen, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Octapharma, 1, 5, Pfizer, 5, Priovant, 1; **C. Mecoli**: None.

Abstract Number: 1208

Neutrophil Activation in Juvenile Dermatomyositis: Associations with Muscle Function and Disease Progression

Jia Shi[1], Yang Wu[2], Aviya Levy[3], Ting Wang[4], Abhinav Janappareddi[5], Payton Hermanson[1], Jorge A. Gonzalez-Chapa[5], Qian Wang[6], Susan Shenoi[7] and Christian Lood[5], [1]University of Washington, Seattle, WA, [2]1. Chinese Academy of Medical Sciences & Peking Union Medical College; 2. Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China; 3. University of Washington, Division of Rheumatology, Seattle, WA, USA, Beijing, China (People's Republic), [3]Rady Children's Hospital, San Diego, CA, [4]Division of Rheumatology, Seattle Children's Hospital and Research Center, Seattle, [5]University of Washington, Division of Rheumatology, Seattle, [6]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [7]Seattle Children's Hospital and Research Center, Mercer Island, WA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is an inflammatory vasculopathy characterized by muscle weakness and systemic inflammation. This study aimed to investigate the clinical utility of neutrophil activation markers, specifically calprotectin (S100A8/A9) and myeloperoxidase (MPO)-DNA complexes, as potential biomarkers for muscle inflammation and predictors of long-term outcomes in JDM.

Methods: Plasma levels of calprotectin and MPO-DNA were quantified using ELISA in JDM (n = 36), juvenile idiopathic arthritis (JIA, n = 13), and healthy controls (HCs, n = 21). Disease severity and muscle function were assessed using the Childhood Myositis Assessment Scale (CMAS), Physician Global Assessment (PGA), and Manual Muscle Testing 8 (MMT8).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

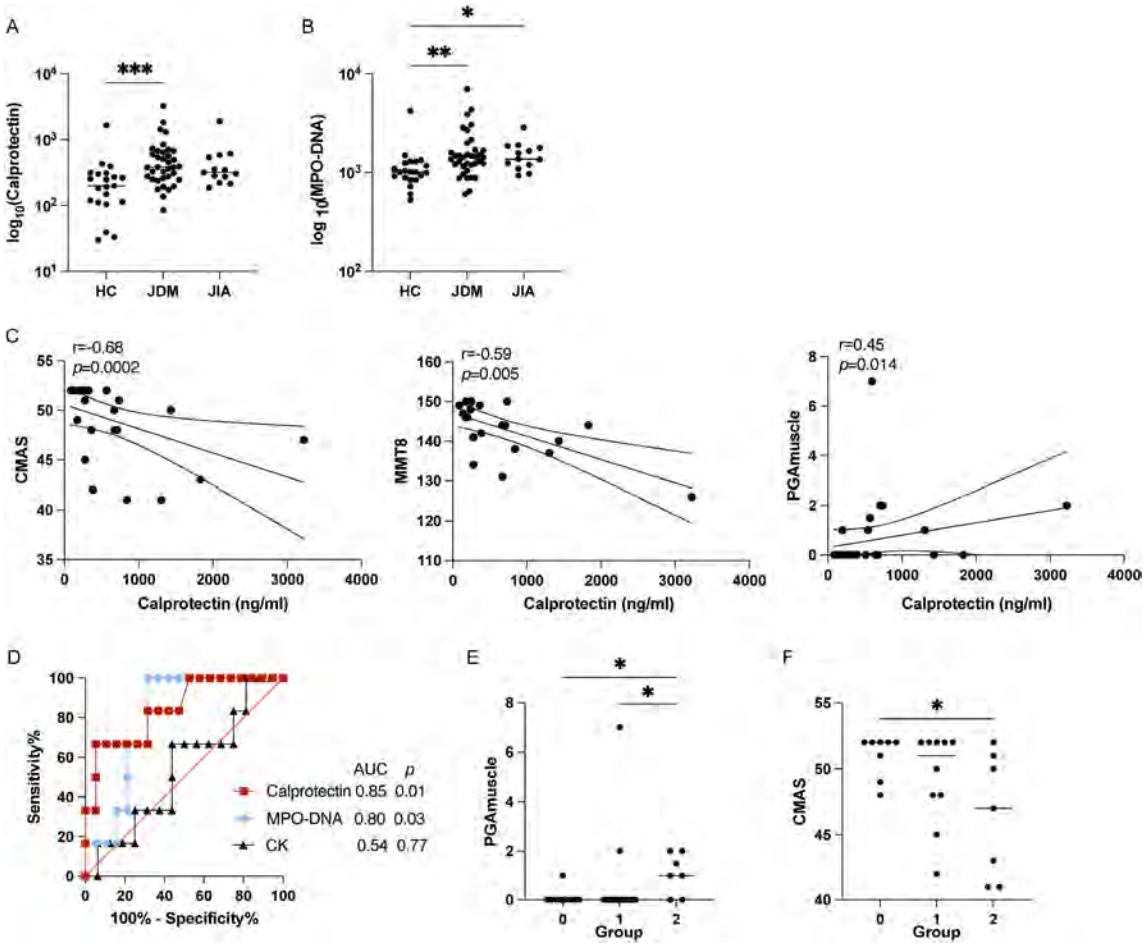


Figure 1. Neutrophil activation levels in JDM and associations with disease activity markers. (A, B) Levels of calprotectin (A) and MPO-DNA (B) in plasma among different groups. (C) Correlation of calprotectin with CMAS, MMT8, and PGA muscle score. (D) ROC curves comparing the performance of calprotectin, MPO-DNA and CK levels in distinguishing active from remission states in JDM patients based on CMAS. Active disease was defined as a CMAS ≤ 47. (E-F) PGA muscle scores (E) and CMAS (F) in JDM patients stratified into three groups based on neutrophil activation marker levels. Group 0: low level of both calprotectin and MPO-DNA; Group 1: elevated level of either biomarker; Group 2: elevated levels of both biomarkers. Statistical analyses by Kruskal-Wallis test, Spearman correlation and Mann-Whitney U test with * p<0.05, ** p<0.01, and *** p<0.001.

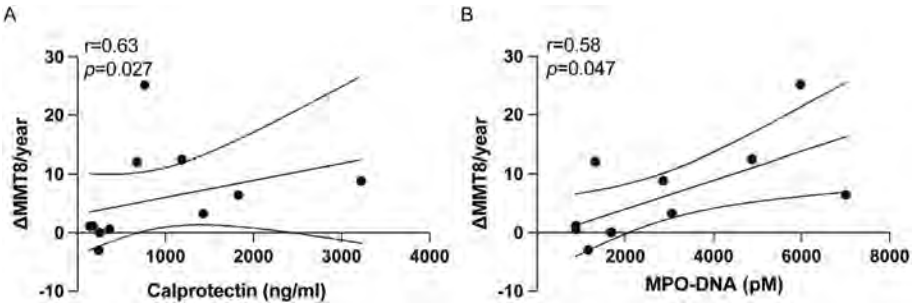


Figure 2. Correlations of neutrophil activation markers and disease progression in JDM. (A-B) Correlation analysis between plasma levels of calprotectin (A) and MPO-DNA (B) and MMT8 progression in JDM. Statistical analyses by Spearman correlation.

Results: JDM patients exhibited significantly higher plasma calprotectin and MPO-DNA levels as compared to HCs (p=0.0008 and p=0.0048, respectively) (Figures 1A-B). Calprotectin levels correlated with muscle function scores (CMAS r=-0.682, p=0.0002; MMT8 r=-0.59, p=0.005; and PGA muscle scores r=0.452, p=0.014) (Figure 1C). ROC analysis demonstrated that baseline calprotectin and MPO-DNA levels could distinguish active disease with high accuracy (AUC = 0.85

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and 0.80, respectively) (Figure 1D). Further stratification showed that patients with elevated levels of both markers had significantly worse disease activity and muscle involvement (Figures 1E-F). Notably, higher baseline levels of these markers correlated with improved MMT8 scores over time (r=0.634, p=0.027; r=0.582, p=0.047) (Figures 2A-B), indicating a predictive role in muscle recovery.

Conclusion: Calprotectin and MPO-DNA represent promising biomarkers for muscle inflammation and functional outcomes in JDM. These results suggest that neutrophil activation plays a key role in JDM pathogenesis and may provide insights into disease monitoring and treatment strategies.

Disclosure: J. Shi: None; **Y. Wu**: None; **A. Levy**: None; **T. Wang**: None; **A. Janappareddi**: None; **P. Hermanson**: None; **J. Gonzalez-Chapa**: None; **Q. Wang**: None; **S. Shenoi**: AbbVie/Abbott, 2, Pfizer, 2, sobi, 2; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11.

Abstract Number: 1209

Beyond Muscle Strength: Functional Performance Measures Enhance Assessment of Disease Activity in Juvenile Dermatomyositis

Jia Shi[1], Alexander Carpenter[2], Christopher Wong[2], Qian Wang[3], Christian Lood[4] and Susan Shenoi[5], [1]University of Washington, Seattle, WA, [2]Division of Rheumatology, Seattle Children's Hospital and Research Center, Seattle, [3]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [4]University of Washington, Division of Rheumatology, Seattle, [5]Seattle Children's Hospital and Research Center, Mercer Island, WA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: To evaluate the measurement properties of functional performance measures (FPMs)—broad jump (BJ) and 10-meter run (10MR)—for assessing muscle function and disease activity in children with juvenile dermatomyositis (JDM), and to assess their added value alongside conventional clinical tools.

Methods: This longitudinal cohort study included 39 children with JDM. BJ and 10MR were assessed alongside standard clinical scores. Construct validity and responsiveness were assessed through cross-sectional and longitudinal analyses (linear mixed-effects models, LMMs).

Results: FPMs correlated significantly with established disease activity and muscle function measures (Figure 1). While 10MR and BJ demonstrated moderate responsiveness (standardized response mean = -0.56 and 0.31, respectively), longitudinal analyses (Figure 2) confirmed that changes in FPMs closely tracked with improvements in Childhood Myositis Assessment Scale (CMAS) and manual muscle testing (MMT8) over time. Within the clinically inactive disease (CID) group, functional heterogeneity was evident (Figure 3A). Cluster analysis based on CMAS and MMT8 identified a subgroup with relatively low strength scores and poor FPM performance (Figures 3B-C), while a more comprehensive four-variable clustering using BJ, 10MR, CMAS, and MMT8 further stratified CID patients into three distinct phenotypes (Figure 3D). Notably, one subgroup exhibited high CMAS/MMT8 scores but reduced FPMs, suggesting residual functional impairment not captured by traditional assessments. Low internal consistency (Cronbach's α =0.44) further suggested that FPMs capture distinct dimensions of muscle function beyond CMAS/MMT8.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

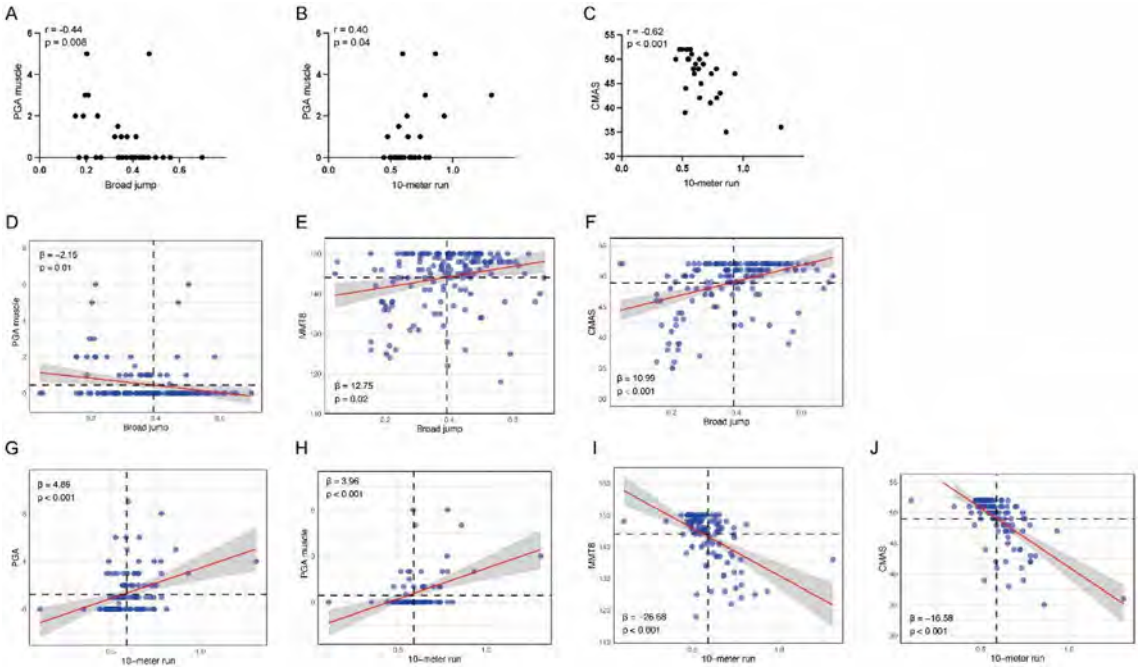


Figure 1. Relationship between FPMs and disease activity scores in JDM. (A-C) Correlation of baseline FPMs (BJ and 10MR) with PGA Muscle (A-B) and CMAS (C). (D-F) Relationship between broad jump and disease activity scores (PGA Muscle, MMT8, and CMAS) across all follow-up data. (G-J) Relationship between the 10-meter run and disease activity scores (PGA, PGA Muscle, MMT8, and CMAS) across all follow-up data. The red line represents the linear regression model fitted to the data, with the shaded area indicating the 95% confidence interval. The regression coefficient (β) and p-value are annotated on the plots. Statistical analyses were performed using Spearman correlation (A-C) and LMM (D-J).

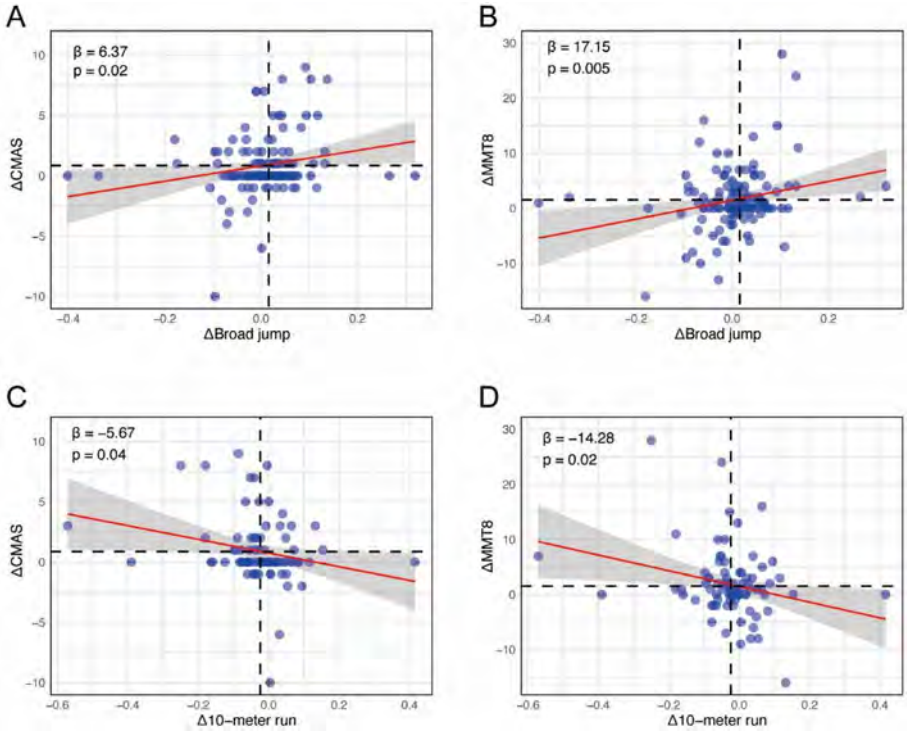


Figure 2. Change in FPMs and disease activity scores between follow-up visits in JDM. (A-B) Relationship between changes in BJ and changes in disease activity scores (ΔCMAS and ΔMMT8, respectively) across all follow-up data. (C-D) Relationship between changes in 10MR and changes in disease activity scores (ΔCMAS and ΔMMT8, respectively) across all follow-up data. The red line represents the linear regression model fitted to the data, with the shaded area indicating the 95% confidence interval. The regression coefficient (β) and p-value are annotated on the plots. Statistical analyses were performed using LMM.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

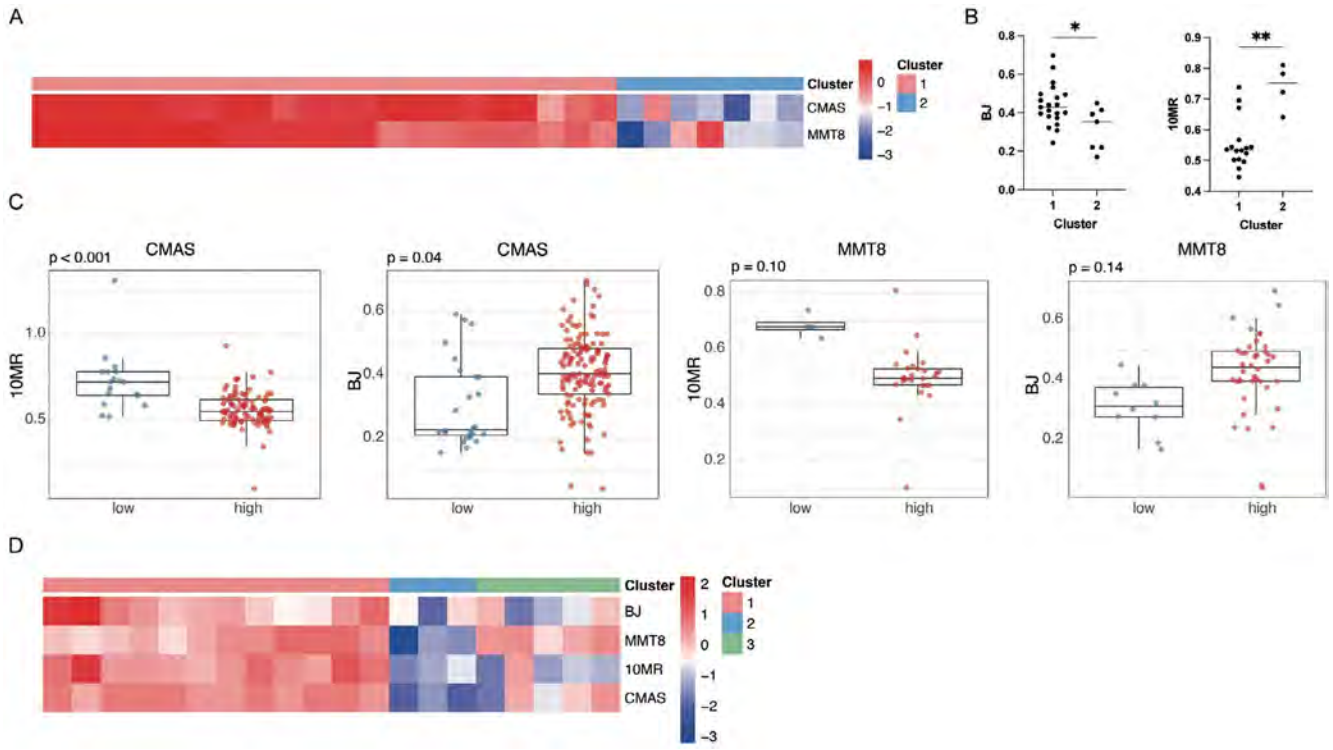


Figure 3. Evaluation of CMAS, MMT8 and functional performances in patients with JDM in clinically inactive disease (CID). (A) Heatmap depicting two patient clusters within the CID group, based on CMAS and MMT8 scores. (B) Comparisons of BJ and 10MR performance between Cluster 1 and Cluster 2. (C) Comparisons of 10MR and BJ performance between high and low CMAS groups, as well as high and low MMT8 groups, in CID patients across all follow-up data. (D) Heatmap depicting three patient clusters within the CID group, based on CMAS, MMT8 scores, BJ and 10MR (inverted). Statistical analyses were performed using the LMM and Mann-Whitney U test with * p<0.05 and ** p<0.01.

Conclusion: FPMs are quick, non-invasive, and clinically feasible tools that demonstrate good measurement properties. By capturing dynamic aspects of muscle function overlooked by CMAS and MMT8, FPMs may enhance clinical assessment and support individualized management in JDM.

Disclosure: J. Shi: None; **A. Carpenter**: None; **C. Wong**: None; **Q. Wang**: None; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11; **S. Shenoi**: AbbVie/Abbott, 2, Pfizer, 2, sobi, 2.

Abstract Number: 1210

Artificial Intelligence-based Capillaroscopy and Laboratory Biomarkers to Predict Disease Activity in Idiopathic Inflammatory Myopathies: Preliminary Data from the Capiami Cohort

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Nailfold videocapillaroscopy (NVC) is a valuable non-invasive tool for assessing microvascular damage in autoimmune diseases. However, its application in idiopathic inflammatory myopathies (IIM) remains limited, partly due to variability in interpretation. Artificial intelligence (AI)-based software offers the potential for objective, standardized capillaroscopic analysis. The CapIAMI project aimed to explore the role of automated NVC evaluation in IIM patients across a large international cohort.

Methods: We conducted an ambispective, observational, international, multicenter study including patients diagnosed with IIM according to established criteria. Standardized NVC images were analyzed using Capillary.io, an AI-based platform extracting quantitative microvascular parameters. Clinical data, laboratory values (CPK, aldolase, LDH, CRP, ESR, and ferritin), and autoantibody profiles were collected at the time of NVC. Disease activity was determined based on clinical

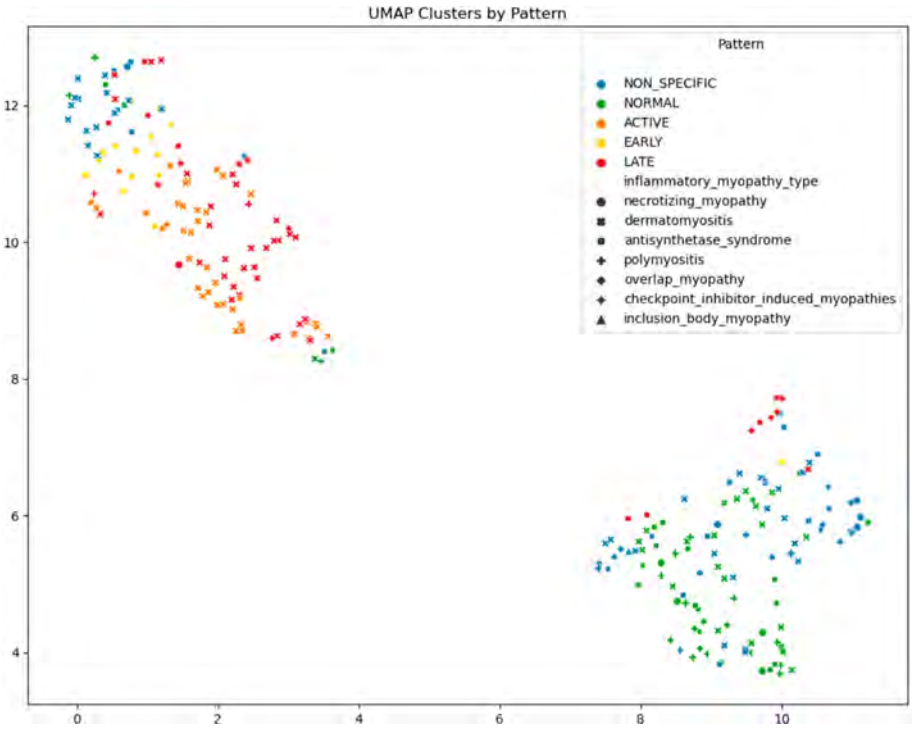


Figure 1. UMAP projection of capillaroscopic variables from CapIAMI patients. Each dot represents an individual capillaroscopy, coloured by capillaroscopic pattern and shaped by IIM subtype. The figure shows distinct clustering based on microvascular characteristics, supporting the potential of AI-assisted stratification in idiopathic inflammatory myopathies.

Table 1. Cohort & Key Clinical Features

Parameter	Value
Patients (n)	272
Age, median (IQR)	58.0 years (41.3–67.0)
Female (%)	68.2 %
Ethnicity (%)	Caucasian 56.2; Latin American 37.7; African American 3.0; Asian 2.6; African 0.4
IIM Subtype (%)	Dermatomyositis 53.7; Antisynthetase syndrome 15.8; Overlap myopathy 11.8; Polymyositis 7.7; Necrotizing autoimmune myopathy 4.0; Inclusion-body myopathy 0.7; Checkpoint inhibitor–induced myopathy 0.4
Active disease (%)	49.3 %
Manifestations (%)	Myositis 80.5; Cutaneous involvement 42.7; Articular symptoms 29.3

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Autoantibody Positivity

Autoantibody	n (%)	Autoantibody	n (%)
Anti–Ro-52	86 (31.6 %)	Anti–SRP	12 (4.4 %)
Anti–Mi-2	54 (19.9 %)	Anti–RNP	10 (3.7 %)
Anti–PM/Scl	36 (13.2 %)	Anti–EJ	9 (3.3 %)
Anti–TIF1γ	28 (10.3 %)	Anti–PL-7	9 (3.3 %)
Anti–Jo-1	26 (9.6 %)	Anti–HMGCR	8 (2.9 %)
Anti–MDA-5	26 (9.6 %)	Anti–KS	5 (1.8 %)
Anti–NXP-2	22 (8.1 %)	Anti–Ha/YRS	4 (1.5 %)
Anti–SAE	20 (7.4 %)	Anti–OJ	2 (0.7 %)
Anti–Ku	20 (7.4 %)	Anti–Zo	2 (0.7 %)
Anti–PL-12	18 (6.6 %)		

evaluation. Predictive models were developed using machine learning algorithms, with performance assessed by cross-validation metrics.

Results: A total of 272 IIM patients from 25 centers were included. The median age was 58.0 years (IQR 41.3–67.0), and 68.2 % were female. Ethnic distribution was 56.2 % Caucasian, 37.7 % Latin American, and 6.0 % other groups. Dermatomyositis was the predominant subtype (53.7 %), followed by antisynthetase syndrome (15.8 %) and overlap myopathy (11.8 %) (Table 1). Clinically active disease was present in 49.3 % of patients. The most frequent active manifestations were myositis (80.5 %), cutaneous involvement (42.7 %), articular symptoms (29.3 %) and interstitial lung disease (ILD) (24.26%) (Table 1).

Patients with active disease exhibited significantly higher serum CK and aldolase, elevated CRP (all $p < 0.05$) and increased prevalence of ILD and late-scleroderma NVC pattern (both $p < 0.001$). Autoantibody profiles are detailed in Table 2. The most prevalent specificities were anti–Ro-52 (31.6 %), anti–Mi-2 (19.9 %) and anti–PM/Scl (13.2 %), with lesser frequencies for other myositis-specific and myositis-associated antibodies.

Combining AI-derived capillaroscopic metrics with laboratory biomarkers yielded an overall precision of 0.746 in cross-validated predictive models. Capillary tortuosity, ramification abnormalities, megacapillary presence and hemorrhagic patterns constituted the principal predictive features, with capillary ramification ($p = 0.005$) and average limb width ($p = 0.026$) remaining independent predictors. UMAP embedding of these features demonstrated clear segregation of early-, active- and late-scleroderma–like patterns from non-specific/normal patterns (Fig. 1).

Conclusion: Automated NVC analysis combined with conventional laboratory biomarkers improves the prediction of disease activity in IIM patients. These preliminary findings underscore the added value of standardized capillaroscopic evaluation as a complementary tool in clinical practice. Further validation in larger cohorts is needed to confirm and expand these observations.

Disclosure: G. Lledó Ibáñez: None; **J. Álvarez-Troncoso**: None; **B. Gracia Tello**: None; **S. Prieto-Gonzalez**: None; **E. Martínez Robles**: None; **D. Cristina-Varela**: None; **S. Molina-Ríos**: None; **L. Sáez Comet**: None; **E. Soliman**: None; **F. Uguña**: None; **M. Mesa**: None; **M. Martín Cascón**: None; **T. Santiago**: None; **G. Santamaría-Peñaloza**: None; **T. Georgiev**: None; **S. Bernal-Macias**: None; **B. Marí-Alfonso**: None; **J. Rodríguez-Solís**: None; **S. Pino Hernández**: Pfizer, 5; **J. Olas**: None; **J. Mosquera Angarita**: None; **E. García- Guijarro**: None; **I. Perales Fraile**: None; **M. Freire Dapena**: None; **I. Pérez de Pedro**: None; **L. Viteri Noël**: None; **E. Ramos ibáñez**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1211

Plasma Levels of miR-133a-3p and miR-1-3p as Potential Biomarkers of Muscle Involvement and Initial Treatment Response in Myositis

Kristina Svobodová[1], Sabína Oreská[1], Lucia Vernerová[2], Dana Dlouhá[3], Hana Wunsch[2], Karel Pavelka[2], Jiri Vencovsky[4], Ladislav Šenolt[5], Michal Vrablik[6], Jaroslav Alois Hubáček[3] and Michal Tomcik[2], [1]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [2]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, [3]Experimental Medicine Center, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [4]Institute of Rheumatology, Praha 8, Czech Republic, [5]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [6]3rd Department of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) involve muscle inflammation. MicroRNAs (miRNAs), such as miR-133a-3p and miR-1-3p, play a key role in gene regulation and muscle repair. Their dysregulated expression contributes to IIM pathogenesis, making them potential biomarkers and therapeutic targets. This study evaluates the expression of miR-133a-3p and miR-1-3p in IIM vs. healthy controls (HC), and the association with muscle involvement and disease-related features, and the impact of initial immunosuppressive therapy.

Methods: 60 patients with IIM were included: 19 males; mean (SD) age 59.1 (12.9) years; disease duration 2.5 (3.5) years; 20 dermatomyositis (DM)/ 25 polymyositis (PM), both without statin history/ 15 statin-induced immune-mediated necrotizing myopathies (IMNM). Follow-up at 6 months of immunosuppressive therapy included 13 patients (5 DM, 5 PM, 3 IMNM) with early disease (disease duration 0.9 (1.3) years). Furthermore, 33 age-/sex-matched HC were included (10 males, age 58.3 (13.4)). Body composition was examined using bioelectric impedance analysis (BIA-2000-M). Total RNA was extracted from plasma with miRNeasy Serum/Plasma Advanced kit (Qiagen). Quantitative PCR was performed using 6 miRCURY LNA

Table 1.

Table 1: Expression of miR-133a-3p and miR-1-3p in IIM and HC

IIM / HC cohorts	miR133a-3p mean (SEM) [log10_RQ to max]	miR-1-3p mean (SEM) [log10_RQ to max]
IIM (n=60)	1.225 (0.074)	1.018 (0.066)
DM (n=20)	1.107 (0.104)	0.897 (0.084)
PM (n=25)	1.071 (0.115)	0.890 (0.104)
IMNM (n=15)	1.637 (0.139)	1.393 (0.129)
HC (n=33)	0.546 (0.037)	0.404 (0.035)
p-value:		
IIM vs. HC	**<0.001**	**<0.001**
DM vs. HC	**0.002**	**0.002**
PM vs. HC	**0.002**	**0.001**
IMNM vs. HC	**<0.001**	**<0.001**
DM vs PM	1.0	1.0
DM vs IMNM	**0.030**	**0.019**
PM vs IMNM	**0.009**	**0.010**

Significant correlations are highlighted in bold ($p<0.05$).
Abbreviations: DM, dermatomyositis; HC, healthy controls; IIM, Idiopathic inflammatory myopathies; IMNM, Immune mediated necrotising myopathy; PM, polymyositis; RQ, Relative Quantification; SEM, Standard Error of the Mean

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2.

Table 2: Correlation of miRNA expression and markers of muscle and metabolic involvment at baseline

	miRNA	Correlated parameter	p-value	Pearson r
IIM (n=60)	**miR133a-3p**	Disease duration; MMT-8; CK; LD; myoglobin; PED; BMR	**0.023; 0.003; <0.001; <0.001; <0.001;** *0.055; 0.080*	-0.300; -0.383; 0.660; 0.622; 0.525; 0.249; 0.295
	miR-1-3p	Disease duration; MMT-8 CK; LD; myoglobin;	*0.054; 0.063* **<0.001; <0.001; <0.001**	-0.252; -0.246; 0.628; 0.520; 0.432
DM (n=20)	**miR133a-3p**	MMT8; CK; LD; myoglobin	*0.079;* **<0.001; <0.001; <0.001**	-0.412; 0.689; 0.841; 0.724
	miR-1-3p	CK; LD; myoglobin	**0.032; 0.001; 0.029**	0.481; 0.680; 0.502
PM (n=25)	**miR133a-3p**	Age; MMT-8; CK; LD; myoglobin; BMI	**0.008;** *0.093;* **<0.001; 0.002; 0.001;** *0.064*	-0.521; -0.351; 0.621; 0.600; 0.610; -0.605
	miR-1-3p	Age; CK; LD; myoglobin; BMI	**0.020; 0.004; 0.006; 0.006;** *0.062*	-0.463; 0.560; 0.531; 0.532; -0.609
IMNM (n=15)	**miR133a-3p**	Disease duration; ESR; CK;LD; myoglobin; PED; BMI; LBM	**<0.001; 0.040; 0.009;** *0.070;* **0.031;** *0.050; 0.052;* **0.041**	-0.860; -0.560; 0.680; 0.500; 0.577; 0.515; -0.703; 0.687
	miR-1-3p	Disease duration; CK; LBM; BMR	**<0.001; 0.005; 0.024;** *0.085*	-0.829; 0.703; 0.735; 0.604

Significant correlations are highlighted in bold (p≤0.05); trends missing the level of statistical significance are highlighted in italics (p = 0.05-0.1).
Abbreviations: IIM, Idiopathic inflammatory myopathies; DM, Dermatomyositis; PM, Polymyositis; IMNM, Immune-Mediated Necrotizing Myopathy; MMT8, Manual Muscle Testing (8 muscle groups); CK, Creatine Kinase; LD, Lactate Dehydrogenase; LBM, Lean Body Mass; BMR, Basal Metabolic Rate; PED, Prednisone Equivalent Dose; BMI, Body Mass Index; ESR,erythrocyte sedimentation rate

Table 3.

Table 3: Changes in disease-related parameters and miRNA expression during the 6-month initial immunosuppressive therapy (n=13)

Parameters	Month 0 mean (SEM)	Month 6 mean (SEM)	p-value
MYOACT	0.08 (0.02)	0.05 (0.01)	**0.007**
MMT-8	62.8 (2.2)	72.2 (2.4)	**0.003**
CK (µkat/L)	36.4 (13.9)	4.9 (2.2)	*0.086*
Myoglobin (µg/L)	942.5 (274.6)	83.8 (23.5)	**0.002**
LD (µkat/L)	8.7 (1.1)	4.1 (0.3)	**0.022**
PED (mg/day)	33.5 (6.2)	13.8 (2.6)	**<0.001**
hsa-miR133a-3p (log10_RQ to max)	1.58 (0.14)	0.93 (0.09)	**0.001**
hsa-miR-1-3p (log10_RQ to max)	1.34 (0.12)	0.81 (0.10)	**0.004**

Significant correlations are highlighted in bold (p<0.05). trends missing the level of statistical significance are highlighted in italics (p = 0.05-0.1).
Abbreviations: MYOACT, Myositis disease aktivity assessment visual analogue scale; MMT-8, Manual Muscle Testing-8; CK, Creatine Kinase; LD, lactate dehydrogenase; PED, Prednisone Equivalent Dose; RQ, Relative Quantification

miRNA PCR assays (Qiagen) with miR-103-3p, miR-191-5p, and let-7a-5p as endogenous controls. miRNA concentration analysis was performed using GenEx software (Multid Analysis AB). Data are presented as mean (SEM).

Results: The expression of miR-133a-3p and miR-1-3p was significantly higher in IIM vs. HC, in all IIM subsets vs. HC, and particularly in IMNM vs. DM and PM (Table 1) and correlated with increased muscle damage markers (CK, LD, myoglobin), decreased muscle strength (MMT8), and shorter disease duration (Table 2). After 6 months of immunosuppressive therapy, miR-133a-3p and miR-1-3p levels significantly decreased, alongside disease activity (MYOACT) and muscle damage markers, while muscle strength (MMT-8) improved (Table 3). A greater miR-133a-3p decrease correlated with a larger decrease in CK (p=0.003; r=0.780) and LD (p=0.030; r=0.623), and strength improvement (p=0.043; r=0.591). Similarly, larger miR-1-3p reduction correlated with greater CK decrease (p=0.010; r=0.705). Higher baseline miR-133a-3p and/or miR-1-3p predicted greater muscle strength improvement (p=0.043; r=0.591) and larger reductions in CK (p=0.007;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

r=0.727 and p=0.017; r=0.671), LD (p=0.010; r=0.707 and p=0.075; r=0.532), and myoglobin (p=0.059; r=0.584, respectively).

Conclusion: The expression of miR-133a-3p and miR-1-3p were significantly higher in IIM vs. HC, in all IIM subsets vs. HC, particularly in IMNM than in DM and PM, reflecting greater muscle damage. The levels were highest in early disease with high activity and declined after 6 months of immunosuppressive therapy, mirroring reduced muscle damage markers and improved strength. Our study demonstrated both miR-133a-3p and miR-1-3p as a potential biomarker of disease activity and muscle damage in IIM, and a potential predictor of initial treatment response in IIM.

Acknowledgment: MH CR 023728, NU21-01-00146, NU21-05-00322, BBMRI.cz-LM2023033, SVV 260638

Disclosure: K. Svobodová: None; **S. Oreská**: None; **L. Vernerová**: None; **D. Dlouhá**: None; **H. Wunsch**: None; **K. Pavelka**: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **J. Vencovsky**: None; **L. Šenolt**: None; **M. Vrablik**: None; **J. Hubáček**: None; **M. Tomcik**: None.

Abstract Number: 1212

Relapse in Idiopathic Inflammatory Myopathies: insights from extended MyoCite and Italian Consortia

Maria Rosa Pellico[1], Cristina Bochicchio[2], Claudia Iannone[3], Lekshmi Minikumari Rahulan[4], Marco Fornaro[5], Ilaria Cavazzana[6], Edoardo Conticini[7], Masataka Kuwana[8], Akira Yoshida[9], Silvia Cavalli[2], Silvia Grazzini[7], Alessia Gatti[10], Giulio Lopinto[11], Paolo Semeraro[12], Thomas Patrick Sheeran[13], Florenzo Iannone[14], Vikas Agarwal[15], Roberto Caporali[16], Nicoletta Del pAPA[1] and Latika Gupta[17], [1]ASST Pini-CTO, Clinical Rheumatology Unit, Milano, Italy, [2]ASST Pini-CTO, Clinical Rheumatology Unit, Milan, Italy, [3]University of Milan, Gaetano Pini CTO, Milano, Milan, Italy, [4]Sanjay Gandhi Postgraduate Institute of Medical sciences Lucknow, Lucknow, Uttar Pradesh, India, [5]Unit of Rheumatology, Department of Precision and Regenerative Medicine, Area Jonica (DiMePRe-J), University of Bari, Italy., Bari, Italy, [6]Rheumatology and Clinical Immunology Unit, Clinical and Experimental Sciences Department, ERN ReCONNET, ASST Spedali Civili of Brescia and University of Brescia, Brescia, Italy, Brescia, Lombardia, Italy, [7]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Italy, Siena, Italy, [8]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [9]Department of Allergy and Rheumatology Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [10]Rheumatology and Clinical Immunology Unit – ERN ReCONNET, ASST Spedali Civili and University of Brescia, Brescia, Lombardia, Italy, [11]Unit of Rheumatology, Department of Precision and Regenerative Medicine, Area Jonica (DiMePRe-J), University of Bari, Italy., Bari, [12]Rheumatology and Clinical Immunology Unit, Clinical and Experimental Sciences Department, ERN ReCONNET, ASST Spedali Civili of Brescia and University of Brescia, Brescia, Italy, Brescia, Italy, [13]Department of Rheumatology, The Royal Wolverhampton NHS Trust, Wolverhampton, UK; Rheumatology Department, Walsall Manor Hospital, Walsall, UK, Wolverhampton, United Kingdom, [14]Rheumatology DiMePReJ, University of Bari, School of Medicine, Bari, Italy, Bari, Italy, [15]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [16]University of Milan and ASST Gaetano Pini-CTO, Milano, Italy, [17]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of rare and heterogeneous diseases. One of the greatest challenges in IIM management is defining and predicting disease flares, which are inconsistently characterized across studies(1–2). The aim of the study was to identify predictors of relapse in a retro-prospective, multicenter IIM cohort during the first two years of disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

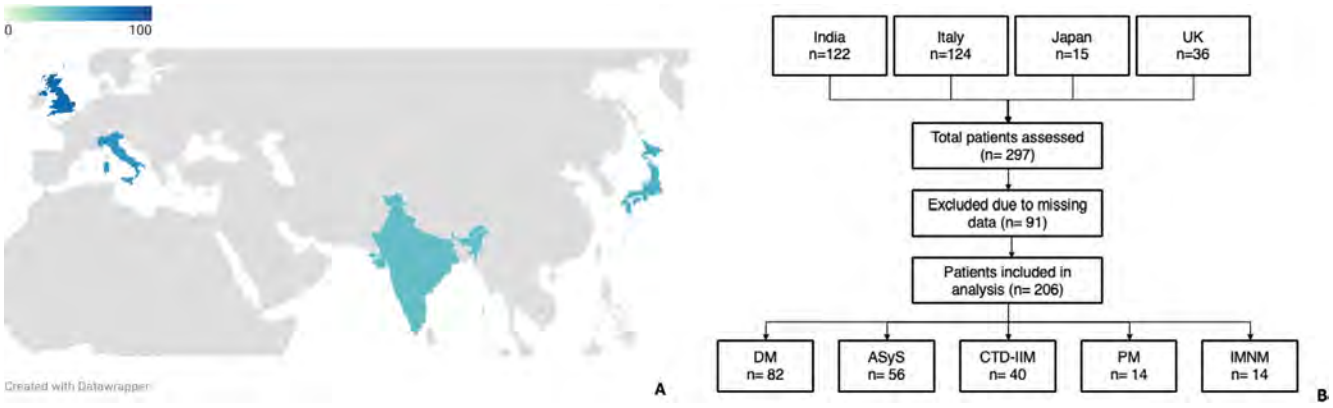
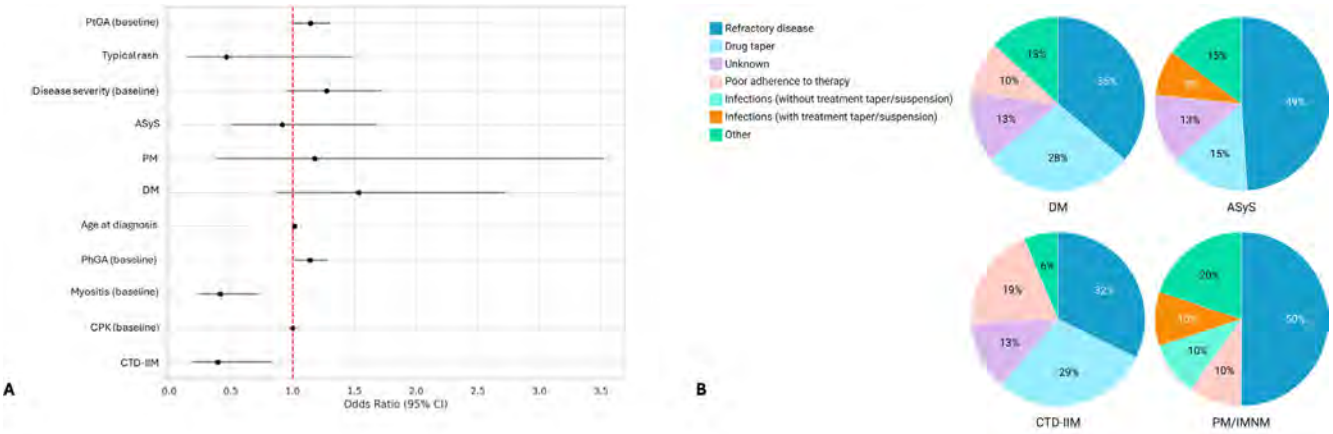


Figure 1A: Percentage of non-monophasic patients in participating centers. 1B: Workflow chart of patients' selection



ASyS: anti-synthetase syndrome; CPK: creatine phosphokinase; CTD-IIM: connective tissue disease-associated idiopathic inflammatory myopathy; DM: dermatomyositis; PM: polymyositis; PhGA: Physician global assessment; PtGA: Patient global assessment.

Figure 2A: Clinical predictors of chronic/relapsing disease in IIM. 2B Causes of relapses in different IIM subsets

Methods: Patients with IIM subsets—dermatomyositis (DM), polymyositis (PM), antisynthetase syndrome (ASyS), connective tissue disease-associated IIM (CTD-IIM), or immune-mediated necrotizing myopathy (IMNM)—were included if aged ≥18 years and had ≥2 years of follow-up. Relapse was defined as any worsening of disease activity requiring escalation of immunosuppressive therapy and/or glucocorticords (GC). Patients were classified as monophasic (M; 0 relapses), polycyclic (P; ≥1 relapse), or chronic continuous (CC; persistent activity) (2). Clinical characteristics across subgroups were compared using chi-square, Mann–Whitney U, or Student's t-test. Predictors were identified through multivariable logistic regression.

Results: Of 297 screened patients, 206 were included (155 F; median age at diagnosis: 46.9 years), distributed as follows: DM (82; 39.8%), ASyS (56; 27.2%), CTD-IIM (40; 19.4%), PM (14; 6.8%) and IMNM (14; 6.8%).

Over the first 2 years, disease trajectories were M in 40.8% of patients (n=84), P in 32.5% (n=67) and CC in the remaining (n=55, 26.7%). PM and IMNM demonstrated a higher propensity for CC or P patterns (64.2% vs 35.8%, p=0.326) although autoantibodies were not predictive.

Among 139 documented relapses, muscle involvement predominated (61.9%), with subtype-specific patterns: PM/IMNM (88.9% muscle), DM (68.4% muscle and skin), and ASyS (61.4% ILD). Refractory disease was primarily associated with

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of monophasic versus non monophasic patients.

	Monophasic (R<1 in the first two years) n=84		Polycyclic and Chronic Continuous (R>=1 in the first two years) n=122		p-value
Female, *n (%)*	66	79%	89	73%	0.226
Age at diagnosis, *median (IQR)*	59.7	55.2-64.2	68.7	53.2-69.5	0.086
Time from first manifestation to diagnosis in months, *median (IQR)*	1.69	4.30	1.55	4.20	0.82
IIM subtype, *n (%)*					
a. DM	33	39%	49	40%	0.137
b. PM	5	6%	9	7%	0.784
c. ASyS	24	29%	32	26%	0.777
d. CTD-IIM	18	21%	22	18%	0.333
e. IMNM	5	6%	9	7%	0.326
Autoantibodies, *n (%)*					
MSA, *n (%)*	66	79%	84	69%	0.256
MAA, *n (%)*	30	36%	42	34%	0.534
Baseline involvement					
Skin, *n (%)*	46	55%	57	47%	0.19
Myositis, *n (%)*	47	56%	85	70%	***0.021**
Carditis, *n (%)*	1	1%	10	8%	***0.023**
Systemic symptoms, *n (%)*	33	39%	60	49%	0.393
Arthritis, *n (%)*	31	37%	52	43%	0.87
Gastrointestinal tract, *n (%)*	8	10%	23	19%	0.125
Respiratory system, *n (%)*	36	43%	54	44%	0.416
Others, *n (%)*	14	17%	30	25%	0.088
CPK, *mean (SD)*	1717	3102	3717	5096	***0.003**
LDH, *mean (SD)*	920	957	1096	1172	0.623
SGOT, *mean (SD)*	115	148	156	149	***0.023**
SGPT, *mean (SD)*	99	122	150	175	***0.004**
PhGA, *mean (SD)*	2.39	2.83	3.9	2.74	***0.001**
PtGA, *mean (SD)*	2.61	3.16	4.52	3.12	***0.001**
MMT8, *mean (SD)*	73.7	9.38	72.9	8.37	0.251
Duration of disease at steroid start in months, *median (IQR)*	0.23	0.63	0.51	1.85	0.968
Steroid pulsed, *n (%)*	48	57%	69	57%	0.514
Steroid after diagnosis, *Induction dose*					
>1 mg/kg	53	63%	39	32%	***0.019**
0.5 to <1 mg/kg	21	25%	30	25%	
<0.5 to 0.25 mg/kg	15	18%	18	15%	
<0.25 mg/kg	4	5%	15	12%	
IVIG after diagnosis, *n (%)*	8	10%	32	26%	***0.004**
Immunosuppressive therapy within 6 months from diagnosis, *n (%)*	44	52%	80	66%	0.56
Duration of disease at immunosuppressant start in months, *median (IQR)*	0.90	2.58	0.81	1.99	0.406

ASyS: anti-synthetase syndrome; CPK: creatine phosphokinase; CTD-IIM: connective tissue disease-associated idiopathic inflammatory myopathy; DM: dermatomyositis; ILD: interstitial lung disease; IMNM: immuno-mediated necrotizing myopathy; IVIG: intravenous immunoglobulins; LDH: lactate dehydrogenase; MAA: myositis associated autoantibodies; MMT8: manual muscle testing 8; MSA: myositis specific autoantibodies; PhGA: Physician global assessment; PM: polymyositis; PtGA: Patient global assessment; SGOT: Serum Glutamic-Oxaloacetic Transaminase; SGPT: Serum Glutamic Pyruvic Transaminase.

relapse (43.2%), followed by treatment-related factors (see Figure 2B). Most relapses (56.5%) occurred while patients were on low-dose GC (≤5mg/day or none) with 44.7% developing within 6 months of stable dosing. Relapses occurred equally during short-term (≤3 months) and long-term (>1 year) stable immunosuppressive therapy (30.2% each).

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

P/CC disease was associated with a more severe phenotype— including elevated muscle enzymes and higher global assessment scores (Ph and Pt). Patients with relapsing patterns more often received low-dose GC at disease onset (< 0.25 mg/kg; 78.9% vs 21.1%, p=0.019) and intravenous immunoglobulin therapy (26.0% vs 10.0%, p=0.004). Multivariable analysis confirmed baseline muscle involvement, CPK levels, and PtGA as independent predictors of relapse.

Conclusion: In this multicentric cohort, relapses occurred in two-thirds of patients, often during a vulnerable period on low-dose GC and within six months of stable therapy. High baseline CPK and PtGA, along with low initial GC dose, independently predicted relapse. These findings highlight the potential value of flare predictors and advocate for standardized definitions of disease activity/relapse in IIM.

References

1. Aggarwal R, et al. ACR/EULAR response criteria for DM/PM. *Ann Rheum Dis*. 2017;76(5):792–801.
2. Constantin T, et al. Relapse and survival in juvenile/adult DM. *Orv Hetil*. 2007;148(42):1989–97.

Disclosure: M. Pellico: None; **C. Bochicchio**: None; **C. Iannone**: None; **L. Minikumari Rahulan**: None; **M. Fornaro**: None; **I. Cavazzana**: None; **E. Conticini**: GlaxoSmithKlein(GSK), 2, 6; **M. Kuwana**: AbbVie, 2, Asahi Kasei Pharma, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 6, GlaxoSmithKlein(GSK), 2, Medical and Biological Laboratories, 5, 9, Mochida, 2, Novartis, 2, Ono Pharmaceuticals, 6; **A. Yoshida**: None; **S. Cavalli**: None; **S. Grazzini**: None; **A. Gatti**: None; **G. Lopinto**: None; **P. Semeraro**: None; **T. Sheeran**: None; **F. Iannone**: None; **V. Agarwal**: None; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Eli Lilly & Co., 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **N. Del pAPA**: None; **L. Gupta**: None.

Abstract Number: 1213

Transitional Changes on High Resolution Computed Tomography (HRCT) in idiopathic inflammatory Myopathy- Associated Interstitial Lung Disease (IIM-ILD)

Sangmee Bae[1], Grace Kim[2], Jihey Lee[2], Daniela Markovic[2], Donald Tashkin[2], Jonathan Goldin[2], Rohit Aggarwal[3] and Christina Charles-Schoeman[4], [1]UCLA Rheumatology, Los Angeles, CA, [2]UCLA, Los Angeles, [3]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA, [4]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: HRCT is used as a surrogate for important histopathological findings when evaluating patients with interstitial lung disease (ILD). Quantitative imaging analysis (QIA) using CT texture-based scores were shown to associate with lung physiology and patient reported outcomes in IIM-ILD. The current work aims to examine changes in HRCT patterns of IIM-ILD as they transition from one pattern to another during follow-up, and compare transition patterns of IIM-ILD to that of ILD related to systemic sclerosis (SSc-ILD).

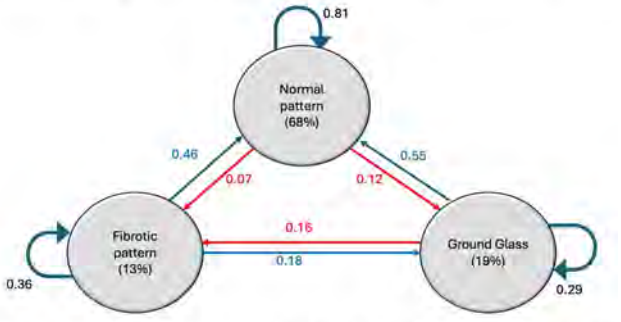
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

	IIM-ILD	SLS II
Demographics		
Age, years	52.3±12.2	52.3±9.7
Sex, Female	48(69%)	105(74%)
Disease variables		
IIM type, Dermatomyositis	26(37%)	-
Antisynthetase	37(53%)	-
Polymyositis	6(9%)	-
IMNM	1(1%)	-
Systemic sclerosis, limited		59(42%)
diffuse		83(58%)
Disease duration, years	3.5±6.6	2.6±1.8
IIM MD global activity VAS	42±19	-
Pt global activity VAS	32±27	-
SSc skin score (mRSS)		
Diffuse SSc	-	20.8±9.4
Limited SSc	-	6.1±3.8
HAQ-DI (0-3)	0.7±0.6	0.7±0.7
PFT at baseline		
FVC % predicted	71±20	66.5±9.1
TLC % predicted	76±17	65.8±11.1
DLCO Hg % predicted	47±29	60.9±12.8
Baseline HRCT QIA		
QGG	16.6±9.3	¶
QLF	12.4±10.7	8.6±6.9
QILD	29.2±18.2	29.5±14.0
Medications		
Mycophenolate Mofetil	40(59%)	69(49%)
Cyclophosphamide	5(7%)	73(51%)
IVIG	16(23%)	
Azathioprine	6(9%)	
Methotrexate	4(6%)	
Plaquenil	13(19%)	
Rituximab	8(11%)	
Prednisone	56(81%)	
Autoantibodies		
Antisynthetase ab	37(53%)	-
Anti-MDA5 ab	9(13%)	-
Anti-SRP ab	1(1%)	-
Anti-Mi2 ab	2(3%)	-
Anti-TIF1g ab	1(1%)	-
Anti-NXP2 ab	2(3%)	-
MAA	5(7%)	-
Unidentified ab/none/unknown	13(19%)	-
Topoisomerase-1 ab	-	61(46%)
RNA polymerase III ab	-	18(13%)
Centromere ab	-	3(2%)
Th/To ab	-	8(6%)

Values are presented as mean±SD IIM-ILD group(n=70) is comprised of 2 separate cohorts: one single-center observational cohort (n=59) and one multicenter clinical trial cohort of antisynthetase ILD (Attack My-ILD ClinicalTrials.gov identifier: NCT03215927, n=11) ¶ Data unavailable at time of abstract submission Abbreviations: IIM, idiopathic inflammatory myopathy; IMNM, immune mediated necrotizing myopathy; VAS, visual analog scale; PFT, pulmonary function test; QIA, quantitative imaging analysis; QGG, quantitative ground glass score; QLF, quantitative lung fibrosis score; QILD, quantitative total ILD score; MAA, myositis associated antibody (Ro, Ku, Pm-scl)

Figure 1. Probabilities of voxelwise transitions from one ILD pattern to another from baseline to follow up in IIM-ILD (n=70)



Values marked alongside arrows are the probability of transition. Values in parentheses are proportions of each pattern at baseline

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of transitional probabilities between IIM-ILD and SSc-ILD

	IIM-ILD (n=36)	SSc-ILD (n=97)	P value
$P_{GG \rightarrow NORML}$	0.50±0.04	0.38±0.02	**0.016**
$P_{Fibro \rightarrow NORML}$	0.43±0.03	0.24±0.01	**<0.001**
$P_{Fibro \rightarrow GG}$	0.18±0.01	0.11±0.01	**<0.001**
$P_{NORML \rightarrow NORML}$	0.78±0.03	0.87±0.01	**0.009**
$P_{GG \rightarrow GG}$	0.29±0.02	0.50±0.01	**<0.001**
$P_{Fibro \rightarrow Fibro}$	0.39±0.04	0.62±0.02	**<0.001**
$P_{NORML \rightarrow GG}$	0.14±0.02	0.10±0.01	0.053
$P_{GG \rightarrow Fibro}$	0.21±0.03	0.14±0.01	0.054
$P_{NORML \rightarrow Fibro}$	0.09±0.02	0.03±0.01	**0.015**

IIM-ILD subgroup of patients with 2 year interval between baseline and follow up to match follow up time in SLS II
Mean±SEM of the probabilities of moving from one pattern to another pattern

Methods: We evaluated changes in the quantitative extent of ground glass, fibrotic pattern and normal lung obtained at baseline and follow-up in HRCT scans. Patients with ILD confirmed by HRCT and on immunosuppressive treatment were included from 2 longitudinal IIM-ILD cohorts. In each within-patient baseline to follow-up HRCT pair, we calculated the transitional probability expressed as a proportion of voxels representing a particular pattern of ILD that changes from the initial pattern to another pattern at follow-up, the denominator being the total number of voxels within the initial pattern at baseline. Net improvements in ground glass and fibrotic patterns were determined by subtracting unfavorable transitional probabilities from favorable ones and statistically analyzed with the null hypothesis of net improvement being 0. In order to compare transitional probability with SSc-ILD, we selected IIM-ILD patients with comparable follow up time between HRCTs to the Scleroderma Lung Study II (SLS II) for which transitional probability had previously been reported using similar methodology (PMID:31430058).

Results: Transitional probability was calculated in 70 IIM-ILD patients that had baseline and follow-up HRCT scans adequate for voxelwise registration. The cohort included 53% antisynthetase and 37% dermatomyositis associated ILD patients with a mean disease duration of 3.5 years (Table 1). Mean transitional probability for each transition pattern is shown in Figure 1. Fifty-five percent of baseline ground glass and 46% of baseline fibrosis transitioned to a normal pattern. Net probabilities of improvement for both ground glass to normal transition ($P_{GG \rightarrow NORML}$ - $P_{NORML \rightarrow GG}$) and fibrosis to normal transition ($P_{Fibro \rightarrow NORML}$ - $P_{NORML \rightarrow Fibro}$) were significant (mean 0.44 and 0.39 respectively, $p < 0.0001$ for both). We compared transitional probabilities of 36 IIM-ILD patients with those in SLS II (Table 2). Favorable transitional probabilities ($P_{GG \rightarrow NORML}$, $P_{Fibro \rightarrow NORML}$, $P_{Fibro \rightarrow GG}$) were significantly greater in IIM-ILD compared to SSc-ILD patients whereas the majority of SSc-ILD remained stable. Unfavorable transitional probabilities ($P_{NORML \rightarrow GG}$, $P_{GG \rightarrow Fibro}$ and $P_{NORML \rightarrow Fibro}$) were overall low in both groups, showing a slight trend to be greater in the IIM-ILD compared to the SSc-ILD group (2/3 comparisons not statistically significant).

Conclusion: Transitional scoring assessment of ILD demonstrated that significant portions of ground glass and fibrotic patterns at baseline transitioned to a normal pattern with treatment in both IIM and SSc patients with ILD. However, IIM-ILD had significantly greater proportions of favorable transition patterns than SSc-ILD.

Disclosure: S. Bae: None; **G. Kim**: UCLA for patent; consultant at Voiant, 2, 10; **J. Lee**: None; **D. Markovic**: None; **D. Tashkin**: None; **J. Goldin**: MEDQIA, 12, Founder; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2; **C. Charles-Schoeman**: AbbVie/Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Immunovant, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2, Sana Biotechnology, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1214

Association of paraoxonase1 Activity with Calcinosis in Patients with Scleroderma and Dermatomyositis : An Exploratory Analysis

Sangmee Bae[1], Srijana Davuluri[2], Brian Lee[3], Sean Lim[4], Daniela Markovic[5], Lorinda Chung[2], David Fiorentino[6] and Christina Charles-Schoeman[7], [1]UCLA Rheumatology, Los Angeles, CA, [2]Stanford University, Stanford, CA, [3]Stanford University, Stanford, [4]Stanford University, Palo Alto, [5]UCLA, Los Angeles, [6]Department of Dermatology, Stanford University Medical Center, Stanford, CA, [7]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1. Baseline clinical characteristics in SSc and DM cohorts

	Systemic Sclerosis				Dermatomyositis			
	Total (n=258)	Calcinosis (N=101)	Without Calcinosis (n=157)	P value	Total (N=652)	Calcinosis (N=85)	Without Calcinosis (n=567)	P value
Age, years	57.0 ± 13.0	57.3 ± 12.8	56.9 ± 13.2	0.91	51.8 ± 15.5	48.4 ± 16.2	52.3 ± 15.2	**<0.001**
Sex, Female	236 (92%)	94 (93%)	14 (92%)	0.84	474 (74%)	64 (77%)	410 (74%)	0.60
Race								
White	192 (80%)	88 (91%)	103 (73%)	**0.001**	407 (66%)	50 (60%)	357 (66%)	0.37
Asian	40(17%)	6 (6%)	34 (24%)		89 (14%)	11 (13%)	78 (15%)	
Black	8(3%)	3 (3%)	5 (4%)		27 (4%)	6 (7%)	21 (4%)	
Ethnicity								
Hispanic	0	0	0	NA	118 (20%)	18 (23%)	100 (20%)	0.59
Not-Hispanic	217 (100%)	89 (100%)	127 (100%)		468 (80%)	60 (77%)	408 (80%)	
Disease duration (months)†	114 ± 116	133± 126	103 ± 108	**0.03**	74 ± 212	89± 101	72± 224	**<0.001**
BMI in kg/m²	25.1±5.4	25.3±5.5	24.9±5.3	0.55	27.3 ± 6.8	27.9 ± 9.3	27.1 ± 6.3	1.00
ESR mm/hr	24.9 ± 21.1	26.8 ± 20.2	23.7 ± 21.7	0.19	28.6 ± 29.4	35.4 ± 31.9	27.4 ± 28.9	**0.04**
CRP mg/L	1.7 ± 3.5	2.2 ± 4.4	1.4 ± 2.9	0.82	4.7 ± 12.4	5.1 ± 8.1	4.7 ± 13.0	0.10
Comorbidities, ever								
ILD	123 (48%)	54 (54%)	69 (45%)	0.21	180 (32%)	20 (27%)	160 (32%)	0.47
Smoking	89 (35%)	34 (34%)	55 (36%)	0.84	69 (14%)	11 (16%)	58 (13%)	0.74
Hypertension	71 (29%)	29 (29%)	42 (29%)	1.00	71 (29%)	29 (29%)	42 (29%)	1.00
Diabetes mellitus	16 (7%)	4 (4%)	12 (8%)	0.28	70 (11%)	11 (13%)	59 (11%)	0.64
Acute MI	4 (2%)	2 (2%)	2 (1%)	1.00	8 (1%)	1 (1%)	7 (1%)	1.00
Ischemic stroke	2 (1%)	1 (1%)	1 (1%)	1.00	14 (2%)	2 (2%)	12 (2%)	1.00
Peripheral artery disease	1 (0%)	1 (1%)	NA	NA	21 (3%)	3 (4%)	18 (3%)	1.00
Congestive heart failure	7 (3%)	1 (1%)	6 (4%)	0.28	9 (1%)	0	9 (2%)	1.00
Medications								
Hydroxychloroquine	47 (20%)	14 (16%)	33 (24%)	0.18	136 (22%)	22 (26%)	114 (21%)	0.39
Methotrexate	25 (11%)	11 (12%)	14 (10%)	0.93	53 (20%)	**14 (41%)**	**39 (17%)**	**0.002**
Azathioprine	6 (3%)	2 (2%)	4 (3%)	1.00	139 (22%)	24 (29%)	115 (21%)	0.15
Rituximab	0	0	0	NA	48/619 (8%)	5 (7%)	42 (8%)	1.00
Mycophenolate	47 (21%)	14 (15%)	33 (24%)	0.16	195 (39%)	10 (29%)	95 (40%)	0.32
IVIG	6 (3%)	3 (3%)	3 (2%)	0.94	156 (25%)	24 (29%)	132 (25%)	0.50
Cyclophosphamide	4 (2%)	NA	4/107 (4%)	0.99	19 (3%)	NA	19 (4%)	1.00
Statin	44 (19%)	20 (22%)	24 (18%)	0.58	74 (12%)	13 (16%)	61 (11%)	0.28
SSc variables								
SSc subtype, Limited	160(62%)	56	103	0.10				
Diffuse	99(38%)	45	54					
mRSS	9[2-18]	9[3-21]	5[2-16]	**0.04**				
Antibody target								
Centromere	91(36%)	41(45%)	49(54)	0.28				
Topoisomerase I	53(20%)	17(31%)	37(69)	0.08				
RNA polymerase III	43(17%)	17(40%)	26(60)	0.83				
U1-RNP	19(7%)	9(47%)	10(53)	0.86				
Pulmonary hypertension	72(28%)	32(31%)	40(25)	0.35				
Renal crisis	18(7%)	9(9%)	9(6)	0.33				
Inflammatory arthritis	145(56)	57(56%)	88(56)	0.95				
Myositis	41(16%)	17(17%)	24(15)	0.74				
Digital ulceration	102(39%)	**56(55%)***	**46(29)**	**<0.0001**				
Digital pitting	87(34%)	43(43%)	44(28)	0.06				
Telangiectasias	209(81%)	**91(90%)***	**117(75)**	**0.001**				
Acro-osteolysis	39(15%)	**22(22%)***	**17(11)**	**0.04**				
GERD	246(95%)	99(98%)	146(93)	0.06				
GAVE	16(6%)	9(9%)	7(4)	0.11				
SIBO	72(28%)	35(35%)	37(24)	0.14				
DM variables								
Antibody target								
MDA5					84(13%)	14(12%)	70(12%)	0.30
Mi2					37(6%)	5(6%)	32(6%)	0.93
SAE					27(4%)	**8(9%)***	**19(3%)**	**0.02**
TIF1γ					182(28%)	22(26%)	160(28%)	0.65
NXP2					59(9%)	**13(15%)***	**45(8%)**	**0.04**
Other					130(20%)	14(16%)	116(20%)	0.38
Raynaud's					143(22%)	21(27%)	122(24%)	0.48
Clinically Amyopathic					277(42%)	31(38%)	246(45%)	0.21
Dysphagia					222(34%)	31(29%)	191(36%)	0.56
Skin ulceration					105(16%)	**21(27%)***	**84(16%)**	**0.03**
Inflammatory arthritis					221(34%)	**38(48%)***	**183(37%)**	**0.049**
CPK, U/L					84[51-197]	88[52-190]	82[51-165]	0.92
Aldolase, U/L					5.8[4.3-8]	5.7[4.5-7.2]	5.8[4.3-8.1]	0.82
CDASI-activity					11[5-21]	13[4-23]	11[5-20]	0.59
CDASI-damage					2[0-4]	**4[1-8]***	**1[1-4]**	**<0.0001**

Values are reported as mean ± SD, median[IQR] and n(%)

P values compare calcinosis yes vs no within disease group. Bolded are p<0.05

†Disease duration defined as time (months) from onset of first non-raynaud symptom in SSc and from symptom onset in DM cohort.

Abbreviations: ILD, interstitial lung disease; mRSS, modified Rodnan Skin Score; GERD, Gastroesophageal reflux disease; GAVE, gastric antral vascular ectasia; SIBO, small intestinal bacterial overgrowth; CDASI, cutaneous disease area and severity index for DM rash

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

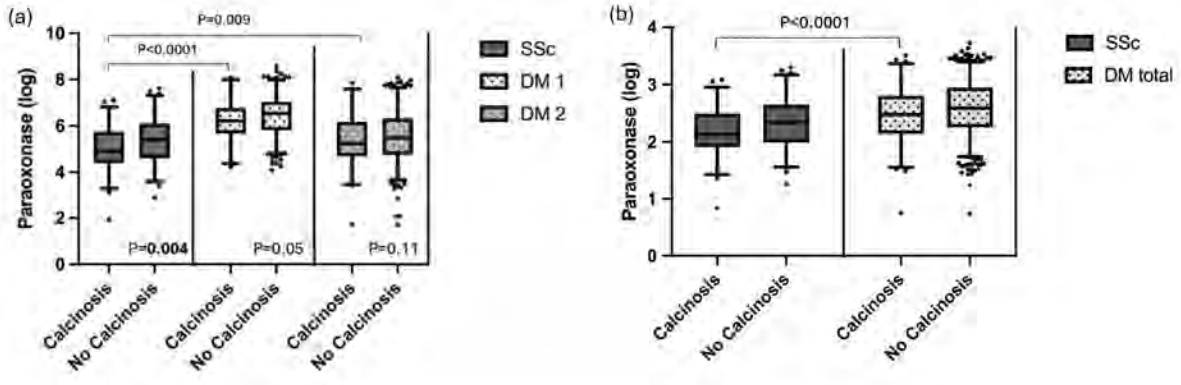
Background/Purpose: Calcinosis is a feature seen in systemic sclerosis (SSc) and dermatomyositis (DM) that leads to significant morbidity and poor quality of life. Inflammatory vasculopathy is hypothesized to play a role in dystrophic mineral deposition. Paraoxonase1 (PON1) is a high-density lipoprotein (HDL) associated protein that protects the vascular endothelium from oxidative injury and damage. The current study aims to assess the association of calcinosis PON1 activity in SSc and DM patients.

Methods: Calcinosis is a feature seen in systemic sclerosis (SSc) and dermatomyositis (DM) that leads to significant morbidity and poor quality of life. Inflammatory vasculopathy is hypothesized to play a role in dystrophic mineral deposition. Paraoxonase1 (PON1) is a high-density lipoprotein (HDL) associated protein that protects the vascular endothelium from oxidative injury and damage. The current study aims to assess the association of calcinosis PON1 activity in SSc and DM patients.

Results: Among 258 SSc patients and 652 DM patients, we identified a total of 186(20%) patients who ever had calcinosis. Calcinosis was more common in SSc (39.6%) compared to DM (13%, p< 0.0001). Calcinosis was associated with longer disease duration in both SSc and DM (Table 1). In SSc, patients with calcinosis were more often white and had higher skin scores, while DM patients with calcinosis were significantly younger, had higher sedimentation rate and had higher incidence of anti SAE and NXP2 antibodies compared to DM without calcinosis (Table 1). Clinical manifestations associated with calcinosis in SSc were digital ulcerations, telangiectasias, and acro-osteolysis, while in DM associated factors were skin ulcers and inflammatory arthritis.

PON1 paraoxonase activity was significantly lower in SSc patients with calcinosis compared to SSc without calcinosis, and a similar trend was seen within each DM cohort (Figure 1-a). Association between calcinosis and low PON1 was significant when the two DM cohorts were combined (Figure 1-b). Multivariate models adjusting for age, sex and disease duration demonstrated that the association between low paraoxonase and calcinosis was significant in SSc, in DM total (DM1+DM2) and in all 3 cohorts combined (SSc+DM1+DM2) (Table 2). SSc patients overall had a significantly lower paraoxonase activity compared to DM (p=0.0002), and SSc patients with calcinosis had the lowest paraoxonase activity.

Figure 1. Paraoxonase in SSc and DM patients with and without calcinosis



Paraoxonase levels compared between patients with and without calcinosis. Box plots for median[IQR]. Paraoxonase is log transformed for normal distribution. (a) comparison within each cohort, (b) comparison within disease subgroup with DM1+DM2 as DM total group. P value by student's t-test

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Unadjusted and Adjusted models of the association between PON1 paraoxonase activity and calcinosis

	All		SSc		DM	
	OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P
Unadjusted	0.73[0.63-0.85]	<0.0001	0.68[0.53-0.88]	0.003	0.84[0.73-0.97]	0.02
Model 1	0.72[0.61-0.84]	<0.0001	0.67[0.52-0.87]	0.003	0.83[0.71-0.96]	0.01
Model 2	0.72[0.61-0.84]	<0.0001	0.68[0.52-0.87]	0.003	0.83[0.71-0.97]	0.02
Model 3	0.68[0.57-0.80]	<0.0001	0.67[0.51-0.87	0.003	0.78[0.65-0.93]	0.005

Multivariate logistic regression for calcinosis ever. Paraoxonase is log transformed for normal distribution. All models adjusted for repeated measures.

Model 1: adjusted for age
Mode 2: adjusted for age and sex
Model 3: adjusted for age, sex and disease duration

Conclusion: In our current work, calcinosis was observed in 40% of SSc and 13% of DM patients. Calcinosis was associated with longer disease duration and ulcerations in both SSc and DM. Impairment in the activity of the PON1 enzyme, which normally protects the vascular endothelium from oxidative injury, was associated with the presence of calcinosis in both DM and SSc patients, suggesting potential involvement in the disease pathogenesis.

Disclosure: S. Bae: None; **S. Davuluri**: None; **B. Lee**: None; **S. Lim**: None; **D. Markovic**: None; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **D. Fiorentino**: None; **C. Charles-Schoeman**: AbbVie/Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Immunovant, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2, Sana Biotechnology, 2.

Abstract Number: 1215

Remission Rates and Predictors in Idiopathic Inflammatory Myopathy Subtypes: Insights from a Single-Center Cohort

Nantakarn Pongtarakulpanit[1], **Sidra Tahir**[2], Varshapriya Suresh[2], Vaidehi Kothari[3], Shiri Keret[4], Eugenia Gkiaouraki[5], Siamak Moghadam-Kia[6], Vladimir Liarski[7], Dana Ascherman[5] and Rohit Aggarwal[8], [1]Mahidol University, University of Pittsburgh, Bangkok, Thailand, [2]Internal medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, [3]University of Pittsburgh Medical Center, Pittsburgh, [4]Bnai Zion Medical Center, Atlit, Israel, [5]University of Pittsburgh, Pittsburgh, PA, [6]University of Pittsburgh Medical Center, Pittsburgh, PA, [7]University of Pittsburgh School of Medicine, Pittsburgh, [8]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: With therapeutic advances in idiopathic inflammatory myopathy (IIM), achieving remission has become an important goal. However, comprehensive data on remission, particularly across IIM subtypes, remain limited. **This stu**dy assessed remission rates and identified predictors of remission in a prospective IIM registry.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Remission after IIM diagnosis

Subtype	Parameters, n (%) or median (Q1, Q3)									
	Remission at 12 months	Drug-free remission at 12 months	Overall remission (ever)	Time to 1st remission (years)	Overall drug-free remission (ever)	Time to 1st drug-free remission (years)	Flare(s) after 1st remission	Time to 1st flare after remission (years)	Remission at last visit	Drug-free remission at last visit
All (n = 430)	15 (3.5)	3 (0.7)	152 (35.3)	3.8 (2.0 – 6.3)	80 (18.6)	5.0 (3.9 – 9.1)	41/152 (27.0)	3.5 (1.6 – 7.0)	121 (28.1)	73 (17)
DM (n = 221)	11 (5.0)	1 (0.5)	94 (42.5)	3.6 (1.8 – 6.1)	51 (23.1)	5.2 (3.8 – 8.5)	25/94 (26.6)	2.4 (1.0 – 7.0)	74 (33.5)	44 (19.9)
ASyS (n = 125)	2 (1.6)	1 (0.8)	35 (28.0)	4.3 (3.0 – 8.3)	19 (15.2)	7.3 (4.3 – 11.1)	11/35 (31.4)	4.0 (2.3 – 8.7)	28 (22.4)	18 (14.4)
IMNM (n = 45)	2 (4.4)	1 (2.2)	15 (33.3)	2.6 (1.7 – 4.6)	8 (17.8)	4.6 (3.7 – 6.7)	2/15 (13.3)	1.7, 3.8*	12 (26.7)	8 (17.8)
PM (n = 39)	0 (0.0)	0 (0.0)	8 (20.5)	12.1 (4.6 – 16.6)	3 (7.7)	2.6, 13.3, 17.7	3/8 (37.5)	4.3, 6.2, 11.0**	7 (17.9)	3 (7.7)

Abbreviations: ASyS, antisynthetase syndrome; DM, dermatomyositis; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; PM, polymyositis

*Time to 1st flare after remission of 2 patients in IMNM subtype (years)

**Time to 1st flare after remission of 3 patients in PM subtype (years)

Table 2. Cox proportional hazard model for predictive factors of first remission in 346 IIM patients followed for ≥ 1 year at the University of Pittsburgh Myositis Center

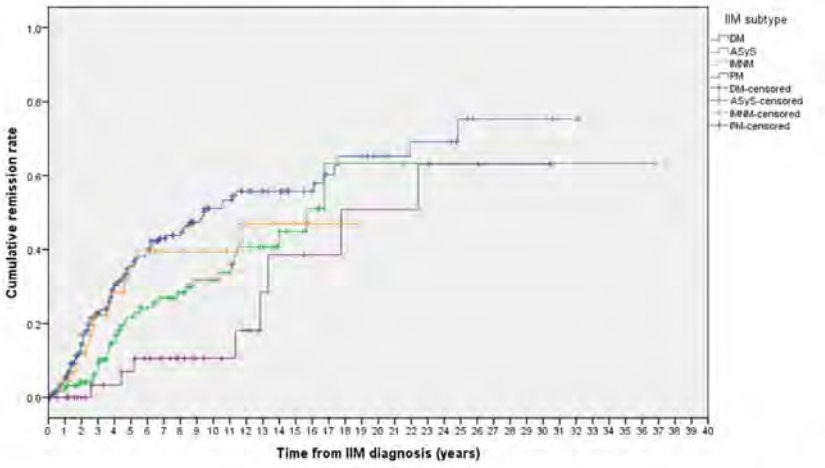
Parameters	Descriptive, mean ± SD or median (Q1, Q3)	Univariable			Multivariable (Forward LR method)		
		HR	95% CI	P-value	HR	95% CI	P-value
Age at diagnosis, years	52.5 ± 14.0	1.01	0.99 -1.02	0.468			
Symptom onset to diagnosis (months)	4.0 (2.0 – 11.0)	1.00	1.00 – 1.00	0.729			
Female	234 (67.6)	0.89	0.62 – 1.28	0.535			
Race							
White	297/333 (89.2)	1.19	0.69 – 2.03	0.534			
Black	29/333 (8.7)	0.51	0.26 – 1.00	0.050[1]			
Other	7/333 (2.0)	8.10	3.50 – 18.73	**<0.001***[1]	9.79	4.12 – 23.27	**<0.001***
Subtype							
DM	182 (52.6)	1.60	1.15 – 2.24	**0.005***[1]			
ASyS	105 (30.3)	0.70	0.48 – 1.03	0.072[1]			
IMNM	35 (10.1)	1.11	0.64 – 1.92	0.720			
PM	24 (6.9)	0.42	0.20 – 0.91	**0.028***[1]	0.37	0.15 – 0.92	**0.033***
Key clinical features							
Dysphagia	106 (30.6)	1.03	0.72 – 1.49	0.867			
Interstitial lung disease	128 (37.0)	0.65	0.46 – 0.93	**0.017***[1]			
Pulmonary hypertension	45 (13.0)	0.49	0.24 – 0.91	**0.023***[1]	0.37	0.18 – 0.73	**0.004***
Cancer	24 (6.9)	1.08	0.53 – 2.20	0.838			
Manual muscle testing (adjusted to full score of 100)	98.8 (90.0 – 100)	1.00	1.00 – 1.00	0.739			
CK (fold of upper limit of normal)	0.94 (0.37 – 5.69)	1.00	1.00 – 1.00	0.637			
Antibodies							
Mi2	22/329 (6.7)	2.31	1.32 – 4.02	**0.003***[1]	1.92	1.09 – 3.37	**0.023***
TIF1-γ	70/329 (21.3)	1.25	0.86 – 1.82	0.250			
NXP2	13/329 (4.0)	1.26	0.59 – 2.77	0.550			
SAE	5/329 (1.5)	0.71	0.17 – 2.91	0.635			
MDA5	14/329 (4.3)	1.86	0.87 – 3.99	0.112			
Jo-1	74/329 (22.5)	0.76	0.50 – 1.15	0.191			
PL7	9/329 (2.7)	1.16	0.37 – 3.64	0.804			
PL12	16/329 (4.9)	0.51	0.16 – 1.61	0.251			
EJ	1/329 (0.3)	0.05	0.00 – 6294.29	0.616			
OJ	5/329 (1.5)	0.05	0.00 – 52.08	0.396			
KS	3/329 (0.9)	1.40	0.35 – 5.65	0.640			
SRP	9/329 (2.7)	1.02	0.32 – 3.19	0.980			
HMG-CR	12/329 (3.6)	0.80	0.30 – 2.17	0.666			
Ku	1/328 (0.3)	0.05	0.00 – 1404.13	0.565			
PM-Scl	1/328 (1.8)	0.73	0.23 – 2.31	0.596			
SSA	43/328 (13.1)	0.53	0.28 – 0.97	**0.041***[1]			
Negative	79/326 (24.2)	1.31	0.90 – 1.89	0.158			

Abbreviations: ASyS, antisynthetase syndrome; CK, creatine kinase; DM, dermatomyositis; HR, hazard ratio; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; PM, polymyositis

*P-value<0.05; [1]Variables inserted into the multivariable Cox proportional model (forward LR method)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Cumulative first remission rate according to IIM subtype



Abbreviations: ASyS, antisynthetase syndrome; DM, dermatomyositis; IIM, idiopathic inflammatory myopathy; IMNM, immune-mediated necrotizing myopathy; PM, polymyositis

Methods: We analyzed data from adult IIM patients enrolled at the University of Pittsburgh Myositis Center between January 2000 and March 2019. The "remission cohort" included 430 patients with a disease duration of ≥1 year or those who died within the first year (categorized as non-remission). We focused on four IIM subtypes: dermatomyositis (DM), antisynthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM), and polymyositis (PM), according to the physician's judgement based on the 2017 EULAR/ACR classification criteria. ASyS was further defined by clinical symptoms and ASyS antibodies, while IMNM was further defined by clinical symptoms and either anti-HMGCR antibody, anti-SRP antibody, or consistent muscle biopsy. Overlap syndromes and inclusion body myositis were excluded. Remission was defined as the absence of disease activity based on expert clinical assessment, either while receiving stable/de-escalating therapy or off medication. Predictive factors for remission were analyzed using a Cox proportional hazard model in a subcohort of 346 patients with ≥1 year of follow-up post-enrollment.

Results: Among 430 patients (67.4% female, 88.5% white, mean age at diagnosis 50.2 ± 14.3 years), the median follow-up time was 5.1 (IQR 1.2 – 10.1) years, and the median disease duration at last visit was 7.5 (IQR 3.1 – 12.4) years. The remission rate at 12 months post-diagnosis was 3.5%, while the overall remission rate was 35.3%. IIM subtype-specific 12-month and overall remission rates were: DM (5.0%, 42.5%), ASyS (1.6%, 28.0%), IMNM (4.4%, 33.3%), and PM (0.0%, 20.5%) (Table 1 and Figure 1). The median time from diagnosis to first remission was 3.8 (IQR 2.0 – 6.3) years. Flares after remission occurred in 27.0% of patients after median 3.5 (IQR 1.6 – 7.0) years. The overall drug-free remission was achieved in 18.6% of patients, with rates by subtype: DM 23.1%, ASyS 15.2%, IMNM 17.8%, and PM 7.7%. In univariate analysis, predictors of higher remission included non-white/black race (i.e., other), DM subtype, and anti-Mi2 antibody, while predictors of lower remission included PM subtype, interstitial lung disease, pulmonary hypertension, and anti-SSA antibody. In multivariate analysis, non-white/black race (HR 9.79, $P<0.001$) and anti-Mi2 antibody (HR 1.92, $P=0.023$) were independently associated with increased remission likelihood, whereas PM subtype (HR 0.37, $P=0.033$) and pulmonary hypertension (HR 0.37, $P=0.004$) were independently associated with decreased remission likelihood (Table 2).

Conclusion: Remission rates vary across IIM subtypes, with the highest rate in DM and the lowest rate in PM. Race, IIM subtype, autoantibody profile, and comorbid pulmonary hypertension significantly influence remission outcomes. These insights can inform individualized management and prognostication of IIM.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Pongtarakulpanit: None; **S. Tahir**: None; **V. Suresh**: None; **V. Kothari**: None; **S. Keret**: None; **E. Gkiaouraki**: None; **S. Moghadam-Kia**: None; **V. Liarski**: None; **D. Ascherman**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

Abstract Number: 1216

Measurement Properties of a Shorter Health Assessment Questionnaire (HAQ-II) in Patients with Inflammatory Myopathies

Sung-Ki Lee[1], Kristin Wipfler[2], Ethan Ritz[3], Burcu Aydemir[4], Kaleb Michaud[5] and Didem Saygin[6], [1]Rush Medical College, Chicago, IL, [2]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [3]Rush Research Informatics Core, Rush University Medical Center, Chicago, IL, [4]Northwestern University Feinberg School of Medicine, Chicago, IL, [5]University of Nebraska Medical Center, Omaha, NE, [6]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of autoimmune disorders characterized by chronic skeletal muscle inflammation leading to muscle weakness and limitations in physical function. Despite the clinical significance of functional impairments in IIM, there are few validated tools of physical function in this population. Even though the Health Assessment Questionnaire (HAQ) is widely accepted, data on its validity are limited. Further, its length and complex scoring system make it cumbersome in clinic, requiring development of a more efficient and validated measure of physical function in these patients. The HAQ-II is a shortened version of the HAQ with 10 items validated in RA. In this study, we aim to assess measurement properties of HAQ-II in evaluation of physical function in individuals with IIM.

Methods: Data were from adults enrolled in FORWARD -The National Databank for Rheumatic Disease- between 1999-2023. Participants had a physician diagnosis of IIM and completed the HAQ-II along with other items related to their disease, comorbidities, pain, fatigue, and quality of life. Internal consistency of HAQ-II was assessed using Cronbach's α. Floor and ceiling effects were calculated by identifying the proportion of minimum and maximum possible HAQ-II scores. Discriminant validity was assessed by comparing differences in baseline HAQ-II scores between relevant subgroups. Construct validity was evaluated by comparing HAQ-II scores and measures of physical health, including SF-36 physical functioning, patient global disease activity, fatigue, and pain using Pearson correlations based on a priori hypotheses derived from the literature. Responsiveness of HAQ-II was assessed using linear mixed models.

Results: A total of 192 participants with IIM (mean age 54.8 [±13.7]; 79.3% female) who completed the HAQ-II (mean 1.1 [±0.7]) were included in the study. Cronbach's α of HAQ-II was 0.93. Floor and ceiling effects were negligible with 7.8% and 0%, respectively. All a priori hypotheses for discriminant validity were met with significant differences in HAQ-II scores between participants with low vs high physical functioning, patient global disease activity, fatigue, and pain levels ($p < 0.0001$) (Table 1). Fifteen out of 17 a priori hypotheses (88.2%) were met for the construct validity of HAQ-II. HAQ-II had weak correlations with symptom duration, age, BMI, Rheumatic Disease Comorbidity Index, SF-36 mental component score, role limitations due to emotional problems and emotional well-being, moderate correlations with pain levels, fatigue levels, health satisfaction, SF-36 general health, and social functioning, and strong correlations with SF-36 physical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Discriminant validity assessment of HAQ-II comparing scores between subgroups of individuals with IIM with low vs high physical functioning, patient global disease activity, fatigue, and pain.

Groups	HAQ-II	
	Mean (SD)	p value
SF-36 physical functioning <45	1.60 (0.53)	<0.0001
SF-36 physical functioning ≥45	0.59 (0.48)	
Patient global disease activity <4	0.60 (0.52)	<0.0001
Patient global disease activity ≥4	1.50 (0.55)	
Fatigue <4.5	0.68 (0.58)	<0.0001
Fatigue ≥4.5	1.42 (0.61)	
Pain <3	0.71 (0.66)	<0.0001
Pain ≥3	1.38 (0.57)	

*Groups stratified by median scores.

Table 2. Construct validity assessment showing a priori hypotheses and observed correlations between HAQ-II and other relevant variables.

Variables	HAQ-II		
	A priori hypotheses	Observed correlations (Rho)	Met?
Age	Weak	-0.005	Yes
Symptom duration	Weak	-0.005	Yes
Body mass index	Weak	0.27	Yes
Rheumatic disease comorbidity index	Weak	0.33	Yes
Pain level	Moderate	0.56	Yes
Fatigue level	Moderate	0.58	Yes
Patient global disease activity	Moderate	0.71	No
Health satisfaction	Moderate	-0.55	Yes
SF-36 PCS	Strong	-0.79	Yes
SF-36 MCS	Weak	-0.29	Yes
SF-36 Health Concepts:			
SF-36 Physical functioning	Strong	-0.87	Yes
SF-36 Role limit due to physical health	Strong	-0.67	No
SF-36 Pain	Moderate	-0.56	Yes
SF-36 General health	Moderate	-0.50	Yes
SF-36 Vitality	Moderate	-0.59	Yes
SF-36 Social functioning	Moderate	-0.60	Yes
SF-36 Role limit due to emotional problems	Weak	-0.36	Yes
SF-36 Emotional well being	Weak	-0.34	Yes

Table 3. Linear mixed models examining the relationship between longitudinal change* in HAQ-II and other outcome variables over time after controlling for age, sex, and obesity.

Variables	HAQ-II	
	Beta [CI]	P value
Pain level	0.08 [0.06 – 0.09]	<0.0001
Fatigue level	0.08 [0.06 – 0.09]	<0.0001
Patient global disease activity	0.07 [0.06 – 0.08]	<0.0001
SF36 Physical Component Score	-0.03 [(-0.04) - (-0.03)]	<0.0001

component score and physical functioning (Table 2). After controlling for age, sex, and obesity, change in HAQ-II was significantly associated with change in pain, fatigue, patient global disease activity, and SF-36 PCS (Table 3).

Conclusion: HAQ-II demonstrated good internal consistency, validity, and responsiveness in assessing physical function in individuals with IIM. Our findings support the HAQ-II as a valid and practical instrument and support its application in both clinical and research settings.

Disclosure: S. Lee: None; **K. Wipfler**: None; **E. Ritz**: None; **B. Aydemir**: None; **K. Michaud**: None; **D. Saygin**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1217

Validation and clincial use of anti-MDA5 test - LIA versus ELISA

TING-YUAN LAN[1], pei-Hsinq lai[2], Tai-Ju Lee[3], Ting-Wei Chang[4], Kuan-Yen Lin[5], Shao-Yu Pai[6] and Ko-Jen Li[7], [1]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan, [2]Taipei City Hospital, Taichung, Taiwan, [3]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan (Republic of China), [4]National Taiwan University Hospital Hsinchu Branch, Taichung, Taiwan, [5]National Taiwan University Hospital, Hsin-Chu Branch, Hsin-Chu City, Taiwan (Republic of China), [6]National Taiwan University Hospital, Taichung City, Taiwan (Republic of China), [7]National Taiwan University Hospital, Taipei, Taiwan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

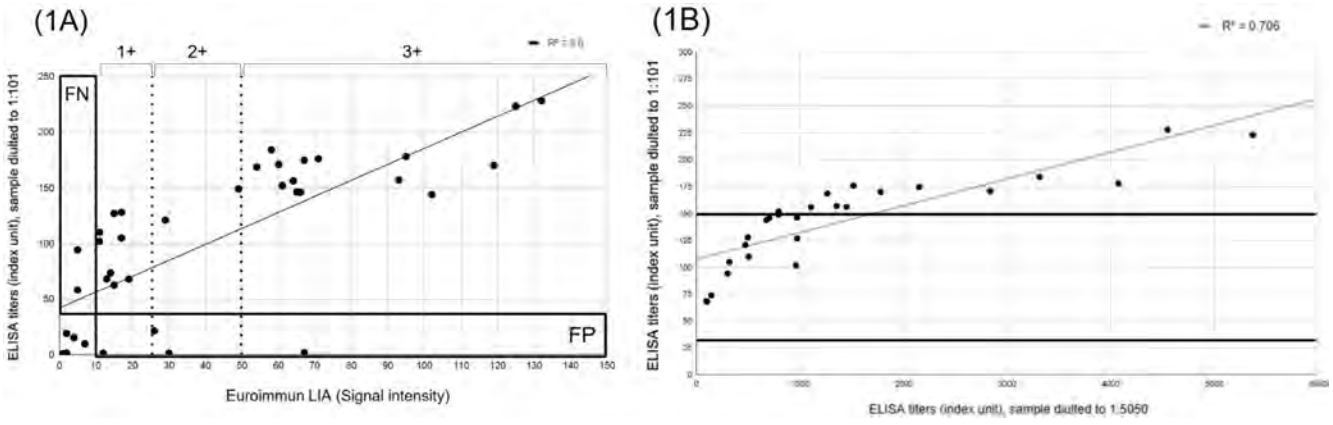
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Although immunoprecipitation (IP) remains the gold standard for detecting myositis autoantibodies, it is technically demanding and not widely available. Line immunoassay (LIA) has become a primary diagnostic tool in many centers but is prone to false positives and negatives, which may lead to inappropriate treatment—particularly in anti-MDA5 patients at risk of rapidly progressive interstitial lung disease (RPILD). Commercial anti-MDA5 ELISA tests have shown comparable performance to IP and may offer prognostic value, especially with additional sample dilution. We aim to validate the performance of LIA for detecting anti-MDA5 using commercial ELISA as reference and explore the clinical utility of ELISA in a Taiwanese medical center.

Methods: Our center uses the Euroimmun 16-antigen LIA panel for myositis antibodies. Samples with anti-MDA5 positivity on LIA and those with clinical features suggestive of anti-MDA5 disease (e.g., RPILD, cutaneous findings) but LIA-negative were further tested using a commercial anti-MDA5 ELISA (MBL, Japan). ELISA was performed at 1:101 dilution per the manufacturer's protocol and at 1:5050 per Gono et al. Two rheumatologists confirmed the final diagnosis based on clinical course.

Results: We analyzed 40 samples from 33 patients. LIA had 4 false positives and 2 false negatives, yielding a sensitivity of 0.93 and specificity of 0.64. Three of four false positives showed moderate or strong LIA signals. Restricting interpretation to moderate/strong positives improved specificity (0.73) but reduced sensitivity (0.62). Both false negatives occurred in RPILD cases: one patient survived after early immunotherapy guided by timely ELISA, while the other died before ELISA results were available. Among the four false positives, two had mechanic's hands but lacked typical anti-MDA5 features, and the other two had ILD due to other causes.



(A) The correlation between LIA signal intensity and ELISA (standard dilution 1:101). (B) The correlation ELISA with standard dilution (1:101) and dilution of 1:5050. Abbreviations: LIA: Line blotting assay, FN: false negative, FP: false positive

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

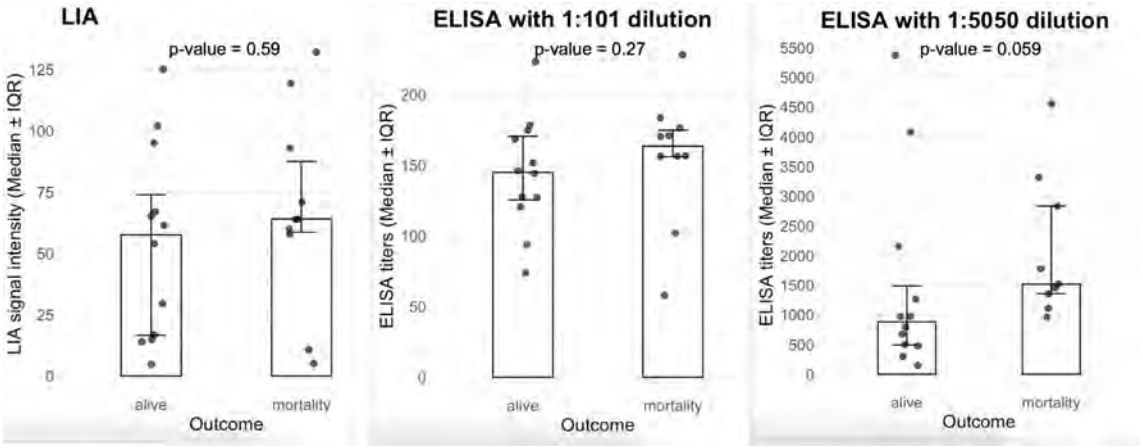


Figure 2: Association of antibody signal intensity (LIA)/ELISA titers and prognosis of patients (morality vs alive).

Among ELISA-positive samples, 45% (13/29) exceeded the 150 IU upper limit at 1:101 dilution, masking antibody titer differences. Dilution to 1:5050 revealed clearer stratification (Figure 1B), with higher titers more strongly associated with poor outcomes (median 1515 vs. 882, p=0.059). In comparison, neither the 1:101 dilution (164 vs. 145 IU, p=0.27) nor LIA signal (64 vs. 57.5, p=0.59) significantly predicted outcome (Figure 2).

Conclusion: Commercial ELISA is a valuable confirmatory tool for anti-MDA5 diagnosis, especially where IP is unavailable and LIA is the standard. ELISA reduces misclassification by LIA and improves treatment guidance. High antibody titers often exceed the ELISA kit's standard detection range, and additional dilution (1:5050) enhances outcome prediction and better identifies high-risk patients.

Disclosure: T. LAN: None; **p. lai**: None; **T. Lee**: None; **T. Chang**: None; **K. Lin**: None; **S. Pai**: None; **K. Li**: None.

Abstract Number: 1218

Social Determinants Shape Health Outcomes in Idiopathic Inflammatory Myopathies: Insights from Lived Experience of 1,252 Patients

Tsvetelina Velikova[1], Kostadin Kostadinov[2], Emilia Naseva[3], Tamar Rubinstein[4], Manali Sarkar[5], Lavanya Mangla[6], Joanna Makowska[7], Raphael Micheroli[8], Leandro ferreryra[9], Linda Kobert[10], Ioannis Parodis[11], Elena Nikiphorou[12], Samuel Shinjo[13], Carlo Vinicio Caballero Uribe[14], Vincenzo Venerito[15], Vikas Agarwal[16], Latika Gupta[17] and COVAD Study Group, [1]Medical Faculty, Sofia University St. Kliment Ohridski, Sofia, Bulgaria, [2]Department of Social Medicine and Public Health, Faculty of Public Health, Medical University, Plovdiv; Health and Quality of Life in a Green and Sustainable Environment Research Group, Strategic Research and Innovation Program for the Development of MU- Plovdiv, Medical University of Plovdiv, Environmental Health Division, Research Institute at Medical University of Plovdiv, Medical University of Plovdiv,, Plovdiv, Bulgaria, [3]Faculty of Public Health, Medical University of Sofia, 15 Acad. Ivan Evstratiev Geshov, 1606 Sofia; Medical Faculty, Sofia University St. Kliment Ohridski, Sofia, Bulgaria, [4]Albert Einstein College of Medicine, White Plains, NY, [5]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India., Mumbai, Maharashtra, India, [6]Maulana Azad Medical College, 2-Bahadurshah Zafar Marg, New Delhi, New Delhi, India, [7]Department of Rheumatology, Medical University of Lodz, Lodz, Poland, [8]University Hospital Zurich, Zurich, Switzerland, [9]HIBA, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [10]The Myositis Association, Columbia, MD, [11]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [12]King's College London, London, United Kingdom, [13]Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [14]Department of Medicine, Hospital Universidad del Norte, Barranquilla, Atlantico, Colombi, Barranquilla, Colombia, [15]Univeristy of Bari \"Aldo Moro\", Italy, Bari, Bari, Italy, [16]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [17]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The impact of social determinants of health (SDoH)—including socioeconomic status, social support, and geographic context—on disease outcomes in idiopathic inflammatory myopathies (IIM) remains underexplored. We aimed to assess the association between SDoH and disease-related patient-reported outcomes (PROs) in patients with IIMs.

Methods: Data were derived from the third phase of the Collating the Voice of Autoimmune Diseases (COVAD) global e-survey, conducted in 111 countries across multiple languages [**Fig.1A**]. Descriptive (median, IQR), comparative, regression, and cluster analyses were used to explore associations between SDoH indicators and key patient-reported outcomes [**Fig.1B**].

Fig.1: A. Themes and variables for the study; B. Survey responses by country; C. Workflow of respondents selection (Anti-synthetase syndrome disease (ASyS), cancer-associated myositis (CAM), dermatomyositis (DM), inclusion body myositis (IBM), juvenile dermatomyositis (JDM), necrotizing autoimmune myopathy (NAM), overlap myositis (OM), and polymyositis (PM).

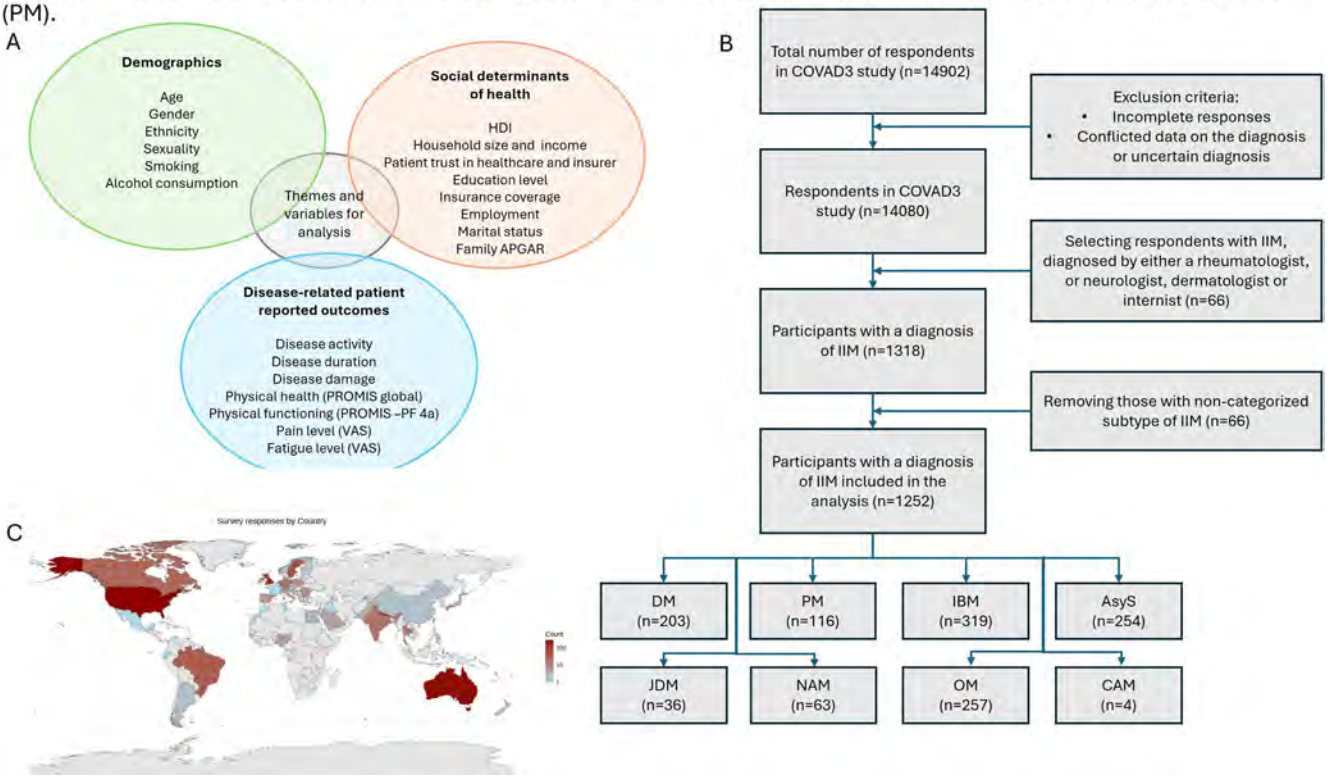


Fig.1: A. Themes and variables for the study; B. Survey responses by country; C. Workflow of respondents selection (Anti-synthetase syndrome disease (ASyS), cancer-associated myositis (CAM), dermatomyositis (DM), inclusion body myositis (IBM), juvenile dermatomyositis (JDM), necrotizing autoimmune myopathy (NAM), overlap myositis (OM), and polymyositis (PM).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig. 2 A. Trust in healthcare; B. APGAR score in IIM subtypes (p<0.001); C. Heatmap of SDoH impact on PROs (Linear or logistic regression analysis, β coefficient, significant results are denoted by *); D. IIM clusters based on the main SDoH and PROs

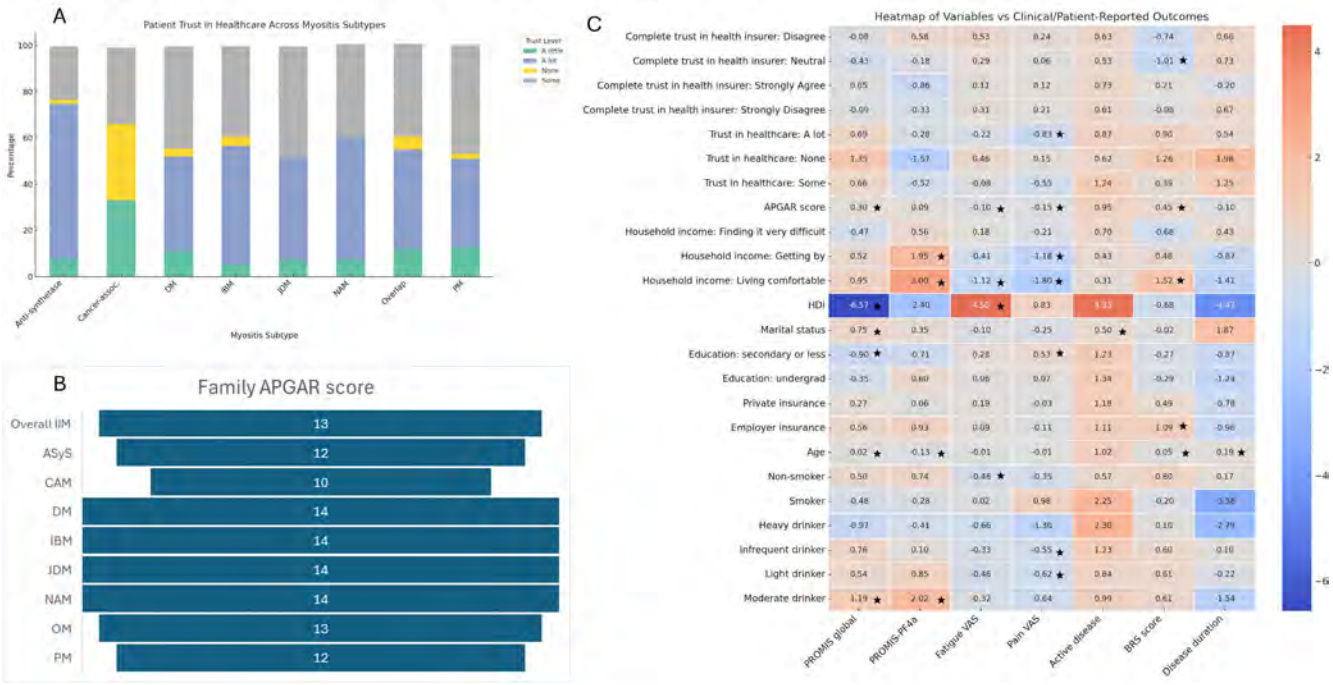


Fig. 2 A. Trust in healthcare; B. APGAR score in IIM subtypes (p<0.001); C. Heatmap of SDoH impact on PROs (Linear or logistic regression analysis, β coefficient, significant results are denoted by *); D. IIM clusters based on the main SDoH and PROs

Table 1. Basic demographics and PROs of the IIM patients included in the study

Characteristic	Overall IIM N = 1,252[1]	ASyS N = 254[1]	CAM N = 4[1]	DM N = 203[1]	IBM N = 319[1]	JDM N = 36[1]	NAM N = 63[1]	OM N = 257[1]	PM N = 116[1]	p-value[2]
Age	59 (47, 70)	51 (44, 60)	49 (28, 74)	55 (46, 65)	72 (66, 77)	31 (24, 42)	59 (49, 67)	56 (42, 64)	58 (45, 65)	<0.001
Gender										<0.001
Female	740 (69%)	147 (64%)	2 (67%)	146 (85%)	128 (45%)	18 (69%)	44 (83%)	178 (85%)	77 (85%)	
Male	323 (30%)	83 (36%)	1 (33%)	26 (15%)	153 (54%)	7 (27%)	9 (17%)	30 (14%)	14 (15%)	
Others	4 (0.4%)	1 (0.4%)	0 (0%)	0 (0%)	1 (0.4%)	1 (3.8%)	0 (0%)	1 (0.5%)	0 (0%)	
Ethnicity										<0.001
Asian	181 (17%)	95 (41%)	1 (33%)	23 (13%)	2 (0.7%)	5 (19%)	3 (5.7%)	39 (18%)	13 (14%)	
Caucasian/White	753 (70%)	117 (50%)	1 (33%)	135 (78%)	258 (91%)	17 (63%)	37 (70%)	133 (62%)	55 (60%)	
Other	143 (13%)	21 (9.0%)	1 (33%)	16 (9.2%)	22 (7.8%)	5 (19%)	13 (25%)	41 (19%)	24 (26%)	
Sexuality										<0.001
Other/Prefer not to say	282 (23%)	33 (13%)	2 (50%)	46 (23%)	47 (15%)	15 (42%)	15 (24%)	93 (36%)	31 (27%)	
Straight/Heterosexual	970 (77%)	221 (87%)	2 (50%)	157 (77%)	272 (85%)	21 (58%)	48 (76%)	164 (64%)	85 (73%)	
Education										0.021
Graduate	260 (26%)	37 (20%)	0 (0%)	45 (27%)	73 (27%)	8 (31%)	12 (24%)	54 (27%)	31 (34%)	
Secondary or less	347 (35%)	58 (32%)	1 (33%)	50 (30%)	116 (42%)	9 (35%)	19 (37%)	60 (30%)	34 (37%)	
Undergrad	387 (39%)	89 (48%)	2 (67%)	71 (43%)	85 (31%)	9 (35%)	20 (39%)	84 (42%)	27 (29%)	
Comorbidity (count)	4.0 (3.0, 7.0)	3.0 (2.0, 5.0)	13.5 (3.5, 32.5)	4.0 (2.0, 7.0)	4.0 (3.0, 7.0)	5.5 (3.0, 13.0)	4.0 (2.0, 6.0)	7.0 (4.0, 11.0)	4.0 (3.0, 7.0)	<0.001
Smoking										<0.001
Ex-smoker	337 (28%)	104 (41%)	0 (0%)	43 (22%)	87 (28%)	6 (17%)	16 (26%)	50 (21%)	31 (29%)	
Non-smoker	815 (68%)	140 (56%)	3 (75%)	146 (75%)	215 (70%)	27 (77%)	41 (66%)	177 (73%)	66 (61%)	
Smoker	54 (4.5%)	8 (3.2%)	1 (25%)	5 (2.6%)	7 (2.3%)	2 (5.7%)	5 (8.1%)	15 (6.2%)	11 (10%)	
Alcohol consumption										<0.001
Don't drink	471 (39%)	68 (27%)	0 (0%)	92 (47%)	95 (31%)	12 (34%)	28 (45%)	126 (52%)	50 (46%)	
Heavy drinker (>=4x/wk)	62 (5.1%)	4 (1.6%)	0 (0%)	2 (1.0%)	41 (13%)	0 (0%)	1 (1.6%)	11 (4.5%)	3 (2.8%)	
Infrequent drinker (<=1x/mo)	379 (31%)	123 (49%)	2 (50%)	51 (26%)	79 (26%)	17 (49%)	13 (21%)	61 (25%)	33 (31%)	
Light drinker (2-4x/mo)	181 (15%)	38 (15%)	2 (50%)	28 (14%)	51 (17%)	6 (17%)	13 (21%)	27 (11%)	16 (15%)	
Moderate drinker (2-3/wk)	113 (9.4%)	19 (7.5%)	0 (0%)	21 (11%)	43 (14%)	0 (0%)	7 (11%)	17 (7.0%)	6 (5.6%)	
Disease duration	8 (3, 16)	8 (3, 17)	13 (2, 23)	5 (2, 15)	8 (4, 13)	21 (10, 27)	3 (1, 6)	8 (3, 20)	8 (4, 13)	<0.001
PROMIS global	12.0 (10.0, 15.0)	12.0 (11.0, 14.0)	17.0 (16.0, 18.0)	12.0 (9.5, 15.0)	13.0 (10.0, 15.0)	13.0 (11.0, 16.0)	11.0 (10.0, 14.0)	12.0 (10.0, 14.0)	12.0 (10.0, 14.0)	0.043
PROMIS PF 4a	11.0 (8.0, 15.0)	12.0 (10.0, 16.0)	15.0 (13.0, 18.0)	14.0 (9.5, 17.0)	8.0 (5.0, 11.0)	14.5 (10.5, 19.0)	10.0 (7.0, 15.0)	12.0 (9.0, 16.0)	12.0 (8.0, 15.0)	<0.001
Resilience (Brief Resilience Scale, BRS)	20.0 (17.0, 24.0)	18.0 (16.0, 21.0)	19.0 (18.0, 20.0)	19.0 (15.0, 23.0)	22.0 (18.0, 24.0)	18.5 (16.0, 22.0)	22.0 (18.0, 24.0)	19.0 (16.0, 23.0)	19.0 (16.0, 23.0)	<0.001
Fatigue VAS	6.00 (5.00, 8.00)	5.00 (4.00, 7.00)	7.00 (0.00, 7.00)	7.00 (5.00, 8.00)	6.00 (5.00, 8.00)	5.00 (4.00, 7.00)	7.00 (5.00, 8.00)	7.00 (5.00, 8.00)	7.00 (5.00, 8.00)	<0.001
Pain VAS	5.00 (2.00, 6.00)	4.50 (3.00, 6.00)	7.00 (1.00, 7.00)	5.00 (3.00, 6.50)	3.00 (1.00, 5.00)	4.00 (2.00, 6.00)	4.00 (1.00, 5.00)	6.00 (3.00, 7.00)	5.00 (3.00, 8.00)	<0.001
Active disease										<0.001
Active by report AND either objective labs/increasing meds/ steroids >10mg/day	539 (84%)	114 (86%)	2 (100%)	87 (74%)	113 (99%)	14 (58%)	30 (77%)	121 (87%)	58 (79%)	
Not active	102 (16%)	18 (14%)	0 (0%)	31 (26%)	1 (0.9%)	10 (42%)	9 (23%)	18 (13%)	15 (21%)	

[1]Median (Q1, Q3); n (%)
[2]Kruskal-Wallis rank sum test; Fisher's Exact Test for Count Data with simulated p-value (based on 2000 replicates)
Anti-synthetase syndrome disease (ASyS), cancer-associated myositis (CAM), dermatomyositis (DM), inclusion body myositis (IBM), juvenile dermatomyositis (JDM), necrotizing autoimmune myopathy (NAM), overlap myositis (OM), and polymyositis (PM).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: From a total of 14902 respondents, 1252 patients with IIM (including DM, PM, IBM, NAM, ASyS, OM, JDM, and CAM), diagnosed by a physician (either a rheumatologist, neurologist, dermatologist or internist), were included [**Fig.1C**]. The median age was 59 (47-70) years, with 69% females, 70% Caucasian/White, 24% holding postgraduate degrees, 32% smokers, and 61% alcohol consumers, with a median disease duration of 8 (3-16) years [**Tab.1**].

Half of IIM patients reported high trust in healthcare, 47.2% had little or some trust, and 3.4% reported none [**Fig.2A**]. In comparison, 74% had insurance, 32.2% trusted in their insurer, 52% live comfortably with the household income, and the median household size was 2 people. Adaptation, partnership, growth, affection, and resolve (APGAR) family score was estimated as 13 (10-15) [**Fig.2B**]. Among the 62% of participants not providing care for others, the majority were men (80%, $p< 0.001$), unlike the women caring for older adults (7.3%, $p=0.001$) and disabled relatives (3.9%, $p=0.016$). The age of retirement was 60 (53-65), with 52% reporting this was because of the IIM diagnosis.

Higher income was associated with better physical function (PROMIS PF 4a, $\beta=3$, $p< 0.001$), less fatigue ($\beta = -1.12$, $p< 0.001$), and reduced pain ($\beta = -1.8$, $p< 0.001$), along with greater resilience (Brief Resilience Score, BRS score ranged 6-30) ($\beta = 1.52$, $p=0.02$). Better family function was positively associated with better overall health perception (PROMIS global, $\beta = 0.3$, $P< 0.001$) and resilience ($\beta = 0.45$, $p< 0.001$), and modestly linked to lower pain levels ($\beta = -0.15$, $p< 0.001$) [**Fig.2C**]. Trust in the insurer and type of insurance coverage were largely unrelated to PROs. Cluster analysis revealed three IIM clusters: (1) characterized by the best PROMIS scores and family function, (2) reflects the most severely affected group, with the lowest PROMIS scores, highest fatigue and pain levels, and the highest disease activity, while the least employed and report low family function, and (3) a younger, high-functioning group but lower HDI and family function.

Conclusion: SDoH play a significant role in influencing the outcomes in IIM. Factors, such as trust in healthcare, financial stability, and social support are associated with improved PROs, while socioeconomic disadvantage increases disease burden. These findings underscore critical priorities for healthcare providers and policymakers.

Disclosure: T. Velikova: None; **K. Kostadinov**: None; **E. Naseva**: None; **T. Rubinstein**: None; **M. Sarkar**: None; **L. Mangla**: None; **J. Makowska**: None; **R. Micheroli**: None; **L. ferreryra**: None; **L. Kobert**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6; **S. Shinjo**: None; **C. Uribe**: None; **V. Venerito**: None; **V. Agarwal**: None; **L. Gupta**: None.

Abstract Number: 1219

anti-ro52 Antibody Identifies Patients with More Severe Lung Disease Among Patients with Idiopathic Inflammatory Myopathy

Vasiliki Syrmou[1], Ioannis Alexiou[2], Christos Liaskos[3], Eleni Patrikiou[3], THEODORA SIMOPOULOU[4], Christina Katsiari[5] and Dimitrios Bogdanos[6], [1]University General Hospital of Larisa, University of Thessaly, Faculty of Medicine, Larisa, Greece, [2]University General Hospital of Larisa, Larissa, Greece, [3]University of Thessaly, Faculty of Medicine, Larisa, Greece, [4]University Hospital of Larissa, Greece, Larissa, Greece, [5]University General Hospital of Larisa, University of Thessaly Faculty of Medicine, Larisa, Greece, [6]Professor, Larissa, Greece

SESSION INFORMATION

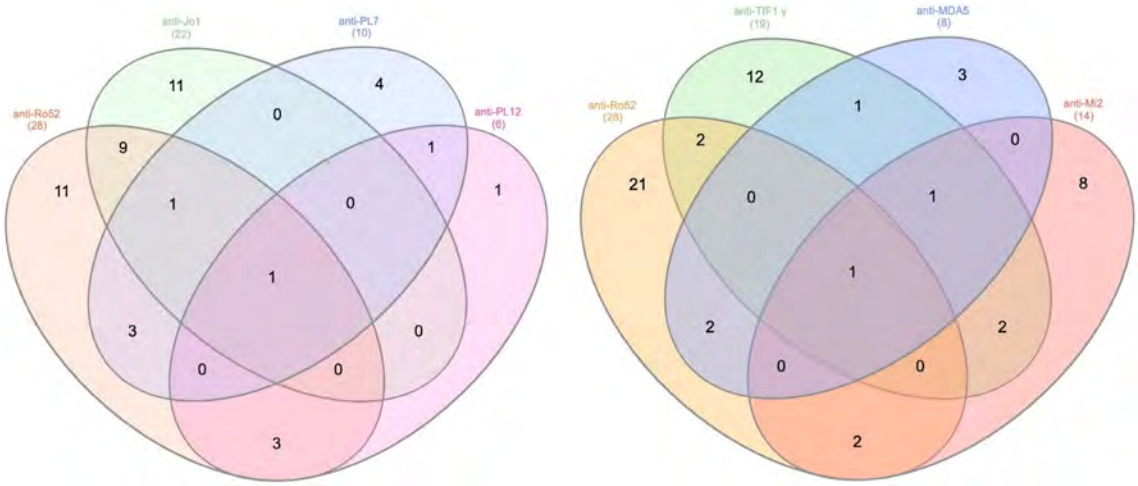
Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

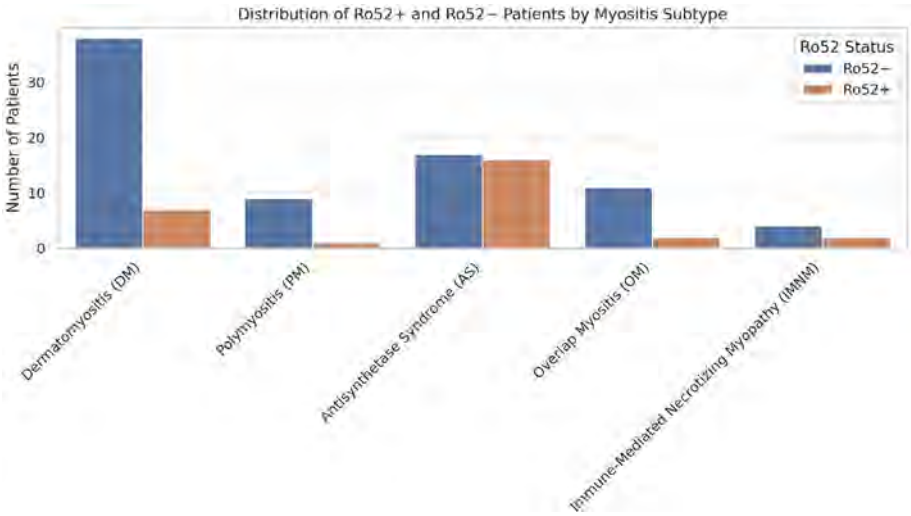
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Venn diagramms depicting coexistence of anti-Ro-52 with with most common MAA (anti-Jo1, anti-PL7, anti-PL12)on the left and most common MSA (anti-TIF1γ, anti-Mi2, anti-MDA5) on the right in our cohort.



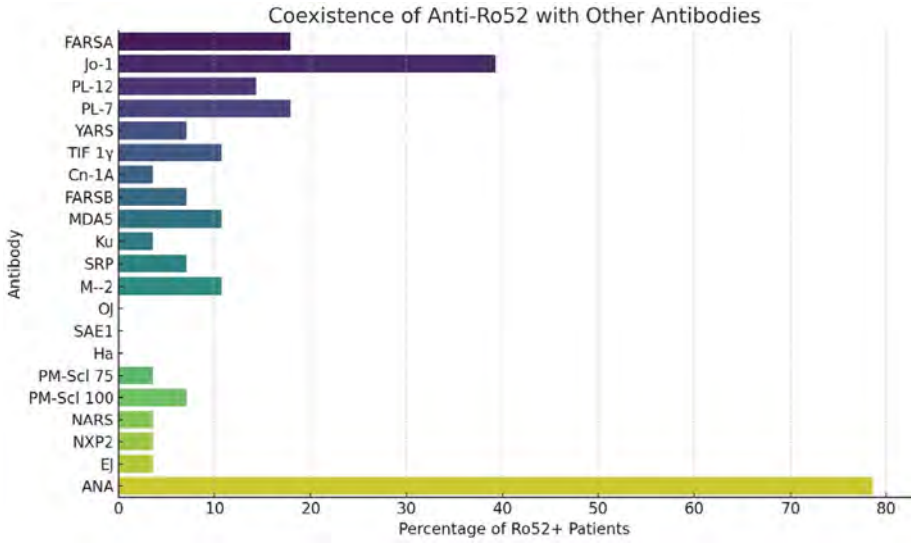
Disease subtypes distribution across our cohort. Blue box represents anti-Ro52(-) while orange box anti-Ro52(+) cases

Background/Purpose: Anti-Ro52 antibodies are commonly detected in idiopathic inflammatory myopathies (IIMs), yet their clinical significance remains incompletely defined. There is evidence that it coexists with anti-synthetase antibodies (ARS). We aimed to investigate the phenotype, survival and antibody coexistence of anti-Ro52 patients within a IIM cohort.

Methods: Retrospective analysis with clinical information regarding skin (CDASI score, typical signs), muscle (MMT-8 score, CPK levels), lung involvement (CT thorax pattern and % predicted Forced Vital Capacity), dysphagia and survival in months, laboratory test (ferritin, LDH, WBC, Hb) and autoantibody profile was performed. Antibody test for Myositis Specific Autoantibodies (MSA) and Myositis Associated Autoantibodies (MAA) was done with myo blot and ANA with indirect immunofluorescence.

Results: A total of 107 patients were analyzed, including 28 (26.2%) positives for anti-Ro52. Anti-Ro52 positivity was significantly associated with antisynthetase syndrome (AS) ($p = 0.009$), with post hoc analysis revealing that AS patients were disproportionately represented among Ro52-positive individuals (standardized residual +2.5). Antibody coexistence was significant for anti-Jo1 ($p=0.001$) and anti-FARS ($p< 0.001$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Bar chart with coexistence of percentage of anti-Ro52 (+) with other autoantibodies

Patients with anti-Ro52 antibodies were diagnosed at a younger age (mean= 55.6 SD ± 12.36 vs. 61.4 years SD ±12.52, p = 0.039) and exhibited significantly lower FVC% at diagnosis (mean=72.1% SD ± 22.21 vs. 88.3% SD ±14.56, p = 0.001). Lung involvement was significantly more frequent in Ro52-positive patients (64.3% vs. 35.4%, p = 0.015), and CT thorax patterns differed by antibody status (p = 0.015), with non-specific interstitial pneumonia (NSIP) more prevalent among Ro52-positive patients (standardized residual +2.1). While overall survival was lower in the Ro52-positive group, the difference was not statistically significant (p=0.39).

No significant differences were observed in malignancy rates, skin involvement (CDASI score and main typical skin signs), muscle involvement (MMT-8 score, CPK levels) . No difference was seen in main commorbidities including Hypertension, diabetes, coronary artery disease, hypothyroidism and osteoporosis (p=ns). Anti-Ro52-(+) patients did not differ in performance status. Although there was a trend towards more severe scores (PS3 or 4)p=0.09.

Conclusion: These findings highlight a potential role of anti-Ro52 as a marker of severe, lung-predominant IIM phenotype but they do not support any other distinct clinical and radiographic profile associated with anti-Ro52 antibodies.

Disclosure: V. Syrmou: None; **I. Alexiou**: None; **C. Liaskos**: None; **E. Patrikiou**: None; **T. SIMOPOULOU**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6; **C. Katsiari**: AbbVie/Abbott, 12, travel support, AstraZeneca, 6, 12, travel support, Boehringer-Ingelheim, 6, 12, travel support, GlaxoSmithKlein(GSK), 6, 12, travel support, Novartis, 12, travel support, UCB, 1, 6, 12, travel support, advisory Boad, Vianex Hellas, 12, travel support, Viatris, 12, travel support; **D. Bogdanos**: Amgen, 6, Boehringer-Ingelheim, 5, GlaxoSmithKlein(GSK), 6, Novartis, 6, Sobi, 5.

Abstract Number: 1220

Predictors of Progressive Pulmonary Fibrosis in Idiopathic Inflammatory Myopathies : a Retrospective Study of 502 Cases

Wei Bian[1], Jian Hao[1], Na zhang[1], Xiaojing Zhang[1], Fumin Qi[1], Yin Zhao[2] and Wei Wei[1], [1]Tianjin Medical University General Hospital, Tianjin, China (People's Republic), [2]Affiliated Hospital of Yunnan University, Yunnan, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table Comparisons in features at baseline between IIM-ILD patients with and without PPF

	IIM-ILD (N=288)	Non-PPF (N=206)	PPF (N=82)	P
Clinical data				
Female-n (%)	218 (75.7)	154 (74.8)	64 (78)	0.557
Age at onset-years	55.5 (47, 62)	54.5 (46, 61)	58 (50, 64)	0.047
Disease duration-months	6 (2, 24)	6.5 (2, 24)	5 (2, 17)	0.141
Follow-up duration-months	53 (29, 76)	47 (29, 71)	61 (29, 81)	0.077
Manifestations				
Fever-n (%)	117 (40.6)	71 (34.5)	46 (56.1)	0.001
Asthenia-n (%)	174 (60.4)	133 (64.6)	41 (50.0)	0.023
Gottron's sign/papules-n (%)	98 (34.0)	66 (32.0)	32 (39.0)	0.259
Mechanic's hands-n (%)	68 (23.7)	52 (25.4)	16 (19.5)	0.292
Oral ulcer-n (%)	15 (5.2)	6 (2.9)	9 (11.0)	0.014
Proximal upper limb weakness-n (%)	63 (21.9)	54 (26.2)	9 (11)	0.005
Neck flexor weakness-n (%)	26 (9.0)	23 (11.2)	3 (3.7)	0.045
Proximal lower limb weakness-n (%)	84 (29.2)	67 (32.5)	17 (20.7)	0.047
MMT-sl	150 (122, 150)	150 (122, 150)	150 (150, 150)	0.015
Arthritis-n (%)	130 (45.1)	94 (45.6)	36 (43.9)	0.790
Raynaud's phenomenon -n (%)	25 (8.7)	20 (9.7)	5 (6.1)	0.326
Laboratory data				
NLR	4.43 (2.41, 6.91)	4.07 (2.37, 6.48)	4.91 (2.74, 8.16)	0.040
CK-U/L	186 (49, 1348)	304 (56, 2213)	115 (37, 527)	0.007
ALB-g/L	33 (30, 37)	34 (30, 37)	32 (29, 36)	0.117
ESR-mm/1h	27 (18, 40)	27 (17, 41)	28.5 (20, 38)	0.704
CRP-mg/dl	0.63 (0.3, 1.58)	0.59 (0.29, 1.35)	0.87 (0.36, 2.14)	0.057
Fer-ng/mL	252.54 (126.95, 662.80)	236.02 (127.08, 620.66)	295.64 (127.0, 815.41)	0.530
CEA-ng/mL	2.27 (1.40, 3.69)	1.95 (1.30, 3.27)	2.83 (1.92, 5.46)	<0.001
CA19-9-U/mL	6.35 (2.27, 13.56)	5.33 (2.02, 12.89)	7.54 (4.00, 16.38)	0.020
HE4-pmol/L	108.25 (71.41, 158.45)	96.25 (66.80, 149.9)	126.36 (80.40, 172.9)	0.052
KL-6-U/mL	687 (342.5, 1186)	607 (330, 1075)	902 (561, 1369)	0.004
Myositis specific autoantibodies				
SAE-n (%)	4 (1.4)	3 (1.5)	1 (1.2)	1.000
NXP2-n (%)	5 (1.8)	5 (2.5)	0 (0)	0.326
MDA5-n (%)	51 (18)	26 (12.9)	25 (30.5)	<0.001
TIF1γ-n (%)	17 (6.0)	15 (7.5)	2 (2.4)	0.166
MI2-n (%)	19 (6.7)	15 (7.4)	4 (4.9)	0.436
Jo-1-n (%)	82 (28.5)	57 (27.7)	25 (30.5)	0.632
OJ-n (%)	3 (1.1)	2 (1.0)	1 (1.2)	1.000
EJ-n (%)	37 (13.1)	22 (10.9)	15 (18.3)	0.096
PL12-n (%)	15 (5.3)	13 (6.5)	2 (2.4)	0.245
PL7-n (%)	25 (8.8)	23 (11.4)	2 (2.4)	0.015
KS-n (%)	1 (0.4)	1 (0.5)	0 (0)	1.000
Zo-n (%)	4 (1.4)	2 (1.0)	2 (2.4)	0.582
SRP-n (%)	22 (7.8)	19 (9.5)	3 (3.7)	0.099
HMGCR-n (%)	1 (0.4)	1 (0.5)	0 (0)	1.000
Myositis associated autoantibodies				
RO52-n (%)	211 (73.3)	146 (70.9)	65 (79.3)	0.146
PM/Scl-n (%)	9 (3.2)	5 (2.5)	4 (4.9)	0.266
Ku-n (%)	13 (4.6)	7 (3.5)	6 (7.3)	0.209
Hest high-resolution CT				
GGO-n (%)	233 (81.2)	160 (78.0)	73 (89.0)	0.032
UIP-n (%)	52 (18.1)	41 (19.9)	11 (13.4)	0.196
NSIP-n (%)	147 (51.0)	98 (47.6)	49 (59.8)	0.062
OP-n (%)	24 (8.3)	16 (7.8)	8 (9.8)	0.582
OP+NSIP-n (%)	34 (11.8)	22 (10.7)	12 (14.6)	0.348
Pulmonary function tests				
FVC%pred-%	75.85±18.11	76.84±16.31	73.71±17.61	0.243
DLCO%pred-%	56.74±16.50	58.78±16.53	52.29±15.66	0.007
Treatment				
Glucocorticoid pulse therapy-n (%)	36 (12.5)	20 (9.7)	16 (19.5)	0.023
Glucocorticoid-n (%)	280 (97.2)	200 (97.1)	80 (97.6)	1.000
Maximum dose of glucocorticoid-mg	80 (40, 160)	80 (40, 160)	80 (40, 200)	0.284
Cyclophosphamide-n (%)	113 (39.2)	80 (38.8)	33 (40.2)	0.825
Intravenous immunoglobulin-n (%)	70 (24.3)	45 (21.8)	25 (30.5)	0.123
Mycophenolate mofetil-n (%)	54 (18.8)	45 (21.8)	9 (11.0)	0.033
Calcineurin inhibitor-n (%)	49 (16.0)	36 (17.5)	13 (15.9)	0.741
Antifibrotic therapy-n (%)	48 (16.7)	31 (15.0)	17 (20.7)	0.283

Values are expressed as numbers (%) or median (25th IQR-75th IQR), as appropriate.

ALB, albumin; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CK, creatine kinase; CRP, C-reactive protein; DLCO, diffusing capacity for carbon monoxide; ESR, erythrocyte sedimentation rate; Fer, ferritin; FVC, forced vital capacity; GGO, ground glass opacity; HE4, human epididymis protein 4; IIM, idiopathic inflammatory myopathy; ILD, interstitial lung disease; KL-6, Krebs von den Lungen-6; MMT, manual muscle test; NLR, neutrophil-to-lymphocyte ratio; NSIP, nonspecific interstitial pneumonia; OP, organizing pneumonia; PPF, progressive pulmonary fibrosis; UIP, usual interstitial pneumonia.

SESSION INFORMATION

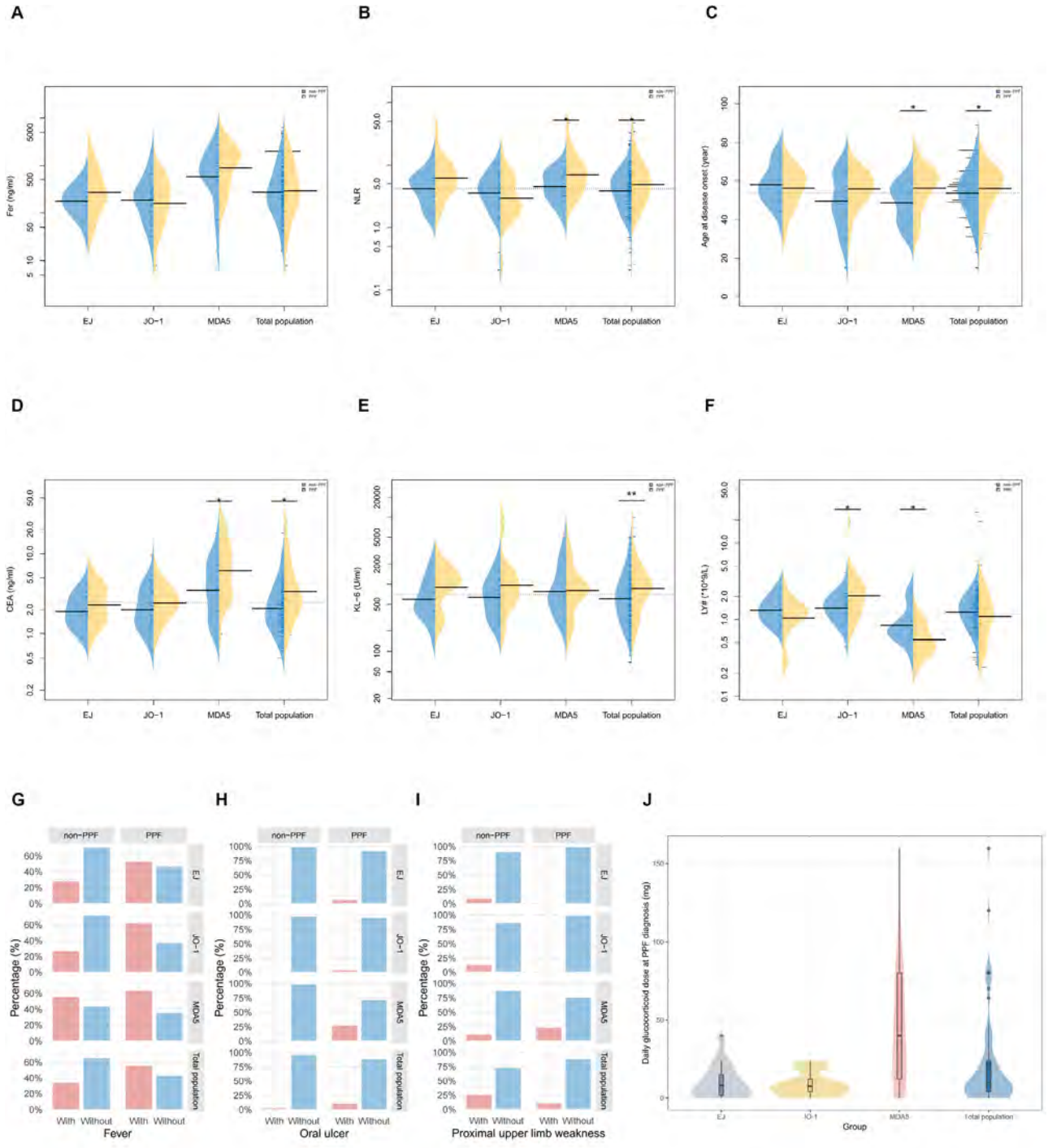
Session Date: Monday, October 27, 2025

Session Title: (1191–1220) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A-F: Laboratory indices and age at disease onset comparisons (PPF=yellow). G-I: Symptom rates (present=red). J: Steroid doses at PPF onset. Statistical significa
CEA, carcinoembryonic antigen; Fer, ferritin; KL-6, Krebs von den Lungen-6; LY#, lymphocyte count, NLR, neutrophil-to-lymphocyte ratio.

Figure PPF-associated features across IIM-ILD subtypes classified by MSA

Background/Purpose: Interstitial lung disease (ILD) in idiopathic inflammatory myopathies (IIM) causes worse prognosis. Some patients develop progressive pulmonary fibrosis (PPF) despite appropriate treatment. Identifying predictors of PPF in IIM patients is crucial for clinical management.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients with IIM hospitalization from 2015 to 2024 were retrospectively collected to identify factors associated with PPF using the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society and Asociación Latinoamericana de Thórax guidelines PPF criteria published in 2022.

Results: ILD presented in 68.5% of IIM patients (344 /502). During follow up, 28.5% (82/288) developed PPF. The median interval from ILD diagnosis to PPF onset was 10 months. The median daily glucocorticoid dose methylprednisolone equivalents at PPF development was 10 mg, among anti-MDA5+ patients it was 40 mg (Figure). In IIM-ILD patients, the top three positive myositis-specific antibodies (MSAs) were anti-Jo-1 (24.1%), anti-MDA5 (21.5%) and anti-EJ (10.8%), and in IIM-PPF patients were anti-MDA5 (30.5%), anti-Jo-1 (29.3%) and anti-EJ (18.3%). Compared to non-ILD patients, those with ILD were older, more frequently anti-Ro52+ (73.3% vs. 39.2%, P< 0.001), and had higher Krebs von den Lungen-6 (KL-6), carcinoembryonic antigen (CEA) at baseline. Among IIM-ILD patients, PPF patients exhibited older age at onset, higher fever (56.1% vs. 34.5%, P=0.001) and oral ulcer prevalence (11% vs. 2.9%, P=0.014), higher CEA [2.83(1.92, 5.46) vs. 1.95(1.3, 3.27) ng/ml, P< 0.001], more frequent anti-MDA5+ (30.5% vs. 12.9%, P< 0.001), and ground-glass opacity on chest high-resolution CT (89% vs. 78%, P=0.032) (Table). In contrast, patients without PPF had higher anti-PL-7 positivity (11.4% vs. 2.4%, P=0.015), better diffusing capacity for carbon monoxide (58.78%±16.53% vs. 52.29% ±15.66%, P=0.007), and more frequent MMF use (21.4% vs. 9.8%, P=0.021) (Table). KL-6 levels remained statistically comparable between baseline and time of PPF (P=0.23). CEA levels were higher in PPF group [2.83 (1.92-5.46) vs. 1.95 (1.30-3.27) ng/ml, P< 0.001] and longitudinal analysis revealed a marked increase from baseline to PPF [2.79(1.59-5.56) vs. 2.84(1.63-4.91) ng/ml, P=0.03]. Multivariate COX analysis identified fever [HR=2.21, 95%CI (1.39, 3.53), P=0.001], oral ulcer [HR=2.44, 95%CI (1.08, 5.50), P=0.031] and CEA [HR=1.11, 95%CI (1,05, 1.17), P< 0.001] as independently risk factors for PPF, while anti-PL7+ [HR=0.075, 95%CI (0.02, 0.36), P=0.001] and proximal upper limb weakness [HR=0.40, 95% CI (0.19, 0.85), P=0.017] as protective factors.

Conclusion: Manifestations of fever, oral ulcer and higher level of CEA at baseline were independently risk factors for PPF, especially among patients with specific autoantibodies. Close monitor of patients' symptom progression and timely scheduling of chest HRCT and PFTs are necessary, when daily glucocorticoid dose tapering to about 10 mg methylprednisolone equivalent. CEA level at baseline may represent a more promising biomarker candidate for identification of PPF.

Disclosure: W. Bian: None; **J. Hao**: None; **N. zhang**: None; **X. Zhang**: None; **F. Qi**: None; **Y. Zhao**: None; **W. Wei**: None.

Abstract Number: 1221

Oxytocin pathway gene BST1 polymorphism rs4273468 genotype GG is negatively associated with Fibromyalgia

Zeeshan Ahmed[1], Koshy Nithin Thomas[2], Shivika Guleria[3], Amita Aggarwal[4] and **Able Lawrence**[3], [1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [2]Christian Medical College, Vellore, Tamil Nadu, India, [3]SGPGIMS, Lucknow, Lucknow, Uttar Pradesh, India, [4]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Oxytocin, also known as love hormone, is important in contextual memory. Oxytocin secreting parvocellular neurons suppress pain through projections to brain and spinal cord besides endocrine action. Optogenetic activation of Oxytocin neurons relieved pain in a rodent model of Fibromyalgia. We had previously shown association of rs6754031 (GG) promoter polymorphism in SCN9A with Fibromyalgia. This hypothalamic expressed voltage sodium channel Nav1.7 is upregulated in stress and its activity is linked to Oxytocin secretion. Hence, we studied SNPs rs4273468, rs3796863 and rs1556314 in genes BST1 (CD157), CD38 and TRPM2 genes involved in hypothalamic Oxytocin secretion. BST1 and CD38 catalyze the formation of cyclic ADP Ribose from NAD+ while TRPM2 is involved in Calcium secretion triggered by cyclic ADP Ribose. The minor alleles of the chosen SNPs are sufficiently common in our population and previously found to be associated with diseases such as Post Traumatic Stress Disorder and Restless Leg Syndrome that are themselves associated with Fibromyalgia

Methods: Patients diagnosed as Fibromyalgia using ACR1990 and/or ACR2016 criteria and consenting to genetic study were included. Healthy subjects with no widespread pain or connective tissue disease or medical comorbidity were taken as controls. Subjects were the same as our prior SCN9A study. DNA was extracted by phenol-chloroform method.

Table 1. Clinical features of FMS cohort

Clinical feature	FMS (n-118)	1990 ACR (n-11)	1990 + 2016 ACR (n-74)	2016 ACR (n-33)	p-value
Female	104 (88%)	11 (100%)	64 (86%)	29 (87%)	0.6
Age (years)	40.6 (±10.3)	40 (±11.8)	39.7 (±10.4)	42.9 (±9.4)	0.3
Age at onset (years)	35 (±9.6)	34 (±10)	34.3 (±9.8)	36.9 (±9)	0.4
WPI	14.6 (±3.6)	12.9 (±4.6)	15.5 (±3)	12.9 (±3.6)	<0.01
SSS	7.8 (±2.5)	2.7 (±1.4)	8.6 (±2.1)	7.9 (±1.7)	<0.01
TP	12.3 (±5)	13.6 (±2)	15.1 (±2.3)	5.5 (±3.4)	<0.01
OSA (STOP BANG)	38 (32%)	1 (9%)	23 (31%)	14 (42%)	0.1
CFS	44 (37%)	1 (9%)	33 (44%)	10 (30%)	0.06
PTSD	19 (16%)	0	15 (20%)	4 (12%)	0.2
RLS	13 (11%)	0	8 (10%)	5 (15%)	0.4

Clinical Characteristics of Fibromyalgia subjects

Table 2 Genotype Analysis

Gene	SNP	Patients			Controls			PValue
BST1	**rs4273468**	AA	AG	**GG**	AA	AG	**GG**	**P=0.001**
		49	68	**1**	44	58	**15**	
CD38	rs3796863	GG	GT	TT	GG	GT	GT	P=0.844
		54	47	17	54	50	14	
TRPM2	rs1556314	GG	GT	TT	GG	GT	TT	P=0.220
		1	32	85	5	26	87	

Genotype Analysis of BST1 CD38 and TRPM2

Table 3 BST1 rs4273468 Recessive (GG) model

Group	BST1	Patients		Controls		PValue
Females	**rs4273468**	AA/AG	**GG**	AA/AG	**GG**	**P<0.001 OR=0.055 (0.0013-0.37)**
		104	**0**	76	**14**	
Males	rs4273468	AA/AG	GG	AA/AG	GG	P=1 (NS)
		13	1	25	1	
Combined	rs4273468	AA/AG	GG	AA/AG	GG	**P<0.001 OR=0.058 (0.0075-0.44)**
		117	1	101	15	

BST1 polymorphism rs4273468 genotype homozygous GG protects from Fibromyalgia

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Genotyping was done by TaqMan real time PCR. All continuous variables among baseline characteristics are expressed in mean (SD) and comparison by one way ANOVA while Fisher's exact test was used for frequency tables. Odds Ratios and confidence intervals were estimated using Logistic Regression using a recessive minor allele (G) model using STATA14

Results: A total of 118 FMS patients (88% female) of mean age of onset 35 (±9.6) years and 118 healthy controls (78% female) of age 34.7 (±10.9) years were included. Clinical features and comorbidities of patients are given in Table 1. Of the 118 patients, 74 were classified Fibromyalgia by both ACR2016 and ACR1990 criteria while 33 and 11 subjects were classified by ACR2016 and ACR1990 alone respectively. All three SNPs were in Hardy Weinberg equilibrium. Homozygous GG allele of BST1 rs4273468 polymorphism was protective with an **Odds Ratio of 0.058 (0.0075-0.44, P< 0.001**). The rs3796863 polymorphism of CD38 and rs1556314 of TRPM2 did not show any association with Fibromyalgia.

Conclusion: This is the first study showing association of BST1/CD157 with Fibromyalgia. This SNP rs4273468 in BST1 has previously been associated with Idiopathic Restless Leg Syndrome. Genes in the Oxytocin secretion pathway names BST1, CD38, TRPM2 and Oxytocin Receptor gene require further study.

Disclosure: Z. Ahmed: None; **K. Thomas**: None; **S. Guleria**: None; **A. Aggarwal**: None; **A. Lawrence**: None.

Abstract Number: 1222

Efficacy of Fasinumab, An Anti-Nerve Growth Factor Monoclonal Antibody, in Managing Chronic Musculoskeletal Pain: A Systematic Review and Meta-Analysis

Ahmed Abouelella[1], Mohammad Alhasan[2], Ahmed Hamoudah[3], Ayman Ibrahim[4], Ola O.A. Abuzied[5], Mansoor Al-Tamimi[6] and Muhammed Elhadi[7], [1]Faculty of Medicine, Benha University, Benha, Al Qalyubiyah, Egypt, [2]Health Education England Internal Medicine Training (Cambridge), Cambridge, United Kingdom, [3]Libyan International University, Sarasota, FL, [4]University of Gezira, Medina, Saudi Arabia, [5]University of Khartoum, Khartoum, Sudan, [6]Faculty of Medicine, Cairo University, Cairo, Egypt, [7]University of Tripoli, Huston, TX

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic musculoskeletal pain can be a significant source of disability and poor quality of life in adults. Many patients do not achieve adequate relief with standard treatments, highlighting the need for novel therapies. Nerve growth factor (NGF), released by pro-inflammatory cells, is crucial in pain signalling, with elevated levels found in chronic pain patients. Fasinumab is a selective nerve-growth factor inhibitor that has shown efficacy in managing musculoskeletal disorders such as osteoarthritis (OA) and chronic low back pain (CLBP).

Methods: We conducted a systematic search in PubMed, Scopus, Embase, Web of Science, ClinicalTrials.gov, and Cochrane through April 25, 2025. Eligible studies were randomized clinical trials (RCTs) comparing the efficacy of Fasinumab against placebo or other analgesics in treating chronic musculoskeletal pain. Two independent reviewers completed screening and data extraction for each study. Primary efficacy outcomes were pooled mean difference from baseline to endpoint for pain levels, represented either as Western Ontario and McMaster Universities Arthritis (WOMAC) index or low back pain intensity (LBPI) numeric rating score, and physical function represented as either WOMAC index or Roland Morris Disability Questionnaire (RMDQ) score. The secondary outcome was pooled change from baseline for Patient Global

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Assessment (PGA). We used a random-effect model for all the analyses conducted. Outcomes were reported as standardized mean difference (SMD) with a 95% confidence interval (CI).

Results: A total of eight RCTs (12118 patients) met the inclusion criteria, comprising seven OA and one CLBP trial. Two trials included NSAIDs as a comparator. The pooled analysis for Fasinumab against placebo indicated statistically significant pain reduction and physical function improvement; SMD (95%CI) = -0.38 (-0.45: -0.3), p< 0.001, and -0.41 (-0.48: -0.33), p< 0.001, respectively. The pooled mean difference against NSAIDs regarding pain level and physical function was statistically significant; SMD (95%) = -0.19 (-0.29: -0.09), p< 0.001, and -0.21 (-0.3: -0.12), p< 0.001, respectively. Additionally, PGA improvement was statistically significant against placebo and NSAIDs; SMD = -0.25 (-0.33: -0.17), p< 0.001, and -0.11 (-0.2: -0.02), p=0.02, respectively.

Conclusion: This meta-analysis shows that Fasinumab has promising results in managing chronic musculoskeletal pain and suggests it may be superior to placebo or conventional analgesics. Further studies involving more intervention arms are needed to come up with a more definitive answer.

Disclosure: A. Abouelella: None; **M. Alhasan**: None; **A. Hamoudah**: None; **A. Ibrahim**: None; **O. O.A. Abuzied**: None; **M. Al-Tamimi**: None; **M. Elhadi**: None.

Abstract Number: 1223

Pain and Fibromyalgia Across Autoimmune and Inflammatory Diseases in the AMP AIM Cohort

Alexis Ogdie[1], Astrid Rasmussen[2], Dana Orange[3], Michelle Petri[4], Caroline Shiboski[5], Rebecca Haberman[6], Mala Masson[7], Daniel Goldman[4], Peter Izmirly[8], Brooke Cohen[9], Jennifer Seifert[10], Jennifer Anolik[11], Wade DeJager[12], Alan Baer[13], Jill Buyon[14], Yvonne Lee[15] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM), [1]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]The Rockefeller University, New York, NY, [4]Johns Hopkins University School of Medicine, Timonium, MD, [5]University of California San Francisco, San Francisco, CA, [6]NYU Langone Health, New York, NY, [7]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [8]New York University Grossman School of Medicine, New York, NY, [9]Yale Physician Associate Program, New Haven, CT, [10]University of Colorado and Oklahoma Medical Research Foundation, Aurora, CO, [11]University of Rochester Medical Center, Rochester, NY, [12]Oklahoma Medical Research Foundation, Oklahoma City, [13]Johns Hopkins University School of Medicine, Baltimore, MD, [14]NYU Grossman School of Medicine, New York, NY, [15]Northwestern University, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The Accelerating Medicines Partnership Autoimmune and Immune-Mediated Diseases (AMP AIM) network seeks to understand the cellular and molecular interactions that lead to inflammation and autoimmune diseases. Pain is among the most common symptoms in patients with these diseases, and up to one third have concomitant fibromyalgia. Little is known about how the experience of chronic pain differs across rheumatic diseases and whether it impacts patients with these conditions similarly or differently. The objective of this study was to examine differences in pain intensity, pain interference, pain distribution, pain catastrophizing, and the prevalence of fibromyalgia (FM) among patients with RA, SLE, PsA, Psoriasis (PsO), Sjögren's disease (SjD), and sicca symptoms without SjD (sicca).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Demographics and Prevalence of Chronic Pain

Table 1. Patient Demographics and Prevalence of Chronic Pain

		Healthy Controls	PsA	PsO	RA	SLE	Sicca without SjD	SjD
	N	22	27	31	39	38	66	55
Age	Age (mean)	46.3 (14.7)	49.7 (11.8)	48.9 (15.7)	58.2 (15.6)	45.8 (17.6)	55.2 (13.6)	60.2 (12)
Sex	Female	17 (77%)	13 (48%)	11 (35%)	33 (85%)	32 (84%)	63 (95%)	51 (93%)
Race	White	16 (73%)	21 (78%)	24 (77%)	27 (69%)	10 (26%)	54 (82%)	42 (76%)
	Black	2 (9%)	0 (0%)	1 (3%)	6 (15%)	19 (50%)	3 (5%)	2 (4%)
Ethnicity	Hispanic	1 (5%)	4 (15%)	2 (6%)	12 (31%)	6 (16%)	8 (12%)	12 (22%)
Education	High school	7 (32%)	9 (33%)	9 (29%)	15 (38%)	14 (37%)	15 (23%)	8 (15%)
	Associates	3 (14%)	3 (11%)	3 (10%)	6 (15%)	4 (11%)	4 (6%)	9 (16%)
	Bachelor's	12 (55%)	14 (52%)	19 (61%)	17 (44%)	19 (50%)	47 (71%)	38 (69%)
Insurance	Private	19 (86%)	20 (74%)	22 (71%)	12 (31%)	20 (53%)	40 (61%)	27 (49%)
	Medicaid	1 (5%)	2 (7%)	1 (3%)	9 (23%)	2 (5%)	2 (3%)	1 (2%)
	Medicare	2 (9%)	4 (15%)	4 (13%)	13 (33%)	7 (18%)	19 (29%)	24 (44%)
Chronic pain	3+ months	4 (18%)	22 (81%)	8 (26%)	32 (82%)	18 (47%)	50 (76%)	27 (49%)
	FMS Criteria	1 (5%)	6 (22%)	0 (0%)	12 (31%)	4 (11%)	20 (30%)	12 (22%)

RA = rheumatoid arthritis; SLE = systemic lupus erythematosus (predominantly those with kidney disease in this cohort); PsA = psoriatic arthritis; PsO = psoriasis without PsA; SjD = Sjogren's Disease; Sicca = sicca symptoms without SjD; FM = fibromyalgia

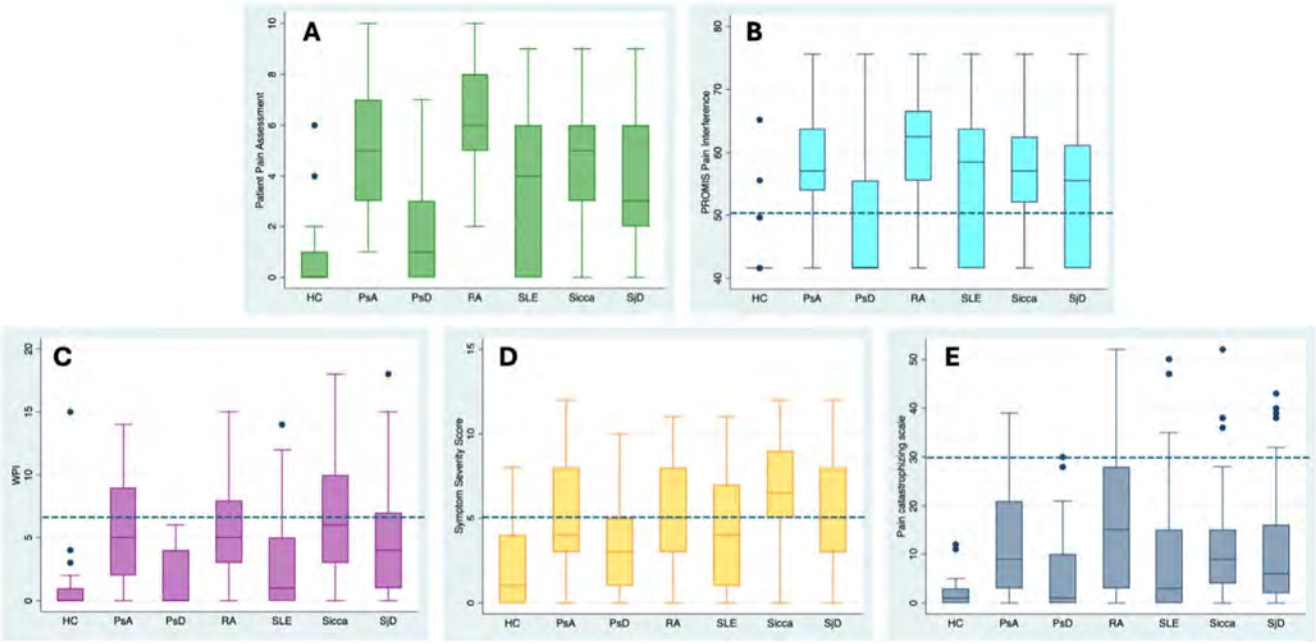


Figure 1. Pain measures across conditions Five pain measures across the enrolled diseases. (A) Pain intensity (0-10); (B) PROMIS Pain Interference scale; (C) WPI; (D) SSS; (E) PCS. Dotted line represents the general population norm (T-score 50) for PROMIS Pain Interference, the cut offs for the 2016 Fibromyalgia criteria for WPI and SSS, and the cut-off for catastrophizing for PCS. Abbreviations: RA = rheumatoid arthritis; SLE = systemic lupus erythematosus (predominantly those with kidney disease in this cohort); PsA = psoriatic arthritis; PsD = psoriasis without PsA; SjD = Sjogren's Disease; Sicca = sicca symptoms without SjD; HC = healthy control

Methods: A common set of patient-reported outcomes was administered to participants in 6 AMP AIM cohorts: RA, SLE (most with nephritis), PsA, PsO, SjD, and Sicca symptoms without SjD. We report demographics and differences among the disease states in the following measures: Pain intensity (0-10) and pain interference (T-score range 41.1-76.3) from the PROMIS-29; Widespread pain index (WPI) as a continuous measure (range 0-19); Symptom Severity Score (SSS) as a continuous measure (range 0-12); FM survey score (sum of WPI and SSS, range 0-31); Pain catastrophizing scale (PCS) (0-52 total score); Presence of FM defined using the 2016 criteria: chronic pain for 3 months or more, pain in 4/5 regions, (WPI ≥

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

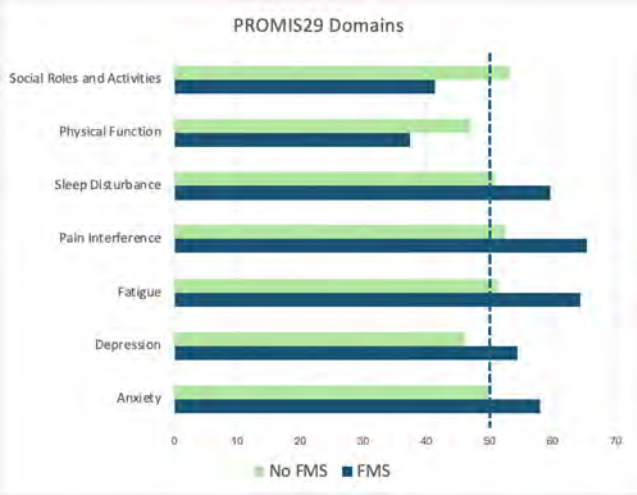


Figure 2. PROMIS29 by 2016 Fibromyalgia criteria The dotted line represents the population norm (50). For social roles and activities and physical function, lower number represent worse outcomes whereas for sleep disturbance, pain interference, fatigue, depression and anxiety, higher numbers represent worse outcomes. Abbreviation: FMS = fibromyalgia syndrome

7 and SSS ≥ 5) or (4 ≤ WPI ≤ 6 and SSS ≥ 9). We examined the differences in each of these PROs by disease and the presence or absence of FM.

Results: Among individuals enrolled in the AMP AIM study (Table 1), 39 participants with RA, 38 with SLE, 27 with PsA, 31 with PsO (without PsA), 55 with SjD, 66 with sicca symptoms but no SjD and 22 healthy controls completed the pain questionnaires. Mean age among the 6 groups varied by disease and ranged from 45 years old in SLE to 60 years in SjD. Sex was predominantly female (80% overall though 49% and 35% in PsA and PsO, respectively). 72% of participants were white, and 61% had a college education or higher. The prevalence of FM was 20% across the various cohorts, highest in participants with RA (31%) and participants with sicca symptoms but no SjD (30%), 22% in SjD, 11% in SLE, 22% in PsA, 5% in healthy controls and not observed in PsO. WPI and SSS scores varied among the groups but were also highest in participants with sicca symptoms but no SjD (Figure 1). PCS was lowest in healthy controls and PsO and similar among the other groups. Across all disease groups, PROMIS 29 scores were worse for participants with FM compared to those without FM (Figure2).

Conclusion: FM prevalence differed among these conditions and was associated with reduced quality of life and greater disease impact. Those with FM had worse PROMIS 29 scores. Patients with RA and those with sicca without SjD had the worst PROs and highest prevalence of FM. This trans-disease study emphasizes the importance of capturing chronic pain and leveraging AMP-AIM to address molecular and cellular mechanisms underlying this health burden.

Disclosure: A. Ogdie: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **D. Orange**: AstraZeneca, 2, Pfizer, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **C. Shiboski**: None; **R. Haberman**: Johnson and Johnson, 1, 5, Novartis, 1; **M. Masson**: None; **D. Goldman**: None; **P. Izmirly**: Hansoh Bio, 2; **B. Cohen**: None; **J. Seifert**: None; **J. Anolik**: None; **W. DeJager**: None; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1.

Abstract Number: 1224

Comparative Effectiveness of Duloxetine versus Pregabalin in Fibromyalgia: A Large-Scale, Real-World Study Across 300,000 Patients

Chukwuemelie Okeke[1], Queeneth Edwards[2], Ufuoma Mamoh[3], Justin Riley Lam[4] and Chekwubejah Uwakwe[5], [1]Maimonides Medical Center, Brooklyn, NY, [2]Department of Epidemiology and Biostatistics, Jiann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, GA, [3]Medstar Health Georgetown University Internal Medicine Residency Program, Baltimore, MD, [4]Jefferson Einstein Hospital, Philadelphia, PA, [5]Nnamdi Azikiwe University Teaching Hospital, Nigeria, Nnewi, Anambra, Nigeria

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia (FM) is a chronic, debilitating condition characterized by widespread pain, fatigue, and cognitive disturbances. Despite the availability of FDA-approved treatments, real-world comparative effectiveness data between duloxetine and pregabalin remain limited, particularly in diverse patient populations. Understanding which agent offers greater clinical durability and fewer adverse outcomes can inform personalized care in rheumatologic practice.

This study aims to compare the real-world effectiveness, tolerability, and healthcare utilization associated with duloxetine and pregabalin among patients diagnosed with fibromyalgia using a large multicenter electronic health record database.

Methods: This is a retrospective cohort study utilizing data from the TriNetX Global Collaborative Network, encompassing over 144 healthcare organizations worldwide. Adult patients (≥18 years) with a diagnosis of fibromyalgia (ICD-10-CM: M79.7) who received either duloxetine (Cohort A: n = 194,834) or pregabalin (Cohort B: n = 114,556) were identified. Patients receiving both drugs were excluded. Propensity score matching (1:1 greedy nearest-neighbor) adjusted for age, sex, comorbidities, and baseline medication use. Primary outcome was treatment durability (time to discontinuation or switch) over 3 years. Secondary outcomes included pain-related ED visits, new-onset psychiatric diagnoses, and adverse event profiles.

Results: Post-matching, each cohort comprised 113,402 patients. Duloxetine demonstrated a significantly longer median time to treatment discontinuation (HR: 0.82; 95% CI: 0.79–0.85; $p < 0.001$) and fewer discontinuation/switch events within 12 months (24.3% vs. 30.9%). Duloxetine users also had reduced pain-related ED visits (RR: 0.76; 95% CI: 0.71–0.81), and lower incidence of new-onset anxiety/depression ($p < 0.01$). In contrast, pregabalin users reported fewer GI side effects but had higher risks of sedation and weight gain (OR: 1.34; 95% CI: 1.29–1.39). Subgroup analyses revealed that patients with pre-existing mood disorders benefited more from duloxetine, whereas pregabalin performed better in elderly populations and those with neuropathic comorbidities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Matched Fibromyalgia Patients Treated with Duloxetine vs. Pregabalin

Characteristic	Duloxetine (N=109,793)	Pregabalin (N=109,793)	p-value	Standardized Difference
Demographics				
Age (years), mean ± SD	60.9 ± 15.1	61.1 ± 14.8	<0.001	0.015
Age at Index, mean ± SD	54.3 ± 15.1	54.5 ± 14.9	0.002	0.013
Female, n (%)	87,532 (79.7%)	87,977 (80.1%)	0.018	0.010
Male, n (%)	18,310 (16.7%)	17,917 (16.3%)	0.024	0.010
White, n (%)	75,219 (68.5%)	75,415 (68.7%)	0.367	0.004
Black or African American, n (%)	12,137 (11.1%)	12,339 (11.2%)	0.171	0.006
Hispanic or Latino, n (%)	7,938 (7.2%)	7,823 (7.1%)	0.342	0.004
Unknown Ethnicity, n (%)	29,992 (27.3%)	30,303 (27.6%)	0.137	0.006
Comorbid Conditions				
Osteoarthritis (M15–M19), n (%)	40,586 (37.0%)	40,815 (37.2%)	0.312	0.004
Disorders of muscle (M60–M63), n (%)	48,340 (44.0%)	48,292 (44.0%)	0.837	0.001
Systemic connective tissue disorders (M30–M36)	11,370 (10.4%)	11,597 (10.6%)	0.113	0.007
Soft tissue disorders (M79), n (%)	78,026 (71.1%)	77,929 (71.0%)	0.648	0.002
Metabolic disorders (E70–E88), n (%)	51,471 (46.9%)	51,695 (47.1%)	0.338	0.004
Obesity/hyperalimentation (E65–E68), n (%)	29,029 (26.4%)	29,158 (26.6%)	0.533	0.003
Diabetes mellitus (E08–E13), n (%)	23,595 (21.5%)	23,835 (21.7%)	0.213	0.005
Nutritional deficiencies (E50–E64), n (%)	24,782 (22.6%)	24,595 (22.4%)	0.339	0.004
Mood disorders (F30–F39), n (%)	44,003 (40.1%)	43,457 (39.6%)	0.017	0.010
Anxiety disorders (F40–F48), n (%)	41,751 (38.0%)	41,526 (37.8%)	0.322	0.004
Substance use disorders (F10–F19), n (%)	26,129 (23.8%)	26,092 (23.8%)	0.853	0.001
Hypertensive diseases (I10–I1A), n (%)	48,290 (44.0%)	49,008 (44.6%)	0.002	0.013
Ischemic heart disease (I20–I25), n (%)	16,017 (14.6%)	16,207 (14.8%)	0.252	0.005
Kidney disease (N17–N19), n (%)	12,848 (11.7%)	12,920 (11.8%)	0.633	0.002

Table 2: Duloxetine (1) and Pregabalin (2) comparison

Cohort	Patients in each Cohort	Patients with outcome	Risk	Risk Difference	Risk Ratio	Odds Ratio	p-value
ED visits							
1	109,793	33,680	0.307	-0.007 (-0.011, -0.003)	0.978 (0.965, 0.990)	0.968 (0.950, 0.985)	0.000
2	109,793	34,454	0.314				
NSAID use							
1	109,793	64,828	0.590	-0.039 (-0.043, -0.035)	0.938 (0.932, 0.944)	0.849 (0.834, 0.863)	0.000
2	109,793	69,115	0.630				
Opioid Use							
1	109,793	61,163	0.557	-0.053 (-0.057, -0.049)	0.914 (0.907, 0.920)	0.805 (0.792, 0.819)	0.000
2	109,793	66,941	0.610				
Suicide							
1	109,793	2,347	0.021	0.005 (0.004, 0.006)	1.286 (1.210, 1.366)	1.292 (1.215, 1.375)	0.000
2	109,793	1,825	0.017				
Depression							
1	109,793	33,410	0.304	0.054 (0.051, 0.058)	1.217 (1.201, 1.234)	1.313 (1.288, 1.337)	0.000
2	109,793	27,443	0.250				
Anxiety							
1	109,793	11,751	0.107	0.019 (0.016, 0.021)	1.213 (1.182, 1.244)	1.238 (1.204, 1.274)	0.000
2	109,793	9,688	0.088				

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In one of the largest real-world analyses of fibromyalgia treatment to date, duloxetine was associated with superior treatment persistence, fewer acute care needs, and improved psychiatric outcomes compared to pregabalin. These results support a precision medicine approach in selecting pharmacologic therapy for FM and call for prospective trials targeting specific patient phenotypes to optimize treatment efficacy and tolerability.

Disclosure: C. Okeke: None; **Q. Edwards**: None; **U. Mamoh**: None; **J. Lam**: None; **C. Uwakwe**: None.

Abstract Number: 1225

Association Between Anxiety and Tender Swollen Joint Difference in Patients with Rheumatoid Arthritis

Clarice Lin[1], Burcu Aydemir[2], Jing Song[3], Lutfiyya muhammad[2], Clifton Bingham[4], Tuhina Neogi[5], Wendy Marder[6], Marcy Bolster[7], Daniel Clauw[8], Dorothy Dunlop[9] and Yvonne Lee[1], [1]Northwestern University, Chicago, IL, [2]Northwestern University Feinberg School of Medicine, Chicago, IL, [3]Northwestern University Feinberg School of Medicine, Worthington, MN, [4]Johns Hopkins University, Baltimore, MD, [5]Boston University School of Medicine, Boston, MA, [6]University of Michigan, Ann Arbor, MI, [7]Massachusetts General Hospital, Concord, MA, [8]Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI, [9]Northwestern University Feinberg School of Medicine, Chicago

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Some patients with rheumatoid arthritis (RA) have pain, despite normalization of inflammatory markers and reduced swollen joint counts. Among these patients, the number of tender joints often exceeds the number of swollen joints. Pollard et al. reported that a tender swollen joint difference (TSJD) ≥ 7 can identify patients with RA and comorbid fibromyalgia, the prototypical nociplastic pain condition.[1] Fibromyalgia and anxiety often co-occur, and previous studies suggest that psychological factors, such as anxiety, may heighten pain sensitivity. The objective of this study is to assess the relationship between anxiety and TSJD, as an indicator of dysregulated CNS pain processing, in patients with RA.

Methods: This analysis used baseline data from the Central Pain in RA (CPIRA) study, which enrolled 295 participants from four academic medical centers between January 2014 to April 2017. Patients met 2010 ACR/EULAR criteria for RA and were either starting DMARDs or switching DMARDs due to lack of efficacy. TSJD was calculated as the number of tender joints minus the number of swollen joints on a 28-joint exam. A higher TSJD indicates greater discrepancy between tender and swollen joint counts. A dichotomous outcome of high vs. low TSJD was defined using a cut-off of ≥ 7 vs. < 7. We

Table 1. Characteristics of Study Participants.

Characteristic	Overall (n = 276)	TSJD < 7 (n = 172)	TSJD ≥ 7 (n = 104)
Age, years	54.7 ± 13.9	54.8 ± 14.9	54.6 ± 12.0
Female (*n*, %)	226 (82%)	137 (80%)	89 (86%)
White (*n*, %)	207 (75%)	131 (76%)	76 (73%)
Body mass index, kg/m^2	28.6 ± 6.7	27.6 ± 6.6	30.2 ± 6.7
RA Symptom Duration, years	12.5 ± 12.7	11.9 ± 12.4	13.5 ± 13.2
Seropositive (*n*, %)	201 (72.8%)	130 (75.6%)	71 (68.3%)
PROMIS Anxiety, t-score	53.8 ± 8.9	52.5 ± 8.4	55.9 ± 9.3
CRP, mg/L	8.0 ± 12.4	8.7 ± 14.1	6.8 ± 8.6

Values represent mean ± SD or n (%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Results of Multivariable Logistic Regression Model, Adjusted Association between Anxiety and Presence of Higher Tender Swollen Joint Difference (TSJD ≥ 7) (n = 276)

Variables	Adjusted OR [95% CI]	p-value
Anxiety, t-score [a]	**1.05 [1.01, 1.08]**	**0.01**
Age, years	1.00 [0.995, 1.003]	0.68
Female	1.12 [0.97, 1.30]	0.12
White	1.01 [0.88, 1.15]	0.92
Seropositivity	0.93 [0.82, 1.06]	0.30
CRP, mg/L	1.00 [0.99, 1.001]	0.17
Body mass index, kg/m^2	**1.01 [1.01, 1.02]**	**<0.001**
RA Symptom Duration, years	1.00 [0.999,1.008]	0.16

a Per 5-unit increase in PROMIS Anxiety T-Score

evaluated associations between PROMIS anxiety t-scores and TSJD using logistic regression. Multivariable logistic regression models were adjusted for age, sex, race, body mass index (BMI), RA symptom duration, seropositivity, and C-reactive protein (CRP).

Results: Among 276 patients with RA (mean age (± SD) 54.7 ± 13.9 years, 82% female), 73% were seropositive for rheumatoid factor and/or anti-cyclic citrullinated peptide, and the mean RA symptom duration was 12.5 ± 12.7 years. The median TSJD was 4.0, (interquartile range of 0-10.3), with 38% having a TSJD of ≥ 7. The mean PROMIS anxiety score was 53.8 ± 8.9. In unadjusted analyses, higher anxiety was significantly associated with presence of higher TSJD (odds ratio [OR] for 5-unit change = 1.05, 95% confidence interval [CI]: 1.02, 1.09). In the multivariable regression model, anxiety remained significantly associated with higher TSJD (OR for 5-unit change = 1.05, 95% CI: 1.01, 1.08) (Table 2). Higher BMI was also significantly associated with higher TSJD.

Conclusion: Greater anxiety was associated with higher TSJD. RA patients with greater TSJD may benefit from a multimodal pain management approach that includes strategies for managing and monitoring symptoms of anxiety.

References:

1. Pollard LC, Kingsley GH, Choy EH, et al. Fibromyalgic rheumatoid arthritis and disease assessment. Rheumatology (Oxford). 2010; 49: 924-9.

Disclosure: C. Lin: None; **B. Aydemir**: None; **J. Song**: None; **L. muhammad**: None; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **T. Neogi**: None; **W. Marder**: None; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **D. Clauw**: Tonix, 2, 5; **D. Dunlop**: None; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1.

Abstract Number: 1226

Preliminary Findings in the Validation of the Modified Pain and Symptom Assessment Tool in Juvenile Fibromyalgia Syndrome

Daniella Schocken[1], Mark Connelly[2], Sabrina Gmuca[3], Andrea Ramirez[4], Mary Ellen Riordan[5], Tracy Ting[6], Susmita Kashikar-Zuck[7] and Jennifer Weiss[8], [1]Children's Mercy Kansas City, Tampa, FL, [2]Children's Mercy Kansas City/University of Missouri-Kansas City School of Medicine, Kansas City, MO, [3]Children's Hospital of Philadelphia, Philadelphia, PA, [4]Baylor College of Medicine, Houston, TX, [5]Hackensack University Medical Center, Hackensack, NJ, [6]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [7]University of Cincinnati College of Medicine; Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Diagnosing juvenile fibromyalgia (JFM) in youth with chronic musculoskeletal (MSK) pain is challenging in the absence of a validated diagnostic tool. The Pain and Symptom Assessment Tool (PSAT) was developed from modifications to the ACR criteria for adult FM (2010) to aid in JFM diagnosis. This ongoing study aims to validate the PSAT as a diagnostic tool by demonstrating how measured differences in pain distribution and accompanying symptoms distinguish JFM from other causes of chronic MSK pain such as JIA or more localized painful disorders.

Methods: This multicenter, cross-sectional observational study enrolled English- and Spanish-speaking adolescents (age range: 11 – 17) with MSK pain of ≥3 months' duration and a clinical diagnosis of JFM, JIA, or localized MSK pain. All participants completed the PSAT, which included both assessment of pain location using the Michigan Body Map© (MBM) and a Symptom Severity Index (SSI) comprised of an inventory of associated symptoms with severity indices for fatigue, nonrestorative sleep, and impaired memory or concentration. One-way ANOVA was performed to look for differences in MBM totals and SSI between diagnostic groups, and post hoc analysis was carried out with Tukey's HSD test to determine the significance of between-group differences. Yunus and Masi's criteria for primary JFM (1985), which include ≥5 tender points on physical exam, were used by study staff as a diagnostic standard with which to evaluate all participants for clinical features consistent with JFM.

Results: A total of 158 participants were enrolled across 5 clinical sites. Participant diagnoses and characteristics are detailed in Figure 1. The average pain intensity rating among study participants was 5.7/10 (sd = 2.2), and 77/158 (49%) participants had ≥5 tender points on physical exam. Yunus and Masi's criteria were fulfilled by 47/60 (78%) participants with a clinical diagnosis of JFM and one participant with JIA. No participants with localized pain met these criteria. MBM totals and SSI both differed between diagnostic groups with $F(2, 155) = 43.43$ ($p < 0.001$, 95% CI [0.26, 1.00]) and $F(2, 155) = 25.79$

	Juvenile Fibromyalgia (n = 60)	*Juvenile Idiopathic Arthritis (n = 40)*	*Localized MSK Pain (n = 58)*	*Total (n = 158)*
Mean Age (sd)	15.6 (1.7)	15.2 (2.0)	14.3 (1.9)	15.0 (1.9)
Gender				
Cis-gender Female (%)	46 (77)	33 (83)	48 (83)	127 (80)
Cis-gender Male (%)	8 (13)	6 (15)	8 (14)	22 (14)
Transgender or Nonbinary (%)	6 (10)	1 (3)	2 (3)	9 (6)
Race				
American Indian or Alaska Native (%)	1 (2)	1 (3)	1 (2)	3 (2)
Asian (%)	3 (5)	0 (0)	1 (2)	4 (3)
Black or African American (%)	2 (3)	1 (3)	7 (12)	10 (6)
White (%)	43 (72)	33 (83)	37 (64)	113 (72)
More than one race (%)	5 (8)	3 (8)	3 (5)	11 (7)
Not reported / unknown (%)	6 (10)	2 (5)	9 (16)	17 (11)
Ethnicity				
Hispanic or Latino (%)	14 (23)	8 (20)	20 (34)	42 (27)
Not Hispanic or Latino (%)	43 (72)	31 (78)	33 (57)	107 (68)
Not reported / unknown (%)	3 (5)	1 (3)	5 (9)	9 (6)
Language				
English (%)	55 (92)	37 (93)	51 (88)	143 (91)
Spanish (%)	5 (8)	3 (8)	7 (12)	15 (9)
Mean Pain Intensity (sd)	6.3 (1.8)	4.7 (2.5)	5.9 (2.1)	5.7 (2.2)
Mean Michigan Body Map total (sd)	15.8 (8.9)	7.1 (5.0)	4.7 (4.9)	9.5 (8.3)
Mean Symptom Severity Index (sd)	8.0 (2.7)	4.6 (3.2)	4.4 (2.9)	5.8 (3.4)
Number of participants with ≥5 tender points (%)	56 (93)	9 (23)	12 (21)	77 (49)
Number of participants meeting Yunus and Masi Criteria (%)	47 (78)	1 (3)	0 (0)	48 (30)

Figure 1: A table providing demographic and clinical characteristics of enrolled participants broken down by diagnosis. Included are age, gender, race, ethnicity, language of study completion, pain intensity, MBM total, SSI, tender point exam findings, and fulfillment of Yunus and Masi's critera.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

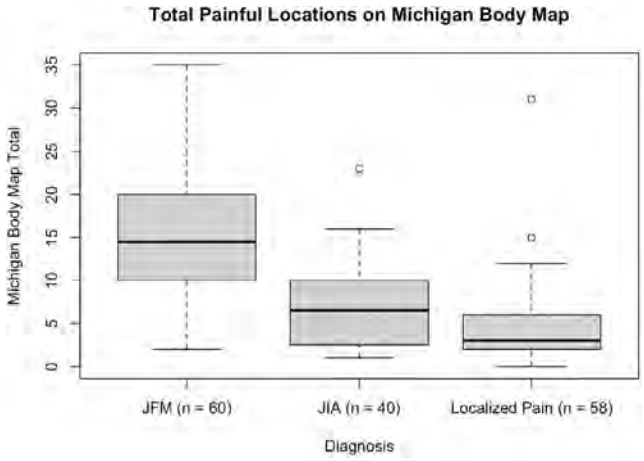


Figure 2: A box plot of total painful locations on Michigan Body Map (MBM) broken down by participant diagnosis. Center bars represent the median. Upper and lower limits of boxes are interquartile ranges. The limits of the whiskers are the full range with significant outliers excluded and plotted separately.

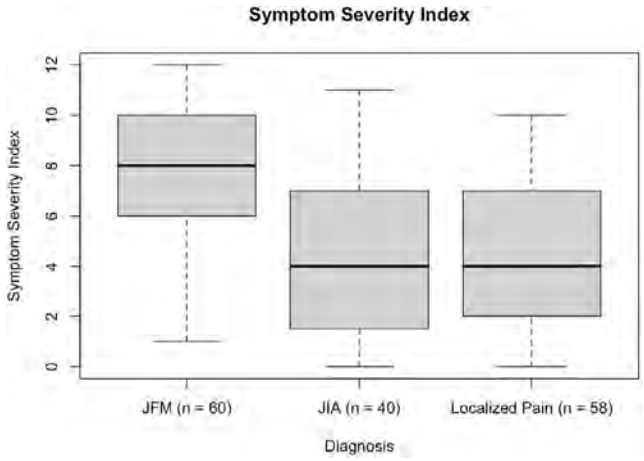


Figure 3: A box plot of participants' Symptom Severity Index (SSI) broken down by diagnosis. Center bars represent the median. Upper and lower limits of boxes are interquartile ranges. The limits of the whiskers are the full range.

($p < 0.001$, 95% CI [0.15, 1.00]), respectively. Post hoc analysis revealed significantly higher MBM totals and SSI among participants with JFM when compared to those with either localized MSK pain or JIA ($p < 0.001$). Figures 2 and 3 illustrate the distribution of MBM totals and SSI across participant diagnoses.

Conclusion: Analysis of these results from PSAT administration to adolescents with chronic MSK pain shows clear differences in measured pain distribution and symptom severity between those participants diagnosed clinically with JFM and those with other chronically painful MSK conditions. As recruitment for this study is ongoing, sensitivity and specificity of the PSAT in comparison with Yunus and Masi's criteria for the diagnosis of JFM will be determined following completion of further data collection and analysis. However, these preliminary results support the utility of the PSAT in distinguishing JFM from other causes of chronic MSK pain in pediatric patients, highlighting a valuable tool to improve the consistency of case definitions in research and ease diagnostic uncertainty in clinical care.

Disclosure: D. Schocken: None; **M. Connelly**: None; **S. Gmuca**: None; **A. Ramirez**: None; **M. Riordan**: None; **T. Ting**: None; **S. Kashikar-Zuck**: None; **J. Weiss**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1227

The Composition of Circulating Immune Cells is Associated with Nociplastic Pain in Patients with Rheumatoid Arthritis

Tyler Therron[1], Meghan Mayer[2], Cecilia Stumpf[3], Gelis Galarcé Lugo[4], Morgan Langereis[5], Kathleen Aren[6], Mary Carns[5], Cally Mills[5], Cheol Min Lee[7], Vanessa Manada De Lobos[2], Carla Marie Cuda[5], Yvonne Lee[5] and **Deborah Rachelle Winter**[8], [1]Northwestern Feinberg School of Medicine, Chicago, IL, [2]Northwestern University, Chicago, [3]Northwestern University, Elmhurst, IL, [4]Northwestern University Feinberg School of Medicine, Zionsville, IN, [5]Northwestern University, Chicago, IL, [6]Northwestern University Division of Rheumatology, Chicago, IL, [7]Northwestern University Feinberg School of Medicine, Chicago, IL, [8]Northwestern University, Skokie, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Over half of patients with RA report clinically meaningful pain, despite treatment with disease-modifying antirheumatic drugs (DMARDs). While joint inflammation is a known cause of pain in patients with rheumatic diseases, emerging data indicate that many patients also suffer from centralized or nociplastic pain. In our prior studies, we have used quantitative sensory testing (QST) to demonstrate that patients with RA have altered CNS pain processing compared to healthy controls and these alterations are associated with clinically meaningful outcomes. However, QST is time-consuming, requires significant assessor training, and is prone to measurement error. There is a critical unmet need to develop quantifiable measurements of the altered cellular state that distinguish patients with centralized pain.

Methods: In this study, we aimed to recruit 50 RA patients with minimal joint inflammation but varying levels of systemic inflammation and pain. All patients consented under the IRB protocol underwent QST to assess centralized pain and provided blood samples for immune profiling using state-of-the-art multi-parameter flow cytometry with a custom panel designed to identify key immune cell types and activation states. Frozen peripheral blood mononuclear cells (PBMCs) from patients in the study with the highest and lowest levels of nociplastic pain were additionally used to generate single-cell RNA-sequencing (scRNA-seq) libraries. These samples were individually labelled using hash tag oligomers (HTO) and pooled for library prep using 10X Genomics technology to reduce batch effect. The resulting sequencing data was processed with cellranger pipeline and analyzed using the Seurat package in R.

Results: We were able to collect 44 usable samples from patients who successfully consented and completed all study requirements. Of these, ~43% reported mild or moderate pain at the time of sample collection as measured by the numeric rating scale. Based on preliminary analyses of scRNA-seq from 6 patients among the highest and lowest pain levels, we annotated 3 subpopulations of T cells (Naïve CD4, Memory CD4, and CD8), NK cells, B cells, Plasma cells, Dendritic cells (DCs), and 2 subpopulations of Monocytes (CD14+ and CD16+/FCGR3A+). The high pain group exhibited decreased proportions of T cells and increased monocytes and DCs compared to the low pain group.

Conclusion: Our preliminary results indicate that the composition of circulating immune cells is associated with nociplastic pain in RA patients. With further analysis, we aim to validate these results in the larger dataset and determine whether there are robust transcriptional changes in specific cell types. Moreover, we are currently in the process of analyzing immunophenotyping data to assess composition and activation across pain levels. These studies provide novel insights into the role of circulating immune cells in altered CNS pain regulation in RA patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Therron: None; **M. Mayer**: None; **C. Stumpf**: None; **G. Galarcé Lugo**: None; **M. Langereis**: None; **K. Aren**: None; **M. Carns**: None; **C. Mills**: None; **C. Lee**: None; **V. Manada De Lobos**: None; **C. Cuda**: None; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1; **D. Winter**: None.

Abstract Number: 1228

Transcending barriers to pain care in rural America: a pragmatic comparative effectiveness trial of evidence-based, on-demand, digital behavioral treatments for chronic pain

Brennan Spiegel[1], Jeffrey Curtis[2], Yashar Eshraghi[3], Maged Guirguis[3], Beth Darnall[4], Christine Rini[5], **Emily Holladay**[6], Mehra Muskaan[1], So Yung Choi[1] and Samuel Eberlein[1], [1]Cedars Sinai, Los Angeles, CA, [2]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [3]University of Queensland Ochsner Medical School, New Orleans, LA, [4]Stanford University School of Medicine, Palo Alto, CA, [5]Northwestern University, Chicago, IL, [6]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Evidence-based behavioral treatments for chronic pain are largely inaccessible, particularly to rural patients. This decentralized randomized controlled trial compared the effectiveness of two digital, evidence-based chronic pain management programs—3D immersive Skills-Based Virtual Reality (EaseVRx+) and interactive pain coping skills training (painTRAINER)—in a rheumatic and musculoskeletal disease (RMD) and chronic pain population.

Methods: Patients were recruited from 3 large health centers and practice networks (Cedars-Sinai Medical Center; the University of Alabama and its affiliated Excellence Network in RheumatoloGY to Innovate Care and High-impact research; Ochsner Health System). Patients meeting study inclusion criteria (qualifying diagnostic code in medical record, primary residence ZIP code defined as rural, aged ≥13, ≥4 pain on 0-10 scale, without history of seizure, etc.) were identified within each participating network. Study coordinators screened individuals by phone; eligible and interested individuals were consented electronically. Participants were required to complete 7 daily baseline surveys which recorded demographics, daily pain intensity as measured by an 11-point pain numeric rating scale (NRS), and daily medication use prior to 1:1 randomization. Participants completed 16 REDCap surveys collecting pain intensity, medication use, and other PROs over 12 weeks. We measured the improvement in pain intensity between baseline and week 8, defined by a minimal clinically important difference (MCID) of 2 points on the standard 11-point numeric rating scale. Secondary outcomes included PROMIS anxiety and pain interference, pain catastrophizing, and pain self-efficacy.

Results: We randomized 330 participants: 169 to EaseVRx+ and 161 to painTRAINER, of which 46.7% were RMD patients. At Week 8, 278 (84.2%) participants completed the primary endpoint, demonstrating a high rate of treatment completion (Table 1). Average pain NRS improved in both arms (mean[SD] 1.22[1.48] units), however the intent-to-treat (ITT) analysis of the primary endpoint found no statistically significant difference in clinically meaningful pain reduction between the EaseVRx+ (22.9% achieving MCID >=2) and painTRAINER arms (32.0%) ($p = 0.088$) (Figure 1).

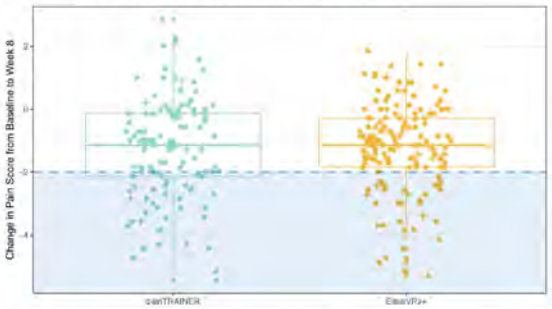
Between baseline and week 8, the mean (SD) changes in PROMIS pain interference, pain catastrophizing, PROMIS anxiety, and pain self-efficacy for Ease VRx+ and painTRAINER were -3.2 (6.0) vs. -4.5 (6.3), -1.7 (3.2) vs. -1.8 (3.5), -0.6 (7.6) vs. -0.3 (7.6), and 0.6 (2.8) vs. 1.5 (2.7), respectively. The group analyses were not statistically significant, except for pain self-efficacy (greater in the painTRAINER arm at weeks 6, 7 and 8) (Figure 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Demographics of Patients who Completed the Primary Endpoint

	Overall 278	painTRAINER 125	EaseVRx+ 153	SMD
Age, median (IQR)	56 (47, 64)	55 (47, 63)	57 (47, 65)	0.077
Female sex (%)	202 (72.7)	89 (71.2)	113 (73.9)	0.060
Race (%)				0.458
White	221 (79.5)	100 (80.0)	121 (79.1)	
Black or African American	35 (12.6)	13 (10.4)	22 (14.4)	
American Indian or Alaska Native	4 (1.4)	1 (0.8)	3 (2.0)	
Asian	4 (1.4)	0 (0.0)	4 (2.6)	
Other	13 (4.7)	11 (8.8)	2 (1.3)	
Unknown	1 (0.4)	0 (0.0)	1 (0.7)	
Ethnicity (%)				0.117
Non-Hispanic or Latino	254 (91.4)	112 (89.6)	142 (92.8)	
Hispanic or Latino	18 (6.5)	10 (8.0)	8 (5.2)	
Unknown	6 (2.2)	3 (2.4)	3 (2.0)	
Education (%)				0.296
No Secondary School or High School	2 (0.7)	1 (0.8)	1 (0.7)	
Some Secondary School or High School	35 (12.6)	14 (11.2)	21 (13.7)	
High School or Secondary School Degree	96 (34.5)	37 (29.6)	59 (38.6)	
Associate's or Technical Degree	70 (25.2)	32 (25.6)	38 (24.8)	
College or Baccalaureate Degree	49 (17.6)	29 (23.2)	20 (13.1)	
Doctoral or Postgraduate Education	26 (9.4)	12 (9.6)	14 (9.2)	
Employment (%)				0.073
Full-time	82 (29.5)	35 (28.0)	47 (30.7)	
Part-time	28 (10.1)	12 (9.6)	16 (10.5)	
Not employed	168 (60.4)	78 (62.4)	90 (58.8)	
Relationship Status (%)				0.307
Married	173 (62.2)	81 (64.8)	92 (60.1)	
Divorced	52 (18.7)	19 (15.2)	33 (21.6)	
Never Married	22 (7.9)	14 (11.2)	8 (5.2)	
Widowed	19 (6.8)	6 (4.8)	13 (8.5)	
Separated	9 (3.2)	4 (3.2)	5 (3.3)	
Domestic Partner	3 (1.1)	1 (0.8)	2 (1.3)	
Income (%)				0.366
Less than $10,000	14 (5.0)	9 (7.2)	5 (3.3)	
$10,000-$24,999	43 (15.5)	15 (12.0)	28 (18.3)	
$25,000-$34,999	27 (9.7)	13 (10.4)	14 (9.2)	
$35,000-$49,999	44 (15.8)	15 (12.0)	29 (19.0)	
$50,000-$74,999	39 (14.0)	19 (15.2)	20 (13.1)	
$75,000-$99,999	34 (12.2)	15 (12.0)	19 (12.4)	
$100,000-$149,999	31 (11.2)	18 (14.4)	13 (8.5)	
$150,000-$199,999	13 (4.7)	7 (5.6)	6 (3.9)	
$200,000 or more	9 (3.2)	4 (3.2)	5 (3.3)	
Prefer not to answer	24 (8.6)	10 (8.0)	14 (9.2)	
Baseline 7-day pain average, mean (SD)	6.20 (1.73)	6.27 (1.74)	6.15 (1.72)	0.072
Baseline 7-day MME average, mean (SD)	448.24 (4762.66)	580.81 (5548.25)	339.93 (4024.67)	0.050
Baseline PROMIS anxiety, mean (SD)	53.56 (9.59)	53.77 (9.50)	53.39 (9.70)	0.039
Baseline Pain Catastrophizing Scale, mean (SD)	8.31 (3.81)	8.14 (3.88)	8.45 (3.77)	0.082
Baseline PROMIS pain interference, mean (SD)	64.25 (6.33)	64.50 (6.45)	64.04 (6.24)	0.072
Baseline Pain Self-Efficacy, mean (SD)	5.88 (3.07)	5.81 (3.19)	5.94 (2.98)	0.043
Primary Diagnosis				0.063
Rheumatology	136 (48.9)	59 (47.2)	77 (50.3)	
Chronic Pain	142 (51.1)	66 (52.8)	76 (49.7)	

Figure 1: ITT Analysis of Pain Intensity Between Baseline and Week 8

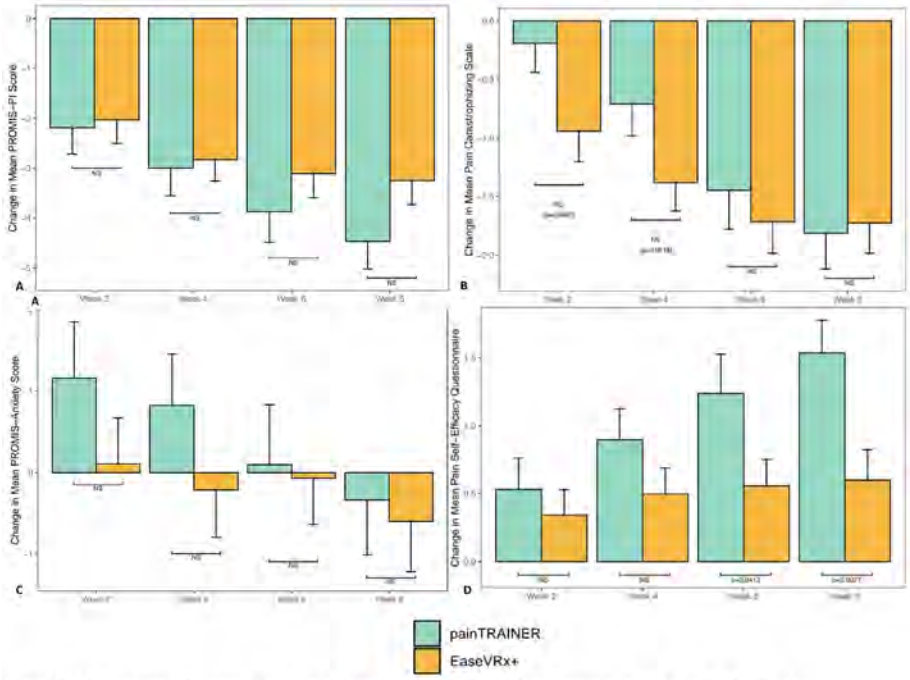


At least 4-response	Freq. (column %)		Chi-squared p-value
	painTRAINER (N=125)	EaseVRx (N=153)	
MCID < 2	85 (68.0%)	118 (77.1%)	0.088
MCID ≥ 2 (Good)	40 (32.0%)	35 (22.9%)	

ITT: Intent-to-treat. MCID: minimal clinically important difference.
Note: ITT analyses of the primary endpoint required responses to at least >=4 of the 7 daily assessments.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Mean Weekly Changes in PROMIS Anxiety and Pain Interference, Pain Catastrophizing, and Pain Self-Efficacy in painTRAINER and EaseVRx+



a. PROMIS Pain Interference, b. Pain Catastrophizing, c. PROMIS Anxiety, d. Pain Self-Efficacy

Conclusion: This trial displays the viability of implementing autonomous (self-paced) digital behavioral treatments for RMDs and chronic pain in rural areas, especially for patients without access to in-person behavioral treatment. EaseVRx+ and painTRAINER are effective and provide accessible behavioral pain treatment for chronic pain and could play a significant role in improving health equity in underserved populations.

Disclosure: B. Spiegel: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **Y. Eshraghi**: None; **M. Guirguis**: avanos inc., 2, Averitas pharma, 2, Boston scientific, 2, Pacira pharm, 2, Saluda medical, 2, Vivex biologics, 2; **B. Darnall**: AppliedVR, 1; **C. Rini**: None; **E. Holladay**: None; **M. Muskaan**: None; **S. Choi**: None; **S. Eberlein**: None.

Abstract Number: 1229

Extent versus impact: Sex-specific burden of chronic pain in older adults

Gillian Fennell[1], Sarah Tilley[2], Sayali Dhamne[3], Angelo Demalia[3], Margaret Clancy[3], Mary Gheller[3], Robert Edwards[4], Emelia J Benjamin[3] and Tuhina Neogi[5], [1]Boston University Medical, Boston, MA, [2]Boston University School of Medicine, Somerville, MA, [3]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, [4]Brigham and Women's Hospital & Harvard Medical School, Boston, MA, [5]Boston University School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Over one third of older Americans experience chronic pain, accompanied by age-related increases in pain-related activity interference (i.e., pain burden). While pain extent (i.e., the number of reported pain sites) is often used as an indicator of this burden, extent tends to plateau or decline after midlife. Thus, it is unclear whether the same pain extent represents the same level of burden in oldest-old adults as it does in younger-old counterparts. Furthermore, there are different ways of assessing pain extent, some of which may better capture the impact of the chronic pain experience. We therefore estimated the prevalence and burden of several chronic pain definitions among older adults by age and sex.

Methods: We used data from a community-based sample of older adults from an ancillary study of the Framingham Heart Study/Omni1. We collected data on number and distribution of pain sites (articular, non-articular, and axial), pain duration, frequency, intensity, and interference with daily activities. We categorized participants with chronic pain (i.e., pain lasting ≥3 months) into 3 extent-based groups: 1) **chronic widespread pain (WSP)** as pain present above and below the waist, on the right and left sides of the body, and in the spine. 2) **chronic multisite pain** as pain occupying ≥3 body sites (and not meeting the WSP definition), and 3) chronic pain in 1-2 pain sites. We additionally characterized participants with bothersome or high-impact chronic pain (**B-HICP**) based upon high pain frequency, intensity, and interference from the Brief Pain Inventory. For each of the 4 pain categorizations, we compared their frequencies across age groups (52-70, 71-80, 81+ years) in a sex-stratified manner and assessed for linear trends. We also assessed mean pain interference from the Brief Pain

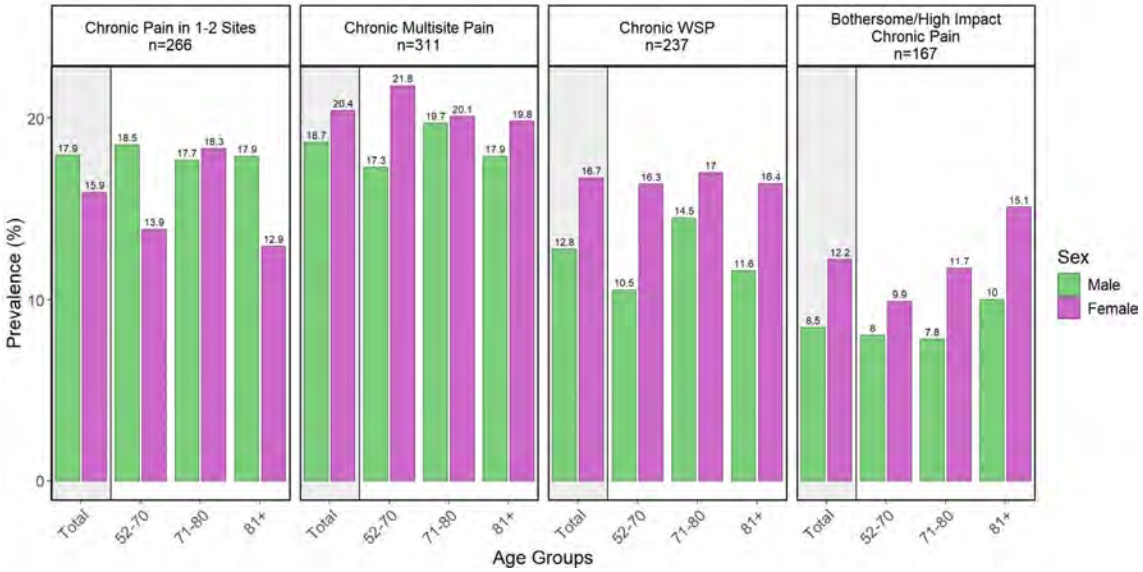


Figure 1: Pain prevalence by classification, stratified by age and sex.

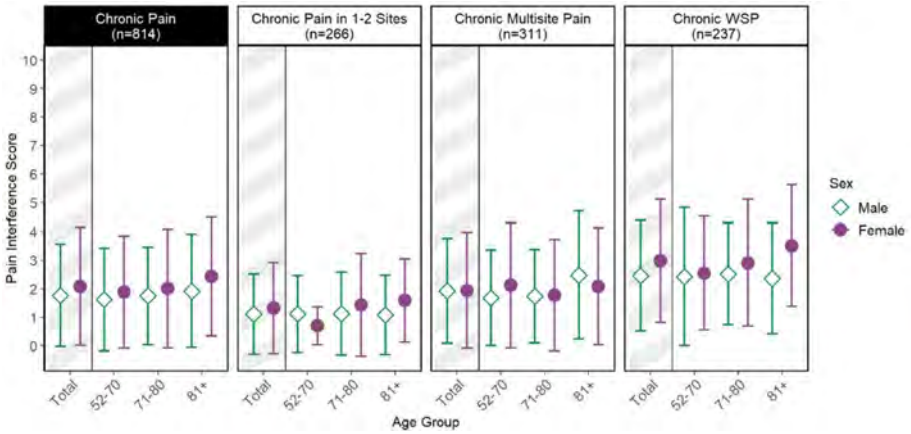


Figure 2: Pain interference score by pain classification, stratified by age and sex.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Inventory for each of the extent-based categorizations across age groups in a sex-specific manner using linear regression. We did not do so for B-HICP because pain interference is included in its definition.

Results: We included 1,584 participants (mean age, 76.1 ± 7.5; range 52-102 years; 56% female), of whom 52% had chronic pain, 36% had chronic multisite pain, 15.6% had chronic WSP, and 10.4% B-HICP (Figure 1). Prevalence of either chronic multisite or WSP did not increase with age ($p>0.05$; Figure 1). However, pain impact—as measured by pain interference and percent whose pain classified as B-HICP—did increase with age for women (both $p< 0.05$; Figures 1 & 2).

Conclusion: Our findings suggest that although pain does not become more widespread with advancing age in either men or women, pain burden does increase with age in women. Thus, similar numbers of pain sites contribute to a greater level of pain burden in oldest-old women than it does in younger-old counterparts. Pain impact measures that incorporate pain frequency, intensity, and pain interference, may better reflect burden than number of pain sites, especially among older women.

Disclosure: G. Fennell: None; **S. Tilley**: None; **S. Dhamne**: None; **A. Demalia**: None; **M. Clancy**: None; **M. Gheller**: None; **R. Edwards**: None; **E. Benjamin**: None; **T. Neogi**: None.

Abstract Number: 1230

Chronic pain phenotypes in older adults: Identifying patterns of musculoskeletal pain and associated burden

Gillian Fennell[1], Sarah Tilley[2], Sayali Dhamne[3], Robert Edwards[4], Mary Gheller[3], Angelo Demalia[3], Margaret Clancy[3], Michael LaValley[5], Emelia J Benjamin[3] and Tuhina Neogi[6], [1]Boston University Medical, Boston, MA, [2]Boston University School of Medicine, Somerville, MA, [3]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, [4]Brigham and Women's Hospital & Harvard Medical School, Boston, MA, [5]Boston University School of Public Health, Arlington, MA, [6]Boston University School of Medicine, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Over a third of older Americans experience chronic pain, typically occupying multiple musculoskeletal body sites. While number of pain sites (NPS) is often touted as a stronger predictor of quality of life and physical functioning than pain location, studies identifying commonly co-occurring pain locations included younger individuals, whose pain location patterns likely vary from older adults with comorbid pain conditions and activity limitations. This study seeks to identify pain location patterns in older adults to elucidate the role of pain location on age-related pain burden.

Methods: We used data from a community-based sample of older adults from an ancillary study of the Framingham Heart Study/Omni1. We collected data on number and distribution of pain sites (articular, non-articular, and axial) on validated body and joint homunculi. We used an agnostic approach to identify patterns of pain locations. Specifically, we conducted a latent class analysis and used traditional model fit statistics (e.g., BIC, AIC, G2) to select the optimal number of classes. After identifying the optimal model, we examined mental and physical health-related quality of life (HRQoL), physical functioning, and pain interference by pain location pattern (i.e., class). For function, we assessed the Nagi functional impairment scale, Rosow-Breslau mobility scale, and Katz activities of daily living (ADLs) index; for pain interference, we used the Brief Pain Inventory, and for HRQOL, we used the mental and physical component scores from the Short Form-12.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Heatmap of Conditional Probabilities

	Class 1 MIN (53.2%) mean age: 76 54% female	Class 2 Hand (21.2%) mean age: 76 57% female	Class 3 JT/AX (12.8%) mean age: 76 58% female	Class 4 Predom LE (7.3%) mean age: 77 53% female	Class 5 Extensive (5.5%) mean age: 76 71% female
Head	0.05	0.1	0.12	0.09	0.34
Chest	0.01	0.02	0.03	0.03	0.1
Abdomen	0.02	0.02	0.03	0.06	0.19
Pelvis	0	0.01	0	0.02	0.19
Neck	0.06	0.18	0.23	0.09	0.57
Upper Back	0.02	0.09	0.11	0.06	0.26
Lower Back	0.21	0.38	0.55	0.38	0.77
Jaw	0	0.01	0.03	0	0.12
Right Upper arm	0.05	0.3	0.43	0.23	0.68
Left Upper arm	0.05	0.23	0.39	0.2	0.78
Right Forearm	0	0.03	0.05	0.03	0.39
Left Forearm	0.01	0.02	0.05	0.05	0.4
Right Hand	0.04	0.79	0.01	0.3	0.89
Left Hand	0.02	0.78	0.01	0.25	0.89
Right Knee	0.11	0.33	0.39	0.38	0.65
Left Knee	0.08	0.34	0.4	0.33	0.67
Right Upper leg	0.02	0.01	0.02	0.35	0.17
Left Upper leg	0.01	0	0.01	0.34	0.24
Right Lower leg	0.01	0.01	0	0.68	0.3
Left Lower leg	0.01	0.01	0	0.69	0.34
Right Foot	0.02	0.2	0.22	0.2	0.67
Left Foot	0.02	0.18	0.23	0.18	0.62
Right Hip/Groin/Buttock	0.05	0.17	0.41	0.35	0.69
Left Hip/Groin/Buttock	0.05	0.13	0.36	0.27	0.69

MIN = minimal pain sites; Hand = predominantly hand/wrist pain; JT/AX = multisite joint and axial pain; Predom LE = predominantly lower extremity pain; Extensive = extensive articular and non-articular multisite pain.

Class	Label	# of sites	≥ 1 Nagi limitation	≥ 1 Rosow-Breslau limitation	≥ 1 ADL limitation	Pain interference	PCS	MCS
1	MIN	0.9	37.1%	19.8%	1.5%	0.77	51.0	55.7
2	Hand	4.4	54.0%	24.9%	0.6%	1.65	46.9	54.9
3	JT/AX	4.4	59.7%	31.6%	3.4%	1.75	45.3	55.8
4	Predom LE	5.8	63.3%	29.1%	6.0%	2.47	44.6	54.7
5	Extensive	11.9	82.0%	48.3%	3.4%	3.66	38.4	53.5

MIN = minimal pain sites; Hand = predominantly hand/wrist pain; JT/AX = multisite joint and axial pain; Predom LE = predominantly lower extremity pain; Extensive = extensive articular and non-articular multisite pain

PCS = physical health-related quality of life; MCS = mental health-related quality of life; ADL = activities of daily living

PCS and **MCS** are T-scores centered on a mean of 50 and an SD of 10. Scores higher than 50 indicate better HRQoL.

Percentages under Nagi, ADL, and Rosow-Breslau are the % of people reporting 1 or more limitation. Participants were coded as having an ADL or Rosow-Breslau limitation if they were unable to do one or more of the below tasks without help from another person. Individuals were coded as having a Nagi limitation is they had "some difficulty," "a lot of difficulty," or were "unable to do" one or more of the tasks listed below.

ADLs include dressing, bathing, toileting, transferring, and eating

Rosow-Breslau: Heavy work around the house, walk 1/2 mile without help (if no, walk 1/4 without help), walk up and down 1 flight of stairs without help.

Nagi: pulling / pushing, stooping / crouching / kneeling, reaching / extending arms below shoulder, reaching / extending arms above shoulder, writing / handling small objects, standing for long periods, lifting / carrying under 10 lbs, lifting / carrying over 10 lbs

Pain interference is an averaged score of seven items on a 0 (no interference) to 10 (completely interferes) scale. Participants were asked how much their pain had interfered with their general activity, mood, walking ability, normal work, social relationships, sleep, and enjoyment of life in the past week. Higher scores indicate greater interference.

Results: We included 1610 participants (mean age, 76.1 ± 7.5 years; 56% Female). The model with 5 classes offered the best model fit. The 5 pain patterns identified in this model included: 1) minimal pain sites (MIN; 53.2%); 2. predominantly hand/wrist pain (Hand; 21.2%); 3. multisite joint and axial pain (JT/AX; 12.8%); 4. predominantly lower extremity pain (Predom LE; 7.3%); and 5. extensive articular and non-articular multisite pain (Extensive; 5.5%). All 5 classes reported some frequency of low back pain, ranging from 21% in the MIN class to 77% in the Extensive class with the Hand and Predom LE class reporting the same frequency (38%). The Extensive class reported the lowest (i.e., worst) HRQoL and physical functioning (Table 1), while the Predom LE class reported both the second-highest average NPS and the second-lowest scores on measures of function. Despite the Hand and JT/AX classes having similar NPS and pain interference scores, the JT/AX class reported worse physical HRQoL and functioning.

Conclusion: We identified pain location patterns with differential patterns of physical functioning, pain, and HRQoL. Overall, higher average NPS was associated with lower (worse) scores on measures of function and HRQoL, but JT/AX reported worse outcomes than the Hand class despite reporting the same mean NPS. Our data suggest that pain location contributes to pain burden beyond NPS. More specifically, lower extremity and/or lower back pain appears to contribute to poor physical HRQoL and functioning outcomes more so than predominantly hand pain.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Fennell: None; **S. Tilley**: None; **S. Dhamne**: None; **R. Edwards**: None; **M. Gheller**: None; **A. Demalia**: None; **M. Clancy**: None; **M. LaValley**: None; **E. Benjamin**: None; **T. Neogi**: None.

Abstract Number: 1231

TNX-102 SL, Cyclobenzaprine HCl Sublingual Tablets, Demonstrates Pain Reduction and Favorable Tolerability in Patients with Fibromyalgia

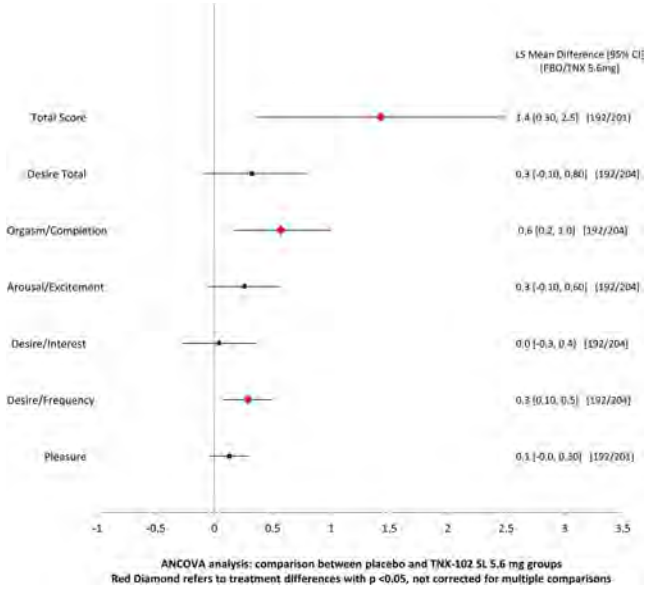
Gregory Sullivan[1], Errol Gould[2], Mary Kelley[1], Jean Engels[1] and Seth Lederman[3], [1]Tonix Pharmaceuticals, Inc., Chatham, NJ, [2]Tonix Pharmaceutical, Inc., Henderson, NV, [3]Tonix Pharmaceuticals, Inc., Austin, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: FDA-approved treatments for fibromyalgia (FM) have historically been limited by intolerable side effects that often lead to poor adherence. TNX-102 SL, a sublingual formulation of cyclobenzaprine, is under evaluation by the FDA as a treatment for FM. TNX-102 SL treatment has shown statistically significant reduction in pain in two Phase 3 studies, including the RESILIENT study reported below. In these studies, TNX-102 SL was generally well tolerated. The tolerability of TNX-102 SL may provide an appealing alternative to existing therapies.

Methods: The RESILIENT study was a 14-week, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of TNX-102 SL in patients with FM. The pre-specified primary endpoint was the change from baseline to Week 14 in the weekly average of daily pain numeric rating scale (NRS) scores, analyzed using a mixed model for repeated measures with multiple imputation for missing data. Exploratory secondary endpoints included assessments of tolerability, such as changes in sexual function (measured by CSFQ-14) and weight gain. Safety evaluations included changes in blood pressure and the incidence of adverse events (AEs).



Changes in Sexual Functioning Questionnaire Change from Baseline to Week 14 in Females

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: TNX-102 SL demonstrated significant improvement in the primary pain endpoint compared to placebo ($p < 0.0001$) at Week 14. Females treated with TNX-102 SL had significantly greater improvements in desire/frequency ($p = 0.010$), orgasm/completion ($p = 0.007$), and total sexual function scores ($p = 0.010$). No significant differences were observed between TNX-102 SL and placebo in weight, systolic, or diastolic blood pressure at Week 14. The most commonly reported AEs were mild to moderate, self-limited events such as transient tongue or mouth numbness and bitter aftertaste, which rarely led to study discontinuation. Systemic AE rates, excluding COVID-19, remained below 4.0%.

Conclusion: TNX-102 SL significantly reduced pain and showed a favorable tolerability profile, including minimal impact on weight and blood pressure, along with its unique mechanism targeting sleep disturbances, supports its potential as a new treatment option for FM. The availability of a well-tolerated treatment may also encourage clinicians to make the diagnosis of fibromyalgia earlier, thereby improving patient outcomes through timely intervention.

Disclosure: G. Sullivan: Tonix Pharmaceuticals, Inc., 3, 11; **E. Gould**: Tonix Pharmaceuticals, Inc., 3, 11; **M. Kelley**: Tonix Pharmaceuticals, Inc., 3, 11; **J. Engels**: Tonix Pharmaceuticals, Inc., 3, 11; **S. Lederman**: Tonix Pharmaceuticals, Inc., 3, 10, 11.

Abstract Number: 1232

Does Social Support Reduce Bodily Pain among African American Women with SLE?: Findings from a Randomized Controlled Trial

Jerik Leung[1], Tomika Caldwell[2], Paul Nietert[3], Clara Dismuke[4], Hetlena Johnson[5], Edith Williams[6] and Everette Keller[3], [1]Emory University, Rollins School of Public Health, Atlanta, GA, [2]Medical University of Souty Carolina, Charleston, [3]Medical University of South Carolina, Charleston, SC, [4]VA Palo Alto Health Care System, Menlo Park, [5]Lupus Community Advocate/Researcher, Columbia, SC, [6]University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Peer mentoring has been shown to be an effective intervention for chronic conditions with evidence to suggest that it might improve health related bodily pain among African American women living with systemic lupus erythematosus (SLE). However, there is a lack of evidence to describe the intervention impact when adjusting for self-management of SLE. The present work aims to determine whether greater patient activation is associated with greater reductions in pain overall and within interventions groups.

Methods: We used a randomized controlled trial (RCT) design with experimental and social support control arms to test the peer approaches to lupus support (PALS) intervention (ClinicalTrials.gov # NCT03734055). Participants were recruited through the Medical University South Carolina (MUSC) P30 Core Center for Clinical Research and have validated diagnosis of SLE according to ACR classification criteria. Mentees (n=274) were randomized to either experimental arm or control arms. Participants in the experimental arm were paired with a peer mentor and received the full intervention condition (twelve 60-minute sessions across 24 weeks) covering self-management topics including: goal setting, effective communication, body image, and sexuality/sexual health. Those randomized into the control arm participated in a support group following the same bi-weekly session schedule but did not receive the tailored materials through a peer mentor. We measured pain and patient activation using the Lupus Quality of Life Questionnaire and Patient Activation Measure (PAM) respectively. Linear mixed models and multivariable models were fit to assess the intervention and impact of PAM on each predictor over time, respectively.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Summary of Fixed Effects

Predictor	Estimate (95% CI)	Type III p-value
Intercept	9.841 (-3.791, 23.474)	0.156
Baseline LUP-QOL BP		
Baseline LUP-QOL BP (Intervention)	-0.283 (-0.4, -0.166)	< 0.001
Baseline LUP-QOL BP (Control)	-0.328 (-0.435, -0.222)	< 0.001
Treatment	-1.639 (-9.995, 6.717)	0.727
Visit		
Visit: Post (6-Months)	-1.176 (-4.749, 2.398)	0.879
Visit: 12-Months	-0.291 (-4.174, 3.592)	
Treatment*Visit		
Treatment*Visit: Intervention*Post (6-Months)	1.199 (-3.9, 6.298)	0.769
Treatment*Visit: Intervention*12-Months	-0.664 (-6.21, 4.88)	
PAM Score	-0.13 (-0.238, -0.021)	0.019
Age		
Age: < 25	Ref	0.688
Age: 25-34	5.89 (-1.939, 13.719)	
Age: 35-44	5.039 (-2.864, 12.941)	
Age: 45-54	6.685 (-1.625, 14.996)	
Age: 55-64	4.814 (-3.639, 13.267)	
Age: 65+	1.3 (-12.045, 14.644)	
Education		
Educ: < HS	Ref	0.324
Educ: HS Grad	5.404 (-2.827, 13.635)	
Educ: Some College	1.431 (-6.236, 9.098)	
Educ: College Grad	0.178 (-7.36, 7.715)	
Married (vs. Non-married)	-2.392 (-7.173, 2.39)	0.325
Insured (vs. Non-insured)	-1.497 (-10.037, 7.043)	0.73

Table 2: Summary of Changes in LUP-QOL Bodily Pain Measures of Time by PAM Measure

LUP-QOL Changes Over Time	Control	Intervention	Control vs. Intervention
PAM Score = 0			
Baseline to 3-Months	-1.269 (-6.98, 4.442); p = NS	-1.308 (-6.714, 4.098); p = NS	NS
Baseline to 6-Months	-2.445 (-8.453, 3.564); p = NS	-1.285 (-6.996, 4.426); p = NS	NS
Baseline to 12-Months	-1.56 (-7.809, 4.689); p = NS	-2.264 (-8.225, 3.697); p = NS	NS
PAM Score = 25			
Baseline to 3-Months	-4.51 (-10.959, 1.938); p = NS	-4.549 (-10.672, 1.573); p = NS	NS
Baseline to 6-Months	-5.686 (-12.281, 0.91); p = NS	-4.526 (-10.897, 1.846); p = NS	NS
Baseline to 12-Months	-4.801 (-11.642, 2.039); p = NS	-5.505 (-12.071, 1.061); p = NS	NS
PAM Score = 50			
Baseline to 3-Months	-7.751 (-15.827, 0.324); p = NS	-7.79 (-15.563, -0.018); p = 0.05	NS
Baseline to 6-Months	-8.927 (-17.024, -0.829); p = 0.031	-7.767 (-15.72, 0.186); p = NS	NS
Baseline to 12-Months	-8.042 (-16.361, 0.276); p = NS	-8.746 (-16.83, -0.662); p = 0.034	NS
PAM Score = 75			
Baseline to 3-Months	-10.993 (-21.168, -0.817); p = 0.034	-11.032 (-20.934, -1.13); p = 0.029	NS
Baseline to 6-Months	-12.168 (-22.284, -2.052); p = 0.018	-11.008 (-21.038, -0.979); p = 0.032	NS
Baseline to 12-Months	-11.284 (-21.594, -0.973); p = 0.032	-11.987 (-22.101, -1.873); p = 0.02	NS
PAM Score = 100			
Baseline to 3-Months	-14.234 (-26.747, -1.721); p = 0.026	-14.273 (-26.536, -2.01); p = 0.023	NS
Baseline to 6-Months	-15.409 (-27.811, -3.007); p = 0.015	-14.249 (-26.604, -1.895); p = 0.024	NS
Baseline to 12-Months	-14.525 (-27.099, -1.951); p = 0.024	-15.228 (-27.635, -2.822); p = 0.016	NS

Results: The demographic characteristics of participants between experimental and social support control arms were generally comparable across age, education, marriage status, and insurance status. Our analysis includes 274 participants, evenly split between experimental and social support control arms. We did not observe statistically significant differences in pain over the study period between experimental and control groups (Table 1). However, across both groups, greater PAM score was associated with decreased pain (b=-0.13, p=0.019) (Table 2).

Conclusion: Those with higher PAM have reduced bodily pain. Additional work is needed to further typologize the varieties of pain experienced by people living with SLE, in addition to understanding the role of social relations and support. Specifically, additional mechanistic work is needed to understand the role of patient activation and to identify potential mediators and moderators of social support and pain among people living with SLE.

Disclosure: J. Leung: None; **T. Caldwell**: None; **P. Nietert**: None; **C. Dismuke**: None; **H. Johnson**: None; **E. Williams**: None; **E. Keller**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1233

Synovial Joint Transcriptomic Differences in Individuals with Knee Osteoarthritis and Neuropathic Pain Symptomology

Joseph Lesnak[1], Michael Zuscik[2], Michael Dayton[2], Craig Hogan[2], Prabil Kaini[2], Andrew Clauw[3], Jennifer Seifert[4], Michael Clay[5], Theodore Price[1] and Larry Moreland[6], [1]University of Texas at Dallas, Dallas, [2]University of Colorado School of Medicine, Aurora, [3]Univ of Colorado, Aurora, CO, [4]University of Colorado and Oklahoma Medical Research Foundation, Aurora, CO, [5]University of Colorado, Aurora, CO, [6]University of Colorado, Denver, CO

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is a painful disease of the synovial joint and is the most common form of arthritis with a large global burden. A subset of individuals with knee OA complain of neuropathic type pain with symptomology of burning, paresthesia, and spontaneous pain in the affected joint. Since nociceptive and neuropathic pain components may require different treatment strategies, it is imperative to understand mechanisms underlying each symptomology. However, it is unknown how changes in the joint may be driving neuropathic like symptoms. Thus, we set out to compare transcriptomic data of synovial joint samples between individuals with and without neuropathic type pain undergoing joint replacement for knee OA.

Methods: A total of 35 individuals (10 males, 25 females) were enrolled who were diagnosed with knee OA by an orthopedic surgeon and undergoing total knee arthroplasty surgery. All individuals completed the painDETECT questionnaire prior to surgery to determine level of neuropathic pain symptomology. Synovial joint samples from the surgical knee were collected and frozen in pulverized dry ice. A painDETECT cutoff score of ≤12 was used to group individuals into low or moderate/high probability of neuropathic pain. RNA was extracted from tissues and bulk RNA sequencing was performed to compare transcriptomic differences between individuals with low (n=25, 8 males, 17 females) and moderate/high painDETECT scores (n=10, 2 males, 8 females). To determine differentially expressed genes (DEGs), the R package DESeq was used to compare differences between low and moderate/high painDETECT score, with sex run as a covariate (DEG: log2fc >0.585, adjusted p-value < 0.1). To make predictions surrounding synovial joint to nociceptor signaling, a ligand receptor interactome was used to intersect upregulated DEG's encoding for ligands with their known receptors on human nociceptive neurons.

Results: A total of 121 DEGs were identified with 115 upregulated and 6 downregulated. Gene pathway assessment of the upregulated genes revealed enrichment of genes responsible for neutrophil degranulation and extracellular matrix organization. The ligand receptor interactome revealed potential interactions between 5 ligands and 24 receptors on human nociceptive neurons. This included interactions with neurotrophic factors such as L1CAM, CBLN4, and NRXN3. These neurotrophic factors bind to several receptors on neurons which have been shown to drive increased nerve growth including DCC, EGFR, and NEO1.

Conclusion: We found a set of upregulated genes specific to individuals with knee OA who complain of neuropathic like pain. These genes revealed potential enhancement of neutrophil degranulation and increased neurite growth in individuals with neuropathic symptoms. Future work will look to validate these targets using cultured human dorsal root ganglion neurons.

Disclosure: J. Lesnak: None; **M. Zuscik**: None; **M. Dayton**: None; **C. Hogan**: None; **P. Kaini**: None; **A. Clauw**: None; **J. Seifert**: None; **M. Clay**: None; **T. Price**: None; **L. Moreland**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1234

Serum Antibodies Against Glial Fibrillary Acidic Protein in Fibromyalgia: A Proof-of-Concept Study

Felipe Massó[1], **Laura Aline Martinez-Martinez**[2], Luis M Amezcua-Guerra[3], Francisco Mercado[4], Angélica Almanza[5] and Manuel Martínez-Lavín[1], [1]Instituto Nacional de Cardiologia Ignacio Chavez, Mexico city, Mexico, [2]Rheumatology Department at National Institute of Cardiology Ignacio Chávez, Mexico City, Federal District, Mexico, [3]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico city, [4]Instituto Nacional de Psiquiatría Ramón del la Fuente Muñiz, Mexico city, Mexico, [5]Instituto Nacional de Psiquiatría Ramón de la Fuente Muñiz, Mexico city, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia (FM) is a stress-related disorder in which dorsal root ganglia (DRG) may play a pivotal pathogenetic role. DRG exhibit unique stress-induced, pro-algesic physio-anatomy, where each pain-sensing nerve fiber soma is tightly encased by metabolically active, immune-competent satellite glial cells (SGCs). Mice receiving IgG from patients with FM display mechanical and cold hypersensitivity and small nerve fiber pathology, in these instances patients IgG is exclusively deposited in mouse DRG SGCs. A subgroup of patients suffering from severe FM harbors anti-SGCs antibodies, although the specific antibody target(s) remain unidentified.

Glial fibrillary acidic protein (GFAP) is an intermediate filament protein serving as an early SGCs activation marker. Different environmental stressors induce GFAP cell-surface expression that could conceivably serve as novel antigen. GFAP antibodies have been implicated in autoimmune encephalomyelitis.

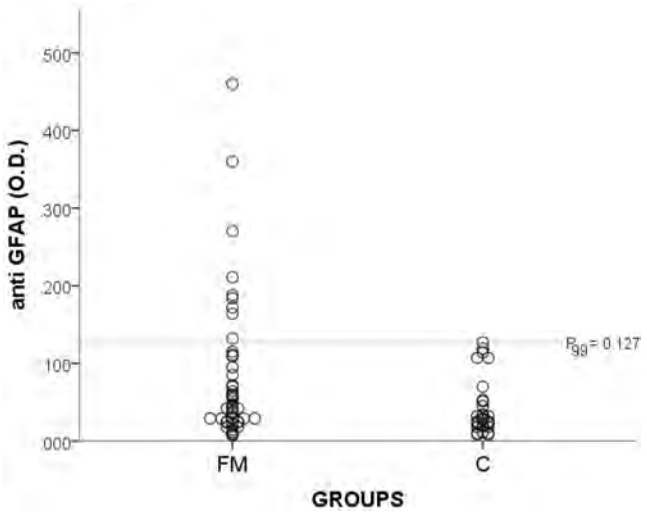
This proof-of-concept study aimed to determine whether the serum of patients suffering from FM contains antibodies against GFAP.

Methods: We included 47 women with "primary" FM (meeting ACR 2010 and Wolfe et al 2016 criteria) without concurrent autoimmune rheumatic disease and 31 age-, sex-, and BMI-matched healthy controls. All participants completed the following standardized clinimetric questionnaires: 2016 Wolfe et al criteria, FIQ-R, COMPASS-31, Small Fiber Symptom Survey, S-LANSS, PHQ-9, GAD-7, IPAQ, and EuroQol-5D.

A sensitive ELISA was developed using recombinant human GFAP (Abcam, Waltham, MA, USA) coated on 96-well plates. Serum samples were incubated overnight, followed by detection with HRP-conjugated anti-human IgG. Each plate included a positive control (commercial anti-GFAP antibody).

Results: Patients with FM exhibited higher GFAP antibody optical densities (OD) compared to controls (median 0.04, 0.02–0.10 vs. 0.02, 0.01–0.05; p = 0.025). Using the controls 99th percentile value (0.127 OD) as cut-off point, 9/47 (19%) of patients suffering from FM tested positive for anti-GFAP antibodies (figure 1). This antibody positivity ratio yields a sensitivity of 19%, specificity of 97%, positive predictive value of 90%, and negative predictive value of 44%. No significant differences in clinimetric scores were observed between GFAP-positive versus GFAP-negative patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



ELISA detection of GFAP antibodies in patients suffering from fibromyalgia (FM) and controls (C) using the controls 99th percentile as threshold for antibody positivity.

Conclusion: A subset of patients suffering from FM harbors serum antibodies against GFAP. Whether these antibodies are more prevalent in cerebrospinal fluid of individuals with FM, as seen in GFAP-associated autoimmune encephalomyelitis, remains to be determined. These early findings suggest that abnormal GFAP expression may play a role in the pathogenesis of FM, warranting further investigation of FM as satellite gliopathy.

Disclosure: F. Massó: None; **L. Martinez-Martinez**: None; **L. Amezcua-Guerra**: None; **F. Mercado**: None; **A. Almanza**: None; **M. Martínez-Lavín**: None.

Abstract Number: 1235

Demystifying Pain in patients with Lupus: How much is it Lupus and How much is it Other Stuff?

Meenakshi Jolly, Rush University, Chicago

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pain in patients with Systemic Lupus Erythematosus (SLE) is not well understood. There is role of active disease in pain (e.g. arthritis, serositis) also referred as Type I symptoms. Other factors e.g. coexistent fibromyalgia (FM), Stress, Fatigue, Sleep and Depression (Type 2 symptoms) may contribute towards pain.

We undertook analyses of data on patients with SLE to better understand Pain using three different measures of Pain. We focused specifically on contribution/s of disease activity, FM, Sleep, Stress, Depression and Fatigue.

Methods: Cross-sectional Data from 122 SLE patients meeting the 1997 ACR classification criteria were analyzed. Pain was measured using Brief Pain Inventory (BPI), SF-36 Bodily Pain (BP) and LupusPRO Pain domain. Disease activity and Flare were measured using SELENA-SLEDAI and SFI. Tools to measure Sleep, Fatigue, Stress, Depression were the Insomnia Severity Index, FACIT-FT, Perceived Stress Scale-PSS and Patient Health Questionnaire-9/PHQ9. FM status was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Univariate Analysis for Pain as the Dependent Variable

Univariate Analysis	BPI (Hi=Worse) Brief Pain	SF-36 BP (Hi=Better) Bodily Pain	LupusPRO-PN (Hi=Better) Pain
N=122	β, 95% CI, p value, R^2	β, 95% CI, p value, R^2	β, 95% CI, p value, R^2
Disease Activity (Total SLEDAI)	0.77, 0.23 to 1.30, 0.005, 0.06	-1.80, -2.87 to -0.73, 0.001, 0.09	-1.26, -2.52 to 0.007, 0.05, 0.03
SLEDAI-Arthritis	13.66, 7.38 to 19.93, <0.001, 0.14	-27.29, -39.91 to -14.67, <0.001, 0.14	-18.88, -33.97 to -3.79, 0.015, 0.05
SFI-Flare	7.82, 1.31 to 14.34, 0.019, 0.09	-14.78, -28.96 to -0.59, 0.04, 0.07	-17.03, -32.25 to -1.81, 0.029, 0.06
Sleep (Insomnia Severity Scale)	0.73, 0.46 to 1.00, <0.001, 0.20	-1.46, -2.01 to -0.91, <0.001, 0.20	-1.69, -2.30 to -1.07, <0.001, 0.21
Stress (Perceived Stress Scale)	1.04, 0.41 to 1.67, 0.001, 0.08	-2.41, -3.67 to -1.15, <0.001, 0.11	-3.19, -4.60 to -1.79, <0.001, 0.15
Fatigue (FACIT-FT)	0.53, 0.38 to 0.68, <0.001, 0.29	-1.20, -1.50 to -0.90, <0.001, 0.36	-1.64, -1.92 to -1.35, <0.001, 0.54
Depression (Patient Health Questionnaire-9)	0.94, 0.61 to 1.27, <0.001, 0.21	-1.90, -2.57 to -1.23, <0.001, 0.22	-2.72, -3.39 to -2.05, <0.001, 0.37
Fibromyalgia Diagnosis	8.40, 2.48 to 14.32, 0.006, 0.06	-11.75, -23.86 to 0.36, 0.06, 0.03	-18.46, -32.40 to -4.52, 0.01, 0.06
Total Tender Points-Self Reported	13.95, 5.37 to 22.53, 0.002, 0.08	-31.86, -48.88 to -14.84, <0.001, 0.11	-37.17, -56.52 to -17.83, <0.001, 0.11

Table 2: Multivariate and Stepwise Regression Models for Pain

		Multivariate Analyses	BPI (Hi=Worse) Brief Pain Inventory	SF-36 BP (Hi=Better) Bodily Pain	LupusPRO-PN (Hi=Better) Pain
		N=122	β, 95% CI, p value, R^2	β, 95% CI, p value, R^2	β, 95% CI, p value, R^2
Model 1		Disease Activity (Total SLEDAI)	**0.66, 0.14 to 1.22, 0.02** R^2 0.07	**-1.56, -2.89 to -0.24, 0.022** R^2 0.05	**-1.50, -2.64 to -0.32, 0.01** R^2 0.10
		SLEDAI-Arthritis	5.21, -1.83 to 12.47, 0.14	-6.85, -23.03 to 9.34, 0.40	-2.67, -19.35 to 12.03, 0.71
		SFI-Flare	0.34, -1.72 to 6.41, 0.19	-6.21, -19.77 to 6.15, 0.31	-5.43, -19.77 to 5.91, 0.34
		Sleep Insomnia Severity Scale	**0.67, 0.24 to 1.1, 0.003**	-0.86, -2.33 to 0.12, 0.078	-0.45, -1.43 to 0.59, 0.54
		Stress (Perceived Stress Scale)	0.15, -1.04 to 0.36, 0.36	-0.52, -2.26 to 0.22, 0.55	-0.18, -1.74 to 1.36, 0.82
		Fatigue (FACIT-FT)	0.12, -0.10 to 0.41, 0.26	-0.37, -0.28 to 0.12, 0.08	**-0.87, -1.50 to -0.24, 0.008**
		Depression (Patient Health Questionnaire-9)	0.48, -0.10 to 0.95, 0.11	-0.53, -1.84 to 0.80, 0.45	**-1.34, -2.56 to -0.11, 0.03**
Model 2	Model 1 + FM	Disease Activity (Total SLEDAI)	0.67, 0.13 to 1.20, 0.14 R^2 0.03	**-1.57, -2.91 to -0.23, 0.02** R^2 0.05	**-1.50, -2.64 to -0.32, 0.01** R^2 0.10
		SLEDAI-Arthritis	5.54, -1.83 to 12.79, 0.13	-6.11, -23.71 to 11.50, 0.49	-2.67, -19.35 to 12.03, 0.71
		SFI-Flare	0.69, -1.27 to 6.65, 0.14	-5.95, -19.43 to 7.11, 0.36	-5.43, -19.77 to 5.91, 0.34
		Sleep Insomnia Severity Scale	**0.69, 0.26 to 1.12, 0.002**	-0.86, -2.33 to 0.56, 0.06	-0.45, -1.43 to 0.59, 0.54
		Stress (Perceived Stress Scale)	0.15, -1.04 to 0.37, 0.26	-0.52, -2.26 to 0.22, 0.55	-0.18, -1.74 to 1.36, 0.82
		Fatigue (FACIT-FT)	0.08, -0.21, 0.37, 0.56	-0.42, -1.35 to 0.50, 0.09	**-0.87, -1.50 to -0.23, 0.008**
		Depression (Patient Health Questionnaire-9)	0.47, -0.12, 0.93, 0.12	-0.59, -1.96 to 0.87, 0.44	**-1.34, -2.56 to -0.11, 0.03**
		Fibromyalgia Diagnosis	4.38, -0.47 to 12.56, 0.27	-5.08, -12.98 to 2.84, 0.59	-0.81, -10.65 to 17.87, 0.64
Model 3	Model 2 in Stepwise Regression		Sleep Insomnia Severity Scale(+), 0.68, 0.25 to 1.10, 0.005 R^2 0.09	Sleep Insomnia Severity Scale(+) -1.34, -2.20 to -0.47, 0.003 R^2 0.06	Fatigue (FACIT-FT) -0.98, -1.55 to -0.41, <0.001 R^2 0.08
			Disease Activity (Total SLEDAI) 0.77, 0.25 to 1.30, 0.005	Disease Activity (Total SLEDAI) -1.02, -2.10 to -0.71, 0.002	Disease Activity (Total SLEDAI) 1.91, 2.69 to -0.86, <0.001
			SLEDAI-Arthritis 9.50, -0.17 to 13.17, 0.06	Fatigue (FACIT-FT) -0.80, -1.40 to -0.41, 0.008	Depression (Patient Health Questionnaire-9) -1.58, -2.56 to -0.60, 0.002
			Depression (Patient Health Questionnaire-9) 0.43, 0.36 to 1.37, 0.003		

determined by chart review and patient reported tender point count. We conducted univariate regression analyses with Pain as the dependent variable and others as independent variables. We next undertook multivariate analyses of significant variables from the univariate analysis (Model 1), with FM (Model 2), and stepwise regression analysis (Model 3). We show chart-based FM results below. Results were similar for tender point counts.

Results: 90% were women; 51% Black, 23% White, 12% Hispanic and 9% Asian. Mean age was 40.7 (13.5) yrs, with Mean (SD) SLEDAI 5.03 (4.0) and SDI 0.61 (0.96). Mean Disease duration was 8.6 (7.2) years. 33% had SFI flare, and 63% were on steroids. 16% had FM. There was a good correlation between the three pain measures (r >0.65). Mean (SD) BPI, BP and PRO-Pain were 11.98 (12.29), 58.71 (24.7) and 69.80 (28.16).

Disease activity (including SLEDAI-arthritis and SFI), Sleep, Stress, Fatigue, Depression and Fibromyalgia were associated with Pain (Table 1) on univariate analysis. On multivariate analysis (Table 2) disease activity, sleep, fatigue and depression were associated with Pain after adjusting for all other variables (R^2 60-70%) %, and the associations were not changed significantly by adding FM to the model. On Stepwise Regression, 3-4 variables explained 56-68% of variance in Pain (Table 2), with disease activity being associated in all the three measures of Pain. In addition, sleep, depression and fatigue were associated with Pain, but not FM or stress.

Conclusion: Pain in SLE is associated with active disease. Latter, along with sleep, fatigue and depression explains more than half of the pain in SLE, indicating that besides controlling disease activity, there may be a role for Biopsychosocial model of care in improving pain in SLE. These models report association and not causation. Longitudinal study models will be tested next.

Disclosure: M. Jolly: LRA, 1, Rush University, 9, 10.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1236

Vestibulocortical Stimulation via Caloric Irrigation in Nociplastic Disease: Therapeutic Effects on Pain, Autonomic Functioning & Quality of Life Measures

Michael Kaplan[1], Alexandra Canori[2], Rebecca Howard[2], Talia Torkian[3], Rebecca Pietro[1], Gabriela Santiago-Pichardo[1], Daniel Clauw[4], David Putrino[2], Yousaf Ali[1], Laura Tabacof[2] and Trung Ngo[5], [1]Division of Rheumatology, Mount Sinai Hospital, New York, [2]Department of Rehabilitation and Human Performance, Icahn School of Medicine at Mount Sinai, New York, [3]Division of Rheumatology, Icahn School of Medicine at Mount sinai, New York, [4]Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI, [5]RECOVER Injury Research Centre, The University of Queensland and Surgical, Treatment & Rehabilitation Service (STARS), Queensland, Australia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia (FM) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) are prototypical nociplastic disorders marked by centralized pain & fatigue, respectively. Nociplastic symptoms — such as fatigue, psychological distress & dysautonomia — commonly complicate rheumatologic diseases and remain difficult to treat, thus highlighting the need for safe, effective & affordable therapies. Vestibulocortical stimulation (VCS) via caloric irrigation is a

FIGURE 1

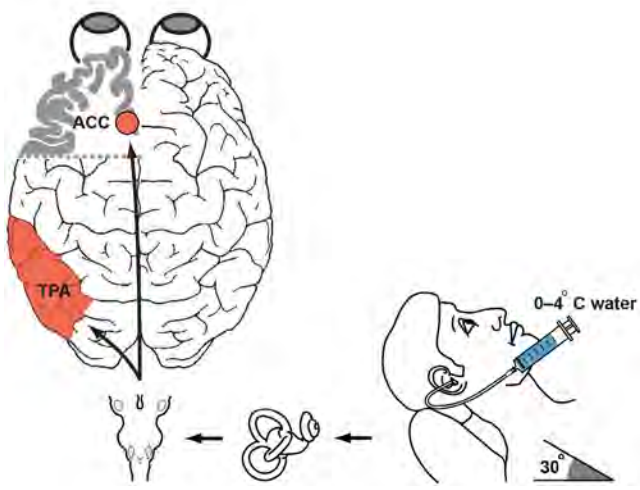


Figure 1: VCS with Caloric Irrigation — From Neurodiagnostic Technique to Therapeutic Neuromodulation Modality. The caloric test — via the vestibulo-ocular reflex — is a simple, low-cost, low-risk, non-invasive and widely used mainstream neurodiagnostic technique for balance problems & brain death, with a long-standing record of safety since its development over a century ago. The technique is routinely performed for example in primary care clinics by family doctors & nurses (for cerumen removal), audiologists, neurologists & ENT physicians. VCS involves irrigation of the external ear canal with warm/cold water (e.g., 1–4° C) while the head is reclined at 30° to the horizontal until nystagmus is observed and vertigo is reported — typically within a few seconds — via stimulation of semicircular canals & brainstem circuits (indicated by the black horizontal arrows). Over recent decades, several brain-imaging studies have shown that cold-water VCS also consistently activates an endogenous highly conserved (>230 million years old) restorative-function network (Ngo & Kaplan, 2023) of predominantly contralateral structures including the anterior cingulate cortex (ACC), temporo-parietal areas (TPA; e.g., temporoparietal junction, superior temporal gyrus, inferior parietal lobe), middle frontal gyrus, insular cortex, thalamus & putamen (in basal ganglia). Correspondingly, the technique's wide-ranging multimodal effects across mood, pain, cognition, attention, perception, beliefs/insight & mobility have been highlighted by remarkable therapeutic benefits shown in adults with often disabling refractory conditions such as nociplastic pain syndromes (e.g., phantom limb & post-stroke thalamic pain, migraine, CRPS/allodynia, spinal cord injury pain, refractory FM — Kaplan et al., 2024); other neurological disorders (e.g., Parkinson's disease, minimally conscious state); and psychiatric illness (e.g., bipolar & schizophrenia spectrum disorders).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

non-invasive neuromodulation technique that has demonstrated rapid analgesic effects in treatment-resistant nociplastic pain (Figure 1).[1] This study aimed to replicate recent findings of VCS-induced analgesia in FM[2] and assess its broader impact on quality of life to inform the design of randomized placebo-controlled trials.

Methods: We conducted a non-randomized open-label effectiveness trial in 39 patients with nociplastic pain & fatigue (mean age = 40.2; 87% female). Twenty-three patients met criteria for ME/CFS (2015 IOM criteria) and 16 met criteria for FM (2011 ACR criteria) +/- ME/CFS. Each participant completed validated electronic patient-reported outcomes at baseline, prior to receiving a single treatment of unilateral right-ear cold-water (4°C) irrigation at 1-2 cc/second. Pain & quality of life measures were reassessed at post-intervention 30 minutes, 1 day, 1 week, 2 weeks & 4 weeks.

Figure 2

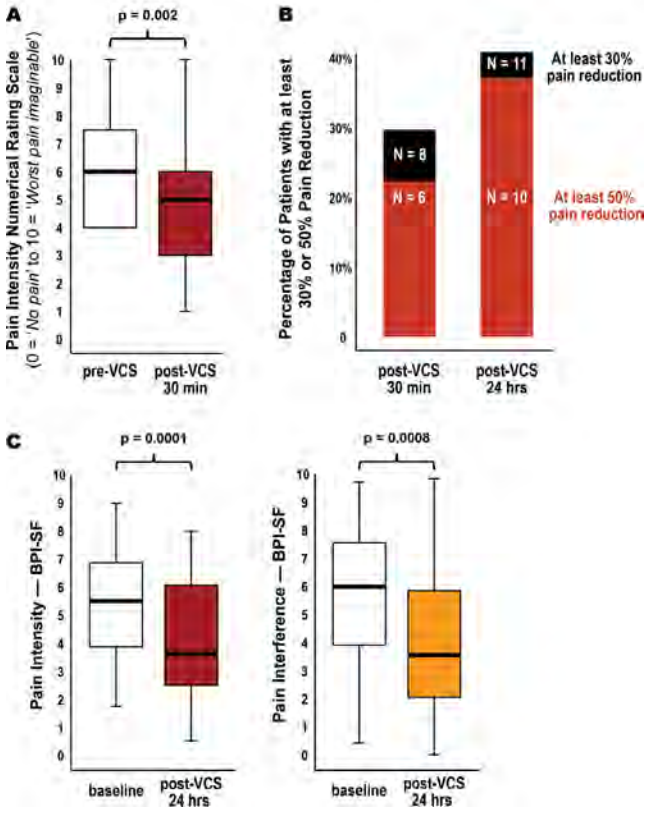


Figure 2. VCS Effects on Pain Measures & Percentage of Participants. (A) Immediate Reduction in Pain Intensity after VCS. The box plot shows the distribution of pain intensity NRS ratings before (pre) and 30 minutes after (post) VCS where 0 = No pain and 10 = Worst pain imaginable. This analysis included participants who experienced at least a 4/10 pre-intervention NRS pain score (N=27). A baseline level of at least 4/10 pain is the standard pain threshold used for inclusion in FM clinical trials. Pain scores were significantly reduced at 30 minutes following the procedure (t = -3.46, p = 0.002). P value is from a paired t-test of pre- and post-VCS pain scores. The bold horizontal bar in each box plot indicates the group's mean pain intensity rating. (B) Percentage of Participants with at least a 30% or 50% Improvement at 30 minutes and 24 hours after VCS. At 30min post-treatment, pain scores decreased by at least 30% in 8 (30%) participants and by at least 50% in 6 (22%) participants. Twenty-four hours after VCS, 11 participants (41%) experienced at least 30% decrease in pain and 10 participants (37%) experienced at least 50% decrease in pain. This analysis included participants who experienced at least a 4/10 pre-intervention NRS pain score (n = 27). The decision to exclude participants with less than 4/10 pain from this analysis was made post-hoc to avoid skewing percentages from participants with baseline scores of 2/10 pain, in which a one-point reduction on the pain scale represented a 50% decrease in pain. (C) Reduction in pain intensity & pain interference (BPI-SF) 24 hours after VCS treatment. The box plots show distribution of BPI-SF pain intensity and pain interference scores for all study participants (n = 39). Paired t tests showed a significant reduction in pain intensity (t = -4.36, p = 0.0008) and pain interference scores (t = -3.67, p = 0.0001). The bold horizontal bar in each box plot indicates the respective group's mean pain intensity & mean pain interference ratings.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

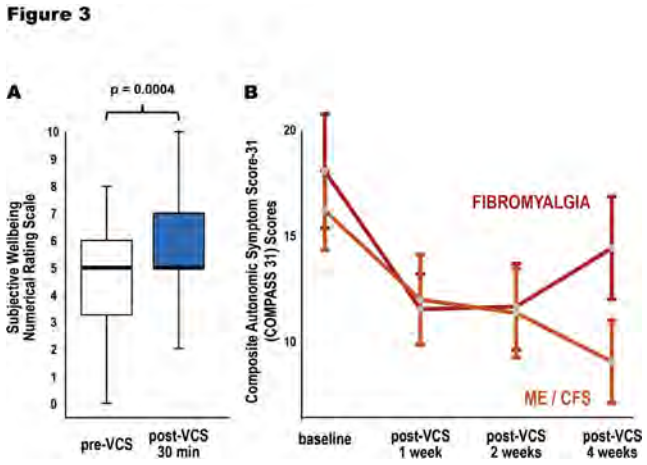


Figure 3. VCS Effects on Subjective Well-being & Autonomic Functioning (A) Immediate Improvement in Subjective Well-Being after VCS. The box plots show the distribution of subjective well-being NRS ratings (0 = lowest quality of life; 10 = best quality of life imaginable) of all study participants (n = 39) before (pre) and 30 minutes after (post) VCS. Overall well-being ratings significantly improved post-procedure (t = 3.89, p <0.001). P value is from paired t-test of pre- & post-VCS ratings. (B) Autonomic Distress Improves for 1 to 4 weeks after VCS. The Composite Autonomic Symptom Score-31 (COMPASS-31) is a validated self-assessment tool used to evaluate the extent of distress secondary to autonomic symptoms. A repeated-measures ANOVA showed COMPASS 31 scores significantly improved over time (p <0.001). Post-hoc comparisons using paired t-tests with Bonferroni correction revealed significant changes in the ME/CFS group (orange line) between baseline and all follow-up timepoints (1 week — t = -3.39, p.adj = 0.016; 2 weeks — t = -3.33, p.adj = 0.019; 4 weeks — t = -3.61, p.adj = 0.019). In the FM group (red line), significant effects were found between baseline and 1 week (t = -3.29, p.adj = 0.049). Beyond one-week post-intervention in the FM group, incomplete data limited our ability to assess the durability of these effects. Nevertheless, the current trial is the first study to demonstrate preliminary findings of VCS therapeutic effects on these autonomic functioning outcome measures in any clinical cohort. All study participants (N=39) were included in analysis.

Results: Regarding pain, 27 of 39 participants reported significant baseline pain intensity (≥4/10). At 30 minutes post-VCS, it significantly decreased (t(26) = -3.46, p = 0.002; Figure 2A) with 30% reporting ≥30% relief and 22% reporting ≥50% relief. At 24 hours post-VCS, 41% achieved ≥30% pain reduction and 37% reported ≥50% improvement (Figure 2B), with significant reductions also found in pain intensity (t(35) = -4.36, p < 0.001) and pain interference (t(35) = -3.67, p < 0.001; Figure 2C). Beyond 24 hours, no significant changes were observed as the study was underpowered to detect effects beyond that timeframe.

Subjective well-being scores increased significantly post-VCS (t(37) = 3.89, p < 0.001; Figure 3A) and autonomic symptom burden (COMPASS-31) decreased over time (F(3,60) = 7.998, p < 0.001; Figure 3B). PROMIS-29 domains showed sustained improvements in anxiety & social role participation at 1, 2, and 4 weeks post-intervention. Fatigue levels remained unchanged and no major adverse events occurred. VCS was safe & well tolerated, with 86.1% of participants reporting a willingness to have the procedure repeated if it reduced pain by half for one week.

Conclusion: These findings provide further open-label trial evidence that VCS offers meaningful relief in nociplastic pain. This study is also the first to show proof-of-concept improvements in autonomic symptoms & quality of life following VCS in nociplastic disease. Large randomized placebo-controlled trials are needed to validate & further advance this simple, bedside procedure into therapeutic standard of care for millions of patients globally suffering with refractory rheumatologic & nociplastic disease.

REFERENCES

1. Ngô T & Kaplan M. Australian Association of Musculoskeletal Medicine (AAMM) conference, 2023.
2. Kaplan M et. al. Pain Med, 2024.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Kaplan: Johnson & Johnson, 1, UpToDate, 9; **A. Canori**: None; **R. Howard**: None; **T. Torkian**: None; **R. Pietro**: None; **G. Santiago-Pichardo**: None; **D. Clauw**: Tonix, 2, 5; **D. Putrino**: BeCareLink, LLC, 4, Precision Recovery, Inc, 4, 8; **Y. Ali**: None; **L. Tabacof**: None; **T. Ngo**: None.

Abstract Number: 1237

Six Month Clinical Outcomes of a Digital Therapeutic Augmented Virtual Care Clinic for Fibromyalgia Management

Michael Rosenbluth[1], Yifei Dai[1], Dianne Shumay[1] and Andrea Chadwick[2], [1]Swing Therapeutics, San Francisco, CA, [2]University of Kansas School of Medicine, Kansas City, KS

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Guidelines for fibromyalgia treatment recommend non-pharmacologic treatment, including cognitive behavioral therapy, alongside medications [1-3]. However, patient access to multi-modal treatment is frequently limited due to a lack of clinics offering integrated care. Early results from a virtual specialty clinic (Swing Care), augmented by an FDA-cleared digital behavioral therapy (Stanza™), have demonstrated significant improvements at 90 days [4]. The purpose of this analysis is to evaluate six-month outcomes of a digital therapeutic augmented virtual specialty clinic for FM.

Methods: A chart review was conducted with IRB approval and consent waiver (Allendale IRB, Old Lyme, CT). FM patients assessed using the 2016 diagnostic criteria received multimodal treatment, combining non-opioid drug and non-drug therapies, including the option of the digital behavioral therapy. Endpoints collected included Patient Global Impression of Change (PGIC), Fibromyalgia Impact Questionnaire-Revised (FIQ-R), Pain Intensity, and Pain Interference (0-10 Likert Scales). Data were collected at baseline, 2, 4, and 6 months. All patients with at least six-month follow-up data were included in analysis.

Table 1. Cohort characteristics, clinical baseline, and outcomes at 6 months.

Cohort			
Female, n (%)	225 (96.6%)		
Age, median (range)	50.0 (22 – 80)		
Clinical Measures	**Baseline**	**Month 6**	***P***
N	233	233	-
FIQ-R, mean (SE)			
Total Score	63.6 (1.2)	48.7 (1.3)	*<.0001*
Function Domain	17.3 (0.4)	13.8 (0.5)	*<.0001*
Impact Domain	13.5 (0.3)	8.6 (0.4)	*<.0001*
Symptoms Domain	32.7 (0.5)	26.3 (0.6)	*<.0001*
Pain (0-best to 10-worst outcome), mean (SE)			
Intensity	6.9 (0.1)	5.4 (0.2)	*<.0001*
Interference	7.3 (0.1)	5.3 (0.2)	*<.0001*

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. PGIC response rate over time (% participants).

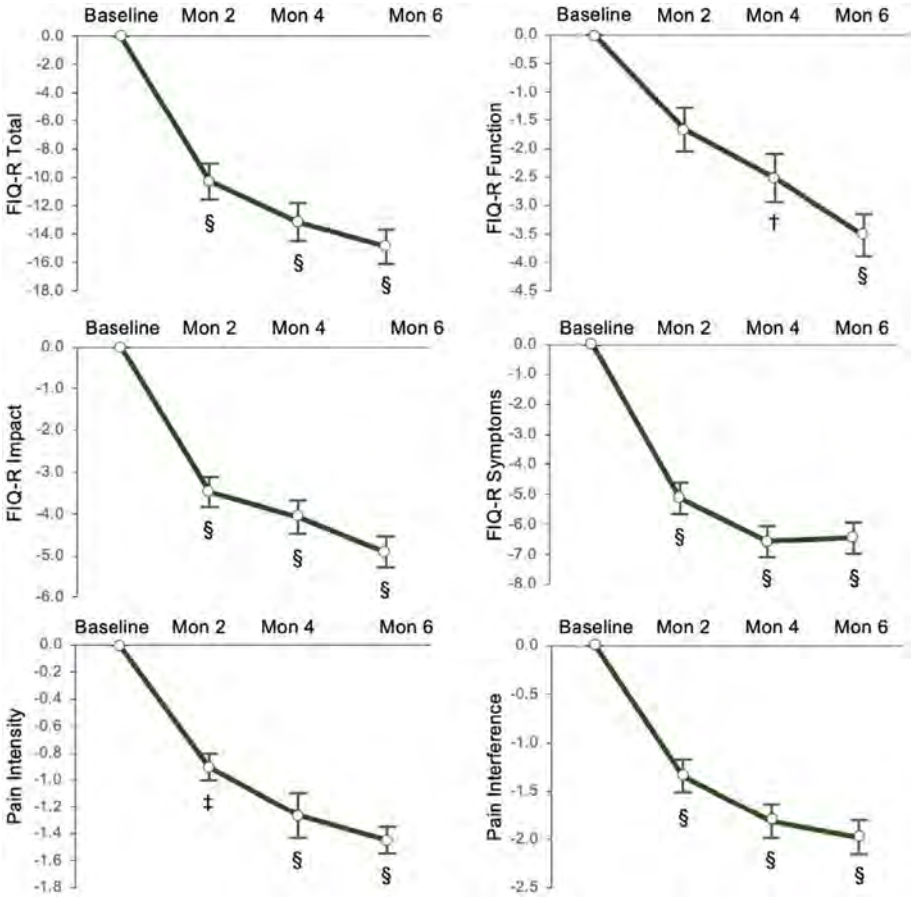


Figure 2. Changes from baseline on the clinical measures. Error bars = one SE. † $p < 0.0100$, ‡ $p < 0.0010$, § $p < 0.0001$.

Results: Outcomes data were available for 233 patients (Table 1). Baseline FIQ-R total score was 63.6 ± 1.2 [mean ± SE] while baseline pain intensity and pain interference scores were 6.9 ± 0.1 and 7.3 ± 0.1 [mean ± SE], respectively (Table 1). At 2 months, 75.5% of patients reported improvement, with 35.4% much improved or better. At 6 months, 88.0% of patients reported improvement, with 55.4% much improved or better (Figure 1). Average FIQ-R total score was significantly reduced at 6 months (by 14.9 ± 1.1 [mean ± SE] points, $p< 0.0001$), with significant improvements starting at 2 months (Figure 2). Significant improvements were also observed in FIQ-R Function, Impact, and Symptom domains ($p< 0.0001$). By six months, pain intensity and pain interference scores were significantly reduced by 1.5 ± 0.1 and 2.0 ± 0.2 [mean ± SE] points, respectively, p values < 0.0001.

Conclusion: Sustained improvements in well-being and reductions in FM severity, pain intensity, and pain interference were demonstrated at the virtual care clinic. These findings highlight the effectiveness of the multidisciplinary approach and the potential of the virtual care clinic as a patient-centered and accessible solution for managing FM.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

[1] Buckhardt CS et al. Guideline for the management of fibromyalgia syndrome pain in adults and children. Glenview Am Pain Soc (APS); (Clinical Pract Guidel no 4). 2005;4:109.
[2] Winslow BT, et al. Fibromyalgia: diagnosis and management. Am Fam Physician. 2023;107(2):137-144.
[3] Fitzcharles MA, et al. 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary. Pain Res Manag. 2013;18(3):119-126.
[4] Shumay D, et al. Society of Behavioral Medicine (SBM) 2024 Annual Meeting.

Disclosure: M. Rosenbluth: Swing Therapeutics, 12,, 3, 4, 8, 10, 11; **Y. Dai**: Swing Therapeutics, 2, 11; **D. Shumay**: Swing Care Provider Group, 3, Swing Therapeutics, 3, 11; **A. Chadwick**: Scilex Pharmaceuticals, 2, Swing Care Provider Group, 4, 8, Swing Therapeutics, 7, 11, Tonix Pharmaceuticals, 2.

Abstract Number: 1238

Pain Is Associated with An Increased Risk of Frailty in Veterans with Rheumatoid Arthritis

Nadine El-ayache[1], Sayuli Bhide[2], Hannah Brubeck[3], Punyasha Roul[4], Bryant England[5], Joshua Baker[6], Grant Cannon[7], Namrata Singh[8], Gary Kunkel[9], Ted Mikuls[5], Patti Katz[10], Dolores Shoback[11], Jose Garcia[12], Pradeep Suri[13], Marianna Gasperi[13], Ariela Orkaby[14], Una Makris[15] and Katherine Wysham[16], [1]VA Puget Sound Health Care System & University of Washington, Seattle, WA, [2]University of Washington, Seattle, WA, [3]VA Puget Sound Health Care System, Seattle, WA, [4]UNMC, Omaha, NE, [5]University of Nebraska Medical Center, Omaha, NE, [6]University of Pennsylvania, Philadelphia, PA, [7]University of Utah and Salt Lake City VA, Salt Lake City, UT, [8]University of Washington, Bellevue, WA, [9]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [10]UCSF, San Rafael, CA, [11]San Francisco VA Medical Center & University of California San Francisco, San Francisco, CA, [12]VA Puget Sound Health Care System, VA GRECC, and University of Washington, Seattle, WA, [13]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, [14]VA Boston Healthcare System & Division of Aging, Brigham and Women's Hospital, Harvard Medical School & VA Geriatrics Research Education and Clinical Center, Boston, MA, [15]UT Southwestern Medical Center and Dallas VA, Dallas, TX, [16]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Frailty, an increased vulnerability to stressors, is commonly associated with aging and functional decline. Pain, prevalent among older adults, contributes to frailty in the general population. Specifically, it has been shown that pain contributes to frailty by increasing exhaustion and decreasing physical activity. Individuals with RA are more likely to experience both higher levels of pain and frailty. However, research evaluating the relationship within the RA population is limited. We examined the relationship between pain and the risk of frailty in RA.

Methods: Data were from the Veterans Affairs Rheumatoid Arthritis (VARA) registry, a multicenter prospective cohort of US Veterans with RA. Pain was assessed by self-report (range 0-10). Frailty was evaluated using the Veterans Affairs Frailty Index (VA-FI), a validated tool derived from ICD-9/10 and CPT codes, with frailty defined as a score >0.2. Characteristics were described at enrollment, stratified by frailty status. We excluded frail participants at baseline and modeled the incidence of a composite outcome of frailty or death. Censoring occurred when people were lost to follow-up and at the end of the study period. Multivariable Cox regression assessed the association between baseline pain and incident frailty, adjusting

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Participants Demographics and RA Disease Characteristics by VAFI Frailty Index Category (non-frail vs frail) at Baseline.

	Total N=3,276	Incident Cohort (Non-Frail at Baseline) N=2,315 (71 %)	Frail at Baseline N=961(29%)
Sociodemographic			
Age (years)	72.8 (10.3)	71.7 (10.7)	75.4 (8.8)
Males	2,809 (86%)	1,986 (86%)	823 (86%)
Race*			
Black	466 (14%)	502 (22%)	138 (14%)
White	2,284 (70%)	1,612 (70%)	672 (70%)
Other	74 (2.3%)	51 (2.2%)	23 (2.4%)
Smoking category*			
Never	688 (21%)	516 (22%)	172 (18%)
Current	774 (24%)	607 (26%)	167 (17%)
Former	1,690 (52%)	1,116 (48%)	574 (60%)
BMI	28.9 (5.8)	28.8 (5.7)	29.1 (6.2)
Pain score	4.4 (2.9)	4.3 (2.9)	4.7 (2.8)
RA disease characteristics			
Anti-CCP positive*	2,375 (73%)	1,741 (75%)	634 (66%)
RF positive*	2,340 (71%)	1,703 (74%)	637 (66%)
Disease Duration (years)	11.4 (11.4)	11.0 (10.9)	12.5 (12.5)
Prednisone use *	987 (30%)	685 (30%)	302 (31%)
csDMARD use *	2,291 (70%)	1,626 (70%)	665 (70%)
bDMARD use *	1,332 (41%)	952 (41%)	380 (40%)
RA disease activity			
DAS28CRP (0-9.4)**	3.4 (2.0)	3.3 (1.4)	3.6 (1.4)
Remission (<2.6)	690 (21%)	517 (22%)	173 (18%)
Low (2.6 to <3.2)	340 (10%)	252 (11%)	88 (9%)
Moderate (3.2 to <5.1)	853 (26%)	597 (26%)	256 (27%)
High (≥5.1)	328 (10%)	223 (10%)	105 (11%)
RDCI	3.5 (2.0)	2.8 (1.8)	5.1 (1.5)

Values are reported as mean (SD) or n (%).Other: American Indian/Alaska Native/Pacific Islander, Asian, and Other/Unknown. Abbreviations: bDMARD, biologic Disease-Modifying Antirheumatic Drugs; CCP, cyclic citrullinated peptide; C-reactive protein; csDMARD, conventional synthetic Disease-Modifying Antirheumatic Drugs; DAS28CRP, Disease Activity Score in 28 joints C-reactive protein, RDCI, Rheumatic Disease Comorbidity Index; RA, rheumatoid arthritis. * >5% missing observations, **>10% missing observations.

Table 2. Multivariable Cox Regression Analyses Assessing the Impact of Pain on Frailty Among Veterans with Rheumatoid Arthritis*

	HR**	95% CI	p-value
Unadjusted	**1.05**	**1.03-1.08**	**<0.0001**
Adjusted	**1.04**	**1.02-1.07**	**0.001**

*Models were adjusted for age, sex, race, disease duration, DAS28CRP, prednisone use, csDMARD use, bDMARD use, RDCI.
**per 1-point increase in pain intensity on a 0 to 10 rating scale

for baseline age, sex, race, BMI, disease duration (years), DAS28-CRP, csDMARD use, bDMARD use, prednisone use, and Rheumatic Disease Comorbidity Index (RDCI).

Results: 3,276 participants, of whom 86% were male, 70% were White, with a mean age of 72.8 ± 10.3 years, were described at baseline (Table 1). 71% were classified as non-frail, and 29% as frail. Frail individuals were older and had longer disease duration and higher pain than non-frail individuals. Individuals included in the incident analysis (N=2,315) were followed for an average of 5.9 years, during which 1,404 individuals (61%) developed frailty or died. Each 1-point increase in baseline self-reported pain was associated with a 4% increased risk in incident frailty (adjusted HR 1.04, 95% CI 1.02–1.07; p = 0.01) (Table 2).

Conclusion: Higher self-reported pain at baseline is associated with a greater risk of incident frailty among people with RA, independent of important patient and disease-related factors, including disease activity. These findings suggest that pain might be a modifiable risk factor for frailty in RA and underscore the need for targeted pain management strategies to mitigate frailty in this vulnerable population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. El-ayache: None; **S. Bhide**: None; **H. Brubeck**: None; **P. Roul**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Baker**: None; **G. Cannon**: None; **N. Singh**: None; **G. Kunkel**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **P. Katz**: None; **D. Shoback**: None; **J. Garcia**: Aveo Oncology, 2, Catalym, 2, Pfizer, 5; **P. Suri**: None; **M. Gasperi**: None; **A. Orkaby**: None; **U. Makris**: None; **K. Wysham**: None.

Abstract Number: 1239

JAK inhibition appears to alter clinical and neurobiological markers of nociplastic pain in rheumatoid arthritis: a 7T MRI Brain study

Kristian Stefanov[1], Andrew McGucken[1], Maxine Arnott[1], Tyrone Lau[1], Norah Aldehmi[1], Vinod Kumar[2], Neil McKay[3], James Dale[4], Lindsay Robertson[5], James Brock[1], Flavia Sunzini[6] and **Neil Basu**[7], [1]University of Glasgow, Glasgow, United Kingdom, [2]NHS Tayside, Dundee, United Kingdom, [3]NHS Lothian, Edinburgh, United Kingdom, [4]NHS Lanarkshire, Wishaw, United Kingdom, [5]NHS Grampian, Aberdeen, United Kingdom, [6]Glasgow University, Glasgow, United Kingdom, [7]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pain remains a prevalent and highly impactful issue for people with rheumatoid arthritis (RA). Among modern day targeted therapies, the janus kinase (JAK) inhibitors are especially effective in reducing RA pain, however the mechanisms of their analgesic action are not fully known, and do not appear to be entirely explained by classical nociceptive pain mediators.

In this study of RA, we hypothesised that filgotinib, a selective JAK-1 inhibitor, additionally modifies nociplastic pain mechanisms, as typified in fibromyalgia (FM). Specifically, we predicted that peripherally driven dimensions of nociplastic pain would be altered as demonstrated by modification of functional brain connectivity between the posterior insula and inferior parietal lobe (IPL), an established neurobiological marker of 'bottom up' nociplastic pain which is most powerfully measured by 7 Tesla (7T) functional MR brain imaging (fMRI).

Methods: A single centre, observational test re-test study of people with moderate to severe RA who have been newly prescribed filogotinib as per standard care. Immediately prior to drug initiation, recruits underwent a clinical evaluation which included the ACR FM 2011 survey criteria (a validated subjective score of nociplastic pain, range 0-31). They then undertook an ultra-high resolution (7T) MRI brain scan, incorporating a 10-minute simultaneous-multi-slice (SMS) echo-planar imaging (EPI) sequence to capture resting state fMRI. During the resting state, subjects were instructed not to undertake any task and to stay awake with their eyes open on a fixation cross. To enable structural co-localisation, a whole-brain T1-weighted structural image was collected using a twice magnetization-prepared rapid gradient echo (MP2RAGE) sequence. Subjects then were invited to return to repeat these measures 12 (±1) weeks later. FMRI data was pre-processed and analysed using statistical parametric mapping (SPM) version 12 and the CONN functional connectivity toolbox, both running on MATLAB 2017a. Seed-based connectivity analyses were applied to determine the connectivity maps informed by our *a priori* determined regions of interest (IPL-Posterior insula). Simple descriptive statistics were employed to derive baseline characterisation and evaluation of longitudinal differences.

Results: Of the n=20 recruited, n=16 (75% female; mean age 56.9 [SD 9.6] years, baseline DAS28 4.6 [SD 1.4]) completed study follow-up. Clinically, this group reported a large and statistically significant change (p= 0.001) in their mean ACR FM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

scores from 14.4 [SD 5.6] to 7.9 [SD 5.4] at follow up. A statistically significant change in functional connectivity between the left IPL and left posterior insula was also observed (p=0.021).

Conclusion: Filgotinib significantly reduced patient reported nociplastic pain, possibly through the attenuation of aberrant posterior insula-IPL brain functional connectivity – a marker of peripherally driven nociplastic pain in RA.

Disclosure: K. Stefanov: None; **A. McGucken**: None; **M. Arnott**: None; **T. Lau**: None; **N. Aldehmi**: None; **V. Kumar**: None; **N. McKay**: Alfa Sigma, 6, Gilead, 2, UCB, 2; **J. Dale**: None; **L. Robertson**: UCB, 12, received funding to attend educational conference EULAR 2023 an 2025; **J. Brock**: None; **F. Sunzini**: None; **N. Basu**: AbbVie, 6, AstraZeneca, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, GSK, 2, 5, MSD, 2, Nesos, 5, Pfizer, 5, 6, Roche, 2, 6, Vifor, 2, 5, 6.

Abstract Number: 1240

Serum Olink Proteomics Identifies Novel Mediators of Pain in Lupus Nephritis Patients Without Extrarenal Clinical Activity

Sarah Keegan[1], **Philip Carlucci**[2], Peter Izmirly[3], Erin Carter[4], Sanchit Sanyal[5], Brooke Cohen[6], Jasmine Shwetar[7], Katie Preisinger[8], Devyn Zaminski[6], Kristina Deonaraine[6], Mala Masson[9], Andrea Fava[10], Judith James[11], Rufei Lu[11], Wade DeJager[12], Chaim Putterman[13], Michael Belmont[14], Richard Furie[15], Maria Dall'Era[16], Diane Kamen[17], Kenneth Kalunian[18], Jennifer Anolik[19], David Wofsy[20], Jennifer Barnas[21], Nir Hacohen[22], Robert Clancy[23], Joel Guthridge[11], Brad Rovin[24], Michelle Petri[25], Jill Buyon[3], Kelly Ruggles[26] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM), Accelerating Medicines Partnership: RA/SLE Network (AMP RA/SLE), [1]NYU Langone, New York, [2]New York University School of Medicine, New York, NY, [3]NYU Grossman School of Medicine, New York, NY, [4]New

Table 1 Clinical characteristics of patients with and without reported pain in the AMP and AMP AIM lupus cohorts without extrarenal clinical activity. Data represented as median [IQR] or N (%). P-value calculated using chi-squared, Fisher's exact, or Mann Whitney U test where appropriate. *1 biopsy with arteriosclerosis and 1 biopsy with an unknown pathology but not lupus nephritis.

	AMP			AMP AIM		
Clinical Characteristic	**Pain N=50**	**No Pain N=28**	p-value	**Pain N=8**	**No Pain N=3**	p-value
Age	35 [27, 44]	33 [26, 42]	0.743	53 [32,61]	27 [25, 36]	0.066
Female	40 (80)	24 (86)	0.759	11 (100)	3 (100)	NA
Race			0.153			0.279
Asian	5 (10)	8 (29)		2 (25)	0 (0)	
Black	26 (52)	9 (32)		5 (63)	1 (33)	
White	11 (22)	7 (25)		0 (0)	1 (33)	
Unreported	8 (16)	4 (14)		1 (13)	1 (33)	
Hispanic	13 (26)	8 (29)	0.797	2 (25)	1 (33)	1
Anti-dsDNA Positive	32 (68) n=47	15 (65) n=23	1	5 (63)	2 (67)	1
Low C3	24 (49) n=49	16 (64) n=25	0.324	2 (25)	0 (0)	1
Low C4	24 (49) n=49	14 (56) n=25	0.628	3 (38)	1 (33)	1
Lupus Nephritis Class			0.397			0.503
Mesangial	0 (0)	0 (0)		1 (13)	1 (33)	
Proliferative	23 (46)	16 (57)		3 (38)	0 (0)	
Membranous	16 (32)	5 (18)		2 (25)	0 (0)	
Mixed	11 (22)	7 (25)		0 (0)	0 (0)	
No lupus nephritis	0 (0)	0 (0)		2 (25)*	2 (67)*	
PROMIS-29 Pain Interference T-Score	61 [56, 65]	42 [42, 42]	<0.001	63 [60, 67]	42 [42, 46]	0.014
Prednisone	25 (50)	23 (82)	0.007	6 (75)	0 (0)	
Prednisone > 20 mg	13 (26)	9 (32)	0.606	0 (0)	0 (0)	NA
Azathioprine	3 (6)	3 (11)	0.661	0 (0)	0 (0)	NA
Cyclophosphamide	1 (2)	1 (4)	1	0 (0)	0 (0)	NA
Hydroxychloroquine	47 (94)	22 (79)	0.063	7 (88)	2 (67)	0.491
Mycophenolate	28 (56)	15 (54)	1	0 (0)	0 (0)	NA
Tacrolimus	4 (8)	3 (11)	0.697	0 (0)	0 (0)	NA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

York University Grossman School of Medicine, New York, NY, [5]Johns Hopkins University School of Medicine, Baltimore, MD, [6]NYU Langone, NYC, [7]New York University School of Medicine, Department of Medicine, New York, [8]NYU Langone, NYU Langone, [9]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [10]Johns Hopkins University, Baltimore, MD, [11]Oklahoma Medical Research Foundation, Oklahoma City, OK, [12]Oklahoma Medical Research Foundation, Oklahoma City, [13]Albert Einstein College of Medicine, Safed, Israel, [14]NYU Langone Health, New York, NY, [15]Division of Rheumatology, Northwell Health, Great Neck, NY, [16]Division of Rheumatology, University of California, San Francisco, CA, [17]Medical University of South Carolina, Johns Island, SC, [18]UC San Diego, La Jolla, CA, [19]University of Rochester Medical Center, Rochester, NY, [20]University of California San Francisco, SF, CA, [21]University of Rochester, Rochester, NY, [22]Broad Institute of MIT Harvard, Cambridge, MA, [23]Columbia University, New York, NY, [24]The Ohio State University, Columbus, OH, [25]Johns Hopkins University School of Medicine, Timonium, MD, [26]NYU Grossman School of Medicine, Brooklyn, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: For patients with lupus nephritis, active disease can be solely renal or include a range of extrarenal signs, such as arthritis or serositis, that can cause pain and decreased quality of life. However, the etiology of pain in the absence of extrarenal clinical activity remains in question, and no clinical trials have evaluated therapies for this potentially debilitating aspect of SLE. The Accelerating Medicines Partnership (AMP) provides an unprecedented opportunity to evaluate molecular mediators of disease in a well-phenotyped multi-ethnic multi-racial cohort of lupus patients enrolled at centers across the US. Accordingly, this study leveraged the AMP and AMP AIM lupus cohorts to evaluate serum proteins associated with patient reported pain specifically in patients without extrarenal clinical activity.

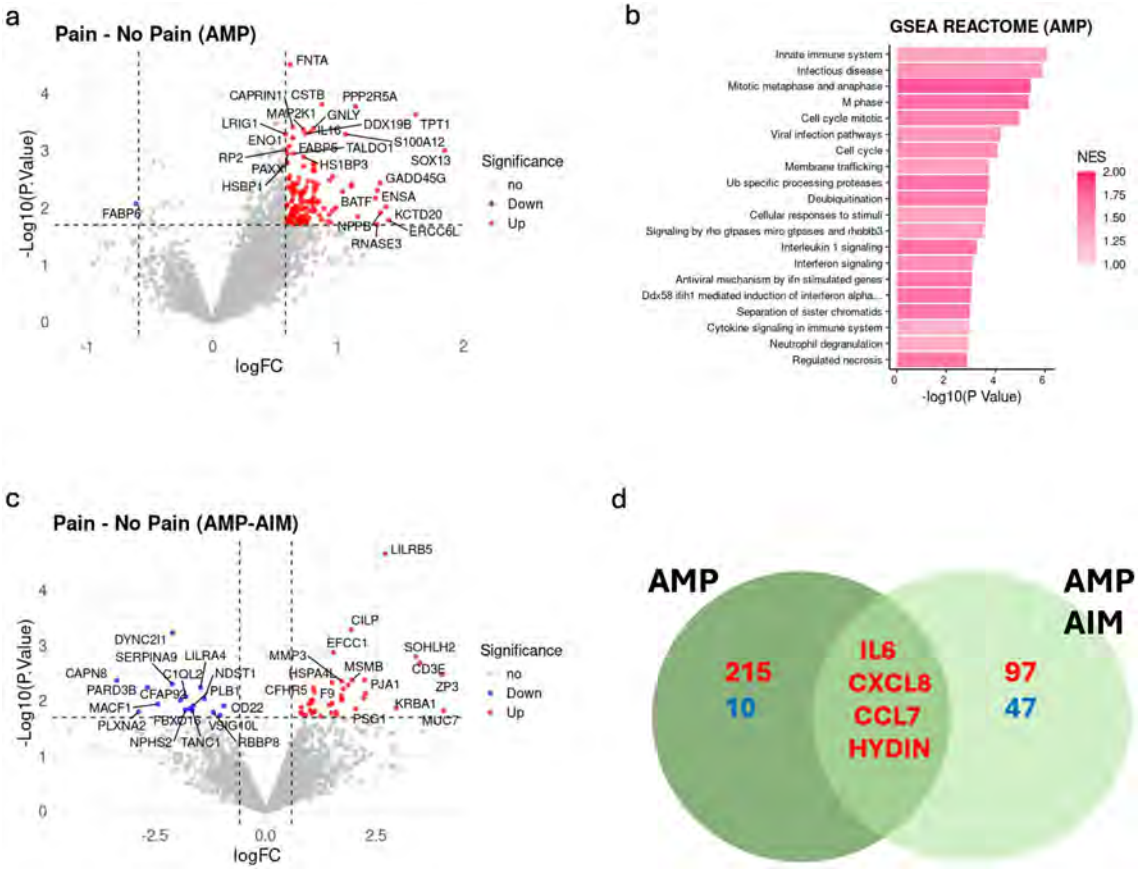
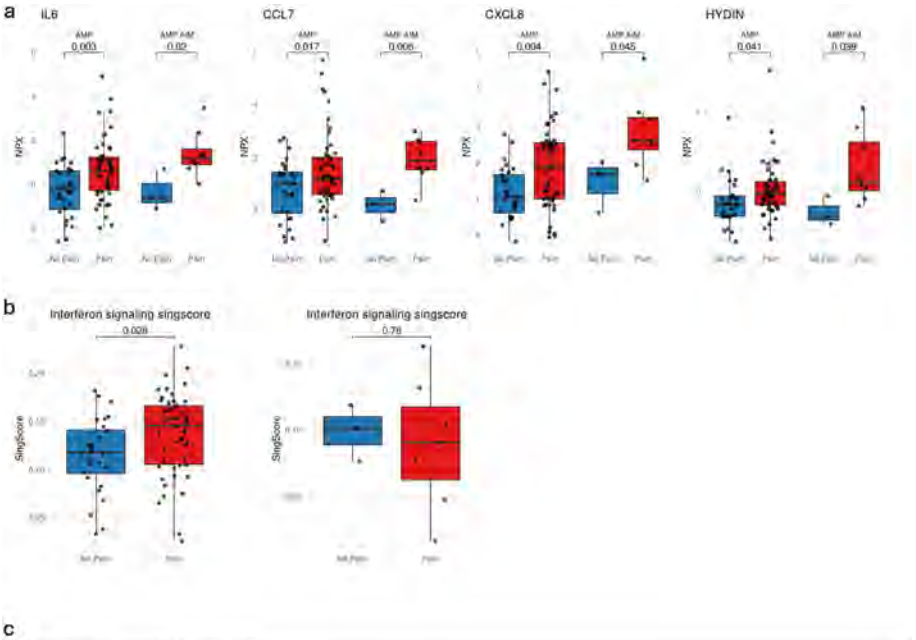


Figure 1 (A) Volcano plot of AMP cohort comparison for Pain vs. No Pain (|logFC| > 1.5, p-value < 0.02). (B) GSEA results for the Reactome pathway database for AMP cohort comparison. (C) Volcano plot of AMP-AIM cohort comparison for Pain vs. No Pain (|logFC| > 1.5, p-value < 0.02). (D) Venn Diagram showing overlap between AMP and AMP AIM differential analysis results (|logFC| > 1.5, p-value < 0.05).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



c

Protein	Citation
IL6	Zhou et al. **Interleukin-6: an emerging regulator of pathological pain.** J Neuroinflammation. 2016, PMID: 27267059
CXCL8	Cambier et al. **The chemokines CXCL8 and CXCL12: molecular and functional properties, role in disease and efforts towards pharmacological intervention.** Cell Mol Immunol. 2023, PMID: 36725964
CCL7	Kwiatkowski et al. **Chemokines CCL2 and CCL7, but not CCL12, play a significant role in the development of pain-related behavior and opioid-induced analgesia**. Cytokine. 2019, PMID: 31003094
HYDIN	Recla et al. **Precise genetic mapping and integrative bioinformatics in Diversity Outbred mice reveals Hydin as a novel pain gene.** Mamm Genome. 2014, PMID: 24700285

Figure 2 (A) Box plots of NPX (normalized protein expression) values for the in common differential proteins between AMP and AMP AIM cohorts when comparing Pain vs. No Pain. (B) Box plots of the Interferon Signaling Singscore for the AMP cohort. (C) Citations showing each of the four protein candidates has been previously associated with pain.

Methods: Pain was assessed using the PROMIS-29 pain interference questionnaire. To limit variability and focus on clinically meaningful outcomes, only patients without clinical extrarenal disease and PROMIS pain interference T scores < 50 (no reported pain interference) or > 55 (abnormal pain interference) were included. The AMP lupus nephritis cohort was used for the discovery analysis (n=28 without pain, n=50 with pain). The AMP AIM lupus cohort, most with renal disease but all chosen without any extrarenal clinical activity, was used for early validation (n=3 without pain, n=8 with pain). Serum proteins were measured using the Olink Explore HT platform. Assays with less than 5 values (AMP) and 1 value (AMP AIM) above limit of detection in either comparison group were excluded. Differential protein expression was evaluated using unadjusted linear models (limma) with candidate proteins considered at log2FC |1.5| and nominal p< 0.05. Pathways were assessed by gene set enrichment analysis (GSEA). An interferon signaling score was calculated by the Singscore method using the proteins in the Reactome "Interferon Signaling" pathway included in the Olink Assay.

Results: The clinical characteristics of the cohorts are described in Table 1. Differential expression analysis revealed 229 (219 up and 10 down) proteins significantly different between patients with vs. without pain and no extrarenal disease in the AMP cohort (Fig 1A). GSEA identified pathways related to innate immune signaling, including interferon, to be associated with pain (Fig 1B). In the validation AMP AIM cohort, there were 148 (101 up and 47 down) proteins significantly associated with pain in the absence of extrarenal activity (Fig 1C). Four proteins—CCL7, IL6, CXCL8, and HYDIN—were significantly elevated in the pain group across both cohorts (Fig 1D and Fig 2A), and all four have been previously linked to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the expression of pain in the literature (Fig 2C). An interferon signaling score significantly associated with pain in AMP but not AMP AIM (Fig 2B).

Conclusion: These data suggest that circulating proteins may be key mediators of pain even in SLE patients without overt extrarenal clinical activity. Experimental evidence from mouse models supports the involvement of the identified candidates: CCL7 in neuropathic pain, IL6 in both neuropathic and nociceptive pain, CXCL8 in nociceptive pain, and HYDIN in nociceptive pain.

Disclosure: S. Keegan: None; **P. Carlucci**: None; **P. Izmirly**: Hansoh Bio, 2; **E. Carter**: None; **S. Sanyal**: None; **B. Cohen**: None; **J. Shwetar**: None; **K. Preisinger**: None; **D. Zaminski**: None; **K. Deonaraine**: None; **M. Masson**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **R. Lu**: None; **W. DeJager**: None; **C. Putterman**: Cullinan, 1, Progentec, 1; **M. Belmont**: None; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **D. Kamen**: None; **K. Kalunian**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Genentech, 1, GlaxoSmithKlein(GSK), 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, Roche, 1; **J. Anolik**: None; **D. Wofsy**: None; **J. Barnas**: None; **N. Hacohen**: Calico Biosciences, 5, Cytoreason, 1, 11, Danger Bio, 1, 11, Moderna, 5, Repertoire Immune Medicines, 1, 11, Takeda, 5; **R. Clancy**: None; **J. Guthridge**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **K. Ruggles**: None.

Abstract Number: 1241

Beyond Pain Severity in Psoriatic Arthritis: Pain Catastrophizing Independently Impacts Disease Burden and Quality of Life

Kyra Chen[1], Uma Scher[2] and **Rebecca Haberman**[3], [1]NYU Grossman School of Medicine and NYU Langone Health Psoriatic Arthritis Center, New York, [2]NYU School of Medicine, Scarsdale, NY, [3]NYU Langone Health, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Pain remains a major burden in psoriatic arthritis (PsA), often persisting despite effective control of synovial inflammation. This persistent pain may prevent patients from achieving remission or meaningful improvements in quality of life (QoL). Although pain severity is typically emphasized in clinical evaluation, emerging evidence suggests that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

psychological contributors—particularly maladaptive cognitive-emotional processes such as pain catastrophizing—may play a critical, underrecognized role. Pain catastrophizing, defined by magnification of symptoms, ruminative thoughts, and a sense of helplessness, is well documented in other chronic pain conditions but remains poorly characterized in PsA. In this study, we assess the prevalence and impact of pain catastrophizing in a real-world PsA population at the NYU Psoriatic Arthritis Center (PAC).

Methods: Consecutive patients meeting CASPAR criteria were enrolled at the NYU PAC into a cross-sectional study of pain and psychosocial features. Participants completed the Pain Catastrophizing Scale (PCS), which includes three subscores (helplessness, magnification, rumination); a total score >30 was considered clinically significant. Depression was defined by PHQ-9 ≥10. Pain severity was rated on a 0–10 scale. Outcomes included Minimal Disease Activity (MDA), low disease activity per cDAPSA (≤13), and multiple QoL indices (EQ-5D, PROMIS-29). Associations between PCS and disease outcomes were assessed via logistic and linear regression, adjusting for pain intensity, depression, and sex.

Results: Among 91 PsA patients, 5 (5.5%) patients met criteria for clinically significant (PCS >30), all of whom were women. Subscale symptom prevalence included helplessness (6), magnification (12), and rumination (3). Higher PCS scores were associated with reduced odds of achieving cDAPSA low disease activity (OR 0.95, 95%CI 0.90–0.99, p=0.022), and a trend toward lower MDA rates (OR 0.95, CI 0.91–1.00, p=0.060). Catastrophizing was associated with poorer QoL (EQ-5D index b=-0.009 95%CI -0.013, -0.006, p < 0.001), with helplessness driving the strongest effect (β = –0.023, 95%CI –0.03 to –0.02, p< 0.001). After adjusting for current pain level, sex, and the presence of active depression, PCS remained independently associated with QoL (b= -0.004, 95%CI -0.01, -0.004, p =0.03), greater pain interference (β = 0.230, 95%CI 0.090–0.370, p=0.002), and reduced participation in social roles (β = –0.338, 95%CI –0.52 to –0.156, p< 0.001). No association was found with physical function (b= -0.91, 95%CI -0.256, -0.074, p =0.276).

Conclusion: Our findings highlight the critical role of psychological pain processing in PsA. Pain catastrophizing—often undetected by standard clinical assessments—exerts a substantial and independent effect on patient-reported outcomes, even after accounting for actual pain intensity and depression. Addressing this process through interventions such as cognitive behavioral therapy or integrative psychosocial support may be necessary to improve holistic disease management and help patients achieve true remission and restoration of function.

Disclosure: K. Chen: None; **U. Scher**: None; **R. Haberman**: Johnson and Johnson, 1, 5, Novartis, 1.

Abstract Number: 1242

Relax the Body: Dual-Agent Nighttime Therapy for Fibromyalgia: Symptom Reduction Using Tricyclic Antidepressants and Muscle Relaxants

Robert Katz[1], Alexandra Katz Small[2], Edwin Moore[3] and Seth Adler[4], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, CHICAGO, IL, [3]University of Illinois Urbana Champaign, CHICAGO, IL, [4]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

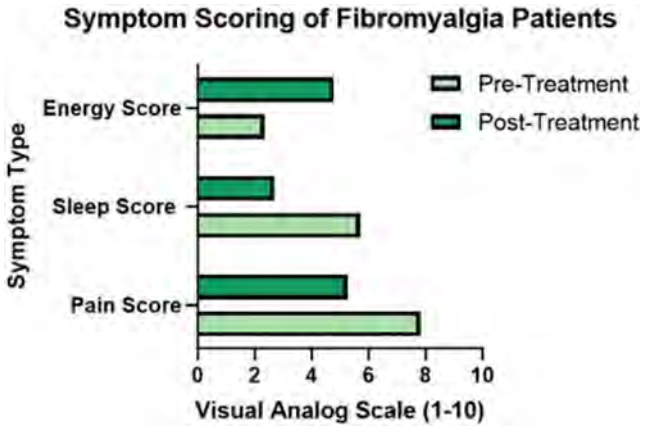


Figure 1. Fibromyalgia Symptom Severity Pre- and Post-Treatment

Background/Purpose: Fibromyalgia (FM) is a multifaceted disorder defined by chronic widespread pain, sleep disruption, fatigue, and cognitive difficulties. Although the predominant theory behind FM pathogenesis involves central sensitization and altered neurotransmitter signaling (e.g., serotonin, norepinephrine, glutamate), emerging evidence suggests peripheral contributors such as increased intramuscular pressure may also play a role. Elevated muscle tension has been correlated with poor sleep quality and higher pain levels, suggesting a cyclical relationship between sleep disturbance and muscular abnormalities. While tricyclic antidepressants (TCAs) have demonstrated some success in relieving FM-related symptoms - particularly sleep and mood disturbances - their use as monotherapy remains insufficient. Furthermore, despite literature on multimodal pharmacologic approaches, no studies to date have examined a combination of TCAs in a dose high enough to achieve uninterrupted sleep and muscle relaxants (MRs) as a targeted therapy for FM. This study explores whether this combination can effectively alleviate symptoms in a clinical population of FM patients.

Methods: We conducted a prospective study of 31 patients (25 females and 6 males) diagnosed with FM using the American College of Rheumatology (ACR) diagnostic criteria. All participants were prescribed a low dose TCA (amitriptyline, doxepin, or trazodone) in the early evening, titrated as needed to induce deep sleep. Once patients reported improved sleep, a nightly muscle relaxant - either cyclobenzaprine or tizanidine - was introduced and gradually increased based on tolerability, up to 30 mg or 24 mg respectively. Visual Analog Scales (VAS) were used to assess changes in pain (0–10), sleep quality (1 = excellent sleep, 10 = no sleep), and energy levels (1 = no energy, 10 = abundant energy) before and after the treatment regimen.

Results: Following treatment, 23 of 31 patients (74%) reported symptomatic improvement. Pain scores on

VAS decreased from a pre-treatment mean of 7.81 to 5.25 post-treatment. Sleep quality improved significantly, with average sleep disruption scores declining from 5.7 to 2.69. Patient-reported energy levels increased from a mean of 2.34 to 4.77. See Figure 1. Eight patients (26%) reported no improvement, and an equal number experienced sedation as a side effect, though no other adverse events were reported. All results were statistically significant with a p-value < 0.01.

Conclusion: This study introduces a novel multimodal pharmacologic regimen combining tricyclic antidepressants and muscle relaxants to target both central and peripheral mechanisms contributing to FM symptomatology. Results suggest that such a combination can improve pain, sleep, and energy in a substantial portion of FM patients, with minimal side effects. Given the limitations of existing monotherapies and the heterogeneity of FM symptoms, this approach warrants further exploration in larger randomized controlled trials. Future studies should also evaluate long-term outcomes and compare this regimen directly with currently approved FM treatments such as duloxetine and pregabalin.

Disclosure: R. Katz: None; **A. Katz Small**: None; **E. Moore**: None; **S. Adler**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1243

Broad Cytokine Dysregulation in Fibromyalgia Patients: A Pilot Immune Profiling Study

Robert Katz[1] and Alexandra Katz Small[2], [1]Rush University Medical Center, Chicago, IL, [2]Rheumatology Associates, CHICAGO, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

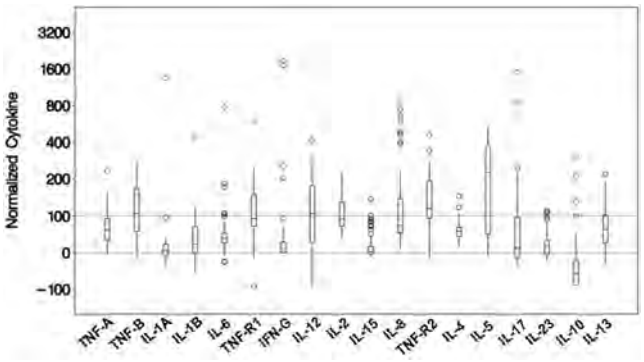
Background/Purpose: Fibromyalgia is a chronic pain syndrome characterized by widespread musculoskeletal pain, fatigue, cognitive disturbances, and poor sleep. Despite accumulating evidence of immune involvement, a clear immunophenotype remains elusive. Previous studies have focused on a limited set of cytokines with inconclusive results. This study aims to explore a broader panel of proinflammatory, anti-inflammatory, and adaptive cytokines to identify immune abnormalities that may contribute to fibromyalgia pathology.

Methods: 46 patients diagnosed with fibromyalgia per the 2016 ACR criteria underwent peripheral blood sampling. Serum levels of 22 cytokines were analyzed at the University of Miami Immunology Lab and compared to age-matched normal controls using a percentile-based cutoff.

Cytokines were categorized as pro-inflammatory (TNF-α, IL-6, IL-8, IL-1α, IL-1β, IFN-γ, IL-17), anti-inflammatory (IL-10, IL-4, IL-13), or adaptive (IL-12, IL-15, IL-23). Levels of soluble cytokine receptors (TNFR1 and TNFR2) were also measured. Levels were deemed abnormal if ≥50% of patients had values greater than the 90th percentile or less than the 10th percentile of the normal range. Flow cytometry was conducted in 25 patients to assess immune cell populations (CD8+, CD26+, CD11a+, CD56+, etc.).

Results: Fibromyalgia patients exhibited elevated levels of TNF-β, IL-5, IL-12, IL-15, IL-23, TNFR1, and TNFR2, suggesting heightened activation of both proinflammatory and adaptive pathways. IL-10, a key anti-inflammatory cytokine, was notably lower than average in most individuals. IL-1β, IL-6, and IL-17 levels exceeded the 90th percentile in a significant subset of patients, indicating innate immune activation. IL-8 elevations correlated with previously reported links to symptom duration.

Flow cytometry revealed reduced frequencies of CD8+, CD26+, and CD11a+ cells, with values below normal in over half of the tested patients



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Fibromyalgia patients demonstrate a coherent dysregulation in immune signaling, characterized by elevations in several proinflammatory and adaptive cytokines alongside suppression of anti-inflammatory mediators such as IL-10. These findings support hypotheses of central sensitization being partially driven by aberrant immune signaling, even in the absence of classical inflammation. IL-10 deficiency and elevated TNF/IL-23 axis components may represent mechanistic targets for therapeutic intervention.

Further research is needed to validate these biomarkers and explore causal mechanisms.

Disclosure: R. Katz: None; **A. Katz Small**: None.

Abstract Number: 1244

PACFiND: Co-Designing Principles To Inform Reconfiguration Of Fibromyalgia Care Across Health Systems

Rosemary Hollick[1], Marcus Beasley[1], Ernest Choy[2], Caroline Cupit[3], Debra Dulake[1], Teresa Finlay[3], Louise Locock[1], Paul McNamee[1], Catherine Pope[3], Elaine Wainwright[1], David Williams[4], Gary Macfarlane[1] and PACFIND study team, [1]University of Aberdeen, Aberdeen, United Kingdom, [2]Division of Infection and Immunity, CREATE Centre, Cardiff University, Cardiff, United Kingdom, [3]University of Oxford, Oxford, United Kingdom, [4]University of Michigan, Michigan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia is a contested and poorly supported condition, characterised by widespread pain, fatigue, and cognitive symptoms, often compounded by stigma and delayed diagnosis. Existing services are fragmented and inconsistent, with high patient and system burden. The PACFiND study (PAtient-centred Care for Fibromyalgia: New pathway Design) aimed to inform new models of care for fibromyalgia.

Methods: A mixed method design integrated systematic literature reviews, surveys of, and interviews with, people with fibromyalgia symptoms/diagnosis and healthcare professionals, analysis of routine healthcare data and service case studies, to explore care pathways for fibromyalgia in the UK. Data collection included over 2,700 survey responses from patients and professionals, 31 in-depth interviews, 12 UK-wide service case studies, and national healthcare data on nearly 100,000

The bus infographic represents a patient-led journey through fibromyalgia care, reflecting the uneven pathway of ups and downs, or flare-ups and remissions of symptoms that people living with fibromyalgia experience. The patient, as driver, reflects autonomy and control, with the bus components symbolising flexible, multidisciplinary support grounded in holistic care principles.

Figure 1. Evidence-based principles of care to guide fibromyalgia service redesign.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

individuals. Findings were synthesised through investigator meetings and structured workshops, involving patients, public representatives, clinicians, commissioners, and policymakers to co-design principles of care to inform new care models.

Results: Findings highlighted delayed and inconsistent approaches to diagnosis, especially in men, and limited post-diagnosis support. Many health professionals questioned the validity of a fibromyalgia diagnosis. Patients often faced a revolving door of referrals across specialties, particularly pain management, gastroenterology, and general surgery, and invasive investigations. They reported substantial out-of-pocket costs, difficulty navigating services, and poor work outcomes. Healthcare professionals expressed uncertainty in making a diagnosis and management, with variable understanding of fibromyalgia as a central sensitisation condition. While medication remains a default, patients voiced strong preferences for personalised, holistic, and non-pharmacological interventions, delivered with empathy and continuity. Community resources, such as support groups, play a key role but lack formal recognition. Insights informed evidence based care principles (Figure 1) and potential delivery across different settings. For example: (1) primary care e.g., family physicians for early recognition, supported by training; (2) specialist input for complex diagnosis and management; and (3) wraparound support, integrating physical, psychological, and peer-led services. These aim to reduce inappropriate referrals, improve experience and outcomes, and enable tailored, appropriate place-based care.

Conclusion: The PACFiND study has co-designed multilevel principles for fibromyalgia care aligned with patient needs and system priorities. While conducted in the UK, the challenges identified—delayed diagnosis, fragmented care, and unmet patient needs—are common across healthcare systems globally, including the US. Although the logistics of implementation may differ, the core principles of integrated, person-centred, and evidence-informed care are widely applicable. This model offers a flexible framework to guide service redesign internationally. Next steps include testing in implementation settings and using economic data to support scale-up.

Disclosure: R. Hollick: None; **M. Beasley**: None; **E. Choy**: AbbVie, 2, 6, Alfasigma, 6, Bio-Cancer, 2, 5, Biocon, 2, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 6, Fresenius Kabi, 2, 6, Gedeon Richter, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 6, Viatris, 2, 6; **C. Cupit**: None; **D. Dulake**: None; **T. Finlay**: None; **L. Locock**: None; **P. McNamee**: None; **C. Pope**: None; **E. Wainwright**: None; **D. Williams**: None; **G. Macfarlane**: None.

Abstract Number: 1245

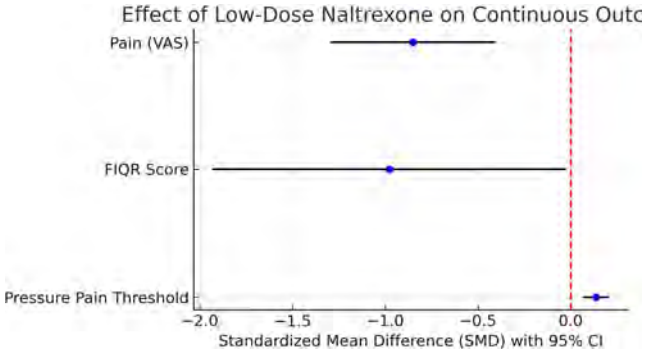
Efficacy And Safety of Low-dose Naltrexone In Fibromyalgia: An Updated Systematic Review And Meta-Analysis of Randomized Controlled Trials (RCTs)

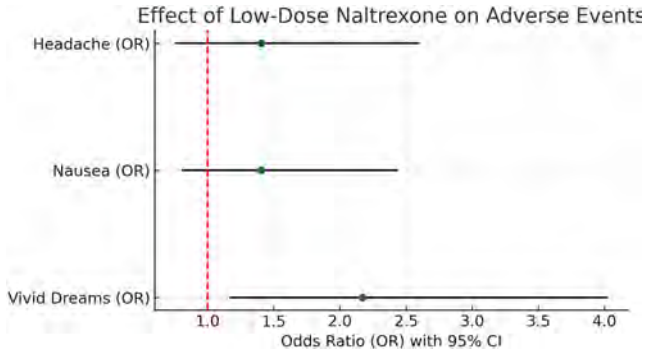
Rubab Rizwan, Sehneet Grewal, Sri Varsha Banda and Mohammad Hazique, Nuvance Health, poughkeepsie, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia is a chronic condition marked by widespread pain that can significantly reduce a patient's quality of life. While low-dose naltrexone (LDN) has emerged as a potential treatment option, its use is not yet well supported by robust evidence, particularly from randomized controlled trials. (RCTs). This study evaluates the effectiveness and safety of LDN in managing symptoms of fibromyalgia.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





Methods: This meta-analysis evaluated the safety and efficacy of LDN in fibromyalgia by systematically reviewing RCTs published through December 2024. Study selection followed PRISMA guideline. Data was analyzed using randome-effect model to calculate the pooled odds ratios (ORs) and Standardized mean difference (SMDs) for the measured outcomes.

Results: A total of five RCTs were included. LDN significantly reduced pain scores compared to placebo, with a pooled SMD of –0.851 (95% CI: –1.290 to –0.412). LDN also improved functional status as measured by the Fibromyalgia Impact Questionnaire Revised (FIQR), with SMD of –0.978 (95% CI: –1.926 to –0.030). Pressure pain threshold showed a small but statistically significant increase in the LDN group (SMD: 0.136; 95% CI: 0.071 to 0.202). Regarding safety, LDN was associated with a higher odds of vivid dreams (OR: 2.17; 95% CI: 1.17 to 4.02), but no significant increase in the risk of headaches (OR: 1.41; 95% CI: 0.76 to 2.60) or nausea (OR: 1.40; 95% CI: 0.81 to 2.43). Heterogeneity ranged from low to moderate across outcomes, and no major safety concerns were identified.

Conclusion: The findings of our analysis indicate that LDN may effectively reduce pain symptoms in patient with fibromyalgia while maintaining the favorable safety profile.

Disclosure: R. Rizwan: None; **S. Grewal**: None; **S. Banda**: None; **M. Hazique**: None.

Abstract Number: 1246

Myo Vs. Myo-fascial Injection for Myofascial Trigger Points. Is There Really a Difference? A Randomized Controlled Trial

Seda Yildiz[1], bugra ince[1] and Halil ibrahim candal[2], [1]izmir sehir hastanesi, izmir, Turkey, [2]izmir sehir hastanesi, izmir

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Primary and Secondary Outcome Measures and Between Group Comparisons

	Myofascial Injection (mean ± sd)				Intramuscular Injection (mean ± sd)				Effect Size (partial squared - ²)	P value
	Pre-treatment	30. minute	Day 3	Week 1	Pre-treatment	30. minute	Day 3	Week 1		
Primer Outcome										
VAS. (cm)	7.16 (1 .60)	4.89 (2.22)	4.44 (1 .84)	4.09 (1 .96)	6.50 (1 .59)	4.08 (2.29)	4.01 (2.26)	3.89 (1 .95)	.OI 1	.479
Secondary Outcome										
PPT (kg/cm2)	4.97 (1 .47)	5.83 (1 .63)	5.76 (1 .54)	5.53 (1 .50)	5.03 (1 .35)	5.65 (1 .49)	5.85 (129)	5.81 (1 .68)	.004	:794
PSFS	14.7 (51)		9.42 (4.53)	8.42 (4.69)	14.1 (5.1)		7.58 (4.52)	6.73 (3.89)	.016	.300

Abbreviations:
VAS: Visual Analog Scale
PPT: Pressure Pain Treshold
PSFS: Patient-Spesific Functional Scale
SD: Standard Deviation

Primary and Secondary Outcome Measures and Between Group Comparisons

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Experimental and clinical studies suggest that fascial structures play a critical role in the pathogenesis and pain mechanisms of myofascial pain syndrome (MTrP). It is proposed that incorporating fascial structures into treatment may enhance therapeutic outcomes. However, no high-quality randomized controlled trials have been conducted to evaluate this hypothesis. This study aims to assess whether including fascial structures in treatment provides additional benefits compared to conventional intramuscular MTrP injections.

Methods: This triple-blind, randomized, parallel-group, single-center prospective study included seventy-six patients aged 18–65 years diagnosed with active MTrP. In the myo-fascial injection group, injections targeted intermuscular fascia, deep fascia, and superficial fascia in addition to MTrP. In the myo-injection group, only intramuscular injections were performed. Pain intensity, pressure pain threshold, and functional status were assessed before treatment and at 30 minutes, 3 days, and 1 week after treatment.

Results: A significant reduction in pain intensity was observed in both groups at all post-treatment time points compared to baseline. The pressure pain threshold increased after treatment but decreased after the third day. Functional status improved in both groups by the third day, and this improvement continued through the first week. However, no significant differences were found between the groups at any time point regarding any measured outcome.

Conclusion: The injection method targeting fascial structures did not provide a significant advantage over the conventional intramuscular trigger point injection method. Further studies are needed to evaluate the long-term effects of including fascial structures in treatment.

Disclosure: s. yildiz: None; **b. ince**: None; **H. candal**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1247

Relation of Measures of Pain Sensitization to Widespread Pain

ZHIQIANG WANG[1], Sarah Tilley[2], Laura Frey Law[3], Cora Lewis[4], Michael Nevitt[5], Kosaku Aoyagi[6], Chunyi Wen[7], Changhai Ding[1] and **Tuhina Neogi**[8], [1]Zhujiang Hospital, Southern Medical University, Guangzhou, China (People's Republic), [2]Boston University School of Medicine, Somerville, MA, [3]Department of Physical Therapy and Rehabilitation Science, Carver College of Medicine, University of Iowa, Iowa City, IA, [4]The University of Alabama at Birmingham, Birmingham, AL, [5]University of California, San Francisco, San Francisco, CA, [6]University of Texas at El Paso, El Paso, TX, [7]The Hong Kong Polytechnic University, Hong Kong, China (People's Republic), [8]Boston University School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1221–1247) Pain in Rheumatic Disease Including Fibromyalgia Poster

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Widespread pain (WSP) is thought to be related to alterations in nociceptive signaling such as pain sensitization. Whether pain sensitization predisposes to an increase in number of pain sites, including the development of WSP, is not known.

Methods: We included participants from the Multicenter Osteoarthritis Study (MOST), a NIH-funded longitudinal cohort, who reported pain sites on a homunculus at baseline and two years later to determine WSP status (defined as pain above and below the waist, on the right and left sides of the body, and axially), and underwent quantitative sensory testing (QST). We assessed baseline pain sensitization (i.e., alterations in ascending nociceptive signaling) using three QST measures: temporal summation (TS) at the wrist, and pressure pain threshold (PPT) at the patella (average of both knees), and PPT at the wrist. Higher TS indicates more pain sensitization, while higher PPT indicates less pain sensitization.

We analyzed the relations of QST to: 1) the presence of WSP at baseline; 2) an increase of at least two painful sites after two years of follow-up; and 3) incident WSP after two years among those who were free of WSP at baseline. We used logistic regression to estimate presence of WSP at baseline, and modified Poisson regression for the longitudinal analyses. We

Table. Associations between quantitative sensory testing measurements and widespread pain § TS Wrist additionally adjusted for study visit due to protocol change. # Adjusted for the following potential confounders: age, sex (for whole sample), BMI, race, site, presence of symptomatic knee OA in at least one knee, depressive symptoms, NSAID use, Opioid use, and Charlson comorbidity index. * Increase in at least two painful sites over 2 years additionally adjusted for baseline number of painful sites. TS: higher values indicate more pain sensitization; PPT: lower values indicate more pain sensitization. Abbreviations: TS, temporal summation; PPT, pressure pain threshold; SD, standard deviation; WSP, widespread pain; CI, confidence interval; OR, odds ratio; RR, risk ratio.

Outcomes	TS Wrist§		PPT Patella (per SD unit increase)		PPT Wrist (per SD unit increase)	
	OR/RR (95% CI)	Forest plots	OR/RR (95% CI)	Forest plots	OR/RR (95% CI)	Forest plots
Cross-sectional presence of baseline WSP Adjusted# OR (95% CI)						
Whole Sample (N=3078)	**1.15 (1.01, 1.32)**		**0.90 (0.84, 0.96)**		**0.87 (0.81, 0.94)**	
Female (n=1776)	**1.26 (1.07, 1.50)**		**0.87 (0.79, 0.95)**		**0.87 (0.78, 0.96)**	
Males (n=1302)	0.98 (0.77, 1.24)		0.94 (0.84, 1.05)		**0.89 (0.80, 0.99)**	
Increase in at least two painful sites over 2 years Adjusted#* RR (95% CI)						
Whole Sample (N=3078)	1.14 (0.97, 1.34)		0.95 (0.88, 1.03)		0.98 (0.91, 1.06)	
Female (n=1776)	1.23 (0.99, 1.52)		0.92 (0.82, 1.02)		0.94 (0.83, 1.06)	
Males (n=1302)	1.06 (0.83, 1.35)		0.99 (0.88, 1.11)		1.02 (0.92, 1.13)	
Incidence of WSP over 2 years (among those free of WSP at baseline) Adjusted# RR (95% CI)						
Whole Sample (N=3078)	1.09 (0.85, 1.39)		0.94 (0.84, 1.07)		0.97 (0.85, 1.09)	
Female (n=1776)	1.20 (0.85, 1.67)		0.85 (0.71, 1.02)		0.88 (0.72, 1.09)	
Males (n=1302)	1.01 (0.71, 1.44)		1.04 (0.88, 1.23)		1.01 (0.86, 1.18)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

secondarily performed sex-stratified analyses given known sex differences in QST. All analyses were adjusted for potential confounders, including age, sex (for analyses of the whole sample), BMI, race, site, presence of symptomatic knee osteoarthritis in at least one knee, depressive symptoms, NSAID use, Opioid use, and Charlson comorbidity index.

Results: We included 3078 participants (mean age 62.7, 57.7% female), of whom 32.2% had WSP at baseline (67.8% female), and 23.5% had an increase in two or more painful sites (59.8% female) at two years of follow-up. Among the 2088 participants free of WSP at baseline (mean age 62.1, 52.9% female), 14.9% had incident WSP (55.9% female) over two years. Cross-sectionally, TS was significantly associated with baseline WSP in the whole sample and in females but not in males (**Table**). PPT at the wrist was inversely associated with baseline WSP in the whole sample and in both sexes, while PPT at the patella was inversely associated in the whole sample and female participants, but not in males (**Table**). There were no significant associations between QST measures and either an increase in at least two painful sites or incidence of WSP after two years of follow-up (**Table**).

Conclusion: Although QST measures were associated with WSP cross-sectionally, they were not associated with incident WSP or increase in number of pain sites over two years. However, the null longitudinal findings may have been limited by the phenomenon of depletion of susceptibles (i.e., those most susceptible had already developed WSP in relation to pain sensitization at an earlier age).

Disclosure: Z. WANG: None; **S. Tilley**: None; **L. Frey Law**: None; **C. Lewis**: None; **M. Nevitt**: None; **K. Aoyagi**: None; **C. Wen**: None; **C. Ding**: None; **T. Neogi**: None.

Abstract Number: 1248

Patient and Clinician Perception and Use of Complementary and Alternative (CAM) Medicine for Rheumatic Disease

Ailia Ali[1], Sarah Sun[1], Faryal Shaikh[1], Tamiko Katsumoto[2], Neha Shah[3], Kimberly Trotter[1] and Pankti Reid[4], [1]University of Chicago, Chicago, IL, [2]Division of Immunology and Rheumatology, Stanford University, Millbrae, CA, [3]Stanford University, Palo Alto, CA, [4]University of Chicago Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Complementary and alternative medicine (CAM) use is increasingly prevalent among patients with rheumatic diseases, yet alignment between patient practices and clinician perspectives remains poorly defined. This study assesses CAM attitudes, usage patterns, and familiarity amongst both rheumatology clinicians and patients.

Methods: An online patient-facing survey and a separate clinician-facing survey evaluated use and perception of CAM in rheumatic diseases. Eligible patients were ≥ 18 years old and actively going to rheumatology clinic. Clinicians included rheumatology MDs, DOs and advanced practice providers. Dissemination of the survey was done virtually through patient advocacy groups, provider organizations, social media, and messaging via electronic medical records. Results were analyzed using descriptive statistics (Chi-square).

Results: 1221 patients with rheumatic disease across the United States completed the patient survey. For patients, if no familiarity with CAM (163 patients or 13% of respondents) was endorsed, the survey was ended. Patient participants were primarily female (88%), and predominantly Caucasian non-Hispanic (64%). The most common rheumatic disease

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Demographics

	TOTAL	%
AGE		
65 and over	463	45%
55-64	279	27%
25-34	37	4%
45-54	184	18%
35-44	68	7%
18-24	7	1%
SEX		
Female	896	88%
Male	128	13%
RACE/ETHNICITY		
Black	217	21%
Caucasian-Non Hispanic	667	64%
American Indian	5	0%
Asian	25	2%
Caucasian-Hispanic	39	4%
Hispanic/Latino	44	4%
Unknown/Not Reported	9	1%
Other	32	3%
RHEUM DISEASE REPORTED		
Rheumatoid arthritis	606	58%
Sjogren's disease	201	19%
Other	198	19%
Systemic lupus erythematosus	162	16%
Systemic sclerosis	136	13%
Psoriatic arthritis	58	6%
Idiopathic inflammatory myopathy	46	4%
Ankylosing spondylitis	25	2%
Vasculitis	24	2%
REASON FOR CAM USE		
Pain management	256	24%
Other (please specify)	89	8%
Overall wellness	151	14%
Reducing inflammation	190	18%
Improving fatigue	16	2%
Improving joint function	60	6%
Stress relief	20	2%
Improving sleep	14	1%
Complementing prescribed medication	60	6%
Weight loss	5	0.50%
HIGHEST EDUCATION LEVEL		
Elementary	3	0%
High School	185	18%
College	482	47%
Master's Degree	260	25%
Doctorate or higher	102	10%
EMPLOYMENT STATUS		
Student	12	1%
Employed part time	83	8%
Employed full time	321	31%
Retired	503	49%
Unemployed	114	11%
ANNUAL INCOME		
$40,000-99,000	369	38%
$0-39,000	284	29%
$100,000-$199,000	244	25%
>200000	69	7%
INSURANCE		
Private	470	45%
Medicare	513	50%
Medicaid	46	4%
Uninsured	6	1%
CAM FAMILIARITY		
Somewhat familiar	439	36%

reported was rheumatoid arthritis (58%) followed by Sjogren's disease (19%). A high proportion of patients reported CAM usage but many were not familiar with CAM and 76% of patients did not find CAM very accessible. Most patients used the internet or social media as their primary source of information on CAM (40%). Half of the patients had Medicare insurance; of these patients, 26% reported daily CAM usage. There was no difference in CAM usage when comparing Medicare vs. non-Medicare patients ($p > 0.05$). Asian respondents reported high daily usage of CAM while Black

23652205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

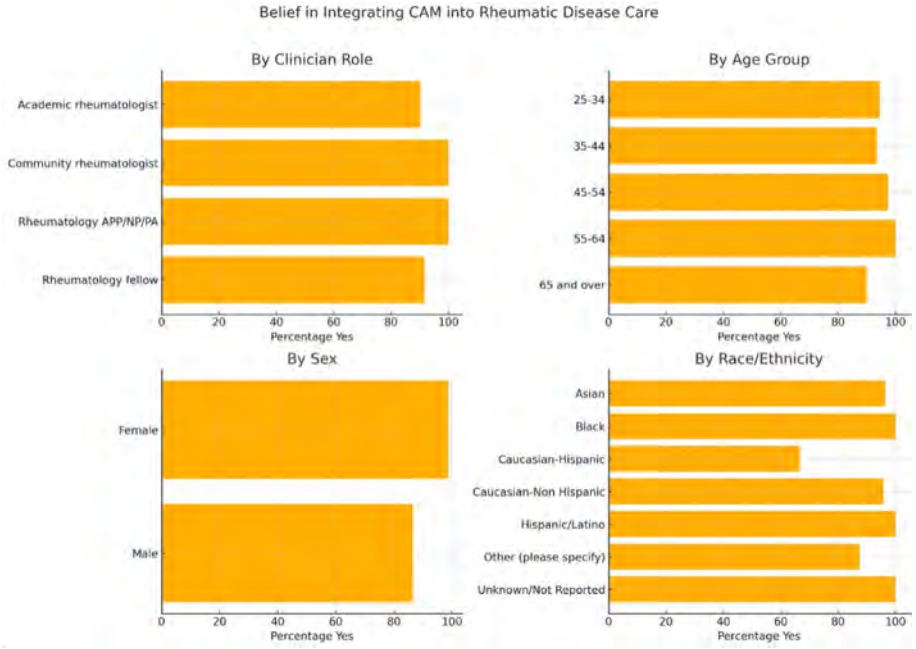


Figure 1: Clinician Belief in Integrating CAM into Rheumatic Disease Care

respondents had a lower daily usage compared to other groups (p=0.02). While patients with higher level education were more likely to use CAM (doctorate or higher with daily: 37.5% and monthly: 12.5% CAM use, master's and college degrees: 35% daily and 7% monthly use), individuals with high school or less education were more likely to never use CAM (35%).

A total of 128 rheumatologists across the United States completed the clinician survey. The majority of respondents were community rheumatologists (47%) and academic rheumatologists (40%). Most were female (66%) and the most common racial background was Asian (42%) and Caucasian-Non Hispanic (38%). Notably, 95.2% of respondents expressed support for integrating CAM therapies into standard rheumatology practice, indicating strong professional interest across practice settings.

Conclusion: CAM usage is prevalent amongst the rheumatic patient population but many patients do not find CAM very accessible and usage varies with different races/ethnicities and education levels. Future implementation needs to focus on more accessible CAM programs. As these patients follow regularly with their rheumatologists, the strong clinician interest for CAM integration into standard rheumatologic care is an opportunity to develop structured education and provide evidence-based resources for patients.

Disclosure: A. Ali: None; **S. Sun**: None; **F. Shaikh**: None; **T. Katsumoto**: Beyond Meat, 12, Unrestricted grant, Sanofi, 5; **N. Shah**: Beyond Meat, 5, Impossible Foods, 11, Oura Ring, 11, Upside Foods, 11; **K. Trotter**: American College of Rheumatology, 1, Gsk, 1, Iridium, 6; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1.

Abstract Number: 1249

Association Between Positive Emotions and Physical Function in Early Rheumatoid Arthritis Patients

Burcu Aydemir[1], Jing Song[2], Lutfiyya muhammad[1], Dorothy Dunlop[3], Rowland Chang[1], Wendy Marder[4], Kevin Deane[5], Clifton Bingham[6], Vivian Bykerk[7], Robert Edwards[8], Judy Moskowitz[1] and Yvonne Lee[9], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Northwestern University Feinberg School of Medicine, Worthington, MN,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[3]Northwestern University Feinberg School of Medicine, Chicago, [4]University of Michigan, Ann Arbor, MI, [5]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [6]Johns Hopkins University, Baltimore, MD, [7]Hospital For Special Surgery, New York, NY, [8]Brigham and Women's Hospital & Harvard Medical School, Boston, MA, [9]Northwestern University, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1. Demographics and Clinical Characteristics of Early RA Patients (n= 106).

	Value
Age, years	51.5 ± 16.5
Female, %	80
White, %	76
Body mass index, kg/m^2	28.8 ± 7.3
RA symptom duration, months	10.8 ± 4.8
Clinical disease activity index (0-76)	17.8 ± 11.6
Swollen joints count (0-28)	4.2 ± 3.4
Tender joint count (0-28)	6.4 ± 6.6
Patient global disease activity (0-10)	3.5 ± 2.5
Assessor global disease activity (0-10)	3.8 ± 2.1
NSAID use, %	21
Steroid use, %	24
DMARD use, %	
Methotrexate	68
Non-methotrexate	19
PROMIS Physical Function, t-score	45.0 ± 8.1
PROMIS Depression, t-score	48.3 ± 7.7
PROMIS Pain Intensity (0-10) ‡	3.8 ± 2.1
Positive Affect subscale (10-50)	31.7 ± 8.0

Note. Value is mean ± standard deviation or %. ‡PROMIS—Global Health 7 assesses pain on average using a numeric rating scale. DMARD, disease modifying antirheumatic drug. PROMIS, Patient-reported outcomes measurement information system.

Table 2. Results of Multivariable Linear Regression Model Estimating Adjusted Association between Positive Affect with Physical Function (n= 106).

Variables	Adjusted Model		
	β	95% CI Φ	p-value
Positive affect €	**1.6**	**0.72, 2.6**	**< 0.001**
Age (years)	**-0.09**	**-0.17, -0.01**	**0.023**
Sex (Female)	-3.0	-6.1, 0.12	0.059
Body mass index (kg/m^2)	-0.17	-0.34, 0.00	0.052
Symptom duration (months)	2.2	-0.63, 5.0	0.13
Swollen joint count (0-28)	0.29	-0.10, 0.69	0.14
Pain Intensity (0-10)	**-1.5**	**-2.2, -0.84**	**< 0.001**
Depression (t-score)	-0.04	-0.22, 0.14	0.7

Φ Confidence intervals (CI) that do not include zero indicate that the effect of that predictor on the outcome is not zero—statistically significant at p < .05.
€ Per 5-unit increase in Positive affect scale corresponded to a 1.6-point improvement in PROMIS Physical Function.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease that can significantly impair physical function and quality of life. While physical symptoms such as joint pain and swelling are primary drivers of disability, psychosocial factors, including emotional well-being, may also influence functional outcomes. Positive affect—defined as the experience of pleasurable emotions and mood—has been associated with better health outcomes in various chronic conditions, but its relationship with physical function in RA, especially in the early stages of the disease, is not well understood. Gaining insight into this relationship early in the disease course is critical, as it may inform more integrated approaches to treatment and improve long-term functional outcomes. This study aimed to evaluate the association between positive affect and physical function in individuals with early, active RA.

Methods: Cross-sectional baseline data were analyzed from adults with early RA enrolled in the on-going Central Pain in RA 2 (CPIRA-2) study. Eligible participants met the ACR/EULAR 1987 or 2010 criteria for RA, had persistent joint symptoms for ≤ 24 months, and active disease. Physical function was assessed by the PROMIS physical function questionnaire, which evaluates the functional capabilities of various body regions and performance of activities of daily living; higher scores indicate better physical functioning. Positive affect was measured with the positive affect subscale of the PANAS self-report questionnaire, a 10-item scale assessing positive emotions such as joy, enthusiasm, and alertness; higher scores reflect greater positive affect. PROMIS instruments were also used to assess symptoms of pain and depression. Descriptive statistics summarized demographic and clinical characteristics. Linear regression models were conducted to estimate unadjusted and adjusted associations between positive affect and physical function. Adjusted models controlled for age, sex, body mass index, swollen joint count, symptom duration, pain, and depression.

Results: Our sample included 106 patients (80% female, 76% white) with mean (SD) age of 51.5 (16.5) years, BMI of 28.8 (7.3) kg/m^2, and RA symptom duration of 10.8 (4.8) months (Table 1). Approximately 61% had mild to severe functional limitations (*t-score* ≤ 45). In unadjusted analysis, greater positive affect (β = 2.4 [95% CI 1.6 to 3.3]) was associated with better physical function. In an adjusted linear regression model, greater positive affect remained associated with physical function; younger age, and lower pain intensity were also significantly associated with better physical function (Table 2).

Conclusion: Greater positive affect was associated with better physical function in patients with early RA, even after adjusting for clinical and demographic factors. Longitudinal investigations are needed to better assess the true directionality of these relationships. Our findings suggest that interventions integrating strategies to enhance emotional well-being alongside effective pain management may help to improve and maintain physical function during the early stages of RA.

Disclosure: B. Aydemir: None; **J. Song**: None; **L. muhammad**: None; **D. Dunlop**: None; **R. Chang**: None; **W. Marder**: None; **K. Deane**: Inova Diagnostics, 1; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **V. Bykerk**: None; **R. Edwards**: None; **J. Moskowitz**: None; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1.

Abstract Number: 1250

Patient Perceptions of the National Tele-Rheumatology Program: A Mixed Methods Study

Alicia Hamblin[1], **Catherine Nasrallah**[2], Cherish Wilson[3], Bernard Ng[4] and gabriela Schmajuk[5], [1]UCSF, San Francisco, CA, [2]University of California San Francisco (UCSF), San Francisco, CA, [3]UCSF / SFVA, San Francisco, CA, [4]Lexington VA, University of Washington, Seattle, [5]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Tele-Medicine Satisfaction Questionnaire Scores for random sample of Veterans participating in the NTRP (N=160)

	Score (Mean (SD))	Score Range (Low-High)
Overall Satisfaction	57.5 (9.6)	14-70
Subdomains		
Quality of Care	32.3 (5.9)	8-40
Similarity to Face to Face	20.8 (3.4)	5-25
Perception of Interaction	4.4 (0.8)	1-5

Table 2: Generated themes with exemplary quotes according to the Healthcare Quality Model (n=102)

Healthcare Quality Model Construct	Themes	Quotes
Safety	Safety from exposures and infections	*"Everything moves so swiftly with this program. It also provides some safety from covid exposure."*
Effectiveness	Effective treatment	*"Everything seems to be going well. I've only seen them one time but the medicine seems to be helping. I like my Dr."*
	Satisfaction with visit outcomes	*"I'm hopeful it'll help. It was good on the teleconference. He did a great job getting it done."*
	Thorough assessment/evaluation	*"I really like this. I thought this was the best evaluation I've ever received. I really liked this Dr. He's amazing! He was very thorough."*
	Experienced/skilled physician	*"Dr. [name] is absolutely the best Dr. at the VA. Very knowledgeable, very approachable, very involved, and very caring."*
	Dissatisfaction with visit outcomes	*"To be honest it was a waste of time. I didn't feel like a lot got solved and it didn't seem like he understood my condition."*
	Dissatisfaction with treatment	*"I feel like we're not making any progress. I don't think I'm improving, and I think it's better to see a Dr. in person."*
	Limited visit time	*"I didn't get to ask all of the questions I wanted to."*
Efficiency	Collaboration between staff members	*"Having the nurse there was great too, you won't find a better nurse. The way they interacted, you would've thought they've been working together for years. It was top notch. I just want this program to keep going... continuity is my drum beat."*
	Organized process	*"It was pretty straight forward. The transition from medical person to Dr. was very smooth"*
	Convenience	*"It was very convenient. I wish more Dr.'s were like [physician name], you have to jump through so many hoops with other Rheumatologists.?*
	Time saving	*"I live 150 miles from the VA so it definitely saved me time."*
	Ease of use	*"It's easy enough to get on and I'm electronically challenged."*
	Lack of clarity on the visit process	*"I would like a better explanation of how it works before the visit starts."*
	Technical difficulties	*"I wish I could see him in person and sometimes it's kind of hard to get on the telehealth call. Sometimes it's hard to hear as well."*
Timeliness	Fast referral/scheduling	*"I'm glad I got an appointment so quickly. it was good."*
	Prescription delays	*"I still haven't received my new medication so it's a little slow moving."*
Patient Centeredness	Supportive team	*"The program has been Johnny on the spot. You're all proactive and I appreciate everything you guys do. It doesn't feel like I'm fighting an uphill battle anymore."*
	Focused on patient needs	*"It fits my needs. I don't have a lot of issues managing my disease, so it works. My Dr. schedules my appointments regularly and I'm overall happy with it."*
	Attentiveness to patient	*"Dr. [name] is amazing. He listens and really takes his time with me. The whole program has been great so far. I'm happy."*
	Comfortable discussion	*"It was better than I thought. Dr. [name] is great and made me feel very at ease."*
	Empathetic and supportive Physician	*"I want to marry him. Does that answer your question?... He's a great Dr... He makes an extra effort."*
	Preference for in-person visits	*"Those are things a Dr. would notice if we were in person so it's hard to not have that face-to-face care."*
	Discomfort with virtual care	*"I'll never do it again. I was really upset when I heard it was a video visit. I want a person; I can't stand this digital useless stuff."*
	Lack of physical examination	*"I really needed a physical exam, and I just can't get that over telehealth."*
	Lack of face-to-face interaction	*"I like the face-to-face interaction better. It's nice to shake your Dr.'s hand."*
Access and equity	Accessible rheumatology care	*"It's been hard to be seen and having that option is incredible. Community care isn't even an option so it's huge for us here. The way this program's set up is wonderful"*
	Difficulty contacting physicians	*"It's a little challenging to reach my Dr. if I have any follow-up questions about my meds."*

*Positives

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Joint display analysis according to the Healthcare Quality framework

Healthcare Quality Construct	TSQ statements
Safety	–
Effectiveness	1. My healthcare provider is able to understand my healthcare condition. 2. Overall, I am satisfied with the quality of service being. 3. I find telemedicine an acceptable way to receive healthcare services. 4. I think the healthcare provided via telemedicine is consistent. 5. I will use telemedicine services again.
Efficiency	1. I can hear my healthcare provider clearly. 2. I can easily talk to my healthcare provider. 3. I can see my healthcare provider as if we met in person. 4. Telemedicine saves me time travelling to hospital or a specialist clinic.
Timeliness	–
Patient centeredness	1. I do receive adequate attention 2. I feel comfortable communicating with my healthcare provider. 3. Telemedicine provides for my healthcare need.
Access and equity	1. I obtain better access to healthcare services by use of telemedicine. 2. I do not need assistance while using the system

Background/Purpose: The national shortage of rheumatology clinicians disproportionately affects over 2.7 million rural Veterans with already limited access to healthcare. To address this gap, the National Tele-Rheumatology Program (NTRP) was developed to connect Veterans with rheumatologists via telehealth. This study aimed to evaluate veteran patient satisfaction with the NTRP using a convergent mixed method analysis.

Methods: We invited a random sample of Veterans who had at least 1 rheumatology encounter via the NTRP to participate in telephone surveys. The first group completed the Telemedicine Satisfaction Questionnaire (TSQ), a validated 14-item instrument assessing quality of care, interaction, and satisfaction. The second group provided qualitative feedback through brief open-ended questions about the NTRP ("*What are things that you liked about the program?*" and "*What are things that you did not like about the program?*"). Quantitative data were analyzed using descriptive statistics and qualitative data were analyzed using a multi-stage thematic approach. Data were integrated through joint display analysis framed by the Healthcare Quality Framework (HQF), including domains of safety, patient-centeredness, effectiveness, efficiency, timeliness, and access and equity.

Results: A total of 160 patients responded to the TSQ (86.9% male, mean (SD) age 63.3 (14.7)). Responses reflected moderate to high satisfaction across all survey items (**Table 1**). 102 patients responded to the open-ended questions (79.4% male, mean (SD) age 63.8 (14.6)). Major themes and corresponding quotes are shown in **Table 2**: Veterans expressed high overall satisfaction with the NTRP, highlighting effective treatments, strong coordination, and the convenience of remote care. Many valued the program's efficiency, safety, and time-saving benefits. However, concerns emerged around technical difficulties, limited visit duration, and the absence of physical examinations. A subset of patients also preferred in-person care, underscoring the need for a tailored approach. The joint display analysis, framed by the HQF (**Table 3**), revealed concordant findings from the survey and open-ended questions, though the TSQ was limited in capturing negative perceptions towards the program around safety and timeliness.

Conclusion: Overall, Veterans reported high satisfaction with the NTRP, especially in domains of quality, effectiveness, and efficiency. Moving forward, efforts should aim to streamline logistics and refine patient selection to ensure telehealth is matched to clinical need and individual preferences. These findings can help inform future telehealth program design and implementation across other specialties serving rural populations.

Disclosure: A. Hamblin: None; **C. Nasrallah**: None; **C. Wilson**: None; **B. Ng**: None; **g. Schmajuk**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1251

Steroids and Me (Sam): engaging and educating steroid-treated patients via patient advocacy partnerships and internet search channels.

Michelle Petri[1], **Martha Stone**[2], John Stone[3], meredith Marinaro[4], Matt Wilkinson[5], Walter Lentfert[6], Camille Kotton[7], Jeffrey Gelfand[8], Jane McDowell[9] and Tricha Shivas[10], [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]Steritas, LLC, Concord, MA, [3]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [4]Novartis, Hartford, CT, [5]UpThereEverywhere, London, United Kingdom, [6]UpThereEverywhere, Charlotte, NC, [7]Harvard Medical School, Boston, MA, [8]UCSF Department of Neurology, Mill Valley, CA, [9]Queens University Belfast, Belfast, United Kingdom, [10]Foundation for Sarcoidosis Research, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: We report on two years of engagement with Sam, a patient-facing program to optimize the use of glucocorticoids and discontinue them when possible. We present aggregated data describing steroid-treated who seek, find, and engage with Sam from two channels: 1) Patient Advocacy Partnerships; and 2) Organic search.

Methods: The design and development of Sam included four steps:

1. Resource Review. A survey of the medical literature and internet for current, scientifically rigorous, patient-focused content on steroid use.
2. Needs Assessment. Workshops with patient advocacy groups and industry leaders; meetings with patient advocates; focus groups with patients; and meetings with industry experts.
3. Construction of portal. Optimized for mobile devices, Sam is co-created with patients and physicians across multiple diseases. User testing and journey validation for learning and tracking are at the core of the platform.
4. Development of learning modules, video snippets, behavioral nudges, and adverse event (AE) tracking capabilities.

Engagement (sample). Patient Advocacy and Google Search results to be updated

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disease specific (sample) Patient Advocacy and Google Search results to be updated

Sam is a companion that provides video and written educational materials and patient reported side effect tracking. The educational content and AE monitoring align with clinical outcome assessments that measure steroid toxicity: Glucocorticoid Toxicity Index (GTI), the GTI-Metabolic Domains (GTI-MD), and the GT-SNAPSHOT, a baseline score of steroid burden.

Results: The engagement of patients with Sam is reported through two channels.

First, the 2025 Patient Advocacy Partnerships include those with the Vasculitis Foundation, the Sarcoidosis Research, the Lupus Research Alliance, IgG4ward! Foundation, Global Asthma & Airways Patient Platform, and the Crohn's and Colitis Foundation. These alliances with advocacy groups have yielded the following insights:

- Strong engagement in learning about steroid-toxicity
- Major interest in tapering, how to talk with doctors, neuropsychiatric side effects
- Multiple articles read
- Multiple side effects tracked
- Substantial engagement and elevated session time

Second, we evaluated 2025 data from individual visitors to Sam who use organic internet searches to learn about a specific steroid induced condition. For example, the query "steroids and brain fog" yielded lessons that patients are:

- Actively seeking knowledge about a steroids in conjunction with one specific side effect
- Successfully finding knowledge on Sam because on high search positions in Google
- Fully engaging in education based - extensive "time spent" on each topic

Conclusion: Steroids and Me (Sam) fills an unmet need for patients who grapple with steroid treatment. Sam engages and informs lay users in plain language, resulting in deeper understanding of the value and pitfalls of steroids. Sam includes steroid side effect mitigation and methods for doctor/patient discussions about safe steroid tapers. Patients from two essential channels (patient advocacy groups and organic search) engage with this unique, highly-curated resource provides education about steroids that leads to patient activation for healthy engagement around steroid use.

Disclosure: M. Petri: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **M. Stone**: argenx, 2; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **m. Marinaro**: None; **M. Wilkinson**: None; **W. Lentfert**: None; **C. Kotton**: None; **J. Gelfand**: None; **J. McDowell**: None; **T. Shivas**: None.

Abstract Number: 1252

Can LLMs Categorize Patient Priorities Like Humans? Comparing AI and Human Coders in Arthritis Nominal Group Discussions

Melissa Mannion[1], Bryce Thornton[1], Bella Mehta[2], Ronan O'Beirne[1], Emily Smitherman[1], Livie Timmerman[3], Shilpa Venkatachalam[4], Jeffrey Curtis[1] and John Osborne[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ, [3]University of Alabama at Birmingham, Gardendale, AL, [4]Global Healthy Living Foundation, New York, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Identifying informational needs of individuals with inflammatory arthritis is critical to enhancing communication and supporting shared decision making between patients, caregivers, and providers. However, qualitative methods require significant human effort, time, and specialized software. Our goal was to determine how effectively a large language model (LLM) could classify thematic categorization with human-labeled data from 2 nominal group technique (NGT) studies of individuals with inflammatory arthritis.

Table 1: Human and large language model (LLM) – assigned themes by participant group in 2 nominal group studies of patient informational needs

Adolescents with JIA		Parents of children with JIA		Adults with inflammatory arthritis	
Human-labeled	LLM-labeled	Human-labeled	LLM-labeled	Human-labeled	LLM-labeled
Cost/Access	Cost/Access	Cost/Access	Cost/Access	Alternative nondrug treatments	Alternative nondrug treatments
Disease Risks	Disease Risks	Disease Risks	Disease Risks	Communication	Communication
Efficacy	Efficacy	Efficacy	Efficacy	Coping	Coping
Lifestyle Effects	Lifestyle Effects	Lifestyle Effects	Lifestyle Effects	Knowledge of Disease	Knowledge of Disease
Medication Administration	Medication Administration	Medication Administration	Medication Administration	Knowledge of Drugs	Knowledge of Drugs
Medication Benefits	Medication Benefits	Medication Benefits	Medication Benefits	Knowledge of Tests	Knowledge of Tests
Medication Interaction	Medication Interaction	Medication Interaction	Medication Interaction	Medication Costs	Medication Costs
Medication Monitoring	Medication Monitoring	Medication Risks	Medication Risks	Right Doctor	Right Doctor
Medication Risks	Medication Risks	Reason	Reason		
Preference	Preference	Trust	Trust		
Reason	Reason		Medication Monitoring		
Support	Support				

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: LLM-Human Interrater Reliability Metrics in Thematic Coding of NGT Responses

Model	Cohen's Kappa: LLM vs Grader 1	Cohen's Kappa: LLM vs Grader 2	Accuracy: LLM vs Grader 1	Accuracy: LLM vs Grader 2	Macro F1 Score: LLM vs Grader 1	Macro F1 Score: LLM vs Grader 2	Krippendorff's Alpha (LLM, Grader 1, Grader 2)	Cohen's Kappa: Grader 1 vs Grader 2
Adolescent NGT groups								
Llama 3.1 8B	0.701	0.604	0.733	0.65	0.692	0.606	0.627	0.574
DeepSeekR1 14B	0.759	0.644	0.783	0.683	0.759	0.638	0.66	0.574
GPT-4.1	0.796	0.719	0.817	0.75	0.802	0.715	0.697	0.574
GPT-4o	0.76	0.684	0.783	0.717	0.771	0.669	0.674	0.574
GPT o4-mini	0.796	0.72	0.817	0.75	0.815	0.734	0.698	0.574
GPT o3-mini	0.795	0.7	0.817	0.733	0.826	0.705	0.691	0.574
Parent NGT groups								
Llama 3.1 8B	0.614	0.466	0.676	0.541	0.552	0.347	0.559	0.593
DeepSeekR1 14B	0.781	0.571	0.811	0.622	0.814	0.412	0.65	0.593
GPT-4.1	0.747	0.474	0.784	0.541	0.698	0.339	0.607	0.593
GPT-4o	0.841	0.535	0.865	0.595	0.831	0.347	0.657	0.593
GPT o4-mini	0.936	0.625	0.946	0.676	0.886	0.504	0.719	0.593
GPT o3-mini	0.904	0.562	0.919	0.622	0.833	0.411	0.687	0.593
Adults with inflammatory arthritis NGT								
Llama 3.1 8B	0.819	0.642	0.852	0.704	0.79	0.615	0.734	0.735
DeepSeekR1 14B	0.955	0.779	0.963	0.815	0.976	0.78	0.824	0.735
GPT-4.1	1	0.735	1	0.778	1	0.759	0.823	0.735
GPT-4o	0.955	0.736	0.963	0.778	0.974	0.758	0.809	0.735
GPT o4-mini	0.955	0.736	0.963	0.778	0.974	0.758	0.809	0.735
GPT o3-mini	0.955	0.736	0.963	0.778	0.974	0.758	0.809	0.735

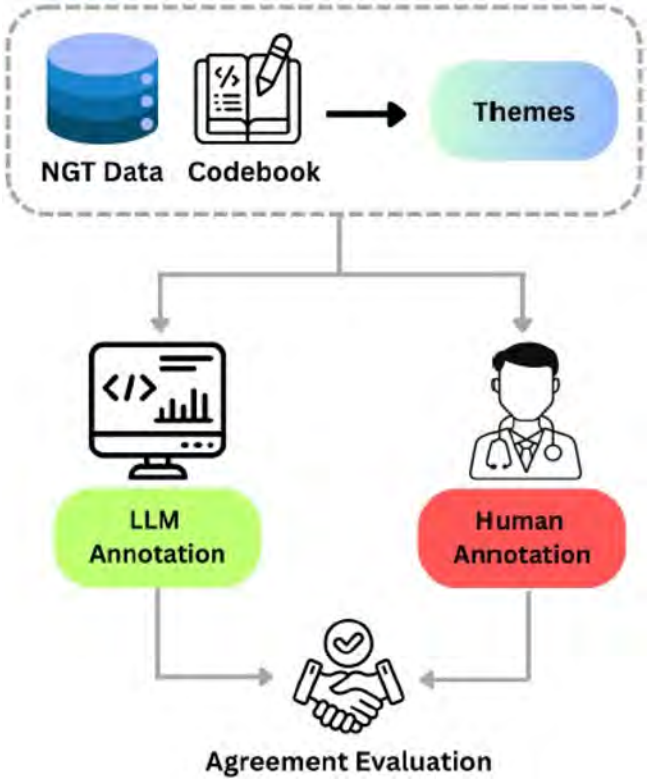


Figure 1: Workflow for Theme Assignment and Agreement Evaluation Between Human Coders and LLMs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We utilized results from 2 separate NGT studies on the informational needs of individuals with inflammatory arthritis. The first identified information patients want prior to medication changes for juvenile idiopathic arthritis (JIA), including 2 virtual parent groups, 1 virtual adolescent group, and 1 asynchronous adolescent group. The second explored information priorities for adults living with inflammatory arthritis, collected over 6 virtual groups. Qualitative responses to the discussion questions were collected and ranked by participants. Responses were manually assigned themes by at least 2 members of the research team (gold standard). Six LLMs, including advanced proprietary models and open-source alternatives, were zero-shot prompted to assign a single best-fit theme from the human-generated codebook to each participant-generated statement. Model-assigned themes were compared to those assigned independently by 2 human coders. A match was defined as exact agreement between the model's theme and the human-coded themes. Performance was evaluated using accuracy, macro F1 score, Cohen's kappa, and Krippendorff alpha relative to each coder.

Results: The adolescent groups had 12 human-labeled and 12 LLM-assigned primary themes; the parent groups had 10 human-labeled and 11 LLM-assigned themes; the adult groups had 8 of each (Table 1). Model accuracy of theme assignment ranged from 65–82% for adolescent statements, 54–95% for parent statements, and 70–100% for adult statements (Table 2). Model agreement with human coders, measured by Cohen's kappa, ranged from 0.70–0.80 for adolescent statements, 0.47–0.94 for parent statements, and 0.64–1.00 for adult statements. Human interrater Cohen's kappa was 0.57 for adolescents, 0.59 for parents, and 0.74 for adults (Table 2).

Conclusion: LLMs can reliably approximate human coding of qualitative themes in NGT data, and in some cases showed stronger agreement with individual coders than the coders had with each other. Human- and model-assigned themes were often similar, with strong agreement across datasets. Models performed best when statements expressed clear, explicit themes but faced challenges with ambiguity or overlapping concepts. Performance was strongest for advanced reasoning models but remained robust across open-source and earlier-generation models. These findings support LLMs as scalable tools for thematic analysis in qualitative research. Future directions include refining prompts to assess statement salience and exploring LLM-guided theme discovery without predefined codebooks for flexible, data-driven identification of emerging concepts.

Disclosure: M. Mannion: None; **B. Thornton**: None; **B. Mehta**: Amgen, 1, Horizon, 1; **R. O'Beirne**: None; **E. Smitherman**: None; **L. Timmerman**: None; **S. Venkatachalam**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **J. Osborne**: None.

Abstract Number: 1253

Patient Reported Outcome Measures: Assessing Resident Physician Acceptance of the Routine Assessment of Patient Index Data 3 Survey and its Impact on Physician-Patient Relationship

Nisha Sapkota[1], Chana Birnbaum[2], Henna Levitansky[2], Yevheniia Andriushchenko[2], Saadia Malik[2], Melissa Andrade[2], Sarang Choi[2] and Sima Terebelo[2], [1]Interfaith Medical Center, One Broolyn Health, Brooklyn, NY, [2]Brookdale Hospital Medical Center, One Brooklyn Health, Brooklyn

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: When treating patients with rheumatological conditions, building a strong physician-patient relationship plays an important role in determining disease outcomes. The Routine Assessment of Patient Index Data 3 (RAPID3) is a patient reported outcome measure which is administered to patients in rheumatology clinics. We initiated use of the RAPID3 assessment in our clinic with the hypothesis that in addition to assessing patient reported outcomes, this tool would help residents better understand the disabling effects of rheumatological diseases and that it would also enhance physician-patient relationships by giving the patient a voice to express themselves and explain the impact of their diseases on their daily lives. This study analyzes the impact of RAPID3 on resident education, doctor-patient relationships, and patient care using a 360-degree assessment of both the resident physician and patient perspectives.

Methods: RAPID3 surveys were administered to all patients (regardless of diagnosis) during their clinic visit, with assistance as needed by the resident physician, and responses were discussed with the patient during the clinic visit, in two resident-staffed outpatient Rheumatology teaching clinics at our institution over a 6-month period. After the clinic visit, patient surveys were administered to patients by research volunteers (CB, HL) who were not part of the medical team. Anonymous surveys were also sent to all resident physicians after each clinic session. The surveys included both yes/no questions as well as 5-point Likert scale questions. The mean plus standard deviation was then calculated for each answer.

Table 1. Resident's responses to the questionnaire used to assess the educational and patient care value of RAPID3 survey. (n=37 resident sample size)

Questions:	Mean ± SD
1. The RAPID3 survey helps me understand my patient better.	4.081 ± 0.759*
2. The RAPID3 survey helps me understand the degree of disability associated with musculoskeletal disease in day to day living of my patient.	4.21 ±0.821*
3. The RAPID3 is a waste of clinic time; it does not help me better understand my patient.	1.94 ±0.941*
4. The RAPID3 slows down patient visits and makes me less efficient.	2.08 ±0.682*
5. From your perspective, are your patients more comfortable with you after the RAPID3 is administered?	0.864 ±0.346**
6. Is there any area which you feel that the RAPID3 does not adequately address?	0.054 ±0.226**
7. Does the RAPID3 enhance the doctor-patient relationship?	0.890 ±0.312**
8. Does the RAPID3 improve your communication with your patient?	0.946 ±0.226**
9. Would you want to see the RAPID3 as regular practice in the Rheumatology clinic moving forward?	0.972 ±0.165**

*Questions 1-4 used a five-point Likert scale, *strongly agree=5, agree=4, neither agree nor disagree=3, disagree=2, strongly disagree=1, Questions 5-9 used no=0 and yes =1.*
**Questions 5-9 used yes/no questions

Table 2. Patient responses to the questionnaire used to assess patients' opinions on the RAPID3 survey (n=148 patient sample size)

Questions:	Mean ± SD
1. The RAPID3 form makes me feel like my disease is better understood by my doctor	4.28 ± 0.738*
2. The RAPID3 helps me explain my disease to the treating doctor	4.24 ± 0.777*
3. The questions on the RAPID3 are too intrusive	1.67 ± 0.832*
4. The RAPID3 helps me explain my pain and level of ability in dealing with problems in my daily activity	4.42 ± 0.738*
5. The RAPID3 asks appropriate questions to help me describe how I am doing	4.33 ± 0.759*
6. The RAPID3 helps me feel more comfortable with the treating doctor	4.29 ±0 .730*
7. I want to see the RAPID3 used at every Rheumatology clinic visit from now on	4.19 ± 0.899*

*Questions used a five-point Likert scale, *strongly agree=5, agree=4, neither agree nor disagree=3, disagree=2, strongly disagree=1*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Resident Belief of Impact of RAPID3 on physician-patient relationships: 89.2% residents agreed/strongly agreed that RAPID3 helped them understand their patient better. 89.2% agreed that RAPID3 helped them get a deeper understanding of the degree of disability patients experience. 86.5% of residents felt that patients were more comfortable with them after completing the survey (Table1).

Resident Acceptance of RAPID3: 91.9% disagreed/strongly disagreed that RAPID3 is a waste of clinic time. 97.3% agreed that the RAPID3 should be a regular part of all future clinics (Table 1).

Patient Acceptance of RAPID3: 86.5% of patients agreed/strongly agreed that the RAPID3 should be used at every visit (Table 2).

Patient Belief of Impact of RAPID3 on physician-patient relationships: 89.9% of patients felt more comfortable with their physician after the survey. 93.3% of patients felt the survey helped the physician better understand the daily impact of disease (Table 2).

Conclusion: RAPID3 was well accepted among patients and residents. It serves as a helpful tool for residents (normally young and healthy) to realize the barriers that patients with rheumatologic and musculoskeletal diseases face. It helped improve patient-physician communication and helped patients feel more comfortable with their physician. Future research may include how to shorten the RAPID3 (i.e., which questions are superfluous) and try to administer RAPID3 regularly prior to visits to always prioritize patient reported outcomes.

Disclosure: N. Sapkota: None; **C. Birnbaum**: None; **H. Levitansky**: None; **Y. Andriushchenko**: None; **S. Malik**: None; **M. Andrade**: None; **S. Choi**: None; **S. Terebelo**: None.

Abstract Number: 1254

Symptom Burden and Treatment Experience in Fibromyalgia: Results From a National Patient Survey

Lesley Arnold[1], Zhao Yang[2], **Parul Houston**[2], Todd Grinnell[2] and Daniel Clauw[3], [1]University of Cincinnati College of Medicine, Cincinnati, OH, [2]Axsome Therapeutics, Inc, New York, NY, [3]Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia (FM) is a chronic, widespread pain disorder driven by dysregulated central pain processing which substantially impairs daily function and quality of life. Approved pharmacotherapies are limited, with no new options introduced in over a decade, and many patients continue to experience burdensome symptoms and impaired daily function despite treatment. A survey of US patients was conducted to understand the current lived experience of people with FM, including their diagnostic journey, impact of disease, and treatment experience.

Methods: The survey was conducted from August-September 2024 among adult patients (≥18 years old) in the US with self-reported FM diagnoses. Respondents, recruited by a third party across a wide range of demographic and care settings, completed a 30-minute online survey assessing diagnosis experience, symptom burden, treatment history, and symptom control.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The survey comprised 500 respondents (94% female). Mean age at diagnosis was 37 years. The average self-reported time of symptom onset was 17 years prior to the survey. On average, nearly 3 years passed between symptom onset and seeing a healthcare provider. Respondents were most often diagnosed by rheumatologists (42%), primary care providers (PCPs; 25%) and pain specialists (9%). Half reported their FM was currently managed by a PCP, 33% by a rheumatologist, and 13% by a pain specialist.

On average, respondents reported experiencing 6 symptoms in the past week; the most prevalent were pain (96%), fatigue (95%), and muscle stiffness/tenderness (88%). Although pain was most common, it was rated less burdensome than waking very tired and lacking energy. The most common comorbidities were anxiety (51%), migraine (48%), and depression (40%); patients reported 5 comorbid medical conditions on average. Most (93%) reported that FM interfered with their ability to accomplish weekly goals.

Among respondents, 46% were taking multiple medications for their FM, 36% were taking a single medication, and 19% had discontinued pharmacotherapy. Among current medications, off-label therapies were most common; most frequently SSRIs/SNRIs or gabapentin (30% each), cyclobenzaprine (20%), and trazodone or tramadol (13% each). Mean duration of use was ≥5 years for all medications, yet 57% of patients described their FM as not well- controlled. Among those who discontinued medication, 68% cited intolerable side effects and 51% lack of efficacy as reasons; cognitive impairment was the most common side effect leading to discontinuation. Nearly two-thirds of all respondents expected medication to offer only partial relief from their symptoms, and 77% expressed concern they would never be pain-free.

Conclusion: This survey found patients with FM frequently experience persistent, burdensome and impactful symptoms, even after years of treatment. Symptom relief and treatment satisfaction were limited, and expectations for future improvement were low. Use of off-label and combination therapies was high, and rates of discontinuation due to side effects or lack of efficacy were common. These findings highlight the continued substantial burden of FM and the need for more effective and better-tolerated treatment options.

Disclosure: L. Arnold: Axsome Therapeutics, 2, Ono Pharmaceutical Co., 2, Scilex, 2; **Z. Yang**: Axsome Therapeutics, Inc., 3; **P. Houston**: Axsome Therapeutics, Inc., 3; **T. Grinnell**: Axsome Therapeutics, Inc., 3; **D. Clauw**: Tonix, 2, 5.

Abstract Number: 1255

Lung Transplantation Outcomes for Pulmonary Sarcoidosis Compared to Idiopathic Pulmonary Fibrosis: A Single Institution Multisite Experience

Reena Yaman[1], Lisa Balistreri[2], Maximiliano Diaz Menindez[3], Sehreen Mumtaz[1], Megan Sullivan[3], Alexander Hochwald[1] and Florentina Berianu[1], [1]Mayo Clinic Florida, Jacksonville, FL, [2]Lee Health, Cape Coral, FL, [3]Mayo Clinic Arizona, Scottsdale, AZ

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pulmonary disease is present in most sarcoidosis cases with up to 10% of patients progressing to advanced lung disease.[1] Pulmonary sarcoidosis accounted for 2.5% of lung transplants in 2015. Idiopathic pulmonary fibrosis (IPF) is a much more common indication for lung transplantation.[2] Post-transplant outcomes for both indications are

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline (pre-transplant) characteristics of idiopathic pulmonary fibrosis and sarcoidosis groups. Statistically significant differences are designated by an asterisk (*).

	Idiopathic pulmonary fibrosis (n=26)	Sarcoidosis (n=13)	p-value
Age, years	65 (51-87)	65 (51-80)	0.66
Male sex	23 (88.5%)	11 (84.6%)	1.00
Smoking history	10 (38.5%)	6 (50.0%)	0.72
Pre-transplant radiographic pattern			
Usual interstitial pneumonia	16 (61.5%)	2 (15.4%)	0.008*
Nonspecific interstitial pneumonia	5 (19.2%)	2 (15.4%)	1.00
Hypersensitivity pneumonitis	1 (3.8%)	1 (7.7%)	1.00
Undefined interstitial disease	2 (7.7%)	5 (38.5%)	0.030*

presumed to be comparable.[1,2] The current study evaluates the experience and outcomes across multiple sites at a single institution.

Methods: All lung transplants occurring at any site between July 2017 and March 2023 were reviewed. Descriptive statistics were performed and compared between pulmonary sarcoidosis and IPF indications via Kruskal-Wallis and Fischer's Exact tests. Survival and pulmonary function test results were compared between groups. Kaplan-Meier curves and hazard ratios were used for survival comparison.

Results: Lung transplantation outcomes for 13 cases of sarcoidosis were compared to 26 age- and gender-matched IPF cases. The most common computed tomography pattern was usual interstitial pneumonia (61.5%) in the IPF group compared to undefined pattern (38.5%) in the sarcoidosis group. Baseline characteristics were otherwise comparable (Table 1). A higher proportion of sarcoidosis patients had improved post-transplant forced vital capacity compared to IPF patients although this difference was not statistically significant (Figure 1). Survival plateaued at 75% in both groups after 5 years with hazard ratio 0.56 (p=0.49) (Figure 2).

Conclusion: Lung transplantation is a feasible treatment strategy for pulmonary sarcoidosis and demonstrated comparable outcomes to IPF in this cohort. Rheumatologists treating sarcoidosis can therefore benefit from familiarity with current lung transplantation referral guidelines, disease-specific indications and contraindications, and multidisciplinary collaboration.

1. Kim JS, Gupta R. Lung transplantation in pulmonary sarcoidosis. *J Autoimmun*. 2023;149:103135. doi:10.1016/j.jaut.2023.103135

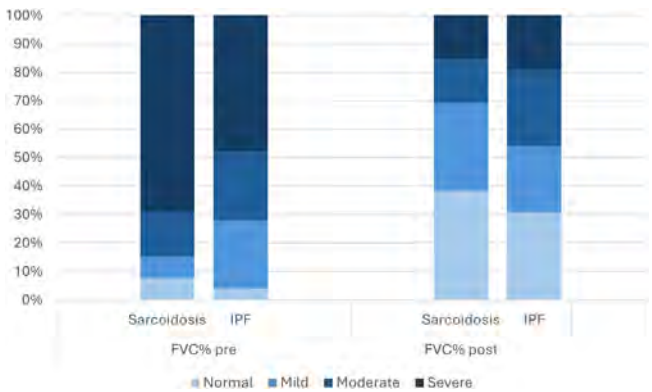


Figure 1. Forced vital capacity (FVC) pre- and post-transplant compared between sarcoidosis and idiopathic pulmonary fibrosis (IPF) groups. FVC scores were categorized as normal (>80%), mildly reduced (60-80%), moderately reduced (50-60%), and severely reduced (<50%). Missing data points were excluded from proportion calculations. Differences were not statistically significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

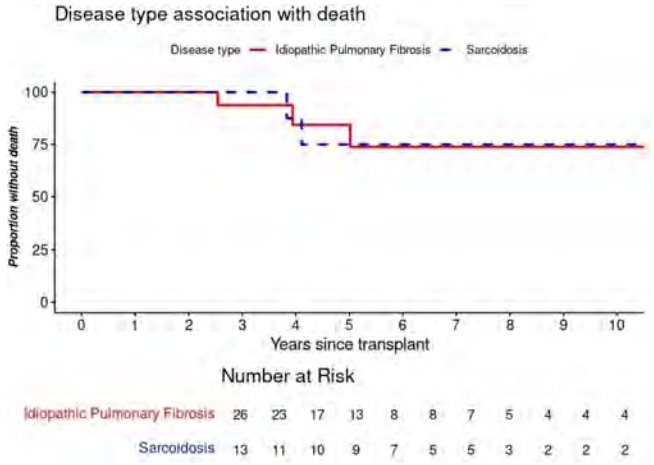


Figure 2. Kaplan-Meier survival curve demonstrating comparable post-transplant survival between idiopathic pulmonary fibrosis (red) and sarcoidosis (blue) groups.

2. Yusen RD, Edwards LB, Kucheryavaya AY, et al. The Registry of the International Society for Heart and Lung Transplantation: thirty-second official adult lung and heart-lung transplantation report—2015; focus theme: early graft failure. *J Heart Lung Transplant*. 2015;34(10):1264-1277. doi:10.1016/j.healun.2015.08.014

Disclosure: R. Yaman: None; **L. Balistreri**: None; **M. Diaz Menindez**: None; **S. Mumtaz**: None; **M. Sullivan**: None; **A. Hochwald**: None; **F. Berianu**: None.

Abstract Number: 1256

Quantitative Analysis of a Pilot Study: Integrating Behavioral Health Services for Patients with Rheumatic Diseases

Shannon Teaw[1], Jessica Link-Malcolm[2], Michelle Ghebranious Farag[3], Dorothy Patterson[2], Jenny Foster[4], Sofia Bereket[2], Urooj Wahid[2], Puneet Bajaj[2], Elizabeth Solow[2], Jennifer Barton[5] and Una Makris[6], [1]UT Southwestern Medical School, Dallas, TX, [2]UT Southwestern Medical Center, Dallas, TX, [3]McGovern Medical School at UT Houston, Houston, TX, [4]UT Southwestern Medical Center, Dallas, [5]VA Portland Health Care System/OHSU, Portland, OR, [6]UT Southwestern Medical Center and Dallas VA, Dallas, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatic diseases (RD) often experience chronic pain, along with comorbid depression and anxiety, which can be addressed using behavioral health (BH) interventions for motivating behavior change and increasing self-management skills. Despite potential benefits, efforts to integrate BH services into rheumatology clinics have been limited. We developed and piloted a single-arm BH program integrated within a rheumatology clinic to evaluate feasibility and trends towards improved patient-reported outcomes (PRO).

Methods: During their clinic visit, adult patients with RD were invited to participate in a pilot BH program. Interested patients were asked to select up to 3 BH goals of interest from a goal elicitation tool (Figure 1). Those who selected at least 1 of the 3 target goals that the BH specialist would focus on were eligible to participate in the telephone-based intervention, which consisted of up to 8, brief, patient-centered sessions, utilizing techniques such as motivational interviewing and mindfulness

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

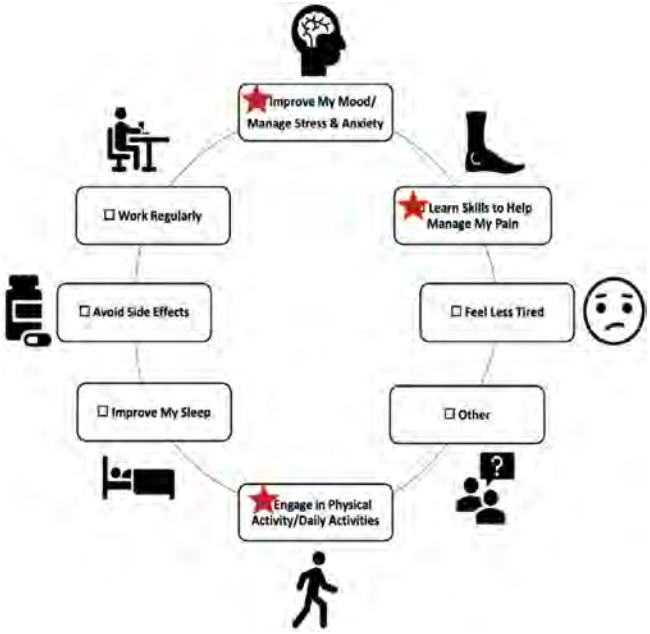


Figure 1. Goals Wheel. Stars indicate BH services offered.

meditation combined with psychoeducation and supplemental apps/videos. PROs for pain interference (PEG-3), pain catastrophizing, depression/anxiety (PHQ-4) and PROMIS measures of fatigue, quality of life (QoL), physical function, sleep and social satisfaction were collected at baseline and during the final BH session. Depending on the normality of distribution, Wilcoxon signed-rank or student T-tests were used to compare baseline and post-intervention scores.

Results: We enrolled 54 participants, 45 completed the baseline assessment, and 39 engaged in at least 1 BH session beyond baseline. Of these, 28 completed the program (i.e., completed a final assessment session). Among the completers, 79% were women and white. Osteoarthritis (32%), rheumatoid arthritis (21%) and psoriatic arthritis (18%) were the most frequent rheumatologic diagnoses. Fifty percent of the sample had a mental health diagnosis code. Most participants (52%) focused on the goal "Improve My Mood/ Manage Stress & Anxiety" and completed the program in 8 sessions (IQR 6, 8). At baseline (n=28), average PEG-3 score was 3.69/10 and PHQ-4 score was 3.32/12. There was improvement in pre-post mean change scores for PEG-3, pain catastrophizing, PHQ-4, fatigue, sleep and QoL; however, no improvement was noted in social satisfaction or physical function (Table 1).

Conclusion: In this pilot study, recruitment and delivery of an integrated BH program was feasible in a busy rheumatology clinic. We found promising trends toward improvement in PROs for several domains, including pain, pain catastrophizing and depression/anxiety. These results warrant future evaluation with a fully powered randomized controlled trial.

Patient Reported Outcomes (PRO)	Median baseline scores	Pre-Post change score	P-value
PEG-3 Pain interference	3.3	-1.14	*p = 0.002
Pain catastrophizing	9.0	-5.39	*p < 0.001
PHQ-4	3.0	-1.50	*p < 0.001
PROMIS Fatigue	14.5	-2.36	*p = 0.003
PROMIS Sleep	13.5	-2.64	*p < 0.001
PROMIS Quality of Life	3.0	0.39	*p = 0.04
PROMIS Social Satisfaction	16.0	1.29	p = 0.057
PROMIS Physical Function	17.5	0.50	p = 0.12

Pain, Enjoyment of Life and General Activity, PEG3 (0-10); Patient Health Questionnaire-4, PHQ4 (0-12); Patient-Reported Outcomes Measurement Information System (PROMIS) (4-20); *p<0.05

Figure 2. Patient Reported Outcomes (PRO) pre-post mean change scores, N=28; *indicates statistical significance

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Teaw: None; **J. Link-Malcolm**: None; **M. Ghebranious Farag**: None; **D. Patterson**: None; **J. Foster**: None; **S. Bereket**: None; **U. Wahid**: None; **P. Bajaj**: None; **E. Solow**: None; **J. Barton**: None; **U. Makris**: None.

Abstract Number: 1257

Integrated Behavioral Health Services for Patients with Rheumatic Diseases: Qualitative Analysis of a Pilot Study

Shannon Teaw[1], Jessica Link-Malcolm[2], Michelle Ghebranious Farag[3], Dorothy Patterson[2], Jenny Foster[4], Sofia Bereket[2], Puneet Bajaj[2], Urooj Wahid[2], Elizabeth Solow[2], Jennifer Barton[5] and Una Makris[6], [1]UT Southwestern Medical School, Dallas, TX, [2]UT Southwestern Medical Center, Dallas, TX, [3]McGovern Medical School at UT Houston, Houston, TX, [4]UT Southwestern Medical Center, Dallas, [5]VA Portland Health Care System/OHSU, Portland, OR, [6]UT Southwestern Medical Center and Dallas VA, Dallas, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatic diseases (RD) often cause pain, fatigue and disability. Depression and anxiety are prevalent comorbidities in RD and ideally managed with behavioral health (BH) strategies. Programs that integrate BH services into rheumatology remain underexplored. Our group conducted a single-arm pilot BH program integrated within rheumatology clinic. This qualitative study explores stakeholder perspectives on barriers and facilitators of integrating BH in rheumatology.

Perspectives on Behavioral Health (BH) Prior to Participating in pilot	Modality of BH Service Delivery and Procedures	Experiences / Perceived Benefits of BH Program	Sustainability and Value
•Participants mostly understood that **health behaviors** were important, but understanding the impact of **mood and anxiety** on health was less common. •Although some participants were well-versed in the connection between stress and RD flare-ups, they did not have the specific skills to change behavior.	•Several participants reported that having their rheumatologist provide a brief introduction about the BH program was helpful and convenient.	•Most participants identified the individualized, patient-centered and goal-focused approach by the BH specialist to be very beneficial.	•Participants reported continuing to use skills and techniques after the BH intervention was completed, as well as intent to use in the future. •Participants appreciated the ability to reference apps, websites, etc., as well as notes some took during sessions
•Participants understood that physical activity benefitted physical health, but they needed help implementing behavioral change to be more active.	•The majority of participants reported it was convenient to meet with the BH specialist in clinic immediately following their rheumatology appointment. •Many felt that meeting the BH specialist in person facilitated participation and rapport-building	•Specific BH skills/ techniques that participants reported were beneficial include mindfulness techniques and breathing exercises (both app-guided and self-guided).	•Some participants reported having shared what they've learned through the pilot program with family members and others, to pay-it-forward.
•Many participants voiced a general understanding that BH could be helpful but lacked specific knowledge and skills to apply it. •Some had never considered the role of BH in RD	•All but one of the participants (who preferred an in-person option) reported that the **telehealth option and short, 20 to 30-minute sessions** were convenient, as they removed transportation barriers and time/scheduling constraints	•Many participants appreciated the accountability associated with regular BH visits, which helped them to experience the benefits of regular practice (i.e., mindfulness, exercise, etc.) and to establish routine habits before managing on their own.	•Given the option, most participants report that they would find it helpful to have booster sessions to reinforce BH skills (q1-3months).
•A few participants expressed initial skepticism about the possibility of BH interventions to improve pain. •Participants, even those voicing skepticism, were open to learning non-medical approaches to managing pain/ flares.	•Two areas several participants identified as needing improvement in this pilot study were **survey burden** (these were required at each session) and **communication challenges** (i.e. contacting the BH specialist)	•Most participants reported improvement in how they viewed their ability to manage their rheumatic disease (i.e., increased confidence, motivation, hope, feelings of control) •The majority of participants also felt more cared for by the institution	•Participants generally agreed that they would pay their usual specialty co-pay if there were costs associated with continuing to receive the BHS. •In most cases this co-pay ranged from $20 to $75.

Figure 1. Rapid Qualitative Analysis (RQA) Matrix of Patient Interviews (N=27)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Perspectives on BH Prior to Participating in BH Program	• "I knew that being active as much as I can is very important to managing my disease. I had never thought before about... emotional triggers" • "Anytime I'm super stressed with work or something personal going on, that's when I'm more inclined to have a flare up." • "Prior to the study, I believed that they could be helpful but kind of lacked the understanding or guidance of how to implement such practices and behaviors."
Modality of BH Service Delivery and Procedures	• "I think that [rheumatologist] knew it would be good for me and that I would be open to it, too." •"If someone would have called me on the phone and told me about the program and I wasn't looking at them and talking to them, then I probably would have said no. Because she approached me in the office and had the demeanor that she did, then I was interested." • "We met in the office, so that was a good thing, and it was really helpful because she saw what I was going through, you know, physically saw."
Experiences / Perceived Benefits of BH Program	• "I felt like that kind of accountability was really helpful in forcing habits that I knew I could develop but never was very diligent about taking the time." • "I went in with no hope and no expectations because I had been told that a lot of my pain was not autoimmune and that it was fibromyalgia...for the breathing to make a difference from the go gave me hope. It never worked before, and she made it so easy to understand from the beginning and it affected my pain levels." • "Overall, I feel like it's really helped my interpretation of pain and how the pain makes me feel. I'm able to deal with it for longer periods of time. It's not as high or I guess as obvious as it used to be."
Sustainability and Value	• "I'm still using the meditation every day, the breathing every day... I think this is something that I'll use forever." • "When in pain or under stress, I will go into a breathing session without even thinking about it." • "I can do this on my own from what she taught me."

Figure 2. Illustrative quotes from Patient Interviews

Methods: Adult patients with any RD were invited to participate in a novel BH program during their rheumatology clinic visit. Participants completed a goal elicitation tool and met with the BH specialist after their visit to discuss the study and determine which of 3 eligible BH goals to focus on. Participants engaged in up to 8 weekly telephone sessions with the BH specialist. After the final session, participants completed a satisfaction survey and semi-structured interview to elicit feedback. Referring rheumatologists and the BH specialist were also interviewed. We used Rapid Qualitative Analysis to identify thematic domains and illustrative quotes.

Introduction and referral to BH	• All agreed that nursing and ancillary staff were an integral part of the introduction to the BH program and helped integrate the BHS in the clinic workflow. •All generally perceived patients as curious about the BH program and open to learning more. Perceived barriers included time, as well as patients not identifying as "sick enough" to require a BH program. •Rheumatologists' introductory pitch to patients is important for framing the program. "I think the way I couched it ...abated some of [the stigma] because I would talk about how [the patient] and I make a plan, but implementing that plan takes a different set of skills and that's where this person [the BH specialist] would come into play...so it wasn't so left field." Per the BH specialist, the rheumatologists' enthusiasm about the program helped minimize stigma.
Who are the most appropriate referrals for the BH program?	•All agreed that referral should not be restricted to certain rheumatic disease diagnoses. •There were slightly contrasting views between rheumatologists regarding the ideal candidate for BH intervention, with one stating a preference for patients with low-to-moderate disease activity. The other rheumatologist, who prior to the BH pilot would have focused on patients with inflammatory conditions, was surprised by the BH outcomes, "It was sort of surprising...it had a broader benefit than I would have expected." This rheumatologist, along with the BH specialist felt all-comers could benefit, "If a patient is in survival mode, it is hard to be in learning mode, but not impossible." •Referrals ultimately should be based on rheumatologist's discretion and patient motivation.
Perceived value of an integrated BH program	•The rheumatologists found value in having a trusted resource they could refer patients to who could assist them in implementing the BH aspects of their treatment plan and provide follow-up care to help the patients reach their goals. "Making small changes is very hard and often times we're asking patients to make major life changes. And it's hard... for patients to... even know where to begin." •Per the BH specialist, the most useful modalities were mindfulness meditation techniques, along with apps patients could utilize on their own time. The BH specialist tailored their approach to each patient and focused on building immediately actionable skills and consistent practice.
Suggestions on future integrated BH programs in rheumatology	•The BH specialist could provide actionable items addressing how the rheumatologist can take the progress a patient has made and apply to their treatment plan. •Establishing an automated referral process utilizing the electronic medical record (EMR). •Extending intervention duration and impact by providing booster sessions or check-ins q 1-3 months.

Figure 3. Rheumatologists and BH Specialist Interview Highlights

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 54 patients enrolled, 39 engaged in BH intervention sessions beyond baseline, and 27 completed post-intervention interviews. Interviewees were primarily female (77.8%) and White (81.5%), with an average age of 56 years. Participants (n=27) selected the following goals: managing mood or stress/anxiety (52%), managing pain (26%), and increasing physical activity (22%). We identified 4 thematic domains: pre-existing perspectives on BH, recruitment/delivery procedures, experiences/perceived benefits, and sustainability/value (Figure 1). While some understood the connection between BH and RD prior to the study, participants expressed a lack of specific skills/motivation to change behavior. Key benefits included the patient-centered, goal-oriented approach and accountability provided by regular sessions (Figure 2 lists illustrative quotes). When asked if BH services added value to their rheumatologic care, all interviewees responded positively, "Yes, definitely" (81%) or "Yes, I think so" (19%). The two rheumatologists and BH specialist provided unique perspectives on barriers and facilitators that could enhance future feasibility and success of a BH program (Figure 3).

Conclusion: The integration of an individualized, goal-focused BH intervention into rheumatology clinics is feasible and perceived as beneficial by patients, rheumatologists and the BH specialist. Results from this pilot program will inform the development of an RCT to evaluate clinical and behavioral outcomes in this population.

Disclosure: S. Teaw: None; **J. Link-Malcolm**: None; **M. Ghebranious Farag**: None; **D. Patterson**: None; **J. Foster**: None; **S. Bereket**: None; **P. Bajaj**: None; **U. Wahid**: None; **E. Solow**: None; **J. Barton**: None; **U. Makris**: None.

Abstract Number: 1258

Upadacitinib in the treatment of Rheumatoid Arthritis - Interstitial Lung Disease. National multicenter study of 25 patients in clinical practice.

Ana Serrano-Combarro[1], Belén Atienza-mateo[2], Leticia del Olmo Perez[3], Sara García-Perez[4], Guillermo Gonzalez Mozo de Rosales[5], Jose Rosas Gómez de Salazar[6], ana Urruticoechea-Arana[7], Andrea García-Valle[8], Jesús Loarce[9], Paula García-Escudero[10], Bryan Josué Flores Robles[11], Rafael B. Melero-González[12], Alicia Garcia[13], Maria Martín López[14], Patricia López Viejo[15], Maria Jose Perez Gaan[16], Nuria Vegas Revenga[17], Angel Garcia-Aparicio[18], M.Pilar Bernabeu Gonzalvez[19], Juan Moreno Morales[20] and Ricardo Blanco[21], [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, PALMA DE MALLORCA/BALEARES, Spain, [3]HGU Nuestra Señora del Prado, Talavera de la Reina, Talavera de la Reina, Spain, [4]Complejo Hospitalario de Vigo, Vigo, Spain, [5]Basurto University Hospital, Bilbao, Spain, [6]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [7]Rheumatology Division. Hospital Universitario Son Espases, Palma de Mallorca, Spain, [8]Rheumatology. Hospital General Río Carrión, Palencia, Castilla y Leon, Spain, [9]Ramón y Cajal University Hospital, Madrid, Spain, [10]Hospital Universitario Álava, Bilbao, Spain, [11]Hospital San Pedro, Logroño, Spain, [12]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [13]Rheumatologist, La Laguna, Spain, [14]Hospital 12 de Octubre, Madrid, Spain, [15]Hospital Severo Ochoa (Leganés), Leganes, Spain, [16]Hospital Universitario Virgen de las Nieves, Granada, Spain, [17]Galdakao- Usansolo University Hospital, Galdakao, Spain, [18]Hospital Universitario de Toledo, Toledo, Spain, [19]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [20]Hospital Universitario Santa Lucia Cartagena, Cartagena, Spain, [21]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept and rituximab are usually the recommended drugs. JAK inhibitors (JAKi) have demonstrated efficacy in RA,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Baseline characteristics of RA-ILD patients treated with UPA.

	UPA (n=25)
Age, years mean±SD	61±9
Women, n (%)	16 (64)
Smoker ever, n (%)	20 (80)
Time since ILD diagnosis, months, median [IQR]	34 [17-47]
RF; ACPA, n (%)	23 (92); 22 (88)
FVC (% of the predicted), mean±SD	88±16
DLCO (% of the predicted), mean±SD	68±23
UIP-like fibrotic pattern on HRCT, n (%)	11 (44)
Joint activity n (%)	23 (96)
Previous immunosuppressive therapy, n (%)	
Conventional*	23 (92)
AntiTNF drugs / Tocilizumab	12 (48); 7 (28)
ABA; RTX	11 (44); 4 (18)
Concomitant immunosuppresive therapy, n (%)	12 (48)
Concomitant antifibrotic therapy, n (%)	0 (0)

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; JAKi, JAK inhibitor; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia. *23 methotrexate, 5 sulfasalazine, 16 leflunomide, 7 hydroxychloroquine

especially tofacitinib and baricitinib. Nonetheless, evidence on eficacy efficacy of other JAKi like Upadacitinib (UPA) in RA-ILD is scarce. Our objective was to assess **a)** the effectiveness and **b)** the safety of UPA in RA-ILD patients.

Methods: National multicenter study of RA-ILD patients on treatment with UPA. We analyzed from baseline the following outcomes: **a)** forced vital capacity (FVC), **b)** diffusing capacity of the lungs for carbon monoxide (DLCO), **c)** high resolution computed tomography (HRCT), **d)** dyspnea (modified Medical Research Council scale), **e)** arthritis activity (DAS28-ESR), and **f**) sparing effect of glucocorticosteroids.

Results: We studied 25 patients (16 women/9 men; mean age 61±9 years) from clinical practice on treatment with UPA. Baseline demographic and clinical characteristics are shown in **Table**. All patients had received disease-modifying antirheumatic drugs (DMARDs) before UPA [conventional DMARDs (n=23; 92%), anti-TNF (12; 48%), Tocilizumab (7;28%), Abatacept (11; 44%) and Rituximab (4;18%)]. Mean baseline values of FVC and DLCO (% predicted) were 88±16, and 68±23, respectively. Patients were followed-up for a median [IQR] of 12 [6-18] months. The evolution of FVC and DLCO remained stable during the first 12 months **(Figure)**. At the end of the follow-up, available chest HRCT images improved/stabilized in all the patients. Stabilization or improvement of dyspnea was found in all the patients. Most patients [12 (67%)] showed articular remission or low activity. UPA was withdrawn in 5 (20%) patients due to ischemic heart disease (n=2), recurrent respiratory infections (n=1), zoster virus infection (n=1) and joint activity (n=1).

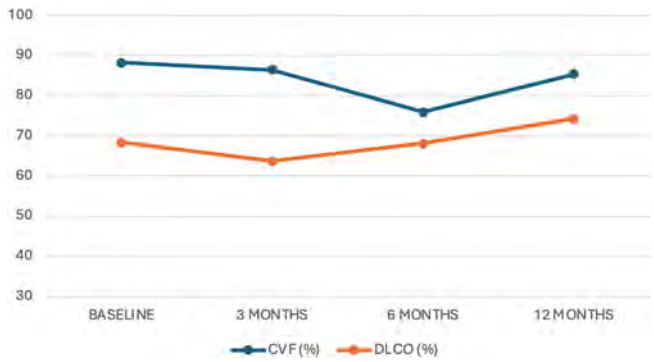


Figure. Evolution of pulmonary function tests (mean % of the predicted FVC and DLCO) in RA-ILD patients with UPA therapy at baseline and 12 months.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: UPA may be useful and safe in controlling the course of both pulmonary and joint disease in RA-ILD patients, even in cases refractory to ABA and/or RTX.

Disclosure: A. Serrano-Combarro: None; **B. Atienza-mateo**: None; **L. del Olmo Perez**: None; **S. García-Perez**: None; **G. Gonzalez Mozo de Rosales**: None; **J. Rosas Gómez de Salazar**: None; **a. Urruticoechea-Arana**: None; **A. García-Valle**: None; **J. Loarce**: None; **P. García-Escudero**: None; **B. Flores Robles**: None; **R. Melero-González**: None; **A. Garcia**: None; **M. Martín López**: None; **P. López Viejo**: None; **M. Perez Gaan**: None; **N. Vegas Revenga**: None; **A. Garcia-Aparicio**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 1, 2, 6, UCB, 6; **M. Bernabeu Gonzalvez**: None; **J. Moreno Morales**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1259

Patient and Caregiver Perspectives on the Burden of Disease in Uncontrolled Gout: A Cross-Sectional Survey Study

Angelo Gaffo[1], Bhavisha Desai[2], Abiola Oladapo[3], Nana Kragh[4], Rebekah Zincavage[5], Brad Padilla[5] and Naomi Schlesinger[6], [1]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [2]Sobi, Glastonbury, CT, [3]Sobi INC, Waltham, MA, [4]Sobi, Kongens Lyngby, Denmark, [5]Stratevi, Boston, [6]Spencer Fox Eccles School of Medicine, University of Utah, Salt Lake City, UT, USA, Salt Lake City, UT

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Many patients with uncontrolled gout (UG) experience symptoms despite being on urate-lowering therapy (ULT), often requiring support from informal caregivers. UG impacts patients and caregivers, yet research remains limited. This real-world study assessed the impact of UG on health-related quality of life (HRQOL) and activities of daily living (ADL) from the perspectives of patients, caregivers, and healthcare professionals in the United States (US). Results presented here focus on patients and caregivers.

Methods: A cross-sectional web-based survey was conducted among patients with UG and caregivers of such patients. Patients included adults (≥18 years) diagnosed with UG (a history of severe gout, defined as ≥2 gout flares within the last 12 months or presence of ≥1 gout tophus; and either currently taking a ULT or previously treated with uricase therapy in the past 18 months). Caregivers were unpaid adults currently caring for an adult with UG. Data collected included demographics, clinical characteristics, treatment information, and patient-reported outcomes (Work Productivity and Activity Impairment [WPAI] and 12-item Short Form Survey version 2 [SF-12v2]). Data were summarized descriptively.

Results: A total of 100 patients (63% male, mean [SD] age 54.3 [13.2] years) and 40 caregivers (73% female, mean [SD] age 55.1 [10.6] years) completed the survey (**Table 1**). Patients were currently using the following ULT treatments: allopurinol (49%), pegloticase (26%), febuxostat (20%), and probenecid (4%). Despite ULT treatment, 35% experienced tophi and 78% reported gout flares. 72% of patients reported a recent serum urate level of ≥6 mg/dL. HRQOL as measured by the SF-12v2 is reported in **Table 2**. Patients had a mean physical component summary (PCS) score of 37.3 (SD: 6.3) and mental component summary (MCS) score of 42.7 (SD: 10.3), which were "well below"[§] and "below" those of the general US population mean of 50 (SD: 10), respectively. The mean caregiver PCS score was 43.3 (SD: 11.7), which was "below" that of the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

	Patients (N=100)	Caregivers (N=40)
Age, years		
Mean (SD)	54.3 (13.2)	55.1 (10.6)
Median (range)	55 (20–80)	56 (30–75)
Gender, % (n)		
Female	37.0 (37)	72.5 (29)
Male	63.0 (63)	27.5 (11)
Caregiver relationship to patient, % (n)		
Spouse/partner	N/A	72.5 (29)
Adult child	N/A	17.5 (7)
Parent	N/A	5.0 (2)
Sibling/stepsibling	N/A	2.5 (1)
Aunt/uncle	N/A	2.5 (1)
Race/ethnicity, % (n)		
Asian or Pacific Islander	5.0 (5)	7.5 (3)
Black or African American	26.0 (26)	22.5 (9)
Hispanic or Latino	14.0 (14)	17.5 (7)
White	47.0 (47)	47.5 (19)
Other	8.0 (8)	2.5 (1)
Employment status, % (n)		
Full-time	46.0 (46)	52.5 (21)
Part-time/self-employed	14.0 (14)	15.0 (6)
Furloughed	1.0 (1)	0.0 (0)
Unemployed	29.0 (29)	30.0 (12)
Homemaker	10.0 (10)	2.5 (1)
Type of employment*, % (n)		
Desk/computer-based	65.6 (40)	N/A
Physically demanding	34.4 (21)	N/A
Number of tophi in the last 6 months**		
Mean (SD)	3.2 (1.7)	N/A
Median (range)	3 (0–8)	N/A
Number of flares in the last 6 months†		
Mean (SD)	3.8 (2.4)	N/A
Median (range)	3 (1–12)	N/A
Months since the last gout flare†		
Mean (SD)	1.6 (1.8)	2 (2.8)‡
Median (range)	1 (0–10)	1 (0–13)‡

*Of those employed (n=61)

**Of those who experienced tophi (n=35)

†Of those who experienced gout flares (n=76)

‡Months since the last gout flare presented for patients assisted by caregivers (n=29)

N/A: Question not asked

general US population, and the MCS score was 45.2 (SD: 11.8). Common issues associated with caring for a patient with UG were stress (40%), inability to carry out a daily routine (35%) and/or work a job (35%), and feelings of being overwhelmed (35%). Over 90% of caregivers reported feeling some level of exhaustion. Overall activity impairment was 60% for patients and 41% for caregivers, measured by the WPAI. Employed patients and caregivers reported 53% and 36% overall work impairment, respectively. Employed patients missed an average of 6.8 (SD: 9.8) hours of work in the past 7 days due to UG, while employed caregivers missed an average of 2.7 (SD: 3.6) hours caring for a patient (**Table 3**).

Conclusion: This is the first study to present data on caregiver burden associated with UG, highlighting significant challenges and reduced HRQOL for caregivers and patients with UG. Both reported HRQOL below the general US population with the largest impact in physical health-related domains, likely due to clinical manifestations of UG for patients, and for caregivers, the physical demands of caring for a patient. Employed individuals also experienced notable work impairment demonstrating the multifaceted impacts of UG.

Table 2. Patient and Caregiver SF-12v2 Scores

SF-12v2 Domain	Patients (N=100) Mean (SD)	Caregivers (N=40) Mean (SD)
Physical component summary (PCS) score	**37.3 (6.3)**	**43.3 (11.7)**
Physical functioning	35.3 (7.8)	41.7 (12.7)
Role - physical	38.5 (7.7)	43.5 (11.5)
Bodily pain	38.2 (9.0)	42.6 (13.5)
General health	38.2 (10.2)	45.0 (12.9)
Mental component summary (MCS) score	**42.7 (10.3)**	**45.2 (11.8)**
Vitality	45.4 (9.4)	49.1 (12.0)
Social functioning	40.5 (9.4)	41.8 (11.3)
Role – emotional	35.9 (10.3)	41.1 (13.9)
Mental health	42.5 (10.8)	45.9 (13.1)

[a]The SF-12v2 scores range from 0 to 100, with higher scores indicating better physical or mental health functioning. The scoring system uses a norm-based approach, where Physical Component Summary (PCS) and Mental Component Summary (MCS) combine the 12 domains in such a way that they compare to a national norm with a mean score of 50.0 and a standard deviation of 10. If the norm-based SF score is 10+ points below the mean, the disease exhibits physical or mental functioning "Well Below" the general population. If it is 5 points to <10 points below, functioning is "Below" average. And scores <5 points below are the "Same or Better" than average.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Patient and Caregiver WPAI Scores

	Patients	Caregivers
Hours worked in past 7 days*		
Mean (SD)	32.2 (10.9)	32.6 (12.2)
Median (range)	34 (0–50)	36 (0–55)
Missed work hours in the past 7 days due to UG*		
Mean (SD)	6.8 (9.8)	2.7 (3.6)
Median (range)	2 (0–40)	0 (0–10)
WPAI percentage scores, mean (SD)		
Absenteeism**	15.0 (19.6)	8.2 (11.0)
Presenteeism**	48.1 (30.4)	31.7 (24.8)
Overall work impairment**	52.5 (31.6)	35.6 (27.5)
Overall activity impairment†	59.9 (25.7)	41.3 (29.1)

Note: WPAI ranges from 0–100%, with high scores indicating greater impairment and less productivity.
*Among those employed (Patients: n=59; Caregivers: n=25).
**Among those employed, 2 patients and 1 caregiver skipped this question (Patients: n=57; Caregivers: n=24).
†Overall activity impairment is presented for all participants (Patients: N=100; Caregivers: N=40).

Disclosure: A. Gaffo: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **B. Desai**: Sobi, 3, 11; **A. Oladapo**: Sobi Inc, 3; **N. Kragh**: Sobi, 3; **R. Zincavage**: Sobi, 2, Stratevi, 3; **B. Padilla**: Sobi, 2, Stratevi, 3; **N. Schlesinger**: Amgen, 1, Arthrosi, 1, Olatec, 1, Protalix, 1, Scilex, 1, Shanton, 1, Sobi, 1.

Abstract Number: 1260

Increasing Zoster Vaccination Rates in Immunosuppressed Veterans at the North Texas VA Medical Center Rheumatology Clinic

Benjamin Gardner[1], Ankitha Lingamaneni[2], Isabel Penabad[3], Jiby Mathew[4], Una Makris[5], Rashmi Arora[6], Swathi Reddy[7] and Nagendra Pokala[8], [1]UTSW, Dallas, TX, [2]University of Texas Southwestern Medical Center, Dallas, TX, [3]UT Southwestern, Dallas, TX, [4]Veteran's Affairs, Rowlett, TX, [5]UT Southwestern Medical Center and Dallas VA, Dallas, TX, [6]VA north texas health centre Dallas, Dallas, TX, [7]UT Southwestern Medical Center / Dallas VA Medical Center, Colleyville, TX, [8]Veterans Affairs North Texas Healthcare System, Dallas, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

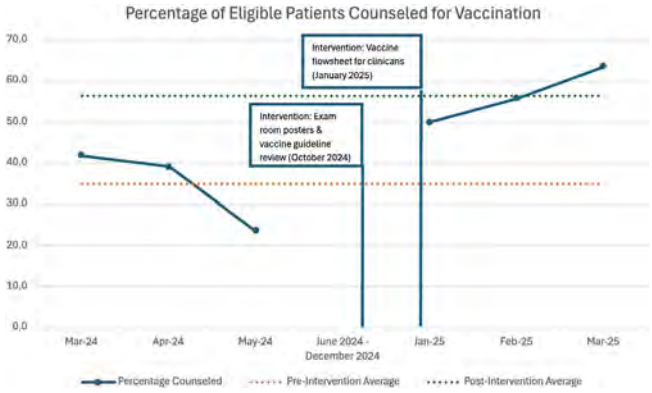
Background/Purpose: Shingles is a painful cutaneous eruption due to the reactivation of latent Varicella zoster virus. Immunocompromised adults, due to a medical condition or immunosuppressive therapies, have a higher risk of shingles. In 2021, recombinant zoster vaccination was formally recommended by the ACIP for adults ages 18-50 who are immunocompromised. Despite this recommendation, zoster vaccination rates in the United States remain low. Our goal is to implement Plan, Do, Study, Act cycles to increase zoster vaccination rates in immunosuppressed patients aged > 18 years at the North Texas VA Medical Center Rheumatology clinic.

Methods: We identified Veterans > 18 years old with rheumatic disease on any immunosuppressive disease-modifying antirheumatic drug and their zoster vaccination status by reviewing charts of patients seen in the VA Rheumatology clinic from March 4, 2024 to May 30, 2024. To obtain baseline vaccination rates, we calculated the proportion of patients who were unvaccinated, partially vaccinated (received 1 of 2 vaccine doses) and fully vaccinated. We developed a process map and identified two areas for intervention (patient and provider education). We created posters for display in exam rooms to increase patient awareness, reviewed vaccination guidelines with rheumatology clinicians, and posted vaccination flowsheets in resident training/ onboarding documents and precepting rooms to improve provider awareness. We then reassessed the data from Jan 2, 2025 to March 31, 2025.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient Characteristics	Baseline (n=390)	Post Intervention (n=398)
Average Age (years)	60.1	59.7
Race		
White	212 (54.4%)	190 (47.7%)
Black	125 (32.1%)	132 (33.2%)
Hispanic	23 (5.9%)	35 (8.8%)
Gender		
Male	309 (79.2%)	324 (81.4%)
Female	81 (20.8%)	74 (18.6%)
Diagnosis		
Seronegative Spondyloarthropathy	152 (39.0%)	149 (37.4%)
Rheumatoid Arthritis	146 (37.4%)	150 (37.7%)
Systemic Lupus Erythematosus	18 (4.6%)	24 (6.0%)

Patient Characteristics



Change in Percentage Counseled for Vaccination

Results: We reviewed 752 charts and identified 390 eligible patients for baseline data. The average age was 60 and 79% were men. The most common diagnoses were spondyloarthropathy (39%) and rheumatoid arthritis (37%). At the time of the visit, 34% of patients were not vaccinated, 10% were partially vaccinated and 56% were fully vaccinated. Among those not fully vaccinated and eligible for vaccination 9% were counseled and immunized within one week, 26% were counseled but not immunized within one week, and 65% were not counseled. Post-intervention we reviewed 798 charts and identified 398 eligible patients. The average age was 60 and 81% were men, with similar rheumatologic diagnoses as baseline sample. At the time of visit, 36% were not vaccinated for zoster, 8% were partially vaccinated, and 56% were fully vaccinated. Among those not fully vaccinated and eligible for zoster vaccination 11% were counseled and immunized within one week of the visit, 46% were counseled but not immunized within one week, and 43% were not counseled.

Conclusion: Among patients eligible for zoster vaccination, our results show an increase in both the percentage of patients who were counseled at their visit and vaccinated within with one week. The percentage of fully vaccinated patients did not increase substantially. Following the above-mentioned interventions, zoster vaccination rates and counseling rates among immunosuppressed individuals improved in our outpatient rheumatology clinic.

Disclosure: B. Gardner: None; **A. Lingamaneni**: None; **I. Penabad**: None; **J. Mathew**: None; **U. Makris**: None; **R. Arora**: None; **S. Reddy**: None; **N. Pokala**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1261

Use of telemedicine to address 'off target' symptoms in psoriatic arthritis (PsA): implementation of PsOWell™ in PsA

Carter Pason[1], Sarah Hopkins Gillespie[1], Joelle Koplin[2], Rachael Hewitt[3], Christine Bundy[3], Ethan Craig[4], Laura Coates[5], Jessica A. Walsh[6] and Alexis Ogdie[7], [1]University of Pennsylvania, Philadelphia, PA, [2]Penn Medicine, Philadelphia, PA, [3]University of Cardiff, Cardiff, United Kingdom, [4]University of Pennsylvania, Wallingford, PA, [5]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [6]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [7]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Approximately 60-70% of patients with PsA do not reach minimal disease activity (MDA) on therapy. However, in many cases, this may not be related to active disease as defined by clinical assessments such as joint count. We hypothesized that "off target" symptoms like fatigue, sleep disturbance, and mood could be addressed by lifestyle behaviors in parallel to standard medical therapy to improve outcomes. The objective of this study was to understand the participant experience in the PsOWell trial through a qualitative process evaluation.

Methods: We conducted the PsOWell pilot? trial among patients with PsA not currently in MDA and with active disease as defined by patient-reported outcomes (PSAID >4 or patient global assessment >4). Patients were required to plan to stay stable on therapy for at least the next 3 months. Patients completed the PSAID and Eq5D at baseline and follow-up within 4-6 months; MDA was recorded at both visits (Figure 1). Between the two primary visits, patients completed two telemedicine visits with a nurse practitioner or clinical research nurse. During these visits, patients chose a target health domain from the Informatree.com site. The provider, trained in motivational interviewing, conducted a first visit using the Action Plan for the corresponding health domain to set goals. A second visit was conducted to check in and modify the plan. The provider took notes for the participant to access through their chart.

The primary outcome was achievement of MDA at the follow up visit. We conducted a qualitative interview at the final visit among the first 25 study completers (target recruitment for the pilot trial is 80 participants). Themes were derived from interviews using content analysis.

Results: We identified recurrent themes about the participants' experiences and the program's impact. The main strengths identified were the ease and convenience of participating via telemedicine and the positive impact of accountability on behavior change. Participants recalled that the nurse practitioners were supportive and provided useful advice to help them execute lifestyle changes. Many participants reported improvements in their chosen health domains.

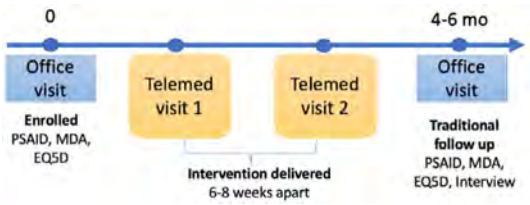


Figure 1. Study Design

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Informatree Health Domains

Primary Topic Selected from Informatree	# of Participants (n=25)
Food and weight	7
Sleep	6
Keeping active	3
Fatigue	4
Mood	2
Pain	3
Tobacco	0
Travel	0
Work	0
Social Support	0
Using treatments	0
Different treatments	0
Intimacy	0
Healthcare appointments	0
Alcohol	0

Opportunities for improvement were also identified. Some participants expressed that their lifestyle changes could be solidified by more frequent follow-up calls, nudging messages, more written resources, and a longer program duration. Some noted that the advice from the NPs could be more specific. Some participants wished that physical symptoms of PsA, such as skin issues, could also be addressed during the telemedicine visit. However, this was beyond the scope of the intervention.

Table 2. Example Quotes

STRENGTHS	**Ease and convenience of telemedicine**	"It was very smooth." "There was no burden." "It saves me close to three to four hours or something like that, which is also a good benefit." "I didn't really rearrange my schedule or anything."
	Accountability	"If what you're trying to do is instill changes in behavior, it's good to be held accountable, but she did it in a very gentle way." "Once you put a responsibility to check in with someone, it makes you more apt to follow through."
	Support	"The care and concern that the person showed, was really good." "It helped to have a support system and helped keep him positive."
	Helpful advice	"She did have some good advice." "She was nice, helpful, and informative." "Open, positive, good feedback."
LIMITATIONS	**More follow-ups**	"… if you want to implement behavioral change […] then I think you might have to touch base a little bit more frequently." "…we could have benefited from an additional follow-up meeting."
	Longer duration	"If the program was to be implemented, having a longer period of time just because it is hard to start a habit." "He wished the support could be constant."
	More documentation or messaging	"…maybe more communication or documentation, just because it kind of fell off my awareness."
	More specific	"[The advice was] not particularly specific."

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The PsOWell program was received well by participants. Many expressed that they achieved positive changes in health behaviors by participating. The program's main strengths are its convenience and being supported and held accountable by the NPs. However, increasing the frequency of check-ins and extending the program duration could strengthen its impact on sustainable behavior change.

Disclosure: C. Pason: None; **S. Hopkins Gillespie**: None; **J. Koplin**: None; **R. Hewitt**: None; **C. Bundy**: None; **E. Craig**: Amgen, 1, Eli Lilly, 6, Janssen, 1, Novartis, 6, Penn Home Infusion, 2, Penn Specialty Pharmacy, 2, Twill Health, 2; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, Moon-Lake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11.

Abstract Number: 1262

Perspectives of Lupus Patients on Quality of Life Measures: A Qualitative Study

Cristina Arriens[1], Fredonna Carthen[2], Alexandre Cammarata-Mouchtouris[1], Judith James[1], Joan Merrill[3] and Motolani Ogunsanya[4], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma, OK, [3]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [4]University of Oklahoma Health Sciences Center, Edmond, OK

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus has profound impact on physical, social, and emotional well-being. Health-related quality of life (HRQOL) measures are increasingly incorporated into lupus research and the US Food and Drug Administration has called for patient-reported outcomes (PROs) to be key endpoints in trials. This study sought to explore which HRQOL instruments are viewed by lupus patients as most relevant and reflective of their lived experience.

Methods: Five 90-minute focus groups were conducted, each with 4-6 participants with SLE. Participants were asked to independently complete six commonly used PRO instruments before the session: The Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-Fatigue), the Lupus Foundation of America Rapid Evaluation of Activity in Lupus (LFA-REAL™), RAND 36-Item Short Form Instrument (SF-36), the Lupus-Quality of Life (Lupus-QoL) Questionnaire, Patients Global Impression of Severity (PGIS-Lupus), and Patients Global Impression of Change (PGIC-Lupus). Time to completion was recorded and written comments were encouraged. A trained moderator guided participants through open-ended discussions exploring instrument ease of use, clarity, relevance, comprehensiveness, and acceptability. Sessions were audio-recorded, transcribed verbatim, and thematically analyzed using an inductive approach.

Results: There were 24 participants aged 29-65 years (33% African American, 13% American Indian, 8% Latinx, and 46% European descent). Demographics are summarized in Table 1. Interrater reliability for qualitative coding was high. Table 2 summarizes the instrument characteristics, completion times, and scores. Most instruments utilized a 4 week recall period; FACIT-Fatigue used 7 days. About 1/3 of participants had difficulty recalling and averaging symptoms over the timespan due to disease variability; others valued the structured reflection. Participants suggested adding items on cognitive dysfunction,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Characteristics. Demographic and SLE disease specific information. All patients met the American College of Rheumatology (ACR)-1997 classification criteria, the Systemic Lupus International Collaborating Clinics (SLICC)-2012 classification criteria, and the 2019 EULAR/ACR Classification Criteria.

Characteristics of Focus Group Participants (n=24)	
Demographics	
Female (n, %)	22 (91.7)
Race/Ethnicity (n, %)	
African American/Black	8 (33.3)
American Indian/Native American	3 (12.5)
Hispanic/Latinx	2 (8.3)
White/Caucasian	11 (45.8)
Age in Yrs (mean ± SD)	45 ± 9.7
Age in Yrs, Range	29-65
SLE Disease Specific	
Duration of SLE in Yrs (mean ± SD)	15.6 ± 6.3
Duration of SLE in Yrs, Range	6.7-30.7
ACR Classification Criteria Total (mean ± SD)	7.0 ± 2.0
SLICC Classification Criteria Total (mean ± SD)	9.0 ± 2.5
EULAR/ACR Classification Criteria Total (mean ± SD)	24.9 ± 10.0
ANA	24 (100.0)
Arthritis	24 (100.0)
Hemolytic Anemia	2 (8.3)
Leukopenia	8 (33.3)
Lymphopenia <1.5K	20 (83.3)
Lymphopenia <1K	17 (70.8)
Thrombocytopenia	4 (16.7)
Malar	12 (50.0)
Discoid	5 (20.8)
Photosensitve Rash	20 (83.3)
Maculopapular Rash	1 (4.2)
Ulcers	19 (79.2)
Alopecia	17 (70.8)
Anti-dsDNA	13 (54.2)
Anti-Sm	8 (33.3)
Anti-cardiolipin Positive	15 (62.5)
Anti-cardiolipin (medium or high)	8 (33.3)
Anti-Beta 2 Glycoprotein	1 (4.2)
Lupus Anticoagulant	1 (4.2)
Complement	17 (70.8)
Pleurisy	14 (58.3)
Pericarditis	5 (20.8)
Renal (Proteinuria, Biopsy Proven LN)	6 (25.0)
Neurologic	5 (20.8)
Fever	12 (50.0)

Table 2. Health Related Quality of Life Instruments. Details the characteristics of each quality of life questionnaire used and presents our participants' data (completion times, overall and comparable subscale scores) organized to facilitate cross-instrument comparison. Notably, while each individual item on the LFA-REAL™ has a maximum score of 100 millimeters, the total possible score for the entire instrument is 700 millimeters. For the purpose of comparing Pain and Appearance domains with other questionnaires, we combined the LFA-REAL™ scores for Joint Pain and Muscle Pain/Aches into a composite "Pain" score, and similarly combined Rash and Hair Loss scores into a composite "Appearance" score.

Health Related Quality of Life Instruments						
	FACIT-Fatigue	**LFA-REAL™**	**RAND SF-36**	**LupusQoL**	**PGIS-Lupus**	**PGIC-Lupus**
Instrument Information						
Number of Items	13	10	36	34	1	1
Recall Period	7 Days	4 Weeks	Variable (Current, 4 Weeks)	4 Weeks	4 Weeks	4 Weeks
Response Scale	Numerical Likert Scale	VAS Linear with Anchor Points	Variable (e.g. Worded Likert, Numerical Likert)	Worded Likert Scale	Worded Likert Scale	Worded Likert Scale
Numerical Range of Responses	0-4	0-100 Millimeters	Variable (e.g. 1-2, 1-5, 1-6)	0-4	0-3	0-4
Worded Range of Responses	Not at All-Very Much	None-Worst Imaginable	Variable (e.g. None-Very Severe)	All of the Time-Never	None-Severe	Much Better-Much Worse
Subscale Domains	Fatigue	Fatigue, Symptoms of Arthritis, Muscle Pain or Aches, Rash, Hair Loss, Fever, Body Symptoms (Chest Pain, Shortness of Breath, Swelling in Legs, and Other)	Energy/Fatigue, Pain, Physical Functioning, Role Limitations due to Physical Health, General Health, Role Limitations due to Emotional Problems, Emotional Well-Being, Social Functioning	Fatigue, Pain, Physical Health, Planning, Body Image, Emotional Health, Intimate Relationship, Burden to Others	Global Lupus Symptom Severity	Global Lupus Symptom Change
Range of Possible Scores	0-52	0-700	0-100	0-100	0-4	0-5
Best Score Possible	52	0	100	100	0	0
Instrument Results in Our SLE Focus Groups						
Time to complete (in Seconds), mean ± SD	77 ± 40	95 ± 43	262 ± 121	349 ± 141	12 ± 8	12 ± 8
Time to complete, mean	1 Min 17 Sec	1 Min 35 Sec	4 Min 22 Sec	5 Min 49 Sec	12 Sec	12 Sec
Total Summary Score, mean ± SD	20 ± 11	277 ± 136	40 ± 18	53 ± 22	1.8 ± 0.8	2.3 ± 0.9
Fatigue Subscale Score, mean ± SD	20 ± 11	63 ± 22	20 ± 18	40 ± 23	N/A	N/A
Pain Subscale Score, mean ± SD	N/A	51 ± 24	43 ± 25	57 ± 25	N/A	N/A
Emotional Subscale Score, mean ± SD	N/A	N/A	58 ± 25	67 ± 22	N/A	N/A
Appearance Subscale Score, mean ± SD	N/A	28 ± 25	N/A	58 ± 26	N/A	N/A

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

headaches, and depression, which they felt were underrepresented and impactful. Difficulty distinguishing lupus-related from comorbid symptoms was a concern, especially with the Lupus QoL, LFA-REAL™, PGIS, and PGIC. The lupus-specific tools and the FACIT-Fatigue were viewed as more relevant. Lupus QoL was preferred by 78% of the participants, alone or combined with the LFA-REAL™ or FACIT-Fatigue, citing its lupus-specific focus, clarity, and coverage of daily function.

Conclusion: This qualitative study provides insights from SLE patients into how well commonly used PRO measures capture their lived experience and symptom burden. The findings may help to determine whether outcome assessments align with priorities and challenges important to patients living with lupus.

Disclosure: C. Arriens: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **F. Carthen**: None; **A. Cammarata-Mouchtouris**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **M. Ogunsanya**: None.

Abstract Number: 1263

Health Literacy diversity among rheumatology patients: insights from a tertiary rheumatology centre

Cristina Calomarde-Gomez[1], Mrinalini Dey[2], Chris Wincup[3], Maria Alonso de Francisco[4], Christina Cheng[5], Richard Osborne[5] and Elena Nikiphorou[6], [1]Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, [2]Centre for Rheumatic Diseases, King's College London, London, United Kingdom, [3]King's College Hospital, London, United Kingdom, [4]H. U. Puerta de Hierro Majadahonda, Tres Cantos, Spain, [5]La Trobe University, Melbourne, Victoria, Australia, [6]King's College London, London, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Health literacy is a potential social determinant of health, fundamental to patient engagement, clinical communication, and long-term outcomes of disease. Understanding health literacy at the individual and population levels are essential to drive equitable, person-centered healthcare.

We aimed to identify and describe health literacy profiles in people with rheumatic and musculoskeletal diseases (RMDs) attending a tertiary rheumatology service.

Methods: Patients attending the rheumatology clinic at King's College Hospital, UK, were invited to complete a survey including the nine-domain Health Literacy Questionnaire (HLQ), socio-demographic and clinical characteristics. Hierarchical cluster analysis, following the Ophelia (Optimising Health Literacy and Access) process (1) was conducted to identify patient subgroups based on the nine HLQ domains and other characteristics.

Results: In total, 263 people with RMDs were included in this study. Eleven distinct clinically relevant clusters were identified (Table 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Cluster analysis of Health Literacy Questionnaire (HLQ) data from 263 patients attending the rheumatology clinic at King's College Hospital. HLQ1 (Feeling understood and supported by health care providers), HLQ2 (Having sufficient information to manage my health), HLQ3 (Actively managing my health), HLQ4 (Social support for health), HLQ5 (Appraisal of health information), HLQ6 (Ability to actively engage with healthcare providers), HLQ7 (Navigating the healthcare system), HLQ8 (Ability to find good health information), HLQ9 (Understand health information well enough to know what to do).

Cluster ID*	% in sample	HLQ1	HLQ2	HLQ3	HLQ4	HLQ5	HLQ6	HLQ7	HLQ8	HLQ9
1	9.5	3.77	3.48	3.43	3.63	3.35	4.59	4.37	4.36	4.68
2	9.1	3.49	3.64	3.77	3.48	3.52	4.42	4.25	4.60	4.76
3	6.1	3.13	3.25	3.00	3.25	3.18	4.63	4.26	4.56	4.73
4	8.0	3.50	3.00	3.15	3.41	3.06	3.88	3.56	3.59	3.69
5	9.9	2.88	3.03	3.12	3.07	3.11	3.96	3.80	4.12	4.19
6	15.2	3.01	2.81	2.91	2.80	2.98	3.74	3.46	3.87	4.13
7	17.1	2.78	2.96	2.95	2.91	2.76	3.66	3.34	3.67	3.91
8	8.0	2.21	2.27	3.10	2.60	2.85	2.91	2.75	3.59	4.17
9	12.2	2.73	2.59	2.51	2.46	2.51	3.28	2.90	3.40	3.50
10	1.5	2.00	1.38	3.90	2.23	3.05	1.30	1.53	2.05	2.80
11	3.4	2.08	1.83	2.22	1.92	1.89	1.93	1.83	2.07	2.78

Clusters 1 (10%) and 2 (9%) exhibited high scores across all HLQ domains, with strong engagement, navigation, and comprehension capabilities. These clusters comprised mainly professionally employed women, with Cluster 1 younger patients (mean 32.8 years) with connective tissue diseases (CTD) and cluster 2 including older patients (mean 55.5 years) with inflammatory arthritis (IA).

Cluster 3 (6%) showed high engagement with limited emotional support. Most were men working in technical or professional roles. Clusters 5 (10%), 6 (15%), 8 (8%), and 9 (12%) showed mixed profiles. For instance, Cluster 5, predominantly women, demonstrated strong information-processing skills but only moderate social support. Cluster 8 had adequate comprehension despite poor support.

Figure 1: Infographic summarising characteristics of individuals within each of the described clústers, including health literacy strengths and needs.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cluster 6 (15%) represented a younger, ethnically diverse group with moderate comprehension, limited support, and high unemployment. Cluster 7 (17%) consisted mainly of older, predominantly white, retired individuals with average literacy levels and low provider engagement.

Clusters 10 (2%) and 11 (3%) reflected the most complex challenges. Cluster 10 revealed a distinct profile of strong self-management despite extremely low support and engagement; members were mostly female, technically trained, and unemployed. Cluster 11, with the lowest scores across all domains, included older, professionally inactive women.

Conclusion: Health literacy among patients at King's College Hospital Rheumatology Clinic is highly variable, with some groups facing substantial barriers to engagement and support. Notable patterns emerged, such as higher health literacy amongst older patients with IA and younger patients with CTD, while lower health literacy in certain domains was associated with unemployment and non-Caucasian ethnicity. Identifying health literacy profiles can support more targeted and equitable approaches to patient communication, care planning, and service design.

Reference

1. Osborne R et al. The Ophelia Manual. The Optimising Health Literacy and Access process to plan and implement National Health Literacy Demonstration Projects.

Disclosure: C. Calomarde-Gomez: None; **M. Dey**: None; **C. Wincup**: None; **M. Alonso de Francisco**: None; **C. Cheng**: None; **R. Osborne**: None; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

Abstract Number: 1264

Breaking the Veil: Preliminary Findings for a Qualitative Analysis of Rheumatoid Arthritis Patient Perspectives on Physical Activity and Mental Healt

Daniel Garcia[1], Vanessa Madrigal[2], Noelia Hernandez[3], Alisha Akinsete[4], Iris Navarro-Millan[5], Ileana Vazquez Otero[6], Ariana Gonzalez Melendez[7], Sarah Young[8] and Monika Safford[2], [1]Weill Cornell, Brooklyn, NY, [2]Weill Cornell Medicine, New York, [3]Weill Cornell Medicine, New York, NY, [4]Weill Cornell Medical Center, New York, NY, [5]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY, [6]Clinica Reuviva, San Juan, PR, [7]Ponce Health Sciences, San Juan, PR, [8]Weill Cornell Medicine, Johnson City, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Approximately 1.3 million Americans have rheumatoid arthritis (RA)[1]. Up to 83% of people with chronic pain, the hallmark symptom of RA also experience anxiety and/or depression[2-5]. Peer coaches, lay individuals who themselves live with the same chronic condition, can be particularly effective at addressing these challenges in people with diabetes and post-partum depression. The purpose of this study was to involve people with RA (PWRA) to inform the adaptation of a proven, effective peer coaching intervention to the context of RA, considering the needs of diverse populations and soliciting input about mental health and physical activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Characteristics	N (%)
Age Mean (stdev)	59.09(11.36)
Female	20(90.90)
White	10(45.45)
Black/African American	2 (9.09)
Hispanic/Latino	13(59.09)
Private Insurance	12(54.54)
Public Insurance	10(45.45)
Full time worker	6(27.27)
Retired-disabled	5(22.72)
Retired-nondisabled	10(45.45)
Unemployed	1(4.54)
<$24,000 per year	7(31.81)
$25-100,000	10(45.45)
> $100,000	5(22.72)
Average Pain (scale 1-10)	4.68
Workout	16
How many times a week do you work out? (Average in days)	4
How long do you work out for? (Average in minutes)	65

Image 1: Demographic Characteristics and Exercise Habits of 22 Participants with RA

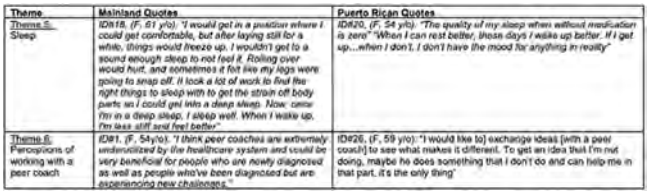
Methods: We conducted semi-structured interviews via teleconference using a topic guide that was informed by Social Cognitive Theory, to elicit the mental and physical experiences of PWRA. Inclusion criteria were: 1) PWRA 18 > years of age, 2) Severe pain interfering significantly with performing activities of daily living over the last 2 weeks, 3) Access to the internet and/or phone, 4) Living in the US including Puerto Rico, and 5) English or Spanish speakers. The topic guide focused on barriers and facilitators related to disease management, mental health, physical activity, and opinions about working with a peer coach (another PWRA trained to coach another PWRA in specific evidence-based health behaviors). Data were analyzed thematically with NVivo software by two independent analysts, highlighting Puerto Rican and Mainland voices.

Results: Of 22 participants, 20 were women, most were >50 years of age, and 5 were residents of Puerto Rico (Image 1). Images 2 and 3 shows the six themes that emerged: (1) Ableism and isolationism: Participants felt a strong sense of separation from their peers without RA; (2) Grief of former self: Many grieved the loss of abilities they had prior to their RA diagnosis, feeling inadequate in tasks they were once self-sufficient at; (3) Resilience: Participants exhibited resilience, adapting their physical and social environments to better support their needs and improve their quality of life; (4) Adaptation of physical activities: Participants emphasized adapting physical activities without causing further injury; (5) Sleep: Participants described challenges with sleep quality that impacted their physical and emotional well-being; and (6) Perception of working with a peer coach: participants valued the guidance of someone with shared experience, who could provide insights into managing pain and mental health.

Theme	Mainland Quotes	Puerto Rican Quotes
Theme 1: Ableism and Isolationism	ID#6 (F,59y/o): "Even my family, to this day, I don't think that they truly understand what I go through. My husband is always shocked when, somehow, they let it be known that they don't understand what I go through on a daily basis. So even the people that I grew up with don't really know how isolating the disease is, how it can make you feel really lonely, how painful it is."	ID#13 (F, 34y/o): "Well, it has been enough from family, friends, my core has decreased considerably but too much, that is, maybe 5 people who were always in my environment, save only 2, because for the same reason, they do not understand the condition, there are people who believe that you are exaggerating, they judge you, and more, and at least save yourself, One of the things that is most important to me is my peace of mind. So, I want to know all those people that I already understood that they had a kind of conflict with the understanding of my condition and moreover, well, I leave them aside."
Theme 2: Grief for former self	ID#1(F, 54y/o): "The mourning, and I think that's probably the better word. I was in mourning for my former abilities and grappling with needing a lot more help than I was used to needing, so it was difficult."	ID#28(F,63y/o): "I don't like to be sitting or lying on a piece of furniture and for me it's even more frustrating because when you lie in bed or whatever and you like to be lying down, it's fine, but when you're a person who is very independent and I help my daughters, I help my mom, I help my granddaughters and then I look like I am in pain, how do I do this? You know, it's very frustrating"
Theme 3: Resilience and tools to cope with diagnosis	*ID#9, (F, 63 y/o) "Well, the benefits of exercise, definitely it helps. Number 1, my emotional state. Whenever I exercise and I'm feeling stronger, feeling like I'm moving better, it immediately just affects my mood. I am always, let's say, more upbeat when there are times that I've noticed in the past that I haven't been able to exercise. I noticed that my mood also changes. Definitely the exercise helps with one's positive state of mind."*	ID#13 (F, 34 y/o): "I just eat and I disconnect, I practice my exercise, and in addition, I talk to myself, I give myself support and everything goes back to normal. But sometimes they don't. Sometimes I do need a little more push"
Theme 4: Adaptation of physical activities	*ID#2, (F,55y/o): "I was playing competitive state league tennis in the state, I played soccer, I played softball, I played all these things, and now all of a sudden, I can't play tennis anymore because my hands swell like sausages every time I try. Realizing I can't do that, but here's what I can do. I can play pickleball because we're playing with a whiffle ball and it's not stressing out my joints the way a tennis ball would, or a tennis racket would."*	ID#20 (F,54 y/o): "At first I couldn't exercise because my feet were swollen and I couldn't move, but then I walked little by little until now I can do a 30-minute exercise routine, at least three times a day, three times a week and yes, on a treadmill, not walking on the road, on the sidewalk, because of the sun, but I do it in a gym, on an electric walker and I can walk, at least I walk my 20 minutes or 30 minutes, it depends on how my body is that day that tells me you can resist a little more and have more courage, and I combine it because as I told you, with music. Relaxing music."

Image 2: Themes and corresponding quotes from Mainland and Puerto Rican participants

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Theme	Mainland Quotes	Puerto Rican Quotes
Theme 5: Sleep	ID#18, (F, 61 y/o): "I would get in a position where I could get comfortable, but after laying still for a while, things would freeze up. I wouldn't get to a sound enough sleep to not feel it. Rolling over would hurt, and sometimes it felt like my legs were going to snap off. It took a lot of work to find the right things to sleep with to get the strain off body parts so I could get into a deep sleep. Now, once I'm in a deep sleep, I sleep well. When I wake up, I'm less stiff and feel better."	ID#20, (F, 54 y/o): "The quality of my sleep when without medication is zero" "When I can rest better, these days I wake up better. If I get up...when I don't, I don't have the mood for anything in reality"
Theme 6: Perceptions of working with a peer coach	ID#1, (F, 54y/o): "I think peer coaches are extremely underutilized by the healthcare system and could be very beneficial for people who are newly diagnosed as well as people who've been diagnosed but are experiencing new challenges."	ID#26, (F, 59 y/o): "I would like to] exchange ideas [with a peer coach] to see what makes it different. To get an idea that I'm not doing, maybe he does something that I don't do and can help me in that part, it's the only thing"

Image 3: Themes and corresponding quotes from Mainland and Puerto Rican participants

Conclusion: PWRA identified several barriers (isolationism, ableism, grief, sleep difficulty) and facilitators (resilience, adaptation) that hold potential for improving mental health and physical activity in this population. This could potentially be achieved by having peer coaches assist in behavioral changes and "breaking the veil" of silence and invisibility through role-modeling behaviors and assisting PWRA to cope with challenges related to living with RA. Further interventions should continue to explore similarities and differences between Puerto Rican and Mainland participants to better tailor RA services to diverse populations.

Disclosure: D. Garcia: None; **V. Madrigal**: None; **N. Hernandez**: None; **A. Akinsete**: None; **I. Navarro-Millan**: None; **I. Vazquez Otero**: None; **A. Gonzalez Melendez**: None; **S. Young**: None; **M. Safford**: MedExplain Health, 1.

Abstract Number: 1265

Patient Portal Awareness and Utilization Across Diverse Rheumatology Populations

Emily Gutowski[1], Joshua Novack[2], Allyson Covello[2], Philip Carlucci[3], Scott Goldberg[1], Mary Guan[4], Marcus Hines[2], Elliot Philips[2], Michael Pillinger[5] and Sara Stream[6], [1]New York University Grossman School of Medicine, Brooklyn, NY, [2]New York University Grossman School of Medicine, New York, NY, [3]New York University School of Medicine, New York, NY, [4]NYU Grossman SOM, Brooklyn, NY, [5]New York University Grossman School of Medicine, New York, NY, [6]New York University Grossman School of Medicine, Great Neck, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatic diseases face complex and chronic diagnoses that require close monitoring and frequent communication with their providers. Given increasing challenges to in-person medical care, including decreased time for clinic visits, physician shortages, and scheduling difficulties, online patient portals serve as important tools to engage patients in their care, allowing them to review test results, schedule appointments, and communicate with physicians. To identify barriers to portal use, we evaluated rheumatology patients' awareness, use, and perceptions of patient portals across three clinical sites: a public safety net hospital, private academic teaching hospital and Veterans Affairs (VA) Hospital.

Methods: We conducted a cross-sectional, survey-based study in outpatient adult rheumatology clinics in three hospitals. During routine visits, surveys were distributed to patients in English or Spanish. Surveys assessed demographics, educational background, familiarity with each hospital system's portal, frequency and reason for portal use, and interest in learning more. Informational handouts on portal capabilities and sign-up instructions were provided.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics of survey respondents.

Table 1

	Public	Private	VA	Total
Number of participants	74	15	50	139
Age, average (st dev)	47 (14.2)	51 (17.6)	62.6 (16.7)	53.1 (17.1)
Female, n (%)	57 (77)	12 (80)	3 (6)	72 (51.8)
Ethnicity, n (%)				
Hispanic	50 (67.6)	5 (33.3)	10 (20)	65 (46.8)
African American	7 (9.5)	6 (40)	18 (36)	31 (22.3)
White	5 (6.8)	2 (13.3)	16 (32)	23 (16.6)
Asian	7 (9.5)	0 (0)	3 (6)	10 (7.2)
Other	4 (5.4)	2 (13.3)	1 (2)	7 (5)
Primary Language, n (%)				
English	44 (59.5)	13 (86.7)	50 (100)	107 (77)
Spanish	30 (40.5)	0 (0)	0 (0)	30 (21.6)
Other	0 (0)	2 (13)	0 (0)	2 (1.4)
Educational Achievement				
Elementary	14 (18.9)	1 (6.7)	0 (0)	15 (10.8)
Middle School	7 (9.5)	3 (20)	13 (26)	23 (16.6)
High School	26 (35.1)	3 (20)	32 (64)	61 (43.9)
College	24 (32.4)	3 (20)	5 (10)	32 (23)
Advanced	2 (2.7)	0 (0)	0 (0)	2 (1.4)
Unknown	1 (1.4)	5 (33.3)	0 (0)	6 (4.3)

Results: 139 patients completed the survey: 50 from the VA, 15 from the private hospital and 74 from the public hospital. The average age was 53.1; 48.2% of respondents were male. Hispanic identity (46.8%) was most common. English was the primary language for 77%. The most reported highest education level was high school (Table 1).

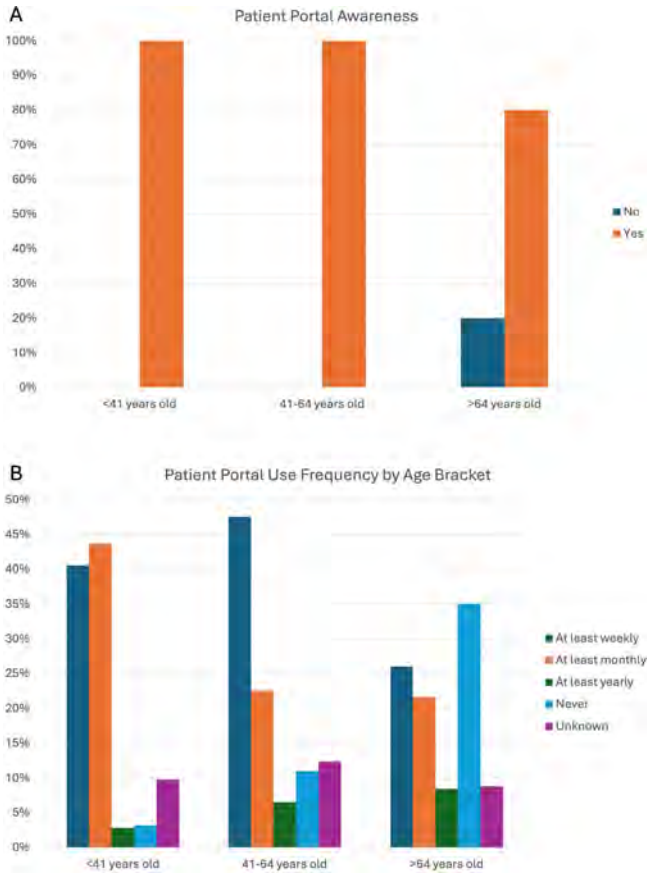


Figure 1. Awareness (A) and use frequency (B) of patient portal by age. Answers for panel A refer to "I am aware of my patient portal."

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

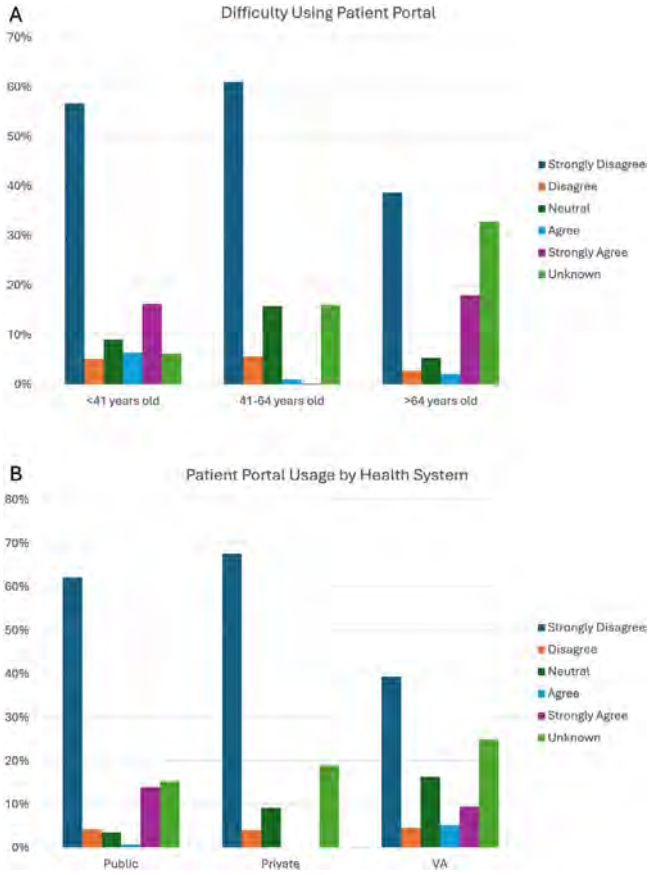


Figure 2. Difficulty using patient portal by age (A) and portal usage by health system (B). Answers refer to "I have trouble using my patient portal" and "I find my patient portal useful for my needs."

93.5% of all patients surveyed were aware of their patient portal, and 71.9% reported using their portal at least once a month. Portal awareness and use declined with age: patients 65 and over were less likely to have internet access or use portals, including a plurality who never used them (Figure 1). Older patients also reported more difficulty navigating portals (Figure 2A). Use varied by hospital, with highest use at the public hospital and lowest at the VA (Figure 2B). At the public hospital, higher educational attainment was associated with increased computer and internet access, whereas computer and internet access were nearly universal at the private hospital, regardless of education.

Conclusion: While awareness of patient portals was high across all sites, actual use was far lower and varied by age and hospital site. Patients 65 and over had the lowest frequency of use, which may be related to reduced access to technology and less favorable attitudes towards portals. Internet and computer access was not universal and varied with educational level, suggesting that access may be a limiting factor. Our findings highlight the need for targeted interventions, such as educational and technical support, as well as alternative communication strategies in those who are unable to utilize patient portals. These efforts would help to increase patient engagement in their medical care, ultimately improving outcomes in rheumatology.

Disclosure: E. Gutowski: Run the List, 12, Creator of podcast (runs ads including those for medical tools, e.g., Open Evidence); **J. Novack**: None; **A. Covello**: None; **P. Carlucci**: None; **S. Goldberg**: None; **M. Guan**: None; **M. Hines**: None; **E. Philips**: None; **M. Pillinger**: Amgen, Federation Bio, Fortress Biotech, Scilex, and SOBI, 2, Convergence Bio, 2; **S. Stream**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1266

Shared Decision Making in Rheumatoid Arthritis: Is RA disease activity associated with patient reported measures of shared decision making pre-SDM intervention?

Jennifer Barton[1], Joshua Baker[2], gabriela Schmajuk[3], Madhavi Valiveti[4], Alexandra Bennett[5], Benjamin Morasco[6], Allison O'Neill[7] and Meike Niederhausen[8], [1]VA Portland Health Care System/OHSU, Portland, OR, [2]University of Pennsylvania, Philadelphia, PA, [3]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [4]VAMC Wilmington, Wilmington, DE, [5]Center to Improve Veteran Involvement in Care (CIVIC) and VA Portland Health Care System, Portland, OR, [6]Center to Improve Veteran Involvement in Care, VA Portland Health Care System, Portland, OR, [7]Center to Improve Veteran Involvement in Care, VA Portland Health Care System, Portland, OR, [8]Oregon Health & Science University/VA Portland Health Care System, Portland, OR

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Shared decision making (SDM) is outlined as the first overarching principle of the treat to target guidelines for rheumatoid arthritis (RA). The quality of SDM varies across patient populations with many patients reporting poor communication around SDM. We sought to measure baseline patient-reported SDM in the usual care phase of an RCT designed to measure the impact of a multicomponent intervention to improve SDM among U.S. Veterans with RA and their clinicians. We also evaluated whether SDM correlated with baseline disease activity during this study phase.

Table 1: Baseline characteristics of Veterans with RA enrolled during the usual care phase of an RCT of a multicomponent intervention to implement shared decision making (SDM)

	Overall	Site			
Measure	N = 213 N (%)	Philadelphia N = 66	Portland N = 89	San Francisco N = 33	Wilmington N = 25
Age					
Mean (SD)	69 (10)	71 (8)	69 (10)	67 (12)	69 (11)
Sex					
Male	158 (75%)	53 (82%)	66 (74%)	22 (69%)	17 (68%)
Female	51 (24%)	12 (18%)	21 (24%)	10 (31%)	8 (32%)
Other/No Response	2 (0.9%)	0 (0%)	2 (2.2%)	0 (0%)	0 (0%)
Race/ethnicity					
American Indian/Alaska Native or Some Other Group	3 (1.4%)	1 (1.5%)	1 (1.1%)	1 (3.1%)	0 (0%)
Asian	1 (0.5%)	0 (0%)	0 (0%)	1 (3.1%)	0 (0%)
Black or African American	48 (23%)	27 (42%)	6 (6.7%)	5 (16%)	10 (40%)
Hispanic or Latino	9 (4.3%)	5 (7.7%)	1 (1.1%)	3 (9.4%)	0 (0%)
Middle Eastern/Northern African	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
White	136 (64%)	31 (48%)	75 (84%)	15 (47%)	15 (60%)
Multiple Races	13 (6.2%)	1 (1.5%)	5 (5.6%)	7 (22%)	0 (0%)
Decline to answer	1 (0.5%)	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)
Health Literacy					
Adequate	161 (79%)	51 (80%)	67 (81%)	25 (76%)	18 (75%)
Limited	43 (21%)	13 (20%)	16 (19%)	8 (24%)	6 (25%)
csDMARDS					
1	153 (78%)	45 (78%)	72 (87%)	26 (84%)	10 (43%)
bDMARDS					
1	112 (57%)	28 (48%)	51 (61%)	13 (42%)	20 (87%)
tsDMARDS					
1	9 (4.6%)	4 (6.9%)	3 (3.6%)	0 (0%)	2 (8.7%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. SDM and disease activity outcomes among US Veterans with RA across 4 sites

	Overall	Site			
Measure	N = 213 N (%)	Philadelphia N = 66	Portland N = 89	San Francisco N = 33	Wilmington N = 25
CollaboRATE Top Score					
No	54 (25%)	17 (26%)	21 (24%)	9 (27%)	7 (29%)
Yes	158 (75%)	49 (74%)	68 (76%)	24 (73%)	17 (71%)
SURE					
No Decisional Conflict	200 (95%)	61 (92%)	87 (98%)	31 (100%)	21 (88%)
Decisional Conflict	10 (4.8%)	5 (7.6%)	2 (2.2%)	0 (0%)	3 (13%)
Rapid3					
Mean (SD)	13.9 (5.2)	14.2 (4.1)	13.9 (6.0)	13.5 (5.9)	13.4 (4.7)

Key: Missing data was <10% for all key variables; CollaboRATE is 3-item measure of SDM (explanation about health issues, elicitation of patient preferences, integration of patient preference into decisions) each scored 0-9 with 9 being highest, if all three questions scored a "9" this is a Top Score; SURE is a 4-item measure of decisional conflict, yes/no response; score of 4 indicates no decisional conflict.

Table 3. RA Disease Activity by level of shared decision making and decisional conflict

		CollaboRATE Top Score			
Measure	Overall N=212	No N=54	Yes N=158	Difference[1]	95% CI[1]
RAPID3					
Mean (SD)	13.8 (5.2)	13.7 (5.0)	13.9 (5.3)	-0.17	-1.9, 1.5
		SURE			
	Overall	No Decisional Conflict	Decisional Conflict	Difference[1]	95% CI[1]
	N=210	N=200	N=10		
RAPID3					
Mean (SD)	13.8 (5.2)	13.7 (5.2)	16.8 (5.3)	-3.1	-7.2, 1.0

[1]Welch Two Sample t-test
Abbreviation: CI = Confidence Interval

Methods: Eligible Veterans with RA and moderate or high disease activity were invited to participate in this stepped-wedge, cluster-randomized trial at 4 U.S. Veterans Health Administration (VA) rheumatology clinics. SDM was assessed during a usual care phase of the trial using two brief, validated patient-reported measures (3-item CollaboRATE; 4-item SURE, yes/no response to: "feeling uncertain," "feeling informed," "feeling clear about values," and "feeling supported in decision-making"). Questionnaires were completed in person on the day of a routine visit along with patient-reported disease activity scores (RAPID3). Participants were also queried on demographics and health literacy. Medications were collected from the medical record. Summary statistics with mean (standard deviation, SD), median, or percentages used for demographics, health literacy, medications, SDM measures, and disease activity. T-tests were used to compare disease activity between SURE scores dichotomized as ≥ 4 vs. < 4 (no decisional conflict v presence of decisional conflict).

Results: 213 adults with RA across 4 sites contributed data during the usual care phases of the study (October 2022-September 2024). Nearly 80% were receiving a conventional synthetic DMARD, 57% a biologic DMARD, and 5% a targeted synthetic DMARD. 75% were male, mean (SD) age 69 (10), 64% white, 23% Black or African American, and 21% had limited health literacy (Table 1). 75% of participants ranked SDM highly on the 3-item CollaboRATE measure (9 out of 9) reflecting top scores. 95% overall reported no decisional conflict by SURE (Table 2). RAPID3 scores did not vary by SDM, however participants with decisional conflict by the SURE measure had slightly higher RAPID3 scores [mean (SD) 16.8 (5.3)] compared with those without decisional conflict [mean (SD) 13.7 (5.2)] though these were not statistically different (Table 3).

Conclusion: One quarter of Veterans with RA and moderate to high disease activity reported suboptimal SDM, which is similar to prior studies among non-Veterans with RA reporting up to 30%, and 5% reported decisional conflict. Ceiling effects of SDM measures present challenges to efficiently and thoroughly measure SDM across many chronic conditions, as identified in this RA population. Future work will use mixed methods to evaluate the effect of a multicomponent intervention on improving SDM and RA disease activity, and whether effects vary by literacy level or other patient- or facility-level characteristics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Barton: None; **J. Baker**: Amgen, 5; **g. Schmajuk**: None; **M. Valiveti**: None; **A. Bennett**: None; **B. Morasco**: None; **A. O'Neill**: None; **M. Niederhausen**: None.

Abstract Number: 1267

Patient Reported Outcomes Predict Subsequent Treatment Intensification Among Rheumatoid Arthritis Patients: Longitudinal PRO Measurement Using a Mobile Health App

Leah Santacroce[1], Misti Paudel[2] and Daniel Solomon[3], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [3]Brigham and Women's Hospital, Newton, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patient Reported Outcomes (PROs) collected via a mobile health application (App) can provide valuable insight into the health of patients with Rheumatoid Arthritis (RA). When collected at frequent intervals, providers can use them to assist in making decisions involving treatment intensification. We conducted a study to determine whether a single PRO score and/or sustained worsening in PROs were associated with future treatment intensification.

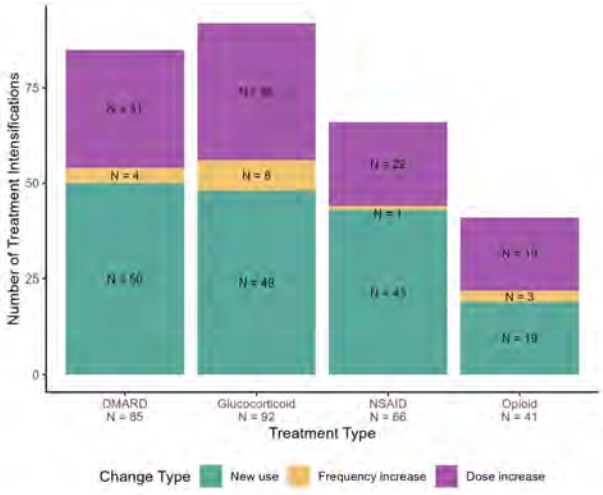
Methods: 150 patients with RA at one academic medical center were prompted to answer 1 of 4 validated PROs every other day through a mobile App ("mPRO") for 1 year; thus, each of the PROs were answered in an 8-day cycle. The PROs included the RA Disease Activity Index 5 (RADAI-5) and PROMIS short forms of pain interference, fatigue, and physical function. Lower function scores are better, where higher scores are worse for the other PROs.

The outcome of interest was RA treatment intensification - an increase in dose, frequency, or new use of any DMARD, NSAID, opioid, or oral glucocorticoid - during the App use period compared to the year prior. We examined 2 aspects of the PRO scores as potential predictors: the short-term PRO score during a given cycle and sustained PRO worsening defined as a clinically significant change compared to the previous measurement that was sustained for 3+ PRO cycles. Treatment intensification at the cycle immediately on or following each PRO score and sustained worsening was assessed. We used latent class mixed models to visualize trajectories of each PRO. Then, we examined mixed-effect logistic regression models to estimate the association between the time-varying PROs and treatment intensification. We conducted sensitivity analysis on a secondary outcome that excluded NSAIDs and opioids.

Results: Of the 150 patients who used the App, 83% were female, 91% were white, 7% had RA for less than 2 years, and the median age was 62 yrs. Over the study period, 284 treatment intensifications occurred among 63 patients, with a mean 1.9 (SD 3.2) changes per participant **(Figure 1)**. **Figure 2** depicts the trajectories of each PRO. The percentage with each trajectory differed by PRO: worsening -- 23% for pain, 18% for fatigue, 26% for function, 10% for RADAI; improvement -- 14% for pain, 12% for fatigue, 8% for function, 9% for RADAI; and stable --63% for pain, 70% for fatigue, 66% for function, 80% for RADAI.

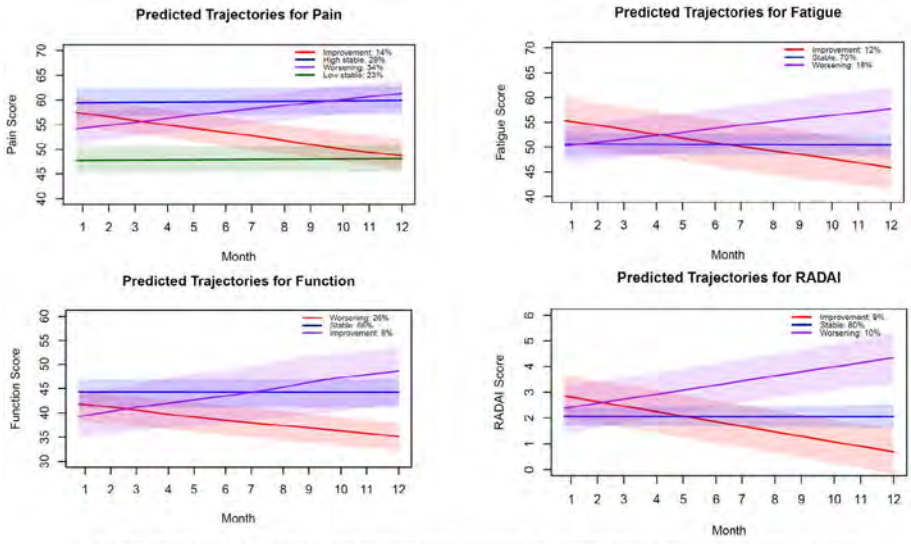
Regression models showed an association with treatment intensification and both short-term PROs and sustained worsening of the PROs. The intensifications were more likely to occur after a sustained worsening of pain interference (OR 2.04, 95% CI 1.10-3.78) or fatigue (OR 2.01, 95% CI 1.13-3.57). All four multivariable models (one for each PRO) had AUCs >

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



*This figure shows 284 treatment intensifications among 63 patients with at least one intensification

Figure 1. Types of treatment intensifications that occurred during a one-year study period among RA patients with at least one intensification.



For Pain, Fatigue, and RADAI higher scores represent worse outcomes, for Function higher scores represent better outcomes

Figure 2. Predicted trajectories of pain interference, fatigue, physical function, and RADAI over one year among patients with RA.

Table 1. The Impact of PRO changes on treatment intensification among patients with RA

PRO:	Pain Model	Fatigue Model	Function Model[1]	RADAI Model
	Odds ratio (95% confidence interval)			
Primary Outcome: All medications				
PRO Score[2]	1.37 (1.15, 1.64)	1.15 (1.01, 1.31)	0.63 (0.51, 0.77)	1.34 (1.17, 1.54)
Sustained PRO worsening[3]	2.04 (1.10, 3.78)	2.01 (1.13, 3.57)	1.09 (0.52, 2.32)	1.66 (0.35, 7.81)
AUC[4]	0.79 (0.74-0.84)	0.76 (0.71-0.81)	0.82 (0.76-0.87)	0.73 (0.67-0.79)
Secondary Outcome: DMARDs and oral glucocorticoids only				
PRO Score	1.43 (1.15, 1.78)	1.18 (1.00, 1.39)	0.55 (0.41, 0.73)	1.32 (1.09, 1.61)
Sustained PRO worsening	2.45 (1.24, 4.84)	2.30 (1.15, 4.61)	1.25 (0.50, 3.13)	1.56 (0.18, 13.2)
AUC	0.70 (0.64-0.75)	0.77 (0.71-0.82)	0.77 (0.71-0.82)	0.75 (0.69-0.81)

All models were adjusted for time, age, sex, and comorbidity index; none of the variables were significant in any model.

[1]Lower function scores are worse, thus odds ratios < 1.0 suggest that worse function is associated with treatment intensification

[2]The Odds Ratios for the PRO score for pain, fatigue, and function are interpreted as a 5-point increase, RADAI is interpreted as a 1-point increase. Higher function is better

[3]The sustained worsening is defined as an increase in 5+ points that remains elevated for 3 or more 8-day cycles for pain and fatigue. Function is defined as a sustained decrease in 5+ points, and RADAI a sustained increase in 1+ points.

[4]Confidence intervals for AUC calculated using bootstrapping

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

0.73, indicating moderate to strong discrimination. Models with the secondary outcome (not NSAIDs or opioids) showed similar results, with some stronger odds ratios but larger confidence intervals **(Table 1)**.

Conclusion: Our results show that longitudinally measured PROs can identify periods of worsening pain and fatigue, which are correlated with subsequent treatment intensification. Frequently assessed PROs can help augment clinical decision-making by providing symptom information between visits.

Disclosure: L. Santacroce: None; **M. Paudel**: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9.

Abstract Number: 1268

Development of the LupusCoach Chatbot: Results of a Focus Group

Leila Khalili[1], Pooja Desai[2], Maya Souvignier[2], Adrienne Pichon[2], Stephen Suh[3], Alberto Nordmann-Gomes[2], Lena Mamykina[2] and Anca Askanase[1], [1]Columbia University Medical Center, New York, NY, [2]Columbia University Irving Medical Center, New York, NY, [3]Columbia University Irving Medical Center, New York City, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Self-management education and coaching are successful interventions for managing chronic health conditions. However, accessibility of in-person coaching is limited; digital coaching is available and has been tested in patients with multiple chronic health conditions, but not in systemic lupus erythematosus (SLE). Building on previous work in collaboration with the biomedical informatics team, the CUIMC Lupus Center team developed a lupus chatbot, *LupusCoach*. The fully scripted chatbot focuses on two areas: 1) weekly educational goal setting for lupus patients that includes lupus specific, lupus clinical trials, and general health information and 2) weekly health management goal setting related to lupus. Here we describe the qualitative feedback of two focus groups evaluating the content and goals for *LupusCoach*.

Methods: Ten diverse lupus patients (all patients met the 2019 ACR/EULAR criteria for SLE) were selected via convenience sampling to give feedback on the chatbot educational content and goals. We conducted two focus groups remotely using video-conferencing software. The focus groups were audio recorded and transcribed verbatim. Reflective thematic analysis was conducted using the NVIVO software.

Results: Thematic analysis across patients from both focus groups identified several main themes relating to participant background and chatbot feedback. Participant background themes included connection between patients and providers, participants' individual experiences with lupus, and strategies for lupus management (Table 1). Themes relating to chatbot feedback included desired features and capabilities, experiences with technology, input on goals and action plans, discussion about informational messages, and user expectations of technology (Table 2). Based on these themes, we made adjustments to *LupusCoach*, specifically by tailoring action plans to different levels of effort. An on-line support community forum was requested, and therefore additional resources for lupus patients were listed on the accompanying FAQ/further information website for *LupusCoach*.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Description of Themes Relating to Participant Background and Experience

Theme	Description	Demonstrative Quote
Connection between patients and providers	Participants expressed the importance of a personal connection with their providers, seeking out the best providers and care, importance of direct communication, importance of goal alignment between patients and providers, and long-term relationship with the right provider.	"I've always had severe joint problems, and [the doctor] discovered that it was because [of] the lupus, but none of the [other] doctors made that connection, so I've been with her since..."
Participants individual experience with lupus	Experiences that participants noted living with lupus included: challenging diagnosis processes/delayed diagnosis, unpredictability of symptoms and flares, invisible symptoms, experiencing balancing lupus and life, the peaks and valleys of living with lupus, and the stigma of living with lupus.	"The most annoying thing about this disease is unpredictability. One day you could be fine and the next moment you're sick with a flare."
Strategies for lupus management	Topics discussed relating to lupus management included social structures for support, identifying triggers for flares, medication management, trial and error in lupus management, and self-management strategies.	"Eventually, you find what works for you or helps along the way. But it's trial and error. It takes time. And also, like being able to read your body and sense for what doesn't work for you and what is working." "But I think there's something to [say for] mental self -care, and the very practical, like take your medicine on time, don't skip your medicine, put the sunscreen, don't go in the sun, drink water, go for a walk, do some movement, do some weight -bearing activity, like all that kind of stuff" "I really kind of had to almost build like a, like a personal code for survival, how to kind of get through it."

Conclusion: Overall, patients gave positive feedback both on the contents and goals of *LupusCoach*. The next step is to beta-test the chatbot and survey a larger group of 10-20 patients, using pre/posttest method, questionnaires, and surveying for satisfaction.

Table 2. Description of Themes Relating to Chatbot Feedback

Theme	Description	Demonstrative Quote
Desired features and capabilities	Participants most commonly expressed the desire for incorporation of AI, sharing ideas with other patients/a community board feature, and a user-friendly interface.	"There should be somewhere on the site if anybody has questions and they want to reach out to others ... [who are] having a problem with this"
Experience with technology	Participants noted that they had they had interacted with other apps that encourage behaviors and engagement in a positive manner and had a high awareness of technology.	"I think that there's something around how the psychological framework of the user is... understood so that there isn't like a sense of shame or failure."
Feedback on goals and action plans	Participants expressed an importance that there is a range of action plans tailored to different levels of effort, that patient expertise impacts goal usefulness, sun protection goals are useful, and the desire for specific action plans.	"But sometimes, if you're bedridden, you can't walk on your own. There needs to be simpler options, accommodations."
Feedback on informational messages	Participants stated that they wanted more information about clinical trials, that messages should be concise and meaningful. Focus group participants gave generally positive feedback on informational messages.	"Maybe I would ask for more [specifics about clinical trials]? What kind of trials are there? ...where can I go?"
User expectations of technology	The participants expected that the chatbot would be tailored to person and personal data, the chatbot content is specific for lupus, and AI will be incorporated.	"I think in some ways the challenge becomes... building enough kind of depth and uniqueness for that lupus patient and that unique profile in terms of what's going to be great for them."

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Khalili: None; **P. Desai**: None; **M. Souvignier**: None; **A. Pichon**: None; **S. Suh**: None; **A. Nordmann-Gomes**: None; **L. Mamykina**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5.

Abstract Number: 1269

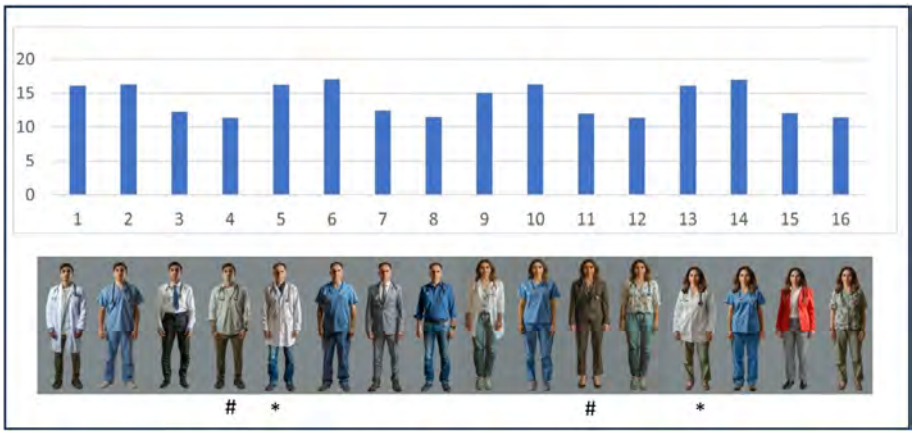
Dress for success: Influence of Rheumatologist Demographics and Attire on Patients with Chronic Inflammatory Arthritis Perceptions

LETICIA LEON[1], LAURA CANO[2], ELENA MORENO[3], GABRIELA CASTILLO[4], GUIDO CORRADI[5], MARTA REDONDO[4], MARIA ISABEL CASADO[5], DALIFER FREITES[6], ALMUDENA TRUCHARTE[4], INMACULADA UREÑA[2] and lydia Abasolo Alcazar[7], [1]Fundación Investigación Biomédica Hospital Clínico San Carlos, IdISSC; Universidad Camilo Jose Cela, MADRID, Madrid, Spain, [2]Hospital Regional Universitario de Málaga, MALAGA, Andalucia, Spain, [3]Fundación Investigación Biomédica Hospital Clínico San Carlos, MADRID, Madrid, Spain, [4]Universidad Camilo Jose Cela, MADRID, Madrid, Spain, [5]Universidad Complutense de Madrid, MADRID, Madrid, Spain, [6]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [7]IdISSC. HCSC, Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Physician sociodemographic factors and attire has been shown to influence patients' trust. This study aimed to determine differences on patient perceptions of rheumatologist professionalism, empathy, reliability and medical safety.

Methods: A multicentre study was conducted from 1 December 2024 to 30 May 2025. Patients with chronic inflammatory arthritis (CIA) receiving biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) were recruited. Demographic and clinical information was collected. Patients completed a questionnaire evaluating 16 standardized photographs, each depicting a fictional rheumatologist with controlled features (race, posture, arm position, facial expression, and use of stethoscope) to minimize nonverbal communication bias. Each physician appeared four times, varying only in attire: formal office wear, scrubs, white coat, and casual clothing. Patients rated the physicians on four criteria—professionalism, empathy, reliability, and medical safety—using a 5-point Likert scale. Additionally, they were asked to select their most and least preferred physicians. A histogram of scores was generated. Statistical differences in sociodemographic preferences were tested with multivariate regression analyses.



Total scores for each physician. *Most preferred physicians; # Least preferred physicians.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 67 patients participated (median age 53 years; 68.6% women). Diagnoses included rheumatoid arthritis (43.3%), spondyloarthritis (34.3%), and psoriatic arthritis (22.4%). In the multivariate analysis of perception criteria, older physicians were rated significantly better than younger physicians across all dimensions assessed ($p < 0.05$). Among these, professionalism was the most highly rated attribute associated with older physicians. No significant differences were found in patient perceptions based on the physician's gender for any of the evaluated criteria. Regarding attire, scrubs received the highest overall ratings [66.71 (SD 10.84)], followed by the white coat [63.59 (SD 11.88)], formal attire [48.80 (SD 18.04)], and casual clothing [45.76 (SD 20.70)]. Patients showed a clear preference for older physicians—both male and female—wearing white coats. Young male physician with casual attire and young female physician with formal office attire were least preferred physicians.

Conclusion: Patients with CIA perceived rheumatologists in scrubs or white coats as more professional, empathetic, reliable, and medically trustworthy than those in formal or casual attire. In addition, older physicians were preferred by patients. Rheumatologists may consider these contextual cues to enhance patient trust and engagement.

Disclosure: L. LEON: None; **L. CANO**: None; **E. MORENO**: None; **G. CASTILLO**: None; **G. CORRADI**: None; **M. REDONDO**: None; **M. CASADO**: None; **D. FREITES**: None; **A. TRUCHARTE**: None; **I. UREÑA**: None; **I. Abasolo Alcazar**: None.

Abstract Number: 1270

Increasing Participation in the FT819 Cell Therapy Trial Amongst People Living with Lupus: A Focus Group Study

Joy Buie[1], Safoah Agyemang[1], Andrew Henry[2], Andrew BitMansour[3], Vaneet Sandhu[4], Debra Zack[5] and **Michael Fisher**[1], [1]Lupus Foundation of America, Washington, DC, [2]Fate Therapeutics, Inc., San Diego, CA, [3]Fate Therapeutics, Inc., San Carlos, CA, [4]Fate Therapeutics, Inc., San Diego, [5]Fate Therapeutics, San Diego

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical trials exploring the safety and efficacy of chimeric antigen receptor (CAR) T-cell therapy for lupus are growing. Challenges linked to recruitment for CAR T-cell clinical trials are likely multifactorial and may include barriers at the healthcare system, provider, and patient level. The aim of this study was to elicit qualitative feedback from people living with systemic lupus erythematosus (SLE) who have the greatest burden of disease to understand attitudes, perceptions, and behaviors related to CAR T-cell therapy clinical trials, specifically the Fate Therapeutics FT819 product.

Methods: A focus group was conducted among people with SLE recruited via the Lupus Foundation of America's Research Accelerated by You (RAY) Registry. Researchers queried RAY for individuals thought to meet inclusion criteria and provided an online screener. Of 205 respondents, 23 were shortlisted based on response timing (5 business days) and alignment with *a priori* inclusion/exclusion criteria. Upon follow-up contact, 6 expressed interest and consented. Five attended a 2-hour virtual focus group in December 2025 via Zoom. Following a slide presentation describing FT819 therapy as an off-the-shelf (uniquely available on-demand) cell therapy with reduced patient burden such as hospitalization requirements, semi-structured questions covered: (1) background and journey to diagnosis and care, (2) general awareness and perceptions of cell therapy, (3) perceptions of FT819 therapy administration, (4) potential benefits and risks of receiving FT819 therapy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Participant Demographics

Characteristics	Category	N	%
Age (years)	Mean (SD) / Range	40 (5.2) / 30 – 45	–
Duration of Disease (years)	Mean (SD) / Range	20 (8.1) / 15 – 38	–
Sex	Female	5	100%
Race	Black/African-American	5	100%
Ethnicity*	Hispanic Non-Hispanic	1 4	20% 80%
Region	Northeast Midwest South West	1 1 3 0	20% 20% 60% 0%
*Ethnicity and race questions were asked separate from one another.			

Table 2. Perceived Benefits of FT819 Therapy

Key Themes	Illustrative Quotes
Improved Quality of Life	• *Just a better quality of life, it seems it would give.* - Participant 3 • *Less pain or no pain, I think that's the biggest benefit of all for me.* - Participant 1 • *Just waking up, feeling good in the morning. Going about my day. Living my life as normal.* - Participant 5
Potential for Remission	• *With the CAR T cell therapy, it sounds like it's more in that direction of, like, you could achieve remission and not just have consistent disease activity or symptoms.* - Participant 2 • *I have seen from some meetings that I've been in that the side effects are low. And the people are in remission and living great lives at this point.* -Participant 1 • *Remission. The potential for remission.* - Participant 4
Relatively Short Hospital Stay (3-day hospitalization after receiving FT819)	• *I would say it's reasonable to me. Three days is nothing compared to the 30 that other stem cell replacement therapies are requiring.* - Participant 1 • *I've done a lot worse with just lupus, so I could do 3 days.* - Participant 4 • *I wouldn't have a problem with that timeline of being in hospital.* - Participant 5

within a clinical trial, and (5) perceptions and acceptability of follow-up and monitoring. The focus group was audio-video recorded, transcribed, and analyzed in Dedoose using content analysis methodology.

Results: Participants included 5 Black/African American female adults, one of whom also identified as Hispanic. All had active SLE affecting one or more major organ systems (Table 1). Results emerged across 3 categories: (1) Initial perceptions of cell therapy, (2) perceptions of FT819 therapy including benefits and concerns (Tables 2 and 3), and (3) willingness to participate in an FT819 trial and expected outcomes. Initial perceptions indicated participants were familiar with and optimistic about cell therapy but also had concerns. Regarding FT819 therapy, participants perceived benefits such as improved quality of life, potential for remission, and a relatively short hospital stay. Participants also expressed concerns about potential adverse reactions or side effects, chemotherapy or mycophenolate requirements, long-term effectiveness, time and travel, hospital care and quality, caregiver needs, and medication cost and coverage (upon FDA approval). Participants also commented on willingness to participate in an FT819 trial, definition of successful treatment, and required duration of clinical effect.

Conclusion: Clinical trials in the U.S. have often failed to include representative samples, leading to a lack of generalizability. This study identified barriers and facilitators to cell therapy trial participation among a purposive sample. The findings can guide activities such as patient engagement, recruitment, and site selection.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Concerns about FT819 Therapy

Key Themes	Illustrative Quotes
Adverse Reactions or Side Effects	• One of the scariest things with taking new medication [is] all the side effects… I just saw a commercial, and it's like 'May cause increased risk for cancer. May affect, you know.' Then, I'm like, what the ****? - Participant 4 • It's just that fear of stopping my medication that I would struggle with, because I had such a life threatening experience… That would be the only thing that would make me hesitate. - Participant 5 • For Benlysta and Saphnelo and other infusion drugs, there can be a higher rate of allergic reactions… So that would be my concern that just the method of delivery… might trigger some sort of allergic reaction. - Participant 2
Chemotherapy/ Mycophenolate Requirement	• I go back to the chemo part. That like terrifies me. So just understanding the side effects from the chemo. How long I would have to do the chemo? - Participant 4 • So, how high of a dosage of [mycophenolate] would you have to be on? Because I've tried that a couple times, I'm actually back on it again, and I'm having bad side effects yet again. - Participant 3 • You know, side effects from chemotherapy or radiation. It's a matter of… Do I stay with this lupus and deal with that or potentially get something else like cancer and have to deal with that as a side effect? - Participant 2
Long-Term Effectiveness	• I would say the you know the long term. What happens after you have that cell therapy replacement? And the years to come, that that is where I have the doubts and the questions, you know, will it return after some? … How long is it? It is it a guarantee? - Participant 1 • I think I would also want to try it. I'm hesitant about it… I think it would just depend on how much more information comes out about this treatment, especially long term studies about how long it might last? … I would be hesitant to stop any and all treatments. - Participant 2 • But my thing would just be kind of like what some of the others are saying. Is this going to work for the long term? - Participant 3
Time and Travel Required for Follow-Up	• The follow up, like the weekly follow up. So like if you had to travel say to New York to get this, and you live in DC or whatever, it is that kind of thing. Where are you gonna have to follow up? - Participant 3 • I think that would help make it easier. To fit it within my life instead of the study itself being the main thing, and I have to fit life around it. - Participant 2 • A lot of the time, like in the clinical trials, they want to reimburse you. But for those that are in my current situation, where I have no income, you would need that travel, the lodging. You would need all of that taken care of ahead of time versus being reimbursed. - Participant 1
Hospital Care and Quality	• I'm always just afraid of additional infection and things like that. You know, the setting itself would have to be obviously highly controlled. That there wouldn't be any kind of infections and things like that. - Participant 3 • [Having] a specific center or a specific rheumatology office that is versed in this, medication, and treatment, that would be a concern. Because I used to work in a hospital, and it's not like they have lupus specialists all over the place. - Participant 4 • I was being evaluated by oncology, and I was one of the only people wearing a mask in the waiting room… Like, cancer patients who are actively taking chemotherapy, [and] doctors and patients weren't even wearing masks. -Participant 2
Caregiver Needs	• If I had to travel outside of where I reside, I wouldn't have a problem with it. But I would have to know ahead of time so that I can prepare, because I don't drive. I need my husband with me. All the time we have children, so. I would definitely need a lot of time to plan ahead. And I would like to make sure he has the resources he needs while I'm going through this. - Participant 5 • So if it's [in my city], sure, I could easily get some family member or something to take me where I need to be. But if I have to go up to Boston or something like that, that's a different story. That would be, having to, again, get my husband to take off work and all that kind of stuff. - Participant 3 • I'm thinking in terms of logistics for caregivers, especially because this is a medication that's going to be impacting our immune system or treatment that's going to impact our immune system, like what changes would they need to make if we're getting this chemotherapy infusion… Do they have to stay out of work or school for a period of? For our own protection? - Participant 2
Medication Cost and Insurance Coverage	• Does my insurance even cover it? … Hopefully, my insurance covers it. And hopefully there's not some huge out of pocket costs. So that's just where my mind goes. - Participant 4 • If I go through this, will I have issues getting back on the medication I was on initially? The concerns I have, I just don't want to recreate a situation for myself when I don't know what's going to happen. - Participant 5 • My thing is like just managing insurance and like work. It just takes so much time. Like a full time job. - Participant 4

Disclosure: J. Buie: Bristol-Myers Squibb(BMS), 1, Fate Therapeutics, 1, Genentech, 1, Novartis, 1; **S. Agyemang**: None; **A. Henry**: Fate Therapeutics, Inc., 3; **A. BitMansour**: Fate Therapeutics, Inc., 3; **V. Sandhu**: Fate Therapeutics Inc, 3; **D. Zack**: Fate Therapeutics, 3; **M. Fisher**: None.

Abstract Number: 1271

Overcoming Obstacles to Care: Survey of Adult Patients with Idiopathic Inflammatory Myopathies (IIM)

Saloni Patolia[1], Carolina Alvarez[2], Jessica Grant[3], Paul Mihas[4], Todd Schwartz[5], Galen Foulke[6], Amanda Nelson[5] and Astia Allenzara[5], [1]UNC Rheumatology, Durham, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]Odum Institute for Reseach in Social Science, Chapel Hill, NC, [4]Odum Institute for Reseach in Social Science, Chapel Hill, [5]Thurston Arthritis Research Center, Chapel Hill, [6]Penn State Health, Hershey, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

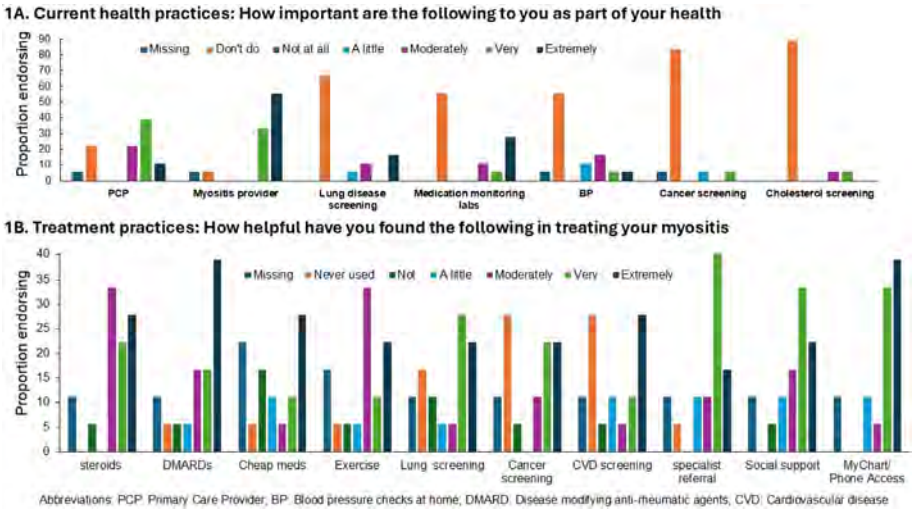
Session Date: Monday, October 27, 2025
Session Title: (1248–1271) Patient Outcomes, Preferences, & Attitudes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

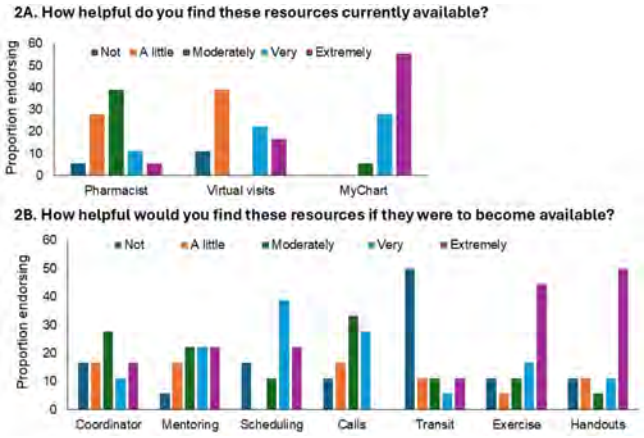
Background/Purpose: Idiopathic inflammatory myopathies (IIM) are heterogenous autoimmune diseases requiring coordinated, patient-centered care. Understanding patient perspectives on diagnosis, treatment, health screening, and barriers to care is essential for optimizing outcomes and improving patient-centered care. We conducted a survey to assess IIM patient attitudes towards treatment, screening, and barriers to care at the University of North Carolina at Chapel Hill Rheumatology clinic.

Methods: A single anonymous survey with two open-ended and 16 discrete questions was developed to elicit perceptions of multimorbidity, a specific focus on screening, and obstacles to care. Patients with IIM were screened for eligibility from chart review prior to their rheumatology clinic appointment and provided with survey access information at the time of the appointment. Participant responses to open ended questions were analyzed with inductive thematic coding by two reviewers.

Table 1. Descriptive Characteristics of Participants		
Demographic characteristics	n	%
Age*		
<45 years old	7	38.9
45-64 years old	7	38.9
>65 years old	2	11.1
Race/Ethnicity**		
Black or African American	5	27.8
More than one	1	5.6
White	7	38.9
White, Hispanic or Latino/a	2	11.1
Gender*		
Female	10	55.6
Male	6	33.3
Education*		
Any college or Graduate degree	12	66.7
High school graduate/GED or equivalent	3	16.7
Less than high school	1	5.6
Income*		
$75,000 or more	4	22.2
$25,000 to $74,999	6	33.3
Less than $25,000	4	22.2
Employment*		
Disabled permanently or temporarily	1	5.6
Retired and not working	2	11.1
Unemployed or looking for work	1	5.6
Working full or part time, student or keeping house	11	61.1
Other	1	5.6
Care characteristics		
Number of additional providers, besides IIM provider that have provided care in the last 6 months?		
1 or 2	9	50
3 or 4	5	27.8
5 or more	3	16.7
None	1	5.6
Sources for health information (check all that apply)		
Websites like ACR or Myositis Association	9	50
Myositis doctor	17	94.4
Primary provider	11	61.1
Wikipedia	2	11.1
Google	8	44.4
Social media	1	5.6
Friends, family, colleagues	4	22.2
Any of the following experienced from medications used to treat myositis? (check all that apply)		
High cost	6	33.3
Not available from pharmacy	2	11.1
Side effects	9	50.0
Not sure why I should take the medication	2	11.1
Interaction with another medication I take	1	5.6
Time from symptoms of myositis to seeing a myositis specialist*		
Less than 4 months	7	38.9
4-12 months	6	33.3
More than a year	3	16.7
Time from symptoms of myositis to starting treatment for myositis*		
Less than 4 months	7	38.9
4-12 months	7	38.9
More than a year	2	11.1
*Category is missing 2 responses; **Category is missing 3 responses, due to rounding, percentages may not sum to 100 percent		

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





Results: Of 62 patients seen during routine ambulatory rheumatology care, 16 completed the survey. Most respondents were female (56%) and working (61%, Table 1). Most participants obtained health information from their IIM provider (94%) followed by their primary care provider (61%). Half of participants did not understand the purpose of one or more of their medications, and a third reported high cost or co-pay of one or more of their medications. Most respondents did not endorse participating in screening practices (Figure 1A). Participants endorsed electronic/phone access to care team, disease modifying anti-rheumatic agents and exercise as components they found helpful in managing their myositis (Figure 1B). For current and future resources, participants noted the electronic patient portal (56%), an exercise program (44%), and educational handouts on IIM (50%) as extremely helpful (Figure 2). Regarding what participants wished their myositis provider understood about their condition, participants discussed uncertainty, "*it comes and goes;*" "[it] *creates feelings of inaptitude and unreliability*" and "*…it seems my muscle pains are dismissed since my bloodwork doesn't show increases in certain levels.*" Regarding what participants would improve about their myositis, many responses focused on a cure, while others expressed a desire to understand "*understanding what I was feeling and facing would help me understand more clearly*" and apply disease understanding to decrease flares: "*what preventative actions I can take to prevent a flare other than medicinal.*"

Conclusion: In this single center survey, we found patients with IIM did not participate in screening (e.g. cancer, cardiovascular). Participants expressed uncertainty/unpredictability as obstacles to care and cited MyChart as helpful alongside a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

desire for informational handouts. These findings highlight the importance of targeted patient education and proactive communication by rheumatologists to address informational gaps and support long-term care engagement.

Disclosure: S. Patolia: None; **C. Alvarez**: None; **J. Grant**: None; **P. Mihas**: None; **T. Schwartz**: None; **G. Foulke**: None; **A. Nelson**: None; **A. Allenzara**: None.

Abstract Number: 1273

Effectiveness of IV Cyclophosphamide and Mycophenolate Mofetil in the Treatment of Pediatric Systemic Lupus Erythematosus with Lupus Nephritis

Adrienne Katrin Guiang-Valerio, University of Santo Tomas Hospital, Mandaluyong, National Capital Region, Philippines

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is more common in children (occurs in 50-82%) compared to adults. Cyclophosphamide (CYC) and mycophenolate mofetil (MMF) are both treatment options for childhood-onset SLE with LN. Both options are included in the recommendations for the management of LN. However, in children, the optimal treatment of LN is still unknown.

Methods: Single center retrospective cohort study included patients ≤18 years old with SLE with nephritis diagnosed between 2008 and 2024.

Results: A total of 231 patients were included in the study. The proportion of participants who were shifted to another treatment due to poor response was significantly higher among those in the MMF group (81.82% vs. 50.00%, p=0.001), while

Comparisons of Renal Response and Outcomes

Table 4.
Between-Group Comparisons of the Renal Response Rates and Outcomes Between the Two Groups among Childhood Systemic Lupus Erythematosus (cSLE) with Lupus Nephritis in the University of Santo Tomas Hospital from January 2008 to September 2024 (N = 231)

Outcomes	Group Allocation (N = 231)		p-value (Two-Tailed)
	Cyclophosphamide Group (CYC; n = 174)	Mycophenolate Mofetil Group (MMF; n = 57)	
Incidence of Complete Renal Response (Per 100 Person-Months; 95% CI)	4.91 (4.12 to 5.82)	4.71 (3.48 to 6.25)	0.818
Renal Response (f, %)			
No Renal Response	10 (5.75%)	4 (7.02%)	0.727
Partial Renal Response	30 (17.24%)	5 (8.77%)	0.122
Complete Renal Response	134 (77.01%)	48 (84.21%)	0.249
Number of Flares (Md, IQR)			
One-Year Post-Treatment	0.00 (0.00 – 1.00)	1.00 (0.00 – 2.00)	0.007*
Two-Year Post-Treatment	0.00 (0.00 – 2.00)	0.00 (0.00 – 4.00)	0.389
Low C3 Levels (f, %)	34 (19.54%)	17 (29.82%)	0.104
Receipt of Hydroxychloroquine (f, %)	172 (98.85%)	56 (98.25%)	0.574
Receipt of ACEI/ARB (f, %)	170 (97.70%)	57 (100.00%)	0.574
Prednisone Daily Dose (mg; Md, IQR)	5.00 (5.00 – 15.00)	5.00 (5.00 – 30.00)	0.190
Methylprednisolone Pulse Therapy (MPPT) Status (f, %)	49 (28.18%)	14 (24.56%)	0.596
Receipt of Rituximab (f, %)	30 (17.24%)	5 (8.77%)	0.122

*Significant at 0.05

Between-Group Comparisons of the Renal Response Rates and Outcomes Between the Two Groups among Childhood Systemic Lupus Erythematosus (cSLE) with Lupus Nephritis in the University of Santo Tomas Hospital from January 2008 to September 2024 (N = 231)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Comparisons of Reasons for Shifting to Another Treatment

Table 3.
Comparative Analyses of the Reasons for Shifting to Another Treatment among Childhood Systemic Lupus Erythematosus (cSLE) with Lupus Nephritis in the University of Santo Tomas Hospital from January 2008 to September 2024 (N = 231)

Outcomes	Group Allocation (N = 231)		p-value (Two-Tailed)
	Cyclophosphamide Group (CYC; n = 174)	Mycophenolate Mofetil Group (MMF; n = 57)	
Completed Induction Phase (f, %)	92 (52.87%)	34 (59.65%)	0.372
Patients Shifted to Another Treatment (f, %)	82 (47.13%)	23 (40.35%)	0.372
Reasons for Shifting Treatment (f, %)			
Poor Response	40 (50.00%)	18 (81.82%)	0.001*
Persistence or Recurrence of Hematuria/Proteinuria	25 (31.25%)	4 (18.18%)	0.057
Transitioned	2 (2.50%)	0 (0.00%)	0.226
Pandemic	2 (2.50%)	0 (0.00%)	0.226
Preference or Request	6 (7.50%)	0 (0.00%)	0.033*
Adverse Events (e.g., Infection, Chest Pain, etc.)	5 (6.25%)	0 (0.00%)	0.053

*Significant at 0.05

Comparative Analyses of the Reasons for Shifting to Another Treatment among Childhood Systemic Lupus Erythematosus (cSLE) with Lupus Nephritis in the University of Santo Tomas Hospital from January 2008 to September 2024 (N = 231)

the proportion of those who were shifted due to preference was higher in CYC group. The overall incidence rate of complete renal response was 4.86 per 100 person-months, 4.91 per person-months in the CYC group and 4.71 per person-months in the MMF group. 77.01% of the CYC group had complete renal response, while the MMF group had a rate of 84.21%. During the first-year post-treatment, the median number of flares was significantly higher in the MMF group compared to CYC. Females were 6.85-times more likely to be shifted to another treatment, while those who received MPPT were 2.86-times less likely to be shifted to another treatment. The odds of being shifted to another treatment decreases by 25% for every 1-milligram increase in the daily dosage of prednisone. Females and having tuberculosis increased the odds of shifting to another treatment by 6.14-times and 4.87-times, respectively. In the CYC group who received RTX were 6.67-times less likely to be shifted to another treatment. The likelihood of shifting from MMF to another treatment decreased by 19.00% for every 1-milligram increase in the daily prednisone dosage.

Conclusion: Both CYC and MMF are effective treatments for cSLE with LN, with CYC showing a faster response time compared to MMF (13 months vs 24 months). The probability of complete renal response at 6 months for those in the CYC group was approximately 80%, while those in the MMF group was about 70%. However, patients who were shifted between treatments had a significantly better renal outcome. Early adjustments in therapy may improve long-term results. A personalized approach considering the patient's clinical characteristics, risk factors, and response to therapy is crucial in managing cSLE with LN.

Disclosure: a. guiang-valerio: None.

Abstract Number: 1274

Analysis of Vaccination Compliance in Patients with Juvenile Idiopathic Arthritis at the Rheumatology Transitional Consultation

Andres Perez Hurtado[1], Jose Ivorra Cortes[2], ELENA GRAU GARCIA[3], Miguel Simeo Vinaixa[4], Iago Alcantara Alvarez[4], Belen Villanueva Manes[5], Alba Maria Torrat Noves[6], Daniel Ramos Castro[7], Pablo Muñoz Martinez[4], Laura mas sanchez[8], Berta López Montesinos[9], Lucía Lacruz Pérez[10] and José Andrés Román Ivorra[11], [1]Hospital Universitario y Politècnico La Fe, Valencia, Comunidad Valenciana, Spain, [2]Hospital Universitario La Fe, Valencia, Comunidad Valenciana, Spain, [3]HUP La Fe, Valencia, Comunidad Valenciana, Spain, [4]Rheumatology Department. HUP La Fe, Valencia, Spain, [5]Hospital La Fe, Valencia, Spain, [6]Hospital Universitari i Politècnic La Fe de Valencia, Valencia, Spain, [7]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [8]Hospital Universitario y Politécnico La Fe, Valencia, Comunidad

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Valenciana, Spain, [9]Pediatric Rheumatology Department. HUP La Fe, Valencia, Spain, [10]Pediatric Rheumatology Department. HUP La Fe, Valencia, Comunidad Valenciana, Spain, [11]Hospital Universitari i Politècnic La Fe, Valencia, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile idiopathic arthritis is the most common group of inflammatory rheumatic diseases in childhood. Its early onset and the immunosuppressive treatments used to control it may interfere with adherence to the established immunisation schedule and increase the risk of infections in adulthood. Little information is available on the magnitude of this problem in clinical practice.

The aim of this study is to assess the degree of compliance with the Spanish vaccination calendar prior to the rheumatology transitional consultation and to analyse different factors that may influence its implementation.

Methods: A single-centre observational retrospective study of patients with JIA (ILAR 2001) included in the rheumatology transitional consultation register (2012-2024) has been performed. Clinical, therapeutic and vaccination data were collected. Given the variability of the vaccination schedule throughout the follow-up period, it was agreed to include vaccines for HBV, Polyomavirus, Haemophilus influenzae B, Diphtheria-Tetanus-Polio (DTaP), Pneumococcal (13-valent), Men. C, Papilloma, Varicella and MMR. The main variables included were: treatment with biological DMARDs or classical DMARDs, years of exposure to biological DMARDs, age at diagnosis and date at the time of transition consultation.

JIA SUBTYPES	N (%)
OLIGOARTICULAR	24 (24.49%)
POLYARTICULAR RF -	24 (24.49%)
POLYARTICULAR RF +	6 (6.12%)
SYSTEMIC	9 (9.18%)
PSORIATIC	5 (5.1%)
ARTHRITIS-ENTHESITIS	24 (24.49%)
UNDIFFERENTIATED	6 (6.12%)

JIA Subtypes

VACCINE	FULL VACCINATION N (%)	VACCINATION EXPOSURE (at least 1 received dose) N (%)
Diphtheria-tetanus-pertussis (DTaP)	60 (61.86%)	87 (89.69%)
Polyomavirus	51 (52.58%)	72 (74.23%)
Haemophilus influenzae B	41 (42.27%)	56 (57.73%)
Hepatitis B Virus	53 (54.64%)	72 (74.23%)
Pneumococcal (13-valent)	22 (22.68%)	56 (57.73%)
Meningococcal C	38 (39.17%)	80 (82.47%)
MMR (Measles, Rubella and Mumps)	49 (50.52%)	78 (80.41%)
Varicella	12 (12.37%)	20 (20.62%)
Papilloma	45 (46.39%)	47 (48.45%)

Vaccination compliance in JIA patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Exposure to the vaccine was considered as having received at least one dose of the vaccine and full vaccination with receiving the doses established in the vaccination schedule of the Valencian Community (Spain)

Logistic regression models were used to study the relationship between the different variables and vaccination compliance.

Results: 98 patients (64.29% female) with a mean age (SD) of 8.65 (4.73) years old at diagnosis and 20.41 (2.54) years old at the rheumatology transition consultation visit, were included. The distribution by JIA subtypes are described in table 1. 53.61% of patients had been treated with biological DMARDs with an average duration of treatment of 18.47 years and 52.04% had been treated with classical DMARDs.

Only 2 patients received the full dose of all the established vaccines and 5 received at least one dose. Table 2 shows the percentage of compliance for each vaccine. Multivariate analysis showed that biological DMARD treatment was associated with lower complete vaccination for MMR (p=0.004), Polyomavuris (p=0.01), H.influenzae B (p=0.02), Men. C (p=0.017), Papilloma (p=0.01) and DTaP (p=0.004). On the other hand, treatment with classical DMARDs was associated with higher exposure to pneumococcal (p=0.004) and HBV (p=0.03) vaccination.

A more recent date at the transition consultation was related to higher percentage of complete vaccination for DtaP (p=0.003), Polyomavuris (p=0.03), Haemophilus Influenzae B (p< 0.001), pneumococcal (p=0.001), Men. C (p=0.034) and Varicella (p=0.001) vaccines.

Conclusion: A low percentage of vaccination exposure and especially a low percentage of complete vaccination was observed for both live and inactivated virus vaccines, mainly related to the biological DMARD prescription. In contrast, treatment with classical DMARDs was associated with higher exposure to pneumococcal and HBV vaccines. Compliance was higher in recent years.

Disclosure: A. Perez Hurtado: None; **J. Ivorra Cortes**: None; **E. GRAU GARCIA**: None; **M. Simeo Vinaixa**: None; **I. Alcantara Alvarez**: None; **B. Villanueva Manes**: None; **A. Torrat Noves**: None; **D. Ramos Castro**: None; **P. Muñoz Martinez**: None; **L. mas sanchez**: None; **B. López Montesinos**: None; **L. Lacruz Pérez**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6.

Abstract Number: 1275

Fostering connections in Pediatric Rheumatology: A Narrative medicine intervention

Anita Dhanrajani[1], Joanne Drew[2], Suzanne Edison[3], Lakshmi Moorthy[4], Ingrid Goh[5], Alicia Garceau[6], Hanna Saltzman[7], Courtney Wells[8], Aviya Levy[9] and Childhood Arthritis and Rheumatology Research Alliance (CARRA) and CARRA Narrative Medicine Workgroup, [1]Manning Family Children's Hospital, Tulane University Medicine, New Orleans, LA, [2]Nationwide Children's Hospital, Columbus, OH, [3]Cure JM foundation, Seattle, WA, [4]Department of Pediatrics, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [5]University of Toronto The Hospital for Sick Children, Toronto, ON, Canada, [6]Self Employed, Indianapolis, [7]University of Utah, Salt Lake City, UT, [8]University of Wisconsin River falls, River Falls, WI, [9]Rady Children's Hospital, San Diego, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient and caregiver characteristics

Total participants in attendance	25
Number of completed responses	21
Diseases reported	JIA, SLE, ANCA vasculitis, Behçet's, Systemic sclerosis, JDM, undiagnosed systemic autoinflammatory disease, Sjögren's, Juvenile immune-mediated necrotizing myopathy, CAPS
Age distribution in years (percent of total)	• 18–30: 8 (38) • 31–40: 2 (9) • 41–50: 5 (24) • 51–60: 6 (29)
Prior narrative medicine experience (percent of total)	• Yes: 4 (19) • No: 17 (81)
Workshop satisfaction (percent of total)	• Satisfied: 7 (33) •Very satisfied: 14 (67)
Level of connection (percent of total)	• Improved: 13 (62) • Same: 5 (24) • Decreased: 3 (14)
Anxiety level (percent of total)	• Improved: 7 (33) • Same: 13 (62) • Worsened: 1 (5)

Legend: JIA = Juvenile Idiopathic Arthritis, SLE = Systemic Lupus Erythematosus, ANCA = Anti neutrophilic cytoplasmic antibody, JDM = Juvenile Dermatomyositis, CAPS = Cryopyrin associated periodic fever syndrome

Patient and caregiver characteristics

Background/Purpose: Patients with chronic diseases often report poor health-related quality of life (QOL) and impaired psychosocial functioning. The current model of healthcare in rheumatology emphasizes evidence-based medicine but does not always address broader dimensions of patient well-being, psychological needs, and QOL. Narrative medicine (NM) is a valuable tool that can be used in healthcare by patients, caregivers, and health care professionals to further explore and understand experiences with illness and caregiving. Allowing patients and caregivers to reconstruct their experiences through self-reflection can be cathartic and has been shown to improve patient reported outcomes and QOL

Methods: The Childhood Arthritis and Rheumatology Research Alliance (CARRA) NM workgroup conducted two 60-minute workshops at its 2025 annual meeting. The first workshop was designed for patients and caregivers affected by rheumatic diseases, while the second targeted pediatric rheumatology healthcare professionals (HCPs). Each workshop was led by

Table 2: Healthcare professionals characteristics

Total participants in attendance	17
Number of complete responses	14
Age distribution (Percent of Total)	• 18–30: 3 (21) • 31–40: 8 (57) • 41–50: 1 (7) • 51–60: 2 (14)
Role in healthcare profession (percent of total)	•Pediatric Rheumatologist: 3 (21) •Fellow in training: 7 (50) •Advanced practice provider: 1 (7) •Research coordinator: 3 (21)
Prior narrative medicine experience (Percent of Total)	• Yes: 2 (14) • No: 12 (86)
Workshop satisfaction (percent of total)	• Satisfied: 3 (21) •Very satisfied: 10 (72) •Neutral: 1 (7)
Level of connection (percent of total)	• Improved: 5 (36) • Same: 6 (43) • Decreased: 3 (21)
Anxiety level (percent of total)	• Improved: 8 (57) • Same: 6 (43) •Worsened: 0 (0)

Healthcare professional characteristics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Experiences of all participants. Image created with wordclouds.com.

Experiences of all participants

facilitators trained in NM. Participants completed a pre-workshop survey to assess their baseline knowledge and prior experience with NM interventions. A post-workshop survey was administered to evaluate feasibility, to understand participant perceptions of intervention, and to assess immediate changes in their feelings of connectedness and anxiety.

Results: Twenty-five participants attended the patient-caregiver workshop, and 17 participants attended the HCP workshop.

Patient-Caregiver Workshop (Table 1): Twenty-four of 25 participants completed the survey. One participant who was under the age of 18 did not take the survey and three surveys were incomplete. Of the 21 valid responses, seven were completed by patients and the remainder by caregivers. Four of the 21 participants had prior NM experience. All respondents reported being satisfied (n=7) or very satisfied (n=14) with the workshop. Free-text responses reflecting participants' experiences and feelings are depicted in Figure 1.

HCP Workshop (Table 2): Participants included pediatric rheumatologists, advanced practice providers, fellows, and research coordinators. Fourteen of 17 participants completed the survey. Thirteen out of 14 participants reported being satisfied (N=X) or very satisfied (N=X) with the workshop. Free-text responses depicting participant experiences and feelings are depicted in Figure 1.

Conclusion: The NM workshops were well received by patients, caregivers, and HCPs with high satisfaction rates. While most participants had no prior NM experience, many respondents found value in the workshop. Further NM interventions with larger samples are required to adequately explore contributing factors impacting participant degree of connection and impact on anxiety. These findings support the feasibility and acceptability of NM interventions in pediatric rheumatology settings.

Disclosure: A. Dhanrajani: None; **J. Drew**: CARRA, 4; **S. Edison**: None; **L. Moorthy**: None; **I. Goh**: None; **A. Garceau**: None; **H. Saltzman**: None; **C. Wells**: None; **A. Levy**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1276

Mental Health Screening Implementation for Pediatric Rheumatology Patients at a Tertiary Academic Medical Center

Bethany Walker[1], Livie Timmerman[2], John Bridges[3], Sara Harbison[4], Carolyn Lacy[5], Jada Lowery[5], Linda McAllister[5], Annelle Reed[6], Eileen Rife[7], Isabell Robles Sanchez[5], Tana Webb[5], Brooke Wyrosdick[5], Melissa Mannion[7] and Emily Smitherman[7], [1]Childrens of Alabama, Trussville, AL, [2]University of Alabama at Birmingham, Gardendale, AL, [3]University of Alabama at Birmingham/Children's of Alabama, Birmingham, AL, [4]Children's Harbor, Birmingham, [5]Children's of Alabama, Birmingham, [6]Children's of Alabama, Birminghan, AL, [7]University of Alabama at Birmingham, birmingham, AL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Pediatric patients living with chronic rheumatic diseases have high rates of anxiety and depression, which can lead to adverse health outcomes. In 2018, The American Board of Pediatrics launched The RoadMap Project to support the emotional needs of patients with chronic diseases. This project provides clinicians with a toolkit and framework for implementing surveillance and assessment of emotional health in pediatric subspecialty practices. Our local pediatric rheumatology clinic utilized the The RoadMap Project framework to develop a workflow for implementing mental health screening questionnaires into routine clinical practices. This quality improvement initiative aimed to assess the prevalence of anxiety and depression within our patient population and ensure timely allocation of resources to help address mental health concerns identified.

Methods: Beginning October 1, 2024, the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder Scale-7 (GAD-7) were piloted in two rheumatology provider clinics for all return visits with patients aged 12 years and older. The nursing staff integrated these questionnaires into the clinical workflow as part of the intake process. Once patients completed the questionnaires, the nursing staff entered scores in a flowsheet within the electronic medical record. A structured response protocol was developed to guide screening responses in real-time. Depending on the severity of symptoms identified, patients were provided a comprehensive mental health educational handout, referred to a licensed counselor within our institution, and/or had a real-time social work consult with safety planning and administration of the Ask Suicide Screening Questions (ASQ) if necessitated. On March 1, 2025 we expanded the screening process to two additional rheumatology provider clinics.

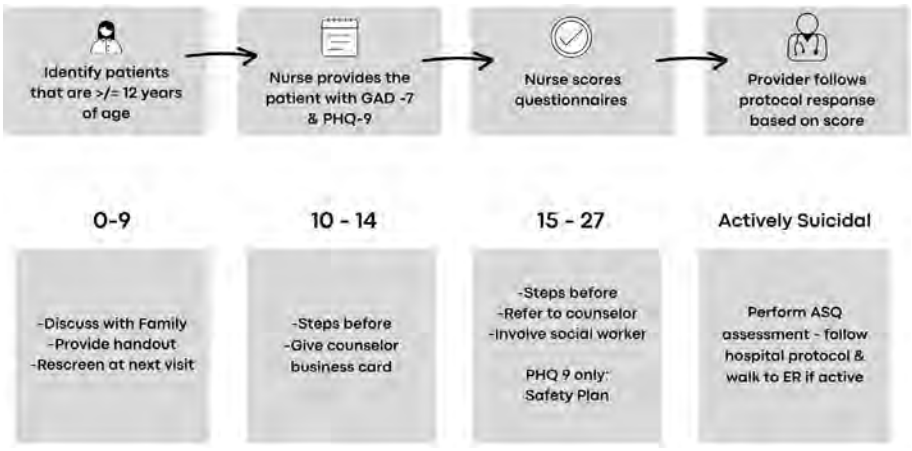


Figure 1. Structured screening and response protocol for PHQ-9 and GAD-7 questionnaires.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: From October 2024 through April 2025, mental health screenings have been completed for a total of 125 patients. Based on PHQ-9 results, 14% of patients reported no depression symptoms, 67% had minimal to mild symptoms (1-9), 9% had moderate symptoms (10-14), and 10% had moderately severe to severe symptoms (15-27). Suicidal ideation was endorsed by six patients, all of whom completed further evaluation using the ASQ tool and none were determined to be actively suicidal at the time of screening. GAD-7 results indicated 21% of patients reported no anxiety symptoms, 53% had minimal to mild symptoms (1-9), 19% had moderate symptoms (10-14), and 7% had severe symptoms (15-21).

Conclusion: We have successfully piloted routine mental health screenings in our pediatric rheumatology clinic, with a plan for complete adoption. In screenings completed to date, we have identified that a majority of pediatric rheumatology patients report mild to moderate symptoms of depression and anxiety, supporting the need for dissemination of mental health screenings as part of standard care. Future efforts will focus on automating the screening process within the electronic medical record to enhance efficiency and sustainability.

Disclosure: B. Walker: None; **L. Timmerman**: None; **J. Bridges**: None; **S. Harbison**: None; **C. Lacy**: None; **J. Lowery**: None; **L. McAllister**: None; **A. Reed**: None; **E. Rife**: None; **I. Robles Sanchez**: None; **T. Webb**: None; **B. Wyrosdick**: None; **M. Mannion**: None; **E. Smitherman**: None.

Abstract Number: 1277

Combination Therapy with Rituximab and Cyclophosphamide for Treating Pediatric Patients with Severe Manifestations of Rheumatic Disease

Eileen Rife[1], Daniel Reiff[2], John Bridges[3], Emily Smitherman[1], randy Cron[1], Matthew Stoll[1], Melissa Mannion[1], Peter Weiser[4] and Livie Timmerman[5], [1]University of Alabama at Birmingham, birmingham, AL, [2]Boys Town Hospital, Omaha, [3]University of Alabama at Birmingham/Children's of Alabama, Birmingham, AL, [4]University of Alabama at Birmingham, Birmingham, [5]University of Alabama at Birmingham, Gardendale, AL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Current practice guidelines recommend either rituximab (RTX) or cyclophosphamide (CYC) for treatment of organ-threatening manifestations of systemic vasculitis or connective tissue disease (e.g., diffuse alveolar hemorrhage, active class III, IV, or V lupus nephritis). These diseases are associated with high mortality and are often refractory to standard therapies. Few studies have evaluated the safety and efficacy of combination therapy with RTX and CYC. We conducted this study to evaluate outcomes in the first 12 months following RTX-CYC combination therapy in pediatric patients with rheumatic diseases.

Methods: Patients who received combination RTX-CYC therapy for a rheumatic disease between January 2020 and February 2023 at a single center were included. The primary outcomes of interest were death and infection requiring hospitalization within 12 months of combination therapy. Secondary outcomes included change in serologic lupus disease activity markers and corticosteroid (CS) dose, flare in disease activity, infusion reactions, and incident hypogammaglobulinemia. Patient demographic information, outpatient medications, laboratory data, and admission data were collected for 12 months post-treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

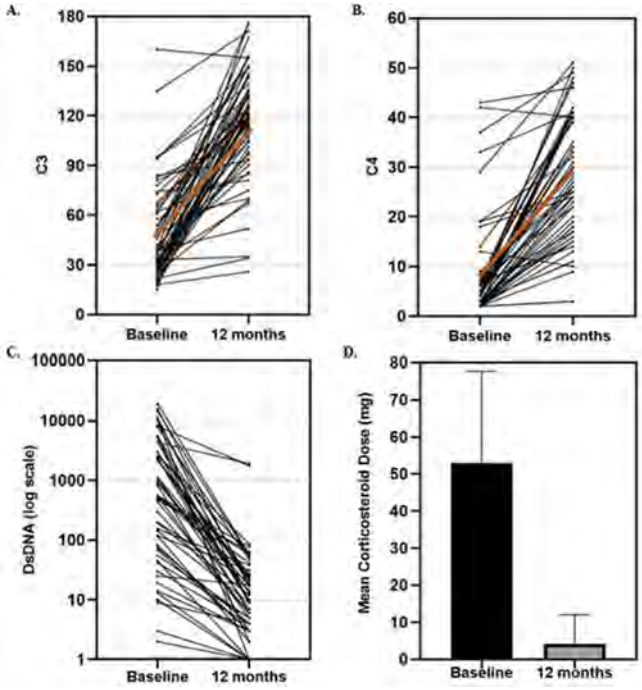


Figure 1. (A) Change in C3 levels in mg/dL – mean 47 ± 29 mg/dL prior to RTX-CYC and 115 ± 34 mg/dL at 12 months. (B) Change in C4 levels in mg/dL – mean 8 ± 10 mg/dL prior to RTX-CYC and 29 ± 13 mg/dL at 12 months. (C) Change in DsDNA levels in IU/mL – mean 2645 ± 4345 IU/mL prior to RTX-CYC and 85 ± 347 IU/mL at 12 months. The brown line represents the regression line. Improvements were significant at $p < 0.0001$. The mean daily prednisone-equivalent dose decreased from 54 mg ± 23.6 to 11 mg ± 9.3, $p<0.0001$ by 12 months (D).

Results: Eighty-nine pediatric patients received combination RTX-CYC therapy for a rheumatic disease during the study period. There were no reported deaths; eight patients (8.9%) were hospitalized with probable or definite infection. Patients with SLE demonstrated significant improvements across all serologic disease activity markers (anti-double stranded DNA antibodies, C3, C4) with $p < 0.0001$. The mean daily prednisone-equivalent dose significantly decreased by the end of the follow-up period from 54 mg ± 23.6 to 11 mg ± 9.3 ($p< 0.0001$), and 54 patients (62%) were able to discontinue CS. Six patients (6.7%) experienced flare of disease and eleven patients (12%) experienced infusion reactions – with 1 patient having a severe reaction to RTX necessitating discontinuation. Twenty-six patients (31%) experienced incident hypogammaglobinemia, with (69%) of cases recovering counts by 24 months.

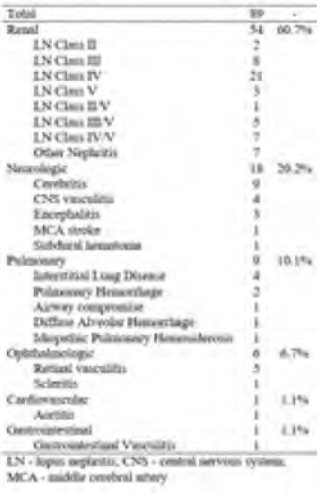
Table 1: Demographics and Rheumatic Diseases, n=89

Age at start of dual therapy, years		
Median (IQR)	14	(12-15)
Sex, No. (%)		
Female	69	77.5%
Race, No. (%)		
White	27	30.3%
Black	60	67.4%
Other	2	2.2%
Ethnicity, No. (%)		
Hispanic	8	9.0%
Non-Hispanic	81	91.0%
Primary Diagnosis, No. (%)	89	
Systemic lupus erythematosus	59	66.3%
ANCA-associated vasculitis	6	6.7%
Sjogren's syndrome	5	5.6%
Retinal Vasculitis	3	3.4%
Idiopathic Pulmonary Hemosiderosis	2	2.2%
IgA Vasculitis	2	
Systemic sclerosis	2	
Vasculitis/arteritis, unspecified	2	
Castleman's Disease	1	1.1%
Mixed Connected Tissue Disease	1	
Nephritic syndrome, unspecified	1	
NMDA Encephalitis	1	
Polyarteritis Nodosa	1	
Relapsing Polychondritis	1	
SAVI	1	
Takayasu's disease	1	

ANCA - antineutrophil cytoplasmic antibody; IgA - Immunoglobulin A; NMDA - N-methyl-D-aspartate; SAVI - STING-associated vasculopathy with onset in infancy; STING - STimulator of INterferon Genes

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Primary Indication for Rituximab and Cyclophosphamide Therapy, n=89



Total	89	-
Renal	54	60.7%
LN Class II	2	
LN Class III	8	
LN Class IV	21	
LN Class V	5	
LN Class II/V	1	
LN Class III/V	5	
LN Class IV/V	7	
Other Nephritis	7	
Neurologic	18	20.2%
Cerebritis	9	
CNS vasculitis	4	
Encephalitis	3	
MCA stroke	1	
Subdural hematoma	1	
Pulmonary	9	10.1%
Interstitial Lung Disease	4	
Pulmonary Hemorrhage	2	
Airway compromise	1	
Diffuse Alveolar Hemorrhage	1	
Idiopathic Pulmonary Hemosiderosis	1	
Ophthalmologic	6	6.7%
Retinal vasculitis	5	
Scleritis	1	
Cardiovascular	1	1.1%
Aortitis	1	
Gastrointestinal	1	1.1%
Gastrointestinal Vasculitis	1	

LN - lupus nephritis, CNS - central nervous system, MCA - middle cerebral artery

Conclusion: Combination therapy with RTX and CYC can be safely administered to children with rheumatic diseases. Risk of serious adverse events, disease flare, and infusion reactions requiring cessation of therapy is uncommon, allowing for effective treatment with decreased CS burden. Prospective controlled trials comparing combination therapy to standard therapy are needed.

Disclosure: E. Rife: None; **D. Reiff**: None; **J. Bridges**: None; **E. Smitherman**: None; **r. Cron**: AbbVie/Abbott, 1, American Board of Pediatrics, 12, Board Question Writer, AS2 Biotherapeutics, 2, CareerPhysician, 1, Neurogene, 2, Pfizer, 1, Sobia, 1, Springer, 9, VIDA Ventures, 2; **M. Stoll**: None; **M. Mannion**: None; **P. Weiser**: None; **L. Timmerman**: None.

Abstract Number: 1278

Differences in Patient and Provider Perception of Functional Status in Adolescents with Lupus

Emily Masi[1], Kimberly Rapoza[2], Tamar Rubinstein[3], Kathy Kenney-Riley[4] and Joyce Hui-Yuen[5], [1]Cohen Children's Medical Center, North New Hyde Park, NY, [2]Mercy College, Dobbs Ferry, NY, [3]Albert Einstein College of Medicine, White Plains, NY, [4]Mercy University, Dobbs Ferry, NY, [5]North Shore LIJ Health System, Great Neck, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patient and provider discordance can negatively impact medication adherence and disease outcomes in pediatric lupus. Functional status is known to greatly affect perception of disease activity and outcomes. We aim to investigate discordance in providers' and patients' assessment of functional status in adolescents with lupus, and relation to disease activity.

Methods: This cross-sectional study enrolled adolescent lupus patients between 2019 and 2022. Functional status was assessed by providers using the American College of Rheumatology classification of global functional status (ACR), and patients using subscales of the KIDSCREEN, PedsQL and PROMIS surveys. Clinical data including disease activity score

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(SLEDAI) and provider global assessment (PGA) were also collected. All analyses were corrected with Benjamini-Hochberg tests. Pearson and Spearman correlations were run among study variables. Mann-Whitney U tests examined differences in ACR groups on functional status variables. Kruskal Wallis analyses were conducted on SLEDAI, functional status ratings and patient and provider global ratings.

Results: 96 participants were enrolled, 77% female, with mean age of 17 (range 12-21) years and mean duration of diagnosis 3.36 (range < 1-12) years. Mean SLEDAI was 5.61 (range 0-38), indicating at least moderate disease activity. Eighty-seven subjects were categorized by providers as ACR Class I (able to perform all daily activities), and 7 as ACR Class II or III (at least some limitation to perform usual daily activities). Norm comparisons with one-sample T-tests found patients reported more fatigue but better physical function on PROMIS subscales, scored worse in all subscales of KIDSCREEN except bullying, and better in physical, emotional, social and school function subscales of the PedsQL compared to population means ($p < .001$). Once adjusted, the ACR categories did not significantly differentiate patients based on any of the patient reported functional subscales. SLEDAIs significantly correlated (Benjamini-Hochberg adjusted to $p < .002$) with PGA and the PedsQL social function subscale, but no other variables. There was no significant differentiation (Class II/ Class III ACR vs. Class I) on patient-rated functional status with the KIDScreen, PROMIS or PedsQL., except for pain intensity ($p=.001$). There were no differences for the SLEDAI, absolute discordance, or the patient global disease rating but there was a significant difference in the provider global disease rating ($p \leq .001$).

Conclusion: Adolescent lupus patients' assessment of function as captured on KIDSCREEN, PedsQL, and PROMIS subscales were more varied than providers' assessments using the ACR. SLEDAI correlated with PGA, but not with patient assessments. These findings suggest that provider-based assessments, may not adequately reflect the functional status of adolescents with lupus as experienced by the patients themselves. While disease activity measures like SLEDAI correlate with provider assessments, they do not align with patient-reported functional outcomes. This discrepancy highlights the need for more comprehensive and patient-centered tools to assess functional status in this population.

Disclosure: E. Masi: None; **K. Rapoza**: None; **T. Rubinstein**: None; **K. Kenney-Riley**: None; **J. Hui-Yuen**: None.

Abstract Number: 1279

Whole Blood Gene Expression Defined Subgroups of Treatment Naïve Children and Adolescents with Childhood-onset Systemic Lupus Erythematosus.

Reagan Reid[1], Huayun Hou[2], Isha Datar[2], Daniela Dominguez[3], Andrea Knight[4], Deborah Levy[5], Lawrence Ng[6], Zhaoyu Ding[2], Michael Wilson[2], Lauren Erdman[7], Eleanor Pullenayegum[2] and Linda Hiraki[5], [1]The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada, [2]SickKids Research Institute, Toronto, ON, Canada, [3]The Hospital for Sick Children, Toronto, Canada, [4]Hospital for Sick Children, Toronto, ON, Canada, [5]The Hospital for Sick Children, Toronto, ON, Canada, [6]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [7]University of Cincinnati, Cincinnati, OH

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is a clinically and genetically heterogeneous disease. We aimed to define subgroups of new diagnosis patients based on treatment naive gene expression profiles. We then examined how subgroup membership related to gene pathways, demographic and clinical features.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Patient Characteristics.

Patient Characteristics n=75	
Sex, Female n (%)	61 (81)
Age years, median (IQR)	13.8 (12.1-15.4)
Inferred Ancestry, n (%)	
East Asian	28 (37)
Admixed/ Amerindian	15 (20)
African	12 (16)
European	12 (16)
South Asian	8 (11)
Lupus Nephritis, n (%)	34 (45)

Table 2 Clinical and demographic features across clusters. P values were obtained from ANOVA for age cluster differences and Fishers exact test for sex, inferred ancestry, and lupus nephritis cluster differences.

	Cluster 1 n=24	Cluster 2 n=41	Cluster 3 n=10	P value
Age years, median (IQR)	13.9 (11.5-15.5)	13.6 (12.2-14.6)	14.5 (13.9-15.7)	0.48
Sex, Female n (%)	21 (88)	31 (76)	9 (90)	0.13
Inferred Ancestry, n (%)				0.41
East Asian	9 (38)	14 (34)	5 (50)	
Admixed/ Amerindian	2 (8)	12 (29)	1 (10)	
African	2 (8)	8 (20)	2 (20)	
European	8 (33)	3 (7)	1 (10)	
South Asian	3 (13)	4 (10)	1 (10)	
Lupus Nephritis, n (%)	6 (25)	24 (59)	4 (40)	0.03

Methods: Participants were diagnosed and followed in a tertiary care Lupus clinic and met SLE classification criteria. Clinical and laboratory data including disease activity and damage indices were prospectively collected and stored in a dedicated database. Participants were genotyped on a multi-ethnic array and ancestry was genetically inferred. Whole blood was collected prior to treatment initiation with glucocorticoids or other potent immunosuppressants, and whole blood transcriptome wide RNA-sequencing was completed. We identified distinct participant clusters based on gene expression profiles using K-means clustering. Clinical and demographic feature differences between clusters were assessed using ANOVA and Fishers exact test. We generated ranked genes lists based on expression profile for each cluster, by comparing each cluster relative to the others using gene set enrichment analysis (gseGO, clusterProfiler). To gain an understanding of the underlying activated/

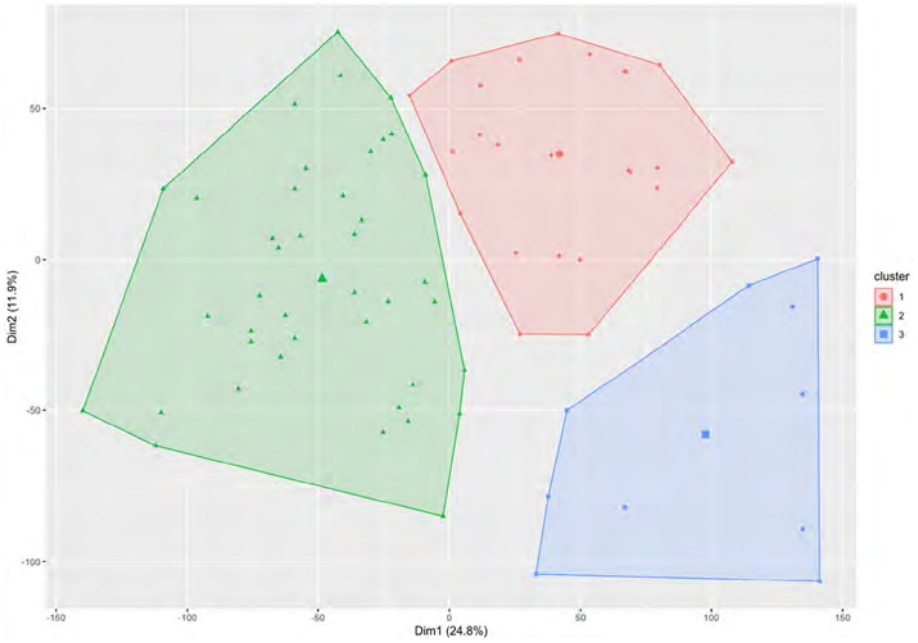


Figure 1 K-means Clusters.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

suppressed processes within each cluster we assessed Gene Ontology (GO) biological processes within each cluster.

Results: The cohort included 75 children and adolescents with cSLE with RNA-sequencing on treatment naïve whole blood samples. Initial K-means plots identified three clusters and one outlier which was excluded resulting in the final cohort. The group was 81% female with a median age at SLE diagnosis of 13.8 years (IQR: 12.1, 15.4).; full participant characteristics are presented in Table 1. We identified three clusters (Figure 1). Clusters differed significantly in proportion of individuals with lupus nephritis (LN) (Cluster 1= 25%, Cluster 2= 59%, Cluster 3= 40%, P= 0.03); the clinical and demographic composition of each cluster is summarized in Table 2. Cluster 1 was characterized by activation of protein synthesis (*RPL10, RPL13, RPS14*) and signaling pathways (*GPR162, FCER1A, CSF1R*), whereas cell cycle processes (CDC16, BCL6, RMI1) were supressed. Cluster 2 showed enrichment of ribosomal related pathways (*UTP20, UTO4, MAK16*) and chromosomal processes (BUB1, NCAPG, MYBL2) while suppressed pathways related to secretory granules (*ATP8B4, ATP11A, CST3*) and innate immune responses (*P2RY1, PIK3CB, MAP1B*). Cluster 3 showed up-regulation of secretory granules and vesicles (*CD177, MMP8, LTF*) while down-regulated pathways were related to ribosomal (*MRPL20, RPS9, RPS3A*) and RNA pathways (*ABT1, RPP38, KARS1*) and the adaptive immune response (*TRAV41, TRAV27, TRGV8)*.

Conclusion: In a clinically heterogeneous, multiethnic cohort of patients with cSLE, treatment naïve whole blood RNAseq genome wide expression generated three discrete clusters of patients. LN was most prevalent in cluster 2 which was characterized by increased activation of ribosomal and chromosomal pathways. Next steps include examining cell specific gene expression pathways.

Disclosure: R. Reid: None; **H. Hou**: None; **I. Datar**: None; **D. Dominguez**: None; **A. Knight**: Pfizer, 6; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **L. Ng**: None; **Z. Ding**: None; **M. Wilson**: None; **L. Erdman**: None; **E. Pullenayegum**: None; **L. Hiraki**: Janssen, 2, 5.

Abstract Number: 1280

Investigating the Association Between SARS-CoV-2 Infection, COVID-19 Vaccination, and Autoimmune Diseases in a Pediatric Population: A comprehensive analysis

Yonatan Butbul Aviel[1], Arad Dotan[2], Dana Arnheim[2] and Cynthia Freiberg[3], [1]Rambam Health Care Campus, Haifa, Israel, [2]Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel, Tel Aviv, Israel, [3]Maccabi Healthcare Services, Tel Aviv, Israel, Tel Aviv

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: During the COVID-19 pandemic there were reports of an increased association between COVID 19 and various autoimmune diseases (AID) in adults. This study aims to investigate the incidence of AIDs in children before and during the pandemic and explores potential links to SARS-CoV-2 vaccination.

Methods: We analyzed 493,705 anonymized medical records from Maccabi Healthcare Services, Israel's second-largest healthcare provider, to study AID incidence during 2014-2022. The study period was divided into three phases: two pre-pandemic phases of equal duration (A and B) and a pandemic phase (C).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1.A

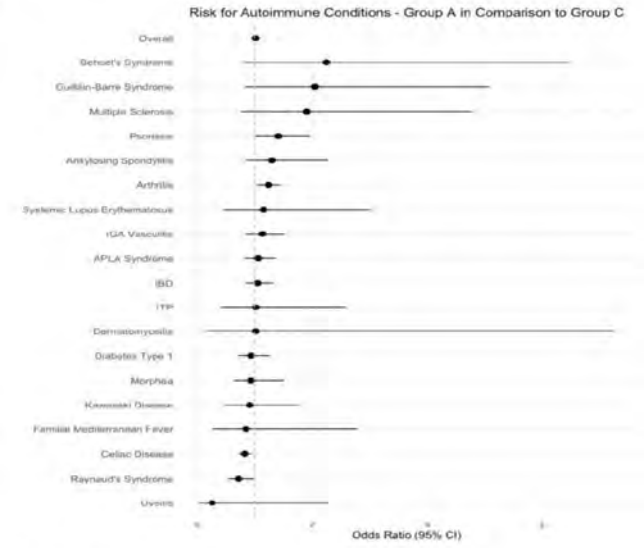


Figure 1.B

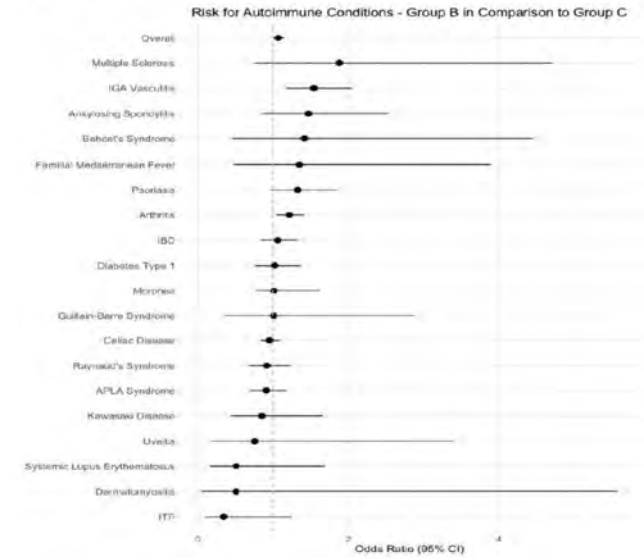


Figure 1.A and B. Multivariable logistic regression analysis comparing the incidence of autoimmune diseases between Group C (pandemic period) and Groups A and B (pre-pandemic periods

Results: Of 4,596 (0.9%) patients diagnosed with an AID in the cohort, incidence rates were 0.9% for Group A (2014-2016), 1.0% for Group B (2017-2019), and 0.9% for Group C (2020-2022) (p = 0.13). Logistic regression showed no significant differences in overall autoimmune disease incidence between the pre-COVID and COVID periods. Notably, specific conditions like celiac disease showed reduced incidence in Group A (OR 0.8309, p = 0.0071) while arthritis was significantly more common in Groups A and B. Additionally, COVID-19 diagnosis was not significantly associated with increased autoimmune disease risk (HR 1.092, p = 0.491); however, receiving at least one COVID vaccine was linked to higher risk (HR 1.2323, p = 0.0033).

Conclusion: Our findings suggest that the overall incidence of new-onset autoimmune diseases in children remained relatively stable during the COVID-19 pandemic. The study indicates a potential association between COVID-19 vaccination and an increased risk of developing autoimmune diseases, necessitating further research to elucidate long-term effects in the pediatric population

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Y. Butbul Aviel: None; **A. Dotan**: None; **D. Arnheim**: None; **C. Freiberg**: None.

Abstract Number: 1281

Ethnic Disparities in Mental Health Screening, Diagnoses, and Outcomes in Patients with Childhood-Onset Systemic Lupus Erythematosus

Alicia Tran[1], Indrani Das[2], Zhaoyu Ding[3], Daniela Dominguez[4], Sefi Kronenberg[5], Lawrence Ng[6], Alene Toulany[1], Gwyneth Zai[7], Deborah Levy[1], Andrea Knight[8] and Linda Hiraki[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]SickKids Research Institute, Toronto, ON, Canada, [4]The Hospital for Sick Children, Toronto, Canada, [5]Holland Bloorview Kids Rehabilitation Hospital, Toronto, ON, Canada, [6]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [7]Centre for Addiction & Mental Health, Toronto, ON, Canada, [8]Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with childhood-onset systemic lupus erythematosus (cSLE) face higher risks of depression and anxiety compared to healthy peers. In 2022, standardized mental health (MH) screening for depression and anxiety was introduced in the cSLE clinic to improve early intervention. While ethnic disparities in accessing MH care have been reported, they remain understudied in cSLE populations. This study examined ethnic differences in the prevalence of elevated symptoms and diagnoses of depression and anxiety among youth with cSLE pre- and post-implementation of standardized MH screening.

Methods: We completed a retrospective study of youth aged ≤ 18 years followed for SLE between January 1, 2000, to December 1, 2024. The cohort was stratified into two periods: pre-implementation (2000-2021) and post-implementation (2022-2024) of standardized MH screening. Ethnicity of patients was grouped into the following categories: European, East Asian, South Asian, African, Latin American, Indigenous American, Admixed (≥2 ethnicities), and Other. Elevated symptoms of depression and anxiety were identified by ever screening positive on any of the following questionnaires: Children's Depressive Inventory (CDI score >13; CDI-2 score ≥20), Patient Health Questionnaire 9-item (PHQ-9 score ≥10), Multidimensional Anxiety Scale for Children (MASC score ≥48; MASC-2 score ≥88), and Generalized Anxiety Disorder 7-item (GAD-7 score ≥10). Diagnoses of depression and anxiety were identified by medical chart review. Univariate and

Table 1. Demographic and clinical features of patients followed for cSLE post-implementation of standardized mental health screening (n=123)

Patient Feature	Total n = 123	European n = 27	East Asian n = 34	South Asian n = 24	African n = 14	Admixed[a] n = 24	p
Female sex (n (%))	107 (87)	23 (85)	31 (91)	20 (83)	11 (79)	22 (92)	0.841
Age at SLE diagnosis, years (median (IQR))	13 (9-15)	14 (9-15)	13 (10-15)	12 (9-15)	13 (10-15)	12 (10-14)	0.740
Duration of follow-up, years (mean (SD))	4.8 (2.8)	5.0 (3.3)	4.7 (2.8)	4.6 (2.6)	4.7 (3.0)	5.1 (2.4)	0.744
SLICC/ACR Damage Index score (median (IQR))	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0.25)	0.924
Neuropsychiatric lupus (NPSLE)	18 (15)	1 (4)	3 (9)	6 (25)	1 (7)	7 (29)	**<0.001**
Lupus nephritis	31 (25)	3 (11)	8 (24)	9 (38)	4 (29)	7 (29)	**0.006**

[a]Admixed category represents patients who had ≥ 2 ethnicities. Includes patients of Admixed (n=18(75)), Latin American (n=5(21)) and Other (n=1(4)) ethnicity. Note: **Bold** indicates significant difference based on $p < 0.05$

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Univariate and multivariable-adjusted odds ratios for association between ethnicity and (1) ever screening positive on the PHQ-9 and (2) screening positive on the PHQ-9 and receiving a depression diagnosis (n=109)

Univariate Analysis	Ever Screened Positive on PHQ-9		Screened Positive on PHQ-9 and Received Depression Diagnosis	
Ethnicity (ref: European)	***OR* (95% CI)**	***p***	***OR* (95% CI)**	***p***
East Asian	1.03 (0.33-3.25)	0.958	0.46 (0.06-3.73)	0.457
South Asian	1.12 (0.32-3.99)	0.857	1.29 (0.20-8.27)	0.791
African	0.30 (0.05-2.04)	0.184	1.17 (0.14-10.03)	0.884
Admixed	1.20 (0.37-3.95)	0.762	1.98 (0.38-10.37)	0.412
Multivariable-Adjusted Analysis	**Ever Screened Positive on PHQ-9**		**Screened Positive on PHQ-9 and Received Depression Diagnosis**	
Ethnicity (ref: European)	***OR* (95% CI)**	***p***	***OR* (95% CI)**	***p***
East Asian	0.75 (0.21-2.63)	0.645	0.39 (0.05-2.94)	0.363
South Asian	0.88 (0.21-3.61)	0.860	1.23 (0.20-7.54)	0.831
African	0.22 (0.01-1.56)	0.189	1.18 (0.14-9.66)	0.880
Admixed	0.81 (0.21-3.14)	0.762	1.83 (0.36-9.38)	0.470
Age	1.03 (0.90-1.20)	0.672	0.96 (0.81-1.15)	0.716
Sex (ref: male)	1.39 (0.37-6.75)	0.643	1.30 (0.23-7.23)	0.779
Duration of follow-up	0.97 (0.70-1.34)	0.840	1.03 (0.63-1.68)	0.931
SLICC/ACR Damage Index score	0.91 (0.53-1.58)	0.749	0.93 (0.51-1.67)	0.804
NPSLE	15.45 (3.07-77.82)	**<0.001**	13.76 (2.55-74.22)	**0.003**
Lupus nephritis	1.68 (0.54-5.12)	0.397	4.22 (0.99-18.04)	0.076

Note: **Bold** indicates significant difference based on $p < 0.05$.

multivariable logistic regression, adjusted for sociodemographic and clinical variables (age, sex, duration of follow-up, disease damage, neuropsychiatric SLE [NPSLE], lupus nephritis), assessed the association of ethnicity with screening outcomes and diagnoses of depression and anxiety.

Results: Among 610 charts reviewed, 560 patients had self-reported ethnicity data and were included in the study. This analysis focuses on 123 patients actively followed post-implementation of standardized screening, during which 109 patients completed both the PHQ-9 and GAD-7. The cohort was predominantly female (87%) with a median age at SLE diagnosis of 13 years (IQR 9-15). Majority of patients were East Asian (28%), European (22%), and Admixed (20%). NPSLE was present in 15% of patients and 25% had lupus nephritis. Ethnicity was not significantly associated with screening completion, screening positivity, or diagnoses of depression or anxiety. In adjusted models, NPSLE was significantly associated with screening positive on the PHQ-9 (OR = 15.45, CI: 3.07-77.82, p = < 0.001) and receiving a depression diagnosis (OR = 13.76, CI: 2.55-74.22, p = 0.003). No significant associations were found between demographic and clinical variables and anxiety-related outcomes.

Table 3. Univariate and multivariable-adjusted odds ratios for association between ethnicity and (1) screening positive on the GAD-7 and (2) screening positive on the GAD-7 and receiving an anxiety diagnosis (n=109)

Univariate Analysis	Ever Screened Positive on GAD-7		Screened Positive on GAD-7 and Received Anxiety Diagnosis	
Ethnicity (ref: European)	***OR* (95% CI)**	***p***	***OR* (95% CI)**	***p***
East Asian	0.88 (0.28-2.82)	0.832	0.54 (0.10-3.00)	0.477
South Asian	0.49 (0.12-2.08)	0.327	0.50 (0.07-3.72)	0.483
African	0.56 (0.11-2.82)	0.467	0.25 (0.01-5.16)	0.297
Admixed	1.43 (0.44-4.64)	0.550	2.16 (0.51-9.11)	0.286
Multivariable-Adjusted Analysis	**Ever Screened Positive on GAD-7**		**Screened Positive on GAD-7 and Received Anxiety Diagnosis**	
Ethnicity (ref: European)	***OR* (95% CI)**	***p***	***OR* (95% CI)**	***p***
East Asian	0.78 (0.23-2.69)	0.699	0.74 (0.12-4.56)	0.753
South Asian	0.41 (0.08-2.06)	0.270	0.89 (0.11-7.12)	0.913
African	0.72 (0.14-3.86	0.706	0.41 (0.02-8.37)	0.551
Admixed	1.56 (0.43-5.60)	0.498	3.18 (0.59-17.28)	0.179
Age	1.05 (0.91-1.22)	0.436	2.65 (0.20-34.91)	0.459
Sex (ref: male)	1.72 (0.42-7.01)	0.445	1.24 (0.98-1.58)	0.083
Duration of follow-up	0.99 (0.73-1.35)	0.956	1.36 (0.76-2.40)	0.337
SLICC/ACR Damage Index score	0.83 (0.46-1.49)	0.544	1.00 (0.53-1.88)	0.997
NPSLE	3.78 (0.86-16.60)	0.081	2.52 (0.47-13.59)	0.324
Lupus nephritis	1.06 (0.36-3.12)	0.921	1.05 (0.24-4.51)	0.958

Note: **Bold** indicates significant difference based on $p < 0.05$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In a large multiethnic cohort of youth with cSLE, we did not observe an association between ethnicity and MH screening or a diagnosis of depression and anxiety. NPSLE was significantly associated with screening positive on the PHQ-9 and receiving a depression diagnosis. Further analyses will assess psychotropic medication use by ethnicity and extend findings to the pre-implementation period.

Disclosure: A. Tran: None; **I. Das**: None; **Z. Ding**: None; **D. Dominguez**: None; **S. Kronenberg**: None; **L. Ng**: None; **A. Toulany**: None; **G. Zai**: None; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **A. Knight**: Pfizer, 6; **L. Hiraki**: Janssen, 2, 5.

Abstract Number: 1282

Real-world use of belimumab in childhood-onset SLE in Spain: cross-sectional analysis from a multicenter study (JULES registry)

Alina-Lucica Boteanu[1], Clara Udaondo[2], Joan Calzada[3], Daniel Clemente Garulo[4], Juan Carlos Nieto Gonzáles[5], Eugenia Enriquez[6], inmaculada Calvo Penades[7], Lourdes Villalobos[8], Belen Sevilla[9], Sara Murias[10], Berta Magallares[11], Ana Capilla[12], Jaime Arroyo[13], Beatriz Bravo[14], Gisela Diez-Cordoves[15], Marisol Camacho[16], Genaro grana[17], Juan Jose Bethencourt[18], Pablo Mesa[19], Natalia Palmou[20], Mireia Lopez Corbeto[21], Judith Sanchez[22], Maria Isabel Gonzalez[23], isabel Patora Granados bautista[24], Clara Moriano[25], Diego Dios[17], Lorena Exposito[26], Alicia Garcia[27], Laura Martin[28], David Fernandez[29], Laura Trujillo[14], Anahy Maria Brandy[30] and CARLOS GUILLEN-ASTETE[31], [1]H.U. Ramn y Cajal, Madrid, Spain, [2]La Paz University Hospital, Madrid, Spain, [3]University Hospital Sant Joan de Deu, Barcelona, Spain, [4]H.U Niño Jesús, Madrid, Spain, [5]H.U Gregorio Marañón, Madrid, Spain, [6]Clnica Universidad de Navarra, Madrid, Spain, [7]Pediatric Rheumatology Department. HUP La Fe, Valencia, Spain, [8]Ramon y Cajal Hospital, MADRID, Spain, [9]Division of Pediatrics, Hospital Universitario San Cecilio, Granada, Spain, [10]H.U Central de Asturias, Oviedo, Spain, [11]Hospital de Sant Pau, Bareclona, [12]H.U de La Merced, Sevilla, Spain, [13]HOSPITAL UNIVERSITARIO LA PAZ, MADRID, [14]H.U Virgen de Las Nieves, Granada, Spain, [15]H. R. U. Malaga, Malaga, Spain, [16]H.U. Virgen del Rocío, Sevilla, Spain, [17]H.U de A Coruña, A Coruña, Spain, [18]H.U. Canarias, Canarias, Spain, [19]H.U Virgen de la Arrixaca, Murcia, Spain, [20]H.U. marques de Valdecilla, Santander, Spain, [21]H.U Vall d´Hebron, Barcelona, Spain, [22]Pediatric Rheumatology Department, Taulí Hospital Universitari-Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Sabadell (Spain)., Sabadell, Spain, [23]H.U. La Fé, Valencia, Spain, [24]H.U Toledo, Toledo, Spain, [25]Hospital Len, LEON, Castilla y Leon, Spain, [26]H.U Canarias, Canarias, Spain, [27]Rheumatologist, La Laguna, Spain, [28]H.R.U Malaga, Malaga, Spain, [29]Complejo Hospitalario Universitario de Vigo, Vigo, Galicia, Spain, [30]Hospital Germans Trias i Pujol, Badalona, Spain, [31]H.U Ramón y Cajal, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: SLE is a multisystemic autoimmune disease with several manifestations. Childhood-onset SLE (cSLE) has a more severe disease course than adult-onset SLE, with a higher frequency and severity of major-organ involvement and damage accrual. Low disease activity is an important goal. Belimumab (BEL) is the first biological drug approved for cSLE.

The aim of this study is to identify whether low lupus disease activity status on BEL is an achievable goal in cSLE and to describe the characteristics of cSLE patients treated with BEL in real world practice included in the JULES registry, a Spanish multicenter, hospital-based, cSLE registry.

Methods: We analyzed cross-sectional data from 67 patients treated with BEL for cSLE from a total of 250 included in the JULES registry. For the description of the cohort, summary statistics of central tendency and dispersion and percentage statistics were used for numerical and categorical variables respectively.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 67 patients (26.8%) of the 250 patients included in the JULES registry were treated with BEL. The mean age to diagnosis was 12.9 (3.2) years, with a mean age at inclusion in the registry of 20.4 (8.3). 86.6% were female. Lupus nephritis (LN) prevalence was 56.1%, arthritis was seen in 74.6% and the most common laboratory abnormalities were leucopenia 68.2%, lymphopenia 62.5%, anti-DNA (89.6%) and hypocomplementemia (94%). The most frequent LN class was IV (23.9%), followed by class III (10.4%) and class II (10.4%). The main reasons for BEL initiation were arthritis (44.8%), muco-cutaneous manifestations (40.3%), systemic manifestations (37.3%), LN (26.9%) and hematological involvement (22.4%). 20.9% of patients initiated BEL in the first 6 months of the disease. The mean duration of BEL treatment was 27.78 months (31.65). The mean SLEDAI and SLICC scores were 3.11 (2.12) and 0.46 (1.25) points respectively. 19.4% of BEL-treated patients have inactive disease (SLEDAI 0-1), 70.1% low disease activity (SLEDAI 2-5), and 10.4% moderate activity. In patients with LN, 32.8% achieved complete remission and 10,4% partial remission, 4.5% experienced an improvement and ESRD was observed only in 3% of patients. 74.6% had managed to completely withdraw prednisone and 77.6% were still on BEL treatment. The reasons for suspension were inefficacy (14.9%), adverse events (4.5%) and complete remission of the symptoms (3%).

Conclusion: In the Spanish cSLE registry (JULES), 26.8% of patients were treated with BEL. In this complex and severe population, BEL is an effective and safe treatment for cSLE, allowing to achieve low disease activity state and corticosteroid withdrawal.

***Funding:** The Spanish registry of juvenile SLE (JULES) is funded by GSK. The author din not recive any grant from GSK

Disclosure: A. Boteanu: GSK, 5, 6; **C. Udaondo**: None; **J. Calzada**: None; **D. Clemente Garulo**: GSK, 6; **J. Nieto Gonzáles**: None; **E. Enriquez**: None; **i. Calvo Penades**: None; **L. Villalobos**: None; **B. Sevilla**: None; **S. Murias**: None; **B. Magallares**: None; **A. Capilla**: None; **J. Arroyo**: None; **B. Bravo**: None; **G. Diez-Cordoves**: None; **M. Camacho**: None; **G. grana**: None; **J. Bethencourt**: None; **P. Mesa**: None; **N. Palmou**: None; **M. Lopez Corbeto**: None; **J. Sanchez**: None; **M. Gonzalez**: None; **i. Granados bautista**: None; **C. Moriano**: None; **D. Dios**: None; **L. Exposito**: None; **A. Garcia**: None; **L. Martin**: None; **D. Fernandez**: None; **L. Trujillo**: None; **A. Brandy**: None; **C. GUILLEN-ASTETE**: None.

Abstract Number: 1283

Impact of Guideline Concordant Care of Renal Outcomes in Childhood-Onset Lupus Nephritis

Alisha Akinsete[1], Orysya Soroka[2], Mangala Rajan[2], Karen Onel[3], Monika Safford[2] and Iris Navarro-Millan[4], [1]Weill Cornell Medical Center, New York, NY, [2]Weill Cornell Medicine, New York, [3]HSS, New York, NY, [4]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: End-stage renal disease (ESRD) is a serious complication of lupus nephritis (LN), yet the effect of guideline-concordant care on this outcome is unclear. Despite the availability of treatment guidelines, adherence remains inconsistent. This study examines the association between guideline-concordant care and adverse renal outcomes in pediatric Medicaid patients with childhood-onset LN.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Description of Quality Indicators for Childhood-Onset Systemic Lupus Erythematosus (cSLE) with Lupus Nephritis (LN)

Quality Indicator	Definition	Numerator	Denominator
SLE Medical Management			
Q1 Hydroxychloroquine use (HCQ)	All patients to be prescribed HCQ annually	Prescription of HCQ at any time in the calendar year	All patients
Q2 Medication Toxicity Surveillance with Complete Blood Count (CBC or LFT) tests	Annual surveillance for toxicity with CBC or LFT tests	CBC or LFT done once per calendar year.	All patients
Q3 Renal Disease Activity	At least 4 Renal Function or Urine test (UA, Up/Ucr, 24hr protein, Cr, cystatin C)	Number of patients with at least 4 tests in the calendar year	All patients
Q4 Lupus Disease Activity Surveillance	At least 4 LUPUS activity tests (C3, C4, dsDNA, ESR)	Number of patients with at least 4 tests in the calendar year	All patients
Nephritis Management			
Q5 Adequate Follow-up	Adequate follow-up while undergoing treatment	At least 4 Evaluation and Management (E & M) visits per calendar year	All patients
Q6 Use of steroid-sparing agents	Use of steroid-sparing agents such as DMARDs and/or Biologics	Prescription of DMARDs and/or Biologics at any time in the calendar year	All patients on glucocorticoids
Q7 Use of ACEi/ARBS for Hypertension or Proteinuria	Patients with hypertension or Proteinuria to be prescribed ACE/ARBS	Prescription of ACEi/ARBS at any time in the calendar year	All patients with HTN or Proteinuria

ACE/ARBS - Angiotensin-Converting Enzyme inhibitors/Angiotensin receptor blockers; DMARDs - Disease-Modifying Antirheumatic Drugs; HTN – Hypertension; UA – Urinalysis; Up/Ucr – Urine protein/Urine creatinine ratio; Cr -Creatinine; C3 – Complement 3; C4 – Complement 4; dsDNA - Double-stranded DNA; ESR - Erythrocyte Sedimentation Rate

Table 2: Childhood-Onset Lupus Nephritis Cohort Baseline Characteristics

	Total	No Adverse Renal Outcome	Adverse Renal Outcome	P value
All n, (%)	420 (100)	361 (86)	59 (14)	
Age, mean, (SD)	15.43 (3.7)	15.3 (3.7)	16.3 (3.3)	0.06
Age Category n, (%)				0.14
5-11	79 (18.8)	71 (19.7)	8 (13.6)	
12-17	227 (54.1)	198 (54.9)	29 (49.2)	
18-21	114 (27.14)	92 (25.5)	22 (37.3)	
Sex				0.27
Female n, (%)	361 (86.0)	313 (86.7)	48 (81.4)	
Male n, (%)	59 (14.1)	48 (13.3)	11 (18.6)	
Race and Ethnicity				0.04
Hispanic n, (%)	53 (12.6)	46 (12.7)	7 (11.9)	
Non-Hispanic Black n, (%)	225 (53.6)	192 (53.2)	33 (55.9)	
Non-Hispanic White n, (%)	60 (14.3)	57 (15.8)	3 (5.1)	
Other n, (%)	36 (8.6)	32 (8.9)	4 (6.8)	
Unknown n, (%)	46 (11.0)	34 (9.4)	12 (20.3)	
Medication severity at baseline*				0.12
No Medication n, (%)	18 (4.3)	15 (3.7)	3 (17.7)	
Steroids only n, (%)	37 (8.8)	34 (8.4)	3 (17.7)	
Mild n, (%)	26 (6.2)	25 (6.2)	1 (5.9)	
Moderate n, (%)	53 (12.6)	52 (12.9)	1 (5.9)	
Severe n, (%)	286 (68.1)	277 (68.7)	9 (52.9)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Performance on each Quality Indicator (QI) for Childhood-Onset Lupus Nephritis (LN) by Adverse Renal Outcomes

Quality Indicator	All	No Adverse Renal Outcome	Adverse Renal Outcome	P value
Q1 Hydroxychloroquine use (HCQ)	70.3	70.7	61.0	0.11
Q2 Medication Toxicity Surveillance with Complete Blood Count and Liver Function (CBC/LFT) tests	88.6	88.5	91.5	0.47
Q3 Renal Disease Activity	82.7	82.7	83.1	0.95
Q4 Disease Activity Surveillance	63.5	63.4	64.4	0.88
Q5 Adequate Follow up	81.2	81.2	81.4	0.97
Q6 Use of steroid-sparing agents	85.6	85.5	87.8	0.68
Q7 Use of ACE/ARBS for Hypertension or Proteinuria	68.5	69.4	51.9	0.007

Data is presented as percentage of number X person years with QI among number of person X exposure years

ACE/ARBS - Angiotensin-Converting Enzyme inhibitors/Angiotensin receptor blockers

Data is presented as percentage of number X person years with QI among number of person X exposure years

Methods: Using Medicaid via Marketscan data from 2011-2022, we identified individuals with LN between the ages of 5 and 21. Patients are required ≥ 3 or more SLE ICD-9 or ICD-10 codes in outpatient visit claims or hospital discharge diagnosis codes at least 30 days apart and have ≥3 ICD-9/ICD-10 for nephritis and a procedure code for renal biopsy. The exposure was the 7 quality indicators (Table 1), and the outcome was the adverse renal outcome (end-stage renal disease, dialysis, or kidney transplant). Descriptive statistics were used to characterized baseline data (Table 2). We compared quality indicator adherence between patients with and without adverse renal outcomes (Table 3). Hazard Ratio was obtained for adverse renal outcomes with quality indicators exposures that reached statistical significance ($p< 0.05$). Annual adjusted rates of adverse renal outcomes were calculated using Poisson regression with robust standard errors. For patients who had multiple years of exposure, we modeled the impact of cumulative quality indicator exposures on renal outcomes with Poisson regression.

Results: We identified 420 children with prevalent childhood-onset LN. The only statically significant difference noted was race and ethnicity where 12.6% were Hispanic, 53.6% Black, 14.3% White, 11.6% Unknown, 8.6% Other (p=0.04) . Adherence to quality indicators was moderate to high (HCQ use: 77.6%, medication toxicity: 88.6 %, renal disease activity monitoring: 87.7%, lupus disease activity monitoring: 63.5%, adequate follow-up: 81.2%, use of steroid-sparing agent: 85.6%, use of ACEi or ARB 68.5%. (Table 3). Use of ACEi/ARBs for HTN or Proteinuria was lower for those with adverse renal outcomes (69.39% vs 51.85%, p=0.007). The risk of adverse renal outcomes is 45% lower for patients with LN with HTN or proteinuria on an ACEi/ARB than those without (age, sex, race adjusted HR 0.55 [95% CI 0.32-0.96). When looking at the cumulative effect of having the ACEi/ARB quality indicator present 2 and 3+ years was statistically significant. Annual Rates of adverse renal outcome at 0 years was statistical higher compared to year 2 and 3+ year respectively (age, sex, race adjusted rates 11.0 [95% CI 6.5-18.6) vs 4.7 [95% CI 2.3-9.6] and 5.6 [95% CI 3.1-10.0]).

Conclusion: Use of ACE inhibitors or ARBs was associated with a lower risk of adverse renal outcomes in children with lupus nephritis, with greater cumulative exposure linked to further risk reduction. Additionally, hydroxychloroquine use showed a trend toward improved renal outcomes, suggesting potential benefit. These findings support the importance of consistent, guideline-based medication use in improving long-term renal health in this population.

Disclosure: A. Akinsete: None; **O. Soroka**: None; **M. Rajan**: Weill Cornell Medicine, 3; **K. Onel**: None; **M. Safford**: MedExplain Health, 1; **I. Navarro-Millan**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1284

Clinical implications of Antiphospholipid Antibodies and Secondary Antiphospholipid Syndrome in Juvenile-onset Systemic Lupus Erythematosus

Daniel Clemente[1], Alina-Lucica Boteanu[2], Clara Udaondo[3], Joan Calzada[4], Juan Carlos Nieto[5], Eugenia Enriquez[6], Inmaculada Calvo[7], Lourdes Villalobos[8], Belen Sevilla[9], Sara Murias[10], Berta Magallares[11], Ana Capilla[12], Jaime Arroyo[13], Beatriz Bravo[14], Gisela Diez-Cordoves[15], Marisol Camacho[16], Genaro grana[17], Juan Jose Bethencourt[18], Pablo Mesa[19], Natalia Palmou[20], Mireia Lopez Corbeto[21], Judith Sanchez[22], Maria Isabel Gonzalez[23], Clara Moriano[24], Diego Dios[17], Lorena Exposito[25], Alicia Garcia[26], Laura Martin[27], David Fernandez[28], Laura Trujillo[14], Anahy Maria Brandy[29], CARLOS GUILLEN-ASTETE[30], lydia Abasolo Alcazar[31] and JULES group, [1]Hospital Infantil Universitario NIño Jesús, Madrid, Madrid, Spain, [2]H.U. Ramn y Cajal, Madrid, Spain, [3]La Paz University Hospital, Madrid, Spain, [4]University Hospital Sant Joan de Deu, Barcelona, Spain, [5]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [6]Clnica Universidad de Navarra, Madrid, Spain, [7]Hospital La Fe, Valencia, Comunidad Valenciana, Spain, [8]Ramon y Cajal Hospital, MADRID, Spain, [9]Division of Pediatrics, Hospital Universitario San Cecilio, Granada, Spain, [10]H.U Central de Asturias, Oviedo, Spain, [11]Hospital de Sant Pau, Bareclona, [12]H.U de La Merced, Sevilla, Spain, [13]HOSPITAL UNIVERSITARIO LA PAZ, MADRID, [14]H.U Virgen de Las Nieves, Granada, Spain, [15]H. R. U. Malaga, Malaga, Spain, [16]H.U. Virgen del Rocío, Sevilla, Spain, [17]H.U de A Coruña, A Coruña, Spain, [18]H.U. Canarias, Canarias, Spain, [19]H.U Virgen de la Arrixaca, Murcia, Spain, [20]H.U. marques de Valdecilla, Santander, Spain, [21]H.U Vall d´Hebron, Barcelona, Spain, [22]Pediatric Rheumatology Department, Taulí Hospital Universitari-Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Sabadell (Spain)., Sabadell, Spain, [23]H.U. La Fé, Valencia, Spain, [24]Hospital Len, LEON, Castilla y Leon, Spain, [25]H.U Canarias, Canarias, Spain, [26]Rheumatologist, La Laguna, Spain, [27]H.R.U Malaga, Malaga, Spain, [28]Complejo Hospitalario Universitario de Vigo, Vigo, Galicia, Spain, [29]Hospital Germans Trias i Pujol, Badalona, Spain, [30]H.U Ramón y Cajal, Madrid, Spain, [31]IdISSC. HCSC, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in juvenile-onset systemic lupus erythematosus (jSLE) patients. We aimed to assess the clinical manifestations of jSLE patients according to the presence of aPL and/or clinical antiphospholipid syndrome (APS).

Methods: Patients from the JULES registry were included. JULES is a Spanish multicenter, hospital-based, retrospective, jSLE registry. Three groups were established: a) SLE without antiphospholipid antibodies (jSLE); b) SLE with antiphospholipid antibodies (jSLE-aPL); c) SLE with secondary antiphospholipid syndrome (jSLE-APS). Clinical manifestations were compared between the 3 groups.

Results: We included 249 patients. 177 patients were classified as jSLE, 50 as jSLE-aPL, and 22 as jSLE-APS. The age of the cases ranged from 5 months to 18 years (mean age 12.65, SD 3.31); 207 patients (83.8%) were female. Regarding cardiovascular risk factors, jSLE-APS patients and jSLE-aPL had higher rates of hypertension and dyslipidemia than those with jSLE ($p< 0.001$). jSLE-APS patients showed higher rates of neurological manifestations ($p< 0.05$) and thrombopenia (63% in jSLE-APS, 30% in jSLE-aPL and 21% in jSLE, $p< 0.01$). The presence of livedo reticularis and Raynaud's syndrome was more frequent in the jSL-aPL group ($p< 0.05$). There were no differences in pulmonary or cardiac manifestations.

Regarding pharmacological treatment, in addition to antiplatelet and anticoagulant therapy, rituximab was used more frequently at the beginning in the jSLE-APS group ($p< 0,05$) and intravenous immunoglobulins in both jSLE-aPL y jSLE-APS groups ($p< 0,01$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: jSLE-APS patients exhibited more severe clinical profiles with higher frequencies of major organ involvement than jSLE-aPL and jSLE patients. Further studies are needed to determine the risk and long-term outcomes of aPL-related events.

Disclosure: D. Clemente: GlaxoSmithKlein(GSK), 6; **A. Boteanu**: GSK, 5, 6; **C. Udaondo**: None; **J. Calzada**: None; **J. Nieto**: None; **E. Enriquez**: None; **I. Calvo**: None; **L. Villalobos**: None; **B. Sevilla**: None; **S. Murias**: None; **B. Magallares**: None; **A. Capilla**: None; **J. Arroyo**: None; **B. Bravo**: None; **G. Diez-Cordoves**: None; **M. Camacho**: None; **G. grana**: None; **J. Bethencourt**: None; **P. Mesa**: None; **N. Palmou**: None; **M. Lopez Corbeto**: None; **J. Sanchez**: None; **M. Gonzalez**: None; **C. Moriano**: None; **D. Dios**: None; **L. Exposito**: None; **A. Garcia**: None; **L. Martin**: None; **D. Fernandez**: None; **L. Trujillo**: None; **A. Brandy**: None; **C. GUILLEN-ASTETE**: None; **I. Abasolo Alcazar**: None.

Abstract Number: 1285

Investigating the Relationship Between Brain Injury Markers and Brain Volume in Children with Systemic Lupus Erythematosus and Healthy Controls

Ganesh Ramanathan[1], Diana Valdes Cabrera[2], Oscar Mwizerwa[3], Justine Ledochowski[2], Tala El Tal[4], Sarah Mossad[5], Ibrahim Mohamed[1], Joanna Law[6], Lawrence Ng[7], Paris Moaf[2], Asha Jeyanathan[6], Adrienne Davis[6], Ann Yeh[6], Linda Hiraki[2], Deborah Levy[2], Zahi Touma[8], Joan Wither[9], Busisiwe Zapparoli[10], Ashley Danguecan[5] and Andrea Knight[5], [1]The Hospital for Sick Children, Brampton, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada, [3]University of Toronto, The Hospital for Sick Children, Toronto, ON, Canada, [4]Children's Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada, [5]Hospital for Sick Children, Toronto, ON, Canada, [6]The Hospital for Sick Children, Toronto, Canada, [7]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [8]University of Toronto, Toronto, ON, Canada, [9]University Health Network, Toronto, ON, Canada, [10]The Hospital for Sick Children, Etobicoke, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with childhood-onset systemic lupus erythematosus (cSLE) are at high risk for neuropsychiatric involvement as disease onset typically occurs during the critical period of adolescent brain development. Previous work has linked serum brain injury markers to systemic inflammation and cSLE disease features. However, the connection between these markers and brain volumetric changes is understudied. We aimed to i) compare serum brain injury markers and brain volumes between cSLE and controls; ii) evaluate the associations between brain injury markers and brain volume parameters; and iii) determine the associations within sub-analysis of the cSLE group.

Methods: This cross-sectional study included cSLE participants (ages 12–17) recruited from the Lupus Clinic at a Canadian tertiary children's hospital (Jan 2020–Dec 2023) and age/sex-matched healthy controls. Serum brain injury markers (serum neurofilament light (sNFL), glial fibrillary acidic protein (GFAP), Tau) were quantified using Simoa Human Neurology 4–Plex B assay (Quanterix, Billerica, MA, USA). T1-weighted MRIs acquired at 3T from cSLE patients and controls were preprocessed with FreeSurfer to automatically segment grey matter, white matter, lateral ventricle, and total brain volumes. Wilcoxon rank-sum tests compared serum brain injury marker levels between both groups and ANCOVA assessed brain volume differences adjusted for age and estimated total intracranial volume (eTIV). Semi-partial Pearson correlations

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

evaluated associations between brain injury markers (adjusted for age) and brain volumes (adjusted for eTIV) in the combined group (cSLE and controls), and in a sub-analysis of the cSLE group.

Results: 56 cSLE participants (mean age=15.1±1.8 years, 86% female) and 43 controls (mean age=15.1±1.7 years, 81% female) were included. GFAP (114.0 vs 74.3 pg/mL) and Tau (3.57 vs 2.58 pg/mL) serum levels were significantly higher in cSLE compared to controls (Figure 1). Adjusted total brain volume [F(1,95)=4.871, p=0.03] and grey matter volume [F(1,95)=5.571, p=0.020] were significantly lower in cSLE compared to controls; there were no differences for white matter and lateral ventricle volume. In the combined group, GFAP had a significant negative correlation with grey matter volume, while both sNFL and GFAP were positively associated with lateral ventricle volume (Table 1). No associations were found

Figure 1: Brain Injury Markers are Higher in cSLE vs. Controls

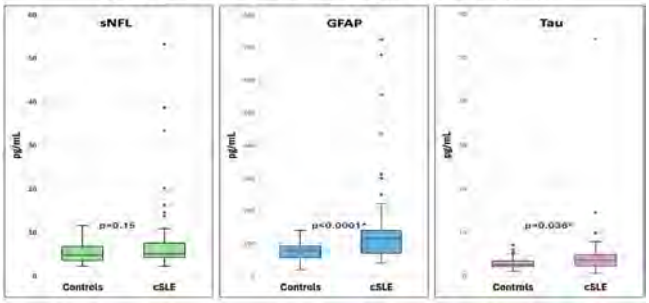


Figure 1: Boxplots showing group differences in serum brain injury marker levels between cSLE and controls. GFAP and Tau were significantly elevated in cSLE group (Wilcoxon rank sum test, $p < 0.05$), with outliers also observed across all brain injury markers for cSLE.

Table 1: Relationship between Brain Injury Markers and Brain Volumes in Combined Cohort of cSLE Patients and Controls (n=99)

	Total Brain Volume	Grey Matter Volume	White Matter Volume	Lateral Ventricle Volume
sNFL	r = -0.136, p = 0.18	r = -0.154, p = 0.13	r = -0.091, p = 0.37	r = 0.228, **p = 0.02**
GFAP	r = -0.155, p = 0.13	r = -0.237, **p = 0.02**	r = -0.041, p = 0.69	r = 0.240, **p = 0.02**
Tau	r = 0.153, p =0.13	r = 0.132, p = 0.19	r = 0.105, p = 0.30	r = 0.024, p = 0.81

Shown are semi-partial Pearson correlations analyzing relationships between serum brain injury markers (adjusted for age) and different brain volumes (adjusted for eTIV). Statistically significant correlations are bolded (p<0.05).

Table 2: Sub-Analysis of Relationship between Brain Injury Markers and Brain Volumes in cSLE only (n=56)

	Total Brain Volume	Grey Matter Volume	White Matter Volume	Lateral Ventricle Volume
sNFL	r = -0.103, p = 0.45	r = -0.125, p = 0.36	r = -0.060, p = 0.66	r = 0.246, p = 0.07
GFAP	r = -0.169, p = 0.21	r = -0.244, p = 0.07	r = -0.024, p = 0.86	r = 0.242, p = 0.07
Tau	r = 0.262, p = 0.05	r = 0.195, p = 0.15	r = 0.173, p = 0.20	r = 0.016, p = 0.91

Shown are semi-partial Pearson correlations analyzing relationships between serum brain injury markers (adjusted for age) and different brain volumes (adjusted for eTIV) in cSLE only. None of the correlations were statistically significant, but the coefficients and directionality of relationships still parallelled that within the combined cohort.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

between Tau and brain volumes. In the cSLE sub-analysis correlations between brain injury markers and brain volumes paralleled the whole group analysis, although not statistically significant (Table 2).

Conclusion: We found elevated serum brain injury markers and reduced total brain and grey matter volumes in patients with cSLE compared to controls. The significant relationships between sNFL/GFAP and grey matter/lateral ventricle volumes in the cohort suggest that these markers are associated with cerebral atrophy. Future studies of larger and longitudinal cohorts will help further explore the relationship between brain inflammation, injury, structure and function.

Disclosure: G. Ramanathan: None; **D. Valdes Cabrera**: None; **O. Mwizerwa**: None; **J. Ledochowski**: None; **T. El Tal**: None; **S. Mossad**: None; **I. Mohamed**: None; **J. Law**: None; **L. Ng**: None; **P. Moaf**: None; **A. Jeyanathan**: None; **A. Davis**: None; **A. Yeh**: Alexion, 5, Novartis, 5, Pfizer, 2, Roche, 1, 5, WIRB-Copernicus Group, 12, DSMB; **L. Hiraki**: Janssen, 2, 5; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **J. Wither**: None; **B. Zapparoli**: None; **A. Danguecan**: None; **A. Knight**: Pfizer, 6.

Abstract Number: 1286

Response to Hydroxychloroquine in Immune Thrombocytopenia in Childhood-Onset Systemic Lupus Erythematosus

Hamada Natour[1], Y. Ingrid Goh[1], Daniela Dominguez[2], Nicholas Gold[1], Lawrence Ng[3], Andrea Knight[4], Earl Silverman[1], Brian Feldman[1], Linda Hiraki[1] and Deborah Levy[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]The Hospital for Sick Children, Toronto, Canada, [3]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [4]Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The management of immune thrombocytopenia in childhood-onset systemic lupus erythematosus (cSLE) is not standardized. We examined the efficacy and safety of hydroxychloroquine (HCQ) as monotherapy for thrombocytopenia in cSLE.

Methods: We retrospectively reviewed the medical records of patients who developed thrombocytopenia (platelet count < 100 $\times 10^9$/L) and were diagnosed with cSLE and followed in the rheumatology clinic at The Hospital for Sick Children (SickKids) between January 2005 and December 2023. In this clinic, structured data, including disease activity (assessed by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)), are prospectively collected at every visit. Definite cSLE was defined by the 2019 EULAR/ACR classification criteria, while patients with incipient cSLE had clinical features of evolving SLE but achieved a EULAR/ACR score below 10. A complete response was defined as a platelet count >100 $\times 10^9$/L with no bleeding. Partial response was defined as a platelet count >30 $\times 10^9$/L with at least a 2-fold increase from the lowest count and no bleeding. Descriptive statistics were used to characterize the study groups and outcomes.

Results: Of the 729 patient records reviewed (68 with incipient lupus and 661 with definite lupus), 153 (21%) patients had thrombocytopenia (Figure 1). Thirty-three patients with thrombocytopenia, secondary to other causes such as medications or infections, were excluded. One hundred twenty patients (79% female) with a median age of 13 years (IQR 10.3 -14.7) and median platelet count of 23 $\times 10^9$/L (IQR 8.0 - 63.0) at the time of thrombocytopenia diagnosis were included. The median lowest platelet count was 10 $\times 10^9$/L (IQR 2 - 40). Disease characteristics are detailed in Table 1. Ninety-five (79%) patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Patients Included in Analysis

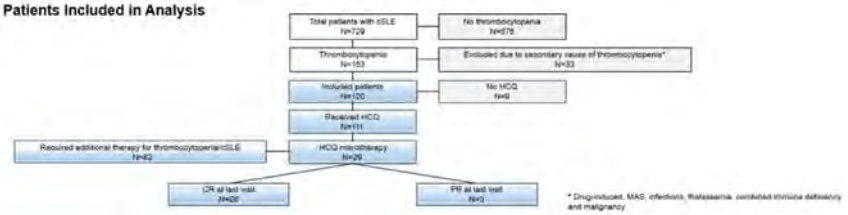


FIGURE 1

Table 1

Table 1. Characteristics of Patients Included in Analysis

	N (%)
Total number of patients (N, %)	120 (100%)
Female (N, %)	95 (79%)
Category of cSLE	
Definite cSLE	95 (79%)
Incipient cSLE	25 (21%)
Features at First Thrombocytopenia	Median (IQR)
Age (years)	13 (10.3-14.7)
Platelet count (x 10^9/L)	23 (8-63)
Features at Lowest Thrombocytopenia	Median (IQR)
Platelet count (x 10^9/L)	10 (2-40)
Hematologic Manifestations	N (%)
Mucosal bleeding	64 (53%)
Autoimmune hemolytic anemia	38 (32%)
Leukopenia	29 (24%)
Features of cSLE	
≥1 Antiphospholipid antibodies	34 (28%)
SLEDAI score for patients with definite cSLE	8 (5.5-10)
Therapy Prescribed to Patients and Response*	
Steroids and/or IVIG prior to HCQ	83 (69%)
Other therapy** prior to HCQ	45 (38%)
Thrombocytopenia response* observed prior to starting HCQ	66 (55%)
HCQ	111 (93%)
Did not receive other therapy after three months of HCQ	29 (24%)
Thrombocytopenia response* observed at patient's most recent clinical encounter	116 (97%)
Side effects with HCQ therapy***	8 (7%)
Discontinued HCQ due to side effects	6 (5%)
Morbidity and Mortality	
Major organ involvement	41 (34%)
SLICC damage score greater than 0 at last follow up	16 (13%)
Death	0

HCQ=hydroxychloroquine, IQR=interquartile range, IVIG=intravenous immunoglobulin, N/A=not applicable, cSLE=systemic lupus erythematosus
*Partial or complete response
**Treated with either one or a combination of azathioprine, mycophenolate mofetil (MMF), eltrombopag, romiplostim, rituximab, cyclophosphamide
***Hyperpigmentation, headaches, myositis, vasculitis, cardiomyopathy, blurred vision, and GI symptoms

Table 2

Table 2. Characteristics of Patients Responding* to HCQ Monotherapy

	Incipient SLE	Definite SLE	Total
	N (%)	N (%)	N (%)
Patients	7 (24%)	22 (76%)	29 (100%)
Female	5 (17%)	21 (72%)	26 (90%)
	Median (IQR)	Median (IQR)	Median (IQR)
Thrombocytopenia duration in months at cSLE diagnosis	9.7 (2-12)	3.2 (0.3-13)	3.7 (1-13)
Follow up duration in months at last visit	35 (27-83)	52 (36-75)	52 (33-75)
Follow up duration in months when started on HCQ	11 (9.5-34.5)	5.3 (1.8-8.4)	7 (2.5-12)
Hematologic Manifestations	N (%)	N (%)	N (%)
Mucosal bleeding	3 (10%)	13 (45%)	16 (55%)
Autoimmune hemolytic anemia	1 (3%)	3 (10%)	4 (14%)
Leukopenia	1 (3%)	6 (21%)	7 (24%)
Features of cSLE			
≥1 Antiphospholipid antibodies	1 (3%)	4 (14%)	5 (7%)
SLEDAI score for patients with definite cSLE	N/A	6 (3.3-8.5)	6 (3.3-8.5)
	Median (IQR)	Median (IQR)	Median (IQR)
Features at First Thrombocytopenia			
Age (in years)	13 (7.4-15.8)	13.3 (11.6-14.2)	13 (11.6-15.1)
Platelet count (x 10^9/L)	22 (15-31)	20.5 (7-52)	22 (8-52)
Features at Lowest Thrombocytopenia			
Platelet count (x 10^9/L)	7 (4-19)	10.5 (2-24)	9 (2-23)
Features when started HCQ			
Platelet count (x 10^9/L)	78 (67-116)	58 (22-127)	77 (24-127)
Therapy Prescribed to Patients and Response	N (%)	N (%)	N (%)
Steroids and/or IVIG prior to HCQ	5 (17%)	11 (38%)	16 (55%)
Other therapy** prior to HCQ	0	2 (7%)	2 (7%)
Thrombocytopenia response*observed prior to starting HCQ	5 (17%)	8 (28%)	13 (45%)
Thrombocytopenia response*observed 3 months after starting HCQ	5 (17%)	17 (59%)	22 (76%)
Thrombocytopenia response*observed at patient's most recent clinical encounter	7 (24%)	22 (76%)	29 (100%)
Side effects with HCQ therapy***	1 (3%)	1 (3%)	2 (7%)
Discontinued HCQ due to side effects	0	1 (3%)	1 (3%)

HCQ=hydroxychloroquine, IQR=interquartile range, IVIG=intravenous immunoglobulin, N/A=not applicable, cSLE=systemic lupus erythematosus
*Partial or complete response
**Treated with either one or a combination of azathioprine, mycophenolate mofetil (MMF), eltrombopag, romiplostim, rituximab, cyclophosphamide
***Hyperpigmentation and headaches

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

had definite, and 25 (21%) had incipient cSLE. The median SLEDAI score at cSLE diagnosis (for definite SLE) was 8 (IQR 5.5 - 16). Eighty-three (69%) of patients were treated with corticosteroids and/or IVIG prior to commencing HCQ, and 45 of them (38%) also required one or more additional treatments for thrombocytopenia (those were azathioprine, mycophenolate mofetil (MMF), eltrombopag, romiplostim, rituximab, or cyclophosphamide). Sixty-six (55%) patients achieved complete or partial responses before initiating HCQ. 111 (93%) patients were treated with HCQ, initiated at a median of 6 months (IQR 2.7 - 12.2) after thrombocytopenia diagnosis at a median platelet count of 77 $\times 10^9$/L (IQR 32.5 - 198.0). Of those, twenty-nine (24%) patients were treated with HCQ monotherapy (Table 2). All 29 responded; 26 had complete responses after a median follow-up of 52 months (IQR 33 - 75). Of the 111 patients who received HCQ during their disease course, eight experienced side effects, and 6 of them had to discontinue the treatment due to these effects.

Conclusion: While most patients initially needed additional treatments, HCQ monotherapy effectively maintained a partial or complete response in thrombocytopenia for over four years in approximately one-quarter of cSLE patients. Further analysis will identify characteristics that predict a positive response to HCQ monotherapy.

Disclosure: H. Natour: None; **Y. Goh**: None; **D. Dominguez**: None; **N. Gold**: None; **L. Ng**: None; **A. Knight**: Pfizer, 6; **E. Silverman**: None; **B. Feldman**: Cabelleta, 1, Pfizer, 12, DSMB; **L. Hiraki**: Janssen, 2, 5; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5.

Abstract Number: 1287

A Clear Pattern of Clinical Presentation in Juvenile Systemic Scleroderma Is Associated with Interstitial Lung Disease

Ivan Foeldvari[1], Kathryn Torok[2], Ozgur Kasapcopur[3], Amra Adrovic[4], Flavio Sztajnbok[5], Maria Teresa Terreri[6], Ana Sakamoto[7], Jordi Anton[8], Raju Khubchandani[9], Sindhu Johnson[10], Gülcan Özomay Baykal[11], Brian Feldman[12], Dieneke Schonenberg-Meinema[13], Sujata Sawhney[14], Vanessa Smith[15], Eslam Al-Abadi[16], Simone Appenzeller[17], Stefanie Hajek[18], Maria Katsicas[19], Mikhail Kostik[20], Suzanne Li[21], Hana Malcova[22], Anjali Patwardhan[23], Walter Alberto Sifuentes-Giraldo[24], Natalia Vasquez-Canizares[25], Tadej Avcin[26], Patricia Costa Reis[27], Siri Opsahl Hetlevik[28], Mahesh Janarthanan[29], Edoardo Marrani[30], Clare Pain[31], Maria Jose Santos[32], Valda Stanevica[33], Sima Abu Alsaoud[34], Ekaterina Alexeeva[35], Cristina Battagliotti[36], Lillemor Berntson[37], blanca e r bica[38], Jürgen Brunner[39], Despina Eleftheriou[40], Liora Harel[41], Tilmann Kallinich[42], Dragana Lazarevic[43], Kirsten Minden[44], Dana Nemcova[45], Susan Nielsen[46], Farzana Nuruzzaman[47], Mihaela Sparchez[48], Yosef Uziel[49] and Nicola Helmus[50], [1]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany, [2]University of Pittsburgh, Pittsburgh, PA, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey, [4]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Turkey, Turkey, [5]UFRJ/UERJ, SAO PAULO, Brazil, [6]UNIFESP, São Paulo, São Paulo, Brazil, [7]Federal University of São Paulo (UNIFESP), São Paulo, São Paulo, Brazil, [8]Hospital Sant Joan de Déu. Universitat de Barcelona, Esplugues de Llobregat (Barcelona), Spain, [9]Jaslok Hospital and Research Center, Mumbai, India, [10]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, [11]Umraniye Training and Research Hospital, Istanbul, Turkey, [12]The Hospital for Sick Children, Toronto, ON, Canada, [13]Emma Children's Hospital, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands, [14]Sir Ganga Ram Hospital, Sector 37 noida, Uttar Pradesh, India, [15]Ghent University Hospital, Gent, Belgium, [16]Birmingham Women's and Children's Hospital NHSFT, Birmingham, United Kingdom, [17]Unicamp, Campinas, São Paulo, Brazil, [18]Deutsches Zentrum für Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Germany, [19]Hospital Garrahan, Buenos Aires, Argentina, [20]Saint-Petersburg State Pediatric Medical University, Saint Petersburg, Russia, [21]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ, [22]Motol University Hospital, Prague, Czech Republic, [23]University of Missouri-Columbia, Columbia, MO, [24]Hospital Universitario Ramón y Cajal, Madrid, Spain, [25]Children's Hospital at Montefiore, Bronx, NY, [26]University Children's Hospital University Medical Center Ljubljana, Ljubljana, Slovenia, [27]Hospital de Santa Maria, Lisbon, Portugal, [28]Oslo University Hospital, Oslo, Norway, [29]SRI RAMACHANDRA INSTITUTE OF HIGHER EDUCATION AND RESEARCH, Chennai, Tamil Nadu, India, [30]Meyer Children Hospital IRCCS, Firenze, Italy, [31]Alder Hey NHS Trust, Liverpool, United Kingdom, [32]Hospital Garcia de Orta, Almada, Lisboa, Portugal, [33]Childrens Clinical University Hospital, Zemgales priekšpilseta, Riga, Latvia, [34]Caritas baby Hospital, Jerusalem, Palestine, [35]National Medical Research Center for Children's Health Federal State Autonomous Institution of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the Russian Federation Ministry of Health and I.M. Sechenov First Moscow State Medical University (Sechenovskiy University), Moscow, Russia, [36]Hospital de Niños Dr Orlando Alassia, Santa Fe, Argentina, [37]Dept. of Women's and Children's Health, Uppsala University, Uppsala, Sweden, [38]UNIVERSIDADE FEDERAL DO RIO DE JANEIRO, Rio de Janeiro, Brazil, [39]Medical University Innsbruck; Department of Pediatrics, Pediatric Rheumatology, Innsbruck, Austria, [40]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [41]Schneider Children's Medical center, Nettnja, Israel, [42]Charite University Medicine Berlin, Berlin, Germany, [43]Dept of Pediatric Rheumatology and Immunology Clinical Center Nis, Faculty of Medicine, University of Niš, Nis, Serbia, [44]German Rheumatism Research Center, Berlin, Germany, [45]Charles University, Prague, Czech Republic, [46]Rigshospitalet, Copenhagen, Denmark, [47]Stony Brook Children's Hospital, Stony Brook, NY, [48]Emergency Clinical Hospital for Children, Cluj-Napoca, Romania, [49]Pediatric Rheumatology Unit, Meir Medical Center, Kfar Saba, Sackler School of Medicine, Tel Aviv University, Kfar Saba, Israel, [50]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile systemic sclerosis(jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. In adult systemic sclerosis is interstitial lung disease (ILD) one of the main leading causes of mortality. High resolution computer tomography (HRCT) is the gold standard to assess ILD. To find risk factors or predictive factors for ILD in jSSc has a significant clinical importance.

Methods: We extracted data from patients till March 2025, who had an HRCT evaluation at the time of inclusion into the juvenile scleroderma inception cohort(jSSclC)(1). We compared the clinical presentation of patients with positive (HRCT+) and negative (HRCT-) findings for ILD.

Results: 216 patients had an HRCT result at time of the inclusion in the cohort. 76 of them were HRCT+. In both groups around 70% of the patients had diffuse subset. Median age at the time of the first non-Raynaud´s presentation was 10.8 and 11.3 in the HRCT+ versus HRCT- group. Median disease duration was around 2 years. Significantly more patients had decreased FVC< 80% (44% versus 25%, p=0.011) and DLCO< 80% (62% versus 36%, p=0.004) in the HRCT + then HRCT- group. Median MRSS was lower in the HRCT+ then HRCT- group (8.5 versus 12.5, p=0.031). Lower number of patients had sclerodactyly in the HRCT+ then HRCT- group (68% versus 81%, p=0.039). Nailfold capillary changes occurred more often in the HRCT+ then in HRCT- group (88% versus 73%, p=0.042). In the HRCT+ group pulmonary hypertension occurred more frequently (14% versus 2%, p=0.001). Oesophageal involvement was more frequent in the HRCT+ group (58% versus 34%, p=0.001). We could not find any significant difference regarding antibody profile, cardiac, renal and musculoskeletal involvement.

Table1. Clinical findings of patients with positive and negative ILD

Patients with and without ILD at time of inclusion	Patients without ILD assessed by HRCT N=140	Patients with ILD assessed by HRCT N=76	p-value
FVC < 80% in assessed group	25% (25/101)	44% (28/64)	0.011
DLCO < 80% in assessed group	36% (26/73)	62% 32/52)	0.004
MRSS, median (IQR)	12 (4.5 – 20) n=136	8.5 (4 – 25) n=74	0.031
Sclerodactyly	81% (108/133)	68% (50/73)	0.039
Nailfold capillary changes	73% (97/132)	86% (61/71)	0.042
Pulmonary Hypertension assessed by US	2% (3/140)	14% (11/76)	0.001
Oesophageal Involvement	34% (48/140)	58% (44/76)	0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: We found a remarkable clinical pattern associated with HRCT+, with increased capillary changes, more frequent oesophageal involvement and pulmonary hypertension and lower MRSS. This pattern may help to predict ILD. We must remark that we had no central reading of the HRCT imaging. We need more patients and more long term observation period to prove our findings.

1. Foeldvari I, Klotsche J, Kasapcopur O, Adrovic A, Terreri MT, Sakamoto AP, et al. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.

Disclosure: I. Foeldvari: None; **K. Torok**: None; **O. Kasapcopur**: None; **A. Adrovic**: None; **F. Sztajnbok**: None; **M. Terreri**: None; **A. Sakamoto**: None; **J. Anton**: None; **R. Khubchandani**: None; **S. Johnson**: None; **G. Özomay Baykal**: None; **B. Feldman**: Cabelleta, 1, Pfizer, 12, DSMB; **D. Schonenberg-Meinema**: None; **S. Sawhney**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **E. Al-Abadi**: None; **S. Appenzeller**: None; **S. Hajek**: None; **M. Katsicas**: None; **M. Kostik**: None; **S. Li**: Boehringer-Ingelheim, 2, Merck/MSD, 12, Spouse was an employee and receiving pension from them; **H. Malcova**: None; **A. Patwardhan**: None; **W. Sifuentes-Giraldo**: None; **N. Vasquez-Canizares**: None; **T. Avcin**: None; **P. Costa Reis**: None; **S. Hetlevik**: None; **M. Janarthanan**: None; **E. Marrani**: None; **C. Pain**: None; **M. Santos**: None; **V. Stanevica**: None; **S. Abu Alsaoud**: None; **E. Alexeeva**: Amgen, 12, 5, AstraZeneca, 6, Biocad, 12, 5, Eli Lilly, 12, 5, Generium, 5, 6, Johnson & Johnson, 5, 6, Novartis, 5, 6, Pfizer, 12, 5, Roche, 6, R-Pharm JSC, 5, 6, Sanofi, 12, 5, Skopinpharm, 6, Sobi, 6, Swixx Biopharma, 6, UCB, 12, 5; **C. Battagliotti**: None; **L. Berntson**: None; **b. bica**: None; **J. Brunner**: None; **D. Eleftheriou**: None; **L. Harel**: None; **T. Kallinich**: None; **D. Lazarevic**: None; **K. Minden**: None; **D. Nemcova**: None; **S. Nielsen**: None; **F. Nuruzzaman**: None; **M. Sparchez**: None; **Y. Uziel**: None; **N. Helmus**: None.

Abstract Number: 1288

Is gastroesophageal reflux a risk for interstitial lung disease in Juvenile systemic sclerosis?

Ivan Foeldvari[1], Kathryn Torok[2], Ozgur Kasapcopur[3], Amra Adrovic[4], Brian Feldman[5], Flavio Sztajnbok[6], Maria Teresa Terreri[7], Ana Sakamoto[8], Jordi Anton[9], Sindhu Johnson[10], Raju Khubchandani[11], Valda Stanevica[12], Gülcan Özomay Baykal[13], Dieneke Schonenberg-Meinema[14], Eslam Al-Abadi[15], Ekaterina Alexeeva[16], Maria Katsicas[17], Sujata Sawhney[18], Vanessa Smith[19], Sima Abu Alsaoud[20], Simone Appenzeller[21], Tadej Avcin[22], Natalia Cabrera[23], Stefanie Hajek[24], Siri Opsahl Hetlevik[25], Mikhail Kostik[26], Thomas Lehman[27], Suzanne Li[28], Hana Malcova[29], Edoardo Marrani[30], Clare Pain[31], Anjali Patwardhan[32], Walter Alberto Sifuentes-Giraldo[33], Natalia Vasquez-Canizares[34], Patricia Costa Reis[35], Mahesh Janarthanan[36], Maria Jose Santos[37], Cristina Battagliotti[38], Lillemor Berntson[39], blanca e r bica[40], Jürgen Brunner[41], Liora Harel[42], Gerd Horneff[43], Daniela Kaiser[44], Jorge Lopez-Benitez[45], Farzana Nuruzzaman[46], Mihaela Sparchez[47], Yosef Uziel[48] and Nicola Helmus[49], [1]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany, [2]University of Pittsburgh, Pittsburgh, PA, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey, [4]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Turkey, Turkey, [5]The Hospital for Sick Children, Toronto, ON, Canada, [6]UFRJ/UERJ, SAO PAULO, Brazil, [7]UNIFESP, São Paulo, São Paulo, Brazil, [8]Federal University of São Paulo (UNIFESP), São Paulo, São Paulo, Brazil, [9]Hospital Sant Joan de Déu. Universitat de Barcelona, Esplugues de Llobregat (Barcelona), Spain, [10]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, [11]Jaslok Hospital and Research Center, Mumbai, India, [12]Childrens Clinical University Hospital, Zemgales priekšpilseta, Riga, Latvia, [13]Umraniye Training and Research Hospital, Istanbul, Turkey, [14]Emma Children's Hospital, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands, [15]Birmingham Women's and Children's Hospital NHSFT, Birmingham, United Kingdom, [16]National Medical Research Center for Children's Health Federal State Autonomous Institution of the Russian Federation Ministry of Health and I.M. Sechenov First Moscow State Medical University (Sechenovskiy University), Moscow, Russia, [17]Hospital Garrahan, Buenos Aires, Argentina, [18]Sir Ganga Ram Hospital, Sector 37 noida, Uttar Pradesh, India, [19]Ghent University Hospital, Gent, Belgium, [20]Caritas baby Hospital, Jerusalem, Palestine, [21]Unicamp, Campinas, São Paulo, Brazil, [22]University Children's Hospital University Medical Center Ljubljana, Ljubljana,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Slovenia, [23]IPS Central: Asunción, Asuncion, Paraguay, [24]Deutsches Zentrum für Kinder- und Jugendrheumatologie, Garmisch-Partenkirchen, Germany, [25]Oslo University Hospital, Oslo, Norway, [26]Saint-Petersburg State Pediatric Medical University, Saint Petersburg, Russia, [27]Hospital for Special Surgery, New York, [28]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ, [29]Motol University Hospital, Prague, Czech Republic, [30]Meyer Children Hospital IRCCS, Firenze, Italy, [31]Alder Hey NHS Trust, Liverpool, United Kingdom, [32]University of Missouri-Columbia, Columbia, MO, [33]Hospital Universitario Ramón y Cajal, Madrid, Spain, [34]Children's Hospital at Montefiore, Bronx, NY, [35]Hospital de Santa Maria, Lisbon, Portugal, [36]SRI RAMACHANDRA INSTITUTE OF HIGHER EDUCATION AND RESEARCH, Chennai, Tamil Nadu, India, [37]Hospital Garcia de Orta, Almada, Lisboa, Portugal, [38]Hospital de Niños Dr Orlando Alassia, Santa Fe, Argentina, [39]Dept. of Women's and Children's Health, Uppsala University, Uppsala, Sweden, [40]UNIVERSIDADE FEDERAL DO RIO DE JANEIRO, Rio de Janeiro, Brazil, [41]Medical University Innsbruck; Department of Pediatrics, Pediatric Rheumatology, Innsbruck, Austria, [42]Schneider Children's Medical center, Nettnja, Israel, [43]Asklepios Klinik, Hamburg, Germany, [44]Childrens Hospital Lucerne, Lucerne, Switzerland, [45]Private Practice, Asuncion, Paraguay, [46]Stony Brook Children's Hospital, Stony Brook, NY, [47]Emergency Clinical Hospital for Children, Cluj-Napoca, Romania, [48]Pediatric Rheumatology Unit, Meir Medical Center, Kfar Saba, Sackler School of Medicine, Tel Aviv University, Kfar Saba, Israel, [49]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Gastroesophageal involvement, particularly reflux, has been identified as a risk factor for development and progression of interstitial lung disease (ILD) in adult systemic sclerosis However, this association has not yet been extensively studied in juvenile systemic sclerosis (jSSc)(1) (2, 3). To further address this gap, the juvenile systemic scleroderma inception cohort(jSScIC) (4) including 279 patients provides an opportunity to investigate the potential link between these two manifestations in the paediatric population.

Methods: We analysed baseline clinical data from all patients enrolled in jSScIC till April 15th, 2025 ~~a~~nd compared the clinical characteristics of patients with and without GR.

Results: We reviewed data of 279 patients: 93 (33%) had reported to have gastroesophageal reflux (GR+). Patients with GR + were more frequently evaluated by barium swallow (32% versus 18%, p=0.006) and endoscopy (22% versus 5%, p=0.041). Approximately 70% of the patients had diffuse cutaneous subset. The Median age at onset of first non-Raynaud presentation was around 11 years. Patients with GR+ had more nailfold capillary changes (91% versus 71%, p=0.001) and telangiectasia (49% versus 30%, p=0.002) compared to GR negative (GR-) patients. GR+ patients were more likely to have lung involvement than GR- patients with higher frequency had FVC< 80% (p=0.05), DLCO< 80% (p=0.001) and ILD as identified by high-resolution CT (p=0.004). The pulmonary function findings GR+ patients had more positive findings for ILD on high resolution CT of the lung as GR- patients (56% versus 37%, p=0.004). No significant differences were observed regarding autoantibody profile, cardiac, renal and musculoskeletal involvement between the groups.

Conclusion: GR+ had a significantly higher prevalence of ILD. Patients reported GR ~~is~~ correlating with an increased frequency of microvascular changes. This findings highlight the importance of assessing all patients for GR to enable timely management of reflux and potentially reduce occurrence/progression for ILD in jSSc. Further long-term studies are needed to prove our hypothesis and support targeted intervention strategies.

1. Ambartsumyan L, Zheng HB, Iyer RS, Soares J, Henstorf G, Stevens AM. Relationship Between Esophageal Abnormalities on Fluoroscopic Esophagram and Pulmonary Function Testing in Juvenile Systemic Sclerosis. Arthritis Care Res (Hoboken). 2019;71(11):1444–9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of patients with and without gastroesophageal reflux in the jSScIC cohort, where we found clinically meaningful difference

	Without GR N=186	With GR N=93	p-value
Nailfold capillary changes	71% (122/173)	91% (81/89)	0.001
Telangiectasia	30% (51/169)	49% (43/87)	0.002
Patient VAS scales 0-100mm (min-max) for Raynaud activity	20 (5 – 50) n=162	45 (20 – 70) n=82	0.011
FVC < 80%	28% (35/125)	42% (31/74)	0.05
DLCO < 80%	33% (30/92)	60% (34/57)	0.001
Abnormal findings on HRCT	37% (51/139)	56% (43/75)	0.004
6-MWT under <10th percentile of normal range	59% (30/51)	78% (25/32)	0.070

DLCO: Diffusing Capacity of the Lung for Carbon Monoxide, FVC: Forced Vital Capacity, GR: gastroesophageal reflux, HRTC: High-Resolution Computed Tomography, jSScIC: juvenile systemic scleroderma inception cohort, 6-MWT: 6-Minute Walk Test, VAS: Visual Analogue Scale

2. Roth E, Bruni C, Petelytska L, Becker MO, Dobrota R, Jordan S, et al. Gastroesophageal reflux disease is associated with a more severe interstitial lung disease in systemic sclerosis in the EUSTAR cohort. Rheumatology (Oxford). 2025.

3. Li JC, Tadros S, Rosser F, Torok KS. Pulmonary Nodules in Juvenile Systemic Sclerosis: A Case-Series from the National Registry for Childhood Onset Scleroderma (NRCOS). Diagnostics (Basel). 2023;13(12).

4. Foeldvari I, Klotsche J, Kasapcopur O, Adrovic A, Terreri MT, Sakamoto AP, et al. Differences Sustained Between Diffuse and Limited Forms of Juvenile Systemic Sclerosis in an Expanded International Cohort. Arthritis Care Res (Hoboken). 2022;74(10):1575–84.

Disclosure: I. Foeldvari: None; **K. Torok**: None; **O. Kasapcopur**: None; **A. Adrovic**: None; **B. Feldman**: Cabelleta, 1, Pfizer, 12, DSMB; **F. Sztajnbok**: None; **M. Terreri**: None; **A. Sakamoto**: None; **J. Anton**: None; **S. Johnson**: None; **R. Khubchandani**: None; **V. Stanevica**: None; **G. Özomay Baykal**: None; **D. Schonenberg-Meinema**: None; **E. Al-Abadi**: None; **E. Alexeeva**: Amgen, 12, 5, AstraZeneca, 6, Biocad, 12, 5, Eli Lilly, 12, 5, Generium, 5, 6, Johnson & Johnson, 5, 6, Novartis, 5, 6, Pfizer, 12, 5, Roche, 6, R-Pharm JSC, 5, 6, Sanofi, 12, 5, Skopinpharm, 6, Sobi, 6, Swixx Biopharma, 6, UCB, 12, 5; **M. Katsicas**: None; **S. Sawhney**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **S. Abu Alsaoud**: None; **S. Appenzeller**: None; **T. Avcin**: None; **N. Cabrera**: None; **S. Hajek**: None; **S. Hetlevik**: None; **M. Kostik**: None; **T. Lehman**: None; **S. Li**: Boehringer-Ingelheim, 2, Merck/MSD, 12, Spouse was an employee and receiving pension from them; **H. Malcova**: None; **E. Marrani**: None; **C. Pain**: None; **A. Patwardhan**: None; **W. Sifuentes-Giraldo**: None; **N. Vasquez-Canizares**: None; **P. Costa Reis**: None; **M. Janarthanan**: None; **M. Santos**: None; **C. Battagliotti**: None; **L. Berntson**: None; **b. bica**: None; **J. Brunner**: None; **L. Harel**: None; **G. Horneff**: Janssen, 5, MSD, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, Sanofi, 6; **D. Kaiser**: None; **J. Lopez-Benitez**: None; **F. Nuruzzaman**: None; **M. Sparchez**: None; **Y. Uziel**: None; **N. Helmus**: None.

Abstract Number: 1289

Longitudinal Exploration of Pain and Disease Characteristics in Youth with Childhood-Onset Lupus

Jida Jaffan[1], Tala El Tal[2], Lawrence Ng[3], Asha Jeyanathan[4], Hunter Hogarth[5], Adrienne Davis[4], Linda Hiraki[5], Deborah Levy[5], Zahi Touma[6], Natoshia Cunningham[7], Ashley Danguecan[8] and Andrea Knight[8], [1]The Hospital for Sick Children/ University of Toronto, Toronto, ON, Canada, [2]Children's Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada, [3]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [4]The Hospital for Sick Children, Toronto, Canada,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[5]The Hospital for Sick Children, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada, [7]Michigan State University, Grand Rapids, MI, [8]Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pain is a common symptom in childhood-onset systemic lupus erythematosus (cSLE) which impacts health-related quality of life. Its relationship to disease measures over time is not fully understood. We aimed to i) examine the course of patient-reported pain behavior (outward expressions of pain, e.g., grimacing) and pain interference (extent to which pain disrupts daily life, e.g., sleep, activities, mood) in patients with cSLE versus controls, and ii) explore relationships between these pain measures and disease characteristics in cSLE.

Methods: We conducted a secondary analysis of data collected from a prospective cohort study of patients with cSLE (meeting SLICC or ACR/EULAR SLE classification criteria) and age/sex-matched healthy controls. Patient-Reported Outcomes Measurement Information System (PROMIS) pain behavior and pain interference T-scores, and disease characteristics (disease duration, glucocorticoid use (current prednisone-equivalent dose, cumulative dose from time of SLE diagnosis), and Physician Global Assessment (PGA)) were collected at two time points: baseline (time of study enrollment) and 1-year follow up. Descriptive statistics summarized group characteristics. Within- and between-group differences in PROMIS scores were analyzed using Mann-Whitney and Wilcoxon signed-rank tests. Associations between PROMIS measures and disease characteristics were examined using Spearman's rank correlation test.

Results: We included 51 youth with cSLE (mean age=15y (SD 1.7), 88% female) and 38 controls (mean age =15y (SD 1.7), 84% female). cSLE disease duration at baseline was median 24 months (IQR 12-45) (Table 1). Compared to controls, cSLE participants pain behavior (baseline: 37 vs 25, p < .001; one-year: 37 vs 29: p = .008) and pain interference (baseline: 46 vs

Table 1: Demographic and Disease Characteristics of cSLE and Controls at Baseline and 1-Year Follow-Up

	cSLE n = 51		Controls n = 38	
	Baseline	**At 1-Year**	**Baseline**	**At 1-Year**
Demographic Characteristics				
Age (years), mean (SD)	15.1 (1.7)	16.0 (1.6)	15.2 (1.7)	16.2 (1.7)
Female, n (%)	45 (88.2)	44 (86.3)	32 (84.2)	33 (86.8)
Self-Reported Ethnicity, n (%)				
Asia	26 (51.0)	-	6 (15.8)	-
Europe	11 (21.6)	-	18 (47.4)	-
Arabia, Africa, and Caribbean Islands	7 (13.7)	-	4 (10.5)	-
America (includes Aboriginal and Latin America)	3 (5.9)	-	3 (7.9)	-
Other	4 (7.8)	-	7 (18.4)	-
Household income below poverty line, n (%)	16 (32.0)	14 (28.0)	4 (10.5)	7 (18.4)
cSLE Disease Characteristics				
Disease duration (months), median (IQR)	24 (12 – 45)	32 (24 – 51)	-	-
SLEDAI-2K, median (IQR)	2 (2 – 6)	2 (0 – 4)	-	-
Active disease (SLEDAI-2K>4), n (%)	14 (27.5)	10 (20.0)	-	-
Disease damage (SLICC Damage Index>0), n (%)	4 (7.8)	7 (13.7)	-	-
Arthritis*, n (%)	30 (58.8)	21 (43.8)		
Nephritis*, n (%)	21 (41.2)	21 (43.8)		
Prednisone-equivalent dose ≥ 5mg/day at visit, n (%)	18 (35.5)	8 (16.7)	-	-
Cumulative glucocorticoid use (g), median (IQR)	2.5 (0.6– 7.2)	4.2 (1.6– 9.2)	-	-

*Missing value for 3 participants at 1-year follow up

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: PROMIS T-Scores at Baseline and 1-Year Follow Up for cSLE and Control Participants, and Within- and Between-Group Comparisons

	cSLE (n=51**)			Controls (n=38)			
PROMIS Measure	Baseline T-Score Mean (SD)	1 Year T-Score Mean (SD)	Within-Group Comparisons	Baseline T-Score Mean (SD)	1 Year T-Score Mean (SD)	Within-Group Comparisons	Between-Group Comparisons
Pain Behavior	38.9 (15.5)	37.2 (14.7)	W= 366, p= 0.954	25.0 (11.3)	29.2 (12.8)	W= 41, p= 0.098	V1: U= 573, **p< 0.001*** V2: U= 655, **p= 0.008***
Pain Interference	45.6 (11.0)	45.7 (10.7)	W= 363, p= 0.868	39.4 (7.7)	40.6 (8.2)	W= 89, p= 0.549	V1: U= 674, **p= 0.007*** V2: U= 704, **p= 0.027***

*Significant at p<0.05
**One patient result missing for Pain Interference at Year1
PROMIS measures reported as standardized T scores with a normative mean of 50 and standard deviation of 10. Higher scores indicate more of the measured trait. Wilcoxon signed-rank tests were used for within-group comparisons, Mann-Whitney U –tests were used for between-group comparisons

Table 3: Exploratory Spearman Correlation Table between PROMIS Pain measures and Disease Characteristics across Baseline and 1-Year Follow-Up for cSLE Participants

	Baseline		1-Year	
	Pain Behavior	Pain Interference	Pain Behavior	Pain Interference
Disease Duration	-0.372* p = 0.007	-0.382* p = 0.005	-0.179 p = 0.218	-0.148 p = 0.310
Physician Global Assessment	0.394* p = 0.004	0.459* p < 0.001	0.389* p = 0.005	0.415* p = 0.003
Current glucocorticoid dose (mg)	0.219 p = 0.123	0.273 p = 0.052	0.078 p = 0.600	0.101 p = 0.499
Cumulative glucocorticoid use (g)	-0.256 p = 0.070	-0.181 p = 0.204	0.108 p = 0.218	0.248 p = 0.105

Spearman Rho and p- value depicted for each correlation
*Significant at p<0.05

39, p = .007; one-year: 46 vs 41, p = .027) were significantly higher (Table 2). Scores remained stable over time within both groups, with no significant mean change at follow-up. For the cSLE group, disease duration negatively correlated with both pain measures at baseline (pain behavior: rho = -.372, p = .007; pain interference: rho = -.382, p = .005), but not at one year follow-up (Table 3). PGA significantly associated with both pain measures for all time points (pain behavior: baseline rho = .394, one-year rho = .389; pain interference: baseline rho = .459, one-year rho = .415, p < .005 for all). Current glucocorticoid dose at visit and cumulative glucocorticoid use did not correlate with pain.

Conclusion: Youth with cSLE report persistently elevated pain interference and pain behavior, underscoring the lasting impact of pain. The association of disease duration with pain weakened over time, initially a negative correlation at baseline and no correlation at one year. This may suggest that early disease manifestations causing pain are controlled (e.g. inflammation), however long-term pain manifestations of SLE may not be. Interestingly, PGA consistently positively correlated with pain indicating that clinicians are sensing and reporting on patient pain in their global assessment, beyond the early manifestations. These findings highlight the importance of furthering our understanding of pain and its causes in youth with SLE

Disclosure: J. Jaffan: None; **T. El Tal**: None; **L. Ng**: None; **A. Jeyanathan**: None; **H. Hogarth**: None; **A. Davis**: None; **L. Hiraki**: Janssen, 2, 5; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **N. Cunningham**: None; **A. Danguecan**: None; **A. Knight**: Pfizer, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1290

Adverse Childhood Experiences: Prevalence and Relationship to Disease and Mental Health Outcomes in Childhood-onset Systemic Lupus Erythematosus (cSLE)

Jin Xuan Zhou[1], Stephanie Fevrier[2], Paris Moaf[2], Lawrence Ng[3], Asha Jeyanathan[4], Louise Boulard[2], Deborah Levy[1], Linda Hiraki[1], Ashley Danguecan[5] and Andrea Knight[5], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]Hospital for Sick Children, Toronto, Canada, [3]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [4]The Hospital for Sick Children, Toronto, Canada, [5]Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) is an autoimmune disease characterized by multi-organ inflammation, alongside high frequencies of mood disorders and cognitive impairment. Adverse Childhood Experiences (ACEs) quantify traumatic childhood events, which have been linked to altered immune response and increased chronic disease risk. Prior studies indicate those with ≥ 4 ACEs, including adults with SLE, face higher risk of worse health outcomes. Limited research exists on ACEs in cSLE. We aimed to describe the prevalence of ACEs among cSLE patients and investigate associations with i) disease activity, ii) patient-reported outcome measures, and iii) self-reported executive function.

Methods: This cross-sectional study analyzed prospective data from cSLE patients aged 13-19 years at the time of assessment. The Pediatric ACEs and Related Life Events Screener (PEARLS) measured 19 self-reported ACEs. Disease activity over the time since diagnosis was measured by the adjusted mean Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K). The Patient Reported Outcomes Information System (PROMIS) Pediatric-37 Profile assessed patient-reported anxiety, depression, and fatigue. The Behavior Rating Inventory of Executive Function (BRIEF-2) Global Executive Composite score measured executive function. The frequency of ACEs types was tabulated, and patients were classified into high-risk (≥ 4 ACEs) and low-risk (≤ 3 ACEs) groups. Associations between ACEs risk group and the outcomes were examined using regression analyses with generalized linear models, adjusted for age.

Results: Of 50 cSLE patients (mean age 15.20 ± 1.86 years, 84% female), 72% reported at least 1 ACE, and 30% reported ≥ 4 ACEs (Table 1). The most common ACEs were caregiver verbal abuse, emotional neglect, and separation, as well as community violence (Figure 1). Being in the high-risk ACEs group compared to low risk, was significantly associated with worse scores for PROMIS anxiety ($p< 0.001$), depression ($p< 0.001$), and fatigue ($p< 0.001$), alongside poorer executive function scores ($p< 0.001$) (Figure 2). No significant associations were observed for disease activity ($p=0.263$).

Conclusion: Within our cSLE cohort, ACEs were substantially prevalent, with almost a third of patients having experienced ≥ 4 ACEs. The high risk group had significantly worse patient-reported outcomes and executive function. These results underscore the impact of ACEs on patient well-being, emphasizing the need for integrated medical and mental health care approaches. Future research should examine these associations in larger cohorts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient demographics, disease characteristics, and outcome measures (n=50)

Demographic Characteristics	cSLE Patients
Age in years, mean (SD)	15.2 (1.9)
Female, n (%)	42 (84)
Low-income families, n (%)	15 (30)
Race and Ethnicity, n (%)	
Asian	27 (54)
Black/African American	8 (16)
White	10 (20)
Other [a]	5 (10)
Self-Identified ACEs Presence (PEARLS), n (%)	
0 ACEs	14 (28)
1 - 3 ACEs	21 (42)
≥ 4 ACEs	15 (30)
Disease Characteristics	
Disease Duration in Years, median (IQR)	0.9 (0.6, 2.5)
Adjusted-mean SLEDAI-2K, median (IQR)	4.0 (2.4, 7.9)
Glucocorticoid use (ever), n (%)	37 (74)
Patient-Reported Outcome Measures (PROMIS-37), mean (SD)	
Fatigue [b]	50.0 (13.3)
Anxiety [b]	48.1 (11.2)
Depression [b]	47.8 (10.5)
Behavior Rating Inventory of Executive Function (BRIEF-2), mean (SD)	
Global Executive Composite [b]	54.3 (10.0)

Note.
[a] Other categories include Latin American (n=3) and multiethnic (n=2) race and ethnicities
[b] Measures are negatively-worded standardized t-scores with a normative mean of 50 and standard deviation of 10. A t-score of 60 indicates outcomes 1 SD worse than average.

Figure 1. Self-Reported Adverse Childhood Experiences (ACEs) in Patients with cSLE: Frequency and Types

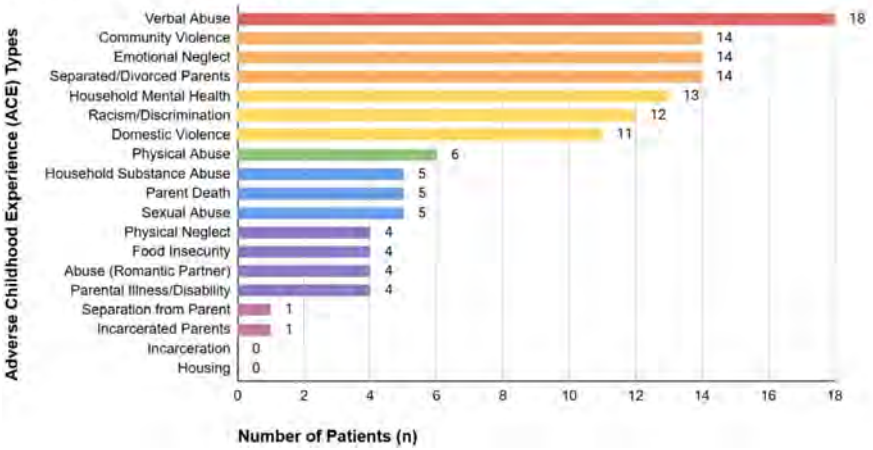


Figure 1 illustrates the distribution of nineteen self-reported adverse childhood experiences (ACEs) types within our cSLE cohort (n=50). Among the total ACEs (n=135) self-reported on the patient PEARLS questionnaire, the most commonly reported ACEs were caregiver verbal abuse (n=18), community violence (n=14), emotional neglect (n=14), and caregiver separation/divorce (n=14).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Relationship between ACEs and Self-Reported cSLE Outcomes

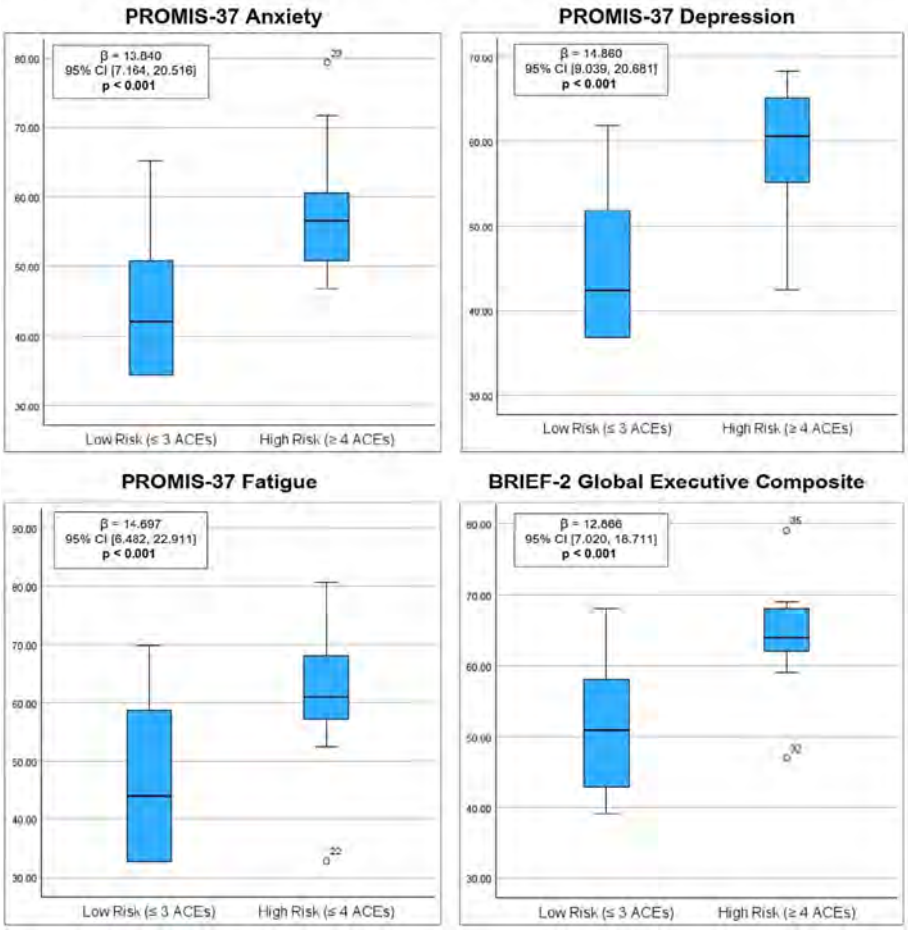


Figure 2 contains four sets of boxplots depicting differences in mean outcome scores between the high-risk and low-risk ACEs groups. Associations show beta coefficients, confidence intervals, and p-values from regression analyses. Regression analyses showed significant associations for worse PROMIS anxiety ($p<0.001$), depression ($p<0.001$), and fatigue ($p<0.001$) scores alongside poorer executive function ($p<0.001$) within the high-risk group. The p-value threshold used for significance was $p<0.05$.

Disclosure: J. Zhou: None; **S. Fevrier**: None; **P. Moaf**: None; **L. Ng**: None; **A. Jeyanathan**: None; **L. Boulard**: None; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **L. Hiraki**: Janssen, 2, 5; **A. Danguecan**: None; **A. Knight**: Pfizer, 6.

Abstract Number: 1291

Gastrointestinal Tract Involvement in Juvenile Systemic Sclerosis: Results from an International Scoping Review of Outcome Measures

Lauren Robinson[1], Lusine Ambartsumyan[2], Emily Willis[3], Aybuke Gunalp[4], Simone Appenzeller[5], Ozgur Kasapcopur[6], Sarah Ishaq[7], Natalia Vasquez Canizares[8] and Suzanne Li[9], [1]Hospital for Special Surgery, New York, NY, [2]Seattle Children's Hospital, Seattle, WA, [3]Royal Manchester Children's Hospital, Manchester, United Kingdom, [4]Cerrahpasa Medicine School, Cerrahpasa, Istanbul, Turkey, [5]Unicamp, Campinas, São Paulo, Brazil, [6]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey, [7]Osteopathic Medicine , Touro College of Osteopathic Medicine, New York, NY, [8]Children's Hospital at Montefiore, New York, NY, [9]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Gastrointestinal (GI) tract involvement is nearly universal in patients with systemic sclerosis (SSc) leading to significant morbidity and mortality. In a North American juvenile SSc (jSSc) registry, GI involvement had the strongest correlation with poorer quality of life (QoL) of any organ system. Esophageal dysmotility is the most common GI manifestation and can lead to moderate to severe malnutrition (identified in 14% of jSSc patients, Stevens et al, 2018). Despite the known prevalence and impact of GI tract pathology in SSc, validated outcomes measures are lacking. The International Juvenile Systemic Sclerosis Outcome Group is working to generate consensus organ-specific outcome measures for use in future jSSc studies. We report findings from our GI scoping literature review with a focus on esophageal measures.

Methods: From 4 databases, 24,849 studies were screened, yielding 277 studies identified by title and abstract of which 134 full text articles were extracted (Figure 1). Each level of screening and extraction required two reviewers. A pediatric gastroenterologist experienced in jSSc care helped guide extractions. Twenty-six GI measures were identified and sorted by GI

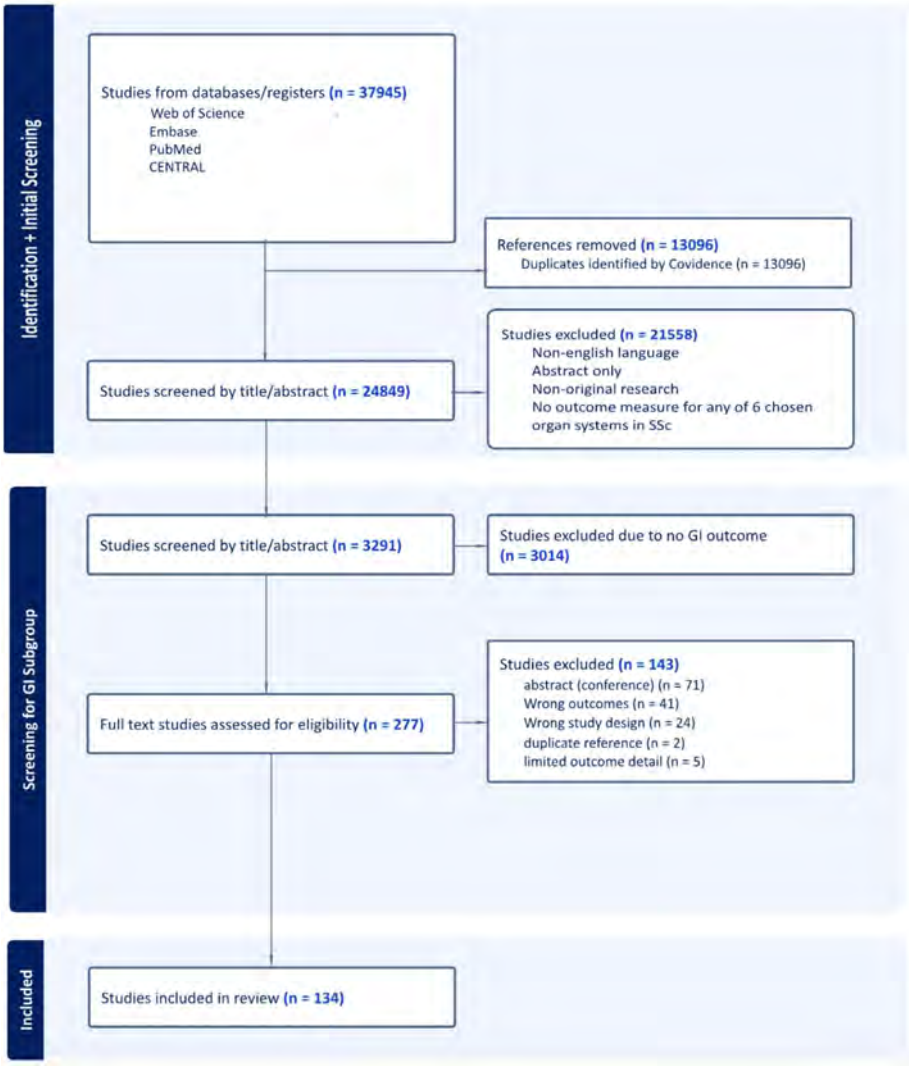


Figure 1: PRISMA systematic review flow diagram

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of SSc Studies on GI Outcome Measures from Scoping Review

Study Type	Number of Studies (%)
Randomized Controlled Trials	5 (3.7%)
Non-randomized/controlled interventional studies	3 (2.2%)
Observational	122 (91.0%)
- Case series	3
- Cohort	83
- Case-control	27
- Cross-sectional	9
Diagnostic test accuracy	4 (3.0%)
GI Region/Topic Studied	**N (%*)**
Oropharynx	10 (7.5%)
Esophagus	87 (64.9%)
Stomach	28 (20.9%)
Small Intestine	21 (15.7%)
Colorectum	27 (20.1%)
Nutrition	16 (11.9%)
GIT/QoL**	42 (31.3%)
Inclusion of juvenile SSc Subjects	**N (%)**
Yes	3 (2.2%)
No	131 (97.8%)

*many studies included more than one GI region/topic, percentages will total >100%
**GIT= UCLA Scleroderma Clinical Trials Consortium Gastrointestinal Tract instrument; QoL= Quality of Life

Table 2: Use and Performance of Esophageal Outcome Measures in SSc

Esophageal Measure		No. Studies using measure (No. included pediatric patients)	No. studies with intervention (No. with significant response to intervention)	No. longitudinal studies (No. with significant change over time)	No. studies with HC group (No. with significant difference SSc vs HC)	No. studies that compared measure to symptoms* (No. with significant symptom correlation)
anatomical	Chest CT (esophageal diameter)	9 (1)	0	1 (1)	0	1 (0)
	EndoFLIP	3 (0)	0	0	1 (1)	0
	Endoscopy	25 (0)	2 (0)	1 (0)	3 (2)	7 (3)
	Esophagram (UGI) / Barium Swallow	7 (1)	0	0	0	4 (1)
functional	Esophageal Manometry	50 (0)	3 (2)	0	12 (12)	13 (7)
	Esophageal Scintigraphy	14 (0)	2 (0)	2 (2)	7 (6)	6 (2)
	pH and/or pH/Impedance	13 (1)	1 (0)	0	3 (3)	1 (1)

No. = number, SSc = systemic sclerosis, HC = healthy control, CT = computerized tomography, EndoFLIP = Endoscopic functional lumen imaging probe, UGI = upper gastrointestinal series
*Including UCLA Scleroderma Clinical Trials Consortium Gastrointestinal Tract 2.0 Instrument (SSc specific GI symptom scale)

region studied. Extracted data included the presence of jSSc patients, significant change in the outcome measure over time or following intervention, ability of the measure to differentiate SSc from healthy controls (HC), and correlation of the measure with symptoms and QoL measures.

Results: Of 134 studies, only 3.7% were randomized control trials (total of 4 GI measures evaluated). Only 2.2% of the studies included pediatric patients. The most commonly studied GI region was the esophagus (64.9%) followed by stomach (20.9%), colorectum (20.1%), small intestine (15.7%), and oropharynx (7.5%). Nutritional outcomes were reported in 11.9% while QoL measures were included in 31.3% of studies (Table 1). Table 2 shows the characteristics of esophageal measures in SSc. 50/87 (57%) esophageal studies reported on esophageal manometry, with endoscopy the next most commonly reported esophageal measure (25/87, 29%). Esophageal manometry was accurately able to differentiate SSc from HC. Very few studies assessed change over time or in response to intervention. Only 4 of the 26 measures (15%) have been studied in jSSc (esophageal manometry, pH probe, chest CT and esophagram/Upper GI). In studies that evaluated the correlation between GI measures and GI symptoms, correlation was inconsistent.

Conclusion: Esophageal manometry is the most widely studied GI outcome measure in SSc. Despite its established use in children with other GI motility disorders (e.g., achalasia), there were no studies that evaluated esophageal manometry in patients with jSSc. Overall, only 2% of the studies included pediatric patients, and < 10% of studies evaluated the ability of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

GI outcome measures to assess response to intervention or change over time. Nearly all measures studied demonstrated inconsistent correlation with GI symptoms. Given the morbidity and impact on QoL associated with GI involvement, our study highlights the need for more studies that evaluate GI involvement in SSc, especially for jSSc.

Disclosure: L. Robinson: None; **L. Ambartsumyan**: None; **E. Willis**: None; **A. Gunalp**: None; **S. Appenzeller**: None; **O. Kasapcopur**: None; **S. Ishaq**: None; **N. Vasquez Canizares**: Boehringer Ingelheim, 2; **S. Li**: Boehringer-Ingelheim, 2, Merck/MSD, 12, Spouse was an employee and receiving pension from them.

Abstract Number: 1292

Childhood-onset Behçet's disease: HLA alleles role on diagnosis and treatment in a Latin American tertiary center

Matheus França[1], Thales Souza[2], Ricardo Machado[3], Vinicius Matias[4], Sylvia Farhat[3], Lia Steuer[3], Luisa Forero[3], Verena Balbi[3], Nadia Emi Aikawa[5], Katia Kozu[3], Clovis Artur Silva[6], Adriana Elias[7] and **Lucia Maria Campos**[8], [1]Instituto da Criança e do Adolescente, Hospital das Clinicas, University of Sao Paulo Medical School, Sao Paulo, Sao Paulo, Brazil, [2]Faculdade de Medicina da Universidade de Brasilia, Brasilia, Distrito Federal, Brazil, [3]Instituto da Criança e do Adolescente, Hospital das Clinicas, Sao Paulo, Sao Paulo, Brazil, [4]Faculdade de Ciências Medicas da Santa Casa de Sao Paulo, Sao Paulo, Sao Paulo, Brazil, [5]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [6]University of São Paulo, São Paulo, São Paulo, Brazil, [7]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas, University of Sao Paulo Medical School, São Paulo, São Paulo, Brazil, [8]Instituto da Criança e do Adolescente, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's disease (BD) is a rare pediatric vasculitis with limited epidemiological data in Latin America centers, especially in children where initial symptoms can be non-specific and disease progression may be protracted. The frequency of HLA-B51, which is associated with increased disease risk, is also lower compared with countries along the Silk-Road. It is possible that in Brazil, a country characterized by mixed population, other HLA alleles might contribute to BD susceptibility. The objective of the study was to identify the HLA alleles in childhood-onset BD patients and characterize clinical manifestations and therapies associated with them.

Methods: The study included 32 childhood-onset BD patients followed at a tertiary and university Pediatric Rheumatology Center in Brazil, diagnosed ≤ 18 years-old, based on expert pediatric rheumatologists' opinion and/or according to the international criteria for BD (ICBD) or the pediatric BD classification criteria (PEDBD). Medical records were reviewed to assess HLA alleles, clinical and therapeutic characteristics of these patients. For further analyses patients were classified according to the presence or absence of HLA-B51 and the groups were compared regarding demographic data, clinical characteristics and treatment.

Results: Demographic data of 32 childhood-onset BD patients were: median age of 4.5(0.5-12) years at diagnosis, female sex in 16(50%) and white ethnicity in 25(78%) of cases. HLA-B51 allele was identified in 16 of 32 patients (50%). Other HLA alleles were found as following: HLA-B15 (n=8), HLA-B35 (n=6), HLA-B42 (n=3), HLA-B53 (n=3), HLA-B39 (n=2), HLA-B58 (n=1), HLA-B57 (n=1), HLA-B52 (n=1) and HLA-B14 (n=1). The presence of other HLA alleles was significantly higher in patients with negative HLA-B51 compared to patients with positive HLA-B51 (75% vs. 38%, p=0.04). HLA-B51 negative

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients were significantly older than HLA-B51 positive patients [7.5 (0.5–12) vs. 3 (0.5–11) years; p=0.02] at diagnosis, in contrast to female sex that was less frequent in the former group (31% vs. 69%, p=0.04). The frequency of patients that fulfilled at least one confirmation criteria (PEDBD and/or ICBD) was similar between groups (57% vs. 44%, p=0.72). Likewise, no differences were observed between the groups regarding clinical manifestations, including fever, oral/genital ulcers, articular, cutaneous, ocular, neurological and gastrointestinal involvement. Further analysis of treatment showed that colchicine use was also similar in both groups (94% vs. 98%, p=0.5). However, HLA-B51 negative patients significantly required the use of additional immunosuppressants agents (60% vs. 23%, p=0.05), especially corticosteroids (56% vs. 19%, p=0.03) and azathioprine (69% vs. 19%, p=0.006).

Conclusion: Patients who were negative for HLA-B51 but positive for other HLA alleles were diagnosed at a later stage and required multiple immunosuppressive therapy. These results indicate that in patients outside the Silk Road, other HLA alleles may be associated with BD and could lead to a delayed diagnosis.

Disclosure: M. França: None; **T. Souza**: None; **R. Machado**: None; **V. Matias**: None; **S. Farhat**: None; **L. Steuer**: None; **L. Forero**: None; **V. Balbi**: None; **N. Aikawa**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **K. Kozu**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **A. Elias**: None; **L. Campos**: None.

Abstract Number: 1293

Synovitis and periarticular soft tissues abnormalities in childhood-onset systemic lupus erythematosus: an ultrasonography study

Marianna Freire[1], Jean Paulo Veronese de Souza[1], Ana Renata Oliveira[1], Renata Kobayasi[2], Vitor Paula[3], Clovis Artur Silva[4] and **Lucia Maria Campos**[5], [1]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clínicas HCFMUSP, São Paulo, Sao Paulo, Sao Paulo, Brazil, [2]Centro de Desenvolvimento de Educação Médica do Hospital das Clínicas HCFMUSP, São Paulo, Sao Paulo, Sao Paulo, Brazil, [3]Pediatric Radiology Unit, Instituto da Criança e do Adolescente, Hospital das Clínicas HCFMUSP, São Paulo, Sao Paulo, Sao Paulo, Brazil, [4]University of São Paulo, São Paulo, São Paulo, Brazil, [5]Instituto da Criança e do Adolescente, São Paulo, São Paulo, Brazil

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal (MSK) involvement occurs in up to 70% of childhood-onset systemic lupus erythematosus (cSLE). MSK ultrasound (US) has emerged as a tool with greater sensitivity than clinical examination for detecting MSK abnormalities in adult SLE. To date, rare case reports and case series have assessed MSK US in cSLE populations, including small sample sizes, limited anatomical scope or restricted to nondominant side evaluations. Therefore, the objectives of this study were to assess MSK US findings in cSLE patients and healthy controls, focusing on joints, tendons, and entheses sites. We also evaluate demographic, clinical, laboratory and treatment parameters in MKS clinically symptomatic compared to asymptomatic cSLE patients.

Methods: A cross-sectional study was performed in a tertiary and university center, evaluating 63 consecutive cSLE patients(ACR1997 and SLICC 2012 criteria) and 20 healthy controls. US evaluations were performed by two experienced sonographers, assessing 36 MSK structures/participant, including 20 joints, 8 tendons, and 8 entheses (Logic 7-GE-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Milwaukee, Wisconsin, USA). ML6-15 MHz and hockey stick L8-18i-D MHz linear array probes were used for images on dominant and nondominant subject sides. MSK US abnormalities were defined according to OMERACT criteria. Patients' records were reviewed for demographic, clinical, laboratory, and therapeutic data.

Results: Median age[14.6(13-16) *vs*. 13(11-16)years, p=0.099] and female sex(73% *vs*. 55%, p=0.902) were similar in cSLE patients and heathy controls. MKS US abnormalities were significantly higher in cSLE compared to controls(79.4% *vs*. 5%, p< 0.001), likewise synovitis(34.9% *vs*. 5%, p=0.009), tenosynovitis(66.7% *vs*. 0%, p< 0.001) and enthesitis(28.6% *vs*. 0%, p=0.004). The most frequent MKS US findings in cSLE patients were knee synovitis(14.3%), wrist extensor tenosynovitis(17.4%), fibular tenosynovitis (20.6%) and quadriceps enthesitis(18.2%). Further analyses of MSK US findings showed significantly higher frequency of enthesitis(50% *vs*. 15.4%, p=0.003) in clinically symptomatic compared to asymptomatic cSLE. The frequencies of any MSK US abnormalities(87.5% *vs*. 74.4%, p=0.337), synovitis(41.7% *vs*. 30.8%, p=0.378), and tenosynovitis(75% *vs*. 61.5%, p=0.271) were alike in clinically symptomatic compared to asymptomatic cSLE patients. No differences were observed between the groups regarding demographic data, SLEDAI-2K, antiphospholipid antibodies, cumulative dose of glucocorticoid and immunosuppressive use (p >0.05).

Conclusion: Our findings demonstrate a high frequency of MSK US abnormalities in cSLE, particularly involving periarticular soft tissues. Subclinical involvement highlights the utility of ultrasound in the early detection of silent abnormalities, which may be important for the diagnosis of both inflammation and structural damage, monitoring and management of cSLE. Further longitudinal studies are necessary to assess the potential of MSK US in predicting disease progression and its impact on treatment decisions.

Disclosure: M. Freire: None; **J. Veronese de Souza**: None; **A. Oliveira**: None; **R. Kobayasi**: None; **V. Paula**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Campos**: None.

Abstract Number: 1294

Implementation of Pneumococcal Vaccination in Patients with Childhood-Onset Systemic Lupus Erythematous

Kristina Ciaglia[1] and **Magan Fosso**[2], [1]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [2]UT Southwestern, Dallas, TX

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Pneumococcal vaccination is critical in patients with childhood-onset systemic lupus erythematosus (cSLE) due to their immunocompromised status and increased susceptibility to serious infections. Despite this, our institution's baseline vaccination rate was 0%. Inadequate documentation compromises patient safety, continuity of care, and may reflect missed vaccination opportunities. A limited on-site vaccine supply further challenged timely administration and follow-up. Our goal was to increase pneumococcal vaccination documentation rates in cSLE patients from 0% to 70% over a 12-month period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective chart review of cSLE patients seen between February and June 2024. To improve documentation and vaccine delivery, we initiated a Plan-Do-Study-Act (PDSA) cycle. Interventions included the development of a standardized documentation template within the electronic health record (EHR), collaboration with key stakeholders (including clinicians, analysts, and nursing staff), and integration of a consistent vaccination process within our rheumatology clinic.

Results: Fifty pediatric patients with cSLE were included in the initial chart review. Of these, 16 had previously received pneumococcal vaccination, but only 2 had appropriate documentation in the EHR. Following implementation of a standardized documentation process, 59 additional patients were identified with non-protective pneumococcal antibody titers. Among these, 8 patients received appropriate vaccination at Scottish Rite: 6 were vaccinated during their clinic visit, and 2 had received the vaccine within 12 months prior. Our clinic vaccination rate went from a baseline of 0% to 13.5% improvement.

Conclusion: Establishing a clear and structured documentation process significantly enhanced the rate of pneumococcal vaccination and documentation in cSLE patients. Accessible, standardized records improved coordination of care and reduced missed opportunities for immunization. On-site vaccine availability also contributed to improved patient follow-through. Continued PDSA cycles, staff feedback, and outcome monitoring will be essential to sustain and expand these improvements.

Disclosure: K. Ciaglia: None; **M. Fosso**: None.

Abstract Number: 1295

Neuropsychiatric Lupus in Children and Adolescents: Understanding Current Practices and Barriers to Care Perceived by Pediatric Rheumatology Clinicians in North America

Martha Rodriguez[1], Ekemini Ogbu[2], Ashley Danguecan[3], Marietta De Guzman[4], Alexandra Theisen[5], Lawrence Ng[6], Andrea Knight[3], Ryann Kammeyer[7] and CARRA NPSLE Workgroup, [1]Riley Hospital For Children at Indiana University, Indianapolis, IN, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Hospital for Sick Children, Toronto, ON, Canada, [4]Baylor College of Medicine, Houston, TX, [5]University of Arkansas, Little Rock, AR, [6]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [7]University of Colorado, Denver, CO

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Neuropsychiatric involvement in Systemic Lupus Erythematosus (NPSLE) is a major cause of morbidity and mortality, particularly among children who are still developing neurologically. Despite this high burden of NPSLE in children it is arguably the least understood manifestation of SLE. Additionally, the care needs of children with NPSLE are complex, requiring multidisciplinary services with varying levels of accessibility. We aimed to understand the current practice of care for evaluation of NPSLE in children, and barriers in accessing multidisciplinary care.

Methods: An electronic survey was conducted among members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) from July to November 2024. It was designed by the CARRA Neuropsychiatric SLE Workgroup, which includes pediatric rheumatologists, neurologists, psychiatrists, psychologists, patients, and caregivers. Eligible participants included physicians, nurse practitioners, and physician assistants who actively care for children with SLE. We collected information on demographics, serum biomarkers, neuroimaging, availability of multidisciplinary support services and barriers to care for patients with NPSLE (15 barriers rated on 5-point Likert scale)

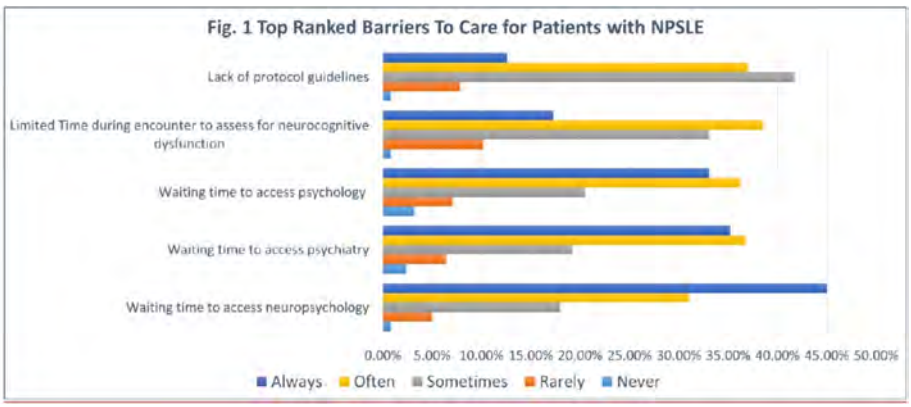
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table I. Current Practice of care for evaluation of NPSLE in children by CARRA Members: Neuroimaging, Neurocognitive Assessment and Mood Screening.

Diagnostic test	N (%)
Neuroimaging	**55 (41%)**
Brain MRI, MRA, MRV w/ and w/o contrast	60 (46%)
Brain MRI w/ and w/o contrast	56 (43%)
Brain MRI w/ and w/o contrast and MRA w/ and w/o contrast	38 (29%)
Brain MRI w/o contrast	4 (3%)
Advanced Neuroimaging	**29 (22%)**
Brain Single-photon emission computer tomography (SPECT)	14 (47%)
Brain Magnetic resonance spectroscopy(MRS)	11(37%)
Brain Positron emission topography (PET)	7 (23%)
Brain Function MRI (fMRI)	5 (17%)
Neurocognitive Assessment	**29 (22%)**
Tests selected by neuropsychologist performing the assessment	95 (73%)
Unsure what is used at their institution	26 (20%)
Mini Mental Status Exam (MMSE)	18 (14%)
Montreal Cognitive Assessment (MOCA)	12 (9%)
Pediatric Automated Neuropsychological Assessment Metrics (Ped-ANAM)	12 (9%)
No access to neurocognitive test	6 (5%)
Mood Disorder Screening	**75 (57%)**
Depression screening	
Patient Health Questionnaire-9 for Depression	66 (50%)
Informal depression screening (screening symptoms of depression)	49 (37%)
I do not formally screen for depression in my practice	24 (18%)
PROMIS Depression Short Form	8 (6%)

Magnetic Resonance Imaging (MRI), Patient-Reported Outcomes Measurement Information System (PROMIS)

Results: Of the 512 eligible respondents, 149 (29%) completed the survey. The findings revealed that only 5% of respondents felt completely confident in evaluating NPSLE on a 5-point Likert scale. The majority (90%) routinely test for antiphospholipid antibodies during the initial evaluation, while fewer test for anti-ribosomal P (46%), anti-neuronal antibodies (18%), aquaporin-4 antibodies (10%), and antiganglioside antibodies (4%). Among those who responded, 19% obtain cerebrospinal fluid (CSF) analysis for all patients with suspected NPSLE, and 41% use neuroimaging. The most common neuroimaging modality was brain MRI, MRV, and MRA with or without contrast (46%), followed by brain MRI with or without contrast (43%). Only 22% of responders use advanced neuroimaging, 31% lack access to advanced imaging at their institution, and 52% were not familiar with the appropriate indications or interpretation of these imaging modalities. Furthermore, 57% screen for mood disorders in all NPSLE patients (Table I). Only 7% of providers have easy access to neuropsychology, and 10% to psychiatry. Waiting time to access neuropsychology, psychiatry and lack of protocol or guidelines were the most common perceived barriers for the evaluation of NPSLE.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study highlights significant variability in current practices for evaluating NPSLE in children, underscoring the need for consensus guidelines to standardize NPSLE evaluation and management Improving timely access to neuropsychology and psychiatry services is essential for proper diagnosis and treatment of NPSLE. Given that these services are often very limited, providing training to rheumatology clinicians on less resource-intensive alternatives (e.g Ped-ANAM validated computerized screening neurocognitive battery or questionnaires) may assist in triaging priority patients for multidisciplinary assessment.

Disclosure: M. Rodriguez: None; **E. Ogbu**: Cartesian Therapeutics, 2; **A. Danguecan**: None; **M. De Guzman**: None; **A. Theisen**: None; **L. Ng**: None; **A. Knight**: Pfizer, 6; **R. Kammeyer**: None.

Abstract Number: 1296

Liver Biopsy Findings in Pediatric SLE: A Large Tertiary Center Experience

Meredith Rae[1], Dawn Gist[2], Kaylani Patel[3], Krupa Mysore[3], Andrea Ramirez[2], Marietta De Guzman[2] and Eyal Muscal[2], [1]Baylor College of Medicine/Texas Children's Hospital, Houston, TX, [2]Baylor College of Medicine, Houston, TX, [3]Baylor College of Medicine/Texas Children's Hospital, Houston

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Distinguishing lupus hepatitis (LH) from autoimmune hepatitis (AIH) in SLE is clinically challenging but critical for guiding treatment duration. The mechanisms differ; AIH results from a T-cell-mediated immune response to liver autoantigens, while LH likely results from hepatic vasculitis, complement activation, and rarely, microvascular occlusive disease.

On biopsy, AIH is characterized by lymphoplasmacytic interface hepatitis and hepatocyte rosettes; LH presents with nonspecific mild lobular or periportal inflammation. Systematic histopathologic studies differentiating AIH and LH in pediatric SLE are lacking.

Methods: With IRB approval, we queried our EMR (1/1/12–3/1/25) for pediatric SLE patients who underwent liver biopsy. Clinical, laboratory and histopathology data were abstracted. Disease activity at biopsy was assessed using the SLEDAI-2K.

Results: During the study period, of the 452 patients with SLE, 12 (2.7%) underwent liver biopsy. In three, liver disease predated SLE diagnosis; biopsies (median six months prior to diagnosis; range 6–32) revealed two AIH and one Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) later diagnosed as possible AIH on repeat biopsy. In the other nine patients, biopsies occurred at a median of one month post diagnosis with SLE (range 0-37). All were performed at least in part to exclude AIH.

One patient diagnosed with AIH before SLE was F-actin IgG positive; the other tested negative for F-actin and anti-LKM. Six out of the nine patients who had negative biopsy findings for AIH were positive for either F-actin, anti-Smooth muscle IgG, or anti-LKM Ab. These patients with positive AIH-associated antibodies but negative biopsy had been pre-treated for a median of one week (range three days-seven months). One patient had three serial liver biopsies, one prior to diagnosis and two after to evaluate for AIH. Peak AST was 211 U/L (range 50-1138) and ALT was 206 U/L (107-1111). Of the nine patients with liver biopsies after diagnosis of SLE, one had AIH, one had MASLD, three had possible drug-related injury (secondary to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics (n=12)

Demographics	*n (%)*
Female	10 (83%)
Hispanic/Latino	6 (50%)
White (non-Hispanic/Latino)	3 (25%)
Black	2 (17%)
Asian	1 (8%)
Clinical features	
Hematologic involvement	9 (75%)
Arthritis	8 (67%)
Mucocutaneous involvement	7 (58%)
Renal involvement	6 (50%)
Antiphospholipid antibody syndrome	5 (42%)
MAS/HLH	2 (17%)
CNS disease	1 (8%)
	Median (range)
SLEDAI score at biopsy (n=9 patients diagnosed with SLE prior to biopsy)	12 (2–20)
Age (years)	13 (9-18)

antibiotics, sertraline, and acetaminophen), and four had nonspecific findings postulated to be SLE-related. Among the four patients with nonspecific findings, all showed mild portal inflammation with infiltrates including plasma cells, lymphocytes, and/or neutrophils. One had mild focal venulitis, one had grade 1 fibrosis, and one had mild hepatocyte ballooning. All had preserved synthetic function.

Of the patients with AIH, two were already on azathioprine and prednisone (15–30 mg) at the time of biopsy and remained on the same regimen; one was initiated on azathioprine and prednisone (2 mg/kg), and another with concurrent lupus nephritis and AIH was started on mycophenolate. Nonspecific biopsy findings did not alter management. At median follow-up of six years (range 0.2–9), none had persistent clinically evident liver disease.

Conclusion: Despite a cohort with active SLE with multi-organ involvement, lupus-related liver manifestations were transient and self-limited. Liver biopsy remains crucial in diagnosis of comorbid AIH since AIH-related autoantibodies were variably detected and may be unreliable in active SLE.

Disclosure: M. Rae: None; **D. Gist**: None; **K. Patel**: None; **K. Mysore**: None; **A. Ramirez**: None; **M. De Guzman**: None; **E. Muscal**: sobi, 1.

Abstract Number: 1297

Biologic Therapy for Refractory Juvenile Scleroderma: a retrospective case-series from a single tertiary care center in Saudi Arabia.

MUNIRA ALMARRI, Deena Alwakeel, Abdulaziz Alrowais and Abdulrahman Asiri, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline demographics and disease characteristics of patients with scleroderma

Patient no.	Age at the disease onset	Age at diagnosis	Sex	Symptoms at onset	Diagnosis	Auto antibodies	Other medications	Age at the initiation of biological treatment	Biological agents dose/Route	Complication and progression at F/U
1	11 yrs 6 mos	12 yrs	M	Diffuse Skin thickening Arthritis Myositis	Systemic sclerderma (Diffuse Sclerderma)	-U1RNP -RNP ANA1/640 -SCL70 -ker	Steriod IVIG MMF Aspirin Amlodipin HCQ	12yrs 6 mos	TCZ 8 mg/kg IV	Raynaud's phenomenon Skin ulcers Enthesitis ILD
2	9 yrs 6 mos	10 yrs	M	Diffuse skin thickening	Systemic sclerderma (Diffuse sclerderma)	ANA 1/5120	Steriod Methotrexate MMF Nifidipin	10yrs 6 mos	TCZ 10 mg/kg IV	Raynaud's phenomenon ILD
3	8 yrs 6 mos	9 yrs	F	Fatigability weight loss Raynauds phenomena muscle pain Skin tightness SOB	Systemic sclerderma (Diffuse Sclerderma)	ANA 1/320 Anti scl75	Steriod IVIG MMF	10 yrs	TCZ 162mg SC every other week	ILD Resolved HTN
4	5 yrs	6 yrs	F	Localized linear lesion in tip of the nose and philtrum	Localized scleroderma	ANA 1/80	Steriod Methotrexate	9 yrs	TCZ 10mg/kg IV	None
5	8 yrs 6 mos	9 yrs	M	Generilaized scleroderma Linear LT LL Left wrist tightness Muscle atrophy Hypopigmented lesion in chest & back	Localized scleroderma (Generilaezd scleroderma)	ANA 1/80	Meilnotrexate	9 yrs 6 mos	TCZ 12 mg/kg IV	Subcutaneous atrophy Joint contraction
6	6 yrs 6 mos	7 yrs	F	Linear lesion of the right side (upper limb lower limb and back) and lower abdomen.	Localized scleroderma (linear scleroderma)	ANA 1/80	Steriod Topical Calcineurin inhibitor Methotrexate MMF	7 5 yrs 6 mos 12 yrs 4 mos	TCZ 10 mg/kg IV TFC 5mg PO BID	Relapse Subcutaneous hyperpigmentation and atrophy
7	11 yrs 6 mos	12 yrs	M	Shiny tight skin in UL & LL & trunk	Localized scleroderma (Generilaezd scleroderma)		Steriod Methotrexate MMF	11 yrs 3 mos	TCZ 8 mg /kg IV	sclerodactyly Joint contraction At elbows wrists, knees & ankles

Background/Purpose: Scleroderma is autoimmune disease that may result in changes to the skin, blood vessels, muscles, and internal organs. It can be either Localized Scleroderma (LS) or Systemic Sclerosis (SSc). Early diagnosis, proper assessment and effective treatment are crucial to improve the long-term outcome.

Tocilizumab, an IL-6 receptor antagonist, and tofacitinib, a JAK inhibitor, have shown promising results in small series and case reports, but pediatric data remain limited.

Table 2: Main outcome measures at the time point of 0, 6th and 12th months of juvenile systemic sclerosis patients treated with tocilizumab.

Patient no.	TCZ treatment duration (months)	Radiological improvement on thorax HRCT at 12th month	DLCO (%) at 0/6/12th month of TCZ treatment	FVC (%) at 0/6/12th month of TCZ treatment	mRSS at 0/6/12th month of TCZ treatment	PGA at 0/6/12th month of TCZ treatment	J4S at 0/6/12th month of TCZ treatment
1	20	+	46/54/71	45/50/72	27/16/12	5/4/3	10/8/5
2	24	+	52/72/78	69/70/74	34/17/8	5/3/2	10/6/3
3	34	+	43/56/76	48/54/72	39/34/23	5/5/3	10/6/5

Table 3: Main outcome measures at the time point of 0, 6th and 12th months of juvenile localized scleroderma patients treated with tocilizumab.

Patient no.	TCZ treatment duration (months)	PGA-A 0/6/12th Months of TCZ treatment	PGA-D 0/6/12th Months of TCZ treatment	LoSSI 0/6/12th Months of TCZ treatment	LoSDI 0/6/12th Months of TCZ treatment
4	22	6/3/1	5/3/2	5/2/1	7/5/4
5	21	5/4/2	5/4/4	38/7/3	17/16/12
6	48	8/4/2	8/6/6	32/8/3	37/27/28
7	7	9/4/NA	8/4/NA	46/8/NA	26/20/NA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 4: Main outcome measures at the time point of 0, 6th and 12th months of juvenile localized scleroderma patients treated with Tofacitinib

Patient no.	TFC treatment duration (months)	PGA-A 0/6/12th Months of TFC treatment	PGA-D 0/6/12th Months of TFC treatment	LoSSI 0/6/12th Months of TFC treatment	LoSDI 0/6/12th Months of TFC treatment
6	12	6/3/1	5/3/3	7/3/1	7/5/4

The current analysis was conducted from a single center in Saudi Arabia to investigate the long-term efficacy and safety of tocilizumab (TCZ) and tofacitinib (TFC) in patients with SSc and LS.

Methods: We conducted a retrospective chart review of pediatric patients diagnosed with LS or SSc who received TCZ or TFC in a single center at Prince Sultan Military Medical City in Saudi Arabia. Overall, seven patients were included in the study (3 Females and 4 Males with a mean age of 9 years (range 6-12 years).

The modified Rodnan skin score (mRSS), carbon-monoxide diffusion capacity (DLCO), thorax high-resolution tomography (HRCT), patient global assessment (PGA), and Juvenile Systemic Sclerosis Severity (J4S) score were used in patients with SSc as endpoints.

The Localized Scleroderma Cutaneous Assessment Tool (LoSCAT) and physician global assessment of activity and damage (PGA-A and PGA-D) were used in patients with localized scleroderma as endpoints to evaluate TCZ and TFC treatment response at 12 months post-treatment.

Results: Seven children with scleroderma were treated with TCZ, in addition to conventional treatment. The median age at the disease onset is 8.5 years (5–11.5) and at the diagnosis is 9 years (6-12).

Three JSS patients with interstitial lung disease were treated with TCZ with a median treatment duration of 19 (14-24) months. All three patients had radiologically confirmed improvement in thorax HRCT at 12 months post-treatment. They had decreased PGA (mean pre-treatment PGA 5 vs. 2.6 post-treatment PGA at 12 months). They had increased DLCO (mean pre-treatment DLCO 47% vs.12 months post-treatment DLCO 72.6% after the TCZ treatment). In all patients, mRSS and the J4S decreased: 33.3 vs. 14.3 and 10 vs. 4.3, respectively.

Three LS patients were treated with TCZ with a median treatment duration of 22 (6 -48) months. They had decreased PGA-A and PGA-D, with mean pre-treatment PGA-A 7 vs 1.7 in 12 months post-treatment, while the mean pre-treatment PGA-D 6.5 vs 4 in 12 months post-treatment. They had also decreased in LoSSI and LoSDI: 25 vs 2.5 and 21.5 vs 14.7, respectively.

One patient with refractory LS was escalated to TFC (5 mg BID) after a partial response to TCZ. She had decreased PGA-A and PGA-D:
pre-treatment 6 vs 1 and 5 vs 3 in 6 months post-treatment, respectively. She had also reduced LoSSI and LoSDI: 7 vs 1 and 7 vs 4, respectively.

TCZ and TFC treatment are tolerated without side effects.

Conclusion: This case series highlights the promising role of Tocilizumab as a therapeutic option in managing refractory pediatric scleroderma in both LS and SSc. Tofacitinib demonstrated also additional benefit in controlling refractory Localized Scleroderma . Long-term studies with a larger number of patients are needed to provide more relevant data.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. ALMARRI: None; **D. Alwakeel**: None; **A. Alrowais**: None; **A. Asiri**: None.

Abstract Number: 1298

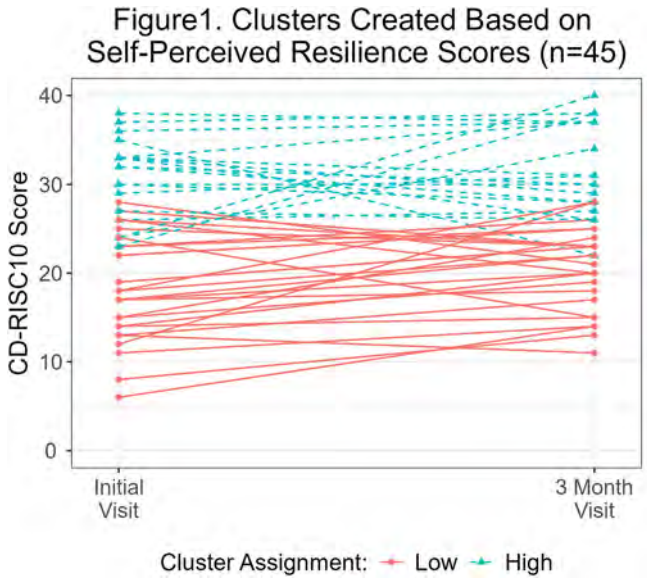
Identifying Psychosocial Profiles in Youth with Chronic Musculoskeletal Pain: A K-Means Clustering Analysis of Resilience Subgroups

Sabrina Gmuca[1], Jan Leonard[2], Alexis Z. Tomlinson[2], Mackenzie McGill[2], **Nellie Butler**[2], Rui Xiao[3], Peter F. Cronholm[3], Tonya M. Palermo[4], Jami F. Young[5], Abby R. Rosenberg[6] and Pamela Weiss[7], [1]Children's Hospital of Philadelphia; University of Pennsylvania, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Washington School of Medicine; Seattle Children's Research Institute, Seattle, [5]Children's Hospital of Philadelphia; University of Pennsylvania, Philadelphia, [6]Dana-Farber Cancer Institute; Boston Children's Hospital; Harvard Medical School, Boston, [7]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Psychological resilience is low among youth with chronic musculoskeletal pain (CMP) at baseline. We aimed to explore resilience profiles among youth with CMP during the first 3-months after the initial clinic visit and their associations with baseline demographics and clinical characteristics as well as changes in psychosocial outcomes over this interval.

Methods: This was a prospective survey study for youth 12-17 years with CMP. Psychological counseling, and physical and occupational therapy were recommended to all youths. Youth completed electronic surveys, including demographics and self-reported psychosocial factors (resilience, benefit finding, hope, mindfulness, pain catastrophizing, self-efficacy, and pain acceptance) at baseline and 3-months. Abstracted baseline data included clinical characteristics and Patient-Reported Outcomes Measurement Information System (PROMIS) measures (fatigue, peer-relationships, and pain interference). Resilience was measured via the Connor-Davidson Resilience Scale 10-item (CD-RISC-10); scores range 0-40 with higher scores



CD-RISC-10= Connor-Davidson Resilience Scale 10-item (range 0-40) with higher scores indicating greater self-perceived psychological resilience.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographics and Clinical Characteristics of Youth with CMP by Cluster

Variable	Overall N = 45[1]	Cluster: Low Resilience n = 27[1]	Cluster: High Resilience n = 18[1]	P-value[2]
Age (Years)				0.87
12	1 (2%)	1 (4%)	0 (0%)	
13	5 (11%)	4 (15%)	1 (6%)	
14	10 (22%)	6 (22%)	4 (22%)	
15	11 (24%)	5 (19%)	6 (33%)	
16	13 (29%)	8 (30%)	5 (28%)	
17	5 (11%)	3 (11%)	2 (11%)	
Race				0.57
Asian	1 (2%)	0 (0%)	1 (6%)	
Black or African American	3 (7%)	1 (4%)	2 (11%)	
White	35 (78%)	22 (81%)	13 (72%)	
More Than One Race	6 (13%)	4 (15%)	2 (11%)	
Ethnicity				0.19
Hispanic or Latino	4 (9%)	4 (15%)	0 (0%)	
NOT Hispanic or Latino	40 (89%)	22 (81%)	18 (100%)	
Prefer not to answer	1 (2%)	1 (4%)	0 (0%)	
Biological Sex				>0.99
Female	39 (87%)	24 (89%)	15 (83%)	
History of Individual Counseling	31 (69%)	23 (85%)	8 (44%)	**0.004**
Currently in Counseling	28 (62%)	21 (78%)	7 (39%)	**0.008**
Currently in Physical Therapy	19 (42%)	13 (48%)	6 (33%)	0.32
Juvenile Fibromyalgia criteria met	25 (56%)	17 (63%)	8 (44%)	0.22
PROMIS Fatigue	64.5 (59.8, 74.0)	69.0 (61.5, 79.0)	60.0 (55.0, 68.0)	**0.010**
PROMIS Peer Relationships	43.5 (39.3, 56.5)	41.0 (37.0, 46.0)	54.0 (43.5, 65.0)	**0.012**
PROMIS Pain Interference	61.4 (51.9, 66.9)	64.1 (61.4, 69.0)	51.6 (45.1, 60.2)	**<0.001**
Verbal Pain Intensity (0-10)	6.0 (4.0, 7.0)	7.0 (6.0, 8.0)	4.5 (3.0, 6.0)	**0.005**
Prior Use of Wheelchair	13 (29%)	11 (41%)	2 (11%)	**0.032**
Psychiatric History[3]				
Anxiety/panic attacks	36 (80%)	24 (89%)	12 (67%)	0.13
Depression	22 (49%)	17 (63%)	5 (28%)	**0.021**
Suicidal	7 (16%)	6 (22%)	1 (6%)	0.22
OCD	7 (16%)	7 (26%)	0 (0%)	**0.031**
Non-suicidal self-injury/cutting	7 (16%)	6 (22%)	1 (6%)	0.22
Suicidality				0.20
Ideation without intent	13 (29%)	8 (30%)	5 (28%)	
Ideation with intent	2 (4%)	2 (7%)	0 (0%)	
Attempt(s)	4 (9%)	4 (15%)	0 (0%)	
None	26 (58%)	13 (48%)	13 (72%)	

[1]n (%); Median (IQR)
[2]Fisher's exact test; Pearson's Chi-squared test; Wilcoxon rank sum test.
PROMIS (Patient-reported outcomes measurement information system) fatigue missing for n=1 and PROMIS peer relationships missing for n=3

indicating greater resilience. The primary outcome was the longitudinal resilience profiles based on CD-RISC-10 scores at baseline and 3-months identified by K-means clustering, an unsupervised machine learning method and a non-hierarchical cluster analysis technique. We examined differences in baseline demographics, clinical characteristics, and PROMIS measures between clusters using Fisher's exact, Pearson's Chi-squared and Wilcoxon rank sum tests, as appropriate. We also

Table 2. Average Within Person Change for Psychosocial Factors at 3-month Follow-up by Resilience Cluster (n=45)

Variable	Overall N = 45[1]	Cluster: Low Resilience n = 27[1]	Cluster: High Resilience n = 18[1]	P-value[2]
Change in CD-RISC10 Score	1.8 (6.1)	2.4 (5.4)	0.8 (7.1)	0.41
Change in Benefit Finding	-0.8 (11.5)	-2.0 (10.7)	1.1 (12.7)	0.40
Change in Hope Scale	1.9 (5.7)	2.1 (5.0)	1.6 (6.7)	0.77
Change in CAMM	1.0 (-1.0, 5.0)	2.0 (-1.0, 4.5)	0.0 (-0.8, 4.3)	0.90
Change in PSES-C	-2.0 (-5.0, 0.0)	-1.0 (-4.0, 1.5)	-3.5 (-8.5, -1.3)	**0.018**
Change in PCS Total Score	-4.2 (10.1)	-3.6 (11.1)	-5.2 (8.8)	0.59
Change in Pain Acceptance	-0.3 (4.5)	0.9 (4.1)	-2.1 (4.5)	**0.031**

Widespread pain index and symptom severity scale score according to the 2010 American College of Rheumatology criteria for fibromyalgia syndrome (Ting VT et al, 2016). Connor-Davidson Resilience Scale 10-item (CD-RISC-10) range 0-40, with higher scores indicating greater resilience. BFSC= Benefit Finding Scale for Children. PCS-C= Pain Catastrophizing Scale, Child report. CHS=Children's Hope Scale. CAMM= The Children and Adolescent Mindfulness Measure. CPAQ-A8= The Chronic Pain Acceptance Questionnaire Adolescent Short Form 8 item. PSES-C=The Pain Self-Efficacy Scale Child. K6= Kessler-6 Psychological Distress Scale.
[1]Median (IQR); Mean (SD)
[2]Wilcoxon rank sum test; Welch Two Sample t-test
*Differences were calculated as the 3-month score minus the initial score. A positive difference indicates the score increased between the initial and 3-month visit, whereas a negative score means the initial score was a higher number than the 3-month score. For all measures, other than PSES-C, higher scores indicate more of the construct.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

explored average within-person changes in psychosocial factors from baseline to follow-up (3-month score minus the initial score) based on cluster.

Results: 45 youths completed the surveys. Median age was 15 (IQR: 14-16) and 87% were female. The number of clusters ranged from 1:5. Based on a within-cluster-sum-of-squares scree plot, the optimal number of clusters was k-2: high (n=18) and low (n=27) resilience clusters (Fig.1). Age, race, ethnicity, and sex were not significantly different between clusters, but those in the low resilience cluster were more likely to have prior and current receipt of counseling (both $p< 0.01$; Table 1). The low resilience cluster had greater self-reported depression and obsessive-compulsive disorder (both $p< 0.05$). The low resilience cluster had worse fatigue, peer relationships, pain interference, and pain intensity at baseline (all $p< 0.05$; Table 1). Within person changes in psychosocial factors from baseline to 3-month follow-up differed by cluster. The high resilience cluster had increased pain self-efficacy but decreased pain acceptance (both $p< 0.05$; Table 2).

Conclusion: We identified 2 resilience clusters among youth with CMP. Those with lower resilience demonstrated greater symptom severity at baseline. Youth with higher resilience demonstrated greater improvements in self-efficacy within 3 months of initiating treatment but decreased pain acceptance. Further characterization of resilience profiles may provide insight into tailored treatment strategies focusing on self-efficacy and pain acceptance in this patient population.

Disclosure: S. Gmuca: None; **J. Leonard**: None; **A. Tomlinson**: None; **M. McGill**: None; **N. Butler**: None; **R. Xiao**: None; **P. Cronholm**: None; **T. Palermo**: None; **J. Young**: None; **A. Rosenberg**: None; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

Abstract Number: 1299

Pediatric Antiphospholipid Syndrome in a Large Tertiary Center

Rasha Elrefai, Marietta De Guzman, Jun Teruya, Vadim Kostousov, Amir Navaei and Olivia Kwan, Baylor College of Medicine, Houston, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Antiphospholipid syndrome (APS) is an autoimmune condition defined as the presence of thrombotic events and/or pregnancy morbidity, accompanied by persistent antiphospholipid antibodies (aPLs). Pediatric APS is rare, often severe, and usually occurs in conjunction with systemic lupus erythematosus (SLE). There currently are no pediatric specific diagnostic or classification criteria for APS. This study aims to describe the characteristics of children with APS in a large tertiary care center.

Methods: With approval from our Institutional Review Board, retrospective descriptive study of patients diagnosed with APS from 2012 to 2025 was performed. The cohort was further stratified into primary APS and secondary APS. Demographic, clinical manifestations, serologies, and treatments were compared between groups. Threshold criteria were defined utilizing the 2023 ACR/EULAR Antiphospholipid Syndrome Classification Criteria threshold of >40 units for moderate/high titer. Statistical analysis for significance was calculated utilizing Fischer exact test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Demographics and clinical manifestations

	All APS n=39	Primary APS n=16	Secondary APS n=23	p value
Median age at diagnosis (IQR)	14 years (5)	14 years (5)	14 years (5)	0.7
Gender				
Male	10 (26%)	6 (38%)	4 (17%)	0.3
Female	29 (74%)	10 (63%)	19 (83%)	0.3
Race/ethnicity				
White Hispanic	22 (56%)	12 (75%)	10 (44%)	0.1
Black/African American	7 (18%)	0 (0%)	7 (30%)	**0.03**
White non-Hispanic	6 (15%)	4 (25%)	2 (9%)	0.2
Asian	4 (10%)	0 (0%)	4 (17%)	0.1
Clinical Manifestations				
Arterial thrombosis	12 (31%)	5 (31%)	7 (30%)	1
Venous thrombosis	18 (46%)	9 (56%)	9 (39%)	0.3
Pulmonary hemorrhage	3 (8%)	1 (6%)	2 (8%)	1
Pulmonary embolism	6 (15%)	1 (6%)	5 (22%)	0.4
Livedoid rash	7 (18%)	2 (12%)	5 (22%)	0.7
APS nephropathy	3 (8%)	1 (6%)	2 (9%)	1
Thrombotic microangiopathy	7 (18%)	2 (13%)	5 (22%)	0.7
Myocardial disease	1 (3%)	0	1 (4%)	1
Cardiac valve disease	6 (15%)	2 (13%)	4 (17%)	1
Adrenal hemorrhage	1 (3%)	1 (6%)	0	0.4
Obstetric	0	0	0	1
Thrombocytopenia	20 (51%)	5 (31%)	15 (65%)	0.05
Autoimmune hemolytic anemia	15 (39%)	4 (25%)	11 (48%)	0.2
Neurologic (stroke/ headache/ seizures)	17 (44%)	5 (31%)	12 (52%)	0.3
CAPS*	7 (18%)	3 (19%)	4 (17%)	1
LAHPS**	1 (3%)	0	1 (4%)	1
Recurrent Events	6 (16%)	4 (25%)	2 (9%)	0.2
ANA positive	36 (92%)	13 (81%)	23 (100%)	0.06
SLEDAI at diagnosis	-	-	17 (IQR 17)	-

*Catastrophic antiphospholipid syndrome, **Lupus anticoagulant hypoprothrombinemia syndrome

Results: Thirty-nine patients were included in the study, 16 (41%) with primary APS and 23 (59%) with secondary APS. Most patients with secondary APS had a diagnosis of SLE and 3 patients with primary APS later developed SLE. Hematologic manifestations were more common in secondary APS. Arterial thrombosis most commonly presented as a stroke. Catastrophic antiphospholipid syndrome (CAPS) was identified in 18% of all patients, all of whom survived. Ten patients with LA hypoprothrombinemia syndrome (LAHPS) were identified, only 1 of whom had APS.

Four (10%) patients had aPL below criteria threshold with negative LA, while 5 (13%) had low titer aPL with positive LA. Persistent positivity was observed in 62% of all APS but only 26% were persistent above threshold. Persistence was statistically more common in the primary APS group; however, above threshold persistence only approached statistical significance. Triple positivity was mostly seen at criteria levels, with only 3 patients having triple positivity at low titers.

Table 2 Laboratory manifestations

aPL positivity	All APS n=39	Primary APS n=16	Secondary APS n=23	p value
Anti B2 glycoprotein IgM	16 (41%)	6 (38%)	10 (44%)	0.8
Anti B2 glycoprotein IgG	12 (31%)	7 (44%)	5 (22%)	0.2
Anticardiolipin IgM	29 (74%)	12 (75%)	17 (74%)	1
Anticardiolipin IgG	26 (67%)	8 (50%)	18 (78%)	0.09
Lupus anticoagulant	33 (85%)	15 (94%)	18 (78%)	0.4
Triple positive	16 (41%)	8 (50%)	8 (35%)	0.5
Persistent positive	24 (62%)	13 (81%)	11 (48%)	0.049
Criteria threshold aPL positivity	**All APS**	**Primary**	**Secondary**	**p value**
Anti B2 glycoprotein IgM	10 (26%)	4 (25%)	6 (26%)	1
Anti B2 glycoprotein IgG	11 (28%)	6 (38%)	5 (22%)	0.3
Anticardiolipin IgM	9 (23%)	4 (25%)	5 (22%)	1
Anticardiolipin IgG	14 (36%)	7 (44%)	7 (30%)	0.5
Triple positive	13 (33%)	7 (44%)	6 (26%)	0.3
Persistent positive	10 (26%)	7 (44%)	3 (13%)	0.06

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 Treatment

Anticoagulation	All APS n=39	Primary APS n=16	Secondary APS n=23	p value
Aspirin	20 (51%)	6 (38%)	14 (61%)	0.2
Direct oral anticoagulant	7 (18%)	4 (25%)	3 (13%)	0.4
Heparin/LMWH*	33 (85%)	12 (75%)	21 (91%)	0.2
Warfarin	14 (36%)	8 (50%)	6 (26%)	0.2
None	2 (5%)	0	2 (9%)	0.5
Immunomodulation	**All APS**	**Primary**	**Secondary**	**p value**
Azathioprine	4 (10%)	1 (6%)	3 (13%)	0.6
Belimumab	2 (5%)	1 (6%)	1 (4%)	1
Cyclophosphamide	10 (26%)	0	10 (43%)	0.002
Eculizumab	4 (10%)	1 (6%)	3 (13%)	0.6
Hydroxychloroquine	36 (92%)	14 (88%)	22 (96%)	0.6
IVIG	11 (28%)	1 (6%)	10 (43%)	0.01
Methotrexate	3 (8%)	1 (6%)	2 (9%)	1
Mycophenolate	18 (46%)	2 (13%)	16 (70%)	0.0008
Plasmapheresis	9 (23%)	2 (13%)	7 (30%)	0.3
Rituximab	26 (67%)	6 (38%)	20 (87%)	0.002
Other	3 (8%)	0	3 (13%)	0.3
None	0	2 (13%)	0	0.2

*Low molecular weight heparin

Anticoagulant treatment was overall similar between the two groups, with heparin-based being most common. While patients with secondary APS received more immunomodulatory therapies, many primary APS patients did receive immunosuppressants, particularly rituximab. Two of the 6 who received rituximab were at the time of progression from primary APS to SLE.

Conclusion: Pediatric APS presents heterogeneously and with severe manifestations. Neurologic manifestations, a non-criteria manifestation, were common in this cohort, as was CAPS. Statistically significant differences between clinical and laboratory manifestations in primary and secondary APS were limited, possibly due to small sample size. Despite the small sample size, this high frequency of severe manifestations suggests APS may be underrecognized in milder cases. About a third of our patients fulfilled the threshold of aPL positive as defined by the most recent classification criteria for APS. This highlights the need for large-scale retrospective and prospective studies to address this definition in pediatric patients.

Disclosure: R. Elrefai: None; **M. De Guzman**: None; **J. Teruya**: None; **V. Kostousov**: None; **A. Navaei**: None; **O. Kwan**: None.

Abstract Number: 1300

International Assessment of cSLE Clinical Remission (cCR) Criteria in Childhood Lupus: Sensitivity Analyses from the UK JSLE Cohort and the CARRA Registry

Chandni Sarker[1], Jennifer Cooper[2], Emily Smitherman[3], Flavia Alves[1], Alexandre Belot[4], Michael Beresford[5], Andreea Jorgensen[1], Eve Smith[6], Laura Lewandowski[7] and **Rebecca Sadun**[8], for the UK JSLE Study Group and the CARRA Registry Investigators, [1]University of Liverpool, Liverpool, United Kingdom, [2]University of Colorado/Children's Hospital Colorado, Aurora, CO, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Hospices Civils de Lyon, Collonges au mont d'or, France, [5]Alder Hey Children's NHS Foundation Trust Hospital, Department of Women's & Children's Health, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom, [6]University of Glasgow, Glasgow, United Kingdom, [7]NIAMS, NIH, Bethesda, MD, [8]Duke University, Durham, NC

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Description of the variations of cCR.

T2T goal	Description of modified criterion associated with variations
Current cCR definition	(1) Clinical SLEDAI score equal to 0, (2) PGA score of < 0.5, (3) prednisolone dose of 0.10 mg/kg/day or a maximum of 5.0 mg/day and no intravenous methylprednisolone, and (4) tolerated standard maintenance immunosuppressive drugs/biological agents.
Variation 1	Removal of 'PGA score' criterion.
Variation 2	Removal of 'tolerated standard immunosuppressive drugs/biological agents' criterion.
Variation 3	Transformation of 'clinical SLEDAI=0' criterion to full SLEDAI-2K=0.
Variation 4	Transformation of 'PGA < 0.5' to equal to 0.
Variation 5	Transformation of 'PGA < 0.5' to ≤ 0.25.
Variation 6	Transformation of 'PGA < 0.5' criterion to ≤ 1.
Variation 7	Transformation of 'prednisolone dose of 0.10 mg/kg/day or maximum of 5 mg/day' to prednisolone dose of 0.10 mg/kg/day or maximum of 2.5 mg/day.
Variation 8	Transformation of 'prednisolone dose of 0.10 mg/kg/day or maximum of 5 mg/day' to prednisolone dose of 0.10 mg/kg/day or maximum of 7.5 mg/day.
Variation 9	Transformation of 'prednisolone dose of 0.10 mg/kg/day or maximum of 5 mg/day' to prednisolone dose of 0.10 mg/kg/day or maximum of 10 mg/day.
cCR, clinical remission on low steroids; PGA, physician global assessment; SLEDAI-2K, systemic lupus erythematosus disease activity index 2000.	

Background/Purpose: Consensus-derived treat-to-target (T2T) goals for childhood-onset SLE (cSLE), including clinical remission on low dose steroids (cCR), have been endorsed by the Paediatric Rheumatology European Society (PReS). This study evaluated whether components of cCR could either be removed or transformed to create modified definitions that provide better protection against high disease activity, as compared to the original consensus-derived cCR.

Methods: Patients from UK JSLE Cohort Study and the CARRA Registry who were < 18 years at diagnosis and met $^{3}4$ ACR/SLICC criteria were included. The components of cCR were either eliminated or transformed as described in Table 1, with 9 variations explored. Prentice-Williams-Peterson (PWP) gap-time models assessed the impact of the new cCR target definitions on high disease activity (SLEDAI-2K ≥10), with the resulting hazard ratios (HRs) compared between original and varied cCR definitions using Student's t-tests. Target attainability was compared between the original cCR and its corresponding variations using Wilcoxon tests.

Results: Data were available from 1,566 cSLE patients (11,965 visits; UK JSLE: n=492, 5,923 visits; CARRA: n=1,074, 6,042 visits). Achieving the original cCR (HR 0.24 [CI 0.18, 0.33]) reduced the hazards of subsequent high disease activity by 76% (p< 0.001, Table 2). Removing the physician global assessment (PGA) criterion (HR 0.31 [CI 0.25, 0.39]) or the criterion for stable immunosuppression (HR 0.27 [CI 0.21, 0.36]) statistically significantly worsened the risk of high disease activity, compared to the original definition (all p< 0.001, Table 2). Transformation of the *clinical* SLEDAI=0 criterion to incorporate *full* SLEDAI-2K=0 (Transformation 3) significantly improved the hazard of high disease activity compared to original

Table 2. Multivariable models showing impact of target attainment on high disease activity.

Description of original and varied cCR targets	Target definitions	Target state attainment at any time point	Significant difference from original cCR
(1) Clinical SLEDAI score equal to 0, (2) PGA score of < 0.5, (3) prednisolone dose of 0.10 mg/kg/day or a maximum of 5.0 mg/day and no intravenous methylprednisolone, and (4) tolerated standard maintenance immunosuppressive drugs/biological agents.	Original cCR	**0.24 (0.18, 0.33); P<0.001**	NA
Removal of 'PGA' criterion.	Variation 1	**0.31 (0.25, 0.39); P<0.001**	**Increased hazards of high disease activity**
Removal of 'stable immunosuppression' criterion.	Variation 2	**0.27 (0.21, 0.36); P<0.001**	**Increased hazards of high disease activity**
Transformation of 'clinical SLEDAI=0' criterion to full SLEDAI-2K=0.	Variation 3	**0.20 (0.13, 0.31); P<0.001**	**Decreased hazards of high disease activity**
Transformation of 'PGA < 0.5' to PGA equal to 0.	Variation 4	**0.26 (0.18, 0.38); P<0.001**	NA
Transformation of 'PGA < 0.5' to PGA ≤ 0.25.	Variation 5	**0.22 (0.16, 0.32); P<0.001**	NA
Transformation of 'PGA < 0.5' to PGA ≤ 1.	Variation 6	**0.29 (0.22, 0.37); P<0.001**	**Increased hazards of high disease activity**
Transformation of 'prednisolone dose of 0.10 mg/kg/day or maximum of 5 mg/day' to 'prednisolone dose of 0.10 mg/kg/day or maximum of 2.5 mg/day.'	Variation 7	**0.24 (0.18, 0.34); P<0.001**	NA
Transformation of 'prednisolone dose of 0.10 mg/kg/day or maximum of 5 mg/day' to 'prednisolone dose of 0.10 mg/kg/day or maximum of 7.5 mg/day.'	Variation 8	**0.24 (0.17, 0.32); P<0.001**	NA
Transformation of 'prednisolone dose of 0.10 mg/kg/day or maximum of 5 mg/day' to 'prednisolone dose of 0.10 mg/kg/day or maximum of 10 mg/day.	Variation 9	**0.24 (0.17, 0.32); P<0.001**	NA
Multivariable Prentice-Williams-Peterson (PWP) gap-time models adjusted for target attainment and significant factors from univariable analyses including history of lupus nephritis within first 6 months, ethnicity, and disease duration. Student's t-test was implemented to compare the hazard ratios (HRs) between original and varied cCR target definitions where a p-value < 0.008 denoted statistical significance. cCR, clinical remission on low steroids; PGA, physician global assessment; SLEDAI-2K, systemic lupus erythematosus disease activity index 2000.			

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cCR ($p < 0.001$, Table 2). However, this transformation significantly increased time-to-target attainment (Original cCR: 18 months vs. Transformation 3: 20 months) and significantly reduced the time spent in target (Original cCR: 11.3 months vs. Transformation 3: 7.4 months).

Conclusion: These analyses demonstrate that PGA and stable immunosuppression are both essential to defining clinical remission. Although transformation of the *clinical* SLEDAI criterion to incorporate the *full* SLEDAI-2K reduced the hazards of high disease activity, this made the definition of remission significantly less attainable, suggesting that the original definition, derived from the adult definition, is optimal for use in cSLE. Further research should evaluate the consensus and varied cCR definitions in their ability to predict and prevent lupus-related damage.

Disclaimer: This study utilized data collected in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. The views expressed are the authors' and do not necessarily represent the view of CARRA.

Acknowledgements: This work could not have been accomplished without the aid of the NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the Arthritis Foundation (AF), and the Centers for Disease Control and Prevention (CDC). We would also like to thank all participants and hospital sites that recruited patients.

Disclosure: C. Sarker: None; **J. Cooper**: Bristol-Myers Squibb(BMS), 1, Sana Biotechnology, 2, Synthekine, 2; **E. Smitherman**: None; **F. Alves**: None; **A. Belot**: None; **M. Beresford**: Novartis, 5; **A. Jorgensen**: None; **E. Smith**: None; **L. Lewandowski**: None; **R. Sadun**: The Expert Institute, 12,.

Abstract Number: 1301

Prevalence, Clinical and Genetic Risk Factors, and Time to Cataract Development in Childhood-onset Systemic Lupus Erythematosus

Sirikarn Tangcheewinsirikul[1], Zhaoyu Ding[2], Nicholas Chan[3], Daniela Dominguez[3], Andrea Knight[4], Deborah Levy[1], Lawrence Ng[5], Earl Silverman[1], Ruud Verstegen[1] and Linda Hiraki[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]SickKids Research Institute, Toronto, ON, Canada, [3]The Hospital for Sick Children, Toronto, Canada, [4]Hospital for Sick Children, Toronto, ON, Canada, [5]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cataracts are a significant ocular complication in childhood-onset systemic lupus erythematosus (cSLE). This study aimed to assess the prevalence, time to cataract development, and clinical and genetic risk factors associated with cataracts in cSLE.

Methods: We conducted a cohort study of children and adolescents diagnosed and followed for cSLE until age 18 years at a tertiary lupus clinic from 1992 to 2023. Genotyping was performed using a multiethnic array, ancestry was genetically inferred and individual polygenic risk scores (PRS) for cataracts were calculated using PRSice. Demographic and clinical variables, including sex, age at SLE diagnosis, disease duration, SLE manifestations, and high-dose glucocorticoid (GC) exposure (defined as ≥2 mg/kg/day or ≥40 mg/day if >30 kg, for at least 30 days). Cataract was diagnosed by an ophthalmologist or optometrist and recorded as part of the Systemic Lupus International Collaborating Clinics Damage Index (SLICC-DI). Summary statistics compared demographic and clinical features between patients with and without cataracts.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Association of cataracts PRS and cataracts in univariate and multivariable adjusted models.

	OR (95%CI)	P	Adjusted OR (95%CI)	P
Polygenic risk score	1.4 (0.2-8.8)	0.73	1.0 (0.1-8.3)	0.98
Male (referent: Female)	1.9 (0.9-3.9)	0.06	1.6 (0.7-3.4)	0.24
Ethnicity (referent: European)				
East Asian	2.2 (0.9-6.1)	0.10	1.8 (0.7-5.3)	0.26
South Asian	2.5 (0.9-7.0)	0.08	1.8 (0.6-5.5)	0.32
Admixed American	**2.8 (1.1-7.9)**	**0.04**	2.6 (0.9-8.0)	0.08
African	0.7 (0.1-2.9)	0.64	0.6 (0.1-2.7)	0.54
High-dose glucocorticoid exposure	**4.4 (1.8-13.0)**	**0.003**	**4.1 (1.7-12.2)**	**0.005**

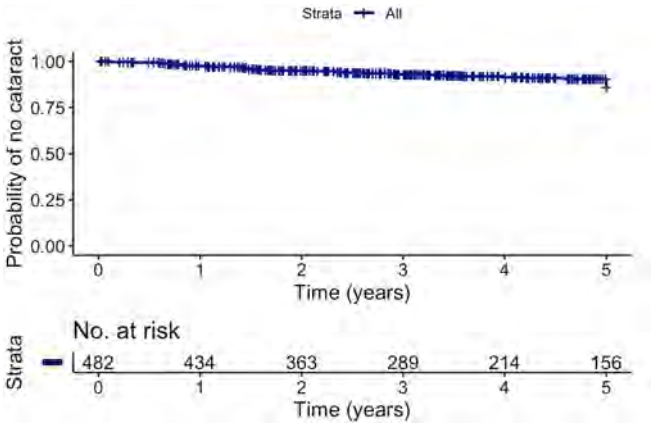


Figure 1. Time to first cataract event in cSLE (n=482).

We completed time to cataract development analyses and estimated the association between clinical features and PRSs with cataract risk in logistic regression models ($P < 0.05$).

Results: Of 482 cSLE patients, 83% were female. The mean age at diagnosis was 13.1±3.1 years, and mean disease duration was 4.5±3.0 years. The cohort was primarily of European (28%) and East Asian (25%) ancestry, followed by South Asian (18%), Admixed American (17%), and African (12%). Lupus nephritis occurred in 42%, and 49% received high-dose GC.

Cataracts were documented in 9% of patients after a mean follow-up of 4.2 years. Cataract prevalence was highest among East Asian (30%), Admixed American (26%), and South Asian (23%) patients but was not statistically significant. High dose GC exposure was associated with cataracts in both univariate and multivariable adjusted models (Table 1).

Cataracts PRS was not associated with odds of cataracts in the univariate or models adjusted for sex, ethnicity and high-dose GC exposure.

Conclusion: In this multiethnic cSLE cohort, 9% developed cataracts within 4.2 years of follow-up. High-dose GC exposure significantly increased cataract risk. We did not observe a significant association between a cataracts-PRS and the odds of developing cataracts in children and adolescents with cSLE. Future studies will include participants with adult-onset SLE.

Disclosure: S. Tangcheewinsirikul: None; **Z. Ding**: None; **N. Chan**: None; **D. Dominguez**: None; **A. Knight**: Pfizer, 6; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **L. Ng**: None; **E. Silverman**: None; **R. Verstegen**: AbbVie/Abbott, 2; **L. Hiraki**: Janssen, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1302

Dose Adjustment was Necessary in Patients with Cryopyrin-Associated Periodic Syndrome Switching from Anakinra to Canakinumab

Soyoung Lee and Hyun Kyung Lee, Chung-Ang University Hospital, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cryopyrin-associated periodic syndrome (CAPS) is a spectrum of rare autoinflammatory disorders caused by mutations in the *NLRP3* gene, leading to excessive interleukin-1β (IL-1 β) activity. IL-1 inhibitors, such as anakinra and canakinumab, are primarily used to treat these patients. In South Korea, anakinra has been the initial treatment of choice for CAPS patients, as canakinumab was only recently reimbursed by the National Health Insurance. Despite varying symptoms and different doses of anakinra, most CAPS patients transitioned from anakinra to canakinumab around the same time following a standardized protocol. The aim of this study is to report the efficacy and potential issues associated with switching from anakinra to canakinumab.

Methods: This study included CAPS patients with confirmed molecular diagnoses who switched from anakinra to canakinumab following its reimbursement approval in August 2024. Canakinumab was injected subcutaneously at a dose of 2mg/kg for patients under 40kg and 150mg for those over 40kg. If clinical response was satisfactory, the same dose was injected every 8 weeks. If not, additional dose was given within one week, up to twice. We prospectively analyzed clinical efficacy, adverse events, and quality of life.

Results: Five patients, including a pair of identical twins, were enrolled in this study (3 NOMID/CINCA, 1 MWS, 1 FCAS). The mean age at the time of the study and at diagnosis was 12.6 years (range: 4-23 years) and 15.8 months (range:1-24 months) respectively. All patients experienced recurrent fever and skin rash. Four patients had sensorineural hearing loss, three patients had hydrocephalus, and one patient had severe bone destruction. The mean dose and duration of anakinra were 3.9 mg/kg (range: 2-5.17 mg/kg) and 8.15 years (range: 1.25-14 years), respectively. Canakinumab was initiated at 2 mg/kg in three patients and 150mg in two patients. An additional dose of canakinumab was required twice in four patients, except for the FCAS patient. One patient, the most severe case, discontinued canakinumab and returned to anakinra at week 26 due to an incomplete response despite the use of the maximum dose. The mean final dose of canakinumab was 5.6 mg/kg (range: 2.8-6.6 mg/kg). Reported adverse events included headache, skin rash, infection, dysaesthesia, dizziness, and hypothermia. These adverse events improved with supportive care and diminished over time. Despite several adverse events, both patients and their families reported high satisfaction, with improvements in physical and emotional functioning.

Conclusion: Canakinumab was effective in CAPS patients, particularly in improving quality of life. However, adjustments in both dosage and dosing interval were necessary from the time of switching from anakinra to canakinumab, depending on the severity of clinical symptoms from the initiation.

Disclosure: S. Lee: None; **H. Lee**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1303

Impact of Fruits and Vegetables Intake on Immune-mediated Inflammatory Diseases:a Two-sample Mendelian Randomization Study

Xuemei Tang, Yuting Zhou, Yuxiao Chen, Xinglin Wu and Qiang Luo, Department of Rheumatology and Immunology, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity, Chongqing, China, Chongqing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

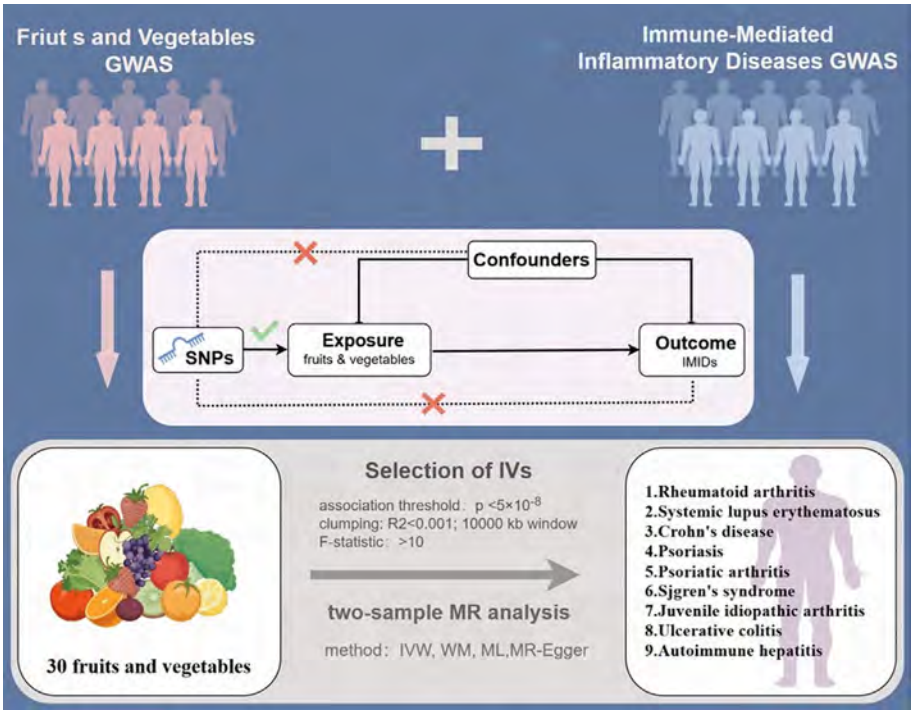
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: A balanced diet can prevent diseases and promote physical and mental health. Accumulating evidence shows that fruits and vegetables (F&Vs) intake is associated with immune-mediated inflammatory diseases (IMIDs). However, it remains uncertain whether there is causality between the two.

Methods: We comprehensively investigated the association between 30 types of F&Vs and IMIDs, using Dietary habits-Target Mendelian Randomization method. GWAS data on exposure and outcome factors were extracted from the IEU database. Ultimately, Steiger test was used to determine the direction of each SNP.



Graphical abstract A graph illustrates the hypothetical impact of fruits & vegetables on IMIDs. The presence of a dotted line indicates a potential direct causal relationship or pleiotropic effect between fruits & vegetables on IMIDs.The two-sample MR study was analyzed using inverse variance weighted (IVW), weighted median (WM), maximum likelihood (ML), and MR-Egger. IMIDs, immune-mediated inflammatory diseases; MR, Mendelian randomization.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

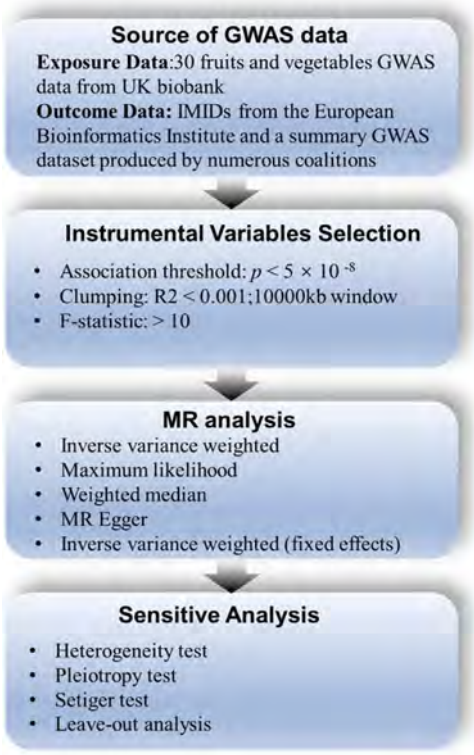


Figure 1. Flowchart of the Mendelian randomization (MR) analysis.

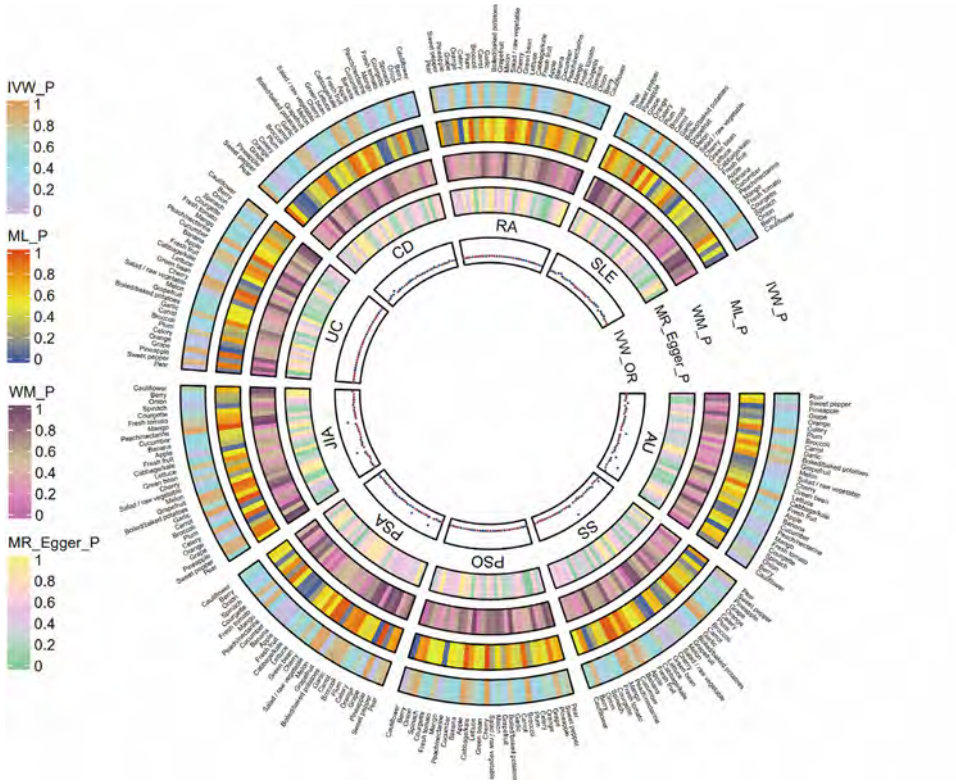


Figure 2. Multiple analysis of F&Vs and IMIDs. IVW, inverse-variance weighted method; WM, weighted median estimator; ML, maximum likelihood; AH, autoimmune hepatitis ; CD, crohn's disease; JIA, juvenile idiopathic arthritis; PsA, psoriasis arthritis; PsO, psoriasis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SS, sjgren's syndrom; UC, ulcerative colitis; F&Vs, fruits and vegetables; IMIDs, immune-mediated inflammatory diseases.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A negative correlation was identified between cauliflower intake and the incidence of psoriasis (OR = 0.993, 95%CI 0.987-0.999, p = 0.016). Inversely, apple intake and onion intake promoted incidence of psoriatic arthritis (OR = 1.864, 95% CI, 1.237-2.809, p = 0.003) and Crohn's disease (OR = 1.850, 95%CI 1.177-2.910, p = 0.008), respectively. Additionally, the findings were consistent across a range of alternative MR methods. Sensitivity analyses did not detect any heterogeneity or pleiotropy in the estimated impact of F&Vs on the risk of developing IMIDs (all p >0.05). Steiger proved that the causal relationship between them was true.

Conclusion: This is the first Dietary habits-Target Mendelian Randomization study to systemically examine the correlation between commonly consumed F&Vs and IMIDs. In conclusion, our findings showed that the intake of cauliflower alleviated psoriasis progression, whereas apple and onion intake promoted psoriatic arthritis and Crohn's disease, respectively.

Disclosure: X. Tang: None; **Y. Zhou**: None; **Y. Chen**: None; **X. Wu**: None; **Q. Luo**: None.

Abstract Number: 1304

The role of PET/CT in evaluating rheumatologic conditions in children with fever of unknown origin - a multicenter study

Neta Berlak[1], Lydia Christodoulou[2], Gil Amarilyo[3], Oded Scheuerman[4], Irit Tirosh[5], Eyal Kristal[6], Ester Forer[7], Amit Carmi[8], Alon Kalter[9] and **Yoel Levinsky**[10], [1]Schneider children's medical center of Israel, Tel Aviv, Israel, [2]Tel Hashomer, Periatric rheumatology unit, Tel Aviv, Israel, [3]Schneider Children's Medical Center of Israel, Kibbutz Maggal, Israel, [4]schneider children's meidcal center of Israel, Petah tikva, Israel, [5]Tel Aviv universty, Ramat Gan, Israel, [6]Soroka medical center Beer Sheva, Beer Sheva, Israel, [7]Soroka medical center, Beer Sheva, Israel, [8]Schneider children's meidcal center of Israel, Tel Aviv, Israel, [9]Schneider children's medical center of ISrael, Petah Tikva, Israel, [10]Schneider Children's Medical Cenetr of Israel, Tel Aviv University, JERUSALEM, Israel

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fever of Unknown Origin (FUO) is a relatively common clinical challenge that is frequently referred for evaluation by pediatric rheumatologists. In many cases, it is necessary to rule out other medical conditions before establishing a rheumatologic diagnosis. 18F-FDG PET/CT is a valuable diagnostic tool that may help identify the fever's source. However, its use in children involves risks, including radiation exposure and the need for sedation. Our aims were To assess the contribution of PET/CT to FUO diagnosis in hospitalized children, and to identify rheumatologic conditions that are either detected through the evaluation or excluded by it. In addition, to identify predictive factors for its diagnostic utility.

Methods: A retrospective cohort study reviewing medical records of children (0-18 years) diagnosed with FUO who underwent PET/CT between 2010 and 2024 in three Israeli medical centers. Clinical and laboratory data were collected, and cases where PET/CT led to a diagnosis were compared to those where it did not.

Results: Among 113 cases, PET/CT contributed to diagnosis in 52 (46%). The majority of diagnoses identified by PET/CT were infectious (53.8%), whereas in cases where PET/CT did not aid in diagnosis, rheumatologic diseases were predominant (66.6%). Of all cases, 21% were ultimately diagnoses with a rheumatologic condition, the most frequent was systemic JIA. Immunodeficiency, low hemoglobin, and low albumin were more frequent in cases where PET/CT was diagnostic, while rash and arthritis were more common in cases where PET/CT did not contribute.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1. Basic demographic and clinical parameters of the study cohort (n=113)	
Age (years)	7.71 ± 5.84
Gender, male	64 (56.6)
Medical background	67 (59.3)
Hospitalization within the last 6 months	63 (56.8)
Length of fever (days)	21 [IQR 14-37]
Medical settings	General ward 94 (83.2) Oncology ward 7 (6.2) PICU 5 (4.4) Ambulatory 7 (6.2)
Imaging before PET-CT	
X-ray	107 (94.7)
US	105 (92.9)
Echocardiography	100 (89.3)
MRI	19 (17.3)
CT	39 (34.5)
Bone scan	15 (13.4)
Empiric treatments before PET-CT	
Antibiotics	86 (76.1)
Glucocorticoids	10 (8.8)
Total length of hospitalization (days)	22 [IQR 14-43]
Death within 3 months of PET-CT	5 (4.8)
Final diagnoses established eventually (versus unknown)	76 (67.3)
Final diagnoses established according to PET-CT results	52 (46)
Final diagnoses - by major groups	Infectious 34 (30.1) Rheumatologic 24 (21.2) Oncologic 14 (12.4) Other 4 (3.5)
[a] The data are presented as N (%) or mead ± SD or median [IQR] as appropriate	

Table 2

Table 3. Demographic and clinical parameters of the cohort (n=113), divided by the diagnostic value of the PET-CT test.

	PET-CT		
Variables[a]	**Aided in diagnosis (n=52)**	**No diagnostic benefit (n=61)**	**P-value**
Age (years)	7.50 ± 5.26	7.90 ± 5.70	0.703
Medical background	32 (61.5)	35 (57.4)	0.654
Oncologic patient	11 (21.2)	6 (9.8)	0.093
Organ transplantation	9 (17.3)	4 (6.6)	0.074
Known genetic disorder	6 (11.5)	4 (6.6)	0.509
Congenital heart disease	3 (5.8)	6 (9.8)	0.503
Known Immunodeficiency	20 (38.5)	12 (19.7)	**0.027**
Hospitalization in the last 6 months	28 (54.9)	35 (58.3)	0.716
Length of fever (days)	30 ± 25	30 ± 27	0.681
Maximal fever (DC)	39.5 ± 0.7	39.5 ± 0.8	0.830
Is there any fever pattern	11 (21.1)	15 (24.6)	0.665
Rash	3 (5.8)	12 (19.7)	**0.03**
Lymphadenopathy or organomegaly	7 (13.5)	7 (11.5)	0.749
Arthritis or arthralgia	3 (5.8)	11 (18)	**0.049**
Hemodynamic instability at any point	8 (15.4)	5 (8.2)	0.233
Laboratory tests			
Total Leukocytes	12.10 ± 12.45	12.25 ± 13.61	0.794
Highest CRP (mg/dL)	14.28 [8.3–18.45]	13.71 [4.8–22]	0.417
Hemoglobin level	8.57 ± 1.50	9.23 ± 1.88	**0.043**
Total platelets	372 ± 300	413 ± 295	0.336
Highest ESR	76 ±59	79 ± 43	0.718
Albumin	3.0 ±0.6	3.3 ±0.6	**0.037**
Ferritin	1329 ± 2723	3532.7 ± 14969.9	0.871
Positive ANA	2 (8.3)	16 (45.7)	**0.002**
LDH elevation	33 (63.5)	27 (44.3)	**0.042**
Final diagnosis group			
Infectious Rheumatologic Oncologic Other	28 (53.8) 8 (15.4) 14 (26.9) 2 (3.8)	6 (25) 16 (66.6) 0 2 (8.3)	**< 0.001**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: PET/CT is an effective diagnostic tool for FUO in children, aiding diagnosis in 46% of cases. Of all cases, 21% were ultimately diagnoses with a rheumatologic condition. However, most were diagnosed without direct findings on the PET/CT, which primarily served to rule out other conditions. Predictive factors for its utility are reported. In appropriate clinical scenarios, PET/CT should be considered as part of the FUO workup in pediatric patients.

Disclosure: N. Berlak: None; **L. Christodoulou**: None; **G. Amarilyo**: None; **O. Scheuerman**: None; **I. Tirosh**: None; **E. Kristal**: None; **E. Forer**: None; **A. Carmi**: None; **A. Kalter**: None; **Y. Levinsky**: None.

Abstract Number: 1305

Clinical outcomes of low-to-moderate–dose glucocorticoids in multisystem inflammatory syndrome in children (MIS-C) - a multicenter study

Nina Shirman[1], Liora Harel[2], Gil Amarilyo[3], Kfir Kaidar[4], Yonatan Butbul Aviel[5], Merav Heshin Bekenstein[6], Mohamad Hamad Saied[7], Ofra Goldzweig[8], Adi Miler[9] and **Yoel Levinsky**[10], [1]Schneider children's medical center of Israe, Tel Aviv, Israel, [2]Schneider Children's Medical center, Nettnja, Israel, [3]Schneider Children's Medical Center of Israel, Kibbutz Maggal, Israel, [4]Pediatric rheumatology, Schneider children's medical center of Israel, Petah Tikva, Israel, [5]Pediatric rheumatology, Technion Faculty of Medicine, Haifa, Israel, [6]Tel Aviv Medical Center Israel, Binyamina, Tel Aviv, Israel, [7]Carmel Medical Centre, Technion Faculty of Medicine, Haifa, Israel, [8]Pediatric rheumatology unit, Kaplan medical canter, Rehovot, Israel, [9]Pediatric rheumatology unit, Technion Faculty of Medicine, Haifa, Israel, [10]Schneider Children's Medical Cenetr of Israel, Tel Aviv University, JERUSALEM, Israel

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1272–1305) Pediatric Rheumatology – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Multisystem Inflammatory Syndrome in Children (MIS-C) is an autoinflammatory disease following SARS-CoV-2 exposure. The optimal treatment strategy remains under investigation, though intravenous immunoglobulin (IVIG) and glucocorticoids are commonly used. While some authors suggest induction with pulse steroids, ACR guidelines recommend initiating low-to-moderate dose glucocorticoids (1-2 mg/kg). This study aimed to assess the response of patients treated with low-to-moderate dose corticosteroids and compare outcomes to a historical cohort treated with pulse steroids.

Methods: A multi-center, retrospective study collected data on patients initially treated with low-to-moderate dose corticosteroids. Clinical and laboratory data were compared to a historical cohort to assess disease severity and outcomes. The primary outcome was treatment escalation after 24 hours. Other outcomes included cardiovascular function, need for adjunctive therapies, and length of hospital stay.

Results: Among 41 patients receiving low-to-moderate dose corticosteroids, 7 (17.1%) required escalation. Overall, 13 (34.2%) needed vasopressors, and 2 (5.3%) required mechanical ventilation. Compared to 26 patients treated with pulse steroids, no differences were found in age, sex, fever characteristics, Kawasaki-like symptoms, or hemodynamic instability. Inflammatory markers (CRP, ESR) were similar, though ferritin was lower in the study group. Hospitalization was longer in the pulse steroid group. An echocardiogram performed post-recovery revealed that 87.5% of the study group had normal cardiac function.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1. A comparison between the group of patients treated with a low/moderate dose of steroids and a historical group treated with high dose (pulse) steroids

	Low/medium steroids dose (n = 41)	Pulse steroids (n=26)	P-value
Gender (M)	29 (70.7%)	16 (61.5%)	0.5941
Age (y)	9.16 ± 4.17	9.11 ± 4.53	0.9633
Medical history, normal	31 (75.6%)	25 (96.2%)	**0.0403**
Fever length (days)	4.45 ± 1.77	4.6 ± 1.58	0.7259
Fever level DC	38.3 ± 1.08	38.6 ± 0.82	0.2303
Cardiac involvement – abnormal echocardiography	15 (51.7%)	15 (57.7%)	0.7876
Cardiac involvement – abnormal echocardiography OR cardiac enzymes	34 (82.9%)	24 (96%)	0.4646
GI involvement	36 (87.8%)	22 (84.6%)	0.7266
Coagulation disorder	26 (63.4%)	17 (65.4%)	1.000
Hemodynamic instability	22 (53.7%)	15 (53.6%)	0.8046
Elevated troponin	27 (81.8%)	17 (73.9%)	0.7866
Kawasaki criteria	4 (9.8%)	2 (7.7%)	1.0000
CRP at presentation	15.85 ± 10.08	20.6 ± 9.2	0.0563
ESR at presentation	52.55 ± 27.73	59.8 ± 21.1	0.2552
Lymphopenia at presentation	27 (65.9%)	21 (87.5%)	0.0798
Thrombocytopenia at presentation	16 (39.0%)	7 (26.9%)	0.4294
Ferritin at presentation	563.91 ± 630.45	975.9 ± 832	**0.0247**
D-dimer at presentation	2,897 ± 3355.2	7368 ± 7085	**0.0009**
Mechanical ventilation (invasive)	2 (5.3%)	4 (15.4%)	0.1972
Vasopressors treatment	13 (34.2%)	10 (38.5%)	0.6058
Total time of hospitalization (hours)	160.4 ± 81.44	211.4 ± 66.2	**0.0093**

Conclusion: Low-to-moderate dose glucocorticoids are effective for most MIS-C patients, with only 17% requiring escalation. No differences were seen in vasopressor or ventilation needs. Given shorter hospital stays and favorable cardiac outcomes, this approach seems appropriate, although pulse steroids may be considered in severe cases. Further research is needed to optimize dosing and duration of therapy.

Disclosure: N. Shirman: None; **L. Harel**: None; **G. Amarilyo**: None; **K. Kaidar**: None; **Y. Butbul Aviel**: None; **M. Heshin Bekenstein**: None; **M. Hamad Saied**: None; **O. Goldzweig**: None; **A. Miler**: None; **Y. Levinsky**: None.

Abstract Number: 1306

Systematic Literature Review of Digital Sleep Outcomes and Endpoints Used to Assess Rheumatoid Arthritis

Anna Fishbein[1], Rachel Lawson[2], Veleka Allen[1], Sophie Wilhelm[1], Tracy Zhang[3], Leanne Williams[1], Karen Chandross[1], Godhuli Chatterjee[4], Markus Kohlmann[5] and Jeffrey Curtis[6], [1]Sanofi, Morristown, NJ, [2]Sanofi, Earley, United Kingdom, [3]Sanofi, Waltham, MA, [4]Sanofi Healthcare India Private Limited, Mumbai, Maharashtra, India, [5]Sanofi, Frankfurt, Germany, [6]University of Alabama at Birmingham, Birmingham, AL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sleep disturbances are prevalent among patients with rheumatoid arthritis (RA), posing a substantial burden to patients and are intricately linked to disease activity and progression. This systematic literature review aimed to 1) identify and evaluate objective digital measures of sleep quality and quantity used in RA research and 2) aggregate present knowledge to inform endpoint selection for future clinical trials.

Methods: A comprehensive search was conducted in Embase, PubMed, and Google Scholar using broad search terms such as "rheumatoid arthritis," "sleep stage," "sleep parameters," "actigraphy," "polysomnography," and "wearable technology." After screening 769 titles and abstracts, 27 articles met inclusion criteria. Data extraction focused on technology used, sleep parameters measured, and correlation between objective and subjective measures.

Results: Three sleep assessment technologies were identified: Polysomnography (PSG;10 studies), wrist/leg actigraphy (16), and novel devices such as armbands and headbands (1). Of these, 8 studies had comparator control patient arms, and 5 studied improvements in sleep in the context of an intervention (e.g. initiation of a biologic therapy such as TNF inhibitors). The most commonly reported sleep parameters were sleep efficiency (SE), sleep latency, total sleep time, wake after sleep onset (WASO), fragmentation index, and number of awakenings. Multiple studies found RA patients experience poor SE (< 85%) and short sleep duration (≤6 hours) (Lee S, etal. 2020, McKenna S, etal. 2018, Katz P, etal. 2021), with 22% of patients experiencing WASO ≥90 minutes nightly (Lee S, etal. 2020). PSG studies confirmed these findings, revealing altered sleep architecture with less stage 2 sleep compared to controls (Bjurström MF, etal. 2017). Sleep disturbance was responsive to advanced therapies, with treatment trials demonstrated improved sleep quality parameters, such as reduced sleep latency and WASO, increase sleep efficiency and deep sleep, as well as sleep quantity with increased total sleep time on anti-TNF therapy (Bjurström MF, etal. 2017, Detert J, etal. 2016, Taylor-Gjevre RM, etal. 2011, Zamarrón C, etal. 2004).

Conclusion: Multiple objective sleep endpoints relevant to RA can be measured with digital technologies to enable sleep assessment. Importantly, patients with RA commonly suffer from sleep disturbance, with the potential for improvement observed in small treatment trials. Further work is needed to better quantify and qualify sleep in patients with RA receiving advanced therapies and explore mechanistic relationships.

Disclosure: A. fishbein: Sanofi, 3; **R. Lawson**: Sanofi, 3; **V. Allen**: Sanofi, 3; **S. Wilhelm**: Sanofi, 3; **T. Zhang**: Sanofi, 3; **L. Williams**: Sanofi, 3; **K. Chandross**: Sanofi, 3; **G. Chatterjee**: Sanofi Healthcare India Private Limited, 3; **M. Kohlmann**: Sanofi, 3; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1307

Plasma levels of monounsaturated fatty acids (MUFAs) positively correlate with disease activity in patients with rheumatoid arthritis (RA)

Martha Belury[1], Rachel Cole[1], Steven Pan[2] and **Beatriz Hanaoka**[2], [1]Ohio State University, Columbus, OH, [2]Oklahoma University Health Sciences Center, Oklahoma City, OK

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) patients have higher body fat percentages, particularly in the abdominal region, which is associated with increased systemic inflammation. Obesity is associated with changes in plasma fatty acid composition, which can affect inflammatory responses. Omega-3 polyunsaturated fatty acids (n3-PUFA) are precursors for anti-inflammatory oxylipins while the roles of n6 PUFAs and monounsaturated fatty acids (MUFAs) remain less well understood. The goal of this study was to investigate FFA composition of plasma of patients with RA and its associations with RA disease activity.

Methods: Cross-sectional study involving 52 RA patients and 30 age-, sex-, and BMI-matched non-RA controls. Participants were evaluated for body mass index (BMI), healthy eating index (HEI), and lipid plasma fatty acid composition after an overnight fast. RA disease activity was assessed using the Clinical Disease Activity Index (CDAI). The correlation between plasma FFAs and CDAI was examined using univariate, Spearman correlation and multivariate linear regression analyses.

Results: Among RA subjects, plasma levels of MUFAs [palmitoleic acid (p=0.022), oleic acid (p=0.001), and gondoic acid (p=0.048)] were higher compared to controls. In contrast, plasma levels of n6 PUFAs [linoleic acid (p=0.031) and arachidonic acid (0.004)] were higher in controls compared to RA patients. Oleic acid ($r = 0.349$, $p = 0.013$) and gondoic acid ($r = 0.435$, $p = 0.002$) showed significant correlations with CDAI. Correlation analyses showed oleic acid ($r = 0.349$, $p = 0.013$) and gondoic acid ($r = 0.435$, $p = 0.002$) significantly correlated with CDAI. Multivariate linear regression analyses revealed CDAI was independently associated with oleic acid ($\beta = 0.09$, 95% CI = 0.02-0.16, $p = 0.014$) and gondoic acid ($\beta = 0.0012$, 95% CI = 0.0005-0.0020, $p = 0.002$), after adjusting for age, sex, BMI, and HEI.

Conclusion: The findings suggest a potential association between elevated plasma MUFAs and disease activity in patients with RA.

Disclosure: M. Belury: None; **R. Cole**: None; **S. Pan**: None; **B. Hanaoka**: None.

Abstract Number: 1308

Predictors of Interstitial Lung Disease Progression in Patients with Rheumatoid Arthritis

Bryant England[1], Austin Wheeler[1], Halie Frideres[2], Scott Matson[3], Geoffrey Thiele[1], Katherine Wysham[4], Grant Cannon[5], Gary Kunkel[6], Gail Kerr[7], Andreas Reimold[8], John Richards[9], Dana Ascherman[10], Paul Monach[11], Joshua Baker[12] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]UNMC Department of Rheumatology, Omaha, NE, [3]University of Kansas, Kansas City, MO, [4]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [5]University of Utah and Salt Lake City VA, Salt Lake City, UT, [6]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [7]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [8]Dallas VA Medical Center, Dallas, TX, [9]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [10]University of Pittsburgh, Pittsburgh, PA, [11]VA Boston Healthcare System, Boston, MA, [12]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of RA-ILD patients stratified by ILD progression.

Variable	Overall (n=347)	ILD progression (n=205)	No progression (n=142)
Age, years	69.5 (9.0)	69.4 (9.1)	69.6 (8.9)
Male sex	91.9%	94.1%	88.7%
White race	75.5%	79.0%	70.4%
Non-Hispanic	89.6%	89.3%	90.1%
Calendar period			
2003-2015	52.4%	73.2%	22.5%
2016-2024	47.6%	26.8%	77.5%
Smoking status			
Never	14.4%	12.7%	16.9%
Former	57.6%	54.6%	62.0%
Current	26.5%	31.2%	19.7%
Missing	1.4%	1.5%	1.4%
BMI, kg/m^2	28.8 (5.0)	28.4 (5.2)	29.4 (4.7)
RA duration, years	12.2 (12.2)	12.5 (12.6)	11.8 (11.7)
Anti-CCP positivity	82.4%	84.7%	78.9%
RF positivity	81.2%	87.2%	71.8%
CDAI	15.3 (12.2)	15.4 (11.9)	15.3 (12.5)
Methotrexate use	35.2%	34.6%	35.9%
Biologic use	16.7%	21.0%	10.6%
Prednisone use	43.2%	55.1%	26.1%
ILD duration, years	1.7 (3.2)	1.6 (3.0)	1.8 (3.4)
UIP pattern	58.8%	67.8%	45.8%
FVC % predicted	80.9 (17.9)	81.1 (17.0)	80.7 (19.3)

Values mean (SD) or %.

Abbreviations: Anti-CCP, anti-cyclic citrullinated peptide antibody, BMI, body mass index; CDAI, clinical disease activity index; FVC, forced vital capacity; ILD, interstitial lung disease; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

Background/Purpose: Interstitial lung disease (ILD) is a frequent extra-articular manifestation of RA predisposing to poor health outcomes. The disease course in RA-ILD is variable, with some patients having stable courses while others experience a more progressive disease course. This variation complicates management decisions, particularly since few predictors of RA-ILD progression have been consistently identified. For example, in some, but not all, prior studies, usual interstitial pneumonia (UIP) ILD pattern has been associated with a more severe disease course. In this study, we aimed to evaluate predictors of RA-ILD progression among participants with ILD in a multicenter, prospective RA cohort.

Methods: We studied RA-ILD patients within the Veterans Affairs Rheumatoid Arthritis registry, a multicenter, prospective cohort of U.S. veterans with RA. RA-ILD was systematically identified, and all cases validated via standardized medical

Table 2. Patient characteristics associated with progression in RA-ILD in a multivariable Cox regression model.

Variable	aHR (95% CI)
Age, per year	**1.03 (1.01, 1.05)**
Female sex	1.19 (0.60, 2.36)
Smoking status	
Never	1 (ref)
Former	**1.60 (1.00, 2.56)**
Current	**1.98 (1.15, 3.40)**
BMI, per kg/m^2	1.01 (0.98, 1.05)
UIP ILD pattern (vs. non-UIP)	**1.46 (1.06, 2.02)**
Calendar period (2016-2024 vs. 2003-2015)	**0.55 (0.38, 0.79)**
RF positivity	1.20 (0.77, 1.87)
CDAI, per 1-unit	1.00 (0.98, 1.01)
Prednisone use	1.33 (0.98, 1.80)
FVC % predicted	
>100	1 (ref)
80-100	1.43 (0.63, 2.15)
60-80	1.37 (0.85, 2.20)
<60	1.43 (0.91, 2.25)

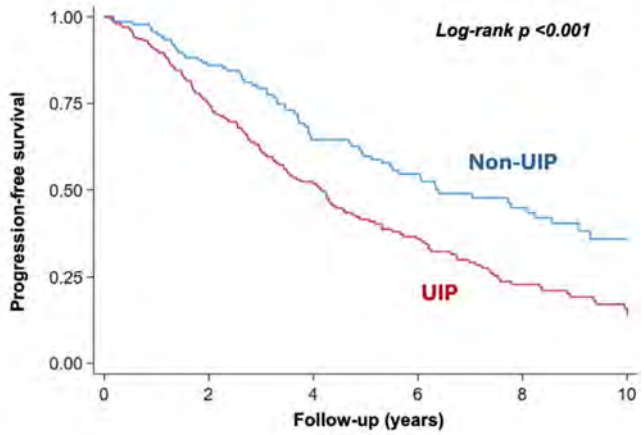
Estimates are adjusted hazard ratios and 95% confidence intervals from a single multivariable model with all listed variables included.

Bolded denotes p value < 0.05

Abbreviations: BMI, body mass index; CDAI, clinical disease activity index; CI, confidence interval; FVC, forced vital capacity; HR, hazard ratio; RA, rheumatoid arthritis; RA-ILD, rheumatoid arthritis-associated interstitial lung disease; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan-Meier plot of progression-free survival by ILD pattern.



Abbreviations: ILD, interstitial lung disease; UIP, usual interstitial pneumonia.

record review, requiring a clinical diagnosis and supportive imaging or biopsy findings. The index date was the later of registry enrollment or ILD diagnosis, to avoid immortal time bias. ILD progression was defined by change in forced vital capacity (FVC; >5% decline over < 3 years follow-up, >10% decline over >3 years of follow-up) or death up to10 years of follow-up. FVC values were obtained from the electronic health record (EHR) manually or with a validated natural language processing (NLP) tool. Candidate predictors included demographics, RA disease characteristics (e.g., autoantibodies, disease activity), and ILD characteristics (e.g., ILD pattern, baseline FVC % predicted). Predictors were obtained from registry and/or EHR data, with ILD pattern determined per treating pulmonologists and/or radiologists. Multivariable Cox regression models were used to identify determinants of progression.

Results: We studied 347 RA-ILD participants (92% male, mean age 69 years, mean ILD duration 1.7 years) (**Table 1**). Over 1,487 patient-years of follow-up, 205 (59%) RA-ILD patients experienced progression. In unadjusted comparisons, those who experienced ILD progression were more likely male, reported White race, initiated follow-up in earlier calendar years, and were more frequently current smokers, RF positive, used prednisone, and had an UIP ILD pattern (**Table 1**). Upon multivariable modeling, factors independently associated with RA-ILD progression included older age (per year aHR 1.03 [1.01, 1.05], smoking status (former vs. never aHR 1.60 [1.00, 2.56]; current vs. never aHR 1.98 [1.15, 3.40], calendar year period (2016-2024 vs. 2003-2015 aHR 0.55 [0.38, 0.79), and UIP ILD pattern (vs. non-UIP aHR 1.46 [1.06, 2.02]) (**Table 2; Figure 1**).

Conclusion: Older age, cigarette smoking history, and UIP ILD pattern were independently associated with RA-ILD progression in this multicenter RA-ILD cohort. These findings may aid in identifying patient subsets most likely to experience ILD progression and who may warrant closer disease monitoring and more aggressive RA-ILD targeted treatment strategies. Additionally, these findings reinforce the importance of smoking cessation in RA-ILD patients.

Disclosure: B. England: Boehringer-Ingelheim, 2, 5; **A. Wheeler**: None; **H. Frideres**: None; **S. Matson**: None; **G. Thiele**: None; **K. Wysham**: None; **G. Cannon**: None; **G. Kunkel**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **A. Reimold**: None; **J. Richards**: None; **D. Ascherman**: None; **P. Monach**: Boehringer-Ingelheim, 2; **J. Baker**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1309

Transcriptomic biomarkers of progression from undifferentiated arthritis to rheumatoid arthritis

Christina Printzis[1], Keerthana Nagesh Prabhu[2], Regina Sakalyte[3], Sigita Stropuviene[3] and **Damini Jawaheer**[1], [1]Northwestern University, Chicago, IL, [2]Washington University in St. Louis, St Louis, MO, [3]Vilnius University, Faculty of Medicine, Institute of Clinical Medicine, Clinic of Rheumatology, Orthopedics Traumatology and Reconstructive Surgery, Vilnius, Lithuania

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: A broad range (6-55%) of patients classified as having undifferentiated arthritis (UA) tend to progress to rheumatoid arthritis (RA), suggesting that UA in these patients may represent the early stages of RA. Our goal was to identify transcriptional biomarkers predictive of progression from UA to RA so that these patients can be differentiated from other UA patients and targeted for early aggressive treatment. We also examined biological changes that accompanied disease progression from UA to RA and spontaneous remission.

Methods: Patients (n=54) with inflammatory arthritis of one or more joints for >4 weeks, but < 12 months, were enrolled in the Vilnius University Hospital Santaros Klinikos Rheumatology Centre early UA cohort and followed prospectively for 12 months. Blood samples were collected at study entry (T0, n=52) and at 12 months (T1, n=35). We examined the transcriptomes at each timepoint using bulk RNA-sequencing. We performed Differential Expression Analysis (a) between UA groups (pre-RA vs pre-remission) at the T0 baseline to identify biomarkers predictive of progression to RA, and (b) within groups (paired samples: T1 vs T0) to assess transcriptional changes associated with progression to RA or spontaneous remission. Genes were considered differentially expressed (DE) using FDR< 0.05 and fold-change >=2. Functional enrichment analysis was also performed.

Results: Of the 54 UA patients, 33 progressed to RA by 12 months, while 21 went into remission. At the T0 baseline, 43 genes were DE between the two UA (pre-RA and pre-remission) groups. These included several genes previously implicated in RA that were over-expressed in the pre-RA group at T0 (e.g. MAOA, DAAM2 and IFI27) and some that were under-expressed (e.g. SOX5, IGLV3-1 and S100B). Functional enrichment analysis identified myeloid cell homeostatis and differentiation pathways significantly enriched among the DE genes. Analysis of samples available at T1 from UA patients who progressed to RA (n=25) or went into remission (n=10), revealed 229 DE genes between the RA and remission groups. These included genes previously associated with RA such as CD177, S100A12, and MMP9 being over-expressed in the RA group, consistent with previous studies, and many immunoglobulin genes being under-expressed. Inflammatory and immune response pathways were significantly enriched among the DE genes. Surprisingly, as UA progressed to RA over time, no significant DE genes were detected between T0 and T1. In contrast, as UA went into remission, 13 genes were DE between T0 and T1, including some genes previously implicated in RA (e.g. CASP5 and OLFM4) which significantly decreased in expression from T0 to T1.

Conclusion: In our cohort, at the pre-RA stage, UA patients exhibited gene expression signatures that may represent predictive biomarkers of progression to RA. The absence of longitudinal transcriptomic changes when UA progressed to RA suggest that molecular mechanisms that drive the disease process in RA were perhaps already under way at the UA (pre-RA) stage, at our study baseline. Remission, on the other hand, was accompanied by decreasing expression of some genes known to have a pro-inflammatory role in RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Printzis: None; **K. Nagesh Prabhu**: None; **R. Sakalyte**: None; **S. Stropuviene**: None; **D. Jawaheer**: None.

Abstract Number: 1310

Naturalized Language Processing Based Extraction of Rheumatoid Arthritis Disease Activity Measures from the Electronic Health Record

Elizabeth Park[1], Iram Kamdar[2], Reid Weisberg[1], Andy Nguyen[1], Joan Bathon[3], Jon Giles[4], Chunhua Weng[5] and Elana Bernstein[1], [1]Columbia University Irving Medical Center, New York, NY, [2]Columbia University Data Science Institute, New York, NY, [3]Columbia University, NEW YORK, NY, [4]Cedars-Sinai Medical Center, New York, NY, [5]Columbia University Department of Biomedical Informatics, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: A treat-to-target approach in rheumatoid arthritis (RA) requires intense monitoring of RA disease activity with measures such as the clinical disease activity index (CDAI). Outside of clinical studies, CDAI may be sparsely recorded by clinicians in real world settings due to their local electronic health record (EHR) systems lacking systematic integration of structured entry forms for CDAI (e.g., homunculus) and variability in documentation practice among clinicians. We hypothesize that most clinicians document CDAI in unstructured free text. Two previous publications developed successful natural language processing (NLP) pipelines extracting CDAI, but the practices were limited to community settings and the Veterans Administration. We explored extracting CDAIs from a large, tertiary academic center EHR with a heterogeneous RA patient population utilizing novel NLP techniques.

Methods: The New York Presbyterian/Columbia University Medical Center Clinical Data Warehouse (NYP/CUMC CDW) contains over 4.5 million patients' data stored in structured and unstructured formats. From a pre-selected group of RA patients in the CDW, a random sample (20%) of free text notes recorded in rheumatology outpatient practices across one EHR system (EPIC) between 2020-2024 were produced. A list of CDAI, its key components, as well as plausible variations in phrasing was generated with expert curation (EP) (Table 1). These keywords, along with serostatus (seropositivity) were extracted using an automated information extraction pipeline, engineered through large language model (LLM) prompts input through Chat GPT-4 Education, a HIPAA compliant, CUMC approved resource (Figure 1).

Table 1. CDAI/Serostatus Terminology Extraction

CDAI Components	CDAI Score Phrasing	Serostatus Terms
Swollen Joint Count: Swollen; SJC; S Tender Joint Count: Tender; TJC; T	"CDAI is..." "CDAI was..." "CDAI was ... today is.." "CDAI went from ... to.."	**Seropositive; Sero+** Rheumatoid Factor (RF) positive; RF+; +RF; RF++; ++RF RF "Number"
Patient Global Assessment Score: Patient Global Assessment of Disease Activity (PGA); Pt Global Score; Pt Score; Pt	"CDAI is <number" "CDAI is >number" "CDAI is number-number"	**Seropositive; Sero+** Anti-citrullinated protein antibodies (CCP) positive; CCP+; CCP++; +CCP; ++CCP CCP "Number"
Physician Global Assessment Score: Physician Global Score; Physician Score; Evaluator Global Assessment of Disease Activity (EGA); Provider Score (Pro); Pr	CDAI Pt/PGA: "Number"; Pr/Pro/EGA: "Number"; SJC/S: "Number"; TJC/T: "Number" = Total Number	**Seronegative; Sero-;** RF negative; negative RF; RF-; -RF CCP negative; negative CCP; CCP-; -CCP

CDAI/Serostatus Terminology Extraction

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

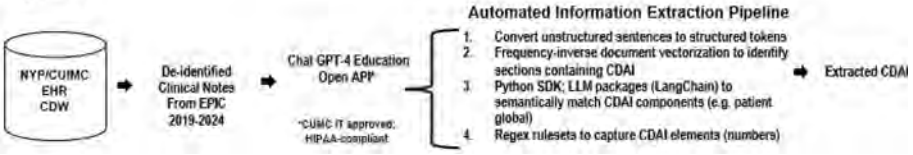
Table 2. Summarized CDAI Extraction

Total RA cohort (n=1,983)*	Prevalence %
CDAI recorded	8.72% (173/1983)
Remission (0-2.8)	34.1% (59/173)
Low Disease Activity (2.9-10.0)	29.4% (51/173)
Moderate disease Activity (10.1-22.0)	17.9% (31/173)
High Disease Activity (22.1-76.0)	17.9% (31/173)
Serologic Status	
Seropositive in total cohort	38.7% (768/1983)
Seropositive in CDAI subset	79.1% (137/173)
Seronegative in total cohort	28.3% (562/1983)
Seronegative in CDAI subset	20.2% (35/173)
Sero status not recorded in total cohort	32.7% (649/1983)
Accuracy	
Precision	0.97
Recall	0.97
F1	0.97

*RA cohort sampled from EHR using International Classification of Disease (ICD) 9 and 10 codes; positive predictive value of 82% when validated against chart review

Summarized CDAI Extraction

Figure 1.



Automated Extraction Pipeline

Results: A total of 1,983 unique RA patients (one note per patient closest to July 1, 2024) were analyzed; 768 (38.7%) were seropositive, 562 (28.3%) were seronegative, and 649 (32.7%) did not have serostatus recorded. The term "CDAI" and its variations were extracted from 173 (8.72%) patients with a median value of 7 (range 0-43). Of the 173 with CDAI recorded, 59 (34.1%) were in remission, 51 (29.4%) had low activity, 31 (17.9%) had moderate activity, and 31 (17.9%) had high activity. Of those with CDAI recorded, 137 (79.1%) were seropositive and 35 (20.2%) were seronegative (Table 2). An expert (EP) performed a chart review of a random 20% sample of the extracted CDAI scores, resulting in a precision of 0.97, recall of 0.97, and F1 score of 0.97.

Conclusion: We demonstrated feasibility and accuracy of a Chat GPT-4 supported NLP/LLM pipeline to extract CDAI scores from a large, academic EHR. At our institution, CDAI appears to be sparsely documented (< 10%) in the sampled portion of notes. Our next steps include: 1) Refining the RA cohort by chart validating those without serostatus (i.e., confirming if they are actual RA cases); 2) Integrating analysis of historical EHRs used prior to EPIC (before 2020) to perform longitudinal extraction of CDAI scores; and 3) Exploring portability of this pipeline to other academic institutions, with the goal of external validation.

Disclosure: E. Park: Amgen, 2, Boehringer Ingelheim, 2, Synthekine, 2; **I. Kamdar**: None; **R. Weisberg**: None; **A. Nguyen**: None; **J. Bathon**: AbbVie/Abbott, 2, Merck, 2, Ono Pharma, 2; **J. Giles**: None; **C. Weng**: None; **E. Bernstein**: AstraZeneca, 5, aTYR, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1311

Decade-Based Trends in First Remission Among Rheumatoid Arthritis Patients: A Population-Based Study

Georges El Hasbani[1], Roslin George[2], Anne Shurtz[1], Cynthia Crowson[3] and Elena myasoedova[2], [1]Mayo Clinic, Rochester, [2]Mayo Clinic, Rochester, MN, [3]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

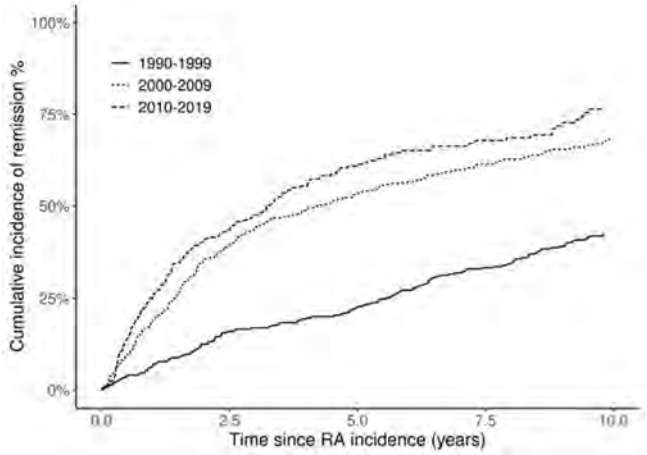
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Early and aggressive treatment of rheumatoid arthritis (RA) has been linked to improved remission rates, but achieving early and sustained remission remains a challenging task. Temporal trends and risk factors for early remission have not been comprehensively studied in longitudinal population-based RA cohorts. We aimed to investigate the likelihood of achieving first remission in RA by decade of RA incidence, serostatus, and by disease modifying drug (DMARD) use.

Methods: Adult residents of a geographically defined area aged ≥18 years who met ≥4 of the 1987 ACR criteria for RA in 1980-2019 were included. All participants were followed until death, last medical contact, or 12/31/2022. Data on RA characteristics, DMARD use (i.e. conventional DMARDs, biologics, targeted synthetic DMARDs), cardiovascular risk factors and comorbidities was manually collected from the medical records. The cumulative incidence of first remission, adjusted for competing risk of death, was evaluated by decade, age, and sex. Cox models were used to examine factors associated with first remission.

Results: The study included 1,098 patients with RA (mean age 55.7, 68.4% female, 62.8% positive for rheumatoid factor (RF) and/or cyclic citrullinated peptide (CCP) antibodies). The cumulative incidence of first remission was higher in persons with RA onset in 2000-2009 and 2010–2019 vs 1990-1999, with 18.9% (95%CI 15.5-23.1%), 25.2% (95% CI 21.3-29.9%) and 6.8% (95% CI 4.4-10.3%) of patients achieving remission in the first year, respectively (**Figure 1**). The likelihood of first remission was higher in patients with RA onset in 2000-2009 (HR 1.75, 95%CI 1.46-2.09) and 2010-2019 (HR 1.79, 95%CI 1.48-2.17) vs 1990-1999.



Cumulative incidence of remission by decade of RA incidence

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Factor	Hazard Ratio (95% Confidence Interval)
Age	1.10 per 10-year increase, (1.05-1.16)
Men vs. women	1.2 (1.04-1.40)
Seropositive vs. seronegative RA	1.23 (1.06-1.43)
Baseline ESR	1.03 per 5 mm/hr increase (1.01-1.04)
Use of methotrexate in the 1st year of RA	1.23 (1.06-1.43)
Use of glucocorticoids in the 1st year of RA	1.21 (1.04-1.42)
Current smoking	0.81 (0.67-0.98)
Non-white race	0.63 (0.48-0.82)

Factors associated with remission

Risk factors associated with the likelihood of first remission included age, sex, seropositivity, baseline ESR, use of methotrexate in first year of RA, use of glucocorticoids in first year of RA, smoking status and race (Table 2). The association between BMI and remission approached statistical significance (HR per 5 unit increase 0.95, 95%CI 0.90-1.01).

The risk of flare after remission was higher in 2000-2009 (HR 1.30, 95%CI 1.07-1.59) and 2010-2019 (HR 1.34, 95%CI 1.08-1.66) vs 1990-1999, and in seropositive vs seronegative patients (HR 1.41, 95%CI 1.18-1.67).

Early exposure to any 2 or more DMARDs (vs 1 DMARD) increased the likelihood of first remission (HR 1.18, 95%CI 1.01-1.38).

Conclusion: The likelihood of achieving first remission in RA has improved across decades. Despite this improvement in remission rates, patients with RA in recent decades were also more likely to flare after remission. DMARD exposure and particularly early use of methotrexate enhances the likelihood of remission. Persons with seropositive and more active RA, men and older patients had higher likelihood of remission, while smoking, higher BMI and non-white race tended to decrease the likelihood of first remission.

Disclosure: G. El Hasbani: None; **R. George**: None; **A. Shurtz**: None; **C. Crowson**: None; **E. myasoedova**: None.

Abstract Number: 1312

Evolution of patients with active rheumatoid arthritis: analysis of disease activity trajectories in a tertiary-care rheumatology department

Elodie Portier[1], Olivier Fogel[2], Terkia Medkour[3], Sophie Hecquet[3] and **Jérôme AVOUAC**[3], [1]Rheumatology department, Bicetre hospital, Le Kremlin Bicetre, France, [2]AP-HP, Paris, France, [3]Rheumatology department, Cochin hospital, Paris, France

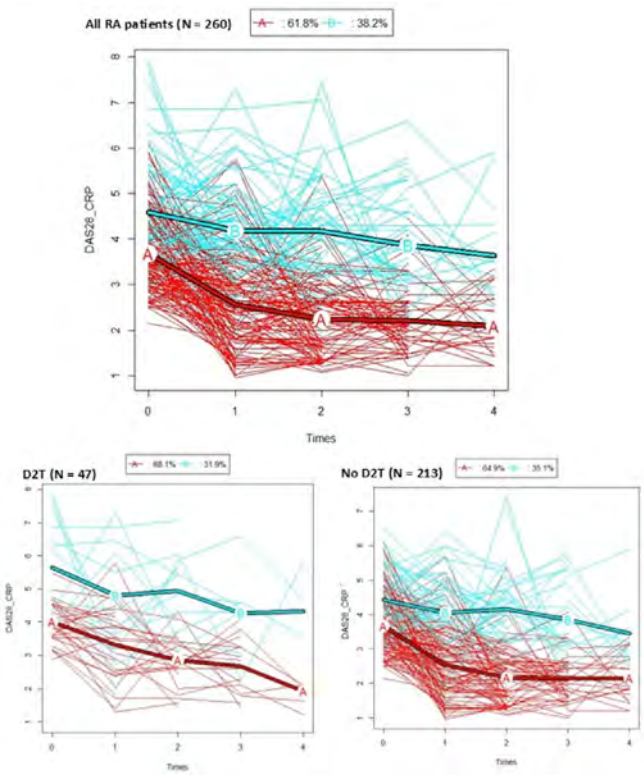
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The objective of this study was to identify clusters of patients with rheumatoid arthritis (RA) in clinical practice, according to evolution of disease activity over time (“trajectories”), when focusing on active RA at inclusion.

Methods: Monocentric study including all RA patients seen from January 2021 to December 2022 in day hospitalization in Cochin Hospital, with active disease at screening (DAS28CRP or ESR ≥ 3.2), and with at least one follow-up visit. DAS28CRP trajectories were identified using k-means clustering. Characteristics at baseline and last-follow up visit

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Trajectories of DAS28CRP during follow-up in all RA population, then according to D2T status.

according to trajectory were described, then analyzed with logistic regression to estimate associations between baseline characteristics and trajectories. Secondary analyses evaluated impact of difficult-to-treat (D2T) status at baseline, and was defined as failure of at least 2 biological (b) or targeted synthetic (ts) DMARDs with different mechanisms of action according to EULAR definition of D2T RA.

Results: Among the 362 patients screened, 260 had at least 2 visits with DAS28CRP values and were included, with a mean follow-up of 24 months (standard deviation, SD 9). Patients were mostly women (87%) of 59 yo, 16 years of disease duration, 81% positive ACPA and 60% erosive status. At baseline, patients had active disease with mean DAS28CRP of 4.1 (SD 1), 4 swollen joints, 6 tender joints, and mean level of CRP of 8 mg/L. They had received a mean of 2 different b/tsDMARDs and 47 (18%) were D2T RA. Two trajectories of DAS28CRP were identified: trajectory A (tA, n=158) with improvement in disease activity over the follow-up period, and trajectory B (tB, n=102) with little change in disease activity (**Figure 1**). At baseline, patients in tB had higher DAS28CRP (4.6 vs 3.7 in tA), more current smokers (23 vs 12%), more D2T status (27 vs 12%), and more treatment with corticosteroids (61 vs 46%) and Janus Kinase inhibitors (JAKi) (9.8 vs 3.2%). Multivariate analysis showed association of trajectories with Body Mass Index (BMI), smoking status, DAS28CRP at baseline and JAKi treatment. At the last visit, patients in tB remained more active than tA with DAS28CRP of 3.9 (vs 2.07) and had received more b/tsDMARDs (3.1 vs 2.3). Finally, 174/260 (67%) had DAS28CRP < 3.2 at the end of follow-up, 149 (94%) in tA and 25 (25%) in tB. There was no difference in trajectories when comparing D2T patients and no-D2T patients (**Figure 1**).

Conclusion: This study revealed two trajectories of RA patients with active disease after a 2-year follow-up, one with achieved remission (tA) and the other with persistent high disease activity (tB). Current smoking and high BMI were the main drivers of tB, these comorbidities are known to be associated with poorer outcomes. Level of DAS28CRP at baseline and use of JAKi were also factors independently associated with trajectories, suggesting higher severity of the disease in these patients. Finally, D2T status had no impact on trajectories. Despite the implementation of a treat-to-target strategy, 75%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of patients following tB did not achieve low disease activity at the end of the follow-up period, highlighting the need for early identification of such patients to ensure timely and optimized management.

Disclosure: E. Portier: None; **O. Fogel**: None; **T. Medkour**: None; **S. Hecquet**: None; **J. AVOUAC**: None.

Abstract Number: 1313

Retrospective Analysis of Factors Associated With Fracture in 2855 Patients With Rheumatoid Arthritis, Stratified by Steroid Use

Jonathan Barnes[1], Hamzah Amin[2] and marwan Bukhari[3], [1]Morecambe Bay NHS Trust, Lancaster, United Kingdom, [2]Lancaster University, Lancaster, United Kingdom, [3]University Hospitals of Morecambe bay NHS foundation trust, Lancaster, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Steroids are used in a proportion of patients with rheumatoid arthritis (RA). Steroids are known to cause a decrease in bone mineral density (BMD), although our recent study suggests a potential for a paradoxically protective effect. We set out to determine if traditional fracture risk factors for fracture are appropriate in those with RA who have been treated with steroids.

The objective of this study was to determine what factors influence fracture in those with rheumatoid arthritis (RA) having received steroid therapy and those who have not, as well as comparing to see if the patterns of fractures are different among those treated with steroids compared to those who have not.

Methods: patients with rheumatoid arthritis (RA) who underwent a DEXA scan at a regional scanner in the North West of England between 2004 and 2021. Demographic data of these patients were collected, including steroid use, alcohol consumption, smoking, secondary osteoporosis, etc., along with the classic FRAX™ risk factors. Bone mineral density (BMD), Z scores and T scores were collected. Group comparisons were performed using t-tests for continuous variables and Chi squared tests for categorical variables, comparing those treated with steroids (past or current) and those not.

Results: 2855 patients were included in the study. Of these patients, 2313 (81.0%) were female, the mean age at scanning was 66.1 (SD ±12.5). Corticosteroid use, either current or prior was reported in 947 patients (33.2%). Fractures were observed in 309 (32.6%) of steroid users and 693 (36.3%) of non-users. Steroid use was not associated with an increase in fractures, rather a reduction - although not statistically significant ($p = 0.057$). Interestingly, among 758 patients currently being treated with steroids, 228 (30.0%) had fractures, compared to those not currently on steroids there were 2097 patients with 774 (36.9%) of those having a fracture. This is suggestive of a protective effect of current steroid use against fracture ($p < 0.01$), although causality cannot be inferred.

The patterns of fractures similar between those having steroid therapy and not, other than forearm fractures which were more common in those without steroid treatment ($p = 0.032$).Traditional FRAX™ factors were not found to be good predictors of fracture in this cohort of patients using steroids, other than femoral neck BMD ($p < 0.01$) and family history of fracture ($p < 0.01$), which both significantly increased fracture risk. Higher total body fat percentage was found to increase fracture risk in both groups of patients ($p < 0.01$), weight was not statistically significant in either group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Classical FRAX™ risk fractures were not significant predictors of fracture in those on steroids with RA, other than family history and femoral neck BMD. The best predictors of fractures in this cohort were bone mineral density analysis, family history, height loss and total fat percentage.

Fracture patterns were similar between those with and without prior or current steroids, other than fractures of the forearm, which were less likely in those steroids on steroids. Further modelling is needed to determine odds ratios of risk factors at specific sites .

Disclosure: J. Barnes: None; **H. Amin**: None; **m. Bukhari**: None.

Abstract Number: 1314

Protein-Specific Anti-Malondialdehyde-Acetaldehyde Antibodies and Cardiovascular Disease Outcomes in Rheumatoid Arthritis

Julia King[1], Michael Duryee[1], Punyasha Roul[2], Katherine Wysham[3], Grant Cannon[4], Gary Kunkel[5], John Richards[6], Isaac Smith[7], Beth Wallace[8], Gail Kerr[9], Andreas Reimold[10], Pascale Schwab[11], Daniel Anderson[12], Wenxian Zhou[13], Joshua Baker[14], Ted Mikuls[1], Bryant England[1] and Tate Johnson[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]UNMC, Omaha, NE, [3]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [6]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [7]Duke University Hospital, Durham, NC, [8]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [9]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [10]Dallas VA Medical Center, Dallas, TX, [11]VA Portland and Oregon Health & Science University, Portland, OR, [12]0587964, Durham, NC, [13]University of Nebraska Medical Center, Bellevue, NE, [14]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular disease (CVD) remains the leading cause of death in rheumatoid arthritis (RA), driven primarily by atherosclerotic CVD (ASCVD) and heart failure (HF). Malondialdehyde-acetaldehyde (MAA) adducts are highly immunogenic post-translational modifications (PTM) that result from oxidative stress. MAA adducts are enriched in serum and synovial fluid from patients with RA, as well as the serum and atheromatous lesions in non-RA patients with coronary artery disease. Given the ongoing need to improve CVD risk stratification and management in RA, our objective was to evaluate the associations of protein-specific anti-MAA antibodies with incident ASCVD and HF outcomes in RA.

Methods: We conducted a cohort study among participants in the multicenter Veterans Affairs RA registry. Antibodies to MAA-modified-albumin, -collagen, -fibrinogen, and -vimentin (IgA, IgG, IgM isotypes) were measured by ELISA on banked serum from registry enrollment. Antibody concentrations were log transformed and standardized (per 1 S.D.), categorized into quartiles, and dichotomized at the highest quartile (high vs. low). Incident ASCVD (fatal or non-fatal myocardial infarction or stroke) and HF (HF hospitalization or HF-related death) were identified using validated administrative algorithms in linked VA, Medicare, and National Death Index data. Patients were followed from enrollment to incident CVD, death, or end of study period (12/2022). The associations of anti-MAA antibodies with incident ASCVD and HF were tested separately in multivariable Cox regression models adjusted for age, sex, race, smoking status, body mass index, comorbidities (hypertension, hyperlipidemia, diabetes, chronic lung disease), seropositivity (for RF and/or anti-CCP), and DAS28.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Association of protein-specific anti-MAA antibody concentrations with incident ASCVD and HF in rheumatoid arthritis*

	ASCVD		Heart Failure	
Anti-MAA-Albumin				
	Per 1 S.D.	*High vs. low*	*Per 1 S.D.*	*High vs. low*
IgG	1.00 (0.88-1.14)	1.08 (0.86-1.35)	0.91 (0.79-1.04)	0.88 (0.68-1.14)
IgM	1.06 (0.94-1.21)	1.08 (0.86-1.36)	0.98 (0.85-1.13)	1.19 (0.93-1.53)
IgA	1.06 (0.94-1.20)	1.07 (0.85-1.34)	0.87 (0.76-1.01)	0.97 (0.75-1.25)
Anti-MAA-Collagen				
	Per 1 S.D.	*High vs. low*	*Per 1 S.D.*	*High vs. low*
IgG	0.93 (0.85-1.03)	0.85 (0.67-1.09)	0.98 (0.88-1.11)	0.97 (0.74-1.26)
IgM	0.92 (0.83-1.01)	0.88 (0.69-1.13)	0.98 (0.88-1.09)	0.95 (0.72-1.24)
IgA	0.93 (0.84-1.04)	1.13 (0.90-1.43)	1.02 (0.91-1.15)	1.04 (0.80-1.36)
Anti-MAA-Fibrinogen				
	Per 1 S.D.	*High vs. low*	*Per 1 S.D.*	*High vs. low*
IgG	0.99 (0.89-1.11)	0.88 (0.69-1.12)	0.78 (0.59-1.04)	0.78 (0.59-1.04)
IgM	0.94 (0.85-1.05)	1.01 (0.79-1.28)	0.98 (0.74-1.28)	0.98 (0.74-1.28)
IgA	1.01 (0.90-1.12)	1.05 (0.83-1.34)	0.85 (0.65-1.13)	0.85 (0.65-1.13)
Anti-MAA-Vimentin				
	Per 1 S.D.	*High vs. low*	*Per 1 S.D.*	*High vs. low*
IgG	1.10 (0.98-1.23)	**1.42 (1.13-1.79)**	1.05 (0.93-1.18)	1.13 (0.87-1.48)
IgM	1.08 (0.96-1.21)	**1.27 (1.01-1.60)**	1.08 (0.95-1.23)	1.25 (0.97-1.61)
IgA	1.08 (0.95-1.22)	**1.30 (1.03-1.64)**	1.07 (0.93-1.23)	1.03 (0.79-1.34)

* Values are hazard ratios (95% confidence intervals) estimated in multivariable Cox regression adjusted for age, sex, race, body mass index, smoking status, CVD risk factors, seropositivity, and DAS28.

High vs. low based on highest quartile (Q4) vs. lower quartiles (Q1-Q3).

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; HF, heart failure; MAA, malondialdehyde acetaldehyde; S.D., standard deviation.

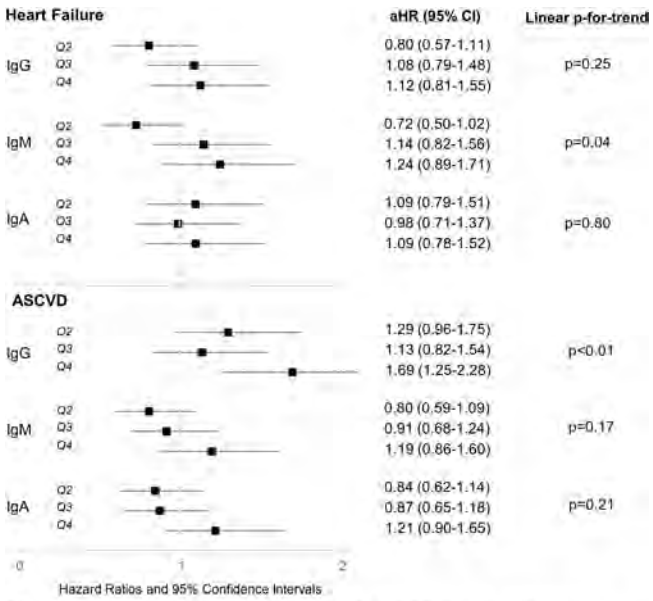


Figure 1. Forest plot illustrating the association of anti-MAA-vimentin isotypes with incident heart failure and ASCVD outcomes. Estimates are hazard ratios adjusted (aHR) for age, sex, race, smoking status, BMI, traditional CVD risk factors, seropositivity, and DAS28. Quartile1 (Q1) is the lowest quartile and serves as the reference (dashed line). A

Figure 1. Association of anti-MAA vimentin quartiles with ASCVD and HF in RA

Results: There were 3,572 participants included in this study (87% male, mean age 64 years, mean DAS28 3.5). Among those without prior ASCVD and HF, we observed 398 incident ASCVD (20.9 events per 1000 person years [PY] over 23,056 PY follow-up) and 327 incident HF events (14.2 per 1000 PY over 19,049 PY follow-up). High values (top vs. lower quartiles) of anti-MAA-vimentin were significantly associated with incident ASCVD for IgG (aHR 1.42, 95% CI 1.13-1.79), IgM (1.27, 1.01-1.60), and IgA isotypes (1.30, 1.03-1.64; **Table 1**). A dose-dependent relationship was observed between IgG anti-MAA-vimentin and incident ASCVD (p< 0.01 for trend across all 4 quartiles; **Figure 1)**. In analyses of all 4 quartiles, higher IgM anti-MAA-vimentin tended to be associated with incident HF (p for trend 0.04; **Figure 1**); findings were not significant for analyses categorized as high vs. low (aHR 1.25, 0.97-1.61; **Table 1**). Other protein-specific anti-MAA antibodies were not associated with ASCVD or HF.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Antibodies against MAA-modified vimentin were independently associated with incident ASCVD in a large, prospective RA cohort. Vimentin, an extracellular matrix protein, commonly undergoes PTM during RA development and MAA is over-expressed in myocardial tissues in animal models of RA. These data support the hypothesis that vimentin modification may serve as a unique driver of ASCVD in RA, and anti-MAA-vimentin antibodies may facilitate CVD risk stratification in RA.

Disclosure: J. King: None; **M. Duryee**: None; **P. Roul**: None; **K. Wysham**: None; **G. Cannon**: None; **G. Kunkel**: None; **J. Richards**: None; **I. Smith**: None; **B. Wallace**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **A. Reimold**: None; **P. Schwab**: None; **D. Anderson**: None; **W. Zhou**: None; **J. Baker**: Amgen, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Johnson**: None.

Abstract Number: 1315

High-resolution thermography and Artificial Intelligence to evaluate and classify Rheumatoid Arthritis

Kale Mayor[1], Joey Mercier[1], Yuxi Long[2], David Robinson[1], Pingzhao Hu[2], Hani El-Gabalawy[1] and Liam O'Neil[1], [1]University of Manitoba, Winnipeg, MB, Canada, [2]Western University, London, ON, Canada

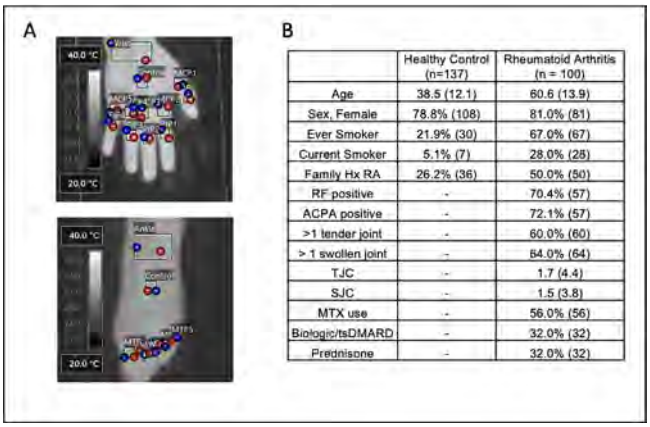
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune polyarthritis that typically affects the small joints of the hands and feet. While imaging modalities such as ultrasound and MRI are valuable for detecting synovitis, their use can be limited by technical requirements and cost. Thermography is a non-invasive imaging technique that captures pixel-level temperature data and has seen growing interest in the assessment of inflammatory arthritis. We aimed to determine if thermal imaging of the hands and feet can effectively distinguish RA patients from healthy controls (HC).

Methods: RA patients were recruited from an academic rheumatology clinic (Winnipeg, Canada). Healthy controls (HC) were recruited through advertising. Thermal images of the dorsal aspects of the hands and feet were captured with a Flir A700 camera. Regions of interest (ROI) were pre-identified as joints commonly affected in RA (Fig1A). ROIs were manually gated, and the max/min/average temperatures were extracted. Data analysis was performed in R to identify temperature differences between groups, followed by machine learning classification. Thermograms were also analyzed using a deep learning model which deployed unsupervised feature extraction (DINOV2) and classification (ElasticNet) in Python.

Results: We recruited 100 RA patients and 137 HC (Fig1B). Principle components analysis using ROI thermogram data revealed clear separation between RA and HC (Fig2A). Differential analysis identified 56 of 114 temperature parameters that were significantly higher in RA patients, for example the maximum temperatures of the right 5th PIP joint (adjusted $p=1.3\times10^{-8}$) and right 4th PIP joint (adjusted $p=7.6\times10^{-8}$). All thermogram parameters (min, max, avg) were increased in joints that were tender or swollen on clinical examination in RA (Fig2C, all p-value < 0.0001). Using thermogram ROI data, XGboost achieved an AUC of .869 to classify RA from control (test set, Fig3A). Rankings of variable importance by SHAP index included average temperatures of L ankle, L Wrist and L 3rd PIP (Fig3B). A computer vision model achieved high performance in classifying RA from controls using entire thermograms (without ROI information), with an AUC of 0.977 and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



	Healthy Control (n=137)	Rheumatoid Arthritis (n = 100)
Age	38.5 (12.1)	60.6 (13.9)
Sex, Female	78.8% (108)	81.0% (81)
Ever Smoker	21.9% (30)	67.0% (67)
Current Smoker	5.1% (7)	28.0% (28)
Family Hx RA	26.2% (36)	50.0% (50)
RF positive	-	70.4% (57)
ACPA positive	-	72.1% (57)
>1 tender joint	-	60.0% (60)
> 1 swollen joint	-	64.0% (64)
TJC	-	1.7 (4.4)
SJC	-	1.5 (3.8)
MTX use	-	56.0% (56)
Biologic/tsDMARD	-	32.0% (32)
Prednisone	-	32.0% (32)

Figure 1 – Thermography of RA patients and healthy controls. (A) Example of thermal images of dorsal hands and feet with gating for regions of interest (ROI). (B) Baseline demographics.

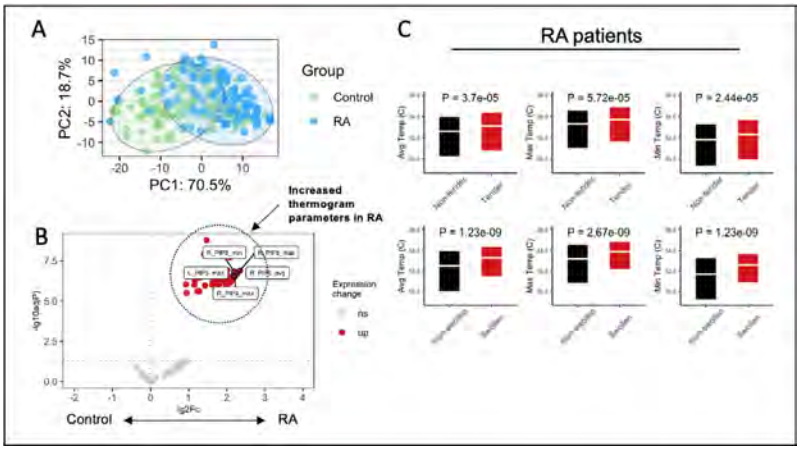
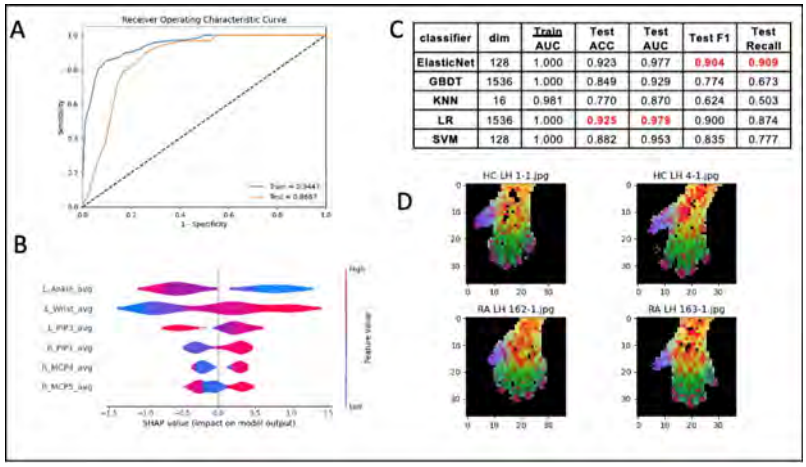


Figure 2: Joint thermography distinguishes RA from healthy controls. (A) Principal components analysis of thermal ROIs. (B) Volcano plot of differential thermal ROI parameters comparing RA and control. (C) Comparison (t-test) of thermal parameters between clinically tender joints (upper) and swollen joints (lower).



classifier	dim	Train AUC	Test ACC	Test AUC	Test F1	Test Recall
ElasticNet	128	1.000	0.923	0.977	0.904	0.909
GBDT	1536	1.000	0.849	0.929	0.774	0.673
KNN	16	0.981	0.770	0.870	0.624	0.503
LR	1536	1.000	0.925	0.979	0.900	0.874
SVM	128	1.000	0.882	0.953	0.835	0.777

Figure 3 – Machine learning to classify RA and controls using thermography. (A) Receiver operator curves derived from an XGboost classifier algorithm (B) SHAP value of the top 6 most important features to classify RA from controls. (C) Summary tables of classifier models used after feature extraction using DINOV2 and multiple classification approaches. (D) Thermal images colorized based on the top 3 features extracted using ElasticNet in the channels red, green and blue.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

recall of 0.909 (Fig. 3C). Principal components from this model were mapped to red, green, and blue channels to visualize thermographic differences between RA and control subjects (Fig. 3D).

Conclusion: Thermal imaging is an inexpensive and readily accessible method for detecting synovitis in the small joints of the hands and can readily discriminate the hand joint of a spectrum of RA patients from those of unaffected healthy controls. As such, this modality may be a cost-effective approach to detecting subtle joint inflammation at the earliest stages of RA onset, for example in individuals with clinically suspect arthralgia.

Disclosure: K. Mayor: None; **J. Mercier**: None; **Y. Long**: None; **D. Robinson**: None; **P. Hu**: None; **H. El-Gabalawy**: None; **L. O'Neil**: None.

Abstract Number: 1316

Predicting mortality of rheumatoid arthritis in China: A nation-wide cohort study

Kangping Huang[1], Shixiong Wei[2], Lan Zhang[3], Xinhao Li[2], Mucong Li[2], Chen Yu[4], Nan Jiang[2], Jiuliang Zhao[2], Yanhong Wang[5], Chanyuan Wu[2], Peng Yin[6], Qian Wang[2], Mengtao Li[2], Xinping Tian[2] and Xiaofeng Zeng[7], [1]Peking Union Medical College, Beijing, Beijing, China (People's Republic), [2]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [3]School of Public Health, Peking University, Beijing, Beijing, China (People's Republic), [4]Peking Union Medical College Hospital, Dong Cheng Qu, Beijing, China (People's Republic), [5]Department of Epidemiology and Biostatistics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, School of Basic Medicine, Peking Union Medical College, Beijing, Beijing, China (People's Republic), [6]National Center for Chronic and NCD Control and Prevention, Chinese Center for Disease Control and Prevention, Xicheng, Beijing, China (People's Republic), [7]Peking Union Medical College Hospital Department of Rheumatology and Clinical Immunology, Beijing, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease associated with increased mortality, primarily due to systemic inflammation and comorbidities. While previous studies have identified some prognostic factors in RA, there remains a lack of robust, clinically applicable tools adapted to the Chinese population. This study aims to develop a predictive model for all-cause mortality in Chinese RA patients using routinely available clinical data.

Methods: The clinical data utilized in this study were obtained from the database of the Chinese Registry of Rheumatoid Arthritis (CREDIT), while the survival outcome data were from the Chinese Center for Disease Control and Prevention (CDC) from October 2003 to December 2021. Variable selection was performed using the least absolute shrinkage and selection operator (LASSO) and univariate Cox regression.A multivariate Cox proportional hazards model was constructed and calibrated. Model performance was assessed using Harrell's C-index and Brier score. External validation was conducted using an independent data as validation set from central China provinces (Henan, Hubei, and Hunan) in China, and data from other provinces was randomly split into training and internal test set. A nomogram was developed based on the final multivariate model to facilitate clinical application.

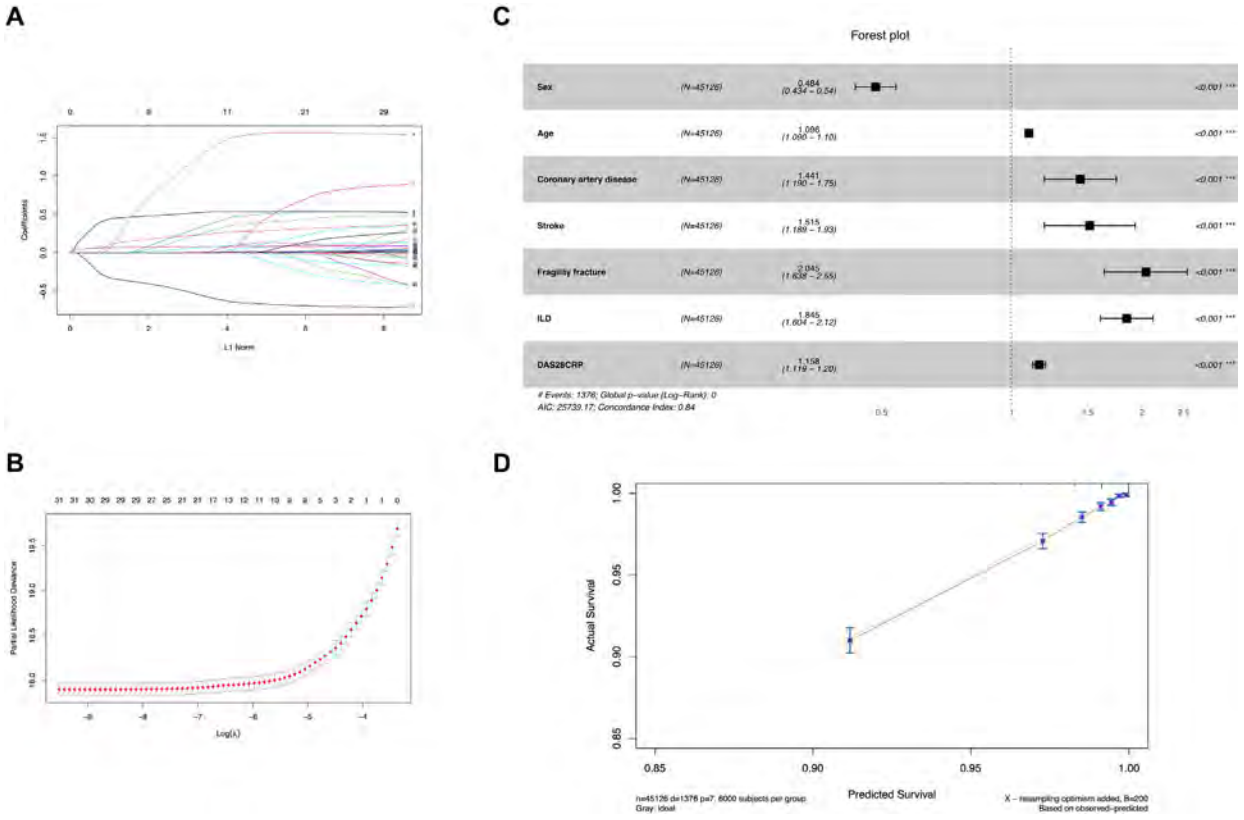
Results: A total of 62,321 patients with complete clinical data (Mean age: 53.13 years, SD: 12.85 years; female: 49,790, 79.9%) from 450 medical centers across the country were included in this study. Among them, 1,901 deaths (3.0%) were recorded during follow-up. 45,126, 12,058, and 5,137 patients were included in training, validation, and test set,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

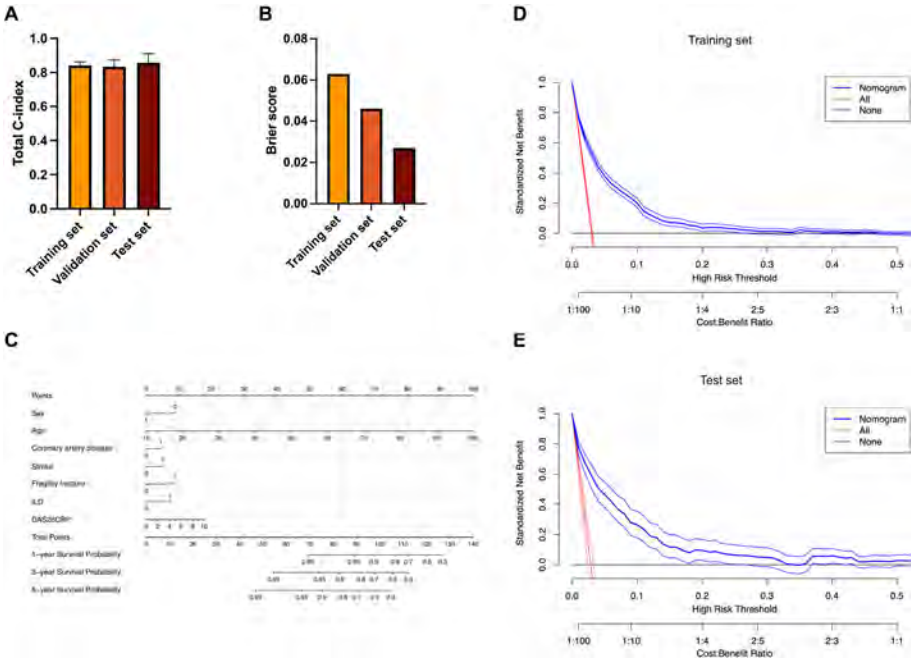
	Overall	Censored	Event	HR	p value
n (%)	62321 (100.0)	60422 (97.0)	1899 (3.0)		
Female (%)	49774 (79.9)	48675 (80.6)	1099 (57.9)	0.34 (0.31-0.37)	<0.001
Age (year) (mean (SD))	53.13 (12.85)	52.68 (12.67)	67.27 (10.30)	1.11 (1.11-1.12)	<0.001
Coronary artery disease (%)	1418 (2.3)	1225 (2.0)	193 (10.2)	5.13 (4.42-5.95)	<0.001
Stroke (%)	815 (1.3)	707 (1.2)	108 (5.7)	5.26 (4.33-6.39)	<0.001
Fragility fracture (%)	1173 (1.9)	1045 (1.7)	128 (6.7)	3.95 (3.3-4.72)	<0.001
Arthroplasty (%)	921 (1.5)	870 (1.4)	51 (2.7)	1.89 (1.43-2.49)	<0.001
Malignancy (%)	753 (1.2)	719 (1.2)	34 (1.8)	1.57 (1.12-2.2)	0.024
ILD (%)	2848 (4.6)	2491 (4.1)	357 (18.8)	4.85 (4.32-5.45)	<0.001
Smoking (%)				1.86 (1.72-2.01)	<0.001
Never smoker	58127 (93.3)	56472 (93.5)	1655 (87.2)		
Ever smoker	1379 (2.2)	1264 (2.1)	115 (6.1)		
Smoker	2815 (4.5)	2686 (4.4)	129 (6.8)		
Family history (%)	1181 (1.9)	1170 (1.9)	11 (0.6)	0.56 (0.31-1.01)	<0.001
Diabetes mellitus (%)	1820 (2.9)	1743 (2.9)	77 (4.1)	2.71 (2.15-3.41)	0.004
Hypertension (%)	4760 (7.7)	4620 (7.6)	160 (8.4)	2.17 (1.84-2.55)	0.225
Hyperlipidemia (%)	1618 (2.6)	1588 (2.6)	30 (1.6)	1.13 (0.79-1.63)	0.006
Joint involvement pattern (%) *				1.17 (1.13-1.21)	<0.001
<= 1 Large joint	4 (0.0)	4 (0.0)	0 (0.0)		
2-10 Large joints	2904 (4.7)	2818 (4.7)	86 (4.5)		
1-3 Small joints	7577 (12.2)	7413 (12.3)	164 (8.6)		
4-10 Small joints	19158 (30.7)	18672 (30.9)	486 (25.6)		
> 10 joints	32678 (52.4)	31515 (52.2)	1163 (61.2)		
Serology (%) †				1.36 (1.21-1.53)	<0.001
Negative RF and ACPA	0 (0.0)	0 (0.0)	0 (0.0)		
Low Positive RF and ACPA	14916 (23.9)	14570 (24.1)	346 (18.2)		
High Positive RF and ACPA	47405 (76.1)	45852 (75.9)	1553 (81.8)		
Symptoms > 6 Weeks (%)	57390 (92.1)	55593 (92.0)	1797 (94.6)	1.31 (1.07-1.6)	<0.001
Positive RF (%)	53934 (86.5)	52227 (86.4)	1707 (89.9)	1.34 (1.16-1.56)	<0.001
Positive ACPA (%)	49991 (80.2)	48448 (80.2)	1543 (81.3)	1 (0.89-1.13)	0.261
Increased ESR at baseline (%)	36793 (59.0)	35297 (58.4)	1496 (78.8)	2.67 (2.39-2.98)	<0.001
Increased CRP at baseline (%)	55770 (89.5)	53973 (89.3)	1797 (94.6)	2.1 (1.72-2.57)	<0.001
Swollen joint count (mean (SD))	7.69 (8.09)	7.63 (8.06)	9.81 (8.73)	1.03 (1.02-1.03)	<0.001
Tender joint counts (mean (SD))	8.46 (8.50)	8.37 (8.47)	11.17 (9.16)	1.03 (1.03-1.04)	<0.001
DAS28ESR (mean (SD))	5.09 (1.74)	5.06 (1.74)	5.87 (1.63)	1.29 (1.25-1.32)	<0.001
DAS28CRP (mean (SD))	4.51 (1.65)	4.48 (1.64)	5.28 (1.59)	1.31 (1.28-1.35)	<0.001
CDAI (mean (SD))	26.10 (17.52)	25.88 (17.47)	33.03 (17.68)	1.02 (1.02-1.02)	<0.001
SDAI (mean (SD))	29.05 (48.75)	28.78 (49.36)	37.54 (20.14)	1 (1-1)	<0.001
Duration of illness (year) (mean (SD))	6.60 (7.80)	6.51 (7.68)	9.45 (10.46)	1.04 (1.03-1.04)	<0.001

	Training	Validation	Test	p value
n (%)	45126 (72.4)	12058 (19.3)	5137 (8.2)	
Female (%)	35818 (79.4)	9696 (80.4)	4260 (82.9)	<0.001
Age (mean (SD))	53.32 (12.83)	52.90 (12.82)	51.96 (13.08)	<0.001

* Detailed definition of classification refers to ACR/EULAR 2010 criteria
† In order to minimizing classification bias, CREDIT registry excludes seronegative RA



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



respectively. Assisted with LASSO method, a multivariate Cox model with sex, age, coronary artery disease (CAD), stroke, fragility fracture, interstitial lung disease (ILD), DAS28CRP was built and calibration curve showed great agreement between predicted and observed 3-year survival probabilities. The model demonstrated consistent discrimination across datasets, with Harrell's C-indices of 0.841 (95% CI: 0.816–0.863) in the training set, 0.857 (0.779–0.911) in the test set, and 0.834 (0.784–0.874) in the validation set. Decision curve analysis indicated that the derived nomogram offers meaningful clinical benefit.

Conclusion: This study developed a robust prediction model for all-cause mortality in patients with RA using routinely collected baseline data. The model offers a practical tool for stratifying patients by prognostic risk, particularly through assessment of comorbidity burden.

Disclosure: K. Huang: None; **S. Wei**: None; **L. Zhang**: None; **X. Li**: None; **M. Li**: None; **C. Yu**: None; **N. Jiang**: None; **J. Zhao**: None; **Y. Wang**: None; **C. Wu**: None; **P. Yin**: None; **Q. Wang**: None; **M. Li**: None; **X. Tian**: None; **X. Zeng**: None.

Abstract Number: 1317

The Association Between Insomnia and Rheumatoid Arthritis: A Systematic Review and Meta-Analysis of 546,822 Patients

Mohamed Abdelsalam[1], Maryam Lasheen[2], Menat Alla Ayman Ali Mahdy[3], Hadeer Hafez[4], Nourhan Abouelella[5], Mohamed Al-Adl[6] and Mohamed Reda Awad[7], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]Misr University For Science and Technology, Helwan, Al Qahirah, Egypt, [3]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [4]6th October University, 6 october, Al Jizah, Egypt, [5]Faculty of Medicine, Misr University for Science and Technology, 6 october, Al Jizah, Egypt, [6]Faculty of medicine Al-Azhar University Cairo, Nasr City, Egypt, [7]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Insomnia and rheumatoid arthritis (RA) are caught in a snowball effect, where chronic pain disrupts sleep and causes poor sleep quality, which in turn increases pain sensitivity. This growing cycle intensifies RA-related symptoms, further impairing patients physical function and psychological well-being. Despite this significant impact, the association between RA and insomnia remains underexplored. This study aims to explore the association between RA, high disease activity, and insomnia to provide deeper insights into its implications.

Methods: We systematically searched PubMed, Web of Science, and Scopus from inception until March 18, 2025, following PRISMA guidelines (Fig. 1). Studies were included if they had a case-control, cohort, or cross-sectional design and confirmed RA diagnosis by a rheumatologist, classification criteria, ICD codes, or self-reported physician diagnosis. Meta-analysis, applying both random- and fixed-effects models, estimated the pooled association between insomnia and RA, comparing RA patients with controls, those with low/remission disease activity versus moderate/high disease activity, and rheumatoid factor (RF) +ve versus RF -ve patients. Data were extracted and analyzed using Review Manager (RevMan), with heterogeneity assessed using I^2.

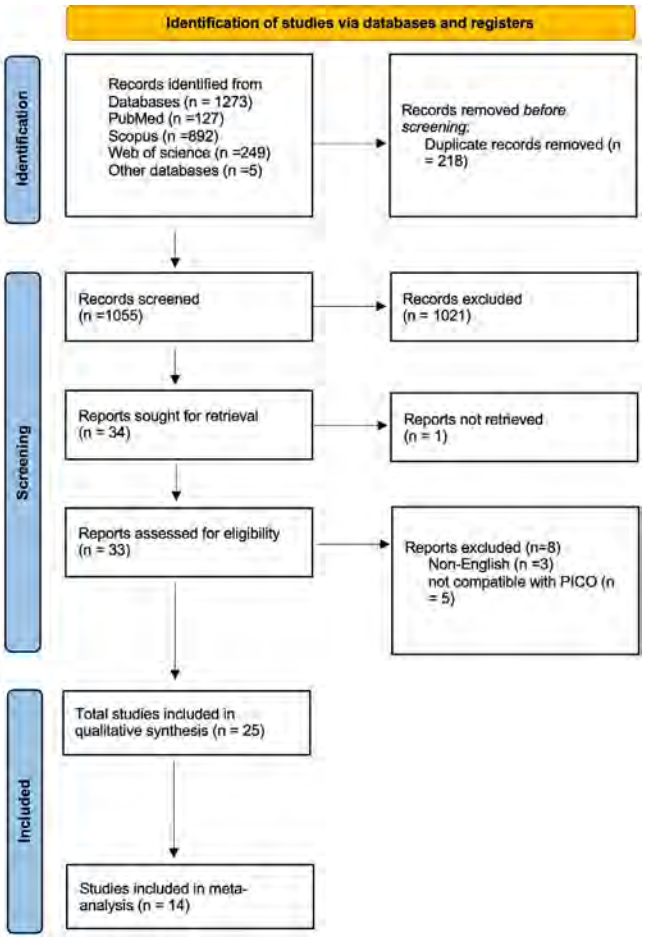


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

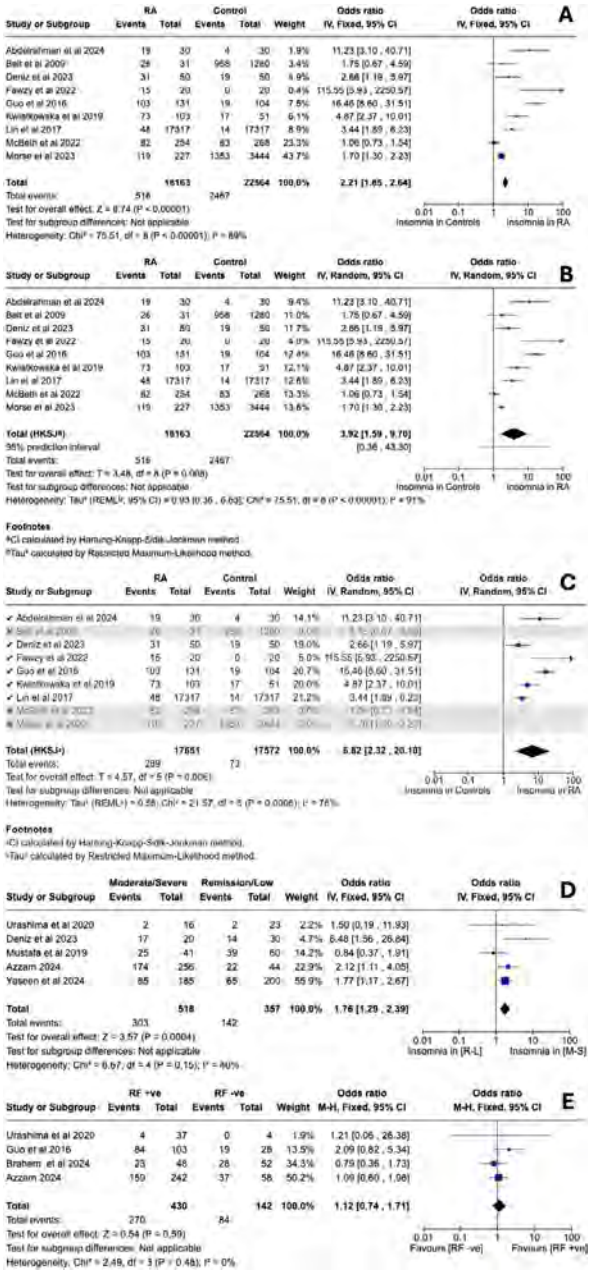
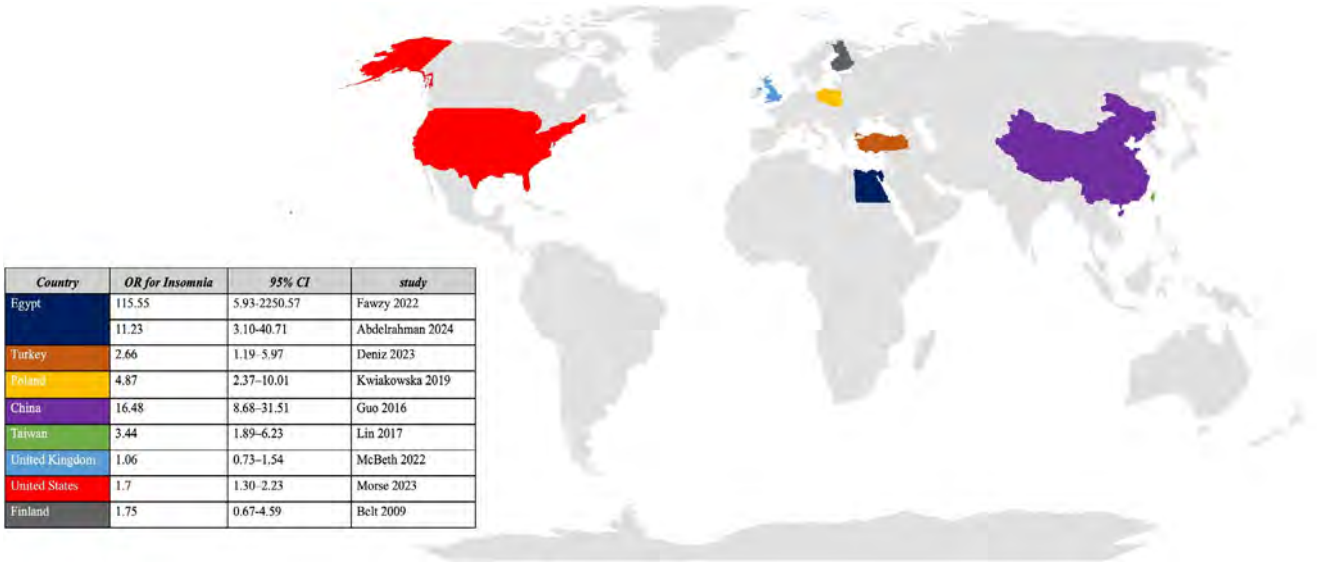


Figure (2) Forest Plots of the Association Between Insomnia, RA, Disease Activity, and RF Status. (A) Fixed-Effects Model: Studies included: Abdelrahman et al. 2024, Belt et al. 2009, Deniz et al. 2023, Fawzy et al. 2022, Guo et al. 2016, Kwiatkowska et al. 2019, Lin et al. 2017, McBeth et al. 2022, Morse et al. 2023. Overall: Significant association between insomnia and RA (OR = 2.21; 95% CI: 1.85–2.64), with considerable heterogeneity (I2=89%). Test for overall effect: Z=8.74 (P<0.00001). Heterogeneity: $\chi2=75.51$, df=8 (P<0.00001). (B) Random-Effects Model: Studies included: Same as fixed-effects model. Overall: Significant association (OR = 3.92; 95% CI: 1.59–9.70), with considerable heterogeneity (I2=91%; $\tau2=0.93$). Test for overall effect: T=3.48 (P=0.008). Heterogeneity: $\chi2=75.51$, df=8 (P<0.00001). (C) Sensitivity Analysis (Excluding Outliers): Studies included: Abdelrahman et al. 2024, Deniz et al. 2023, Fawzy et al. 2022, Guo et al. 2016, Kwiatkowska et al. 2019, Lin et al. 2017. Excluded studies: Belt et al. 2009, McBeth et al. 2022, Morse et al. 2023. Overall: Stronger association (OR = 6.82; 95% CI: 2.32–20.10), with reduced but substantial heterogeneity (I2=76%; $\tau2=0.58$). Test for overall effect: T=4.57 (P=0.006). Heterogeneity: $\chi2=21.57$, df=5 (P=0.0006). Insomnia was consistently associated with RA across models, with the strongest effect observed after excluding outliers (OR = 6.82). (D) Insomnia in Moderate/Severe RA vs. Remission/Low RA: Studies included: Urashima 2020, Deniz 2023, Azzam 2024, Mustafa 2019, Yassen 2024. Overall: Significant association between moderate/severe insomnia and RA (OR = 1.76; 95% CI: 1.29–2.39), with moderate heterogeneity (I2=40%). Test for overall effect: Z=3.57 (P=0.0004). Heterogeneity: $\chi2=6.67$, df=4 (P=0.15). (E) RF-Positive vs. RF-Negative Status in RA: Studies included: Urashima 2020, Guo 2016, Brahem 2024, Azzam 2024. Overall: Non-significant association between Insomnia and RF positivity in RA (OR = 1.12; 95% CI: 0.74–1.71), with no heterogeneity (I2=0%). Test for overall effect: Z=0.54 (P=0.59). Heterogeneity: $\chi2=2.49$, df=3 (P=0.48). Heterogeneity was high in all analyses, likely due to variability in study designs and populations. CI, confidence interval; df, degrees of freedom; OR, odds ratio; I2, heterogeneity index; $\tau2$, Tau-squared; RF, Rheumatoid Factor; RA, Rheumatoid Arthritis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Country	OR for Insomnia	95% CI	study
Egypt	115.55	5.93-2250.57	Fawzy 2022
	11.23	3.10-40.71	Abdelrahman 2024
Turkey	2.66	1.19–5.97	Deniz 2023
Poland	4.87	2.37–10.01	Kwiakowska 2019
China	16.48	8.68–31.51	Guo 2016
Taiwan	3.44	1.89–6.23	Lin 2017
United Kingdom	1.06	0.73–1.54	McBeth 2022
United States	1.7	1.30–2.23	Morse 2023
Finland	1.75	0.67-4.59	Belt 2009

Figure (3) Map of Insomnia Odds Ratios (ORs) for RA by Country Countries included: Egypt, Turkey, Poland, China, Taiwan, United Kingdom, United States, Finland. Accompanying table: Provides country-specific odds ratios (ORs), 95% confidence intervals (CIs), and associated studies. Map powered by Bing.

Results: The literature search yielded 1,273 articles. We included 25 in the qualitative synthesis and 14 studies in the meta-analysis, encompassing 546,822 and 41,565 patients, respectively. Nine studies explored the association between insomnia and RA. Both fixed- and random-effects models showed significantly higher odds of insomnia in RA patients compared to controls (OR: 2.21; 95% CI 1.85 – 2.64, $p < 0.00001$) and (OR: 3.92; 95% CI 1.59 – 9.7, $p = 0.008$), respectively, with considerable heterogeneity. Sensitivity analysis revealed that RA patients had nearly seven times higher odds of experiencing insomnia (OR: 6.82; 95% CI: 2.32–20.1, $p = 0.006$). Five studies compared insomnia in RA patients based on disease activity. Patients with moderate/high disease activity had higher odds of insomnia (OR: 1.76; 95% CI 1.29–2.39, $p = 0.0004$). RF +ve RA patients had higher but not statistically significant odds of insomnia (OR 1.12; 95% CI 0.74–1.71, $p = 0.59$) (Fig. 2). Among the countries with insomnia in both the RA and control groups, China had the highest odds of insomnia (OR: 16.48; 95% CI 8.68 – 31.51) and UK had the lowest odds (OR: 1.06; 95% CI 0.73 – 1.54) (Fig. 3).

Conclusion: This meta-analysis is the first to assess the association between RA, high disease activity, and insomnia, revealing that RA patients had almost 4 times higher the odds of insomnia than controls and patients with moderate/high disease activity had nearly double the odds of insomnia than those with low/remission disease activity. These findings underscore the need for greater awareness among patients and healthcare providers, as well as the importance of developing targeted interventions to improve both sleep and disease management in RA. Further large-scale studies are needed to better understand the relationship between RF and insomnia in RA patients.

Disclosure: M. Abdelsalam: None; **M. Lasheen**: None; **M. Mahdy**: None; **H. Hafez**: None; **N. Abouelella**: None; **M. Al-Adl**: None; **M. Awad**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1318

Diagnostic Delay in Rheumatoid Arthritis and its Impact on Radiographic Outcomes: A Systematic Review and Meta-analysis of 100,066 Patients

Mohamed Abdelsalam[1], Menat Alla Ayman Ali Mahdy[2], Bassant Elaraby Elsayed Badwy[2], Maryam Lasheen[3], Omar Sameh Nabil El Sedafy[1], Hadeer Hafez[4] and Mohamed Reda Awad[5], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [3]Misr University For Science and Technology, Helwan, Al Qahirah, Egypt, [4]6th October University, 6 october, Al Jizah, Egypt, [5]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Timely diagnosis is the cornerstone of effective rheumatoid arthritis (RA) management, with early treatment shown to significantly improve outcomes through a treat-to-target strategy. While diagnostic delay has been well-characterized in axial spondyloarthritis (axSpA), there remains a significant research gap in understanding diagnostic delays specific to RA, causing many patients to miss the critical "window of opportunity" to prevent irreversible joint damage. This study aims to evaluate the extent of diagnostic delay in RA across multiple countries and examine its impact on radiographic joint damage, with emphasis on erosive outcomes.

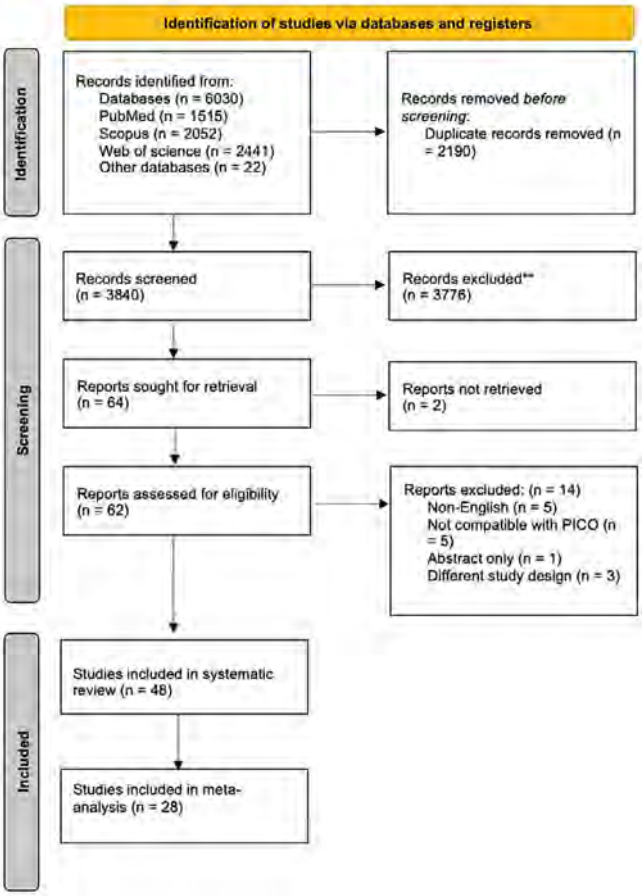


Figure (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

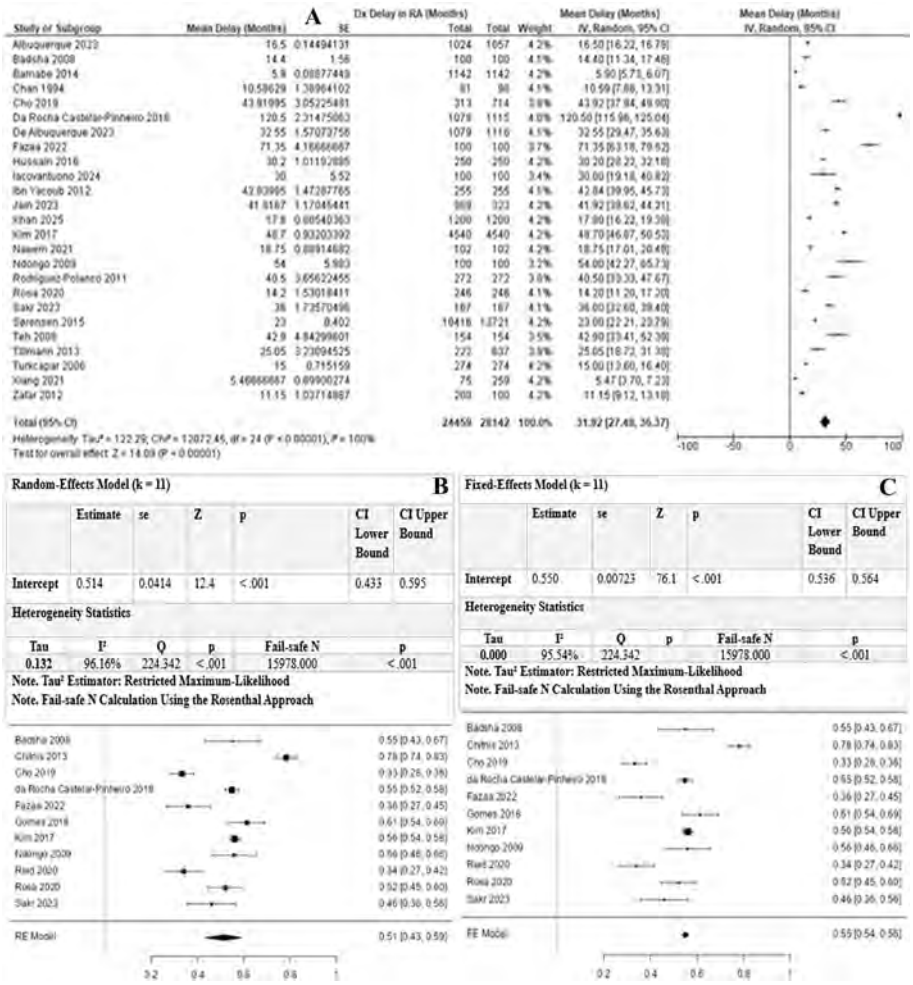
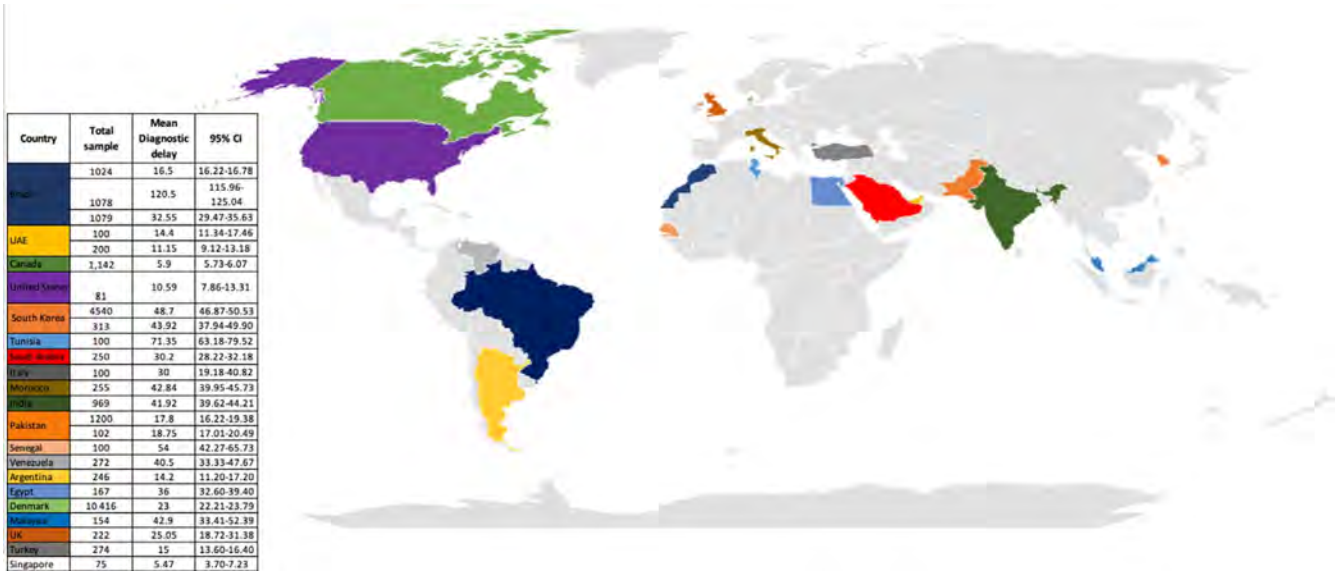


Figure (2) Forest Plots of Diagnostic Delay and Radiographic Damage Prevalence in Rheumatoid Arthritis (RA). (A) Mean Diagnostic Delay (Months): Studies included: Albuquerque 2023, Badsha 2008, Barnabe 2014, Chan 1994, Cho 2019, da Rocha Castelar-Pinheiro 2018, de Albuquerque 2023, Fazaa 2022, Hussain 2016, Iacovantuono 2024, Ibn Yacoub 2012, Jain 2023, Khan 2025, Kim 2017, Naeem 2021, Ndongo 2009, Rodríguez-Polanco 2011, Rosa 2020, Sakr 2023, Sørensen 2015, Teh 2008, Tillmann 2013, Turkcapar 2006, Xiang 2021, Zafar 2012. Overall: Pooled mean diagnostic delay = 31.92 months (95% CI: 27.48–36.37), with considerable heterogeneity (I2 =100% I2 =100%, Tau2=122.2). Test for overall effect: Z= 14.09 (P < 0.00001) Z=14.09(P<0.00001). (C) and (B) Prevalence of Radiographic Damage (Random- and Fixed-Effects Models): Random-effects model: Pooled prevalence = 0.51 (95% CI: 0.43–0.59), with considerable heterogeneity (I2 = 96.16%) I2 =96.16%, Tau2= 0.132). Fixed-effects model: Pooled prevalence = 0.55 (95% CI: 0.54–0.56). Studies included: Badsha 2008, Chitins 2013, Cho 2019, Da Rocha Castelar-Pinheiro 2018, Fazaa 2022, Gomes 2018, Kim 2017, Ndongo 2009, Riad 2020,Rosa 2020, Sakr 2023. CI, confidence interval; RA, rheumatoid arthritis; Tau2 , between-study variance; I2 , heterogeneity index.

Methods: We systematically searched PubMed, Web of Science, and Scopus from inception until April 5th, 2025 following PRISMA guidelines (Fig.1) for observational studies reporting diagnostic delay and radiographic outcomes in RA. Studies were included if RA diagnosis was confirmed by a rheumatologist according to a classification criteria. Diagnostic delays were extracted if reported as mean (SD) or median (IQR). Meta-analyses were conducted for the pooled mean diagnostic delay and prevalence of radiographic damage in delayed diagnosis patients. Heterogeneity was assessed using I^2 statistics following Cochrane guidelines.

Results: A total of 48 studies were identified encompassing 100,066 participants of which 28 were included in the meta-analysis encompassing 15,226 participants. The pooled mean diagnostic delay was 31.92 months (95% CI: 27.48, 36.37) with considerable heterogeneity (I^2 = 100%, τ^2 = 122.29) (Fig. 2). Radiographic outcomes, primarily bone erosions, were reported in a subset of studies. The pooled proportion of patients with radiographic joint damage was 51.4% (95% CI:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Country	Total sample	Mean Diagnostic delay	95% CI
[illegible]	1024	16.5	16.22-16.78
[illegible]	1078	120.5	115.96-125.04
[illegible]	1079	32.55	29.47-35.63
UAE	100	14.4	11.34-17.46
	200	11.15	9.12-13.18
Canada	1,142	5.9	5.73-6.07
United States	81	10.59	7.86-13.31
South Korea	4540	48.7	46.87-50.53
	313	43.92	37.94-49.90
Tunisia	100	71.35	63.18-79.52
Saudi Arabia	250	30.2	28.22-32.18
Italy	100	30	19.18-40.82
Morocco	255	42.84	39.95-45.73
India	969	41.92	39.62-44.21
Pakistan	1200	17.8	16.22-19.38
	102	18.75	17.01-20.49
Senegal	100	54	42.27-65.73
Venezuela	272	40.5	33.33-47.67
Argentina	246	14.2	11.20-17.20
Egypt	167	36	32.60-39.40
Denmark	10416	23	22.21-23.79
Malaysia	154	42.9	33.41-52.39
UK	222	25.05	18.72-31.38
Turkey	274	15	13.60-16.40
Singapore	75	5.47	3.70-7.23

Figure (3) Map of Mean Diagnostic Delay in Months for RA by Country Countries included: United Arab Emirates (UAE), Canada, United States, South Korea, Italy, Morocco, India, Pakistan, Venezuela, Argentina, Denmark, Malaysia, Brazil, Turkey, Tunisia, Saudi Arabia, Senegal, Egypt, UK , and Singapore. The accompanying table provides sample size, mean delay, and 95% CI for each country. Map powered by Bing.

43.3%, 59.5%), with considerable heterogeneity (I^2 = 96.16%) (Fig. 2). There was marked geographic variation in diagnostic delay, with reported mean delays ranging from 5.47 months in Singapore to 120.5 months in Brazil (Fig. 3).

Conclusion: This is the first systematic review and meta-analysis to evaluate diagnostic delay in RA. It revealed a significant mean diagnostic delay, with over half of the patients exhibiting radiographic erosions. These findings highlight critical gaps in early disease recognition, which hinder the implementation of the treat-to-target approach and contribute to irreversible structural damage. The development of clear diagnostic criteria and expansion in the use of diagnostic technologies such as ultrasonography are vital to facilitate earlier detection.

Disclosure: M. Abdelsalam: None; **M. Mahdy**: None; **B. Badwy**: None; **M. Lasheen**: None; **O. El Sedafy**: None; **H. Hafez**: None; **M. Awad**: None.

Abstract Number: 1319

The Association of Rheumatoid Arthritis in Patients with Vitiligo: Systematic Review and Meta-Analysis

Nattanicha Chaisrimaneepan[1], thunyaporn Khoruamklang[2], Pitchaporn Yingchoncharoen[3], Tulaton Sodsri[4] and Miriam Paz[3], [1]Texas Tech University Health Sciences Center, Lubbock, TX, [2]2Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University, bangkok, Thailand, [3]Texas Tech University Health Sciences Center, Lubbock, [4]Department of Medicine, Texas Tech University Health Sciences Center, Bangkok, Thailand

SESSION INFORMATION

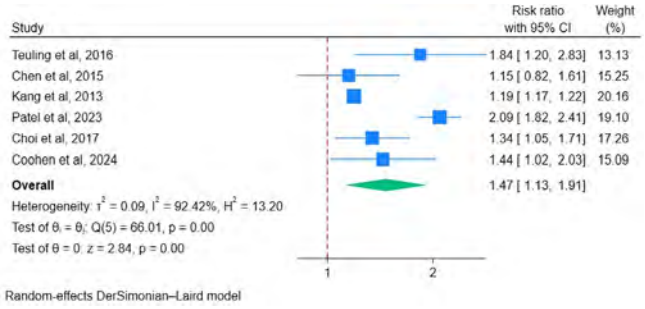
Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest plot of the meta-analysis of rheumatoid arthritis in patients with vitiligo

Background/Purpose: Vitiligo is associated with many autoimmune diseases, but its association with rheumatic disease has not been well-defined. Therefore, we conducted a systematic review and meta-analysis to study the association of vitiligo and occurrence of rheumatoid arthritis.

Methods: A comprehensive literature review was conducted by searching for published

articles indexed in Pubmed, Embase, Google Scholar, and MEDLINE databases from inception through

January 2025. Identify all observational studies that compared the incidence or risk of developing rheumatoid arthritis (RA) in vitiligo patients compared to non-vitiligo. Pooled risk ratio (RR) and 95% confidence interval (CI) were calculated using a random-effect model, DerSimonian and Laird. Publication bias was analyzed with the Egger test.

Results: A total of 262 articles were identified. Following PRISMA for study selection, 6 studies fulfilled the inclusion criteria and were included in the meta-analysis. The risk of developing rheumatoid arthritis among vitiligo patients was significantly higher than in non-vitiligo patients with the pooled RR of 1.47, 95% CI 1.13-1.91: I^2 92.42%. Publication bias analyzed by the Egger test showed no small-study effects with p value of 0.83.

Conclusion: This analysis found that vitiligo is associated with a higher risk of developing rheumatoid arthritis. Further investigation is required to determine the causal relationship.

Disclosure: N. Chaisrimaneepan: None; **t. Khoruamklang**: None; **P. Yingchoncharoen**: None; **T. Sodsri**: None; **M. Paz**: None.

Abstract Number: 1320

Trends In Incidence and Risk factors For Incident Venous Thromboembolism in Patients with Rheumatoid Arthritis: A Population-Based Retrospective Cohort Study

Noah Frechette[1], Elena myasoedova[1], Iqra Javed[1], Roslin George[1], Sara Achenbach[2] and Cynthia Crowson[3], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, [3]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Risk factors for DVT in patients with RA

Parameter	HR (CI)
Age (years) per 10-year increase	1.52 (1.31-1.76)
Obesity (BMI≥30 kg/m²)	1.86 (1.26-2.75)
Charlson comorbidity index	1.17 (1.06-1.28)
Rheumatoid Nodules*	2.88 (1.86-4.47)
Severe extra-articular manifestations of RA*	2.67 (1.42-5.03)
Biologic use*	2.36 (1.22-4.55)

* w/in the first year of meeting RA criteria

Background/Purpose: Venous thromboembolism (VTE) is more common in patients with rheumatoid arthritis (RA) and can present as deep vein thrombosis (DVT) or pulmonary embolism (PE). The changing risks of VTE in patients with RA over time and in relation to RA disease characteristics and treatments have not been comprehensively studied in longitudinal population-based cohorts. We aimed to estimate the risk of incident VTE (PE and DVT) in patients with RA vs the general population, to identify risk factors for VTE, mortality after VTE and time trends of VTE in RA.

Methods: This retrospective population-based cohort study included residents of a geographically defined area, meeting the 1987 ACR RA criteria in 1980-2019 and comparators from the same population with similar demographics. DVT/PE were identified by >2 ICD 9/10 codes >30 days apart and confirmed by manual record review. Cox proportional hazards models were used to compare incident VTE in RA vs. non-RA cohort, adjusting for demographics, smoking and obesity. Cumulative incidence of DVT, PE and total VTE was estimated, adjusting for competing risk of death. Cox models were used to examine risk factors for VTE in RA and to compare mortality in RA vs non-RA.

Results: 2818 individuals were included: 1409 with RA (62% RF/CCP-positive) and 1409 without RA, mean age 55.9 years, 68% women in both groups. Mean follow-up: 14.0 and 14.9 years in the RA and non-RA cohort respectively. DVT developed in 105 and 52 people with and without RA respectively. PE developed in 84 and 55 people with and without RA respectively. Persons with RA had a significantly increased risk of incident DVT (HR 2.26, 95%CI 1.62-3.17) and PE (HR 1.61, 95%CI 1.14-2.27). There was a significant difference in RA as a risk factor for VTE in two of the decades: 1980-1989 (HR 1.57; 95%CI 0.86-2.89), 1990-1999 (HR 2.68, 95%CI 1.55-4.63), 2000-2009 (HR1.80, 95%CI 1.13-2.86), 2010-2019 (HR 1.74, 95%CI 0.95-3.17). There was a significant increase in PE risk in both persons with RA onset after 2000s vs before 2000s (HR 2.00, 95%CI 1.21-3.32) and in the non-RA cohort (HR 2.70, 95%CI 1.38-5.28). Adjusted for age, sex, and calendar year, risk factors for DVT in RA included age, BMI >30 kg/m2, Charlson comorbidity index, rheumatoid nodules, severe extra-articular manifestations, and treatment with biologic in first year (Table 1). Risk factors for PE in RA included age, current and former smoking, BMI >30 kg/m2, rheumatoid nodules, large joint swelling, and

Table 2. Risk factors for PE in patients with RA

Parameter	HR (CI)
Age (years) per 10-year increase	1.53 (1.29-1.81)
Smoking status	
Current	2.16 (1.17-3.99)
Former	2.24 (1.36-3.71)
Obesity (BMI≥30 kg/m²)	2.29 (1.48-3.53)
Rheumatoid Nodules*	2.14 (1.26-3.63)
Large joint swelling*	1.66 (1.04-2.66)
Any remission visit*	0.47 (0.23-0.94)
Biologic use*	2.87 (1.46-5.62)

* w/in the first year of meeting RA criteria

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

treatment with biologic in first year. Remission in the first year was associated with lower PE risk (Table 2). Patients with RA were more likely to die following VTE (HR 1.52, 95%CI 1.04-2.21), adjusting for age, sex and year of VTE.

Conclusion: The risk of DVT and PE, and mortality following any VTE event were significantly increased in patients with RA vs non-RA. Several RA disease characteristics were associated with increased risk of DVT and PE. Remission was associated with reduced PE risk, underscoring benefits of tight control of RA disease activity. Despite recent RA treatment advancements, the risk of VTE in RA did not decline after 2000s, like the non-RA population trends. Better understanding of these indicators presents future research areas to improve care of patients with RA at risk of VTE.

Disclosure: N. Frechette: None; **E. myasoedova**: None; **I. Javed**: None; **R. George**: None; **S. Achenbach**: None; **C. Crowson**: None.

Abstract Number: 1321

Efficacy and safety of janus kinase inhibitors in diffuse interstitial lung disease in rheumatoid arthritis. Systematic review

Olga Compán[1], Marta Ibañez[2], Olga Martínez[3], Carolina Cristina Chacón[4], Ricardo López Pérez[3], Borja Felices López[3], Belén Miguel Ibáñez[3], Laura Blanco[4], Sergio Cimadevila Santiago[3], Ana Isabel Turrión Nieves[3], Manuel Cipriano Martin Martinez[3], Cristina Hidalgo Calleja[4], Carlos Montilla[4] and Susana Gómez[4], [1]Rheumatology Service, University Hospital of Salamanca, Carbajosa de la Sagrada, 37191, Spain, [2]Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [3]Hospital Universitario de Salamanca, Salamanca, Castilla y Leon, Spain, [4]Rheumatology Service, University Hospital of Salamanca, Salamanca, Castilla y Leon, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a relatively common serious extra-articular complication in rheumatoid arthritis (RA). Although there have been great advances, we do not have strong evidence of the efficacy of the different drugs in the treatment of this complication, which is even scarcer compared to janus kinase inhibitors (JAKi).

To systematically evaluate the evidence published in the literature on the efficacy and safety of JAKi in the treatment of RA-associated ILD.

Methods: Literature searches were carried out in the Pubmed, Cochrane Library, Embase and Scopus databases between 01/01/2019 and 01/07/24, according to the Cochrane Manual and the PRISMA guidelines. A combination of the terms and their synonyms "janus kinase inhibitors", "interstitial lung disease" and "rheumatoid arthritis" were used. Two independent reviewers participated, using a third if there was no agreement.

Results: Of a total of 387 references obtained in the initial search, a total of 10 original, 8 retrospective and 2 prospective studies were finally included, including 4 communications. We found no randomised trials, meta-analyses or systematic reviews. Tables 1 and 2 show the characteristics of the included studies, demographic data and clinical characteristics of the patients. The mean age range of the patients oscillated from 59 to 74 years, with a variable percentage of women, generally close to 60%. The follow-up range was from 6 to 36 months. The time of evolution of RA in the included patients varied between 7 and 16 years, with positivity for rheumatoid factor (RF) and anti-citrullinated peptide antibody (ACPA) greater than

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic data and clinical characteristics of the patients.

Author, Year	Female N (%)	Age (range)	Personal history smoking (%)	Evolution time RA	RF+/ACPA+ (%)	ILD pattern, N (%)	Type of JAKi and dose	JAKi and DMARDs combination	GC	Previous use DMARDs or JAKi, N (%)
Tsuji, A., 2024	14 (66.7%)	74	ABT 9 (1.3%), JAKi 30.8%	8 years ABT, 10 años JAKi	ABT 85.7% 85.1%, JAKi 100%-100%	ABT UIP, N= 3 (14.3%), NSIP 18(85.7%); JAKi UIP n=4 (15.4%), NSIP N= 17 (80.9%)	NS	NS	NS	ABT n = 13 (28.9%), JAKi n=21 (60.8%)
Tanikella, M., 2022	51 (69.5%)	59.5 ±7.77	NS	7.41 ±5.23 years (7.55 ABT, 7.33 JAKi)	ABT 63.6% 52.3%, JAKi 61.3% 81.6%	NS	TOF 5mg 12h o. BAR 4mg/dia	JAKi 100% monotherapy, ABT 100% concomitant DMARDs	GC medium-onset ABT 5.3/ JAKi 3.3	ABT 18 (26.4%), JAKi 11 (15.3%)
Valero-Juliano, J. A., 2022	4 (26%)	71 (63–88)	80%	18 years	100%-100%	UIP 7 (41%), pUIP2(12%), NSIP 3(18%), ON 1 (6%), NS 4 (24%)	BAR, 4mg n=12(70%), 2mg n=2 (30%)	NS	NS	ABT 14 (82%)
Serrano-Cumplido, A., 2023	37 (84.9%)	66 ±10	82%	NS	98%-98%	UIP 30(55%)	BAR	monotherapy 45%	NS	47(87%): ABT (30.9%), TOCI (34.39%), RTX (10.18%)
Tanaka, A., 2023	45 (69%)	59.3	ND	7.7 years	83.7%/80.9%	NS	NS	NS	NS	2nd line 100%
Kobayasi, T. 2022	27.4% RA-ILD, 52.2% RA no ILD	61 (37-69) RA-ILD, 56 (46-66) RA no ILD	44.7% RA-ILD, 43.8% RA no ILD	128 months RA-ILD, 110 months RA no ILD	RA-ILD 78.3%/83.2% RA no ILD 68.8%/81.6%	RA-ILD: 26.3% UIP, 54.3% NSIP, 9.15% NS	NS	NS	RA-ILD 13(28.3%); RA no ILD 2(4 (34.24%)	18(54%)
Mochizuki T., 2020	ABT 18 (94.7%), JAKi 10 (90.9%)	ABT 73.5 ±7.7 Vs JAKi 71.0 ±7.7	ABT 1 (5.3%) JAKi 2 (18.2%)	ABT 15.2 ± 6.8 years Vs JAKi 15.6 ± 8.9	100%, ABT 89.5% JAKi66.9%	UIP) ABT 3(4.2%) JAKi 2 (5.4%) UIPno6) ABT 9 (18.8%) JAKi 9(47.7%) Indeterminate) ABT 8(5.2%) JAKi 2(2.5%)	NS	NS	ABT 4 (21.0%) JAKi 4 (36.4%)	ABT 8 (42.1%); JAKi 9 (81.8%)
Navarro F., 2021	20 (66.72%)	68.87±01.46 ± 71.70)	NS	12.86 ± 7.61 years	88.37% 81.40%	UIP 25 (58%), NSIP 5 (11%), LIP 3(4%), Emphysema-fibrosis1(2%) Indeterminate10(23%)	BAR 30(6%); TOF 9 (20%); FILGO y UPA 5 (7%)	16 (16.30%) concomitant MTX	20(60.47%)	TNFi 18(44%) RTX 12 (28%), ABT 16 (38%), TOCI 13(30%)
Bejarano, M. F., 2019	9 (60%)	64,4 ±10,52	NS	9 (4-40) years	NS	NS	TOF 10mg/d	7 (47%) monotherapy; 8 (53%) concomitant DMARDs N=3 (35%) MTX	NS	5 (33%)
Wang, S., 2023	39 (50%)	NS	TOF+IGU, 4 (16.7%), comorbis groups) (10.2%)	TOF–IGU 15.3±8.6 years IGU+DMARDs 14.5±12.5 years DMARDs14.2±11.4	TOF+IGU 83.3/87.5% IGU+ DMARDs 88.4/ 90.8%, DMARDs 85.7/82.1%	NS	TOF 5mg,2 veces al día+IGU 25mg/2 dia	NS	allowed ≤15 mg daily of prednisone	NS

N= number/size, Age: mean or median in years, RA=Rheumatoid arthritis, RF= Rheumatoid factor, ACPA= anti-citrullinated peptide antibody, ILD= interstitial lung disease., JAKi= janus kinase inhibitor, DMARDs= conventional synthetic disease-modifying drugs, GC= glucocorticoids, DMARDs= biological disease-modifying drugs, ABT=Abatacept, BAR= baricitinib, NS = not specified, UIP= Usual Interstitial Neumonia, NSIP= non-specific interstitial pneumonia, OP= Organized pneumonia, CTD= connective tissue disease pulmonary, FILGO= filgotinib, UPA= upadacitinib, TNFi= tumor necrosis factor inhibitor , TOF= tofacitinib, IGU= ignatinod. This table has been done by myself.

80% in most cases. The patterns of ILD reported are highly variable, with the first in frequency being usual interstitial pneumonia (UIP) in most studies (up to 58%), followed by non-specific interstitial pneumonia (NSIP). The most frequently used JAKi were tofacitinib and barititinib, which were prescribed as monotherapy in more than half of the patients (60-100%). The methods of assessment of the ILD were highly variable, pulmonary function tests are included (PFT) and high-resolution computed tomography (HRCT). Improved or stabilized HRCT images in more than 80% of patients. Regarding PFT, stabilization was achieved in more than 70% of patients, with a worsening of carbon monoxide difussion capacity test (DLCO) in only 1 study. Only 2 cases of acute exacerbation of ILD were reported in one study, with 1; the rest of the adverse events

Table 2. Characteristics of the included studies

Author, Year	Study design/ follow up; N	Pulmonary function test results	HRCT results	Overall result	Security	Conclusions
Tsuji, A., 2024	Retrospective case-control study at 1 centre. 21 months. (2015–2020) N=21 total.	NS	Significant improvement of the GGO with TAKi (p=0.03), not in fibrosis or in the two parameters with ABT	IMPROVEMENT	ABT and TAKi N=7 No acute exacerbations of ILD.	JAKi is as safe and effective as ABT. There are no differences in persistence (p=0.716), pulmonary complications (p= 0.465) or reasons for discontinuation.
Tanikella, M., 2022	Retrospective multi-at 1 centre. 18 months. N= 51 (TJAKi: 44/ABA)	FVC, ABT pre: 81.38 ± 4.40; post: 82.25 ± 21.07/ JAKi pre: 81.18–5.07; post: 79.10 9– 14.02. DLCO ABT: pre: 60.89 ± 8.2; post: 61.26 ± 11.23. JAKi pre: 59.72 ± 8.36; post: 60.25 ± 12.04.	No statistically significant changes in fibrosis on HRCT. Just in ABA, showed stability or improvement of RA-ILD in 83.9% and 88.6% of patients	STABILITY / IMPROVEMENT	NS	JAKi or ABA were related to the stability or improvement of RA-ILD in 83.9% and 88.6%. The duration of RA is the only variable associated with worsening of RA-ILD on linear mixed with JAKi.
Valero-Juliano, J. A., 2022	Retrospective study at 1 centre. 24 months, until 2020. N= 17	FVC pre: 80% ± 19.03; 1111; post 94% (87–107), DLCO pre: 80% (70-87.5); post: 85% (74-87)	10 patients HRCT available. N= 9 stable (53%), improvement 2 (9%)	STABILITY / IMPROVEMENT	5%	Good performance of JAK (81–10%), the most frequent cause of discontinuation was Non Failure. It was found kept lung function stable
Serrano-Cumplido, A., 2023	Retrospective study. Multicenter study., 37 months N= 37 (33 BAR)	FVC pre: 87±22, DLCO pre: 71 ± 23. Stabilization in the first 12 months	HRCT available (improvement/stabilized 82%	STABILITY / IMPROVEMENT	N= 1 Interventions= due to pneumonia. No acute exacerbation of ILD	JAKi, especially BAR may be useful and safe to control loss, and relax disease in RA-ILD .
Umeda A. 2023	Retrospective study at 1 centre. 2.8 years (2014– 2022) N= 50	NS	Increase in FC reticular opacities more in 8 (16%) in TJAKi(20) 5 vs 0 (0%) JAKi (p= 0.01)	STABILITY	NS	Worsening on HRCT , particularly reticular opacities, less in the period with JAKi=5, (16%) vs DMARDs (8 –40%) JAKi did not stabilize GGO worse, rather it could stabilize it.
Kobayasi T., 2022	Prospective study. Multicenter study. 12 months. N= 41 RA-ILD /87 RA no ILD	RA-ILD: increase FEV1 y FVC statistically significant of FEV1 pre0 and post: 82.11 ± 82.44, FVC pre0 and post: 83.6% ± 82.8. Deterioration FVC>10% in 7 (11.7%) *Clinical deterioration due to no significant clinical improvement (dyspnea in 44.6% patients)	NS	STABILITY	Infections 6.3/100 patients year RA-ILD, 2.4/100 patients year RA no ILD. Infections: same group: exacerbations RA-ILD 23%, in RA no ILD 6.4%.	Statistically significant increase in both FEV1 and FVC in the RA-ILD group; however, not considered clinically significant.
Mochizuki T. 2020	Retrospective study at 1 centre. 1 year (2017 – 2020). Study RA-ILD subgroup. ABT19/ JAKi 21	NS	1) ILD improved, defined by HRCT ABT 2 (10.5%) VS JAKi 3 (14.2%) p= 0.011)	STABILITY		No significant difference was observed in the deterioration of known ILD between the ABT and JAKi groups (p = 0.011)
Navarro F., 2021	Retrospective study. Multicenter study. 19.1 months (2018– 2022). N= 43	FVC: stable 22/28 (78.57%); improvement 3/28 (10.71%); worsening 3/28 (10.71%); Not significant. DLCO stable 18/25 (72%) improvement 2/25 (8%); worsening 5/25 (20%). Slight decrease in DLCO if significant.	Stability 37/43 (86.05%), deterioration 4/43 (9.30%) and improvement 2 (4.65%).	STABILITY	Adverse events with BAR: 1 (4.76%) severe urinary infection, and 2 (9.52%) severe exacerbations of ILD, 1 of them death.	JAKi can stabilize more than 2/3 of patients (about 80%) on DLCO as FVC. In HRCT stability or improvement in 80%, with no differences between JAKi.
Bejarano, M. F., 2019	Retrospective study. Multicenter study 12 months. N= 15	FVC: start <80% 3 patients and >80% in 2. At 12 months, 4 FVC >80%, 10= 4 (27%) grade 3-4 dyspnea at onset. Improvement in dyspnea scale in 8 patients, rest stable.	No progression was observed on HRCT at 12 months in any of the patients evaluated.	STABILITY / IMPROVEMENT	NS	No patient had worsening of dyspnea, with improvement in some. The pulmonary function test were stable, and in 4 patients there was improvement. No progression was observed on HRCT in any patient.
Wang, S., 2023	Prospective study at 1 centre. At least 6 months (2020– 2022). N= 78. TOF+IGU: 24 IGU+ DMARDs: 26; DMARDs 28	DLCO decreased in all groups although without statistically significant differences. FVC does increase significantly (P = 0.013) in the TOF+IGU group compared to DMARDs.	TOF+IGU slight progress GGO in HRCT, without significant differences Vs DMARDs (P = 0.359). Fibrosis on HRCT significant improvement, compared to DMARDs (P = 0.031). IGU+ DMARDs as DMARDs alone, worsening fibrosis	IMPROVEMENT	1 herpes zoster in group TOF+IGU	The TOF+IGU group shows a statistically significant improvement with respect to the UIP pattern at HRCT (P = 0.031), and although the ground glass score slightly increases, this is not significant. There is also a significant increase in FVC compared to DMARDs (P = 0.013).

JAKi= janus kinase inhibitors, DMARDs= conventional synthetic disease-modifying drugs, No sample size, HRCT= thoracic high-resolution computed tomography, ABA: Abatacept, (who not specified, RA= Rheumatoid arthritis , ILD= interstitial lung disease, TOF= tofacitinib, BAR= baricitinib, %FVC= predicted forced vital capacity, %DLCO= predicted diffusing capacity for carbon monoxide, FEV1= Maximum expiration volume in the first second of forced expiration, DMARDs= biological disease-modifying drugs, MTX= methotrexate, UIP= Usual Interstitial Neumonia, IGU= ignatinod, GGO= ground glass opacities, pre=pre-treatment, post= post-treatment. This table has been done by myself.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(AEs) are comparable to what is expected with the safety profile of JAKi, although a higher incidence of such AEs is reported in patients with AR-ILD compared to those with RA without ILD.

Conclusion: JAK inhibitors could be a useful treatment strategy in maintaining stability in RA-associated ILD, including improvement.

The low prevalence of ILD during treatment with JAKi suggests that perhaps we should rethink the treatment algorithm in rheumatoid arthritis, even more so in young patients, without contraindications and at risk of developing ILD.

Prospective, randomized, controlled studies are needed to confirm this hypothesis.

Disclosure: O. Compán: None; **M. Ibañez**: None; **O. Martínez**: None; **C. Chacón**: None; **R. López Pérez**: None; **B. Felices López**: None; **B. Miguel Ibáñez**: None; **L. Blanco**: None; **S. Cimadevila Santiago**: None; **A. Turrión Nieves**: None; **M. Martin Martinez**: None; **C. Hidalgo Calleja**: None; **C. Montilla**: None; **S. Gómez**: None.

Abstract Number: 1322

High Rheumatoid Factor Titers and Biologic Persistence in RA: Beyond TNF Inhibitors

Sara Salas Santamaría[1], Marta Chao Moreira[2], Manuel Juárez[3], Marta Novella-Navarro[2], Pilar Nozal[2], Ana Martínez[2], Carolina Tornero[4], Cristina Bohorquez[5], Ana Sánchez[2], Carmen Cámara[2], Eduardo López[2], Eugenio de Miguel[2] and Chamaida Plasencia-Rodríguez[2], [1]Hospital Universitario La Paz, Miranda de Ebro, Castilla y Leon, Spain, [2]Hospital Universitario La Paz, Madrid, Spain, [3]Rheumatology Unit, Hospital Universitario La Paz, IdiPAZ, Madrid, Spain, [4]Hospital La Paz, Madrid, Spain, [5]La Paz University Hospital, Alcalá De Henares, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid factor (RF), an autoantibody targeting the Fc portion of IgG, is one of the most studied biomarkers in rheumatoid arthritis (RA). High RF titers have been associated with a more aggressive disease course and reduced efficacy of certain biologic DMARDs (bDMARDs), particularly monoclonal anti-TNF agents. RF levels ≥203 IU/mL have been linked to lower serum drug levels and reduced treatment persistence in these therapies. However, this association has not been observed with pegylated TNFi, and its impact on non-TNFi monoclonal antibodies remains unclear.

Methods: We conducted a retrospective longitudinal study of RA patients from our hospital treated with Certolizumab (CZP), Rituximab (RTX), and/or Tocilizumab (TCZ) as up to third-line therapy. Sociodemographic data, use of csDMARDs, bDMARDs, corticosteroids, RF levels at bDMARD initiation, and baseline and 6-month clinical and analytical inflammatory markers were collected (ET approval PI 6366). Drug discontinuation dates and reasons, up to December 31, 2024, were recorded. Patients were grouped by bDMARD received, and comparisons were made using Chi-square or Fisher's exact test for categorical variables, and ANOVA or Kruskal-Wallis for continuous variables. Kaplan-Meier analysis was used to assess drug survival, overall and stratified by RF levels (High; HL ≥203 IU/mL vs. Low; LL < 203 IU/mL).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographic and clinical characteristics of patients.

Treatment	CZP SC (N=43)	RTX (N=46)	TCZ (N=97)	p value	p value
Sociodemographic characteristics					
Sex, female n(%)	37 (86.0%)	37 (80.4%)	83 (85.6%)	0.576[1]	1.000[1]
Age (years)				**< 0.001[2]**	**0.004[2]**
- Median (IQR)	46.6 (39.8- 62.1)	63.5 (55.9-68.7)	57.5 (48.6-65.1)		
BMI					
- Median (IQR)	24.5 (21.6-29.7)	25.7 (23.7-30.9)	26.7 (23.4- 28.6)	0.104[2]	0.122[2]
Smoking status, n(%)				0.602[1]	0.799[1]
- Current	6 (14,3%)	9 (19.6%)	19 (19,6%)		
- Previous	12 (28.6%)	16 (34.8%)	28 (28.9%)		
- Nonsmoker	24 (57.1%)	21 (45.7%)	50 (51.5%)		
Disease duration until treatment (years)				0.059[2]	0.082[2]
- Median (IQR)	8.2 (4.2-11.6)	13.8 (5.0-22.0)	11.3 (5.1-18.3)		
Disease duration until 12/31/24 (years)				0.141[2]	0.037[2]
- Median (IQR)	17.0 (13.4-20.9)	21.9 (12.0-31.4)	19.6 (14.7-26.0)		
Serological characteristics					
CRP mg/L				0.384[2]	0.881[2]
- Median (IQR)	5.0 (2,2-14.4)	9.2 (1.5-19.0)	4.6 (1.0-16.7)		
RF status n(%)	29 (67.4%)	38 (82.6%)	66 (74.2%)	0.140[1]	0.418[1]
RF levels				0.178[1]	0.049[1]
- Low: <203 IU/mL	32 (74.4%)	14 (56.0%)	55 (78.6%		
- High: ≥203 IU/mL	11 (25.6%)	11 (44.0%)	15 (21.4%)		
ACPA status, n(%)	40 (93.0%)	37 (88.1%)	73 (79.3%)	0.483[1]	**0.049[1]**
Clinical characteristics					
DAS28, mean (SD)	4.8 (1.3)	4.7 (1.4)	4.5 (1.5)	0.729[3]	0.188[3]
Basal TJC, mean (SD)	8.4 (7.7)	6.7 (5.4)	15.0 (81.9)	0.484[2]	0.201[2]
Basal SJC, mean (SD)	6.5 (5.4)	6.7 (5.0)	4.7 (3.9)	0.666[2]	0.130[2]
Basal SDAI, mean (SD)	25.6 (15.0)	23.9 (11.5)	21.8 (13.2)	0.962[2]	0.302[2]
Basal HAQ, mean (SD)	7.4 (4.9)	10.7 (4.8)	8.8 (6.4)	**0.004[2]**	0.296[2]
Treatment characteristics					
Prev DMARD	40 (95.2%)	41 (89.1%)	85 (87.6%)	0.437[1]	0.228[1]
MTX use, n(%)	20 (47.6%)	25 (54.3%)	62 (63.9%)	0.670[1]	0.091[1]
Prednisone use, n(%)	21 (50.0%)	30 (65.2%)	58 (59.8%)	0.195[1]	0.352[1]
N° prev bDMARDs,n(%)				**< 0.001[1]**	**< 0.001[1]**
0	35 (81.4%)	9 (19.6%)	43 (44.8%)		
1	6 (14.0%)	31 (67.4%)	49 (51.0%)		
2	2 (4.7%)	6 (13.0%)	4 (4.2%)		
N° prev TNFI., n(%)				**< 0.001[1]**	**< 0.001[1]**
0	39 (90.7%)	20 (43.5%)	49 (51.0%)		
1	4 (9.3%)	22 (47.8%)	44 (45.8%)		
2	0 (0.0%)	4 (8.7%)	3 (3.1%)		

[1] Fisher's Exact Test for Count Data. [2] Kruskal-Wallis rank sum test. [3] Linear Model ANOVA.

BMI: Body mass index; CRP: C-reactive protein; RF: Rheumatoid factor; ACPA: Anti-citrullinated peptide antibodies; DAS28: 28-joint Disease Activity Score 28; TJC: Tender joint count; SJC: Swollen joint count; SDAI: Simplified Disease Activity Index; HAQ: Health Assessment Questionnaire; DMARD: Disease- modifying drug; MTX: Methotrexate; bDMARDs: Biologic disease- modifying drugs; TNFi: Tumor Necrosis Factor inhibitors.

Results: A total of 186 patients with RA were included: 43 (23%) received CZP, 46 (25%) RTX, and 97 (52%) TCZ, with no significant sociodemographic differences between groups (Table 1). Baseline DAS28 and SDAI scores were comparable across treatments. In addition, näive patients to b/tsDMARDs were more frequent in CZP group (81% in CZP vs. 19% in RTX vs. 45% in TCZ, p< 0.001). At 6 months after the initiation of bDMARD, patients with high RF levels treated with TCZ showed higher disease activity (DAS28, SDAI) than those with lower RF levels (Table 2), whereas no statistically significant differences in activity were observed in the other treatment groups based on RF levels. Overall, 66% discontinued treatment (22 CZP, 30 RTX and 71 TCZ); 36% due to inefficacy (10 CZP, 5 RTX and 29 TCZ). In survival analysis, RF levels did not

Table 2. Comparison of DAS28, SDAI, and CRP at 6 months according to RF levels.

		RF < 203 UI/mL	RF ≥ 203 UI/mL	p value
CERTOLIZUMAB	6M-DAS28, mean (SD)	2,5 (0,8)	3,2 (0,9)	0.057[1]
	6M-SDAI, median (IQR)	4,8 (2,4-8,8)	6,1 (3,1-11,4)	0.597[2]
	6M-CRP, median (IQR)	1,8 (0,9-3,9)	0,9 (0,6-3,6)	0.514[2]
RITUXIMAB	6M-DAS28, mean (SD)	3,8 (1,6)	4,4 (1,0)	0.353[1]
	6M-SDAI, mean (SD)	15,8 (12,1)	20,2 (10,8)	0.478[1]
	6M-CRP, median (IQR)	4,8 (1,2-6,2)	8,4 (1,1-12,3)	0.552[2]
TOCILIZUMAB	6M-DAS28, mean (SD)	2,8 (1,2)	3,6 (1,1)	**0.034[1]**
	6M-SDAI, median (IQR)	8,3 (2,2-12,1)	10,1 (8,0-18,5)	**0.050[2]**
	6M-CRP, median (IQR)	0,8 (0,2-0,9)	0,5 (0,3-1,6)	0.912[2]

[1] ANOVA. [2] Kruskal-Wallis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

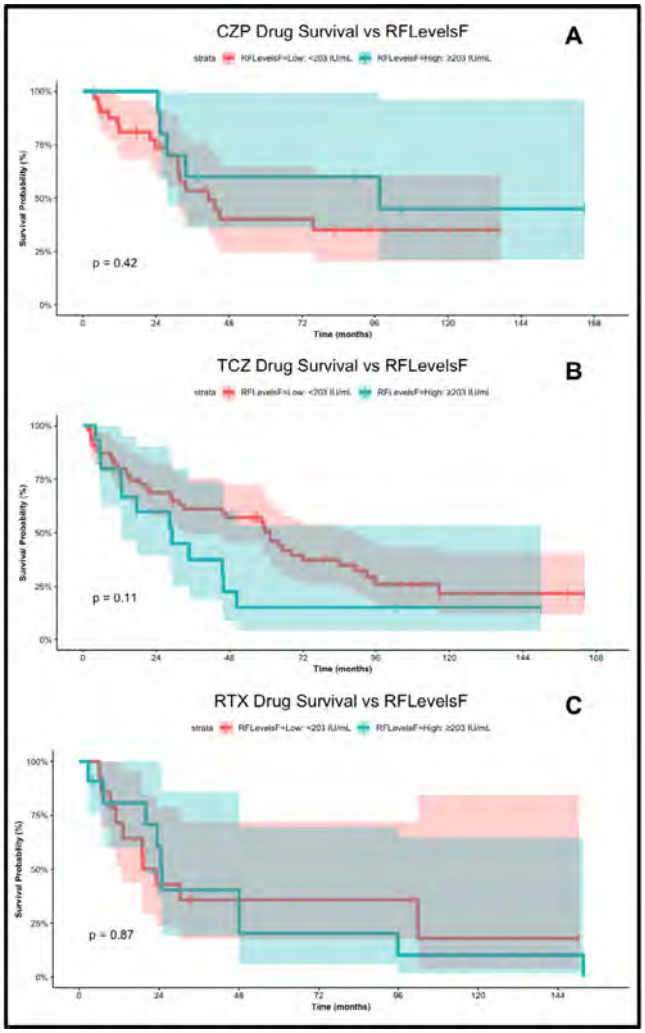


Figure 1. Survival drugs analysis (global) vs RF levels. A: Certolizumab Drug Survival vs RFLevels; B: Tocilizumab Drug Survival vs RFLevels; C: Rituximab Drug Survival vs RFLevels

influence drug persistence in CZP, with a similar curve in both subgroups regardless of RF levels (99.9 in HL vs. 76.9 in LL months, p=0.42) (Figure 1A). The same occurs in the RTX group (Figure 1C), even showing a slightly higher median in the group with higher RF titres (45.1 in HL vs. 55.1 in LL months, p=0.87), consistent with the molecule's mechanism of action. However, when looking at the patients treated with TCZ (Figure 1B), the drug survival mean tended to be lower in patients in the group with RF ≥203 although no statistically significant (46.1 in HL vs 70.8 in LL months, p=0.11).

Conclusion: Patients with RF levels above 203 IU/mL did not show significant differences in drug survival for CZP or RTX. Nevertheless, TCZ showed a poorer short-term clinical response and a trend toward shorter drug survival and in patients with high RF levels. These findings suggest that RF levels might influence the persistence and effectiveness of certain bDMARDs, particularly TCZ, and warrant further investigation in studies with larger sample sizes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Salas Santamaría: None; **M. Chao Moreira**: None; **M. Juárez**: Gebro Pharma, 6; **M. Novella-Navarro**: None; **P. Nozal**: None; **A. Martínez**: None; **C. Tornero**: None; **C. Bohorquez**: None; **A. Sánchez**: None; **C. Cámara**: None; **E. López**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6.

Abstract Number: 1323

Efficacy of Olokizumab in Treating Comorbid Depression in Patients with Rheumatoid Arthritis: Results of a Single-Center Randomized Controlled Trial

Tatiana Lisitsyna[1], Anton Abramkin[2], Dmitry Veltishchev[3], **Sofia Kuzkina**[4], Anastasia Borisova[2], Vasily Ignatiev[5], Mikhail Samsonov[6] and Eugeny Nasonov[2], [1]Thromboinflammation Laboratory of the Department of Systemic Rheumatic Diseases V.A.Nasonova Research Institute of Rheumatology, Moskva, Russia, [2]V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, [3]V.A.Nasonova Research Institute of Rheumatology, Moscow, Russia, [4]R-Pharm, Moscow, Russia, [5]"R-Pharm", JSC, Moscow, Russia, [6]RPharm, Brussels, Belgium

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin (IL)-6 plays an important role in the pathogenesis of depression in rheumatoid arthritis (RA) patients. IL-6 inhibitors used to treat patients with RA may also have an antidepressant effect.

The objective of this study is to evaluate the effectiveness of 24-week IL-6 inhibitor therapy with olokizumab (OKZ) in combination with or without psychopharmacotherapy (PPT) in patients with moderate to high RA activity.

Methods: According to ICD-10, a psychiatrist diagnosed varying severity of depression (chronic or recurrent) in all patients during a semi-structured interview. At week 0, all patients were randomized using sequential numbers in a 2:2:1 ratio into one of three groups: in the group 1, patients received conventional synthetic disease modifying antirheumatic drugs

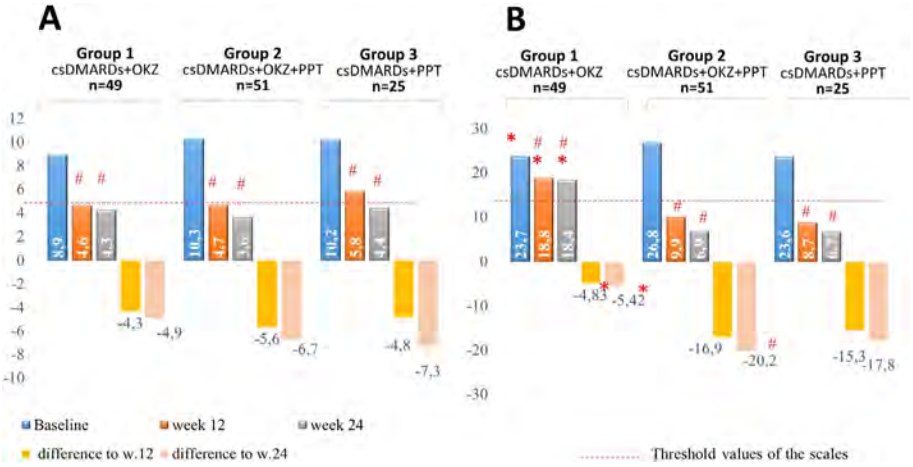


Figure 1. The dynamics of depression severity depending on therapy Note: A, The dynamics of depression severity according to the PHQ-9 self-questionnaire, score B, The dynamics of depression severity according to the MADRS scale, score; * p<0,05 comparison between groups; # p<0,05 comparison between baseline and weeks 12/24 in the group; csDMARDs - conventional synthetic disease modifying antirheumatic drugs; OKZ – olokizumab: PPT - psychopharmacotherapy

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

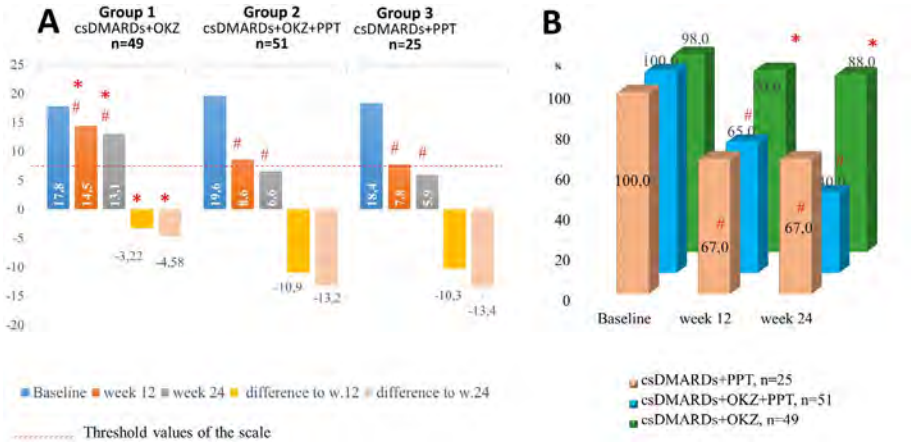


Figure 2. The dynamics of anxiety severity and the proportion of patients without anxiety according to the HAM-A scale by week 24 Note: A, The dynamics of anxiety severity on the Hamilton scale, score; B, The proportion of patients with clinically significant anxiety on the Hamilton scale; * p<0,05 comparison between groups; # p<0,05 comparison between baseline and weeks 12/24 in the group; csDMARDs - conventional synthetic disease modifying antirheumatic drugs; OKZ – olokizumab: PPT - psychopharmacotherapy

(csDMARDs)+OKZ 64 mg subcutaneously once every 4 weeks (q4w) (n=49); in the group 2, patients received csDMARDs +OKZ 64 mg subcutaneously q4w along with PPT (n=51); in the group 3, patients received csDMARDs + PPT (n=25). The study duration was 24 weeks. The severity of depression was assessed using the PHQ-9 and MADRS scales; while anxiety was assessed using the HAM–A scale. Projective experimental psychological techniques were also used.

Results: A total of 125 patients with RA were included, 102 (81,6%) of them being women. The average age of the patients was 48,5±12,6 years; the majority of the patients (86.4%) had high RA activity and stable 12-week therapy with csDMARDs was ineffective . Additionally, 34 (27,2%) patients had shown inefficacy of one or more biological DMARDs. After 12 and 24 weeks of therapy, a significant decrease in the severity of depression and anxiety was observed in all patients' groups. However, the differences between the final and initial values of the scales filled in by a psychiatrist were statistically significantly greater ($p< 0.001$) in the groups of patients receiving PPT: in group 2 ($\Delta MADRS_{24-0}$=-20.2±6.57; $\Delta HAM\text{-}A_{24-0}$ =-13.2±5.68) and group 3 ($\Delta MADRS_{24-0}$=-17.8±4.73; $\Delta HAM\text{-}A_{24-0}$=-13.4±4.41), compared with group 1 ($\Delta MADRS_{24-0}$=-5.42±7.14; $\Delta HAM\text{-}A_{24-0}$=-4.58±6.80). There were no significant differences between the groups according to the PHQ-9 depression questionnaire (respectively, in group 1, $\Delta PHQ\text{-}9_{24-0}$=-4.89±4.87; in group 2, $\Delta PHQ\text{-}9_{24-0}$ =-6.73±4.97; in group 3, $\Delta PHQ\text{-}9_{24-0}$=-7.26±5.58), despite a greater decrease in the severity of depression in groups with

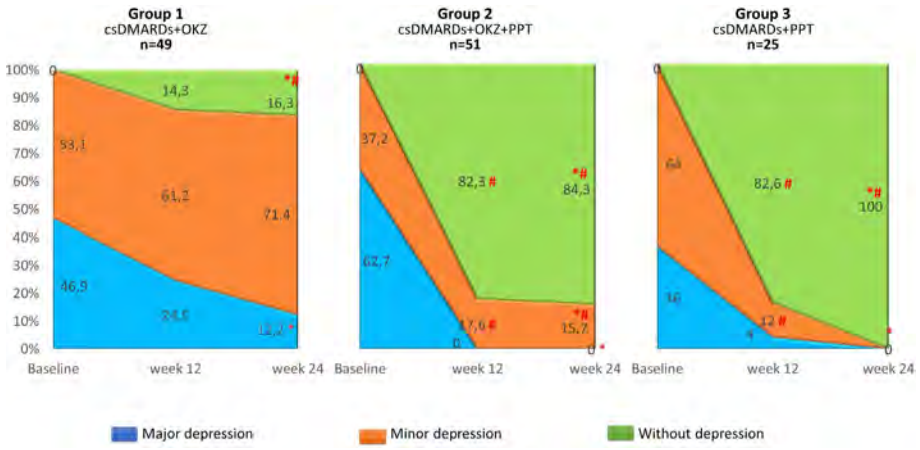


Figure 3. The dynamics of the incidence of major/ minor depression according to DSM-5 criteria depending on therapy Note: csDMARDs - conventional synthetic disease modifying antirheumatic drugs; OKZ – olokizumab: PPT – psychopharmacotherapy; * p<0,05 (comparison between baseline and week.24 in Groups); # p<0,001 (comparison between Group 1 and Groups 2-3)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

PPT. According to a semi-structured interview with a psychiatrist and projective experimental psychological techniques, the proportion of patients without depression 24 weeks after the start of therapy was significantly higher in the groups receiving PPT: 84.3% in group 2, 100% in group 3, and 16.3% in group 1.

Conclusion: In patients with moderate/high RA activity and comorbid depression, OKZ without PPT can lead to a decrease in severity of depression in 51% of patients with RA, with complete regression of depressive symptoms observed in 16.3% of patients, mainly those with minor depression. OKZ therapy without PPT also reduces the severity of anxiety, but does not eliminate it completely. The combination of OKZ and PPT is optimal for achieving complete regression of depression and anxiety in this category of RA patients.

Disclosure: T. Lisitsyna: R-Pharm, JSC, 6; **A. Abramkin**: None; **D. Veltishchev**: None; **S. Kuzkina**: R-Pharm, JSC, 3; **A. Borisova**: None; **V. Ignatiev**: R-Pharm, JSC, 3; **M. Samsonov**: R-Pharm, JSC, 3; **E. Nasonov**: None.

Abstract Number: 1324

Similar Negative Effects of Fatigue on Physical Activity in Persons with Rheumatoid Arthritis and Healthy Controls: A Patient-Control Study

Maartje Cox[1], Kyra Theunissen[2], Kenneth Meijer[2], Annick Timmermans[3], **Sofia Ramiro**[4], Annelies Boonen[5] and Guy Plasqui[2], [1]Australian National Phenome Centre - Murdoch University, Booragoon, Western Australia, Australia, [2]Maastricht University, Maastricht, Netherlands, [3]Universiteit Hasselt, Hasselt, [4]Leiden University Medical Center, Bunde, Netherlands, [5]Maastricht University Medical Centre+ & Maastricht University, Maastricht, Limburg, Netherlands

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: People with rheumatoid arthritis (pwRA) are prone to fall short of the World Health Organization's physical activity (PA) recommendations due to perceived fatigue and pain. Given the high prevalence of fatigue and its impact on health-related quality of life and social participation, this study investigated objectively measured PA patterns and the association between PA and self-reported fatigue in pwRA compared to healthy controls (HC).

Methods: In this observational cross-sectional study, pwRA (DAS28 > 2.6) and HC wore a tri-axial accelerometer (ActiGraph wGT3X-BT, ActiGraph LLC) on one ankle for ≥4 days. Accelerometer-based outcomes included vector magnitude counts/min (square root of summed sagittal, frontal, and vertical axes' counts/min squared – primary outcome), step count, and time spent in moderate-to-vigorous intensity PA. Data were separated by day and time (weekday/weekend; daytime/evening) to investigate PA patterns. Fatigue severity was assessed using the Fatigue Severity Scale (FSS, 0–7). Associations between fatigue, RA status, and PA were examined using multilevel generalized estimating equations models (patient and day-timing as levels). Interactions between RA and fatigue were tested. Manual forward selection identified multivariable associations adjusted for confounders.

Results: Participants included 23 pwRA (20 females, age 52 (SD 13), FSS 4.7 (1.4)) and 18 HC (14 females, age 52 (11), FSS 2.1 (1.0)). Vector magnitude counts/min were lower in pwRA than HC at any time, with non-significant differences on weekday daytime (1534.3 (691.3) in pwRA vs 1802.6 (610.6) in HC), and larger differences on weekday evenings (880.7 (491.4) vs 1457.3 (572.7)) (Figure 1). Step count was also lower in pwRA (587 (226) vs 724 (224) steps/h), as was time spent in moderate-to-vigorous PA (1.6 (1.4) vs 2.7 (1.5) min/h). No interaction was found between fatigue and RA, indicating that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

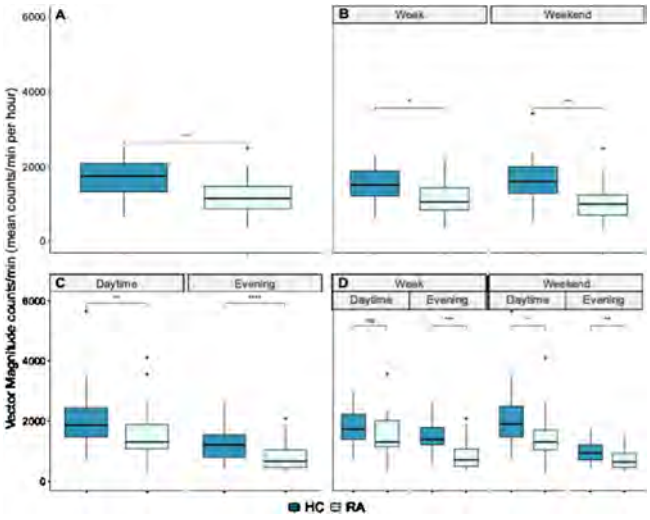


Figure 1: Vector Magnitude counts per minute (mean counts/min per hour) measured in rheumatoid arthritis patients (RA) and healthy controls (HC) overall (A), on weekdays as compared to the weekend (B), during the day and during the evening (C), and separated by day as well as timing of the day (D). ns p > .05, * p < .05, ** p < .01, *** p < .001, **** p < .0001

Table 1: Effect of RA vs HC on the Vector Magnitude Counts per Minute in univariable and multivariable Generalized Estimating Equations analyses

	Univariable model	Multivariable model
Variables	**Coefficient (95% CI)**	**Coefficient (95% CI)**
Age (years)	2.48 (-9.53; 14.50)	ns
Male vs Female	136.46 (-315.00; 587.91)	ns
BMI (kg/m²)	-47.14 (-78.60; -15.67)	-27.18 (-50.73; -3.62)
FFM (kg)	-6.20 (-24.68; 12.28)	ns
RA vs HC	-467.72 (-768.40; -167.05)	-330.63 (-650.45; -10.81)
FSS (0-7)	-117.06 (-216.04; -18.09)	-43.89 (-135.26; 47.48)
Weekend vs Week	-24.48 (-301.03; 252.07)	§
Evening vs Daytime	-724.93 (-945.42; -504.44)	§
Day-Timing:		
Weekend-Daytime	Reference	Reference
Weekday-Daytime	-123.89 (-509.31; 261.54)	-129.66 (-527.19; 267.87)
Weekday-Evening	-687.07 (-1059.60; -314.54)	-723.68 (-1091.19; -356.16)
Weekend-Evening	-942.19 (-1287.31; -597.07)	-970.77 (-1322.72; -618.82)

§Variables Weekend vs Week and Evening vs Daytime were not considered for the multivariable model, since the variable Day-Timing combines the information from both these variables

ns: variable not significant in the univariable model and not a confounder for RA vs HC and therefore not included in the multivariable model

BMI, Body Mass Index; FFM, Fat Free Mass; FSS, Fatigue Severity Scale

fatigue affected PA similarly in both groups. Likewise, no interaction between group and day-timing was observed, suggesting comparable daily PA patterns in pwRA and HC. RA was significantly and negatively associated with vector magnitude counts/min after adjusting for confounders (β = -330.63; 95% CI = -650.45 to -10.81; Table 1). In the multivariable model, lower vector magnitude counts/min was seen in pwRA, persons with higher fatigue severity (β = -43.89; 95% CI = -135.26 to 47.48), and in persons with higher BMI (β = -27.18; 95% CI = -50.73 to -3.62). BMI, RA presence, and fatigue were similarly negatively associated with step count and time spent in moderate-to-vigorous PA.

Conclusion: pwRA performed less objectively measured PA than HC. Fatigue was inversely associated with PA, with no differential impact between groups. Future research should examine the role of transient vs persistent fatigue, employability, inflammation, and medication use in PA participation. This may identify which patients are most at risk of falling short of PA guidelines and help design effective interventions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Cox: None; **K. Theunissen**: None; **K. Meijer**: None; **A. Timmermans**: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **A. Boonen**: AbbVie/Abbott, 5, Alfasigma, 2, Celgene, 5, Eli Lilly, 2, Novartis, 2, Sandoz, 2, UCB, 2; **G. Plasqui**: None.

Abstract Number: 1325

Plasma Matrix Metalloproteinases and Heart Failure Outcomes in Rheumatoid Arthritis

Tate Johnson[1], Michael Duryee[1], Punyasha Roul[2], Grant Cannon[3], Gary Kunkel[4], Beth Wallace[5], Isaac Smith[6], John Richards[7], Katherine Wysham[8], Gail Kerr[9], Andreas Reimold[10], Pascale Schwab[11], Daniel Anderson[12], Joshua Baker[13], Geoffrey Thiele[1], Ted Mikuls[1] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]UNMC, Omaha, NE, [3]University of Utah and Salt Lake City VA, Salt Lake City, UT, [4]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [5]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [6]Duke University Hospital, Durham, NC, [7]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [8]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [9]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [10]Dallas VA Medical Center, Dallas, TX, [11]VA Portland and Oregon Health & Science University, Portland, OR, [12]0587964, Durham, NC, [13]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The mechanisms of heart failure (HF) risk in RA remain incompletely understood. HF with preserved ejection fraction (HFpEF) is over-represented in RA, which may be a result of chronic inflammation leading to cardiac remodeling and fibrosis. Matrix metalloproteinases (MMPs) are involved in extracellular matrix remodeling, upregulated in RA circulation and synovium, and associate with RA-interstitial lung disease, another fibrotic extra-articular manifestation in RA. We aimed to evaluate the association of plasma MMP concentrations with HF and HF subtype risk in RA.

Methods: In a multicenter, prospective cohort of US Veterans with RA, MMP-1, -3, -7, and -9 were measured from banked plasma at enrollment, using R-PLEX immunoassays (MesoScale Diagnostics). Analyte concentrations were log-transformed and standardized, categorized into quartiles, and dichotomized as high (quartile 4) vs. low (quartiles 1-3). Incident HF was defined as an outpatient HF diagnosis (2+ diagnostic codes at least 30 days apart), HF hospitalization or HF-related death in linked VA, Medicare, and National Death Index data. HF subtypes (HF with reduced EF [HFrEF] < 40%, HFpEF ≥50%) were defined using the most proximate left ventricular EF prior to or < 30 days after HF event (if prior EF was missing), extracted from clinical notes using a validated natural language processing tool. Participants without HF at baseline were

Table 1. Association of Plasma MMP Quartiles with Incident Heart Failure in RA

Table 1. Association of plasma matrix metalloproteinase quartiles with incident heart failure in RA*

	MMP-1	MMP-3	MMP-7	MMP-9
Per S.D.	1.11 (1.00-1.23)	1.10 (0.99-1.22)	1.21 (1.09-1.35)	1.00 (0.91-1.10)
Per Quartile				
Q1	*Ref*	*Ref*	*Ref*	*Ref*
Q2	1.02 (0.77-1.35)	1.03 (0.78-1.36)	1.07 (0.82-1.41)	1.38 (1.06-1.79)
Q3	1.06 (0.80-1.41)	1.20 (0.92-1.56)	1.06 (0.80-1.40)	1.00 (0.76-1.31)
Q4	1.26 (0.96-1.67)	1.24 (0.94-1.64)	1.68 (1.27-2.22)	1.17 (0.90-1.53)
p-for-trend	0.08	0.07	<0.01	0.71

*Estimates are hazard ratios (95% confidence interval) adjusted for age, sex, race, smoking status, body mass index, ischemic heart disease, hypertension, diabetes, and DAS28 in Cox regression models. Quartile 1 (Q1) is the lowest quartile and serves as the reference (Ref) category. P-for-trend assessed in a linear fashion across MMP quartiles.

Abbreviations: MMP, matrix metalloproteinase; RA, rheumatoid arthritis; SD, standard deviation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

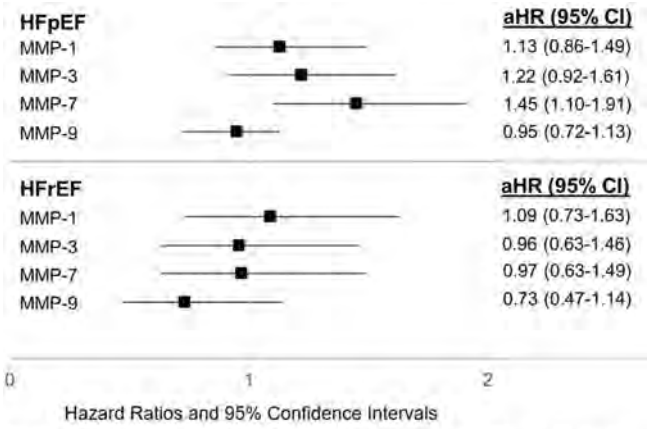


Figure 1. Association of high (quartile 4) vs. low (quartiles 1-3) matrix metalloproteinase (MMP) concentrations with HF subtypes in RA. Forest plot illustrating the association of plasma MMP concentrations with incident heart failure with preserved (HFpEF) and reduced (HFrEF) ejection fraction in RA. Estimates are hazard ratios adjusted (aHR) for age, sex, race, smoking status, body mass index, ischemic heart disease, hypertension, diabetes, and DAS28.

Table 2. Matrix metalloproteinase concentrations and risk of HF-related hospitalization or death in RA patients with prevalent HF

	Per 1 S.D.	High vs. low**
MMP-1	1.11 (0.88-1.41)	1.53 (0.98-2.38)
MMP-3	1.14 (0.88-1.47)	1.53 (0.94-2.48)
MMP-7	**1.40 (1.11-1.76)**	**1.91 (1.23-2.97)**
MMP-9	0.91 (0.73-1.15)	1.07 (0.66-1.72)

* Estimates are hazard ratios (95% CI) adjusted for age, sex, race, smoking status, BMI, ischemic heart disease, hypertension, diabetes, and DAS28 in Cox regression models restricted to RA patients with prevalent HF (N=349)
** High = quartile 4, low = quartiles 1-3
Bold denotes p value < 0.05

followed to incident HF, death, or end of study period (4/2022). The association of MMPs with incident HF and HF subtypes was estimated in multivariable Cox regression models adjusted for age, sex, race, smoking status, BMI, ischemic heart disease, hypertension, diabetes, and DAS28 at baseline. Among patients with prevalent HF, the association of MMPs with risk of future HF hospitalization and HF-related death was tested using similar multivariable Cox regression models.

Results: Among 2,855 participants without HF at baseline (mean age 63 years, 86% male, mean DAS28 3.5) 488 HF diagnoses (N=115 HFrEF, 246 HFpEF) were identified over a median follow up of 7 years. In fully adjusted models, MMP-7 was associated with incident HF risk (per 1 SD aHR 1.21 [1.09-1.35]; **Table 1**) in a dose-dependent manner (quartile (Q)4 vs. Q1 aHR 1.68 [1.27-2.22], p-for-trend < 0.01). This was driven by a stronger association with HFpEF (high vs. low aHR 1.45 [1.10-1.91]; **Figure 1**) compared with HFrEF (high vs. low aHR 0.97 [0.63-1.49]). While a trend toward higher HF risk was observed with higher MMP-1 (Q4 vs. Q1 aHR 1.26 [0.96-1.67], p-for-trend = 0.08) and MMP-3 quartiles (Q4 vs. Q1 aHR 1.24 [0.94-1.64], p-for-trend = 0.07), these were not significant (**Table 1**). Among patients with prevalent HF (N=349), MMP-7 was associated with future HF hospitalization and HF-related death (high vs. low aHR 1.91 [1.23-2.97]; **Table 2**).

Conclusion: MMP-7 was associated with incident HFpEF and a higher risk of HF hospitalization or HF-related death in RA patients with prevalent HF, independent of traditional risk factors and RA disease activity. These findings support MMPs may play a role in cardiac remodeling and dysfunction in RA. Continued research is needed to incorporate these findings into clinical risk stratification and HF prevention strategies in RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Johnson: None; **M. Duryee**: None; **P. Roul**: None; **G. Cannon**: None; **G. Kunkel**: None; **B. Wallace**: None; **I. Smith**: None; **J. Richards**: None; **K. Wysham**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **A. Reimold**: None; **P. Schwab**: None; **D. Anderson**: None; **J. Baker**: Amgen, 5; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 1326

Association Between Physical Function and Nutritional Status in Rheumatoid Arthritis Patients

Yasumori Sobue[1], Mochihito Suzuki[2], Yoshifumi Ohashi[3], Shuji Asai[2] and Shiro Imagama[2], [1]Sobue Orthopedic Clinic Yatomi, Aichi, Japan, [2]Nagoya University Graduate School of Medicine, Nagoya, Japan, [3]Aichi Medical University, Graduate School of Medicine, Aichi, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

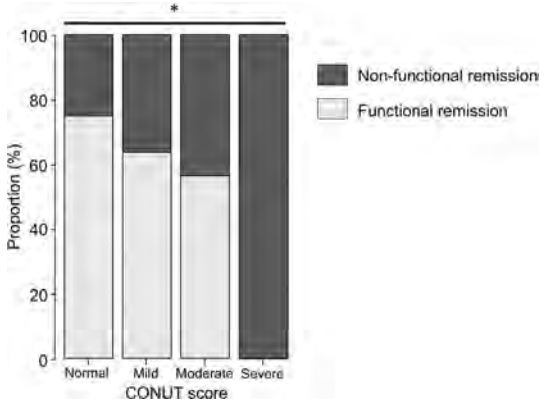
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic inflammatory disease that primarily affects the joints but also has substantial implications for physical function. Persistent inflammation may contribute to malnutrition, which in turn can lead to muscle weakness and impaired physical function. While the association between inflammation and nutrition has been reported (1), few studies have examined how nutritional status relates specifically to physical function in RA. This study aimed to investigate the association between nutritional status and physical function in patients with RA.

Methods: Among the 686 patients seen between June and August 2024, this cross-sectional study included 613 RA patients with available background data, including Controlling Nutritional Status (CONUT) scores and Health Assessment Questionnaire-Disability Index (HAQ-DI). The CONUT score, calculated based on serum albumin, total cholesterol, and total lymphocyte count, is a simple and objective tool for assessing the nutritional status of RA patients (2). Nutritional status was classified as normal (0–1 points), mild (2–4 points), moderate (5–8 points), or severe (9–12 points), with a score of ≥2 indicating nutritional risk. Physical function was assessed using the HAQ-DI, with a score of ≤0.5 defined as functional remission. Multivariable logistic regression analysis was conducted to examine the association between nutritional risk and functional



Proportions of Patients with Functional Remission Across CONUT Score Categories. Functional remission was defined as a HAQ-DI score of ≤0.5. Nutritional status based on the CONUT score was classified as normal (0–1), mild (2–4), moderate (5–8), and severe (9–12). A P-value of <0.001 was determined using the Cochran–Armitage trend test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

remission, adjusting for relevant background factors including age, disease duration, and the Clinical Disease Activity Index (CDAI).

Results: Among the 613 patients (74.2% female), 431 (70.3%) achieved functional remission. The prevalence of non-remission increased with the severity of nutritional risk: 25.2% in the normal, 36.3% in the mild, 43.8% in the moderate, and 100% in the severe CONUT categories (Figure). The mean age (functional remission/non-remission) was 67.1 ±13.2/72.1±13.7 years, disease duration was 12.1±9.2/16.9±11.4 years, CDAI was 3.7±5.2/11.8±9.6, and CONUT score was 1.21±1.23/1.62±1.55, all of which showed significant differences between the groups. Nutritional risk (CONUT score ≥2) was more prevalent in patients without functional remission than in those with remission (47.3% vs. 33.9%, $p < 0.001$). In multivariable logistic regression analysis adjusted for age, disease duration, and CDAI, nutritional risk was significantly associated with non-remission (odds ratio: 1.86, 95% CI: 1.19–2.91).

Conclusion: Nutritional risk was significantly associated with poor physical function in RA patients. Since physical function is a key determinant of quality of life in RA, early identification and management of nutritional risk may contribute to maintaining better function and improving overall outcomes. Nutritional interventions should be considered as part of comprehensive care in RA, especially for those not achieving functional remission.

Disclosure: Y. Sobue: None; **M. Suzuki**: None; **Y. Ohashi**: None; **S. Asai**: None; **S. Imagama**: None.

Abstract Number: 1327

Systematic Review of Mobility in Rheumatoid Arthritis with Digitally Measured Objective Assessment

Anna fishbein[1], Rachel Lawson[2], Veleka Allen[1], Xiaozhong Zhang[3], Laura Chambre[4], Stephen Ruhmel[1], Sophie Wilhelm[1], Fredric Marrache[5], Maria Wiekowski[1], Markus Kohlmann[6] and Jeffrey Curtis[7], [1]Sanofi, Morristown, NJ, [2]Sanofi, Earley, United Kingdom, [3]Sanofi, Chengdu, China (People's Republic), [4]Sanofi, Cambridge, MA, [5]Sanofi, Gentilly, France, [6]Sanofi, Frankfurt, Germany, [7]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) are less physically active than the general population, and these activity differences can be measured through digital devices. This systematic review examined various mechanisms by which mobility has been objectively measured in RA patients and highlighted findings on common digital endpoints related to mobility.

Methods: We performed a literature search using PubMed and Embase databases through August 2024 with search terms including mobility, physical activity, physical function, sedentary behavior, walking, and digital measurement technologies. After removing duplicates, 715 titles were screened, with 105 meeting inclusion criteria (Figure 1). Studies were categorized by primary aim: validation of digital technology, descriptive observational studies, assessment of interventions (e.g. initiation of RA treatment), and digital technology as a monitoring intervention itself. Technology used was assessed based on manuscript categorization.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

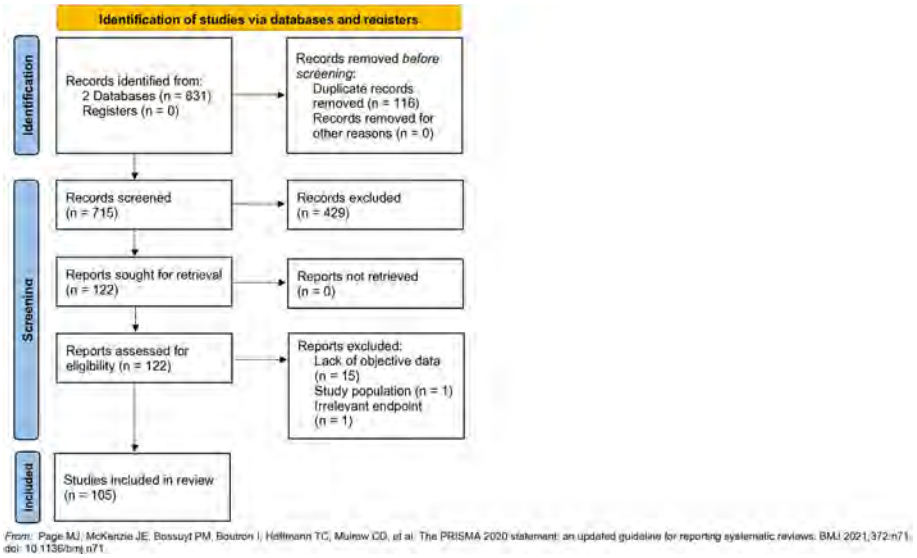


Figure 1: PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources

Results: Among the 105 studies, 28 (26.7%) validated digital technology, 41 (39.0%) were descriptive observational studies, 30 (28.6%) assessed interventions, and 6 (5.7%) used digital technology as intervention. Accelerometers were the most commonly used digital device (n=54, 51.4%), followed by activity monitors (n=19, 18.1%), pedometers (n=6, 5.7%), and smartwatches (n=3, 2.9%). Commonly measured digital endpoints included daily step counts, sedentary time/behavior, and time spent in different physical activity intensities. RA patients showed greater sedentary behavior (9-10 h/day), and significantly less moderate-to-vigorous physical activity ($p < 0.001$) compared to matched controls (Belau MH, et al. 2024). Only 5-17% of RA patients met recommended physical activity guidelines (Bell K, et al. 2022, Khoja SS, et al. 2016). Patients with controlled disease showed greater physical activity than those with active disease (Barami T, et al. 2017). Physical activity was inversely related to fatigue (Rongen-van Dartel SA, et al. 2014) and positively associated with improved mood (Hegarty RSM, et al. 2015) and quality of life (Bell K, et al. 2022). Diurnal patterns revealed reduced activity in afternoons/evenings, with morning stiffness affecting early day mobility (Keogh A, et al. 2020, Prioreschi A, et al. 2013).

Conclusion: We identified numerous ways in which mobility is objectively measured in patients with RA by digital tools, with accelerometers as the predominant technology and step counts, sedentary time, and activity intensity as the key endpoints. Findings suggest that patients with RA are more sedentary and less active than healthy controls, with disease activity significantly influencing mobility patterns. Future work is planned to conduct a meta-analysis of findings described in this abstract.

Disclosure: A. fishbein: Sanofi, 3; **R. Lawson**: Sanofi, 3; **V. Allen**: Sanofi, 3; **X. Zhang**: Sanofi, 3; **L. Chambre**: Sanofi, 3; **S. Ruhmel**: Sanofi, 3; **S. Wilhelm**: Sanofi, 3; **F. Marrache**: Sanofi, 3; **M. Wiekowski**: Sanofi, 3; **M. Kohlmann**: Sanofi, 3; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1328

Mortality Trends of Hypertension in Patients with Rheumatoid Arthritis in the United States (1999–2020)

Rameez Qasim[1], Khadija Mohib[2], Muhammad Ali[3], Umm E Aimen Minhas[4], Abu-bakr Ahmed[5] and **Areeba Minhaj**[6], [1]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [2]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, [3]Dow International Medical College, Karachi, Sindh, Pakistan, [4]Allama Iqbal Medical College, Lahore, Pakistan, [5]Kirk Kerkorian School of Medicine, Las Vegas, NV, [6]University of South Dakota, sioux falls, SD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Hypertension is highly prevalent among patients with rheumatoid arthritis (RA) and significantly increases the risk of cardiovascular disease (CVD). Despite this established relationship, there is limited data on long-term mortality trends related to hypertension in patients with RA in the United States.

Methods: We used the CDC WONDER database to analyze mortality data from 1999 to 2020. Individuals aged 25 years and older who died with both hypertension and RA were identified using ICD codes I10–I15 (hypertension) and M06, M08.0 (rheumatoid arthritis). Age-adjusted mortality rates (AAMR) per 100,000 population were calculated. Joinpoint regression analysis was used to determine Average Annual Percent Change (AAPC), with statistical significance assessed via p-values. Mortality trends were stratified by gender, race/ethnicity, U.S. Census region, and urbanization level.

Results: Between 1999 and 2020, the age-adjusted mortality rate for individuals with both hypertension and RA increased from 3.9 to 14.0 per 100,000 population, with total deaths reaching 3,793 in 2020. Female mortality rates rose more sharply than male rates (AAMR 5.2 to 18.2 vs. 3.7 to 8.3), with AAPCs of -6.9 (95% CI: -7.3 to -6.6) and -6.3 (95% CI: -6.7 to -5.8), respectively. Nonmetropolitan areas had consistently higher mortality rates compared to metropolitan areas, increasing from an AAMR of 5.0 to 17.4 versus 3.7 to 13.4 (AAPC -6.3 vs. -7.0). Regionally, the South had the highest mortality rate in 2020 (AAMR 12.4), while the Northeast had the lowest (AAMR 8.9). Among racial and ethnic groups, Black or African American individuals had the highest mortality (AAMR 15.6; AAPC -6.7), followed by Hispanics or Latinos (AAMR 16.4; AAPC -8.2) and Whites (AAMR 10.4; AAPC -6.5). Mortality increased notably in adults aged 75 and older in 2020, likely influenced by the COVID-19 pandemic.

Conclusion: Hypertension-related mortality in patients with rheumatoid arthritis has risen significantly over the past two decades, with notable disparities across gender, geographic regions, racial and ethnic groups, and urbanization status. These findings underscore the need for targeted interventions and improved cardiovascular risk management strategies in this high-risk population.

Disclosure: R. Qasim: None; **K. Mohib**: None; **M. Ali**: None; **U. Minhas**: None; **A. Ahmed**: None; **A. Minhaj**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1329

Relationship Between Circulating Bacterial Small RNAs, Methotrexate Response, and Microbiome in New Onset Rheumatoid Arthritis

Carolina Ramirez-Becerra[1], Tulsi Joishy[2], Sheau-Chiann Chen[2], Marisol Ramirez-Solano[2], Quanhu Sheng[2], Peter Turnbaugh[3], Carles Ubeda[4], Renuka Nayak[5], Rebecca Blank[6], Jose Scher[7] and Michelle Ormseth[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, [3]University of California, San Francisco, San Francisco, CA, [4]Fisabio, Madrid, [5]University of California, San Francisco (UCSF), San Francisco, CA, [6]NYU Langone Health, New York, NY, [7]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Microbiome and microbial products are possible contributors and predictors to methotrexate (MTX) response variability. Bacterial small RNAs (sRNAs) are found in human plasma and can alter host gene expression and immune function. The purpose of this study was to determine 1) if circulating bacterial sRNAs are associated with response to MTX in patients with new onset RA (NORA), 2) whether sRNAs aligning to stool microbiome taxa that are associated with MTX response also are associated with MTX response, and 3) the overall relationship between circulating bacterial sRNAs and stool microbiome.

Methods: The study included a training cohort of 26 NORA and validation cohort of 20 NORA patients who were studied previously for relationship between microbiome and MTX response. Participants met ACR/EULAR 2010 classification criteria for RA, were treatment naïve at the time of plasma collection, and were followed for treatment response to MTX at 4 months. Plasma sRNAs from both cohorts (n=46) were sequenced and aligned to bacterial genomes using the TIGER pipeline. Individual bacterial sRNA sequences and taxa counts were compared in methotrexate responders (MTX-R) versus non-responders (MTX-NR) by DESeq2. Spearman's rank correlation test was used to measure the association between plasma small RNAs and the stool microbiome.

Results: Demographic data are included in **Table 1**. Twelve bacterial sRNAs were enriched in the plasma of MTX-R versus MTX-NR in both the training and validation cohorts and included tRNA derived RNAs (tDRs) and ribosomal derived RNAs (rDRs) mapping to genera such as *Prevotella, Bacteroides, Porphyromonas, Ruminococcus, Blautia*, and *Clostridium*. Stool OTUs corresponding to *Bacteroides and Prevotella*, were abundant and significantly enriched in MTX-R versus MTX-NR in the training cohort as previously reported, and plasma sRNAs aligning to these taxa were also enriched in MTX-R versus MTX-NR in the same participants (p=0.04 and p=0.01, respectively). However, Clostridiales family and Ruminococcus genus that were decreased in MTX-R versus MTX-NR in the prior report were altered in plasma bacterial sRNAs of the same taxa but in the opposite direction (**Figure 1**). Combining training and validation cohorts, the overall correlation between the stool microbiome and respective plasma bacterial sRNA taxa counts was poor; however, several stool taxa were associated with the total abundance of bacterial sRNAs in plasma (**Figure 2**).

Conclusion: Consistent with findings that stool *Prevotella* and *Bacteroides* were increased in MTX-R, plasma sRNAs aligning to these taxa were similarly enriched in MTX-R versus MTX-NR. Moreover, increased abundance of specific plasma sRNAs aligning to *Prevotella* and *Bacteroides* were reproducibly enriched in MTX-R in two cohorts, positioning them as potential predictors of clinical response to MTX. Future studies will be needed to replicate these findings and determine the role of these specific bacterial sRNAs on MTX response and how they may gain entry to human circulation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical data, for training and validation cohort.

	Training cohort N=26	Validation cohort N=20
Age, years	37.0 [30.3, 58.3]	46.0 [38.5, 50.3]
Female	19 (73)	15 (75)
Ethnicity		
Caucasian or Hispanic White, n (%)	13 (50)	10 (50)
Hispanic, n (%)	8 (31)	5 (25)
African American/African n (%)	1 (4)	3 (15)
Others, n (%)	4 (15)	2 (10)
Disease duration, months	3.0 [2.0, 5.0]	3.5 [2.0, 5.0]
Disease activity parameters		
ESR, mm/h	27.5 [19.3, 42.8]	30.0 [19.5, 44.5]
CRP, mg/l	14.5 [10.6, 25.6]	8.2 [3.5, 23.7]
Tender joints count, units	10 [5, 14]	8 [6, 12]
Swollen joints count, units	7 [3, 12]	11 [6, 16]
DAS28 score at baseline, units	5.4 [4.8, 6.3]	5.9 [5.2, 6.6]
DAS28 score at month 4, units	3.7 [2.8, 5.2]	4.4 [2.6, 5.1]
DAS28 score change at month 4, units	1.5 [0.4, 2.5]	1.2 [0.7, 2.7]
Autoantibody status		
IgM-RF positive, n (%)	24 (92)	20 (100)
ACPA positive, n (%)	25 (96)	18 (90)
IgM-RF and/or ACPA positive, n (%)	26 (100)	20 (100)
IgM-RF titer, kU/l	113.0 [48.5, 209.3]	126.5 [34.3, 498.5]
ACPA titer, kAU/l	89.3 [15.3, 250.0]	250.0 [181.3, 250.0]
Methotrexate response 4 months		
MTX-R, n (%)	10 (39)	8 (40)

Continuous data are presented as median [first quartile, third quartile] for continuous variables and number (%) for categorical variables. ESR= erythrocyte sedimentation rate, CRP=C-reactive protein, DAS28= disease activity score, TJC= tender joint count, SJC= swollen joint count, RF=rheumatoid factor, ACPA=anti-citrullinated protein antibody, MTX-R = methotrexate responder.

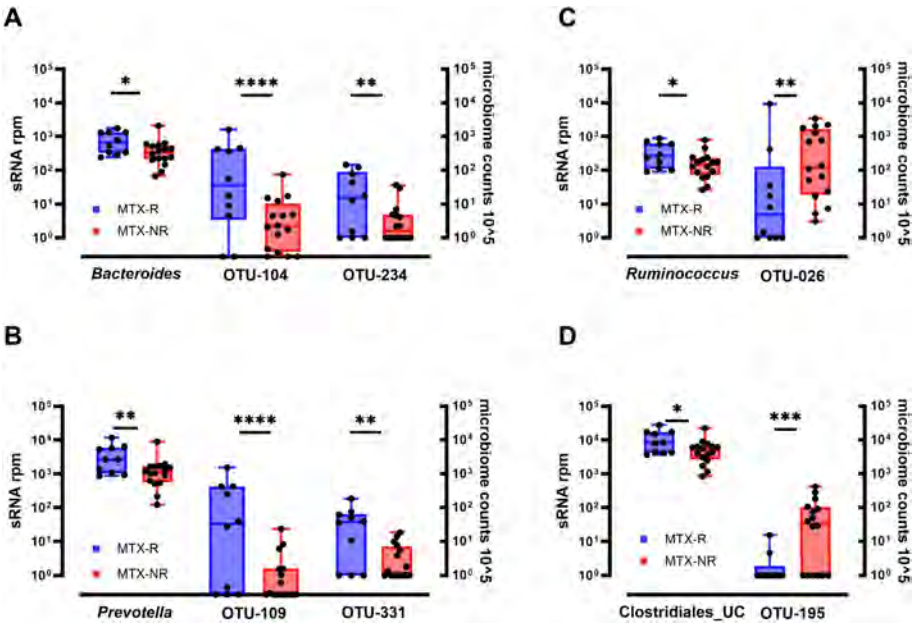
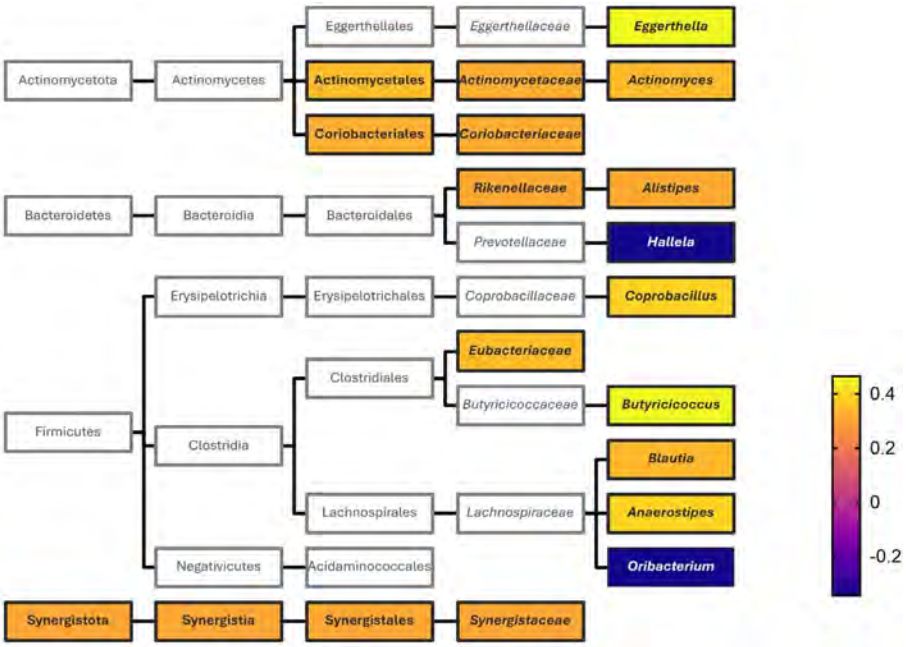


Figure 1. Highly abundant (>0.01% in ≥1 group) and significantly altered stool OTUs in methotrexate responders (MTX-R) versus methotrexate non-responders (MTX-NR) (q < 0.05 by DESeq2) (as previously presented in Artacho et al Arthritis Rheumatol 2021;73(6):9310942) and their aligned plasma sRNAs in the training cohort.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Stool microbiome genera and respective phylogeny significantly associated with the total abundance of bacterial sRNAs in plasma. Color scale refers to Spearman correlation coefficient.

Disclosure: C. Ramirez-Becerra: None; **T. Joishy**: None; **S. Chen**: None; **M. Ramirez-Solano**: None; **Q. Sheng**: None; **P. Turnbaugh**: None; **C. Ubeda**: None; **R. Nayak**: None; **R. Blank**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **M. Ormseth**: None.

Abstract Number: 1330

Sex and reproductive stage modify the role of endogenous estrogens on coronary atherosclerosis in rheumatoid arthritis and differences reflect effects on inflammation and cholesterol metabolism

George Karpouzas[1], Bianca Papotti[2], Sarah Ormseth[3], Marcella Palumbo[2], Matthew Budoff[1] and Nicoletta Ronda[2], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]University of Parma, Parma, Italy, [3]The Lundquist Institute for Biomedical Innovation, Torrance, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Endogenous estrogens associate with cardioprotective benefits in the general population. Yet, dual pro- and anti-inflammatory effects were described in autoimmune states depending on concentration, disease entity and stage, cell-type involved, target organ environment, and intracellular metabolism. We here explore associations between endogenous estrogens, coronary atherosclerosis and cardiovascular risk in patients with rheumatoid arthritis (RA). Since RA activity is higher in females, especially after menopause, and inflammation is linked to cardiovascular risk, we interrogated whether these relationships varied by sex and menopause and whether they reflected differences in inflammation and lipoprotein functions influencing cell cholesterol homeostasis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

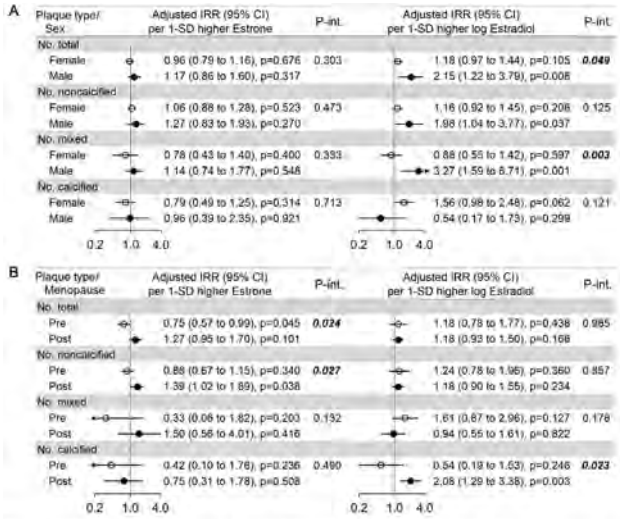


Figure 1 (A) Influence of sex on the association of estrone and estradiol with various plaque types. All models adjusted for age, hypertension, diabetes, HDLc, waist circumference, and menopause. (B) Influence of reproductive stage on the association of estrone and estradiol with various plaque types. All models adjusted for age, hypertension, diabetes, HDLc, and waist circumference.

Methods: Computed tomography angiography evaluated coronary atherosclerosis in 140 patients without known cardiovascular disease from a single-center. Serum estrone and 17-b-estradiol were measured with Elisa. Serum cholesterol loading capacity (CLC) on macrophages, which enhances atherosclerosis, was measured in THP-1 monocyte-derived macrophages. High-density lipoprotein cholesterol efflux capacity from macrophages via ATP-binding-cassette-A1 (ABCA1-CEC) and G1 transporters (ABCG1-CEC), which attenuates atherogenesis, was assessed in J774 macrophages and Chinese hamster ovary cells.

Results: Estrone and estradiol associated with higher coronary artery calcium score (p for interaction 0.023) and estradiol with more coronary plaques (p-for-interaction 0.048) in males but not females. Estrone was linked to fewer plaques in premenopausal women (p for interaction 0.043), while both estrone and estradiol associated with more plaques in

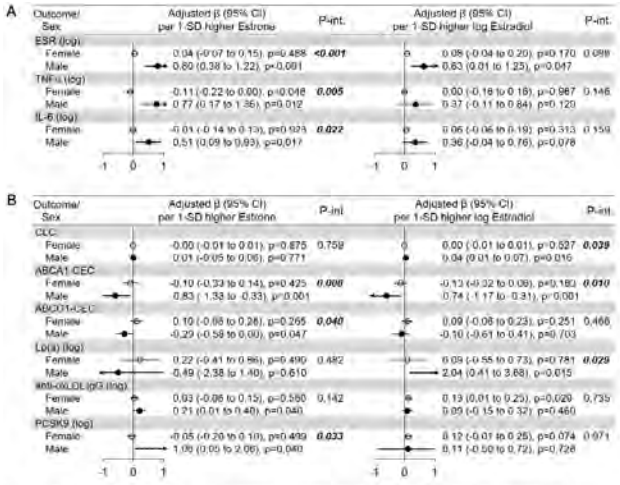


Figure 2 (A) Influence of sex on the association of estrone and estradiol with measures of inflammation. All models adjusted for age, hypertension, diabetes, HDLc, waist circumference, and menopause. **(B)** Influence of sex on the association of estrone and estradiol with lipoprotein parameters, anti-oxLDL IgG and PCSK9. All models adjusted for age, hypertension, diabetes, HDLc, CRP and waist circumference.
ESR, erythrocyte sedimentation rate; TNFa: tumor necrosis factor a; IL-6, interleukin-6; CLC, serum cholesterol loading capacity; ABCA1-CEC, cholesterol efflux through the ABCA1 transporter; ABCG1-CEC, cholesterol efflux through the ABCG1 transporter; Lp(a), lipoprotein(a); anti-oxLDL IgG, IgG antibodies against oxidized LDL; PCSK9, proprotein convertase subtilisin Kexin type-9; 95% CI, 95% confidence interval; SD, standard deviation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

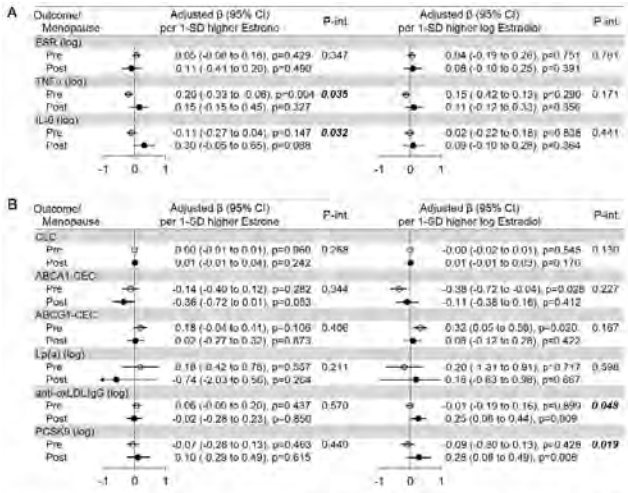


Figure 3 (A) Influence of reproductive status on the association of estrone and estradiol with measures of inflammation. All models adjusted for age, hypertension, diabetes, HDLc, waist circumference, and menopause. **(B)** Influence of reproductive stage on the association of estrone and estradiol with parameters of lipoprotein parameters, anti-oxLDL IgG and PCSK9. All models adjusted for age, hypertension, diabetes, HDLc, CRP and waist circumference. ESR, erythrocyte sedimentation rate; TNFa: tumor necrosis factor a; IL-6, interleukin-6; CLC, serum cholesterol loading capacity; ABCA1-CEC, cholesterol efflux through the ABCA1 transporter; ABCG1-CEC, cholesterol efflux through the ABCG1 transporter; Lp(a), lipoprotein(a); anti-oxLDL IgG, IgG antibodies against oxidized LDL; PCSK9, proprotein convertase subtilisin Kexin type-9; 95% CI, 95% confidence interval; SD, standard deviation

postmenopausal women (Figure 1A and B). Estrone associated with higher proatherogenic cytokine levels in males (Figure 2A) and in postmenopausal women, but lower levels in premenopausal women (Figure 3A). Likewise, estrone inversely associated with ABCA1-CEC (p-for-interaction 0.008) and ABCG1-CEC (p for interaction 0.040) in males (Figure 2B and 3B), while estradiol positively associated with CLC (p for interaction 0.044) and inversely with ABCA1-CEC (p-for-interaction 0.010) in males. Estrone, but not estradiol, inversely associated with cardiovascular risk (adjusted hazards ratio 0.43 [95% confidence interval 0.21-0.86] per standard deviation increase), particularly among premenopausal women (p for interaction=0.015).

Conclusion: Sex and reproductive status modified the effect of endogenous estrogens on coronary atherosclerosis in RA and their associations with inflammation and lipoprotein functions impacting on cholesterol homeostasis. Importantly, estrone levels inversely associated with cardiovascular risk independently of ASCVD score and coronary plaque burden, and further optimized risk estimates.

Disclosure: G. Karpouzas: Janssen, 1, Pfizer, 5, Scipher, 2; **B. Papotti**: None; **S. Ormseth**: None; **M. Palumbo**: None; **M. Budoff**: None; **N. Ronda**: None.

Abstract Number: 1331

anti-beta-2-glycoprotein-1 Iga Antibodies Facilitate Macrophage Cholesterol Loading and Influence Coronary Atherosclerosis Progression in a Dose-dependent Manner in Rheumatoid Arthritis

George Karpouzas[1], Bianca Papotti[2], Sarah Ormseth[3], Marcella Palumbo[2], Matthew Budoff[1] and Nicoletta Ronda[2], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]University of Parma, Parma, Italy, [3]The Lundquist Institute for Biomedical Innovation, Torrance, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Changes in serum cholesterol loading capacity (CLC) on macrophages were linked to coronary plaque progression in rheumatoid arthritis (RA). Inflammation, LDL oxidation and autoantibodies influenced macrophage cholesterol loading and plaque burden directly and indirectly. Oxidized LDL formed complexes with beta-2-glycoprotein-1 (b2GPI)—an antiatherogenic protein in serum and plaque—in both RA and controls. Complexes can be then bound by anti-b2GPI antibodies. Anti-b2GPI Ab, particularly of the IgA isotype, independently promoted coronary plaque progression in RA; yet the precise mechanisms remain speculative. We hypothesized that anti-b2GPI IgA may promote atherosclerosis progression by influencing oxidized LDL-mediated cholesterol loading on arterial macrophages.

Methods: Coronary CT angiography evaluated atherosclerosis (noncalcified, mixed, or calcified plaques) in 100 patients without cardiovascular disease at baseline and follow-up 6.9±0.4 years later. Presence of 5 plaques and lesions rendering greater than 50% stenosis were deemed extensive and obstructive disease respectively. CLC was measured as intracellular cholesterol content in serum treated human THP-1 monocyte-derived macrophages with a fluorimetric assay. Serum anti-b2GPI IgA were measured with ELISA at baseline and positivity was confirmed 12 weeks later. Negative binomial regression and logistic regression evaluated the influence of anti-b2GPI IgA on the relationship between CLC change and number of new plaques and likelihood of noncalcified plaque formation and new extensive or obstructive disease respectively.

Results: A significant interaction between CLC change and anti-b2GPI IgA titers on plaque progression was observed. Specifically, increasing anti-b2GPI IgA titers associated with more new plaques overall (p for interaction=0.005), higher likelihood of new noncalcified plaque formation (p for interaction=0.023) and new extensive or obstructive disease (p for interaction=0.043) only at the highest tertile of CLC change (Figure 1). This suggested that anti-b2GPI IgA may be involved in macrophage cholesterol loading by oxidized LDL in a dose-dependent manner. Anti-b2GPI IgA may also determine the composition of newly formed plaques in the context of increasing CLC change (Figure 2). CLC change associated with a greater likelihood of higher-risk noncalcified plaque progression in the presence (odds ratio 2.82, 95% confidence interval 1.40-5.67) but not absence of anti-b2GPI IgA (p for interaction=0.005). In contrast, CLC change associated with a greater likelihood of lower-risk calcified plaque progression in the absence (odds ratio 1.48, 95% confidence interval 1.19-1.84) but not presence of anti-b2GPI IgA (p for interaction=0.046).

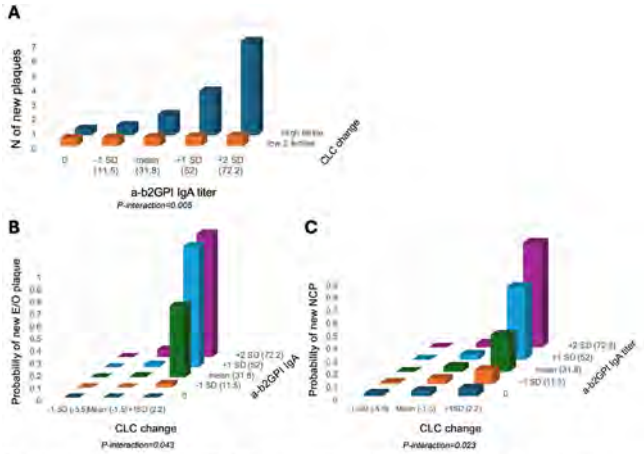


Figure 1. Increasing anti-b2GPI IgA titers associate with **A.** greater number of new plaques overall, **B.** greater likelihood of new extensive or obstructive disease and **C.** greater likelihood of new noncalcified plaques at the highest tertile of CLC change, but not the lower ones.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

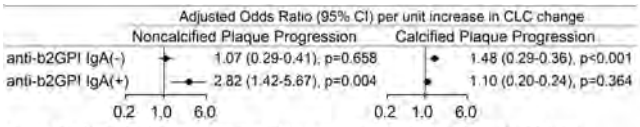


Figure 2. Effect of CLC on per-segment plaque progression stratified by anti-b2GPI-IgA positivity. All models adjust for 10-year atherosclerotic cardiovascular disease risk score, low-density lipoprotein cholesterol, body mass index, statin exposure during follow-up, and baseline plaque.

Conclusion: Anti-b2GPI IgA may facilitate macrophage cholesterol loading and influence coronary plaque progression and composition in a dose dependent manner, specifically at high levels of CLC change. Anti-b2GPI IgA may bind oxidized LDL/b2GP1 complexes to FcA receptors on arterial macrophages, promote cholesterol loading and atherosclerosis progression.

Disclosure: G. Karpouzas: Janssen, 1, Pfizer, 5, Scipher, 2; **B. Papotti**: None; **S. Ormseth**: None; **M. Palumbo**: None; **M. Budoff**: None; **N. Ronda**: None.

Abstract Number: 1332

Mid-Infrared Spectroscopy for Enhanced Diagnosis of Rheumatic Diseases

Gilad Halpert[1], Yair Dankner[2], Eri Govrin[1], Abdulla Watad[3], Omer Gendelman[1], Shlomo Segev[1], Yehuda Shoenfeld[1] and Howard Amital[1], [1]Sheba Medical Center, Ramat Gan, Israel, [2]Shenkar College of Engineering and Design, Ramar Gan, Israel, [3]Tel Hashomer Medical Center, Ramat Gan, Israel

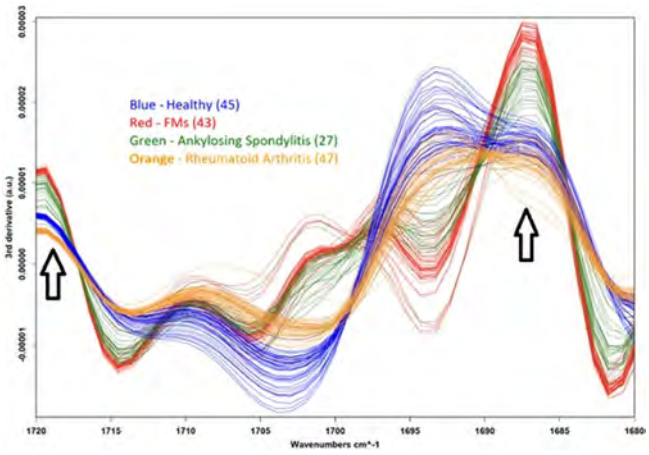
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Spectral analysis of liquid biopsies has recently emerged as a promising, non-invasive approach to improve the diagnosis of various pathologies. Our objective was to develop a rapid and precise strategy to differentiate among clinically challenging rheumatic inflammatory and autoimmune diseases, as well as to assess their severity, by analyzing the spectral properties of peripheral blood.

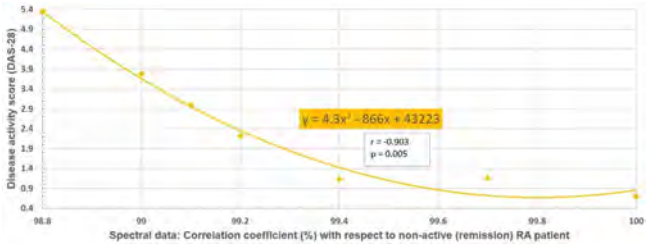
Methods: We recruited patients with rheumatoid arthritis (RA, n=47), ankylosing spondylitis (AS, n=27), fibromyalgia syndrome (FMs, n=43), along with healthy controls (n=45). Disease activity was assessed using the Disease Activity Score-28 (DAS-28) for RA, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for AS, and the Fibromyalgia Impact Questionnaire (FIQ) for FMs. Plasma concentrations of inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-17A and IFN-γ) were quantified via U-Plex ELISA (Meso Scale Diagnostics, USA). Peripheral blood mononuclear cells (PBMC) were isolated by standard density-gradient centrifugation (Lymphoprep™). Mid-infrared (Mid-IR) spectra were acquired from plasma and PBMC's supernatants using a Bruker V80 Fourier-transform infrared (FTIR) spectrometer. Correlation coefficient analysis was performed to relate specific spectral features to clinical scores and cytokine levels.

Results: Spectral analysis of plasma samples generated distinct spectral "fingerprints" that reliably distinguished FMs patients from those with RA, AS and healthy controls (Fig. 1). Notably, several infrared spectral features showed strong correlations with RA disease activity (e.g., DAS28) (Fig.2) and inflammatory cytokine levels (e.g. IL-6, IL-17A), indicating that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

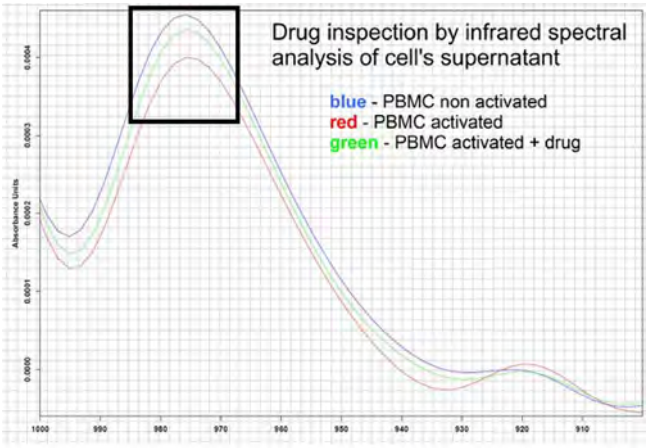


Mid-IR spectral analysis of plasma samples distinguishes fibromyalgia syndrome (FMs) patients (n=43) from other rheumatic inflammatory/autoimmune diseases: rheumatoid arthritis (n=47), ankylosing spondylitis (n=27), and healthy controls (n=45). Black arrows indicate specific optical windows where clear differentiation between the groups is observed, even to the naked eye of a rheumatologist or immunologist. The analysis considers the third derivative of the absorption data with respect to the wavenumbers (cm^{-1}).



A significant correlation between disease activity score of RA patients and spectral data of their plasma. A parabolic relationship between the disease activity score (DAS-28, y-axis) and the spectral data (correlation coefficient in percentage, x-axis). The absorption spectra of plasma derived from RA patients were measured. The correlation coefficient between the spectra and a reference spectrum was calculated (y-axis). The reference can be the average of a healthy control group or an RA patient in remission. The results align with expectations: the closer the spectrum is to the reference (higher correlation coefficient), the healthier the patient (lower DAS28 score). r = -0.903, p value = 0.005.

spectral markers reflect underlying inflammatory burden. Furthermore, spectral analysis of PBMC-derived supernatants from rheumatic patients, following activation (LPS/PHA) and treatment with anti-inflammatory drugs, corelated with biological data reflecting the inflammatory status of the cells (Fig. 3).



Spectral analysis, at a specific optical window, of PBMC-derived supernatants from rheumatic patients revealed spectral peaks (black square) that correlate with the in vitro status of the cells: non-activated cells (blue curve), inflammatory activation (red curve, shifted downward compared to the blue curve), or activation plus anti-inflammatory drug (green curve, shifted back toward the blue curve). The spectral results are consistent with biological findings.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Integrating Mid-IR spectral profiling of liquid biopsies (such as patients-derived plasma or -immune cells' supernatants) with established clinical and biological parameters provides a powerful, non-invasive modality for differential diagnosis and severity stratification of rheumatic diseases. This approach has the potential to improve diagnostic accuracy and guide personalized treatment strategies in rheumatology.

Disclosure: G. Halpert: None; **Y. Dankner**: None; **E. Govrin**: None; **A. Watad**: AbbVie/Abbott, 1, 6, Celgene, 1, 6, Eli Lilly, 1, 6, Janssen, 1, 6, Neopharm, 1, 6, Novartis, 1, 6; **O. Gendelman**: None; **S. Segev**: None; **Y. Shoenfeld**: None; **H. Amital**: None.

Abstract Number: 1333

Assessment of Lipid Abnormalities After Initiation of a JAK Inhibitor in Rheumatoid Arthritis in Clinical Practice

Salomé Abdellaoui[1], Omar Al Tabaa[1], Sophie Hecquet[1], Alice Combier[1], Sandrine Carves[1], Olivier Fogel[2], Yannick Allanore[3] and **Jérôme Avouac**[4], [1]Rheumatology department, Cochin Hospital, Paris, France, [2]AP-HP, Paris, France, [3]Université Paris Cité, Paris, France, [4]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: rheumatoid arthritis (RA) is characterized by a lipid paradox induced by systemic inflammation. JAK inhibitors (JAKi) have been associated with a short-term increase in total cholesterol (TC), LDL and HDL fractions, which could be a direct effect of the drug, or indirectly related to drug-induced systemic inflammation reduction. The aim of this study was to investigate the course of TC levels and fractions following the introduction of a JAKi.

Methods: Retrospective study conducted at a single center, encompassing all RA patients who initiated JAKi therapy between 2019 and 2023. The study population included patients who had at least two follow-up visits and had a lipid panel available at the time of enrollment. Patients who had received statin therapy at the time of enrollment were excluded.

The primary endpoint was defined as changes in TC and fractions at 6 months from the initiation of JAKi treatment. Secondary endpoints included the study of factors associated with changes in TC and fraction at 6 months, and changes in TC and fractions between the first and last available visits.

Results: 85 RA patients (68 women, 80%) met the inclusion criteria, with a mean age of 59± 13 years and a mean disease duration of 19.5± 12.4 years; 73 (86%) and 76 (89%) patients were rheumatoid factor and ACPA positive respectively, and 66 (78%) had bone erosions. 22 patients received baricitinib, 7 tofacitinib, 38 upadacitinib and 18 filgotinib. The DAS28-CRP at inclusion was 4.09± 1.26 with a mean CRP of 10±14 mg/L. Comorbidities, concomitant treatments and lipid profile at inclusion are presented in **Tables 1** and **2**. At inclusion, TC and HDL cholesterol (HDL-C) levels correlated negatively with CRP (respectively r=-0.23, p=0.042 and r=-0.25, p=0.040), but not with DAS28 or DAS28-CRP. This correlation was not observed for LDL and triglycerides.

At 6 months, there was a significant increase in TC (+0.17±0.37 g/L, p=0.016) and HDL-C (+0.09±0.19g/L, p=0.017), but not LDL-C (+0.02±0.31, p=0.68) (**Table 2**). This increase was inversely correlated with the reduction in CRP concentrations (-6±10 mg/L) upon JAKi (TC: r=-0.31, p=0.033 and HDL-C: r=-0.32, p=0.042). This increase was not associated with the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient characteristics

	JAKi (n=85)
Demographics	
Age (years), mean ± SD	59±13
Women, n (%)	68 (80)
Basic features of the disease	
Disease duration (years), mean ± SD	19.5±12.4
Rheumatoid factor positive, n (%)	73 (86)
Positive anti-CCP2 antibodies, n (%)	76 (89)
Bone erosions, n (%)	66 (78)
Extra-articular manifestations	32 (38)
Basic disease activity :	
Tender joints, mean± SD	5.7±5.4
Swollen joints, mean ± SD	4.5±4.8
Patient's overall assessment of disease, mean ± SD	63±25
SAR28, mean ± SD	4.65±1.36
DAS28-CRP, mean ± SD	4.09±1.23
ESR (mmH1), mean ± SD	30±25
CRP (mg/L), mean ± SD	10.1±13.7
Comorbidities	
Active / former smokers, n (%)	11 (13) / 27 (32)
Hypertension, n (%)	19 (22)
Diabetes mellitus, n (%)	8 (9)
Hypercholesterolemia (without statin treatment), n (%)	18 (21)
BMI, kg/m2, mean ± SD	24.9± 5.1
BMI >30 kg/m2, n (%)	16 (19)
Atherosclerotic cardiovascular disease, n (%)	3 (3.5)
History of ischemic stroke, n (%)	3 (3.5)
History of venous thromboembolism, n (%)	6 (7)
History of serious infection, n (%)	3 (3.5)
History of herpes zoster, n (%)	10 (12)
Previous neoplasia, n (%)	11 (13)
≥65 years and/or at least one CV risk factor, n (%)	60 (71)
>50 years AND at least one additional CV risk factor, n (%)	72 (85)
Treatments received	
Current use of corticosteroids, n (%)	60 (71)
Corticosteroid dose, mg/day, mean± DS	4.3±3.4
Current use of a conventional DMARD, n (%)	62 (73)
Current use of MTX, n (%)	49 (58)
JAKi targeted therapeutic line, mean± SD	3±2

Table 2: Changes in total cholesterol and fractions

	Inclusion	Visit M6	Delta M6-inclusion	p-value	Final visit	Delta Final - M6	p-value
Total cholesterol (g/L)	1.98±0.43	2.15±0.40	+0.17±0.37	0.016	1.96±0.39	-0.11±0.21	0.042
LDL cholesterol (g/L)	1.15±0.36	1.17±0.34	+0.02±0.31	0.68	1.16±0.67	-0.01±0.61	0.74
HDL cholesterol (g/L)	0.65±0.23	0.74±0.27	+0.09±0.19	0.017	0.63±0.17	-0.11±0.16	0.031
Triglycerides (g/L)	1.36±0.88	1.19±0.59	-0.16±0.61	0.16	1.07±0.54	-0.12±0.33	0.17

use of corticosteroids or methotrexate, nor with the course of the number of tender and swollen joints. At the last available visit (20±15 months after the onset of JAKi), there was a drop in TC and particularly in its HDL fraction compared with the first visit, with values close to those at the inclusion visit (**Table 2**). Statins were prescribed for 9 patients during the follow-up period, all of whom had known dyslipidemia at inclusion (10.6%).

Conclusion: This study confirms a transient increase in TC and TC fractions under JAKi, linked to the drug-induced reduction in systemic inflammation. These lipid abnormalities were regressive in the majority of patients. The clinical consequences of this elevation remain to be determined in the context of the cardiovascular tolerance of JAKi.

Disclosure: S. Abdellaoui: None; **O. Al Tabaa**: None; **S. Hecquet**: None; **A. Combier**: None; **S. Carves**: None; **O. Fogel**: None; **Y. Allanore**: None; **J. Avouac**: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1334

Cardiac Biomarkers and Prediction of Major Cardiovascular Events in Rheumatoid Arthritis: Results from the ESPOIR Cohort

manon lesturgie[1], Fiona Oudart[1], Anne Cauvet[2], Virginie Gonzalez[2], Bruno Fautrel[3], Arnaud Constantin[4], Nathalie Rincheval[5], Yannick Allanore[6] and **Jérôme Avouac**[7], [1]INSERM U1016, Paris, France, [2]INSERMU1016, Paris, France, [3]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [4]Hôpital Pierre-Paul Riquet, CHU Purpan, Toulouse, France, [5]Institut de Recherche Clinique EA2415, Université de Montpellier, Département de Statistiques, Montpellier, France, [6]Université Paris Cité, Paris, France, [7]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) experience premature mortality, largely due to cardiovascular (CV) disease. The increased CV risk is due to both the underlying systemic inflammation and the interaction between RA and traditional CV risk factors. Individual CV risk assessment in RA patients is complex because tools validated for the general population have not been adapted to account for disease activity. The use of biomarkers may help to refine risk stratification.

The aim of this study was to evaluate the predictive value of two cardiac biomarkers for major CV events in RA patients.

Methods: This prospective cohort study included patients from the ESPOIR cohort who met the 2010 ACR/EULAR classification criteria for RA and had no prior history of CV events at baseline. Serum levels of high-sensitivity cardiac troponin T (Hs-cTnT, a marker of myocardial injury) and soluble ST2 (a marker of inflammation and myocardial fibrosis) were measured at baseline using electrochemiluminescence and ELISA, respectively. The primary outcome was the occurrence of major CV events (myocardial infarction, ischemic stroke, and CV death) during the observation period.

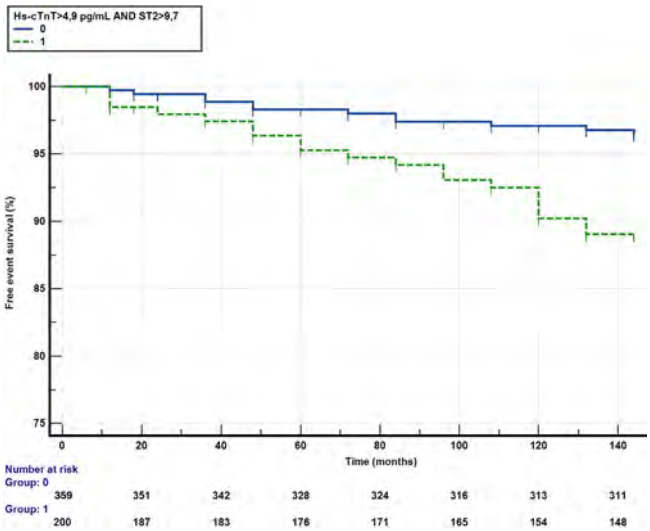


Figure 1: Kaplan-Meier curve illustrating CV event-free survival based on Hs-cTnT and ST2 concentrations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We analyzed 559 patients (425 women, 76%) with available data and biomarker measurements. The mean (SD) age was 49 (12) years, and the mean (SD) disease duration was 104 (211) days. Among these patients, 228 (41%) and 253 (45%) were positive for rheumatoid factors and anti-CCP antibodies, respectively, and 218 (39%) had bone erosions. The mean (SD) DAS28 was 5.26 (1.27).

Thirty-three major CV events were identified over a mean (SD) follow-up of 130 (34) months. Baseline mean (SD) Hs-cTnT and ST2 levels were 6.5 (13.8) pg/mL and 5.2 (1.3) ng/mL, respectively, and both correlated with age (r=0.53, p< 0.001 and r=0.22, p< 0.001) and the Framingham risk score (r=0.63, p< 0.001 and r=0.18, p=0.003). Mean ST2 levels were significantly higher in patients with at least two CV risk factors (22.3 (18.8) vs. 15.8 (11.5) ng/mL, p< 0.001).

The area under the curve (AUC) for Hs-cTnT in predicting major CV events was 0.71 (p=0.002), with a sensitivity of 72% and specificity of 60% at a threshold of 4.9 pg/mL. The AUC for ST2 was 0.69 (p=0.019), with a sensitivity of 97% and specificity of 32% at a threshold of 9.7 ng/mL. Elevated levels of Hs-cTnT (>4.9 pg/mL) and ST2 (>9.7 ng/mL) were predictive of major CV events (hazard ratios [HR]: 2.59, 95% confidence interval [CI] 1.31–5.13 and 3.23, 95% CI 1.43–7.27, respectively). The predictive value was higher when both biomarkers were elevated (HR 3.49, 95% CI 1.68–7.24). This combination remained predictive after adjusting for DAS28, CRP, methotrexate exposure, and traditional CV risk factors (adjusted HR 2.22, 95% CI 1.01–4.92).

Conclusion: These two cardiac biomarkers were identified as predictors of major CV events in this prospective RA cohort. The combination of Hs-cTnT and ST2 may improve CV risk stratification in RA patients. Adding these biomarkers to non-specific CV risk scores could better identify patients requiring advanced CV evaluation.

Disclosure: m. lesturgie: None; **F. Oudart**: None; **A. Cauvet**: None; **V. Gonzalez**: None; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **A. Constantin**: None; **N. Rincheval**: None; **Y. Allanore**: None; **J. Avouac**: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6.

Abstract Number: 1335

Chest x-Ray and pulmonary function tests are not sensitive for screening intertitial lung disease in reumatoid arthritis

Jesús Loarce[1], Alonso Sebastián González Montes[2], SONIA JIMENEZ BARRIOS[3], Mauro Ferre-Sanfrancisco[4], Verónica García García[5] and Javier Bachiller[6], [1]Ramón y Cajal University Hospital, Madrid, Spain, [2]Ramón y Cajal university hospital, Madrid, Madrid, Spain, [3]Hospital Universitario Ramón y Cajal, Madrid, Spain, [4]Department of Rheumatology, Hospital Universitario Ramon y Cajal, Madrid, Spain, Madrid, Madrid, Spain, [5]Ramón y Cajal University Hospital, MADRID, Spain, [6]Hospital Ramon y Cajal, Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a frequent and severe complication of rheumatoid arthritis (RA). Although early diagnosis and screening of ILD in RA patients with risk factors is recommended, there is no current consensus on how to perform screening of ILD in these patients. Spanish guidelines (SER-SEPAR screening criteria) recommend

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	No ILD (n=212)	ILD (n=58)	P value
Sex (women)	156 (73.6%)	35 (60.3%)	0.05
Age (years), mean (SD)	63.1	68.3	**0.004**
Smoker/previous smoker, n (%)	145 (69%)	39 (67.2%)	0.069
Dyspnoea/cough > 3 months	32 (15.1%)	19 (32.8%)	**0.002**
Lung crackles	15 (7.1%)	23 (40.4%)	**P<0.001**
RF +	165 (78.2%)	53 (91.4%)	**0.023**
ACPA +	185 (88.5%)	54 (93.1%)	0.313
Moderate-high disease activity	39 (18.7%)	15 (26.8%)	0.18
Family history of ILD	1 (0.5%)	2 (3.4%)	**0.025**
FVC %, mean (SD)	89.1 (18.9)	89.6 (39.2)	0.87
FVC < 80%	36 (23.1%)	17 (32.1%)	0.193
DLCO %, mean (SD)	87.8 (26)	78.7 (27.8)	**0.037**
DLCO < 80%	49 (35.3%)	27 (52.9%)	**0.027**
Abnormal CXR	17 (14.2%)	19 (47.5%)	**<0.001**

Table 1. Characteristic of RA patients with and without ILD.
RA=rheumatoid arthritis, ILD=interstitial lung disease, RF=rheumatoid factor, ACPA= Anti-citrullinated protein antibodies, CXR: chest-Xray FVC=forced vital capacity, DLCO= diffusing capacity of lung for carbon monoxide

chest x-ray (CXR) and pulmonary function test (PFT) to patients with dyspnoea or cough > 3 months and asymptomatic patients with an intermediate risk for ILD. Portuguese guidelines recommend CXR and PFT as screening in patients without symptoms or risk factors for ILD. ACR/CHEST guidelines conditionally recommend against screening with CXR but considers screening with PFT.

The aim of this study is to assess the diagnostic yield of CXR and PFT for diagnosing ILD in patients with RA.

Methods: This is a retrospective study that included patients with RA fulfilling ACR/EULAR 2010 classification criteria that had a thoracic computerized tomography (CT) between 01/01/2020 and 31/12/2024. ILD was diagnosed according to the CT results. CXR and PFT (spirometry and diffusing capacity of lung for carbon monoxide [DLCO]) performed a maximum of 12 months previous to the CT were reviewed. CXR were interpreted blindly to the patient clinical data and classified as normal or abnormal (which included findings suggestive of ILD or another lung pathology that would require a CT). Sensitivity and specificity were calculated for each item individually and combined for diagnosing ILD, using CT as the gold standard.

	CXR	FVC<80%	DLCO<80%	Combined
All patients (n=270)				
- Sensitivity	45.9%	32.4%	62.2%	70.3%
- Specificity	87.5%	75%	61.3%	50%
Asymptomatic patients (screening situation)* (n=201)				
- Sensitivity	28.6%	14.3%	42.9%	57.1%
- Specificity	86.7%	78.3%	65%	56.7%
Symptomatic patients (n=69)**				
- Sensitivity	56.5%	43.5%	73.9%	78.3%
- Specificity	90%	65%	50%	30%
SER-SEPAR criteria* (n=93)**				
- Sensitivity	50%	12.5%	62.5%	75%
- Specificity	89.9%	71.1%	66.7%	48.9%

Table 2. Sensitivity and specificity of CXR and PFT
CXR: chest-Xray, FVC=forced vital capacity, DLCO= diffusing capacity of lung for carbon monoxide
*Asymptomatic patients: patients without lung crackles and without respiratory symptoms (cough or dyspnoea > 3 months)
**Symptomatic patients: patients with lung crackles or respiratory symptoms (cough or dyspnoea > 3 months)
***Indication for a chest-Xray and PFT for ILD screening according to SER-SEPAR criteria

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We compared patients with ILD and without ILD using χ2 (with Fisher correction as appropriate) for categorical variables and t test/Mann-Whitney test for quantitative variables.

Results: A total of 270 patients with RA and a CT were included, and 58 patients (21.5%) had ILD. The patient's characteristics are represented in table 1. A total of 204 (75.6%) patients had PFT and 160 (59.3%) had CXR performed. In the bivariate analysis, we observed a significant difference between patients without ILD and patients with ILD for abnormal CXR (14.2% vs 47.5%, p< 0.001) and DLCO< 80% (35.3% vs 52.9%, p=0.037). No significant differences were observed for FVC.

The sensitivity and specificity for CXR, FVC< 80%, DLCO < 80% and the combined (abnormal CXR and/or abnormal PFT) results are represented in table 2. The best results were obtained for CXR due to high specificity, but sensitivity was low in all groups.

Conclusion: The diagnostic yield of CXR and PFT is low for ILD diagnosis, especially in patients without respiratory symptoms or lung crackles. Other strategies should be adopted for screening of ILD in patients with RA.

Disclosure: J. Loarce: None; **A. González Montes**: None; **S. JIMENEZ BARRIOS**: None; **M. Ferre-Sanfrancisco**: None; **V. García García**: None; **J. Bachiller**: None.

Abstract Number: 1336

Effectiveness of new initiators of tofacitinib and other biologic/targeted synthetic DMARDs in patients with rheumatoid arthritis

Katherine Liao[1], Chandrasekar Gopalakrishnan[2], Jinoos Yazdany[3], Griffith Bell[4], Suraj Mothi[5], Genevieve Gauthier[6], Arne Yndestad[7] and Milena Gianfrancesco[8], [1]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, USA, Boston, MA, [2]OM1 Inc, Boston, MA, USA, Boston, [3]UCSF, San Francisco, CA, [4]Pfizer Inc, New York, NY, USA, Boston, MA, [5]OM1 Inc, Boston, MA, USA, Boston, MA, [6]Pfizer Canada ULC, Kirkland, QC, Canada, Montreal, Canada, [7]Pfizer Inc, Oslo, Norway, Oslo, Norway, [8]Pfizer Inc, New York, NY, USA, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Though the efficacy and safety profile of tofacitinib in RA has been established in prior trials, the effectiveness of tofacitinib in routine care settings compared to biologic DMARDs (bDMARDs) is limited.

This observational cohort study of RA patients (pts) evaluated the real-world effectiveness of tofacitinib compared to select bDMARDs overall and within relevant subgroups of demographic and clinical characteristics using data from OM1 PremiOM™ RA (OM1, Boston, MA), a multisource dataset with linked claims and EHR data on RA pts in the US.

Methods: Pts with RA aged ≥18 years initiating tofacitinib or select bDMARDs (tumor necrosis factor inhibitors (TNFi); abatacept; interleukin 6 inhibitors (IL-6i)) from 01 January 2013 – 13 March 2024 and with ≥1 Clinical Disease Activity Index (CDAI) score in 45 days prior to and including the index date were included. Stabilized inverse probability treatment weights (sIPTW) were calculated to adjust for demographics, treatment history, and comorbidities). Crude incidence rates (IRs) per 1000 pt-years (PYs) were calculated to estimate the first record of CDAI remission (≤ 2.8) measured at 6- and 12-months.

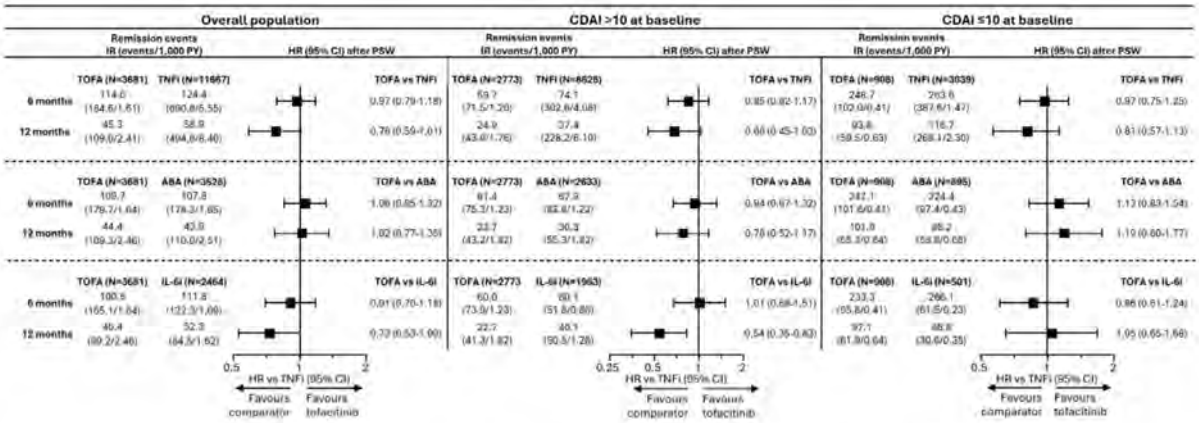
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Demographics/clinical characteristics of RA patients initiating treatment, before propensity score weighting

	Tofacitinib	TNFi	Abatacept	IL-6i
N	3,681	11,667	3,528	2,464
Age at index (years), mean (SD)	57.9 (12.3)	58.1 (13.7)	61.1 (13.1)	60.5 (12.8)
Female, n (%)	2,997 (81.4%)	9,171 (78.6%)	2,898 (82.1%)	1,982 (80.4%)
Disease Duration ≥ 2 years, n (%)	2,407 (65.4%)	5,683 (48.7%)	2,185 (61.9%)	1,726 (70.0%)
Number of previous b/tsDMARD, n (%)				
0	1,087 (29.5%)	7,192 (61.6%)	1,219 (34.6%)	478 (19.4%)
1	1,247 (33.9%)	2,902 (24.9%)	1,209 (34.3%)	763 (31.0%)
2	787 (21.4%)	944 (8.1%)	678 (19.2%)	627 (25.4%)
3	375 (10.2%)	350 (3.0%)	292 (8.3%)	338 (13.7%)
≥4	185 (5.0%)	279 (2.4%)	130 (3.7%)	258 (10.5%)
Charlson Comorbidity Index, mean (SD)	2.0 (1.6)	1.9 (1.6)	2.2 (1.7)	2.2 (1.9)
Prior csDMARD use, n (%)	3,113 (84.6%)	9,769 (83.7%)	2,936 (83.2%)	2,018 (81.9%)
Prior corticosteroid use, n (%)	2,414 (65.6%)	7,224 (61.9%)	2,343 (66.4%)	1,720 (69.8%)
Baseline obesity (BMI > 30 kg/m2), mean (SD))	30.6 (7.1)	30.5 (7.3)	30.5 (7.3)	30.5 (7.3)
Baseline CDAI score, mean (SD)[b]	19.8 (12.7)	19.1 (12.4)	19.6 (12.5)	20.9 (12.5)
Baseline CDAI score category, n (%)[b]				
Remission: 0.0-2.8	87 (5.9%)	115 (4.7%)	62 (4.3%)	42 (4.1%)
Low activity: 2.9-10.0	247 (16.8%)	386 (15.7%)	267 (18.6%)	129 (12.6%)
Moderate activity: 10.1-22.0	584 (39.7%)	978 (39.7%)	587 (41.0%)	420 (41.1%)
High activity: 22.1-76.0	554 (37.6%)	985 (40.0%)	517 (36.1%)	432 (42.2%)

TNFi=adalimumab, certolizumab pegol, etanercept, golimumab, infliximab; IL-6i= tocilizumab or sarilumab; b/tsDMARD = biologic or targeted synthetic DMARDs; csDMARD = conventional synthetic DMARD; SD, standard deviation
[a]Assessed during the baseline period, defined as all available data prior to and including the index date (date of treatment initiation), unless otherwise stated. For obesity and lab measures, the most recent value over the baseline period was used. Patients diagnosed with concomitant indications for tofacitinib (PsA, UC, pcJIA) anytime prior to cohort entry date were excluded (required at least 2 diagnosis codes at least 30 days apart)
[b]Most recent value in the 45 days prior to and including the index date.

Cox regression with robust standard errors were used to calculate weighted hazard ratios (HRs) and 95% confidence intervals (CIs) overall and stratified by baseline CDAI >/≤ 10. Subgroup analyses by pre-specified variables of interest were conducted to assess heterogeneity of treatment effect (HTE) among pts with baseline CDAI >10.

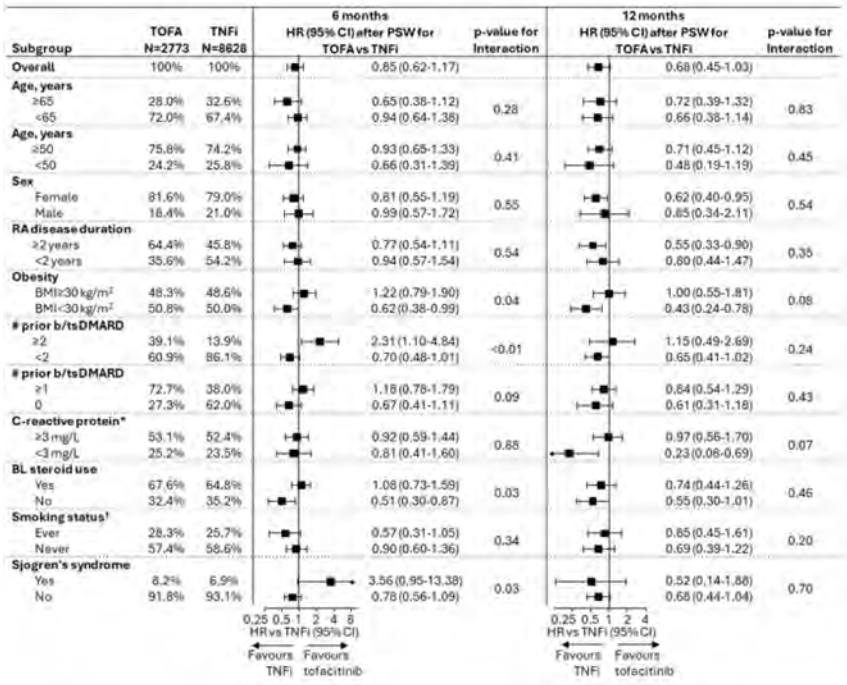


Baseline covariates used to estimate IPTW included: age, sex, race (black, white, other, unknown/not documented), ethnicity (Hispanic, non-Hispanic, unknown/ not documented), insurance status (commercial, Medicare, Medicaid, multiple, other, unknown/ not documented), geographic census region (Northeast, Midwest, West, South, unknown), BMI (<18.5, 18.5-<25, 25-<30, ≥30 kg/m2, unknown), year of index, RA disease duration (<2, ≥2 years), RA disease activity (CDAI score 0-2.8, 2.9-10, 10.1-22.0, 22.1-76.0), Charlson Comorbidity Index (continuous and categorical: 0-1, 2-3, 4-5, ≥6), comorbidities (cardiovascular disease, COPD, fibromyalgia, malignancies, osteoporosis, type 1 diabetes, type 2 diabetes, Sjögren's syndrome), smoking status (ever, never, unknown), hospitalization, laboratory results (RF positive, negative, unknown), anti-CCP (positive, negative, unknown), CRP (<3, ≥3 mg/L, unknown), prior use of medications (csDMARD, bDMARD, tsDMARD), count of prior b/tsDMARD (0, 1, 2, 3, ≥4), and corticosteroid use.

ABA, abatacept; BMI, body mass index; CCP, cyclic citrullinated peptide; CDAI, clinical disease activity index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; HR, hazard ratio; IL-6i; interleukin-6 inhibitor; IR, incidence rate; N, number of evaluable patients; PSW, propensity score weighting; PY, patient years; RA, rheumatoid arthritis; RF, rheumatoid factor; TNFi, tumor necrosis factor; TOFA, tofacitinib.

Figure 1. Effectiveness of tofacitinib vs bDMARDs in achieving remission (CDAI ≤ 2.8) at 6 and 12 months

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



*CRP was unknown in 21.7% (tofacitinib) and 24.2% (TNFi) of patients. †Smoking status was unknown in 14.3% (tofacitinib) and 15.8% (TNFi) of patients.

BMI, body mass index; CCP, cyclic citrullinated peptide; CDAI, clinical disease activity index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; HR, hazard ratio; IL-6i; interleukin-6 inhibitor; IR, incidence rate; N, number of evaluable patients; PSW, propensity score weighting; PY, patient years; RA, rheumatoid arthritis; RF, rheumatoid factor; TNFi, tumor necrosis factor; TOFA, tofacitinib.

Figure 2. Effectiveness of tofacitinib vs TNFi in achieving remission (CDAI ≤ 2.8) at 6 and 12 months, by subgroup.

Results: In total, 21,340 pts were included (tofacitinib, N=3,681; TNFi, N=11,667; abatacept, N=3,528; IL-6i, N=2,464) (Table). Mean age at index date ranged from 58-62 years, and proportion with disease duration ≥ 2 years ranged from 48.7%-70.0%. At baseline, 36.6% of pts initiating tofacitinib had used ≥ 2 prior biologic or targeted synthetic DMARDs (b/tsDMARDs) vs TNFi (13.5%), abatacept (31.2%) and IL-6i (49.6%). Comorbidities and CDAI scores at baseline were similar between cohorts. Treatment switch rates were higher among tofacitinib (5.7-12.9%) vs. comparator (1.7-3.5%) pts at 6- and 12-months, while treatment discontinuation rates were slightly lower (33.8-51.6% vs. 36.6-63.0%).

In the main sIPTW analysis, there were no statistically significant differences in the rate of achieving remission between treatments at 6- and 12-months (Fig 1). Results were consistent when stratifying pts by baseline CDAI >/≤ 10, apart from a lower rate of remission for tofacitinib compared to IL-6i at 12 months among those with baseline CDAI >10 (HR = 0.54, 95% CI 0.35-0.83). Subgroup analyses suggested HTE among pts with obesity (BMI ≥30kg/m2), ≥2 prior biologic or targeted synthetic DMARDs, prior corticosteroid use, and Sjogren's syndrome for tofacitinib compared to TNFi among pts with baseline CDAI >10 at 6 months (p-interaction < 0.05), but not 12 months (Fig 2).

Conclusion: In this large cohort study using real-world data, no significant differences were found in achieving remission between treatments among the overall RA population. Subgroup analyses suggest some potential HTE; however, interpretation is limited by low event rates, missing data, and potential residual confounding.

Disclosure: K. Liao: Merck, 2; **C. Gopalakrishnan**: OM1, Inc, 3, 11; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **G. Bell**: Pfizer, 3, 11; **S. Mothi**: OM1, 3, 11; **G. Gauthier**: Pfizer, 3, 11; **A. Yndestad**: Pfizer, 3, 11; **M. Gianfrancesco**: Pfizer, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1337

The Association Between Glucagon-Like Peptide-1 Receptor Agonist and Rheumatoid Arthritis: A Population-Based Case Control Study

Ariel Israel[1], Fadi Hassan[2], Jalal Kurtam[2], Jamal Awad[2], Eugene Merzon[1] and **Mohammad Naffaa**[3], [1]Leumit Health Services, Tel-Aviv, Israel, [2]Galilee Medical Center, Nahariya, Israel, [3]The Azriel's Faculty of Medicine, Bar-Ilan University, Safed, Israel; The Rheumatology Unity, Galilee Medical Center, Naharyia, Israel

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The increasing use of glucagon-like peptide-1 receptor agonists (GLP1-RAs) for diabetes mellitus (DM) and weight loss has the potential modify the risk for rheumatoid arthritis (RA) development. In this study we aimed to explore the association between GLP1-RA use and RA development.

Methods: This case-control study utilized the Leumit Health Services (LHS) computerized database. Cases were defined as adult RA patients (≥18 years) registered in the database up to December 31, 2023, using ICD-9 code 714.0, who also were prescribed conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) or diagnosed with RA by a rheumatologist. Each case was matched with five controls based on age, gender, and socioeconomic status from the same database. The primary exposure was the use of either liraglutide, dulaglutide, or semaglutide within the 5 years preceding the

Table 1 - Baseline Characteristics of Study and the Control Groups

Characteristic	RA n=4405	Controls n=22025	p-value
Age (years)	52.5 ± 15.1	52.5 ± 15.1	0.96
Female, n (%)	3,174 (72.1 %)	18,570 (72.1 %)	1.00
BMI (Kg/m²)	28.3±5.9	27.8±5.8	<0.001
Socioeconomic status			
0-3	138 (3.3%)	690 (3.3%)	1.00
4-6	1,134 (27.0%)	5,670 (27.0%)	1.00
7-9	1,032 (24.6%)	5,160 (24.6%)	1.00
10-11	951 (22.7%)	4,755 (22.7%)	1.00
12-14	712 (17.0%)	3,560 (17.0%)	1.00
15	232 (5.5%)	1,160 (5.5%)	1.00
Missing	206 (4.7%)	1,030 (4.7%)	1.00
Smoking status			
Active smoker	813 (19.2 %)	3,664 (18.2 %)	0.12
Past smoker	104 (2.46 %)	416 (2.06 %)	0.11
Non-smoker	3,318 (78.4 %)	16,078 (79.8 %)	**0.04**
Comorbidities			
Ischemic heart disease	284 (6.45 %)	1,303 (5.92 %)	0.18
Diabetes mellitus	696 (15.8 %)	3,046 (13.8 %)	**<0.001**
COPD	276 (6.27 %)	900 (4.09 %)	**<0.001**
Chronic kidney disease	60 (1.36 %)	298 (1.35 %)	0.94
CVA	65 (1.48 %)	365 (1.66 %)	0.43
Cirrhosis	4 (0.09 %)	39 (0.18 %)	0.30
Osteoporosis	484 (11.0 %)	1,881 (8.5 %)	**<0.001**
Hypothyroidism	362 (8.2 %)	1,351 (6.1 %)	**<0.001**
Inflammatory bowel disease	47 (1.07 %)	139 (0.63 %)	**0.003**
Fibromyalgia	224 (5.1%)	397 (1.8%)	**<0.001**
Malignancies			
Breast carcinoma	70 (1.59 %)	353 (1.60 %)	1.00
Colon carcinoma	21 (0.48%)	137 (0.62%)	0.29
Lung carcinoma	10 (0.23 %)	40 (0.18 %)	0.57
Pancreatic carcinoma	1 (0.02 %)	8 (0.04 %)	1.00
Prostatic carcinoma	15 (0.34 %)	104 (0.47 %)	0.27
Melanoma	12 (0.27 %)	71 (0.32 %)	0.66

RA – Rheumatoid arthritis; BMI – Body mass index; SES – Socioeconomic status; COPD – Chronic obstructive pulmonary disease; CVA – Cerebrovascular accident.
Bold styling indicates clinical significance.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 – Univariate analysis of the associations between GLP1-RA Use and RA

GLP1-RA Agent	RA Cases Exposure (%) N=4,405	Controls Exposure (%) N=22,025	Odds Ratio (95% CI)	p-value
Liraglutide	50 (1.14%)	182 (0.83%)	1.38 (0.99 to 1.90)	0.051
Dulaglutide	19 (0.43%)	62 (0.28%)	1.54 (0.87 to 2.60)	0.101
Semaglutide	40 (0.91%)	145 (0.66%)	1.38 (0.95 to 1.98)	0.075

GLP1-RA - Glucagon-like peptide-1 receptor agonists; RA – Rheumatoid arthritis; CI – Confidence interval.
Bold styling indicates clinical significance.

Table 3 –Adjusted multivariate analysis for factors associated with RA

Variable	Odds Ratio (CI)	p-value
Liraglutide	1.25 (0.90 to 1.73)	0.18
Dulaglutide	1.26 (0.74 to 2.15)	0.40
Semaglutide	1.13 (0.76 to 1.67)	0.56
Age	1.11 (1.00 to 1.23)	0.06
Past smoking	1.24 (0.99 to 1.54)	0.06
Active smoking	1.08 (0.99 to 1.18)	0.08
DM	1.18 (1.07 to 1.31)	**0.001**

GLP1-RA - Glucagon-like peptide-1 receptor agonists; RA – Rheumatoid arthritis; CI – Confidence interval; DM – Diabetes mellitus.
Bold styling indicates clinical significance.

RA diagnosis (index date). Demographic variables, smoking status, comorbidities, and malignancy history were collected at the index date. Univariate and multivariable logistic regression analyses were performed to evaluate the association between GLP1-RA usage and RA, with the multivariable model adjusting for potential confounders. A p-value of less than 0.05 was considered statistically significant. Ethical approval for the study was obtained from the LHS Institutional Review Board.

Results: The study included 4,405 RA patients and 22,025 matched controls. Baseline characteristics revealed that RA patients had a significantly higher BMI and a greater prevalence of several comorbidities including DM, chronic obstructive pulmonary disease, osteoporosis, hypothyroidism, inflammatory bowel disease, and fibromyalgia (Table 1). GLP1-RA use was non-significantly associated with RA: liraglutide (OR 1.38, p=0.051), dulaglutide (OR 1.54, p=0.101), and semaglutide (OR 1.38, p=0.075) (Table 2). After adjusting for age, smoking status, and DM in a multivariate model, these associations remained non-significant (Table 3). Notably, DM was identified as an independent risk factor for RA (adjusted OR 1.18, p=0.001) (Table 3).

Conclusion: Our findings demonstrated that GLP1-RAs exposure was not associated with a decreased incidence of RA, but rather the exposure trended towards increased incidence. DM was the only variable that was significantly associated with incident RA, pointing to the potential role of metabolic dysregulation in the development of autoimmune disease. Further prospective, interventional studies are warranted to understand the effect of GLP1-RA on the risk of developing RA.

Disclosure: A. Israel: None; **F. Hassan**: None; **J. Kurtam**: None; **J. Awad**: None; **E. Merzon**: None; **M. Naffaa**: AbbVie, 5, 6, BI, 5, Eli Lilly, 6, Pfizer, 6, Roche, 6.

Abstract Number: 1338

Short-Chain Fatty Acids and Their Gut Microbial Metabolic Pathways Distinguish Rheumatoid Arthritis in Discordant Monozygotic Twins

Rebecca Blank[1], Kevin Bu[2], Xinyuan Zhang[3], Weixi Chen[4], Ian Cunningham[4], jeremy sokolove[5], Lauren Lahey[6], Adriana Heguy[4], Rhina Medina[4], Carles Ubeda[7], Renuka Nayak[8], Jiyuan Hu[4], Adam Cantor[9], Jakleen Lee[9], Frances Williams[10], Jose Clemente[2] and Jose Scher[11], [1]NYU Langone Health, New York, NY, [2]Icahn School of Medicine at Mount Sinai, New York,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

NY, [3]Kings College London, London, United Kingdom, [4]NYU Grossman School of Medicine, New York, [5]odyssey, Berwyn, PA, [6]Stanford, Palo Alto, [7]Fisabio, Madrid, [8]University of California, San Francisco (UCSF), San Francisco, CA, [9]Icahn School of Medicine, New York, [10]Kings College London, London, [11]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Although genetic factors have been identified in the pathogenesis of RA, the concordance rate in monozygotic (MZ) twins is low, suggesting that other factors contribute to disease development. Further, the relative contribution of such non-genetic elements in identical twins has not been characterized. Here, we aimed to measure host and microbial biomarkers of RA by studying MZ twin pairs discordant for disease using a multi-omics approach.

Methods: Eight pairs of MZ twins discordant for RA (n=16; Table 1) were enrolled in the United States (US). Gut microbiome was assessed using shotgun metagenomic sequencing. Autoantibodies, cytokines, and other plasma proteins were measured in both plasma and feces. Levels of short-chain fatty acids (SCFA) from serum and feces were quantified using gas chromatography mass spectrometry (GC-MS). A metagenomic dataset from a geographically distinct cohort of MZ twins discordant for RA (n=14, Table 2) from TwinsUK was used to validate the findings.

Results: While overall microbiome diversity and composition did not significantly differ between twin pairs in either cohort, we observed a decrease in *Blautia faecis*, a SCFA producer, in RA affected US twins (Fig. 1 A). Affected US twins had higher concentrations of both fecal and plasma citrullinated and non-citrullinated autoantibodies, as well as significantly lower concentrations of fecal butyrate and propionate (Fig. 1 B,C). TwinsUK RA discordant pairs showed comparable differences

Table 1: US Cohort demographics and clinical information.

Characteristic	Unaffected (n = 8)	RA (n = 8)	p-value
Age- years, mean (median)	56.3 (58.0)	56.3 (58.0)	1
Female- n (%)	7 (87.5)	7 (87.5)	1
White/Caucasian- n (%)	8 (100)	8 (100)	1
Disease duration, years, mean (median)	–	7.0 (4.0)	–
Disease activity parameters			
TJC-28, mean (median)	–	10.4 (9.5)	–
SJC-28, mean (median)	–	6.25 (4.0)	–
DAS 28-CRP, mean (median)	–	4.02 (4.0)	–
Serum CCP antibody, units, mean (SD)	13314 (36841)	27203 (33538)	0.117
Medication use ever			
Prednisone, n (%)	–	4 (50.0)	–
Methotrexate, n (%)	–	6 (75.0)	–
Biologic agent, n (%)	–	5 (62.5)	–

TJC = tender joint count; SJC = swollen joint count; DAS28-CRP = Disease activity score-C reactive protein; CCP = cyclic citrullinated peptide

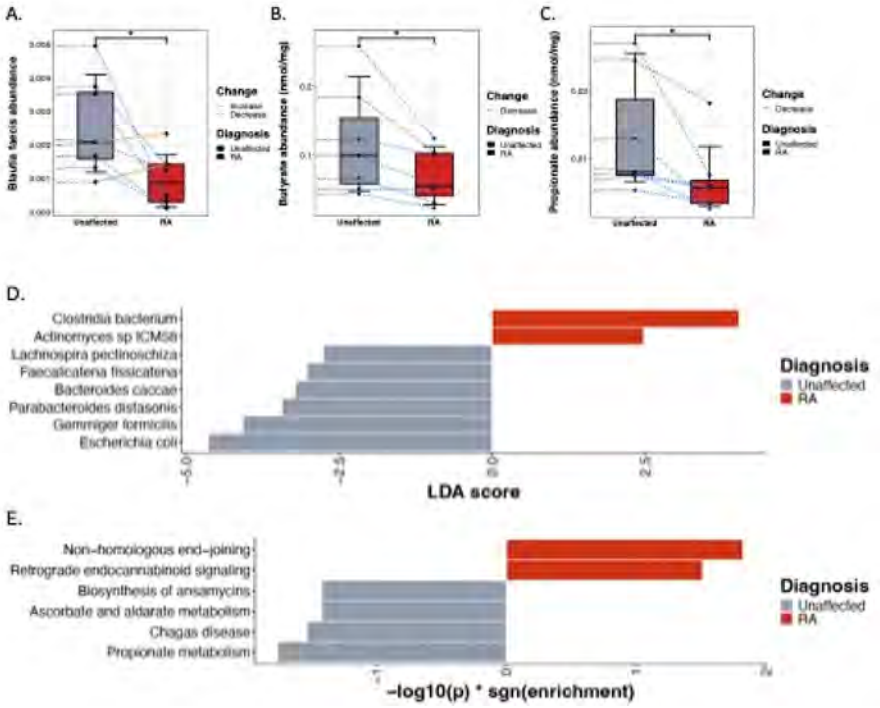
Table 2. TwinsUK sample demographics and clinical information.

Characteristic	Unaffected (n = 7)	RA (n = 7)	p-value
Age- years, mean (median)	63.4 (68)	63.4 (68)	1
Female- n (%)	7 (100)	7 (100)	1
White/Caucasian- n (%)	7 (100)	7 (100)	1
Serum CCP antibody, U/ml, mean (SD)	1.17 (0.41)	95 (116)	0.0047
Medication use ever			
Sulfasalazine, n (%)	–	2 (28.6)	–
Methotrexate, n (%)	–	5 (71.4)	–
Biologic agent, n (%)	–	3 (42.9)	–

CCP = cyclic citrullinated peptide

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Gut bacterial composition, predicted functional pathways, and fecal SCFA concentration in affected and unaffected twins in US and UK cohorts. (A-C are US cohort; D-E are UK cohort.) (A) Boxplot showing distribution of *B. faecis* abundance in unaffected and affected US twins. Fecal concentration of butyrate (B) and propionate (C) in unaffected and affected US twins. (D) Linear discriminant analysis Effect Size (LEfSe) showing differential species in unaffected twins compared to affected twins in UK cohort. *Gemmiger* and *Faecalicatena* are SCFA producers. (E) Barplot of Wilcoxon effect sizes for differential pathways in UK cohort. *p<0.05, **p<0.01.



using metagenomic-based taxa- and pathways-features. SCFA producing bacteria and pathways were depleted in TwinsUK RA affected twins (Fig 1 D,E).

Conclusion: Multi-omic biomarkers differentiate MZ twins discordant for RA. *Blautia faecis*, which is associated with SCFA production and reduced inflammatory cytokine expression, was decreased in US affected twins. Similarly, SCFA, which are known to have immune modulatory effects, were decreased in affected twins, suggesting further bi-directional interactions between inflammation at the gut barrier and disease state. We observed similar changes in SCFA producing taxa between unaffected and affected twins in a geographically distinct twin cohort. If confirmed in larger cohorts, exhaustive multi-omic approaches may improve our understanding of RA pathogenesis. Future work should focus on the potential for SCFA in diagnostics and therapeutics.

Disclosure: R. Blank: None; **K. Bu**: None; **X. Zhang**: None; **W. Chen**: None; **I. Cunningham**: None; **j. sokolove**: Odyssey Therapeutics, 3, Roivant, 3; **L. Lahey**: Bristol-Myers Squibb(BMS), 3; **A. Heguy**: None; **R. Medina**: None; **C. Ubeda**: None; **R. Nayak**: None; **J. Hu**: None; **A. Cantor**: None; **J. Lee**: None; **F. Williams**: None; **J. Clemente**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1339

Inflammatory Rheumatic Diseases in IDH-mutated Myeloid Neoplasms: Clinical Spectrum and Response to IDH Inhibitors

Romain Stammler[1], Peter Chen[2], Orianne Debeaupuis[2], Lin Pierre Zhao[1], Mirabelle Ruyer Thompson[1], Eve Zakine[1], Julien Rossignol[1], Lauriane Goldwirt[1], Thibault Comont[3], Mael Heiblig[4], Lionel Ades[1], Marie Sebert[1], Jean-sébastien Allain[5], Julien Campagne[6], Marie Anne Couturier[7], Marina Cumin[8], Marie Caroline Dalmas[9], Guillaume Denis[10], Cecile Devloo[11], Adrien De Voeght[12], Louis Drevon[1], Pierre Duffau[13], Sophie georgin-Lavialle[14], Delphine Gobert[1], Noemie Abisror[15], Olivier Kosmider[16], Fréderic Rieux-Laucat[2], Estibaliz LAZARO[17], Jean Guillaume Lopez[18], Alexandre Maria[19], Wladimir Mauhin[20], Julie Merindol[21], Claire Merlot[22], Tristan Mirault[1], Laurent Pascal[23], François Perrin[24], Emmanuel Raffoux[1], Ramy Rahme[25], Damien Roos-Weil[1], Benjamin Terrier[26], Benjamin Torreau[27], Olivier Fain[1], Pierre Fenaux[1], Pierre Hirsch[1], Vincent Jachiet[1], Jerome Hadjadj[1] and Arsène Mekinian[28], [1]Assistance Publique des Hôpitaux de Paris, Paris, France, [2]Imagine Institute, Paris, France, [3]Centre Hospitalier Universitaire Toulouse Institut Universitaire du Cancer Toulouse Oncopole, Toulouse, France, [4]Lyon-Sud Hospital, Hospices Civils de Lyon, Paris and Université Claude Bernard, Lyon, France, [5]Scorff-Lorient Hospital, Lorient, France, [6]Hospital Robert Schuman, Metz, France, [7]Centre Hospitalier Régional et Universitaire de Brest, Brest, France, [8]Centre hospitalier de Libourne, Libourne, France, [9]Strasbourg University Hospital Center, Strasbourg, France, [10]Centre Hospitalier Rochefort, Rochefort, France, [11]Centre hospitalier de Dieppe, Dieppe, France, [12]CHU of Liège, Liège, Belgium, [13]Groupe Hospitalier Saint-André, Bordeaux, France, [14]Sorbonne university, Tenon hospital, DMU3ID, CEREMAIA, ERN RITA, Paris, France, [15]Internal Medicine, CHU Saint-Antoine, Paris, France, [16]AP-HP, Hopital Cochin, Institut Cochin, CNRS UMR8104, INSERM U1016 Université Paris Cité Paris France., PARIS, France, [17]Bordeaux University Hospital, Pessac, France, [18]Dupuytren University Hospital, Limoges, France, [19]Saint-Eloi Hospital, Montpellier, France, [20]Croix Saint Simon Hospital, Paris, France, [21]University Hospital of Nice, Nice, France, [22]Centre hospitaliser d'Orléans, Orléans, France, [23]Hôpital Saint-Vincent de Paul, Lille, France, [24]Centre Hospitalier de Saint-Nazaire, Saint Nazaire, France, [25]Assistance Publique des Hôpitaux de Paris, Bobigny, France, [26]Cochin Hospital, Paris, France, [27]Internal Medicine and Immunology, CHU Tours, Tours, France, [28]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France

SESSION INFORMATION

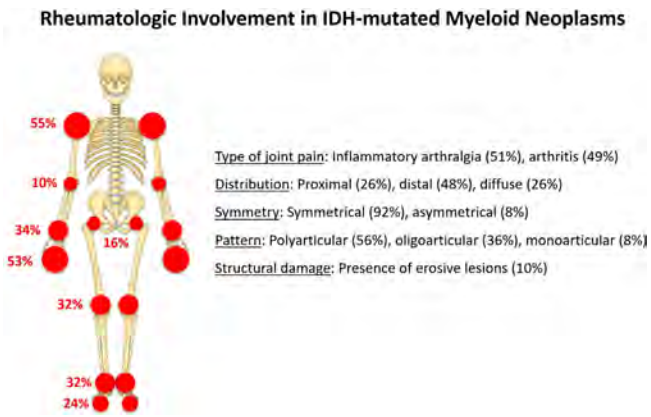
Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Clonal hematopoiesis has emerged as a key contributor to systemic inflammation, bridging hematologic and immune-mediated inflammatory disorders (IMIDs). Isocitrate dehydrogenase 1 and 2 (IDH1/2) somatic mutations, typically found in myeloid neoplasms (MN), may be overrepresented in patients with both MN and IMIDs. This study aimed to characterize the clinical, immunological, and molecular features of IDH-mutated MN associated with IMIDs, and to assess outcomes and treatment responses, particularly to IDH inhibitors.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

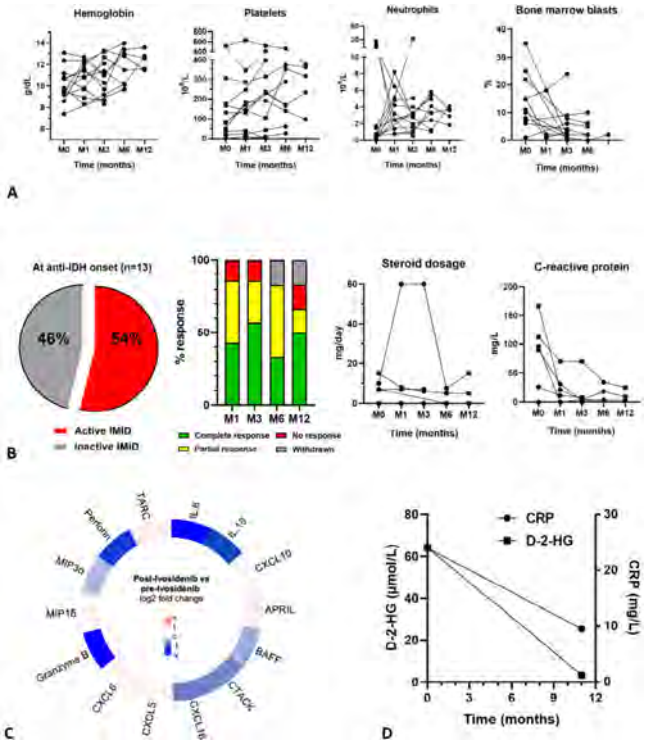


Figure 2: Efficacy of anti-IDH inhibitors on IMID patients with IDH-mutated myeloid neoplasm Legend: (A) Hematological parameters (hemoglobin, platelets, neutrophils, and bone marrow blasts) during follow-up (M0, M1, M3, M6 and M12). Each dot represents an individual patient; (B) Proportion of patients with active versus inactive IMID at anti-IDH onset (left), evolution of inflammatory response rates over time (middle), and longitudinal changes in steroid dosage (mg/day) and C-reactive protein (mg/L) in 7 patients with active IMID (right); (C) Cytokine profile pre- and post-ivosidenib (anti-IDH1) in one patient showing log2 fold changes in circulating cytokines and chemokines, with upregulated (red) and down-regulated (blue) markers; (D) D-2-HG and CRP levels evolution under anti-IDH1 inhibitor in one patient. CRP: C-reactive protein; IMID: immune-mediated inflammatory disorder; VAF: variant allele frequency

Methods: We conducted a multicenter retrospective cohort study of 50 patients with IDH-mutated MN and IMIDs (IDH^{mut} group), compared to 61 patients with MN and IMIDs without IDH mutations (IDH^{wt} group). Clinical and biological characteristics, survival outcomes, therapeutic responses, cytokine profiles, and circulating immune cell populations were assessed.

Results: Fifty patients (25 (50%) male, median age 73 (54-85) years) with IDH-mutated MN and IMID (MN-IMID-IDH^{mut} group) were included. Twenty-seven (54%), 22 (44%) and 1 (2%) patients respectively displayed IDH1, IDH2, both mutations. Thirty-six (72%) had MDS and 14 (28%) patients had CMML. The most common inflammatory manifestations were musculoskeletal in 39 (78%) patients, cutaneous in 22 (44%) and vascular in 12 (24%). Musculoskeletal involvement was inflammatory arthralgia without synovitis in 20 (51%) patients and arthritis in 19 (49%). These symptoms were predominantly symmetrical (92%) and polyarticular (56%), with common involvement of both proximal and distal joints such as the shoulders (55%), hands (53%), and wrists (34%). Erosive lesions were infrequent (10%). The most frequent underlying IMIDs diagnosis were seronegative arthritis in 17 (34%) patients, polymyalgia rheumatica in 13 (26%) and giant cell arteritis in 8 (16%).

Compared to the IDH^{wt} group, patients in the IDH^{mut} group were more frequently female (50% vs 25%, p = 0.006) and older (73 (54-85) vs 69 (20-86) years, p=0.038). Musculoskeletal manifestations were significantly more common in the IDH-mutated group (78% vs 54%, p=0.009), whereas cutaneous, digestive, and renal manifestations were significantly less frequent. Polymyalgia rheumatica was significantly more common in the IDH^{mut} group (26% vs 8%, p=0.011). A specific cytokine signature with significant higher expression of several chemokines implicated in monocyte and dendritic cells recruitment to inflamed tissues was identified.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table: Characteristics of IMID patients with IDH-mutated versus IDH-wild type myeloid neoplasms Continuous variables are presented as medians (range), while categorical variables are presented as counts (percentage). Abbreviations: IMID: immune-mediated inflammatory disorders; MN: myeloid neoplasm; SD: standard deviation; Footnote: * complex karyotype (i.e. >= 3 anomalies) ; ** other (n=4) including del20q (n=2), del5p (n=1),+19+21 (n=1) ; *** other (n=10) including del20q (n=3), -Y (n=2), del5q (n=1), -7 (n=1), del7q (n=1), del4q (n=1); **** inflammatory backpain; ***** other (n=7) including inflammatory back pain (n=2); myalgia (n=5)

	IDH^{mut} (n=50)	IDH^{wt} (n=61)	p-value
Demographics			
Male-sex	25 (50%)	46 (75%)	**0.006**
Age at MN diagnosis (years)	73 (54-85)	69 (20-86)	**0.038**
Hematological parameters			
Myelodysplastic neoplasms	36 (72%)	33 (54%)	0.053
Chronic myelomonocytic leukemia	14 (28%)	28 (46%)	0.266
Hemoglobin (g/L)	10.8 (8-14.4)	10.3 (6-15.1)	**0.01**
Platelets (G/L)	199 (24-961)	153 (10-845)	**<0.001**
Leukocytes (G/L)	3.5 (1.1-16)	6 (2.1-91)	**<0.001**
Neutrophils (G/L)	1.2 (0.2-11.5)	3.6 (0.3-56)	**0.002**
Monocytes (G/L)	0.4 (0-5.1)	0.9 (0.1-12)	0.057
Dysgranulopoiesis	39/45 (87%)	14/21 (67%)	0.249
Dyserythropoiesis	24/45 (53%)	5/14 (36%)	0.151
Dysmegakaryopoiesis	29/45 (64%)	6/14 (43%)	0.192
Bone marrow blasts (%)	1 (0-15)	1,7 (0-14)	0.055
Abnormal marrow cytogenetics	10 (20%)	22/60 (37%)	
Trisomy 8	4/10 (40%)	6/23 (26%)	
Complex karyotype *	2/10 (20%)	6/23 (26%)	
Other	4/10 (40%) **	10/23 (43%) ***	
			0.061
Low IPSS-M (≤0)	39 (78%)	36/55 (65%)	0.155
Low IPPS-R (≤ 3.5)	40 (80%)	40/55 (73%)	0.382
IMID-related parameters			
IMID diagnoses before MN diagnosis	28/48 (58%)	37/61 (62%)	0.841
Delay between IMID and MN diagnoses (months)	18 (0-224)	11 (0-96)	0.322
Clinical features			
Musculoskeletal	39 (78%)	33 (54%)	**0.009**
Inflammatory arthralgia without synovitis	20/39 (51%)	18/33 (54%)	
Arthritis	19/39 (49%)	12/33 (36%)	
Other	1/39 (3%) ****	7/33 (21%) *****	
Skin	22 (44%)	39 (64%)	**0.036**
Neutrophilic dermatosis	6/22 (27%)	11/39 (28%)	
Purpura	4/22 (18%)	6/39 (15%)	
Other	12/22 (54%)	22/39 (56%)	
Non-infectious fever	17 (34%)	25 (41%)	0.450
Pulmonary	10 (20%)	10 (16%)	0.625
Ocular	7 (14%)	6 (10%)	0.497
Nervous system	6 (12%)	5 (8%)	0.505
Venous thrombosis	4 (8%)	3 (5%)	0.506
Digestive	2 (4%)	12 (20%)	**0.013**
Cardiac	1 (2%)	7 (11%)	0.055
Renal	0 (0%)	8 (13%)	**0.008**
Clonulitis	0 (0%)	4 (6%)	0.065
Biological features			
C-reactive protein during flare (mg/L)	40 (0-300)	62 (0-450)	0.480
IMID diagnostic			
Seronegative arthritis	17 (34%)	15 (25%)	0.276
Polymyalgia rheumatica	13 (26%)	5 (8%)	**0.011**
Giant cell arteritis	8 (16%)	6 (10%)	0.330
Sjogren syndrome	4 (8%)	1 (2%)	0.108
Systemic sclerosis	2 (4%)	0 (0%)	0.115
Inflammatory bowel disease	3 (6%)	7 (11%)	0.316
Rheumatoid arthritis	2 (4%)	0 (0%)	0.135
Spondyloarthritis	1 (2%)	0 (0%)	0.267
Follow-up			
Median follow up (months)	31 (1-166)	38 (1-123)	0.645
Alive at last follow-up	36 (72%)	46 (59%)	0.134
Progression to acute myeloid leukemia	10 (20%)	7 (11%)	0.215

Inflammatory efficacy of biologics targeting inflammation and azacitidine were limited with an overall response rate below 25% at 3 months and below 10% at 12 months. Seven patients with active inflammatory disease received IDH inhibitors. The iORR was 86% at 3 months, 83% at 6 months and 66% at 12 months. All of the 7 patients displayed a hematological response.

Conclusion: This study suggests that *IDH* mutations may contribute to a distinct disease phenotype, marked by a predominance of inflammatory rheumatologic manifestations, particularly polymyalgia rheumatica. These findings highlight new therapeutic opportunities, including the use of targeted anti-IDH therapies.

Disclosure: R. Stammler: None; **P. Chen**: None; **O. Debeaupuis**: None; **L. Zhao**: None; **M. Ruyer Thompson**: None; **E. Zakine**: None; **J. Rossignol**: None; **L. Goldwirt**: None; **T. Comont**: AbbVie, 6, Amgen, 6, BMS, 2, 6, CSL Behring, 6, Griffols, 6, Novartis, 2, 5, 6; **M. Heiblig**: AbbVie, 2, Astellas, 2, Blueprint, 2, BMS/Celgebe, 2, Jazz Pharmaceuticals, 2, Servier, 2; **L. Ades**: None; **M. Sebert**: None; **J. Allain**: None; **J. Campagne**: None; **M. Couturier**: None; **M. Cumin**: None; **M. Dalmas**: None; **G. Denis**: None; **C. Devloo**: None; **A. De Voeght**: None; **L. Drevon**: None; **P. Duffau**: None; **S. georgin-Lavialle**: Novartis, 2, Sobi, 2; **D. Gobert**: None; **N. Abisror**: Roche, 5; **O. Kosmider**: None; **F. Rieux-Laucat**: None; **E. LAZARO**: None; **J. Lopez**: None; **A. Maria**: None; **W. Mauhin**: None; **J. Merindol**: None; **C. Merlot**:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

None; **T. Mirault**: None; **L. Pascal**: None; **F. Perrin**: None; **E. Raffoux**: None; **R. Rahme**: None; **D. Roos-Weil**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **B. Torreau**: None; **O. Fain**: None; **P. Fenaux**: None; **P. Hirsch**: None; **V. Jachiet**: None; **J. Hadjadj**: None; **A. Mekinian**: Roche, 5.

Abstract Number: 1340

Does Moderate Alcohol Use Lower Disease Activity Among Patients with Rheumatoid Arthritis?

Sarah Crisci[1], Joshua Baker[2], Kevin Kane[3], George Reed[4], Dimitrios Pappas[5] and Joel Kremer[6], [1]New York University, New York, NY, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Massachusetts Lowell, Lowell, MA, [4]University of Massachusetts Chan Medical School, Worcester, MA, [5]CorEvitas, New York, NY, [6]The Corrona Research Foundation, Delray Beach, FL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The relationship between alcohol use and disease activity among patients with rheumatoid arthritis (RA) remains controversial. Several studies have concluded that moderate drinking may be beneficial for individuals with RA. However, recent concerns about residual confounding have arisen within studies aimed at understanding causal risks of alcohol. This is because non-drinkers may have stopped consuming alcohol because of adverse health. Recent efforts in epidemiologic studies to define occasional use of alcohol as the reference may help reduce this bias. This study aimed to explore associations between alcohol use and clinical disease activity index (CDAI) among RA patients in a large sample, comparing the estimates of association when using non-drinkers or, alternatively, occasional drinkers as the comparison group.

Methods: This cross-sectional study assessed the association between disease activity and frequency of alcohol use, using data from the CorEvitas Rheumatoid Arthritis Registry, a prospective, observational, multi-site study of adults with RA. All patients in the Registry were provided-diagnosed. One visit per patient was randomly chosen, excluding the enrollment visit or last visit. Drinking is patient reported and divided into 6 categories. The association of mean CDAI with drinking categories was estimated using linear regression. A series of nested models adjusted for demographics and drug use, +comorbidities, and +pain and psychosocial factors. Estimates used "Not at All" or "Occasionally" as the reference category in the models.

Results: A total of 30,995 adults with non-missing confounding variables were included in this study. Non-drinkers had higher rates of disability, comorbidities (including diabetes, CAD, CHF, hypertension, obesity, and fibromyalgia), opioid use, depression, and anxiety; as well as higher scores for physician and patient global assessments, tender and swollen joints, pain, and fatigue compared to other categories (Table 1).

Compared to non-drinkers, any amount of drinking was associated with a lower CDAI with the greatest apparent benefit observed for moderate drinkers. [Unadjusted β: -3.65 (95 % CI: -4.16, -3.14)]. This was somewhat attenuated with adjustment for confounders [Fully adjusted β: -2.42 (95% CI: -2.91, -1.93)] (Table 2). The unadjusted estimate for moderate drinkers was reduced substantially when using occasional drinkers as the reference group. [Unadjusted β: -1.85 (95% CI -2.43, -1.17)] and was further attenuated with adjustment [β: -1.11 (95% CI: -1.66, -0.56)]. Figure 1 shows the mean difference in CDAI for the fully adjusted models.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics by alcohol use frequency

	Drink Categories						
	Not at all	Occasionally	1-3 drinks per week	4-6 drinks per week	1-2 drinks daily	3 drinks or more daily	Test
N (%)	17,743 (57.2%)	4,241 (13.7%)	4,293 (13.9%)	1,930 (6.2%)	2,249 (7.3%)	539 (1.7%)	
Sex at birth							
Male	3,607 (20.3%)	734 (17.3%)	1,028 (23.9%)	623 (32.3%)	814 (36.2%)	307 (57.0%)	<0.001
Female	14,136 (79.7%)	3,507 (82.7%)	3,265 (76.1%)	1,307 (67.7%)	1,435 (63.8%)	232 (43.0%)	
Age	63.5 (12.8)	59.3 (13.2)	59.0 (13.5)	57.5 (12.9)	63.3 (13.0)	60.3 (12.0)	<0.001
Smoking status							
Never	9,768 (55.1%)	2,293 (54.1%)	2,195 (51.1%)	934 (48.4%)	907 (40.3%)	159 (29.5%)	<0.001
Previous	3,748 (21.1%)	975 (23.0%)	1,001 (23.3%)	485 (25.1%)	676 (30.1%)	165 (30.6%)	
Current	4,227 (23.8%)	973 (22.9%)	1,097 (25.6%)	511 (26.5%)	666 (29.6%)	215 (39.9%)	
Disabled	2,877 (16.2%)	421 (9.9%)	308 (7.2%)	112 (5.8%)	109 (4.8%)	49 (9.1%)	<0.001
Biol/TS Use	8,948 (50.4%)	2,262 (53.3%)	2,337 (54.4%)	1,093 (56.6%)	1,237 (55.0%)	303 (56.2%)	<0.001
Number of prior biol/TS naïve							
Naive	5,697 (32.1%)	1,270 (29.9%)	1,296 (30.2%)	530 (27.5%)	650 (28.9%)	158 (29.3%)	<0.001
1	5,871 (33.1%)	1,486 (35.0%)	1,571 (36.6%)	760 (39.4%)	808 (35.9%)	216 (40.1%)	
2	2,979 (16.8%)	734 (17.3%)	723 (16.8%)	352 (18.2%)	389 (17.3%)	85 (15.8%)	
3	1,537 (8.7%)	368 (8.6%)	368 (8.6%)	139 (7.2%)	205 (9.1%)	38 (7.1%)	
4	851 (4.8%)	193 (4.6%)	194 (4.5%)	83 (4.3%)	116 (5.2%)	20 (3.7%)	
5+	808 (4.6%)	192 (4.5%)	141 (3.3%)	66 (3.4%)	81 (3.6%)	22 (4.1%)	
Prednisone use							
No Prednisone	13,956 (78.7%)	3,487 (82.2%)	3,598 (83.8%)	1,623 (84.1%)	1,873 (83.3%)	456 (84.6%)	<0.001
Pred <5mg	841 (4.7%)	161 (3.8%)	183 (4.3%)	71 (3.7%)	79 (3.5%)	13 (2.4%)	
Pred >=5mg	2,946 (16.6%)	593 (14.0%)	512 (11.9%)	236 (12.2%)	297 (13.2%)	70 (13.0%)	
MTX Use							
No MTX	8,427 (47.5%)	1,994 (47.0%)	1,982 (46.2%)	1,010 (52.3%)	1,228 (54.6%)	332 (61.6%)	<0.001
MTX <12.5mg	1,846 (10.4%)	458 (10.8%)	493 (11.5%)	174 (9.0%)	229 (10.2%)	49 (9.1%)	
MTX >=12.5mg	7,470 (42.1%)	1,789 (42.2%)	1,818 (42.3%)	746 (38.7%)	792 (35.2%)	158 (29.3%)	
Patient pain assessment	37.1 (29.0)	32.0 (27.7)	28.3 (26.4)	26.1 (25.7)	26.7 (25.1)	29.8 (27.4)	<0.001
Patient global assessment	34.7 (27.6)	29.1 (25.9)	26.2 (25.0)	24.2 (24.4)	24.5 (23.9)	28.6 (26.6)	<0.001
Patient fatigues assessment	39.6 (30.5)	36.2 (29.6)	32.6 (28.6)	30.1 (27.8)	29.3 (27.8)	31.6 (29.5)	<0.001
28 joints: tender	3.5 (5.8)	2.9 (5.2)	2.5 (4.7)	2.2 (4.5)	2.3 (4.4)	2.5 (4.6)	<0.001
28 joints: swollen	2.5 (4.1)	2.1 (3.6)	1.8 (3.2)	1.7 (3.3)	1.9 (3.5)	2.4 (4.1)	<0.001
Physician global assessment scale	19.1 (19.9)	16.6 (18.8)	14.8 (17.2)	13.7 (16.9)	14.2 (16.8)	16.7 (19.5)	<0.001
Stiffness in the morning	12,948 (73.7%)	3,012 (71.6%)	2,924 (68.7%)	1,299 (67.8%)	1,497 (67.1%)	376 (70.4%)	<0.001
HAQ-DI	0.9 (0.7)	0.7 (0.7)	0.6 (0.6)	0.5 (0.6)	0.5 (0.6)	0.5 (0.6)	<0.001
hx of Diabetes	2,328 (13.1%)	401 (9.5%)	268 (6.2%)	86 (4.5%)	109 (4.8%)	38 (7.1%)	<0.001
hx CAD	328 (1.8%)	51 (1.2%)	54 (1.3%)	20 (1.0%)	34 (1.5%)	6 (1.1%)	0.002
hx CHF	357 (2.0%)	49 (1.2%)	40 (0.9%)	14 (0.7%)	31 (1.4%)	5 (0.9%)	<0.001
hx Hypertension	7,204 (40.6%)	1,316 (31.0%)	1,214 (28.3%)	534 (27.7%)	746 (33.2%)	185 (34.3%)	<0.001
hx Liver Disease	445 (2.5%)	120 (2.8%)	100 (2.3%)	46 (2.4%)	58 (2.6%)	8 (1.5%)	0.436
hx Chronic Kidney Disease	55 (0.3%)	17 (0.4%)	16 (0.4%)	4 (0.2%)	6 (0.3%)	0 (0.0%)	0.545
hx Lung Disease	30 (0.2%)	8 (0.2%)	4 (0.1%)	2 (0.1%)	3 (0.1%)	0 (0.0%)	0.72
hx Cancer	1,920 (10.8%)	402 (9.5%)	437 (10.2%)	163 (8.4%)	275 (12.2%)	46 (8.5%)	<0.001
hx Fibromyalgia	537 (3.0%)	97 (2.3%)	94 (2.2%)	42 (2.2%)	51 (2.3%)	10 (1.9%)	0.002
Pt reported Depression	2,280 (12.9%)	519 (12.2%)	373 (8.7%)	170 (8.8%)	177 (7.9%)	63 (11.7%)	<0.001
Pt reported Anxiety	2,602 (14.7%)	566 (13.3%)	493 (11.5%)	203 (10.5%)	227 (10.1%)	77 (14.3%)	<0.001
NSAIDs use	9,310 (52.5%)	2,302 (54.3%)	2,298 (53.5%)	1,020 (52.8%)	1,206 (53.6%)	267 (49.5%)	0.148
Opioid use	4,410 (24.9%)	853 (20.1%)	651 (15.2%)	248 (12.8%)	316 (14.1%)	89 (16.5%)	<0.001
BMI	30.3 (7.7)	30.3 (7.5)	29.0 (6.8)	28.5 (6.4)	27.8 (6.1)	28.8 (6.2)	<0.001
Duration of RA	12.4 (10.7)	11.8 (10.2)	11.8 (9.9)	11.5 (9.5)	12.6 (10.5)	11.1 (9.6)	<0.001
CDAI	11.4 (11.5)	9.6 (10.5)	8.4 (9.5)	7.7 (9.4)	8.0 (9.3)	9.4 (10.4)	<0.001
Charlson Comorbidity Index	1.4 (0.7)	1.3 (0.6)	1.3 (0.5)	1.2 (0.5)	1.3 (0.6)	1.2 (0.5)	<0.001
CCI							
1	12,032 (67.8%)	3,212 (75.7%)	3,347 (78.0%)	1,575 (81.6%)	1,697 (75.5%)	426 (79.0%)	<0.001
2	4,366 (24.6%)	807 (19.0%)	787 (18.3%)	304 (15.8%)	462 (20.5%)	95 (17.6%)	
3+	1,345 (7.6%)	222 (5.2%)	159 (3.7%)	51 (2.6%)	90 (4.0%)	18 (3.3%)	

Note: using test pearson across levels of drink6 for sex, smoking status, disabled, previous biologic use, Prednisone dose group, MTX dose group, Morning stiffness, History of diabetes, History of CAD, History of CHF, History of cancer, History of lung disease, History of chronic kidney disease, History of fibromyalgia, Hypertension, History of liver disease, Depression, Anxiety, NSAID use, Opioid use, CDAI cat4, and CCI group.
Note: using test kwallis across levels of drink6 for Age, Pain, Patient global assessment, Fatigue, Tender joints, Swollen joints, Physician global assessment, HAQ, BMI, Duration, CDAI, and CCI.
Note: Marital status, Site US region, Work status, Education, Weight (lbs), and BMI categories not shown for space considerations.

Conclusion: Light to moderate alcohol use was associated with lower disease activity in patients with RA, with moderate users seeing the biggest reduction in CDAI. However, the amount of observed benefit was far less when comparing moderate use to occasional use and after adjustment for confounding factors. These data raise questions regarding the accuracy of the estimated benefit of alcohol from prior studies where non-drinkers were used as the reference group and suggests that residual confounding is likely. A biologic mechanism for a benefit of alcohol effect is not known.

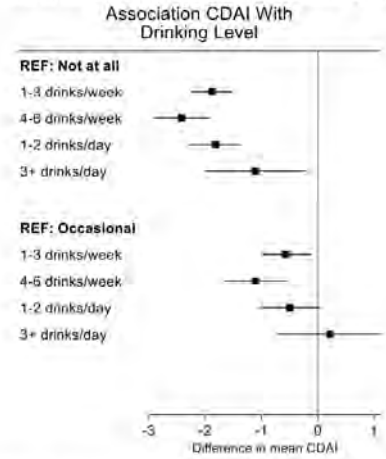
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Estimated CDAI by drinking category using tiered models
Coefficients represent difference in CDAI from reference group

Mean change in CDAI from reference group [95% CI]	Unadjusted	Adjusted demographics and drug use	Adjusted + Comorbidities	Adjusted + Pain and psychosocial factors
Using non-drinkers as reference group				
Not at All	Reference	Reference	Reference	Reference
Occasionally	-1.80 [-2.17, -1.44]	-1.94 [-2.30, -1.59]	-1.85 [-2.20, -1.49]	-1.31 [-1.66, -0.96]
1-3 drinks/week	-2.98 [-3.34, -2.62]	-2.80 [-3.16, -2.45]	-2.66 [-3.01, -2.30]	-1.88 [-2.23, -1.53]
4-6 drinks/week	-3.65 [-4.16, -3.14]	-3.50 [-4.00, -3.00]	-3.33 [-3.83, -2.83]	-2.42 [-2.91, -1.93]
1-2 drinks/day	-3.34 [-3.81, -2.86]	-2.84 [-3.31, -2.37]	-2.67 [-3.14, -2.20]	-1.81 [-2.27, -1.35]
3+ drinks daily	-2.01 [-2.94, -1.09]	-1.71 [-3.31, -2.37]	-1.56 [-2.47, -0.66]	-1.11 [-2.00, -0.22]
Using occasional drinkers as reference group				
Not at All	1.80 [1.44, 2.17]	1.94 [1.59, 2.30]	1.85 [1.49, 2.20]	1.31 [0.96, 1.66]
Occasionally	Reference	Reference	Reference	Reference
1-3 drinks/week	-1.17 [-1.63, -0.71]	-0.86 [-1.31, -0.42]	-0.81 [-1.26, -0.37]	-0.57 [-1.00, -0.13]
4-6 drinks/week	-1.85 [-2.43, -1.27]	-1.56 [-2.13, -1.00]	-1.49 [-2.05, -0.92]	-1.11 [-1.66, -0.56]
1-2 drinks/day	-1.53 [-2.08, -0.98]	-0.90 [-1.44, -0.36]	-0.82 [-1.37, -0.28]	-0.50 [-1.03, 0.03]
3+ drinks daily	-0.21 [-1.18, 0.76]	0.23 [-0.72, 1.18]	0.28 [-0.67, 1.23]	0.21 [-0.72, 1.13]

Demographic and drug use: Sex, age, duration of RA, BMI, smoking, prednisone use, MTX use, Biologic/tsDMARD use.
+ Comorbidities: Diabetes, HTN, Liver Disease, CAD, CHF, Kidney disease, Lung disease, Cancer
+ Pain and psychosocial: Pt reported depression, pt reported anxiety, fibromyalgia, education, disabled.

Figure 1: Difference in Mean CDAI in fully adjusted models using "Not At All" or "Occasionally" as the reference group



Adjusted for: Demographic and drug use: Sex, age, duration of RA, BMI, smoking, prednisone use, MTX use, Biologic/tsDMARD use + Comorbidities: Diabetes, HTN, Liver Disease, CAD, CHF, Kidney disease, Lung disease, Cancer + Pain and psychosocial: Pt reported depression, pt reported anxiety, fibromyalgia, education, disabled.

Difference in Mean CDAI in fully adjusted models using "Not At All" or "Occasionally" as the reference group

Disclosure: S. Crisci: CorEvitas, part of Thermo Fisher Scientific, 3; **J. Baker**: Amgen, 5; **K. Kane**: None; **G. Reed**: CorEvitas, part of Thermo Fisher Scientific, 2, Corrona Research Foundation, 2; **D. Pappas**: AbbVie/Abbott, 2, CorEvitas, Part of Thermofisher, 3, 11, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4, Novartis, 2, Roche, 2; **J. Kremer**: CorEvitas (part of ThermoFisher), 1, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1341

Physical Function Across Age in Patients With Rheumatoid Arthritis and Population Controls: A Cross-Sectional Study of Four Performance Measures

Saskia Truijen[1], Annelies Boonen[1], Sofia Ramiro[2] and Marloes van Onna[1], [1]Maastricht University Medical Centre+ & Maastricht University, Maastricht, Limburg, Netherlands, [2]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) may accelerate age-related functional decline compared to the general population. This study aimed to examine whether four performance measures of physical function differ between older patients with RA and population controls, and whether this decline is stronger with increasing age in patients with RA.

Methods: Cross-sectional data of patients with RA and population controls without inflammatory rheumatic disease aged 55–85 years from the STudying Aging in Rheumatoid arthritis (STAR) study was used. Physical function was assessed using four measures. All participants completed the self-reported Cochin hand functional disability questionnaire (18 items; 0=no

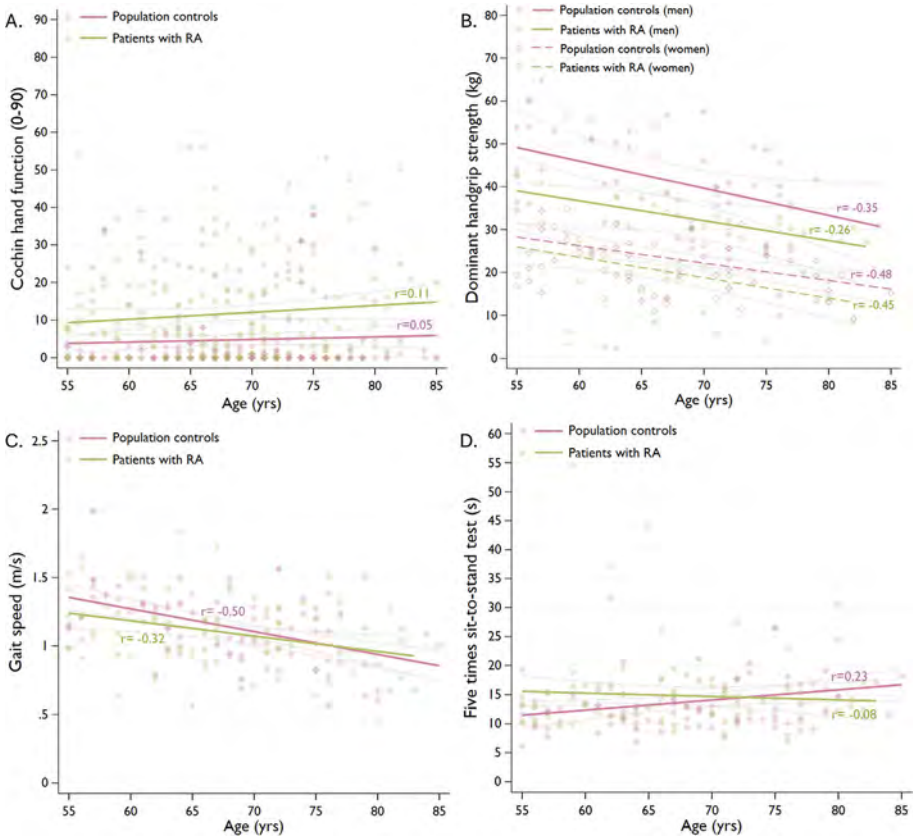


Figure 1. A) The Cochin hand function scale by age, stratified for population controls (n=209; r=0.05) and patients with RA (n=197; r=0.11) B) Observed dominant handgrip strength (kg) by age, stratified for population controls (men: n=38; r=-0.35, women: n=52; r=-0.48) and patients with RA (men: n=39; r=-0.26, women: n=38; r=-0.45) C) Gait speed (m/s) by age, stratified for population controls (n=90; r=-0.50) and patients with RA (n=78; r=-0.32) D) Five times sit-to-stand test (s) by age, stratified for population controls (n=90; r=0.23) and patients with RA (n=78; r=-0.08)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Associations between group (RA vs control), adjusted for age and sex, and (thresholds of) functional ability assessed by the Cochin hand function scale (n=406), dominant handgrip strength, gait speed and five-times sit-to-stand test (n=168)

Linear regression		Dominant handgrip strength (kg) β (95% CI)	Gait speed (m/s) β (95% CI)	Five times sit-to-stand test (s) β (95% CI)
Age, *years*	-	-0.36 (-0.56 to -0.15)	-0.01 (-0.02 to -0.01)	0.06 (-0.07–0.18)
Sex, *women*	-	-11.34 (-15.39 to -7.30)	-0.10 (-0.18 to -0.03)	0.35 (-1.51–2.21)
Group, *patient with RA*	-	-4.70 (-7.68 to -1.72)	-0.04 (-0.12–0.03)	1.21 (-0.66–3.08)
Height, *cm* [1]	-	0.33 (0.12–0.53)	-	-
Logistic regression	**Cochin hand function scale score ≥1 vs. 0** [2] OR (95% CI)	**Diminished dominant handgrip strength (kg) according to Fried criteria** [3] OR (95% CI)	**Gait speed <0.8 m/s** [4] OR (95% CI)	**Five-times sit-to-stand test >15.0 s** [4] OR (95% CI)
Age, *years*	1.03 (1.00–1.06)	1.10 (1.05–1.15)	1.12 (1.05–1.20)	1.04 (1.00–1.09)
Sex, *women*	2.31 (1.48–3.61)	1.47 (0.72–2.98)	1.57 (0.57–4.34)	0.91 (0.47–1.77)
Group, *patient with RA*	4.90 (3.15–7.62)	2.51 (1.23–5.12)	2.45 (0.88–6.79)	1.81 (0.93–3.54)

[1] Handgrip strength was adjusted for height to account for body size differences
[2] Interaction $p<0.05$, however, not considered clinically relevant after stratification
[3] Based on the threshold for dominant hand grip strength of the Fried frailty criteria, stratified for gender and BMI quartiles:
Men: BMI ≤24 HGS ≤29 kg, BMI 24.1–26.0 HGS ≤30 kg, BMI 26.1–28.0 HGS ≤30 kg, BMI >28.0 HGS ≤32 kg
Women: BMI ≤23 HGS ≤17 kg, BMI 23.1–26.0 HGS ≤17.3 kg, BMI 26.1–29.0 HGS ≤18 kg, BMI >29.0 HGS ≤21 kg
[4] Based on the threshold for low performance (slow walking speed <0.8 m/s) and low strength (chair stand >15.0 s for five rises) according to the European Working Group on Sarcopenia in Older People.

functional hand disability, 90=maximal disability; score ≥1 = impaired). In a subpopulation, additional physical measurements were conducted: grip strength of the dominant hand measured with a dynamometer (kg; fulfilling sex- and BMI-specific Fried frailty criteria = impaired), gait speed using the four-meter walk test (< 0.8 m/s = impaired), and the Five Times Sit-to-Stand Test (FTSST) (>15.0s = impaired). Correlations between age and outcomes of physical function were explored separately for RA patients and controls and visualized using scatter plots. Linear and logistic regressions assessed age and sex adjusted associations between group (RA vs. control) and outcome, and the interaction age*group. Due to a left-skewed distribution, Cochin scores were only analyzed using logistic regression (≥1 vs. 0).

Results: A total of 416 persons were included: 197 patients with RA (mean age 68 ± 7, 62% women) and 209 population controls (mean age 68 ± 7, 60% women). The subpopulation consisted of 168 persons: 78 patients with RA (mean age 67 ± 8, 51% women) and 90 controls (mean age 68 ± 7, 58% women). Age correlated moderately with gait speed in controls and handgrip strength in female controls, but correlated weakly for all other comparisons (Figure 1A-D). For self-reported handfunction, RA patients were more likely to report a functional disability (score ≥1) (OR=4.9, 95%CI: 3.2–7.6) (Table 1). For hand grip strength, patients with RA had lower handgrip strength (β=-4.7, 95%CI: -7.7 to -1.7) and were more likely to meet the Fried criteria for low grip strength (OR=2.5, 95%CI: 1.2–5.1), as compared to controls. For gait speed and FTSST, no associations with RA were observed. A significant interaction between age and group was only observed for the Cochin scale, however, after stratification this was not considered clinically relevant.

Conclusion: These findings suggest that while RA leads to lower physical functioning compared to controls, this effect does not differ across age. Functional decline in RA may be more disease-specific than age-driven, highlighting the importance of early management of RA. The results may also indicate that current RA treatment may be effective in limiting excessive functional decline later in life, by reducing cumulative joint damage over time.

Disclosure: S. Truijen: None; **A. Boonen**: AbbVie/Abbott, 5, Alfasigma, 2, Celgene, 5, Eli Lilly, 2, Novartis, 2, Sandoz, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **M. van Onna**: Alfasigma, 2, Novartis, 2, Pfizer, 2, 5, ReumaNederland, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1342

The Impact of Age on Health-Related Quality of Life in Patients With Rheumatoid Arthritis Compared to Population Controls: A Cross-Sectional Analysis

Saskia Truijen[1], Annelies Boonen[1], Sofia Ramiro[2] and Marloes van Onna[1], [1]Maastricht University Medical Centre+ & Maastricht University, Maastricht, Limburg, Netherlands, [2]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: As the population ages, rheumatologists will increasingly care for older persons with rheumatoid arthritis (RA). Aging comes with specific challenges of which rheumatologists are currently insufficiently aware. Among others, there is limited understanding of how older age affects aspects of Health-Related Quality of Life (HRQoL) and whether the impact of age is different compared to controls.

Methods: Cross-sectional data of patients with RA and population controls without inflammatory rheumatic disease aged 55–85 years from the STudying Aging in Rheumatoid arthritis (STAR) study was used. HRQoL was assessed by the eight domains of the self-reported 36-item Short Form (SF-36) Health Survey Questionnaire (score 0–100: 0=worst, 100=best). Linear regression was used to test potential interactions between five age categories (ref 55–59 years) and group (RA/control), while adjusting for sex, with $p_{interaction}<0.10$ considered statistically significant. In subsequent multivariable linear regressions, body mass index (BMI), the no. of self-reported painful joints (Rheumatoid Arthritis Disease Activity Index (RADAI); score 0–48), physical function (Health Assessment Questionnaire (HAQ); score 0–3) and comorbidities (Charlson Comorbidity Index (CCI); score 0, 1, ≥2) were added to explore potential confounding of age category and group.

Results: A total of 406 participants were included: 197 patients with RA (mean age 68±7, 62% women) and 209 population controls (mean age 68±7, 60% women). Across all eight HRQoL domains, patients with RA reported lower scores than controls (∼10–20 points lower on average). For bodily pain (BP), general health (GH), role emotional (RE) and mental health (MH), no differential effect of age category between patients and controls were observed ($p_{interaction}\geq0.10$) (Table 1). For physical functioning (PF), role physical (RP), social functioning (SF) and vitality (VT), interactions between RA/control and age categories were significant. Scores for PF and SF tended to be worse in patients with RA aged 75–85 years compared to the

Table 1. Linear regression analyses of the association between age (category), sex, group and SF-36 domain scores (n=406)

	SF36 BP β (95% CI)	SF36 GH β (95% CI)	SF36 RE β (95% CI)	SF36 MH β (95% CI)
Age category, *years*				
55-59	*reference*	*reference*	*reference*	*reference*
60-64	3.2 (-3.8–10.2)	2.5 (-3.7–8.9)	0.7 (-9.9–11.4)	0.7 (-4.4–5.8)
65-69	1.8 (-4.7–8.2)	0.0 (-5.8–5.8)	2.8 (-7.0–12.6)	2.3 (-2.4–7.0)
70-74	1.4 (-5.2–8.0)	1.3 (-4.6–7.3)	3.3 (-6.8–13.5)	-0.5 (-5.3–4.4)
75-85	-5.5 (-12.5–1.4)	-3.6 (-9.9–2.7)	1.3 (-9.3–11.9)	1.3 (-3.7–6.4)
Sex, *women*	-4.8 (-8.9 to -0.7)	-0.8 (-4.5–2.9)	2.2 (-4.1–8.4)	-4.5 (-7.4 to -1.5)
Group, *RA*	-13.4 (-17.4 to -9.4)	-16.9 (-20.5 to -13.3)	-10.5 (-16.6 to -4.4)	-4.7 (-7.6 to -1.8)

BP Bodily Pain; GH General Health; RE Role Emotional; MH Mental Health; RA Rheumatoid Arthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Linear regression analyses of the association between age (category), group and sex and SF-36 domain scores, stratified for patients with RA (n=197) and controls (n=209)

	SF36 PF RA β (95% CI)	SF36 PF Control β (95% CI)	SF36 RP RA β (95% CI)	SF36 RP Control β (95% CI)	SF36 SF RA β (95% CI)	SF36 SF Control β (95% CI)	SF36 VT RA β (95% CI)	SF36 VT Control β (95% CI)
Age category, *years*								
65-69	*reference*	*reference*	*reference*	*reference*	*reference*	*reference*	*reference*	*reference*
60-64	-2.6 (-12.6–7.6)	2.7 (-8.5–11.9)	0.7 (-20.3–20.8)	13.1 (-4.1–30.3)	-7.0 (-18.1–4.0)	9.0 (-0.3–18.3)	-1.0 (-10.4–8.4)	11.7 (3.2–20.2)
65-69	-5.4 (-14.6–4.0)	0.2 (-8.3–8.8)	-2.1 (-21.8–16.8)	17.4 (1.6–33.2)	-1.3 (-11.8–8.9)	7.4 (-1.2–15.9)	3.8 (-5.8–12.3)	11.9 (4.1–19.7)
70-74	-7.3 (-17.0–2.5)	-2.4 (-11.1–6.3)	-3.1 (-22.9–16.6)	22.2 (6.6–38.4)	-6.0 (-16.8–4.6)	8.7 (0.2–17.6)	-0.3 (-9.4–8.8)	13.1 (5.1–21.1)
75-85	-20.1 (-30.5 to -9.7)	-8.4 (-17.4–0.6)	-9.4 (-30.5–11.6)	12.1 (-4.8–28.9)	-16.0 (-27.3 to -4.7)	6.7 (-2.4–15.8)	-1.1 (-10.7–8.5)	9.5 (1.3–17.8)
Sex, *women*	-5.3 (-11.5–1.0)	-8.7 (-13.9 to -3.5)	-7.1 (-19.9–5.7)	-0.5 (-10.2–9.2)	-3.2 (-10.1–3.6)	-4.1 (-9.4–1.1)	-3.8 (-9.6–2.1)	-0.1 (-10.9 to -1.4)

PF Physical Functioning; RP Role Physical; SF Social Functioning; VT Vitality; RA Rheumatoid Arthritis

youngest group, but remained unchanged (PF) or even improved (SF) in controls aged 70–74 years (Table 2). No effect of age on scores for RP and VT were observed in patients, while better scores with increasing age were observed in controls, specifically in those 70–74 years. After adjusting for health-related confounders, the impact of RA on RE, MH, BP and GH reduced or disappeared, and a positive age effect emerged in those aged 75–85 years for MH and 70–74 for BP (data not shown). For domains that had to be stratified, the effect of age was (i) attenuated for PF among RA patients, (ii) unchanged for VT and SF in patients and controls and (iii) stronger for RP in controls aged 75–85 years.

Conclusion: These findings suggest that age-related changes in HRQoL differ between patients with RA and controls, by age category, and SF-36 domain. Older RA patients begin at a lower baseline, experience a decline in physical functioning, and miss the age-related improvements seen in controls in role physical, vitality and social functioning. Clinicians should more aware of these differences and gain more attention on supporting psychosocial well-being in older patients with RA.

Disclosure: S. Truijen: None; **A. Boonen**: AbbVie/Abbott, 5, Alfasigma, 2, Celgene, 5, Eli Lilly, 2, Novartis, 2, Sandoz, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **M. van Onna**: Alfasigma, 2, Novartis, 2, Pfizer, 2, 5, ReumaNederland, 5.

Abstract Number: 1343

Six-Minute Walk Distance as a Functional Measure in Rheumatoid Arthritis-associated Interstitial Lung Disease Reflecting Both Lung and Joint Involvement

Sung Hae Chang[1], You-Jung Ha[2], Sung Won Lee[3], Misti Paudel[4], Gregory McDermott[5], Qianru Zhang[6], Min Uk Kim[7], Jeong Seok Lee[8], Chan Ho Park[9], Ji-Won Kim[10], Jang Woo Ha[11], SANGWAN CHUNG[12], Eun Ha Kang[13], Yeon-Ah Lee[12], Yong-Beom Park[14], Jung-Yoon Choe[15], Eun Young Lee[16], Jeffrey Sparks[17] and KORAIL Cohort Study Group, [1]Soonchunhyang University College of Medicine, Cheonan, MA, South Korea, [2]Seoul National University Bundang Hospital, Seongnam, South Korea, [3]Soon Chun Hyang University Hospital, Seoul, South Korea, [4]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [5]Brigham and Women's Hospital, Brookline, MA, [6]Harvard Medical School, Boston, MA, [7]SMG-SNU Boramae Medical Center, Seoul, Republic of Korea, [8]Korea Advanced Institute of Science and Technology, KAIST, DaeJeon, Republic of Korea, [9]Soonchunhyang University College of Medicine, Cheonan, Republic of Korea, [10]Daegu Catholic University School of Medicine, Nam-gu, Daegu, Republic of Korea, [11]Division of Rheumatology, Department of Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, Seodaemun-gu, Seoul, Republic of Korea, [12]Kyung Hee University Medical Center, seoul, Republic of Korea, [13]Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [14]Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, [15]Division of Rheumatology, Department of Internal Medicine, Daegu Catholic University School of Medicine, Daegu, Republic of Korea, [16]Seoul National University College of Medicine, Seoul, South Korea, [17]Brigham and Women's Hospital, Boston, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The six-minute walk distance (6MWD) measures functional capacity in cardiopulmonary diseases, predicts mortality in interstitial lung disease (ILD), and is used as an endpoint in trials. In RA, 6MWD correlates with patient-reported outcomes and adverse cardiovascular events, yet few studies investigate 6MWD in RA-ILD.

Methods: We performed a cross-sectional analysis using baseline data from the Korean RA-ILD (KORAIL) cohort, a multicenter prospective study. RA was diagnosed based on the 2010 ACR/EULAR criteria, and ILD was confirmed by chest CT imaging. Participants were assessed for RA disease activity using the DAS28 and laboratory tests, including ESR and CRP. ILD status was evaluated by chest CT and pulmonary function tests, including forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and diffusing capacity of the lung for carbon monoxide (DLCO). The expected lower limit of the six-minute walk distance (eLL-6MWD) was calculated based on age, sex, height, and weight. Associations of 6MWD or having a 6MWD below the expected lower limit (eLL-6MWD) with predictors were analyzed using linear or logistic regression, while their associations with progression or mortality were analyzed using Cox regression, adjusting for age, sex, height, and weight.

Results: We analyzed 141 patients with RA-ILD (mean age 66.7 years, 32.6% male, 61.7% with the usual interstitial pneumonia [UIP] pattern). The median RA duration was 6.0 years (interquartile range [IQR] 1.2 to 10.7), and the median ILD duration was 1.5 years (IQR 0.2 to 4.6). The mean DAS28-ESR score was 4.1 (standard deviation [SD] 1.4), with 70.7% of patients having moderate/high disease activity. ILD extent >10% on chest CT was present in 40.4%. The mean FVC% was 84.2 (SD 17.3), DLCO% was 71.3 (SD 19.4), and 6MWD was 339 meters (SD 113). Overall, 49.6% had a 6MWD below the eLL-6MWD. Participants with moderate or high disease activity demonstrated shorter six-minute walk distances (6MWD) compared to those in remission or low disease activity (β -50.3) (Table 1). Higher HAQ scores were also associated with shorter 6MWD (β -50.1) and higher ESR and CRP levels (ESR: -30.5 per SD; CRP: β -23.1 per SD). Higher FEV_1%, FVC

Table 1. Factors associated with 6-minute walk distance in meters among patients with RA-ILD.

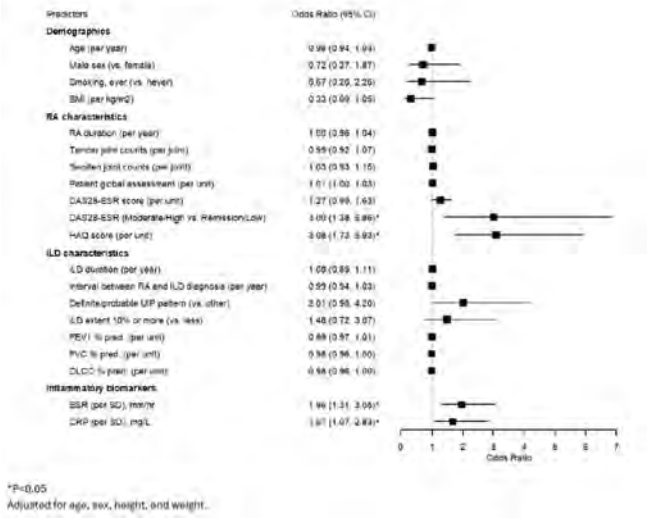
	β-coefficient (95 % CI) *	P*
Demographics		
Age (per year)	**-4.0 (-6.3, -1.8)**	**<0.01**
Male sex (vs. female)	25.6 (-23.8, 74.9)	0.31
Smoking, ever (vs. never)	18.1 (-43.8, 79.2)	0.56
BMI (per kg/m²)	19.0 (-36.0, 73.9)	0.50
RA characteristics		
RA duration (per year)	-1.1 (-3.3, 1.0)	0.29
Tender joint count (per joint)	0.4 (-3.6, 4.5)	0.83
Swollen joint count (per joint)	-1.4 (-6.6, 3.8)	0.60
Patient global assessment (per unit)	-0.6 (-1.2, 0.1)	0.11
DAS28-ESR score (per unit)	-11.6 (-24.0, 0.8)	0.07
DAS28-ESR (category)		
Moderate/high (vs. remission/low)	**-50.3 (-88.3, -12.3)**	**0.01**
HAQ score (per unit)	**-50.1 (-73.7, -26.6)**	**<0.01**
ILD characteristics		
ILD duration (per year)	-4.0 (-9.7, 1.7)	0.17
Interval between RA and ILD diagnosis (per year)	-0.4 (-2.8, 1.9)	0.71
Definite/probable UIP pattern (vs. other)	-26.0 (62.4, 10.5)	0.16
ILD extent 10 % or more (vs. less)	-35.5 (-72.0, 1.1)	0.057
FEV_1 % pred. (per unit)	**1.1 (0.3, 2.0)**	**0.01**
FVC % pred. (per unit)	**1.5 (0.4, 2.5)**	**0.01**
DLCO % pred. (per unit)	**1.2 (0.3, 2.1)**	**0.01**
Inflammatory biomarkers		
ESR (per SD), mm/hr	**-30.5 (-47.6, -13.3)**	**<0.01**
CRP (per SD), mg/L	**-23.1 (-40.5, -5.9)**	**0.01**

*Adjusted for age, sex, height, and weight.

Bolded values are statistically significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Factors associated with a 6-minute walk distance of less than expected lower limit (adjusted for age, sex, height, and weight) among patients with RA-ILD.



*P<0.05
Adjusted for age, sex, height, and weight.

%, and DLCO% were associated with longer 6MWD (FEV_1%: β 1.1, FVC%: β 1.5, DLCO%: β 1.2). The odds of having a 6MWD below eLL-6MWD were higher among participants with moderate or high disease activity (odds ratio [OR] 3.00), higher HAQ score (OR 3.08 per unit), higher ESR (OR 1.96 per SD), and higher CRP (OR 1.67 per SD) (Figure 1).

No significant associations were observed between 6MWD and ILD progression (hazard ratio [HR] 1.00 per meter, 95%CI 1.00 to 1.00) or all-cause mortality (HR 1.00 per meter, 95%CI 0.99 to 1.00), nor between 6MWD below eLL-6MWD and ILD progression (HR 1.23, 95%CI 0.68 to 2.22) or all-cause mortality (OR 1.85, 95%CI 0.71 to 4.81).

Conclusion: In RA-ILD, older age, moderate/high RA disease activity, worse HAQ, and increased ESR and CRP were associated with shorter 6MWD, while high FEV1%, FVC%, and DLCO% were associated with longer 6MWD. Collectively, these results suggest that the 6MWD test may provide a simple functional assessment that encompasses pulmonary function as well as RA-related disease activity and function.

Disclosure: S. Chang: None; **Y. Ha**: None; **S. Lee**: None; **M. Paudel**: None; **G. McDermott**: None; **Q. Zhang**: None; **M. Kim**: None; **J. Lee**: None; **C. Park**: None; **J. Kim**: None; **J. Ha**: Samsung Bioepis, 5; **S. CHUNG**: None; **E. Kang**: None; **Y. Lee**: None; **Y. Park**: Samsung Bioepis, 5; **J. Choe**: Samsung Bioepis, 5; **E. Lee**: IMbiologics, 1, Samsung Bioepis, 5; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 1344

Exploring the Factors Associated with the Discontinuation of Tofacitinib in Patients with Rheumatoid Arthritis: A Retrospective Cohort Study

Yao Fan Fang[1], Ping-Han Tsai[2] and yen Fu CHEN[3], [1]Chang Gung memorial hopspital, Linkou, Taipei, New Taipei, Taiwan (Republic of China), [2]Chang Gung memorial hospital, linkou, Taipei, Taiwan (Republic of China), [3]Chang Gung memorial hospital linkou, taipei, Taiwan (Republic of China)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

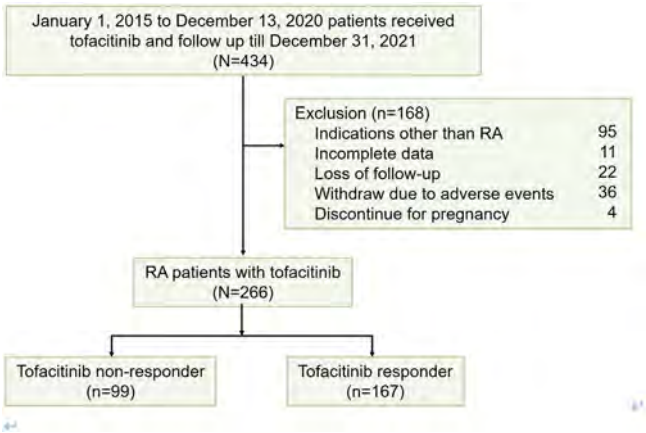


Figure 1 Flowchart for identifying rheumatoid arthritis patients with tofacitinib in Chang Gung memorial hospital. RA, rheumatoid arthritis.

Table 2. Multivariate Cox regression analysis: adjusted hazard ratio of the factors for tofacitinib in RA patients

Variable	Multivariate 1* HR (95% CI)	Multivariate 2†† HR (95% CI)	Multivariate 3††† HR (95% CI)
Male vs. Female	0.722 (0.400-1.302)	0.649 (0.339-1.243)	0.682 (0.268-1.734)
Age	1.000 (0.984-1.017)	0.998 (0.979-1.017)	1.015 (0.992-1.038)
RA disease duration	1.008 (0.968-1.049)	1.007 (0.963-1.053)	1.010 (0.958-1.065)
bDMARDs-experienced vs. bDMARDs-naïve	1.992* (1.265-3.139)	—	—
Prior TNFis vs. bDMARDs-naïve	—	2.152* (1.351-3.426)	—
Prior non-TNFis vs. bDMARDs-naïve	—	—	1.760* (1.012-3.606)

*, $p<0.05$. † 266 subjects with 155 bDMARDs-experienced, adjusting for gender, age, RA disease duration; †† 217 subjects with 95 prior TNFis, adjusting for gender, age, RA disease duration; ††† 171 subjects with 49 non-TNFis, adjusting for gender, age, RA disease duration.
RA, rheumatoid arthritis; HR, hazard ratio; CI, confidence interval; bDMARDs, biological DMARDs; TNFis, tumor necrosis factor inhibitors.

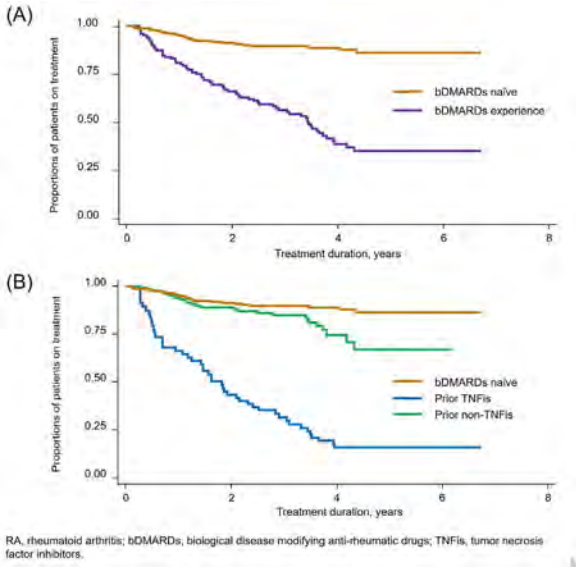


Figure 2. A) Drug survival curve for comparing RA patients with bDMARDs-näive and bDMARDs-experienced (B) Drug survival curve of comparing RA with prior TNFis, prior non-TNFis and bDMARDs näive.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Tofacitinib is the first oral targeted synthetic disease-modify anti-rheumatic drug for patients with moderate to severe rheumatoid arthritis [1]. This study aimed to identify the factors associated with the discontinuation of tofacitinib in patients with RA in clinical practice.

Methods: RA patients who received tofacitinib between 2015 and 2020 were included in this observational cohort study. The patients were followed for at least one year, ending on December 31, 2022. A tofacitinib non-responder was defined as a patient who required discontinuation or switch to another bDMARD. Conversely, tofacitinib responders were defined as those who could continue to receive tofacitinib without experiencing a loss of efficacy or severe adverse events. Univariate and multivariate Cox regression analyses and Kaplan–Meier survival curve analysis were used to investigate the factors associated with the discontinuation of tofacitinib.

Results: A total of 266 patients were enrolled. The average age of the patients was 57.07 ± 12.07 years, and 99 (37.2%) were tofacitinib non-responders. Univariate analysis revealed that the non-responders had a lower rate of concomitant hydroxychloroquine treatment, and higher rates of leflunomide, biological disease-modifying antirheumatic drug (bDMARD), and tumor necrosis factor inhibitor (TNFi) treatment compared to the responders. Cox regression adjusted analysis indicated that prior bDMARD treatment (hazard ratio (HR) = 1.423, 95% confidence interval (CI) = 1.024, 1.976, p = 0.036), prior TNFi treatment (HR = 1.605, 95% CI = 1.165, 2.212, p = 0.004), and prior non-TNFi treatment (HR = 1.326, 95% CI = 1.012, 2.075, p = 0.048) were associated with a higher non-response rate. Moreover, Kaplan–Meier survival curve analysis revealed that the patients with prior bDMARD treatment had a higher non-response rate.

Conclusion: The RA patients who received tofacitinib in this study had a good response rate, and the average non-response rate was around 37% after two years of treatment. The main factor associated with an inadequate response to tofacitinib was prior bDMARD treatment. Prior TNFi treatment was the strongest factor associated with a non-response to tofacitinib. Patients with a non-response to tofacitinib may consider bDMARDs with other mechanisms if previous treatment with TNFis was unsuccessful.

Disclosure: y. fang: None; **P. Tsai**: None; **y. CHEN**: None.

Abstract Number: 1345

Upregulated TLR Signaling Identified in Difficult-to-Treat RA: A Propensity Score–Matched Transcriptome Study

YOSHINORI NISHIURA[1], YOSHIHARU SATO[2], YU NAKAI[1], MOE TOKUNAGA[1], KENTA SHIDAHARA[1] and YOSHINOBU KOYAMA[3], [1]Japan Red Cross Okayama Hospital, Okayama-shi, Okayama, Japan, [2]DNA Chip Research Inc., Kawasaki-shi, Kanagawa, Japan, [3]Japanese Red Cross Okayama Hospital, Okayama, Okayama, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Difficult-to-treat rheumatoid arthritis (D2T-RA) represents a clinically challenging RA subset defined by failure to achieve disease control despite multiple conventional and advanced therapies. The immunopathogenesis of D2T-RA remains poorly understood. Prior studies suggest that elevated pretreatment type I interferon (IFN) signatures are associated with poor responses to tumor necrosis factor inhibitors (TNFi). Although Janus kinase (JAK) inhibitors, which modulate multiple cytokine pathways, are widely used, D2T-RA persists in a subset of patients. This study aimed to elucidate the immunological basis of D2T-RA through transcriptomic comparisons between propensity score–matched D2T and non-D2T patients.

Methods: Peripheral blood samples were obtained from 473 RA patients enrolled at the Department of Rheumatology, Japanese Red Cross Okayama Hospital, between March 2012 and September 2023, prior to initiation of new treatments. Based on EULAR criteria, 14 patients were identified as D2T, and 459 as non-D2T, the latter confirmed by at least two years of follow-up. Propensity score matching (1:1) was performed using age, DAS28-ESR, and the number of prior medications, yielding 13 matched pairs. RNA sequencing was conducted, and differentially expressed genes (DEGs) were identified using the LRM Paired-edgeR approach. Subsequent analyses included hierarchical clustering, Gene Ontology (GO) and pathway enrichment analyses, and weighted gene co-expression network analysis (WGCNA).

Results: At least 11 of 14 D2T patients demonstrated inadequate responses to JAK inhibitors. A total of 2,875 DEGs ($P < 0.05$) were identified, among which 288 genes with transcripts per million (TPM) ≥ 1 in either group were subjected to further analysis. Hierarchical clustering did not distinctly segregate D2T from non-D2T patients. Of these 288 genes, 114 were upregulated (positive DEGs) and 174 downregulated (negative DEGs) in the D2T group. GO analysis of the positive DEGs revealed enrichment of genes associated with immunity, particularly those involved in T cell function, innate immunity, and Toll-like receptor (TLR) signaling—most notably, the TLR7 pathway. Pathway analysis confirmed significant upregulation of TLR-related pathways. WGCNA identified five modules, one of which was enriched for TLR-associated genes.

Conclusion: This transcriptomic study identified marked upregulation of TLR signaling, especially TLR7-associated pathways, in patients with D2T-RA. These findings suggest that dysregulated TLR signaling may play a central role in the pathogenesis of treatment-refractory RA and offer potential insights for targeted therapeutic strategies.

Disclosure: Y. NISHIURA: None; **Y. SATO**: None; **Y. NAKAI**: None; **M. TOKUNAGA**: None; **K. SHIDAHARA**: None; **Y. KOYAMA**: AstraZeneca, 5, Novartis, 5, Ono, 5.

Abstract Number: 1346

Preliminary Result of Investigating the Response of Conventional Disease-Modifying Antirheumatic Drugs (cDMARDs) Associated SNPs: One Cohort Study

YU Chen[1], Chien-Sheng Wu[2], Jacob Shujui Hsu[3] and Pei-Lung Chen[4], [1]Division of Rheumatology, Allergy and Immunology, Far Eastern Memorial Hospital, New Taipei City, Taiwan, R.O.C. Graduate Institute of Medical Genomics and Proteomics, National Taiwan University, Taipei, Taiwan, R.O.C., New Taipei City, Taiwan (Republic of China), [2]Division

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

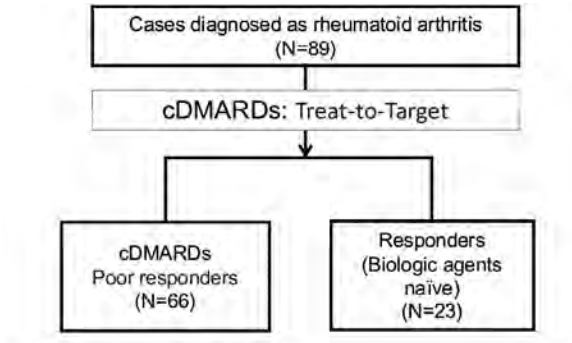
of Rheumatology, Allergy and Immunology, Far Eastern Memorial Hospital, New Taipei City, Taiwan, R.O.C., New Taipei city, Taiwan (Republic of China), [3]Graduate Institute of Medical Genomics and Proteomics, National Taiwan University, Taipei, Taiwan, R.O.C., Taipei city, Taiwan (Republic of China), [4]Graduate Institute of Medical Genomics and Proteomics, National Taiwan University, Taipei, Taiwan, R.O.C., Taipei, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1306–1346) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

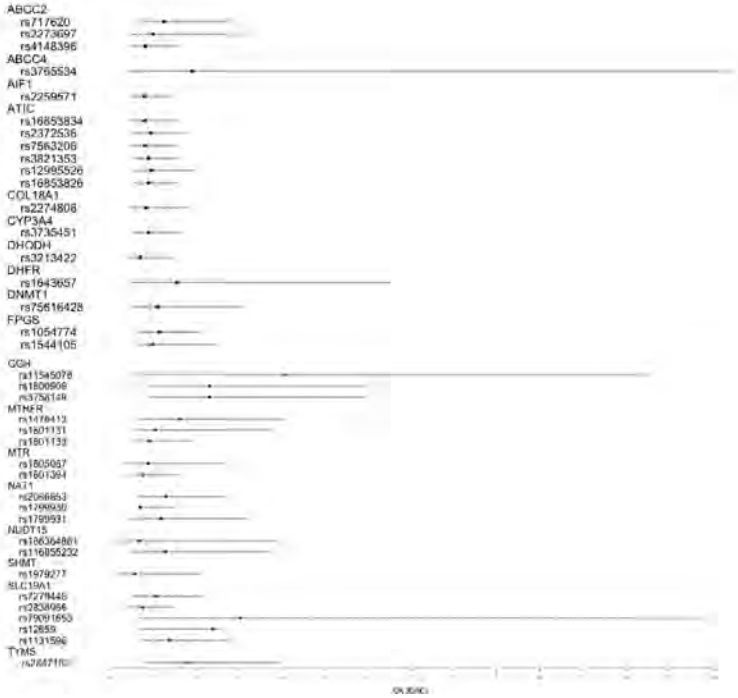
Background/Purpose: Multiple Single-Nucleotide Polymorphisms (SNPs), including those in the methotrexate and azathioprine metabolic pathways, are associated with poor response to conventional disease-modifying anti-rheumatic drugs (cDMARDs) in Caucasians with rheumatoid arthritis. This retrospective cohort study aimed to investigate the association between SNPs and cDMARDs in responders and poor responders.

Methods: cDMARDs responders were defined as patients who had received standard treatment for at least 6 months and had not yet used biological agents. Poor responders were defined as patients who had received cDMARD therapy for at least 6 months and subsequently required treatment with biological agents. Genotype analysis was performed using *Axiom Genome-Wide TPM 2.0 Array Plate*, specifically designed for our population and contained 752,922 probes per array plat. A total of 38 SNPs were selected in *AMPD*, *ATIC*, *DHFR*, *FPGS, GGH, ITPA*, *MTHFR*, *SLC19A1* and *TYMS* genes, which affect the methotrexate and azathioprine metabolic pathways. The distribution of allele frequency, odds ratio (OR), and 95% confidence intervals (CI) were calculated to evaluate the association between the categorical variables. A p-value of < 0.05 was considered to be statistically significant.



Clinical characteristics

cDMARDs	Poor responders	Responders	P vaule
Age	58.8 ± 11.3	57.4 ± 10.6	0.5951
Female (%)	48 (73%)	15 (68%)	0.6707
RF	315.52 ± 578.46	333.74 ± 554	0.8825
anti-CCP	189.21 ± 165	103.7 ± 135.3	0.01137*
1st CRP	1.76 ± 2.68	1.44 ± 2.63	0.5215
1st ESR	34.5 ± 22.7	32.64 ± 25.6	0.6758
ΔCRP 6M	-0.70± 2.72	-1.34 ± 2.84	0.2342
ΔESR 6M	-8.21 ± 22.71	-13.02 ± 26.17	0.3153



Flow chart and Result of OR CI95% illustrated by forest plot

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Approximately 724,985.3 ± 416.1 (mean ± standard deviation) of SNP per sample met quality control requirements. SNPs affecting the methotrexate and azathioprine metabolic pathways were then selected. A total of 89 study participants including 66 DMARDs poor responders and 23 DMARDs responders were included in this study. There were no significant differences in age and sex between the two groups. Serum anti-CCP levels were significantly higher in the cDMARDs poor responder group (189.2 versus 103.7 U/mL, p = 0.011*). The distribution of allele frequency of the selected 38 SNPs and 2 in *GHH* (rs1800909 and rs3758149) were statistically different between the two groups (p =0.04062*, OR = 2.31, 95% CI: 0.91–5.31), and were associated with lower methotrexate efficacy.

Conclusion: The pharmacogenetics effects of cDMARDs poor responders could not be demonstrated in this study due to the small sample size. However, two SNPs (rs1800909 and rs3758149) in *GHH* which affect the methotrexate metabolic pathway were significantly different between the two groups. These SNPs exhibited a tendency towards an increasing OR. These genotypes can be presented as cDMARDs poor responders in our cohort.

Disclosure: Y. Chen: None; **C. Wu**: None; **J. Hsu**: None; **P. Chen**: None.

Abstract Number: 1347

The Better Disease-modifying antirheumatic drug (DMARD)? Efficacy and Safety of Methotrexate Versus Leflunomide Monotherapy in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis

Aakanksha Pitliya[1], Srivatsa Surya Vasudevan[2], Sarthak Sharma[3], Bijay Mukesh Jeswani[4], Tanya Ratnani[5] and Rajesh Thirumaran[6], [1]Mercy Catholic Medical Center, Darby, PA, Clifton Heights, PA, [2]Louisiana State University Health Sciences Center, Shreveport, LA, [3]Government Medical College, Jammu, Jammu, Jammu and Kashmir, India, [4]GCS Medical College, Hospital and Research Center, Ahmedabad, Gujarat, India, [5]Chhattisgarh Institute of Medical Sciences, Bilaspur, Chhattisgarh, India, [6]Mercy Catholic Medical Center, Darby, PA

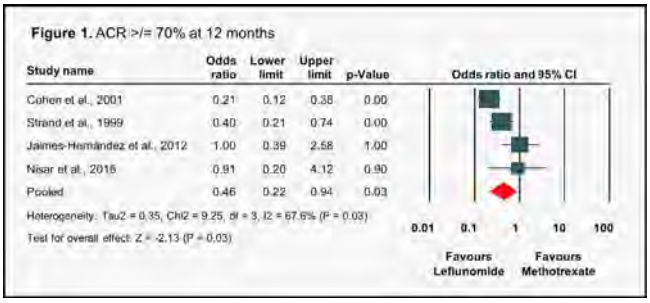
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate (MTX) and leflunomide (LEF) are commonly used disease-modifying antirheumatic drugs (DMARDs) in the treatment of rheumatoid arthritis (RA). While both are widely prescribed, their comparative efficacy and safety remain a subject of clinical debate. This systematic review and meta-analysis aimed to evaluate and compare the efficacy and safety outcomes of MTX and LEF monotherapies in RA patients.

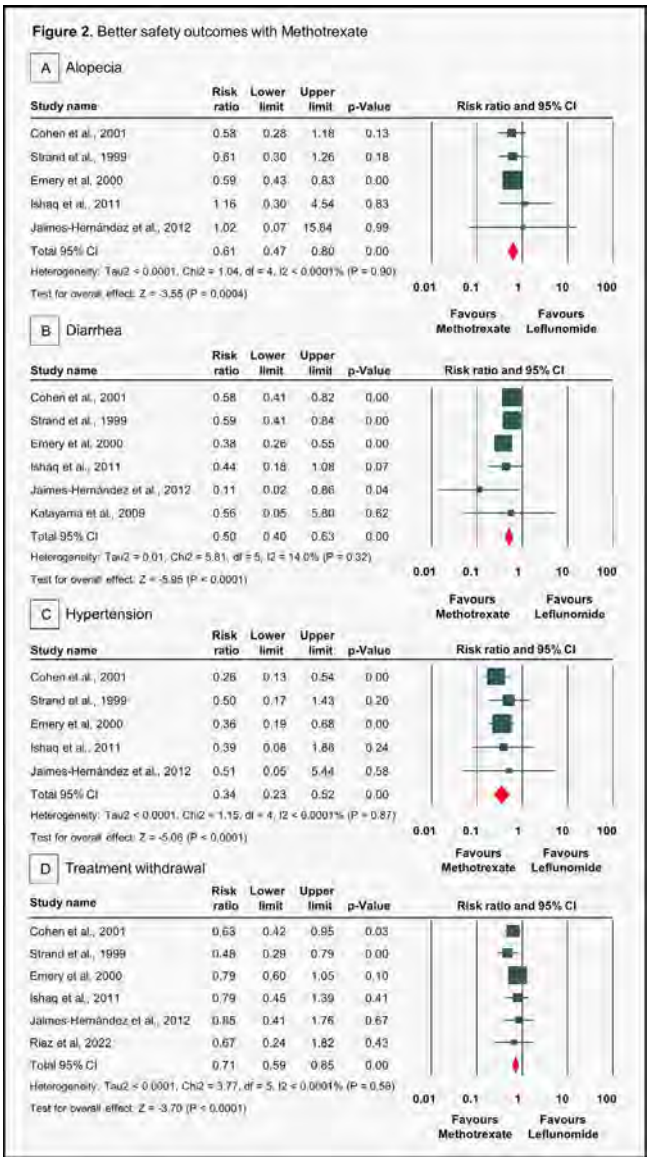
Methods: We conducted a systematic review and Meta-analysis using PRISMA guidelines. A comprehensive literature search was conducted in Medline, Embase, and the Cochrane Library from inception to 2025 to identify clinical trials and observational studies comparing MTX and LEF. A total of 7920 articles were initially identified. After removing duplicates and screening titles and abstracts, 39 full-text articles were reviewed, and 10 studies met the inclusion criteria. The quality analysis was conducted by two independent reviewers using the Cochrane RoB 2 for RCTs and the Newcastle Ottawa tool for observational studies. Primary outcomes were comparative efficacy and safety of both drugs. A random-effects model was used to perform meta-analyses, with odds ratios (ORs) calculated for efficacy outcomes and risk ratios (RRs) for safety outcomes to compare the two treatment groups. Heterogeneity among studies may affect the comparability of outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Ten studies were included for comparative analysis, comprising 6 RCTs and 4 observational studies, with a total of 5514 participants (2059 in the LEF group and 3455 in the MTX group). The study population had a mean age of approximately 51.5 ± 0.21 years and a female predominance of 78.39%. Efficacy analysis revealed that methotrexate was significantly less effective than leflunomide in achieving a 70% improvement in ACR response (ACR ≥70) at

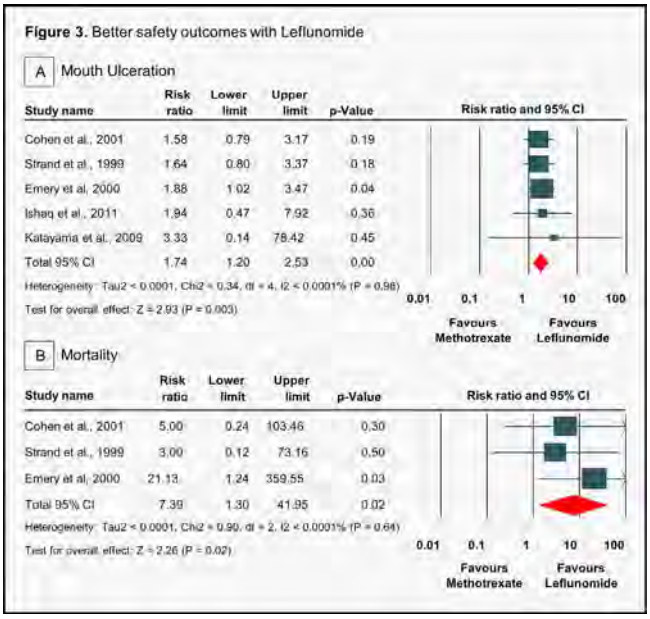


Comparison of the statistically significant efficacy of Methotrexate and Leflunomide



Comparison of safety outcomes: Methotrexate and Leflunomide with Methotrexate showing superior outcomes

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparison of safety outcomes: Methotrexate and Leflunomide, with Leflunomide showing superior outcomes

12 months (OR 0.46, 95% CI 0.22–0.94, p = 0.03) (Figure 1). No other ACR response comparisons at 12 or 24 months showed statistically significant differences between the two treatments. Regarding safety outcomes, methotrexate was associated with a lower risk of diarrhea (RR 0.50, 95% CI 0.40–0.63, p < 0.001), alopecia (RR 0.61, 95% CI 0.47–0.80, p = 0.0004), withdrawal due to adverse events (RR 0.71, 95% CI 0.59–0.85, p = 0.0002), and hypertension (RR 0.34, 95% CI 0.23–0.52, p < 0.001) compared to leflunomide (Figure 2). However, it was associated with a higher risk of mouth ulceration (RR 1.74, 95% CI 1.20–2.53, p = 0.003) and mortality (RR 7.39, 95% CI 1.30–41.95, p = 0.02) (Figure 3).

Conclusion: This meta-analysis demonstrates significant differences in both efficacy and safety outcomes between the two treatment groups. Leflunomide showed superior efficacy compared to methotrexate in achieving a high-level ACR response at 12 months, while methotrexate was associated with a more favorable safety profile, including lower risks of diarrhea, alopecia, hypertension, and treatment withdrawal.

Disclosure: A. Pitliya: None; **S. Vasudevan**: None; **S. Sharma**: None; **B. Jeswani**: None; **T. Ratnani**: None; **R. Thirumaran**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1348

Real World Evaluation on the Effectiveness of Baricitinib or Other Treatments in Patients With Rheumatoid Arthritis: Data from the European and Non-European Cohorts of the RA-BE-REAL Study

Rieke Alten[1], Gerd Burmester[2], Marco Matucci-Cerinic[3], Jens Gerwien[4], Walid Fakhouri[4], Samuel Ogwu[4], Ewa Haladyj[4], Inmaculada De La Torre[4], Bruno Fautrel[5] and **AJ Fernandez**[4], [1]SCHLOSSPARK KLINK, Teaching Hospital of University Medicine Berlin, Department of Internal Medicine and Rheumatology, Berlin, Germany, [2]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [3]University San Raffaele Milano, Milano, Milan, Italy, [4]Eli Lilly and Company, Indiana Polis, IN, [5]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Here, we provide descriptive baseline characteristics and effectiveness outcomes of Baricitinib (BARI) and other ts/bDMARDs at 24-month (24M) in both European (EU) and non-European regions (OEU) regions, in addition to the effectiveness of BARI in EU countries at 36M, from the RA-BE-REAL study.

Methods: Patients (N=1322) with rheumatoid arthritis (RA) from five EU countries (France, Germany, Italy, Spain, and UK) and three OEU countries (Australia, Canada, and Saudi Arabia) initiated BARI 2 mg or 4 mg (Cohort A) or any other targeted synthetic (ts) or biologic (b) disease-modifying antirheumatic drugs (DMARDs)(Cohort B) as per label requirements for the first time. Response rates for remission (REM) and low disease activity (LDA) were determined by the Clinical Disease Activity Index (CDAI), and patient's assessment of pain using the 100 mm pain visual analog scale (VAS).

Results: A summary of patient characteristics identified higher baseline disease activity in OEU countries however, improvements in disease activity and pain were observed in both regions at 24M, **Table 1**.

Table 1: Baseline data and effectiveness of treatment at 24M

Baseline Data	EU Region N=1071		OEU Region N=251		Overall EU & OEU Regions N=1322
	Baricitinib Cohort A N=511	Other ts/bDMARDs Cohort B N=560	Baricitinib Cohort A N=115	Other ts/bDMARDs Cohort B N=136	
Age, years	59.2 *(13.24)*	57.1 *(13.86)*	59.9 *(12.41)*	57.0 *(12.95)*	58.1 (13.44)
Disease duration, years	10.0 (9.06)	9.0 (9.70)	10.4 (9.68)	8.2 (8.83)	9.4 (9.38)
ts/bDMARD treatment prior enrolment, n (%)					
Naïve	246 (48.1)	343 (61.3)	45 (39.1)	67 (49.3)	701 (53.0)
Any ts/bDMARD	265 (51.9)	217 (38.8)	70 (60.9)	69 (50.7)	621 (47.0)
Monotherapy, n (%)	258 (50.5)	176 (31.4)	29 (25.2)	33 (24.3)	496 (37.5)
Swollen joint count	5.0 (4.78)	4.6 (4.78)	7.3 (6.77)	8.5 (6.61)	5.4 (5.32)
Tender joint count	7.1 (6.09)	7.6 (6.40)	8.6 (7.03)	10.5 (7.74)	7.8 (6.55)
CDAI	23.7 (11.66)	23.5 (12.23)	26.8 (14.77)	31.0 (14.96)	24.6 (12.73)
Pain VAS	58.9 (22.94)	56.6 (24.28)	56.7 (24.66)	62.4 (21.33)	58.0 (23.57)

Effectiveness Data	EU Region N=725		OEU Region N=193		Overall EU & OEU Regions N=918
	Baricitinib Cohort A N=339	Other ts/bDMARDs Cohort B N=386	Baricitinib Cohort A N=86	Other ts/bDMARDs Cohort B N=107	
CDAI, CFB	-15.3 (12.43)	-11.7 (12.58)	-20.0 (15.95)	-22.2 (18.24)	-14.8 (13.97)
Pain VAS, CFB	-24.4 (30.10)	-17.2 (30.23)	-22.5 (29.59)	-21.5 (28.59)	-20.8 (30.06)

Values represent mean (SD) unless otherwise stated. Abbreviations: M, months; EU, European; OEU, non-European; ts/bDMARD, targeted synthetic or biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; VAS, visual analog scale (mm); CFB, Change from baseline.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Effectiveness of BARI at 24M and 36M in the EU subgroup

	Baseline n/N=469/511	CFB at 24M n/N=275/339	CFB at 36M n/N=255/315
CDAI, mean (SD)	23.7 (11.66)	-15.3 (12.43)	-14.2 (13.14)
Pain VAS, mean (SD)	58.9 (22.94)	-24.4 (30.10)	-23.6 (31.34)
CDAI REM, n (%)	1 (0.2)	65 (23.6)	69 (27.1)
CDAI LDA, n (%)	42 (9.0)	123 (44.7)	120 (47.1)

Abbreviations: Bari, baricitinib; M, months; EU, European; CFB, Change from Baseline; CDAI, Clinical Disease Activity Index; VAS, visual analog scale (mm); REM, Remission; LDA, low disease activity.

Effectiveness results at 24M within the EU and OEU subgroups mirrored the overall effectiveness data. The overall CDAI mean CFB at 24M was -13.3 (12.63) in the EU and -21.2 (17.19) in the OEU regions. The mean CFB in pain VAS was -20.6 (30.36) and -21.9 (28.97) in EU and OEU regions, respectively. Most patients within the EU and OEU subgroups achieved CDAI REM or LDA by 24M (EU: 68.3% Cohort A [23.6% REM, 44.7% LDA], 61.4% Cohort B [23.1% REM, 38.3% LDA]; OEU: 70.8% Cohort A [27.7% REM, 43.1% LDA], 65.4% Cohort B [24.4% REM, 41.0% LDA]), with results numerically favoring BARI.

Patients treated with BARI in the EU subgroup were followed up for 36M, and improvements in disease activity and pain were maintained from baseline, **Table 2**.

Conclusion: Baseline clinical characteristics indicated that OEU patients exhibited higher disease activity, with similar improvements observed in EU and OEU patients treated with BARI. Effectiveness outcomes within EU and OEU subgroups reflected overall results, with results numerically favoring BARI. Effectiveness outcomes in the EU population of patients treated with BARI demonstrated a sustained response over 36M.

Disclosure: R. Alten: Abbvie, 6, Abbvie, BMS, Celltrion, Chugai, Galapagos, Janssen, Eli Lilly and Company, Novartis, Pfizer, Roche, UCB, and Viatris, 2, BMS, 6, Celltrion, 6, Chugai, 6, Eli Lilly and Company, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6, Viatris, 6; **G. Burmester**: Celltrion, 6, Chugai, 6, Fresenius, 6, Gedeon Richter, 6, Sanofi, 6; **M. Matucci-Cerinic**: None; **J. Gerwien**: Eli Lilly and Company, 3, 11; **W. Fakhouri**: Eli Lilly and Company, 3, 11; **S. Ogwu**: Eli Lilly and Company, 3, 6; **E. Haladyj**: Eli Lilly and Company, 3, 6; **I. De La Torre**: Eli Lilly and Company, 3, 11; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **A. Fernandez**: Eli Lilly and Company, 3, 11.

Abstract Number: 1349

Achievement of Treatment Targets and Maintenance of Response with Upadacitinib in Patients with Moderate-to-severe Rheumatoid Arthritis in a Real-world Setting: Final 2-year Outcomes from the UPHOLD Study

Andrew Ostor[1], Eugen feist[2], Prodromos Sidiropoulos[3], Jérôme Avouac[4], Martin Rebella[5], Rajaie Namas[6], Erin McDearmon-Blondell[7], Ivan Lagunes[8], Tianming Gao[9], Tim Shaw[7] and Suzan Attar[10], [1]Australian National University, Canberra, Australia, [2]Helios Department of Rheumatology, Vogelsang-Gommern, Germany, [3]Department of Rheumatology, Clinical Immunology and Allergy, University Hospital of Heraklion, Heraklion, Greece, [4]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France, [5]Hospital de Clínicas, Facultad de Medicina, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [6]Medical Subspecialties Institute, Division of Rheumatology, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates, [7]AbbVie Inc., North Chicago, IL, [8]Abbvie Inc, North Chicago, IL, [9]AbbVie, North Chicago, IL, [10]King Abdulaziz University, Saudi Arabia, Jeddah, Saudi Arabia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

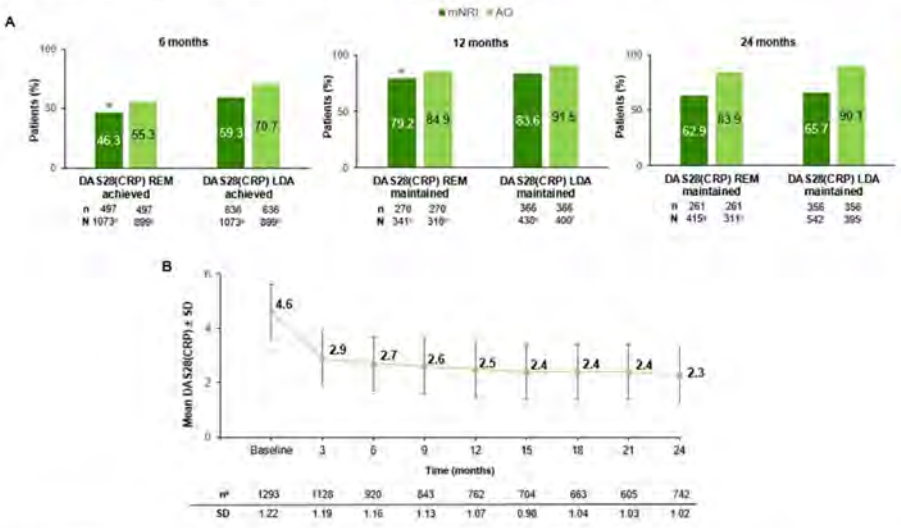
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: We evaluated long-term achievement of treatment targets, sustained clinical response, and safety of upadacitinib (UPA) over 2 years in patients with moderate-to-severe rheumatoid arthritis (RA).

Methods: UPHOLD (NCT04497597) is an observational cohort study of UPA-naïve adults with RA (data collected: 16 October 2020-15 May 2024). Co-primary endpoints were achievement of DAS28(CRP) remission < 2.6 (6 months) and maintenance of DAS28(CRP) remission (or ≤0.6-point increase) at 12 months (analyzed by modified non-responder imputation (NRI) or as observed [AO]). mFAS1 included patients in FAS (receiving ≥1 UPA dose) who completed 6 months and those who discontinued before 6 months; mFAS2 included patients achieving DAS28(CRP) remission within mFAS1 who completed 12 months and those discontinuing between 6 and 12 months. Key endpoints were proportion achieving/maintaining DAS28(CRP) low disease activity (LDA≤3.2); maintaining DAS28(CRP) remission/LDA by treatment strategy (UPA monotherapy or csDMARD combined) and prior therapy exposure (ts/bDMARD-naïve, ts/bDMARD-experienced, tsDMARD-experienced or TNF inhibitor only-experienced); mean DAS28(CRP) values; proportion in each DAS28(CRP)/CDAI/SDAI disease category; PROs change from baseline.

Results: 1699 of 1715 total participants received ≥1 UPA dose (FAS; UPA monotherapy [48.3%], +/- csDMARDs [51.7%]). 1029 (60.0%) completed 24 months and 686 (40.0%) prematurely discontinued (lack of efficacy [15.2%], adverse events [9.5%] and loss to follow-up [5.5%]). 1524 participants received prior therapy (≥1 bDMARD [64.3%] and ≥1 tsDMARD [18.3%]). In mFAS1 (n=1073, 6 months), 46.3% (mNRI) and 55.3% (AO) achieved DAS28(CRP) remission. In mFAS2 (n=341, 12 months), 79.2% (mNRI) and 84.9% (AO) maintained DAS28(CRP) remission. Similar trends for 6 and 12 months were observed with higher rates for DAS28(CRP) LDA (Figure 1A). Of 6-month responders, most maintained response until the end of the study at 24 months (DAS28(CRP) remission: 62.9% [mNRI]; 83.9% [AO]; DAS28(CRP) LDA: 65.7% [mNRI]; 90.1% [AO]) (Figure 1A). DAS28(CRP), CDAI(≤2.8) and SDAI(≤3.3) remission was achieved at 24 months in 66.8%, 36.1%

Figure 1. Effectiveness: (**A**) Achievement of DAS28(CRP) remission (<2.6) and LDA (≤3.2) and maintenance of response through 24 months; and (**B**) decrease in mean DAS28(CRP) per analysis visit in patients with moderate-to-severe RA treated with UPA through 24 months



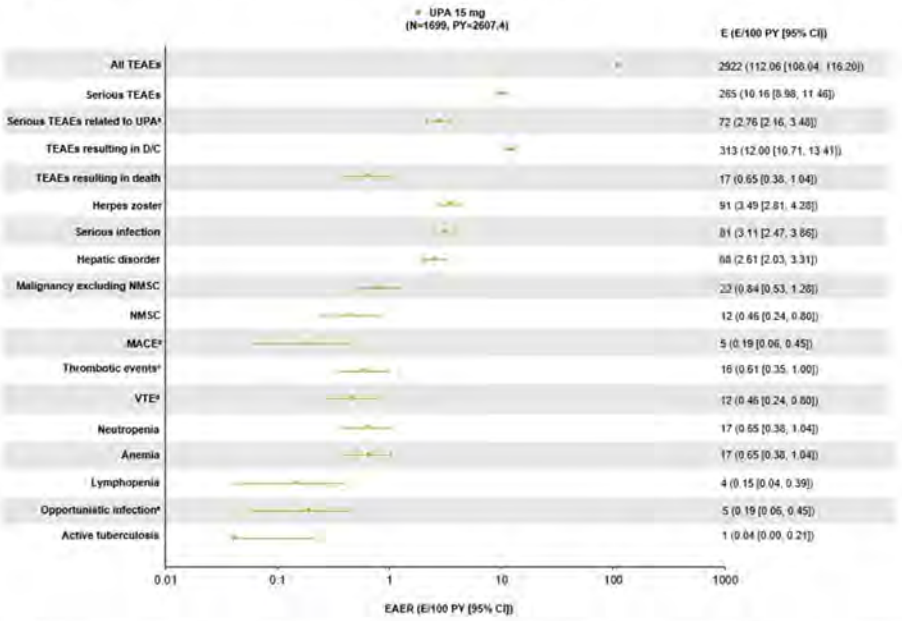
*Co-primary endpoints.

[a]mFAS1: FAS patients who completed 6 months of treatment and had DAS28(CRP) data available or discontinued the study for any reason before month 6. [b]mFAS1 patients with non-missing DAS28(CRP) data. [c]mFAS2: mFAS1 patients who achieved REM at 6 months, completed 12 months of treatment and had DAS28(CRP) data available, or discontinued the study for any reason between 6 and 12 months. [d]mFAS2 patients with non-missing DAS28(CRP) data. [e]mFAS1 patients who achieved LDA at 6 months, completed 12 months of treatment and had DAS28(CRP) data available, or discontinued the study between 6 and 12 months. [f]mFAS1 patients who achieved LDA at 6 months, completed 12 months of treatment and had DAS28(CRP) data available. [g]FAS patients who achieved REM at 6 months, completed 24 months of treatment and had DAS28(CRP) data available at 6 and 24 months, or discontinued the study between 6 and 24 months. [h]FAS patients who achieved REM at 6 months, completed 24 months of treatment and had DAS28(CRP) data available at 6 and 24 months. [i]FAS patients who achieved LDA at 6 months, had DAS28(CRP) data available at 6 and 24 months, and continued to receive UPA at 24 months or discontinued the study between 6 and 24 months. [j]FAS patients who achieved LDA at 6 months, had DAS28(CRP) data available at 6 and 24 months, and continued to receive UPA at 24 months. [k]Patients with non-missing data.

AO, as observed; DAS28(CRP), disease activity score in 28 joints using C-reactive protein; FAS, full analysis set; LDA, low disease activity; mFAS, modified FAS; mNRI, modified non-responder imputation; RA, rheumatoid arthritis; REM, remission; SD, standard deviation; UPA, upadacitinib.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Safety: EAERs of TEAEs in patients with moderate-to-severe RA treated with UPA



Safety was evaluated by assessing all TEAEs (AEs occurring after the first dose of study drug and up to 30 days after the last dose of study drug) occurring in the FAS up to the data cutoff date of 15 May 2024. There were no reported events of gastrointestinal perforation. [a]Reasonable possibility. [b]Includes cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. [c]Includes VTE, other venous thrombosis, and arterial thromboembolic events. [d]Includes deep vein thrombosis, venous thromboembolism, and pulmonary embolism. [e]Excluding herpes zoster and active tuberculosis.

AE, adverse event; CI, confidence interval; D/C, discontinuation; E, event; EAER, exposure-adjusted event rate; FAS, full analysis set; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PY, patient-years; RA, rheumatoid arthritis; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolic events.

and 36.7% participants, respectively (FAS; AO). Mean DAS28(CRP) decreased from 4.6 at baseline to 2.9 (3 months) and 2.3 (24 months) (Figure 1B). Improvements were observed regardless of UPA monotherapy/csDMARD combined treatment or prior therapy exposure in all assessed PROs at 3 months and maintained or improved through 24 months. 2922 TEAEs and 265 serious TEAEs were reported. Rates of herpes zoster, serious infection, hepatic disorder, malignancy excluding non-melanoma skin cancer (NMSC), NMSC, VTE and MACE were consistent with previous UPA safety data (Figure 2).[2]

Conclusion: UPA was effective in treating RA in RW practice. About half of patients treated with UPA achieved DAS28(CRP) remission at 6 months; almost 80% maintained remission at 12 months and >60% at 2 years (mNRI). The benefit–risk profile remains consistent with phase 3 clinical trials.[1,2]

References

1. Conaghan, PG et al. *Rheumatol Adv Pract* 2023;7(1):rkad017.
2. Burmester, GR et al. *RMD Open* 2023;9:e002735.

Disclosure: A. Ostor: AbbVie Inc., 1, 2, 12, Clinical Trials, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Eli Lilly, 1, 2, 12, Clinical Trials, GlaxoSmithKlein, 1, 2, 12, Clinical Trials, Janssen, 1, 2, 12, Clinical Trials, Merck, 2, 5, Novartis, 1, 2, 12, Clinical Trials, Pfizer, 1, 2, 12, Clinical Trials, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **E. feist**: AB2Bio, 6, AbbVie/Abbott, 6, Alfasigma, 6, AstraZeneca, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Galapagos, 6, Hexal, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6, Roche/Chugai, 6, R-Pharm, JSC, 6, Sandoz, 6, Sanofi, 6, Sobi, 6, UCB, 6; **P. Sidiropoulos**: None; **J. Avouac**: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6; **M. Rebella**: None; **R. Namas**: AbbVie/Abbott, 5, 6;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

E. McDearmon-Blondell: AbbVie/Abbott, 3, 11; **I. Lagunes**: AbbVie, 3, 11; **T. Gao**: AbbVie, 3, 11; **T. Shaw**: AbbVie/Abbott, 3, 11; **S. Attar**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 5, 6, Gilead, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Hikma, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Organon, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Sandoz, 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6.

Abstract Number: 1350

Initial Biologic Therapy Improves Sexual Function in Female Patients with Rheumatoid Arthritis: A 6 Month Follow-Up Study

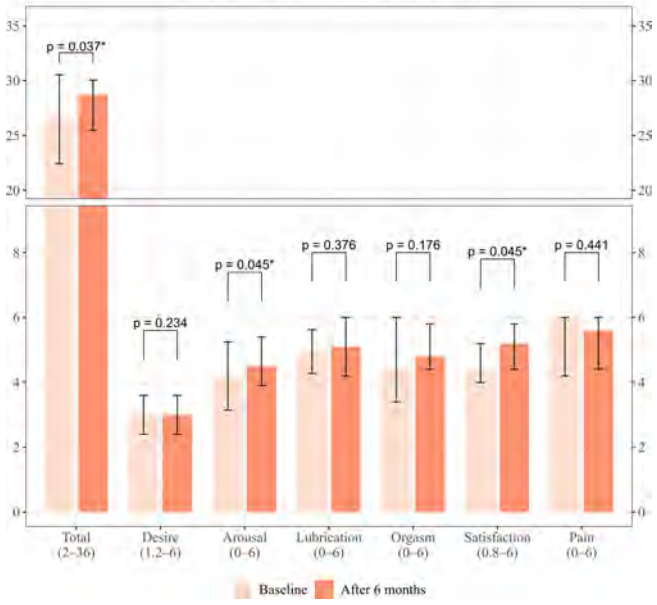
Daniel Zavada[1], Barbora Vala[2], Adela Navratilova[2], Veronika Losterova[2], Lenka Moravcova[2], Jiri Vencovsky[3], Ladislav Šenolt[4], Karel Pavelka[5] and Michal Tomcik[5], [1]Institute of Rheumatology, Prague; Charles University, Third Faculty of Medicine, Hlavní mesto Praha, Czech Republic, [2]Institute of Rheumatology, Praha, Czech Republic, [3]Institute of Rheumatology, Praha 8, Czech Republic, [4]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [5]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) significantly impacts quality of life in multiple domains. This study aimed to evaluate the impact of initial biologic/targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) therapy on sexual function in women with RA and sought to assess changes in sexual function over six months of treatment and identify clinical and laboratory predictors of these changes.

Figure 1. Female Sexual Function Index
Before and after b/tsDMARD therapy (n = 23)



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

Characteristic (score range: worst - best)	Total n = 23
Age [years]	49.19 (39.39, 54.93)
Seropositivity	16 (73%)
DAS-28-CRP	5.52 (4.74, 6.40)
DAS-28-ESR	5.63 (5.38, 6.40)
CRP [mg/L]	7.17 (5.56, 17.75)
ESR [m/hours]	13.00 (9.00, 20.00)
Biological Therapy - Agent	
adalimumab	11 (48%)
baricitinib	1 (4.3%)
certolizumab pegol	3 (13%)
etanercept	8 (35%)
Biological Therapy - MoA	
TNFa inhibitor	22 (96%)
JAK inhibitor	1 (4.3%)
HAQ (3-0)	1.38 (1.00, 1.63)
MDHAQ-RAPID3 (30-0)	15.70 (12.00, 18.20)
EuroQol (0-1)	0.62 (0.09, 0.69)
SF-36 Mental Component Score (5.5–63.6)	38.78 (34.42, 46.70)
SF-36 Physical Component Score (16.6–57.9)	26.56 (21.93, 31.12)

Table 1 shows the baseline characteristics of our patient cohort. Data are presented as median (IQR) for continuous and n (%) for categorical variables. Acronyms: CRP, Creactive protein; DAS-28, Disease Activity Score 28; ED; ESR, Erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; MDHAQ – RAPID3, Multidimensional Health Assessment Questionnaire; SF-36, Short Form Health Survey Questionnaire.

Methods: Women with RA indicated for b/tsDMARD therapy within the Czech ATTRA registry were recruited. Participants completed the Female Sexual Function Index (FSFI; higher scores indicate better sexual function) at baseline (M0) and after six months (M6). Routine clinical and laboratory data were collected, with patient-reported outcomes regarding function and quality of life (Health Assessment Questionnaire (HAQ), 36-Item Short Form Health Survey (SF-36), EuroQoL 5-Dimension Questionnaire (EuroQoL), and Multidimensional Health Assessment Questionnaire (MDHAQ)). Comparisons were performed using the Wilcoxon test, p-values adjusted for multiple comparisons using the Benjamini-Hochberg method. Selection of baseline predictors with improvement in IIEF domains was performed using LASSO regression. Associations with FSFI improvement were assessed using bivariate screening.

Results: Out of 36 screened patients, 23 sexually active women completed the questionnaires at both time intervals (Table 1). The baseline prevalence of sexual dysfunction was 47% (defined as the published cutoff of FSFI Total < 26.55).

At the 6-month follow-up, b/tsDMARD therapy had a significant positive effect on inflammation (ESR, CRP), disease activity (DAS28-ESR, DAS28–CRP), function, and quality of life (HAQ, MDHAQ, SF-36, and EuroQoL) ($p < 0.05$ for all).

Table 2. Predictors of Sexual Function Improvement

IIEF Domain (follow-up – baseline)	Coefficients
FSFI Total	FSFI Satisfaction (-0.91), HAQ (0.77), Cardiovascular Disease (-0.7), FSFI Total (-0.4)
FSFI Desire	FSFI Desire (-0.19), FSFI Total (-0.09), HAQ (0.05)
FSFI Arousal	FSFI Arousal (-0.18), HAQ (0.01)
FSFI Lubrication	-
FSFI Orgasm	FSFI Orgasm (-0.56), HAQ (0.27), Weight (0.21), Importance of Sexual Activity (0.19), Swollen Joint Count (-0.18), Cardiovascular Disease (-0.15), Tender Joint Count (-0.13), FSFI Satisfaction (-0.08), NSAID use (0.07), FSFI Lubrication (0.07), Disease activity reported by the patient (0.06), Metabolic disease (-0.05), Age (-0.02)
FSFI Satisfaction	FSFI Satisfaction (-0.21), NSAID use (0.03)
FSFI Pain	-

Table 2 shows the baseline predictors associated with improvements in FSFI domains. These variables were selected using the LASSO regression method – we are reporting the standardized coefficients to better report the effect of the variables. Acronyms: FSFI, Female Sexual Function Index; HAQ, Health Assessment Questionnaire.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Regarding sexual function, we observed small but significant benefits in the FSFI Total Score (from 26.65 to 28.7, p=0.037), as well as in the domain of Arousal (from 4.2 to 4.5, p=0.0453) and Satisfaction (from 4.4 to 5.2, p=0.0453) (Figure 1). The 6M follow-up prevalence of sexual dysfunction was 30%

In bivariate analysis, improvements in sexual function correlated with reduced inflammation (CRP), lower disease activity (DAS28-CRP, DAS28-ESR, SDAI), and improved function/quality of life (HAQ, EuroQoL, SF-36).

LASSO regression identified baseline FSFI domain scores as the strongest predictors of improvements in sexual function. However, weaker but relevant predictors were also observed (Table 2).

Conclusion: Women with RA experienced modest but significant improvements in sexual function (particularly in the domain of Arousal and Satisfaction) after six months of initial b/tsDMARD therapy. These changes were associated with reduced inflammation, better physical function, and improved quality of life. Further research is needed to confirm these associations and elucidate underlying mechanisms.

Supported by MHCR 023728

Disclosure: D. Zavada: None; **B. Vala**: None; **A. Navratilova**: None; **V. Losterova**: None; **L. Moravcova**: None; **J. Vencovsky**: None; **L. Šenolt**: None; **K. Pavelka**: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **M. Tomcik**: None.

Abstract Number: 1351

Are Glucocorticoids Associated with Worse Overall Survival Among Rheumatoid Arthritis Patients Treated with Immune Checkpoint Inhibitors? The Confounding Effect of Dexamethasone

Deanna Jannat-Khah[1], Jeffrey Curtis[2], Fenglong Xie[3], Ashish Saxena[4] and Anne R. Bass[1], [1]Hospital For Special Surgery, New York, NY, [2]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [3]The University of Alabama at Birmingham, Birmingham, AL, [4]Weill Cornell Medicine, New York

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Previous studies suggest that glucocorticoids are associated with worse survival in patients receiving immune checkpoint inhibitors (ICI). This is an important issue for Rheumatoid Arthritis (RA) patients initiating ICI since they may require glucocorticoids for RA disease control or management of immune related adverse events. Glucocorticoids are also used for cancer palliation, and for this indication dexamethasone is the preferred formulation. We investigated the association between glucocorticoid use and type and overall survival (OS) among patients with pre-existing RA treated with ICI for non-small cell lung cancer (NSCLC).

Methods: We used a curated Medicare claims dataset (2010-2019) that consists of a 100% sample of patients with RA. Inclusion criteria: Age ≥ 66 years; RA preceding NSCLC diagnosis initiating nivolumab, pembrolizumab or atezolizumab (during dates approved only for metastatic/ stage 4 cancer, to homogenize cancer stage).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Demographic and Clinical Characteristics Rheumatoid Arthritis Patients with Non-Small Cell Lung Cancer Treated with Immune Checkpoint Inhibitors from Medicare Fee for Service Claims Data.

		All Patients		
Factor	Total N (%)	No Glucocorticoids	Glucocorticoids	p-value
N	779	300 (39)	479 (61)	
Age, mean (SD)	74.69 (7.21)	75.3 (6.9)	74.3 (7.4)	0.067
White race	684 (87.8)	225 (85)	429 (89.6)	0.22
Female	507 (65.1)	207 (69)	300 (62.6)	0.07
Chronic lung disease*	352 (45.2)	134 (44.7)	218 (45.5)	0.82
DMARDs in the 91 days after ICI initiation	34 (4.4)	<11	Redacted	0.14
Modified Elixhauser score median (IQR)	1.8 (1.26, 2.6)	2 (1.2, 2.6)	1.8 (1.2, 2.6)	0.13
Radiation ever	511 (65.6)	200 (66.7)	311 (64.9)	0.62
Second line ICI or ICI plus chemotherapy	458 (58.8)	173 (57.7)	285 (59.5)	0.61
ICI plus chemotherapy	119 (15.3)	48 (16)	71 (14.8)	0.66
ICI Duration, median (IQR)	84 (21, 244)	92.5 (0, 262)	84 (28, 233)	0.43
Death	610 (85.8)	240 (80)	370 (77.2)	0.36
Time from ICI initiation to death, median (IQR)	207 (78.5, 431.5)	175 (48, 386)	228 (101, 467)	<0.001
Any Glucocorticoid use	479 (61.5)	N/A	479 (100)	N/A
Average glucocorticoid dose, median (IQR)	7.91 (4.07, 13.19)	N/A	7.91 (4.07, 13.19)	N/A
Non-dexamethasone glucocorticoid use	363 (54.8)	N/A	363 (75.78)	N/A
Non-dexamethasone glucocorticoid dose, median (IQR)	7.69 (3.35, 13.02)	N/A	7.69 (3.51, 13.02)	N/A
Dexamethasone use	116 (15)	N/A	116 (24)	N/A
Average daily dexamethasone dose, median (IQR)	7.91 (5.27, 15.82)	N/A	7.91 (5.27, 15.82)	N/A

* Chronic lung disease is defined as Interstitial Lung Disease or Chronic Obstructive Pulmonary Disease
Per the data use agreement with the Centers for Medicare and Medicaid, values less than 11 are not reported
Unknown or missing values: Race: N=36 (4.7%); Hispanic ethnicity N=70 (9%)

Kaplan Meier (KM) curves and 90-day landmark Cox proportional hazard (PH) models were created to measure OS from first ICI initiation, stratified by glucocorticoid (GC) use in the first 90 days. Adjusted models controlled for age, sex, race, ethnicity, interstitial lung disease, chronic obstructive pulmonary disease, prior radiation, year of ICI initiation, modified Elixhauser score, first- or second-line ICI, concomitant chemotherapy. Steroid use was modeled both as binary (KM curves) and as a continuous variable. Schoenfeld residuals were used to assess the PH assumption. Patients were followed through 12/31/2019, or time of death.

Results: We identified 779 eligible RA patients with mean age 74.7 (SD 7.2) years, 87.8% White, 65% female. Among these, 479 (61%) were treated with GCs in the first 90 day. GC users had similar demographics to the overall cohort (table 1). Among GC users, median dose was 7.9 mg prednisone equivalents/day [IQR 4.1,13.2]. In KM analyses, glucocorticoid

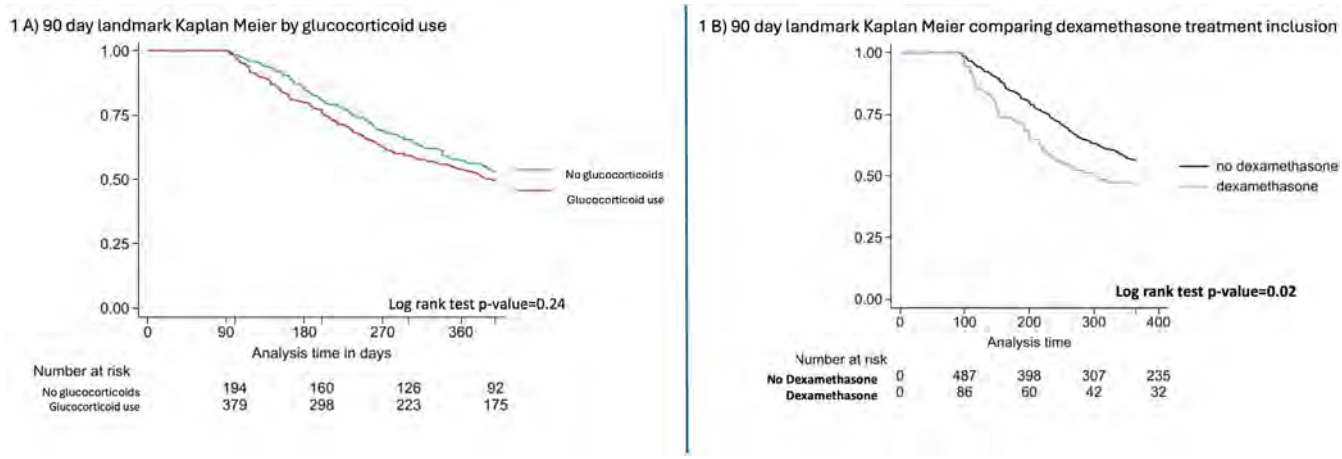


Figure 1 A) 90 day landmark Kaplan Meier by glucocorticoid use; B) 90 day landmark Kaplan Meier comparing dexamethasone treatment inclusion

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

use (yes/no) was associated a non-significant trend towards worse overall survival (Figure 1a). In a separate KM curve, dexamethasone use was associated with worse OS compared to non-users (Figure 1b).

In adjusted models, higher mean glucocorticoid dose was associated with worse overall survival (aHR 1.08 [95%CI 1.01, 1.16]), but in a sensitivity analysis that excluded dexamethasone-treated patients, the association of glucocorticoid dose with overall survival disappeared [HR 0.91 95%CI [0.83, 1.01].

Conclusion: Glucocorticoids used to treat RA and irAE were not associated with worse survival in NSCLC patients with RA after exclusion of dexamethasone-treatment. Dexamethasone, often given palliatively at high doses to alleviate work of breathing, nausea and/or brain edema in cancer patients, should be excluded (or reason for censoring) from studies assessing the association between glucocorticoid use and survival in patients with RA.

Disclosure: D. Jannat-Khah: AstraZeneca, 11, CytoDyn, 11; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **F. Xie**: None; **A. Saxena**: AstraZeneca, 5, Galvanize Therapeutics, 6; **A. Bass**: None.

Abstract Number: 1352

Prediction of 5-Year Fracture Risk in Rheumatoid and Psoriatic Arthritis Using REMS Technology

Marco Di Paola[1], **Edmund J MacLaughlin**[2], Kathleen Methric[3], Maurizio Muratore[4], Gianmarco Del Vecchio[5], Giusy Peluso[6], Ernesto Casciaro[1], Fabiola Rosa Contaldo[7], Fiorella Anna Lombardi[1], Paola Pisani[1], Francesco Conversano[1] and Sergio Casciaro[1], [1]Institute of Clinical Physiology, National Research Council, Lecce, Puglia, Italy, [2]Rheumatology Associates of Delmarva and BoneVue Diagnostics, Easton, MD, [3]BoneVue Diagnostics, Catonsville, MD, [4]ASL- LE, "Vito Fazzi" Hospital, Lecce, Puglia, Italy, [5]Department of Research and Development, Echolight S.p.a., Lecce, Puglia, Italy, [6]Department of Innovative Engineering, University of Salento, Lecce, Puglia, Italy, [7]Department of Biological and Environmental Sciences and Technologies, University of Salento, University of Salento, Lecce, Puglia, Italy

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune arthritis, including Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PA), are among the most common forms of inflammatory joint diseases. These conditions affect joints and surrounding structures, often leading to systemic skeletal complications and an increased risk of fragility fractures. Treatment typically involves steroids-based therapy, mostly glucocorticoids, which are known to enhance bone resorption and reduce bone strength. Radiofrequency Echographic Multi-Spectrometry (REMS) is a non-ionizing technology that represents the alternative to the current standard Dual X-Ray Absorptiometry (DXA) and allows to predict the imminent (within 5 years) fracture risk (FR). Therefore, the aim of the present study is to assess the REMS-based 5-years FR in a cohort of patients with RA and PA.

Methods: REMS automatically analyses the raw, unprocessed backscattered radiofrequency signals by comparing them to a proprietary reference database, extracting both quantitative (BMD, T- and Z-score) and qualitative (bone microarchitecture via Fragility Score, FS) data. Furthermore, the REMS-measured parameters are integrated into a progressive fracture risk classification system consisting of 7 risk levels, R1 to R7, each corresponding to a defined probability of imminent FR. To assess the potential impact of steroid therapy on risk classification, a logistic regression analysis was carried out.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A cohort of RA and PA patients (n = 56, Caucasian, both genders), who either received (n = 28, median age: 65.5 years old, 50% women under 65) or did not receive (n = 28, median age: 45 years old, 92.8% women under 65) steroids-based therapy underwent REMS scans at femoral neck. The FR analysis on hips revealed that 5.4% of the patients were classified in R1, 44.6% in R3, 48.2% in R5 and 1.8% in R7. Notably, 78.6% of the patients classified in the high-risk classes (R5-R7) were undergoing a steroid-based therapy, whereas 78.6% of those in the low-risk classes (R1-R4) were not receiving steroid treatment. The results from logistic regression showed an OR = 12,83 (95% CI = 3.57-46.15; $p <$ 0.0001), indicating a strong and statistically significant association between steroid use and high fracture risk. Since the steroids-based patients showed a high FS (36.25 ± 8.44), it means that information of bone quality plays a greater impact on the FR probability, aligning with current literature stating that steroids-induced bone loss is more trabecular than cortical.

Conclusion: The analysis confirmed the detrimental impact that a steroid-based therapy can exert on the skeletal system, especially on the trabecular architecture, thus highlighting the potentiality of REMS to directly measure FR through the integration of data from both bone quality and quantity analysis. Furthermore, considering that the annual cost of providing care for osteoporotic fractures in USA is estimated to increase to $95 Bln in 2040, the presented approach will allow potential cost savings through effective prevention strategies, such as reducing the incidence of subsequent fractures in patients facing challenges to access bone test like women < 65.

Disclosure: M. Di Paola: None; **E. MacLaughlin**: None; **K. Methric**: None; **M. Muratore**: None; **G. Del Vecchio**: None; **G. Peluso**: None; **E. Casciaro**: None; **F. Contaldo**: None; **F. Lombardi**: None; **P. Pisani**: None; **F. Conversano**: None; **S. Casciaro**: None.

Abstract Number: 1353

Phase 3 Study of the Efficacy, Safety and Immunogenicity of the Proposed Tocilizumab Biosimilar RGB-19, Intravenously Administered to Participants With Active Rheumatoid Arthritis: 52-Week Data

Gerd Burmester[1], Hiroaki Matsuno[2], Ernest Choy[3], Masato Okada[4], Roshan Dias[5], Károly Horvát-Karajz[5], Gordana Dancer[5], Yusuke Karibe[6], Suguru Masuda[6], Joachim Kiefer[5] and Paul Emery[7], [1]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [2]Matsuno Clinic for Rheumatic Disease, Toyama, and Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, [3]Division of Infection and Immunity, CREATE Centre, Cardiff University, Cardiff, United Kingdom, [4]Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, [5]Gedeon Richter Plc, Budapest, Hungary, [6]Mochida Pharmaceutical Co., Ltd, Tokyo, Japan, [7]University of Leeds, Leeds, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: RGB-19 is a proposed biosimilar to tocilizumab, a monoclonal antibody that competitively inhibits the binding of interleukin-6 (IL-6) to its receptor. Results of a Phase 3 study (jRCT2031220512) assessing the clinical equivalence in efficacy between RGB-19 and reference tocilizumab at Week 12, and comparing secondary efficacy, safety and immunogenicity outcomes up to Week 24, have been previously reported.[1] Here, secondary outcomes up to Week 52 (safety to Week 54) are reported.

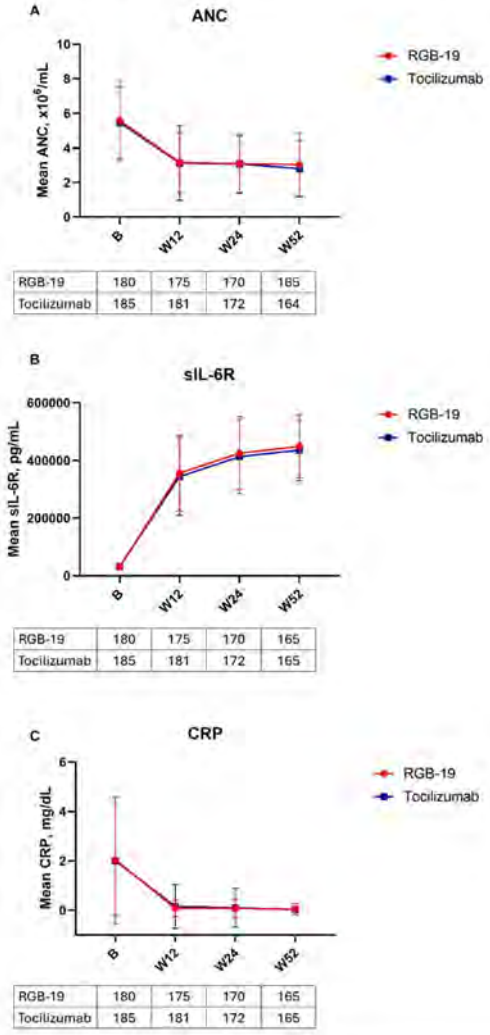
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Efficacy outcomes at Week 52 (full analysis set)

	RGB-19 N=165	Tocilizumab N=164	Adjusted mean difference[c]
DAS28-ESR descriptive analysis[a]			
Mean value (SD)	1.66 (0.94)	1.92 (1.15)	-
Mean CfB (SD)	−4.54 (1.09)	−4.17 (1.15)	
DAS28-ESR ANCOVA analysis[b]			
Adjusted mean CfB (SE) [two-sided 95 % CI]	−4.42 (0.09)	−4.14 (0.09)	−0.28 [−0.49 to −0.07]
	RGB-19 N=165	**Tocilizumab N=164**	**Difference point estimate (95% CI)[c]**
CDAI remission rate, %[d]	47.9	40.6*	7.3 (−3.4 to 17.7)
DAS28-ESR <2.6 achievement rate, %	84.2	76.8	7.4 (−1.2 to 15.9)
ACR20 achievement rate, %	98.2	93.3*	4.8 (0.4 to 9.9)
ACR50 achievement rate, %	86.7	81.8*	4.8 (−3.1 to 12.7)
ACR70 achievement rate, %	71.5	62.4*	9.1 (−1.1 to 19.0)
EULAR response rate, %[f]	100.0	99.4	0.6 (−1.7 to 3.4)
SDAI remission rate, %[g]	53.3	43.0*	10.3 (−0.5 to 20.7)

ACR, American College of Rheumatology; ANCOVA, analysis of covariance; CDAI, Clinical Disease Activity Index; CfB, change from baseline; CI, confidence interval; DAS28-ESR, Disease Activity Score in 28 joints-erythrocyte sedimentation rate; DMARD, disease-modifying anti-rheumatic drug; EULAR, European League Against Rheumatism; N, number of participants analyzed; SD, standard deviation; SDAI, Simplified Disease Activity Index; SE, standard error.
[a]Imputation method: observed case. [b]ANCOVA model: included the treatment group and the administration history of biological DMARDs as factors, and DAS28-ESR score at baseline as the covariate, if data were missing due to the occurrence of an intercurrent event, DAS28-ESR at each time point was imputed using the multiple imputation method under the assumption of missing at random. Cases analyzed: RGB-19 N=162; tocilizumab N=161; [c]RGB-19 group − tocilizumab group. [d]Remission defined as SDAI ≤3.3 or CDAI ≤2.8; [e]N=163; [f]EULAR response rate consists of participants with a "good response" (improvement in DAS28-ESR >1.2 for those with low disease activity [DAS28-ESR ≤3.2]) or "moderate response" (improvement of >0.6 to ≤1.2 for those with low or moderate disease activity [DAS28-ESR ≤5.1]) or improvement in of >1.2 for those with moderate or high disease activity (DAS28-ESR >3.2)

Figure. Mean (SD) pharmacodynamic outcomes at Week 52 (PD analysis set)



ANC, absolute neutrophil count; B, baseline; CRP, C-reactive protein; PD, pharmacodynamic; SD, standard deviation; sIL-6R, soluble interleukin-6 receptor; W, week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Safety outcomes at end of follow-up period, Week 54 (safety analysis set)

	RGB-19 N=182	Tocilizumab N=186
TEAEs, n	695	773
Participants with ≥1 TEAE, n (%)	164 (90.1)	173 (93.0)
Participants with AEs leading to treatment discontinuation, n (%)	5 (2.7)	14 (7.5)
Participants with AEs leading to death, n (%)	0	1 (0.5)*
Severe AEs, n	7	19
Participants with ≥1 severe AE, n (%)	6 (3.3)	17 (9.1)
Serious AEs, n	7	21
Participants with ≥1 serious AE, n (%)	6 (3.3)	18 (9.7)
ADRs, n	235	253
Participants with ≥1 ADR, n (%)	100 (54.9)	109 (58.6)
Participants with ADRs leading to treatment discontinuation, n (%)	5 (2.7)	9 (4.8)
Participants with ADRs leading to death, n (%)	0	0
Severe ADRs, n	2	11
Participants with ≥1 severe ADRs, n (%)	2 (1.1)	9 (4.8)
Serious ADRs, n	3	12
Participants with ≥1 serious ADRs, n (%)	3 (1.6)	9 (4.8)

ADR were defined as treatment-related TEAEs.
ADR, adverse drug reaction; AE, adverse event; N, number of participants analyzed; TEAE, treatment-emergent adverse event.
*Severe renal injury, which considered not to be correlated to tocilizumab administration.

Methods: This Phase 3, randomized, double-blind study enrolled Japanese adults with active rheumatoid arthritis and an inadequate response to methotrexate, a baseline Disease Activity Score based on 28 joints with erythrocyte sedimentation rate (DAS28-ESR) of ≥3.2, and swollen/tender joints (≥6 from 66/68). Participants were randomized 1:1 to intravenous infusions of either RGB-19 8 mg/kg or tocilizumab 8 mg/kg, administered every 4 weeks to Week 52, and participants were followed to Week 54. The primary endpoint was the mean change from baseline (CfB) in DAS28-ESR at Week 12 (previously reported).[1] Key secondary outcomes included efficacy, serum concentration, pharmacodynamics (PD; absolute neutrophil count [ANC], C-reactive protein [CRP], and soluble IL-6 receptor [sIL-6R]), and immunogenicity up to Week 52, and safety up to Week 54.

Results: Overall, 368 participants were randomized. A total of 335 participants completed the secondary evaluation period from Week 12 to Week 52 (RGB-19 n=169; tocilizumab n=166). The most common reason for withdrawal from the secondary evaluation period was adverse events (AEs; RGB-19 n=3; tocilizumab n=8). Baseline demographics were balanced between groups, as previously reported.[1]

The CfB in DAS28-ESR at Week 52 was similar between groups (confidence intervals within the primary endpoint equivalence margin of ±0.6; **Table 1**). Achievement/disease remission rates (American College of Rheumatology [ACR] 20/50/70, Simplified Disease Activity Index [SDAI], Clinical Disease Activity Index [CDAI], and European League Against Rheumatism [EULAR]) were also similar up to Week 52 (**Table 1**). Mean serum concentration time profiles and ANC, CRP, and sIL-6R PD outcomes were all similar between groups up to Week 52 (**Figure**).

Safety profiles were similar between groups, with comparable incidences of treatment-emergent AEs, and adverse drug reactions up to Week 54 (**Table 2**). The incidence of treatment-emergent antidrug antibodies (RGB-19 2.7%, tocilizumab 5.4%) and neutralizing antibodies (RGB-19 2.7%, tocilizumab 4.3%) was similarly low in both groups.

Conclusion: Similar efficacy, serum drug concentration, PD, safety and immunogenicity outcomes were shown for RGB-19 and tocilizumab up to the end of this Phase 3 study. These results support previously reported data that demonstrated the clinical equivalence in efficacy at Week 12 and similarity in secondary outcomes between treatments at Week 24.[1]

Reference

1. Choy E, et al. European Alliance of Associations for Rheumatology Congress 2025. Abstract 1398.

Disclosure: G. Burmester: Celltrion, 6, Chugai, 6, Fresenius, 6, Gedeon Richter, 6, Sanofi, 6; **H. Matsuno**: Chugai Pharmaceutical, 6, Daiichi Sankyo, 6, Eli Lilly, 6, Mochida Pharmaceutical, 2, Nichi-Iko Pharmaceutical, 2; **E. Choy**: AbbVie, 2, 6, Alfasigma, 6, Bio-Cancer, 2, 5, Biocon, 2, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 6, Fresenius Kabi, 2, 6, Gedeon Richter, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 6, Viatris, 2, 6; **M. Okada**:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Astellas, 6, Eli Lilly and Company, 6, GSK, 6, Janssen, 6; **R. Dias**: Gedeon Richter, 3; **K. Horvát-Karajz**: Gedeon Richter, 3; **G. Dancer**: Gedeon Richter, 3; **Y. Karibe**: Mochida Pharmaceutical Co., Ltd, 3; **S. Masuda**: Mochida Pharmaceutical Co., Ltd, 3; **J. Kiefer**: Gedeon Richter, 3; **P. Emery**: Abbvie, 1, Activa, 1, Anaptysbio, 1, Astra-Zeneca, 1, BMS, 1, Boehringer Ingelheim, 1, Galapagos, 1, Gedeon Richter, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, Novartis, 1.

Abstract Number: 1354

Effect of Ivarmacitinib on Joint Swelling and Tenderness in Patients with Moderate-to-severe Rheumatoid Arthritis: A Post-hoc Study of a Phase III Clinical Trial

Hongtao Jin, Huifang Guo, Yuxiang Han and Meng Ding, The Second Hospital of Hebei Medical University, Shijiazhuang, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Joint swelling and tenderness are major symptoms of rheumatoid arthritis (RA). This post-hoc analysis evaluated the effect of ivarmacitinib (SHR0302), a selective Janus kinase 1 inhibitor, on joint swelling and tenderness in patients with moderate-to-severe RA, using data from a phase III clinical trial (NCT04333771, Liu J, Jiang Y, Zhang S, et al. Ivarmacitinib, a selective Janus kinase 1 inhibitor, in patients with moderate-to-severe active rheumatoid arthritis and inadequate response to conventional synthetic DMARDs: results from a phase III randomised clinical trial. Ann Rheum Dis. Published online November 27, 2024. doi:10.1136/ard-2024-226385).

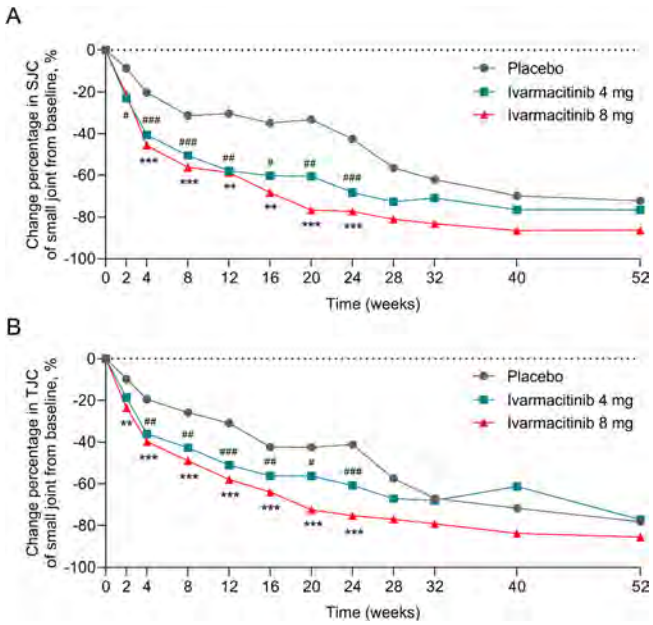


Figure 1. Comparison of the change in SJC and TJC of small joints from baseline between groups. **, P <0.01 between placebo vs. Ivarmacitinib 8 mg; ***, P <0.001 between placebo vs. Ivarmacitinib 8 mg. #, P <0.05 between placebo vs. Ivarmacitinib 4 mg; ##, P <0.01 between placebo vs. Ivarmacitinib 4 mg; ###, P <0.001 between placebo vs. Ivarmacitinib 4 mg.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

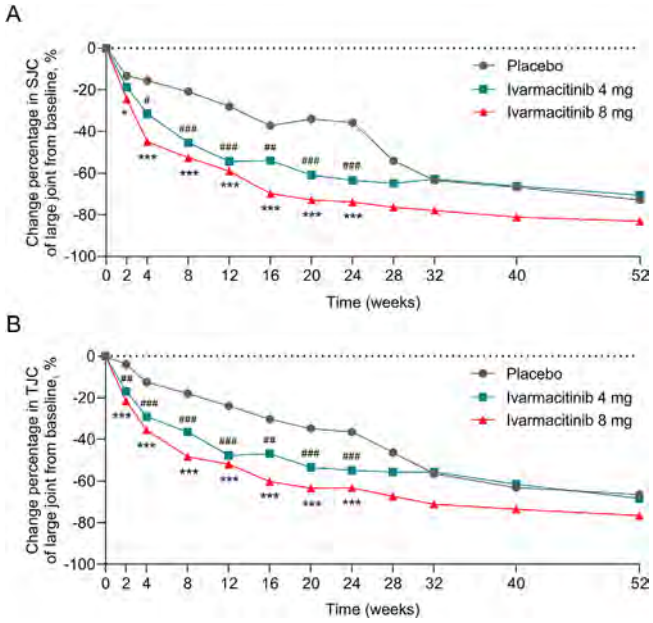


Figure 2. Comparison of the change in SJC and TJC of large joints from baseline between groups. *, P <0.05 between placebo vs. Ivarmacitinib 8 mg; **, P <0.01 between placebo vs. Ivarmacitinib 8 mg; ***, P <0.001 between placebo vs. Ivarmacitinib 8 mg. #, P <0.05 between placebo vs. Ivarmacitinib 4 mg; ##, P <0.01 between placebo vs. Ivarmacitinib 4 mg; ###, P <0.001 between placebo vs. Ivarmacitinib 4 mg.

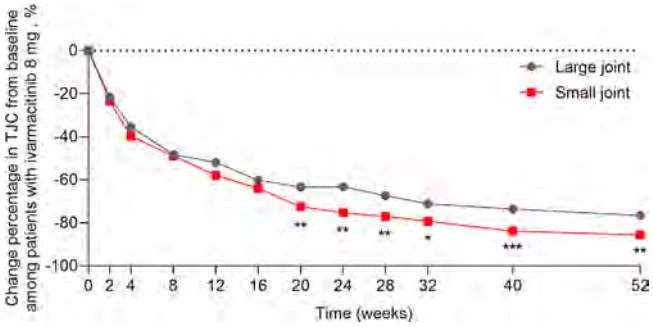


Figure 3. Comparison of the change in TJC from baseline between small joints and large joints in ivarmacitinib 8 mg group. *, P <0.05; **, P <0.01; ***, P <0.001 between small joints and large joints.

Methods: Patients were randomized to receive ivarmacitinib 4 mg (n=189), ivarmacitinib 8 mg (n=189) or placebo (n=188) for 24 weeks. At week 24, patients in the placebo group switched to ivarmacitinib 4 mg, while others continued the initial regimen until 52 weeks. Changes in swollen joint count (SJC) and tender joint count (TJC) from baseline were compared between groups and between small (metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists) and large joints (shoulders, elbows, hips, knees, and ankles).

Results: During the initial 24 weeks, both ivarmacitinib groups demonstrated greater reductions in SJC and TJC of both small and large joints compared to placebo. From week 24 to 52, both ivarmacitinib 4 mg and 8 mg groups showed sustained benefits in improving SJC and TJC of small and large joints. (**Figure 1** and **Figure 2**). In addition, ivarmacitinib 4 mg and placebo/placebo-ivarmacitinib 4 mg groups presented no difference in SJC or TJC reduction between small joints and large joints at most timepoints. However, ivarmacitinib 8 mg group demonstrated greater reduction of TJC in small joints compared with large joints from week 20 to week 52 (**Figure 3**).

Conclusion: Ivarmacitinib significantly improves joint swelling and tenderness in patients with moderate-to-severe RA. Moreover, ivarmacitinib 8 mg provides superior long-term benefits in improving tenderness of small joints than large joints.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Jin: None; **H. Guo**: None; **Y. Han**: None; **M. Ding**: None.

Abstract Number: 1355

Use of parenteral compared to oral glucocorticoids in early rheumatoid arthritis is superior for chance ofbeing off steroids and escalation of therapy at 1 year

Andreu Fernandez Codina[1], Marie-France Valois[2], Susan J. Bartlett[3], Mishquatul Wahed[4], Hugues Allard-Chamard[5], Louis Bessette[6], Glen Hazlewood[7], Carol Hitchon[8], Bindee Kuriya[9], Vivian Bykerk[10], **Janet Pope**[11] and CATCH investigators, [1]Western University, London, ON, Canada, [2]McGill University, Pointe-Claire, QC, Canada, [3]McGill University, Beaconsfield, QC, Canada, [4]Western University, Windsor, ON, Canada, [5]Université de Sherbrooke, Sherbrooke, Canada, [6]Centre de l'Ostoporose et de Rhumatologie de Qubec, Quebec, QC, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]University of Manitoba, Winnipeg, MB, Canada, [9]University of Toronto - Toronto, Toronto, ON, Canada, [10]Hospital for Special Surgery, New York, NY, [11]University of Western Ontario, London, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

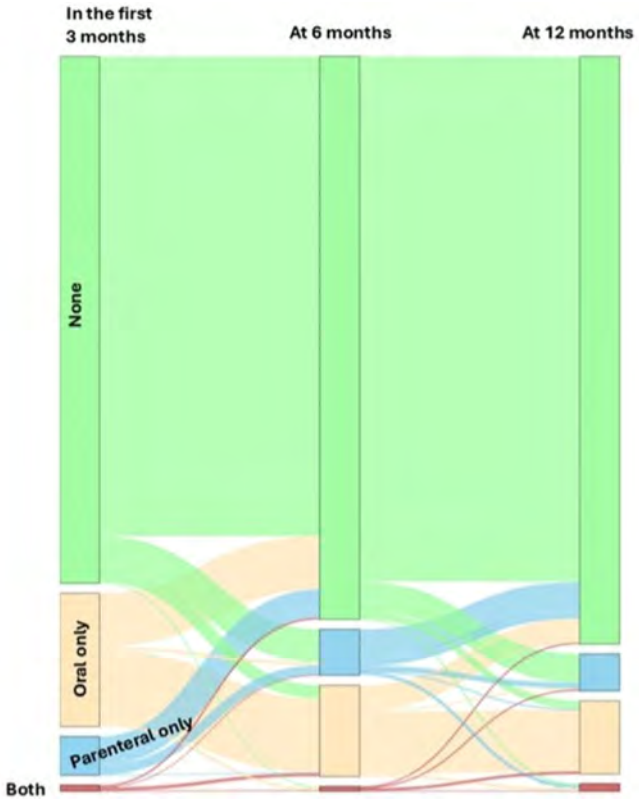
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The 2023 EULAR recommendations for the management of Rheumatoid Arthritis (RA) emphasizes the importance of limiting the dose and duration of glucocorticoids (GC) used in early disease. However, no recommendation about the preferred route of GC administration is available, nor is it known if GC route is associated with total

Table 1. Multivariate logistic regression estimating the odds for GC and advanced therapy use over time



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

GC exposure. In this study we describe the route of GC administration in patients with early RA (ERA), and determine if GC route is associated with the likelihood of being GC-free and/or requiring advanced therapy at 12 months.

Methods: Participants included newly diagnosed RA patients (symptoms < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) between (dates) and excluded if they reported GC use 90 days prior to baseline, were on advanced therapy by 3 months, or had < 12 months. Patients were stratified by use of GC during the first 3 months of follow-up: none; oral only; parenteral only (intramuscular or intraarticular); or both (oral +parenteral). Multivariate logistic regression adjusted by confounders was used to calculate the OR of GC use at 6 and 12 months and/or progression to advanced therapies (biologics or JAKi).

Results: The sample included 2,222 ERA patients. Mean (SD) age was 55 (15), disease duration 5.5 (3) months, 73% were female, and 86% were white, 69% were initially on methotrexate (MTX) at a mean dose of 20.1 (4.2) mg/week. Mean CDAI at baseline and 12-month scores were 26 (14) and 7.5 (8.6). The majority (1,661; 75%) received no GC; oral-only GC was 421 (19%); parenteral-only GC was 121 (5%), and both oral and parenteral was 19 (1%). Mean CDAI at baseline was lowest in the no GC and highest in those receiving both (24.1 vs 31.6, vs 30.2, vs 32.8, p< 0.0001), but no differences were observed among groups at 12 months. GC and advanced therapeutics at 12 months were: 8% and 7% (no GC); 47% and 14% (oral); 26% and 14% (parenteral); 63% and 16% (both). Table 1 shows that any GC use, particularly oral-only, increases odds of chronic GC use at 6 and 12 months, as well as advanced therapy utilization. Figure 1 features a Sankey diagram illustrating changes in GC use over 12 months.

Conclusion: Initial use of GC is low despite EULAR recommendations suggesting their use for patients with higher baseline disease activity. Among patients with active early RA, those receiving parenteral GC were half as likely to remain on GC at 12 months, compared to those using oral GC. Both GC groups had similar rates of use of advanced treatment use, which were higher compared to the no GC group. Parenteral GC use may support earlier discontinuation of steroids.

Disclosure: A. Fernandez Codina: Amgen, 2, AstraZeneca, 2, Bayer, 2, Boehringer-Ingelheim, 2, Mallinckrodt, 2, Sanofi, 2, Vifor pharma, 2; **M. Valois**: None; **S. Bartlett**: Accord, 2, Nordic, 2, PROMIS Health Organization, 4, Sandoz, 2; **M. Wahed**: None; **H. Allard-Chamard**: AbbVie, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 1, 5, 6, GlaxoSmithKlein(GSK), 1, Janssen, 1, 5, 6, Kabi, 1, 5, 6, Novartis, 1, 6, Otsuka, 1, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Sobi, 1, 5, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, 5, 6, Fresenius Kabi, 2, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, TEVA, 2, 6, UCB, 2, 5, 6; **G. Hazlewood**: None; **C. Hitchon**: Accord, 1, AstraZeneca, 2, Fresenius-Kabi, 2, Pfizer, 2, Sandoz, 2; **B. Kuriya**: AbbVie/Abbott, 1, Pfizer, 1, UCB, 1; **V. Bykerk**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, E.R. Squibb & Sons, 2, Janssen, 2, L.L.C, 2, Organon, 2, Pfizer, 2; **J. Pope**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Frese, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mallinckrodt Pharmaceuticals, 2, 5, Merck/MSD, 2, Mitsubishi Tanabe Pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2, Sanofi, 2, Teva, 2, UCB, 2, Viatris, 2.

Abstract Number: 1356

Use of (MSB11456), the first tocilizumab biosimilar approved for rheumatoid arthritis: 6-month data from an international observational study

Jonathan Kay[1], Eugen feist[2], Ernest Choy[3], Joerg Kaufmann[4], Ernest Wong[5], Hector Corominas[6], René-Marc Flipo[7], Jérôme Avouac[8], María América López Lasanta[9], Joelle Monnet[10], Peter Baker[11], Maria Romanova Michailidi[12], Fabrizio Dolfi[11] and Graziella Pourcel[13], [1]UMass Chan Medical School, Worcester, MA, [2]Helios Department of Rheumatology, Vogelsang-Gommern, Germany, [3]Division of Infection and Immunity, CREATE Centre, Cardiff University, Cardiff, United Kingdom, [4]NA, Ludwigsfelde, Germany, [5]Portsmouth Hospitals University NHS Trust, Portsmouth, United Kingdom, [6]Hospital de Sant Pau, Barcelona, Spain, [7]Université de Lille, CHU Lille, Service de rhumatologie, Lille,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

France, Lille, France, [8]Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France, [9]Hospital Universitario Vall d´ Hebron, Barcelona, Spain, [10]Fresenius Kabi SwissBioSim, Eysins, Switzerland, [11]Fresenius Kabi Biopharma, Eysins, Switzerland, [12]University of Geneva, Eysins, Switzerland, [13]Fresenius Kabi Biopharma, Eyzins, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Although most healthcare professionals are convinced of the quality, safety, and favorable economic impact of biosimilars, their routine use is not yet widespread. MSB11456 is the first tocilizumab biosimilar approved for both IV and subcutaneous administration. Its biosimilarity to the originator has been demonstrated in an extensive non-clinical and clinical program in patients with moderate-to-severe rheumatoid arthritis (RA).

The aim of RUBY, a multinational, prospective non-interventional study, is to evaluate the use of MSB11456 (either in initiation or switch) in RA patients over 12 months, assess persistence rate at 6 months after treatment initiation, and identify factors associated with treatment persistence for at least 12 months.

Methods: Adult RA patients were included; those participating in any interventional clinical trial were excluded. The primary endpoint was the persistence on MSB11456 by 6 months after treatment initiation. Data collected included basic clinical characteristics, inflammatory disease history, current clinical status including disease activity score (DAS28-CRP), and adverse events at each follow-up visit up to 12 months. Data are presented using descriptive statistics. A logistic regression model will be employed to identify potential predictive factors of persistence at 12 months. We present here patient baseline characteristics, and 6-months intermediate results.

Results: 241 RA patients in Germany (219), UK (17) and Spain (5) completed the 6-month follow-up visit. At MSB11456 initiation, the median duration of RA was 10.5 years. 59.3% patients were naïve to tocilizumab, whereas 40.7 % switched from the originator. Patient characteristics at baseline, are summarized in **Table 1**. The most frequent comorbidity was hypertension (48.5%) and most frequent extra-articular manifestations were rheumatoid nodules (9.1%), Raynaud's phenomenon (2.1%) and pulmonary fibrosis (2.1%). MSB11456 was administered as monotherapy in 52.3% patients, mainly by subcutaneous route (78%) using often the autoinjector. DAS28-CRP disease activity improved at 6 months, with high rates of low-disease activity and remission (**Table 2**). Corticosteroids (CS) dose decreased in 28/82 (34.2%) tocilizumab-naïve patients (in which 13 patients < 5 mg/day or discontinuing CS). By 6 months, 127 patients (53%) experienced at least one adverse event (AE), of which 66 (27%) had AE(s) possibly attributable to MSB11456 that led to permanent discontinuation in 22 (9%) patients **At 6 months, 86% of patients remained on MSB11456**. Among patients with comorbidities, no worsening in existing conditions was observed, with high persistence rates (86.5% to 100%) **(Table 3)**.

Table 1: Patient characteristics at baseline

		Baseline (N=241)
Age	Median [Min, Max]	60.0 [53.0 - 69.0]
Gender	Male	61/241 (25.3%)
	Female	180/241 (74.7%)
BMI	Median [Min, Max]	26.85 [23.42 - 31.14]
Comorbidities	Hypertension n (%)	117 (48.5)
	Cardiac Disease n (%)	37 (15.4)
	Diabetes n (%)	32 (13.3)
	Stroke n (%)	8 (2.3)

BMI, body mass index.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Patients with DAS28-CRP at baseline and at 6 months of FK-tocilizumab treatment

		Baseline (N=176)	6 months (N=139)
	Median [Min, Max]	3.3 [1.6 - 4.1]	1.9 [1.3 - 2.7]
DAS28-CRP categorical	Remission (< 2.6)	70 (39.8%)	96 (69.1%)
	Low disease activity (2.6- <3.2)	15 (8.5%)	17 (12.2%)
	Moderate disease activity (3.2- <5.1)	72 (40.9%)	24 (17.3%)
	High disease activity (>=5.1)	19 (10.8%)	2 (1.4%)

Sites chose between ESR or CRP to calculate DAS28 scores. As of the abstract, 139 of 176 patients had completed Month 6 or discontinued. All patients will complete Month 6 or discontinue before ACR 2025.

Table 3: Patients with comorbidities at baseline and at 6 months of FK-tocilizumab treatment

Comorbidity	Baseline			6 Months				
	N valid	Severity		N valid	Severity	Evolution	Persistence rate	Main discontinuation cause
Hypertension	117	Mild	61 (52%)	105	Mild	55 (52%)	100% stable	89.7%	AE
		Moderate	56 (48%)		Moderate	50 (48%)			
		Severe	0%		Severe	0%			
Cardiac disease	37	Mild	11 (30%)	31	Mild	10 (32%)	100% stable	88.5%	Patient withdraw consent
		Moderate	22 (60%)		Moderate	17 (55%)			
		Severe	4 (10%)		Severe	4 (13%)			
Diabetes	32	Mild	18 (56%)	32	Mild	18 (56%)	100% stable	87.5%	Patient withdraw consent
		Moderate	12 (38%)		Moderate	12 (38%)			
		Severe	2 (6%)		Severe	2 (6%)			
Stroke	8	Mild	5 (63%)	8	Mild	5 (63%)	100% stable	100%	NA
		Moderate	3 (38%)		Moderate	3 (38%)			
		Severe	0%		Severe	0%			

Conclusion: The RUBY study evaluates the real-world use of the first tocilizumab biosimilar to treat RA. Results at 6-months demonstrate high persistence on treatment with improvement in RA disease activity and no worsening of cardiovascular comorbidities. Further study will examine factors influencing treatment persistence at 12 months in clinical practice.

Disclosure: J. Kay: Biogen, 5, Celltrion, Inc., 2, Gate Bioscience, 2, Immunitas Therapeutics, 2, Immunovant, Inc., 2, Istesso, Ltd, 2, Kolon TissueGeje, Inc, 1, Organon, LLC, 2, Sana Biotechnology, Inc., 2, Santa Ana Bio, Inc., 2, Spyre Therapeutics, 2, Wolters Kluwer NV, 9; **E. feist**: AB2Bio, 6, AbbVie/Abbott, 6, Alfasigma, 6, AstraZeneca, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Galapagos, 6, Hexal, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6, Roche/Chugai, 6, R-Pharm, JSC, 6, Sandoz, 6, Sanofi, 6, Sobi, 6, UCB, 6; **E. Choy**: AbbVie, 2, 6, Alfasigma, 6, Bio-Cancer, 2, 5, Biocon, 2, Biogen, 2, 5, Chugai Pharma, 2, 6, Eli Lilly, 6, Fresenius Kabi, 2, 6, Gedeon Richter, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 6, Viatris, 2, 6; **J. Kaufmann**: None; **E. Wong**: None; **H. Corominas**: None; **R. Flipo**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6; **J. Avouac**: AbbVie, 2, 6, Alfasigma S.p.A., 6, BMS, 5, 6, Celltrion, 6, Eli Lilly & Co., 6, Fresenius Kabi, 5, Galapagos, 2, 6, Novartis, 5, 6, Pfizer, 5, 6; **M. López Lasanta**: None; **J. Monnet**: Fresenius Kabi SwissBioSim GmbH, 3; **P. Baker**: Fresenius Kabi SwissBioSim GmbH, 3; **M. Romanova Michailidi**: Fresenius Kabi SwissBioSim GmbH, 3; **F. Dolfi**: None; **G. Pourcel**: None.

Abstract Number: 1357

Measuring Rheumatoid Arthritis Outcomes Using Machine Learning Imputed Disease Activity Scores

Jue Hou[1], Feiqing Huang[2], Gregory McDermott[3], Jun Wen[4], Mary Jeffway[3], Ying Qi[5], Yunqing Han[3], Tianrun Cai[6], Florence Bourgeois[4], Katherine Liao[7] and Tianxi Cai[2], [1]University of Minnesota, Minneapolis, MN, [2]Harvard T.H. Chan School of Public Health, Boston, [3]Brigham and Women's Hospital, Boston, [4]Harvard Medical School, Boston, [5]Brigham and Women's Hospital, Boston, [6]Brigham and Women's Hospital, Boston, MA, [7]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, USA, Boston, MA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Validated rheumatoid arthritis (RA) disease activity measures such as the Disease Activity Score-28 (DAS28) are used in clinical trials but not universally recorded in routine clinical care. Lack of readily available disease activity measures limits the use of electronic health records (EHRs) for generating real-world evidence (RWE) on RA treatment effectiveness. However, the key components of RA disease activity measures such as DAS28, including physical examination findings and laboratory assessments, are often documented in the EHRs, presenting an opportunity to determine disease activity using computational algorithms. The objective of this study was to produce scalable EHR RA disease activity metrics and conduct a test case comparing outcomes among RA patients switching from one tumor necrosis factor inhibitor (TNFi) to another vs changing mechanism of action (MOA).

Methods: We used data from a large EHR-based RA cohort (n=35,235) from a large multihospital healthcare system in the United States with natural language processing of clinical notes, coded EHR data, and laboratory results. A subset of these patients (n=1,579) was co-enrolled in an established RA disease registry and had planned assessment of RA disease activity by formal DAS28-CRP every 6 months. We developed a scalable **m**achine learning **i**mputed **d**isease **a**ctivity **s**core (miDAS) using EHRs, computed aggregating semi-supervised and supervised learning approaches that combine DAS28-CPR measurements from the registry subset and large RA EHR cohort without DAS28-CRP. Using miDAS, we defined longitudinal moderate to severe RA disease activity (DAS28-CRP >3.2 or miDAS >0.365) over the full EHR cohort. We identified the patients who initiated TNFi and either 1) cycled to a second TNFi or 2) switched to a biologic DMARD or targeted-synthetic DMARD with another MOA. We then conducted the RWE study comparing the disease activity following the two treatment strategies. The primary outcome was the rate of medium to high disease activity 1 year after treatment switching adjusted for potential confounding using doubly robust causal modeling.

	Corresponding patients in BRASS Registry, N (%)	Patients in EHR Cohort Included in Clinical Use Case, N (%)	p-value‡
Cohort size	71	2,119	
Age at RA diagnosis, median years (IQR)	63 (51-71)	62 (54-73)	0.895
Sex			
Female	60 (84.5)	1,668 (79.7)	0.378
Male	11 (15.5)	431 (20.3)	
Race			
American Indian	0 (0.0)	7 (0.3)	0.514
Asian	2 (2.8)	62 (2.9)	
Black	4 (5.6)	113 (5.3)	
White	61 (85.9)	1,744 (82.3)	
Other	4 (5.6)	193 (9.1)	
RA disease duration at index date, median years (IQR)	3.91 (1.79-6.24)	3.05 (1.45-5.93)	0.337
Treatment duration with first TNF inhibitor, median years (IQR)	2.07 (0.76-4.50)	1.44 (0.55-3.52)	0.125
miDAS at initiation of first TNF inhibitor	0.20 (0.08-0.46)	0.22 (0.10-0.44)	0.8
miDAS at initiation of third-line therapy	0.37 (0.15-0.75)	0.33 (0.16-0.59)	0.14
DAS28-CRP at initiation of second bDMARD or tsDMARD therapy	2.53 (1.90-3.53)	-	-

‡ P-values from univariate two sample tests comparing characteristics between patients in the two cohorts

Patient characteristics according to data source

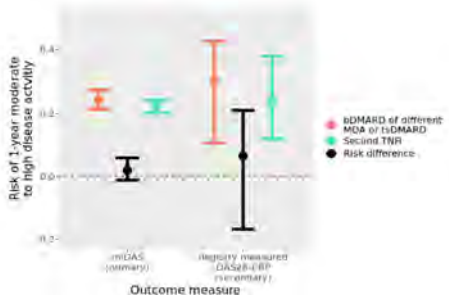
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	miDAS*	LATTE	Adaptive Lasso	xgBoost	Random Forest
All registry visits (N=9414)	0.829	0.812	0.780	0.807	0.821
1-year disease activity (N=238)	0.813	0.779	0.765	0.776	0.833

* The final miDAS was created by combining LATTE, adaptive Lasso, xgBoost and random forest through a linear ensemble

Accuracy of miDAS and its machine learning components for classifying moderate to high disease activity as measured by area under curve

Estimated treatment effects on 1-year RA disease activity with 95% confidence intervals (vertical bars). After adjustment, we observed no statistically significant difference in RA disease activity at 1-year when comparing treatment with a second TNF inhibitor vs bDMARD with a different mechanism of action or tsDMARD using either miDAS or registry DAS28-CRP values, though confidence intervals were more narrow using miDAS as the outcome measure.



Treatment outcomes in clinical use case

Results: A total of 2,119 RA patients were included with baseline characteristics listed in **Table 1**. Cross-validated against registry outcomes, miDAS achieved area-under-reception-operator-curve (AUC) for classifying moderate to high disease activity 0.829 (**Table 2**). There was no significant difference in risk of moderate to high disease activity at 1 year between TNFi cycling vs. MOA switching (average risk difference 1.9% [95% CI, -1.2% to 5.8%]) (**Figure 1**).

Conclusion: We used longitudinal electronic health records data and computational algorithms to derive and validate a disease activity measure (miDAS) with strong agreement with DAS28-CRP scores recorded in registry. This technique will allow for future real-world studies assessing RA treatments with imputed disease activity as an outcome. We also performed a proof-of-concept study demonstrating that switching mechanism of action after discontinuation of first TNFi did not result in significant difference in 1-year disease activity compared to cycling to a second TNFi.

Disclosure: J. Hou: None; **F. Huang**: None; **G. McDermott**: None; **J. Wen**: None; **M. Jeffway**: None; **Y. Qi**: None; **Y. Han**: None; **T. Cai**: None; **F. Bourgeois**: None; **K. Liao**: Merck, 2; **T. Cai**: None.

Abstract Number: 1358

Real-World Evidence for the Superiority of Subcutaneous Methotrexate in RA: A Comparative Observational Study with Ultrasonographic Assessment

Masatsugu Komagamine[1], Sari Taguchi[2], Masataka Komagamine[2], Tetsuji Naka[1] and Minoru Fujimoto[1], [1]Division of Allergy and Rheumatology, Department of Internal Medicine, Iwate Medical University, Morioka, Japan, [2]Komagamine Rheumatology and Orthopedic Clinic, Morioka, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate (MTX) is a foundational agent in the management of rheumatoid arthritis (RA). While oral MTX is widely prescribed, its subcutaneous (SC) formulation may enhance bioavailability and reduce gastrointestinal intolerance. Despite these theoretical advantages, real-world comparative data—particularly incorporating musculoskeletal ultrasound (MSUS)—remain sparse. This study aimed to compare clinical efficacy, sonographic synovial response, and safety between SC and oral MTX, adjusting for potential confounders such as MTX dosage and baseline disease activity.

Methods: In this retrospective observational study, we analyzed 96 RA patients from two Japanese centers who initiated either SC MTX (n = 75) or oral MTX (n = 21) between April 2022 and March 2025. All patients fulfilled the 2010 ACR/EULAR criteria. Disease activity indices—including TJC28, SJC28, DAS28-CRP, SDAI, and CDAI—were assessed at baseline and at 1, 3, and 6 months. Serial MSUS assessments were performed in the SC group to evaluate synovitis using power Doppler (PD) and gray scale (GS) imaging (semi-quantitative scale 0–3). Multivariable linear regression models were applied to adjust for baseline scores and MTX starting doses.

Results: At 6 months, SC MTX was associated with significantly greater reductions in TJC28 (–4.0 vs. –1.0; p = 0.0229), DAS28-CRP (–1.28 vs. –0.57; p = 0.0117), SDAI (–6.8 vs. –2.0; p = 0.0005), and CDAI (–7.3 vs. –2.8; p = 0.0414). SJC28 changes did not differ significantly (p = 0.8711). Multivariable analysis adjusting for baseline MTX dose confirmed the superiority of SC MTX in improving DAS28-CRP (β = –0.74, p = 0.005), CDAI (β = –7.15, p < 0.001), SDAI (β = –7.15, p < 0.001), and TJC28 (β = –2.34, p = 0.036), while no significant difference was observed for SJC28 (β = –0.61, p = 0.438). PD and GS scores declined steadily in the SC group, although PD signals recurred in some patients at month 6. No serious adverse events were observed. Mild hepatic and renal function changes occurred more frequently in the oral MTX group, though not significantly.

Table 1. Baseline Demographic and Clinical Characteristics

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Metoject (n=75)	Oral MTX (n=21)	P-value
Mean age ± SD (years)	60.8 ± 13.1	59.4 ± 11.4	0.57
Female, %	85.5	90.1	0.74
Disease duration, mean ± SD (years)	15.9 ± 11.5	5.8 ± 3.5	<0.001
ACPA positive, %	88.2	70.0	0.08
RF positive, %	89.3	80.9	0.33
Smoking history, %	6.6	11.1	0.61
Concomitant steroid use, %	53.3	66.6	0.31
Steinbrocker class (I / II / III / IV), %	34.6 / 24 / 20 / 21.3	95.2 / 4.7 / 0 / 0	<0.001
Metoject dosage (7.5 / 10 / 12 / 15 mg), %	36.8 / 24 / 29.3 / 9.3	N/A	N/A
Oral MTX dosage (2 / 4 / 6 / 8 / 10 / 12 mg), %	N/A	4.7 / 4.7 / 19 / 19 / 23.8 / 28.6	N/A

N/A: not applicable

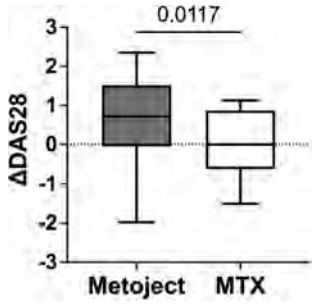


Figure 2. Longitudinal changes in disease activity indices DAS28-CRP scores at baseline, 1, 3, and 6 months in the subcutaneous and oral MTX groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

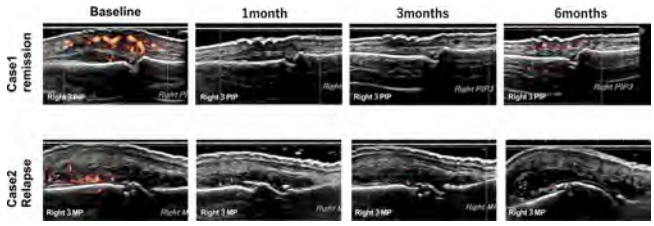


Figure 3. Ultrasound findings in the subcutaneous MTX group Representative musculoskeletal ultrasound (MSUS) images demonstrating resolution (upper panel) and recurrence (lower panel) of power Doppler (PD) signal at baseline, 3 months, and 6 months.

Conclusion: Subcutaneous MTX demonstrated enhanced clinical and ultrasonographic outcomes compared to oral MTX, independent of baseline disease activity or starting dose. These findings support broader adoption of SC MTX as a practical and effective strategy for RA management prior to escalation to biologic agents. The inclusion of imaging and dose-adjusted outcomes strengthens the generalizability and clinical relevance of this study.

Disclosure: M. Komagamine: None; **S. Taguchi**: None; **M. Komagamine**: None; **T. Naka**: None; **M. Fujimoto**: None.

Abstract Number: 1359

Comparative Safety Outcomes of Tofacitinib Versus Upadacitinib in Patients with Rheumatoid Arthritis: A Retrospective Cohort Study

Maya Khasho[1], Ahmad Alomari[2], Reem Elmusa[3] and Rafal Ali[4], [1]University of central florida, Gainesville, FL, [2]UCF- North Florida hospital, Gainesville, FL, [3]UCF/ HCA - North florida hospital, Gainesville, FL, [4]Jefferson Einstein Philadelphia, Lansdale, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disease affecting synovial joints, often leading to joint destruction if untreated. Disease-modifying antirheumatic drugs (DMARDs), including Janus kinase (JAK) inhibitors like tofacitinib and upadacitinib, are essential for managing RA to achieve remission or low disease activity. However, JAK inhibitors are associated with adverse effects such as venous thromboembolism, malignancy, cerebrovascular and cardiovascular events, infections, and hyperlipidemia. Here is a comparative safety data between tofacitinib and upadacitinib.

Methods: We included RA patients aged ≥18 years, identified by ICD-10 codes, who initiated tofacitinib (n=20,305) or upadacitinib (n=6,281). The index event was the first RA diagnosis with corresponding medication. Propensity score matching (1:1) was performed based on demographics, comorbidities (e.g., diabetes, hyperlipidemia, hypertension), and concurrent medications (e.g., methotrexate, TNF inhibitors). Post-matching, 6,276 patients per cohort were analyzed. Outcomes within five years post-treatment initiation included acute myocardial infarction, cerebral infarction, venous thrombosis/embolism, diverticular disease, pneumonia, herpes zoster, depression, hyperlipidemia, suicidal ideation, lymphoma/leukemia, basal cell carcinoma (BCC), squamous cell carcinoma (SCC), transaminitis, and neutropenia. Patients with prior occurrences were excluded. Risk ratios (RR) with 95% confidence intervals (CI) were calculated.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Patient Characteristics of Study groups, Before and After Propensity Score Matching

Characteristics	Before Matching			Std diff.	After Matching			Std diff.
	Tofacitinib	Upadacitinib	P-Value		Tofacitinib	Upadacitinib	P-Value	
Demographics								
Age at index, mean ± SD	57.4 ± 13.7	56.2 ± 13.5	<0.0001	0.0866	55.8 ± 13.9	56.2 ± 13.5	0.0711	0.0322
Female, (%)	78.26	76.89	0.0228	0.0327	77.31	76.90	0.5807	0.0099
Race (%)								
White	65.94	67.08	0.0977	0.0240	66.78	67.07	0.7327	0.0061
Black	10.75	8.98	<0.0001	0.0594	9.27	8.99	0.5770	0.0100
Hispanic or Latino	7.83	9.66	<0.0001	0.0649	9.56	9.672	0.8322	0.0038
Unknown	14.86	16.26	<0.0001	0.0385	16.48	16.25	0.7355	0.0060
Diagnoses (%)								
Rheumatoid arthritis	100.0	100.0	-	-	100.0	100.0	-	-
Hypertension	39.19	40.19	0.1596	0.0203	38.45	40.17	0.0484	0.0352
Hyperlipidemia	30.89	34.01	<0.0001	0.0665	32.90	33.96	0.2117	0.0223
Obesity	15.39	18.89	<0.0001	0.0930	18.24	18.86	0.3705	0.0160
Diabetes mellitus	15.27	16.14	0.0950	0.0240	15.60	16.14	0.4062	0.0148
Chronic kidney disease	5.97	6.53	0.1060	0.0231	6.07	6.53	0.2868	0.0190
Inflammatory bowel disease	6.2	5.56	0.0613	0.0274	4.87	5.56	0.0844	0.0308
Tobacco use	3.49	3.92	0.1095	0.0228	3.76	3.90	0.6756	0.0075

Results: After matching, each cohort included 6,276 RA patients. Tofacitinib was associated with higher risks of cerebral infarction (RR=1.694, 95% CI 1.29–2.24, P< 0.0001), acute myocardial infarction (RR=2.43, 95% CI 1.858–3.17, P< 0.0001), venous thrombosis/embolism (RR=1.465, 95% CI 1.182–1.818, P=0.0005), diverticular disease (RR=1.373, 95% CI 1.176–1.604, P< 0.0001), pneumonia (RR=1.73, 95% CI 1.472–2.034, P< 0.0001), herpes zoster (RR=1.413, 95% CI 1.157–1.725, P=0.0006), hyperlipidemia (RR=1.24, 95% CI 1.126–1.366, P< 0.0001), and depression (RR=1.453, 95% CI 1.287–1.640, P< 0.0001) compared to upadacitinib. No significant differences were found for suicidal ideation, lymphoid/hematopoietic malignancies, BCC, SCC, transaminitis, or neutropenia as shown in the table below

Conclusion: RA patients treated with tofacitinib have increased risks of cardiovascular events, venous thrombosis/embolism, diverticular disease, pneumonia, herpes zoster, hyperlipidemia, and depression compared to those on upadacitinib. Prospective studies are needed to confirm these findings and investigate underlying mechanisms. Continuous monitoring of patient safety profiles is essential in RA management

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Safety Outcomes in RA Patients: Tofacitinib vS. Upadacitinib

Table 2: Safety Outcomes in RA Patients: Tofacitinib vs. Upadacitinib

Outcomes		Tofacitinib	Upadacitinib	RR (95% CI), P value
Acute myocardial infarction	*Patients with outcome (%)*	161 (2.629%)	74 (1.209%)	2.175 (1.656–2.858), p < 0.0001
Cerebral infarction (stroke)	*Patients with outcome (%)*	131 (2.141%)	81 (1.320%)	1.622 (1.232–2.135), p = 0.0005
Venous thrombosis/embolism	*Patients with outcome (%)*	198 (3.268%)	136 (2.230%)	1.465 (1.182–1.818), p = 0.0005
Pneumonia	*Patients with outcome (%)*	381 (6.602%)	221 (3.816%)	1.73 (1.472- 2.034) P <0.0001
Diverticular disease	*Patients with outcome (%)*	364 (6.233%)	258 (4.538%)	1.373 (1.176–1.604), p < 0.0001
Elevation levels of liver transaminase levels	*Patients with outcome (%)*	178 (2.894%)	149 (2.455%)	1.179 (0.951–1.462) p= 0.1322
Neutropenia	*Patients with outcome (%)*	79 (1.273%)	62 (1.004%)	1.267 (0.910–1.764), p = 0.1594
Malignant neoplasms (lymphoid/hematopoietic)	*Patients with outcome (%)*	44 (0.709%)	30 (0.482%)	1.47 (0.925–2.335), p = 0.1006
Squamous cell carcinoma of the skin	*Patients with outcome (%)*	39 (0.623%)	30 (0.480%)	1.299 (0.808–2.088), p = 0.2787

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Safety Outcomes in RA Patients: Tofacitinib vS. Upadacitinib (continued)

Table 2: Safety Outcomes in RA Patients: Tofacitinib vs. Upadacitinib (continued)				
Basal cell carcinoma of the skin	*Patients with outcome (%)*	35 (0.562%)	24 (0.388%)	1.455 (0.867–2.443), p = 0.1530
Herpes zoster	*Patients with outcome (%)*	226 (3.732%)	159 (2.642%)	1.413 (1.157–1.725), p = 0.0006
Hyperlipidemia	*Patients with outcome (%)*	779 (16.975%)	632 (13.692%)	1.24 (1.126–1.366) p < 0.0001
Depression	*Patients with outcome (%)*	593 (11.893%)	393 (8.186%)	1.453 (1.287–1.640), p < 0.0001
Suicidal ideation	*Patients with outcome (%)*	35 (0.562%)	25 (0.403%)	1.395 (0.836 –2.328) P 0.2006

Disclosure: M. Khasho: None; **A. Alomari**: None; **R. Elmusa**: None; **R. Ali**: None.

Abstract Number: 1360

Evaluating Causal Effects of Biologic and Targeted Synthetic Disease-modifying Anti-rheumatic Drugs Targets in Rheumatoid Arthritis Using Mendelian Randomisation

Mihye Kwon[1], Chung-il Joung[1] and Young Soo Song[2], [1]Konyang University Hospital, Daejeon, Republic of Korea, [2]Konyang University Hospital, Daejeon, Taejon-jikhalsi, Republic of Korea

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease in which biologic and targeted synthetic DMARDs (bDMARDs, tsDMARDs) have substantially improved clinical outcomes. While randomized controlled trials (RCTs) support their clinical use, RCTs have limitations in cost, generalizability, and long-term risk assessment. Mendelian randomization (MR), using genetic variants as proxies for drug target modulation, provides an alternative approach for inferring causality. This study aimed to assess whether genetically proxied modulation of known therapeutic targets is causally associated with RA risk, thereby validating drug efficacy from a genetic perspective.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Summary of Mendelian Randomization estimates and results from sensitivity analyses.

Dataset	Exposure	Outcome	SNP no.	Two Sample MR analysis				Sensitivity analysis			
				MR method	Beta	SE	P value	Egger-intercept	P value	Cochran's Q	P value
ieu-a-834	TNF	RA	106	Weighted median	-0.66	0.05	0.00	-0.07	0.05	2041.22	0.00
	LTA	RA	70	MR Egger	-1.65	0.39	0.00	0.10	0.04	1170.26	0.00
	FCGR2B	RA	128	IVW	0.09	0.01	0.00	0.01	0.09	33.17	1.00
	FCGR2C	RA	66	MR Egger	-0.30	0.06	0.00	0.08	0.00	193.93	0.00
	CD86	RA	125	IVW	0.28	0.03	0.00	0.00	0.44	26.39	1.00
	CTLA4	RA	152	MR Egger	-0.16	0.07	0.03	-0.08	0.00	94.15	1.00
	IL1R1	RA	149	MR Egger	0.48	0.08	0.00	-0.04	0.00	64.57	1.00
	JAK1	RA	16	IVW	-0.31	0.14	0.03	0.09	0.36	0.18	1.00
FinnGen Seropositive	TNF	RA	265	Weighted median	-0.63	0.03	0.00	-0.09	0.00	5292.53	0.00
	FCGR1A	RA	40	IVW	0.09	0.01	0.00	0.01	0.83	3.87	1.00
	FCGR2B	RA	502	MR Egger	0.09	0.01	0.00	0.02	0.00	571.45	0.01
	MS4A1	RA	92	MR Egger	1.00	0.21	0.00	-0.03	0.00	18.98	1.00
	IL6R	RA	178	MR Egger	-0.87	0.11	0.00	0.04	0.00	97.96	1.00
	IL1R1	RA	256	IVW	-0.08	0.02	0.00	0.00	0.67	106.87	1.00
	JAK1	RA	21	MR Egger	-1.44	0.57	0.02	0.08	0.04	6.66	1.00
FinnGen Seronegative	TNF	RA	265	Weighted median	-0.60	0.04	0.00	-0.11	0.00	1984.60	0.00
	FCGR2B	RA	502	MR Egger	0.03	0.01	0.01	0.02	0.00	417.25	1.00
	FCGR3B	RA	227	IVW	-0.16	0.02	0.00	-0.01	0.06	150.25	1.00
	CD80	RA	101	MR Egger	1.73	0.51	0.00	-0.07	0.03	115.18	0.13
	CD86	RA	295	Weighted median	0.18	0.04	0.00	0.02	0.00	145.11	1.00
	CTLA4	RA	240	Weighted median	-0.83	0.04	0.00	-0.07	0.00	252.09	0.25
	MS4A1	RA	92	IVW	0.74	0.08	0.00	-0.02	0.11	81.86	0.74
	IL6R	RA	178	IVW	-0.48	0.04	0.00	0.02	0.06	111.88	1.00
	IL1R1	RA	256	Weighted median	-0.77	0.04	0.00	0.00	0.93	341.40	0.00
	JAK1	RA	21	IVW	-1.65	0.18	0.00	0.07	0.22	26.23	0.16
	JAK2	RA	351	Weighted median	-0.06	0.02	0.00	-0.01	0.02	116.88	1.00

Methods: We applied a two-sample drug-target MR framework using cis-eQTLs from the eQTLGen Consortium for 18 gene targets corresponding to approved RA therapies. Outcome datasets included three large RA GWASs: a pan-European cohort (ieu-a-834), and two Finnish FinnGen cohorts stratified by seropositivity. Three MR methods (inverse variance weighted, MR-Egger, weighted median) were applied. Sensitivity analyses included MR-PRESSO, Steiger directionality, heterogeneity testing, and Bayesian colocalization. Results were interpreted based on convergence across methods, consistency in directionality, and robustness to pleiotropy.

Results: Across three independent datasets, TNF, FCGR2B, IL1R1, and JAK1 consistently demonstrated statistically significant and directionally concordant associations with RA risk, affirming their causal relevance. TNF and JAK1 were negatively associated with RA, consistent with their known therapeutic effects. FCGR2B and IL1R1 also showed strong associations, supporting their roles as immune regulators. Colocalization analysis identified a shared causal variant for CTLA4 in the

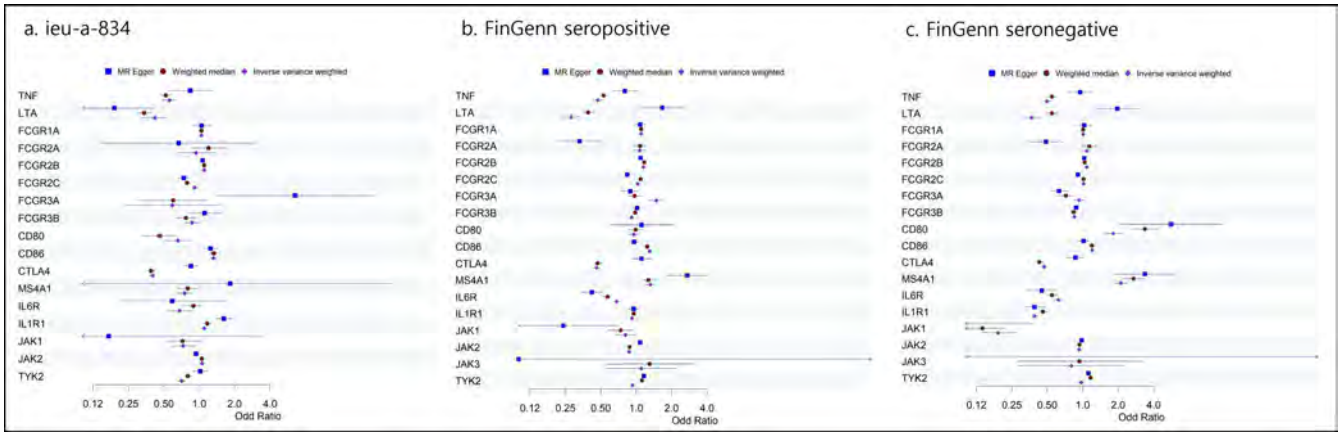


Figure 1. Forest plots of Mendelian randomization estimates for 18 candidate genes across three rheumatoid arthritis GWAS datasets

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

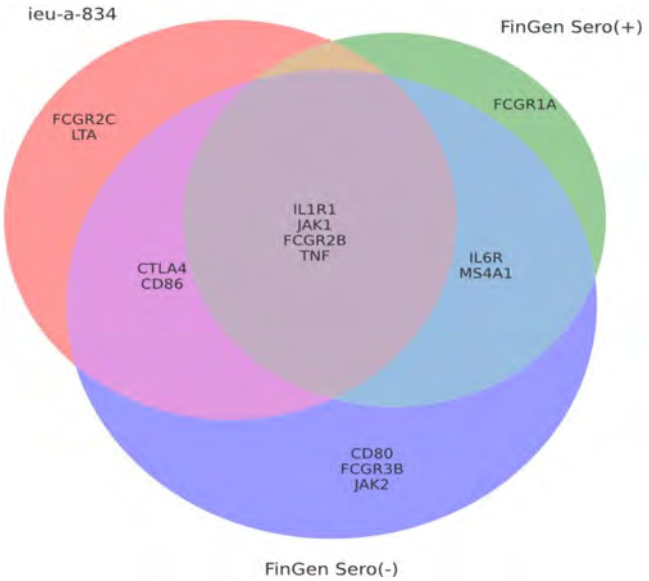


Figure 2. Venn diagram showing genes significantly associated with RA in each dataset

pan-European cohort (PP.H4 = 1.0), while TNF and LTA showed distinct variants. Other genes such as MS4A1 (CD20), IL6R, and CTLA4 demonstrated inconsistent or dataset-specific effects, indicating population-dependent signals or context-specific relevance. A multitarget MR of abatacept-related genes (CD80, CD86, CTLA4) also showed a significant protective effect. Discrepancy analysis revealed that beta estimates and standard errors varied by cohort, underscoring the importance of dataset selection.

Conclusion: This study is the first to apply a systematic drug-target MR framework to validate approved RA therapies. MR reliably recapitulated the effects of known therapeutic targets such as TNF, JAK1, and FCGR2B. Integration with colocalization analysis enhanced causal interpretation, particularly for CTLA4. However, inconsistent findings for MS4A1 and IL1R1 across cohorts highlight the need for population-specific and tissue-specific validation. Our findings demonstrate the utility of MR in therapeutic target evaluation and support its use alongside RCT data in future drug development and repurposing strategies.

Disclosure: M. Kwon: None; **C. Joung**: None; **Y. Song**: None.

Abstract Number: 1361

Efficacy of Telitacicept in the treatment of Connective tissue disease-associated interstitial lung disease: A Potential therapeutic option

Mingfang Sun[1], Xue Chen[2], Ying Zhou[2], Yanlong Yang[2], Fei Xiao[2] and huanzi dai[2], [1]Daping Hospital, chongqing, China (People's Republic), [2]Daping Hospital & Research Institute of Surgery, Army Medical University, Chongqing, PR China., Chongqing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table1:Patient clinical characteristics at baseline（pSS-ILD）

Case number	Age/Sex	BMI	ASA	SSA	SSB	RO-52	Observation period	Clinical involvement at baseline: Xerostomia	Xerophthalmia	Lung (LD)	IgG (8.7-17 g/L)	C3 (0.9-1.8 g/L)	C4 (0.1-0.4 G/L)	CRP (0-8 mg/L)	ESR (0-20 mm/h)	Ferritin (23.9-336.2 ng/ml)	PaO2/FiO2	6MWT (m)	FVC (%)	DLCO (%)	ESSDAI	ESSPRI
1	52F	22.9	+	+	+	+	Baseline	+	+	+	17.34	1.14	0.14	31.21	107	286.61	327	212	85.6	33.3	10	7
							12 W	+	+	+	6.55	0.8	0.16	0.5	6	425.55	410	226	97.7	52.8	3	4
							24 W	+	+	+	5.81	0.99	0.5	0.5	20	470	450	245	105.8	51.4	3	3
2	55F	22.1	+	+	+	+	Baseline	+	+	+	8.39	0.72	0.14	0.5	9	254.66	480	456	89.3	82.9	5	5
							12 W	+	+	+	9.07	1	0.2	0.5	5	281.11	475	460	99	86.2	5	3
							24 W	+	+	+	6.69	0.79	0.17	0.5	5	572.16	482	458	96.7	87.3	5	5
3	58M	20.9	+	+	+	+	Baseline	+	+	+	14.9	0.91	0.1	0.81	73	357.05	435.3	503	81.7	52.4	14	4
							12 W	+	+	+	9.25	0.96	0.07	0.5	10	350.2	430	572	91.9	70.1	12	3
							24 W	+	+	+	7.68	0.67	0.07	0.5	11	109.71	442	596	98.7	66.5	10	2
4	58M	30	+	+	+	+	Baseline	+	+	+	12.14	42.4	1.09	0.5	73	658.47	257	201	91.4	64.9	2	3
							12 W	+	+	+	7.55	57.4	1.07	0.5	5	352.1	283	224	105.2	90.6	2	5
							24 W	+	+	+	8.37	40.8	1.17	0.5	3	126.84	364	375	112.4	99.4	2	2
5	54M	28.2	+	+	+	+	Baseline	+	+	+	38.85	0.96	0.2	0.5	7	18.6	432	468	101	91.2	17	3
							12 W	+	+	+	37.02	0.68	0.18	0.5	13	59.61	429	460	108	91.3	15	3
							24 W	+	+	+	24.95	1.14	0.25	0.5	6	25.5	441	470	111.9	91.7	13	2
6	49M	22.5	+	+	+	+	Baseline	+	+	+	17.52	0.89	0.11	5.04	73	373.74	395	285	75.4	54.3	5	5
							12 W	+	+	+	15.15	0.87	0.13	0.5	69	161.28	384	297	86.3	77.8	4	2
							24 W	+	+	+	11.99	0.99	0.15	0.5	23	85.74	390	391	95.2	76.8	3	2
7	48M	22.1	+	+	+	+	Baseline	+	+	+	28.86	1.13	0.28	2.79	30	201.59	404	252	87.6	81.3	4	3
							12 W	+	+	+	9.69	1.12	0.32	1.69	19	214.64	413	276	92.5	90.2	3	2
							24 W	+	+	+	11.93	1.24	0.35	1.81	31	242.31	468	331	98.7	93.4	3	2
8	49M	27.1	+	+	+	+	Baseline	+	+	+	37.18	0.91	0.12	9.91	48	116.32	319	-	72.8	57.1	6	4
							12 W	+	+	+	8.65	0.86	0.18	0.5	3	324.2	325	275	76	62.3	3	3
							24 W	+	+	+	5.89	0.97	0.2	0.5	5	98.7	318	302	89.7	88	4	3
9	46M	24.9	+	+	+	+	Baseline	+	+	+	32.75	1.18	0.34	5.91	11	609.5	342	319	84.5	64.1	5	6
							12 W	+	+	+	6.18	1.13	0.24	0.5	6	307.2	393	338	75.1	67.6	4	5
							24 W	+	+	+	7.36	1.14	0.11	0.5	7	201.3	399	329	91.2	76.8	4	3
10	49M	23.1	+	+	+	+	Baseline	+	+	+	14.74	0.97	0.14	0.75	28	135.6	421	401	73.3	68.8	5	3
							12 W	+	+	+	9.72	1.06	0.17	1.52	5	98.6	409	397	87	70.5	2	2
							24 W	+	+	+	10.24	1.09	0.17	0.5	7	111.5	441	405	90.6	84.4	2	3

Table 3:Patient clinical characteristics at baseline（RA-ILD）

Case number	Age/Sex	BMI	Observation period	RF (0-30 KJU/L)	CCP (0-2.99)	CRP (0-8 mg/L)	ESR (0-20 mm/h)	PaO2/FiO2	6MWT (m)	FVC (%)	DLCO (%)	DAS28 (ESR)
1	58/M	20.8	Baseline	296	0.5	5.48	30	376	389	53.5	46.5	6.62
			12 W	68.8	0.5	1.36	19	395	401	71.9	54	3.88
			24 W	27.7	0.5	4.92	20	390	390	72.9	55.5	2.78
2	68/M	21.6	Baseline	446	112.6	5.76	6	451	396	65.5	89.3	2.54
			12 W	215.8	91.5	0.5	5	443	384	82.7	99.7	4.41
			24 W	307.75	274.1	21.72	11	450	390	81.6	75.8	2.47
3	72/F	21	Baseline	690	300	0.5	13	395	482	98.2	93.9	1.39
			12 W	745	300	0.5	6	385	468	117.3	103.1	2.03
			24 W	342.37	300	0.5	7	390	480	120	104	1.64
4	60/F	23.9	Baseline	309.03	300	0.82	33	390	401	105.5	60.7	2.63
			12 W	385.89	300	2.07	6	383	392	97.4	72	2.33
			24 W	176.39	300	3.11	81	395	387	106.1	53.8	2.13
5	71/M	21.5	Baseline	340.87	293.45	6.02	67	410	451	151.2	89.6	2.63
			12 W	79.86	252.3	2.89	34	423	460	118.9	66.6	2.33
			24 W	52.34	197.4	0.5	23	430	465	128.7	69.6	2.33

Table 2:Patient clinical characteristics at baseline（ASS-ILD）

Case number	Age/Sex	BMI	ARS	MEAS	Observation period	Clinical involvement at baseline: Skin	Muscle	Joint	Lung (LD)	CK (30-200 U/L)	LDH (120-250 U/L)	ALT (7-40 U/L)	AST (13-35 U/L)	CRP (0-8 mg/L)	ESR (0-20 mm/h)	Ferritin (13-300 ng/ml)	IgG (8.7-17 g/L)	PaO2/FiO2	6MWT (m)	SGRTX
1	52/F	19.5	RO-1	-	Baseline	-	-	+	+	70.7	211	15.6	24.7	1.06	29	412	11.99	380	420	80
					12 W	-	-	+	+	52.9	162	11.2	16.2	0.5	11	58.93	8.53	459	451	80
					24 W	-	-	+	+	39.1	186.5	11.8	18.9	0.5	8	101.17	8.71	411	420	80
2	45/F	21.9	PL-12	-	Baseline	-	-	-	+	167.4	547.5	22.8	43.9	15.78	52	462.8	10.52	395	380	60
					12 W	-	-	-	+	81.5	162.9	13.6	14.1	0.5	20	141.5	8.18	420	532	80
					24 W	-	-	-	+	51.2	182.1	10.9	15.9	0.5	12	143	7.43	458	540	80
3	47/F	27.4	RO-1	-	Baseline	+	-	-	+	71.3	232.6	15.9	15.9	0.5	37	50.48	15.04	384	592	80
					12 W	+	-	-	+	55.6	147.6	19.6	14.4	0.5	9	80.4	8.7	412	560	80
					24 W	+	-	-	+	74.1	191.2	23.1	17.6	0.5	19	62.54	6.79	433	576	80
4	66/F	28.1	PL-12	-	Baseline	+	-	-	+	52.4	198.1	46.7	62.4	28.61	76.5	2161.21	9.49	299	380	60
					12 W	+	-	-	+	63.6	264	90.4	57.4	4.51	14	132.19	9.66	223	390	60
					24 W	+	-	-	+	55.1	271.4	59.6	40.8	3.62	15	128.93	8.8	352	457	60
5	56/M	22.2	RJ	-	Baseline	+	+	+	+	612.3	437.5	162.2	179.9	31.04	23	1275.16	13.14	285	260	48
					12 W	+	+	+	+	748	277.1	64.7	66.5	10.8	15	607.84	11.87	334	264	54
					24 W	+	+	+	+	98.6	195.4	26	19.5	2.6	9	89.5	7.61	372	359	65
6	75/F	21.5	PL-12	-	Baseline	+	+	+	+	949.3	503.3	35.5	50.3	23.87	71	871.74	24.12	270	300	70
					12 W	+	+	+	+	221.5	284	14.9	19	14.86	65	161.28	9.28	334	384	70
					24 W	+	+	+	+	151.7	290.2	9.7	16	8.56	22	85.74	7.29	382	420	70
7	65/M	22.6	RO-1	-	Baseline	-	+	-	+	1093	282.5	178.5	210.9	2.79	35	153.62	19.67	276	312	70
					12 W	-	+	-	+	28.4	175.9	17.6	20.6	0.5	6	166.89	5.66	390	398	76
					24 W	-	-	-	+	65.3	207.7	33.3	30.5	0.5	9	171.47	6.56	409	432	78
8	49/M	23.6	-	+	Baseline	+	+	+	+	850.8	475.4	47.4	92.2	18.22	29	1243.2	14.34	273	288	65
					12 W	+	+	+	+	58.6	295.6	25.2	33.1	2.5	16	574.33	7.23	386	437	80
					24 W	+	+	+	+	55.6	227.9	16.2	24.6	0.64	23	291.22	5.35	428	495	77
9	73/W	22.5	-	-	Baseline	+	+	+	+	11,075.3	791.5	360	258.5	14.41	51	982.53	7.68	400	200	40
					12 W	+	+	+	+	2060.8	504	93.9	27.5	0.5	8	185.97	6.25	426	470	59
					24 W	+	+	+	+	1980.2	307	31.7	24.2	2.93	5	202.13	6.67	438	485	66
10	81/F	22.7	+	+	Baseline	+	+	+	+	2905	619.9	192	94.2	7.4	69	123.9	23.57	357	270	74
					12 W	+	+	+	+	777	350.9	80.9	49.2	0.71	23	98.28	12.9	408	310	77
					24 W	+	+	+	+	68	334	34.2	37	0.61	15	65.26	9.42	460	370	78

Background/Purpose: Connective tissue disease-associated interstitial lung disease(CTD-ILD) represents a significant cause of mortality among patients. Presently, research on treatment options for CTD-ILD is limited, with most evidence derived from studies involving patients with systemic sclerosis-associated ILD (SSc-ILD). Each type of CTD possesses unique clinical characteristics, and the concurrent ILD manifestations vary, necessitating tailored treatment strategies. Furthermore, there is a lack of consensus regarding the timing, dosage, duration, and tapering of various medications.

Methods: Patients with severe ILD, characterized by pronounced shortness of breath and an oxygenation index below 300, were treated with a combination of glucocorticoids (GCs), Rituximab (RTX) at a dosage of 375 mg/m^2 per week for four weeks, and Telitacicept at a dosage of 160 mg per week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1:Chest CT scans at baseline and after 6 months of treament（pSS-ILD）

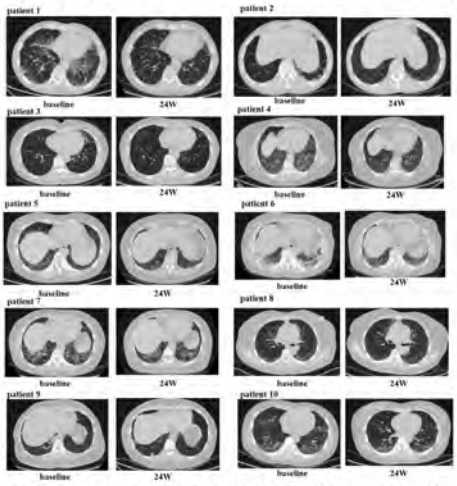


Figure 2:Chest CT scans at baseline and after 6 months of treament（ASS-ILD）

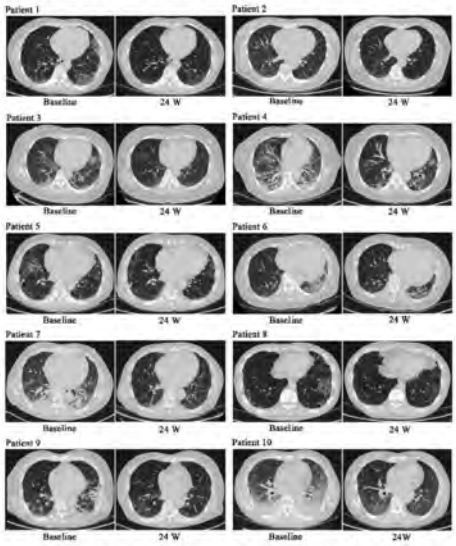
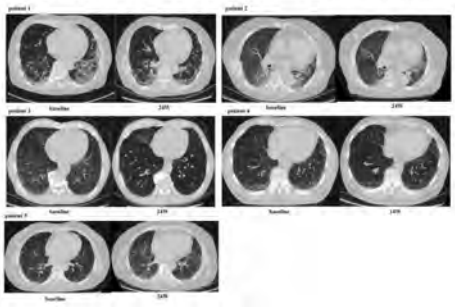


Figure 3:Chest CT scans at baseline and after 6 months of treament（RA-ILD）



Patients with refractory CTD-ILD who do not respond adequately to glucocorticoids (GCs) combined with conventional immunosuppressants, those who struggle to reduce GC dosage, those at high risk of infection, those who refuse high-dose GCs or traditional therapies, and those with additional connective tissue diseases or other systemic damage were treated with Telitacicept 160 mg, administered subcutaneously once a week. Follow up observation for 24 weeks, gradually reducing hormones and immunosuppressant, observing the improvement of CTD and ILD conditions in patients, as well as whether there are adverse reactions such as infection, allergies, organ damage.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of twenty-five patients were included in the study, ten patients with pSS-associated ILD, ten patients with ASS-associated ILD and five patients with RA-ILD. During the treatment process, no adverse reactions were found in all 25 patients. All patients gradually reduced prednisone to 5-7.5 mg/day, while Telitacicept was extended to 160 mg/two weeks. The disease activity has decreased. Chest CT scans revealed varying degrees of reduction in bilateral lung lesions, and lung function demonstrated significant improvement, with FVC% and DLCO% increased, along with the 6MWT elevated.

Conclusion: This is the first clinical trial of the use of Telitacicept for the treatment of CTD-ILD. Our work indicates that the treatment of PSS-ILD, ASS-ILD, RA-ILD by using Telitacicept has achieved good therapeutic effects. Currently, there is insufficient evidence regarding the efficacy of Telitacicept for treating CTD-ILD. This clinical trial suggests that Telitacicept could be a potential option for CTD-ILD.

Disclosure: M. Sun: None; **X. Chen**: None; **Y. Zhou**: None; **Y. Yang**: None; **F. Xiao**: None; **h. dai**: None.

Abstract Number: 1362

Multimodal Spatial and Single-Cell Profiling of Synovial Tissue Reveals Macrophage Programs Associated with Biologic TherapyTreatment Response in Rheumatoid Arthritis

Mohammad Daud Khan[1], Matthew Dapas[2], Salina T Dominguez[1], Tyler Therron[3], Kathleen Aren[4], Mary Carns[5], Hadijat Makinde[5], Arthur M Mandelin[1], Eric M Ruderman[1], John F Seagrist[5], Ruth Misha[1], Carla Marie Cuda[5], Harris R Perlman[5] and Deborah Rachelle Winter[6], [1]Northwestern University, Chicago, [2]Northwestern University Feinberg School of Medicine, Chicago, IL, [3]Northwestern Feinberg School of Medicine, Chicago, IL, [4]Northwestern University Division of Rheumatology, Chicago, IL, [5]Northwestern University, Chicago, IL, [6]Northwestern University, Skokie, IL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease driven by persistent synovial inflammation and progressive joint damage. Selecting an effective biologic therapy remains a costly, time-consuming trial-and-error process, as blood-based biomarkers poorly predict therapeutic response. In this study, we analyzed synovial tissue from RA patients by integrating single-cell and spatial transcriptomics to identify tissue-resident immune populations, particularly macrophage subsets, associated with response or resistance to therapy

Methods: Samples from minimally invasive, ultrasound-guided synovial biopsies were collected at baseline (n=15) and 12-week follow-up (n=6) from RA patients prior to start of a new DMARD (responders n=8; non-responders n=6; dropped out n=1) under IRB-approved protocols with informed consent. Samples were dissociated, enriched for $CD45^+$ or $CD45^+CD11b^+$ cells, and processed on the 10X Genomics Chromium platform to generate libraries for single-cell RNA sequencing with cell-surface protein detection (CITE-seq). Adjacent sections were analyzed with 10X Xenium (n=3, 196-gene panel) and NanoString CosMx (n=1, 1,000-gene panel) platforms to profile spatially resolved gene expression of synovial tissue at single-cell resolution.

Results: From the synovial CITE-seq analysis, five major immune populations were identified: myeloid cells, T cells, B cells, plasma cells, and mast cells. Clinical response stratification of patients revealed that baseline samples from non-responders exhibited increased T cells proportions compared to responders. However, the T cell to myeloid ratio tended to decrease in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

these patients following therapy. In the myeloid compartment, the FCN1+S100A12 macrophage subpopulation was enriched in non-responders, but decreased after treatment. On the other hand, the MERTK^{+}LYVE1^{+} and TIMD4 subpopulations were depleted in responders but both increased after treatment. Spatial molecular imaging by CosMx revealed layered tissue organization, with transcriptionally distinct macrophages (including MERTK+LYVE1+) and fibroblasts at the synovial lining, and sub-lining macrophages, stromal, vascular, and immune cells occupying interstitial and perivascular zones. Xenium spatial profiling confirmed a compartmentalized immune–stromal landscape with lymphocytes forming discrete follicle-like clusters, supporting spatially organized immune–stromal niches in RA.

Conclusion: Our results demonstrating that TIMD4^{+} and SPP1^{+} macrophages in non-responders reflects persistent synovial inflammation despite therapy, whilesynovial lining MERTK^{+}LYVE1^{+} and TIMD4+ expansion indicates a broader tissue-adaptive programmacrophages are enriched in responders support prior observations that these cells are necessary for synovial health. The opposing trends in the myeloid compartment suggest that deciphering the interactions between cells is critical to understanding treatment response. Our integrated single-cell and spatial analysis highlights macrophage subset dynamics and immune–stromal organization linked to treatment outcomes, offering new insights into RA pathogenesis and therapeutic resistance.

Disclosure: M. Khan: None; **M. Dapas**: None; **S. Dominguez**: None; **T. Therron**: None; **K. Aren**: None; **M. Carns**: None; **H. Makinde**: None; **A. Mandelin**: None; **E. Ruderman**: None; **J. Seagrist**: None; **R. Misha**: None; **C. Cuda**: None; **H. Perlman**: AbbVie/Abbott, 2; **D. Winter**: None.

Abstract Number: 1363

Evaluation of the Clinical Outcome of Baricitinib in Patients with Rheumatoid Arthritis from Multi-center Collaborative Study in Japan: Sub-analysis for Difficult-to-treat RA.

Naoki Kondo and Nariaki Hao, Division of Orthopedic Surgery, Niigata University Medical and Dental General Hospital, Niigata, Japan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The aim is to examine the efficacy and safety of baricitinib (BARI) in Japanese rheumatoid arthritis (RA) patients in real clinical practice and is to perform a subgroup analysis dividing cases into difficult-to-treat RA (D2TRA) and non-D2TRA.

Methods: This study involved 192 patients with RA (39 men, 153 women) who were administered with BARI. We examined patient background, treatment response at 52 weeks after initiation, continuation rate, and adverse events. We analyzed cases categorized as meeting the definition of D2TRA and those that did not in a similar manner.

Results: The mean age of enrolled patients was 66.0±13 years, and the mean disease duration was 13.4±11.4 years. Rheumatoid factor and anti-CCP antibody were positive in 77% and 76% of patients, respectively, with 9.9% of patients being negative for both antibodies. Prednisolone (PSL) and methotrexate (MTX) were co-administered in 74 cases (5.5 ±3.3 mg/day) and 85 cases (7.9±2.7 mg/week), respectively. There were 56 naive cases of biological agents/JAK inhibitors,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table1. The demographic data of difficult-to-treat RA (D2TRA) and non D2TRA groups. Rheumatoid factor value at the baseline in D2TRA shows significantly higher than that in nonD2TRA.

Table 1

	D2TRA	Non D2TRA	
Cases	62	130	
Men: Women	11: 51	28:102	
Age (years old)	63 [26-83]	68 [35-91]	
RA duration (years)	14 [1.7-31]	13.1 [0.1-54.9]	
2mg: 4mg of baricitinib dose/day	22:40	66:64	
% of 4mg of baricitinib	63	49	
Anti-CCP antibody :Positivity rate (%)	86	82	
Anti-CCP Ab Titer (IU/l)	269 [0.5-1200]	263 [0.5-1958	
RF; Positivity rate (%)	88 %	89 %	
RF Titer (IU/l)	262 [5-2261]	138 [5- 1720]	p<0.05

58 cases who received a second agent, and 78 cases who were introduced to agents after the third. The continuation rate at 52 weeks after starting BARI was 76%, and CDAI and DAS28-ESR(4) significantly decreased from 17.3±11.2, 4.0±1.5 to 5.2±4.5 ($p< 0.05$), 2.6±0.9 ($p< 0.05$), respectively. The number of PSL co-administered cases at 52 weeks decreased to 38 cases (3.7±2.1 mg). The occurrence of herpes zoster during the observation period was 4 cases (2.1%). Events leading to the discontinuation of BARI included 32 cases of primary ineffectiveness, 3 cases of secondary ineffectiveness, 10 cases of adverse events (disseminated herpes zoster, pericarditis, dizziness, onset of dermatomyositis, diverticulitis, death due to pneumonia, urticaria, anemia, ileus, mood discomfort), and 1 unknown case. There were 62 cases of D2TRA and 130 of non-D2TRA. No significant differences were found in the ratio of females, age at initiation, disease duration of RA, proportion of the initial BARI dose of 4 mg/day, positive rate or titer of anti-CCP antibodies. While there was no difference in the positive rate of rheumatoid factor, the RF levels were significantly higher in D2TRA (262 vs 138 IU/l, $p< 0.05$). The continuation rate at 52 weeks after starting BARI was 62% for D2TRA and 81% for non-D2TRA, but no significant difference was observed. CDAI significantly decreased from initiation to 52 weeks, with no significant difference between the two groups. The DAS28-ESR(4) before initiation was 4.27 for D2TRA and 4.00 for non-D2TRA, showing no significant difference, but it was significantly higher for D2TRA at 52 weeks after initiation (2.94 vs 2.47, $p< 0.05$). The DAS remission rate was 40% for D2TRA and 65% for non-D2TRA. The ineffectiveness discontinuation cases were 26% for D2TRA and 15% for non-D2TRA. The discontinuation cases due to adverse events were 8% for D2TRA and 4.6% for non-D2TRA, with no significant differences observed.

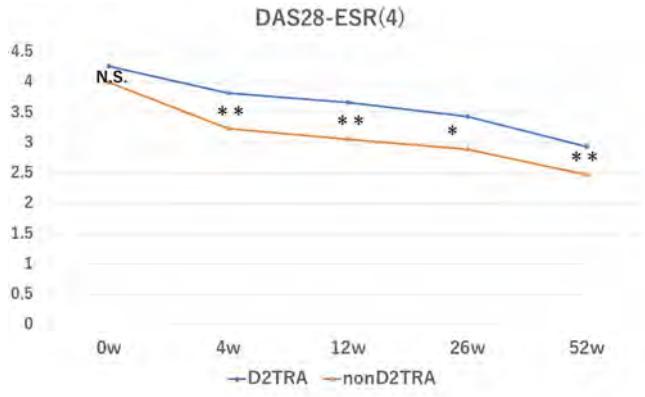


Figure 1

Figure 1. The time course of DAS28-ESR(4) after the baricitinib. In the administration of baricitinib, no significant difference between the difficult-to-treat RA (D2TRA) and non D2TRA. However, 4, 12, 26, and 52 weeks after the administration, DAS28-ESR(4) in D2TRA is significantly higher than that in nonD2TRA. N.S.; not significant difference, *; $p<0.05$, **; $p<0.01$.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: BARI significantly reduced disease activity and showed a high continuation rate. Serious adverse events were infrequent, confirming efficacy and safety in real clinical practice. BARI did not demonstrate the comparable efficacy in D2TRA cases compared to non-D2TRA.

Disclosure: N. Kondo: None; **N. Hao**: None.

Abstract Number: 1364

Efficacy Of Ayurvedic Treatment Versus Placebo, Each In Combination With Methotrexate In Early RA Over 20 Weeks: An Exploratory Randomized Control Trial

Prativa Priyadarshani Sethi[1], Venkatesh Srinivasa Pai[2], Rajat Ranka[2], Avneet Kumar Gupta[3], Ashish Baweja[4], ritu sangwan[5], Abhishek Rai[6], Sryla Punjadath[1] and Nithya Maskani[2], [1]All India Institute of Medical Sciences, Rishikesh, Rishikesh, Uttarakhand, India, [2]AIIMS RISHIKESH, Rishikesh, Uttarakhand, India, [3]AIIMS RISHIKESH, Lucknow, Uttar Pradesh, India, [4]Medanta, The Medicity, Gurugram, New Delhi, Delhi, India, [5]AIIMS ,Rishikesh, Rishikesh, Uttarakhand, India, [6]AIIMS ,RISHIKESH, Bhilai, Chhattisgarh, India

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Early rheumatoid arthritis (RA) is a critical therapeutic window where prompt treatment targeting remission or low disease activity can significantly reduce long-term disability and systemic complications. Methotrexate (MTX) remains the standard of care, but interest in complementary approaches, particularly Ayurveda—a WHO-recognized traditional Indian medical system with anti-inflammatory and immunomodulatory properties—is increasing. A prior pilot RCT suggested potential benefit of Ayurvedic formulations when combined with MTX, without added toxicity. We conducted a double-blind, randomized controlled trial to evaluate the efficacy and safety of combining Ayurvedic treatment with methotrexate versus methotrexate with placebo in early RA, hypothesizing greater benefit with combination therapy in early disease.

Methods: This exploratory, double-blind RCT was conducted over 15 months (Aug 2023–Dec 2024) in patients fulfilling 2010 ACR/EULAR RA criteria with ≤1 year disease duration. Patients (n=140) were randomized into two groups: MTX + Ayurveda (n=70) or MTX + Placebo (n=70). Ayurvedic treatment included Panchkol churna, Erand oil, Rasna Saptak Kwath, and Singhnad guggul administered sequentially alongside stable MTX dosing (15–25 mg/week). Blinding was maintained for participants and outcome assessors. Data were represented in mean (SD) and analysed as treated. Fisher's exact test and Chi-Square tests were used for categorical variables. Group comparisons were done at baseline and 20 weeks using t-tests and Wilcoxon-Mann Whitney U Test for parametric and nonparametric data respectively (figure 1).

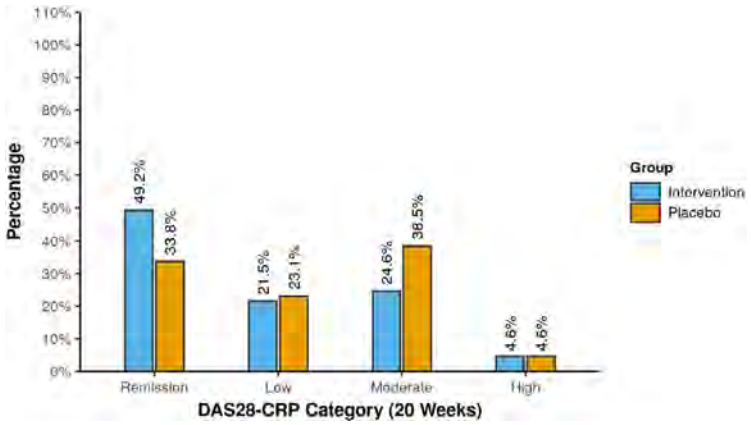
Results: Of 140 enrolled, 130 patients completed 20 weeks. There was no statistical significant difference among two groups in terms of baseline disease activity including age, rheumatoid factor and anti-CCP positivity. At 20 weeks, numerically more patients in the Ayurveda + MTX (49.2%) arm achieved remission as compared to placebo+ MTX (33.8%) by DAS28CRP, though between-group differences were not statistically significant (Figure 2). However, mean reduction in DAS28-CRP, DAS28-ESR, CDAI, and SDAI scores from baseline to 20 weeks was significantly greater in the combination arm ($p< 0.05$ for all). ACR20 and ACR50 response rates were also significantly higher in the Ayurveda + MTX group (ACR20: 90.8% vs 70.8%, p=0.007; ACR50: 81.5% vs 60.0%, p=0.012) (Figure 3). Adverse events, mostly gastrointestinal, were comparable between groups and mild.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disease activity	Ayurveda + MTX Mean (SD)		Placebo + MTX Mean (SD)		20 weeks-Baseline
	Baseline	20 weeks	Baseline	20 weeks	P value
TJC	12.31 (8.06)	2.45 (3.18)	9.64 (7.84)	2.75 (3.27)	0.012
SJC	5.84 (4.86)	0.82 (1.88)	4.90 (4.37)	0.86 (1.51)	0.097
PtGA	8.11 (2.03)	3.41 (1.64)	8.03 (2.30)	4.01 (2.10)	0.150
PhGA	7.69 (2.22)	2.37 (1.97)	7.44 (2.75)	2.88 (2.14)	0.205
ESR (mm/Hr)	56.50 (32.76)	28.71 (17.17)	49.51 (24.61)	31.74 (16.67)	0.018
CRP (mg/L)	25.88 (34.97)	6.24 (12.66)	19.59 (26.36)	6.65 (6.52)	0.018
DAS28-CRP	**5.51 (1.29)**	**2.73 (1.15)**	**5.13 (1.20)**	**3.03 (1.11)**	**0.003**
DAS28-ESR	**6.25 (1.15)**	**3.46 (1.20)**	**5.92 (1.12)**	**3.76 (1.15)**	**0.008**
CDAI	**33.93 (13.79)**	**9.04 (7.61)**	**29.93 (13.29)**	**10.50 (7.89)**	**0.019**
SDAI	**36.46 (15.65)**	**9.67 (8.24)**	**31.78 (14.23)**	**11.17 (8.14)**	**0.011**
HAQDI	1.35 (0.70)	0.29 (0.35)	1.18 (0.62)	0.25 (0.34)	0.385
Remission rate at 20 Weeks (DAS28-CRP), n (%)					
	Intervention	Placebo	Total	P value	
Remission	**32 (49.2%)**	**22 (33.8%)**	**54 (41.5%)**	0.266	
Low	14 (21.5%)	15 (23.1%)	29 (22.3%)		
Moderate	16 (24.6%)	25 (38.5%)	41 (31.5%)		
High	3 (4.6%)	3 (4.6%)	6 (4.6%)		
ACR Response Rate					
	Ayurveda + MTX, n (%)	Placebo + MTX, n (%)	χ^2	P value	
ACR20	**59 (90.8%)**	**46 (70.8%)**	**7.131**	**0.007**	
ACR50	**53 (81.5%)**	**39 (60.0%)**	**6.284**	**0.012**	
ACR70	24 (36.9%)	18 (27.7%)	0.879	0.348	
Adverse Reactions					
	Ayurveda + MTX, (n=70)	Placebo + MTX, (n=70)	P value		
Upper GI	19 (27.1%)	18 (25.7%)	0.848		
Lower GI	11 (15.7%)	6 (8.6%)	0.196		
Constitutional	7 (10.0%)	8 (11.4%)	0.785		
Lab Abnormalities	2 (2.9%)	1 (1.4%)	1.000		

Significant associations (p<0.05) indicated in bold letters, Abbreviations: MTX: methotrexate, SD: standard deviation, DAS28: Disease activity score in 28 joints, ESR: Erythrocyte sedimentation rate, CRP: C- Reactive Protein, CDAI: Clinical disease activity score, SDAI: Simplified disease activity score, HAQDI: Health assessment questionnaire disability index, ACR: America college of rheumatology, GI: gastrointestinal

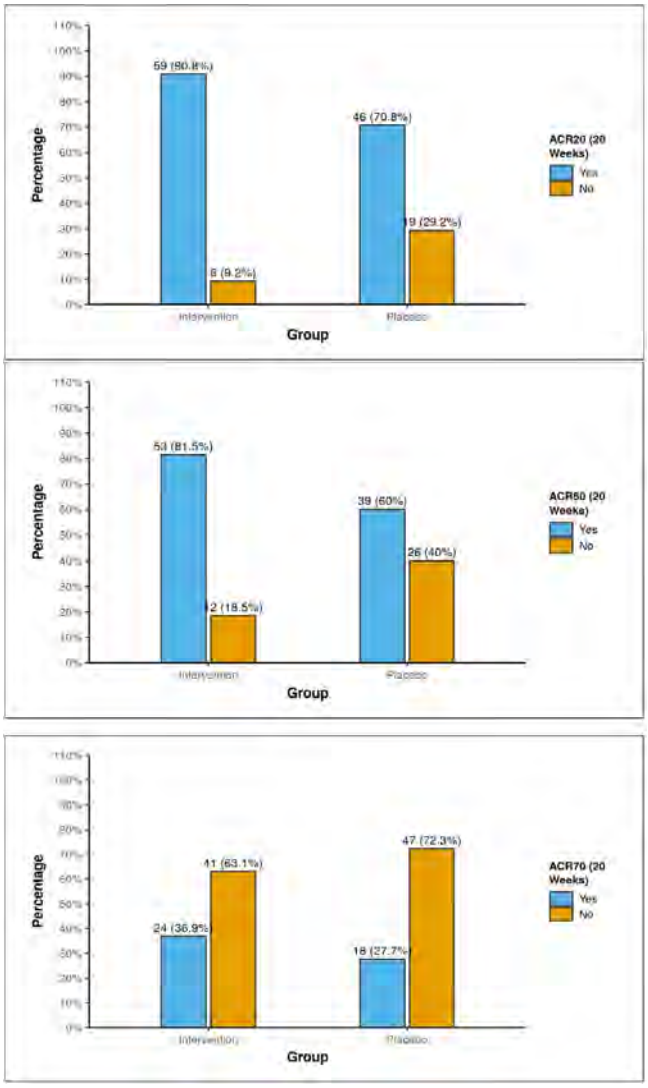
Comparison of disease activity, remission and response rate at 20 weeks between intervention and placebo groups



Remission rate between two groups as per DAS28CRP composite disease activity index

Conclusion: In early RA, adjunctive Ayurvedic therapy with methotrexate led to significantly greater improvements in disease activity and ACR response rates over 20 weeks, with a favorable safety profile. These findings support further investigation of integrative approaches in early disease stages, balancing traditional systems with modern clinical rigor to optimize patient outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



ACR response rate between two groups

Disclosure: P. Sethi: None; **V. Pai**: None; **R. Ranka**: None; **A. Gupta**: None; **A. Baweja**: None; **r. sangwan**: None; **A. Rai**: None; **S. Punjadath**: None; **N. Maskani**: None.

Abstract Number: 1365

Economic impact of early treatment and strict disease control in rheumatoid arthritis: a cost-minimization approach concerning biological therapy

Raianni Rúbia Pacheco Silva[1], Daniel da Silva Pereira Curado[2], Paula Cristina Montina[2], Everton Nunes da Silva[3], Ana Paula Monteiro Gomides[2], Rina Dalva Neubarth Giorgi[4], Leticia Rocha Pereira[5], Sebastião Cezar Radominski[6], Ivanio Alves Pereira[7], Maria Fernanda Brandão de Resende Guimarães[8], Manoel Barros Bertolo[9], Paulo Louzada Junior[10], Maria de Fátima Lobato da Cunha Sauma[11], Karina Rossi Bonfiglioli[5], Claiton Viegas Brenol[12], Geraldo da Rocha Castelar Pinheiro[13], Cleandro Pires de Albuquerque[2] and Licia Maria Henrique da Mota[14], [1]Universidade de Brasília, Brasília, Distrito Federal, Brazil, [2]Universidade de Brasília, Brasília, Brazil, [3]Universidade de Brasília, brasilia, Brazil, [4]IAMSPE, São Paulo, Brazil, [5]Hospital do Servidor Público Estadual de São Paulo, São Paulo, Brazil, [6]UFPR, Curitiba, Brazil, [7]UFSC, Florianopolis, Brazil, [8]UFMG, Belo Horizonte, Brazil, [9]Unicamp, Campinas, Brazil, [10]USP-RP, Ribeirão Preto, Brazil, [11]UFPA, Belem, Brazil, [12]UFRGS, Porto Alegre, Brazil, [13]UERJ, Rio de Janeiro, Brazil, [14]UNB, Brasilia, Distrito Federal, Brazil

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, progressive, potentially disabling autoimmune disease, with substantial economic burden, particularly related to its high-cost pharmacological treatment. Early treatment, goal-oriented management (treat to target, T2T), and strict disease control have been shown to modify the course of the disease, and might influence its economic impact.This cost-minimization study aimed to estimate the financial impact associated with biological disease-modifying antirheumatic drugs (bDMARDs) use in patients with RA treated with a strict control strategy versus conventional management under real-life conditions.

Methods: 256 participants meeting the ACR/EULAR 2010 classification criteria for RA, diagnosed within one year of symptoms onset, distributed into one strict control and three conventional management groups (64 patients per group) were assessed. Cost data for a comprehensive range of bDMARDs available in clinical practice during the study period (2018–2022) were sourced from public procurement records, based on annual maintenance doses in adults with RA. Potential cost reduction was estimated by multiplying the difference in bDMARD usage proportions by the weighted cost (based on market share) over one- and five-year horizons. Deterministic (Tornado diagram) and probabilistic (Monte Carlo) sensitivity analyses were performed using minimum and maximum parameter values to address uncertainty. A 95% confidence interval (CI) was applied to the proportional differences in bDMARD use between groups. Beta distributions were used for proportions (bDMARD use and market share), and gamma distributions for costs and patient counts. All costs are presented in U.S. dollars, adjusted for inflation to reflect May 2024 price levels.

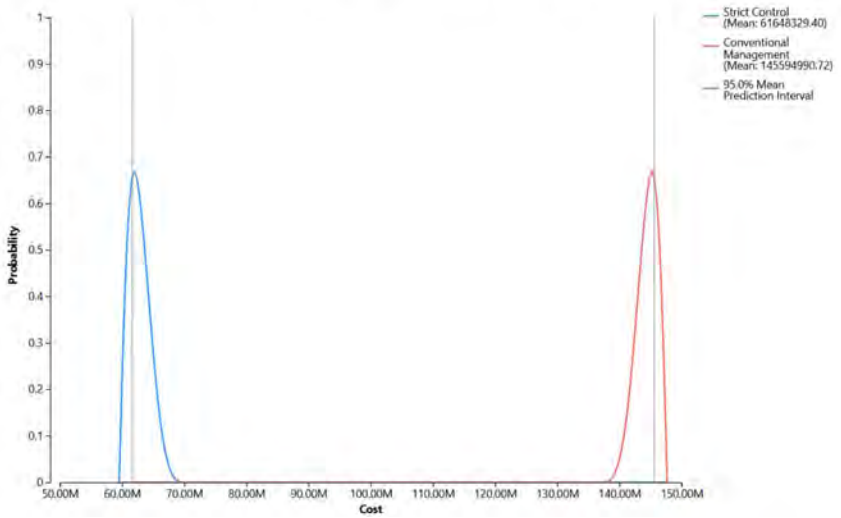
Results: Table 1 summarizes the background characteristics and clinical outcomes of the study groups. Average annual spending on bDMARDs during the study period amounted to approximately USD 151 million. National projections based on the strict control scenario suggested potential annual savings of USD 83.94 (95% CI: USD 40.13–113.97) million in 2024, representing a 55.6% (95% CI: 26.6%-75.5%) reduction in bDMARD expenditures compared to conventional management. Assuming stable population size, therapeutic strategies, and drug prices, cumulative savings over five years could reach up to USD 419.73 (95%CI: USD 200,65 - USD 569,85) million (Figures 1 and 2).

Table 1 – Comparison of Early Rheumatoid Arthritis Treatment: Strict Control vs. Conventional Management

	Comparison Groups				
	Strict Control*	Convencional** 1	Convencional** 2	Convencional** 3	p-valor †
Clinical Characteristics	N=64	N=64	N=64	N=64	
Female Sex (%)	95,3	89,1	87,5	81,3	0,103
White Race (%)	57,5	59,1	59,4	57,8	0,055
Positive FR (%)	75,0	75,0	78,1	67,7	0,594
Age, Mean (SD)	53,0 (13,3)	55,6 (11,3)	51,7 (13,9)	54,7 (10,3)	0,306
Education years, Mean (SD)	7,9 (4,8)	8,1 (4,5)	9,1 (4,2)	8,8 (4,3)	0,412
Disease Duration, Mean (SD)	54,6 (51,9)	103,9 (48,7)	90,1 (46,1)	98,6 (48,0)	0,120
Corticosteroid Use (%)	1,6	54,7	59,4	54,7	<0,001§
bDMARD Use (%)	14,1	37,5	28,1	34,4	0,017§
Erosive Disease (%)	7,9	47,6	44,4	50,8	<0,001§
DAS28-ESR Remission (%)	48,4	16,4	28,8	33,3	0,002§
HAQ-DI Score, Mean (SD)	0,55 (0,63)	1,03 (0,74)	0,82 (0,71)	0,75 (0,73)	0,002§
DAS28-ESR Score, Mean (SD)	2,9 (1,3)	3,61 (0,74)	3,4 (1,3)	3,2 (1,4)	0,018§

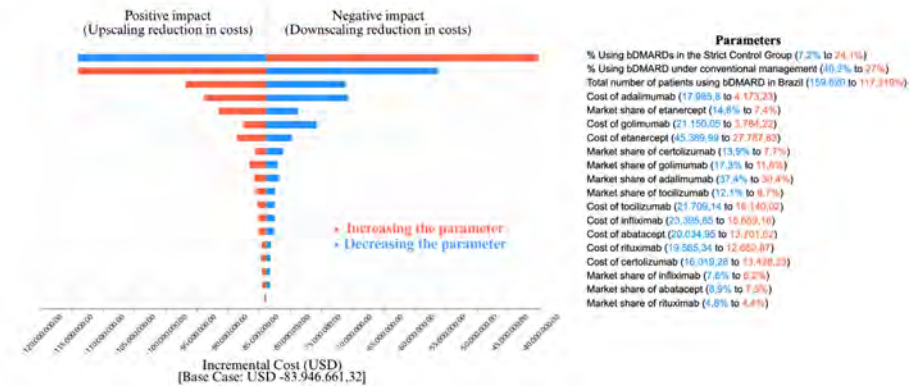
Legend: * Strict disease control group. ** Groups under conventional management of Rheumatoid Arthritis. † For categorical variables, Pearson's chi-square test was used for comparisons; for continuous variables, analysis of variance (ANOVA) with Welch's correction was applied when appropriate. § Characteristics for which at least one group significantly differed from the others ($p < 0.05$).

Figure 1. Distribution of bDMARD-Related Costs Across the Analyzed Rheumatoid Arthritis Treatment Strategies (Strict Control vs. Conventional Management), Considering the Population Eligible for bDMARD Therapy Within the Public Healthcare System



Legend: biological disease-modifying antirheumatic drugs (bDMARD)

Figure 2. Deterministic Sensitive Analysis (Tornado Diagram) of the projected incremental cost of strict disease control vs. conventional management, concerning bDMARD utilization for the treatment of rheumatoid arthritis, at current prices in 2024, expressed in American Dollars (USD).



Conclusion: A strict control strategy compared to conventional management in early RA showed substantial expenditure reductions concerning the usage of bDMARD, along with improved clinical outcomes. These findings support that, under real-life conditions of healthcare systems, the implementation of strict disease control in early RA is a feasible and potentially cost-saving approach.

Disclosure: R. Pacheco Silva: None; **D. da Silva Pereira Curado**: None; **P. Montina**: None; **E. Nunes da Silva**: None; **A. Monteiro Gomides**: None; **R. Neubarth Giorgi**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **L. Rocha Pereira**: None; **S. Radominski**: AbbVie/Abbott, 6, Amgen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Pfizer, 6, Roche, 6; **I. Alves Pereira**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, Pfizer, 6, Roche, 6, UCB, 6; **M. Brandão de Resende Guimarães**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **M. Barros Bertolo**: AbbVie/Abbott, 6, Pfizer, 6; **P. Louzada Junior**: None; **M. Lobato da Cunha Sauma**: None; **K. Rossi Bonfiglioli**: None; **C. Viegas Brenol**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **G. da Rocha Castelar Pinheiro**: None; **C. Pires de Albuquerque**: None; **L. Henrique da Mota**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1366

Cost Per Responder Analysis of Certolizumab Pegol Versus Adalimumab in Patients with Moderate to Severe Active Rheumatoid Arthritis and High Rheumatoid Factor Levels: A Payer Perspective from Canada and Brazil

Rémi Marty[1], Baran Ufuktepe[2], Nicola Tilt[3], Flore Decuypere[4], Angela Blake[3], Sandeep Kiri[3] and Mohammed Soomro[3], [1]UCB Pharma, Brussels, Belgium, Anderlecht, Belgium, [2]UCB Pharma Istanbul, Turkey, istanbul, Turkey, [3]UCB Pharma, Slough, United Kingdom, Slough, United Kingdom, [4]UCB Pharma Brussels, Belgium, Brussels, Belgium

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: According to the 2022 EULAR recommendations for the management of rheumatoid arthritis (RA), the presence of rheumatoid factor (RF), particularly at high levels, is recognised as a poor prognostic factor.[1] In patients with poor prognosis who fail to achieve treatment targets with initial conventional synthetic DMARD (csDMARD) therapy, the addition of a biological DMARD (bDMARD) is recommended.[2,3] Despite this recommendation, patients with high RF levels are associated with reduced response to monoclonal anti-TNF therapies.[4] Certolizumab pegol (CZP), a TNF inhibitor without a fragment crystallizable (Fc) region, may offer improved efficacy for these patients.[5,6] Given the unmet need in patients with RA and high RF levels, who are less likely to respond to Fc-containing TNF inhibitors and are considered at poor prognostic risk, we evaluated the cost per responder (CPR) for CZP versus adalimumab (ADA) to support value-based treatment decisions from the perspective of Canada and Brazil over a 104 week time horizon.

Methods: A 104-week (Wk) CPR model was developed using data from EXXELERATE,[7] a phase IV, randomised, head-to-head trial comparing CZP plus methotrexate (MTX) with ADA plus MTX, in patients with moderate to severe RA. Response rates were defined by achievement of low disease activity (LDA), measured as a Disease Activity Score 28 joints-C-reactive protein (DAS28-CRP) ≤2.7. CPR at Wk104 was calculated by multiplying the total number of doses administered over 104 weeks by the drug acquisition cost divided by the corresponding response rate. Treatment regimens followed the approved product labels: CZP 400 mg at Weeks 0, 2, and 4, followed by 200 mg every 2 weeks; ADA 40 mg every other week. Average prices were considered to derive ADA biosimilar costs.

Results: At Wk104, the LDA achievement rates were higher with CZP compared to ADA (42.5% vs 25.5%). The cost per LDA achievement for CZP vs ADA respectively, was CAD 94,348 vs CAD 97,828 in Canada, and BRL 156,203 vs BRL 793,888 in Brazil (Table 1 and 2).

A sensitivity analysis was performed to test the robustness of these findings under varying list-to-net pricing assumptions. Across multiple scenarios, CZP consistently maintained a more favourable cost profile compared to ADA, highlighting its potential value under a range of pricing conditions.

Conclusion: At Wk104, CZP at list price demonstrated a lower CPR compared to ADA biosimilar price in both Canada and Brazil. These findings suggest that, for patients with moderate to severe active rheumatoid arthritis and high rheumatoid factor levels, CZP may offer a more personalised and cost-effective treatment strategy, supporting more efficient allocation of healthcare resources and potentially reducing the budgetary burden for payers in Canadian and Brazilian healthcare settings.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Canada - Cost Per Responder in Local Currency

TNF-Alfa Inhibitors	LDA Response probability at Wk104 (%)[a]	Cost per patient over 104 weeks (CAD)	Cost per responder (CAD)
Certolizumab 400mg Wk 0, 2, and 4, then 200 mg Q2W	42.45	40,053	94,348
Adalimumab 40mg every other week	25.53	24,977	97,828

TNF: tumour necrosis factor; LDA: low disease activity; Q2W: every 2 weeks; Wk: week; CAD: Canadian dollar.

Table 2: Brazil - Cost Per Responder in Local Currency

TNF-Alfa Inhibitors	LDA Response probability at Wk104 (%)[a]	Cost per patient over 104 weeks (BRL)	Cost per responder (BRL)
Certolizumab 400mg Wk 0, 2, and 4, then 200 mg Q2W	42.45	66,312	156,203
Adalimumab 40mg every other week	25.53	202,695	793,888

TNF: tumour necrosis factor; LDA: low disease activity; Q2W: every 2 weeks; Wk: week; BRL: Brazilian Real.

References: 1. Smolen JS. Ann Rheum Dis. 2023;82(1):3–18; **2**. Cuchacovich M. Clin Rheumatol 2014;33(12):1707–14; **3**. Takeuchi T. Arthritis Res 2017;19:194, **4**. Pappas DA. Rheumatol Int 2021;41:585–93; **5**. Bidgood SR. ACR 2024; **6**. Smolen JS. Rheumatology. 2024;63(11):3015–24; **7**. Smolen JS. Lancet 2016; 388(10061):2763-2774.

Disclosure: R. Marty: UCB, 3, 11; **B. Ufuktepe**: UCB Pharma, 3, 11; **N. Tilt**: UCB, 3, 11; **F. Decuypere**: UCB, 3, 11; **A. Blake**: UCB, 3, 11; **S. Kiri**: UCB, 3, 11; **M. Soomro**: UCB, 3, 11.

Abstract Number: 1367

Molecular Signature Response Classifier Identifies Contribution of GLP-1 Therapy to TNF Inhibitor Response in Rheumatoid Arthritis Patients

Lixia Zhang[1], Angus Wong[2], Alex Jones[2], Sherry Guardiano[2], Reginald Seeto[2] and **Ryan T, Phan**[3], [1]Scipher Medicine, Plainsboro, NJ, [2]Scipher Medicine, Waltham, [3]Scipher Medicine, Los Gatos

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Tumor necrosis factor-α inhibitors (TNFi) are extensively utilized in the management of rheumatoid arthritis (RA). Therapeutic responses remain highly heterogeneous. Emerging evidence suggests glucagon-like peptide-1 (GLP-1) plays a role in the regulation of inflammatory processes relevant to RA pathophysiology and may influence TNFi efficacy in RA patients[1,2]. This study reports evidence of GLP-1 therapy contributing to TNFi response, documented by a validated molecular signature response classifier (MSRC) that predicts TNFi treatment outcomes[3].

Methods: Data obtained from two independent RA patient cohorts: NETWORK-004, an observational clinical study of 259 samples from 152 unique eligible patients designed to evaluate and validate MSRC[3] performance and real-world evidence (RWE) from 34,795 RA patients treated by 1623 physicians across 962 rheumatology clinics in 48 states in the US. GLP-1 treatment records obtained from open claims databases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics for NETWORK-004 study and Real-world cohort

	Category	NETWORK-004	Real World Cohort
Number of Unique Patient		152	34795
Number of Unique Practices		73	962
Number of Unique Physicians		N/A	1623
Gender (%)	Female	119 (78.3)	27266 (78.4)
	Male	33 (21.7)	7481 (21.5)
	Unknown	0 (0)	48 (0.1)
Ethnicity (%)	Not Hispanic or Latino	113 (74.3)	N/A
	Hispanic or Latino	35 (23.0)	N/A
	Not Reported	4 (2.6)	N/A
Age (mean (SD))		57.18 (14.18)	59.30 (16.09)
BMI (mean (SD))		30.76 (7.65)	30.08 (6.74)
BMI Category	Less than 30	73 (48.0)	18896 (54.3)
	Greater or equal to 30	79 (52.0)	15899 (45.7)
Patient Global Assessment (mean (SD))		52.74 (23.77)	53.04 (26.45)
Anti-CCP result (%)	Negative	77 (50.7)	20957 (60.2)
	Positive	75 (49.3)	13176 (37.9)
	Unknown	0 (0)	662 (1.9)

MSRC scores, ranging from 1 to 25, were evaluated for each patient. A higher MSRC score predicts greater likelihood of inadequate TNFi response. MSRC ≥18.5 is classified as having a very high likelihood of inadequate response.

Results: Study participants demographic information reported in table 1. The analysis of NETWORK-004 demonstrated although no direct linear correlation of body mass index (BMI) and MSRC was observed, a larger proportion of patients with BMI ≥30 (40.9%) compared to BMI < 30 (4.7%) exhibited MSRC score ≥18.5. The difference statistically constitutes a 9-fold increase (Fig 1a). Remarkedly, modeling BMI reduction of 10% to 20% would result in a reduction of MSRC median 8.4% to 17.6%, respectively, indicating that decreasing BMI may lead to decreasing the likelihood of inadequate TNFi response (Fig 1b).

Consistent with these findings, examination of the RWE cohort revealed that a larger proportion of patients with BMI ≥30 (24.1%) exhibited very high likelihood of inadequate TNFi response compared to BMI <30 (4.7%), documented by MSRC score ≥18.5 (Fig 2a). The impact of GLP-1 exposure in the RWE cohort was evaluated. Analysis showed GLP-1 patients

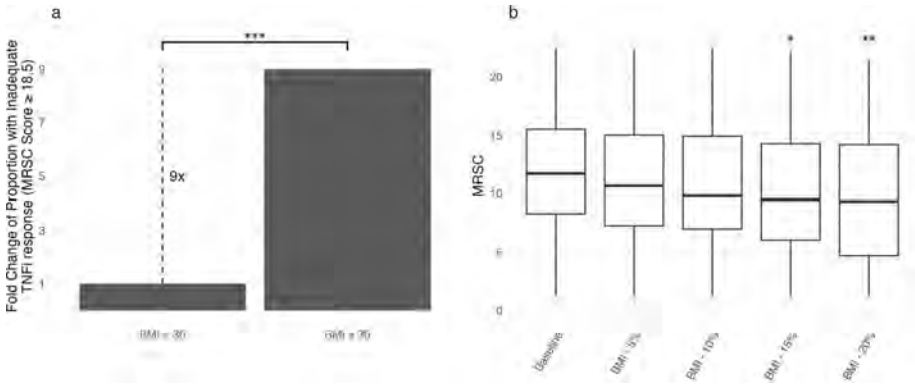


Figure 1. BMI Association between inadequate TNFi response predicted by MSRC in NETWORK-004 study. Figure 1a illustrates a 9-fold increase in the proportion of patients with MSRC scores ≥18.5 (<5% chance of TNFi response) among those with BMI ≥30 comparing to those with BMI < 30 in the NETWORK-004 cohort, as shown in bar charts with fold change on the y-axis. Figure 1b demonstrates the modeled downward shift in MSRC scores corresponding to hypothetical BMI reductions ranging from 5% to 20% relative to baseline.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

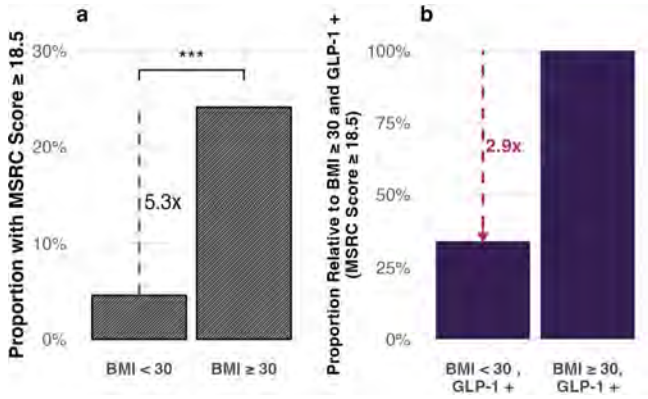


Figure 2. Real-world evidence from MSRC tested cohort. Figure 1a displays shaded bar charts presenting the proportion of patients with MSRC scores ≥18.5 (<5% chance of TNFi response), stratified by BMI group (BMI <30 vs. BMI ≥30) in the overall cohort, demonstrating a 5.3-fold increase in the higher BMI group. P-values were calculated using chi-square tests. Figure 1b depicts the proportion relative to BMI ≥30 among patients with concurrent or prior GLP-1 treatment, where a reduced 2.9-fold difference is presented.

achieving BMI < 30 demonstrated a significant reduction in TNFi inadequate response (9.0%) compared to patients with BMI ≥30 (26.5%). The reduction is approximately 194% and equivalent to 2.9-fold decreased likelihood of inadequate TNFi response for GLP-1 patients achieving BMI < 30 (Fig 2b).

Conclusion: In this study, GLP-1-based interventions, traditionally employed in the treatment of metabolic diseases, enhanced TNFi therapeutic efficacy in specific RA patient subgroups. Future randomized clinical trials are warranted to validate the efficacy of GLP-1 receptor agonists and TNF inhibition combined therapies for RA and potentially other autoimmune diseases. In precision medicine, MSRC can serve as a biomarker to identify patients who may benefit from these combinatorial therapeutic regimens.

1. Mehdi SF et al. *Front Immunol*. 2023;14:1148209.
2. Bendotti G et al. *Pharmacol Res*. 2022;182:106320.
3. Cohen S et al. *Rheumatol Ther*. 2021;8(3):1159–1176.

Disclosure: L. Zhang: Scipher Medicine, 3; **A. Wong**: Scipher Medicine, 3; **A. Jones**: Scipher Medicine, 3; **S. Guardiano**: Scipher Medicine, 3; **R. Seeto**: Scipher Medicine, 3, 4; **R. Phan**: Scipher Medicine, 2, 3.

Abstract Number: 1368

Thrombocytosis Predicts Response to Biologic and Targeted Synthetic DMARDs in Rheumatoid Arthritis: Data from the Korean KOBIO Registry

Se Hee Kim[1] and kyung-Ann Lee[2], [1]Kyung Hee University College of Medicine, Seoul, Republic of Korea, [2]Soonchunhyang University Hospital Seoul: Soonchunhyang University Hospital, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aimed to evaluate the clinical characteristics of thrombocytosis, its relationship with disease activity and joint involvement, and its influence on the effectiveness of biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) in patients with rheumatoid arthritis (RA).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Risk factors for thrombocytosis in patients with RA were analyzed using logistic regression analysis. SJC, swollen joint count; TJC, tender joint count; WBC, white blood cell; ESR, erythrocyte sediment rat; CRP, C-reactive protein; DAS28-CRP, Disease Activity Score in 28 joints based on C-reactive protein; SDAI, Simple Disease Activity Index; RAPID, Routine Assessment of Patient Index Data; DM, diabetes mellitus; BOOP, bronchiolitis obliterans organizing pneumonia; PGA, patient's global assessment; PhGA, physician's global assessment. *statistically significant (p<0.005). ** statistically significant (p<0.010).

Risk Factor	Univariable analysis		Multivariable analysis	
	OR (95%CI)	p-value	OR (95%CI)	p-value
SJC	1.006(0.929-1.088)	0.889	-	-
TJC	0.986(0.923-1.050)	0.652	-	-
WBC	1.000(1.000-1.000)	<0.001*	1.000(1.000-1.000)	<0.001*
Hemoglobin	0.803(0.678-0.952)	0.011*	0.797(0.675-0.941)	0.007*
ESR	1.021(1.013-1.030)	<0.001*	1.028(1.020-1.036)	<0.001*
CRP	1.063(0.982-1.150)	0.130	-	-
DAS28-CRP	1.361(0.712-2.603)	0.351	-	-
SDAI	0.989(0.910-1.075)	0.793	-	-
RAPID	1.005(0.952-1.061)	0.862	-	-
DM	0.567(0.308-1.044)	0.069**	-	-
BOOP	0.743(0.011-51.827)	0.891	-	-
PGA	1.100(0.910-1.331)	0.325	-	-
PhGA	0.935(0.784-1.115)	0.455	-	-

Methods: Data from 2,104 patients with RA from the Korean College of Rheumatology Biologics and Targeted Therapy registry were analyzed. Thrombocytosis was defined as a platelet count >450 × 10^9/L. Baseline demographics, comorbidities, laboratory results, joint involvement, and disease activity indices (DAS28, SDAI, CDAI, RAPID3, ESR, CRP) were compared between patients with and without thrombocytosis. Responses to b/tsDMARDs over 1 year were assessed using ACR and EULAR criteria. Logistic regression identified independent predictors of thrombocytosis.

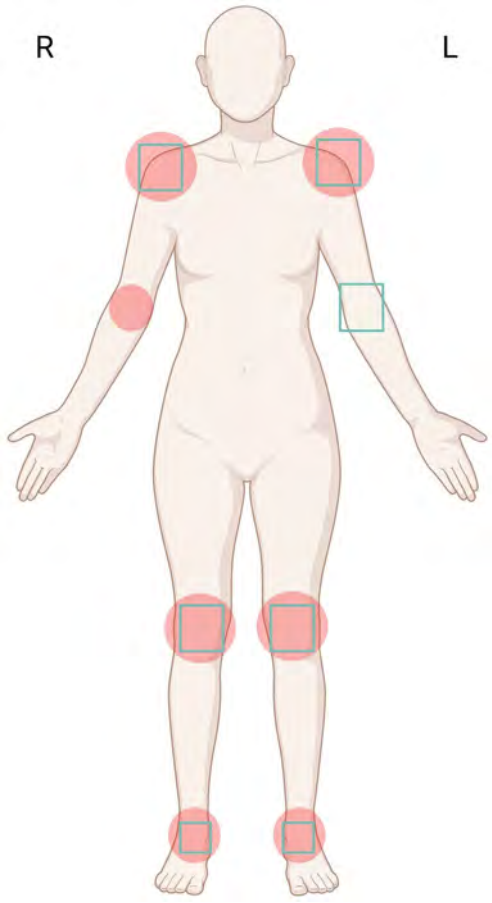


Figure. Involvement of swollen and tender joints in the thrombocytosis group. Swollen and tender joint involvement was more frequent in the thrombocytosis group. Transparent red circles indicate greater involvement of swollen joints, while green squares represent joints with increased tenderness in the thrombocytosis group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

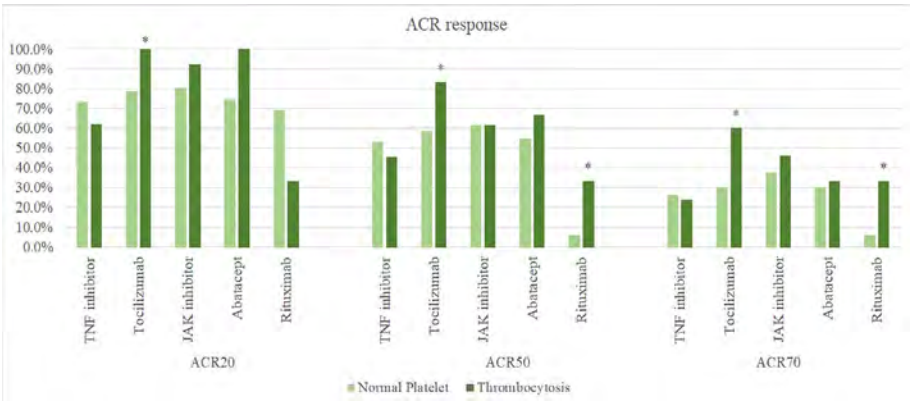


Figure. ACR response according to b/tsDMARDs. ACR, American College of Rheumatology; b/tsDMARDs, biologic and targeted synthetic disease-modifying antirheumatic drugs; TNF, tumor necrosis factor; JAK, Janus kinase. *statistically significant (p<0.005).

Results: Thrombocytosis was found in 97 patients (4.6%). Compared to those with normal platelet counts, these patients had significantly higher ESR, CRP, and WBC counts, lower hemoglobin, higher disease activity scores, and more frequent large joint involvement. Anemia, diabetes, obesity, and bronchiolitis obliterans organizing pneumonia were also more common. At 1 year, ACR70 response rate was significantly higher in the thrombocytosis group (39.2% vs. 29.0%, p=0.041), while ACR20 and ACR50 responses were similar. IL-6 inhibitors, particularly tocilizumab, were more effective in patients with thrombocytosis, achieving higher ACR20/50/70 responses and greater reductions in platelet count and inflammatory markers. Other b/tsDMARDs, such as TNF and JAK inhibitors displayed favorable but non-significant trends. Multivariate logistic regression identified higher WBC count, lower hemoglobin, and elevated ESR as independent predictors of thrombocytosis in RA.

Conclusion: Thrombocytosis in RA indicates increased disease activity and greater joint involvement. Monitoring platelet counts helps assess disease severity and tailor treatments, particularly IL-6 targeting therapies.

Disclosure: S. Kim: None; **k. Lee**: None.

Abstract Number: 1369

Impact of SGLT2 Inhibitors and GLP-1 Agonists on RA Flares in Patients on DMARD Therapy: A Retrospective Study

Shreya Sakthivel[1], Mitch Karpman[2], Liam Oland[3] and Amer Aldamouk[4], [1]Anne Arundel Medical Center, Washington DC, DC, [2]Anne Arundel Medical Center, Annapolis, [3]Saba University School of Medicine, Annapolis, [4]Anne Arundel Medical Center, Washington, DC

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease driven by T- and B-cell activation and pro-inflammatory cytokines such as TNF-α and IL-6 and is managed by disease-modifying antirheumatic drugs (DMARDs) [1]. SGLT2 inhibitors and GLP-1 receptor agonists, developed for type 2 diabetes, have shown cardiovascular, renal, and potential anti-inflammatory benefits via reduced cytokine production and macrophage activation [2-5]. Clinical data on their

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

Characteristics	DMARDs Only (n=12214)	DMARDs + SGLT2i (n=226)	DMARDs + GLP-1 RA (n=329)
Demographics			
Female, n (%)	9,475 (77.6%)	136 (60.2%)	274 (83.3%)
Male, n (%)	2,739 (22.4%)	90 (39.8%)	55 (16.7%)
White, n (%)	7,520 (61.6%)	112 (49.6%)	219 (66.6%)
Black or African American, n (%)	1,335 (10.9%)	40 (17.7%)	63 (19.1%)
Hispanic/Latino, n (%)	1,025 (8.4%)	22 (9.7%)	32 (9.7%)
Other, n (%)	3,359 (27.5%)	74 (32.7%)	47 (14.3%)
Clinical Characteristics			
Tobacco user, n (%)	366 (3%)	14 (6.2%)	10 (3%)
Diabetes Mellitus, n (%)	1,588 (13%)	147 (65%)	158 (48%)
Hypertension, n (%)	4,275 (35%)	151 (67%)	171 (52%)
Hyperlipidemia, n (%)	3,420 (28%)	154 (68%)	164 (50%)
Stroke, n (%)	244 (2%)	20 (9%)	7 (2%)
Congestive Heart Failure, n (%)	733 (6%)	95 (42%)	16 (4.9%)
Myocardial Infarction, n (%)	366 (3%)	32 (14%)	10 (3%)
Obesity, n (%)	2,076 (17%)	72 (32%)	217 (66%)
CKD (≥Stage 3), n (%)	489 (4%)	41 (18%)	16 (5%)
RA-Specific Characteristics			
Age of Earliest DMARD use, mean ± SD	57.2 ± 15.0	64.9 ± 11.5	52.0 ± 12.5
Number of DMARDs at baseline, mean ± SD	1.70 ± 1.35	1.81 ± 2.69	2.51 ± 2.18
Number of DMARDs at end, mean ± SD	1.57 ± 1.11	1.49 ± 1.01	1.31 ± 1.31
bDMARD and tsDMARD use, n (%)	5,252 (43%)	94.92 (42%)	180.9 (55%)
Baseline ESR (mm/hr), mean ± SD	23.4 ± 22.5	32.9 ± 29.9	23.9 ± 21.1
Baseline CRP (mg/L), mean ± SD	11.9 ± 30.0	13.5 ± 34.9	9.09 ± 7.3

This table compares demographics, clinical comorbidities, and RA-specific characteristics among patients on DMARDs only, DMARDs + SGLT2 inhibitors, and DMARDs + GLP-1 receptor agonists.

Table 2. Flare Outcomes by Group

Flare Outcome	DMARDs Only	DMARDs + GLP-1	DMARDs + SGLT2i
RA Flare Composite Score, mean ± SD	1.12 ± 2.44	1.71 ± 3.79	1.30± 1.78
IV Methylprednisolone, n (%)			
0	9,909 (81.1%)	225 (68.4%)	181 (80.1%)
1	752 (6.2%)	39 (11.9%)	8 (3.5%)
2	480 (3.9%)	17 (5.2%)	6 (2.7%)
3+	1,073 (8.8%)	48 (14.6%)	31 (13.7%)
Oral Prednisone, n (%)			
0	9,107 (74.6%)	208 (63.2%)	167 (73.9%)
1	1,841 (15.1%)	75 (22.8%)	29 (12.8%)
2	602 (4.9%)	24 (7.3%)	11 (4.9%)
3+	664 (5.4%)	22 (6.7%)	19 (8.4%)
Intra-articular steroid Injection, n (%)			
0	11,065 (90.6%)	266 (80.9%)	193 (85.4%)
1	732 (6%)	47 (14.3%)	17 (7.5%)
2	212 (1.7%)	6 (1.8%)	8 (3.5)
3+	205 (1.7%)	10 (3.0%)	8 (3.5%)
Increase CRP ≥ 10 above baseline, n (%)			
No	11,476 (94.0%)	315 (95.7%)	207 (91.6%)
Yes	738 (6.0%)	14.0 (4.3%)	19 (8.4%)
Increase ESR ≥ 20 above baseline, n (%)			
No	11,370 (93.1%)	305 (92.7%)	203 (89.8%)
Yes	844 (6.9%)	24 (7.3%)	23 (10.2%)
DMARDs Escalation			
No escalation	9,911 (81.1%)	268 (81.5%)	187 (82.7%)
Yes escalation	2,303 (18.9)	61 (18.5)	39 (17.3)

This table shows the number of patients in each group who experienced flare-related events. The RA Flare Composite Score was calculated per patient to reflect total flare burden: 1 point each for oral prednisone use, elevated CRP (≥10 mg/L), elevated ESR (≥20 mm/h), and DMARD escalation; IV steroids and joint injections counted as 1 point per three counts. Higher scores reflect more flare activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. RA Flare Status Pre- and Post-Initiation of GLP1 or SGLT2i

	Pre- initiation of medication, n (%)	Post-initiation of medication, n (%)	p-value
DMARDs + GLP-1 (n=329)	135 (41.0%)	68 (20.7%)	0.1525
DMARDs + SGLT2i (n=226)	77 (34.1%)	27 (12.0%)	0.0407

This table shows the number and percentage of patients who experienced a flare before and after starting GLP-1 receptor agonists or SGLT2 inhibitors.

effect in RA is limited. This study examines the association between SGLT2 or GLP-1 use and RA flare outcomes in DMARD-treated patients using real-world retrospective data.

Methods: A retrospective cohort study was conducted using TriNetX data between 2019 and 2024. Adults with RA and >12 months follow-up after DMARD initiation were included and categorized into: (1) DMARDs only, (2) DMARDs + SGLT2 inhibitor, and (3) DMARDs + GLP-1 receptor agonist. Patients with other inflammatory arthritides, malignancy, transplant, pregnancy, combined SGLT2/GLP-1 use, or prolonged prednisone use (>3 months) were excluded. Data included demographics, comorbidities, treatment timing, short-term oral prednisone, IV methylprednisolone, joint injections, ESR/CRP, and DMARD changes. RA flares were defined using a composite of: IV methylprednisolone, intra-articular injection, oral prednisone use less than 3 months, number of DMARD escalation, or increased CRP (≥10 mg/L) or ESR (≥20 mm/h).

Results: In Table 1, the GLP-1 group had the highest baseline DMARD count (mean 2.51), lowest end count (mean 1.31). ESR and CRP were most elevated in the SGLT2i group. Table 2 reports significantly different flare burden scores ($p = 0.00006$): DMARDs-only (1.12 ± 2.44), DMARDs+GLP-1 (1.71 ± 3.79), and DMARDs+SGLT2i (1.30 ± 1.78). Flare proxies such as IV steroids, joint injections, and inflammatory marker elevations were more common in the GLP-1 group. The composite flare burden score included oral prednisone use (1 point if present), IV methylprednisolone and joint injections (1 point per three administrations), frequency of CRP ≥10 mg/L, frequency of ESR ≥20 mm/hr, and if DMARD escalation was present. Flare proxies like IV steroids, injections, and inflammatory marker elevations were more frequent in the GLP-1 group. These findings suggest a possible association between GLP-1 use and higher flare burden, though further adjustment for baseline differences is needed. Table 3 shows patients with post-initiation flare declined significantly in the SGLT2i group (34.1% to 12.0%, $p = 0.0407$) and non-significantly in the GLP-1 group (41.0% to 20.7%, $p = 0.1525$). Limitations include lack of standardized disease activity measures (e.g., DAS28), potential confounding factors, and the inability to include DMARD escalation in pre-treatment and post-treatment analysis.

Conclusion: The use of SGLT2i was associated with a significant reduction in RA flares. GLP-1 showed a non-significant trend toward flare reduction, though this may reflect higher baseline RA severity which may influence the trend. These findings support the need for further prospective studies to validate the anti-inflammatory potential of SGLT2 inhibitors in RA and further explore the effect of GLP-1 on RA flare.

Disclosure: S. Sakthivel: None; **M. Karpman**: None; **L. Oland**: None; **A. Aldamouk**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1370

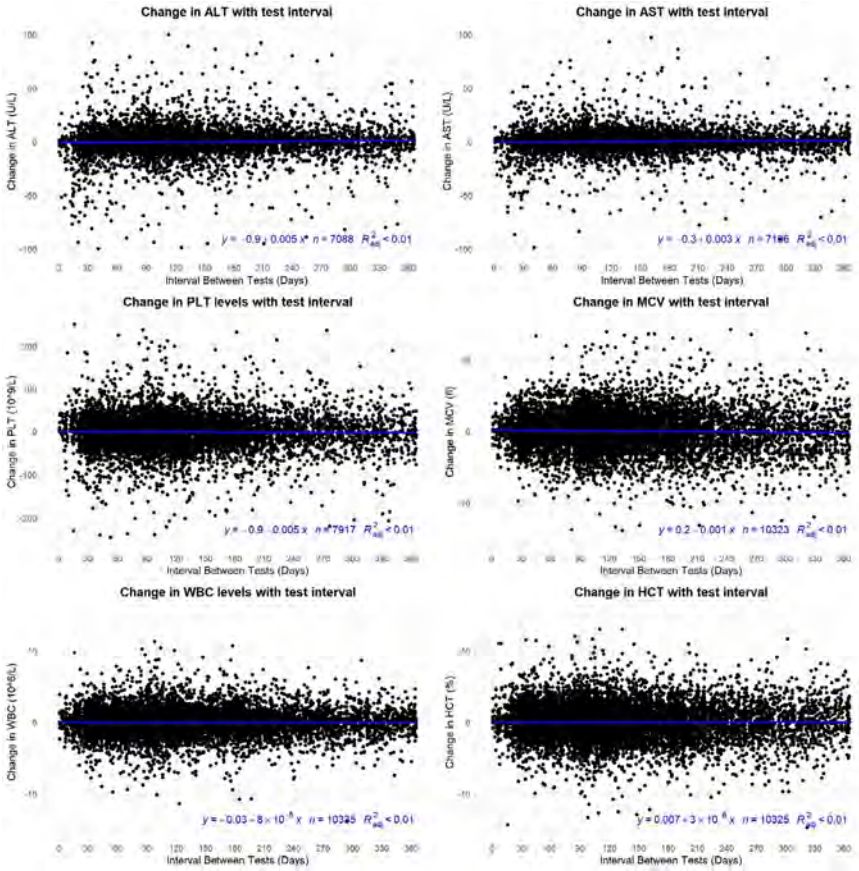
Impact of Six-Month Monitoring Compared to Three-Month Monitoring of Labs for Methotrexate Toxicity

Spencer Simko[1], Sohini Mukherjee[2], Ray Zhang[2], Puneet Bajaj[3] and Bonnie Bermas[4], [1]University of Texas Southwestern, Dallas, TX, [2]University of Texas Southwestern, Dallas, [3]UT Southwestern Medical Center, Dallas, TX, [4]UTSouthwestern.edu, Dallas, TX

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

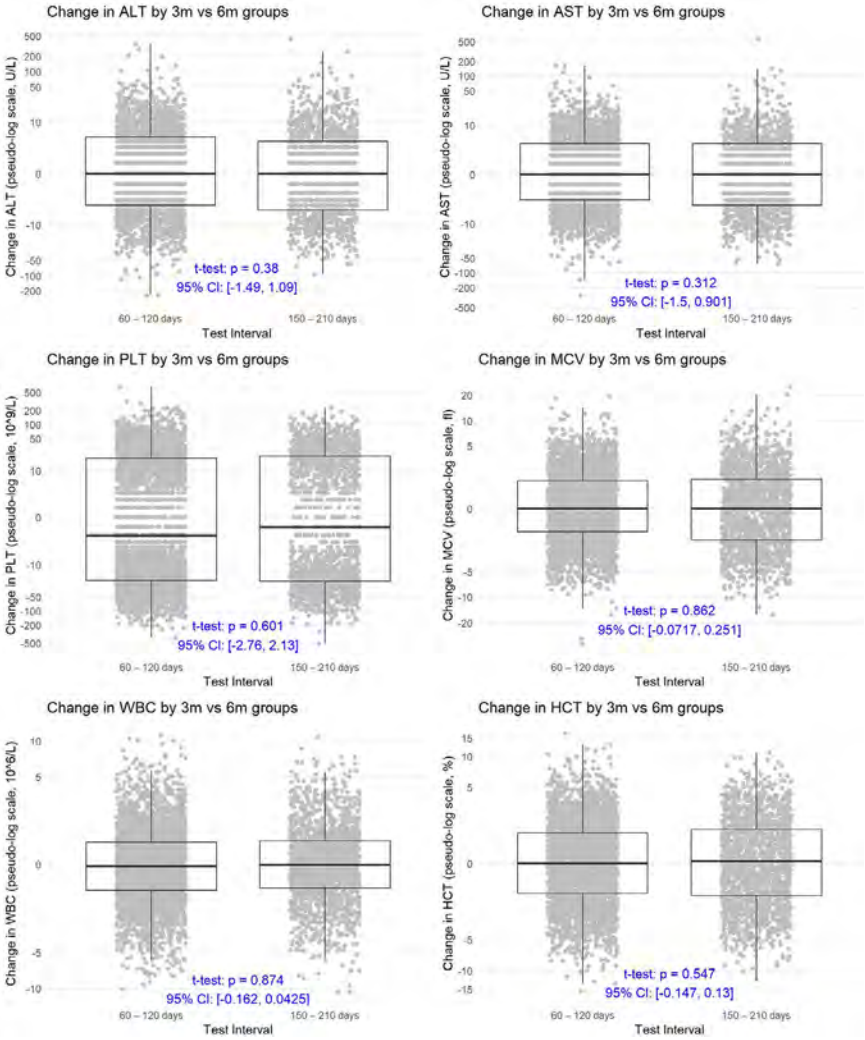
Background/Purpose: Current rheumatology treatment guidelines recommend lab monitoring for methotrexate toxicity at three-month intervals for established patients. We sought to evaluate whether monitoring labs at six-month intervals instead of recommended intervals was associated with more frequent reporting of lab test abnormalities.

Methods: We performed a retrospective analysis on patients at a large academic medical center who were taking methotrexate and who had at least two laboratory measurements of ALT, AST, PLT, WBC, MCV or HCT. Data for 3,821 patients spanning 2017–2024 were extracted from the electronic health record. Query parameters included patient MRN, sex, BMI, birth date, encounter date, methotrexate prescriptions, HCT, MCV, PLT, WBC, ALT, and AST. Only encounters in which the



Linear regression of test level changes vs. time interval between tests in patients taking MTX longer than 90 days

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparing changes in LFT and CBC across 2 different testing intervals: 60 – 120 days and 150 – 210 days for patients taking MTX longer than 90 days. A one-tailed t-test was performed with the p-value reported on the figure and a two-tailed 95% confidence interval for the difference in means was calculated.

patient was prescribed MTX more than 90 days prior were analyzed in order to exclude patients new to methotrexate. We plotted the changes in lab values from one encounter to the next against their respective test intervals and conducted linear regression analysis. We defined two different testing intervals: 3 months (2-4 months) and 6 months (5-7 months) and tested whether there was a difference in the mean change in lab value between the two testing intervals. We tested whether

Table 1. Percent of lab values starting in a clinically normal range that crossed a clinically concerning threshold in the subsequent test for two different testing intervals representing 3 months and 6 months in patients taking MTX longer than 90 days. Odds-ratio that the longer interval was associated with abnormal lab values adjusted by age, sex and BMI is also reported. The upper limit of normal (ULN) was established as 35 U/L (females) or 50 U/L (males) for ALT, as 50 U/L for AST. The lower limit of normal (LLN) was established as than 35% (female) or 37% (male) for HCT.

	Clinically Relevant Value	60 – 120 days	150 – 210 days	Δ% P-value	Adj-OR	Adj-OR P-value
ALT	>2x ULN	1.2%	1.7%	0.28	1.38	0.26
AST	>2x ULN	0.4%	0.9%	0.08	2.38	0.05
WBC	<4x10^6/L	3.8%	3.8%	1	0.99	0.93
HCT	<LLN	4.7%	5.8%	0.11	1.27	0.08
MCV	>100 fl	2.9%	2.6%	0.58	0.94	0.72
PLT	<100x10^9/L	0.1%	0.0%	0.42	-	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients were more likely to transition from a clinically normal lab value to a lab value exceeding a clinically relevant threshold in either testing interval group.

Results: There was no correlation between test frequency and ALT, AST, WBC, HCT, MCV or PLT count (R-squared < 0.01, Figure 1). Additionally, the average change between tests in these lab values was not different when measured every six months compared to every three months (Table 2). Patients tested at six months were not more likely to develop an abnormal lab result after a previously normal result compared to patients tested at three months (Figure 2).

Conclusion: Monitoring routine labs for methotrexate therapy using a six-month interval was not worse than monitoring at three months for detecting impactful lab abnormalities. The current ACR guideline to perform the measurements at three months may not be necessary and should be re-evaluated for cost-effectiveness and unnecessary patient burden.

Disclosure: S. Simko: None; **S. Mukherjee**: Galderma, 3; **R. Zhang**: None; **P. Bajaj**: None; **B. Bermas**: None.

Abstract Number: 1371

Effect of bDMARDs and tsDMARDS on diffuse interstitial lung disease associated with rheumatoid arthritis: systematic review and meta-analysis

Stéphane HILLIQUIN[1], Enrico VISMARA[1], Virginia BERLENGIERO[2] and Jérôme AVOUAC[3], [1]Département de Rhumatologie, Hôpital Cochin, Assistance publique des Hôpitaux de Paris, Université Paris-Cité, Paris, France, PARIS, France, [2]Rheumatoloy Department, Cochin Hospital, PARIS, France, [3]Rheumatology department, Cochin hospital, Paris, France

SESSION INFORMATION

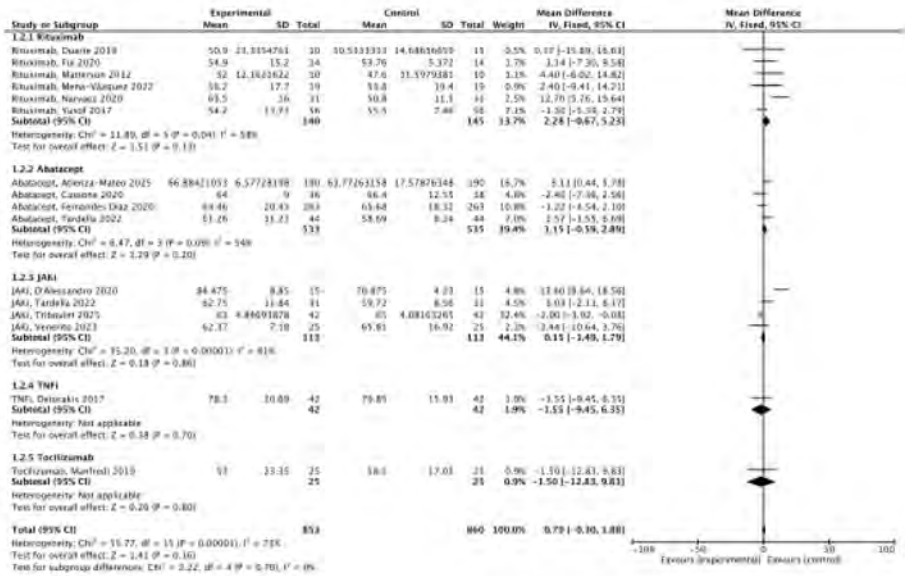
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a severe complication of rheumatoid arthritis (RA), associated with increased morbidity and mortality. The pulmonary safety of biologic (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) in RA-ILD remains unclear due to limited and heterogeneous data. **The aim** is to assess the impact of bDMARDs and tsDMARDs on interstitial lung disease in rheumatoid arthritis.

Methods: The SLR aimed to include all reports of controlled trials and observational studies of biological and targeted synthetic disease-modifying antirheumatic drugs (DMARDs) used in patients with a diagnosis of RA, defined as fulfilment of the 1987 ACR criteria or 2010 ACR/EULAR criteria. We searched PubMed and Cochrane databases for English articles published until 2025 using the keywords « interstitial lung disease AND "Arthritis, Rheumatoid"[Mesh]) AND "Arthritis, Rheumatoid/therapy"[Mesh] ». The MA was performed with Review Manager (RevMan v.5.4.1) software with the inverse variance method on FVC and DLCO parameters.

Results: Out of 861 abstracts screened, 15 observational studies were included, evaluating the effects of abatacept, rituximab, tocilizumab, TNF inhibitors (TNFi), and Janus kinase inhibitors (JAKi) on RA-ILD. These studies collectively involved 958 patients (mean age: 65 years; 57% female) with a mean disease duration of 115 months. Among the ILD patterns, usual

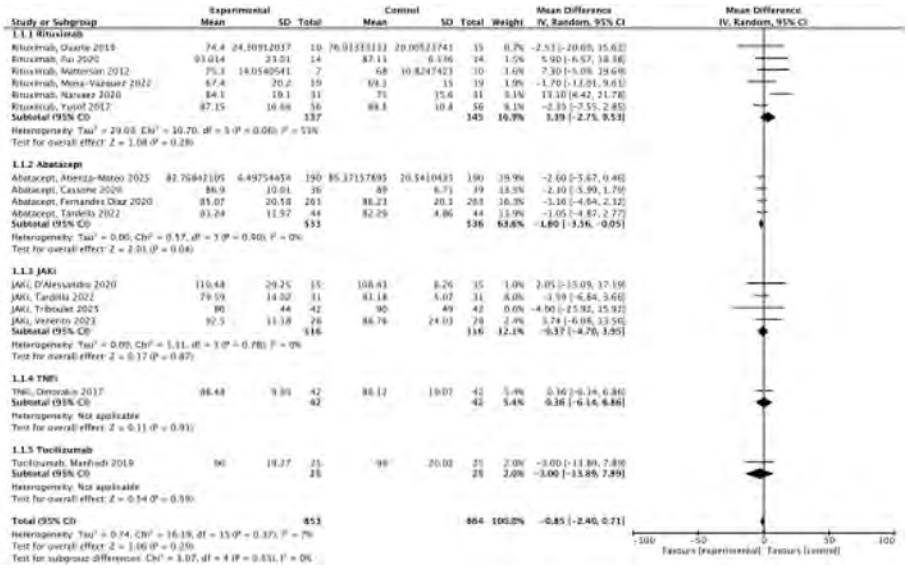
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



interstitial pneumonia (UIP) accounted for 48% and non-specific interstitial pneumonia (NSIP) for 40%. Data on changes in DLCO and FVC were available from 6 studies on rituximab, 4 on abatacept, 4 on JAK inhibitors, 1 on TNFi, and 1 on tocilizumab.

Analysis of FVC (%) variation before and after treatment revealed no significant overall change across all therapies (mean difference: -0.85%, 95% CI [-2.40, 0.71]; p=0.29). Rituximab was the only agent associated with a potential increase in mean FVC (+3.39%, 95% CI [-2.75, 9.53]), although this difference did not reach statistical significance (p=0.28). Similarly, DLCO values remained stable following treatment (mean difference: +0.79, 95% CI [-0.30, 1.88]; p=0.16). No statistically significant differences were observed between the individual treatment groups.

Conclusion: In conclusion, while bDMARDs and tsDMARDs show potential in stabilizing pulmonary function in RA-ILD, no significant differences were observed between treatments, highlighting the need for further research to clarify their impact on interstitial lung disease progression.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. HILLIQUIN: None; **E. VISMARA**: None; **V. BERLENGIERO**: None; **J. AVOUAC**: None.

Abstract Number: 1372

Treatment Patterns and Outcomes After Janus Kinase Inhibitor Discontinuation in Rheumatoid Arthritis: A Real-World Cohort Study

Sungwon Ko[1], Young-Eun Kim[1], Soo Min Ahn[1], Ji Seon Oh[1], Yong-Gil Kim[1], Chang-Keun Lee[2], Bin Yoo[1] and Seokchan Hong[1], [1]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea, Seoul, Republic of Korea, [2]Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Janus kinase (JAK) inhibitors are recommended for patients with rheumatoid arthritis (RA) who have an inadequate response to conventional synthetic or biologic disease-modifying antirheumatic drugs (csDMARDs or bDMARDs). However, evidence is limited regarding optimal treatment strategies following JAK inhibitor failure. This study aimed to evaluate real-world treatment patterns after JAK inhibitor discontinuation and to compare the efficacy and drug retention rates among different bDMARD classes in this context.

Methods: This retrospective study included patients with RA who discontinued JAK inhibitors due to inefficacy or intolerance between August 2015 and March 2025 and subsequently switched to an alternative bDMARDs. Changes in disease activity, as measured by the Disease Activity Score in 28 joints using ESR (DAS28-ESR), were assessed at 6 months post-switch, and drug retention rates were compared across three bDMARD groups: TNF inhibitors, IL-6R inhibitors, and other bDMARDs. Low disease activity (LDA) was defined as DAS28-ESR score < 3.2.

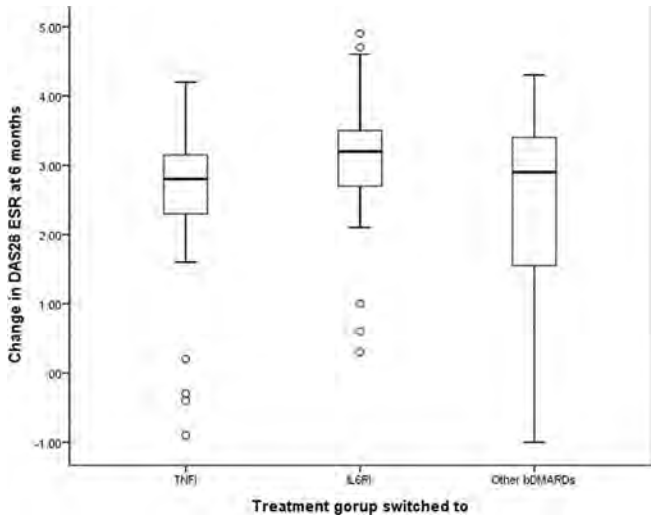


Figure 1. Change in DAS28-ESR over 6months following bDMARD switch after JAK inhibitor discontinuation. Statistical comparisons between groups were performed using the Mann–Whitney U test with Bonferroni correction. Adjusted p-values: 0.027 (TNF inhibitor vs. IL-6R inhibitor), 0.378 (IL-6R inhibitor vs. other bDMARDs), and 1.000 (other bDMARDs vs. TNF inhibitor).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 151 patients who discontinued JAK inhibitors, 59 (39.1%) switched to TNF inhibitors (adalimumab N=33, etanercept N=16, golimumab N=9, infliximab N=1), 69 (45.7%) to IL-6R inhibitors, and 23 (15.2%) to other bDMARDs (abatacept N=19, rituximab N=4). Among them, 113 patients (40 TNF inhibitor group, 53 IL-6R inhibitor group, and 20 other bDMARD group) remained on therapy for at least 6 months and were included in the efficacy and drug retention analyses. Baseline characteristics were generally comparable across the groups, although patients in other bDMARDs group were older and had a higher number of prior bDMARDs. Baseline DAS28-ESR was also significantly higher in the other bDMARD group than in the IL-6R inhibitor group ($p = 0.012$).

At 6 months, patients who switched to IL-6R inhibitors showed significantly greater improvement in DAS28-ESR compared to those who switched to TNF inhibitors (adjusted $p = 0.027$). No significant differences were observed between IL-6R inhibitors and other bDMARDs (adjusted $p = 0.378$), or between TNF inhibitors and other bDMARDs (adjusted $p = 1.000$). LDA was achieved in 83.0% (44/53) of the IL-6R inhibitor group, compared to 62.5% (25/40) in the TNF inhibitor group and 60.0% (12/20) in the other bDMARD group. The overall group difference was statistically significant ($p = 0.042$), but pairwise comparisons did not remain significant after Bonferroni correction (TNF vs. IL-6R: adjusted $p = 0.075$; TNF vs. other bDMARDs: adjusted $p = 1.000$; IL-6R vs. other bDMARDs: adjusted $p = 0.114$). Drug retention rates did not differ significantly among the three groups ($p = 0.249$).

Conclusion: In this real-world cohort of RA patients who discontinued JAK inhibitors, IL-6R inhibitors were the most frequently selected subsequent therapy and were associated with greater clinical improvement at 6 months compared to TNF inhibitors. However, drug retention rates were comparable across all bDMARD classes. These findings provide insight into treatment decisions and outcomes following JAK inhibitor failure in RA management.

Disclosure: S. Ko: None; **Y. Kim**: None; **S. Ahn**: None; **J. Oh**: None; **Y. Kim**: None; **C. Lee**: Samsung Bioepis, 5; **B. Yoo**: None; **S. Hong**: None.

Abstract Number: 1373

Effect of JAK Inhibitors on Bone Mineral Density in Rheumatoid Arthritis Patients with Osteoporosis: A Comparative Study with Biologics

Sungwon Ko[1], Young-Eun Kim[1], Soo Min Ahn[1], Ji Seon Oh[1], Yong-Gil Kim[1], Chang-Keun Lee[2], Bin Yoo[1] and Seokchan Hong[1], [1]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea, Seoul, Republic of Korea, [2]Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoporosis is more prevalent in patients with rheumatoid arthritis (RA) than in the general population. Janus kinase (JAK) inhibitors and tumor necrosis factor (TNF) inhibitors are widely used in RA treatment; these drugs effectively reduce disease activity and prevent joint destruction by suppressing inflammation. However, their effects on bone mineral density (BMD) remain unclear. Thus, this study aims to compare BMD changes in RA patients with osteoporosis treated with JAK inhibitors versus TNF inhibitors, thereby providing insights into their impact on bone metabolism and informing optimal treatment strategies for osteoporosis management in RA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical characteristics of RA patients undergoing osteoporosis treatment: Comparison between JAK inhibitor users and TNF inhibitor users.

	JAK inhibitor (n = 23)	TNF inhibitor (n = 13)	P
Age, years	66.0 (62.5 – 71.0)	59.0 (54.0 – 65.0)	0.14
Female	23 (100)	12 (92.3)	0.99
Body mass index, kg/m²	22.4 (20.7–23.9)	24.7 (23.5–24.7)	0.21
Duration of RA, years	17.0 (3.3–38.8)	22.8 (5.9–40.2)	0.51
Treatment of osteoporosis			0.82
Bisphosphonate	13 (56.5)	7 (53.8)	
Denosumzb	8 (34.8)	5 (38.5)	
Teriparatide	1 (4.3)	0	
Zoledroic acid	1 (4.3)	0	
Romosozumab	0	1 (7.7)	
Initial BMD, T-score			
Lumbar spine	-2.9 (0.5)	-2.8 (0.5)	0.36
Femur neck	-2.2 (0.6)	-1.7 (0.6)	0.71
Follow-up BMD, T-score			
Lumbar spine	-2.9 (0.7)	-2.7 (0.4)	0.23
Femur neck	-2.2 (0.6)	-1.9 (0.7)	0.35
% change in BMD			
Lumbar spine	3.9 (1.9–5.8)	3.3 (2.2–8.2)	0.50
Femur neck	2.3 (0.7–2.7)	1.8 (1.1–2.2)	0.61

BMD, bone mineral density; JAK, Janus kinase; TNF, tumor necrosis factor; RA, rheumatoid arthritis

Methods: This retrospective study included RA patients diagnosed with osteoporosis who were treated with either TNF inhibitors or JAK inhibitors at a tertiary referral center between January 2005 and December 2024. Areal BMD (g/cm^2) was measured at the lumbar spine, femoral neck, trochanter, and total femur using dual-energy X-ray absorptiometry. The rate of BMD change was expressed as the annualized percentage change between the initial and follow-up measurements

Results: Among RA patients who received biologics (n = 23) and JAK inhibitors (n = 13), 23 (100.0%) and 12 (92.3%) were women, respectively. The mean ages at initial BMD measurement for these patients were 66.0 years (IQR, 62.5–71.0 years) and 59.0 years (IQR, 54.0–65.0 years), respectively (P = 0.14). There was no significant difference in baseline clinical characteristics, including laboratory data and baseline BMD, between the two groups. With osteoporosis treatment, follow-up areal BMD was significantly increased compared with the initial value at the lumbar spine and femur neck in RA patients, regardless of concomitant use of JAK inhibitors or TNF inhibitors. Further, no statistically significant differences were observed in annualized BMD changes between RA patients receiving TNF inhibitors and JAK inhibitors (P = 0.83).

Conclusion: In RA patients receiving osteoporosis treatment, JAK inhibitors did not provide a significant additional effect on bone formation compared with TNF inhibitors.

Disclosure: S. Ko: None; **Y. Kim**: None; **S. Ahn**: None; **J. Oh**: None; **Y. Kim**: None; **C. Lee**: Samsung Bioepis, 5; **B. Yoo**: None; **S. Hong**: None.

Abstract Number: 1374

AZD1163, a Novel Bispecific Human Antibody Targeting PAD2/4 Enzymes Responsible for Generating Citrullinated Protein Auto-antigens in Rheumatoid Arthritis, Demonstrates Dose-dependent Inhibition of Systemic PAD Activity in Healthy Volunteers

Susanne Prothon[1], Jacob Leander[1], Ulla Seppälä[1], Eduard Molins[2], Mia Collins[1], Nicholas White[3], Ivonne Puente[1], Andre Santa Maria[1], Gary Sims[4], David Han[5], Obada Al Hamdan[6], Ronald Goldwater[7], Emon Khan[8] and David Close[9], [1]AstraZeneca, Gothenburg, Sweden, [2]AstraZeneca, Barcelona, Spain, [3]AstraZeneca, Cambridge, United Kingdom, [4]AstraZeneca, Gaithersburg, [5]Parexel, Los Angeles, [6]Parexel, Berlin, Germany, [7]Parexel, Baltimore, [8]BioPharmaceuticals

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

R&D, Late Respiratory and Immunology, AstraZeneca, Academy House, Cambridge, United Kingdom, [9]AstraZeneca, Royston, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: AZD1163 is a novel bispecific antibody that inhibits the activity of extracellular Peptidyl Arginine Deiminases (PADs) 2 and 4, enzymes responsible for protein citrullination in patients with Rheumatoid Arthritis (RA). In susceptible individuals, citrullinated proteins activate a cascade of T cell driven events, promoting B cell maturation and activation, leading to the production of pathogenic anti-citrullinated protein antibodies (ACPA). ACPAs are associated with a worse prognosis, often translating to more severe joint damage and a rapidly progressing disease course. In vitro, AZD1163 inhibits protein citrullination and increased PAD activity present in serum and synovial fluid from patients with RA. The aim is to present the first clinical findings on AZD1163 safety and tolerability, pharmacokinetic properties, and pharmacodynamic effect of AZD1163 on systemic PAD enzyme activity in healthy volunteers.

Methods: This randomized, double-blind, placebo-controlled Phase I study (NCT06103877) in healthy participants comprised of two parts: Part A consisted of nine single-ascending dose (SAD) cohorts, each receiving AZD1163 mg intravenous infusion or placebo, where one dose level was administered subcutaneously (SC). In the first two cohorts, 2 participants received AZD1163 and 1 received placebo. Subsequent cohorts had 6 (or 8 for the SC cohort) participants on AZD1163 and 2 (or 3 for the SC cohort) on placebo. Part B included two multiple-ascending dose (MAD) cohorts dosed twice, two weeks apart (Q2W), with either AZD1163 SC or placebo. In each cohort, 6 participants received AZD1163 and 3 received placebo. Safety and tolerability were assessed through the evaluation of adverse events, clinical chemistry/hematology, ECG, and vital signs. PK characteristics and immunogenic profile of AZD1163 were evaluated through repeated sampling in serum. Inhibition of solid phase bound histone H3 citrullination (% change from baseline) was used to demonstrate *ex vivo* AZD1163 target engagement.

Results: Sixty-five participants were included in the SAD and eighteen in the MAD. A dose proportional exposure increase was observed for AZD1163, with maximum concentration occurring 10 days post-SC dose. The bioavailability following SC dosing was estimated at 65 %. Mean systemic clearance was 0.15 L/day and the mean elimination half-life was 38 days. A significant, dose dependent inhibition of PAD2/4 activity was observed, with maximum inhibition exceeding 95%, confirming target engagement. Anti-drug antibodies (ADA) incidence was low at 6.7% among AZD1163 recipients. Adverse events were few and escalating doses were well-tolerated. No trends were evident in vital assessments, lab values, or ECGs.

Conclusion: This first-in-human study of a novel bispecific antibody inhibiting PAD 2 and 4 enzymes, demonstrated that Q2W dosing of AZD1163 was well tolerated in healthy volunteers, with favorable PK characteristics in the dose range studied. Target engagement was demonstrated by inhibition of PAD2/4 activity *ex vivo* in plasma. Results generated from this Phase I study, supports the further evaluation of AZD1163 in patients with RA.

Disclosure: S. Prothon: AstraZeneca, 3; **J. Leander**: AstraZeneca, 3; **U. Seppälä**: AstraZeneca, 3; **E. Molins**: AstraZeneca, 3; **M. Collins**: AstraZeneca, 3; **N. White**: AstraZeneca, 3; **I. Puente**: AstraZeneca, 3; **A. Santa Maria**: AstraZeneca, 3; **G. Sims**: AstraZeneca, 3; **D. Han**: Parexel, 2; **O. Al Hamdan**: Parexel, 2; **R. Goldwater**: Parexel, 2; **E. Khan**: AstraZeneca, 3; **D. Close**: AstraZeneca, 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1375

86-96% of Rheumatoid Arthritis (RA) Patients with RA Who Have 0 or 1 Swollen Joint or Tender Joint but Are Classified as Moderate/high on RA Indices Have 1-9 Comorbidities Recognized on a Multidimensional Health Assessment Questionnaire (MDHAQ)

Theodore Pincus[1], Juan Schmukler[1] and Tengfei Li[2], [1]Rush University Medical Center, Chicago, IL, [2]Rush, chicago, IL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1347–1375) Rheumatoid Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) guidelines suggest management according to "treat-to-target," with escalation of treatment in patients with moderate/high (M/H) DAS28 (disease activity score 28) or CDAI (clinical disease activity index) according to shared decisions toward low activity/remission (R/L). It is recognized that elevated RA clinical core data set measures and indices may be seen in the absence of inflammatory activity in RA patients with comorbid joint damage and/or fibromyalgia. A multidimensional health assessment questionnaire (MDHAQ) includes queries to screen for fatigue, back pain, neck pain, headache, problems with sleep or thinking, and indices to screen for anxiety, depression and fibromyalgia. Analyses were performed of RA patients with 0 or 1 swollen and tender joint counts (SJC & TJC), who met criteria for remission according to these measures, but who were classified as M/H on DAS28-ESR (disease activity score 28–erythrocyte sedimentation rate) , CDAI (clinical disease activity index), or RAPID3 (routine assessment of patient index data) and would be regarded as candidates for escalation of therapy, to identify comorbidities found on the MDHAQ which may explain the elevated index scores.

Methods: Unselected patients with RA seen in routine care completed an MDHAQ prior to seeing the rheumatologist, who performed a standard 28 joint count. DAS28–ESR, CDAI, and RAPID3 were computed, and patients were classified as L/R or M/H. The proportion of patients who were identified as having each of 9 generally non-inflammatory comorbidities on the MDHAQ and any of 9 was computed for each index, recognizing that these comorbidities may reflect inflammation in certain patients.

Results: In 173 patients with RA seen in 2021, SJC and TJC 0 or 1 was found in 73 (42%), of whom 7%, 34%, and 58% were classified as M/H according to DAS28-ESR, CDAI, and RAPID3, respectively. Among these patients, positive MDHAQ screening was seen in 29-33% for anxiety , 26-33% for depression, 17-38% for fibromyalgia, 67-81% for fatigue >3/10,

SJC0,1 TJC0,1	n (%)	a.Anxiety	b. Depression	c. Fibromyalgia	d.Fatigue >3/10	e.Back pain	f.Neck pain	g.Headache	h. Sleep prblms	i.Think prblms	j. Any a-i
DAS28-ESR R/L	60 (90%)	1 0 (17%)	7 (12%)	4 (8%)	23 (40%)	23 (38%)	24 (40%)	8 (13%)	19 (32%)	7 (12%)	41 (68%)
M/H	7 (10%)	2 (33%)	2 (33%)	1 (17%)	4 (67%)	4 (57%)	4 (57%)	0 (0%)	3 (43%)	0 (0%)	6 (86%)
CDAI R/L	47 (66%)	6 (13%)	3 (7%)	0 (0%)	12 (26%)	12 (26%)	17 (36%)	2 (4%)	10 (21%)	1 (2%)	27 (57%)
M/H	24 (34%)	8 (33%)	8 (33%)	6 (38%)	17 (81%)	16 (67%)	13 (54%)	7 (29%)	15 (63%)	8 (33%)	23 (96%)
RAPID3 R/L	30 (42%)	2 (7%)	0 (0%)	0 (0%)	3 (10%)	9 (30%)	10 (33%)	0 (0%)	3 (10%)	0 (0%)	14 (47%)
M/H	42 (58%)	12 (29%)	11 (26%)	6 (19%)	26 (67%)	20 (48%)	21 (50%)	9 (21%)	22 (52%)	9 (21%)	37 (88%)

Proportion of Rheumatoid arthritis patients with 0 and 1 swollen (SJC) and tender (TJC) joints on a 28 joint count who reported positive responses for 9 comorbidities within the MDHAQ vs classification as DAS28–ESR, CDAI, or RAPID3 remission/low (R/L) or moderate/high (M/H)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

48-67% for back pain, 50-57% for neck pain, 0-21% for headache, 43-63% for problems with sleep and 0-33% for problems with thinking. One of the 9 comorbidities was seen in 86-96% of patients with SJC and TJC 0 or 1, who were classified as M/H (Table). In patients with SJC and TJC 0 or 1 who were classified as R/L, 47%-68% reported one of the 9 symptoms. The proportion reporting each symptom was higher in the M/H group for all 3 indices other than two symptoms reported by none of 7 patients with 0 or 1 SJC and TJC who were classified as DAS28–ESR M/H (Table).

Conclusion: In 173 patients with RA seen in 2021 who met SJC and TJC criteria for remission but were classified as DAS28-ESR, CDAI, or RAPID3, 86-96% reported one of 9 non-inflammatory comorbidities on the MDHAQ found on the MDHAQ. One limitation is that it is possible that one or more comorbidities identified as "non-inflammatory" may result from inflammation in certain patients. Nonetheless, the MDHAQ, which is completed by most patients in 5-10 minutes and is available in the February 2025 release of the Epic electronic medical record (EMR), can be helpful to interpret RA index scores for treat-to-target, description of outcomes, and general patient management.

Disclosure: T. Pincus: Medical history services, LLC, 8, 9, 10; **J. Schmukler**: None; **T. Li**: None.

Abstract Number: 1376

A Systematic Literature Review on the Economic Burden of Sjögren's Disease

Nora Sandorfi[1], Lisa Shea[2], **Alexander Keenan**[2], Elizabeth Adamson[2], Federico Zazzetti[3], Soumya Chakravarty[4], Donna Gotshall[5], Jyotika Gandhi[6], Sandip Ranjan[6] and Esen Akpek[7], [1]University of Pennsylvania, Philadelphia, PA, USA, Philadelphia, [2]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [3]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [4]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [5]Sjögren's Disease Patient, Hickory, NC, USA, Hickory, NC, [6]Putnam Associates, Gurugram, India, Gurugram, India, [7]Johns Hopkins Jerome L. Greene Sjögren's Syndrome Center, Baltimore, MD USA, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a chronic systemic autoantibody driven disorder characterized by glandular dysfunction that typically presents with oral and ocular dryness, fatigue, and pain. Ninety percent of affected individuals are female, and the condition imposes significant clinical, humanistic, and economic burden. Limited information is known regarding the total economic burden associated with SjD including direct, indirect, or societal costs and the implications for patients living with SjD. We conducted a systematic literature review (SLR) to identify, evaluate, and summarize the economic burden on patients with SjD. The SLR was supplemented by a roundtable discussion of patients living with SjD to add additional insight and context regarding the burden of disease.

Methods: The SLR was developed using the PRISMA reporting guidelines for systematic reviews and conducted using the MEDLINE and Embase databases (via OvidSP), covering the period from January 1, 2014 to April 12, 2024. Additional searches were performed in the bibliographies of relevant studies, Google Scholar, disease-specific websites, and conference proceedings. Data were extracted to report on healthcare resource utilization (HCRU), direct medical costs, as well as indirect and societal costs. A focus group discussion of patients living with SjD generated qualitative insights to identify themes across diagnosis, treatment, and burden of disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Studies measuring total direct health care resource utilization

Study	Country	Study population	Metric	Costs
McCormick 2015	Canada	SjD vs non-SjD	Total cost (CAD) PPPY, mean (IQR); times increase	11,748 (9,640–13,856) vs 4,213 (3,762–4,665); 2.8x
Perera 2018	USA	SjD vs non-SjD	1. Total all-cause cost (USD) PPPY, mean; times increase 2. SjD-related cost (USD) PPPY, mean; times increase	1. 10,729 vs 6,534; 1.6x 2. 2,214 vs 1,503; 1.5x
Yao 2018	China	SjD (with DED) vs non-SjD	Total cost (CNY) PPPY, mean, times increase	7,637 vs 1,179; 6.5x
Chan 2021	Canada	SjD (with DED) vs non-SjD	Total cost (CAD) PPPY, mean; times increase	2,689 vs 2,203; 1.2x
Westerlund 2021	Sweden	SjD vs non-SjD	Total cost (SEK) per patient, median (IQR); times increase	23,735 (9,907–58,180) vs 8,128 (2,822–24,540); 2.9x
Cafaro 2024	Italy	SjD vs non-SjD	Total cost (Euro) PPPY, mean; times increase	1,171 vs 372; 3.1x
Birt 2017	USA	Post- vs pre-diagnosis of SjD	1. Total cost (USD) PPPY, mean; times increase 2. SjD-related cost (USD) PPPY, mean	20,417 vs 14,612; 1.4x 1,742 vs NA
Kim 2020	Korea	SjD	Total cost (USD) PPPY, mean	503 in 2012 and 643 in 2016
McCoy 2022	USA	SjD	Total cost (USD) PPPY, mean	5,748
Bowman 2017	UK	SjD subgroups (rituximab vs PBO)	Total cost (GBP) per patient over 48 weeks, mean; times increase	10,752 vs 2,672; 4.0x
Perera 2018	USA	SjD subgroups (extra-glandular vs glandular disease only)	Total cost (USD) PPPY, mean; times increase	14,387 vs 4,878; 2.9x
Alemao 2019	USA	SjD subgroups with RA (abatacept vs anti-TNFs)	Total adjusted* cost (USD) per patient per 180-days, mean; times increase	17,050 vs 27,469; 0.6x
Lee 2022	USA	SjD subgroups (with vs without interstitial lung disease)	Total cost (USD) per patient per 180-days, mean; times increase	23,192 vs 8,648; 2.7x
Ndife 2022	USA	SjD subgroups (ESSDAI ≥5 vs ESSDAI <5)	Total cost (USD) PPPY, mean; times increase	15,656 vs 11,165; 1.4x
Seror 2024	France	SjD subgroups (with other autoimmune disease vs SjD only)	Total cost (Euro) PPPY, mean; times increase	8,819 vs 5,780 in 2011; 1.5x 13,273 vs 9,710 in 2018; 1.4x

DED, dry eye disease; ESSDAI, EULAR Sjögren Syndrome Patient Reported Index; ILD, IQR, NA, not available; PBO, placebo; PPPY, per patient per year; pSS, primary Sjögren's syndrome; RA, rheumatoid arthritis; SjD, Sjögren's disease; TNF, tumor necrosis factor.

Results: A total of 53 publications (43 unique studies) reported outcomes related to economic burden of SjD. The studies were performed across many countries, predominately in North America (23) and Europe (13). The publications reflected 23 studies reporting on HCRU, with 18 assessing direct and/or indirect costs. Direct health care costs for patients with SjD were, on average, 2.8 times higher than for patients without SjD (**Table 1**). Direct patient out-of-pockets costs were not measured in any study. The studies underscore that patients with SjD require more frequent hospitalizations, outpatient visits, emergency room care, and dental visits compared to the patients without SjD. Productivity loss was reported in 15 studies. On average, patients with SjD had two times higher total indirect costs (**Table 2**). The studies also highlighted significant societal costs associated with SjD, including a higher likelihood of early retirement, reduced work hours, and

Table 2. Studies measuring indirect costs for patients with SjD

Study	Country	Study population	Metric	Costs
Chan 2021	Canada	1. SjD (with dry eye disease) vs non-SjD 2. SjD with dry eye disease by severity (overall vs mild vs moderate vs severe)	Indirect cost (CAD) PPPY, mean; times increase	1. 41,094 vs 17,694; 2.3x 2. 24,331 (presenteeism: 19,304; absenteeism: 2,702) vs 5,961 vs 16,525 vs 25,485
Yao 2018	China	SjD (with dry eye disease) vs non-SjD	Indirect cost (CNY) PPPY, mean; times increase	828 vs 487; 1.7x
McCormick 2019	Canada	SjD	Indirect cost (CAD) per patient, mean	Weekly cost: 377 (presenteeism: 320; absenteeism: 191) Annual cost: 14,092

PPPY, per patient per year; SjD, Sjögren's disease.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

part-time work due to health. The patients interviewed confirmed they were unable to work due to disease impact and fatigue as well as an inability to afford living alone and experiences of financial insecurity.

Conclusion: Current published studies demonstrate that SjD results in considerable healthcare costs, loss of productivity, and a profound financial burden on both individuals and healthcare systems, highlighting an increased need for inpatient care and extended stays. Indirect costs, primarily arising from lost productivity, further amplify the economic burden of SjD. In total, these costs highlight a significant economic and societal burden of SjD, reflecting both direct healthcare costs and significant indirect costs.

Disclosure: N. Sandorfi: Bristol-Myers Squibb(BMS), 2, Immunovant, 1, Johnson & Johnson, 1, 2, Novartis, 1; **L. Shea**: Johnson & Johnson, 3, 11; **A. Keenan**: Johnson & Johnson, 3, 11; **E. Adamson**: Johnson & Johnson, 3, 11; **F. Zazzetti**: Johnson & Johnson, 3, 11; **S. Chakravarty**: Johnson & Johnson, 3, 11; **D. Gotshall**: None; **J. Gandhi**: Johnson & Johnson, 12, Employer received funding from Johnson & Johnson to conduct study; **S. Ranjan**: Johnson & Johnson, 12, Employer received funding from Johnson & Johnson to conduct study; **E. Akpek**: Abbvie, 2, 6, Alcon, 2, 6, Baush & Lomb, 2, 6, Department of Defense, 5, Dompe, 2, 5, 6, Iolyx, 2, 6, Johnson & Johnson, 2, 6, National Institutes of Health, 5, Novaliq, 2, 6, Novartis, 5, Phycin Inc., 2, 6, Thea, 2, 6, Up-To-Date, 9, W. L. Gore & Assoc., 2, 6.

Abstract Number: 1377

Humanistic Burden of Sjögren's Disease: A Systematic Review of Treatment Efficacy on Health-Related Quality-of-Life

Esen Akpek[1], Elizabeth Adamson[2], Lisa Shea[2], Federico Zazzetti[3], Soumya Chakravarty[4], Sandip Ranjan[5], Ravi Potluri[6] and **Alexander Keenan**[2], [1]Johns Hopkins Jerome L. Greene Sjögren's Syndrome Center, Baltimore, MD USA, Baltimore, MD, [2]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [3]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [4]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [5]Putnam Associates, Gurugram, India, Gurugram, India, [6]Putnam Associates, Boston, MA, USA, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a chronic systemic autoimmune disorder that imposes significant clinical, humanistic, and economic burdens on patients. It is associated with multiple comorbidities and significant heterogeneity in disease manifestation, including an increased risk of lymphoma, which further exacerbate its impact. Despite numerous drugs (such as rituximab and abatacept) having been tested, there are currently no approved treatments for the disease. While some drugs are prescribed to help relieve symptoms, many patients report inadequate relief, which exacerbates the emotional and social impact of the disease. We conducted a systematic literature review (SLR) to identify, summarize, and evaluate the existing evidence on the impact of treatments on the humanistic burden of SjD, with a particular focus on their impact on patients' health-related quality of life (HRQoL).

Methods: The SLR was conducted using the MEDLINE and Embase databases (via OvidSP), covering the period from January 1, 2014 to April 12, 2024 for publications in the English language. Additional searches were performed in the bibliographies of relevant studies, Google Scholar, disease-specific websites, and conference proceedings. Articles were screened, and data were extracted to report on HRQoL outcomes, including disease-specific instruments (EULAR Sjögren's Syndrome Patient-Reported Index [ESSPRI]), generic tools (European Quality of Life 5 Dimensions [EQ-5D], Short

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Study characteristics of publications on systemic treatments for Sjögren's disease

Study	Study design	Study population	Intervention (n)	Comparator (n)	Patient characteristics: age, mean (SD); female, %	HRQoL questionnaires used
Devauchelle-Pensec 2014	RCT, DB	pSS	Rituximab (63)	PBO (57)	52.9 (13.3); 90.5%	VAS, SF-36
Bowman 2017	RCT, DB	pSS	Rituximab (67)	PBO (66)	54.3 (11.5); 94%	ESSPRI, VAS, SF-36
Dorner 2018	RCT, DB	pSS	Leniolisib (20)	PBO (10)	NR	ESSPRI, SF-36, MFI, VAS
Van 2020, de Wolff 2022	RCT Ph III DB + OLE	pSS	Abatacept (40)	PBO (40)	48 (15); 92.5%	ESSPRI, FSFI, SF-36, MFI, EQ-5D-5L
Baer 2021	RCT, Ph III DB	pSS	Abatacept (92)	PBO (95)	51.2 (12.3); 92.4%	ESSPRI, patients GDA, PROMIS-Fatigue, FSFI
Tsuboi 2023	Cohort study	SS with RA	Abatacept (68)	–	56.1 (12.5); 100%	ESSPRI
Shao 2021	RCT, SB	pSS	Iguratimod (44)	PBO (19)	49.5 (12.3); 91.7%	ESSPRI, VAS, PGA
Clair 2023	RCT, Ph II DB	SS	Dazodalibep (54)	PBO (55)	NR	ESSPRI, FACIT-F, OSDI, PGI
Felten, 2021	RCT, DB	pSS	Tocilizumab (55)	PBO (55)	50.9 (12.4); 98.2%	ESSPRI, NAS, SF-36, HADS
Mariette 2015	Non RCT	pSS	Belimumab (30)	–	49.5 (16.5); 100%	ESSPRI, VAS
Kedor 2016	Non RCT	pSS	Cyclosporin (30)	–	54.9 (11.1); 96.7%	SF-36, VAS, HAQ-DI
Papas 2018	RCT, Ph IIA DB	pSS	Iscalimab (21)	PBO (11)	NR	ESSPRI, MFI, VAS, SF-36
Liu 2019	RCT, DB	pSS	TGP (211)	PBO (103)	48.9 (12.2); 97.2%	ESSPRI, VAS
Chen 2021	RCT, DB	pSS	TCM (28)	PBO (14)	58.4 (10.5); 100%	ESSPRI, PGA, VAS, SF-36
Bentley 2023	RCT, Ph IIA DB	pSS	Petesicatib (38)	PBO (37)	52.3 (11.8); 97.3%	ESSPRI, SF-36
Fisher 2019	RCT, Ph II, DB	pSS	RSLV-132 (22)	PBO (8)	NR	PRO-F
Guan 2020	Cohort study	pSS	HCQ (230)	Non-HCQ (153)	47.6 (12.8); 94%	WHO-BREF, ESSPRI, and PSQI
Cornec 2017	RCT	pSS	Rituximab by systemic activity groups: Low (29) vs moderate (57) vs high (34)		54.2; NR	ESSPRI, VAS, and SF-36

DB, double blind; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Level Version; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; FACIT-F, Functional Assessment of Cancer Therapy: Fatigue; FSFI, Female Sexual Function Index; GDA, Global Disease Activity; HADS, Hospital Anxiety and Depression Scale; HAQ-DI, Health Assessment Questionnaire – Disability Index; HCQ, Hydroxychloroquine; HRQoL, Health-related quality of life; MFI, Multidimensional Fatigue Inventory; NAS, Numeric Analog Scale; OLE, open label extension; OSDI, Ocular Surface Disease Index; PBO, placebo; PGA, Physician Global Assessment; PGI, Patient Global Impressions; Ph, phase; PROMIS, Patient Reported Outcome Measurement Information System; pSS; primary Sjögren's syndrome; SB, single blind; SF-36: Short form–36 Health Survey; SS, Sjögren's syndrome; TCM, traditional Chinese medicine; TGP, total glucosides of peony; VAS, Visual Analogue Scale.

form–36 Health Survey [SF-36], Visual Analogue Scale [VAS]), and specific HRQoL domains such as pain, fatigue, activity participation, anxiety, depression, ocular health, oral health, and sexual health.

Results: Twenty-nine publications reporting the effect of treatment on humanistic burden outcomes of SjD were identified (19 related to systemic treatments and 10 to non-systematic/non-pharmacological interventions; **Table 1**). In randomized controlled trials (RCTs) involving rituximab, leniolisib, and abatacept, no significant differences in ESSPRI scores were found between treatment and placebo groups, indicating similar levels of symptom burden reduction (**Table 2**). In contrast, iguratimod and dazodalibep demonstrated significant improvements in overall ESSPRI scores compared to placebo in small or local trials. An RCT of tocilizumab failed to show significant improvements in anxiety or depression outcomes compared to the control group (**Table 3**). Use of systemic treatments was found to result in non-significant improvements in fatigue, oral dryness, and ocular dryness compared to placebo. Non-pharmacological interventions, including exercise-based therapies and traditional Chinese medicine, also showed inconsistent effects on HRQoL.

Table 2. Impact of systemic treatments on ESSPRI score

Study	Intervention vs comparator (n)	Metric	Overall	Dryness	Fatigue	Pain
Bowman 2017	Rituximab (66) vs PBO (67)	Wk 48 MTD (95% CI), p-value	0.54 (–0.12, 1.20), 0.1087	NR	NR	NR
Dorner 2018	Leniolisib (20) vs PBO (10)	NR	Not significant	NR	NR	NR
Van Nimwegen 2020	Abatacept (40) vs PBO (40)	1. Wk 24 difference of median CFB 2. Wk 24 MTD (95% CI), p-value	1. –1.0 vs –0.6 2. –5.0 (–12.7, 2.8), 0.208	1. NR 2. –0.3 (–0.9, 0.4), 0.455	1. NR 2. –2.6 (–14.1, 9.0), 0.664	1. NR 2. –5.2 (–14.5, 4.2), 0.279
de Wolff 2022	Abatacept (40) vs PBO (40)	Wk 48 difference of median CFB	–2.0 vs –1.3	–1.0 vs 0.0	–2.5 vs –1.0	–3.0 vs –2.0
Baer 2021	Abatacept (92) vs PBO (95)	1. Mean CFB (SD) 2. MTD (95% CI)	1. –1.3 (0.3) vs –1.5 (0.3) 2. 0.3 (–0.3, 0.8)	1. –0.8 (0.3) vs –1.0 (0.3) 2. 0.2 (–0.5, 0.8)	1. –1.3 (0.3) vs –1.6 (0.3) 2. 0.3 (–0.4, 0.9)	1. –1.1 (0.3) vs –1.5 (0.3) 2. 0.3 (–0.3, 1.0)
Tsuboi 2023	Abatacept (32)	Wk 52 CFB	–1.1	–0.6	–0.7	–2.3
Shao 2021	Iguratimod (44) vs PBO (22)	Wk 24 Mean CFB (IQR), p-value	–1.4 (–1.9, 0.8), 0.024 vs –0.3 (–0.8, 0.4), 0.528	NR	NR	NR
Clair 2023	Dazodalibep (54) vs PBO (55)	1. LS Mean CFB (SE) 2. MTD (SE), p-value	1. –1.80 (0.23) vs –0.53 (0.23) 2. –1.27 (0.33), 0.0002	NR	NR	NR
Felten 2021	Tocilizumab (55) vs PBO (52)	1. Wk 24 mean CFB 2. Difference in CFB between groups	1. –0.6 vs –0.2 2. –0.4 (–1.0, 0.3)	NR	NR	NR
Mariette 2015	Belimumab (30)	Mean CFB (95% CI), p-value	–0.8 (–1.5, –0.2), 0.0174	NR	NR	NR
Papas 2018	Iscalimab (21) vs PBO (10)	Wk 12 MTD (95% CI)	–0.83 (–2.2, 0.6)	NR	NR	NR
Liu 2019	TGP (211) vs PBO (103)	Mean CFB	–0.21 vs –0.09	NR	NR	NR
Chen 2021	TCM (28) vs PBO (14)	Mean CFB (SD), p-value	–0.62 (1.6) vs –0.91 (1.3), 0.557	–1.14 (1.7) vs –0.93 (1.7), 0.706	–0.75 (2.7) vs –0.93 (2.5), 0.836	–0.07 (2.1) vs –0.86 (1.9), 0.242
Bentley 2023	Petesicatib (38) vs PBO (37)	MTD (95% CI), p-value	–0.22 (–1.08, 0.64), 0.6077	NR	NR	NR

CFB, change from baseline; CI, confidence interval; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; IQR, interquartile range; MTD, mean treatment difference; NR, not reported; PBO, placebo; SE, standard error; TCM, traditional Chinese medicine; TGP, total glucosides of peony; Wk, week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Impact of systemic treatments on fatigue, ocular health, and oral health

Study	Intervention vs comparator (n)	Metric	Fatigue	Ocular health	Oral health
Devauchelle-Pensec 2014	Rituximab (63) vs PBO (57)	1. Wk 24 CFB 2. Wk 24 MTD (95% CI), p-value	1. VAS: 20.1 vs 10.8 2. VAS: 9.3 (−2.0, 20.5), 0.105	NR.	NR.
Bowman 2017	Rituximab (67) vs PBO (66)	Wk 48 MTD (95% CI), p-value	VAS: 2.10 (−5.89, 10.09), 0.6053	NR.	VAS: 4.06 (−12.01 to 3.89)
Dorner 2018	Leniolisib (20) vs PBO (10)	p-value	ESSPRI-F: >0.05 MFI: >0.05	NR.	NR.
van Nimwegen 2019	Abatacept (40) vs PBO (40)	Wk 24 MTD, median (IQR), p-value	MFI: −0.8 (−2.8, 1.2), >0.05 ESSPRI-F: −2.6 (−14.1, 9.0), 0.664	NRS: 0.0 (−0.8, 0.9), >0.05	NRS: −0.6 (−10.1, 8.9), 0.902
de Wolff 2022	Abatacept (40) vs PBO (BL:37; follow up: 36)	Wk 48 CFB median (IQR), p-value	ESSPRI-F: 5.0 (3.8, 7.0), <0.001 vs 6.0 (4.0, 8.0), 0.50 MFI: 13.0 (10.0, 16.3), 0.001 vs 13.0 (11.8, 17.5), 0.492	NR.	NR.
Baer 2021	Abatacept (92) vs PBO (95)	1.Wk 24 CFB (SD) 2. Wk 24 MTD (95% CI), p-value	1. PROMIS-F: −5.6 (1.2) vs −5.6 (1.1) 2. PROMIS-F: 0.04 (−2.3, 2.4), >0.05 1. ESSPRI-F: −1.3 (0.3) vs −1.6 (0.3) 2. ESSPRI-F: 0.3 (−0.4, 0.9), >0.05	1. NRS: −0.9 (0.3) vs −1.0 (0.3)	1. NRS: −1.3 (0.3) vs −1.2 (0.3)
Clair 2023	Dazodaliben (54) vs PBO (55)	CFB mean (SE), p-value	FACIT-F: 8.1 (1.4) vs 2.8 (1.4), 0.0095	OSDI: −14.0 (3.0) vs −8.5 (2.9), 0.001	NR.
Felten 2021	Tocilizumab (55) vs PBO (52)	Wk 24 mean, p-value	FACIT-F: 25.2 (12.9) vs 27.6 (13.5), >0.05 NAS: 6.5 (2.5) vs 6.6 (2.6), >0.05	NR.	NR.
Papas 2018	Iscalimab (21) vs PBO (10)	Wk 12 MTD (95% CI)	MFI: −9.15 (−20.25, 1.96)	NR.	NR.
Fisher 2019	RSLV-132 (22) vs PBO (8)	CFB mean, p-value	PRO-F mental component: 1.53 vs 0.06, 0.046 PRO-F physical component: 0.8 vs 0.06, 0.142	NR.	NR.
Liu 2019	TGP (211) vs PBO (103)	Wk 24 CFB (SD), p-value	VAS: −0.8 (2.1) vs 0 (2.0)	VAS: −1.0 (2.1) vs −0.27 (1.0)	VAS: −1.4 (2.2) vs −0.7 (1.8), 0.019
Chen 2021	TCM (28) vs PBO (14)	CFB mean (SD), p-value	ESSPRI-F: −0.7 (2.6) vs −0.9 (2.5), 0.836	NR.	NR.

CFB, change from baseline; ESSPRI-F, EULAR Sjögren's Syndrome Patient Reported Index-Fatigue; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; IQR, interquartile range; MFI, Multidimensional Fatigue Inventory; MTD, mean treatment difference; NAS, Numerical Analog Scale; NR, not reported; NRS, Numerical Rating Scale; OSDI, Ocular Surface Disease Index; PRO-F, Profile of Fatigue; PROFAD-SSI, Profile of Fatigue and Discomfort-Sicca Symptoms Inventory; PROMIS-F, Patient-Reported Outcomes Measurement Information System-Fatigue; SD, standard deviation; SE, standard error; TCM, traditional Chinese medicine; TGP, total glucosides of peony; VAS, Visual Analogue Scale; VAS-F, Visual Analogue Scale-Fatigue; Wk, week.

Conclusion: Both systemic treatments and non-pharmacological interventions have generally shown limited efficacy in reducing the HRQoL burden in SjD. Although some treatments have demonstrated potential, these findings are primarily derived from clinical studies with small sample sizes and require validation. There remains a significant unmet need for therapies that can effectively alleviate the quality-of-life burden in patients with SjD.

Disclosure: E. Akpek: Abbvie, 2, 6, Alcon, 2, 6, Baush & Lomb, 2, 6, Department of Defense, 5, Dompe, 2, 5, 6, Iolyx, 2, 6, Johnson & Johnson, 2, 6, National Institutes of Health, 5, Novaliq, 2, 6, Novartis, 5, Phycin Inc., 2, 6, Thea, 2, 6, UpToDate, 9, W. L. Gore & Assoc., 2, 6; **E. Adamson**: Johnson & Johnson, 3, 11; **L. Shea**: Johnson & Johnson, 3, 11; **F. Zazzetti**: Johnson & Johnson, 3, 11; **S. Chakravarty**: Johnson & Johnson, 3, 11; **S. Ranjan**: Johnson & Johnson, 12, Employer received funding from Johnson & Johnson to conduct study; **R. Potluri**: Johnson & Johnson, 12, Employer received funding from Johnson & Johnson to conduct study; **A. Keenan**: Johnson & Johnson, 3, 11.

Abstract Number: 1378

Prevalence of Central Nervous System Manifestations in Sjögren's Disease

Arun Varadhachary[1], Ghaith Noaiseh[2], Katherine Hammitt[3], Julie Frantsve-Hawley[3], Paula Barreras Cortes[4], Shamik Bhattacharyya[5], E. Sherwood Brown[6], Drew Carey[7], Robert Fox[8], Brent Goodman[9], Thomas Grader-Beck[10], Janet Lewis[11], Stephen Maitz[12], Steven Mandel[13], Jenifer McCombe[14], Astrid Rasmussen[15], George Sarka[16], Daniel Wallace[17], Frederick Vivino[18], Rochelle Zak[19], Nancy Carteron[20], R Hal Scofield[15] and Steven Carsons[21], [1]Washington University in St. Louis, St. Louis, MO, [2]University of Kansas Medical Center, Kansas City, KS, [3]Sjogren's Foundation, Reston, VA, [4]Cedars Sinai, Los Angeles, CA, [5]Brigham and Women's Hospital, Malden, MA, [6]UT Southwestern Medical Center, Dallas, TX, [7]Johns Hopkins University School of Medicine, Baltimore, MD, [8]Rheumatology Clinic, San Diego, CA, [9]HonorHealth, Scottsdale, AZ, [10]Johns Hopkins, Reisterstown, MD, [11]University of Virginia, Charlottesville, VA, [12]U.S. Department of Veterans Affairs, Coatesville, PA, [13]Donald and Barbara Zucker School of Medicine and Hofstra/Northwell, Hempstead, NY, [14]University of Alberta, Edmonton, AB, Canada, [15]Oklahoma Medical Research Foundation, Oklahoma City, OK, [16]Cedars-Sinai Medical Center, Laguna Hills, CA, [17]Cedars Sinai Medical Center, Studio City, CA, [18]University of Pennsylvania, Bryn Mawr, PA, [19]UCSF Health, San Francisco, CA, [20]University of California, Berkeley & San Francisco, Angwin, CA, [21]NYU Long Island School of Medicine, Mineola, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sjögren's disease is a systemic autoimmune disorder with diverse clinical manifestations affecting multiple organ systems. While dry mouth, dry eyes, fatigue and pain are the most common features, involvement of the central nervous system (CNS) is increasingly reported among Sjögren's patients. CNS manifestations may precede Sjögren's diagnosis and can occur in the absence of classic sicca symptoms, potentially leading to delayed or missed diagnoses. To better understand the neurological aspects, we conducted a scoping review and meta-analysis to characterize the prevalence of CNS manifestations in Sjögren's disease.

Methods: The Sjögren's Foundation convened an expert panel to conduct this scoping review as part of a broader CNS guideline project. We searched PubMed, Embase, and ECRI for articles containing prevalence data on CNS manifestations in Sjögren's from 1980 to September 16, 2024. All articles were screened in duplicate by members of the panel using predefined inclusion criteria (>17 years of age; any sex, gender, ethnicity, or location; any study design; published in English). Studies that were not conducted in a general Sjögren's population were excluded. One author (JFH) extracted data on event counts and total sample size, and a second author (AV) conducted an audit of the extracted data. We used the meta package in R to conduct random-effects meta-analyses of proportions. To stabilize the variance of proportions, we used the Freeman-Tukey double arcsine transformation. We estimated between-study heterogeneity using the restricted maximum likelihood (REML) method.

Results: Our literature search resulted in 20,549 citations. After duplicates were removed, we screened 17,305. 110 articles met the inclusion criteria. Prevalence data for the following CNS manifestations were identified: anxiety, aseptic meningitis, bipolar, brain stem-related symptoms, central sensitization, cerebellar syndrome, cerebral vasculitis, cerebral vascular disease, chronic fatigue syndrome, cognitive dysfunction/impairment, dementia, demyelinating diseases, depression, encephalopathy/delirium, fibromyalgia, headache, insomnia, long-COVID-CNS manifestations, migraine, movement disorders, multiple sclerosis, myelopathy, neuromyelitis optica spectrum disorder, optic neuritis, Parkinson's disease, psychosis, restless leg syndrome, schizophrenia, seizure disorder, stroke, transverse myelitis. Meta-analysis of proportions for each of these CNS manifestations will be presented.

Conclusion: This scoping review and meta-analysis of proportions highlights the prevalence of CNS manifestations in individuals with Sjögren's. By systematically identifying and quantifying these neurological features, this study provides critical insights to inform earlier recognition, prompt referral, and improved multidisciplinary management of Sjögren's disease. These results also support the need for future guidelines and research focused specifically on CNS manifestations to enhance care for this complex patient population.

Disclosure: A. Varadhachary: Alexion, 1, Argenx, 1, 2, Biogen, 5, 6, Blue Oak NX, 1, 11, Capricor, 5, Edgewise, 5, Genentech, 5, Lexeo, 5; **G. Noaiseh**: None; **K. Hammitt**: None; **J. Frantsve-Hawley**: None; **P. Barreras Cortes**: None; **S. Bhattacharyya**: Alexion Pharmaceuticals, 1, 5, Amgen, 1, Roche, 5, UCB, 5; **E. Brown**: None; **D. Carey**: None; **R. Fox**: Novartis, 2; **B. Goodman**: None; **T. Grader-Beck**: Argenx, 5, 12, Consulting fees, Bristol-Myers Squibb(BMS), 5, 12, Consulting fees, Novartis, 5, 12, Consulting fees; **J. Lewis**: None; **S. Maitz**: None; **S. Mandel**: None; **J. McCombe**: None; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **G. Sarka**: None; **D. Wallace**: PPD, 2; **F. Vivino**: Bristol-Myers Squibb, 2; **R. Zak**: None; **N. Carteron**: Bristol-Myers Squibb(BMS), 1; **R. Scofield**: IQVIA, 1, Jannsen Pharmaceuticals, 1; **S. Carsons**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1379

Renal tubular acidosis in Sjögren's disease and non-Sjögren's sicca in an Oklahoma cohort

Biji T Kurien[1], Martha Tsaliki[2] and R Hal Scofield[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]OMRF, Oklahoma City, OK

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Renal involvement in primary Sjögren's disease (pSjD) is a well-known extraglandular manifestation with a prevalence of 5-14% in several studies. Mostly, it affects the renal tubules through tubulointerstitial nephritis, resembling lymphocytic infiltration in the exocrine glands. Distal renal tubular acidosis (RTA), rather than proximal RTA, is the most frequent tubular dysfunction in SjD. We hypothesized that RTA occurs in SjD and non-SjD sicca and will be found in those with high urinary pH, and that it will correlate with serum hypokalemia and bicarbonate.

Methods: We screened urinary and serum metabolic data from primary SjD, incomplete SjD, and healthy controls from the database maintained by Oklahoma Sjögren's Syndrome Center of Research Translation at the Oklahoma Medical Research Foundation (OMRF). This work was part of a study approved by the Institutional Review Board of OMRF and the University of Oklahoma Health Sciences Center.

Results: We found data for urinary pH and metabolic profile in 504 pSjD, 725 incomplete Sjögren's, and 13 healthy controls. Sixty pSjD, 115 non-Sjögren's sicca subjects, and 2 healthy controls had a urinary pH greater than 7.5. Of these 23 SjD, 46 incomplete SjD and 1 healthy control had a pH greater than 8. Seven SjD subjects had a urinary pH of 8.5, while 2 had a pH of 9. Two each of incomplete Sjögren's had a pH of 8.5 and 9. The 23 SjD subjects had a significantly higher alkaline pH compared to incomplete Sjögren's (pH 8.24 ±0.275 Vs 8.06 ±0.224 respectively, p= 0.01). All the 60 pSjD or 115 non-Sjögren's sicca subjects had a highly significant alkaline pH compared to healthy controls (p< 0.0001). However, very interestingly, there was no significant difference in bicarbonate, potassium, or chloride levels between the SjD, incomplete SjD, or the controls in subjects. Anion gap was within normal range in the SjD, non-Sjögren's sicca, and healthy controls. While the SjD and non-Sjögren's sicca subjects with highly alkaline urinary pH may have specific tubular defects that hinder urine acidification, the defects may not be severe enough to bring about RTA in our cohort.

Conclusion: Higher urinary pH is found in SjD compared to non-Sjögren's sicca, and healthy controls. However, the defect in urine acidification does not appear to be related to RTA in our cohort.

Disclosure: B. Kurien: None; **M. Tsaliki**: None; **R. Scofield**: IQVIA, 1, Jannsen Pharmaceuticals, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1380

Phenotyping Neuropathic Pain in Sjögren's Disease: A Cluster-Based Approach

Beatrice Dei[1], Stefano Donati[1], Gaetano La Rocca[2], Giovanni Fulvio[1], Federico Fattorini[1], Antonello Sulis[1], Michele Moretti[1], Elena Elefante[1], Francesco Ferro[3], Giulia Ricci[4], Marta Mosca[5] and **Chiara Baldini**[5], [1]Rheumatology Unit, University of Pisa, Pisa, Toscana, Italy, [2]University of Pisa, Rheumatology Unit, Pisa, Pisa, Italy, [3]Clinical and Experimental Medicine Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Pisa, Italy, [4]Neurology Unit, University of Pisa, Pisa, Toscana, Italy, [5]University of Pisa, Pisa, Pisa, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Neuropathic pain (NeP) is increasingly recognized as a relevant symptom domain in primary Sjögren's disease (SjD), contributing to the disease burden beyond glandular involvement. Despite its potential impact on quality of life, the clinical and patient-reported (PROs) outcomes associated with NeP in SjD remain incompletely understood.

Aim of this study is to investigate the prevalence of NeP in patients with SjD, and identify its associations with clinical features, immunological markers, and PROs including fatigue, pain severity, small fiber symptoms, and emotional distress.

Methods: We conducted a cross-sectional analysis of 112 (105 F:7 M) patients diagnosed with SjD according to ACR/EULAR criteria. NeP was assessed using the DN4 questionnaire (cut-off ≥4). Extra glandular manifestations were prospectively assessed following the ESSDAI. PROs included the ESSPRI, FACIT-Fatigue, VAS items, and the Hospital Anxiety and Depression Scale (HADS). Fibromyalgia was diagnosed according to ACR 2016 criteria. Immunological data included SSA/SSB status, gammaglobulin fractions, complement levels, and histological findings. The SFNSL was administered to assess symptoms related to small fiber neuropathy. Logistic regression models were used to identify independent predictors of neuropathic pain and K-means clustering was applied to DN4 scores to explore phenotypic subgroups.

Results: NeP (DN4 ≥4) was identified in 25% (28/112) of SjD patients. Coexisting fibromyalgia was present in 31.5% (35/112) of the cohort. Patients with NeP had significantly higher fibromyalgia severity scores, ESSPRI, HADSA, HADSD and lower FACIT scores (Fig 1). In multivariate logistic regression, fibromyalgia severity (OR = 1.13, p = 0.017), ESSPRI

Table 1: DN4-based Clusters: Clinical features and Patient-Reported Outcomes

Variable	Cluster 1 (High DN4)	Cluster 2 (Moderate DN4)	Cluster 3 (Low DN4)	p-value
				0.003
Duration of disease (years)	7.4	14.4	8.7	
Age at evaluation (years)	61.2	64.7	62.1	ns
FACIT score	23.8	29.2	38.3	0.001
HADS-A (Anxiety)	12.7	9.8	6.1	0.001
HADS-D (Depression)	9.7	9.3	5.3	0.001
ESSPRI	8.63	7.26	5.53	0.001
VAS Dryness	8	7.36	6.26	0.003
VAS Ocular	9.2	7.45	5.98	0.001
VAS Oral	8.3	7.52	6.09	0.008
VAS Fatigue	8.3	7.76	5.54	0.0001
VAS Pain	8.6	6.94	4.72	0.0001
SFNSL Total	49.9	31	15.5	0.0001
Fibromyalgia Severity	17.4	13.9	5.02	0.0001
C3 (mg/dL)	112	128.9	113.8	ns
C4 (mg/dL)	21.05	24.13	20.64	ns
IgG (mg/dL)	1415	1325	1356	ns
IgA (mg/dL)	228	263	250	ns
IgM (mg/dL)	154	144	122	ns
Focus score	1.21	1.51	1.9	ns
ESSDAI score	2.5	1.66	2.88	ns
SSA (%)	50	64.7	68.2	0.02

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

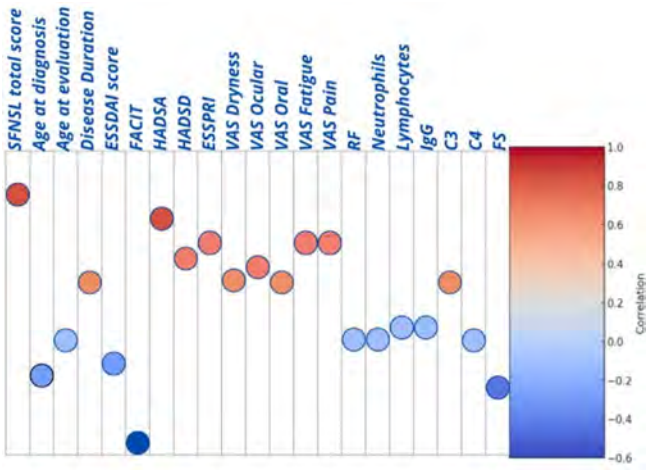


Figure 1: Correlations between DN4 and clinical, histological and laboratory features in SjD

(OR = 1.99, p = 0.024), and FACIT (OR = 0.91, p = 0.032) emerged as independent predictors of NeP. ESSDAI scores did not differ between groups.

Cluster analysis identified three distinct DN4-based phenotypes: high NeP (n=10, DN4≈8), moderate NeP (n=34, DN4≈5), and low/negligible NeP (n=68, DN4≈1) (Table1). These clusters differed significantly in total fibromyalgia score ($p < 0.001$), fatigue ($p < 0.001$), VAS pain, dryness, and SFNSL scores (all $p < 0.001$) (Fig 2). Disease duration was shorter in the high NeP cluster ($p = 0.003$). No significant differences were observed in systemic disease activity (ESSDAI), complement levels, or focus score. A significant association was found between DN4 clusters and SSA status ($p = 0.002$), with SSA-negative patients more frequently classified in higher DN4 clusters. Notably, a strong convergence was observed between DN4 and SFNSL scores ($r=0.754$, $p< 0.001$), supporting the reliability of NeP identification through both tools in this population.

Conclusion: Neuropathic pain defines a distinct symptomatic phenotype in SjD, associated with greater symptom burden, fibromyalgia, and SSA-negativity. Unsupervised clustering highlights the existence of clinically meaningful subgroups based on NeP severity, which are not mirrored by systemic inflammation. These findings underscore the need for comprehensive symptom profiling in SjD beyond conventional immunological and systemic markers.

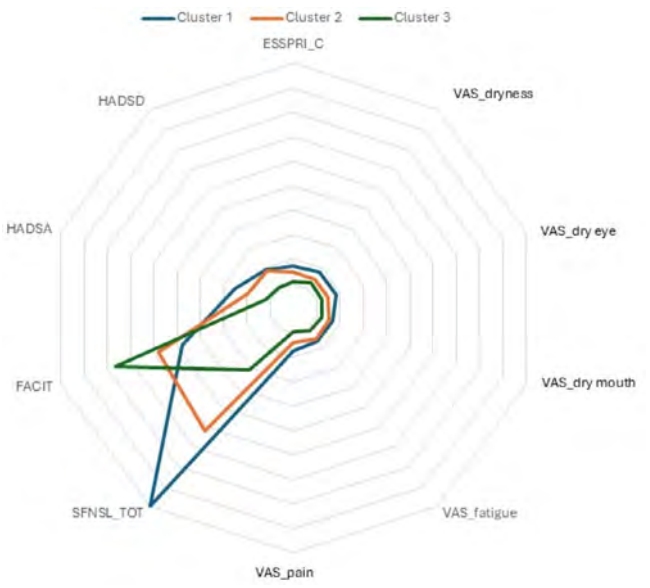


Figure 2: Radar Chart Depicting Differences in Patient-Reported Outcomes Across DN4-Based Clusters"

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: B. Dei: None; **S. Donati**: None; **G. La Rocca**: None; **G. Fulvio**: None; **F. Fattorini**: None; **A. Sulis**: None; **M. Moretti**: None; **E. Elefante**: None; **F. Ferro**: None; **G. Ricci**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **C. Baldini**: None.

Abstract Number: 1381

Self-Reported and Actigraphic Sleep and Circadian Rhythm Disruptions in Patients with Sjögren's Disease: Associations with Disease Activity and Patient-Reported Outcomes

Caterina Di Pede[1], Alessandro Colitta[2], Marco Di Galante[3], Simone Bruno[4], Stefano Donati[1], Beatrice Dei[1], Giovanni Fulvio[1], Gaetano La Rocca[5], Rosaria Talarico[6], Marta Mosca[1], **Chiara Baldini**[7] and Ugo Faraguna[4], [1]Rheumatology Unit, University of Pisa, Pisa, Toscana, Italy, [2]Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa, Toscana, Italy, [3]Sleepacta srl, Montacchiello, Pisa, Italy, Pisa, Toscana, Italy, [4]Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa., Pisa, Toscana, Italy, [5]University of Pisa, Rheumatology Unit, Pisa, Pisa, Italy, [6]Azienda Ospedaliero Universitaria Pisana, Pisa, Pisa, Italy, [7]University of Pisa, Pisa, Pisa, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with Sjögren's Disease (SjD) frequently report debilitating symptoms such as pain, fatigue, and dryness, significantly impacting health-related quality of life. Although sleep disturbances in SjD are well documented, only a few studies have objectively assessed sleep using wrist actigraphy, and none have explored circadian rhythm alterations or their clinical correlates. This study aimed to: (1) evaluate differences in self-reported and actigraphic sleep and circadian parameters between SjD patients and healthy controls (HCs); and (2) examine associations between these disruptions and clinical indices, including disease activity and patient-reported outcomes.

Table 1: Self-reported and Actigraphic Sleep and Circadian Rhythm Parameters in SjD and HCs

Variable	HCs N = 40	SjD N = 46	p-value
Age, mean (SD)	54 (9)	56 (13)	0.4
BMI, mean (SD)	23.33 (3.63)	23.28 (3.37)	>0.9
Female, n (%)	40 (100)	46 (100)	ns
Sleep Health, mean (SD)	3.65 (1.10)	2.80 (0.91)	<0.001
PSQI, mean (SD)	7.2 (2.8)	9.6 (3.6)	<0.001
TST, mean (SD)	7.04 (1.27)	7.14 (1.58)	0.8
WASO, mean (SD)	59 (33)	94 (44)	<0.001
SE, n (%)	88 (6)	82 (10)	<0.001
SRI, n (%)	79 (10)	78 (12)	0.8
Mid-sleep Point, mean (SD)	27 (21)	50 (21)	<0.001
rMEQ, mean (SD)	17.4 (3.7)	16.9 (3.5)	0.5
ESS, mean (SD)	6.4 (3.1)	8.1 (4.4)	0.046
Acrophase, mean (SD)	14.94 (0.86)	15.41 (1.12)	0.033
Amplitude, mean (SD)	0.39 (0.08)	0.40 (0.06)	0.3

BMI: Body-Mass Index (kg/m^2); PSQI: Pittsburgh Sleep Quality Index; TST: Total Sleep Time (hours); WASO: Wake After Sleep Onset (minutes); SE: Sleep Efficiency (%); Sleep Regularity Index (%); rMEQ: reduced Morningness-Eveningness Questionnaire; ESS: Epworth Sleepiness Scale; MESOR: Midline-Estimating Statistic Of Rhythm

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

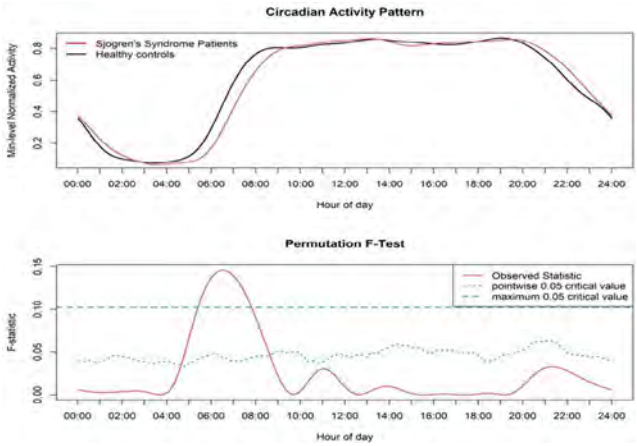


Fig.1 F-Test for 24h-circadian activity

Methods: In this cross-sectional study, we enrolled female SjD patients meeting the 2016 ACR/EULAR criteria, along with age-, sex-, and BMI-matched HCs. Participants underwent 7-day wrist actigraphy. Subjective measures included the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and reduced Morningness-Eveningness Questionnaire (rMEQ). Circadian rhythm parameters were estimated using both parametric and non-parametric methods. Patient-reported outcomes included the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Functional Assessment of Chronic Illness Therapy (FACIT), and Hospital Anxiety and Depression Scale (HADS). Disease activity was assessed using the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI).

Results: Forty-six SjD patients and forty HCs were included. Compared to controls, SjD patients reported poorer sleep quality (higher PSQI scores) and greater daytime sleepiness (higher ESS). Actigraphy revealed lower sleep efficiency (SE), increased wake after sleep onset (WASO), an earlier sleep midpoint, and a significantly advanced sleep midpoint and acrophase, indicating an objective shift towards eveningness (Table 1, Fig 1).

Table 2: Multiple Linear Regression Models Exploring Associations Between ESSPRI, HADS, and Sleep–Circadian Parameters

Independent Variables	ESSDAI β, p	ESSPRI β, p	HADS β,p	Age β, p	BMI β, p	R2	Adjusted R2
Sleep Health	-0.02 (0.6)	-0.01 (0.9)	-0.04 (0.14)	-0.01 (0.4)	-0.08 (0.059)	0.221	0.103
PSQI	-0.03 (0.8)	0.51 (0.024)	0.23 (0.003)	-0.05 (0.2)	-0.25 (0.054)	0.572	0.507
ESS	0.13 (0.5)	0.54 (0.13)	-0.07 (0.6)	-0.04 (0.5)	0.42 (0.046)	0.212	0.093
TST	0.15 (0.050)	-0.03 (0.8)	-0.05 (0.2)	0.03 (0.2)	0.01 (0.9)	0.215	0.096
SE	0.20 (0.7)	0.73 (0.3)	-0.53 (0.030)	-0.13 (0.3)	-0.18 (0.7)	0.206	0.085
WASO	-0.06 (>0.9)	-4.3 (0.2)	2.1 (0.068)	1.2 (0.038)	0.87 (0.7)	0.218	0.1
SRI	-1.3 (0.030)	0.37 (0.7)	0.15 (0.6)	-0.12 (0.4)	-0.79 (0.2)	0.219	0.101
Midpoint	-0.03 (>0.9)	-2.2 (0.2)	1.0 (0.063)	0.57 (0.036)	0.43 (0.7)	0.222	0.104
rMEQ	0.27 (0.13)	-0.38 (0.2)	0.01 (>0.9)	0.06 (0.2)	0.21 (0.2)	0.166	0.039
TST Misperception	-0.06 (0.5)	0.02 (>0.9)	-0.06 (0.3)	0.00 (0.9)	0.01 (>0.9)	0.056	-0.087
SE Misperception	-0.60 (0.6)	-0.83 (0.6)	-1.3 (0.027)	0.38 (0.2)	0.76 (0.5)	0.268	0.158
Acrophase	0.02 (0.7)	-0.01 (>0.9)	-0.04 (0.3)	0.00 (>0.9)	-0.01 (0.9)	0.078	-0.062
Amplitude	0.00 (0.5)	0.00 (0.6)	0.00 (0.8)	0.00 (0.6)	0.00 (0.7)	0.066	-0.075
MESOR	-0.01 (0.008)	0.00 (0.5)	0.00 (0.4)	0.00 (0.8)	0.00 (0.8)	0.199	0.078
Daily Steps	-558 (0.020)	467 (0.2)	-278 (0.031)	12 (0.8)	-151 (0.5)	0.231	0.114

[1] PSQI: Pittsburgh Sleep Quality Index; ESS: Epworth Sleepiness Scale; TST: Total Sleep Time (hours); SE: Sleep Efficiency (%); WASO: Wake After Sleep Onset (minutes); SRI: Sleep Regularity Index (%); rMEQ: reduced Morningness-Eveningness Questionnaire); MESOR: Midline-Estimating Statistic Of Rhythm.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Higher ESSPRI and HADS scores were associated with worse subjective sleep quality, greater sleepiness, lower total sleep time, reduced sleep efficiency, and increased WASO. Higher ESSDAI scores correlated with reduced daytime activity levels (lower MESOR) and fewer daily steps. Sensitivity analyses suggested that greater disease activity was linked to longer total sleep time and reduced sleep regularity (Table 2).

Conclusion: Conclusions: SjD is associated with both subjective and objective disruptions in sleep and circadian rhythms. These alterations correlate with disease activity and patient-reported outcomes, especially fatigue, mood disturbances, and physical inactivity. Circadian rhythm dysregulation may represent an underrecognized aspect of SjD, with potential implications for future therapeutic approaches.

Disclosure: C. Di Pede: None; **A. Colitta**: None; **M. Di Galante**: None; **S. Bruno**: None; **S. Donati**: None; **B. Dei**: None; **G. Fulvio**: None; **G. La Rocca**: None; **R. Talarico**: None; **M. Mosca**: None; **C. Baldini**: None; **U. Faraguna**: None.

Abstract Number: 1382

Interstitial lung disease in primary sjögren syndrome: pathochrony, seronegative cases, and Risk of progressive pulmonary fibrosis

Delia Reina[1], Paula Estrada-Alarcón[2], Daniel Roig-Vilaseca[1], Dacia Cerdà[1], Vanessa Navarro-Angeles[3], oscar Camacho[1], Sergi Herdia[4], Marta lópez-Gómez[1], Silvia Gacía-Díaz[1], Paola Vidal Montal[5], Pol Maymó-Paituvi[6], martí Aguilar-Coll[7] and Javier Narváez[8], [1]Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain, [2]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [3]Department of Rheumatology, Complex Universitari Hospitalari Moisès Broggi, Sant Joan Despí, Barcelona, Spain, Sant Joan Despí, Barcelona, Spain, [4]Complex Hospitalari Moisès Broggi, Barcelona, Spain, [5]Bellvitge University Hospital, Barcelona, Spain, [6]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [7]Hospital Universitari de Bellvitge, Barcelona, Spain, [8]Hospital Universitari de Bellvitge, L'Hospitalet; Barcelona, Barcelona, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a chronic autoimmune disorder primarily targeting exocrine glands. A significant extraglandular manifestation is interstitial lung disease (ILD), which contributes to considerable morbidity and can adversely affect patient outcomes. Our aim is to describe the clinical characteristics and disease course of a primary Sjögren's syndrome-associated ILD (pSS-ILD) cohort, with a specific focus on the proportion progressing to progressive pulmonary fibrosis (PPF).

Methods: This multicenter, retrospective, observational study included patients with pSS-ILD confirmed by high-resolution chest CT (HRCT). Diagnosis of pSS was based on anti-SSA/Ro positivity, salivary gland biopsy, or salivary gland ultrasound (grade 2 or 3 according to OMERACT SG US definitions).

Results: A total of 45 patients (91% women) were included, with a mean age at ILD diagnosis of 67 years (SD: 11). ILD preceded pSS diagnosis in 78% (35/45), with a median lead time of 8 months (IQR: 4–17). In 22% (10/45), ILD developed after pSS, with a median interval of 48 months (IQR: 21–64.5). Anti-SSA/Ro antibodies were present in 38% (16/42), anti-SSB/La in 24.5% (11/45), and 38% (17/45) were seronegative.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1: Basal and follow-up general, immunological, clinical, radiological and treatment characteristics of our cohort of patients with Sjogren Disease (SjD) and interstitial lung disease (ILD), n=45.

General Characteristics:	
Sex, W:M (% women)	10:1 (91)
Age at ILD diagnosis, mean (SD)	67.0 (11)
ILD first;SS after, n (%)	35 (78)
Total follow-up, months, median [Q1-Q3]	56 [30-84]
Months between ILD and SjD, median [Q1-Q3]	8 [4-17]
Immunological characteristics:	
ANA positive, n (%)	36 (73%)
Anti-SSA/Ro, n=42 (%)	16 (38%)
RF, n (%)	15 (33%)
Anti-SSB/La, n (%)	11 (24.5%)
Hypergammaglobulinemia, n (%)	23 (47%)
Cryoglobulins, n (%)	1 (6%)(n=16)
Sjögren's disease characteristics:	
Raynaud's phenomenon, n (%)	8 (17)
Parotidomegalia, n(%)	7 (15)
Vasculitis, n(%)	0
Skin involvement, n(%)	0
Arthritis, n (%)	11 (23.4)
Renal disease, n (%)	4 (8.5)
Peripheral neuropathy, n(%)	2 (4.3)
Lymphoma, n (%)	2 (4.3)
Liver involvement, n (%)	2 (4.3)
ILD basal characteristics:	
NSIP, n (%)	26 (58)
OP, n (%)	9 (20)
LIP, n (%)	4 (9)
UIP, n (%)	6 (13)
ILD treatment, n=43	
GC, any dose, n (%)	33 (77)
GC initial dose, mg/day, mean (SD)	32 (14)
Conventional immunosuppressive, n, (%)	33 (77)
Rituximab, n (%)	11 (25.6)
Abatacept, n (%)	1 (2.3)
Antifibrotic, n (%)	10 (26)
ILD follow-up characteristics:	
Follow-up FVC, %, mean (SD)	83 (30)
Follow-up DLCO, %, mean (SD)	55 (26)
6 min walking distance, mts.; mean (SD)	341 (120)
CT follow-up, months, median [Q1-Q3]	31 [15-70]
Oxygen requirement	11 (24)

Radiologically, 58% (26/45) had nonspecific interstitial pneumonia (NSIP), including 14 with fibrotic NSIP; 13% (6/45) had usual interstitial pneumonia (UIP); 20% (9/45) had organizing pneumonia (OP) or NSIP with OP; and 9% (4/45) had lymphocytic interstitial pneumonia (LIP). Follicular bronchiolitis was found in 38% (17/45).

At ILD diagnosis, mean %pFVC was 84.4 ± 21.5 (IQR: 70.8–101.7), %pDLCO was 62.2 ± 17.3 (IQR: 48–76), and 6MWT distance was 371 ± 114 m (IQR: 306–422). Mean ESSDAI was 12 (SD: 5; IQR: 7–16).

Treatment included glucocorticoids in 77% (33/43; mean prednisone dose: 32 ± 14 mg/day), immunosuppressants in 77% (mycophenolate in 31, azathioprine in 2), and biologics in 28% (rituximab in 11, abatacept in 1). Antifibrotic therapy (nintedanib or pirfenidone) was initiated in 26% (10/43) due to progression to PPF.

After a median follow-up of 56 months (IQR: 30–84), 24% (11/45) required oxygen therapy due to chronic respiratory failure, 4% (2/45) were referred for lung transplantation, and 18% (8/45) died due to ILD progression or infections.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: ILD was the initial or predominant manifestation leading to pSS diagnosis in 78% of cases. Seronegative status was common (38%), highlighting the need to consider pSS in ILD patients with sicca symptoms. At least 26% progressed to PPF and required antifibrotic therapy.

Disclosure: D. Reina: None; **P. Estrada-Alarcón**: None; **D. Roig-Vilaseca**: None; **D. Cerdà**: None; **V. Navarro-Angeles**: None; **o. Camacho**: None; **S. Herdia**: None; **M. lópez-Gómez**: None; **S. Gacía-Díaz**: None; **P. Vidal Montal**: None; **P. Maymó-Paituvi**: None; **m. Aguilar-Coll**: None; **J. Narváez**: None.

Abstract Number: 1383

Obesity in Primary Sjogren's Disease

Gabriela Hernandez-Molina[1], Donaji Gómez-Velasco[2], Ariel Garcia-Torralba[2], Carlos Aguilar-Salinas[2] and Ivette Cruz-Bautista[2], [1]Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Federal District, Mexico, [2]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Obesity is an excessive fat accumulation that presents a risk to health. Little is known about the relationship between obesity and Sjögren's disease (SjD). We evaluated the prevalence of obesity in a cohort of patients with primary SjD, as measured by anthropometric indices such as body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), as well as with a body composition variable, the fat mass index (FMI). We also assessed the association of obesity with clinical and serologic features, disease activity, damage, and symptoms (sicca/fatigue/pain).

Methods: We included 91 patients with SjD. We registered demographics, comorbidities, glandular/ extraglandular and serologic variables. We assessed the Schirmer-I test and non-stimulated salivary flow, and scored the cumulative ESSDAI, SSDDI and ESSPRI scores. We measured the body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR). We defined obesity as a BMI ≥30 kg/m^2. Central obesity was defined as WC >90 cm and >80 cm; or by a WHR >0.90 and >0.85, for men and women, respectively. All patients underwent bioimpedance analysis (BIA) to measure body fat mass index (FMI). An elevated/high FMI according to BIA definitions was classified as obese (≥9.3 kg/m^2 for women and ≥6.2 kg/m^2 for men).

Results: 97.8% were women with a mean age of 54.4±12.8 years, and a median disease duration of 10 years. The prevalence of obesity was 19.7%, 52.7%, 52.7% and 40.6%, according to the BMI, WC, WH, and FMI, respectively. When we compared obese vs non-obese patients according to BMI, the first group had a higher prevalence of anti-Ro/SSA antibodies (90.4% vs 66.7%), and were more likely to have hypertension (25% vs 6.7%).

When we compared obese vs non-obese patients according to their WC, the obese group had a longer disease duration (13 vs 9 years) and a higher cumulative ESSDAI score (12 vs 6.5 points). They were also more likely to have parotid gland enlargement (58.1% vs 34.5%), and higher globulin levels (3.9 vs 3.5 g/dL). In logistic regression analysis, the variables that remained associated with obesity were disease duration (OR 1.06 95% CI 0.99-1.1, p=0.05) and the SSDDI score (OR 1.36, 95% CI 1.04-1.7, p=0.02). A similar finding was observed when we compared obese patients according to the WHR with their counterpart (SSDDI score OR 1.31, 95% CI 1.01-1.69, p=0.03)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patients with obesity according to the FMI were more likely to have parotid gland enlargement (54.1% vs. 31.4%), neurologic involvement (35.1 vs 13.5%), higher cumulative ESSDAI scores (11 vs 7 points) , higher SSDDI scores (3 vs 2 points), and higher globulin levels (3.8 vs 3.6 g/dL). These patients were also more likely to have hypertension (24.3% vs 9.3%). In the logistic regression analysis, the variable that was again associated with obesity was the SSDDI score (OR 1.50, 95% CI 1.1-1.9, p=0.005).

Conclusion: According to BMI, at least 20% of patients were obese, this prevalence increased to 40% when BIA was used, with a higher prevalence found in central obesity. Obesity was associated with accrual damage. Our results may have implications for weight reduction in this patient group.

Disclosure: G. Hernandez-Molina: None; **D. Gómez-Velasco**: None; **A. Garcia-Torralba**: None; **C. Aguilar-Salinas**: None; **I. Cruz-Bautista**: None.

Abstract Number: 1384

Systematic Review of Therapies for Central Nervous System Manifestations in Sjögren's Disease

Ghaith Noaiseh[1], Arun Varadhachary[2], Katherine Hammitt[3], Julie Frantsve-Hawley[3], Paula Barreras Cortes[4], Shamik Bhattacharyya[5], E. Sherwood Brown[6], Drew Carey[7], Robert Fox[8], Brent Goodman[9], Thomas Grader-Beck[10], Janet Lewis[11], Stephen Maitz[12], Steven Mandel[13], Jenifer McCombe[14], Astrid Rasmussen[15], George Sarka[16], Daniel Wallace[17], Frederick Vivino[18], Rochelle Zak[19], Nancy Carteron[20], R Hal Scofield[15] and Steven Carsons[21], [1]University of Kansas Medical Center, Kansas City, KS, [2]Washington University in St. Louis, St. Louis, MO, [3]Sjogren's Foundation, Reston, VA, [4]Cedars Sinai, Los Angeles, CA, [5]Brigham and Women's Hospital, Malden, MA, [6]UT Southwestern Medical Center, Dallas, TX, [7]Johns Hopkins University School of Medicine, Baltimore, MD, [8]Rheumatology Clinic, San Diego, CA, [9]HonorHealth, Scottsdale, AZ, [10]Johns Hopkins, Reisterstown, MD, [11]University of Virginia, Charlottesville, VA, [12]U.S. Department of Veterans Affairs, Coatesville, PA, [13]Donald and Barbara Zucker School of Medicine and Hofstra/Northwell, Hempstead, NY, [14]University of Alberta, Edmonton, AB, Canada, [15]Oklahoma Medical Research Foundation, Oklahoma City, OK, [16]Cedars-Sinai Medical Center, Laguna Hills, CA, [17]Cedars Sinai Medical Center, Studio City, CA, [18]University of Pennsylvania, Bryn Mawr, PA, [19]UCSF Health, San Francisco, CA, [20]University of California, Berkeley & San Francisco, Angwin, CA, [21]NYU Long Island School of Medicine, Mineola, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease is recognized as a multifaceted autoimmune disease impacting almost any organ or body system. Of particular importance is the central nervous system (CNS) involvement, which may manifest before classic sicca symptoms. The Sjögren's Foundation is conducting a systematic review on the treatment of CNS manifestations, the conclusions of which will inform the development of clinical practice guidelines and advance patient outcomes in an often underrecognized aspect of Sjögren's.

Methods: The Sjögren's Foundation convened an expert panel to conduct a systematic review as part of a broader CNS guideline project. Our PICO question was: *What are effective treatments for Sjögren's patients >17 years of age with or without an accompanying rheumatic or non-rheumatic autoimmune disorder who are diagnosed with any central nervous system manifestation?* Outcomes of interest include mortality, disability, health-related quality of life, any qualitative or quantitative measures of clinically relevant improvement, symptom stabilization, serious adverse events specific to Sjögren's, activities of daily living, effects on family or caregivers, healthcare resource utilization, and cost-effectiveness. In

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

anticipation of very limited direct evidence in a Sjögren's population, evidence on treating CNS manifestations in lupus was included as an indirect source of evidence. We searched PubMed, Embase, and ECRI for articles containing prevalence data on 53 CNS manifestations in Sjögren's disease from 1980 to September 16, 2024. All articles were screened in duplicate by members of the panel using predefined inclusion criteria (>17 years of age; any sex, gender, ethnicity or location; any treatment, published in English). Exclusions were narrative reviews, editorials, case reports, and case series with < 4 cases.

Results: Our initial literature search resulted in 20,549 citations. After duplicates were removed, we screened 17,305. 16,222 articles were excluded based on title and abstract review, and 1083 articles are undergoing full-text review. Due to insufficient data for conducting a meta-analysis, summative narrative results will be presented.

Conclusion: Our preliminary findings underscore both the complexity and the critical importance of accurately identifying and managing CNS manifestations in Sjögren's disease. Although the initial literature search yielded a high volume of citations, a substantial number did not meet the inclusion criteria, underscoring the relative scarcity of robust data on this topic. Given the limited available evidence specific to Sjögren's disease, the decision to include parallel data from lupus research provides a necessary indirect comparison to inform clinical decision-making. The results of this systematic review will be essential for developing rigorous, evidence-based recommendations on the evaluation and management of CNS manifestations in Sjögren's disease.

Disclosure: G. Noaiseh: None; **A. Varadhachary**: Alexion, 1, Argenx, 1, 2, Biogen, 5, 6, Blue Oak NX, 1, 11, Capricor, 5, Edgewise, 5, Genentech, 5, Lexeo, 5; **K. Hammitt**: None; **J. Frantsve-Hawley**: None; **P. Barreras Cortes**: None; **S. Bhattacharyya**: Alexion Pharmaceuticals, 1, 5, Amgen, 1, Roche, 5, UCB, 5; **E. Brown**: None; **D. Carey**: None; **R. Fox**: Novartis, 2; **B. Goodman**: None; **T. Grader-Beck**: Argenx, 5, 12, Consulting fees, Bristol-Myers Squibb(BMS), 5, 12, Consulting fees, Novartis, 5, 12, Consulting fees; **J. Lewis**: None; **S. Maitz**: None; **S. Mandel**: None; **J. McCombe**: None; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **G. Sarka**: None; **D. Wallace**: PPD, 2; **F. Vivino**: Bristol-Myers Squibb, 2; **R. Zak**: None; **N. Carteron**: Bristol-Myers Squibb(BMS), 1; **R. Scofield**: IQVIA, 1, Jannsen Pharmaceuticals, 1; **S. Carsons**: None.

Abstract Number: 1385

Characterizing Isolated Dryness Phenotypes in Sjögren's Syndrome

Giovanni Fulvio[1], Rossana Izzetti[2], Francesco Gulia[2], Valentina Donati[3], Gaetano La Rocca[4], Inmaculada Concepción Navarro García[5], Beatrice Dei[1], Francesco Ferro[6], Marta Mosca[7] and Chiara Baldini[7], [1]Rheumatology Unit, University of Pisa, Pisa, Toscana, Italy, [2]University of Pisa, Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, Unit of Dentistry and Oral Surgery, Pisa, Italy, [3]Azienda Ospedaliero-Universitaria Pisana (AOUP), Unit of Pathological Anatomy 2, Pisa, Italy, [4]University of Pisa, Rheumatology Unit, Pisa, Pisa, Italy, [5]University of Pisa, Clinical and Experimental Medicine, Rheumatology Unit, Pisa, Italy, [6]Clinical and Experimental Medicine Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Pisa, Italy, [7]University of Pisa, Pisa, Pisa, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Ocular and oral dryness, occurring in isolation, represent distinct phenotypic subsets within Sjögren's disease (SjD). However, potential differences in glandular imaging findings and pathophysiological mechanisms have not yet been adequately investigated. This study investigates how isolated ocular, isolated oral, and combined dryness

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

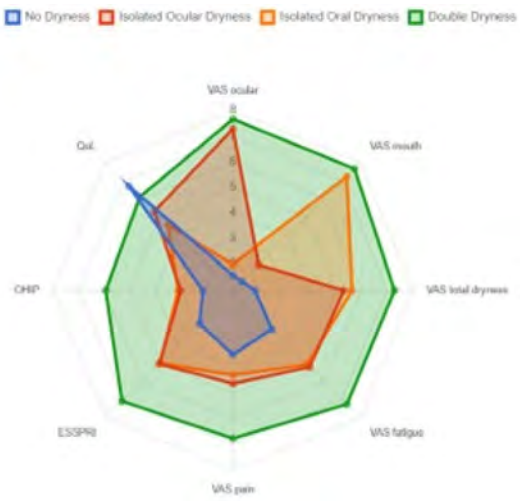


Figure 1 - Comparative Analysis of Patient-Reported Outcomes Across Dryness Phenotypes in Sjögren's Syndrome This radar chart illustrates the differences in various patient-reported outcomes including quality of life (QoL), Oral Health Impact Profile (OHIP), EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), and Visual Analogue Scale (VAS) assessments for ocular and oral dryness, total dryness, pain, and fatigue. Each colour represents a different group: no dryness (blue), isolated ocular dryness (red), isolated oral dryness (orange), and double dryness (green), highlighting their respective impacts on the dimensions assessed.

phenotypes in SjD differ with respect to ultrasonographic patterns, histological findings, functional test outcomes, and patient-reported metrics

Methods: We retrospectively reviewed patients diagnosed with SjD based on the 2016 EULAR/ACR criteria from January 2017 to December 2024. All participants underwent labial gland biopsies and comprehensive imaging using high-frequency ultrasonography: 18 MHz for major salivary glands (SGUS), 48 MHz for lacrimal glands (LGUHFUS), and 70 MHz for labial salivary glands (LSGUHFUS). A semiquantitative OMERACT score (0–3) was used to define abnormal imaging (score ≥2).

Table 1 - Demographic and Clinical Characteristics of Sjögren's Syndrome Patients by Dryness Phenotype This table presents a comprehensive comparison of demographic and clinical parameters among Sjögren's syndrome patients categorized into no dryness, isolated ocular dryness, isolated oral dryness, double dryness, and combined isolated ocular or oral dryness groups. Key parameters include age, gender distribution, Ocular Surface Disease Index (OSDI), unstimulated salivary flow rate (USWR), Schirmer's test scores, Focus Score, Ectopic Lymphoid Structures (ELS), Major Salivary Gland Ultrasonography (SGUS), Lacrimal Gland Ultrasonography (LGUHFUS), labial salivary glands (LSGUHFUS) and EULAR Sjögren's syndrome disease activity index (ESSDAI).

	No Dryness	Isolated Ocular Dryness	Isolated Oral Dryness	Double Dryness	p-value
Age	51.4±6.2	52.3±3.8	56.8±3.5	56.6±2.2	0.147
Gender	1/22 (4.5%)	4/32 (12.5%)	2/24 (8.3%)	9/113 (8.0%)	0.764
OSDI	5,1±2.4	15,8±3.6	7,9±3.5	18,2±2.1	**0,001**
USWR	3,5±1.7	3,7±1.1	2,9±1.5	1,8±0.4	**0.002**
Schirmer	12,2±3.5	5,6±2.0	6,2±2.4	5,0±0.8	**0**
Focus Score	2,0±0.8	1,3±0.32	1,4±0.36	1,9±0.4	0.24
ELS	2,1±1.1	1,3±0.5	2,3±1.3	2,1±0.5	0.362
SGUS	4,1±2.1	3,3±1.6	5,6±2.2	4,9±1.0	0.333
LGUHFUS	2,0±0	2,0±2	2,7±0.6	2,4±0.4	0.807
LSGUHFUS	1,8±0.4	1,8±0.4	1,7±0.4	1,9±0.2	0.813
ESSDAI	4,7±1.2	2,8±1.1	3,9±1.4	5,6±1.1	**0.045**

	No Dryness	Isolated ocular or oral dryness	Double Dryness	p-value
Age	51.4±6.2	54.2±3.7	56.6±2.2	0.163
Gender	1/22 (4.5%)	6/56 (10.7%)	9/113 (8.0%)	0.656
OSDI	5,1±2.4	12.5±2.7	18,2±2.1	**0,001**
USWR	3,5±1.7	3.32±0.9	1,8±0.4	**0.001**
Schirmer	12,2±3.5	5.96±1.6	5,0±0.8	**0,001**
Focus Score	2,0±0.8	1.3±0.2	1,9±0.4	0.123
ELS	2,1±1.1	1.7±0.6	2,1±0.5	0.597
SGUS	4,1±2.1	4.4±1.3	4,9±1.0	0.729
LGUHFUS	2,0±0	2.3±1.0	2,4±0.4	0.884
LSGUHFUS	1,8±0.4	1.8±0.3	1,9±0.2	0.76
ESSDAI	4,7±1.2	3.3±0.9	5,6±1.1	**0.023**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient-reported outcome (PRO) included the ESSPRI, OSDI, OHIP, and VAS scores for oral and ocular dryness. Dryness was categorized into four groups based on VAS scores: no dryness (VAS ocular< 5, VAS oral < 5), isolated ocular dryness (VAS ocular ≥5, VAS oral < 5), isolated oral dryness, (VAS ocular< 5, VAS oral ≥5) and double dryness (VAS ocular≥5, VAS oral≥5). In addition, patients presenting with either ocular dryness or oral dryness were analyzed separately. Systemic disease activity was evaluated using the ESSDAI score while functional assessment included unstimulated salivary flow rate (USWR) and the Schirmer's test

Results: Among 191 SjD patients (mean age 55.3 ± 1.9 years; 8.4% male), 22 had no dryness, 32 isolated ocular, 24 isolated oral, and 113 both symptoms. PROs scores followed a gradient, with the double dryness group reporting the highest symptom burden, the no dryness group the lowest, and the isolated dryness groups falling in between (see Fig.1). Quality of Life (QoL) scores were higher in the no dryness group. Patients with isolated ocular dryness exhibited lower Schirmer's test values compared to those with no dryness and isolated oral dryness (5.6±2.0 vs 12.2±3.5 and 6.2±2.4 respectively), but higher than double dryness (5.0±0.8, p< 0.001). Similarly, patients with isolated oral dryness had lower USWR than those with no dryness or isolated ocular dryness (2.9±1.5 vs 3.5±1.7 and 3.7±1.1 respectively), but higher than patients with double dryness (1.8±0.4) (Tab.1). No significant differences were observed in labial salivary gland histology or in the ultrasonographic findings of the lacrimal, labial, and major salivary glands. Finally, ESSDAI scores were lower in isolated ocular (2.8 ±1.1) and oral dryness (3.9±1.4) compared to no dryness (4.7±1.2) or double dryness (5.6±1.1)

Conclusion: In SjD isolated ocular and oral dryness are linked to specific functional deficits in the lacrimal and salivary glands, respectively. However, these isolated forms do not exhibit significant differences in histological features or glandular ultrasonographic findings. Clinically, isolated dryness appears to define a milder and distinct phenotype of SjD, marked by limited systemic involvement and a moderate burden on patient-reported outcomes

Disclosure: G. Fulvio: None; **R. Izzetti**: None; **F. Gulia**: None; **V. Donati**: None; **G. La Rocca**: None; **I. Navarro García**: None; **B. Dei**: None; **F. Ferro**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **C. Baldini**: None.

Abstract Number: 1386

Characterization and Progression of Localized Amyloidosis in Sjogren's Syndrome: Evidence Long-Term (1995-2025) Follow-Up of a Cohort compared to Literature Review.

Hoang Nguyen[1], Philip Moresco[2], Antoine Chiu[2], Asha Patnaik[3] and Peter Gorevic[4], [1]Stony Brook University-Renaissance School of Medicine- Department of Rheumatology, Jamaica, NY, [2]Stony Brook University -Renaissance School of Medicine, Stony Brook, NY, [3]Stony Brook University Hospital, Stony Brook, NY, [4]Stony Brook University, Stony Brook, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: -Sjogren's syndrome (SS) is a chronic autoimmune disorder, defined by keratoconjunctivitis sicca (KCS), specific serologies, and a significant risk of extra-exocrine disease manifestations and B-cell lymphoma[1].

- Amyloidosis is the local or systemic accumulation of abnormal protein aggregates[2].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient Number	Age of SS Diagnosis	Age of Amyloidosis Diagnosis	Length of F/U (Years)	Location(s) of Amyloid	Amyloid Typing	Serum IFE and/or Urine IFE	Kappa/Lambda Ratio	Systemic Progression
1	38	38	9	Pulmonary	AL(λ)	(-)	0.49	None
2	26	41	2	Pulmonary	AL(λ) & AL(κ)	(-)	1.48	None
3	60	68	15	Cutaneous	AL(λ)	(-)	N/A	None
4	51	73	11	Pulmonary	AL(κ)	(-)	0.97	Yes
5	49	56	3	Pulmonary	AL(λ)	(-)	1.36	None
6	54	59	21	Cutaneous	AL(λ)	(-)	N/A	None
7	17	37	1	Cutaneous	AL(λ)	(-)	1.73	None
8	32	41	7	Breast → Pulmonary	AL(λ)	(-)	1.02	None

Cohort Characteristics

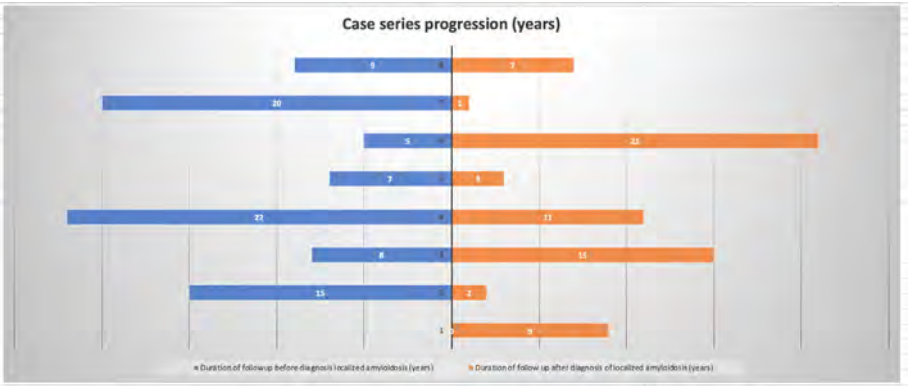
-Localized amyloidosis is a known, but rare, complication of SS[3], and is poorly characterized as to long-term course and treatment options.

-We report a case series of eight individuals with SS and localized amyloidosis, followed for an average of 8.65 years (range 1-21 years). Our results were compared to literature review to compile a description of localized amyloidosis in the setting of SS.

Methods: Our eight-patient cohort was seen and followed by PG over a 30-year period as part of an amyloidosis referral practice. PubMed was searched through January 2025 for the terms: amyloidosis, amyloid, Sjogren's syndrome, and their combinations.

Results: -In our cohort, the average age of SS at diagnosis was 40.9 (range 17-54). The average age at the time of amyloidosis diagnosis was 51.6 (range 37-73). 7/8 patients developed amyloid after being diagnosed with KCS/SS 12.3 years prior (range 5-22). In the remaining patient, SS and amyloidosis were diagnosed concurrently. The diagnosis of amyloidosis was made by immunohistochemistry and amyloid typing by sequence analysis, including mass spectrometry (7/8 patients). All samples stained positive for Congo red, and 8/8 were the AL subtype. Six patients had AL (λ), one had AL (κ), and in one patient both light chain types were present. All eight patients initially presented with localized amyloidosis, with no indication of systemic disease on detailed work-up. Of these patients, 4 had pulmonary amyloidosis, 3 had cutaneous amyloidosis, and 1 had intraparenchymal breast amyloidosis (**Figure 1A**). During the averaged 8.6 year follow-up (range 1-21), only the patient with intraparenchymal breast amyloid progressed to have systemic disease. In this patient, a pulmonary amyloid lesion presented six years after the original amyloid diagnosis. The remaining seven patients have had stable disease (**Figure 1B**; **Table 1**).

-We performed a literature search for articles published on SS and amyloidosis and found 55 publications comprising 74 total patients. The mean age of diagnosis of SS was 52, while amyloidosis was diagnosed at 59. The predominant subtype was AL (κ) (39.7%), followed by AL (λ) (19.05%). Most patients presented with local amyloidosis (92.68%) with the most



Case series progression follow-up

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

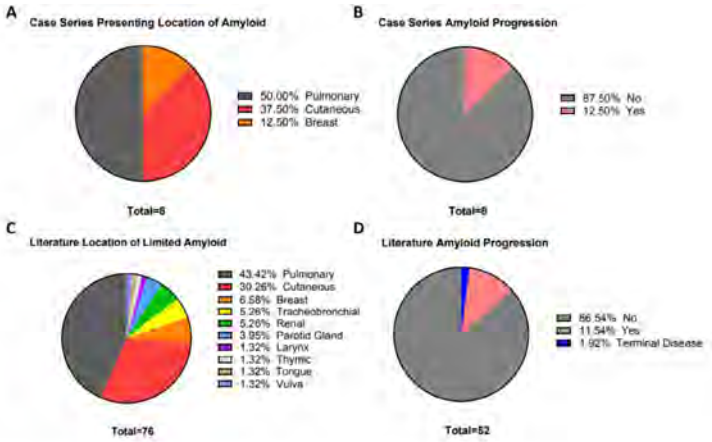


Figure 1: Location of amyloid in case series (**A**) or literature search (**C**) and disease progression in case series (**B**) or literature search (**D**).

Location of localized amyloid and disease progression in case series versus literature review.

common location being pulmonary (43.42%), cutaneous (30.26%), and breast (6.58%) (**Figure 1C**). Of those reported, 86.54% with localized disease did not have disease progression, 11.54% did have progression, and one patient had terminal disease (**Figure 1D**).

Conclusion: -In our long-term follow-up of amyloidosis in SS, we monitored for local and systemic progression for an average duration 8.6 years (range 1-21 years).

-Between our cohort and our literature search, we find the most common location for amyloidosis in SS is pulmonary, then cutaneous, and finally breast.

-While the majority of cases are stable and do not progress, a subset of patients do, requiring close monitoring.

Disclosure: H. Nguyen: None; **P. Moresco**: None; **A. Chiu**: None; **A. Patnaik**: None; **P. Gorevic**: None.

Abstract Number: 1387

Demographic and Clinical Characteristics of Patients Diagnosed With Sjögren's Disease Using Electronic Health Records and Linked Claims Data From the US Excellence Network in RheumatoloGY (ENRGY) Practice-Based Research Network

Jeffrey Curtis[1], Emily Holladay[2], Antton Egana[3], Anjana Lalla[3], Yujie Su[4], Fenglong Xie[5], Amy Mudano[4], Shanette Daigle[4] and Sara McCoy[6], [1]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [2]University of Alabama at Birmingham, Edmond, OK, [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [4]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [5]The University of Alabama at Birmingham, Birmingham, AL, [6]University of Wisconsin–Madison, Madison, WI

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

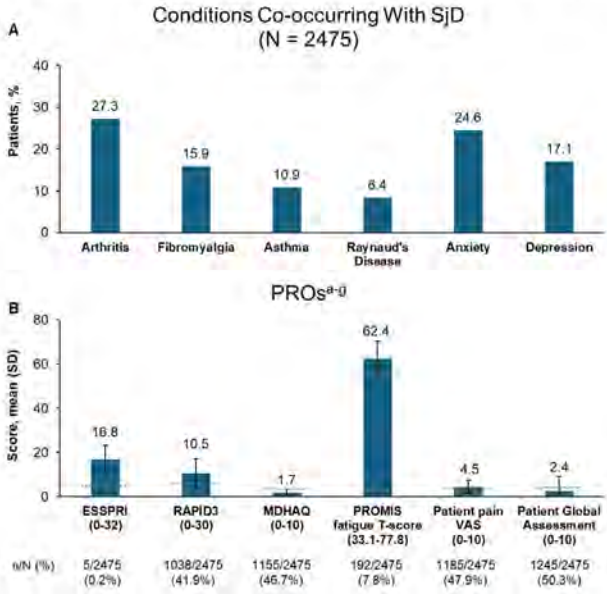
Table 1. Patient Demographics and Clinical Characteristics

Characteristic	Total population (N=2475)	No overlapping autoimmune conditions (n=1427)	Overlapping autoimmune conditions (n=1048)
Age, mean (SD), years	52.8 (12.9)	52.7 (13.2)	53.2 (12.4)
Female, n (%)	2272 (91.8)	1316 (92.2)	956 (91.2)
Overlapping autoimmune conditions, n (%)			
Juvenile/rheumatoid arthritis	11 (0.4)	NA	11 (1.0)
Myositis	20 (0.8)	NA	20 (1.9)
Systemic lupus erythematosus	386 (15.6)	NA	386 (36.8)
Systemic sclerosis	55 (2.2)	NA	55 (5.2)
Any asthenia-polyalgia symptoms, n (%)	2175 (87.9)	1254 (87.9)	921 (87.9)
Arthralgia (joint pain)	1758 (71.0)	1006 (70.5)	752 (71.8)
Fatigue	1302 (52.6)	760 (53.3)	542 (51.7)
Myalgia (muscle pain)	570 (23.0)	356 (24.9)	214 (20.4)
Any extraglandular symptom, n (%)	1751 (70.7)	718 (68.5)	1,033 (72.4)
Prevalent extraglandular symptoms, n (%)			
Dermatitis	694 (28.0)	420 (29.4)	274 (26.1)
Dysphagia	254 (10.3)	144 (10.1)	110 (10.5)
Headaches	698 (28.2)	405 (28.4)	293 (28.0)
Lymphadenopathy	157 (6.3)	96 (6.7)	61 (5.8)
Raynaud's disease	236 (9.5)	115 (8.1)	121 (11.5)
SS-A/Ro antibody positive, n/M[a] (%)	492/1447 (34.0)	270/869 (31.1)	222/578 (38.4)

NA, not applicable; SS-A, Sjogren's syndrome-related antigen A. a n/M is the number of patients with positive test/number of evaluable patients.

Background/Purpose: Sjögren's disease (SjD) is a chronic autoimmune disease characterized by systemic symptoms such as dryness, fatigue, musculoskeletal pain, and extraglandular manifestations. SjD may overlap with other autoimmune diseases like systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA). This analysis characterized the demographics, clinical characteristics, and patient-reported outcomes (PROs) of patients with SjD treated in a rheumatology setting and evaluated comorbidities 12 months post-diagnosis.

Figure 1. (**A**) Proportion of Patients With Conditions Co-Occurring With SjD at 12 Months Post-Index and (**B**) Mean PRO Scores Collected Closest to Index Up to 12 Months Post Diagnosis



ESSPRI, EULAR Sjogren's Syndrome Patient Reported Index; MDHAQ, Multidimensional Health Assessment Questionnaire; n/N, number of patients evaluated/total patient population; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; RAPID3, Routine Assessment of Patient Index Data 3; SjD, Sjögren disease; VAS, visual analog scale. a Gray dotted lines represent cutoff points for moderate disease for each PRO. b ESSPRI score of ≥5 indicates unsatisfactory symptom status. c RAPID3 disease severity states are defined as remission (≤3), low (3.1-6), moderate (6.1-12), and high (≥12). d MDHAQ physical function score of 3.3 to 6.6 indicates moderate limitation of physical function. e PROMIS fatigue T-score is defined as normal (≤50), mild (50-55), moderate (55-65), and severe (≥65). f Patient pain VAS is defined as mild (≤3.4), moderate (3.5-7.4), and severe (≥7.5). g Patient Global Assessment is defined as mild disease (≤3), moderate (4.1 to <7), and severe (≥7).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Adult patients in the Excellence Network in RheumatoloGY (ENRGY) rheumatology network with ≥2 ICD-9 and ICD-10-CM codes for SjD diagnoses ≥28 to ≤365 days apart from January 2017 through February 2023 were included in this retrospective analysis of electronic health record (EHR) data. Prior to diagnosis by a rheumatologist, patients were required to have ≥12 months without an SjD diagnosis. Patient EHR data were linked to administrative claims from the Komodo Health database. The index date was defined as the date of the first SjD diagnosis. Demographic and clinical data were captured at index. Clinical manifestations and PRO outcomes collected closest to and within 12 months before or after index were reported

Results: Among 2475 patients, 91.8% were female and the mean (SD) age was 52.9 (12.9) years. Dryness symptoms were common (55.8%) prior to diagnosis, including dry eyes (22.4%) and mouth (10.8%). Asthenia-polyalgia was the most commonly occurring symptom in the pre-index period (87.9%), including arthralgia (71.0%), fatigue (52.6%), or myalgia (23.0%) (**Table 1**). Many patients had ≥1 extraglandular symptom (70.7%) (**Table 1**). Among the 58.5% of patients who underwent SS-A antibody testing, 34.0% tested positive. Diagnostic procedures including salivary gland ultrasound (15.4%) were infrequent, and magnetic resonance sialography, ocular surface staining test, and unstimulated whole saliva flow test were rare (< 0.1%). Anxiety (35.9%) and depression (27.1%) were common, and 42.3% had overlapping autoimmune diseases pre- and post-index, such as RA (29.1%), SLE (15.6%), and systemic sclerosis (2.2%). Patient characteristics were similar irrespective of overlapping autoimmune disease (**Table 1**). Frequent comorbidities 12 months post-diagnosis included arthritis, anxiety, Raynaud's disease, depression, and fibromyalgia (**Figure 1**). Mean (SD) PRO scores included EULAR Sjögren's Syndrome Patient Reported Index (16.8 [6.5]; n=5), Routine Assessment of Patient Index Data 3 (10.5 [6.6]; n=1038), Pain 0-10 (4.5 [2.9]; n=1185), and Patient Global Assessment (2.4 [6.6]; n=1245).

Conclusion: This analysis of EHR data revealed a range of extraglandular symptoms and comorbidities with SjD. Diagnostic procedures were infrequent, and common symptoms like dryness were under-reported. PRO scores indicated high disease burden, with high rates of anxiety, depression, and arthritis—the latter most commonly co-occurring 1 year post-diagnosis. These findings reveal the complex clinical challenges faced by patients with SjD.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **E. Holladay**: None; **A. Egana**: Novartis, 3; **A. Lalla**: Novartis, 3; **Y. Su**: None; **F. Xie**: None; **A. Mudano**: None; **S. Daigle**: None; **S. McCoy**: Amgen, 2, Aurinia, 2, iCell, 2, Kiniksa, 2, Novartis, 2, Otsuka, 2, TearSolutions, 2, Visterra, 2.

Abstract Number: 1388

Positive predictive value of various diagnostic codes for the classification of primary Sjögren's syndrome

Kaci Clement[1], Cynthia Crowson[2], sarah Achenbach[1], Elena myasoedova[1], eva carmona[3], Robert Vassallo[1], Vanessa Kronzer[1] and elena Joerns[3], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Stewartvillle, MN, [3]Mayo Clinic, Rochester

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Table 1: Definitive, probable, possible, or unlikely classification of primary Sjögren's syndrome using the 2016 ACR-EULAR classification criteria

Classification Designation	Criteria
Definitive	Meets ACR-EULAR classification criteria
Probable	Positive serology (SSA) with other supporting characteristics* or being treated for Sjögren's by a rheumatologist
Possible	Positive serology (SSA)
Unlikely	Does not meet any diagnostic criteria and alternate diagnosis is suspected.

*Supporting characteristics include presence of renal tubular acidosis, polyclonal hypergammaglobulinemia, autonomic neuropathy, elevated inflammatory markers, lymphoma, fevers, weight loss, lymphadenopathy, glandular swelling, unexplained rashes, lung involvement, joint pain, in the absence of alternative explanation.

Background/Purpose: Primary Sjögren's syndrome is a multisystem autoimmune disorder characterized by progressive dysfunction of exocrine glands leading to symptoms of keratoconjunctivitis and xerostomia.

There is no cure for Sjögren's syndrome, however a multidisciplinary approach with care from a rheumatologist, dentist, and ophthalmologist can be adopted to help manage symptoms. Diagnosis of the condition can be difficult due to the overlap between Sjögren's syndrome and other diseases. In 2016 the ACR-EULAR classification criteria for primary Sjögren's syndrome were established. Application of these classification criteria, especially for enrollment in clinical trials, can help differentiate between primary Sjögren's syndrome and patients that need further evaluation. Accurate classification of patients is crucial for their treatment and prognosis.

Methods: We analyzed a quaternary medical center-based biobank cohort identifying patients with 2+ ICD codes associated with Sjögren's syndrome. This was done as a subset of a study investigating patients with interstitial lung disease (ILD) within the biobank, Patients also had 2+ codes associated with ILD as well as 1+ codes for computed tomography scan of the chest. Patient records were manually reviewed for information leading to a definitive, probable, possible, or unlikely classification of primary Sjögren's syndrome using the 2016 ACR-EULAR classification criteria (Table 1). Patient characteristics were compared using Kruskal-Wallis and chi-square tests. We calculated positive predictive value (PPV) for each of the ICD codes associated with Sjögren's syndrome to assess whether code-based algorithms could be used to predict definitive Sjögren's syndrome.

Table 2: Characteristics of patients with 2+ diagnostic codes for Sjögren's syndrome

Characteristic	Definitive n=14 (17) n(%)	Probable n=23 (28) n(%)	Possible n=20 (24) n(%)	Unlikely n=26 (31) n(%)	Total n=83 (100) n(%)	p-value
Age at 2nd Sjögren's code, mean(SD)	59.7(9.8)	67.4(10.6)	68.0(14.9)	60.2(10.7)	64.0(12.1)	**0.017**
Female sex	14(100)	17(74)	19(95)	14(54)	64(77)	**0.001**
Positive anti-SSA	13(93)	20(87)	3(15)	0(0)	36(43)	**<0.001**
Positive Schirmer test	5(36)	1(4)	0(0)	2(8)	8(10)	**0.003**
Lip biopsy performed	8(57)	6(26)	2(10)	4(15)	20(24)	**0.009**
Ocular staining score>5 (or Van Bijsterveld)	2(14)	0(0)	0(0)	0(0)	2(2)	**0.018**
Immunomodulatory therapy	11(79)	15(65)	2(10)	1(4)	29(35)	**<0.001**
Peripheral neuropathy	1(7)	1(4)	3(15)	2(8)	7(8)	0.645
Glandular swelling	2(14)	1(4)	2(10)	1(4)	6(7)	0.573
Polyclonal hypergammaglobulinemia	2(14)	11(48)	2(10)	1(4)	16(19)	**0.001**
Joint involvement	3(21)	8(35)	4(20)	2(8)	17(20)	0.138
Interstitial lung disease	6(43)	13(57)	5(25)	3(12)	27(33)	**0.006**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: PPV of various ICD codes in predicting definitive Sjögren's syndrome classification subtypes

ICD-10 Code*	Definitive (n=14) n (PPV)	Probable (n=23) n (PPV)	Possible (n=20) n (PPV)	Unlikely (n=26) n (PPV)
M35.00 (Unspecified Sjögren / SICCA)	11 (0.26)	13 (0.30)	13 (0.30)	6 (0.14)
M35.01 (Keratoconjunctivitis Sjögren/SICCA)	2 (0.33)	0 (0)	3 (0.50)	1 (0.17)
M35.02 (Sjögren/SICCA with lung involvement)	2 (1)	0 (0)	0 (0)	0 (0)
M35.05 (Sjögren/SICCA with inflammatory arthritis)	0 (0)	0 (0)	0 (0)	1 (1)
M35.09 (Sjögren/SICCA with other organ involvement)	1 (1)	0 (0)	0 (0)	0 (0)
ICD-9 710.2 (SICCA syndrome)	12 (0.21)	18 (0.32)	9 (0.16)	17 (0.30)

PPV – positive predictive value, ICD – International Classification of Disease

*2+ codes 30+ days apart at any point in time

Results: Eighty-three patients with codes of interest were identified within the biobank cohort (Table 2). Of these 83 patients, 14 (17%) fit classification criteria for definitive Sjögren's syndrome, 23 (28%) - for probable Sjögren's syndrome, 20 (24%) -for possible Sjögren's syndrome, and 26 (31%) were unlikely to be classified with primary Sjögren's syndrome. Positive anti-SSA (Ro) was the most common classification criteria seen among the 71 (86%) patients who underwent serological testing in the cohort. Diagnosis of Sjögren's syndrome by a rheumatologist was noted in 55% of the total cohort but in 100% of the definitive subgroup. None of the ICD codes had a high PPV for definitive Sjögren's syndrome category by chart review (Table 3).

Conclusion: This work highlights the difficulty with the classification of Sjögren's syndrome even within a group of patients that have multiple diagnostic codes for the condition. A large proportion of patients had missing data, many did not have serological or clinical testing available for review. Continued education for providers who are likely to evaluate patients for Sjögren's syndrome in their clinic, such as primary care or ophthalmology, is crucial to improve diagnosis and patient care. Future directions include development of an algorithm to help accurately classify patients with definitive Sjögren's syndrome without extensive chart review.

Disclosure: K. Clement: None; **C. Crowson**: None; **s. Achenbach**: None; **E. myasoedova**: None; **e. carmona**: Boehringer-Ingelheim (SEPAR), 6, vitalograph, 6; **R. Vassallo**: Regeneron, 6, Rion LLC, 11, Sanofi, 2; **V. Kronzer**: None; **e. Joerns**: Boehringer-Ingelheim, 1.

Abstract Number: 1389

Association of Dry Eye Severity with Salivary Flow in Patients with Primary Sjögren's Syndrome

Janett C. Riega-Torres[1], **Karina Palomo-Arnaud**[2], Jose Martinez-Delgado[3], Fernando Morales-Wong[3], Jesus Mohamed-Hamsho[3], Valeria Mata-Riega[2], Irma Cantu-Zapata[2], Luis Medina-Gomez[2], Miguel Betancourt-De la Torre[2], Aritze Chong-Amezcua[2], Dionicio A. Galarza-Delgado[4] and Karim Mohamed-Noriega[3], [1]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [2]Hospital Universitario "Dr. José Eleuterio González", Rheumatology, Monterrey, Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Hospital Universitario "Dr. José Eleuterio González", Ofthalmology, Monterrey, Nuevo León, Monterrey, Nuevo Leon, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sjögren's Syndrome (SS) is a multisystemic autoimmune disease that causes hypofunction of salivary and lacrimal glands, manifesting in xerostomia and xerophthalmia among other systemic manifestations. Unstimulated whole salivary flow rate (UWSF) is a test used to quantify saliva production, a decrease in USWF rate impacts the quality of life in patients with SS. Similarly, dry eye tests are useful tools in everyday clinical practice to identify inflammatory damage to the ocular surface. An abnormal UWSF, along with positive serology, a reduced Schirmer's test, and a positive minor salivary gland biopsy is included in the 2016 ACR/EULAR SS classification criteria. However, the association between UWSF and dry eye tests is poorly known. We aimed to explore if there is an association between UWSF and dry eye severity.

Methods: A cohort of rheumatic patients with dry eye disease (DED) (2015-2024) was analyzed. Patients aged 18-years or older, with DED symptoms and primary SS diagnosis (according to ACR-EULAR 2016 criteria) were included. Patients were divided into two groups according to UWSF in 5 minutes (group 1: UWSF ≤0.5 ml/5min, group 2: UWSF >0.5 ml/5min). MSG biopsy, tear film osmolarity (OSM), matrix metalloproteinase 9 (MMP-9), Ocular Surface Disease Index (OSDI), Tear break-up time (TBUT), SICCA Ocular Surface Staining (SICCA OSS), and Schirmer tear test with and without anesthesia (STT) were evaluated. Only the worst eye was included, which was selected as the eye with the higher SICCA OSS score. Associations and results were presented using (frequencies [%], mean ± SD, median [IQR]), and we used Chi^2, Mann-Whitney U, or Student's tests as appropriate. Institutional ethics committee approval was received; all participants provided written informed consent.

Results: Eighty-nine patients with primary SS were included, the mean age was 52.6 ± 12.8 years, and 97.7% (87/89) were women. Forty-three (48.3%) patients had a UWSF ≤0.5 ml/5 min, and 46 (51.7%) patients had a UWSF >0.5 ml/5 min. We observed a higher proportion of patients with positive MMP-9 in the UWSF ≤0.5 ml/5 min group (15/43,34.9%) than those with a UWSF >0.5 ml/5 min (7/46,15.2%; p=0.041). Patients with UWSF ≤0.5 ml/5 min also showed higher OSDI scores (48.85 ± 27.83) than patients with UWSF >0.5 ml/5 min (34.76 ± 21.58; p=0.010). There was no difference in SICCA OSS scores, Schirmer's tear test with or without anesthesia, tear film osmolarity, and tear break-up time.

Conclusion: Patients with low salivary flow had greater ocular surface damage and more dry eye disease symptoms.

Table 1. Dry eye severity according to unstimulated whole salivary flow rate (UWSF) among patients with Sjögren's Syndrome.

	All N= 89	Low salivary flow (≤0.5 ml/5 min) N=43	Normal Salivary flow (>0.5 ml/5 min) N=46	p-value*
Age, years, mean ± SD	52.6 ± 12.8	54.45 ± 13.08	50.91 ± 12.27	0.200
Sex, n (%)				0.167
Female	87 (97.7%)	43 (100%)	44 (95.7%)	
Male	2 (2.2%)	0 (0.0%)	2 (4.3%)	
Positive MSG biopsy, n (%)	72 (80.0%)	34 (79.1%)	38 (82.6%)	0.497
Positive MMP-9, n (%)	22 (24.4%)	15 (34.9%)	7 (15.2%)	**0.041**
OSDI score, mean ± SD	41.72 ± 25.7	48.85 ± 27.83	34.76 ± 21.58	**0.010**
SICCA OSS score, mean ± SD	6.63 ± 3.69	7.68 ± 3.4	6.35 ± 3.74	0.164
Schirmer's tear test w/o anesthesia, median (IQR)	7 (0-35)	7 (0-35)	8.5 (0-35)	0.715
Schirmer's tear test with anesthesia, median (IQR)	5 (1-35)	5 (1-35)	6 (1-31)	0.389
TBUT, median (IQR)	4 (1-15)	4 (1-15)	4 (1-15)	0.642
Tear film osmolarity, median (IQR)	310 (277-397)	307 (277-397)	310 (281-351)	0.752

UWSF= Unstimulated Whole Salivary Flow rate, MSG= minor salivary gland, MMP-9= Matrix metalloproteinase 9, OSDI= Ocular Surface Disease Index, SICCA OSS= SICCA ocular surface staining, STT= Schirmer tear test with and without anesthesia, TBUT= tear break-up time.

*Comparison between UWSF ≤0.5 ml/5 min and UWSF >0.5 ml/5 min.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Riega-Torres: None; **K. Palomo-Arnaud**: None; **J. Martinez-Delgado**: None; **F. Morales-Wong**: None; **J. Mohamed-Hamsho**: None; **V. Mata-Riega**: None; **I. Cantu-Zapata**: None; **L. Medina-Gomez**: None; **M. Betancourt-De la Torre**: None; **A. Chong-Amezcua**: None; **D. Galarza-Delgado**: None; **K. Mohamed-Noriega**: None.

Abstract Number: 1390

Cystic Lung Disease and Autoantibodies in Lymphocytic Interstitial Pneumonia: Exploring the Impact of Sjögren's Syndrome

KARLA CHACON[1], ALBERTO ALEJANDRO MARQUEZ-SANCHEZ[1], Jorge Rojas-Serrano[2] and MAYRA MEJÍA[1], [1]Instituto Nacional de Enfermedades Respiratorias, CIUDAD DE MEXICO, Distrito Federal, Mexico, [2]Instituto Nacional de Enfermedades Respiratorias, Mexico City, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Lymphocytic interstitial pneumonia (LIP) is a rare interstitial lung disease, most commonly associated with Sjögren's syndrome, but it may also occur in the context of other autoimmune diseases. Despite its low prevalence, LIP can significantly impact patients' quality of life, particularly in cases progressing to severe pulmonary restriction. Accurate characterization of LIP is essential, as early diagnosis can guide timely interventions, including consideration for lung transplantation in advanced cases.

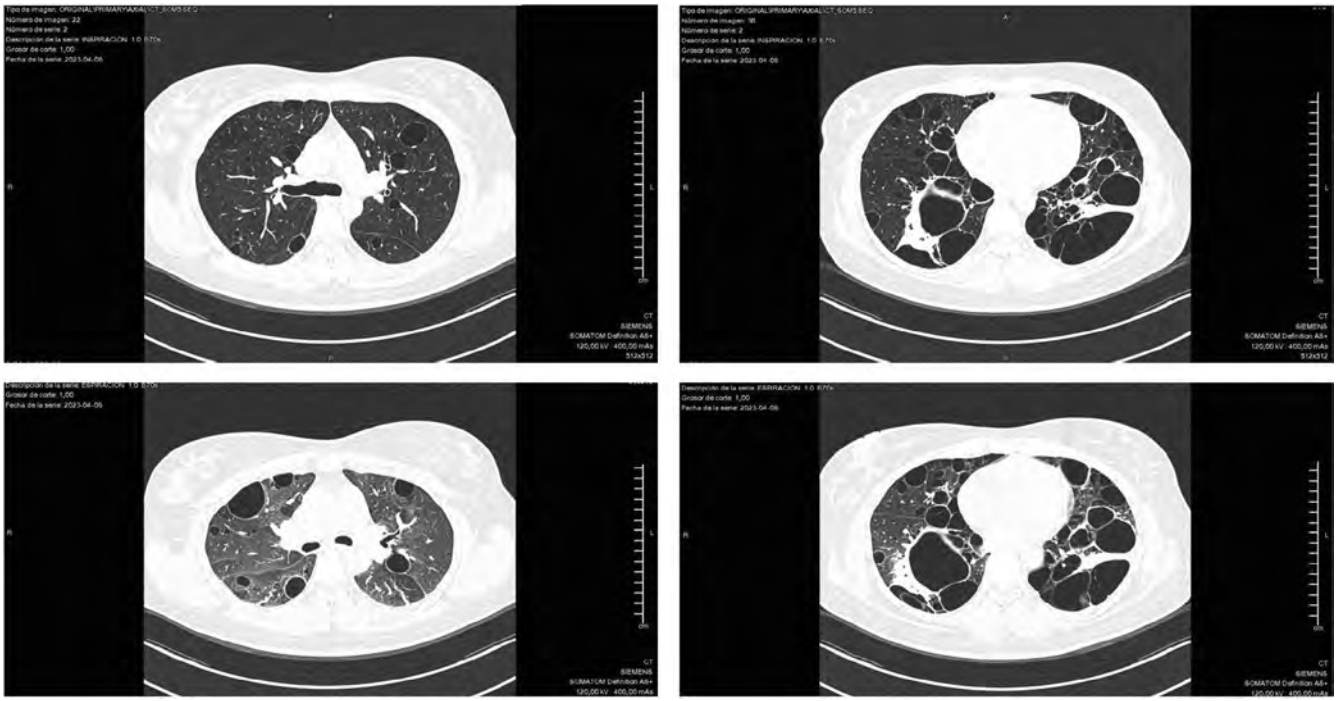
Methods: We conducted a cross-sectional study of patients with lymphocytic interstitial pneumonia (LIP) diagnosed by multidisciplinary consensus between rheumatology and pulmonology. Clinical, serological, and functional variables were systematically collected. Pulmonary function tests included forced vital capacity (FVC); a restrictive pattern was defined as FVC < 80% of predicted. Chest CT scans were evaluated for the number and size of pulmonary cysts. Cystic disease was considered diffuse when more than 10 cysts were identified. The largest cyst in each patient was measured along its longest axis and reported in millimeters.

Table 1. Comparison of Clinical, Serological, and Radiological Characteristics in Patients With Lymphocytic Interstitial Pneumonia According to Sjögren's Status

Variables	Total n=46	Sjögren's n = 27	Non Sjögren's n=19	p
Age, years (mean ± SD)	62.15 ± 12.71	64.59 ± 12.68	58.68 ± 12.25	0.12
Female, n (%)	40 (86.96)	24 (88.89)	16 (84.21)	0.64
Ever smoke, n (%)	11 (23.91)	7 (25.93)	4 (21.05)	0.70
Arthritis, n (%)	21 (45.65)	13 (48.15)	8 (42.11)	0.68
Sicca syndrome, n (%)				0.49
Ocular dryness	2 (4.35)	1 (3.72)	1 (5.26)	
Dry mouth	7 (15.22)	5 (18.52)	2 (10.53)	
Both	23 (50)	15 (55.56)	8 (42.11)	
ANA positive, n/N (%)	35/38 (92.11)	24/24 (100)	11/14 (78.57)	**0.01**
Anti Ro positive, n/N (%)	19/37 (51.35)	15/21 (71.43)	4/16 (25)	**<0.01**
High titter Anti Ro, n(%)	16 (43.24)	13 (61.9)	3 (18.75)	**<0.05**
Anti La positive, n/N (%)	16/35 (45.71)	13/20 (65)	3/15 (20)	**<0.05**
Rheumatoid factor positive, n/N (%)	12/31 (38.71)	7/19 (36.84)	5/12 (41.67)	0.78
Salivery gland biopsy				0.63
Focus score <1	2/12 (16.67)	2 (18.18)	0	
Focus score ≥1	10/12 (83.33)	9 (81.82)	1 (100)	
Serum IgG level, mg/dL (n=40)	1565 ± 572.22	1587.92 ± 512.22	1529.26 ± 680.08	0.75
Serum IgM level, mg/dL (n=40)	152.6 ± 110.09	135.04 ± 75.05	181.86 ± 150.45	0.19
Serum C3 level, g/L (n=37)	112.54 ± 29.54	112.47 ± 30.47	112.64 ± 29.06	0.98
Serum C4 level, g/L (n=37)	22.12 ± 11.05	21.56 ± 11.49	23.05 ± 10.63	0.69
High titter IgG >2000 mg/dL, n (%)	10 (25)	6 (24)	4 (26.67)	0.85
Reduced FVC<80%, n/N (%)	16/37 (43.24)	9/21 (42.86)	7 (43.75)	0.95
Cyst number>10	38 (82.61)	24 (88.89)	14 (73.68)	0.18
Largest cyst size, mm (median ± SD)	28.04 ± 22.01	33.81 ± 26.03	19.84 ± 10.58	**0.03**

Comparison of Clinical, Serological, and Radiological Characteristics in Patients With Lymphocytic Interstitial Pneumonia According to Sjögren's Status

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Chest CT of a Patient With Sjögren's Syndrome and Lymphocytic Interstitial Pneumonia Showing Cysts >10 mm in Diameter; A–B: Inspiratory Phase, C–D: Expiratory Phase

Results: A total of 46 patients with LIP were included; 58.7% had associated Sjögren's syndrome. Other autoimmune diagnoses included rheumatoid arthritis (10.9%), rheumatoid arthritis with Sjögren's overlap (6.5%), systemic sclerosis (8.7%), lupus (2.2%), antisynthetase syndrome (2.2%), and interstitial pneumonia with autoimmune features (IPAF) (2.2%). Four patients (8.7%) had no identifiable autoimmune disease.There were no significant differences in age, sex, smoking history, or pulmonary function between groups. Sjögren's patients had a higher prevalence of ANA positivity (100% vs 78.6%, p=0.01), anti-Ro (71.4% vs 25%, p< 0.01), and anti-La antibodies (65% vs 20%, p< 0.05). High-titer anti-Ro was significantly more frequent in the Sjögren's group (61.9% vs 18.8%, p< 0.05). Serum immunoglobulin levels, complement levels, and the proportion of patients with IgG >2000 mg/dL did not differ significantly. Although diffuse cystic disease (defined as >10 cysts) was common in both groups (88.9% vs 73.7%, p=0.18), the largest cyst size was significantly greater in patients with Sjögren's (33.8 ± 26.0 mm vs 19.8 ± 10.6 mm, p=0.03).

Conclusion: In this cohort of patients with LIP, those with Sjögren's syndrome exhibited a more pronounced autoimmune profile and significantly larger cysts, despite similar lung function. These findings support the hypothesis that LIP in Sjögren's may represent a distinct immunopathologic phenotype, potentially driven by exaggerated bronchus-associated lymphoid tissue (BALT) hyperplasia. Early recognition of this phenotype may inform prognosis and guide decisions regarding close monitoring or early referral for lung transplantation.

Disclosure: K. CHACON: None; **A. MARQUEZ-SANCHEZ**: None; **J. Rojas-Serrano**: None; **M. MEJÍA**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1391

Assessment of Anti-ssa/ro Testing Across Various Commercial Laboratories in the United States to Reduce the Burden of Surveillance in Pregnant Women with No History of Fetal Atrioventricular Block (fAVB)

Mala Masson[1], Bettina Cuneo[2], Philip Carlucci[3], Peter Izmirly[4], Justin Brandt[5], Colin Phoon[6], Ashley Roman[6], Amit Saxena[7], Michael Belmont[5], Christina Penfield[6], Young Mi Lee[6], Julie Nusbaum[5], Andrew Rubenstein[6], Elena Sinkovskaya[8], Alfred Abuhamad[8], Gary Satou[9], Whitnee Hogan[10], Anita Moon-Grady[11], Lisa Howley[12], Mary Donofrio[13], Stephanie Levasseur[14], Miwa Geiger[15], Sonal Owens[16], Kristopher Cumbermack[17], Jyothi Matta[18], Gary Joffe[19], Christopher Lindblade[20], Caitlin Haxel[21], Katherine Kohari[22], Joshua Copel[22], James Strainic[23], Tam Doan[24], Conisha Holloman[24], Stacy Killen[25], Theresa Tacy[26], Michelle Kaplinski[26], Nalani Sachan[6], Nicola Fraser[6], Robert Clancy[14] and Jill Buyon[6], [1]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [2]University of Arizona College of Medicine, Tucson, AZ, [3]New York University School of Medicine, New York, NY, [4]New York University Grossman School of Medicine, New York, NY, [5]NYU Langone Health, New York, NY, [6]NYU Grossman School of Medicine, New York, NY, [7]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [8]Eastern Virginia Medical School, Norfolk, VA, [9]University of California Los Angeles, Los Angeles, CA, [10]University of Utah, Salt Lake City, UT, [11]University of California San Francisco, San Francisco, CA, [12]Midwest Fetal Care Center, Children's Minnesota/ Allina Health, Minneapolis, MN, [13]Children's National Hospital, Washington, DC, [14]Columbia University, New York, NY, [15]Mount Sinai School of Medicine, New York, NY, [16]University of Michigan, Ann Arbo, MI, [17]University of Kentucky, Lexington, KY, [18]University of Louisville, Louisville, KY, [19]Perinatal Associates of New Mexico, Albuquerque, NM, [20]Phoenix Children's Hospital, Phoenix, AZ, [21]University of Vermont Children's Hospital, Burlington, VT, [22]Yale University, New Haven, CT, [23]UH Rainbow Babies, Cleveland, OH, [24]Baylor College of Medicine, Houston, TX, [25]Vanderbilt University, Nashville, TN, [26]Stanford University, Stanford, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: For women with Sjögren's disease, the risk of Fetal Atrioventricular Block (fAVB) is a critical aspect in pregnancy counseling. To date, the most reliable predictor of fAVB is a previously affected child, followed by high titer Anti-SSA/Ro52 and 60 antibody titers. In advising on risk for women without an affected child, physicians face the challenge of interpreting different reporting units and upper limits of commercial assay values. Accordingly, this current study leveraged a prospective, anti-SSA/Ro positive pregnancy cohort to compare results obtained from commercial laboratories across the U.S. to those measured in a central research laboratory. The goal was to identify commercial values that would associate with a low risk of fAVB and reduce the need for standard of care surveillance.

Table 1: Anti-SSA/Ro Testing Across Eight Laboratories.

Commercial Laboratory	Negative	Positive Range	Total Patients	Positive below upper limit and < 1000 EU for both anti-Ro52 + 60	Positive below upper limit and > 1000 EU for either anti-Ro52 or 60	Positive above upper limit but < 1000 EU for both anti-Ro52 + 60	Positive above upper limit and > 1000 EU for either anti-Ro52 or Ro 60
ARUP	< 40	Linear, no limit	74	N/A- See Table 2	N/A- See Table 2	N/A- See Table 2	N/A- See Table 2
Bioplex	< 1.0	1 - >8 no specificity	354	66/81	15/81	49/273	224/273
Mayo Labs	≤ 19.9	Anti Ro52 20 - >1374.8 Anti Ro60 20 - >1885.3	21	8/10	2/10	0/11	11 /11
Minnesota Healthpartners	< 6.9	7 - >240 no specificity	21	10/12	2/12	0/9	9/9
UCSF China Basin Labs	< 20	Anti-Ro52 20 - >1300 Anti-Ro60 20 - >1300	17	6/6	0/6	0/11	11/11
SHC Lab	< 20	20 - >100 no specificity	15	4/7	3/7	0/8	8/8
UCLA Lab	< 20	20 - >80 no specificity	13	6/6	0/6	0/7	7/7
Yale New Haven Lab	< 7.0	7 - >240 no specificity	11	2/3	1/3	1/8	7/8

Table 2: Spearman's Rank Correlation Coefficient Between ARUP Laboratory and NYU Research Laboratory.

	Anti-52kd	Anti-60kd
Spearman's Rank Correlation Coefficient	0.7788	0.7497
r^2	0.6065	0.5621
P-value	2.22E-16	1.53E-14
Covariance	360.0137	346.661
Sample size (n)	74	74

Methods: Seven hundred and sixty-six pregnant subjects from 24 centers who tested positive for anti-SSA/Ro (either anti-Ro52 or anti-Ro60 or both) in their local commercial assay were referred to STOP BLOQ for prospective evaluation by home fetal Doppler to rapidly identify emergent fAVB. Eight laboratories were included in this analysis, each testing at least 10 subjects (capturing 526 study participants). The values and descriptors of ranges are provided in Table 1. Each sample was tested for anti-Ro52kD (recombinant antigen) and Ro60kD (native antigen) in the central NYU research lab at serial dilutions ranging from 1:100 to 1:100,000. A threshold titer for risk of fAVB was set at 1,000 ELISA units (EU) for either anti-Ro52kD or Ro60kD based on the evaluation of 50 subjects with a child affected by fAVB (Buyon, A&R, 2023). None of the 10 cases of fAVB in STOP BLOQ were < 1000 EU for either anti Ro52kd or 60kD.

Results: Only one of the commercial laboratories, ARUP (tested in 74), provided a linear range of positivity for both anti Ro52kD and Ro60kD. Previous studies identified a risk threshold at 110 arbitrary units (AU) for each specificity (Kaizer, AJOG, 2022). For anti-Ro52, 29 were > 110 AU and all but one was > 1000 EU. For anti-Ro60 44 were > 110 AU and all but 6 were > 1000 EU. Overall, the values for ARUP and NYU were strongly correlated (Table 2). Seven of the 8 commercial laboratories provided a negative cutoff and an upper threshold for positivity. Three hundred and fifty-four patients were tested using the BioPlex assay. Of 81 below the upper limit > 8, 66 did not meet the research risk threshold and none had an affected child. Of 273 above the upper limit, 224 exceeded the threshold risk of 1000 EU for either anti-Ro52kD or 60kD (PPV: 82%; NPV: 81%), 5 of which developed fAVB. Twenty-one pregnant subjects were tested in the Mayo labs. Of 10 below the commercial lab upper limit, 8 did not meet the research risk threshold. Of the 11 that exceed the commercial lab upper limit, all exceed the research risk threshold. Values for the 6 other commercial labs are detailed in Table 1.

Conclusion: These data provide a framework for evaluating commercial values to guide fetal surveillance of anti-SSA/Ro pregnancies. However, there are inconsistencies in the ability of a test result to associate with risk, with most labs demonstrating that anti-SSA/Ro below the positive upper limit are not at risk, but for a few, predictions are less reliable.

Disclosure: M. Masson: None; **B. Cuneo**: None; **P. Carlucci**: None; **P. Izmirly**: Hansoh Bio, 2; **J. Brandt**: None; **C. Phoon**: None; **A. Roman**: None; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **M. Belmont**: None; **C. Penfield**: None; **Y. Lee**: None; **J. Nusbaum**: None; **A. Rubenstein**: None; **E. Sinkovskaya**: None; **A. Abuhamad**: None; **G. Satou**: None; **W. Hogan**: None; **A. Moon-Grady**: None; **L. Howley**: GE Healthcare, 2; **M. Donofrio**: None; **S. Levasseur**: None; **M. Geiger**: Brightheart, 2; **S. Owens**: None; **K. Cumbermack**: None; **J. Matta**: None; **G. Joffe**: None; **C. Lindblade**: None; **C. Haxel**: None; **K. Kohari**: Myriad, 5, Natera, 5; **J. Copel**: Janssen, 1, 2; **J. Strainic**: None; **T. Doan**: None; **C. Holloman**: None; **S. Killen**: None; **T. Tacy**: None; **M. Kaplinski**: None; **N. Sachan**: None; **N. Fraser**: None; **R. Clancy**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1392

Cancer Mortality in Sjogren's Disease: Disproportionate Increase in Mortality from Cancers in Sjogren's Disease Relative to All-Cancers

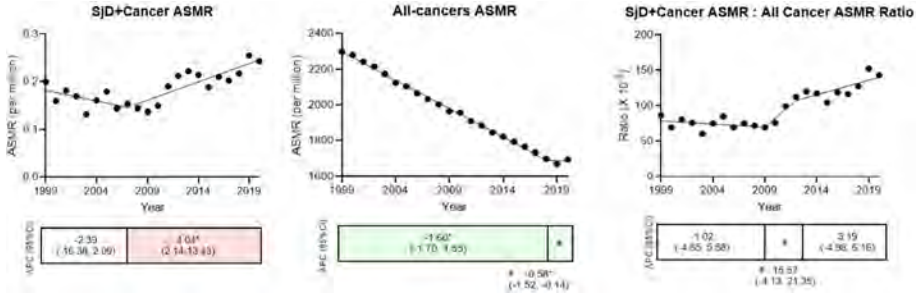
Margaret Essien and Ram Singh, UCLA David Geffen School of Medicine, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD), an autoimmune condition with chronic inflammation in exocrine glands, is associated with increased risks of cancers. The impact of cancer on mortality from SjD is not well documented. Here, we assessed trends associated with mortality from cancer in SjD across the US over a 22-year period.

Methods: This is a population-based study using a national mortality database and census data covering all U.S. residents. We calculated age-standardized mortality rates (ASMR) for cancer in SjD (SjD-C) and all-cancers, overall and by demographic variables. For comparison, we calculated ASMRs for SjD, non-Hodgkin's lymphoma that is the commonest malignancy in SjD, and another autoimmune disease dermatopolymyositis. We performed joinpoint trend analysis to estimate annual percent change (APC) in ASMRs, and Chi-square statistics with Yates's correction to compare changes in different cancer deaths over time.

Results: SjD was recorded as a cause of death in 7,817 decedents from 1999 through 2020. Of these, 1,395 (17.8%) had both SjD AND cancer recorded as multiple causes of death. During the same time-period, the number of all-cancer deaths was 8,096,904. The ASMRs for SjD-C initially showed a decreasing trend (p=NS), but significantly increased in the last decade at an APC of 4.04% (95% CI, 2.14-13.43; 2007-2020). In contrast, the all-cancers ASMRs decreased throughout the 22-year period. The average APC for the entire 1999-2020 was 1.54% (95% CI, 0.43-3.19) for SjD-C ASMR and -1.50% (95% CI, -1.58% to -1.46%) for all-cancer ASMRs. Mortality from dermatopolymyositis-associated cancers and non-Hodgkin's lymphoma decreased during the study period. The SjD-C mortality rates were higher in females than males, non-Hispanic whites than other race/ethnic groups, ≥65-years old than in 0-64-years, and decedents in the West than in other census regions. Proportions of hematological cancer deaths decreased, whereas lung cancer deaths increased in SjD during the last decade.



Trends in ASMR for SjD+cancer and all-cancers, and Ratio of SjD+cancer to all cancer Mortality Rates, 1999-2020. Green bars indicate a statistically significant decreasing trend, Red bars indicate a statistically significant increasing trend, and White bars indicate that the trend is not statistically significant. *p<0.05.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this nationwide, population-based study, cancer mortality in SjD exhibited an increasing trend in the last decade, while all-cancer mortality continually decreased. Prospective, population-based studies are needed to identify causes underlying this increase.

Disclosure: M. Essien: None; **R. Singh**: None.

Abstract Number: 1393

Prevalence of Sjögren's Disease in the United States - A Retrospective Cohort Study Among a Commercially Insured Population (2019-2023)

Minoti Ganguli, Annie Kilby, Ahva Shahabi and Tsu-Chieh Jay Lin, Amgen Inc., Thousand Oaks, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a systemic autoimmune condition characterized by diverse clinical manifestations, which often complicates diagnosis and disease management[1]. Previous epidemiological estimates of SjD prevalence in the US have varied significantly due to differences in methodologies and data sources[2]. Consequently, SjD is frequently underdiagnosed or misclassified, affecting accurate prevalence estimates and complicating clinical decision-making[1].

This retrospective cohort study aims to characterize temporal trends in the annual prevalence of overall diagnosed SjD, including SjD without overlapping autoimmune conditions and SjD with overlapping autoimmune conditions (systemic lupus erythematosus, rheumatoid arthritis and ankylosing spondylitis) among commercially insured adult patients in the US (2019–2023).

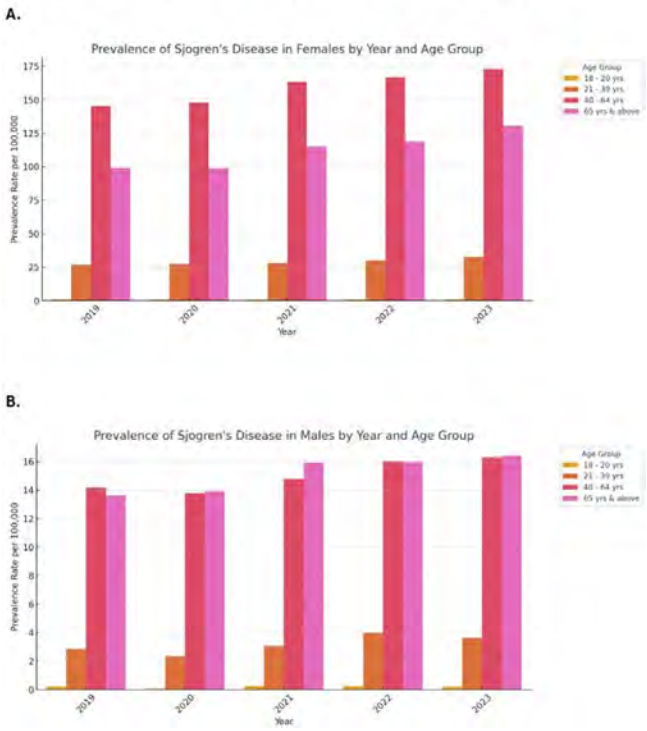
Methods: This retrospective cohort study utilized data from the Optum Clinformatics® Data Mart database, encompassing US adults (≥18 years) with Commercial or Medicare Advantage insurance. Patients with ≥1 inpatient or ≥2 outpatient claims for SjD (ICD-10: M35.x) during the period of interest (POI) from 2019–2023 were considered as prevalent cases. Annual prevalence was calculated by dividing the number of identified SjD patients by the total number of eligible enrollees during each annual POI prevalence was age and sex standardized to the US population using the US Census and reported as a rate (per 100,000 persons). A one-year lookback period prior to each POI was used to ascertain disease status. Generalized linear regression was employed to assess temporal trends.

Table 1 – Prevalence of overall diagnosed Sjögren Disease and Sjögren Disease without and with overlapping autoimmune conditions

Year	Overall diagnosed Sjögren Disease	Sjögren without autoimmune conditions	Sjögren Disease with overlapping autoimmune conditions
2019	195.95	144.48	51.48
2020	197.93	145.81	52.12
2021	223.99	165.37	58.62
2022	239.20	177.57	61.64
2023	259.20	192.76	66.44

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

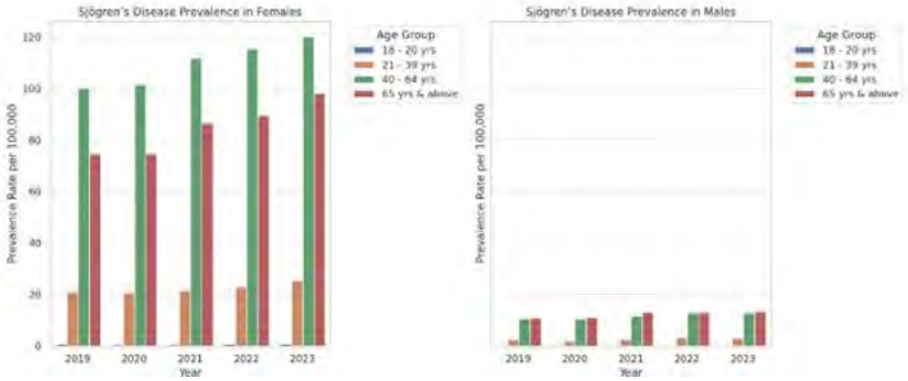
Fig 1: Age- and sex-adjusted prevalence of overall diagnosed Sjögren's Disease



Results: Between 2019 and 2023, the prevalence proportion per 100,000 persons steadily increased from 195.95 to 259.20 in overall diagnosed SjD, from 144.48 to 192.76 in SjD without overlapping autoimmune conditions, and from 51.48 to 66.44 in SjD with overlapping autoimmune conditions. The prevalence of overall diagnosed SjD and those without any overlapping autoimmune conditions was higher in women (vs men) and in the age groups 45–64 and ≥65 years (Fig 1a and 1b). Generalized linear regression showed statistically significant increasing trend in prevalence over time ($p< 0.01$) for overall diagnosed SjD in the US.

Conclusion: Findings from this large, claims-based analysis indicate a rising trend in diagnosed SjD, including SjD without and with overlapping autoimmune conditions, among adults from 2019–2023. The increasing prevalence in the US indicates an unmet need and disease burden, especially among women aged ≥40 years. This highlights the need for improved

Fig 2: Age- and sex-adjusted prevalence of Sjögren's Disease without any overlapping autoimmune conditions



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

treatment and management strategies. Future work should explore if the observed trend is driven by increased awareness for screening, changes in clinical practice, or true changes in incidence.

References:

1. Mariette, X, et al. (2018). Primary Sjögren's Syndrome. N Engl J Med, 378(10), 931-939.
2. Brito-Zerón, P, et al. (2016). Sjögren syndrome. Nat Rev Dis Primers, 2, 16047.

Disclosure: M. Ganguli: Amgen, 3, 11; **A. Kilby**: Amgen, 3, 11; **A. Shahabi**: Amgen, 3, 11; **T. Jay Lin**: Amgen, 3, 11.

Abstract Number: 1394

Burden of Comorbidities Across EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) Domains: Treatment Prevalence Among Commercially Insured Sjögren's Patients in the United States

Minoti Ganguli, Annie Kilby, Ahva Shahabi and Tsu-Chieh Jay Lin, Amgen Inc., Thousand Oaks, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a systemic disorder characterized by exocrine gland inflammation, leading to dry eyes/mouth, and multiple organ systems involvement[1]. The European League Against Rheumatism (EULAR) developed the Sjögren's Syndrome Disease Activity Index (ESSDAI) to capture systemic disease activity across clinical domains, to monitor disease progression and guide treatment[2].

Patients with SjD often have comorbidities across multiple ESSDAI domains – musculoskeletal, central nervous system (CNS), hematological, pulmonary, renal, and others – significantly affecting morbidity, quality of life, and clinical management strategy [3].

This study evaluates the prevalence of ESSDAI domain-specific comorbidities and treatment in patients diagnosed with SjD as well as those without any overlapping autoimmune conditions (2019–2023).

Methods: A retrospective cohort study using Optum Clinformatics® Data Mart (2019–2023) included adults (≥18 years) with ≥1 inpatient or ≥2 outpatient SjD claims. All relevant domain-specific comorbidities were identified using ≥2 ICD-10-CM diagnosis codes/year. Treatments assessed included biologics, immunosuppressants, NSAIDs, opioids, and neuropathic agents. Descriptive analyses were conducted for overall SjD patients and SjD patients without overlapping autoimmune disease, by calendar year.

Results: In the overall SjD patients (n=38,456) and SjD patients without overlapping autoimmune conditions (n=24,657), majority were female (90.6%, 89.3%), most were aged ≥65 years (62.8%, 66.2%), and predominantly identified as non-Hispanic (77.6%, 78.9%) and White (68.1%, 69.6%), followed by Black (10.3%, 9.3%) and Asian (2.6%, 2.7%).

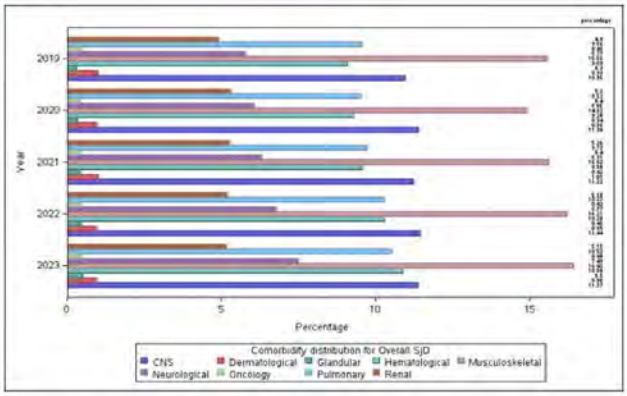
In the overall SjD cohort, musculoskeletal comorbidities were the most prevalent (15.66-16.42%) while CNS involvement was highest in those without overlapping autoimmune conditions (8.88-9.20%). Both cohorts showed consistently high rates of hematological, pulmonary, and neurological domains. In both cohorts, fibromyalgia was the most prevalent CNS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

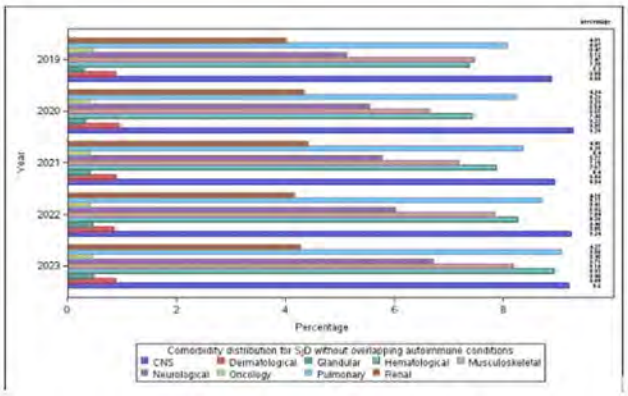
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig 1: Annual Prevalence Trends of ESSDAI Domain Comorbidities in patients with overall SjD and SjD without overlapping autoimmune disease (2019–2023)

A.



B.



condition (~8–10%), hypokalemia was the leading renal comorbidity (up to 4.34%), and anemia was highest among hematological conditions (7.80–9.28%).

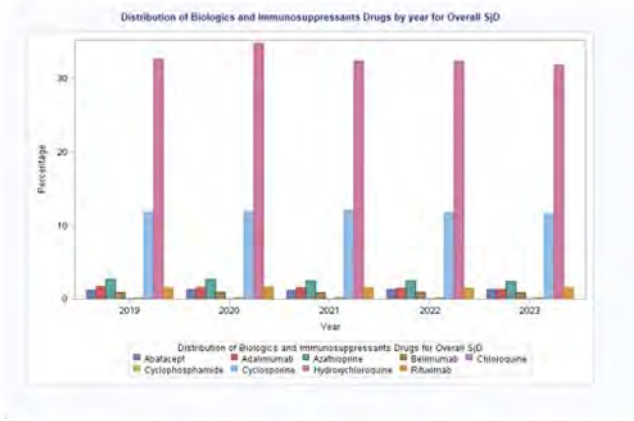
SjD patients without overlapping autoimmune conditions had lower comorbidity prevalence versus overall SjD cohort (Table 1). Top treatments for both cohorts included hydroxychloroquine (32.8% vs. 28%), cyclosporine (~12%), azathioprine, rituximab, and adalimumab (Figure 2). The overall SjD patient cohort had consistently higher treatment rates.

Table 1. Most Prevalent ESSDAI domains in both Overall Sjögren's Disease and Sjögren's Disease without overlapping autoimmune conditions, 2019-2023

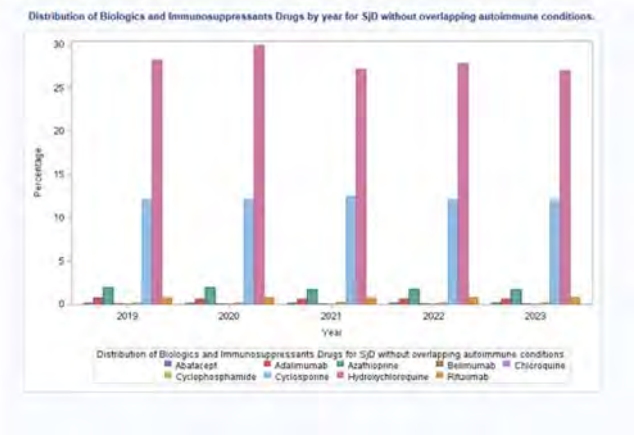
	2019	2019	2020	2020	2021	2021	2022	2022	2023	2023
Comorbidity	Prevalence (%) among Overall Sjögren	Prevalence (%) among Sjögren's without overlapping autoimmune disease	Prevalence (%) among Overall Sjögren	Prevalence (%) among Sjögren's without overlapping autoimmune disease	Prevalence (%) among Overall Sjögren	Prevalence (%) among Sjögren's without overlapping autoimmune disease	Prevalence (%) among Overall Sjögren	Prevalence (%) among Sjögren's without overlapping autoimmune disease	Prevalence (%) among Overall Sjögren	Prevalence (%) among Sjögren's without overlapping autoimmune disease
Musculoskeletal	15.56	7.47	14.92	6.65	15.62	7.18	16.21	7.84	16.42	8.18
Central nervous system (CNS)	10.95	8.88	11.39	9.20	11.22	9.04	11.44	9.24	11.37	9.20
Hematological	9.09	7.38	9.28	7.43	8.58	7.87	10.28	8.26	10.88	8.93
Pulmonary	9.56	8.07	9.53	8.23	9.72	8.36	10.27	8.71	10.52	9.06
Neurological	5.77	5.12	6.05	5.54	6.31	5.77	6.77	6.02	7.49	6.71

Fig 2 - Top 5 Pharmacological Treatments in A) overall SjD and B) SjD without overlapping autoimmune conditions, (2019-2023)

A.



B.



Conclusion: Musculoskeletal, CNS, hematologic, pulmonary and neurological domains contribute substantially to high comorbidity burden in overall SjD patients and those without overlapping autoimmune conditions. High comorbidity and treatment rates were seen in both overall SjD and SjD without overlapping autoimmune conditions suggest a more complex disease phenotype, underscoring the need for targeted treatment strategies.

References

1. Mariette, X, et al. (2018). N Engl J Med, 378(10), 931-939.
2. Seror, R, et al. (2015). Ann Rheum Dis, 74(5), 859-866.
3. Brito-Zerón, P, et al. (2016). Nat Rev Dis Primers, 2(1), 16047.

Disclosure: M. Ganguli: Amgen, 3, 11; **A. Kilby**: Amgen, 3, 11; **A. Shahabi**: Amgen, 3, 11; **T. Jay Lin**: Amgen, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1395

A Comparative Study of Yao Syndrome and Primary Sjögren's Syndrome

Nayaab Bakshi[1], Christopher Loh[2], Song Wu[3] and Qingping Yao[3], [1]Stony Brook University, Dix Hills, NY, [2]Stony Brook University, Lake Grove, NY, [3]Stony Brook University, Stony Brook, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Yao syndrome (YAOS, OMIM 617321) is formerly named Nucleotide-binding oligomerization domain containing protein 2 (NOD2)-associated autoinflammatory disease affecting multiorgan systems characterized by recurrent fever, dermatitis, arthralgias, gastrointestinal, sicca symptoms, eyelid swelling, and distal leg swelling. Sicca symptoms are common in YAOS, which can be confused with Sjögren's syndrome. This study aimed to compare the clinical and laboratory characteristics between YAOS and primary Sjögren's Syndrome (pSS).

Methods: A retrospective study of 27 adult patients with YAOS seen in the Center of Autoinflammatory Disease at Stony Brook University Hospital between 2015 and 2025 was conducted. YAOS was diagnosed based on our prior published criteria in the American Journal of Medicine in 2017. Since the presence of certain NOD2 gene mutations is required for the diagnosis of YAOS, a periodic fever syndrome gene panel was performed for all these patients. To compare patients with pSS, we also performed a chart review of 29 adult patients with pSS diagnosed in the same Institution during the same period. Patients with pSS were diagnosed based on the 2016 ACR/EULAR diagnostic criteria. Categorical variables were compared between the YAOS and pSS groups using either Fisher's exact test or the Chi-squared test. Continuous variables were compared using two-sample t-tests.

Results: In both YAOS and pSS groups, females were predominant, and an overwhelming majority of patients were Caucasian. Disease onset occurred at an earlier age in YAOS than pSS (27.7 ± 13.9 vs. 42.7 ± 15.2 years, p = 0.002). Although Sicca symptoms were common in both diseases, compared with pSS, several presentations were significantly more frequent in YAOS, including fever (66.7% vs. 10.3%, P=0.00002), rash (100% vs. 24.1%, $p < 0.000001$), eyelid swelling (52% vs. 0%, $p = 4.1 \times 10^{-5}$), abdominal pain (70.4% vs. 20.7%, p = 5.2 × 10-4), and non-bloody diarrhea (51.9% vs. 14.3%, p = 0.007) (Table to be presented). In addition, oral ulcers, chest pain, arthralgia, and asthma were more common in YAOS. All patients with pSS had positive autoantibodies, SSA in particular, whereas patients with YAOS did not have elevated autoantibodies in general.

Conclusion: While both YAOS and pSS share sicca symptoms, YAOS possesses a characteristic manifestation and distinctive clinical constellation from pSS. Since therapeutic approaches and outcomes differ between these two conditions, this study will further increase awareness of YAOS, an underdiagnosed disease, to avoid diagnostic confusion.

References:

Yao Q et al. A Systematic Analysis of Treatment and Outcomes of NOD2-Associated Autoinflammatory Disease. Am J Med. 2017 Mar;130(3):365.e13-365.e18.
Nomani H et al. Comprehensive clinical phenotype, genotype and therapy in Yao syndrome. Front Immunol. 2024 Sep 20;15:1458118.

Disclosure: N. Bakshi: None; **C. Loh**: None; **S. Wu**: None; **Q. Yao**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1396

Influence of Age on Daily Impairment, Patient Empowerment, Activation and Engagement in Patients with Sjögren's Disease

Esra Sevimli[1], Berceste Polat[2], Busra Sari[3], Can Akmansoy[2], Burcu Aksoy[4], Omur Mumcu[5], Hatice Kalender[3], Aysegul Avcu[6], Mustafa Erdogan[7], Nur Sisman[8], Farida Fortune[9], Gonca Mumcu[10] and **Nevsun Inanc**[7], [1]1Institute of Health Sciences, Marmara University, Department of Health Management, Istanbul, Turkey, [2]Marmara University, Faculty of Dentistry, Istanbul, Turkey, [3]Institute of Health Sciences, Marmara University, Department of Health Management, Istanbul, Turkey, [4]Istanbul University-Cerrahpasa, Institute of Postgraduate Education, Department of Health Management, Istanbul, Turkey, [5]Yeditepe University, Faculty of Dentistry, Istanbul, Turkey, [6]Marmara University, Istanbul, Turkey, [7]Marmara University, School of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [8]Marmara University, Faculty of Health Sciences, Istanbul, Turkey, [9]Barts and The London School of Medicine and Dentistry, Centre Immunobiology and Regenerative Medicine, Queen Mary University of London, London, United Kingdom, [10]Faculty of Dentistry, Istanbul Okan University, Istanbul, Turkey

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patient-centred care and improvement of daily life are the main components in chronic disease management. The aim of the study was to determine associations among age, Patient Empowerment, Engagement, and Activation status and Daily impairment in patients with Sjögren disease (SjD).

Methods: In this cross-sectional study, 164 patients with SjD (F/M: 157/7; mean age: 54.4±12.4 years, disease duration: 9.02±7.14 years) were included. Data were collected by clinical examinations and a questionnaire.

The Patient Empowerment (n=7 items), Engagement (n=7 items), and Activation (n=7 items) Survey (PEEAS) scale, the 5-Level EQ-5D scale (EQ-5D-5L) for quality-of-life status (high score: good QoL status) as well as the EULAR SS Patient Reported Index (ESSPRI) score were used in the study. High scores reflected Empowered, Engaged and Active patients (7-35 points in each group) in PEEAS and good self-reported health status (0-100 mm: the best health status) whereas high score of Work Productivity and Activity Impairment (WPAI)-Daily impairment and ESSPRI score were associated with poor conditions.

After preliminary analysis, moderation analysis was used to test the influence of age as a third variable (Z), on the relationship between dependent (Y; WPAI, PEEAS) and independent (X; self-reported health status) variables.

Results: Increase in age was correlated with decreases in scores of EQ-5D-5L (0.62±0.21), self-reported general health status (61.92 ±11.59), Empowerment, Engagement and Activation subgroups (26,65±4.33; 26.68±4.20; 25.10±6.20)($p< 0.05$). Moreover, an elevated WPAI-Daily impairment score (43.59±22.20) was correlated with poorer self-reported general health status and younger age ($p< 0.05$). According to Moderator analysis, the negative impacts of self-reported health status (X) on WPAI-Daily impairment were stronger in young (Z) patients ($p< 0.05$). Similar relation was not seen for PEEAS subgroups for young patients ($p >0.05$).

Low EQ-5D-5L score as well as elevated ESSPRI score (6.48±1.64) and long duration for ocular dryness were also associated with poor scores of Empowerment, Engagement and Activation in PEEAS scale (25.10±6.20)($p< 0.05$).

Conclusion: This study highlights the relationships between age, self-reported health status, patient empowerment, engagement, and those actively patient in their management. In addition, younger individuals who have poorer health perception may experience greater impairment on a daily basis. Prolonged ocular dryness emphasizes the importance of tailored interventions to enhance patient-centred care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Sevimli: None; **B. Polat**: None; **B. Sari**: None; **C. Akmansoy**: None; **B. Aksoy**: None; **O. Mumcu**: None; **H. Kalender**: None; **A. Avcu**: None; **M. Erdogan**: None; **N. Sisman**: None; **F. Fortune**: None; **G. Mumcu**: None; **N. Inanc**: AbbVie/Abbott, 6, Amgen, 6, Janssen, 6, Novartis, 6, Pfizer, 5, 6, Roche, 6, UCB, 6.

Abstract Number: 1397

Cardiovascular And Cerebrovascular Risk In Sjögren's Disease: Results From A Prospective Multicenter Cohort.

Olga Rusinovich[1], Zulema Plaza[2], Monica Fernandez Castro[3], Jose Rosas Gómez de Salazar[4], Victor Martinez-Taboada[5], Alex Olive[6], Raúl Menor Almagro[7], Belén Serrano-Benavente[8], Judit Font-Urgelles[9], Angel Garcia-Aparicio[10], Sara Manrique-Arija[11], Jesús Alberto Garcia Vadillo[12], Ruth Lopez-Gonzalez[13], Javier Narváez[14], Maria Beatriz Rodriguez[15], Carlos Galisteo[16], Jorge Juan Gonzalez Martin[17], Paloma Vela Casasempere[18], Cristina Bohorquez[19], MARIA CELIA ERAUSQUIN ARRUABARRENA[20], Beatriz Paredes-Romero[21], Leyre Riancho-Zarrabeitia[22], Sheila Melchor Diaz[23], José María Pego-Reigosa[24], Sergi Herdia[25], Clara Moriano[26], Mª Angeles Blazquez Cañamero[27], Paula Estrada-Alarcón[28], Enrique Judez[29], Nerea Alcorta-Lorenzo[30], Consuelo Ramos Giraldez[31], Fernando Sánchez-Alonso[32] and Jose Luis Andreu[33] On behalf SJÖGRENSER PROS Group, part of the Spanish Society of Rheumatology Systemic Autoimmune Diseases Study Group (EASSER), [1]Puerta de Hierro University Hospital, Boadilla del Monte, Spain, [2]Research Unit, Spanish Society of Rheumatology, Madrid, Spain, Madrid, Spain, [3]PUERTA DE HIERRO HOSPITAL, Madrid, Spain, [4]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [5]Facultad de Medicina. Universidad de Cantabria, Santander, Spain, [6]Solo practice, Barcelona, Spain, [7]Department of Rheumatology, Hospital de Jerez, Spain, Puerto De Santa Mara, Spain, [8]Hospital Gregorio Marañon, Madrid, Spain, [9]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [10]Hospital Universitario de Toledo, Toledo, Spain, [11]Hospital Regional Universitario Mlaga, Malaga, Spain, [12]Hospital Universitario La Princesa, Madrid, Spain, [13]Zamora Health Complex, Salamanca, Spain, [14]Hospital Universitario de Bellvitge, Barcelona, Spain, [15]Canarias University Hospital, La Laguna- Tenerife, Spain, [16]Hospital Parc Taulí, Sabadel, Sabadel, Spain, [17]HM Sanchinarro Univeristary Hospital, Madrid, Spain, [18]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [19]La Paz University Hospital, Alcal De Henares, Spain, [20]Dr Negrin University Hospital, Ls Palmas, Spain, [21]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, San Sebastian de los Reyes, Spain, [22]Rheumatology Department. Hospital Sierrallana, Torrelavega, Spain, [23]12 de Octubre University Hospital, Madrid, Spain, [24]Department of Rheumatology, University Hospital of Vigo, Vigo, Spain; IRIDIS Group (Investigation in Rheumatology and Immune-Diseases), Galicia Sur Health Research Institute, Vigo, Spain, [25]Complex Hospitalari Moisès Broggi, Barcelona, Spain, [26]Hospital Len, LEON, Castilla y Leon, Spain, [27]Hospital Ramon y Cajal, Madrid, Spain, [28]Complex Universitari Hospital Moisès Broggi, Barcelona, Spain, [29]Albacete University Hospital, Albacete, Spain, [30]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [31]Hospital Universitario Virgen de Valme, Servicio de Reumatología, Seville, Spain, [32]Sociedad Española de Reumatología, Madrid, Spain, [33]Hospital Universitario Puerta de Hierro, Majadahonda, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: To evaluate the incidence of cardiovascular and cerebrovascular events (CVEs) in patients with Sjögren's Disease (SjD), focusing on major adverse cardiovascular events (MACE), defined as non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death. Additional objectives were to identify both traditional and disease-specific risk factors associated with CVEs; to assess CV risk using the SCORE2 algorithm and compare predicted versus observed event rates; to examine the impact of CVEs on all-cause mortality; and to determine the prevalence of conventional cardiovascular risk factors (CVRFs) within this population.

Methods: We conducted a prospective, multicenter observational study including 314 patients with SjD who met the 2002 AECG classification criteria. Median follow-up was 9.5 years. Clinical, serological, demographic variables, CVRFs, and CVEs were recorded. Independent predictors of MACE and overall CVEs were identified using multivariate Cox proportional hazards regression models. Cardiovascular risk was estimated using the SCORE2 algorithm. Expected event rates were calculated by summing individual predicted probabilities. CV mortality was compared to the general population using

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Cardiovascular Risk Factors in the SjögrenSER-PROS Cohort.

Variable	Men	Women	Total
Age, median [IQR], years	65.4 [59.2 - 74.6]	58.4 [50.7 - 66.8]	58.7 [50.7 - 67.1]
Disease duration, median [IQR], years	3.9 [1.9 - 5.6]	7.0 [3.2 - 12.2]	6.8 [3.0 - 12.0]
Smoking			
Former smoker, n (%)	10 (58.8)	45 (15.2)	55 (17.6)
Current smoker, n (%)	2 (11.8)	24 (8.1)	26 (8.3)
Alcohol			
0-5 UBE, n (%)	8 (53.3)	23 (11.3)	31 (14.2)
BMI			
BMI 25-29.9 kg/m², n (%)	4 (36.4)	71 (33.3)	75 (33.5)
BMI ≥30 kg/m², n (%)	4 (36.4)	39 (18.3)	43 (19.2)
Diabetes Mellitus, n (%)	1 (5.9)	18 (6.1)	19 (6.1)
Hypertension, n (%)	5 (29.4)	78 (26.3)	83 (26.4)
Dyslipidemia, n (%)	7 (41.2)	97 (32.7)	104 (33.1)
Cholesterol >200 mg/dL, n (%)	1 (6.7)	130 (48.2)	131 (46.0)
Cholesterol >240 mg/dL, n (%)	0 (0.0)	39 (14.4)	39 (13.7)
LDL Cholesterol ≥ 130 mg/dL, n (%)	2 (18.2)	74 (40.7)	76 (39.4)
HDL Cholesterol: Men < 40 mg/dL, Women < 50 mg/dL, n (%)	6 (54.6)	141 (75.8)	147 (74.6)
Triglycerides ≥ 150 mg/dL, n (%)	3 (23.1)	29 (12.1)	32 (12.7)

standardized mortality rate (SMR), based on official data from the Spanish National Institute of Statistics. Relative risk (RR) of all-cause mortality was assessed according to the presence of prior or incident CVEs.

Results: Among 314 patients (94.6% women; median age 58.7 [IQR 50.7–67.1]), 29 CV events occurred: pericarditis (1.27%), conduction abnormalities (1.27%), ischemic heart disease (1.59%), heart failure (1.59%), peripheral artery disease (0.95%), and cerebrovascular events (2.55%). Seventeen patients (5.41%) experienced MACE: 7 non-fatal strokes (2.23%), 5 non-fatal myocardial infarctions (1.59%), and 5 cardiovascular deaths (1.59%). Among the 130 patients with complete SCORE2 data, the expected number of events was 5.74 (4.41%), while 11 events (8.46%) were observed, including 6 MACE (4.62%) and 5 non-MACE events (3.85%).

Independent predictors of CV events were age (OR 1.06; 95% CI 1.01–1.14), cryoglobulinemia (OR 10.13; 95% CI 1.63–62.88), glucocorticoid use (OR 3.44; 95% CI 1.29–9.19), and antiphospholipid antibodies (OR 5.33; 95% CI 1.15–24.79). Predictors of MACE included age (OR 1.07; 95% CI 1.01–1.14), cryoglobulinemia (OR 10.41; 95% CI 1.37–79.26), and glucocorticoid use (OR 3.53; 95% CI 1.00–12.51). See the prevalence of traditional CVRFs in Table 1. CV mortality accounted for 11.9% of all deaths. The SMR for CV mortality was 5.09 (95% CI 5.08–5.11). Previous CVEs were significantly associated with increased all-cause mortality (RR 3.27; 95% CI 1.90–5.63).

Conclusion: Sjögren's Disease is associated with a significantly increased incidence of cardiovascular events, exceeding predicted risk estimates. Disease-specific factors—including cryoglobulinemia, glucocorticoid exposure, and the presence of antiphospholipid antibodies—emerge as independent contributors to this elevated burden. Cardiovascular mortality was fivefold higher than expected, and prior CV events were strong predictors of all-cause mortality.

Disclosure: O. Rusinovich: None; **Z. Plaza**: None; **M. Fernandez Castro**: None; **J. Rosas Gómez de Salazar**: None; **V. Martinez-Taboada**: None; **A. Olive**: None; **R. Menor Almagro**: None; **B. Serrano-Benavente**: None; **J. Font-Urgelles**: None; **A. Garcia-Aparicio**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 1, 2, 6, UCB, 6; **S. Manrique-Arija**: None; **J. Garcia Vadillo**: None; **R. Lopez-Gonzalez**: None; **J. Narváez**: None; **M. Rodriguez**: None; **C. Galisteo**: None; **J. Gonzalez Martin**: None; **P. Vela Casasempere**: None; **C. Bohorquez**: None;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

M. ERAUSQUIN ARRUABARRENA: None; **B. Paredes-Romero**: None; **L. Riancho-Zarrabeitia**: None; **S. Melchor Diaz**: None; **J. Pego-Reigosa**: AstraZeneca, 1, 5, 6, GlaxoSmithKline (GSK), 1, 5, 6, Otsuka, 1, 6; **S. Herdia**: None; **C. Moriano**: None; **M. Blazquez Cañamero**: Astrazeneca, 12, conference registrations, Gsk, 6, Novartis, 12, conference registrations, Rubio, 12, conference registrations; **P. Estrada-Alarcón**: None; **E. Judez**: None; **N. Alcorta-Lorenzo**: None; **C. Ramos Giraldez**: None; **F. Sánchez-Alonso**: None; **J. Andreu**: None.

Abstract Number: 1398

Reproductive Challenges and Cardiovascular Risks in Sjögren's Syndrome and Systemic Sclerosis: A Meta-Analysis of Fertility, Pregnancy Outcomes, and Maternal Cardiac Health

R. Mohamad Javier[1], Bernadus Bramantyo[2], Arkan Berlian[3], Mahardika Nugraha[4], Azzura Simanulang[1], Eko Setyo Herwanto[5], Athaya Febriantyo Purnomo[6], Jonathan Jonathan[7], Ananingati Ananingati[5], Budi Prakoso[8] and Aisyah Rizki Nirmala Hanum[5], [1]University of Indonesia Hospital, Jakarta Selatan, Jakarta Raya, Indonesia, [2]Sardjito General Hospital, Daerah Istimewa Yogyakarta, Yogyakarta, Indonesia, [3]Dr. Cipto Mangunkusumo Hospital, Jakarta Barat, Jakarta Raya, Indonesia, [4]Universitas Islam Sultan Agung, KOTA SEMARANG, Jawa Tengah, Indonesia, [5]Universitas Muhammadiyah Malang, Malang, Jawa Timur, Indonesia, [6]Saiful Anwar General Hospita, Malang, Jawa Timur, Indonesia, [7]RSUD Kalideres, Jakarta, Jakarta Raya, Indonesia, [8]Department of Internal Medicine, RST dr Soepraoen, Malang, Jawa Timur, Indonesia

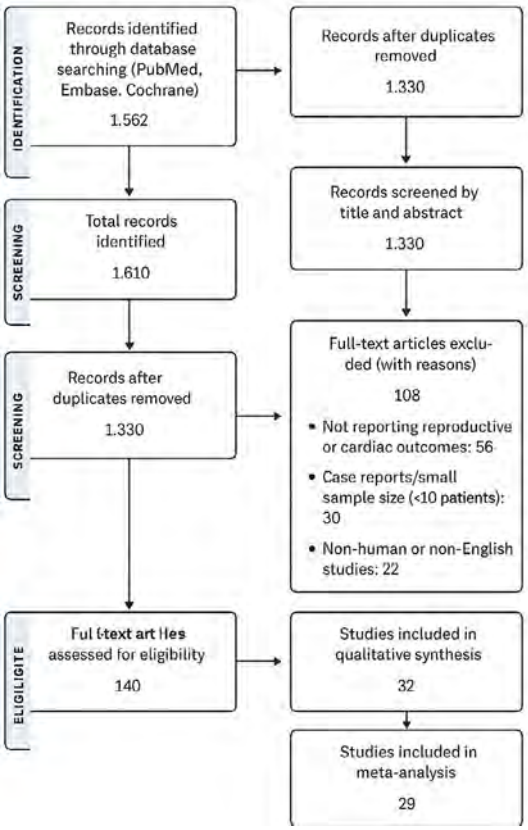
SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

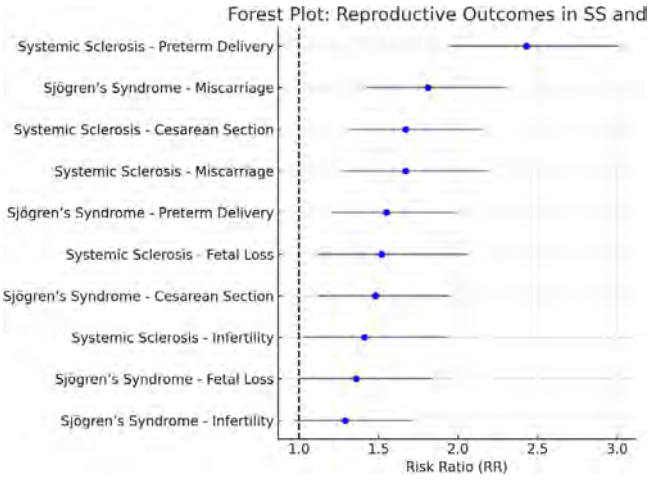
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

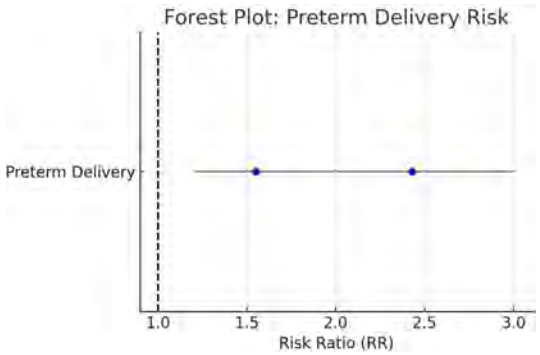


PRISMA Flow Diagram

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot: Reproductive Outcome in SS and Systemic Sclerosis



Forest Plot: Preterm Delivery Risk

Background/Purpose: Autoimmune rheumatic diseases such as Sjögren's Syndrome (SS) and Systemic Sclerosis (SSc) can significantly impact reproductive health and increase maternal cardiovascular risk. These conditions are associated with fertility challenges, obstetric complications, and cardiac events during pregnancy, necessitating a thorough understanding for optimal maternal care. Evaluate reproductive outcomes and cardiac complications in women of reproductive age diagnosed with SS or SSc, including fertility status, pregnancy loss, preterm birth, cesarean delivery, and maternal cardiac morbidity.

Methods: A systematic search of PubMed, Embase, and Cochrane Library databases was conducted up to 2020. Eligible studies reported fertility and/or pregnancy outcomes in women with SS or SSc, with or without comparison to healthy controls. Data were pooled using a random-effects model, and heterogeneity was assessed using the I^2 statistic.

Results: A total of 32 studies comprising 4,820 women (SS: 2,140; SSc: 2,680) were included. Compared to controls, women with SS had a 1.8-fold increased risk of miscarriage (RR: 1.81, 95% CI: 1.42–2.30), while those with SSc showed a 2.4-fold increase in preterm delivery (RR: 2.43, 95% CI: 1.95–3.01). Fertility rates were modestly decreased in both groups (SS: –15%, SSc: –22%). Cardiac complications were significantly higher in SSc pregnancies, with elevated rates of arrhythmias (RR: 3.10, 95% CI: 2.05–4.70), preeclampsia (RR: 2.75), and heart failure events (RR: 2.12). Cesarean delivery was more common in both groups (SS: RR 1.48; SSc: RR 1.67).

Conclusion: Women with Sjögren's Syndrome and Systemic Sclerosis are at increased risk of adverse reproductive and cardiac outcomes. These findings highlight the need for preconception risk assessment, specialized obstetric care, and interdisciplinary collaboration to improve maternal and fetal outcomes in this high-risk population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Javier: None; **B. Bramantyo**: None; **A. Berlian**: None; **M. Nugraha**: None; **A. Simanulang**: None; **E. Herwanto**: None; **A. Purnomo**: None; **J. Jonathan**: None; **A. Ananingati**: None; **B. Prakoso**: None; **A. Hanum**: None.

Abstract Number: 1399

Significance of Antiphospholipid Antibodies in Patients with Sjogren's Disease

Rashmi Thimmapuram[1], Ahmad Alkhatib[2], Joshua Baker[3], Mehrdad Maz[4] and Ghaith Noaiseh[2], [1]University of Kansas Medical Center, Westwood, KS, [2]University of Kansas Medical Center, Kansas City, KS, [3]University of Pennsylvania, Philadelphia, PA, [4]The University of Kansas Medical Center, Kansas City, KS

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: A few reports have evaluated the frequency of antiphospholipid antibodies (aPL) in Sjogren's disease (SjD) and their association with SjD or Antiphospholipid Antibody Syndrome (APS) manifestations. Some authors have suggested an association between presence of aPL and peripheral neuropathy, hypergammaglobulinemia, stroke, and venous thrombosis. Our aim was to assess the frequency of aPL detected in a cohort of well-characterized SjD patients and determine their correlation with key phenotypic features of SjD and clinical manifestations of APS.

Methods: We performed a retrospective chart review of 117 consecutive patients seen at SjD specialty clinic at the University of Kansas Medical Center meeting the 2016 ACR/EULAR classification criteria for SjD who were tested for aPL. All patients underwent testing for anti-cardiolipin antibodies (ACL) IgG/IgM, anti-beta-2-glycoprotein-1 antibodies (B2GP-1) IgG/IgM, and lupus anticoagulants, including Dilute Russell's Viper Venom Time (DRVVT) and hexagonal phase phospholipid neutralization assay (HPPNA). Clinical, laboratory, and histological manifestations of both SjD and APS were collected. Statistical analyses included Chi-squared, Fisher's exact test, and Student t-tests, as appropriate.

Table 1. 16 SjD patients with positive aPL. F = female, M = male, WP = weakly positive (25-39.9 GPL), MHP = moderate-high positive (> 40 GPL), NA = not available, N = No, Y = Yes, VTE = venous thromboembolism, ART = arterial thrombosis, MI = myocardial infarction, CVA = cerebrovascular accident, CAPS = catastrophic antiphospholipid syndrome, TCP = thrombocytopenia, (+) = positive test, (-) = negative test.

Patient	Age (y)	Gender	ACL IgG	ACL IgM	B2GP-1 IgG	B2GP-1 IgM	Hexagonal assay	DRVVT	Twice	VTE	ART	MI	CVA	Obstetric APS	CAPS	TCP
1	43	F	-	-	-	-	+	-	N	N	N	N	N	N	N	N
2	77	F	-	WP	-	-	-	-	N	N	Y	N	N	N	N	N
3	47	F	-	WP	-	-	-	NA	N	N	N	N	N	N	N	N
4	74	F	-	WP	-	WP	-	-	N	N	N	N	N	N	N	N
5	59	M	-	-	-	-	-	+	Y	Y	N	N	N	N	N	Y
6	74	F	WP	-	WP	-	-	-	N	N	N	N	N	N	N	Y
7	55	F	-	-	-	-	-	+	N	N	N	N	N	N	N	N
8	68	F	-	MHP	-	MHP	-	+	Y	Y	N	N	N	N	N	N
9	74	F	-	-	-	-	+	+	N	N	N	N	N	N	N	Y
10	60	F	-	-	-	-	+	+	N	N	N	N	N	N	N	N
11	78	M	-	-	-	-	+	-	N	N	N	N	N	N	N	N
12	45	F	-	-	-	-	+	-	Y	N	N	N	N	N	N	N
13	81	F	-	WP	-	WP	-	-	N	N	N	N	N	N	N	N
14	48	F	-	-	-	-	+	-	N	N	N	N	N	N	N	N
15	65	F	MHP	-	MHP	-	-	-	Y	N	Y	Y	N	N	N	N
16	39	F	-	-	-	-	NA	*	Y	N	N	N	N	N	N	N

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Features of SjD and APS by aPL status. ILD = interstitial lung disease, LAD = lymphadenopathy, PNS = peripheral nervous system, CNS = central nervous system, MGUS = monoclonal gammopathy of uncertain significance, TCP = thrombocytopenia, VTE = venous thromboembolism, ART = arterial thrombosis, MI = myocardial infarction, CVA = cerebrovascular accident.

	Positive aPL (n=16)		Negative aPL (n=101)		
Category	#	%	#	%	p-value
Fatigue	8	50%	64	63%	0.41
Inflammatory arthritis	10	63%	68	67%	0.78
Interstitial nephritis/cryo-associated glomerulonephritis	0	0%	1	1%	1.00
Purpura/cutaneous vasculitis	1	6%	7	7%	1.00
Raynaud's phenomenon	3	19%	35	35%	0.21
Pulmonary involvement	2	13%	17	17%	0.66
ILD	2	13%	13	13%	1.00
Splenomegaly	0	0%	7	7%	0.59
LAD	3	19%	13	13%	0.52
Lymphoma	0	0%	6	6%	0.32
Constitutional symptoms	2	13%	16	16%	0.73
Parotid gland swelling	4	25%	30	30%	0.70
Myositis	1	6%	0	0%	0.14
PNS involvement	3	19%	30	30%	0.37
CNS involvement	1	6%	9	9%	0.72
Autonomic dysfunction	1	6%	10	10%	1.00
SSA positive	10	63%	70	69%	0.58
SSB positive	6	38%	35	35%	0.82
RF positive	7	44%	34	34%	0.43
Low C3	1	6%	4	4%	0.51
Low C4	1	6%	3	3%	0.45
Hypergammaglobulinemia	6	38%	30	30%	0.77
MGUS	9	56%	23	23%	0.01
Lymphopenia	4	25%	38	38%	0.33
Neutropenia	3	19%	19	19%	1.00
TCP	3	19%	6	6%	0.11
Anemia	2	13%	17	17%	1.00
VTE	2	13%	2	2%	1.00
Unprovked VTE	1	6%	6	6%	1.00
ART	2	13%	0	0%	0.02
MI	1	6%	0	0%	0.14
CVA	2	2%	0	0%	1.00

Results: 103 patients (88%) were females, mean age was 54.6 +/- 13.9 years, 100 patients (85%) were white, and mean disease duration was 2.9 years. Of the 117 SjD patients, 16 (13.7%) had at least one positive testing for antiphospholipid antibodies (Table 1). Only 3 patients (2.5%) met criteria for APS. Detection of aPL was associated with monoclonal gammopathy (56.25% of aPL-positive vs 22.77% of aPL-negative, p = 0.012) and arterial thrombosis (12.5% vs 0%, p = 0.02). We did not observe any other association with clinical, laboratory, or histological parameters (Table 2). Of the 16 patients with positive aPL, 5 patients (31%) had aPL positivity confirmed at least 12 weeks apart whereas 11 patients (69%) had aPL checked only once. There was no association between the number of occurrences of aPL positivity and monoclonal gammopathy (46% of one-time aPL positive vs 80% of two time-aPL positive, p = 0.31) or arterial thrombosis (1% of one-time aPL positive vs 20% of two-time aPL positive, p = 1).

Conclusion: A minority of patients with SjD had aPL and an even smaller group met the criteria for APS. Detection of aPL was associated with the presence of monoclonal gammopathy and arterial thrombosis. Larger studies are necessary to determine the clinical significance and utility of screening for antiphospholipid antibodies in SjD, particularly in those with monoclonal gammopathy.

Disclosure: R. Thimmapuram: None; **A. Alkhatib**: None; **J. Baker**: Amgen, 5; **M. Maz**: None; **G. Noaiseh**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1400

Beyond the Glands: Hypogammaglobulinemia as a Clue to Peripheral Neuropathy in Sjogren's Disease

Renata Fróes Ramos de Lima[1], Regis Sewa Marques[2], Zoraida Sachetto[3] and Alisson Pugliesi[4], [1]Universidade Estadual de Campinas (UNICAMP), Campinas, Sao Paulo, Brazil, [2]Universidade Estadual de Campinas, Campinas, Sao Paulo, Brazil, [3]UNIVERSIDADE ESTADUAL DE CAMPINAS, UNICAMP, Campinas, Sao Paulo, Brazil, [4]Unicamp, Campinas, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Sjogren's disease (SjD) is a systemic autoimmune disorder characterized by inflammatory involvement of the exocrine glands and extra-glandular manifestations. Among the latter, there is a growing interest in the study of neurological involvement, as the prevalence and association factors are still divergent in the literature. Thus, the objective was to evaluate the frequency of neurological manifestations in SjD, as well as the laboratory factors associated with the disease.

Methods: This retrospective observational study reviewed the electronic medical records of patients diagnosed with SjD, according to the 2002 or 2016 ACR criteria, at a tertiary outpatient clinic. Only patients over 18 years of age with the primary form of the disease were included. Patients with neurological manifestations were assessed and reviewed to determine whether the manifestations could be attributed to SjD. When attributable, their types and frequencies in the study population and their association factors were described. Inferential analysis was performed by comparing patients with neurological manifestations and those without neurological manifestations with regard to the presence of anti-Ro, anti-La, ANA, rheumatoid factor, C3, C4, cryoglobulins, hypergammaglobulinemia or hypogammaglobulinemia using Fischer and Chi Square statistical methods and, if necessary, multivariate analysis with logistic regression.

Results: 92 patients with SjD were evaluated. A prevalence of 17,39% neurological manifestations was found in the context of SjD in the peripheral nervous system (PNS). The main types of PNS found were ganglionopathy, sensitive neuropathy, multiple mononeuritis, fine fiber neuropathy and sensitive-motor neuropathy and are illustrated in figure 1. The two patients with CNS manifestations were attributed to concomitant Neuromyelitis Optica Spectrum Disease. Thus, a comparative inferential analysis was carried out between laboratory markers and the presence of PNS manifestations. In the univariate analysis, only hypogammaglobulinemia showed a significant statical association (p = 0.008). This association also occurred in the multivariate analysis, using rituximab as a covariate (p = 0,010). Table 1 shows the results obtained after statistical analysis.

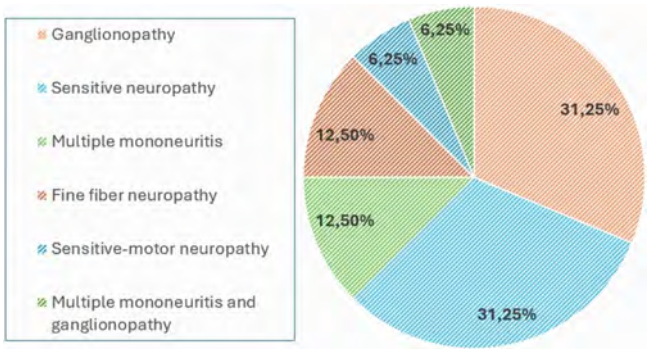


Figure 1: Types of neurological manifestations of PNS attributable to Sjögren's disease

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Statistical analysis comparing patients with Sjögren's Disease with and without associated peripheral neuropathy

Clinical/ Laboratory markers	PNS absent	PNS present	P-value
Extraglandular manifestation	49/76 (64,5%)	11/16 (68%)	p = 0,97
C3	6/76 (7,9%)	2/16 (12%)	p = 0,9276
C4	16/76 (21%)	3/16 (18%)	p = 1
C3 or C4	19/76 (25%)	3/16 (18%)	p = 1
ANA	74/76 (97,4%)	15/16 (93%)	p = 1
Anti-Ro	74/76 (97,4%)	15/16 (93%)	p = 1
Anti-LA	38/76 (50%)	11/16 (68%)	p = 0,3288
Cryoglobulins	7/76 (9,2%)	5/16 (31%)	p = 0,1104
Rheumatoide factor	45/76 (59,2%)	11/16 (68%)	p = 0,9623
Hypergammaglobulinemia	37/76 (48,7%)	6/16 (37,5%)	p = 0,2771
Hypogammaglobulinemia	9/76 (11,8%)	7/16 (43%)	p = 0,008* p = 0,010**

NOTE: * Univariate analysis / ** Multivariate analysis

Conclusion: In our sample, we found a prevalence of approximately 17,39% of neurological manifestations, with only PNS involvement attributable to SjD. The two CNS manifestations found to be immune in nature were attributed to the Neuromyelitis Optica spectrum disorder. Hypogammaglobulinemia, independent of rituximab use, was the only variable associated with PNS manifestations.

Disclosure: R. Fróes Ramos de Lima: None; **R. Sewa Marques**: None; **Z. Sachetto**: None; **A. Pugliesi**: None.

Abstract Number: 1401

Real World Treatment Patterns and Health Care Resource Use in Patients With Newly Diagnosed Sjögren's Disease (SjD) in the United States

Sara McCoy[1], Anjana Lalla[2], Nilesh Choudhary[3], Shraddha Chatterjee[3], Shiwani Prasad[3] and Antton Egana[2], [1]University of Wisconsin–Madison, Madison, WI, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]Novartis India, Hyderabad, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: SjD is a chronic, systemic, progressive autoimmune disease characterized by dry mouth and eyes, but it is often accompanied by extraglandular symptoms and signs that affect the entire body. About two-thirds of SjD occurs alone; the remaining one-third is associated with other autoimmune connective tissue diseases such as RA, SLE, or systemic sclerosis. This analysis describes treatment patterns and health care resource use (HCRU) over 12 months in US patients newly diagnosed with SjD.

Methods: This retrospective cohort analysis included adult patients with a first diagnosis (index date) of sicca syndrome or SjD (*ICD-9-CM*: 710.2; *ICD-10-CM*: M35.0-9, M35A-C; together termed SjD here) from October 2015 through March 2023 (identification period) and a second diagnosis within 28 to 365 days of first diagnosis in the Optum EHR database. Patients had ≥12 months pre-index documented clinical history with no record of a SjD diagnosis (baseline period), as well as ≥12 months follow-up post index (follow-up period). Treatment patterns and HCRU were assessed during the follow-up period. Patients' HCRU and medication use in the baseline and follow-up periods were reported descriptively.

Results: Of the 35,035 patients with SjD who met the inclusion criteria, 67.2% had SjD only whereas 32.8% had SjD occurring with other autoimmune conditions such as RA, SLE, and systemic sclerosis (SjD+other). HCRU for all patients with SjD increased from the baseline to follow-up period, irrespective of whether patients had SjD only or SjD+other (**Table 1**). An

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. All-Cause HCRU During Baseline and Follow-Up Periods for the Overall Cohort, Patients With SjD Only, and Patients With SjD and Overlapping Autoimmune Disease.

HCRU	Overall Cohort (N=35,035)		SjD+Other[a] (n=11,503)		SjD Only (n=23,532)	
	Baseline	Follow-Up	Baseline	Follow-Up	Baseline	Follow-Up
≥1 OP visit, n (%)	31,502 (89.9)	34,889 (99.6)	10,493 (91.2)	11,466 (99.7)	21,009 (89.3)	23,423 (99.5)
OP visits, mean (SD), PPPY	15.0 (16.2)	20.3 (18.8)	15.5 (16.5)	22.0 (19.7)	14.7 (16.1)	19.4 (18.3)
OP visits, median (IQR), PPPY	10.0 (4.0-20.0)	15.0 (8.0-27.0)	10.0 (4.0-21.0)	16.0 (8.0-29.0)	10.0 (4.0-20.0)	14.0 (7.0-25.0)
≥1 IP admission, n (%)	1741 (5.0)	4126 (11.8)	677 (5.9)	1871 (16.3)	1064 (4.5)	2255 (9.6)
IP visits, mean (SD), PPPY	1.3 (0.8)	1.6 (1.1)	1.4 (0.8)	1.7 (1.2)	1.3 (0.8)	1.6 (1.1)
IP visits, median (IQR), PPPY	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)
≥1 ED visit, n (%)	5788 (16.5)	7303 (20.8)	2264 (19.7)	2863 (24.9)	3524 (15.)	4440 (18.9%)
Mean (SD), PPPY	2.0 (2.5)	2.1 (2.3)	2.1 (3.2)	2.2 (2.9)	1.9 (1.9)	2.0 (1.9)
Median (IQR), PPPY	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-3.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
SjD-specific diagnostic procedures, n (%)	9976 (28.5)	14,447 (41.2)	3032 (26.4)	4183 (36.4)	6944 (29.5)	10,264 (43.6)
Mean (SD), PPPY	1.8 (1.1)	2.0 (1.4)	1.7 (1.0)	1.9 (1.3)	1.8 (1.2)	2.0 (1.4)
Median (IQR), PPPY	1.0 (1.0-2.0)	2.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-2.0)
SSA (Ro) antibody test, n (%)	6738 (19.2)	8734 (24.9)	2321 (20.2)	3062 (26.6)	4417 (18.8)	5672 (24.1)
SSB (La) antibody test, n (%)	6748 (19.3)	8758 (25.0)	2323 (20.2)	3062 (26.6)	4425 (18.8)	5696 (24.2)
Schirmer test, n (%)	2936 (8.4)	5568 (15.9)	630 (5.5)	1114 (9.7)	2306 (9.8)	4454 (18.9)
Salivary gland ultrasound, n (%)	1069 (3.1)	1435 (4.1)	308 (2.7)	415 (3.6)	761 (3.2)	1020 (4.3)
Salivary or lacrimal gland biopsy, n (%)	155 (0.4)	560 (1.6)	27 (0.2)	104 (0.9)	128 (0.5)	456 (1.9)
Ocular surface staining test, n (%)	13 (0.0)	27 (0.1)	3 (0.0)	5 (0.0)	10 (0.0)	22 (0.1)
Unstimulated whole saliva flow test, n (%)	6 (0.0)	9 (0.0)	1 (0.0)	3 (0.0)	5 (0.0)	6 (0.0)
Magnetic resonance sialography, n (%)	4 (0.0)	11 (0.0)	0	2 (0.0)	4 (0.0)	9 (0.0)
Lab tests,[b] n (%)	19,348 (55.2)	26,151 (74.6)	7090 (61.6)	9375 (81.5)	12,258 (52.1)	16,776 (71.3)
Mean (SD), PPPY	3.5 (3.8)	4.3 (5.2)	3.8 (3.8)	5.2 (5.8)	3.3 (3.5)	3.9 (4.8)
Median (IQR), PPPY	2.0 (1.0-4.0)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	4.0 (2.0-6.0)	2.0 (1.0-4.0)	3.0 (1.0-5.0)
Imaging,[c] n (%)	9315 (26.6)	12,905 (36.8)	3154 (27.4)	4539 (39.5)	6161 (26.2)	8366 (35.6)
Mean (SD), PPPY	1.8 (1.7)	2.3 (2.7)	1.9 (1.8)	2.5 (3.0)	1.8 (1.7)	2.2 (2.4)
Median (IQR), PPPY	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)

ED, emergency department; IP, inpatient; IQR, interquartile range; OP, outpatient; PPPY, per patient per year; SjD, Sjögren disease; SSA, Sjögren's-syndrome-related antigen A; SSB, Sjögren's-syndrome-related antigen B. a Associated autoimmune conditions were looked in all available pre-index and 1 year post-index period. b Lab tests include the following: parotidectomy, punctal occlusion, antinuclear antibodies, rheumatoid factor, Anti-double stranded DNA (dsDNA%) test (for associated lupus), beta 2 microglobulin, complement C3, complement C4, complete blood count with differential, comprehensive metabolic panel, cryoglobulins, cyclic citrullinated peptide (associated rheumatoid arthritis), free light chain, lactate dehydrogenase, myositis antibodies, pulmonary function test, scleroderma antibodies, serum protein electrophoresis, uric acid, urine protein electrophoresis. c Imaging includes chest x-rays, computed tomography scans, magnetic resonance imaging, and ultrasound.

increase in patients with HCRU from baseline to follow-up was observed across all HCRU categories (all-cause outpatient visits [OP, 89.9% vs 99.6%], inpatient admissions [IP, 5.0% vs 11.8%], emergency department visits [ED, 16.5% vs 20.8%], SjD-specific diagnostic procedures [28.5% vs 41.2%], lab tests [55.2% vs 74.6%], and imaging [26.6% vs 36.8%]). A higher proportion of SjD+other patients had an IP visit in the follow-up period compared with SjD only patients. In addition to the increase in the proportion of patients with any HCRU during the follow-up period, the mean (SD) number of IP, ED, and lab visits per patient per year (PPPY) increased slightly in the follow-period vs baseline, with a substantial increase in OP visits (**Table 1**). Mean OP visits PPPY increased to a greater extent in the SjD+other group (41% increase) vs the SjD only group (32% increase). The 3 most commonly prescribed treatment classes in the overall cohort were systemic corticosteroids (42.8%), antidepressants (32.2%), and hydroxychloroquine and antimalarials (29.0%) (**Table 2**). This trend was similar for the SjD+other cohort; however, in the SjD only cohort, NSAIDs were among the top 3 classes along with systemic corticosteroids and antidepressants. Conventional DMARDs and biologic DMARDs were used by 14.2% and 5.6% of patients, respectively, in the follow-up period.

Table 2. Treatment Classes During Baseline and Follow-Up Periods for the Overall Cohort, Patients With SjD Only, and Patients With SjD and Overlapping Autoimmune Disease.

SjD-specific drugs prescribed, n (%)	Overall Cohort (N=35,035)		SjD+Other[a] (n=11,503)		SjD Only (n=23,532)	
	Baseline	Follow-Up	Baseline	Follow-Up	Baseline	Follow-Up
Anticonvulsants	4594 (13.1)	6844 (19.5)	1769 (15.4)	2660 (23.1)	2825 (12.0)	4184 (17.8)
Antidepressants	8769 (25.0)	11,275 (32.2)	3192 (27.7)	4164 (36.2)	5577 (23.7)	7111 (30.2)
Diuretics	4857 (13.3)	6021 (17.2)	1616 (14.0)	2188 (19.0)	041 (12.9)	3833 (16.3)
bDMARDs (non-TNFis)	435 (1.2)	855 (2.4)	368 (3.2)	707 (6.1)	67 (0.3)	148 (0.6)
bDMARDs (TNFis)	688 (2.0)	1129 (3.2)	576 (5.0)	926 (8.1)	112 (0.5)	203 (0.9)
csDMARDs	2458 (7.0)	4983 (14.2)	2013 (17.5)	3581 (31.1)	445 (1.9)	1402 (6.0)
Hydroxychloroquine and antimalarials	4110 (11.7)	10,167 (29.0)	2591 (22.5)	4923 (42.8)	1519 (6.5)	5244 (22.3)
Estrogen-related treatment	1412 (4.0)	1690 (4.8)	481 (4.2)	551 (4.8)	931 (4.0)	1139 (4.8)
Hormone replacement therapy	334 (1.0)	633 (1.8)	132 (1.1)	262 (2.3)	202 (0.9)	371 (1.6)
Metformin	1886 (5.4)	2160 (6.2)	544 (4.7)	631 (5.5)	1342 (5.7)	1529 (6.5)
Muscarinic agonists	390 (4.0)	4846 (13.8)	561 (4.9)	1769 (15.4)	829 (3.5)	3077 (13.1)
Prescription eye drops	1763 (5.0)	4266 (12.2)	503 (4.4)	1044 (9.1)	1260 (5.4)	3222 (13.7)
Saliva substitute	59 (0.2)	298 (0.9)	17 (0.1)	117 (1.0)	42 (0.2)	181 (0.8)
Systemic corticosteroids	10,490 (29.9)	14,993 (42.8)	4410 (38.3)	6349 (55.2)	6080 (25.8)	8644 (36.7)
Topical corticosteroids	3303 (9.4)	4111 (11.7)	1101 (9.6)	1398 (12.2)	202 (9.4)	2713 (11.5)
Systemic NSAIDs	7052 (20.1)	9472 (27.0)	2721 (23.7)	3680 (32.0)	4331 (18.4)	5792 (24.6)
Topical NSAIDs	1308 (3.7)	2079 (5.9)	518 (4.5)	829 (7.2)	790 (3.4)	1250 (5.3)

bDMARDs, biologic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; NSAIDs, nonsteroidal anti-inflammatory drugs; SjD, Sjögren's disease; TNFi, tumor necrosis factor inhibitor. a Associated autoimmune conditions were looked in all available pre-index and 1 year post-index period.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This real-world analysis confirmed that patients with newly diagnosed SjD alone or with other autoimmune diseases have high disease burden within 12 months of diagnosis as demonstrated by increases in HCRU, largely driven by greater use of OP, IP, and ED services. Although treatment use increased during follow-up, biologic use was limited.

Disclosure: S. McCoy: Amgen, 2, Aurinia, 2, iCell, 2, Kiniksa, 2, Novartis, 2, Otsuka, 2, TearSolutions, 2, Visterra, 2; **A. Lalla**: Novartis, 3; **N. Choudhary**: Novartis, 3; **S. Chatterjee**: Novartis, 3; **S. Prasad**: Novartis, 3; **A. Egana**: Novartis, 3.

Abstract Number: 1402

Understanding Fatigue Through Patients' Eyes: Development of a Novel Questionnaire Capturing the Complexity of Real-Life Fatigue in Sjögren's Disease

Saviana Gandolfo[1], Flavia Riccio[2], Mariachiara Visconti[3], Corrado Parlati[3], Nicola Della Rossa[4], Enrico Tirri[5] and Francesco Ciccia[3], [1]Rheumatology Unit, Ospedale del mare, Naples, Naples, Naples, Italy, [2]Rheumatology Section, University of Campania L. Vanvitelli, Naples, Italy, Napoli, Italy, [3]Rheumatology Section, University of Campania L. Vanvitelli, Naples, Italy, Naples, Italy, [4]Rheumatology Section, University of Campania L. Vanvitelli, Naples, Italy, Naples, [5]Rheumatology Unit, Ospedale del mare, Naples, Italy, Naples, Italy

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Fatigue is one of the most frequent, debilitating and impactful symptoms for patients with Sjögren's Disease (SjD), and one of the most challenging to measure. To date, there are no PROs fully capturing fatigue as experienced by patients in their daily lives.

The purpose of this study was to define a new PRO for assessing fatigue and its impact on the quality of life of patients with SjD, based on lived experiences and their own definitions of fatigue.

Methods: Inspired by an essay written by a patient with SjD on the Sjögren's Foundation website (1), a new fatigue questionnaire, including 15 distinct types of fatigue (basic, rebound, sudden, weather-related, molten lead phenomenon, tired-wired, flare-related, fatigue related to other physical causes, fatigue-related concentration impairment, stress/distress/anxiety/depression SDAD-related fatigue, not sleeping well fatigue, normal aging fatigue, chronic illness fatigue, fatigue from trying to keep up with family and friends without a chronic illness, and doctor fatigue) was created and administered to SjD patients. Correlations with ESSPRI, ESSDAI, clinical and laboratory parameters were analyzed.

Results: 90 consecutive patients (female 93.4%) fulfilling SjD ACR/EULAR 2016 criteria, mean age 57.1 years (range 21–82), completed the questionnaire. The most frequently reported types of fatigue were SDAD(88.9%), basic (86.7%), and rebound (86.7%), while the least reported was weather-related (60%). Among all types, the SDAD had the highest impact on quality of life (mean impact score 82.8%). Males more frequently reported SDAD (100%), doctor fatigue (100%), and not sleeping well (83.4%), while females reported rebound (89.3%), basic (88.1%), and SDAD (88.1%). Younger and older patients reported basic fatigue more frequently (85.7% and 100%, respectively), compared to middle-aged groups, reporting SDAD(36–59 years: 92.1%; 60–70 years: 87.5%). Rebound was the only type correlating with disease duration (r=0.22, p0.03). Although SDAD was the most frequently reported and impacting type, it did not significantly correlate with ESSPRI,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

whereas strong correlations were observed between ESSPRI and other types, particularly basic (r=0.54, p< 0.0001) and rebound (r=0.50, p< 0.0001). Certain types of fatigue strongly correlated with each other, such as basic and rebound (r=0.90, p< 0.0001), or specifically with other symptoms, such as flare-related and VASglobal pain (r=0.41, p< 0.0001). No correlations were observed with ESSDAI or lab parameters, except for the molten lead phenomenon with CRP (r=0.55, p0.007).

Conclusion: This novel SjD fatigue questionnaire captures aspects of real-life fatigue previously underrepresented in existing PROs, and reveals heterogeneity in patient experiences. These differences, along with the clustering of fatigue types and symptoms, underscore the importance of a fatigue-based patient profiling, with potential implications for pathophysiological understanding and personalized treatment. Ongoing efforts focus on validating the questionnaire, stratifying patients based on fatigue, and establishing its role as an outcome measure.

1.https://sjogrens.org/blog/2019/13-types-of-sjogrens-fatigue

Disclosure: S. Gandolfo: None; **F. Riccio**: None; **M. Visconti**: None; **C. Parlati**: None; **N. Della Rossa**: None; **E. Tirri**: None; **F. Ciccia**: None.

Abstract Number: 1403

Treatment of sleep apnoea syndrome in patients with primary Sjögren's disease improves symptoms and activity of disease

Anna Kuhn[1], Magdalena Seng[2], Björn Christian Frye[3], Sebastian Fähndrich[3], Lydia Vollmer[3], Jacques-eric GOTTENBERG[4], Florian Kollert[5], Reinhard Voll[6] and **Stephanie Finzel**[7], [1]University Medical Center, Department of Rheumatology and Clinical Immunology, Freiburg, Germany, Freiburg, Germany, [2]University Medical Center, Department of Rheumatology and Clinical Immunology, Freiburg, Germany; University Medical Center, Department of Radiology and Nuclear medicine, Basel, Switzerland, Freiburg, Germany, [3]University Medical Center, Department of Pulmonology, Freiburg, Germany, Freiburg, Germany, [4]Hautepierre Hospital, STRASBOURG, Alsace, France, [5]University Medical Center, Department of Rheumatology and Clinical Immunology, Freiburg, Germany; Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, University of Bern, Bern; Switzerland Department of Rheumatology, University Hospital Basel, Basel, Switzerland, Basel, Switzerland, [6]University Medical Center Freiburg, Freiburg, Germany, [7]Department of Rheumatology and Clinical Immunology, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: About 70% of patients with primary Sjögren's disease (pSjD) suffer from fatigue. Fatigue is associated with functional deficits(1), leading to anxiety, depression and reduced quality of life. Recent studies showed that sleep apnea syndrome (SAS) is common in patients with pSjD(2,3).

We aimed to determine the prevalence of SAS in pSjD patients and to examine to what extent SAS treatment could improve fatigue and disease activity in pSjD.

Methods: We report the 4-week (W4), 3-month (V2) and 6-month (V3) data of patients included between 2019-2024. Three different cohorts (pSjD, psoriatic arthritis (PsA) and patients with SAS without underlying rheumatologic disease (SAS+)) were screened for SAS and compared. All patients with pSjD and PsA fulfilled the respective ACR/EULAR criteria for their diseases. An apnoea-hypopnoea index >5/h triggered treatment with CPAP or positional therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Delta of p-values between V1 and week 4 (W4), between V1 and V2 (ΔV2) and between V1 and V3 (ΔV3)

	pSjD+ ΔW4	pSjD- ΔW4	PsA+ ΔW4	PsA- ΔW4	SAS+ ΔW4	pSjD+ ΔV2	pSjD- ΔV2	PsA+ ΔV2	PsA- ΔV2	SAS+ ΔV2	pSjD+ ΔV3	pSjD- ΔV3	PsA+ ΔV3	PsA- ΔV3	SAS+ ΔV3
ESSDAI	n.a.	n.a.	n.a.	n.a.	n.a.	0.617	0.248	n.a.	n.a.	n.a.	**0.003**	0.882	n.a.	n.a.	n.a.
ESSPRI	*0.054*	*0.074*	n.a.	n.a.	n.a.	0.154	0.344	n.a.	n.a.	n.a.	**0.043**	0.396	n.a.	n.a.	n.a.
FACIT	*0.074*	0.915	0.300	0.294	0.139	0.109	0.735	**0.012**	**0.036**	**0.008**	0.096	0.192	**0.034**	0.592	**0.017**
PHQ-9	0.206	0.578	0.423	**0.017**	0.249	0.553	0.614	**0.020**	0.097	0.064	0.467	0.370	**0.035**	0.080	0.156
Tender Joint Count	n.a.	n.a.	n.a.	n.a.	n.a.	0.407	0.668	1.000	**0.036**	0.477	0.063	0.835	1.000	0.219	0.419
EPS	0.489	0.136	0.289	0.456	0.233	0.202	0.306	*0.053*	0.594	*0.072*	0.775	1.000	**0.014**	0.842	0.386
Health WHOQOL-BREF	0.681	0.241	0.184	0.347	0.192	0.104	0.718	**0.042**	0.758	0.838	0.591	0.131	0.374	0.598	0.172
Soc WHOQOL-BREF	*0.063*	*0.096*	0.775	0.830	0.785	**0.017**	0.157	0.665	0.937	0.756	*0.059*	0.792	0.317	0.331	0.741
Env WHOQOL-BREF	0.332	0.215	0.423	0.119	0.332	0.599	0.351	**0.044**	0.328	0.360	0.775	0.568	0.186	0.407	0.386

SAS+: non-rheumatological patients with sleep apnea syndrome; pSjD+: patients with primary Sjögren's disease with initiation of therapy after sleep apnea syndrome diagnosis; pSjD-: patients with primary Sjögren's disease without sleep apnea syndrome or without initiation of therapy after sleep apnea syndrome diagnosis; PsA+: patients with psoriatic arthritis with initiation of therapy after sleep apnea syndrome diagnosis; PsA-: patients with Psoriatic arthritis without sleep apnea syndrome or without initiation of therapy after sleep apnea syndrome diagnosis; ESSDAI: EULAR Sjögren's syndrome disease activity index; FACIT: Functional Assessment of Chronic Illness Therapy; ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index; PHQ-9: Patient Health Questionnaire-9; EPS: Epworth Sleepiness Scale; WHOQOL-BREF: World Health Organization Quality of Life Questionnaire, short form (soc: social, env: environmental). Values in bold are statistically significant, values in italics trended towards significance.

Assessments after W4 comprised fatigue (FACIT), visual analogue scale for pain and quality of life, depression (PHQ-9), quality of life (WHOQOL-BREF), daytime sleepiness (EPS) and ESSPRI. Assessments at inclusion (V1), V2 and V3: CRP and ESSDAI. Level of significance was set at a p-value < 0.05.

Results: The Departments of Rheumatology and Clinical Immunology, University Medical Center in Freiburg and Strasbourg examined 41 patients with pSjD (age 54.98 ± 12.36) and 21 patients with PsA (age 56.00 ± 9.12) for SAS. The SAS+ control group (age 58.46 ± 9.90) comprised of 13 individuals. The pSjD+ patients were significantly older than the pSjD- patients (p=0.00076). In pSjD, 15/41 (36.6%) of patients were diagnosed with SAS; 13/15 were treated with CPAP or positional therapy (pSjD+). In PsA, 11/ 21 patients had SAS; 8/11 received CPAP or positional therapy (PsA+). In SAS, 13/13 received CPAP treatment.

Between V1 and V2, and V1 and V3, the FACIT score improved significantly in SAS+ and PsA+ patients (p=0.008, p=0.012; p=0.017, p=0.034). Furthermore, in patients with pSjD+, the ESSDAI and ESSPRI (improved domains: fatigue and limb pain) scores improved significantly between V1 and V3 (p=0.003; p=0.043), while the Soc WHOQOL-BREF score significantly decreased between V1 and V2 (p=0.017). In PsA+ patients the PHQ-9 score improved significantly between V1 and V2 (p=0.020), and V1 and V3 (p=0.035), the Health WHOQOL-BREF and the Env WHOQOL-BREF scores improved significantly between V1 and V2 (p=0.042; p=0.044), the EPS between V1 and V3 (p=0.014). Table 1 gives further details.

Interestingly in PsA- patients, the following significant improvements were noted: joint tenderness between V1 and V2 (p=0.036), PHQ-9 between V1 and W4 (p=0.017), and FACIT between V1 and V2 (p=0.036).

Conclusion: SAS affected 36.6% of pSjD patients, which is within the range of analyses published in literature. In individuals with pSjD, adequate SAS treatment markedly reduced disease activity and symptoms; this implies that SAS screening in pSjD is in general appropriate.

Successful immunosuppressive treatment might positively influence PHQ-9 and FACIT in PsA- patients.

Disclosure: A. Kuhn: None; **M. Seng**: None; **B. Frye**: None; **S. Fähndrich**: CSL-Behring, Astra Zeneca, GSK, 2, 6; **L. Vollmer**: None; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **F. Kollert**: Roche, 2; **R. Voll**: None; **S. Finzel**: AbbVie/Abbott, 6, Alfasigma/Galapagos, 6, 12, meeting or travel grant, AstraZeneca, 2, Biotest, 6, 12, meeting or travel grant, Celltrion, 6, Chugai, 6, Eli Lilly, 12, meeting or travel grant, GlaxoSmithKlein(GSK),

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 6, Johnson&Johnson, 2, 6, 12, meeting or travel grant, Novartis, 2, 6, 12, meeting or travel grant, NovoNordisk, 2, Sobi, 12, meeting or travel grant, UCB, 2, 6, 12, meeting or travel grant.

Abstract Number: 1404

Higher cardiovascular risk and lymphoma development in primary Sjögren's Syndrome with extraglandular involvement

Teresa Blázquez Sánchez[1], Antía García Fernández[1], Jorge Mairal Monesma[2], Arantxa Torres Roselló[3], Elena Heras Recuero[4], Raquel Largo Carazo[5], Juan Antonio Martínez López[6] and Miguel A. González-Gay[7], [1]Fundacion Jiménez Díaz, Madrid, Madrid, Spain, [2]Instituto de Investigacion Fundación Jiménez Díaz, Madrid, Spain, [3]Fundacion Jiménez Díaz, Madrid, Spain, [4]Hospital Fundacion Jimenez Dias, Madrid, Spain, [5]Instituto de Investigacion Fundacion Jiménez Díaz, Madrid, Spain, [6]Hospital Universitario Fundacion Jimenez Diaz, Madrid, Spain, [7]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1376–1404) Sjögren's Disease – Basic & Clinical Science Poster II: Clinical Manifestations and Health Outcomes

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Sjögren's syndrome (pSS) can have a systemic involvement with extraglandular manifestations, which are associated with more severe disease and with higher risk of complications, such as lymphoma. pSS has also been associated with an increased prevalence of cardiovascular risk (CV) factors and cardiovascular disease. The aim of the study was to describe the clinical characteristics of a cohort of Spanish patients with pSS from a tertiary hospital and to analyze the rates of CV factors and lymphoma between groups.

Methods: A retrospective descriptive study of patients with a diagnosis of pSS between January 1990 and December 2024 who met the ACR/EULAR 2016 classification criteria for pSS, in follow-up in a tertiary hospital in Madrid, Spain.

Patients diagnosed with other systemic connective tissue diseases were excluded. Patients with glandular involvement were compared to patients with systemic involvement (extraglandular). Categorical variables were presented as proportions or percentages, whereas continuous variables were reported as means with standard deviations (SD). Group comparisons were conducted using the Student's t-test or the χ^2test, as appropriate.

Results: A total of 110 patients were included, 39 (35.5%) had extraglandular involvement. Main characteristics are reported in Table 1. There were no differences regarding age, sex, time in follow up and smoking status. Cardiovascular risk (CV) factors were similarly distributed between groups, but a higher proportion of patients with extraglandular involvement had more than 1 CV risk factor. No cardiovascular events were reported after pSS diagnosis. Articular involvement was the most frequent followed by Raynaud, peripheral nervous system and interstitial lung disease.

Regarding neoplasia, 14.5% of patients developed malignancies, rates were higher in extraglandular patients. The reported incidence rate of lymphoma was 4.54 per 100 patients with pSS, being 2.82 per 100 patients in the glandular group and 7.69 per 100 patients in the extraglandular group.

Hydroxychloroquine was the main treatment in both groups, with higher rates of corticosteroids, rituximab and immunosuppressive treatments in patients with extraglandular involvement, as expected.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of patients included in the study.

	Glandular	Extraglandular	Total	*p value*
Patients, n (%)	71 (64.5)	39 (35.5)	110 (100)	-
Age at diagnosis, years, mean (SD)	56 (15.4)	53 (14.7)	55 (15.2)	0.303
Disease duration, years, mean (SD)	6.9 (6,5)	7.8 (7,8)	7.2 (6.9)	0.547
Sex Women, n (%)	65 (91.5)	34 (87.2)	99 (90)	0.515
Former smoker, n (%) Active smoker, n (%)	18 (25.7) 4 (4.3)	7 (17.9) 3 (7.7)	25 (22.9) 7 (6.4)	0.477 0.697
Hypertension, n (%) DL, n (%) DM, n (%)	17 (23.6) 18 (25) 6 (8.3)	13 (34.2) 14 (36.8) 5 (13.2)	30 (27.3) 32 (29.1) 11 (10)	0.373 0.280 0.518
>1 CV risk factor, n (%) CV risk factors, mean (SD)	27 (38) 0.5 (0,8)	21 (53.8) 0.8 (0.9)	48 (43.6) 0.6 (0.8)	0.238 0.08
Diagnosis Positivity for SS-A/SS-B antibodies, n (%)	63 (87.5)	35 (92.1)	98 (89.1)	1
Schirmer test performed, n (%) - Positive, n (%)	28 (39.4) 22/28 (78.6)	18 (46.2) 17/18 (94.4)	46 (41.8) 39/46 (84.8)	0.547 0.220
Glandular ultrasound performed, n (%) - Nonspecific, n (%) - Diagnostic, n (%)	49 (69.0) 4/49 (8.16) 38/49 (77.5)	24 (61.5) 2/24 (8.3) 15/24 (62.5)	73 (66.4) 6/73 (8.2) 53/73 (72.6)	0.527 0.291 0.493
Glandular biopsy performed, n (%) - Positive, n (%)	26 (37.5) 19/26 (73)	15 (36.8) 14/15 (93.3)	41 (37.3) 33/41 (80.5)	1 0.386
Manifestations Xerostomia, n (%) Xerophthalmia, n (%) Raynaud's phenomenon, n (%) Leukocytoclastic vasculitis, n (%) ILD, n (%) Myositis, n (%) Myalgia, n (%)	62 (86.1) 63 (87.3) 0 (0) 0 (0) 0 (0) 0 (0) 5 (7.0)	34 (89.5) 33 (86.8) 13 (33.3) 4 (10.5) 6 (15) 1 (2.6) 6 (15.4)	96 (87.3) 96 (87.3) 13 (11.8) 4 (3.6) 6 (5.5) 1 (0.9) 11 (10.0)	0.560 1.000 <0.001* 0.014* 0.002* 0.355 0.193
PNS, n (%) CNS, n (%) Arthritis, n (%) Renal, n (%) Asthenia, n (%)	0 (0) 0 (0) 0 (0) 0 (0) 15 (21.1)	7 (18.4) 1 (2.6) 18 (46.2) 2 (5) 11 (28.2)	7 (6.4) 1 (0.9) 18 (16.4) 2 (1.8) 26 (23.6)	<0.001* 0.355 <0.001 0.295 0.483
Neoplasia, n (%) Lymphoma, n (%) Leukemia, n (%) Solid tumor, n (%)	8 (9.9) 2/8 (25) 1/8 (12.5) 5/8 (62.5)	9 (23.1) 3/9 (33.3) 1/9 (11.1) 6/9 (66.7)	16 (14.5) 5/16 (31.3) 2/16 (12.5) 11/16 (68.8)	0,127 0.344 1 1
Serological profile RF+, n (%) ANA+, n (%) Ro+, n (%) Ro-52+, n (%) Ro-60+, n (%) La+, n (%)	34 (49.3) 61 (88.4) 61 (88.4) 42 (75) 47 (83.9) 27 (39.7)	23 (60.5) 37 (94.9) 35 (89.7) 29 (78.4) 31 (88.6) 18 (46.2)	57 (53.3) 98 (90.7) 96 (88.9) 71 (76.3) 78 (85.7) 45 (42.1)	1 0.324 1 0.806 0.759 0.517
Treatment Hydroxychloroquine, n (%) IS, n (%) Rituximab, n (%) Prednisone, n (%)	12 (17.1) 1 (1.4) 0 (0) 3 (4.3)	12 (30.8) 8 (20.5) 8 (20.5) 9 (23.1)	24 (22.0) 9 (8.2) 8 (7.3) 12 (11)	0.147 0.001* <0.001* 0.008*

CNS: Central Nervous System; CRF: Cardiovascular Risk Factors; DL: Dyslipidemia; DM: Diabetes Mellitus; ILD: Interstitial Lung Disease; IS: Immunosuppressants; PNS: Peripheral Nervous System; RF: Rheumatoid Factor

Conclusion: Patients with extraglandular involvement in pSS present significantly more severe systemic manifestations with more frequent use of immunosuppressive therapies. They showed a higher cardiovascular risk burden and a considerable prevalence of neoplasia, particularly lymphomas.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Blázquez Sánchez: None; **A. García Fernández**: None; **J. Mairal Monesma**: None; **A. Torres Roselló**: None; **E. Heras Recuero**: None; **R. Largo Carazo**: None; **J. Martínez López**: None; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2.

Abstract Number: 1405

A Combined Score of Syndesmophytes and Facet Joint Ankylosis Improves Sensitivity to Spinal Structural Damage Progression in Axial Spondyloarthritis

Ana Bento da Silva[1], Floris A. van Gaalen[1], Robert Landewé[2], Manouk de Hooge[3], Mary Lucy Marques[4], Miranda van Lunteren[1], Liese de Bruin[1], Gizem Ayan[5], Xenofon Baraliakos[6], Monique Reijnierse[7], Jürgen Braun[8], Désirée Van Der Heijde[1] and Sofia Ramiro[9], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [3]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [4]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [5]Ankara Research and Training Hospital, Ankara, Turkey, [6]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [7]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [8]Ruhr-University, Bochum, Germany; and Rheumatologische Versorgungszentrum (RVZ) Steglitz, Berlin, Germany, [9]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

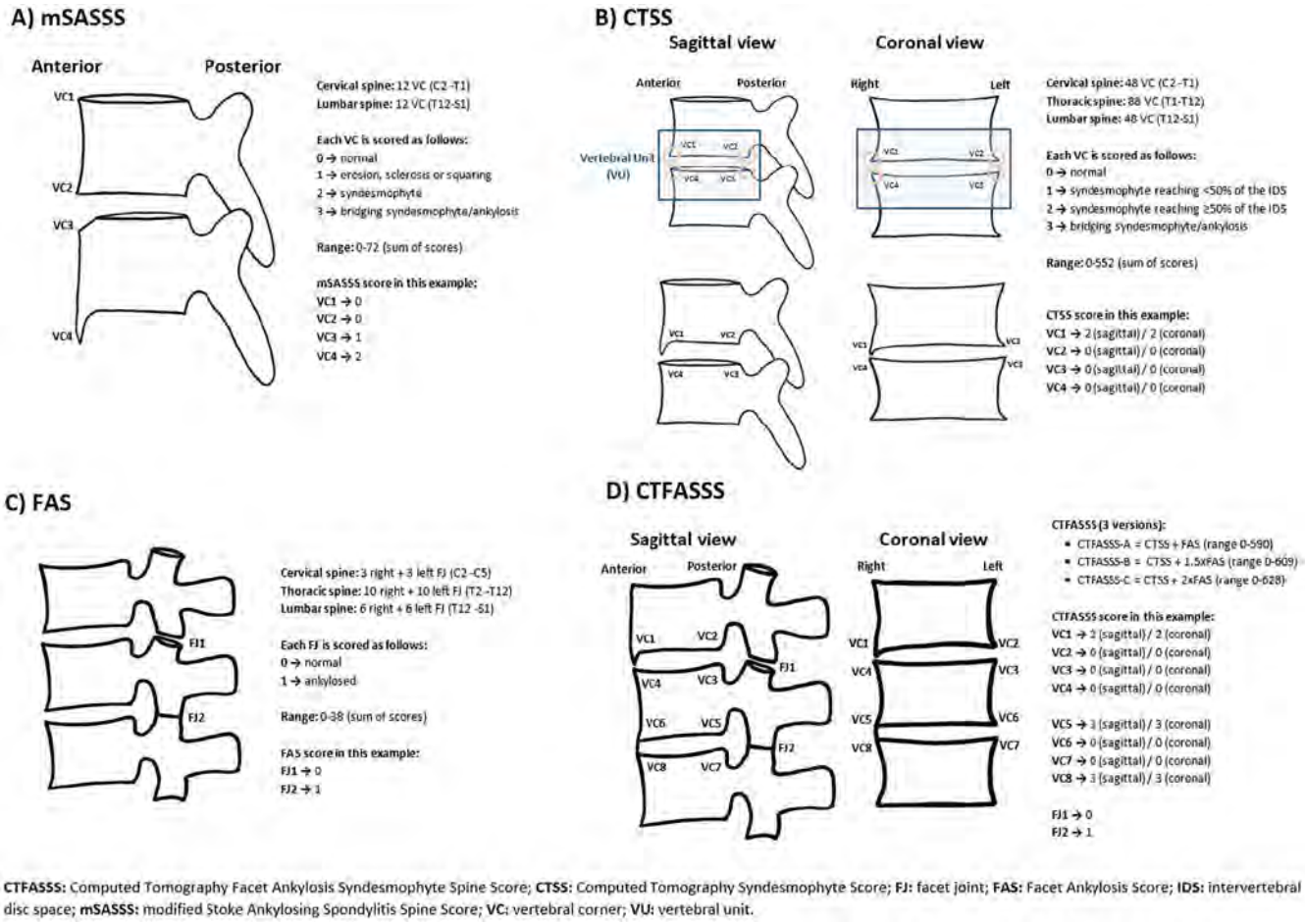
Session Time: 10:30AM–12:30PM

Background/Purpose: The computed tomography (CT) syndesmophyte score (CTSS) has shown to be more sensitive in capturing spinal structural damage progression in axial SpA (axSpA), compared to the current gold standard, the modified Stoke Ankylosis Spondylitis Spine Score (mSASSS) (de Koning A *et al*, Ann Rheum Dis 2018). Additionally, assessing facet joint ankylosis (FJA) on CT seems promising in further detecting progression (Stal R *et al*, Rheumatology 2020). We investigated whether a score combining syndesmophytes and FJA is more sensitive than CTSS for assessing spinal damage progression in axSpA.

Methods: Data from the Sensitive Imaging in Ankylosing Spondylitis cohort were used, including axSpA patients fulfilling the modified New York criteria and with ≥1 syndesmophyte. Conventional radiography (CR) and low-dose computed tomography (ldCT) of the spine were performed at baseline and 2 years (2Y) and scored by 3 (CR) or 2 (ldCT) central readers, blinded for time order. Syndesmophytes were assessed on CR and ldCT by the mSASSS and CTSS, respectively (Figure 1). The presence of FJA was evaluated on ldCT with the facet ankylosis score (FAS) on 19 facet joints (levels C5-T2 excluded due to poor visibility). The total mSASSS, CTSS and FAS were calculated per reader at each timepoint. Three versions of a combined score of syndesmophytes and FJA were proposed and computed by adding the CTSS and FAS while giving equal weight to both components (CT facet ankylosis syndesmophyte spine score A [CTFASSS-A]), 50% (CTFASSS-B) or 100% more weight to FAS (CTFASSS-C). Change scores were calculated per reader by subtracting the baseline from the 2Y score and then averaged across readers. The number of patients with positive and negative change as well as net change >0 and >0.5 were calculated for each score and compared. The total number of new or growing syndesmophytes and new FJA were calculated per reader and then averaged across readers.

Results: Forty-eight patients were included: mean (SD) age of 49 (9.7) years, 85% male, 81% HLA-B27+. Between baseline and 2Y, progression of spinal damage was observed as assessed by all scores: mean (SD) mSASSS 18.3 (14.3) vs 20.4 (15.1), CTSS 161.6 (127.1) vs 179.5 (132.3), FAS 8.2 (9.8) vs 9.4 (10.2). CTFASSS changed from 169.8 (134.5)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CTFASSS: Computed Tomography Facet Ankylosis Syndesmophyte Spine Score; **CTSS:** Computed Tomography Syndesmophyte Score; **FJ:** facet joint; **FAS:** Facet Ankylosis Score; **IDS:** intervertebral disc space; **mSASSS:** modified Stoke Ankylosing Spondylitis Spine Score; **VC:** vertebral corner; **VU:** vertebral unit.

Figure 1. Schematic representation to guide the calculation of the mSASSS (A), CTSS (B), FAS (C) and CTFASSS (D)

(CTFASSS-A), 174.0 (138.4) (CTFASSS-B) and 178.1 (142.3) (CTFASSS-C) at baseline to 188.9 (140.0), 193.6 (143.9) and 198.3 (147.9) at 2Y, respectively.

After 2Y, CTFASSS-A, CTFASSS-B and CTFASSS-C detected any net change in a higher percentage of patients compared to CTSS (96% vs 83%) and, most notably, to mSASSS (96% vs 46%) and FAS (96% vs 48%) (Table 1A). Moreover,

Table 1. Number of axSpA patients with spinal structural damage progression on low-dose computed tomography (n=48)

A. According to change in spinal structural damage scores

	mSASSS*	CTSS	FAS	CTFASSS-A (CTSS + FAS)	CTFASSS-B (CTSS + 1.5 x FAS)	CTFASSS-C (CTSS + 2 x FAS)
Change >0, n (%)						
Positive	24 (65)	43 (90)	27 (56)	47 (98)	47 (98)	47 (98)
Negative	7 (20)	3 (6.3)	4 (8.3)	1 (2.1)	1 (2.1)	1 (2.1)
Net progression$	17 (46)	40 (83)	23 (48)	46 (96)	46 (96)	46 (96)
Change >0.5, n (%)						
Positive	22 (59)	43 (90)	23 (48)	45 (94)	47 (98)	47 (98)
Negative	6 (16)	3 (6.3)	2 (4.2)	1 (2.1)	1 (2.1)	1 (2.1)
Net progression$	16 (43)	40 (83)	21 (44)	44 (92)	46 (96)	46 (96)

B. According to syndesmophyte and facet joint ankylosis development

	Total number of new lesions&	Mean (SD)	Range	≥1, n(%)#	≥2, n(%)#	≥3, n(%)#
New syndesmophytes	327	6.8 (7.0)	0-33	35 (73)	31 (65)	22 (46)
Growing syndesmophytes	145	3.0 (2.5)	0-8	25 (52)	19 (40)	14 (29)
New or growing syndesmophytes	472	9.8 (8.3)	0-37	41 (85)	36 (75)	28 (58)
New facet joint ankylosis	73	1.5 (2.0)	0-8	11 (23)	10 (21)	6 (13)
New/growing syndesmophytes and FJA	545	11.3 (9.0)	0-42	41 (85)	38 (79)	33 (69)

* Retrieved from: de Koning A *et al. Ann Rheum Dis* 2018;77:293-299 (n=37).
$ Net progression: number of patients with positive progression minus number of patients with negative progression.
& Total number of new lesions (out of 48 patients) is the average across both readers.
# Agreement between both readers was required on the presence of ≥1, ≥2 and ≥3 lesions.
axSpA: axial spondyloarthritis; **CTFASSS:** Computed Tomography Facet Ankylosis Syndesmophyte Spine Score; **CTSS:** Computed Tomography Syndesmophyte Score; **FAS:** Facet Ankylosis Score; **mSASSS:** modified Stoke Ankylosis Spondylitis Spine Score.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

considering all 48 patients, 472 new or growing syndesmophytes and 73 new FJA were detected on ldCT, denoting that the combined score captured 1.15 times more new bone formation than CTSS (545 vs 472 new lesions) (Table 1B).

Conclusion: A combined score assessing syndesmophytes and FJA captures more spinal structural damage progression in axSpA than assessing syndesmophytes alone. With respect to sensitivity to change, all CTFASSS proposals performed similarly, with the simple addition of CTSS and FAS (CTFASSS-A) being the most straightforward approach. However, further validation will define which is the best combination.

Disclosure: A. Bento da Silva: None; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **M. de Hooge**: UCB pharma, 2; **M. Marques**: Novartis, 2, 6; **M. van Lunteren**: None; **L. de Bruin**: None; **G. Ayan**: None; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **M. Reijnierse**: None; **J. Braun**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1406

A Combined Score of Facet Joint Ankylosis and Syndesmophyte Development Correlates Well with Spinal Mobility in Axial Spondyloarthritis

Ana Bento da Silva[1], Floris A. van Gaalen[1], Robert Landewé[2], Manouk de Hooge[3], Mary Lucy Marques[4], Miranda van Lunteren[1], Liese de Bruin[1], Gizem Ayan[5], Xenofon Baraliakos[6], Monique Reijnierse[7], Jürgen Braun[8], Désirée Van Der Heijde[1] and Sofia Ramiro[9], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [3]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [4]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [5]Ankara Research and Training Hospital, Ankara, Turkey, [6]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [7]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [8]Ruhr-University, Bochum, Germany; and Rheumatologische Versorgungszentrum (RVZ) Steglitz, Berlin, Germany, [9]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Spearman's correlation between spinal structural damage scores and spinal mobility (at baseline, n=46)*

	mSASSS	CTSS	FAS	CTFASSS-A (CTSS + FAS)	CTFASSS-B (CTSS + 1.5 x FAS)	CTFASSS-C (CTSS + 2 x FAS)
	r_s	r_s	r_s	r_s	r_s	r_s
Spinal mobility						
Occiput-to-wall distance	0.50	0.64	0.64	0.65	0.66	0.66
Lateral spinal flexion	-0.61	-0.72	-0.53	-0.72	-0.72	-0.73
Modified Schober test	-0.41	-0.50	-0.40	-0.50	-0.50	-0.50
Cervical rotation	-0.49	-0.58	-0.62	-0.58	-0.59	-0.59
Chest expansion	-0.32	-0.49	-0.31	-0.49	-0.49	-0.48
Composite measure						
BASMI	0.60	0.71	0.65	0.71	0.72	0.72

* Aggregate scores (average across readers) were used. Higher r_s values mean higher strength of the association; the following cutoffs were applied (Castro MP *et al*, *Clin Rheumatol* 2016;35(7):1777-87):
Low: 0.00-0.20; Fair: 0.21-0.40; Moderate: 0.41-0.60; Substantial: 0.61-0.80; Excellent: 0.81-1.00
BASMI: Bath Ankylosing Spondylitis Metrology Index; **CTFASSS:** Computed Tomography Facet Ankylosis Syndesmophyte Spine Score; **CTSS:** Computed Tomography Syndesmophyte Score; **FAS:** Facet Ankylosis Score; **mSASSS:** modified Stoke Ankylosis Spondylitis Spine Score; r_s: Spearman's rho.

Background/Purpose: In axial SpA (axSpA), the computed tomography (CT) syndesmophyte score (CTSS) has shown to capture more spinal structural damage progression and to better correlate with spinal mobility than the modified Stoke Ankylosis Spondylitis Spine Score (mSASSS, the current gold standard) (Stal R *et al*, *RMD Open* 2023). Recently, a combined score of syndesmophyte and facet joint ankylosis (FJA) development has been proposed as a more sensitive instrument in capturing damage progression. We aimed to assess whether this combined score retains good correlation with spinal mobility compared to current measurement instruments.

Methods: Data from the Sensitive Imaging in Ankylosing Spondylitis cohort were used, including axSpA patients fulfilling the modified New York criteria and with ≥1 syndesmophyte. Conventional radiography (CR) and low-dose computed tomography (ldCT) of the spine were performed at baseline (BL) and scored by 3 (CR) or 2 (ldCT) central readers, blinded for time order. Syndesmophytes were assessed on CR and ldCT by the mSASSS and CTSS, respectively. FJA was evaluated on ldCT with the facet ankylosis score (FAS) on 19 facet joints (levels C5-T2 excluded due to poor visibility, range: 0-38). Three different versions of a combined score of FJA and syndesmophyte development (the CT facet ankylosis syndesmophyte spine score, CTFASSS) were proposed and computed by adding the CTSS and FAS while giving equal weight to both components (CTFASSS-A = CTSS + FAS), 50% more weight to FAS (CTFASSS-B = CTSS + 1.5xFAS) or 100% more weight to FAS (CTFASSS-C = CTSS + 2xFAS). At BL, the following spinal mobility measures were evaluated: occiput-to-wall distance (OWD), lateral spinal flexion (LSF), modified Schober test (mSchober), cervical rotation and chest expansion. The composite score BASMI was calculated. Correlations between each spinal structural damage score and spinal mobility were assessed at BL with Spearman's rank correlation coefficients and compared. A cumulative probability plot was created to better illustrate correlations between CTFASSS and BASMI.

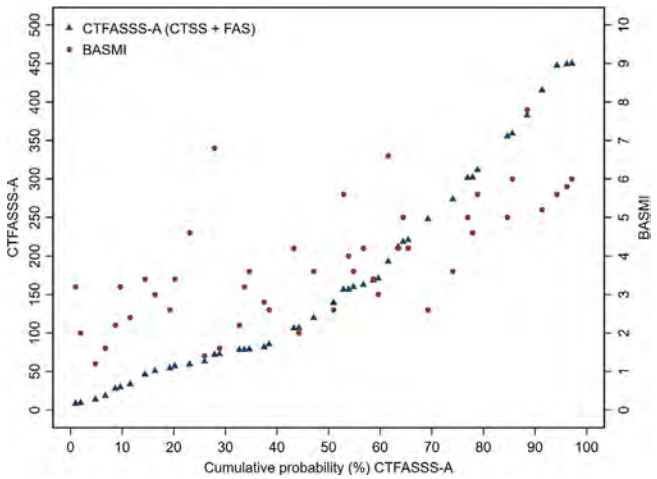


Figure 1. Cumulative probability plot representing the relationship between BASMI and CTFASSS-A (BASMI: Bath Ankylosing Spondylitis Metrology Index; CTFASSS-A: Computed Tomography Facet Ankylosis Syndesmophyte Spine Score version A; CTSS: Computed Tomography Syndesmophyte Score; FAS: Facet Ankylosis Score)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Forty-six patients had data available for all structural damage scores and spinal mobility measures at BL: mean (SD) age of 47 (9.6) years, 87% male, 83% HLA-B27+. All versions of the CTFASSS showed substantial correlations with OWD (CTFASSS-A: r_s 0.65; CTFASSS-B and CTFASSS-C: r_s 0.66) and LSF (CTFASSS-A and CTFASSS-B: r_s -0.72; CTFASSS-C: r_s -0.73) and moderate correlations with the other measures, to a similar degree to that observed for CTSS, but better than mSASSS (Table 1). Notably, compared to mSASSS, FAS alone correlated better with OWD (r_s 0.64 vs 0.50) and cervical rotation (r_s -0.62 vs -0.49). However, no additional benefit was obtained with a CTFASSS score attributing more weight to FAS compared to the simple sum of the components (i.e. CTFASSS-A). Although substantial correlations were observed between all imaging scores and BASMI, better results were seen with CTSS and CTFASSS (Figure 1).

Conclusion: A composite score assessing syndesmophytes and FJA correlates with spinal mobility similarly well as CTSS but better than mSASSS, supporting the validity of the combined score in assessing spinal damage progression in axSpA.

Disclosure: A. Bento da Silva: None; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **M. de Hooge**: UCB pharma, 2; **M. Marques**: Novartis, 2, 6; **M. van Lunteren**: None; **L. de Bruin**: None; **G. Ayan**: None; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **M. Reijnierse**: None; **J. Braun**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1407

Trends in Diagnostic Timing and Clinical Features of Axial Spondyloarthritis by Sex and Clinical Subtype: A Multicenter Cohort Over Seven Decades

Carla Saad[1], Rafael Bassara Macedo[2], Maria Eduarda Veiga[1], Claudia Marques[3], Gustavo Resende[4], Adriana Marinho[5], Andressa Soares[6], Cleandro Pires[7], Débora Rodrigues[8], Glaucio Castro[9], Guilherme Bulbol[10], Jamile Carneiro[11], José Mauro Fernandes[12], Manuella Ochtrop[13], Maria Bernadete Gavi[14], Michel Yazbek[15], Nara Cavalcanti[16], Natalia Machado[17], Olivio Malheiro[18], Rejane Vieira[19], Ricardo Lage[18], Rita Menin[20], Rywka Golebiovski[21], Sandra Ribeiro[10], Thauana Oliveira[21], Tysciana Brito[22], Valquiria Diniz[14], Marcelo Pinheiro[23] and Percival Sampaio-Barros[24], [1]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [3]Hospital das Clínicas da Universidade Federal de Pernambuco (UFPE) - PE, Recife, Brazil, [4]Hospital das Clinicas UFMG, Belo Horizonte, Brazil, [5]Fundação Hospital do Acre - AC, Rio Branco, Brazil, [6]Hospital Universitário da Universidade Federal de Santa Catarina (UFSC) - SC, Florianópolis, Brazil, [7]UNB, Brasilia, Distrito Federal, Brazil, [8]Fundação Hospital do Acre - AC, Rio Branco, Acre, Brazil, [9]Hospital Governador Celso Ramos (HCR) - SC, Florianópolis, Santa Catarina, Brazil, [10]Faculdade de Medicina da Universidade Federal do Amazonas (UFAM) - AM, Manaus, Amazonas, Brazil, [11]Hospital de Base do Distrito Federal (HBDF) - DF, Brasilia, Distrito Federal, Brazil,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[12]Universidade Federal do Maranhão (UFMA) - MA, São Luiz, Maranhao, Brazil, [13]Hospital Universitário Pedro Ernesto / UERJ - RJ, Rio de Janeiro, Rio de Janeiro, Brazil, [14]Universidade Federal do Espírito Santo (UFES) - ES, Vitória, Espirito Santo, Brazil, [15]Universidade Estadual de Campinas (UNICAMP) - SP, Campinhas, Sao Paulo, Brazil, [16]Hospital das Clínicas da Universidade Federal de Pernambuco (UFPE) - PE, Recife, Pernambuco, Brazil, [17]Universidade Fedral do Paraná (UFPR) - PR, Curitiba, Parana, Brazil, [18]Hospital das Clínicas da Universidade Federal de Minas Gerais (UFMG) - MG, Belo Horizonte, Minas Gerais, Brazil, [19]Universidade Estadual do Ceará (UECE) - CE, Fortaleza, Ceara, Brazil, [20]Faculdade de Medicina de São José do Rio Preto (FAMERP) - SP, São José do Rio Preto, Sao Paulo, Brazil, [21]Escola Paulista de Medicina (EPM) - Universidade Federal de São Paulo (UNIFESP) - SP, São Paulo, Sao Paulo, Brazil, [22]Faculdade de Medicina da Universidade Federal do Amazonas (UFAM) - AM, Manaus, Brazil, [23]UNIFESP/ EPM, São Paulo, São Paulo, Brazil, [24]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial Spondyloarthritis (axSpA) frequently eludes early recognition, particularly before structural sacroiliitis becomes visible. We analyzed decade-specific diagnosis delay, clinical subtype distribution, and first-symptom profiles in men and women within a nationwide cohort to assess the impact of updating classification criteria on presentation patterns.

Methods: This was a cross-sectional data analysis from the Brazilian Spondyloarthritis Registry (RBE), including 19 centers nationwide. All patients included were diagnosed with axSpA by a rheumatologist and met the ASAS classification criteria for axSpA. Patients were grouped by the decade in which their first SpA-related symptom.

Results: A total of 791 patients were included, whose disease onset (initial symptoms) occurred between 1961 and 2024. A male predominance was observed (n = 547, 69.2%). Notably, all patients with disease onset before 1970 were male, but female representation increased progressively according to the decade of disease onset (30% in the 1970s to 50% in the 2020s). The mean diagnosis delay interval dropped from 41.7 ± 4.2 years in the 1960s (n=3) to 1.9 ± 1.5 years in 2020–2024 (n=18) (Figure 1). Diagnostic delay decreased similarly in both sexes across decades (p for interaction = 0.971). In each decade of initial symptom, delay was comparable between men and women, with no significant differences observed (all p > 0.05) (Figure 2). Radiographic axSpA (r-axSpA) accounted for all cases before 2009 and declined to 83.3 % by 2020–2024 as non-radiographic axSpA (nr-axSpA) reached 16.7 %. Diagnosis delay improved markedly for both subtypes (p< 0,001). Low back pain was the dominant initial symptom over the decades varying from 90.0% to 81.1%. Regarding symptoms, men reported more hip pain than women (23.2% vs. 8,6%, p< 0.001). Initial symptoms with upper-limb arthritis, dactylitis,

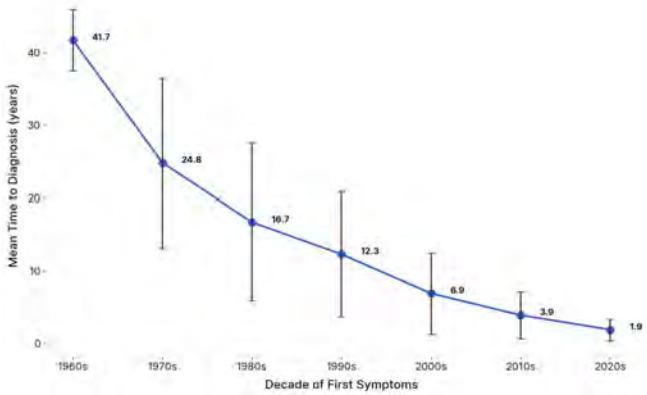


Figure 1. Overall Diagnostic Delay by Initial Symptom Decade

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

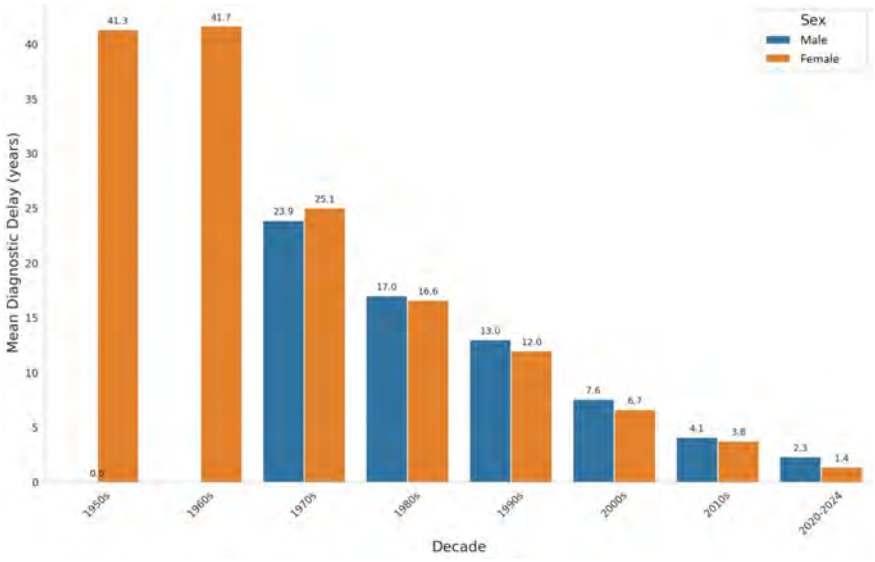


Figure 2. Comparison of Mean Diagnostic Delay by Sex and Initial Symptom Decade

cervical pain, buttock pain was similar between men and women (p >0.05). **Compared to radiographic disease, non-radiographic axSpA showed more hip pain as initial symptom (23.2% vs. 8.2%, p=0.024), while frequencies of upper-limb arthritis, lower-limb arthritis, and back pain were similar (**p >0.05).

Conclusion: These findings suggest a significant improvement in the recognition of axSpA in recent decades, possibly related to the adoption of new axSpA biomarkers, such as the use of magnetic resonance imaging, as well as increased awareness of the disease. This progress has led to greater recognition of previously underdiagnosed female patients. The growing proportion of non-radiographic axSpA highlights the need for early imaging-based referral protocols and management strategies.

Disclosure: C. Saad: None; **R. Bassara Macedo**: None; **M. Veiga**: None; **C. Marques**: None; **G. Resende**: None; **A. Marinho**: None; **A. Soares**: None; **C. Pires**: None; **D. Rodrigues**: None; **G. Castro**: None; **G. Bulbol**: None; **J. Carneiro**: None; **J. Fernandes**: None; **M. Ochtrop**: None; **M. Gavi**: None; **M. Yazbek**: None; **N. Cavalcanti**: None; **N. Machado**: None; **O. Malheiro**: None; **R. Vieira**: None; **R. Lage**: None; **R. Menin**: None; **R. Golebiovski**: None; **S. Ribeiro**: None; **T. Oliveira**: None; **T. Brito**: None; **V. Diniz**: None; **M. Pinheiro**: AbbVie/Abbott, 2, Johnson & Johnson, 2, UCB, 2; **P. Sampaio-Barros**: None.

Abstract Number: 1408

When Damage and Disability Diverge: Unraveling Sex-Based Drivers of Axial Spondyloarthritis Burden

Claudia Marques[1], Gustavo Resende[2], **Carla Saad**[3], Adriana Marinho[4], Andressa Soares[5], Beatriz Paiva[6], Cleandro Pires[7], Débora Rodrigues[8], Glaucio Castro[9], Guilherme Bulbol[10], Jamile Carneiro[11], Manuella Ochtrop[12], José Mauro Fernandes[13], Maria Bernadete Gavi[14], Maria Eduarda Veiga[3], Michel Yazbek[15], Nara Cavalcanti[16], Natalia Machado[17], Olivio Malheiro[18], Rafael Bassara Macedo[19], Rejane Vieira[20], Ricardo Lage[18], Rita Menin[21], Rywka Golebiovski[22], Sandra Ribeiro[10], Thauana Oliveira[22], Valquiria Diniz[14], Percival Sampaio-Barros[23] and Marcelo Pinheiro[24], [1]Hospital das Clinicas - Universidade Federal de Pernambuco - UFPE, Recife, Pernambuco, Brazil, [2]Hospital das Clinicas UFMG, Belo Horizonte, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Fundação Hospital do Acre - AC, Rio Branco, Brazil, [5]Hospital Universitário da Universidade Federal de Santa Catarina (UFSC) - SC, Florianópolis, Brazil, [6]Faculdade de Medicina da Universidade Federal do Amazonas (UFAM) - AM, Manaus, Brazil, [7]UNB, Brasilia, Distrito Federal, Brazil, [8]Fundação Hospital do Acre -

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

AC, Rio Branco, Acre, Brazil, [9]Hospital Governador Celso Ramos (HCR) - SC, Florianópolis, Santa Catarina, Brazil, [10]Faculdade de Medicina da Universidade Federal do Amazonas (UFAM) - AM, Manaus, Amazonas, Brazil, [11]Hospital de Base do Distrito Federal (HBDF) - DF, Brasilia, Distrito Federal, Brazil, [12]Hospital Universitário Pedro Ernesto / UERJ - RJ, Rio de Janeiro, Rio de Janeiro, Brazil, [13]Universidade Federal do Maranhão (UFMA) - MA, São Luiz, Maranhao, Brazil, [14]Universidade Federal do Espírito Santo (UFES) - ES, Vitória, Espirito Santo, Brazil, [15]Universidade Estadual de Campinas (UNICAMP) - SP, Campinhas, Sao Paulo, Brazil, [16]Hospital das Clínicas da Universidade Federal de Pernambuco (UFPE) - PE, Recife, Pernambuco, Brazil, [17]Universidade Fedral do Paraná (UFPR) - PR, Curitiba, Parana, Brazil, [18]Hospital das Clínicas da Universidade Federal de Minas Gerais (UFMG) - MG, Belo Horizonte, Minas Gerais, Brazil, [19]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [20]Universidade Estadual do Ceará (UECE) - CE, Fortaleza, Ceara, Brazil, [21]Faculdade de Medicina de São José do Rio Preto (FAMERP) - SP, São José do Rio Preto, Sao Paulo, Brazil, [22]Escola Paulista de Medicina (EPM) - Universidade Federal de São Paulo (UNIFESP) - SP, São Paulo, Sao Paulo, Brazil, [23]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [24]UNIFESP/ EPM, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Sex differences in axial spondyloarthritis (axSpA) are well recognized, but their clinical consequences remain understudied in real-world settings. This study aimed to assess sex-based differences in demographic, clinical, functional, and treatment-related characteristics among patients with axSpA, and to explore sex-specific predictors of disease burden

Methods: Cross-sectional analysis of patients with axSpA enrolled in the Brazilian Registry of Spondyloarthritis (RBE), a multicenter, observational cohort involving 46 referral centers across Brazil. Eligible participants were adults diagnosed with SpA and classified according to ASAS criteria. Disease activity and impact were assessed using validated indices: BASDAI, ASDAS-CRP, BASFI, BASMI, ASQoL, and mSASSS. Sex-stratified multivariable linear regression models were developed to identify independent predictors of disease activity, function, mobility, and quality of life. Model assumptions and multicollinearity were evaluated, and results were expressed as unstandardized beta coefficients with 95% confidence intervals.

Results: A total of 828 patients were included: 568 (68.6%) males and 260 (31.4%) females, with a similar median age between groups (p = 0.351). Although HLA-B27 positivity has been more frequent in males (71.0% vs. 29.0%; p = 0.009), the family history of SpA was more frequently reported by females (26.2% vs. 17.2%; p = 0.002), as well as anxiety (18.6% vs. 9.6%; p< 0.001; OR 2.14), depression (18.2% vs. 5.8%; p< 0.001; OR 3.58), and fibromyalgia (23.0% vs. 5.8%; p< 0.001; OR 4.80). Figure 1 illustrates significantly higher scores of BASDAI, ASDAS-CRP, BASFI, and ASQoL in women, while men had worse BASMI. Correlation matrices showed stronger associations between patient-reported outcomes in women and a stronger mSASSS–BASMI correlation in men. Multivariable models revealed distinct sex-specific patterns. In women, functional limitation (BASFI) and patient global assessment were consistent predictors across outcomes. In men, disease burden was associated with root joint pain, enthesitis, comorbidities (fibromyalgia, depression), and work status. Complementary logistic regression identified fibromyalgia, depression, family history, and higher BASDAI as independent correlates of female sex, while HLA-B27 positivity, hip limitation, and higher BASMI were associated with male sex.

Conclusion: These findings highlight contrasting profiles of axSpA by sex: a predominantly functional and subjective burden in women, and a more structural axial damage and inflammatory phenotype in men. Tailored assessment strategies may improve disease evaluation and management in both groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

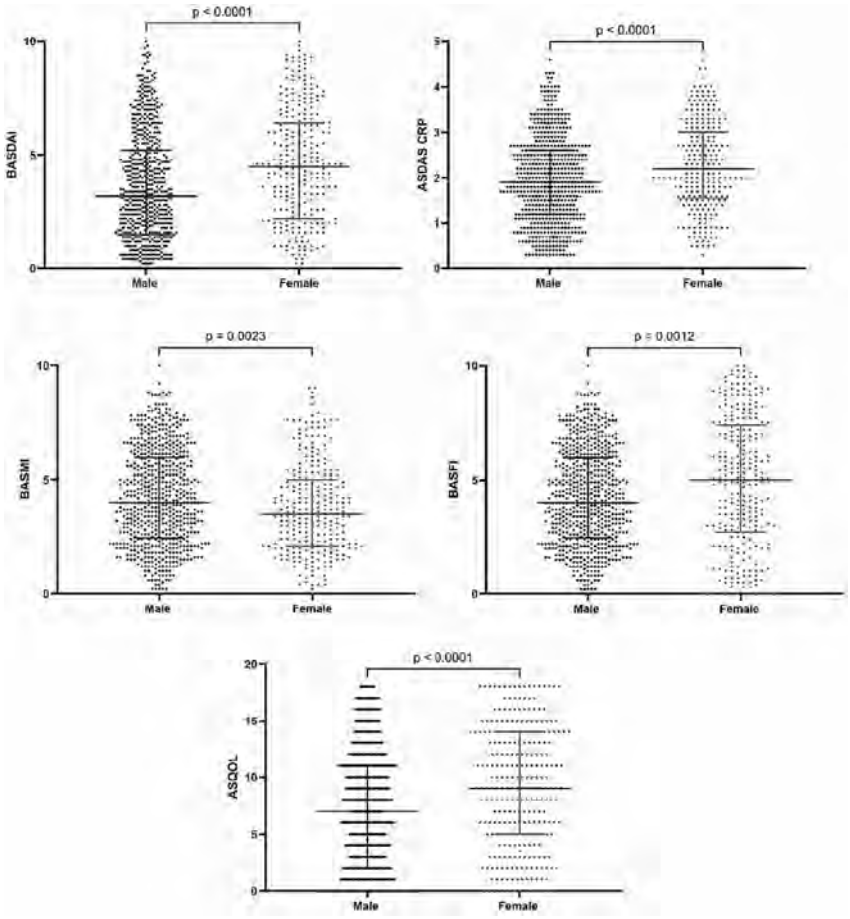


Figure 1. Sex-based comparison of disease activity, function, mobility, and quality of life in patients with axial spondyloarthritis

Disclosure: C. Marques: None; **G. Resende**: None; **C. Saad**: None; **A. Marinho**: None; **A. Soares**: None; **B. Paiva**: None; **C. Pires**: None; **D. Rodrigues**: None; **G. Castro**: None; **G. Bulbol**: None; **J. Carneiro**: None; **M. Ochtrop**: None; **J. Fernandes**: None; **M. Gavi**: None; **M. Veiga**: None; **M. Yazbek**: None; **N. Cavalcanti**: None; **N. Machado**: None; **O. Malheiro**: None; **R. Bassara Macedo**: None; **R. Vieira**: None; **R. Lage**: None; **R. Menin**: None; **R. Golebiovski**: None; **S. Ribeiro**: None; **T. Oliveira**: None; **V. Diniz**: None; **P. Sampaio-Barros**: None; **M. Pinheiro**: AbbVie/Abbott, 2, Johnson & Johnson, 2, UCB, 2.

Abstract Number: 1409

The impact of depression in axial spondyloarthritis: Epidemiological insights from the Ankylosing Spondylitis Registry of Ireland (ASRI)

Conall Mac Gearailt[1], Rebecca O'Farrell[2], Mohamed Eltahir[3], Brian Hallahan[3], Andrew Smyth[4], Finbar O'Shea[5] and Gillian Fitzgerald[3], [1]Galway University Hospital, Galway, Galway, Ireland, [2]Sligo University Hospital, Sligo, Ireland, [3]Galway University Hospital, Galway, Ireland, [4]University of Galway, Galway, Ireland, [5]St James's Hospital and Trinity College Dublin, Dublin, Dublin, Ireland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographics and clinical characteristics

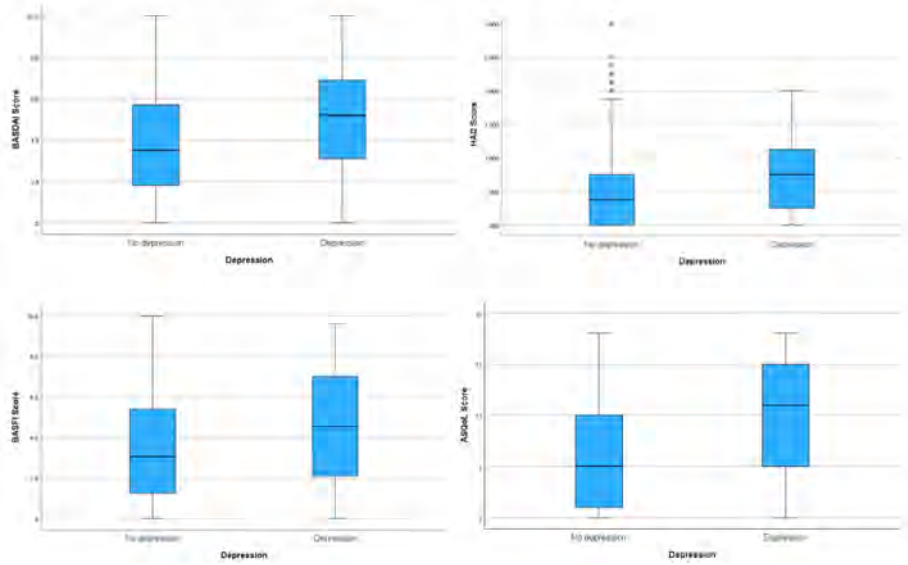
Demographics	
Total Participants	914
Age, Mean (SD)	45.85 (12.63)
Year born, n (%)	
• 1930-1949	63 (6.9)
• 1950-1959	130 (14.2)
• 1960-1969	219 (24)
• 1970-1979	257 (28.1)
• 1980-1989	196 (21.4)
• 1990-	49 (5.4)
Caucasian, n (%)	885 (96.8)
Male, n (%)	687 (75.2)
Ever Smoker, n (%)	527 (57.5)
HLA B27 positive, n (%)	631 (68.8)
Psoriasis, n (%)	150 (16.4)
Inflammatory Bowel Disease, n (%)	96 (10.5)
Uveitis, n (%)	308 (33.7%)
Dactylitis, n (%)	60 (6.6%)
Peripheral arthritis, n (%)	276 (30.2)
Enthesitis, n (%)	162 (17.7)
Disease Characteristics	
Disease Duration, median (25^{th},75^{th})	20.89 (10.25, 25)
Delay to diagnosis (25^{th},75^{th})	5.0 (2.0, 11.0)
Patient Reported Outcomes	
BASDAI, mean (SD)	4.0 (2.4)
BASFI, mean (SD)	3.6 (2.6)
HAQ, median (25^{th}, 75^{th})	0.4 (0.0,0.8)
ASQoL, mean (SD)	6.1 (5.0)

Background/Purpose: The burden of comorbidities in Axial Spondyloarthritis (axSpA) is increasingly recognised and contributes to the concept of difficult-to-treat axSpA (D2T-axSpA). The need to assess for non-inflammatory causes of uncontrolled disease is vital. We aim to characterise the prevalence and impact of depression in an Irish axSpA cohort.

Methods: The Ankylosing Spondylitis Registry of Ireland is a well-established observational multi-centre study of clinically diagnosed axSpA patients in Ireland. This study was conducted within the framework of ASRI. Depression was identified using a participant-reported physician-confirmed diagnosis.

Comorbidities and medication history were compiled using structured interviews. Validated outcome measures including Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Health Assessment Questionnaire (HAQ), Bath Ankylosing Spondylitis Functional Index (BASFI) and Ankylosing Spondylitis Quality of Life (ASQoL) scale were recorded.

Figure 1. Association between depression and disease activity



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: At analysis, 914 participants were enrolled in the registry (75.3% male, mean age 45.85). Basic demographics are available at Table 1. In total, depression was reported in 94 (10.3%) participants. A significant association between age group and depression (p=0.049) was observed, with higher prevalence in older cohorts.

Participants with comorbid depression had a higher prevalence of peripheral manifestations of axSpA compared to their peers without depression: peripheral arthritis was more common in those with depression (42.9% vs 29.6% without depression; p< 0.01); 27.5% of patients with depression had enthesitis vs 16.8% of those without depression (p< 0.01); psoriasis was present in 25.3% of cases with depression vs 15.7% of those without depression (p=0.02). No differences were found in dactylitis (6.6% in both groups; p=0.60) or inflammatory bowel disease (13.3% vs 10.4%; p=0.24). No statistical difference between genders was seen when assessing depression in this cohort (11.1% male vs 13% female, p=0.59).

Participants with depression had significantly (p< 0.001) higher disease activity scores compared to those without, including BASDAI (5.04 vs 3.81), HAQ (0.76 vs 0.49), BASFI (4.56 vs 3.46) and ASQoL (9.93 vs 6.07) (Figure 1). Unemployment status also differed significantly (p< 0.01) between those with (28.7%) and without depression (16.6%). Depression was also more prevalent in homemakers (13.8% vs 4.9%; p< 0.01).

Conclusion: In an Irish axSpA cohort, depression is a prominent factor affecting approximately 1 in 10 participants. Depression is significantly associated with higher disease activity, poorer functional status, and increased peripheral manifestations indicating a greater burden of disease in these patients.

Disclosure: C. Mac Gearailt: AbbVie/Abbott, 12, Support to attend conference, Celltrion, 12, Support to attend conference, Pfizer, 12, Support to attend conference; **R. O'Farrell**: None; **M. Eltahir**: Novartis, 12, Support to attend conference; **B. Hallahan**: None; **A. Smyth**: None; **F. O'Shea**: None; **G. Fitzgerald**: None.

Abstract Number: 1410

Examining the Interchangeability of Two Different Patient-Reported Global Assessment Measures in an Observational Axial Spondyloarthritis Cohort

Connor Vershel[1], Mark Hwang[2], John Reveille[3], Seokhun Kim[4], Matthew A. Brown[5], Michael Weisman[6], Mariko Ishimori[6] and Michael Ward[7], [1]Department of Internal Medicine, Division of Rheumatology, John P. and Katherine G. McGovern School of Medicine at the University of Texas Health Science Center at Houston, Houston, TX, [2]UTHealth Houston, Houston, TX, [3]Department of Medicine, University of Texas Medical Center, Houston, TX, [4]UTHealth Houston, Houston, [5]Genomics England, London, United Kingdom, [6]Cedars-Sinai Medical Center, LOS ANGELES, CA, [7]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, US Department of Health and Human Services, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: In axial spondyloarthritis cohorts, patient reported outcomes are vital for tracking disease progression and response to therapy. However, many cohorts enrolled prior to the development and validation of the ASDAS-CRP as a generally accepted standard measurement of disease activity. Our goal is to formally assess if patient global assessment (PGA) activity prior to ASDAS can be used when the modern questionnaire is unavailable.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

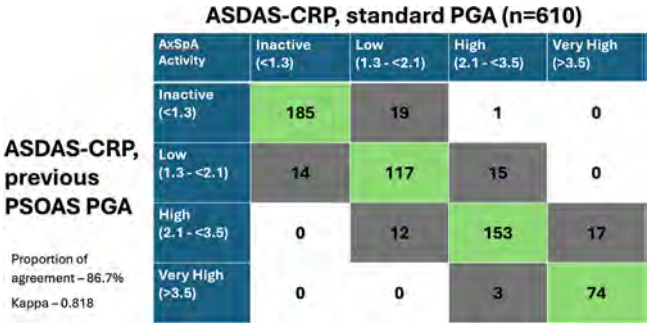


Figure 1. Agreement table comparing ASDAS-CRP calculated with the previous PSOAS PGA measure and the ASDAS-CRP with standard PGA, including weighted Cohen's kappa coefficient.

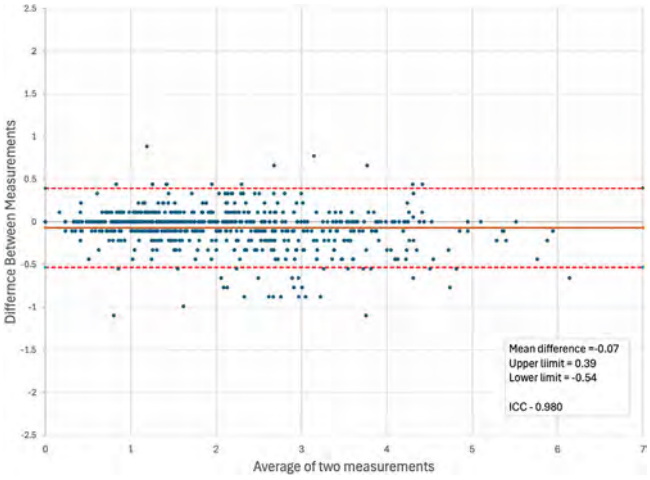


Figure 2. Bland-Altman Plot assessing agreement between ASDAS-CRP calculated with the previous PSOAS PGA measure and the ASDAS-CRP with standard PGA.

Methods: Data from the Prospective Study of Outcomes in Ankylosing Spondylitis (PSOAS) observational cohort were analyzed. Patients met Modified New York (mNY) criteria for AS and assessed their global disease activity during study visits. Before the development of ASDAS-CRP, global disease activity was rated on a numeric rating scale with the prompt: "Considering all the ways that your ankylosing spondylitis affects you, rate how you are doing." The currently used ASDAS global prompt instead asks: "How active was your spondylitis on average during the last week?"

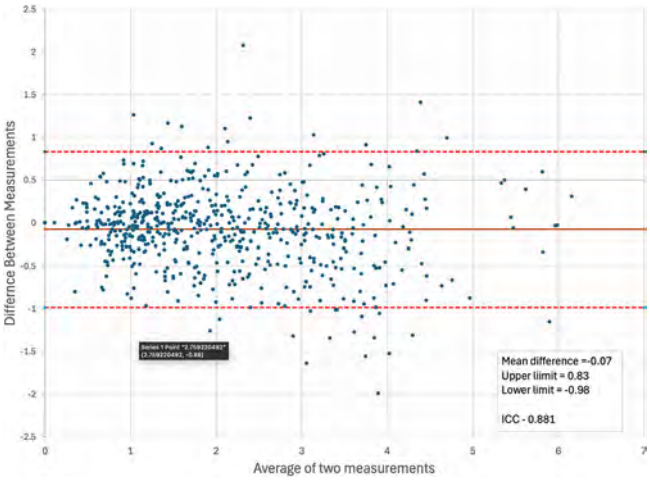


Figure 3. Bland-Altman plot assessing agreement between ASDAS-ESR and ASDAS-CRP

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We analyzed patients with visits that included both the older global score and the ASDAS global score to assess agreement between the two measures; ASDAS-CRP was calculated using both the older global assessment compared to the standard ASDAS global assessment. We also compared the standard ASDAS-CRP and ASDAS-ESR. We compared ASDAS disease activity categories between the comparisons and calculated weighted Cohen's Kappa coefficients. We also compared the older vs. newer global single-item scores with intraclass correlation coefficients (ICC) to evaluate agreement.

Results: 610 unique patient visits were analyzed. The proportion of agreement of ASDAS-CRP calculated with the old PGA compared to the newer PGA was 86.7% based on disease activity categories with Cohen's Kappa Coefficient of 0.818 (values of 0.81 – 1.00 are considered perfect agreement). The ICC was calculated using a two-way random effects model and was 0.980, consistent with excellent agreement. In other studies, the proportion of agreement of ASDAS-CRP to ASDAS-ESR has been calculated based on disease severity categories. In our study, this proportion was 72.6% with Kappa Coefficient of 0.62, which is similar to other studies.

Conclusion: Prior measures of PGA utilized before the validation of ASDAS-CRP are a valid substitution for the PGA in the ASDAS-CRP based on calculation of a Kappa Coefficient showing perfect agreement. This is important in scenarios where investigators are calculating the ASDAS-CRP in patients who were a part of observational cohorts prior to its development.

Disclosure: C. Vershel: None; **M. Hwang**: None; **J. Reveille**: Surf Therapeutics, 5; **S. Kim**: None; **M. Brown**: Clementia, 2, Grey Wolf Therapeutics, 2, Incyte, 2, Ipsen, 2, Novartis, 6, Pfizer, 2, 6, Regeneron, 2, UCB, 5, Xinthera, 2; **M. Weisman**: Spyre Therapeutics, 1, 2; **M. Ishimori**: None; **M. Ward**: Advanced Clinical LLC, 2, KSQ therapeutics, 2.

Abstract Number: 1411

Defining Minimal Disease Activity (MDA) in Psoriatic Arthritis (PsA) with the inclusion of Psoriatic Arthritis Impact of Disease (PsAID) scores rather than Health Assessment Questionnaire (HAQ)

Conor Coyle[1], Sarah Yazji[2], Sruthi Murthy[3], Philip Helliwell[4], Andra Balanescu[5], Juan Cañete[6], Emmanuelle Dernis[7], Uta Kiltz[8], Ying Ying Leung[9], Ana-Maria Orbai[10], PENELOPE PALOMINOS[11], Josef Smolen[12], Maarten de Wit[13], Laure Gossec[14] and Laura Coates[15], [1]Oxford University Hospitals, Reading, United Kingdom, [2]South Texas Health System GME Consortium, Texas A&M College of Medicine, Texas, USA, College Station, TX, [3]Oxford University Hospitals NHS Foundation Trust, Oxford, UK, Oxford, United Kingdom, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK, Leeds, United Kingdom, [5]UNIVERSITY OF MEDICINE AND PHARMACY CAROL DAVILA, Bucharest, Romania, [6]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [7]Rheumatology Department, Le Mans Central Hospital, Le Mans, France, LE MANS, France, [8]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [9]Rheumatology Department, Singapore General Hospital, Singapore, Singapore, Singapore, Singapore, [10]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [11]Hospital Lifeplus Litoral Norte, Xangri-lá, Brazil, Porto Alegre, Rio Grande do Sul, Brazil, [12]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria, Vienna, Austria, [13]Patient Research Partner, Stichting Tools, Amsterdam, Netherlands, [14]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [15]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

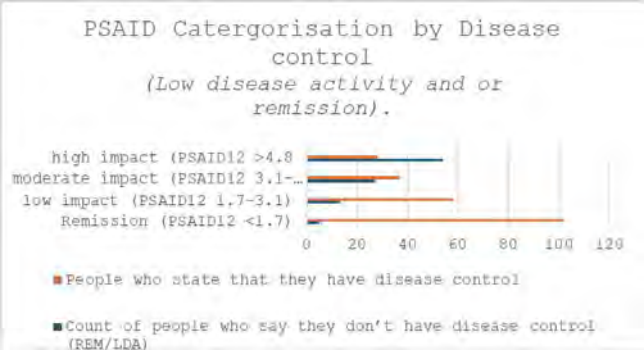


Figure 1: Patient REM/LDA compared to PsAID categories

Table 1: Sensitivity, specificity, PPV and NPV for each MDA definition using Patient REM/LDA as a gold standard

	Patient REM/LDA n=308	Standard MDA-HAQ	MDA-PsAIDrem	MDA-PsAIDlow
All patients n=308	Sensitivity	67.1	58.1	66.2
	Specificity	79.7	86.5	82.4
	Positive predictive value	91.3	93.2	92.3
	Negative predictive value	43.4	39.5	43.6
Patients over 65 years n=51	Sensitivity	63.4	56.1	68.3
	Specificity	80.0	90.0	80.0
	Positive predictive value	92.9	95.8	93.3
	Negative predictive value	34.8	33.3	38.1

Background/Purpose: Treat to target management is recommended in psoriatic arthritis (PsA) to improve disease control and patient quality of life. Minimal disease activity (MDA) criteria for PsA are a recommended target for treatment. However, the criteria include the health assessment questionnaire (HAQ) which may not always align or be responsive to changes in disease activity or accurately represent disease activity in older patients.

We aimed to test if the new PsA impact of disease (PsAID) score categories of remission and low impact can be used as an alternative item within the MDA criteria and whether this may better reflect patient opinion of disease remission/ Low disease activity (REM/LDA) than the HAQ.

Methods: A post-hoc analysis of data from the Remission/Flare in PsA (ReFlaP) study utilised real world data from adults with PsA for >2 years (NCT03119805). Data included HAQ, PSAID, and patient self-assessment of REM/LDA at clinic visits in 14 countries between 2017-2019. Patients with missing MDA/PsAID/REM data were excluded.

Patients were classified as meeting MDA (5/7 items) and very low disease activity (VLDA; 7/7 items) using either HAQ< 0.5 or PsAID thresholds. PsAID12 was categorised as REM < 1.7; Low impact 1.7-3.1; Moderate impact >3.1-4.8; high impact >4.8. Analysis included summary statistics and chi-squared analysis for categorical variables (p for significance < 0.01) and was performed in SPSS v 30.0.

Results: A total of 308 (164 M, 144 F) patients were included in the analysis (median age 53, IQR 43, 61). 171 were receiving biologic medication and 186 conventional DMARDs. At the baseline visit 234 (131M, 103F) patients reported that they felt that they were in REM/LDA. At baseline, using PSAID12 cut-offs, 126 were in remission and 65 in low impact. 94.4% of those in PsAID remission and 80.0% of those in low impact self-reported that they identified that they were in REM/LDA (figure 1).

There was a significant correlation at both visits between PSAID12 and HAQ scores and good agreement between MDA using HAQ as an item and MDA using PsAID as an item (89.0% for PsAID-rem and 91.0 for PsAID-low). Using the standard MDA-HAQ as a reference, MDA-PsAIDrem and MDA-PsAIDlow had sensitivity 82.6% and 90.7% and specificity was 97.1% and 91.2%.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Using patient reported REM/LDA as a gold standard, sensitivity, specificity, positive and negative predictive values were calculated for all the patients and separately for those over 65 years of age (table 1).

Conclusion: Patient perspective on disease severity is an important variable which is challenging to quantify. Using PsAID remission/low impact (≤3.1) instead of HAQ≤0.5 within the MDA showed very good agreement with a standard MDA assessment. The different MDA definitions showed similar agreement with patient opinion of REM/LDA in the full population.

We propose that PSAID12 category of remission/LDA (< 3.1) could be used as an alternative to HAQ< 0.5 in the MDA criteria and may correlate slightly better with patient opinion in those over 65 years old.

Disclosure: C. Coyle: None; **S. Yazji**: None; **S. Murthy**: None; **P. Helliwell**: None; **A. Balanescu**: AbbVie/Abbott, 1, 6, Amgen, 2, 6, Angellini, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Ewopharma, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sobi, 2, 6, Stada, 2, 6, Theramex, 6, UCB, 2, 6; **J. Cañete**: None; **E. Dernis**: None; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **Y. Leung**: None; **A. Orbai**: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB, 2; **P. PALOMINOS**: None; **J. Smolen**: None; **M. de Wit**: Celgene, 2, Eli Lilly, 2, Janssen-Cilag, 2, Pfizer, 2, UCB, 2; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1412

Classification of sacroiliits using an artificial intelligence model

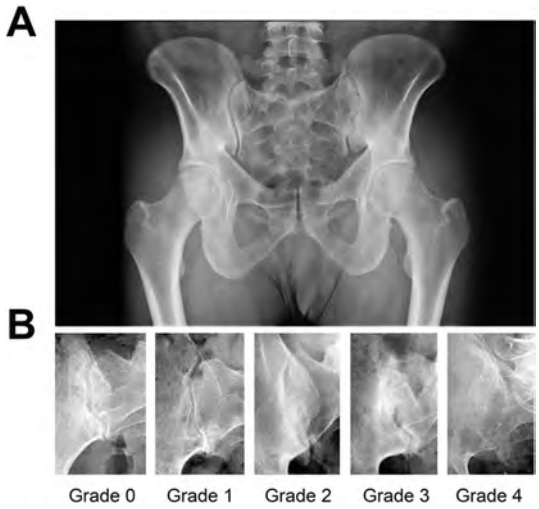
Esther Fernández Guill[1], Yazmina Bautista Mártir[2], Eduardo Fernández Jover[3] and Irene Cases Susarte[4], [1]Sociedad Española de Reumatologia, Murcia, Spain, [2]Sociedad Española de Medicina de Familia, Murcia, Spain, [3]Universidad Miguel Hernandez, Alicante, Spain, [4]Sociedad Española de Radiologia, Murcia, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial Spondyloarthritis (axSpA) is a chronic inflammatory disease that mainly involvessacroiliac joints and spine. It is caused by ankylosing spondylitis and other rheumatic diseases and affects mostly young adults, leading to a decreased quality of life and complications if not diagnosed promptly. Conventional radiographs of sacroiliac joints are the first imaging technique in patients with suspected axSpA. However, the diagnosis of sacroiliitis remains subject to significant intrapersonal and interpersonal variation, especially in the early stages. The ability to identify meaningful patterns in large data sets makes machine learning very attractive for screening of diseases such as axSpA.

The objective is to To develop and validate a new approach based on artificial intelligence techniques for the automatic classification of the grade of sacroiliitis on conventional radiographs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Examples of pelvic X-rays. A. Normal X-ray. B. Imaging representation of sacroiliitis according to the New York criteria.

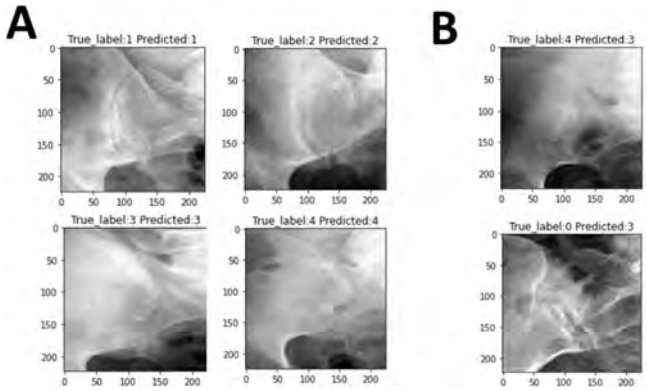


Figure 2. Examples of correct (A) and incorrect (B) results.

class	precision	recall	f1-score	support(samples)
0	0.68	0.50	0.58	30
1	0.29	0.15	0.20	13
2	0.42	0.70	0.53	27
3	0.32	0.35	0.33	20
4	0.64	0.41	0.50	17
metric avg	0.47	0.42	0.43	107
weighted avg	0.49	0.47	0.46	107

Results using a single XGBoost model to fit the sacroiliitis dataset.

class	precision	recall	f1-score	support(samples)
0	0.64	0.60	0.62	30
1	0.00	0.00	0.00	13
2	0.47	0.63	0.54	27
3	0.58	0.70	0.64	20
4	0.80	0.71	0.75	17
metric avg	0.50	0.53	0.51	107
weighted avg	0.54	0.57	0.55	107

Results using a combined CNN-XGBoost model to fit the sacroiliitis dataset.

Figure 3. Above initial results using a single XGBoost model to fit the sacroiliitis dataset. Below final results using a combined CNN-XGBoost model to fit the sacroiliitis dataset

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We included 267 X-ray images of patients with clinical suggestion of axSpA. Images were reviewed by 3 rheumatologists and 1 radiologist who graded the severity of sacroiliitis according to the New York criteria (Figure 1 and 2). We performed some pre processing steps using Fiji, median filter, manual adjustment and data augmentation. For model training we used 10-fold stratified cross-validation. Grayscales images were expanded to 3 identical channels and images were resized for the ResNet50, EfficientNetV2S and Xception Backbones. At first we used transfer learning technique by combining a base CNN model as feature extractor, with a top dense stack customized. For the base model, several flavors of Resnet, EfficienNet and Inception architectures were used, besides a custom designed CNN core for basic comparison. We also used XGBoost.

Results: First results were disappointing (Figure 3). To improve performance, we used the XGBoost ensemble learning combined with CNN based onResNet50 architecture. We kept the convolutional kernel, and eliminated the top classifier. A tensor of shape was used as the input for the XGBoost model. After grid search for optimizing XGBoost, we obtained an accuracy of 57% (Figure 3) Therefore, we found that the sensitivity (recall) for all classes was over 60%, except for Class 1 which was misclassified.

Conclusion: -Our trained model successfully detected the grade of sacroiliitis with an accuracy over 60 %.-With further improvement and validation this approach could be helpful to aid the detection and classification of radiographic sacroiliitis

Disclosure: E. Fernández Guill: None; **Y. Bautista Mártir**: None; **E. Fernández Jover**: None; **I. Cases Susarte**: None.

Abstract Number: 1413

Restless Legs Syndrome in Patients with Psoriatic Arthritis: Association with Inflammatory, Clinical Parameters, and Comorbidities

Esther Toledano[1], Carlos Villegas[2], Carolina Cristina Chacón[3], Cristina Hidalgo Calleja[3], Belén Miguel[3], Laura Blanco[3], Ana Turrión[4], Olga Compán[5], Manuel Martín[4], Susana Gómez[3] and Carlos Montilla[3], [1]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Spain, [2]Faculty of Medicine, University of Salamanca, Salamanca, Spain, [3]Rheumatology Service, University Hospital of Salamanca, Salamanca, Castilla y Leon, Spain, [4]Rheumatology Service, University Hospital of Salamanca, Salamanca, Spain, [5]Rheumatology Service, University Hospital of Salamanca, Carbajosa de la Sagrada, 37191, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Restless legs syndrome (RLS) is a chronic neurological disorder associated with brain iron metabolism. Although RLS has been linked to various immune-mediated inflammatory diseases, such as psoriatic arthritis (PsA), little is known about the influence of inflammation on this association or the impact of RLS on disease activity, disease burden, and other comorbidities. The objective is to evaluate the prevalence of restless legs syndrome (RLS) in patients with psoriatic arthritis (PsA) and its association with clinical, inflammatory, functional characteristics, and comorbidities.

Methods: This is a cross-sectional observational study including 230 PsA patients. RLS screening was performed using the International Restless Legs Syndrome Study Group questionnaire, with diagnostic confirmation by a neurologist. Demographic data, disease activity (measured by DAPSA), functionality (measured by HAQ), disease impact (measured by PsAID), and comorbidities (anxiety, depression, sleep quality, obesity, and fibromyalgia) were collected.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variable	All (n= 230)	RLS (n=46)	No RLS (n= 184)	p
Age, years	54.6 ± 11.3	51.3 ± 11.9	53.4 ± 11.2	0.2
Sex (woman/man)	104/126	24/22	80/104	0.2
Time since onset (years)	8 (9)	8 (9)	10 (10)	0.9
Smoking status, N (%)				
Smoker (current or former)	166 (72)	33 (72)	133 (72)	0.9
Never smoker	64 (28)	13 (28)	51 (28)	
Smoking, pack-years	12.9 ± 20	18.0 ± 18.6	14.5 ± 9.2	0.3
Iron	87.0 (43)	88.0 (42)	87.0 (43)	0.8
Ferritin	124.0 (164)	92 (135)	96 (168)	0.2
Transferrin saturation	27.2 (13.9)	27.5 (14.4)	26.9 (13.7)	0.6
Total iron binding capacity	325 (66)	316 (47)	328 (65)	0.07
Creatinine	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.6
csDMARDs (N/%)	170 (74)	36 (78)	134 (73)	0.7
Methotrexate	129 (56)	29 (63)	100 (54)	
Sulfasalazine	32 (14)	5 (11)	27 (15)	
Leflunomide	9 (4)	2 (4)	7 (4)	
tsDMARDs or bDMARDs, N (%)	64 (29)	16 (25)	48 (28)	
TNFi	47 (17)	11 (14)	36 (19)	
Secukinumab	10 (7)	2 (8)	8 (6)	
Ustekinumab	3 (1)	2 (1)	1 (2)	0.8
Tofacitinib	3 (2)	2 (3)	1 (1)	
Apremilast	2 (1)	0	2 (1)	
Failure of tsDMARDs or bDMARDs, N (%)	28 (12)	16 (17)	12 (11)	0.2
Clinical presentation, N (%)				
Peripheral	194 (85)	37 (80)	157 (85)	0.6
Mixed	30 (12)	7 (15)	23 (13)	
Axial	6 (3)	2 (5)	4 (2)	
Dactylitis (yes/no) (%)	36/194 (15)	3/43 (6)	33/151 (18)	0.07
mMASES	1.4 ± 2.4	1.8 ± 2.5	1.3 ± 2.3	0.2
PASI	1.8 ± 2.6	1.7 ± 2.2	1.8 ± 2.7	0.9
PsAID (Item 3)	4,0 ± 3.0	5,7 ± 2.1	3.6 ± 2.9	0.001
FACIT-F	38.0 (16)	30.5 (21)	39.0 (13)	0.001

Abbreviations: bDMARD: Biologic Disease-Modifying Antirheumatic Drug; csDMARD: Conventional Synthetic Disease-Modifying Antirheumatic Drug; FACIT-F: *Functional Assessment of Chronic Illness Therapy*; mMASES: Modified Maastricht Ankylosing Spondylitis Enthesitis Score; n: Number; PASI: *Psoriasis Area Severity Index*; SD: Standard Deviation; PSAID: *Psoriatic Arthritis Impact of Disease*; TNFi: Tumor Necrosis Factor Inhibitor; tsDMARD: Targeted Synthetic Disease-Modifying Antirheumatic Drug.

Results: RLS was confirmed in 46 patients (20%). Patients with RLS showed a higher frequency of polyarthritis (27% vs. 6%; p< 0.001), a greater number of swollen joints (2.0 vs. 1.4; p=0.04), increased fatigue (p< 0.001), higher disease activity (p< 0.001), greater disease impact (p< 0.001), and poorer functionality (p=0.01). RLS was associated with higher rates of anxiety, depression, and poor sleep quality (all p< 0.001).

In the regression analysis, polyarthritis (OR: 1.03; 95% CI: 1.00–1.9; p=0.04) and skin problems (OR: 1.4; 95% CI: 1.03–2.0; p=0.03) were significantly associated with the presence of RLS.

Conclusion: RLS is common in patients with PsA and is associated with poorer functionality, higher disease burden, increased fatigue, anxiety, depression, and worse sleep quality. Inflammation and psoriasis-related symptoms could be related to the presence of RLS in these patients.

Disclosure: E. Toledano: None; **C. Villegas**: None; **C. Chacón**: None; **C. Hidalgo Calleja**: None; **B. Miguel**: None; **L. Blanco**: None; **A. Turrión**: None; **O. Compán**: None; **M. Martín**: None; **S. Gómez**: None; **C. Montilla**: None.

Abstract Number: 1414

Multidimensional Assessment to Differentiate Early Psoriatic Arthritis from Cutaneous Psoriasis

Eugeniu Russu[1], Victor Cazac[2], Mircea Betiu[3], Alesea Nistor[3] and Liliana Groppa[4], [1]"Nicolae Testemitanu" State Medical and Pharmaceutical University; "Timofei Moşneaga" Republican Clinical Hospital, Chisinau, Moldova, [2]Norwalk Hospital, Nuvance Health, Connecticut, [3]State Medical and Pharmaceutical University "Nicolae Testemițanu", Chisinau, Chisinau, Moldova, [4]State Medical and Pharmaceutical University "Nicolae Testemițanu", Chisinau, Moldova

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) develops in ∼20-30% of psoriasis patients. However, early PsA diagnosis is challenging due to heterogeneous, subtle symptoms and overlap with psoriasis without arthritis (PsO). Even a brief diagnostic delay (∼6 months) can lead to joint erosions and functional decline. We aimed to address this unmet need by identifying early clinical/imaging markers and developing a composite index for timely PsA detection.

Methods: We analyzed a retrospective case-control dataset (2014-2022) of 100 early PsA patients (≤2-year duration) and 100 psoriasis-only controls. All subjects underwent standardized clinical evaluation of tender/swollen joint counts (TJC, SJC), morning stiffness, enthesitis, and dactylitis, non-specific inflammatory biomarkers (ESR and CRP) along with musculoskeletal ultrasound and MRI imaging. A composite index (φAPs) was derived using multivariate logistic regression to integrate significant clinical and imaging predictors. Model performance (sensitivity, specificity, ROC area) was assessed and internally validated via bootstrap resampling.

Results: Early PsA patients demonstrated significantly elevated inflammatory activity compared to PsO controls. The mean TJC was 7.5±0.5 in early PsA vs 2.2±0.5 in PsO (p=0.0032), and the SJC was 4.5±0.3 vs 2.9±0.7 (p=0.0057), respectively. Morning stiffness duration was markedly longer in early PsA (37.7±5.5 minutes vs 10.2±4.5 minutes, $p< 0.001$). Enthesitis was present in 78% of PsA cases vs 31% in PsO (p=0.00023). Dactylitis affected 65.6% of early PsA patients, compared to 9% in PsO ($p< 0.001$), predominantly involving toes II–IV and fingers IV–V.

Non-specific inflammatory biomarkers (ESR and CRP) were significantly elevated in early PsA: mean ESR was 37.8 ±2.4 mm/h vs 15.2±2.1 mm/h (p=0.0071); CRP was 36.25±2.23 mg/L vs 8.12±3.14 mg/L (p=0.0056). MRI detected tenosynovitis in 89.3% and early bone erosions in 40.4% of cases. Power Doppler ultrasonography identified active synovial proliferation in 91.7% and entheseal changes in key anatomical locations.

The composite predictive model (φAPs), which integrates clinical and laboratory variables, demonstrated a sensitivity of 89% and specificity of 84% for early PsA identification. ROC curve analysis yielded an AUC of 0.91. Internal validation by 1,000 bootstrap replicates confirmed model robustness. In subgroup PsA analyses, φPsA values ≥2.3 correlated with confirmed early PsA in 92% of cases, while values < 1.8 excluded PsA in 95%. The most informative variables contributing to the model were dactylitis, enthesitis, and CRP elevation.

Conclusion: This composite clinical-imaging model greatly enhances early PsA recognition in psoriasis patients, enabling earlier intervention to prevent irreversible joint damage. By incorporating hallmark features like enthesitis and dactylitis, it helps clinicians distinguish incipient PsA from psoriasis alone at the earliest stages. External validation is underway to establish the φAPs index as a practical tool that improves clinical decision-making and patient outcomes.

Disclosure: E. Russu: None; **V. Cazac**: None; **M. Betiu**: None; **A. Nistor**: None; **L. Groppa**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1415

The Association of Handedness with Radiographic Damage in Patients with Psoriatic Arthritis

Fadi Kharouf[1], Shahad Al-Matar[2], Virginia Carrizo Abarza[3], Pankti Mehta[4], Shangyi Gao[5], Daniel Pereira[6], Richard Cook[7], Vinod Chandran[8], Denis Poddubnyy[9] and Dafna D. Gladman[10], [1]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [2]University of alberta, Edmonton, AB, Canada, [3]Toronto Western Hospital - University of Toronto, Toronto, ON, Canada, [4]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [5]Gladman-Krembil Psoriatic Arthritis Research Program, Centre for Prognosis Studies in the Rheumatic Diseases, Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, Toronto, ON, Canada, [6]University Health Network, Toronto, ON, Canada, [7]University of Waterloo, Waterloo, Canada, [8]University of Toronto, Toronto, ON, Canada, [9]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [10]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Mechanical stress is known to trigger and exacerbate psoriatic arthritis (PsA). Based on the hypothesis that biomechanical stress is greater in the dominant extremity, we aimed to investigate the association between handedness and radiographic damage in PsA.

Table 1. Baseline characteristics (clinic entry).

Variable	Overall (n=359)	Right-handed (n=324)	Left-handed (n=35)	p-value
Demographic features				
Age in years, mean (SD)	43.7 (12.9)	43.2 (12.7)	48.1 (13.8)	**0.03**
Sex (male), n (%)	204 (57.0)	185 (57.3)	19 (54.3)	0.87
Ethnicity White, n (%)	299 (84.7)	270 (84.6)	29 (85.3)	1.00
Duration of PsA in years, mean (SD)	4.8 (6.7)	4.6 (6.6)	6.4 (7.6)	0.15
Duration of PsC in years, mean (SD)	15.8 (14.0)	14.9 (13.2)	24.6 (17.7)	**<0.01**
BMI in kg/m², mean (SD)	28.3 (6.2)	28.0 (6.0)	30.8 (6.8)	**0.01**
Disease-related features				
SJC (0-66), median [IQR]	2.0 [0.0, 5.0]	1.5 [0.0, 3.6]	1.0 [0.0, 4.5]	0.71
Dactylitis, n (%)	97 (27.4)	90 (28.2)	7 (20.0)	0.40
Nail Disease, n (%)	209 (61.7)	183 (63.1)	17 (50.0)	0.19
PASI (0-72), median [IQR]	1.6 [0.0, 3.6]	1.6 [0.0, 3.6]	0.9 [0.0, 6.7]	0.97
DAPSA, median [IQR]	16.3 [8.7, 27.5]	16.3 [8.7, 26.0]	16.6 [9.2, 28.0]	0.70
mSS score, median [IQR]	0.0 [0.0, 7.0]	0.0 [0.0, 6.0]	2.0 [0.0, 12.5]	0.12
mSS on the right side, median [IQR]	0.0 [0.0, 4.0]	0.0 [0.0, 3.00]	2.0 [0.0, 6.0]	0.05
mSS on the right hand, median [IQR]	0.0 [0.0, 2.0]	0.0 [0.0, 2.0]	0.0 [0.0, 4.5]	0.11
mSS on the right foot, median [IQR]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 2.0]	0.07
mSS on the left side, median [IQR]	0.0 [0.0, 4.0]	0.0 [0.0, 3.0]	0.0 [0.0, 7.0]	0.12
mSS on the left hand, median [IQR]	0.0 [0.0, 2.0]	0.0 [0.0, 2.0]	0.0 [0.0, 5.5]	0.20
mSS on the left foot, median [IQR]	0.0 [0.0, 0.00]	0.0 [0.0, 0.0]	0.0 [0.0, 2.0]	0.23
Syndesmophytes and/or sacroiliitis, n (%)	92 (25.8)	74 (26.1)	6 (20.0)	0.61
Pharmacotherapy				
NSAIDs, n (%)	235 (65.5)	216 (66.7)	19 (54.3)	0.20
csDMARDs, n (%)	144 (40.1)	128 (39.5)	16 (45.7)	0.60
b/tsDMARDs, n (%)	50 (13.9)	45 (13.9)	5 (14.3)	1.00

PsA: Psoriatic Arthritis, PsC: Psoriasis, BMI: Body Mass Index, SJC: Swollen Joint Count, PASI: Psoriasis Area and Severity Index, DAPSA: Disease Activity in Psoriatic Arthritis, mSS: Modified Steinbrocker Score, NSAIDs: Non-Steroidal Anti-Inflammatory Drugs, csDMARDs: Conventional Synthetic Disease-Modifying Antirheumatic Drugs, b/tsDMARDs: Biologic or Targeted Synthetic DMARDs

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Linear mixed models analyzing the association between handedness and peripheral damage.

Variable*	Estimate	95% CI		p-value
Outcome: Total (four-limb) mSS				
Left-handedness	7.59	-0.88	16.07	0.08
Outcome: Total mSS in the hands				
Left handedness	6.34	0.24	12.44	**0.04**
Outcome: Total mSS in the feet				
Left handedness	1.30	-1.77	4.38	0.41
Outcome: Total right-sided mSS				
Left-handedness	3.82	-0.54	8.17	0.09
Outcome: Total left-sided mSS				
Left-handedness	3.79	-0.52	8.09	0.09
Outcome: Right-hand mSS				
Left-handedness	2.98	-0.17	6.13	0.07
Outcome: Left-hand mSS				
Left-handedness	3.37	0.25	6.48	**0.04**
Outcome: Right-foot mSS				
Left-handedness	0.87	-0.74	2.49	0.29
Outcome: Left-foot mSS				
Left-handedness	0.44	-1.12	2.00	0.58

CI, confidence interval; mSS, modified Steinbrocker score
*Models are adjusted for baseline age, psoriasis duration, and BMI

Methods: We included PsA patients from a prospective observational cohort. Handedness was determined by self-report of the writing hand. To assess the relationship between handedness and peripheral joint damage, we used linear mixed models (LMMs) with the modified Steinbrocker score (mSS) as the outcome. We studied the association of handedness with total mSS, total hand or foot mSS, single-sided mSS, and single-sided hand or foot mSS. As no known confounders exist between the exposure (handedness) and the outcome (radiographic damage), models were adjusted only for variables that were imbalanced between groups and are known to be associated with peripheral damage.

Results: Among 359 patients, 324 (90.3%) were right-handed and 35 (9.7%) were left-handed **(Table 1)**. At baseline (clinic entry), the mean (SD) age was 43.7 (12.9) years. Compared to right-handed individuals, left-handed patients were older, had longer psoriasis duration, and higher BMI. In LMMs adjusted for these variables **(Figure 1 and Table 2)**, left-handedness was associated with a trend toward higher total mSS (β = 7.59, 95% CI -0.88 to 16.07). A significant association was observed with higher total hand mSS (β = 6.34, 95% CI 0.24 to 12.22). Similar trends were seen in side-specific analyses: left-handedness was associated with higher mSS on both right and left sides (β = 3.82, 95% CI -0.54 to 8.17; β = 3.79, 95% CI -0.52 to 8.09, respectively). Notably, left-handedness was linked to significantly higher left-hand mSS (β = 3.37, 95% CI 0.25 to 6.48), whereas the association with right-hand mSS was weaker (β = 2.98, 95% CI -0.17 to 6.13). Associations with foot mSS—both unilateral and bilateral—were less pronounced.

Conclusion: In PsA, where right-handedness predominates, left-handed individuals appear to experience greater peripheral joint damage, particularly in the hands, with a stronger effect observed in the left hand. Mechanical stress from daily activities—shaped by tools and environments predominantly designed for right-handed individuals—may contribute to this pattern. Potential cross-laterality (e.g., left-handedness with right-foot dominance) may attenuate observed patterns of foot involvement.

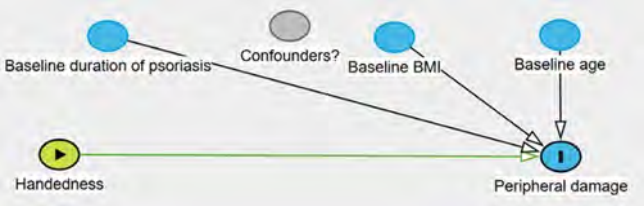


Figure 1. DAG showing the relationship between the exposure (handedness) and outcome (peripheral damage) in our model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: F. Kharouf: None; **S. Al-Matar**: None; **V. Carrizo Abarza**: None; **P. Mehta**: None; **S. Gao**: None; **D. Pereira**: None; **R. Cook**: None; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5.

Abstract Number: 1416

Structural Damage Progression in the Spine in Patients with Psoriatic Arthritis: Findings from a Longitudinal Cohort Study

Fadi Kharouf[1], Pankti Mehta[2], Virginia Carrizo Abarza[3], Shangyi Gao[4], Daniel Pereira[5], Dafna D. Gladman[6], Vinod Chandran[7] and Denis Poddubnyy[8], [1]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [2]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [3]Toronto Western Hospital - University of Toronto, Toronto, ON, Canada, [4]Gladman-Krembil Psoriatic Arthritis Research Program, Centre for Prognosis Studies in the Rheumatic Diseases, Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, Toronto, ON, Canada, [5]University Health Network, Toronto, ON, Canada, [6]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [7]University of Toronto, Toronto, ON, Canada, [8]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial involvement is one of the key features of psoriatic arthritis (PsA) and is associated with increased disease burden. However, rates and predictors of structural damage progression in the spine in PsA are not well defined. This study aimed to explore associations between factors reflecting activity and severity across PsA domains and the development and progression of structural damage in the spine in a large longitudinal cohort.

Methods: We analyzed patients from a prospective longitudinal PsA cohort. Axial damage was assessed using two outcomes: (1) syndesmophyte development (binary), and (2) modified Stoke Ankylosing Spondylitis Spine Score (mSASSS, continuous). Cox proportional hazards models were used for syndesmophyte development, and generalized estimating equation (GEE) models were used for mSASSS progression. Variables reflecting activity/severity included cDAPSA, swollen joint count (SJC), SPARCC enthesitis score, dactylitis, nail involvement, PASI, modified Steinbrocker score, radiographic sacroiliitis score (sum of grades on two sides; range 0-8), BASDAI, ESR, and CRP. Multivariable models were adjusted for potential confounders, including age, sex, PsA duration, BMI, smoking status, decade of observation, HLA-B*27, HLA-A*29 (known to be associated with a reduced risk of axial disease), radiographic sacroiliitis score (where appropriate), NSAID use, and biologic or targeted synthetic (b/ts) DMARD use.

Lastly, we conducted sensitivity analyses stratified by observation period (pre-2000 vs. 2000 and beyond).

Results: The study included 1584 patients with PsA, with a median age of 45 years [IQR: 34.3–54.7]. At baseline (clinic entry), 218 patients (13.8%) had syndesmophytes. The median mSASSS was 0 [IQR: 0–0], while the mean (SD) was 1.6 (6.2). Over the study follow-up period, 166 of the 922 individuals (18.0%) without syndesmophytes at baseline who had repeat spine X-rays developed syndesmophytes, with a median time to development of 5.8 years [IQR: 2.4, 9.9].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Univariable Cox and GEE Models for Syndesmophyte Development and mSASSS Progression.

	Syndesmophyte Development		mSASSS Progression	
Variable	**HR**	**95% CI**	**Estimate**	**95% CI**
Age in years (1-unit increase)	1.00	0.99–1.01	0.05	**0.02–0.07**
Sex (Reference: Female)	2.15	**1.55–2.98**	1.07	**0.53–1.61**
PsA duration in years (1-unit increase)	1.02	**1.004–1.04**	0.09	**0.04–0.13**
BMI in kg/m2 (1-unit increase)	1.03	**1.001–1.05**	0.01	-0.03–0.05
Smoking Status (Reference: Never smoker)				
Current	0.71	0.43–1.20	0.85	-0.12–1.82
Past	0.58	0.30–1.09	0.80	-0.19–1.78
Decade of Observation (Reference: 1978-1988)				
1989–1999	0.84	0.60–1.19	0.01	-0.61–0.62
2000–2010	0.26	**0.17–0.40**	0.38	-0.34–1.09
2011–2025	0.16	**0.08–0.33**	-0.41	-0.85–0.04
SJC (1-unit increase)	0.99	0.95–1.04	-0.03	-0.07–0.001
cDAPSA (1-unit increase)	0.95	0.89–1.01	0.13	-0.05–0.31
SPARCC Enthesitis Score (1-unit increase)	0.70	**0.52–0.93**	-0.07	**-0.13 – -0.02**
Dactylitis	1.78	**1.25–2.54**	-0.56	**-0.88 – -0.23**
PASI (1-unit increase)	1.01	0.99–1.03	0.06	-0.002–0.11
Nail Disease	1.91	**1.25–2.90**	-0.17	-0.76–0.41
Modified Steinbrocker Score (1-unit increase)	1.01	**1.01–1.014**	0.03	**0.01–0.05**
Radiographic Sacroiliitis Score* (1-unit increase)	1.16	**1.09–1.24**	0.66	**0.35–0.97**
BASDAI (1-unit increase)	1.09	0.87–1.38	-0.01	-0.16–0.14
ESR (1-unit increase)	1.01	**1.01–1.02**	0.00	-0.01–0.02
CRP (1-unit increase)	1.00	0.96–1.03	0.05	**0.002–0.10**
HLA-B*27	1.95	**1.37–2.78**	1.58	-0.28–3.44
HLA-A*29	0.59	0.30–1.18	-0.61	**-1.20 – -0.03**
NSAIDs	1.28	0.91–1.78	-0.33	-0.89–0.23
Biologic or targeted synthetic DMARDs	0.43	**0.25–0.72**	1.13	**0.16–2.10**

Abbreviations: HR: Hazard Ratio, CI: Confidence Interval, PsA: Psoriatic Arthritis, BMI: Body Mass Index, SJC: Swollen Joint Count, cDAPSA: Composite Disease Activity Index for Psoriatic Arthritis, SPARCC: Spondyloarthritis Research Consortium of Canada, PASI: Psoriasis Area and Severity Index, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ESR: Erythrocyte Sedimentation Rate, CRP: C-Reactive Protein, HLA: Human Leukocyte Antigen, NSAIDs: Non-Steroidal Anti-Inflammatory Drugs, DMARDs: Disease-Modifying Anti-Rheumatic Drugs. *Sum of the two sides (0-8)

Figure 1 shows a Kaplan-Meier curve of syndesmophyte-free survival, with the results of the univariable models shown in **Table 1**. In multivariable Cox models **(Figure 2A)**, higher ESR (HR 1.02, 95% CI 1.01–1.03) and radiographic sacroiliitis score (HR 1.19, 95% CI 1.07–1.32) were significantly associated with syndesmophyte development. In multivariable GEE

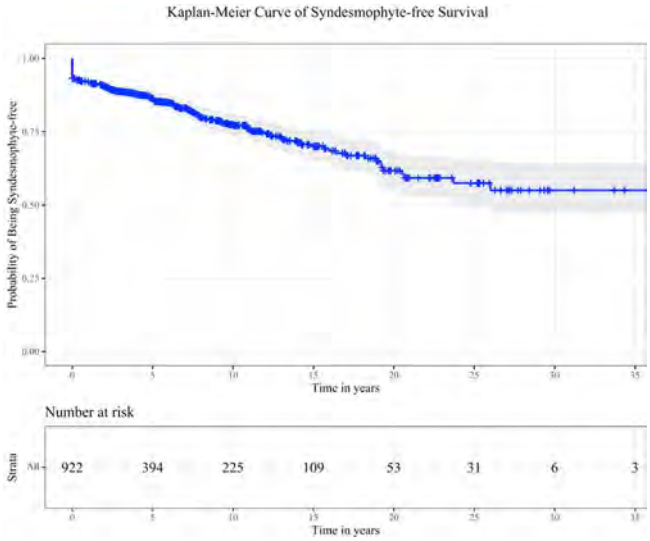


Figure 1. Kaplan–Meier survival analysis depicting the probability of remaining syndesmophyte-free over time.

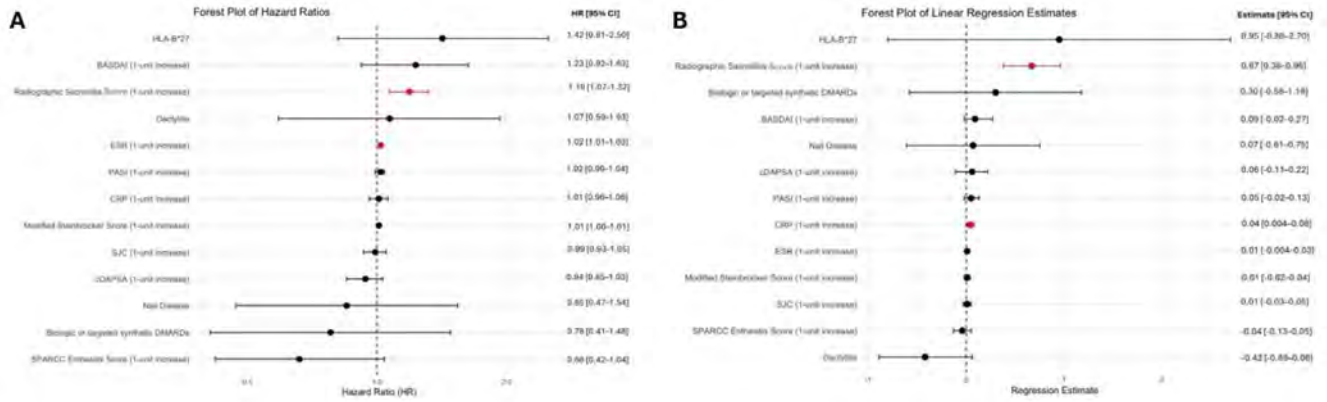


Figure 2. A: Multivariable Cox proportional hazards models identifying factors associated with syndesmophyte development in patients with psoriatic arthritis (PsA). B: Multivariable generalized estimating equation (GEE) models identifying factors associated with mSASSS progression among PsA patients. Abbreviations: HLA-B*27: Human Leukocyte Antigen B*27; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: Erythrocyte Sedimentation Rate; PASI: Psoriasis Area and Severity Index; CRP: C-Reactive Protein; SJC: Swollen Joint Count; cDAPSA: Clinical Disease Activity Index for Psoriatic Arthritis; DMARDs: Disease-Modifying Antirheumatic Drugs; SPARCC: Spondyloarthritis Research Consortium of Canada.

models **(Figure 2B)**, higher CRP (estimate 0.04, 95% CI 0.004–0.08) and sacroiliitis score (estimate 0.70, 95% CI 0.40–1.00) were associated with mSASSS progression. Sensitivity analyses confirmed consistent findings across observation periods.

Conclusion: Systemic inflammation, reflected by elevated ESR and CRP levels, was the strongest predictor of radiographic spinal progression in axial PsA. Radiographic sacroiliitis also showed an association with structural damage in the spine in PsA.

Disclosure: F. Kharouf: None; **P. Mehta**: None; **V. Carrizo Abarza**: None; **S. Gao**: None; **D. Pereira**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6.

Abstract Number: 1417

Common Causes of Hospitalization in Spondyloarthritis Patients: A Nationwide Analysis

Faria Sami[1], Maria I. (\"Maio\") Danila[2], Liron Caplan[3] and Rouhin Sen[4], [1]The University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [3]Medicine Service, Rocky Mountain Regional VAMC, Aurora, CO, [4]University of Alabama at Birmingham, Department of Medicine, Division of Clinical Immunology & Rheumatology, Birmingham

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic Characteristics of Hospitalized Patients with AxSpA, PsA and IBD- A arthritis

Characteristic	AxSpA n= 139130	PsA n=223745	IBD-associated Arthritis n=1880
Female (%)	46.0%	57.6%	62.4%
Mean Age (years ± SD)	60.3 ± 16.9	61.2 ± 13.8	46.2 ± 17.3
White (%)	77.8%	85.4%	73.4%
African American (%)	8.1%	28.3%	11.2%
Hispanic (%)	6.1%	4.9%	6.5%
Asian/Pacific Islander (%)	1.9%	1.5%	1.2%
Length of Stay (days)	5.5 ± 6.9	4.9 (SD not provided)	5.2 ± 5.8
Total Charge (USD)	79,120.3 ± 122,456	63,346 ± 84,431	60,177.05 ± 79,654.53
In-patient Mortality (%)	1.8%	1.6%	1.0%

Abbreviations: *AxSpA: axial spondylarthritis; PsA: Psoriatic Arthritis; IBD: Inflammatory Bowel Disease.*

Table 2: Distribution of Principal Diagnosis Categories Among Hospitalized Patients with AxSpA, PsA, and IBD-A Arthritis Hospitalization in NIS 2016-2020.

Principal Diagnosis Category	AxSpA (%)	PsA (%)	IBD-associated Arthritis (%)
Rheumatological	25.9	14.0	14.6
Cardiovascular	10.7	15.8	2.4
Infection	9.6	10.6	13.2
Injury/Poisoning	13.8	9.5	3.6
Gastrointestinal	10.8	11.5	47.3
Respiratory	6.0	7.7	4.1
Neoplasm	3.1	4.3	1.2
Genitourinary	3.7	4.4	1.7
Endocrine	2.4	4.1	1.2
Psychiatry	3.0	3.4	0.7
Neurologic	2.5	2.6	2.6
Skin	1.8	5.3	2.4
Obstetric	2.0	1.4	1.4
Eye/Ear	0.2	0.3	0.2

Abbreviations: *AxSpA: axial spondylarthritis; PsA: Psoriatic Arthritis; IBD-A: Inflammatory Bowel Disease.*

Background/Purpose: Axial spondylarthritis (AxSpA), psoriatic arthritis (PsA), and inflammatory bowel disease-associated arthritis (IBD-A) are chronic inflammatory conditions with systemic involvement, leading to substantial morbidity and health-care utilization. There is a paucity of national-level data on reasons for hospitalizations in patients with these conditions. We aimed to identify major diagnostic categories for hospitalizations and top reasons for hospitalization among patients with AxSpA, PsA, and IBD-A, using a large United States population-based database.

Methods: We conducted a retrospective cohort study using the National Inpatient Sample (NIS) from 2016 to 2020. The NIS is the largest inpatient hospitalization database in the U.S., representing 20% of hospitalizations from all non-federal acute care hospitals. We identified patients with a primary or secondary diagnosis of AxSpA, PsA, or IBD-A using ICD-10 codes. Principal diagnoses for hospitalization were analyzed and categorized into major diagnostic categories. Weighted analyses were performed to calculate national estimates of hospitalization reasons and determine the top principal diagnoses for each disease group.

Table 3: Most Common Principal Diagnoses among Spondylarthritis Hospitalizations in NIS 2016-2020

Disease Group	Five Most Prevalent Principal Diagnosis (% hospitalizations)				
AxSpA n= 139130	Sacroiliitis, not elsewhere classified 7.6%	Sepsis, unspecific 5.3%	Acute kidney failure 1.3%	Pneumonia 1.2%	Primary OA of hip, unilateral 1.0%
PsA n=223745	Sepsis, unspecified 6.5%	Primary OA of knees 3.5%	NSTEMI 1.7%	Pneumonia 1.6%	Acute kidney failure 1.5%
IBD-associated arthritis N=1880	Ulcerative Colitis 12.2 %	Sepsis 10.6%	Crohn's Disease with and without complications 6.0%	Enterocolitis due to Clostridium difficile with and without toxic megacolon 4.4%	Primary Osteoarthritis of Right Shoulder 1.9%

Abbreviations: *AxSpA: axial spondylarthritis; PsA: Psoriatic Arthritis; IBD-A: Inflammatory Bowel Disease.*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 139,130 AxSpA, 223,745 PsA, and 1,880 IBD-A hospitalizations were analyzed. Demographics for the study cohort appear in Table 1. The top five most frequent major diagnostic categories for each group are summarized below [Table 2]:

- **AxSpA:** 1) Rheumatological disorder, 2) Injury/Poisoning, 3) Gastrointestinal disorders, 4) Cardiovascular disease, 5) Infections.
- **PsA:** 1) Cardiovascular disease, 2) Rheumatological, 3) Gastrointestinal disorders, 4) Infections, 5) Injury/Poisoning.
- **IBD-A:** 1) Gastrointestinal disorders, 2) Rheumatological disorder, 3) Infection, 4) Respiratory conditions, 5) Injury/Poisoning.

The leading principal diagnoses [Table 3] for AxSpA included sacroiliitis (7.6%), sepsis (5.3%), and acute renal injury (1.3%). For PsA, the top principal diagnoses included sepsis (6.5 %), primary osteoarthritis of the knee (3.5%), and non-ST-elevated myocardial injury (1.7 %). IBD-A population was most frequently admitted for ulcerative colitis (12.2%), followed by sepsis (10.6%), and then Crohn's disease with and without complications (6.0%)

Conclusion: Hospitalization patterns in AxSpA, PsA, and IBD-A differ by disease type but share common themes of rheumatological, cardiovascular disease, infectious, injury/poisoning, and gastrointestinal involvement. These findings may highlight key areas for targeted management and preventive efforts to optimize healthcare resource utilization and improve quality care for patients

Disclosure: F. Sami: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5; **L. Caplan**: None; **R. Sen**: None.

Abstract Number: 1418

Impact of Type 2 Diabetes Mellitus on Cardiovascular Outcomes in Patients with Ankylosing Spondylitis on NSAID Therapy

Godbless Ajenaghughrure[1], Sila Mateo Faxas[2], **Gurjot Singh**[3], Nirys Mateo Faxas[4], Kim Nguyen[3], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Trihealth Good Samaritan Hospital, Cincinnati, OH, [2]Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with ankylosing spondylitis (AS) have increased cardiovascular risk, potentially exacerbated by NSAID therapy. However, the additional impact of Type 2 diabetes mellitus (T2DM) in this population remains poorly characterized.

Methods: We conducted a retrospective cohort study using the TriNetX global federated health research network across 100 healthcare organizations. Two cohorts of adult patients (18-99 years) with AS on non-salicylate NSAIDs were analyzed: Cohort 1 with T2DM (n=9,499) and Cohort 2 without T2DM (n=9,499), propensity-score matched for demographic and clinical characteristics. Cardiovascular outcomes were assessed over a 5-year follow-up period (1825 days) after index date.

Results: Patients with AS on NSAID therapy and comorbid T2DM demonstrated significantly higher rates of major adverse cardiovascular events compared to matched patients without T2DM. Specifically, risk ratios (RR) and hazard ratios (HR) were significantly elevated for: mortality (RR 2.03, 95% CI 1.79-2.29; HR 1.95, 95% CI 1.72-2.21), cardiac arrest (RR 3.51, 95% CI 2.44-5.06; HR 3.37, 95% CI 2.34-4.86), atrial fibrillation (RR 2.97, 95% CI 2.60-3.39; HR 2.92, 95% CI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2.55-3.35), heart failure (RR 2.73, 95% CI 2.48-2.99; HR 2.76, 95% CI 2.50-3.04), cerebral infarction (RR 2.29, 95% CI 1.93-2.73; HR 2.59, 95% CI 2.02-3.32), and ventricular arrhythmias (RR 2.16, 95% CI 1.73-2.73; HR 2.09, 95% CI 1.66-2.64). Additionally, patients with T2DM had significantly higher rates of requiring pacemaker implantation (RR 2.44, 95% CI 2.09-2.84) and experiencing pulmonary complications including pulmonary hypertension (RR 2.26, 95% CI 1.93-2.64) and pulmonary embolism (RR 3.55, 95% CI 2.36-5.36).

Conclusion: T2DM significantly amplifies cardiovascular risk in patients with ankylosing spondylitis on NSAID therapy. This represents the largest analysis to date quantifying this increased risk across multiple cardiac outcomes. These findings highlight the need for enhanced cardiovascular monitoring and risk mitigation strategies in this high-risk population

Disclosure: G. Ajenaghughrure: None; **S. Mateo Faxas**: None; **G. Singh**: None; **N. Mateo Faxas**: None; **K. Nguyen**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 1419

Effectivenss of an educational program on non-radiographic axial spondyloarthritis

Hideto Kameda[1], Toshihide Shuto[2], Akimichi Morita[3], Yasuharu Nakashima[4], Kiyoshi Matsui[5], Masaaki Mori[6] and Masahiro Yamamura[7], [1]Department of Internal Medicine, Toho University, Tokyo, Japan, [2]Chiyoda Hospital, Hyuga, Japan, [3]Department of Geriatric and Environmental Dermatology, Graduate School of Medical Sciences, Nagoya City University, Nagoya, Japan, [4]Kyushu University, Fukuoka, Japan, [5]Amagasaki Chuo Hospital, Amagasaki, Japan, [6]Institute of Science Tokyo, Tokyo, Japan, [7]Okayama Saiseikai General Hospital, Okayama, Japan

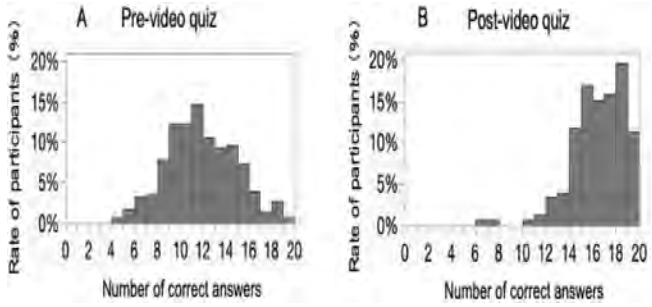
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Non-radiographic axial spondyloarthritis (nr-axSpA) is a relatively new disease concept. We developed an educational program to promote early and appropriate referral to specialists based on a correct understanding of nr-axSpA. The objective of this study was to analyze the outcomes and challenges identified through the educational program.

Methods: The program targeted physicians in internal medicine, orthopedics, and dermatology, as well as other healthcare professionals. A 30-minute educational video on nr-axSpA was uploaded to the official website of the society. A 30-question quiz was created to assess knowledge before and after watching the video. Upon accessing the website, participants first answered 20 questions. After completing this initial quiz, they were allowed to watch the video. Following the viewing, they answered another set of 20 questions—10 of which were identical to those from the pre-video quiz, and the remaining 10 were new. Anonymous response data were analyzed to assess changes in correct answer rates before and after the video, and to explore pre-video correct answer rates by participant background.

Results: From April 2023 to September 2024, 420 healthcare professionals registered for the program. Membership distribution was as follows: 88% were members of the Japan College of Rheumatology, 25% of the Japanese Orthopaedic Association, 11% of the Japan Spondyloarthritis Society, and 4% of the Japanese Society for Psoriasis Research. A total of 316 participants completed the pre-video quiz, with a median correct answer rate of 55% (range: 20–100%; Figure 1A). After viewing the video, 180 participants completed the post-video quiz, achieving a median correct answer rate of 80% (range: 30–100%; Figure 1B). A paired test revealed a significant improvement in the correct answer rate from 57% to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



The distribution of the correct answer rates of the pre- and post-video quiz.

80% ($p < 0.0001$). For the identical 10 questions, the correct response rate significantly increased from 55% before viewing to 86% after viewing ($p = 0.0033$). Even for different questions, there was a trend toward improvement, with correct responses increasing from 61% before viewing to 75% after viewing ($p = 0.20$). No correlation was observed between years of professional experience in spondyloarthritis and pre-video correct answer rates (correlation coefficient $r^2 = 0.0042$).

Conclusion: The educational program demonstrated clear benefits, indicating that when nr-axSpA is suspected, referral to specialists or clinicians with relevant training–rather than relying primarily on years of clinical experience in spondyloarthritis–may be both appropriate and advantageous.

Disclosure: H. Kameda: AbbVie, 2, 6, Amgen, 2, 6, Asahi Kasei Pharma Co., 2, 5, 6, BMS, 6, Eisai, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Mitsubishi-Tanabe, 6, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, Taisho, 2, 5, UCB, 2, 6; **T. Shuto**: AbbVie, 6, Asahi Kasei, 6, Astellas, 6, Ayumi, 6, Boehringer Ingelheim, 6, Chugai, 7, Daiichi Sankyo, 6, Eli Lilly, 6, Kyowa Kirin, 6, Mitsubishi Tanabe, 6, Novartis, 6, UCB, 6; **A. Morita**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Kyowa Kirin, 2, 5, 6, LEO Pharma, 2, 5, 6, Maruho, 2, 5, 6, Sun Pharma Japan, 2, 5, 6, Taiho Pharmaceutical, 2, 5, 6, Torii Pharmaceutical, 2, 5, 6, UCB Japan, 2, 5, 6, Ushio, 2, 5, 6; **Y. Nakashima**: AbbVie/Abbott, 6, Aimedic MMT, 6, Amgen, 6, Asahi Kasei, 6, Astellas, 6, Ayumi, 5, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly, 6, Heart Organization, 6, Hisamitsu, 6, Johnson&Johnson, 6, Kaken, 6, Kyocera, 5, 6, Kyowa Kirin, 6, Nippon Kayaku, 6, Nippon Zoki, 6, Pfizer, 6, Seikagaku Corporation, 6, Stryker, 6, Teijin Healthcare, 6, Tsumura, 6, UCB, 6; **K. Matsui**: Asahi Kasei, 5, 6, Astellas, 6, Chugai, 5, 6, Eli Lilly, 6, Taisho, 6; **M. Mori**: AbbVie/Abbott, 2, 6, Asahi Kasei, 6, AstraZeneca, 1, 2, 6, Ayumi, 5, 6, Bristol-Myers, 6, Chugai, 6, Dai-ichi Sangyo, 1, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Human Life CORD, 5, IQVIA, 6, Japan Blood, 6, Lightnix, 2, Medac, 6, Meiji Seika, 6, Mitsubishi-Tanabe, 6, MSD, 6, Novartis, 6, Pfizer, 6, Sanofi, 6, Shionogi, 6, SRL, 6, Taisho, 5, 6, Takeda, 6, Viatris, 6; **M. Yamamura**: AbbVie/Abbott, 6, Astellas, 6, Ayumi, 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, Novartis, 6, Otsuka, 6, UCB, 6.

Abstract Number: 1420

A Nationwide Analysis of In-Hospital Mortality in Adult Ankylosing Spondylitis

Isadora Small[1], Anuya Natu[2] and Augustine Manadan[3], [1]The Latin School of Chicago, Chicago, IL, [2]John H Stroger, Jr. Hospital of Cook County, Chicago, IL, [3]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease with systemic complications that may contribute to increased mortality risk. This study examines the characteristics and causes of in-hospital death among adult AS patients in the United States using a claims-based database.

Methods: A retrospective analysis of all adult hospitalizations with a diagnosis of AS (ICD-10: M45) in the National Inpatient Sample (NIS) database (2017 - 2021) was conducted. Descriptive statistics were used to analyze demographics, hospital length of stay (LOS), insurance status, total hospital charges, and causes of death categorized by ICD-10 codes.

Results: Of the 96,330 adult AS hospitalizations in the 2017 - 2021 NIS database, 2,390 (2.5%) died in the hospital (Table 1). AS patients who died compared to those discharged alive were more likely to be male (79.7% vs. 62.9%; $p < 0.001$), were older (median age 73 vs. 62 years; $p < 0.001$), had longer median hospital LOS (7 vs. 4 days; $p < 0.001$), had higher median total hospital charges ($104,275 vs. $44,345; $p < 0.001$), more Medicare (73.6% vs. 54.6%; $p < 0.001$), less Medicaid (4.8% vs. 10.3%; $p < 0.001$), less private insurance (16.3% vs. 30.1%; $p < 0.001$), and a lower percentage of the top household income quartile (18.6% vs. 24.9%; $p = 0.002$). Racial distribution did not significantly differ between groups.

The causes of in-hospital death of AS patients as determined by their "principal ICD-10 billing diagnosis category" were as follows: injury/poisoning (29.1%), infections (22.0%), cardiovascular (CV) diseases (11.3%), respiratory diseases (11.1%), hematologic/oncologic conditions (7.5%), gastrointestinal diseases (5.0%), genitourinary diseases (3.1%), factors influencing health status (1.5%), rheumatologic diseases (1.3%), neurologic diseases (0.8%), endocrine diseases (0.6%), and other causes (0.6%) (Table 2).

The most common specific injury diagnosis was traumatic subdural hemorrhage (ICD-10: S06.5X0A) (table 3), followed by fractures of the thoracic (ICD-10: S22.089A, S22.088A, S22.078A, S22.069A, S22.079A), cervical (ICD-10: S12.300A, S12.400A, S12.490A, S12.200A), and lumbar vertebrae (ICD-10: S32.019A). Severe spinal cord injuries (ICD-10: S14.115A, S24.102A, S24.103A, S14.106A), traumatic subarachnoid hemorrhage (ICD-10: S06.6X0A), and thoracic trauma, including hemothorax and hemopneumothorax (ICD-10: S27.1XXA, S27.2XXA), were also frequent (Table 3).

Table 1. Descriptive Characteristics of Adult Ankylosing Spondylitis Patients from 2017 - 2021 National Inpatient Sample Database (n = 96,330). Abbreviations: AS = ankylosing spondylitis; n = number; IQR = interquartile range

Characteristic	Discharged Alive (n= 93,940)	In-Hospital Deaths (n=2,390)	P value
Male, n (%)	59,085 (62.9%)	1,905 (79.7%)	<0.001
Age, median (IQR) years	62 (49-73)	73 (64-81)	<0.001
Age Distribution, n (%)			
18-40 years	11,860 (12.6%)	35 (1.5%)	<0.001
40-60 years	29,445 (31.3%)	350 (14.6%)	<0.001
60-80 years	41,325 (44.0%)	1,330 (55.6%)	<0.001
> 80 years	11,310 (12.0%)	675 (28.2%)	<0.001
Race, n (%)			
White	74,965 (79.8%)	1,935 (81.0%)	0.531
African American	6,050 (6.4%)	110 (4.6%)	0.106
Hispanic	5,635 (6.0%)	145 (6.1%)	0.950
Asian or Pacific Islander	1,855 (2.0%)	55 (2.3%)	0.613
Native American	825 (0.9%)	15 (0.6%)	0.561
Other Race	2,100 (2.2%)	55 (2.3%)	0.924
Median Household Income, n (%)			
Income Quartile 1	20,630 (22.0%)	595 (24.9%)	0.123
Income Quartile 2	23,390 (25.0%)	665 (27.8%)	0.147
Income Quartile 3	25,115 (26.7%)	655 (27.4%)	0.742
Income Quartile 4	23,375 (24.9%)	445 (18.6%)	0.002
Length of Stay, median (IQR)	4 (2-7)	7 (3-12)	<0.001
Insurance Type, n (%)			
Medicare	51,260 (54.6%)	1,760 (73.6%)	<0.001
Medicaid	9,640 (10.3%)	115 (4.8%)	<0.001
Private Insurance	28,265 (30.1%)	390 (16.3%)	<0.001
Self-Pay	1,730 (1.8%)	55 (2.3%)	0.465
No Charge	95 (0.1%)	0 (0%)	0.488
Other Insurance	2,840 (3.0%)	70 (2.9%)	0.905
Total Hospital Charges, median (IQR)	$44,345 (23,105- 90,437)	$104,275 (44,682- 228,396)	<0.001

Table 2. Causes for In-Hospital Death of Adult Ankylosing Spondylitis Patients from the National Inpatient Sample Database 2017 - 2021 (n = 2,390). Abbreviations: AS = ankylosing spondylitis; n = number; NR = not reported as below permitted reporting threshold rules for National Inpatient Sample

ICD 10 Diagnostic Category	In-hospital deaths, n (%)
Injury/Poison	695 (29.1%)
Infections	525 (22.0%)
Cardiovascular	270 (11.3%)
Respiratory	265 (11.1%)
Hematology/Oncology	180 (7.5%)
Gastrointestinal	120 (5.0%)
Genitourinary	75 (3.1%)
Factors influencing health status	35 (1.5%)
Rheumatologic	30 (1.3%)
Neurologic	20 (0.8%)
Endocrine	15 (0.6%)
Other	15 (0.6%)
Skin	NR
Psychiatry	NR
Eye/Ear	0 (0%)
Obstetrics	0 (0%)
Perinatal	0 (0%)
Congenital	0 (0%)
External Causes	0 (0%)

Table 3: Top Injury Causes of In-Hospital Death in Adult AS patients from National Inpatient Sample Database.

Top Injury Causes of In-Hospital Death in Adult AS patients from National Inpatient Sample Database	Number of Deaths
Traumatic subdural hemorrhage without loss of consciousness, initial encounter S06.5X0A	40
Unspecified fracture of T11-T12 vertebra, initial encounter for closed fracture S22.089A	35
Unspecified displaced fracture of fourth cervical vertebra, initial encounter for closed fracture S12.300A	25
Unspecified fracture of first lumbar vertebra, initial encounter for closed fracture S32.019A	20
Complete lesion at C5 level of cervical spinal cord, initial encounter S14.115A	20
Other fracture of T11-T12 vertebra, initial encounter for closed fracture S22.088A	20
Other fracture of T9-T10 vertebra, initial encounter for closed fracture S22.078A	20
Unspecified fracture of T7-T8 vertebra, initial encounter for closed fracture S22.069A	20
Unspecified fracture of T9-T10 vertebra, initial encounter for closed fracture S22.079A	15
Traumatic subdural hemorrhage with loss of consciousness of unspecified duration, initial encounter S06.5X9A	15
Unspecified displaced fracture of fifth cervical vertebra, initial encounter for closed fracture S12.400A	15
Traumatic subarachnoid hemorrhage without loss of consciousness, initial encounter S06.6X0A	15
Unstable burst fracture of T11-T12 vertebra, initial encounter for closed fracture S22.082A	15
Traumatic hemothorax, initial encounter S27.1XXA	≤10
Unspecified injury at T2-T6 level of thoracic spinal cord, initial encounter S24.102A	≤10
Traumatic hemopneumothorax, initial encounter S27.2XXA	≤10
Other displaced fracture of fifth cervical vertebra, initial encounter for closed fracture S12.490A	≤10
Unspecified injury at T7-T10 level of thoracic spinal cord, initial encounter S24.103A	≤10
Unspecified displaced fracture of third cervical vertebra, initial encounter for closed fracture S12.200A	≤10
Unspecified injury at C6 level of cervical spinal cord, initial encounter S14.106A	≤10

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our analysis represents the only report to date to comprehensively study AS inpatients on a U.S. national level. Over 1 of 50 AS hospitalizations ended in death, and they were predominantly older males, most of whom had Medicare insurance. Injury-related conditions were the most frequent cause of death. The leading injury diagnoses were brain bleeds, vertebral fractures, and spinal cord injuries. Further research is needed to explore the factors contributing to injuries and falls in AS patients.

Disclosure: I. Small: None; **A. Natu**: None; **A. Manadan**: None.

Abstract Number: 1421

Impact of Psoriatic Arthritis Disease Activity and Fatigue on Subjective Cognitive Decline ("Brainfog")

Lily Mikolajczak[1], Helena Kuhn[1], Leslie Harrold[2] and George Reed[3], [1]Kuchnir Dermatology and Dermatologic Surgery, Milford, MA, [2]CorEvitas, Northborough, MA, [3]University of Massachusetts Chan Medical School, Worcester, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with psoriatic arthritis often report having brain fog, describing symptoms such as forgetfulness, difficulty thinking and memory issues. It has been hypothesized that these symptoms, consistent with subjective cognitive decline, may be the result of fatigue, depression, associated chronic pain and inflammation. We proposed to explore the association between disease activity and subjective cognitive decline when taking into account patient factors, comorbidities and PsA characteristics.

Methods: We identified patients with a diagnosis of PsA from the CorEvitas PsA/SpA registry with a visit between 7/22/2013-10/20/2024 that included information on Minimal Disease Activity (MDA) and confounding covariates of interest. MDA assesses joint pain, swelling, skin involvement, physical function and pain, making it a comprehensive assessment of disease activity. Subjective Cognitive Decline (SCD) or "Brainfog", was defined as the patient indicating problems thinking/confusion or problems with memory/forgetfulness. The association of MDA (achievement of ≥5 of the 7 criteria) with SCD was estimated using logistic regression models controlling for demographic (age, sex, education), behavior (smoking, drinking), BMI, disease duration, modified Charlson Comorbidity Index, fibromyalgia, medication use (narcotics, analgesics, NSAIDs, biologic/targeted synthetic DMARDs), patient reported fatigue, depression, and anxiety. Odds Ratios (ORs) with 95% confidence intervals are presented to estimate risk of SCD in those not in MDA vs those in MDA. The proportion with SCD is estimated based on the number of MDA criteria met.

Results: There were 4077 eligible PsA patients. Of those, 315 (7.7%) were missing at least one covariate of interest. Of the remaining 3762 patients, 385 or 10.2%, indicated SCD (3% for those in MDA and 16% in those not in MDA). Table 1 breaks out selected covariates by SCD or not. Those reporting SCD were more often female, had more comorbidities including fibromyalgia, as well as fatigue, anxiety and depression. Figure 1 illustrates ORs comparing risk of SCD in those not in MDA vs those in MDA for a series of tiered models that illustrate the adjusted ORs for nested inclusion of key covariates. Unadjusted OR= 5.33 [95% CI: 4.0, 7.10] and after adjustment for demographics, behavior, BMI, comorbidities, and medications OR=4.34 [3.21, 5.87]. Adding "Fatigue" reduces the OR=2.15 [1.54, 3.01]. Patient depression and anxiety had less

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1.

Table 1. PsA Patient Characteristics by Subjective Cognitive Dysfunction (SCD)

	Reported SCD N=385 (10%)	No reported SCD N=3,377 (90%)	P value
Age in years (SD)	59.2 (13.7)	57.5 (13.4)	0.024
Female, n (%)	269 (70%)	1,865 (55%)	<0.001
Education, n (%)			0.056
Primary	9 (2%)	36 (1%)	
High school	105 (28%)	677 (26%)	
College/University	268 (70%)	2464 (73%)	
Smoking, n (%)			0.046
Never	205 (54%)	1911 (57%)	
Former	124 (32%)	1122 (33%)	
Current	55 (12%)	344 (10%)	
Alcohol use, n (%)			<0.001
Nondrinker	228 (59%)	1513 (45%)	
Social drinker	130 (34%)	1552 (46%)	
High risk drinker	27 (7%)	312 (9%)	
BMI categories, n (%)			
Underweight	4 (1.0%)	36 (1%)	0.015
Normal weight	70 (18%)	524 (16%)	
Overweight	90 (23%)	1,000 (30%)	
Obesity stage I	91 (24%)	893 (26%)	
Obesity stage II	130 (34%)	924 (27%)	
Disease duration in years (SD)	9.4 (8.7)	10.6 (9.2)	0.017
Modified Charlson Comorbidity Index, n (%)			<0.001
1	239 (63%)	2451 (73%)	
2	93 (24%)	742 (22%)	
3+	53 (14%)	184 (5%)	
Disease duration in years (SD)	9.4 (8.7)	10.598 (9.2)	0.017
History of fibromyalgia, n (%)	48 (13%)	182 (5%)	<0.001
Use of narcotics or opioids, n (%)	36 (9%)	182 (5%)	0.003
Use of analgesics	47 (12%)	169 (5%)	<0.001
Use of NSAIDs	124 (32%)	1082 (32%)	0.947
Number of prior b/fs DMARDs			0.037
None	23 (6%)	279 (8%)	
1	104 (27%)	1097 (33%)	
2	98 (26%)	788 (23%)	
3+	160 (42%)	1221 (36%)	
Patient fatigue (0-100), mean (SD)	63.4 (24.2)	38.6 (28.7)	<0.001
Patient reported depression, n (%)	155 (41%)	184 (5%)	<0.001
Patient reported anxiety, n (%)	148 (38%)	238 (7%)	<0.001

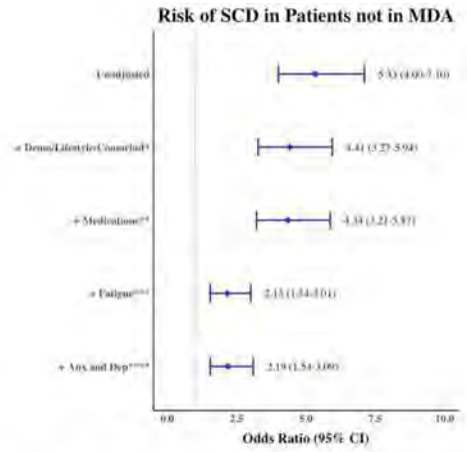


Figure 1: Risk of SCD in PsA patients not in MDA vs in MDA

Models

*Demo/Lifestyle/Comorbid: demographics (age, sex, education), behavior (smoking, drinking), BMI, disease duration, modified Charlson Comorbidity Index, and fibromyalgia

**+ Medications: adds in (narcotics, analgesics, nsaids, biologic/targeted synthetic DMARDs)

***+Fatigue: adds in patient fatigue

***+Anx and Dep: adds in patient anxiety and patient depression

Figure 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

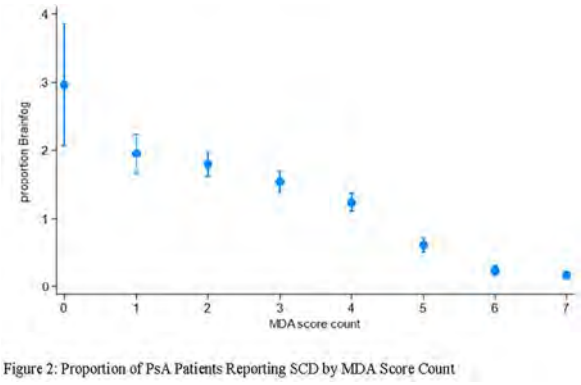


Figure 2: Proportion of PsA Patients Reporting SCD by MDA Score Count

Figure 2.

of an impact (OR= 3.53 and 3.72, respectively). Figure 2 illustrates the proportion of SCD by the number of criteria met for achieving MDA showing decreasing SCD with additional indicators of MDA.

Conclusion: Not achieving MDA shows a high risk of SCD (OR >4) adjusting for differences in patient characteristics. Adjusting for fatigue reduces the associated risk of SCD with not being in MDA, suggesting a potential mechanism for the impact of disease activity. However, it does not completely explain the association. The monotonic association of SCD with MDA markers illustrates this is not a threshold effect. Additional longitudinal analyses are planned to elucidate the impact of PsA disease activity on a patient's cognitive well-being.

Disclosure: L. Mikolajczak: None; **H. Kuhn**: Castle Biosciences, 6, Pfizer, 6; **L. Harrold**: CorEvitas, 3, Pfizer, 2; **G. Reed**: CorEviitas, LLC, 2, Corrona Research Foundation, 2.

Abstract Number: 1422

Assessment of Difficulties, Modifications and Use of Work Adaptations in Patients with Axial Spondyloarthritis: Validation of the Dificultax and Modal Questionnaires

Mariana Benegas[1], Maria Victoria Martire[2], Leandro ferreryra[3], Hernan Maldonado[4], Carla Airoldi[5], Luciana Casalla[6], Joan Manuel Dapeña[7], Etel Saturansky[8], Eliana Serrano[7], Julieta Morbiducci[9], Aixa Lucia Merce[10], Natalia Zamora[11], Javier Federico Flores Trejo[12], Fernando Sommerfleck[13], Emilio Buschiazzo[14], Hernan Molina[15], Cecilia Castro[16] and Romina Nieto[17], [1]sanatorio Mendez, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [2]Hospital San Roque, La plata, Buenos Aires, Argentina, [3]HIBA, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [4], Hospital San Antonio de Padua, Rio cuarto, Cordoba, Argentina, [5]Hospital Provincial de Rosario, Rosario, Santa Fe, Argentina, [6]Centro medio GENEA, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [7]Sanatorio Dr Julio Méndez, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [8]Sanatorio Méndez, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [9]Hospital General de Agudos Bernardino Rivadavia, Capital Federal, Ciudad Autonoma de Buenos Aires, Argentina, [10]Hospital General de Agudos Bernardino Rivadavia, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [11]HIGA San José, pergamino, Buenos Aires, Argentina, [12]Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [13]Sanatorio Julio Mendez, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [14], Hospital Sr. del Milagro, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [15]Instituto CER, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [16]Hospital Z.G.A Dr. Isidoro Iriarte de Quilmes, Quilmes, Buenos Aires, Argentina, [17]Centro Regional de Enfermedades Autoinmunes y Reumáticas, GO-CREAR, Rosario, Argentina, Rosario, Argentina

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Spearman correlations between DificuLtAx and ModAL scores (n = 72).

Variable	DificuLtAx		ModAL	
	r	p	r	p
Tender joint count	0.41	**0.001**	0.35	**0.003**
Swollen joint count	0.32	**0.006**	0.16	0.2
Fatigue VAS	0.53	**0.001**	0.55	**0.001**
BASDAI	0.65	**0.001**	0.55	**0.001**
BASFI	0.59	**0.001**	0.40	**0.001**
ASDAS-ESR	0.59	**0.001**	0.53	**0.001**
ASDAS-CRP	0.58	**0.001**	0.44	**0.001**
ASAS-HI	0.61	**0.001**	0.41	**0.001**
Work-productivity VAS (WPAI Q5)	0.58	**0.001**	0.57	**0.001**
Activity-impairment VAS (WPAI Q6)	0.68	**0.001**	0.72	**0.001**
Absenteeism (WPAI)	0.54	**0.001**	0.55	**0.001**
Presenteeism (WPAI)	0.58	**0.001**	0.67	**0.001**
Work-productivity loss (WPAI)	0.64	**0.001**	0.70	**0.001**

Abbreviations: VAS = visual analogue scale; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; ASDAS = Ankylosing Spondylitis Disease Activity Score; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; ASAS-HI = Assessment of SpondyloArthritis International Society-Health Index; WPAI = Work Productivity and Activity Impairment Questionnaire.

Background/Purpose: DificuLtAR and ModAL, two spanish-language questionnaires that assess work difficulties and workplace adaptations, were originally developed and validated for rheumatoid arthritis (RA). Their performance in axial spondyloarthritis (axSpA) remains unknown.

Objective: (1) to validate DificuLtAR and ModAL in axSpA (2) Identify factors associated with work difficulties and the use of workplace modifications and adaptations reported by employed patients with axSpA.

Methods: An adaptation of the DificuLtAR for EspAax (DificuLtAx) questionnaire was made, Both questionnaires were applied to patients ≥18 years old, both genders, with a diagnosis of axSpA (ASAS-2009) and actively working. Cronbach's alpha (DifficuLtAx=0.92 and ModAL=0.83) and construct validity were explored through factor analysis. The Eigenvalue values for a single factor (DificuLtAx=0.89 and ModAL=0.81) and correlation coefficients greater than 0.40 for all questions of both questionnaires after varimax rotation were aceptable. Spearman correlation coefficients, Mann-Whitney or Kruskal-Wallis tests, were calculated. ($p < 0.05$).

Results: 72 patients were included, 72% men, median age 42 years (IQR 37-53), disease duration 97 months (IQR 40-156), 54% B27positive, and 67% radiographic. The median ASDAS-PCR 2 (IQR 1-3) and BASFI 3.5 (IQR 2-5). 58% were in formal salaried employment and the median WPAI (labor productivity) was 0 (IQR 0-44). The greatest difficulties were sitting or standing for prolonged periods of time (75%) and working crouched (84%) and the most frequent modifications were taking breaks (78%) and furniture changes (45%). The median DificuLtAx 5 (IQR 2-9) and ModAL 3.5 (IQR 2-6), with a correlation between both of rho: 0.67 (p 0.001). See correlations Table 1. Female gender 5.5 vs 3.5 (p 0.001) and boss's knowledge of the disease 4 vs 3 (p 0.05), were associated with greater modifications.

Conclusion: DificuLtAx and ModAL showed good reliability and construct validity. The main work difficulties were to remain seated or standing and to work crouching/kneeling, and the most frequent modifications were to take breaks and modify the furniture; these were more common in women and in those in whom the boss was aware of the disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: m. benegas: None; **M. Martire**: None; **L. ferreryra**: None; **H. Maldonado**: None; **C. Airoldi**: None; **L. Casalla**: None; **J. Dapeña**: None; **E. Saturansky**: None; **E. Serrano**: None; **J. Morbiducci**: None; **A. Merce**: None; **N. Zamora**: None; **J. Flores Trejo**: None; **F. Sommerfleck**: None; **E. Buschiazzo**: None; **H. Molina**: None; **C. Castro**: None; **R. Nieto**: None.

Abstract Number: 1423

Genetic and Cytokine Correlates in Ankylosing Spondylitis: rs27038 polymorphism of ERAP1 gene and IL-17 Interactions : A Case-Control Study

Meghna Gavali[1], Husna Fatima[2], Bhavya Sirivelu[3], Nishanth S[3] and Noorjahan M[3], [1]nizam's institute of medical sciences ,Hyderabad, Hyderabad, Telangana, India, [2]Nizami Institute of Medical Sciences, Hyderabad, Telangana, India, [3]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing Spondylitis (AS) is a chronic inflammatory disorder primarily affecting the axial skeleton and associated with HLA-B27. Non-HLA genes, including ERAP1 (Endoplasmic Reticulum Aminopeptidase 1), also play a role in pathogenesis by influencing peptide trimming and cytokine regulation. The rs27038 SNP in ERAP1 may affect antigen processing and inflammatory responses. IL-17, a key proinflammatory cytokine, is central to AS immunopathology. This study investigates the association of ERAP1 rs27038 SNP with AS susceptibility, IL-17 levels, and disease severity.There is limited data on ERAP1 gene polymorphisms and IL-17 levels in Indian patients with Ankylosing Spondylitis, despite genetic and immunological differences across populations. This study addresses the gap by exploring the association of ERAP1 rs27038 and IL-17 in South Indian AS patients, aiming to improve early diagnosis and guide population-specific therapeutic approaches.

Methods: A case-control study included 75 AS patients (modified New York criteria) and 25 age- and sex-matched healthy controls from a tertiary care centre in South India . Clinical parameters (BASDAI, ESR, hsCRP) were recorded. Genomic DNA was extracted, amplified using qPCR and rs27038 SNP genotyping was done via Sanger's sequencing. Serum IL-17 was quantified by ELISA. Genotypic and allelic frequencies were compared using Chi-square test. IL-17 levels were compared using the ManWhithey U test. Correlations with disease activity were analyzed using Spearman's rank correlation.

Results: Serum IL-17 levels were significantly elevated in AS patients (median 48.39 pg/mL) compared to controls (median 8.78 pg/mL, p=0.0002). The ERAP1 rs27038 polymorphism showed significant association with AS susceptibility, with the A allele being more frequent in cases than controls (22% vs. 8%, p=0.03, OR=3.15, 95% CI: 1.05-9.24). Serum IL-17 demonstrated good diagnostic performance (AUC=0.848, 95% CI: 0.755-0.917), comparable to hsCRP (AUC=0.843). Il-17 showed a significant correlation with hsCRP levels (rho=0.353, p=0.0009), but did not show association with BASDAI/ASDAS (rho=0.120, p=0.34; rho=0.13, p=0.31 respectively). Logistic regression identified HLA-B27 positivity (OR=38.25), elevated ESR (OR=1.095), and Patient Global Assessment (OR=1.94) as independent predictors of AS. However, no significant associations were found between rs27038 genotypes and IL-17 levels.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of patients with ankylosing spondylitis

Characteristics	AS patients $n = 75$ (%)
Smoking	11 (14.6)
Disease duration (years) Median(IQR)	5 (3.2 - 9)
Age	32 (24.2 - 41.7)
Gender M / F	65 (86.6) / 10 (13.4)
SpA Features as defined by ASAS Criteria	
Peripheral Arthritis	46 (61.3)
Enthesitis	28 (37.3)
Family History of SpA	6 (8)
Dactylitis	7(9.3)
Uveitis	5 (6.6)
Psoriasis	2 (2.6)
IBD	8 (10.6)
HLA B27 POSITIVE	58 (77.3)
Disease activity measures	
MEAN BASDAI Mean $\pm$ SD)	3.7 $\pm$ 2.27
MEAN ASDAS Mean $\pm$ SD	3.09 $\pm$ 1.12
Radiological Features	
Hip Involvement	9 (12)
Syndesmophytes	23 (30.6)
Treatment History	
NSAIDS	66 (88)
DMARDS : SAAZ MTX JAK-(Tofacitinib)	33 (44) 12 (16) 9 (12)
BIOLOGICAL AGENTS: Adalimumab	33 (44)

Conclusion: Our findings support the role of both IL-17-mediated inflammation and ERAP1 genetic variants in AS pathogenesis. Serum IL-17 could serve as a valuable biomarker for AS diagnosis, potentially enabling earlier detection and intervention. The ERAP1 rs27038 polymorphism contributes to AS susceptibility but appears to act through pathways independent of IL-17 regulation. These results provide insights into AS pathogenesis and suggest potential applications in diagnosis, risk assessment, and targeted therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

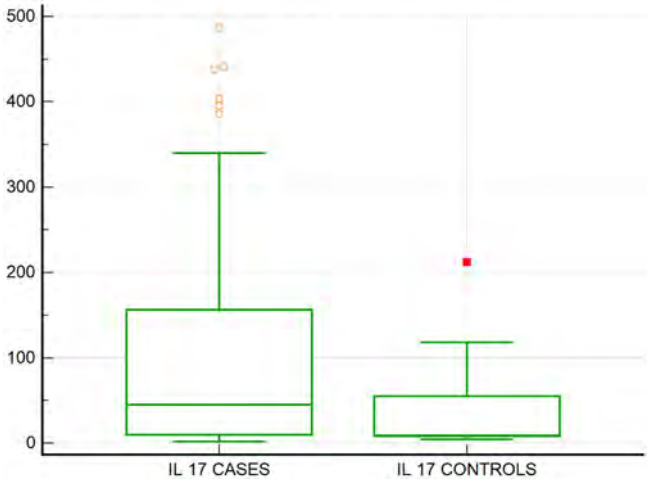


Figure1: Serum IL-17(pg/mL) in Cases vs Controls (P = 0.0002)

Table 2: Genotype distribution and allele frequency of rs27038 SNP in study population

rs27038	Genotype	Controls (N) N (%	Cases (N) N (%)	Cases (N) N (%) OR (95% CI,)	*X2 p-values*
Genotype frequency	G/G	20 (83.3)	45 (63.8) 4 (5.4	1.00	
	G/A	4 (16.7)	25 (33.8)	3.0 (0.90-1.03)	0.07
	A/A	0 (0)	4 (5.4)	0.47 (0.26-0.83	
Allele	G	44 (0.92)	115 (0.78)	1.00	
	A	4 (0.08)	33 (0.22)	**3.15 (1.05-9.24)**	**0.03***
HWE(p)		0.75	0.74		

Disclosure: M. Gavali: None; **H. Fatima**: None; **B. Sirivelu**: None; **N. S**: None; **N. M**: None.

Abstract Number: 1424

Mapping Central Nervous System Responses To Painful Stimuli In Patients With Axial Spondyloarthritis

Mohamad Bittar[1], Yvonne Lee[2], Atul Deodhar[3], Jennifer Barton[4] and Alexander Stevens[1], [1]Oregon Health & Science University, Portland, OR, [2]Northwestern University, Chicago, IL, [3]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [4]VA Portland Health Care System/OHSU, Portland, OR

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

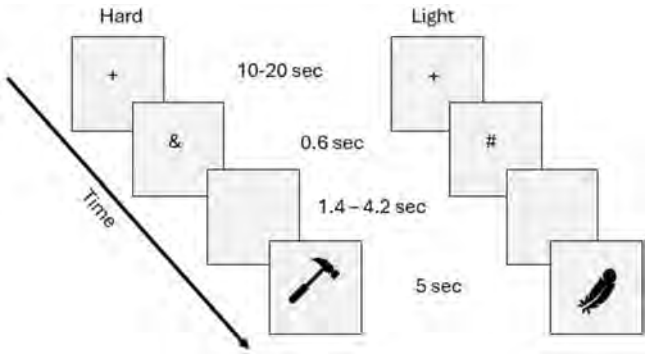


Fig. 1. Illustration of the fMRI tactile pressure task. The painful and light trials differ only in the stimulus cues (&,#) and the stimulus pressure. The crosshair is present during the variable inter-trial interval. The post-cue interval (1.4 – 4.2s) is jittered to permit deconvolution of the cue and stimulus hemodynamic responses.

Background/Purpose: Chronic pain is one of the common causes of disability in axial spondyloarthritis (axSpA). The mechanism behind this pain is not well understood, hindering the development of safe and efficacious treatments. The aim of this exploratory study is to examine differences in brain responses to painful stimuli between axSpA patients and healthy controls (HC).

Methods: Six axSpA patients and 6 age-and-sex matched HC underwent functional brain magnetic resonance imaging (fMRI) while tactile pressure to the thumbnail was applied: a light pressure (LSTIM) that is perceived but not painful, and a hard pressure (HSTIM) rated as a 1 pain, on a scale of 0-10 (Fig 1). A visual cue appeared 1.4 – 4.2 seconds prior to the stimulus, indicating a light or hard level of the subsequent stimulus. Analysis of fMRI data was exploratory due to small sample size. AxSpA and HC groups were combined to maximize power to detect signal changes associated with the pressure task. Areas with increased signal were used to create regions of interest (ROIs), which were then analyzed for group effects, using repeated measures mixed effects models.

Results: AxSpA patients were 50% females, had a mean age of 40 and mean ASDAS-CRP score of 2.7. The visual cue conditions produced increased signal throughout the brain, including areas in the occipitotemporal pathway, anterior insula, frontal operculum, medial superior frontal gyrus, and parietofrontal (PF) complex. Signal decreases were seen in areas typically associated with the default mode network (DMN). The tactile stimulation produced increased signal throughout the

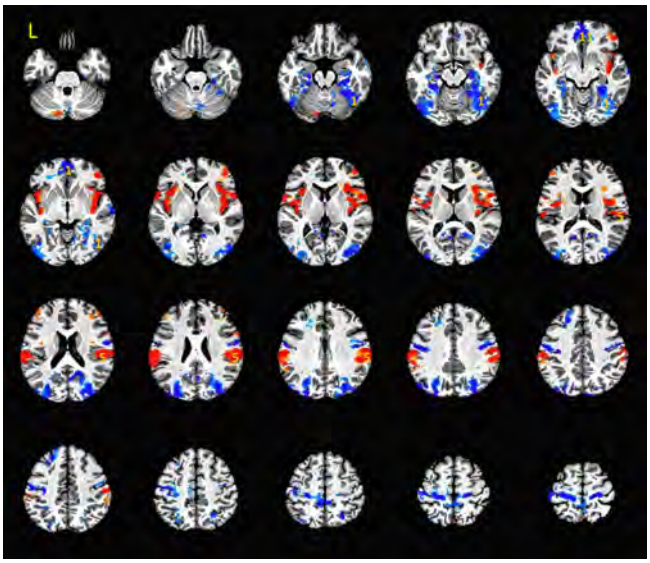


Fig. 2: Combined whole-brain analysis showing hyperactive (red) and hypoactive (blue) regions of interest (ROIs) following pressure stimulus. Numbers indicate ROIs with significant effects shown in Fig. 3.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

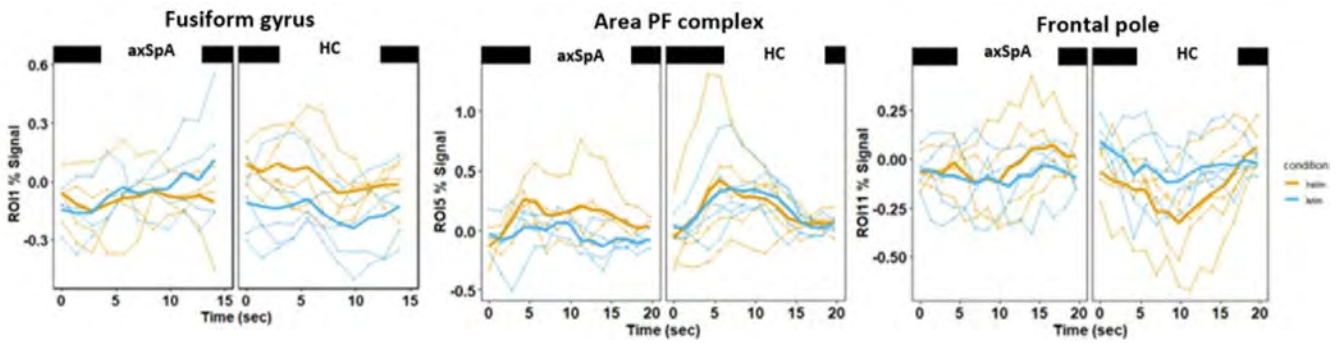


Fig. 3. Signal response achieving statistical significance ($p<0.05$) of ROIs to LSTIM (blue) and HSTIM (yellow) in axSpA and HC. ROI: region of interest. LSTIM: light pressure. HSTIM: hard painful pressure. axSpA: axial spondyloarthritis. HC: healthy control.

insula bilaterally, somatomotor areas along the central sulcus, fusiform gyrus, middle frontal gyrus, and the area at the PF junction (Fig 2). Decreased activity was seen in occipitotemporal areas, occipitoparietal areas, frontal pole, and precentral sulcus, bilaterally.

When comparing axSpA vs HC responses to LSTIM and HSTIM (within and between groups), there were statistically significant differences in 3 ROIs: the fusiform gyrus, the PF junction, and the frontal pole (Fig 3). At the level of the fusiform gyrus (involved in visual processing and pain anticipation), axSpA patients had a decreased signal over time in response to HSTIM compared to LSTIM, while the opposite was seen in HC. The PF junction, which is part of the salience network (SN), is involved in cognitive functions and pain processing. AxSpA patients had more pronounced response with HSTIM compared to LSTIM at the level of the PF complex compared with no difference in stimulus response in HC. The frontal pole, including the anterior cingulate cortex and medial prefrontal cortex, and part of the DMN, is involved in cognitive functions and modulating chronic pain. In the axSpA group, there was an increased signal over time in response to HSTIM compared to LSTIM; this signal was decreased in HC.

Conclusion: In this proof-of-concept exploratory study, patients with active axSpA had altered brain response to painful stimuli at regions encompassing SN and DMN, which have been previously implicated in chronic pain conditions. Further studies are planned to characterize central nervous system dysregulation and its role in chronic pain in larger cohorts of axSpA patients.

Disclosure: M. Bittar: None; **Y. Lee**: CVS Health, 12, GE Healthcare, 12, Tonix, 1; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **J. Barton**: None; **A. Stevens**: None.

Abstract Number: 1425

Quantifying Functional Impact of Structural Damage in Psoriatic Arthritis: Insights from a Long-Term Prospective Cohort

Pankti Mehta[1], Shangyi Gao[2], Virginia Carrizo Abarza[3], Fadi Kharouf[4], Dafna D. Gladman[5], Vinod Chandran[6] and Denis Poddubnyy[7], [1]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [2]Gladman-Krembil Psoriatic Arthritis Research Program, Centre for Prognosis Studies in the Rheumatic Diseases, Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, Toronto, ON, Canada, [3]University of Toronto, Toronto, [4]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada, [7]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) significantly affects physical function (PF), which is influenced by both disease activity and structural damage. Despite its clinical importance, there is limited quantitative data on how radiographic damage impacts PF in PsA. This study aimed to assess the relationship between radiographic damage and PF in PsA patients.

Methods: We analyzed data from a large, prospectively enrolled cohort of PsA patients followed since 1978. Assessments were performed every six months, including evaluations of disease activity, patient-reported outcomes, and treatment details. Radiographs were obtained every two years. Disease activity was measured by swollen joint count (SJC), and PF was assessed using the Health Assessment Questionnaire (HAQ; 0-3) and the Short Form 36 (SF-36) PF domain score (0-100). Radiographic damage was scored using the modified Steinbrocker scoring system (mSS, 0-168). Only patients with PF data collected within three months of their radiographs were included in the analysis.

Baseline characteristics at enrollment were summarized. Cumulative probability plots were created to illustrate visit-to-visit changes in both mSS scores and PF scores. Multivariable linear mixed models (LMM) were used to examine the association between PF measures (HAQ and SF-36 PF) and mSS, adjusting for covariates including age at PsA diagnosis, disease activity (SJC at the time of radiographs), sex, and disease duration. Further, we assessed the severity of joint damage (any joint graded 2, 3, or 4) and the number of severely damaged joints (graded 2, 3, or 4) per patient for their association with SF-36 PF using LMM, adjusting for SJC, age at PsA diagnosis, sex, and disease duration.

Results: Among 1,177 patients, the mean age at enrollment was 44.61 ± 12.76 years, and 657 (55.8%) were male. The median mSS was 2 (IQR 0, 8.5), HAQ was 0.62 (IQR 0.12, 1.12), and SF-36 PF score was 60 (IQR 35, 85) at enrollment. The mSS change scores in relation to the corresponding HAQ and SF-36 PF change scores are presented in Figure 1.

The mSS showed significant associations with both HAQ (b = 0.003, 95% CI 0.002 to 0.004) and SF-36 PF (-0.10; 95% CI -0.15 to -0.05), after adjusting for disease activity (SJC), age at PsA diagnosis, sex, and disease duration (Table 1). While the presence of a damaged joint was not significantly associated with PF, the number of severely damaged joints (graded 2, 3,

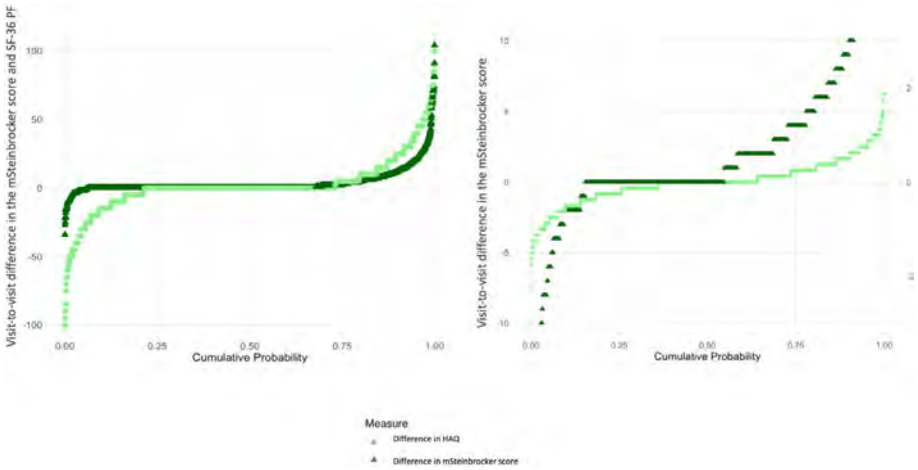


Figure 1: Cumulative probability plots reflecting visit-to-visit change scores of the modified Steinbrocker score with SF-36 PF (A) and HAQ (B)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Association between mSteinbrocker score and physical function using multivariable linear mixed models

	HAQ, 0-3				SF-36 PF, 0-100			
	Estimate	95% CI		p-value	Estimate	95% CI	p-value	
Modified Steinbrocker's score, 0-168	0.003	0.002	0.004	<0.001	-0.10	-0.15	-0.05	<0.001
SJC, 0-68	0.039	0.034	0.044	<0.001	-1.54	-1.77	-1.30	<0.001
Age at PsA diagnosis, years	0.005	0.003	0.008	<0.001	-0.19	-0.30	-0.07	0.002
Sex, male	-0.298	-0.365	-0.231	<0.001	12.30	9.35	15.26	<0.001
Duration of PsA, years	0.006	0.004	0.009	<0.001	-0.20	-0.31	-0.08	<0.001

Abbreviations: SF: Short Form, HAQ: Health Assessment Questionnaire, SJC: Swollen Joint Count, PsA: Psoriatic Arthritis

or 4) per patient was significantly associated with both HAQ (b = 0.01, 95% CI 0.001 to 0.01) and SF-36 PF (-0.22, 95% CI -0.37 to -0.07).

Conclusion: Structural damage, as quantified by the mSS , is significantly associated with physical function in PsA, independent of disease activity and other factors. Specifically, a one-unit increase in the mSS corresponds to a 0.003 increase in HAQ and 0.10 decrease in SF-36 PF. While the presence of a single damaged joint does not notably affect PF, the cumulative number of severely damaged joints is significantly associated with a decline in PF. These findings underscore the importance of early diagnosis and effective management of PsA to preserve physical function and prevent structural damage.

Disclosure: P. Mehta: None; **S. Gao**: None; **V. Carrizo Abarza**: None; **F. Kharouf**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6.

Abstract Number: 1426

Understanding the Drivers of BASDAI and Back Pain Scores in Psoriatic Arthritis

Pankti Mehta[1], Fadi Kharouf[2], Virginia Carrizo Abarza[3], Shangyi Gao[4], Dafna D. Gladman[5], Vinod Chandran[6] and Denis Poddubnyy[7], [1]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [2]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [3]University of Toronto, Toronto, [4]Gladman-Krembil Psoriatic Arthritis Research Program, Centre for Prognosis Studies in the Rheumatic Diseases, Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Ontario, Canada, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada, [7]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

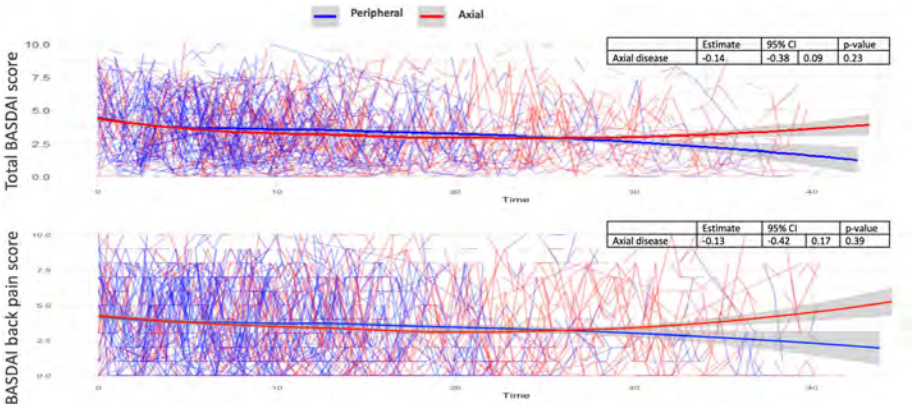


Figure 1: Smooth trajectories of BASDAI and BASDAI back pain over follow-up

Background/Purpose: The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is the most commonly used tool to assess axial disease in psoriatic arthritis (PsA). However, five of its six questions focus on general disease activity rather than being specific to axial involvement. Furthermore, back pain itself is a non-specific symptom and is potentially affected by many factors. This raises concerns regarding the utility of the BASDAI back pain question for monitoring axial disease in a multidomain disease like PsA. We aimed to evaluate the utility of the BASDAI and its back pain subscore in assessing axial disease in patients with PsA.

Methods: Patients with available BASDAI scores (done every 6 months after 1999) were selected from a large longitudinally assessed PsA cohort initiated in 1978. These patients are followed every six months with comprehensive documentation of demographic data, clinical and patient-reported outcomes, and treatment details. Axial disease was defined as sacroiliitis (modified New York criteria) and/or syndesmophytes. The trend of BASDAI and back pain was studied across axial and peripheral subgroups over the follow-up duration. The association of axial disease with total BASDAI and BASDAI back pain scores was studied using multivariable linear mixed models (LMM) for the whole cohort, adjusting for swollen joint count (SJC), tender joint count (TJC), enthesitis, dactylitis, Psoriasis Area and Severity Index (PASI), modified Steinbrocker score, and drug use. Drivers of BASDAI and BASDAI back pain scores were studied in the peripheral and axial subgroups using multivariable GEE models.

Results: Of 1,059 patients, 610 (57.6%) had peripheral disease, 449 (42.39%) had axial involvement at any time over their follow-up. The mean age was 44.4 years (SD 12.8), with 55.9% being males.

The BASDAI and back pain scores were similar between the axial and peripheral subgroups (Figure 1).

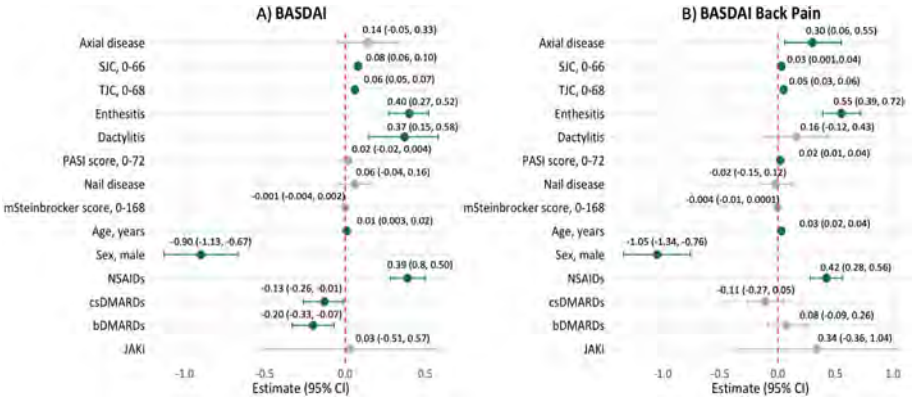


Figure 2: Multivariable linear mixed models for association of axial disease with BASDAI and BASDAI back pain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

When compared to patients with peripheral disease, the presence of axial involvement did not show an association with BASDAI [β -0.14 (-0.05 to 0.33)] after adjustment for confounders. However, the presence of axial disease was associated with a small but significant effect on the BASDAI back pain subscore [β 0.3 (0.06 to 0.55)] as compared to peripheral disease. (Figure 2)

Among patients with axial disease, higher BASDAI back pain scores were positively associated with TJC [β 0.06 (95% CI: 0.074–0.08)], enthesitis [0.49 (0.25-0.74)], PASI score [0.03 (90.02–0.05)], along with age and sex. In patients with peripheral disease only, BASDAI back pain was significantly driven by SJC [0.05 (0.01-0.08], TJC [0.05 (0.03-0.07)], enthesitis [0.62 (0.40-0.84)] and PASI score [0.04 (0.02-0.07)] along with age and sex.

Conclusion: BASDAI and BASDAI back pain scores are influenced by age, sex, peripheral joint (arthritis, enthesitis), and skin involvement in PsA, regardless of axial involvement. Similar factors drive this association in patients with axial and peripheral disease. These findings highlight that the BASDAI back pain question is not a reliable outcome measure for assessing axial disease in PsA

Disclosure: P. Mehta: None; **F. Kharouf**: None; **V. Carrizo Abarza**: None; **S. Gao**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6.

Abstract Number: 1427

Impact of Biologic Therapy on Subclinical Atherosclerosis and Ventricular Function in Psoriatic Arthritis

Rebeca L. Polina-Lugo[1], Oscar Azael Garza-Flores[2], Fernanda M. Garcia-Garcia[3], Esteban C. Garza-Gonzalez[4], Ricardo I. De la Rosa-Vazquez[5], Victoria P. Limas-Martínez[5], Annette Dominguez-Guerra[5], Jesus Alberto Cardenas-de la Garza[6], Iris J. Colunga-Pedraza[3], Dionicio A. Galarza-Delgado[3], Jose R Azpiri-Lopez[7], Victor M Fraga-Enriquez[8] and Diego Azamat Salcedo Almanza[9], [1]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, San Nicolas de los Garza, Nuevo Leon, Mexico, [5]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [6]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [7]Cardiology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [8]Cardiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [9]Radiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of carotid ultrasound

	Patients with biologic therapy (n=49)	Patients without biologic therapy (n=49)	P-Value
Age, years, mean ± SD	51.9±11.7	51.9±10.53	0.98
Women, n (%)	27 (55.1)	27 (55.7)	1.00
Diabetes, n (%)	17 (14.2)	17 (34.6)	0.13
Hypertension, n (%)	17 (34.6)	17 (34.6)	1.0
Dyslipidemia, n (%)	26 (53.6)	16 (32.6)	**0.04**
Active smoking, n (%)	11 (22.4)	12 (24.4)	0.80
Disease duration, years, median (IQR)	12 (7.0-20.0)	8 (3.0-16.0)	0.10
DAPSA, median, (IQR)	13.2 (7.2-22.0)	15.1 (11.0-33.0)	0.15
BMI, mean ± SD	29.1±5.3	30.5±5.7	0.20
Subclinical atherosclerosis			
Carotid plaque, n (%)	21 (42.8)	20 (40.8)	0.54
Unilateral plaque, n (%)	13 (26.5)	8 (16.3)	0.21
Bilateral plaque, n (%)	8 (16.3)	12 (24.4)	0.31

SD, Standard deviation; IQR, Interquartile range; DAPSA, Disease Activity Index for Psoriatic Arthritis; BMI, Body mass index.

Background/Purpose: Patients with psoriatic arthritis (PsA) have an increased cardiovascular (CV) risk due to a higher prevalence of comorbidities and chronic systemic inflammation. In those with an inadequate response to conventional synthetic disease-modifying antirheumatic drugs, biologic therapy is recommended. Previous studies have shown that inhibition of proinflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-1, and IL-6, exerts beneficial effects on cardiac function and could prevent the development of atherosclerosis. However, current evidence remains limited. For this reason, we aim to associate the use of biologic therapy with the presence of subclinical atherosclerosis and left ventricular (LV) function in patients with PsA.

Methods: A Cross-sectional, descriptive, comparative study was conducted. Patients aged 30 to 75 with PsA who met the 2006 CASPAR Classification criteria were included. Those with CV disease history were excluded. Patients were divided into two groups: those without biologic therapy and those receiving biologic treatment for at least one month. Patients receiving biologic therapy were matched 1:1 based on age, sex, and the presence of at least two cardiovascular risk comorbidities.

Carotid ultrasound was performed on 98 participants, carotid plaque (CP) was defined as a diffuse carotid intima-media thickness (IMT) ≥1.2 mm or focal thickness ≥0.8 mm. The transthoracic echocardiogram was performed on 60 patients, which included left ventricular mass index (LVMI), relative wall thickness (RWT), and left ventricular ejection fraction (LVEF). Subclinical systolic dysfunction (SSD) of the left ventricle (LV) was defined as a global longitudinal strain (GLS) >-18%. Group distribution was evaluated using the Kolmogorov-Smirnov test. Comparisons were made using the Chi-square, T-student, or Mann-Whitney U tests. A p-value ≤0.05 was considered statistically significant.

Table 2. Transthoracic echocardiogram characteristics

	Patients with biologic therapy (n=30)	Patients without biologic therapy (n=30)	P-Value
Age, years, mean ± SD	54.0±13.0	55.1±12.2	0.73
Women, n (%)	18 (60.0)	18 (60.0)	1.0
Diabetes, n (%)	6 (20.0)	7 (34.6)	0.75
Hypertension, n (%)	12 (40.0)	7 (23.3)	0.16
Dyslipidemia, n (%)	17 (56.6)	13 (43.3)	0.30
Active smoking, n (%)	9 (30.0)	9 (30.0)	0.36
Disease duration, years, mean ± SD	18.0±11.3	11.7±11.8	**0.04**
DAPSA, mean ± SD	18.4±14.8	22.8±23.6	0.40
BMI, mean ± SD	30.2±5.7	28.9±4.8	0.37
Left Ventricular assessment			
LVMI, mean ± SD	86.7±32.1	100±51.6	0.21
RWT, median (IQR)	0.42 (0.34-0.46)	0.40 (0.37-0.47)	0.77
LVEF, mean ± SD	60.8±6.0	60.1±5.0	0.64
E/E' ratio, mean ± SD	8.0±2.0	8.3±2.6	0.45
SSD, n (%)	4 (13.3)	3 (10.0)	0.61
GLS, mean ± SD	-19.7±2.5	-19.9±4.0	0.83

SD, Standard deviation; IQR, Interquartile range; DAPSA, Disease Activity index for Psoriatic Arthritis; BMI, Body mass index; LVMI, left ventricular mass index; RWT, relative wall thickness; LVEF, left ventricular ejection fraction; SSD, subclinical systolic dysfunction.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In both populations, most patients were women with anti-TNF therapy. Among the 98 patients who underwent carotid ultrasound (Table 1), the median duration of biologic treatment was 26 months (IQR 12–60). Dyslipidemia was significantly more prevalent in the biologic therapy group (p=0.041), while no significant differences were found for other comorbidities. The prevalence of CP was lower in patients not receiving biologic therapy (40.8%, p=0.54).

In the group of 60 patients who underwent echocardiography (Table 2), 30 were receiving biologic therapy, with a mean treatment duration of 44.0 ± 50.7 months. No significant differences in CV risk comorbidities were observed between groups. The LVMI was higher in patients without biologic therapy, but other echocardiographic parameters showed no statistically significant differences.

Conclusion: According to our data, biological therapy is not associated with the prevalence of carotid plaque or left ventricular function. However, this may be due to the short duration of biological therapy use among patients. While biologics are essential for managing disease activity, larger prospective studies are needed to determine their impact on CV risk assessment.

Disclosure: R. Polina-Lugo: None; **O. Garza-Flores**: None; **F. Garcia-Garcia**: None; **E. Garza-Gonzalez**: None; **R. De la Rosa-Vazquez**: None; **V. Limas-Martínez**: None; **A. Dominguez-Guerra**: None; **J. Cardenas-de la Garza**: None; **I. Colunga-Pedraza**: None; **D. Galarza-Delgado**: None; **J. Azpiri-Lopez**: None; **V. Fraga-Enriquez**: None; **D. Salcedo Almanza**: None.

Abstract Number: 1428

Ankylosing Spondylitis Related Mortality Trends in USA from 1999-2020: Analysis of CDC Wonder Database

Sanjana Thimmannagari[1], Shiamak Cooper[2], Asim Khanfar[1] and Candrika Dini Khairani[1], [1]Rochester General Hospital, Rochester, NY, [2]Rochester General Hospital, Irondequoit, NY

SESSION INFORMATION

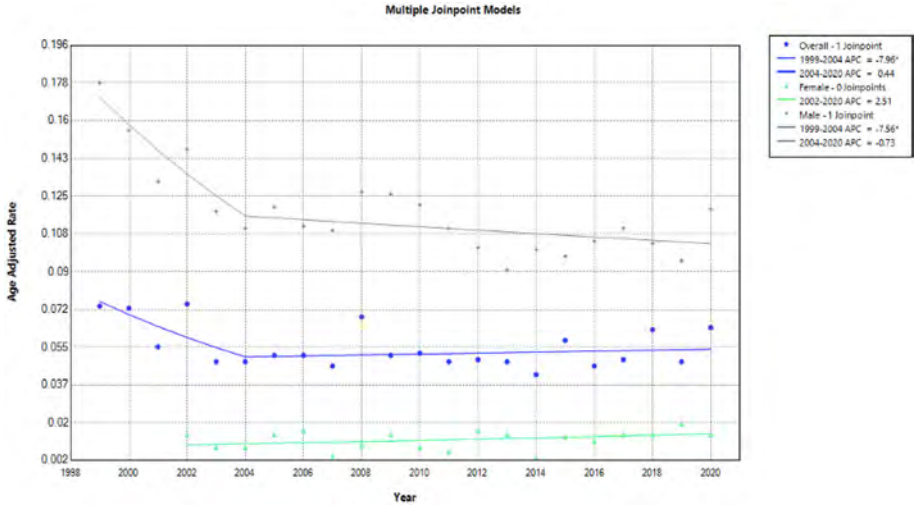
Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing spondylitis is a significant cause of mortality and morbidity in the United States (US), with a prevalence of 0.2%–0.5%. However, trends in mortality among patients with ankylosing spondylitis in the US remain unclear. Therefore, we aim to analyze mortality trends in patients with ankylosing spondylitis in the US from 1999 to 2020, stratified by year, sex, and rural-urban status.

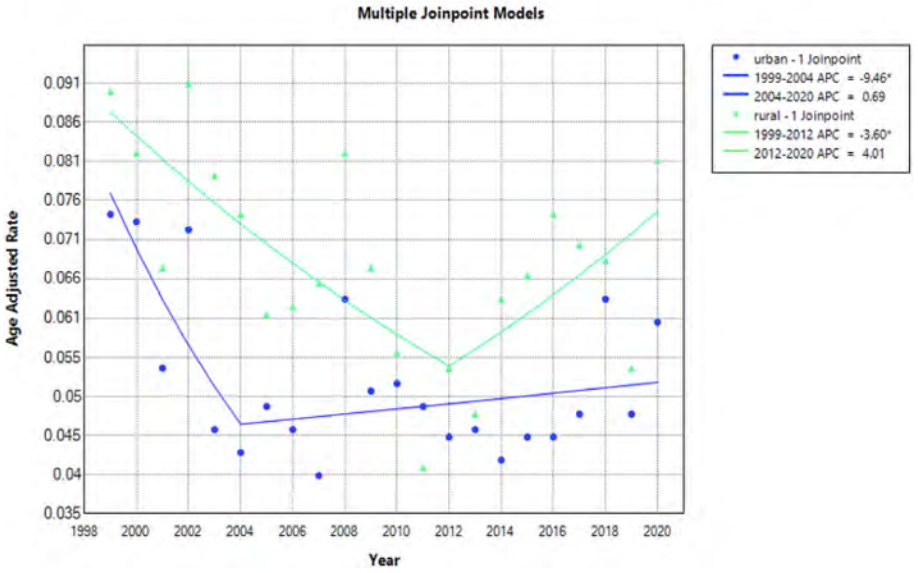
Methods: Age-adjusted mortality rates (AAMR) per 100,000 individuals were obtained from the Centers of Disease Control and Prevention WONDER database from the years of 1999-2020. Joinpoint regression was applied to calculate the annual percentage change (APC) to evaluate significant differences in the change of AAMR over time.

Results: A total of 4405 deaths occurred in patients with Ankylosing Spondylitis from 1999 to 2020. The AAMR declined from 1999 to 2004 (APC -7.96 [-23.02, -1.43]) and remained stable from 2004 to 2020 (APC 0.44 [-0.95, 8.57]). Among females, AAMRs were stable from 2002 to 2020 (APC 2.51 [-0.99, 6.68]). Among males, the AAMR declined from 1999 to 2004 (APC -7.56 [-18.71, -2.31]) and remained stable from 2004 to 2020 (APC -0.73 [-1.76, 4.68]). The AAMR in urban

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Annual Percentage Change in Ankylosing Spondylitis-Related Mortality by Year and Gender



Annual Percentage Change in Ankylosing Spondylitis-Related Mortality by Urban Status

areas declined from 1999 to 2004 (APC -9.46 [-25.62, -1.70]) and remained stable from 2004 to 2020 (APC 0.69 [-0.99, 9.63]). In rural areas, the AAMR declined from 1999 to 2012 (APC -3.60 [-11.60, -1.57]) and then increased from 2012 to 2020 (APC 4.01 [-0.001, 18.745]).

Conclusion: From 1999 to 2020, ankylosing spondylitis mortality initially declined but later plateau. Mortality rates remained constant in females and urban areas, while rural areas had increased mortality after 2012. These potential disparities warrant further research into quality of care delivered and phenotype of disease based on sex and rural status.

Disclosure: S. Thimmannagari: None; **S. Cooper**: None; **A. Khanfar**: None; **C. Khairani**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1429

Survival Outcomes in Elderly Patients with Axial Spondyloarthritis and Concomitant Cancer

Savannah Bowman[1], Mei Li[2], Xiudong Lei[3], Hui Zhao[3], Juan Ruiz[4], Sharon H. Giordano[3], Alexis Ogdie[5] and Maria Suarez-Almazor[6], [1]Baylor College of Medicine, Houston, [2]The University of Texas Health Science Center at Houston, Houston, [3]The University of Texas MD Anderson Cancer Center, Houston, [4]Hospital Alemán, Buenos Aires, Argentina, [5]University of Pennsylvania, Philadelphia, PA, [6]MD Anderson Cancer Center, Houston, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is associated with several comorbidities, including cancer. Prior studies have shown that elderly patients with rheumatoid arthritis and concomitant breast or prostate cancer have worse survival outcomes than patients with cancer alone. Our objective was to examine survival outcomes in elderly patients with recently diagnosed cancer, with or without axSpA, as there are currently no studies investigating survival outcomes in this population.

Methods: We conducted a population-based study using Medicare claims linked to the Surveillance, Epidemiology, and End Results (SEER) to examine overall survival (OS) and cancer-specific survival (CSS) in patients aged ≥ 66 with 1 of the 4 most common types of cancer (breast, prostate, lung, colorectal) diagnosed between 2006-2019 with or without axSpA. Patients in the axSpA cohorts were required to have ≥2 claims with an ICD 9/10 diagnosis of axSpA. For the non-axSpA cancer controls, we excluded patients with claims for connective tissue diseases. Patients with axSpA were matched to 2-5 controls using cancer type, age at cancer diagnosis, sex, stage, and year of cancer diagnosis. We investigated OS and CSS (censored at 5 years). Kaplan-Meier (KM) analysis and log-rank tests assessed survival time in patients with or without axSpA. Cox proportional hazard regression models were performed for each cancer, with analysis adjusted for competing risks for CSS.

Results: There were a total of 6103 patients (2061 breast, 1988 prostate, 1234 lung, 820 colorectal) with axSpA matched with 29,004 controls in this study (Table 1). Mean ages ranged from 74 (breast, prostate, lung) to 77 (colorectal) (Table 1). Table 2 shows the results of 5-year OS and CSS estimates and Cox regressions within each type of cancer. No statistically significant differences were observed in OS or CSS between patients with or without axSpA, for breast, prostate or lung cancer. For colorectal cancer, patients with axSpA had a decreased risk of death compared to patients without axSpA: 5-year

Table 1: Distribution of baseline demographics for matched axSpA and non-axSpA patients by cancer types.

	Breast		Prostate		Lung		Colorectal	
	axSpA	Non-axSpA	axSpA	Non-axSpA	axSpA	Non-axSpA	axSpA	Non-axSpA
Total patients	2061	9727	1988	9600	1234	5747	820	3930
Mean age (SD)	74.46 (6.23)	74.46 (6.26)	73.61 (5.59)	73.58 (5.60)	74.64 (5.82)	74.58 (5.77)	77.20 (6.76)	77.15 (6.74)
Sex (%)								
Female	2061 (100)	9727 (100)	--	--	815 (66.05)	3742 (65.11)	534 (65.12)	2539 (64.61)
Male	--	--	1988 (100)	9600 (100)	419 (33.95)	2005 (34.89)	286 (34.88)	1391 (35.39)
Race/ Ethnicity (%)								
Hispanic	83 (4.03)	590 (6.07)	83 (4.18)	615 (6.41)	29 (2.35)	269 (4.68)	51 (6.22)	260 (6.62)
White	1822 (88.40)	7942 (81.65)	1716 (86.32)	7615 (79.32)	1133 (91.82)	4802 (83.56)	724 (88.29)	3179 (80.89)
Black	101 (4.90)	631 (6.94)	114 (5.73)	864 (9.00)	47 (3.81)	374 (6.51)	21 (2.56)	286 (7.28)
Other	55 (2.67)	564 (5.80)	75 (3.77)	506 (5.27)	25 (2.03)	302 (5.25)	24 (2.93)	205 (5.22)
Cancer Extent (%)								
In situ	168 (8.15)	791 (8.13)	--	--	NR (NR)	NR (NR)	26 (3.17)	123 (3.13)
Localized	1458 (70.74)	6859 (70.52)	1632 (82.09)	7879 (82.07)	>575 (>46.60)	>2690 (>46.80)	433 (52.80)	2072 (52.72)
Regional	382 (18.53)	1823 (18.74)	228 (11.47)	1102 (11.48)	373 (30.23)	1739 (30.26)	309 (37.68)	1484 (37.76)
Distant	53 (2.57)	254 (2.61)	128 (6.44)	619 (6.45)	274 (22.20)	1307 (22.74)	52 (6.34)	251 (6.39)

Patients with axSpA were matched to controls using cancer type, age at cancer diagnosis, sex, stage, and year of cancer diagnosis (within 2 years).
Abbreviations: axSpA= axial spondyloarthritis, SD= standard deviation, NR = not reportable due to Centers for Medicare & Medicaid Services suppression rule for cell size < 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Survival outcomes and hazard ratios (HR) for patients with or without axSpA.

	Breast	Prostate	Lung	Colorectal
OVERALL SURVIVAL				
5-year probability (95% CI)				
axSpA	0.83 (0.81-0.85)	0.81 (0.79-0.83)	0.41 (0.37-0.44)	0.67 (0.63-0.71)
Non-axSpA	0.83 (0.82-0.83)	0.82 (0.81-0.83)	0.41 (0.40-0.43)	0.63 (0.61-0.65)
Log-rank p value	0.81	0.17	0.85	**0.03**
HR (95% CI)*	0.87 (0.76-1.00)	0.95 (0.84-1.08)	0.94 (0.86-1.03)	**0.72 (0.62-0.83)**
p value	0.051	0.44	0.18	**<0.0001**
CANCER-SPECIFIC SURVIVAL				
5-year probability (95% CI)				
axSpA 5-year	0.95 (0.94-0.96)	0.96 (0.95-0.97)	0.68 (0.65-0.71)	0.91 (0.88-0.93)
Non-axSpA 5 year	0.96 (0.95-0.96)	0.96 (0.95-0.96)	0.71 (0.70-0.73)	0.87 (0.86-0.89)
Log-rank p value	0.47	0.82	0.34	**0.02**
HR (95% CI)*	1.07 (0.80-1.43)	1.00 (0.75-1.35)	1.10 (0.96-1.25)	**0.73 (0.55-0.97)**
p value	0.64	0.99	0.16	**0.03**

*Cox regression with non-axSpA group as reference value, adjusted for covariates. Covariates included cancer stage, cancer subtype (for breast cancer: hormone receptor positive, HER2-positive, and triple negative; for lung cancer: small cell, adenocarcinoma, and squamous cell carcinoma), age at diagnosis, frailty index, marital status, cancer treatment (surgery, radiation, chemotherapy, and hormonal therapy where applicable), Charlson comorbidity index, Yost socioeconomic quintile, and poverty quartile.
Abbreviations: axSpA= axial spondyloarthritis, HR= hazard ratio, CI= confidence interval.

OS hazard ratio (HR): 0.72 (95% CI: 0.62-0.83, p=< 0.0001) and CSS HR: 0.73 (95% CI: 0.55-0.97, p=0.03) (Table 2).

Conclusion: Elderly patients with axSpA and concomitant breast, prostate, and lung cancer had similar OS and CSS compared to patients with cancer alone. Elderly patients with axSpA and concomitant colorectal cancer were associated with increased OS and CSS compared to patients without axSpA. Further research is needed to explore the potential reasons for longer survival in elderly patients with colorectal cancer and axSpA compared to those without axSpA.

Disclosure: S. Bowman: None; **M. Li**: None; **X. Lei**: None; **H. Zhao**: None; **J. Ruiz**: None; **S. Giordano**: None; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **M. Suarez-Almazor**: Novartis, 5, SetPoint Medical, 2, Syneos Health, 2.

Abstract Number: 1430

Redefining BASDAI cut-offs: implications for patients' eligibility for initiating biologic disease-modifying antirheumatic treatment in axial spondyloarthritis

Stylianos Georgiadis[1], Lykke Ørnbjerg[1], Brigitte Michelsen[2], Tore K. Kvien[2], Mehrdad Shoae Kazemi[1], Bente Glintborg[1], Anne Gitte Loft[3], Rita Fonseca[4], Helena Santos[5], Andreas Reich[6], Anne C. Regierer[6], Jarno Rutanen[7], Laura Kuusalo[8], Gary Macfarlane[9], Gareth T. Jones[9], Adrian Ciurea[10], Michael J. Nissen[11], Bjorn Gudbjornsson[12], Olafur Palsson[13], Ziga Rotar[14], Katja Perdan Pirkmajer[15], Daniela Di Giuseppe[16], Merete Hetland[17] and Mikkel Ostergaard[18], [1]Rigshospitalet, Glostrup, Denmark, [2]Diakonhjemmet Hospital, Oslo, Norway, [3]Aarhus University Hospital, Aarhus, Denmark, [4]Unidade Local de Saúde de Entre Douro e Vouga, Santa Maria da Feira, Portugal, [5]Instituto Português de Reumatologia, Lisbon, Portugal, [6]German Rheumatology Research Center, Berlin, Germany, [7]Tampere University Hospital, Tampere, Finland, [8]Turku University Hospital, Turku, Finland, [9]University of Aberdeen, Aberdeen, United Kingdom, [10]University Hospital Zurich, Zurich, Switzerland, [11]Geneva University Hospital, Geneva, Switzerland, [12]Landspitali University Hospital; Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [13]University of Iceland, Reykjavik, Iceland, [14]University Medical Centre Ljubljana, Ziri, Slovenia, [15]University Medical Centre Ljubljana, Ljubljana, Slovenia, [16]Karolinska Institutet, Department of Medicine Solna, Clinical Epidemiology Division, Stockholm, Stockholms Lan, Sweden, [17]Copenhagen Center for Arthritis Research (COPECARE) and DANBIO, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; Department of Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark, [18]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: In patients with axial spondyloarthritis (axSpA), high disease activity is a key indication for biological disease-modifying antirheumatic drug (bDMARD) initiation. The Axial Spondyloarthritis Disease Activity Score (ASDAS) criterion (ASDAS≥2.1) is recommended for defining high disease activity, but the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) criterion (BASDAI≥4) can be used if ASDAS is unavailable [1]. We aimed to compare a newly proposed BASDAI cut-off for high disease activity (BASDAI≥2.5) [2] with ASDAS≥2.1 as an eligibility criterion for bDMARD initiation.

Methods: Prospectively collected real-world data from registries participating in the European Spondyloarthritis (EuroSpA) collaboration were analysed. Patients with axSpA initiating a tumour necrosis factor inhibitor or an interleukin-17A inhibitor as their first bDMARD between 2015 and 2023 were included. Analyses were limited to patients who had complete data on ASDAS and BASDAI at baseline and had attended a 6-month visit. Patients were categorised into 4 subgroups according to baseline ASDAS (≥2.1) and BASDAI (≥2.5) cut-offs for high disease activity. Treatment effect was assessed at 6 months by the Assessment of SpondyloArthritis international Society (ASAS) response measures (ASAS20 and ASAS40). Logistic regression analyses were performed to compare the achievement of treatment effect according to the ASDAS (≥2.1) and BASDAI (≥2.5) cut-offs for high disease activity.

Results: We analysed data from 6,329 patients with axSpA from 9 European registries. Most patients (n=5,753; 91%) fulfilled both ASDAS (≥2.1) and BASDAI (≥2.5) eligibility criteria at baseline, while 243 (4%) patients fulfilled neither of them (Table 1). The number of patients fulfilling either ASDAS or BASDAI criterion alone were 161 (3%) and 172 (3%), respectively. Baseline patient characteristics in the overall cohort and in subgroups are presented in Table 1. The subgroup fulfilling both eligibility criteria demonstrated the highest ASAS20 and ASAS40 responses at 6 months (68% and 52%, respectively) (Table 2). Among patients who only fulfilled the ASDAS or BASDAI criterion alone, similar ASAS20 (37% and 39%) and ASAS40 (17% and 15%) responses were achieved. The results of the regression analyses showed that fulfilling either ASDAS or BASDAI criterion was significantly associated with achieving ASAS20 and ASAS40 responses (Figure 1). When both criteria were included in the regression analyses, ASDAS≥2.1 and BASDAI≥2.5 were positive predictors of treatment effect at 6 months.

Table 1. Baseline patient characteristics in overall cohort and in subgroups according to baseline ASDAS and BASDAI cut-off values for high disease activity

Patient characteristic	Overall cohort n=6,329	ASDAS≥2.1 and BASDAI≥2.5 n=5,753 (91%)	ASDAS≥2.1 and BASDAI<2.5 n=161 (3%)	BASDAI≥2.5 and BASDAI≥2.5 n=172 (3%)	ASDAS<2.1 and BASDAI<2.5 n=243 (4%)
Age at treatment start, years	42 (33-51)	42 (33-51)	40 (31-49)	40 (33-48)	40 (32-49)
Time since diagnosis, years	2 (1-8)	2 (1-8)	2 (1-8)	3 (1-7)	3 (1-8)
Time since symptom onset, years	8 (3-16)	8 (3-16)	8 (2-14)	8 (3-14)	6 (2-13)
Male, n (%)	3,807 (60%)	3,438 (60%)	112 (70%)	93 (54%)	164 (67%)
BMI, kg/m²	26.2 (23.2-29.3)	26.3 (23.3-30.0)	24.8 (22.2-27.7)	25.0 (23.1-27.3)	25.1 (22.6-27.5)
Smoking status, current, n (%)	1,841 (31%)	1,709 (32%)	43 (29%)	37 (23%)	52 (24%)
Radiographic axSpA*, n (%)	2,723 (84%)	2,621 (84%)	38 (78%)	29 (67%)	35 (71%)
Concomitant csDMARD, n (%)	1,612 (28%)	1,449 (27%)	50 (34%)	51 (32%)	62 (29%)
HLA-B27 positive, n (%)	4,459 (78%)	4,067 (78%)	108 (77%)	115 (82%)	169 (79%)
CRP, mg/l	10.7 (4.0-21.0)	11.1 (4.2-22.0)	18.0 (11.0-30.0)	1.8 (1.0-3.0)	3.0 (1.0-6.0)
Patient pain assessment, 0-10	7 (5-8)	7 (5-8)	3 (2-4)	3 (2-4)	2 (1-3)
Patient fatigue assessment, 0-10	7 (5-8)	7 (6-8)	2 (1-4)	4 (3-6)	2 (1-3)
Patient global assessment, 0-10	7 (5-8)	7 (6-8)	3 (2-5)	3 (2-4)	2 (1-3)
Physician global assessment, 0-10	6 (3-7)	6 (4-7)	4 (2-6)	3 (2-5)	2 (1-5)
HAQ, 0-3	1.0 (0.6-1.4)	1.0 (0.6-1.4)	0.6 (0.2-0.8)	0.5 (0.2-0.8)	0.2 (0.1-0.5)
BASDAI, 0-10	6.0 (4.6-7.3)	6.2 (5.0-7.4)	1.9 (1.5-2.3)	3.4 (2.9-3.9)	1.5 (0.9-1.9)
BASFI, 0-10	4.9 (2.8-6.7)	5.2 (3.3-6.9)	1.4 (0.6-2.4)	2.2 (1.0-3.4)	0.9 (0.3-1.7)
ASDAS	3.6 (3.0-4.3)	3.7 (3.2-4.3)	2.5 (2.3-2.9)	1.9 (1.7-2.0)	1.5 (1.2-1.8)

Values are given as median (25th-75th percentile) unless otherwise stated. Results were calculated based on available data. *Radiographic axSpA was defined by bilateral grade 2–4 or unilateral grade 3–4 sacroiliitis on plain radiographs, according to the modified New York criteria (30).

ASAS: Assessment of SpondyloArthritis international Society, ASDAS: Axial Spondyloarthritis Disease Activity Score based on CRP, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, bDMARD: biologic Disease-Modifying Anti-Rheumatic Drug, BMI: Body Mass Index, csDMARD: conventional synthetic Disease-Modifying Anti-Rheumatic Drug, CRP: C-reactive protein, HAQ: Health Assessment Questionnaire, HLA-B27: Human Leukocyte Antigen B27, GDP: gross domestic product.

Table 2. Treatment effect at 6 months in overall cohort and in subgroups according to baseline ASDAS and BASDAI cut-off values for high disease activity

	Overall cohort	ASDAS≥2.1 and BASDAI≥2.5	ASDAS≥2.1 and BASDAI<2.5	BASDAI≥2.5 and BASDAI≥2.5	ASDAS<2.1 and BASDAI<2.5
Response measure	n=6,329	n=5,753 (91%)	n=161 (3%)	n=172 (3%)	n=243 (4%)
ASAS20	3,767 (65%)	3,611 (68%)	53 (37%)	61 (39%)	42 (19%)
ASAS40	2,824 (48%)	2,759 (52%)	25 (17%)	24 (15%)	16 (7%)

Values are given as number (percentage). Percentages were calculated based on available ASAS20 and ASAS40 data at 6 months.

ASAS: Assessment of SpondyloArthritis International Society; ASDAS: Axial Spondyloarthritis Disease Activity Score based on CRP; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

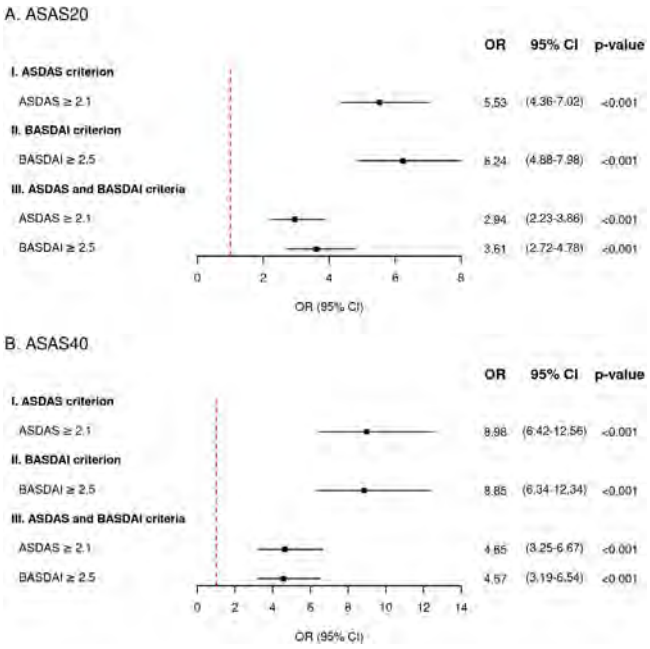


Figure 1. Forest plots of odds ratios with 95% confidence intervals for achieving ASAS 20 and ASAS40 at 6 months derived by logistic regression models including I. ASDAS criterion alone, II. BASDAI critetion alone, and III. both ASDAS and BASDAI criteria. Logistic regression analyses were adjusted for sex, age and GDP per capita (1,000$), as a proxy for socio-economic status of registries. ASAS: Assessment of SpondyloArthritis international Society; ASDAS: Axial Spondyloarthritis Disease Activity Score based on CRP; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CI: confidence interval; OR: odds ratio.

Conclusion: In a multinational European cohort, similar numbers of patients were eligible for treatment with bDMARDs when applying either ASDAS≥2.1 or BASDAI≥2.5 as the eligibility criterion. Patients with ASDAS≥2.1 and BASDAI≥2.5 demonstrated the best response to bDMARD treatment. These findings support the use of BASDAI≥2.5 as an indication for biologic treatment in axSpA, particularly when ASDAS is not available.

References

1. Ramiro *et al*. (2023). *Ann Rheum Dis*, 82(1), 19-34.
2. Georgiadis *et al*. (2025). Under review.

Disclosure: S. Georgiadis: Novartis, 5, UCB, 5; **L. Ørnbjerg**: Novartis, UCB, 5; **B. Michelsen**: Novartis, 2, 5, Pfizer, 5; **T. Kvien**: Abbvie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 5, Celltrion, 2, Galapagos, 2, 5, Gilead, 2, Grünenthal, 6, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 2, 6, UCB, 2, 5, 6; **M. Shoae Kazemi**: None; **B. Glintborg**: alfasigma, 5, Eli Lilly, 5, Pfizer, 5, Sandoz, 5; **A. Loft**: Janssen, 6, UCB, 1, 6; **R. Fonseca**: None; **H. Santos**: Abbvie, 2, 6, Eli Lilly, 6, Janssen, 6, Novartis, 6, Pfizer, 2, 6; **A. Reich**: None; **A. Regierer**: Amgen, 6, Pharma Deutschland, 6; **J. Rutanen**: None; **L. Kuusalo**: None; **G. Macfarlane**: None; **G. Jones**: Amgen, 5, Pfizer, 5, Shionogi, 5, UCB, 6; **A. Ciurea**: None; **M. Nissen**: AbbVie/Abbott, 2, 12, Payment to institution, Amgen, 2, 12, Payment to institution, Eli Lilly, 2, 12, Payment

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

to institution, Janssen, 2, 6, 12, Support for conference participation. Payment to institution, Novartis, 2, 5, 6, 12, Payment to institution, Pfizer, 2, 12, Payment to institution, UCB, 2, 12, Support for conference participation. Payment to institution; **B. Gudbjornsson**: None; **O. Palsson**: None; **Z. Rotar**: None; **K. Perdan Pirkmajer**: None; **D. Di Giuseppe**: None; **M. Hetland**: AbbVie/Abbott, 1, 5, Alfasigma, 5, Eli Lilly, 5, Novartis, 6, Pfizer, 5, 6, Sandoz, 5, 6, UCB, 5, 6; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6.

Abstract Number: 1431

Radiographic Sacroiliitis in Psoriatic Arthritis: Clinical, Laboratory, and Spinal Radiographic Correlates in an Indian Cohort

SUBIN PHILIP[1], RITESH KUMAR MISHRA[2], RIZWANA NAUSHAD[1], Lovely Kumari[3], Vishnu Koneru[4], Aishwarya Gopal[5], Christina Mariaselvam[6], Chengappa Kavadichanda[7], Ananthakrishnan Ramesh[1], Molly Thabah[1] and VIR SINGH NEGI[1], [1]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, PUDUCHERRY, Puducherry, India, [2]JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH, Bhubaneswar, India, [3]Jawaharlal Institute of Postgraduate Medical Education and Research,PUDUCHERRY, PUDUCHERRY, Puducherry, India, [4]JIPMER, Hyderabad, Telangana, India, [5]Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, Puducherry, India, [6]Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, Puducherry, India, [7]Jawaharlal Institute of Postgraduate Medical Education and Research, pondicherry, Puducherry, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial involvement in psoriatic arthritis (PsA) is variable and influences treatment choices. Data on axial PsA in Indian patients, especially its clinical and radiographic features, are limited. We aimed to describe these features and their association with radiographic sacroiliitis in an Indian PsA cohort.

Methods: Patients with PsA fulfilling CASPAR criteria were enrolled between April 2024 and March 2025. Demographic, clinical, and laboratory data were collected. Pelvis and spine radiographs were independently scored for sacroiliitis (modified New York criteria) and spinal damage by modified Stokes ankylosing spondylitis score (mSASSS). Patients were stratified by sacroiliitis status, and group comparisons were made using appropriate statistical tests and odds ratios (ORs).

Results: Of 182 consecutively enrolled patients (table 1), radiographic sacroiliitis was present in 85 (46.7%). Thirty of these 85 (35%) radiographic sacroiliitis patients had no clinical axial symptoms. Asymmetric oligoarthritis was the most common pattern of presentation observed as per Moll and Wright Classification (figure-1A). Radiographic sacroiliitis patients were older (mean age 49.6 vs. 45.3 years, p=0.01), had longer disease duration (median 6 vs. 3 years, p=0.01). Axial symptoms (spondylitis ± inflammatory back pain) were more frequent in the sacroiliitis group (51.9% vs. 29.9%, p=0.04; OR 2.5, 95% CI 1.3–4.6), including *HLA-B*27* positivity (16.9% vs. 1.0%, p< 0.001; OR 19.2, 95% CI 2.4–151.0). Other clinical features, including peripheral disease patterns, nail changes, enthesitis, dactylitis, and inflammatory markers did not significantly differ.

On spinal radiography (table 2), lumbosacral (LS) spine bridging syndesmophytes were significantly more frequent (35.3% vs. 8.0%, p< 0.001; OR 6.3, 95% CI 2.5–15.0), and LS spine mSASS were higher (median 8 vs. 4, p=0.001). Cervical spine syndesmophytes were also more common in the sacroiliitis group (70.6% vs. 54.4%, p=0.03). The C5, C6, and L4 vertebrae were most frequently involved, and were also frequently damaged with syndesmophytes including non-marginal bridging

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Clinical and lab parameters of Psoriatic Arthritis with or without Radiographic Sacroiliitis

Variable	Total (n=182)	Sacroiliitis Absent n=97	Sacroiliitis Present n= 85	OR (95% CI), P Value
Demographic				
Age (years), mean	47.4 (11.3)	45.3 (11.1)	49.6 (10.8)	**0.01**
Age at Onset	41.9 (11.2)	40.8(10.4)	42.9(11.9)	**0.01**
Age>40 years	140 (75.3)	66(68)	70(82.4)	**2.1(1.0-4.4), 0.04**
Sex Male Female	93 (50) 93 (50)	48 (49.5) 49 (50.5)	44 (51.8) 41 (48.2)	0.95(0.7-1.2), 0.76
Total Duration of disease, years (IQR)	4 (2-8)	3 (2-7)	6 (2-10)	**0.01**
Early Disease (<2 years)	69 (37.1)	44 (45.4)	23 (27.1)	**0.4(0.2-0.8), 0.01**
Employed Unemployed	127 (68.3) 59 (31.2)	69 (71.1) 28 (28.9)	56(65.9) 29(54.1)	0.7(0.4-1.4), 0.5
H/o Smoking	29 (15.6)	16 (16.5)	12 (14.1)	0.8(0.3-1.8), 0.68
Family History of AIRD	21 (11.3)	10 (10.3)	9 (10.6)	1(0.3-2.8), 1.00
Clinical				
H/o Inflammatory Back Pain	99 (53.2)	44 (45.4)	55 (63.5)	**2(1.1-3.8), 0.017**
BMI	25.3 (4.9)	25.5 (5.2)	25.3 (4.7)	0.82
Obesity (BMI>25)	95 (51.1)	50 (51.5)	44 (51.8)	1.0(0.56-1.8), 1.0
Swollen Joint Count (IQR)	1 (0-2)	0 (0-2)	1 (0-2)	0.16
Tender Joint Count (IQR)	2 (0-3)	2 (0-3)	2 (0-3)	0.42
Active Joints	127 (68.3)	66 (67)	61 (69.4)	1.1(0.5-2), 0.75
Nail Changes of Psoriasis	88 (47.3)	47(48.5)	41 (47.1)	0.9(0.5-1.6), 0.8
Dactylitis	48 (25.8)	25 (25.8)	22(25.9)	1(0.5-1.9), 1.00
Uveitis	1 (0.5)	0	1 (1.1)	0.4(0.3-0.5), 0.46
Enthesitis	71 (38)	39 (40.2)	30 (35.3)	0.8(0.4-1.4), 0.85
MASES	0 (0-1)	0.46 (0-1)	0.55 (0-1)	**0.02**
Modified Schober, cm	5.18 (1.4)	5.48 (1.3)	4.85 (1.4)	**0.003**
Tragus to Wall, cm	10.86 (2.9)	10.37 (2.9)	11.35 (2.7)	**0.02**
Cervical Rotation	78.4 (12.5)	81.6 (8.0)	74.9 (15.6)	**0.00**
Cervical Restriction <75 degrees	50 (26.9)	19 (18.6)	31 (35.3)	**2.3(1.2-4.7), 0.01**
BASMI	2.42 (1.09)	2.11 (0.86)	2.76 (1.23)	**0.00**
DAPSA	20.8 (14.4-32.1)	20 (14.3-30.7)	22 (14-33)	0.16
ASDAS CRP	5.9 (3.6-11.1)	5.8 (3.7-10.1)	6.7 (4.2-12.2)	0.20
hsCRP (g/L)	8.34 (3.8-16.1)	7.8 (3.4-14.8)	8.8 (5.1-18.6)	0.20
Elevated hsCRP	147 (79)	73 (75.3)	74 (84.7)	1.8(0.8-3), 0.14
*HLA-B*27* Positive	14 (7.5)	1 (1)	13 (16.9)	**19.2(2.4-151), 0.00**
Wright and Moll classification				
Asymmetric Oligoarthritis	108 (58.1)	55 (56.7)	49 (57.6)	1(0.5-1.8), 1.00
Symmetric Polyarthritis	70 (37.6)	39 (40.2)	31 (36.5)	0.8(0.4-1.5), 0.64
DIP Predominant	22 (11.8)	12 (12.4)	10 (11.8)	0.9(0.3-2.3), 1.00
Spondylitis +/- Sacroiliitis (classified based on symptoms of Inflammatory Back pain and Examination)	74 (39.8)	29 (29.9)	44 (51.9)	**2.5(1.3-4.6), 0.04**
Treatment Characteristics	**Methotrexate : 163 (87.6), Sulfasalazine : 14 (7.5), Leflunomide : 9 (4.6), NSAIDs: 21 (11.3), bDMARDs: 13 (7)**			

Results expressed as mean ± standard deviation, median (IQR) or frequency (%)

ones (figure-1B). Though age at onset, age >40 years, history of inflammatory back pain, MASES, Bath Ankylosing Spondylitis Metrology Index (BASMI) components, restriction of cervical rotation, cervical spine radiological changes including bridging syndesmophytes as well as mSASSS were also significantly higher on univariate analysis. But on multivariate logistic

Table 2: Cervical and lumbosacral spine radiological involvement in PsA patients with or without radiographic sacroiliitis

Variable	**Total n=182**	**Sacroiliitis Absent n=97**	**Sacroiliitis Present n= 85**	**OR (95% CI), P Value**
Cervical Spine				
Any Change*	125 (67.2)	58 (61.1)	64(73.5)	**1.9 (1-3.6), 0.05**
Erosions or Squaring or Sclerosis	54 (29)	31(34.4)	23 (27)	0.7(0.3-1.3), 0.32
Syndesmophytes	109 (58.6)	49(54.4)	60 (70.6)	**2(1-3.7), 0.03**
Bridging Syndesmophytes	58 (31.2)	23 (25.6)	35 (41.2)	**2(1-3.8), 0.037**
mSASS	4 (0-9)	4.0 (0-7)	7.0 (0-12)	**0.006**
Lumbosacral Spine				
Any Changes*	138 (74.2)	68 (77.3)	70 (82.4)	1.3(0.6-2.9), 0.45
Erosions or Squaring or Sclerosis	43 (23.1)	22 (26.1)	19 (23.5)	0.9(0.4-1.8), 1.0
Syndesmophytes	132 (71)	64 (72.7)	68 (80)	1.5(0.7-3), 0.28
Bridging Syndesmophytes	37 (19)	7 (8)	30 (35.3)	**6.3(2.5-15), 0.00**
Lumbosacral Spine mSASS	6 (2-11)	4 (2-8)	8 (3-13)	**0.001**
Total mSASS	11 (4-19)	9 (4-16)	13 (5-24)	**0.000**
SI Joint Changes (Grade)	**Asymmetric/Unilateral:** 44 (31.2%), **Any:** 108 (68.8%), **Grade 1:** 43 (14.3%), **Grade 2:** 45 (15%), **Grade 3:** 75 (25%), **Grade 4:** 21 (6.9%)			

*Includes erosions, squaring, sclerosis or syndesmophytes. Results are expressed as mean ± standard deviation, median (25th -75th IQR) or frequency (%). ***Abbreviations***: mSASSS, modified Stokes Ankylosing Spondylitis Spinal Score.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

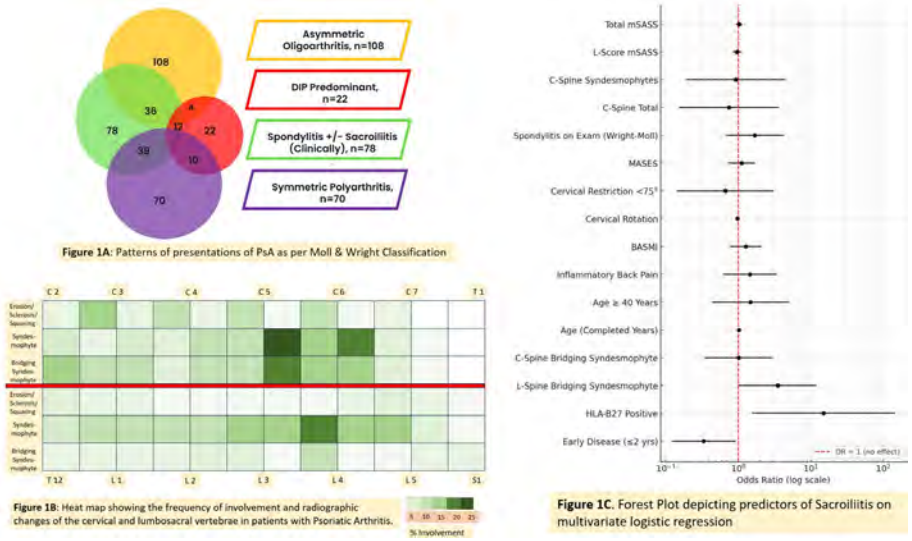


Figure 1A: Patterns of presentations of PsA as per Moll & Wright Classification Figure 1B: Heat map showing the frequency of involvement and radiographic changes of the cervical and lumbosacral vertebrae in patients with Psoriatic Arthritis. Figure 1C. Forest Plot depicting predictors of Sacroiliitis on multivariate logistic regression

regression only *HLA-B*27*, LS spine bridging syndesmophytes emerged as independent predictors of radiographic sacroiliitis (figure-1C), while shorter disease duration was associated with low odds of radiographic sacroiliitis.

Conclusion: Radiographic sacroiliitis was prevalent in nearly 47% patients in this Indian PsA cohort, often occurring without clinical axial symptoms. *HLA-B*27* positivity, and LS spine bridging syndesmophytes were significantly associated with sacroiliitis, while those with disease duration < 2 years had a lower odds of sacroiliitis. These findings support the role of early routine imaging to detect subclinical axial involvement and guide management.

Disclosure: S. PHILIP: None; **R. MISHRA**: None; **R. NAUSHAD**: None; **L. Kumari**: None; **V. Koneru**: None; **A. Gopal**: None; **C. Mariaselvam**: None; **C. Kavadichanda**: None; **A. Ramesh**: None; **M. Thabah**: None; **V. NEGI**: None.

Abstract Number: 1432

Long-term Radiographic Progression in Early versus Established Axial Spondyloarthritis: A 12-Year Observational Study

Tae-Hwan Kim[1], Bora Nam[2], Jung Ho Yang[3], So-Young Bang[4], Ji Hui Shin[5], Seunghun Lee[6] and **Tae-jong Kim**[7], [1]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, South Korea, [3]Department of Preventive Medicine, Graduate School of Chonnam National University, Gwangju, Republic of Korea, [4]Hanyang University, Seoul, Republic of Korea, [5]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [6]College of Medicine, Hanyang University, Seoul, Republic of Korea, [7]Department of Rheumatology, Chonnam National University Medical School and Hospital, Gwang-Ju, South Korea

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1 Comparative Analysis of Baseline Clinical Characteristics Categorized by ASAS Early axSpA Definition

Characteristics	Early (n = 115)	Established (n = 330)	P - value
Duration from Axial Symptom Onset to Diagnosis, (Mean ± SD)	0.80 ± 0.77	8.17 ± 5.92	<0.001
Sex (female), (%)	17 (14.7)	27 (8.2)	0.041
Age at spinal symptom onset, (Mean ± SD)	27.52 ± 9.69	20.81 ± 8.05	<0.001
Familial History, (%)	11 (9.6)	27 (8.2)	0.648
History of Psoriasis, (%)	8 (6.9)	6 (1.8)	0.012
History of Inflammatory Bowel Disease, (%)	0 (0.0)	4 (1.2)	0.577
History of Uveitis, (%)	42 (36.5)	143 (43.3)	0.194
History of Peripheral Arthritis, (%)	61 (53.0)	140 (42.4)	0.049
CRP, (Mean ± SD)	3.15 ± 3.41	2.58 ± 2.79	0.111
HLA-B27, (%)	111 (96.5)	317 (96.1)	>0.999

axSpA: axial spondyloarthritis; TNF: tumor necrosis factor; CRP: C reactive protein; HLA: human leukocyte antigen; mSASSS: the modified Stokes AS Spinal Score

Table 2

Table 2 Univariable and Multivariable Analysis of mSASSS change over 12 years in Patients According to ASAS Early axSpA Definition

Characteristics	Univariable			Multivariable		
	Coefficients	95% CI	*P* - value	Coefficients	95% CI	*P* - value
Sex (female)	-0.434	-0.795, -0.073	0.018	-0.405	-0.755, -0.054	0.024
Age at the onset of spinal symptom	0.009	-0.003, 0.021	0.161	0.009	-0.004, 0.021	0.177
History of Uveitis	0.355	0.137, 0.572	0.001	0.379	0.169, 0.590	<0.001
History of Peripheral Arthritis	-0.578	-0.789, -0.367	<0.001	-0.61	-0.830, -0.391	<0.001
Time averaged CRP	0.021	-0.029, 0.071	0.408	0.044	-0.005, 0.094	0.077
HLA-B27	0.073	-0.492, 0.639	0.799			
Proportion of TNF-α blocker Exposure	-0.09	-0.343, 0.162	0.482			
Early axial Spondyloarthritis (ASAS definition)	-0.201	-0.448, 0.046	0.111	-0.147	-0.399, 0.105	0.253

axSpA: axial spondyloarthritis; CRP: C reactive protein; HLA: human leukocyte antigen; mSASSS: the modified Stokes AS Spinal Score; TNF: tumor necrosis factor.

Background/Purpose: This study evaluates the impact of the ASAS definition of early axial spondyloarthritis (axSpA) on radiographic progression over a 12-year period, utilizing the Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) to compare early and established disease stages.

Methods: Data from the Korean spondyloarthropathy registry were used in this retrospective observational study to categorize patients into early or established axSpA according to the ASAS criteria. Radiographic progression was assessed through annual changes in mSASSS, scored independently by two radiologists. Linear regression and other statistical analyses were performed to examine the correlation between early axSpA status and radiographic progression, adjusting for relevant covariates.

Results: The study included time intervals at 0-4, 0-6, 0-8, 0-10, and 0-12 years, involving 445 patients. Results showed no statistically significant differences in mSASSS changes between the early and established axSpA groups, suggesting similar rates of progression irrespective of TNF-α blocker therapy. Both univariable and multivariable analyses demonstrated that early axSpA status did not significantly impact changes in mSASSS.

Conclusion: Our findings indicate that the ASAS criteria for early stage axSpA do not significantly affect long-term radiographic outcomes, challenging the assumption that early identification and treatment of axSpA based on these criteria alter radiographic progression.

Disclosure: T. Kim: Samsung Bioepis, 5; **B. Nam**: None; **J. Yang**: None; **S. Bang**: None; **J. Shin**: None; **S. Lee**: None; **T. Kim**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1433

Identifying Predictors of Difficult-to-Manage Axial Spondyloarthritis: Real-World Insights from a Taiwanese Registry Cohort

Yen-An Chang and Ming-Han Chen, Division of Allergy, Immunology & Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, Taipei, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1405–1433) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The concept of Difficult-to-Manage Axial Spondyloarthritis (D2M-ax-SpA) was recently introduced by the Assessment of Spondyloarthritis International Society (ASAS). According to this new definition, D2M-ax-SpA is characterized by (a) failure of ≥2 biologic or targeted synthetic DMARDs (b/tsDMARDs) with different mechanisms of action (MOAs), (b) persistent disease activity, and (c) symptoms considered problematic by either the patient or rheumatologist.

This study is among the first to evaluate the real-world prevalence and clinical predictors of D2M-ax-SpA using this newly proposed definition.

Methods: We conducted a retrospective cohort study of patients with axial spondyloarthritis (ax-SpA) enrolled between January 2009 and December 2021 at Taipei Veterans General Hospital. Inclusion criteria included fulfillment of the ASAS classification criteria and ≥6 months of follow-up. Patients were categorized into three groups: D2M-ax-SpA (per ASAS definition), those treated with b/tsDMARDs with only one MOA, and those who never received b/tsDMARDs. Demographic, radiographic, and laboratory data were analyzed. Group comparisons were performed using the Mann–Whitney U and Fisher's exact tests. Univariate and multivariate logistic regression were conducted to identify predictors of D2M-ax-SpA, and ROC curve analysis was applied to assess the predictive performance of laboratory markers.

Results: Among 560 patients with ax-SpA (all HLA-B27 positive), 20 (3.6%) met the criteria for D2M-ax-SpA. Ninety-four patients received b/tsDMARDs with a single MOA, while 446 were treatment-naïve to b/tsDMARDs. Compared to the other groups, patients with D2M-ax-SpA had significantly longer disease duration (median 3890 vs. 3292 and 2034 days, $p< 0.01$), more frequent peripheral arthritis ($p< 0.01$), higher grades of sacroiliitis on plain radiography ($p< 0.01$), and elevated ESR and CRP levels ($p< 0.01$). In multivariate analysis, peripheral arthritis emerged as an independent predictor of D2M-ax-SpA (OR: 4.68, 95% CI: 1.74–12.60, $p=0.0022$). ROC analysis demonstrated that ESR and CRP were strong predictive markers, each with an AUC of 0.785 ($p< 0.0001$), and optimal thresholds identified as ESR >20 mm/hr and CRP >0.99 mg/dL.

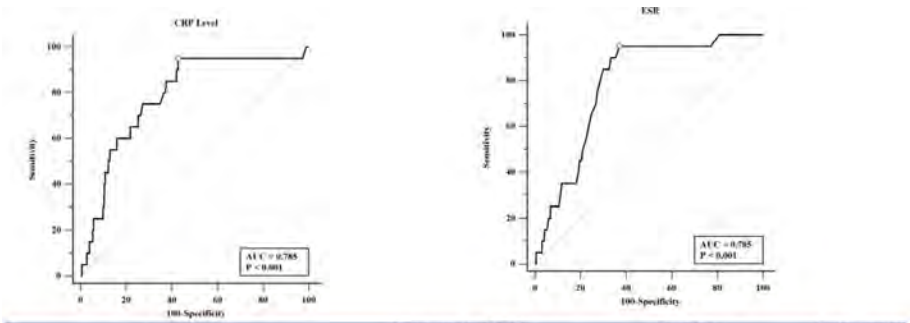
	D2M (n=20)	MOA1 (n=94)	no biologics (n=448)	P value
age at diagnosis (median)	35	30	30	0.441
age at diagnosis>30	12 (60%)	45 (47.87%)	220 (49.33%)	0.611
disease duration (days)	3890	3292	2034.5	<0.01
gender				
male	12 (60%)	72 (76.60%)	338 (75.78%)	0.265
female	8 (40%)	22 (23.40%)	108 (24.22%)	
symptom/signs				
uveitis	3 (15%)	8 (8.51%)	55 (12.33%)	0.524
peripheral	10 (50%)	22 (23.40%)	42 (9.42%)	<0.01
enthesitis	3 (15%)	20 (21.28%)	48 (10.76%)	0.019
sacroiliitis	3	3	2	<0.01
syndesmophyte	5 (25%)	32 (34.04%)	90 (20.18%)	0.014
Lab data				
ESR	33.5	39	10	<0.01
CRP	2.69	1.75	0.4	<0.01

Baseline Characteristics of the Axial Spondyloarthritis Cohort at Taipei Veterans General Hospital

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	univariate analysis			multivariate analysis		
	odds ratio	95% CI	P value	odds ratio	95% CI	P value
gender	2.1026	0.8412 to 5.2554	0.1118			
uveitis	1.43	0.3979 to 5.1128	0.59			
peripheral	6.70	2.6400 to 17.4449	<0.01	4.6848	1.7420 to 12.5993	0.0022
enthesitis	0.9	0.2439 to 3.3244	0.87			
sacroiliitis	1.979	1.1813 to 3.3154	0.0095	1.6291	0.9442 to 2.8109	0.0795
syndesmophyte	0.37	0.1042 to 1.3135	0.12			
ESR	1.0291	1.0144 to 1.0439	<0.01	1.0153	0.9969 to 1.0340	0.1047
CRP	1.2391	1.0929 to 1.4048	0.008	1.0772	0.9165 to 1.2661	0.3669

Univariate and Multivariate Logistic Regression Analysis Identifying Predictors of Difficult-to-Manage Axial Spondyloarthritis (D2M-ax-SpA)



	Area under ROC	P value	Cutoff point
ESR	0.785	<0.0001	>20
CRP	0.785	<0.0001	>0.99

Receiver Operating Characteristic (ROC) Curve Analysis of Laboratory Markers Predicting D2M-ax-SpA

Conclusion: This study provides the first real-world evidence on the clinical characteristics and predictors of D2M-ax-SpA using the newly proposed ASAS criteria. Peripheral arthritis and elevated inflammatory markers (ESR, CRP) were strongly associated with treatment resistance. These findings highlight the importance of early identification of high-risk patients, which may inform treatment selection and improve long-term outcomes. Further prospective studies in larger, multi-ethnic cohorts are warranted to validate these results.

Disclosure: Y. Chang: None; **M. Chen**: None.

Abstract Number: 1434

Safety of Prescription NSAIDs in Adults with IBD: Data from a Large Administrative Claims Cohort

Adam Mayer[1], Rui Xiao[2], Meenakshi Bewtra[3], Michael George[4] and Pamela Weiss[5], [1]University of Pennsylvania/ Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]University of Pennsylvania, Philadelphia, [4]University of Pennsylvania, Philadelphia, PA, [5]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

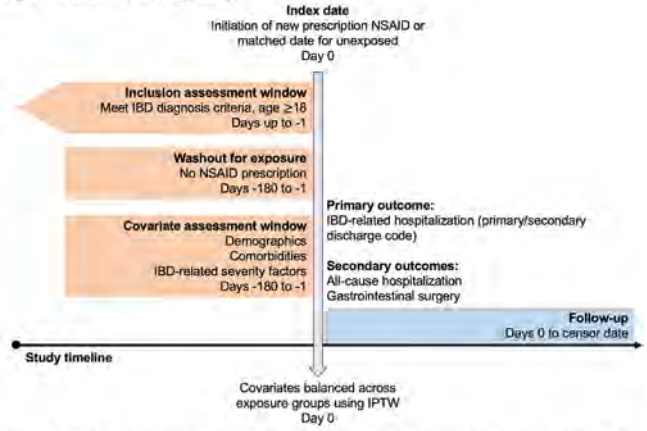
Session Time: 10:30AM–12:30PM

Background/Purpose: The potential that nonsteroidal anti-inflammatory drugs (NSAIDs) may precipitate flares of inflammatory bowel disease (IBD) has limited their use in managing joint pain in this population. We tested whether use of NSAIDs is associated with a clinically important risk of IBD-related hospitalization using a non-inferiority design.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Overview of study design



Legend: NSAID: Nonsteroidal anti-inflammatory drug; IBD: inflammatory bowel disease; IPTW: inverse probability of treatment weighting. Subjects were censored at the end of continuous enrollment, end of study period, or ≥6 months from last NSAID fill. Cox proportional hazards models for primary and secondary outcomes were adjusted for covariates that did not achieve balance by propensity scores.

Methods: This retrospective cohort study of IBD patients used administrative claims data from Optum's de-identified Clinformatics Data Mart Database (2000-2022). Patients with a new NSAID prescription fill ("exposed") were matched to those without an NSAID fill during the study period ("unexposed") by age and calendar year when IBD criteria were met (**Figure 1**). The index date for exposed patients was date of first NSAID fill; unexposed patients were assigned a matched index date based on time from meeting IBD criteria. A propensity score was calculated to balance covariates across exposure groups. The primary outcome was IBD-related hospitalization, defined as any hospitalization >1 day duration with an IBD diagnosis code as the primary or secondary discharge code. Secondary outcomes included all-cause hospitalization and gastrointestinal surgery, defined by Current Procedural Terminology codes. Propensity score-based inverse probability of treatment weighted (IPTW) Cox proportional hazards models evaluated the association between NSAID exposure and time to each primary and secondary outcome across IBD subtypes. A hazard ratio (HR) of 1.2 was set as the pre-specified non-inferiority margin based on discussions with IBD content experts on acceptable risk.

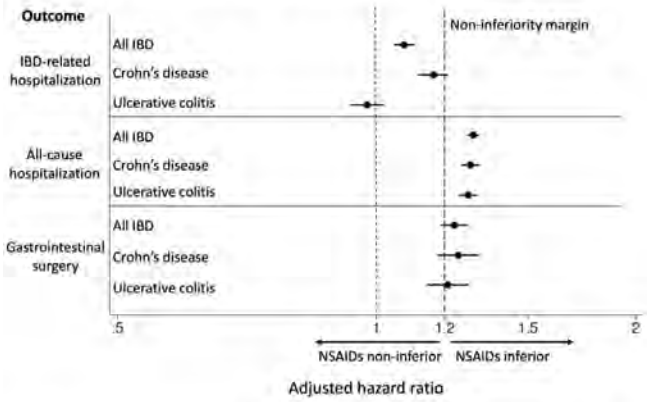
Results: Among 269,304 patients with IBD, 29.7% were NSAID exposed (**Table 1**). In the IPTW-weighted Cox model, NSAID exposure was associated with a small increase in IBD-related hospitalization in the overall IBD cohort (HR 1.08, 95% CI 1.05-1.11; **Figure 2**) but demonstrated non-inferiority (upper limit of confidence interval < 1.20). Exposed patients experienced an adjusted 0.06 IBD-related hospitalizations/person-year versus 0.05 events/person-year in the unexposed

Table 1. Unweighted cohort characteristics stratified by NSAID exposure

Factor	Total N (%) (N=269,304)	NSAID Exposed N (%) (N=79,872)	Unexposed N (%) (N=189,432)
Age, median (IQR)	52 (39, 66)	52 (40, 65)	52 (39, 66)
Female sex	155,098 (57.6)	47,477 (59.4)	107,621 (56.8)
Follow-up time (yrs), median (IQR)	0.95 (0.48, 2.78)	0.57 (0.52, 2.04)	1.15 (0.37, 3.03)
IBD subtype			
Crohn's disease	114,497 (42.5)	33,302 (41.7)	81,195 (42.9)
Ulcerative colitis	118,285 (43.9)	34,890 (43.7)	83,395 (44.0)
Indeterminate colitis	36,522 (13.6)	11,680 (14.6)	24,842 (13.1)
CCI, median (IQR)	0 (0, 2)	0 (0, 2)	0 (0, 1)
CD severity index, median (IQR)	2 (1, 4)	2 (1, 5)	2 (1, 4)
UC severity index, median (IQR)	3 (0, 6)	3 (0, 6)	3 (0, 5)
Opioid use	64,378 (23.9)	26,603 (33.3)	37,775 (19.9)
Glucocorticoid use	76,393 (28.4)	27,787 (34.8)	48,606 (25.7)
csDMARD use	111,161 (41.3)	33,028 (41.4)	78,133 (41.2)
b/tsDMARD use	39,286 (14.6)	11,297 (14.1)	27,989 (14.8)
Joint pain	106,147 (39.4)	39,643 (49.6)	66,504 (35.1)
Chronic pain	116,967 (43.4)	45,737 (56.0)	71,230 (36.9)
Gastrointestinal bleed	66,809 (24.8)	22,047 (27.6)	44,762 (23.6)

Legend: NSAID: Nonsteroidal anti-inflammatory drug; IQR: interquartile range; yrs: years; CD: Crohn's disease; UC: ulcerative colitis; CCI: Charlson comorbidity index; csDMARD: conventional synthetic disease modifying anti-rheumatic drug; b/tsDMARD: biologic/targeted synthetic disease modifying anti-rheumatic drug

Figure 2. Association between prescription NSAID exposure and time to IBD-related hospitalization, all-cause hospitalization, and gastrointestinal surgery across IBD subtypes.



Legend: Vertical dashed lines indicate: 1) null hazard ratio 1.0 and 2) the prespecified non-inferiority margin of hazard ratio 1.2 based on clinically-acceptable risk defined by IBD content experts. X-axis is log-transformed. NSAID: Nonsteroidal anti-inflammatory drug; IBD: inflammatory bowel disease

group (absolute risk difference 0.007, number needed to harm 137). No significant increase in IBD-related hospitalization was seen in the ulcerative colitis subgroup (HR 0.96, 95% CI 0.91-1.01), but there was a significant increase in those with Crohn's disease (HR 1.16, 95% CI 1.11-1.21), with non-inferiority not met. There were significantly higher rates of gastrointestinal surgery (overall HR 1.23, 95% CI 1.19-1.28) and all-cause hospitalization (overall HR 1.30, 95% CI 1.28-1.32) with neither meeting non-inferiority.

Conclusion: Prescription NSAID exposure was associated with a numerically small risk of IBD-related hospitalization below the pre-specified non-inferiority threshold. Risk was not seen in patients with ulcerative colitis, while small magnitude risks were present in those with Crohn's disease. These results challenge the current paradigm of avoiding NSAIDs in all patients with IBD and suggest that the benefits of NSAIDs may outweigh small possible risks for many patients with significant joint disease.

Disclosure: A. Mayer: None; **R. Xiao**: None; **M. Bewtra**: AbbVie/Abbott, 2, 6, GlaxoSmithKlein(GSK), 5, Iterative Health, 5, Johnson & Johnson, 2, 5, Pfizer, 2, Takeda, 5; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

Abstract Number: 1435

Impact of Treatment With Upadacitinib on Non-Nociceptive Pain and Its Relevance for the Presence of Residual Symptoms in Axial Spondyloarthritis: Results from a Multicountry Observational Study

Denis Poddubnyy[1], Victoria Navarro-Compan[2], Neil Basu[3], Mohammad Naffaa[4], Tianming Gao[5], Christopher Saffore[6], Jamie Urbanik[7], Bhumik Parikh[8], Peter Taylor[9] and Philip J. Mease[10], [1]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [2]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [3]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom, [4]The Azriel's Faculty of Medicine, Bar-Ilan University, Safed, Israel; The Rheumatology Unity, Galilee Medical Center, Naharyia, Israel, [5]AbbVie, North Chicago, IL, [6]AbbVie Inc., waukegan, IL, [7]AbbVie, Grayslake, IL, [8]AbbVie, Hillsborough Township, NJ, [9]University of Oxford, Oxford, United Kingdom,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[10]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA

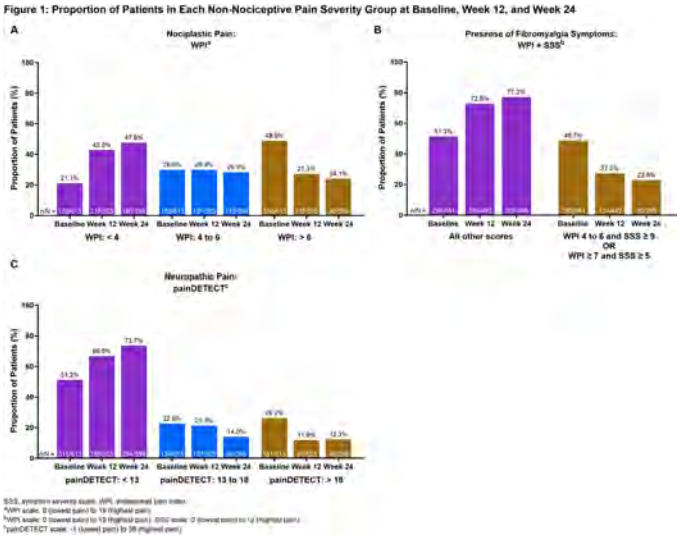
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Upadacitinib (UPA), an oral JAK inhibitor, has demonstrated improvements in inflammation and nociceptive pain in late phase clinical trials of patients with axSpA.[1,2,3] However, patients may also experience non-nociceptive pain via altered central nervous system modulation (nociplastic), including fibromyalgia (FM), or peripheral nervous system damage (neuropathic). This post hoc analysis of a real-world study in patients with axSpA examined the impact of UPA treatment on non-nociceptive pain and the association of non-nociceptive pain with residual symptoms, sleep disturbance, anxiety, and depression.

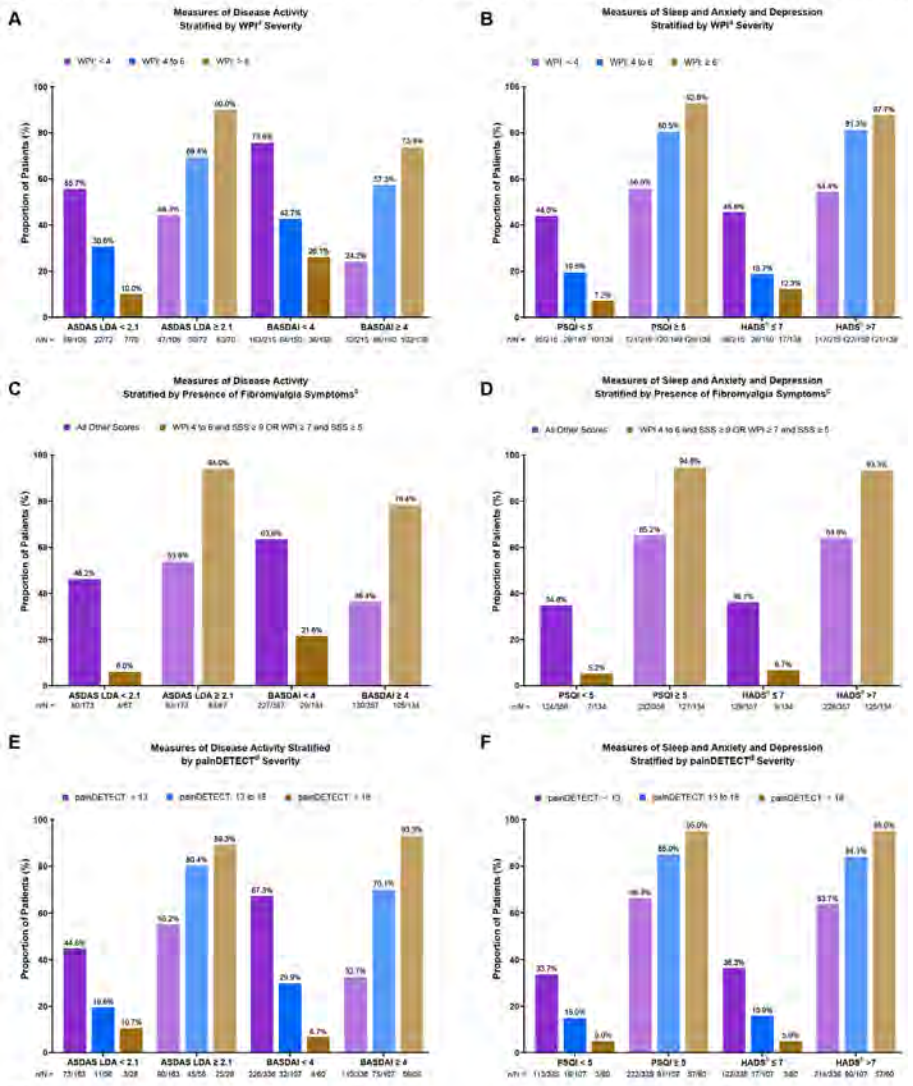
Methods: UPSTAND was a 12-month, multicountry, noninterventional, observational study evaluating the effectiveness of UPA on pain in adult patients with axSpA. Safety from UPSTAND has been previously analyzed.[4] This analysis used interim data collected after all patients completed at least week (wk) 12. Patients were grouped by severity of neuropathic pain, as captured by painDETECT (< 13, 13-18, and > 18) or severity of nociplastic pain, as captured by widespread pain index (WPI: < 4, 4-6, and > 6). While patients demonstrating active symptoms of FM per clinical diagnosis were excluded from UPSTAND, WPI and symptom severity score (SSS) were used together to assess the presence of nociplastic pain fulfilling FM criteria as per Wolfe et al. 2016: WPI 4-6 and SSS ≥ 9 or WPI ≥ 7 and SSS ≥ 5.[5] All other scores (absence of FM) were grouped together. The proportion of patients in each group was reported at baseline (BL) and wk 12. For those with available data, the proportion of patients in each group was reported at wk 24. The association of non-nociceptive pain with measures of disease activity, sleep quality, and symptoms of anxiety/depression was assessed by analyzing the proportion of patients in each group at wk 12 that did or did not achieve ASDAS low disease activity (ASDAS LDA; < 2.1), BASDAI < 4, Pittsburgh Sleep Quality Index Score < 5, and Hospital Anxiety and Depression Scale ≤ 7 at wk 12. The change from BL in total back pain, nocturnal back pain, fatigue (BASDAI question 1), and BASFI at wk 12 was reported for each group.

Figure 1: Proportion of Patients in Each Non-Nociceptive Pain Severity Group at Baseline, Week 12, and Week 24



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Achievement of Response at Week 12 Stratified by Non-Nociceptive Pain Severity at Week 12



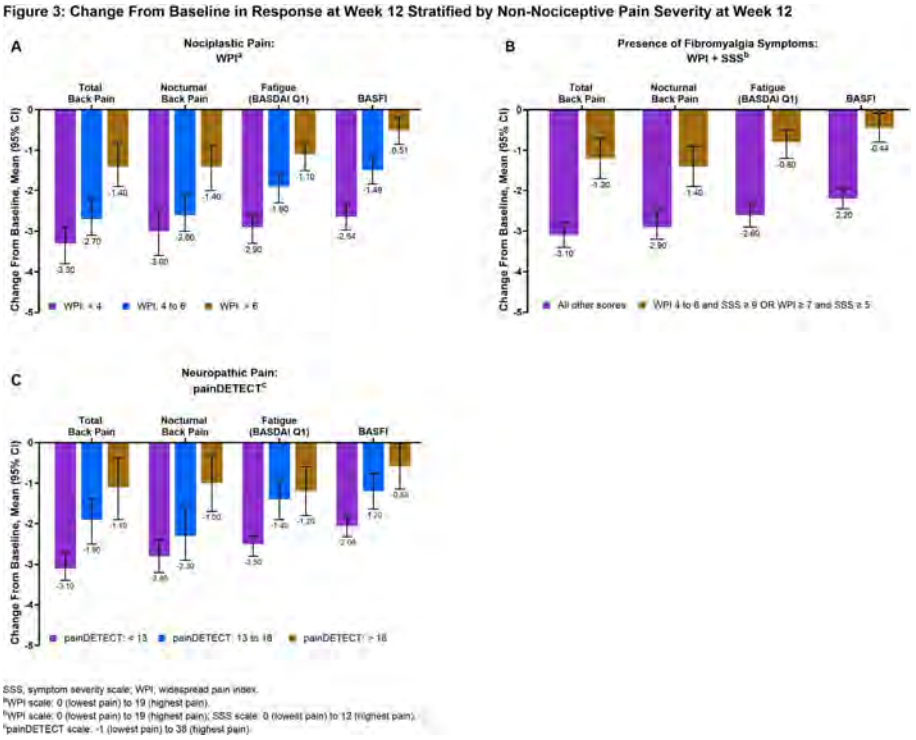
SSS, symptom severity scale; WPI, widespread pain index.
[a]WPI scale: 0 (lowest pain) to 19 (highest pain).
[b]HADS ≤ 7 indicates no depression. Scale: 0 to 21.
[c]WPI scale: 0 (lowest pain) to 19 (highest pain); SSS scale: 0 (lowest pain) to 12 (highest pain).
[d]painDETECT scale: −1 (lowest pain) to 38 (highest pain).

Results: Overall, UPA treatment was associated with a reduction in the burden of nociplastic and neuropathic pain over time (**Figure 1**). The proportion of patients in the least severe pain groups increased from BL over time; the proportion of patients in the more severe pain groups or meeting criteria for FM decreased over time. Non-nociceptive pain at wk 12 was associated with residual symptoms, anxiety/depression, and poor sleep (**Figure 2**). The presence of non-nociceptive pain was associated with smaller improvements in total back pain, nocturnal back pain, fatigue, and BASFI from BL to wk 12 (**Figure 3**).

Conclusion: In patients with axSpA, treatment with UPA was associated with improvements in non-nociceptive pain. Non-nociceptive pain was associated with residual symptoms, sleep disturbance, signs of anxiety/ depression, and fatigue.

1. van der Heijde D, et al. *Lancet*. 2019;394:2108-17.
2. van der Heijde D, et al. *Ann Rheum Dis*. 2022;81:1515-23.
3. Deodhar A, et al. *Lancet*. 2022;400:369-79.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



4. Poddubnyy D, et al. [abstract]. *Ann Rheum Dis*. 2025;83:1.
5. Wolfe F, et al. *Semin Arthritis Rheum*. 2016;46:319-29.

Disclosure: D. Poddubnyy: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **N. Basu**: AbbVie, 6, AstraZeneca, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, GSK, 2, 5, MSD, 2, Nesos, 5, Pfizer, 5, 6, Roche, 2, 6, Vifor, 2, 5, 6; **M. Naffaa**: AbbVie, 5, 6, BI, 5, Eli Lilly, 6, Pfizer, 6, Roche, 6; **T. Gao**: AbbVie, 3, 11; **C. Saffore**: AbbVie, 3, 11; **J. Urbanik**: AbbVie, 3, 11; **B. Parikh**: AbbVie, 3, 11; **P. Taylor**: AbbVie, 2, Acelyrin, Inc., 2, Alfasigma S.p.A., 2, 5, Biogen, 2, Eli Lilly & Co., 2, Fresenius Kabi, 2, Gilead, 2, Immunovant, 2, Moonlake, 2, Nordic Pharma, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB, 2; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6.

Abstract Number: 1436

Angiogenesis Markers in Difficult to Treat Psoriatic Arthritis Patients

Devy Zisman[1], Amir Haddad[2], Dunia Araide[3], Noa Hayat[2], Tal Gazitt[4], Joy Feld[5], Michal Aizenberg Peleg[1], Muhanad Abu-Elhija[1], Ameen Batheesh[1], Abdulla Watad[6], Alina Simanovich[1], Nili Stein[1], Kateryna Milman[2] and Michal Amit Rahat[1], [1]Carmel Medical Center, Haifa, Israel, [2]Carmel Medical Centre, Haifa, Israel, [3]The Ruth and Bruce Rappaport Faculty of Medicine, Technion, Haifa, HaZafon, Israel, [4]Carmel Hospital, Haifa, Israel, [5]Carmel and Zvulun Medical Centre, Haifa, Israel, [6]Tel Hashomer Medical Center, Ramat Gan, Israel

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Difficult to treat (D2T) psoriatic arthritis (PsA) presents a state of active inflammatory disease manifestations despite therapy with at least two biologic disease modifying anti-rheumatic drugs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs) with two different mechanisms of action. Inflammation and angiogenesis are interlinked processes. EMMPRIN/CD147, a multi-functional protein that can induce the expression of the pro-angiogenic matrix metalloproteinases (MMPs) and vascular-endothelial-growth factor (VEGF), also regulates the expression of the anti-angiogenic factor endostatin.

We aimed to assess the levels of pro- and anti-angiogenic factors in patients with D2T PsA patients compared to non-D2T PsA patients.

Methods: We determined the serum levels of the pro-angiogenic factors EMMPRIN/CD147, VEGF, MMP-9, MMP-9 activity, and the anti-angiogenic factors endostatin and Thrombospondin-1 (Tsp-1) in D2T PsA patients and in non-D2T controls who were stratified into two subgroups based on exposure to bDMARDs / tsDMARDS or to conventional DMARDs (biologic naïve) from a well-defined database. Each patient with D2T PsA was matched with at least one non-D2T patient of similar age and disease duration. The visit with the highest scores of articular and skin manifestations in the database was chosen for each patient. The serum levels of the biomarkers were evaluated using sandwich ELISA, and the MMP-9 activity was determined by the cleavage of its fluorescent substrate. The three patient groups were compared using Kruksal-Wallis ANOVA followed by Dunn's multiple comparisons test.

Results: 23 patients with D2T PsA, accounting for 6.7% of the database population, were matched with 25 non-D2T bDMARDs /tsDMARDs-experienced PsA controls and to 25 non-D2T biologic naive patients. The mean age of the study groups was 62.32±15.48 years with a disease duration of 19.38±11.12 years. All patients had active disease, but the D2T group had higher scores of enthesitis compared to the non-D2T bDMARDs/tsDMARDs group and higher tender and swollen joint counts and HAQ scores compared to the non-D2T biologic naïve group. No significant differences were observed in the mean dactylitis or psoriasis area and severity index (PASI) scores, nor in other patient-related outcomes among the three groups. Comparing between the D2T patients, the non-D2T biologic experienced patients, and the non-D2T biologic-naïve patients, higher levels of EMMPRIN/CD147 (26.4±1.4, 19.4±0.88, 19.7±0.86 ng/ml, respectively, $p< 0.001$), endostatin (60.9±2.8, 52.1±1.56, 50.1±1.4 ng/ml, respectively, $p< 0.048$), and of MMP-9 activity (123,861±9,446, 90,067±5,620, 89,328±6,258 RFU, respectively, $p< 0.017$) were found in the DTT group. No statistically significant differences were found in the levels of VEGF and Tsp-1 between the three groups.

Conclusion: Higher level of CD147, and increased activity of MMP-9, which we have previously linked to the regulation of the anti-angiogenic factor endostatin, were detected in D2T PsA patients' serum, suggesting their possible use as biomarkers, and indicating the complexity of the angiogenetic process in these patients, which merit further investigation.

Disclosure: D. Zisman: AbbVie/Abbott, 1, 6, AstraZeneca, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 1, Neopharm, 1, 6, Novartis, 6, Pfizer, 1, 5; **A. Haddad**: AbbVie/Abbott, 6, AstraZeneca, 6, Janssen, 6, Novartis, 6; **D. Araide**: None; **N. Hayat**: None; **T. Gazitt**: None; **J. Feld**: AbbVie/Abbott, 6; **M. Aizenberg Peleg**: None; **M. Abu-Elhija**: None; **A. Batheesh**: None; **A. Watad**: AbbVie/Abbott, 1, 6, Celgene, 1, 6, Eli Lilly, 1, 6, Janssen, 1, 6, Neopharm, 1, 6, Novartis, 1, 6; **A. Simanovich**: None; **N. Stein**: None; **K. Milman**: None; **M. Amit Rahat**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1437

Characterization of ORKA-002, a Novel Extended Half-life Monoclonal Antibody Targeting IL-17A/F for the Treatment of Psoriasis and Other Indications

Byron Kwan[1], Joseph Merola[2], Andrew Blauvelt[3], Daniel Rios[1], Joana Ministro[1], Jacob Milligan[1], Ghassan Fayad[1], Christopher Finch[4], **Eugenia Levi**[5], Joseph Senn[5], Jason Oh[1] and Hussam Shaheen[1], [1]Paragon Therapeutics, Waltham, MA, [2]UT Southwestern Medical Center, Dallas, TX, [3]Blauvelt Consulting, LLC, Annapolis, MD, [4]Oruka Therapeutics, Menlo Park, CA, [5]Oruka Therapeutics, Waltham, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin 17 (IL-17) is a pro-inflammatory cytokine that has been implicated in the pathogenesis of multiple autoimmune conditions, including psoriasis and psoriatic arthritis (PsA). The IL-17 family of cytokines includes 6 members (IL-17A to IL-17F). Both IL-17A and IL-17F are key drivers in the pathogenesis of psoriatic disease, being highly overexpressed in psoriatic plaques and the inflamed synovium of patients with PsA. Recently, a biologic targeting both IL-17A and IL-17F, bimekizumab (BIME), has demonstrated high efficacy that exceeds therapies targeting IL-17A only. ORKA-002 is a novel, extended half-life, humanized, monoclonal antibody that binds to IL-17A/F with high affinity. ORKA-002 has been engineered to have optimized properties with the aim of delivering an enhanced clinical profile compared to currently available treatments for psoriasis and other inflammatory diseases.

Methods: ORKA-002 was evaluated across multiple *in vitro* and *ex vivo* assays alongside BIME. Binding affinity to IL-17A and IL-17F was determined by surface plasmon resonance (SPR). Antagonism of IL-17A and IL-17F signaling was assessed through NFκB activation assays in reporter cell lines. Inhibition of IL-17A-induced or IL-17F-induced IL-6 secretion was measured *in vitro* using normal human dermal fibroblasts. Half-life extension was evaluated via pharmacokinetic (PK) analysis in cynomolgus monkeys following a single bolus dose of ORKA-002.

Results: ORKA-002 bound specifically to human IL-17A and IL-17F with high affinity. IL-17A/F binding affinity and functional potencies for IL-17A/F antagonism were comparable to BIME. In cynomolgus monkeys, ORKA-002 demonstrated a significantly extended half-life relative to BIME. Predictive simulations, based on allometric scaling of ORKA-002 PK parameters, suggest that in humans, subcutaneous maintenance dosing every four to six months could sustain high antibody exposures.

Conclusion: ORKA-002 exhibits high selectivity and affinity for IL-17A and IL-17F *in vitro*, potent inhibition of downstream cellular signaling *ex vivo*, and an extended half-life in non-human primates compared to BIME. These characteristics could result in comparable or increased efficacy compared to BIME with just two to three doses of ORKA-002 a year. Pre-clinical evidence for ORKA-002 reported here may lead to therapeutic improvements for psoriatic disease and other inflammatory conditions amenable to IL-17 inhibition. Clinical studies are planned to explore this potential.

Disclosure: B. Kwan: Paragon Therapeutics, 3; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **A. Blauvelt**: Oruka Therapeutics,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

4, 11; **D. Rios**: Paragon Therapeutics, 3; **J. Ministro**: Paragon Therapeutics, 3; **J. Milligan**: Paragon Therapeutics, 3; **G. Fayad**: Paragon Therapeutics, 3; **C. Finch**: Oruka Therapeutics, 3; **E. Levi**: Oruka Therapeutics, 3; **J. Senn**: Oruka Therapeutics, 3; **J. Oh**: Paragon Therapeutics, 3; **H. Shaheen**: Paragon Therapeutics, 3.

Abstract Number: 1438

Similar Efficacy of Bimekizumab in Two Clinical Endotypes of Axial Spondyloarthritis: 2-Year Results from Two Phase 3 Studies and Their Open-Label Extension

Félicie Costantino[1], Ann-Sophie De Craemer[2], Filip Van den Bosch[2], Maxime Breban[3], Vanessa Taieb[4], Diana Voiniciuc[5], Natasha de Peyrecave[6], Dirk Elewaut[7] and Maria-Antonietta D'Agostino[8], [1]Department of Rheumatology, Ambroise Paré Hospital, AP-HP, Paris, France and Infection & Inflammation, UMR 1173, Inserm, UVSQ/Université Paris Saclay, Montigny-Le-Bretonneux, France, [2]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [3]CHU Ambroise-Paré, Boulogne-Billancourt, France, [4]UCB, Colombes, France, [5]UCB, Slough, United Kingdom, [6]UCB, Brussels, Belgium, [7]VIB Center for Inflammation Research, and Ghent University Hospital, Department of Rheumatology, Ghent, Belgium, [8]Department of Rheumatology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease mainly affecting the sacroiliac joints and spine.[1] Peripheral manifestations are common, contributing to disease burden.[2] Two clinical axSpA endotypes have been identified by cluster analyses: patients (pts) with predominantly axial disease (i.e., Endotype A), and pts with axial and peripheral manifestations (i.e., Endotype B; associated with higher disease activity and reduced quality of life).[3–5]

Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown sustained efficacy and safety to Week (Wk) 104 across the full disease spectrum of axSpA in the phase 3 studies BE MOBILE 1 and 2 and their open-label extension (OLE).[6] Here, we report efficacy and safety of BKZ to Wk 104 by endotype to evaluate differences in treatment response.

Methods: Study designs of BE MOBILE 1 (NCT03928704; non-radiographic axSpA), BE MOBILE 2 (NCT03928743; radiographic axSpA) and their OLE (NCT04436640) have been reported previously.[7] From Wk 16, all pts received subcutaneous BKZ 160 mg every 4 weeks. At Wk 52, eligible pts could enroll in the OLE.

Pts pooled across studies were categorized into endotypes by a validated classification and regression tree (CART) clustering algorithm using baseline characteristics.[3]

Retention and efficacy data to Wk 104 are reported for all randomized pts (N=586). ASAS40 response and ASDAS major improvement (ASDAS-MI) are reported with non-responder imputation (NRI); ASDAS low disease activity (LDA) and ASDAS change from baseline are reported with multiple imputation (MI). Safety data are reported in pts receiving ≥1 BKZ dose (N=574).

Results: Of the 586 pts in BE MOBILE 1 and 2 and their OLE, 402 (68.6%) were categorized into Endotype A, and 184 (31.4%) into Endotype B. Baseline characteristics by endotype are shown in the **Table**. Kaplan-Meier retention rate at Wk 104 was 83.9% in both endotypes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Patient demographics and baseline characteristics, stratified by endotype

	Endotype A *Predominantly Axial Manifestations*		Endotype B *Axial and Peripheral Manifestations*		Overall
Mean (SD) unless otherwise specified	PBO → BKZ 160 mg Q4W n=169	BKZ 160 mg Q4W n=234	PBO → BKZ 160 mg Q4W n=69	BKZ 160 mg Q4W n=115	N=586
Age, years	39.0 (11.6)	40.5 (11.4)	40.2 (13.4)	40.4 (12.6)	40.0 (11.9)
Sex, male, n (%)	110 (65.5)	161 (68.8)	35 (50.7)	72 (62.6)	378 (64.5)
HLA-B27 positive, n (%)	132 (78.6)	197 (84.2)	55 (79.7)	97 (84.3)	481 (82.1)
Symptom duration, years	9.9 (8.4)	12.5 (10.8)	11.4 (10.0)	12.1 (10.0)	11.5 (9.9)
Age at axSpA onset, years	29.6 (8.6)	28.6 (8.3)	29.3 (8.4)	28.8 (8.6)	29.0 (8.5)
ASDAS	3.6 (0.7)	3.6 (0.8)[b]	3.8 (0.8)	4.0 (0.8)	3.7 (0.8)[b]
BASFI	5.0 (2.2)	5.1 (2.2)	5.8 (2.0)	5.9 (2.1)	5.3 (2.2)
ASQoL	8.4 (4.2)	8.8 (4.7)	10.5 (4.4)	10.1 (4.6)	9.1 (4.5)
SF-36 PCS	35.2 (8.6)	34.7 (8.3)[a]	31.3 (8.4)	32.5 (8.4)	34.0 (8.5)[a]
hs-CRP, mg/L, median (Q1, Q3)	7.0 (2.7, 13.2)	6.2 (1.8, 15.5)	5.9 (1.7, 19.8)	9.1 (2.6, 21.0)	7.0 (2.2, 15.9)
History of peripheral manifestations, n (%)					
Peripheral arthritis	24 (14.3)	21 (9.0)	69 (100)	115 (100)	229 (39.1)
Enthesitis[c]	94 (56.0)	133 (56.8)	65 (94.2)	93 (80.9)	385 (65.7)
Dactylitis	5 (3.0)	8 (3.4)	11 (15.9)	18 (15.7)	42 (7.2)
Uveitis	30 (17.9)	31 (13.2)	15 (21.7)	21 (18.3)	97 (16.6)
Psoriasis	10 (6.0)	13 (5.6)	7 (10.1)	12 (10.4)	42 (7.2)
Inflammatory bowel disease	2 (1.2)	3 (1.3)	0	3 (2.6)	8 (1.4)

Randomized sets. The Classification and Regression Tree (CART) clustering algorithm used to stratify patients into endotypes was based on the following baseline characteristics: sex, onset age <40 years, disease duration <2 years, HLA-B27 status and presence of arthritis, enthesitis, dactylitis, uveitis, psoriasis, and inflammatory bowel disease. Unlike the published algorithm, buttock pain, triggering infection and NSAID response were not used to determine endotype, as these data were not collected in BE MOBILE 1 and 2. [a] n=233; [b] n=585; [c] Enthesitis is defined as MASES >0 at baseline. ASDAS: Axial Spondyloarthritis Disease Activity Score; ASQoL: Ankylosing Spondylitis Quality of Life; axSpA: axial spondyloarthritis; BASFI: Bath Ankylosing Spondylitis Functional Index; BKZ: bimekizumab; CART: Classification and Regression Tree; hs-CRP: high sensitivity C-reactive protein; HLA: human leukocyte antigen; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; NSAID: non-steroidal anti-inflammatory drug; PBO: placebo; PCS: physical component summary; Q: quartile; Q4W: every four weeks; SD: standard deviation; SF-36: 36-Item Short Form Health Survey.

At Wk 16, higher ASAS40 response rates were observed with BKZ vs PBO in both endotypes, sustained to Wk 104 with continuous BKZ (Endotype A: 49.1%; Endotype B: 56.5%; **Figure 1A**). Trends were largely similar for ASDAS-MI and ASDAS LDA (**Figure 1B–C**).

Reductions from baseline in ASDAS were greater in both endotypes with BKZ vs PBO at Wk 16 and sustained to Wk 104 with continuous BKZ (A: –1.7; B: –2.0; **Figure 1D**). Greater differences in responses with BKZ vs PBO were observed in Endotype B vs Endotype A.

The safety profile of BKZ was consistent across endotypes (treatment-emergent adverse events [TEAEs]: A: 89.1% [352/395], B: 90.5% [162/179]; serious TEAEs: A: 12.2% [48/395], B: 13.4% [24/179]).

Conclusion: BKZ showed comparable retention, efficacy, and safety to Wk 104 in pts with predominantly axial disease and with axial and peripheral manifestations. These data suggest pts with axSpA have improved outcomes with BKZ regardless of endotype.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

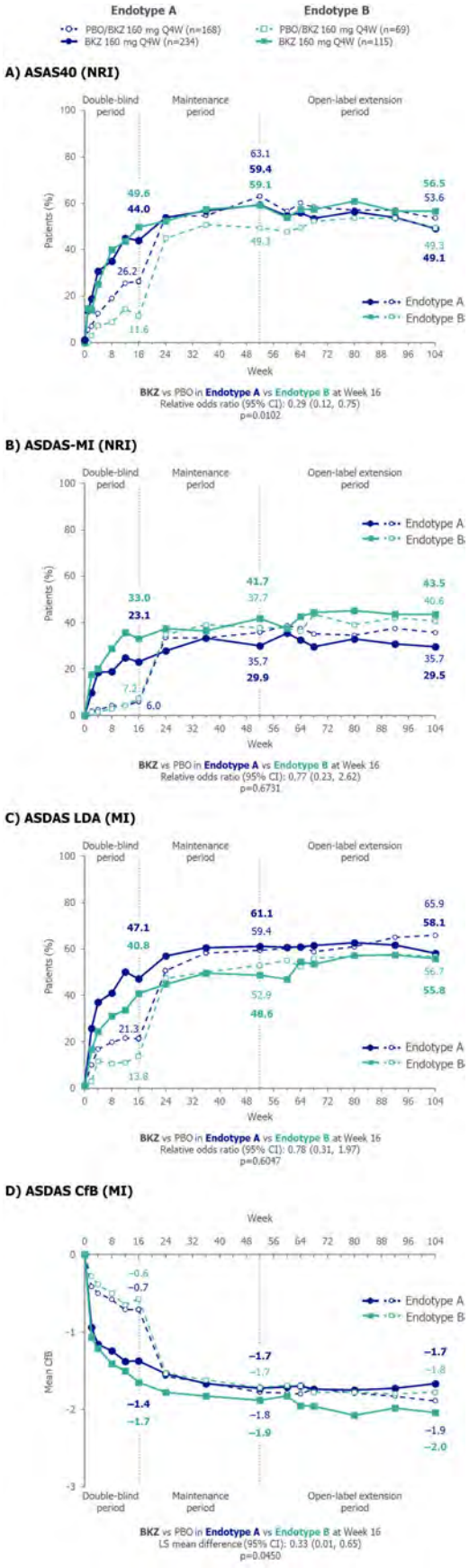


Figure 1. ASAS40, ASDAS-MI, ASDAS LDA and change from baseline in ASDAS to Week 104, stratified by endotype

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References: 1. Navarro-Compán V. Lancet 2025;405:159–72; **2**. De Winter JJ. Arthritis Res Ther 2016;18:196; **3**. Costantino F. Rheumatology 2022;61:3289–98; **4**. De Craemer A-S. Rheumatology 2022;61:3279–88; **5**. Costantino F. Arthritis Rheumatol 2016;68:1660–8; **6**. Baraliakos X. Rheumatology 2025;keaf009; **7**. Baraliakos X. Ann Rheum Dis 2024;83:199–213.

Disclosure: F. Costantino: AbbVie, 2, 6, Amgen, 2, 6, Celltrion, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, UCB, 2, 6; **A. De Craemer**: UCB, 6; **F. Van den Bosch**: AbbVie, 2, 6, Alfasigma, 2, Amgen, 2, 6, Eli Lilly, 2, Galapagos, 2, Grey Wolf Therapeutics, 2, Janssen, 2, 6, Merck, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **M. Breban**: MSD, 5, Novartis, 2, 5, UCB, 2; **V. Taieb**: UCB, 3, 12, Shareholder; **D. Voiniciuc**: UCB, 7, Veramed, 3; **N. de Peyrecave**: UCB, 3; **D. Elewaut**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6, UCB, 2, 6; **M. D'Agostino**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 1439

Bimekizumab in Psoriatic Arthritis. A real-world prospective study. Comparison of its efficacy in bDMARD-naive and IL-17A-experienced patients

Vassiliki Poulia[1], Eleni Sampatakaki[2], Dimitrios Katsifis-Nezis[3], Maria Pappa[3], Evangelia Mole[4], Sousana Gazi[4], Elpida Skouvaklidou[5], Nikolaos Kougkas[5], Maria Polyzou[6], Loukia Koutsogeorgopoulou[6], Ioannis Xynogalas[7], Anastasios Karamanakos[7], Konstantinos D Vassilakis[1], Evangelos Papadimitriou[8], Charalampos Papagoras[8], Gerasimos Evangelatos[9], Nafsika Gerolymatou[10], Paraskevi V Voulgari[10] and **George E Fragoulis**[1], [1]First Department of Propedeutic and Internal Medicine, Joint Academic Rheumatology program, National and Kapodistrian University of Athens, Athens, Attiki, Greece, [2]Joint Academic Rheumatology Program, Attikon University Hospital, National and Kapodistrian University of Athens, School of Medicine, 4th Department of Internal Medicine, Athens, Greece, Athens, Attiki, Greece, [3]Rheumatology and Clinical Immunology Unit, 4th Department of Internal Medicine, Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, Athens, Attiki, Greece, [4]Rheumatology department, KAT General Hospital of Attica, Athens, Attiki, Greece, [5]4th Department of Internal Medicine, Aristotle University, Thessaloniki, Thessaloniki, Greece, [6]Department of Pathophysiology, Joint Academic Rheumatology program, National and Kapodistrian University of Athens, Athens, Attiki, Greece, [7]Department of Rheumatology, Evangelismos General Hospital, Athens, Attiki, Greece, [8]First Department of Internal Medicine, University Hospital of Alexandroupolis, Democritus University of Thrace, Alexandroupolis, Evros, Greece, [9]Third Department of Medicine, National and Kapodistrian University of Athens, School of Medicine, Sotiria Hospital, Athens, Attiki, Greece, [10]Department of Rheumatology, School of Health Sciences, Faculty of Medicine, University of Ioannina, Ioannina, Ioannina, Greece

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Bimekizumab, a dual IL-17 A and F blocker, has recently been added in the therapeutic rheumatologist's armamentarium of PsA, but real-world evidence is lacking. Phase 3 trials have suggested that its efficacy between TNFi-naïve and TNFi experienced patients is not significantly different. In this nationwide study we aimed to comparatively examine the efficacy of bimekizumab in biologic(b)/ targeted synthetic(ts)-DMARD-naive and IL-17Ai-experienced PsA patients.

Methods: Consecutive PsA patients, either b/ts-DMARD-naïve (Group 1) or IL-17Ai- experienced (Group 2) followed up from October 2024 – January 2025 were prospectively included and assessed at time-0 (commencement of bimekizumab) and at month-3. There were no exclusion criteria. The following characteristics were recorded: demographics, clinical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table-1: Demographic and clinical characteristics of b/tsDMARD-naive and IL-17A experienced PsA patients included in the study

	PsA (n=33)		
	b/tsDMARD-naive (n=14)	IL-17A experienced (n=19)	p-value
Demographics			
Sex (females), n (%)	6 (42.9)	12 (63.2)	0.247
Age (years) mean ± S.D.	48.9 ± 14.0	53.7 ± 10.2	0.262
BMI (kg/m²) median (Q3-Q1)	25.2 (39.4-23.2)	30.7 (38-21)	0.328
Current Smoking, n (%)	3 (21.4)	9 (47.4)	0.126
Clinical			
Axial involvement, n (%)	3 (21.4)	7 (36.8)	0.309
Enthesitis, n (%)	4 (36.4)	12 (63.2)	**0.049**
Dactylitis, n (%)	4 (36.4)	3 (15.8)	0.375
Skin, n (%)	13 (92.9)	18 (94.7)	0.823
Nail disease, n (%)	4 (36.4)	12 (63.2)	**0.049**
Eye involvement, n (%)	0 (0.0)	1 (5.3)	0.383
IBD, n (%)	0 (0.0)	0 (0.0)	1.000

b/tsDMARD: biologic/target synthetic DMARD; IBD: Inflammatory bowel disease

features (peripheral arthritis, axial involvement, dactylitis, enthesitis, psoriasis, nail-, eye- and bowel- involvement) present throughout the disease , as well as laboratory parameters, clinical features and disease activity scores at time-0 and at month-3. Treatment characteristics (concurrent conventional synthetic (cs) DMARDs, previous bDMARDs treatment if any and reason for bimekizumab discontinuation, if so) were also recorded. Difference between scores was expressed as Delta (Δ) (score at time-0 minus score at month-3).

Results: In total 33 patients were enrolled. Fourteen patients were b/tsDMARD-naïve (Group 1) and 19 were IL-17Ai-experienced (Group 2). csDMARDs were co-administered in 50% and 42.1% of patients, respectively. In Group 2, 7 were switched directly from another IL-17Ai to bimekizumab, while 12 received other b/tsDMARDs in-between. Of note, 42.1% of patients in Group 2 had failed in two different IL-17A-inhibitors.

No significant differences were detected in the characteristics between the two groups apart from enthesitis and nail disease which were slightly more common in the latter (Table-1). At month 3, Disease Activity index for PsA (DAPSA) was significantly improved in both groups (Group 1; p=0.001, Group 2; p=0.002) (Table-2), while ΔDAPSA was comparable (Group 1; 10.8 ±14.6, Group 2; 15.5 ±13.1, p=0.258). Number of tender count joints (TJC)/ swollen count joints (SJC), as well as Body Surface Area (BSA) and ESR were also significantly improved for both groups (Table-2). ΔESR (Group 1; 12.0±12.5, Group 2;

Table 2. Comparison of Disease Activity Between Baseline time-0 and month-3 in b/tsDMARD-naive and IL-17A–Experienced Patients With Psoriatic Arthritis (PsA)

	b/tsDMARD-naive (n=14)		p-value	IL-17A-experienced (n=19)		p-value
	time-0	Month-3		time-0	Month-3	
DAPSA	29.0 (38.1-15.0)	7.8 (9.0-5.0)	**0.001**	18.5 (26.0-10.0)	7.0 (12.0-4.4)	**0.002**
TJC	4 (10-1)	0 (1-0)	**0.003**	4 (10-1)	1 (2-0)	**0.006**
SJC	2.5 (7-1)	0 (1-0)	**0.003**	2 (5-1)	0 (2-0)	**0.006**
Enthesitis, n (%)	2 (14.3)	0 (0.0)	0.142	6 (31.6)	4 (21.1)	0.283
Dactylitis, n (%)	2 (14.3)	0 (0.0)	0.142	0 (0.0)	0 (0.0)	1.000
BSA	6.0 (10.0-2.0)	0.0 (1.0-0.0)	**0.007**	1.0 (4.0-0.0)	0.0 (2.0-0.0)	**0.024**
Nail	4 (36.4)	4 (28.6)	1.000	7 (36.8)	6 (31.6)	0.732
ASDAS* mean ± S.D.	2.8 (1.4-3.2)	2.0 (1.0-3.6)	0.691	2.6 (2.0-3.9)	1.5 (1.1-3.0)	**0.003**
ESR mean ± S.D.	38 ± 28	18.5 ± 13.7	**0.029**	22 ± 15	12.5 ± 8.2	**0.021**
CRP	2.0 (14.0-1.0)	1.5 (3.0-01)	0.129	3.0 (7.5-0.2)	0.5 (5.0-0.0)	0.219

Values are presented as median (Q3–Q1) unless otherwise indicated. p-value in bold indicates statistically significant difference (p<0.05) b/tsDMARD: biologic/target synthetic DMARD; DAPSA: Disease Activity in Psoriatic Arthritis; TJC: Tender Joint Count; SJC: Swollen Joint Count; BSA: Body Surface Area affected by psoriasis; ASDAS: Ankylosing Spondylitis Disease Activity Score Nail: nail involvement in psoriatic disease. *ASDAS is calculated based on CRP

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

16.6 ±28.8, p=0.813), as well as ΔTJC (Group 1; 4.2±6.0, Group 2; 4.8±4.8, p=0.741) and ΔSJC (Group 1; 2.3±3.7, Group 2; 3.5±3.6, p=0.338) were comparable between groups. ΔBSA was significantly higher for the Group 1 (Group 1; 5.6±4.2, Group 2; 2.6±6.5, p=0.007). Finally, in the whole cohort, Ankylosing Spondylitis Disease Activity Score was also significantly improved (time-0; 2.64±0.75, month-3; 1.95±0.96, p=0.01), This was also evident when Group 2 was analyzed separately, as Group 1 included only 3 patients with axial disease (Table-2). Two patients (6.1%) developed oral candidiasis.

Conclusion: In this real-world prospective study, we found that at 3 months bimekizumab is equally effective in b/tsDMARDs and IL-17A-experienced patients in almost all aspects of PsA. Also, bimekizumab was found to be effective for axial-PsA.

Disclosure: V. Poulia: None; **E. Sampatakaki**: None; **D. Katsifis-Nezis**: None; **M. Pappa**: None; **E. Mole**: None; **S. Gazi**: None; **E. Skouvaklidou**: None; **N. Kougkas**: None; **M. Polyzou**: None; **L. Koutsogeorgopoulou**: None; **I. Xynogalas**: None; **A. Karamanakos**: None; **K. Vassilakis**: None; **E. Papadimitriou**: None; **C. Papagoras**: None; **G. Evangelatos**: None; **N. Gerolymatou**: None; **P. Voulgari**: None; **G. Fragoulis**: None.

Abstract Number: 1440

Comparison of standard and tapered dose of biologic treatments in patients with axial spondyloarthritis

MÜSLÜM FIRAT İKİKARDEŞ[1], EMRAH KOÇ[1], **GEZMIS KIMYON**[2], EMİNE DUYGU ERSOZLU[1] and TAYYIBE SALER[1], [1]ADANA SEHİR HASTANESİ, ADANA, Turkey, [2]MUSTAFA KEMAL UNIVERSITY, HATAY, Turkey

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: We aimed to compare the demographic and clinical characteristics of the patients with axial spondyloarthritis (aSpA) receiving standard-dose versus tapered-dose biologic disease-modifying antirheumatic drugs (bDMARD).

Methods: The patients with aSpA who visited the rheumatology outpatient clinics at our hospital between 1 October 2017 and 31 October 2023 were retrospectively analyzed. The patient's data were collected between 1 December 2023 and 30 November 2024. The demographic and clinical characteristics of the patients were compared between groups.

Results: A total of 251 patients were included in the study, with 105 patients in bDMARD tapered dose group (TDG) and 146 patients in standard dose group (SDG). Compared to SDG, there were more male patients in the TDG (75.2% vs. 57.5%, p=0.004). In the TDG, lower rates of obesity (27.6% vs. 47.9%, p=0.001), chronic disease (55.2% vs. 68.5%, p=0.032), fibromyalgia syndrome (FMS) (1.9% vs. 10.3%, p=0.009), ≥3 different bDMARDs usage (4,8% vs 26%, p=0,000), and nonsteroidal anti-inflammatory drug usage (23,8% vs 48,6%, p=0,000) were found. The TDG had a longer disease duration (median: 152 vs. 130 months, p=0.009), lower erythrocyte sedimentation rate (median: 5 mm/h vs. 8 mm/h, p=0.000), C-reactive protein (median: 3,1 mg/L vs 4,05 mg/L, p=0,033), current ankylosing spondylitis disease activity score-C-reactive protein level (median: 1.2 vs. 1.7, p=0.000), and a higher remission rate (87.6% vs. 58.2%, p=0.000). The most frequently used bDMARD in the TDG was etanercept (31,4%, 25 mg and 50 mg forms), and the second

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

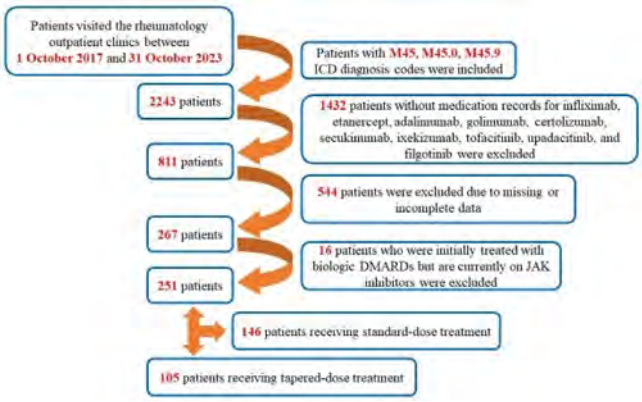


Figure 1: Flowchart of the study population selection

most commonly used was golimumab (%21,9). Compared to other bDMARDs, maintenance duration at the tapered dose of etanercept was longer (median: 102 vs 61 months, p=0.002).

Conclusion: bDMARD tapering was more frequently performed in male patients who do not have obesity, chronic diseases, or FMS. Etanercept was a drug that was most commonly tapered.

Table 1: Comparison of baseline characteristics between the tapered-dose and standard-dose groups

Characteristics	Tapered-dose group n= 105	Standard-dose group n= 146	P-value
Age at diagnosis, year (mean±SD)	35±10,8	35±10	0,658
Male, n (%)	**79 (%75,2)**	**84 (%57,5)**	**0,004**
Obesity, yes, n (%)	**29 (%27,6)**	**70 (%47,9)**	**0,001**
Current smoking, yes, n (%)	54 (%51,4)	74 (%50,7)	0,907
University graduate, yes, n (%)	24 (%22,8)	24 (%16,4)	0,202
Married, yes, n (%)	92 (%87,6)	122 (%83,6)	0,371
Family history of SpA, yes, n (%)	40 (%38,1)	52 (%35,6)	0,688
Chronic disease, yes, n (%)	**58 (%55,2)**	**100 (%68,5)**	**0,032**
Psychiatric disorders, yes, n (%)	15 (%14,3)	27 (%18,5)	0,378
Diabetes mellitus, yes, n (%)	13 (%12,4)	15 (%10,3)	0,601
Polyneuropathy, yes, n (%)	4 (%3,8)	15 (%10,3)	0,056
Osteoporosis, yes, n (%)	7 (%6,7)	10 (%6,8)	0,955
Fibromyalgia syndrome, yes, n (%)	**2 (%1,9)**	**15 (%10,3)**	**0,009**
History of enthesitis, yes, n (%)	42 (%40)	74 (%50,7)	0,094
History of peripheral arthritis, yes, n (%)	31 (%29,5)	49 (%33,6)	0,498
History of uveitis, yes, n (%)	23 (%21,9)	19 (%13)	0,063
Psoriasis, yes, n (%)	3 (%2,9)	3 (%2,1)	0,681
IBD, yes, n (%)	1 (%1)	8 (%5,5)	0,057
Disease duration, month, median (min-max)	152 (23-197)	130 (12-196)	0,009
Disease duration, n (%)			
≤60 ay	4 (%3,8)	35 (%24)	
61-120 ay	26 (%24,8)	34 (%23,3)	0,000
>120 ay	75 (%71,4)	77 (%52,7)	
Radiographic aSpA, n (%)	76 (%72,4)	92 (%63)	0,120
***HLA-B27, positive, n (%)**	27 (%64,3)	45 (%51,1)	0,158
Current CRP, mg/L, median (min-max)	3,1 (0,5-24)	4,05 (0,8-61,7)	0,033
Current ESH, mm/h, median (min-max)	5 (2-36)	8 (2-54)	0,000
Current ASDAS-CRP, median (min-max)	1,2 (0,6-3,4)	1,7 (0,6-4,8)	0,000
Current ASDAS-CRP remission rate, n (%)	92 (87,6%)	85 (58,2%)	0,000
Current treatment, n (%)			
İnfliximab	12 (%11,4)	24 (%16,4)	
Etanercept	33 (%31,4)	23 (%15,8)	
Adalimumab	20 (%19)	52 (%35,7)	0,000
Golimumab	23 (%21,9)	11 (%7,5)	
Certolizumab	16 (%15,3)	18 (%12,3)	
Secukinumab	1 (%1)	18 (%12,3)	
Number of bDMARD used			
1	63 (%60)	77 (%52,7)	
2	37 (%35,2)	31 (%21,3)	0,000
≥3	5 (%4,8)	38 (%26)	
Exercise, n (%)	41 (%39)	49 (%33,6)	0,371
NSAID use, n (%)	25 (%23,8)	71 (%48,6)	0,000

ASDAS: ankylosing spondylitis disease activity score, aSpA: axial spondyloarthritis, bDMARD: biologic disease-modifying antirheumatic drugs, CRP: C-reactive protein, ESH: erythrocyte sedimentation rate, SpA:spondyloarthritis, HLA: human leukocyte antigen, IBD:inflammatory bowel disease, NSAID: nonsteroidal antiinflammatory drug
**Statistical analysis was performed on a total of 130 patients, including 42 patients in the tapered-dose group and 88 patients in the standard-dose group, who had available HLA-B27 data*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Dose, dosing interval, time to dose tapering, duration of treatment at the tapered dose, and total treatment duration of the current bDMARD in patients from the tapered-dose group

bDMARD	Dose	Dosing interval, median (min-max) (day)	Time to dose tapering, median (min-max) (month)	Duration of treatment at tapered dose, median (min-max) (month)	Total treatment duration, median (min-max) (month)
İnfliximab	5 mg/kg	90 (70-120)	22 (12-113)	78 (27-159)	126 (77-184)
Etanercept	25 mg	6 (5-7)	14 (12-17)	133 (125-142)	148 (142-154)
Etanercept	50 mg	13 (10-30)	18 (11-86)	102 (4-155)	121 (46 -191)
Adalimumab	40 mg	20 (17-30)	24 (9-128)	27 (3-145)	58 (12-165)
Golimumab	50 mg	45 (34-55)	21 (12-107)	99 (29-124)	121 (71-138)
Certolizumab	200 mg	24 (17-30)	22 (11-57)	30 (5-81)	70 (19-95)
Secukinumab	150 mg	45	23	38	61

bDMARD: biologic disease-modifying antirheumatic drugs

Disclosure: M. İKİKARDEŞ: None; **E. KOÇ**: None; **g. KIMYON**: None; **E. ERSOZLU**: None; **T. SALER**: None.

Abstract Number: 1441

Efficacy and Safety of Vunakizumab in Patients with Active Ankylosing Spondylitis by Cigarette Smoking Status: A Post Hoc Analysis of a Randomized, Double-blind, Phase 2/3 Study

Hongbin Li[1] and Huilin Li[2], [1]Affiliated Hospital of Inner Mongolia Medical University, Hohhot, Nei Mongol, China (People's Republic), [2]Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Vunakizumab, a humanized anti-interleukin-17A monoclonal antibody, has shown significant efficacy and favorable safety in patients with active ankylosing spondylitis (AS), leading to its approval in China. This analysis aims to evaluate the impact of cigarette smoking status on the efficacy and safety of vunakizumab in patients with active AS.

Methods: This post hoc analysis used data from a randomized, double-blind, adaptive, seamless, phase 2/3 trial (NCT04840485) of vunakizumab in adult patients with active AS who were confirmed by radiographic evidence and met the modified New York criteria. In phase 2, eligible patients were randomized (2:2:1) to receive subcutaneous vunakizumab 120 mg, 240 mg, or placebo at weeks 0, 2, 4, 8, and 12. In phase 3, patients were randomized (2:1) to receive vunakizumab 120 mg (the optimal dose selected from phase 2) or placebo. In both phases, all patients continued to receive subcutaneous vunakizumab every 4 weeks from week 16 to week 32. The primary endpoint was the proportion of patients with at least 20% improvement in Assessment of SpondyloArthritis International Society (ASAS20) response criteria at week 16. This analysis pooled baseline, efficacy and safety data for patients receiving vunakizumab 120 mg or placebo in phase 2 and 3. Subgroup analyses were performed based on smoking status (never/former smoker or current smoker). Efficacy outcomes included ASAS20, ASAS40 and ASAS5/6. Logistic regression models were used to estimate the treatment difference in each subgroup, with stratification factors (weight, prior exposure to tumor necrosis factor-α inhibitors) as covariates. Safety was also assessed.

Results: A total of 440 patients were included in the analysis. Of these, 279 patients were never/former smokers (vunakizumab, n=182; placebo, n=97), and 161 patients were current smokers (vunakizumab, n=112; placebo, n=49). Baseline demographics and clinical characteristics were comparable between treatment arms within smoking status subgroups. The efficacy outcomes (ASAS20, ASAS40, ASAS5/6) from week 2 to week 16 are presented in Table 1. At week 16, among

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. ASAS responses from week 2 to week 16 by smoking status

	Never/former smoker (N=279)			Current smoker (N=161)			
	Placebo (N=97)	Vunakizumab (N=182)	OR (95% CI)	Placebo (N=49)	Vunakizumab (N=112)	OR (95% CI)	$P_{interaction}$
Week 2							
ASAS20	13 (13.40)	71 (39.01)	4.18 (2.16, 8.06)	4 (8.16)	29 (25.89)	3.93 (1.29, 11.93)	0.9164
ASAS40	3 (3.09)	30 (16.48)	6.41 (1.89, 21.69)	0	9 (8.04)	NR (NE, NE)	0.9719
ASAS5/6	8 (8.25)	52 (28.57)	4.44 (2.01, 9.81)	0	22 (19.64)	NR (NE, NE)	0.9733
Week 4							
ASAS20	29 (29.90)	93 (51.10)	2.44 (1.44, 4.11)	9 (18.37)	50 (44.64)	3.63 (1.60, 8.22)	0.4244
ASAS40	12 (12.37)	56 (30.77)	3.17 (1.60, 6.27)	3 (6.12)	19 (16.96)	3.15 (0.88, 11.22)	0.9862
ASAS5/6	14 (14.43)	67 (36.81)	3.43 (1.80, 6.51)	4 (8.16)	37 (33.04)	5.79 (1.93, 17.38)	0.4294
Week 8							
ASAS20	38 (39.18)	100 (54.95)	1.89 (1.14, 3.13)	12 (24.49)	65 (58.04)	4.33 (2.03, 9.22)	0.0711
ASAS40	18 (18.56)	67 (36.81)	2.55 (1.41, 4.62)	6 (12.24)	34 (30.36)	3.25 (1.26, 8.39)	0.6890
ASAS5/6	20 (20.62)	73 (40.11)	2.54 (1.43, 4.53)	5 (10.20)	46 (41.07)	6.29 (2.31, 17.14)	0.1166
Week 12							
ASAS20	36 (37.11)	114 (62.64)	2.89 (1.73, 4.82)	16 (32.65)	69 (61.61)	3.51 (1.71, 7.19)	0.7266
ASAS40	24 (24.74)	67 (36.81)	1.79 (1.03, 3.11)	9 (18.37)	44 (39.29)	3.09 (1.35, 7.05)	0.3211
ASAS5/6	19 (19.59)	92 (50.55)	4.20 (2.35, 7.50)	10 (20.41)	54 (48.21)	3.79 (1.71, 8.38)	0.8059
Week 16							
ASAS20	45 (46.39)	123 (67.58)	2.44 (1.47, 4.06)	17 (34.69)	70 (62.50)	3.26 (1.61, 6.63)	0.5402
ASAS40	24 (24.74)	84 (46.15)	2.63 (1.52, 4.55)	11 (22.45)	52 (46.43)	3.03 (1.40, 6.56)	0.7855
ASAS5/6	22 (22.68)	106 (58.24)	4.72 (2.69, 8.26)	11 (22.45)	57 (50.89)	3.78 (1.75, 8.19)	0.6309

Notes: ASAS20 response was defined as at least 20% improvement in ASAS criteria; ASAS40 response was defined as at least 40% improvement in ASAS criteria; ASAS5/6 response was defined as at least 20% improvement in five of the six ASAS domains; ASAS domains comprised Bath Ankylosing Spondylitis Functional Index, total back pain, patient global assessment, inflammation/morning stiffness, spinal mobility, and high-sensitive C-reactive protein. ASAS, Assessment of SpondyloArthritis International Society.

If patients withdrew from the study before 16 weeks, missing data were imputed using the Non-Responder Imputation (NRI) method.

For each visit, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a logistic regression model, with stratification factors (weight, prior exposure to tumor necrosis factor-α inhibitors) as covariates.

One-sided interaction P values were calculated using a logistic regression model, adjusting for stratification factors (weight, prior exposure to tumor necrosis factor-α inhibitors), subgroups (smoking status), and treatment-subgroup interactions.

never/former smokers, the ASAS20 response rates were 67.58% for vunakizumab and 46.39% for placebo (OR: 2.44; 95% confidence interval [CI]: 1.47, 4.06; nominal P=0.0006); among current smokers, the ASAS20 response rates were 62.50% for vunakizumab and 34.69% for placebo (OR: 3.26; 95% CI: 1.61, 6.63; nominal P=0.0011). Moreover, vunakizumab showed a rapid onset of action, with a higher ASAS20 response rate observed as early as week 2 compared to placebo in both subgroups. This elevated ASAS20 response was sustained through week 32 in both subgroups (Figure 1). Furthermore, no treatment-subgroup interaction term was observed for ASAS20, ASAS40 and ASAS5/6 responses from week 2 to week 16 (Table 1). The incidence of treatment-emergent adverse events (TEAEs) was similar across treatment arms within smoking status subgroups. During the 32-week treatment period, the majority of TEAEs were mild to moderate in severity.

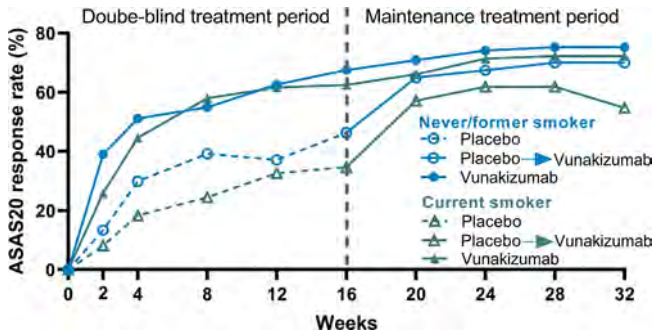


Figure 1. ASAS20 response rate from week 0 to week 32 by smoking status. Patients who received placebo from week 0 to week 16 were switched to receiving vunakizumab 120 mg after week 16 and those initially receiving vunakizumab 120 mg continued receiving vunakizumab 120 mg. ASAS20 response was defined as at least 20% improvement in ASAS criteria. ASAS, Assessment of SpondyloArthritis International Society.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Vunakizumab 120 mg showed significant efficacy and favorable safety in patients with active AS, regardless of cigarette smoking status.

Disclosure: H. Li: None; **H. Li**: None.

Abstract Number: 1442

Modulation of Soluble Biomarkers of Cartilage and Bone Turnover and Inflammation by Zasocitinib (TAK-279), an Oral, Allosteric, Highly Selective and Potent TYK2 Inhibitor, is Associated with Clinical Response in Patients with Active Psoriatic Arthritis

Amit Choudhury[1], Jie Cheng[2], Feng Hong[1], Sachin Kumar[1], Ayumu Sugiura[3], Jay Tang[1], Banishree Saha[1], Vinayagam Arunachalam[3], Ting Hong[3], Elena Tomaselli Muensterman[1], Haakan Wennbo[3], Paresh Thakker[1] and **Iain McInnes**[4], [1]Takeda Development Center Americas, Inc., Cambridge, MA, [2]Takeda Development Center Americas, Inc., Cambridge, MA, [3]Takeda Development Center Americas, Inc, Cambridge, MA, [4]University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

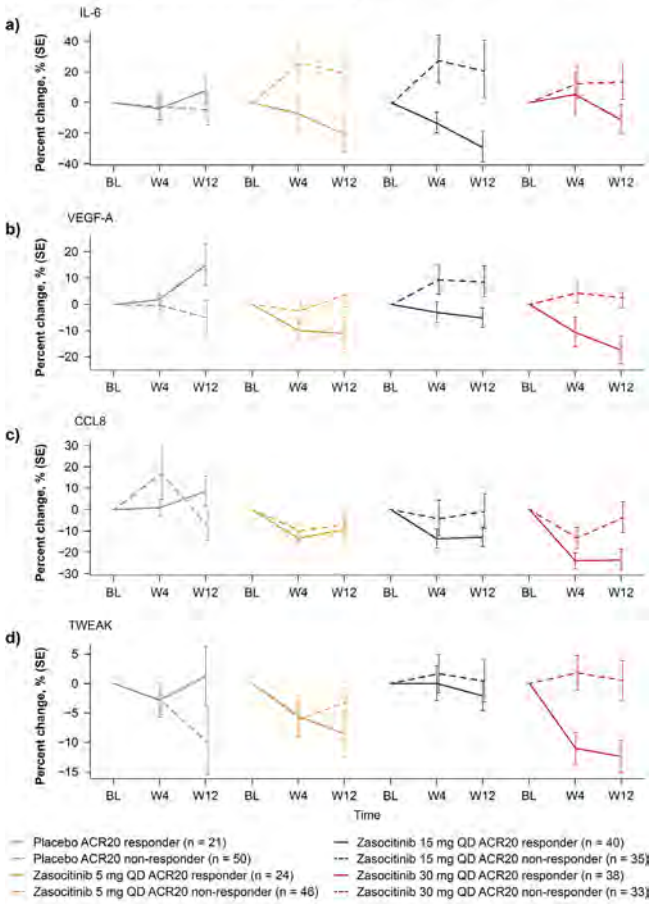
Background/Purpose: As a chronic inflammatory disease, PsA is marked by cartilage and bone turnover and articular inflammation. Accordingly, elevated levels of inflammation and bone metabolism are observed in PsA. Zasocitinib (TAK-279) is an oral, allosteric, highly selective and potent tyrosine kinase 2 (TYK2) inhibitor under clinical investigation for PsA treatment. In a phase 2b study in patients with active PsA (NCT05153148), ACR20 response rates were significantly greater with zasocitinib 15 mg or 30 mg once daily versus placebo (PBO) at Week 12 (primary endpoint; both $p = 0.002$). This study evaluated the longitudinal impact of zasocitinib on biomarkers of cartilage and bone turnover and inflammation in patients with active PsA, including associations between biomarker changes and clinical response.

Methods: In this multicenter, double-blind, PBO-controlled, dose-ranging phase 2b study, patients with active PsA were randomized 1:1:1:1 to zasocitinib 5, 15 or 30 mg or PBO, once daily for 12 weeks. Blood samples were collected at baseline (day 1), Week 4 and Week 12 (pre-dose, if applicable). Plasma biomarkers, including IL-6, colony stimulating factor 1 (CSF1), vascular endothelial growth factor A (VEGF-A), monocyte chemoattractant protein-2 (CCL8), tumor necrosis factor-like weak inducer of apoptosis (TWEAK), type VI collagen degradation marker (C6M), and matrix metalloprotease 3 (MMP3) were measured using the Olink Explore HT or Nordic (C6M) platforms. Longitudinal biomarker changes were modeled using a mixed-effect model, with baseline value, treatment, time and treatment–time interaction as fixed effects and patient as a random effect. Associations with clinical response (ACR20) were measured using absolute area under the receiving operator characteristic curve (abs AUC), adjusted for permutation.

Results: Overall, among 290 treated patients (zasocitinib or PBO), least-squares mean reductions in IL-6 and CSF1 at Week 4 and VEGF-A at Week 12 were associated with ACR20 response (abs AUC: 0.637, 0.627 and 0.637, respectively; $p = 0.018$, 0.036 and 0.018, respectively). Among ACR20 responders, zasocitinib-treated patients generally showed dose-dependent reductions from baseline in IL-6, VEGF-A, CCL8 and TWEAK at both Weeks 4 and 12 (**Figure 1**); in contrast, reductions from baseline in these parameters were not consistently observed in ACR20 non-responders, suggesting a link to intercurrent disease activity. At Week 4, dose-dependent C6M reductions were seen in patients receiving zasocitinib

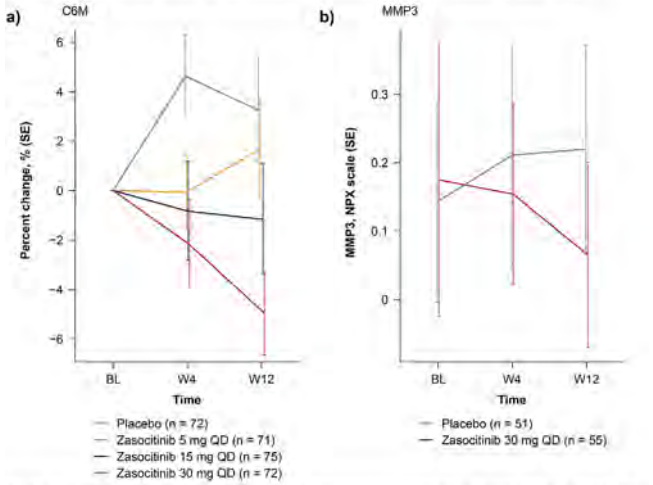
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Zasocitinib treatment resulted in dose-dependent reductions in IL-6 (a), VEGF-A (b), CCL8 (c) and TWEAK (d) in ACR20 responders from baseline to Week 12.



Biomarker levels, reported on a relative and log2 scale as normalized protein expression values, in each treatment group were quantified at different time points and were compared between treatment groups. To calculate change from baseline, the normalized protein expression for biomarkers of interest at baseline was subtracted from the normalized protein expression at each time point (baseline, Week 4 and Week 12) for each patient. The longitudinal change from baseline for each biomarker was modeled using a mixed effect model, with baseline value, treatment, time and treatment–time interaction as fixed effects, and the patient as the random effect. The least-squares mean and standard error were plotted for each biomarker at each time point. ACR20 responders were defined as patients who achieved ACR20 response at Week 12.
ACR, American College of Rheumatology; BL, baseline; CCL8, monocyte chemoattractant protein-2; IL-6, interleukin 6; QD, once daily; SE, standard error; TWEAK, tumor necrosis factor-like weak inducer of apoptosis; VEGF-A, vascular endothelial growth factor A; W, Week.

Figure 2. Dose-dependent reductions were observed in serum C6M in patients receiving zasocitinib 15 mg and 30 mg at Week 12, compared with placebo (a). Zasocitinib 30 mg reduced serum levels of MMP3 at Week 12 (b).



To calculate change from baseline, the normalized protein expression for biomarkers of interest at baseline was subtracted from the normalized protein expression at each time point (baseline, Week 4 and Week 12) for each patient. The longitudinal change from baseline for each biomarker was modeled using a mixed effect model, with baseline value, treatment, time and treatment–time interaction as fixed effects, and the patient as the random effect. The least-squares mean and standard error were plotted for each biomarker at each time point.
BL, baseline; C6M, type VI collagen degradation marker; MMP3, matrix metalloprotease 3; NPX, normalized protein expression; QD, once daily; SE, standard error; W, Week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

15 mg and 30 mg, with significant reductions versus PBO (0.94-fold [$p < 0.05$] and 0.93-fold [$p < 0.01$], respectively); at Week 12 zasocitinib 30 mg had significant reductions in plasma C6M versus PBO (0.92-fold, $p < 0.01$; **Figure 2a**) and from baseline (5% reduction, $p < 0.01$). Zasocitinib 30 mg also reduced plasma MMP3 levels at Week 12 (**Figure 2b**).

Conclusion: Zasocitinib modulates biomarkers of cartilage and bone turnover and articular tissue inflammation in patients with active PsA as early as Week 4, with changes linked to ACR20 clinical response. Zasocitinib 30 mg significantly reduced bone turnover biomarkers at Week 12 versus PBO. Ongoing phase 3 studies (NCT06671483 and NCT06671496) are examining TYK2 inhibition in PsA.

Disclosure: A. Choudhury: Takeda Development Center Americas, Inc., 3, 11; **J. Cheng**: Takeda Development Center Americas, Inc., 3, 11; **F. Hong**: Takeda Development Center Americas, Inc., 3, 11; **S. Kumar**: Takeda Development Center Americas, Inc., 3, 11; **A. Sugiura**: Takeda Development Center Americas. Inc., 3, 11; **J. Tang**: Takeda Development Center Americas, Inc., 3, 11; **B. Saha**: Takeda Development Center Americas, Inc., 3, 11; **V. Arunachalam**: Takeda Development Center Americas, Inc., 3, 11; **T. Hong**: Takeda Development Center Americas, Inc., 3, 11; **E. Muensterman**: Takeda Development Center Americas, Inc., 3, 11; **H. Wennbo**: Takeda Development Center Americas, Inc., 3, 11; **P. Thakker**: Takeda Development Center Americas, Inc., 3, 11; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1443

Long-Term Safety and Efficacy of Upadacitinib in Patients With Psoriatic Arthritis: 5-Year Results From the Phase 3 SELECT-PsA 1 Study

Iain McInnes[1], Koji Kato[2], Marina Magrey[3], Joseph Merola[4], mitsumasa kishimoto[5], Derek Haaland[6], Ivan Lagunes[7], Laura Coates[8], Yanxi Liu[9], Erin Mancl[10], Bhumik Parikh[11] and Charles Phillips[12], [1]University of Glasgow, Glasgow, United Kingdom, [2]Abbvie. Inc, North Chicago, IL, [3]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH, [4]UT Southwestern Medical Center, Dallas, TX, [5]Kyorin University School of Medicine, Tokyo, Japan, [6]The Waterside Clinic, Oro Medonte, ON, Canada, [7]Abbvie Inc, North Chicago, IL, [8]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [9]Abbvie Inc, Florham Park, NJ, [10]AbbVie, Chicago, IL, [11]AbbVie, Hillsborough Township, NJ, [12]AbbVie Inc, Princeton, NJ

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

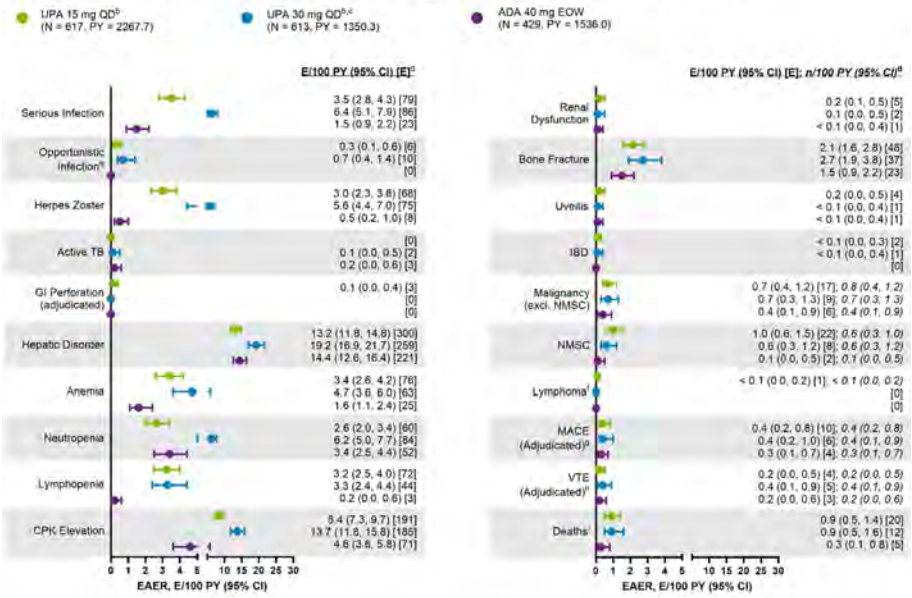
Session Time: 10:30AM–12:30PM

Background/Purpose: We evaluated safety and efficacy of upadacitinib (UPA) versus adalimumab (ADA) at week 260 (5-years) from the long-term extension of SELECT-PsA 1.

Methods: Randomized patients with PsA received UPA 15mg once daily, UPA 30mg once daily, ADA 40mg every other week, or placebo for 24 weeks. At week 24, placebo groups switched to UPA15 or UPA30. Following approval of UPA15, patients on UPA30 switched to UPA15; earliest switch at week 104; data not presented). TEAEs were summarized for patients who received ≥1 dose of the drug using all 5-year data. Safety data are presented as exposure-adjusted event rates (EAERs; events per 100 patient-years) and exposure-adjusted incidence rates (EAIRs; patients per 100 patient-years). Efficacy endpoints were analyzed using nonresponder imputation (NRI) and as observed (AO) (binary endpoints), or mixed-effect model repeated measures and AO (continuous endpoints; P values are nominal).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure: Exposure-Adjusted Event Rates of Treatment-Emergent Adverse Events at Week 260 (5 Years)[a]



ADA, adalimumab; CPK, creatine phosphokinase; E, event; EAER, exposure-adjusted event rate; EAIR, exposure-adjusted incidence rate; EOW, every other week; GI, gastrointestinal; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PY, patient-year; QD, once daily; TB, tuberculosis; UPA, upadacitinib; VTE, venous thromboembolism.

[a]Treatment-emergent adverse events are defined as psoriasis events with onset on or after the first dose of study drug and ≤ 30 days after the last dose for UPA or ≤ 70 days for ADA.

[b]Includes patients treated with placebo that switched to UPA.

[c]Following a protocol amendment, all patients on UPA 30 mg switched to UPA 15 mg (earliest switch at week 104). For patients who switched from UPA 30 mg to UPA 15 mg, adverse events and exposure to UPA 30 mg were censored at the time of dose switch.

[d]Data are presented as EAERs (defined as E/100 PYs [95% CI] [number of E]) or as EARs (derived as n/100 PY [95% CI]) for a subset of treatment-emergent adverse events. For EAERs, total patient exposure was used with multiple events in the same patient included. For EARs, patients were censored at the time of the first event.

[e]Opportunistic infections excluding tuberculosis and herpes zoster.

[f]There was one case of abnormal lymphocyte morphology with UPA 15 mg, which is reported here, as this preferred term is included in the Malignant Lymphoma Standardised MedDRA Query, but it was not confirmed to be a true lymphoma.

[g]Defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.

[h]Includes deep vein thrombosis and pulmonary embolism (fatal and non-fatal).

Both treatment-emergent and nontreatment-emergent deaths are included. Deaths (listed by preferred term) include 20 with UPA 15 mg (1 cardiovascular death, 4 COVID-19, 3 COVID-19 pneumonia, 1 haematemesis, 1 lower respiratory tract infection, 1 metastatic lung cancer, 1 multiple organ dysfunction syndrome, 1 myocardial infarction, 1 pulmonary embolism, 1 road traffic accident, 1 sepsis, shock, 1 sudden cardiovascular death, 3 sudden death), 12 with UPA 30 mg (1 arteriosclerosis of coronary artery, 1 cardiac arrest, 1 circulatory collapse, 1 COVID-19, 5 COVID-19 pneumonia, 1 interstitial lung disease, 1 myocardial infarction, 1 pulmonary embolism), and 5 with ADA (1 acute myocardial infarction, 1 COVID-19 pneumonia, 1 drowning, 1 road traffic accident, 1 suicide).

Table. Efficacy Endpoints at Week 260 (5 Years)

Endpoint	UPA 15 mg QD		UPA 30 mg QD[a]		ADA 40 mg EOW	
Proportion of patients, % (95% CI)	AO	NRI	AO	NRI	AO	NRI
ACR20	n/N = 233/258 90.3 (86.7, 93.9)	n/N = 229/429 53.4 (48.7, 58.1)	n/N = 226/261 86.6 (82.5, 90.7)	n/N = 219/423 51.8 (47.0, 56.5)	n/N = 227/263 86.3 (82.2, 90.5)	n/N = 223/429 52.0 (47.3, 56.7)
ACR50	n/N = 188/262 71.8 (66.3, 77.2)	n/N = 189/429 44.1 (39.4, 48.8)	n/N = 185/260 71.2 (65.6, 76.7)	n/N = 181/423 42.8 (38.1, 47.5)	n/N = 174/262 66.4 (60.7, 72.1)	n/N = 169/429 39.4 (34.8, 44.0)
ACR70	n/N = 123/261 47.1 (41.1, 53.2)	n/N = 126/429 29.4 (25.1, 33.7)	n/N = 125/258 48.4 (42.4, 54.5)	n/N = 125/423 29.6 (25.2, 33.9)	n/N = 117/262 44.7 (38.6, 50.7)	n/N = 124/429 28.9 (24.6, 33.2)
MDA	n/N = 156/265 58.9 (52.9, 64.8)	n/N = 145/429 33.8 (29.3, 38.3)	n/N = 163/261 62.5 (56.6, 68.3)	n/N = 155/423 36.6 (32.1, 41.2)	n/N = 144/262 55.0 (48.9, 61.0)	n/N = 146/429 34.0 (29.5, 38.5)
PASI75[b]	n/N = 105/134 78.4 (71.4, 85.3)	n/N = 96/214 44.9 (38.2, 51.5)	n/N = 103/129 79.8 (72.9, 86.8)	n/N = 99/210 47.1 (40.4, 53.9)[#]	n/N = 115/135 85.2 (79.2, 91.2)	n/N = 79/211 37.4 (30.9, 44.0)
PASI90[b]	n/N = 90/134 67.2 (59.2, 75.1)	n/N = 83/214 38.8 (32.3, 45.3)	n/N = 85/129 65.9 (57.7, 74.1)	n/N = 81/210 38.6 (32.0, 45.2)	n/N = 97/135 71.9 (64.3, 79.4)	n/N = 69/211 32.7 (26.4, 39.0)
PASI100[b]	n/N = 63/134 47.0 (38.6, 55.5)	n/N = 59/214 27.6 (21.6, 33.6)	n/N = 68/129 52.7 (44.1, 61.3)	n/N = 65/210 31.0 (24.7, 37.2)	n/N = 69/135 51.1 (42.7, 59.5)	n/N = 48/211 22.7 (17.1, 28.4)
Resolution of enthesitis by LEI[c]	n/N = 145/174 83.3 (77.8, 88.9)	n/N = 122/270 45.2 (39.2, 51.1)[**]	n/N = 139/162 85.8 (80.4, 91.2)	n/N = 126/268 47.0 (41.0, 53.0)[###]	n/N = 135/163 82.8 (77.0, 88.6)	n/N = 86/265 32.5 (26.8, 38.1)
Resolution of dactylitis by LDI[d]	n/N = 91/92 98.9 (96.8, 100.0)	n/N = 77/136 56.6 (48.3, 64.9)	n/N = 81/84 96.4 (92.5, 100.0)	n/N = 71/127 55.9 (47.3, 64.5)	n/N = 91/92 98.9 (96.8, 100.0)	n/N = 60/127 47.2 (38.6, 55.9)
Change from baseline, LS mean (95% CI) or mean (SD)[e]	Descriptive (AO)	MMRM (AO)	Descriptive (AO)	MMRM (AO)	Descriptive (AO)	MMRM (AO)
HAQ-DI	n = 260 -0.59 (0.62)	n = 421 -0.53 (-0.58, -0.48)	n = 262 -0.59 (0.59)	n = 419 -0.54 (-0.59, -0.48)[#]	n = 262 -0.51 (0.58)	n = 425 -0.46 (-0.51, -0.40)
Patient's assessment of pain (NRS)	n = 260 -3.7 (2.5)	n = 421 -3.3 (-3.5, -3.0)	n = 262 -3.6 (2.6)	n = 419 -3.2 (-3.5, -3.0)	n = 262 -3.4 (2.6)	n = 425 -3.1 (-3.4, -2.9)
BASDAI[f]	n = 86 -3.35 (2.28)	n = 137 -3.22 (-3.60, -2.84)	n = 88 -3.47 (2.37)	n = 137 -3.18 (-3.56, -2.79)	n = 78 -3.07 (2.67)	n = 123 -3.02 (-3.43, -2.61)
ASDAS[f]	n = 83 -1.69 (1.10)	n = 137 -1.56 (-1.76, -1.37)	n = 83 -1.90 (1.17)	n = 137 -1.63 (-1.82, -1.44)	n = 74 -1.54 (1.22)	n = 123 -1.49 (-1.69, -1.29)
mTSS	n = 252 0.24 (2.71)	n = 264 0.23 (-0.02, 0.48)	n = 244 0.19 (1.38)	n = 259 0.20 (-0.06, 0.46)	N = 246 0.23 (1.63)	n = 259 0.22 (-0.04, 0.48)

ACR20/50/70, ≥ 20%/50%/70% improvement in ACR criteria; ADA, adalimumab; AO, as observed; EOW, every other week; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; LS mean, least squares mean; MDA, minimal disease activity; MMRM, mixed effected model repeated measurement; mTSS, modified total Sharp/van der Heijde Score; NRI, nonresponder imputation; NRS, numeric rating scale; PASI75/90/100, ≥ 75%/90%/100% improvement in PASI; QD, once daily; UPA, upadacitinib.

[a]Following a protocol amendment, all patients on UPA 30 mg switched to UPA 15 mg (earliest switch at week 104); data are presented by originally randomized treatment.

[b]In patients with psoriasis affecting ≥ 3% of body surface area at baseline.

[c]In patients with LEI > 0 at baseline; resolution LEI = 0.

[d]In patients with LDI > 0 at baseline; resolution LDI = 0.

[e]Data shown as LS Mean (95% CI) for MMRM and mean (SD) for AO.

[f]In patients with psoriatic spondylitis at baseline.

For NRI and MMRM analyses, nominal *P < .01 UPA 15 mg versus ADA; nominal #P < .05, ###P < .001 UPA 30 mg versus ADA.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 1704 patients received ≥1 dose and 983 (57.7%) completed 260 weeks. Most common reasons for discontinuation were AEs (8.4%), withdrawal of consent (6.2%), and lack of efficacy (4.7%). UPA's safety profile through week 260 (5-years) was comparable to ADA and consistent with week 104 and 152 data. Rates of malignancy excluding nonmelanoma skin cancer (NMSC), VTE, and MACE were low compared to historical comparators and generally similar across treatments. Serious infection, herpes zoster, anemia, lymphopenia, creatine phosphokinase (CPK) elevation, and NMSC rates were higher with UPA versus ADA; serious infection, herpes zoster, anemia, neutropenia, and CPK elevation were higher with UPA30 versus UPA15. Death rates (EAERs) were the same across UPA treatment groups and similar (< 1.0 difference) with ADA; COVID-19/COVID-19 pneumonia was the most common cause. UPA15 achieved ≥20%/50%/70% improvement in ACR response criteria (ACR20/50/70) and minimal disease activity (MDA) comparable to ADA at week 260 (AO). PASI (PASI75/90/100) improvements were also comparable between UPA15 and ADA at week 260 (AO). Using the more conservative NRI, responses were comparable for UPA15 versus ADA at week 260. HAQ-DI and patient assessment of pain changes were consistent through week 260 and comparable between UPA15 versus ADA (AO). Mean change in modified total Sharp/van der Heijde Score (mTSS) at week 260 was similar across treatments.

Conclusion: In patients with PsA and inadequate response/intolerance to ≥1 non-biologic DMARD, no new safety risks were identified with UPA up to 5 years; its safety profile remained consistent with ADA. Efficacy responses were generally maintained over time and comparable to ADA at 5 years.

1. McInnes I, et al. *N Engl J Med*. 2021;384:1227-39.
2. McInnes I, et al. *Rheumatol Ther*. 2023;10:275-92.
3. McInnes I, et al. *Ann Rheum Dis*. 2023 [Abstract].
4. Burmester G, et al. *RMD Open*. 2023;9:e002735.

Disclosure: I. McInnes: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **K. Kato**: AbbVie, 3, 11; **M. Magrey**: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **D. Haaland**: AbbVie, 1, 5, 6, Adiga Life Sciences, 5, Amgen, 1, 5, 6, AstraZeneca, 1, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Can-Fite pharma, 5, Celgene, 5, Eli Lilly, 5, 6, Gilead, 5, GlaxoSmithKlein(GSK), 1, 5, 6, Janssen, 1, 5, 6, Merck/MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Regeneron, 5, Roche, 1, 6, Sanofi Genzyme, 1, 5, 6, Takeda, 1, 6, UCB, 5, 6; **I. Lagunes**: AbbVie, 3, 11; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **Y. Liu**: AbbVie, 3, 11; **E. Mancl**: AbbVie, 3, 11; **B. Parikh**: AbbVie, 3, 11; **C. Phillips**: AbbVie, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1444

Real-world comparative effectiveness of tofacitinib, tumor necrosis factor inhibitors, and interleukin-17 inhibitors among patients with axial spondyloarthritis

Jeffrey Curtis[1], Genevieve Gauthier[2], Lara Fallon[3], David Gruben[3], You-Li Ling[4], Matthew Brouillette[3], Arne Yndestad[5], Yu hong[6] and Mona Kelkar[6], [1]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [2]Pfizer Canada ULC, Kirkland, QC, Canada, Montreal, Canada, [3]Pfizer Inc, New York, NY, USA, New York, [4]Pfizer Inc, New York, NY, USA, New York, NY, [5]Pfizer Inc, Oslo, Norway, Oslo, Norway, [6]Genesis Research Group, Hoboken, NJ, USA, New York

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: : In the context of an expanding therapeutic landscape and absence of head-to-head trials in axial spondyloarthritis (axSpA), data on direct comparison of effectiveness between the JAK inhibitor tofacitinib (TOFA) and other advanced therapies (AT), i.e., inhibitors of tumor necrosis factor (TNFi) and interleukin-17 (IL-17i) in patients (pts) with axSpA is lacking.

To compare real-world effectiveness of TOFA, TNFi, and IL-17i using an adapted version of a claims-based treatment (tx) effectiveness algorithm applied to the Komodo Healthcare Map®, a large US administrative claims database.

Methods: Adults with axSpA who initiated ≥1 selected AT on/after Dec 14 2021 (tofacitinib FDA approval date for ankylosing spondylitis) were selected and required to have continuous healthcare enrollment for ≥12 months before and ≥6 months after the index date (date of AT initiation). Pts could contribute multiple tx episodes of the analysis (i.e. multiple index dates) if they switched to a different AT over the study period. Pts with >1 AT administered/prescribed on the index date were excluded. Pts were classified into cohorts based on the AT initiated on each index date: (1) TOFA (2) TNFi (adalimumab, golimumab, infliximab, etanercept, certolizumab) and (3) IL-17i (ixekizumab, secukinumab). Propensity score weighting (PSW) was used to adjust for baseline confounders.

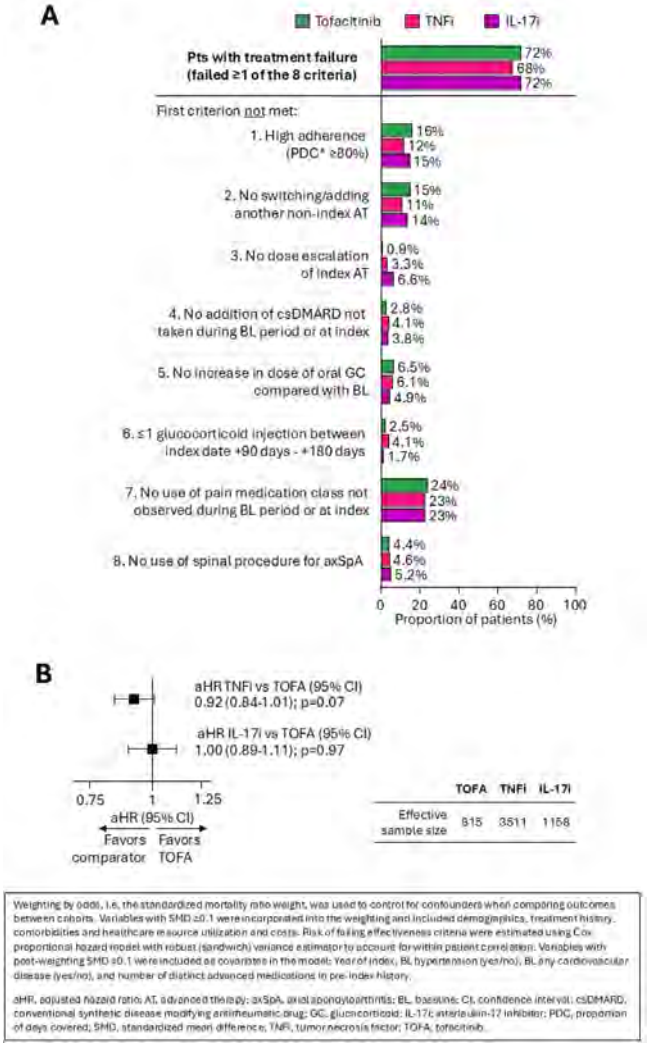
The proportion of pts fulfilling all effectiveness criteria over the 6-month study period was reported. Lack of effectiveness (i.e. not meeting all 8 effectiveness criteria) was compared between TOFA vs TNFi and TOFA vs IL-17i cohorts using Cox Proportional Hazards model with robust variance estimator to account for within patient correlation (multiple tx episodes). Results were reported as weighted hazard ratios (HR) and 95% confidence intervals.

Results: A total of 829 TOFA, 14,056 TNF and 4,472 IL-17i pts were included. Mean age at index ranged from 47 to 48 years; proportion of female range from 65% to 69%. In the pre-index period, 60% of TOFA pts had used ≥2 prior ATs, vs. 14% for the TNFi and 40% for the IL-17i cohort. Prior to PS weighting, use of steroid, opioid, non-opioid pain medications and csDMARDs at baseline was higher in the TOFA vs the TNFi and IL-17i cohorts.

After PS weighting, 28%, 32%, and 28% of pts in the TOFA, TNFi, and IL-17i cohorts met all effectiveness criteria. No difference in risk of effectiveness failure was found between cohorts: TNFi vs TOFA: HR=0.92 (0.84-1.01); IL-17i vs TOFA: HR=1.00 (0.89-1.11). Most common events associated with effectiveness failure were: use of a new pain medication class, low adherence to index tx, and switching/adding another non-index AT for axSpA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Effectiveness failure within 6 months in patients with axSpA initiating treatment with tofacitinib *versus* TNFi or IL-17i.



Weighting by odds, i.e. the standardized mortality ratio weight, was used to control for confounders when comparing outcomes between cohorts. Variables with SMD ≥0.1 were incorporated into the weighting and included demographics, treatment history, comorbidities and healthcare resource utilization and costs. Risk of failing effectiveness criteria were estimated using Cox proportional hazard model with robust (sandwich) variance estimator to account for within patient correlation. Variables with post-weighting SMD ≥0.1 were included as covariates in the model: Year of index, BL hypertension (yes/no), BL any cardiovascular disease (yes/no), and number of distinct advanced medications in pre-index history.

aHR, adjusted hazard ratio; AT, advanced therapy; axSpA, axial spondyloarthritis; BL, baseline; CI, confidence interval; csDMARD, conventional synthetic disease modifying antirheumatic drug; GC, glucocorticoid; IL-17i, interleukin-17 inhibitor; PDC, proportion of days covered; SMD, standardized mean difference; TNFi, tumor necrosis factor; TOFA, tofacitinib.

Conclusion: In this study using real-world data, pts with axSpA who initiated TOFA, TNFi, or IL-17i had similar effectiveness within the first 6 months of tx initiation. Overall response rate to TOFA in this real-world cohort, assessed using a claims-based effectiveness algorithm, was comparable ASDAS major improvement rates and numerically lower than ASAS40 response rates observed in published tofacitinib AS clinical trials. Longer term follow-up will allow confirmation of the robustness of these conclusions.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **G. Gauthier**: Pfizer, 3, 11; **L. Fallon**: Pfizer Inc, 3, 11; **D. Gruben**: Pfizer Inc, 3, 11; **Y. Ling**: Pfizer, 3, 11; **M. Brouillette**: Pfizer Inc, 3, 11; **A. Yndestad**: Pfizer, 3, 11; **Y. hong**: Genesis Research Group, 3, Pfizer, 2; **M. Kelkar**: Genesis Research Group, 3, Pfizer, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1445

Patient Characteristics, and Physician-Reported Treatment Effectiveness and Treatment Satisfaction with Bimekizumab for Axial Spondyloarthritis in the United States: Interim Analysis from a Real-World Study

Jessica A. Walsh[1], Abhijeet Danve[2], Isabel Truman[3], Dan Twigg[3], Hervé Besson[4] and Helena Roque[5], [1]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [2]Section of Rheumatology, Department of Medicine, Yale School of Medicine, New Haven, CT, [3]Adelphi Real World, Bollington, United Kingdom, [4]UCB, Breda, Netherlands, [5]UCB, Brussels, Belgium

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory condition affecting the sacroiliac joints and spine.[1] Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A and has demonstrated long-term clinical efficacy and safety in patients (pts) with axSpA across the full disease spectrum (non-radiographic [nr-]axSpA and radiographic [r-]axSpA).[2,3] BKZ was approved for axSpA treatment in the US in September 2024.[4]

This first presentation of BKZ real-world clinical data from the US describes physician-reported pt characteristics, including treatment history and disease severity, of pts with axSpA initiating BKZ in routine clinical practice in the US, and physician-reported effectiveness of BKZ treatment and satisfaction with disease control.

Methods: Interim data were drawn from the Adelphi Real World BKZ axSpA Plus Disease Specific Programme™, an ongoing cross-sectional survey in Canada, France, Germany, Italy, Japan, Spain, the UK and the US. Physician questionnaires on pts with PsA or axSpA undergoing BKZ treatment began in July 2024, staggered by country based on BKZ reimbursement; completion expected September 2025. Interim data from the US axSpA population are reported (data cut April 22 2025).

Physicians completed a questionnaire per patient at most recent visit including current and retrospective questions (answered as perceived by physicians and/or by medical records). We present pt characteristics at BKZ initiation, physician-reported overall disease severity (mild, moderate or severe; as perceived by physicians) at BKZ initiation and most recent visit, and physician satisfaction with disease control, at most recent visit (stratified by BKZ treatment duration [TD]: < 3, 3–6 or >6 months).

Pts with mild axSpA at BKZ initiation were excluded and no TD-related inclusion criteria were imposed. All analyses are descriptive; observed data reported.

Results: At interim data cut, 10 physicians provided data for 43 BKZ-treated pts with axSpA and available TD information **(Table)**.

Between BKZ initiation and most recent visit, physicians reported overall disease severity improvements with BKZ for all TDs including < 3 months, suggesting rapid treatment response. By the most recent visit, most pts had mild overall disease severity and none had severe disease severity **(Figure 1)**, demonstrating sustained improvements in disease control. At the most recent visit, physicians were satisfied/very satisfied with treatment for almost all pts across TD groups **(Figure 2)**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Characteristics and demographics of patients with available BKZ treatment duration data, at BKZ initiation, in the Adelphi Real World BKZ axSpA Plus Disease Specific Programme™

Baseline characteristic *(mean [SD] unless otherwise stated)*	**All patients in interim analysis[a]**
Age, years	39.5 (13.3)
Sex, n (%)[b]	
Male	26 (60)
Female	17 (40)
Diagnosed axSpA subtype, n (%)	
nr-axSpA	20 (47)
r-axSpA	23 (53)
Ethnicity, n (%)	
White	37 (86)
Black	2 (5)
South or Central American Native	1 (2)
East or Southeast Asian	1 (2)
South Asian	1 (2)
Middle Eastern or North African	1 (2)
Time since onset of axSpA symptoms,[c] years	5.6 (7.9)
Time since axSpA diagnosis,[d] years	2.6 (2.5)
Physician-reported overall disease severity at initiation, n (%)	
Moderate	29 (67)
Severe	14 (33)
BKZ treatment duration, months	7.6 (6.3)
BKZ treatment duration categories, n (%)	
<3 months	7 (16)
3–6 months	17 (40)
>6 months	19 (44)
Current advanced therapy treatment line,[e] n (%)	
1st line[f]	17 (40)
2nd line	20 (47)
3rd line or later	6 (14)
csDMARD prescribed concomitantly, yes, n (%)	11 (26)

Includes all patients with available treatment duration data. For each recruited patient, physicians completed Patient Reported Forms at most recent physician visit; baseline characteristics and demographics were collected retrospectively using physician-reported information and details from patients' medical records. [a] N=43 unless otherwise stated; [b] Biological sex, as recorded on patient medical records; categories were male, female and intersex, no patients were reported as intersex; [c] n=30; [d] n=42; [e] An advanced therapy is considered to be a prior biologic DMARD, targeted synthetic DMARD or JAK inhibitor; [f] No prior exposure to advanced therapy. axSpA: axial spondyloarthritis; BKZ: bimekizumab; csDMARD: conventional synthetic DMARD; DMARD: disease-modifying antirheumatic drug; nr-axSpA: non-radiographic axSpA; r-axSpA: radiographic axSpA; SD: standard deviation.

Conclusion: In real-world settings, physician-reported disease severity improved over time in BKZ-treated pts with axSpA regardless of TD. Physicians were satisfied/very satisfied with almost all pts' disease control on BKZ treatment across all TD groups. These results from routine clinical practice complement the rapid and sustained effectiveness of BKZ in pts with axSpA previously observed in phase 3 trials.

References: 1. Navarro-Compán V. Lancet 2025;405:159–72; **2**. Deodhar A. RMD Open 2025;11:e005081; **3**. Baraliakos X. Rheumatology 2025;keaf009; **4**. FDA. 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761151s009lbl.pdf.

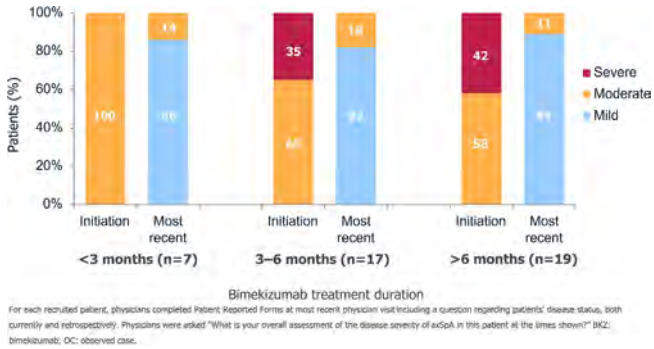


Figure 1. Physician-reported overall disease severity at treatment initiation and most recent visit, stratified by BKZ treatment duration (OC)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

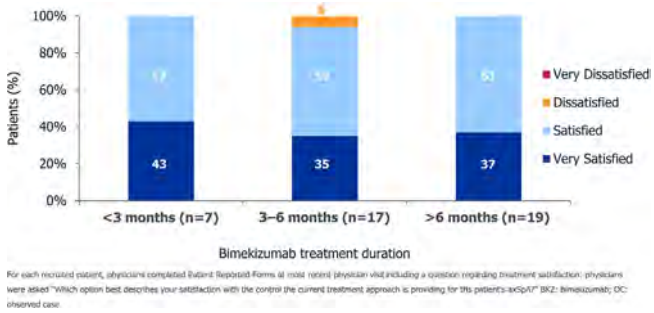


Figure 2. Physician-reported overall treatment satisfaction at most recent visit, stratified by BKZ treatment duration (OC)

Disclosure: J. Walsh: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **A. Danve**: AbbVie, 2, Amgen, 2, Eli Lilly, 5, Janssen, 2, Novartis, 2, 5; **I. Truman**: AbbVie, 2, Adelphi Real World, 3; **D. Twigg**: Adelphi Real World, 3; **H. Besson**: UCB, 3, 11; **H. Roque**: UCB, 3.

Abstract Number: 1446

Persistence of Second-line Treatment in Anti-TNF-experienced Axial Spondyloarthritis Patients: Comparing Cycling Anti–TNF vs Switching to a Different Mechanism of Action

José Miguel Senabre[1], Lucia Otero[2], Jerusalén Calvo[3], Vega Jovaní[4], Javier Manero-Ruiz[5], Rabadán Elena[6], Eugenia Enriquez[7], Yanira Pérez[8], Alicia Garcia[9], Francisca Sivera[10], Olga Martínez[11], María Colazo Burlato[12], Diana Sueiro[13], Fernando Sánchez-Alonso[14] and Isabel Castrejón Fernández[15], [1]Hospital Marina Baixa, Villajoyosa/Vila Joiosa, La, Comunidad Valenciana, Spain, [2]Spanish Society of Rheumatology, Madrid, Spain, [3]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [4]Hospital General Universitario de Alicante, Reumatología, Alicante, Alicante, Comunidad Valenciana, Spain, [5]Hospital Miguel Servet, Zaragoza, Spain, [6]Hospital Universitario Príncipe de Asturias, Alcala de Henares, Spain, [7]Clinica Universidad de Navarra, Madrid, Spain, [8]Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain, [9]Rheumatologist, La Laguna, Spain, [10]Hospital General Universitario Elda, Elda, Spain, [11]Hospital Universitario de Salamanca, Salamanca, Castilla y Leon, Spain, [12]Hospital Universitario de Burgos, Burgos, Spain, [13]Complexo Hospitalario Universitario de Ourense, Ourense, [14]Sociedad Española de Reumatología, Madrid, Spain, [15]MD, PhD, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Failure of a first-line anti-TNF in axial spondyloarthritis (axSpA) is common, and when it occurs, there are no randomized clinical trials (RCTs) comparing the option of switching to a drug with a different mechanism of action (MoA) or cycling to a different anti-TNF. The aim of this study is to evaluate whether these treatment strategies influence the retention to second-line therapy after failure of first-line anti-TNF.

Methods: Data were obtained from the nationwide prospective registry BIOBADASER (Spanish Registry of Adverse Events of Targeted Therapies in Rheumatic Diseases). Patients diagnosed with axSpA who had failed a first TNFi and were starting a second advanced treatment (anti-TNF, IL17 inhibitors or JAK inhibitors) after 2016 were included in the study. Demographic variables, presence of HLA-B27, axSpA manifestations, as well as start and end dates of treatment and reasons for discontinuation were included in the study. Retention rates of the different drugs were estimated using Kaplan-Meier curves and Log rank test, considering discontinuation due to inefficacy or loss of efficacy as a completion event. Predictors of discontinuation were examined using the Cox multivariate regression model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

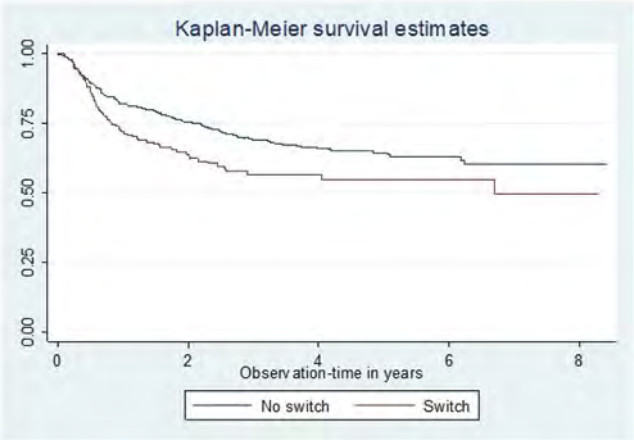


Figure 1. Kaplan - Meier survival estimates

Results: A total of 827 axSpA patients who met inclusion criteria were included in the analysis, 603 (72.9%) continued to another TNFi and 224 (27.1%) switched to different MoA (90.6% to an IL-17 inhibitor). Of all patients, 306 (37.0%) were female, mean (SD) age at treatment initiation was 48.4 (13.0) years, 697 (84.3%) had radiographic axSpA and 547 (66.1%) were HLA-B27 positive, with a mean disease duration of 9.8 (9.8) years.

No statistically significant differences in baseline characteristics were found between the two groups, except for a higher percentage of patients initiating second-line treatment after 2020 in the switch cohort versus the cycling cohort (60.3% vs 45.4%; $p < 0.001$).

The one-year retention rate until inefficacy was significantly higher in the cycling cohort compared to the switching cohort (82.3%; 95%CI [78.8 - 85.4] vs 71.3% [64.5 - 77.1]; Log Rank < 0,01) (Figure 1).

In the univariate analysis, switching to a different MoA was associated with a higher probability of treatment discontinuation (HR: 1.49 [1.14 - 1.90]; p = 0.004) (Table 1). This finding was confirmed in the multivariate analysis (HR: 1.50 [1.14–1.98]; p = 0.004). Other significant predictors of increased risk of discontinuation were obesity (HR: 1.57 [1.11–2.23]; p = 0.011) and nr-axSpA diagnosis (HR: 1.74 [1.23 - 2.44]; p = 0,002). In contrast, HLA-B27 positivity (HR: 0.70 [0.52–0.94]; p = 0.017) and second-line treatment initiation after 2020 (HR: 0.61 [0.46 - 0.80]; p < 0,001) were associated with a lower probability of discontinuation, suggesting a protective effect (Table 1).

Table 1. Univariate and Multivariate models.

	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Switch (reference: no switch)	1.49 (1.14 - 1.95)	**0.004**	1.50 (1.14 - 1.98)	**0.004**
Female (reference: male)	1.13 (0.87 - 1.47)	0.345	0.98 (0.74 - 1.30)	0.891
Rx axSpA (reference: No Rx axSpA)	1.81 (1.33 - 2.46)	**<0.001**	1.74 (1.23 - 2.44)	**0.002**
Age at treatment initiation	1.00 (0.99 - 1.01)	0.901	1.00 (0.99 - 1.01)	0.687
HLA-B27 positive (reference: HLA-B27 negative)	0.62 (0.47 - 0.83)	**0.001**	0.70 (0.52 - 0.94)	**0.017**
Obesity (BMI > 30) (reference: BMI < 25)	1.61 (1.15 - 2.26)	**0.006**	1.57 (1.11 - 2.23)	**0.011**
Year of second-line treatment initiation 2021-2024 (reference 2016-2020)	0.68 (0.51 – 0.89)	**0.005**	0.61 (0.46 - 0.80)	**<0.001**
Tobacco use: current (reference never)	0.94 (0.69 - 1.27)	0.676		
First line anti-TNF (reference adalimumab)				
Etanercept	1.12 (0.82 - 1.53)	0.463		
Infliximab	0.74 (0.49 - 1.13)	0.161		
Certolizumab pegol	0.91 (0.50 - 1.66)	0.770		
Golimumab	1.27 (0.84 - 1.92)	0.253		

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion:

1. In patients with axSpA, cycling to another anti-TNF agent after first-line anti-TNF failure is associated with a lower risk of discontinuation compared to switching to a treatment with a different mechanism of action.
2. HLA-B27 positivity and treatment initiation after 2020 were also associated with a lower risk of discontinuation.
3. In contrast, obesity and nr-axSpA diagnosis were associated with higher risk of discontinuation.

Disclosure: J. Senabre: None; **L. Otero**: None; **J. Calvo**: None; **V. Jovaní**: None; **J. Manero-Ruiz**: None; **R. Elena**: None; **E. Enriquez**: None; **Y. Pérez**: None; **A. Garcia**: None; **F. Sivera**: None; **O. Martínez**: None; **M. Colazo Burlato**: None; **D. Sueiro**: None; **F. Sánchez-Alonso**: None; **I. Castrejón Fernández**: None.

Abstract Number: 1447

Long-term impact of secukinumab on the prevention of psoriatic arthritis in patients with psoriasis: a 5-year pooled analysis of the ERASURE, FIXTURE and SCULPTURE studies

Ulrich Mrowietz[1], **Laura Coates**[2], Diamant Thaçi[3], Mark Lebwohl[4], Bardur Sigurgeirsson[5], Richard B. Warren[6], Richard G. Langley[7], Andreas Clemens[8], Cynthia Vizcaya[8], Weibin Bao[9], Kim Hoyt[10], Lara Gómez[11] and Robert Bissonnette[12], [1]Department of Dermatology, University Medical Center Schleswig-Holstein, Kiel, Germany, [2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [3]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany, [4]Icahn School of Medicine at Mount Sinai, New York, NY, [5]University of Iceland, Faculty of Medicine, Department of Dermatology, Reykjavik, Iceland, [6]Dermatology Centre, Northern Care Alliance, NHS Foundation Trust & Division of Musculoskeletal and Dermatological Sciences, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom, [7]Dalhousie University, Halifax, NS, Canada, [8]Novartis Pharma AG, Basel, Switzerland, [9]Novartis Pharmaceuticals Corporation, Hanover, NJ, [10]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [11]Novartis Farmaceutica, Madrid, Spain, [12]Innovaderm, Montreal, Québec, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Secukinumab is a fully human monoclonal antibody that selectively inhibits interleukin-17A, demonstrating robust and sustained efficacy in moderate to severe psoriasis (PsO) and psoriatic arthritis (PsA) with a good safety profile in long-term trials.[1-3] Besides its efficacy in PsA, secukinumab may have a preventive effect in patients with PsO without clinical signs of PsA. Pooled clinical trials of secukinumab (ERASURE, FIXTURE and SCULPTURE) provide valuable data sets that can help in understanding PsA prevention with secukinumab treatment. This study aimed to explore the efficacy of secukinumab in preventing PsA in patients with PsO using pooled data from the ERASURE, FIXTURE and SCULPTURE trials and to indirectly compare these data with historical data in patients who were biologic-naïve.[4]

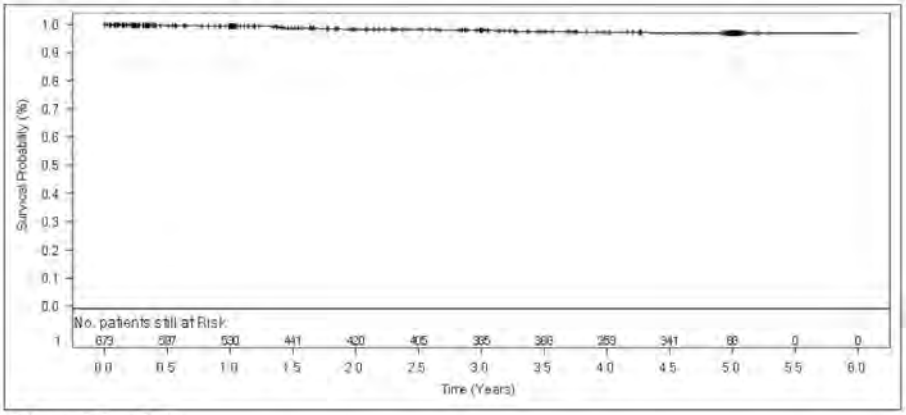
Methods: Patients with moderate to severe PsO (with no medical history of PsA at baseline) who were treated with secukinumab 300 mg through up to 5-year follow-up were included in this analysis. The incidence of PsA within the studies was assessed using exposure-adjusted incidence rates (EAIRs; incidence rate/100 patient-years [PY]). The preferred term 'psoriatic arthropathy' in the reported adverse events was used to capture the incident PsA. The time to develop PsA was estimated using Kaplan-Meier analysis. Efficacy was measured using Psoriasis Area and Severity Index (PASI) 90 and 100 responders (as observed data).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Efficacy of secukinumab in patients with psoriasis without PsA at baseline over a 5-year follow-up period.

Endpoints	Study population (N)	Year 1	Year 2	Year 3	Year 4	≥Year 5
PASI 100 n/M (%)	673	242/570 (42.5)	139/334 (41.6)	115/316 (36.4)	107/290 (36.9)	92/252 (36.5)
PASI 90 n/M (%)	673	407/570 (71.4)	217/334 (65.0)	187/316 (59.2)	188/290 (64.8)	161/252 (63.9)

M, number of patients under evaluation; n, number of responders; N, number of patients in the study population; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis.



PsA, psoriatic arthritis.

Figure 1: Kaplan-Meier Curve for PsA development in patients with psoriasis without PsA at baseline over a 5-year follow-up period.

Results: Overall, 673 patients with active PsO without PsA were included in the analysis (mean age: 45.2 years; male: 71.8%; mean body mass index: 28.9 kg/m^2; mean time since diagnosis: 16.1 years). In total, 8% (N=54), 11.3% (N=76), 34.5% (N=232) and 46.2% (N=311) patients had < 2, 2-< 5, 5-< 15 and ≥15 years of disease duration, respectively. Overall, 18.3% of patients were biologic-experienced before the start of secukinumab. All patients had a PASI score of ≥10. After 5 years of treatment and a total exposure of 1831 PY, most patients (659/673 patients; 97.9%) did not experience PsA (**Fig. 1**). This translates into an EAIR of 0.76 (95% CI: 0.42,1.28). An 8-year prospective observational study previously reported a yearly PsA incidence rate of 2.7/100 patients in biologic-naïve patients with PsO without PsA.[4] When we indirectly compared these data with current data from pooled clinical trials, we found that incidence rate of PsA development was ~72% lower with secukinumab. At Year 5 of secukinumab treatment, 36.5% and 63.9% of patients achieved skin clearance (PASI 100) and PASI 90, respectively (**Table 1**).

Conclusion: These findings support the hypothesis that secukinumab may prevent PsA development in patients with PsO and suggest a potential protective effect against PsA. Additionally, secukinumab-treated patients demonstrated effective and sustained long-term control over skin clearance.

References:

1. Langley RG, et al. Br J Dermatol. 2023;188:198-207
2. Bissonnette R, et al. J Eur Acad Dermatol Venereol. 2018;32:1507-14.
3. Sun R, et al. Dermatol Ther (Heidelb). 2024;14:729-43.
4. Eder L. Arthritis Rheumatol. 2016;68:915-23.

Disclosure: U. Mrowietz: AbbVie, 1, 5, 6, Aditxt, 1, Almirall, 1, Amgen, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Immunic Therapeutics, 1, Janssen-Cilag, 1, LEO Pharma, 1, Merck/MSD, 1, Novartis, 1, Phi-Stone, 1, selectION, 1, Sharp & Dohme, 1, 5, 6, UCB, 1, UNION therapeutics, 1, 5, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **D. Thaçi**: AbbVie, 1, 2, 5, 12, Investigator, Almirall, 1, 2, 12, Investigator, Amgen, 1, 2, 12, Investigator, Boehringer-Ingelheim, 1, 2, 12, Investigator, Bristol Myers Squibb, 1, 2, 12, Investigator, Celltrion, 1, 2, 12, Investigator, Eli Lilly and Company, 1, 2, 12, Investigator, Fresenius-Kabi, 2, 5, Galderma, 1, 2, 12, Investigator, Johnson & Johnson, 1, 2, 12, Investigator, Kyowa Kirin, 1, 2, 12, Investigator, L'Oreal, 1, 2, 12, Investigator, LEO Pharma, 1, 2, 5, 12, Investigator, New Bridge, 1, 2, 12, Investigator, Novartis, 1, 2, 12, Investigator, Pfizer, 1, 2, 12, Investigator, Regeneron, 1, 2, 12, Investigator, Samsung, 1, 2, 12, Investigator, Sanofi, 1, 2, 12, Investigator, Sun-Pharma, 1, 2, 5, Target-RWE, 1, 2, 12, Investigator, UCB, 1, 2, 12, Investigator, Vichy, 1, 2, 12, Investigator; **M. Lebwohl**: AbbVie, 5, Almirall, 2, AltruBio Inc, 2, Apogee Therapeutics, 2, Arcutis Biotherapeutics, 2, 5, AstraZeneca, 2, Atomwise, 2, Avotres, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, Cara Therapeutics, 5, Castle Biosciences, 2, Celltrion Biosciences, 2, Clexio Biosciences, 5, CorEvitas, 2, Dermavant, 2, 5, Dermsquared, 2, Eli Lilly, 5, Evommune, Inc, 2, Facilitation of International Dermatology Education, 2, Forte Biosciences, 12, Facilitation of International Dermatology Education, Galderma, 12, Facilitation of International Dermatology Education, Genentech, 12, Facilitation of International Dermatology Education, Incyte, 5, 12, Facilitation of International Dermatology Education, Inozyme, 5, Janssen, 5, LEO Pharma, 12, Facilitation of International Dermatology Education, Meiji Seika Pharma, 12, Facilitation of International Dermatology Education, Mindera, 12, Facilitation of International Dermatology Education, Mirium Pharmaceuticals, 2, Mount Sinai, 3, Pfizer, 5, 12, Facilitation of International Dermatology Education, Sanofi-Regeneron, 5, 12, Facilitation of International Dermatology Education, Seanergy, 12, Facilitation of International Dermatology Education, Strata, 12, Facilitation of International Dermatology Education, Takeda, 12, Facilitation of International Dermatology Education, Trevi Therapeutics, 12, Facilitation of International Dermatology Education, UCB, 5, Verrica Pharmaceuticals, 2; **B. Sigurgeirsson**: Novartis, 12,; **R. Warren**: AbbVie, 2, 5, 6, Almirall, 2, 5, 6, Amgen, 2, 5, Arena, 2, Astellas, 2, Avillion, 2, Biogen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 6, Celgene, 2, 5, DICE Therapeutics, 2, Eli Lilly and Company, 2, 5, 6, GSK, 2, Janssen, 2, 5, 6, LEO Pharma, 2, 5, Meiji Pharma, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, RAPT Therapeutics, 2, Sanofi, 2, Sun Pharma, 2, UCB, 2, 5, Union, 2; **R. Langley**: AbbVie, 1, 6, 12, Principal investigator, Amgen, 1, 6, 12, Principal investigator, Boehringer-Ingelheim, 1, 12, Principal investigator, Celgene, 1, 6, 12, Principal Investigator, Eli Lilly and Company, 1, 6, 12, Principal Investigator, LEO Pharma, 1, 6, 12, Principal Investigator, Merck, 1, 6, 12, Principal Investigator, Novartis, 1, 6, 12, Principal Investigator, Pfizer, 1, 6, 12, Principal Investigator, UCB, 1, 12, Principal Investigator; **A. Clemens**: Novartis, 3; **C. Vizcaya**: Novartis, 3; **W. Bao**: Novartis, 3, 11; **K. Hoyt**: Novartis, 3; **L. Gómez**: Novartis, 3; **R. Bissonnette**: AbbVie, Alumis, Amgen, Anaptys-Bio, Arcutis, BMS/Celgene, Dermavant, Eli Lilly, J&J (Janssen), LEO Pharma, Nimbus, Takeda, UCB Pharma, Ventyx-Bio, Vyne, 12, 1, 2, 5, 6, Innovaderm Research, 3, 8, Xencor, Zai Lab and Zura Bio, 12, 1, 2, 5, 6.

Abstract Number: 1448

Influence of Sex on the Therapeutic Persistence of Guselkumab in Psoriatic Disease: a Retrospective National Cohort Study

Laure Gossec[1], Pascal Claudepierre[2], Arnaud Constantin[3], Denis Jullien[4], Samira Chaalal[5], Julie Baraut[5], Laure Cipiere[5], Laurène Gautier[6], Pierre Lemire[7] and Thierry Passeron[8], [1]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [2]Department of Rheumatology, CHU Henri Mondor, AP-HP, Créteil, France, Creteil, France, [3]Department of Rheumatology, Toulouse University Hospital, Toulouse University and INSERM U1291, France, Toulouse, France, [4]Hospices Civils de Lyon, Hôpital E. Herriot Department of Dermatologie, Lyon F-69003 ; CIRI, Centre International de Recherche en Infectiologie, Team EIA : Epidermal immunity & Allergy, INSERM, U1111; Univ Lyon; Université de Lyon 1; Ecole Normale Supérieure de Lyon; CNRS, UMR 5308, Lyon, France., Lyon, France, [5]Johnson & Johnson, Issy les moulineaux, France, [6]Johnson & Johson, Issy les Moulineaux, France, [7]IQVIA, Real World Solutions, Paris, France, Paris, France, [8]Johnson & Johnson, Nice, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic disease, including psoriasis (Pso) and psoriatic arthritis (PsA), seems to affect male and female patients differently in clinical presentation, disease progression and advanced treatment response[1]. Sex influence on biologics has been described in bio-naive PsA population[2] previously, and this study investigates the sex impact on guselkumab (GUS) persistence in overall, bio-naive and bio-experienced Pso and/or PsA patients.

Methods: This study used data from the French administrative healthcare claims database (SNDS) on all adults with psoriatic disease who received their first GUS dispensation (index date) between 2019 and 2022. Patients were followed until death, treatment discontinuation or the end of the study period (12/31/2023). Two sub-groups were identified in the overall population of patients with a psoriatic disease, using surrogate markers of diagnosis: i) Pso patients (without PsA) and ii) PsA patients (with or without Pso). Treatment persistence for GUS depending on sex (i.e., the duration of treatment from initiation to discontinuation, defined as a drug-free interval of at least 120 days after the last dispensation of GUS) was estimated using the Kaplan-Meier method.

Results: Among the 9,478 patients who received at least one dispensation of GUS between 2019 and 2022, a total of 8,603 adult patients initiated treatment for psoriatic disease: 6,872 (79.9%) were Pso patients and 1,731 (20.1%) PsA patients. Males represented 55.6%, 58.2% and 54.8% of the overall, Pso and PsA populations, respectively. During the 5-year period before GUS initiation, 59.7% of patients had received at least one conventional disease-modifying antirheumatic drug

Table: Persistence of guselkumab

Population	Stratification	N (%)	Persistence (%) - 95% CI					
			12 months		24 months		36 months	
Psoriatic disease	Overall	8603 (100)	71.8	70.3-73.2	58.2	56.6-59.7	49.8	48.1-51.4
	Male	4783 (55.6)	74.4	72.4-76.3	60.8	58.7-62.7	52.5	50.2-54.8
	Female	3820 (44.4)	68.5	66.2-70.6	54.9	52.6-57.2	46.4	43.8-48.9
Pso	Overall	6872 (100)	73.6	72-75.2	59.6	57.9-61.3	51.2	49.3-53
	Male	4001 (58.2)	75.9	73.7-78	61.8	59.5-63.9	53.4	51-55.7
	Female	2871 (41.8)	70.4	67.8-72.9	56.6	54-59.2	48.1	45.1-51
PsA	Overall	1731 (100)	64.4	61-67.5	52.5	49-55.9	44.1	-*
	Male	782 (45.2)	66.5	61.4-71.1	56.0	50.8-60.9	48.0	-*
	Female	949 (54.8)	62.6	58-66.8	49.7	44.9-54.1	40.7	-*

*The follow-up of the PsA population was not sufficient to evaluate robustly the persistence at 36 months.

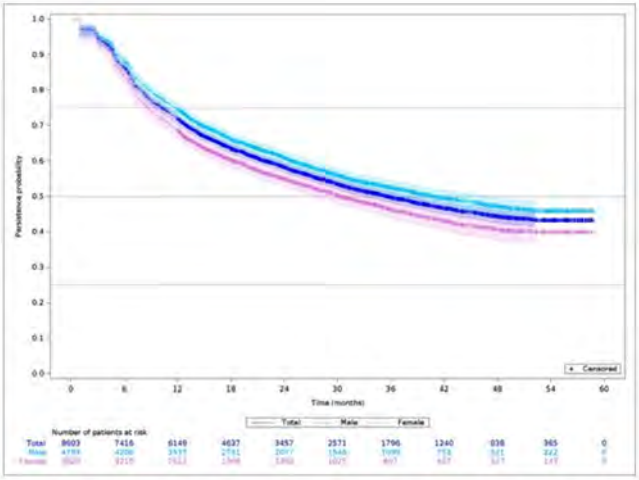


Figure: Persistence of guselkumab according to sex in psoriatic patients (overall population)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(DMARD) (Pso: 58.2%; PsA: 65.8%), and 61.8% had received at least one biologic DMARD (Pso: 57.2%; PsA: 79.8%). For overall population, persistence rates of GUS treatment at 12 months, 24 months, and 36 months were 71.8%, 58.2%, and 49.8% respectively, with 74.4%, 60.8%, and 52.5% for males and 68.5%, 54.9%, and 46.4% for females. For the Pso population, persistence rates were 73.6% at 12 months, 59.6% at 24 months and 51.2% at 36 months, with respectively 75.9%, 61.8% and 53.4% for males and 70.4%, 56.6% and 48.1% for females. For the PsA group, persistence rates were 64.4% at 12 months and 52.5% at 24 months, with respectively 66.5% and 56.0% for males and 62.6% and 49.7% for females. (Figure & Table). The median times to discontinuation were 35.6 months [95% CI: 33.6-38.0] for the overall population, 40.7 months [95% CI: 37.9-45,8] for males and 30.2 months [95% CI: 28.0-33.0] for females.

Conclusion: Consistent with previous findings showing that TNFi and IL-17i treatment persistence was lower for female PsA patients than for male, our results highlight the sex influence on GUS persistence in psoriatic disease, including PsO and PsA patients. These findings suggest that sex-related factors may influence treatment outcomes, emphasizing the need for tailored treatment strategies to enhance persistence in psoriatic disease management.

[1]Tarannum S et al., Nat Rev Rheumatol. 2022 Sep;18(9):513-526
[2] Pina Vegas L et al., RMD Open. 2023 Dec 19;9(4):e003570

Disclosure: L. Gossec: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **P. Claudepierre**: Johnson & Johnson, 1, 2, 6; **A. Constantin**: Johnson & Johnson, 1, 2, 6; **D. Jullien**: Johnson & Johnson, 1, 2, 6; **S. Chaalal**: None; **J. Baraut**: None; **L. Cipiere**: None; **L. Gautier**: None; **P. Lemire**: None; **T. Passeron**: Johnson & Johnson, 1, 2, 6.

Abstract Number: 1449

Bimekizumab Demonstrated Comparable One-Year Efficacy in Male and Female Patients with Axial Spondyloarthritis: Results from Two Phase 3 Studies

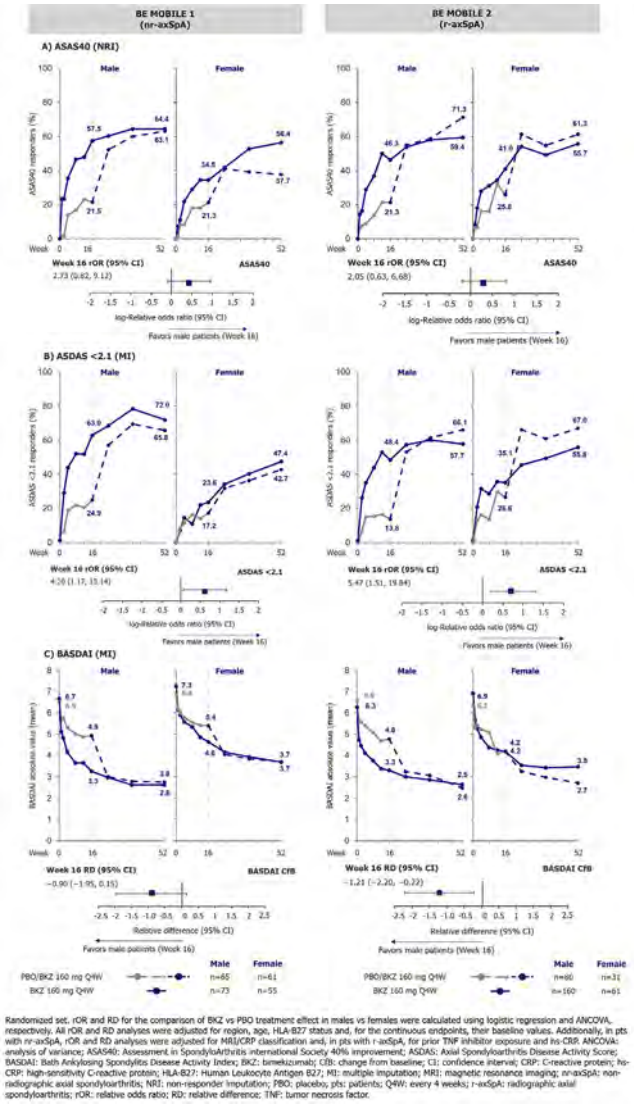
Lianne S. Gensler[1], Sofia Ramiro[2], Denis Poddubnyy[3], Marina Magrey[4], Irene E. van der Horst-Bruinsma[5], Atul Deodhar[6], Vanessa Taieb[7], Diana Voiniciuc[8], Natasha de Peyrecave[9] and Martin Rudwaleit[10], [1]Department of Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, [2]Leiden University Medical Center, Bunde, Netherlands, [3]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [4]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH, [5]Department of Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands, [6]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [7]UCB, Colombes, France, [8]UCB, Slough, United Kingdom, [9]UCB, Brussels, Belgium, [10]Bielefeld University, Medical School and University Medical Centre OWL, Klinikum Bielefeld, Department of Rheumatology, Bielefeld, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. BKZ has shown sustained efficacy to Week (Wk) 52 in patients (pts) with non-radiographic/radiographic axial spondyloarthritis (nr-/r-axSpA) in the BE MOBILE 1 and 2 studies.[1,2] Studies have shown male and female pts with axSpA can experience different disease manifestations, clinical burden and treatment efficacy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Randomized set. rOR and RD for the comparison of BKZ vs PBO treatment effect in males vs females were calculated using logistic regression and ANCOVA, respectively. All rOR and RD analyses were adjusted for region, age, HLA-B27 status and, for the continuous endpoints, their baseline values. Additionally, in pts with nr-axSpA, rOR and RD analyses were adjusted for MRI/CRP classification and, in pts with r-axSpA, for prior TNF inhibitor exposure and hs-CRP. ANCOVA: analysis of variance; ASAS40: Assessment in Spondyloarthritis international Society 40% improvement; ASDAS: Axial Spondyloarthritis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; CRP: C-reactive protein; hs-CRP: high-sensitivity C-reactive protein; HLA-B27: Human Leukocyte Antigen B27; MI: multiple imputation; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; PBO: placebo, pts: patients; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; rOR: relative odds ratio; RD: relative difference; TNF: tumor necrosis factor.

Figure 1. ASAS40, ASDAS <2.1 and BASDAI to Week 52 and relative odds ratios and relative differences at Week 16, stratified by sex

Here, we assess efficacy of BKZ treatment to Wk52 in pts across the full axSpA disease spectrum, focusing on potential sex-based differences.

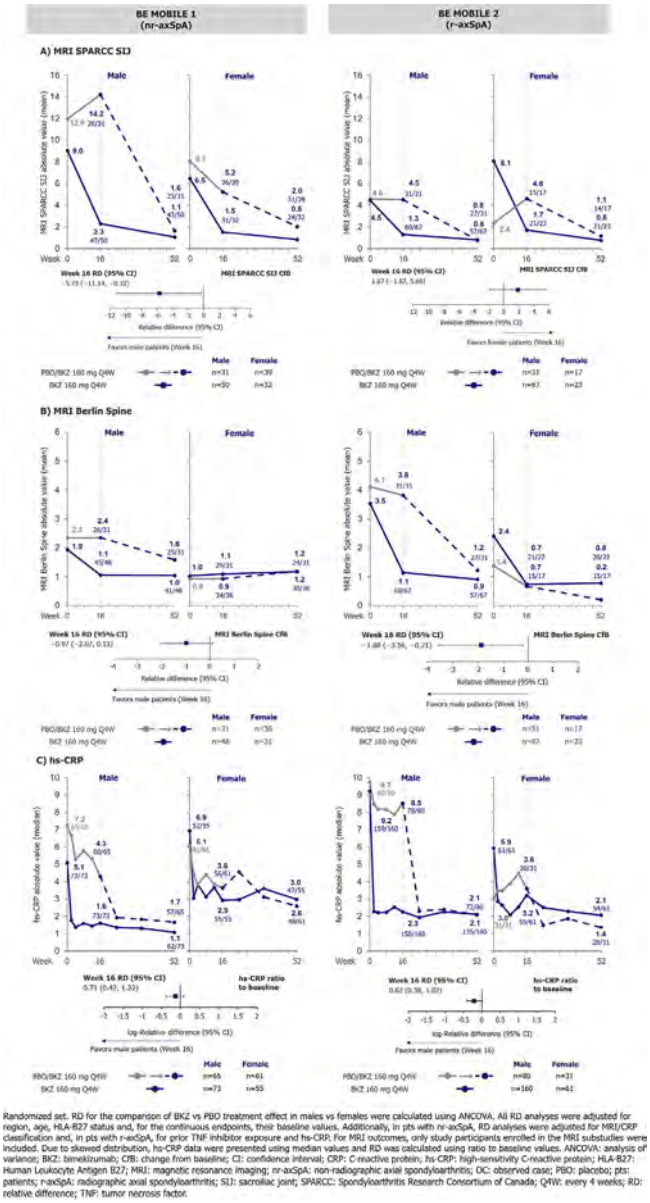
Methods: BE MOBILE 1 (NCT03928704) and 2 (NCT03928743) both comprised a 16-wk double-blind and 36-wk maintenance period. Pts were randomized to receive subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO); from Wk16, all received BKZ 160 mg Q4W.

Outcomes reported to Wk52, stratified by sex, include ASAS40, ASDAS < 2.1, BASDAI, Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) and objective signs of inflammation (OSI; MRI SPARCC SIJ, MRI Berlin spine and hs-CRP).

Results: 254 pts (M=138, F=116) were randomized in BE MOBILE 1 and 332 pts (M=240, F=92) were randomized in BE MOBILE 2; of these, 220/254 and 298/332 completed to Wk52.

Baseline (BL) differences between males and females included longer mean symptom duration (years) in females (**nr-axSpA**: 7.2 vs 11.1; **r-axSpA**: 12.9 vs 15.0) and lower HLA-B27 positivity (%) in females (**nr-axSpA**: 84.8 vs 69.0; **r-axSpA**: 88.3 vs 78.3). Across BKZ and PBO-randomized pts at BL, males had lower mean ASQoL scores vs females (**nr-axSpA:** BKZ: 8.5

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Randomized set. RD for the comparison of BKZ vs PBO treatment effect in males vs females were calculated using ANCOVA. All RD analyses were adjusted for region, age, HLA-B27 status and, for the continuous endpoints, their baseline values. Additionally, in pts with nr-axSpA, RD analyses were adjusted for MRI/CRP classification and, in pts with r-axSpA, for prior TNF inhibitor exposure and hs-CRP. For MRI outcomes, only study participants enrolled in the MRI substudies were included. Due to skewed distribution, hs-CRP data were presented using median values and RD was calculated using ratio to baseline values. ANCOVA: analysis of variance; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; CRP: C-reactive protein; hs-CRP: high-sensitivity C-reactive protein; HLA-B27: Human Leukocyte Antigen B27; MRI: magnetic resonance imaging; nr-axSpA: non-radiographic axial spondyloarthritis; OC: observed case; PBO: placebo; pts: patients; r-axSpA: radiographic axial spondyloarthritis; SIJ: sacroiliac joint; SPARCC: Spondyloarthritis Research Consortium of Canada; Q4W: every 4 weeks; RD: relative difference; TNF: tumor necrosis factor.

Figure 2. MRI SPARCC SIJ, MRI Berlin spine score and hs-CRP absolute values to Week 52 and relative differences at Week 16, stratified by sex (OC)

vs 10.8, PBO: 8.6 vs 10.2; **r-axSpA:** BKZ: 8.3 vs 11.1, PBO: 8.4 vs 9.0), and generally had higher mean OSI values.

Across ASAS40, ASDAS < 2.1 and BASDAI change from BL (CfB), a pattern of higher BKZ vs PBO treatment effect in males vs females at Wk16 was reflected in the relative odds ratios (rORs) and relative differences (RDs) at this timepoint (**Figure 1**). At Wk52, response rates were higher/comparable in males vs females with nr-axSpA/r-axSpA respectively. Full results of ASAS40, ASDAS < 2.1 and BASDAI can be seen in **Figure 1**.

For ASQoL, males and females showed improvements with BKZ at Wk16 (**nr-axSpA**: –5.5 vs –4.8; **r-axSpA**: –4.8 vs –5.5) compared with PBO (**nr-axSpA**: –2.1 vs –2.9; **r-axSpA**: –3.1 vs –3.7). Improvements continued to Wk52 with BKZ (**nr-axSpA:** BKZ: –5.7 vs –6.2, PBO/BKZ: –5.5 vs –5.1; **r-axSpA:** BKZ: –5.4 vs –6.5, PBO/BKZ: –5.5 vs –5.8).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

For CfB in OSI outcomes, RDs generally indicated a higher BKZ vs PBO treatment effect in males vs females at Wk16 (-**Figure 2**). However, absolute OSI values in males and females were generally comparable at Wk16, with values maintained or improved to Wk52 (**Figure 2**).

Conclusion: The treatment effect of BKZ vs PBO at Wk16 tended to be higher among male vs female pts with axSpA. However, at Wk52 female pts showed marked improvement and comparable efficacy to male pts following longer-term treatment with BKZ. Overall, efficacy of BKZ in clinical, patient-reported, and OSI outcomes was demonstrated in both pt populations across the full axSpA disease spectrum.

References: 1. van der Heijde D. Ann Rheum Dis 2023;82(4):515–26; **2**. Baraliakos X. Ann Rheum Dis 2024;83 (2):199–213.

Disclosure: L. Gensler: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **M. Magrey**: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **I. van der Horst-Bruinsma**: AbbVie, 2, 5, 12, Fees received for lectures, BMS, 12, Fees received for lectures, Eli Lilly, 2, MSD, 2, 5, 12, Fees received for lectures, Novartis, 2, Pfizer, 5, 12, Fees received for lectures, UCB, 2, 5; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **V. Taieb**: UCB, 3, 12, Shareholder; **D. Voiniciuc**: UCB, 7, Veramed, 3; **N. de Peyrecave**: UCB, 3; **M. Rudwaleit**: AbbVie, 2, Boehringer Ingelheim, 2, Janssen, 2, 6, Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2.

Abstract Number: 1450

The Novel Digital Therapeutic Axia Improves Disease Activity, Functionality, and Quality of Life in Axial Spondyloarthritis Patients: Results from a Randomized Controlled Trial (Bechterew-App Trial)

Patrick-Pascal Strunz[1], Tobias Heusinger[2], Maxime Le Maire[2], Anna Fleischer[3], Karsten Sebastian Luetkens[4], Patricia Possler[2], Michael Gernert[1], Hannah Labinsky[5], Robert Leppich[6], Astrid Schmieder[7], Ludwig Hammel[8], Billy Sperlich[9], Matthias Fröhlich[1] and **Marc Schmalzing**[10], [1]University Hospital of Wuerzburg, Department of Medicine II, Rheumatology/ Immunology, Wuerzburg, Germany, [2]University of Wuerzburg, Wuerzburg, Germany, [3]University Hospital of Wuerzburg, Department of Medicine II, Psychosomatics, Wuerzburg, Germany, [4]University Hospital of Wuerzburg, Institute of Diagnostic and Interventional Radiology, Wuerzburg, Germany, [5]University Hospital of Wuerzburg, Würzburg, Germany, [6]University Hospital of Wuerzburg, Chair of Software Engineering (Informatik II), Department of Computer Science, Wuerzburg, Germany, [7]University Hospital Würzburg, Department of Dermatology, Venereology, and Allergology, Wuerzburg, Germany, [8]Deutsche Vereinigung Morbus Bechterew e. V., Schweinfurt, Germany, [9]Integrative and Experimental Exercise Science and Training, Institute for Sports Science, Wuerzburg, Germany, [10]Department of Medicine II, Rheumatology/ Immunology,University Hospital of Wuerzburg, Wuerzburg, Bayern, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

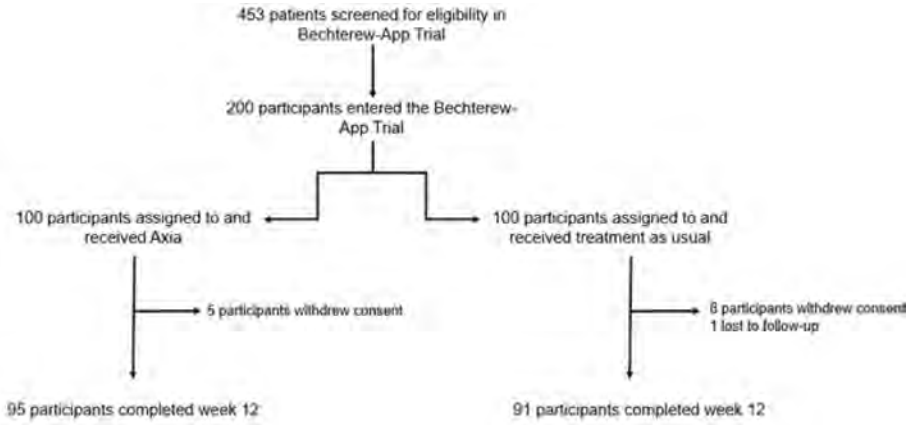
Session Time: 10:30AM–12:30PM

Background/Purpose: Axia is a novel digital therapeutic (DTx) specifically designed for patients with axial spondyloarthritis (axSpA), in compliance with the European Medical Device Regulation (MDR). Axia delivers an innovative, app-based

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Intervention (n=95)	Control (n=92)
Mean age; years (SD)	50 (12)	51 (11)
BASDAI; absolute (SD)	5.32 (1.31)	5.02 (1.26)
Female Proportion; % (n)	74% (70)	59% (54)
NSAIDs; % (n)	55% (52)	62% (57)
bDMARD or tsDMARD usage; % (n)	56.3% (53)	60.2% (55)
Physical Therapy		
Professional Physiotherapy		
Once per week; % (n)	56% (53)	60% (55)
No Physiotherapy; % (n)	44% (42)	40% (37)
Home-based Exercise; % (n)	39% (37)	41% (38)
Functional training; % (n)	31% (29)	34% (31)
Other Sports; % (n)	32% (30)	34% (31)

Baseline characteristics of the study population



Flowchart and trial design of the Bechterew-App Trial

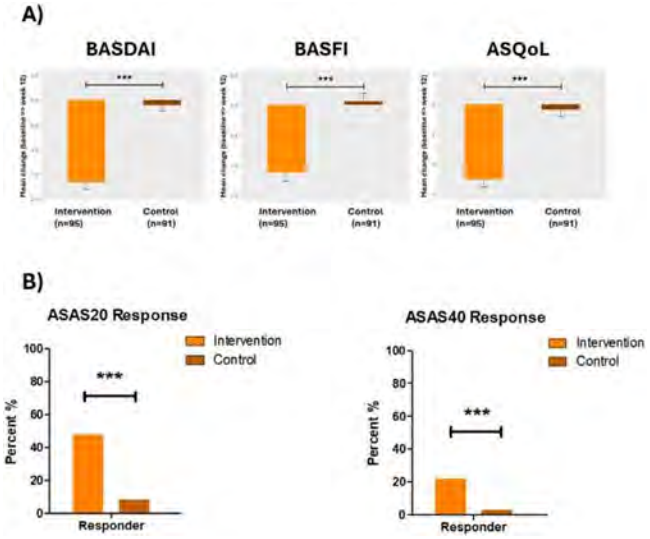
intervention combining individualized home exercise programs, patient education, and comprehensive disease management, incorporating structured gamification elements to support long-term adherence. To date, no DTx targeting rheumatic diseases has been convincingly demonstrated to improve disease activity.

The Bechterew-App Trial was designed as a nationwide, randomized, controlled interventional trial (RCT) to assess the efficacy of Axia over a 12-week period in German axSpA patients with stable pharmacotherapy.

Methods: In this 12-week RCT, 200 patients with axSpA receiving stable pharmacotherapy were randomized (1:1) to either using Axia (intervention group) or treatment as usual (control group) (Figure 1 and Figure 2). The primary endpoints are improvements in disease activity, measured by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); disease-specific functionality, assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI); and disease-specific quality of life, evaluated using the Ankylosing Spondylitis Quality of Life questionnaire (ASQoL). Secondary endpoints include responder analyses based on the Assessment of Spondyloarthritis International Society (ASAS)20 and ASAS40 response criteria.

Results: Of the 200 axSpA patients enrolled in the trial, 186 participants (95 in the intervention group and 91 in the control group) completed the study (Figure 2). Apart from a slightly higher proportion of female participants, no significant differences were observed between the groups at baseline (Figure 1). Participants in the Axia intervention group demonstrated significant and clinically meaningful improvements in disease activity (BASDAI: –1.66 [SD 1.41] vs. control: –0.11 [1.15];

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Results of the Bechterew-App Trial A) The intervention group showed improvements in mean BASDAI, BASFI and ASQoL The analysis was conducted using ANCOVA, adjusted for baseline values and sex. ***: p < 0.001. Abbreviations: ASQoL, Ankylosing Spondylitis Quality of Life Questionnaire; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index. B) Efficacy of Axia assessed by ASAS20 and ASAS40 response criteria. ASAS20 response was defined as an improvement of at least 20% and at least 1 unit (on a 0–10 scale) from baseline in three of four domains (spinal pain [BASDAI question 2], spinal inflammation [mean of BASDAI questions 5 and 6], physical function [BASFI], and patient global assessment by visual analogue scale [VAS]), with no worsening in the remaining domain (defined as a deterioration of ≥20% or ≥1 unit). ASAS40 response required an improvement of at least 40% and 2 units in three of the four domains without worsening in the fourth. ***: p < 0.001. Abbreviations: ASAS, Assessment of Spondyloarthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index.

p< 0.001), functional status (BASFI: −1.12 [1.40] vs. control: 0.06 [1.31]; p< 0.001), and disease-specific quality of life (ASQoL: –2.51 [2.55] vs. control: –0.16 [2.26]; p< 0.001), without meaningful changes in the control group (Figure 3A). Furthermore, a significantly higher proportion of patients in the intervention group achieved an ASAS20 response compared to the control group (51% vs. 9%; p< 0.001), and the ASAS40 response rate was also markedly higher (23% vs. 3%; p< 0.001) (Figure 3B). No concerning safety signals were detected.

Conclusion: In this 12-week RCT involving axSpA patients receiving stable pharmacotherapy, the DTx Axia significantly improved disease activity, functional status, and disease-specific quality of life. These findings support the potential of Axia as a novel therapeutic option for patients with axSpA.

Disclosure: P. Strunz: None; **T. Heusinger**: Applimeda GmbH, 12, 4, 8; **M. Le Maire**: Applimeda GmbH, 12, 4, 8; **A. Fleischer**: None; **K. Luetkens**: None; **P. Possler**: None; **M. Gernert**: None; **H. Labinsky**: None; **R. Leppich**: Applimeda GmbH, 12, 4, 8; **A. Schmieder**: None; **L. Hammel**: None; **B. Sperlich**: None; **M. Fröhlich**: None; **M. Schmalzing**: None.

Abstract Number: 1451

Bimekizumab was Efficacious Regardless of Age, BMI, CRP, or HLA-B27 Status: 1-Year Results from Two Phase 3 Studies

Marina Magrey[1], Helena Marzo-Ortega[2], Yuho Kadono[3], David Nicholls[4], Martin Rudwaleit[5], Atul Deodhar[6], Gaëlle Varkas[7], Chetan Prajapati[8], Sarah Kavanagh[9] and Victoria Navarro-Compan[10], [1]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH, [2]NIHR Leeds Biomedical Research Centre, The Leeds Teaching Hospitals NHS Trust and Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom, [3]Department of Orthopaedic Surgery, Saitama Medical University, Saitama, [4]Clinical Trials Unit,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University of the Sunshine Coast, Queensland, Australia, [5]Bielefeld University, Medical School and University Medical Centre OWL, Klinikum Bielefeld, Department of Rheumatology, Bielefeld, Germany, [6]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [7]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [8]UCB, Slough, United Kingdom, [9]UCB, Morrisville, NC, [10]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

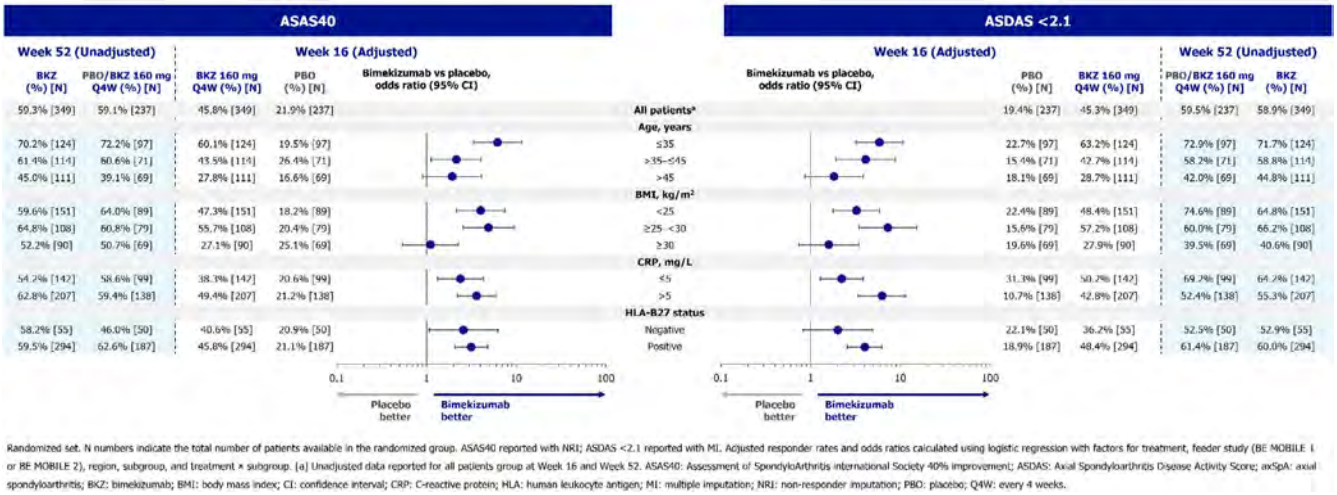
Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown efficacy to Week (Wk) 52 in patients (pts) with axial spondyloarthritis (axSpA).[1] BKZ has shown comparable efficacy to 1 year (yr) across sexes,[2] and to 2 yrs in differing symptom durations;[3] the effect of other pt characteristics has not yet been reported. We report BKZ clinical outcomes to 1 yr in pts with axSpA stratified by age, BMI, CRP, and HLA-B27 status.

Methods: In BE MOBILE 1 and 2 (NCT03928704; NCT03928743), pts were randomized to subcutaneous BKZ 160 mg every 4 wks (Q4W) or placebo (PBO); all pts received BKZ Q4W from Wk 16–52.

To Wk 52, we analyzed proportions of pts achieving ASAS40 and ASDAS < 2.1, and change from baseline (CfB) in ASDAS, BASDAI, ASQoL, and objective signs of inflammation (OSI; MRI SPARCC SIJ and MRI Berlin Spine). Pooled pts were stratified by baseline age (≤35, >35–≤45, >45 yrs), BMI (< 25, ≥25–< 30, ≥30 kg/m^2), CRP (≤5, >5 mg/L), and HLA-B27 status (negative, positive). Binary endpoints used non-responder imputation; continuous endpoints used multiple imputation. OSI measures used observed case.

To compare Wk 16 BKZ treatment effect vs PBO stratified by subgroup, adjusted odds ratios and least squares (LS) mean differences were calculated using logistic regression and ANCOVA, respectively. No p values are provided due to the post hoc nature of analyses.

Results: Of 586 pooled pts, 349 and 237 were randomized to BKZ and PBO at baseline, respectively. Generally, larger improvements in clinical outcomes were seen for BKZ vs PBO across all subgroups at Wk 16; improvements were sustained/further improved to Wk 52 in all pts (**Figures 1–3**).



Randomized set. N numbers indicate the total number of patients available in the randomized group. ASAS40 reported with NRI; ASDAS <2.1 reported with MI. Adjusted responder rates and odds ratios calculated using logistic regression with factors for treatment, feeder study (BE MOBILE 1 or BE MOBILE 2), region, subgroup, and treatment × subgroup. [a] Unadjusted data reported for all patients group at Week 16 and Week 52. ASAS40: Assessment of SpondyloArthritis international Society 40% improvement; ASDAS: Axial Spondyloarthritis Disease Activity Score; axSpA: axial spondyloarthritis; BKZ: bimekizumab; BMI: body mass index; CI: confidence interval; CRP: C-reactive protein; HLA: human leukocyte antigen; MI: multiple imputation; NRI: non-responder imputation; PBO: placebo; Q4W: every 4 weeks.

Figure 1. Patients achieving ASAS40 (NRI) and ASDAS <2.1 (MI) at Week 16 and Week 52, stratified by baseline characteristic subgroups

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

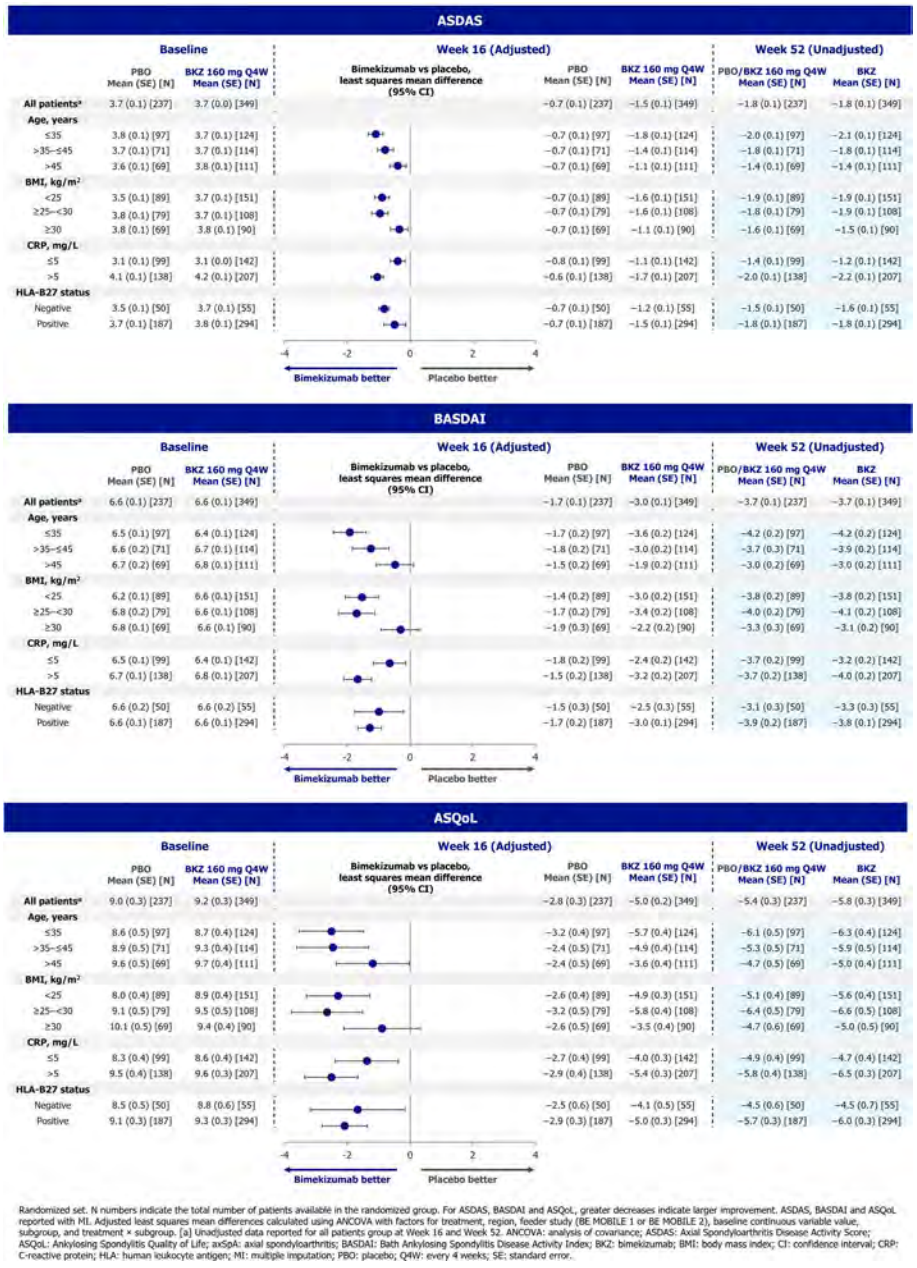


Figure 2. Mean change from baseline in ASDAS, BASDAI and ASQoL at Week 16 and Week 52, stratified by baseline characteristic subgroups (MI)

For ASAS40/ASDAS < 2.1, numeric differences in the proportions of pts achieving outcomes were detected between BKZ vs PBO at Wk 16 across subgroups except age >45 yrs, BMI ≥30 kg/m^2, and HLA-B27 negativity (ASDAS < 2.1 only). Within respective subgroups, at Wk 52, proportions achieving ASAS40/ASDAS < 2.1 were numerically higher in BKZ-randomized pts with age ≤35 yrs, BMI ≥25–< 30 kg/m^2, or HLA-B27 positivity (**Figure 1**).

For ASDAS/BASDAI/ASQoL, numeric differences in LS mean CfB were detected for BKZ vs PBO at Wk 16 across most subgroups except for age >45 yrs (BASDAI only), and BMI ≥30 kg/m^2 (BASDAI/ASQoL only). Within respective subgroups, at Wk 52, numerically larger improvements in mean CfB ASDAS/BASDAI/ASQoL were observed in BKZ-randomized pts with age ≤35 yrs, BMI ≥25–< 30 kg/m^2, CRP >5 mg/L, and HLA-B27 positivity (**Figure 2**).

For OSI, numeric differences in LS mean CfB were detected for BKZ vs PBO at Wk 16 across subgroups except for age >45 yrs and HLA-B27 negativity, BMI ≥30 kg/m^2 (MRI SPARCC SIJ only), and BMI < 25 kg/m^2 and CRP ≤5 mg/L (MRI Berlin

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

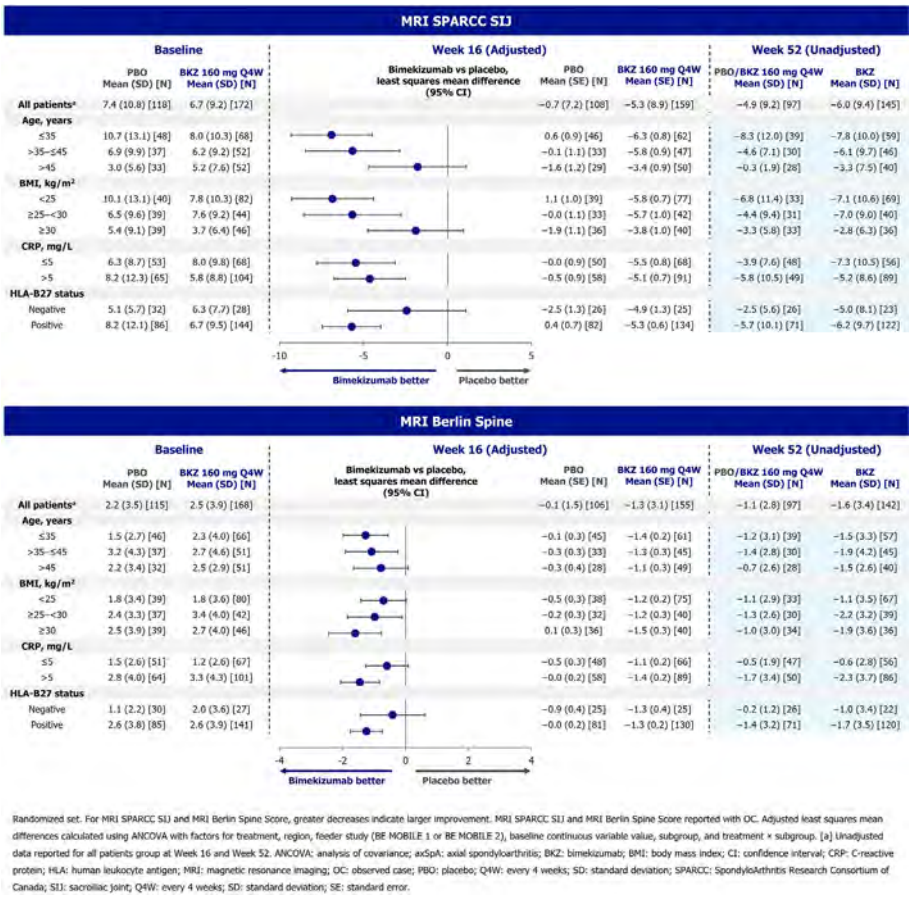


Figure 3. Mean change from baseline in MRI SPARCC SIJ and MRI Berlin Spine Score at Week 16 and Week 52, stratified by baseline characteristic subgroups (OC)

Spine only). Within respective subgroups, at Wk 52, numerically larger OSI improvements were seen in HLA-B27 positive pts only (**Figure 3**).

Conclusion: BKZ generally demonstrated greater improvements in clinical outcomes vs PBO at Wk 16. Improvements were sustained to 1 yr in pts with axSpA, regardless of pt demographics and baseline clinical presentation.

References: 1. Baraliakos X. Ann Rheum Dis 2024;83:199–213. **2**. Rudwaleit M. EULAR 2025; Poster POS0920. **3**. Ramiro S. ACR 2024; Poster 2352.

Disclosure: M. Magrey: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **H. Marzo-Ortega**: AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 6, UCB, 2, 5, 6; **Y. Kadono**: AbbVie, 6, Eli Lilly, 6, Novartis, 6, UCB, 6; **D. Nicholls**: AbbVie, 1, 5, 6, AstraZeneca, 1, 6, BMS, 5, Eli Lilly, 5, Gilead, 5, Incannex, 5, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Servatus, 5, Sun Pharma, 5, UCB, 1, 5, 6; **M. Rudwaleit**: AbbVie, 2, Boehringer Ingelheim, 2, Janssen, 2, 6, Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **G. Varkas**: AbbVie, 2, 5, 6, Amgen, 2, 6, Celltrion, 2, 5, 6, EG, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, MSD, 5, Novartis, 2, 6, Pfizer, 2, 5, 6, Takeda, 5, UCB, 2, 6; **C. Prajapati**: UCB, 7, Veramed, 3; **S. Kavanagh**: Aclipse Therapeutics, 2, Aliada Therapeutics, 2, Allay Therapeutics, 2, Autobahn Therapeutics, 2, Cognition Therapeutics, 2, Colorado Prevention Center, 2, Karuna Therapeutics, 2, Kisbee Therapeutics, 2, LB Pharmaceuticals, 2, Nesos, 2, Novartis, 2, Onward Medical,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, PharPoint Research, 2, Summit Analytical, 2, Therini Bio, 2, Tonix Pharmaceuticals, 2, Tornado Therapeutics, 2, UCB, 2, 3, Whitsell Innovations, 2, Worldwide Clinical Trials, 2, Zosano Pharma, 2; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1452

Clinical and Demographic Characteristics of Treatment-Refractory Axial Spondyloarthritis: Data from the Greek AxSpA Registry

Nikolaos Kougkas[1], Konstantinos Tsafis[2], Dimitrios Deligeorgakis[3], Vasileios Papadopoulos[4], Nikolaos Fytanidis[5], Michail Krikelis[6], Evangelia Mole[7], Sousana Gazi[7], Nikolaos Koletsos[8], EVRIPIDIS KALTSONOUDIS[9], Paraskevi V Voulgari[10], Anastasios Karamanakos[11], Maria Pappa[12], Maria Tektonidou[13], Petros Sfikakis[14], Kalliopi Klavdianou[15], aggelos Banos[16], Eleni Kalavri[17], Konstantinos Kottas[18], Gkikas Katsifis[18], MARIA KONSTA[19], Eleftheria Grika[20], Charalampos Sfontouris[20], Evgenia Mavrea[21], Christos Koutsianas[22], Evangelia Kataxaki[23], Eleni Sampatakaki[24], Konstantina Zoupidou[25], Pelagia Katsimpri[26], Alexios Iliopoulos[27], Georgios Iliopoulos[28], Dimitrios Daousis[29], Ilias Bournazos[30], DIMITRIOS KAROKIS[31], Dimos Patrikos[32], Theodoros Dimitroulas[3], Dimitrios Vassilopoulos[21], George E Fragoulis[33] and Charalampos Papagoras[34], [1]4th Department of Internal Medicine, Aristotle University, Thessaloniki, Thessaloniki, Greece, [2]Hippokration University Hospital, Medical School, Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece, Thessaloniki, Thessaloniki, Greece, [3]Hippokration University Hospital, Medical School, Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece, Thessaloniki, Greece, [4]Department of Medicine Democritus University of Thrace, Laboratory of Anatomy, Alexandroupolis, Greece, Alexandroupolis, Evros, Greece, [5]University Hospital of Alexandroupolis, Democritus University of Thrace, First Department of Internal Medicine, Alexandroupolis, Greece, Alexandroupolis, Greece, [6]KAT Hospital, Athens, Department of Rheumatology, Athens, Greece, Athens, Attiki, Greece, [7]Rheumatology department, KAT General Hospital of Attica, Athens, Attiki, Greece, [8]School of Health Sciences, Faculty of Medicine, University of Ioannina, Department of Rheumatology, Ioannina, Greece, Ioannina, Ioannina, Greece, [9]Rheumatology Clinic, University of Ioannina, IOANNINA, Ioannina, Greece, [10]Department of Rheumatology, School of Health Sciences, Faculty of Medicine, University of Ioannina, Ioannina, Ioannina, Greece, [11]Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine, General Hospital of Athens "Laiko", First Department of Propedeutic and Internal Medicine, Athens, Greece, Athens, Greece, [12]Rheumatology and Clinical Immunology Unit, 4th Department of Internal Medicine, Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, Athens, Attiki, Greece, [13]National and Kapodistrian University of Athens, Athens, Greece, [14]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [15]Asklepieion" General Hospital, Athens, Department of Rheumatology, Athens, Greece, Kaisariani Athens, Greece, [16]Asklepieion" General Hospital, Athens, Department of Rheumatology, Athens, Greece, Athens, Attiki, Greece, [17]"Asklepieion" General Hospital, Athens, Department of Rheumatology, Athens, Greece, Athens, Greece, [18]Naval Hospital of Athens, Rheumatology Clinic, Athens, Greece, Athens, Greece, [19]Sismanoglion Hospital, Athens, Greece, Marousi, Attiki, Greece, [20]Evaggelismos Athens General Hospital, Department of Rheumatology, Athens, Greece, Athens, Greece, [21]Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine, General Hospital of Athens "Hippokration", Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine and Laboratory, Athens, Greece, Athens, Greece, [22]Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine, General Hospital of Athens "Hippokration", Athens, Greece, [23]General Hospital Elefsinas Thriaseio,Attica, Rheumatology Department, Athens, Greece, Athens, Greece, [24]Joint Academic Rheumatology Program, Attikon University Hospital, National and Kapodistrian University of Athens, School of Medicine, 4th Department of Internal Medicine, Athens, Greece, Athens, Attiki, Greece, [25]Joint Academic Rheumatology Program, Attikon University Hospital, National and Kapodistrian University of Athens, School of Medicine, 4th Department of Internal Medicine, Athens, Greece, Athens, Greece, [26]Joint Rheumatology Program, University of Athens Medical School, Athens, Greece, [27]417 Army Share Fund Hospital (NIMTS), Department of Rheumatology, Athens, Greece, ZOGRAFOU, Greece, [28]Patras University Hospital, University of Patras Medical School, Department of Rheumatology, Patras, Greece, Patras, Akhaia, Greece, [29]Patras University Hospital, University of Patras Medical School, Department of Rheumatology, Patras, Greece, Patra, Greece, [30]Private practice, Athens, Greece, Athens, Greece, [31]Private practice, Patras, Greece, Patras, Greece, [32]Private practice, Athens, Greece, Ag. Paraskevi, Greece, [33]First Department of Propedeutic and Internal Medicine, Joint Academic Rheumatology program, National and Kapodistrian University of Athens, Athens, Attiki, Greece, [34]First Department of Internal Medicine, University Hospital of Alexandroupolis, Democritus University of Thrace, Alexandroupolis, Evros, Greece

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (AxSpA) is a chronic inflammatory disease that significantly impairs quality of life. Although biologic and targeted synthetic DMARDs (b/tsDMARDs) have improved disease control, a subset of patients remains treatment-refractory (TR), failing to achieve effective control of inflammation despite sequential use of multiple advanced therapies. This TR subgroup forms part of the broader group of difficult-to-manage (D2M) AxSpA patients. ASAS recently proposed a definition for both D2M and TR to guide research into these special populations [1].

Objectives: To describe the demographic and clinical features of treatment-refractory AxSpA patients in Greece and compare them with the non-TR subgroups.

Methods: Data were retrieved from the Greek AxSpA Registry, a prospective cohort (2022–2023) including patients fulfilling the 1984 modified New York criteria for radiographic AxSpA or the 2009 ASAS criteria for non-radiographic AxSpA. Patients were classified into three groups: non-D2M, D2M non-TR, and TR. TR patients met both of the following criteria: (1) inadequate response, defined as ASDAS ≥2.1 despite treatment with ≥2 b/tsDMARDs with different mechanisms, and (2) objective evidence of persistent inflammation (CRP >0.5 mg/dL). Demographics, clinical, radiographic features and comorbidities were compared among groups.

Table 1. Comparison of characteristics between Treatment Refractory (TR), non-TR Difficult-to-manage (D2M) and non-D2M patients with AxSpA

Variable	Non-D2M (n=355)	Non-TR D2M (n=18)	TR D2M (n=22)	p-value
Age, mean±SD, years	49.7 ± 14.6	51.2 ± 12.3	53.9 ± 9.7	0.387
Male gender, *n (%)*	250 (70)	11 (61)	13 (59)	0.395
Unemployed, *n (%)*	22 (6)	**5 (28)***	3 (14)	**0.008**
Radiographic AxSpA, *n (%)*	241 (70)	10 (56)	17 (77)	0.304
Disease duration since diagnosis, median (IQR), years	9 (4–17)	7 (5–12)	17 (8–23)	0.068
HLA-B27 positive, *n (%)*	192 (78)	**8 (57)****	13 (100)	0.026
BASDAI, median (IQR)	1.6 (0.6–2.8)	**4.9 (4.0–6.0)***	**4.4 (3.6–6.1)***	**<0.001**
ASDAS, median (IQR)	1.3 (0.9–1.7)	**2.9 (2.4–3.1)***	**3.1 (2.3–4.1)***	**<0.001**
BASFI, median (IQR)	1.8 (0.5–3.0)	**5.0 (4.4–6.2)***	**4.9 (3.9–8.0)***	**<0.001**
Global VAS, median (IQR)	1 (1–3)	**6 (4–7)***	**4 (3–8)***	**<0.001**
Pain VAS, median (IQR)	1 (0–2)	**5 (4–8)***	**4 (3–7)***	**<0.001**
CRP, median (IQR), mg/dL	0.3 (0.2–0.7)	0.4 (0.3–1.9)	**1.1 (0.9–2.1)***	**<0.001**
Syndesmophytes, *n (%)*	139 (39)	5 (28)	**15 (68)*****	**0.014**
Spine sections with syndesmophytes, median (IQR)	0 (0 – 2)	0 (0 – 1)	**1 (0 – 2)*****	0.012
Hip involvement (ever), *n (%)*	87 (25)	8 (44)	**10 (45)***	**0.021**
BMI ≥25 kg/m², n (%)	192 (59)	11 (69)	**19 (95)***	**0.005**
Current smokers, *n (%)*	114 (33)	7 (44)	**13 (65)***	**0.012**
Depression, *n (%)*	45 (13)	**7 (39)***	6 (30)	**0.002**
Number of comorbidities†, median (IQR)	0 (0–1)	**2 (1–3)***	**3 (1–3)***	**0.004**
Number of prior b/tsDMARDs, median (IQR)	0 (0–1)	**1 (1–3)***	**2 (1–3)***	**<0.001**

† Includes BMI ≥25 kg/m², arterial hypertension, dyslipidemia, diabetes mellitus, atherosclerotic disease, chronic obstructive pulmonary disease, osteoporosis, cancer
*Asterisks denote significant difference: * vs non-D2M, ** vs non-D2M AND TR, ***vs non-D2M AND non-TR D2M*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Out of 395 AxSpA patients included in this analysis, 355 (89.9%) were classified as non-D2M and 40 (10.1%) as D2M, among whom 22 (5.6%) patients met criteria for TR disease. There was no significant difference regarding age, gender, disease duration and proportion of radiographic disease among the three groups (Table 1). However, compared to non-D2M patients, TR patients, as well as non-TR D2M patients, exhibited significantly higher BASDAI, ASDAS, BASFI, Global and Pain VAS ($p< 0.001$ for all), as well as a higher number of comorbidities ($p=0.004$). However, depression was more frequent in the non-TR D2M group only ($p=0.002$). Particularly TR patients had significantly more syndesmophytes, more frequent hip involvement, and were more often overweight and current smokers. Finally, in our cohort all TR patients were HLA B27 positive, compared to 57% of non-TR D2M and 78% of non-D2M patients ($p=0.026$).

Conclusion: Treatment-refractory AxSpA represents a subgroup of D2M patients with severe disease, characterized by persistent inflammation, functional impairment, more advanced structural damage, despite extensive use of advanced therapies, and multiple comorbidities. Early identification and implementation of tailored multidisciplinary care is needed to improve outcomes in this population.

References

1 Poddubnyy D et al. The Assessment of SpondyloArthritis International Society (ASAS) Consensus-Based Expert Definition of Difficult-to-Manage, including Treatment-Refractory, Axial Spondyloarthritis. Ann Rheum Dis. 2025;84(4):538-546

Acknowledgement

The registry on which this study was based received funding from the Greek Rheumatology Society. The authors are grateful to the study participants

Disclosure: N. Kougkas: None; **K. Tsafis**: None; **D. Deligeorgakis**: None; **V. Papadopoulos**: None; **N. Fytanidis**: None; **M. Krikelis**: None; **E. Mole**: None; **S. Gazi**: None; **N. Koletsos**: None; **E. KALTSONOUDIS**: None; **P. Voulgari**: None; **A. Karamanakos**: None; **M. Pappa**: None; **M. Tektonidou**: None; **P. Sfikakis**: None; **K. Klavdianou**: None; **a. Banos**: None; **E. Kalavri**: None; **K. Kottas**: None; **G. Katsifis**: None; **M. KONSTA**: None; **E. Grika**: None; **C. Sfontouris**: None; **E. Mavrea**: None; **C. Koutsianas**: None; **E. Kataxaki**: None; **E. Sampatakaki**: None; **K. Zoupidou**: None; **P. Katsimpri**: None; **A. Iliopoulos**: None; **G. Iliopoulos**: None; **D. Daousis**: None; **I. Bournazos**: None; **D. KAROKIS**: None; **D. Patrikos**: None; **T. Dimitroulas**: None; **D. Vassilopoulos**: None; **G. Fragoulis**: None; **C. Papagoras**: None.

Abstract Number: 1453

Real-World Comparative Effectiveness of Upadacitinib in Psoriatic Arthritis: Evaluation of Switching to Upadacitinib Versus Tumor Necrosis Factor Inhibitors or Interleukin-17 Inhibitors After First-Line Tumor Necrosis Factor Inhibitors

Philip J. Mease[1], William Tillett[2], Xiaolan Ye[3], Christopher Saffore[4], Molly Edwards[5], Isabel Truman[5], Sophie Barlow[6], Jayne Stigler[7], Bhumik Parikh[8] and Daniel Aletaha[9], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, United Kingdom, [3]AbbVie Inc., Mettawa, IL, [4]AbbVie Inc., waukegan, IL, [5]Adelphi Real World, Bollington, United Kingdom, [6]AbbVie, North Chicago, IL, [7]AbbVie, Round Lake, IL, [8]AbbVie, Hillsborough Township, NJ, [9]Medical University Vienna, Wien, Austria

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The aim of this study was to compare the effectiveness of switching from a first-line TNFi to upadacitinib (UPA), an oral JAKi, versus cycling to another TNFi or switching from a TNFi to an IL-17 inhibitor (IL-17i) on tender and swollen joint involvement in patients with PsA.

Methods: Data were drawn from the Adelphi Real World Spondylarthritis (SpA) V and VI Disease Specific Programmes™, cross-sectional surveys administered to physicians (rheumatologists, dermatologists, and internal medicine specialists) and their consulting patients in routine clinical practice in Germany, France, Italy, Spain, the United Kingdom, and the United States (SpA VI only), with respective data collection periods from March 2021 to November 2021 for SpA V and from June 2023 to June 2024 for SpA VI. Adult patients with PsA who switched treatment from a TNFi in the first line of advanced therapy to another advanced therapy were stratified by the second-line therapy of interest: TNFi to UPA, TNFi to TNFi, or TNFi to IL-17i. The outcome of physician-reported assessment of both TJC ≤ 1 and SJC ≤ 1 was evaluated ≥ 3 months from treatment switch. Patient demographics and clinical characteristics were balanced using inverse-probability-weighted regression adjustment (IPWRA).The covariates balanced within the IPWRA were age, sex, Charlson Comorbidity Index (CCI), and severity at initiation of second-line therapy as reported by their physician for the weighting and regression adjustment stage, and additionally second-line treatment duration was used for the regression adjustment stage. The regression analyses were conducted separately for comparisons between TNFi to UPA and TNFi to TNFi as well as between TNFi to UPA and TNFi to IL-17i.

Results: Of the 320 patients included in the analysis who switched from a first-line TNFi, 101 switched to UPA, 96 switched to a second TNFi, and 123 switched to an IL-17i. Patient demographics are presented in **Table 1**. The most commonly used first-line TNFi in each group was adalimumab. The most commonly used second-line therapy in the TNFi to TNFi group was

Table 1: Patient Demographics and Characteristics

Parameter	TNFi to UPA N = 101	TNFi to TNFi N = 96	TNFi to IL-17i N = 123
Age, mean (SD)	45.9 (10.1)	51.1 (13.7)	48.4 (10.4)
Sex, n (%)			
Male	48 (48)	47 (49)	60 (49)
Female	53 (52)	49 (51)	63 (51)
Charlson Comorbidity Index, mean (SD)	0.1 (0.5)	0.1 (0.5)	0.2 (0.7)
Time since PsA diagnosis, years, mean (SD)	5.8 (3.7) n = 100	8.3 (7.1) n = 90	7.0 (5.4) n = 110
TNFi received as first-line, n (%)			
Adalimumab	85 (84)	61 (64)	95 (77)
Etanercept	8 (8)	22 (23)	18 (15)
Infliximab	2 (2)	8 (8)	3 (2)
Certolizumab-pegol	3 (3)	2 (2)	5 (4)
Golimumab	3 (3)	3 (3)	2 (2)
Advanced therapy received as second-line, n (%)			
Adalimumab	-	58 (60)	-
Etanercept	-	9 (9)	-
Infliximab	-	9 (9)	-
Certolizumab-Pegol	-	9 (9)	-
Golimumab	-	11 (11)	-
Secukinumab	-	-	76 (62)
Ixekizumab	-	-	45 (37)
Bimekizumab	-	-	2 (2)
Upadacitinib	101 (100)	-	-
Concurrent csDMARD use, n (%)	12 (12)	23 (24)	30 (24)
Prior csDMARD use, n (%)	77 (76)	69 (72)	95 (77)
Duration of first line TNFi, years, mean (SD)	2.8 (2.7)	1.9 (2.0)	2.7 (2.6)
Duration of current advanced therapy, years, mean (SD)	0.9 (0.5)	2.6 (3.1)	2.1 (1.5)
Reasons for switch, n (%)			
Joint condition worsened	45 (45)	39 (41)	65 (53)
Skin condition worsened	24 (24)	13 (14)	56 (46)
Secondary lack of efficacy (loss of response after initial response)	38 (38)	13 (14)	41 (34)
Disease activity worsened	16 (16)	5 (5)	10 (8)
Formulary driven switch	1 (1)	22 (23)	1 (1)
Disease severity[a] at second-line treatment initiation, n (%)			
Mild	8 (8)	11 (11)	9 (7)
Moderate	57 (56)	56 (58)	83 (67)
Severe	36 (36)	29 (30)	31 (25)
TJC at second-line treatment initiation, mean (SD)	7.7 (7.8) n = 101	8.4 (8.8) n = 29	7.9 (9.3) n = 70
SJC at second-line treatment initiation, mean (SD)	5.0 (7.0) n = 101	5.6 (6.3) n = 29	4.6 (7.8) n = 70

[a]Disease severity assessed by physician's definition of mild, moderate, and severe when completing the survey.
csDMARD, conventional synthetic DMARD; IL-17i, IL-17 inhibitor; TNFi, TNF inhibitor; UPA, upadacitinib

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

adalimumab while secukinumab was the most used second-line therapy in the TNFi to IL-17i group. The most frequent reason for switching reported by the physician was a worsening of the joints. At the time of switch, most patients had a physician-reported assessment of moderate/severe disease severity (TNFi to UPA: 92%; TNFi to TNFi: 89%; TNFi to IL-17i: 93%). After adjustment via IPWRA, significantly more patients in the TNFi to UPA group had physician-reported assessment of both TJC and SJC ≤ 1 at the time of data collection compared with patients in the TNFi to TNFi group (94% vs. 76%; $P = .0342$) and the TNFi to IL-17i group (91% vs. 72%; $P = .0123$) (**Figure 1**).

Conclusion: In this real-world study, a higher proportion of patients who switched from their first TNFi advanced therapy to UPA as their second-line advanced therapy had both TJC ≤ 1 AND SJC ≤1 than cycling to a second TNFi or switching to an IL-17i. The results demonstrate that switching to UPA after a TNFi may benefit patients with PsA.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ono Pharma, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6; **X. Ye**: AbbVie, 3, 11; **C. Saffore**: AbbVie, 3, 11; **M. Edwards**: AbbVie, 2, Adelphi Real World, 3; **I. Truman**: AbbVie, 2, Adelphi Real World, 3; **S. Barlow**: AbbVie/Abbott, 3, 11; **J. Stigler**: AbbVie, 3, 11; **B. Parikh**: AbbVie, 3, 11; **D. Aletaha**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sanofi, 6.

Abstract Number: 1454

Long-Term Safety and Tolerability of Bimekizumab Treatment Across Phase 2b and Phase 3 Studies in Patients with Axial Spondyloarthritis or Psoriatic Arthritis: 3-Year Update from the Phase 3 Studies

Philip J. Mease[1], Denis Poddubnyy[2], Rajan Bajracharya[3], Barbara Ink[3], Myriam Manente[4], Luke Peterson[5], Katy White[6], Peter Nash[7] and Lianne S. Gensler[8], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany, [3]UCB, Slough, England, United Kingdom, [4]UCB, Braine-L'Alleud, Belgium, [5]UCB, Morrisville, NC, [6]UCB, Slough, United Kingdom, [7]School of Medicine, Griffith University, Brisbane, Australia, [8]Department of Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A.

Previous analyses of phase (Ph)2b/3 safety data (data cut-off: July 2023) demonstrated that BKZ was generally well tolerated by patients (pts) with axial spondyloarthritis (axSpA; exposure: 2,513.8 patient-years [PY]) and psoriatic arthritis (PsA; exposure: 3,655.9 PY) longer-term over ∼2 years.[1] Here, we present updated safety analyses from these studies, including another year of BKZ exposure from the ongoing Ph3 open-label extensions (OLEs).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Safety data are reported for two pools, each comprising one Ph2b and two Ph3 studies and their OLEs, in pts with axSpA (non-radiographic and radiographic) and PsA, respectively (**Figure**).[1]

Exposure-adjusted incidence rates (EAIR)/100 PY and n (%) are reported for treatment-emergent adverse events (TEAEs; classified using MedDRA v19.0) among pts who received ≥1 dose of subcutaneous BKZ 160 mg every four weeks (wks; Q4W) in any treatment period. Data are reported to the data-cuts of September 2024 (axSpA) or August 2024 (PsA) in the ongoing BE MOVING and BE VITAL OLEs (corresponding with ≥156 wks of total Ph3 study participation; **Figure**).

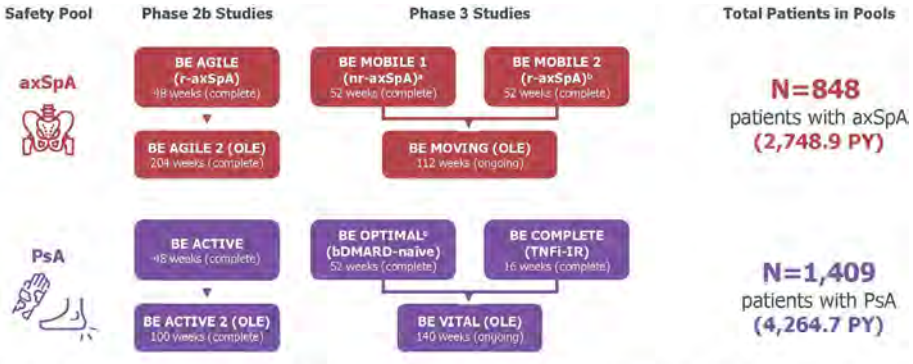
Results: The axSpA safety pool included 848 pts (2,748.9 PY); the PsA safety pool included 1,409 pts (4,264.7 PY; **Figure**).

Comparison of safety data with previous analyses did not indicate an increase in EAIRs of the majority of TEAEs; some TEAEs demonstrated an EAIR decrease with longer BKZ exposure, including *Candida* infections.[1] The 3 most frequently reported TEAEs in pts with axSpA and PsA (by preferred term) were corona virus infection, nasopharyngitis, and upper respiratory tract infection (**Table**).

Safety topics of interest are reported in the **Table**. Serious infections occurred at an EAIR/100 PY of 1.4 in pts with axSpA and 1.2 in PsA. The EAIR/100 PY of fungal infections was 8.1 in axSpA and 7.1 in PsA. Most fungal infections were muco-cutaneous and mild/moderate in severity; oral candidiasis was the most common fungal infection. Permanent BKZ discontinuation due to oral candidiasis was infrequent (axSpA: 0.2/100 PY; PsA: 0.3/100 PY). No systemic fungal infections were reported.

No cases of active tuberculosis, histoplasmosis, coccidioidomycosis or blastomycosis were reported in any study.

The EAIR/100 PY of hepatic events was 4.9 in axSpA and 4.6 in PsA; most were transient liver enzyme abnormalities (**Table**; no confirmed cases of Hy's law). For adjudicated definite/probable IBD, the EAIR/100 PY was 0.7 in axSpA and 0.2 in PsA. The uveitis EAIR/100 PY was 1.2 in axSpA and 0.1 in PsA.



Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown; including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 2b/3 studies. Duration of overall treatment period shown; BKZ treatment duration by data-cut varied between patients, depending on study duration and initial randomization in the feeder studies. [a] Patients with nr-axSpA met Assessment of SpondyloArthritis international Society (ASAS) classification criteria. Patients with radiographic sacroiliitis were excluded; [b] Patients with r-axSpA met modified New York criteria and fulfilled ASAS classification criteria; [c] BE OPTIMAL also included an adalimumab treatment arm. Data from patients treated with adalimumab were not included in the PsA safety pool prior to switching to BKZ, but were included following the switch. ASAS: Assessment of SpondyloArthritis international Society; axSpA: axial spondyloarthritis; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; nr-axSpA: non-radiographic axSpA; OLE: open-label extension; PsA: psoriatic arthritis; PY: patient-year; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; TNFi-IR: tumor necrosis factor inhibitor inadequate response.

BE AGILE: NCT02963506; BE AGILE 2: NCT03355573; BE MOBILE 1: NCT03928704; BE MOBILE 2: NCT03928743; BE MOVING: NCT04436640; BE ACTIVE: NCT02969525; BE ACTIVE 2: NCT03347110; BE OPTIMAL: NCT03895203; BE COMPLETE: NCT03896581; BE VITAL: NCT04009499.

Figure. The two safety pools (axSpA, PsA) of patients treated with BKZ 160 mg Q4W across six phase 2b/3 studies and their open-label extensions

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Summary of TEAEs reported up to the phase 3 data cut (axSpA: September 2024; PsA: August 2024)

	axSpA	PsA
TEAEs (MedDRA v19.0) n (%) [EAIR/100 PY]	BKZ 160 mg Q4W (N=848; exposure 2,748.9 PY)	BKZ 160 mg Q4W (N=1,409; exposure 4,264.7 PY)
Any TEAE	777 (91.6) [128.0]	1,256 (89.1) [122.5]
Severe TEAEs	79 (9.3) [3.0]	132 (9.4) [3.2]
Study discontinuations due to TEAEs	61 (7.2) [2.2]	114 (8.1) [2.7]
Drug-related TEAEs[a]	417 (49.2) [24.3]	590 (41.9) [20.3]
Serious TEAEs[b]	127 (15.0) [5.0]	216 (15.3) [5.5]
Deaths	3 (0.4) [0.1][c]	5 (0.4) [0.1][c]
Most common TEAEs,[d] by preferred term		
Corona virus infection	206 (24.3) [8.5]	318 (22.6) [8.7]
Nasopharyngitis	194 (22.9) [8.3]	231 (16.4) [6.2]
Upper respiratory tract infection	123 (14.5) [4.9]	203 (14.4) [5.2]
Oral candidiasis	86 (10.1) [3.4]	138 (9.8) [3.5]
Headache	62 (7.3) [2.4]	90 (6.4) [2.2]
Diarrhea	61 (7.2) [2.3]	91 (6.5) [2.2]
Hypertension	58 (6.8) [2.2]	92 (6.5) [2.3]
Safety topics of interest		
Fungal infections	188 (22.2) [8.1]	266 (18.9) [7.1]
Candida infections	104 (12.3) [4.1]	171 (12.1) [4.3]
Oral candidiasis	86 (10.1) [3.4]	138 (9.8) [3.5]
Fungal infections NEC	85 (10.0) [3.3]	118 (8.4) [2.9]
Tinea infections	25 (2.9) [0.9]	22 (1.6) [0.5]
Systemic infections	0	0
Serious infections	37 (4.4) [1.4]	51 (3.6) [1.2]
Opportunistic infections	16 (1.9) [0.6]	29 (2.1) [0.7]
Active tuberculosis	0	0
Hepatic events[e]	121 (14.3) [4.9]	177 (12.6) [4.6]
Elevated liver enzymes[f]	93 (11.0) [3.7]	145 (10.3) [3.7]
ALT or AST >3× ULN[g]	49 (5.8) [1.9]	73 (5.2) [1.8]
ALT or AST >5× ULN[g]	21 (2.5) [0.8]	23 (1.6) [0.5]
Adjudicated MACE	4 (0.5) [0.1]	13 (0.9) [0.3]
Malignancies (excluding NMSC)	10 (1.2) [0.4]	24 (1.7) [0.6]
Neutropenia[h]	14 (1.7) [0.5]	45 (3.2) [1.1]
Adjudicated SIB[i]	3 (0.4) [0.1]	2 (0.1) [0.0]
Administration/injection site reaction	28 (3.3) [1.0]	36 (2.6) [0.9]
Adjudicated definite or probable IBD	19 (2.2) [0.7][j]	9 (0.6) [0.2][j]
With prior history[k]	3 (20.0) [6.0]	1 (7.7) [2.6]
Without prior history[l]	16 (1.9) [0.6]	8 (0.6) [0.2]
Uveitis[m]	33 (3.9) [1.2]	4 (0.3) [0.1]
With prior history[n]	20 (15.4) [5.0]	2 (9.5) [4.0]
Without prior history[o]	13 (1.8) [0.6]	2 (0.1) [0.0]

Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown; including all patients who received ≥1 dose of BKZ 160 mg Q4W. [a] Per investigator assessment; [b] Serious TEAEs met one or more of the following criteria: death, life-threatening event, significant or persistent disability/incapacity, congenital anomaly/birth defect, important medical event that may jeopardize the patient and may require medical/surgical intervention to prevent one of the previous mentioned outcomes, or initial inpatient hospitalization/prolongation of hospitalization; [c] No deaths were considered drug-related by the investigator in any study. No deaths reported in additional year of follow-up (Since July 2023); [d] TEAEs occurring in ≥6% of patients in both the axSpA and PsA patient pools; [e] Includes events described as drug-related hepatic disorders, excluding liver neoplasms; [f] Elevated liver enzymes include the following preferred terms reported as adverse events: increased/abnormal levels of ALT, AST, blood bilirubin, gamma-glutamyltransferase, hepatic enzyme, liver function test, total bile acids or transaminases; [g] axSpA: n=847; PsA: n=1,407; [h] Neutropenia includes additional preferred terms identified based on UCB-defined search criteria; [i] All patients had a history of psychiatric disorders or ongoing traumatic and stressful circumstances; [j] Crohn's disease: axSpA, n=10 (1.2%); PsA, n=2 (0.1%); ulcerative colitis: axSpA, n=6 (0.7%); PsA, n=2 (0.1%); unclassified: axSpA, n=5 (0.6%); PsA, n=5 (0.4%); [k] axSpA, n=15; PsA, n=13; [l] axSpA, n=833; PsA, n=1,396; [m] Includes the preferred terms autoimmune uveitis, iridocyclitis, iritis, and uveitis; [n] axSpA, n=130; PsA, n=21; [o] axSpA, n=718; PsA, n=1,388.

ALT: alanine transaminase; AST: aspartate aminotransferase; axSpA: axial spondyloarthritis; BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; IBD: inflammatory bowel disease; MACE: major adverse cardiovascular event; NEC: not elsewhere classified; NMSC: non-melanoma skin cancer; PsA: psoriatic arthritis; PY: patient-years; Q4W: every four weeks; SIB: suicidal ideation or behavior; TEAE: treatment-emergent adverse event; ULN: upper limit of normal.

Rates of suicidal ideation/behavior were low, and no cases of completed suicide were reported (**Table**). Rates of other safety topics of interest (major adverse cardiovascular events, malignancies, neutropenia, administration/injection site reactions) are shown in the **Table**.

No additional deaths occurred since the previous data-cut (**Table**).

Conclusion: With an additional year of exposure, the long-term safety profile of BKZ in pts with axSpA and PsA remained consistent with prior analyses; no new safety signals or concerns were raised.[1]

References: 1. Mease PJ. Arthritis Rheumatol 2024;76(suppl 9). Abstract 2367.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6; **R. Bajracharya**: UCB, 3, 11; **B. Ink**: AbbVie, 11, GSK, 11, UCB, 3, 11; **M. Manente**: UCB, 3, 11; **L. Peterson**: UCB, 3, 11; **K. White**: UCB, 3, 11; **P. Nash**: AbbVie, 2, 5, 6, Amgen, 5, AstraZeneca, 2, 5, 6, BMS, 2, 5, 6, Eli Lilly, 2, 5,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Servatus, 2, 6, UCB, 2, 5, 6, Xencor, 2, 5; **L. Gensler**: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5.

Abstract Number: 1455

Sonelokimab in Patients With Active Psoriatic Arthritis Who Are Naive to Biologic DMARDs: Phase 2 ARGO Analysis and Phase 3 IZAR-1 Study Design

Philip J. Mease[1], Laure Gossec[2], Atul Deodhar[3], Xenofon Baraliakos[4], Frank Behrens[5], Joseph F Merola[6], Lihi Eder[7], Ana-Maria Orbai[8], Andreas Ramming[9], Iain McInnes[10], Alexis Ogdie[11], Dennis McGonagle[12], Christopher Ritchlin[13], Nuala Brennan[14], Ben Porter-Brown[14], Eva Cullen[14], Matthew R. Thomas[14], Marius Albulescu[14], Alex Godwood[14], Kristian Reich[15] and Laura Coates[16], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [3]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [4]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [5]Rheumatology, Immunology - Inflammation Medicine, University Hospital Goethe-University & Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Frankfurt am Main, Germany, [6]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [7]University of Toronto, Toronto, ON, Canada, [8]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [9]Department of Internal Medicine 3, Rheumatology & Immunology, Friedrich-Alexander-University (FAU) & Universitätsklinikum Erlangen, Erlangen, Germany, [10]University of Glasgow, Glasgow, United Kingdom, [11]University of Pennsylvania, Philadelphia, PA, [12]Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom, [13]University of Rochester Medical Center, Canandaigua, NY, [14]MoonLake Immunotherapeutics AG, Zug, Switzerland, [15]MoonLake Immunotherapeutics AG and Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, Zug, Switzerland, [16]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Sonelokimab (SLK), a novel Nanobody that binds to both IL-17A and IL-17F with similarly high affinity, is designed to target difficult-to-reach sites of inflammation due to its small size and albumin-binding domain. ARGO was a Phase 2 trial of SLK in active PsA, which met its primary endpoint of ACR50 vs. placebo at Week (W) 12 for SLK 60mg and 120mg (with induction [WI]). Here, we report W24 data in the ARGO trial from a subset of patients naive to bDMARDs (prior biologic use was a stratification factor). We also describe the design of the Phase 3 IZAR-1 trial, which will further evaluate SLK 60mg WI and SLK 60mg with no induction (NI) in this patient population.

Methods: ARGO (NCT05640245) was a 24-week, global, randomized, placebo-controlled, double-blind trial of adults with active PsA (TJC68 ≥3 and SJC66 ≥3). Three SLK doses were assessed: 60mg NI (Q4W), SLK 60mg WI, and SLK 120mg WI (induction doses at W0, 2, 4, and 6; Q4W from W8). In this exploratory analysis, we assessed outcomes at W24 in patients without prior bDMARD exposure treated with SLK 60mg with or without induction (IZAR-1 doses).

Results: Of the 207 patients enrolled in ARGO (**Table**), 171 patients (82.6%) were naive to bDMARDs. SLK 60mg resulted in clinical responses at W24 in patients naive to bDMARDs (SLK 60mg WI, n=34; SLK 60mg NI, n=33), including ACR50 (SLK 60mg WI: 61.8%; SLK 60mg NI: 63.6%), the higher threshold of ACR70 (SLK 60mg WI: 41.2%; SLK 60mg NI: 45.5%), and the composite endpoint of minimal disease activity ([MDA]; SLK 60mg WI: 58.8%; SLK 60mg NI: 48.5%). For patients naive to bDMARDs with skin involvement (SLK 60mg WI, n=22; SLK 60mg NI, n=28), treatment with SLK resulted in notable PASI 90 (SLK 60mg WI: 81.8%; SLK 60mg NI: 67.9%) and PASI 100 responses (SLK 60mg WI: 68.2%; SLK 60mg NI: 57.1%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

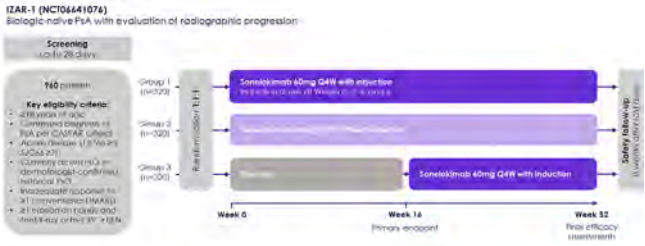
Table. Baseline characteristics from the ARGO trial

Table. Baseline characteristics from the ARGO trial

	All patients (N=207)	SLK 60mg Q4W NI (n=41)	SLK 60mg Q4W WI (n=41)
Age at screening, years, mean (SD)	48.6 (12.7)	50.3 (13.9)	47.5 (12.7)
Female, %	49.3	51.2	48.8
BMI [kg/m²], mean (SD)	29.0 (5.7)	29.6 (5.4)	27.7 (4.8)
Duration of PsA [years], mean (SD)	5.4 (5.8)	6.0 (5.7)	6.2 (7.4)
Naive to bDMARDs, n (%)	171 (82.6)	33 (80.5)	34 (82.9)
Concomitant non-biologic DMARD, %	74.4	82.9	68.3
Concomitant MTX, %	71.0	80.5	58.5
TJC68, mean (SD)	17.0 (12.4)	18.0 (12.2)	16.9 (14.1)
SJC66, mean (SD)	9.4 (7.1)	10.7 (8.2)	9.1 (7.1)
Affected BSA ≥3%, %	69.4	78.0	63.4
PASI [BSA ≥3%], mean (SD)	7.2 (6.6)	8.7 (5.7)	8.0 (9.7)
DAPSA score, mean (SD)	38.9 (18.9)	41.5 (20.5)	38.5 (19.6)

bDMARD, biologic disease-modifying anti-rheumatic drug; BMI, body mass index; BSA, body surface area; DAPSA, Disease Activity in Psoriatic Arthritis; DMARD, disease-modifying anti-rheumatic drug; MTX, metholrexate; NI, no induction; PsA, psoriatic arthritis; Q4W, every 4 weeks; SD, standard deviation; SJC66, 66 swollen joint count; SLK, sonelokimab; TJC68, 68 tender joint count; WI, with induction.

Figure. Study design



CASPAR, Classification Criteria for Psoriatic Arthritis; DMARD, disease-modifying anti-rheumatic drug; hs-CRP, high-sensitivity C-reactive protein; PsA, psoriatic arthritis; PsO, psoriasis; Q4W, every 4 weeks; SJC66, 66 swollen joint count; TJC68, 68 tender joint count; ULN, upper limit of normal.

Figure. Study design

SLK was well tolerated, with a safety profile consistent with IL-17 inhibition. Based on these findings, we have designed a 52-week, global, randomized, double-blind, PBO-controlled, Phase 3 trial in this patient population (IZAR-1; NCT06641076; **Figure**). An estimated 960 patients will be randomized 1:1:1 to receive SLK 60mg Q4W WI, SLK 60mg Q4W NI, or PBO (SLK 60mg WI from W16). Given the results from ARGO, this sample size should provide sufficient power to demonstrate a statistically significant difference for each SLK arm vs. PBO on the primary outcome of ACR50 at W16. Eligible participants will have a confirmed diagnosis of PsA (CASPAR criteria), active disease (TJC68 ≥3; SJC66 ≥3), currently active or dermatologist-confirmed historical psoriasis, inadequate response to ≥1 conventional DMARD, and ≥1 erosion on hands-and-feet X-ray or hs-CRP > the ULN. Key secondary outcomes (all vs. PBO at W16) include ACR20, PASI 90, and MDA; the PROs HAQ-DI and SF-36 Physical Component Summary; and radiographic progression (vdH-mTSS).

Conclusion: The Phase 2 ARGO study demonstrated high levels of clinical response with SLK, including in patients with active PsA naive to bDMARDs. The randomized Phase 3 IZAR-1 study will further assess outcomes with SLK in patients naive to bDMARDs and is actively recruiting, including at sites across the USA.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

X. Baraliakos: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **F. Behrens**: AbbVie, 2, 6, 12, Support for attending meetings and/or travel, Acelyrin, 2, 6, Amgen, 2, 6, AstraZeneca, 6, Chugai Pharmaceuticals, 2, 5, 6, Cilag, 2, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 2, Janssen Pharmaceuticals, 2, 5, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 5, Sandoz, 6, UCB, 2, 6, 12, Support for attending meetings and/or travel; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **A. Orbai**: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB, 2; **A. Ramming**: Boehringer-Ingelheim, 2, Johnson & Johnson, 2, MoonLake Immunotherapeutics AG, 2, 5, Novartis Pharma GmbH, 2, UCB, 2; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **D. McGonagle**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, MoonLake Immunotherapeutics AG, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sobi, 2, 5, 6, UCB, 2, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **N. Brennan**: MoonLake Immunotherapeutics AG, 3, 11; **B. Porter-Brown**: MoonLake Immunotherapetics, 3, 11, Sanofi, 3, 11; **E. Cullen**: MoonLake Immunotherapeutics AG, 3, 11; **M. Thomas**: MoonLake Immunotherapeutics AG, 3, 11; **M. Albulescu**: MoonLake Immunotherapeutics, 3, 11; **A. Godwood**: MoonLake Immunotherapeutics, 3, 11; **K. Reich**: AbbVie, 1, 6, 12, Participated in clinical trials, Almirall, 1, 6, 12, Participated in clinical trials, Amgen, 1, 6, 12, Participated in clinical trials, Boehringer Ingelheim, 1, 6, 12, Participated in clinical trials, Bristol-Myers Squibb(BMS), 1, 6, 12, Participated in clinical trials, Eli Lilly, 1, 6, 12, Participated in clinical trials, Galderma, 1, 6, 12, Participated in clinical trials, Janssen-Cilag, 1, 6, 12, Participated in clinical trials, Kyowa Kirin, 1, 6, 12, Participated in clinical trials, LEO Pharma, 1, 6, 12, Participated in clinical trials, Medac, 1, 6, 12, participated in clinical trials, MoonLake Immunotherapeutics AG, 3, 11, Novartis, 1, 6, 12, participated in clinical trials, Ocean Pharma, 1, 6, 12, participated in clinical trials, Pfizer, 1, 6, 12, participated in clinical trials, Sanofi, 1, 6, 12, participated in clinical trials, UCB, 1, 6, 12, participated in clinical trials; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1456

Long-Term Safety of Tildrakizumab Through Week 208 in Patients With Psoriatic Arthritis: Results From the Phase 2b Open-Label Extension Study

Philip J. Mease[1], Saima Chohan[2], Ferran José Garcia Fructuoso[3], Michael E Luggen[4], Proton Rahman[5], Siba Raychaudhuri[6], Alice B. Gottlieb[7], Richard Chou[8], Marek Honczarenko[8], Benjamin P Soule[8], Shantanu Mehta[8], Tushar Nishandar[9], Arvind Tripathi[8] and Mudgal Kothekar[10], [1]Department of Rheumatology, Providence-Swedish Medical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Center and University of Washington, Seattle, WA, [2]Arizona Arthritis and Rheumatology Research, PLLC, Pheonix, AZ, [3]Servicio de Reumatología, Hospital CIMA Sanitas, Paseo Manuel Girona, Barcelona, Spain, [4]Division of Rheumatology, Allergy, and Immunology, University of Cincinnati College of Medicine, Cincinnati, OH, [5]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada, [6]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [7]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX, [8]Sun Pharmaceutical Industries, Inc., Princeton, NJ, [9]Sun Pharmaceutical Industries Limited, Andheri (E), Mumbai, India, [10]Sun Pharma Advanced Research Company Limited, Andheri (E), Princeton, NJ

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Tildrakizumab (TIL) is an anti–IL-23 p19 monoclonal antibody approved for the treatment of adults with moderate-to-severe plaque psoriasis. In a Phase 2b trial in patients with active psoriatic arthritis (PsA; NCT02980692), TIL treatment significantly improved joint and skin symptoms and was well tolerated for up to 52 weeks. An open-label long-term extension (LTE) of that trial evaluated the safety of TIL through Week (W)208 of treatment in patients with active PsA.

Methods: Patients who completed treatment in the Phase 2b parent study, achieved ACR20 response at W52, and had sufficient clinical benefit per the investigator were eligible for the LTE. Patients continued to receive the same dose of TIL as in the parent study (200 mg every 4 weeks, 200 mg every 12 weeks [Q12W], or 100 mg Q12W) until parent study database lock (at least 52 weeks of treatment), after which all patients received TIL 100 mg Q12W through W208. Safety was assessed in all patients who entered the LTE and received ≥1 dose of TIL based on frequency and severity of adverse events (AEs); frequency of serious AEs (SAEs), AEs of special interest (AESIs), and AEs of clinical interest (AECIs); and presence of antidrug antibodies (ADAs) to TIL. Analyses were based on the treatment received.

Results: Of 303 patients from the parent study screened, 281 entered the LTE and received ≥1 dose of TIL, and 205 completed treatment through W208 (Table 1).

Any AEs, treatment-related AEs, SAEs, and treatment-related SAEs occurred in 79.7% (224/281), 19.6% (55/281), 14.2% (40/281), and 0.7% (2/281) of patients, respectively (Table 2). The most common treatment-related AEs were upper respiratory tract infection (3.2%) and nasopharyngitis (2.5%). A total of 6.0% (17/281) and 2.5% (7/281) of patients discontinued the study due to AEs and treatment-related AEs, respectively (Table 2), most due to infections and infestations. AESIs were reported in 4.6% (13/281) of patients and included infections and infestations (1.8%); cardiac disorders (1.1%; included 2 acute myocardial infarction events confirmed as major adverse cardiovascular events, not related to the study drug); malignancies (n = 2; 0.7%); respiratory, thoracic, and mediastinal disorders (n = 2; 0.7%); and vascular disorders (n = 1; 0.4%;

Table 1. Disposition and baseline demographics of patients who entered the LTE study

	TIL200 Q4W* n = 5	TIL200 Q12W* n = 22	TIL100 Q12W n = 49	TIL200 Q4W to TIL100 Q12W n = 54	TIL200 Q12W to TIL100 Q12W n = 151	Total N = 281
Completed treatment	0	0	33 (67.3)	46 (85.2)	126 (83.4)	205 (73.0)
Discontinued treatment	5 (100.0)	22 (100.0)	16 (32.7)	8 (14.8)	25 (16.6)	76 (27.0)
Age, years, mean ± SD	65.0 ± 12.0	53.8 ± 14.8	50.6 ± 11.4	49.9 ± 13.5	48.3 ± 11.5	49.7 ± 12.6
Sex						
Male	4 (80.0)	9 (40.9)	21 (42.9)	21 (38.9)	74 (49.0)	129 (45.9)
Female	1 (20.0)	13 (59.1)	28 (57.1)	33 (61.1)	77 (51.0)	152 (54.1)
Race						
White	5 (100.0)	21 (95.5)	48 (98.0)	53 (98.1)	147 (97.4)	274 (97.5)
Black or African American	0	1 (4.5)	1 (2.0)	0	2 (1.3)	4 (1.4)
Other	0	0	0	1 (1.9)	2 (1.3)	3 (1.1)

Data are shown as n (%) unless otherwise indicated.

*Patients discontinued the LTE prior to switching to TIL100 Q12W.

LTE, long-term extension; Q4W, once every 4 weeks; Q12W, once every 12 weeks; SD, standard deviation; TIL100, tildrakizumab 100 mg; TIL200, tildrakizumab 200 mg.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Summary of AEs in the LTE study

	TIL200 Q4W n = 5	TIL200 Q12W n = 22	TIL100 Q12W n = 49	TIL200 Q4W to TIL100 Q12W n = 54	TIL200 Q12W to TIL100 Q12W n = 151	Total N = 281
≥1 AE	5 (100.0)	14 (63.6)	36 (73.5)	44 (81.5)	125 (82.8)	224 (79.7)
Treatment-related AE	1 (20.0)	4 (18.2)	11 (22.4)	10 (18.5)	29 (19.2)	55 (19.6)
SAE	3 (60.0)	3 (13.1)	7 (14.3)	3 (5.6)	25 (16.6)	40 (14.2)
Treatment-related SAE	1 (20.0)	0	1 (2.0)	0	0	2 (0.7)
AEs leading to discontinuation	3 (60.0)	5 (22.7)	4 (8.2)	2 (3.7)	3 (2.0)	17 (6.0)
Treatment-related AEs leading to discontinuation[a]	1 (20.0)	1 (4.5)	3 (6.1)	2 (3.7)	0	7 (2.5)
AEs leading to death	0	1 (4.5)	0	0	1 (0.7)	2 (0.7)
AESIs[b]	1 (20.0)	1 (4.5)	3 (6.1)	1 (1.9)	7 (4.6)	13 (4.6)
Infections and infestations	1 (20.0)	0	2 (4.1)	0	2 (1.3)	5 (1.8)
Abdominal abscess	1 (20.0)	0	0	0	0	1 (0.4)
COVID-19 pneumonia	0	0	0	0	2 (1.3)	2 (0.7)
Intestinal sepsis	0	0	1 (2.0)	0	0	1 (0.4)
Septic shock	0	0	1 (2.0)	0	0	1 (0.4)
Upper respiratory tract infection	0	0	1 (2.0)	0	0	1 (0.4)
Urinary tract infection	0	0	1 (2.0)	0	0	1 (0.4)
Cardiac disorders	0	0	0	0	3 (2.0)	3 (1.1)
Acute myocardial infarction	0	0	0	0	2 (1.3)	2 (0.7)
Cardiac failure	0	0	0	0	1 (0.7)	1 (0.4)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	0	0	0	0	2 (1.3)	2 (0.7)
Adenocarcinoma metastatic	0	0	0	0	1 (0.7)	1 (0.4)
Invasive ductal breast carcinoma	0	0	0	0	1 (0.7)	1 (0.4)
Respiratory, thoracic, and mediastinal disorders	0	0	1 (2.0)	1 (1.9)	0	2 (0.7)
Bronchitis chronic	0	0	0	1 (1.9)	0	1 (0.4)
Interstitial lung disease	0	0	1 (2.0)	0	0	1 (0.4)
Vascular disorders	0	1 (4.5)	0	0	0	1 (0.4)
Aortic dissection	0	1 (4.5)	0	0	0	1 (0.4)
AECIs	0	0	0	0	1 (0.7)	1 (0.4)

Data are shown as n (%).

[a]Includes 1 patient each with gastritis, hyperbilirubinemia, nonalcoholic steatohepatitis, abdominal abscess, intestinal sepsis, pulmonary tuberculosis, septic shock, urinary tract infection, or arthritis.

[b]AESIs included severe infections, malignancies, confirmed major adverse cardiovascular events, and drug-related hypersensitivity reactions. Totals for the number of patients at the system organ class level may not align with the sum of patients with events at the preferred term level since a patient may report ≥2 different AESIs within the system organ class level.

AE, adverse event; AECI, adverse event of clinical interest; AESI, adverse event of special interest; COVID-19, coronavirus disease 2019; LTE, long-term extension; Q4W, once every 4 weeks; Q12W, once every 12 weeks; SAE, serious adverse event; TIL100, tildrakizumab 100 mg; TIL200, tildrakizumab 200 mg.

Table 3. Summary of ADA immunogenicity status and neutralizing antibodies in the LTE study

	TIL200 Q4W n = 5	TIL200 Q12W n = 22	TIL100 Q12W n = 49	TIL200 Q4W to TIL100 Q12W n = 54	TIL200 Q12W to TIL100 Q12W n = 151	Total N = 281
Evaluable patients						
Conclusive	2 (40.0)	11 (50.0)	48 (98.0)	53 (98.1)	150 (99.3)	264 (94.0)
Inconclusive[a]	2 (40.0)	4 (18.2)	0	1 (1.9)	1 (0.7)	8 (2.8)
Missing	1 (20.0)	7 (31.8)	1 (2.0)	0	0	9 (3.2)
Immunogenicity status						
Negative[b]	2 (40.0)	11 (50.0)	47 (95.9)	51 (94.4)	142 (94.0)	253 (90.0)
Non-treatment-emergent positive[c]	0	0	1 (2.0)	2 (3.7)	5 (3.3)	8 (2.8)
Treatment-emergent positive[d]	0	0	0	0	3 (2.0)	3 (1.1)
Neutralizing antibody, non–treatment-emergent						
Neutralizing negative	0	0	0	0	0	0
Neutralizing positive	0	0	0	0	2 (1.3)	2 (0.7)
Neutralizing antibody, treatment-emergent						
Neutralizing negative	0	0	0	0	0	0
Neutralizing positive	0	0	0	0	1 (0.7)	1 (0.4)

Data are shown as n (%).

[a]Patients who had negative pretreatment and post-dose samples and whose last post-dose sample had a tildrakizumab concentration at or above the drug tolerance limit for the ADA assay.

[b]Patients who had negative pretreatment and post-dose samples and whose last post-dose sample had a tildrakizumab concentration below the drug tolerance limit for the ADA assay.

[c]Patients who had a positive pretreatment sample and all negative post-dose samples or who had positive pretreatment and post-dose samples with a titer increase <2-fold post-dose.

[d]Patients who had a negative pretreatment sample and ≥1 positive post-dose sample (treatment-induced positive) or who had positive pretreatment and post-dose samples with a titer increase ≥2-fold post-dose (treatment-boosted positive).

ADA, antidrug antibody; LTE, long-term extension; Q4W, once every 4 weeks; Q12W, once every 12 weeks; TIL100, tildrakizumab 100 mg; TIL200, tildrakizumab 200 mg.

Table 2). Only 1 AECI (viral infection) occurred during the LTE. AEs leading to death were reported in 2 patients (1 aortic dissection and 1 metastatic adenocarcinoma), both deemed unrelated to the study drug (Table 2).

A total of 2.8% (8/281) and 1.1% (3/281) of patients were positive for non–treatment-emergent (TE) and TE ADAs, respectively; 0.7% (2/281) and 0.4% (1/281) had non–TE and TE neutralizing antibodies (nAbs; Table 3). Patients' TE ADA-positive or nAb-positive statuses were not associated with AEs of hypersensitivity or injection-site reactions, AESIs, or AECIs. The effects of ADAs and nAbs on TIL clearance could not be quantified due to the low number of ADA-positive patients.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The safety of TIL was maintained through W208 of treatment in patients with PsA, with no new safety signals. These data support continued development of TIL to treat patients with active PsA.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **S. Chohan**: Arizona Arthritis and Rheumatology Associates, 12, Partner; **F. Garcia Fructuoso**: AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, Gedeon Richter, 2, 5, 6, MedImmune, 2, 5, 6, Nichi-Iko, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi-Aventis, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6; **M. Luggen**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Eli Lilly, 2, 5, 6, Genentech, 2, 5, 6, Nichi-Iko, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Priovant Therapeutics, 2, 5, 6, R-Pharm, 2, 5, 6, Sun Pharma, 2, 5, 6; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **S. Raychaudhuri**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **A. Gottlieb**: Amgen, 2, 4, 6, Avalo Therapeutics, 5, BMS, 5, Eli Lilly and Company, 2, 4, 6, Highlights Therapeutics, 2, 4, 6, Janssen, 2, 4, 5, 6, MoonLake Immunotherapeutics, 5, Novartis, 2, 4, 6, Sanofi, 2, 4, 6, Sun Pharma, 2, 4, 6, Takeda, 2, 4, 6, Teva, 2, 4, 6, UCB, 2, 4, 5, 6; **R. Chou**: Sun Pharmaceutical Industries, Inc., 3; **M. Honczarenko**: Sun Pharmaceutical Industries, Inc., 3; **B. Soule**: Sun Pharmaceutical Industries, Inc., 3; **S. Mehta**: Sun Pharmaceutical Industries, Inc., 3; **T. Nishandar**: Sun Pharmaceutical Industries Limited, 3; **A. Tripathi**: Sun Pharmaceutical Industries, Inc., 3; **M. Kothekar**: Sun Pharma Advanced Research Company Limited, 3, 11.

Abstract Number: 1457

Real-world Patient Trajectories in Psoriasis and Psoriatic Arthritis: a Retrospective Study

Philip J. Mease[1], Qi Wei[2], Lawrence Huang[3], Jason Hawkes[4], Clive Liu[5], Ying Wu[6], Tony Wang[7], Anthony Hager[8] and Jennifer Hadlock[3], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Institute for Systems Biology, Seattle, WA, [3]Institute for Systems Biology, Seattle, [4]Oregon Medical Research Center, Portland, OR, [5]Bellevue Dermatology, Bellevue, [6]Bristol Myers Squibb, Princeton, NJ, [7]Bristol Meyers Squib, Princeton, NJ, [8]Bristol Myers Squibb, Seattle, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Real world data from community healthcare systems can provide insights into patient trajectories with psoriasis (PsO) and psoriatic arthritis (PsA): baseline characteristics, patterns of treatment, and transitions between PsO and PsA.

Methods: Patients with a new PsO or PsA diagnosis were identified from 51 hospitals and 1,085 clinics in Providence Health & Services, which serves urban centers and rural catchment areas across seven states in the Western US. The study period was Jan 1, 2011 to Aug 31, 2023. The PsO cohort index time t_0 was the first diagnosis of PsO without PsA, and the PsA t_0 was the first diagnosis of PsA. Baseline characteristics were determined by the most recent results during the year before t_0. Medication use was observed for 6 months after t_0. For the PsO cohort, we analyzed time-to-onset of PsA. For the PsA cohort, we analyzed time-to-augmentation and time-to-discontinuation for the first line of systemic immunomodulatory therapy (excluding steroids and NSAIDs). Time-to-event analyses were conducted using Aalen-Johansen survival estimators. Patients were right-censored at the end of their most recent encounter or at the end of the study period, whichever came first, and death considered as a competing outcome.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of patients with PsO or PsA at time of first records diagnosis * Jan 1, 2011 to Aug 31, 2023

Characteristic	psoriasis† n (%)	psoriatic arthritis n (%)
Total	88975	23083
Age, median [Q1,Q3]	54 [39,66]	58 [44,65]
Age range, years		
18-49	37419 (42.1)	8172 (35.4)
50-74	42498 (47.8)	13004 (56.3)
75+	9058 (10.2)	1907 (8.3)
Ethnicity		
Hispanic	6437 (7.2)	1480 (6.4)
Not Hispanic	79389 (89.2)	20885 (90.5)
Unknown	3149 (3.5)	718 (3.1)
Race		
AI/AN	339 (0.4)	75 (0.3)
Asian	5652 (6.4)	880 (3.8)
Black	1460 (1.6)	231 (1.0)
NHPI	260 (0.3)	46 (0.2)
White	69515 (78.1)	19143 (82.9)
Unknown	11749 (13.2)	2708 (11.7)
Sex		
Male	40430 (45.4)	9449 (40.9)
Female	48532 (54.6)	13633 (59.1)
Body mass index (BMI) kg/m²	28.5 (24.8,33.5)	29.7 (25.6,34.9)
Systolic blood pressure, median [Q1,Q3] mmHg	124.0 [114.0,137.0]	126.0 [116.0,138.0]
Diastolic blood pressure, median [Q1,Q3] mmHg	76.0 [68.0,82.0]	77.0 [70.0,84.0]
Co-occurring IMIDs		
Inflammatory bowel disease	1325 (1.5)	403 (1.7)
Rheumatoid arthritis ‡	1604 (1.8)	1840 (8.0)
Axial spondyloarthritis	423 (0.5)	573 (2.5)
Multiple sclerosis	434 (0.5)	106 (0.5)
Autoimmune skin disease	411 (0.5)	96 (0.4)
Systemic lupus erythematosus	408 (0.5)	311 (1.3)
Sjögren's syndrome	281 (0.3)	223 (1.0)
Co-occurring conditions		
Mental health condition	24886 (28.0)	6387 (27.7)
Hypertension	20774 (23.3)	5443 (23.6)
Diabetes (type 1 and type 2)	9134 (10.3)	2453 (10.6)
Cardiac arrhythmia	6831 (7.7)	1883 (8.2)
Migraine	5980 (6.7)	1973 (8.5)
Arteriosclerotic vascular disease	5792 (6.5)	1495 (6.5)
Chronic kidney disease	4027 (4.5)	1136 (4.9)
Osteoporosis	3679 (4.1)	1218 (5.3)
Gout	2898 (3.3)	1089 (4.7)
Heart failure	2761 (3.1)	688 (3.0)
Malignant neoplasm of skin	2571 (2.9)	448 (1.9)
Ischemic heart disease	2390 (2.7)	669 (2.9)
Fibromyalgia	1913 (2.2)	1530 (6.6)
Tobacco use (ever)	25192 (28.3)	6502 (28.2)
Area deprivation index, national > 5th decile	11607 (13.0)	4202 (18.2)
Area deprivation index, state > 5th decile	32513 (36.5)	9327 (40.4)

Data are n (%) or median (IQR). IMID = immune-mediated inflammatory disease. IQR = interquartile range. AI/AN, American Indian and Alaska Native. NHPI, Native Hawaiian and other Pacific Islander. NA = not applicable. For binary variables, p values are calculated by the Fisher's exact method; for categorical variables, p-values are calculated by the Chi-squared test of independence; for continuous variables, p-values are calculated by the Mann-Whitney U test. *Time of first diagnosis is defined as the first noted date of a patient's diagnosis or the first time they came to Providence for care. Total patients with Psoriasis diagnosis, excluding patients with pre-existing PsA diagnosis. Diagnoses in EHR may reflect initial misdiagnosis of rheumatoid arthritis prior to diagnosis of PsA.

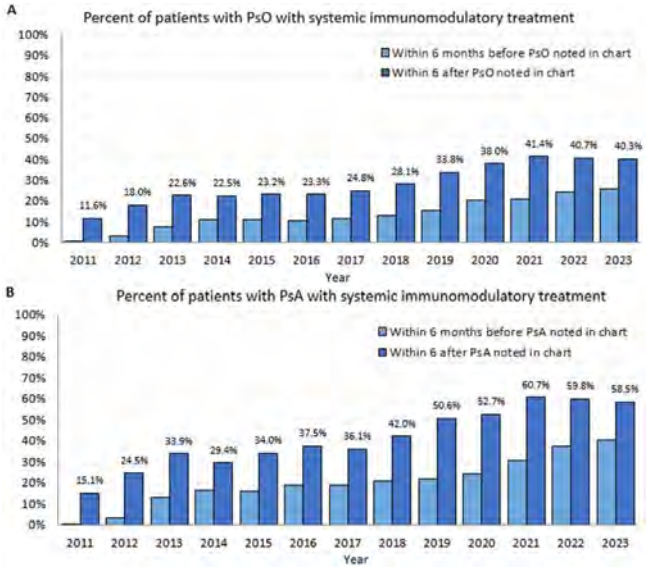


Figure 1. (A) Patients' systemic immunomodulatory treatment six months prior to the first diagnosis and six months after the first diagnosis. (A) Patients with Psoriasis condition and without pre-existing Psoriatic arthritis (PsA) condition (B) Patients with PsA condition. Systemic immunomodulatory treatment includes medications used for PsO, PsA, but not steroids or NSAIDs. Time of first diagnosis is defined as the first noted date of a patient's diagnosis within the healthcare system

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

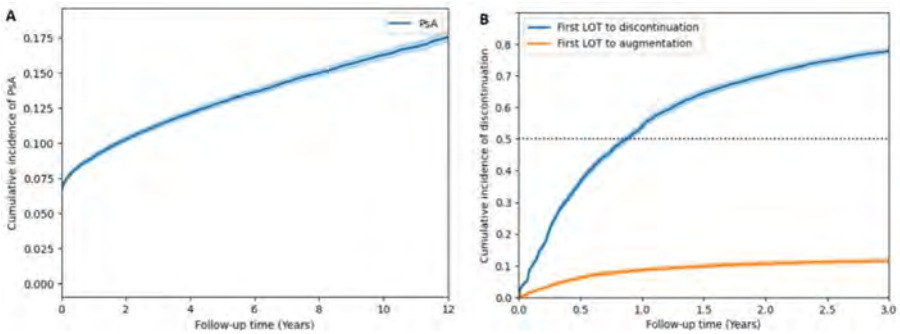


Figure 2: (A) Cumulative incidence of new Psoriatic Arthritis (PsA) diagnoses over time. The Y-axis represents the cumulative incidence (%) of patients newly diagnosed with PsA, while the X-axis shows follow-up time in years. (B) Time from first line systems immunomodulatory medication (other than steroids or NSAIDS) of patients with PsA diagnoses to discontinuation (blue) or augmentation (orange). The Y-axis represents the cumulative incidence (%), while the X-axis shows follow-up time in years.

Results: Of 96,533 patients with PsO, 7,558 (7.8%) had PsA at the time PsO was first reported. There were 88,975 patients with PsO without PsA (median age 54, 54.6% female) and 23,083 patients with PsA (median age 56, 59.1% female). See Table 1 for baseline characteristics. Within 6 months after t_0, patients use of systemic immunomodulatory medications included the following classes: steroid (PsO 16.7%, PsA 19.9%), antimetabolite (PsO 1.8%, PsA 11.6%), TNF-α inhibitor (PsO 1.5%, PsA 11.6%), calcineurin inhibitor (PsO 1.0%, PsA 0.5%), PDE4 inhibitor (PsO 0.8%, PsA 3.5%), IL-17 inhibitor (PsO 0.6%, PsA 3.3%), IL-23 inhibitors (PsO 0.6%, PsA 0.9%), IL-12/23 inhibitor (PsO 0.5%, PsA 1.2%), JAK inhibitor (PsO 0.1%, PsA 0.9%), and TYK2 inhibitor (PsO 0.0001%, PsA 0.0001%). The percentage of patients with systemic immunomodulatory medications within 6 months after t_0 (excluding steroids and NSAIDs) increased from 2011 (PsO 11.6%, PsA 15.1%) to 2023 (PsO 40.3%, PsA 58.5%). Time from PsO to PsA (Figure 1a) and time from the first PsA systemic immunomodulatory line of treatment to discontinuation or augmentation (Figure 1b) are shown below.

Conclusion: Data from a large community health system provides new insight into real world trajectories for patients with PsO and PsA. At the time of first reported PsO diagnosis, many patients have additional chronic medical conditions. The numbers of patients with PsA with systemic immunomodulatory treatment has increased since 2011 but remains lower than reported in studies conducted in academic centers, consistent with the 2016 MAPP survey.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **Q. Wei**: None; **L. Huang**: None; **J. Hawkes**: AbbVie, 2, 5, Acelyrin, 5, Allakos, 5, Alumis, 5, Amgen, 5, Apogee, 2, 5, Arcutis, 2, Blueprint Medicines, 2, Boehringer-Ingelheim, 2, 6, Boxer Capital LLC, 2, Bristol Meyers Squibb, 2, 6, CellDex, 5, Concert Pharmaceuticals, 5, Dermavant, 2, 6, Eli Lilly, 2, 5, 6, Gladerma, 2, 6, Incyte, 5, Johnson & Johnson, 2, 5, 6, LEO, 2, 5, Novartis, 2, 5, 6, Oruka, 2, 5, Regeneron, 2, 6, Sanofi, 2, 5, 6, Sun Pharma, 2, 5, Takeda, 2, 5, UCB, 2, 6; **C. Liu**: AbbVie, 5, 6, Arcutis, 5, 6, Boehringer-Ingelheim, 5, 6, Bristol Meyers Squibb, 5, 6, Dermavant, 5, 6, Eli Lilly, 5, 6, Incyte, 5, 6, Johnson & Johnson, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Regeneron, 5, 6, Sanofi, 5, 6, Takeda, 5, 6, UCB, 5, 6; **Y. Wu**: Bristol Meyers Squibb, 3; **T. Wang**: Bristol Meyers Squibb, 3; **A. Hager**: Bristol Meyers Squibb, 3; **J. Hadlock**: Bristol Meyers Squibb, 5, Gilead, 5, Johnson & Johnson, 5, Novartis, 5, Pfizer, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1458

Clinical Efficacy of Bimekizumab Treatment up to 2 Years Across Patients with Psoriatic Arthritis and Varying Baseline Joint Involvement: Results from a Post Hoc Analysis of Two Pooled Phase 3 Studies

Philip J. Mease[1], Laure Gossec[2], Hideto Kameda[3], David Nicholls[4], Proton Rahman[5], Barbara Ink[6], Rajan Bajracharya[6], Patrick Healy[7] and Laura Coates[8], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [3]Department of Internal Medicine, Toho University, Tokyo, Japan, [4]Clinical Trials Unit, University of the Sunshine Coast, Queensland, Australia, [5]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada, [6]UCB, Slough, England, United Kingdom, [7]UCB, Morrisville, NC, [8]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients (pts) in PsA clinical trials often have greater joint involvement than in the clinical setting due to trial inclusion criteria,[1] thus it is important to assess treatment efficacy in pts with varying degrees of joint involvement. We investigated the efficacy of bimekizumab (BKZ), a selective inhibitor of interleukin (IL)-17F in addition to IL-17A, in subgroups of pts with varying joint involvement at baseline (BL), using data pooled from two phase 3 studies.

Methods: Post hoc analysis assessed subcutaneous BKZ 160 mg every 4 weeks (wks; Q4W) in pts with PsA and varying BL joint involvement. Pts were grouped by BL swollen joint count (SJC); thresholds defined based on quartile boundaries at BL (SJC ≤5 / 6–≤7 / 8–≤12 / >12). Due to small pt numbers with 3/4 SJC at BL, pts with 5 SJC were included in the first quartile; pt numbers in each quartile therefore vary.

Table. Baseline demographics and disease characteristics, reported by baseline joint involvement

	Joint involvement							
	SJC ≤5		SJC 6–≤7		SJC 8–≤12		SJC >12	
Mean (SD) unless otherwise specified	PBO n=139	BKZ 160 mg Q4W n=231	PBO n=71	BKZ 160 mg Q4W n=139	PBO n=81	BKZ 160 mg Q4W n=176	PBO n=100	BKZ 160 mg Q4W n=152
Age, years	49.6 (13.2)	47.9 (13.2)	49.8 (12.0)	49.6 (12.8)	49.3 (11.1)	49.5 (11.6)	49.4 (12.0)	50.2 (12.1)
Sex, male, n (%)	65 (46.8)	112 (48.5)	34 (44.7)	54 (38.8)	43 (43.4)	82 (46.6)	45 (45.0)	83 (54.6)
BMI, kg/m^2	28.0 (5.1)	28.4 (6.0)	31.0 (6.7)	29.7 (7.6)	30.1 (6.3)	30.6 (7.1)	29.5 (5.4)	30.0 (6.1)
Time since PsA diagnosis, years	6.0 (6.5)	6.4 (7.1)[a]	7.8 (7.8)	7.8 (9.1)[b]	7.2 (8.2)[c]	7.5 (9.4)[d]	6.7 (6.9)[c]	8.3 (9.0)[e]
cDMARD use at baseline, n (%)	73 (52.5)	147 (63.6)	46 (60.5)	85 (61.2)	61 (61.6)	111 (63.1)	77 (77.0)	97 (63.8)
BSA affected by psoriasis ≥3%, n (%)	65 (46.8)	129 (55.8)	45 (59.2)	64 (46.0)	56 (56.6)	100 (56.8)	62 (62.0)	100 (65.8)
PASI score[f]	8.6 (6.2)	9.2 (8.0)	8.2 (4.8)	8.1 (7.7)	7.2 (5.1)	9.0 (8.0)	8.4 (7.3)	9.5 (8.1)
SJC	4.2 (0.8)	4.1 (0.8)	6.4 (0.6)	6.4 (0.5)	9.6 (1.4)	9.6 (1.4)	20.2 (8.6)	19.2 (7.7)
TJC	10.7 (7.9)	10.8 (8.4)	13.5 (9.9)	15.3 (10.3)	18.1 (9.9)	18.0 (9.6)	30.6 (14.5)	28.8 (14.3)
Enthesitis (LEI >0), n (%)	37 (26.6)	64 (27.7)	16 (21.1)	50 (36.0)	20 (20.2)	71 (40.3)	33 (33.0)	64 (42.1)
LEI score[g]	2.5 (1.4)	2.4 (1.5)	3.3 (1.8)	2.3 (1.4)	2.9 (1.5)	2.5 (1.5)	3.2 (1.5)	3.0 (1.4)
Pain VAS[h]	52.3 (26.5)	49.3 (25.6)[i]	55.0 (21.6)	53.3 (24.6)	61.4 (22.4)	57.5 (22.9)	66.4 (19.7)	64.3 (20.7)
HAQ-DI	0.80 (0.60)	0.75 (0.58)[j]	0.81 (0.58)	0.87 (0.58)	1.03 (0.57)	0.92 (0.59)	1.14 (0.72)	1.03 (0.59)
PtGA	55.8 (24.8)	51.9 (24.4)[j]	56.1 (21.1)	53.9 (24.7)	62.0 (23.6)	59.1 (20.9)	66.9 (19.7)	64.0 (20.5)

Randomized set. Due to the small number of patients with 3 SJC (n=85) and 4 SJC (n=143) at BL, pts with 5 SJC (n=142) were included in the first quartile. [a] n=226; [b] n=138; [c] n=98; [d] n=174; [e] n=151; [f] In patients with BSA affected by psoriasis ≥3%; [g] In patients with enthesitis at baseline (LEI >0); [h] Pain VAS assessed using Patient's Assessment of Arthritis Pain VAS (0 [no pain] to 100 [most severe pain]); [i] n=230. BKZ: bimekizumab; BMI: body mass index; BSA: body surface area; HAQ-DI: Health Assessment Questionnaire – Disability Index; LEI: Leeds Enthesitis Index; PASI: Psoriasis Area and Severity Index; PBO: placebo; PsA: psoriatic arthritis; PtGA: patient's global assessment; Q4W: every four weeks; SD: standard deviation; SJC: swollen joint count; VAS: visual analog scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

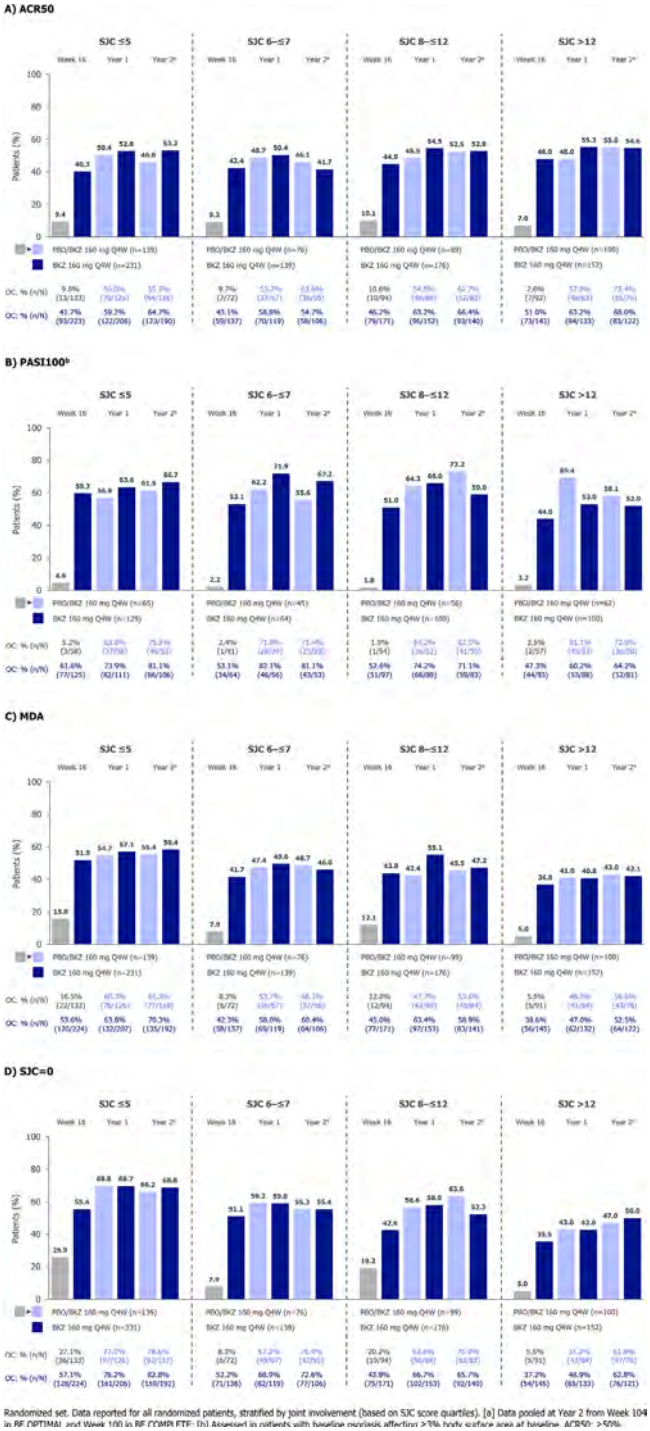


Figure 1. (A) ACR50, (B) PASI100, (C) MDA, and (D) SJC=0 responders at Week 16, Year 1, and Year 2, reported by baseline joint involvement (NRI, OC)

Pts were pooled from the BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve) and BE COMPLETE (NCT03896581; TNF inhibitor inadequate response/intolerance [TNFi-IR]) trials. As trials were different sizes (BE OPTIMAL 431 BKZ, 281 PBO; BE COMPLETE 267 BKZ, 133 PBO), proportions of bDMARD-naïve and TNFi-IR pts are not equal per quartile. Inclusion criteria for each trial included ≥3 tender and swollen joints. Both had a 16-wk double-blind, placebo (PBO)-controlled period. Pts completing Wk 52 of BE OPTIMAL or Wk 16 of BE COMPLETE could enter BE VITAL (NCT04009499; open-label extension), in which all pts received BKZ. BE OPTIMAL included a reference arm (adalimumab 40 mg Q2W); data not reported due to small pt numbers in SJC quartiles.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

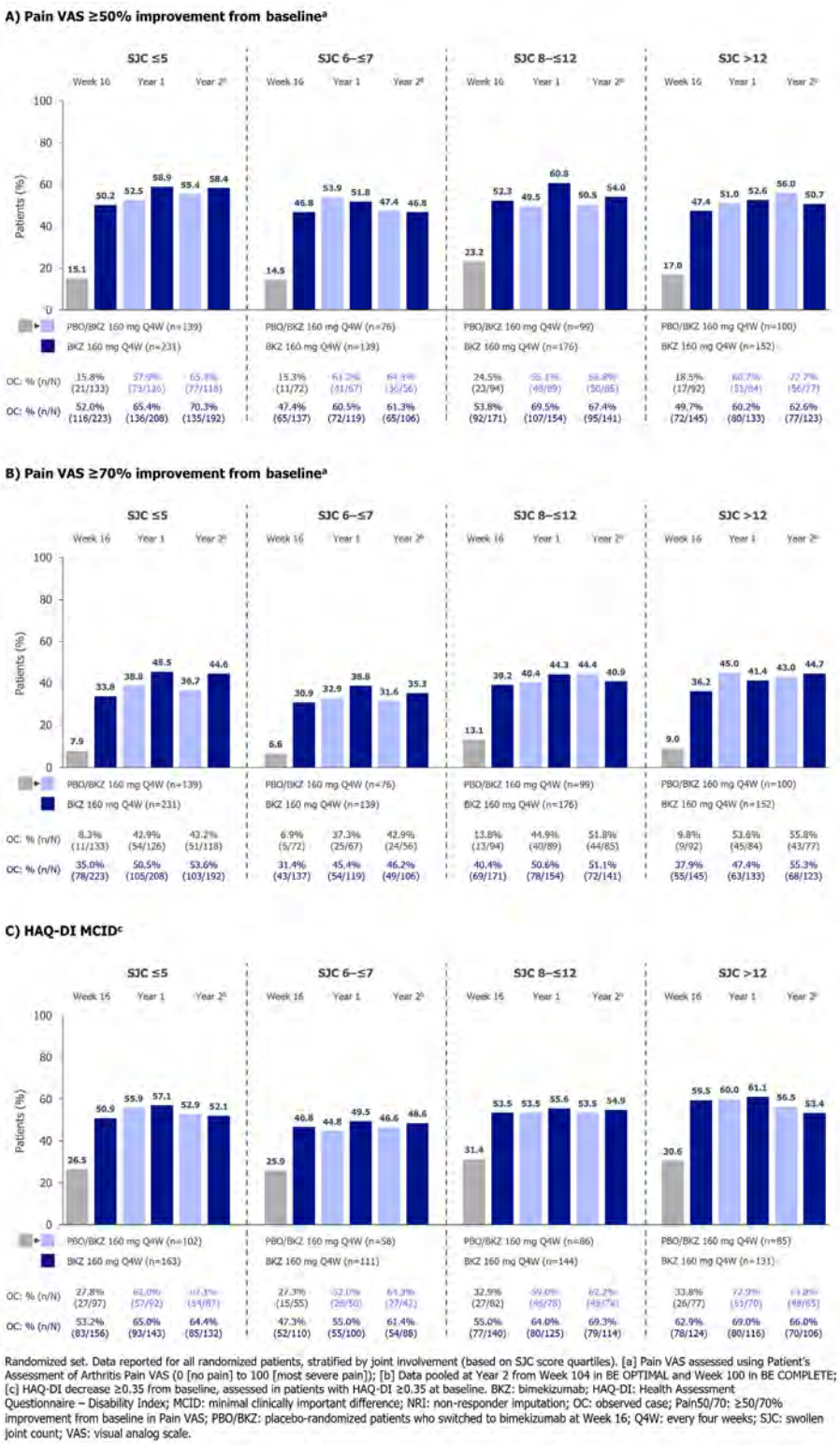


Figure 2. (A) Pain50, (B) Pain70, and (C) HAQ-DI MCID responders at Week 16, Year 1, and Year 2, reported by baseline joint involvement (NRI, OC)

Outcomes reported: ACR ≥50% improvement, Psoriasis Area and Severity Index 100% improvement, minimal disease activity, SJC=0, Pain visual analog scale ≥50/70% improvement from BL, Health Assessment Questionnaire – Disability Index minimal clinically important difference (≥0.35 decrease from BL in pts with BL score ≥0.35). Data are pooled across

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

both trials (non-responder imputation; observed case). Data are reported by randomization group at Wk 16, Year 1 (Wk 52), and Year 2 (pooled Wk 104/100 from BE OPTIMAL/BE COMPLETE).

Results: At BL, 370 pts had SJC ≤5, 215 had 6–≤7, 275 had 8–≤12, and 252 had >12. Demographic and disease characteristics by BL SJC are presented in the **Table**.

At Wk 16, BKZ-treated pts demonstrated numerically greater improvements in joint, skin, composite, and patient-reported outcomes vs PBO, across pts with varying BL joint involvement. For all domains assessed, improvements were sustained to 2 years in BKZ-randomized pts, with robust efficacy across pts with varying BL joint involvement (**Figure 1–2**). For pts who switched from PBO to BKZ at Wk 16, improvements in efficacy similar to BKZ-randomized pts with varying BL joint involvement were reported to Year 1 and sustained to Year 2.

Conclusion: In pts with PsA and varying BL joint involvement, BKZ treatment demonstrated greater improvements vs PBO across disease domains at Wk 16, and improvements were sustained to 2 years. Robust efficacy was observed across all groups of pts with varying BL joint involvement, reflecting the broader range of pts seen in clinical practice.

References: 1. Alle G. J Rheum 2025;52:138–44.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **H. Kameda**: AbbVie, 2, 6, Amgen, 2, 6, Asahi Kasei Pharma Co., 2, 5, 6, BMS, 6, Eisai, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Mitsubishi-Tanabe, 6, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, Taisho, 2, 5, UCB, 2, 6; **D. Nicholls**: AbbVie, 1, 5, 6, AstraZeneca, 1, 6, BMS, 5, Eli Lilly, 5, Gilead, 5, Incannex, 5, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Servatus, 5, Sun Pharma, 5, UCB, 1, 5, 6; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **B. Ink**: AbbVie, 11, GSK, 11, UCB, 3, 11; **R. Bajracharya**: UCB, 3, 11; **P. Healy**: UCB, 3, 11; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1459

Fungal Infections, Including *Candida*, in Patients With Active Psoriatic Arthritis (PsA) Treated With Secukinumab: A Pooled Analysis of 9 Phase 3 Trials

Shikha Singla[1], Linda Grinnell-Merrick[2], Weibin Bao[3], Artem Zharkov[4] and Abhijeet Danve[5], [1]Medical College of Wisconsin, Milwaukee, WI, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]Novartis Pharmaceuticals Corporation, Hanover, NJ, [4]Novartis Pharma AG, Basel, Switzerland, [5]Section of Rheumatology, Department of Medicine, Yale School of Medicine, New Haven, CT

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: PsA is a chronic inflammatory disease characterized by joint pain, swelling and stiffness, and is often accompanied by cutaneous changes linked to psoriasis. Patients receiving treatment with an IL-17 inhibitor, such as secukinumab (SEC), reported higher incidence of *Candida* and other fungal infections. The objective of this post hoc analysis is to describe the incidence, severity, seriousness, and type of fungal infections, including *Candida*, among patients with PsA treated with SEC.

Methods: This post hoc analysis included patients with active PsA from a pooled population of 9 phase 3 clinical trials who received SEC 150 mg, SEC 300 mg, or placebo (PBO). Following the PBO-controlled period, patients randomized to PBO were switched to SEC 150 mg or SEC 300 mg while patients randomized at baseline to receive either dose of SEC continued the same dose. Baseline demographic and clinical characteristics are reported in patients with or without ≥1 fungal infection adverse event during the entire treatment period. Incidence of fungal infections, including *Candida*, are reported for the PBO-controlled period and through the entire treatment period. Characteristics of infections including the specific types (defined by MedDRA preferred term), severity grades, and infections resulting in treatment discontinuation are reported through the entire treatment period.

Results: Overall, 2416 and 932 patients with active PsA receiving SEC or PBO, respectively, were included. A total of 167 (6.9%) patients receiving SEC reported ≥1 fungal infection through the entire treatment period, and most (62.3%) were female. Female patients comprised 51.8% of the entire study population and the mean age was 48.6 years. During the PBO-controlled period, rates of total fungal infections were infrequent in each treatment group (exposure adjusted incidence rate [EAIR] per 100 patient years [95% CI], SEC 150 mg: 3.97 [2.17-6.66], SEC 300 mg: 10.04 [6.04-15.67], PBO: 4.45 [2.37-7.61]). EAIRs of *Candida* infections were also infrequent in patients receiving either SEC 150 mg (2.54 [1.16-4.83]), SEC 300 mg (5.78 [2.89-10.34]), or PBO (2.04 [0.75-4.45], **Table 1**). Through the entire treatment period, the rates of total fungal infections (SEC 150 mg: 3.86 [3.05-4.81], SEC 300 mg: 4.68 [3.75-5.77] and *Candida* infections (SEC 150 mg: 1.86 [1.33-2.55], SEC 300 mg: 2.18 [1.57-2.95]) did not increase. The majority of fungal infections, including *Candida*, in patients receiving any SEC in the entire treatment period were mild or moderate (99.6%). One severe fungal infection (0.04%) was reported in the SEC 150 mg group (-**Figure 1**). The vast majority (83.1% of total fungal infections and 89.7% of *Candida* infections) were fully resolved before the end of the treatment period (**Figure 2**), and 2 (0.8%) infections resulted in treatment discontinuation.

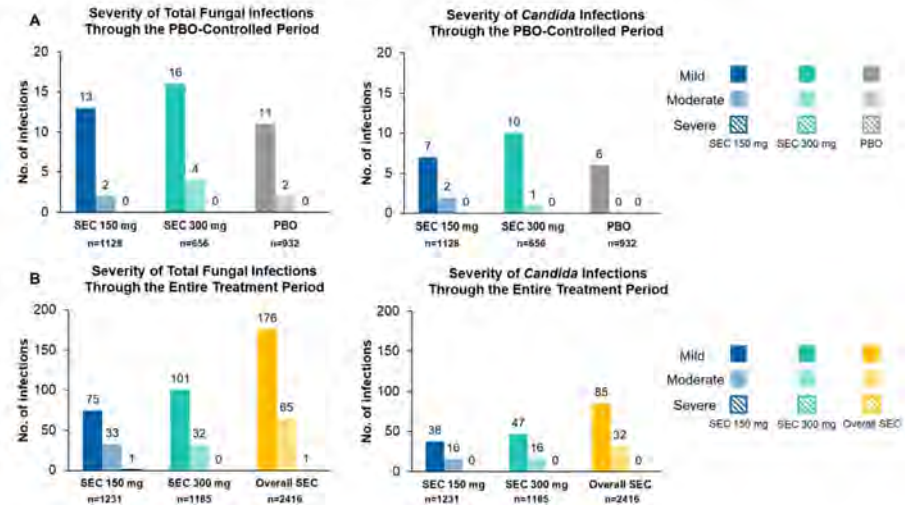
Table 1. Fungal Infections, Including *Candida*, During the PBO-Controlled Period in Patients With PsA Receiving Secukinumab

Infection type, EAIR (95% CI)[a,b]	SEC 150 mg (n=1128)	SEC 300 mg (n=656)	PBO (n=932)
Total fungal infections	3.97 (2.17-6.66)	10.04 (6.04-15.67)	4.45 (2.37-7.61)
Candida infections	2.54 (1.16-4.83)	5.78 (2.89-10.34)	2.04 (0.75-4.45)
Oral candidiasis	0.85 (0.17-2.47)	2.09 (0.57-5.35)	0.34 (0.01-1.89)
Vulvovaginal candidiasis	1.13 (0.31-2.89)	1.57 (0.32-4.58)	1.36 (0.37-3.48)
Candida infection	0.00 (0.00-1.04)	1.04 (0.13-3.77	0.00 (0.00-1.25)
Oesophageal candidiasis	0.28 (0.01-1.57)	0.52 (0.01-2.90)	0.00 (0.00-1.25)
Genital candidiasis	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.00 (0.00-1.25)
Oropharyngeal candidiasis	0.00 (0.00-1.04)	0.52 (0.01-2.91)	0.00 (0.00-1.25)
Balantis candida	0.00 (0.00-1.04)	0.00 (0.00-1.92)	0.34 (0.01-1.89)
Fungal infections (NEC)[c]	1.13 (0.31-2.89)	2.09 (0.57-5.34)	1.36 (0.37-3.49)
Fungal foot infection	0.00 (0.00-1.04)	0.52 (0.01-2.90)	0.00 (0.00-1.25)
Fungal infection	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.00 (0.00-1.25)
Fungal rhinitis	0.00 (0.00-1.04)	0.52 (0.01-2.90)	0.00 (0.00-1.25)
Fungal skin infection	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.34 (0.01-1.89)
Genital infection fungal	0.00 (0.00-1.04)	0.52 (0.01-2.90)	0.00 (0.00-1.25)
Mastitis fungal	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.00 (0.00-1.25)
Oral fungal infection	0.00 (0.00-1.04)	0.52 (0.01-2.90)	0.34 (0.01-1.89)
Vulvovaginal mycotic infection	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.34 (0.01-1.89)
Otitis external fungal	0.00 (0.00-1.04)	0.00 (0.00-1.92)	0.34 (0.01-1.89)
Tinea infections	0.56 (0.07-2.04)	2.09 (0.57-5.35)	1.02 (0.21-2.99)
Body tinea	0.00 (0.00-1.04)	1.04 (0.13-3.77)	0.34 (0.01-1.89)
Tinea pedis	0.00 (0.00-1.04)	1.04 (0.13-3.77)	0.00 (0.00-1.25)
Tinea cruris	0.00 (0.00-1.04)	0.52 (0.01-2.90)	0.00 (0.00-1.25)
Tinea versicolour	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.34 (0.01-1.89)
Trichophytosis	0.28 (0.01-1.57)	0.00 (0.00-1.92)	0.00 (0.00-1.25)
Dermatophytosis	0.00 (0.00-1.04)	0.00 (0.00-1.92)	0.34 (0.01-1.89)

EAIR, exposure adjusted incidence rate per 100 patient-years; MedDRA, Medical Dictionary of Regulatory Activities; NEC, not elsewhere classifiable; PBO, placebo; SEC, secukinumab. a MedDRA preferred term. b A patient with multiple occurrences of an infection while receiving 1 treatment was counted only once in the infection category for that treatment. c NEC denotes infections that were not specifically classified into any of the MedDRA preferred terms.

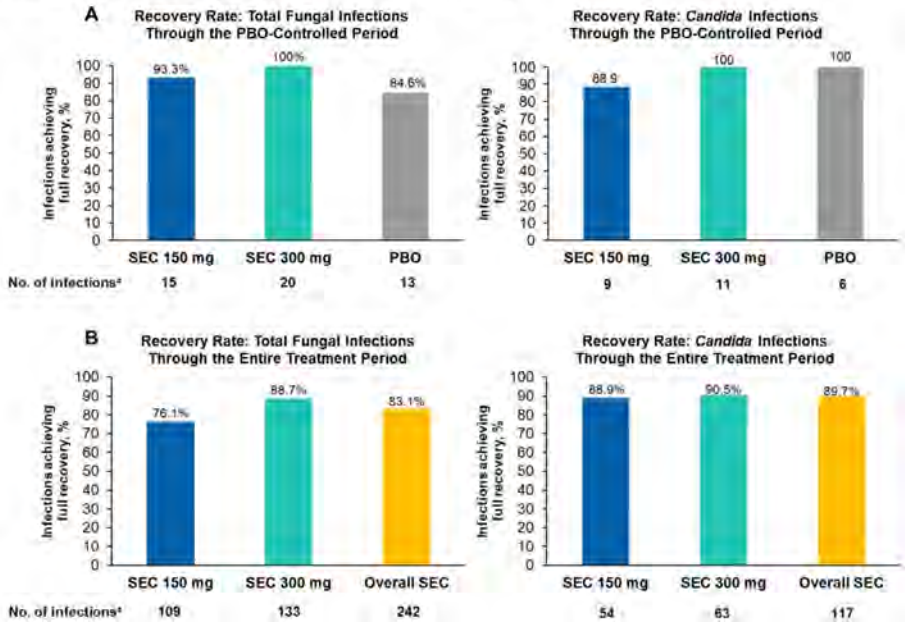
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Severity of Total Fungal and *Candida* Infections Through (**A**) the PBO-Controlled Period and (**B**) the Entire Treatment Period[a]



PBO, placebo; SEC, secukinumab. a Infections are reported as the number of infections per treatment arm.

Figure 2. Recovery Rates of Total Fungal and *Candida* Infections Through (**A**) the PBO-Controlled Period and (**B**) the Entire Treatment Period



PBO, placebo; SEC, secukinumab. a Total number of infections through the indicated time.

Conclusion: Fungal infections, including *Candida*, were infrequent with incidence rates not increasing throughout the entire treatment period. Fungal infections during treatment with SEC were mild or moderate in most instances and most infections were fully resolved before the end of treatment, allowing almost all patients to continue treatment.

Disclosure: S. Singla: AbbVie/Abbott, 2, Eli Lilly, 5, Janssen, 2, 6, Prometheus Biosciences, 5, UCB, 2; **L. Grinnell-Merrick**: Novartis, 3, 11; **W. Bao**: Novartis, 3, 11; **A. Zharkov**: Novartis, 3, 11; **A. Danve**: AbbVie, 2, Amgen, 2, Eli Lilly, 5, Janssen, 2, Novartis, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1460

Effect of Guselkumab and IL-17 Inhibitors on Work Productivity and Activity Impairment in Psoriatic Arthritis: 6-Month Results of the PsABIOnd Observational Study

Stefan Siebert[1], Mohamed Sharaf[2], Frank Behrens[3], Proton Rahman[4], mitsumasa kishimoto[5], Enrique R. Soriano[6], Emmanouil Rampakakis[7], László Köleséri[8], Karissa Lozenski[9], Ruben Queiro[10], Ennio Lubrano[11] and Laure Gossec[12], [1]University of Glasgow, Glasgow, United Kingdom, [2]Janssen - Johnson & Johnson, Dubai, United Arab Emirates, [3]Goethe-University & Fraunhofer ITMP, Frankfurt, Germany, [4]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada, [5]Kyorin University School of Medicine, Tokyo, Japan, [6]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires and University Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [7]JSS Medical Research, Montréal, QC, Canada, [8]IQVIA, Budapest, Hungary, [9]Johnson & Johnson, Horsham, PA, [10]Hospital Universitario Central de Asturias, Oviedo. Asturias, Spain, [11]Department of Medicine, Università deglia Studi del Molise, CAMPOBASSO, Italy, [12]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

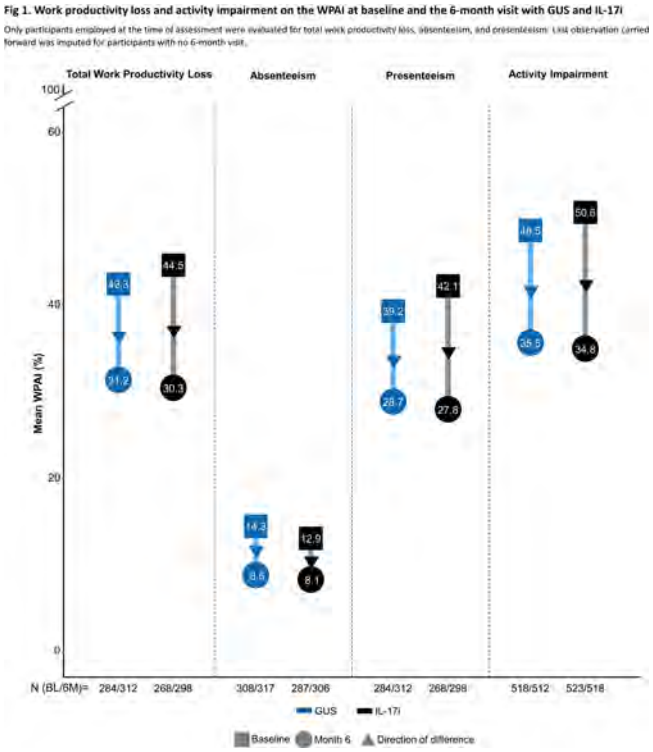
Background/Purpose: Work impairment is a key issue in PsA. Biologic treatments can improve work status in patients (pts) with PsA; however, there is lack of comparative real-world data for different modes of action, e.g. IL-23 and IL-17 inhibitors (i). The current analysis aimed to assess PsA pt-reported outcomes (PRO), specifically work productivity, activity impairment, and disease impact after 6 months of treatment with guselkumab (GUS) and IL-17i.

Methods: PsABIOnd (NCT05049798) is a global (20 countries) observational study in PsA pts starting GUS or IL-17i as 1st-to-4th line of biologic therapy per standard of care.[1] Here, the full population of the PsABIOnd study was analyzed over the first 6 months of follow-up. Work productivity (overall work productivity loss, absenteeism, presenteeism) and activity impairment were assessed via the Work Productivity and Activity Impairment Questionnaire (WPAI; 0-100).[2] Pt-reported disease impact was assessed using the PsA Impact of Disease-12 (PsAID-12; 0-10),[3] including the mean total score and proportions of pts achieving minimal clinically important improvement (MCII; improvement by ≥1.4; among pts with BL PsAID-12 score ≥1.4). All analyses were performed according to initial treatment group allocation and treatment comparison was based on 95% confidence intervals (CI).

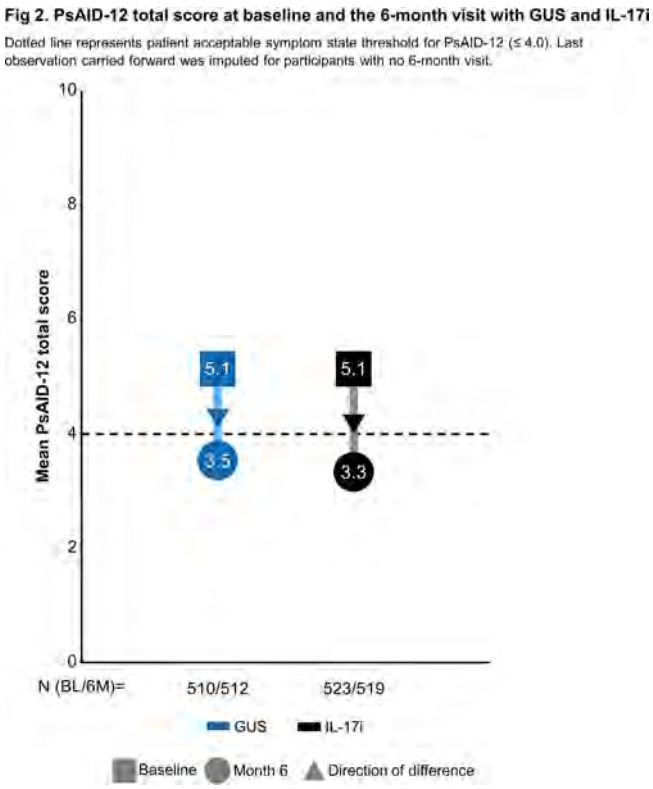
Results: 1134 pts were analyzed; 555 and 579 received GUS or IL-17i, respectively, as their initial treatment. Mean age (53.2/53.5 yrs), sex (60.4%/59.2% female), and prior exposure to a targeted drug (63.4%/62.3%) were comparable for GUS/IL-17i. Mean overall baseline work productivity loss (42.3%/44.5% for GUS/IL17i groups), absenteeism (14.3%/12.9%), presenteeism (39.2%/42.1%), activity impairment (48.5%/50.6%), and mean baseline PsAID-12 total score (5.1/5.1) were also similar between groups.

At the 6-month visit, comparable improvements were observed in all WPAI outcomes with GUS and IL-17i. Mean (95% CI) improvements in GUS/IL-17i were: overall work productivity loss (-13.1 [-16.5, -9.7]/-13.8 [-17.5, -10.1]%), absenteeism (-6.4 [-10.4, -2.4]/-2.5 [-5.1, 0.2]%), presenteeism (-12.5 [-15.7, -9.3]/-14.0 [-17.5, -10.5]%), activity impairment (-13.1 [-15.4, -10.8]/-15.7 [-18.2, -13.1]%; **Fig 1**). Mean PsAID-12 total scores also improved significantly (-1.6 [-1.7, -1.4]/-1.8 [-2.0, -1.6]) reaching levels (3.5/3.3) indicative of symptom impact below the pt acceptable symptom state threshold (≤ 4.0) in both groups (**Fig 2**). Rates of pts achieving PsAID-12 MCII at 6 months were also comparable (54.7%/55.9%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Conclusion: By 6 months of treatment in real-world, improvements in work productivity and ability to perform daily activities were observed with both GUS and IL-17i which were paralleled with clinically meaningful improvements in pt-reported multi-domain disease impact. Based on overlapping CIs, improvements in PROs were comparable between the two modes of



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

action. These results may be useful for reimbursement decisions and healthcare provider/pt shared treatment decision-making.

References

1. Siebert S. Rheumatol Ther. 2023;10(2):489
2. Teilly MC. Parmacoeconomics. 1993; 4(5):353
3. Gossec L. Ann Rheum Dis. 2014;73(6):1012

Disclosure: S. Siebert: AbbVie, 6, Amgen, 6, AstraZeneca, 6, BMS, 5, Boehringer-Ingelheim, 5, Eli Lilly, 5, GlaxoSmithKlein, 5, Johnson & Johnson, 5, 6, Novartis, 6, Pfizer, 6, Syncona, 6, Teijin Pharma, 6, UCB, 5, 6; **M. Sharaf**: Johnson & Johnson, 3, 11; **F. Behrens**: AbbVie, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genzyme, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 5, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 6, UCB, 2, 6; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **E. Soriano**: AbbVie, 5, 6, BMS, 5, 6, Eli Lilly, 5, 6, GSK, 5, 6, J&J, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Raffo, 5, 6, UCB, 5, 6; **E. Rampakakis**: Johnson & Johnson, 2, JSS Medical Research, 3; **L. Köleséri**: IQVIA, 3, Johnson & Johnson, 2; **K. Lozenski**: BMS, 11, Johnson & Johnson, 3, 11; **R. Queiro**: AbbVie, 2, 5, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Johnson & Johnson, 2, 5, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6; **E. Lubrano**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GlaxoSmithKlein, 6, Johnson & Johnson, 6, Novartis, 6, UCB, 6; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5.

Abstract Number: 1461

Digital Behavioral Therapy Improves Outcome in Patients With Axial Spondyloarthritis And Persistent Pain: Results From a Randomized Controlled Trial

David Kiefer[1], Yade Sonkaya[2], Dietmar Krause[3], Markus Voglau[4], Bernhard Mintrop[5], Imke Redeker[6], Xenofon Baraliakos[7] and **Uta Kiltz**[7], [1]Ruhr-Universitét Bochum; Private practice of rheumatology, Hattingen, Germany, Herne, Germany, [2]Ruhr-Universität Bochum, Herne, Germany, [3]Elisabeth-Gruppe, Herne, Germany, Essen, Germany, [4]myself, Oldenburg, Germany, [5]Private rheumatology practice, Hattingen, Germany, [6]Ruhr University Bochum, Bochum, Germany, [7]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is often associated with persistent pain despite effective anti-inflammatory treatment, substantially impacting patients' quality of life. Digital health applications (DiGAs) provide an innovative approach to address multidimensional aspects of chronic pain through psychological and behavioral strategies. Our objective was to assess the impact of a DiGA utilizing the acceptance and commitment therapy (ACT) on disease outcomes, including the West Haven-Yale Multidimensional Pain Inventory (MPI), in axSpA patients experiencing chronic back pain despite stable pharmacological therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics stratified by group and user activity

Characteristics		Intervention group total (n=73)	Active App Users (n=44)	Inactive App Users (n=29)	SOC patients (n=63)
Age (years)		46.8 (13)	47.3 (12)	46.2 (12.4)	50.9 (11.4)
Gender, female, n (%)		36 (49.3)	23 (52.3)	13 (44.8)	27 (42.9)
Time (years) since axSpA diagnosis		13.3 (13)	13.2 (13.7)	13.6 (12.4)	15.2 (12.7)
No. of patients on bDMARD, n (%)		47 (64.4)	29 (65.9)	18 (64.3)	42 (66.6)
No. of patients on tsDMARD, n (%)		5 (6.8)	4 (9.1)	1 (3.4)	3 (4.8)
No. of previous b-DMARDs		1.6 (1.4)	1.7 (1.5)	1.5 (1.6)	1.4 (1.1)
Physician global assessment (PhGA), 0-10		3 (1.5)	2.7 (1.6)	3.3 (1.3)	2.9 (1.2)
ASDAS, 0-10		2.7 (0.8)	2.6 (0.8)	2.9 (0.7)	2.9 (0.8)
BASFI, 0-10		4.6 (2.4)	4.5 (2.5)	4.8 (2.1)	4.9 (2.3)
BASMI		3 (1.4)	3.3 (1.3)	2.6 (1.4)	3.4 (1.6)
ASAS Health Index, 0-17		8.1 (3.5)	7.9 (3.7)	8.3 (3.3)	8 (3.8)
PainDETECT >18, n (%)		13 (29.5)	13 (29.5)	6 (21.4)	22 (36.0)
MPI	Pain severity (0-6)	3.4 (1.1)	3.1 (1.2)	3.8 (0.9)	3.84 (1.2)
	Pain-related life interference (0-6)	3.4 (1.1)	3.3 (1.3)	3.7 (0.6)	3.6 (1)
	Affective distress (0-6)	3.2 (1.2)	3.1 (1.3)	3.4 (1.1)	3.2 (1.2)
	Social support (0-6)	3.4 (1.9)	3.3 (2.0)	3.5 (1.7)	3.8 (1.5)
	Life control (0-6)	3.8 (1.2)	4.0 (1.2)	3.2 (1.1)	3.5 (1)
HADS-D, 0-21		7.9 (4.3)	7.6 (4.5)	8.3 (3.9)	9 (5.3)
HADS-A, 0-21		8.5 (4.4)	8.3 (4.6)	9.0 (4.1)	9 (4.3)
SF-36 (PCS), 0-100		33.5 (8.3)	33.5 (9.6)	33.5 (6.1)	32,6 (7.4)
SF-36 (MCS), 0-100		41,7 (12.2)	42.6 (12.2)	40.4 (12.2)	42,1 (13.1)

Values are presented as mean (standard deviation), unless otherwise indicated; ASAS: Assessment of Spondyloarthritis International Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; FIQ: Fibromyalgia Impact Questionnaire; HADS: Hospital Anxiety and Depression Scale; MPI (D): Multidimensional Pain Inventory; NRS: Numerical rating scale; NSAID: Nonsteroidal anti-inflammatory drug; PAM 13: Patient Activation Measure-13; SF-36: Short Form 36; PCS: Physical component summary (PCS); MCS: Mental component summary

Methods: This unblinded, monocentric, randomized controlled trial (1:1) compared an intervention group receiving the ACT-app with a standard of care (SOC) group. The ACT app provided behavioral therapy in seven interactive lessons. Patients were followed for 12 weeks. The primary outcome was MPI pain-related life interference; secondary outcomes included pain severity, affective distress and other patient reported outcomes (PRO). The Patient Global Impression of Change (PGIC) was used to evaluate patients' subjective perception of overall change during the study. Acceptance of the DiGA was assessed

Figure 1: Change of clinical characteristics stratified by group

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

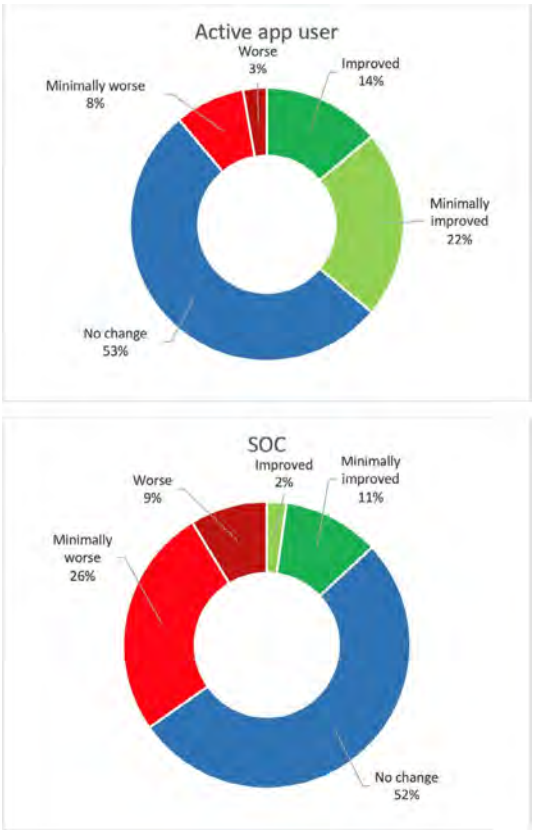


Figure 2: Patient Global Impression of Change (PGIC) Categories: Comparison Between Active App Users and Standard of care (SOC) Group

using the Net promoter score (NRS 0-10). Linear models estimating the effect of the ACT-app on the change of MPI pain-related life interference (model 1) and affective distress (model 2), with adjustments made for their respective baseline values, were calculated.

Results: A total of 136 patients were randomized to the intervention (n=73) with ACT-app and SOC group (n=63) without ACT-app (table 1). Among intervention patients, 44 actively used ACT-app, while 29 either did not receive the app code by their health insurance company or did not use the ACT-app at all. At week 12, all lessons in the ACT-app were fully completed by 19 (43%) patients in the intervention group. Baseline characteristics, including MPI scores, were comparable between groups (table 1). Active app users showed a significant reduction in pain-related interference ($p< 0.05$) as well as in other outcomes (figure 1). The improvements in pain-related life interference (model1: -0.36, 95% CI: -0.73 to 0.01) and affective distress related to the disease (model 2: -0.4, 95% CI: -0.84,0.003) were greater compared to SOC patients. Overall acceptance was moderate (Net Promoter Score 5.8 (4.3)).

Conclusion: The ACT-app demonstrated a meaningful reduction in pain-related interference, supporting that the use of DIGAs might become a supplementary tool in managing pain for axSpA patients. However, a substantial number of patients experienced challenges to use the app actively.

Disclosure: D. Kiefer: AbbVie/Abbott, 2, 5, Alpha sigma, 2, 6, UCB, 1, 2, 6; **Y. Sonkaya**: None; **D. Krause**: None; **M. Voglau**: None; **B. Mintrop**: None; **I. Redeker**: None; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5.

Abstract Number: 1462

Five-Year Results of Secukinumab on Minimal Disease Activity (MDA) Components and the Impact of Biologic Treatment Status on Effectiveness and Safety in Patients With Psoriatic Arthritis: Real-World Data From the SERENA Study

Uta Kiltz[1], Petros Sfikakis[2], Andreas Bounas[3], Nicola Gullick[4], Eric LESPESSAILLES[5], Jan Brandt-Juergens[6], Rasho Rashkov[7], Cynthia Vizcaya[8], Andreas Clemens[8], Kim Hoyt[9], Weibin Bao[10] and Karl Gaffney[11], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [3]'OLYMPION', General Clinic of Patra, Patra, Greece, [4]Rheumatology Department, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, Coventry, United Kingdom, [5]University Hospital of Orléans, Orleans, France, [6]Rheumatologische Schwerpunktpraxis, Berlin, Germany, [7]Clinic of Rheumatology, University Hospital St. Ivan Rilski, Sofia, Bulgaria, [8]Novartis Pharma AG, Basel, Switzerland, [9]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [10]Novartis Pharmaceuticals Corporation, Hanover, NJ, [11]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Secukinumab has demonstrated long-lasting efficacy and a favorable safety profile across multiple clinical trials and domains of psoriatic disease. Real-world data provides additional valuable information on the long-term outcomes of secukinumab in routine clinical practice. Secukinumab has shown high retention rates and sustained effectiveness in patients with psoriatic arthritis (PsA) and radiographic axial spondyloarthritis (r-axSPA) during 5 years of follow-up in

Table 1: Demographics and baseline characteristics

Characteristics*	PsA (N = 522)
Age (years)	52.5 ± 12.0
Male, n (%)	234 (44.8)
Weight (kg)	83.6 ± 17.6
Body mass index (kg/m²)	28.7 ± 5.5
Caucasian race, n (%)	491 (94.1)
Time since diagnosis (years)	8.6 ± 7.4
Smoking status, n (%)	
Current	113 (21.6)
Former	89 (17.0)
Never	260 (49.8)
Previous biologic exposure prior to start of secukinumab, n (%)	
No biologics pre-treatment	164 (31.4)
1 biologics pre-treatment	147 (28.2)
2 biologics pre-treatments	88 (16.9)
3 or more biologics pre-treatments	123 (23.6)

*mean ± SD otherwise indicated. N, number of patients in populations; n, number of patients with non-missing data; PsA, psoriatic arthritis; SD, standard deviation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

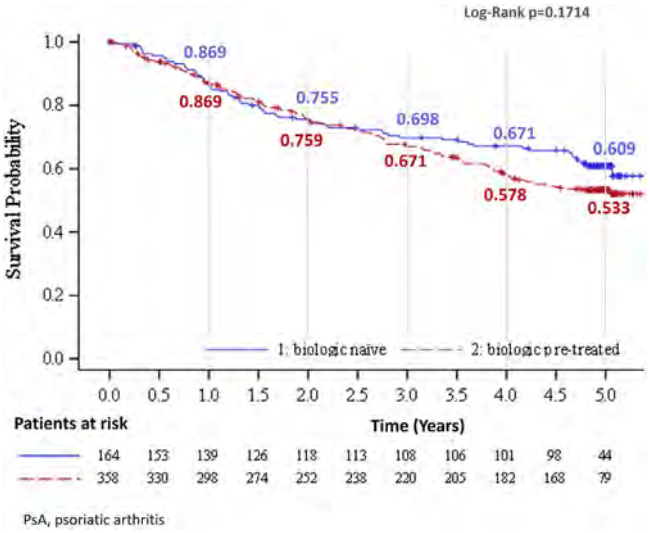


Figure 1. Kaplan-Meier estimates of the retention rate of secukinumab by biologic-experienced vs biologic-naïve in PsA cohort

Figure 2. MDA response (components of MDA criteria)

the SERENA study. This post hoc analysis assesses minimal disease activity (MDA) components and retention rates in biologic-naïve and biologic-experienced patients during the study period.

Methods: SERENA (CAIN457A3403) was a non-interventional, prospective real-world study conducted across 19 countries in patients with moderate to severe chronic plaque-type psoriasis, active PsA, or r-axSpA, who had received secukinumab for ≥16 weeks before enrollment. The different components within the MDA assessment were evaluated for patients achieving the following criteria: tender joint count (TJC ≤1), swollen joint count (SJC ≤1), Psoriasis Area and Surface Index (PASI ≤1) or body surface area (BSA ≤3), patient pain visual analogue scale (VAS ≤15 mm), Health Assessment Questionnaire Disability Index (HAQ-DI ≤0.5), and tender entheseal points (TEP ≤1) from years 1 to 5. Secukinumab retention rate was derived from Kaplan-Meier estimates for the proportion of patients who had been treated with secukinumab from years 1 to 5.

Results: Overall, 522 patients with PsA were included in the analysis. The mean age at inclusion was 52.5 years, 44.8% male. The mean ± SD BMI was 28.7 ± 5.5 kg/m^2 and mean time since diagnosis was 8.6 ± 7.4 years (**Table 1**). Before inclusion in the study, the patients had been receiving secukinumab treatment for a mean duration of 1 year, and 68.6% had previous biologic exposure. Secukinumab retention rates were numerically higher in the biologic-naïve subgroup compared with the biologic-experienced subgroup, from years 2.5 onwards (**Figure 1**). The percentage of patients reaching the threshold of the different components within the MDA assessment are shown in **Figure 2**. Since the patient's global assessment (≤20) was not collected, it was not possible to report the overall MDA. There were no new safety signals in this subanalysis of patients with PsA.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this real-world data analysis, secukinumab demonstrated sustained clinical effectiveness and a favorable safety profile in patients with PsA over 5 years of observation. Retention rates remained high throughout the observation time, with no statistically significant differences observed in biologic naïve or pre-treated patients. Importantly, secukinumab demonstrated sustained long-term remission across all six collected components of the MDA criteria. These results reinforce the long-term value of secukinumab in managing multiple PsA domains in routine clinical practice.

Disclosure: U. Kiltz: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **P. Sfikakis**: None; **A. Bounas**: AbbVie, 6, Aenorasis, 6, Amgen, 6, Bausch Health, 6, FARAN, 6, Genesis Pharma, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, MSD, 6, Novartis, 6, Pfizer, 6, UCB, 6; **N. Gullick**: AbbVie, 2, 5, 6, Alfasigma, 2, AstraZeneca, 5, Eli Lilly, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Takeda, 2, UCB, 2, 5, 6; **E. LESPESSAILLES**: AbbVie, 5, 6, Amgen, 2, 5, 6, Eli Lilly, 2, 5, 6, Expanscience, 2, 6, Galapagos, 6, MSD, 2, 5, 6, Novartis, 5, UCB, 5; **J. Brandt-Juergens**: AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Medac, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **R. Rashkov**: AbbVie, 12, Consultancy fees and speaker honoraria, Amgen, 12, Consultancy fees and speaker honoraria, Janssen, 12, Consultancy fees and speaker honoraria, MSD, 12, Consultancy fees and speaker honoraria, Novartis, 12, Consultancy fees and speaker honoraria, Pfizer, 12, Consultancy fees and speaker honoraria, Roche, 12, Consultancy fees and speaker honoraria, UCB, 12, Consultancy fees and speaker honoraria; **C. Vizcaya**: Novartis, 3; **A. Clemens**: Novartis, 3; **K. Hoyt**: Novartis, 3; **W. Bao**: Novartis, 3, 11; **K. Gaffney**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1463

Effective Prevention of Psoriatic Arthritis with Secukinumab: A 5-Year Observation from the SERENA Study

Uta Kiltz[1], Petros Sfikakis[2], Andreas Bounas[3], Nicola Gullick[4], Eric LESPESSAILLES[5], Jan Brandt-Juergens[6], Rasho Rashkov[7], Cynthia Vizcaya[8], Andreas Clemens[8], Weibin Bao[9] and Karl Gaffney[10], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [3]'OLYMPION', General Clinic of Patra, Patra, Greece, [4]Rheumatology Department, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, Coventry, United Kingdom, [5]University Hospital of Orléans, Orleans, France, [6]Rheumatologische Schwerpunktpraxis, Berlin, Germany, [7]Clinic of Rheumatology, University Hospital St. Ivan Rilski, Sofia, Bulgaria, [8]Novartis Pharma AG, Basel, Switzerland, [9]Novartis Pharmaceuticals Corporation, Hanover, NJ, [10]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Secukinumab, an IL-17A inhibitor, has well-established effectiveness in the treatment of psoriasis (PsO) and psoriatic arthritis (PsA) in both long-term clinical trials and the real world.[1,2] There is an intense discussion if biologics can prevent the development of PsA in patients with psoriasis without PsA with nail involvement (higher risk patient group). SERENA is a large, longitudinal, observational study conducted at 438 sites across Europe in adult patients with moderate to severe chronic plaque PsO, active PsA and radiographic axial spondyloarthritis.[2] The observations will be put into perspective to historical evidence regarding patients with PsO without PsA not previously treated with biologics[3]. Here we evaluate the 5-year effectiveness of secukinumab in prevention of PsA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Effectiveness of secukinumab in patients with PsO without PsA and with nail involvement at inclusion

Endpoints	Study population	Year 1	Year 2	Year 3	Year 4	≥Year 5
PASI 100 n/M (%)	292	62/221 (28.1)	56/208 (26.9)	49/174 (28.2)	42/131 (32.1)	47/122 (38.5)
PASI 90 n/M (%)	292	119/221 (53.8)	113/208 (54.3)	95/174 (54.6)	76/131 (58.0)	77/122 (63.1)
PGA 0/1 response, n/M (%)	292	75/104 (72.1)	71/94 (75.5)	60/78 (76.9)	48/67 (71.6)	41/52 (78.8)

M, number of patients under evaluation; n, number of responders; N, number of patients in the study population; PASI Psoriasis Area and Severity Index, PGA, Physician's Global Assessment; PsA, psoriatic arthritis

Methods: Patients received secukinumab treatment for ≥16 weeks before enrolment into the study. In the subgroup of patients with PsO without PsA and nail involvement at the study entry, we analysed the incidence of PsA from inclusion into the study to the 5-year follow up. We describe the outcomes as exposure adjusted incidence rates (EAIR) of developing PsA during the 5-year follow-up, in terms of per 100 patient-years. Descriptive statistics of effectiveness assessments were based on observed data.

Results: Overall, 292 patients with active PsO with nail involvement without PsA were included in the analysis (mean age at study enrolment, 49.2 years; male, 79.8%; mean body mass index, 29.3 kg/m^2; mean time since diagnosis, 17.8 years). 28.8% had previous biologic exposure before the start of secukinumab. After 5 years of study enrolment and a total exposure of 1022 patient-years, most patients (287/292 patients; 98.3%) did not develop PsA. This translates into a yearly, exposure adjusted incidence rate (EAIR) of 0.49 (95% CI: 0.16,1.14). Secukinumab treatment resulted in a sustained control over skin changes as assessed by Psoriasis Area and Severity Index (PASI) and Physician's Global Assessment (PGA) 0/1 response, with 39% of patients achieving skin clearance (PASI 100) after 5 years (**Table 1**). Approximately 63% of patients achieved PASI 90 after 5 years (**Table 1**).

Conclusion: Previously, an 8-year prospective observational study in patients with PsO (including 35% of patients with nail involvement) without PsA reported a yearly incidence rate of PsA of 2.7 per 100 patients not treated with a biologic[3]. SERENA is one of the largest real-world studies in Europe observing the effect of secukinumab over 5 years. Long-term secukinumab treatment in patients with PsO with nail involvement without PsA resulted in an ~82% reduction of the annual incidence rate of PsA in comparison to historic non-biologic treated patients. These results suggest that secukinumab may be effective in preventing PsA in patients with PsO. Secukinumab-treated patients also achieved sustained long-term control over skin changes.

References:

1. Blair HA. Drugs 2021;81(4): 483-494. doi: 10.1007/s40265-021-01476-3.
2. Kiltz U, et al. Rheumatol Ther. 2022;9(4): 1129-1142. doi: 10.1007/s40744-022-00460-x.
3. Eder L. Arthritis Rheumatol. 2016;68(4):915-23. doi: 10.1002/art.39494.

Disclosure: U. Kiltz: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **P. Sfikakis**: None; **A. Bounas**: AbbVie, 6, Aenorasis, 6, Amgen, 6, Bausch Health, 6, FARAN, 6, Genesis Pharma, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, MSD, 6, Novartis, 6, Pfizer, 6, UCB, 6; **N. Gullick**: AbbVie, 2, 5, 6, Alfasigma, 2, AstraZeneca, 5, Eli Lilly, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Takeda, 2, UCB, 2, 5, 6; **E. LESPESSAILLES**: AbbVie, 5, 6, Amgen, 2, 5, 6, Eli Lilly, 2, 5, 6, Expanscience, 2, 6, Galapagos, 6, MSD, 2, 5, 6, Novartis, 5, UCB, 5; **J. Brandt-Juergens**: AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Medac, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **R. Rashkov**: AbbVie, 12, Consultancy fees and speaker honoraria, Amgen, 12, Consultancy fees and speaker honoraria, Janssen,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

12, Consultancy fees and speaker honoraria, MSD, 12, Consultancy fees and speaker honoraria, Novartis, 12, Consultancy fees and speaker honoraria, Pfizer, 12, Consultancy fees and speaker honoraria, Roche, 12, Consultancy fees and speaker honoraria, UCB, 12, Consultancy fees and speaker honoraria; **C. Vizcaya**: Novartis, 3; **A. Clemens**: Novartis, 3; **W. Bao**: Novartis, 3, 11; **K. Gaffney**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1464

Incidence of Major Adverse Cardiovascular Events (MACE) in Psoriasis, Psoriatic Arthritis and Axial Spondyloarthritis Patients With and Without Cardiovascular Risk Factors Treated With Secukinumab: Five-Year Safety Data from the Real-World SERENA Study

Uta Kiltz[1], Petros Sfikakis[2], Andreas Bounas[3], Nicola Gullick[4], Eric LESPESSAILLES[5], Jan Brandt-Juergens[6], Rasho Rashkov[7], Cynthia Vizcaya[8], Andreas Clemens[8], Lara Gómez[9], Kim Hoyt[10], Weibin Bao[11] and Karl Gaffney[12], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [3]'OLYMPION', General Clinic of Patra, Patra, Greece, [4]Rheumatology Department, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, Coventry, United Kingdom, [5]University Hospital of Orléans, Orleans, France, [6]Rheumatologische Schwerpunktpraxis, Berlin, Germany, [7]Clinic of Rheumatology, University Hospital St. Ivan Rilski, Sofia, Bulgaria, [8]Novartis Pharma AG, Basel, Switzerland, [9]Novartis Farmaceutica, Madrid, Spain, [10]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [11]Novartis Pharmaceuticals Corporation, Hanover, NJ, [12]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with psoriasis (PsO), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA) are at increased risk of major adverse cardiovascular events (MACE) due to systemic inflammation and cardiometabolic burden. Secukinumab, a fully human interleukin (IL)-17A inhibitor, has demonstrated long-term efficacy and safety across multiple indications. We assessed the 5-year incidence of MACE and baseline cardiovascular (CV) risk factors in patients with and without CV risk factors who were treated with secukinumab in the real-world SERENA study.

Methods: SERENA (CAIN457A3403) is a non-interventional, prospective real-world study conducted across 19 countries in patients with moderate to severe chronic PsO, PsA, or radiographic axSpA (r-axSpA), who received secukinumab for ≥16 weeks before enrollment. MACE were defined using MedDRA v26.1 (including myocardial infarction, stroke, and CV

Table 1. Baseline demographic and clinical characteristics

	Psoriasis		Psoriatic arthritis		Radiographic axSpA	
	Patients with MACE (n=24)	Patients without MACE (n=1818)	Patients with MACE (n=7)	Patients without MACE (n=572)	Patients with MACE (n=4)	Patients without MACE (n=502)
Age (years), mean ± SD	61.13 ± 11.8	48.07 ± 13.5	57.0 ± 13.0	52.37 ± 11.9	52.0 ± 8.9	46.25 ± 11.7
Females, n (%)	5 (20.8)	598 (32.9)	5 (71.4)	319 (55.8)	0 (0.0)	203 (40.4)
Disease duration, n*	24	1799	7	567	4	502
<2, n (%)	2 (8.3)	163 (9.1)	2 (28.6)	84 (14.8)	1 (25.0)	87 (17.3)
2-<5, n (%)	2 (8.3)	193 (10.7)	1 (14.3)	147 (25.9)	0 (0.0)	118 (23.5)
5-≤15, n (%)	10 (41.7)	561 (31.2)	3 (42.9)	236 (41.6)	2 (50.0)	191 (38.0)
≥15, n (%)	10 (41.7)	882 (49.0)	1 (14.3)	100 (17.6)	1 (25.0)	106 (21.1)
BMI (kg/m²), n*	20	1393	3	472	2	426
Mean ± SD	30.91 ± 6.7	28.75 ± 6.1	29.63 ± 3.8	28.72 ± 5.6	29.60 ± 6.6	27.02 ± 4.9
BMI ≥30 kg/m², n (%)	9 (37.5)	488 (26.9)	1 (14.3)	165 (28.8)	1 (25.0)	110 (21.9)
Diabetes, n (%)	3 (12.5)	173 (9.5)	3 (42.9)	65 (11.4)	0 (0.0)	31 (6.2)

n*, number of patients with non-missing data. axSpA, axial spondyloarthritis; BMI, body mass index; MACE, major adverse cardiovascular event; SD, standard deviation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

death). Exposure-adjusted incidence rates (EAIRs) were calculated per 100 patient-years (PY). Descriptive comparisons of CV risk factors (age ≥60 years, BMI ≥30 kg/m^2, disease duration ≥15 years, and diabetes) were performed between patients with and without MACE. No formal statistical comparisons were made.

Results: Among 2927 patients (PsO: 1842; PsA: 579; r-axSpA: 506), 35 MACE were reported during 9679 PY: 24 in PsO, 7 in PsA, and 4 in r-axSpA. EAIRs were 0.39 (95% CI: 0.25 - 0.58), 0.38 (0.15 - 0.78), and 0.23 (0.06 - 0.60) per 100 PY, respectively; equivalent to 3.9, 3.8, and 2.3 events per 1000 PY. These rates are lower than those reported in biologic-naïve psoriatic disease cohorts (14.5–16.4/1000 PY),[1,2] as well as in patients with and without prior biologic experience: 7.4/1000 PY in PsA and 6.0/1000 PY in axSpA[3]. Among patients who experienced MACE, 42.9% were ≥60 years old, 31.4% were obese, 34.3% had long-standing disease (≥15 years), and 17.1% had diabetes vs 9.3% in non-MACE patients. Most events occurred in individuals with traditional CV risk factors, however there was no meaningful difference in baseline characteristics compared to patients who did not experience MACE (**Table 1**). No multivariable analysis was conducted due to the low event count.

Conclusion: These results support the favorable long-term CV safety profile of secukinumab in patients with PsO, PsA, and axSpA. Over five years of treatment in a real-world setting, MACE were infrequent, and incidence rates remained low and stable across indications, including patients with baseline CV risk. The lower observed incidence than that reported in biologic-naïve cohorts,[1-3] is in line with the hypothesis that IL-17A inhibition with secukinumab may help reduce the incidence of MACE in these populations.

Disclosure: U. Kiltz: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **P. Sfikakis**: None; **A. Bounas**: AbbVie, 6, Aenorasis, 6, Amgen, 6, Bausch Health, 6, FARAN, 6, Genesis Pharma, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, MSD, 6, Novartis, 6, Pfizer, 6, UCB, 6; **N. Gullick**: AbbVie, 2, 5, 6, Alfasigma, 2, AstraZeneca, 5, Eli Lilly, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Takeda, 2, UCB, 2, 5, 6; **E. LESPESSAILLES**: AbbVie, 5, 6, Amgen, 2, 5, 6, Eli Lilly, 2, 5, 6, Expanscience, 2, 6, Galapagos, 6, MSD, 2, 5, 6, Novartis, 5, UCB, 5; **J. Brandt-Juergens**: AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Medac, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **R. Rashkov**: AbbVie, 12, Consultancy fees and speaker honoraria, Amgen, 12, Consultancy fees and speaker honoraria, Janssen, 12, Consultancy fees and speaker honoraria, MSD, 12, Consultancy fees and speaker honoraria, Novartis, 12, Consultancy fees and speaker honoraria, Pfizer, 12, Consultancy fees and speaker honoraria, Roche, 12, Consultancy fees and speaker honoraria, UCB, 12, Consultancy fees and speaker honoraria; **C. Vizcaya**: Novartis, 3; **A. Clemens**: Novartis, 3; **L. Gómez**: Novartis, 3; **K. Hoyt**: Novartis, 3; **W. Bao**: Novartis, 3, 11; **K. Gaffney**: AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Gilead, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 1465

Sustainability of Clinical Response Through 2 Years Among Upadacitinib-Treated Patients With Axial Spondyloarthritis: Data From the SELECT-AXIS 1 and SELECT-AXIS 2 Trials

Victoria Navarro-Compan[1], Philip J. Mease[2], Lianne S. Gensler[3], Martin Rudwaleit[4], Yael Klionsky[5], Jayne Stigler[6], Erin Mancl[7], Shirley Chen[8], Jamie Urbanik[9] and Xenofon Baraliakos[10], [1]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]Department of Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, [4]Bielefeld University, Medical School and University Medical Centre OWL, Klinikum Bielefeld, Department of Rheumatology, Bielefeld, Germany, [5]Division of Rheumatology, Department of Medicine, Wake Forest School of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medicine, Winston-Salem, NC, [6]AbbVie, Round Lake, IL, [7]AbbVie, Chicago, IL, [8]AbbVie, Somerset, NJ, [9]AbbVie, Grayslake, IL, [10]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

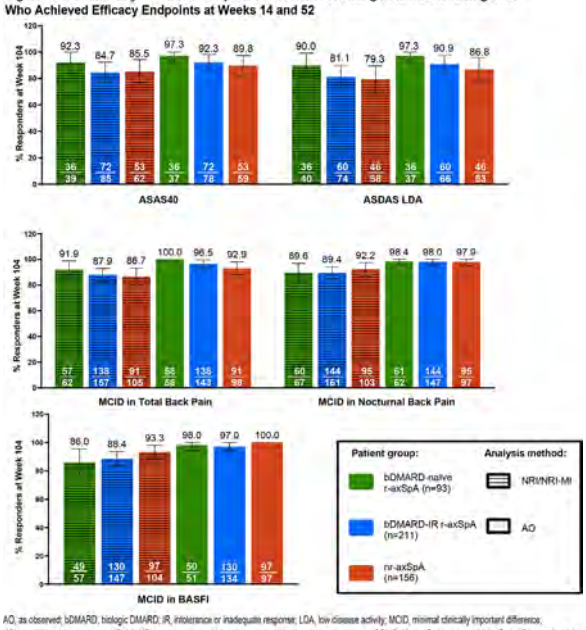
Session Date: Monday, October 27, 2025
Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Treatment with the oral JAK inhibitor upadacitinib (UPA) has shown efficacy and safety in patients with active axial spondyloarthritis (axSpA), including both radiographic (r-axSpA, historically known as ankylosing spondylitis [AS]) and non-radiographic (nr-axSpA). This therapeutic benefit was observed among patients who are naïve to biologic DMARDs (bDMARD-naïve) as well as those with an intolerance or inadequate response to biologic DMARDs (bDMARD-IR). Sustainability of response was previously demonstrated through week 52 among patients who achieved clinical responses at week 14.[1] This post hoc analysis evaluated the long-term sustainability of clinical outcomes through 2 years (104 weeks) in UPA-treated patients with axSpA from the SELECT-AXIS 1 and SELECT-AXIS 2 clinical trials.

Methods: Data from SELECT-AXIS 1 (bDMARD-naïve r-axSpA) and SELECT-AXIS 2 (two studies: bDMARD-IR r-axSpA and nr-axSpA which included a population with 33% bDMARD-IR and 67% bDMARD-naïve) were assessed in this post hoc analysis. Sustained treatment response at week 104 was evaluated in patients receiving UPA 15 mg once daily who achieved responses at both weeks 14 and 52. Endpoints included ASAS40 response, ASDAS low disease activity (LDA; score < 2.1), and achievement of a minimal clinically important difference (MCID) in total and nocturnal back pain (≥ 1.0 decrease) and in BASFI (≥ 0.6 decrease).[2] Data were analyzed using nonresponder imputation (NRI), NRI with multiple imputation (NRI-MI) for COVID-19 missing data, and as observed (AO). Sankey diagrams were used to illustrate ASDAS LDA achievement through week 104 using AO and NRI (with AO-NRI as appropriate) analyses.

Results: A total of 460 patients were included in this analysis (bDMARD-naïve r-axSpA, N = 93; bDMARD-IR r-axSpA, N = 211; nr-axSpA, N = 156). Among patients who achieved ASAS40 at weeks 14 and 52, most sustained this response at

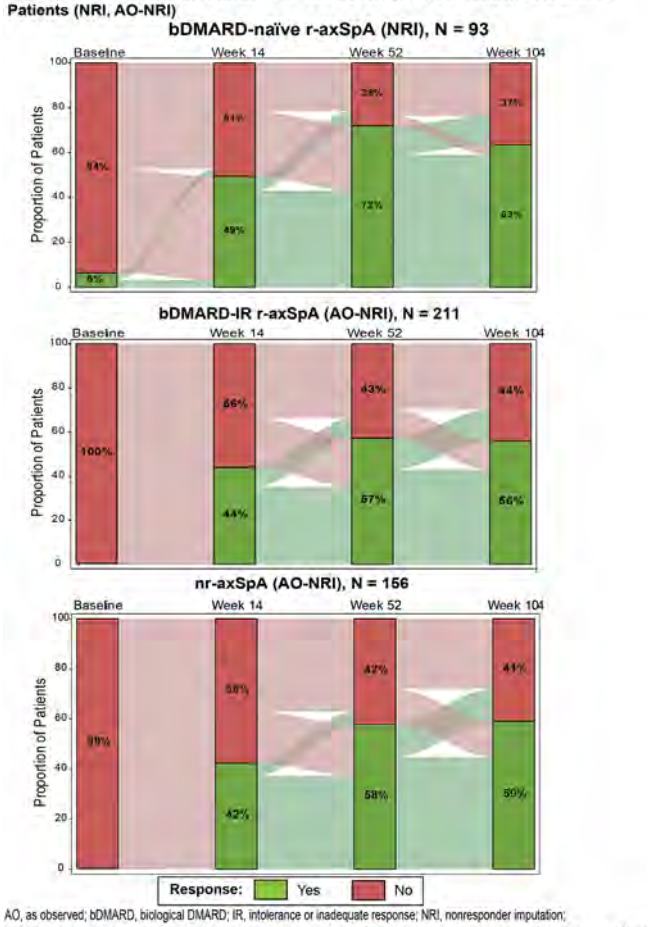
Figure 1. Sustainability of Clinical Response at Week 104 Among Patients Receiving UPA Who Achieved Efficacy Endpoints at Weeks 14 and 52



AO, as observed; bDMARD, biologic DMARD; IR, intolerance or inadequate response; LDA, low disease activity; MCID, minimal clinically important difference; NRI, nonresponder imputation; NRI-MI, NRI incorporating multiple imputations to handle missing data due to COVID-19; r-axSpA, radiographic axSpA; UPA, upadacitinib.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Achievement of ASDAS Low Disease Activity Over Time in UPA-treated Patients (NRI, AO-NRI)



AO, as observed; bDMARD, biological DMARD; IR, intolerance or inadequate response; NRI, nonresponder imputation; NRI-MI, NRI incorporating multiple imputation to handle missing data due to COVID-19; r-axSpA, radiographic axSpA; UPA, upadacitinib. AO-NRI was utilized in bDMARD-IR AS and nr-axSpA to ensure consistent categorization as responses would vary with NRI-MI.

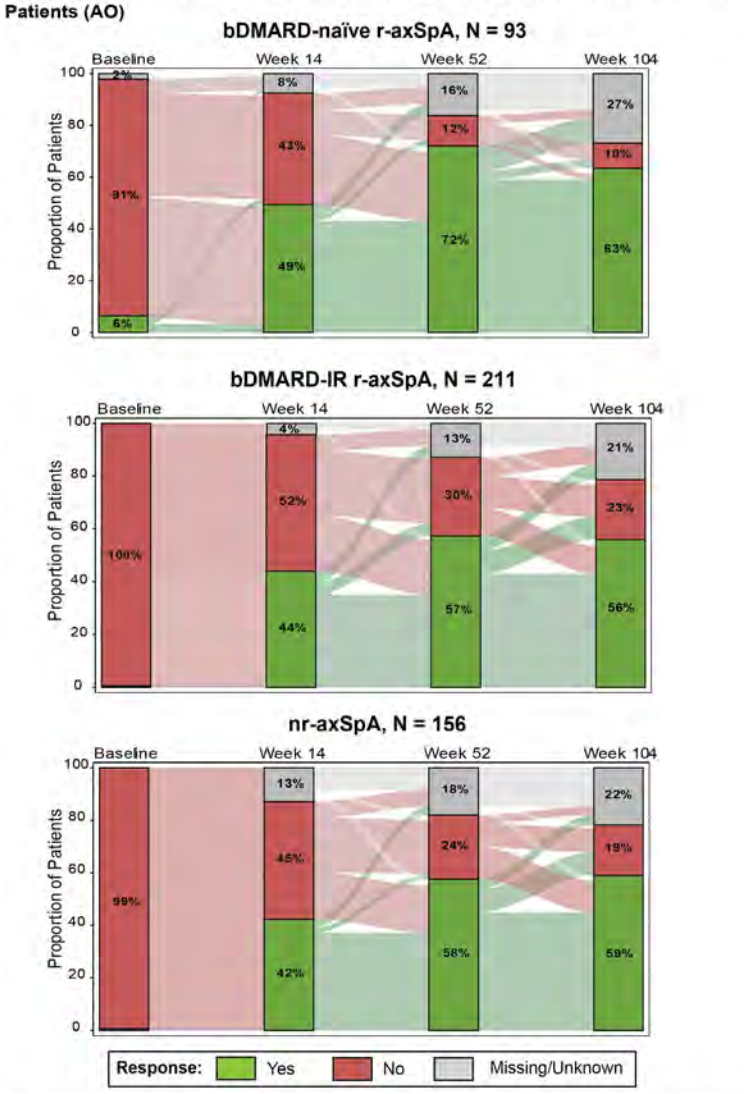
week 104 (bDMARD-naïve r-axSpA: NRI, 92.3%; AO, 97.3%; bDMARD-IR r-axSpA: NRI-MI, 84.7%; AO, 92.3%; nr-axSpA: NRI-MI, 85.5%; AO, 89.8%) (**Fig 1**). Most UPA-treated patients who achieved ASDAS LDA at weeks 14 and 52 sustained that response at week 104 (bDMARD-naïve r-axSpA: NRI, 90.0%; AO, 97.3%; bDMARD-IR r-axSpA: NRI-MI, 81.1%; AO, 90.9%; nr-axSpA: NRI-MI, 79.3%; AO, 86.8%). Similar maintenance of response was observed for achievement of MCID in total back pain (NRI: range, 86.7% to 91.9%; AO: range, 92.9% to 100.0%), nocturnal back pain (NRI-MI: range, 89.4% to 92.2%; AO: range, 97.9% to 98.4%), and BASFI (NRI-MI: range, 86.0% to 93.3%; AO: range, 97.0% to 100.0%). In a longitudinal analysis, the long-term sustainability of ASDAS LDA was further examined over time (**Fig 2 & 3**), demonstrating an increased proportion of patients achieving ASDAS LDA from baseline to weeks 14, 52, and 104.

Conclusion: Patients treated with UPA who showed response at weeks 14 and 52 continued to maintain those responses in disease activity (ASAS40 and ASDAS LDA), total back pain, nocturnal back pain, and physical function at week 104. These findings highlight the consistent and long-term efficacy of UPA across the full spectrum of axSpA.

1. Navarro-Compán V, et al. *Arthritis Rheumatol*. 2023;75 [Abstract].
2. Kviatkovsky MJ, et al. *J Rheumatol*. 2016;43:1680-86.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3: Achievement of ASDAS Low Disease Activity Over Time in UPA-treated Patients (AO)



AO, as observed; bDMARD, biological DMARD; IR, intolerance or inadequate response; r-axSpA, radiographic axSpA; UPA, upadacitinib.

Disclosure: V. Navarro-Compan: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **L. Gensler**: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **M. Rudwaleit**: AbbVie, 2, Boehringer Ingelheim, 2, Janssen, 2, 6, Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **Y. Klionsky**: Amgen, 1, 2, AstraZeneca, 1, 2, Johnson&Johnson, 1, 2, Lilly, 1, 2, Mediq, 1, 2; **J. Stigler**: AbbVie, 3, 11; **E. Mancl**: AbbVie, 3, 11; **S. Chen**: AbbVie, 3, 12, provided statistical analysis support that was funded by AbbVie, Tigermed-BDM Inc, 3; **J. Urbanik**: AbbVie, 3, 11; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1466

Impact of Bimekizumab on Spinal MRI Inflammation and Structural Lesions in Patients with Radiographic Axial Spondyloarthritis: 2-Year CANDEN Scoring Results from a Phase 3 Study and Its Open-Label Extension

Walter P. Maksymowych[1], Robert G. W. Lambert[2], Victoria Navarro-Compan[3], Xenofon Baraliakos[4], Jason Coarse[5], Natasha de Peyrecave[6] and Mikkel Ostergaard[7], [1]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [2]University of Alberta, Department of Radiology & Diagnostic Imaging, Edmonton, AB, Canada, [3]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [4]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [5]UCB, Morrisville, NC, [6]UCB, Brussels, Belgium, [7]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1434–1466) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Spinal inflammation and structural progression are key features of radiographic axial spondyloarthritis (r-axSpA).[1] Canada-Denmark (CANDEN) scoring enables anatomical-based assessments of MRI inflammatory and structural lesions by spinal compartment.[2,3]

Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown sustained efficacy and safety to 2 years in patients (pts) with r-axSpA in the phase 3 study BE MOBILE 2 and its open-label extension (OLE), and to 5 years in a phase 2b study.[4,5]

Here, from BE MOBILE 2 and its OLE, we present the first 2-year evaluation of the effects of a biologic treatment (i.e., BKZ) on spinal MRI inflammatory and structural lesions in pts with r-axSpA using CANDEN scoring.

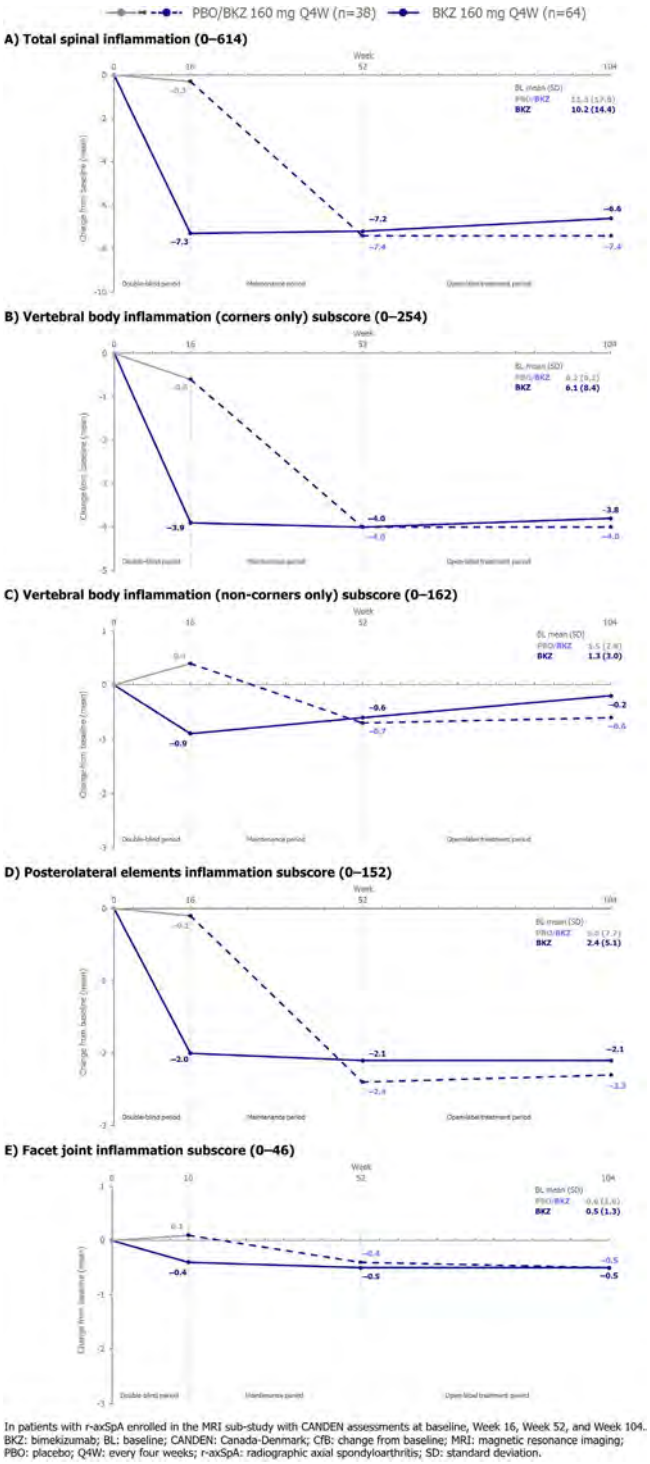
Methods: In BE MOBILE 2 (NCT03928743), pts with r-axSpA were randomized to subcutaneous BKZ 160 mg every 4 weeks (wks) or placebo (PBO); from Wk 16, all received BKZ. At Wk 52, eligible pts could enroll in the OLE (BE MOVING; NCT04436640).[4]

Post hoc CANDEN scoring assessments were conducted in pts enrolled in the MRI sub-study who had evaluable spinal MRIs at all four timepoints: baseline, Wk 16, 52, and 104. All readers were blinded to timepoint. We report mean change from baseline (CfB) at Wk 16, 52, and 104 in total spinal inflammation score and subscores for inflammation in vertebral bodies (corners and non-corners), posterolateral elements, and facet joints, and total spinal structural lesions scores (fat, erosions, new bone formation). All data use observed case.

Results: 140/332 (42.2%) pts in BE MOBILE 2 had MRIs eligible for CANDEN scoring. 102 pts had CANDEN scores at baseline, Wk 16, 52, and 104 (PBO/BKZ: n=38; BKZ: n=64). Baseline characteristics of these pts were largely comparable between treatment arms and with the overall population.

A greater reduction from baseline in total spinal inflammation was seen at Wk 16 with BKZ vs PBO. After switching to BKZ at Wk 16, PBO-randomized pts had an improvement from baseline comparable to BKZ-randomized patients at Wk 52, both of which were largely sustained at Wk 104 (**Figure 1A**). This was also observed for vertebral body (corners only) and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



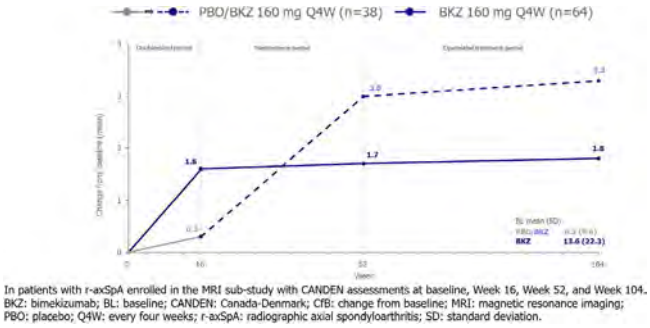
In patients with r-axSpA enrolled in the MRI sub-study with CANDEN assessments at baseline, Week 16, Week 52, and Week 104.
BKZ: bimekizumab; BL: baseline; CANDEN: Canada-Denmark; CfB: change from baseline; MRI: magnetic resonance imaging; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation.

Figure 1. Change from baseline in CANDEN total inflammation score and subscores to Week 104 (observed case)

posterolateral elements inflammation (**Figure 1B, 1D**). Data for vertebral body (non-corners only) and facet joint inflammation are shown in **Figure 1C, 1E**.

At Wk 16, a greater increase from baseline in fat lesions was seen with BKZ vs PBO. BKZ-randomized pts had minimal change in fat lesions from Wk 16 to Wk 104. After switching to BKZ, PBO-randomized pts had an increase in fat lesions at Wk 52 and then minimal change at Wk 104 (**Figure 2**). Minimal changes were observed in new bone formation and erosion to Wk 104.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



In patients with r-axSpA enrolled in the MRI sub-study with CANDEN assessments at baseline, Week 16, Week 52, and Week 104. BKZ: bimekizumab; BL: baseline; CANDEN: Canada-Denmark; CfB: change from baseline; MRI: magnetic resonance imaging; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axial spondyloarthritis; SD: standard deviation.

Figure 2. Change from baseline in CANDEN total fat lesion score to Week 104 (observed case)

Conclusion: In pts with r-axSpA, comprehensive scoring of spinal inflammatory and structural lesions using CANDEN showed BKZ led to a rapid and sustained long-term reduction in individual components of spinal MRI inflammation, an initial increase in fat lesions with minimal subsequent change, and minimal changes in new bone formation and erosion over two years.

References: 1. Navarro-Compán V. Lancet 2025;405:159–72; **2**. Tu L. Front Immunol 2021;12:700260; **3**. Krabbe S. RMD Open 2019;5:e001057; **4**. Baraliakos X. Rheumatology 2025;keaf009; **5**. Deodhar A. RMD Open 2025;11: e005081.

Disclosure: W. Maksymowych: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Lambert**: AbbVie, 2, CARE Arthritis and Image Analysis Group, 2; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **J. Coarse**: UCB, 3, 11; **N. de Peyrecave**: UCB, 3; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6.

Abstract Number: 1467

Risk Factors Associated with Chronic Kidney Disease and End-Stage Kidney Disease in Patients with Newly Diagnosed Lupus Nephritis

Aakash V. Patel[1], Lingxiao Zhang[2], Hyon K. Choi[3] and April Jorge[4], [1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [4]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Characteristics of Patients with Newly Diagnosed, Biopsy-Proven Lupus Nephritis

Characteristics	All Patients (n=387)
Age, mean (SD)	38.9 (16.1)
Female, n (%)	321 (82.9)
Race/Ethnicity, n (%)	
White	166 (42.9)
Black	99 (25.6)
Asian	45 (11.6)
Hispanic	20 (5.2)
Other	57 (14.7)
Charlson Comorbidity Index, mean (SD)	2.3 (1.6)
SLE Severity Index, n (%)	
Mild	103 (26.6)
Moderate	239 (61.8)
Severe	45 (11.6)
Comorbidities, n (%)	
Type 2 Diabetes	22 (5.7)
Hypertension	196 (50.7)
Hyperlipidemia	61 (15.8)
Obesity	37 (9.6)
Heart Failure	39 (10.1)
Tobacco Use	38 (9.8)
Antiphospholipid Antibody Syndrome	20 (5.2)
End-Stage Kidney Disease	22 (5.7)
Perinatal, n (%)	23 (5.9)
Clinical /Laboratory Data	
Estimated GFR, mL/min/1.73 m^2, mean (SD)	68.9 (35.1)
eGFR < 60 mL/min/1.73 m^2, n (%)	111 (28.7)
Urine Protein, mg, mean (SD)	528.4 (1249.4)
Double Stranded DNA, n (%)	266 (68.7)
Hypocomplementemia, n (%)	295 (81.5)
Lupus Nephritis Class, n (%)	
Class III Only	62 (16.0)
Class III + V	34 (8.8)
Class IV Only	112 (28.9)
Class IV + V	54 (14.0)
Class V Only	86 (22.2)
Class V + II	12 (3.1)
Class VI	3 (0.8)
Not Classified	24 (6.2)
Time to Biopsy, Days, median (IQR)	51 (8-298)
Medication Use, n (%)	
Systemic Glucocorticoids	282 (72.9)
Hydroxychloroquine	191 (49.4)
Immunosuppressant	134 (34.6)
SGLT2i	3 (0.8)
GLP-1 RA	9 (0.9)
ACEi or ARB	152 (39.3)

SLE, systemic lupus erythematosus; GFR, glomerular filtration rate; SGLT2i, sodium-glucose cotransporter-2 inhibitor; GLP-1RA, glucagon-like peptide-1 receptor agonist; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker

Background/Purpose: Lupus nephritis (LN) affects over half of patients with systemic lupus erythematosus (SLE) and is associated with an increased risk for adverse kidney outcomes. We sought to identify risk factors for chronic kidney disease (CKD) and end-stage kidney disease (ESKD) in patients with newly diagnosed LN.

Table 2: Risks of Chronic Kidney Disease Stage ≥3 and End-Stage Kidney Disease at 5 Years Among Patients with Newly Diagnosed, Biopsy-Proven Lupus Nephritis

Outcome	≤ 90 Days to Biopsy	> 90 Days to Biopsy	No HCQ Use at Baseline	HCQ Use at Baseline	No ACEi or ARB Use at Baseline	ACEi or ARB Use at Baseline	Chronicity Index ≤3	Chronicity Index >3
Chronic Kidney Disease Stage ≥3								
All Patients								
N Events in 5 Years	65	53	60	58	65	53	-	-
Incidence Rate (per 100 person-yrs)	11.87	16.3	14.86	12.37	10.71	19.95	-	-
Unadjusted Hazard Ratio	1.00 (ref)	1.31 (0.91-1.88)	1.00 (ref)	0.83 (0.58-1.19)	1.00 (ref)	1.76 (1.23-2.53)	-	-
Adjusted Hazard Ratio[a]	1.00 (ref)	1.16 (0.80-1.70)	1.00 (ref)	0.95 (0.63-1.43)	1.00 (ref)	1.35 (0.90-2.03)	-	-
Membranoproliferative LN[b]								
N Events in 5 Years	52	32	41	43	51	33	27	15
Incidence Rate (per 100 person-yrs)	14.02	17.54	16.94	13.82	12.89	20.93	11.96	41.14
Unadjusted Hazard Ratio	1.00 (ref)	1.21 (0.78-1.87)	1.00 (ref)	1.21 (0.78-1.87)	1.00 (ref)	1.54 (0.99-2.39)	1.00 (ref)	2.82 (1.47-5.42)
Adjusted Hazard Ratio[a]	1.00 (ref)	1.19 (0.74-1.90)	1.00 (ref)	0.78 (0.47-1.28)	1.00 (ref)	1.24 (0.75-2.05)	1.00 (ref)	2.94 (1.44-5.99)
Membranoproliferative LN[b] without Prior Immunosuppression								
N Events in 5 Years	35	14	30	19	32	17	13	10
Incidence Rate (per 100 person-yrs)	14.17	16.28	15.22	13.98	12.21	23.97	8.8	42.68
Unadjusted Hazard Ratio	1.00 (ref)	1.18 (0.64-2.20)	1.00 (ref)	0.92 (0.52-1.64)	1.00 (ref)	1.86 (1.03-3.35)	1.00 (ref)	3.75 (1.59-8.86)
Adjusted Hazard Ratio[a]	1.00 (ref)	1.10 (0.58-2.10)	1.00 (ref)	0.96 (0.51-1.81)	1.00 (ref)	1.32 (0.69-2.53)	1.00 (ref)	3.79 (1.47-9.81)
End-Stage Kidney Disease								
All Patients								
N Events in 5 Years	20	18	25	13	20	18	-	-
Incidence Rate (per 100 person-yrs)	2.39	3.14	3.78	1.74	2.33	3.28	-	-
Unadjusted Hazard Ratio	1.00 (ref)	1.28 (0.68-2.42)	1.00 (ref)	0.47 (0.24-0.92)	1.00 (ref)	1.40 (0.74-2.65)	-	-
Adjusted Hazard Ratio[a]	1.00 (ref)	1.21 (0.62-2.34)	1.00 (ref)	0.55 (0.26-1.16)	1.00 (ref)	0.83 (0.41-1.67)	-	-
Membranoproliferative LN[b]								
N Events in 5 Years	15	11	17	9	14	12	2	6
Incidence Rate (per 100 person-yrs)	2.44	3.22	3.93	1.72	2.32	3.39	0.58	7.37
Unadjusted Hazard Ratio	1.00 (ref)	1.28 (0.59-2.78)	1.00 (ref)	0.45 (0.20-1.01)	1.00 (ref)	1.46 (0.67-3.15)	1.00 (ref)	12.39 (2.45-62.77)
Adjusted Hazard Ratio[a]	1.00 (ref)	1.51 (0.66-3.44)	1.00 (ref)	0.49 (0.20-1.21)	1.00 (ref)	0.85 (0.36-2.03)	1.00 (ref)	12.27 (2.16-69.67)
Membranoproliferative LN[b] without Prior Immunosuppression								
N Events in 5 Years	11	7	14	4	11	7	1	4
Incidence Rate (per 100 person-yrs)	2.65	4.51	4.05	1.78	2.87	3.74	0.46	9
Unadjusted Hazard Ratio	1.00 (ref)	1.63 (0.64-4.26)	1.00 (ref)	0.46 (0.15-1.39)	1.00 (ref)	1.28 (0.50-3.31)	1.00 (ref)	20.06 (2.18-184.69)
Adjusted Hazard Ratio[a]	1.00 (ref)	1.87 (0.69-5.07)	1.00 (ref)	0.47 (0.15-1.46)	1.00 (ref)	0.64 (0.22-1.82)	1.00 (ref)	70.43 (2.68-1852.16)

LN, lupus nephritis; HCQ, hydroxychloroquine; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker
[a]Hazard ratio adjusted for age, sex, race, baseline diabetes and hypertension, and prior treatment with an immunosuppressive medication
[b]Membranoproliferative lupus nephritis includes patients with any component of class III or class IV disease on kidney biopsy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We identified an inception cohort of patients with biopsy-proven LN in the Mass General Brigham health system. We included patients with an index kidney biopsy between 2001-2024, excluding those with prior kidney transplant, and with available laboratory signs of LN prior to the index kidney biopsy. These included a spot or timed urine protein estimating ≥500mg/24 hr or microalbumin ≥300mg/24 hr, urinalysis with ≥2+ protein, or RBC casts. We assessed the effect of time between the first abnormal LN laboratory sign and kidney biopsy (>90 days versus ≤90 days), chronicity index score on kidney biopsy (>3 compared to ≤3), as well as the use of hydroxychloroquine (HCQ) and an ACEi or ARB in the 12 months prior to kidney biopsy, on subsequent kidney outcomes. Primary outcomes included new-onset CKD stage ≥3 and ESKD through 5 years following the first kidney biopsy. We used Cox proportional hazards regression, adjusting for age, sex, race and ethnicity, diagnoses of diabetes and hypertension, and prior SLE immunosuppressant use (including oral and biologic immunosuppressants but not glucocorticoids). We also performed subgroup analyses among patients with membranoproliferative LN (class III or IV +/- class II or V) as well as those with membranoproliferative LN who had not received treatment with an immunosuppressant prior to the kidney biopsy.

Results: There were 387 patients with newly diagnosed, biopsy-proven LN with a mean age of 38.9 years (SD 16.1); 83% were female, 43% were White, and 26% were Black **(Table 1)**. Two-thirds of patients had membranoproliferative LN and one-third had previously received treatment with an immunosuppressive agent. Among those with membranoproliferative LN, a chronicity index score >3 on the first kidney biopsy was associated with an increased risk of new-onset CKD stage ≥3 and ESKD (adjusted HR [aHR] 2.94 [95% CI 1.44-5.99] and 12.27 [95% CI 2.16-69.67], respectively **(Table 2)**. The risk increased further among those with membranoproliferative LN without prior immunosuppressant use (aHR 3.79 [95% CI 1.47-9.81] and 70.43 [95% CI 2.68-1852.16], respectively. The rates of CKD and ESKD were numerically higher with a longer time to kidney biopsy from the first LN laboratory sign. Treatment with HCQ at baseline was protective against new-onset ESKD in unadjusted HRs, but did not reach statistical significance in the adjusted models.

Conclusion: In this cohort of patients with newly diagnosed LN on kidney biopsy, a higher chronicity index score was associated with a substantially increased risk of new-onset CKD stage ≥3 and ESKD. A duration of more than 90 days to kidney biopsy from the first LN laboratory sign may also portend an increased risk of these adverse kidney outcomes though did not reach statistical significance. HCQ use may be protective. Our data is limited by a small sample size. These findings highlight risk factors associated with a worse prognosis among newly diagnosed patients with LN.

Disclosure: A. Patel: None; **L. Zhang**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **A. Jorge**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 1468

A Hipaa-compliant LLM for Personalized Therapeutic Decision-making in Lupus Nephritis

Abhimanyu Amarnani[1], Zaynab Marzuk[2] and H Michael Belmont[3], [1]New York University Grossman School of Medicine, New York, NY, [2]NYU Langone / FHC, brooklyn, NY, [3]NYU School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is the most significant driver of morbidity and mortality in patients with systemic lupus erythematosus (SLE). The ACR 2024 lupus nephritis treatment guidelines (PMID: 40127995) emphasize the importance of intensive induction of LN flares with initiation of dual and/or triple therapy. The guidelines also recommend prompt

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

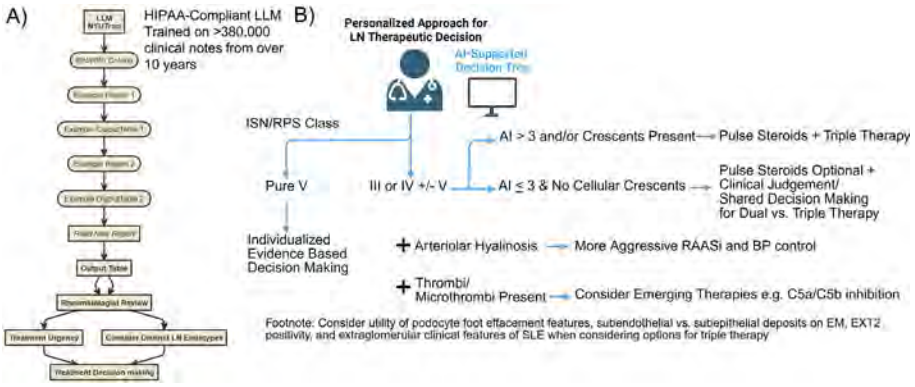


Figure 1. A) The organizational scheme for a HIPAA-compliant LLM is proposed as a clinical support tool for practicing rheumatologists. Our internal HIPAA-compliant LLM initially provides summary information regarding ISN/RPS LN classification criteria. Then, our additional prompt engineering includes two example input unstructured renal biopsy reports, with two paired ideal output organizational tables as well. Finally, a new LN biopsy report is introduced that the LLM reviews and summarizes. B) Proposed personalized approach for LN therapeutic decision utilizing AI-assisted rheumatologist review of renal biopsy reports. A clinical decision-making framework for rheumatologists includes stratifying patients by class (proliferative vs. pure class V vs. mixed classes), AI score, and the presence or absence of crescents, arteriolar hyalinosis, thrombi, and microthrombi. If AI >3 and/or crescents are present, pulse steroids and triple therapy should be strongly considered. However, if AI <3 and crescents are absent, dual therapy versus triple therapy, pulse steroids with or without cyclophosphamide can be optionally used, and these decisions should be guided by shared physician-patient decision-making. Additionally, arteriolar hyalinosis and thrombi/microthrombi may simultaneously prompt RAASi and complement-based therapies (e.g., C5a/C5b inhibitors), respectively.

pulse steroid therapy for both proliferative and pure membranous nephritis. However, these recommendations are conditional, and the necessity for the same treatment intensity for all LN, without regard for other features on biopsy (e.g. crescents, high activity index (AI)), is less certain. Recent data indicate that an AI of $\leq$3 predicts a more favorable prognosis, supporting the concept that a subset of patients can achieve sustained remission without pulse steroids (PMID: 39521057,40180257). Therefore, an evidence-based individualized treatment approach is essential for LN patients, prompting us to create a clinical decision-making support tool to stratify patients for treating providers.

Methods: We used a local HIPAA-compliant large language model (LLM), NYUTron, trained on 10 years of data from 387,144 patients (PMID: 37286606), currently used for clinical predictive modeling in our hospital system. This model organized renal biopsy reports into tabular data of AI, chronicity indices, crescents, sclerosis, thrombi, immunofluorescence, deposits, exostin2 staining, interstitial fibrosis, tubular atrophy, and arterial intimal fibrosis. Prompt engineering involved summarizing ISN/RPS criteria and ideal table examples (Fig 1A). We reviewed renal biopsies from 1/2024 to 3/2025 with ICD-10 SLE diagnoses, comparing results with LLM output to validate accuracy.

Results: 70 renal biopsies were included, with narrative reports generated by 10 renal pathologists (Arkana labs). Of these, four had limited specimens (< 10 glomeruli) or alternate pathology (e.g., focal segmental glomerular sclerosis, acute tubular injury, or lupus podocytopathy), all correctly identified by the LLM (100% accuracy). For ISN/RPS classifications, the LLM correctly assigned A (active), C (chronic), or A/C lesions in 65 of 66 biopsies (98.5% accuracy). The LLM demonstrated 100% accuracy in reporting microthrombi (6/70 biopsies) and cellular/fibrocellular crescents (23/70 biopsies) (Table 1). Arteriolar hyalinosis was accurately identified in 69 of 70 biopsies (98.6% accuracy). This LLM's retrospective renal biopsy summarization, validated by physician review, shows the feasibility of identifying relevant features in SLE renal biopsies to aid in individualized therapy plans (Fig 1B).

Conclusion: This study highlights our LLM's accuracy in analyzing LN renal biopsies, identifying key pathological features linked to poor prognosis. Summarizing these features can facilitate personalized therapy approaches through risk stratification, ultimately improving lupus nephritis treatment outcomes with further validation. We will focus next on fine-tuning our LLM model and integrating biopsy reports with unstructured rheumatologist notes and patient outcomes, aiming to deploy this model in a future prospective, single-arm trial.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical and pathological characteristics of the standardized cohort (N = 70). Summarizes our single-center patient cohort's clinical and pathological characteristics (N=70), including demographic data, lupus nephritis (LN) classification, activity and chronicity indices, and specific histological features. These features were all designated using our local LLM and validated by an independent physician review of each input renal biopsy report. *In one of the biopsies, a patient carrying a prior Class IV LN diagnosis underwent repeat biopsy to evaluate for recurrent lupus nephritis. They were noted to have sclerosing lupus nephritis, which one can argue classifies them as VI. Of note, our LLM noted on pathology report review remote active LN, with predominantly chronic features, and the histology of class IV disease, considered the case IV(C). **For another biopsy, where only mild arterial intimal fibrosis was noted upon physician review, our LLM still classified this case as mild arterial hyalinosis. Our model maintains a low threshold for highlighting any evidence of early arterial fibrotic disease, which may help prompt necessary aggressive blood pressure management in our patients.

CHARACTERISTICS	N	%
MEAN AGE (AGE RANGE), YEAR	37.2 (14-67)	
SEX	N=70	
MALE	8	11.4%
FEMALE	62	88.6%
LN CLASSIFICATION	N = 66	
I	3	4.5%
II	7	10.6%
III	10	15.2%
III+V	8	12.1%
IV*	13	19.7%
IV +V	9	13.6%
V	16	24.2%
TOTAL ACTIVITY INDEX SCORE (0-24)	N= 62	
0	23	37.1%
1	4	6.5%
2	5	8.1%
3	5	8.1%
>3	25	40.3%
TOTAL CHRONICITY INDEX (0-12)	N= 61	
0	14	21.9%
1	8	12.5%
2	14	21.9%
>2	28	43.8%
SEGMENTAL SCLEROSIS	N= 69	
PRESENT	34	49.3%
ABSENT	35	50.7%
INTERSTITIAL FIBROSIS	N=68	
MILD/MINIMUM	35	51.5%
MILD/MODERATE	1	1.5%
MODERATE	9	13.2%
SEVERE	4	5.9%
NONE/ABSENT	19	27.9%
TUBULAR ATROPHY	N= 68	
MILD/MINIMUM	33	48.5%
MILD/MODERATE	1	1.5%
MODERATE	9	13.2%
SEVERE	4	5.9%
NONE/ABSENT	21	30.9%
ARTERIAL INTIMAL FIBROSIS	N= 69	
MILD	15	21.7%
MILD/MODERATE	1	1.4%
MODERATE	14	20.3%
SEVERE	9	13.0%
NONE/ABSENT	30	43.5%
ARTERIOLAR HYALINOSIS	N=70	
PRESENT	22	31.4%
ABSENT**	48	48.0%
CELLULAR/FIBROCELLULAR CRESCENTS	N=70	
0	47	67.1%
1	8	11.4%
2	8	11.4%
4	1	1.4%
5	1	1.4%
6	3	4.3%
9	1	1.4%
11	1	1.4%

Disclosure: A. Amarnani: None; **Z. Marzuk**: None; **H. Belmont**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1469

Remission, Low Level Disease Activity State (LLDAS) and Relapse in Patients With Early-Onset, Adult-Onset and Late-Onset Systemic Lupus Erythematosus

Adriana Vázquez-Hernández[1], Emilio Godinez-Lazarini[2], Erik Cimé-Aké[2] and Hilda Fragoso-Loyo[3], [1]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Immunology and Rheumatology Department, Mexico City, Distrito Federal, Mexico, [2]Instituto Nacional de Ciencias Médicas y Nutrición. Salvador Zubirán. Immunology and Rheumatology Department, Mexico City, Mexico, [3]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: In systemic lupus erythematosus (SLE), differences have been observed between patients of different ages at onset. This study evaluates remission, low disease activity, and relapse in patients with SLE at different ages of onset.

Table 1. Demographic, clinical, auto-antibodies and treatment of studied patients. Data are expressed as number (percentage) or median (interquartile range). Statistical analysis: Chi-square test was used for nominal variables, and the Kruskal-Wallis test was used for numerical variables. APS: antiphospholipid syndrome, SAH: systemic arterial hypertension, AIHA: autoimmune hemolytic anemia, SLEDAI-2K: SLE disease activity index 2000, SDI: SLICC/ACR damage index, LLDAS: low level disease activity state, ACLF: acute on chronic liver failure. *Statistically significant.

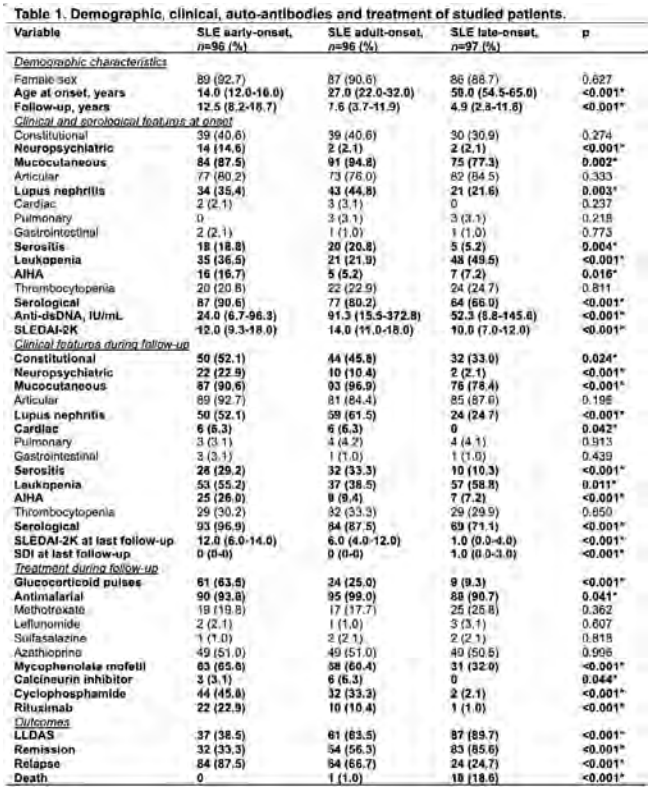


Table 1. Demographic, clinical, auto-antibodies and treatment of studied patients.

Variable	SLE early-onset, *n*=96 (%)	SLE adult-onset, *n*=96 (%)	SLE late-onset, *n*=97 (%)	p
Demographic characteristics				
Female sex	89 (92.7)	87 (90.6)	86 (88.7)	0.627
Age at onset, years	**14.0 (12.0-16.0)**	**27.0 (22.0-32.0)**	**58.0 (54.5-65.0)**	**<0.001***
Follow-up, years	**12.5 (8.2-18.7)**	**7.6 (3.7-11.9)**	**4.9 (2.8-11.8)**	**<0.001***
Clinical and serological features at onset				
Constitutional	39 (40.6)	39 (40.6)	30 (30.9)	0.274
Neuropsychiatric	**14 (14.6)**	**2 (2.1)**	**2 (2.1)**	**<0.001***
Mucocutaneous	**84 (87.5)**	**91 (94.8)**	**75 (77.3)**	**0.002***
Articular	77 (80.2)	73 (76.0)	82 (84.5)	0.333
Lupus nephritis	**34 (35.4)**	**43 (44.8)**	**21 (21.6)**	**0.003***
Cardiac	2 (2.1)	3 (3.1)	0	0.237
Pulmonary	0	3 (3.1)	3 (3.1)	0.218
Gastrointestinal	2 (2.1)	1 (1.0)	1 (1.0)	0.773
Serositis	**18 (18.8)**	**20 (20.8)**	**5 (5.2)**	**0.004***
Leukopenia	**35 (36.5)**	**21 (21.9)**	**48 (49.5)**	**<0.001***
AIHA	**16 (16.7)**	**5 (5.2)**	**7 (7.2)**	**0.016***
Thrombocytopenia	20 (20.8)	22 (22.9)	24 (24.7)	0.811
Serological	**87 (90.6)**	**77 (80.2)**	**64 (66.0)**	**<0.001***
Anti-dsDNA, IU/mL	**24.0 (6.7-96.3)**	**91.3 (15.5-372.8)**	**52.3 (8.8-145.6)**	**<0.001***
SLEDAI-2K	**12.0 (9.3-18.0)**	**14.0 (11.0-18.0)**	**10.0 (7.0-12.0)**	**<0.001***
Clinical features during follow-up				
Constitutional	**50 (52.1)**	**44 (45.8)**	**32 (33.0)**	**0.024***
Neuropsychiatric	**22 (22.9)**	**10 (10.4)**	**2 (2.1)**	**<0.001***
Mucocutaneous	**87 (90.6)**	**93 (96.9)**	**76 (78.4)**	**<0.001***
Articular	89 (92.7)	81 (84.4)	85 (87.6)	0.196
Lupus nephritis	**50 (52.1)**	**59 (61.5)**	**24 (24.7)**	**<0.001***
Cardiac	**6 (6.3)**	**6 (6.3)**	**0**	**0.042***
Pulmonary	3 (3.1)	4 (4.2)	4 (4.1)	0.913
Gastrointestinal	3 (3.1)	1 (1.0)	1 (1.0)	0.439
Serositis	**28 (29.2)**	**32 (33.3)**	**10 (10.3)**	**<0.001***
Leukopenia	**53 (55.2)**	**37 (38.5)**	**57 (58.8)**	**0.011***
AIHA	**25 (26.0)**	**9 (9.4)**	**7 (7.2)**	**<0.001***
Thrombocytopenia	29 (30.2)	32 (33.3)	29 (29.9)	0.850
Serological	**93 (96.9)**	**84 (87.5)**	**69 (71.1)**	**<0.001***
SLEDAI-2K at last follow-up	**12.0 (6.0-14.0)**	**6.0 (4.0-12.0)**	**1.0 (0.0-4.0)**	**<0.001***
SDI at last follow-up	**0 (0-0)**	**0 (0-0)**	**1.0 (0.0-3.0)**	**<0.001***
Treatment during follow-up				
Glucocorticoid pulses	**61 (63.5)**	**24 (25.0)**	**9 (9.3)**	**<0.001***
Antimalarial	**90 (93.8)**	**95 (99.0)**	**88 (90.7)**	**0.041***
Methotrexate	19 (19.8)	17 (17.7)	25 (25.8)	0.362
Leflunomide	2 (2.1)	1 (1.0)	3 (3.1)	0.607
Sulfasalazine	1 (1.0)	2 (2.1)	2 (2.1)	0.818
Azathioprine	49 (51.0)	49 (51.0)	49 (50.5)	0.996
Mycophenolate mofetil	**63 (65.6)**	**58 (60.4)**	**31 (32.0)**	**<0.001***
Calcineurin inhibitor	**3 (3.1)**	**6 (6.3)**	**0**	**0.044***
Cyclophosphamide	**44 (45.8)**	**32 (33.3)**	**2 (2.1)**	**<0.001***
Rituximab	**22 (22.9)**	**10 (10.4)**	**1 (1.0)**	**<0.001***
Outcomes				
LLDAS	**37 (38.5)**	**61 (63.5)**	**87 (89.7)**	**<0.001***
Remission	**32 (33.3)**	**54 (56.3)**	**83 (85.6)**	**<0.001***
Relapse	**84 (87.5)**	**84 (66.7)**	**24 (24.7)**	**<0.001***
Death	**0**	**1 (1.0)**	**18 (18.6)**	**<0.001***

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Factors associated with relapses in SLE patients (n=289). Data are expressed as median (interquartile range). Statistical analysis: the log rank test was used for univariate analysis, and the Cox regression with Bonferroni correction was used for multivariate analysis. NPSLE: neuropsychiatric SLE, LN: lupus nephritis, aCL: anti-cardiolipin, aβ2GPI: anti-β2 glycoprotein I. *Statistically significant.

Table 2. Factors associated with relapses in SLE patients (n=289).

	Relapse-free survival, years (median and 95% CI)		Univariate analysis	Multivariate analysis		
Variable	Present	Absent	p	HR (95% CI)	p	Adj. p
SLE early-onset	**1.7 (0.6-5.2)**	**3.3 (1.9-6.6)**	**<0.001**	**1.9 (1.4-2.8)**	**<0.001**	**0.008***
Constitutional activity at onset	**1.9 (0.6-4.0)**	**3.3 (1.9-8.1)**	**<0.001**	**1.6 (1.2-2.2)**	**0.006**	**0.048***
Serositis at onset	2.5 (0.9-4.9)	3.0 (1.0-7.0)	0.023	1.2 (0.8-1.8)	0.508	-
NPSLE during follow-up	1.8 (0.7-4.1)	3.0 (1.1-7.0)	0.001	1.4 (0.9-2.2)	0.224	-
LN during follow-up	**2.4 (0.9-5.5)**	**3.1 (1.5-7.0)**	**<0.001**	**1.7 (1.2-2.4)**	**0.003**	**0.024***
IgM aCL	2.1 (0.8-5.0)	3.1 (1.7-6.4)	<0.001	1.7 (1.1-2.6)	0.011	0.088
IgG aβ2GPI	2.7 (0.8-6.2)	2.8 (1.1-5.9)	0.047	1.0 (0.6-1.7)	0.904	-
IgM aβ2GPI	1.9 (0.6-4.0)	2.9 (1.4-6.0)	0.003	1.1 (0.6-1.8)	0.798	-

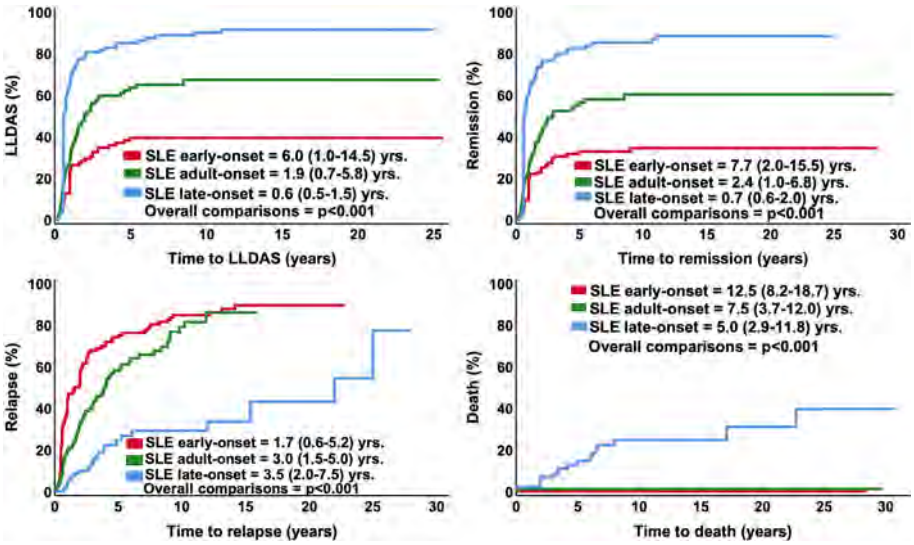


Figure 1. Survival analysis of the outcomes according to SLE groups (n=289). Statistical analysis: the log rank test was used to find differences in time to different outcomes comparing the age of onset of SLE groups. LLDAS: low level disease activity state.

Methods: Design: Retrospective cohort study. We included patients classified with SLE according to the EULAR/ACR 2019 criteria, divided into three groups based on age at onset: early-onset (SLEe < 18 years), adult-onset (SLEa 18–49 years), and late-onset (SLEl ≥50 years). We excluded patients with other autoimmune diseases, except for antiphospholipid syndrome or Sjögren's syndrome. Information was collected through medical record review to obtain demographic data, disease characteristics (disease activity assessed by SLEDAI-2K, accrual damage by SLICC/ACR-DI, autoantibodies, and treatment); and outcomes (remission defined according to DORIS; low disease activity defined according to LLDAS and relapse defined by SELENA-SLEDAI Flare Index). The analysis period began at the date of diagnosis and included all rheumatology follow-up visits until relapse, death, or the last recorded rheumatology visit before December 2024. Demographic and disease characteristics were recorded at onset and during the follow-up period. Outcomes were assessed during follow-up.

Results: We included 289 SLE patients: 96 in the SLEe, 96 in the SLEa and 97 in the SLEl group. A total 90.5% were women. At disease onset, patients in the SLEa group exhibited higher disease activity compared to the other groups. Neuropsychiatric manifestations were more frequent in the SLEe group, whereas mucocutaneous manifestations and lupus nephritis were more prevalent in the SLEa group (Table 1). SLEa group compared to SLEe and SLEl had more prevalence of positive anti-cardiolipin IgG (46.2% vs. 34.2% vs 14%, p< 0.001), IgM (54.9% vs. 50.6% vs. 20.9%, p< 0.001) and positive lupus anticoagulant (27.3% vs. 16.9% vs. 7.1%, p=0.002). In contrast, SLEe group showed a higher prevalence of positive anti-β2 glycoprotein I compared to SLEa and SLEl (IgG: 29.9% vs. 22.7% vs. 1.2%, p< 0.001; IgM: 38.2% vs. 21.3% vs. 9.3%, p< 0.001). Differences in treatment among the groups are summarized in Table 1. Remission and LLDAS were more frequently achieved in the SLEl group compared to the SLEe and SLEa groups. Relapses were more frequent in SLEe group compared to the other groups (Table 1). Moreover, severe relapses were more common in SLEe patients than in

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

those with SLEa or SLEl (63.5% vs. 42.7% vs. 14.4%, p< 0.001). Risk factors associated with relapse in studied patients included SLEe (HR 1.9, 95% CI, 1.4-2.8, p=0.008), constitutional manifestations at onset (HR 1.6, 95% CI, 1.2-2.2, p=0.048) and lupus nephritis during follow-up (HR 1.7, 95% CI, 1.2-2.4, p=0.024) (Table 2). Deaths occurred predominantly in SLEl group, with infections being the leading cause. Survival analysis of the outcomes is presented in Figure 1.

Conclusion: Patients with SLEe experienced more frequent relapses, while those with SLEl more often achieved remission and low disease activity. SLEe, constitutional manifestations at onset and lupus nephritis during follow-up were identified as risk factors for relapse.

Disclosure: A. Vázquez-Hernández: None; **E. Godinez-Lazarini**: None; **E. Cimé-Aké**: None; **H. Fragoso-Loyo**: None.

Abstract Number: 1470

Why Do Some Lupus Patients Skip Their Mycophenolate Mofetil? A Multi-Factorial Assessment of Patient Compliance

Nidaa Bukhari[1], **Ali Rizvi**[1], Jian sun[1], Zerai Manna[2], Paul Schaughency[3], Suraj Rajasimhan[4] and Sarfaraz Hasni[1], [1]National Institutes of Health, BETHESDA, MD, [2]NIH, Bethesda, MD, [3]NIAID, NIH, Bethesda, MD, [4]National Institutes of Health, Columbia, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Nonadherence to medication is a significant confounder in assessing treatment efficacy for systemic lupus erythematosus (SLE), with rates reported up to 75% depending on the measurement method. Mycophenolate mofetil (MMF) presents unique adherence challenges due to twice-daily dosing, large pill size, and gastrointestinal side effects. Measuring serum mycophenolic acid (MPA: active metabolite of MMF) levels have been used to gauge compliance. However, MPA levels are costly, unavailable during patient encounters, and only performed by a few labs. In this study, we aimed to determine the most reliable predictor of adherence to MMF in SLE patients using multiple modalities. Barriers to compliance were also explored.

Methods: Adult patients with SLE on stable MMF dosing for at least six weeks followed at the outpatient clinic under the NIH longitudinal cohort study, were included. Patients with significant renal dysfunction (eGFR < 30 mL/min/1.73m^2) or hypoalbuminemia (albumin < 3.5 g/dL) were excluded. Adherence was assessed using four methods: (1) Serum MPA trough levels were measured after an overnight fast and prior to the morning dose, with MPA < 1 mcg/mL considered nonadherent; (2) Pharmacy refill percentage was calculated as the proportion of MMF doses dispensed over the prescribed interval, with ≥80% considered adherent; (3) Patient self-assessment was quantified using modified Medication Adherence Self-Report Inventory (MASRI), with adherence defined as ≥80% by visual analog scale; and (4) Treating clinicians, blinded to MASRI scores and refill data, rated adherence using a 0–10 Likert scale. Patients were asked to provide reasons for non-compliance. Demographic and clinical data were collected via chart review and standardized survey. Comparisons between adherent and nonadherent groups were performed using t-tests and chi-square analyses, and correlations between adherence measures were assessed using Pearson coefficients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Measures of MMF adherence

	Non-adherent mean (SD)	Adherent mean (SD)	p-value
N	17	44	
Age	39.24 (10.80)	43.23 (10.08)	0.179
BMI kg/m^2	32.61 (10.96)	28.83 (7.27)	0.122
Disease Duration (years)	10.06 (5.83)	12.11 (8.06)	0.343
Number of comorbidities	4.47 (5.37)	5.75 (5.44)	0.412
Number of medications	6.59 (3.34)	8.36 (3.88)	0.102
Dosage in mg	2,215.29 (725.17)	1,890.00 (819.70)	0.157
Refill percentage	0.66 (0.33)	0.89 (0.11)	<0.001
SELENA-SLEDAI Score	3.70 (3.71)	3.45 (4.59)	0.845
Physician rating	7.94 (1.76)	7.93 (1.64)	0.984
MASRI rating	83.24 (26.76)	92.41 (14.18)	0.087

Table 2. Demographic and Miscellaneous variables

		Non-Adherent	Adherent	p-value
n		17	44	
Ethnicity (%)	African American	6 (35.3)	7 (15.9)	0.17
	Asian	2 (11.8)	8 (18.2)	
	Caucasian	0 (0.0)	6 (13.6)	
	Hispanic	9 (52.9)	23 (52.3)	
Sex (%)	Female	16 (94.1)	39 (88.6)	0.87
	Male	1 (5.9)	5 (11.4)	
Depression (%)	N	15 (88.2)	43 (97.7)	0.38
	Y	2 (11.8)	1 (2.3)	
Marital status (%)	Single/unmarried/widowed	12 (70.6)	19 (43.2)	0.1
	Married	5 (29.4)	25 (56.8)	
Antibiotics (%)	N	15 (88.2)	38 (86.4)	1
	Y	2 (11.8)	6 (13.6)	
MMF With Food (%)	N	6 (35.3)	17 (38.6)	0.27
	Y	10 (58.8)	27 (61.4)	
	Y	1 (5.9)	0 (0.0)	
Side Effects (%)	N	14 (82.4)	39 (88.6)	0.82
	Y	3 (17.6)	5 (11.4)	
PPI (%)	N	12 (70.6)	27 (61.4)	0.71
	Y	5 (29.4)	17 (38.6)	
Education Level (%)	High school or lower	9 (52.9)	22 (50.0)	0.67
	Some college	4 (23.5)	6 (13.6)	
	College Graduate	4 (23.5)	12 (27.3)	
	Post-graduate	0 (0.0)	3 (6.8)	
	Not disclosed	0 (0.0)	1 (2.3)	

Results: Of the 61 patients on stable MMF, 44 (72.1%) were classified as adherent based on MPA trough levels > 1mcg/ml. Pharmacy refill percentage was the only variable significantly associated with adherence: adherent patients had a higher mean refill percentage (0.89 ± 0.11) compared to nonadherent patients (0.66 ± 0.33; $p < 0.001$; r=0.47)(Table 1). Self-reported adherence (MASRI) trended higher in the adherent group (92.4 ± 14.2 vs. 83.2 ± 26.8; p=0.087. Physician compliance rating was similar in both groups (adherent mean (SD) 7.93(1.64) vs non-adherent 7.94(1.76) p=0.98). There was a trend toward higher adherence among married patients (56.8% vs. 29.4%, p=0.10). Age, BMI, number of

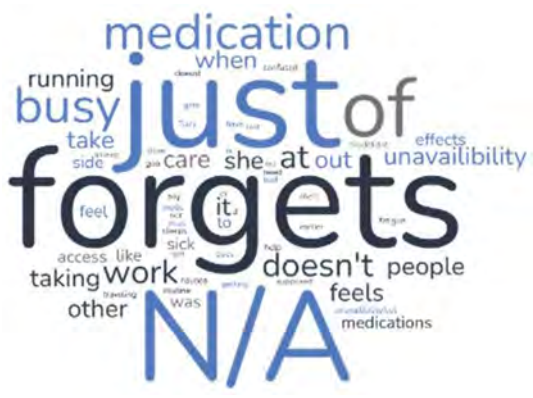


Figure 1. Word Cloud generated from patient responses. Reasons given for nonadherence

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

comorbidities, total number of medications, and MMF dosage were similar between groups. No significant differences were observed in ethnicity, sex, education, side effects, or MMF intake with food (Table 2). Forgetfulness and medication access were the most commonly identified barriers (Figure 1).

Conclusion: Only pharmacy refill percentage reliably predicted MMF adherence. Compliance can be improved by providing social support and using a reliable medication reminder system.

Disclosure: N. Bukhari: None; **A. Rizvi**: None; **J. sun**: None; **Z. Manna**: None; **P. Schaughency**: None; **S. Rajasimhan**: None; **S. Hasni**: None.

Abstract Number: 1471

Prevalence and Clinical Outcomes of Hemophagocytic Lymphohistiocytosis in Systemic Lupus Erythematosus: A Multi-Institutional Cohort Study

Amir Daneshvar[1], Julia Wajsberg[1], Chelsea Guan[1], Keri Ann Pfeil[1], Elleson Harper[1], Lindsay Frumker[2], Meghan Gump[1] and Omer Pamuk[3], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]University hospitals Cleveland medical center, Highland Heights, OH, [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystem involvement. A rare but life-threatening hyper-inflammatory hematological complication of SLE is hemophagocytic lymphohistiocytosis (HLH). This study aims to determine the prevalence of HLH among SLE patients and to compare clinical characteristics and outcomes between SLE patients with and without HLH.

Methods: In this study, we utilized data from the TriNetX global research network, which includes electronic medical records from 101 healthcare organizations. Our search in the TriNetX yielded 130,187 patients with SLE (ICD-10: M32), of which 448 patients had a diagnosis of HLH (ICD-10: D76.1) and 129,739 did not have an HLH diagnosis. Propensity score matching was performed using 59 demographic and clinical variables, yielding two well-balanced cohorts of 443 patients each. Variables studied included baseline patient demographics, clinical manifestations/comorbidities, and autoantibody profile. Outcomes analyzed included mortality, laboratory findings, and medication usage. Kaplan-Meier curve and log-rank test were used for survival analysis. Statistical significance was defined as a p-value of < 0.05.

Results: The prevalence of HLH among the general SLE population was 0.34%. Prior to propensity matching, higher rates of HLH were seen in males (26.1% vs 13.4%), African-American (35.3% vs 24.7%) and Asian populations (16.1% vs 7.5%) (all p-values $<$ 0.001). Clinical manifestations such as glomerular disease, anti-phospholipid syndrome, seizures & epilepsy, and pericarditis (all p-values < 0.001) as well as pleurisy ($p=0.008$) were seen more frequently in HLH patients before propensity matching (Table 1).

After matching, SLE patients with HLH were significantly more likely to have positive Ro/SSA (14.9% vs. 7.2%), RNP (11.3% vs. 4.3%) autoantibodies, low C3 complement (44.7% vs. 29.3%) and low C4 complement (30.5% vs. 20.1%) (all p values $<$ 0.001) (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic Characteristics and Clinical Manifestations/Comorbidities of Patients With Systemic Lupus Erythematosus With and Without Hemophagocytic Lymphohistiocytosis Before and After Propensity Matching.

	Before Matching			After Propensity Matching		
Variable	SLE w HLH (N=448)	SLE wo HLH (N=129,739)	p-value	SLE w HLH (N=443)	SLE wo HLH (N=443)	p-value
Demographics						
Age at index (Mean ± SD)	31.8 ± 16.6	46.6 ± 17.2	**<0.001**	32.0 ± 16.6	30.9 ± 16.6	0.319
Female	331 (73.9%)	112,314 (86.6%)	**<0.001**	330 (74.5%)	308 (69.5%)	0.111
African-American	158 (35.3%)	32,033 (24.7%)	**<0.001**	157 (35.4%)	146 (33.0%)	0.436
White	124 (27.7%)	63,113 (48.6%)	**<0.001**	121 (27.3%)	115 (26.0%)	0.648
Hispanic	49 (10.9%	12,181 (9.4%)	0.262	49 (11.1%)	47 (10.6%)	0.829
Asian	72 (16.1%)	9,700 (7.5%)	**<0.001**	72 (16.3%)	75 (16.9%)	0.786
Clinical manifestations & comorbidities						
Glomerular disease	116 (25.9%)	7,633 (5.9%)	**<0.001**	111 (25.1%)	109 (24.6%)	0.876
ESRD	21 (4.7%)	4,619 (3.6%)	0.199	20 (4.5%)	21 (4.7%)	0.873
APS	30 (6.7%)	4,909 (3.8%)	**<0.001**	29 (6.5%)	24 (5.4%)	0.479
Venous emboli/ thrombosis	35 (7.8%)	5,214 (4.0%)	**<0.001**	34 (7.7%)	32 (7.2%)	0.798
Discoid lupus	36 (8.0%)	10,811 (8.3%)	0.820	35 (7.9%)	25 (5.6%)	0.181
Seizures/Epilepsy	30 (6.7%)	4,215 (3.2%)	**<0.001**	30 (6.8%)	40 (9.0%)	0.213
Inflammatory arthritis	78 (17.4%)	24, 558 (18.9%)	0.413	75 (16.9%)	74 (16.7%)	0.928
Pleurisy	10 (2.2%)	1,277 (1.0%)	**0.008**	10 (2.3%)	10 (2.3%)	1.0
Acute pericarditis	14 (3.1%)	937 (0.7%)	**<0.001**	12 (2.7%)	10 (2.3%)	0.666
Sjogren's syndrome	30 (6.7%	12,015 (9.3%)	0.061	30 (6.8%)	21 (4.7%)	0.194
Hemolytic anemia	88 (19.6%)	3,230 (2.5%)	**<0.001**	85 (19.2%)	76 (17.2%)	0.433
Neutropenia	77 (17.2%)	2,228 (1.7%)	**<0.001**	72 (16.3%)	66 (14.9%)	0.578
Lymphocytopenia	37 (8.3%)	985 (0.8%)	**<0.001**	35 (7.9%)	26 (5.9%)	0.232
ITP	10 (2.2%)	1,846 (1.4%)	0.149	10 (2.3%)	11 (2.5%)	0.825
Thrombocytopenia	127 (28.3%)	6,015 (4.6%)	**<0.001**	123 (27.8%)	121 (27.3%)	0.880
Tobacco use	25 (5.6%)	11,933 (9.2%)	**0.008**	25 (5.6%)	18 (4.1%)	0.274
Type 2 Diabetes	31 (6.9%	13,480 (10.4%)	**0.016**	31 (7.0%)	20 (4.5%)	0.113
Hypertension	118 (26.3)	42,176 (32.5%)	**0.005**	117 (26.4%)	107 (24.2%)	0.440

Table 2: Medication Treatment and Autoantibody Profile of Patients With Systemic Lupus Erythematosus With and Without Hemophagocytic Lymphohistiocytosis Before and After Propensity Matching.

	Before Matching			After Propensity Matching		
Variable	SLE w HLH (N=448)	SLE wo HLH (N=129,739)	p-value	SLE w HLH (N=443)	SLE wo HLH (N=443)	p-value
Medications						
Hydroxychloroquine	277 (61.8%)	55,682 (42.9%)	**<0.001**	273 (61.6%)	282 (63.7%)	0.532
Glucocorticoids	368 (82.1%)	70,179 (54.1%)	**<0.001**	363 (81.9%)	365 (82.4%)	0.861
Azathioprine	36 (8.0%)	6,552 (5.1%)	**0.004**	36 (8.1%)	28 (6.3%)	0.299
Mycophenolate mofetil	111 (24.8%)	10,625 (8.2%)	**<0.001**	109 (24.6%)	112 (25.3%)	0.816
Mycophenolic acid	31 (6.9%)	3,081 (2.4%)	**<0.001**	31 (7.0%)	25 (5.6%)	0.407
Cyclophosphamide	54 (12.1%)	1,948 (1.5%)	**<0.001**	51 (11.5%)	47 (10.6%)	0.668
Methotrexate	28 (6.3%)	8,588 (6.6%)	0.754	28 (6.3%)	23 (5.2%)	0.471
Belimumab	10 (2.2%)	2,040 (1.6%)	0.263	10 (2.3%)	10 (2.3%)	1.0
Rituximab	43 (9.6%)	1,755 (1.4%)	**<0.001**	43 (9.7%)	32 (7.2%)	0.184
Autoimmune labs						
DsDNA	102 (22.8%)	14,568 (11.2%)	**<0.001**	102 (23.0%)	80 (18.1%)	0.067
Ro/SSA	67 (15.0%)	7,097 (5.5%)	**<0.001**	66 (14.9%)	32 (7.2%)	**<0.001**
La/SSB	62 (13.8%)	7,518 (5.8%)	**<0.001**	62 (14.0%)	41 (9.3%)	0.028
RNP	51 (11.4%)	4,660 (3.6%)	**<0.001**	50 (11.3%)	19 (4.3%)	**<0.001**
Sm	10 (2.2%)	146 (0.1%)	**<0.001**	10 (2.3%)	10 (2.3%)	1.0
Ribosomal-P	19 (4.2%)	564 (0.4%)	**<0.001**	19 (4.3%)	11 (2.5%)	0.137
Low complement C3	201 (44.9%)	11,151 (8.6%)	**<0.001**	198 (44.7%)	130 (29.3%)	**<0.001**
Low complement C4	138 (30.8%)	6,801 (5.2%)	**<0.001**	135 (30.5%)	89 (20.1%)	**<0.001**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

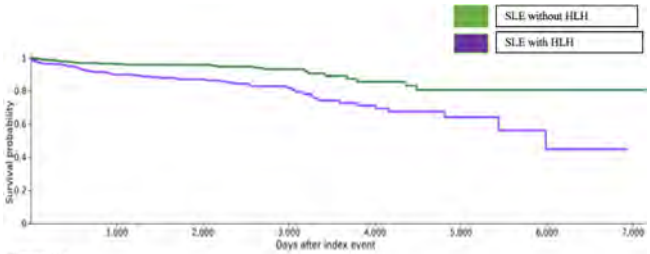


Figure 1A

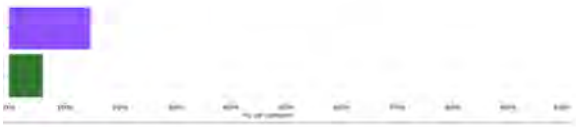


Figure 1B

Figure 1A: Survival Probability in Systemic Lupus Erythematosus Patients With and Without Hemophagocytic Lymphohistiocytosis Using Kaplan-Meier Survival Analysis Figure 1B: Mortality Rate Data in Systemic Lupus Erythematosus Patients With and Without Hemophagocytic Lymphohistiocytosis

Kaplan-Meier survival analysis revealed that HLH is a significantly poor prognostic factor in SLE patients , with diminished survival probability compared to patients without HLH (HR: 2.62, 95% CI: 1.67-4.1, p< 0.001). During the study period, 14.7% of patients with HLH died and 6.1% of patients without HLH died (RR: 2.41, 95% CI: 1.57-3.70) (Figure 1A & 1B).

Conclusion: HLH is an uncommon but clinically significant complication of SLE, associated with hypocomplementemia, distinct autoantibody patterns, and markedly increased mortality. These findings underscore the need for heightened clinical awareness and timely intervention in SLE patients presenting with features suggestive of HLH.

Disclosure: A. Daneshvar: None; **J. Wajsberg**: None; **C. Guan**: None; **K. Pfeil**: None; **E. Harper**: None; **L. Frumker**: None; **M. Gump**: None; **O. Pamuk**: None.

Abstract Number: 1472

Characteristics and Predictors of LLDAS in Survivors of Early Active Lupus: Insights from a Decade-Long Cohort

Amirtha Gopalan[1], keerthi vardhan yerram[2], Mahesh Gaikwad[2] and Liza rajasekhar[3], [1]Nizams Institute of Medical Sciences, Hyderabad, Hyderabad, Telangana, India, [2]Nizams institute of medical sciences, hyderabad, Andhra Pradesh, India, [3]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: LLDAS is a desirable state in lupus, with ongoing global reports on its durability and outcomes. The relationship between LLDAS, baseline characteristics, and drug efficacy is unknown. A university hospital's SLE registry (since 1998) describes the frequency, duration, and outcomes after achieving LLDAS in patients followed for ≥5 years.

Methods: Patients fulfilling the updated 1997 ACR or 2012 SLICC criteria with at least one follow-up clinic visit annually for a minimum of five years, were included. The registry records baseline disease characteristics, SLEDAI score, SLICC/ACR

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 - Baseline characteristics of study population (n=307)

Descriptor	Frequency (%) or Mean ± SD or Median (IQR)
Age at onset of symptoms (years)	22.9 ± 8.2
Juvenile onset lupus; n (%)	86 (27.9)
Median time to diagnosis (in years)	0.5 (0.2-1.2)
Median followup time (years)	7.7 (5.4 - 11.3)
anti-dsDNA positive ever; n (%)	258 (83.7)
Hypocomplementemia ever; n (%)	194 (63)
SLEDAI score at first visit Adult onset Juvenile onset	 13.9 ± 6.5 15.3 ± 6.7
BILAG A/B ever • Constitutional • Mucocutaneous • Musculoskeletal • Renal • Hematological • Cardiorespiratory • Gastrointestinal • Ophthalmic • Neuropsychiatric	 145 (47) 220 (71) 206 (66) 152 (49) 108 (35) 76 (24) 25 (8) 13 (4) 94 (30)
Immunosuppres medication use ever Cyclophosphamide Rituximab Mycophenolate	 184 (60) 19 (6.1) 80 (26)
Patients with HDAS before onset of LLDAS	266 (86)

Damage Index, serologies, and treatment in each clinic visit and is approved by the Institutional Ethics Committee. Records with missing data on clinical SLEDAI in more than 3 contiguous visits or deaths/ lost followup within 5 years and when the disease course could not be inferred by registry notes were excluded. HDAS before LLDAS was defined by either 1 BILAG A, 2 BILAG B, or clinical SLEDAI >6. LLDAS was scored if all five predefined criteria (Franklyn K et al) were fulfilled. LLDAS50 was recorded if at least half of the observation period was spent in LLDAS.

The study used non-parametric descriptive statistics for summarizing non-normally distributed data and generalized estimating equations (GEE) to identify predictors of LLDAS50. Group comparisons were performed using Mann-Whitney U tests and Chi-square tests as appropriate.

Aim - To characterize the attainment and maintenance of LLDAS over time in a cohort of SLE

Objectives

To determine frequency, predictor and time to flare following LLDAS

To identify the frequency and predictors of LLDAS50

Results: This study included a cohort of 307 (282 females) patients (Table 1) with 2679.6 patient-years of observation, averaging 3.15 ± 3.4 observations per patient per year. A large proportion (266 of 307, 86%) exhibited HDAS before achieving their first LLDAS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Characteristics of LLDAS achiever's (n=291) stratified by prior High Disease Activity Status (HDAS)

Descriptor	Prior HDAS (n=266)	No prior HDAS (n=41)	P value
Mean (SD) baseline SLEDAI	15.66 (6.06)	5.51 (1.3)	**<0.0001**
Median number of BILAG A/B domains at baseline	3 (3-4)	2 (1-3)	**<0.01**
Lupus nephritis ever; n (%)	156 (59)	9 (21)	**<0.0001**
Medication use ever Cyclophosphamide Rituximab Mycophenolate	 173 (65) 17 (6.3) 73 (27)	 11 (26) 2 (4.8) 7 (14.5)	 **<0.0001** 0.08 **< 0.0001**
LLDAS ever; n (%)	253 (95.4)	41 (97.6)	0.30
Time to first LLDAS	2 (1-4.1)	1.17 (0.9-4)	0.2
Duration of first LLDAS	3.8 (1.9-6.1)	4.8 (2.4-7.7)	0.06
Median percentage of time spent in LLDAS	73.2 (48.5- 90.3)	86.1 (69.9 - 93.7)	**<0.001**
Flares after LLDAS_1 • 0 • 1 • 2 • >2 • Missing data	 118 (44) 70 (26) 45 (17) 9 (3.3) 17 (6.3)	 26 (63) 8 (19.5) 7 (17) 0 (0) 0 (0)	0.2
Median time to flare	2.84 (1.41-4.80)	3.67 (1.75-5.15)	0.34
% of LLDAS-50 achievers	195 (73.3)	32 (78)	0.65
Severe flares after LLDAS_1	106 (40)	7 (17)	0.008
Ever flare after steroid taper Yes No Missing data	 126 (47) 122 (45) 18 (6.7)	 12 (29) 24 (58.5) 3 (7.3)	**0.02**
Ever flare after IS taper Yes No Missing data	 112 (42) 129 (48) 24 (9)	 9 (22) 26 (63) 4 (9.7)	**0.04**

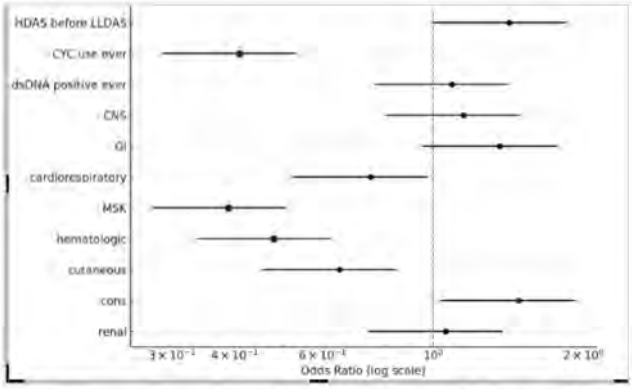


Figure 1 illustrates the predictors of failure to achieve LLDAS-50, derived from a multivariate Generalized Estimating Equation (GEE) model. The forest plot presents odds ratios (ORs) and 95% confidence intervals on a logarithmic scale, with the vertical dashed line representing the null value (OR = 1). Variables with ORs to the left of this line are associated with reduced odds of spending at least 50% of time in LLDAS. Black dots represent predictors included in the model, while red-circled black dots highlight statistically significant negative predictors ($p < 0.05$). Notably, cyclophosphamide use, hematologic involvement, and musculoskeletal involvement were significantly associated with lower likelihood of achieving LLDAS-50. Other clinical domains such as CNS, renal, and cardiorespiratory involvement, though included in the model, did not demonstrate statistically significant associations.

Figure 1: Predictors of LLDAS50

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

During the observation period 291 (94.7%) achieved LLDAS, 142 maintained it till last visit while 228 (78%) attained LLDAS50. Flares occurred in 154 patients (severe in 111). Median (IQR) time to flare was 2.89 (1.48, 4.95) years. Most (45%) flares occurred within 2 years of first attaining LLDAS. Differences in LLDAS characteristics in patients with and without prior HDAS is presented in Table 2.

GEE models showed that patients with hematologic or musculoskeletal involvement (OR and p value 0.48, 0.011; 0.39, 0.04 respectively) or cyclophosphamide use (OR 0.41, p 0.01) did not attain LLDAS50 (Figure 1).

At their last recorded visit, 194/291 (66%) patients were in LLDAS with one-third (102 of 307) off glucocorticoids. SDI was 0 in 43.4%, with some damage present in the others.

Limitations: This study does not include patients who died or were lost to follow-up within five years of first being seen at the hospital. Periods of non-compliance are not reliably captured.

Conclusion: In patients attending lupus clinic for more than five years, LLDAS is achieved by most early active lupus survivors but not often sustained. Patients with hematological and musculoskeletal involvement are less likely to achieve LLDAS50. High initial disease activity is associated with reduced time in LLDAS, earlier, more severe flares and flares after steroid/IS taper.

Disclosure: A. Gopalan: None; **k. yerram**: None; **M. Gaikwad**: None; **L. rajasekhar**: None.

Abstract Number: 1473

Comparison of Three Different Double-Stranded DNA Antibody Assays in the Diagnosis of Systemic Lupus Erythematosus

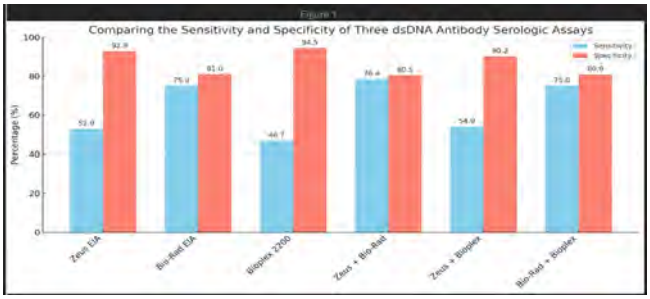
Anika Morgado[1], Sowmika Rao[2], Lili Tao[1] and Narender Annapureddy[3], [1]Vanderbilt University Medical centre, Nashville, [2]Vanderbilt University Medical Center, Nashville, [3]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Double-stranded DNA (dsDNA) antibodies are among the most specific biomarkers for systemic lupus erythematosus (SLE). They are associated with disease activity and are incorporated into widely accepted lupus activity indices. Additionally, dsDNA antibody titers have been linked to lupus nephritis, with improvements in titers serving as important predictors of renal response. However, serologic testing for these antibodies has limitations, as antibody positivity does not always correlate with clinical SLE. Several assays are available for detecting dsDNA antibodies in serum, including the ZEUS dsDNA enzyme-linked immunosorbent semi-quantitative assay, the Bio-Rad Anti-dsDNA semi-quantitative enzyme immunoassay, and the BioPlex 2200 multiplex flow immunoassay. This study aimed to evaluate and compare the diagnostic performance of these three assays to better elucidate their clinical utility in diagnosing SLE.

Methods: A total of 78 cross-sectional serum samples from patients seen at Vanderbilt University Medical Center between November 2024 and April 2025 were analyzed using the three dsDNA antibody assays. Among these, 36 patients had a diagnosis of SLE, of whom 26 had a SLE Disease Activity Index (SLEDAI) score greater than zero (excluding points for

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



dsDNA positivity). The remaining samples were from patients without SLE. Concordance rates between the assays were calculated, and the sensitivity and specificity of each assay, as well as combinations of assays, were assessed. Equivocal or indeterminate results were considered negative for the purposes of this analysis.

Results: The concordance rate between the Bio-Rad and BioPlex 2200 assays was 73.3%, between ZEUS and Bio-Rad was 67.6%, and between ZEUS and BioPlex 2200 was 78.5%. The Bio-Rad assay had the highest sensitivity at 75%, but the lowest specificity at 80.9%. The ZEUS and BioPlex 2200 assays demonstrated high specificity at 92.9% and 94.5%, respectively, though their sensitivity was lower at 52.9% and 46.7%. The sensitivity and specificity of a combination of these assays is depicted in Figure 1.

Conclusion: The performance of the three dsDNA antibody assays varied considerably. Concordance among the assays was suboptimal, and no single assay achieved both high sensitivity and specificity. These findings also indicate that using a combination of assays, for example through sequential testing, unfortunately does not significantly improve sensitivity or specificity of these tests. Ultimately, the results of this study suggest that existing assays, while useful adjuncts in assisting with the diagnosis of SLE, should continue to be interpreted with caution without corresponding clinical correlation given existing limitations in their diagnostic accuracy.

Disclosure: A. Morgado: None; **S. Rao**: None; **L. Tao**: None; **N. Annapureddy**: AstraZeneca, 1, GlaxoSmithKlein(GSK), 2.

Abstract Number: 1474

Rethinking Heart Risk Prediction for Lupus Patients

Aretha On[1], Xiwei Yang[1], Shae Chambers[2], Hammad Ali[3], Touraj Khosravi-Hafshejani[3], Lais Lopes Almeida Gomes[2], Rui Feng[4], Kevin Jon Williams[5] and Victoria Werth[6], [1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, U.S./Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, U.S., Philadelphia, PA, [4]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, Pennsylvania, Philadelphia, PA, [5]Department of Cardiovascular Sciences, Department of Medicine, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, USA, Philadelphia, PA, [6]University of Pennsylvania, Wynnewood, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

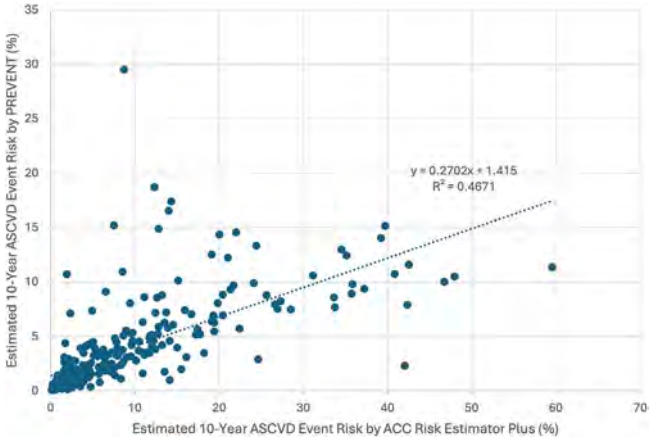


Figure 1. Pearson's Correlation Between Estimated 10-Year ASCVD Event Risk by PREVENT Calculator and Estimated 10-Year ASCVD Event Risk by ACC Risk Estimator Plus for the Lupus Erythematosus Cohort. The two calculators used to estimate the risk of a future atherosclerotic cardiovascular disease (ASCVD) event for individual patients within the primary prevention lupus erythematosus (LE) cohort with sufficient data in electronic medical records were the 10-year ASCVD event risk generated by the PREVENT Calculator (y-axis) versus the ACC ASCVD Risk Estimator Plus (x-axis). Two estimates of ASCVD event risk for each of the 278 eligible patients with LE. Each dot represents an individual patient.

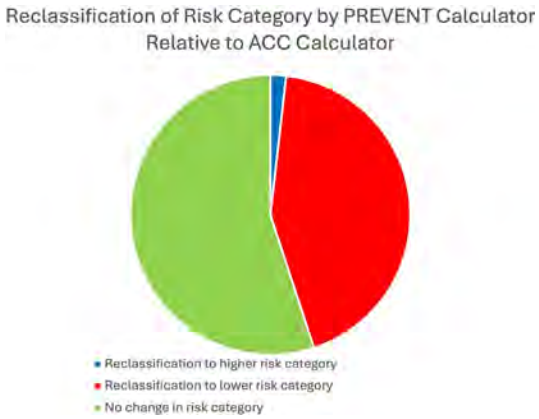


Figure 2. Distribution of Risk Category Change Using the PREVENT Calculator Compared to the ACC ASCVD Risk Estimator Plus (ACC) Calculator

Background/Purpose: Patients with lupus erythematosus (LE) are at an increased risk of clinical events from atherosclerotic cardiovascular disease (ASCVD), yet the accuracy of risk estimation tools in this population remains unclear. Here, we compared the new American Heart Association cardiovascular risk calculator, PREVENT, with the previous ACC ASCVD Risk Estimator Plus (ACC) in our longitudinal cohort of patients with cutaneous LE without (CLE-only) or with (CLE+SLE) concurrent systemic LE.

Methods: Utilizing our prospective longitudinal database of patients with LE, we conducted a retrospective chart review to estimate the risk of an ASCVD event in the next 10 years ("10-year ASCVD event risk") using both calculators, incorporating optional variables when available.

Results: A highly significant correlation was identified between the two calculators ($p< 10^{-15}$), but with considerable scatter (r^2=0.47) (Figure 1). The PREVENT calculator consistently generated far lower estimates of 10-year ASCVD event risk (median 2.33%, IQR 0.79%-5.16%) compared with the ACC calculator (median 4.65%, IQR 1.30%-11.98%; $p< 10^{-15}$ by the Wilcoxon signed-rank test), consistent with previous studies. Subtype analyses revealed significant differences between the two calculators for CLE-only patients and for CLE+SLE patients as well ($p< 10^{-15}$), although no significant difference was observed within PREVENT-generated scores between these two subgroups (p=0.11). Clinical management of ASCVD is

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

typically driven by risk category, and the PREVENT calculator reclassified 43.2% (120 out of 278) of the lupus patients to a lower category than was assigned by the ACC calculator (Figure 2).

Conclusion: Given an actual 10-year ASCVD event *rate* of 13.5% in this cohort (Zhao M et al. 2023), both calculators underestimated risk, with PREVENT underestimating more significantly. These findings highlight the need for caution when using PREVENT for LE patients. Overall, there is a need for better cardiovascular risk assessment and management for patients with lupus erythematosus.

Disclosure: A. On: None; **X. Yang**: None; **S. Chambers**: None; **H. Ali**: None; **T. Khosravi-Hafshejani**: Pfizer, 1; **L. Lopes Almeida Gomes**: None; **R. Feng**: None; **K. Williams**: None; **V. Werth**: AbbVie/Abbott, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta Bio, 2, Calyx, 2, CSL Behring, 5, Cugene, 2, Eli Lilly, 2, EMD Serona, 2, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 5, Immunovant, 2, Janssen, 2, Kwoya Kirin, 2, Merck/MSD, 2, Novartis, 2, Nuvig, 2, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, Rome Pharmaceuticals, 5, Sanofi, 2, Takeda, 2, UCB, 2, 2, Ventus, 2, Viela, 5.

Abstract Number: 1475

Humoral immune responses to real-world recombinant zoster vaccination in systemic lupus erythematosus

Arielle Mendel[1], Maximilien Lora[2], Sasha Bernatsky[3], Paul Fortin[4], Michaël Desjardins[5], Joyce Rauch[6], Chantal Sauvageau[7], Evelyne Vinet[3] and Ines Colmegna[8], [1]McGill University Health Centre, Montreal, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, [3]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [4]Centre ARThrite - CHU de Québec - Université Laval, Quebec, QC, Canada, [5]Centre Hospitalier de l'Université de Montréal (CHUM)), Montreal, QC, Canada, [6]McGill University, Hampstead, Canada, [7]Institut national de santé publique du Québec, Quebec City, QC, Canada, [8]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are at increased risk for herpes zoster (HZ) and its complications. Exposure to immunosuppressants (IS) at the time of the 2-dose recombinant zoster vaccine (RZV) may attenuate responses. We evaluated humoral immune responses to the RZV in a longitudinal SLE cohort, including individuals exposed and unexposed to IS.

Methods: Cohort participants meet ACR SLE criteria and have clinical data and biospecimens collected annually. We selected participants who received ≥1 RZV dose according to the provincial registry (2018-2024) and had available serum samples before vaccination plus at ≥1 time point after the first and/or second RZV dose. We determined serum anti-Varicella Zoster Virus glycoprotein E antibody (anti-gE Ab) concentrations using an enzyme-linked immunosorbent assay (ELISA, ReVacc Scientific, USA). We defined the humoral response threshold as a ≥4-fold increase in anti-gE Ab concentration compared to pre-vaccination titres. We determined the proportion of RZV recipients above the response threshold (RZV response rate), compared RZV responses according to IS exposure, and evaluated the persistence of humoral responses over time.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of SLE cohort participants

Characteristic	Overall (n=46)
Age at first RZV vaccination, mean years (SD)	59.5 (12)
Female sex, n (%)	39 (85)
Race/ethnicity, n (%)	
Asian	6 (13)
Black	2 (4)
Indigenous	1 (2)
White	37 (80)
SLE duration, mean years (SD)	22.0 (12.6)
Previous herpes zoster (self-report), n (%)	16/45 (36)
SLE medications at vaccination, n (%) *	
None	6 (13)
Antimalarial only	19 (41)
Prednisone (≤10 mg/day)	5 (11)
Mycophenolate	10 (22)
Methotrexate	4 (9)
Azathioprine	4 (9)
Belimumab	4 (9)
Abatacept	1 (2)
Tacrolimus	1 (2)
Timing of samples and RZV doses, median months (IQR)	
Time from pre-vaccination sample to first RZV dose	13.0 (6-31)
Time from first RZV dose to first sample collection	9.1 (3-17)
Time from second RZV dose to first sample collection	10.5 (6-21)
Time between RZV doses	2.6 (2-5)

*Unless indicated, participants could be on ≥1 SLE medication

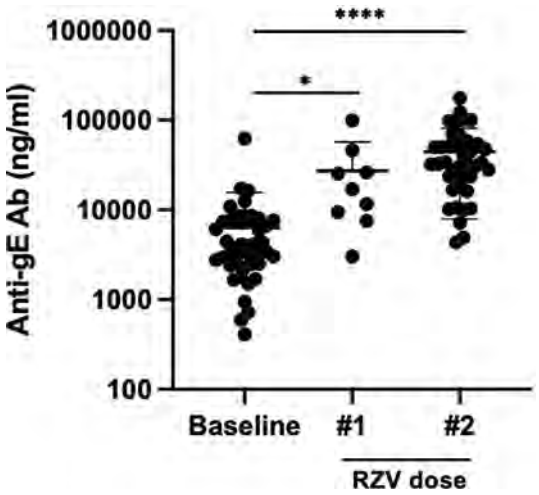


Figure 1. Anti-gE Ab concentrations (ng/mL) pre-vaccination, and after first and second RZV dose

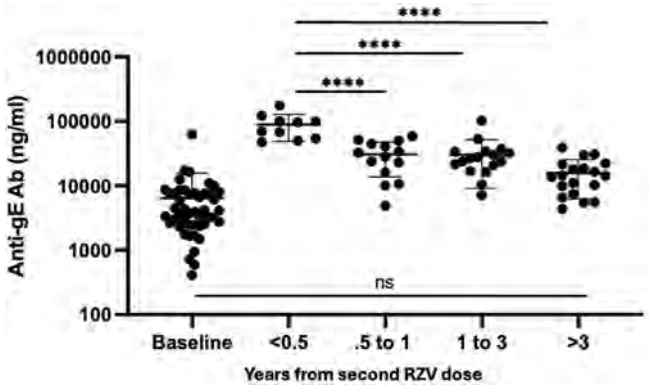


Figure 2. Anti-gE Ab concentrations (ng/mL) at baseline and over time after the 2-dose RZV

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We tested baseline and post-vaccine samples from 46 SLE cohort participants, 9 with samples collected after one RZV dose and 40 with samples collected after two doses (Table 1). All were seropositive for anti-gE Ab at baseline and 45/46 (98%) had an increase in anti-gE Ab concentrations following ≥1 RZV doses. The RZV response threshold was met in 5/9 (56%) at a median of 9 months (IQR 3-17) from the first RZV dose, and in 26/40 (65%) at a median of 11 months (IQR 6-21) from the second dose (mean ± SD anti-gE Ab concentration 27291 ± 29949 ng/ml post-first dose and 46471 ± 36933 ng/ml post-second dose, compared to 6341 ± 9270 ng/ml at baseline, Figure 1). Response rates to two doses were similar in those unexposed (15/22, 68%) and exposed to IS (11/18, 61%) at the time of vaccination, and in those who received 2 RZV doses ≤65 days apart (8/12, 67%) versus >65 days apart (18/28, 64%). Anti-gE Ab concentrations decreased according to time since vaccination (Figure 2), and in samples drawn ≥3 years post-vaccination, mean (±SD) anti-gE Ab concentration was not significantly different from baseline (15775 ± 9562 ng/ml versus 6417 ± 9184 ng/ml).

Conclusion: We detected a humoral response in most (68%) patients with SLE who received 2 doses of RZV, regardless of background treatment. However, increases in anti-gE Ab appear to return to baseline concentrations ≥3 years post vaccination.

Disclosure: A. Mendel: None; **M. Lora**: None; **S. Bernatsky**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1; **M. Desjardins**: None; **J. Rauch**: None; **C. Sauvageau**: None; **E. Vinet**: None; **I. Colmegna**: None.

Abstract Number: 1476

Autoimmune Hemolytic Anemia in Systemic Lupus Erythematosus: A Meta-analysis of Prevalence and Clinical Correlates

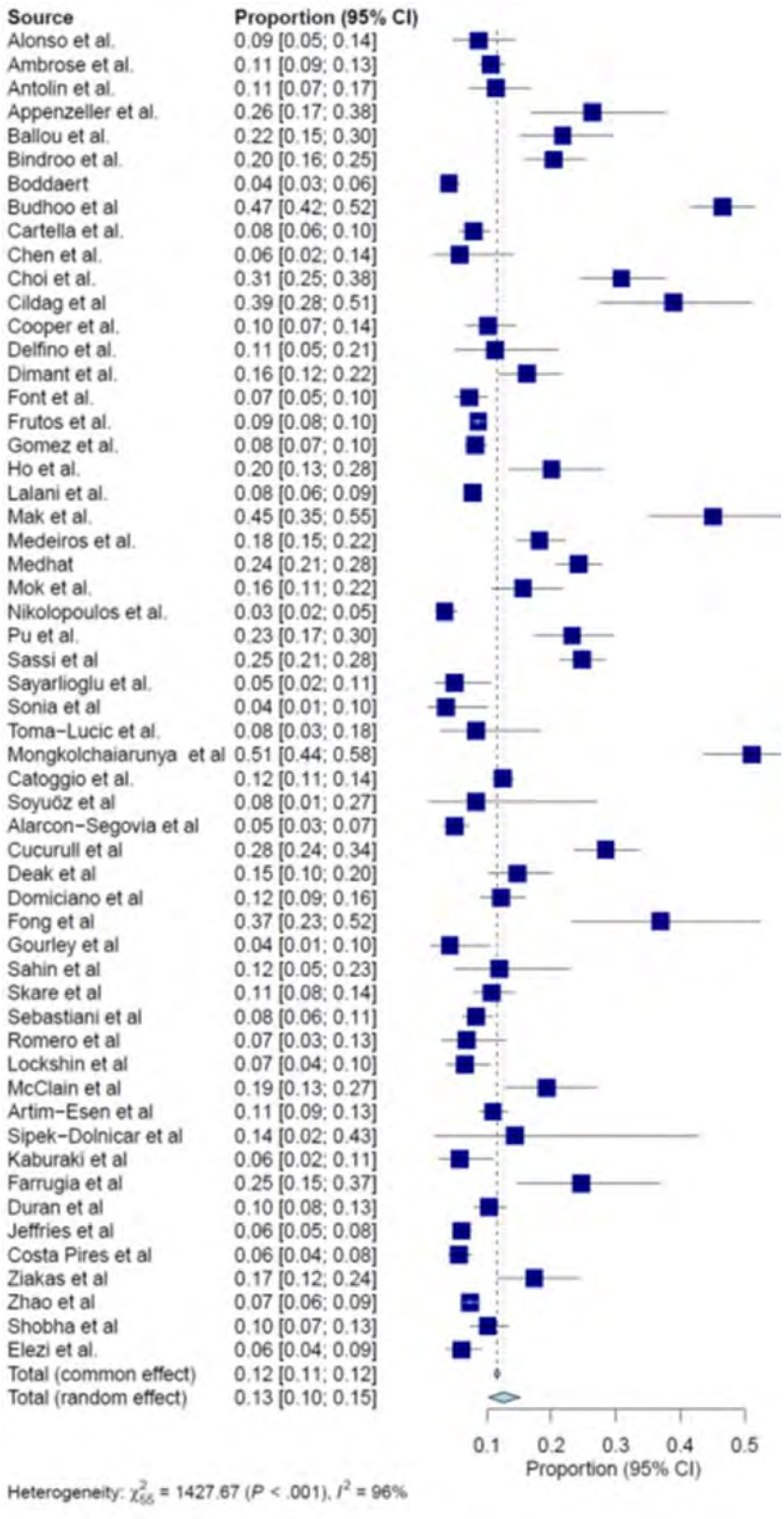
Bana Shawareb[1], Muhannad Haddadin[1], Ansaam Daoud[2] and Omer Pamuk[3], [1]Cleveland Clinic Akron General, Akron, OH, [2]Case Western Reserve University/University Hospitals, Cleveland, OH, [3]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by widespread immune dysregulation and multi-organ involvement. Autoimmune hemolytic anemia (AIHA), marked by antibody-mediated red blood cell destruction, is a common hematological complication of SLE. The overlap of SLE and AIHA represents a distinct clinical phenotype with diagnostic challenges. This study examined the frequency of AIHA in SLE and its association with other clinical manifestations of SLE.

Methods: The systematic review and meta-analysis adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and checklists. A comprehensive literature search was conducted using PubMed (1959–2025) with the keywords "systemic lupus erythematosus," "lupus," "hemolytic anemia," "autoimmune hemolytic anemia," "AIHA," and "hematologic manifestations. Studies reporting the frequency of AIHA in SLE patients were screened, and eligible articles were included to estimate AIHA prevalence and assess associations with other clinical features of SLE. A random effects model was used to pool AIHA frequency across SLE studies, with forest plots generated for composite estimates and corresponding 95% confidence intervals (CI). Study heterogeneity was assessed using the I^2 statistic. Correlation analyses were performed to evaluate associations between AIHA and specific SLE features.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot diagram representing the studies included in the meta-analysis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1, showing the correlation between AIHA and other SLE manifestations

Correlations

		n_AIHA	Leukopenia	Lymphopenia	Thrombocytopenia	LN	Serositis	NPSLE	APLA	Thrombosis	
n_AIHA	Pearson Correlation	1	.960**	.799**	.788**	.794**	.627**	.760**	.633**	.394	.885**
	Sig. (2-tailed)		<.001	<.001	<.001	<.001	<.001	<.001	<.001	.205	<.001
	N	56	9	34	23	51	37	41	35	12	19
n_Coombs	Pearson Correlation	.960**	1	.937**	.963	.961**	.887	.988**	.975*	.789	.917
	Sig. (2-tailed)	<.001		.002	.175	<.001	.113	.002	.025	.421	.261
	N	9	9	7	3	9	4	5	4	3	3
Leukopenia	Pearson Correlation	.799**	.937**	1	.960**	.995**	.974**	.982**	.615**	.994**	.842**
	Sig. (2-tailed)	<.001	.002		<.001	<.001	<.001	<.001	.001	<.001	.002
	N	34	7	34	20	32	27	31	25	7	10
Lymphopenia	Pearson Correlation	.788**	.963	.960**	1	.969**	.908**	.983**	.807**	.533	.267
	Sig. (2-tailed)	<.001	.175	<.001		<.001	<.001	<.001	<.001	.467	.809
	N	23	3	20	23	22	19	21	18	4	6
Thrombocytopenia	Pearson Correlation	.794**	.961**	.995**	.969**	1	.939**	.980**	.638**	.812**	.901**
	Sig. (2-tailed)	<.001	<.001	<.001	<.001		<.001	<.001	<.001	.002	<.001
	N	51	9	32	22	51	35	39	34	11	18
LN	Pearson Correlation	.627**	.887	.974**	.908**	.939**	1	.959**	.801**	.859**	.866**
	Sig. (2-tailed)	<.001	.113	<.001	<.001	<.001		<.001	<.001	.001	<.001
	N	37	4	27	19	35	37	34	31	10	11
Serositis	Pearson Correlation	.760**	.988**	.982**	.983**	.980**	.959**	1	.775**	.842**	.937**
	Sig. (2-tailed)	<.001	.002	<.001	<.001	<.001	<.001		<.001	.001	<.001
	N	41	5	31	21	39	34	41	32	11	11
NPSLE	Pearson Correlation	.633**	.975*	.615**	.807**	.638**	.801**	.775**	1	.772**	.757*
	Sig. (2-tailed)	<.001	.025	.001	<.001	<.001	<.001	<.001		.009	.018
	N	35	4	25	18	34	31	32	35	10	9
APLA	Pearson Correlation	.394	.789	.994**	.533	.812**	.859**	.842**	.772**	1	.746
	Sig. (2-tailed)	.205	.421	<.001	.467	.002	.001	.001	.009		.148
	N	12	3	7	4	11	10	11	10	12	5
Thrombosis	Pearson Correlation	.885**	.917	.842**	.267	.901**	.886**	.937**	.757*	.746	1
	Sig. (2-tailed)	<.001	.261	.002	.609	<.001	<.001	<.001	.018	.148	
	N	19	3	10	6	18	11	11	9	5	19

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Results: Fifty-six studies reported the frequency of AIHA in 25,549 SLE patients. The overall AIHA prevalence was 12.5% (95% CI: 10.3-15.1) using a random-effects model, selected due to substantial inter-study heterogeneity (I^2 = 96%). While most patients were female, gender-stratified AIHA analyses were limited by inconsistent reporting. Across the included studies, Pearson Correlation Analysis showed that AIHA frequency was significantly correlated with a positive Coombs test (r=0.96, p< 0.001), leukopenia (r=0.79, p< 0.001), lymphopenia (r=0.78, p< 0.001), thrombocytopenia (r=0.79, p< 0.001), lupus nephritis (LN) (r=0.62, p< 0.001), serositis (r=0.76, p< 0.001), neuropsychiatric SLE (NPSLE) (r=0.63, p< 0.001) and thrombosis (r=0.88, p< 0.001).

Conclusion: This study demonstrates that AIHA is present in approximately 1 in 8 patients with SLE (12.5%) and that it frequently co-occurs with Coombs positivity, cytopenias, thrombosis, serositis, LN, and NPSLE—all key markers of major organ involvement. These findings support AIHA as a hallmark hematologic manifestation of SLE, with potential utility as a marker of disease burden and prognostic significance. Further prospective studies are warranted to define the prognostic implications of AIHA and its possible role in SLE disease stratification, monitoring, and therapeutic decision-making in SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2, showing the studies included in the meta-analysis

Study	Year	Country	Design	Sample size
Alonso et al.	2012	Spain	Cohort	150
Ambrose et al.	2016	United Kingdom	Cohort	924
Antolin et al.	1995	Spain	Cohort	194
Appenzeller et al.	2022	Brazil	Cohort	76
Ballou et al.	1982	USA	Cohort	138
Bindroo et al.	2023	India	Cross-sectional	305
Boddaert	2004	France	Retrospective	756
Budhoo et al	2017	South Africa	Retrospective	408
Cartella et al.	2013	Italy	Retrospective	535
Chen et al.	2009	Taiwan	Cohort	69
Choi et al.	2015	Korea	Cohort	201
Cildag et al	2019	Turkey	Retrospective	72
Cooper et al.	2002	USA	Cohort	265
Delfino et al.	2020	Brazil	Cohort	71
Dimant et al.	1979	USA	Cohort	234
Font et al.	1998	Spain	Prospective	430
Frutos et al.	2021	Spain	Cohort	3619
Gomez et al.	2006	Spain	Cohort	363
Ho et al.	1998	China	Cohort	125
Latani et al.	2010	Canada	Cohort	1528
Mak et al.	1998	China	Retrospective	102
Medeiros et al.	2016	Brazil	Cohort	414
Medhat	2020	Egypt	Retrospective	575
Mok et al.	2000	Japan	Cohort	186
Nikolopoulos et al.	2020	Greece	Cohort	555
Pu et al.	2000	Taiwan	Cohort	194
Sassi et al	2017	Brazil	Retrospective	598
Sayarlioglu et al.	2005	Turkey	Cohort	120
Sonia et al	2017	Tunisia	Retrospective	83
Tomic-Lucic et al.	2013	USA	Cohort	60
Mongkolchaiarunya et al	2023	Thailand	Cohort	123
Catoggio et al.	2014	Latin America	Cohort	1480
Soyuöz et al	2017	Turkey	Retrospective	24
Alarcon-Segovia et al	1989	Mexico	Prospective	500
Cucurull et al	1999	Spain & Columbia	Retrospective	320
Deak et al	2014	Hungary	Retrospective	224
Domiciano et al	2010	Brazil	Cohort	362
Fong et al	1992	UK	Prospective	46
Gourley et al	1996	Ireland	Cohort	95
Sahin et al	2007	Turkey	Cohort	59
Skare et al	2017	Brazil	Retrospective	373
Sebastiani et al	1999	Europe	Retrospective	575
Romero et al	1998	Spain	Cohort	118
Lockshin et al	2000	USA	Prospective	243
McClain et al	2004	USA	Retrospective	130
Artim-Esen et al	2014	Turkey	Retrospective	852
Sipek-Dolnicar et al	2002	Slovenia	Retrospective	14
Kaburaki et al	1995	Japan	Retrospective	140
Farrugia et al	1992	USA	Retrospective	65
Duran et al	2008	USA	Cohort	628
Jeffries et al	2008	USA	Retrospective	1251
Costa Pires et al	2021	UK	Retrospective	707
Ziakas et al	2005	Greece	Retrospective	150
Zhao et al	NA	China	Retrospective	96
Shobha et al	2023	India	Prospective	415
Elezi et al	2016	Turkey	Retrospective	333

Disclosure: B. Shawareb: None; **M. Haddadin**: None; **A. Daoud**: None; **O. Pamuk**: None.

Abstract Number: 1477

Can Large Language Models Support Clinical Decision-Making in Atypical SLE? A Comparative Analysis

Beste Acar[1], Berkay Aktas[1], Oguzhan Omer Kizilkaya[1], Zekayi Kutlubay[2] and serdal Ugurlu[3], [1]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Dermatology, Istanbul, Turkey, Istanbul, Istanbul, Turkey, [3]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: This study evaluates the contributions of large language models (LLMs) in clinical decision-making for atypical presentations of systemic lupus erythematosus (SLE). It focuses on the models' ability to assist with diagnosis, further investigations and treatment planning. Diagnostic and treatment recommendations from LLMs were compared with those of treating physicians and the relative strengths of each LLM were assessed. To our knowledge, this is the first study to assess LLMs in both diagnosis and management of atypical SLE. The LLMs used in the study are Claude 3 Opus, GPT-4o Mini and Gemini 2.0 Flash.

Methods: A PubMed search identified case reports published after April 2024, ensuring cases were not part of the LLMs' prior training data. Of 95 studies reviewed, 24 cases from 23 studies were included, involving atypical SLE presentations that did not meet established classification criteria. Exclusion criteria were prior SLE diagnosis, insufficient diagnostic information or unavailable full texts.

Clinical data including symptoms, laboratory, imaging findings and medical history were extracted, standardized and entered into LLMs for diagnosis, further investigations and treatment planning. Models operated without web access, relying entirely on internal knowledge. Antinuclear antibody (ANA) testing was prioritized for its high sensitivity and the timing and frequency of ANA requests were evaluated as indicators of SLE suspicion. The models' ability to identify SLE and its ranking in differential diagnoses were assessed. Initial and long-term treatment recommendations were compared with those of treating physicians.

Results: All LLMs successfully suggested SLE as a differential diagnosis in every case. While Gemini mostly ranked SLE first, Claude requested ANA more frequently but neither difference was significant. However, GPT prioritized ANA significantly earlier (p=0.011). Table 1 shows model comparisons.

Initial treatment was similar across models, suggesting corticosteroids as first-line therapy. Long-term treatment plans varied; Claude aligned most with treating physicians' long-term plans, while GPT often proposed guideline-consistent alternatives, such as mycophenolate mofetil (MMF) or hydroxychloroquine (HCQ).

In one case, all LLMs recommended HCQ despite the contraindication due to optic nerve atrophy, highlighting limitations in safety considerations. GPT and Gemini more frequently recalled rare differentials such as Aicardi-Goutières and Evans syndromes, whereas Claude more often assigned direct SLE diagnoses with fewer alternatives.

Table 1. Performance Comparison of LLMs in Diagnostic and Treatment Decisions for Atypical SLE Cases

	Claude	Gemini	GPT	p-value
SLE Diagnosis Mentioned	24 (100.0)	24 (100.0)	24 (100.0)	NA
Rank of the SLE Diagnosis	1.29 (0.55)	1.08 (0.28)	1.21 (0.41)	0.247
Request for ANA	23 (95.8)	21 (87.5)	22 (91.7)	0.580
Rank of ANA Request	4.88 (3.64)	3.21 (2.11)	2.55 (1.65)	**0.011**
Initial Treatment Aligning with Treating Physician	23 (95.8)	22 (91.7)	21 (87.5)	0.580
Long-Term Treatment Aligning with Treating Physician	13 (56.5)	13 (56.5)	10 (45.5)	0.684

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The lack of a non-SLE control group limited the assessment of false-positives and diagnostic specificity, raising concerns about potential overdiagnosis, particularly with GPT's early ANA prioritization.

Conclusion: LLMs effectively prioritized ANA testing, supporting early SLE consideration in complex cases. They showed strong diagnostic performance and appropriate initial treatment suggestions. However, variability in long-term management and limited safety considerations remain. The lack of a non-SLE control group limits specificity analysis and highlights the need for further research to improve clinical use.

Disclosure: B. Acar: None; **B. Aktas**: None; **O. Kizilkaya**: None; **Z. Kutlubay**: None; **s. Ugurlu**: None.

Abstract Number: 1478

Construction and Validation of a Prediction Model of Cognitive Dysfunction in Patients with Systemic Lupus Erythematosus

Bin Zhou[1], QIn Huang[2], Pan Wang[3] and Qiguo Cui[4], [1]Nanfang Hospital, Guangzhou, Guangdong, China (People's Republic), [2]Nanfang Hospital, Guangzhou, China (People's Republic), [3]southern medical university Nanfang Hospital, Guangzhou, China (People's Republic), [4]Southern Medical Univercity Nanfang Hospital, guang zhou, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

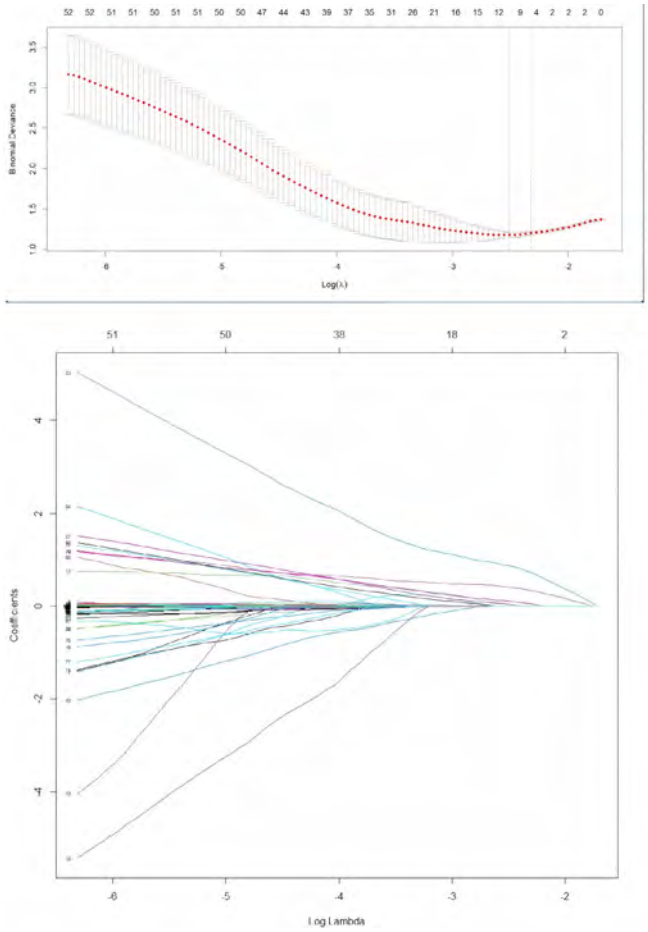
Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organs. Cognitive dysfunction (CD) is a common but often underestimated complication in SLE patients, seriously affecting their quality of life. The purpose of this study was to analyze the clinical data of SLE patients, screen effective predictors, and construct and validate a prediction model for the early identification of cognitive impairment in SLE patients.

Methods: The training cohort included 100 SLE patients. Baseline characteristics, clinical data, and laboratory and imaging data during hospitalization were screened using least absolute shrinkage and selection operator (LASSO) and logistic regression to construct a predictive risk score. The derived score represents an estimate of the risk of developing cognitive dysfunction in patients with SLE. A nomogram was constructed, and its accuracy and predictive performance were evaluated using the area under the receiver operating characteristic curve (AUC), calibration curves, and clinical decision curves. For the validation cohort, data were prospectively collected from 47 SLE patients.

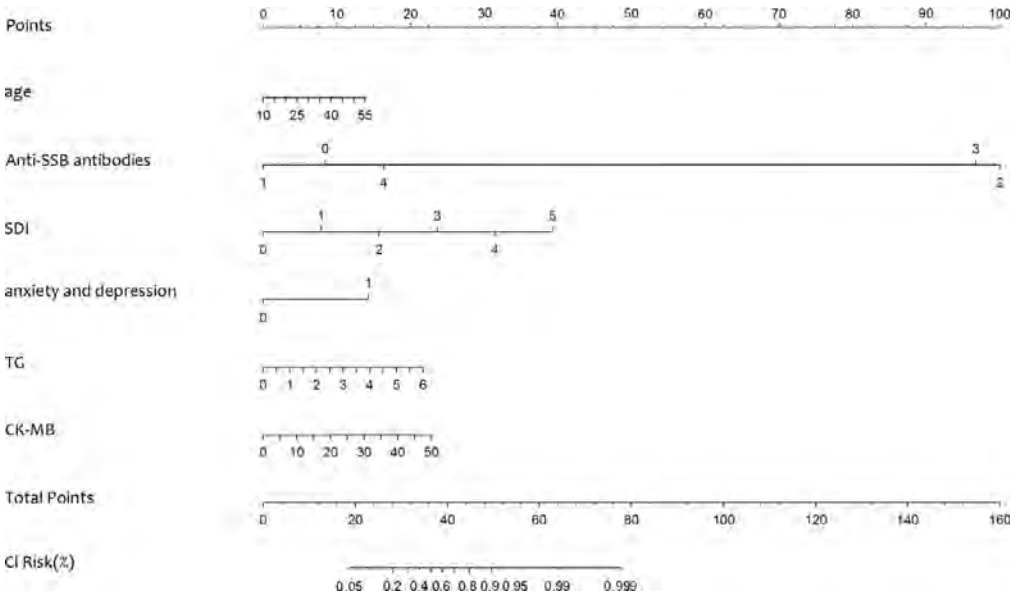
Results: Six important predictors were screened out by LASSO regression: age, SDI, anxiety and depression, creatine kinase isoenzymes(CK-MB), triglycerides (TG), and anti-SSB antibodies, and a prediction model nomogram for SLE-CD was constructed. In the training cohort, the AUC of the model was 0.887 (critical value: 0.571, sensitivity: 0.821, specificity: 0.841, Youden index: 0.662). In the validation cohort, the AUC of the model was 0.877 (critical value: 0.526, sensitivity: 0.810, specificity: 0.846, Youden index: 0.656). The calibration curve showed that the predicted probability was highly consistent with the actual observed value, and the clinical decision curve suggested that the model had clinical application value within a wide range of thresholds.

Conclusion: The constructed SLE-CD prediction model showed good predictive efficacy in the training and validation cohorts and has potential clinical application value.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

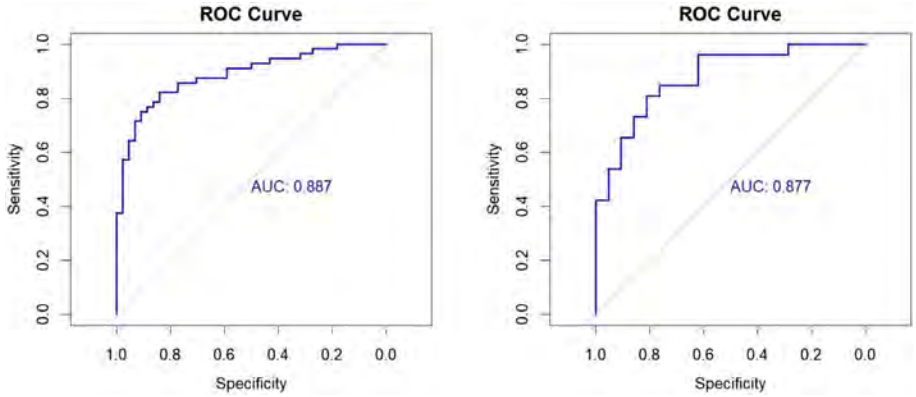


Binomial deviance vs. log(λ) and Coefficient paths for different variables



Nomogram for predicting cognitive impairment in SLE patients incorporating age, Anti-SSB,SDI,anxiety depression,TG and CK-MB.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



ROC curve for cognitive impairment prediction in the training cohort (AUC: 0.887, cut-off value:0.571, sensitivity:0.821, specificity: 0.841, Youden index: 0.662) and validation cohort (AUC: 0.877, cut-off value: 0.526, sensitivity: 0.810, specificity: 0.846, Youden index: 0.656).

Disclosure: B. Zhou: None; **Q. Huang**: None; **P. Wang**: None; **Q. Cui**: None.

Abstract Number: 1479

Validation of Attention, Memory, and Frontal-Executive Abilities Screening Test (AMFAST) in Systemic Lupus Erythematosus (SLE), a prospective single-center study in The Bronx

Chen Chao[1], Garrett Thomas[2], Catherine O'Brien[2], Davina Chen[3], Sundus Mian[4], Tamar Rubinstein[5], Noa Schwartz[4] and Bryan Freilich[2], [1]Rheumatology Division, Department of Medicine, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, NY, [2]Department of Psychiatry, Montefiore Medical Center, Bronx, NY, [3]Division of Rheumatology, Department of Medicine, Montefiore Medical Center, New Rochelle, NY, [4]Division of Rheumatology, Department of Medicine, Montefiore Medical Center, New York, NY, [5]Albert Einstein College of Medicine, White Plains, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Up to 80% of Systemic Lupus Erythematosus (SLE) patients experience cognitive dysfunction (CD), which is a top distressing symptom affecting their quality of life.(1) This process is poorly understood and often a diagnostic challenge due to mild and nonspecific symptoms. The current gold-standard diagnostic tool, the comprehensive neuropsychological (CNP) testing, is time-consuming and requires specialized training. Other tests, such as the Automated Neuropsychological Assessment Metric (ANAM) or the Montreal Cognitive Assessment (MoCA), can be impractical in busy clinical settings or focus more on memory deficits that are less relevant than impairment in processing speed and executive function in young SLE patients. We propose using a novel tool, the Attention, Memory, and Frontal-Executive Abilities Screening Test (AMFAST), which is a 10-minute pen-and-paper test that has shown excellent sensitivity and specificity for neurologic pathologies within a large age range.(2) Our aim is to validate AMFAST as a bedside screening tool for detecting CD in adult SLE patients.

Methods: This IRB-approved longitudinal study assessed a cohort of 31 adult SLE patients from the Lupus Clinic at Montefiore Medical Center between 2023 and 2025. English-speaking patients with no pre-existing, non-SLE-related neurological conditions were recruited. Participants underwent AMFAST testing in the clinic, followed by a CNP battery evaluation administered by a blinded neuropsychologist within two weeks. Patients were then classified into two groups: those

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

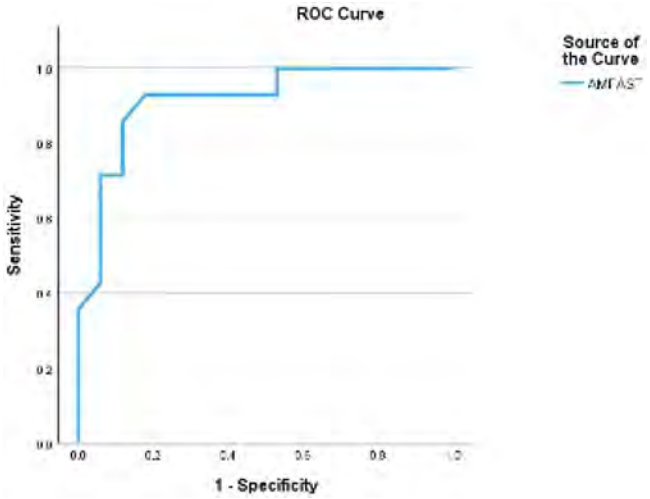


Figure 1: Receiver operating characteristic (ROC) of AMFAST test

Table 1: Baseline demographics

Characteristics	AMFAST population (n = 31)
Gender (n [%])	
Male	2 (6.5%)
Female	29 (93.5%)
Race & ethnicity (n [%])	
Black	19 (61.3%)
Asian	1 (3.2%)
Hispanic	11 (35.5%)
Education (mean [SD])	14.94 (2.66)

exhibiting CD, defined by scoring below one standard deviation (SD) on at least six of the 24 measures, and those without cognitive impairment (NCD).(3) A receiver operating characteristic (ROC) curve analysis was conducted to evaluate the correlation between AMFAST scores and CNP test battery performance.

Results: Participants had a mean age of 43 years (range 23-70) and were 93.5% female (Table 1). Based on the CNP battery tests, 14 out of 31 patients (45.2%) were classified as having CD. The mean score on the AMFAST test was 79.23 (SD = 18.1). ROC analysis demonstrated excellent diagnostic discrimination for the AMFAST test, with AUC of 0.92 (Figure 1). This indicates that AMFAST is highly effective in distinguishing between individuals with CD and NCD. AMFAST cutoff score of 83 had the best balance of sensitivity (93%) with specificity (82%), where overall, it was able to correctly classify 27 out of 31 cases (87.1%).(Table 2)

Conclusion: Our single-center findings confirm the robustness of AMFAST in screening SLE patients at risk of cognitive impairment. It is a simple bedside screening tool demonstrating promising results for identifying CD in SLE patients. The test's ease of administration with high sensitivity and specificity makes it an attractive clinical tool for early identification of CD, enabling timely intervention. Although our study provides valuable insights, further research is warranted.

Reference

(1) Lupus Foundation of America: Patient Voices Report (2017)
(2) Freilich BM, et al. Validation of AMFAST. Assessment (2020)
(3) Freilich BM, et al. Validation of AMFAST in children, adolescents, and young adults. Child Neurops (2023)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: AMFAST Score with sensitivity and specificity based on different cut-off. In grey, the best cutoff

AMFAST Score	Sensitivity	Specificity	Youden
78	0.786	0.882	0.668
79	0.857	0.882	0.739
80	0.857	0.882	0.739
81	0.929	0.824	0.739
82	0.929	0.824	0.753
83	0.929	0.824	0.753
84	0.929	0.765	0.694
85	0.929	0.706	0.635
86	0.929	0.706	0.635
87	0.929	0.706	0.635
88	0.929	0.706	0.635
89	0.929	0.647	0.576

Disclosure: C. Chao: None; **G. Thomas**: None; **C. O'Brien**: None; **D. Chen**: None; **S. Mian**: None; **T. Rubinstein**: None; **N. Schwartz**: None; **B. Freilich**: None.

Abstract Number: 1480

Urinary Biomarkers Detect Proliferative Lupus Nephritis in SLE Patients with Subclinical Proteinuria.

CHEN-YU LEE[1], Rufei Lu[2], Carla Guthridge[2], Wade DeJager[3], Jennifer Barnas[4], Jennifer Anolik[5], H Michael Belmont[6], Judith James[2], Jill Buyon[7], Brad Rovin[8], Michelle Petri[9], Joel Guthridge[2], Andrea Fava[1] and the Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network and the Accelerating Medicines Partnership in RA/SLE Network, [1]Johns Hopkins University, Baltimore, MD, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Oklahoma Medical Research Foundation, Oklahoma City, [4]University of Rochester, Rochester, NY, [5]University of Rochester Medical Center, Rochester, NY, [6]NYU School of Medicine, New York, NY, [7]NYU Grossman School of Medicine, New York, NY, [8]The Ohio State University, Columbus, OH, [9]Johns Hopkins University School of Medicine, Timonium, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Early treatment is critical to prevent irreversible kidney damage in lupus nephritis (LN). Current guidelines recommend kidney biopsy when the urine protein-to-creatinine ratio (UPCR) reaches ≥0.5 g/g. However, one-third of patients with UPCR between 0.25–0.5 g/g already harbor ISN Class III or IV ± V LN. While urinary biomarkers can detect active LN in patients with UPCR >0.5, their utility at lower proteinuria thresholds remains unclear. We analyzed candidate urinary biomarkers in SLE patients undergoing kidney biopsy at the initial onset of UPCR 0.25–0.49 g/g to identify molecular signatures of clinically underestimated LN that could support earlier diagnosis and treatment.

Methods: SLE patients with no history of LN, UPCR 0.250–0.49 g/g, and at least one additional LN risk factor (non-White race, low C3, low C4, anti-dsDNA positivity, or active urine sediment) were prospectively enrolled (KP1; n=21). For comparison, we analyzed a cohort of SLE patients with UPCR >0.5 undergoing clinically indicated kidney biopsy (AMP; n=282), and healthy controls (HC; n=31). Urine samples were collected near the time of biopsy, and 5,416 proteins were quantified using the Olink Explore HT platform. We focused on eight candidate biomarkers previously associated with histological activity, fibrosis, and future kidney function loss: IL16, CD163, CD206 (MRC1), PR3 (PRTN3), Galectin-1 (LGALS1), Tenascin-C (TNC), BAFF (TNFSF13B), and C9.

Results: In this interim analysis, 13 of 21 low proteinuria patients (62%) had biopsy-confirmed LN, including 3 (14%) with Class III and 5 (24%) with Class V (**Table 1**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Characteristics and Histopathologic Features at Time of Biopsy. # one patient had UPCR >0.5 at screening but 0.099 on repeat pre biopsy.

	KP1 (N=21)	AMP (N=282)
Sex - n(%)		
Female	19 (90.5%)	242 (85.8%)
Male	2 (9.5%)	37 (13.1%)
Race - n(%)		
Black	10 (47.6%)	121 (42.9%)
White	7 (33.3%)	84 (29.8%)
Asian	0 (0%)	41 (14.5%)
Other	4 (19.0%)	36 (12.8%)
Age		
Mean (SD)	44.8 (17.9)	36.8 (11.9)
ISN Class		
No_LN	8 (38.1%)	12 (4.3%)
I	1 (4.8%)	5 (1.8%)
II	4 (19.0%)	16 (5.7%)
III	3 (14.3%)	50 (17.7%)
III+V	0 (0%)	33 (11.7%)
IV	0 (0%)	42 (14.9%)
IV+V	0 (0%)	21 (7.4%)
V	5 (23.8%)	64 (22.7%)
VI	0 (0%)	20 (7.1%)
Activity*		
Median [Min, Max]	0 [0, 4.00]	4.00 [0, 18.0]
Chronicity**		
Median [Min, Max]	0 [0, 3.00]	3.00 [0, 9.00]
Urine Protein/Creatinine		
Median [Min, Max]	0.349 [0.254, 0.484]	1.91 [0.0990, 12.7]#
eGFR CKD-EPI***		
Mean (SD)	100 (23.1)	86.4 (35.8)

*p < 0.01 between KP1 and AMP

**p < 0.01 between KP1 and AMP

***No significant difference between KP1 and AMP

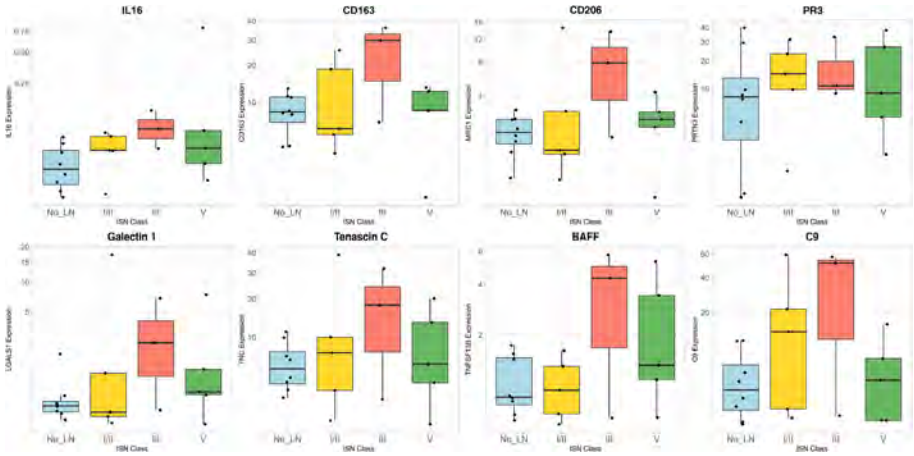


Figure 1. Urinary biomarkers of inflammation and fibrosis are elevated in early lupus nephritis across ISN classes. Boxplots display expression levels of inflammation-associated markers (IL16, CD163, CD206 [MRC1], PR3 [PRTN3], Galectin-1 [LGALS1], BAFF [TNFSF13B], and C9) and the myofibroblast marker Tenascin C [TNC] in early LN biopsies. Among the eight KP1 patients without histologic LN, six (75%) exhibited 20–30% foot process effacement, two (25%) showed glomerulosclerosis, five had atherosclerosis, and one had IgA nephropathy. Proteins are expressed as normalized protein expression (NPX) and normalized by plate controls.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

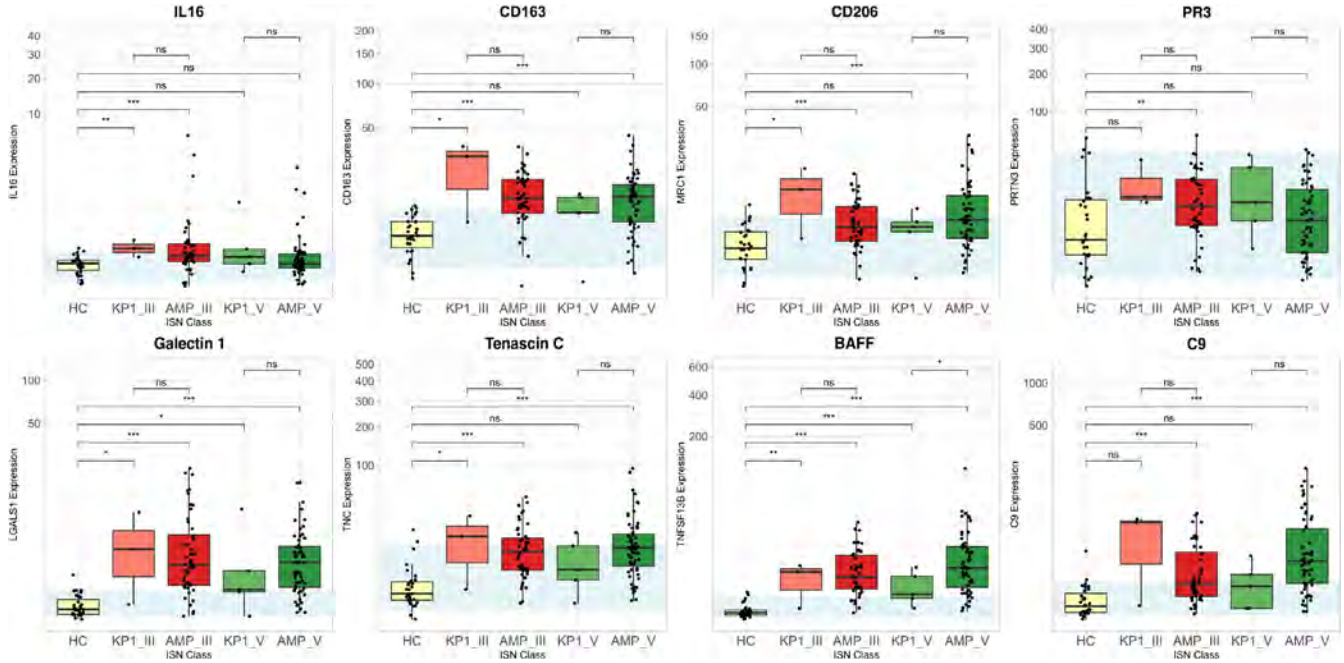


Figure 2. Urinary inflammatory and fibrotic protein expression is elevated in early and established proliferative and membranous lupus nephritis. Boxplots show expression levels of eight candidate biomarkers—IL16, CD163, CD206 (MRC1), PR3 (PRTN3), Galectin-1 (LGALS1), BAFF (TNFSF13B), C9, and Tenascin-C (TNC)—in urine samples from patients with low proteinuria LN (UPCR <0.5, KP1), high proteinuria LN (UPCR >= 0.5, AMP), and healthy controls (HC). KP1 Class III patients exhibited similar biomarker profiles to AMP Class III patients, suggesting early molecular activation despite subclinical proteinuria. Class V patients in both cohorts also showed enrichment of fibrotic markers (Tenascin-C). The blue shaded area represents the 5th to 95th percentile range of protein expression in HC. Statistical comparisons were performed using the Wilcoxon test. *p < 0.05; **p < 0.01; ***p < 0.001.

Compared to UPCR >0.5 SLE patients, low proteinuria patients had higher eGFR (but not statistically significant) and lower NIH activity and chronicity indices, suggesting earlier stages of inflammation and fibrosis.

Although the sample size limited statistical power, patients with Class III LN showed elevated levels of multiple candidate biomarkers—including CD163, CD206, IL16, Galectin-1, BAFF, C9, and Tenascin-C—compared to those with no LN (**Figure 1**).

All eight biomarkers were significantly enriched in low proteinuria Class III patients, mirroring the Class III profile in high proteinuria patients (**Figure 2**). This suggests that proliferative LN is already molecularly active at lower proteinuria levels, with signatures of M1/M2 macrophage activation (CD163, CD206), B cell stimulation (BAFF), complement activation (C9), and fibrotic remodeling (Tenascin C). Importantly, biomarker levels in KP1 Class III patients were comparable to those in AMP patients with UPCR >0.5, indicating that proteinuria alone underestimates the degree of renal inflammation. Notably, Class V patients in both KP1 and AMP cohorts showed elevated Tenascin-C, highlighting a pro-repair/fibrotic signature even in early membranous LN.

Conclusion: Urinary biomarkers may detect proliferative LN in SLE patients with subclinical proteinuria. These findings support the potential of biomarker-guided strategies to enable screening as well as earlier diagnosis and intervention in lupus nephritis. Ongoing analysis of the full 5,416-protein panel aims to elucidate early mechanisms of LN and identify novel targets for timely intervention.

Disclosure: C. LEE: None; **R. Lu**: None; **C. Guthridge**: None; **W. DeJager**: None; **J. Barnas**: None; **J. Anolik**: None; **H. Belmont**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sciences, 2, UCB, 2; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. Guthridge**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2.

Abstract Number: 1481

Duffy Antigen Screening in Systemic Lupus Erythematosus Patients with Neutropenia: A Quality Improvement Initiative

Divya Sudireddy[1], Jason Yang[2], Huseyin Berk Degirmenci[3], Eva Petrow[2] and Michael York[4], [1]Boston Medical Center, Westborough, MA, [2]Boston Medical Center, Boston, MA, [3]Boston University Medical Center, Boston, MA, [4]Boston University, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Laboratory monitoring for patients with systemic lupus erythematosus (SLE) is essential for assessing disease activity and detecting treatment-related adverse effects, including cytopenias. Neutropenia in particular may result from immunosuppressive medications. In patients with chronic neutropenia, providers may discontinue immunosuppressive medications out of concern for drug-induced myelosuppression. However, individuals with Duffy null (Fy[a–b–]) red blood cell phenotype, more common among those of African ancestry, have lower baseline absolute neutrophil counts without increased infection risk. The neutropenia associated with Duffy null phenotype may be misattributed to medication-related toxicity leading to inappropriate discontinuation of effective immunosuppressive therapy. We aimed to assess the frequency of Duffy antigen screening in SLE patients with neutropenia at an urban safety-net hospital and implemented a quality improvement (QI) intervention to increase screening.

Table 1: Duffy Antigen Screening Outcomes in SLE Patients with Neutropenia

SLE patients with neutropenia = 62

Metric	Pre Intervention	Post Intervention	Total	Race
Number of Patients screened for Duffy antigen	6	9	15	12=African American 1= Asian 1=Caucasian 1=Other
Number of Patients with Duffy Null Phenotype	5	7	12	11=African American 1 = other

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We used Epic's electronic health record (EHR) Slicer Dicer tool to identify patients with SLE and concurrent neutropenia at a single safety net hospital and reviewed the medical records to confirm presence of chronic neutropenia. We conducted an educational session for rheumatologists on the clinical relevance of the Duffy null phenotype and facilitated coordinated ordering of the test. We assessed whether a Duffy antigen screen had been performed and documented the results prior to and 2-months following the intervention.

Results: We identified 78 patients with SLE and leukopenia within the prior year, of whom 62 had neutropenia confirmed by medical record review. Prior to the intervention, 6 patients (9.7%) had undergone Duffy antigen testing, 5 of whom were Duffy null. Following the intervention, an additional 9 patients were screened over a 2-month period, increasing the post-intervention screening frequency to 14.5% (9/62). Among the 9 patients screened post-intervention, 7 had the Duffy null phenotype. Overall, 11 of the 12 patients identified as Duffy null were African American. (Table 1)

Conclusion: Our QI initiative led to a 4.8% absolute increase in Duffy antigen screening frequency in a 2-month post-intervention period. However, overall screening remained suboptimal. Given the higher prevalence of Duffy null phenotype in patients of African ancestry, which constitute a large percentage of SLE patients, recognizing this phenotype is important to prevent unnecessary medication changes that could compromise disease management. Future efforts to be considered include integrating electronic decision support tools, such as a Best Practice Advisory (BPA), to promote routine screening in SLE patients with chronic neutropenia. Our goal is to implement a more streamlined and automated process to ensure Duffy null antigen testing is routinely conducted.

Disclosure: D. Sudireddy: None; **J. Yang**: None; **H. Degirmenci**: None; **E. Petrow**: None; **M. York**: None.

Abstract Number: 1482

Evaluation of T Cell Subpopulations, CD4/CD8 Ratio and p16INK4a in Patients with Systemic Lupus Erythematosus and Cognitive Impairment

Erik Cimé-Aké[1], Guadalupe Lima[1], Emilio Godinez-Lazarini[1], Sandra Juárez[1], Hilda Marín-López[1], Amairani Gómez-Rodríguez[1], Daniela Flores-Hernández[1], Ileana Flores-Hernández[1], Diego F. Hernández-Ramírez[1], Luis Llorente[1] and Hilda Fragoso-Loyo[2], [1]Instituto Nacional de Ciencias Médicas y Nutrición. Salvador Zubirán. Immunology and Rheumatology Department, Mexico City, Mexico, [2]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Cognitive impairment (CI) in systemic lupus erythematosus (SLE) may be associated with different T cell subpopulations distribution and chronic pro-inflammatory state in which immunosenescence could be involved. This study investigates the distribution of T cell subpopulations and immunosenescent markers in SLE patients with CI.

Methods: We included women aged 18-50 years, classified with SLE according to the EULAR/ACR 2019 criteria. Women with other autoimmune diseases except antiphospholipid syndrome or Sjögren's syndrome, administration of any biologic drug < 6 months prior to study entry, clinical SLEDAI-2K >0, SDI ≥1, current prednisone >7.5 mg/day, education level ≤6 years, pregnancy or premature ovarian failure, active infection, malignant disease, history of other neuropsychiatric manifestations, other chronic comorbidities or major depressive disorder were excluded. We also include healthy women

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, subpopulations and immunosenescence markers of studied patients.

Variable		SLE with CI, *n*=15	SLE without CI, *n*=15	HC, *n*=15	p
Demographic and clinical characteristics					
Age, years		41.9 (38.2-48.4)	39.4 (27.2-43.3)	42.2 (34.7-51.8)	0.333
Educational level, years		**10.2 (8.2-13.3)**	**15.5 (12.2-16.4)**	**19.1 (14.2-26.4)**	**0.004***
Disease duration, years		**16.0 (11.7-20.0)**	**10.1 (5.8-15.7)**	-	**0.032***
Clinical SLEDAI-2K		0 (0-0)	0 (0-0)	-	0.335
SDI		0 (0-0)	0 (0-0)	-	1.000
CD4+					
CD3+/CD4+	%	46.4 (25.9-58.1)	53.8 (47.1-58.9)	57.9 (52.7-61.3)	0.117
Naive	**%**	**21.9 (13.4-26.6)**	**31.1 (17.3-47.7)**	**31.5 (29.7-45.2)**	**0.012***
CM	%	32.8 (18.3-42.9)	35.8 (14.8-44.3)	28.0 (26.5-42.2)	0.994
EM	%	36.3 (18.8-52.1)	26.5 (14.9-36.2)	29.0 (18.3-37.1)	0.248
TEMRA	%	3.3 (1.3-6.3)	1.6 (0.7-16.6)	2.5 (0.9-4.4)	0.304
CD8+					
CD3+/CD8+	**%**	**48.1 (35.0-67.4)**	**36.5 (31.9-44.0)**	**30.9 (20.1-39.8)**	**0.023***
Naive	%	27.7 (5.6-51.1)	32.6 (21.1-43.2)	15.8 (8.0-34.0)	0.336
CM	%	4.2 (1.6-8.6)	6.0 (0.9-14.2)	6.8 (4.7-7.9)	0.736
EM	%	18.3 (15.0-28.5)	17.1 (11.4-27.1)	27.2 (18.6-50.4)	0.086
TEMRA	%	19.3 (3.8-29.2)	9.8 (4.2-24.4)	6.0 (2.4-20.4)	0.192
Immunosenescence markers					
Inverted ratio CD4+CD8+, n (%)		**8 (53.3)**	**3 (20.0)**	**0 (0)**	**0.003***
p16INK4a, ddCT		**1.6 (1.0-2.3)**	**0.8 (0.4-2.2)**	**0.6 (0.5-1.0)**	**0.005***

Data are expressed as proportions (percentages) or medians (interquartile ranges). Statistical analysis: Chi-square or Fisher's exact tests were used for nominal variables, the Kruskal-Wallis test was used for numerical variables. CM: central memory, EM: effector memory, TEMRA: effector memory T cells re-expressing CD45RA. *Statistically significant.

(HC) paired for age ±5 years. We applied a neurocognitive battery, assessing eight cognitive domains: concentration, verbal memory, visuospatial memory, language, processing speed, motor speed, problem solving and executive function. CI was defined when a subject had scores ≥2 standard deviation below the mean of the normative data in at least one cognitive domain. According to the neurocognitive assessment patients were classified as: SLE with CI, SLE without CI and HC. The lymphocyte subpopulation profile for each patient was determined by flow cytometry. A CD4+/CD8+ ratio of < 1 (inverted ratio) was considered a marker of immunosenescence. The relative expression of the p16INK4a gene in CD3+ T lymphocytes was considered another marker of immunosenescence and was assessed through CD3+ cell purification from peripheral blood, RNA extraction, qPCR, and evaluation of relative expression (ddCT) normalized to the housekeeping gene GAPDH. Demographic and clinical data were also recorded.

Results: Fifteen patients in each group were included. The median age of patients studied was similar. SLE patients with CI had lower educational level than the SLE without CI and HC, and longer disease duration compared to SLE patients without CI. Disease activity and accrual damage was similar between the SLE groups (Table 1). In SLE patients with CI, the most frequently impaired cognitive domain was motor speed (73.3%), followed by visuospatial memory (33.3%), processing speed (13.3%), verbal memory (6.6%), language (6.6%), and problem solving (6.6%) (Figure 1). SLE patients with CI had significant lower levels of naive CD4+T cells and higher levels of CD8+ T cells compared to the other groups. The proportion of inverted CD4+/CD8+ ratio and relative expression of p16INK4a were greater in SLE with CI compared to SLE without CI and HC

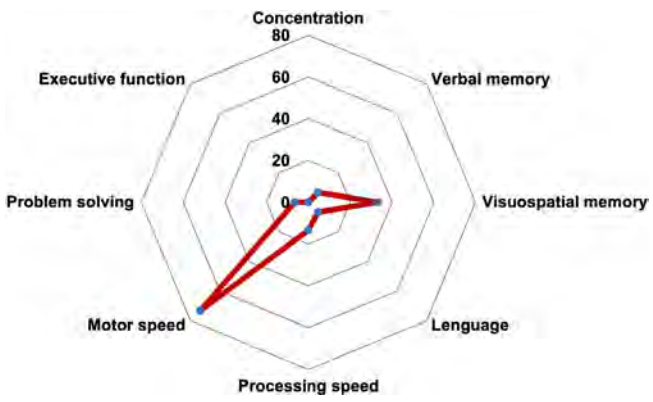


Figure 1. Impaired cognitive domains in SLE patients with CI. Data are expressed as percentages.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

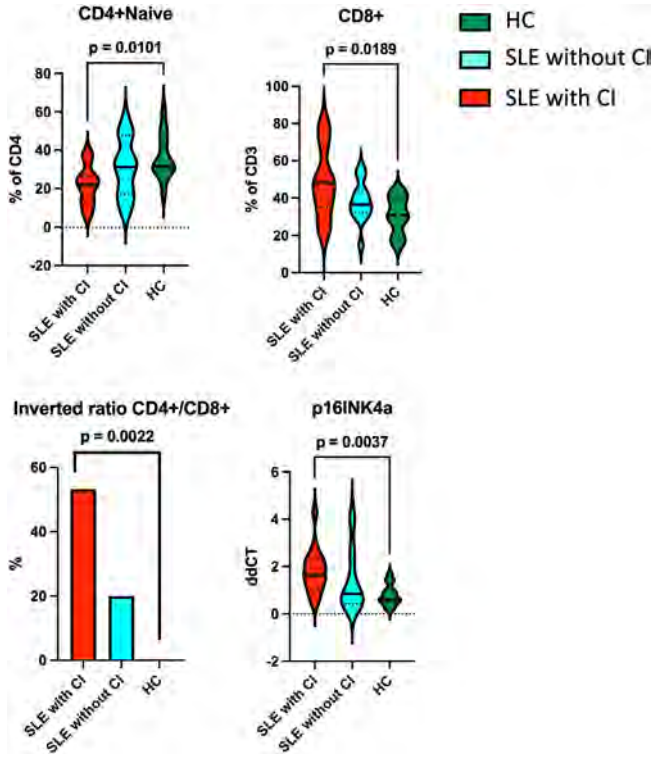


Figure 2. Statistical significant differences in subpopulations and senescent markers in T cells of studied patients. HC: healthy control, SLE: systemic lupus erythematosus, CI: cognitive impairment.

groups (53.3% vs. 20.0% vs. 0%, p=0.003 and 1.6 [1.0-2.3] ddCT vs. 0.8 [0.4-2.2] ddCT vs. 0.6 [0.5-1.0] ddCT, p=0.005, respectively) (Table 1, Figure 2).

Conclusion: In SLE with CI there were lower levels of naïve CD4+ T-cells, higher levels of CD8+ T cells and greater presence of immunosenescence markers compared to SLE without CI and HC. The study suggests the possibility that immunosenescence may play a role in CI in SLE.

Disclosure: E. Cimé-Aké: None; **G. Lima**: None; **E. Godinez-Lazarini**: None; **S. Juárez**: None; **H. Marín-López**: None; **A. Gómez-Rodríguez**: None; **D. Flores-Hernández**: None; **I. Flores-Hernández**: None; **D. Hernández-Ramírez**: None; **L. Llorente**: None; **H. Fragoso-Loyo**: None.

Abstract Number: 1483

Evidence of Early Cardiovascular Dysfunction in Young Systemic Lupus Erythematosus Patients Compared to Older Healthy Controls

Fernanda M. Garcia-Garcia[1], Oscar Azael Garza-Flores[2], Esteban C. Garza-Gonzalez[3], Rebeca L. Polina-Lugo[4], Leslie Y. Lopez-Cantú[1], Dionicio A. Galarza-Delgado[1], Iris J. Colunga-Pedraza[1], Jesus Alberto Cardenas-de la Garza[5], Jose R Azpiri-Lopez[6] and Victor M Fraga-Enriquez[7], [1]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, San Nicolas de los Garza, Nuevo Leon, Mexico, [4]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [5]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [6]Cardiology Service, Hospital

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Cardiovascular Risk Characteristics

Variable	Young SLE Patients n= 64	Older Healthy Controls n= 76	p-value
Age, median (IQR)	25.00 (22.00 – 34.00)	55.00 (50.00 – 61.25)	**< .001**
Women, n (%)	58 (90.62)	49 (64.47)	**< .001**
CV risk factors			
BMI, kg/m², mean ± SD	23.79 ± 4.49	27.84 ± 4.66	**< .001**
Obesity, n (%)	4 (6.25)	12 (15.78)	0.070
DM, n (%)	1 (1.56)	16 (21.05)	**< .001**
HTN, n (%)	10 (15.62)	22 (28.94)	0.060
DLP, n (%)	6 (9.37)	29 (38.15)	**< .001**
Smoking, n (%)	11 (17.18)	25 (32.89)	**0.034**
Laboratory Parameters			
HbA1c, mean ± SD	5.03 ± 1.13	5.77 ± 1.32	**0.012**
CRP, mg/dL, median (IQR)	0.46 (0.26 – 0.74)	0.40 (0.24 – 0.56)	0.212
ESR, mm/h, median (IQR)	20.50 (11.00 – 39.50)	16 (7.00 – 27.00)	**0.050**
Treatment			
Prednisone, n (%)	54 (84.37)	–	**< .001**
Hydroxychloroquine, n (%)	56 (87.5)	–	**< .001**
Antihypertensive, n (%)	14 (21.87)	9 (11.84)	0.203
Statin, n (%)	10 (15.62)	12 (15.78)	0.533

Values are presented as mean ± SD or median (IQR), as appropriate. SD, Standard Deviation; IQR, Interquartile Range; SLE, Systemic Lupus Erythematosus; CV, Cardiovascular; BMI, Body Mass Index; DM, Diabetes Mellitus; HTN, Hypertension; DLP, Dyslipidemia; CRP, C-Reactive Protein; ESR, Erythrocyte Sedimentation Rate. Bold values indicate statistical significance at $p < 0.05$.

Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [7]Cardiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by systemic inflammation and accelerated atherosclerosis, leading to increased cardiovascular (CV) risk. While CV disease typically affects older individuals, SLE patients may develop subclinical CV damage at a younger age due to chronic inflammation. Emerging echocardiographic techniques, including left ventricular ejection fraction (LVEF), global longitudinal strain (GLS) and pulmonary artery systolic pressure (PASP), enable early detection of CV dysfunction before clinical manifestations arise. This study aimed to evaluate subclinical CV alterations in young SLE patients compared to older healthy controls.

Methods: A cross-sectional study was conducted, enrolling patients aged ≤39 years who met the 2019 ACR/EULAR classification criteria for SLE, and a control group of healthy adults aged ≥40 years without rheumatic disease, recruited from a preventive cardio-rheumatology clinic. Individuals with a history of CV disease were excluded.

Table 2. Echocardiographic Parameters

Variable	Young SLE Patients n= 64	Older Healthy Controls n= 76	p-value
Left Ventricular Function			
LVEF, mean ± SD	59.04 ± 8.35	62.53 ± 5.17	**0.006**
GLS, mean ± SD	-18.99 ± 2.96	-20.84 ± 3.52	**0.010**
RWT, median (IQR)	0.293 (0.259 – 0.352)	0.342 (0.270 – 0.432)	**0.023**
LVMI, g/m², mean ± SD	66.38 ± 21.21	84.05 ± 29.18	**< .001**
E' wave, median (IQR)	0.16 (0.13 – 0.18)	0.12 (0.11 – 0.14)	**0.002**
E/e' ratio, mean ± SD	6.96 ± 2.47	8.47 ± 2.31	**< .001**
Deceleration Time, ms, median (IQR)	163 (149 – 187)	215 (187 – 255)	**< .001**
Right Ventricular Function			
TAPSE, mm, median (IQR)	21.00 (19.25 – 24.00)	18.00 (2.20 – 24.00)	**0.004**
PASP, mmHg, mean ± SD	24.03 ± 8.07	19.60 ± 8.18	**0.028**
S' velocity, cm/s, median (IQR)	13.00 (11.00 – 14.00)	12.00 (11.00 – 14.00)	0.305

Values are presented as mean ± SD or median (IQR), as appropriate. SD, Standard Deviation; IQR, Interquartile Range; SLE, Systemic Lupus Erythematosus; LVEF, Left Ventricular Ejection Fraction; GLS, Global Longitudinal Strain; RWT, Relative Wall Thickness; LVMI, Left Ventricular Mass Index; TAPSE, Tricuspid Annular Plane Systolic Excursion; PASP, Pulmonary Artery Systolic Pressure; S' velocity, Peak Systolic Velocity of the Tricuspid Annulus. Bold values indicate statistical significance at $p < 0.05$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Demographic data, CV risk factors (hypertension, diabetes, dyslipidemia, and body mass index), and echocardiographic parameters were collected. All echocardiograms were performed by a single board-certified echocardiographer using standardized protocols, including B-mode, M-mode, spectral Doppler, color Doppler, and tissue Doppler imaging. Cardiac geometry, systolic and diastolic function were assessed and classified according to the 2016 ASE/EACVI guidelines. Data normality was evaluated using the Kolmogorov–Smirnov test. Between-group comparisons were conducted using Student's t-test, Chi-square test, or Mann–Whitney U test, as appropriate. A p-value of ≤0.05 was considered statistically significant.

Results: A total of 140 participants were included: 64 young SLE patients and 76 older healthy controls. Median age was 25.00 years in the SLE group and 55.00 years in controls ($p < 0.001$), with a higher proportion of women among SLE patients (90.62% vs. 64.47%; $p < 0.001$). SLE patients also had a lower body mass index ($p < 0.001$), and a lower prevalence of diabetes mellitus ($p < 0.001$), dyslipidemia ($p < 0.001$), and smoking ($p = 0.034$). HbA1c was also lower in SLE ($p = 0.012$), while erythrocyte sedimentation rate was higher ($p = 0.050$).

Echocardiography revealed reduced LVEF (59.04 vs. 62.53, $p = 0.006$) and impaired GLS **(–18.99 vs. –20.84**, $p = 0.010$) in SLE patients, while LVMI ($p < 0.001$) and RWT ($p = 0.023$) were higher in controls. Diastolic function assessment showed a higher E′ wave in SLE patients ($p = 0.002$), with lower E/e′ ratio ($p < 0.001$) and deceleration time ($p < 0.001$). TAPSE ($p = 0.004$) and PASP (**24.03 vs. 19.60 mmHg**, $p = 0.028$) were also higher in SLE.

Conclusion: Our findings indicate that young SLE patients may exhibit early echocardiographic alterations compared to older healthy individuals, including reduced myocardial strain, elevated pulmonary pressures, and impaired diastolic function. Notably, these differences were present despite a lower burden of traditional metabolic risk factors. These findings underscore subclinical CV impairment in young SLE patients and reinforce the need for routine CV monitoring in this population.

Disclosure: F. Garcia-Garcia: None; **O. Garza-Flores**: None; **E. Garza-Gonzalez**: None; **R. Polina-Lugo**: None; **L. Lopez-Cantú**: None; **D. Galarza-Delgado**: None; **I. Colunga-Pedraza**: None; **J. Cardenas-de la Garza**: None; **J. Azpiri-Lopez**: None; **V. Fraga-Enriquez**: None.

Abstract Number: 1484

Decoding the Impact of Systemic Lupus Erythematosus on Transcatheter Aortic Valve Implantation: A Nationwide population-based Study

Mariana Vanoye Tamez[1], **Freya Shah**[2], Neel Patel[3] and siddharth Agrawal[2], [1]New York Medical College / Landmark Medical Center, Providence, RI, [2]landmark medical center, Cumberland, RI, [3]University of Tennessee, Nashville

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with autoimmune connective tissue disease, such as Systemic Lupus Erythematosus (SLE), are at higher risk for developing aortic valve pathology. However, the impact of the presence of SLE on outcomes of Transcatheter aortic valve implantation (TAVI) has not been well described in the literature. We studied mortality, complications, readmission rates, and length of stay on a propensity-matched national cohort of SLE patients undergoing TAVI.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We queried the Nationwide readmission database from 2016-2020 using ICD 10 codes to extract the baseline population who underwent the TAVR procedure. Patients were identified and divided into two groups based on the presence of SLE. The Clinical outcomes were assessed at index admissions and readmissions using chi-square statistics, univariate and multivariate regression analysis using STATA v.17

Results: A total of 320,353 weighted index hospitalizations with TAVI were identified from 2016 to 2020. Out of which 1,348 patients had SLE while 319,005 patients did not. The mean age of the SLE group was 72.12 +/- 10.53 years while the non-SLE group was 79 +/- 8.53 years.

The non-SLE group had a statistically significant higher prevalence of hyperlipidemia (73.21% vs 69.74%, p:< 0.001); smoking (35.64% vs 30.06%, p:0.0116); and prior PCI (19.4% vs 13.23%, p:0.0007); prior CABG (15.88% vs 10.06; p:0.0003) compared to the SLE group. While the SLE group had a higher prevalence of pulmonary disease (25.28% vs 20.58%, p: 0.01); hypothyroidism (26.92% vs 18.6%, p< 0.0001); anemia (8.38% vs 5.15%, p:0.00014) and liver disease (2.71% vs 1.51%, p:0.0256).

There was no statistically significant difference in the crude and propensity-matched in-hospital outcomes including death, acute kidney injury, acute stroke, heart failure, myocardial infarction, use of mechanical circulatory support, post-procedural bleeding, cardiac tamponade, and Major adverse cardiac and cerebrovascular events (MACCE) among SLE and non-SLE groups. The multivariate regression analysis did not show statistically significant higher odds of SLE for the outcomes mentioned above.

The mean length of stay at index hospitalization in the SLE group was 5.63 +/- 8.44 days while the non-SLE group was 4.14 +/- 6.21 days. The SLE patients had higher rates of hospital readmission at 1 month (10.01% vs 9.31%) and 6 months (18.02% vs 13.05%).

Conclusion: In conclusion, SLE does not appear to be a risk factor for in-hospital mortality and the studied post-procedural complications in patients undergoing TAVI. However, patients with SLE who underwent TAVI were younger and differed significantly at baseline comorbidities, compared to patients without SLE. Patients with SLE had longer lengths of stay and higher readmission rates after TAVI.

Disclosure: M. Vanoye Tamez: None; **F. Shah**: None; **N. Patel**: None; **s. Agrawal**: None.

Abstract Number: 1485

Lupus Under the Lens: Fibrinogen-to-Albumin Ratio as a Novel Inflammatory Index

Guru Vijay Chagalakondu and Vijaya prasanna Parimi, ESIC Medical College and Super Specilaity Hospital, hyderabad, Telangana, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

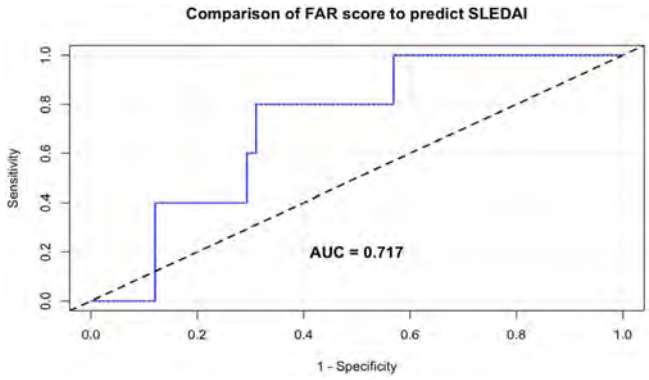


Fig 1: Comparison of FAR score to predict SLE disease activity.

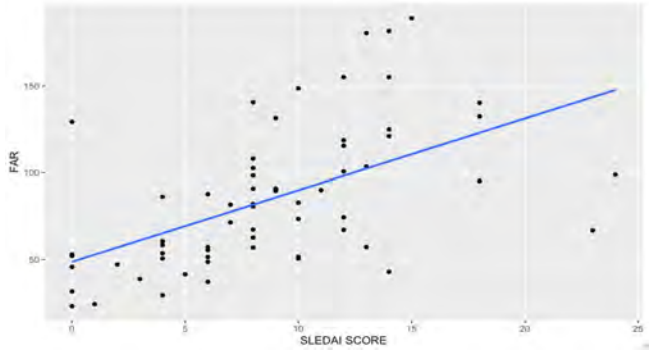


Fig 2: Scatter plot of SLEDAI Score and FAR Score in the study cohort.

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune condition presenting with unpredictable varying levels of severity. Thus, constant monitoring of disease activity is required. The fibrinogen-to-albumin ratio, is an emerging marker which can be used as a cost effective surrogate marker of disease activity in countries with limited resources.

Methods: In a cross-sectional observational study, 63 adult patients with SLE, were included in the study, conducted over a duration of one year, in the Department of Rheumatology, of a tertiary care centre. exclusion criterion included pregnancy, diabetes mellitus, active infections and presence of other autoimmune conditions. Clinical evaluation and laboratory assessments (including fibrinogen, albumin, ESR, CRP, complements, anti-dsDNA, UPCR, and 24-hour urine protein) were recorded. Disease activity was categorized using SLEDAI-2K as stable, mild, moderate, or severe. FAR was calculated, and its correlation with SLEDAI was assessed using Pearson's r. Receiver operating characteristic (ROC) analysis determined FAR's diagnostic accuracy in identifying severe disease.

Results: The cohort was predominantly female (95.2%), with a mean age of 32.2±8.9 years and mean disease duration of 4.9±4.1 years. The mean SLEDAI score was 8.7±5.4; FAR averaged 84.7±40.7. FAR exhibited a strong positive correlation with SLEDAI (r=0.645, $p< 0.001$). ROC analysis revealed an AUROC of 0.717 (p=0.028) for FAR in identifying severe disease. At a cut-off of ≥95.3, FAR predicted severe SLE with 80% sensitivity, 69% specificity, and an impressive 97.6% negative predictive value

Conclusion: Fibrinogen-to-albumin ratio demonstrates a strong correlation with SLE disease activity and offers moderate diagnostic accuracy in distinguishing severe flares. owing to its cost-effectiveness, it can be used a practical biomarker for SLE disease activity surveillance.

Disclosure: g. Chagalakondu: None; **V. Parimi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1486

Systemic Lupus Erythematosus and Statins in GLADEL 2.0: Are Cardiovascular Risk Prevention Guidelines Being Followed?

Ileana C. Reynosa-Silva[1], Iris J. Colunga-Pedraza[2], Guillermina Harvey[3], Dionicio A. Galarza-Delgado[2], Jose R Azpiri-Lopez[4], Fernanda M. Garcia-Garcia[2], Oscar Azael Garza-Flores[5], Marina Scolnik[6], Gisela Subils[7], CINTIA OTADUY[8], Veronica Saurit[9], Valeria Arturi[10], Leonel Berbotto[11], Guillermo Pons-Estel[12], Luciana Gonzalez Lucero[13], Melissa Brenda Serna Góngora[14], Maria de los Angeles Gargiulo[15], Cecilia Pisoni[16], Maria Elena Crespo[17], Mónica Sánchez Guamán[18], Vitalina de Souza Barbosa[19], Andrese Aline Gasparin[20], Henrique Ataide Mariz[21], Francinne Ribeiro[22], Eduardo Borba[23], Edgard dos Reis-Neto[24], Iris Guerra Herrera[25], Maria Loreto Massardo[26], Gustavo Aroca Martínez[27], Carlos Alberto Caas[28], Gerardo Quintana-Lopez[29], Carlos Toro-Gutierrez[30], Mario Moreno Alvarez[31], MIGUEL SAAVEDRA[32], Margarita Portela Hernández[33], Hilda Fragoso-Loyo[34], Luis M Amezcua-Guerra[35], Ignacio García-De la Torre[36], Jorge Isaac Velasco Santos[37], Jorge Antonio Esquivel Valerio[38], Jhonatan Losanto[39], Magaly Alva Linares[40], Manuel Ugarte-Gil[41], Katiuzka Zuñiga Corrales[42], Roberto Muñoz-Louis[43], Carina Pizzarossa[44], Gonzalo Silveira[45], Federico Zazzetti[46], Ashley Orillion[47] and Gloria Vásquez[48] on behalf of Grupo Latino Americano De Estudio de Lupus (GLADEL). Study Group of PANLAR, [1]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Universidad Nacional de Rosario, Rosario, Argentina, Rosario, Argentina, [4]Cardiology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [5]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [6]Hospital Italiano de Buenos Aires, Argentina, Buenos Aires, Argentina, [7]Hospital Italiano de Córdoba, Córdoba, Argentina, Córdoba, Argentina, [8]Servicio de Reumatología Hospital Córdoba y Sanatorio Allende, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Córdoba, Argentina, Crdoba, Argentina, [9]Hospital Privado Universitario de Cordoba, Córdoba, Argentina, Crdoba, Argentina, [10]Hospital San Martin de La Plata, La Plata, Argentina, La Plata, Argentina, [11]Sanatorio Británico; Rosario, Argentina, Rosario, Argentina, [12]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR); Rosario, Argentina, Rosario, Argentina, [13]Hospital Ángel C. Padilla, Tucumán, Argentina, Tucumán, Argentina, [14]Hospital J.M Ramos Mejía, Buenos Aires, Argentina;, Buenos Aires, Argentina, [15]Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires; Buenos Aires, Argentina, Buenos Aires, Argentina, [16]CEMIC Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno", Buenos Aires, Argentina, Ciudad Autonoma Buenos Aires, Argentina, [17]Hospital Señor del Milagro Salta, Salta, Argentina, Salta, Argentina, [18]Hospital General de Agudos Dr. Juan A. Fernández, Buenos Aires, Argentina, Buenos Aires, Argentina, [19]Hospital das Clinicas da Universidade Federal de Goias, Goiania, Brazil, Goiania, Brazil, [20]Hospital de Clínicas de Porto Alegre, Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil, Porto Alegre, Brazil, [21]Universidad Federal de Pernambuco, Recife, Brazil, Recife, Brazil, [22]Hospital Universitário Pedro Ernesto - Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, Rio De Janeiro, Rio de Janeiro, Brazil, [23]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, So Paulo, Brazil, [24]Escola Paulista de Medicina / Universidade federal de São Paulo (EPM / Unifesp), São Paulo, Brazil, So Paulo, Brazil, [25]Hospital del Salvador Santiago de Chile, Santiago, Chile, Santiago, Chile, [26]Facultad de Medicina y Ciencia, Universidad San Sebastián, Santiago, Chile, Santiago, Chile, [27]Universidad Simón Bolívar, Barranquilla, Colombia y Clínica de la Costa, Barranquilla, Colombia, [28]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia, Cali, Colombia, [29]Facultad de Medicina, Universidad Nacional de Colombia; Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogotá, Colombia, [30]Pontificia Universidad Javeriana de Cali, Cali, Colombia, Cali, Colombia, [31]Universidad de Especialidades Espíritu Santo, Guayaquil, Ecuador, Guayaquil, Ecuador, [32]Hospital de Especialidades Dr. Antonio Fraga Mouret, Centro Médico Nacional La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico, MEXICO, Mexico, [33]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico, Mexico City, Mexico, [34]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico, [35]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico city, [36]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, Guadalajara, Jalisco, Mexico, [37]Facultad de Medicina de la Universidad Autónoma de San Luis Potosí y Hospital Central "Dr. Ignacio Morones Prieto" San Luis Potosí, Mexico, San Luis Potosí, Mexico, [38]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [39]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, San Lorenzo, Paraguay, [40]Hospital Nacional Edgardo Rebagliati Martins-EsSalud, Lima, Peru, Lima, Peru, [41]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [42]Hospital Nacional Cayetano Heredia, Universidad Peruana Cayetano Heredia, San Martín de Porres, Peru, San Martín de Porres, Peru, [43]Hospital Docente Padre Billini, Santo Domingo, Distrito Nacional, Dominican Republic, [44]Hospital de Clínicas, Facultad de Medicina, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [45]Facultad de Medicina - Universidad de la República, Montevideo, Uruguay, Montevideo, Uruguay, [46]Johnson &

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Johnson, Horsham, PA, USA, Ambler, PA, [47]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [48]Sede de Investigación Universitaria (SIU), Universidad de Antioquia (UDEA), Medellín, Colombia., Medellín, Colombia

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients (pts) with systemic lupus erythematosus (SLE) have a significantly increased risk of atherosclerotic cardiovascular disease (ASCVD). EULAR recommends a comprehensive assessment and management of cardiovascular risk (CVR), following general population guidelines (Drosos GC et al, Ann Rheum Dis 2022). Statin therapy plays a key role in reducing CVR and preventing ASCVD events (Yousef Yengej FA et al, Neth J Med 2017). This study aimed to determine the proportion of pts with SLE eligible for statin use for primary ASCVD prevention, based on American and European CVR guidelines.

Methods: This was an observational and cross-sectional study of GLADEL 2.0, a multi-ethnic Latin-American SLE cohort. Demographics, comorbidities, medications, disease activity, and laboratory data were analyzed. Statin eligibility was determined using the 2019 American College of Cardiology/American Heart Association (ACC/AHA) and the 2021 European Society of Cardiology (ESC) guidelines. CVR was assessed using the ASCVD risk calculator from the ACC/AHA, Systemic

Table 1. Baseline clinical characteristics, disease activity, damage index and treatments

	Total (N=1083)
Age, years, median (Q1, Q3)	35.4 (15.6, 77.5)
≥40 years, n (%)	394 (36.4)
Female, n (%)	970 (89.6)
Mestizo, n (%)	701 (64.7)
Obesity, n (%)	187 (18.5)
Disease duration, years, median (Q1, Q3)	5.6 (0.6, 61.6)
SLEDAI, median (Q1, Q3)	5 (0, 57)
SDI, median (Q1, Q3)	0 (0, 9)
HDL-c (mg/dL), median (Q1, Q3), n=504	49 (11, 102)
LDL-c (mg/dL), median (Q1, Q3), n=480	103 (28, 328)
Triglycerides (mg/dL), median (Q1, Q3), n= 557	124 (32, 619)
Diabetes, n (%)	45 (4.2)
Hypertension, n (%)	293 (27.2)
Dyslipidemia, n (%)	129 (12)
Active smoking, n (%)	54 (5.1)
Chronic kidney disease, n (%)	61 (5.6)
Acute myocardial infarction, n (%)	8 (0.7)
Statins, n (%)	155 (20.4)
Prednisone, n (%)	758 (72.5)
Hydroxychloroquine, n (%)	876 (84)

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index

Table 2. Comparison of clinical characteristics based on their age group.

	< 40 years	≥ 40 years	*P* value
Obesity, n (%)	102 (15.8)	85 (23.3)	0.0031[2]
Disease duration, years, median (Q1, Q3)	4.1 (0.2 28.9)	9.9 (0.6, 61.6)	<0.0001[1]
SLEDAI, median (Q1, Q3)	6 (0, 57)	3 (0, 38)	<0.0001[1]
HDL-c, mg/dL, median (Q1, Q3), n=504	47 (11, 102)	52 (15, 100)	0.0003[1]
LDL-c, mg/dL, median (Q1, Q3), n=480	105.5 (37, 241)	101 (28, 328)	0.1404[1]
Triglycerides, mg/dL, median (Q1, Q3), n=557	123 (39, 619)	127 (32, 525)	0.4044[1]
Diabetes, n (%)	12 (1.7)	33 (8.4)	<.0001[2]
Active smoking, n (%)	30 (4.5)	24 (6.2)	0.0503[2]
Statins, n (%)	94 (19.8)	61 (21.3)	0.0510[2]
Prednisone, n (%)	525 (78.5)	233 (61.8)	<.0001[2]

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

[1]Kruskal-Wallis p-value; [2]Chi-Square p-value.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Coronary Risk Evaluation 2 (SCORE2), and Pan American Health Organization (PAHO) risk scores. Cohen's Kappa coefficient was used to determine inter-guideline agreement. Both guidelines only consider pts ≥40 years of age as candidates for CVR prevention with statins, due to eligibility dependence on CVR scores. Therefore, a comparative analysis was conducted between pts above and below this age threshold.

Results: Among 1083 pts in the GLADEL 2.0 SLE cohort, only 394 (36.4%) were older than 40 years of age; demographic characteristics are shown in Table 1. ACC/AHA could only be calculated for 164 pts, PAHO for 351 pts, and SCORE2 for 181 pts. Most of these pts were categorized as having a low CVR, regardless of the calculator used. A total of 15 pts were indicated to receive statin therapy based on European guidelines; among these, only 5 (33%) had a previous prescription for a statin. Among 50 pts eligible for statin therapy based on American guidelines, only 13 (26%) had been prescribed them. Inter-guideline agreement on statin eligibility was fair (Cohen's Kappa = 0.35; 95% CI: 0.15–0.55). Pts under 40 years of age were more obese and had higher disease activity compared with those older than 40 years of age (Table 2).

Conclusion: This study reveals a gap in the management of CVR among pts with SLE in the GLADEL 2.0 cohort, as only a small percentage are candidates for statin therapy, primarily due to the predominance of younger pts under age 40. Traditional CVR assessment tools fail to encompass this group, which is at an elevated risk for accelerated atherosclerosis. Among eligible pts, statin prescribing rates remain low, suggesting a missed opportunity in proactive cardiovascular prevention. The moderate agreement between differing guidelines highlights the inconsistency in risk assessment and management approaches for this population. There is a need for tailored strategies to comprehensively evaluate and address CVR in younger pts with chronic inflammatory conditions like SLE. Implementing more inclusive guidelines could enhance preventative measures and improve outcomes for pts at increased risk for ASCVD.

Disclosure: I. Reynosa-Silva: None; **I. Colunga-Pedraza**: None; **G. Harvey**: None; **D. Galarza-Delgado**: None; **J. Azpiri-Lopez**: None; **F. Garcia-Garcia**: None; **O. Garza-Flores**: None; **M. Scolnik**: AstraZeneca, 2, 5, 6, GSK, 1, 5, 6, Janssen, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6; **G. Subils**: None; **C. OTADUY**: None; **V. Saurit**: None; **V. Arturi**: None; **L. Berbotto**: None; **G. Pons-Estel**: AstraZeneca, 1, 2, 5, 6, Boehringer Ingelheim, 1, 2, 5, 6, GSK, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6, RemeGen, 1, 2, 5, 6, Sanofi, 1, 3, 5, 6, Werfen Diagnostics, 1, 2, 5, 6; **L. Lucero**: None; **M. Serna Góngora**: None; **M. Gargiulo**: None; **C. Pisoni**: None; **M. Crespo**: None; **M. Guamán**: None; **V. Barbosa**: None; **A. Gasparin**: None; **H. Mariz**: None; **F. Ribeiro**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. dos Reis-Neto**: None; **I. Guerra Herrera**: None; **M. Massardo**: None; **G. Aroca Martínez**: None; **C. Casas**: None; **G. Quintana-Lopez**: None; **C. Toro-Gutierrez**: None; **M. Moreno Alvarez**: None; **M. SAAVEDRA**: None; **M. Portela Hernández**: None; **H. Fragoso-Loyo**: None; **L. Amezcua-Guerra**: None; **I. García-De la Torre**: None; **J. Velasco Santos**: None; **J. Esquivel Valerio**: None; **J. Losanto**: None; **M. Alva Linares**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **K. Zuñiga Corrales**: None; **R. Muñoz-Louis**: None; **C. Pizzarossa**: None; **G. Silveira**: None; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **G. Vásquez**: None.

Abstract Number: 1487

Whole Health Empowerment for Endotypes of Lupus (WHEEL) Program: User Testing Findings on Feasibility, Acceptability, and Opportunities for Intervention Refinement

Jennifer Rogers[1], Amanda Eudy[2], Connor Drake[3], Tamara Somers[4], David Pisetsky[5], Christie Clipper[6], Ralph Snyderman[7], Anna Batsakes[6], Leigh Saner[6], Dana Burshell[3], Mithu Maheswaranathan[4], Lisa Criscione-Schreiber[4], Rebecca Sadun[8], Nathaniel Harris[5], Kai Sun[8], Kelsey Dunn[6], Jenny Herndon[6], Vonne Jacobs[6] and Megan Clowse[9], [1]Duke,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Durham, NC, [2]Duke University, Raleigh, NC, [3]Duke University School of Medicine, Durham, [4]Duke University School of Medicine, Durham, NC, [5]Duke University Medical Center, Durham, NC, [6]Duke University, Durham, [7]Duke Center for Personalized Health Care, Durham, NC, [8]Duke University, Durham, NC, [9]Duke University, Chapel Hill, NC

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: To improve quality of life (QoL) in individuals with SLE, we developed the Whole Health Empowerment for Endotypes of Lupus (WHEEL) program—a 4-month, biweekly, virtual, SLE-specific peer support curriculum. Adapted from an existing evidenced-based group visit model and delivered by certified health coaches, WHEEL promotes self-care and engagement through education, goal setting, mindfulness, and group discussion (Fig 1). The current study conducted user testing to assess feasibility and acceptability. To optimize group dynamics and shared experience, participants were stratified into two Type 2 SLE endotypes: Intermittent (symptoms aligning with Type 1 activity) and Persistent (symptoms persisting despite Type 1 remission).

Methods: Adults with SLE (2012 SLICC or 2019 ACR/EULAR criteria) with ≥3 visits in an academic registry were screened for potential inclusion based on SLEDAI, Type 1 and Type 2 physician global assessments (PGA; 3-point visual analog scales), and the polysymptomatic distress (PSD) score. *High Type 1 SLE activity* was defined as clinical SLEDAI ≥4, SLEDAI ≥6, renal SLEDAI ≥4, or PGA ≥1. *High Type 2 SLE activity* was defined as Type 2 PGA ≥1 or PSD ≥8. Patients without high Type 2 SLE activity were not eligible.

User Testing Cohorts

- Persistent Type 2 SLE (SLE-P): High Type 1 SLE activity at < 30% and high Type 2 SLE activity at ≥50% of visits
- Intermittent Type 2 SLE (SLE-I): Fluctuating Type 2 SLE activity

User testing consisted of 8 group sessions, 2 individual health coach sessions, development of personal goals, and pre/post surveys. Feasibility and acceptability were assessed via accrual, attendance, attrition, satisfaction, and fidelity. Progress achieved on personal goals further informed feasibility. Whole Health Assessment and PROMIS surveys explored preliminary efficacy.

Results: We enrolled 5 women in each cohort (100% accrual). While race and ethnicity were similar between cohorts, the average age of the SLE-P cohort was 10 years older. Nine participants completed the program with 1 early withdrawal from SLE-P. Over 80% of all group sessions were attended, and 8 participants attended all but 1 group session. On average, participants set 3 personal goals. All participants made progress on at least 1 goal, and 7 of 9 participants achieved ≥1 personal goal.

Figure 1a. Aspects of the WHEEL program. 1b. Components of each WHEEL group session

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Anonymous feedback from User testing participants

"I liked being able to communicate with others who were on a similar journey and also learn through their goals. I enjoyed having a place to check in and talk about progress or setbacks. I also enjoyed learning about my condition"
"I liked the group aspect of the program in addition to the educational information provided about this disease I must learn to live with and manage."
"How all of it the educational parts, self-care, goals, and support from other women all works in tandem and produces a great program."
"This group was very beneficial, and I hope it continues for other patients. I never knew how much I needed this group until I started attending the sessions."
"Maybe a little longer. It seems to go by quickly."
"I like the activity at the end of each session week. It helps to keep me honest and accountable."

Table 2. Lupus Outcomes Pre and Post WHEEL intervention

	Intermittent		Persistent	
	Pre-WHEEL n=5	Post-WHEEL n=5	Pre-WHEEL n=5	Post-WHEEL n=4
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
PROMIS Measures				
Pain Intensity	**59 (55-65)**	**52 (50-60)**	65 (60-72)	66 (62-71)
Pain Interference	**67 (62-68)**	**56 (56-65)**	67 (64-67)	64 (60-67)
Self-Efficacy: Medications	41 (36-41)	44 (39-46)	**48 (43-54)**	**53 (46-58)**
Self-Efficacy: Symptoms	44 (43-46)	44 (41-48)	43 (37-45)	45 (42-46)
Whole Health Assessment				
Movement and Exercise	30 (25-42)	56 (43-90)	47 (38-65)	63 (40-75)
Nutrition	50 (50-50)	70 (45-70)	55 (46-67)	70 (58-80)
Rest	20 (10-25)	50 (35-75)	32 (15-44)	33 (25-45)
Purpose and Meaning in Life	74 (70-75)	80 (54-90)	89 (54-100)	82 (44-98)
Stress	40 (29-60)	80 (47-80)	69 (34-100)	70 (34-95)
Physical environment	80 (70-100)	100 (83-100)	99 (74-100)	92 (77-100)
Relationships	80 (50-90)	80 (50-95)	90 (72-100)	100 (90-100)
Personal and Professional Goals	70 (50-80)	60 (56-86)	60 (48-80)	39 (23-66)
Lupus Medications	85 (75-90)	87 (84-90)	100 (98-100)	100 (96-100)
Trust in healthcare	94 (80-95)	94 (84-95)	100 (95-100)	99 (82-100)

Scoring: Scoring for PROMIS Pain Measures: High score = more pain. Scoring for PROMIS Self-Efficacy: High score = more self-efficacy. Whole Health Assessment scored 0-100 with higher score = better. Bolded scores indicate statistically significant improvements.

Program fidelity was high (98%). Participants reported excellent program satisfaction (96%) and provided overwhelmingly positive feedback (Table 1).

Post-WHEEL, PROMIS pain intensity and pain interference scores improved in SLE-I, while PROMIS medication self-efficacy improved in SLE-P (Table 2). Both cohorts reported gains in Whole Health nutrition and movement/activity; SLE-I additionally showed improvement in rest, purpose, stress, and environment, whereas SLE-P improved in relationships.

Conclusion: The WHEEL program was developed to improve quality of life in SLE. User testing demonstrated strong accrual, retention, acceptance, fidelity, and satisfaction. Participants progressed toward personal health goals and exhibited improvement across several outcome domains. Findings support the feasibility of a multi-modal, whole health approach for SLE and are informing adaptations of the WHEEL program.

Disclosure: J. Rogers: AstraZeneca, 1, 1, Aurinia, 2, 5, Exagen, 5, Immunovant, 2, 5; **A. Eudy**: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **C. Drake**: ZealCare, 12, 10; **T. Somers**: None; **D. Pisetsky**: Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **C. Clipper**: None; **R. Snyderman**: DNAnexus, 4, Heartland Whole Health Institute, 4, iRhythm Technologies, 4, OrthoTheapeutics, Inc., 1, ZealCare, 4; **A. Batsakes**: None; **L. Saner**: None; **D. Burshell**: Immunovant, 5; **M. Maheswaranathan**: AstraZeneca, 2, UCB, 2; **L. Criscione-Schreiber**: UCB, 5; **R. Sadun**: The Expert Institute, 12,; **N. Harris**: None; **K. Sun**: Aurinia, 2; **K. Dunn**: None; **J. Herndon**: None; **V. Jacobs**: None; **M. Clowse**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1488

Limited Concordance Between anti-dsDNA Assays and Association with Lupus Nephritis

Jessica Dai[1], Peter Izmirly[2], Jill Buyon[3] and H Michael Belmont[4], [1]New York University Grossman School of Medicine, Tenafly, NJ, [2]New York University Grossman School of Medicine, New York, NY, [3]NYU Grossman School of Medicine, New York, NY, [4]NYU School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-dsDNA antibodies are a key diagnostic marker of systemic lupus erythematosus (SLE), often associated with active disease. Its presence is detected using various commercial assays including enzyme-linked immunosorbent assay (EIA), multiplexed flow immune assay (MFIA) and the Crithidia lucilae immunofluorescence assay (CLIFT), which differ in sensitivity, specificity and methodology. This variability complicates interpretation of anti-dsDNA results in relation to disease activity. Using a multiethnic, longitudinal SLE cohort, the analysis compares anti-dsDNA measurements by CLIFT, EIA and MFIA with disease activity.

Methods: Patients with SLE from Bellevue Hospital Center were included. All patients fulfilled SLE criteria by at least one method: American College of Rheumatology (ACR), Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) and/or 2019 ACR/European League Against Rheumatism (EULAR) classification criteria. A change in commercial anti-dsDNA antibody testing from enzyme immunoassay (EIA) to multiplex flow immunoassay (MFIA) on April 1, 2024, served as a natural point for analysis. Patients with anti-dsDNA results by EIA, CLIFT and MFIA within one year before and after this transition were identified. Titre and concordance or discordance among assays and association with ACR criteria lupus nephritis (LN) were analyzed.

Results: Of the 135 patients with SLE, 50% were Hispanic, 30% were Black, 17% were Asian, and 4% were unknown. Paired testing with EIA and CLIFT was performed in 103 patients, and MFIA and CLIFT in 104 patients. Comparison between CLIFT and EIA revealed that 57% of patients had consistently concordant results, 31% showed fluctuating concordance, and 12% were consistently discordant (Figure 1). Similarly, 60% of patients had concordant results between CLIFT and MFIA, 13% fluctuated, and 27% were consistently discordant. Following the transition from EIA to MFIA in April, 109 patients demonstrated concordant results between EIA and MFIA, while 26 had discordant findings. Among 68 patients with ACR criteria LN, 20 tested positive by EIA, 22 by MFIA and 29 by CLIFT. The specificity and sensitivity for detecting LN were 77% and 26% for EIA, 73% and 32% for MFIA, and 47% and 47% for CLIFT, respectively.

Conclusion: This cohort demonstrates that current anti-dsDNA antibody testing using CLIFT, in conjunction with EIA or MFIA shows limited concordance. Despite EIA and MFIA being similar immunoassays, 23% of patients exhibited discordant results following the laboratory decision to change assay. In our cohort, CLIFT had the lowest specificity for identifying patients with LN. Moreover, failing to identify anti-dsDNA antibody positive status by restricted method testing can have

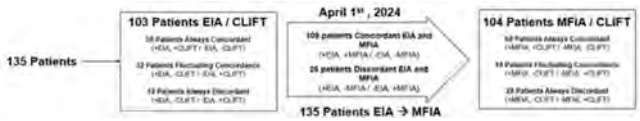


Figure 1. Flow diagram illustrating concordance and discordance of EIA and CLIFT or MFIA and CLIFT as well as the transition from EIA to MFIA immunoassays.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

an impact on meeting SLE disease classification criteria and/or accurately determining disease activity. These findings suggest incorporating multiple dsDNA antibody assays may enhance the accuracy of SLE classification and ensure more reliable assessment of disease activity during routine monitoring.

Disclosure: J. Dai: None; **P. Izmirly**: Hansoh Bio, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **H. Belmont**: None.

Abstract Number: 1489

Impact of Menopause on Long-Term Outcomes in Patients with Systemic Lupus Erythematosus

Lorena López, **José Bretón** and Luis Vilá, University of Puerto Rico Medical Sciences Campus, San Juan, PR

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Women of childbearing age are more prone to developing autoimmune diseases, suggesting a role for sex hormones, particularly estrogens, in regulating both cellular and humoral immunity. During menopause, estrogen levels decline significantly, which may affect the immune system and, in turn, influence clinical outcomes in systemic lupus

Table 1. SLE manifestations, disease activity, disease damage, lupus pharmacologic treatment, comorbidities, disease exacerbations, and hospitalizations (n=43).

	Pre-menopausal period	Post-menopausal period	p-value
SLE manifestations, %			
Malar rash	69.8	25.6	<0.001
Discoid rash	4.6	4.6	>0.999
Oral ulcers	65.1	23.3	<0.001
Photosensitivity	86.0	55.8	0.002
Arthritis	67.4	65.1	>0.999
Serositis	9.3	2.3	0.164
Renal involvement	46.5	27.9	0.075
Neurological involvement	48.8	23.2	0.013
Anemia	34.9	6.9	0.003
Leukopenia	46.5	16.3	0.004
Lymphopenia	55.8	28.5	0.010
Thrombocytopenia	18.6	4.65	0.043
Serology, %			
Low C3 complement	44.1	14.1	0.002
Low C4 complement	41.9	14.1	0.004
Elevated anti-dsDNA antibodies	76.7	16.2	<0.001
SLEDAI*, mean score (SD)	7.8 (4.7)	3.7 (2.9)	<0.001
SDI, mean score (SD)	0.6 (1.0)	0.9 (1.1)	0.241
SLE treatment, %			
Glucocorticoids	95.3	67.4	0.005
Hydroxychloroquine	90.7	69.8	0.016
Mycophenolate mofetil	20.9	41.9	0.034
Azathioprine	32.6	16.2	0.081
Methotrexate	14.0	9.3	0.521
Tacrolimus	9.3	18.6	0.222
Cyclophosphamide	18.6	4.7	0.050
Rituximab	2.3	0.0	>0.999
Selected comorbidities, %			
Arterial hypertension	65.1	11.6	<0.001
Diabetes mellitus	16.3	14.0	0.765
Dyslipidemia	23.3	16.2	0.414
Hypothyroidism	14.0	11.6	0.755
Malignancy	0.0	14.0	<0.001
SLE flare not requiring hospitalization, %	34.9	16.3	0.082
SLE flare requiring hospitalization, %	0.0	4.7	0.454
Hospitalization (any cause), %	65.1	79.0	0.229

*Highest yearly score was used to calculate mean. SLE: Systemic lupus erythematosus; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SD: Standard deviation; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

erythematosus (SLE). However, the impact of menopause on patients with SLE has not been widely studied. Therefore, we aimed to assess the long-term outcomes of SLE patients after menopause.

Methods: A retrospective cohort study was conducted involving women with SLE, classified according to the 1997 revised American College of Rheumatology criteria, from a university-based center in Puerto Rico who had undergone menopause. The premenopausal and postmenopausal periods were compared in terms of SLE manifestations, disease activity (assessed using the Systemic Lupus Erythematosus Disease Activity Index), damage accrual (measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index), incident comorbidities, disease exacerbations, and hospitalizations. Variables were evaluated annually before and after menopause. Paired analyses were used to compare outcomes between the premenopausal and postmenopausal periods.

Results: Out of 309 female patients, 80 were identified as postmenopausal. Thirty-seven were excluded due to hysterectomy prior to menopause, SLE diagnosis at or after menopause, or an unclear date of menopause. A total of 43 patients were included in the analysis. The mean (standard deviation [SD]) ages at SLE diagnosis, menopause, and last visit were 33.6 (9.1), 46.5 (5.6), and 57.2 (9.0) years, respectively. The mean (SD) durations of SLE before and after menopause were 13.7 (10.9) and 12.0 (6.5) years, respectively. Table 1 summarizes the data for the 43 postmenopausal women included in the analysis. Compared to the premenopausal period, the postmenopausal period was associated with significantly lower frequencies of malar rash, photosensitivity, neurologic involvement, anemia, leukopenia, lymphopenia, and thrombocytopenia. These patients also had significantly lower disease activity and reduced exposure to glucocorticoids and hydroxychloroquine compared to the premenopausal period. While the occurrence of arterial hypertension was more frequent in the premenopausal period, new-onset malignancy was more common in post menopause. No significant differences in damage accrual were observed between the two periods.

Conclusion: In this cohort of patients with SLE, the postmenopausal period was associated with a significant decrease in disease activity and clinical manifestations—particularly mucocutaneous, neurologic, and hematologic involvement—as well as reduced exposure to glucocorticoids and hydroxychloroquine. These findings suggest that the hormonal changes accompanying menopause may influence the long-term course of SLE.

Disclosure: L. López: None; **J. Bretón**: None; **L. Vilá**: None.

Abstract Number: 1490

Vitamin D Deficiency and Its Relationship with Inflammatory Biomarkers in SLE: A Focus on Neutrophil-to-Lymphocyte Ratio

judith hernández-Sánchez[1], Beatriz Tejera Segura[2], Luis Bausá Gimeno[1], Doryan García Olivas[1], Patricia González Terrats[1], MA Acosta Mérida[1], Diana Botello Corzo[1], Daniel Batista perdomo[1], Sergio Machin González[1], F Javier Nóvoa Medina[1] and Jose Angel Hernandez[3], [1]Rheumatology Department. Hospital Universitario Insular de Gran Canaria, Las palmas, Spain, [2]Hospital Insular de Gran Canaria, Las palmas, Spain, [3]Hospital Universitario Insular de Gran Canaria, Las Palmas de Gran CanariaHospital, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of SLE patients and their association with serum vitamin D leves

Variables	Vitamin D (median ±standard desviation)	P value
Age	52 ±12.7	0.86
Sex		
- Female	31.4±10,4	0.286
- Male	27.5±7.75	
Clinical manifestations		
- Neuropsychiatric	**No:** 31.1±10.1 **Yes:** 30.9±11.9	0.661
- Serositis	31±10.5 vs 31.3±8.9	0.687
- Renal disease	31.2±10.7 vs 30.5±9.31	0.757
- Arthritis	32±9.5 vs 30.9±10.4	0.511
- Skin disease	32.8±10.2 vs 30.4±10.2	0.514
- Haematological disease	31.7±11 vs 30.3±9.4	0.409
- APS	30.4±9.5 vs 34.8±13.2	0.120
Treatments		
- HCQ	34.7±11.2 vs 30.3±9.9	0.857
- DMARDs	30.9±11.5 vs 31.2±9.5	0.651
- Biological treatment	31.4±10.5 vs 30.2±9.6	0.825
- Prednisone	30.6±10.2 vs 33±10.4	0.228
Comorbidities		
- Smoker	31.4±9.9 vs 27.4±13.3	**0.070**
- Hypertension	32.4±9.2 vs 29.5±11.2	0.083
- Dyslipemia	31.2±8.7 vs 30,7±13	0.571
- Diabetes	31.6±9.5 vs 25.8±14.9	**0.048**
SLEDAI -2K	1.6±2.4	0.777
Organ Damage**	33.3±9.8 vs 28.6±10.2	**0.008**
Neutrophil-lymphocyte ratio	2.4±3.24	**0.024**
Platelet-lymphocyte ratio	168±104.2	0.406

*APS : antiphospholipid syndrome
*HCQ: Hydroxychloroquine
*SLEDAI-2K: Systemic Lupus Erythematosus Systemic Index 2000
**Organ damage measured by SLICC/ACR damage index

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect multiple organs. Vitamin D levels have been associated with disease activity in SLE, and the neutrophil-to-lymphocyte ratio (NLR) has emerged as a potential marker of inflammation in autoimmune conditions, including SLE. However, the relationship between vitamin D and NLR in SLE patients remains unclear and requires further investigation.

Objective: To evaluate the association between serum vitamin D levels and the neutrophil-to-lymphocyte ratio (NLR) in patients with SLE.

Methods: We performed a cross-sectional study including 188 patients with systemic lupus erythematosus (SLE), recruited from a specialized outpatient clinic. All individuals met the 2019 EULAR/ACR classification criteria for SLE. Clinical and laboratory data were extracted from electronic medical records (SLEDAI-2K scores, comorbidities, current treatments, and serum 25-hydroxyvitamin D [25(OH)D] levels. The NLR was calculated using absolute counts from complete blood counts obtained on the same day. Data distribution was assessed using the Kolmogorov–Smirnov test. Group comparisons were performed using the Student's t-test or Mann–Whitney U test, as appropriate. The relationship between vitamin D levels and NLR was evaluated through Spearman's rank correlation and multivariable linear regression, adjusting for potential confounders. Statistical significance was set at $p < 0.05$. Analyses were conducted using STATA MP-Parallel Edition 17.0.

Results: The description of the main demographic, clinical, comorbidity, and analytical variables, along with their association with vitamin D levels (treated as a continuous variable), is presented in **Table 1**. Serum vitamin D levels were inversely correlated with NLR ($r = –0.195$; $p = 0.024$). Patients with organ damage had significantly lower vitamin D levels compared to those without (28.6 ± 10.2 vs. 33.3 ± 9.8 ng/mL; $p = 0.008$). A trend toward lower vitamin D levels was observed in patients with diabetes ($p = 0.048$). No significant differences were found regarding disease activity, sex, or other clinical manifestations. In the multivariable regression analysis, log-transformed vitamin D was significantly negatively associated with NLR (coef. -1.40, $p = 0.002$), indicating that higher vitamin D levels are linked to lower NLR. However, no significant associations were found between NLR and other variables sex, age, disease activity (SLEDAI2K), or organ damage (**Table 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Linear Regression Analysis of Factors Associated with Neutrophil-to-Lymphocyte Ratio in Systemic Lupus Erythematosus Patients

Variable	Coefficient (β)	Standard Error (SE)	t-value	p-value	95% Confidence Interval
Log(Vitamin D)	**-1.40**	**0.45**	**-3.11**	**0.002**	**(-2.29, -0.51)**
Sex (Male vs. Female)	-0.50	0.57	-0.87	0.39	(-1.63, 0.64)
Age (years)	-0.01	0.01	-0.86	0.39	(-0.04, 0.01)
SLEDAI-2K (Disease Activity)	0.09	0.07	1.38	0.17	(-0.04, 0.22)
Organ Damage	0.19	0.33	0.58	0.56	(-0.47, 0.85)

Conclusion: Vitamin D levels are inversely associated with the neutrophil-to-lymphocyte ratio in SLE patients, suggesting that vitamin D may play a role in immune modulation. Further research is necessary to explore the potential therapeutic effects of vitamin D in lupus management.

Disclosure: j. hernández-Sánchez: None; **B. Tejera Segura**: None; **L. Bausá Gimeno**: None; **D. García Olivas**: None; **P. González Terrats**: None; **M. Acosta Mérida**: None; **D. Botello Corzo**: None; **D. Batista perdomo**: None; **S. Machin González**: None; **F. Nóvoa Medina**: None; **J. Hernandez**: None.

Abstract Number: 1491

Feasibility of Extrarenal Systemic Lupus Erythematosus Disease Modification in GLADEL 2.0, a Latin American Cohort

julián Barahona-correa[1], Santiago Bernal-Macías[2], Daniel Fernandez[3], Óscar Muñoz[2], Lucia Hernández[4], Erika Susana Palacios Santillan[5], Laura Maurelli[6], Paula Alba[7], Veronica Saurit[8], Lucila Garcia[9], María Emilia Sattler[10], Maria Constanza Bertolaccini[11], Marina Laura Micelli[12], Graciela Gomez[13], Micaela A. Cosatti[14], Ana Carolina Ralle[15], Joaquín Martinez Serventi[16], Ana Silva[17], ODIRLEI MONTICIELO[18], Ángela Luzia Branco Pinto Duarte[19], Laíssa Cristina Alves Alvino[20], Eduardo Borba[21], Eloisa Bonfa[21], Edgard dos Reis-Neto[22], Iris Guerra Herrera[23], Milena Mimica[24], Gustavo Aroca Martínez[25], Lorena Gómez Escorcia[26], Carlos Alberto Caas[27], Gerardo Quintana-Lopez[28], Carlos Toro-Gutierrez[29], José Maximiliano Martínez Pérez[30], Reyna Elizabeth Sánchez-Briones[31], Mario Pérez Cristóbal[32], Eduardo Martin-Nares[33], Yaneli Juarez-Vicuña[34], Ignacio García-Valladares[35], Rodrigo Ortiz Hernández[36], Jorge Antonio Esquivel Valerio[37], Maria Isabel Acosta[38], Astrid Paats[39], Jorge Cieza Calderón[40], Manuel Ugarte-Gil[41], Armando Calvo[42], Rodamin Ambiorix Alvarez Santana[43], Analía Cánepa[44], Carina Pizzarossa[44], Federico Zazzetti[45], Ashley Orillion[46] and Cristina Drenkard[47] on behalf of Grupo Latino Americano De Estudio de Lupus (GLADEL). Study Group of PANLAR, [1]Colombian Association of Rheumatology (ASOREUMA), Bogotá, Colombia; Hospital Universitario San Ignacio, Bogotá, Colombia, Bogotá, Colombia, [2]Hospital Universitario San Ignacio, Bogotá, Colombia, Bogotá, Colombia, [3]Facultad de Medicina, Pontificia Universidad Javeriana, Bogotá, Colombia; Departamento de Medicina Interna, Unidad de Reumatología, Hospital Universitario San Ignacio, Bogotá, Colombia, BOGOTA, Colombia, [4]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina, Rosario, Argentina, [5]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, Buenos Aires, Argentina, [6]Hospital Italiano de Córdoba, Córdoba, Argentina, Córdoba, Argentina, [7]Hospital Córdoba y Sanatorio Allende, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Córdoba, Argentina, Cordoba, Argentina, [8]Hospital Privado Universitario de Cordoba, Córdoba, Argentina, Crdoba, Argentina, [9]Hospital San Martin de La Plata, La Plata, Argentina, La Plata, Argentina, [10]Sanatorio Británico, Rosario, Argentina, Rosario, Argentina, [11]Hospital Ángel C. Padilla, Tucumán, Argentina, Tucumán, Argentina, [12]Hospital J.M Ramos Mejía, Buenos Aires, Argentina, Buenos Aires, [13]Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires, Buenos Aires, Argentina, Buenos Aires, Argentina, [14]CEMIC Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno," Buenos Aires, Argentina, Buenos Aires, Argentina, [15]Hospital Señor del Milagro Salta, Salta, Argentina, Salta, Argentina, [16]Hospital General de Agudos Dr. Juan A. Fernández, Buenos Aires, Argentina, Buenos Aires, Argentina, [17]Hospital das Clinicas da Universidade Federal de Goias, Goiania, Brazil, Goiania, Brazil, [18]Hospital de Clínicas de Porto Alegre, Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil, PORTO ALEGRE, Rio Grande do Sul, Brazil, [19]Universidad Federal de Pernambuco, Recife, Brazil, Recife, Brazil, [20]Hospital Universitário Pedro Ernesto -

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, Rio de Janeiro, Brazil, [21]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, So Paulo, Brazil, [22]Escola Paulista de Medicina / Universidade federal de São Paulo (EPM / Unifesp), São Paulo, Brazil, So Paulo, Brazil, [23]Hospital del Salvador Santiago de Chile, Santiago, Chile, Santiago, Chile, [24]Facultad de Medicina y Ciencia, Universidad San Sebastián, Santiago, Chile, Santiago, Chile, [25]Universidad Simón Bolívar, Barranquilla, Colombia y Clínica de la Costa, Barranquilla, Colombia, [26]Clínica de la Costa y Universidad Simón Bolívar Barranquilla, Barranquilla, Colombia, Barranquilla, Colombia, [27]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia, Cali, Colombia, [28]Facultad de Medicina, Universidad Nacional de Colombia; Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogotá, Colombia, [29]Pontificia Universidad Javeriana de Cali, Cali, Colombia, Cali, Colombia, [30]Universidad de Especialidades Espíritu Santo, Guayaquil, Ecuador, Guayaquil, Ecuador, [31]Hospital de Especialidades Dr. Antonio Fraga Mouret, Centro Médico Nacional La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico, Mexico City, Mexico, [32]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico, Mexico City, Mexico, [33]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico, [34]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [35]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, Guadalajara, Mexico, [36]Facultad de Medicina de la Universidad Autónoma de San Luis Potosí y Hospital Central "Dr. Ignacio Morones Prieto," San Luis Potosi, Mexico, San Luis Potosi, Mexico, [37]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [38]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asuncion, Paraguay, [39]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asuncin, Paraguay, [40]Hospital Nacional Edgardo Rebagliati Martins-EsSalud, Lima, Peru, Lima, Peru, [41]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [42]Hospital Nacional Cayetano Heredia Universidad Peruana Cayetano Heredia, Lima, Peru, Jess Mara, Peru, [43]Hospital Docente Padre Billini, Santo Domingo, Distrito Nacional, Dominican Republic, [44]Hospital de Clínicas, Facultad de Medicina, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [45]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [46]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [47]Rollins School of Public Health, Emory University, Atlanta, Georgia, USA, Acworth, GA

Table 1. Baseline sociodemographics and their differences among patients with SLE who did and did not achieve extrarenal disease modification over time

		Extra Renal Disease Modification at each Time Point					
	Month 12 (N=709)		Month 24 (N=663)		Month 36 (N=482)		Month 48 (N=372)	
Baseline Descriptor	Yes (N=111)	No (N=598)	Yes (N=115)	No (N=548)	Yes (N=92)	No (N=390)	Yes (N=73)	No (N=299)
Age at diagnosis, years, median (IQR)	26 (19-33.5)	27 (20-36)	27 (20-36)	26 (20-34)	27 (21-37)	26 (20-33)	29 (21-39)	27 (20-35)
Age at enrollment, years, median (IQR)	33 (25.5-42)	36 (27-45)	33 (27-42)	36 (28-46)	34.5 (27.5-44)	36 (28-46)	35 (29-45)	36 (29-47)
Sex at birth, n (%)								
Female	104 (93.7%)	534 (89.3%)	101 (87.8%)	496 (90.5%)	**75 (81.5%)**	**329 (92.1%)**	**59 (80.8%)**	**280 (91.5%)**
Male	7 (6.3%)	64 (10.7%)	14 (12.2%)	52 (9.5%)	**17 (18.5%)**	**25 (7.9%)**	**14 (19.2%)**	**26 (8.5%)**
Ethnicity, n (%)								
White	30 (27.3%)	183 (30.8%)	37 (32.5%)	153 (28.1%)	24 (26	109 (29.7%)	23 (31.5%)	94 (31.1%)
Mestizo	68 (61.8%)	363 (61.1%)	71 (62.3%)	344 (63.2%)	56 (61.5%)	226 (62.8%)	43 (58.9%)	183 (60.6%)
African Latin American	12 (10.9%)	47 (7.9%)	6 (5.2%)	47 (8.6%)	11 (12.1%)	26 (7.7%)	7 (9.6%)	25 (8.3%)
Other		1 (0.2%)						
Country of birth, n (%)								
Argentina	35 (31.5%)	193 (32.3%)	36 (31.3%)	151 (27.6%)	30 (32.6%)	107 (26.1%)	21 (28.8%)	68 (29.1%)
Brazil	21 (18.9%)	128 (21.4%)	26 (22.6%)	125 (22.8%)	25 (31.8%)	72 (19.8%)	20 (27.4%)	64 (20.9%)
Chile	2 (1.8%)	23 (3.8%)	2 (1.7%)	22 (4%)	-	14 (3.8%)	-	5 (1.8%)
Colombia	18 (16.2%)	40 (6.7%)	6 (5.2%)	31 (5.7%)	2 (2.2%)	16 (4.3%)	4 (5.5%)	21 (6.9%)
Dominican Republic	4 (3.6%)	15 (2.5%)	2 (1.7%)	12 (2.2%)	3 (3.3%)	9 (2.4%)	2 (2.7%)	8 (2.6%)
Ecuador	2 (1.8%)	12 (2%)	1 (0.9%)	8 (1.5%)	-	8 (2.2%)	-	4 (1.3%)
Honduras	-	1 (0.2%)	-	-	-	-	-	-
Mexico	15 (13.5%)	81 (13.5%)	15 (13%)	66 (12.1%)	15 (16.3%)	55 (14.9%)	19 (26%)	52 (17%)
Paraguay	4 (3.6%)	43 (7.2%)	8 (7%)	34 (6.2%)	7 (7.6%)	26 (7.1%)	1 (1.4%)	16 (5.2%)
Peru	7 (6.3%)	27 (4.5%)	11 (9.6%)	44 (8%)	3 (3.3%)	34 (9.2%)	3 (4.1%)	30 (9.8%)
Uruguay	3 (2.7%)	33 (5.5%)	7 (6.1%)	32 (5.8%)	3 (3.3%)	27 (7.3%)	3 (4.1%)	17 (5.6%)
Venezuela	-	2 (0.3%)	1 (0.9%)	1 (0.2%)	-	-	-	-
Marital status, n (%)								
Married-Concubine	48 (46.5%)	247 (43%)	55 (48.7%)	233 (43.3%)	41 (46.6%)	154 (42.7%)	31 (44.9%)	133 (44.9%)
Separated-Divorced	4 (3.8%)	38 (6.6%)	7 (6.2%)	37 (6.9%)	7 (7.9%)	28 (7.8%)	6 (8.7%)	20 (6.8%)
Single	50 (54.1%)	281 (49%)	49 (43.4%)	260 (48.3%)	40 (44.4%)	175 (48.5%)	30 (43.5%)	139 (47%)
Widow	2 (1.9%)	6 (1.4%)	2 (1.8%)	8 (1.5%)	2 (2.2%)	4 (1.1%)	2 (2.9%)	4 (1.4%)
Education, years, median (IQR)	**14 (11-16)**	**13 (11-16)**	**14 (11-16)**	**13 (11-16)**	**12.5 (11-16)**	**13 (11-16)**	**12 (11-16)**	**13 (11-16)**
Employment status, n (%)								
Full/Partial Work	**52 (45.5%)**	**322 (56.3%)**	51 (55%)	293 (54.7%)	41 (46.1%)	207 (56%)	36 (53.9%)	165 (56.7%)
Retired	**2 (1.7%)**	**33 (5.8%)**	3 (2.7%)	23 (4.4%)	4 (4.5%)	20 (5.8%)	6 (8.5%)	19 (6.4%)
Student	**19 (17.1%)**	**55 (9.7%)**	13 (11.7%)	52 (10.1%)	12 (13.5%)	29 (8.1%)	4 (5.8%)	24 (8.1%)
Unemployed	**33 (31.4%)**	**156 (27.6%)**	34 (30.8%)	159 (30.8%)	32 (36%)	101 (28.3%)	23 (32.4%)	88 (29.7%)
Socioeconomic status, n (%)								
High	2 (1.9%)	16 (2.7%)	4 (3.5%)	13 (2.4%)	**5 (5.5%)**	**9 (2.4%)**	4 (5.6%)	11 (3.6%)
Middle high	18 (16.7%)	131 (22.3%)	21 (18.6%)	119 (22.1%)	**11 (12.1%)**	**87 (23.6%)**	10 (14.1%)	84 (30.9%)
Middle	43 (39.8%)	200 (34%)	46 (40.5%)	176 (33.1%)	**31 (34.1%)**	**130 (35.2%)**	27 (38%)	124 (40.8%)
Middle low	31 (28.7%)	175 (29.8%)	24 (21.2%)	170 (31.6%)	**28 (30.8%)**	**107 (29.1%)**	26 (36.2%)	84 (27.6%)
Low	14 (13%)	66 (11.2%)	18 (14.2%)	58 (10.8%)	**16 (17.6%)**	**35 (9.5%)**	10 (14.1%)	23 (7.5%)
Medical coverage, n (%)								
Full coverage	66 (66%)	299 (50.7%)	64 (57.7%)	297 (54.6%)	**44 (49.4%)**	**215 (59.1%)**	39 (54.9%)	186 (61.4%)
Partial coverage	14 (12.7%)	85 (14.4%)	11 (9.9%)	75 (13.8%)	**8 (9%)**	**50 (13.4%)**	13 (18.3%)	45 (14.9%)
Without coverage	30 (27.3%)	206 (34.9%)	36 (32.4%)	172 (31.6%)	**37 (41.6%)**	**93 (25.5%)**	19 (26.8%)	72 (23.8%)

Composite definition of extrarenal SLE disease modification. Included: (i) a significant reduction in SLEDAI (>3 points), (ii) none severe flares, and (iii) ≤10 mg/day of prednisone for months 0-12 and ≤5 mg/day prednisone-equivalent for years 2-5. Values presented in bold represent significant differences of baseline descriptors between disease modification groups at the corresponding time point (p<0.05). The number of patients decreased at each time point due to either insufficient time in the cohort or loss of follow-up. Comparisons were performed using a Chi-squared test for qualitative variables or a non-parametric t-test for continuous variables. Abbreviations: IQR, interquartile range.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The concept of disease modification (DM) has been recently introduced to improve the long-term care of patients (pts) with SLE. DM is defined as 'the minimization of disease activity with the fewest treatment (tx)-associated toxicities and slowing/preventing organ damage progression.' To claim DM ultimately requires delayed or prevented progression of organ damage beyond 5 years. The concept of DM is valuable for assessing 'whether an intervention is on track for achieving DM at the 5-year mark,' based on interim evaluations during the first 5 years. Latin American pts with SLE are prone to poorer outcomes, which are associated with both disease severity and social determinants of health (SDH). This preliminary study evaluates the prevalence of extrarenal DM in Latin American pts with SLE and examines differences in SDH and tx between those who did and did not achieve extrarenal DM.

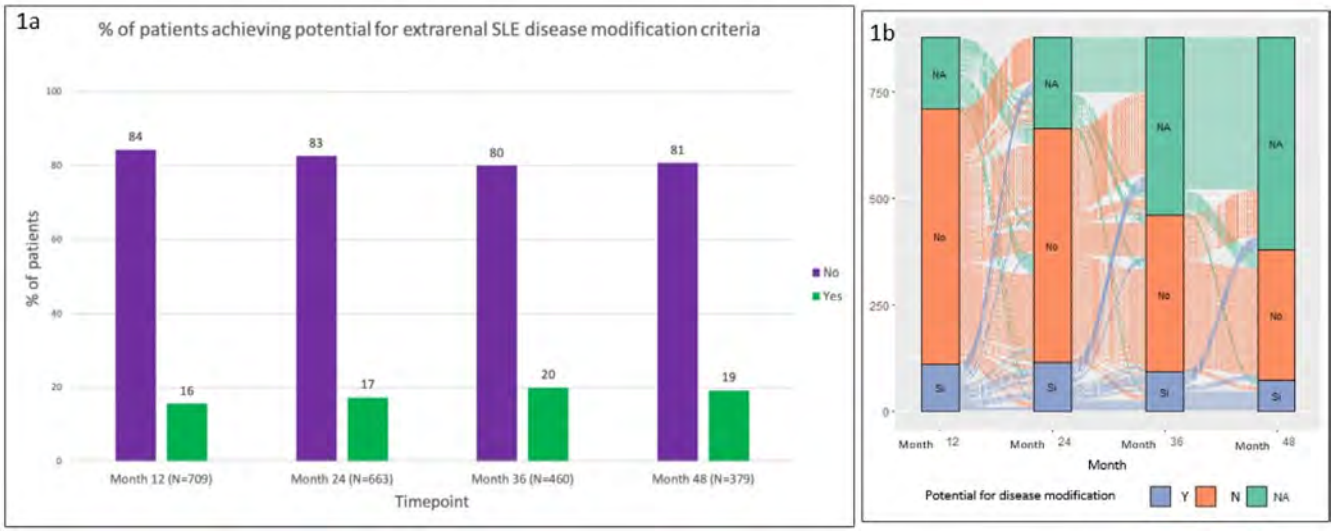


Figure 1. Percentage of patients achieving potential for extrarenal SLE disease modification (A) and disease modification trajectory (B)

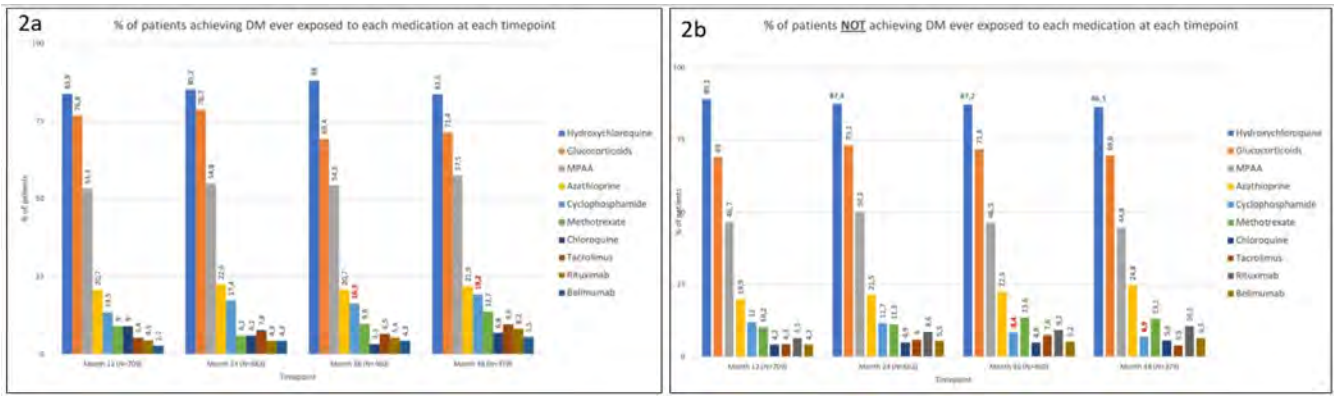


Figure 2. Medication exposure in patients who did (A) and (B) did not achieve DM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: GLADEL 2.0 is a longitudinal cohort assessing the incidence and prevalence of SLE. Forty-three centers from 10 Latin-American countries enrolled pts ≥18 years of age who fulfilled the 1982/1997 ACR and/or the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE. The composite definition of DM for extrarenal SLE included: (i) a significant reduction in SLE Disease Activity Index (SLEDAI; >3 points), (ii) no severe flares, and (iii) ≤10 mg/day of prednisone for months 0–12 and ≤5 mg/day prednisone-equivalent for years 2–5. Pts with complete data at baseline, 12, 24, 36, 48, and 60 months were analyzed. We compared baseline SDH and exposure to medications between pts who did and did not achieve DM criteria over time.

Results: Among 1083 pts who entered the GLADEL 2.0 cohort, 709 had the baseline data needed to fulfill DM criteria. Table 1 shows differences in demographic and SDH data by extrarenal DM achievement groups over time. Data from month 60 were not analyzed as data were available for only 64 pts. Although educational attainment varied between groups and genders at each time point, a higher proportion of pts achieved DM among men compared to women at the 36 and 48-month marks. Overall, the proportion of pts achieving DM criteria ranged between 16%–20% across time points (Fig 1a). Figure 1b shows DM trajectories during follow-up. Medication exposure is depicted in Fig 2. A higher number of pts achieving extrarenal DM at months 36 and 48 received cyclophosphamide.

Conclusion: In this preliminary investigation, up to 20% of Latin American pts with SLE achieved extrarenal DM. The study highlights critical disparities, indicating that pts with lower educational attainment and women were less likely to achieve DM. Our findings suggest that specific medication exposure plays a significant role in extrarenal DM achievement, particularly with medications like cyclophosphamide. These results underscore the importance of addressing SDH and tailoring tx strategies to improve outcomes for marginalized groups within this population. Continued research is essential to discern the independent contributions of SDH and different tx modalities on achieving extrarenal DM, ultimately aiming to enhance long-term care and pt quality of life.

Disclosure: j. Barahona-correa: Colombian Association of Rheumatology (ASOREUMA), 12, Supported by the Colombian Association of Rheumatology (ASOREUMA); **S. Bernal-Macías**: None; **D. Fernandez**: None; **Ó. Muñoz**: None; **L. Hernández**: None; **E. Palacios Santillan**: None; **L. Maurelli**: None; **P. Alba**: None; **V. Saurit**: None; **L. Garcia**: None; **M. Sattler**: None; **M. Bertolaccini**: None; **M. Micelli**: None; **G. Gomez**: None; **M. Cosatti**: None; **A. Ralle**: None; **J. Serventi**: None; **A. Silva**: AstraZeneca, 6, GSK, 6; **O. MONTICIELO**: None; **Á. Duarte**: None; **L. Alves Alvino**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. dos Reis-Neto**: None; **I. Guerra Herrera**: None; **M. Mimica**: None; **G. Aroca Martínez**: None; **L. Gómez Escorcia**: None; **C. Casas**: None; **G. Quintana-Lopez**: None; **C. Toro-Gutierrez**: None; **J. Martínez Pérez**: None; **R. Sánchez-Briones**: None; **M. Pérez Cristóbal**: None; **E. Martin-Nares**: None; **Y. Juarez-Vicuña**: None; **I. García-Valladares**: None; **R. Hernández**: None; **J. Esquivel Valerio**: None; **M. Acosta**: None; **A. Paats**: None; **J. Calderón**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **A. Calvo**: None; **R. Alvarez Santana**: None; **A. Cánepa**: None; **C. Pizzarossa**: None; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **C. Drenkard**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1492

Prevalence and Risk Factors of Gynecologic Cancers in Female Patients with Systemic Lupus Erythematosus

Katherine Moseley[1], Dulaney Wilson[2], Emily Vara[1] and Diane Kamen[3], [1]Medical University of South Carolina, Charleston, SC, [2]Medical University of South Carolina, Charleston, [3]Medical University of South Carolina, Johns Island, SC

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic systemic autoimmune disorder that is nine times more prevalent in women. Patients with SLE are at an overall increased risk of cancer and may additionally have an increased risk of specific female reproductive cancers. This increase in cancer risk may be attributed to factors such as chronic inflammation, immunosuppression with decreased clearance of oncogenic viral infections, or treatment medication exposure. Our objective was to investigate if specific SLE clinical disease characteristics and sociodemographic factors are associated with gynecologic cancer in female patients with SLE.

Table 1. Baseline Demographic Characteristics and Cancer Prevalence for Female SLE Patients and Controls

Characteristics	SLE Patients n = 800 (%)	Controls n = 499 (%)	p-value
Age at Baseline Visit			0.61
0 to 17	54 (6.8)	29 (5.8)	
18 to 30	204 (25.5)	111 (22.2)	
30 to 40	163 (20.4)	105 (21.0)	
40 to 50	181 (22.6)	114 (22.8)	
50 to 60	119 (14.9)	89 (17.8)	
60+	79 (9.9)	51 (10.2)	
Race			**<0.001**
Black	576 (72.0)	441 (88.4)	
White	193 (24.1)	58 (11.6)	
Other	31 (3.9)	0 (0.0)	
Ethnicity			**0.006**
Hispanic	25 (3.1)	4 (0.8)	
Not Hispanic	775 (96.9)	495 (99.2)	
Education			0.40
Less than high school	42 (6.8)	38 (8.5)	
High school graduate	34 (5.5)	19 (4.2)	
College graduate	542 (87.7)	392 (87.3)	
Data not provided	182 (22.8)	50 (10.0)	
Insurance			**<0.001**
Public	255 (37.7)	76 (17.5)	
Private	387 (57.2)	335 (77.0)	
Uninsured	34 (5.0)	24 (5.5)	
Data not provided	124 (15.5)	64 (12.8)	
History of Nicotine Use			0.19
Current use	66 (9.0)	41 (8.9)	
Former use	115 (15.7)	55 (11.9)	
Never	553 (75.3)	365 (79.2)	
Data not provided	66 (8.3)	38 (7.6)	
Cancer Diagnosis			
Any malignancy	68 (8.5)	18 (3.6)	**<0.001**
Gynecologic cancer	14 (1.8)	1 (0.2)	**0.01**
Breast cancer	14 (1.8)	1 (0.2)	**0.01**
Cervical cancer	5 (0.6)	1 (0.2)	0.42

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. SLE Disease Characteristics and Association with Cancer (All or Gynecologic) in Female Patients with SLE

Characteristics	No Cancer n = 732	Any Cancer n = 68		Gynecologic Cancer n = 14	
	Frequency (%) w Associated Characteristic	Frequency (%) w Associated Characteristic	p-value	Frequency (%) w Associated Characteristic	p-value
Age at Baseline Visit (Mean Years)			**<0.001**		**<0.001**
0 to 17	54 (7.4)	0 (0.0)		0 (0.0)	
18 to 30	198 (27.0)	6 (8.8)		3 (21.4)	
30 to 40	153 (20.9)	10 (14.7)		2 (14.3)	
40 to 50	161 (22.0)	20 (29.4)		5 (35.7)	
50 to 60	105 (14.3)	14 (20.6)		4 (28.6)	
60+	61 (8.3)	18 (26.5)		0 (0.0)	
Race			**<0.001**		**<0.001**
Black	545 (74.5)	37 (54.4)		6 (42.9)	
White	156 (21.3)	31 (45.6)		8 (57.1)	
Other	31 (4.2)	0 (0.0)		0 (0.0)	
Nicotine Use History			**0.001**		**0.006**
Current Nicotine Use	61 (9.2)	5 (7.4)		1 (7.1)	
Former Nicotine Use	94 (14.1)	21 (30.9)		3 (21.4)	
Never	511 (76.7)	42 (61.8)		10 (71.4)	
SLE Clinical Characteristics					
Onset of SLE in Childhood (<18yo)	117 (18.5)	7 (11.7)	0.19	2 (14.3)	0.40
SDI Excl. Malignancy (Mean Score)	1.8±2.2	2.4±2.4	0.09	4.2±3.6	**0.04**
High Organ Damage (SDI >=2)	253 (39.0)	38 (59.4)	**0.002**	8 (72.7)	**0.004**
Proliferative Lupus Nephritis	184 (25.1)	10 (14.7)	0.05	2 (14.3)	0.16
Membranous Lupus Nephritis	133 (18.2)	9 (13.2)	0.31	2 (14.3)	0.59
Medication Use (Ever)					
Prednisone	421 (57.5)	42 (61.8)	0.50	10 (71.4)	0.57
Biologic	124 (16.9)	11 (16.2)	0.87	2 (14.3)	0.97
Hydroxychloroquine	609 (83.2)	52 (76.5)	0.16	13 (92.9)	0.07
Azathioprine	238 (32.5)	22 (32.4)	0.98	7 (50.0)	0.29
Mycophenolate	328 (44.8)	31 (45.6)	0.90	7 (50.0)	0.93
Methotrexate	112 (15.3)	11 (16.2)	0.85	4 (28.6)	0.35
Cyclophosphamide	81 (11.1)	8 (11.8)	0.86	2 (14.3)	0.93
Serology (Ever)					
Anti-dsDNA antibodies	459 (62.7)	41 (60.3)	0.69	10 (71.4)	0.58
Anti-Smith antibodies	73 (10.0)	1 (1.5)	**0.02**	0 (0.0)	0.07
Antiphospholipid antibodies	84 (11.5)	8 (11.8)	0.94	6 (42.9)	**<0.001**
Direct Coombs Test Positive	11 (1.5)	0 (0.0)	0.61	0 (0.0)	0.55
Anti-RNP antibodies	31 (4.2)	1 (1.5)	0.27	0. (0.0)	0.51
Anti-SSA antibodies	97 (13.3)	5 (7.4)	0.16	1 (7.1)	0.38
Anti-SSB antibodies	33 (4.5)	0 (0.0)	0.10	0 (0.0)	0.20
Low complement	291 (39.8)	27 (39.7)	0.99	8 (57.1)	0.33

Methods: We conducted a retrospective study utilizing our institutional ongoing longitudinal registry with a study population which included females ≥18 years of age, meeting classification criteria for SLE, and non-SLE population-matched female controls. Sociodemographic information and medical history were obtained from patient interviews and medical record information recorded in the registry. SLE disease damage was measured using SLICC Damage Index (SDI), modified for this study by excluding malignancy from the total score. Gynecologic cancers included any cancer of the female reproductive tract. Statistical analyses were Chi-squared test, Fisher's exact test, two-sided t-test, and ANOVA, as appropriate, with significance determined by p-values < 0.05.

Results: Table 1 shows baseline demographic characteristics of the study population, comparing patients with SLE (n=800) to controls (n=499). Overall malignancy prevalence was higher among patients (8.5%) compared to controls (3.6%, $p< 0.001$), including a higher prevalence of breast cancer and gynecologic cancer. Of the 800 included female SLE patients (**Table 2**), 68 (8.5%) had been diagnosed with cancer, 14 (20.6%) of which had gynecologic cancers. Older age at baseline, and history of nicotine use were associated with a significantly higher prevalence of cancer and gynecologic cancers. Although the patients with SLE were disproportionately Black (74.5%) compared to White (21.3%), patients with gynecologic cancer were more likely to be White (57.1%, $p< 0.001$). The modified SDI score was associated with gynecologic cancers ($p=0.04$), while SDI score >2 was associated with both overall cancer ($p=0.002$) and gynecologic cancers ($p=0.004$). No significant association was found with childhood onset of SLE, lupus nephritis, or exposure to specific SLE medications. While most of the studied serologic markers did not correlate with the presence of cancer, a positive association between the presence of antiphospholipid antibodies and gynecologic cancers was found ($p< 0.001$).

Conclusion: Our findings provide insight into which SLE disease characteristics may be associated with gynecologic cancers for our cohort of female patients with SLE. The primary SLE disease characteristic found to correlate with gynecologic cancers was a higher modified SDI, while no association was found with SLE treatment medications, although overall cancer numbers were low. These results support ongoing investigation into additional risk and preventative factors for gynecologic cancers in patients with SLE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Moseley: None; **D. Wilson**: None; **E. Vara**: None; **D. Kamen**: None.

Abstract Number: 1493

Long-Term Outcomes in Systemic Lupus Erythematosus Patients Infected with SARS-CoV-2: Variant-Specific Analysis of Pre-Delta/Delta and Omicron Periods

Lilliana Serrano-Arroyo, César Rosado-Bloise and Luis Vilá, University of Puerto Rico Medical Sciences Campus, San Juan, PR

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The post-acute sequelae of SARS-CoV-2 infection may involve low-grade inflammation, immune dysregulation, and endothelial dysfunction. Therefore, it would not be surprising if SARS-CoV-2 negatively impacts the clinical outcomes of patients with autoimmune disorders such as systemic lupus erythematosus (SLE). Previously, we reported that COVID-19 did not significantly affect the short-term outcomes of patients with SLE during the Pre-Delta/Delta and Omicron waves. Therefore, we sought to evaluate the long-term outcomes in these patient groups.

Methods: We studied a cohort of adults (≥21 years) with SLE (per 1997 American College of Rheumatology classification criteria), from a single center in Puerto Rico. Patients with confirmed COVID-19 infection during the pre-Delta/Delta (March 2020–November 2021) and the Omicron periods (December 2021–December 2022) were compared. Participants were followed at 12- and 24-month post-infection to evaluate SLE flares, disease activity (measured by the Systemic Lupus Erythematosus Activity Index), damage accrual (based on the Systemic Lupus International Collaborating Clinics/American College

Table 1. Clinical Outcomes and pharmacologic treatment in SLE patients with COVID-19: Pre-Delta/Delta period at 12- and 24-months post-infection (n=18).

Characteristics	At baseline	After baseline to 12 months	p-value	>12 months to 24 months	p-value
Age, mean (SD) years	41.9 (9.4)	--	--	--	--
Sex, % female	94.4	--	--	--	--
SLE duration, median (25th-75th) years	10.0 (7.0-15.0)	--	--	--	--
COVID-19 vaccinated, %	5.6	--	--	--	--
SLE flare, %	0.0	0.0	--	5.6	>0.999
SLEDAI, median (25th-75th)	0.0 (0.0-1.0)	0.0 (0.0-2.0)	0.125	0.0 (0.0-3.0)	0.453
SDI, median (25th-75th)	1.0 (0.0-3.0)	1.0 (0.0-3.0)	>0.999	1.0 (0.0-3.0)	>0.999
SLE therapy, %					
Corticosteroids	55.6	55.6	>0.999	50.0	>0.999
Hydroxychloroquine	66.7	72.2	0.317	66.7	>0.999
Mycophenolate mofetil	38.9	44.4	0.317	44.4	0.317
Azathioprine	5.6	5.6	>0.999	5.6	>0.999
Methotrexate	0.0	0.0	--	0.0	--
Tacrolimus	0.0	0.0	--	0.0	--
Belimumab	0.0	0.0	--	0.0	--
Rituximab	0.0	0.0	--	0.0	--
Cyclophosphamide	0.0	0.0	--	0.0	--

*Highest yearly score was used to calculate median. SLE: Systemic lupus erythematosus; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SD: Standard deviation; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical Outcomes and pharmacologic treatment in SLE patients with COVID-19: Omicron period at 12- and 24-months post-infection (n=130).

Characteristics	At baseline	After baseline to 12 months	p-value	>12 months to 24 months	p-value
Age, mean (SD)	45.8 (12.6)	--	--	--	--
Sex, % female	95.4	--	--	--	--
SLE duration, median (25th-75th) years	15.0 (8.0-20.0)	--	--	--	--
COVID-19 vaccinated, %	96.2	--	--	--	--
SLE flare, n (%)	4 (3.1)	5 (3.8)	>0.999	10 (7.7)	0.109
SLEDAI, median (25th-75th)	1.0 (0.0-2.0)	2.0 (0.0-4.0)	0.003	1.0 (0.0-4.0)	0.033
SDI, median (25th-75th)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	>0.999	1.0 (0.0-2.0)	>0.999
SLE therapy, n (%)					
Corticosteroids	56.9	57.7	>0.999	54.6	0.629
Hydroxychloroquine	83.1	79.2	0.180	75.4	0.013
Mycophenolate mofetil	38.5	37.7	>0.999	37.7	>0.999
Azathioprine	9.2	12.3	0.289	13.1	0.180
Methotrexate	3.8	3.8	>0.999	3.1	>0.999
Tacrolimus	3.1	6.2	0.125	6.2	0.125
Belimumab	0.8	0.8	>0.999	0.8	>0.999
Rituximab	0.0	0.0	--	0.8	>0.999
Cyclophosphamide	0.0	0.0	--	0.0	--

*Highest yearly score was used to calculate median. SLE: Systemic lupus erythematosus; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; SD: Standard deviation; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index

of Rheumatology damage index [SDI]), and lupus pharmacologic treatment. Outcomes were compared between baseline and 12- and 24-follow-up periods for pre-Delta/Delta and Omicron groups using paired analyses.

Results: A total of 148 patients with SLE were studied: 18 from the pre-Delta/Delta period and 130 from the Omicron period. None of the patients died during the follow-up. Tables 1 and 2 present demographic characteristics, SLE flares, SLEDAI scores, SDI scores, and pharmacologic therapy at the time of SARS-CoV-2 infection (baseline), as well as at 12 and 24 months. A slight but statistically significant increase in SLEDAI scores was observed at 12 and 24 months in the Omicron group. Hydroxychloroquine exposure was significantly lower in this group at 24 months. No significant differences in other outcome measures or pharmacologic treatments were noted for the study groups at 12- and 24-months post–COVID-19.

Conclusion: In this cohort of SLE patients infected with SARS-CoV-2 during the pre-Delta/Delta and Omicron periods, long-term outcomes were favorable. Aside from a slight increase in disease activity and reduced hydroxychloroquine exposure in the Omicron group, there was no increase in lupus flares, damage accrual, or use of other immunosuppressive therapies in either group.

Disclosure: L. Serrano-Arroyo: None; **C. Rosado-Bloise**: None; **L. Vilá**: None.

Abstract Number: 1494

Comparing Childhood-Onset Versus Adult-Onset Systemic Lupus Erythematosus Young Adults' Lived Employment Experiences

NILOFAR JAHAGHI[1], Michael Golding[2], Fareha Nishat[3], Kaitlyn Merrill[2], Diane Lacaille[4], Umut Oguzoglu[2], Roberta Woodgate[2], Jennifer Stinson[5], Christine Peschken[6], Zahi Touma[7], Jennifer Protudjer[2] and **Lily Lim**[6], [1]Karolinska Institutet, Stockholm, Sweden, [2]University of Manitoba, Winnipeg, Canada, [3]University of Toronto, Toronto, Canada, [4]Arthritis Research Canada, University of British Columbia, Vancouver, BC, Canada, [5]The Hospital for Sick Children, Toronto, ON, Canada, [6]University of Manitoba, Winnipeg, MB, Canada, [7]University of Toronto, Toronto, ON, Canada

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Young adulthood (18-30 years) is a life stage with many transitions. Young adults with Systemic Lupus Erythematosus must navigate this period while living with a devastating illness. Young adults with childhood-onset SLE (cSLE) have more time to adapt compared to adult-onset SLE (aSLE) patients. Thus, lived experiences of young adults with cSLE may differ from their aSLE counterparts. We aimed to compare the lived employment (school and work) experiences of young adults with cSLE and aSLE.

Methods: Participants were recruited from 3 rheumatology clinics in Canada for individual semi-structured, English language qualitative interviews. Participants completed a pre-interview questionnaire (socio-demographics, SLE history and work characteristics). Semi-structured interviews were conducted by video/phone, transcribed verbatim, double-coded and analyzed using thematic analysis. Divergence is defined as differences in articulating experiences under the same theme.

Results: 34 SLE patients: 16 (47%) cSLE, 18 (53%) aSLE, were interviewed. There were 25 females, 7 males, 2 non-binary. Median ages were 21 (cSLE) and 28 years (aSLE). 59% of cSLE and 76% of aSLE participants were working. Major organ involvements were present in 56% (similar in cSLE and aSLE and disease duration).

There were 4 main themes and 10 sub-themes. Diverging subthemes are highlighted below:

1) *Decreased productivity (subthemes: physical tasks and cognitive performance):* Both groups endorsed fatigue, cSLE group changed course to reduce fatigue while aSLE group tried to push through. cSLE group avoided flares by planning ahead but aSLE group dealt with flares as they occurred and were forced to change course. Though both groups report brain fog, cSLE group described attention problems but aSLE group memory problems.

2) *Interference with employment (subthemes: changing career path, losing/quitting job/ school, and medical encounters):* cSLE group planned their career by making different choices before entering the workplace but the aSLE group had to change their work.

3) *Social relations (subthemes: interference with social relations, and social support needs):* The cSLE group had to learn to prioritize their health over social activities but the aSLE group prioritized their health.

4) *Flexibility (subthemes: autonomy in different settings):* While both groups desired autonomy, the cSLE group was better able to access it compared to the aSLE group.

Conclusion: While young adults with cSLE and aSLE face similar challenges during employment, they also have different lived experiences. This may also reflect differences in age, life stage, and type of employment (school vs. work) between the 2 groups. Interventions targeting the challenges identified in young adulthood offer an opportunity for change with large potential future effects. Late cSLE teens and early post-diagnosis aSLE patients could be offered interventions to help them gain and sustain productive employment.

Disclosure: N. JAHAGHI: None; **M. Golding**: None; **F. Nishat**: None; **K. Merrill**: None; **D. Lacaille**: None; **U. Oguzoglu**: None; **R. Woodgate**: None; **J. Stinson**: None; **C. Peschken**: None; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **J. Protudjer**: None; **L. Lim**: Pfizer, 12, Speaker.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1495

Comparing the 0-10 Physician Global Assessment Scale to Categorical Disease Activity States among Pediatric Patients with SLE

Livie Timmerman[1], Melissa Mannion[2] and Emily Smitherman[2], [1]University of Alabama at Birmingham, Gardendale, AL, [2]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The Physician Global Assessment (PGA) is used to measure disease activity on a 0–10 scale for many pediatric rheumatic conditions. However, the thresholds at which 0-10 PGA scores correspond to clinically defined categories (inactive, mild, moderate, severe), or a 0-3 scale as utilized in childhood lupus low disease activity state (cLLDAS), are not standardized. Understanding the relationship between 0–10 and 0–3 PGA may clarify if the 0–3 scale is necessary for cLLDAS or whether a transformed 0–10 scale could serve as an acceptable substitute. Our objective was to define 0-10 PGA score thresholds that correspond to clinician-assigned categorical disease activity levels using statistical modeling and predicted probabilities.

Methods: We analyzed electronic health record (EHR) data collected from a tertiary care pediatric rheumatology clinic between December 2021 and February 2023. We identified ambulatory visits for SLE using a clinician-documented structured field. Our EHR documentation included structured fields to collect: 1) 0-10 PGA (21 points with 0.5 increments), built as a drop-down menu; 2) a categorical "Disease Activity Assessment" with radio buttons for "Inactive", "Mild", "Moderate", and "Severe" arranged in a row, representing 0-3 PGA anchored values. We calculated descriptive statistics for PGA by clinician-assigned disease activity category. PGA was then evaluated as a continuous predictor of disease activity category using ordinal logistic regression. Predicted probabilities of each disease activity category were estimated using margins from the ordinal model. We then derived PGA thresholds and calculated the frequency of visits within each PGA category compared to clinician-assigned categories.

Results: We analyzed 190 visits < ![if !supportAnnotations] >[ES1]< ![endif] > < ![if !supportAnnotations] >[LT2]< ![endif] > < ![if !supportAnnotations] >[MM3]< ![endif] > for SLE with both 0-10 PGA and disease activity category completed (Figure 1). Clinician-assigned categories were Inactive for 50% of visits (PGA median 0, IQR 0-0), Mild 42% (1.0, 1-2), and Moderate 8% (3.75, 2.25-5). Each 1-point increase in PGA more than doubled the odds of being assigned to a higher disease activity category (OR = 2.08, 95% CI: 1.57–2.59, p < 0.001). Visits with PGA ≤0.5 had >80% probability of clinician-assigned

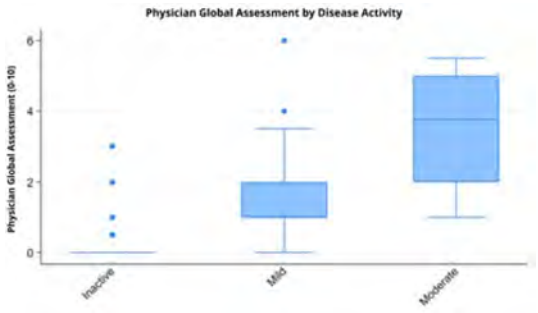


Figure 1. Distribution of 0-10 Physician Global Assessment Scores by Clinician-Assigned Disease Activity Assessment Category (inactive, mild, moderate) across 190 Pediatric Rheumatology Encounters for SLE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Predicted Probability of Clinician-Assigned Disease Activity (PGA) Category by 0-10 Physical Global Assessment (PGA) Score

PGA	Pr(Inactive)	Pr(Mild)	Pr(Moderate)
0	83%	17%	<1%
1	38%	61%	<1%
2	7%	88%	5%
3	<1%	70%	29%
4	<0.1%	23%	77%
5-10	≈0%	<1%	≈99%

Table 2. Number of visits within each Physician Global Assessment (PGA) Threshold cross-tabulated with Clinician-Assigned Disease Activity Category

PGA Range	Inactive Category, n (%)	Mild Category, n (%)	Moderate Category, n (%)
0-0.5	90 (94%)	11 (14%)	0
1-3.5	6 (6%)	66 (83%)	7 (50%)
4-10	0 (0%)	3 (3%)	7 (50%)

inactive category, 1-3.5 had the highest probability of mild, and ≥5 had >95% probability of moderate (Table 1). PGA 0-0.5 identified 94% of the visits assigned inactive, 1-3.5 identified 83% of the visits assigned mild, and 4-10 identified 50% of the visits assigned moderate (Table 2),

Conclusion: In children with SLE, 0-10 PGA scores are strongly aligned with clinician-assigned disease activity categories, supporting transformation between the 2 scales. Using a 21-point 0-10 PGA scale, we propose that 0-10 PGA ≤3.5 corresponds to cLLDAS criteria and 0-10 PGA ≤0.5 corresponds to clinical remission criteria, suggesting a modification from strict mathematical transformation. Aligning the cLLDAS 0-3 PGA scale to 0-10 scale used in other pediatric rheumatic conditions is likely to increase reliability of collection in routine clinical practice.

Disclosure: L. Timmerman: None; **M. Mannion**: None; **E. Smitherman**: None.

Abstract Number: 1496

Demyelinating Syndromes in Systemic Lupus Erythematosus: A 23-Year Retrospective Analysis of Clinical Features and Treatment Outcomes from a Tertiary Care Center

Manikandan Gopal[1], Ashish Jacob Mathew[2] and john mathew[3], [1]christian medical college, Vellore, India, [2]Christian Medical College, Vellore, Tamil Nadu, India, [3]Christian Medical college , Vellore , India, Vellore, Tamil Nadu, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) with acute myelitis or optic neuritis is rare and causes significant morbidity. Data on these conditions remain limited. This study aimed to evaluate the clinical profile and outcomes of patients presenting with demyelinating syndromes (transverse myelitis or optic neuritis) in SLE.

Methods: A retrospective chart review was conducted, identifying patients diagnosed with SLE and myelitis or optic neuritis at our center between 2000 and 2023. SLE was diagnosed using ACR-EULAR 2019 criteria. The Expanded Disability Status Scale (EDSS) was used to assess disability levels. Data were analyzed using descriptive statistics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Demographics and Clinical Characteristics

Table 1: Patient Demographics and Clinical Characteristics

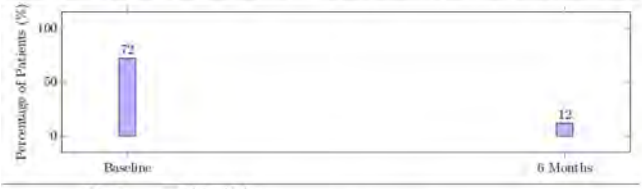
Characteristic	Value
Number of patients	25
Sex	100% (25/25) female
Age (years, mean ± SD)	27.04 ± 9.69
SLEDAI (mean ± SD)	17.72 ± 6.88
Demyelination as initial SLE manifestation	24% (6/25)
Time to nadir ≤ 24 hours	64% (16/25)
Motor deficit	88% (22/25)
Sensory level involvement	88% (22/25)
Urinary retention	72% (18/25)
Optic neuritis	16% (4/25)
Thoracic cord involvement (MRI)	88% (22/25)
Longitudinally extensive myelitis (MRI)	53% (13/25)
ANA positive	100% (25/25)
Low complements	76% (19/25)
Aquaporin-4 antibody positive	12% (3/25)

Table 2: Treatment and Outcomes

Table 1: Treatment and Outcomes

Treatment/Outcome	Value
Pulse methylprednisolone	92% (23/25)
Cyclophosphamide	68% (17/25)
Severe disability at baseline (EDSS > 5)	72% (18/25)
Severe disability at 6 months (EDSS > 5)	12% (3/25)
Relapse after treatment	12% (3/25)
Mortality (sepsis)	4% (1/25)
Optic atrophy within 1 year (optic neuritis patients)	0% (0/4)

Figure 1: Expanded Disability Status Scale (EDSS > 5) Score Distribution and Criteria



Score	Description
0.0	Normal neurological exam, no disability.
1.0–1.5	No disability, minimal signs in one or more functional systems.
2.0–2.5	Minimal disability in one or two functional systems.
3.0–3.5	Moderate disability in one functional system or mild disability in multiple systems, fully ambulatory.
4.0–4.5	Significant disability but ambulatory without aid, able to walk 300–500 meters.
5.0–5.5	Disability severe enough to impair daily activities, able to walk 100–200 meters without aid.
6.0	Requires unilateral assistance (cane/crutch) to walk about 100 meters.
6.5–7.5	Requires bilateral assistance or wheelchair for mobility.
8.0–9.5	Restricted to bed, with varying degrees of retained function.
10.0	Death due to disease.

Figure 1: EDSS (Expanded Disability Status Scale) Score at baseline and 6 month and EDSS Criteria

Results: A total of 25 female patients were identified with a mean age of 27.04 ± 9.69 years. The interval between SLE diagnosis and onset of demyelination varied widely, with 24% of patients presenting with demyelination as an initial manifestation. The mean SLEDAI was 17.72± 6.88. Sixteen patients (64%) reached the nadir of clinical presentation within 24 hours. Severe impairments included motor deficit (88%), sensory level involvement (88%), urinary retention (72%), and optic neuritis (16%). MRI was abnormal in all cases, with thoracic cord involvement in 88%, longitudinally extensive myelitis in 53%, and area postrema involvement in 8.3%. ANA was positive in all patients, 76% had low complements, and 12% tested positive for aquaporin-4 antibodies. Pulse methylprednisolone was administered to 92%; cyclophosphamide (68%) was the most used second-line therapy. At baseline, 72% had severe disability (EDSS > 5), which improved after six months,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

with only 12% retaining severe disability. Three patients relapsed after treatment and one patient succumbed to sepsis. No patients with optic neuritis developed optic atrophy within one year.

Conclusion: Demyelinating syndromes in SLE primarily affect young females and correlate with high disease activity. Early immunosuppressive therapy leads to improved outcomes , though some patients retain residual disability, underscoring the need for prompt intervention.

Disclosure: M. Gopal: None; **A. Jacob Mathew**: None; **j. mathew**: None.

Abstract Number: 1497

Acute Care Utilization in Patients with Antiphospholipid Syndrome And/or Systemic Lupus Erythematosus

Megan Barber[1], Fengjuan Yang[2], Leslie Skeith[2], Danielle Southern[3] and Ann Clarke[1], [1]Division of Rheumatology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]University of Calgary, Calgary, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Little is known about acute care utilization in patients with APS and/or SLE. This study focuses on hospitalizations, intensive care unit (ICU) admissions and emergency department (ED) visits, in patients with APS and/or SLE, both one year prior to and after identification of positive aPLs or diagnosis with SLE, compared to a control population.

Methods: Patients from our observational aPL/APS and SLE registries were included. Patients had persistently positive aPL (medium positive [40-80 GPU] or high positive [>80 GPU] anticardiolipin or anti-beta-2 glycoprotein 1 or a positive lupus anticoagulant test, measured at least 12 weeks apart) and/or fulfilled ACR or SLICC SLE classification criteria. Patients diagnosed with APS clinically met revised Sapporo Criteria. The index date was defined as the date that persistently positive aPL were first identified or that SLE classification criteria were met. Acute care utilization one year prior to and after the index date was determined. Data were sourced from several provincial health-related databases in Alberta, Canada. Acute care utilization was compared to age, sex, and geographic matched controls, excluding individuals with testing for aPLs, ANA, ENA or anti dsDNA or those with any practitioner claim codes or ICD codes for SLE or APS. Controls were assigned the index date of their matched case. Descriptive statistics were used to summarize baseline demographics and acute care utilization. Conditional logistic regressions were applied to assess differences between cases and matched controls for binary outcomes, generalized linear mixed Poisson regression models for discrete count and Gamma regression models for continuous outcomes, accounting for matched pairs.

Table 1: Baseline characteristics at index date

Characteristics	APS	APS Control	SLE	SLE Control
N	65	325	440	2,200
Mean age at index date (years, SD)	36.03 (16.06)	36.02(16.06)	35.04 (15.77)	35.04 (15.76)
Female, N (%)	51 (78.46%)	255 (78.46%)	396 (90.00%)	1980 (90.00%)
Urban region of residence, N (%)	55 (84.62%)	275 (84.62%)	394 (89.55%)	1970 (89.55%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Acute care utilization one year prior to, and one year after index date

Year	Utilization	APS	APS Control	P Value	SLE	SLE Control	P Value
	N	65	325		440	2,200	
	Availability of inpatient data						
Prior to index date	N (%)	50 (76.92%)	245 (75.38%)	0.6939	281 (63.86%)	1374 (62.45%)	0.2847
After index date	N (%)	54 (83.08%)	277 (85.23%)	0.9974	291 (66.14%)	1,523 (69.23%)	<0.0001*
	Hospitalizations						
Prior to index date	N (%)	12 (24.00%)	9 (3.67%)	<0.0001*	39 (13.88%)	68 (4.95%)	<0.0001*
	Mean (Std)	1.92(1.08)	2.00(1.22)	0.8939	1.69 (1.10)	1.29(0.57)	0.1015
	(Median, IQR)	2.00 (1.00-2.00)	2.00 (1.00-2.00)	0.8939	1.00 (1.00-2.00)	1.00 (1.00-1.50)	0.1015
After index date	N (%)	23 (42.59%)	13 (4.69%)	<0.0001*	96 (32.99%)	74 (4.86%)	<0.0001*
	Mean (Std)	2.65 (2.01)	1.92 (1.32)	0.1775	1.99(1.71)	1.27(0.73)	0.0012*
	(Median, IQR)	2.00 (1.00-4.00)	2.00 (1.00-2.00)	0.1775	1.00 (1.00-2.00)	1.00 (1.00-1.00)	0.0012*
	Hospitalizations - length of stay, days						
Prior to index date	Mean (Std)	6.25(3.37)	4.80 (6.12)	0.8044	6.12 (6.44)	5.97 (11.18)	0.9098
	(Median, IQR)	4.50 (2.75-5.00)	3.00 (1.00-5.00)	0.8044	3.00 (2.00-7.50)	2.00 (1.75-5.00)	0.9098
After index date	Mean (Std)	7.60 (6.06)	7.83 (13.26)	0.9502	8.10(8.51)	4.78 (10.01)	0.0323*
	(Median, IQR)	7.00 (3.50-7.00)	2.00 (1.50-7.00)	0.9502	5.75(3.00-9.00)	2.00 (1.00-3.00)	0.0323*
	ICU admissions						
Prior to index date	N (%)	0 (0.00%)	1 (0.41%)	0.9983	0 (0.00%)	3 (0.22%)	0.9976
	Mean (Std)	-	1(-)	-	-	1.00(0.00)	-
	(Median, IQR)	-	1.00(1.00-1.00)	-	-	1.00(1.00-1.00)	-
After index date	N (%)	2 (3.70%)	2 (0.72%)	0.1075	3 (1.03%)	1 (0.07%)	0.0190*
	Mean (Std)	2.50 (2.12)	1.50 (0.71)	-	2.00 (1.73)	2(-)	-
	(Median, IQR)	2.50 (1.00-4.00)	1.50 (1.00-2.00)		1.00 (1.00-4.00)	2.00 (2.00-2.00)	-
	Availability of outpatient data						
Prior to index date	N (%)	50 (76.92%)	246 (75.69%)	0.7563	284 (64.55%)	1384 (62.91%)	0.2216
After index date	N (%)	54 (83.08%)	277 (85.23%)	0.9974	297(67.50%)	1,535 (69.77%)	0.0045*
	ED Visits						
Prior to index date	N (%)	27 (54.00%)	41 (16.67%)	<0.0001*	131 (46.13%)	220 (15.90%)	<0.0001*
	Mean (Std)	3.78(3.41)	3.07 (2.07)	0.1412	2.47 (2.26)	1.85 (1.46)	0.0001*
	(Median, IQR)	2.00 (2.00-4.00)	2.00 (2.00-4.00)	0.1412	2.00 (1.00-3.00)	1.00 (1.00-2.00)	0.0001*
After index date	N (%)	32 (59.26%)	37 (13.36%)	<0.0001*	141 (47.47%)	225 (14.66%)	<0.0001*
	Mean (Std)	4.50 (3.86)	3.27 (2.77)	0.0119*	2.82(2.23)	1.77 (1.53)	<0.0001*
	(Median, IQR)	4.00 (2.00-4.00)	2.00 (2.00-4.00)	0.0119*	2.00 (1.00-4.00)	1.00 (1.00-2.00)	<0.0001*

Note:
Availability of data is based on participants' active status in the Alberta Provincial Registry and availability of the Discharge Abstract Database (since April 1, 2002) and National Ambulatory Care Reporting System (since April 1, 2001) in Alberta.
*$P < 0.05$ indicates a statistically significant difference.
- Statistical Analyses were not performed due to the small sample size.

Results: 459 patients participated: 65 with APS (+/- SLE), and 440 with SLE (+/- aPL) (Table 1). There were 2,525 matched controls randomly selected. One year prior to the index date, patients with APS and/or SLE had significantly higher rates of hospitalizations compared to their respective control groups (all $p < 0.0001$) (24.0% in APS vs. 3.7% in controls, and 13.9% in SLE vs. 5.0% in controls). ED visits rates were also higher in APS (54.0% vs. 16.7%) and SLE (46.1% vs. 15.9%) groups.

One-year post-index date, healthcare utilization remained significantly higher in patients with APS and/or SLE. Hospitalization rates rose to 42.6% in APS and 33.0% in SLE, both significantly higher than their controls (4.7% and 4.9%, respectively; $p < 0.0001$). SLE patients also had longer hospital stays (5.75 (3.00-9.00) vs. 2.00 (1.00-3.00) median days, p = 0.0323) and more hospitalizations (1.00 (1.00 -2.00) vs. 1.00 (1.00 -1.00), p = 0.0012). ICU admissions rates were higher in SLE patients than controls (1.03% vs. 0.07%, $p = 0.0190$). ED visit rates remained elevated in APS (59.3% vs. 13.4%) and SLE (47.5% vs. 14.7%) groups, with significantly higher mean visit counts in both (p = 0.0119 for APS; p < 0.0001 for SLE) (Table 2).

Conclusion: Patients with APS and/or SLE have a higher rate of hospitalizations and ED presentations compared to a control population, both one year prior to and after the first identification of positive aPLs or diagnosis of SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Barber: AstraZeneca, 1, GlaxoSmithKlein(GSK), 1; **F. Yang**: None; **L. Skeith**: CSL Behring, 2, 5, Leo Pharma, 6, Sanofi, 6; **D. Southern**: None; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(-GSK), 2, 5, Novartis, 2, Roche, 2.

Abstract Number: 1498

Both Race and Socioeconomic Status Affect Mortality in SLE

Gursimran Kaur[1], Daniel Goldman[2], Andrea Fava[3], Laurence Magder[4] and **Michelle Petri**[2], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Timonium, MD, [3]Johns Hopkins University, Baltimore, MD, [4]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: A recent meta-analysis found an overall 2.87-fold increase in all-cause mortality in systemic lupus erythematosus (SLE) with cause-specific increases in renal disease, infections, cardiovascular disease, stroke and cancer. An increase in mortality due to lupus nephritis was found between 2015-2020. Yen et al examined SLE mortality in the United States from 1968 to 2013. Multiple logistic regression found sex (male), race (blacks) and region (the South) were associated with SLE mortality. We evaluated the role of different demographic variables on mortality outcomes in systemic lupus erythematosus (SLE) in a large single-center cohort.

Methods: Using data from the cohort and the National Death Index, we analyzed demographic and clinical information to discover links between demographic characteristics and mortality. Cox proportional hazards models were used to assess the independent effects of age, gender, race/ethnicity, education and socioeconomic status on mortality risk while controlling for disease activity and comorbidities. Given the strong non-linear relationship between age and mortality, all estimated associations with mortality are adjusted for age at diagnosis and age at diagnosis squared.

Table 1. Predictors of Mortality based on a Cox Proportional Hazard Model

Variable	Level	N of patients	Number (%) of deaths	Age-adjusted hazard ratios (95% CI)	P-value
All		3021	628 (21%)		
Sex	Female	2773	561 (20%)	1.00 (Ref. Group)	--
	Male	248	67 (27%)	**1.40 (1.090, 1.82)**	**0.0098**
Race	White	1575	301 (19%)	1.00 (Ref. Group)	--
	Black	1183	316 (27%)	**1.76 (1.50, 2.07)**	**<0.0001**
	Other	263	11 (4%)	**0.36 (0.20, 0.66)**	**0.0009**
Education	≥12 yrs	2619	484 (18%)	1.00 (Ref. Group)	--
	12 yrs	230	105 (46%)	**2.28 (1.93, 2.77)**	**<0.0001**
Household Income	>$40,000/yr	1530	182 (12%)	1.00 (Ref. Group)	--
	<$40,000/yr	1100	357 (32%)	**2.32 (1.96, 2.93)**	**<0.0001**
Decade of Diagnosis	Pre-1990	578	254 (44%)	1.00 (Ref. Group)	--
	1990-2000	898	228 (25%)	0.53 (0.43, 0.65)	<0.0001
	2000-2010	910	129 (14%)	0.42 (0.33, 0.53)	<0.0001
	Post 2010	635	17 (3%)	0.20 (0.12, 0.34)	<0.0001
Age at Diagnosis (yrs)	<15	156	26 (17%)	1.00 (Ref. Group)	--
	15-20	367	70 (19%)	1.32 (0.84, 2.09)	0.23
	20-25	474	73 (15%)	1.03 (0.65, 1.62)	0.91
	25-30	497	91 (18%)	1.25 (0.80, 2.00)	0.32
	30-35	392	72 (18%)	1.31 (0.83, 2.07)	0.25
	35-40	340	64 (19%)	1.52 (0.95, 2.42)	0.080
	40-45	251	60 (24%)	1.92 (1.20, 3.08)	0.0070
	45-50	198	44 (22%)	1.92 (1.17, 3.15)	0.010
	50-55	134	37 (28%)	2.75 (1.64, 4.62)	0.0001
	55-60	88	34 (39%)	5.00 (2.93, 8.41)	<0.0001
	>60	124	57 (46%)	8.40 (5.18, 13.6)	<0.0001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariable Model of Predictors of Mortality

	Hazard Ratios (95%CI)	P-value
Male gender	1.57 (1.19, 2.07)	0.0014
Black race vs White	1.41 (1.17, 1.69)	0.0003
Other race vs. White	0.52 (0.29, 0.98)	0.042
Less than 12 years of Education	1.40 (1.11, 1.77)	0.0053
Household Income less than or equal to $40,000	1.73 (1.42, 2.11)	<0.0001
Decade of Diagnosis		
Pre 1990		
1990-2000	0.63 (0.51, 0.78)	<0.0001
2000-2010	0.53 (0.40, 0.70)	<0.0001
2010+	0.24 (0.12, 0.44)	<0.0001

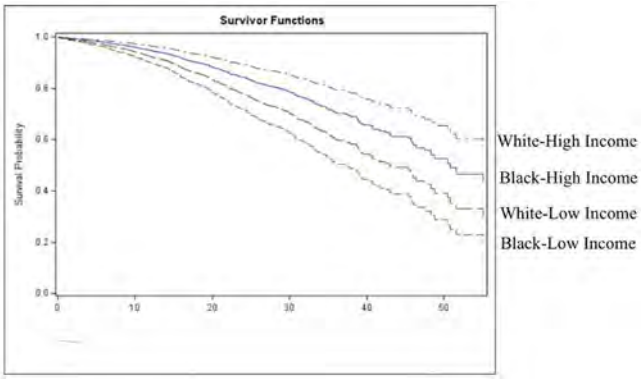


Figure 1. Estimated probability of survival by years since diagnosis by Race and Income

Results: Of the 3,021 patients included from the cohort, 628 deaths were recorded. They were 89% female, 34% had a household income of more than $40,000, and 82% had 12 years or more years of education. They were 48% White, 50% Black, 1% East Asian and 1% Other or mixed racial background. Male gender (p=0.0098), Black race vs White (p< 0.0001), less than 12 years of education (p< 0.0001), and household income of less than or equal to $40,000 (p< 0.0001) were associated with increased mortality in both univariate (Table 1) and multivariable (Table 2) models. Decreased mortality was observed for those diagnosed with lupus after 1990 (Table 1, Table 2). White race with high income had the lowest mortality, and black race with low income had the highest mortality (Figure 1).

Conclusion: Patel et al, in a meta-analysis, found that Blacks had higher mortality than Whites, but could not comment on socioeconomic factors. In the Eight Americas study, Falasinnu et al found that Blacks sharing the same social and geographic contexts as Whites had higher mortality, but SLE mortality did not vary between socially advantaged and disadvantaged Blacks. Our results, using individual patient data to measure socioeconomic status in 2 ways (household income and education) clearly contradict the Eight Americas study. Race and socioeconomic status both played a role in mortality risk in SLE, even in a single center of excellence (where access to care and medication were not issues). Our single center study was able to use actual individual patient household income and education, and not infer it from zip codes or county of residence. Black race with high income had better survival than white race with low income.

Disclosure: G. Kaur: None; **D. Goldman**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **L. Magder**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2.

Abstract Number: 1499

Predictors of Proteinuria Flares in Biopsy Positive Lupus Nephritis

Michelle Petri[1], Andrea Fava[2], Daniel Goldman[1] and Laurence Magder[3], [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]Johns Hopkins University, Baltimore, MD, [3]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Over 20% of lupus nephritis (LN) patients progress to end stage kidney disease. One of the most important predictors is renal flare.

Methods: The analysis is based on members of a longitudinal SLE cohort who had biopsy-proven lupus nephritis. The analysis includes all cohort visits that occurred after the positive biopsy. Two cohort visits, separated by less than 120 days in which the urine protein-creatinine ratio (UPCR) was measured, were referred to as a set of "paired visits". A proteinuria flare was defined as an increase in UPCR of 500 mg/gm or more in a pair of visits. We calculated the proportion of paired visits that exhibited a proteinuria flare in subgroups of paired visits defined by various patient characteristics. The association between patient characteristics and risk of a proteinuria flare was quantified using odds ratios from a logistic regression model fit with GEE to account for the fact that each patient contributed more than one set of paired visits. A multivariate equation to predict the risk of a proteinuria flare was developed using a forward-stepwise approach, considering each of the variables in Tables 1 in turn, and adding the variable that led to the greatest reduction in Quasi-likelihood Information Criterion (QIC).

Results: In 524 biopsy proven LN patients there were 776 proteinuria flares, with a mean $\pm$ SD of 1.48 $\pm$ 2.59 flares per patient. The patients were 88% female, 31% White, 51% Black, and 17% Other. Table 1 shows the univariate analysis of associates of proteinuria flare. African-American race, younger age, low C3 and lower household income predicted flares.

Table 1. Rates of proteinuria flares based on demographics

Variable	Level	N paired visits	Number (%) of proteinuria flares	Odds Ratio (95% CI)	P-value
All		8584	776 (9%)		
Sex	Female	7720	683 (9%)	1.00 (Ref. Group)	--
	Male	864	93 (11%)	1.24(0.99,1.56)	0.0629
Race	White	2710	151 (6%)	1.00 (Ref. Group)	--
	African-American	4479	474 (11%)	2.01(1.66,2.42)	0.0000
	Other	1395	151 (11%)	2.06(1.63,2.60)	0.0000
Age group (years)	<30	1557	214 (14%)	1.00 (Ref. Group)	--
	30-44	3938	341 (9%)	0.59(0.50,0.71)	0.0000
	45-59	2474	184 (7%)	0.50(0.41,0.62)	0.0000
	60+	615	37 (6%)	0.40(0.28,0.58)	0.0000
Days since Biopsy	<180	405	61 (15%)	1.00 (Ref. Group)	--
	180-365	273	28 (10%)	0.64(0.40,1.04)	0.0708
	>365	7906	687 (9%)	0.54(0.40,0.71)	0.0000
Years since SLE diagnosis	<2	431	48 (11%)	1.00 (Ref. Group)	--
	2-5	906	98 (11%)	0.97(0.67,1.40)	0.8608
	5+	7246	630 (9%)	0.76(0.56,1.04)	0.0835
Diabetes	No	7628	675 (9%)	1.00 (Ref. Group)	--
	Yes	956	101 (11%)	1.22(0.98,1.52)	0.0816
Income	Low	2186	224 (10%)	1.00 (Ref. Group)	--
	Medium	3267	293 (9%)	0.86(0.72,1.04)	0.1145
	High	3007	242 (8%)	0.77(0.63,0.93)	0.0063
Education	No college	2805	270 (10%)	1.00 (Ref. Group)	--
	Some college	3891	341 (9%)	0.90(0.76,1.07)	0.2271
	Some graduate sch	1856	160 (9%)	0.89(0.72,1.09)	0.2460

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Rates of proteinuria flares based on clinical history, recent clinical measures and recent treatments

Variable	Level	N paired visits	Number (%) of proteinuria flares	Odds Ratio (95% CI)	P-value
History of anti-dsDNA	No	1313	115 (9%)	1.00 (Ref. Group)	--
	Yes	7271	661 (9%)	1.04(0.85,1.28)	0.6991
History of low C3	No	1264	94 (7%)	1.00 (Ref. Group)	--
	Yes	7320	682 (9%)	1.28(1.02,1.60)	0.0317
History of low C4	No	1909	157 (8%)	1.00 (Ref. Group)	--
	Yes	6675	619 (9%)	1.14(0.95,1.37)	0.1589
History of anti Sm	No	4692	388 (8%)	1.00 (Ref. Group)	--
	Yes	3892	388 (10%)	1.23(1.06,1.42)	0.0063
History of anti RNP	No	4733	333 (7%)	1.00 (Ref. Group)	--
	Yes	3851	443 (12%)	1.72(1.48,1.99)	0.0000
History of anti-Ro	No	4426	389 (9%)	1.00 (Ref. Group)	--
	Yes	4158	387 (9%)	1.07(0.92,1.23)	0.4026
Recent Low C3	No	6378	483 (8%)	1.00 (Ref. Group)	--
	Yes	2206	293 (13%)	1.87(1.60,2.18)	0.0000
Recent Low C4	No	7173	599 (8%)	1.00 (Ref. Group)	--
	Yes	1411	177 (13%)	1.57(1.32,1.88)	0.0000
Recent Anti-dsDNA	No	4974	408 (8%)	1.00 (Ref. Group)	--
	Yes	3447	348 (10%)	1.26(1.08,1.46)	0.0029
Recent SLEDAI	0	2295	160 (7%)	1.00 (Ref. Group)	--
	1-2	2180	150 (7%)	0.99(0.78,1.24)	0.9047
	3+	4085	463 (11%)	1.71(1.41,2.06)	0.0000
Recent Serum Creatinine	<0.8	2678	193 (7%)	1.00 (Ref. Group)	--
	0.8-1.19	3628	249 (7%)	0.95(0.78,1.15)	0.5974
	1.2+	2239	327 (15%)	2.20(1.83,2.66)	0.0000
Recent Urine Protein/Creatinine Ratio	<0.5	5586	229 (4%)	1.00 (Ref. Group)	--
	0.5-0.99	1201	185 (15%)	4.26(3.47,5.23)	0.0000
	1.0+	1797	362 (20%)	5.90(4.95,7.03)	0.0000
Recent Prednisone Dose	None	4188	274 (7%)	1.00 (Ref. Group)	--
	<7	2468	217 (9%)	1.36(1.13,1.64)	0.0010
	7-14	1150	139 (12%)	1.96(1.58,2.44)	0.0000
	15+	746	145 (19%)	3.45(2.77,4.29)	0.0000
Recent Hydroxychloroquine use	No	1406	139 (10%)	1.00 (Ref. Group)	--
	Yes	7178	637 (9%)	0.89(0.73,1.08)	0.2265
Recent Immunosuppressant use	No	1726	118 (7%)	1.00 (Ref. Group)	--
	Yes	6857	657 (10%)	1.44(1.18,1.77)	0.0004
Recent ACE inhibitors/ ARBs use	No	2758	276 (10%)	1.00 (Ref. Group)	--
	Yes	5824	498 (9%)	0.84(0.72,0.98)	0.0280
Recent Calcium Channel Blocker use	No	6800	570 (8%)	1.00 (Ref. Group)	--
	Yes	1782	205 (12%)	1.42(1.20,1.68)	0.0000
Recent Diuretics use	No	6222	487 (8%)	1.00 (Ref. Group)	--
	Yes	2360	287 (12%)	1.63(1.40,1.90)	0.0000
Recent NSAIDs use	No	8141	762 (9%)	1.00 (Ref. Group)	--
	Yes	442	13 (3%)	0.29(0.17,0.51)	0.0000

All recent serologies (low C3, low C4 or high anti-dsDNA), higher SLEDAI, UPCR > 500 mg and higher serum creatinine all predicted proteinuria flare. Hydroxychloroquine use did not protect against proteinuria flare, but anti-hypertensive drug use did. NSAID use protected against proteinuria flare. Table 2 shows the final multivariate model. Higher serum creatinine, higher UPCR, younger age, African-American race, low C3, low C4 and anti-Ro predicted proteinuria flares. Protective factors included ACE-inhibitor/ARB use, age over 45, and NSAIDs.

Conclusion: Reduction of proteinuria flares is an essential goal to prevent progression to end-stage kidney disease, as each flare leads to additional loss of nephrons and podocytes. Our study could not address adherence to medication, a key factor in renal flare. We did find pathways that are essential: ACE-inhibitor/ARB use is protective. Treatments that normalize low C3 and low C4 would be hypothesized to also be key in preventing flares. One shocking finding was that NSAID use (which we counsel patients to avoid) was protective, even in the multiple variable model.

Table 3. Multivariate model to predict a proteinuria flare

Variable	Comparison	Odds Ratio (95% CI	P-value
Recent Serum Creatinine	0.8-1.2 vs <0.8	1.19 (0.94, 1.51)	0.15625
	1.2+ vs <0.8	2.27 (1.79, 2.87)	0.00000
Recent UPCR	0.5-0.99 vs <0.5	2.72 (2.13, 3.47)	0.00000
	1.0+ vs <0.5	2.61 (2.19, 3.59)	0.00000
History of Anti-Ro	Yes vs No	1.31 (1.05, 1.62)	0.01446
Recent low C3	Yes vs No	1.48 (1.18, 1.86)	0.00068
Age group (years)	30-44 vs <30	0.60 (0.47, 0.77)	0.00007
	45-59 vs < 30	0.56 (0.41, 0.77)	0.00032
	60+ vs < 30	0.57 (0.36, 0.91)	0.01916
Recent Diuretic use	Yes vs No	1.31 (1.09, 1.58)	0.00416
Recent ACE inhibitors/ ARBs use	Yes vs No	0.61 (0.50, 0.75)	0.00000
Recent NSAIDs use	Yes vs No	0.46 (0.26, 0.81)	0.00748
Race	African-American vs. White	1.31 (1.00, 1.72)	0.05046
	Other vs. White	1.37 (0.98, 1.92)	0.06273
Recent low C4	Yes vs No	1.40 (1.07, 1.82)	0.01288
Diabetes	Yes vs No	1.33 (0.95, 1.86)	0.10194

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Petri: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **D. Goldman**: None; **L. Magder**: None.

Abstract Number: 1500

Prognostic Impact of Thrombocytopenia on Morbidity and Mortality in Systemic Lupus Erythematosus: A Retrospective Single-Center Study

Milad Heydari-Kamjani[1], Amir Daneshvar[2], Dana Nachawati[2], Elleson Harper[2], Keri Ann Pfeil[2], Meghan Gump[2], Lindsay Frumker[3] and Omer Pamuk[1], [1]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [2]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [3]University hospitals Cleveland medical center, Highland Heights, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease with heterogeneous hematologic manifestations. Thrombocytopenia (TP) in SLE may be associated with major organ involvement and poor prognosis. Our study aimed to evaluate the frequency and prognostic significance of TP in a large, single-center SLE cohort.

Methods: We conducted a retrospective cross-sectional study using data from the SLE cohort at University Hospitals Cleveland Medical Center. Patients met 2019 EULAR/ACR classification criteria for SLE. Clinical, demographic, immunologic, and outcome variables were extracted to assess associations with a history of TP, defined as any documented platelet count $< 150 \times 10^9$/L. Chi-square (χ^2) tests were used to assess the relationship between TP and categorical variables, including clinical manifestations, laboratory markers, medication use, and mortality. To determine independent risk factors for TP in SLE patients, multivariate logistic regression analysis was performed. Parameters which were found significant in univariate analysis were utilized in logistic regression analysis. A two-sided p-value of < 0.05 is considered statistically significant. The study was IRB-approved.

Results: Among the 279 SLE patients, 105 (37.6%) had a history of TP. TP was significantly associated with several immunologic and clinical features. Patients with TP were more likely to have leukopenia (74.3% vs. 37.9%, $p < .001$), lymphopenia (83.8% vs. 36.8%, $p < .001$), low C3 (41.9% vs. 13.8%, $p < .001$), and low C4 (37.1% vs. 13.8%, $p < .001$). There was a non-statistical trend toward higher anti-dsDNA antibody positivity (57.7% vs. 46.5%, $p = .072$). TP was associated with major organ involvement including increased rates of lupus nephritis (41.0% vs. 18.4%, $p < .001$), ESRD (21.9% vs. 2.3%, $p < .001$), CNS involvement (17.1% vs. 9.2%, $p = .049$), cerebrovascular events (20.0% vs. 4.1%, $p < .001$), and thrombotic events (25.0% vs. 9.8%, $p < .001$). Additionally, in this cohort, they had an approximately 6.8-fold higher risk of mortality (7.5% vs. 1.1%, $p = 0.039$). Use of immunosuppressive therapies, including mycophenolate mofetil (48.6% vs. 26.4%, $p < .001$) and rituximab (11.4% vs. 3.5%, $p = .013$), was also significantly more common among patients with TP. In contrast,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline demographics and comorbid conditions in SLE with and without thrombocytopenia.

Variables	SLE without Thrombocytopenia (n = 174)	SLE with Thrombocytopenia (n = 105)	p-value
Gender			
Female	158 (90.8%)	94 (89.5%)	0.65
Race			0.51[1]
White	76 (43.7%)	42 (40%)	-
African American	86 (49.4%)	59 (56.2%)	-
Asian	5 (2.9%)	1 (1.0%)	-
Ethnicity			0.24[2]
Non-Hispanic ethnicity	170 (97.7%)	100 (95.2%)	-
Comorbidities			
Smoking	45 (25.6%)	33 (31.4%)	0.77
Hypertension	73 (42.4%)	55 (52.4%)	0.10
Diabetes mellitus	19 (11.0%)	19 (18.1%)	0.098
Coronary artery disease	11 (6.4%)	13 (12.4%)	0.086
Malignancy	15 (8.7%)	15 (14.3%)	0.14

[1] p-value from Pearson chi-square test comparing overall race distribution between groups.

[2] p-value from Pearson chi-square test comparing overall distribution of ethnicity categories across groups.

Table 2: Comparison of serologic markers in SLE patients with and without thrombocytopenia.

Variables	SLE without Thrombocytopenia (n = 174)	SLE with Thrombocytopenia (n = 105)	p-value
Leukopenia	66 (37.9%)	78 (74.3%)	**<.001**
Lymphopenia	64 (36.8%)	88 (83.8%)	**<.001**
Low C3	24 (13.8%)	44 (41.9%)	**<.001**
Low C4	24 (13.8%)	39 (37.1%)	**<.001**
dsDNA antibody	80 (46.5%)	60 (57.7%)	0.07
Anti-Sm antibody	37 (21.5%)	24 (23.1%)	0.76
Ro/SSA antibody	57 (33.1%)	35 (33.7%)	0.93
La/SSB antibody	19 (11.0%)	12 (11.5%)	0.90
Chromatin antibody	50 (28.9%)	39 (37.1%)	0.15
RNP antibody	59 (34.3%)	40 (38.5%)	0.48
Lupus anticoagulant	17 (13.4%)	18 (20.0%)	0.19

Table 3: Clinical manifestation of SLE patients with and without thrombocytopenia.

Variables	SLE without Thrombocytopenia (n = 174)	SLE with Thrombocytopenia (n = 105)	p-value
Malar rash	58 (33.3%)	35 (33.3%)	1
Discoid rash	12 (6.9%)	8 (7.6%)	0.821
Photosensitivity	31 (17.8%)	26 (24.8%)	0.163
Oral ulcers	25 (14.4%)	11 (10.5%)	0.348
Alopecia	29 (16.7%)	16 (15.2%)	0.753
Arthritis	129 (74.1%)	75 (71.4%)	0.621
Pleuritis	22 (12.6%)	19 (18.1%)	0.213
Pericarditis	16 (9.2%)	15 (14.3%)	0.19
Lupus nephritis	32 (18.4%)	43 (41.0%)	**<.001**
End-stage renal disease	4 (2.3%)	23 (21.9%)	**<.001**
CNS involvement	16 (9.2%)	18 (17.1%)	**0.049**
Cerebrovascular disease	7 (4.1%)	21 (20.0%)	**<.001**
Thrombosis	17 (9.8%)	26 (25.0%)	**<.001**
Mortality	1 (1.1%)	4 (7.5%)	**0.039**

there were no statistically significant differences between patients with and without TP in terms of gender, race, ethnicity, or comorbid conditions such as hypertension, diabetes mellitus, coronary artery disease, or malignancy. Multivariate logistic regression analysis showed that lymphopenia (OR: 7.6, 95%CI: 1.5-38.5, p=0.014) and the presence of cerebrovascular disease (OR: 37, 95%CI: 2.1-647.2, p=0.013) are independent factors associated with TP in our SLE cohort.

Conclusion: TP in SLE is significantly associated with leukopenia, lymphopenia, and decreased C3/C4. It is also linked to severe clinical manifestations, including lupus nephritis, ESRD, CNS and cerebrovascular events, thrombosis and increased mortality. Multivariate analysis confirmed that lymphopenia and cerebrovascular disease are independent predictors of TP. These findings support TP as a powerful prognostic marker in SLE.

Disclosure: M. Heydari-Kamjani: None; **A. Daneshvar**: None; **D. Nachawati**: None; **E. Harper**: None; **K. Pfeil**: None; **M. Gump**: None; **L. Frumker**: None; **O. Pamuk**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1501

Thrombocytopenia in SLE: A Hidden Prognostic Marker of Increased Mortality and Adverse Outcomes - Results from Real World Data

Milad Heydari-Kamjani[1], Amir Daneshvar[2], Chelsea Guan[2], Elleson Harper[2], Keri Ann Pfeil[2], Lindsay Frumker[3], Meghan Gump[2] and Omer Pamuk[1], [1]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [2]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [3]University hospitals Cleveland medical center, Highland Heights, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogeneous hematologic manifestations. Thrombocytopenia (TP) in SLE may be associated with major organ involvement and poor prognosis. In this study, we aimed to evaluate the frequency and prognostic significance of TP in a large, multi-center, real-world SLE cohort.

Methods: We conducted a retrospective cohort study using the TriNetX Research Network, a de-identified, federated electronic health record database (accessed March 20, 2025). Adult patients (≥18 years) with SLE (ICD-10: M32.9) and TP (ICD-10: D69.6), with at least one follow-up encounter, were included. A 1:1 propensity score matching was performed using 41 variables including demographics, comorbidities, and medication exposures to balance baseline characteristics. Continuous and categorical variables were compared using t-tests and chi-squared tests ($\alpha = 0.05$).

Table 1: Baseline characteristics and comorbidities in patients with SLE with and without thrombocytopenia before and after propensity score matching.

Variables	Before Matching			After Matching		
	SLE-TP (n = 17,407)	SLE-non-TP (n = 118,640)	P-Value	SLE-TP (n = 17,097)	SLE-non-TP (n = 17,097)	P-Value
Demographics						
Age at Index (Mean ± SD)	46.7 ± 18.8	46.6 ± 17.0	0.31	46.8 ± 18.8	46.6 ± 18.0	0.247
Female	14,207 (81.6%)	103,696 (87.4%)	**<0.001**	13,991 (81.8%)	13,912 (81.4%)	0.27
African American	5,118 (29.4%)	28,684 (24.2%)	**<0.001**	5,017 (29.3%)	5,255 (30.7%)	**0.005**
White	7,958 (45.7%)	58,121 (49.0%)	**<0.001**	7,836 (45.8%)	7,776 (45.5%)	0.515
Asian	1,308 (7.5%)	8,733 (7.4%)	0.47	1,283 (7.5%)	1,253 (7.3%)	0.53
Comorbid conditions						
Overweight and obesity	2,876 (16.5%)	16,309 (13.7%)	**<0.001**	2,792 (16.3%)	2,678 (15.7%)	0.093
Type 2 diabetes mellitus	2,531 (14.5%)	11,837 (10.0%)	**<0.001**	2,440 (14.3%)	2,562 (15.0%)	0.062
Hypertension	7,418 (42.6%)	37,242 (31.4%)	**<0.001**	7,183 (42.0%)	7,226 (42.3%)	0.638
Nicotine dependence	1,988 (11.4%)	10,960 (9.2%)	**<0.001**	1,933 (11.3%)	1,843 (10.8%)	0.12
Alcohol disorders	571 (3.3%)	1,732 (1.5%)	**<0.001**	545 (3.2%)	565 (3.3%)	0.542
SLE related manifestations						
Inflammatory arthritis	3,392 (19.5%)	22,247 (18.8%)	**0.021**	3,326 (19.5%)	3,228 (18.9%)	0.178
Pleurisy	204 (1.2%)	1,122 (0.9%)	**0.005**	200 (1.2%)	184 (1.1%)	0.412
Acute pericarditis	213 (1.2%)	786 (0.7%)	**<0.001**	199 (1.2%)	209 (1.2%)	0.618
Discoid lupus	1,683 (9.7%)	9,622 (8.1%)	**<0.001**	1,645 (9.6%)	1,609 (9.4%)	0.507
scLE	148 (0.9%)	772 (0.7%)	0.003	146 (0.9%)	131 (0.8%)	0.365
Glomerular disease	1,793 (10.3%)	6,295 (5.3%)	**<0.001**	1,669 (9.8%)	1,688 (9.9%)	0.73
End-stage renal disease	1,595 (9.2%)	3,253 (2.7%)	**<0.001**	1,456 (8.5%)	1,461 (8.5%)	0.923
APS	1,335 (7.7%)	3,704 (3.1%)	**<0.001**	1,256 (7.3%)	1,249 (7.3%)	0.884
Arterial and venous thrombosis	1,526 (8.8%)	4,004 (3.4%)	**<0.001**	1,383 (8.1%)	1,361 (8.0%)	0.661
Epilepsy and seizures	926 (5.3%)	3,561 (3.0%)	**<0.001**	869 (5.1%)	803 (4.7%)	0.098
Peripheral neuropathy	611 (3.5%)	4,418 (3.7%)	0.163	599 (3.5%)	509 (3.0%)	**0.006**
Sjögren syndrome	1,367 (7.9%)	10,913 (9.2%)	**<0.001**	1,349 (7.9%)	1,271 (7.4%)	0.113
Hemolytic anemias	1,263 (7.3%)	2,218 (1.9%)	**<0.001**	1,107 (6.5%)	1,083 (6.3%)	0.596

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Serologic profile and immunosuppressive medication use in SLE patients with and without thrombocytopenia before and after propensity score matching.

Variables	Before Matching			After Matching		
	SLE-TP (n = 17,407)	SLE-non-TP (n = 118,640)	P-Value	SLE-TP (n = 17,097)	SLE-non-TP (n = 17,097)	P-Value
Immunologic profiles						
dsDNA	2,435 (14%)	12,619 (14%)	**<0.001**	2,364 (13.8%)	2,114 (12.4%)	0.65
Ro/SSA	1,254 (7.2%)	6,019 (7.2%)	0.434	1,217 (7.1%)	1,047 (6.1%)	0.169
La/SSB	1,287 (7.4%)	6,366 (7.4%)	**0.031**	1,247 (7.3%)	1,012 (5.9%)	**0.013**
RNP	836 (4.8%)	4,063 (4.8%)	0.091	800 (4.7%)	704 (4.1%)	0.791
Complement C3	7,554 (43.4%)	39,862 (33.6%)	<0.001	7,317 (42.8%)	6,575 (38.5%)	**0.001**
Complement C4	7,387 (42.4%)	40,243 (33.9%)	<0.001	7,158 (41.9%)	6,537 (38.2%)	**<0.001**
Medications						
Hydroxychloroquine	7,902 (45.4%)	50,272 (42.4%)	**<0.001**	7,714 (45.1%)	7,725 (45.2%)	0.905
Glucocorticoids	11,380 (65.4%)	62,482 (52.7%)	**<0.001**	11,079 (64.8%)	11,029 (64.5%)	0.572
Azathioprine	1,171 (6.7%)	5,625 (4.7%)	**<0.001**	1,130 (6.6%)	1,137 (6.7%)	0.879
Mycophenolate mofetil	2,384 (13.7%)	8,895 (7.5%)	**<0.001**	2,258 (13.2%)	2,337 (13.7%)	0.21
Cyclophosphamide	581 (3.3%)	1,486 (1.3%)	**<0.001**	507 (3.0%)	498 (2.9%)	0.773
Belimumab	175 (1.0%)	1,958 (1.7%)	**<0.001**	172 (1.0%)	157 (0.9%)	0.406
Rituximab	714 (4.1%)	1,137 (1.0%)	**<0.001**	592 (3.5%)	588 (3.4%)	0.906

Results: A total of 17,407 patients with SLE and TP (SLE-TP) and 118,640 without TP (SLE-non-TP) were identified, with SLE-TP comprising 14.7% of the cohort. Before matching, SLE-TP patients were more likely to be male and African American ($p < 0.001$) and had significantly higher frequencies of inflammatory arthritis, pleurisy, glomerular disease, antiphospholipid syndrome, seizure, and hemolytic anemia (all $p < 0.05$). Comorbidities including obesity, type 2 diabetes, and hypertension were also more common in the SLE-TP group (all $p < 0.001$)

After matching, African American patients were slightly less prevalent in the SLE-TP group compared to the SLE-non-TP group (29.3% vs. 30.7%, $p = 0.005$). SLE-TP patients had significantly higher rates of peripheral neuropathy ($p = 0.006$), La/SSB autoantibody ($p = 0.013$), low C3 ($p = 0.001$), and low C4 ($p < 0.001$) (Table 1 and Table 2). There was a trend toward higher obesity in the SLE-TP group ($p = 0.093$). Use of immunosuppressive medications was not significantly different between the matched groups (Table 2).

During the study period, 3,182 (18.6%) SLE-TP patients and 1,368 (8.0%) SLE-non-TP patients died (relative risk [RR]: 2.33; 95% CI: 2.19–2.47) (Figure 1A). Survival analysis showed significantly worse prognosis in the SLE-TP group (hazard ratio [HR]: 1.94; 95% CI: 1.83–2.07; $p < 0.001$) (Figure 1B), indicating that SLE patients who had thrombocytopenia exhibited a significantly lower survival probability compared to those without this condition.

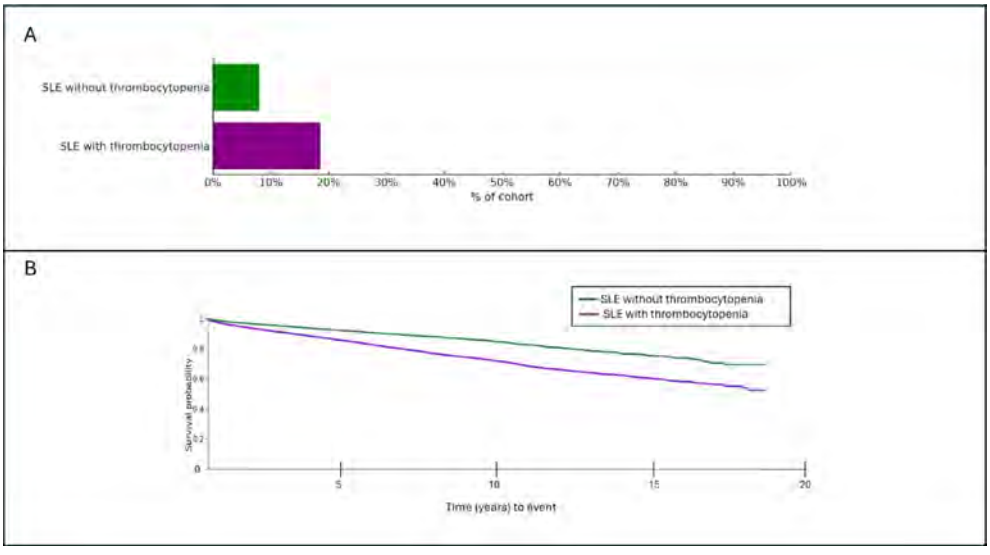


Figure 1: Impact of thrombocytopenia in SLE on mortality and survival in patients with and without thrombocytopenia.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The presence of La/SSB autoantibody, hypocomplementemia (low C3 and C4), and peripheral neuropathy are the immunological and clinical features most strongly associated with SLE-TP. More importantly, this group faces over a twofold increase in mortality with survival analysis confirming a significantly worse prognosis. These findings confirm thrombocytopenia as a powerful prognostic marker in SLE, indicating that low platelet counts are linked to substantially worse outcomes and nearly double the risk of death.

Disclosure: M. Heydari-Kamjani: None; **A. Daneshvar**: None; **C. Guan**: None; **E. Harper**: None; **K. Pfeil**: None; **L. Frumker**: None; **M. Gump**: None; **O. Pamuk**: None.

Abstract Number: 1502

Prevalence and Associated Factors of Autoimmune Hepatitis and Primary Sclerosing Cholangitis in Systemic Lupus Erythematosus: A Systematic Review and Meta-Analysis

Bisma Shaikh[1], Sarfaraz Hasni[2] and **Omer Pamuk**[3], [1]Jinnah Sindh Medical University, Karachi, Pakistan, [2]NIH/NIAMS, Bethesda, MD, [3]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune, chronic disorder characterized by multisystem organ involvement. The hepatic involvement in SLE is categorized as a primary or secondary disease, which incorporates drug-induced liver injury, vascular disorders, alternative hepatic comorbidities, and concurrent autoimmune liver diseases (AILDs). The most prevalent AILDs include autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC), which may manifest alone or concurrently. The primary aim of this study is to perform a systematic review of the literature to determine the relationship between SLE and AILDs.

Methods: We searched the literature using PubMed and Cochrane Library up to 2024 for studies investigating the frequency of AIH, and PBC in patients with SLE and other connective tissue diseases (CTDs). Abstracts presented at international conferences and references of relevant articles have been also reviewed, without any restrictions, between 1959 and 2024. We used the terms 'systemic lupus erythematosus', 'lupus', 'autoimmune liver disease', 'autoimmune hepatitis',

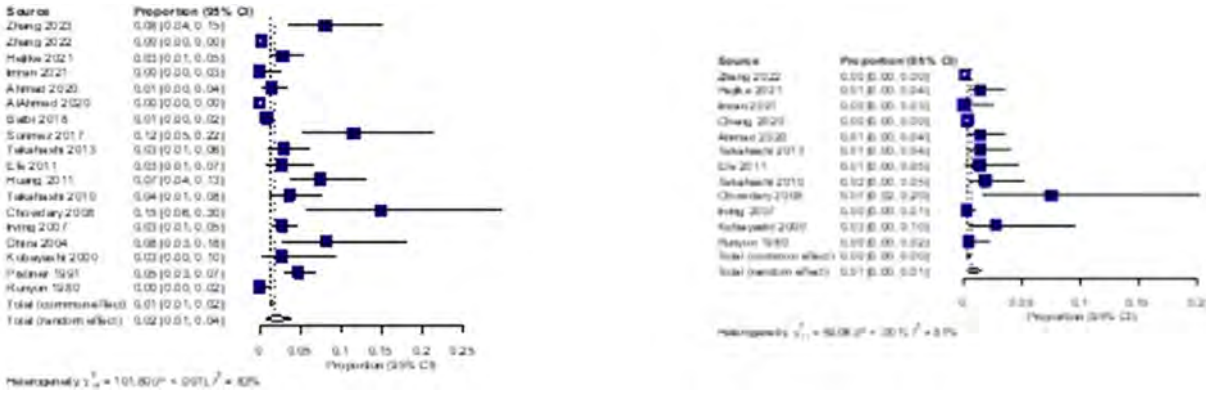


Figure 1A. The prevalence of AIH in patients with SLE. Figure 1B. The frequency of PBC in SLE group.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2A. The rate of SLE in patients with AIH. Figure 2B. The prevalence of SLE in patients with PBC.

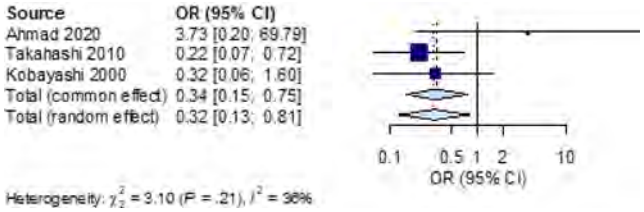


Figure 3. The comparison of the frequency of PBC in patients with SLE and other CTDs.

'primary sclerosing cholangitis', and 'primary biliary cirrhosis'. To detect the frequency of AIH and PSC in the SLE series, a random effect model was used. Forest plots were created to summarize composite data, generating frequencies, odd ratio (OR), and corresponding 95% CI for each subgroup. The I^2 statistic was utilized to evaluate heterogeneity between studies.

Results: Our literature search yielded 1745 articles. After reviewing the titles and abstracts, 254 articles merited full-text review. A total of 29 manuscripts met our eligibility criteria. The pooled cohorts included a total of 58,052 SLE and/or AIH/PBC patients. A random effects model was used to detect the prevalence of AIH/PSC in SLE patients. Eighteen eligible studies comprising 7,651 SLE patients evaluated the frequency of AIH in patients with SLE. The frequency of AIH was 1.88% (95%CI: 0.87-4.01) (Figure 1A). The frequency of PBC was analyzed in 12 studies including 12,538 patients with SLE. The prevalence of PBC was 0.67% (95%CI: 0.30-1.48)) (Figure 1B). Three studies that investigated the frequency of SLE in patients with AIH containing 17,358 patients were included in our analysis. The frequency of SLE was 5.12% (95%CI: 0.98-22.75) in patients with AIH (Figure 2A). Six studies provided data on SLE in patients with PBC (a total of 2,814 PBC patients). The frequency of SLE was found 3.17% (95%CI: 2.26-4.45) in patients with PBC (Figure 2B). Three studies-including 1161 SLE patients provided data comparing the frequency of AIH and PBC between SLE and other CTDs. SLE and other CTD groups showed similar frequencies of AIH (OR: 1.39, 95%CI: 0.31-6.23, p >0.05). The frequency of PBC was found to be lower in SLE than in other CTD groups (OR: 0.32, 95%CI: 0.13-0.81, p= 0.0003) (Figure 3).

Conclusion: Our study showed autoimmune liver diseases such as AIH and PBC are more common in SLE than in the general population. Pooled data revealed that SLE is also relatively common in AIH and PBC. Patients with AIH and PBC need to be screened for concomitant SLE.

Disclosure: B. Shaikh: None; **S. Hasni**: None; **O. Pamuk**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1503

Lupus Disease Activity Adversely Affects the Quality of Life but not Intimate Relationship and Sexual Function in Indian Female Lupus Patients

Ranjan Gupta, Nilanchali Singh, Nisha Jawaliya, Rudra Prosad Goswami, Soniya Dhiman and Parul baisoya, All India Institute of Medical Sciences, New Delhi, Delhi, India

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) disease activity can affect the normal functioning of the patients. This functioning in various domains can be assessed using quality of life (QoL) tools like Lupus QoL which is a disease specific QoL tool. Similarly, sexual function can be measured by tools like Female Sexual Function Index (FSFI) which is not an SLE specific instrument. We aimed to assess the impact of lupus disease activity on QoL and sexual function of female SLE patients from India.

Methods: We recruited 160 SLE (all females; Mean (±SD) age 28.75 (±8.07) years) patients satisfying ACR/EULAR 2019 classification criteria. A formal disease activity assessment was done using SLEDAI. Lupus QoL instrument in Hindi was used to assess the QoL. Briefly, a transformed domain wise score was calculated based on the responses in each of the 8 domains and a cumulative score for the instrument was calculated by adding the individual transformed domain scores and dividing it by the number of contributory domains. Sexual function in these ladies was assessed using the FSFI instrument (Hindi Version) and a domain wise score calculated in 6 domains. For FSFI, patients were divided into 2 groups based on having sexual intercourse within the last month: Sexually active (SA) and sexually inactive (SI). Age matched healthy ladies were recruited as healthy controls (HC) for comparison of FSFI scores in SA and SI groups. Continuous variables were expressed as Mean (±SD). Unpaired t-test was used to compare the scores and Spearman's correlation coefficient was used to express correlation. A p-value< 0.05 was considered significant.

Results: Mean SLEDAI for all the patients was 4.88 (±3.22). Lupus QoL had worst scores in Fatigue domain and best in the physical health domain. (Table) In Lupus QoL, physical health, pain, planning, burden to others, emotional health, fatigue and the total QoL scores showed a modest negative correlation with SLEDAI. (Table 1)

A total of 89 patients out of 160 (55.62%) and 35 (45.45%) ladies among the HC (n=77), reported having a sexual intercourse within the past 1 month. The scores in all domains of FSFI were compared for these. A total of 146 out of 160 patients (91%) and 75 out of 77 HC (97%) had an FSFI score < 26.55 putting them at risk for developing sexual dysfunction (p >0.05).

Table 1. Domain wise and total scores for Lupus Quality of Life tool for lupus patients and their correlation with disease activity (SLEDAI)

Lupus QoL domains	All Patients	Spearman's Correlation coefficient w.r.t SLEDAI	p-value
Physical Health	67.39 (±27.46)	-0.25	**0.002**
Pain Score	65.082 (±29.95)	-0.26	**0.001**
Planning Score	67.31 (±29.21)	-0.19	**0.019**
Intimate Relationship	64.58 (±29.79)	-0.16	0.08
Burden to Others	57.943 (±31.92)	-0.25	**0.001**
Emotional Health	57.89 (±29.64)	-0.25	**0.002**
Body Image	57.44 (±30.26)	-0.10	0.23
Fatigue Score	57.13 (±27.56)	-0.19	**0.015**
Total Score	**61.76 (±24.19)**	**-0.26**	**0.001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparison of the domain wise and total Female Sexual Function Index mean (±SD) scores among patients and healthy females

	Patients (n=160)		Healthy Controls (n=77)	
	Sexually Active	Sexually Inactive	Sexually Active	Sexually Inact
FSFI Domains				
Desire	4.04 (±1.16)	3.43 (±0.99)	3.77 (±1.17)	5.6 (±0.74)
Arousal	3.52 (±1.12)		3.16 (±1.13)	
Lubrication	4.17 (±0.72)		3.8 (±0.88)	
Orgasm	3.57 (±0.93)		3.48 (±0.94)	
Satisfaction	2.46 (±1.44)		2.45 (±1.61)	
Pain	4.71 (±1.23)*		4.02 (±1.37)	
Total Score	**22.49 (±3.99)***		**20.71 (±4.38)**	

*Significant when compared to healthy controls

For SI patients and HC, the scores only in the desire domain were compared which were not different. However, among the SA patients, scores in the pain domain and total FSFI scores were significantly better ($p < 0.05$ for both) as compared to HC. (Table 2) Neither any of the individual domains nor the total FSFI score correlated with SLEDAI.

Conclusion: The QoL in Indian SLE patients is the worst in the fatigue domain and best in the physical health domain. Except the intimate relationship and the body image scores in the QoL, all the scores and the total QoL score is adversely affected by disease activity. Sexual function in Indian female SLE patients is better than age matched HC even though 91% patients are at risk of developing sexual dysfunction. Absence of correlation of SLEDAI with the FSFI scores & intimate relationship domain of the QoL suggests that disease activity does not affect sexual function in these patients.

Disclosure: R. Gupta: None; **N. Singh**: None; **N. Jawaliya**: None; **R. Goswami**: None; **S. Dhiman**: None; **P. baisoya**: None.

Abstract Number: 1504

High prevalence of clonal hematopoiesis of indeterminate potential (CHIP) somatic mutations in a cohort of 1,073 SLE participants

Richard Oppong[1], Joanne Nititham[2], Ashira Blazer[3], Manuel Ugarte-Gil[4], Jinoos Yazdany[5], Maria Dall'Era[6], Alexander Bick[7], Lindsey Criswell[2] and Cristina Lanata[8], [1]National Institutes of Health, Bethesda, MD, [2]NIH/NHGRI, Bethesda, MD, [3]University of Maryland Baltimore, Baltimore, Maryland, [4]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [5]UCSF, San Francisco, CA, [6]Division of Rheumatology, University of California, San Francisco, CA, [7]Vanderbilt University, Nashville, TN, [8]NIH/NHGRI, Bethesda

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Clonal hematopoiesis of indeterminate potential (CHIP) is characterized by the presence of somatic mutations in hematopoietic stem cells that lead to the expansion of a genetically distinct blood cell clone. CHIP is associated with increasing age, chronic inflammatory states and an elevated risk of cardiovascular events. The prevalence of CHIP mutations in healthy individuals is ~**10%** among those over age 65. In this study, we aimed to investigate the prevalence and mutational landscape of CHIP, as well as its association with clinical outcomes, in a large, multi-ethnic cohort of individuals with SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We analyzed 1,073 individuals with SLE across four cohorts for CHIP using a hybrid capture–based targeted sequencing panel encompassing 22 canonical CHIP-associated genes, sequenced at high depth. Raw reads were aligned and processed following GATK Best Practices. Somatic mutation calling and filtering was done by GATK Mutect2 and annotated via ANNOVAR. Rigorous filters were applied to exclude potential germline mutations and artifacts. Variants were classified as exonic or deleterious mutations (defined by CADD Phred score >20). Statistical models evaluated associations between CHIP mutation status and SLE ACR classification criteria, and cardiovascular outcomes, adjusting for age, sex, disease duration, cohort and race/ethnicity.

Results: The mean age of participants was 44.7 (SD 14.4), with a disease duration of 13.2 years (SD 9.8). Exonic CHIP mutations were identified in 47% of participants, with 31% harboring deleterious CHIP mutations. The most frequently mutated genes were *SETBP1* (16.3% exonic, 14% deleterious) and *DNMT3A* (11.4% exonic, 15.2% deleterious). The burden of deleterious CHIP mutations increased by 25.9% per decade of life ($p = 0.002$), and both age at diagnosis and disease duration were significantly associated with the presence of exonic ($p = 0.003$, $p = 0.011$) and deleterious mutations ($p = 0.008$, $p = 0.019$). While overall CHIP mutation status was not significantly associated with the ACR classification criteria or cardiovascular outcomes, gene-specific associations emerged. For instance, mutations in *IDH1* and *IDH2* were associated with hematologic involvement ($p = 0.004$ and $p = 0.015$, respectively), while mutations in *KRAS* and *MPL* were associated with a history of stroke ($p = 0.008$ and $p = 0.02$, respectively). Additionally, *SETBP1, DNMT3A, ASXL1, KIT*, and *IDH2* showed gene-phenotype associations with renal and immunologic manifestations.

Conclusion: SLE may influence the prevalence of CHIP mutations relative to the general population, as both disease duration and age at diagnosis are important risk factors. While global CHIP status was not associated with ACR criteria, specific associations have been observed between CHIP and adverse clinical outcomes including stroke, renal and hematologic involvement. These findings highlight the need for longitudinal studies to investigate the causal role of CHIP mutations for these outcomes in SLE.

Disclosure: R. Oppong: None; **J. Nititham**: None; **A. Blazer**: AstraZeneca, 2, GlaxoSmithKlein(GSK), 5, 12, Medical educators network; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **A. Bick**: None; **L. Criswell**: None; **C. Lanata**: None.

Abstract Number: 1505

Discordance Between Physician and Patient Global Assessment of Disease Activity in a Large Multicenter Prospective SLE Cohort in the U.S. and Canada

Romy Kallas[1], Naiva Manuela Piatchou Donfack[1], Deanna Jannat-Khah[1], Cynthia Aranow[2], Cristina Arriens[3], Jill Buyon[4], Megan Clowse[5], Maria Dall'Era[6], Richard Furie[7], Ellen Ginzler[8], Jennifer Grossman[9], Kenneth Kalunian[10], Diane Kamen[11], Kichul Ko[12], William McCune[13], Brad Rovin[14], Francisco Sanchez-Guerrero[15], Saira Sheikh[16], Kyriakos Kirou[1] and Timothy Niewold[17], [1]Hospital for Special Surgery, New York, NY, [2]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]NYU Grossman School of Medicine, New York, NY, [5]Duke University, Chapel Hill, NC, [6]Division of Rheumatology, University of California, San Francisco, CA, [7]Division of Rheumatology, Northwell Health, Great Neck, NY, [8]SUNY Downstate Health Sciences University, New York, NY, [9]UCLA, Sherman Oaks, CA, [10]UC San Diego, La Jolla, CA, [11]Medical University of South Carolina, Johns Island, SC, [12]The University of Chicago, Chicago, IL, [13]U Michigan, Ann Arbor, MI, [14]The Ohio State University, Columbus, OH, [15]University Health Network/Sinai Health system, Toronto, ON, Canada, [16]University of North Carolina at Chapel Hill, Chapel Hill, NC, [17]Hospital for Special Surgery, New York, New York

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Understanding the discordance between patient- and physician-reported disease assessment scores is essential for incorporating patient-reported outcomes into disease activity measures and identifying gaps between physician and patient perception of disease activity. Our objective is to identify factors associated with discordance between Patient Global Assessment (PtGA) and Physician Global Assessment (PGA) scores in a large multicenter SLE cohort.

Methods: The Lupus Clinical Trials Consortium (LCTC) is a prospective cohort of SLE patients from U.S. and Canadian centers. Data were collected during biannual routine visits. Discordance was defined as PtGA minus PGA, with positive discordance indicating higher scoring of disease activity by the patient as compared to their physician. Multivariable linear mixed effects regression evaluated associations between discordance and patient characteristics. Multivariable mixed effects logistic regression was performed to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between positive discordance and patient characteristics. All statistical analyses were performed in RStudio, with a significance level set at 0.05.

Results: The study included 1,349 SLE patients. Patients who met 4 of 11 ACR criteria for SLE and had baseline PtGA and PGA scores available were included. Mean age at diagnosis was 29.3 (±12.4) years, with an average disease duration of 12 years. The cohort was 48% White and 37% Black. Mean PGA and PtGA scores were 0.72 and 0.92, respectively (range 0 to 3); 60% of patients rated their disease as more severe than their physician. Black patients had 0.09 lower discordance than White patients (95% CI [-0.17, 0.00], p=0.043). College-educated patients had 0.11 lower discordance than those without a degree (95% CI [-0.19, -0.04], p=0.002). Current smokers showed 0.16 higher discordance than never-smokers (95% CI [0.04, 0.28], p=0.01). Patients needing help with daily activities had nearly double the odds of positive discordance (OR=1.96, 95% CI [1.36, 2.83], p< 0.001). Government insurance was associated with increased odds of positive discordance (OR=1.55, 95% CI [1.01, 2.38], p=0.044). Each point increase in SELENA SLEDAI score was linked to a 15% decrease in odds of positive discordance (OR=0.85, 95% CI [0.82, 0.89], p< 0.001). Patients with arthritis, renal disease, or neurologic disorder had 41% (OR=0.59, 95% CI [0.38, 0.91], p=0.018), 35% (OR=0.65, 95% CI [0.47, 0.90], p=0.01), and 38% (OR=0.62, 95% CI [0.40, 0.97], p=0.037) lower odds, respectively, of rating disease activity higher than physicians. No association was found between discordance and medication adherence, hospitalizations, or disability.

Conclusion: In this large SLE cohort, most patients rated their disease as more severe than their physicians. Functional limitations and governmental insurance were key predictors of higher patient-rated disease activity. In contrast, disease activity measured by SLEDAI and certain organ manifestations were linked to lower odds of positive discordance.

Disclosure: R. Kallas: None; **N. Piatchou Donfack**: EMD Serono, 3; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **C. Arriens**: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Clowse**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **E. Ginzler**: None; **J. Grossman**: artiva, 5, exact sciences, 11, illumina, 11, iqvia, 11, Merck/MSD, 11, Novartis, 5; **K. Kalunian**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Genentech,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1, GlaxoSmithKlein(GSK), 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, Roche, 1; **D. Kamen**: None; **K. Ko**: None; **W. McCune**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **F. Sanchez-Guerrero**: None; **S. Sheikh**: AstraZeneca, 1, Aurinia Pharmaceuticals, 5, Biogen, 1, Cabaletta Bio, 5, GlaxoSmithKlein(GSK), 1; **K. Kirou**: AMPEL Biosolutions, 5, Bristol-Myers Squibb(BMS), 5, Novartis, 5; **T. Niewold**: AstraZeneca, 2, Pioneering Medicines, 2, Progentec, 2, 4, Zenas, 5.

Abstract Number: 1506

Perspectives on Clinical Trial Participation for Novel Advanced Therapies: A Focus Group Study in Systemic Lupus Erythematosus (SLE)

Olivia A. Stein[1], Jennifer Lee[1], Evelyne Vinet[2], Arielle Mendel[3], Christian Pineau[4], Leanne Mielczarek[5] and **Sasha Bernatsky**[2], [1]Research Institute of the McGill University Health Centre, Montreal, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [3]McGill University Health Centre, Montreal, Canada, [4]McGill University, Montréal, QC, Canada, [5]Lupus Canada, Newmarket, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Our objective is to identify barriers and facilitators perceived by people with systemic lupus erythematosus (SLE) regarding participation in clinical trials for novel/advanced agents, such as cellular therapies.

Methods: Adults from our SLE research cohort were invited to participate in 1-hour virtual focus groups concerning their perspectives on clinical trials for novel/advanced SLE therapies. Sessions, facilitated by trained moderators using standardized questions, were recorded and transcribed. An inductive thematic analysis approach was used to code the data and generate themes/sub-themes.

Results: Nineteen patients participated in four focus groups (two in English, two in French). The mean age (range) was 50.0 (21-77) years and mean disease duration was 21.4 years. Most (90%) of participants were female and 79% (15/19) were White, with the remainder being Black, Asian, and Hispanic. Six major themes emerged: two barriers and four facilitators to trial participation. The first barrier was time and logistical constraints, such as employment and travel. The second was risk aversion, including subthemes of concerns of SLE flare, drug side effects and early-phase trials. Facilitators included receiving clear, detailed clinical trial information. Disease instability was another driver, making patients increasingly willing to accept elevated health risks, time commitment and/or logistical challenges. Desire to support the lupus community was also an important factor. Finally, access in clinical trials to mental health counsellors, peer support, and close medical follow-up were strong facilitators of participation.

Conclusion: We identified potential barriers and facilitators/driving factors for SLE patients regarding clinical trial participation, which are particularly relevant for novel/advanced agents like cellular therapies.

Disclosure: O. Stein: None; **J. Lee**: None; **E. Vinet**: None; **A. Mendel**: None; **C. Pineau**: None; **L. Mielczarek**: None; **S. Bernatsky**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1507

Temporal Trends in the Incidence of Systemic Lupus Erythematosus (SLE) in the United States (US): Holding Steady?

Sasha Bernatsky[1], Sharon Dowell[2], Brittany Banbury[3], Jeffrey Curtis[4], Grace Wright[5], Emily Holladay[6], Amy Mudano[7], Cristiano Moura[8] and Gail Kerr[9], [1]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [2]NEA Baptist Memorial Hospital, Jonesboro, AR, [3]Mount Sinai Beth Israel, Brooklyn, NY, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Grace C Wright MD PC, New York, NY, [6]University of Alabama at Birmingham, Edmond, OK, [7]Foundation for Advancing Science, Technology, Education and Research (FASTER), Birmingham, AL, [8]Research Institute of the McGill University Health Center, Montréal, Canada, [9]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Since SLE is associated with significant morbidity and healthcare burden, estimates of SLE incidence are needed to inform research and public health initiatives, including rheumatology workforce planning. SLE incidence estimates may be affected by health care access or care-seeking behaviour (which may have been altered during COVID-19 pandemic years i.e. 2020-2022) and/or by changing environmental factors (e.g. viral triggers, climate change). Our objective is to estimate annual SLE incidence rates over time, using real-world US data.

Methods: Using the Merative™ MarketScan® Commercial (+/-Medicare Supplemental) databases, we identified adults (18+) with $\geq$ 2 years of continuous enrollment and no SLE diagnoses during those 2 years between Jan. 2016-Dec. 2022. Among these, a 20% random sample was selected for analysis. Time zero was the first qualifying date for cohort entry. Incident SLE was defined by International Classification of Diseases diagnostic codes, based on ≥2 physician visits ≥8 weeks apart within two years and/or ≥1 hospitalization. Individuals were followed from time zero until the earliest of SLE diagnosis, health plan disenrollment, or end of follow-up. Annual SLE incidence rates were calculated with 95% confidence intervals (CI). We report incidence overall and stratified by sex, and female-specific rates were further stratified according to whether person-time was contributed during reproductive age (age younger than 52). We assessed age (continuous) and sex in a multivariate hazard regression predicting SLE onset, controlling for calendar year.

Table 1: Annual SLE incidence by 10,000 person-years with 95% CI, US MarketScan, 2016-2022*

Table 1: Annual SLE incidence by 10,000 person-years with 95% CI, US MarketScan, 2016-2022*

	Years						
Group	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**
Overall	14.0 (12.5-15.6)	10.6 (9.3-12.2)	12.1 (10.6-13.8)	11.7 (10.2-13.4)	13.5 (11.9-15.3)	14.3 (12.5-16.2)	9.7 (8.2-11.4)
Sex							
Female	23.4 (20.7-26.3)	17.8 (15.4-20.5)	20.3 (17.6-23.4)	20.1 (17.4-23.1)	23.0 (20.1-26.3)	24.0 (20.8-27.6)	16.4 (13.7-19.5)
Male	3.2 (2.2-4.4)	2.4 (1.6-3.7)	2.9 (1.9-4.2)	2.4 (1.5-3.7)	3.0 (2-4.4)	3.5 (2.3-5.1)	2.4 (1.4-3.8)
Reproductive years (female only)							
Reproductive (18-51 years)	24.7 (21.3-28.5)	19.3 (16.1-23)	22.2 (18.6-26.4)	24.3 (20.5-28.6)	26.4 (22.4-31)	28.7 (24.3-33.7)	17.6 (14-21.7)
Older (52+ years)	21.2 (17.1-25.9)	15.4 (11.9-19.7)	17.4 (13.5-22.1)	13.6 (10.2-17.8)	18.0 (14-22.8)	16.6 (12.5-21.7)	14.5 (10.6-19.5)

*Incidence rate (95% confidence interval)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We analyzed 4.6 million individuals followed an average of 2.8 years (standard deviation, SD 2.2); 52.6% were female, and mean age at time zero was 43.1 years (SD 14.8). During this period, 1,593 new SLE cases (89.2% female) were identified across 12.9 million person-years (12.3 events per 100,000 person-years). There was no clear difference in incidence comparing 2020-2022 (12.6 events per 100,000 person-years) versus 2016-2019 (12.2 events per 100,000 person-years). In any given calendar year, the incidence was (as expected) much greater among females than males (Table 1). Overall, women had a higher incidence during reproductive years (23.3 events per 100,000 person-years; 95% CI 21.9-24.9) versus later (16.8 events per 100,000 person-years; 95% CI 15.3-18.5). In multivariate models, hazard ratios (HR) for female sex was 7.47 (95% CI 6.38-8.75) and for age (continuous),1.00 (95% CI 1.00, 1.01).

Conclusion: These clinically relevant real-world data suggest SLE incidence in the US is holding steady, during the period 2016-2022. Potential limitations of our analyses include selection bias (all individuals had private insurance), short average follow-up time period, and possible outcome misclassification, including the possibility that some prevalent SLE cases were mis-characterized as incident. Additional/ongoing analyses will consider other important factors, such as urban-versus-rural residence, race/ethnicity, and environmental exposures over a longer time period.

Disclosure: S. Bernatsky: None; **S. Dowell**: J&J, 6; **B. Banbury**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **G. Wright**: AbbVie/Abbott, 2, 5, 6, AstraZeneca, 2, 5, 6, Bristol-Myers Squibb(BMS), 1, 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Scipher Medicine, 2, 5, 6, UCB, 2, 5, 6; **E. Holladay**: None; **A. Mudano**: None; **C. Moura**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2.

Abstract Number: 1508

Dissecting the Role of T Cell Subsets and Complements in Lupus Pathogenesis in Systemic Lupus Erythematosus Patients with Obesity

Sheila Serin[1], Megan Schluentz[1], Chandana Keshavamurthy[1], Alexandra Reese[1], Sneha Centala[1], Bettina Boone[1], Samantha Ahrens[2], William Davis[3], Robert Quinet[1], Jerald Zakem[4], Samina Hayat[5], Sarwat Umer[6], Teresa leeth[7], Daniyal Nadeem[7] and Xin Zhang[8], [1]Department of Rheumatology, Ochsner Health, New Orleans, LA, [2]Multi-specialty Clinical Research, Ochsner Health, New Orleans, LA, [3]Ochsner Health System, New Orleans, LA, [4]Ochsner Health Systems, Metairie, LA, [5]Louisiana state university Shreveport, Shreveport, LA, [6]LSUHSC Shreveport, Shreveport, LA, [7]Louisiana State University Health Science, Shreveport, LA, [8]Ochsner Medical Center, New Orleans, LA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by systemic inflammation, autoantibody production, and multiorgan involvement. Although genetic, hormonal, and environmental factors are known contributors to disease development, the role of obesity – a growing epidemic in the United States – remains underexplored in SLE. Evidence suggests that adipose tissue in obese individuals secretes inflammatory mediators, which may influence immune function and disease activity. Our published study showed that a high-fat diet accelerates lupus development and autoimmunity in MRL/lpr lupus-prone mice. Here, we examined immune cell profiles (especially T cell

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

subsets), clinical manifestations, and laboratory parameters in non-obese, overweight, and obese SLE patients to explore the immunometabolic link between obesity and lupus pathogenesis.

Methods: Peripheral blood specimens were collected from 56 consented SLE patients: 15 (27%) non-obese (BMI ≤ 25kg/m2), 12 (21%) overweight (BMI 25-30kg/m2), and 29 (52%) obese (BMI ≥ 30 kg/m2). Multiparameter flow cytometry and serial gating were used to examine immune cell populations in patients' blood. Clinical data including demographic information, body mass index (BMI), SLE disease activity (SLEDAI), titers of anti-dsDNA antibody, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and complement (C3, C4) levels were extracted from Epic electronic medical record system. Statistical significance and correlation among groups were determined by Student's t-test and Chi-squared test. Two-tailed $p < 0.05$ was considered significant.

Results: SLE patients included in this study were 96.4% female, 71.4% African American, 21.4% Caucasian American, 3.6% Asian, and 3.6% Hispanic/Latino. Obese and overweight lupus patients had a significantly higher CRP ($p < 0.01$) compared to the non-obese patients. The percentage of patients with severe lupus (SLEDAI > 6) was significantly higher in the obese (21.7%) and overweight (8.3%) groups than the non-obese group (0%). In addition, a higher percentage of lupus with skin lesions was found in the obese (27.3%) and overweight (17.9%) groups than the non-obese group (0%). Flow cytometry results revealed a significantly higher frequency of circulating CD4+ T helper cells (especially CCR4+CCR6- Th2 cells and CD4+ICOS+ T follicular helper cells) in obese and overweight lupus patients, compared to non-obese lupus patients ($p < 0.05$, $p < 0.01$, respectively). Interestingly, these increased frequencies of circulating Th2 ($r=0.8910$) and Tfh helper cells ($r=0.5902$) in obese SLE patients were significantly correlated to SLEDAI level ($p < 0.05$), whereas the increased levels of complement levels (C3 and C4) in obese SLE patients were closely correlated to patients' BMI levels ($p < 0.05$).

Conclusion: Our results showed that obese and overweight lupus patients had an altered Th2 and Tfh cell profile and dysfunctional clinical features with worse outcomes. The increased level of complement is due to obesity, not autoimmunity. Further mechanism studies may provide insight into lupus pathogenesis and treatment strategies for obese SLE patients.

Disclosure: S. Serin: None; **M. Schluentz**: None; **C. Keshavamurthy**: None; **A. Reese**: None; **S. Centala**: None; **B. Boone**: None; **S. Ahrens**: None; **W. Davis**: None; **R. Quinet**: None; **J. Zakem**: None; **S. Hayat**: None; **S. Umer**: None; **T. Ieeth**: None; **D. Nadeem**: None; **X. Zhang**: None.

Abstract Number: 1509

Outcome of Newly Diagnosed SLE with Serositis and Its Clinical Features in Daily Clinical Practice: A Single Center Study

Shuzo Sato, Kaito Moriuchi, So Yamamoto, Hiroki Nibu, Takahito Sakamoto, Shotaro Ogawa, Kenji Saito, Yuya Sumichika, Shuhei Yoshida, Haruki Matsumoto, Jumpei Temmoku and Tomoyuki Asano, Fukushima Medical University, Fukushima, Fukushima, Japan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Past reports have shown that serositis is a risk factor for organ damage in patients with SLE. However, the distinct clinical features of newly onset SLE with serositis remain unclear. This study aims to elucidate specific clinical features of SLE with serositis at initial onset compared to those without.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1 Clinical features of newly-onset SLE patients with serositis compared to those without

Clinical items mean SD, (%)	No-serositis (n = 47)	Serositis (n = 35)	p
Age (mean SD)	36.7 ± 16.5	36.3 ± 14.9	N.S
Male/Female (female %)	5/42 (89.4%)	2/33 (94.3%)	N.S
Observation period (months)	61.0 ± 45.1	63.1 ± 40.4	N.S
Lupus nephritis	27/47 (57.4)	24/35 (68.6)	N.S
Neuropsychiatric SLE	11/47 (23.4)	8/35 (22.9)	N.S
SLEDAI*	16.6 ± 6.97	20.7 ± 9.18	0.036
SDI (end of follow up) *	0.51 ± 0.86	0.97 ± 1.04	0.022
Outcome (alive)	38/41 (92.7)	31/32 (96.9)	N.S
Severe infections (need hospitalization)	12/47 (25.5)	6/35 (17.1)	N.S
Complication of Sjogren's syndrome	18/47 (38.3)	10/35 (28.6)	N.S
Anti-SSA positive	31 (66.0)	23 (65.7)	N.S
Low complement C3/C4*	37 (78.7)	33 (94.3)	0.045
PSL doses (mg/day)*	37.3 ± 18.1	51.3 ± 11.6	<0.001
mPSL pulse therapy (yes)*	22 (46.8)	30 (85.7)	<0.001
Hydroxychloroquine (HCQ)	24 (51.1)	23 (65.7)	N.S
Flare (during the observation period, person)	17 (36.2)	13 (37.1)	N.S
flare with serositis (any serositis/total times of all flare)*	2/24 (8.3)	6/15 (40.0)	0.025
lupus peritonitis/enteritis (times/all flare)*	0/24 (0)	4/15 (26.7)	0.017

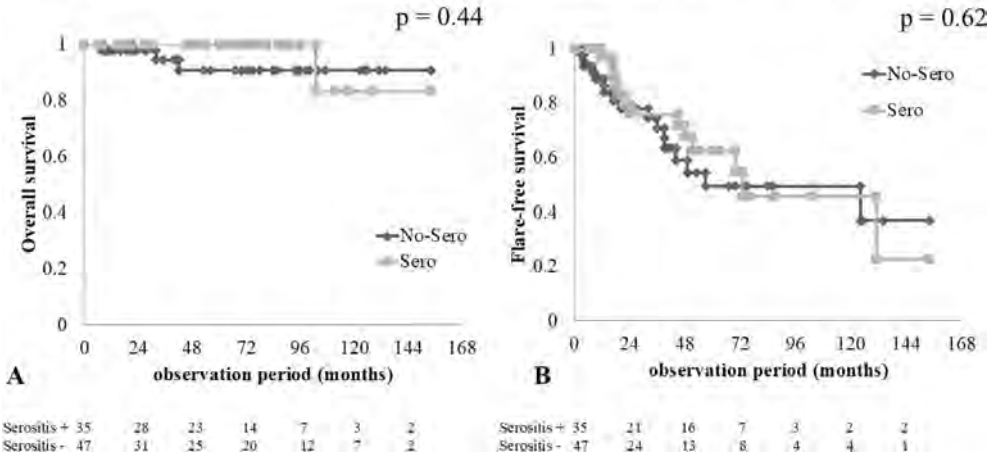
*p < 0.05
N.S. Not significant

Clinical features of newly-onset SLE patients with serositis compared to those without

Methods: This study is a retrospective inception cohort design. Newly diagnosed patients with SLE treated in the Department of Rheumatology at Fukushima Medical University Hospital between 2011 and 2023 were included. Patients who followed up for over 6 months were selected for this study. Those with newly onset SLE with serositis, which includes pericarditis, pleuritis, and peritonitis, were classified as the serositis group. Clinical features, including age, sex, disease duration, SLE symptoms, laboratory data, disease activity, organ damage, and treatment, were compared with those without serositis (no-serositis group). Cumulative overall survival and flare-free survival were also compared between the two groups using Kaplan-Meier analysis.

Results: Among 95 patients with newly onset SLE treated in our department, 82 patients were included. The mean age was 36.5 years, and 75 patients were female (91.8%). The mean observation period was 61.9 months, and the mean SLEDAI score was 18.4. Among the 82 patients, 35 (42.7%) had serositis at the initial disease onset. The comparison of clinical characteristics between the serositis group (35 patients) and no-serositis group (47 patients) is shown in Figure 1. General characteristics were similar between the two groups, except for higher SLEDAI scores and lower complement levels in the serositis group. The serositis group showed a significantly increased number of flares with serositis compared to no-serositis group. Additionally, the SDI scores at the end of follow-up were significantly higher in the serositis group. In terms of therapy,

Figure 2 Kaplan-Meier analyses between Serositis group and No-serositis group



Kaplan-Meier analyses between newly-onset SLE with serositis group and those without (no-serositis group)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

significantly higher PSL doses and increased frequencies of mPSL pulse therapy were observed in the serositis group. Kaplan-Meier analysis revealed similar cumulative overall and flare-free survival rates between the two groups (Figure 2). We further analyzed the risk factors for organ damage accrual (SDI of 1 or more) in patients with newly onset SLE. Logistic regression analysis indicated that age and serositis were independent risk factors for damage accrual (odds ratio: age 1.05, 95%CI 1.01-1.09; serositis 2.74, 95%CI 1.01-7.40, respectively, $p< 0.05$).

Conclusion: Newly onset SLE with serositis may demonstrate higher organ damage accrual compared to that without serositis. More frequent flare-ups of serositis/enteritis may occur in newly onset SLE with serositis.

Disclosure: S. Sato: AbbVie/Abbott, 6, Asahi-Kasei Pharma, 5, 6, AstraZeneca, 6, Chugai Pharmaceutical, 5, 6, Eisai Pharmaceutical, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 6, Ono Pharmaceutical, 6, Taisho Pharmaceutical, 6, Tanabe Mitsubishi Pharmaceutical, 6; **K. Moriuchi**: None; **S. Yamamoto**: None; **H. Nibu**: None; **T. Sakamoto**: None; **S. Ogawa**: None; **K. Saito**: None; **Y. Sumichika**: None; **S. Yoshida**: None; **H. Matsumoto**: None; **J. Temmoku**: None; **T. Asano**: None.

Abstract Number: 1510

Biomarker landscape for neuropsychiatric involvement in patient with systemic lupus erythematosus

Sitian Zang[1], Ranran Yao[2] and Zhanguo Li[3], [1]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China (People's Republic), [2]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China (People's Republic), [3]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, Beijing, Beijing, China (People's Republic)

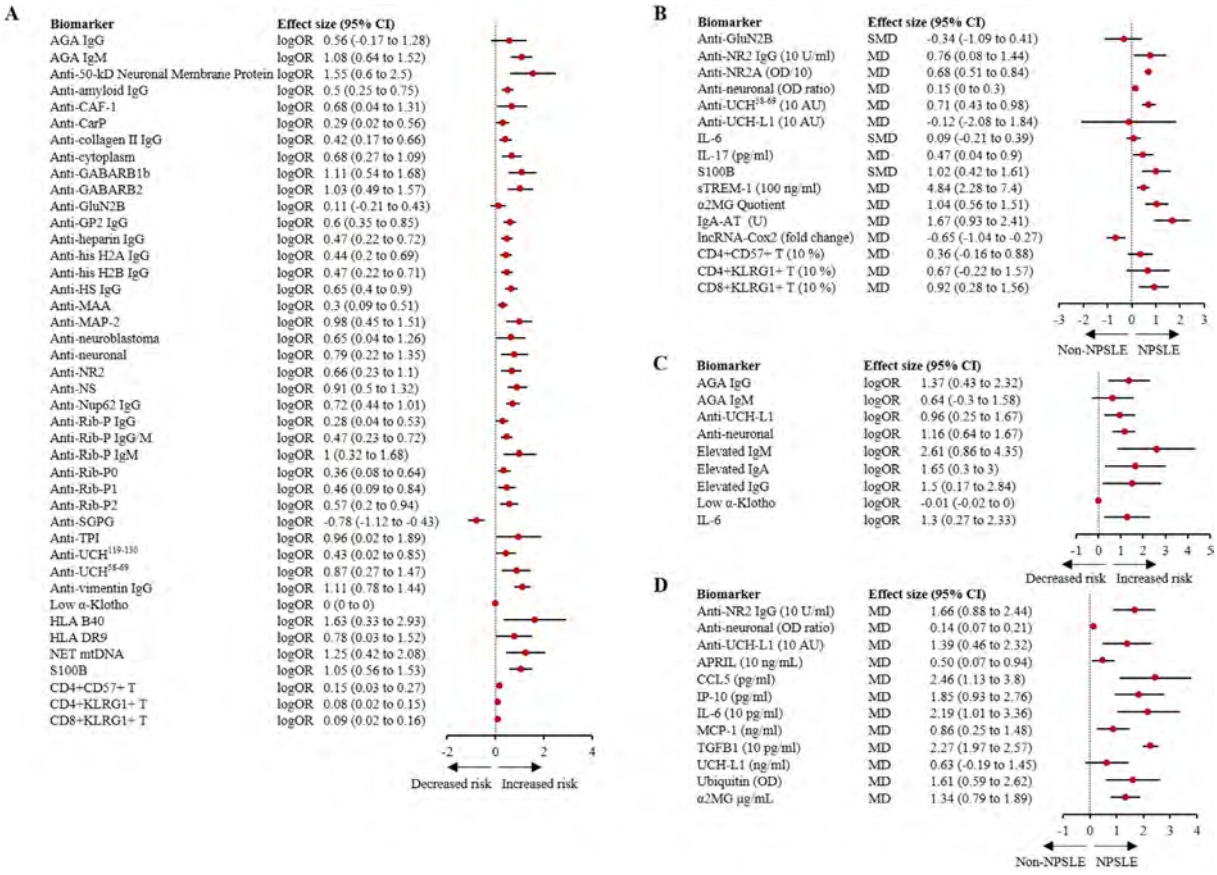
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multifactorial autoimmune disease result in substantial organs or systems damage or even fatal. The estimated number of global patients with SLE was up to 4 million, and the annually newly diagnosed number was 0.37 million. Neuropsychiatric damage, comprising the overwhelming majority of the manifestations, are lethal.

Methods: A comprehensive search strategy on the associations between biomarkers and organ or system involvement was developed and implemented across multiple databases, including Embase, PubMed and Web of Science, from inception to 1 June, 2023. Additionally, reference lists of key reviews, meta-analyses, and primary studies were hand-searched to identify potential articles not captured in the initial database queries to maximize the inclusion of relevant studies. We pooled effect estimates by DerSimonian-Laird random-effects model when $I2 > 50\%$ or p value for Q less than 0.1, and performed sensitivity analyses by sequentially omitting one study at a time to assess the impact of each individual study on the pooled effect estimates. Otherwise, we use the fixed effects model.

Results: Of the 24,279 citations identified, 5,056 full-text was screened, and 229 publications was included in the studies, involving 42464 patients with lupus, of them, 8550 patients with neuropsychiatric involvement, spanning 38 countries and territories. There are 39 blood and seven CSF biomarkers uniquely associated with the risk of neuropsychiatric involvement in patients with SLE, and mean difference between patients with versus without neuropsychiatric involvement in SLE of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Effect size of biomarkers in patients with VS without neuropsychiatric involvement. A-B, blood biomarkers. C-D, cerebrospinal fluid biomarkers.

11 blood and 11 cerebrospinal fluid (CSF) biomarkers are statistically significant. Anti-neuronal abs (odd ratio [OR] 14.31, 95% confidence interval (CI) 4.41 to 46.45) in CSF are associated with the risk of neuropsychiatric involvement in patients with SLE, and the quality of evidence is moderate because of consistency, low risk of bias and large effect. Besides, anti-neuronal abs (OR 6.1, 95%CI 1.65 to 22.59) in blood are associated with the risk of neuropsychiatric involvement. The blood and CSF level of anti-neuronal abs in patients with versus without neuropsychiatric involvement are significantly higher. Anti-N-methyl-D-aspartate receptor subtype NR2a/2b antibody (anti-NR2 antibody) in blood are associated with the risk of neuropsychiatric involvement in patients with SLE (OR 4.6, 95%CI 1.70 to 12.47), the blood level of Anti-NR2 IgG (mean difference [MD] 7.6, 95%CI 0.84 to 14.36 U/ml) and anti-NR2A (MD 0.07, 0.05 to 0.08 OD), CSF Anti-NR2 IgG (MD 16.62, 95%CI 8.83 to 24.41 U/ml) in patients with versus without neuropsychiatric involvement are significantly higher. Blood low CSF α-Klotho have excellent diagnostic accuracy for predicting neuropsychiatric involvement in patients with SLE, and the sensitivity, specificity, and AUC is 82.3%, 96.0%, and 0.94, respectively.

Conclusion: Multiple biomarkers have diagnostic value for neuropsychiatric involvement in patients with SLE, which may be used in clinical diagnosis in the future to reduce the disease burden caused by neuropsychiatric involvement.

Disclosure: S. Zang: None; **R. Yao**: None; **Z. Li**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1511

Mental Health and Medical Burden: The Impact of Depression on Length of Stay in Lupus Patients

Sophia Chang Stauffer[1], Huan Chang[2], Parth Desai[3], Elaine Adams[4], William Galanter[5] and Axi Patel[6], [1]Mount Sinai Hospital, Sinai Urban Health Institute and Univ.of Illinois @ Chicago, Dept Medicine, Div. Endocrinology, Chicago, IL, [2]University of Illinois at Chicago, Div Rheumatology and Jesse Brown VA Medical Center, Chicago, IL, [3]University of Texas Southwestern Medical Center, Dallas, TX, [4]Jesse Brown VA Medical Center, Chicago, IL, [5]University of Illinois at Chicago, Division of General Internal Medicine, Chicago, IL, [6]University of Illinois at Chicago, Div Rheumatology, Chicago, IL

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Depression is more common in patients with systemic lupus erythematosus (SLE) than in the general population. Individuals with SLE and a mental health condition have higher rates of healthcare use than those without mental health conditions, but the effect of SLE and depression on hospitalization has not been studied. In this pilot study we assess the impact of co-morbid depression on in-hospital mortality, length of hospital stay (LOS), and hospital charges in patients admitted for SLE.

Methods: We utilized the 2022 National Inpatient Sample (NIS) to identify adult hospitalizations with a primary diagnosis of SLE, further categorizing patients into those with coexisting depression (SLE+DEP) and those without (SLE only) based on ICD-10 codes across secondary diagnoses. Survey weights were applied to generate national estimates. We conducted 1:3 propensity score matching (PSM) using a nearest-neighbor algorithm with a caliper of 0.1, adjusting for demographic and clinical covariates. Balance diagnostics confirmed improved covariate balance post-matching. Outcomes assessed included length of stay (LOS), and in-hospital mortality.

Results: Of an estimated 8,180 weighted SLE hospitalizations, 110 had coexisting depression diagnoses. Patients in the SLE+DEP group were predominantly female (90.9%) and older (mean age 46.7 ± 16.8 years) compared with the SLE-only group (88.0% female; mean age 38.9 ± 15.2 years). Mean LOS was longer among SLE+DEP patients (9.0 vs. 7.2 days), though not statistically significant in unadjusted models. Mean total hospital charges were lower in the SLE+DEP group ($70,478 vs. $99,755), with no observed in-hospital mortality among the depressed cohort versus 0.87% among the non-depressed cohort.

Conclusion: Currently there is no standard of care for mental health monitoring and treatment for SLE patients. Our data suggest that hospitalized patients with diagnoses of SLE and depression have significantly longer lengths of stay than those with a diagnosis of SLE only. Our data also suggest a trend between longer stays and lower cost. Our data were limited by the information available in the dataset, which does not include intensity of care. Additionally, our pilot study includes only 1 year of data and the cohorts differed in mean age. Nevertheless, our study reveals intriguing findings that could have

Table 1. Baseline Characteristics

VARIABLE	SLE Only (n=8,070)	SLE + Depression (n=110)	P-value/Notable Difference
Female, n (%)	7,094 (88.0%)	100 (90.9%)	0.66
Mean Age (years)	38.9 ± 15.2	46.7 ± 16.8	< 0.01

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Unadjusted Outcomes

UNADJUSTED OUTCOMES			
VARIABLE	SLE Only (n=8,070)	SLE + Depression (n=110)	P-value/Notable Difference
Mean Total Charges ($)	99,755	70,478	p = 0.86
In-Hospital Mortality	0.87%	0%	p = 0.67
Mean LOS (Days)	7.2 ± 9.2	9.0 ± 10.7	p = 0.32

Table 3. Adjusted Outcomes

ADJUSTED OUTCOMES			
	Average Treatment Effect on the Treated (ATT)	95% Confidence Interval	P-value
In-Hospital Mortality	-4.5% (NS)	-13.2% to +4.1%	0.305
LOS (Days)	+2.32 days	+1.47 to +3.17	<0.001

important ramifications for inpatient care of SLE patients. More investigation is needed to elucidate the complexities of co-morbid SLE and depression and how they can impact patient healthcare needs and utilization in context.

Disclosure: S. Chang Stauffer: None; **H. Chang**: None; **P. Desai**: None; **E. Adams**: None; **W. Galanter**: None; **A. Patel**: None.

Abstract Number: 1512

anti-u1-rnp Antibody Positivity Is Associated with Elevated Interferon Score in SLE Irrespective of Disease Activity: A Transcriptome Analysis in Japanese Patients

Takemichi Matsui[1], Yumi Tsuchida[2], Takahiro Itamiya[2], Mineto Ota[2], Toshihiko Komai[2], Haruka Tsuchiya[2], Hirofumi Shoda[2], Tomohisa Okamura[2] and Keishi Fujio[2], [1]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, [2]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: With the introduction of anifrolumab to clinical practice, there is a growing interest in identifying factors associated with IFN activity in patients with SLE. An association between IFN gene signature and anti-U1-RNP antibody positivity has been reported. However, data from Asians are scarce. In this study, we investigated serological parameters associated with the IFN gene signature in patients with SLE, as well as its association with disease activity.

Methods: We utilized transcriptome data from 130 Japanese patients diagnosed with SLE from the ImmuNexUT database. IFN score was defined as the average normalized expression levels of *IFI27*, *IFI44*, *IFI44L*, and *RSAD2*. The associations between clinical parameters and the IFN score were assessed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

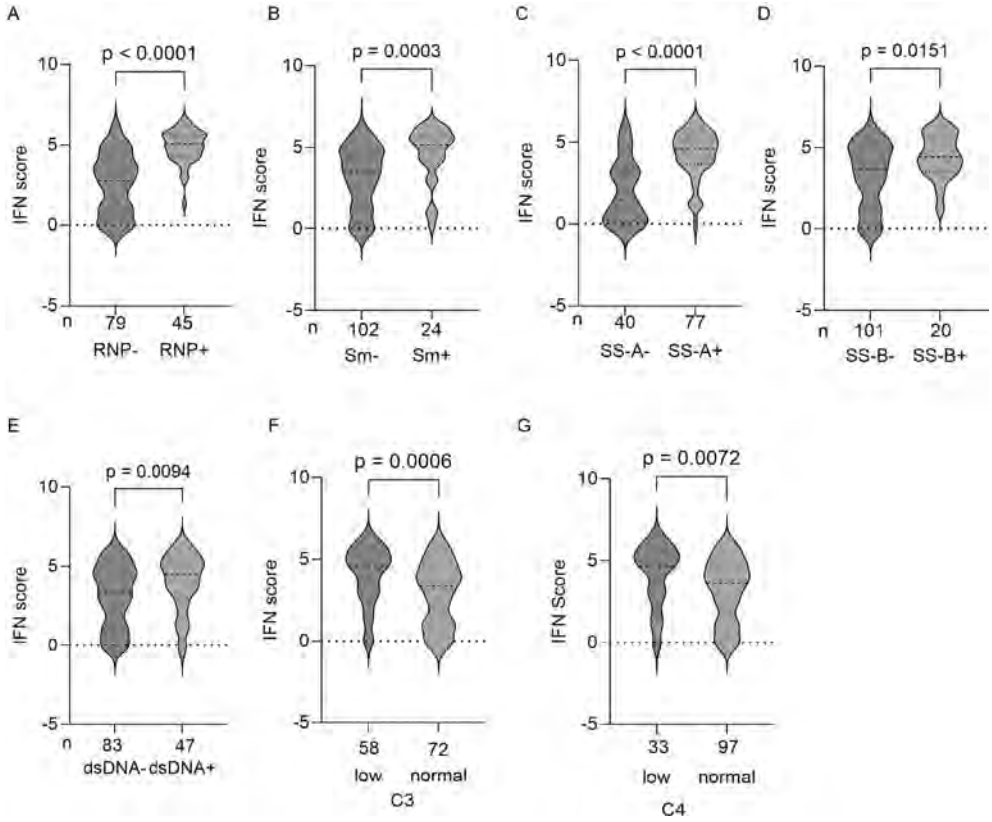


Figure 1: IFN Score and Serological Characteristics (A–E) IFN scores according to the anti-U1-RNP (A), anti-Sm (B), anti-SS-A (C), anti-SS-B (D), and anti-dsDNA (E) antibody statuses. (F and G) IFN scores according to C3 (F) and C4 (G) levels.

Results: The IFN scores showed a bimodal distribution; therefore, the patients were divided into two groups according to a cutoff score of 1.6. Of the 130 patients, 31 and 99 were classified into the low and high IFN groups, respectively. Clinical characteristics of patients in each group are shown in Table 1. Notably, disease activity was higher in the high IFN than the low IFN group (median [IQR] SLEDAI-2K score: 5 [2–9] vs. 2 [0–2], $p < 0.0001$). The IFN score was higher in patients positive for anti-U1-RNP antibodies (median [IQR]: 5.0 [4.3–5.4] vs. 2.8 [0.9–4.1]), anti-Sm antibodies (median [IQR]: 3.5 [1.4–4.7] vs. 5.1 [4.0–5.6]), anti-SSA antibodies (median [IQR]: 4.6 [3.7–5.3] vs. 1.4 [0.2–3.4]), anti-SSB antibodies (median [IQR]: 4.4 [3.5–5.6] vs. 3.7 [1.4–5.0]), and anti-dsDNA antibodies (median [IQR]: 4.5 [3.0–5.4] vs. 3.3 [1.2–4.7]) compared with patients negative for these autoantibodies (Figure 1A–E). Classification and regression tree analysis indicated anti-U1-RNP antibody positivity as the most important serological predictor of the IFN score (Figure 2A). Even among patients who are

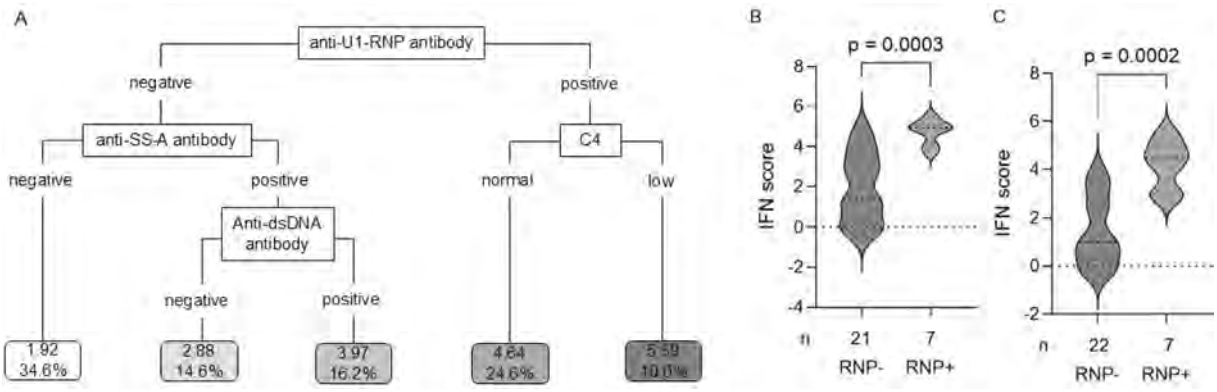


Figure 2: The IFN score and anti-U1-RNP Antibody Status (A) Classification and regression tree analysis of serological factors associated with the IFN score. The numbers in the boxes indicate the average IFN score in each group and the percentage of patients in that group. (B, C) IFN scores in serologically active, clinically quiescent patients (B) and inactive patients (C) according to anti-U1-RNP antibody status.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Clinical Characteristics of Patients in the Low and High IFN Groups

Table 1. Clinical characteristics of patients in the low and high IFN groups

	Low IFN (n=31)	High IFN (n=99)	
Age, years, mean ± SD	48.2 ± 12.1	45.8 ± 13.1	n.s.
Sex (female), n (%)	29 (93.5%)	91 (91.9%)	n.s.
Disease duration, years, median (IQR)	12 (5-20)	14 (3-18)	n.s.
SLEDAI-2K score, median (IQR)	2 (0-2)	5 (2-9)	$p<0.0001$
Treatment			
Glucocorticoids, n (%)	28 (90.3%)	81 (81.8%)	n.s.
PSL (mg), median (IQR)	5 (4–5)	5 (3–7.5)	n.s.
PSL ≥ 10 mg	2 (6.5%)	11 (11.1%)	n.s.
HCQ, n (%)	14 (45.2%)	46 (46.5%)	n.s.
Tacrolimus, n (%)	10 (32.3%)	17 (17.2%)	n.s.
CyA, n (%)	1 (3.2%)	11 (11.1%)	n.s.
MMF, n (%)	9 (29.0%)	21 (21.2%)	n.s.
Azathioprine, n (%)	2 (6.5%)	10 (10.1%)	n.s.
Symptoms during the entire disease course			
Lupus nephritis, n (%)	20 (64.5%)	59 (60.0%)	n.s.
Arthritis, n (%)	23 (74.2%)	70 (70.7%)	n.s.
Mucocutaneous, n (%)	19 (61.3%)	77 (73.7%)	n.s.
Leukopenia, n (%)	25 (80.6%)	86 (86.9%)	n.s.
Thrombocytopenia, n (%)	8 (25.8%)	29 (29.3%)	n.s.
Active symptoms			
Lupus nephritis, n (%)	1 (3.2%)	28 (28.3%)	$p=0.0035$
Arthritis, n (%)	3 (9.7%)	20 (20.2%)	n.s.
Mucocutaneous, n (%)	2 (6.5%)	36 (36.4%)	$p=0.0014$
Leukopenia, n (%)	0 (0.0%)	9 (9.1%)	n.s.
Thrombocytopenia, n (%)	0 (0.0%)	7 (7.1%)	n.s.

SD: standard deviation; IQR: interquartile range; PSL: prednisolone (for patients taking glucocorticoids other than PSL, the equivalent doses were calculated); HCQ: hydroxychloroquine; CyA: cyclosporin A; MMF: mycophenolate mofetil.

serologically active clinically quiescent (SACQ) and among patients who were both serologically and clinically inactive, the IFN score was higher in anti-U1-RNP antibody positive patients compared to negative patients (median [IQR]: 4.7 [4.1–5.1] vs. 1.4 [0.2–5.0], p = 0.0003 for SACQ, Figure 2B; median [IQR]: 4.5 [3.0–5.1] vs. 1.0 [0.3–2.6], p = 0.0002 for inactive, Figure 2C). Among SACQ patient and inactive patients, all patients positive for anti-U1-RNP antibodies belonged to the high IFN group while less than half of the patients negative for anti-U1-RNP antibodies belonged to the high IFN group (8/8 (100%) vs 10/21 (47.2%), p=0.03 for SACQ and 7/7 (100%) vs 8/22 (27.6%), p=0.01).

Conclusion: Autoantibody profiles, especially anti-U1-RNP antibodies, are useful for predicting IFN scores. Anti-U1-RNP antibody-positive patients have high IFN scores irrespective of disease activity.

Disclosure: T. Matsui: None; **Y. Tsuchida**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Daiichi-Sankyo, 6, Eisai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Novartis, 6; **T. Itamiya**: None; **M. Ota**: None; **T. Komai**: AbbVie, 6, AstraZeneca, 6, Eisai, 6, Eli Lilly, 2, 6, GlaxoSmithKlein(GSK), 5, 6, Kissei, 6, Mitsubishi Tanabe Pharma, 6, Novartis, 6; **H. Tsuchiya**: AbbVie, 5, 6, Amgen, 6, Asahi Kasei, 6, Astellas, 6, Bristol-Myers Squibb, 6, Chugai, 6, Daii chi-Sankyo, 6, Eisai, 6, Eli Lilly, 6, Gilead, 6, Jansen, 6, Mochida, 5, Novartis, 6, Sanofi, 6, Takeda, 5, Tanabe Mitsubishi, 6, UCB, 6; **H. Shoda**: None; **T. Okamura**: Asahi Kasei, 6, Bristol-Myers Squibb, 6, Chugai Pharmaceutical, 5; **K. Fujio**: AbbVie/Abbott, 5, 6, Alexion Pharma, 6, Asahi Kasei Pharma, 5, 6, Astellas, 6, AstraZeneca, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Chugai, 5, 6, Daiichi-Sankyo, 6, Eisai, 6, Eli Lilly, 5, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Novartis, 1, 6, Pfizer, 6, Taisho, 6, Tanabe Mitsubishi, 6, Tsumura, 6, UCB, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1513

Race, Renal Failure, and Risk: A five-to-ten year retrospective cohort study of Racial differences in outcomes of patients with dialysis-dependent Lupus nephritis

Ufuoma Mamoh[1], Queeneth Edwards[2], Chukwuemelie Okeke[3], Justin Riley Lam[4], Soziema Salia[5] and Christhopher Haas[6], [1]Medstar Health Georgetown University Internal Medicine Residency Program, Baltimore, MD, [2]Georgia Southern University, Statesboro, GA, [3]Maimonides Medical Center, Brooklyn, NY, [4]Albert Einstein Medical Center, Philadelphia, PA, [5]MedStar Health Georgetown University (Baltimore) Internal Medicine Program, Baltimore, MD, [6]MedStar Health Georgetown University (Baltimore) Internal Medicine Program, Baltimore

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that disproportionately affects racial and ethnic minority populations, particularly Black/African American and Hispanic/Latino individuals. In 50% of patients with SLE, Lupus nephritis typically develops within 5 years of diagnosis. These patients have an increased risk of developing ESRD. This study evaluates the racial disparities in clinical outcomes of adults diagnosed with SLE and dialysis-dependent ESRD over 20 years, between Black/African American and Hispanic/Latino populations.

Methods: This retrospective cohort study utilized TriNetX Global Collaborative Network data, encompassing over 144 healthcare organizations. Adults (age >18 years) with a diagnosis of systemic lupus erythematosus (SLE), end-stage renal disease (ESRD), and who were on dialysis within the past 20 years were included in the study. We classified two

Table 1. Demographic Comparison of Blacks and Hispanics – Pre- and Post-Propensity Score Matching

Characteristic	Blacks (Pre-Match, N=2,101)	Hispanics (Pre-Match, N=1,007)	Blacks (Post-Match, N=965)	Hispanics (Post-Match, N=965)
Age (Years)	53.0 ± 15.5	50.3 ± 15.9	50.0 ±15.2	50.4 ± 15.9
Age at Index	46.0 ± 15.6	43.2 ± 16.0	42.9 ± 15.1	43.2 ± 15.9
Female (%)	81.5%	77.3%	79.3%	77.5%
Male (%)	18.5%	22.7%	20.7%	22.5%
Overweight/Obesity (%)	19.1%	17.7%	16.1%	17.7%
Diabetes mellitus (%)	22.8%	23.7%	22.4%	23.8%
Metabolic Disorders (%)	47.5%	48.7%	47.5%	48.6%
Hypertension (%)	60.9%	59.8%	57.4%	59.7%
Neoplasms (%)	20.3%	17.6%	16.6%	17.6%
Chronic Resp. Disease (%)	18.4%	11.9%	11.8%	11.9%
Cardiovascular medications	64.0%	60.3%	58.9%	60.3%
Adrenal corticosteroids	52.3%	49.2%	48.8%	49.2%
Immune suppressants	29.2%	27.4%	26.9%	27.5%
Immunological agents, other	13.0%	14.5%	14.8%	14.4%

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical Outcomes after Propensity Matching

Outcome	Blacks	Hispanics	Statistical Test Risk Difference:	Hazard Ratio (95% CI)	Odds Ratio (95% CI)
All-cause Mortality	446 / 2683 (16.6%)	271 / 2669 (10.2%)	0.065 (0.047,0.0830)	1.700 (1.462,1.977)	1.764 (1.501-2.074)
MI (Ischemic Heart Disease)	442 / 2092 (20.2%)	375/2081 (18.2%)	0.022 (-0.002,0.045)	1.194 (1.039,1.372)	1.150 (0.985-1.342)
Stroke	157 /2514 (6.2%)	112 /2557 (4.4%)	0.019 (0.006,0.031)	1.486 (1.166–1.894)	1.454 (1.134-1.865)

cohorts: Cohort A (Black or African American, n=7491), and Cohort B (Hispanic/Latino, n=2723). Exclusion criteria included patients younger than 18 or diagnosed more than 20 years ago. Propensity score matching was applied to balance demographics, diagnoses, and medications. The outcomes measured were all-cause mortality, myocardial ischemia (MI), and stroke.

Results: After matching, each cohort included 2690 patients. The average age was 50 years in both Cohorts. Both cohorts were predominantly female (79.3% and 77.5%). Blacks had a significantly higher odds of all-cause mortality than Hispanic patients [16.6% vs 10.2%; OR 1.764; 95% (CI = 1.501,2.074)]. There was a higher odds of stroke in black patients compared to Hispanic patients [6.2% vs 4.4% OR 1.454; 95% (CI = 1.134, 1.865)]. There was no significant difference in the odds of MI [OR 1.150, 95% (CI = 0.985, 1.342)].

Conclusion: These findings suggest the racial disparities in clinical outcomes in patients with dialysis-dependent ESRD secondary to lupus nephritis. Black patients had higher odds of all-cause mortality and stroke compared to their Hispanic counterparts, despite comparable baseline characteristics. Posulated reasons include differences in quality and access to healthcare and health-promoting resources, differences in healthcare utilization patterns, differences in comorbid disease patterns, and underlying epigenetic patterns. These results highlight the need for tailored interventions and equitable healthcare delivery to mitigate outcome disparities and further investigations to determine the underlying processes causing these differences in results

References:

1. Mahajan A, Amelio J, Gairy K, et al. Systemic lupus erythematosus, lupus nephritis and end-stage renal disease: a pragmatic review mapping disease severity and progression. Lupus. 2020;29(9):1011-1020. doi:10.1177/0961203320932219
2. 2. Xipell M, Lledó GM, Egan AC, et al. From systemic lupus erythematosus to lupus nephritis: The evolving road to targeted therapies. Autoimmun Rev. 2023;22(10):103404. doi:10.1016/j.autrev.2023.103404

Disclosure: U. Mamoh: None; **Q. Edwards**: None; **C. Okeke**: None; **J. Lam**: None; **S. Salia**: None; **C. Haas**: None.

Abstract Number: 1514

Serum Antigenome Profiling Reveals Diagnostic Models for Systemic Lupus Erythematosus

Yan Wang[1], Lulu Cao[2], Mengze Xu[3], Jian Lu[3], Jing He[1], Fanlei Hu[4] and Zhanguo Li[5], [1]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, Beijing, China (People's Republic), [2]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, Beijing, [3]State Key Laboratory of Protein and Plant Gene Research, Center for Bioinformatics, School of Life Sciences, Peking University, Beijing, China., Beijing, Beijing, China (People's Republic), [4]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China (People's Republic), [5]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, Beijing, Beijing, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) exhibits profound clinical and pathogenic heterogeneity, complicating diagnosis and treatment. Identifying subtype-specific biomarkers might intrinsically link to organ involvement.

Methods: Patients with SLE were classified into five subgroups, including renal, hematologic, mucocutaneous, neuropsychiatric, and cardiopulmonary subtypes. Serum antigens were captured by purified IgG from a cohort consisting of 10 SLE patients per subgroup, together with sex- and age-matched 10 rheumatoid arthritis (RA), 10 Sjogren's syndrome (pSS), 10 anti-synthetase syndrome (ASS) patients and 10 healthy controls. Affinity Chromatography-purified autoantigens were set to liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis and machine learning to identify pathogenic molecules in different groups of SLE patients. The significantly upregulated and downregulated proteins with fold change > 2 ($p < 0.05$) were selected.

Results: We identified 39, 32, 36, 13 and 12 differentially expressed (DE) autoantigens in renal, hematological, mucocutaneous, neuropsychiatric, and cardiopulmonary subtypes, respectively. Based on the newly identified autoantigens, including CH60, FABPS, CREG1, ODO2, and TRY3, diagnostic prediction models were further constructed for SLE subtypes with renal, hematological, mucocutaneous, neuropsychiatric, and cardiopulmonary involvement. The average accuracy and AUC of the 5 groups were 92%/0.96, 93%/1.00, 95%/1.00, 89%/0.98, and 84%/0.99, respectively. The predominant autoantigens were enriched in distinct molecular pathways correlating with the clinical manifestations. Signal pathways were analyzed among these DE autoantigens.

Conclusion: These findings reveal SLE subtype-specific immune signatures, offering novel biomarkers for clinical stratification and potential targeted therapeutics.

Disclosure: Y. Wang: None; **L. Cao**: None; **M. Xu**: None; **J. Lu**: None; **J. He**: None; **F. Hu**: None; **Z. Li**: None.

Abstract Number: 1515

Machine Learning–defined Subtypes of Systemic Lupus Erythematosus Identify Distinct Immunologic and Molecular Signatures

Yuke Hou[1], Bo Wei[2], Jingyuan Liang[3], Yujia Zhai[4], Yan Wang[5], Haihong Yao[1] and Zhanguo Li[6], [1]Peking University People's Hospital, Beijing, Beijing, China (People's Republic), [2]Zhongshan Hospital Xiamen University, Xiamen, Fujian, China (People's Republic), [3]North China University Of Science And Technology Affiliated Hospital, Tianjin, Tianjin, China (People's Republic), [4]Bayannur City Hospital, Bayannur, Nei Mongol, China (People's Republic), [5]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, Beijing, China (People's Republic), [6]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, Beijing, Beijing, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

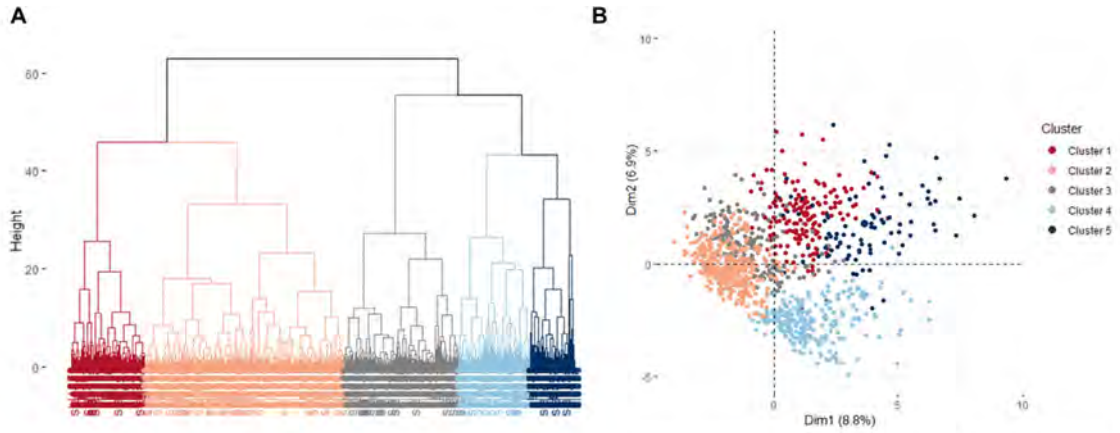


Figure 1. Hierarchical clustering tree and cluster reduction factor maps of systemic lupus erythematosus (SLE). (A) Five SLE clusters were defined by hierarchical cluster analysis. (B) Factor maps of each cluster, colored by cluster affiliation.

Hierarchical clustering tree and cluster reduction factor maps of systemic lupus erythematosus (SLE)

Background/Purpose: To refine clinical subtypes of systemic lupus erythematosus (SLE) using unsupervised machine learning, and to elucidate the molecular basis of disease heterogeneity through integrated immune, proteomic, and transcriptomic profiling.

Methods: We enrolled 1,065 SLE patients hospitalized at Peking University People's Hospital between 2012–2024. Unsupervised hierarchical clustering was applied to integrated clinical and laboratory variables. Peripheral blood lymphocyte subsets were assessed to characterize immunologic divergence across clusters. One-year prospective follow-up was conducted to evaluate therapeutic responses. Multi-omics profiling—including serum proteomics (LC-MS/MS) and transcriptomics (bulk RNA-seq) of peripheral blood mononuclear cells—was performed in subtype-stratified patients and age-/sex-matched healthy controls. Differential expression and enrichment analyses were used to define cluster-specific molecular signatures.

Results: Unsupervised machine learning identified SLE subtypes: Cluster 1 exhibited nephritis, high disease activity, and anti-Sm positivity; Cluster 2 had skin/mucosal involvement with low inflammation; Cluster 3 was defined by neuropsychiatric manifestations and anti-U1RNP/SSA positivity; Cluster 4 featured anemia, leukopenia, and thrombocytopenia (85.9%), with Coombs positivity and antiphospholipid antibody enrichment; Cluster 5 involved serosal/vascular complications with older age and elevated LDH. Immune cell profiling revealed distinct T, B, and NK subset distributions. Rituximab was most effective in Cluster 5 ($\beta = 0.286$, $p < 0.001$), while cyclophosphamide benefited Cluster 3 ($\beta = 0.284$, $p < 0.001$). Cluster 2 showed the highest LLDAS (46.4%) and steroid tapering; Cluster 4 had the highest SLEDAI < 4 rate (84.1%). In addition, multi-omics analyses identified key cluster-enriched molecules: APOA4 and LAMC1 in Cluster 1; CXCL7 and CCL18 in Cluster 2 ; S100A7 and ACTN4 in Cluster 3 ; IGHG1 and SERPINA1 in Cluster 4; THBS1 and LOX in Cluster 5. Transcriptomics revealed shared upregulation of interferon-inducible genes (e.g., IFI44, IFITM1) and cluster-specific cytokines (e.g., WNT5B, KRT5, BDNF), highlighting distinct pathogenic pathways that parallel clinical phenotypes.

Conclusion: Machine learning–guided subtyping uncovers clinically and molecularly distinct SLE subgroups. These findings support biologically informed stratification and might lay the groundwork for precision therapy in SLE.

Disclosure: Y. Hou: None; **B. Wei**: None; **J. Liang**: None; **Y. Zhai**: None; **Y. Wang**: None; **H. Yao**: None; **Z. Li**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1516

The Benefits of SGLT2i on GFR Slope and Proteinuria in SLE Depend on Subgroups of Diabetes Mellitus and Baseline eGFR

Jennifer Lee[1], Andrea Fava[2], Daniel Goldman[3], Laurence Magder[4] and **Michelle Petri**[3], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Timonium, MD, [4]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1467–1516) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) affects over 50% of SLE patients. Twenty percent of LN patients develop end-stage renal disease (ESRD) within 10 years. The 2021 CREDENCE trial and subsequent studies in the general population demonstrated that sodium-glucose co-transporter 2 inhibitors (SGLT2i) were shown to slow the progression of chronic kidney disease in type 2 diabetes patients. However, experience in SLE is limited. We investigated changes in eGFR and proteinuria in SLE patients following SGLT2i initiation.

Methods: We studied 109 SLE patients longitudinally (86% female; 32% White, 60% African-American, 9% Other, 32% with diabetes, 60% with eGFR< 60, and 58% with UPCR< 0.50 gm) who started taking SGLT2i and had at least one clinical visit within three years before and/or after treatment initiation. eGFR was calculated using the 2021 CKD-EPI creatinine equation, and proteinuria was assessed using the urine protein-creatinine ratio (UPCR**)**. Longitudinal mixed effects regression models with random slopes and intercepts were used to estimate changes in eGFR and UPCR before and after SGLT2i initiation. Models included terms for immediate level change and slope change starting 30 days after SGLT2i initiation, assuming linear trends in eGFR or UPCR. Subgroup analyses were done for diabetes mellitus status and baseline kidney function (eGFR < 60 vs. ≥60 mL/min/1.73m^2).

Results: In the cohort, the mean annual decline in eGFR before SGLT2i initiation was -2.0 (P=0.0002). The immediate change in eGFR post SGLT2i showed a decline of -1.4 (P=0.17). The eGFR slope post SGLT2i improved by 0.43 (P=0.63, Table 1). The initial decline followed by improvement in GFR slope were similar to the results of the CREDENCE trial, but did not reach statistical significance.

The improvement in eGFR slope was greater in those with diabetes and in those with eGFR < 60 (Table 2). This same benefit was shown in those with UPCR < 0.50g at SGLT2i initiation (Table 2, p=0.036) and also in those with UPCR < 0.30g at SGLT2i initiation (p=0.043).

Table 1. Estimated impact of SGLT2 on eGFR and mean Urine Protein-Creatinine ratio.

Subgroup	*Outcome*	*Effect*	*Estimate (95% CI)*	*P-value*
All (n=109)	eGFR	Annual decline before SGLT2i	-2.0 (-3.1, -1.0)	0.0002
		Immediate change	-1.4 (-3.5, 0.6)	0.17
		Change in slope after SGLT2i	0.43 (-1.3, 2.2)	0.63
	UPCR	Annual increase before SGLT2i	0.10 (-0.01, 0.20)	0.074
		Immediate change	-0.14 (-0.30, 0.02)	0.083
		Change in slope after SGLT2i	**-0.27 (-0.40, -0.13)**	**0.0001**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Estimated impact of SGLT2 on eGFR and mean Urine Protein-Creatinine ratio for subgroups based on diabetes mellitus status and baseline UPCR.

Subgroup	*Outcome*	*Effect*	*Estimate (95% CI)*	*P-value*
No Diabetes (n=77)	eGFR	Annual decline before SGLT2i	-1.9 (-3.1, -0.7)	0.0018
		Immediate change	-1.0 (-3.2, 1.3)	0.40
		Change in slope after SGLT2i	-0.54 (-2.6, 1.5)	0.61
	UPCR	Annual increase before SGLT2i	0.12 (-0.01, 0.24)	0.063
		Immediate change	-0.15 (-0.34, 0.03)	0.097
		Change in slope after SGLT2i	**-0.34 (-0.51, -0.18)**	**<0.0001**
With Diabetes (n=32)	eGFR	Annual decline before SGLT2i	-2.5 (-4.7, -3.1)	0.026
		Immediate change	-2.7 (-7.3, 1.8)	0.24
		Change in slope after SGLT2i	2.5 (-0.8, 5.8)	0.14
	UPCR	Annual increase before SGLT2i	-0.00 (-0.19, 0.19)	0.99
		Immediate change	-0.04 (-0.35, 0.28)	0.81
		Change in slope after SGLT2i	-0.11 (-0.35, 0.13)	0.36
eGFR ≥60 (n=43)	eGFR	Annual decline before SGLT2i	-0.7 (-2.5, 1.2)	0.47
		Immediate change	-3.2 (-6.8, 0.3)	0.08
		Change in slope after SGLT2i	-0.4 (-3.2, 2.4)	0.79
	UPCR	Annual increase before SGLT2i	0.17 (-0.05, 0.40)	0.13
		Immediate change	-0.13 (-0.44, 0.18)	0.41
		Change in slope after SGLT2i	**-0.55 (-0.78, -0.32)**	**<0.0001**
eGFR <60 (n=64)	eGFR	Annual decline before SGLT2i	-3.1 (-4.3, -1.8)	<0.0001
		Immediate change	-0.0 (-2.4, 2.4)	0.98
		Change in slope after SGLT2i	1.2 (-1.0, 3.4)	0.30
	UPCR	Annual increase before SGLT2i	0.06 (-0.04, 0.15)	0.23
		Immediate change	-0.16 (-0.32, -0.01)	0.040
		Change in slope after SGLT2i	0.02 (-0.13, 0.17)	0.77
UPCR>=0.5 (n=44)	eGFR	Annual increase before SGLT2i	-1.8 (-3.4, -0.3)	0.022
		Immediate change	-0.3 (-3.4, 2.7)	0.82
		Change in slope after SGLT2i	-2.2 (-4.8, 0.4)	0.10
UPCR<0.5 (n=60)	eGFR	Annual increase before SGLT2i	-2.2 (-3.7, -0.8)	0.0026
		Immediate change	-2.1 (-4.9, 0.6)	0.13
		Change in slope after SGLT2i	**2.6 (0.1, 5.0)**	**0.036**
UPCR>=0.3 (n=57)	eGFR	Annual increase before SGLT2i	-1.6 (-3.1, -0.2)	0.025
		Immediate change	-1.7 (-4.5, 1.1)	0.24
		Change in slope after SGLT2i	-1.4 (-3.8, 1.0)	0.26
UPCR<0.3 (n=47)	eGFR	Annual increase before SGLT2i	-2.6 (-4.2, -1.1)	0.0011
		Immediate change	-0.7 (-3.6, 2.3)	0.65
		Change in slope after SGLT2i	**2.7 (0.1, 5.3)**	**0.043**

Next we looked at the effect of SGLT2i on UPCR. There was a significant reduction in the UPCR after starting SGLT2i in all SLE patients (Table 1). Contrary to the eGFR effects, the benefit was statistically significant in those without diabetes (Table 2, p< 0.001) and with baseline eGFR >60 (Table 2, p< 0.001).

Conclusion: In this analysis, SGLT2i use did not significantly reduce eGFR decline (although the results were in the correct direction), but had a significant improvement on proteinuria. This differs from the 2022 Phase I/II trial in SLE by Wang et al, which found the opposite to be true. Our subgroup effects are fascinating and go in opposite directions. The benefit of SGLT2i on GFR slope is seen in those WITH and GFR < 60 (neither were significant). In particular, protection of GFR slope was seen in those with LOW levels of UPCR, such as < 0.50 g and < 0.30 g. The benefit of SGLT2i on proteinuria is seen in the all patient analysis (p=0.0001) and in those without diabetes (p< 0.001) and eGFR > 60 (p< 0.0001). Both GFR protection and reduction in proteinuria are desirable goals in SLE, but our study found that GFR protection was not statistically significant in the all patient analysis, whereas proteinuria reduction was.

Disclosure: J. Lee: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **D. Goldman**: None; **L. Magder**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1517

The Chinese Experience with Telitacicept in Lupus Nephritis Management: 51-Patient Cohort Analysis on Therapeutic Outcomes and Safety Parameters

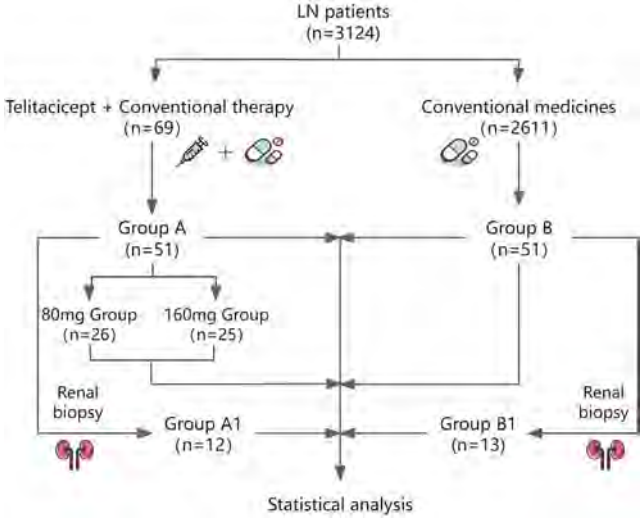
Aijing Liu[1], Fei Chang[2] and Qiuhong Xu[1], [1]Department of Rheumatology and Immunology, The Second Hospital of Hebei Medical University, Shijiazhuang, China (People's Republic), [2]Department of Rheumatology and Immunology, The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

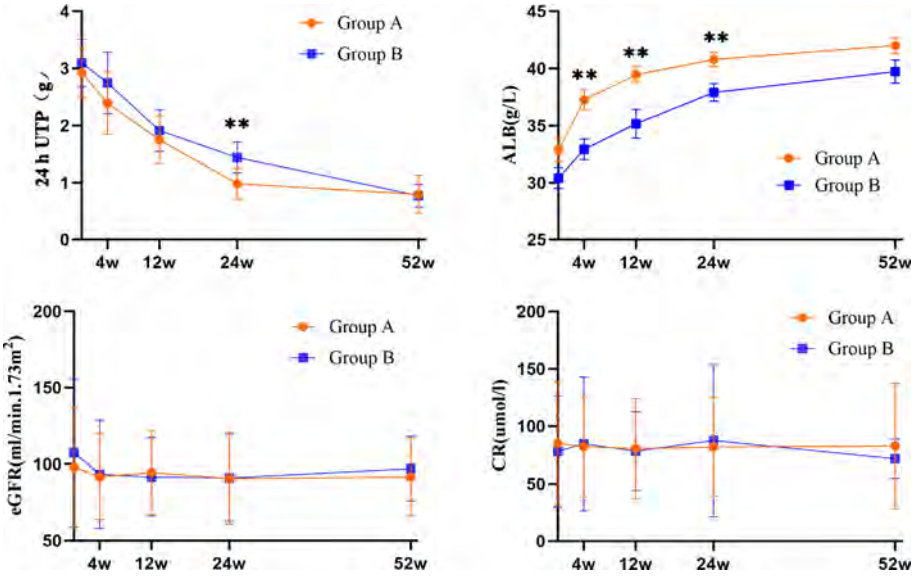
Background/Purpose: Lupus nephritis (LN), affects 30%-50% of systemic lupus erythematosus (SLE) patients, a major contributor to SLE-related mortality. Telitacicept, an innovative recombinant fusion protein, disrupts the interaction between BLyS/APRIL and their receptors, thereby effectively curbing B lymphocyte proliferation and maturation. While both Phase I and Phase II clinical trials have substantiated Telitacicept's efficacy in ameliorating SLE progression, its therapeutic potential in LN remains underexplored, with limited data on efficacy and safety. To evaluate the real-world efficacy and safety of Telitacicept in LN patients at a single center, we aim to furnish evidence for B-cell-targeted therapeutic strategies in LN management.

Methods: A total of 51 LN patients treated with Telitacicept combined therapy (Group A) and 51 matched controls receiving conventional therapy (Group B) in the Second Hospital of Hebei Medical University from March 2021 to January 2024 were enrolled in the retrospective study. Clinical data, including laboratory results, disease activity, renal response rates, and adverse events (AEs) were collected at 4, 12, 24, and 52 weeks. Further, LN patients confirmed by renal biopsy were divided into Group A1 (n=12) and Group B1 (n=13), and clinical data were compared and analyzed based on different pathological types. Additionally, Group A patients were stratified by telitacicept dosage (160mg and 80mg) and compared with Group B.



Flow chart of the study

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparisons of renal indexes in LN patients with Telitacicept group and conventional therapy group. (24h urinary total protein, serum albumin, eGFR and serum creatinine in LN patients of Group A and Group B) **P<0.01.

Results: 1. Compared to Group B, Group A showed substantial improvement in serum albumin from week 4 to week 24 and reduced 24-hour urine protein at week 24 (P< 0.05). The systemic lupus erythematosus responder index 4 and complete renal response (CRR) rate in Group A were 71.88% and 87.5%, respectively, significantly higher than those in Group B (P=0.030 and P=0.050). At weeks 12 and 24, complement 3 (C3), C4, and immunoglobulins (Ig) in Group A improved notably, with faster IgG reduction (P< 0.05). Anti-dsDNA antibodies decreased at week 52 (P< 0.05). From week 4 to week 52, glucocorticoid (GC) use was considerably lower in Group A (P< 0.05).

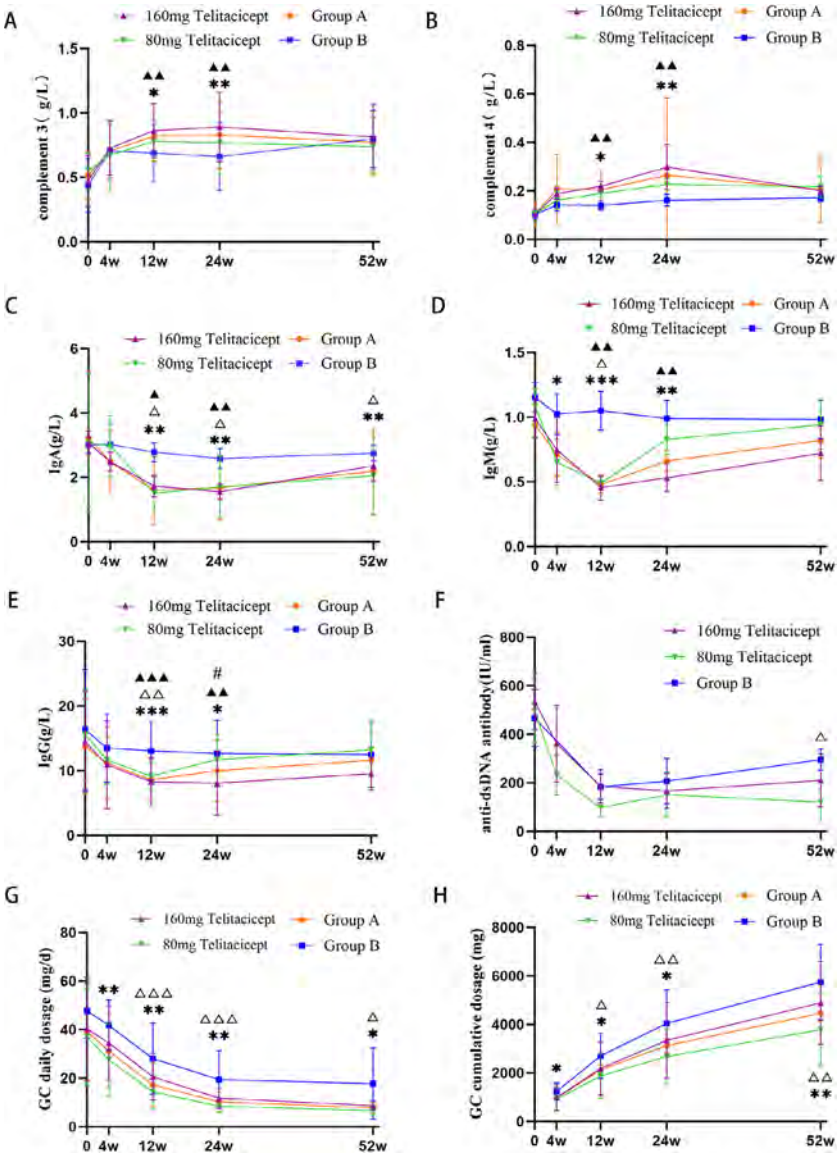
2. Compared to Group B1, type IV LN patients in Group A1 showed improved C3, C4 and reduced GC use at 24 week (P< 0.05). Type V LN patients had lower GC use and increased C3 at week 52 (P=0.037). CRR rates were 91.67% (A1) vs. 76.92% (B1) (P=0.315). The partial RR rates were 8.33% and 23.08%, where type IV accounted for 100% and 66.67%, respectively, with no statistical analysis due to small sample size.

3. 160 mg of Telitacicept reduced IgG more effectively than 80mg group at week 24 (P=0.025).

4. AE rates were 23.5% (Group A) and 19.6% (Group B) (P=0.350) respectively, with infections being the most common. No severe AEs were reported in Telitacicept group.

Conclusion: Compared to conventional therapy, Telitacicept combined therapy remarkably reduces proteinuria, improves immunological markers, enhances CRR, and effectively reduces GC use in LN patients. The 160mg dose is more effective in reducing IgG. Telitacicept is safe, with no severe AEs reported.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparisons of immunological indexes and glucocorticoid dosage in LN patients with different Telitacicept dosage group and conventional therapy group. A. Complement 3(C3); B. C4; C.Immunoglobulin (Ig) A; D. Ig M; E. Ig G; F. Anti-dsDNA antibody; G. Glucocorticoid daily doage; H. Glucocorticoid cumulative dosage. *P<0.05,**P<0.01,***P<0.001, Group A vs Group B; ▲P<0.05,▲▲P<0.01,▲▲▲P<0.001, 160mg vs Group B;△P<0.05,△△P<0.01,△△△P<0.001, 80mg vs Group B; # P<0.05-160mg vs.80mg.

Disclosure: A. Liu: None; **F. Chang**: None; **Q. Xu**: None.

Abstract Number: 1518

Efficacy and Safety of Anifrolumab in Discoid Lupus: A Meta-Analysis of the Literature

Ali Ali[1], Neelay Purohit[2], Ciji Robinson[2], Amanda Darzi[3] and Alireza Meysami[4], [1]Department of Internal Medicine, Division of Rheumatology, Henry Ford Health System, Canton, MI, [2]Department of Internal Medicine, Division of Rheumatology, Henry Ford Health System, Detroit, MI, [3]Department of Internal Medicine, Henry Ford Health System, Detroit, MI, [4]Henry Ford Health, Detroit, MI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

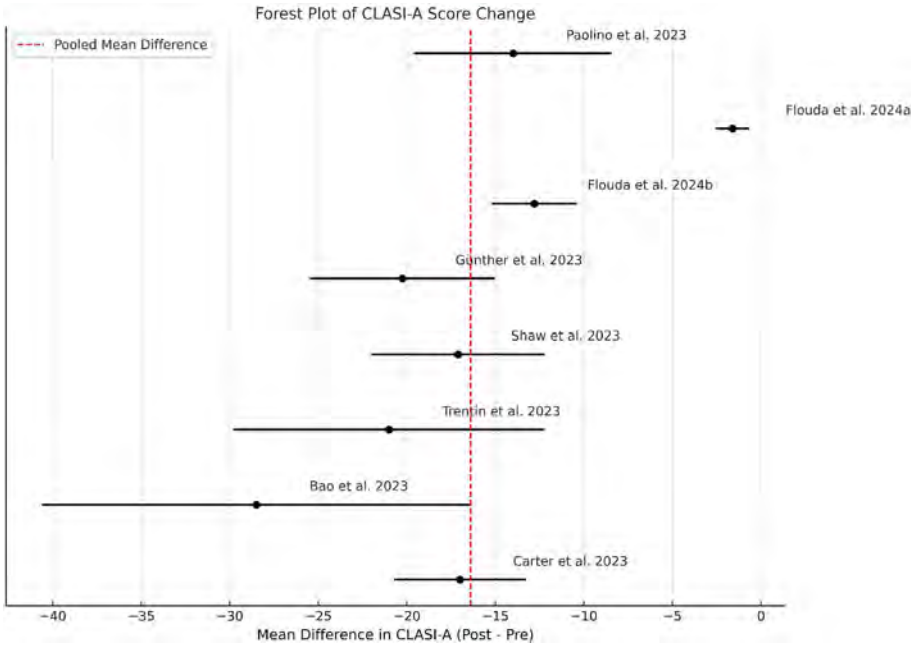
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Anifrolumab, a monoclonal antibody targeting the type I interferon receptor, demonstrated clinical efficacy in systemic lupus erythematosus in the pivotal TULIP-2 trial[1]. However, its role in discoid lupus erythematosus (DLE) remains less well defined. Emerging case-based studies indicate potential benefit in refractory DLE[2]. This review aims to evaluate the clinical role of anifrolumab in DLE using a focused literature review and meta-analysis.

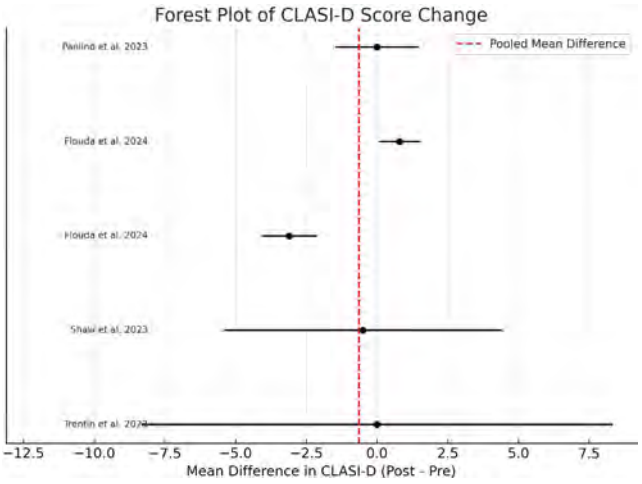
Methods: To evaluate the clinical role of anifrolumab in DLE, we conducted a comprehensive literature search of MEDLINE and EMBASE for studies published between January 2015 and April 2025. We prioritized studies that reported Cutaneous Lupus Erythematosus Disease Area and Severity Index – Activity (CLASI-A) and – Damage (CLASI-D) scores to ensure a standardized assessment of treatment response. We included 8 studies (n = 36) for CLASI-A and 5 studies (n = 25) for CLASI-D. A random-effects meta-analysis using the DerSimonian-Laird method was applied. In studies lacking reported variability, we estimated standard deviations as 25% of the mean, consistent with methods used in prior meta-analyses of small clinical samples. All patients had received hydroxychloroquine and at least one prior immunosuppressive therapy.

Results: The meta-analysis demonstrated a significant reduction in CLASI-A scores among 36 patients with available data, with a pooled mean difference of –16.41 (95% CI: –19.72 to –13.10; $p < 0.001$; $I^2 = 97.9\%$), indicating meaningful improvement in disease activity. For CLASI-D, assessed in 25 patients, the pooled mean difference was –0.63 (95% CI: –2.33 to 1.06; $p = 0.465$; $I^2 = 78.2\%$), suggesting no statistically significant change in cutaneous damage. Among the 89 patients included across all studies, only 36 had CLASI-A scores and 25 had CLASI-D scores reported. Most patients also exhibited features of systemic lupus, including arthritis, serologic abnormalities, or other systemic involvement. Although the remaining cases lacked formal CLASI documentation, most were described as having improvement in their skin disease based on physician assessment or clinical descriptors. Average CLASI-A scores dropped from approximately 14.7 at baseline to 2.0 after treatment, while CLASI-D decreased from 4.9 to 3.0. No hospitalizations or deaths were reported. Six patients developed mucocutaneous herpes simplex virus (HSV) or varicella-zoster virus (VZV) infections, including one case of herpes zoster



Forest Plot of CLASI-A Score Change

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot of CLASI-D Score Change

oticus. Among 22 patients with corticosteroid data, the average prednisone dose was reduced from 13.75 mg/day to 2.5 mg/day following anifrolumab treatment.

Conclusion: Anifrolumab appears effective and well tolerated in DLE, particularly in reducing disease activity and corticosteroid burden. Its impact on reversing cutaneous damage is limited. These findings support its role as a targeted therapy for DLE. While promising, the results are based on a small sample size and retrospective data, underscoring the need for validation in larger, prospective studies.

References:

1. Furie R et al. *N Engl J Med*. 2020;382(3):211-221.
2. Shaw K et al. *Arthritis Rheumatol*. 2023;75(Suppl 9).

Disclosure: A. Ali: None; **N. Purohit**: None; **C. Robinson**: None; **A. Darzi**: None; **A. Meysami**: Amgen, 1, 2, 6, AstraZeneca, 1, GlaxoSmithKlein(GSK), 1, Janssen, 1, Zenas, 1.

Abstract Number: 1519

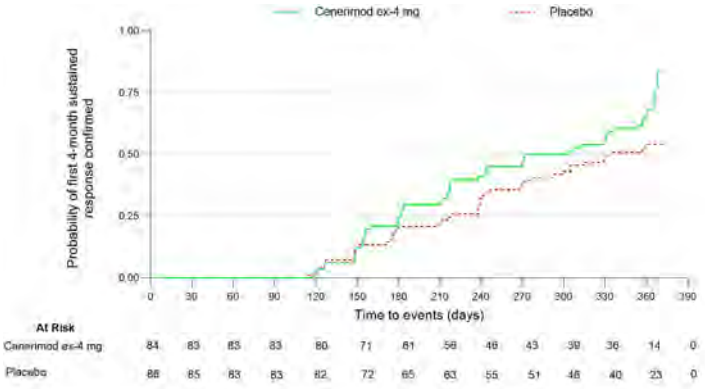
Post-hoc Analysis of Sustained Response Over Time in Systemic Lupus Erythematosus Patients Treated with Cenerimod in CARE (Phase 2 B) Study

Anca Askanase[1], Bruno Flamion[2], Ouali Berkani[2] and Cecile Dubois[2], [1]Columbia University Medical Center, New York, NY, [2]Viatris Innovation, Allschwil, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



	Cenerimod ex-4 mg N=85	Placebo N=86
Number of subjects with at least one event (%)	54 (63.5)	43 (50.0)
Number of subjects without event [a] (%)	30 (35.3)	43 (50.0)
Kaplan-Meier estimate (days)		
Median (95% CI)	304 (217, 354)	334 (272, NE)
Treatment effect		
Hazard-ratio versus Placebo [b] (95% CI)	1.431 (0.958, 2.139)	

NE = Value not estimated.
[a] Censored at the date of the last non-missing mSLEDAI-2K assessment.
[b] Cox proportional hazard model adjusted for stratification factors (oral corticosteroids dose and mSLEDAI-2K)

4-month sustained response in mSLEDAI-2K of Cenerimod ex-4 mg group as compared to the placebo

Background/Purpose: Cenerimod is a highly selective $S1P_1$ receptor modulator which is undergoing trials for potential therapeutic benefits in autoimmune disease, including Systemic Lupus Erythematous (SLE). The Phase 2b CARE study (NCT03742037) evaluated the efficacy and safety of cenerimod at doses 0.5, 1, 2, and 4 mg in moderate to severe SLE patients. Patients in the 0.5, 1, 2 mg, and placebo arms continued the study drug for an additional 6 months. Patients assigned to cenerimod 4 mg arm were randomly assigned (1:1) to either cenerimod 2 mg or placebo for another 6 months, designated herein as cenerimod Ex-4 mg group. All patients who had received cenerimod 4 mg for the first 6 months were included in the analysis irrespective of their treatment assignment in the next 6 months to either 2 mg or placebo. Safety outcomes were monitored for 12 months.

This post-hoc analysis was performed to assess sustained responses in mSLEDAI-2K (defined as a decrease of ≥4 points from baseline for 4 consecutive monthly assessments) vs placebo over a period of 12 months.

Methods: The treatment effect was estimated for each treatment group vs placebo using a Cox proportional hazards model stratified by baseline oral corticosteroid and mSLEDAI-2K. Hazard ratios and 95% confidence interval were derived from the model. The analysis was performed over the 12-month period and the initial randomization was used as the basis for group allocation.

Results: 427 patients were randomized, 85 patients each in the 0.5, 1, and 4 mg arms and 86 patients each in the 2 mg and placebo arms. Median age was 42 years (range 18–72), 406 (95%) were female, and 337 (79%) White.

A sustained response in mSLEDAI-2K score was observed in 63.5% of the patients in the cenerimod Ex-4mg group as compared to 50.0% of those in the placebo group. The median time is the time by when the event has occurred in 50% of the study subjects. The median time to the first confirmation of a 4-month sustained response in mSLEDAI-2K was estimated at 304 days in cenerimod Ex-4mg group vs 334 days in placebo group. The hazard ratio was estimated at 1.43 in cenerimod Ex-4mg group, suggesting that this group has a 43% greater chance of experiencing a 4-month sustained response in mSLEDAI-2K as compared to the placebo group (Figure 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This analysis showed that over a period of 12 months, patients in the cenerimod Ex-4 mg group were 1.43 times more likely to achieve a 4-month sustained response than those receiving placebo.

The ongoing confirmatory Phase 3 program OPUS (NCT05648500 and NCT05672576) will further evaluate the safety and efficacy of 4 mg cenerimod in adults with SLE.

Disclosure: A. Askanase: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **B. Flamion**: Viatris Innovation, 3; **O. Berkani**: Viatris Innovation, 3; **C. Dubois**: Viatris Innovation, 3.

Abstract Number: 1520

Long-Term Effects of Obinutuzumab on Kidney Function in Lupus Nephritis

Bahtiyar Toz[1], Himanshu Vashistha[2] and Richard Furie[3], [1]Zucker School of Medicine at Hofstra/ Northwell, Queens, NY, [2]Northwell Health, Great Neck, NY, [3]Division of Rheumatology, Northwell Health, Great Neck, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Biologic treatments for lupus nephritis (LN) have improved short-term outcomes. Obinutuzumab (OBI), an anti-CD20 monoclonal antibody, demonstrated efficacy in the NOBILITY and REGENCY trials; however, long-term real-world data are limited.

Table 1: Baseline Demographics and Clinical Characteristics

Baseline Characteristics and Demographics (N=26)	
Age, years	32.0 (28–39)
Female, no (%)	20 (77%)
Disease duration (year)	13 (9-16)
Serum creatinine, mg/dL, median (IQR)	1.1 (0.8–1.5)
eGFR, mL/min/1.73 m2, median (IQR)	77 (55–108)
Baseline UPCR, g/d, median (IQR)	4.6 (2–6.7)
Anti- dsDNA, median (IQR)	320 (50–1000)
C3 <90 mg/dL, median (IQR)	71 (55 - 79)
C4 <12mg/dL, median (IQR)	11 (7.5– 16)
Kidney biopsy ISN/RPS class before OBI	Class III (5), Class IV (8), Class V (1), Class IV and V (8), Class III and V (3), and podocytopathy (2).
Class IV LN – no. (%)	16 (62%)
Concomitant Class V LN- no. (%)	12 (46%)
Activity Index, median (IQR)	6 (4-7)
Chronicity Index, median (IQR)	3 (1-4)
Post-Obi follow up (months), median (IQR)	27 (17-61)
Concomitant immunosuppressants	MMF (17), HCQ (22), steroid (20), AZA (1), MTX (1), Voclo (1)
Previous Therapies Prior to Obinutuzumab	MMF (26), RTX (7), BEL (7), CYC (3), AZA (4), VOC (3)

Abbreviations: eGFR, estimated glomerular filtration rate; UPCR, urine protein-to-creatinine ratio; MMF, mycophenolate mofetil; RTX, rituximab; BEL, belimumab; CYC, cyclophosphamide; HCQ, hydroxychloroquine; AZA, azathioprine; MTX, methotrexate; VOC, voclosporin

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Adverse Events Associated with Obinutuzumab

Adverse Events			
	Number of Patients	Severity	Timeline
Infection			
Acute gastroenteritis	2	Grade 1	1 mo and 4 mo
UTI	1	Grade 2	2 mo
Herpes zoster	1	Grade 2	4 mo
URI	2	Grade 2	5 mo
	1	Grade 2	2 mo
COVID-19	1	Grade 3	7 mo
	1	Grade 1	6 wk
Orchitis	1	Grade 3	15 mo
Herpetic lip lesion	1	Grade 1	6 mo
Infusion-related reaction			
Headache	2	Grade 1	
Transient paresthesia	1	Grade 1	
Arthralgia	2	Grade 1	
Hematologic			
Drug-induced thrombocytopenia	1	Grade 3	10 d
Drug-induced neutropenia	1	Grade 1	6 mo
Other			
Scleritis	1	Grade 1	6 mo
Exacerbation of eczema	1	Grade 1	2 mo
Atypical squamous cells of undetermined significance+HPV	1	N/A	24 mo

Abbreviations: AE, adverse event; URI, upper respiratory infection; UTI, urinary tract infection; HPV, human papillomavirus; ASCUS, which stands for atypical squamous cells of undetermined significance; mo, months; wk, weeks; d, days

Methods: We conducted a retrospective single-center study of 26 LN patients (pts) who received at least 1g of OBI between 2015 and 2025. Clinical and laboratory data were collected to assess longitudinal changes in serum creatinine, eGFR, urine protein-to-creatinine ratio (UPCR), and B cells. A mixed-effects model was used to analyze changes in eGFR and UPCR over 48 months. Three pts with progressive renal decline either initiated hemodialysis or were lost to follow-up. B cell reconstitution kinetics, LN flare rates, and adverse events (AE) were analyzed.

Renal responses were classified as complete, partial, or no response. Complete (CR) and partial remission (PR) were defined as follows: CR: UPCR < 0.5 and eGFR ≥85% of baseline; PR: ≥50% reduction in UPCR from baseline, UPCR < 1 (or < 3 if baseline was ≥3), and eGFR ≥85% of baseline.

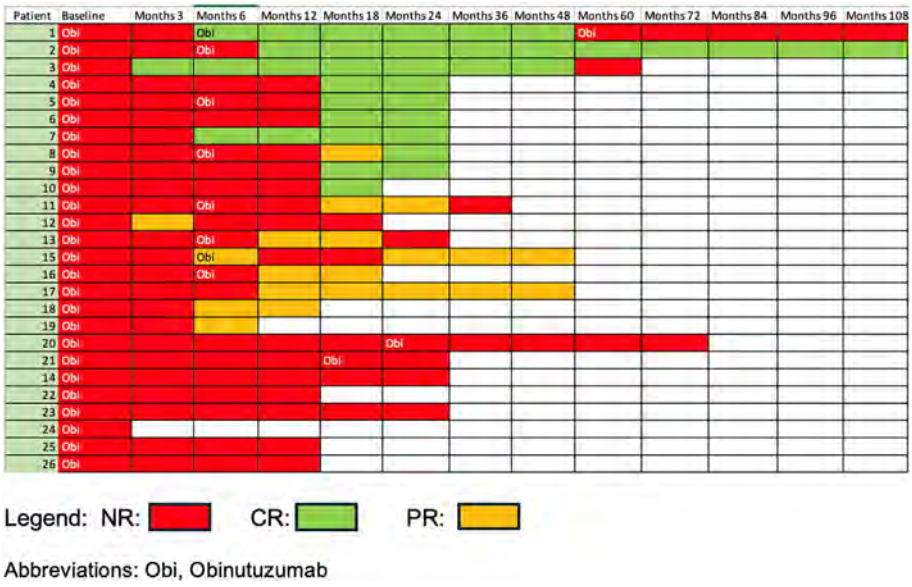


Fig 1. Longitudinal Treatment Responses in Patients Receiving Obinutuzumab Between 2015 and 2025

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 26 pts who received OBI, 25 with adequate follow-up were analyzed (Table 1). UPCR levels decreased significantly over time ($p < 0.001$). There was no statistically significant difference in eGFR across time points.

By 24 months, CR was achieved in 10 pts (40%), PR in 8 (32%), and NR in 7 pts (28%) (Fig. 1). Most CR and PR responses occurred between 6-18 months. Of 6 pts who flared, 2 CR pts flared 5 years after receipt of OBI, and 4 PR pts flared within 1 year. Nine pts in the CR and PR groups were able to discontinue steroids. Among the 7 pts who previously received rituximab, 3 did not respond to OBI.

Across response groups, baseline UPCR values were similar: CR: 4.5; PR: 5.5; NR: 4.7 ($p = 0.78$). Pts achieving CR had a significantly higher baseline mean eGFR compared to NR (102 vs 58 mL/min/1.73 m^2; $p = 0.014$). The mean difference in baseline eGFR between PR (80) and NR (58) was not significant ($p = 0.32$). Over 24 months, 50% of CR pts demonstrated stable or improved eGFR (mean change: +36%), and 50% had a decrease in eGFR (mean change: –7%). In the PR group, 83% of pts had stable or improved eGFR (mean change: +19%), and 17% had a decrease. When combined (CR + PR), 62% of pts had stable or improved eGFR (mean change +31%), while 38% had a decline in eGFR (mean change -6%).

No significant association was found between baseline LN class and response outcome.

Peripheral B cell counts decreased from a median of 48 cells/μL (IQR 12–121) at baseline to 3 cells/μL (IQR 1–39) at ~6 months. Reconstitution began by 12 months (median 14, IQR 0–55) and continued through 24 months (median 41, IQR 5–87). Of 12 pts with B cell data through 24 months, a total of 8, 11, and 12 repleted (>10 cells/ μL) at 12, 18, and 24 months, respectively.

AEs occurred in 18 pts, mostly mild or moderate. Infections and infusion-related reactions were the most common, with most events occurring within 6 months (Table 2).

Conclusion: Despite inadequate responses to prior therapies, two-thirds of our cohort achieved CR or PR. AEs were generally mild. These findings support the potential role of OBI as a long-term therapeutic option in LN.

Disclosure: B. Toz: None; **H. Vashistha**: None; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2.

Abstract Number: 1521

Kidney-Related Outcomes With Obinutuzumab in Patients With Active Lupus Nephritis: A Pre-Specified Exploratory Analysis of the Clinical Trial Data

Brad Rovin[1], William Pendergraft[2], Liz Lightstone[3], Eric Daugas[4], Richard Furie[5], Theodore Omachi[2], Imran Hassan[6], Elsa Martins[7], Thomas Schindler[7], Jay Garg[2], Luis Quintana[8], Piotr Leszczyński[9] and Ana Malvar[10], [1]The Ohio State University, Columbus, OH, [2]Genentech, Inc., South San Francisco, CA, [3]Department of Immunology and Inflammation, Faculty of Medicine, Imperial College London, London, England, United Kingdom, [4]Department of Nephrology, Hospital Bichat - Claude-Bernard, Paris, France, [5]Division of Rheumatology, Northwell Health, Great Neck, NY, [6]Hoffmann-La Roche Ltd, Mississauga, ON, Canada, [7]F. Hoffmann-La Roche Ltd, Basel, Switzerland, [8]Department of Nephrology, Hospital Clinic, Barcelona, Spain, [9]Department of Internal Medicine and Metabolic Diseases, Poznan University of Medical Sciences, Poznan, Poland, [10]Organización Médica de Investigación, Buenos Aires, Argentina

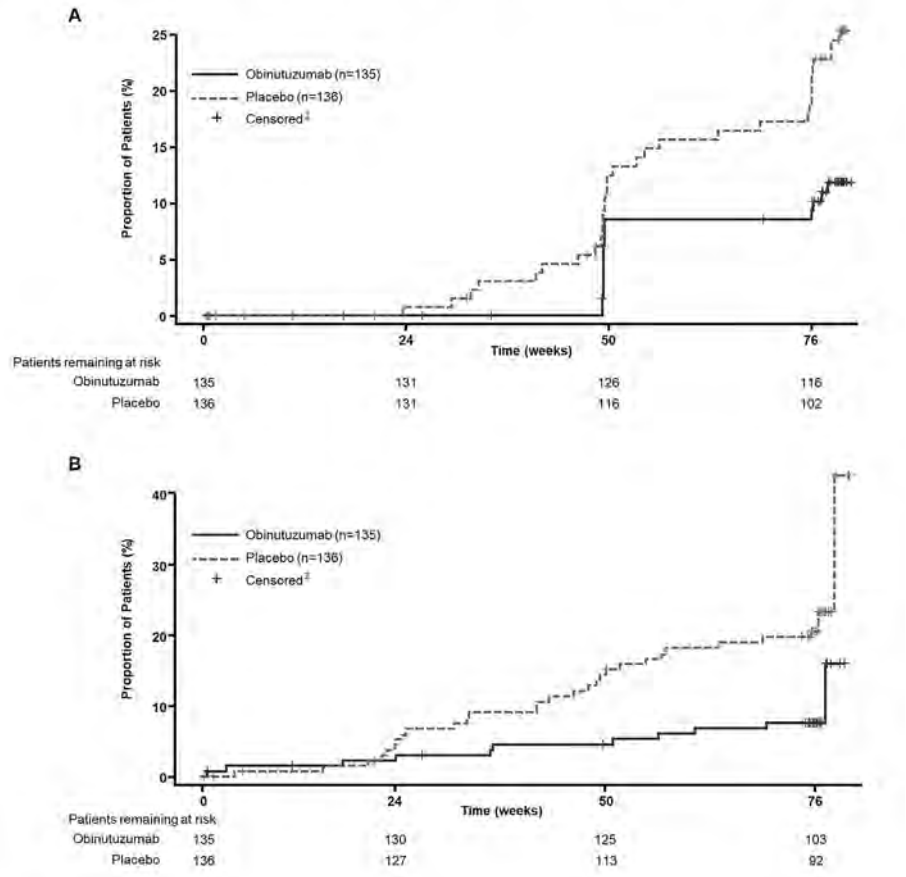
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is the most common, severe, organ-threatening manifestation of systemic lupus erythematosus (SLE). The randomized, double-blind, placebo-controlled, Phase III REGENCY trial (NCT04221477) demonstrated superiority of obinutuzumab over placebo for achievement of complete renal response at Week 76 when added to standard therapy (mycophenolate mofetil plus glucocorticoids) in patients with active LN. This study assessed the effects of obinutuzumab on time to LN flare, time to an unfavorable kidney outcome and annualized estimated glomerular filtration rate (eGFR) slope during the REGENCY trial.

Figure 1: Time to A) Lupus Nephritis Flare* from Week 24 through Week 76 and B) an Unfavorable Kidney Outcome†



eGFR, estimated glomerular filtration rate; LN, lupus nephritis; UPCR, urine protein-to-creatinine ratio.

*LN flare from Week 24, diagnosed if one of the following conditions occurred: eGFR decrease >20% compared with Week 24 in patients with UPCR >1 g/g and/or cellular casts; UPCR increase (A) to >1 g/g if Week 24 UPCR was <0.2 g/g, (B) to >2 g/g if Week 24 UPCR was 0.2-1 g/g or (C) to double if Week 24 UPCR was >1 g/g; receipt of rescue therapy, except for corticosteroid-only rescue. †Time to unfavourable kidney outcome, assessed from baseline to Week 76, was defined as the first of the following events: death, doubling of serum creatinine or treatment failure. ‡Patients who experienced early study withdrawal before experiencing the event were censored at the time of the study withdrawal. Patients who completed a 76-week treatment period and did not experience the event were censored at the upper limit of the Week 76 visit window in the LN flare group and censored at Week 76 in the unfavourable kidney outcome.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. eGFR Slope From Week 12 to Week 76

eGFR (mL/min/1.73m²/year)	Obinutuzumab n=135	Placebo n=136
Estimated eGFR slope (SE)	−0.71 (1.46)	−4.39 (1.46)
95% CI	−3.55 to 2.14	−7.24 to 1.54
Difference in eGFR slope (SE)	3.68 (2.06)	
95% CI	−0.35 to 7.72	
P value	0.073	

The eGFR slope was analyzed using a mixed effect model with random intercept and random slope. The difference in eGFR slope shows annualized difference.

eGFR, estimated glomerular filtration rate; SE, standard error.

Methods: In the REGENCY study, all patients met the ACR classification criteria for SLE and had biopsy-proven proliferative LN. In this pre-specified analysis of REGENCY, time to LN flare was assessed between Weeks 24 and 76 by Cox regression. The composite outcome of death, doubling of serum creatinine or treatment failure was defined as an unfavorable kidney outcome. Time to an unfavorable kidney outcome from baseline to Week 76 was also assessed by Cox regression after stratifying for race and region. Finally, linear mixed-effects modelling was used to assess eGFR slope between Weeks 12 and 76. These analyses were not controlled for type I error.

Results: Between Weeks 24 and 76, the proportion of patients with LN flare was lower in the obinutuzumab arm (11.1%) compared with the placebo arm (23.5%), with a hazard ratio of 0.44 (95% CI, 0.24 to 0.82; *P*=0.0074) (**Figure 1A**). The proportion of patients with unfavorable kidney outcomes in the obinutuzumab arm (8.10%) was also lower compared with the placebo arm (21.30%), with a hazard ratio of 0.37 (95% CI, 0.18 to 0.75; *P*=0.0039) (**Figure 1B**). Numerical attenuation of eGFR decline from Week 12 to Week 76 was observed in the obinutuzumab arm with the annualized eGFR slope calculated as –0.71 (SE=1.454) compared with –4.39 (SE=1.454) in the placebo arm, with a difference in eGFR slope of 3.68 (SE=2.055; *P*=0.0732), favoring patients treated with obinutuzumab (**Table 1**).

Conclusion: This pre-specified exploratory analysis of the REGENCY trial demonstrated that obinutuzumab significantly reduced the occurrence of LN flares and unfavorable kidney outcomes and attenuated the annualized decline in kidney function compared with placebo-treated patients. Together with the significantly higher proportion of patients achieving a complete renal response in the obinutuzumab arm, these findings suggest that obinutuzumab affords long-term kidney survival benefits compared with standard therapy.

Disclosure: B. Rovin: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **W. Pendergraft**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; **L. Lightstone**: Alexion, 2, AstraZeneca, 2, F. Hoffman-La Roche Ltd, 2, GlaxoSmithKline, 2, Kezar, 2, Novartis, 2, Otsuka, 2, Pfizer, 2; **E. Daugas**: Alexion, 12, Support for Attending Meetings and Travel, Amgen, 2, AstraZeneca, 2, 6, 12, Support for Attending Meetings and Travel, CSL, 12, Support for Attending Meetings and Travel, GlaxoSmithKline, 2, 6, 12, Support for Attending Meetings and Travel, Novartis, 2, Otsuka, 2, 12, Support for Attending Meetings and Travel, Vifor, 12, Support for Attending Meetings and Travel; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **T. Omachi**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech, 3; **I. Hassan**: F. Hoffmann-La Roche Ltd, 3; **E. Martins**: F. Hoffman-La Roche Ltd, 3; **T. Schindler**: F. Hoffman-La Roche Ltd, 3, 12, Shareholder; **J. Garg**: F. Hoffman-La Roche Ltd, 12, Shareholder, Genentech Inc., 3; **L. Quintana**: Genentech Inc., 2, GlaxoSmithKline, 2, Otsuka, 2; **P. Leszczyński**: None; **A. Malvar**: Bristol-Myers Squibb(BMS), 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Kezar, 2, Novartis, 2, Pfizer, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1522

Outcomes of Continuing Hydroxychloroquine following Renal Transplant in Patients with Lupus Nephritis: A retrospective Cohort Study using the TrinetX database

Carlos Pena[1], Irene Tan[2], Rafal Ali[3], Arthur Lau[4], Shahrzad Abdollahi[5], Fabian Rodriguez Quinonez[6] and Marianne Meshreky[7], [1]Jefferson Einstein Philadelphia, Wynnewood, PA, [2]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA, [3]Jefferson Einstein Philadelphia, Lansdale, PA, [4]Jefferson Einstein Hospital, Maple Glen, PA, [5]Jefferson Einstein Hospital, Philadelphia, PA, [6]Einstein Medical Center Philadelphia, Philadelphia, PA, [7]St. Mary's Hospital, Philadelphia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Evidence of kidney disease occurs in up to one half of patients with SLE, and approximately 10% of the patients with lupus nephritis (LN) will go on to develop end stage renal disease (ESKD). Kidney transplantation is a safe and effective treatment for ESKD secondary to LN; and is associated with improved patient survival. of ESKD has been described as associated with a decrease in extrarenal manifestations of SLE following kidney transplantation when patients are placed on anti-rejection immunosuppressive therapy. Hydroxychloroquine (HCQ) has often been described as a medication with significant benefits and improving overall survival in patients with SLE regardless of their disease activity. With this in mind, we sought to explore outcomes of continuing HCQ following renal transplant in patients with LN.

Methods: In this retrospective, observational cohort study, we explore various outcomes in patients with SLE and kidney transplant status receiving hydroxychloroquine following transplant compared to those with SLE and kidney transplant status who did not receive HCQ following transplant.

We utilized the TrinetX database, which includes electronic health records from over 80 different global healthcare organizations. We created two groups: the first cohort included patients with SLE, kidney transplant status and HCQ (2855 patients), and the second cohort included patients SLE, kidney transplant status not on HCQ (4627 patients). The outcomes investigated were cerebral infarction, MACE risk, deceased, and ESKD (occurring within 3 years after transplant and receiving HCQ vs not receiving it "index event"), using International Classification of Diseases, Tenth Revision (ICD-10) codes. We excluded patients with these outcomes prior to undergoing kidney transplant and/or starting the medication.

Results: After propensity score matching, it was noted that between the cohorts, there was no difference between each group for developing cerebral infarction (2.757% vs 2.709 %), with a risk ratio of 1.018, p-value of 0.919 with a 95% CI (0.726,1.426). There was a reduced risk in all-cause mortality in the first (HCQ) cohort (3.271% vs 5.452%), with a risk ratio of 0.6, p-value of 0.0002 with a 95% CI (0.458,0.786). For MACE risk, there was no difference between groups (5.075% vs 4.588%), with a risk ratio of 1.106, p-value of 0.4366 with a 95% CI (0.858, 1.426). Lastly, the HCQ cohort had increased risk of developing ESKD following kidney transplant (40.015% vs 16.918%) with a risk ratio of 1.49, p-value < 0.0001 with a 95% CI (1.323, 1.678).

Conclusion: In SLE patients status post kidney transplantation, hydroxychloroquine (HCQ) use was associated with a significantly reduced risk of all-cause mortality, suggesting a potential survival benefit. However, HCQ use was also linked to a substantially increased risk of progression to end-stage kidney disease. No significant differences were observed in the risk of cerebral infarction or major adverse cardiovascular events (MACE). These findings suggest a complex and context-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

dependent risk–benefit profile for HCQ in the post-transplant setting, emphasizing the need for individualized therapeutic strategies and further prospective investigation.

Disclosure: C. Pena: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial; **R. Ali**: None; **A. Lau**: None; **S. Abdollahi**: None; **F. Rodriguez Quinonez**: None; **M. Meshreky**: None.

Abstract Number: 1523

Genetic architecture and translational insights for SLE progression from preclinical stages

Lida Wang[1], havell Markus[1], Laura Carrel[1], Nancy Olsen[2], Galen Foulke[3] and **Dajiang Liu**[1], [1]Penn State College of Medicine, Hershey, PA, [2]Penn State University/Milton S Hershey, Hershey, PA, [3]Penn State Health, Hershey, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE), have a preclinical phase where individuals display a subset of symptoms, but do not meet the full diagnostic criteria. Identifying genetic variants influencing the progression from preclinical stage is crucial, since autoimmunity can quickly cause irreversible organ damage. Biobanks with electronic health records are valuable for studying disease progression but can be underpowered due to limited number of diseases cases. We previously developed genetic prediction scores (GPS, Wang, Markus et al, Nature Communications, 2025) that can predict the progression of SLE from preclinical stages. Compared to conventional genetic risk scores calculated from SLE case-control

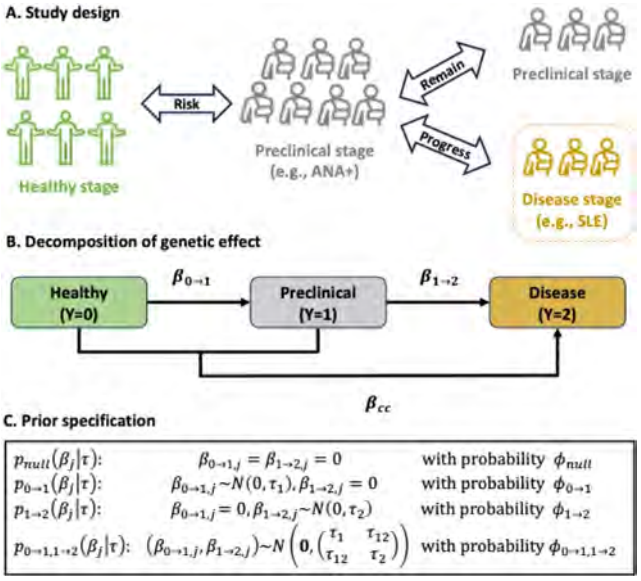


Fig 1. Study design and the key model for the method to detect genetic associations with progression phenotype. Panel A: each SLE patients will undergo a preclinical stage. Panel B. We will decompose the genetic effects into effects influencing healthy to preclinical progressions and the effects influencing preclinical to SLE progressions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

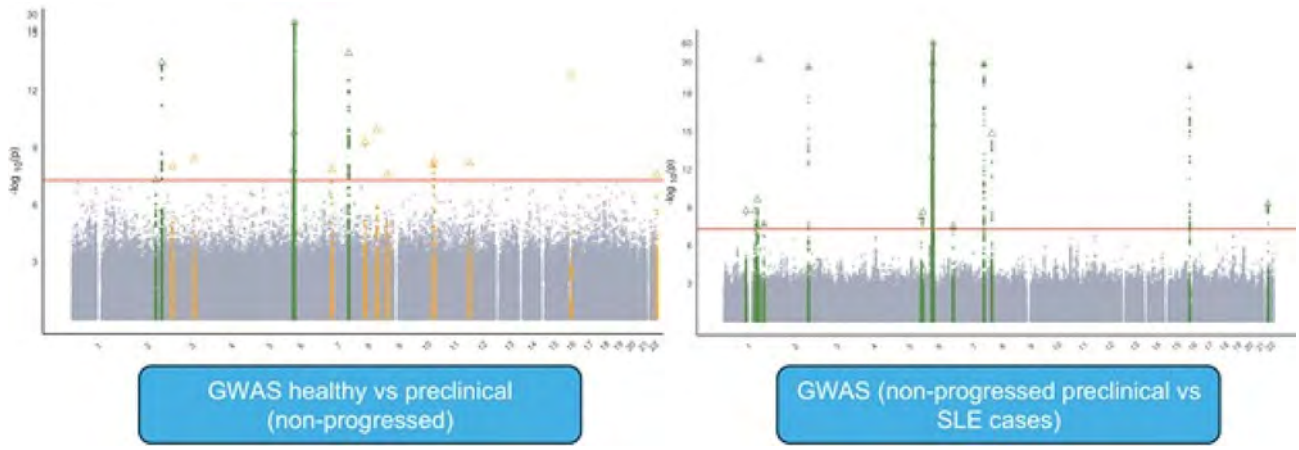


Fig 2. GWAS identifies distinct loci influencing different stages of SLE progression. Left panel: GWAS hits influencing healthy to preclinical stage progressions. Right panel: GWAS hits influencing preclinical to SLE progressions. Green color shows loci identified previously from case-control studies and yellow color shows loci unique to SLE progression traits.

studies, the GPS method increases the accuracy of risk prediction by ~20%-1000%. Despite the progress, individual variants associated with SLE progressions remain elusive. More powerful methods are needed to understand the etiology of preclinical SLE.

Methods: Almost SLE cases will undergo a preclinical stage with positive antinuclear antibody. Leveraging this insight, we can break the genetic effects influencing healthy → SLE transition into the effects influencing healthy → preclinical and that influencing preclinical → SLE transition, leading a novel Bayesian model to detect genetic association with progression (GAP). GAP borrows strength from the large sample sizes of SLE case-control studies and improves power of GWAS for progression phenotypes (Fig 1). We also developed a novel drug repurposing pipeline that leverages GAP results to identify compounds capable of slowing down the preclinical → SLE progression by reversing the expression levels of causal genes in disease-relevant cell types including B cells.

Results: We apply GAP to identify genetic associations with preclinical → SLE progressions, integrating BioVU biobank (749 SLE cases, 2,784 preclinical individuals, 46,174 controls) and case-control GWAS summary statistics from six different studies (14,355 cases and 505,956 controls). We identified 4 and 17 novel loci for control → preclinical and preclinical → SLE progressions (Fig 2). Intriguingly, two causal variants in *IRF5* are colocalized with eQTLs from different genes, emphasizing the importance of resolving phenotype heterogeneities due to different disease stages. Leveraging our drug-repurposing pipeline, we identify several novel drugs, leukotriene receptor antagonist (montelukast) and TNF-α inhibitors (pentoxifylline and lenalidomide). We also confirmed the effectiveness of hydroxychloroquine for slowing down SLE progression, a drug that is frequently prescribed but lacking solid scientific support.

Conclusion: Our results reveal distinct genetic architecture of healthy → preclinical and preclinical → SLE progressions. The novel genes and putative drugs we identify will inform clinical studies and accelerate the therapeutic development for slowing the progression of SLE from preclinical stages.

Disclosure: L. Wang: None; **h. Markus**: None; **L. Carrel**: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5; **G. Foulke**: None; **D. Liu**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1524

Hydroxychloroquine Reduces Autoantibody Levels in Persons at Risk for Systemic Lupus Erythematosus

David Karp[1], Prithvi Raj[1], Changsong Zhu[1], Dajiang Liu[2], Duanping Liao[2] and Nancy Olsen[3], [1]UT Southwestern Medical Center, Dallas, TX, [2]Penn State College of Medicine, Hershey, PA, [3]Penn State University/Milton S Hershey, Hershey, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The Study of Antimalarials in Incomplete Lupus Erythematosus (SMILE, NCT03030118) was a double-blind, randomized, placebo-controlled study of hydroxychloroquine (HCQ) to prevent the development of lupus in people at risk. Participants had an ANA of ≥1:80 and one or two but not three 2012 SLICC criteria for the classification of SLE. They were randomized to either 400 mg/d of HCQ (200 mg for participants under 40kg) or matching placebo (PBO). They were followed for up to 24 months for the development of new SLICC criteria. 187 individuals were enrolled in the trial. Biospecimens were collected every three months for mechanistic studies. The objective of this study was to assess the effect of HCQ on the level of antibodies to a panel of 120 potential autoantigens.

Methods: Serum was collected from SMILE participants at baseline and every three months for a total of 24 months or until they met SLICC classification criteria for SLE. IgG and IgM antibodies to 120 antigens previously demonstrated in patients with SLE and other autoimmune diseases were quantified by fluorescence intensity on antigen microarrays. Signal intensity was normalized to total IgG or IgM for each sample and log_2transformed for analysis. Levels of individual autoantibodies were compared at baseline and at the last study visit and significance determined using a paired t-test. Nominal p values were corrected for multiple comparisons by Benjamini-Hochberg at a False-Discovery Rate of 0.05.

Results: 152 of the 187 SMILE participants had informative pairs of serum samples. These included 46 individuals who got HCQ and 50 who got PBO and did not develop new SLICC criteria over 24 months (“Non-Progressors”, NP); 16 individuals who got HCQ and 16 who got PBO who developed a second SLICC criterion in addition to the ANA (“Progressors”, PR); 12 individuals who got HCQ and 12 who got PBO who developed criteria for classification of lupus (“Developed SLE”, DS).The Progressors and Developed SLE individuals were combined (PRDS) for comparison to the NP.

In the group of participants who received HCQ, 93 of 120 antibodies levels were significantly lower at the end of the study compared to 6 of 120 antibodies in the group that received PBO ($p = 2.2x10^{-6}$, Fisher’s exact test). Table 1 shows the results by treatment group and study outcome. No IgG antibody levels were significantly increased at the end of the study and no IgM antibody levels were significantly affected by hydroxychloroquine in the SMILE study.

Table 1: Effect of Hydroxychloroquine on Autoantibody Levels

	Participant Outcome			
	Non-Progressors		Progressors and Developed SLE	
Treatment[1]	N[2]	Median % decrease (range)[3]	N	Median (range)
HCQ	62	13.4 (8.8-46.4)	73	19.4 (9.6-52.7)
PBO	5	17.7 (13.9-37.5)	1	18.5

[1]HCQ: Hydroxychloroquine; PBO: Placebo.
[2]Number of antibodies with lower mean levels at the end of the study having a corrected p value < 0.05; 42 antibodies were in common between outcomes such that there were 93 total in the HCQ treatment group.
[3]Percentage decrease from first visit to end of study

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Mean Decreases in Autoantibody levels for Select Antigens in Individuals Receiving Hydroxychloroquine

Antigen	Non-Progressors	Progressors and Developed SLE
Glomerular Basement Membrane	NS	28.5%, p = 0.004
Genomic DNA	40.1%, p = 0.004[1]	52.6%, p = 0.003
Histone 2B	46.4%, p = 0.02	21.0%, p = 0.03
Nucleolin	NS	32.8%, p = 0.003
Nucleosome	NS	23.6%, p = 0.006
Thyroglobulin	23.1%, p = 0.003	30.8%, p = 0.009
Thyroid Peroxidase	12.7%, p = 0.004	19.4%, p = 0.015
U1-RNP-C	NS	22.3%, p = 0.01

[1]p values corrected for multiple comparisons by Benjamin-Hochberg.

The median decrease in autoantibody level was 13.4% for the NP participants and 19.4% for the PRDS participants. The maximum decreases were 46.4% for the NP participants and 52.7% for the PRDS participants. Decreases in mean autoantibody levels in response to hydroxychloroquine varied. The mean decreases in antibody titers for select antigens are shown in Table 2.

Conclusion: In a cohort of individuals at risk for the development of systemic lupus erythematosus, treatment with hydroxychloroquine resulted in significant decreases in autoantibody levels measured against a diverse panel of antigens. This feature of treatment with hydroxychloroquine may be a factor in the clinical efficacy of this agent.

Disclosure: D. Karp: Ampel Biosciences, 2, Biogen, 5, Bristol-Myers Squibb(BMS), 5, Caribou, 1, Eli Lilly, 5, Novartis, 5, Sanofi, 1, UCB, 5, Zura, 1; **P. Raj**: None; **C. Zhu**: None; **D. Liu**: None; **D. Liao**: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5.

Abstract Number: 1525

Rituximab super-responders: characteristics of patients with more than 3 years response to a single cycle of treatment

Md Yuzaiful Md Yusof[1], Junaid Patel[2], Paul Emery[3] and **Ed Vital**[3], [1]University of Leeds, Leeds, United Kingdom, [2]University of Leeds, Leeds, [3]University of Leeds, Leeds, England, United Kingdom

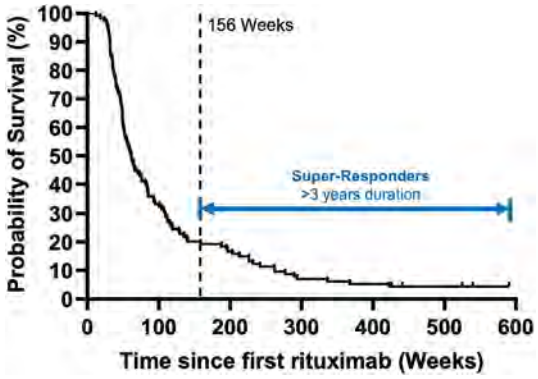
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Emerging therapies such as CD19 CAR-T-cells have been reported to induce deeper B-cell depletion and thereby drug-free remission up to 18 months. With rituximab, we showed that efficacy is related to depth of depletion and rate of repopulation, which are highly variable, and related to FCGR genotype[1]. We have observed "RTX-super-responders" with sustained remission after one cycle of RTX. The objectives of this study were to assess a) incidence of RTX-super-response, b) factors associated with sustained remission.

Methods: We conducted an observational study of RTX-treated SLE patients in a single centre over 20 years with on-demand retreatment . Usual practice was to continue concomitant immunosuppressants but taper glucocorticoids. Univariable and multivariable logistic regression analyses were performed to identify factors associated with RTX long-response, with $p < 0.1$ associated with the deviance used for inclusion into the model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Relapse-free survival after first cycle of rituximab

	Median (IQR) SLEDAI-2K				Median (IQR) Plasmablast (x10^9/L)		
	Baseline	6-Month	2-Year	3-Year	Baseline	6-Month	3-year
RTX-Super Responder on IS (n=15)	9 (6-13)	1 (0-2)	1 (0-2)	1 (0-2)	0.0048 (0.0035-0.0092)	<0.0001 (0.0000-0.0001)	0.0023 (0.0007-0.0051)
IS-Free RTX Super-Responder (n=8)	10 (8-14)	3 (2-4)	2 (1-3)	2 (0-2)	0.0062 (0.0020-0.0110)	0.0002 (0.0000-0.0003)	0.0007 (0.0003-0.0012)

IS = oral immunosuppressant

Disease activity and plasmablast repopulation

Results: Of 149 first-cycle-RTX-treated patients, 114 were included in the study [excluded due to non-response in Cycle 1=17; received fixed retreatment at 6-9 months=15; deaths within the first 3 years=2; and discontinued RTX due to psoriasis=1]. Based on survival curve, we defined super-responders as >3 years. This occurred in 23/114 patients (20%) with median (IQR) duration of response 263 (212,423) weeks.

At baseline, RTX-super-responders had: mean (SD) age 35 (14) years, 20/23 (87%) female, ancestry European=9/23 (39%); South Asian=6/23 (26%), Chinese/SE Asian=2/23 (9%); African=5/23 (22%); and Mixed=1/23 (4%], concurrent APS 6/23 (26%), disease duration 2.8 (1,5) years, median (IQR) SLEDAI-2K 11 (7-15), and median (IQR) numeric BILAG score 21 (13-25). Sustained suppression of plasmablasts was observed at 3 years: median (IQR) 0.0008 (0.0002-0.0045). 8/23 RTX-super-responders (34.8%) were either not prescribed immunosuppressants or withdrew them during follow up (drug free remission).

In multivariable analysis of all 114 patients, RTX-super-response was associated with non-European ancestry (OR 4.6, 95% CI 1.6-12.7)) and concurrent APS, (3.2, 0.99-10.35). Longer disease duration (0.89,0.80-0.99 per year) was associated with lower odds of RTX-super-response. No other factors (age, sex, anti-dsDNA+, low C3/C4, number of antibodies, concomitant immunosuppressant, disease activity score, and active BILAG A/B in 5 most frequent domains) were predictive.

Conclusion: Sustained drug-free remission is not confined to patients who have received CAR-T CD19. 1 in 5 RTX-treated patients had >3 years response to their first cycle, and 1 in 12 had sustained, immunosuppressant-free remission. RTX-super-responders have patient characteristics denoting disease severity (early disease, non-European ancestry and APS), and marked suppression of plasmablast repopulation. This suggests that sustained drug-free remission is a feature of the overall immune environment rather than the modality of B cell killing. Future work will include more detailed biomarker evaluation of this cohort.

Disclosure: M. Md Yusof: GlaxoSmithKlein(GSK), 1, Novartis, 1, 6, UCB, 2, 6; **J. Patel**: None; **P. Emery**: Abbvie, 1, Activa, 1, Anaptysbio, 1, Astra-Zeneca, 1, BMS, 1, Boehringer Ingelheim, 1, Galapagos, 1, Gedeon Richter, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, Novartis, 1; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6.

Abstract Number: 1526

Guidance For Corticosteroid Tapering In Patients With Systemic Lupus Erythematosus: Results From An International Delphi Consensus Project

Ed Vital[1], George Bertsias[2], Andrea Doria[3], Sindhu Johnson[4], Sarah Mackie[5], Sandra Navarra[6], Bas Nijmeijer[7], Ayobami Olojo[7], Bernardo A. Pons-Estel[8], Onno Teng[9] and Jinoos Yazdany[10], [1]University of Leeds, Leeds, England, United Kingdom, [2]Rheumatology and Clinical Immunology, University Hospital of Heraklion and University of Crete Medical School and Foundation for Research and Technology-Hellas (FORTH), Infections and Immunity, Institute of Molecular Biology and Biotechnology, Heraklion, Greece, [3]University of Padova, Padova, Italy, [4]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, [5]University of Leeds, Leeds, United Kingdom, [6]University of Santo Tomas, Manila, Philippines, [7]AstraZeneca, Cambridge, United Kingdom, [8]Grupo Oroño - Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina, [9]Leiden University Medical Center, Leiderdorp, Netherlands, [10]UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite guidelines for SLE emphasizing the importance of tapering corticosteroids (CS), detailed recommendations on how to taper are limited. The purpose of this modified Delphi consensus exercise is to develop consensus-based guidance for tapering CS in patients with SLE, including specific tapering regimens.

Methods: *Delphi Rounds*

Following a literature and guideline review, candidate statements were grouped into three topics:

1) CS-tapering regimens in lupus: general considerations

2) Managing flares and patients with high risk of flare during CS tapering

3) Managing CS-associated toxicity and CS withdrawal symptoms

Open-ended and multiple-choice questions were also included, and example CS-tapering regimens for different disease severities were proposed. Results were obtained over two rounds of online surveys, with Round 1 results supporting the development of Round 2. In Round 2, respondents were asked to vote for which regimens they deemed acceptable for use in clinical practice and could vote for multiple regimens per patient scenario.

Respondents
Snowball sampling was used to identify a global interdisciplinary group of experts to participate in the Delphi rounds.

Defining consensus

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Summary of recommended CS-tapering regimens. *Respondents could choose multiple schemes that they considered acceptable; †CS-tapering regimen is the reduced-dose regimen from the KDIGO 2024 guidelines for lupus nephritis; ‡respondents voted that the regimen for active lupus nephritis could also be used in severe non-renal SLE as per Table 2. CS, corticosteroid; IV, intravenous; KDIGO, Kidney Disease: Improving Global Outcomes

Patient characteristics	Timing	CS dose		Respondents who agreed regimens are acceptable in clinical practice (%)
Mild SLE **(CS initiation and tapering)**	Week 1 2 3 4	Oral prednisone equivalent (mg/day) 10–15 5–10 2.5–5 0 if lupus is controlled		87.2
Moderate SLE **(CS initiation and tapering)**	Optional day 1–3	**With or without*** IV methylprednisolone pulses 0.125–0.5 g/day (for up to 3 days)		Regimen with or without IV pulses: 93.6 Regimen with IV pulses: 59.6 Regimen without IV pulses: 67.0
	Week 1 2 3 4 5 6 7 8 9 10 11 12 13 14 >15	Oral prednisone equivalent (mg/day) 20–30 20–25 15–20 15–20 10–15 10–15 5–10 5–10 2.5–7.5 2.5–7.5 0–5 0–5 0–2.5 0–2.5 0 if lupus is controlled		
Patients with severe non-renal SLE or active lupus nephritis†‡ **(CS initiation and tapering)**	Day 1–3	IV methylprednisolone pulses 0.25–0.5 g/day up to 3 days as initial treatment		74.5
	Week 0–2 3–4 5–6 7–8 9–10 11–12 13–14 15–16 17–18 19–20 21–24 >25	Oral prednisone equivalent (mg/day) 0.5–0.6 mg/kg (up to 40) 0.3–0.4 mg/kg 15 10 7.5 5 2.5 2.5 2.5 2.5 2.5 <2.5		
Patients on long-term, low-dose CS treatment	Faster regimen: Week 1–2 3–4 5–6 7–8 9–10 11–12	Oral prednisone equivalent (mg/day) where 1 mg tablets **are** available 5 4 3 2 1 0	Oral prednisone equivalent (mg/day) where 1 mg tablets **are not** available 5 5 and 2.5 on alternating days 2.5 2.5 2.5 and 0 on alternating days 0	62.8
	Slower regimen: Month 1 2 3 4 5 6	Oral prednisone equivalent (mg/day) if 1 mg tablets **are** available 5 4 3 2 1 0	Oral prednisone equivalent (mg/day) if 1 mg tablets **are not** available 5 5 and 2.5 on alternating days 2.5 2.5 2.5 and 0 on alternating days 0	67.0

In Round 1, respondents were asked to rate their agreement with the candidate statements using a nine-point Likert scale, with a rating of 1–3 indicating disagreement, 4–6 indicating neutrality, and 7–9 indicating agreement. Consensus was defined as ≥70% of respondents voting either ≤3 (disagreement) or ≥7 (agreement). In Round 2, respondents were presented with the mean ratings from Round 1, their own Round 1 ratings, and the opportunity to revise their rating.

Results: Of the 124 respondents invited, 101 (81%) completed Round 1 and, of these, 94 (93%) completed Round 2. Respondents who completed both rounds were from 30 countries and comprised 79 rheumatologists, 11 nephrologists, three dermatologists, and one internist. Of the eight example

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Consensus received on final CS-tapering voting statements. CS, corticosteroid; dsDNA, double-stranded DNA; IV, intravenous

Topic 1: CS-tapering regimens in lupus: general considerations	Consensus (%)
When initiating treatment in a patient with mild disease, IV methylprednisolone pulses should be used	Disagreement (84.0)
When initiating treatment in a patient with moderate disease, IV methylprednisolone pulses could be used	Agreement (71.3)
When initiating treatment in a patient with severe disease, IV methylprednisolone pulses should be used	Agreement (93.6)
In non-renal SLE, CS tapering should only be initiated as soon as clinical manifestations significantly improve, rather than having a pre-planned tapering regimen	Agreement (84.0)
In non-renal SLE, whenever CS are initiated, there should be a tapering scheme	Agreement (76.6)
In moderate and severe disease, CS tapering should be initiated after initiation of an adequate immunosuppressant or biologic	Agreement (88.3)
In mild disease, CS tapering should be initiated after initiation of an adequate immunosuppressant or biologic	No consensus
Long-term prednisone maintenance should be avoided (tapering of CS to 0 mg should always be attempted)	Agreement (77.7)
Long-term prednisone could be used to control disease activity at the lowest effective dose if other options have had a lack of response	Agreement (86.2)
CS dose should be titrated to the lowest possible dosage (comment: the lowest possible dose does not need to be a multiple of 5 mg/day, eg 3 or 4 mg/day could also be used, if available)	Agreement (93.6)
In patients for whom complete CS withdrawal is not possible, physicians should aim for a target dosage of ≤2.5 mg/day when the patient is in remission	Agreement (83.0)
In patients for whom complete CS withdrawal is not possible, physicians should aim for a target dosage as low as possible, but not exceeding 5 mg/day, when the patient is in a state of low disease activity	Agreement (95.1)
Antimalarials are recommended for all patients, unless contraindicated	Agreement (98.9)
Immunosuppressants or biologics should be used to increase the likelihood of success during CS tapering	Agreement (97.9)
Immunosuppressants or biologics should be optimized if previous CS-tapering attempts have failed	Agreement (100.0)
In patients who have already attempted CS tapering, but the treatment plan has failed, standard of care should be re-evaluated and biologics should be considered	Agreement (95.7)
Adrenal insufficiency should be tested for when initiating CS tapering in stable patients on long-term low-dose CS	No consensus
Plasma cortisol levels (circadian rhythm) should be measured throughout a CS-tapering regimen	Disagreement (86.2)
Clinicians should engage in shared decision-making	Agreement (96.8)
Shared decision-making should be documented	Agreement (88.3)
The same CS-tapering regimen(s) that can be used for patients with severe active lupus nephritis can also be used for patients with severe non-renal SLE disease activity or severe flares	Agreement (88.3)
CS tapering should be slower for patients who have already attempted CS tapering, but the treatment plan has failed	Agreement (87.2)
Topic 2: Managing flares and patients with a high risk of flare during CS tapering	
The slower CS-tapering regimen (the 6-month regimen for patients on long-term low-dose CS) is acceptable for a patient with high anti-dsDNA antibodies and/or low complement	Agreement (86.2)
One or more standard-of-care drugs other than CS should be added for patients with overt/undisputed persistent very active serology (eg high titer of anti-dsDNA or low complement)	Agreement (84.0)
IV methylprednisolone pulses may be used to control flares during CS tapering in patients with severe disease	Agreement (88.3)
If a flare occurs during tapering in patients with mild or moderate disease, CS dose should be increased according to the activity and severity of the flare and tapering resumed once disease control is established	Agreement (90.4)
If a moderate or severe flare occurs, a new CS induction regimen adapted to the severity of flare may be required (comment: this can potentially include IV methylprednisolone)	Agreement (94.7)
Topic 3: Managing CS-associated toxicity and withdrawal symptoms	
Patients on long-term CS treatment should be educated about adrenal insufficiency during CS tapering	Agreement (90.4)
Patients should be educated on how to manage CS during periods of acute illness/stress	Agreement (95.7)
In patients at high risk of CS-associated toxicities, a faster tapering schedule should be recommended	Agreement (86.2)
In patients that have previously experienced CS-associated toxicities, a faster tapering schedule should be recommended	Agreement (93.6)
In patients at high risk of CS-associated toxicities, a CS-sparing regimen should be recommended from the beginning of treatment	Agreement (93.6)
CS tapering may need to be extremely rapid in patients with serous CS-related maculopathy to prevent blindness	Agreement (91.5)

CS-tapering regimens presented, three achieved ≥70% agreement that they would be acceptable to use in clinical practice (regimens for mild SLE, moderate SLE, and lupus nephritis or severe SLE). The regimens that received the highest agreement in Round 2 for each patient scenario are presented in Table 1. Consensus for either agreement or disagreement was achieved in 31/33 statements in Round 2 (Table 2).

Conclusion: This consensus-based guidance will support physicians in choosing a CS-tapering approach for patients with SLE across different clinical scenarios. The next step is to obtain the patient perspective on these results to ensure that patient preferences are considered when initiating CS tapering, followed by dissemination into routine practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Vital: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6; **G. Bertsias**: AbbVie, 6, AstraZeneca, 2, 5, 6, Eli Lilly, 2, 6, GSK, 2, 5, 6, MSD, 5, Novartis, 2, 6, Otsuka, 6, Pfizer, 6; **A. Doria**: AbbVie, 6, AstraZeneca, 2, 6, Biogen, 2, 6, BMS, 2, 6, GSK, 2, 6, MSD, 2, Otsuka, 2, 6; **S. Johnson**: None; **S. Mackie**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, Fresenius Kabi, 6, Novartis, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, UCB, 6, Vifor, 6; **S. Navarra**: Astellas, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Biogen, 2, 12, Independent Data Monitoring Committee, Viatris (Idorsia), 2, 6; **B. Nijmeijer**: AstraZeneca, 3; **A. Olojo**: AstraZeneca, 3, 11; **B. Pons-Estel**: AstraZeneca, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 5, 6, Novartis, 6, Roche, 5; **O. Teng**: GlaxoSmithKlein(GSK), 5, Vifor, 5; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2.

Abstract Number: 1527

Lupus Nephritis Clinical Practice Guidelines: Critical Appraisal and Quality Comparison Using the AGREE II Tool

Egla Samantha Sanchez-Peralta[1], Hector Alejandro Martinez-Espinosa[1], Karla Paola Moncada-Flores[2], Margarita Isabel Alarcon-Jarquin[3], Dionicio A. Galarza-Delgado[4], Diana E. Flores-Alvarado[1] and Gabriel Figueroa-Parra[5], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [2]Internal Medicine, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [5]Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: About a half of the patients with systemic lupus erythematosus (SLE) can present lupus nephritis (LN) throughout the course of their disease, representing one of the most severe manifestations of SLE. Patients with LN could develop end-stage kidney disease which carry an important burden of morbidity and mortality. In order to improve the quality of care of patients with LN, several medical associations have developed clinical practice guidelines (CPG) and recommendations. However, the quality of care of these patients might be impacted by the quality of the CPG. To evaluate the quality of LN CPG, we aimed to critically appraise and compare the LN CPG from the main international medical associations.

Table 1. Comparison of the methodological quality of lupus nephritis guidelines across six domains of the AGREE II tool.

Domain	GLADEL	EULAR/ERA	EULAR	KDIGO	APLAR	ACR	p-value
1. Scope and purpose	6.2 (1)	6.3 (1)	5.7 (2.1)	7 (0)	5.5 (2.3)	7 (0)	0.346
2. Stakeholder involvement	5.3 (1)	4.5 (2.9)	6 (0.9)	4.7 (2.3)	4.3 (2)	6.7 (0.5)	0.190
3. Rigor of development	5.3 (1.9)	4.9 (2.1)	6.7 (0.7)	6.6 (0.7)	5.6 (1.2)	5.3 (1.9)	**0.005**
4. Clarity of presentation	7 (0)	7 (0)	7 (0)	7 (0)	6 (1.3)	7 (0)	0.215
5. Applicability	4.1 (1.4)	3.5 (1.9)	3.3 (1.5)	5.3 (1.8)	4.1 (2.2)	4 (2.4)	0.344
6. Editorial independence	7 (0)	6.8 (0.5)	7 (0)	7 (0)	5.5 (3)	5.3 (1.7)	0.339
Overall judgement	5 (1.4)	5.5 (0.7)	5 (1.4)	6 (0)	5.5 (0.7)	6 (0)	0.595
Final score	5.8 (1.1)	5.5 (1.4)	5.9 (1.4)	6.3 (1)	5.2 (0.8)	5.9 (1.2)	-

Numbers represents mean (SD).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

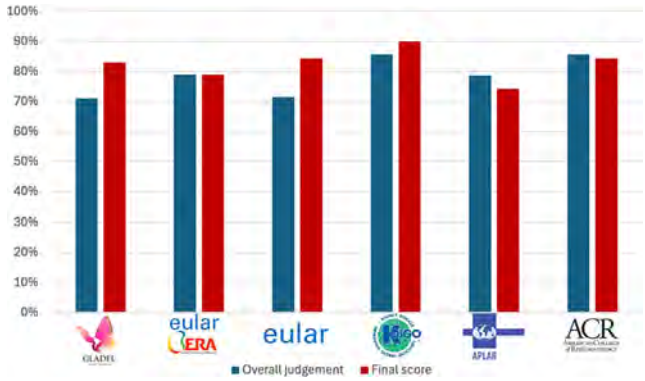


Figure 1. Overall judgement and final scores of AGREE II instrument across six clinical practice guidelines for LN.

Methods: We included globally representative CPG published in the last ten years that focused on LN or SLE including recommendations for renal involvement. We used the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument. It comprised of 23 items organized into 6 quality domains: 1) Scope and purpose; 2) Stakeholder involvement; 3) Rigor of development; 4) Clarity of presentation; 5) Applicability; and 6) Editorial independence. It also includes two final overall assessment items that requires to make overall judgements of the practice guideline while considering how the 23 items were rated. Two appraisers review each CPG and any supplementals. The average score for each item was considered to calculate the final scores by domain. The results are presented for each CPG. Guidelines scores were compared overall and by domain. Descriptive statistical analysis was performed. ANOVA test was employed to evaluate the differences between the six domains of the AGREE instrument. A p-value < 0.05 was considered statistically significant.

Results: We included six CPGs that evaluated SLE and/or LN, published between 2018 and 2025. The oldest CPG appraised was GLADEL (2018), and the newest was ACR (2025). Four CPGs were developed by rheumatology associations (GLADEL, EULAR, APLAR, ACR), one by a nephrology association (KDIGO), and one was a collaboration of both rheumatology and nephrology (EULAR/ERA). Most CPGs involved both rheumatologists and nephrologists, except for KDIGO (only nephrologists) and GLADEL (only rheumatologists). Four out of the six CPGs took into consideration the patient's preferences in the making of their recommendations (EULAR, APLAR, GLADEL, ACR). The CPG with the highest final score was KDIGO (6.3/7 points), and the lowest was APLAR (5.2/7 points). The domain with the lowest score across all CPGs was domain five (Applicability), with a mean of 4/7 points. On the contrary, domain four (Clarity of Presentation) was the highest graded (6.8/7 points) (**Figure 1**). When comparing scores of each domain between the six CPGs, only the domain 3 (Rigor of development) showed a significant difference ($F= 5.120$, $p= 0.005$) (**Table 1**).

Conclusion: The findings highlight areas for improvement in guideline development, particularly in making recommendations more applicable to diverse patient populations.

Disclosure: E. Sanchez-Peralta: None; **H. Martinez-Espinosa**: None; **K. Moncada-Flores**: None; **M. Alarcon-Jarquin**: None; **D. Galarza-Delgado**: None; **D. Flores-Alvarado**: None; **G. Figueroa-Parra**: None.

Abstract Number: 1528

Influence of Prednisone use over cardiovascular risk in patients with Systemic Lupus Erythematosus

Esteban C. Garza-Gonzalez[1], Fernanda M. Garcia-Garcia[2], Oscar Azael Garza-Flores[3], Rebeca L. Polina-Lugo[4], Leslie Y. Lopez-Cantú[2], Jose R Azpiri-Lopez[5], Iris J. Colunga-Pedraza[2], Jesus Alberto Cardenas-de la Garza[6], Dionicio A. Galarza-Delgado[2] and Diego Azamat Salcedo Almanza[7], [1]Rheumatology Service, Hospital Universitario Dr. José Eleuterio

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

González, Universidad Autónoma de Nuevo León, San Nicolas de los Garza, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Guadalupe, Mexico, [4]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [5]Cardiology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [6]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [7]Radiology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic multisystem autoimmune disease associated with increased morbidity and mortality, particularly due to cardiovascular complications. Atherosclerotic cardiovascular disease (ASCVD) has emerged as one of the leading causes of death in young patients with SLE. This elevated cardiovascular risk cannot be fully explained by traditional risk factors alone, suggesting that disease-specific mechanisms, including chronic inflammation, immune dysregulation, and treatment-related factors, play a pivotal role. We aimed to evaluate the impact of prednisone in patients with SLE on lipid profile and the risk of subclinical atherosclerosis.

Methods: A cross-sectional, comparative, and analytical case-control study was conducted. Eighty patients, older than 18 years, who met the classification criteria for SLE according to ACR/EULAR 2019 criteria guidelines were enrolled.Carotid ultrasound was accomplished in 34 patients, and the presence of plaque was recorded, defined as wall thickening greater than 50%, or a focal region with a measurement greater than 1.5 mm that protrudes into the lumen. CIMT was also

Table 1 Demographic data

	SLE on Prednisone n=65	SLE without Prednisone n=15	*p* value
Age, mean ± SD	35.32 ± 11.67	42.6 ± 15.63	**0.045**
Female, n (%)	58 (82.23%)	13 (86.66 %)	0.770
Cardiovascular Risk Factors			
Weight, kg, mean ± SD	66.44 ± 16.87	71.08 ± 14.14	0.327
Height, m, mean ± SD	1.58 ± 0.06	1.60 ± 0.08	0.488
BMI, ± SD	26.3 ± 6.42	27.63 ± 4.95	0.457
Obesity, n (%)	13 (20%)	3 (20%)	1
Waist-Hip Ratio, mean ± SD	0.85 ± 0.5	0.84 ± 0.06	0.423
DM, n (%)	4 (6.15%)	1 (6.66%)	0.941
HTN, n (%)	15 (23.07%)	2 (13.33%)	0.406
DLP, n (%)	6 (9.23%)	4 (26.66%)	0.060
Smoking, n (%)	4 (6.15%)	2 (13.33%)	0.340
Treatment			
DMARDs, n (%)	39 (60%)	1 (6.66%)	**<0.001**
HCQ/CQ, n (%)	30 (46.15%)	12 (80%)	**0.016**
ACE inhibitors/ARBs, n (%)	19 (29.68%)	2 (13,33%)	0.060
Statins, n (%)	13 (20%)	3 (20%)	0.889
Lipid Profile			
COL Total, mg/dL, mean ± SD	186.03 ± 63.63	155.46 ± 27.18	0.073
VLDL, mg/dL, median, (p25 - p75)	1 (0-1)	18.1 (11.62 - 23.8)	**0.049**
LDL, mg/dL, mean ± SD	38.92 ± 26.85	62.15 ± 30.99	**0.004**
HDL, mg/dL, median (p25 - p75)	68.5 (51.3 - 106)	60.9 (44.2 - 92.05)	0.467
Ratio COL:HDL, median (p25 - p75)	2 (2 - 3)	2 (1.5 - 3.5)	0.701
TG, mg/dL, mean ± SD	132.18 ± 47.7	127.09 ± 55.23	0.718
Glucose Levels			
Glucose, mg/dL, median (p25 - p75)	87.7 (82 - 94)	93 (91.2 - 98.8)	**0.007**
HbA1c, mean ± SD	5.10 ± 1.04	5.52 ± 1.13	0.172

BMI, Body Mass Index; DM, Diabetes Mellitus; HTN, Hypertension; DLP, Dyslipidemia; HCQ/CD, Hydroxicloroquine/Chloroquine; ACE, Angiotensin Converting Enzyme; ARBs, Angiotensin II Receptor Blockers;DMARDs, Disease Modifying Antirheumatic Drugs; COL, Cholesterol; VLDL, Very Low Density Lipid; LDL, Low Density Lipid; HDL, High Density Lipid; TG, Triglycerides; HbA1c, Hemoglobin A1c; SD, Standard Deviation; p25, Percentile 25; p75, Percentil 75.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 Carotid Ultrasound

	SLE on Prednisone n=24	SLE without Prednisone n=10	*p* value
Carotid Ultrasound			
Carotid Plaque, n (%)	0 (0%)	1 (10%)	0.116
Right CIMT, mm, mean ± SD	0.43 ± 0.069	0.52 ± 0.17	**0.046**
Right Intimal Hyperplasia, n (%)	1 (4.16%)	1 (10%)	0.510
Right Plaque, n (%)	0 (0%)	1 (10%)	0.116
Left CIMT, mm, mean ± SD	0.43 ± 0.5	0.5 ± 0.18	0.118
Left Intimal Hyperplasia, n (%)	0 (0%)	1 (10%)	0.116
Left Plaque, n (%)	0 (0%)	1 (10%)	0.116
Bilateral Plaques, n (%)	0 (0%)	1 (10%)	0.116

CIMT, Carotid Intima-Media Thickness; SD, Standard Deviation; p25, Percentile 25; p75, Percentil 75.

registered. The descriptive analysis was done with frequencies (%), mean (± SD), median (q25-q75), and comparisons with Chi square and Student's T, accordingly. We considered $p < 0.05$ as statistically significant. Statistical analysis was performed using SPSS version 25 (IBM, New York, USA).

Results: In this cohort study of patients with SLE, those receiving prednisone were significantly younger (35.32 ± 11.67 vs. 42.6 ± 15.63 years, $p = 0.045$) and more frequently treated with DMARDs (39 [60%] vs 1 [6.66%] $p < 0.001$), while hydroxychloroquine/chloroquine use was higher in the non-prednisone group ($p = 0.018$). There were no significant differences in traditional cardiovascular risk factors like obesity, diabetes, hypertension, or smoking. Despite the known adverse metabolic effects of corticosteroids, patients not on prednisone had significantly higher levels of VLDL ($p = 0.049$), LDL cholesterol ($p = 0.004$), and fasting glucose ($p = 0.007$), suggesting a paradoxical trend toward a worse metabolic profile in those without steroids (Table 1). In a subset of 34 patients who underwent carotid ultrasound, right carotid intima-media thickness (CIMT) was also significantly greater in the non-prednisone group (0.43 ± 0.069 vs 0.52 ± 0.17 $p = 0.046$), indicating more subclinical atherosclerosis (table 2).

Conclusion: This study suggests that in patients with SLE, prednisone use despite its known metabolic side effects, was paradoxically associated with a more favorable lipid and glucose profile, as well as lower carotid intima-media thickness, compared to those not on prednisone. There were no significant differences in traditional cardiovascular risk factors or carotid plaque presence. These findings indicate that the anti-inflammatory effects of prednisone may, in certain contexts, mitigate metabolic and vascular risks, potentially reducing subclinical atherosclerosis. However, further longitudinal studies are needed to better understand its long-term cardiovascular impact in SLE.

Disclosure: E. Garza-Gonzalez: None; **F. Garcia-Garcia**: None; **O. Garza-Flores**: None; **R. Polina-Lugo**: None; **L. Lopez-Cantú**: None; **J. Azpiri-Lopez**: None; **I. Colunga-Pedraza**: None; **J. Cardenas-de la Garza**: None; **D. Galarza-Delgado**: None; **D. Salcedo Almanza**: None.

Abstract Number: 1529

Updated Phase 1 Trial Data Assessing the Tolerability, Efficacy, Pharmacokinetics, and Pharmacodynamics of BMS-986353 (CC-97540), a CD19-directed Chimeric Antigen Receptor T Cell Therapy Using a Next-Generation Process for Severe, Refractory SLE

Georg Schett[1], David Simon[2], Margrit Wiesendanger[3], Anca Askanase[4], Vikas Majithia[5], Neil Kramer[6], Jacques Morel[7], Philip J. Mease[8], Ellen De Langhe[9], Amit Saxena[10], dominique Farge[11], Alain Lescoat[12], Alisha Desai[13], Griff McTume[14], Whitney Handy[14], Sharmila Das[13], Jerill Thorpe[14], Alexis Melton[14], Ashley Koegel[14] and Emily Littlejohn[15], [1]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [2]Department of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Germany, [3]Icahn School of Medicine at Mount Sinai, New York, NY, [4]Columbia University Medical Center, New York, NY, [5]Mayo Clinic Hospital, Jacksonville, FL, [6]Overlook Medical Center; Atlantic Medical Group, Atlantic Health System, Summit, NJ, [7]CHU and University of Montpellier, Montpellier, France, [8]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [9]University Hospitals Leuven, Leuven, Belgium, [10]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [11]Hôpital Saint-Louis, Paris, France, [12]CHU Rennes University Hospital, Rennes, France, [13]Bristol Myers Squibb, Princeton, NJ, [14]Bristol Myers Squibb, Princeton, [15]Cleveland Clinic, Cleveland, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: BMS-986353 (CC-97540; CD19 NEX-T) is a CD19-directed chimeric antigen receptor (CAR) T cell therapy that expresses the same CAR as lisocabtagene maraleucel (liso-cel); it is manufactured via the NEX-T™ process to reduce manufacturing time and optimize phenotypic attributes. In Breakfree-1 trial (NCT05869955), BMS-986353 showed promising initial safety and efficacy in pts with severe refractory SLE.[1] Here, we report updated data on BMS-986353 in the SLE cohort.

Methods: This phase 1, multicenter trial assesses safety and efficacy of BMS-986353 in pts with severe, treatment-resistant autoimmune diseases. Inclusion criteria required active disease (BILAG A score) and an inadequate response to ≥ 2 immunosuppressants and steroids. After lymphodepletion, a single BMS-986353 infusion was administered at 2 dose levels (DLs) to optimize risk–benefit in SLE: DL1, 10×10^6; DL2, 25×10^6 CAR+ T cells. All pts were weaned off lupus-directed therapies by day 29 post-infusion. Primary endpoint was safety.

Results: As of March 17, 2025, 26 pts with SLE were enrolled; 19 were treated with BMS-986353 (DL1, n=13; DL2, n=6), with 17 (DL1, n=11) evaluable for efficacy. Median age: 30.0 (18–49) years. Median follow-up (range): 181.0 (7–488) days. Four and 15 pts had BILAG A cardiorespiratory and BILAG A renal involvement, respectively, and had refractory disease despite multiple prior therapies (median [range]: 7.0 [4–11]).

Lower frequency and grade (gr) of adverse events were observed in DL1 vs DL2. Gr 3/4 neutropenia occurred in 46.2% (DL1) versus 83.3% (DL2); all events resolved. There were no gr 3/4 thrombocytopenia or prolonged cytopenias at either DL. Low gr cytokine release syndrome (CRS) occurred in 61.5% at DL1 (**Table**) versus 100% at DL2; no gr ≥3 CRS events

	DL1 (n = 13)	
	CRS	ICANS
Any grade, n (%)		
Grade 1	7 (53.8)	0
Grade 2	1 (7.7)	0
Grade 3	0	0
Grade 4–5	0	0
Median onset (range), days	7.5 (2–11)	0
Median duration[a] (range), days	2.0 (1–5)	0
Treatments, n (%)		
Tocilizumab	4 (30.8)	–
Steroids	3 (23.1)	0

[a]Multiple events occurring within 7 days from each other are considered as 1 episode. CRS, cytokine release syndrome; DL, dose level; ICANS, immune effector cell-associated neurotoxicity syndrome.

CRS and ICANS at Part B expansion dose.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

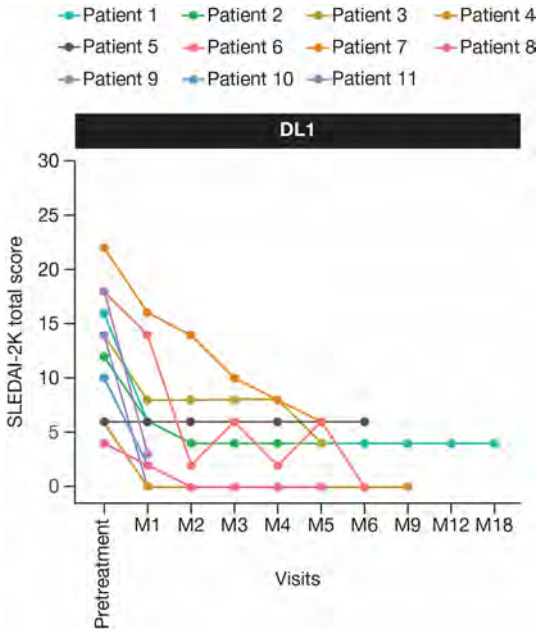


Figure 1. Total SLEDAI-2K score following BMS-986353 treatment in the SLE efficacy-evaluable population at DL1. DL, dose level; M, month; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

were observed at either DL. Immune effector cell-associated neurotoxicity syndrome (ICANS) was not observed at DL1; 2 gr 3 ICANS events occurred at DL2. All CRS and ICANS were brief and reversible. DL1 was selected for expansion in Part B based on the improved safety profile at DL1 in Part A.

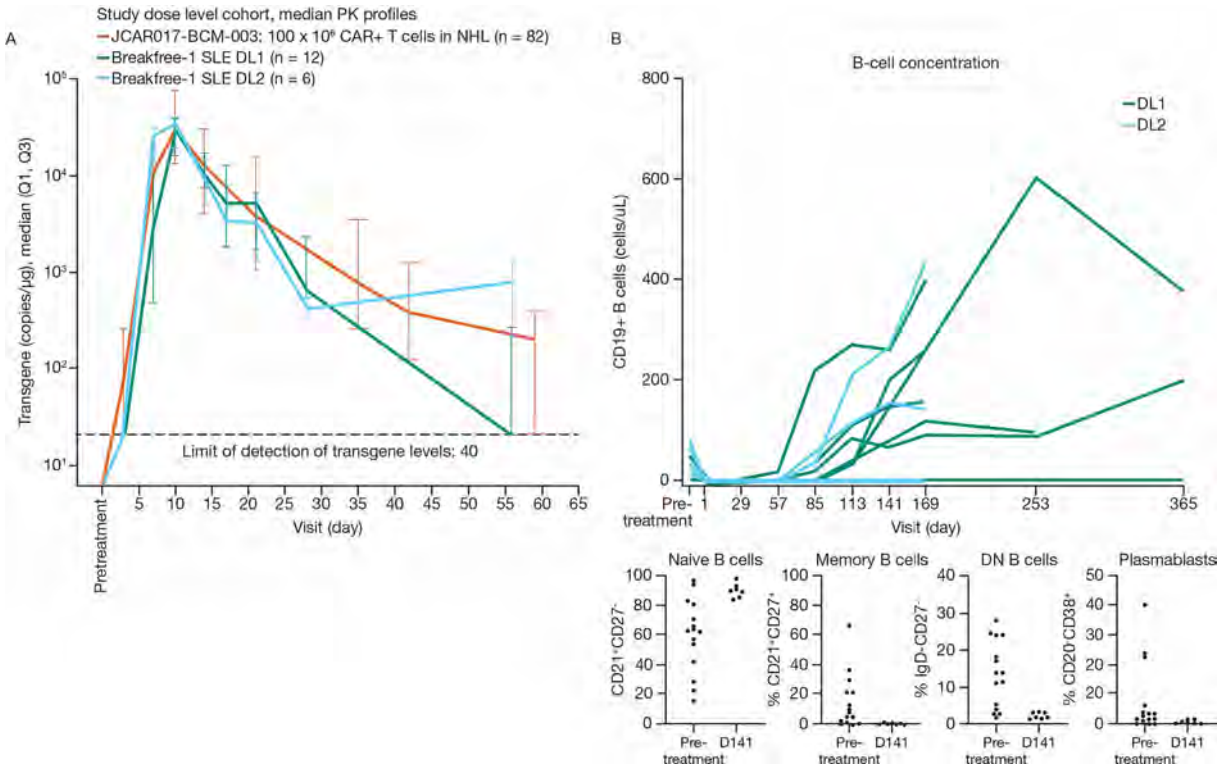


Figure 2. Median transgene PK profiles (A) and peripheral B cell concentration and phenotype (B) following BMS-986353 treatment in the SLE population. PK were analyzed using droplet PCR and pharmacodynamics were evaluated via flow cytometry. DL, dose level; DN, double negative; PCR, polymerase chain reaction; PK, pharmacokinetics; SLE, systemic lupus erythematosus.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

After BMS-986353 administration, most evaluable pts experienced a substantial improvement in disease activity as assessed by a significant reduction in SLEDAI-2000K (2K) and Physician's Global Assessment (PGA) scores; with 6 months of follow-up, DL1 pts had a median 9 point reduction in SLEDAI-2K score (**Fig 1**) and a 90% improvement in PGA. No clinically meaningful differences in efficacy outcomes were observed between DLs.

Double-stranded DNA and serum complement (C3 or C4) had significant titer reduction or normalized over time for pts with abnormal values at screening. All pts showed robust CAR T cell expansion compared with liso-cel and complete peripheral blood B-cell depletion at both DLs with primarily naive repopulating B cells (**Fig 2**).

Conclusion: These data show a manageable safety profile and preliminary clinical benefit of BMS-986353 for pts with severe, treatment-resistant SLE, suggesting BMS-986353 may be a potential therapeutic option.

Reference: 1. Schett G, et al. *Arthritis Rheumatol* 2024;76(suppl 9).

Medical writing: Alexus Shirk, PhD (Caudex, an IPG Health Company), funded by Bristol Myers Squibb.

Disclosure: G. Schett: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **D. Simon**: AbbVie, 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, Janssen-Cilag, 2, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Lilly, 2, 6, Medac, 2, 6, Novartis, 2, 6, UCB, 2, 6; **M. Wiesendanger**: Bristol-Myers Squibb(BMS), 1, 6; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **V. Majithia**: None; **N. Kramer**: Amgen, 11, AstraZeneca, 5, 6, Becton Dickinson, 11, Bristol-Myers Squibb(BMS), 2, 5, GlaxoSmithKlein(GSK), 5, 6, Immunic, 11, Johnson & Johnson, 11, Pfizer, 11, Protagonist Therapeutics, 11, Stryker, 11, UpToDate, 12, author; **J. Morel**: AbbVie, 2, 5, 6, Biocon, 6, Biogen, 6, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 6, Galapagos, 2, 6, GlaxoSmithKline, 2, 6, Lilly, 2, 6, Medac, 6, Mylan/Viatris, 6, Nordic Pharma, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche/Chugai, 6, Sanofi, 2, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **E. De Langhe**: AC Immune, 1; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **d. Farge**: None; **A. Lescoat**: None; **A. Desai**: Bristol-Myers Squibb(BMS), 3; **G. McTume**: Bristol Myers Squibb, 3; **W. Handy**: Bristol Myers Squibb, 3; **S. Das**: Bristol-Myers Squibb(BMS), 3, 11, Deciphera Pharmaceuticals, 2; **J. Thorpe**: Bristol-Myers Squibb(BMS), 3; **A. Melton**: Bristol Myers Squibb, 3; **A. Koegel**: Bristol-Myers Squibb(BMS), 3, 11; **E. Littlejohn**: Bristol Myers Squibb, 2, 5, 6, Synthekine, 5.

Abstract Number: 1530

The Renal Activity Index for Lupus Identifies and Predicts Complete Renal Remission or Absence of Kidney Involvement in Systemic Lupus Erythematosus

Guillermo Pons-Estel[1], Rosana Quintana[1], Romina Nieto[1], Hermine Brunner[2], Marina Scolnik[3], Carmen Funes Soaje[4], Paula Alba[5], Veronica Saurit[6], Mercedes Garcia[7], GUILLERMO ARIEL BERBOTTO[8], Inés Verónica Bellomio[9], Mario Eduardo Kerzberg[10], Graciela Gomez[11], Cecilia Pisoni[12], Vicente Juarez[13], Ana Malvar[14], Nalzio Silva[15], ODIRLEI MONTICIELO[16], Henrique Mariz[17], Francinne Ribeiro[18], Eduardo Borba[19], Eloisa Bonfa[19], Edgard Torres dos Reis-Neto[20], Iris Guerra Herrera[21], Maria Loreto Massardo[22], Gustavo Aroca-Martínez[23], Lorena Gómez Escorcia[24], Carlos Alberto Casas[25], Gerardo Quintana-Lopez[26], Carlos Toro-Gutierrez[27], Mario Moreno Alvarez[28], MIGUEL SAAVEDRA[29], Margarita Portela Hernández[30], Hilda Fragoso-Loyo[31], Luis H Silveira[32], Ignacio García-De la Torre[33], Carlos Abud-Mendoza[34], Jorge Antonio Esquivel Valerio[35], Maria Isabel Acosta[36], Astrid Paats[37], Claudia S. Mora-Trujillo[38], Manuel Ugarte-Gil[39],

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Armando Calvo[40], Roberto Muñoz-Louis[41], Martin Rebella[42], Alvaro Danza[43], Federico Zazzetti[44], Ashley Orillion[45], Urbano Sbarigia[46] and Bernardo A. Pons-Estel[47], [1]Centro Regional de Enfermedades Autoinmunes y Reumáticas, GO-CREAR, Rosario, Argentina, Rosario, Argentina, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Hospital Italiano de Buenos Aires, Argentina, Buenos Aires, Argentina, [4]Hospital Italiano de Córdoba, Córdoba, Argentina, Cordoba, Argentina, [5]Hospital Córdoba y Sanatorio Allende, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Córdoba, Argentina, Cordoba, Argentina, [6]Hospital Privado Universitario de Cordoba, Córdoba, Argentina, Córdoba, Argentina, [7]Hospital Interzonal General de Agudos "General San Martín" de la plata, La Plata, Argentina, [8]Sanatorio Británico, Rosario, Argentina, ROSARIO, Argentina, [9]Hospital Padilla, Tucumán, Argentina, San Miguel de Tucumán, Argentina, [10]Hospital J.M Ramos Mejía, Buenos Aires, Argentina, CABA, Argentina, [11]Instituto de Investigaciones Médicas Alfredo Lanari, Universidad de Buenos Aires, Buenos Aires, Argentina, Buenos Aires, Argentina, [12]CEMIC Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno", Buenos Aires, Argentina, Ciudad Autonoma Buenos Aires, Argentina, [13]Hospital Señor del Milagro Salta, Salta, Argentina, Salta, Argentina, [14]Organización Médica de Investigación, Buenos Aires, Argentina, [15]Hospital das Clinicas da Universidade Federal de Goias, Goias, Brazil, Goiânia, Brazil, [16]Hospital de Clínicas de Porto Alegre, Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil, PORTO ALEGRE, Rio Grande do Sul, Brazil, [17]Universidad Federal de Pernambuco, Pernambuco, Brazil, Pernambuco, Brazil, [18]Hospital Universitário Pedro Ernesto - Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, Rio De Janeiro, Rio de Janeiro, Brazil, [19]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [20]Universidad Federal São Paulo, São Paulo, Brazil, São Paulo, Brazil, [21]Hospital del Salvador Santiago de Chile, Santiago, Chile, Santiago, Chile, [22]Facultad de Medicina y Ciencia, Universidad San Sebastián, Santiago, Chile, Santiago, Chile, [23]Clínica de la Costa y Universidad Simón Bolívar, Barranquilla, Colombia, barranquilla, Colombia, [24]Clínica de la Costa y Universidad Simón Bolívar Barranquilla, Barranquilla, Colombia, Barranquilla, Colombia, [25]Fundación Valle del Lili, Universidad Icesi, Cali, Colombia, Cali, Colombia, [26]Facultad de Medicina, Universidad Nacional de Colombia; Hospital Universitario Fundación Santa Fe de Bogotá; Hospital Universitario Nacional de Colombia, Bogotá, Colombia, Bogotá, Colombia, [27]Pontificia Universidad Javeriana de Cali, Cali, Colombia, Cali, Colombia, [28]Universidad de Especialidades Espíritu Santo, Guayaquil, Ecuador, Guayaquil, Ecuador, [29]Hospital de Especialidades Dr. Antonio Fraga Mouret, Centro Médico Nacional La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico, MEXICO, Mexico, [30]Hospital de Especialidades del Centro Médico Nacional SXXI, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico, Mexico City, Mexico, [31]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, Mexico City, Mexico, [32]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [33]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, Guadalajara, Jalisco, Mexico, [34]Facultad de Medicina de la Universidad Autónoma de San Luis Potosí y Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí, Mexico, San Luis Potosí, Mexico, [35]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [36]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asuncion, Paraguay, [37]Facultad de Ciencias Medicas, Universidad Nacional de Asunción, San Lorenzo, Paraguay, Asuncion, Paraguay, [38]Hospital Nacional Edgardo Rebagliati Martins-EsSalud, Lima, Peru, Lima, Peru, [39]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [40]Hospital Nacional Cayetano Heredia Universidad Peruana Cayetano Heredia, Lima, Peru, Jesús Maria, Peru, [41]Hospital Docente Padre Billini, Santo Domingo, Distrito Nacional, Dominican Republic, [42]Hospital de Clínicas, Facultad de Medicina, UDELAR, Montevideo, Uruguay, Montevideo, Uruguay, [43]Médica Uruguaya, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay, Montevideo, Uruguay, [44]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [45]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [46]Johnson & Johnson, Beerse, Belgium, [47]Grupo Oroño - Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Argentina

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Effective, non-invasive disease activity and treatment response assessments are needed for patients with systemic lupus erythematosus (SLE), especially if associated with kidney disease, i.e. lupus nephritis (LN). The treatment goal of LN is to achieve complete renal remission (CRR). Proteinuria of >0.5 g/day can prompt a kidney biopsy to diagnose LN. The Renal Activity Index for Lupus (RAIL) measures the degree of kidney inflammation. The RAIL-score is calculated from the creatinine-adjusted RAIL biomarkers (neutrophil gelatinase-associated lipocalin [NGAL], kidney injury

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics & RAIL-scores over time

Variable	T0 (n=69)	T1 (n=58)	T2 (n=59)
Complete Renal Response, n (%)	37 (54%)	51 (88%)	55 (93%)
RAIL-Cr score	3.74 (2.72, 4.88)	3.47 (2.47, 4.12)	3.46 (2.43, 4.62)
Time to SLE diagnosis (months), median (Q1, Q3)	28 (21-36)		
Age at cohort entry (years), median (Q1, Q3)	37 (25-44)		
Ethnicity Caucasian / Mestizo, n (%)	10 (15.5%) / 58 (84%)		
Proteinuria	0.36 (0.12, 1.7)	0.16 (0.1, 0.3)	0.13 (0.1, 0.29)
Hematuria	19 (28%)	7 (12%)	3 (5%)
C3 / C4, low	61 (88%) / 57 (83%)	14 (24%) / 15 (26%)	16 (27%) / 18 (31%)
SLEDAI total score (range)	6 (2, 13)	2 (0, 4)	2 (0, 4)
SDI total score (range)	0 (0, 1)	0 (0, 1)	0 (0, 1)
Treatments n (%)			
ACE/ARB	37 (54%)		
Azathioprine	9 (13%)		
Prednisone / Steroids pulses	56 (81%) / 12 (17%)		
Antimalarials	65 (94%)		
Cyclophosphamide	9 (13%)	12 (21%)	4 (7%)
Mycophenolate mofetil	24 (35%)	21 (36%)	34 (58%)
Tacrolimus	3 (4%)	2 (3.5%)	4 (7%)

ACE= angiotensin-converting enzyme; ARB=angiotensin receptor blockers Cr=creatinine; RAIL= Renal Activity Index for Lupus; SDI=SLICC/ACR Damage Index; SLE=systemic lupus erythematosus; SLEDAI=Systemic Lupus Erythematosus Disease Activity Index; T0=at enrollment; T1=at 6 months; T2=at 12 months

molecule-1 [KIM-1], monocyte chemoattractant protein-1 [MCP-1], adiponectin, hemopexin, ceruloplasmin) and higher scores indicate higher kidney inflammation.[1] This study evaluated 1) the role of RAIL to distinguish CRR status and identify the cut-point for RAIL; **2)** the role of RAIL in predicting change in CRR status over time.

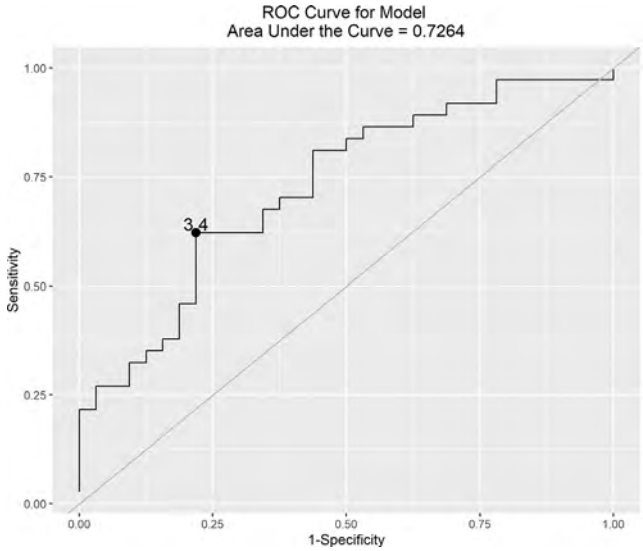


Figure 1. ROC curve for model

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Urine samples collected from 69 SLE adult patients with and without LN were studied longitudinally at enrollment into the GLADEL cohort (T0), at 6 months (T1) and 12 months (T2). Absolute scores and changes in RAIL-scores over time were assessed for presence of CRR status (proteinuria of < 0.5 g/day) by logistical regression models. The Youden Index optimal cut-points on the receiver operating characteristic (ROC) curves were calculated.

Results: For 186 visits from 51 (74%; 91% female) patients with LN and 18 (26%) patients without LN diagnosis, patient characteristics and disease courses are shown in **Table 1**. RAIL-scores were correlated with renal-SLEDAI (r=0.46; p< 0.0001) and proteinuria (r=0.37; p=0.002). Considering all visits (CRR present/absent=146/40), mean (SD) RAIL-scores with CRR-status were 1.17 (1.53) lower than without CRR (p=0.023; area under the ROC curve =0.73), as shown in **Figure 1**, RAIL scores of no more than 3.4 identified CRR-status with 78% specificity (Positive Predictive Value [PPV]=0.77, sensitivity=62). Patients who newly achieved CRR-status at the next visit had a mean (SD) RAIL-score decrease of 1.0 (1.524) since the last visit (Percentage Variance Value [PVV]=82%, p=0.0024) and a further decrease of ≥0.57 of achieving CRR at the next visit.

Conclusion: RAIL-scores are significantly lower with CRR-status in LN and decreases of 1.0 between visits >0.57 or larger may predict future CRR achievement.

Disclosure: G. Pons-Estel: AstraZeneca, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen, 1, 6; **R. Quintana**: None; **R. Nieto**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **M. Scolnik**: AstraZeneca, 2, 5, 6, GSK, 1, 5, 6, Janssen, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6; **C. Funes Soaje**: None; **P. Alba**: None; **V. Saurit**: None; **M. Garcia**: None; **G. BERBOTTO**: None; **I. Bellomio**: None; **M. Kerzberg**: None; **G. Gomez**: None; **C. Pisoni**: None; **V. Juarez**: None; **A. Malvar**: Bristol-Myers Squibb(BMS), 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Kezar, 2, Novartis, 2, Pfizer, 2; **N. Silva**: None; **O. MONTICIELO**: None; **H. Mariz**: None; **F. Ribeiro**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Torres dos Reis-Neto**: None; **I. Guerra Herrera**: None; **M. Massardo**: None; **G. Aroca-Martínez**: None; **L. Gómez Escorcia**: None; **C. Casas**: None; **G. Quintana-Lopez**: None; **C. Toro-Gutierrez**: None; **M. Moreno Alvarez**: None; **M. SAAVEDRA**: None; **M. Portela Hernández**: None; **H. Fragoso-Loyo**: None; **L. Silveira**: None; **I. García-De la Torre**: None; **C. Abud-Mendoza**: None; **J. Esquivel Valerio**: None; **M. Acosta**: None; **A. Paats**: None; **C. Mora-Trujillo**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **A. Calvo**: None; **R. Muñoz-Louis**: None; **M. Rebella**: None; **A. Danza**: None; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **U. Sbarigia**: Johnson and Johnson, 11; **B. Pons-Estel**: AstraZeneca, 5, 6, GlaxoSmithKlein(GSK), 5, 6, Janssen, 5, 6, Novartis, 6, Roche, 5.

Abstract Number: 1531

Achieving Remission and Low Disease Activity with Belimumab versus Placebo in Patients with SLE Excluding the Glucocorticoid Component from Target Definitions: A Post Hoc Analysis of Five Phase 3 Trials

Ioannis Parodis[1], Julius Lindblom[2], Roger A. Levy[3], Alexander Tsoi[1], Margherita Zen[4], Dionysis Nikolopoulos[5], Munther Khamashta[6], Ryan Tomlinson[7], Anca Askanase[8], Ronald van Vollenhoven[9] and Mandana Nikpour[10], [1]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [2]Karolinska Institutet, Stockholm, Sweden, [3]GSK, Specialty Care, Global Medical Affairs, Collegeville, PA,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[4]University of Padua, Department of Medicine, Division of Rheumatology, Padua, Italy, [5]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [6]GSK, Medical Affairs, Dubai, United Arab Emirates, [7]GSK, Development – R&D, Collegeville, PA, [8]Columbia University Medical Center, New York, NY, [9]Amsterdam Rheumatology and Immunology Center, Amsterdam University Medical Centers, Department of Rheumatology, Amsterdam, Netherlands, [10]University of Sydney School of Public Health and Department of Rheumatology, Royal Prince Alfred Hospital, Sydney, Victoria, Australia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: An integrated post hoc analysis of five Phase 3 trials in adults with SLE showed greater benefit of belimumab (BEL) than placebo (PBO), plus standard therapy (ST), in attaining Definition of Remission In SLE (DORIS) and Lupus Low Disease Activity State (LLDAS).[1] As these trials were conducted before glucocorticoid (GC) tapering recommendations were introduced,[2] tapering was not mandated, resulting in prolonged GC courses in a large proportion of patients (pts), impacting attainability of DORIS and LLDAS.[1] Assessed here was attainment of DORIS and LLDAS in these trials using definitions excluding the GC requirement (non-GC-DORIS and non-GC-LLDAS).

Methods: This post hoc analysis pooled data for adults with active SLE from five trials (BLISS-76 [GSK Study 110751; NCT00410384], BLISS-52 [110752; NCT00424476], North East Asia [113750; NCT01345253], BLISS-SC [112341; NCT01484496], EMBRACE [115471; NCT01632241]) receiving BEL (10 mg/kg/month IV or 200 mg/week [wk] subcutaneous) or PBO, plus ST. Non-GC-DORIS and non-GC-LLDAS (defined in Figure 1) attainment rates were calculated and compared between BEL and PBO using modified Poisson regression adjusted for trial variance in all pts and

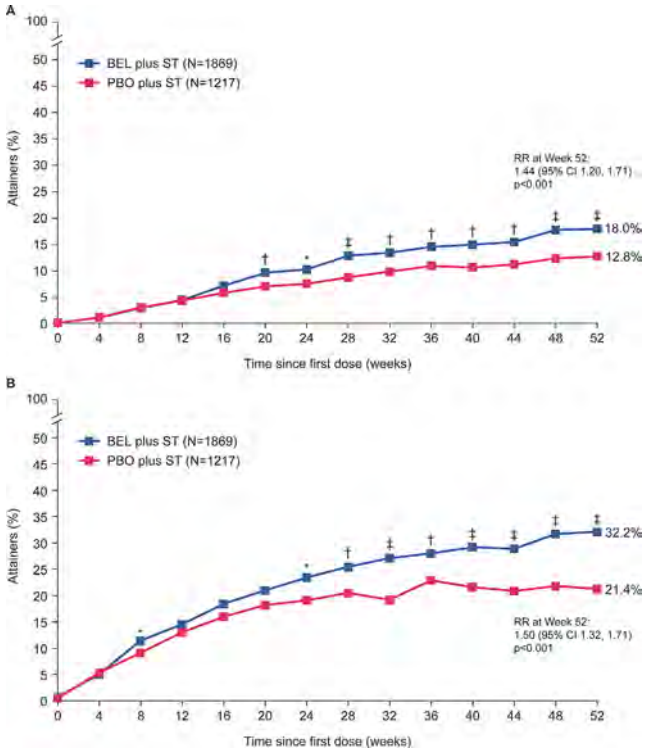


Figure 1. Attainment of (A) non-GC-DORIS and (B) non-GC-LLDAS up to Wk 52 in the overall population. *p<0.05; †p<0.01; ‡p<0.001. Non-GC-DORIS: clinical SLEDAI=0 (irrespective of serological activity), PGA <0.5. Non-GC-LLDAS: SLEDAI-2K ≤4 with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever), no hemolytic anemia or gastrointestinal activity, and no new features of SLE disease activity (using SLEDAI-2K) compared with the previous assessment, PGA ≤1. PGA, Physician's Global assessment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

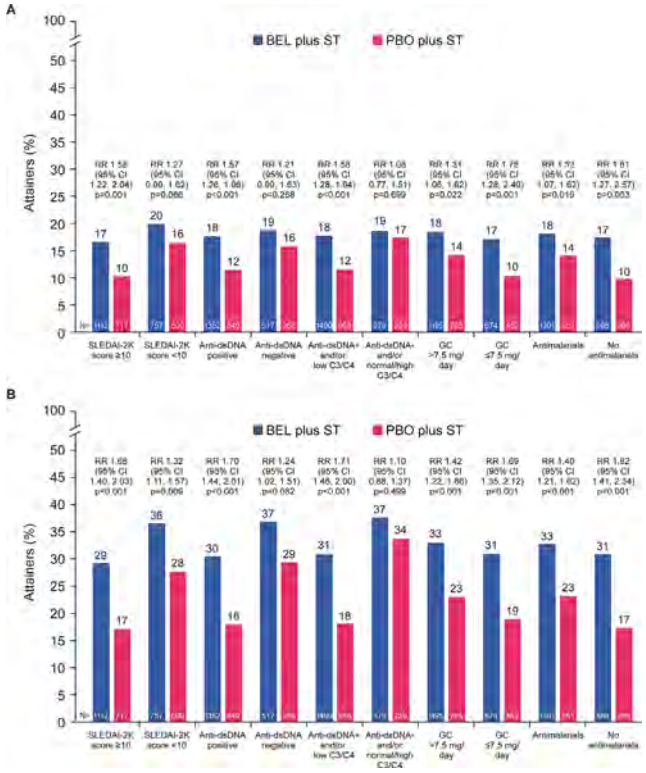


Figure 2. Attainment of (A) non-GC-DORIS and (B) non-GC-LLDAS at Wk 52 in pt subgroups defined by baseline characteristics. C, complement component.

subgroups based on baseline/pt characteristics (SLEDAI-2K score, anti-dsDNA positivity, complement levels, GC dose, antimalarial use, race).

Results: Included were 1869 BEL and 1217 PBO pts. At Wk 52, non-GC-DORIS and non-GC-LLDAS attainment rates were higher with BEL versus PBO (**Figure 1**). Significance maintained to Wk 52 was reached by Wk 20 for non-GC-DORIS and Wk 24 for non-GC-LLDAS. At Wk 52, significantly greater proportions of BEL versus PBO pts were in non-GC-DORIS and non-GC-LLDAS across most subgroups (**Figure 2**); for baseline SLEDAI-2K score ≥10, maintained from as early as Wk 16 (non-GC-DORIS remission: risk ratio, RR [95% CI]: 1.95 [1.20, 3.16], p=0.009; non-GC-LLDAS: 1.54 [1.17, 2.02], p=0.003).

At Wk 52, non-GC-DORIS and non-GC-LLDAS attainment rates were higher with BEL versus PBO for Asian (BEL n=698, PBO n=405; non-GC-DORIS: RR [95% CI]: 1.60 [1.13, 2.27], p=0.013; non-GC-LLDAS: 1.59 [1.25, 2.02], p=0.001) and White pts (n=596, n=436; 1.66 [1.23, 2.25], p=0.002; 1.76 [1.42, 2.19], p< 0.001); numerical differences were seen for pts of Black African ancestry (n=403, n=229; 1.13 [0.76, 1.69], p=0.577; 1.14 [0.86, 1.51]; p=0.438) and Indigenous American pts (n=172, n=147; 1.17 [0.80, 1.71], p=0.496; 1.35 [1.00, 1.82], p=0.117).

Conclusion: When analyzing data from past trials, it is key to consider context, timing, and effects of confounding factors. GC taper was not mandated in the BEL trial protocols and was not part of the assessment of BEL benefit. In this analysis, BEL was associated with higher attainment of both DORIS and LLDAS versus PBO in all pts and most subgroups. Attainment rates were ~2-fold higher than reported with full DORIS and LLDAS definitions.[1] This analysis corroborates benefits of BEL over PBO, plus ST, in inducing remission and low disease activity in pts with SLE.

Funding: GSK; Parodis research group

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

1 Parodis I et al. *Lancet Rheumatol* 2024;6:E751–61
2 Bertsias G, Yazdany *J. Lancet Rheumatol* 2024;6:E734–5

Original presentation: EULAR 2025

Disclosure: I. Parodis: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5; **J. Lindblom**: None; **R. Levy**: GSK, 3, 8; **A. Tsoi**: None; **M. Zen**: AbbVie, 6, AstraZeneca, 6, GSK, 6, Otsuka, 6; **D. Nikolopoulos**: None; **M. Khamashta**: GSK, 12,, 3; **R. Tomlinson**: GSK, 12,, 3; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **R. van Vollenhoven**: AbbVie, 2, 6, AstraZeneca, 2, Biogen, 2, Biotest, 2, BMS, 2, Galapagos, 2, 6, Gilead, 2, GSK, 6, Janssen, 2, 6, Pfizer, 2, 5, 6, Roche, 5, 6, Sanofi, 2, Servier, 2, UCB, 2, 6, Vielabio, 2; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer Ingelheim, 2, 5, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6.

Abstract Number: 1532

Preliminary Safety, Efficacy, and Cellular Kinetics of CTA313, a CD19/BCMA Dual-Targeted Universal CAR-T Therapy, for Active Systemic Lupus Erythematosus

Hanwei Wang[1], Yue Xie[2], Guojiao Yang[3], Lu Han[3], Jiangtao Ren[4], Yali Zhou[4], Wengang Ge[3], **Jan Davidson-Moncada**[4] and Huan Zhou[5], [1]The Third People's Hospital of Bengbu, Beng bu, China (People's Republic), [2]Bioheng Therapeutics Limited, Nan Jing Shi, China (People's Republic), [3]Bioheng Therapeutics Co., Limited, Nanjing, China (People's Republic), [4]Bioheng Therapeutics Co., Limited, Nan Jing, China (People's Republic), [5]Clinical Research Hospital of the First Affiliated Hospital of Anhui Medical University, Hefei, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: SLE is characterized by B cell activation, autoantibody production and autoreactivity. Recently, CAR-T therapy has emerged as a promising strategy to deplete autoreactive B cells and induce sustained remission. CTA313 is a CD19/BCMA dual-targeted "off-the-shelf" universal CAR-T product with T cell receptor and human leukocyte antigen class knockout, as well as ANSWER^{TM} inhibitory molecule overexpression to resist host immune rejection - leading

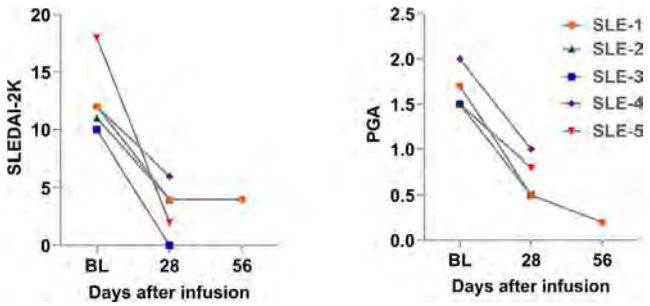


Figure 1. SLEDAI-2K score and PGA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

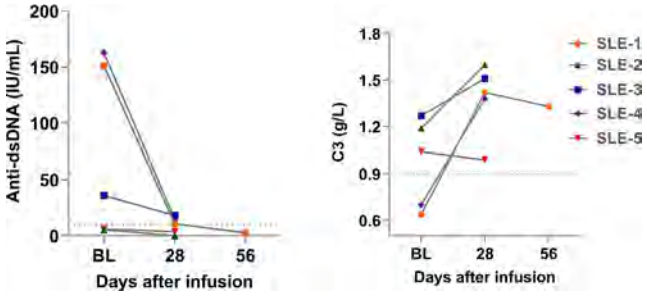


Figure 2. Anti-dsDNA antibodies and complement C3

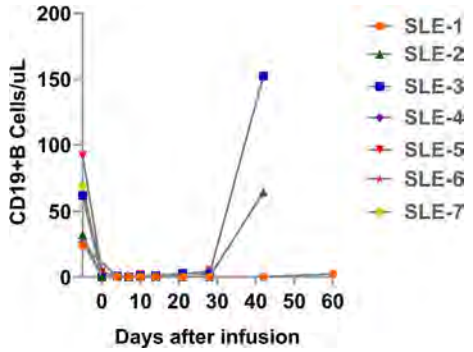


Figure 3. B cells

to increased expansion and persistence in the context of standard dose lymphodepletion. The study aims to evaluate the safety, efficacy and cellular kinetics of CTA313 in patients with active SLE.

Methods: Patients received a single administration of CTA313 treatment at 2 dose levels (DLs): DL1 as 3×10^6 CAR+ T cells/kg, DL2 as 6×10^6 CAR+ T cells/kg following lymphodepletion with cyclophosphamide (300 mg/m^2, day -5 to -3) and fludarabine (30 mg/m^2, day -5 to -3). Cellular kinetics are measured by quantitative PCR and flow cytometry; pharmacodynamics assessments include quantification of B cells, complement (C3/C4), and autoantibodies. Clinical activity assessments include disease activity scores (SLEDAI-2K), Physician's Global Assessment (PGA) and renal outcome measures.

Results: As of April 30, 2025, seven patients with active SLE received CTA313 at two doses, DL1 (n=3), DL2 (n=4). Six (86%) patients were female, median age 43 (22-50) years, median disease duration 6 (1.3-13.0) years, and 2 patients had lupus nephritis. All patients had been previously treated with steroids and immunosuppressive drugs, including hydroxychloroquine (n=7), tacrolimus (n=7), mycophenolate mofetil (n=4), cyclosporine A (n=2), thalidomide (n=2), and methotrexate (n=1), and one patient received belimumab.

To date, treatment has been well tolerated with only Grade 1 cytokine release syndrome (CRS) observed in four of seven patients; no neurotoxicity, GvHD or infections were reported. Hypogammaglobulinemia, which did not require intravenous immunoglobulin treatment, was a common adverse event.

With 5 patients reaching initial disease assessment, preliminary efficacy indicated reductions in SLEDAI-2K and PGA. All 5 patients achieved SRI-4 response, and 4 of 5 patients achieved Lupus Low Disease Activity State (LLDAS). Importantly, three patients discontinued all immunosuppressive agents, including glucocorticoids, achieving drug-free remission. Autoantibodies levels declined, accompanied with increasing level of C3. Meanwhile, 24-hour proteinuria significantly decreased in 2 patients with lupus nephritis. PK analysis revealed median peak expansion (C_{max}) of 286,265 copies/ug DNA by qPCR at Day 7-10. Complete B cell depletion was observed by Day 4-7 post-infusion. To date, B cell recovery was observed in 3 patients, with median B cell aplasia of 42 days. In patients who achieved anti-dsDNA antibody eradication, the antibody remained undetectable despite B cell reconstitution.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Preliminary data from this trial suggest favorable safety, CAR T cell expansion, B cell depletion and promising clinical activity of CTA313 in active SLE. Ongoing follow up and dose escalation in additional patients will provide insights into long term safety and efficacy.

Disclosure: H. Wang: None; **Y. Xie**: None; **G. Yang**: None; **L. Han**: None; **J. Ren**: None; **Y. Zhou**: None; **W. Ge**: None; **J. Davidson-Moncada**: None; **H. Zhou**: None.

Abstract Number: 1533

Belimumab Is Associated with Early Improvement in Disease Activity Measures Among Patients with Systemic Lupus Erythematosus in the US

Yan Chen[1], Maral DerSarkissian[1], Shumin Rui[1], Justin Clark[1], Daniel Moldaver[2], **Jeffrey J. Ellis**[3], Karen Worley[3] and Aarat M Patel[4], [1]Analysis Group, Los Angeles, CA, [2]GSK, Global Real-World Evidence & Health Outcomes Research, Toronto, ON, Canada, [3]GSK, Global Real-World Evidence & Health Outcomes Research, Collegeville, PA, [4]GSK, US Medical Affairs, Durham, NC

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Belimumab (BEL), a B-cell modulator mAb that selectively inhibits soluble B-lymphocyte stimulator and reduces autoreactive B cells that drive lupus disease activity, is approved for SLE and LN in adults and children.[1] While early response to BEL has been demonstrated to occur within weeks for several key clinical endpoints,[2] robust real-world evidence is limited regarding the characteristics of patients who experience early improvement in SLE disease activity measures (DAM). To address this knowledge gap, we identified key predictors of early improvement in SLE DAM among patients with SLE in the US.

Methods: This retrospective, longitudinal cohort study (GSK Study 222157) used electronic health record data from the Specialty Networks rheumatology practice database. Eligible patients were aged ≥18 years, diagnosed with SLE, initiated either subcutaneous or intravenous BEL (9/1/2011–12/25/2024; defined index), and had ≥12 months of pre-index (defined the baseline period) and ≥2 months of post-index clinical activity. For the analysis of each SLE DAM, patients had ≥1 record of disease activity with a nonzero value in baseline and ≥1 record of the same DAM within 2 months post-index. Early improvement in each DAM was evaluated within 2 months post-index and defined as presence of ≥1 observation that was less than the mean baseline score (at the patient level) minus its minimal important difference (0.5×standard deviation of baseline DAM) or value of 0. Predictors of early improvement for patient pain index (PPI), Health Assessment Questionnaire Disability Index (HAQ-DI), swollen joint count (SJC), and tender joint count (TJC) were assessed separately and in ≥1 of these measures on aggregate using a least absolute shrinkage and selection operator (LASSO) regression model. Predictors assessed at baseline included age, sex, race, year of index, baseline DAM, SLE disease severity, organ damage, Quan-Charlson Comorbidity Index (QCCI), and comorbidities.

Results: Overall, 684 patients were included, 54.7% (n=374) of whom experienced early (within 2 months) improvement in ≥1 DAM on aggregate. Early improvement in PPI, HAQ-DI, SJC, and TJC was experienced by 41.2%, 32.5%, 48.7%, and 38.8% of patients, respectively (**Table 1**). Demographics and clinical characteristics of patients with improvement in ≥1 DAM versus those without improvement are summarized in **Table 2**. LASSO identified male sex (vs female) (odds ratio [OR; 95% confidence interval (CI)]: 2.25 [1.03, 5.29]), minority race (vs White) (OR [95% CI]: 1.77 [1.21, 2.60]), and baseline

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. SLE disease activity measures during the 12-month baseline period and 2 months post-BEL initiation. *For all four SLE disease activity measures, higher values indicate greater disease activity; †for patients with multiple measurements of the same SLE disease activity during the baseline period, the mean value was used to represent the patient's baseline level; ‡for patients with multiple SLE activity measurements 2 months post-BEL initiation, the mean value was used. IQR, interquartile range; SD, standard deviation.

	PPI (scale* 0–10)	HAQ-DI (scale* 0–10)	SJC (scale* 0–28)	TJC (scale* 0–28)
	n=616	n=280	n=154	n=214
Baseline†				
Mean (SD)	5.2 (2.3)	2.7 (1.8)	3.6 (3.5)	6.2 (5.7)
Median (IQR)	5.3 (3.5, 7.0)	2.9 (1.8, 4.3)	4.4 (2.7, 7.0)	7.0 (5.0, 12.0)
MID	1.1	0.9	1.8	2.9
2 months post-BEL initiation‡				
Mean (SD)	5.0 (2.7)	2.6 (1.9)	3.7 (4.7)	6.7 (7.0)
Median (IQR)	5.0 (3.0, 7.0)	2.3 (1.0, 4.0)	2.0 (0.0, 5.5)	4.0 (1.0, 10.5)
Early improvement				
n (%)	254 (41.2)	91 (32.5)	75 (48.7)	83 (38.8)
Mean (SD)	3.3 (2.5)	1.9 (1.9)	1.0 (2.1)	2.4 (3.8)
Median (IQR)	3.0 (1.0, 5.0)	1.5 (0.2, 3.0)	0.0 (0.0, 1.0)	0.7 (0.0, 3.0)

Table 2. Patient demographics and clinical characteristics by SLE disease activity improvements during the 12-month baseline period. *SLE disease severity was identified using a previously published algorithm based on validated measures of SLE activity and the consensus of expert clinical opinion; †organ damage was identified by ≥3 outpatient diagnoses (within the same organ system) for any of the medical conditions associated with organ damage.

Characteristics	Early improvement in ≥1 SLE disease activity measure on aggregate	
	Yes (n=374)	No (n=310)
Demographic characteristics		
Age at index, years		
Mean (SD)	49.4 (14.2)	50.3 (14.1)
Median (IQR)	49.0 (39.0, 60.0)	49.0 (39.0, 61.0)
Female sex, n (%)	352 (94.1)	301 (97.1)
Race, n (%)		
American Indian/Alaskan Native	0 (0.0)	1 (0.3)
Asian	4 (1.1)	2 (0.6)
Black/African American	78 (20.9)	40 (12.9)
Native Hawaiian/Other Pacific Islander	1 (0.3)	0 (0.0)
White	205 (54.8)	216 (69.7)
Multiple Race	2 (0.5)	1 (0.3)
Unknown	84 (22.5)	50 (16.1)
Clinical characteristics		
SLE disease severity*, n (%)		
Mild	102 (27.3)	112 (36.1)
Moderate	256 (68.4)	183 (59.0)
Severe	16 (4.3)	15 (4.8)
Any organ damage†, n (%)	43 (11.5)	39 (12.6)
Quan-Charlson Comorbidity Index, mean (SD)	1.1 (0.9)	1.2 (1.1)

Table 3. LASSO-selected predictors of early improvement in SLE disease activity measures*. *ORs and 95% CIs were estimated from a logistic regression model using only covariates selected by the LASSO procedure. The tuning parameter that results in the lowest misclassification error was chosen for the LASSO procedure; †"minority" includes American Indian/Alaskan Native, Asian, Black/African American, Native Hawaiian/Other Pacific Islander, and individuals identifying as multiple races.

Variable	OR (95% CI) Early improvement in ≥1 SLE disease activity measure on aggregate N=684
Demographic characteristics	
Sex	
Male vs female	2.25 (1.03, 5.29)
Race	
Minority† vs White	1.77 (1.21, 2.60)
Unknown vs White	2.29 (1.46, 3.65)
Clinical characteristics	
SLE disease severity	
Moderate or severe vs mild	1.50 (1.08, 2.10)
Comorbidities of interest	
Reynaud's phenomenon	1.74 (1.06, 2.91)
Hypertension	0.51 (0.32, 0.82)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

moderate/severe SLE (vs mild) (OR [95% CI]: 1.50 [1.08, 2.10]) as predictors of early improvement in ≥1 SLE DAM on aggregate (**Table 3**).

Conclusion: Greater than half of patients with SLE initiating BEL experienced early (within 2 months) improvement in burdensome dimensions of disease activity (e.g. pain and joint involvement), demonstrating the rapid therapeutic effect of BEL. Moderate/severe SLE and non-White race were predictive of early improvement, suggesting a potentially greater treatment benefit of BEL in these subgroups.

Funding: GSK

References

1 GSK. Benlysta US prescribing information. 2024
2 Fanouriakis A et al. *Lupus Sci Med* 2019;8;6(1):e000310

Disclosure: Y. Chen: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **M. DerSarkissian**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **S. Rui**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **J. Clark**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **D. Moldaver**: GSK, 3, 8; **J. Ellis**: GSK, 12,, 3, 8; **K. Worley**: GSK, 12,, 3; **A. Patel**: GSK, 12,, 3, University of Virginia, 3, 12, Volunteer Faculty at the University of Virginia, Virginia Society of Rheumatology and The Paediatric Society of the African League Against Rheumatism, 4.

Abstract Number: 1534

Rapid Oral Glucocorticoid Discontinuation or Dose Reduction Among US Patients with SLE Receiving Belimumab in a Real-World Setting

Yan Chen[1], Maral DerSarkissian[1], Shumin Rui[1], Justin Clark[1], Daniel Moldaver[2], **Jeffrey J. Ellis**[3], Karen Worley[3] and Aarat M Patel[4], [1]Analysis Group, Los Angeles, CA, [2]GSK, Global Real-World Evidence & Health Outcomes Research, Toronto, ON, Canada, [3]GSK, Global Real-World Evidence & Health Outcomes Research, Collegeville, PA, [4]GSK, US Medical Affairs, Durham, NC

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Belimumab (BEL), a B-cell modulator mAb that selectively inhibits soluble B-lymphocyte stimulator and reduces autoreactive B cells that drive lupus disease activity, is approved for SLE and LN in adults and children.[1] Prolonged oral glucocorticoid (OGC) use can lead to organ damage, and OGC reduction is an important treatment goal in SLE. BEL has been shown to reduce OGC use in the real world; however, limited evidence exists regarding the characteristics of patients who are able to reduce OGC use with BEL. We studied OGC reduction or discontinuation within 6 months of BEL initiation in patients with SLE in US clinical practice and aimed to identify patient characteristics that may support prediction of early OGC dose reduction or discontinuation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient baseline demographics and clinical characteristics by early OGC dose reduction by ≥50% or discontinuation*. *≥50% OGC dose reduction was defined as ≥50% decrease in the average daily dose of OGC from baseline, and discontinuation of OGC was defined for a patient who was expected to be using an OGC as of the index date and did not have another OGC prescription for >120 days after the end of the days' supply of the previous OGC prescription; †within 57 days post-index; ‡this group includes patients who reached OGC dose reduction by ≥50% or discontinuation more than 57 days post-index and patients who did not reach this outcome. IQR, interquartile range; SD, standard deviation.

Characteristics	Early† OGC dose reduction by ≥50% or discontinuation	
	Yes (n=136)	No‡ (n=405)
Age at index, years		
Mean (SD)	50.3 (14.1)	48.3 (13.2)
Median (IQR)	51.0 (39.0, 59.0)	48.0 (39.0, 57.0)
Female sex, n (%)	126 (93)	382 (94)
Race, n (%)		
American Indian/Alaskan Native	1 (0.7)	2 (0.5)
Asian	1 (0.7)	4 (1.0)
Black/African American	32 (23.5)	90 (22.2)
White	76 (55.9)	241 (59.5)
Multiple Race	1 (0.7)	2 (0.5)
Unknown	25 (18.4)	66 (16.3)
SLE disease severity, n (%)		
Mild	30 (22.1)	125 (30.9)
Moderate	101 (74.3)	271 (66.9)
Severe	5 (3.7)	9 (2.2)
Any organ damage, n (%)	13 (9.6)	39 (9.6)
Quan-Charlson Comorbidity Index, mean (SD)	1.1 (0.5)	1.0 (0.4)

Table 2. LASSO-selected predictors of early OGC dose reduction or discontinuation*. *ORs and 95% CIs were estimated from a logistic regression model using only covariates selected by the LASSO procedure. The tuning parameter that results in the lowest deviance was chosen for the LASSO procedure; †within 57 days post-index. CI, confidence interval; OR, odds ratio.

Variable	OR (95% CI)
	Early† OGC dose reduction by ≥50% or discontinuation
	N=541
Demographic characteristics	
Age at index, every 5 years	1.07 (0.99, 1.15)
Clinical characteristics	
SLE disease severity	
Moderate or severe vs mild	1.64 (1.04, 2.65)
Comorbidities of interest	
Myositis/myalgia	0.66 (0.41, 1.04)
Rheumatoid arthritis	1.59 (0.98, 2.54)
Hematologic disorders	1.34 (0.84, 2.13)
Hypertension	0.55 (0.24, 1.13)

Methods: This retrospective, longitudinal cohort study (GSK Study 222157) used health record data from the Specialty Networks rheumatology practice database. Eligible patients were aged ≥18 years, diagnosed with SLE, initiated either subcutaneous (SC) or intravenous (IV) BEL (9/1/2011–4/25/2024; defined index), had ≥12 months of pre-index (defined as baseline period) and ≥10 months of post-index clinical activity, ≥1 OGC prescription with dose information (in prednisone-equivalent units), and no OGC discontinuation during baseline. To ensure sufficient exposure, within 3 months of index prescription, SC BEL initiators were required to have ≥1 SC or ≥1 IV BEL record while IV BEL initiators were required to have ≥1 SC or ≥2 IV BEL records. OGC dose reduction by ≥50% or discontinuation (≥120 consecutive days without OGC supply) within 6 months was defined as "early" if it occurred within the first quartile of the time from index to either event calculated across all patients, using a data-driven approach. Predictors of early OGC dose reduction or discontinuation were identified using a least absolute shrinkage and selection operator (LASSO) logistic regression model. Candidate predictors included age, sex, race, year of index, SLE disease severity, organ damage, Quan-Charlson Comorbidity Index, and comorbidities.

Results: Among 541 patients included in the study, approximately half (50.8%, n=275) achieved ≥50% OGC dose reduction or discontinuation within 6 months of initiating BEL. Median time to ≥50% dose reduction or discontinuation was 177 days and 25% (n=136) of patients achieved this outcome in < 2 months (57 days). Patients with early (i.e. within 57 days) OGC reduction or discontinuation were slightly older than those without (50.3 vs 48.3 years), a greater proportion had

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

moderate (74.3% vs 66.9%) or severe (3.7% vs 2.2%) SLE, but the same proportion (9.6%) had evidence of baseline organ damage (**Table 1**). LASSO regression identified moderate/severe SLE at baseline (vs mild) (odds ratio [95% confidence interval]: 1.64 [1.04, 2.65]) as a predictor of early OGC dose reduction or discontinuation (**Table 2**).

Conclusion: Among patients initiating BEL treatment for SLE, half achieved OGC discontinuation or dose reduction by ≥50% within 6 months. This outcome was achieved by 25% of patients within 2 months of BEL initiation, with this earlier benefit more likely in patients who had moderate/severe SLE.

Funding: GSK

Reference

1 GSK. Benlysta US prescribing information. 2024

Disclosure: Y. Chen: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **M. DerSarkissian**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **S. Rui**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **J. Clark**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **D. Moldaver**: GSK, 3, 8; **J. Ellis**: GSK, 12,, 3, 8; **K. Worley**: GSK, 12,, 3; **A. Patel**: GSK, 12,, 3, University of Virginia, 3, 12, Volunteer Faculty at the University of Virginia, Virginia Society of Rheumatology and The Paediatric Society of the African League Against Rheumatism, 4.

Abstract Number: 1535

INB-619 - A Novel Gamma-Delta (γδ) T cell Engager to Target B cells in Autoimmune Diseases

Lei Ding, Yanjie Li, Mariska ter Haak, Sadhak Sengupta, Kate Rochlin and **Lawrence Lamb**, IN8bio, Inc., New York, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: T cell engagers (TCEs) redirect T cells to bind target cells by linking T cells with target-associated antigens expressed on cells responsible for disease pathology. Most TCEs to-date target alpha-beta (αβ) T cells, binding both an antigen such as CD20 on the cell of interest and CD3 on the T cell. This approach is complex, requiring CD3 detuning due to the risks of T cell exhaustion and severe, potentially life-threatening complications such as cytokine release syndrome (CRS). Gamma delta (γδ) T cells offer a promising alternative due to their innate MHC-independent cell killing and low production of CRS-associated cytokines. INB-619, a novel pan-γδ TCE that exhibits specific targeting of CD19+ B cells, including those from SLE patients with active disease. INB-619 induces potent cytotoxicity and drives robust activation and expansion of Vδ1and Vδ2 T cells. These unique properties potentially solve the challenge of current B cell depleting TCE's, where dysfunctional immune cells, tissue-resident B cells and potential toxicities may limit the depth of B cell depletion. These findings position INB-619 as a promising therapeutic candidate for autoimmune indications.

Methods: INB-619 binding and activation specificity were confirmed by co-incubation of a 1:1 ratio of NALM-6 ALL (CD19+) or CD19- cell lines with expanded γδ T cells at increasing concentrations of INB-619. PBMC from healthy donors (n=2) and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

from subjects with active SLE (n=3) were exposed at DAY 0 to 5nM of INB-619 and assessed over 10 days for lymphocyte phenotype, expression of cell surface activation/ degranulation markers, and secreted cytokines (N = 3).

Results: INB-619 bound specifically to CD19+ NALM-6 and to γδ T cells and induced specific and dose-dependent γδ T cell cytotoxicity and upregulation of CD107a, PD-1, and CD69 at EC50 values from 26 to 51 pM but showed no specific activity against a CD19- cell line. Complete depletion of B cells from healthy and SLE donor PBMC were shown over a 10-day incubation period. In all cases, γδ T cells showed robust expansion of both CD27+CD45RA+ and CD27+/-CD45RA- populations reflecting the Vδ1 and Vδ2 populations, respectively. INB-619-expanded PBMC also exhibited a favorable cytokine release profile, with no detectable or minimal release of cytokines associated with CRS such as IL-4, IL-6, IL-10, and IL-17α. Concentrations of IgG1 and IgM in the coculture supernatants of all three SLE donors significantly decreased in TCE treatment groups concurrent with B cell depletion, with a correlation between the level of B cell depletion and γδ T expansion.

Conclusion: INB-619 is a novel CD19-targeting γδ TCE that expands both major γδ T cell subtypes sufficiently to eliminate a large population of B cells in vitro. The combined expansion and activation of tissue-resident Vδ1 and circulating Vδ2 populations, with the favorable cytokine pattern evidenced here, suggests that INB-619 could provide deep B cell depletion with a clinically relevant improvement in safety over current methods.

Disclosure: L. Ding: IN8bio, Inc., 3; **Y. Li**: IN8bio, Inc., 3; **M. ter Haak**: IN8bio, Inc., 3; **S. Sengupta**: IN8bio, Inc., 3; **K. Rochlin**: IN8bio, Inc., 4; **L. Lamb**: IN8bio, Inc., 4.

Abstract Number: 1536

Evaluating Systemic Lupus Erythematosus Remission Among Patients Initiating Belimumab in a Real-World Setting in the USA

Aarat M Patel[1], Renee L. Gennarelli[2], Temitope Bello[2], Ali Bonakdar[2] and Karen Worley[3], [1]GSK, US Medical Affairs, Durham, NC, [2]Cencora, Real-World Evidence, Conshohocken, PA, [3]GSK, Global Real-World Evidence & Health Outcomes Research, Collegeville, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The Definition Of Remission In SLE (DORIS) criteria were developed to provide alignment on defining remission in patients with SLE.[1,2] Belimumab (BEL) treatment increases the proportion of patients with SLE in DORIS remission.[3] Several real-world studies have evaluated DORIS remission in BEL-treated patients with SLE[4,5,6]; however, data are limited for patients in the USA.

Methods: This retrospective, observational cohort study (GSK Study 222161) assessed remission among adult patients with SLE receiving BEL in a real-world setting in the USA using the OM1 PremiOM SLE dataset (OM1, Inc, Boston, MA, USA). Study period: Jan 1, 2013, to May 31, 2024. Eligible patients had ≥1 BEL pharmacy/medical encounter during the identification period (Jan 1, 2014, [index: first BEL receipt during identification period] to Oct 31, 2023). Primary objective: determine the proportion of patients achieving SLE remission (DORIS definition by proxy: SLEDAI score=0 [no disease activity]; Physician's Global Assessment [PGA] < 2; prednisone equivalent dose ≤5 mg/day) at 28, 48, and 52 weeks (wks) post–BEL initiation. Secondary objectives included: describe SLEDAI scores and PGA before BEL and 28, 48, and 52 wks post–

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographics and clinical characteristics.* *The baseline period was defined as the period that begins 12 months prior to the index date up to and excluding the index date. CCI, Charlson Comorbidity Index; SD, standard deviation.

	Patients meeting inclusion criteria (N=398)
Age (years), mean (SD)	51 (14)
Female, n (%)	375 (94.2)
Race, n (%)	
White	283 (71.1)
Black or African American	66 (16.6)
Other	24 (6.0)
Asian	5 (1.3)
Multiracial	3 (0.8)
American Indian or Alaska Native	0
Native Hawaiian or Other Pacific Islander	0
Missing/unknown	17 (4.3)
Insurance payor type, n (%)	
Commercial	262 (65.8)
Medicare	105 (26.4)
Medicaid	26 (6.5)
Missing/unknown	5 (1.3)
Geographic region, n (%)	
South	344 (86.4)
Midwest	24 (6.0)
Northeast	18 (4.5)
West	12 (3.0)
CCI score, mean (SD)	1.7 (1.3)
Affected organ systems, n (%)	
Neuropsychiatric	61 (15.3)
Cardiovascular	48 (12.1)
Diabetes	44 (11.1)
Ocular	33 (8.3)
Musculoskeletal	30 (7.5)
Renal	15 (3.8)
Malignancy (excluding dysplasia)	14 (3.5)
Gastrointestinal	6 (1.5)

BEL initiation. Two censoring approaches assessed estimate robustness (last available score: earlier of (1) latest available SLEDAI or PGA score in follow-up period and (2) end of follow-up; end of follow-up: earlier of 52 wks post-index, last activity date, or date of data cutoff). Analyses were descriptive.

Table 2. Proportion of patients achieving real-world SLE remission (per DORIS proxy), no disease activity (per SLEDAI), and PGA-based threshold for remission. *The two censoring approaches were utilized to assess the robustness of estimates: the last available score which was the earlier of latest available PGA or SLEDAI score in the follow-up period (not carried forward) and end of follow-up, and the end of follow-up which was the earlier of 52 weeks post-index, last activity date or date of data cutoff; †the proportion of patients achieving SLE remission (per DORIS proxy) at 28, 48, and 52 weeks after initiating therapy with belimumab defined as SLEDAI score=0, PGA score <2, and prednisone-equivalent dose ≤5 mg/day; ‡the proportion of patients with no disease activity (per SLEDAI; SLEDAI=0); §the proportion of patients with at least one PGA score meeting the predefined threshold for remission (<2). CI, confidence interval.

	Point estimate (95% CI)		
Censoring approach*	**28 weeks**	**48 weeks**	**52 weeks**
Proportion of patients achieving real-world SLE remission (per DORIS proxy)†			
Last available score censoring approach	7.7% (4.7, 10.7)	25.9% (18.8, 32.4)	28.3% (19.8, 35.9)
End of follow-up censoring approach	5.0% (2.9, 7.1)	13.0% (9.5, 16.3)	13.8% (10.3, 17.2)
Proportion of patients achieving no disease activity (per SLEDAI)‡			
Last available score censoring approach	21.3% (16.8, 25.6)	40.7% (33.3, 47.3)	45.8% (36.6, 53.7)
End of follow-up censoring approach	18.6% (14.7, 22.3)	28.1% (23.5, 32.4)	29.5% (24.8, 33.9)
Proportion of patients achieving PGA-based remission threshold§			
Last available score censoring approach	45.9% (40.4, 51.0)	60.6% (54.2, 66.1)	68.5% (58.2, 76.3)
End of follow-up censoring approach	43.7% (38.6, 48.4)	54.6% (49.4, 59.3)	56.3% (51.1, 60.9)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Overall, 398 patients were included (Table 1). Estimates were sensitive to censoring approach (Table 2). By last available score, point estimates for the proportion of patients achieving SLE remission (per DORIS proxy) increased from 7.7% at 28 wks to 25.9% at 48 wks and 28.3% at 52 wks post–BEL initiation. The proportion of patients achieving no disease activity (SLEDAI=0) within 28 wks was 21.3%, increasing to 45.8% within 52 wks post–BEL initiation. The proportion of patients achieving PGA-based remission thresholds increased from 45.9% at 28 wks to 68.5% at 52 wks. By end of follow-up approach, the proportion of patients achieving SLE remission increased from 5.0% at 28 wks to 13.0% at 48 wks and 13.8% at 52 wks post–BEL initiation. Point estimates for the proportion of patients achieving no disease activity were 18.6% within 28 wks post–BEL initiation increasing to 29.5% within 52 wks. The proportion of patients achieving PGA-based remission thresholds was 43.7% at 28 wks and 56.3% at 52 wks.

Conclusion: This study demonstrates the achievement of real-world remission targets for patients with SLE initiating BEL in the USA, with DORIS remission criteria being reached within 28 wks for about 5–8% of patients, and within 52 weeks for 14–28% of patients.

Funding: GSK

References

[1]van Vollenhoven R et al. Ann Rheum Dis 2017;76:554–61
[2]van Vollenhoven RF et al. Lupus Sci Med 2021;8:e000538
[3]Parodis I et al. Lancet Rheumatol 2024;6(11):e751–61
[4]Nikoloudaki M et al. Front Immunol 2023;13:1074044
[5]Su Z et al. Arthritis Res Ther 2024;26:163
[6]Altabás-González I et al. Rheumatology 2025;64:276–82
Original presentation: CCR-East 2025

Disclosure: A. Patel: GSK, 12,, 3, University of Virginia, 3, 12, Volunteer Faculty at the University of Virginia, Virginia Society of Rheumatology and The Paediatric Society of the African League Against Rheumatism, 4; **R. Gennarelli**: Cencora, 3; **T. Bello**: Cencora, 3; **A. Bonakdar**: Cencora, 3; **K. Worley**: GSK, 12,, 3.

Abstract Number: 1537

Local Immune effector Cell-Associated Toxicity Syndrome (LICATS) in CAR T-cell treated patients with Autoimmune Disease

Melanie Hagen[1], Fabian Müller[2], Andreas Wirsching[1], Soraya Kharboutli[3], Silvia Spoerl[3], Christina Duesing[4], Tobias Krickau[5], Markus Metzler[5], Simon Völkl[3], Michael Aigner[3], Sascha Kretschmann[3], Ingrid Vasova[3], Marc Saake[5], Stefan Schliep[5], Torsten Kubacki[6], Nicolas Hunzelmann[6], Laura Bucci[1], Jule Taubmann[7], Christina Bergmann[1], Andrea-Hermina Györfi[8], Sascha Dietrich[9], Jörg Distler[10], Ricardo Grieshaber-Bouyer[11], Andreas Mackensen[12] and Georg Schett[13], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]University Hospital of Erlangen, Erlangen, Germany, [3]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [4]Klinik für Rheumatologie, Dösseldorf, Germany, [5]Friedrich-Alexander-Universität Erlangen-Nürnberg, University Hospital Erlangen, Erlangen, Germany, [6]University and University Hospital Cologne, Cologne, Germany, Cologne, Germany, [7]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [8]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany, [9]Heinrich Heine University Duesseldorf, University Hospital Duesseldorf, Duesseldorf, Germany, [10]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [11]University Hospital Erlangen, Erlangen, Germany, [12]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) and Uniklinikum

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Erlangen, Erlangen, Germany, [13]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: CD19-targeting chimeric antigen receptor (CAR) T-cell therapy has revolutionized treatment strategies for severe B-cell driven autoimmune diseases (AID) like Systemic Lupus erythematosus (SLE), Systemic Sclerosis (SSc) or Idiopathic Inflammatory Myositis (IIM). Cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS) and hematotoxicity are the most common and best described side effects, but little is known about AID-specific adverse events (1,2).

Purpose of our study was to describe a new form of toxicity – Local Immune effector cell-Associated Toxicity Syndrome (LICATS), related to the treatment of patients with autoimmune disease (AID) with CD19-targeting chimeric antigen receptor (CAR) T-cells.

Methods: AID patients receiving CD19-CAR T-cell therapy in Erlangen and Duesseldorf with a follow-up of at least 30 days were assessed for organ-specific LICATS occurring after CAR T-cell infusion. Observed reactions were documented according to localization, time, duration and graded for severity (grade 1: spontaneous resolution; grade 2: glucocorticoid use; grade 3: glucocorticoid use plus prolonged hospital stay; grade 4: intensive care treatment). No systemic events, such as fever, chills, nausea, fatigue, diffuse pain/hypersensitivity or hemodynamic changes were classified as LICATS to

	SLE	IIM	SSc	Total
Patients				
Number of patients, N (%)	20 (51.3)	6 (15.4)	13 (33.3)	39
Female, n (%)	15 (75)	5 (83.3)	5 (38.5)	25 (64-1)
Age, years (median)	34	37,5	37,5	36
Disease duration, years (median)	3	2	2,5	3
Number patients with LICATS, N (%)	16 (80)	4 (66.7)	10 (76.9)	30 (76.9)
Number of LICATS events, N (%)	34 (63)	6 (11.1)	14 (25.9)	54
Day of occurence, days (median)	13	12	20	14
Duration of event, days (median)	7	14	14	11
Severity of events				
Grade 1, N (%)	21 (61.8)	3 (50)	11 (78.6)	35 (64.8)
Grade 2, N (%)	12 (35.3)	2 (33.3)	2 (14.3)	16 (29.6)
Grade 3, N (%)	1 (2.9)	1 (16.7)	1 (7.1)	3 (5.6)
Grade 4, N (%)	0	0	0	0
Organs Involved				
Kidneys; N (%)	11 (91.7)	0	1 (8.3)	12 (22.2)
Skin, N (%)	18 (94.7)	0	1 (5.3)	19 (35.2)
Muscle, N (%)	0	3 (60)	2 (40)	5 (8.8)
Heart, N (%)	0	0	2 (100)	2 (3.5)
Lungs, N (%)	1 (33.3)	1 (33.3)	1 (33.3)	3 (5.3)
Gastrointestinal, N (%)	0	0	3 (100)	3 (5.3)
Joints, N (%)	4 (40)	2 (20)	4 (40)	10 (18.5)

Demographics, Incidence and organ involvement of LICATS.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

separate it from CRS. Furthermore, per definition, LICATS were time-limited events that spontaneously regressed or stopped after a short course of glucocorticoid treatment in order to distinguish it from recurrence of AID.

Results: Between March 2021 and October 2024, 39 patients with AID were treated with CD19-CAR T-cells (20 systemic lupus erythematosus, SLE; 13 systemic sclerosis, SSc; 6 idiopathic inflammatory myositis, IIM). 25 patients (64.1%) were females. Median age was 36 years [22;43.5]. 54 local reactions, which we termed "Local Immune effector Cell-Associated Toxicity Syndrome" (LICATS) were recorded, affecting overall 30 patients (76.9%) with median (IQR) time of onset of 14 [5;21] days and a median duration of 11 [5;14] days. LICATS exclusively occurred during the B-cell aplasia phase and only involved organs previously affected by the respective AID. Most frequent affected organs were the skin (N=19, 35.2%) and the kidneys (N=12, 22.2%). Most LICATS were mild (grade 1: 35, grade 2: 16). Only three LICATS were grade 3. All LICATS resolved without sequelae.

Conclusion: LICATS is a new form of toxicity in CD19-CAR T-cell treated patients with AID, most likely based on the cleansing of immune cells from the affected organs. It is self-limited, organ-specific and usually mild in its intensity.

References:

< !1. Müller F, Taubmann J, Bucci L, et al. CD19 CAR T-Cell Therapy in Autoimmune Disease - A Case Series with Follow-up. *N Engl J Med*. 2024; 390:687-700.

< !2. Isaacs JD. CAR T Cells - A New Horizon for Autoimmunity?. *N Engl J Med*. 2024; 390:758-759.

Disclosure: M. Hagen: None; **F. Müller**: AbbVie/Abbott, 6, ArgoBIO, 2, AstraZeneca, 2, 6, Beigene, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CRISPR Therapeutics, 2, EcoR1, 2, Incyte, 6, Janssen, 2, 6, Kite/Gilead, 2, 5, 6, Merck/MSD, 6, Miltenyi, 2, 6, Novartis, 2, 6, Pfizer, 6, Sobi, 2, 6, Takeda, 6; **A. Wirsching**: None; **S. Kharboutli**: None; **S. Spoerl**: None; **C. Duesing**: None; **T. Krickau**: None; **M. Metzler**: None; **S. Völkl**: None; **M. Aigner**: None; **S. Kretschmann**: None; **I. Vasova**: None; **M. Saake**: None; **S. Schliep**: None; **T. Kubacki**: None; **N. Hunzelmann**: None; **L. Bucci**: None; **J. Taubmann**: None; **C. Bergmann**: Kyverna Therapeutics, Inc., 5; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6; **S. Dietrich**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6; **A. Mackensen**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6.

Abstract Number: 1538

Safety, Pharmacodynamics, and Efficacy of a Novel Plasmacytoid Dendritic Cells Targeting Antibody in Healthy Adults and Patients with SLE or Cutaneous Lupus Erythematosus with Active Skin Lesions: A First-In-Human Study of KK4277

Minoru Hasegawa[1], Jun Kinoshita[2], Shigeki Otsubo[3], Kana Yamada[3], Ehsanollah Esfandiari[4] and the KK4277 Investigators, [1]Division of Medicine, University of Fukui, Yoshida-gun, Fukui, Japan, [2]Kyowa Kirin Co., Ltd., Chiyoda-ku, Tokyo, Japan, [3]Kyowa Kirin Co., Ltd., Tokyo, Japan, [4]Kyowa kirin International plc, London, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

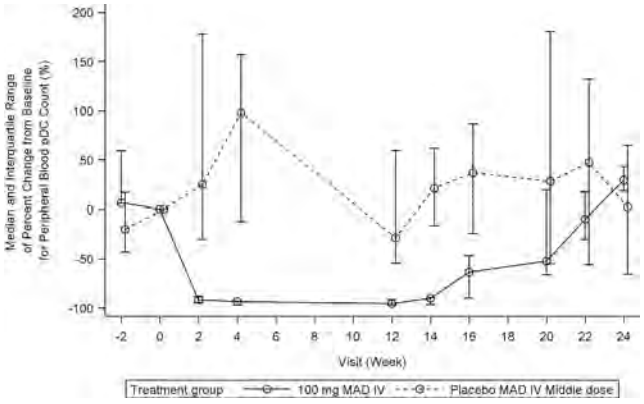


Figure 1: Median and interquartile range of percent change from baseline for peripheral blood pDC count (%) in 100 mg/body IV

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Plasmacytoid dendritic cells (pDCs) are known to be the main source of type 1 interferon (IFN), which is the cause of various autoimmune diseases. The increased accumulation of pDCs in tissues is associated with inflammation and damage in Lupus. KK4277 is a monoclonal antibody targeting pDCs with its unique dual mode of action that directly depletes pDCs by enhanced Antibody-Dependent-Cellular-Cytotoxicity activity and independently inhibits type 1 IFN production from pDCs.

Methods: This was a first-in-human study that consisted of a randomized, placebo-controlled, double-blind, single-dose ascending study in Japanese and non-Asian healthy men (Part 1) and a multicenter, randomized, placebo-controlled, double-blind, multiple-dose ascending study in SLE or Cutaneous Lupus Erythematosus (CLE) Asian patients with active skin lesions (Part 2) (NCT05411016). In Part 1, healthy adult men were enrolled in eight cohorts for intravenous (IV) administration, 0.005 to 150 mg/body and four cohorts for subcutaneous (SC) administration, 100 to 300 mg/body (n=8 for each cohort). In Part 2, SLE or CLE patients who had active skin lesions without any disease severity requirements were enrolled in 5 mg/body cohort. The patients with CLE Disease Area and Severity Index Activity (CLASI-A) score of ≥8 were enrolled in 100 mg/body cohort. Participants received KK4277 or placebo intravenously with their standard of care every 2 weeks for 6 doses, followed by safety observation until Week 24. pDC and myxovirus resistance protein A (MxA) in skin were measured in addition to pDC and type 1 IFN signature in blood. CLASI-A score was assessed by investigators through the study. Another cohort of SC multiple administrations was undergoing at the time of data cut-off, and the data is not included.

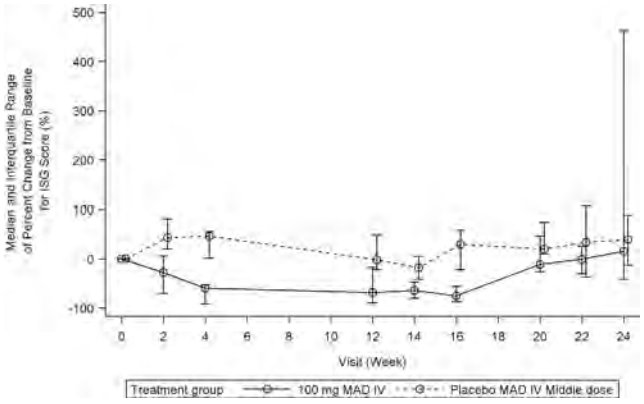


Figure 2: Median and interquartile range of percent change from baseline for Type 1 IFN signature (%) in 100 mg/body IV

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In Part 1, 97 subjects were enrolled. No serious or severe adverse event (AE) occurred. The tolerability of up to 150 mg/body IV and 300 mg/body SC was confirmed. More than a 90% reduction in blood pDCs was observed at 5 mg/body or higher doses, and the duration of the reduction increased in a dose-dependent manner. In part 2, 21 subjects were enrolled and received the study treatment. In 100 mg/body IV (KK4277: 8, Placebo: 4), more than a 90% reduction in blood pDCs was observed in the KK4277 group after the first administration and maintained until Week 14 (Figure 1). The median change in type 1 IFN signature was -69% in the KK4277 group and -2% in the placebo group at Week 12 (Figure 2). Three and two skin samples were provided in the KK4277 and placebo group, respectively, and a great reduction of pDC and MxA was obtained in all KK4277-treated individuals. Whereas the median change of CLASI-A score at Week 12 was not clearly different between the groups (KK4277: -62%, placebo: -56%), numerically huge improvements were observed in several subjects in the KK4277 group, including severe patients. No serious or severe AE was observed. The proportion of AE incidences was similar between the groups (KK4277: 63%, placebo: 75%).

Conclusion: Multiple doses of 100 mg/body IV were tolerable. KK4277 greatly depleted pDC in blood and skin and reduced type I IFN. A proof of pharmacological action was obtained. An additional study is expected for further evaluation in Lupus.

Disclosure: M. Hasegawa: Kyowa Kirin Co.,Ltd., 2, 5, 6, Maruho, 5, 6, Nippon Boehringer Ingelheim Co., Ltd., 5, 6; **J. Kinoshita**: Kyowa kirin, 3; **S. Otsubo**: Kyowa Kirin, 3; **K. Yamada**: Kyowa Kirin, 3; **E. Esfandiari**: Kyowa Kirin, 3.

Abstract Number: 1539

The Impact Of Interferon Signature On Anifrolumab Efficacy And Safety In Systemic Lupus Erythematosus: A Systematic Review And Meta-analysis

Muhammad Usman Hashmi[1], Paramarajan Piranavan[2], Yasmeen Sufi[3], Zaira Nasir[4], Zainab Azhar[5], Shamaem Tariq[5], Hamas Ul Hudaibia[5], IMRAN SAEED[6], Aayet Zulfiqar[5], Natasha Rasool[2], Anum Faiz[7] and RARE (Rahmah Academy of Research Excellence), [1]Rahmah Academy of Research Excellence, Islamabad, Pakistan., Islamabad, Pakistan, [2]University of Kentucky, Louisville, KY, [3]Karachi Medical & Dental College, Karachi, Karachi, Pakistan, [4]Rawalpindi Medical University, Rawalpindi, Pakistan., Islamabad, Pakistan, [5]Rawalpindi Medical University,Rawalpindi, Pakistan., Rawalpindi, Pakistan, [6]Nishtar Medical University,Multan, Pakistan., Multan, Pakistan, [7]Jinnah Hospital Lahore, Pakistan, Lahore, Pakistan

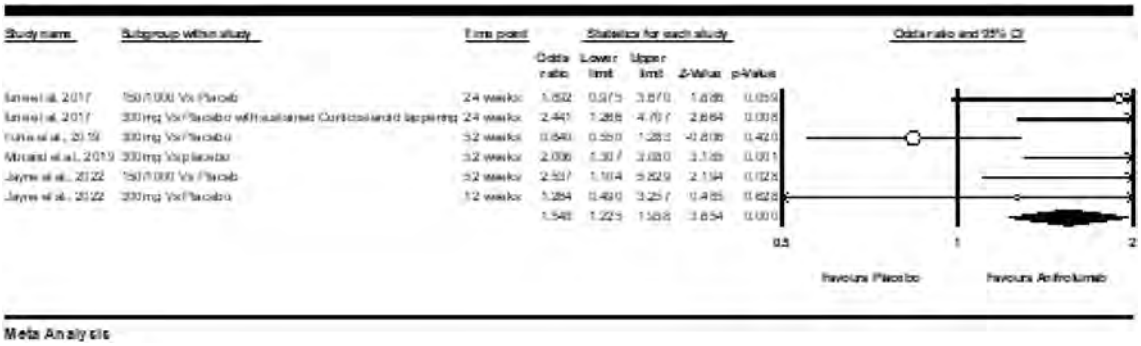
SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

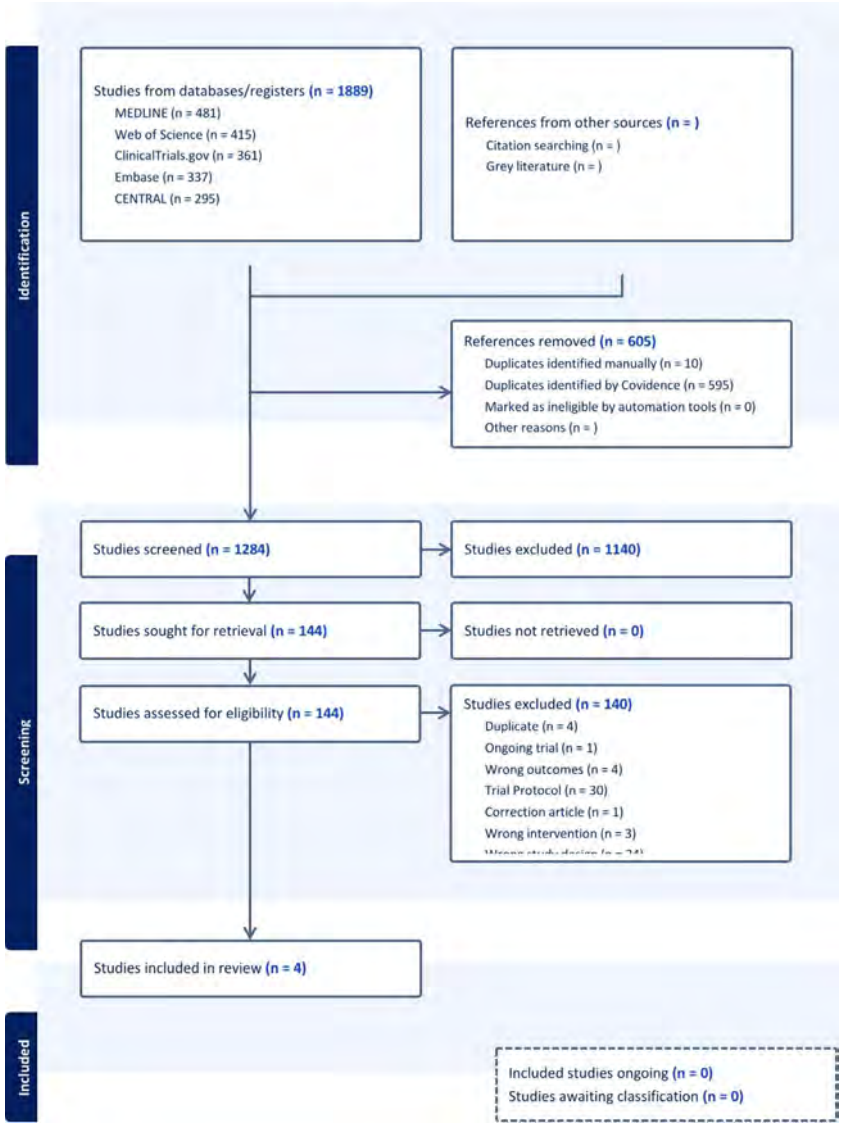
Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

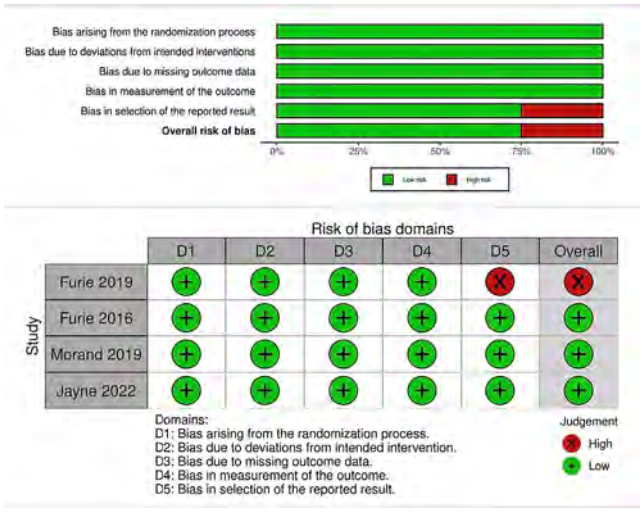


The forest plots showing efficacy of Anifroulomab

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



PRISMA Flow Chart Showing The Details of Included Databases and Studies



PLOTS FOR RISK OF BIAS ASSESSMENT

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Type I interferon (IFN) signaling is central to systemic lupus erythematosus (SLE) pathogenesis, and anifrolumab, a monoclonal antibody targeting the IFN-α receptor (IFNAR), has emerged as a promising therapy. This systematic review evaluates the impact of baseline IFN signature on anifrolumab's efficacy and safety and synthesizes its overall clinical profile in SLE.

Methods: A comprehensive systematic review was conducted in accordance with PRISMA guidelines. We analyzed data from four randomized controlled trials (RCTs, n = 1,271 patients) comparing anifrolumab (150–1,000 mg) to placebo. Primary outcomes included SLE Responder Index-4 (SRI-4), BILAG-Based Composite Lupus Assessment (BICLA), and IFN signature-stratified efficacy/safety. Secondary outcomes assessed pooled efficacy and adverse events. Risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool across five domains. Two reviewers independently evaluated the studies, and discrepancies were resolved by consensus.

Results: Patients with high baseline IFN signatures (measured via 4- or 21-gene assays) demonstrated superior clinical responses. In phase 3 trials, anifrolumab 300 mg achieved significantly higher BICLA response rates versus placebo (47.8% vs. 31.3%, *p* < 0.001), particularly in high IFN subgroups. SRI-4 responses were 36.1% (anifrolumab) vs. 40.2% (placebo) in TULIP-1 (*p* = 0.03), with enhanced efficacy in IFN-high patients. In lupus nephritis, an intensified anifrolumab regimen (900 mg induction) reduced urine protein-creatinine ratio (UPCR) in 84.3% vs. 73.5% placebo. However, IFN-high patients faced elevated infection risks (e.g., herpes zoster: 10/45 vs. 8/49 placebo). Pooled analysis revealed anifrolumab increased SRI-4 likelihood (RR = 1.4, 95% CI: 1.1–1.8) but raised serious infections (13.9% vs. 16.3% placebo). Upper respiratory infections (15–30%) and infusion reactions (10–15%) were common. Most included RCTs showed low risk of bias.

Conclusion: Anifrolumab is efficacious in SLE, with maximal benefit in IFN-high patients, though this subgroup requires vigilant monitoring for infections. These findings underscore the IFN signature's role as a predictive biomarker and highlight the need for personalized risk-benefit assessment in SLE management.

Disclosure: M. Hashmi: None; **P. Piranavan**: None; **Y. Sufi**: None; **Z. Nasir**: None; **Z. Azhar**: None; **S. Tariq**: None; **H. Ul Hudaibia**: None; **I. SAEED**: None; **A. Zulfiqar**: None; **N. Rasool**: None; **A. Faiz**: None.

Abstract Number: 1541

Tofacitinib versus Belimumab in maintenance therapy of Systemic Lupus Erythematosus: A Real-World Study of the CSTAR cohort

Qizhi Yuan[1], Qinli Qin[2], Leyao Ma[1] and Mengtao Li[3], [1]Peking Union Medical College Hospital, Beijing, China (People's Republic), [2]Dongguan Kanghua Hospital, Dongguan, Guangdong, China (People's Republic), [3]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with multi-organ involvements and recurrent relapses. The objectives of treatment include ensuring long-term patient survival, preventing disease relapses and organ damage. Belimumab(BEL) is a humanized monoclonal antibody that targets B-Cell Activating Factor of the TNF Family(BAFF) and has been approved as the first antibody to treat SLE. Tofacitinib(TOFA) functions as an inhibitor of Janus kinase (JAK). Previous study demonstrated the safety and efficacy of TOFA in treating mucocutaneous involvement and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

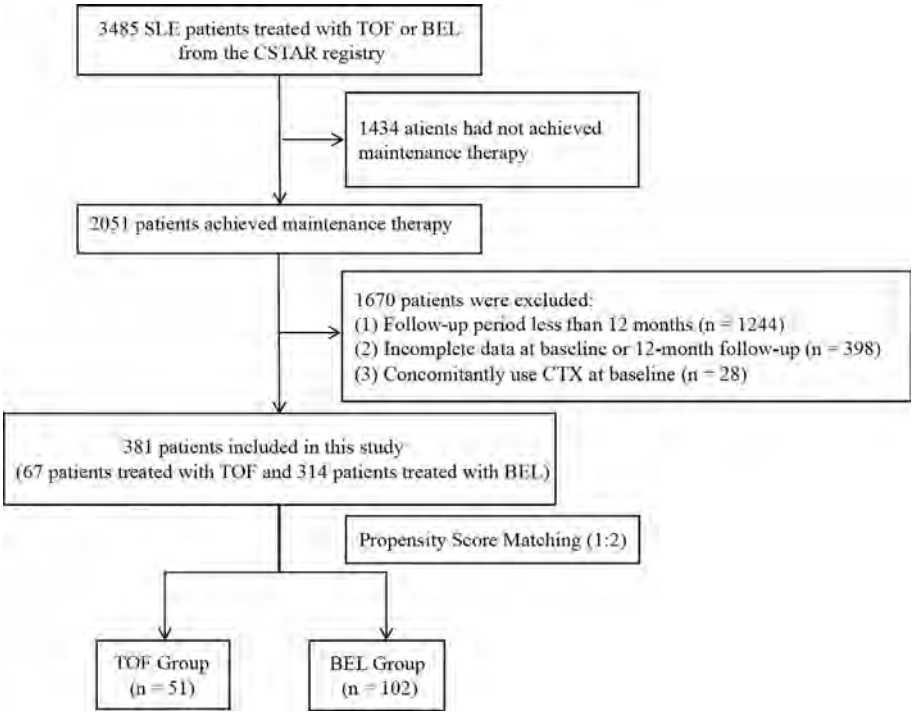


Fig.1. Study flow chart. Abbreviations: BEL, belimumab; CSTAR, the Chinese Systemic Lupus Erythematosus Treatment and Research group; CTX, cyclophosphamide; TOF, tofacitinib.

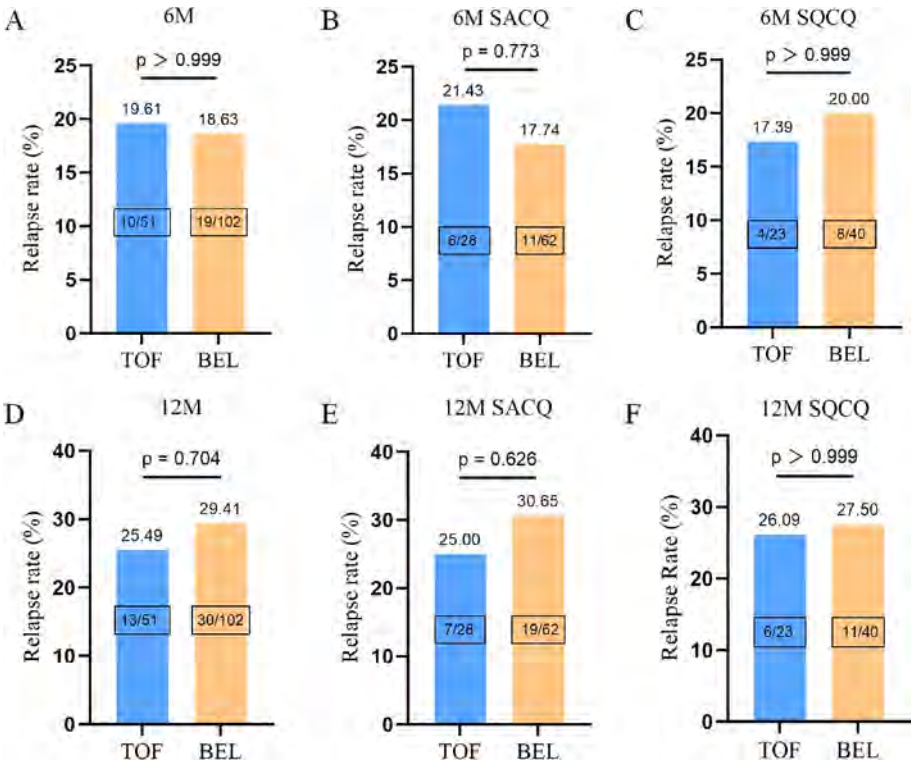


Fig.2. Relapse rate of TOF versus BEL within 6 months and 12 months. (A-C) Comparison of total relapse rates, relapse rates of SACQ sungroup, relapse rates of SQCQ sungroup between TOF and BEL within 6 months. Numbers represent percentages of all patients (%). (D-F) Comparison of total relapse rates, relapse rates of SACQ sungroup, relapse rates of SQCQ sungroup between TOF and BEL within 12 months. Numbers represent percentages of all patients (%). Abbreviations: SACQ, serologically active clinical quiescence. SQCQ, serologically quiescent clinical quiescent.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

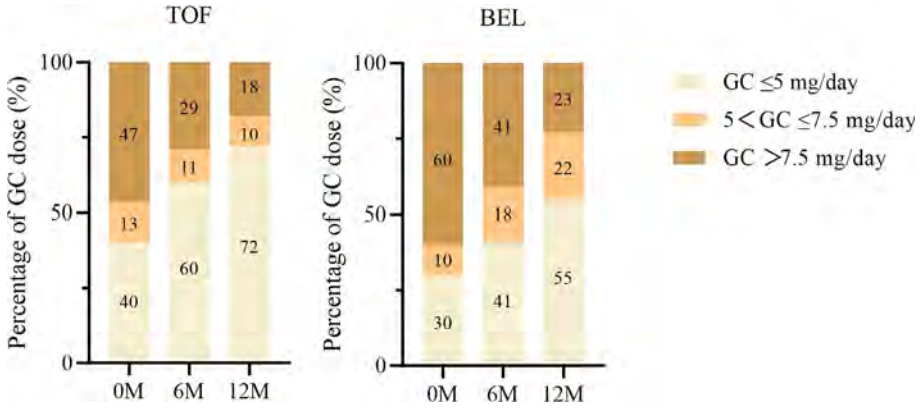


Fig.3. Change of GC dosage(prednisone equivalent) regarding the effectiveness of TOF versus BEL

arthritis in lupus. TOFA showed the potential efficacy to faster reach BICLA (BILAG-based Composite Lupus Assessment) response than belimumab in patients with mild to moderate SLE. However, the long-term effect of TOFA versus BEL in maintenance therapy of SLE remains unknown.We conducted this study to compare efficacy and safety of TOFA and BEL in maintenance therapy of SLE.

Methods: We conducted a real-world, multicenter, retrospective cohort study based on the Chinese SLE Treatment and Research Registry (CSTAR). Maintenance therapy was defined as treatment after achieving a clinical Systemic Lupus Erythematosus Disease Activity Index (cSLEDAI) score of zero. A total of 51 patients treated with TOF and 102 patients treated with BEL were enrolled through propensity score matching. The primary endpoint was the 12-month disease relapse rate, as defined by the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI Flare Index (SFI).

Results: No statistically significant difference in relapse rates were observed between the TOF group and the BEL group within 6 and 12 months (19.61% vs. 18.63%, $p > 0.999$; 25.49% vs. 29.41%, $p = 0.704$). Subgroup analysis of the serologically active clinical quiescence (SACQ) patients also showed no significant difference between two groups (6 months: 21.43% vs. 17.74%, $p = 0.773$; 12 months: 25% vs. 30.65%, $p=0.626$). A gradual decline in C3 levels in the TOF group, while the BEL group showed a physiological increase over time. C4 levels increased within the first 6 months but gradually returned to baseline by 12 months in both groups. The glucocorticoid dosage curves for both groups exhibited a descending trend. Four patients in the TOF group and one patient in the BEL group reported adverse events during the one-year follow-up.

Conclusion: Tofacitinib demonstrated potentially comparable effects to belimumab in the maintenance treatment of SLE, both drugs can aid in tappering off glucocorticoid.

Disclosure: Q. Yuan: None; **Q. Qin**: None; **L. Ma**: None; **M. Li**: None.

Abstract Number: 1542

Alternative Definitions of Moderate Flares That Simulate Clinical Practice in Systemic Lupus Erythematosus: Post Hoc Exploration of Moderate Flares in Patients Treated with Dapirolizumab Pegol in a 48-week Phase 3 Trial

Richard Furie[1], George Bertsias[2], Lucy Carter[3], Eric Morand[4], Marta Mosca[5], Marilyn Pike[6], Vanessa Taieb[7], Annette Nelde[8], Ed Vital[9] and Christian Stach[10], [1]Division of Rheumatology, Northwell Health, Great Neck, NY, [2]Rheumatology and Clinical Immunology, University Hospital of Heraklion and University of Crete Medical School and Foundation for Research and Technology-Hellas (FORTH), Infections and Immunity, Institute of Molecular Biology and Biotechnology,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Heraklion, Greece, [3]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [4]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [5]University of Pisa, Pisa, Pisa, Italy, [6]Rheumatology, MedPharm Consulting, Inc., Bethesda, MD, [7]UCB, Colombes, France, [8]Biogen, Baar, Switzerland, [9]University of Leeds, Leeds, England, United Kingdom, [10]UCB, Monheim am Rhein, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite the evolution of various flare definitions and their inclusion in SLE clinical trials, moderate flares tend to be underestimated in trials owing to their evaluation based on a single time interval as opposed to multiple intervals. Dapirolizumab pegol (DZP) is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[1,2] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain. In the phase 3 PHOENYCS GO trial (NCT04294667) of DZP in SLE, the primary endpoint, BILAG-based Composite Lupus Assessment (BICLA) response at Week (Wk) 48, was met.[3] Additionally, through Wk 48, a lower proportion of patients (pts) receiving DZP plus standard of care (DZP+SOC) vs placebo (PBO)+SOC had BILAG 2004 severe flares (11.6% vs 23.4%; nominal p=0.0257).[3] We report moderate flare outcomes from PHOENYCS GO and explore alternative definitions to more accurately estimate their frequency.

Methods: PHOENYCS GO was a 48-wk, randomized, double-blind, PBO-controlled trial. Pts were randomized 2:1 to intravenous DZP 24 mg/kg+SOC or PBO+SOC every 4 wks. Pre-specified analyses defined a BILAG 2004 severe flare as ≥1 BILAG 2004 Grade A due to a new/worse individual item(s), and a BILAG 2004 moderate flare as ≥2 BILAG 2004 Grade Bs due to new/worse individual items in different organ systems at the same visit. Post hoc analyses included two alternative definitions of BILAG 2004 moderate flares that allowed for ≥2 BILAG 2004 Grade Bs due to new/worse individual items in different organ systems to occur across either: (1) up to 2 consecutive visits and (2) up to 3 consecutive visits, all visits 4 wks apart (**Figure 1**).

Table. Baseline demographics and disease characteristics

	DZP+SOC n=208	PBO+SOC n=107
Age, years, mean (SD)	43.5 (12.3)	41.5 (12.4)
Female, n (%)	193 (92.8)	100 (93.5)
Time since first diagnosis of SLE, years, mean (SD)	10.1 (7.9)	9.8 (8.5)
SLEDAI-2K, mean (SD)	10.7 (3.5)	11.2 (3.4)
SLEDAI-2K ≥10, n (%)	140 (67.3)	79 (73.8)
BILAG 2004 total score, mean (SD)	18.4 (4.0)	18.7 (4.4)
Concomitant SLE medications at baseline, n (%)	208 (100.0)	107 (100.0)
Antimalarials	166 (79.8)	91 (85.0)
Systemic glucocorticoids	171 (82.2)	87 (81.3)
Immunosuppressants	129 (62.0)	70 (65.4)
Systemic glucocorticoid dose >7.5 mg/day, n (%)	105 (50.5)	51 (47.7)
Glucocorticoid dose, mg/day, mean (SD)	7.9 (5.9)	9.6 (8.1)

Full analysis set.
BILAG: British Isles Lupus Assessment Group; DZP: dapirolizumab pegol; PBO: placebo; SD: standard deviation; SLE: systemic lupus erythematosus; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index-2K; SOC: standard of care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

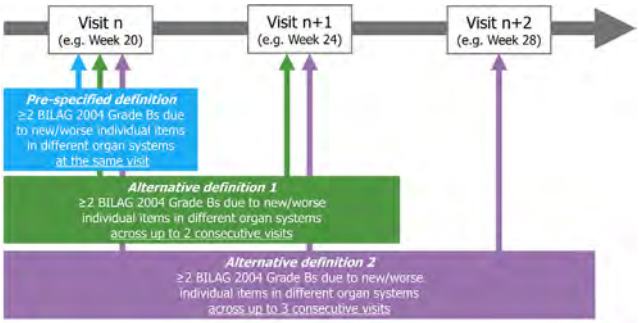
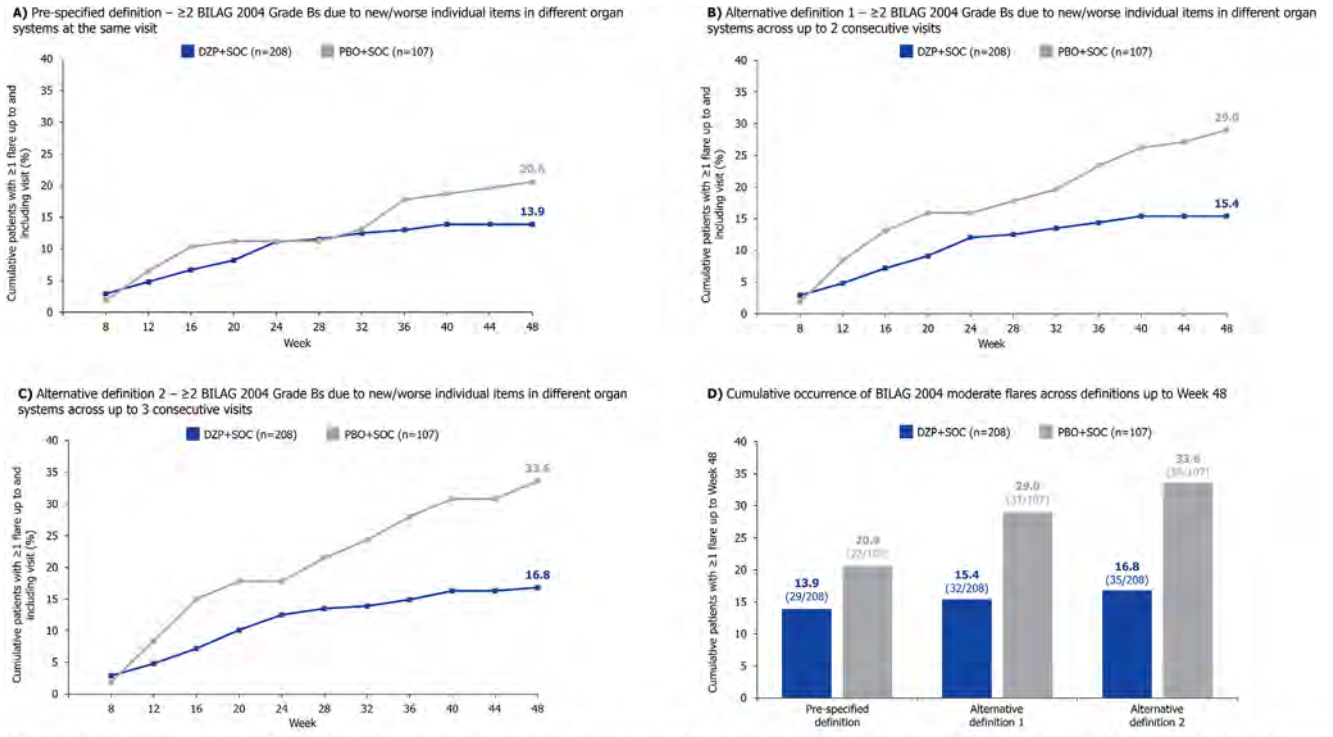


Figure 1. Pre-specified and alternative definitions of BILAG 2004 moderate flares

Results: Baseline characteristics are presented in the **Table**. At Wk 48, by the pre-specified definition, 13.9% (29/208) vs 20.6% (22/107) of pts receiving DZP+SOC vs PBO+SOC, respectively, had BILAG 2004 moderate flares. By alternative definition 1, BILAG 2004 moderate flares occurred in 15.4% (32/208) vs 29.0% (31/107) of pts receiving DZP+SOC vs PBO +SOC, respectively. By alternative definition 2, BILAG 2004 moderate flares occurred in 16.8% (35/208) vs 33.6% (36/107) of pts receiving DZP+SOC vs PBO+SOC, respectively (**Figure 2**). Time to BILAG 2004 moderate/severe flares through Wk 48 was shorter for pts receiving DZP+SOC vs PBO+SOC by all definitions.

Conclusion: Pts treated with DZP+SOC had fewer BILAG 2004 moderate flares, by all definitions considered, vs those treated with PBO+SOC. When allowing for longer time intervals over consecutive visits to evaluate moderate flares with the alternative definitions, greater rates of BILAG 2004 moderate flares were observed, particularly for pts receiving PBO +SOC, and greater differentiation between DZP+SOC and PBO+SOC was also observed. These results confirm a need to re-evaluate how flares are captured in SLE clinical trials; the alternative definitions of flares explored may better simulate clinical practice than the native definition of BILAG 2004 moderate flares.



Full analysis set; OC. A composite strategy was used for Escape Treatment Intervention 2, where missing data were counted as a severe flare at the time point of the intercurrent event, even if the event was after permanent discontinuation of study medication, as long as the event was ≤5 weeks after the last infusion. A composite strategy was used for Escape Treatment Intervention 3, where missing data were counted as a moderate flare. A treatment policy strategy was used for Escape Treatment Intervention 1, where data observed after the intercurrent event were considered for the analysis. A hypothetical strategy was used for permanent discontinuation of study drug or premature withdrawal from study, where data values >5 weeks after the last infusion were set to missing.
BILAG 2004: British Isles Lupus Assessment Group 2004; DZP: dapirolizumab pegol; OC: observed case; PBO: placebo; SOC: standard of care.

Figure 2. Cumulative occurrence of BILAG 2004 moderate flares across definitions

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References: 1. Powlesland AS. Annals Rheum Dis 2024;83 (suppl 1):261; **2**. Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); **3**. Clowse M. Arthritis Rheumatol 2024;76 (suppl 9).

Disclosure: R. Furie: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **G. Bertsias**: AbbVie, 6, AstraZeneca, 2, 5, 6, Eli Lilly, 2, 6, GSK, 2, 5, 6, MSD, 5, Novartis, 2, 6, Otsuka, 6, Pfizer, 6; **L. Carter**: Alumis Inc., 12, Paid instructor, UCB, 2; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **M. Pike**: AstraZeneca, 2, BMS, 2, UCB, 2; **V. Taieb**: UCB, 3, 12, Shareholder; **A. Nelde**: Biogen, 3, 12, Shareholder; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6; **C. Stach**: UCB, 3, 12, Shareholder.

Abstract Number: 1543

Low-Dose Aspirin Therapy in Patients with Type 2 Diabetes and Systemic Lupus Erythematosus: A Propensity-Matched Cohort Study

Sila Mateo Faxas[1], Godbless Ajenaghughrure[2], Kim Nguyen[3], Nirys Mateo Faxas[4], Gurjot Singh[3], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Good Samaritan Hospital, Cincinnati, OH, [2]Trihealth Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with both Type 2 diabetes mellitus (T2DM) and systemic lupus erythematosus (SLE) face an increased risk of cardiovascular complications due to the compounding effects of both conditions. While low-dose aspirin is commonly prescribed for cardioprotection, its specific benefits in this dual-diagnosis population remain unclear. This study aimed to evaluate the impact of low-dose aspirin (81mg) on cardiovascular and other clinical outcomes in patients with both T2DM and SLE.

Methods: Using the TriNetX global federated health research network encompassing 101 healthcare organizations, we conducted a retrospective propensity score-matched cohort study of adults (18-99 years) with both T2DM and SLE diagnoses. Patients were divided into cohorts receiving low-dose aspirin (81mg) (n=14,221) or no aspirin (n=14,221). Propensity score matching was performed to balance demographics and comorbidities between groups. Primary outcomes included mortality, cardiac arrest, cardiovascular events, and other complications measured during a 365-day follow-up period after index date. Hazard ratios (HR) and 95% confidence intervals were calculated using survival analysis.

Results: After propensity score matching, patients receiving low-dose aspirin had significantly lower rates of all-cause mortality (HR 1.471, 95% CI 1.330-1.626, p< 0.001), cardiac arrest (HR 2.369, 95% CI 1.884-2.979, p< 0.001), sepsis (HR 1.748, 95% CI 1.601-1.909, p< 0.001), acute kidney failure (HR 1.767, 95% CI 1.660-1.880, p< 0.001), and atrial fibrillation (HR 1.836, 95% CI 1.697-1.986, p< 0.001) compared to non-aspirin users. The aspirin group also showed lower incidence of cerebral infarction (HR, 1.838, 95% CI 1.591-2.123, p< 0.001), ventricular tachycardia (HR 2.163, 95% CI

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1.808-2.587, p< 0.001), and heart failure (HR 1.713, 95% CI 1.583-1.852, p< 0.001). Notably, aspirin users had significantly lower rates of hypoglycemic events (HR 1.992, 95% CI 1.612-2.462, p< 0.001).

Conclusion: In patients with both T2DM and SLE, low-dose aspirin therapy was associated with significantly reduced risk of mortality and major cardiovascular complications. The protective effect extended to renal outcomes and hypoglycemic events. These findings support the use of low-dose aspirin as part of comprehensive cardiovascular risk management in this high-risk population. Future prospective trials are needed to confirm these observations and optimize therapeutic strategies.

Disclosure: S. Mateo Faxas: None; **G. Ajenaghughrure**: None; **K. Nguyen**: None; **N. Mateo Faxas**: None; **G. Singh**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 1544

Voclosporin in Lupus Nephritis: Meta-Analysis of 6-Month and 1-Year Efficacy with 1-Year Safety Outcomes

Sri Laxmi Priya Sunkara[1], Ravi Medarametla[2], Megha Kotha[3] and Wael Jarjour[4], [1]White river medical center, batesville, AR, [2]Mamata Medical College, Guntur, Andhra Pradesh, India, [3]Ohio State University, Columbus, OH, [4]The Ohio State University, Columbus, OH

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN), is the most sever organ manifestation of systemic lupus erythematosus (SLE) and it contributes significantly to morbidity and mortality. . Standard therapies—high-dose corticosteroids combined with mycophenolate mofetil or cyclophosphamide—achieve complete renal remission in a limited subset of patients and carry substantial toxicity. Calcineurin inhibitors (CNIs) target immune dysregulation and podocyte injury. Voclosporin, a novel CNI, inhibits T-cell activation and reduces proteinuria, offering potential therapeutic benefit in LN.

Figure 1a: Complete Renal Response at 6 Months

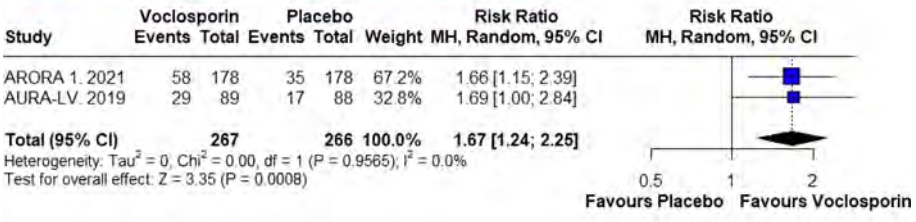


Figure 1b: Complete Renal Response at 1 Year

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2a: Any Adverse Events

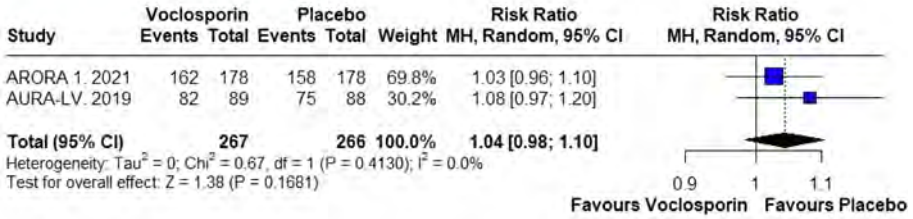


Figure 2b: Serious Adverse Events

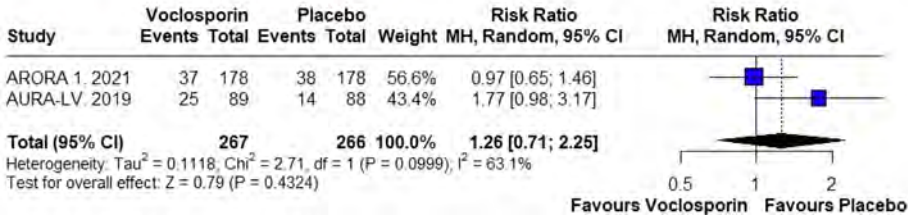


Figure 3a: Infections

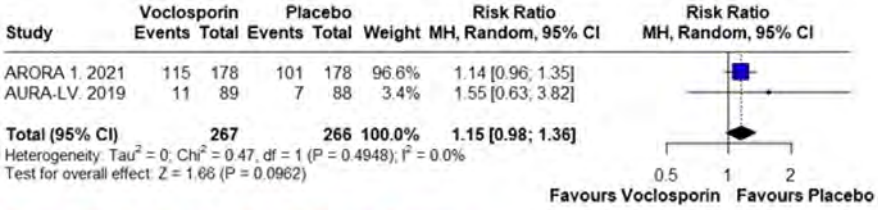


Figure 3b: Gastrointestinal Adverse Events

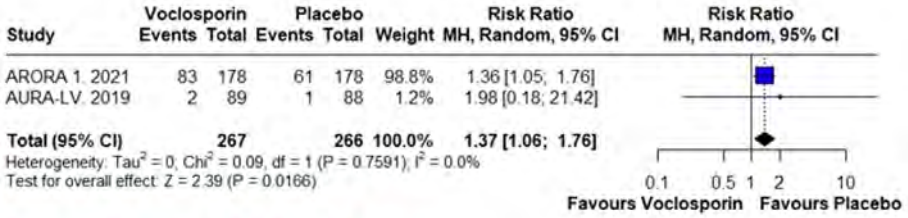
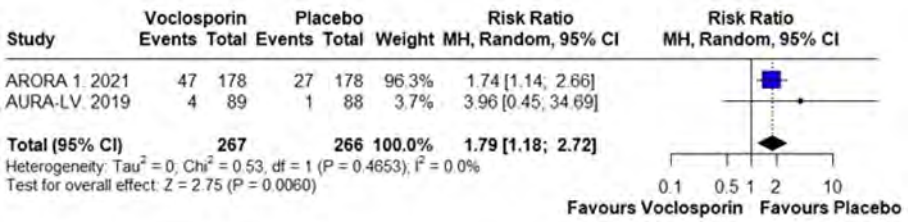


Figure 3c: Neurological Adverse Events



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A systematic search of PubMed, Embase, and Cochrane databases was conducted for English-language studies evaluating voclosporin in LN and reporting relevant efficacy or safety outcomes. Two randomized controlled trials met inclusion criteria. Data were pooled using inverse variance weighting with a random-effects model in R Studio. Forest plots were used to illustrate pooled effect estimates, and heterogeneity was assessed.

Results: A total of 533 patients from two studies were included. Voclosporin significantly increased complete renal response (CRR) at 6 months (RR 1.67; 95% CI: 1.24–2.25; p=0.0008) and 1 year (RR 1.91; 95% CI: 1.48–2.48; p< 0.0001) compared to placebo. Rates of overall adverse events (RR 1.04; 95% CI: 0.98–1.10; p=0.16), serious adverse events (RR 1.26; 95% CI: 0.71–2.25; p=0.43), and infections (RR 1.15; 95% CI: 0.98–1.36; p=0.096) were similar between groups. However, voclosporin was associated with significantly higher gastrointestinal (RR 1.37; 95% CI: 1.06–1.76; p=0.016) and neurological adverse events (RR 1.79; 95% CI: 1.18–2.72; p=0.006) at 1 year.

Conclusion: Voclosporin significantly improves CRR at 6 months and 1 year in patients with LN, with an overall safety profile comparable to placebo. However, gastrointestinal and neurological adverse events were more common. Further studies are needed to assess long-term outcomes, define steroid-sparing protocols, optimize dosing, and evaluate efficacy across diverse populations to determine voclosporin's definitive role in LN treatment.

Disclosure: S. Sunkara: None; **R. Medarametla**: None; **M. Kotha**: None; **W. Jarjour**: None.

Abstract Number: 1545

Efficacy and Safety of Subcutaneous Anifrolumab in Systemic Lupus Erythematosus: Interim Analysis of a Phase 3 Randomized Placebo-controlled Study

Susan Manzi[1], Ian Bruce[2], Eric Morand[3], Richard Furie[4], Yoshiya Tanaka[5], Patricia Puzio[6], Emon Khan[7], Jenny Wissmar[8], Michael Song[9] and Catharina Lindholm[10], [1]Lupus Center of Excellence, Autoimmunity Institute, Allegheny Health Network, Pittsburgh, PA, [2]Centre for Public Health, Faculty of Medicine, Health and Life Sciences, Queen's University, Belfast, Manchester, United Kingdom, [3]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [4]Division of Rheumatology, Northwell Health, Great Neck, NY, [5]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [6]BioPharmaceuticals R&D, AstraZeneca US, Gaithersburg, MD, [7]BioPharmaceuticals R&D, Late Respiratory and Immunology, AstraZeneca, Academy House, Cambridge, United Kingdom, [8]BioPharmaceuticals R&D, Late-Stage Development, Respiratory & Immunology, AstraZeneca, Gothenburg, Sweden, [9]BioPharmaceuticals R&D, Late Clinical Development Immunology, AstraZeneca, Boston, MA, [10]BioPharmaceuticals R&D, Late Clinical Development Immunology, AstraZeneca, Gothenburg, Sweden

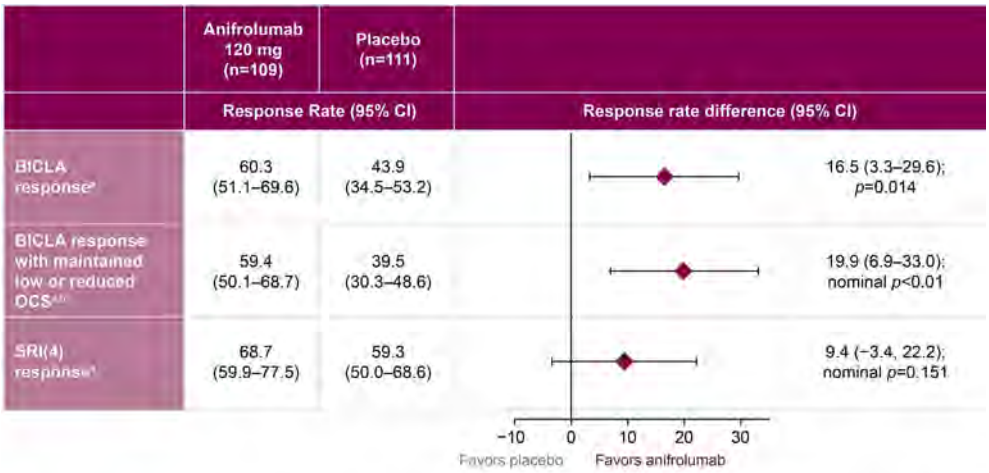
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Intravenous (IV) anifrolumab (300 mg, every 4 weeks [Q4W]) is an approved biologic add-on therapy for moderate to severe SLE;[1] a subcutaneous (SC) formulation may allow for greater personalization of treatment. Here, we report interim results from a global phase 3 study evaluating the efficacy and safety of SC anifrolumab in patients with moderate to severe SLE.

Methods: In TULIP-SC (NCT04877691), eligible adult patients with SLE (revised 1997 ACR criteria) were randomized 1:1 to receive weekly (QW) anifrolumab 120 mg SC or placebo plus standard therapy during a 52-week double-blind treatment period. This pre-planned interim analysis (IA) of 346 patients was conducted once 220 patients completed the double-blind treatment period or discontinued.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



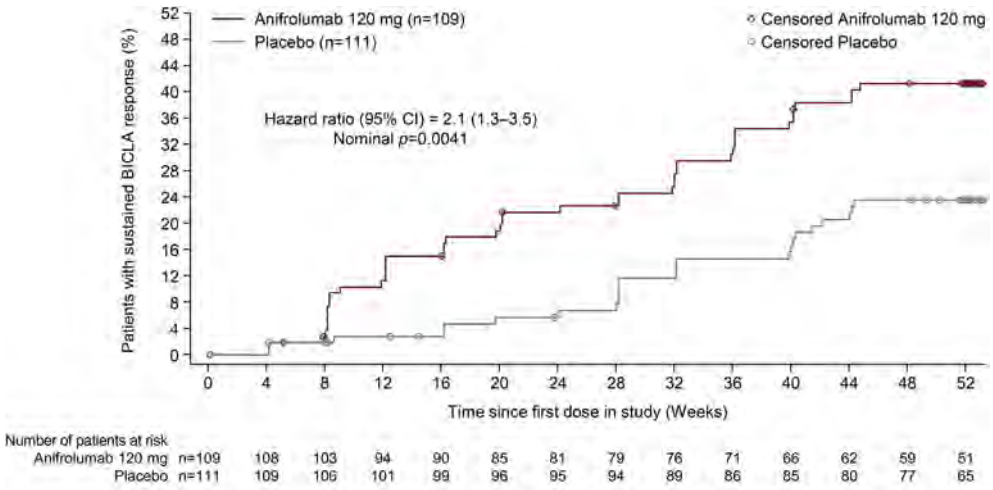
[a]The responder rates (percentages) were estimated using stratified CMH, adjusting for the stratification factors; [b]Maintained low or reduced OCS use through Week 52 is defined as follows: if baseline OCS ≥10 mg/day, an OCS dose of ≤7.5 mg/day prednisone or equivalent must be achieved by Week 40 and maintained from Week 40 to Week 52; if baseline OCS <10 mg/day, an OCS dose at Week 40 must be ≤ the OCS dose at baseline and maintained from Week 40 to Week 52.

Only patients with non-missing covariates/stratification factors were included in the interim analyses. Stratification factor levels = baseline IFNGS-high and SLEDAI <10 points, baseline IFNGS-high and SLEDAI ≥10 points, and baseline IFNGS-low.

BICLA, BILAG-based Composite Lupus Assessment; CI, confidence interval; CMH, Cochran-Mantel–Haenszel; IFNGS, type I interferon gene signature status; MAR, missing at random; OCS, oral corticosteroids; SRI, SLE Responder Index; TULIP, Treatment of Uncontrolled Lupus via the Interferon Pathway.

Figure 1: Interim efficacy results at Week 52 of the phase 3 TULIP-SC trial of weekly subcutaneous anifrolumab alongside standard therapy

Efficacy was assessed in the IA set (n=220); the safety set included all randomized patients who received ≥1 dose at time of IA data cut-off (n=346). The difference between groups in the proportions of BILAG-based Composite Lupus Assessment (BICLA) responders (primary endpoint; stratified Cochran-Mantel–Haenszel approach) was assessed at Week 52. Key secondary endpoints (proportions of BICLA responders whose oral corticosteroid [OCS] dose from Week 40 through Week 52 was ≤7.5 mg/day if baseline [BL] was ≥10 mg/day or ≤BL if BL was < 10 mg/day, time to first BICLA response sustained to Week 52, and time to first flare) and the proportion of patients achieving SLE Responder Index response (SRI[4]) at Week 52 were also assessed.



Kaplan-Meier estimate with 95% CI for each treatment group. Hazard ratios and 95% CIs were estimated using a Cox regression model with treatment groups and stratification factors.

BICLA, BILAG-based Composite Lupus Assessment; CI, confidence interval; SC, subcutaneous; TULIP, Treatment of Uncontrolled Lupus via the Interferon Pathway.

Figure 2: Time to first BICLA response sustained up to, and including, Week 52 during the phase 3 TULIP-SC trial of weekly subcutaneous anifrolumab alongside standard therapy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Baseline demographics and key clinical characteristics were balanced between groups (anifrolumab: n=109, mean [standard deviation] age=43.0 [12.4] years, SLEDAI-2K score=11.3 [3.8]; placebo n=111, mean age=42.3 [11.4] years, SLEDAI-2K score=10.5 [2.9]), with similar discontinuation (21.1% vs 21.6%).

The primary endpoint was met: 60.3% vs 43.9% of patients achieved a BICLA response at Week 52 with anifrolumab vs placebo, respectively (**Figure 1**; difference [95% CI]=16.5% [3.3–29.6%]; p=0.014). At Week 52, the proportion of BICLA responders who met the OCS dosing criteria, and the proportion achieving SRI(4) were numerically greater with anifrolumab vs placebo (**Figure 1**). Patients receiving anifrolumab vs placebo were around twice as likely to achieve a BICLA response sustained through Week 52 (**Figure 2**). The risk of flare over 52 weeks with anifrolumab vs placebo was numerically lower (HR [95% CI]=0.69 [0.4–1.1]; nominal p=0.093).

The incidence of adverse events (AEs) was 74.4% (131/176) vs 71.2% (121/170) with anifrolumab and placebo treatment, respectively; similar proportions of serious AEs (10.8% vs 8.8%) and serious infections (6.3% vs 3.5%) were reported. Injection site reactions (ISR) occurred in 15.3% vs 17.1% with anifrolumab and placebo treatment, respectively. Most AEs, including ISRs, were of mild to moderate intensity.

Conclusion: Treatment with anifrolumab 120 mg SC QW provided a statistically significant and clinically meaningful benefit in overall disease activity over standard therapy and was well tolerated; the efficacy and safety profile was consistent with the approved IV 300 mg anifrolumab treatment regimen.[1]

1. Saphnelo Prescribing Information. http://www.azpicentral.com/pi.html?product=saphnelo.

Disclosure: S. Manzi: AstraZeneca, 2, CAQH, 1, Cartesian, 1, 2, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, Lily, 2, Lupus Foundation of America, 4, UCB Advisory Board, 2; **I. Bruce**: AstraZeneca, 2, 5, 6, BMS, 2, Cabaletta Bio, 2, GSK, 2, 5, 6, Janssen, 5, 6, Lilly, 2, Novartis, 5, Otsuka, 5, UCB, 2; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **P. Puzio**: AstraZeneca, 3; **E. Khan**: AstraZeneca, 3; **J. Wissmar**: AstraZeneca, 3; **M. Song**: AstraZeneca, 3, 11; **C. Lindholm**: AstraZeneca, 3.

Abstract Number: 1546

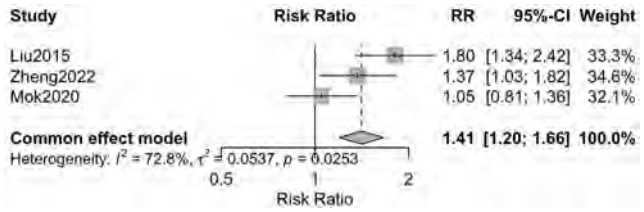
Tacrolimus Versus Voclosporin for Active Lupus Nephritis: A Comparative Meta-analysis of Renal Response

Urvi Zala[1] and Rushi Patel[2], [1]Loyola MacNeal Hospital, Berwyn, IL, Oak Park, IL, [2]Baptist Hospitals of Southeast Texas, Beumont, TX

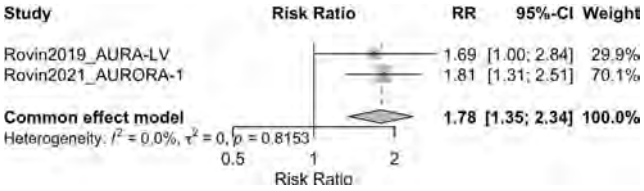
SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest plot for Tacrolimus trials



Forest plot Voclosporin trials

Background/Purpose: Lupus nephritis (LN) is seen in approximately 40–60 % of patients with systemic lupus erythematosus (SLE) and contributes significantly to morbidity and mortality in this population. The definitive diagnosis is made with a kidney biopsy, and disease severity is classified according to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) system, which guides management. The approach to active class III and IV LN involves glucocorticoids and mycophenolate mofetil (MMF), with the addition of calcineurin inhibitors (CNIs) based on patient characteristics. CNIs exert potent immunosuppressive effects by blocking T-lymphocyte activation and inhibiting the production of interleukin-2 and have traditionally been used as immunosuppression in renal transplantation. Through this meta-analysis, we aim to compare the use of the CNIs tacrolimus (TAC) and Voclosporin (VOC) in active LN.

Methods: A comprehensive review of PubMed, Scopus, and the Cochrane Library was performed to locate relevant clinical trials. Five randomized controlled trials (n = 1 311) met inclusion criteria. Three trials compared TAC with conventional induction regimens (cyclophosphamide or MMF; n = 777). Two placebo-controlled trials evaluated VOC on an MMF/low-dose-steroid background (n = 534). Pooled risk ratios (RRs) were determined using Mantel–Haenszel common-effect and random-effects models. Heterogeneity among studies was evaluated with I^2 and τ^2 metrics. An indirect Bucher comparison was conducted to analyze differences between TAC and VOC. A p-value < 0.05 was considered statistically significant.

Results: We evaluated five studies in total with the network meta-analysis framework. TAC was associated with a significant increase in complete/partial renal response (RR = 1.41; 95 % CI 1.20–1.66; p < 0.0001), although substantial heterogeneity was present (I^2 = 72.8 %, τ^2 = 0.054). A random-effects synthesis attenuated the estimate (RR = 1.36; 95 % CI 1.00–1.86; p = 0.048). VOC significantly improved renal response (common-effect RR = 1.78; 95 % CI 1.35–2.34; p < 0.0001) with no observed between-study heterogeneity (I^2 = 0 %). An indirect Bucher comparison of pooled random-effects estimates showed no statistically significant difference between TAC and VOC (log RR = –0.23; SE = 0.164); the corresponding RR was 0.79 (95 % CI 0.58–1.09).

Conclusion: Based on this meta-analysis, both calcineurin inhibitors improve short-term renal response in active lupus nephritis when added to standard care. Voclosporin shows a larger and more consistent benefit across trials (RR 1.78), whereas tacrolimus exhibits greater between-study variability. Nevertheless, the indirect Bucher comparison does not establish the clear superiority of either drug. These findings highlight the need for additional studies that directly compare calcineurin inhibitors, with particular emphasis on their relative efficacy, safety, and patient adherence.

Disclosure: U. Zala: None; **R. Patel**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1547

Anifrolumab in Systemic Lupus Erythematosus with Renal Involvement: National Multicenter Registry in Clinical Practice

Vanesa Calvo-Río[1], Carmen Secada-Gómez[1], Blanca Garcia-Magallon[2], Deseada Palma-Sanchez[3], Andrea García-Valle[4], Irati Urionaguena Onaindia[5], Adrián Mayo-Juanatey[6], Paúl Hernández Velasco[7], GUILLERMO GONZALEZ ARRIBAS[8], Ana Pareja-Martínez[9], Montserrat Corteguera[10], Guillen Sada Urmeneta[11], Paz Collado Ramos[12], Jose Luis Tandaipan[13], Juan Roberto Miguelez Sanchez[14] and Ricardo Blanco[1], [1]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [2]Rheumatology. Hospital Universitario Puerta de Hierro, Madrid, Spain, [3]Rheumatology. Hospital Rafael Méndez, Lorca, Murcia, Spain, [4]Rheumatology. Hospital General Río Carrión, Palencia, Castilla y Leon, Spain, [5]Rheumatology.Hospital Galdakao, Vizcaya, Pais Vasco, Spain, [6]Hospital Universitario Doctor Peset, Valencia, Comunidad Valenciana, Spain, [7]Nephrology, Hospital Universitario 12 de Octubre, Madrid. Spain, Madrid, Madrid, Spain, [8]Facultativo especialista, PALMA DE MALLORCA, Galicia, Spain, [9]Rheumatology. Hospital Universitario Infanta Leonor, Madrid, Madrid, Spain, [10]Rheumatology. Complejo Asistencial de Ávila, Ávila, Castilla y Leon, Spain, [11]Rheumatology. Hospital Reina Sofía, Tudela, Navarra, Spain, [12]Department of Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain,, MADRID, Madrid, Spain, [13]Rheumatology. Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Spain, [14]Department of Rheumatology, Hospital Universtiario de Móstoles, Madrid, Spain, Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus Nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE), occurring in up to 50% of patients. Currently, Anifrolumab (ANI) is approved for moderate-to-severe SLE, based on clinical trials excluding active LN **(1,2)**. In LN, an elevated type I IFN gene signature (IFNGS) is associated with increased disease activity, high proteinuria levels, and therapeutic failure **(3)**.

In patients with LN treated with ANI in clinical practice in Spain, our aim was to assess the effectiveness and safety of ANI.

Methods: Observational multicenter study of patients diagnosed with SLE (EULAR/ACR 2019 classification criteria), treated with ANI who presented renal involvement (renal insufficiency and/or hematuria and/or proteinuria). Data were collected from medical records up to January 31 2025. Demographic, clinical, laboratory, and pathologic variables were evaluated, along with previous and concomitant therapies, disease activity indices (SLE-DAS, SLEDAI-2K, PGA), organ damage index (SLICC SDI), and safety.

Results: We studied 18 patients (16 women/2 men), mean age of 38.16±10.35 years (range 20-63 years), from 14 hospitals. Baseline characteristics, prior treatment before starting ANI and LN subtypes are summarized in TABLE. The most common renal manifestations at ANI initiation were proteinuria (n=9, 50%), hematuria (n=5; 27.8%), and renal insufficiency (n=2; 11.1%).

The mean number of immunosuppressive treatments (synthetic/biologic) received prior to ANI was 4.3 ± 2.4 (range 1-12). All of them had received belimumab, and 15 mycophenolate mofetil. The standard ANI regimen was 300 mg every 4 weeks, except in two patients who received loading doses (900 mg/4 weeks for 3 months, then 300 mg/4 weeks).

In addition to corticosteroids, ANI was administered concomitantly with antimalarials (n=16), mycophenolate mofetil (n=11), tacrolimus (n=4), azathioprine (n=2), methotrexate (n=1), and voclosporin (n=1). A rapid (from the first month) and maintained significant improvement was observed in: a) disease activity (SLE-DAS, SLEDAI-2K, PGA) (Figure 1) b) immunologic markers

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Clinical manifestations at the time of anifrolumab initiation and previously treatments. Abbreviations in alphabetical order: ANI: anifrolumab; AZA: azathioprine; BLM: belimumab; CYM: cyclophosp-hamide; MMF: mycophenolate mofetil; MP: methylprednisolone; MTX: methotrexate; LN: lupus nephritis; RTX: rituximab

Clinical manifestations before ANI initiation	N (%)
joints	17 (94.4%)
skin	15 (83.3%)
hematological	13 (72.2%)
alopecia	6 (33.3%)
serositis	6 (33.3%)
oral ulcers	5 (27.8%)
neuropsychiatric	1 (5.5%)
gastrointestinal	1 (5.5%)
Kidney involvement at ANI initiation	
proteinuria	9 (50%)
hematuria	5 (27.8%)
renal insufficiency	2 (11.1%)
LN subtypes	
class III	7 (36.9%)
class IV	6 (33.3%)
class II	1 (5.6%)
class III+V	1 (5.6%)
Unknown	3 (16.7%)
Treatments before ANI initiation	
antimalarials	17 (94.4%)
BLM	18 (100%)
MMF	15 (83.3%)
AZA	8 (44.4%)
CYM	8 (44.4%)
MTX	8 (44.4%)
RTX	7 (38.9%)
tacrolimus	4 (22.2%)
Concomitant treatment with ANI	
antimalarials	16 (88.9%)
MMF	11 (61.1%)
tacrolimus	4 (22.2%)
AZA	2 (11.1%)
MTX	1 (5.5%)
CYM	1 (5.5%)

(decrease in anti-dsDNA antibody titers and normalization of C3 and C4 levels) c) renal parameters (reduction in creatinine, proteinuria and improvement in glomerular filtration rate) (Figure 2).

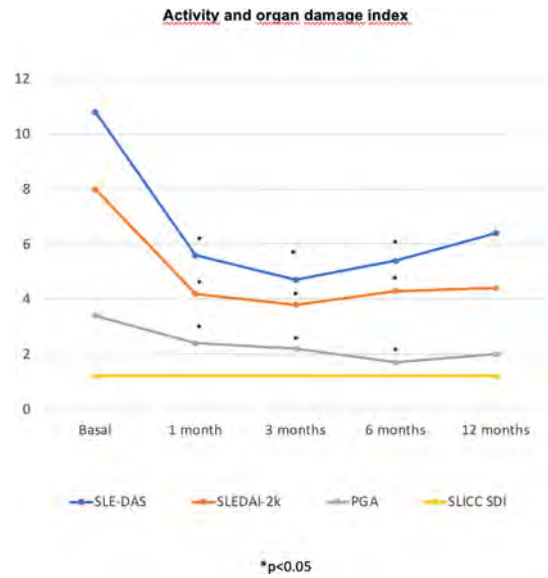


Figure 1. Evolution of activity and organ damage index after the initiation of anifrolumab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

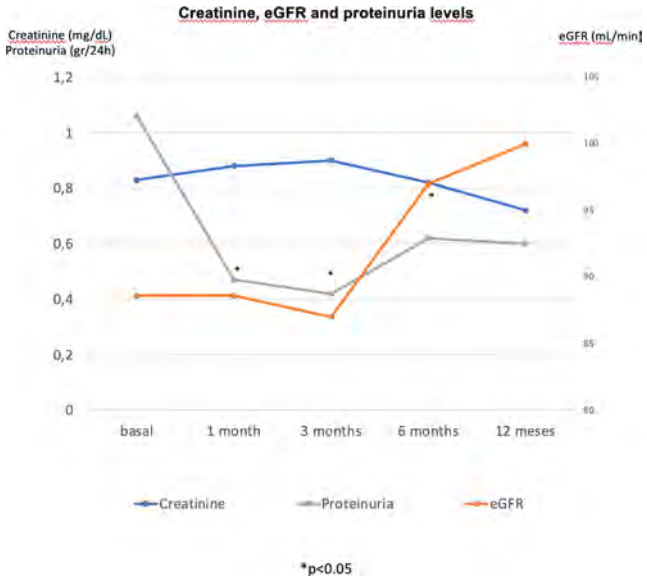


Figure 2. Evolution of creatinine levels, glomerular filtration rate and proteinuria (g/24h) after the initiation of anifrolumab.

After a mean follow-up of 8.8 ± 5.5 months, a reduction in the number of relapses was observed, from a median [IQR] of 2 [0-3] to 0 [0-0]. The organ damage index remained stable. All 18 patients remained on ANI, and the most relevant adverse events were herpes zoster (n=1) and hidradenitis suppurativa (n=1). The prednisone dose was decreased from 9.2±7.9 mg/day to 3.3±2 mg/day (p= 0.1).

Conclusion: To our knowledge, this is the first real-life study of ANI in LN. In refractory patients to multiple immunosuppressive therapies, we observed a rapid and maintained effectiveness in SLE activity and renal manifestations, with a good safety profile. These preliminary data should be confirmed in clinical trials.

Disclosure: V. Calvo-Río: AstraZeneca, 6, MSD, Roche, AbbVie, Lilly, Celgene, Grünenthal, and UCB Pharma, 2, 6; **C. Secada-Gómez**: None; **B. Garcia-Magallon**: AstraZeneca, 12,, 6; **D. Palma-Sanchez**: None; **A. García-Valle**: None; **I. Urionaguena Onaindia**: None; **A. Mayo-Juanatey**: None; **P. Hernández Velasco**: None; **G. GONZALEZ ARRIBAS**: None; **A. Pareja-Martínez**: None; **M. Corteguera**: None; **G. Sada Urmeneta**: None; **P. Collado Ramos**: None; **J. Tandaipan**: None; **J. Miguelez Sanchez**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1548

Anifrolumab in Systemic Lupus Erythematosus. Spanish Multicenter Registry in Clinical Practice

Vanesa Calvo-Río[1], Carmen Secada-Gómez[1], Miriam Retuerto Guerrero[2], Judit Font-Urgelles[3], Ivette Casafont-Solé[3], Adrián Mayo-Juanatey[4], Juan José Alegre-Sancho[5], DALIFER FREITES[6], Cristina Hormigos Martin[7], Noemí Garrido[8], GUILLERMO GONZALEZ ARRIBAS[9], Juan Roberto Miguelez Sanchez[10], Andrea García-Valle[11], Marta Ibañez[12], Fernando Lozano Morillo[13], Ángel García Manzanares[14], Sebastián Sandoval-Moreno[15], Josefina Cortés-Hernández[16], Deseada Palma-Sanchez[17], LETICIA LOJO-OLIVEIRA[18], Evelin Cervantes[19], Paz Collado Ramos[20], cristina arciniega Larios[21], Luis Sala[22], Eztizen Labrador-Sánchez[23], Cilia Peralta-Ginés[24], Nahia Plaza-Aulestia[25], Irati Urionaguena Onaindia[26], Miguel Medina Malone[27], Jose Rosas Gómez de Salazar[28], Montserrat Corteguera[29], Laura Cebrian[30], Fred Anton Pages[31], Jose Ramón Lamua-Riazuelo[32], María Dolores Fábregas Canales[33], María José Alados Hernández[34], Marta Garijo Bufort[35], Anna Pamies[36], Luis Sarabia[37], Rodrigo Aguirre-del-Pino[38], José Ángel Cabezas Lefler[39], alvaro seijas[38], Carmen Carrasco-Cubero[40], Ana López-Cerón Cofiño[41], Vera Ortiz-Santamaria[42], Santos Castañeda[43], Maria Laino[44], Carmen

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ordás Calvo[45], Celia arconada[46], ana Urruticoechea-Arana[47], Blanca Garcia-Magallon[48], Ana Valeria Acosta Alfaro[49], Samuel Leal Rodriguez[50], Marina Salido Olivares[7], Patricia Lavilla Villar[51], Anahy Maria Brandy[3], Inmaculada Ros Vilamajo[52], Alvaro García Martos[53], Berta Magallares[54], Guillen Sada Urmeneta[55], Cristina Córdoba Martín[56], Elena Riera Alonso[57], Carmen Bejerano-Herreria[58] and Ricardo Blanco,<58, [1]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [2]Complejo Asistencial Universitario de Leon, Leon, Castilla y Leon, Spain, [3]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [4]Hospital Universitario Doctor Peset, Valencia, Comunidad Valenciana, Spain, [5]Hospital Universitario Doctor Peset, Valencia, Spain, [6]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [7]Hospital Clínico San Carlos, Madrid, Spain, [8]Hospital Universitario Virgen del Rocío, Sevilla, Andalucia, Spain, [9]Facultativo especialista, PALMA DE MALLORCA, Galicia, Spain, [10]Department of Rheumatology, Hospital Universtiario de Móstoles, Madrid, Spain, Madrid, Madrid, Spain, [11]Rheumatology. Hospital General Río Carrión, Palencia, Castilla y Leon, Spain, [12]Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [13]Hospital Central de La Defensa Gómez Ulla, Madrid, Madrid, Spain, [14]Hospital Universitario de Torrevieja, Alicante, Spain, [15]Hospital Universitario Vall D'Hebron, Barcelona, Spain, [16]Hospital Universitari Vall d'Hebron-Universitat Autónoma de Barcelona, Barcelona, Spain, [17]Rheumatology. Hospital Rafael Méndez, Lorca, Murcia, Spain, [18]Hospital Universitario Infanta Leonor, Madrid, Spain, [19]Hospital Provincial de Pontevedra, Pontevedra, Spain, [20]Department of Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain,, MADRID, Madrid, Spain, [21]Hospital de Mérida, Badajoz, Spain, [22]Hospital Universitario de Torrejón, Madrid, Spain, [23]Hospital General de La Rioja, Logroño, Spain, [24]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [25]Hospital Galdakao, Vizcaya, Spain, [26]Rheumatology.Hospital Galdakao, Vizcaya, Pais Vasco, Spain, [27]Hospital de Calahorra, Calahorra, Spain, [28]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [29]Rheumatology. Complejo Asistencial de Ávila, Ávila, Castilla y Leon, Spain, [30]Department of Rheumatology, Hospital Universitario Infanta Leonor / Universidad Complutense de Madrid, Madrid, Spain, Madrid, Spain, [31]Hospital General de Segovia, Segovia, Spain, [32]Hospital Universitario del Henares, Madrid, Spain, [33]Hospital de Barbastro, Huesca, Spain, [34]Hospital Universitario Puerta del Mar, Cadiz, Spain, [35]Hospital de Sagunto, Valencia, Spain, [36]Hospital Verge de la Cinta, Tortosa, Tarragona, Spain, [37]Complejo Hospitalario de Jaén, Jaén, Spain, [38]Hospital Universitario Lucus Augusti, Lugo, Spain, [39]Complejo Asistencial de Zamora, Zamora, Spain, [40]Complejo Hospitalario Universitario de Badajoz, Badajoz, Spain, [41]Hospital Santa Bárbara, Soria, Spain, [42]Hospital General de Granollers, Barcelona, Spain, [43]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [44]Hospital Universitario de Navarra, Pamplona, Spain, [45]Hospital Universitario de Cabueñes, Gijón, Spain, [46]Hospital universitario de Getafe, Getafe, Madrid, Spain, [47]Rheumatology Division. Hospital Universitario Son Espases, Palma de Mallorca, Spain, [48]Rheumatology, Hospital Universitario Puerta de Hierro, Madrid, Spain, [49]Hospital Universitario Infanta Sofia; Universidad Europea de Madrid; FIIB HUIS-HUHEN, Madrid, Spain, [50]Hospital Universitario La Fe, Valencia, Valencia, Spain, [51]Hospital General de Villalba, Collado Villalba, Madrid, Spain, [52]Hospital Son Llàtzer, Palma de Mallorca, Spain, [53]Hospital del Tajo, Aranjuez, Madrid, Spain, [54]Hospital de Sant Pau, Barcelona, Spain, [55]Rheumatology, Hospital Reina Sofía, Tudela, Spain, [56]Hospital Universitario Nuestra Señora de la Candelaria, Santa Cruz de Tenerife, Tenerife, Spain, [57]Hospital Universitari Mùtua Terrassa, Terrassa, Spain, [58]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain.

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Anifrolumab (ANI) is a human monoclonal antibody that binds to the type I interferon receptor subunit 1 (IFNAR1). ANI was approved by Spanish authorities for the treatment of adults with moderate to severe systemic lupus erythematosus (SLE) with positive autoantibodies, in combination with standard treatment.

In patients with SLE treated with ANI in clinical practice in Spain, our aim was to assess a) the profile of patients receiving ANI b) effectiveness and c) safety.

Methods: Observational multicenter study of patients diagnosed with SLE (EULAR/ACR 2019 classification criteria) treated with ANI. Data were collected from medical records up to April 31st 2025. Demographic, clinical, laboratory, and pathologic variables were evaluated, along with previous and concomitant therapies, disease activity indices (SLE-DAS, SLEDAI-2K, PGA), organ damage index (SDI), and safety were evaluated.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Clinical manifestations and treatments received before starting anifrolumab Abbreviations in alphabetical order: ANI: anifrolumab; AZA: azathioprine; BLM: belimumab; CsA: cyclosporine; CYM: cyclophosphamide; MMF: mycophenolate mofetil; MP: methylprednisolone; MTX: Methotrexate; RTX: rituximab

Clinical manifestations at ANI initiation	N (%)
articular	180 (87.8%)
cutaneous	163 (79.1%)
hematological	132 (65%)
oral ulcers	98 (47.8%)
alopecia	90 (43.7%)
renal	57 (27.8%)
serositis	45 (21.8%)
neuropsychiatric	28 (13.6%)
digestive	17 (8.3%)
Therapy before ANI	
antimalarials	198 (97%)
BLM	137 (66.9%)
MMF	84 (41.4%)
AZA	84 (41.4%)
MP boluses	62 (30.4%)
RTX	59 (29.1%)
MTX	59 (29.1%)
CYM	30 (14.8%)
tacrolimus	19 (9.3%)
Concomitant therapy with ANI	
oral steroids	167 (82.3%)
antimalarials	158 (80.2%)
MMF	49 (24.6%)
MTX	34 (17%)
AZA	22 (11%)
tacrolimus	8 (4%)
RTX	7 (3.5%)
leflunomide	3 (2.6%)
sulfones	2 (1.4%)
CYM	1 (0.5%)
anakinra	1 (0.5%)

Results: 206 patients (183 females/23 males), mean age 44.6 ± 12.6 years (range 15-90 years) (54 hospitals) were included. Baseline characteristics of patients and prior treatment before starting ANI are summarized in TABLE.

The main reason for starting ANI was clinical activity: cutaneous (n=124, 61.7%), articular (n=98, 48.5%), hematological (n=55, 27.2%), corticosteroid dependence (n=11, 5.4%), renal (n=8, 4%), serositis (n=6, 3%), serious adverse events with other immunosuppressants (n=4, 1.9%), neurological (n=2, 1%), and Kikuchi disease (n=1, 0.5%).

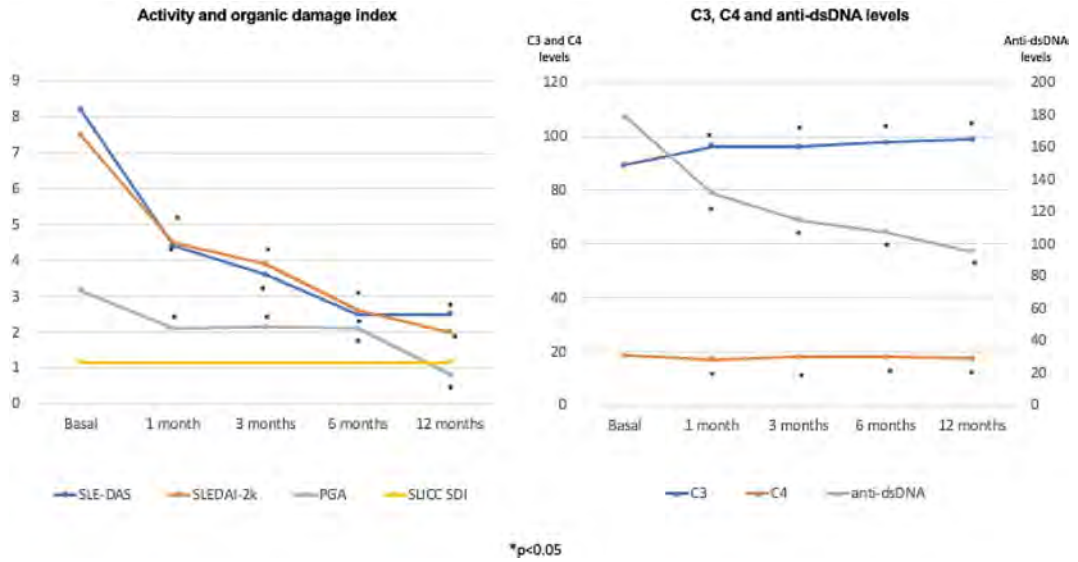


Figure 1. Evolution of C3, C4 and anti-dsDNA levels and activity and organ damage indices after starting anifrolumab.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

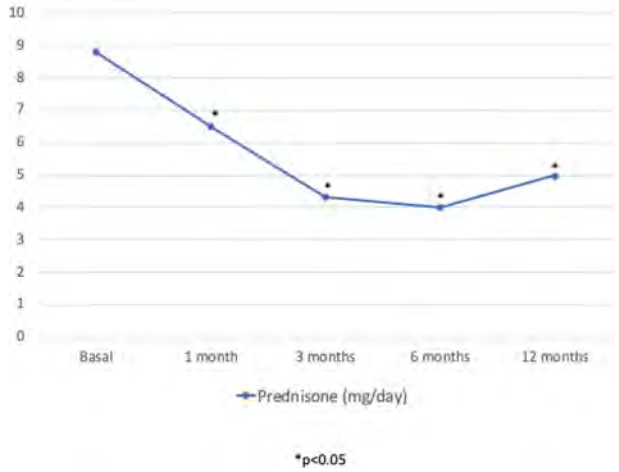


Figure 2. Reduction in prednisone dosage after initiation of anifrolumab.

The mean number of immunosuppressants (synthetic/biologic) received prior to ANI was 2.5±1.6 (range 0-8). All patients received 300 mg/4 weeks of ANI except two patients with renal involvement who received a loading dose (900 mg/4 weeks x3 months followed by 300 mg/4 weeks). In addition to corticosteroids and antimalarials, ANI was administered in many cases concomitantly with other immunomodulator drug (TABLE).

A rapid (from the 1st month) and maintained significant improvement was observed in: a) disease activity (SLE-DAS, SLEDAI-2K, PGA) (Figure 1) b) immunologic markers (decrease in anti-dsDNA antibody titers and normalization of C3 and C4 levels) (Figure 1) and c) prednisone dose (**Figure 2**). The organ damage index remained stable.

After a mean follow-up of 7.5 ± 5.3 months, a reduction in the number of relapses was observed, from a median [IQR] of 2 [1-6] prior ANI to 0 [0-0] after ANI ($p < 0.001$). The most relevant adverse events were: herpes zoster (n=5), headache (n=3), upper respiratory tract infection (n=3), pneumonia (n=3), arterial hypotension (n=2), hidradenitis suppurativa (n=2) and vaginal candidiasis (n=2). In the follow-up, 20 patients discontinued treatment due to primary failure (n=8), secondary failure (n=3), severe infections (n=6), hypotension (n=1), acute anterior uveitis (n=1), and pregnancy desire (n=1).

Conclusion: As in clinical trials, a rapid and maintained effectiveness was observed; even in severe and refractory patients. ANI was used in monotherapy or combined with other immunosuppressive drugs, including other biological therapies. The safety profile was acceptable with the limitation of short follow-up.

Disclosure: V. Calvo-Río: AstraZeneca, 6, MSD, Roche, AbbVie, Lilly, Celgene, Grünenthal, and UCB Pharma, 2, 6; **C. Secada-Gómez**: None; **M. Retuerto Guerrero**: None; **J. Font-Urgelles**: None; **I. Casafont-Solé**: None; **A. Mayo-Juanatey**: None; **J. Alegre-Sancho**: None; **D. FREITES**: None; **C. Hormigos Martin**: None; **N. Garrido**: None; **G. GONZALEZ ARRIBAS**: None; **J. Miguelez Sanchez**: None; **A. García-Valle**: None; **M. Ibañez**: None; **F. Lozano Morillo**: None; **Á. García Manzanares**: None; **S. Sandoval-Moreno**: None; **J. Cortés-Hernández**: AstraZeneca, 6, Bristol-Myers Squibb (BMS), 1, GlaxoSmithKline (GSK), 6, Novartis, 1, 5, 6; **D. Palma-Sanchez**: None; **L. LOJO-OLIVEIRA**: None; **E. Cervantes**: None; **P. Collado Ramos**: None; **c. arciniega Larios**: None; **L. Sala**: None; **E. Labrador-Sánchez**: None; **C. Peralta-Ginés**: None; **N. Plaza-Aulestia**: None; **I. Urionaguena Onaindia**: None; **M. Medina Malone**: None; **J. Rosas Gómez de Salazar**: None; **M. Corteguera**: None; **L. Cebrian**: None; **F. Anton Pages**: None; **J. Lamua-Riazuelo**: None; **M. Fábregas Canales**: None; **M. Alados Hernández**: None; **M. Garijo Bufort**: None; **A. Pamies**: None; **L. Sarabia**: None; **R. Aguirre-del-Pino**: None; **J. Cabezas Lefler**: None; **a. seijas**: None; **C. Carrasco-Cubero**: None; **A. López-Cerón Cofiño**: None; **V. Ortiz-Santamaria**: None; **S. Castañeda**: None; **M. Laino**: None; **C. Ordás Calvo**: None; **C. arconada**: None; **a. Urruticoechea-Arana**: None; **B. Garcia-Magallon**:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

AstraZeneca, 6, 12; **A. Acosta Alfaro**: None; **S. Leal Rodriguez**: None; **M. Salido Olivares**: None; **P. Lavilla Villar**: None; **A. Brandy**: None; **I. Ros Vilamajo**: None; **A. García Martos**: None; B. Magallares: None; **G. Sada Urmeneta**: None; **C. Córdoba Martín**: None; **E. Riera Alonso**: None; **C. Bejerano-Herreria**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb (BMS), 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1549

Improvement in Joint Activity in Adults with Systemic Lupus Erythematosus Treated with Anifrolumab: Results from a Real-World Cohort

Vasileios Kyttaris[1], Dan Persons[2], Gelareh Atefi[3] and Mawuena Binka[4], [1]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, [2]Trio Health, Louisville, CO, [3]AstraZeneca, Wilmington, DE, [4]Former Employee of AstraZeneca, Wilmington, DE

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory arthritis is a cardinal manifestation of systemic lupus erythematosus (SLE), limiting joint mobility and adversely affecting quality of life.[1] Joint activity in SLE can be quantified using Tender Joint Counts and Swollen Joint Counts, providing concrete data for the evaluation of treatment effectiveness.[2] Clinical trials have shown reductions in swollen and tender joint counts in patients treated with the type I interferon inhibitor anifrolumab, compared to placebo.[3] In this study, we assess changes in inflammatory arthritis before and after anifrolumab initiation among adults with SLE receiving treatment in real-world settings.

TABLE 1: Baseline Characteristics of the Study Population

CHARACTERISTIC	STUDY POPULATION (N=54)
AGE, YEARS, MEDIAN (IQR)	53 (44-61)
SEX, N (%)	
Female	51 (94%)
Male	<3
RACE / ETHNICITY, N (%)	
Black or African American	11 (20%)
Other	19 (35%)
White	24 (44%)
US RESIDENCE, N (%)	
South	34 (63%)
West	17 (31%)
Other	<3
PAYER TYPE, N (%)	
Commercial	26 (48%)
Medicaid	8 (15%)
Medicare	8 (15%)
Other	12 (22%)
DRUG CLASSES RECEIVED WITHIN 6 MONTHS BEFORE INDEX, N (%)	
Only Antimalarials	13 (24%)
Only Biologics	5 (9%)
Only Immunosuppressants	5 (9%)
Antimalarials + Biologics	6 (11%)
Antimalarials + Immunosuppressants	7 (13%)
Biologics + Immunosuppressants	<5
Antimalarials + Biologics + Immunosuppressants	11 (20%)
No known prior treatment (Antimalarials, Biologics, or Immunosuppressants)	<5

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 2: Joint Activity within the Study Population

	Patients assessed	Swollen Joint Assessment			Tender Joint Assessment		
Period	N	Patients with inflammatory arthritis, N (%)	Mean number of active joints	SD	Patients with inflammatory arthritis, N (%)	Mean number of active joints	SD
Baseline	54	29 (54%)	2.9	4.2	37 (69%)	6.5	7.3
Period 1	54	25 (46%)	2.4	3.9	33 (61%)	5.0	6.3
Period 2	54	22 (41%)	2.2	3.9	30 (56%)	3.7	5.2

Baseline: 0-6 months pre-index; Period 1: 0-6 months post-index; Period 2: >6-12 months post-index.
Inflammatory arthritis: joint count ≥1.

TABLE 3: Joint Activity among Patients with Inflammatory Arthritis at Baseline

	Swollen Joint Assessment				Tender Joint Assessment			
	Patients with inflammatory arthritis		Number of active joints		Patients with inflammatory arthritis		Number of active joints	
	N	%	Mean	SD	N	%	Mean	SD
Baseline	29	100%	5.4	4.5	37	100%	9.5	7.1
Period 1	23	79%	4.3	4.5	32	86%	6.7	6.1
Period 2	19	66%	4.0	4.6	27	73%	5.2	5.7

Baseline: 0-6 months pre-index; Period 1: 0-6 months post-index; Period 2: >6-12 months post-index.
Inflammatory arthritis: joint count ≥1.

Methods: This retrospective, observational cohort study included data from adult patients with SLE in the American Rheumatology Network initiating anifrolumab (index date) from August 2, 2021 to May 31, 2023. Eligible patients adhered to anifrolumab, defined as having 6 or more infusions in a 12-month period. Tender and Swollen Joint Counts (28 joints) were captured during 6-month intervals: 6 months pre-index (baseline); 0-6 months post-index (follow-up Period 1); >6-12 months post-index (follow-up Period 2). All patients were required to have at least one joint count assessment performed in each of the 6-month intervals, with the result closest to the end of each interval being assessed. Inflammatory arthritis (joint activity) was defined as having Tender Joint Counts or Swollen Joint Counts ≥1.

Results: Of the 54 included participants, 94% were female and 44% white [TABLE 1]. The median age was 53 years (IQR 44-61). A declining number of patients had swollen joints (Baseline: 54%; Period 1: 46%; Period 2: 41%) and joint tenderness (Baseline: 69%; Period 1: 61%; Period 2: 56%) during the first year of anifrolumab therapy [TABLE 2]. Joint tenderness (37/54) occurred more frequently than joint swelling (29/54) at baseline [TABLE 3]. In patients experiencing joint swelling prior to initiation of anifrolumab, the mean (SD) number of swollen joints progressively decreased from 9.5 (7.1) joints per patient in the Baseline period to 5.2 (5.7) in Period 2. Similarly, in patients with joint tenderness at baseline, the mean (SD) number of tender joints decreased from 5.4 (4.5) to 4.0 (4.6) joints per patient [TABLE 3]. After at least six months of receiving anifrolumab treatment, 34% (10/29) of patients with joint swelling and 27% (10/37) of those with joint tenderness at baseline had no joint activity.

Conclusion: In this real-world cohort, patients with SLE on anifrolumab therapy had marked improvement, with reductions in both swollen and tender joints observed within six months of treatment initiation. After at least six months of receiving anifrolumab treatment, approximately one-third of patients with active inflammatory arthritis became asymptomatic. These findings contribute to the growing body of evidence supporting improvement of inflammatory arthritis with anifrolumab therapy.

1. Grossman JM. Best Pract Res Clin Rheumatol. 2009;23(4): 495-506.
2. Bell CF, et al. Rheumatol Ther. 2023;10:261–74.
3. Morand EF, et al. Lancet Rheumatol. 2022;4(4);e282-e292.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Kyttaris: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2; **D. Persons**: AstraZeneca, 5; **G. Atefi**: AstraZeneca, 3; **M. Binka**: AstraZeneca, 3.

Abstract Number: 1550

Real-World Outcomes of Anifrolumab in Systemic Lupus Erythematosus Patients at Toronto Lupus Program

Virginia Carrizo Abarza[1], Qixuan Li[2], Teresa Semalulu[3], Justin Smith[3], Pankti Mehta[4], Fadi Kharouf[5], Dafna D. Gladman[6], Laura Whitall Garcia[7] and Zahi Touma[3], [1]Toronto Western Hospital - University of Toronto, Toronto, ON, Canada, [2]Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [3]University of Toronto, Toronto, ON, Canada, [4]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [5]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [6]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [7]University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II

Session Type: Poster Session B

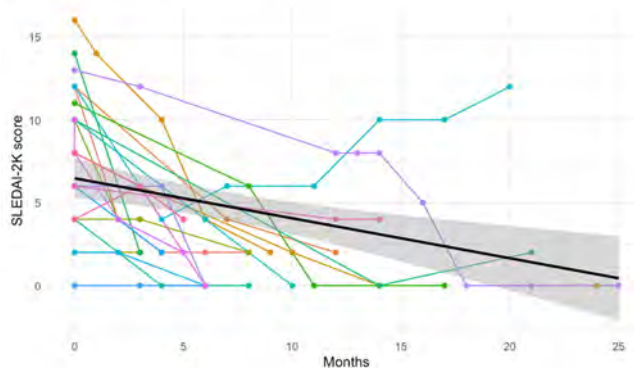
Session Time: 10:30AM–12:30PM

Background/Purpose: Anifrolumab (ANI) is a human monoclonal antibody targeting the type I interferon receptor subunit 1 (IFNAR1), blocking interferon activity and reducing disease activity in systemic lupus erythematosus (SLE). Real-world evidence is essential to understand its use and outcomes. This study aimed to describe the clinical profiles of SLE patients treated with anifrolumab for ≥3 months at the Toronto Lupus Program and to assess its efficacy and safety.

Methods: We included patients from the University of Toronto Lupus Cohort who met the 2019 EULAR/ACR classification criteria and had received anifrolumab for ≥3 months. Demographics, clinical and lab data, prior and concomitant therapies, and disease activity indices (SLEDAI-2K, CLASI, and PGA) were recorded at baseline and during follow-up. Time to symptom resolution, prednisone dose, infections, and treatment discontinuation were also assessed.

Results: Twenty-three patients (73.9% female) with a mean age of 40.4 years and mean SLE duration of 12.7 years were included. Cumulative organ involvement at anifrolumab initiation included mucocutaneous (100%), musculoskeletal (73.9%), serositis (34.8%), hematologic (34.8%), renal (30.4%), neuropsychiatric (21.7%), and persistent fever (8.7%).

Figure 1
SLEDAI-2K Scores Over Time.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The main reasons for initiating anifrolumab included skin rash (n = 20, 87.0%), musculoskeletal involvement (n = 15, 65.2%), alopecia (n = 8, 34.8%), along with the presence of concomitant hematological involvement (leukopenia) and shrinking lung syndrome. Mean follow-up was 8.4 months.

All patients were on prednisone at initiation; 82.6% were also on hydroxychloroquine. Concomitant immunosuppressives included mycophenolate (47.8%), methotrexate (17.4%), or both (4.3%). Prednisone decreased from 13.2 mg/day to 4.0 mg/day, and 69.6% discontinued it. Immunosuppressives were reduced or stopped in 52.2%. SLEDAI-2K scores decreased significantly over time (Figure 1). Median time to rash resolution was 57 days; full symptom resolution occurred in a median of 131 days.

Anifrolumab was discontinued in two patients: one after 20 months to start another biologic for lupus nephritis, and one due to refractory molluscum contagiosum after 14 months. No additional adverse events were reported.

Anifrolumab demonstrated significant effectiveness in reducing disease activity and corticosteroid use in SLE, with a favorable safety profile.

Conclusion: Anifrolumab demonstrated significant effectiveness in reducing disease activity and corticosteroid use in SLE, with a favorable safety profile.

Disclosure: V. Carrizo Abarza: None; **Q. Li**: None; **T. Semalulu**: None; **J. Smith**: None; **P. Mehta**: None; **F. Kharouf**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Whitall Garcia**: None; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2.

Abstract Number: 1551

Disease Burden and Treatment Preferences for Systemic Lupus Erythematosus: Results from a Global Real-World Survey

Zahi Touma[1], Christopher Saffore[2], Karim Masri[3], Jerry Clewell[3], Emily Goddard[4], Grace O'Neill[4], Madelane Foxall[4] and Karen H. Costenbader[5], [1]University of Toronto, Toronto, ON, Canada, [2]AbbVie Inc., waukegan, IL, [3]AbbVie Inc., North Chicago, IL, [4]Adelphi Real World, Bollington, United Kingdom, [5]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: As new treatment options for systemic lupus erythematosus (SLE) become available, understanding patient burden and preferences is key to optimizing shared decision-making. This study evaluated patient burden and physician/patient treatment preferences through a global real-world survey.

Methods: Data were drawn from the 2024 Adelphi Lupus Disease Specific Programme™, a cross-sectional survey with retrospective data collection of rheumatologists and their patients with SLE in Germany, Italy, Spain and the US from Jul 2024 – Jan 2025; physicians provided data for their next 6 consulting patients with SLE. Physicians reported patient demographics, clinical characteristics (including SLE Disease Activity Index [SLEDAI]), and treatment preferences. Patients self-reported

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographics and clinical characteristics of patients with SLE across the US and Europe collected from the 2024 Adelphi Lupus Disease Specific Programme™ – all data physician reported unless otherwise specified

	Overall (n = 1194)
Age (years), mean (SD)	43.3 (13.7)
Female, n (%)	1007 (84)
Region, n (%)	
Europe [1]	630 (53)
US	564 (47)
Race/Ethnicity, n (%)	
White	864 (72)
Black or African American/African or Caribbean	197 (16)
Other	135 (11)
Hispanic, Latin or Spanish origin (US only patients), n (%) *(n=564)*	
Yes	93 (11)
No	500 (89)
Don't know	1 (<1)
Disease duration (years), median (IQR) *(n=1051)*[1]	2.8 (1.1, 6.6)
Time since onset of SLE symptoms (years), median (IQR) *(n=853)*[1]	3.8 (1.6, 8.3)
SLEDAI Score, n (%)	
0 no activity	360 (30)
1-5 mild	188 (16)
6-10 moderate	238 (20)
>10 severe	408 (34)
Current treatment, n (%)	
Anti-malarials	389 (70)
Immunosuppressants	264 (47)
Steroids	438 (37)
Belimumab	275 (23)
IV	*64 (23)*
SC	*211 (77)*
Anifrolumab	83 (7)
Rituximab	45 (4)
Top 5 current symptoms, n (%)	
Joint tenderness	584 (49)
Fatigue	540 (45)
Joint stiffness	373 (31)
Photosensitivity	324 (27)
Malar / Butterfly rash	238 (20)
Top 5 organ(s) / area(s) of the body currently actively involved, n (%)	
Musculoskeletal	765 (64)
Constitutional (e.g. fatigue, fever, weight change)	684 (57)
Mucocutaneous	674 (56)
Neuropsychiatric	240 (20)
Renal	213 (18)
(Patient reported) FACIT-Fatigue, mean (SD) *(n=363)*[1]	36.3 (10.5)
(Patient reported) FACIT-Fatigue, n (%)	
No/mild fatigue (>40)	141 (39)
Moderate fatigue (30-40)	127 (35)
Severe fatigue (<30)	95 (26)

[1]*Indicates variation in sample sizes due to exclusion of unknown data*

Abbreviations: FACIT – functional assessment of chronic illness therapy, IQR – interquartile range, IV – intravenous, SC – subcutaneous, SD – standard deviation, SLEDAI – systemic lupus erythematosus disease activity index

[1] Europe in this study is represented by Germany, Italy, and Spain.

treatment preferences for their SLE and quality of life via the Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-Fatigue). Patients and physicians rated their preference for four treatment modes including an oral pill once or twice per day, self-administered subcutaneous (SC) injection every week, or intravenous [IV] injection every 4 weeks. All analyses were descriptive.

Results: Overall, 176 physicians across the US (n=71) and Europe (n=105) reported data for 1,194 patients of which 47% were from the US and 53% from Europe. Patients' mean (SD) age was 43.3 (13.7), 72% were White, 84% female, with a median (IQR) disease duration of 2.8 (1.1, 6.6) years **(Table 1)**. Most patients (54%) had moderate/severe disease activity as defined by a SLEDAI score >6. The most reported organs affected were musculoskeletal (64%), constitutional (57%) and mucocutaneous (56%). Joint tenderness (49%), fatigue (45%), and joint stiffness (31%) were the most prevalent symptoms; 61% of patients reported moderate or severe fatigue via FACIT-Fatigue. Current treatment with injectable biologics at data collection included 23% on belimumab, 7% on anifrolumab, and 4% on rituximab. Physician-reported reasons for initiation of patient's current treatment were overall efficacy (99%), safety (55%), treatment administration (39%), quality of life (38%), and cost (23%) **(Figure 1a)**. When asked to choose among the four administration modes, a once daily oral pill was most preferred by both patients and physicians: 60% of patients and 77% of physicians respectively **(Figure 1b, Figure 1c)**. An oral pill twice daily was the least preferred option by both patients and physicians, but following this option

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Physician and Patient Treatment Preferences for SLE across the US and Europe collected from the 2024 Adelphi Lupus Disease Specific Programme™

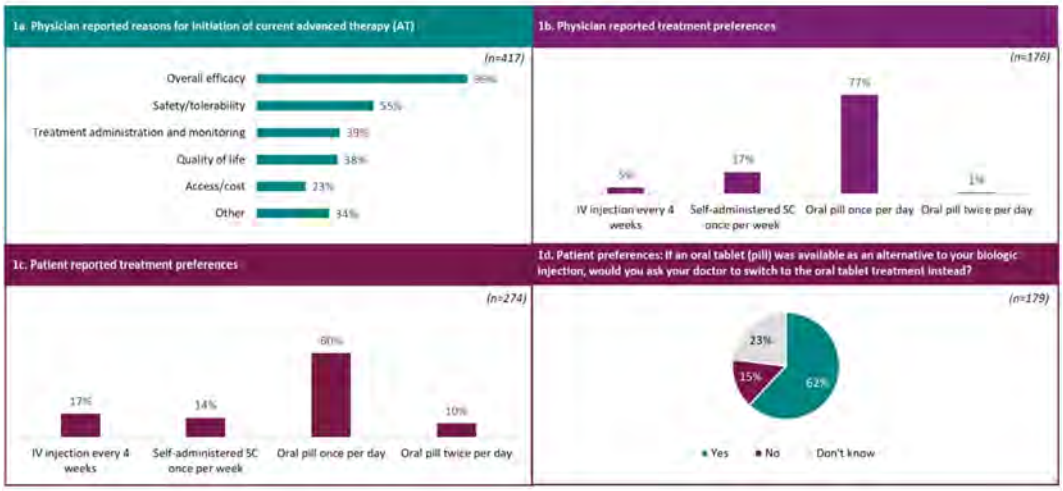


Figure 1a is derived from the physician reported patient sample, 1b is derived from the physician survey sample pertaining to physician perceptions and behaviors around SLE treatment and management, and figures 1c and 1d are derived from the patient reported sample.

there was some discordance with patients more likely to choose the every-4-week IV injection where physicians chose the weekly SC injection. There were 62% of patients who indicated they would ask their doctor to switch to an oral pill if one was available as an alternative to their biologic injection **(Figure 1d)**.

Conclusion: Despite the availability of injectable advanced treatments, patients with SLE continue to have a high disease burden. Overall efficacy, safety, and treatment administration were reported as key reasons for treatment choice by SLE treating physicians. A once-daily oral pill was the preferred route and frequency of administration by both physicians and patients. These findings may help optimize shared decision-making in SLE.

Disclosure: Z. Touma: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **C. Saffore**: AbbVie, 3, 11; **K. Masri**: AbbVie, 3, 11; **J. Clewell**: AbbVie, 3, 11; **E. Goddard**: Adelphi Real World, 3; **G. O'Neill**: Adelphi Real World, 3; **M. Foxall**: Adelphi Real World, 3; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 1552

Treatment With Anifrolumab Prevents Long-Term Cardiovascular Damage Accrual Compared With Real-World Standard of Care in Patients With Systemic Lupus Erythematosus: Findings From the LASER Study

Zahi Touma[1], Ian Bruce[2], Richard Furie[3], Eric Morand[4], Raj Tummala[5], Shelly Chandran[6], Gabriel Abreu[7], Jacob Knagenhjelm[7], Cathy Emmas[8], Lyra Agustin[8], Alessandra Venerus[9], Tarana Mehdikhanova[10], Zheyuan Yang[10] and Miina Waratani[8], [1]University of Toronto, Toronto, ON, Canada, [2]Centre for Public Health, Faculty of Medicine, Health and Life Sciences, Queen's University, Belfast, Manchester, United Kingdom, [3]Division of Rheumatology, Northwell Health, Great Neck, NY, [4]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [5]AstraZeneca, BioPharmaceuticals R&D, Gaithersburg, Gaithersburg, MD, [6]AstraZeneca, Medical & Scientific Affairs, R&I, Mississauga, ON, Canada, [7]AstraZeneca, BioPharmaceuticals R&D, Gothenburg, Sweden, [8]AstraZeneca,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

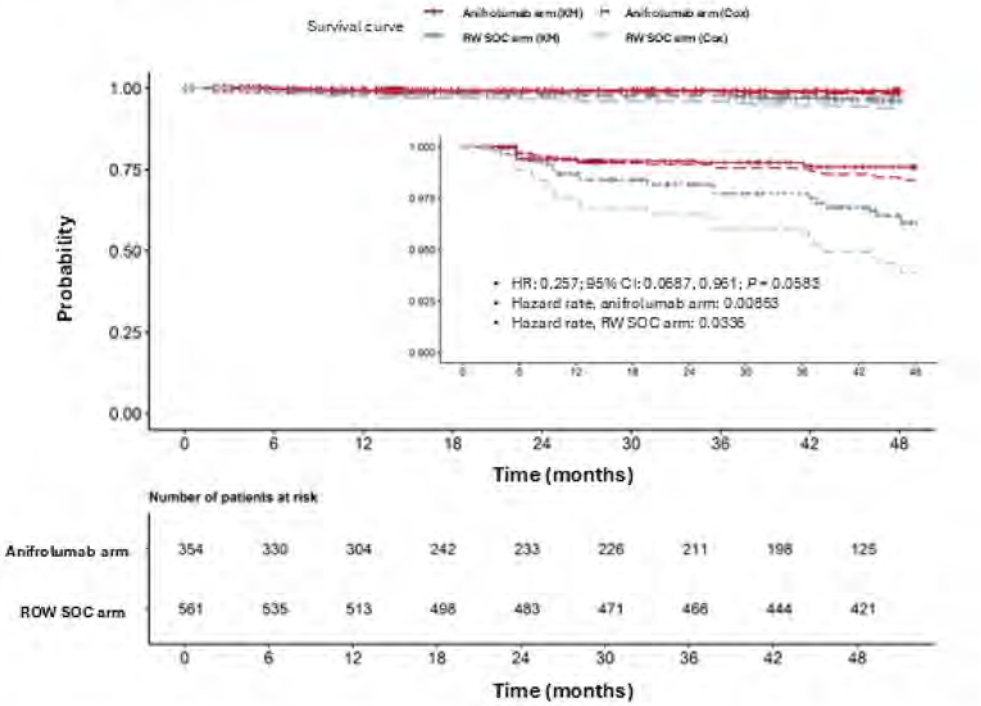
BioPharmaceuticals Medical, Cambridge, United Kingdom, [9]IQVIA, EMEA Real World Methods and Evidence Generation, Milan, Italy, [10]IQVIA, EMEA Real World Methods and Evidence Generation, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1517–1552) Systemic Lupus Erythematosus – Treatment Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) can develop cardiovascular (CV) damage (angina, myocardial infarction, ventricular dysfunction, valvular disease, or pericarditis for 6 months/pericardiectomy) particularly in patients with uncontrolled disease activity, flares, or under long-term glucocorticoid use. The Treatment of Uncontrolled Lupus via the Interferon Pathway (TULIP) trials and long-term extension (LTE) study demonstrated that anifrolumab can control disease activity and reduce the need for glucocorticoid use. However, evaluation of the long-term effects of anifrolumab on CV damage remains limited by patient attrition in the placebo arm and clinical trial duration. The purpose of this analysis—the Long-Term Organ Damage: Anifrolumab versus Real-World Standard of Care in Adult Patients with Active SLE (LASER; NCT06485674)—was to (1) assess the mean CV damage accrual at 4 years, and (2) estimate time to first CV event up to 4 years of therapy in adult patients with moderately to severely active SLE treated with anifrolumab or real-world standard of care (RW SOC).

Figure 1. Time to first cardiovascular event from the index date[a]



HR and hazard rates reported in **Figure 1** refer to the effect estimates by the Cox model, with the hazard rate in each arm averaged across the observed period. The Cox regression model for SMRW (untreated) + IPCW was further adjusted for SLEDAI score and proteinuria level at the index date, as these variables remained unbalanced after weighting (i.e., SMD >0.2).

[a]Restricted mean survival time, and minimum and maximum survival times, were derived while accounting for the combined SMRW + IPCW weights (i.e., the raw survival times were weighted). Hence, some extreme weighted values are beyond the 48 months of observed time.

HR, hazard ratio; **IPCW**, inverse probability of censoring weighting; **KM**, Kaplan–Meier; **RW SOC**, real-world standard of care; **SDI**, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; **SLEDAI**, Systemic Lupus Erythematosus Disease Activity Index; **SMD**, standardized mean difference; **SMRW**, standardized mortality ratio weighting.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Change in cardiovascular SDI from baseline to year 4

Estimand	Type of regression analysis	Method	Parameter	TULIP cohort	UTLC cohort	Mean difference of change in SDI between groups	95% CI	Robust SE	P-value
Main analysis									
ATC	Linear regression[a]	SMRW (untreated) + IPCW[b]	N	354	561	−0.046	−0.074, −0.018	0.014	0.008
			Mean change in SDI	0.005	0.045				
			Robust SE	0.004	0.013				
			95% CI	−0.002, 0.013	0.021, 0.071				
Sensitivity analysis									
ATT	Linear regression	SMRW (untreated) + IPCW[c]	N	354	561	−0.063	−0.119, −0.007	0.029	0.001
			Mean change in SDI	0.013	0.076				
			Robust SE	0.009	0.027				
			95% CI	−0.005, 0.031	0.023, 0.129				
ATO	Linear regression	PSM[d]	N	110	110	−0.036	−0.096, 0.010	0.024	0.161
			Mean change in SDI	0.017	0.036				
			Robust SE	0.012	0.021				
			95% CI	−0.007, 0.041	0.014, 0.097				

To account for the impact of informative censoring, IPCW was utilized. Censoring weights were calculated from the ratio of stabilized censoring probability to censoring probability.

[a]The linear regression model for SMRW (untreated) + IPCW was further adjusted for SLEDAI score and proteinuria level at the index date, as these variables remained unbalanced after weighting (i.e., SMD > 0.2).

[b]Treatment weights were calculated using SMRW method, with the UTLC cohort as the target population (ATC) for the main analysis (SMRW [untreated] + IPCW).

[c]Treatment weights were calculated using SMRW method, with the TULIP cohort as the target population (ATT) for the sensitivity analysis (SMRW (treated) + IPCW).

[d]The PSM method was applied to estimate ATO in patients with ≥208 weeks of follow-up. Nearest-neighbor matching with replacement was applied to estimate propensity scores within a caliper value defined as 20% of the standard deviation for the distribution of the propensity score variable in the full sample.

ATC, average treatment effect in the control population; **ATO**, average treatment effect in the overlap population; **ATT**, average treatment effect in the treated population; **CI**, confidence interval; **IPCW**, inverse probability of censoring weighting; **PSM**, propensity score matching; **SDI**, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; **SE**, standard error; **SLEDAI**, Systemic Lupus Erythematosus Disease Activity Index; **SMD**, standardized mean difference; **SMRW**, standardized mortality ratio weighting; **TULIP**, Treatment of Uncontrolled Lupus via the Interferon Pathway; **UTLC**, University of Toronto Lupus Clinic.

Table 2. Description of time to first cardiovascular event from index date

Time	Parameters	TULIP[a]	UTLC[a]
Total	Number of patients	354	561
	Number of events	5	17
	Number of censored patients	348	544
	Restricted mean (SE)[b]	51.21 (146.18)	42.39 (15.57)
	Median	Not reached	Not reached
	Q1–Q3	N/A–N/A	N/A–N/A
	Minimum–Maximum[b]	0.0564–1888.99	0.0518–149.47
6 months	Number of patients	330	535
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	1.00 (0.99, 1.00)
12 months	Number of patients	304	513
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.99 (0.98, 1.00)
18 months	Number of patients	242	498
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.98 (0.97, 1.00)
24 months	Number of patients	233	483
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.98 (0.97, 0.99)
30 months	Number of patients	226	471
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.98 (0.96, 0.99)
36 months	Number of patients	211	456
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.98 (0.96, 0.99)
42 months	Number of patients	198	444
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.97 (0.96, 0.99)
48 months	Number of patients	125	421
	Probability[c] (95% CI)	0.99 (0.98, 1.00)	0.96 (0.95, 0.98)

[a]Administrative censoring at 4 years post-index was applied to both cohorts for comparability of follow-up periods.

[b]Restricted mean survival time, and minimum and maximum survival times, were derived while accounting for the combined SMRW + IPCW weights (i.e., the raw survival times were weighted). Hence, some extreme weighted values are beyond the 48 months of observed time.

[c]Kaplan–Meier estimates of survival probability were produced based on a weighted population using SMRW and IPCW (ATC estimand). The number of patients/events in the life table is reported as per observed data (i.e., without weighting applied).

ATC, average treatment effect in the control population; **CI**, confidence interval; **IPCW**, inverse probability of censoring weighting; **N/A**, not applicable; **Q**, quartile; **SE**, standard error; **SMRW**, standardized mortality ratio weighting; **TULIP**, Treatment of Uncontrolled Lupus via the Interferon Pathway; **UTLC**, University of Toronto Lupus Clinic.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This analysis used an external control arm of patients who received RW SOC from the University of Toronto Lupus Clinic (UTLC). Patients assigned to anifrolumab 300 mg in the TULIP-1 and -2 trials were included in the anifrolumab arm (n = 354). Patients from the UTLC registry (n = 561) with matching eligibility criteria comprised the RW SOC arm. Baseline confounding and possible informative loss to follow-up were accounted for using propensity scores (PS) and inverse probability censoring weights, respectively. Fourteen known predictors of CV damage were included in the PS models, and predictors that appeared imbalanced after PS weighting (e.g., standardized mean difference ≥ 0.2) were included as independent covariates in the outcome model. Mean changes in CV-related Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) from baseline to year 4 were estimated using weighted linear regression models in the average treatment effect in the control (ATC), treated (ATT), and overlap (ATO) groups. Time to first CV event up to 4 years was assessed using Kaplan–Meier estimators and a Cox proportional hazards regression model.

Results: Baseline patient characteristics were adequately balanced after PS weighting. Patients in the anifrolumab arm accrued (on average) 0.046 fewer CV SDI points (95% confidence interval [CI]: –0.074, –0.018; $P = 0.008$) at 4 years compared with patients in the RW SOC arm (**Table 1**). Results were consistent across ATC and ATT groups. A total of 6 patients in the anifrolumab arm vs 17 patients in the RW SOC arm experienced CV events (**Table 2**). Patients in the anifrolumab arm were 74.3% less likely to experience a CV event over 4 years compared to patients in the RW SOC arm (hazard ratio, 0.257; 95% CI: 0.0687, 0.961; $P = 0.0583$; **Figure 1**).

Conclusion: Patients who received anifrolumab in the TULIP trials and LTE accumulated less CV damage at 4 years compared with patients who received RW SOC in an external control arm. These results support the added benefit of anifrolumab to RW SOC in preventing long-term CV organ damage in patients with moderately to severely active SLE.

Disclosure: Z. Touma: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **I. Bruce**: AstraZeneca, 2, 5, 6, BMS, 2, Cabaletta Bio, 2, GSK, 2, 5, 6, Janssen, 5, 6, Lilly, 2, Novartis, 5, Otsuka, 5, UCB, 2; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **R. Tummala**: AstraZeneca, 3; **S. Chandran**: AstraZeneca, 3, 11; **G. Abreu**: AstraZeneca, 3; **J. Knagenhjelm**: AstraZeneca, 3, 11; **C. Emmas**: AstraZeneca, 3, 11; **L. Agustin**: AstraZeneca Pharmaceuticals, 3, 11; **A. Venerus**: None; **T. Mehdikhanova**: None; **Z. Yang**: AstraZeneca, 2; **M. Waratani**: AstraZeneca, 3.

Abstract Number: 1553

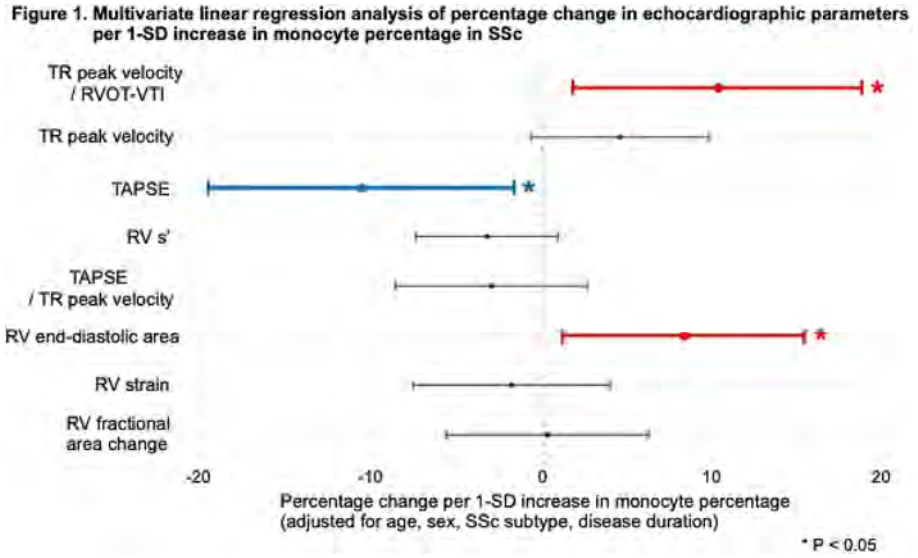
Circulating Monocyte Level Is Associated With Pulmonary Vascular Disease and Right Ventricular Dysfunction in Systemic Sclerosis

Ai Yaku[1], Bong Joon Kim[2], Hidenori Yaku[1], Carrie Richardson[2], Michael Cuttica[2], Ruben Mylvaganam[2], Vera Rigolin[2], Matthew Feinstein[2] and Sanjiv Shah[1], [1]Northwestern University, Chicago, IL, [2]Northwestern University, Chicago

SESSION INFORMATION

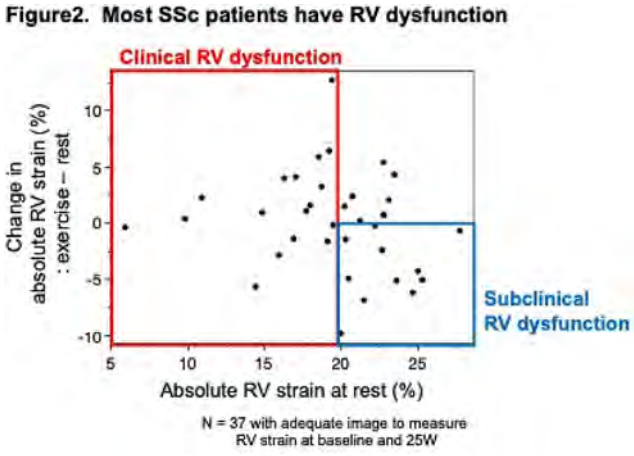
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Background/Purpose: Pulmonary arterial hypertension associated with systemic sclerosis (SSc-PAH) is a life-threatening condition with obliterative pulmonary vascular remodeling, right ventricular (RV) dysfunction, and poor prognosis. Despite therapeutic advances, SSc-PAH remains a critical unmet clinical need due to its complex pathophysiology and lack of effective treatments. Chronic inflammation and immune dysregulation are believed to play a pivotal role in disease progression, but specific immune mechanisms remain poorly understood. Early detection of pulmonary hypertension (PH) and RV dysfunction is also a major challenge in clinical practice. To address this, we employed exercise echocardiography to unmask early RV dysfunction and PH and sought to elucidate the relationship between circulating immune subsets and PH and RV dysfunction severity in patients with SSc.

Methods: We prospectively enrolled 96 participants: 41 SSc-PH patients, 23 SSc-nonPH patients, 15 idiopathic PAH patients, and 17 age- and sex-matched controls. All participants underwent resting and exercise echocardiography, 6-minute walk test, electrocardiography, clinical assessments, and blood tests. We evaluated associations between immune cell subsets in peripheral blood and echocardiographic parameters of PH severity and RV function both at rest and during exercise, using univariate and multivariate linear regression models adjusted for age, sex, SSc subtype, and disease duration.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Immune cell subset distributions did not differ significantly among the groups. However, increased monocyte percentage in SSc patients was associated with greater RV end-diastolic area, higher tricuspid regurgitation velocity peak velocity (TRV)/RV outflow tract velocity time integral (RVOT-VTI) which is an echo estimate of total pulmonary resistance, and reduced tricuspid annular plane systolic excursion (TAPSE)/TRV ratio which is an indicator of worse RV-pulmonary arterial coupling (**Figure 1**). These associations remained significant after adjustment for covariates. Exercise echocardiography revealed that most SSc patients (81%) had RV dysfunction, including subclinical RV dysfunction (change in absolute RV strain from rest to exercise [ΔRV strain] < 0) or clinical RV dysfunction (absolute resting RV strain < 20%) (**Figure 2**). Notably, higher monocyte percentage was associated with worse RV contractile reserve (ΔRV strain from rest to 25W exercise): multivariable β = -1.71, 95% CI: -3.31 to -0.113, p = 0.037.

Conclusion: Increased levels of circulating monocytes are associated with greater PH severity and RV dysfunction in SSc. Dysregulation of the innate immune system potentially links cardiopulmonary dysfunction/remodeling in SSc.

Disclosure: A. Yaku: None; **B. Kim**: None; **H. Yaku**: None; **C. Richardson**: Cabaletta Bio, 2; **M. Cuttica**: None; **R. Mylvaganam**: Janssen, 2, Roivant Sciences, 2, United Therapuetics, 2, 6; **V. Rigolin**: Amgen, 11, AstraZeneca, 11, Bristol-Myers Squibb(BMS), 11, Edwards Lifesciences, 11, Merck/Schering Plough, 11, Pfizer, 11, Regeneron, 11, Viatris, 11; **M. Feinstein**: None; **S. Shah**: None.

Abstract Number: 1554

Demographic, Clinical, and Mortality Trends in Scleroderma Patients with Gastric Antral Vascular Ectasia (GAVE): A National Inpatient Analysis

Akanksha Sharma[1], Veera Durga Vaishnavi Kurra[2] and Neev Mehta[3], [1]UPMC Mercy hospital, Pittsburgh, PA, Pittsburgh, PA, [2]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [3]Lahey Hospital and Medical Center, Burlington, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Gastric antral vascular ectasia (GAVE), commonly known as "watermelon stomach," is a rare but potentially severe gastrointestinal manifestation in systemic sclerosis (SSc). Despite its known association with SSc, data regarding demographic patterns, comorbidity profiles, and inpatient mortality among this subset remain limited. This study aimed to analyze the factors associated with GAVE in hospitalized SSc patients, including age, sex, comorbidities, and mortality, using a national inpatient dataset.

Methods: A retrospective cohort study was conducted using an extensive national inpatient database to identify patients with scleroderma, stratifying them by the presence or absence of GAVE. Patient demographics, comorbidities, and inpatient mortality were compared using logistic regression and descriptive statistics. Odds ratios (ORs), standard errors, 95% confidence intervals (CIs), and p-values were reported to assess statistical significance.

Results: Among 152,971 hospitalized SSc patients, 24,451 (1.62%) had a diagnosis of GAVE. Patients with GAVE were older (mean age 68.9 vs. 63.4) and predominantly female. There were no statistically significant sex-based differences in GAVE prevalence (p=0.7498), but racial differences were significant (p=0.0002), with White and Asian patients more commonly affected. Several comorbidities were significantly associated with GAVE in SSc, including chronic kidney disease

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Logistic Regression of In-Hospital Mortality in Scleroderma Patients

Table 1. Logistic Regression of In-Hospital Mortality in Scleroderma Patients

Variable	Odds Ratio	Standard Error	p-value	95% Confidence Interval	Interpretation
Age	1.01	0.00	0.000	1.01 1.02	Increased age associated with higher mortality
Female (vs Male)	0.74	0.05	0.000	0.65 – 0.85	Female sex protective
COPD	1.20	0.08	0.003	1.07 – 1.38	Higher mortality with COPD
Diabetes Mellitus	1.00	0.073	0.950	N/A	No significant effect
Obesity	0.70	0.066	0.000	0.59 – 0.86	Protective effect
Acute Kidney Injury (AKI)	4.10	0.29	0.000	3.77 – 4.67	Strong association with mortality
Chronic Kidney Disease (CKD)	1.56	0.108	0.000	1.36 – 1.79	Increased mortality risk
Hypertension	0.50	0.035	0.000	0.44 – 0.58	Protective effect
Coronary Artery Disease	1.07	0.69	0.265	0.95 1.22	Not significant
Cancer	1.00	0.73	0.990	0.24 – 4.18	Not significant
Myositis	0.67	0.159	0.083	0.41 – 1.05	Not significant
Heart Failure	2.28	1.12	0.000	2.05 – 2.50	Strong predictor of mortality
Myocarditis	2.40	1.06	0.043	1.02 – 5.70	Significant association
Pulmonary Hypertension	1.70	0.386	0.020	1.09 – 2.65	Significant association
Pulmonary Fibrosis	1.60	0.125	0.000	1.40 1.90	Significant association
GERD	0.58	0.033	0.000	0.52 – 0.65	Protective effect
GAVE	0.90	0.203	0.650	0.58 – 1.40	Not significant

(CKD) (p=0.0000), coronary artery disease (p=0.0000), heart failure (p=0.0000), pulmonary fibrosis (p=0.0064), and GERD (p=0.0025).

Table 2. Prevalence of Comorbidities in Scleroderma Patients

Table 2. Prevalence of Comorbidities in Scleroderma Patients

Comorbidity	Present	(N. %)	95% CI	Absent (N. %)	95% CI
COPD	29,281	(19.41%)	18.91–19.93	121,652 (80.58%)	80.07–81.09
Diabetes Mellitus	25,055	(16.56%)	16.11–17.03	125,860 (83.43%)	82.97–83.89
Obesity	16,602	(11.03%)	10.65–11.43	134,332 (88.96%)	88.57–89.35
Acute Kidney Injury	32,753	(21.71%)	21.24–22.21	118,182 (78.28%)	77.79–78.76
Chronic Kidney Disease	20,225	(13.36%)	12.92–13.82	130,709 (86.63%)	86.18–87.08
Hypertension	46,035	(30.54%)	29.99–31.11	104,900 (69.45%)	68.88–70.01
Coronary Artery Disease	33,507	(22.22%)	21.72–22.75	117,427 (77.78%)	77.25–78.28
Cancer	150	(0.13%)	0.10–0.19	150,784 (99.86%)	99.81–99.90
Myositis	2,837	(1.87%)	1.72–2.05	148,067 (98.12%)	97.95–98.28
Heart Failure	48,450	(32.12%)	31.51–32.73	102,485 (67.88%)	67.27–68.49
Myocarditis	302	(0.19%)	0.14–0.25	150,633 (99.81%)	99.75–99.86
Pulmonary Hypertension	1,358	(0.90%)	0.79–1.02	149,577 (99.10%)	98.98–99.21
Pulmonary Fibrosis	15,546	(10.26%)	9.88–10.65	135,389 (89.74%)	89.36–90.12
Polyarthritis	302	(0.17%)	0.13–0.23	150,633 (99.83%)	99.78–99.87
GERD	70,185	(46.54%)	45.87–47.21	80,750 (53.46%)	52.79–54.13
GAVE	24,451	(1.62%)	1.48–1.78	148,520 (98.38%)	98.22–98.52

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Comparison of Scleroderma Patients With and Without GAVE

Table 3. Comparison of Scleroderma Patients With and Without GAVE

Variable	With GAVE (N)	Without GAVE (N)	p-value
Demographics			
Male	3,751	20,700	0.7498
Female	20,710	3,741	—
Mean Age	68.9	63.4	—
Race			0.0002
White	18,265	16,333	
African-American	2,029	3,790	
Asian	3,301	3,032	
American Indian/Alaska Native	416	5,184	
Native Hawaiian/Pacific Islander	48	222	
Multiple Categories Reported	406	536	
Comorbidities			
COPD	5,648	18,803	0.0536
Diabetes Mellitus	4,010	20,441	0.9088
Obesity	2,298	22,152	0.2556
AKI	5,942	18,509	0.1631
CKD	6,101	18,350	0.0000
Hypertension	6,499	17,952	0.0597
Coronary Artery Disease	7,401	17,050	0.0000
Cancer	0	24,451	0.4132

Logistic regression for inpatient mortality in SSc patients revealed increasing age was a significant risk factor (OR 1.01, CI 1.01–1.02, p< 0.001). Male sex (OR 1.35) and African American race did not significantly impact mortality. AKI (OR 4.1), CKD (OR 1.56), heart failure (OR 2.28), myocarditis (OR 2.4), pulmonary hypertension (OR 1.7), and pulmonary fibrosis (OR 1.6) were all independently associated with increased inpatient mortality. Interestingly, obesity (OR 0.7), hypertension (OR 0.5), and GERD (OR 0.58) appeared to be protective. GAVE itself was not significantly associated with mortality (OR 0.9, CI 0.58–1.4, p=0.65).

Conclusion: This national inpatient analysis highlights significant demographic and comorbidity trends in SSc patients with GAVE. While GAVE is associated with distinct clinical features and comorbidities, it was not independently linked to an increase in inpatient mortality. Instead, traditional predictors such as AKI, heart failure, and pulmonary complications played a more prominent role in poor outcomes. Understanding these patterns may guide risk stratification and improve multidisciplinary care strategies in scleroderma.

Disclosure: A. Sharma: None; **V. Kurra**: None; **N. Mehta**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1555

Prevalence of Organ Involvement and Baseline Predictors of Disease Progression in Patients with Limited Cutaneous Systemic Sclerosis: Insights from the CONQUER Database

Alain Lescoat[1], Virginia Steen[2], Monica Harding[3], John VanBuren[3], Brian Skaug[4], Shervin Assassi[5], Maureen Mayes[6], Zsuzsanna McMahan[7], Elana Bernstein[8], Flavia Castelino[9], Lorinda Chung[10], Luke Evnin[11], Tracy Frech[12], Jessica Gordon[13], Faye Hant[14], Laura Hummers[15], Kimberly Lakin[13], Dorota Lebiedz-Odrobina[3], Yiming Luo[16], Ashima Makol[17], Jerry Molitor[18], Duncan Moore[19], Carrie Richardson[19], Nora Sandorfi[20], Ami Shah[15], Ankoor Shah[21], Elizabeth Volkmann[22], Carleigh Zahn[23] and Dinesh Khanna[24], [1]CHU Rennes - University Rennes, Rennes, France, [2]Georgetown University School of Medicine, Washington, DC, [3]University of Utah, Salt Lake City, UT, [4]UTHealth Houston Division of Rheumatology, Houston, TX, [5]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [6]UT Health Houston Division of Rheumatology, Houston, TX, [7]UT Health Houston, Houston, TX, [8]Columbia University Irving Medical Center, New York, NY, [9]Massachusetts General Hospital, Boston, MA, [10]Stanford University, Stanford, CA, [11]Scleroderma Research Foundation, San Francisco, CA, [12]Vanderbilt University Medical Center, Nashville, TN, [13]Hospital for Special Surgery, New York, NY, [14]Medical University of South Carolina, Charleston, SC, [15]Johns Hopkins Rheumatology, Baltimore, MD, [16]Columbia University Irving Medical Center, New York, [17]Mayo Clinic, Rochester, MN, [18]University of Minnesota, Minneapolis, MN, [19]Northwestern University, Chicago, [20]University of Pennsylvania, Philadelphia, PA, USA, Philadelphia, [21]Duke University, Durham, NC, [22]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA, [23]University of Michigan, Ann Arbor, [24]University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is characterized by a wide range of clinical manifestations and available interventions still lack overall efficacy. Limited cutaneous SSc (lcSSc) and sine scleroderma constitute more than 60% of all SSc patients. Despite this high prevalence, there is a lack of high quality randomized controlled trials conducted for lcSSc. Acquiring high quality data on the natural history of early lcSSc will help design trials with a higher probability of success. CONQUER is a multicenter US-based cohort of patients with early SSc (less than 5 years after first non-Raynaud (RP) symptom), uniquely allowing assessment of the early phases of SSc.

This analysis of CONQUER aimed to describe the prevalence of organ involvement in lcSSc patients and to define the onset of key scleroderma manifestations during follow-up. Baseline characteristics predicting disease progression were also identified.

Methods: All patients from the CONQUER multicenter US cohort with physician diagnosed sine scleroderma or lcSSc at baseline were included. Patients were defined as progressors if they experienced one or more of the following events: New renal crisis, Interstitial Lung disease (ILD) progression (relative loss of ≥15% of FVC as compared to first available FVC or onset of FVC less than 80% with ILD), onset of heart failure (LVEF≤40%), pulmonary arterial hypertension on right heart catheterization, gastrointestinal dysmotility requiring enteral or parenteral nutrition, digital ulcer (DU) or gangrene, or death.

Results: 275 patients were included, with a mean (SD) disease duration of 2.6 (1.39) years since first non-RP and 6.2 (8.51) years since RP. Baseline manifestations included: active digital ulcers in 29.5%, ILD in 34.9%, SSc-related cardiac involvement in 12.4% and renal crisis in 1.5%. Only 14 patients (5%) were identified as progressors in the first 12 month of follow-up. Twenty-nine patients (11%) were identified as progressors in the first 24 months of follow-up. The main reasons

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of baseline characteristics between progression and non-progressors after 24 months of follow-up

	Progressor within 24 months of baseline			
	Non-progressors (N = 246)	Progressors (N = 29)	Odds ratio (95% CI)	P-value
Age (years) at baseline visit	52.9 (13.67)	52.7 (14.84)	1.00 (0.97, 1.03)	0.94
Sex				0.90
Male	36 (14.6%)	4 (13.8%)	0.93 (0.26, 2.58)	
Female	210 (85.4%)	25 (86.2%)	Reference	
Non-Hispanic White	184 (74.8%)	25 (86.2%)	2.04 (0.75, 7.13)	0.17
ANA/Autoantibody classification				0.07
Centromere	88 (35.8%)	6 (20.7%)	Reference	
SCL 70	55 (22.4%)	12 (41.4%)	3.20 (1.17, 9.65)	
Other	82 (33.3%)	9 (31%)	1.61 (0.56, 4.99)	
Raynaud's phenomenon as first symptom	188 (76.4%)	24 (82.8%)	1.48 (0.58, 4.55)	0.43
Disease duration from date of first Raynaud's symptom to baseline visit (years)	6.1 (8.33)	7.1 (10.06)	1.01 (0.97, 1.05)	0.56
Disease duration from date of first non-Raynaud's symptom to baseline visit (years)	2.6 (1.37)	3.0 (1.54)	1.21 (0.91, 1.62)	0.19
Disease duration from date of earliest SSc symptom (Raynaud's or non-Raynaud's) to baseline visit (years)	6.1 (8.12)	7.0 (9.92)	1.01 (0.96, 1.05)	0.62
C-reactive protein (CRP) (mg/dL)	1.8 (3.83)	1.8 (2.51)	1.00 (0.84, 1.11)	0.98
Baseline skin thickening	230 (93.5%)	28 (96.6%)	1.95 (0.37, 35.80)	0.49
Hand swelling/Puffy fingers	195 (79.3%)	19 (65.5%)	0.50 (0.22, 1.17)	0.11
Baseline finger involvement	228 (92.7%)	28 (96.6%)	2.21 (0.43, 40.50)	0.40
Baseline telangiectasia	147 (59.8%)	20 (69.0%)	1.65 (0.72, 4.12)	0.24
Baseline digital gangrene	10 (4.1%)	2 (6.9%)	1.80 (0.27, 7.31)	0.49
Baseline active digital ulcers	71 (28.9%)	10 (34.5%)	1.35 (0.58, 3.03)	0.48
Baseline calcinosis	9 (3.7%)	2 (6.9%)	2.00 (0.29, 8.29)	0.42
Baseline reflux	94 (38.2%)	11 (37.9%)	0.98 (0.42, 2.23)	0.97
Baseline GI symptoms (other than reflux)	146 (59.3%)	17 (58.6%)	0.96 (0.42, 2.34)	0.92
Baseline joint involvement	58 (23.6%)	7 (24.1%)	1.06 (0.40, 2.52)	0.90
Baseline Dyspnea (NYHA) Class II, III, or IV	82 (33.3%)	17 (58.6%)	3.05 (1.38, 7.01)	0.006
Baseline ILD diagnosis	78 (31.7%)	18 (62.1%)	4.10 (1.45, 14.69)	0.007
Baseline FVC % predicted < 80%	52 (21.1%)	12 (41.4%)	2.44 (1.06, 5.46)	0.04
FVC % predicted	91.5 (17.44)	78.7 (22.33)	0.96 (0.94, 0.98)	<0.001
Baseline DLCO % predicted < 80%	96 (39.0%)	20 (69.0%)	3.26 (1.42, 8.15)	0.005
DLCO % predicted	81.7 (25.14)	71.3 (23.45)	0.98 (0.97, 1.00)	0.06
Baseline pulmonary hypertension	11 (4.5%)	2 (6.9%)	1.58 (0.24, 6.30)	0.56
Baseline SSc-related cardiac involvement	29 (11.8%)	5 (17.2%)	1.50 (0.48, 4.02)	0.46
Baseline renal crisis	3 (1.2%)	1 (3.4%)	3.05 (0.15, 24.82)	0.39

for progression at 24 months were ILD progression (55.2%) and new DU (17.2%) during follow-up. Baseline characteristics predicting progression (**Table 1**) were positivity for anti-topoisomerase-1 antibody (antiTOPO) compared to anti centromere (OR 3.20, 95%CI(1.17-9.65)), the presence of ILD (OR 4.10, 95%CI(1.45-14.69)), the presence of dyspnea (NYHA II, III or IV) (OR 3.05, 95%CI(1.38-7.01), FVC (%pred) less than 80% (OR 2.44, 95%CI(1.06-5.46)), and DLCO (%pred) less than 80% (OR 3.26, 95%CI(1.42-8.15)).

Conclusion: In the CONQUER database of patients with early SSc, 5% and 11% of patients with lcSSc or sine scleroderma experienced disease progression at 12 and 24 months, respectively. This low rate of progression suggests that clinical trials including lcSSc or sine scleroderma patients with early disease may benefit from a trial duration of 24 months. Predictors of progression within the first 24 months included antiTOPO, ILD and cardiopulmonary-related parameters (DLCO, FVC (pred) or dyspnea). Incorporating lcSSc patients with antiTOPO and presence of ILD may help enrich clinical trials with lcSSc patients more likely to show disease progression.

Disclosure: A. Lescoat: None; **V. Steen**: None; **M. Harding**: None; **J. VanBuren**: None; **B. Skaug**: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **E. Bernstein**: AstraZeneca, 5, aTYR, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **L. Evnin**: None; **T. Frech**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **F. Hant**: None; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **K. Lakin**: None; **D. Lebiedz-Odrobina**: None; **Y. Luo**: None; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **J. Molitor**: None; **D. Moore**: AstraZeneca, 5; **C. Richardson**: Cabaletta Bio, 2; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 1, Johnson & Johnson, 1, 2, Novartis, 1; **A. Shah**: None; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **C. Zahn**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2.

Abstract Number: 1556

Latent Profiles of Parenchymal Abnormalities and Vascular Features Measured by Quantitative CT Identifies a Subgroup of Systemic Sclerosis Patients With a Greater Lung Function Decline Over Time

Alicia Hinze[1], Nishanth Katurkuri[2], Robert Vassallo[2], Ami Shah[3], Ryan Lennon[2], Brian Bartholmai[2] and Cynthia Crowson[4], [1]Mayo Clinic - Rochester, MN, Rochester, MN, [2]Mayo Clinic, Rochester, MN, [3]Johns Hopkins Rheumatology, Baltimore, MD, [4]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The clinical course of interstitial lung disease (ILD) in systemic sclerosis (SSc) is highly variable--some patients experience progressive loss of lung function while others remain stable. Although risk factors such as early disease, diffuse cutaneous subtype, Black race, and >20% ILD on baseline CT increase the likelihood of progression, ILD progression can also occur in their absence. This study aimed to develop radiomic profiles linked to pulmonary function decline by analyzing quantitative CT measures of lung parenchymal and vascular abnormalities in early SSc.

Methods: A retrospective cohort of adult (≥18 yrs) patients with systemic sclerosis (SSc) seen at an academic center (1/1/2007–12/31/2018) was identified using ICD-9/10 codes. Records were reviewed, and patients included if they met ACR/EULAR 2013 SSc classification criteria or ≥3/5 CREST criteria and had ILD. Inclusion required a baseline high-resolution CT (HRCT) ±2 yrs of SSc diagnosis and a PFT ±6 mo. of HRCT. Patients with infection, pleural effusion, cardiogenic edema, or non-SSc ILD were excluded. CALIPER software quantified six lung features (normal, ground glass opacities (GGO), reticular densities (RD), honeycombing (HC), hyperlucency, and pulmonary vascular related structures (PVRS)) by lung zone (upper/middle/lower, central/peripheral). Each feature was expressed as a % of lung volume for that zone. Percent predicted forced vital capacity (ppFVC) was standardized using the GLI 2022 equations.[1] Latent Profile Analysis (LPA)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Demographics, Clinical Characteristics, Pulmonary Function Studies (PFTs), and Quantitative CT Values with Comparison Between Latent Profile 1 (LP1) and Latent Profile 2 (LP2)

Table 1. Baseline Demographics, Clinical Characteristics, Pulmonary Function Studies (PFTs), and Quantitative CT Values with Comparison Between Latent Profile 1 (LP1) and Latent Profile 2 (LP2)

Covariates	Total Cohort N = 116	Latent Profile 1 (LP1) N = 76	Latent Profile 2 (LP2) N = 40	LP1 vs LP2
	N (%) or median (IQR)	N (%) or median (IQR)	N (%) or median (IQR)	P-Value
Age at SSc dx, yrs	58 (49, 68)	57 (49, 67)	58 (50, 70)	0.39
Female Sex	73 (63)	50 (66)	23 (58)	0.38
Race				
White Caucasian	98 (85)	66 (87)	32 (80)	0.61
Black or AA	5 (4)	3 (4)	2 (5)	
Other/unknown	13 (11)	7 (9)	6 (15)	
Ever Smoker	57/115 (50)	39/75 (52)	18 (45)	0.21
1st non-RP sx to HRCT, yrs	1.3 (0.6, 2.5) n=111	1.1 (0.6, 2.2) n=73	1.5 (0.7, 3.3) n=38	0.23
ILD dx to HRCT, yrs	0.0 (0.0, 0.6)	0.0 (0.0, 0.2)	0.5 (0.0, 1.3)	<0.001
SSc subtype				
Sine/Limited	78/115 (68)	50 (66)	28/39 (72)	0.81
Diffuse	37/115 (32)	26 (34)	11/39 (28)	
Clinical Characteristics				
Digital ulcers/pits	38/92 (41)	27/60 (45)	11/32 (34)	0.32
Abnormal NC	59/86 (69)	41/54 (76)	18/32 (56)	0.06
Telangiectasias	62/102 (61)	37/67 (55)	25/35 (71)	0.11
Calcinosis	10/93 (11)	6/63 (10)	4/30 (13)	0.58
GERD	96/114 (84)	66/75 (88)	30/39 (77)	0.12
SRC	3/113 (3)	2/73 (3)	1 (3)	0.94
TFR	5/29 (17)	3/18 (17)	2/11 (18)	0.92
Myositis	20/112 (18)	15/74 (20)	5/38 (13)	0.35
Synovitis	22/115 (19)	16 (21)	6/39 (15)	0.46
Pre-cap PH by RHC*	16/22 (59)	8/10 (80)	8/12 (67)	0.19
Autoantibodies				
Scl70	30/115 (26)	21/75 (28)	9 (23)	0.52
RNA Pol III	13/51 (26)	7/38 (18)	6/13 (46)	0.048
Centromere	13/106 (12)	8/70 (11)	5/36 (14)	0.72
PFTs, median (IQR)				
ppFVC	82 (70, 94)	85 (74, 97)	75 (62, 83)	<0.001
ppDLCO	61 (46, 77) n=111	64 (56, 78) n=73	49 (34, 69) n=38	0.002
ppTLC	57 (51, 64) n=84	58 (53, 64) n=49	52 (29, 76) n=35	0.007
CALIPER, median (IQR)				
ILD%	13 (7, 21)	11 (6, 15)	23 (13, 38)	<0.001
GGO%	10 (5, 17)	9 (4, 13)	17 (9, 32)	<0.001
RD%	1.9 (0.9, 3.6)	1.3 (0.7, 2.4)	3.5 (2.2, 6.5)	<0.001
HC%	0.0 (0.0, 0.1)	0.0 (0.0, 0.0)	0.1 (0.0, 0.2)	<0.001
Hyperlucency%	0.1 (0.0, 0.6)	0.1 (0.0, 0.7)	0.1 (0.0, 0.5)	0.332
Normal%	83 (74, 90)	86 (80, 91)	71 (57, 83)	<0.001
PVRS%	3.3 (2.4, 4.1)	2.7 (2.1, 3.5)	4.4 (3.8, 5.5)	<0.001

AA: African American; GERD: gastroesophogeal reflux disease; GGO: ground glass opacities; HC: honeycombing; HRCT: high-resolution computed tomography; NC: nailfold capillaries; PFT: pulmonary function test; PH: pulmonary hypertension including both isolated pre-capillary PH (mean pulmonary artery pressure (mPAP) >20mmHg, pulmonary vascular resistence (PVR) >2.0 Woods Units (WU), pulmonary capillary wedge pressure (PCWP) <15mmHg) or combined pre-/post-capillary PH (mPAP >20mmHg, PVR >2.0 WU, PCWP ≥15mmHg); ppDLCO: percent predicted DLCO diffusing lung capacity of the lung for carbon monoxide; ppFVC: forced vital capacity; ppTLC: total lung capacity; PVRS: pulmonary related vascular structures; RD: reticular densities; RHC: right heart catheterization; RP: Raynaud's Phenomenon; SRC: scleroderma renal crisis; SSc: systemic sclerosis; TFR: tendon friction rubs

identified radiomic clusters from CALIPER measurements. Mixed effects models estimated annual ppFVC decline by cluster, adjusting for baseline ppFVC, including linear and quadratic effects for the change over time.

Table 2. Estimated Difference in the Change in ppFVC per year for Latent Profile 2 Compared to Latent Profile 1

Table 2. Estimated Difference in the Change in ppFVC per year for Latent Profile 2 Compared to Latent Profile 1

Covariate	Model 1		Model 2	
	Δ ppFVC	p-value	Δ ppFVC	p-value
Expected change per year (slope)	1.11 (-0.04 – 2.26)	0.062	0.69 (-1.66 – 3.05)	0.57
Quadratic change per year	-0.12 (-0.15 – -0.08)	<0.001	-0.12 (-0.15, -0.08)	<0.001
LP2*	-2.66 (-4.65 – -0.67)	0.011	-2.18 (-4.35 – 0.01)	0.054
ppFVC at HRCT (per 10%)*	-0.66 (-1.19 – -0.14)	0.017	-0.60 (-1.16 – -0.04)	0.041
Age at HRCT, per 10y*			-0.69 (-1.43 – 0.06)	0.075
Female*			0.22 (-1.72 – 2.16)	0.83
ILD duration, y*†			-0.13 (-0.38 – 0.12)	0.33
Scl70(+)*			-1.35 (-3.35 – 0.65)	0.19
Diffuse cutaneous*			0.04 (-1.92 – 2.00)	0.97

*Interaction with expected slope
† log-transformed (base 2)
HRCT: high-resolution computed tomography; LPA: Latent Profile Analysis; ppFVC: Percent Predicted Forced Vital Capacity

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

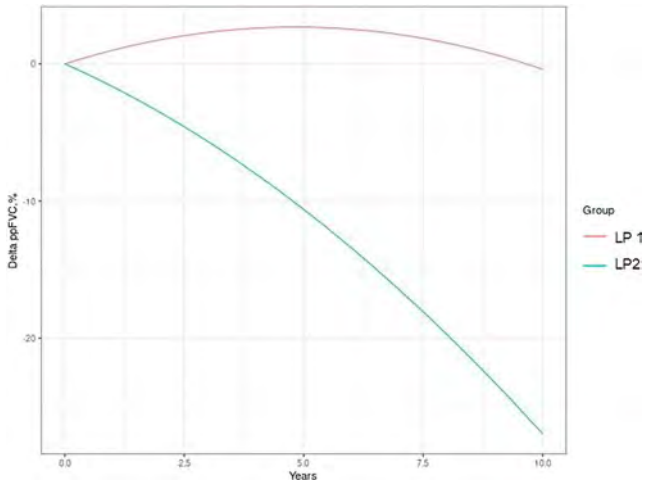


Figure 1. Difference in the Estimated Rate of Decline in percent predicted FVC (ppFVC) per year for Latent Profile (LP) 1 vs. LP 2, adjusting for age, sex, baseline ppFVC, ILD duration, diffuse cutaneous disease, and a positive Scl70

Results: Of 1,399 SSc patients identified, 712 had ILD, 315 had a CT ±2 yrs of SSc diagnosis, and 116 met inclusion criteria with ≥1 follow-up PFT. LPA identified two radiomic profiles (LP1 & LP2). LP1 had lower percentages of ILD, GGO, RD, HC, and PVRS (Table 1). There were no significant differences in demographics, smoking history, SSc dx. dur., subtype or other clinical features, anti-Scl70, or anti-centromere Abs (Table 1). RNA Pol III was less frequent in LP1 than LP2 (18% vs. 46%, p=0.048). LP1 had a shorter interval from ILD dx. to HRCT (median 0.0 vs. 0.5 yrs; p< 0.001), and better lung function at baseline (median ppFVC (85% vs. 75%) and ppDLCO (64% vs. 49%), both p< 0.001). In longitudinal analysis, LP2 had a faster rate of ppFVC decline: -2.66% per year (95% CI: –4.65 to –0.67; p=0.011) relative to LP1, adjusting for baseline ppFVC (Table 2, Model 1). This association was slightly attenuated after adjusting for age, sex, ILD dur., Scl-70(+), and diffuse subtype (–2.18% per year; 95% CI: –4.35 to 0.01; p=0.054; Table 2, Model 2; Fig 1).

Conclusion: Two early SSc-ILD radiomic phenotypes were identified. Frequencies of clinical risk factors for ILD progression were similar between profiles. One radiomic profile was associated with greater parenchymal and vascular abnormalities and faster lung function decline. Imaging-based phenotyping using radiomic biomarkers may enhance risk stratification and identify patients at higher risk for ILD progression.

Ref. 1. Bowerman, C. et. Al., AJRCCM, 2022.

Disclosure: A. Hinze: None; **N. Katurkuri**: None; **R. Vassallo**: Regeneron, 6, Rion LLC, 11, Sanofi, 2; **A. Shah**: None; **R. Lennon**: None; **B. Bartholmai**: None; **C. Crowson**: None.

Abstract Number: 1557

Association Between Thoracic Muscle and Fat Area and Density and Pulmonary Function in Systemic Sclerosis

Aradhna Agarwal[1], Niki Pradhan[1], James St. Clair[2], Dinesh Khanna[3] and Elana Bernstein[4], [1]Columbia University Medical Center, New York, NY, [2]University of Michigan, Ann Arbor, [3]University of Michigan, Ann Arbor, MI, [4]Columbia University, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics stratified by sex

Variable	All patients (n=104)	Men (n=20)	Women (n=84)	p-value
Age, median (IQR), years	55.0 (44.0, 62.0)	57.0 (53.0, 61.0)	53.0 (42.0, 62.5)	0.21[a]
Anthropometrics, mean (SD)				
Height, cm	165.1 (8.8)	175.1 (8.3)	162.8 (7.3)	<0.001[a]
Weight, kg	76.1 (22.8)	92.3 (29.6)	72.3 (19.0)	<0.001[a]
BMI, kg/m²	27.7 (7.1)	30.1 (9.4)	27.1 (6.4)	0.10[a]
Race, no (%)				0.30[b]
White	80.0 (76.9)	16.0 (80.0)	64.0 (76.2)	
African American	10.0 (9.6)	2.0 (10.0)	8.0 (9.5)	
Asian	4.0 (3.9)	0.0 (0.0)	4.0 (4.8)	
Other/Decline to answer	10.0 (9.6)	2.0 (10.0)	8.0 (9.5)	
Hispanic ethnicity, no. (%)	15.0 (14.6)	7.0 (36.8)	8.0 (9.5)	<0.01[b]
Smoking status, no. (%)				0.078[b]
Never	68.0 (66.7)	11.0 (61.1)	57.0 (67.9)	
Former	31.0 (30.4)	5.0 (27.8)	26.0 (40.0)	
Current	3.0 (2.9)	2.0 (11.1)	1.0 (1.2)	
Years from first non-Raynaud's symptom, median (IQR)	1.1 (0.8, 2.8)	1.5 (1.0, 3.1)	1.7 (1.0, 3.4)	0.44[a]
Baseline mRSS, median (IQR)	8.5 (3.0, 17.0)	8.0 (2.0, 29.0)	9.0 (3.0, 16.0)	0.23[a]
Diffuse cutaneous SSc subtype at baseline, no (%)	59.0 (57.8)	14.0 (70.0)	45.0 (54.9)	0.22[b]
Autoantibody status, no. (%)				
ANA	91.0 (89.2)	18.0 (90.0)	73.0 (89.0)	0.88[b]
Anti-centromere	26.0 (25.5)	2.0 (10.0)	24.0 (29.3)	0.20[b]
Anti-Scl-70	33.0 (31.7)	5.0 (25.0)	28.0 (33.3)	0.10[b]
Anti-RNAP3	26.0 (25.2)	5.0 (26.3)	21.0 (25.0)	0.70[b]
Pulmonary Function Tests				
FVC, % predicted, mean (SD)	84.8 (21.2)	75.0 (29.1)	87.0 (18.7)	0.033[a]
FEV1, % predicted, mean (SD)	84.9 (19.4)	77.9 (30.5)	86.5 (15.9)	0.10[a]
DLCO, % predicted, mean (SD)	71.6 (23.3)	66.3 (29.5)	72.9 (21.7)	0.32[a]
Body Composition, median (IQR)				
Total Pectoralis Muscle Area, cm²	26.2 (21.5, 31.4)	39.1 (32.8, 48.4)	24.7 (20.3, 28.2)	<0.001[a]
Pectoralis Muscle Density, HU	25.3 (20.1, 32.7)	31.4 (22.7, 36.5)	24.9 (19.2, 31.7)	0.40[a]
Total Subcutaneous Fat Area, cm²	49.2 (28.3, 71.8)	32.5 (19.3, 43.3)	54.8 (30.0, 76.7)	<0.01[a]
Subcutaneous Fat Density, HU	-104.3 (-110.4, -98.3)	-100.2 (-107.7, -93.9)	-105.4 (-110.8, -99.4)	0.14[a]
Muscle/Fat Ratio	0.4 (0.2, 0.7)	0.9 (0.7, 1.7)	0.3 (0.2, 0.6)	<0.001[a]

[a] t-test for continuous variables

[b] chi2 for categorical variables > 20% expected cell counts less than 5

[c] Fisher exact for categorical variables < 20% expected cell counts less than 5

IQR = interquartile range; SD = standard deviation; cm = centimeters; kg = kilograms; m² = meters squared; no. = number; mRSS = modified Rodnan skin score; ANA = antinuclear antibody; anti-Scl-70 = anti-topoisomerase I antibody; anti-RNAP3 = RNA polymerase 3 antibody; FVC = forced vital capacity; FEV1 = forced expiratory volume in one second; DLCO = diffusion capacity for carbon monoxide; HU = Hounsfield units

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of mortality in systemic sclerosis (SSc). Little is known about the association between body composition and lung function in SSc. Thoracic computed tomography (CT) scans are routinely obtained in SSc patients to screen for ILD. Accessory respiratory muscles and subcutaneous fat (SF) measurements can be calculated from these CT scans. Our aim was to examine the association between thoracic body composition and pulmonary function in SSc patients.

Table 2. Association between body composition parameters and %predicted FVC

Body Composition Parameter	Unadjusted			Adjusted*		
	No.	β coefficient (95% CI)	p-value	No.	β coefficient (95% CI)	p-value
Pectoralis Muscle Area	93	-0.45 (-0.89, -0.008)	0.046	87	-0.28 (-0.84, 0.38)	0.41
Pectoralis Muscle Density	94	-0.013 (-0.26, 0.25)	0.92	88	0.054 (-0.24, 0.35)	0.71
Subcutaneous Fat Area	91	0.0036 (-0.13, 0.14)	0.95	85	0.019 (-0.15, 0.19)	0.83
Subcutaneous Fat Density	94	-0.56 (-0.98, -0.14)	0.010	85	-0.77 (-1.20, -0.35)	0.001
Muscle/Fat Ratio	91	-6.72 (-13.16, -0.28)	0.041	85	-7.44 (-14.96, 0.066)	0.052

* Adjusted for age, sex, height, weight, smoking history, disease duration from first non-Raynaud's symptom, disease subtype (diffuse versus limited), presence of anti-topoisomerase I autoantibody

No: number; CI: confidence interval

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: SSc patients who met ACR/EULAR 2013 classification criteria were recruited longitudinally from the Scleroderma Programs at two academic medical centers. We performed a cross-sectional analysis using baseline thoracic CTs and baseline pulmonary function tests. Pectoralis muscle and SF area and density from thoracic CT scans were measured using ImageJ. Pectoralis muscle area to SF area ratio (MFR) was calculated. To evaluate the relationship between pectoralis muscle and SF area and density and MFR (exposures) and the % predicted forced vital capacity (ppFVC) (outcome), we performed unadjusted and multivariable-adjusted linear regression analyses. The multivariable regression model was adjusted for potential confounders of the relationship between body composition and ppFVC, including age, sex, height, weight, disease duration, smoking status, SSc subtype, and Scl-70 positivity.

Results: One hundred-four CT scans from SSc participants were analyzed. The median (interquartile range [IQR]) age was 55.0 (44.0, 62.0) years (Table 1). The mean (standard deviation [SD]) BMI was 27.7 (7.08) kg/m^2. The majority were female (80.8%) and white (76.9%). The median (IQR) disease duration was 1.1 (0.8, 2.8) years from first non-Raynaud's symptom. Men were taller, weighed more, and had larger muscle and fat area than women. Men had lower ppFVC than women (75.0% vs 87.0%, p = 0.03). In unadjusted analyses, the following body composition measures were inversely associated with ppFVC: pectoralis muscle area (PMA) (β coefficient = -0.45, 95% confidence interval [CI] -0.89 to -0.008), SF density (β coefficient -0.56, 95% CI -0.98 to -0.14), and MFR (β coefficient = -6.72, 95% CI -13.18 to -0.28) (Table 2). In a multivariable-adjusted model, SF density remained statistically significantly inversely associated with ppFVC (β coefficient = -0.77, 95% CI -1.20 to -0.35). MFR was inversely associated with ppFVC, but only approached statistical significance (β coefficient = -7.44, 95% CI -14.96 to 0.066). There was no association between PMA and ppFVC in the multivariable-adjusted model.

Conclusion: SF density was statistically significantly inversely associated with ppFVC in a multivariable-adjusted regression model. MFR was also inversely associated with ppFVC in the adjusted model, but only approached statistical significance. High SF density and MFR may be risk factors for diminished ppFVC. However, it remains unknown whether thoracic muscle and fat composition can predict ppFVC over time. Prospective studies are needed to determine whether thoracic body composition can predict outcomes in SSc-ILD.

Disclosure: A. Agarwal: None; **N. Pradhan**: None; **J. St. Clair**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **E. Bernstein**: AstraZeneca, 5, aTyr, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2.

Abstract Number: 1558

Gastrointestinal Symptom Severity Is Associated with Worse Patient-reported Outcomes and Dietary Patterns in Systemic Sclerosis: A Single Center Prospective Study

Thomas Guedens[1], Elvira Lesmana[2], Adam Edwinson[3], Margaret Breen-Lyles[1], Anukul Karn[4], Madhusudan Grover[1] and **Ashima Makol**[3], [1]Mayo Clinic, Rochester, Rochester, MN, [2]Mayo Clinic, Rochester, USA, Rochester, MN, [3]Mayo Clinic, Rochester, MN, [4]Trinity Health Livonia, Farmington Hills, MI

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Dietary patterns among systemic sclerosis patients with variable GI symptom severity (none – mild vs moderate – very severe, based on UCLA GIT 2.0) vs healthy volunteers. All data are presented as mean (standard deviation). BMI = body mass index; MUFA = mono-unsaturated fatty acids; PUFA = poly-unsaturated fatty acids; SFA = saturated fatty acids. *Note: Post-hoc analysis to assess statistically significant intergroup differences using a Dunn's multiple comparison test. 'a' denotes significant differences between None – Mild vs Healthy, 'b' between None – Mild vs Moderate – Very Severe, and 'c' between Moderate – Very Severe vs Healthy.

Variable	None - Mild (n = 42)	Moderate - Very Severe (n = 46)	Healthy (n = 18)	p value	Post-hoc p value*
BMI	25.7 (5.8)	28.2 (6.9)	29.0 (4.8)	0.05	/
Total caloric intake, kcal	1735 (793)	1712 (799)	1733 (748)	0.92	/
Total carbohydrates, % caloric intake	45.4 (6.8)	44.2 (9.9)	44.1 (6.9)	0.78	/
Total fat, % caloric intake	37.6 (5.8)	37.8 (7.5)	36.0 (4.2)	0.63	/
Total protein, % caloric intake	17.3 (3.4)	16.6 (3.6)	19.1 (4.6)	0.16	/
Animal protein, % caloric intake	11.6 (3.6)	11.9 (4.1)	13.2 (4.9)	0.59	/
Vegetable protein, % caloric intake	5.74 (2.61)	4.73 (1.72)	5.85 (1.51)	**0.005**	**0.045[b] 0.01[c]**
Fiber, g	20.1 (9.5)	16.2 (9.0)	19.3 (9.2)	0.09	/
Percentage of caloric intake from meat, poultry, and fish	21.8 (10.5)	22.2 (13.9)	28.5 (16.5)	0.20	/
Percentage of caloric intake from meat	8.48 (7.86)	11.93 (11.86)	9.90 (7.92)	0.42	/
Total fruit, cup equivalents/1000 kcal	0.91 (0.68)	0.65 (0.48)	0.62 (0.47)	0.18	/
Total whole fruit, cup equivalents/1000 kcal	0.82 (0.65)	0.55 (0.44)	0.52 (0.43)	0.10	
Legumes (beans and peas), cup equivalents/1000 kcal	0.05 (0.08)	0.03 (0.06)	0.05 (0.07)	0.17	/
Total vegetables, cup equivalents/1000 kcal	1.19 (1.06)	1.02 (0.70)	1.24 (0.64)	0.18	/
Whole grains, ounce equivalents/1000 kcal	0.33 (0.33)	0.27 (0.28)	0.65 (0.40)	**<0.001**	**0.001[b] <0.001[c]**
Refined grains, ounce equivalents/1000 kcal	1.75 (0.82)	1.86 (0.71)	2.03 (1.10)	0.64	/
Total dairy, cup equivalents/1000 kcal	1.12 (0.60)	1.12 (0.65)	0.96 (0.44)	0.71	/
Sodium, g/1000 kcal	1.68 (0.29)	1.75 (0.45)	1.88 (0.60)	0.56	/
Empty calories, % caloric intake	15.1 (4.07)	12.5 (5.17)	16.2 (3.50)	**0.01**	**0.046[b] 0.02[c]**
Fatty acids, ratio (MUFA+PUFA)/SFA	1.83 (0.61)	1.67 (0.62)	1.82 (0.30)	**0.02**	**0.04[c]**
Alcohol, % caloric intake	3.06 (4.79)	4.26 (7.69)	3.31 (4.32)	0.90	/
Added sugars, % caloric intake	7.68 (2.95)	9.89 (7.16)	7.21 (4.12)	0.32	/
Healthy Eating Index (2010) Score	66.4 (12.7)	59.1 (11.6)	66.9 (12.2)	**0.01**	**0.01[b] 0.04[c]**

Background/Purpose: Systemic sclerosis (SSc) is a rare multisystem auto-immune disease characterized by peripheral vasculopathy and widespread fibrosis of the skin and internal organs. Up to 90% of SSc patients experience gastrointestinal (GI) symptoms ranging from mild to very severe. We aimed to explore how GI symptom severity correlates with dietary intake patterns and patient-reported outcome measures in SSc patients.

Methods: Adult (>18 years old) SSc patients meeting the ACR/EULAR 2013 criteria were prospectively recruited and stratified into those with none-to-mild and moderate-to-very severe GI symptoms based on The University of California Los Angeles Scleroderma Clinical Trials Consortium gastrointestinal tract 2.0 (UCLA GIT 2.0) scores.[1] Patients completed a food frequency questionnaire to assess dietary intake which was compared to historically obtained healthy volunteer dietary data. Patient-reported outcomes were assessed using a range of validated questionnaires. All variables were compared using Mann-Whitney U tests and Kruskal-Wallis tests and correlated using Spearman's rank correlation.

Results: 94 SSc participants (79 females; mean 58±12 years) were enrolled. The average UCLA GIT 2.0 score was 0.6±0.4 and participants were categorized as having none to mild (n=47, 50%), and moderate to very severe GI symptoms (n=47, 50%). Compared to healthy volunteers or those with none to mild GI symptoms, patients with moderate to very severe GI symptoms had a lower intake of vegetable proteins and empty calories as well as lower healthy eating index (HEI) scores (Table 1). Patients with moderate to very severe GI symptoms also consumed more saturated fatty acids compared to healthy volunteers. Regardless of GI symptoms, SSc patients consumed fewer whole grains compared to healthy volunteers. Additionally, patients with moderate to very severe GI symptoms reported worse physical and social function, higher levels of fatigue, pain and anxiety, and more bowel movements which were also softer when compared to those with none

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Patient-reported outcomes in systemic sclerosis patients based on UCLA GIT 2.0 scores. All data are presented as mean (standard deviation), n. PROMIS = Patient-Reported Outcomes Measurement Information System; HADS = Hospital Anxiety and Depression Scale; SHAQ = Scleroderma Health Assessment Questionnaire; PtGA = Patient Global Assessment.

Variable	None - Mild (n = 47)	Moderate - Very Severe (n = 47)	p value
PROMIS 29 v2.1			
Physical Function	45.6 (9.0), 47	41.7 (8.8), 47	**0.03**
Anxiety	49.7 (8.1), 47	51.0 (9.7), 47	0.57
Depression	48.2 (8.7), 47	51.1 (9.2), 47	0.11
Fatigue	52.4 (10.6), 47	58.8 (9.5), 47	**0.001**
Sleep Disturbance	51.5 (6.3), 47	52.9 (8.3), 47	0.55
Social Functioning	50.5 (9.7), 47	45.7 (7.9), 47	**0.02**
Pain Interference	53.5 (8.9), 47	58.6 (8.8), 47	**0.01**
Pain Intensity	2.9 (2.1), 47	4.1 (2.6), 47	**0.02**
HADS			
Anxiety	4.5 (3.5), 47	6.4 (3.6), 47	**0.01**
Depression	3.5 (3.2), 47	4.7 (3.4), 47	0.06
SHAQ			
Dressing and Grooming	0.30 (0.52), 47	0.48 (0.61), 47	0.08
Arising	0.28 (0.51), 47	0.45 (0.61), 47	0.11
Eating	0.40 (0.66), 47	0.54 (0.75), 47	0.46
Walking	0.28 (0.48), 47	0.54 (0.68), 47	**0.04**
Hygiene	0.42 (0.61), 47	0.70 (0.72), 47	**0.04**
Reach	0.39 (0.63), 47	0.78 (0.79), 47	**0.01**
Grip	0.26 (0.48), 47	0.38 (0.49), 47	0.11
Activities	0.40 (0.51), 47	0.67 (0.68), 47	**0.04**
Total SHAQ Score	0.34 (0.43), 47	0.57 (0.52), 47	**0.03**
PtGA	3.0 (2.2), 47	4.3 (2.5), 47	**0.01**
7-day bowel diary			
Frequency (weekly)	10.7 (5.4), 42	15.4 (7.6), 43	**<0.001**
Consistency (Bristol)	4.0 (0.8), 42	4.8 (1.1), 43	**<0.001**

to mild GI symptoms (Table 2). Harder stool consistency correlated with higher HEI scores (r=0.42, p< 0.001) and a higher intake of fiber (r=0.40, p< 0.001) and vegetable protein (r=0.44, p< 0.001).

Conclusion: In this large prospective single center cohort of well characterized SSc patients, those with moderate to very severe GI symptoms exhibited suboptimal dietary intake and reported worse physical and social functioning as well as higher levels of pain, fatigue and anxiety. Future studies are needed to understand the mechanistic influence of diet in SSc patients and its impact on GI symptoms and other patient-reported outcomes.

Disclosure: T. Guedens: None; **E. Lesmana**: None; **A. Edwinson**: None; **M. Breen-Lyles**: None; **A. Karn**: None; **M. Grover**: Alfa-Sigma, 5, Takeda, 5; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial.

Abstract Number: 1559

Anti-cytolethal Distending Toxin Antibodies in Systemic Sclerosis: Associations with Gastrointestinal Disease and Immune Dysregulation

Francesca Romana Di Ciommo[1], Livia Casciola-Rosen[2], **Ashish Balar**[3], Ami Shah[4], Michael Hughes[5], Walter Morales[6], Mark Pimentel[7], Brittany L Adler[8] and Zsuzsanna McMahan[9], [1]La Sapienza University of Rome, Rome, Italy, [2]Johns Hopkins University, Baltimore, MD, [3]UTHealth Houston, Houston, TX, [4]Johns Hopkins Rheumatology, Baltimore, MD, [5]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom, [6]Cedars-Sinai Medical Center, Los Angeles, CA, [7]Karsh Division of Gastroenterology and MAST Program, Cedars-Sinai Medical Center, Los Angeles, CA, [8]Johns Hopkins University School of Medicine, Baltimore, MD, [9]UT Health Houston, Houston, TX

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti- Cytolethal Distending Toxin (CDT) antibodies may serve as biomarkers for post-infectious autoimmunity and aid in clinical risk stratification. In this study, we aimed to determine the prevalence of anti-CDT antibodies in a large, well-characterized cohort of patients with systemic sclerosis (SSc) and to examine associations with gastrointestinal (GI) and extraintestinal clinical features and other SSc-related antibodies.

Methods: Sera from 130 well-characterized patients with SSc enriched for GI disease were screened for anti-CDT antibodies by ELISA. Clinical features, UCLA GIT 2.0-assessed symptoms, and autoantibody profiles were compared between patients with and without anti-CDT antibodies.

Results: Anti-CDT antibodies were detected in 18% (23/130) of SSc patients. Patients with anti-CDT antibodies more frequently had significant GI disease (87% vs. 71%; p=0.19) and were significantly more likely to have antibodies to U11/U12 (RNPC3) (35% vs. 4%; p< 0.001), U1RNP (26% vs. 8%; p=0.018), and topoisomerase-1 (30% vs. 12%; p=0.044). UCLA GIT Soilage scores were significantly higher (worse) among anti-CDT -positive patients [1 (1, 2) vs. 0 (0, 2); p=0.037]. In multivariable analyses, anti-CDT antibodies remained significantly associated with anti-U11/U12 (RNPC3) [OR 19.0 (4.3, 83.4);

Table 1. Comparison of demographic, clinical and serological features between anti-CDT antibody positive and negative patients with systemic sclerosis. SD= standard deviation; IQR = interquartile range; FVC = forced vital capacity; DLco =diffusing capacity for carbon monoxide; RVSP = right ventricular systolic pressure; p= p-value. § Disease duration from any first symptom to the date of the serum sample collection. ‡ Maximum Medsger severity score ever recorded in the database; FVC and DLco are represented by the minimum values ever recorded. *UCLA GIT 2.0, University of California Los Angeles Scleroderma Clinical Trials Consortium gastrointestinal tract 2.0. † Statistically significant.

Features	Anti-CDT antibody positive patients (n=23)	Anti-CDT antibody negative patients (n=107)	P
Age, mean ± SD years	58 ± 15	56 ± 12	0.42
Disease Duration, median (IQR) years §	10 (7-24)	11 (5-19)	0.49
Male, n° (%)	1 (4)	15 (14)	0.30
White, n° (%)	16 (70)	83 (79)	0.41
Cutaneous Subtype, diffuse, n° (%)	10 (43)	27 (26)	0.13
Tendon friction rub, n° (%) ‡	2 (9)	8 (8)	1.00
Calcinosis, n° (%) ‡	8 (35)	40 (39)	0.81
Raynaud's phenomenon > 1, n° (%) ‡	10 (43)	38 (36)	0.49
Cardiac involvement > 1, n° (%) ‡	3 (15)	7 (10)	0.69
Lung involvement > 1, n° (%) ‡	10 (58)	42 (61)	0.88
Gastrointestinal involvement ≥ 1, n° (%) ‡	20 (87)	76 (71)	0.19
Muscle weakness > 1, n° (%)	5 (22)	9 (9)	0.08
Skeletal myopathy, n° (%) ‡	8 (35)	18 (18)	0.09
Sicca complex, n° (%)	20 (87)	88 (87)	1.00
Death, n° (%)	0 (0)	11 (10)	0.21
Pulmonary function, mean ± SD			
Minimum FVC % predicted	77 ± 19	84 ± 21	0.15
Minimum DLco % predicted	62 ± 23	60 ± 21	0.64
RVSP, median (IQR) mm Hg	33 (28-37)	35 (26-42)	0.62
Autoantibodies n° (%)			
Anti-topoisomerase-1	6 (30)	10 (12)	**0.04 †**
Anti-centromere	7 (35)	38 (45)	0.41
Anti-RNA polymerase 3	1 (5)	8 (10)	1.00
Anti–Pm- Scl	2 (10)	3 (4)	0.24
Anti–U3 RNP	3 (13)	6 (6)	0.20
Anti- ThTo	0 (0)	1 (1)	1.00
Anti- Ku	0 (0)	1 (1)	1.00
Anti–U1 RNP	6 (26)	8 (8)	**0.02†**
Anti–U11/U12 (RNPC3)	8 (35)	4 (4)	**<0.01†**
Anti-Gephryn	2 (9)	5 (5)	0.61
Anti–Ro 52	10 (43)	32 (30)	0.23
Anti-M2 (mitochondrial)	4 (17)	14 (13)	0.52
UCLA GIT, median (IQR)*			
Reflux score	1.1 (0.6-2.0)	1.1 (0.8-1.8)	0.95
Distention/bloating score	2.2 (1.5-3.0)	2 (1.2-2.8)	0.37
Soilage score	1.0 (1.0-2.0)	0.0 (0.0-2.0)	**0.037†**
Diarrhea score	1.0 (1.0-1.5)	1.0 (0.5-1.5)	0.17
Constipation score	1.2 (0.5-1.8)	1.0 (0.5-1.8)	0.49
Total score	1.1 (0.8-1.6)	0.9 (0.5-1.6)	0.35

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Statistical models assessing the association between anti–CDT–positive patients with systemic sclerosis and clinical, serological features. † Statistically significant. *Values are odds ratio (95% confidence interval).

Characteristic	Univariate logistic regression	Conditional logistic adjusted for age, disease duration and sex: model 1*	Conditional logistic including all significant variables: model 2 *
Age	1.02 (0.98- 1.06)	\	1.022 (0.97-1.08)
Disease duration	1.01 (0.97-1.05)	\	1.026 (0.97-1.08)
Sex (female)	3.59 (0.45-28.62)	\	7.97 (0.80-79.46)
Anti–U1 RNP	**4.37 (1.35-14.17) †**	**7.22 (1.87- 27.85) †**	**7.55 (1.38-41.44) †**
Anti–RNPC- 3	**13.73 (3.68-51.24) †**	**19.01 (4.33-83.43) †**	**18.24 (2.56-130.03) †**
Anti-topoisomerase-1	3.17 (0.99-10.14)	**4.65 (1.29-16.77) †**	**6.25 (1.41-27.70) †**

p=< 0.001), anti-U1RNP antibodies [OR 7.2 (1.9, 27.9); p=0.004] and anti-topoisomerase-1 antibodies [OR 4.7 (1.3, 16.8); p=0.019], even after adjusting for potential confounders.

Conclusion: Anti-CDT antibodies may serve as markers of post-infectious autoimmunity and are strongly associated with SSc-specific autoantibodies linked to severe, progressive GI disease. Understanding the connection between anti-CDT antibodies and autoimmune mechanisms may provide insight into disease pathogenesis.

Disclosure: F. Di Ciommo: None; **L. Casciola-Rosen**: None; **A. Balar**: None; **A. Shah**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5; **W. Morales**: None; **M. Pimentel**: Bausch Health, 2, 5, Cylinder Health Inc, 12,, 2, Dieta Health, 2, Ferring Pharmaceuticals Inc., 2, Gemelli Biotech, 12,, 12, licensing agreement, Salvo Health, 12,, 2, Vivante Health Inc., 2; **B. Adler**: None; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2.

Abstract Number: 1560

Longitudinal assessment of circulating fibroblast activation protein in systemic sclerosis-associated interstitial lung disease

Bo Broens[1], Conny van der Laken[1], Iris Simons[1], Tamara Dekker[1], Jan Willem Duitman[1] and Alexandre Voskuijl[2], [1]Amsterdam UMC, Amsterdam, Netherlands, [2]Amsterdam University Medical Center, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis-associated interstitial lung disease (SSc-ILD) is difficult to manage due to the heterogeneous disease course. There is a high need for biomarkers to identify patients at high risk for ILD progression. Fibroblast activation protein (FAP) has gained interest as a biomarker to reflect fibrotic activity. As circulating FAP (cFAP) can be measured in blood, we aimed to investigate the value of cFAP in SSc-ILD.

Methods: cFAP concentrations were determined in plasma samples of 210 SSc patients and 13 controls using an enzyme-linked immunosorbent assay. We compared cFAP levels in (repeated longitudinal) samples between SSc patients, with and without ILD (n=63 and n=147, respectively) and controls. Furthermore, we investigated the correlation between cFAP and ILD progression at follow-up (defined as forced vital capacity (FVC) decline ≥5%). In an exploratory analysis, we also investigated if cFAP was associated with other disease-related clinical features and all-cause mortality.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

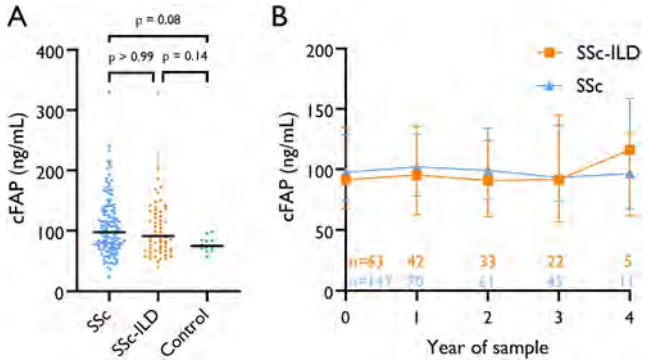


Figure 1. cFAP levels in patients with SSc - with and without ILD - and controls

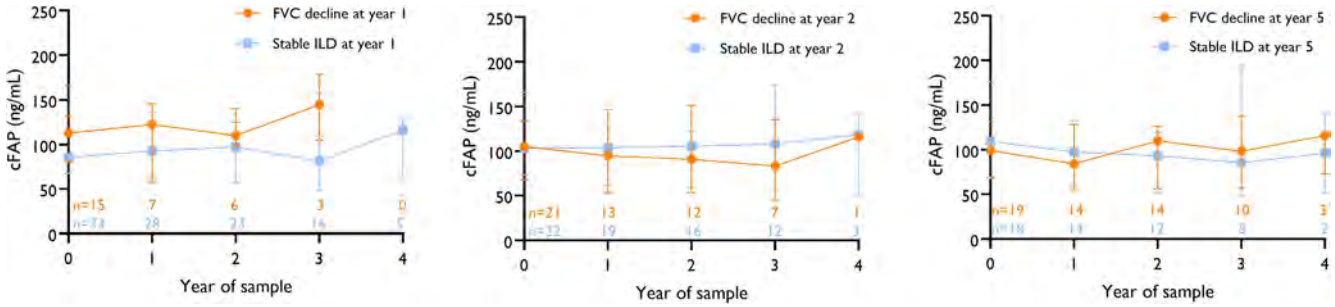


Figure 2. cFAP concentrations plotted over time in SSc patients that did or did not develop ILD progression at 1, 2 and 5 years of follow-up

Table 1. Baseline cFAP is not associated with ILD progression during follow-up

FVC decline ≥5%	ILD progression n (%)	ILD progression cFAP (ng/mL)	No ILD progression cFAP (ng/mL)	Logistic regression analysis
Year 1	15/48 (31.3%)	113.0 ± 51.3	86.0 ± 98.8	p=0.52
Year 2	21/43 (48.8%)	105.4 ± 66.3	103.5 ± 92.4	p=0.30
Year 5	19/37 (51.4%)	99.3 ± 64.1	109.7 ± 107.3	p=0.99

Results: cFAP levels were not different between SSc patients, with and without ILD, both at baseline (median 91.5 and 97.7 ng/mL; p >0.99) or during follow-up (Figure 1). Additionally, no differences were found between the cFAP levels of SSc patients, with or without ILD, and controls (median 76.9 ng/mL; p=0.08 and p=0.14). Furthermore, we found no correlations between cFAP at baseline and ILD progression at 1, 2 and 5 years of follow-up (Table 1 and Figure 2). In the entire SSc cohort, cFAP levels were elevated at baseline in patients with higher skin scores (mRSS ≥10 compared to mRSS < 10; p=0.01). Lastly, there was no association between cFAP and all-cause mortality at 5 and 10 years of follow-up.

Conclusion: In conclusion, cFAP does not seem useful as a biomarker in SSc-ILD. The relationship between cFAP and skin deserves additional investigation.

Disclosure: B. Broens: None; **C. van der Laken**: None; **I. Simons**: None; **T. Dekker**: None; **J. Duitman**: None; **A. Voskuijl**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1561

Usefulness of HRCT in screening of interstitial lung disease in patients with systemic sclerosis without risk factors of clinical suspicion

Carlos de la Puente-Bujidos[1], Antia Garcia Fernandez[2], Verónica García García[1], Jesús Loarce[3] and Sandra Garrote-Corral[1], [1]Ramón y Cajal University Hospital, Madrid, Spain, [2]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain, [3]Ramón y Cajal University Hospital, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: In 2019 a European expert consensus suggested that all patients with systemic sclerosis (SSc) should be screened with HRCT for interstitial lung disease (ILD) at diagnosis, regardless of the presence of risk factors (RF). However, in the absence of RF or suggestive symptoms or signs, the probability of finding ILD is low. Our aim was to assess rate of ILD and its severity in the absence of clinical suspicion (CS) or RF for ILD in patients with SSc at diagnosis.

Methods: Retrospective study of patients with a recent diagnosis of SSc from January 2020 to January 2025 who were under follow up in a dedicated SSc clinic in Madrid, Spain. Patients with CS and/or RF for ILD were compared with those without CF or RF. CS was defined as presence of dyspnea or crackles. RF were defined as ATA+, diffuse cutaneous

Table 1: Main clinical characteristics regarding presence of CS or RF for ILD

	CS or RF -	CS or RF +	Cohort	p value
n (%)	26 (41.3)	37 (58.7)	63 (100)	-
Female, n (%)	23 (88.5)	32 (86.5)	55 (87.3)	1
Age at diagnosis, years, mean (SD)	58.5 (12.4)	59.5 (13.9)	59.1 (13.2)	0.77
Time in follow up after diagnosis, months, mean (SD)	32.6 (17.5)	25.5 (15.4)	28.4 (16.5)	0.092
First non-Raynaud's symptom <3 years, n (%)	13 (54.2)	22 (59.5)	35 (55.6)	0.683
Race, n (%)				0.581
Caucasian	20 (76.9)	24 (64.9)	44 (69.8)	
Hispanic	4 (15.4)	8 (21.6)	12 (9)	
African	2 (7.7)	2 (5.4)	4 (6.3)	
Asian	0 (0)	2 (5.4)	2 (3.2)	
Arabic	0 (0)	1 (2.7)	1 (1.6)	
Smoking status, n (%)				0.018*
Active	0 (0)	9 (24.3)	9 (14.3)	
Former	9 (34.6)	7 (18.9)	16 (25.4)	
Never	17 (65.4)	21 (56.8)	38 (60.3)	
ATA, n (%)	0 (0)	12 (32.4)	12 (19)	0.001*
ACA, n (%)	17 (65.4)	17 (45.9)	34 (54)	0.199
Capillaroscopy pattern				
normal, n (%)	2 (7.7)	5 (13.9)	7 (11.1)	0.447
Early, n (%)	17 (65.4)	10 (27.8)	27 (42.9)	0.004*
Active, n (%)	4 (15.4)	17 (47.2)	21 (33.3)	0.014*
Late, n (%)	0 (0)	2 (5.6)	2 (3.2)	0.505
Non-specific, n (%)	3 (11.5)	2 (5.6)	5 (7.9)	0.641
Cutaneous				0.101
Diffuse, n (%)	0 (0)	3 (8.1)	3 (4.8)	
Limited, n (%)	20 (76.9)	31 (83.8)	51 (81)	
sine, n (%)	6 (23.1)	3 (8.1)	9 (14.3)	
Esophageal , n (%)	12 (60)	19 (44.2)	31 (49.2)	0.287
Articular, n (%)	6 (23.1)	9 (24.3)	15 (23.8)	1
Telangiectasias, n (%)	12 (46.2)	17 (45.9)	29 (46)	0.987
Calcinosis, n (%)	1 (3.8)	1 (2.7)	2 (3.2)	0.799
Digital ulcers, n (%)	3 (11.5)	11 (29.7)	14 (22.2)	0.126
ILD, n (%)	3 (11.5)	17 (45.9)	20 (31.7)	0.005*
Dyspnea, n (%)	0 (0)	25 (67.6)	25 (39.7)	<0.0001*
Crackles, n (%)	0 (0)	13 (35.1)	13 (20.6)	<0.0001*
Cough, n (%)	1 (3.8)	9 (24.3)	10 (15.9)	0.037*
CRP> 6mg/L, n (%)	1 (3.8)	8 (21.6)	9 (14.3)	0.047*

ACA, anticentromere antibodies; ATA, antitopoisomerase antibodies; CRP, C-reactive protein; CS, clinical suspicion; RF, risk factors; ILD, interstitial lung disease; SD, standard deviation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: HRCT findings, PFT and treatment regarding presence of CS or RF

	CS or RF -	CS or RF +	total cohort	p value
n, (%)	26 (41.3)	37 (58.7)	63 (100)	-
Abnormal PFT at baseline, n (%)	3/25 (12)	13/34 (38.2)	16/59 (27.1)	0.038*
FVC, % median (IQR)	95.1 (12.6)	84.1 (19.7)	88.8 (17.8)	0.02*
DLCO, % median (IQR)	87.3 (21.2)	72.4 (20.1)	78.8 (21.7)	0.01*
ILD pattern, n (%)				0.042*
NSIP	1 (3.8)	12 (32.4)	13 (20.6)	
UIP	0 (0)	0 (0)	0 (0)	
Probable UIP	0 (0)	1 (2.7)	1 (1.6)	
Indetermined for UIP	1 (3.8)	1 (2.7)	2 (3.2)	
Others	1 (3.8)	3 (8.1	4 (11.1)	
Scleroderma related - Esophageal dilation, n (%)	3 (11.5)	12 (32.4)	15 (23.8)	0.074
- Pulmonary artery enlargement, n (%)	0 (0)	5 (13.5)	5 (7.9)	0.071
IS*, n (%)	4 (15.4)	16 (43.2)	35 (55.6)	0.028*
IS-ILD, n (%)	0 (0)	10 (27)	10 (15.9)	0.004*
Antifibrotic therapy, n (%)	0 (0)	4 (10.8)	4 (6.3)	0.136

*ILD and non ILD indication for IS
CS, clinical suspicion; RF risk factors; ILD, interstitial lung disease; IS, immunosuppression; PFT, pulmonary function tests.

involvement or active smokers. Severe ILD was defined as disease characterized either by progression observed in PFT or the requirement for immunosuppressive and/or antifibrotic treatment. Categorical variables were described as proportions and/or percentages, while continuous variables were shown as mean or median and standard deviation (SD) or interquartile range (IQR). The Student t test and X^2 test were used to compare data, when appropriate.

Results: 70 patients were diagnosed of SSc during the study period, 90% were screened with HRCT at diagnosis, therefore 63 patients were analyzed. Main characteristics are reported in Table 1. There were no differences in age, sex, race, presence of ACA, time in follow up and organ involvement other than ILD between both groups. In 26 (41.3%) patients there were no CS or RF for ILD. ILD was diagnosed in 3 (11.5%) patients without RF or CS compared to 18 (45.9%) in the group with CS and/or RF ($p< 0.001$). After a mean of 28.4 months of follow-up, none of the patients in the group without CS or RF required treatment for ILD, compared to 10 patients (27%) and 4 patients (10.8%) in the other group who required IS and antifibrotic therapy, respectively (Table 2). Serial pulmonary function tests (PFT) were available in 15/20 (75%) patients with ILD, 2/3 patients without CS or RF had serial PFT, both without deterioration. On the contrary, 13/17 patients with CS and ILD had serial PFT, 53.8% had deterioration of PFT at baseline and 38.5% showed worsening during follow-up. There were no differences in time in follow-up PFT between groups (no CS mean 41.5 months [SD 16.3], CS: mean 32.3 months [SD 12.3], p=0.361).

Conclusion: In our cohort, in absence of CS or RF for ILD, only 11.5% had ILD and none required IS or antifibrotic therapy. Despite the presence of ILD in HRCT at diagnosis, the presence of CS or RF seems to be a key factor identifying patients requiring treatment or in risk of progression during initial follow up. It is necessary to be very cautious with the interpretation of radiological findings in patients without RF because their clinical significance is probably minimal.

Disclosure: C. de la Puente-Bujidos: None; **A. Garcia Fernandez**: None; **V. García García**: None; **J. Loarce**: None; **S. Garrote-Corral**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1562

Vasodilation with Prostanoids Influences Progression of Systemic Sclerosis-Associated Interstitial Lung Disease: a EUSTAR Cohort Study

adela cristina sarbu[1], Liubov Petelytska[2], lorenzo tofani[3], Gianluca Moroncini[4], Alexandra Balbir-Gurman[5], elisabetta zanatta[6], Jörg Henes[7], paolo airò[8], Marco Matucci-Cerinic[9], Ana Maria Gheorghiu[10], antonella marcoccia[11], branimir Anić[12], Jelena Colic[13], Daniel Furst[14], julia Spierings[15], Francesco Del Galdo[16], Britta Maurer[17], Anna-Maria Hoffmann-Vold[18], Oliver Distler[19] and **Cosimo Bruni**[20], [1]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland. • Department of Rheumatology and Immunology, Bern University Hospital, University of Bern, Bern, Switzerland, bern, Swaziland, [2]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland. • Dept Internal Medicine #3, Bogomolets National Medical University, Kyiv, Ukraine, Kyiv, Ukraine, [3]Department of Statistics, Informatics and Applications, University of Florence, Florence, Italy, firenze, Italy, [4]Department of Internal Medicine, Marche University Hospital, Clinica Medica, Ancona, Italy, Ancona, Italy, [5]• Rheumatology Institute, Rambam Health Care Campus, Rappaport Faculty of Medicine, Tecchnion, Haifa, Israel, Haifa, Israel, [6]Padova University Hospital, Rheumatology Unit, Padova, Italy, padova, Italy, [7]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology, and Rheumatology, University Hospital Tübingen, Tuebingen, Germany, [8]Rheumatology and Clinical Immunology Unit, ASST Spedali Civili of Brescia, University of Brescia, Brescia, Italy, brescia, Italy, [9]University San Raffaele Milano, Milano, Milan, Italy, [10]Spitalul Clinic Dr. Ion Cantacuzino, Bucharest, Romania, [11]Centro di Riferimento Interdisciplinare per la Sclerosi Sistemica (CRIIS), Roma, Italy, rome, Italy, [12]Department of Internal Medicine, Division of Clinical Immunology and Rheumatology, University of Zagreb, School of Medicine, University Hospital Center Zagreb, Croatia, zagreb, Croatia, [13]Institute of Rheumatology Belgrade, Belgrade, Serbia, Belgrade, Serbia, [14]Southern California Scleroderma and Rheumatology Center, Los Angeles, CA, [15]Department of Rheumatology & Clinical Immunology, University Medical Center, Ultrecht, The Netherlands, Utrecht, Netherlands, [16]University of Leeds, Leeds, United Kingdom, [17]Department of Rheumatology & Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [18]Oslo University Hospital, Oslo, Norway, [19]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [20]University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Although most vasoactive vasodilating drugs (VVDs) exert anti-fibrotic effects in pre-clinical studies, randomized controlled trials assessing their efficacy in systemic sclerosis-associated interstitial lung disease (SSc-ILD) have shown mixed results. Therefore, we assessed the impact of VVDs on functional progression of SSc-ILD in an observational, real-life setting.

Methods: We identified SSc patients with ILD diagnosed on computed tomography, follow-up pulmonary function tests (PFTs) and treatment data in the EUSTAR database and excluded those with pulmonary hypertension on right heart catheterization or with systolic pulmonary artery pressure on echocardiography >50mmHg at any timepoint. VVDs included endothelin-receptor antagonists, phosphodiesterase-5 inhibitors and prostanoids, administered for at least 3 months in the observation period.

Five definitions of ILD progression within 12±3 months were tested:

A) Forced vital capacity (FVC) decline≥10%, or 5-9% with diffusion capacity for carbon oxide (DLCO) decline ≥15%

B) FVC decline ≥5% or DLCO decline ≥10%

C) FVC decline ≥10%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the study population at baseline and across all visits. Biologic Disease-Modifying Anti-Rheumatic Drug (bDMARD), conventional synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARD), diffusing capacity for carbon monoxide (DLCO), digital ulcer (DU), endothelin-receptor antagonists (ERA), forced vital capacity (FVC), New York heart association (NYHA), phosphodiesterase-5 inhibitors (PDE5i)

Parameter	At Baseline	Ever during observation including baseline	Among all visits
Female sex, n (%)	1544 (79%)		81.6%
Age, mean (SD)	55 (13)		56 (13)
Disease duration (years), mean (SD)	9 (8)		11 (8)
Diffuse subset, n (%)	972 (49.8%)		48.6%
Anti-Scl70 positive, n (%)	1082 (55.4%)		57.6 %
DU ever, n (%)	655 (33.6%)		44.8%
Increased inflammatory biomarkers, n (%)	461 (23.6%)		22.4%
FVC%, mean (SD)	86 (21)		86 (21)
DLco%, mean (SD)	62 (19)		62 (19)
bDMARDs, n (%)		178 (9.1%)	9.2%
csDMARDs, n (%)		978 (50.1%)	56.6%
Glucocorticoids >10 mg/day, n (%)		206 (10.6%)	12.4%
ERAs, n (%)		351 (18.0%)	20.2%
PDE5i, n (%)		156 (8.0%)	9.6%
Prostanoids, n (%)		457 (23.4%)	25.7%
Progression A) FVC decline ≥10%, or 5-9% DLCO decline ≥15%			18.3%
Progression B) FVC decline ≥5% or DLCO decline ≥10%			42.1%
Progression C) FVC decline ≥10%			13.2%
Progression D) FVC decline ≥5%			28.2%
Progression E) Worsening of NYHA class.			17.5%

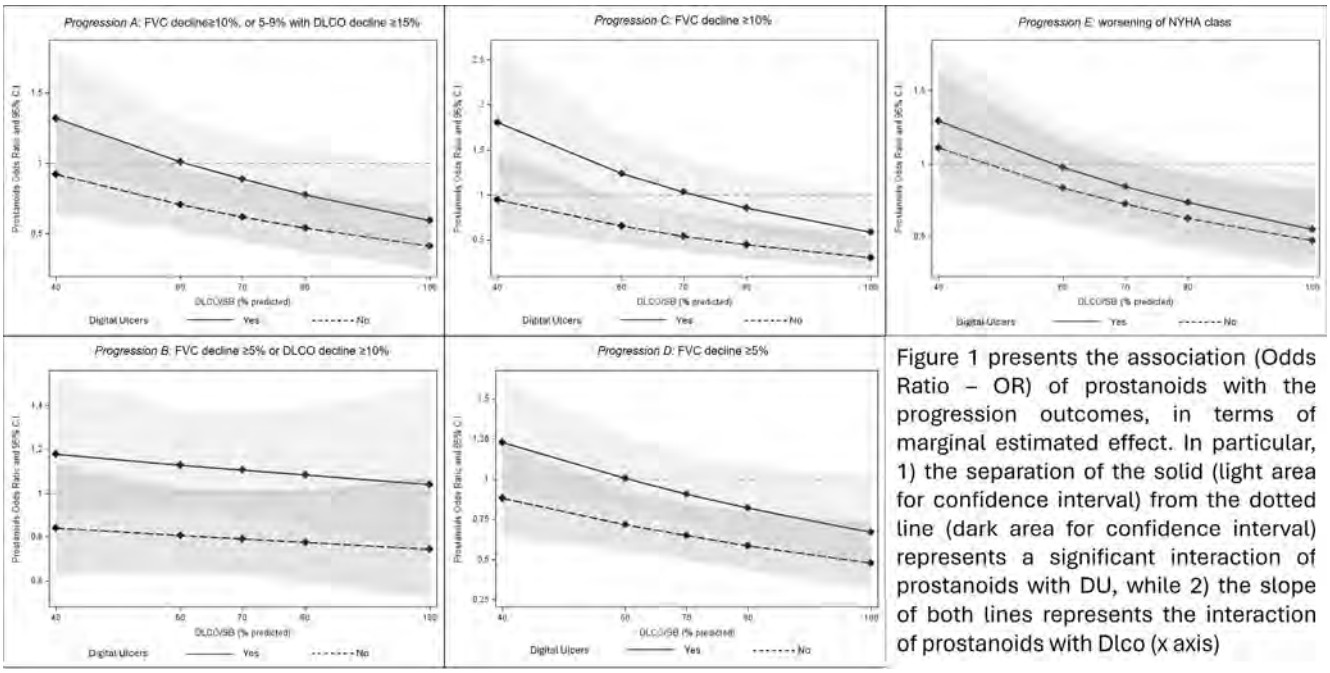


Figure 1 presents the association (Odds Ratio – OR) of prostanoids with the progression outcomes, in terms of marginal estimated effect. In particular, 1) the separation of the solid (light area for confidence interval) from the dotted line (dark area for confidence interval) represents a significant interaction of prostanoids with DU, while 2) the slope of both lines represents the interaction of prostanoids with Dlco (x axis)

Figure 1.

D) FVC decline ≥5%

E) Worsening of NYHA class.

Generalized estimated equation mixed models were performed separately for each ILD progression outcome.

A Cox regression model with time-dependent variables was applied for the survival analysis, with mortality as outcome.

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Interaction terms were computed between VVDs and markers of peripheral/pulmonary vasculopathy (digital ulcers – DU, DLCO).

All models were adjusted for known risk factors for ILD progression or mortality and ongoing immunosuppression.

Results: Among 5360 yearly visits of 1950 SSc-ILD patients, progression events ranged from 13 to 42%, according to the definition used (Table 1). Similarly, exposure to VVDs varied from 10 to 25% of the visits, with prostanoids being the most frequent.

The interaction of prostanoids and DU was associated with progression A (p=0.057), B (p=0.028), C (p=0.006) and D (p=0.048). This translated into a protective effect of prostanoids against PFT decline in patients without DU, compared to patients with DU (Figures A-D).

Additionally, prostanoids interacted significantly with DLCO, and this associated significantly with all progression definitions (A: p=0.022, B: p=0.003; C: p=0.001; D: p=0.023; E: p=0.010). Figures A-E show how higher DLCO values impact positively on the effectiveness of prostanoids.

Combining all effects, prostanoids significantly associated with less PFT progression when used in patients without DU and with DLCO >70%, while DLCO values >100% would be needed for prostanoids to exert similar effects in DU patients.

Over a median follow-up of 5.7 (2.8-9.9) years, 178/1950 (15.6%) SSc-ILD patients died. In the survival analysis, VVDs did not show any significant, independent impact on mortality.

Conclusion: Exposure to prostanoids is associated with lower risk of ILD progression in patients with mild vasculopathy (absence of DU, higher DLCO). Given our positive preliminary results on short-term progression, but the lack of independent impact on mortality, further studies are needed to confirm the beneficial effects of prostanoids on SSc-ILD.

Disclosure: a. sarbu: None; **L. Petelytska**: Swiss National Research Foundation/Scholars at risk, 5; **I. tofani**: None; **G. Moroncini**: None; **A. Balbir-Gurman**: None; **e. zanatta**: None; **J. Henes**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 1, 6, Eli Lilly, 1, Janssen, 1, 6, Novartis, 1, 1, 6, 6, Otsuka, 1, Pfizer, 1, Roche, 1, SOBI, 1, UCB, 1, 6; **p. airò**: Amgen, 12, meeting/travel support, CSL Behring, 12, meeting/travel support, Eli Lilly, 12, meeting/travel support, Janssen, 6, 12, meeting/travel support, Novartis, 6; **M. Matucci-Cerinic**: None; **A. Gheorghiu**: Boehringer-Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5; **a. marcoccia**: None; **b. Anić**: None; **J. Colic**: None; **D. Furst**: AbbVie/Abbott, 2, 5, Actelion, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cytori, 2, NIH, 5, Novartis, 2, 5, Pfizer, 2, 2, 5, 5, Roche-Genentech, 2, 5; **j. Spierings**: None; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **B. Maurer**: AbbVie/Abbott, 5, Actelion, 12, Congress support, Boehringer-Ingelheim, 1, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Medtalk, 12, Congress support, Mepha, 12, Congress support, Merck/MSD, 12, Congress support, Novartis, 2, 5, 6, Otsuka, 6, Pfizer, 12, Congress support, Protogen, 5, Roche, 12, Congress support, UCB, 12, Congress support; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Bruni**: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5.

Abstract Number: 1563

RESET-SSc: Clinical Trial Evaluating Rese-cel (Resecabtagene Autoleucel), A Fully Human, Autologous 4-1BB CD19-CAR T Cell Therapy in Systemic Sclerosis

Dinesh Khanna[1], Monalisa Ghosh[1], Ankoor Shah[2], Sonali Bracken[3], george georges[4], Carrie Richardson[5], Pei-Suen Tsou[1], Charles Ross[6], Carleigh Zahn[1], Courtney Little[7], Carl diCasoli[7], Mikaela Raymond[7], Adreeja GuhaRay[7], Jenell Volkov[7], Daniel Nunez[7], Thomas Furmanak[7], Jason Stadanlick[7], Larissa Ishikawa[7], Zachary Vorndran[7], Alexandra Ellis[7], Jazmean Williams[7], Steve Flanagan[7], Quynh Lam[8], Domenick Braccia[8], Fatemeh Hadi-Nezhad[8], Raj Tummala[8], Samik Basu[7] and David Chang[9], [1]University of Michigan, Ann Arbor, MI, [2]Duke University, Durham, NC, [3]Duke University Medical Center, Durham, NC, USA, Apex, NC, [4]Northwestern Medicine, Evanston, IL, [5]Northwestern University, Chicago, IL, [6]University of Michigan, Ann Arbor, [7]Cabaletta Bio, Philadelphia, PA, [8]Cabaletta Bio, Philadelphia, [9]Cabaletta Bio, Bryn Mawr, PA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The treatment goals for systemic sclerosis (SSc) are to control disease activity, limit progression of organ damage and decrease long-term morbidity and mortality. Therapies providing durable clinical responses without requiring chronic administration are lacking. Rese-cel (formerly CABA-201) is a fully human, autologous 4-1BB CD19-CAR T cell therapy designed to deeply and transiently deplete CD19 positive cells following a weight-based, single infusion to enable an "immune system reset" with the potential for durable response without chronic immunomodulatory (IM) therapy. RESET-SScTM (NCT06328777) is an ongoing Phase 1/2 trial evaluating rese-cel in 2 independent cohorts of adults with SSc and either severe skin or organ involvement.

Methods: Eligible patients were 18 to 75 years with SSc. A weight-based infusion of $1x10^6$ CAR T cells/kg was administered following preconditioning with fludarabine and cyclophosphamide. All non-glucocorticoid (GC) IM agents were stopped by Day -5. Adverse events, modified Rodnan skin score (mRSS), pulmonary function test (PFTs), nailfold capillaroscopy (NFC) and use of IM medications were evaluated. CAR T cells and B cells were profiled in peripheral blood pre- and post-infusion by digital PCR and flow cytometry, respectively. Serum cytokines were measured using the mesoscale discovery platform. Inguinal lymph node biopsies were taken from SSc-Skin-1 before and 21-days after rese-cel under a biorepository at University of Michigan; tissue was labeled for B cells (CD19, CD20, and PAX5, not shown) and T cells (CD3).

Results: As of 31 March 2025, 2 patients were infused with rese-cel (Table 1); SSc-Skin-2 did not have sufficient follow-up for efficacy or translational assessments. A third patient was recently infused.

SSc-Skin-1 had grade 2 cytokine release syndrome (CRS) but no dose-limiting toxicity (DLT) or immune effector cell-associated neurotoxicity syndrome (ICANS). SSc-Skin-2 experienced grade 3 ICANS based on a transient period of isolated confusion without seizures, motor findings, or signs of cerebral edema, which resolved in < 2 days with GC alone.

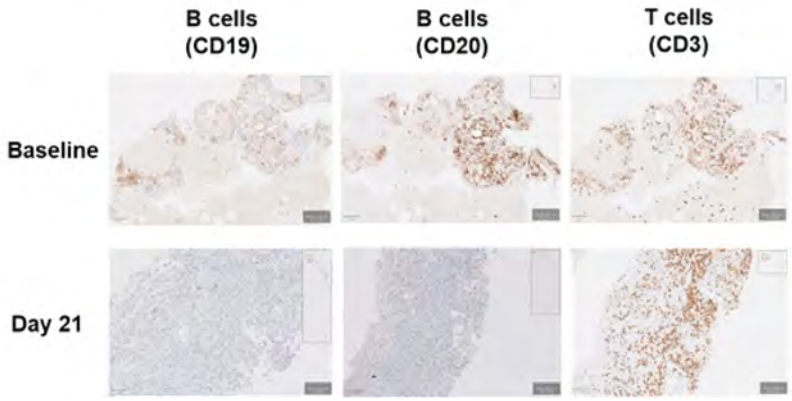
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

	RESET-SSc	
Patient / Cohort	**SSc-Skin-1** (Severe skin cohort)	**SSc-Skin-2** (Severe skin cohort)
Age, sex	66 F	55 F
Disease duration (y)	~2	~0.5
Autoantibodies	RNA P III	Scl-70
Baseline* mRSS	**42**	**38**
Baseline* PFTs (% predicted)	FVC: 91 DLCO: 70	FVC: 93 DLCO: 58
ILD present / absent	Present	Absent
Therapies at Screening	MMF (1500 mg BID)	MMF (1500 mg BID), GC
Other prior therapies	BRX (as part of a trial), HCQ	None
Prednisone dose at Screening (mg/day)	N/A	5
Duration of follow-up	6 months	2 weeks

As of 31 March 2025
*Baseline disease activity = activity before preconditioning.
BRX, brentuximab vedotin; DLCO=diffusing capacity of the lungs for carbon monoxide; FVC=forced vital capacity; GC, glucocorticoid; HCQ, hydroxychloroquine; MMF, mycophenolate mofetil; mRSS, modified Rodnan skin score; PFT=pulmonary function test; RESET, REstoring SElf-Tolerance; RNA P III, RNA polymerase III; SSc, systemic sclerosis; y, years.
Cabaletta Bio: Data on file

Figure 1. B cells depleted from LN tissue at Day 21 post-infusion in SSc-Skin-1.



SSc-Skin-1 showed improvement on mRSS, PFT and NFC at 6 months off all IM therapy. MRSS gradually improved from 42 to 34. NFC showed preliminary evidence of improvement of capillary density and size.

SSc-Skin-1 exhibited robust expansion of rese-cel that peaked at Day 15 post-infusion and was undetectable by Day 29. Serum IFNγ levels increased post-infusion and peaked prior to rese-cel peak expansion. Peripheral B cells were rapidly reduced in circulation by Day 15 and in lymphoid tissue (Figure 1) at Day 21. B cells reconstituted by 8 weeks post-infusion with a transitional naïve phenotype (CD19+CD20+CD38++CD24++) and switched to predominantly mature naïve by 6 months.

Conclusion: Data from the first SSc patient infused with rese-cel shows early IM-free clinical response and acceptable safety profile in the setting of CAR T cell expansion and complete peripheral and lymph node B cell depletion. These initial data suggest the potential for rese-cel to reset the immune system in SSc, allowing patients to achieve meaningful clinical responses off all IM therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: D. Khanna: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **M. Ghosh**: Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Fate, 5, Kite, 5, Miltenyi, 5, Novartis, 5; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **S. Bracken**: None; **g. georges**: Cabaletta Bio, 5; **C. Richardson**: Cabaletta Bio, 2; **P. Tsou**: None; **C. Ross**: None; **C. Zahn**: None; **C. Little**: Cabaletta Bio, 3; **C. diCasoli**: Cabaletta Bio, 3; **M. Raymond**: Cabaletta Bio, 3; **A. GuhaRay**: Cabaletta Bio, 3; **J. Volkov**: Cabaletta Bio, 3; **D. Nunez**: Cabaletta Bio, 3; **T. Furmanak**: Cabaletta Bio, 3; **J. Stadanlick**: Cabaletta Bio, 3; **L. Ishikawa**: Cabaletta Bio, 3; **Z. Vorndran**: Cabaletta Bio, 3; **A. Ellis**: Cabaletta Bio, 3; **J. Williams**: Cabaletta Bio, 3; **S. Flanagan**: Cabaletta Bio, 3; **Q. Lam**: Cabaletta Bio, 3; **D. Braccia**: Cabaletta Bio, 3; **F. Hadi-Nezhad**: Cabaletta Bio, 3; **R. Tummala**: Cabaletta Bio, 3; **S. Basu**: Cabaletta Bio, 12,, 3, 11; **D. Chang**: Cabaletta Bio, 3.

Abstract Number: 1564

Validation of a Composite Endpoint for Systemic Sclerosis-Associated Interstitial Lung Disease

Elizabeth Volkmann[1], Holly Wilhalme[2], Samuel Good[2], Grace Kim[2], Jonathan Goldin[2], Michael Roth[2] and Donald Tashkin[2], [1]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA, [2]UCLA, Los Angeles

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The forced vital capacity (FVC) is the most commonly used endpoint in registrational trials for systemic sclerosis-associated interstitial lung disease (SSc-ILD). However, the FVC has known methodological pitfalls, is affected by extra-pulmonary manifestations of SSc and may not be clinically meaningful to patients. Composite endpoints offer promising benefits for SSc-ILD trials in augmenting trial statistical efficiency and including patient-centered components.

Methods: We previously developed a composite endpoint for SSc-ILD using data from the Scleroderma Lung Study (SLS) I, comprised of the FVC, Transitional Dyspnea Index (TDI), Health Assessment Questionnaire Disability Index (HAQ-DI), and the quantitative extent of radiological fibrosis in the zone of maximum fibrosis (QLF-ZM), which demonstrated a more robust treatment effect of cyclophosphamide (CYC) versus placebo than the FVC alone [1]. The purpose of this study was to validate this composite endpoint using data from the SLS II (comparing CYC versus mycophenolate [MMF]). A secondary goal was to determine how the composite endpoint predicted long-term mortality in SLS I and II compared with the change in FVC.

Results: Seventy-two of the 142 randomized participants in SLS II had all of composite endpoint components assessed at 24 months and were included in this analysis. The composite endpoint distributions for SLS I and II were similar (Figure 1). In both SLS I and II, the standardized effect size as determined by Cohen's d was greater when the composite endpoint model was applied than when the FVC alone model was applied (Table 1). In SLS I and II, the composite endpoint was a better predictor of long-term mortality (HR 0.76 vs 0.98 and 0.59 vs. 0.98, for the composite index vs. FVC based on Cox proportional hazards models in SLS I and II, respectively), although both analyses were likely underpowered to detect statistical significance (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

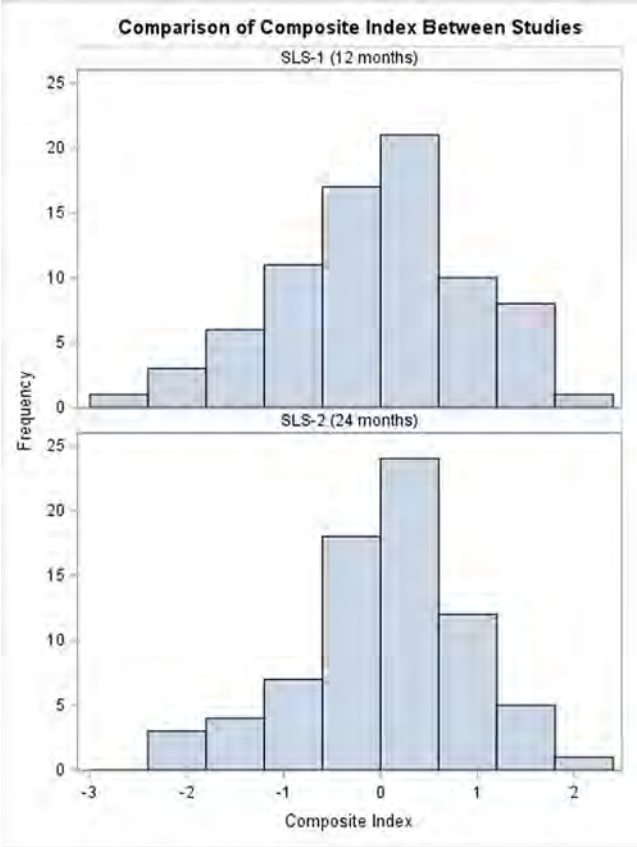


Figure 1. Histogram of composite index distributions in SLS I (top, composite endpoint measured at 12 months) and SLS II (bottom, composite endpoint measured at 24 months). In SLS II, the composite index had a mean (SD) of 0.06 (0.86), indicating slightly reduced variability compared to SLS I (standard normal). This variation may reflect differences in the two cohorts, rates of disease progression, and/or collection timepoints.

Conclusion: The results of this post-hoc analysis provide further evidence that a composite endpoint for SSc-ILD comprised of radiological, physiological and patient-reported outcomes is a promising endpoint for SSc-ILD trials. The composite endpoint may also serve to reduce the sample size required in clinical trials as more patients are needed to detect a significant treatment effect when a single outcome, such as the FVC, is used.

Table 1. Comparison of the treatment effects between the composite endpoint model and the FVC model in SLS I and II.

	Composite Endpoint Model	FVC Model
SLS I		
Treatment Effect (CYC vs. placebo)	Estimate 0.696 (SE 0.193), p=0.0006	Estimate 3.019 (SE 1.885), p=0.1133
Cohen's d (Standardized Effect Size)[1]	0.848	0.359
Sample Size Needed to Detect Treatment Effect (per group)[2]	23	123
SLS II		
Treatment Effect (CYC vs. MMF)[3]	Estimate 0.061 (SE 0.153), p=0.692	Estimate -0.184 (SE 1.594), p=0.909
Cohen's d (Standardized Effect Size)	0.094	-0.071

[1]Note that the root mean squared error from the adjusted linear model is used as the denominator of the effect size.
[2]Sample size calculation assumes a two-sample t-test with 80% power and alpha of 0.05.
[3]In SLS II, there was no significant difference in the FVC endpoint, nor any of the other efficacy endpoints included in the composite endpoint, between patients randomized to CYC vs. MMF; therefore, a sample size calculation was not performed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Cox proportional hazards model analysis for predicting long-term mortality in SLS I and II: Comparison of using the composite endpoint vs. the change in FVC. Follow up time for patients in SLS I and II was up to 12 and 8 years, respectively, from the time the first patient was randomized in each study.

Dataset	Number of Deaths/Total	Hazard Ratio (CI)	P-Value	C-Statistic
SLS I				
Composite Index (12 months)	27/77	0.763 (0.529 - 1.099)	0.1462	0.61
Change in FVC (12 months)	27/77	0.982 (0.956 - 1.008)	0.1642	0.58
SLS II				
Composite Index (24 months)	4/69	0.589 (0.190 - 1.830)	0.3604	0.71
FVC (24 months)	4/69	0.980 (0.897 - 1.071)	0.6575	0.59

References: 1. Volkmann ER, et al. Rheumatology (Sunnyvale). 2015;5:154.

Disclosure: E. Volkmann: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **H. Wilhalme**: None; **S. Good**: None; **G. Kim**: UCLA for patent; consultant at Voiant, 2, 10; **J. Goldin**: MEDQIA, 12, Founder; **M. Roth**: Genentech, 5; **D. Tashkin**: None.

Abstract Number: 1565

Association of the Gastrointestinal (GI) Microbiome and GI Symptoms in Systemic Sclerosis: An International, Multi-center, Observational Study

Zsuzsanna McMahan[1], Swapna Joshi[2], Jennifer Labus[2], Arissa Young[2], Andrea Low[3], Vanessa Smith[4], Susanna Proudman[5], Antonia Valenzuela[6], Phoebe Hunter[7], Kristofer Andréasson[8], Ezinne Aja[2], Jonathan Jacobs[2] and **Elizabeth Volkmann**[9], [1]UT Health Houston, Houston, TX, [2]UCLA, Los Angeles, [3]Singapore General Hospital, SingHealth; Duke-NUS, Singapore, Singapore, [4]Ghent University Hospital, Gent, Belgium, [5]Royal Adelaide Hospital and University of Adelaide, Medindie, South Australia, Australia, [6]Pontificia Universidad Catolica de Chile, Santiago, Chile, [7]Royal Adelaide Hospital, Adelaide, Australia, [8]Skåne University Hospital, Department of Rheumatology, Lund, Sweden, Lund, Sweden, [9]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: GI disease is highly prevalent in systemic sclerosis (SSc) and adversely affects quality of life and survival in SSc. The pathogenesis of GI disease in SSc is poorly understood; however, accumulating evidence suggests that alterations in the GI microbiome occur early in the SSc disease course [1] and are associated with specific SSc phenotypes [2]. No prior studies have investigated whether specific bacterial species associate with GI symptoms. The purpose of this study was to identify bacterial species associated with GI symptom severity in patients with SSc from across the world.

Methods: SSc patients from 7 SSc centers across 5 continents provided a stool sample. Shotgun metagenomic sequencing was performed using the Illumina NovaSeq 6000 to characterize microbial composition at the species level. The UCLA GIT 2.0 was administered at the time of the stool collection to evaluate GI symptom severity. Multivariate Sparse Partial Least Squares Regression (sPLS-R) was used to examine whether there was a species signature associated with GI symptom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

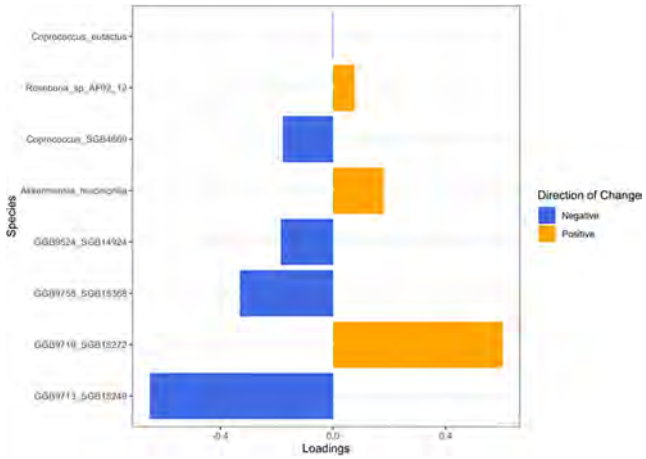


Figure 1. Feature loadings on the species-derived Total GIT 2.0 symptom severity signature from sPLS-R analysis (N=172). Features are ranked from highest (bottom) to lowest (top); species with higher loadings (i.e., weights) contributed the most to the signature score. For each species, positive and negative loadings reflect positive (orange bars) and negative association (blue bars) between that species and Total GIT 2.0 scores.

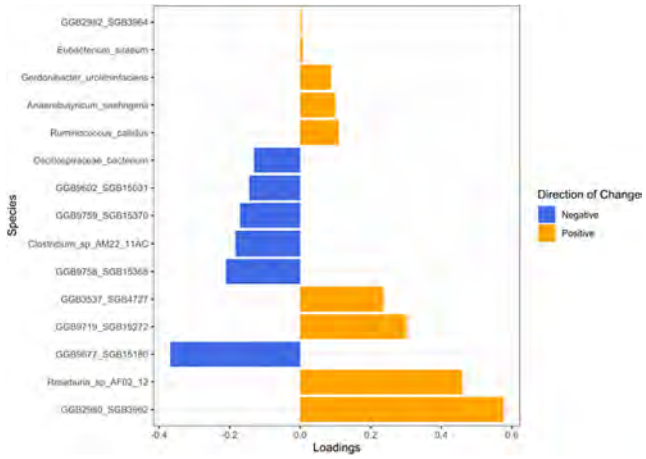


Figure 2. Feature loadings on the species-derived constipation severity signature from sPLS-R analysis (N=172). Features are ranked from highest (bottom) to lowest (top); species with higher loadings (i.e., weights) contributed the most to the signature score. For each species, positive and negative loadings reflect positive (orange bars) and negative association (blue bars) between that species and constipation scores.

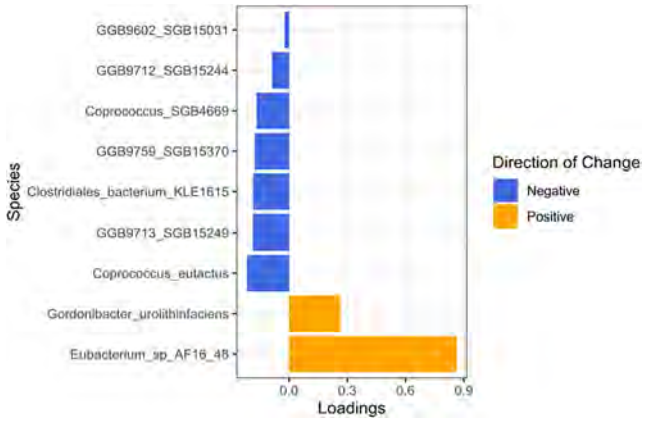


Figure 3. Feature loadings on the species-derived distension severity signature from sPLS-R analysis (N=172). Features are ranked from highest (bottom) to lowest (top); species with higher loadings (i.e., weights) contributed the most to the signature score. For each species, positive and negative loadings reflect positive (orange bars) and negative association (blue bars) between that species and distension scores.

23265205, 2025, S9, Downloaded from https://acgjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

severity, controlling for body mass index, current proton pump inhibitor use, current supplemental probiotic use, current or prior immunomodulatory therapy, presence of small intestinal bacterial overgrowth, interstitial lung disease and study site.

Results: Of the 274 participants, 83.5% were female, and 13.9% had SIBO. The mean (SD) disease duration was 9.49 (9.29) years. Among 257 bacterial species, the multivariate s-PLS-R identified a linear combination of 8 species associated with total GIT 2.0 score (r=0.38 (95% CI 0.24, 0.50), t(170)=5.29, p< 0.0001) (Figure 1). In terms of specific lower GI symptoms, s-PLS-R identified a linear combination of 15 species associated with constipation score (r=0.45 (95%CI 0.32, 0.56), t(171)=6.60, p< 0.0001) (Figure 2) and a linear combination of 9 species associated with distension score (r=0.37 (95%CI 0.23, 0.49), t(174)=5.18, p< 0.0001) (Figure 3). Six of the 8 species associated with total GIT 2.0 scores overlapped with species associated with either constipation or distension scores.

Conclusion: The results of this cross-sectional, international study demonstrate that the abundance of specific intestinal bacterial species in patients with SSc is associated with the severity of GI disease. These species and/or their metabolic products may serve as markers of GI disease severity in SSc and potentially contribute to SSc-GI pathogenesis.

References

1. Bellando-Randone S, et al. RMD Open. 2024;10:e004647.
2. Andréasson K, et al. ACR Open Rheumatol. 2022;4:417–25.

Disclosure: Z. McMahan: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **S. Joshi**: None; **J. Labus**: None; **A. Young**: None; **A. Low**: Boehringer-Ingelheim, 2, 5, 6, 12, Support for attending meetings; DSMB, Janssen, 2, 6, Neuquin Biopharm Pte Ltd, 1, Novartis, 6; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **S. Proudman**: Boehringer-Ingelheim, 5, 6, Janssen, 5, 6, Merck/MSD, 1; **A. Valenzuela**: None; **P. Hunter**: None; **K. Andréasson**: Janssen, 6; **E. Aja**: None; **J. Jacobs**: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5.

Abstract Number: 1566

Factors Associated with Patient and Physician Global Assessments in Early Systemic Sclerosis

Ellen Romich[1], Alexis Ogdie[2], Peter Merkel[3], Alisa Stephens Shields[3], Jessica Alvey[4], Shervin Assassi[5], Elana Bernstein[6], Sonali Bracken[7], Flavia Castelino[8], Lorinda Chung[9], Luke Evnin[10], Tracy Frech[11], Jessica Gordon[12], Faye Hant[13], Monica Harding[14], Laura Hummers[15], Dinesh Khanna[16], Kimberly Lakin[12], Dorota Lebiedz-Odrobina[14], Yiming Luo[6], Ashima Makol[17], Maureen Mayes[18], Zsuzsanna McMahan[19], Jerry Molitor[20], Duncan Moore[21], Carrie Richardson[22], Ami Shah[15], Ankoor Shah[23], Brian Skaug[24], Virginia Steen[25], John VanBuren[14], Elizabeth Volkmann[26], Carleigh Zahn[16], Nora Sandorfi[3] and the CONQUER Investigators, [1]University of Pennsylvania, Media, PA, [2]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [3]University of Pennsylvania, Philadelphia, PA, [4]Utah Data Coordinating Center, University of Utah, Salt Lake City, UT, [5]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [6]Columbia University, New York, NY, [7]Duke University Medical Center, Durham, NC, USA, Apex, NC, [8]Massachusetts General Hospital, Boston, MA, [9]Stanford University, Stanford, CA, [10]Scleroderma Research Foundation, San Francisco, CA, [11]Vanderbilt University Medical Center, Nashville, TN, [12]Hospital for Special Surgery, New York, NY, [13]Medical University of South Carolina, Charleston, SC, [14]University of Utah, Salt Lake City, UT, [15]Johns Hopkins Rheumatology, Baltimore, MD, [16]University of Michigan, Ann Arbor, MI, [17]Mayo Clinic, Rochester, MN, [18]UT Health Houston Division of Rheumatology, Houston, TX, [19]UT Health Houston, Houston, TX, [20]University of Minnesota, Minneapolis, MN, [21]Northwestern Memorial Hospital, Chicago, IL, [22]Northwestern University, Chicago, IL, [23]Duke University, Durham, NC, [24]UTHealth Houston Division of Rheumatology, Houston, TX, [25]Georgetown University School of Medicine, Washington, DC, [26]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Global assessments by patients and physicians provide unique but complementary perspectives of disease severity. This study aimed to determine the clinical and patient-reported factors associated with patient and physician global assessments in systemic sclerosis.

Methods: Adult patients with early systemic sclerosis (SSc) (< 5 years from first non-Raynaud's phenomenon symptom) from the COllaborative National QUality and Efficacy Registry (CONQUER) were included. Global disease assessments by patients (PtGA) and physicians (PhGA)(0-10, higher is worse, 7-day recall), clinical evaluations, and patient-reported outcomes were collected at enrollment. Multivariable linear regression models determined factors associated with each global assessment using i) pre-specified clinical variables only (Model 1), and ii) clinical variables plus patient-reported outcomes (Model 2). Relative weight analysis (RWA), an approach to evaluate variable importance among correlated variables, determined the relative importance of each factor as a portion of the total variance explained by the models.

Results: Data from 1113 patients (83% female, 35% limited cutaneous disease, mean (standard deviation, SD) disease duration 2.5 (1.4) years) are included **(Table 1)**. Mean (SD) global assessment scores at enrollment were 4.2 (2.6) and 3.5 (2.0) among patients and physicians, respectively (p< 0.001). Clinical variables explained 20% of the variability in the PtGA and 42% of the variability in the PhGA. Clinical and patient-reported variables explained 39% of the variability in the PtGA and 49% of the variability in the PhGA. RWA from Model 1 identified modified Rodnan skin score (mRSS) and New York Heart Association (NYHA) Function Class as clinical variables with the highest importance for both PtGA and PhGA **(Figure 1a, 1b)**. RWA from Model 2 demonstrated a shift in the most important contributors to PtGA from clinical measures to patient-reported measures including overall pain/discomfort (16.1%), PROMIS physical function (9.7%), PROMIS Pain

Table 1. Demographics and clinical characteristics at enrollment of patients with systemic sclerosis

Number of patients	1113
Age at baseline visit (years)	52.5 (13.56)
Female sex	927 (83.3%)
Race/ethnicity	
Hispanic	120 (10.8%)
Non-Hispanic White	770 (69.2%)
Non-Hispanic Black or African American	123 (11.1%)
Non-Hispanic Asian	70 (6.3%)
Non-Hispanic Other	25 (2.2%)
Unknown	5 (0.4%)
Disease duration at enrollment (years)	2.5 (1.42)
Limited cutaneous disease	387 (34.8%)
ANA/Autoantibody classification	
Centromere	201 (18.1%)
Scl-70	275 (24.7%)
RNA Polymerase III	241 (21.7%)
Two sub-serologies	55 (4.9%)
ANA only (no sub-serology)	81 (7.3%)
ANA negative or Other*	141 (12.7%)
Modified Rodnan Skin Score (mRSS)	12.3 (10.98)
ILD diagnosis	
ILD present	414 (37.2%)
ILD absent	323 (29.0%)
Unknown, no HRCT performed	376 (33.8%)
Renal crisis	42 (3.8%)
Global Assessments	
Physician Global Assessment (0-10)	3.5 (2.04)
Patient Global Assessment (0-10)	4.2 (2.56)

Values presented as n (%) or mean (standard deviation). *Other includes U1 anti-ribonucleoprotein, anti-polymyositis-scleroderma, anti-fibrillarin, anti-Th/To, anti-Ku, anti-Ro, anti-Ro, anti-La antibodies. Global assessments are rated from 0 (excellent health in past 7 days) to 10 (worst possible health). ANA, anti-nuclear antibody; ILD, interstitial lung disease; HRCT, high-resolution computed tomography chest imaging; RNA polymerase III, anti-ribonucleic acid polymerase III antibody; Scl-70, anti-topoisomerase antibody

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

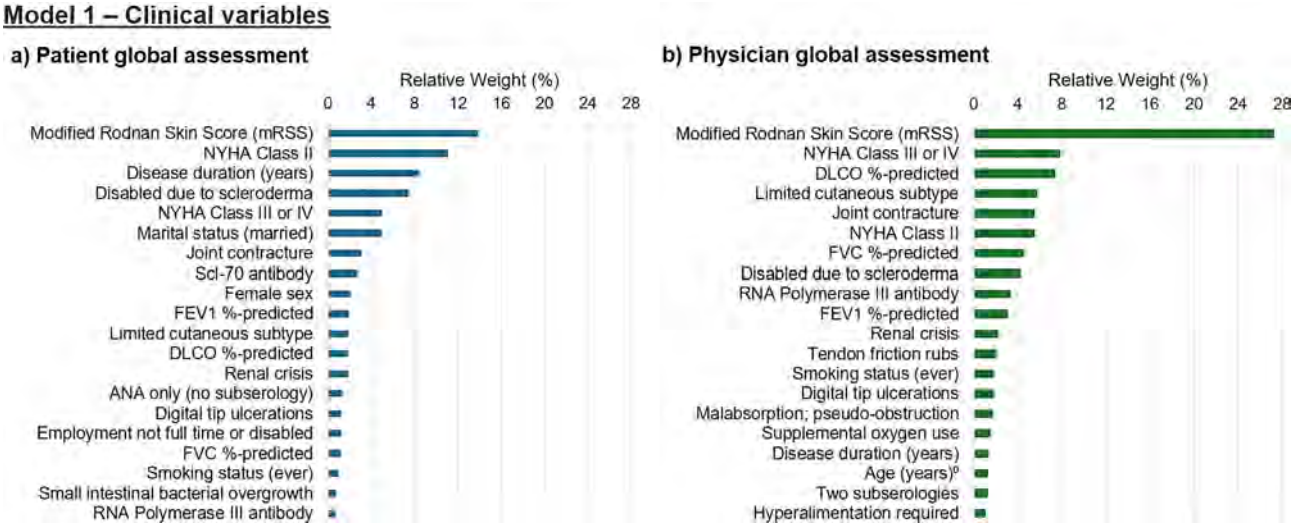


Figure 1. Relative weights of clinical variables associated with the patient and physician global assessment of disease in systemic sclerosis. Relative weight analysis (RWA) using enrollment visit data determined the relative importance of clinical variables (Model 1) associated with the a) patient global assessment and b) physician global assessment. Relative weights (%) indicate the proportion of variance explained by the variable out of the total variance explained by the model. Plots depict the 20 variables with the highest relative weights. For the patient global, R-squared = 0.20 and the 20 variables shown account for 74% of the total variance. For the physician global, R-squared = 0.42 and the 20 variables shown account for 90% of the total variance. Abbreviations: DLCO, diffusing capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NYHA, New York Heart Association; PROMIS, Patient-reported outcomes measurement information system; RNA polymerase III, anti-ribonucleic acid polymerase III antibody; Scl-70, anti-topoisomerase antibody; SHAQ, Scleroderma Health Assessment Questionnaire; VAS, visual analogue scale.

Interference (9.4%), Patient Skin Assessment (8.7%), and PROMIS Social Roles (6.9%) **(Figure 2a)**. For the PhGA, RWA based on Model 2 demonstrated that mRSS (13.1%), NYHA Class III/IV (7.2%), Patient Skin Assessment (6.5%), diffusing capacity of the lung for carbon monoxide (DLCO) %-predicted (5.4%), and overall pain/discomfort (5.0%) had the highest importance **(Figure 2b)**.

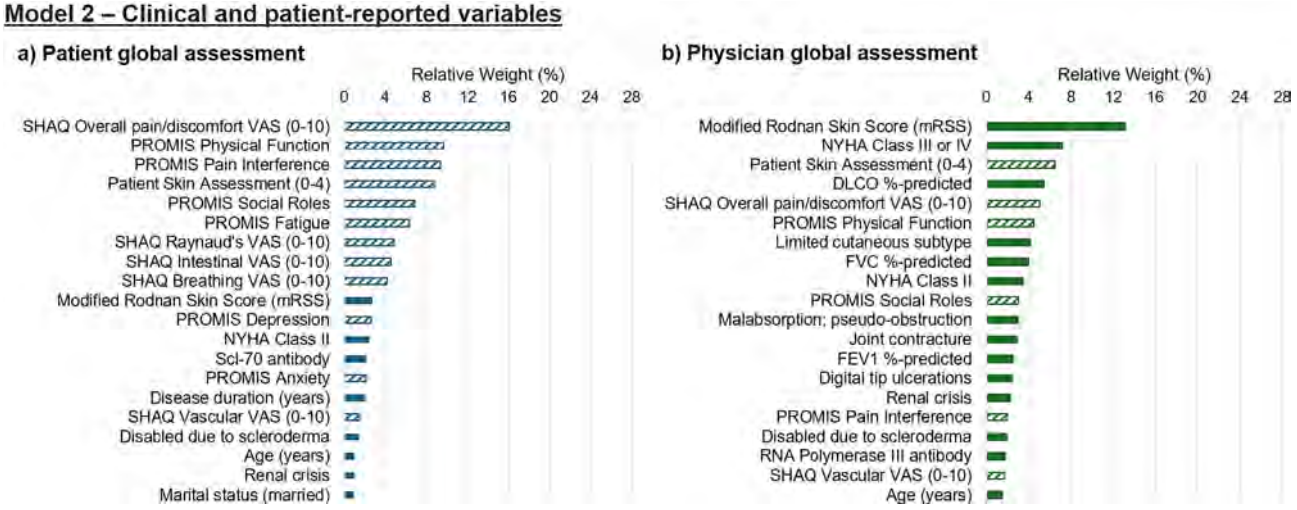


Figure 2. Relative weights of clinical and patient-reported variables associated with the patient and physician global assessments of disease in systemic sclerosis. Relative weight analysis (RWA) using enrollment visit data determined the relative importance of clinical and patient-reported variables (Model 2) associated with the a) patient global assessment and b) physician global assessment. Plots depict the 20 variables with the highest relative weights. Patient-reported variables are indicated by striped bars. For the patient global, R-squared = 0.39 and the 20 variables shown account for 90% of the total variance. For the physician global, R-squared = 0.49 and the 20 variables shown account for 79% of the total variance. Abbreviations: DLCO, diffusing capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NYHA, New York Heart Association; PROMIS, Patient-reported outcomes measurement information system; RNA polymerase III, anti-ribonucleic acid polymerase III antibody; Scl-70, anti-topoisomerase antibody; SHAQ, Scleroderma Health Assessment Questionnaire; VAS, visual analogue scale.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Factors associated with global assessments in early SSc differ between patients and physicians. Measures of skin involvement and functional status are important contributors to both PtGA and PhGA. However, the PtGA is most influenced by health-related quality of life symptoms that are not well-captured with traditional disease measures. The PhGA is influenced more heavily by traditional clinical factors, but physicians may underestimate the impact of patients' symptom burden. These findings highlight the broad impact of patients' experiences and the importance of collecting both patient- and clinician-reported outcomes in research in SSc.

Disclosure: E. Romich: Lungpacer Medical, Inc., 11, Teva Pharmaceuticals, 12, Spouse employment; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **A. Stephens Shields**: None; **J. Alvey**: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **E. Bernstein**: AstraZeneca, 5, aTyr, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **S. Bracken**: None; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **L. Evnin**: None; **T. Frech**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **F. Hant**: None; **M. Harding**: None; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(-GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **K. Lakin**: None; **D. Lebiedz-Odrobina**: None; **Y. Luo**: None; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **J. Molitor**: None; **D. Moore**: AstraZeneca, 5; **C. Richardson**: Cabaletta Bio, 2; **A. Shah**: None; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **B. Skaug**: None; **V. Steen**: None; **J. VanBuren**: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **C. Zahn**: None; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 2, Janssen, 2, Novartis, 1.

Abstract Number: 1567

Deep-learning analysis of HRCT images predicts progression and mortality in systemic sclerosis-related interstitial lung disease

Enrico De Lorenzis[1], Rosa D'Abronzo[2], Pier Giacomo Cerasuolo[3], Lucio Calandriello[4], Gabriella Alonzi[3], Giuseppe Cicchetti[2], gerlando Natalello[3], Bruno Iovene[5], Lucia Lanzo[3], Francesco Varone[6], Giacomo Sgalla[7], Luca Richeldi[8], anna Rita Larici[4], Maria Antonietta D'Agostino[3] and Silvia Laura Bosello[9], [1]Catholic University of the Sacred Heart, Roma, Rome, Italy, [2]Division of Radiology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy, [3]Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [4]Division of Radiology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [5]Division of Rheumatology - Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Rome, Italy, [6]Division of Respiratory Medicine - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [7]Catholic University of the Sacred Heart, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Rome, Italy,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[8]Division of Respiratory Medicine - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italy, [9]Division of Rheumatology and Clinical Immunology - Catholic University of the Sacred Heart, Rome, Italy, Rome, Italy

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a major complication in systemic sclerosis (SSc) patients, associated with substantial morbidity and mortality. Functional, imaging, and clinical measures of lung involvement could be biased in SSc due to its multiorgan nature and extra-articular involvement (e.g., cardiac, musculoskeletal). Artificial intelligence (AI) reading of high-resolution computed tomography (HRCT) has emerged as a novel tool for the objective and reliable assessment of pulmonary diseases. The aim of this study is to correlate AVIEW measures, an Deep learning based software for HRCT image assessment, with ILD-progression and disease-related mortality in SSc patients.

Methods: The AVIEW software (Coreline Soft, South Korea) was employed to analyze HRCT images from a cohort of consecutive SSc-ILD patients at baseline and after 24±3 months. Quantitative analyses included lung volume, texture, airways, and vascular anatomy. Baseline metrics were assessed for their association with ILD progression, defined by clinical, functional, and imaging criteria based on the INBUILD study parameters over 24 months. Furthermore, changes in AVIEW-derived measurements between consecutive HRCT evaluations over the 24-month period were analyzed for their association with SSc-related mortality during the subsequent 36 months. All absolute measurements were normalized to body surface area.

Results: A total of 146 HRCT scans from 73 SSc-ILD patients were assessed (mean age 58.4±14.3 years; male 16.4%; diffuse skin variant 49.3%). Thirty-one patients (42.4%) experienced ILD progression, which was predicted at baseline by higher percentages of ground glass opacities (GGO) (p=0.05) and reticulation (p=0.05), higher subpleural vessel volumes (p=0.017), and a tendency toward larger distal airways (p=0.066). Serial evaluations demonstrated that INBUILD progression was associated with a reduction in the percentage of normal lung (p=0.044) and absolute volumes (p=0.009), without significant changes in reticulation, GGO, vessels, or airways when considered individually.

Twelve patients died due to SSc within 36 months following the second HRCT evaluation. Patients in the upper quartile for changes in reticular score and airway volume exhibited a higher mortality risk, independent of INBUILD progression (reticular score: OR 3.30, 95% CI 1.03–10.61, p=0.045; airway volume: OR 3.37, 95% CI 1.08–10.51, p=0.036).

Conclusion: Deep learning-based assessment in SSc-ILD identified distinct modifications and prognostic significance in lung anatomical components, offering potential improvements in patient evaluation and stratification beyond conventional clinical tools.

Disclosure: E. De Lorenzis: None; **R. D'Abronzo**: None; **P. Cerasuolo**: None; **L. Calandriello**: None; **G. Alonzi**: None; **G. Cicchetti**: None; **g. Natalello**: None; **B. Iovene**: None; **L. Lanzo**: None; **F. Varone**: None; **G. Sgalla**: None; **L. Richeldi**: None; **a. Larici**: None; **M. D'Agostino**: Bristol-Myers Squibb(BMS), 5; **S. Bosello**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1568

A Novel Endothelial Cell Profiling Assay to Identify Systemic Sclerosis Patient Characteristics at the Endothelial Cell Level

Eva Hoekstra[1], Rudmer Postma[1], Nils Steinz[2], Wieke van Oostveen[1], Roel Bijkerk[1], Vincent van Duinen[2], Rachel Knevel[2], Tom Huizinga[2], Anton jan van Zonneveld[1], Jeska de Vries-Bouwstra[2] and Cynthia Fehres[1], [1]Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands, [2]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Vasculopathy, a hallmark clinical feature in systemic sclerosis (SSc), is a consequence of endothelial cell (EC) damage and dysfunction and might precede tissue fibrosis. Clinical disease progression in SSc is highly heterogeneous, with some patients developing severe fibrotic complications while others are affected by severe vascular complications including pulmonary arterial hypertension (PAH). The underlying mechanisms of this variability are poorly understood. We hypothesize that these distinct clinical phenotypes can be identified at the EC level. The objective is to investigate whether SSc patient plasma induces specific EC profiles and to examine correlations between these EC signatures and patients' clinical features.

Methods: Human umbilical vein endothelial cells (HUVECs) were exposed to 25% citrate plasma from SSc patients from the Leiden CCISS cohort (n = 199; 61 at baseline, and 69 at baseline and 1-year follow-up) and healthy controls (HC; n = 35), according to previously published protocol (Postma RJ, 2024; doi:10.1016/j.gastha.2023.10.006). After staining, Max-projections of 9 z-steps with 0.7 μm step size were acquired using a high content confocal microscope. Single-cell morphological profiles were computed from the images and averaged to create single-patient profiles (Fig 1). The Leiden algorithm was used to detect densely connected clusters in the constructed dataset. Performance of Support Vector Machine models predicting different clinical characteristics was evaluated by repeated cross validation. Sankey plots were generated to visualize transitions between clusters after 1 year of follow-up. Validation experiments are pending.

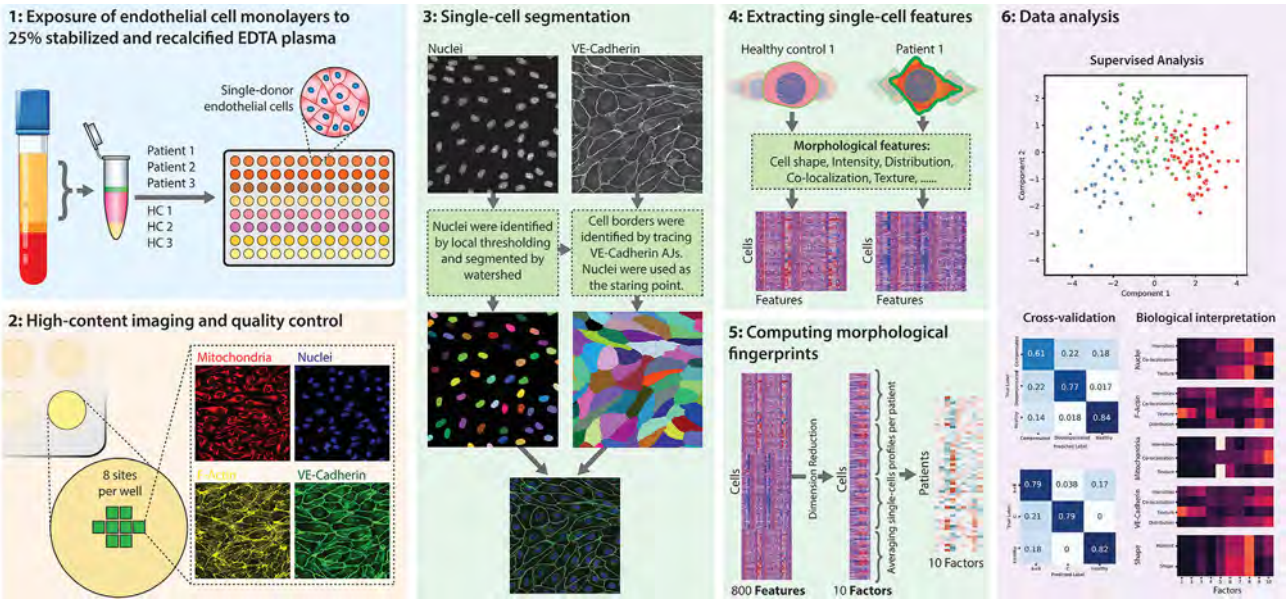


Figure 1. Morphological profiling on endothelial cell level.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

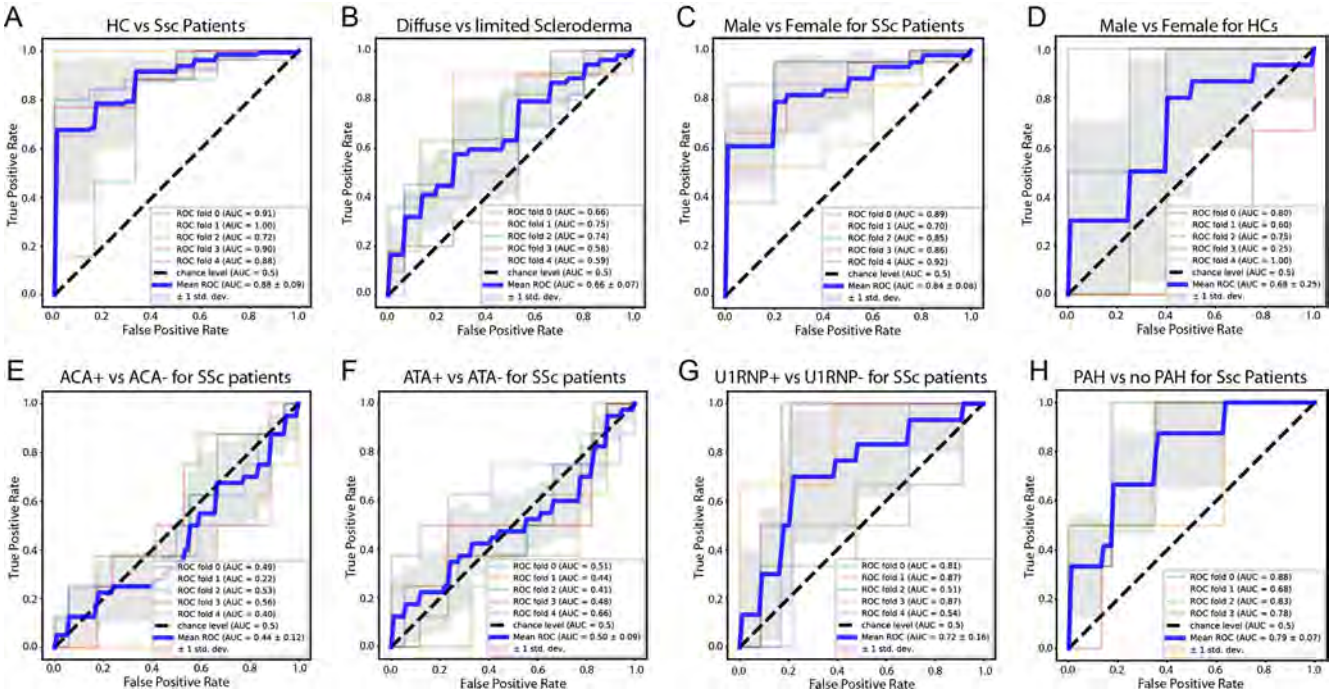


Figure 2. ROC curves of cross validation of SVM models with clinical characteristics.

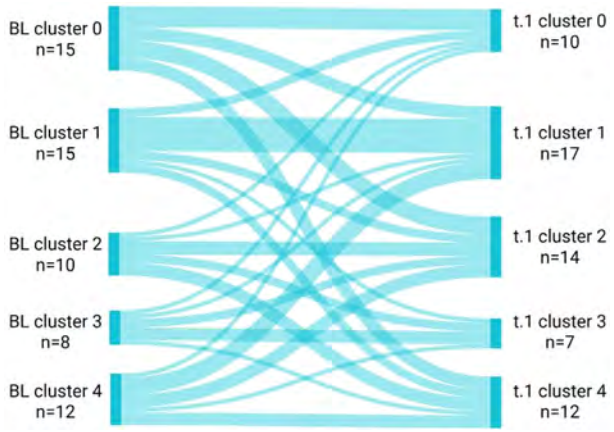


Figure 3. Transition of patients between cluster at baseline to cluster at 1-year follow-up.

Results: Graph-based cluster analysis of the morphological profiles identified 6 separate clusters, with high similarity between all 6-cluster solutions (adj. RAND index: 0.92). Cluster 6 represented outliers of the experiment and was therefore excluded from further analysis. HCs were predominantly found in cluster 0 (27.3%) and cluster 3 (55.9%). Figure 2 shows different SVM models that classify clinical features based on morphological data, specifically discriminating well between HC and patients (AUC 0.88 ± 0.09). Among patients, U1RNP+ patients and PAH patients showed distinct EC profiles (Fig 2). Strikingly, among patients EC profiles were clearly different between males and females, but this was not the case in HC (AUC 0.84 ± 0.08, and 0.68 ± 0.25, respectively). After 1 year follow up most patients (64.2%) migrated to a different cluster (Fig 3); patients who migrated from an SSc cluster to a HC enriched cluster (n = 8) showed stable, mild disease, whereas 50% of patients who migrated from a HC enriched to an SSc cluster (n=7/14) had disease progression.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Distinct morphological endothelial cell profiles were identified in SSc, especially for PAH. Interestingly, male and female EC profiles could be discriminated more clearly in SSc than in HC, indicating that sex-differences in SSc could be identified at the EC level. After 1 year follow-up, patients more often switched than remained in their original cluster, suggesting EC clusters could potentially reflect disease activity.

Disclosure: E. Hoekstra: None; **R. Postma**: None; **N. Steinz**: None; **W. van Oostveen**: None; **R. Bijkerk**: None; **V. van Duinen**: None; **R. Knevel**: None; **T. Huizinga**: None; **A. van Zonneveld**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **C. Fehres**: None.

Abstract Number: 1569

Can We Use Patient Reported Outcomes For Home-monitoring in SSc?

Eva Hoekstra[1], Katherine van der Wouden[2], Queeny Madari[1], Saad Ahmed[3], Lianne Kwant[1], Ada Hortensius-Varkevisser[1], Emiel Marges[1], Jacopo Ciaffi[4], Anne Schouffoer[5], Tom Huizinga[6] and Jeska de Vries-Bouwstra[6], [1]Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands, [2]Leiden University Medical Center and Amsterdam University Medical Center, Leiden, Zuid-Holland, Netherlands, [3]LUMC, Leiden, Netherlands, [4]IRCCS Istituto Ortopedico Rizzoli, Bologna, Bologna, Italy, [5]HagaZiekenhuis the Hague, the Hague, Netherlands, [6]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Home-monitoring is a suitable strategy to reduce the frequency of hospital visits, and alleviate strain on healthcare resources. However, in systemic sclerosis (SSc) this is challenging because of the heterogenous nature of the disease with regards to multi-organ involvement and trajectories of disease. The aim of this study was to explore the feasibility of using patient reported outcomes measures (PROMs) for home-monitoring by: (1) studying the association between

Table 1. Baseline characteristics of SSc patients in the CCISS cohort.

	Total (n = 767)	Stable disease* (n = 174)
Age (years)	55.2 ± 13.9	51.4 ± 13.4
Female, n (%)	596 (78)	133 (76)
Disease subset, n (%)		
- Non-cutaneous	170 (22)	34 (20)
- Limited cutaneous	427 (55.8)	84 (48)
- Diffuse cutaneous	168 (22)	44 (25)
Non RP duration (years)	7.2 (0.5 – 8.0)	2.5 (0.6 – 7.0)
Ever smoking, n (%)	402 (52)	80 (46)
ANA, n (%)	730 (95)	156 (90)
ATA, n (%)	181 (24)	42 (24)
ACA, n (%)	323 (42)	66 (38)
mRSS	3 (0 – 7)	3 (0 – 6)
Digital ulcers, n (%)	102 (12)	16 (9)
ILD on HRCT, n (%)	281 (37)	63 (36)
PAH, n (%)	21 (3)	3 (2)
FVC (%)	96.9 ± 20.4	100.4 ± 20.7
DLCO (%)	68.2 ± 18.8	69.2 ± 16.4
Immunosuppressive use (any), n (%)	222 (29)	47 (27)
- Methotrexate, n (%)	96 (13)	24 (14)
- Mycophenolate mofetil, n (%)	31 (3)	7 (4)
- Corticosteroids, n (%)	81 (11)	15 (9)
- Hydroxychloroquine, n (%)	40 (5)	9 (5)

*Stable disease defined as patients who had ≥ 3 consecutive progression-free visits.
Parametric data are reported as mean ± SD, non-parametric data as median (IQR).
Abbreviations. SSc: systemic sclerosis; ACA: anti-centromere antibody; GAVE: gastric antral vascular ectasia; ILD: interstitial lung disease; PAH: pulmonary arterial hypertension; FVC: forced vital capacity; DLCO: diffusing capacity for carbon monoxide.
Immunosuppressives include: methotrexate, mycophenolate mofetil, corticosteroids, hydroxychloroquine, cyclophosphamide and azathioprine.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Responses to SF-1 and SF-2 in the CCISS cohort.

In general, would you say your health is:		Compared to one year ago, how would you rate your health in general now?	
Total number of responses	3186	Total number of responses	3186
Excellent	40 (1.3)	Much better now	169 (5.3)
Very good	151 (4.7)	Somewhat better now	334 (10.5)
Good	986 (30.9)	About the same	1286 (40.4)
Fair	1620 (50.8)	Somewhat worse now	1091 (34.2)
Poor	389 (12.2)	Much worse now	306 (9.6)

Table 3. Diagnostic test accuracy of patient reported health in stable SSc.

"In general, how would you rate your health?"	No disease progression (n = 148)	Disease progression (n = 26)
Excellent	4 (80.0)	1 (20.0)
Very good	10 (76.9)	3 (23.1)
Good	50 (90.9)	5 (9.1)
Fair	68 (81.0)	16 (19.0)
Poor	16 (94.1)	1 (5.9)
Diagnostic test accuracy for the comparison "excellent + very good" versus "fair + poor": - Sensitivity: 81.0% - Specificity: 1.6% - Positive predictive value: 16.8% - Negative predictive value: 80.0%		
"Compared to one year ago, how would you rate your health in general now?"	No disease progression (n = 148)	Disease progression (n = 26)
Much better	6 (85.7)	1 (14.3)
Somewhat better	13 (92.9)	1 (7.1)
About the same	64 (84.2)	12 (15.8)
Somewhat worse	50 (82.0)	11 (18.0)
Much worse	15 (93.8)	1 (6.3)
Diagnostic test accuracy for the comparison "somewhat worse + much worse" versus "much better + somewhat better": - Sensitivity: 85.7% - Specificity: 22.6% - Positive predictive value: 15.6% - Negative predictive value: 90.5%		

PROMs assessing general health (question 1 and 2 of the 36-Item Short Form Health Survey [SF-36]) and disease progression, and (2) studying the discriminative ability of these PROMs to identify patients with active disease.

Methods: SSc patients fulfilling ACR/EULAR 2013 criteria, with complete SF-36 data, were included from the prospective Leiden CCISS cohort. The first two questions of the SF-36 comprise: "In general, how would you rate your health?" (SF-1) and "Compared to one year ago, how would you rate your health in general?" (SF-2), with possible responses on a 5-point ordinal scale. Disease progression was defined as a worsening of mRSS ≥ 5 and 25%, or ≥ 10% relative decrease in forced vital capacity (FVC), or ≥10% relative decrease in diffusing capacity for carbon monoxide (DLCO), compared to the previous visit). Considering informative follow-up and within-subject correlation we performed mixed-effects logistic regression correcting for age and sex to estimate the association between SF-1 and SF-2 response and disease progression, including time as a fixed effect and random intercept for each patient. A sensitivity analysis was performed in patients who had had three consecutive 'disease progression free' – visits, to determine diagnostic test accuracy of SF-1 and SF-2 for disease progression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In total, 767 SSc patients (n=3186 visits) were identified. Mean age of included patients was 55.2 ± 13.9 years, and 78% was female. Disease progression occurred in 287 patients (n=548 visits; Table 1 and 2). After correcting for age and sex both SF-1 and SF-2 response were not associated with disease progression (very good β -0.2 [-1.4-1.0], good β 0.4 [-0.7 – 1.4], fair β 0.6 [-0.5 – 1.6], poor β 0.7 [-0.4 – 1.8]; and somewhat better β 0.2 [-0.3 – 0.8], about the same β -0.3 [-0.8 – 0.2], somewhat worse β -0.1 [-0.8 – 0.3], much worse β -0.3 [-0.8 – 0.3]). In total, 174 patients (n=1279 visits) had three consecutive progression-free visits. In this subgroup, disease progression was observed in 26 visits. Both SF-1 and SF2 showed good sensitivity (>80%) and NPV (≥80%) to identify the patients with progression (Table 3).

Conclusion: Patient reported general health and change in health, as assessed with SF-36, are not associated with disease progression in the general SSc population, and are therefore not helpful for home-monitoring purposes for this population. However, when selecting a subgroup of patients with stable and mild disease for ≥ 3 years, general PROMs show good sensitivity and negative predictive value to identify patients with stable disease. We conclude that general PROMs hold potential for implementation in home-monitoring of SSc patients with mild disease.

Disclosure: E. Hoekstra: None; **K. van der Wouden**: None; **Q. Madari**: None; **S. Ahmed**: Janssen, 5; **L. Kwant**: None; **A. Hortensius-Varkevisser**: None; **E. Marges**: None; **J. Ciaffi**: None; **A. Schouffoer**: None; **T. Huizinga**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5.

Abstract Number: 1570

Hydroxychloroquine and Disease Progression in Systemic Sclerosis: Insights from Antibody-Stratified Survival Analyses

Francesco Bonomi[1], Ilaria Bisconti[2], Ilenia Mallia[3], Greta Pellegrino[4], Gabriele Ciuti[5], Gloria Muolo[2], Martina Salerno[2], Simona Truglia[2], Cristiano Barbetta[3], Silvia Peretti[5], Serena Guiducci[6], Valeria Riccieri[7] and Silvia Bellando Randone[3], [1]University Hospital Careggi, Florence, Florence, Toscana, Italy, [2]Sapienza University of Rome, Rome, Rome, Italy, [3]University of Florence, Florence, Italy, [4]Rheumatology Unit, IRCCS Ospedale Galeazzi Sant'Ambrogio, Milano, Italy; Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy, [5]University Hospital Careggi, Florence, Italy, [6]Division of Rheumatology, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, Florence, Italy, [7]Sapienza University of Rome, Rheumatology Clinic, Rome, Italy, Roma, Italy

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is an antimalarial drug that interferes with dendritic cells and monocytes, acidifies endosomes, and modulates toll-like receptors, reducing autoimmune responses and cell proliferation through autophagy inhibition. HCQ is widely used in rheumatic diseases for its immunomodulatory properties and is often prescribed in systemic sclerosis (SSc), despite the lack of confirmation of its efficacy in randomized trials.

The aim the study was to compare disease progression trajectories between HCQ-treated and -untreated SSc patients.

Methods: This retrospective, multicenter observational study included patients diagnosed with SSc according to the ACR/EULAR 2013 criteria, recruited from two Italian Rheumatology centers. Patients were grouped based on HCQ treatment. Demographic, clinical, serological, and capillaroscopic (NVC) data, as well as concomitant therapies, were recorded at baseline. At 6, 12-, 24-, 36-, and 60-months follow-up visits disease progression was determined according to validated criteria (Khanna D, 2016; Hoffmann-Vold AM, 2024) encompassing cutaneous, pulmonary, cardiac, and musculoskeletal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of demographical data and symptoms in SSc patients with or without treatment with hydroxychloroquine (HCQ). ANA: anti-nuclear antibodies; lcSSc: limited cutaneous SSc; dcSSc: diffuse cutaneous SSc; ssSSc: SSc sine scleroderma

	SSc without HCQ (n=134)	SSc with HCQ (n=167)	missing	p
Age, mean (SD)	56 (13.3)	55.2 (15)	0	0.637
Disease duration years, mean (SD)	1.93 (3.84)	2.54 (5.62)	0	0.269
Female, n (%)	116 (86.5)	153 (91.6)	0	0.157
ANA, n (%)	126 (94.0)	157 (94.0)	2	0.771
Anti-centromere antibodies, n (%)	49 (36.6)	85 (50.9)	5	**0.036**
Anti-topoisomerase I antibodies, n (%)	60 (44.8)	43 (25.7)	5	**<0.001**
Anti RNA polymerase III antibodies, n (%)	3 (2.2)	7 (4.2)	5	0.578
lcSSc, n (%) dcSSc, n (%) ssSSc, n (%)	85 (63.4) 35 (26.1) 14 (10.4)	120 (71.9) 30 (18.0) 17 (10.2)	0	0.215
mRSS, mean (SD)	5 (7)	3 (5)	10	**0.004**
Raynaud's phenomenon, n (%)	133 (99.3)	157 (94.0)	0	0.026
Puffy fingers, n (%)	81 (60.4)	99 (59.3)	0	0.258
Digital ulcers, n (%)	13 (9.7)	19 (11.4)	0	0.779
Digital pitting scars, n (%)	16 (11.9)	29 (17.4)	0	0.250
Teleangectasias, n (%)	33 (24.6)	52 (31.1)	0	0.263
Interstitial lung disease, n (%)	42 (31.3)	22 (13.2)	0	**<0.001**
Gastro-esophageal reflux, n (%)	55 (41.0)	69 (41.3)	0	>0.999
Dysphagia, n (%)	22 (16.4)	28 (16.8)	0	>0.999
Diarrhea, n (%)	6 (4.5)	8 (4.8)	0	>0.999
Nailvideocapillaroscopic pattern 0 normal, n (%) 1 early, n (%) 2 active, n (%) 3 late, n (%)	 14 (10.4) 28 (20.9) 50 (37.3) 21 (15.7)	 50 (29.9) 43 (25.7) 62 (37.1) 12 (7.2)	21	**0.006**
Corticosteroid, n (%)	35 (26.1)	46 (27.5)	0	0.884
Mycofenolate mofetil, n (%)	22 (16.4)	8 (4.8)	0	**0.002**
Methotrexate, n (%)	8 (6.0)	4 (2.4)	0	0.143
Tocilizumab, n (%)	1 (0.7)	1 (0.6)	0	>0.999
Rituximab, n (%)	2 (1.5)	3 (1.8)	0	>0.999
Cyclophosphamide, n (%)	2 (1.5)	3 (1.8)	0	>0.999
Calcium channel blockers, n (%)	53 (47.0)	66 (39.0)	0	0.235
Pentoxyphilline, n (%)	22 (16.4)	27 (16.2)	0	>0.999
Iloprost, n (%)	19 (14.2)	15 (9.0)	0	0.218
Sildenafil, n (%)	6 (4.5)	15 (9.0)	0	0.195
Endothelin receptor antagonist, n (%)	17 (12.7)	22 (13.2)	0	>0.999
Nintedanib, n (%)	2 (1.5)	0 (0.0)	0	0.197

domains, or the need to escalate immunosuppressive therapy. Progression-free survival was defined as the absence of worsening or new organ involvement. To test the study hypothesis Kaplan-Meier survival curves and Cox proportional hazards models were applied, stratifying the population by antibody profile (anticentromere, ACA+ or anti-topoisomerase I, Scl70+).

Results: A total of 301 patients with SSc were included (167 in the HCQ group and 134 in the non-HCQ group). Baseline characteristics were broadly similar between groups (Table 1), with no significant differences in age or disease duration. The HCQ group had a higher prevalence of ACA+ (50.8% vs 36.5%, p=0.036), and a lower prevalence of Scl70+ (25.7% vs 44.7%, p< 0.001) and interstitial lung disease (ILD, 13.1% vs 31.3%, p< 0.001). Mean mRSS was lower in the HCQ group (3±5 vs 5±7, p=0.004), while MMF use was more frequent in non-HCQ group (13.1% vs 6.0%, p=0.002). Kaplan-Meier curves demonstrated significant differences in progression-free survival between HCQ-treated patients in both ACA+ and Scl70+ (p< 0.001) subgroups (Figure 1).

In multivariable Cox regression models, HCQ treatment was independently associated with a reduced hazard of progression in both ACA+ (n=134, events=16; HR=0.05, 95% CI 0.01–0.25) and Scl70+ (n=103, events=39; HR=0.14, 95% CI 0.06–0.34) subgroups. However, baseline imbalances and confounding by indication may partially explain these associations.

Older age was also linked to reduced risk (HR=0.95, 95%CI 0.91–0.99) among ACA+ patients, while MMF showed a protective association (HR=0.37, 95%CI 0.15–0.88) in Scl70+ group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

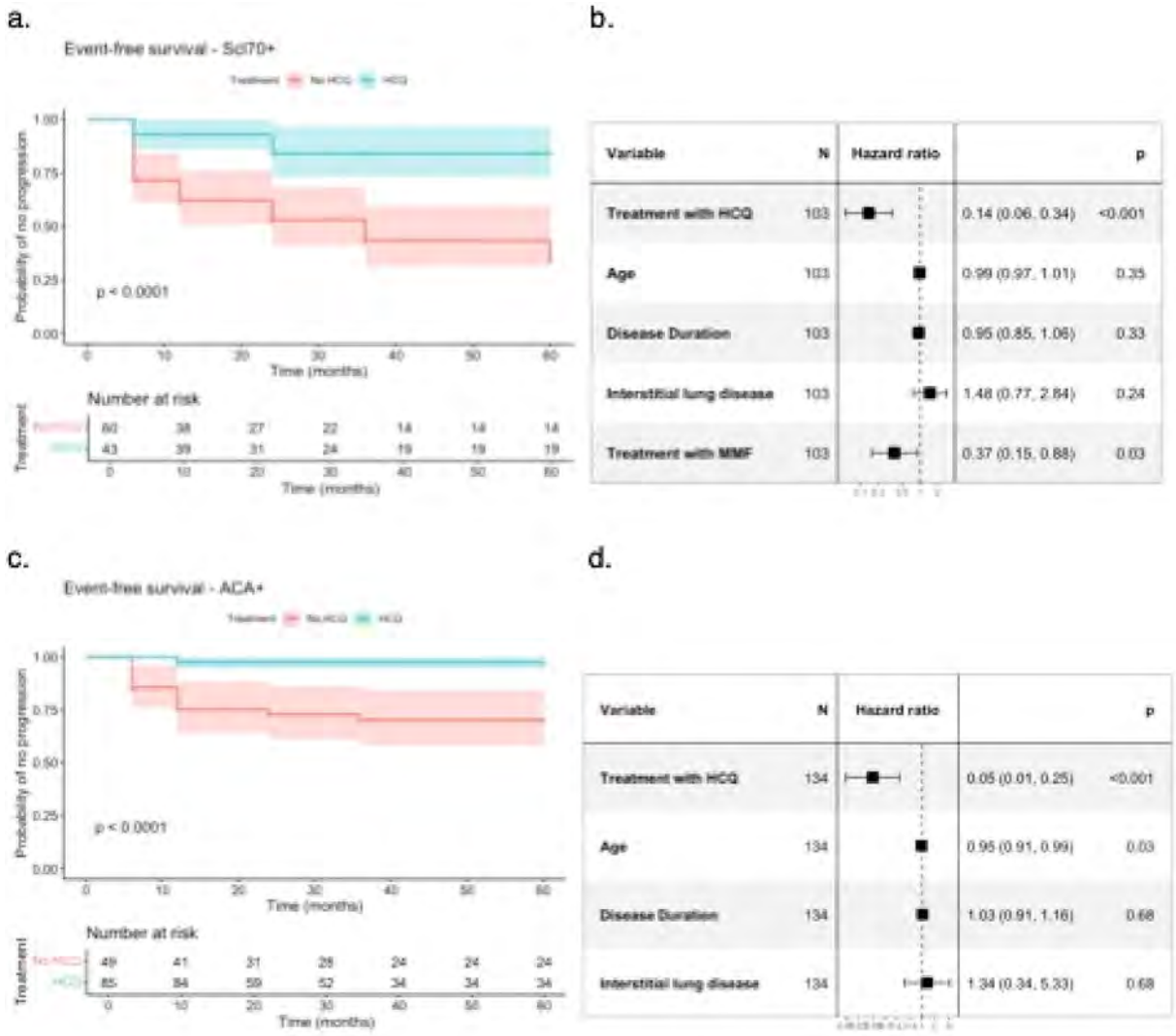


Figure 1. a. Kaplan-Meier curve showing the probability of remaining free from immunosuppressive therapy intensification in anti-Scl70 positive SSc patients, stratified by HCQ treatment. b. Forest plot illustrating the hazard ratios for progression in anti-Scl70 positive SSc patients. c. Kaplan-Meier curve showing the probability of remaining free from immunosuppressive therapy intensification in ACA-positive SSc patients, stratified by HCQ treatment. d. Forest plot illustrating the hazard ratios for progression in ACA-positive SSc patients.

Conclusion: In this retrospective study, HCQ use was associated with a lower risk of disease progression in patients with SSc, in both ACA+ and Scl70+ subgroups, over a 60 -months follow-up period. While the findings might suggest a potential protective role of HCQ, they must be interpreted with caution due to residual confounding. Prospective studies are warranted to validate these results.

Disclosure: F. Bonomi: Boehringer-Ingelheim, 6; **I. Bisconti**: None; **I. Mallia**: None; **G. Pellegrino**: None; **G. Ciuti**: None; **G. Muolo**: None; **M. Salerno**: None; **S. Truglia**: None; **C. Barbetta**: None; **S. Peretti**: None; **S. Guiducci**: None; **V. Riccieri**: None; **S. Bellando Randone**: Boehringer-Ingelheim, 2, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1571

Spatial Transcriptomics of Perivascular Subepidermal Regions in Very Early Systemic Sclerosis Unveils Cellular and Mitochondrial Stress-Driven Innate Immune Signatures that Initiate Stromal Remodeling

Ifeoluwa Emmanuel Bamigbola[1], Jayakumar Vadakekolathu[1], Stefano Di Donato[2], Vishal Kakkar[3], Rebecca Ross[4], Yasser El-Sherbiny[1] and **Francesco Del Galdo**[3], [1]1Nottingham Trent University, Department of Biosciences, School of Science and Technology, Nottingham, United Kingdom, [2]University of Leeds, Canosa Sannita, Chieti, Italy, [3]University of Leeds, Leeds, United Kingdom, [4]Medicine and Health, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: The skin from patients with Very Early Diagnosis of Systemic Sclerosis (VEDOSS) already exhibits fibrotic alterations such as collagen deposition and perivascular infiltration (1), despite the absence of clinically detectable skin thickening. A distinct immune-mediated structural organization across the epidermis, sub-epidermal region, and dermis, is involved in both early and late stages of SSc [2] The sub-epidermal perivascular area, located between these layers, serves as a crucial immune-fibro-vascular niche that may play a role in early fibrotic remodeling useful for determining SSc progression and identifying novel therapeutic applications.

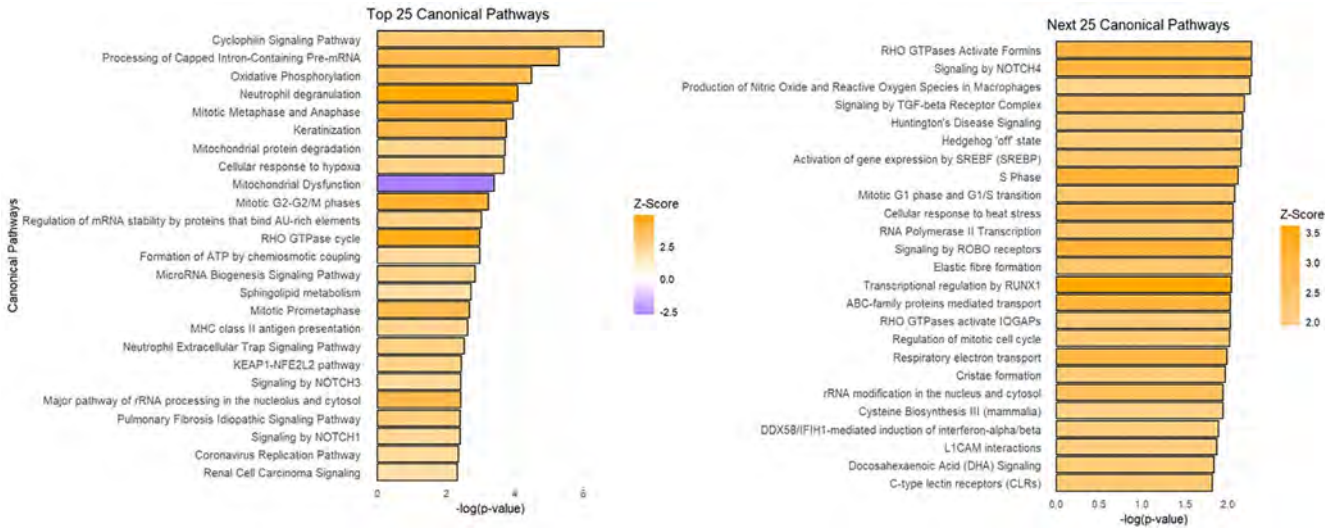
Objectives: To identify key signaling and cell types involved in the sub-epidermal perivascular regions within Very Early Diagnosis of Systemic Sclerosis (VEDOSS) compared to those with established disease and healthy control using spatial transcriptomic analyses.

Methods: We employed digital spatial transcriptomics to map whole genome transcriptome expression in the area immediately surrounding CD34-stained vessels in the sub-epidermal regions. Differentially expressed genes ($p < 0.05$, log2FC >0) were analyzed to identify relevant canonical pathways and biological processes.

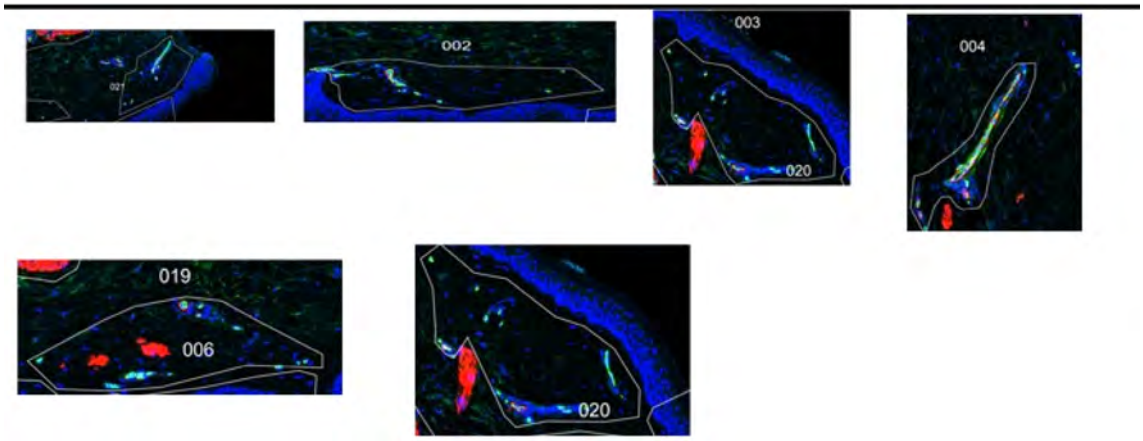
Results: Six skin biopsies from VEDOSS were compared with six biopsies from healthy individuals or patients with developed systemic sclerosis (SSc). Cell deconvolution revealed that the sub-epidermal region was dominated by diverse fibroblast subsets and vascular endothelial cells, with notable representation of immune populations such as T cells and macrophages. Disease-associated shifts included early depletion of secretory papillary fibroblasts in VEDOSS, enrichment of lymphatic endothelial cells, and progressive erythrocyte loss. Pathway Analysis of the sub-epidermal region in VEDOSS compared to healthy controls revealed significant upregulation of key stress and immune-related pathways. Notable among these were Cellular response to hypoxia, Oxidative Phosphorylation, Neutrophil Degranulation, Mitochondrial Dysfunction, and pulmonary idiopathic fibrosis signaling pathway. Key genes significantly upregulated included cyclophilin A, CD47, ATP5MG, COX10, NDUFB9, S100A4, COL1A1, COL16A1, COL17A1, COL21A1, FN1, PIK3R2, PIK3C2B, PDGFRB, implying cellular remodeling and stromal transitions through associated signaling pathways involved in fibrosis.

Conclusion: We demonstrate that the sub-epidermal perivascular region is a transcriptionally dynamic niche in VEDOSS skin, where early immune, metabolic, and fibrotic reprogramming converges to initiate stromal remodeling before the onset of clinically detectable fibrosis and progression to SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Ingenuity Pathway Analysis (IPA) of differentially expressed genes (DEGs) from the subepidermal region of interest (ROI), comparing VEDOSS with healthy controls. Pathways with an absolute z-score > 2 and p-value < 0.001 were considered significantly activated ($z \geq 2$) or inhibited ($z \leq -2$). Orange are predicted activated pathways and blue predicted inhibited.



Representative examples of subepidermal regions of interest (ROIs) selected from the 54 ROIs analyzed.

References:

[1] R[1] R. L. Ross *et al*., "Biological hallmarks of systemic sclerosis are present in the skin and serum of patients with Very Early Diagnosis of Systemic Sclerosis (VEDOSS)," *Rheumatology*, p. keae698, Dec. 2024, doi: 10.1093/rheumatology/keae698.

[2] Z. Li *et al*., "Mapping spatially-resolved transcriptomes in systemic sclerosis," *bioRxiv*, p. 2025.01.14.632962, Jan. 2025, doi: 10.1101/2025.01.14.632962.

Disclosure: I. Bamigbola: None; **J. Vadakekolathu**: None; **S. Di Donato**: None; **V. Kakkar**: None; **R. Ross**: None; **Y. El-Sherbiny**: None; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1572

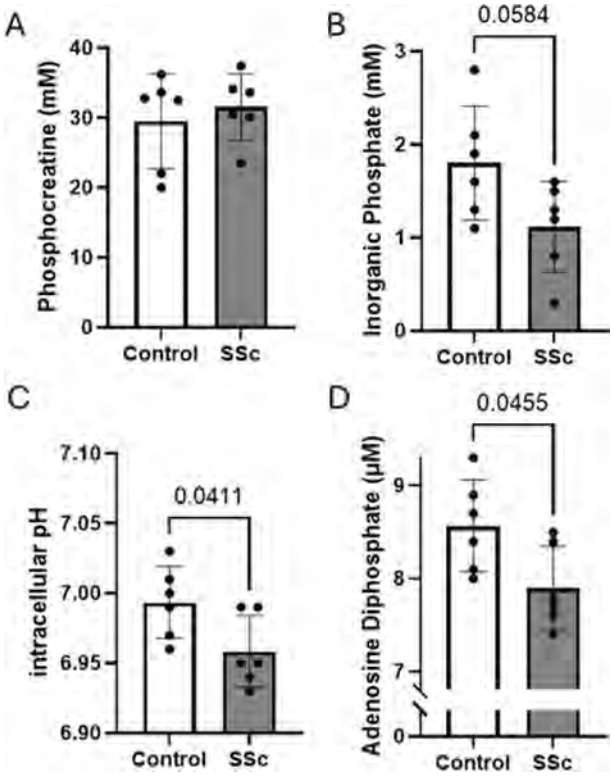
Compromised intracellular oxygen availability and severe mitochondrial dysfunction in the skeletal muscle of patients with systemic sclerosis

Gwenael Layec[1], Tracy Frech[2] and Anthony Donato[3], [1]University of Nebraska, Omaha, NE, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Salt Lake Veterans Affairs Medical Center, Salt Lake City, UT

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

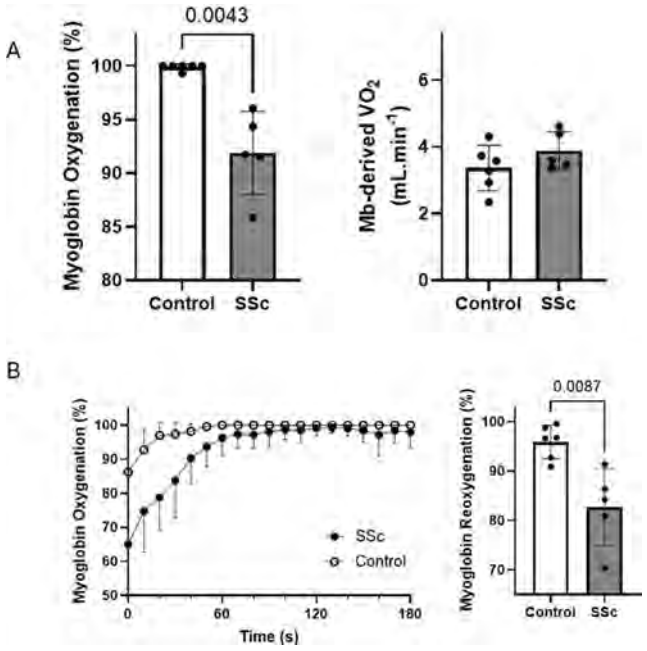
Background/Purpose: Muscle weakness and fatigue are frequent manifestations associated with systemic sclerosis (SSc). However, significant gaps remain in our understanding of the effects of SSc on skeletal muscle oxygenation and mitochondrial function. Using a non-invasive approach combining phosphorus- (31P) and proton- (1H) MRS of deoxy-myoglobin (dMb), the purpose of this study was to examine intracellular oxygen (O2) availability, muscle energetics, and mitochondrial function *in vivo* in the plantar flexor muscles of SSc patients and age-matched healthy controls.

Methods: Six adult with SSc and six healthy controls volunteered to participate in this study after signing a written informed consent. All patients were ANA positive with a SSc-specific antibody with a disease duration of less than 7 years disease duration from first non-Raynaud's phenomenon. No patients were classified as a myositis overlap. After familiarization, individual WRmax was determined during an incremental dynamic plantar flexion exercise to exhaustion (1 min stages). On a separate day, subjects performed two short bouts of submaximal plantar flexion at ~ 40% of WRmax (frequency of 1 Hz)

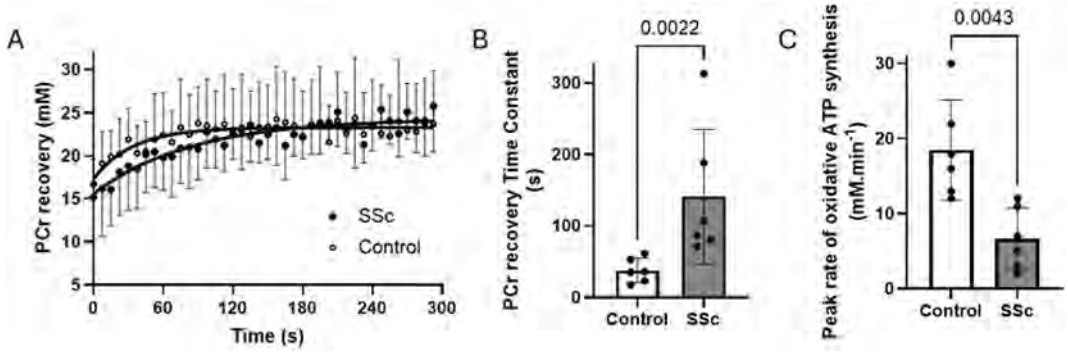


Resting concentrations of phosphocreatine (A), inorganic phosphate (B), intracellular pH (C), and adenosine diphosphate (D) in healthy controls and systemic sclerosis patients. Values are presented as mean ± SD with individual data (n = 6 in both groups).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Resting myoglobin oxygen saturation (left panel) and myoglobin-derived O2 consumption (right panel) in healthy controls and systemic sclerosis patients (A) and Post-exercise myoglobin reoxygenation kinetics (left panel) and the corresponding mean Mb O2 level during the first minute of recovery (right panel) in healthy controls and systemic sclerosis patients (B). Values are presented as mean ± SD with individual data (n = 6 in healthy control; n = 5 in SSc).



Post-exercise phosphocreatine resynthesis kinetics (A) and the corresponding time constant of the monoexponential fit of the individual data (B) in healthy controls and systemic sclerosis patients. Figure 3C displays the estimated peak rate of mitochondrial ATP synthesis in healthy controls and systemic sclerosis patients. Values are presented as mean ± SD with individual data (n = 6 in both groups).

in the whole-body MR system to assess skeletal muscle mitochondrial function and intracellular oxygenation, respectively. Specifically, after 4 min of data collection at rest, subjects exercised for 4 min followed by 5 min of recovery while 31P-MRS was continuously recorded. After ∼20 min of rest, this protocol was repeated using 1H-MRS of deoxy-myoglobin (dMb). At the end of this second protocol, an air-cuff wrapped above the knee was inflated to 250 mmHg for 8 min to achieve complete vascular occlusion and determine the maximum dMb signal. Due to safety concerns, the circulatory occlusion was not completed in one of the SSc patients. All experimental trials were performed in a thermoneutral environment with participants in an overnight fasted state.

Results: Resting concentrations of phosphocreatine, inorganic phosphate, intracellular pH, and adenosine diphosphate in HC and SSc patients are shown in Figure 1. Values are presented as mean ± SD with individual data (n = 6 in both groups). As shown in Figure 2, at rest SSc patients demonstrated significantly lower MbO2 saturation in the calf (SSc: 93 ± 4 % and controls: 99.9 ± 0.3%), although myoglobin-derived O2 consumption and phosphocreatine resynthesis kinetics [PCr] were

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

not significantly different between groups. During the post-exercise recovery period Mb reoxygenation was delayed in patients with SSc as indicated by the significantly lower mean Mb O2 saturation in the calf muscle of SSc patients during the first min of recovery compared with healthy controls (SSc: 83 ± 8 % and controls: 96 ± 3 %). As a result of this limited O2 supply, both the PCr recovery time constant and the peak rate of mitochondrial ATP synthesis (Vmax) were markedly lower in SSc patients than healthy controls (Vmax, SSc: 6.7 ± 4.1 mM·min-1 and 18.4 ± 6.7 mM·min-1) (Figure 3).

Conclusion: These findings suggest that both compromised intracellular O2 availability and impaired mitochondrial oxidative phosphorylation capacity play a central role in the development of muscle weakness and fatigue experienced by SSc patients.

Disclosure: G. Layec: None; **T. Frech**: None; **A. Donato**: None.

Abstract Number: 1574

A Rise in Serum KL-6 Levels Predicts Subsequent Progressive Pulmonary Fibrosis in Patients with Systemic Sclerosis-associated Interstitial Lung Disease

Keina Yomono[1], Suiyuan Huang[2], Dinesh Khanna[2] and Masataka Kuwana[3], [1]Nippon Medical School, Bunkyo-ku, Tokyo, Japan, [2]University of Michigan, Ann Arbor, MI, [3]Nippon Medical School Graduate School of Medicine, Tokyo, Japan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is leading cause of morbidity and mortality in patients with systemic sclerosis (SSc). Given the high variable clinical course of SSc-associated ILD (SSc-ILD), accurate prediction of ILD progression is crucial for both clinical practice and trial designing. Circulating biomarkers have emerged as convenient, non-invasive tools for the diagnosis and prognostication of SSc-ILD. Among these, elevated levels of Krebs von den Lungen-6 (KL-6), a marker for alveolar epithelial injury, has been consistently associated with subsequent decline in forced vital capacity (FVC) and progression to end-stage lung disease [1,2]. However, it remains unclear whether serial changes in KL-6 levels can predict ILD progression. This study aimed to determine whether rising KL-6 levels are predictive of progressive pulmonary fibrosis (PPF) in patients with SSc-ILD using a single-center prospective cohort.

Methods: A total of 136 patients with SSc-ILD were enrolled from a prospective SSc registry at Nippon Medical School Hospital. Patients were categorized into PPF and non-PPF groups based on the proposed criteria [3]. Baseline characteristics were compared between the groups, and a Cox proportional hazards model was used to identify baseline predictors of PPF. To assess the prognostic significance of dynamic KL-6 changes, a time-varying Cox model was applied using KL-6 measurements taken 12 and 6 months prior to either the first PPF event (PPF group) or the last follow-up visit (non-PPF group). KL-6 values were log2-transformed to facilitate interpretation per doubling. Models were adjusted for clinically relevant covariates.

Results: Over a median follow-up of 34 months, 26 patients (19%) developed PPF. Comparison to the non-PPF group, the PPF group had higher prevalence of anti-topoisomerase I antibody (P = 0.034), and a greater ILD extent on high-resolution computed tomography (HRCT) (P = 0.012). Baseline serum KL-6 levels were significantly higher in the PPF group

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics stratified by the presence or absence of PPF in patients with SSc-ILD

Variable	Non-PPF* (n = 110)	PPF* (n = 26)	*P*-value**
Age at baseline (years)	56.9 (15.2)	55.1 (14.0)	0.60
Female	98 (89.1%)	19 (73.1%)	0.054
Disease duration (months)	26.5 (6.0–67.0)	12.0 (5.0–26.0)	**0.025**
dcSSc	71 (64.5%)	16 (61.5%)	0.77
SSc-related autoantibody			
Anti-topoisomerase I	55 (50.0%)	19 (73.1%)	**0.034**
Anti-centromere	14 (12.7%)	1 (3.8%)	0.30
Anti-RNA polymerase III	13 (11.8%)	0 (0%)	0.073
mRSS	6 (2–13)	5 (2–12)	0.63
Raynaud's phenomenon	95 (86.4%)	23 (88.5%)	1.00
Tendon friction rubs	22 (20.0%)	5 (19.2%)	0.93
Digital ulcer	15 (14%)	2 (7.7%)	0.53
Laboratory parameters			
CRP (mg/L)	1.00 (0.50–2.70) (n = 108)	0.80 (0.40–2.30) (n=26)	0.48
KL-6 (U/mL)	609 (384–939) (n=104)	963 (640–1,365) (n=25)	**0.009**
Chest HRCT findings			
ILD extent on HRCT (%)	8 (4–18)	16 (8–22)	**0.012**
UIP pattern	11 (10.1%) (n = 109)	6 (23.1%)	0.097
Pulmonary function test			
FVC (L)	2.26 (1.84–2.84) (n=102)	2.38 (2.11–3.00) (n=25)	0.33
FVC (% predicted) (%)	88.5 (75.6–104.0) (n=102)	83.2 (75.4–97.1) (n=25)	0.53
DL_{CO} (% predicted) (%)	73.0 (58.4–86.5) (n=91)	75.7 (45.2–84.0) (n=21)	0.60
ILD extensive disease	32 (31.4%) (n = 102)	11 (44.0%) (n=25)	0.34

*Mean (SD); Median (IQR); n (%), **Wilcoxon rank sum test; Fisher's exact test, Pearson's Chi-squared test
CRP: C-reactive protein; dcSSc: diffuse cutaneous systemic sclerosis; DL_{CO}: diffusing capacity for carbon monoxide; ESR: erythrocyte sedimentation rate; mRSS: modified Rodnan total skin thickness score; GI: gastrointestinal; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; IQR: interquartile range; KL-6: Krebs von den Lungen-6; PAH: pulmonary hypertension; FVC: forced vital capacity; PPF: progressive pulmonary fibrosis; SD: standard deviation; SSc-ILD: systemic sclerosis-associated ILD; UIP: unusual interstitial pneumonia

(P = 0.009). In the Cox model, positive anti-topoisomerase I antibody was associated with 236% higher risk of future PPF development (HR: 3.36, 95% confidence interval (CI): 1.17-9.62, P = 0.024), while ILD extent, usual interstitial pneumonia (UIP) pattern on HRCT, and FVC didn't show significant association. In the time-varying Cox model, a doubling of KL-6 levels was associated with 72% higher risk of subsequent PPF (HR 1.72; 95% CI 1.09–2.71; P = 0.020). This association remained significant and was even strengthened after adjusting for clinically relevant covariates, including anti-topoisomerase I antibody status (HR 2.17; 95% CI 1.06–4.45; P = 0.034).

Conclusion: A rise in serum KL-6 levels was significantly associated with the near-term development of PPF in patients with SSc-ILD. These findings support the use of serial KL-6 measurements as a non-invasive biomarker to monitor disease progression and guide clinical decision-making in SSc-ILD.

Reference

[1] *J Rheumatol* 2016; 43: 1825
[2] *Arthritis Rheumatol* 2019; 71: 2059
[3] *Am J Respir Crit Care Med* 2022; 205: e18

Disclosure: K. Yomono: None; **S. Huang**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **M. Kuwana**: AbbVie, 2, Asahi Kasei Pharma, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 6, GlaxoSmithKlein(GSK), 2, Medical and Biological Laboratories, 5, 9, Mochida, 2, Novartis, 2, Ono Pharmaceuticals, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1575

Clinical presentation, course, treatment and outcome of juvenile onset versus adult onset mixed connective tissue disease patients: a multicenter retrospective cohort.

Kevin Chevalier[1], Brigitte Bader-Meunier[2], Isabelle Kone-Paut[3], Benjamin Torreau[4], Marc Michel[5], Bertrand Godeau[5], Christian AGARD[6], Thomas Papo[7], Karim Sacré[8], Raphaele Seror[9], Xavier Mariette[10], Cacoub Patrice[11], Ygal Benhamou[12], Mathilde Leclercq[13], Cécile goujard[14], Olivier Lambotte[3], Bernard Bonnotte[15], Maxime Samson[16], Félix Ackermann[17], Jean Schmidt[18], Pierre Duhaut[18], Jean-Emmanuel Kahn[19], Thomas Hanslik[19], Nathalie Costedoat-Chalumeau[20], Benjamin Terrier[20], Alexis REGENT[21], bertrand Dunogue[22], Pascal Cohen[23], Véronique Le Guern[20], Eric HACHULLA[24], Luc Mouthon[22] and Benjamin Chaigne[22], [1]Université Paris Cité, Montrouge, France, [2]Necker hospital, Paris, France, [3]Bicêtre hospital, Kremlin Bicêtre, France, [4]Internal Medicine and Immunology, CHU Tours, Tours, France, [5]Henri Mondor hospital, Créteil, France, [6]Internal medicine, Nantes University Hospital, Nantes, France, [7]Bichat hospital, Paris, France, [8]Department of Internal Medicine, Bichat University Hospital, Université Paris Cité, AP-HP, Paris, France, Paris, France, [9]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [10]Université Paris-Saclay, Le Kremlin Bicetre, France, [11]Department of Internal Medicine and Clinical Immunology, Sorbonne Universités, AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Centre national de références Maladies Autoimmunes et systémiques rares, Centre national de références Maladies Autoinflammatoires rares et Amylose inflammatoire (CEREMAIA), INSERM, UMR S959, Immunology-Immunopathology-Immunotherapy (I3), Paris, France, Paris, France, [12]Internal Medicine, CHU Rouen, Rouen, France, [13]Rouen hospital, Rouen, France, [14]Université Paris Saclay, Department of Internal Medicine and Clinical Immunology, Bicêtre Hospital, APHP, UMR1184 Inserm, CEA, Le Kremlin Bicêtre, France, Kremlin Bicêtre, France, [15]Internal medicine and clinical immunology, Université Bourgogne Europe , CHU Dijon Bourgogne, Dijon, France, [16]CHU Dijon Bourgogne, Dijon, France, [17]Foch hospital, Suresnes, France, [18]Amiens hospital, Amiens, France, [19]Ambroise Paré hospital, Boulogne, France, [20]Cochin hospital, Paris, France, [21]Hopital Cochin, Paris, France, [22]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [23]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [24]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-Immunes et Auto-Inflammatoires Rares du Nord, Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille, France, Lille, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Mixed connective tissue disease (MCTD) is an entity defined by clinical features of differentiated connective tissue diseases (dCTD), such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), or idiopathic inflammatory myopathies (IIM) and the presence of autoantibodies directed toward ribonucleoprotein U1. Although juvenile onset MCTD (jMCTD) occurs in 7-23% of all MCTD cases, few studies have examined the course of jMCTD patients. The aim of the present study was to describe the characteristics, treatments, long-term outcomes of jMCTD, in comparison to adult onset MCTD patients.

Methods: We conducted a multicentric case-control, retrospective, observational, and longitudinal study in the French MCTD cohort. Adult and jMCTD patients were included if they fulfilled, at time of disease onset, at least one of the 4 sets of MCTD diagnosis criteria without fulfilling any current classification criteria for a dCTD. jMCTD patients were defined by an age < 18 years old (y.o) at disease onset. For each jMCTD, 3 adult controls were randomly matched for sex, date of inclusion and follow-up duration.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 – Comparison of clinical characteristics at baseline between juvenile and adult onset MCTD patients

Characteristic	All patients (n=188)	Juvenile onset (n=47)	Adult onset (n=141)	p-value
Female	172 (91.5)	44 (93.6)	128 (90.8)	0.5
Age at diagnosis (y.o.)	30.5 [18 - 42.3]	14 [11-16]	36 [29-45]	< 0.0001
Ethnic group				0.1
Caucasian	123 (65.4)	32 (68.1)	91 (64.5)	
Afro-Caribbean ancestry	53 (28.2)	15 (31.9)	38 (27)	
Asian ancestry	12 (6.4)	0 (0)	12 (8.5)	
Clinical findings				
Fever	21 (11.2)	7 (14.9)	14 (9.9)	0.4
Raynaud's phenomenon	169 (89.9)	42 (89.4)	127 (90.1)	0.8
Puffy fingers	73 (38.8)	8 (17)	65 (46.1)	< 0.0001
Sclerodactyly	4 (2.1)	0 (0)	4 (2.8)	-
Digital tip ulcers	4 (2.1)	2 (4.3)	2 (1.4)	-
Cracked fingertips	2 (1.1)	0 (0)	2 (1.4)	-
Telangiectasias	3 (1.6)	0 (0)	3 (2.1)	-
Skin pigmentation disorder	7 (3.7)	2 (4.3)	5 (3.5)	-
Acute cutaneous lupus	3 (1.6)	0 (0)	3 (2.1)	-
Photosensitivity	9 (4.8)	3 (6.4)	6 (4.3)	-
Livedo	4 (2.1)	1 (2.1)	3 (2.1)	-
Alopecia	9 (4.8)	1 (2.1)	8 (5.7)	-
Arthralgia	154 (81.9)	37 (78.7)	117 (83)	0.5
Synovitis	42 (22.3)	13 (27.7)	29 (20.6)	0.2
Myalgia	67 (35.6)	19 (40.4)	48 (34)	0.4
Seritis (pericarditis/pleurisis)	7 (3.7)	0 (0)	7 (5)	-
Peripheral neuropathy	0 (0)	0 (0)	8 (5.7)	-
Gastroesophageal reflux	27 (14.4)	3 (6.4)	24 (17)	-
Dysphagia	2 (1.1)	1 (2.1)	1 (0.7)	-
Renal disease	5 (2.7)	3 (6.4)	2 (1.4)	-
Dyspnea	33 (17.6)	9 (19.1)	24 (17)	0.8
Pulmonary hypertension	5 (2.7)	0 (0)	5 (3.5)	-
ILD	24 (12.8)	5 (10.6)	19 (13.5)	0.6
PF	2 (1.1)	0 (0)	2 (1.4)	-
Parotid swelling	7 (3.7)	3 (6.4)	4 (2.8)	-
Subjective oral dryness	23 (12.2)	2 (4.3)	21 (14.9)	-
Subjective ocular dryness	15 (8)	2 (4.3)	13 (9.2)	-
Lymphadenopathy	28 (14.9)	5 (10.6)	23 (16.3)	0.3

Data are presented as number (percentage) or median with interquartile range. P-value were calculated thanks to Chi-squared test or Fisher's exact test as appropriate for qualitative variables and T-test or Wilcoxon rank sum test as appropriate for quantitative variables
ILD: interstitial lung disease; MCTD: mixed connective tissue disease; n= number; PF: pulmonary fibrosis, y.o.: years old

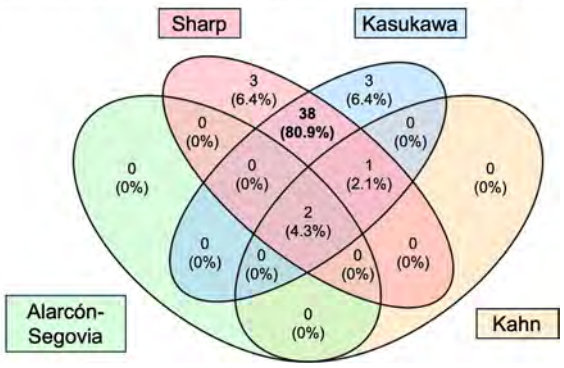
Table 2 – Comparison on the outcomes between juvenile and adult onset MCTD patients

Characteristic	All patients (n=188)	Juvenile onset (n=47)	Adult onset (n=141)	p-value
Follow-up (months)	118 [80-193.5]	118 [79-194]	118 [80-193]	> 0.9
Outcomes				
Pulmonary hypertension	14 (7.4)	2 (4.3)	12 (8.5)	0.5
ILD	56 (29.8)	11 (23.4)	45 (31.9)	0.3
PF	24 (12.8)	5 (10.6)	19 (13.5)	0.6
Remission	91 (48.4)	29 (61.7)	62 (44)	0.04
Death	8 (4.3)	1 (2.1)	7 (5)	-
Evolution towards dCTD	60 (31.9)	17 (36.2)	43 (30.5)	0.5
SLE	29 (15.4)	10 (21.3)	19 (13.5)	0.2
SSc	33 (17.6)	8 (17)	25 (17.7)	> 0.99
IIM	5 (2.7)	3 (6.4)	2 (1.4)	-
RA	2 (1.1)	0 (0)	2 (1.4)	-
SjD	8 (4.3)	1 (2.1)	7 (5)	-
Overlap	11 (5.9)	2 (4.3)	9 (6.4)	-

Data are presented as number (percentage). P-value were calculated thanks to Chi-squared test or Fisher's exact test as appropriate
dCTD: differentiated connective tissue disease; IIM: idiopathic inflammatory myopathies; ILD: interstitial lung disease; MCTD: mixed connective tissue disease; n: number; PF: pulmonary fibrosis; RA: rheumatoid arthritis; SjD: Sjögren's disease; SLE: systemic lupus erythematosus; SSc: systemic sclerosis

Results: Forty-seven jMCTD patients (44 (93.6%) girls with a median age of 14 [11-16] y.o) at disease onset were included. Forty-four (93.6%) patients met either Sharp or Kasukawa diagnostic criteria and 41 (87.2%) met both diagnostic criteria while none met other classification criteria without fulfilling Sharp or Kasukawa criteria (**Figure 1**). At diagnosis, jMCTD patients had less frequently puffy fingers ($p < 0.0001$) and higher creatine kinase level ($p< 0.001$) compared to adult-onset

Figure 1. Numbers (percentages) of juvenile onset patients fulfilling diagnosis criteria for mixed connective tissue disease.



patients (**Table 1**). Among jMCTD, 26 (55.3%) had received hydroxychloroquine at MCTD diagnosis and 45 (95.7%) during follow-up. jMCTD patients were treated with higher dose of glucocorticoids (p=0.02) and more frequently with rituximab (p=0.01) than adults. After 118 [79-194] months follow-up, jMCTD patients had less frequently puffy fingers (p=0.003), oral dryness (p=0.02) but more renal disease (p=0.02) and were more often in remission than adult-onset patients (p=0.04). In addition, 2 (4.3%) jMCTD patients developed pulmonary hypertension (vs. 12, 8.5% in adults; p=0.5), 11 (23.4%) interstitial lung disease (*vs*. 45, 31.9%; p=0.3 in adults) and 1 (3.1%) died (*vs*. 7, 5% in adults). Seventeen (36.2%) jMCTD patients evolved toward a dCTD (*vs*. 43, 30.5% in adult-onset, p=0.5) (**Table 2**). During follow-up, occurrence of dyspnea (p=0.02), restrictive pattern (p=0.002) or altered DLCO on pulmonary function tests (p=0.005), lymphopenia (p=0.03), and hypergammaglobulinemia (p=0.05), were associated with absence of remission.

Conclusion: This works reports that jMCTD and adult-onset patients share the same phenotype. As for adult-onset patients, Sharp and Kasukawa criteria are sufficient to diagnose MCTD. It shows that jMCTD are treated with higher doses of GC and more frequently with rituximab than adult-onset patients. Importantly, jMCTD patients develop more frequently renal disease but more often reach remission, especially in the absence of respiratory function impairment, as compared to adult-onset patients.

Disclosure: K. Chevalier: None; **B. Bader-Meunier**: None; **I. Kone-Paut**: None; **B. Torreau**: None; **M. Michel**: None; **B. Godeau**: None; **C. AGARD**: None; **T. Papo**: None; **K. Sacré**: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **C. Patrice**: None; **Y. Benhamou**: None; **M. Leclercq**: None; **C. goujard**: None; **O. Lambotte**: None; **B. Bonnotte**: Boehringer-Ingelheim, 2, Chugai, 2, Novartis, 2, Vifor Pharma, 2; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2; **F. Ackermann**: None; **J. Schmidt**: None; **P. Duhaut**: None; **J. Kahn**: None; **T. Hanslik**: None; **N. Costedoat-Chalumeau**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **A. REGENT**: Novartis, 2; **b. Dunogue**: None; **P. Cohen**: Roche, 5; **V. Le Guern**: AstraZeneca, 12, attending meetings and travel., Bristol-Myers Squibb(BMS), 6, Novartis, 2; **E. HACHULLA**: None; **L. Mouthon**: None; **B. Chaigne**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1576

Impact of COVID-19 Infection on Fibrosis Progression in CTD-Associated ILD: An AI-Based Quantitative CT Study

Kyung-Ann Lee[1], Hyun-Sook Kim[2] and Boda Nam[3], [1]Soonchunhyang University Hospital Seoul: Soonchunhyang University Hospital, Seoul, Republic of Korea, [2]Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea, [3]Chung-Ang University Hospital, Seoul, Republic of Korea

SESSION INFORMATION

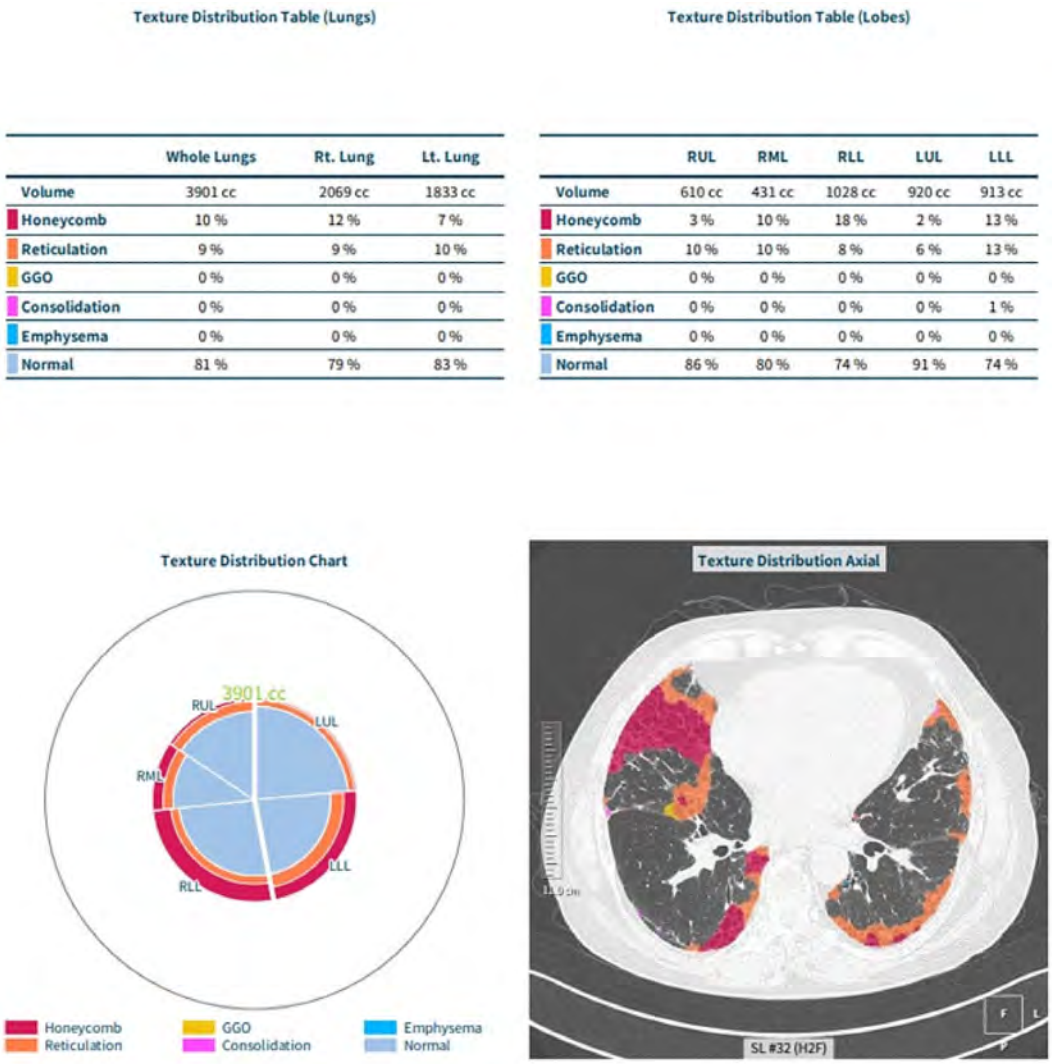
Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Pulmonary fibrosis is a recognized sequela of severe COVID-19 pneumonia, but its additive impact on pre-existing interstitial lung disease (ILD)—particularly in patients with connective tissue disease (CTD)—remains poorly



	Whole Lungs	Rt. Lung	Lt. Lung
Volume	3901 cc	2069 cc	1833 cc
Honeycomb	10 %	12 %	7 %
Reticulation	9 %	9 %	10 %
GGO	0 %	0 %	0 %
Consolidation	0 %	0 %	0 %
Emphysema	0 %	0 %	0 %
Normal	81 %	79 %	83 %

	RUL	RML	RLL	LUL	LLL
Volume	610 cc	431 cc	1028 cc	920 cc	913 cc
Honeycomb	3 %	10 %	18 %	2 %	13 %
Reticulation	10 %	10 %	8 %	6 %	13 %
GGO	0 %	0 %	0 %	0 %	0 %
Consolidation	0 %	0 %	0 %	0 %	1 %
Emphysema	0 %	0 %	0 %	0 %	0 %
Normal	86 %	80 %	74 %	91 %	74 %

Figure 1. AI-based Quantitative CT (QCT) Analysis Example Representative output of automated lung texture classification in a CTD-ILD patient using QCT. Distribution of honeycombing, reticulation, and normal parenchyma are quantified in tables (upper panels), a polar chart (lower left), and an axial HRCT image with overlaid classification (lower right). Color coding corresponds to specific radiologic textures (legend below chart).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

understood. This study aimed to assess the effect of prior COVID-19 infection on fibrosis progression in CTD-associated ILD (CTD-ILD) using artificial intelligence (AI)-based quantitative CT (QCT) analysis.

Methods: We conducted a single-center retrospective study of CTD-ILD patients with confirmed COVID-19 pneumonia who underwent at least two high-resolution CT (HRCT) scans: one within 18 months before infection and one ≥6 months after infection. Only follow-up scans obtained >1 year post-infection were included in the final analysis. Controls were CTD-ILD patients without a history of COVID-19, matched for baseline HRCT and follow-up interval (12–18 months). Fibrosis progression was quantified using both visual and AI-based QCT analysis (Figure 1). Clinical characteristics, pulmonary function tests (PFTs), and immunosuppressive treatment history were collected. Multivariable linear regression identified independent predictors of fibrosis progression.

Results: A total of 110 patients were included (COVID-19 group: n=53; control group: n=57). The cohort comprised various CTD subtypes: systemic sclerosis (54.7%), Sjögren's syndrome (23.2%), rheumatoid arthritis (15.8%), polymyositis (3.2%), dermatomyositis (1.1%), and mixed connective tissue disease (2.1%). Baseline CTD subtype, COVID-19 treatment history, baseline PFTs, and initial fibrosis extent and pattern were comparable between groups. At follow-up, the COVID-19 group showed a significantly greater extent of reticulation on QCT (3.1% vs. 1.4%, p=0.044) and a trend toward increased honeycombing. Multivariable analysis revealed that prior COVID-19 infection (β=4.332, p=0.044), older age (β=0.211, p=0.004), lower baseline FVC (β=–0.187, p=0.001), and rituximab use (β=6.607, p=0.022) were independently associated with greater fibrosis scores (Table 1).

Conclusion: In CTD-ILD patients, prior COVID-19 infection was independently associated with increased fibrosis progression on follow-up CT. These findings highlight the long-term pulmonary impact of COVID-19 in a vulnerable population, warranting close radiologic surveillance and personalized management strategies.

Table 1. Linear Regression Analyses for Factors Associated with Increased Fibrosis Scores on AI-based QCT

Disclosure: k. Lee: None; **H. Kim**: None; **B. Nam**: None.

Abstract Number: 1577

Intravenous cyclophosphamide in the treatment of progressive interstitial lung diseases associated with systemic sclerosis: a prospective randomized trial versus placebo (SCLEROCYC)

Luc Mouthon[1], David Launay[2], Sylvie leroy[3], Christian AGARD[4], Yannick Allanore[5], Alice berezne[1], Emmanuel Bergot[6], Boris Bienvenu[7], Benjamin Chaigne[1], Pascal Cohen[8], Bruno Crestani[9], Anca Corondan[10], bertrand Dunogue[1], Christian Lavigne[11], Jonathan London[12], Jean-Marc Naccache[10], Gabriel Baron[13], Alexis REGENT[14], Benjamin Terrier[15], Zahir AMOURA[16], Charles Marquette[10] and Philippe Ravaud[13], [1]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [2]Univ. Lille, Inserm, CHU Lille, Department of Internal Medicine and Clinical Immunology, Reference Center for Rare Autoimmune and Autoinflammatory diseases (CERAINOM), U1286 - INFINITE - Institute for Translational Research in Inflammation, Lille, France. National Reference Center for Pulmonary Arterial Hypertension (Pulmotension), Lille, France, Lille Cedex, France, [3]AP HP, Paris, France, [4]Internal medicine, Nantes University Hospital, Nantes, France, [5]Université Paris Cité, Paris, France, [6]CHU, Caen, France, [7]Saint Joseph Hospital, Marseille, France, [8]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [9]CHU, Paris, France, [10]NA, Paris, France, [11]CHU, Angers, France, [12]Hôpital Croix-Saint-Simon, Paris, France, [13]Hôtel-Dieu, Université Paris Cité,, Paris, France, [14]Hopital Cochin, Paris, France, [15]Cochin Hospital, Paris, France, [16]APHP, Paris, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of death in patients with systemic sclerosis (SSc). Randomized controlled trials favoured the use of cyclophosphamide (CYC) for treating SSc related ILD (SSc-ILD) (1,2). However, the effects of CYC waned after an additional year off therapy (3) and patients included did not fulfil progressive ILD criteria.

Methods: We conducted a randomized, prospective, double-blind, placebo-controlled multicenter trial to evaluate the efficacy and safety of CYC in combination with prednisone in patients with progressive SSc-ILD (Clinical trial NCT01570764).

Patients (≥ 18 years old) with SSc (defined by the American College of Rheumatology (ACR) and/or Leroy and Medsger criteria) and progressive SSc-ILD (defined as ≥ 10% decrease in forced vital capacity (FVC) and/or total lung capacity (TLC), and/or ≥ 15% decrease in diffusing capacity of the lung for carbon monoxide (DLCO) within 3 to 18 months prior to inclusion) were randomly assigned, in a 1:1 ratio, to receive either 0.7 g/m^2 (maximum 1200 mg) of intravenous (IV) CYC every 4 weeks during 12 months, or placebo. Both groups received 15 mg/day prednisone. The primary endpoint was the proportion of patients who improved or stabilized FVC at 12 months.

Results: Forty patients (13 males and 27 females, 24 (60%) with diffuse cutaneous SSc) were included between January 2013 and March 2017, with 20 patients randomized to each group. In the primary endpoint analysis, the proportion of patients who improved or stabilized FVC at 12 months was 17/20 (85%) in the CYC group and 16/20 (80%) and in the placebo group (relative risk (RR) 1.06 95% confidence interval (CI) (0.51 to 2.19)).

Sensitivity analyses showed that the mean change from baseline in FVC at 12 months was 252.1 mL (122.8 to 381.4) in the CYC group and 3.8 mL (-129.3 to 136.9) in the placebo group (mean difference 248.3 (64.3 to 432.4)). The mean change from baseline in the health assessment questionnaire (HAQ) was lower at 12 months in the CYC group (-0.23 [-0.43; -0.02]) compared to the placebo group (0.27 [0.06; 0.48]) (mean difference -0.50 (-0.79 to -0.21)). Similarly, the mean change in the scleroderma-HAQ was significantly lower in the CYC group (-0.22 (-0.42; -0.02)) compared to the placebo group (0.28 (0.08; 0.48)) (mean difference -0.50 (-0.78 to -0.21)). The mean change in the physical component of the SF-36 was also greater in the CYC group (5.5 (0.9; 10.1)) than in the placebo group (-2.6 (-7.0; 1.9)) (mean difference 8.1 (1.7 to 14.3)). There was no significant difference in the mental component scale of the SF-36, nor in DLCO, New York Health Association, or six-minute walk distance. The proportion of patients who developed severe adverse events was similar between the groups ((5/20 (25%) in the CYC group vs. 7/20 (35%) in the placebo group). Two patients died, one in each group.

Conclusion: In patients with progressive SSc-ILD, treatment with oral prednisone and IV CYC did not significantly increase the proportion of patients who improved or stabilized FVC and/or DLCO at 12 months. However, it significantly increasedFVC, and improved HAQ, Scleroderma-HAQ scores, and the physical component of the SF-36 at 12 months.

Disclosure: L. Mouthon: None; **D. Launay**: AstraZeneca, 2, 6, BioCryst, 6, 12, travel grants, CSL Behring, 2, 6, Shire, 12, travel grants, Takeda, 2, 6; **S. Ieroy**: None; **C. AGARD**: None; **Y. Allanore**: None; **A. berezne**: None; **E. Bergot**: None; **B. Bienvenu**: None; **B. Chaigne**: None; **P. Cohen**: Roche, 5; **B. Crestani**: None; **A. Corondan**: None; **b. Dunogue**: None; **C. Lavigne**: None; **J. London**: None; **J. Naccache**: None; **G. Baron**: None; **A. REGENT**: Novartis, 2; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **Z. AMOURA**: AstraZeneca, 6, Bristol-Myers Squibb(BMS), 6, GlaxoSmithKlein(GSK), 6, Merck/MSD, 6, Novartis, 6, Roche, 6; **C. Marquette**: None; **P. Ravaud**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1578

Use of the CD19/CD3 T cell engager blinatumomab in refractory diffuse systemic sclerosis : a case series

Marc Scherlinger[1], Yannick dieudonne[2], Anna Molto[3], Emmanuel Chatelus[4], aurelien Guffroy[5], Thierry Martin[2], Jacques-eric GOTTENBERG[6], Celestine Simand[7], Anne El Aatmani[8], Justine Decroocq[9], Eden Sebbag[1], Jean Sibilia[10], Jérôme AVOUAC[11] and C3I : Club for Innovating Immunotherapies in IMIDs., [1]Rheumatology Department, National Center for Rare autoimmune disease RESO,Strasbourg University Hospital, Strasbourg, France, [2]Immunology Department, National Center for Rare autoimmune disease RESO,Strasbourg University Hospital, Strasbourg, France, [3]Assistance Publique Hôpitauxde Paris, Paris, France, [4]Department of Rheumatology, University Hospital Strasbourg, France, Strasbourg, France, [5]CHU de Strasbourg, Strasbourg, [6]Hautepierre Hospital, STRASBOURG, Alsace, France, [7]ICANS, Strasbourg, France, [8]CHU de Strasbourg, Strasbourg, France, [9]APHP, Paris, France, [10]Rheumatology Department, National Center for Rare autoimmune disease RESO,Strasbourg University Hospital, Strasbourg, Alsace, France, [11]Rheumatology department, Cochin hospital, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose:

Systemic sclerosis (SSc) is a severe autoimmune disease with limited treatments. While anti-CD19 CAR T-cell therapy shows promise, its use is limited by cost and complexity. Blinatumomab, a bispecific T-cell engager targeting CD3 and CD19, may offer a simpler and more affordable alternative and may be effective in severe SSc.

We aim to evaluate the safety and effectiveness of blinatumomab in managing severe refractory systemic sclerosis in real-world settings.

Methods: Patients with severe, refractory, Scl70-positive SSc were considered for treatment with blinatumomab following a multidisciplinary review to validate its off-label use. Informed, written consent was obtained from patients to participate in a translational study evaluating the impact of blinatumomab on their immune system. The treatment protocol included premedication with hydrocortisone (100 mg), acetaminophen (1 g), and dexchlorpheniramine (5 mg), followed by continuous intravenous infusion of blinatumomab at 9 µg/day for 7 days, then 28 µg/day for another 7 days. Patients were closely monitored in a hospital setting throughout the intravenous treatment phase and then followed ambulatorily.

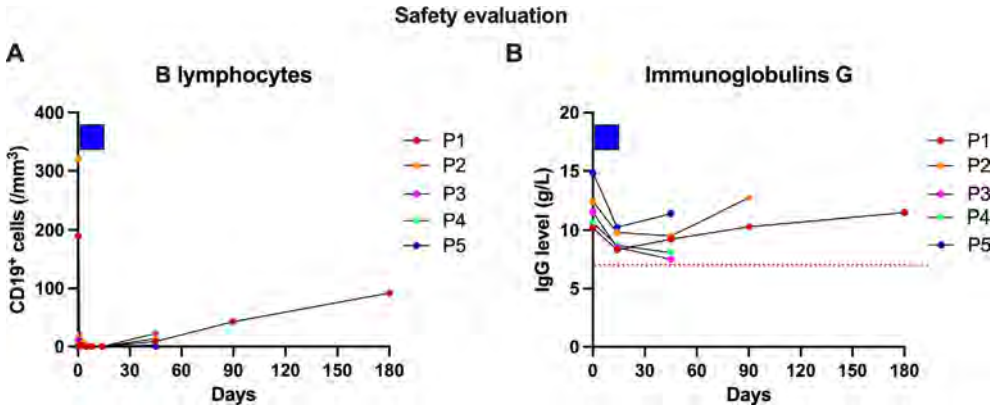


Figure 1: Safety evaluation after blinatumomab treatment. (A) Peripheral CD19+ B cells, (B) total immunoglobulin levels.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

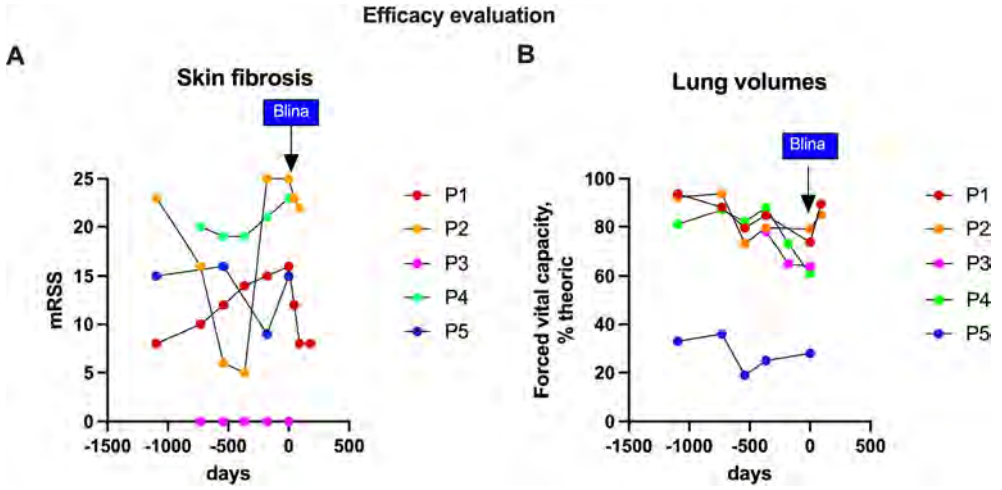


Figure 2: Efficacy evaluation blinatumomab treatment. (A) modified Rodnan Skin Score (mRSS), and (B) forced Vital capacity (FVC) expressed in % of the theoric value.

Results: Five patients from three different departments were included in the study: four women (P1, P2, P3,P4) and one man (P5) of median age 64 (IQR : 61-65) years. All patients had recent (≤6 years) and progressive Scl70-positive SSc that was refractory to a median of four immunosuppressive therapies (3-8), including autologous stem cell transplantation for P2. The median modified Rodnan skin score (mRSS) was 16 (15-23). All patients had fibrosing interstitial lung disease; four had cardiac fibrosis and one had pulmonary hypertension.

At the time of submission, all patients had received the complete treatment.. During infusion, 4 patients developped a grade 1 cytokine release syndrome (isolated fever) treated with acetaminophen, and one a grade 2 (fever and transient hypotension) that was treated with acetaminophen and fluids without need for tocilizumab. No Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) was observed.

All patient completed month 1 of follow-up, two completed month 3 and one month 6. Peripheral B-cell depletion was complete by day 3, persisted until day 14, and B cell repopulation was seen at month 1 (**Fig. 1A**). Despite a small decrease in total IgG, all patients remained above the lower limit (**Fig. 1B**). There was no impact on post-vaccination serologies, and no severe infections during follow-up was identified.

Clinically, a notable decrease in mRSS was observed in the two patients who completed the 3-month follow-up (**Fig. 2A**). While antinuclear and anti-Scl70 antibodies remained unchanged post-treatment, there was a marked reduction in the type I interferon signature. Pulmonary function, as indicated by lung volumes (e.g., forced vital capacity), showed significant improvement after treatment (**Fig. 2B**). B-cell receptor (BCR) sequencing is currently underway.

Conclusion: This real-world study indicates that blinatumomab is safe for use in systemic sclerosis and may lead to clinically significant improvements, including benefits for skin and lung manifestations.

Disclosure: M. Scherlinger: Abbvie, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Fresenius Kabi, 2, Galapagos, 2, GlaxoSmithKlein(GSK), 2, Innate pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2; **Y. dieudonne**: None; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **E. Chatelus**: None; **a. Guffroy**: None; **T. Martin**: None; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **C. Simand**: None; **A. El Aatmani**: None; **J. Decroocq**: None; **E. Sebbag**: None; **J. Sibilia**: None; **J. AVOUAC**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1579

Exploring the Pulmonary Vascular Changes on Computed Tomography in predicting progression and mortality of Systemic Sclerosis-associated Interstitial Lung Disease

Maria Iacovantuono[1], Nicholas landini[2], lisa Jungblut[3], Florian Käs[4], Rucsandra Dobrota[5], Sinziana Muraru[6], Carina Mihai[7], Muriel Elhai[8], Mike Becker[9], Maria Sole Chimenti[10], Thomas Frauenfelder[3], Anna-Maria Hoffmann-Vold[11], Oliver Distler[12] and Cosimo Bruni[13], [1]Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, Tor Vergata University, Rome, Italy. Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Spinete, Italy, [2]Department of Radiological Sciences, Oncology and Pathology, "Sapienza" University, Policlinico Umberto I, Rome, Italy. Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Rueil Malmaison, France, [3]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, zurich, Switzerland, [4]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Zurich, Switzerland, [5]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [6]University of Zurich, University Hospital Zurich, Zurich, Switzerland, [7]University Hospital Zurich, University of Zurich, Zurich, Switzerland, [8]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, Schlieren, Switzerland, [9]Dept. of Rheumatology, University Hospital Zurich, Zurich, Switzerland, [10]Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, Tor Vergata University, Rome, Italy, Roma, Italy, [11]Oslo University Hospital, Oslo, Norway, [12]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [13]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is the main cause of mortality in systemic sclerosis (SSc). Among radiomics features, the automated quantification of pulmonary vascular volume (PVV) on high-resolution computed tomography (HRCT) was predictive of survival and functional changes in idiopathic pulmonary fibrosis (IPF) and rheumatoid arthritis (RA)-associated ILD (Jacob, 2018). In SSc, PVV was associated with ILD severity (extent on HRCT, pulmonary function tests values: pFVC%, pDLCO%). Here, we explored the predictive value of CT-derived radiomics features for mortality and ILD progression in SSc-ILD.

Methods: We included SSc patients from a single referral centre with ILD present on HRCT and at least one follow-up visit. The progression analysis focused on patients with lung function repeated within 12±3 months. ILD progression was defined as at least one of the following:

- FVC relative decline ≥ 10 %
- FVC relative decline ≥ 10 % or FVC 5-9% and DLCO relative decline ≥ 15%
- FVC absolute decline ≥ 5%
- FVC absolute decline ≥ 5 or DLCO absolute decline ≥ 10%

HRCT scans underwent lung texture analysis (LTA, Imbio). The percentage distribution of ground-glass, reticular, honeycombing (the latter two defining “fibrotic alterations”), hyperlucency, normal lung and PVV was quantified in upper, middle and lower zones and the whole lung.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table I. Clinical and functional characteristics of the study population. ACA: anti-centromere antibodies; ATA: anti-topoisomerase I antibodies; ARA: anti-RNA polymerase III antibodies; antiPm-Scl: anti-PM-scleroderma-antibodies; dcSSc: diffuse cutaneous systemic sclerosis; NVC: nail-fold videocapillaroscopy; NYHA: New York Hearth Association; pFVC%: predicted forced vital capacity; pDLCO/SB%: predicted diffusion of the lung for carbon monoxide on single breath; 6MWT: 6 minutes walking test Increased inflammatory markers defined as ESR or/and CRP above normal levels

	Progression				**Mortality**			
	Any ILD progression n (%) = 64 (40)	**No ILD progression n (%) = 96 (60)**	**n data available**	**p-value**	**Death n (%) = 65 (24.3)**	**Alive n (%) = 202 (75.7)**	**n data available**	**p-value**
Age at baseline, years (mean, S.D.)	58.5/64 (13.9)	57.5/95 (13.2)	159	0.7	66.8 (11.3)	56.7 (14.1)	267	**<0.01**
Male sex, n (%)	12 (18.8)	23 (24)	160	0.4	19 (29.2)	44 (21.8)	267	0.2
Disease duration, years (median, IQR)	6.3 (1.5-18.2)	7.5 (3.3-15.1)	160	0.7	5.9 (2.4-13.1)	6.1 (1.9-16.2)	267	**<0.01**
Smoking ever, n (%)	19 (29.7)	28 (29.2)	160	0.9	24 (36.9)	49 (24.3)	267	**0.05**
SSc autoantibodies, n (%)								
ACA	15/64 (23.4)	19/95 (20)	159	0.6	12/65 (18.5)	51/200 (25.5)	265	0.2
ATA	32 (50)	45 (46.9)	160	0.7	28/65 (43.1)	91/201 (45.3)	266	0.8
ARA	10/64 (15.6)	17/95 (17.9)	159	0.7	7/60 (11.7)	31/197 (15.7)	257	0.4
antiPm/Scl	11 (17.2)	19 (19.8)	160	0.7	11/60 (18.3)	36/198 (18.2)	258	0.9
dcSSc, n (%)	26 (40.6)	33 (34.4)	160	0.4	27 (41.5)	65 (32.2)	267	0.2
Scleroderma pattern on NVC, n (%)	1 (1.6)	3 (3.1)	160	0.7	30/41 (73.2)	124/165 (75.2)	206	0.8
Scleroderma renal crisis, n (%)	40/52 (76.9)	58/80 (72.5)	132	0.6	4 (6.2)	2 (1)	267	**0.03**
Digital Ulcers ever, n (%)	17 (26.6)	45 (46.9)	160	**0.01**	21 (32.3)	60 (29.7)	267	0.7
Pitting scars ever, n (%)	23 (35.9)	43 (44.8)	160	0.3	21 (32.3)	70 (34.7)	267	0.7
Puffy Fingers, n (%)	43 (67.2)	68 (70.8)	160	0.6	36 (55.4)	150 (74.3)	267	**<0.01**
Teleangectasia, n (%)	42 (65.6)	55 (57.3)	160	0.3	50 (76.9)	113 (55.9)	267	**<0.01**
Joint involvement, n (%)	16 (25)	25 (26)	160	0.9	15 (23.1)	46 (22.8)	267	>0.9
Calcinosis, n (%)	2/37 (5.4)	6/60 (10)	97	0.7	2/24 (8.3)	12/117 (10.3)	141	>0.9
Increased inflammatory markers, n (%)	7 (10.9)	24 (25)	160	**0.03**	18 (27.7)	32 (15.8)	267	**0.03**
SCOpE score, (mean, SD)					12.7 (4.4)	7.6 (3.9)	267	**<0.01**
Dyspnoea NYHA ≥ II, n (%)	33 (51.6)	49 (51)	160	0.9	45 (69.2)	97 (48)	267	**<0.01**
O2 saturation at rest (mean, S.D.)	97.2/61 (2.1)	97.2/88 (3.4)	149	0.9	96.1/52 (2.9)	97.6/181 (1.9)	233	**<0.01**
pFVC % (mean, S.D.)	95.4 (16.9)	83.2 (20.2)	160	**<0.01**	84/57 (25.9)	91.1/199 (18.6)	256	0.06
pDLCO/SB % (mean, S.D.)	72.6 (19.8)	60.9 (20.4)	160	**<0.01**	51.5/58 (20.6)	69.8/200 (21.3)	258	**<0.01**
6MWT, (mean, S.D.)	538.8/61 (108.1)	512.8/89 (109.7)	150	0.2	415.6/53 (124)	530.9/183 (108)	236	**<0.01**

Survival analysis was performed from the first ILD-positive CT until last contact (death or alive status), using Cox proportional hazards models, with radiomics parameters adjusted for the SCOpE score (Elhai, 2017). Radiomics predictors of ILD progression were assessed using the logistic Generalized Estimating Equations (GEE), adjusted for established risk factors.

Results: Among 267 SSc-ILD patients, 65 (24%) deaths were recorded over a median follow up of 42 (27-110) months. Patients who died were older, clinically and functionally more severely impaired (Table I) and with higher extent of PVV% and parenchymal alterations in all lung zones (Table II). In a multivariable Cox model, the PVV% of the upper zones (HR 1.28, 95% CI 1.12-1.47) and the SCOpE score (HR 1.22, 95% CI 1.15-1.28) independently predicted mortality (Fig IA).

Among the 261 yearly follow-ups from 160 SSc-ILD patients, we recorded 99 episodes of ILD progression (38%), occurring in 64 patients (40%). Patients with progressive ILD had more frequently increased inflammatory markers, better-preserved pulmonary function tests (Table I), but comparable radiomics changes versus non-progressors (Table II). In a multivariable model integrating clinical and radiomics predictors selected through univariable analysis, only pDLCO% (OR 1.02, 95% CI 1.01-1.04) and pFVC% (OR 1.03, 95% CI 1.01-1.05) were independently associated with ILD progression (Fig IB). Comparable results were obtained when each progression definition was analysed separately.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table II. Distribution of radiomics parameters in the total lungs among systemic sclerosis patients with progressive disease or death Fibrotic alterations = reticular pattern + honeycombing

	ILD progression n (%) = 64 (40)	No ILD progression n (%) = 96 (60)	p-value	Death n (%) = 65 (24.3)	Alive n (%) = 202 (75.7)	p-value
Median (IQR)			TOTAL LUNGS			
fibrotic alterations	0.85 (0.50-1.31)	1.19 (0.61-2.62)	**0.01**	2.25 (0.63-6.50)	0.84 (0.46-1.68)	**<0.01**
ground glass	1.99 (0.35-5.23)	2.88 (0.75-10.71)	0.38	5.88 (0.29-26.06)	1.41 (0.27-5.04)	**<0.01**
reticular	0.78 (0.44-1.24)	1.1 (0.59-2.36)	**0.02**	2.23 (0.41-1.63)	0.75 (0.59-5.71)	**<0.01**
honeycombing	0.03 (0.01-0.07)	0.04 (0.02-0.09)	**0.05**	0.04 (0.03-0.15)	0.03 (0.02-0.07)	0.44
hyperlucent	2.11 (0.26-5.02)	1.85 (0.32-6.54)	0.16	0.93 (0.2-5.26)	2 (0.35-5.91)	0.98
normal lung	92.88 (85.56-96.03)	88.28 (75-94.81)	0.06	76.43 (58.54-91.81)	92.37 (83.5-96.66)	**<0.01**
vessel	1.67 (1.43-2.14)	1.91 (1.43-2.51)	0.20	2.9 (1.57-4.98)	1.65 (1.29-2.17)	**<0.01**
			UPPER ZONE			
fibrotic alterations	0.17 (0.02-0.38)	0.27 (0.05-0.72)	0.30	0.90 (0.03-4.65)	0.13 (0.02-0.51)	**<0.01**
ground glass	0.08 (0-0.54)	0.11 (0.03-0.89)	0.59	0.74 (0.01-10.70)	0.03 (0-0.47)	**<0.01**
reticular	0.16 (0.02-0.36)	0.24 (0.03-0.66)	0.33	0.77 (0.03-4.51)	0.12 (0.02-0.42)	**<0.01**
honeycombing	0 (0-0.02)	0. (0-0.05)	**0.03**	0.01 (0-0.07)	0.01 (0-0.27)	0.08
hyperlucent	1.84 (0.22-7.47)	1.31 (0.49-5.85)	0.14	1.13 (0.24-2.64)	1.13 (0.39-5.88)	0.86
normal lung	96.58 (87-98.85)	95.83 (79.89-98.40)	0.10	88.37 (75.68-98.1)	97.25 (90.11-98.85)	**<0.01**
vessel	1.16 (0.97-1.35)	1.20 (0.99-1.56)	0.38	1.74 (1.04-3.37)	1.07 (0.92-1.45)	**<0.01**
			MIDDLE ZONE			
fibrotic alterations	0.67 (0.28-1.17)	0.85 (0.41-1.74)	0.14	1.93 (0.56-5.43)	0.72 (0.27-1.29)	**<0.01**
ground glass	0.88 (0.4-3.07)	1.18 (0.44-5.14)	0.48	2.85 (0.49-25.26)	0.69 (0.25-2.84)	**<0.01**
reticular	0.64 (0.26-1.09)	0.70 (0.38-1.70)	0.16	1.93 (0.52-5.25)	0.70 (0.25-1.16)	**<0.01**
honeycombing	0.02 (0.01-0.06)	0.02 (0-0.04)	0.32	0.03 (0.02-0.10)	0.02 (0.01-0.04)	0.547
hyperlucent	1.37 (0.15-4.1)	1.37 (0.22-5.59)	0.19	0.87 (0.24-3.08)	1.37 (0.27-4.51)	0.902
normal lung	95.22 (87.61-97.4)	90.86 (79.5-97.01)	0.13	86.08 (55.77-96.29)	94.99 (86.87-97.42)	**<0.01**
vessel	2.16 (1.78-2.70)	2.28 (1.70-2.80)	0.44	3.11 (1.78-5.37)	2.11 (1.70-2.64)	**<0.01**
			LOWER ZONE			
fibrotic alterations	1.77 (1.03-3.29)	1.90 (1.11-4.99)	**0.01**	4.54 (1.30-12.69)	1.66 (0.83-3.76)	**<0.01**
ground glass	5.86 (0.63-16.15)	6.27 (1.38-25.52)	0.75	11.31 (0.61-48.6)	3.55 (0.45-12.76)	**<0.01**
reticular	1.64 (0.98-3.17)	1.84 (1-4.80)	**0.02**	3.98 (1.21-11.10)	1.55 (0.79-3.45)	**<0.01**
honeycombing	0.06 (0.02-0.12)	0.06 (0.02-0.16)	**0.03**	0.07 (0.02-0.35)	0.05 (0.02-0.13)	0.416
hyperlucent	0.82 (0.08-4.58)	1.69 (0.12-4.60)	**0.02**	0.71 (0.12-4.60)	1.01 (0.11-4.59)	0.550
normal lung	87.46 (77.16-93.96)	84.28 (53.16-93.51)	0.09	62.95 (22.02-93.07)	87.66 (72.63-93.96)	**<0.01**
vessel	1.62 (1.27-2.21)	1.76 (1.22-2.85)	0.28	3.77 (1.40-7.06)	1.58 (1.14-2.28)	**<0.01**

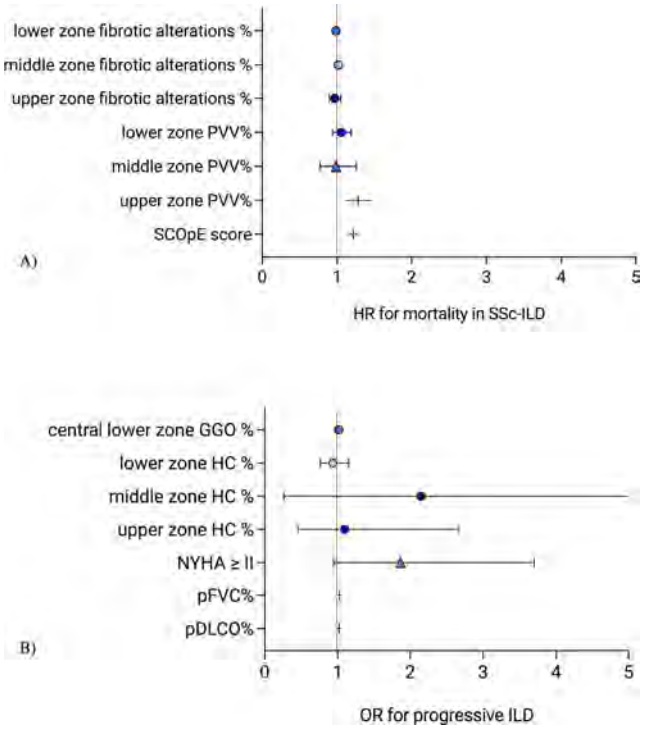


Fig I. Forrest plot showing predictive radiomics and clinical risk factors for mortality (IA) and progression (IB).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In line withRA-ILD and IPF, PVV% of the upper zones significantly predicts mortality in SSc-ILD. Conversely, we could not detect radiomics predictors for ILD progression. Further studies are needed to support the identification of patients at risk of ILD progression and prompt therapeutic interventions.

Disclosure: M. Iacovantuono: Eli Lilly, 12, congress support, EULAR long-term research felloship, 5; **N. Iandini**: None; **I. Jungblut**: None; **F. Käs**: None; **R. Dobrota**: Actelion, 5, 6, Amgen, 6, Boehringer-Ingelheim, 6, Iten-Kohaut, 5, Otsuka, 6, Pfizer, 5, Walter und Gertrud Siegenthaler Fellowship, 5; **S. Muraru**: AstraZeneca, 12, congress support; **C. Mihai**: Boehringer Ingelheim, 2, 12, congress support, Janssen, 2, MED Talks Switzerland, 6, Medbase, 6, MedTrix, 6, Mepha, 6, Novartis, 6, PlayToKnow, 6; **M. Elhai**: AstraZeneca, 12, Congress support, Boehringer-Ingelheim, 6, FOREUM, 5, Iten Kohaut foundation, 5, Janssen, 12, Congress support, Kurt und Senta Herrmann foundation, 5, Novartis, 5, Pfizer, 5, University Zurich, 5; **M. Becker**: Foundation for research in Rheumatology (FOREUM), 5, GSK, 6, 12, congress support, Novartis Foundation for Medical-biological Research, 5, 6, Vifor, 6, 12, congress support; **M. Chimenti**: None; **T. Frauenfelder**: AstraZeneca, 2, Bayer, 6, Siemens, 6; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Bruni**: Boehringer Ingelheim, 2, EMDO Foundation, 5, Iten-Kohaut Foundation, 5, Scleroderma Clinical Trials Consortium (SCTC), 5, Scleroderma Research Foundation (SRF), 2.

Abstract Number: 1580

Lung Vasculature Quantification on Computed Tomography Predicts New Onset of Interstitial Lung Disease in Systemic Sclerosis

Maria Iacovantuono[1], Nicholas Iandini[2], Iisa Jungblut[3], Gesa Sauer[4], Rucsandra Dobrota[5], Sinziana Muraru[6], Muriel Elhai[7], Carina Mihai[8], Mike Becker[9], Maria Sole Chimenti[10], Thomas Frauenfelder[3], Anna-Maria Hoffmann-Vold[11], Oliver Distler[12] and Cosimo Bruni[13], [1]Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, Tor Vergata University, Rome, Italy. Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Spinete, Italy, [2]Department of Radiological Sciences, Oncology and Pathology, "Sapienza" University, Policlinico Umberto I, Rome, Italy. Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, Rueil Malmaison, France, [3]Institute for Diagnostic and Interventional Radiology, University Hospital Zurich, University Zurich, Zurich, Switzerland, zurich, Switzerland, [4]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, zurich, Switzerland, [5]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [6]University of Zurich, University Hospital Zurich, Zurich, Switzerland, [7]University Hospital zurich, Zurich, Switzerland, [8]University Hospital Zurich, University of Zurich, Zurich, Switzerland, [9]Dept. of Rheumatology, University Hospital Zurich, Zurich, Switzerland, [10]Rheumatology, Allergology and Clinical Immunology, Department of Systems Medicine, Tor Vergata University, Rome, Italy, Roma, Italy, [11]Oslo University Hospital, Oslo, Norway, [12]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [13]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Interstitial lung disease (ILD) is highly prevalent in systemic sclerosis (SSc) and a leading cause of mortality. Recent studies have identified clinical risk factors for new onset of ILD at both 1-year and long-term follow-up (1,2), still not optimally identifying patients at high risk. Pulmonary vascular volume (PVV%) quantified on high-resolution computed tomography (HRCT) is associated with both presence and severity of SSc-ILD (3).

In this study, we investigate the potential of radiomics in identifying patients with risk of developing ILD.

Methods: We included patients from a single SSc referral centre, with no ILD on baseline HRCT and at least one clinical and HRCT follow-up. Images 1) were assessed by experienced thoracic radiologist for presence/absence of ILD at all timepoints, 2) underwent lung texture analysis (LTA, Imbio), quantifying PVV, normal lung, lung pathologies (hyperlucency, ground-glass, reticular, honeycombing), as percentage of the lung volume, both for whole lungs and for upper, middle, lower zones.

Univariable and multivariable prediction models were developed to identify radiomics risk factors for ILD onset, using Cox regression and generalizes estimating equation (GEE) analysis for ILD onset ever and at 1-year, the latter allowing for multiple observations of the same patient. Both models were adjusted for the established clinical risk factors (1,2).

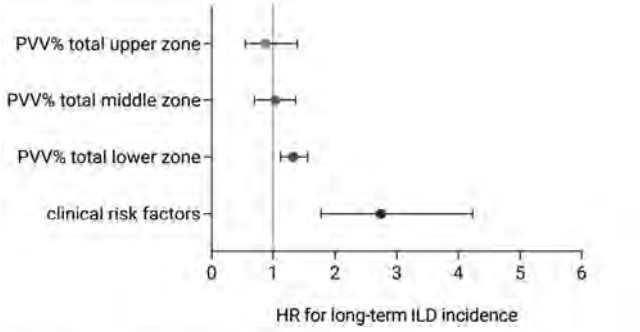
Table I. Clinical characteristics and functional features of SSc patients with and without ILD onset ever and ILD onset 1-year ACA: anti-centromere antibodies ATA: anti-topoisomerase I antibodies; ARA: anti-RNA polymerase III antibodies; antiPm/Scl: anti-PM-scleroderma-antibodies; dcSSc: diffuse cutaneous systemic sclerosis; NVC: nailfold videocapillaroscopy; NYHA: New York Hearth Association; pFVC%: predicted forced vital capacity; pDLCO/SB%: predicted diffusion of the lung for carbon monoxide on single breath; 6MWT: 6 minutes walking test; SD: standard deviation. Increased inflammatory markers defined as ESR or/and CRP above normal limit

	ILD onset ever n (%) = 54 (21.8)	No ILD n (%) = 194 (78.2)	n data available	p-value	ILD onset 1 year n (%) = 22 (11.4)	No ILD at 1 year n (%) = 171 (88.6)	n data available	p-value
Age at baseline, years (mean, S.D.)	54.4 (13.5)	54.41 (13.8)	248	0.9	55.3 (15.2)	57 (14.3)	193	0.6
Male sex, n (%)	11 (20.4)	18 (9.3)	248	**0.03**	6 (27.3)	19 (11.1)	193	**0.03**
Disease duration, years (median, IQR)	2.5 (1-9.1)	6.20 (2.2-19.3)	248	**0.02**	5.2 (2.1-10.7)	7.4 (2.6-22.1)	193	0.2
Smoking ever, n (%)	13/53 (24.5)	57/194 (29.4)	247	0.5	8/22 (36.4)	57/170 (33.5)	192	0.8
SSc autoantibodies, n (%)								
ACA	23/53 (43.4)	145/194 (74.7)	247	**<0.01**	9/22 (40.9)	117/170 (68.8)	192	**<0.01**
ATA	14/53 (26.4)	17/192 (8.9)	245	**<0.01**	6/22 (27.3)	22/169 (13)	191	0.1
ARA	9/53 (17)	26/190 (13.7)	243	0.5	5/22 (22.7)	27/168 (16.1)	190	0.5
Anti-Pm/Scl	5/53 (9.4)	8/188 (4.3)	241	0.2	1/22 (4.5)	9/168 (5.4)	190	0.9
dcSSc, n (%)	12/53 (22.6)	22/194 (11.3)	247	**<0.01**	8/22 (36.4)	23/170 (13.5)	192	**<0.01**
Scleroderma pattern on NVC, n (%)	30/40 (75)	120/159 (75.5)	199	0.9	11/19 (57.9)	110/149 (73.8)	168	0.2
Digital Ulcers ever, n (%)	12/53 (22.6)	30/194 (15.5)	247	0.2	5/22 (22.7)	42/170 (24.7)	192	0.9
Pitting scars ever, n (%)	17/53 (32.1)	60/247 (24.3)	194	0.1	6/22 (27.3)	48/170 (28.2)	192	0.9
Puffy Fingers, n (%)	32/53 (60.4)	120/194 (61.9)	247	0.8	13/22 (59.1)	108/170 (63.5)	192	0.7
Teleangiectasias, n (%)	30/53 (56.6)	107/194 (55.2)	247	0.8	10/22 (45.5)	106/170 (62.4)	192	0.1
Joint involvement, n (%)	9/53 (17)	31/194 (16)	247	0.9	7/22 (31.8)	50/170 (29.4)	192	0.8
Calcinosis, n (%)	4/22 (18.2)	10/95 (10.5)	117	0.3	0/14 (0)	19/112 (17)	126	0.1
Increased inflammatory markers, n (%)	7/53 (13.2)	18/194 (9.3)	247	0.4	2/22 (9.1)	11/170 (6.5)	192	0.7
NYHA ≥ II, n (%)	21/53 (39.6)	95/247 (38.5)	194	0.8	9/22 (40.9)	68/170 (40)	192	0.9
O2 saturation at rest, (mean, S.D.)	97.2/46 (1.6)	97.5/168 (1.9)	214	0.3	97.7/21 (1.9)	97.7/149 (1.8)	170	0.8
pFVC % (mean, S.D.)	100.9/52 (15.9)	98.9/192 (15.3)	244	0.4	93.7 (11.5)	98.5 (14.9)	193	0.2
pDLCO/SB % (mean, S.D.)	76.4/53 (19.8)	79.7/192 (18.7)	245	0.3	73.5/22 (14.5)	77.1/169 (18.9)	191	0.4
6MWT, (mean, S.D.)	535.8/46 (104.7)	552.5/171 (118.3)	217	0.4	525.1/21 (134.1)	547.3/152 (114.4)	173	0.1

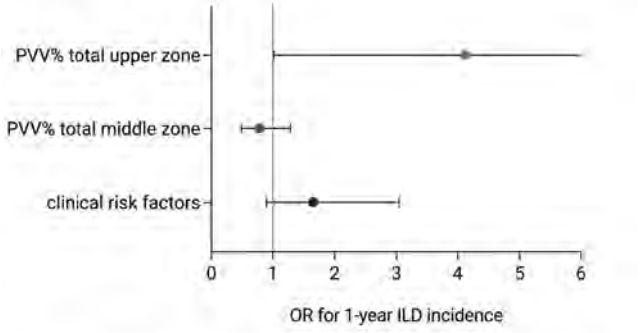
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table II. Distribution of parenchymal and vascular radiomics parameters among SSc patients with and without ILD-onset ever. Data are presented as percentage of lung volume (total or upper/middle/lower zone). PVV: pulmonary vascular volume

	ILD onset (ever) n (%) = 54 (21.8)	No ILD onset (ever) n (%) = 194 (78.2)	p-value
% of lung volume	**TOTAL LUNGS**		
	median (IQR)		
ground glass	0.29 (0.14-1.48)	0.22 (0.10-0.56)	0.20
reticular	0.49 (0.23-0.71)	0.29 (0.15-0.59)	0.80
honeycombing	0.03 (0.01-0.06)	0.03 (0-0.05)	0.37
hyperlucent	2.24 (0.71-5.60)	3.15 (0.94-9.08)	0.14
normal lung	95.89 (91.35-96.98)	94.8 (87.63-97)	0.33
PVV	**1.55 (1.30-2)**	**1.4 (1.20-1.69)**	**0.04**
	UPPER ZONE		
ground glass	0.01 (0.01-0.36)	0.01 (0.01-0.07)	0.66
reticular	0.11 (0.02-0.38)	0.04 (0.01-0.21)	0.90
honeycombing	0 (0-0.03)	0.01 (0-0.01)	0.46
hyperlucent	1.19 (0.31-3.73)	1.98 (0.53-7)	0.31
normal lung	97.49 (93.82-98.85)	96.93 (89.11-98.85)	0.41
PVV	**1.07 (0.88-1.38)**	**0.94 (0.76-1.06)**	**0.03**
	MIDDLE ZONE		
ground glass	0.49 (0.14-1.58)	0.27 (0.09-0.69)	0.35
reticular	0.55 (0.19-0.81)	0.29 (0.14-0.66)	0.71
honeycombing	0.02 (0.01-0.58)	0.02 (0.01-0.03)	0.44
hyperlucent	1.41 (0.46-5.89)	2.59 (0.68-8.62)	0.07
normal lung	95.98 (90.90-97.42)	95.46 (87.10-97.42)	0.17
PVV	**1.99 (1.69-2.55)**	**1.81 (1.62-2.16)**	**0.03**
	LOWER ZONE		
ground glass	0.40 (0.22-2.02)	0.28 (0.09-0.60)	0.15
reticular	0.55 (0.23-1.34)	0.39 (0.14-1.05)	0.70
honeycombing	0.03 (0.01-0.07)	0.03 (0-0.10)	0.06
hyperlucent	**1.84 (0.42-5.44)**	**5.13 (1.52-14.24)**	**<0.01**
normal lung	94.19 (90.15-97.32)	92.66 (90.90-97.42)	0.22
PVV	**1.31 (1.05-1.82)**	**1.10 (0.89-1.51)**	**0.04**



A) clinic risk score incorporates age, sex, SSc specific autoantibodies, pDLCO%, inflammatory markers, DUs, NYHA class ≥ II, haemoglobin levels in long-term ILD analysis



B) clinic risk score incorporates age, sex, SSc specific autoantibodies, pDLCO%, inflammatory markers, NYHA class ≥ II, haemoglobin levels in the 1-year analysis

Fig I: Forrest plot showing predictive radiomics and clinical risk factors for long-term ILD incidence (A) and 1-year ILD incidence (B)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 248 SSc patients with no ILD at baseline HRCT, new onset of ILD occurred in 54 (22%) cases over a median follow-up of 39 (24-72) months. Patients developing ILD were more frequently males, with diffuse skin involvement, anti-topoisomerase I antibodies and shorter disease duration (Table I, left panel). Additionally, patients with new onset ILD over the study period presented higher values of PVV across all lung zones at baseline HRCT (Table II). In multivariable Cox regression analysis, new ILD onset was independently predicted by PVV% from the whole lung [HR 1.054 (1.030-1.078)], as well as from each individual zone. When integrating the PVV% of each single zone with the clinic risk factors in the multivariable analysis, we observed the significant, independent impact of the lower zone PVV% [HR 1.217 (1.113–1.332)], in addition to the known risk associated with clinical features [HR 3.281 (2.145–5.021)] (Fig IA).

Focusing on 1-year ILD onset, we analysed 279 follow-up visits from 193 patients and observed 22 (11.4%) new onset ILD (Table I, right panel). On univariable GEE, we confirmed the association of PVV from the whole lung on ILD onset, with particular focus on the middle and upper zones, alongside the clinical risk factors. When tested in a multivariable model adjusted for clinical risk factors, PVV% of the upper zone remained significantly associated with ILD onset [OR 4.127 (1.016–16.761)] (Fig IB).

Conclusion: PVV% from HRCT scans of SSc patients without ILD can predict new onset of ILD at both 1-year and long-term follow-up, supporting the use of radiomics in clinical risk phenotyping.

References

1. Petelytska, L., et al., Arthritis Rheumatol, 2023
2. Hoa S, et al., Arthritis Rheumatol. 2025
3. Occhipinti M, et al., PLoS One. 2019

Disclosure: M. Iacovantuono: Eli Lilly, 12, congress support, EULAR long-term research felloship, 5; **N. Iandini**: None; **I. Jungblut**: None; **G. Sauer**: Schweizerische Gesellschaft für Rheumatologie, 12, Congress support EULAR 2023; **R. Dobrota**: Actelion, 5, 6, Amgen, 6, Boehringer-Ingelheim, 6, Iten-Kohaut, 5, Otsuka, 6, Pfizer, 5, Walter und Gertrud Siegenthaler Fellowship, 5; **S. Muraru**: AstraZeneca, 12, congress support; **M. Elhai**: Astrazeneca, 12, congress support, Boehringer Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5, Iten Kohaut foundation, 5, Janssen, 12, congress support, Kurt und Senta Herrmann foundation, 5, Novartis Foundation for Bio-Medical Research, 5, pfizer, 5, University Zurich, 5; **C. Mihai**: Boehringer Ingelheim, 2, 12, congress support, Janssen, 2, MED Talks Switzerland, 6, Medbase, 6, MedTrix, 6, Mepha, 6, Novartis, 6, PlayToKnow, 6; **M. Becker**: Foundation for research in Rheumatology (FOREUM), 5, GSK, 6, 12, congress support, Novartis Foundation for Medical-biological Research, 5, 6, Vifor, 6, 12, congress support; **M. Chimenti**: None; **T. Frauenfelder**: AstraZeneca, 2, Bayer, 6, Siemens, 6; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Bruni**: Boehringer Ingelheim, 2, EMDO Foundation, 5, Iten-Kohaut Foundation, 5, Scleroderma Clinical Trials Consortium (SCTC), 5, Scleroderma Research Foundation (SRF), 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1581

The Overall Prevalence and Associated Disease Characteristics of Calcinosis in Systemic Sclerosis: a Systematic Review and Meta-analysis

Marie-Elise Martel[1], Zélie Guitton[2], Aurélien Chepy[1], SEBASTIEN SANGES[3], Eric Hachulla[4], David Launay[1] and Vincent Sobanski[5], [1]Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE - Institut de Recherche Translationnelle en Inflammation, Lille, France., Lille, France, [2]CH Lens, Lens, France, [3]Medecine Interne CHRU Lille, Lille, France, [4]University of Lille, LILLE, France, [5]Université de Lille, Lille, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Calcinosis is a high-burden, key manifestation of systemic sclerosis (SSc), with a challenging therapeutic management. Yet, its precise prevalence and association with SSc charcateristics remain poorly defined. This study aimed to (i) assess the overall prevalence of calcinosis in SSc, and (ii) describe its association with clinical and serological phenotypes of SSc, through a systematic review of the literature with meta-analysis.

Methods: A systematic review of the literature available from inception to September 2024 was carried out in Pubmed, Embase and Web of Science databases. Meta-analyses were performed using collected data on demographic, clinical, biological and imaging characteristics of SSc patients with and without calcinosis.

Results: Eighty-one studies corresponding to a total of 18,643 SSc patients from 37 different countries were included in the meta-analysis. In this population, the overall prevalence of calcinosis was 24% (95% confidence interval [CI]: 21-27), with a high degree of heterogeneity (I^2 = 90.4%, p het < 0.001). Meta-regression revealed that the publication date (p = 0.02) and country (p = 0.001) of each report, could partially explain this observed disparity across studies. Calcinosis screening method also influenced its prevalence. When calcinosis diagnosis was based exclusively on clinical examination, its prevalence was 21% (95%CI: 16-27), whereas it increased to 28% (95%CI: 21-35) when the diagnosis was radiographic, alone or combined with clinical examination (p = 0.04) (**Figure 1**). Calcinosis was positively associated with female gender (OR: 1.43 [1.17; 1.76]), a longer disease duration (14.5 years vs 11.1 years, p = 0,03), pulmonary hypertension (OR: 1.76

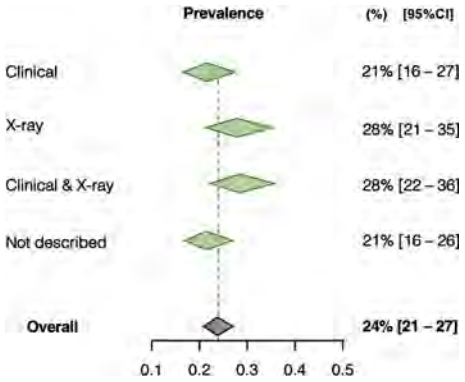
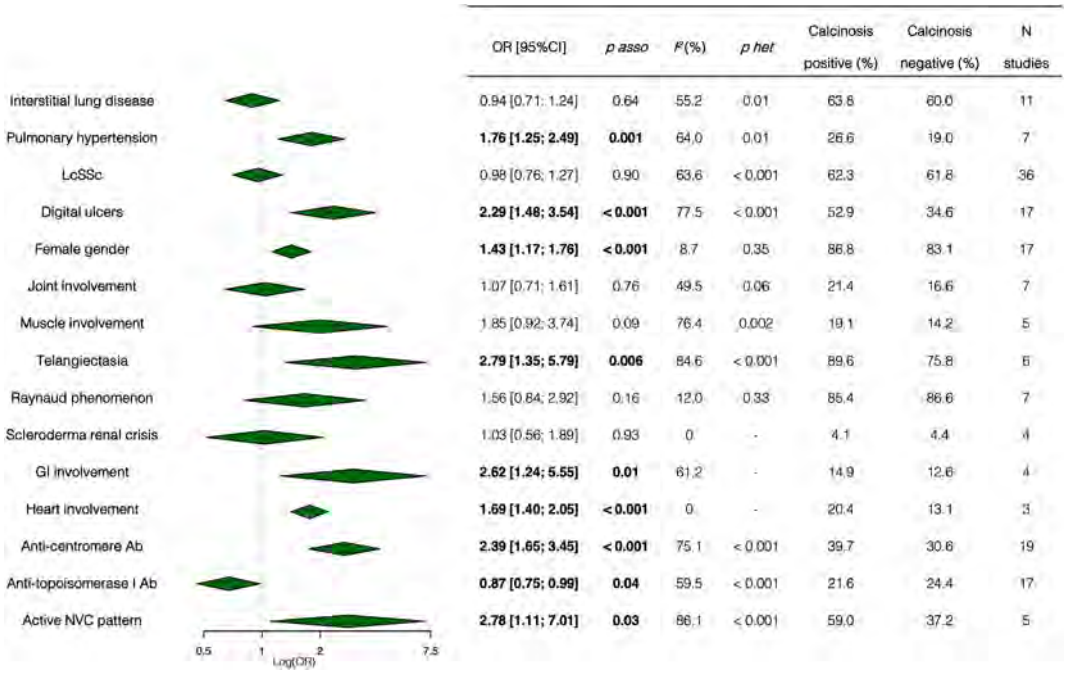


Figure 1. Prevalence of calcinosis in SSc patients, according to the diagnostic method. Diamonds represent the pooled prevalence for each diagnostic method and the overall prevalence.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



	OR [95%CI]	*p asso*	I^2(%)	*p het*	Calcinosis positive (%)	Calcinosis negative (%)	N studies
Interstitial lung disease	0.94 [0.71; 1.24]	0.64	55.2	0.01	63.8	60.0	11
Pulmonary hypertension	**1.76 [1.25; 2.49]**	**0.001**	64.0	0.01	26.6	19.0	7
LcSSc	0.98 [0.76; 1.27]	0.90	63.6	< 0.001	62.3	61.8	36
Digital ulcers	**2.29 [1.48; 3.54]**	**< 0.001**	77.5	< 0.001	52.9	34.6	17
Female gender	**1.43 [1.17; 1.76]**	**< 0.001**	8.7	0.35	86.8	83.1	17
Joint involvement	1.07 [0.71; 1.61]	0.76	49.5	0.06	21.4	16.6	7
Muscle involvement	1.85 [0.92; 3.74]	0.09	76.4	0.002	19.1	14.2	5
Telangiectasia	**2.79 [1.35; 5.79]**	**0.006**	84.6	< 0.001	89.6	75.8	6
Raynaud phenomenon	1.56 [0.84; 2.92]	0.16	12.0	0.33	85.4	86.6	7
Scleroderma renal crisis	1.03 [0.56; 1.89]	0.93	0	-	4.1	4.4	4
GI involvement	**2.62 [1.24; 5.55]**	**0.01**	61.2	-	14.9	12.6	4
Heart involvement	**1.69 [1.40; 2.05]**	**< 0.001**	0	-	20.4	13.1	3
Anti-centromere Ab	**2.39 [1.65; 3.45]**	**< 0.001**	75.1	< 0.001	39.7	30.6	19
Anti-topoisomerase I Ab	**0.87 [0.75; 0.99]**	**0.04**	59.5	< 0.001	21.6	24.4	17
Active NVC pattern	**2.78 [1.11; 7.01]**	**0.03**	86.1	< 0.001	59.0	37.2	5

Figure 2. Association between calcinosis and SSc features. p asso: p-value for association, p het: p-value for heterogeneity, LcSSc: limited cutaneous systemic sclerosis, GI involvement: gastrointestinal involvement, Ab: antibodies, NVC: nailfold video capillaroscopy. Statistically significant associations are represented in bold.

[1.25-2.49]), digital ulcerations (OR: 2.29 [1.48; 3.54]), telangiectasia (OR: 2.79 [1.35; 5.79], an active nailfold capillaroscopy pattern (OR: 2.78 [1.11-7.01]), anti-centromere antibodies (ACA) (OR: 2.39 [1.65; 3.45] and, negatively associated with anti-topoisomerase I antibodies (OR: 0.86 [0.75; 0.99]). A positive association was also found between calcinosis and heart (OR: 1.69 [1.40; 2.05] or gastro-intestinal involvement (OR: 2.62 [1.24; 5.55]), but with a small number of studies (**Figure 2**). No statistically significant association was found between calcinosis and other available clinical features, including cutaneous subset.

Conclusion: Calcinosis is a highly prevalent clinical finding in SSc, occurring in almost one out of four SSc patients. Our work confirmed that, across multiple centers worldwide, calcinosis preferentially develops in female patients, with ACA, and a predominantly vascular phenotype. These findings also highlight the potential clinical relevance of a more systematic radiological evaluation of calcinosis, both to prevent a destructive local evolution, and to identify SSc patients who require closer monitoring of vascular complications, especially pulmonary hypertension. Further studies are needed to decipher the precise implication of vascular involvement in this manifestation, with the prospect of new therapeutic opportunities.

Disclosure: M. Martel: None; **Z. Guitton**: None; **A. Chepy**: None; **S. SANGES**: BioCryst, 5, 12, meeting fees, Grifols, 2, Merck/MSD, 5, 6, Novartis, 2, 12, meeting fees, Sanofi-Genzyme, 12, meeting fees, Shire, 12, meeting fees, SOBI, 12, meeting fees, Takeda, 2; **E. Hachulla**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, Pfizer, 5, Roche-Chugai, 5, Sanofi-Genzyme, 2, 5, Sobi, 5; **D. Launay**: None; **V. Sobanski**: Boehringer-Ingelheim, 2, 6, CSL Behring, 5, Fresenius Kabi, 2, 6, Grifols, 2, 5, 6, Ultragenyx, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1582

Risk factors for incident digital ischemic complications in systemic sclerosis in the Collaborative National Quality and Efficacy Registry (CONQUER)

Marissa Savoie[1], Monica Harding[2], John VanBuren[2], Shervin Assassi[3], Elana Bernstein[4], Lorinda Chung[5], Luke Evnin[6], Tracy Frech[7], Jessica Gordon[1], Faye Hant[8], Laura Hummers[9], Dinesh Khanna[10], Kimberly Lakin[1], Dorota Lebiedz-Odrobina[2], Yiming Luo[4], Ashima Makol[11], Maureen Mayes[12], Zsuzsanna McMahan[13], Jerry Molitor[14], Duncan Moore[15], Carrie Richardson[16], Nora Sandorfi[17], Ami Shah[9], Ankoor Shah[18], Brian Skaug[19], Virginia Steen[20], Elizabeth Volkmann[21], Carleigh Zahn[10] and Flavia Castelino[22], [1]Hospital for Special Surgery, New York, NY, [2]University of Utah, Salt Lake City, UT, [3]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [4]Columbia University, New York, NY, [5]Stanford University, Stanford, CA, [6]Scleroderma Research Foundation, Brisbane, CA, [7]Vanderbilt University Medical Center, Nashville, TN, [8]Medical University of South Carolina, Charleston, SC, [9]Johns Hopkins Rheumatology, Baltimore, MD, [10]University of Michigan, Ann Arbor, MI, [11]Mayo Clinic, Rochester, MN, [12]UT Health Houston Division of Rheumatology, Houston, TX, [13]UT Health Houston, Houston, TX, [14]University of Minnesota, Minneapolis, MN, [15]Northwestern Memorial Hospital, Chicago, IL, [16]Northwestern University, Chicago, IL, [17]University of Pennsylvania, Philadelphia, PA, [18]Duke University, Durham, NC, [19]UTHealth Houston Division of Rheumatology, Houston, TX, [20]Georgetown University School of Medicine, Washington, DC, [21]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA, [22]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: There have not been large US-based studies of digital pitting scars (DPS) and digital ischemic ulcers (DIU) in systemic sclerosis. Utilizing the Collaborative National Quality and Efficacy Registry (CONQUER) cohort, we describe the prevalence, incidence, and quality of life impact of DPS and DIU and determine factors associated with the development of DPS or DIU.

Methods: CONQUER is a US-based, prospective, multi-center cohort of adults (age ≥18) with SSc who meet 2013 ACR/EULAR Classification Criteria and have a disease duration ≤5 years from first non-Raynaud's symptom at enrollment. As of December 31st, 2024, 1113 participants with mean follow-up of 24 months were enrolled. At each visit, investigators noted the presence of DPS and DIU and collected demographic, clinical and laboratory variables. Multivariable logistic regression models were designed using directed acyclic graphs.

Results: The mean age at study entry was 52.5 years, 83% were female, 65% had diffuse cutaneous SSc and 64% had interstitial lung disease. At baseline, 20% had current DPS and 5% had DIU. Younger age at baseline, non-Hispanic Black or African American race, telangiectasias of face or lips, and positive Scl-70 antibody were associated with DPS at baseline (Table 1). Younger age was associated with DIU at baseline (Table 1). In contrast to the variables associated with DPS, positive Scl-70 antibody was associated with lower odds of DIU at baseline. During the first year in CONQUER, 14% developed new DPS and 15% developed new DIU. Analyses of demographic and SSc-related factors did not reveal significant predictors for time to development of first DPS or DIU (Figures 1 and 2). The presence of DIU, but not DPS, was associated with higher PROMIS-29 scales (worse symptom burden) from anxiety (OR 1.38, 95% CI 1.05 to 1.81), depression (OR 1.57, 95% CI 1.18 to 2.10), and pain (OR 1.40, 95% CI 1.04 to 1.89).

Conclusion: In this large, prospective US cohort of participants with early SSc, 14% developed DPS and 15% developed DIU in the first year of study. Non-Hispanic Black or African American race and younger age were associated with DPS, while

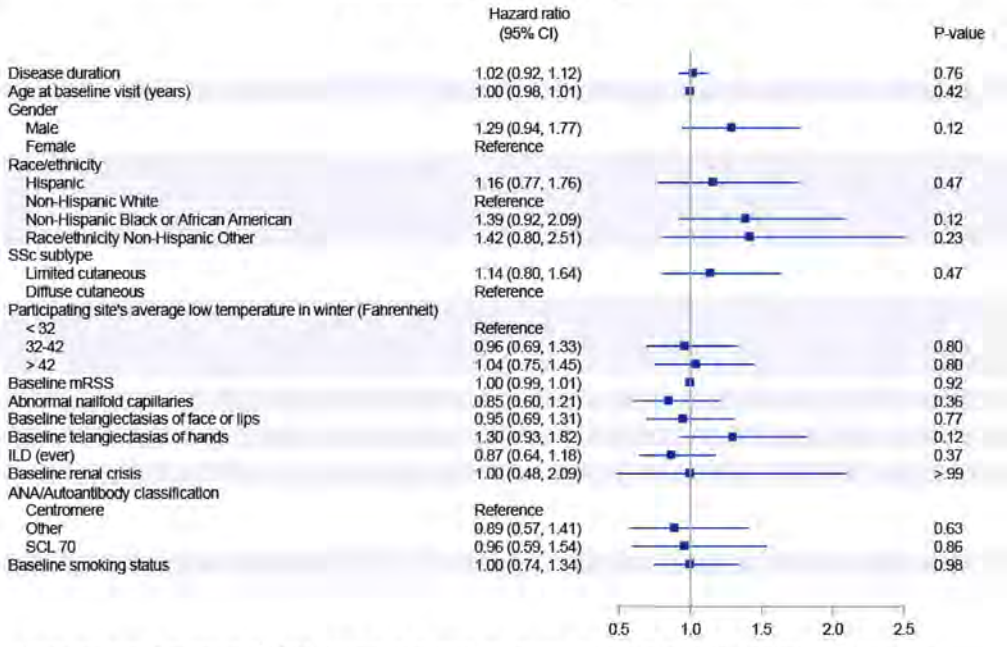
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Multivariable logistic regression of systemic sclerosis (SSc) characteristics and vascular risk factors with the presence of digital pitting scars and digital ischemic ulcers at baseline

	Baseline digital pitting scars N=150			Baseline digital ischemic ulcers N=40		
	N (%) or mean (standard deviation)	Odds ratio (95% CI)	P-value	N (%) or mean (standard deviation)	Odds ratio (95% CI)	P-value
Disease duration from date of first non-Raynaud's symptom to baseline visit (years)	3 (1.4)	1.07 (0.92, 1.24)	0.39	2 (1.3)	0.92 (0.70, 1.18)	0.51
Age at baseline visit (years)	48 (13.1)	0.97 (0.96, 0.99)	0.001	48 (17.5)	0.97 (0.95, 1.00)	0.029
Sex			0.060			0.61
Male	38 (25.3%)	1.58 (0.98, 2.53)		8 (20.0%)	1.26 (0.50, 2.92)	
Female	112 (74.7%)	Reference		32 (80.0%)	Reference	
Race/ethnicity[1]			0.006			0.65
Hispanic	16 (10.7%)	0.84 (0.43, 1.56)		4 (10.0%)	0.71 (0.19, 2.03)	
Non-Hispanic White	98 (65.3%)	Reference		29 (72.5%)	Reference	
Non-Hispanic Black or African American	26 (17.3%)	2.63 (1.41, 4.86)		5 (12.5%)	0.90 (0.28, 2.47)	
Non-Hispanic Other	10 (6.7%)	0.66 (0.29, 1.37)		2 (5.0%)	0.43 (0.07, 1.60)	
Participating site's average low temperature in winter (Fahrenheit)			0.15			0.31
< 32	52 (34.9%)	Reference		14 (35.0%)	Reference	
32-42	52 (34.9%)	0.77 (0.48, 1.22)		18 (45.0%)	0.87 (0.40, 1.94)	
> 42	45 (30.2%)	1.24 (0.75, 2.06)		8 (20.0%)	0.50 (0.18, 1.29)	
SSc subtype			0.70			0.36
Limited cutaneous	38 (25.3%)	0.90 (0.53, 1.52)		10 (25.0%)	0.63 (0.23, 1.68)	
Diffuse cutaneous	112 (74.7%)	Reference		30 (75.0%)	Reference	
Modified Rodnan Skin Score	14 (10.6)	1.02 (0.99, 1.04)	0.18	16 (12.3)	1.03 (1.00, 1.07)	0.088
Abnormal nailfold capillaries	124 (82.7%)	1.12 (0.69, 1.89)	0.65	28 (70.0%)	0.53 (0.25, 1.16)	0.11
Telangiectasias of face or lips	85 (56.7%)	1.91 (1.23, 3.00)	0.004	12 (30.0%)	0.47 (0.20, 1.05)	0.068
Telangiectasias of hands	47 (31.3%)	1.33 (0.84, 2.12)	0.23	7 (17.5%)	0.81 (0.30, 2.01)	0.66
ILD (ever)	96 (64.0%)	0.82 (0.54, 1.26)	0.37	24 (60.0%)	0.92 (0.45, 1.93)	0.83
History of renal crisis	5 (3.3%)	0.64 (0.20, 1.76)	0.41	3 (7.5%)	1.49 (0.30, 5.42)	0.59
ANA/Autoantibody classification[2]			0.031			<.001
Centromere	16 (10.7%)	Reference		12 (30.0%)	Reference	
Scl 70	60 (40.0%)	2.15 (1.09, 4.38)		11 (27.5%)	0.20 (0.07, 0.57)	
Other	74 (49.3%)	1.29 (0.68, 2.56)		17 (42.5%)	0.16 (0.06, 0.41)	
Smoking status	49 (32.7%)	1.19 (0.77, 1.83)	0.42	13 (32.5%)	1.00 (0.47, 2.07)	> 99

Variables considered, but not included due to missingness: Pulmonary arterial hypertension, Pulmonary hypertension, Pulmonary Hypertension related to left heart disease, ESR (mm/Hr), C-reactive protein (CRP), NT-proBNP ≥ 210 pg/mL
[1]Non-Hispanic Asian and Non-Hispanic Other were collapsed into Non-Hispanic Other
[2]In ANA/Autoantibody classification, "other" category includes: ANA negative, RNA Polymerase III, U1 RNP, U3 RNP, Th/To, PM SCL, KU, or isolated ANA.

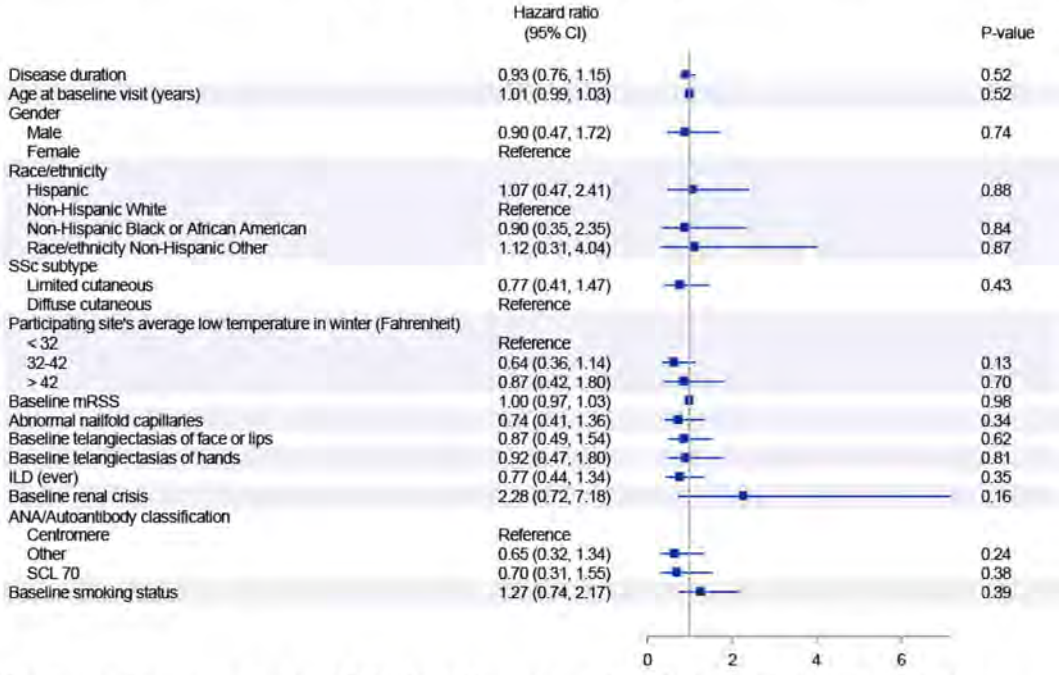
Figure 1: Survival analysis of demographic and systemic sclerosis-related factors in association with time to digital pitting scar



Participants with presence of digital pitting scar at baseline are not included in analysis. Analysis uses time from baseline to first digital pitting scars (months).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Survival analysis of demographic and systemic sclerosis-related factors in association with time to ischemic digital ulcers



Participants with presence of ischemic digital ulcers at baseline are not included in analysis. Analysis uses time from baseline to first ischemic digital ulcers (months).

younger age was associated with DIU. Although we did not identify significant predictors of incident DPS or DIU, DIU were associated with worse symptom burden. These findings underscore the importance of early vascular assessment in SSc and support further study to reduce ischemic complications and improve patient outcomes.

Disclosure: M. Savoie: None; **M. Harding**: None; **J. VanBuren**: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **E. Bernstein**: AstraZeneca, 5, aTyr, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **L. Evnin**: None; **T. Frech**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **F. Hant**: None; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **K. Lakin**: None; **D. Lebiedz-Odrobina**: None; **Y. Luo**: None; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **J. Molitor**: None; **D. Moore**: AstraZeneca, 5; **C. Richardson**: Cabaletta Bio, 2; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 2, Janssen, 2, Novartis, 1; **A. Shah**: None; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **B. Skaug**: None; **V. Steen**: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **C. Zahn**: None; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1583

Epidemiology, Outcome and Expenditures of Hospitalized Patients with Systemic Sclerosis: National Inpatient Sample 2021

Patompong Ungprasert[1] and Paul Kroner[2], [1]Cleveland Clinic, Cleveland, OH, Cleveland Heights, OH, [2]Riverside Health System, Newport News, VA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The inpatient epidemiology, morbidity, mortality, and healthcare expenditures of patients with systemic sclerosis (SSc) are not well-characterized. This study aims to utilize a nationwide inpatient database to better describe these parameters.

Methods: Patients with SSc were identified in the 2021 Nationwide Inpatient Sample (NIS) using ICD-10-CM codes. The NIS is the largest all-payer inpatient database in the United States, encompassing data from over 4,000 non-federal acute care hospitals, and is representative of all U.S. acute care hospitalizations. A comparison cohort without SSc was created for comparative analysis. Extracted data included demographics, primary admission diagnoses, length of stay, mortality, morbidity, expenditures, and comorbidities. Comparative analyses were adjusted for age, sex, ethnicity, Charlson Comorbidity Index, payer type, income, and hospital characteristics.

Results: The inpatient prevalence of SSc was 86.7 per 100,000 admissions. The most common primary admission diagnoses among SSc patients were sepsis (22.7%), hypertension with heart failure (14.4%), and COVID-19 infection (11.5%). The SSc cohort was predominantly female (84.2%) with a mean age of 63.5 years. Compared with non-SSc hospitalizations, those with SSc had significantly longer hospital stays (by 0.7 days; 95% CI: 0.5–0.9) and higher costs, including an adjusted mean increase of $3,277 (95% CI: $2,051–$4,504) in total hospital costs and $11,801 (95% CI: $6,485–$17,116) in total hospitalization charges. Patients with SSc also experienced worse outcomes, including higher risk of in-hospital mortality (adjusted OR 1.42; 95% CI: 1.26–1.61), shock (OR 1.30; 95% CI: 1.17–1.44), systemic inflammatory response syndrome (OR 1.32; 95% CI: 1.01–1.74), and acute respiratory distress syndrome (OR 1.45; 95% CI: 1.12–1.87). Additionally, hospitalized SSc patients had a higher prevalence of multiple comorbidities compared to the control group (see Table 1).

Table 1: Adjust odds ratio comparing comorbidity between hospitalized patients with systemic sclerosis and comparators without systemic sclerosis

Table 1: Adjust odds ratio comparing comorbidity between hospitalized patients with systemic sclerosis and comparators without systemic sclerosis

	Adjusted OR	95% CI	p-value
Pulmonary hypertension	7.21	6.68-7.78	<0.01
Interstitial lung disease	26.33	23.83-29.10	<0.01
Sjögren's syndrome	21.42	19.21-23.87	<0.01
Osteoporosis	2.41	2.18-2.67	<0.01
Hypertension	1.25	1.17-1.34	<0.01
Myocardial infarction	0.97	0.87-1.09	0.63
Mesenteric ischemia	1.42	0.90-2.22	0.13
Chronic kidney disease	0.92	0.85-1.04	0.23
Autoimmune thyroid disease	2.79	2.10-3.70	<0.01

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The inpatient prevalence of SSc is substantially higher than its prevalence in the general population, suggesting that individuals with SSc require inpatient care more frequently. SSc hospitalizations are associated with poorer clinical outcomes and significantly higher healthcare expenditures.

Disclosure: P. Ungprasert: None; **P. Kroner**: None.

Abstract Number: 1584

Evaluation of Adverse Childhood Experiences in Systemic Sclerosis: Prevalence and Patient Characteristics

Samuel Good[1], Nahal Ghanoongooi[1], Ju Young Lee[2], Arissa Young[3] and Elizabeth Volkmann[1], [1]David Geffen School of Medicine at University of California, Los Angeles, Department of Medicine, Division of Rheumatology, Los Angeles, CA, [2]David Geffen School of Medicine at University of California, Los Angeles, Department of Medicine, Los Angeles, CA, [3]UCLA, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: There is growing evidence that trauma, and in particular adverse childhood experiences (ACEs), play a role in the pathogenesis and exacerbation of systemic autoimmune disease.[1] ACEs likely affect autoimmunity through multiple pathways, including pro-inflammatory processes and associations with psychosocial influences on the development of autoimmunity, such as substance use and mental health disorders. To date, no studies have evaluated the association between ACEs and disease manifestations in systemic sclerosis (SSc). The purpose of this study is to evaluate the prevalence of ACEs in SSc patients and to describe the clinical characteristics of patients with SSc with high adversity.

Methods: We recruited consecutive patients who met 2013 ACR/EULAR criteria for SSc seen in our UCLA Scleroderma Center from September 4, 2024 to April 9, 2025. The Adverse Childhood Experiences Questionnaire (ACE-Q), was administered to assess the frequency of ACEs experienced by respondents.[2] The ACE-Q categorizes ACEs into 2 subdomains: abuse/neglect and household dysfunction. Descriptive statistics were used to demonstrate the demographic and clinical characteristics of patients with SSc with high vs. low-moderate total ACE-Q scores based on the validated threshold for high adversity (4 or more ACEs). This threshold is associated with significantly elevated risk for severe and complex health problems.[2]

Results: Among 98 patients with SSc, 85 (86.7%) were female, 63 (64.3%) identified as White, 34 (34.6%) had diffuse cutaneous disease, and 59 (60.2%) had ILD (**Table 1**). In the total SSc population, 63 (64.2%) patients reported at least one ACE, and 22 (22.4%) reported 4 or more ACEs (**Table 1**). The mean number of ACEs was 2.02 (SE 0.23) for the entire SSc cohort (**Figure 1**). The proportion of patients with ILD was numerically higher in the high adversity compared with low to moderate adversity groups (68.2% vs. 57.9%, respectively).

Conclusion: The majority of patients with SSc reported at least one ACE, and the prevalence of high adversity was greater in SSc patients compared with the general population in the US (22.4% vs. 17.3%, respectively).[3] The high prevalence of ACEs and, in particular high adversity, in this SSc cohort highlights the need for further research into the effects of trauma on SSc pathogenesis. Moreover, the finding that high adversity was more prevalent in patients with ILD warrants future investigation into the relationship between trauma and the diverse clinical phenotypes of SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Characteristics of SSc Population, Stratified by Low to Moderate versus High Adversity.

	Low to Moderate Adversity (0-3 ACEs) (N=76)	High Adversity (4+ ACEs) (N=22)	Total (N=98)
Sex			
Male	11 (14.5%)	2 (9.1%)	13 (13.3%)
Female	65 (85.5%)	20 (90.9%)	85 (86.7%)
Age			
20-39 years	8 (10.5%)	2 (9.1%)	10 (10.2%)
40-59 years	33 (43.4%)	10 (45.5%)	43 (43.9%)
60-79 years	31 (40.8%)	9 (40.9%)	40 (40.8%)
80+ years	4 (5.3%)	1 (4.5%)	5 (5.1%)
Race			
White	46 (60.5%)	17 (77%)	63 (64.3%)
Asian	6 (7.9%)	0 (0.0%)	6 (6.1%)
Native Hawaiian or other Pacific Islander	1 (1.3%)	0 (0.0%)	1 (1.0%)
More than one race	2 (2.6%)	0 (0.0%)	2 (2.0%)
Hispanic			
No	45 (59.2%)	15 (68.1%)	60 (61.2%)
Yes	18 (23.6%)	5 (22.7%)	23 (23.5%)
Cutaneous Subtype			
Limited	43 (56.6%)	13 (59.1%)	56 (57.1%)
Diffuse	28 (36.8%)	6 (27.3%)	34 (34.6%)
Sine	5 (6.6%)	2 (9.1%)	7 (7.1%)
ILD			
No	32 (42.1%)	7 (31.8%)	39 (39.8%)
Yes	44 (57.9%)	15 (68.2%)	59 (60.2%)
Number of ACEs			
0	35 (46.1%)	0 (0.0%)	35 (35.7%)
1	17 (22.4%)	0 (0.0%)	17 (17.3%)
2	11 (14.5%)	0 (0.0%)	11 (11.2%)
3	13 (17.1%)	0 (0.0%)	13 (13.3%)
4	0 (0.0%)	8 (36.4%)	8 (8.2%)
5	0 (0.0%)	6 (27.3%)	6 (6.1%)
6	0 (0.0%)	2 (9.1%)	2 (2.0%)
7	0 (0.0%)	4 (18.2%)	4 (4.1%)
9	0 (0.0%)	2 (9.1%)	2 (2.0%)

Abbreviations: ACE=Adverse Childhood Experiences

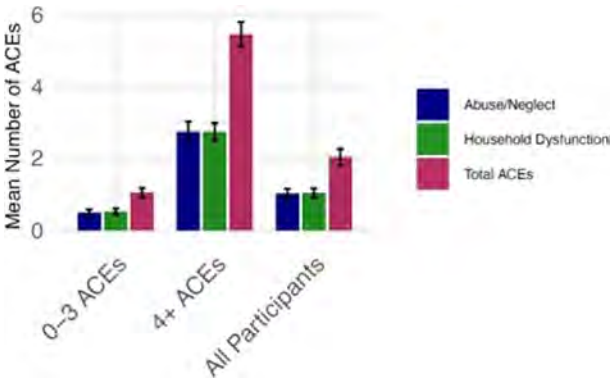


Figure 2: Bar Graph of Mean number of ACEs, Stratified by Low to Moderate Adversity (0-3 ACEs) as Compared to High Adversity (4+ ACEs).

Citations

1. Ploesser M, et al. The link between traumatic stress and autoimmune rheumatic diseases: A systematic scoping review. *Semin Arthritis Rheum*. 2024;69:152558. doi:10.1016/j.semarthrit.2024.152558

2. Felitti VJ, et al. Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*. 1998;14 (4):245-258. doi:10.1016/S0749-3797(98)00017-8

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3. Swedo EA, et al. Prevalence of Adverse Childhood Experiences Among U.S. Adults - Behavioral Risk Factor Surveillance System, 2011-2020. *MMWR Morb Mortal Wkly Rep*. 2023;72(26):707-715. doi:10.15585/mmwr.mm7226a2

Disclosure: S. Good: None; **N. Ghanoongooi**: None; **J. Lee**: None; **A. Young**: None; **E. Volkmann**: None.

Abstract Number: 1586

Real-World Safety and Efficacy of JAK Inhibitors in Systemic Sclerosis: A Propensity-Matched EUSTAR Study

Stefano Di Donato[1], Marie-Elise Truchetet[2], Marco Minerba[3], Oliver Distler[4], JUAN JOSE ALEGRE SANCHO[5], Yolanda Braun Moscovici[6], Christina Bergmann[7], Petros Sfikakis[8], Jeska de Vries-Bouwstra[9], Murray Baron[10], Silvia Bellando-Randone[11], Lorenzo Dagna[12], Christopher Denton[13], Madelon Vonk[14], Vanessa Smith[15], Ivan Castellvi[16], Gabriela Riemekasten[17], Andra Balanescu[18], Masataka Kuwana[19], Maria De Santis[20], Kamal Solanki[21], Anastas Batalov[22], Vahan Mukuchyan[23], Marco Matucci-Cerinic[24], Yannick Allanore[25], Francesco Del Galdo[26], Michael Hughes[27] and The EUSTAR Centers Collaborators, [1]University of Leeds, Canosa Sannita, Chieti, Italy, [2]Bordeaux University Hospital, Bordeaux, France, [3]Campus Bio-Medico University of Rome, Taranto, Taranto, Italy, [4]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [5]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain, [6]Rambam Heath Care Campus, Haifa, Israel, [7]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [8]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [9]Leiden University Medical Center, Leiden, Netherlands, [10]Self employed, Montral, Canada, [11]University of Florence, Florence, Florence, Italy, [12]Ospedale San Raffaele, Milano, Italy, [13]University College London, UK, London, United Kingdom, [14]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, [15]Ghent University Hospital, Gent, Belgium, [16]Hospital Universitari de la Santa Creu i Sant Pau, Sant Just Desvern, Spain, [17]University Clinic Schleswit-Holstein (UKSH), Lbeck, Germany, [18]UNIVERSITY OF MEDICINE AND PHARMACY CAROL DAVILA, Bucharest, Romania, [19]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [20]Humanitas University, Pieve Emanuele, Italy, [21]Waikato Hospital, Hamilton, New Zealand, [22]Medical University of Plovdiv, Plovdiv, Bulgaria, [23]"Erebuni" Medical Center, Yerevan, Armenia, [24]University San Raffaele Milano, Milano, Milan, Italy, [25]Universit Paris Cit, Paris, France, [26]University of Leeds, Leeds, United Kingdom, [27]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a complex systemic autoimmune disease characterized by vasculopathy, fibrosis, and immune dysregulation. While JAK inhibitors (JAKi) have shown promising immunomodulatory and antifibrotic effects in early-phase studies, their real-world impact on SSc patients remains poorly studied. We aimed to assess safety and explore the efficacy in JAKi-treated SSc patients compared to conventional immunosuppressants.

Methods: We conducted a longitudinal retrospective cohort study within the European Scleroderma Trials and Research group (EUSTAR) database. Patients receiving JAK inhibitors (JAKi) were matched 1:5 to patients initiating mycophenolate mofetil (MMF), rituximab (RTX), or methotrexate (MTX) using nearest-neighbour propensity score matching based on age, sex, disease duration, antibody profile, skin subset, presence of digital ulcers (DUs), and baseline lung function.

Primary outcomes included adverse events and drug survival (time to permanent discontinuation). Efficacy endpoints were change in FVC% and mRSS at 12 and 24 months, improvement in swollen joint count (SJC) in patients with synovitis, time to new DUs, and a composite disease progression outcome (new PAH, SRC, or ILD progression). Safety events, reasons for discontinuation, and use of vasodilators were also recorded. Time-to-event analyses were performed using Kaplan–Meier

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical features of the study cohort stratified by treatment.

Characteristic	JAKi N = 36[1]	MMF N = 180[1]	MTX N = 180[1]	RTX N = 180[1]	p-value[2]	q-value[3]
Follow up (months)	44 (26, 71)	50 (25, 87)	48 (25, 89)	50 (22, 86)	0.8	0.9
Disease duration (months)	76 (38, 161)	82 (40, 138)	94 (45, 160)	78 (46, 133)	0.5	0.7
Age at baseline	57 (51, 63)	57 (48, 67)	57 (47, 68)	55 (45, 63)	0.2	0.3
Sex					0.3	0.4
Female	29 (81%)	144 (80%)	156 (87%)	143 (79%)		
Male	7 (19%)	36 (20%)	24 (13%)	37 (21%)		
Leroy subset					0.058	0.13
Diffuse cutaneous	12 (33%)	59 (33%)	53 (29%)	72 (40%)		
Limited cutaneous	24 (67%)	121 (67%)	127 (71%)	108 (60%)		
Anti Topoisomerase I	14 (39%)	76 (42%)	80 (44%)	74 (41%)	0.9	>0.9
Anti Centromere	10 (28%)	30 (17%)	44 (24%)	24 (13%)	0.021	0.054
Anti RNA Polymerase III	3 (8.3%)	6 (6.4%)	7 (8.4%)	9 (10%)	0.8	>0.9
Mycophenolate Mofetil	0 (0%)	180 (100%)	8 (4.4%)	20 (11%)	<0.001	<0.001
Rituximab	0 (0%)	6 (3.3%)	10 (5.6%)	180 (100%)	<0.001	<0.001
Methotrexate	14 (39%)	10 (5.6%)	180 (100%)	19 (11%)	<0.001	<0.001
Endothelin Receptor Antagonists	6 (17%)	13 (7.2%)	20 (11%)	11 (6.1%)	0.10	0.2
Calcium Channel Blockers	11 (31%)	28 (16%)	31 (17%)	19 (11%)	0.018	0.053
Phosphodiesterase Inhibitors	8 (22%)	11 (6.1%)	9 (5.0%)	7 (3.9%)	0.003	0.016
Forced Vital Capacity %	96 (85, 109)	87 (81, 110)	94 (88, 101)	89 (82, 105)	0.3	0.4
Diffusing Lung Capacity co %	69 (58, 80)	57 (56, 75)	69 (57, 73)	58 (57, 70)	<0.001	<0.001
Pitting Scars	7 (19%)	82 (46%)	56 (31%)	68 (38%)	0.004	0.017
History of DUs	15 (42%)	81 (55%)	77 (52%)	79 (55%)	0.5	0.7
Active DUs at baseline	10 (28%)	51 (28%)	54 (30%)	49 (27%)	>0.9	>0.9
Telangiectasia	19 (53%)	139 (77%)	130 (72%)	122 (68%)	0.017	0.053
Calcinosis	8 (22%)	16 (16%)	16 (17%)	14 (15%)	0.8	0.9
Pulmonary Arterial Hypertension	4 (11%)	9 (13%)	16 (19%)	14 (16%)	0.7	0.8

[1] Median (Q1, Q3); n (%)

[2] Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test

[3] False discovery rate correction for multiple testing

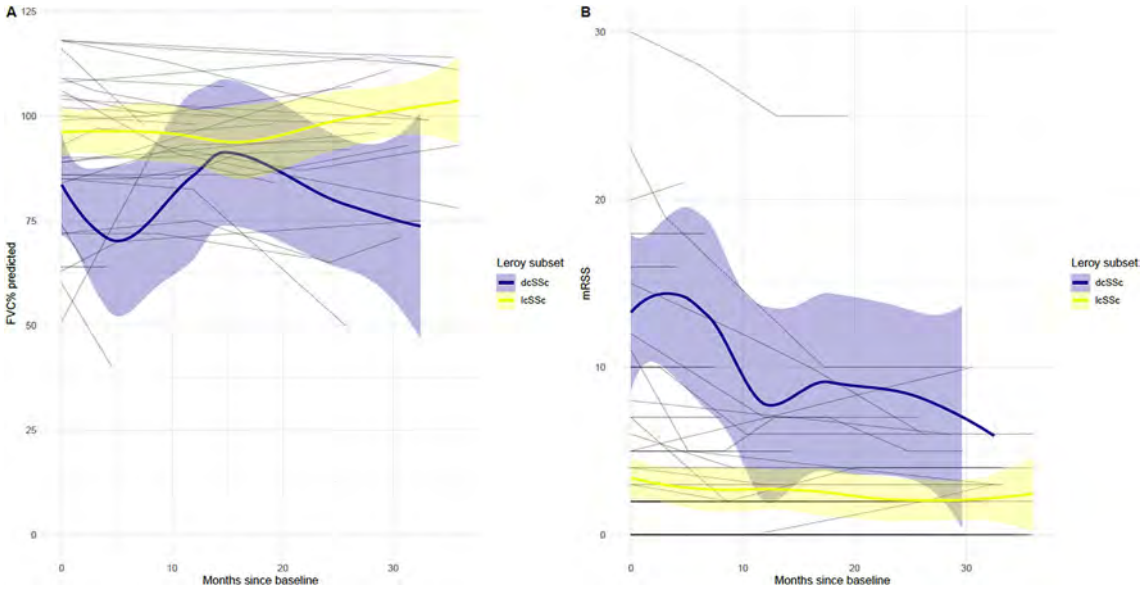


Figure 1. Longitudinal trends of pulmonary function (A) and skin fibrosis (B) in patients treated with JAK inhibitors, stratified by Leroy cutaneous subset.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and restricted mean survival time (RMST); continuous outcomes were analysed via linear models and paired tests. Follow-up was censored at drug discontinuation for patients without outcome events.

Results: We included 36 JAKi-treated patients (44% baricitinib, 42% tofacitinib, 14% upadacitinib), predominantly female (81%), with a median disease duration of 76 months. Over 98.7 patient-years, 23 adverse events occurred (23.3/100 patient-years), including 12 infections (8 severe, 1 fatal), 7 lab abnormalities, and 3 malignancies. JAKi was permanently discontinued in 14 patients (39%), and transiently interrupted in 7 (19%).

At 12 months, FVC remained stable (+1.7%, p=0.530); skin fibrosis improved modestly (–1.1 mRSS, p=0.036), particularly in diffuse cutaneous SSc. Swollen joint count improved in patients with baseline synovitis (median –1, p=0.052). No new calcinosis developed, and two pre-existing cases improved.

Time-to-event analyses over 60 months showed comparable risk of recurrent digital ulcers and composite progression events between JAKi and matched MMF, RTX, and MTX arms (RMST differences non-significant; DU log-rank p=0.24). JAKi-treated patients had similar or slightly better RMST for disease progression versus MTX (+3.1 months), though differences did not reach significance.

Conclusion: In this cohort, treatment with JAK inhibitors was not associated with an increased risk of fibrosing or vascular complications compared to conventional immunosuppressive therapies. While these findings suggest a favourable safety profile and potential efficacy of JAKi in SSc, prospective, controlled studies are needed to confirm these results and to explore their potential disease-modifying effects.

Disclosure: S. Di Donato: None; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2; **M. Minerba**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **J. ALEGRE SANCHO**: None; **Y. Braun Moscovici**: None; **C. Bergmann**: None; **P. Sfikakis**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **M. Baron**: None; **S. Bellando-Randone**: Boehringer-Ingelheim, 2, 6; **L. Dagna**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **M. Vonk**: Boehringer-Ingelheim, 2, 6, 12, Travel grants, Janssen, 2, 6, 12, travel grants, Merck/MSD, 6; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **I. Castellvi**: None; **G. Riemekasten**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 2, 6, Galapagos, 6, Janssen, 2, 6, Merck/MSD, 6, Novartis, 6, Roche, 6, Sanofi, 5; **A. Balanescu**: AbbVie/Abbott, 1, 6, Amgen, 2, 6, Angellini, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Ewopharma, 6, Janssen, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sobi, 2, 6, Stada, 2, 6, Theramex, 6, UCB, 2, 6; **M. Kuwana**: AbbVie, 2, Asahi Kasei Pharma, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 6, GlaxoSmithKlein(GSK), 2, Medical and Biological Laboratories, 5, 9, Mochida, 2, Novartis, 2, Ono Pharmaceuticals, 6; **M. De Santis**: Boehringer-Ingelheim, 2, 6; **K. Solanki**: Apollo Hospitals Educational and Research Foundations, 12, Honorary adjunct professor; **A. Batalov**: None; **V. Mukuchyan**: None; **M. Matucci-Cerinic**: None; **Y. Allanore**: None; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **M. Hughes**: Janssen, 5, 6, UCB, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1587

Longitudinal Clinical Response to JAK Inhibitors in Systemic Sclerosis: A Real-Life Multicentric Study Across Clinical Domains

Stefano Di Donato[1], JUAN JOSE ALEGRE SANCHO[2], Anastas Batalov[3], Zguro Batalov[4], Silvia Bellando-Randone[5], carmela coccia[6], Marco de Pinto[7], Dilia Giuggioli[8] and Michael Hughes[9], [1]University of Leeds, Canosa Sannita, Chieti, Italy, [2]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain, [3]Medical University of Plovdiv, Plovdiv, Bulgaria, [4]UMHAT Kaspela, Ploudiv, Bulgaria, [5]University of Florence, Florence, Florence, Italy, [6]Rheumatology Unit, Department of Experimental and Clinical Medicine, University of Florence, Firenze, Italy, [7]Azienda Ospedaliero Universitaria Policlinico di Modena, Parma, Parma, Italy, [8]Scleroderma Unit, Rheumatology Unit, University Hospital of Modena and Reggio Emilia, Modena, Italy, Modena, Italy, [9]Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, Manchester, England, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: JAK inhibitors (JAKi) have shown promising early results in systemic sclerosis (SSc) patients, yet real-world data on their longitudinal effects across different disease domains remain limited. We aimed to explore the safety and intra-patient evolution of pulmonary, cutaneous, and articular parameters in a well-characterized cohort of SSc patients treated with JAKi, using standardized efficacy metrics over 12 and 24 months.

Methods: Ours was an international, multi-center longitudinal retrospective cohort study. Continuous variables were reported as means (SD) or medians (IQR) as appropriate and categorical variables were reported as counts (%). Incidence rates were calculated per 100 patient-years, and descriptive statistics were used for calcinosis and DU events. To assess treatment efficacy, we evaluated changes in FVC%, DLCO%, modified Rodnan skin score (mRSS), tender and swollen joint counts (TJC, SJC), digital ulcers (DU), and calcinosis status. Baseline was defined as the first available measurement at JAKi initiation; follow-up values were taken within a ±2-month window from 12 and 24 months. For each parameter, the primary outcome was the delta from baseline. Paired comparisons used the Wilcoxon signed-rank test. Effect size was quantified using standardized mean change (SMC). Analyses were performed in R (version 4.3.3).

Results: Among the 32 patients treated with the 4 avaliable JAK inhibitors, the median (IQR) follow-up time on treatment was 16.9 (10.3-31.8) months, with a range from 1.4 to 52.0 months, amounting to 52.8 patient-years. At 12 months, pulmonary function parameters (FVC% and DLCO%) remained stable over time. Although small positive changes were observed (SMC +0.22 for FVC and +0.23 for DLCO), neither reached statistical significance (p=0.10 and p=0.33, respectively) (Figure 1A and 1B). At 12 months, the median mRSS showed a significant improvement (p=0.030), with an SMC of -0.29 (Figure 1C). Similarly, both TJC and SJC showed decreases, (p=0.0002 and p=0.0012, respectively) with SMCs of -1.19 for TJC and -0.69 for SJC (Figure 1D and 1E). At 24 months, mRSS, TJC, and SJC showed numerical improvements which were marginally significant for joints domain (SMC: -0.21, -1.13, and -1.14; p=0.17, p=0.054, and p=0.058, respectively). FVC% and DLCO% remained stable with no significant changes. Among 11 patients with calcinosis at baseline, 5 (45.5%) showed improvement, 3 (27.3%) experienced worsening, and 3 (27.3%) remained stable during follow-up. During follow-up, 10 patients developed at least one episode of active DUs, corresponding to an incidence rate of 21 events per 100 patient-years. Among patients treated with glucocorticoids (n=15), a trend toward dose tapering over time was observed (-0.038 mg/month), although borderline significant (p=0.1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline clinical and demographic parameter of the JAK inhibitor-treated Systemic Sclerosis cohort.

Characteristic	Patients N = 32[1]
LeRoy subset	
Diffuse cutaneous	13 (41%)
Limited cutaneous	19 (59%)
ANA positive	31 (97%)
Rheumatoid Factor	7 (22%)
Anti CCP	2 (6.3%)
Anti Ro52	2 (6.3%)
Anti Centromere	8 (25%)
Anti Topoisomerase I	12 (38%)
Anti RNA polymerase III	2 (6.3%)
Pitting scars	14 (44%)
Telangiectasia	21 (66%)
History of Digital Ulcers	22 (69%)
Active Digital Ulcers	7 (22%)
Puffy fingers	17 (53%)
Calcinosis	11 (34%)
Acro osteolysis	3 (9.4%)
Pulmonary Arterial Hypertension	8 (25%)
Interstitial Lung Disease	16 (50%)
Glucocorticoids treatment	15 (47%)
Forced Vital Capacity (% predicted)	92 (78, 108)
Diffusing Lung Capacity (% predicted)	71 (57, 84)
Swollen Joints Count	4.0 (2.0, 10.0)
Tender Joints Count	6.0 (2.5, 10.0)
Raised C-reactive protein	10 (31%)
Antiplatelets treatment	8 (25%)
Mycophenolate Mofetil	3 (9.4%)
Calcium Channel Blockers	11 (34%)
Endothelin Receptors Antagonists	7 (22%)
Phosphodiesterase 5 inhibitors	10 (31%)
Iloprost	6 (19%)
Methotrexate	12 (38%)
Leflunomide	2 (6.3%)
Tocilizumab	1 (3.1%)
Nintedanib	1 (3.1%)
Rituximab	1 (3.1%)
Cyclophosphamide	0 (0%)
JAK inhibitor type	
Baricitinib	10 (31%)
Filgotinib	7 (22%)
Tofacitinib	10 (31%)
Upadacitinib	5 (16%)

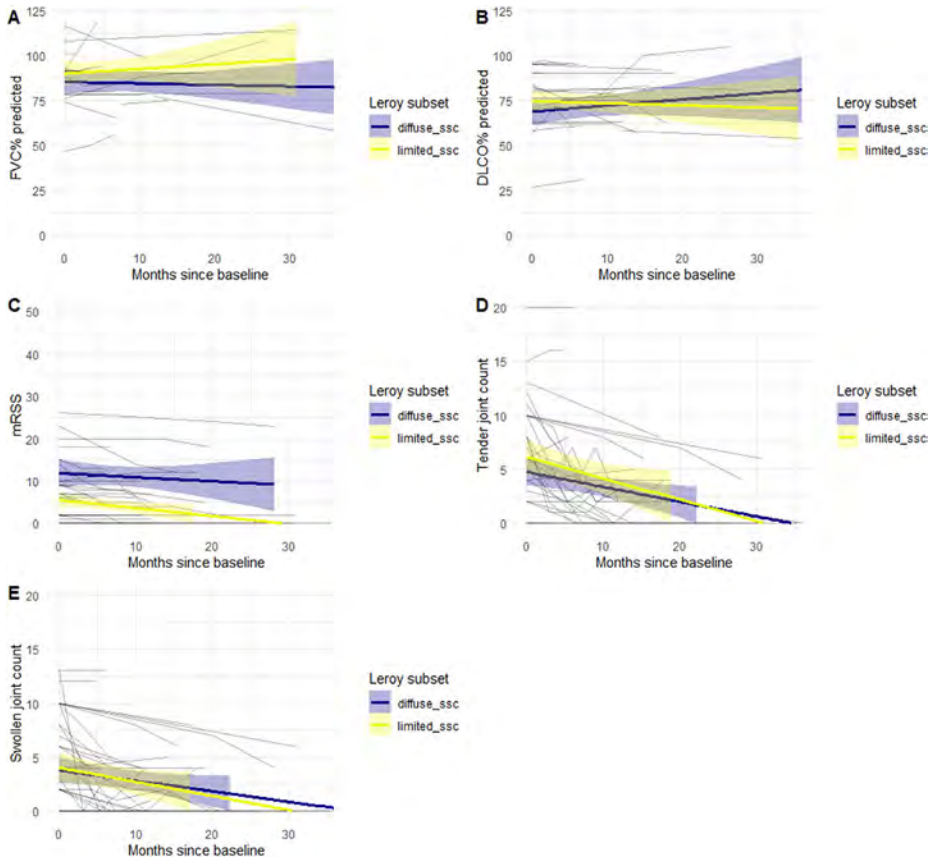


Figure 1. Longitudinal changes in clinical parameters during JAK inhibitor treatment in systemic sclerosis. (A) FVC% predicted, (B) DLCO% predicted, (C) modified Rodnan skin score (mRSS), (D) tender joint count (TJC), and (E) swollen joint count (SJC), stratified by LeRoy subset. Each line represents an individual patient; solid lines and shaded areas represent linear trends with 95% confidence intervals.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this real-life SSc cohort, JAK inhibitors were associated with significant improvements in skin and joint involvement. Importantly, pulmonary function remained stable over time, suggesting a potential disease-modifying effect across multiple clinical domains. A steroid sparing effect was noted, and with improvement in calcinosis seen in some treated patients.

Disclosure: S. Di Donato: None; **J. ALEGRE SANCHO**: None; **A. Batalov**: None; **Z. Batalov**: None; **S. Bellando-Randone**: Boehringer-Ingelheim, 2, 6; **c. coccia**: None; **M. de Pinto**: None; **D. Giuggioli**: None; **M. Hughes**: Janssen, 5, 6, UCB, 5.

Abstract Number: 1588

Prevalence Of Oral Manifestations And Their Association With Clinical And Serological Profile In Systemic Sclerosis Patients- An Indian Study

Vijaya prasanna Parimi[1], **Tejaswini Ramineni**[2], Pradeep S Anand[3], Vineeta Shobha[4], Padmanabha Shenoy[5], Geetabali Sircar[6], kaushik Basu[7], Anna C Das[4], Geetha Amritrao Kale[4], indranil sarkar[8], Shinie Razil Goveas[4], Biswarup Sengupta[8], Caseena Kareem[9], Yogananth Sakthivel[4], Soma Halder Biswas[7] and Neel Nallulwar[8], [1]ESIC Medical College and Super Specilaity Hospital, hyderabad, Telangana, India, [2]Esic Medical College And Hospital, Sanathnagar, Hyderabad, Telangana, India, [3]ESIC MEDICAL COLLEGE AND HOSPITAL, HYDERABAD, Telangana, India, [4]St. John's Medical College Hospital, Bangalore, Bangalore, Karnataka, India, [5]Shenoy's CARE, Kochi, Kerala, India, [6]West Bengal Medical Education Service, Kolkata, West Bengal, India, [7]Medical College, Kolkata, kolkata, West Bengal, India, [8]IPGMER, Kolkata, kolkata, West Bengal, India, [9]CARE, Kochi, kochi, Kerala, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

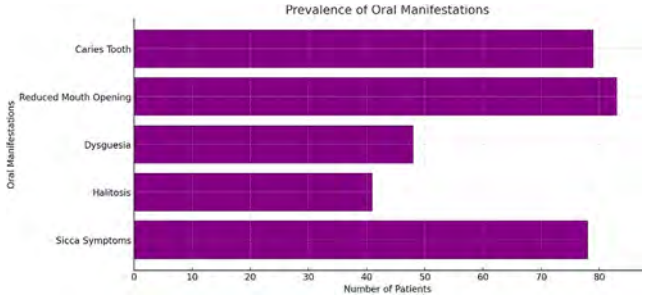
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSC) is a chronic, multisystem autoimmune disease characterized by immune dysfunction, microangiopathy, and tissue remodelling. Orofacial manifestations, including xerostomia, microstomia, tooth decay, and periodontitis, affect up to 80% of SSC patients and significantly impact their quality of life. Despite their prevalence, these manifestations are often neglected compared to more life-threatening complications such as lung or kidney involvement. This study was designed to estimate the prevalence of oral-manifestations and to find their association with clinical and serological profiles in SSC patients.

Methods: A multi-centre study was conducted involving 131 SSC patients fulfilling ACR/EULAR-criteria. Comprehensive clinical-evaluation was performed including Modified-Rodnan-Skin-Score (MRSS) for skin tightness and Medsger's-disease-severity-score for organ involvement. Oral-manifestations like presence of sicca symptoms, GERD were noted. Standardised-questionnaires like, Indian Cochin hand function Scale (ICHFS), Mouth Handicap in Systemic Sclerosis Scale (MHISS) were used to assess functional-impairment. Oro-facial health was evaluated using standardized dental indices such as Debri-Index(DI), Calculus-index(CI), number of missing-teeth, tooth-mobility, probing-depth(PD), gingival-bleeding (GB) and Clinical-attachment-level(CAL), Recession(REC) by a periodontist. Statistical-analysis was conducted using SPSS software V20, with statistical significance set at $p < 0.05$.

Results: Among 131 SSC patients, 45 were Limited Cutaneous SSC (LCSSC), 83 were Diffuse Cutaneous SSC (DCSSC) and 3 were sine scleroderma. The mean age was 42 years. Prevalence of oral manifestations like sicca symptoms was 59.5%, halitosis was 31.3%, Dysguesia was 36.6%, Reduced mouth opening was 63.4%, caries tooth was 60.3%%. Most of the oral manifestations were seen with a higher prevalence in DCSSC. Among the dental-examination findings, GB20,30,40, mean CAL, mean REC, DI and CI were higher in DSCC. The patients with early-disease (< 5 years from first non-Raynauds symptom) constituted 43.5% and late-disease constituted 56.5%. All the oral-manifestations and dental-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Prevalence Of Oral Manifestations In Systemic Sclerosis Patients

	LC SSC	DC SSC	P VALUE
ICHFS	14.64	16.45	**0.01***
MHISS	9.14	8.82	**0.02***

Functional Measures Among Limited and Diffuse Cutaneous Systemic Sclerosis Patients

	EARLY	LATE	P VALUE
ICHFS	14.0	20.2	**0.02***
MHISS	12.4	14.0	0.31

Functional Measures Among Early and Late Systemic Sclerosis Patients

examination findings were higher in patients with late disease. The IC-HFS is higher in DCSSC patients with a mean score of 16.45 ($p < 0.05$) and among those with late disease with a mean score of 20.2($p < 0.05$). Disease severity assessed by Medsger's score correlated positively with DCSSC, periodonditis, missing teeth, teeth mobility, GB, mean REC.

Conclusion: In this multicentre study, DCSSC exhibited significantly higher oral and dental manifestations with increased IC-HFS scores, GERD, reduced mouth opening, greater number of missing-teeth and periodontitis. Patients with late disease had more pronounced oral-manifestations and higher CAL, REC scores. These findings suggest that DCSSC and extended disease-duration are associated with more severe oral health complications, highlighting the importance of early dental intervention. Disease severity as assessed by Medsgers-score correlated-positively with presence of periodontitis indicating its possible role in disease pathogenesis.

Disclosure: V. Parimi: None; **T. Ramineni**: None; **P. Anand**: None; **V. Shobha**: None; **P. Shenoy**: None; **G. Sircar**: None; **k. Basu**: None; **A. Das**: None; **G. Kale**: None; **i. sarkar**: None; **S. Goveas**: None; **B. Sengupta**: None; **C. Kareem**: None; **Y. Sakthivel**: None; **S. Biswas**: None; **N. Nallulwar**: None.

Abstract Number: 1589

Nintedanib in Systemic Sclerosis-Associated Interstitial Lung disease: Real-World Cohort Study on Tolerability and Discontinuation

Punchalee Kaenmuang[1], Nina Goldman[2], Arthihai Srirangan[1], Fiammetta Danzo[1], Wing-Ho Yip[1], Ali Taki[3], Shereen Boreland[1], Benedetta Vitri[1], Carmel JW. Stock[1], Christopher Denton[4], Athol U. Wells[1], **Voon H. Ong**[5], Piersante Sestini[6] and Elisabetta A. Renzoni[1], [1]Interstitial Lung Disease Unit, Royal Brompton Hospital, Guy's and St Thomas' National Health Service Foundation Trust, London, England, United Kingdom, [2]Division of Medicine, Centre for Rheumatology, University College London, London, England, United Kingdom, [3]Royal Free Hospital, London, England, United Kingdom, [4]University College London, UK, London, United Kingdom, [5]Division of Medicine, Centre for Rheumatology, University College London, London, United Kingdom, [6]Department of Medical and Surgical Sciences and Neurosciences, University of Siena, Siena, Toscana, Italy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

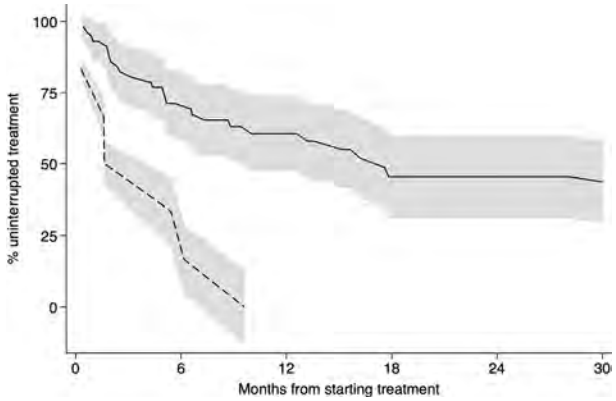


Figure 1 Smoothed representation of the Kaplan-Meier survival curve showing the proportion of patients remaining on uninterrupted treatment over time, stratified by body mass index (BMI) (<18.5 vs ≥18.5 kg/m^2). The dashed line represents patients with BMI<18.5 kg/m^2; the solid line represents patients with ≥18.5 kg/m^2. Shaded areas represent the 95% Confidence Interval (C.I).

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Nintedanib slows the progression of systemic sclerosis-associated interstitial lung disease (SSc-ILD). However, potential high discontinuation rates due to adverse side-effects raise concerns about its tolerability in this patient group.

Methods: In this multicenter study, nintedanib tolerability and body weight changes were assessed. Nintedanib interruption was defined as any interruptions due to treatment-related side effects. Predictors of nintedanib interruption were assessed using logistic regression, with multivariable analysis adjusting for potential confounders. Fisher's exact test was used when complete separation precluded logistic regression and time to first treatment interruption was analysed by Cox proportional hazards analysis. The Wilcoxon signed-rank test was used to compare body weight changes before and after nintedanib initiation.

Results: Among 63 patients (mean age 56.5±13.8 years, 22% male and 56% ever smokers), 76.2% received nintedanib 150 mg twice daily, the remainder 100 mg twice daily. Both concomitant mycophenolate mofetil use and baseline gastrointestinal (GI) symptoms were reported in 85.7% of patients. Patient-reported GI symptoms included diarrhoea (58.7%, 41.3% requiring loperamide), reflux (47.6%), weight loss (38.1%), and nausea/vomiting (33.3%). Over a median follow up of 22.2 months (95% CI 18.1-26.2), Nintedanib was interrupted in 50.8% of patients. Older age ($p< 0.03$ on univariable and multivariable analyses) and BMI <18.5 kg/m^2 ($p = 0.024$) were significant predictors of interruption. Patients with BMI <18.5 kg/m^2 had a significantly shorter time to treatment interruption compared to those with higher BMI (Figure 1) and remained significant after adjustment for FVC or DLCO and demographic variables. Baseline GI symptoms and concurrent Disease-Modifying Antirheumatic Drugs used were not associated with interruption. Most patients who experienced interruption were able to restart treatment, either at reduced or full dose. Permanent discontinuation occurred in 22.2%, with no significant risk factors identified. Mean weight loss over 12 (±6)months after initiation was 1.93 kg (95% CI: 0.64-3.22, p=0.0041), significantly greater than in the 12 (±6)months before treatment (1.38 kg) (p=0.0008).

Conclusion: Among patients with SSc-ILD treated with nintedanib, adverse effects and weight loss frequently led to treatment interruptions. Older age and lower BMI were significant predictors of interruption, while no clear predictors of permanent discontinuation were identified, such as baseline GI symptoms, larger studies are needed to confirm these findings. Most patients were able to resume treatment, underscoring the need for close monitoring and accessible healthcare professional support.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Kaenmuang: None; **N. Goldman**: None; **A. Srirangan**: None; **F. Danzo**: None; **W. Yip**: None; **A. Taki**: None; **S. Boreland**: None; **B. Vitri**: None; **C. Stock**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **A. Wells**: Boehringer Ingelheim, 2, 6, Chiesi, 2, Roche, 2, Veracyte, 2; **V. Ong**: Boehringer-Ingelheim, 6; **P. Sestini**: None; **E. Renzoni**: Boehringer-Ingelheim, 1, 6.

Abstract Number: 1590

Association of Levels of Soluble CD13 with Clinical Features and Fibrosis in Systemic Sclerosis Patients

Yuzo Ikari[1], Poulami Dey[2], James St. Clair[3], Anna Webber[4], Caroline Foster[5], Yi-Chen Chen[5], Ramadan Ali[6], Dinesh Khanna[7], David Fox[8] and Pei-Suen Tsou[7], [1]Division of Rheumatology, Department of Medicine, Showa Medical University School of Medicine, Tokyo, Japan, [2]Michigan Medicine, Ann Arbor, MI, [3]University of Michigan, Ann Arbor, [4]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [5]Division of Rheumatology, Department of Internal Medicine, University of Michigan, ANN ARBOR, MI, [6]University of Michigan, Ann Arobr, MI, [7]University of Michigan, Ann Arbor, MI, [8]University of Michigan, Dexter, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Soluble CD13 (sCD13), released by the cleavage of cell surface CD13 by matrix metalloproteinase-14 (MMP14), has potent proinflammatory, angiogenic, and arthritogenic activities. The receptors for sCD13 are bradykinin receptor B1 (B1R) and protease-activated receptor 4 (PAR4). Building on our recent study showing that the sCD13-B1R axis was critically involved in promoting fibrosis in systemic sclerosis (SSc)[1], we hypothesized that plasma sCD13 levels are associated with SSc clinical features. This study aimed to measure plasma sCD13 levels in SSc patients and examine their correlations with disease phenotype, vascular complications, skin and lung fibrosis, and other clinical characteristics. The expression of genes associated with the sCD13-B1R pathway was also examined in peripheral blood cells.

Methods: Plasma sCD13 was measured using ELISA. SSc patients and healthy controls were recruited at the University of Michigan Scleroderma Program. Three patient cohorts were used to evaluate sCD13 levels for disease subtypes, vascular involvement, and early disease. Clinical data was recorded. Vascular complications were defined as a history of at least one of the following: digital ulcers, pulmonary arterial hypertension, or SSc renal crisis. Transcriptomic data from the GEO dataset GSE181228 was extracted to evaluate genes relevant to CD13 in peripheral blood cells. Statistical analyses were performed using t-tests, chi-square tests, and correlation analysis, and $p < 0.05$ was considered significant.

Results: Plasma sCD13 levels were significantly higher in diffuse cutaneous (dc)SSc patients compared to limited cutaneous SSc patients and healthy controls. There was no significant association between vascular complications and plasma sCD13 levels in SSc patients with vascular complications compared to those without. Among early-stage SSc patients (diagnosed within 3 years of disease onset), there was no significant difference in mRSS between the high and low sCD13 groups (Table 1). However, the change in mRSS at one-year follow-up showed a significant decrease in the high sCD13 patient group (Figure 1). The transcriptomic analysis showed that *ANPEP* (gene encoding CD13), *MMP14* and *F2RL3* (encoding PAR4) were upregulated in SSc patients compared to healthy controls, and a positive correlation was observed between *ANPEP* and *MMP14*, as well as between *ANPEP* and *F2RL3*. Furthermore, significant positive correlations were observed between *ANPEP* and *TGFB1* or *IL6*, as well as between *MMP14* and *TGFB1* or *IL6*. *F2RL3* also showed a significant correlation with *TGFB1* (Figure 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of patients with early-onset SSc and comparison between High and Low sCD13 status High sCD13 status was defined as plasma values exceeding 384.3 ng/mL. SSc, systemic sclerosis; sCD13 soluble CD13; SD, standard deviation; IQR, interquartile range; mRSS, modified Rodnan skin score; ILD, interstitial lung disease, PAH, pulmonary arterial hypertension; FVC, forced vital capacity; DLCO, diffusing capacity of the lung for carbon monoxide.

		sCD13 status		
Clinical variables	Overall SSc N = 74	High N = 46	Low N = 28	*P* value
Age, mean (SD), y	54.4 (12.3)	53.2 (11.7)	56.3 (13.0)	0.30
Male, n (%)	18 (24.3)	10 (78.2)	8 (71.4)	0.50
Race White, n (%)	62 (83.8)	37 (80.4)	25 (89.2)	0.52
Black, n (%)	8 (10.8)	7 (15.2)	1 (3.6)	0.25
Asian, n (%)	1 (1.4)	0 (0)	1 (3.6)	0.36
American Indian, n (%)	1 (1.4)	1 (2.2)	0 (0)	>0.99
Other, n (%)	2 (2.7)	1 (2.2)	1 (3.6)	>0.99
Ethnicity Hispanic, n (%)	6 (8.1)	3 (6.5)	3 (10.7)	0.67
Diffuse cutaneous variant, n (%)	61 (82.4)	38 (82.6)	23 (82.1)	>0.99
Disease duration, median (IQR), y	1.54 (0.86 – 2.13)	1.63 (0.94 – 2.10)	1.47 (0.72 – 2.56)	0.74
Anti centromere positive, n (%)	8 (10.8)	3 (6.5)	5 (17.9)	0.15
Anti Scl-70 positive, n (%)	16 (21.6)	10 (21.7)	6 (21.4)	0.97
Anti RNA polymerase positive, n (%)	26 (35.1)	14 (30.4)	12 (42.8)	0.28
Anti RNP positive, n (%)	11 (14.9)	8 (17.4)	3 (10.7)	0.52
Baseline mRSS, median (IQR)	16.5 (10 - 24)	18 (10 - 24)	13 (4.8 – 20.5)	0.87
mRSS at 1 year, median (IQR)	10 (5 - 16)	10 (5 – 13)	10.5 (4.8 – 20.3)	0.56
ΔmRSS (Change), median (IQR)	-2.5 (-8 - 0)	-6.5 (-11.8 - -0.3)	-0.5 (-0.25 - 0)	0.003
Raynaud, n (%)	69 (93.2)	43 (93.4)	26 (92.9)	>0.99
Skin telangiectasia, n (%)	30 (40.5)	22 (47.8)	8 (26.6)	0.10
Nail-fold capillary abnormalities, n (%)	38 (50.0)	23 (50)	14 (50)	>0.99
Skin calcinosis, n (%)	5 (5.4)	4 (8.7)	0 (0)	0.29
Digital ulcers, n (%)	12 (16.2)	8 (17.4)	4 (14.3)	>0.99
ILD, n (%)	33 (44.6)	20 (43.4)	13 (46.4)	>0.80
PAH, n (%)	4 (5.4)	2 (4.3)	2 (7.1)	>0.63
Renal crisis, n (%)	5 (6.8)	3 (6.5)	2 (7.1)	>0.99
Synovitis, n (%)	6 (8.1)	4 (8.7)	2 (7.1)	>0.99
Myositis, n (%)	4 (5.4)	3 (6.5)	1 (3.6)	>0.99
Baseline FVC, % of predicted, mean (SD)	90.6 (18.1)	92.5 (19.5)	87.2 (14.7)	0.13
Baseline DLCO, % of predicted, mean (SD)	78.3 (22.4)	81.1 (22.3)	74.2 (18.6)	0.13
Immunosuppressive treatment, n (%)	39 (52.7)	27 (58.7)	12 (42.9)	0.19
Glucocorticoid use, n (%)	7 (9.4)	4 (8.7)	3 (10.7)	>0.99
sCD13, mean (SD), ng/mL	425.6 (92.9)	480.0 (72.8)	336.0 (34.5)	<0.001

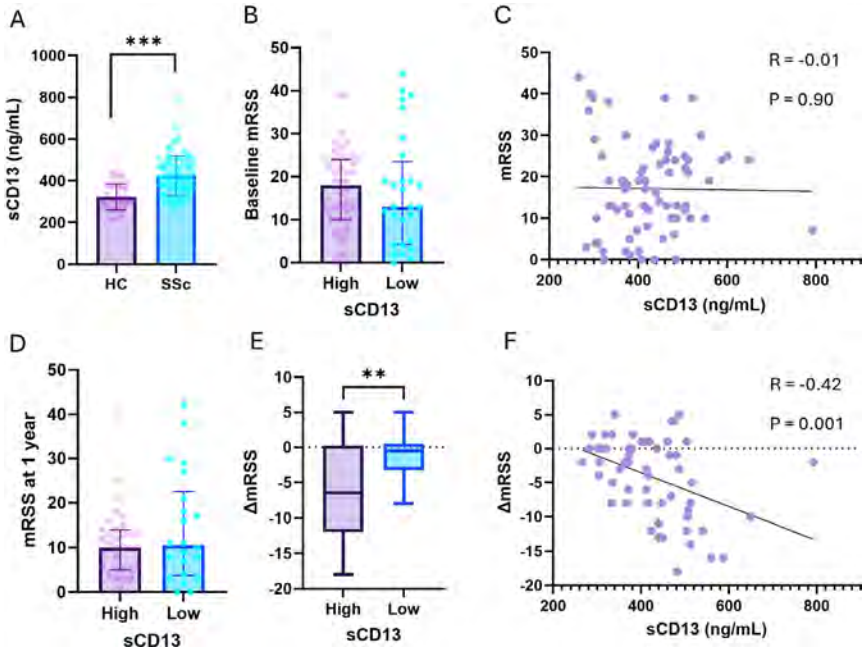


Figure 1. Comparison of mRSS changes between High and Low sCD13 groups in SSc patients within 3 years of disease onset. (A) Plasma sCD13 levels were significantly higher in SSc patients within 3 years of disease onset compared to HC. (B) No significant difference in baseline mRSS was observed between the high and low sCD13 groups. (C) No significant correlation was observed between plasma sCD13 levels and baseline mRSS. (D) mRSS measured one year follow up visit showed no significant difference between the high and low sCD13 groups. (E) The change in mRSS (ΔmRSS) over one year showed a significant decrease in the high sCD13 group. (F) A significant negative correlation was observed between ΔmRSS over one year and plasma sCD13 levels. Results are expressed as mean ± SD or median [IQR]. *P < 0.05, **P < 0.01, ***P < 0.001. sCD13, soluble CD13; HC, healthy controls; SSc, systemic sclerosis; mRSS, modified Rodnan skin score; SD, standard deviation; IQR, interquartile range.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

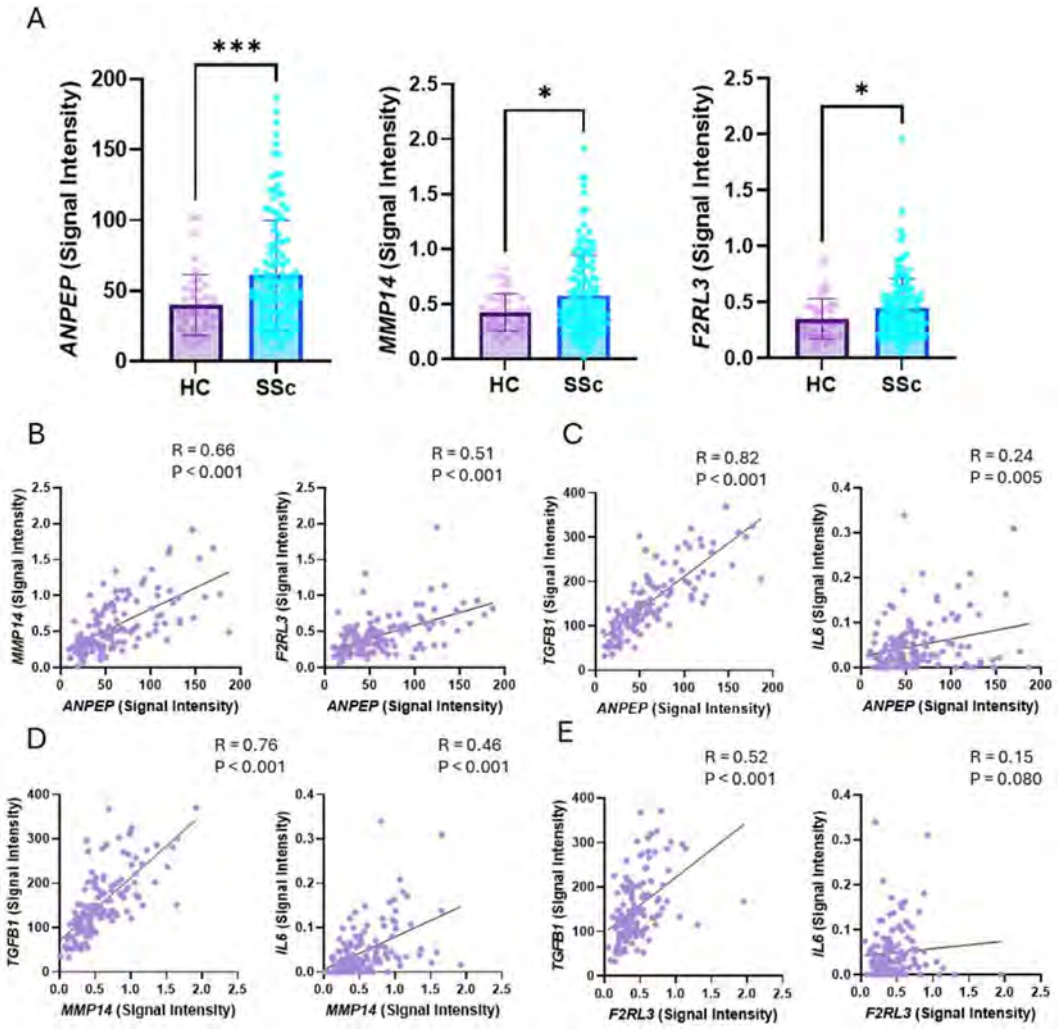


Figure 2. Evaluation of CD13, MMP14 and PAR4 expression in SSc patients and healthy controls (A) Expression levels of ANPEP, MMP14 and F2RL3 were significantly higher in SSc patients compared to healthy controls. (B) ANPEP expression levels were significantly and positively associated with MMP14 and F2RL3. (C) ANPEP, MMP14 and F2RL3 expression levels showed a significant correlation with TGFB1 and IL6, key cytokines involved in fibrosis and inflammation in SSc, although the correlation between F2RL3 and IL6 was not statistically significant (P = 0.08). Results are expressed as mean ± SD. *P < 0.05, **P < 0.01, ***P < 0.001. Significance was determined by (A) Mann-Whitney test and (B-C) Spearman correlation. SSc, systemic sclerosis.

Conclusion: Our study showed that the increased plasma sCD13 levels in patients with SSc did not correlate with the clinical features of the disease. Given that sCD13 is elevated in dcSSc patients and that it promotes myofibroblast transformation in SSc skin, these results suggest that tissue-level sCD13 might be more significant than systemic levels. In addition, MMP14 and CD13 expression on blood cells, potentially enhanced by TGF-β and IL-6, could influence circulating CD13 levels in SSc.

1. Muraoka S et al. Targeting CD13/Aminopeptidase N as a Novel Therapeutic Approach for Scleroderma Fibrosis. Arthritis Rheumatol. 2025;77(1):80-91.

Disclosure: Y. Ikari: None; **P. Dey**: None; **J. St. Clair**: None; **A. Webber**: None; **C. Foster**: None; **Y. Chen**: None; **R. Ali**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **D. Fox**: None; **P. Tsou**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1591

Novel autoantibodies in patients with systemic sclerosis and gastrointestinal dysfunction provide insight into disease pathogenesis

Zsuzsanna McMahan[1], Claudia Pedroza[2], Katie Lee[3], Bingrui Chen[3], Ami Shah[4], Jody Hooper[5], Srinivas Puttapaka[6], Livia Casciola-Rosen[7] and Subhash Kulkarni[8], [1]UT Health Houston, Houston, TX, [2]UTHealth Houston Institute for Clinical Research & Learning Health Care, Texas, TX, [3]UTHealth Houston, Houston, TX, [4]Johns Hopkins Rheumatology, Baltimore, MD, [5]Stanford University, Stanford, CA, [6]BIDMC/Harvard, Boston, MA, [7]Johns Hopkins University, Baltimore, MD, [8]BIDMC, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1553–1591) Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Gastrointestinal (GI) dysfunction is common and often debilitating in systemic sclerosis (SSc). Though it affects most patients, mechanisms are poorly understood and biomarkers for risk stratification and disease activity are limited. Here we sought to identify novel autoantibodies in patients with SSc GI disease and to determine whether they provide insight into clinical phenotype and disease mechanism.

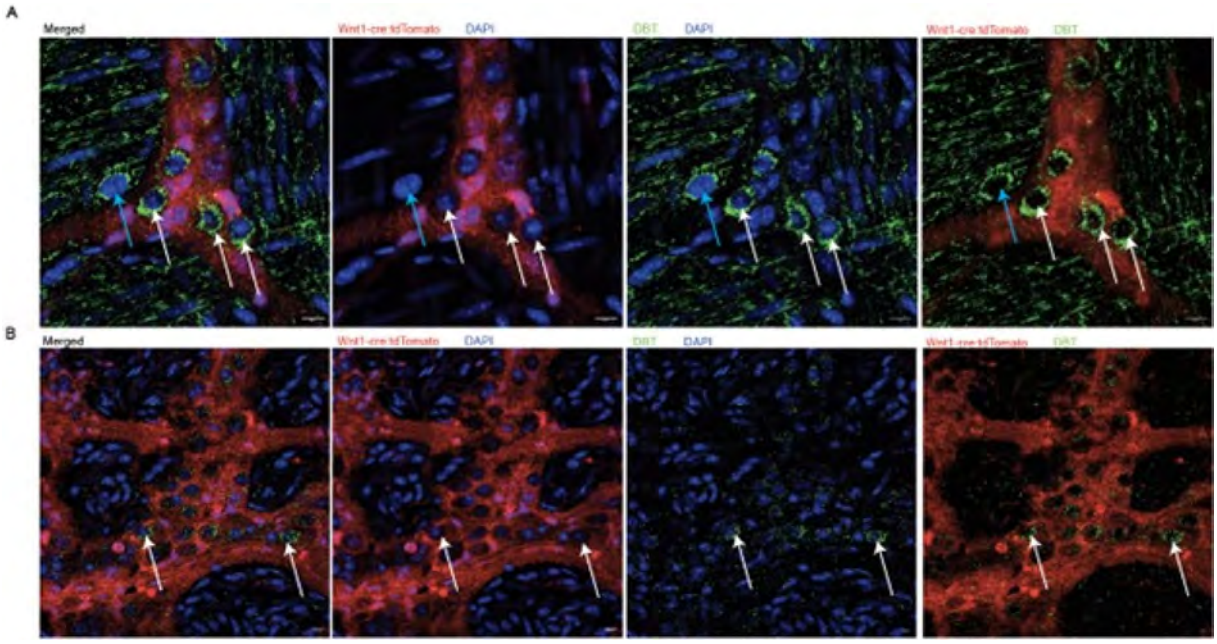


Figure 1: DBT staining of murine LMMP. Mitochondria-specific enzyme DBT is expressed abundantly by MENs in the adult ENS. Immunostaining adult murine (A) small intestinal and (B) colonic longitudinal muscle – containing myenteric plexus (LM-MP) tissues from a neural crest lineage fate mapping mouse model Wnt1-cre:tdTomato, where tdTomato (red) labels all derivatives of the neural crest, with commercially available anti-DBT antibodies (green), which labels the mitochondria-specific Dihydrolipoamide Branched Chain Transacylase (DBT) enzyme (also known as the E2 subunit of the branched-chain alpha-keto acid dehydrogenase complex (BCKD)) shows that DBT protein is localized specifically in the tdTomato-negative non-neural crest cells of the tissue. Mesoderm-derived enteric neurons (MENs, white arrows) in (A) small intestinal LM-MP show abundant expression of DBT, while (B) colonic MENs show relatively reduced abundance of MENs. Nuclei are labeled with DAPI (blue). Scale bar = 10 μm.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

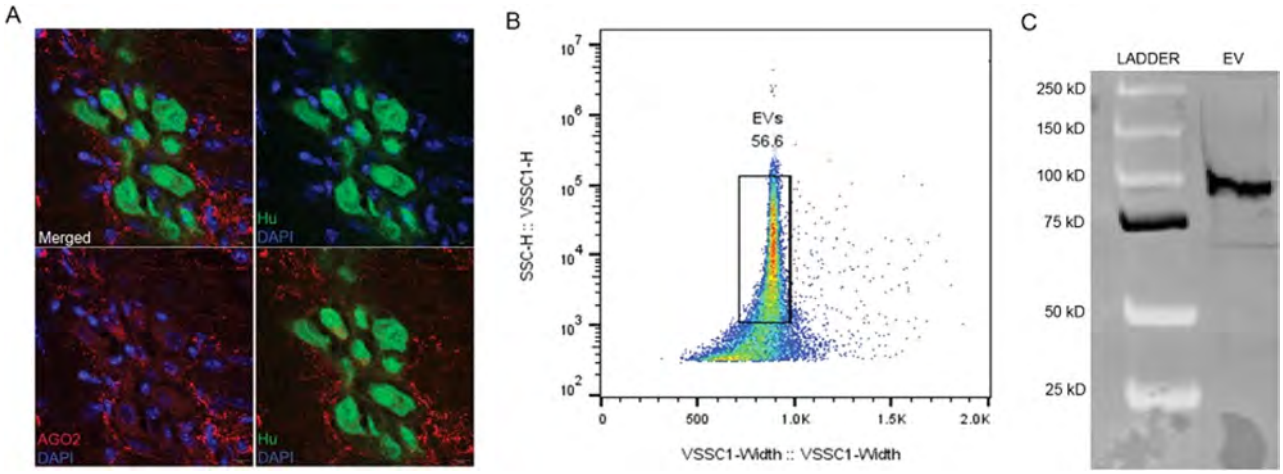


Figure 2: AGO staining of LMMP. Small intestinal ENS releases AGO2-containing extracellular vesicles (EVs). (A) Immunostaining adult murine small intestinal longitudinal muscle – containing myenteric plexus (LM-MP) tissues with antibodies against neuronal marker Hu (green) and EV-marker AGO2 (Argonaut 2, red) shows presence of AGO2 around the Hu-labeled neurons, showing that the neurons release AGO2. (B) Short-term cultured preparations of adult murine small intestinal LM-MP release significant amounts of EVs in the culture media, as assessed by nanoparticle-detecting flow cytometry. (C) Western blot of isolated EVs from cultured LM-MP (shown in (B)) when assayed for the presence of AGO2 (estimated size of 99 kD) using anti-AGO2 antibodies shows a strong and specific band around 100kD providing evidence that small intestinal ENS releases abundant AGO2-containing EVs.

Methods: Sera from patients from the Gastrointestinal Assessment Protocol (GAP), a subcohort of a large Scleroderma Research Registry, were screened for novel autoantibodies. Immunoprecipitations performed with murine myenteric plexus lysates were on-bead digested, and autoantigens were identified by mass spectrometry and then validated. Prevalence was determined, and clinical features associated with the validated autoantibodies were identified using both an all-comers cohort (n=179) and the GAP cohort (n=140). We also examined whether the identified specificities, anti-AGO and anti-DBT antibodies, associated with other known SSc antibodies using an unbiased clustering analysis. The expression of AGO2 and DBT in murine GI tract tissue was then examined by immunohistochemistry. Extracellular vesicles released by ENS and associated cells were captured from cultured longitudinal muscles – containing myenteric plexus (LM-MP) tissues, and their size, abundance, and presence of AGO protein as EV-associated cargo was ascertained by flow cytometry and western blot, respectively.

Results: Using sera from SSc patients with GI dysmotility, we identified AGO1, AGO2, and DBT as candidate autoantigens, which were validated in subsequent cohorts. Anti-AGO antibodies were present in 9.4% (17/179) and anti-DBT in < 1% (1/178) of patients in the all-comers cohort, but absent in healthy controls (0/38 for anti-AGO, 0/36 for anti-DBT). Anti-AGO–positive patients had significantly more GI-related social problems (p=0.02), stomachaches (p=0.005), bloating

Table 1. Gastrointestinal symptom severity is associated with anti-Ago2 antibodies in the all-comers cohort

UCLA GIT 2.0 domain and subdomain	Anti-Ago2 positive	Anti-Ago2 negative	p-value
Reflux (total score)	0.8 (0, 1.9)	0.4 (0, 0.8)	0.45
Acid reflux	2 (0, 2)	0 (0, 1)	0.07
Distention (total score)	1.3 (0.5, 2)	0.5 (0, 1.3)	0.20
Bloating	2 (1, 2)	1 (0, 1)	0.06
Soilage (total score)	0 (0, 1)	0 (0, 0)	0.43
Diarrhea (total score)	0.5 (0, 1.5)	0 (0, 0.5)	0.13
Loose stools	1 (0, 2.5)	0 (0, 1)	**0.04**
Social functioning (total score)	0.3 (0, 1)	0 (0, 0.3)	0.08
Stomachache or pain	0 (0, 1)	0 (0, 0)	**<0.01**
Bloated sensation	1 (0, 2)	0 (0, 1)	**0.02**
Emotional well-being (total score)	0.3 (0, 0.9)	0 (0, 0.3)	0.08
Feel worried or anxious about your bowel problems	1 (0, 2)	0 (0, 1)	**0.01**
Fear of not finding a bathroom	0 (0, 1)	0 (0, 0)	**0.02**
Constipation (total score)	0.8 (0, 1.6)	0.1 (0, 0.8)	0.14
Harder time emptying bowels	1 (0, 2.5)	0 (0, 1)	0.06
Hard stools	0.5 (0, 2)	0 (0, 1)	0.07
Total GIT score	0.8 (0.1, 1.1)	0.3 (0.1, 0.6)	0.09

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(p=0.02), and emotional distress including worry (p=0.012) and fear (p=0.02). In a GI-enriched validation cohort, anti-AGO antibodies were found in 11% (15/140), with higher titers correlating with more severe constipation (p=0.03) and bloating (p=0.02). Conversely, anti-DBT antibodies, present in 3% (4/126), were associated with significantly less constipation (p=0.02). Immunofluorescence demonstrated that anti-DBT antibodies specifically target mesodermal-derived enteric neurons and smooth muscle, while anti-AGO antibodies may target AGO2-containing extracellular vesicles (EV's) released from the gut.

Conclusion: Antibodies in patients with SSc may provide insight into distinct clinical phenotypes and disease mechanism(s). Understanding the targets of the immune response and identifying immune biomarkers may shed light on important mechanisms of disease and novel therapies.

Disclosure: Z. McMahan: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **C. Pedroza**: Medicem, 5; **K. Lee**: None; **B. Chen**: None; **A. Shah**: None; **J. Hooper**: None; **S. Puttapaka**: None; **L. Casciola-Rosen**: None; **S. Kulkarni**: None.

Abstract Number: 1592

Mepolizumab to Benralizumab Switch in Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Adrien Cottu[1], Irene Mattioli[2], Xavier Puéchal[3], Loic Guillevin[4], Mathieu Groh[5], Camille Taillé[6], Maxime Samson[7], Pascal Cathébras[8], Halil Yildiz[9], Grégory Pugnet[10], Stéphane Jouneau[11], Marie-Charlotte Besse[12], François Lifermann[13], Jean-Philippe Martellosio[14], Laurent Guilleminault[15], Colas Tcherakian[16], Yann Nguyen[17], Claire Demoreuil[18], Philippe Guilpain[19], Giacomo Emmi[20] and Benjamin Terrier[21], [1]Internal medicine departement, Cochin Hospital, Paris, France, [2]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, [3]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [4]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [5]Hôpital Foch, Suresnes, France, [6]Bichat hospital, APHP, Paris, France, [7]CHU Dijon Bourgogne, Dijon, France, [8]Internal medicine department, CHU St-Etienne, Saint-Etienne, France, [9]Internal medicine department, Saint-Luc, Saint-Luc, France, [10]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France, [11]Respiratory Medicine, Université de Rennes 1, CHU Pontchaillou, Rennes, France, [12]Tours University Hospital, 37000 tours, Ile-de-France, France, [13]Internal Medicine, CH de Dax, Dax, France, [14]Internal medicine department, CHU Poitiers, Poitiers, France, [15]CHU Toulouse, Toulouse University, Toulouse, France, [16]Pneumology department, Foch, Suresnes, France, [17]Department of Internal Medicine, Beaujon Hospital, AP-HP Nord, Université Paris Cité, Clichy, France, Clichy, France, [18]Internal medicine department, Brest CHU, Brest, France, [19]Internal medicine department, CHU Montpellier, Montpellier, France, [20]Department of Medical, Surgery and Health Sciences, University of Trieste, Italy and Clinical Medicine and Rheumatology Unit, Cattinara University Hospital, Trieste, Italy, Trieste, Italy, [21]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Glucocorticoid (GC)-dependent asthma and ENT exacerbations may persist in more than half of patients with eosinophilic granulomatosis with polyangiitis (EGPA). Mepolizumab and benralizumab, monoclonal antibodies targeting IL-5 and its receptor, respectively, have demonstrated comparable remission rates in patients with relapsing or refractory EGPA. As mepolizumab was the first approved agent for the treatment of EGPA, a switch to benralizumab is often considered in case of failure of mepolizumab. We aimed to describe the use of benralizumab after mepolizumab failure in patients with refractory EGPA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective multicenter European study of patients with EGPA according to ACR/EULAR classification criteria 2022 who received benralizumab after mepolizumab for inadequate disease control. Complete response was defined as no disease activity (BVAS=0) and a prednisone-equivalent dose ≤4 mg/day, and partial response as no disease activity and a prednisone-equivalent dose >4 mg/day.

Results: Fifty-nine patients (median age 55 years [IQR 47; 63]) were included. ANCA was positive in 18 (31%) patients at the time of EGPA diagnosis. Mepolizumab was initiated at a median of 4 years [1; 9] after diagnosis, mainly for uncontrolled asthma (100%) and/or ENT manifestations (61%). The majority of patients received a dose of 100 mg/month (76%), while 14 (24%) received a dose of 300 mg/month. Mepolizumab was discontinued due to lack of efficacy or partial efficacy in 27 (46%) and 25 (42%) patients, respectively, while 7 patients (12%) experienced a respiratory relapse after an initial complete response.

Benralizumab was started a median of 15 months [11; 24] after starting mepolizumab at a dose of 30 mg every 8 weeks in all but one patient. The median follow-up for benralizumab was 33 months [23; 43]. Complete response was achieved in 23 patients (39%) and partial response in 14 patients (24%). However, only 11 of the 23 patients maintained a complete response at the last follow-up. GCs were discontinued in 35 patients (59%) but restarted in 11 (31%). Six patients (10%) experienced a relapse of vasculitis during follow-up, a median of 25 months [16; 25] after starting benralizumab.

Primary refractoriness to mepolizumab to mepolizumab (OR 4.46, 95% CI 1.44–13.83) and the presence of ENT manifestations at the time of benralizumab initiation (OR 4.00, 95% CI 1.22–13.13) were associated with lack of response to benralizumab. FEV1 and eosinophil count at the start of benralizumab were not associated with response.

Conclusion: After mepolizumab failure, switching to benralizumab provides a complete response and GC withdrawal in one third of patients. However, this efficacy declines over time in half of the patients. These data suggest that targeting a pathway other than IL-5 may be more effective in patients who do not respond to mepolizumab.

Disclosure: A. Cottu: None; **I. Mattioli**: None; **X. Puéchal**: Roche, 5; **L. Guillevin**: Roche, 5; **M. Groh**: None; **C. Taillé**: None; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2; **P. Cathébras**: None; **H. Yildiz**: None; **G. Pugnet**: None; **S. Jouneau**: Roche, 5; **M. Besse**: None; **F. Lifermann**: None; **J. Martellosio**: None; **L. Guilleminault**: None; **C. Tcherakian**: None; **Y. Nguyen**: None; **C. Demoreuil**: None; **P. Guilpain**: None; **G. Emmi**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 1593

Comparison of rituximab induction and maintenance regimens in ANCA-associated vasculitis: PK/PD modelling approach in real-world patients

Blaise Pasquiers[1], Benoit Blanchet[2], Xavier Puéchal[3], Xavier Declèves[1], Pascal Cohen[4], Claire Goulvestre[1], Marion Casadevall[1], Ines Benhabiles[1], Michel Vidal[1], David Ternant[1], **Benjamin Terrier**[5] and Alicja Puszkiel[6], [1]Hopital Cochin, Paris, France, [2]National Referral Centre for Rare Autoimmune and Systemic Diseases, Hôpital Cochin, Paris, France, [3]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [4]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [5]Cochin Hospital, Paris, France, [6]Cochin Hospital, Paris

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: For the treatment of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), rituximab (RTX) may be given as a 4-dose regimen (375 mg/m^2 weekly for 4 weeks) or a 2-dose regimen (1000 mg on day 0 and 14, D0-D14) to induce remission. Once the remission is achieved, RTX is administered in the maintenance phase (starting 4 to 6 months after the first induction dose) at 500 mg every 6 months (Q6M) for 18 months or at 1000 mg every 4 months (Q4M) for 20 months. In the absence of direct comparison of these dosing regimens, there is a need to better define the optimal regimen as well as the duration of the maintenance phase in order to improve the risk-benefit ratio while reducing treatment costs. We aimed to provide pharmacokinetic-pharmacodynamic (PK/PD) rationale for the selection of optimal induction and maintenance dosing regimens in AAV using a population modeling approach based on longitudinal data (RTX concentrations, MPO-ANCA, PR3-ANCA and gammaglobulins) from a real-world cohort.

Methods: A total of 121 patients with 296 plasma RTX concentrations (99 and 197 in the induction and maintenance phases, respectively), 439 ANCA levels (215 in the induction, 224 in the maintenance) and 559 gammaglobulin levels (249 in the induction, 310 in the maintenance) were included in the analysis. The modeling of the effect of plasma RTX concentrations on gammaglobulin and ANCA levels over time was preformed using non-linear mixed effects models in Monolix Suite. Simulations of induction (375 mg/m^2 weekly for 4 weeks, 1000 mg D0-D14) and maintenance regimens (500 mg every 6 months [Q6M], 500 mg Q6M starting at month 4, 1000 mg Q4M, 500 mg Q4M) were performed in 1000 virtual patients with the final PK/PD model. Dosing regimens were compared based on the percentage of patients in serological remission and at risk of hypogammaglobulinemia. In addition, a utility score was calculated taking into account both the expected gain in efficacy and the increased risk of adverse events with increased drug exposure.

Results: The final PK/PD model satisfactorily described the relationship between RTX concentrations, gammaglobulins and ANCA levels over time. Simulations showed that both induction regimens resulted in a similar number of patients achieving serological remission and hypogammaglobulinemia at 6 months (Table 1). In the maintenance phase, increasing the dose (1000 mg) or frequency of administration (Q4M versus Q6M) was associated with a higher number of patients with serological remission at month 24 but also with higher risk of hypogammaglobulinemia (Table 2). Starting the maintenance phase earlier, i.e. 500 mg Q6M from month 4 versus from month 6, was associated with a higher number of patients with negative MPO-ANCA and PR3-ANCA at month 24 (68% versus 59% for MPO-ANCA and 58% versus 46% for PR3-ANCA, respectively). Based on the benefit-risk ratio, both 500 mg Q6M and 500 mg Q4M regimens appear to be optimal for maintenance therapy.

Table 1.

Table 1. Comparison of rituximab induction regimens.

Time after first induction dose	Percentage of patients with MPO-ANCA < 20 U/mL		Percentage of patients with PR3-ANCA < 20 U/mL		Percentage of patients with gammaglobulins < 6 g/L		Median plasma rituximab concentration (mg/L) (10^{th}-90^{th} percentile)	
	375 mg/m^2 Q1W	1000 mg D0–D14	375 mg/m^2 Q1W	1000 mg D0–D14	375 mg/m^2 Q1W	1000 mg D0–D14	375 mg/m^2 Q1W	1000 mg D0–D14
4 months	45	50	41	38	81	75	38.5 (7.94, 101)	25.4 (5.32, 67.9)
6 months	50	55	46	42	49	43	10.3 (<1.0, 46.1)	6.78 (<1.0, 30.0)

MPO-ANCA, myeloperoxidase antineutrophil cytoplasmic antibodies; PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibodies; D0, day 0; D14, day 14; Q1W, every week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2.

Table 2. Comparison of rituximab maintenance regimens.

	500 mg Q6M (MAINRITSAN regimen)	500 mg Q6M, start at month 4	500 mg Q4W	1000 mg Q4W (RITAZAREM regimen)
Median rituximab $C_{trough,ss}$ (mg/L) (10^{th}, 90^{th} percentile)[a]	1.53 (<1.0, 8.16)	1.61 (<1.0, 8.54)	5.77 (1.03, 19.2)	11.1 (1.81, 40.3)
Percentage of patients with rituximab plasma concentration < 4 mg/L at month 3 after the 1st maintenance dose	16	13	14	6.2
Percentage of patients with MPO-ANCA < 20 U/mL				
12 months	52	62	67	67
24 months	59	68	75	79
Percentage of patients with PR3-ANCA < 20 U/mL				
12 months	49	55	56	65
24 months	46	58	65	77
Percentage of patients with gammaglobulins < 6 g/L				
Before 3rd cycle[b]	18	19	38	50
At the end of treatment[c]	17	19	20	28

MPO-ANCA, myeloperoxidase antineutrophil cytoplasmic antibodies; PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibodies; Q4W, every 4 months; Q6W, every 6 months.

[a] $C_{trough,ss}$ was extracted at month 20 for 500 mg Q4M and 1000 Q4M regimens, at month 22 for 500 mg Q6M start at 4 month regimen and at month 24 for 500 mg Q6M regimen

[b] % of patients with hypogammaglobulinemia was extracted at month 12 for 500 QM4 and 1000 mg Q4M regimens, at month 16 for 500 mg Q6M start at month 4 and at month 18 for 500 mg Q6M

[c] % of patients with hypogammaglobulinemia was extracted at month 26 for 500 QM4 and 1000 mg Q4M regimens, at month 28 for 500 mg Q6M start at month 4 and at month 30 for 500 mg Q6M

Conclusion: This first PK/PD study may inform clinical decisions regarding the choice between different rituximab induction and maintenance regimens in AAV patients in daily practice.

Disclosure: B. Pasquiers: None; **B. Blanchet**: None; **X. Puéchal**: Roche, 5; **X. Declèves**: None; **P. Cohen**: Roche, 5; **C. Goulvestre**: None; **M. Casadevall**: None; **I. Benhabiles**: None; **M. Vidal**: None; **D. Ternant**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **A. Puszkiel**: None.

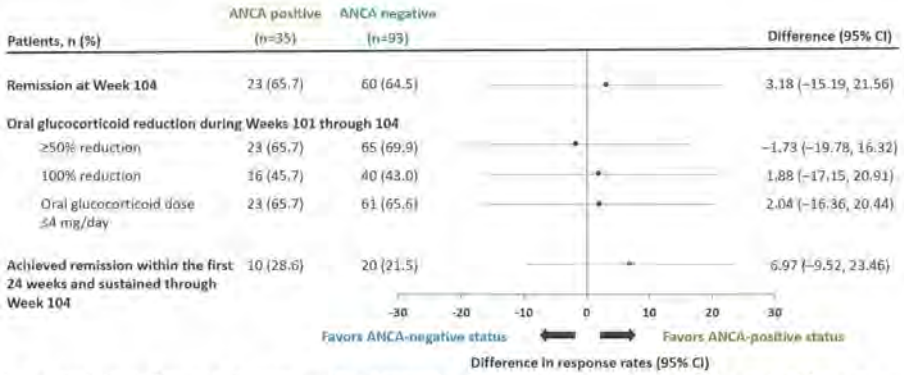
Abstract Number: 1594

Two-Year Efficacy of Anti-Interleukin-5/Receptor Therapies According to Anti-Neutrophil Cytoplasmic Antibodies Status in Patients with Eosinophilic Granulomatosis with Polyangiitis

Benjamin Terrier[1], David Jayne[2], Bernhard Hellmich[3], Nancy Agmon-Levin[4], Parameswaran Nair[5], Lena Börjesson Sjö[6], Priya Jain[7], Aadarsh Lal[8], Sofia Necander[9], Claire Walton[10], Peter Merkel[11] and Michael Wechsler[12], [1]Cochin Hospital, Paris, France, [2]University of Cambridge, Cambridge, United Kingdom, [3]Klinik für Innere Medizin, Rheumatologie, Pneumologie, Nephrologie und Diabetologie, Medius Kliniken, Akademisches Lehrkrankenhaus der Universität Tübingen, Kirchheim unter Teck, Germany, [4]Clinical Immunology, Angioedema and Allergy, Sheba Medical Center, Ramat Gan, Israel, [5]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, ON, Canada, [6]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca,, Gothenburg, Sweden, [7]BioPharmaceuticals Medical, AstraZeneca, Cambridge, United Kingdom, [8]Respiratory & Immunology, AstraZeneca, Bengaluru, Karnataka, India, [9]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [10]Late-Stage Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom, [11]University of Pennsylvania, Philadelphia, PA, [12]Department of Medicine, National Jewish Health, Denver

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Efficacy endpoints by ANCA status



Rates and the difference in rates were estimated using marginal standardization method from a logistic regression model. For BVAS = 0, covariates included ANCA-positive status, baseline OGC dose, and baseline BVAS. For others, the covariates included ANCA-positive status, baseline OGC dose, baseline BVAS, and region.

Remission was defined as BVAS = 0 and OGC dose ≤4 mg/day (patients achieving remission who had, at any subsequent visit, a BVAS = 1 that did not require an increase in OGC dose >4 mg/day or any other significant clinical intervention/investigation, were considered to be in continued remission).

BVAS, Birmingham Vasculitis Activity Score; CI, confidence interval; OGC, oral glucocorticoids.

Table 1. Baseline characteristics by ANCA status of patients with eosinophilic granulomatosis with polyangiitis in the MANDARA open-label extension phase

Characteristic	ANCA-positive status (n=35)	ANCA-negative status (n=93)
Age, years		
Mean (SD)	56.4 (13.16)	51.4 (14.09)
Female, n (%)	15 (42.9)	62 (66.7)
Time since diagnosis of EGPA, years		
Mean (SD)	4.25 (4.271)	5.68 (6.153)
Min, max	0.6, 15.0	0.6, 38.0
EGPA disease characteristics (ever), n (%)		
Asthma	35 (100.0)	93 (100.0)
Eosinophilia	35 (100.0)	93 (100.0)
Biopsy evidence of eosinophilic vasculitis/inflammation*	14 (40.0)	36 (38.7)
Neuropathy †	24 (68.6)	52 (55.9)
Nonfixed pulmonary infiltrates	23 (65.7)	61 (65.6)
Sino-nasal abnormality	30 (85.7)	87 (93.5)
Cardiomyopathy ‡	7 (20.0)	22 (23.7)
Glomerulonephritis	3 (8.6)	1 (1.1)
Palpable purpura	7 (20.0)	10 (10.8)
Dose of prednisolone or prednisone, mg/day		
Mean (SD)	10.39 (4.485)	11.37 (5.675)
Median (min, max)	10.0 (5.0, 25.0)	10.0 (7.5, 40.0)
Immunosuppressive therapy, n (%)	12 (34.3)	35 (37.6)
Birmingham Vasculitis Activity Score (BVAS)		
Mean (SD)	2.1 (3.53)	1.9 (2.97)
>0, n (%)	19 (54.3)	40 (43.0)
=0, n (%)	16 (45.7)	53 (57.0)
Vasculitis Damage Index (VDI)		
Mean (SD)	4.0 (1.52)	4.0 (1.79)
6-item Asthma Control Questionnaire (ACQ-6)		
Mean (SD)	1.44 (1.241)	1.19 (1.013)
≥1.5, n (%)	17 (48.6)	37 (39.8)
Sino-Nasal Outcomes Test 22 (SNOT-22) total score		
Mean (SD)	30.8 (23.17)	30.2 (20.12)

*A biopsy showing histopathological evidence of eosinophilic vasculitis, perivascular eosinophilic infiltration, or eosinophil-rich granulomatous inflammation.
†Mono- or polyneuropathy (motor deficit or nerve conduction abnormality).
‡Established by echocardiography or magnetic resonance imaging.
EGPA, eosinophilic granulomatosis with polyangiitis; ANCA, anti-neutrophil cytoplasmic antibodies; max, maximum; min, minimum; SD, standard deviation

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The MANDARA trial (NCT04157348) demonstrated that after two years of anti-interleukin-5/receptor (anti-IL-5/R) therapy over 60% of patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA) without active organ- or life-threatening disease manifestations achieved remission, and more than 40% discontinued oral glucocorticoids (OGCs). The clinical presentation of EGPA may vary with anti-neutrophil cytoplasmic antibodies (ANCA) status. ANCA-positive patients may exhibit more "vasculitic" features, such as glomerulonephritis, while ANCA-negative patients may tend toward manifestations thought driven by eosinophilic inflammation, such as cardiomyopathy, although there is some overlap of symptoms. Consequently, both ANCA-positive and ANCA-negative patients with EGPA can present with a range of disease manifestations. This analysis evaluated the efficacy of anti-IL-5/R therapies in patients with EGPA according to ANCA status over the combined double-blind (DB) and first year of the ongoing open-label extension (OLE) period in MANDARA.

Methods: Following the 52-week DB period, eligible patients entered the OLE, where they either continued benralizumab or switched from mepolizumab to benralizumab. Remission was defined as Birmingham Vasculitis Activity Score (BVAS) = 0 and oral glucocorticoid (OGC) ≤4 mg/day. The OGC-sparing capacity of the anti-IL-5/R therapies was also assessed, as was disease activity (BVAS and Vasculitis Damage Index [VDI]). Data from both study phases were pooled to evaluate remission and OGC reduction over two years (up to Week 104) according to patients' ANCA status. ANCA-positive patients were defined as those positive for myeloperoxidase (MPO)-ANCA and/or proteinase 3 (PR3)-ANCA at study screening or with a historical record of ANCA-positivity.

Results: Of the 128 patients that entered the OLE 35 (27.3%) were ANCA-positive and 93 (72.7%) were ANCA-negative at the beginning of the double-blind period of the study (baseline). BVAS and VDI scores were similar between the ANCA-positive and -negative groups at baseline, whereas the proportion of patients who had an ACQ-6 score ≥1.5 was higher, and the time since diagnosis was shorter in the ANCA-positive versus -negative group (**Table 1**). At Week 104, the proportion of patients achieving remission was similar regardless of ANCA status (ANCA-positive: 65.7%, ANCA-negative: 64.5%; difference: 3.18; 95% confidence interval [CI]: –15.19, 21.56, p=0.7341) (**Figure 1**). During Weeks 101 through 104, 65.7% and 69.9% in the ANCA-positive and -negative groups, respectively, had a reduction in OGC dose of ≥50% from baseline, and 45.7% versus 43.0%, respectively, were fully withdrawn from OGCs. The proportion of patients with ≥1 relapse was similar between ANCA-positive (37.1%) and ANCA-negative groups (44.1%). Most patients had ≤3 or no relapses (ANCA-positive: 97.1%; ANCA-negative: 93.5%).

Conclusion: This analysis demonstrated that in patients without active organ- or life-threatening EGPA, historic or baseline ANCA status is not associated with response to treatment with anti-IL-5/R therapies.

Disclosure: B. Terrier: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **D. Jayne**: Alentis, 2, 11, Amgen, 2, 6, AstraZeneca, 1, 2, 6, Aurinia, 1, 11, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, ChemoCentryx, 2, 6, Chinook, 1, Chugai, 2, 6, CSL Vifor, 2, 6, Fate, 2, GlaxoSmithKlein(GSK), 2, 6, GSK, 1, Hansa, 1, Novartis, 1, 2, 6, Otsuka, 2, Roche, 2, 6, Takeda, 1, 2, 6; **B. Hellmich**: AbbVie, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Chugai, 2, 6, CSL Vifor, 2, 6, GlaxoSmithKlein(GSK), 2, 6, InflaRx, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Phadia, 2, 6, Roche, 2, 6; **N. Agmon-Levin**: Amgen, 2, AstraZeneca, 2, Boehringer, 2, Bristol Myers Squibb, 2, Chemocentryx, 2, Chugai, 2, GlaxoSmithKline, 2, Novartis, 2, Roche, 2, Takeda, 2, Vifor Pharma, 2; **P. Nair**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Arrowhead Pharmaceuticals, 6, AstraZeneca, 5, 6, CSL Behring, 6, Cyclomedica, 5, Equillium, 5, Foresee, 5, Genentech, 5, GlaxoSmithKlein(GSK), 6, Sanofi, 5, 6, Teva, 5; **L. Börjesson Sjö**: AstraZeneca, 3, 11; **P. Jain**: AstraZeneca, 3, 11; **A. Lal**: AstraZeneca, 3, 11; **S. Necander**: AstraZeneca, 3, 11; **C. Walton**: AstraZeneca, 3, 11; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **M. Wechsler**: allakos, 1, 2, 6, Amgen, 1, 2, 6, Areteia Therapeutics, 1, 2, 6, Arrowhead Pharmaceuticals, 1, 2, 6, AstraZeneca, 1, 2, 6, Avalo Therapeutics, 1, 2, 6, Celldex, 1, 2, 6, Connect Biopharma, 1, 2, 6, Eli Lilly, 1, 2, 6, Equillium, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Incyte, 1, 2, 6, Kinaset, 1, 2, 6, Kymera, 1, 2, 6, Merck, 1, 2, 6, Phylaxis, 1, 2, 6, Pulmatrix, 1, 2, 6, Rapt Therapeutics, 1, 2, 6, Recludix Pharma, 1, 2, 6, Regeneron Pharmaceuticals, 1, 2, 6, Roche/Genentech, 1, 2, 6, Sanofi/Genzyme, 1, 2, 6, Sentien, 1, 2, 6, Sound Biologics, 1, 2, 6, Tetherex Pharmaceuticals, 1, 2, 6, Uniquity Bio, 1, 2, 6, Upstream Bio, 1, 2, 6, Verona Pharma, 1, 2, 6, Zurabio, 1, 2, 6.

Abstract Number: 1595

Subcordal Stenosis is a Glucocorticoid-Responsive Manifestation of Granulomatosis with Polyangiitis

Brendan Denvir[1], Brendan Antiochos[2], Philip Seo[3] and Alexander Hillel[3], [1]Johns Hopkins, Baltimore, MD, [2]Johns Hopkins, CLARKSVILLE, MD, [3]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Subglottic stenosis (SGS) is a recognized manifestation of granulomatosis with polyangiitis (GPA), occurring in 8–23% of patients. A distinct variant, identified in this study, involves edema of the inferior true vocal folds, termed "subcordal stenosis." This pattern results in significant narrowing at a higher airway level than typical SGS, often extending inferiorly to involve the conventional subglottic region. Based on clinical observations, this pattern appears particularly responsive to glucocorticoid therapy. The objective of this study was to characterize the clinical presentation and treatment outcomes of subcordal stenosis and compare it to typical SGS associated with GPA. We hypothesized that patients with subcordal disease would require fewer dilations within two years of SGS diagnosis due to its glucocorticoid responsiveness.

Methods: Following IRB approval, we reviewed records of patients treated for SGS at the Johns Hopkins Vasculitis Center, identifying two groups: patients with subcordal involvement and those with typical SGS. Patients were excluded if they were procedurally treated for SGS before being seen at our institution. Subcordal cases were identified by searching laryngoscopy reports for "subcordal" and confirmed by otolaryngologist review as narrowing at the inferior true vocal folds (Figure 1).

Baseline demographic and clinical characteristics were obtained through chart review. Longitudinal data on immunosuppressive treatments (start and stop dates) and tracheal dilation procedures were also collected. The number of tracheal dilations at two years was compared between groups using the Wilcoxon rank-sum test. Time-to-event analyses were performed, and Kaplan-Meier curves were compared using the log-rank test. All statistical analyses were conducted using R.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

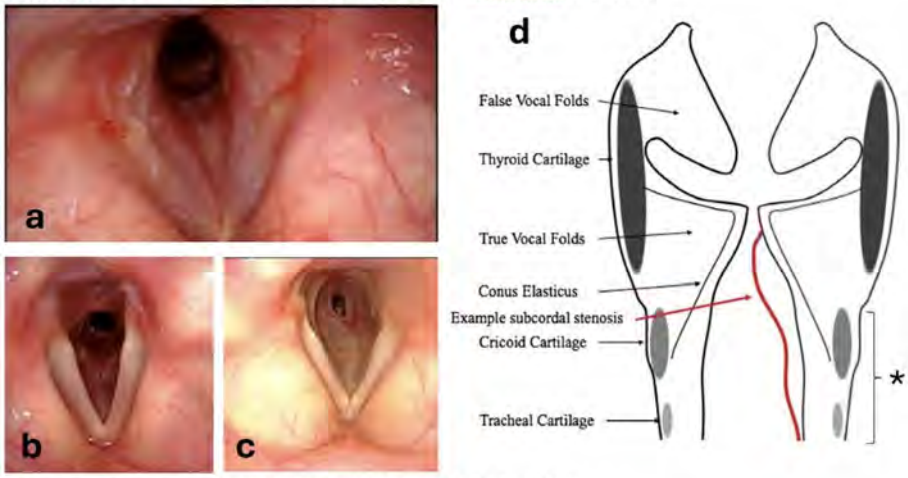
Table 1. Baseline demographic, clinical, and treatment characteristics, and outcome comparisons between SGS patients with and without subcordal involvement

	Subcordal Involvement n=11	No Subcordal Involvement n=38	p-value*
Demographics			
Age, mean (sd)	44.5 (12.3)	42.6 (15.3)	0.69
Female, n (%)	7 (63.6)	28 (73.7)	0.71
Male, n (%)	4 (36.3)	10 (26.3)	
Diagnosis			
GPA, n (%)	8 (72.7)	33 (86.8)	0.50
Severe	3 (27.3)	4 (10.5)	0.18
Non-severe	5 (45.5)	29 (76.3)	
ANCA positive	7 (63.6)	26 (68.4)	0.81
Idiopathic SGS, n (%)	3 (27.3)	5 (13.2)	
Airway Involvement			
Subglottic	5 (45.4)	38 (100)	-
Subcordal	11 (100)	0 (0)	-
Airway Symptoms, n (%)			
Dyspnea	9 (81.8)	29 (76.3)	1
Stridor	5 (45.5)	15 (39.5)	0.74
Cough	2 (18.2)	6 (15.8)	1
Dysphonia	5 (45.5)	12 (31.6)	0.48
Immunosuppression, n (%)			
Prednisone	10 (90.9)	27 (71.1)	0.41
Rituximab	3 (27.3)	13 (34.2)	1
Methotrexate	2 (18.2)	13 (34.2)	0.46
Azathioprine	3 (27.3)	4 (10.5)	0.12
Leflunomide	3 (27.2)	3 (7.9)	0.18
Cyclophosphamide	1 (9.1)	1 (2.6)	0.40
Mycophenolate mofetil	0 (0)	1 (2.6)	1
Outcomes at 2 Year Follow-up			
Tracheal Dilations, median (IQR)	0 (0-1)	1 (0-2.75)	0.049
Patients with 0 dilations, n (%)	6 (54.5)	11 (28.9)	0.23

*Statistical comparisons between groups were made using fisher's exact tests, t-tests and wilcoxon rank sum tests where appropriate.
Immunosuppression indicates medication patients were on in the first year after airway disease diagnosis

Results: Baseline characteristics of SGS patients with and without subcordal involvement are summarized in Table 1. Most patients in both groups had GPA diagnosed by rheumatologists. Five patients with subcordal disease also had typical subglottic involvement, while six had isolated subcordal disease. Among patients with subcordal involvement, 10 of 11 received

Figure 1. Representative laryngoscopic images of subglottic stenosis with and without subcordal involvement and animated depiction of subcordal stenosis.



Panel A: Subcordal stenosis with swelling and erythema of the inferior TVF.
Panel B: Typical SGS-GPA appearance with stenosis starting distal to the inferior TVF.
Panel C: Typical iSGS with 80% stenosis distal to the inferior TVF.
Panel D: Animated depiction of laryngeal anatomy highlighting the area of subcordal stenosis. The asterisk (*) indicates the typical level of subglottic stenosis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

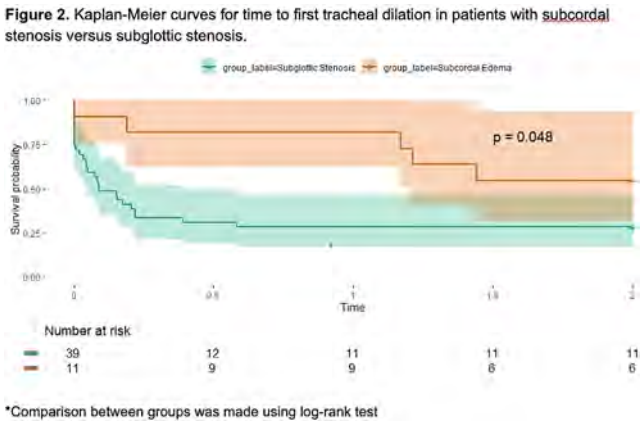


Figure 2. Kaplan-Meier curves for time to first tracheal dilation in patients with subcordal stenosis versus subglottic stenosis.

*Comparison between groups was made using log-rank test

prednisone at the time of SGS diagnosis. Patients with subcordal disease underwent fewer dilations within two years compared to those without subcordal involvement (median 0 vs. 1 dilation, p = 0.05, Table 1). Kaplan-Meier analysis showed that patients with subcordal involvement had a significantly longer time to first dilation, with a median of 792 days compared to 44 days in those without subcordal disease (p = 0.048, Figure 2).

Conclusion: Among patients with SGS seen at our vasculitis center (most of whom have GPA), those with subcordal involvement exhibit a reduced need for tracheal dilation and a longer interval before first dilation compared to patients without subcordal disease. These findings likely reflect greater corticosteroid responsiveness in patients with subcordal airway involvement.

Disclosure: B. Denvir: None; **B. Antiochos**: None; **P. Seo**: None; **A. Hillel**: Airiver, Inc, 2.

Abstract Number: 1596

GPA-Associated Tracheobronchial Stenosis: Immunosuppressant Use and Dilation Frequency

Brendan Denvir[1], Alexander Hillel[2], Ami Shah[3], Ji Soo Kim[1], Philip Seo[2] and Brendan Antiochos[4], [1]Johns Hopkins, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins Rheumatology, Baltimore, MD, [4]Johns Hopkins, CLARKSVILLE, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Granulomatosis with polyangiitis (GPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis that affects all levels of the respiratory tract. Tracheobronchial stenosis (TBS) occurs in 8–23% of patients with GPA and may cause life-threatening airway compromise requiring repeated tracheal dilation. Despite advances in GPA treatment, TBS remains difficult to manage, with frequent relapses and high procedural burden. The objective of this study was to evaluate the relationship between observed immunosuppressant use and tracheal dilation frequency in patients with TBS-GPA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We queried our electronic health record for patients with GPA and TBS evaluated at Johns Hopkins Medical Institute between January 2003 and September 2024. Diagnoses were confirmed by retrospective chart review. Baseline demographic and clinical characteristics, immunosuppressant exposure, and tracheal dilation procedure dates were extracted. We performed longitudinal analyses using annual dilation count as our outcome measure, and time-varying binary indicators of immunosuppressant use as categorical predictor variables. Data from an example patient is depicted in Figure 1. A multivariate mixed effects Poisson regression model was used to assess the association between immunosuppressant exposures (rituximab, cyclophosphamide, methotrexate, azathioprine, leflunomide, and mycophenolate) and annual tracheal dilation count, adjusting for age, sex, years since TBS diagnosis, ANCA status (positive vs. negative), and GPA disease severity (non-severe vs. severe). A random intercept term was included to account for patient-level variability in dilation frequency.

Results: A total of 52 patients with tracheobronchial GPA were included in the analysis, with a mean follow-up duration of 9.9 years. Baseline clinical characteristics and immunosuppressant exposures are summarized in Table 1. In the adjusted mixed-effects Poisson regression model, patient-years on leflunomide were associated with a 68% lower incidence of tracheal dilations compared to periods off leflunomide (IRR 0.32, $p < 0.001$), while patient-years on rituximab were associated with a 40% lower incidence compared to periods off rituximab (IRR 0.57, $p = 0.021$) (Table 2). No statistically significant associations were observed for methotrexate, azathioprine, cyclophosphamide, or mycophenolate. Among other tested covariates, time since TBS diagnosis and age over 40 were also associated with lower dilation frequency (Table 2).

Table 1. Baseline demographic, clinical, and treatment characteristics of patients with tracheobronchial GPA.

	Overall (n = 52)
Sex, n (%)	
Male	17 (32.7)
Female	35 (67.3)
Age	
Age, mean (sd)	36.8 (16.6)
Age over 40 at TBS diagnosis, n (%)	24 (46.2)
Serologies*, n (%)	
ANCA positive	41 (78.8)
PR3-ANCA	31 (59.6)
MPO-ANCA	10 (19.2)
GPA Severity	
Severe	10 (19.2)
Non severe	42 (80.8)
Organ Involvement†, n (%)	
Sinonasal	47 (90.4)
Pulmonary	28 (53.8)
Renal	9 (17.3)
Neurologic	2 (3.8)
Ophthalmologic	6 (11.5)
Skin/Mucous membranes	17 (32.7)
General‡	22 (43.3)
Medication¶, n (%)	
Rituximab	30 (57.7)
Methotrexate	22 (42.3)
Leflunomide	16 (30.8)
Azathioprine	13 (25.0)
Cyclophosphamide	5 (9.6)
Mycophenolate mofetil	4 (7.7)

* PR3-ANCA positivity was defined as either a positive anti-PR3 antibody by ELISA or a positive c-ANCA by indirect immunofluorescence. MPO-ANCA positivity was defined as either a positive anti-MPO antibody or a positive p-ANCA.
† Organ involvement adapted from Birmingham Vasculitis Activity Score and Vasculitis Damage Index. ‡ General = arthralgia, arthritis, myalgia, fever (> 38C), or weight loss (> 2 kg).
¶ Medications received at any point during the follow-up period.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Incidence rate ratios estimated from univariate models and multivariate mixed effects Poisson regression model of tracheal dilation incidence

	Univariate Models		Multivariate model	
	IRR (95% CI)	p-value	IRR (95% CI)	p-value*
Immunosuppressants				
Rituximab	0.87 (0.64, 1.17)	0.343	0.57 (0.37, 0.96)	0.021
Methotrexate	0.73 (0.52, 1.04)	0.079	1.26 (0.78, 2.03)	0.350
Leflunomide	0.60 (0.37, 0.99)	0.047	0.32 (0.18, 0.66)	<0.001
Azathioprine	1.60 (1.12, 2.28)	0.009	0.70 (0.41, 1.20)	0.190
Cyclophosphamide †	1.16 (0.16, 8.27)	0.88	-	-
Mycophenolate mofetil †	0.57 (0.21, 1.54)	0.27	-	-
Additional Covariates				
Years from TBS diagnosis	0.93 (0.90, 0.95)	<0.001	0.94 (0.89, 0.96)	<0.001
Age over 40 at TBS diagnosis	0.50 (0.38, 0.66)	<0.001	0.45 (0.26, 0.95)	0.022
Female Sex	0.36 (0.14, 0.85)	0.03	0.85 (0.44, 1.68)	0.652
Severe Disease ‡	1.89 (1.43, 2.49)	<0.001	1.91 (0.90, 4.18)	0.121
ANCA status ¶	2.95 (1.85, 4.72)	<0.001	1.83 (0.73, 4.31)	0.205

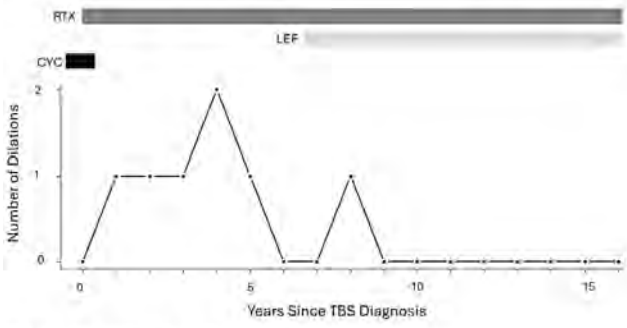
*P-value less than 0.0125 is significant after Bonferroni correction adjusting for multiple comparisons

† Cyclophosphamide and mycophenolate mofetil were not included in the final multivariate model due to limited use in our sample (fewer than 6 patients on each medication), and poorer model performance with their inclusion

‡ Severe GPA was defined by the presence of glomerulonephritis, diffuse alveolar hemorrhage, or mononeuritis. All other patients were non-severe.

¶ ANCA status was positive if c-ANCA, p-ANCA, anti-PR3 antibody, or anti-MPO antibody were positive at vasculitis diagnosis.

Figure 1. Example patient's annual dilation counts over time with corresponding immunosuppressant exposure data.



RTX = Rituximab, LEF = leflunomide, CYC = cyclophosphamide.

Conclusion: Leflunomide and rituximab (but not methotrexate or azathioprine) were associated with significantly fewer tracheal dilations in patients with tracheobronchial GPA. Older age and longer time since diagnosis were also associated with reduced dilation frequency.

Disclosure: B. Denvir: None; **A. Hillel**: Airiver, Inc, 2; **A. Shah**: None; **J. Kim**: None; **P. Seo**: None; **B. Antiochos**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1597

Effectiveness and Safety of Rituximab Biosimilars in Small Vessel Vasculitis: a Systematic Literature Review

Caitlyn Kanters[1], Joo Young Lee[2], Christian Pagnoux[3], Lillian Barra[4], Jean-Paul Makhzoum[5] and Arielle Mendel[6], [1]McGill University, Montreal, Canada, [2]Research institute of the McGill University Health Center, Montreal, QC, Canada, [3]Mount Sinai Hospital, University Health Network, Toronto, and Canadian Vasculitis Research Network (CanVasc), Toronto, ON, Canada, [4]Western University, London, ON, Canada, [5]University of Montreal, Montreal, [6]McGill University Health Centre, Montreal, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: To evaluate the safety and effectiveness of rituximab biosimilars in the treatment of small vessel vasculitis.

Methods: The Medline, CINAHL, Cochrane, Embase and Web of Science databases were searched from inception until May 7, 2025 to identify all studies (full-length manuscripts or abstracts) including $^{3}5$ adults diagnosed with any small vessel vasculitis treated with a rituximab biosimilar for induction or maintenance of remission, including switching from the originator to a biosimilar. Effectiveness outcomes were clinical remission (Birmingham Vasculitis Activity Score = 0) and relapse, while serious adverse events, serious infections, hypersensitivity reactions, late-onset neutropenia and hypogammaglobulinemia were safety outcomes.

Table 1. Rituximab biosimilars in small vessel vasculitis: study characteristics and outcomes

	N= patients receiving biosimilar	Vasculitis subtype	Age, median years [IQR]	Treatment phase (N)	Median follow-up, months [IQR]	Remission or clinical response , n(%)	Relapse (any time point), n (%)	Serious infections (any time point), n (%)
Full text articles								
Antonelou, M. et al (2022)	130	AAV	66 [54-76]	Induction (67)	8 [4-12]	Remission at 3 months: 62 (93%)	1 (2%)	14 (21%)
			65 [52-74]	Maintenance (63)	19 [16-21]	NR	2 (3%)	21 (33)
Jae-Cheol Jo et al. (2023)	15	AAV	59 (range 22-79)	Induction	6 (all)	Any improvement in BVAS at 6 months: 7 (47%)	NR	1 (7%)^
Kwon, H.C. et al (2020)	15	AAV	57.5 [13.5]	Induction	26 [57.7]	NR	8 (53%)	NR
Mittal, S. et al (2021)	77	AAV	40 [29-53]	Induction (60)	27 [10-40]	Remission at 6 months: 36/60 (60%)	14 (23%)*	18 (23%)
				Maintenance (57)	27 [10-40]	NR	7 (12%)	
Vacchi, C. et al. (2019)	51	CV	68 [21]	Induction	NR	Improvement at 6 months: renal 14/15 (93%), peripheral nervous system 24/30 (80%)	NR	0 (0%) at 1 month
Abstracts								
Smitienko, I. et al (2018)	45	AAV	NR	Induction (12)	12 (IQR NR)	Median BVAS at 6 months: 0 (IQR 0-2)	NR	8 (18%)
				Maintenance (33)	12 (IQR NR)	Median BVAS at 6 months: 0 (IQR 0-1)	0 (0%)^	
Sartorelli, S (2021)	56	AAV	NR	Induction	20 [10-24]	Remission at 6 months: 48 (92%)	0 (0%)^	2 (4%)^
Tansley, S. et al. (2019)	8	AAV	NR	Switch*	NR	NR	3 (38%)	NR
Vural, A. et al (2022)	43	AAV	Mean 40.7 (SD 17.3)	Switch*	6 (all)	NR	1 (2%)^	0 (0%)^
Mendel, A. et al (2024)	126	AAV	Mean 57.1 (SD 17.40	Induction (74)	6 (all)	Remission at 6 months: 66/71 (93%)	1 (1%)^	NR
				Maintenance (36)	6 (all)	Remission at 6 months: 100%	0 (0%)^	NR
				Switch (16)*	6 (all)	Remission at 6 months: 100%	0 (0%)^	NR

AAV: ANCA-associated vasculitis, CV: cryoglobulinemic vasculitis, NR: not reported, IQR: interquartile range, SD: standard deviation, BVAS: Birmingham Vasculitis Activity Index
*During maintenance
^ Outcome at 6 months

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 1,628 publications screened, 69 underwent full text review, and ten (5 full text articles, 5 abstracts) reporting on 566 patients treated with rituximab biosimilars were included (n=9 ANCA-associated vasculitis [AAV], n=1 cryoglobulinemic vasculitis [CV]). Seven studies were retrospective, while three were prospective. Most studies reported on the biosimilar Truxima (n=6), while Ruxience, Acelbia and Reditux were evaluated in one study each, and biosimilar type was not indicated in one abstract. Due to heterogeneous outcome reporting, we did not perform a meta-analysis. Follow-up ranged from 5-27 months after first rituximab biosimilar dose. Among studies evaluating a rituximab biosimilar for AAV induction (n=7), clinical remission at 6 months ranged from 60-93%, and relapses occurred in 0-23% of patients by 6 months (reported in 3 studies each). Among studies assessing a rituximab biosimilar for AAV maintenance (n=6), relapses occurred in 0-2% by 6 months (three studies). Of 3 studies evaluating outcomes after switching from originator to biosimilar in stable AAV, two reported sustained remission in 98-100% of patients at 6 months, while one observed relapses in 3/8 patients (timeframe undefined). In the CV study, renal parameters improved in 14/15 (93%) patients and peripheral neuropathy improved in 24/30 (80%) at 6 months. Three studies reported ≥1 serious infection in 0-7% of patients by 6 months. Five studies reported hypersensitivity reactions (2-14%). Hypogammaglobulinemia occurred in 4% and 31% of patients, and late-onset neutropenia in 2% and13% of patients (reported in two studies each). Four studies compared a rituximab biosimilar to the originator (3 AAV, 1 CV), with no significant differences found in terms of remission, relapse, serious adverse events, or infections.

Conclusion: We did not identify any randomized studies of biosimilar rituximab for small-vessel vasculitis, and observational data is limited. The biosimilars studied in AAV appear to have safety and effectiveness similar to historical randomized controlled trials and observational studies of the originator molecule.

Disclosure: C. Kanters: None; **J. Lee**: None; **C. Pagnoux**: amgen, 1, 2, 6, Astra zeneca, 1, 6, csl vifor, 1, 2, 6, gsk, 1, 2, 6, Novartis, 2, ns pharma, 1, otsuka, 1, 2, 5, 6, Pfizer, 2, 6; **L. Barra**: GlaxoSmithKlein(GSK), 6, Otsuka, 5, 6, Pfizer, 5, 6; **J. Makhzoum**: AbbVie/Abbott, 5, Amgen, 6, AstraZeneca, 5, 6, GlaxoSmithKlein(GSK), 6, Janssen, 5, KabiCare, 6, Novartis, 5, Otsuka, 6, Roche, 6, Sanofi, 6; **A. Mendel**: None.

Abstract Number: 1598

Use of JAK Inhibitors in Medium- and Small-Sized Vasculitides: a Retrospective Multicenter Study

Caterina Ricordi[1], elena treppo[2], Pavel Novikov[3], Paul Russo[4], Luca moroni[5], Angelo Fassio[6], Paolo Delvino[7], hervé lobbes[8], Chiara Marvisi[1], Francesco Muratore[1], Xavier Puéchal[9], Carlo Salvarani[1] and Benjamin Terrier[10], [1]Unit of Rheumatology, Azienda USL - IRCCS di Reggio Emilia, and University of Modena and Reggio Emilia, Reggio Emilia, Italy, [2]Division of Rheumatology, Department of Medicine, University of Udine, Udine, Italy, [3]Sechenov University, Moscow, Russia, [4]Royal Adelaide Hospital, Clinical Immunology and Allergy, Adelaide, Australia, [5]IRCCS San Raffaele, Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Milan, Italy, [6]University of Verona, Department of Medicine, Unit of Rheumatology, Verona, Italy, [7]University of Milano-Bicocca, Monza, Monza and Brianza, Italy, [8]Department of Internal Medicine, Hôpital Estaing, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, France, [9]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [10]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Demographic and clinical features of the 14 patients with small- to medium-sized vessel vasculitis treated with JAKi

Patient	Sex	Age at JAKi initiation (years)	Diagnosis	Disease duration (months)	Previous immuno-suppressants	JAKi	Clinical manifestations at JAKi initiation	JAKi treatment duration (months)	Clinical evaluation at last FU	JAK at last FU
1	F	50	IgA vasculitis	6.5	CYC, RTX, MTX, CysA, TAC, dapsone	TOFA	articular, cutaneous	8.7	active disease	stopped (VTE)
2	F	72	Cryoglo-bulinemic vasculitis	40.6	RTX	BARI	systemic, articular, cutaneous, PNS	45.6	complete remission	ongoing
3	F	80	GPA	0.9	MTX, CysA, TCZ, antiTNF, abatacept	TOFA	systemic, articular, ENT	35.1	complete remission	stopped (hepato-toxicity)
4	M	57	Cryoglo-bulinemic vasculitis	9.8	RTX, MTX, TCZ, anti-TNF, abatacept	UPA	systemic, articular	4.3	complete remission	ongoing
5	F	56	PAN	296.1	CYC, RTX, MTX, TCZ	UPA	systemic, articular, cutaneous, ocular, GI	2.3	active disease	stopped (inefficacy)
6	F	51	MPA	2.1	AZA, MTX, HCQ	UPA	articular, pulmonary, ENT	31.4	complete remission	ongoing
7	F	49	GPA	19.3	RTX, MTX, antiTNF, HCQ	UPA	articular, ocular, PNS, CNS	27.4	complete remission	ongoing
8	F	43	GPA	39.1	RTX, MTX	TOFA	systemic, ENT	4.6	partial remission	ongoing
9	F	33	GPA	45.5	RTX, AZA, TCZ, antiTNF	TOFA	systemic, articular, cutaneous, ocular	2.8	partial remission	ongoing
10	F	64	GPA	7.6	CYC, RTX,	TOFA	ocular	12.6	complete remission	ongoing
11	F	76	PAN	194.2	CYC, RTX, AZA, MTX, CysA, TCZ	TOFA	systemic, articular, cutaneous	2.6	active disease	ongoing
12	M	64	PAN	110.6	CYC, AZA, MTX, MMF, CysA, TCZ	UPA	systemic, articular, cutaneous	24.3	partial remission	ongoing
13	F	24	GPA	7.1	RTX	BARI	systemic, articular, cutaneous	4	partial remission	ongoing
14	M	69	MPA	68.9	CYC, RTX, AZA, MMF	UPA	systemic, articular, ENT, PNS	6	complete remission	ongoing

AZA= azathioprine; BARI= baricitinib; CNS= central nervous system; CYC= cyclophosphamide; CysA= cyclosporin A; ENT: ear, nose, throat; GI= gastro-intestinal; GPA= granulomatosis with polyangiitis; HCQ= hydroxychloroquine; JAKi= janus kinase inhibitors; MMF= mycophenolate mofetil; MPA= microscopic polyangiitis; MTX= methotrexate; PAN= polyarteritis nodosa; PNS= peripheral nervous system; RTX= rituximab; TAC=tacrolimus TCZ= tocilizumab; TNF= tumor necrosis factor; TOFA= tofacitinib; UPA= upadacitinib; VTE=venous thromboembolism

Background/Purpose: Medium- and small-vessel vasculitides (MVV and SVV) are a heterogeneous group of inflammatory diseases affecting the vascular wall. Current treatment strategies are based on a combination of glucocorticoids (GCs) and disease modifying anti-rheumatic drugs (DMARDs), but relapses, GC dependence and treatment-related toxicity remain major challenges. In preclinical studies, the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway has emerged as a key regulator of chronic vascular inflammation. To date, data on the use of JAK inhibitors (JAKi) in clinical practice remains limited. This study aimed to evaluate the off-label use of JAKi in MVV and SVV, focusing on patient characteristics, therapeutic efficacy, and safety outcomes in multiple centers worldwide.

Methods: This was a retrospective, multicenter, observational study that collected real-world data on adult patients who met the classification criteria for MVV or SVV and were treated with JAKi. Data were extracted from electronic medical records. Complete response (CR) was defined as BVAS =0 and prednisone ≤5 mg/day, partial response (PR) as BVAS =0 and prednisone between 6 and 10 mg/day, and active vasculitis as BVAS≥1 regardless of prednisone dose.

Results: Fourteen patients (6 granulomatosis with polyangiitis, 2 microscopic polyangiitis, 3 polyarteritis nodosa, 2 cryoglobulinemic vasculitis, and 1 IgA vasculitis) from 8 different centers were included (Table). The median age was 57 (IQR 49-68) years. JAKi were prescribed for refractory disease in 12/14 (85.7%) and for GC sparing in 4/14 (28.6%). The median disease duration prior to JAKi initiation was 2.4 years (IQR 0.6-3.1). Among the JAKi, tofacitinib and upadactinib were used in 6/14 (42.85%) and baricitinib in 2/14 (14.3%) patients, respectively. At JAKi initiation, 13/14 (92.8%) patients were still receiving GCs at a median prednisone dose of 13.75 mg/day (IQR 7.5-20). JAKi were prescribed alone in 8/14 (47.1%) patients, in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

combination with conventional synthetic DMARDs in 4/14 (28.6%) and with biologic DMARDs in 2/14 (14.3%). After a median follow-up of 7.4 months (IQR 4.1-26.6), JAKi achieved an overall response in 11/14 (78.6%) patients (7 CR and 4 PR). Three patients (21.4%) relapsed while on JAKi, including a major relapse that led to discontinuation of JAKi in one patient. Two other patients discontinued JAKi due to adverse events (1 hepatic toxicity and 1 venous thromboembolism). Twelve infections occurred in 5/14 (35.7%) patients, including 6 viral (among which 4 SARS-CoV-2 infections) and 6 bacterial infections. Of the 12 infections, 8 occurred with upadactinib, 3 with tofacitinib and 1 with baricitinib. At the last follow-up, 11/14 (78.6%) were still taking JAKi.

Conclusion: JAK inhibitors may offer a promising therapeutic alternative for refractory vasculitis. However, the risk of adverse events, especially infections, emphasizes the need for careful patient selection and prophylactic measures. Further prospective studies are needed to define the efficacy, safety and optimal role of JAKi in the treatment of MVV and SVV.

Disclosure: c. ricordi: None; **e. treppo**: None; **P. Novikov**: None; **P. Russo**: None; **L. moroni**: None; **A. Fassio**: None; **P. Delvino**: None; **h. lobbes**: None; **C. Marvisi**: None; **F. Muratore**: None; **X. Puéchal**: Roche, 5; **C. Salvarani**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 1599

Cyclophosphamide versus Rituximab in the treatment of Anca-associated Vasculitis: Adverse events and Relapses

Fabricio Benavides Villanueva[1], Diana Prieto-Peña[2], Vanesa Calvo-Río[3], Monica Renuncio-García[4], Adrian Martin-Gutierrez[5], Amparo Sanchez-Lopez[6], Claudia Poo-fernandez[7], maria Rodríguez-Vidriales[8] and Ricardo Blanco[3], [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Immunopathology Group,Santander, Spain, Santander, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [3]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [4]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain, [5]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Piélagos, Spain, [6]Division of Dermatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain, [7]Division of Pneumology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain, [8]Division of Nephrology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis include Granulomatosis with Polyangiitis (GPA), Microscopic Polyangiitis (MPA), and Eosinophilic Granulomatosis with Polyangiitis (EGPA). EGPA presents a different pathogenic, clinical, and therapeutic entity. However, international therapeutical recommendations (ACR, EULAR and KDIGO), epidemiological studies and clinical trials (RAVE and RITUXVAS) (1-4) include MPA and GPA as a combined group. Cyclophosphamide (CYC) and Rituximab (RTX) are considered the first-line therapeutic option in MPA and GPA. RAVE and RITUXVAS trials have demonstrated similar efficacy and safety with CYC and RTX. However, these studies are often limited in follow-up time, which may influence on the results.

Objectives: To compare safety and relapse rates between CYC and RTX.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	CYCLOPHOSPHAMIDE (n=48)	RITUXIMAB (n=39)	p
Age mean±SD	65.7±13.4	57.4±14.8	0.813
Men/ Women, n (% men)	23/25 (48)	20/19 (51)	0.830
Mean follow-up ±SD (months)	17.4±23	31.5±26.1	**0.0046***
ANCA VASCULITIS SUBTYPES			
MPA	24 (50)	17 (43.5)	0.66
GPA	17 (35.4)	14 (36)	> 0.99
EGPA	2 (4.1)	6 (15.3)	0.132
CLINICAL MANIFESTATIONS			
Constitutional symptoms, n (%)	33(68.7)	26(66.7)	>0.99
Renal involvement, n (%)	43 (89.5)	18 (46.1)	**<0.0001***
Pulmonary involvement, n (%)	26 (54.2)	27 (69.2)	0.187
Joint involvement, n (%)	16 (33.3)	15 (38.4)	0.657
ENT involvement, n (%)	11 (22.9)	15 (38.4)	0.158
Abdominal involvement, n (%)	14 (29.1)	1 (2.6)	**0.001***
PNS involvement, n (%)	6 (12.5)	9 (23)	0.256
Ocular involvement, n (%)	6 (12.5)	6 (15.4)	0.761
Cutaneous involvement, n (%)	4 (8.3)	6 (15.4)	0.331
CNS involvement, n (%)	2 (4.1)	2 (5.1)	>0.99
ANALITYCAL FINDINGS			
CRP (mg/dL), median [IQR]	2.8 [0.4-10.4]	4.5 [1.4-11]	**0.704**
ESR mm/1st hour, median [IQR]	61 [38.2-92]	59.5 [34 -93.5]	0.705
ANCA Positive, n (%)	43(89.5)	34 (87.1)	0.693
MPO-ANCA, n (%)	31 (72)	23 (67.7)	0.802
PR3-ANCA, n (%)	12 (28)	11 (32.3)	0.802

*p-value with statistical significance ($p < 0.05$) according to Fisher's exact test for qualitative variables and the Mann–Whitney U test for quantitative variables.
Abbreviations (in alphabetical order): ANCA: Anti-neutrophil cytoplasmic antibodies; CNS: Central Nervous System; EGPA: Eosinophilic granulomatous polyangiitis; ENT: ears, nose and throat; GPA: Granulomatosis with polyangiitis; MPA: Microscopic polyangiitis; MPO-ANCA: ANCA specific for myeloperoxidase; n: number; PNS: Peripheral nervous System; PR3-ANCA: ANCA specific for proteinase 3; SD: Standard Deviation.

TABLE 1. Clinical characteristics and analytical findings of 87 patients with ANCA associated Vasculitis treated with CYC and RTX. Data were obtained at moment of diagnosis.

	CYCLOPHOSPHAMIDE (n=48)	RITUXIMAB (N=39)	p
MAIN ADVERSE EVENTS, n (%) /EAIR /100PY	40 (83.3) / 4.78	22 (56.4) /1.78	**0.0085***
SEVERE INFECTIONS	28 (58.3) /3.34	13 (33.3)/ 1	**0.0304***
NON-INFECTIOUS PULMONAR	9 (18.7) /1	7 (18) /0.56	> 0.99
MACE	9 (18.7)/1	3 (7.7) /0.24	0.211
RENAL COMPLICATIONS	6 (12.5) /0.7	1 (2.6) /0.08	0.123
NEPLASMS	4 (8.3) /0.4	3 (7.7) /0.24	> 0.99
RELAPSE, n (%)	7 (14.6) /0.8	2 (5.1) /0.16	0.178

p-value with statistical significance ($p < 0.05$) according to Fisher's exact test for qualitative variables.
Abbreviations. MACE: major cardiovascular event.

TABLE 2. Adverse Events and Relapse in 87 patients with ANCA associated Vasculitis treated with CYC and RTX.

Methods: Observational study of 196 patients diagnosed with ANCA-associated vasculitis at a referral hospital in northern Spain from January 1, 2000, to December 31, 2024. Classification of ANCA vasculitis was based on the 2022 ACR/EULAR criteria. Depending on the induction therapy administered, patients were divided into two groups: **i)** Patients treated exclusively with CYC and **ii)** with RTX. Patients who received both treatments at any time during follow-up were excluded. Rates of Adverse effects are expressed as the exposure-adjusted incidence rate (EAIR) per 100 person years (PY).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 87 patients were finally included (44 women/43 men); 48 received CYC and 30 received RTX, mean ages at diagnosis of 65.7±13.4 and 57.4±14.8 years, respectively. MPA was the most frequent vasculitis subtype in both groups. Most clinical and laboratory features were similar, except for renal and abdominal involvement that was more common in the CYC group (**Table 1**).

Despite a shorter mean follow-up in patients in the CYM group (17.4±23 vs 31.5±26.1 months), they present significantly more serious adverse events (83.3% vs. 56.4%; p= 0.0085) EAIR of 4.78 /100 PY Vs 1.78/100 PY. The most frequent adverse effect was severe infections (58% vs. 33.3%; p= 0.0304) with a EAIR of XX/100 PY on the CYP group Vs a EAIR of XX/ 100 PY on the RTX group. (**Table 2**).

No significant differences were found for other adverse events. During follow-up, relapses occurred more frequently in the CYC group (14% vs 5.1%; p= 0.178) with an EAIR of 0.8 and 0.16 respectively. (**Table 2**).

Conclusion: In our series, patients treated with CYC had statistically more frequently severe infections and a trend to higher relapse rates.

Disclosure: F. Benavides Villanueva: None; **D. Prieto-Peña**: None; **V. Calvo-Río**: AstraZeneca, 6, MSD, Roche, AbbVie, Lilly, Celgene, Grünenthal, and UCB Pharma, 2, 6; **M. Renuncio-García**: None; **A. Martin-Gutierrez**: None; **A. Sanchez-Lopez**: None; **C. Poo-fernandez**: None; **m. Rodríguez-Vidriales**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1600

Real-world clinical effectiveness of Benralizumab for Eosinophilic Granulomatosis with Polyangiitis: a National multicenter study

Fabricio Benavides Villanueva[1], Andrea Tristan-Alonso[2], Carlos Martinez-Rivera[3], Alicia Padilla-Galo[4], Marina Blanco-Aparicio[5] and Ricardo Blanco[6], [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Immunopathology Group,Santander, Spain, Santander, Spain, [2]Division of Pneumology, Hospital Universitario Puerta del Hierro, Madrid, Spain, Majadahonda, Madrid, Spain, [3]Division of Pneumology, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, Barcelona, Catalonia, Spain, [4]Division of Pneumology, Hospital Universitario Virgen de la Victoria, Málaga, Spain, Malaga, Andalucia, Spain, [5]Division of Pneumology, Hospital Universitario A Coruña, A Coruña, Spain, A coruña, Galicia, Spain, [6]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Benralizumab is approved for eosinophil-driven conditions, like eosinophilic asthma. Recently, the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA) authorized its use for eosinophilic granulomatosis with polyangiitis (EGPA). However, real-world evidence remains limited. This study aims to evaluate the clinical effectiveness of benralizumab for EGPA in routine clinical practice on multiple centers.

Methods: We conducted an observational multicenter study with patients diagnosed with EGPA according to the 2022 EULAR/ACR classification criteria who received benralizumab treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Clinical and Laboratory Characteristics of 23 Patients with EGPA Prior to Benralizumab Treatment.

	EGPA (n=23)
Age at diagnosis mean ±SD	58.5±13
Men/ women, n (% men)	8/15 (65.2)
CLINICAL MANIFESTATIONS SINCE DIAGNOSIS	
Pulmonary involvement, n (%)	23 (100)
Asthma	23 (100)
Pulmonary Infiltrates	14 (60.8)
ENT involvement, n (%)	21 (91.3)
Sinusitis	16 (76.1)
Nasal polyps	21 (100)
Constitutional symptoms, n (%)	16 (69.5)
CNS/CNP involvement, n (%)	9 (39.1)
Cutaneous involvement, n (%)	5 (21.7)
Abdominal involvement, n (%)	3 (13)
Renal involvement, n (%)	3 (13)
ANALYTICAL FINDINGS DIAGNOSIS	
Eosinophilia, n(%) (>500 cell/uL)	23 (100)
Eosinophiles (/mm3), median [IQR]	865 [740-1100]
IgE (UI/L), median [IQR]	225 [57-360.5]
ANCA Positive, n (%)	16 (69.5)
PREVIOUS IMMUNOSUPPRESSANT TREATMENT, n (%)	
Biologic treatment, n(%)	10 (43.4)
Azathioprine, n(%)	5 (21.7)
Methotrexate, n(%)	3 (13)
Mycophenolate mofetil, n(%)	2 (8.7)
Cyclophospharnide, n(%)	2 (8.7)

Abbreviations (in alphabetical order):
ANCA: Anti-neutrophil cytoplasmic antibodies; CNS: Central Nervous System; EGPA: Eosinophilic granulomatous polyangiitis; ENT: ears, nose and throat, n: number; PNS: Peripheral nervous System; SD: Standard Deviation

Effectiveness was assessed through clinical improvement, laboratory findings, pulmonary function, and corticosteroid-sparing effects. Clinical parameters were monitored throughout follow-up. Analytical outcomes included eosinophil count (>500 cells/μL) and IgE level improvement (>100 IU/L). Pulmonary function was evaluated using forced expiratory volume in the first second (FEV_1) and the FEV_1/FVC ratio.

Data were extracted from medical records up to April 30, 2025. Results were expressed as percentages, means ± standard deviation (SD), or medians [interquartile range, IQR]. Comparisons of continuous variables over time were conducted by Wilcoxon test.

Results: We included 23 patients (15 women/8 men); mean age of 58.5±13 years. Baseline clinical and laboratory characteristics before benralizumab initiation are summarized in Table 1. The most common manifestation was asthma (100%), followed by ENT involvement (91.3%), constitutional symptoms (76.1%), neurologic involvement (39.1%), cutaneous manifestations (21.7%), and renal (13% each).

Before treatment, all patients exhibited eosinophilia (median 865 [740-1100] eosinophils/mm^3). Elevated serum IgE in 56.5%; (median 225 [57-360.5] IU/L), and ANCA positivity in 69.5%. Previous immunosuppressive therapies included azathioprine (22%), methotrexate (13.6%), mycophenolate mofetil (9%), and cyclophosphamide (9%). Prior biologic therapies were used in 43.4%. Most commonly were Mepolizumab (50%), Omalizumab (40%), and Reslizumab (10%).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

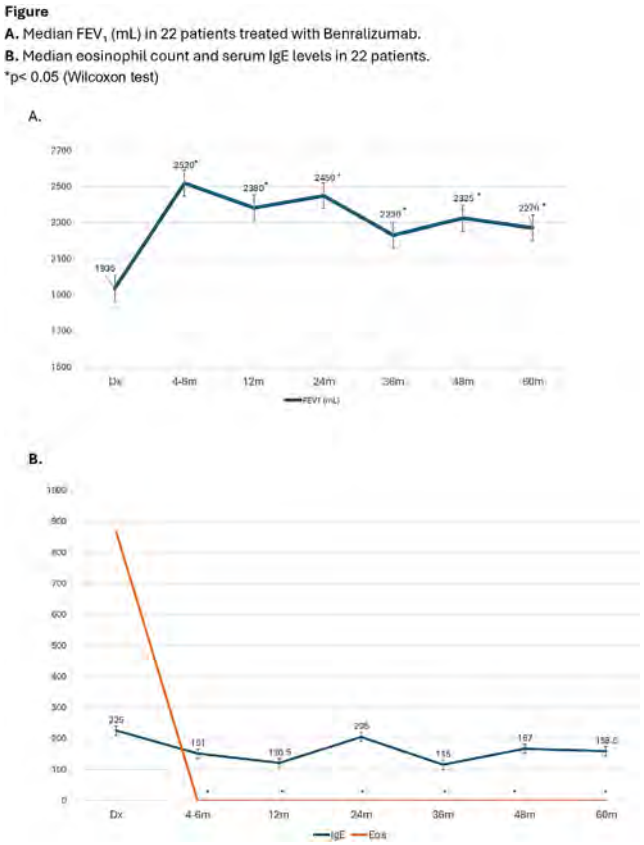


Figure A. Median FEV_1 (mL) in 22 patients treated with Benralizumab. B. Median eosinophil count and serum IgE levels in 22 patients. *p< 0.05 (Wilcoxon test)

Benralizumab was initiated a mean of 4.6±4 years post-EGPA diagnosis (30 mg subcutaneously every 4 weeks). Showed a rapid and sustained improvements over 60 months: **a)** FEV_1 increased from median 1935 [1545-2680] to 2270 [2192.5-2460] mL (p=0.0312), **b)** eosinophil counts dropped from 850 [740-1100]/mm^3 to 0 [0-0] (p< 0.0001), **c)** serum IgE levels decreased from 225 [57-360] (IU/mL) to 158.5 [115-217] IU/mL; (p=0.125) and, **d)** prednisone dose from 5 mg/day [2.5-10] to 0 [0-0]; (p=< 0.0001)

After a mean follow-up of 42.4±20.7 months 78.2% of patients remained in remission. Disease relapse occurred in 3 (13%) (2 respiratory, 1 systemic), while 2 patients discontinued therapy due to inadequate clinical response.

Conclusion: Benralizumab demonstrated rapid and sustained effectiveness, even in patients with severe and refractory EGPA, consistent with findings from clinical trials. These preliminary real-world data highlight its therapeutic potential, but further validation in larger cohorts with extended follow-up is necessary to establish its role in routine clinical practice.

Disclosure: F. Benavides Villanueva: None; **A. Tristan-Alonso**: None; **C. Martinez-Rivera**: None; **A. Padilla-Galo**: None; **M. Blanco-Aparicio**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1601

Obinutuzumab Induces and Maintains Remission in Refractory or Relapsing ANCA-Associated Vasculitis – A Case Series

Helen Au[1], Christian Löffler[2], Hartmut Mahrhofer[1], Bastian Walz[1] and Bernhard Hellmich[1], [1]Klinik für Innere Medizin, Rheumatologie und Immunologie, medius Klinik Kirchheim, Kirchheim unter Teck, Germany, [2]Medizinische Klinik V, Nephrology, Endocrinology, Hypertensiology and Rheumatology, Universitaetsmedizin Mannheim, University of Heidelberg, Mannheim, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: B-cell depletion with anti-CD20 therapy is the current cornerstone of management in organ- or life-threatening ANCA-associated vasculitis (AAV). Guidelines recommend the use of rituximab or cyclophosphamide for remission induction and rituximab for remission maintenance. Compared with rituximab, obinutuzumab is a newer humanized type 2 anti-CD20 monoclonal antibody and is postulated to result in deeper tissue B cell depletion. It has an emerging role in rituximab-intolerant patients and in rituximab-refractory disease. To date, only nine cases in two case series have been published on the use of obinutuzumab in rituximab-intolerant patients with AAV.

Methods: This single-centre case series reports the clinical outcomes of five patients who received obinutuzumab therapy for refractory or relapsing PR3+ granulomatosis with polyangiitis (GPA). All patients satisfied the 2022 ACR/EULAR classification criteria for GPA. Review of electronic health records was undertaken for patient demographics, disease manifestations, previous treatments, indication for obinutuzumab, clinical and laboratory outcomes, and potential complications.

Table 1: Patient demographics, disease manifestations, indications for obinutuzumab, and treatment history

Table 1: Patient demographics, disease manifestations, indications for obinutuzumab, and treatment history

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age/ Sex	69 F	53 F	54 F	34 F	38 M
Disease	PR3+ GPA Diagnosed 2021	PR3+ GPA Diagnosed 2000	PR3+ GPA Diagnosed 2023	PR3+ GPA Diagnosed 2023	PR3+ GPA Diagnosed Aug 2023
Indication for obinutuzumab	Relapsing disease on rituximab maintenance. Refractory to cyclophosphamide induction.	Multiple relapses with ENT, eye, joint, and neurological involvement. Rituximab allergy	Steroid-dependent episcleritis/ scleritis that developed during cyclophosphamide induction and was refractory to rituximab	Refractory disease despite rituximab and cyclophosphamide induction, avacopan, IVIG	Refractory disease despite rituximab and cyclophosphamide induction
Manifestations at time of obinutuzumab administration	BVAS 7 Middle ear effusion with conductive hearing loss New saddle-nose deformity	BVAS 8 Nasal crusting Scleritis Inflammatory arthritis Sensory polyneuropathy Elevated PR3: 188 U/mL	BVAS 1 Episcleritis/ scleritis Elevated PR3: 14 U/mL	BVAS 6 Sinusitis Mastoiditis New saddle-nose deformity Elevated PR3: 14 U/mL	BVAS 4 Progressive maxillary sinusitis with bony destruction Optic nerve involvement Elevated PR3: 87 U/mL
Previous manifestations	Mononeuritis multiplex, sensory axonal polyneuropathy, ischaemic colitis, sinusitis	Glomerulonephritis Alveolar hemorrhage	Pansinusitis Pauci-immune glomerulonephritis	Sinusitis Mastoiditis with facial nerve palsy Mixed hearing loss	
Previous treatment (in chronological order)	Prednisolone Cyclophosphamide induction Rituximab induction	Prednisolone Cyclophosphamide (> 30g) Azathioprine Rituximab induction Methotrexate Leflunomide Mycophenolate mofetil IVIG Tacrolimus	Prednisolone Cyclophosphamide Azathioprine Rituximab induction Topical ciclosporin	Prednisolone Rituximab induction IVIG Cyclophosphamide induction Avacopan Mastoid decompression and tympanoplasty	Prednisolone Methotrexate Mepolizumab Rituximab induction Cyclophosphamide induction IVIG

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: In refractory/ relapsing AAV, obinutuzumab use facilitated glucocorticoid reduction to ≤ 5mg prednisolone daily

Table 2: Obinutuzumab dosing details and daily glucocorticoid dosage					
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Timing of obinutuzumab administration	Jul 2023: 1000mg x1 Jun 2024 1000mg x1 Feb 2025: 1000mg x1	Feb 2021: 1000mg x1 Aug 2021: 1000mg X1 May 2022: 1000mg X1 Jan 2023: 1000mg X1 Jan 2024: 1000mg X1 Dec 2024: 1000mg X1	Mar 2024: 1000mg x2 Jan 2025: 1000mg x1	July 2024: 1000mg x2 Jan 2025: 1000mg x1	Jan 2025: 1000mg x2
Daily glucocorticoid dose at obinutuzumab commencement and at last follow-up	Commencement: Prednisolone 20mg Follow-up: Prednisolone 5mg	Commencement: Prednisolone 8mg Completely weaned since July 2022	Commencement: Prednisolone 15mg Follow-up: Prednisolone 5mg	Commencement: Prednisolone 5mg Follow-up: Prednisolone 2.5mg	Commencement: Prednisolone 15mg Follow-up: Prednisolone 5mg

Results: One male and four female patients with refractory or relapsing GPA received obinutuzumab. Three had multi-system involvement while one had isolated episcleritis/scleritis and another, severe isolated ENT disease. All patients had refractory or relapsing disease despite guideline-directed induction therapy with rituximab and cyclophosphamide. For induction of disease remission, obinutuzumab was administered at one or two doses of 1000mg at week 0 and week 2. Maintenance treatment consisted of single 1000mg infusions at six- to twelve- monthly intervals. Obinutuzumab was effective in inducing and maintaining disease remission. Those patients with detectable ANCA titres at time of obinutuzumab treatment seroconverted from positive to negative. During a median follow-up of 14 months (range: 4-51 months), obinutuzumab was well tolerated with two infections noted (sinusitis and moderate SARS-CoV-2 infection requiring prolonged antiviral treatment).

Conclusion: This case series illustrating the use of obinutuzumab in five patients with GPA adds to the limited published literature. Obinutuzumab shows promise in the management of rituximab-refractory or relapsing AAV and appears to be efficacious and well tolerated. Results of use thereof in larger clinical studies are awaited.

Disclosure: H. Au: None; **C. Löffler**: None; **H. Mahrhofer**: None; **B. Walz**: None; **B. Hellmich**: CSL Vifor, 2, 6.

Abstract Number: 1602

Biomarkers of Innate Immune Activation to Identify Non-Response to Rituximab in Granulomatosis with Polyangiitis

Irene Carrión-Barberà[1], Jorge A. Gonzalez-Chapa[2], David Cuthbertson[3], Nader Khalidi[4], Curry Koening[5], Carol Langford[6], Carol McAlear[7], Paul Monach[8], Larry Moreland[9], Christian Pagnoux[10], Philip Seo[11], Ulrich Specks[12], Kenneth Warrington[12], Peter Merkel[7], Christian Lood[2] and Vasculitis Clinical Research Consortium, [1]Department of Rheumatology. Hospital del Mar, Barcelona, Spain, [2]University of Washington, Division of Rheumatology, Seattle, [3]University of South Florida, Tampa, [4]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Canada, [5]University of Texas Dell Medical School, Austin, TX, [6]Cleveland Clinic, Moreland Hills, OH, [7]University of Pennsylvania, Philadelphia, PA, [8]VA Boston Healthcare System, Boston, MA, [9]University of Colorado, Denver, CO, [10]Mount Sinai Hospital, University Health Network, Toronto, and Canadian Vasculitis Research Network (CanVasc), Toronto, ON, Canada, [11]Johns Hopkins University, Baltimore, MD, [12]Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Innate immune activation plays a key role in granulomatosis with polyangiitis (GPA), contributing to vascular inflammation via neutrophil extracellular traps, immune complexation (IC), and endothelial injury. Its role in response to rituximab (RTX) remains unclear. We aimed to evaluate changes in innate immune markers before and after RTX and assess their ability to predict remission and treatment response.

Methods: Ten plasma biomarkers reflecting neutrophil and platelet activation, endothelial injury, and IC were measured pre- and 6–12 months post-RTX. Skewed biomarkers were log-transformed or dichotomized. Changes over time were assessed using linear or generalized linear mixed-effects models. Confounders were selected systematically using iterative linear regression models, excluding aliased and collinear variables. Non-response was defined as < 50% BVAS/WG

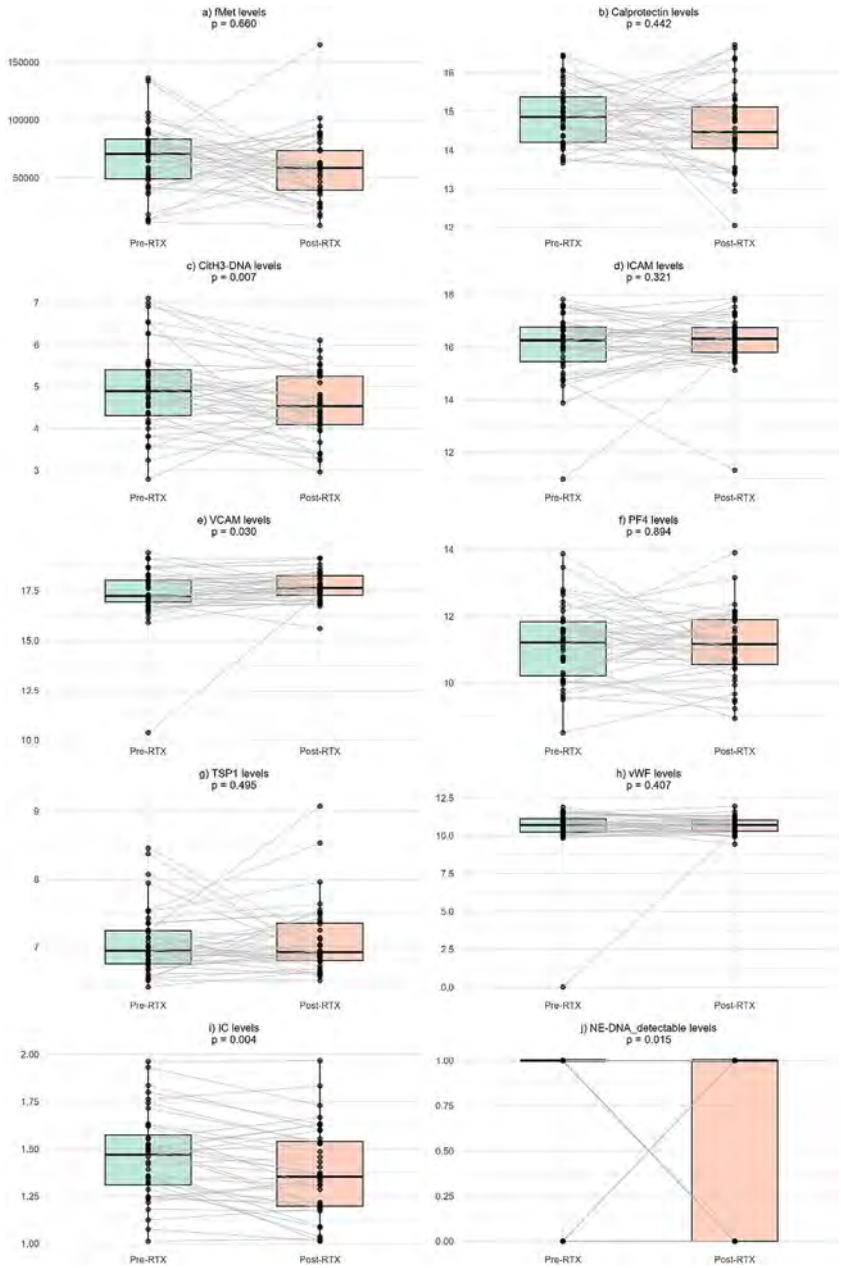


Figure 1: Comparison of the biomarker's levels pre- and post-RTX. fMet: N-Formylmethionine; CitH3-DNA: Citrullinated histone H3-DNA complex; ICAM: Intercellular adhesion molecule 1; VCAM: Vascular cell adhesion molecule 1 (VCAM-1); PF4: Platelet factor 4 complement; TSP1: Thrombospondin 1, vWF: Von Willebrand factor; IC: Immune complexation; NE-DNA: Neutrophil Elastase-DNA Complexes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

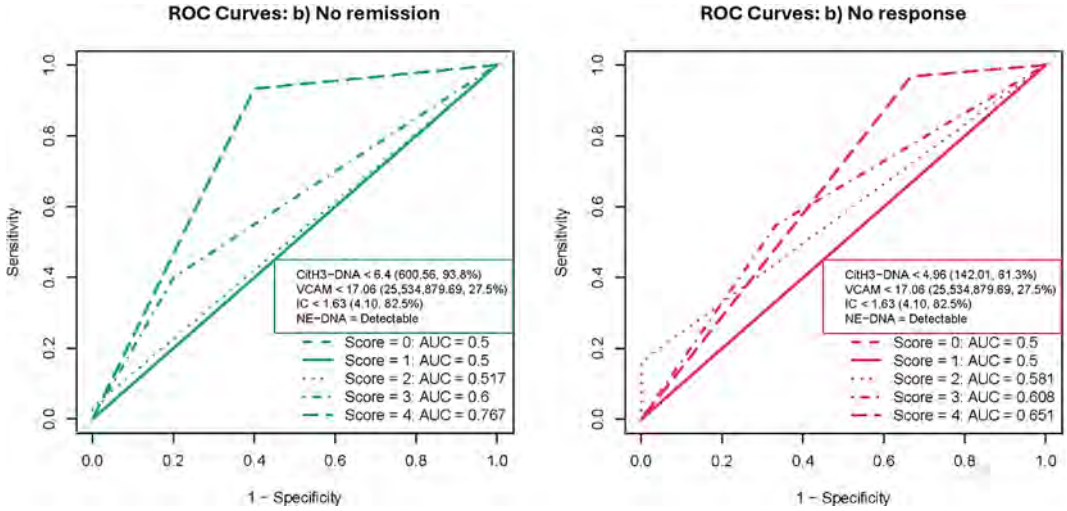


Figure 2: Receiving operating characteristics (ROC) curves and areas under the curve (AUC) of no remission (a), no response (b). Scores 1 to 4 refers to the number of biomarkers that are positive according to the thresholds and their direction specified in the figure. Numbers next to the biomarkers inside the square indicate logarithmic value (raw value, percentile). CitH3-DNA: Citrullinated histone H3-DNA complex; VCAM: Vascular cell adhesion molecule 1 (VCAM-1); IC: Immune complexation; NE-DNA: Neutrophil Elastase-DNA Complexes.

reduction without new symptoms; non-remission as BVAS/WG > 0. Wilcoxon and Fisher's tests compared trajectories by outcome. ROC curves and Youden index thresholds were used to evaluate predictive performance.

Combined biomarker scores we constructed to predict non-response/non-remission and calculated individual biomarker thresholds based on ROC-derived Youden index from pre-treatment samples. These thresholds were applied to generate a simple score (0–4), summing the number of positive biomarkers within those that significantly changed post-RTX. Areas under the curve (AUC) were calculated for each cutoff (score 0–4). A weighted score was derived from logistic regression, and DeLong's test was used to compare performance.

Results: Forty GPA patients were included (median age 53 [interquartile range 38–65], 58% female, 90% White). Thirty-four (85%) were PR3-ANCA+, 3 (7.5%) MPO-ANCA+ and 3 (7.5%) missing. Pre-RTX median BVAS/WG was 3.0, dropping to 0.0 post-RTX. Ten patients (25%) did not reach remission; 9 (23%) failed to respond.

Citrullinated histone H3-DNA complexes (CitH3-DNA), IC, and neutrophil elastase–DNA complexes (NE-DNA) levels decreased significantly post-RTX; vascular cell adhesion molecule 1 (VCAM) increased (**Figure 1**). Baseline biomarkers individually did not differentiate outcomes. However, a combined score of 4 positive biomarkers according to the thresholds and direction specified in **Figure 2** best identified non-responders across definitions: AUC ranged from 0.767 to 0.651. For lack of remission, score 4 had: sensitivity = 0.93, specificity = 0.60, positive predictive value (PPV) = 0.88, negative predictive value (NPV) = 0.75; for lack of response: sensitivity = 0.97, specificity = 0.33, PPV = 0.83, NPV = 0.75. Weighted scores did not significantly outperform the simple score.

Conclusion: A combined score of 4 innate immune biomarkers—CitH3-DNA, VCAM, IC, and NE-DNA—identifies patients who fail to achieve remission or response after RTX treatment. The simple additive score performed consistently across outcome definitions and was not improved by weighting. While promising for stratifying non-responders prior to B-cell–depleting therapy, this score requires external validation before clinical application.

Disclosure: I. Carrión-Barberà: AstraZeneca, 6, GlaxoSmithKlein(GSK), 2; **J. Gonzalez-Chapa**: None; **D. Cuthbertson**: None; **N. Khalidi**: AbbVie/Abbott, 2, 5, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 5, GlaxoSmithKlein(-GSK), 2, 6, Mallinckrodt, 2, NS Pharma, 5, Otsuka, 2, 6, Roche, 2, 6, Sanofi, 2, 5; **C. Koening**: Amgen, 1, Boehringer-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ingelheim, 1; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **C. McAlear**: None; **P. Monach**: Boehringer-Ingelheim, 2; **L. Moreland**: None; **C. Pagnoux**: amgen, 1, 2, 6, Astra zeneca, 1, 6, csl vifor, 1, 2, 6, gsk, 1, 2, 6, Novartis, 2, ns pharma, 1, otsuka, 1, 2, 5, 6, Pfizer, 2, 6; **P. Seo**: None; **U. Specks**: Amgen, 1, 2, 5, Argenx, 2, AstraZeneca, 1, 5, Boehringer-Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 5, CSL Vifor, 1, Genentech, 5, GlaxoSmithKlein(GSK), 5, Mayo Foundation for Education and Research, 9, Melodia Therapeutics, 2, NorthStar Medical Radioisotopes, 5, Novartis, 1, 2, 5, NS Pharma, 5, UpToDate, 9; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11.

Abstract Number: 1603

SGLT-2 Inhibitors are Associated with Lower Risk of End Stage Renal Disease (ESRD) and Lower Mortality in ANCA-associated Vasculitis With Kidney Involvement

Julia Foos[1], Naveed Shah[2] and Nezam Altorok[3], [1]Unversity of Toledo College of Medicine and Life Sciences, Toledo, [2]University of Toledo College of Medicine and Life Sciences, Toledo, [3]The University of Toledo, Toledo, OH

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA-associated vasculitis encompasses three main conditions: Granulomatosis with Polyangiitis (GPA, previously called Wegener's granulomatosis), Eosinophilic Granulomatosis with Polyangiitis (EGPA, previously called Churg-Strauss), and microscopic polyangiitis. These three conditions are known to cause kidney issues. SGLT-2 inhibitors (SGLT-2i) have demonstrated the ability to protect some aspects of kidney function in patients with Type 2 diabetes. This study intends to investigate effects of SGLT-2 inhibitors on renal-related outcome measures in patients with ANCA-associated vasculitis and Type 2 diabetes.

Methods: This retrospective cohort study used TriNetX, a global, federated network of databases that provides de-identified data of over 113 million patients. We used all applicable ICD-10 codes to identify patients with GPA, EGPA, or microscopic polyangiitis and Type 2 diabetes, and if they take SLGT-2i for diabetes treatment. The participants in the study ranged from ages 18-80 years and were balanced based on age and sex. These cohorts filtered out patients who had received a previous diagnosis/procedure of Chronic Kidney Disease (CKD), End Stage Renal Disease (ESRD), unclassified kidney disorders, dialysis, and kidney transplant.

Results: We identified 219 patients who used SGLT-2i at time of diagnosis of ANCA-associated vasculitis with kidney involvement. Among these patients, we identified lower incidence of ESRD in patients who used SGLT-2i compared to age- and sex-matched controls. Age at index was 62.9 in the SGLT-2i group, and 64.1 in the control group. Specifically, we identified 33 patients who took SGLT-2i and were diagnosed with ESRD, compared to the 57 patients who did not take SGLT-2i (p=0.003). 10 patients on SGLT-2i received kidney transplants, and 0 became infected. 18 patients received kidney transplants but did not take SLGT-2 inhibitors, and 10 of their transplants became infected (p=0.001). We did not find

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

statistically significant difference in outcomes related to kidney transplant status (p=0.115) and dialysis services (p=0.062). Moreover, patients with ANCA-associated vasculitis who used SGLT2 inhibitors had a survival probability (outcomes: ESRD, stage 5 CKD, dialysis services, kidney transplant status, or kidney transplant infection) of 90% five years after meeting the selected criteria, as opposed to the 72% who did not take SGLT-2i (p=0.03).

Conclusion: Patients with ANCA-associated vasculitis who used SGLT-2i at time of diagnosis of ANCA-associated vasculitis had lower risk of ESRD and kidney transplant infection (p< 0.05). Also, significantly lower 5-year mortality was found in SGLT-2i users. These findings highlight a potential survival and nephroprotective role of SGLT-2i in ANCA-associated vasculitis.

Disclosure: J. Foos: None; **N. Shah**: None; **N. Altorok**: None.

Abstract Number: 1604

Impact and risk factors of anti-rituximab antibodies in small-vessel vasculitis: a multicenter retrospective study

Lucas Khellaf[1], Raphaele Seror[2], caterina ricordi[3], stephanie chhun[4], audes gleizes[4], hervé lobbes[5], clara pouchelon[6], marie Charlotte Besse[7], Jean-Emmanuel Kahn[8], sabine revuz[9], Marina Cumin[10], Dimitri Titeca-Beauport[11], Matthias Papo[6], Philippe Rémy[6], marie Desprets[12], florian garo[13], Charles Ronsin[14], Salima Hacein-Bey-Abina[6], Amélie Servettaz[15], Cacoub Patrice[16], Xavier Puéchal[17] and Benjamin Terrier[18], [1]AP-HP, Paris, [2]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [3]Unit of Rheumatology, Azienda USL - IRCCS di Reggio Emilia, and University of Modena and Reggio Emilia, Reggio Emilia, Italy, [4]APHP, Paris, Ile-de-France, France, [5]Department of Internal Medicine, Hôpital Estaing, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, France, [6]APHP, Paris, France, [7]CHU Tours, Tours, France, [8]Ambroise Paré hospital, Boulogne, France, [9]CHU de la Réunion, Réunion, France, [10]Centre hospitalier de Libourne, Libourne, France, [11]CHU Amiens, Amiens, France, [12]CH Chôlet, Cholet, France, [13]CHU Nîmes, Nîmes, France, [14]CHU Nantes, Nantes, France, [15]Internal Medicine, CHU Reims, Reims, France, [16]Department of Internal Medicine and Clinical Immunology, Sorbonne Universités, AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Centre national de références Maladies Autoimmunes et systémiques rares, Centre national de références Maladies Autoinflammatoires rares et Amylose inflammatoire (CEREMAIA), INSERM, UMR S959, Immunology-Immunopathology-Immunotherapy (I3), Paris, France, Paris, France, [17]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [18]Cochin Hospital, Paris, France

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Small vessel vasculitis mainly includes ANCA-associated vasculitis (AAV) and cryoglobulinemic vasculitis (CV), leading to significant organ damage. Rituximab (RTX), an anti-CD20 monoclonal antibody, has improved the prognosis by targeting B cells[1]. Anti-RTX antibodies (ARA) are detrimental in primary membranous glomerulonephritis[2] and rheumatoid arthritis but their impact in small vessel vasculitis remains unclear. We aimed to evaluate the impact of ARAs on disease progression, treatment response and prognosis in patients with AAV and CV.

Methods: We retrospectively identified patients with AAV or CV who developed ARA through two immunology laboratories and the French Vasculitis Study Group. ARA positivity was defined by an undetectable serum RTX level with high anti-RTX antibody titer (>20%). We evaluated demographic, clinical, and laboratory data; CD19+ B-cell counts at 6 months; and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

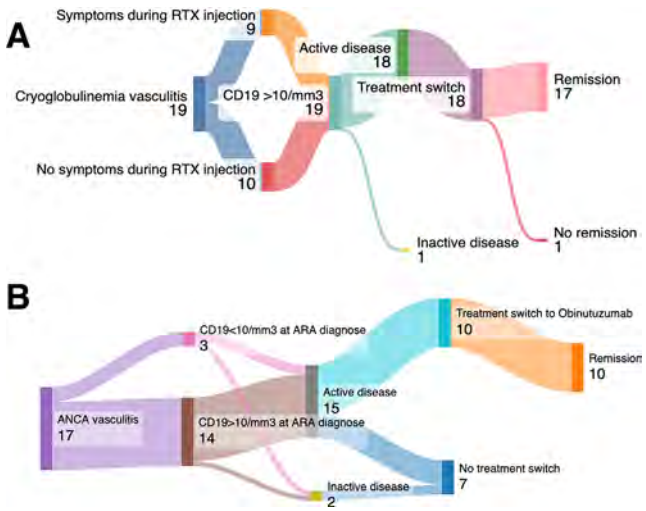


Figure 1. Sankey Diagram of Clinical Features, CD19 Reconstitution, and Treatment Outcomes in Cryoglobulinemic and ANCA-Associated Vasculitis Cohorts. A. Cyroglobulinemic vasculitis ARA's cohort: Among 19 patients with cryoglobulinemic vasculitis who developed anti-rituximab antibodies (ARA), half experienced infusion-related symptoms during rituximab (RTX) administration. All 19 showed CD19+ reconstitution (>10 cells/mm^3) at the time of ARA detection; 18 had active disease and were switched to an alternative therapy, leading to remission in 17 cases (1 remained with persistent disease). B. ANCA-associated vasculitis patients with ARA, 14 exhibited CD19+ reconstitution (>10 cells/mm^3) and 3 maintained depletion (<10 cells/mm^3). Fifteen had active disease, of whom 10 were switched to obinutuzumab—achieving remission in all—and 7 continued their previous regimen without switch (2 were inactive at ARA diagnosis).

Table 1 Baseline features, treatment regimens and follow-up outcomes of the study cohorts. A. Comparison between CV patients without anti-rituximab antibodies (CryoVas cohort, N = 321) versus those with detectable anti-rituximab antibodies (ARA cryoglobulinemia, N = 19). B. Comparison between patients with ANCA-associated ARA (N = 202) versus ARA-ANCA patients with detectable anti-rituximab antibodies (N = 17).

A

Variable	Overall N = 340[1]	CryoVas cohort N = 321[1]	ARA Cryoglobulinemia N = 19[1]	p-value[2]
Inclusion characteristics				
Age	64 [54, 73]	64 [55, 74]	56 [34, 67]	**0.012**
Female	223 (66)	207 (66)	16 (84)	0.10
Weight, kg	63 [54, 73]	63 [54, 74]	58 [54, 69]	0.4
B lineage hemopathy	33 / 327 (10)	30 (9.7)	3 (16)	0.4
Connective tissue disease	87 (26)	73 (23)	14 (73)	**<0.001**
Sjogren disease	95 (28)	76 (24)	19 (100)	**<0.001**
Essential	117 (34)	117 (36)	0 (0)	**0.004**
Digital Ulcers	61 (18)	59 (18)	2 (11)	0.5
Purpura	256 (75)	240 (75)	16 (84)	0.4
Digital Ulcers	61 (18)	59 (18)	2 (11)	0.5
Peripheral neuropathy	168 (49)	157 (49)	11 (58)	0.4
Kidney involvment	113 (33)	106 (33)	7 (37)	0.7
C4 (g/l) at inclusion	0.04 [0.02, 0.12]	0.04 [0.02, 0.12]	0.01 [0.00, 0.06]	**<0.001**
Rituximab	75 (24)	57 (20)	19 (100)	**<0.001**
Rituximab injection schedule				
Weekly 375 mg/m² for 4 weeks regimen	52 (68)	45 (79)	7 (37)	**<0.001**
RTX 1 g protocol (Day 1 and Day 15)	18 (23)	6 (10)	12 (63)	**<0.001**
Follow-up				
Refractory/Relapse	173 (54)	155 (48)	18 (95)	**<0.001**
Clinical response to treatment switch	77 (26)	59 (21)	18 (95)	**<0.001**
Death	49 (14)	48 (15)	1 (5.3)	0.3

[1]Median [Q1, Q3]; n / N (%)

B

Variable	Overall N = 219[1]	ANCA control N = 202[1]	ARA ANCA N = 17[1]	p-value[2]
Inclusion characteristics				
Age	53 [36, 67]	53 [36, 66]	66 [43, 70]	0.2
Female	123 (56)	113 (56)	10 (59)	0.9
Granulomatosis with Polyangiitis	168 (77)	160 (79)	8 (47)	**0.022**
Microscopic Polyangiitis	47 (21)	39 (19)	8 (47)	**0.039**
Eosinophilic Granulomatosis with Polyangiitis	4 (2)	3 (2)	1 (6)	0.4
Purpura	34 (16)	31 (15)	3 (19)	0.8
Kidney involvement	110 (50)	101 (50)	13 (76)	**0.021**
Pulmonary involvement	130 (59)	125 (62)	5 (29)	**0.048**
Peripheral neuropathy	39 (18)	33 (16)	6 (35)	0.179
Serum creatinine (µmol/L)	77 [64, 122]	76 [63, 110]	140 [80, 215]	**0.015**
Treatment received				
RTX 1 g protocol (Day 1 and Day 15)	57 (26)	49 (24)	8 (47)	**0.048**
Rituximab 375 mg/m² weekly × 4	136 (62)	127 (63)	9 (53)	0.4
Corticosteroids	211 (97)	195 (98)	16 (94)	0.4
Rituximab	193 (88)	176 (87)	17 (100)	0.2
Plasma exchange	21 (9.6)	21 (10)	0 (0)	0.5
Cyclophosphamid	85 (39)	82 (41)	3 6 (19)	0.19
Azathioprine	69 (32)	67 (33)	2 / 16 (13)	0.10
Follow-up				
Refractory/Relapse	**75 (34)**	**60 (30)**	**15 (88)**	**<0.001**
Treatment switch during follow-up	**17 (4)**	**6 (3.0)**	**11 (65)**	**<0.001**
CD19 count at month 6 (/mm³)	**0 [0, 3]**	**0 [0, 1]**	**45 [10, 110]**	**<0.001**
Death	16 (4)	15 (7.5)	1 (5.9)	>0.9

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Univariable and multivariable predictors of anti-rituximab antibody development in small-vessel vasculitis. A. illustrates the associations between key clinical factors and anti-rituximab antibody (ARA) positivity in cryoglobulinemic vasculitis (CV), using both univariable and multivariable Firth-penalized logistic regression. B. presents the same analyses for ANCA-associated vasculitis (AAV). Odds ratios and 95% confidence intervals were estimated via the logistf package; multivariable models adjust for all variables shown in each panel.

A

Cryoglobulinemic vasculitis

		Univariable			Multivariable		
Variable	N	Odd Ratio	95% CI	p-value	Odd Ratio	95% CI	p-value
Age ≤40 years	340	5.37	[1.84 - 14.5]	**0.003**	9.21	[1.29 - 65.8]	**0.027**
Sjogren disease	340	39.6	[9.79 – 362]	**<0.001**	31.2	[3.64– 268]	**<0.001**
Symptoms during RTX injection	340	116	[28.5 – 667]	**<0.001**	25.6	[3.30 – 198]	**0.002**
RTX 1g protocol (Day 1 and Day 15)	71	11.9	[3.68 - 43.4]	**<0.001**	10.1	[2.33 - 43.8]	**0.024**

Abbreviation: CI = Confidence Interval; RTX = Rituximab

Odds Ratio and 95% CI estimated via Firth's penalized logistic regression (logistf)

B

ANCA associated vasculitis

		Univariable			Multivariable		
Variable	N	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Microscopic polyangiitis	219	3.70	[1.35 - 10.0]	0.012	3.48	[1.21 - 10.0]	**0.021**
Kidney involvement	219	3.00	[1.06 - 10.2]	0.037	3.36	[1.01 - 11.2]	**0.048**
Mononeuritis multiplex	215	4.67	[1.54 - 13.3]	0.008	3.58	[1.19 - 10.8]	**0.023**
RTX 1g protocol (day 1 and day 15)	219	2.77	[1.02 - 7.44]	0.046	4.87	[1.59 - 14.9]	**0.006**

Abbreviation: CI = Confidence Interval; RTX = Rituximab

Odds Ratio and 95% CI estimated via Firth's penalized logistic regression (logistf).

outcomes including relapse or refractory disease. We also analyzed two control cohorts (one for AAV, one for CV) to assess risk factors for immunization.

Results: Thirty-six patients with ARA-positive vasculitis were included (median age 58 IQR [42-69]; 75% female), including 19 CV (all associated with Sjögren's syndrome) and 17 AAV. The most common organ involvement was skin (59%), peripheral nerve (42%), and kidney (41%). Patients received a median of five RTX infusions prior to ARA detection, with a median interval of 11 months (IQR [5-25]) from RTX initiation. Notably, 38% experienced serum sickness-like reactions during infusions prior to ARA identification. CD19+ B cells were detectable in 91% of patients at the time of ARA detection, and 91% had active disease at that time.

After ARA detection, 27 patients (75%) required a change in therapy, with obinutuzumab being the most common alternative (50%), while others received cyclophosphamide, belimumab or ofatumumab. Clinical remission was achieved in 96% of patients, with 92% achieving B-cell depletion after switching (**Figure 1**).

We next compared baseline and follow-up data between patients and controls (**Table 1**). In the CV group, variables independently associated with the detection of ARA were Sjogren's syndrome (adjusted OR 31.2; 95%CI 3.4-268; p=0.001), age ≤40 years (aOR 9.21; 95%CI 1.29–65.8; p=0.027), reactions during RTX infusions (aOR 25.6; 95%CI 3.30–198; p=0.002) and the use of RTX regimen 1 gram on days 1 and 15 (aOR 10.1; 95%CI 2.33–43.8; p=0.002). In the AAV group, variables independently associated with the detection of ARA were microscopic polyangiitis (aOR 3.7; 95%CI 1.21–10.0; p=0.021), renal involvement (aOR 3.36; 95%CI 1.01–11.2; p=0.048) and mononeuritis multiplex (aOR 3.58; 95% CI [1.19–10.8]; p=0.023), and the use of RTX regimen 1 gram on days 1 and 15 (aOR 4.87; 95%CI 1.59-14.9; p=0.006) (**Table 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In conclusion, ARA detection is associated with younger age, Sjogren's syndrome and infusion-related reactions in cryolgobulinemia vasculitis, and with microscopic polyangiitis, renal involvement, and mononeuritis multiplex in AAV, with the RTX regimen of 1 gram on days 1 and 15 being associated with ARA detection in both vasculitis. Monitoring and switching to obinutuzumab may improve outcomes.

Disclosure: L. Khellaf: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **c. ricordi**: None; **s. chhun**: None; **a. gleizes**: None; **h. lobbes**: None; **c. pouchelon**: None; **m. Besse**: None; **J. Kahn**: None; **s. revuz**: None; **M. Cumin**: None; **D. Titeca-Beauport**: None; **M. Papo**: None; **P. Rémy**: None; **m. Desprets**: None; **f. garo**: None; **C. Ronsin**: None; **S. Hacein-Bey-Abina**: None; **A. Servettaz**: None; **C. Patrice**: None; **X. Puéchal**: Roche, 5; **B. Terrier**: Amgen, 1, Astra-Zeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 1605

Combined Anti-IL-5/IL-5R and Dupilumab Therapy in Eosinophilic Granulomatosis with Polyangiitis: A European Retrospective Study

Miriam Guerini[1], Pavel Novikov[2], Roberto Padoan[3], Georgina Espigol-Frigole[4], Jan Willem Cohen Tervaert[5], Vincent Grobost[6], Laurent Guilleminault[7], Jan Walter Schroeder[8], Bernhard Hellmich[9], Joana Martins-Martinho[10], Camillo Ribi[11], Mathieu Groh[12] and Benjamin Terrier[13], [1]IRCCS Policlinico S. Matteo, University of Pavia, Pavia, Italy, [2]Sechenov University, Moscow, Russia, [3]University of Padova, Padova, Italy, [4]Hospital Clnic de Barcelona, Barcelona, Spain, [5]University of Alberta, Edmonton, AB, Canada, [6]Internal medicine, CHU Clermont Ferrand Estaing, Clermont Ferrand, France, [7]CHU Toulouse, Toulouse University, Toulouse, France, [8]ASST Grande Ospedale Metropolitano Niguarda, Milano, Italy, [9]Klinik für Innere Medizin, Rheumatologie und Immunologie, medius Klinik Kirchheim, Kirchheim unter Teck, Germany, [10]ULS Santa Maria, Lisbon, Portugal, [11]Lausanne University Hospital / University of Lausanne, Lausanne, Switzerland, [12]Hôpital Foch, Suresnes, France, [13]Cochin Hospital, Paris, France

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a small-vessel vasculitis characterized by asthma, ear, nose, and throat (ENT) symptoms, eosinophilia, and systemic involvement. Despite the use of anti-interleukin (IL)-5/IL-5R therapies, asthma or primarily ENT symptoms may persist. Dupilumab (anti-IL-4Rα) is approved for severe asthma and chronic rhinosinusitis but has been associated with drug-induced eosinophilia and EGPA flares. Given their complementary mechanisms, the combination of anti-IL-5/IL-5R and dupilumab may improve disease control in patients with EGPA. We report the safety and efficacy of this off-label combination in relapsing/refractory EGPA.

Methods: This European, multicenter, retrospective study included EGPA patients fulfilling 2022 ACR/EULAR classification criteria treated with anti-IL-5/IL-5R in combination with dupilumab for relapsed or refractory disease. Complete response (CR) was defined as BVAS=0 and prednisone dose ≤4 mg/day, partial response (PR) as BVAS=0 and prednisone dose >4 mg/day. Failure was defined as inability to reduce GCs ≤7.5 mg/day due to persistently active disease, vasculitis relapse, and/or worsening of asthma or ENT symptoms, and requiring treatment escalation.

Results: Sixteen patients received the combination therapy, with mepolizumab or benralizumab in 8 cases each. Twelve patients (75%) received the addition of dupilumab to ongoing anti-IL-5/IL-5R, 6 for uncontrolled ENT symptoms, 5 for both uncontrolled ENT and asthma symptoms, and 1 for uncontrolled asthma. The remaining 4 patients (25%) received the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

addition of anti-IL-5/IL-5R to dupilumab for drug-induced eosinophilia associated with vasculitis relapse in 3 and for uncontrolled ENT symptoms/asthma in 3.

Safety analysis showed no serious adverse events, with only two patients experiencing mild-to-moderate adverse events.

Thirteen patients with ≥3 months of follow-up were analyzed for efficacy (median follow-up 6 (3-12) months). At the start of combination therapy, the median prednisone dose was 5 mg/day (0-10), decreasing to 4.38 mg/day (0-6.25) at 3 months and 3.75 mg/day (1.25-5) at 6 months. In patients with dupilumab-induced eosinophilia, the addition of anti-IL-5/IL-5R reduced eosinophil counts from 1600/μL (1082-4000) to 170/μL (90-465) at 3 months and remained 170/μL (165-175) at 6 months. No eosinophilia occurred when dupilumab was added to anti-IL-5/IL-5R.

At 3 months, 4/13 (31%) and 1/13 (8%) achieved CR and PR, respectively, while 3/13 (23%) had treatment failure. At 6 months (data available for 11 patients), 5/11 (45%) and 3/11 (27%) achieved CR and PR, respectively, and at 9 months, CR was achieved in all patients with available follow-up, except for the 3 patients with initial treatment failure.

Conclusion: The combination of anti-IL-5/IL-5R and dupilumab in this small case series was safe and appeared to be an effective option in EGPA patients with uncontrolled ENT manifestations while on anti-IL-5/IL-5R or in patients with dupilumab-induced hypereosinophilia and EGPA manifestations, with optimal response requiring at least 6 months of treatment.

Disclosure: M. Guerini: None; **P. Novikov**: None; **R. Padoan**: None; **G. Espigol-Frigole**: None; **J. Cohen Tervaert**: AbbVie/Abbott, 6, GlaxoSmithKlein(GSK), 6, Hoffmann-La Roche, 6, IDMC InflaRx, 12, Chair, Mallinckrodt Pharmaceuticals, 2, Medexus, 6, Merck/MSD, 2, Novartis, 2, Pfizer, 6, Sanofi, 6; **V. Grobost**: None; **L. Guilleminault**: None; **J. Schroeder**: None; **B. Hellmich**: CSL Vifor, 2, 6; **J. Martins-Martinho**: None; **C. Ribi**: None; **M. Groh**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 1606

One Year Real-World Effectiveness with Avacopan in Granulomatosis with Polyangiitis and Microscopic Polyangiitis in a Large Healthcare System

Naomi Patel[1], Andrew King[2], Madison Negron[3], Zachary Williams[4], Ana Fernandes[1], Nora Shepherd[2], Colebrooke Johnson[1], Guy Katz[1], Belen Arevalo Molina[1], Elizabeth Ibiloye[5], Sam Oh[6], Zachary Wallace[7] and Sebastian H Unizony[8], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Harvard Extension School, Medford, MA, [4]Massachusetts General Hospital, Nancy, KY, [5]Amgen Inc, Thousand Oaks, CA, [6]Amgen Inc, South San Francisco, CA, [7]Massachusetts General Hospital, Newton, MA, [8]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Avacopan has been approved for adjunctive use in adults with severe active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in the US. Here we describe 12-month effectiveness and safety outcomes for avacopan users in a large healthcare system.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Individuals Prescribed Avacopan for GPA/MPA

Characteristic at time of prescription	N=119
Age, years, mean (SD)	59.4 (16.2)
Female, n (%)	83 (69.8)
Race, n (%)	
Asian	7 (5.9)
Black	6 (5.0)
White	96 (80.6)
Other	9 (7.6)
Unknown	1 (0.8)
Hispanic ethnicity, n (%)	11 (9.2)
AAV status, n (%)	
Newly diagnosed	79 (66.4)
Relapsed	40 (33.6)
AAV phenotype, n (%)	
GPA	60 (50.4)
MPA	59 (49.6)
ANCA type, n (%)	
MPO-ANCA+	66 (55.5)
PR3-ANCA+	40 (33.6)
Dual positive	2 (1.7)
Negative	11 (9.2)
BVAS v3, median (IQR)	12 (8, 17)
Setting of avacopan prescription, n (%)	
Inpatient	37 (31.1)
Outpatient	82 (68.9)
Prescribing provider specialty, n (%)	
Rheumatology	60 (50.4)
Nephrology	59 (49.6)
Concomitant immunosuppression,* n (%)	
Rituximab ± csDMARD	65 (54.6)
Cyclophosphamide ± csDMARD	6 (5.0)
Rituximab and cyclophosphamide ± csDMARD	39 (32.8)
Other csDMARD	2 (1.7)
None	7 (5.9)
GPA/MPA-related cumulative GC exposure in the 3 months prior to prescription, prednisone-equivalent mg, median (IQR)	1252.6 (540.0, 3507.1)
GPA/MPA-related cumulative GC exposure in the 12 months prior to prescription, prednisone-equivalent mg, median (IQR)	2275.0 (970.0, 4100.0)

AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; BVAS v3, Birmingham Vasculitis Activity Score version 3; csDMARD, conventional synthetic disease modifying antirheumatic drug; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; IQR, interquartile range; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PR3, proteinase 3.
*Rituximab and cyclophosphamide use were considered to be baseline use if received within 5 weeks of avacopan initiation; other medications were considered if prescribed at baseline. csDMARDs included methotrexate (n=6), azathioprine (n=2), and mycophenolate (n=1).

Methods: This ongoing retrospective cohort study involves patients prescribed avacopan for GPA or MPA from 12/1/21-4/1/24. Data from 12 months pre- and post-avacopan prescription are reported. As in the ADVOCATE trial, sustained remission at month 12 is defined as a Birmingham Vasculitis Activity Score version 3 (BVAS v3) of 0 at months 6 and 12 with no glucocorticoid (GC) use for GPA/MPA for 1 month before months 6 and 12, and no relapse from months 6-12. Relapse is assessed after 1 month and is defined as: 1) ≥1 major BVAS v3 item, 2) ≥3 minor items, or 3) 1 or 2 minor items for ≥2 consecutive visits. Increase in BVAS v3 of < 3 and absence of major items defines a minor relapse; all others are defined as a major relapse. We also assessed other disease- and treatment-related outcomes, including the Glucocorticoid Toxicity Index-Metabolic Domains (GTI-MD).

Results: Among 119 patients prescribed avacopan, the mean age was 59.4 years; most were female (83, 70%), newly diagnosed (79, 66%), had GPA (60, 50%), and were MPO-ANCA+ (66, 55%) (**Table 1**). The median (IQR) baseline BVAS v3 was 12 (8, 17). Most patients received concomitant rituximab (65, 55%), cyclophosphamide (6, 5%), or both (39, 33%). Sixteen (13%) did not initiate avacopan, with the most common reasons being insurance denial (n=5) or high copay (n=3). Of the 103 (87%) initiating avacopan, organ involvement included the kidneys (58, 56%), lungs (50, 49%) and ear, nose, or throat (ENT) (43, 42%) (**Table 2**).

Table 2. Baseline Disease and Treatment-Related Characteristics of Individuals who Initiated Avacopan for GPA/MPA

Characteristic	N=103
Time from avacopan prescription to initiation, days, median (IQR)	10 (3, 22)
Initiated in ≤14 days of prescription, n (%)	68 (66.0)
Initiated in ≤21 days of prescription, n (%)	76 (73.8)
GPA/MPA-related GC use at baseline, n (%)	92 (89.3)
Prednisone-equivalent GC dose at time of initiation among those on GCs, mg, median (IQR)	40 (20, 60)
BVAS v3 at prescription, median (IQR)	12 (8, 17)
Organ involvement* at initiation, n (%)	
Kidney	58 (56.3)
Lung	50 (48.5)
Ear, nose, or throat	43 (41.8)
≥1 dialysis session at or within 30 days following initiation, n (%)	10 (9.7)
Baseline eGFR among those with kidney involvement and not on dialysis (n=49), ml/min/1.73m², median (IQR)	35 (20, 57)

BVAS v3, Birmingham Vasculitis Activity Score version 3; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis
*Defined by presence of any BVAS v3 criterion for respective organ system

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Clinical Outcomes Among Those who Initiated Avacopan for GPA/MPA

General Effectiveness and Safety	N=95*
Remission at month 6#	61 (64.2)
Relapse between months 6-12#, n (%)	3 (3.2)
Major, n (%)	1 (1.1)
Minor, n (%)	2 (2.1)
Sustained remission at month 12#, n (%)	58 (61.1)
BVAS v3 of 0 at month 12, n (%)	90 (94.7)
GC-free at month 12, n (%)	83 (87.4)
Days to GC discontinuation among those off GCs at month 12, median (IQR) (n=72)	84 (56, 175)
≤5mg prednisone equivalent daily dose at month 12 among those on GCs for GPA/MPA at 12 months, n (%) (n=12)	3 (25)
Cumulative GC exposure between initiation and month 12, prednisone-equivalent mg, median (IQR)	1050 (280, 2030)
Remaining on avacopan at month 12, n (%)	38 (40.0)
Days to avacopan discontinuation among those off at month 12, median (IQR)	203 (140, 324)
Reasons for avacopan discontinuation (n=57)	
Completed provider's planned treatment course, n (%)	33 (57.9)
Days to discontinuation among those who completed planned course, median (IQR)	273 (181, 365)
Self-discontinued, n (%)	3 (5.3)
Aminotransferase elevation, n (%)	3 (5.3)
Other adverse event, n (%)	11 (19.3)
Other or unknown, n (%)	7 (12.3)
Glucocorticoid Toxicity	
GTI-MD Cumulative Worsening Score (CWS), median (IQR)	29.0 (19.0, 51.0)
GTI-MD Aggregate Improvement Score (AIS), median (IQR)§	0.0 (-19.0, 23.0)
Blood Pressure Domain AIS >0, n (%)	39 (41.1)
Body Mass Index Domain AIS >0, n (%)	20 (21.1)
Lipid Metabolism Domain AIS >0, n (%)	17 (17.9)
Glucose Tolerance Domain AIS >0, n (%)	5 (5.3)
Outcomes Among Those with Specific Baseline Organ Involvement	
Sustained remission among those with kidney involvement#, n (%) (n=54)	37 (68.5)
eGFR among those not on dialysis at month 12 (n=49), ml/min/1.73m², median (IQR)	44 (29, 71)
Sustained remission among those with ENT involvement#, n (%) (n=42)	25 (59.5)
Sustained remission among those with lung involvement#, n (%) (n=44)	26 (59.1)

BVAS v3, Birmingham Vasculitis Activity Score version 3; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; GTI-MD, Glucocorticoid Toxicity Index-Metabolic Domains; ENT, ear, nose, or throat

*Table includes those with available data at month 12, excluding 4 people who died by month 12 (with causes of COVID-19 infection, diffuse alveolar hemorrhage due to AAV, necrotizing bacterial pneumonia, and decompensated heart failure) and 4 who were lost to follow-up

#Sustained remission defined as remission at months 6 and 12 (BVAS v3 of 0 and no GCs for GPA/MPA within 1 month before month 6 or month 12, respectively), without relapse between months 6 and 12. Relapse was defined as the return (after prior improvement) of vasculitis activity by 1 or 2 minor BVAS v3 items for ≥2 consecutive clinical visits, ≥1 major BVAS v3 item, ≥3 minor BVAS v3 items. Increase in the BVAS v3 of <3 and absence of major items defines a minor relapse; all others are defined as major.

§Aggregate Improvement Scores are the sum of scores from 0-3, 3-6, & 6-12 months; negative scores indicate improvement, zero indicates no change, and positive scores indicate net worsening over 12 months.

Among 95 with available 12-month follow-up data, 61 (64%) were in remission at month 6, while at month 12, 90 (95%) had a BVAS v3=0, 83 (87%) were GC-free, and 58 (61%) had sustained remission (**Table 3**). Three patients relapsed (1 major, 2 minor) between months 6 and 12. Overall, 38 (40%) were still on avacopan at 12 months and 57 (60%) discontinued therapy before 12 months mostly due to completion of the provider's planned treatment course (33/57, 58%) or adverse events (14/57, 25%). The median (IQR) cumulative prednisone-equivalent GC exposure over 12 months was 1050 (280, 2030) mg. Among 84 patients on GCs at baseline, 72 discontinued GCs after a median (IQR) of 84 (56, 175) days, and 12 remained on GCs at 12 months (range of 1.25-20 prednisone-equivalent mg daily). Sustained remission was similar in those with baseline kidney, lung, or ENT involvement.

The most common GTI-MD domain with net worsening (i.e., Aggregate Improvement Score [AIS] > 0) was Blood Pressure (41%), followed by Body Mass Index (21%), Lipid Metabolism (18%), & Glucose Tolerance (5%). The majority (53, 56%) had no net worsening of metabolic GC toxicity over 12 months (i.e., AIS ≤0), indicating either net improvement or no change.

Conclusion: In this real-world cohort of individuals with GPA or MPA, among those with 1-year follow-up, most avacopan users discontinued GCs within 3 months and had sustained remission at 12 months, and a minority had avacopan-related adverse events and/or worsening of GC toxicity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Patel: Amgen, 5; **A. King**: None; **M. Negron**: None; **Z. Williams**: None; **A. Fernandes**: None; **N. Shepherd**: None; **C. Johnson**: None; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **B. Arevalo Molina**: Amgen, 2; **E. Ibiloye**: Amgen, 3, 11, AstraZeneca, 3, 11; **S. Oh**: Amgen, 3, 11; **Z. Wallace**: Amgen, 3; **S. Unizony**: Harvard Pilgrim Healthcare, 2, IQVIA, 2, Sanofi, 2.

Abstract Number: 1607

Antibiotic Prophylaxis During Treatment of Anca-associated Vasculitis with Rituximab: Data from a Multicenter Cohort

Natasha Le Blanc[1], Lillian Barra[2], Sasha Bernatsky[3], Alison Clifford[4], Mojtaba Dabaghjamanesh[5], Natasha Dehghan[6], Aurore Fifi-Mah[7], Jean-Paul Makhzoum[8], Nataliya Milman[9], Medha Soowamber[10], Nader Khalidi[11], Christian Pagnoux[10], Rosalie-Selene Meunier[12], Jan Willem Cohen Tervaert[4], Elaine Yacyshyn[4] and Arielle Mendel[13], [1]McGill University, Montreal, Canada, [2]Western University, London, ON, Canada, [3]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [4]University of Alberta, Edmonton, AB, Canada, [5]Self employed, Richmond Hill, ON, Canada, [6]University of British Columbia - Vancouver, Vancouver, BC, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]Universite de Montreal, Montreal, Canada, [9]the Ottawa Hospital, Ottawa, ON, Canada, [10]Mount Sinai Hospital, Toronto, ON, Canada, [11]McMaster University, Hamilton, ON, Canada, [12]Hopital du Sacre-Coeur-de-Montreal, Montreal, QC, Canada, [13]McGill University Health Centre, Montréal, QC, Canada

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Antibiotic prophylaxis is recommended during initial treatment of ANCA-associated vasculitis (AAV). We assessed characteristics associated with prophylaxis within a Canadian multicenter AAV cohort starting rituximab (RTX) for either induction or maintenance of remission.

Methods: We performed a secondary analysis of baseline characteristics from the Biosimilars in ANCA-associated Vasculitis compared to the Originator (BRAVO) cohort, including adults with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who started RTX induction or maintenance (either the originator or a biosimilar) at cohort entry. We stratified characteristics (at time of starting RTX induction or maintenance, as applicable) according to concurrent antibiotic prophylaxis (e.g. trimethoprim sulfamethoxazole [TMP-SMX], dapsone, atovaquone), and compared groups using 95% confidence interval (CI) for the differences in mean or proportion, or the Mann Whitney *U* test as applicable. Characteristics of interest included demographics, current prednisone dose, disease activity, disease duration and prior relapse. Univariable and multivariable logistic regressions assessed the association of covariates of interest with prophylaxis.

Results: Of the 200 participants in BRAVO, 126 initiated induction and 58 initiated maintenance at baseline. [Table 1]. The proportion taking prophylaxis at the start of induction (81%) and maintenance (79%) was similar, whereas 98 (96%) of the induction group and 39 (85%) of the maintenance group were receiving prednisone at baseline. TMP-SMX was the most commonly used antibiotic during induction (95%) and maintenance (89%), with the remainder being primarily atovaquone (2% induction, 11% maintenance) and dapsone (2% in induction).

In the induction group, any prednisone use (OR 4.9; 95% CI 1.1-21.4), prednisone ≥20 mg/day (OR 6.5; CI 2.5-17.0) and baseline Birmingham Vasculitis Activity Score (BVAS) (OR for each point 1.2; 95 CI 1.1-1.3) were associated with antibiotic prophylaxis, while use of other concurrent immunosuppressants (OR 0.3; 95% CI 0.1-0.8) and having ≥1 prior relapse (0.3 OR; 95% CI 0.1-0.9) were negatively associated with prophylaxis. In multivariable analyses, daily prednisone dose ≥20 mg

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of the BRAVO cohort at the time of initiating induction or maintenance rituximab according to antibiotic prophylaxis

	Induction (n=126)		Maintenance (n=58)	
	prophylaxis (n=102)	prophylaxis (n=24)	prophylaxis (n=46)	prophylaxis (n=12)
Age, mean (SD)	54.8 (19.7)	60.2 (12.7)	58.8 (15)	53.8 (14)
Female sex, n (%)	54 (53)*	18 (75)*	22 (48)	3 (25)
White race/ethnicity, n (%)	82 (80)	16 (70)	37 (80)	9 (75)
Highest education				
Post-secondary	57 (56)	17 (71)	31 (67)	6 (50)
< Post-secondary	31 (30)	3 (13)	10 (22)	4 (33)
Unknown	14 (14)	4 (16)	5 (11)	2 (17)
Diagnosis (n,%)				
GPA	69 (68)	19 (79)	32 (70)	8 (67)
MPA	33 (32)	5 (21)	14 (30)	4 (33)
Disease duration, median years (IQR)	0.63 (0.11-5.2)**	4.2 (0.9-10.1)**	0.78 (0.6-4.4)	2.4 (1.2-8.8)
≥ 1 prior relapse, n (%)	50 (49)*	18 (75)*	14 (30)	4 (33)
Manifestations at diagnosis/flare, n (%)				
Ear, nose, or throat	57 (56)	13 (54)	24 (52)	7 (58)
Pulmonary	56 (55)	11 (46)	32 (70)	6 (50)
Alveolar hemorrhage	29 (28)	4 (17)	18 (39)	4 (33)
Glomerulonephritis	55 (54)	8 (33)	29 (63)	6 (50)
Hemodialysis or creatinine > 500 µmol/L	8 (7)	2 (8)	7 (15)	2 (17)
Prior treatment, n (%)				
Cyclophosphamide	37 (36)	12 (50)	29 (63)	7 (58)
RTX induction	14 (14)	6 (25)	17 (37)	5 (42)
BVAS, mean (SD)	14 (7.5)*	7.6 (5.9)*	0.98 (2.5)*	0 (0)*
VDI, mean (SD)	1.58 (2)	2.04 (1.6)	2.7 (2.3)	2.5 (2.6)
Prednisone use (yes/no), n (%)	98 (96)*	20 (83)*	39 (85)*	6 (50)*
Prednisone median mg/day (IQR)	40.0 (20-60)**	10.0 (5-30.0)**	5 (5-10)	2.5 (0-10)
Other current immunosuppressant	13 (13)*	8 (33)*	3 (7)	1 (8)

Abbreviations: SD, standard deviation; IQR, interquartile range; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; RTX, rituximab; BVAS, Birmingham Vasculitis Activity Score; VDI, Vasculitis Damage Index

*the 95% CI for difference in mean or proportion excludes the null value

** p<0.05 (Mann-Whitney-U test)

(adjusted OR 3.4; 95% CI 1.2-10.0) and BVAS (aOR 1.1, 95% 1.0-1.2) remained associated with prophylaxis. In the maintenance group, prednisone use was also associated with prophylaxis in adjusted analyses (aOR 6.1, 95% CI 1.3-27.0).

Conclusion: In this multicenter cohort initiating RTX for induction or maintenance, 80% of the participants were taking antibiotic prophylaxis, which is higher than reported in other cohorts. During the induction and maintenance period, concurrent prednisone was associated with prophylaxis, as was higher disease activity during induction. Our findings provide additional insight into the patterns of antibiotic prophylaxis use in AAV.

Table 2. Univariable and multivariable logistic regression for factors associated with antibiotic prophylaxis, Induction group (n=126)

	Univariable		Multivariable	
	Odds ratio	95% CI	Odds ratio	95% CI
Age (years)	1	0.9-1.0	1	0.9-1.0
Female sex	0.4	0.1-1.0	0.4	0.1-1.2
White race/ethnicity	1.8	0.7-5.0	-	-
Post secondary education	0.35	0.1-1.1	-	-
Disease duration (years)	0.9	0.9-1.0	-	-
≥ 1 prior relapse	**0.3**	**0.1-0.9**	0.7	0.2-2.2
BVAS	**1.2**	**1.1-1.3**	**1.1**	**1.01-1.2**
VDI	0.9	0.7-1.1	-	-
Prednisone use (yes/no)	**4.9**	**1.1-21.3**	-	-
Prednisone ≥ 20mg per day (vs. none)	**6.5**	**2.5-17.0**	**3.4**	**1.6-10.0**
Other current immunosuppressant	**0.3**	**0.1-0.8**	0.4	0.1-1.4

Abbreviations: SD, standard deviation; IQR, interquartile range; BVAS, Birmingham Vasculitis Activity Score; VDI, Vasculitis Damage

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Univariable and multivariable logistic regression for factors associated with antibiotic prophylaxis, Maintenance group (n= 58)

	Univariable		Multivariable	
	Odds ratio	95% CI	Odds ratio	95% CI
Age (years)	1	1.0-1.1	1	1.0-1.1
Female sex	2.8	0.7-11.5	3.6	0.7-17.7
White race/ethnicity	1.4	0.3-6.1	-	-
Post secondary education	1.4	0.4-4.6	-	-
Disease duration (years)	1	1.0-1.1	-	-
≥ 1 prior relapse	0.9	0.2-3.4	-	-
BVAS	50.8	0.0-99	-	-
VDI	1	0.8-1.4	-	-
Prednisone use (yes/no)	5.6	1.4-22.3	6.1	1.4-27.0
Other current immunosuppressant	0.8	0.1-8.1	-	-

Abbreviations: SD, standard deviation; IQR, interquartile range; BVAS, Birmingham Vasculitis Activity Score; VDI, Vasculitis Damage Index

Disclosure: N. Le Blanc: None; **L. Barra**: GlaxoSmithKlein(GSK), 6, Otsuka, 5, 6, Pfizer, 5, 6; **S. Bernatsky**: None; **A. Clifford**: AbbVie/Abbott, 1, UCB, 1, 6; **M. Dabaghjamanesh**: None; **N. Dehghan**: None; **A. Fifi-Mah**: frenesius-kabi, 12, Travel, Janssen, 6, Novartis, 6, Organon, 6, Otsuka, 6, Pfizer, 5, 6; **J. Makhzoum**: AbbVie/Abbott, 12, Investigator, Astra-Zeneca, 6, 12, Investigator, GlaxoSmithKlein(GSK), 6, Janssen, 12, Investigator, Novartis, 12, Investigator, Otsuka, 6, Roche, 6, Sanofi, 6; **N. Milman**: Abbvie, 1, Boehringer Ingelheim, 1, 6, Fresenium-Kabi, 1, 6, Gilead, 1, GlaxoSmithKlein(GSK), 6, Novartis, 1, Otsuka, 1, Sandoz, 1, TEVA, 1; **M. Soowamber**: AbbVie/Abbott, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Otsuka, 1, 6; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 6, Mallinckrodt, 6, NS Pharma, 5, Otsuka, 6, Roche, 2, Sanofi, 5; **C. Pagnoux**: AstraZeneca, 1, ChemoCentryx, 1, GlaxoSmithKlein(GSK), 1, 5, InflaRx GmbH, 1, otsuka, 1, 5, Pfizer, 1, 5, Roche, 1, 5; **R. Meunier**: AstraZeneca, 12, Investigator, Novartis, 12, Investigator; **J. Cohen Tervaert**: AbbVie/Abbott, 6, GlaxoSmithKlein(GSK), 6, Hoffmann-La Roche, 6, IDMC InflaRx, 12, Chair, Mallinckrodt Pharmaceuticals, 2, Medexus, 6, Merck/MSD, 2, Novartis, 2, Pfizer, 6, Sanofi, 6; **E. Yacyshyn**: None; **A. Mendel**: None.

Abstract Number: 1608

Efficacy of Anti-IL-5/R Therapies on Specific Disease Manifestations of Eosinophilic Granulomatosis with Polyangiitis

Peter Merkel[1], Arnaud Bourdin[2], Bernhard Hellmich[3], Nader Khalidi[4], David Jackson[5], David Jayne[6], Parameswaran Nair[7], Christian Pagnoux[8], Ulrich Specks[9], Benjamin Terrier[10], Lena Börjesson Sjö[11], Priya Jain[12], Aadarsh Lal[13], Sofia Necander[14], Claire Walton[15] and Michael Wechsler[16], [1]University of Pennsylvania, Philadelphia, PA, [2]Department of Respiratory Diseases, Montpellier University Hospitals, Arnaud de Villeneuve Hospital, Montpellier, France, [3]Klinik für Innere Medizin, Rheumatologie, Pneumologie, Nephrologie und Diabetologie, Medius Kliniken, Akademisches Lehrkrankenhaus der Universität Tübingen, Kirchheim unter Teck, Germany, [4]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Canada, [5]Guy's Severe Asthma Centre, Guy's and St Thomas' NHS Trust, London, and School of Immunology and Microbial Sciences, King's College London, London, United Kingdom, [6]University of Cambridge, Cambridge, United Kingdom, [7]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, ON, Canada, [8]Mount Sinai Hospital, University Health Network, Toronto, and Canadian Vasculitis Research Network (CanVasc), Toronto, ON, Canada, [9]Mayo Clinic, Rochester, MN, [10]Cochin Hospital, Paris, France, [11]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca,, Gothenburg, Sweden, [12]BioPharmaceuticals Medical, AstraZeneca, Cambridge, United Kingdom, [13]Respiratory & Immunology, AstraZeneca, Bengaluru, Karnataka, India, [14]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [15]Late-Stage Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom, [16]Department of Medicine, National Jewish Health, Denver

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Results from the 1-year double-blind period and first year of the open-label extension (OLE) of the MANDARA trial (NCT04157348) demonstrated that over 60% of patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA), with active non-severe disease at baseline, achieved remission. Additionally, more than 40% discontinued oral glucocorticoids after treatment with anti-interleukin-5/Receptor (anti-IL-5/R) therapies. This analysis focuses on changes in individual items of active disease and long-term damage in EGPA over the same two-year period.

Methods: Patients (without active life- or organ-threatening manifestations at the start of the trial) who completed the randomized double-blind period, could enter the OLE, during which they continued benralizumab (benra/benra n=66) or switched from mepolizumab to benralizumab (mepo/benra n=62). The protocol encouraged reduction in oral glucocorticoids. Disease activity was measured by the Birmingham Vasculitis Activity Score (BVAS), while items of damage were measured by the Vasculitis Damage Index (VDI) for the trial participants over two years (up to Week 104).

Results: In total, 128 patients entered the OLE. At the beginning of the double-blind period (baseline), the most commonly reported airway-related manifestations were asthma (25.8% of patients), paranasal sinus involvement (15.6%), and bloody nasal discharge/crusts/ulcers/granulomata (14.1%). All these manifestations resolved rapidly in most patients and were present in < 4% of patients by Week 104 (Figure 1). Sensory peripheral neuropathy (9.4%), arthralgia/arthritis (7.8%), and myalgia (6.3%) were the most reported non-airway manifestations at baseline, and their frequency also decreased rapidly to < 3% by Week 104. Cutaneous (3.9%) and renal manifestations (1.6%) were infrequent at baseline and either resolved

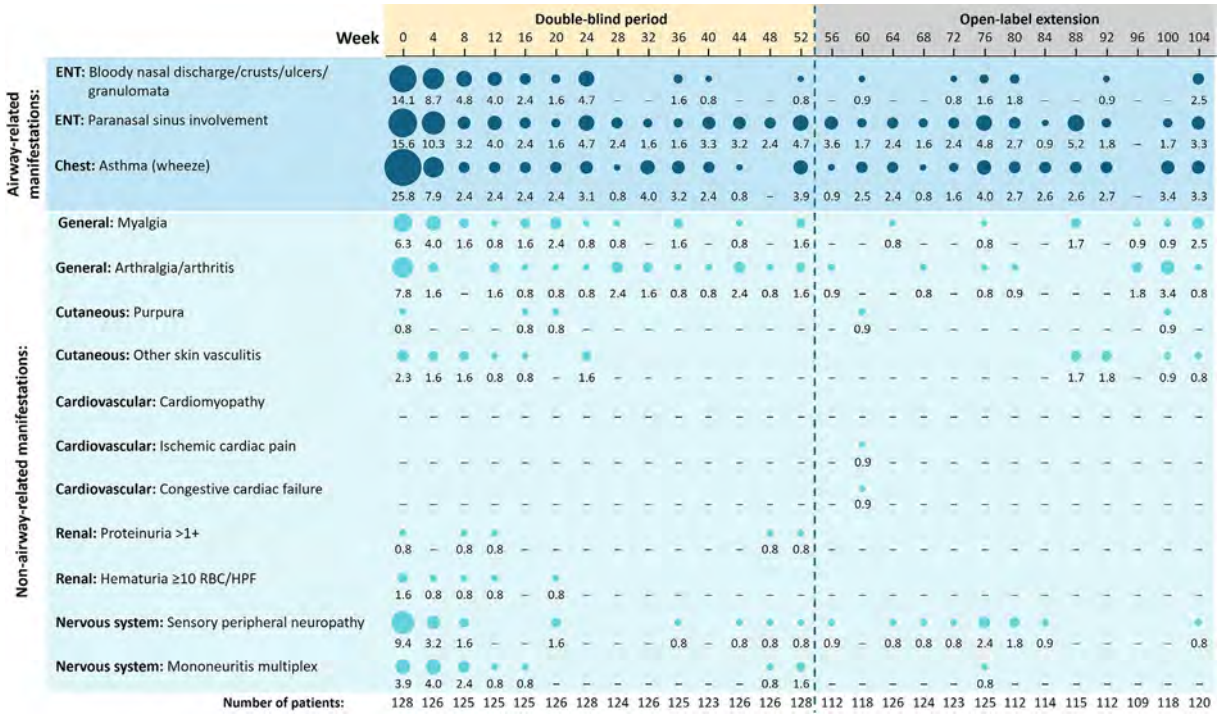


Figure 1. Summary of select manifestations of eosinophilic granulomatosis with polyangiitis up to Week 104 of the MANDARA trial Corresponding percentage of patients is shown beneath each bubble. Manifestations are categorized according to the BVAS. BVAS, Birmingham Vasculitis Activity Score; ENT, ear, nose, and throat; HPF, high power field; RBC, red blood cells.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

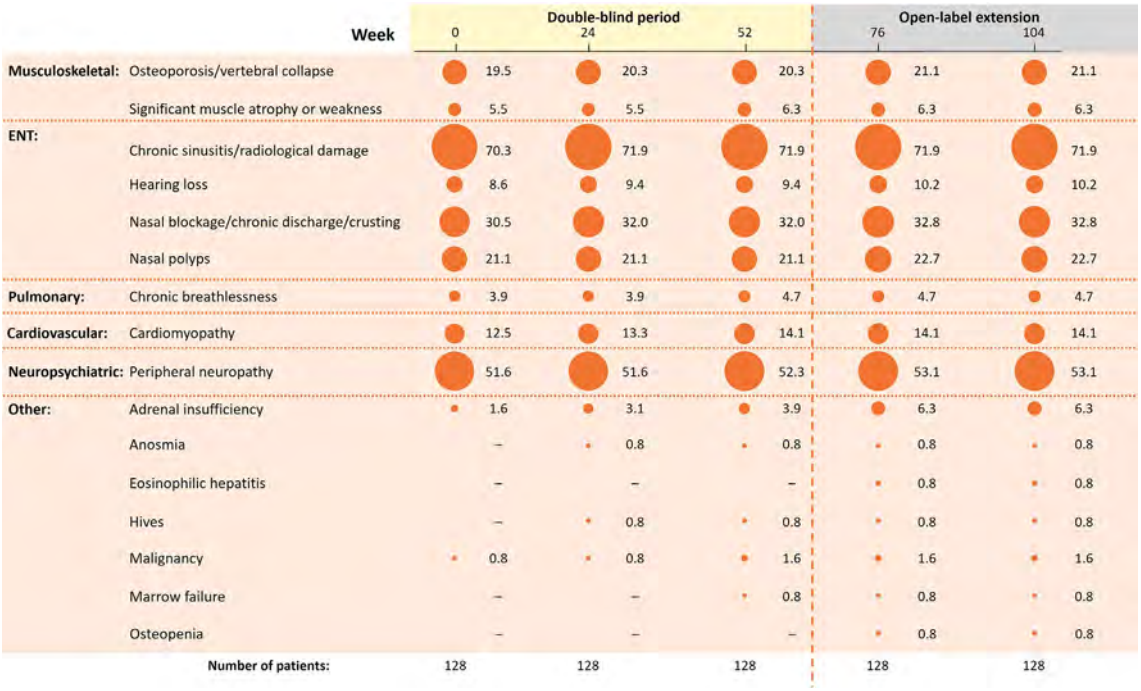


Figure 2. Summary of items of damage in patients with eosinophilic granulomatosis with polyangiitis up to Week 104 of the MANDARA trial Corresponding percentage of patients is shown beneath each bubble, as measured by VDI. ENT, ear, nose, and throat; VDI, Vasculitis Damage Index.

or affected < 1% of patients by Week 104. Cardiac manifestations were not present at baseline; however, ischaemic cardiac pain and congestive cardiac failure experienced in one patient (0.9%), were present at Week 60.

Overall, there were 29 new items of damage in 25 patients recorded up to Week 104, with 18 occurring in the double-blind period, and 11 during the first year of the OLE (Figure 2).

Conclusion: Among patients with EGPA, after two years of treatment with anti-IL-5/R therapies, mostly associated with substantial reductions in oral glucocorticoids, there is little disease progressive organ damage, suggesting a durable effect of treatment with mepolizumab and benralizumab for reducing both airway-and non-airway-related manifestations of disease.

Disclosure: P. Merkel: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **A. Bourdin**: Amgen, 2, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Chiesi, 2, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Novartis, 2, 6, Sanofi Regeneron, 2, 6; **B. Hellmich**: AbbVie, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Chugai, 2, 6, CSL Vifor, 2, 6, GlaxoSmithKlein(GSK), 2, 6, InflaRx, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Phadia, 2, 6, Roche, 2, 6; **N. Khalidi**: AbbVie/Abbott, 2, 5, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 5, GlaxoSmithKlein(GSK), 2, 6, Mallinckrodt, 2, NS Pharma, 5, Otsuka, 2, 6, Roche, 2, 6, Sanofi, 2, 5; **D. Jackson**: AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 6, Chiesi, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Sanofi Regeneron, 2, 6; **D. Jayne**: Alentis, 2, 11, Amgen, 2, 6, AstraZeneca, 1, 2, 6, Aurinia, 1, 11, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, ChemoCentryx, 2, 6, Chinook, 1, Chugai, 2, 6, CSL Vifor, 2, 6, Fate, 2, GlaxoSmithKlein(GSK), 2, 6, GSK, 1, Hansa, 1, Novartis, 1, 2, 6, Otsuka, 2, Roche, 2, 6, Takeda, 1, 2, 6; **P. Nair**: Arrowhead Pharmaceuticals, 6, AstraZeneca, 5, 6, CSL Behring, 6, Cyclomedica, 5, Equillium, 5, Foresee, 5, Genentech, 5, GlaxoSmithKlein(GSK), 6, Sanofi, 5, 6, Teva, 5; **C. Pagnoux**: amgen, 1, 2, 6, Astra zeneca, 1, 6, csl vifor, 1, 2, 6, gsk, 1, 2, 6, Novartis, 2, ns

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pharma, 1, otsuka, 1, 2, 5, 6, Pfizer, 2, 6; **U. Specks**: Amgen, 1, 2, 5, Argenx, 2, AstraZeneca, 1, 5, Boehringer-Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 5, CSL Vifor, 1, Genentech, 5, GlaxoSmithKlein(GSK), 5, Mayo Foundation for Education and Research, 9, Melodia Therapeutics, 2, NorthStar Medical Radioisotopes, 5, Novartis, 1, 2, 5, NS Pharma, 5, UpToDate, 9; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **L. Börjesson Sjö**: AstraZeneca, 3, 11; **P. Jain**: AstraZeneca, 3, 11; **A. Lal**: AstraZeneca, 3, 11; **S. Necander**: AstraZeneca, 3, 11; **C. Walton**: AstraZeneca, 3, 11; **M. Wechsler**: allakos, 1, 2, 6, Amgen, 1, 2, 6, Areteia Therapeutics, 1, 2, 6, Arrowhead Pharmaceuticals, 1, 2, 6, AstraZeneca, 1, 2, 6, Avalo Therapeutics, 1, 2, 6, Celldex, 1, 2, 6, Connect Biopharma, 1, 2, 6, Eli Lilly, 1, 2, 6, Equillium, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Incyte, 1, 2, 6, Kinaset, 1, 2, 6, Kymera, 1, 2, 6, Merck, 1, 2, 6, Phylaxis, 1, 2, 6, Pulmatrix, 1, 2, 6, Rapt Therapeutics, 1, 2, 6, Recludix Pharma, 1, 2, 6, Regeneron Pharmaceuticals, 1, 2, 6, Roche/Genentech, 1, 2, 6, Sanofi/Genzyme, 1, 2, 6, Sentien, 1, 2, 6, Sound Biologics, 1, 2, 6, Tetherex Pharmaceuticals, 1, 2, 6, Uniquity Bio, 1, 2, 6, Upstream Bio, 1, 2, 6, Verona Pharma, 1, 2, 6, Zurabio, 1, 2, 6.

Abstract Number: 1609

A Multicenter Prospective Longitudinal Observational Study to Determine Safety of Extended Treatment with Rituximab in Maintaining Remission in Patients with ANCA Associated Vasculitis (AAV) - An Interim Analysis

Ravi Kumar U[1], Anoop Chitrabhanu[2], Ramya Janardana[3], Avinash Jain[4], Nitty Mathews[5], Rutvi Dave[5], Prabhu Vasantha Kumar[6], ashish mathew[5], john mathew[5], Prasanna Samuel[5], Arul Rajamurugan[2], Vineeta Shobha[3] and ruchika goel[5], [1]Christian Medical college, Vellore, India, Bengaluru, Karnataka, India, [2]Madras Medical College, Chennai, India, Chennai, Tamil Nadu, India, [3]St. John's Medical College, Bengaluru , India, Bangalore, Karnataka, India, [4]SMS Medical College and Hospital, Jaipur, India, JAIPUR, Rajasthan, India, [5]Christian Medical college , Vellore , India, Vellore, Tamil Nadu, India, [6]Christian Medical College, Vellore, Tamil Nadu, India, Vellore, Tamil Nadu, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

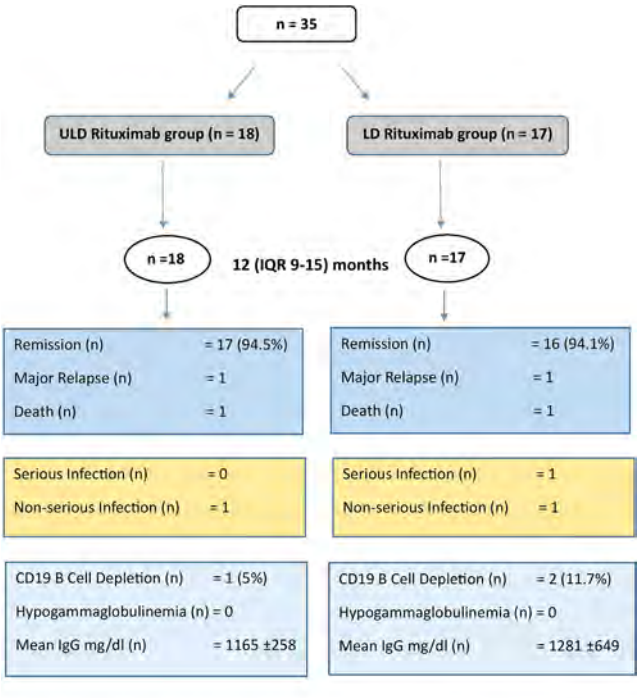
Background/Purpose: Rituximab (RTX) has been shown to achieve high remission-induction and sustained maintenance rates across multiple studies and clinical trials in patients with AAV. The optimal dose and duration of rituximab for maintenance of remission in ANCA vasculitis (AAV) remains a matter of debate. In this interim analysis of an ongoing study, we aimed to compare the relapse rate, B cell depletion rate and hypogammaglobulinemia after receiving fixed protocol ultra-low dose (200mg, ULD biannually) and low dose (500mg, LD biannually) rituximab for maintenance of remission in patients with AAV.

Methods: Patients satisfying ACR / EULAR criteria for either Granulomatosis with polyangiitis (GPA) or Microscopic polyangiitis (MPA), in complete remission and receiving rituximab maintenance therapy for > 12 months, were recruited across 4 centres in India between 1st April 2023 - 1st February 2025. Based on the dose of maintenance rituximab used as per physician's discretion, the patients were subdivided into either LD or ULD group. Details of clinical presentation, disease activity as assessed by BVASvs3 and laboratory investigations were collected prospectively at recruitment (T0), 3 monthly follow up until the last follow up visit or relapse whichever occurred earlier. Remission was defined as Birmingham Vasculitis activity score (new/worsening) (BVAS) = 0 while relapses were defined as (BVAS) ≥ 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table-1: Baseline clinical and laboratory details of the patients with AAV treated with ULD and LD maintenance rituximab, *NS-Not significant

VARIABLE	ULD Group (n = 18)	LD group (n = 17)	P value
Age at diagnosis, mean (years)	34 ± 11.2	45 ± 14.1	0.01
Disease duration, median (years, IQR)	4 (3-6)	2 (6-12)	0.01
Gender F/M, (n)	12/6	11/6	-
Diagnosis GPA/MPA., (n)	17/1	13/4	-
Mean BVAS at diagnosis	12.3 ± 7.9	11.4 ± 9.2	NS
Organ involvement at diagnosis (n)			
1. ENT	16	12	NS
2. Eye	7	5	NS
3. Constitutional	10	8	NS
4. Musculoskeletal	6	7	NS
5. Renal	9	7	NS
6. CNS	1	1	NS
7. PNS	4	7	NS
8. Pulmonary	13	12	NS
9. Cardiac	0	1	NS
10. GIT	4	1	NS
11. Cutaneous	8	5	NS
Laboratory parameters			
1. Mean IgG, mg/dl(T0)	1215.5 ± 339	1240.8 ± 501	NS
2. Mean CD19 B cell count(T0)	100.2 ± 105.6	122.7 ± 179.9	NS
3. Mean CD19 B cell percentage (T0)	4.4 ± 4.5	5.9 ± 7.6	NS
Treatment history -Prior Induction (n)			
1. Cyclophosphamide	7	5	NS
2. Mycophenolate	7	7	NS
3. Rituximab	11	12	NS
Mean Steroid dosage mg/day (T0)	0.8±2.2	0.6±1.6	NS
Mean cumulative Rituximab dose in mg (T0)	3405 ± 1360	3294 ± 1263	NS



*B cell depletion defined as peripheral CD19+ B cell ≤ 0.01% of total lymphocytes

Figure-1: Flow chart depicting outcomes of patients with AAV treated with ULD and LD maintenance rituximab

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 35 patients (GPA= 30, MPA = 5) recruited, 18 and 17 patients received ULD and LD maintenance rituximab respectively. The clinical details at diagnosis and T0 visits are depicted in (Table-1). All the parameters at diagnosis except age and disease duration were similar in both groups (Table-1).

During median follow-up of 12 (IQR 9-15) months (Figure 1), 1 patient given LD rituximab had major flare with renal involvement (BVAS=11) at 6 months while another 1 patient developed sepsis at 15 months follow up and died. Among patients receiving ULD rituximab, one developed exacerbation of colitis and succumbed. None of the patients in either group developed hypogammaglobulinemia during follow up. The CD19 B cell count, and IgG levels at the last visit did not differ significantly between LD and ULD group.

Conclusion: In this proof-of-concept study, frequency of relapse, mortality, B cell depletion and adverse events were comparable between both LD and ULD rituximab group.

Disclosure: R. Kumar U: None; **A. Chitrabhanu**: None; **R. Janardana**: None; **A. Jain**: None; **N. Mathews**: None; **R. Dave**: None; **P. Vasantha Kumar**: None; **a. mathew**: None; **j. mathew**: None; **P. Samuel**: None; **A. Rajamurugan**: None; **V. Shobha**: None; **r. goel**: None.

Abstract Number: 1610

Early Mepolizumab Initiation Enables High Glucocorticoid and Immunosuppressant Discontinuation Rates in EGPA: A Retrospective Cohort Study of 35 Patients

Takashi Yamane[1], Ayaka Inoue[2], Noriaki Yasuda[2], Takahisa Ohnishi[3] and Akira Hashiramoto[4], [1]Kakogawa Central City Hospital, Kobe, Hyogo, Japan, [2]Kakogawa Central City Hospital, Kakogawa, Japan, [3]Kakogawa Central City Hospital, Kobe, Japan, [4]Department of Biophysics, Kobe University Graduate School of Health Sciences, Kobe, Japan

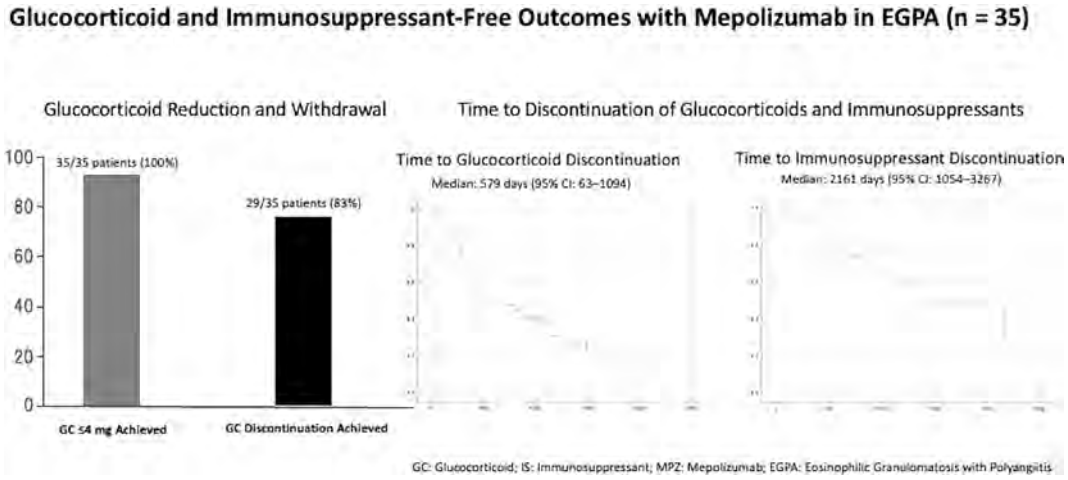
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

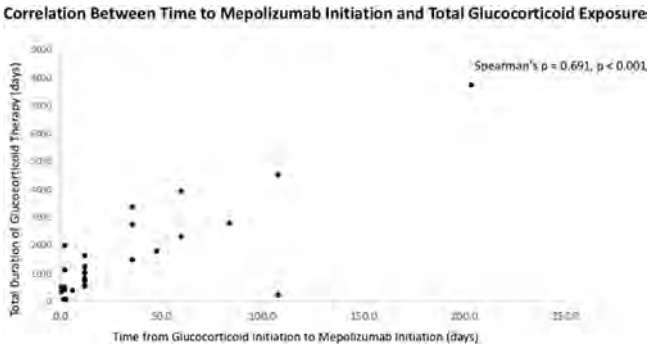
Background/Purpose: Mepolizumab (MPZ), an anti–interleukin-5 monoclonal antibody, has shown efficacy in reducing glucocorticoid (GC) dosage and sustaining remission in eosinophilic granulomatosis with polyangiitis (EGPA). This study investigated real-world outcomes of GC and immunosuppressant (IS) discontinuation, and the clinical predictors of successful shift to MPZ monotherapy.

Methods: We conducted a retrospective cohort study of 35 EGPA patients treated with MPZ and GC for ≥48 weeks. Patients were stratified by antineutrophil cytoplasmic antibody (ANCA) status and IS use. Outcomes included the proportion of patients achieving GC ≤4 mg/day and GC/IS discontinuation. GC exposure, time to withdrawal, and predictors were analyzed using Wilcoxon signed-rank, Mann–Whitney U, log-rank tests, and Cox proportional hazards models. Correlations were assessed by Spearman's coefficient.

Results: All patients (35/35) achieved GC tapering to ≤4 mg/day. GC was completely discontinued in 29 patients (83%), and 13 (37%) discontinued both GC and IS, achieving sustained MPZ monotherapy. The median time to GC-free status was 579 days (95% CI: 63–1094), while the median time to IS-free status was 2161 days (95% CI: 1054–3267). A significant

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





negative correlation was observed between time from GC initiation to MPZ initiation and total GC duration (ρ = 0.691, p < 0.001), suggesting the benefit of early MPZ initiation. ANCA-negative patients achieved GC-free status more rapidly than ANCA-positive patients (p = 0.038). IS use did not significantly affect GC discontinuation time, though non-IS users tended to discontinue GC earlier (p = 0.040).

Predictors of Combined Glucocorticoid and Immunosuppressant Discontinuation Under Mepolizumab Monotherapy

At onset	Univariate HR (95%CI)	P	Multivariate HR (95%CI)	P
Sex(female)	**2.2(1.0-4.5)**	**0.007**	1.3(0.5-3.2)	0.553
Age	1.0(0.9-1.0)	0.486		
ANCA positive	0.7(0.3-1.6)	0.386		
Eos	1.0(1.0-1.0)	0.360		
CRP	0.9(0.8-1.0)	0.079		
FFS	0.7(0.4-1.1)	0.121		
Nasal	1.8(0.8-3.9)	0.155		
Asthma	2.0(0.5-8.9)	0.352		
Neurological	**0.3(0.1-0.8)**	**0.021**	0.3(0.12-0.9)	0.035
Cardiovasular	1.4(0.5-4.1)	0.533		
Renal	2.3(0.9-5.6)	0.078		

At MPZ initiation	Univariate HR (95%CI)	P	Multivariate HR (95%CI)	P
Onset to MPZ	0.9(0.9-1.0)	0.403		
History of relapse	**0.4(0.2-0.9)**	**0.036**	0.4(0.2-1.2)	0.101
Concomitant IS	**2.8(1.2-6.8)**	**0.023**	1.8(0.7-4.7)	0.254
GC dose	1.0(0.9-1.0)	0.449		

Cox Proportional Hazards Regression Analysis

HR: Hazard Ratio; CI: Confidence Interval; MPZ: Mepolizumab; IS: Immunosuppressants; GC: glucocorticoid

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Univariate Cox regression identified female sex (HR 2.2, 95% CI: 1.0–4.5, p = 0.007), absence of neurological involvement (HR 0.3, 95% CI: 0.1–0.8, p = 0.021), and no history of relapse (HR 0.4, 95% CI: 0.2–0.9, p = 0.036) as significant predictors of GC/IS discontinuation. In multivariate analysis, neurological involvement remained an independent predictor (HR 0.3, 95% CI: 0.12–0.9, p = 0.035).

Conclusion: MPZ facilitated tapering to low-dose GC in all patients and enabled complete GC discontinuation in the majority, with some patients achieving IS-free status. Early MPZ initiation significantly shortened GC exposure. ANCA-negative status and absence of neurological involvement were associated with more favorable outcomes. These findings support the treatment with MPZ monotherapy as a feasible long-term treatment strategy in selected EGPA patients.

Disclosure: T. Yamane: GlaxoSmithKlein(GSK), 6; **A. Inoue**: None; **N. Yasuda**: None; **T. Ohnishi**: None; **A. Hashiramoto**: Eli Lilly, 5.

Abstract Number: 1611

Effectiveness of Avacopan and Its Impact on Serum Calprotectin in MPA/GPA Patients Receiving Rituximab-Based Remission Induction: A Single-Center Study

Yusuke Ushio[1], Hiromi Shimada[2], Taichi Miyagi[3], Koichi Sugihara[2], Mao Mizusaki[2], Rina Mino[2], Kanako Chujo[3], Naoto Manabe[3], Mayuko Wada[2], Shusaku Nakashima[2] and Hiroaki Dobashi[2], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita District, Kagawa, Japan, [2]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa, Japan, [3]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1592–1611) Vasculitis – ANCA-Associated Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Avacopan, an oral C5a receptor antagonist, offers a promising glucocorticoid (GC)-sparing option for patients with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). Although randomized trials have demonstrated its efficacy, real-world data, particularly in combination with rituximab-based induction, remain limited. Moreover, reliable biomarkers for monitoring avacopan treatment response are yet to be established. This study aimed to evaluate the effectiveness of avacopan and its impact on serum biomarkers—especially calprotectin—in MPA/GPA patients receiving rituximab for remission induction.

Methods: We retrospectively analyzed MPA/GPA patients who received rituximab-based induction therapy between January 2019 and December 2024, followed for at least 12 months. Patients were divided into those who received avacopan (avacopan group) and those who did not (non-avacopan group) during induction therapy. The primary endpoint was GC-free remission (defined as BVAS = 0 with complete GC withdrawal). Cumulative GC dose by month 12 was also assessed. In the avacopan group, serum calprotectin (S100A8/A9) and C5a levels were measured at baseline and month 3. Statistical comparisons between two groups were performed using the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Paired t-tests were used to assess within-group changes in biomarkers. Pearson's correlation coefficient was used to examine the relationship between changes in biomarkers and BVAS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	avacopan group (N = 21)	non–avacopan group (N = 26)	p
Age, years	73.0 (67.0–83.0)	76.5 (70.3–80.0)	0.645
Sex, Female, n (%)	9 (42.9)	18 (69.2)	0.084
Newly diagnosed, n (%)	12 (57.1)	16 (61.5)	0.775
Relapsed, n (%)	9 (42.9)	10 (38.5)	0.775
ANCA status			
PR3-ANCA positive, n (%)	(0)	0 (0)	-
MPO-ANCA positive, n (%)	18 (85.7)	23 (88.5)	1.000
negative, n (%)	3 (14.3)	3 (11.5)	1.000
Type of vasculitis			
GPA, n (%)	3 (14.3)	10 (38.5)	0.102
MPA, n (%)	18 (85.7)	16 (61.5)	0.102
Birmingham Vasculitis Activity Score (BVAS)	10.0 (8.5–16.5)	13.0 (7.5–18.0)	0.492
Organ involvement (BVAS ≥ 1) †			
General	14 (66.7)	16 (61.5)	0.768
Renal	11 (52.4)	17 (65.4)	0.390
Chest	9 (42.9)	7 (26.9)	0.355
Nervous system	7 (33.3)	7 (26.9)	0.752
Ear, nose, and throat	3 (14.3)	3 (11.5)	1.000
Mucous membranes or eyes	2 (9.5)	4 (15.4)	0.678
Cutaneous	1 (4.8)	5 (19.2)	0.204
Vasculitis Damage Index (VDI)	0 (0–1.0)	0 (0–1.0)	0.694
Year in which the treatment was initiated			
2022–2024	21 (100.0)	4 (15.4)	< 0.001**
Treatment up to 6 months			
Rituximab, n (%)	21 (100.0)	26 (100.0)	-
Use of any GC, n (%)	21 (100.0)	26 (100.0)	-
Intravenous GC pulse, n (%) ‡	3 (14.3)	3 (11.5)	1.000
The initial daily GC dose (prednisolone-equivalent), mg/day	30.0 (21.3–46.5)	40.0 (30.0–50.0)	0.253
Avacopan	21 (100.0)	-	-
Days from baseline to the initiation of avacopan, day	11.0 (7.5–17.0)	-	-
Additional treatment from 6 to 12 months			
Rituximab (maintenance), n (%) §	18 (85.7)	9 (34.6)	< 0.001**
Azathioprine, n (%)	0 (0)	7 (26.9)	0.012*

Data are presented as median (interquartile range) or as numbers (%), unless otherwise indicated.
ANCA: anti-neutrophil cytoplasmic antibody; PR3: proteinase 3; MPO: myeloperoxidase; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; BVAS: Birmingham Vasculitis Activity Score; RTX: rituximab; GC: glucocorticoids.
† Organ involvement was based on the Birmingham Vasculitis Activity Score ≥ 1.
‡ An infusion of methylprednisolone was administered at a dose of 500 or 1000 mg per day for 3 consecutive days.
§ A single dose of rituximab (375 mg/m²) was administered when CD19+ B-lymphocytes reappeared in peripheral blood.
For statistical analyses, *p < 0.05, **p < 0.01. P-value: Wilcoxon rank sum test, Fisher's exact test.

Figure 1. Baseline characteristics of the patients.

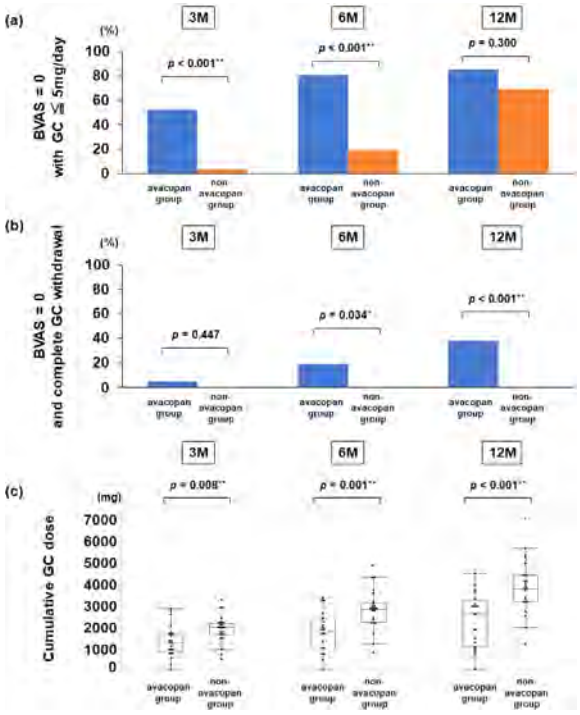


Figure 2. Comparison of remission status and cumulative GC dose between the two groups. (a) Proportion of patients achieving BVAS = 0 with GC ≦ 5 mg/day. (b) Proportion of patients achieving BVAS = 0 and complete GC withdrawal (GC-free remission). (c) Cumulative GC dose through month 12.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

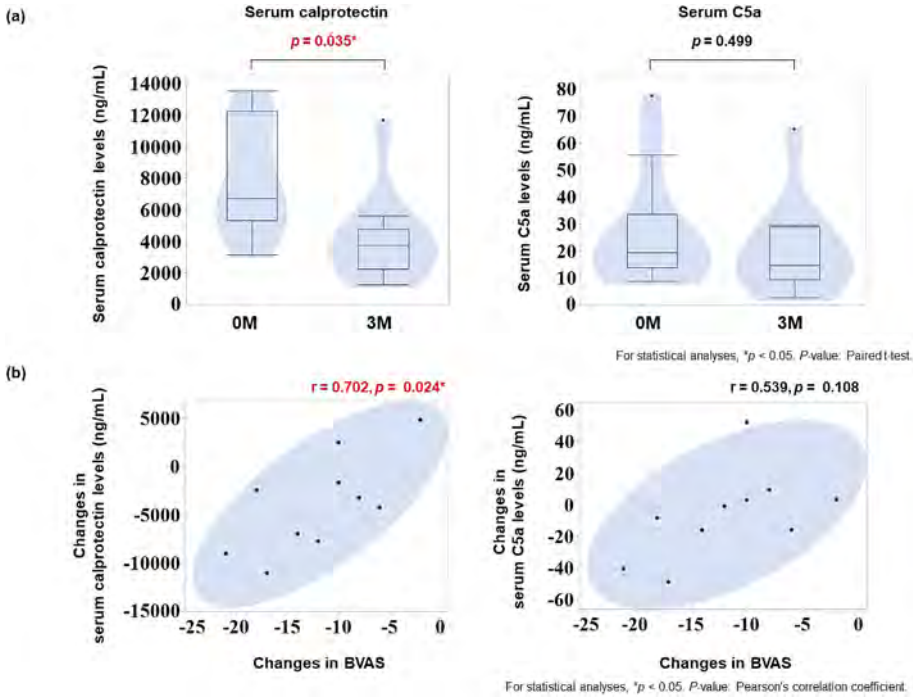


Figure 3. Serum biomarker changes and correlations with disease activity. (a) Changes in serum calprotectin and C5a levels from baseline to month 3. (b) Correlation between changes in BVAS and changes in serum calprotectin or C5a levels.

Results: A total of 47 patients were included (avacopan group: n = 21; non-avacopan group: n = 26). Baseline characteristics are shown in Figure 1. GC-free remission rate was significantly higher in the avacopan group at month 6 (19.1% vs. 0%, p = 0.034) and month 12 (38.1% vs. 0%, p < 0.001) (Figure 2). Cumulative GC dose at month 12 was significantly lower in the avacopan group (2343.2 ± 1242.3 mg vs. 4037.7 ± 1208.7 mg, p < 0.001). In the avacopan group, serum calprotectin levels significantly declined from 8082.1 ± 3624.6 ng/mL to 4170.5 ± 2975.8 ng/mL at month 3 (p = 0.035), and this change strongly correlated with BVAS improvement (r = 0.702, p = 0.024). In contrast, no significant change was observed in serum C5a levels (Figure 3).

Conclusion: Among MPA/GPA patients receiving rituximab-based induction therapy, avacopan enabled significant GC dose reduction while achieving clinical remission. Serum calprotectin decreased in response to treatment and correlated with disease activity, highlighting its potential as a real-world biomarker for monitoring avacopan efficacy.

Disclosure: Y. Ushio: None; **H. Shimada**: None; **T. Miyagi**: None; **K. Sugihara**: None; **M. Mizusaki**: None; **R. Mino**: None; **K. Chujo**: None; **N. Manabe**: None; **M. Wada**: None; **S. Nakashima**: None; **H. Dobashi**: None.

Abstract Number: 1612

Window of opportunity with tocilizumab therapy in giant cell arteritis. Multicenter study of 471 patients of clinical practice

Adrian Martin-Gutierrez[1], Javier Loricera[2], Diana Prieto-Peña[3], Vicente Aldasoro Cáceres[4], Olga Maiz[5], Eugenio de Miguel[6], Eva Galíndez Agirregoikoa[7], Ivan Ferraz Amaro[8], Santos Castañeda[9], Ricardo Blanco[10] and Tocilizumab in Giant Cell Arteritis Spanish Collaborative Group, [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Pilagos, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [4]Hospital Universitario de Navarra, Pamplona, Spain, [5]Hospital Universitario de Donosti, Donostia, Spain, [6]Hospital Universitario

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

La Paz, Madrid, Spain, [7]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [8]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [9]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [10]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Tocilizumab (TCZ) is the only biological drug currently approved for the treatment of giant cell arteritis (GCA), regardless of GCA duration. The "window of opportunity" is an increasingly widespread in different immune mediated inflammatory diseases, such as rheumatoid arthritis or psoriatic arthritis. Window of opportunity is usually defined as the chance of achieving remission depending on early treatment. Our aim was to assess the window of opportunity in a wide series of GCA patients treated with TCZ in clinical practice.

Table 1. Main clinical characteristics of GCA at initiation of tocilizumab.

	Overall n=471	Newly Diagnosed GCA n=91	Refractory GCA n=380	*P*
Age at diagnosis, years mean ± SD	72.1±9.1	74.2±8.6	71.6±9.1	**0.0353**
Sex, female/male n (% female	342/129 (72.6)	60/31 (65.9)	282/98(74.2)	0.1177
PHENOTYPES				
Cranial phenotype, n (%)	218 (46.3)	50 (54.9)	168 (44.2)	0.0650
Extracranial phenotype, n (%)	82 (17.5)	15 (16.5)	67 (17.6)	0.8784
Mixed phenotype, n (%)	171 (36.3)	26 (28.6)	145 (38.2)	0.0909
CRITERIA				
GiACTA, n (%)	276 (64.3)	53 (71.6)	223 (62.8)	0.1822
ACR 1990, n (%)	344 (74.1)	70 (76.9)	274 (73.5)	0.5935
ACR/LVV, n (%)	277 (81)	49 (72.1)	228 (83.2)	0.0560
Cardiovascular risk factors, n (%)				
High blood pressure	272 (61.4)	49 (55.1)	223 (63)	0.1815
Dyslipidemia	241 (54.4)	54 (60.7)	187 (52.8)	0.2336
Diabetes	81 (18.3)	16 (18)	65 (18.4)	0.4710
Previous or current smoking history	47 (10.5)	16 (18)	31 (8.7)	**0.0189**
SYSTEMIC MANIFESTATIONS, n (%)				
PMR	284 (60.9)	57 (63.3)	227 (60.4)	0.6323
Constitutional syndrome	175 (37.5)	34 (37.8)	141 (37.4)	0.9999
Fever	57 (12.2)	14 (15.5)	43 (11.4)	0.2853
Aortitis	196 (47.7)	33 (39.2)	163 (49.8)	0.0879
ISCHEMIC MANIFESTATIONS, n (%)				
Headache	258 (55.6)	58 (65.9)	200 (53.2)	**0.0422**
Jaw claudication	112 (25)	28 (31.5)	84 (23.4)	0.1325
Visual impairment	80 (17)	32 (35.2)	48 (12.7)	**0.0020**
Stroke	5 (1.1)	2 (2.2)	3 (0.8)	0.2552
LABORATORY				
ESR, mm/1 st hour, median [IQR]	30 [11-56]	46 [16.5-81.5]	27 [10-50]	**0.0005**
CRP, mg/dL, median [IQR]	1.4 [0.4-3.39]	2.1 [0.6-8.5]	1.3 [0.4-2.9]	**0.0003**
POSITIVE TEMPORAL ARTERY BIOPSY, n (%)	201 (61.8)	40 (63.5)	161 (61.5)	0.8853
Previous conventional synthetic DMARDs, n (%)	258 (54.8)	18 (19.8)	240 (63.2)	**<0.0001**
MTX	236 (50.1)	17 (18.6)	219 (57.6)	**<0.0001**
AZA	12 (2.5)	0 (0)	12 (3.2)	**0.1349**
SSZ	3 (0.6)	1 (1.1)	2 (0.5)	**0.4756**
HCQ/CQ	2 (0.4)	0 (0)	2 (0.5)	0.9999
MMF	1 (0.2)	0 (0)	1 (0.3)	0.9999
LFN	3 (0.6)	0 (0)	3 (0.8)	0.9999
CyA	1 (0.2)	0 (0)	1 (0.3)	0.9999
Previous biological therapy, n (%)	12 (2.5)	0 (0)	12 (3.2)	0.3221
GLUCOCORTICOIDS AT TCZ INITIATION				
Prednisone at TCZ initiation, mg/day, median [IQR]	20 [10-40]	40 [20-50]	15 [10-30]	**<0.0001**
TOCILIZUMAB				
Intravenous/subcutaneous, n/n (% intravenous)	238/233 (50.4)	36/55 (39.6)	202/178 (53.2)	**0.0202**
Monotherapy/combination, n/n (% monotherapy)	353/118 (74.9)	81/10 (89)	272/108 (71.6)	**0.0001**

Abbreviations: ABA : abatacept ; ACR: American College of Rheumatology; ACR/LVV: Large vessel vasculitis criteria of GCA ACR with a positive image suggestive for aortitis; ADA : adalimumab ; AZA: azathioprine; CQ: chloroquine; CRP: C-reactive protein ; CyA : cyclophosphamide; DMARDs : disease-modifying antirheumatic drugs; ESR: erythrocyte sedimentation rate ; ETN : etanercept ; HCQ: hydroxychloroquine; IFX: infliximab; IQR: interquartile range; LFN: leflunomide ; MMF: mycophenolate mofetil; n : number; PET/CT: positron emission tomography scan; PMR: polymyalgia rheumatica; RTX: rituximab; SD: standard deviation; SSZ: sulfasalazine; TCZ: tocilizumab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariable analysis through logistic regression of associative factors with EULAR remission at 24 months of initiation of TCZ

	Univariable		Multivariable	
	OR (IC 95%)	p	OR (IC 95%)	p
Age at diagnosis, years mean ± SD	0.997 (0.957-1.039)	0.8830		
Sex, female/male n (% female)	0.943 (0.419-2.119)	0.8688		
Months from GCA diagnosis to TCZ initiation, median [IQR]	0.990 (0.978-1.002)	0.0912	0.985 (0.970-1.000)	0.051
Newly diagnosed GCA, n (%)	0.373 (0.081-1.716)	0.2054		
VASCULAR PHENOTYPES				
Cranial phenotype, n (%)	0.752 (0.357-1.584)	0.4529		
Extracranial phenotype, n (%)	1.622 (0.612-4.301)	0.3310		
Mixed phenotype, n (%)	0.973 (0.447-2.119)	0.9450		
CARDIOVASCULAR RISK FACTORS				
High blood pressure, n (%)	1.344 (0.601-3.008)	0.4713		
Dyslipidemia, n (%)	1.040 (0.482-2.243)	0.9205		
Diabetes, n (%)	0.548 (0.175-1.716)	0.3015		
Previous or current smoking history, n (%)	0.554 (0.173 -1.772)	0.3193		
SYSTEMIC MANIFESTATIONS				
PMR, n (%)	1.500 (0.659 -3.413)	0.3337		
Constitutional syndrome, n (%)	1.514 (0.718-3.195)	0.2758		
Fever, n (%)	1.594 (0.507-5.008)	0.4248		
Aortitis, n (%)	0.563 (0.240-1.316)	0.1848	1.592 (0.630-4.021)	0.325
ISCHEMIC MANIFESTATIONS				
Headache, n (%)	1.913 (0.886-4.132)	0.0986	0.734 (0.290-1.854)	0.513
Jaw claudication, n (%)	1.043 (0.421-2.586)	0.9268		
Visual impairment, n (%)	0.947 (0.321-2.792)	0.9217		
Stroke, n (%)	(0-)	0.9999		
LABORATORY				
ESR, mm/1 st hour, median [IQR]	0.999 (0.986-1.012)	0.8906		
CRP, mg/dL, median [IQR]	1.018 (0.906-1.143)	0.7673		
Previous conventional synthetic DMARDs, n (%)	0.187 (0.176-1.404)	0.1872	1.371 (0.443-4.241)	0.584
Prednisone at TCZ initiation, mg/day, median [IQR]	0.989 (0.970-1.007)	0.2376		
TOCILIZUMAB SCHEDULE				
Intravenous, n (%)	1.182 (0.507-2.664)	0.7227		
Monotherapy, n (%)	1.123 (0.528-2.388)	0.7633		

Abbreviations: CRP: C-reactive protein; DMARDs: disease-modifying antirheumatic drugs; ESR: erythrocyte sedimentation rate; IQR: interquartile range; n: number; PMR: polymyalgia rheumatica; SD: standard deviation; TCZ: tocilizumab.
In this analysis, EULAR remission is the dependent variable.

Methods: Multicenter observational study of GCA patients treated with TCZ. Accordingly, to definitions of clinical trials in GCA, two groups of GCA were considered, "newly diagnosed GCA" and "relapsing GCA" depending on GCA diagnosis was made ≤6 or >6 weeks before initiation of TCZ, respectively. Window of opportunity in GCA was defined as the chance of achieving GCA-EULAR remission criteria (clinical and analytical remission). In addition, a multivariable study of associative factors with window of opportunity at 24 months of initiation of TCZ was conducted (logistic regression analysis).

Results: 471 patients (n=342; 72.6% female); mean age: 73.5±9 years were included. "Newly GCA" were 91 (19.3%) patients and "relapsing GCA", 380 (80.7%). In the newly diagnosed GCA, headache and visual impairment were statistically more frequent and median ESR and CRP were higher (**Table 1**).

After 52 weeks of treatment, EULAR remission was similar regardless of time to TCZ initiation (**Figure 1A,B&C**), and GCA phenotypes (**Figure 1D**). In the multivariable analysis there was a non-statistically higher trend to a EULAR remission when TCZ initiation was shorter from GCA diagnosis, OR 0.985 (0.970-1.000) (**Table 2**).

Conclusion: In contrast with the "window of opportunity" observed in other immune mediated inflammatory diseases, a delay in the initiation of TCZ therapy in GCA may not decrease its effectiveness (EULAR remission) in clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

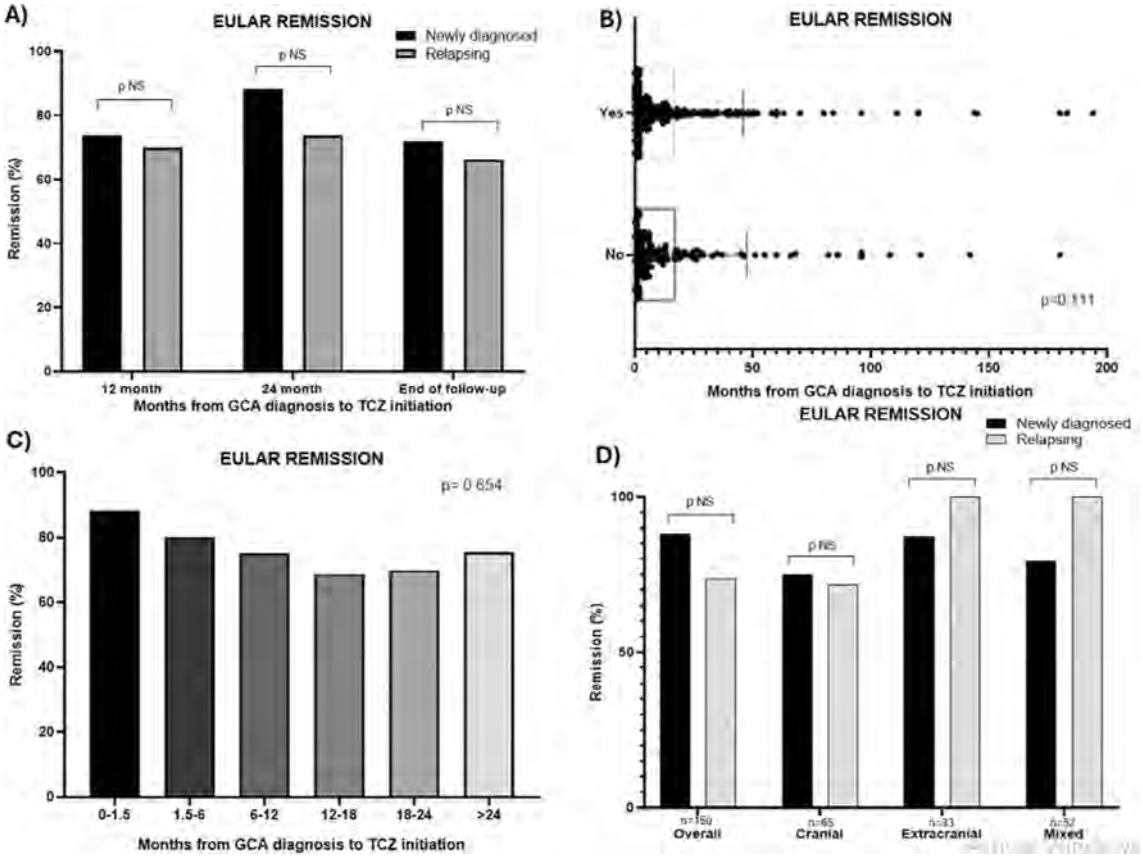


Figure. EULAR remission (Window of opportunity) according to the time of tocilizumab initiation since GCA diagnosis.

Disclosure: A. Martin-Gutierrez: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **D. Prieto-Peña**: None; **V. Aldasoro Cáceres**: None; **O. Maiz**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **E. Galíndez Agirregoikoa**: None; **I. Ferraz Amaro**: None; **S. Castañeda**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1613

Switching From Reference Tocilizumab to Biosimilar in Giant Cell Arteritis: Effectiveness and Safety in a Multicenter Study of 38 Patients

Adrian Martin-Gutierrez[1], Fernando Lopez Gutierrez[2], Javier Loricera[3], Juan Molina-Collada[4], Juan Carlos Nieto[5], Marina Sánchez-Lucas[6], Maite silva[7], Patricia Moya Albarado[8], Eztizen Labrador-Sanchez[9], Ivan Ferraz Amaro[10] and Ricardo Blanco[11], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Piélagos, Spain, [2]Hospital Universitario Marqués de Valdecilla, Immunopathology Group -IDIVAL, Reumatología, Santander, Santander, Spain, [3]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [4]Department of Rheumatology, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Spain, [5]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [6]Hospital General Universitario Gregorio Marañón, Madrid, Madrid, Spain, [7]Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas, A Coruña, Spain, A Coruña, Galicia, Spain, [8]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [9]Hospital Universitario San Pedro, Laguardia, Spain, [10]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [11]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: The cost of original biologics may limit treatment access. Biosimilars are biologics that are structurally highly similar and functionally equivalent to the approved reference product, providing the opportunity to improve access to treatment. Tocilizumab (TCZ)-biosimilar have showed therapeutic equivalence in rheumatoid arthritis. To date, there are no studies evaluating the effectiveness and safety of the switch to TCZ-biosimilar in GCA. The aim of this study is to assess the effectiveness and safety of switching from TCZ-reference product to TCZ-biosimilar in GCA patients in clinical practice.

Methods: Retrospective, multicentre, real-world clinical practice study of GCA patients who switched from TCZ-reference product to TCZ-biosimilar. We assessed a) effectiveness including clinical and laboratory parameters, and EULAR definition of remission (absence of signs and symptoms and normalization of acute phase reactants) (5), b) dose of prednisone, and c)

Feature	Value
Demographic features	
Age at TCZ biosimilar initiation, years (mean±SD)	74.1±9.0
Sex, women/men (% women)	26/12 (68.4)
GCA criteria, n (%)	
ACR 1990	26 (72.2)
ACR/EULAR 2022	38 (100)
Biopsy-proven GCA/biopsy performed (% biopsy-proven GCA)	10/17 (58.8)
Time receiving TCZ originator, mean±SD	36.1±27.7
TCZmono/TCZcombo (%TCZmono)	34/4 (89.5)
GCA phenotype, n (%)	
Cranial GCA	14 (36.8)
Extracranial GCA	14 (38.9)
Mixed GCA	10 (26.3)

TABLE. Main features of the 30 GCA patients who were switched from TCZ - reference product to TCZ- biosimiliar.

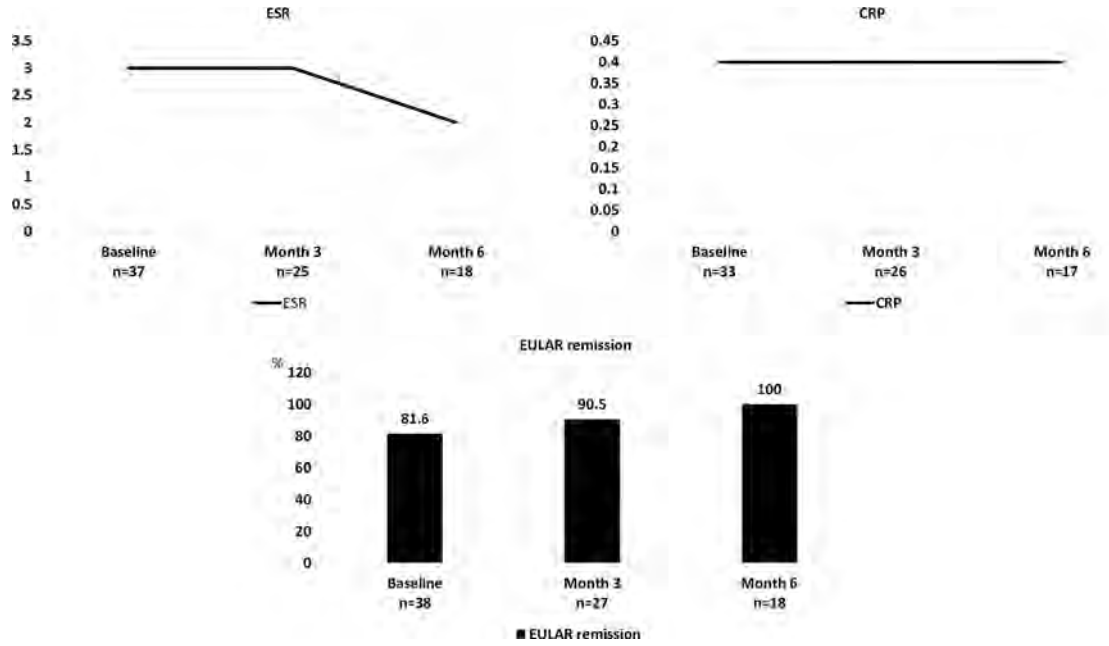


FIGURE. Median ESR, CRP and daily prednisone dose, and EULAR remission of the 38 GCA patients who were switched from TCZ - reference product to TCZ- biosimiliar.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

side effects. Comparisons were performed between baseline and 3rd, and 6th months using McNeemar´s test for binary variables and T-student test for continuous variables

Results: A total of 38 patients (68.4% females, mean age 74.1 years) who were switched from TCZ-reference product to TCZ-biosimilar were included for analysis **(TABLE)**. The GCA phenotypes were: cranial (n=14; 36.8%), extracranial (n=14; 38.9%) and mixed (n=10; 26.3%). The patients had received TCZ-reference product for 36.1±27.7 months. Tyenne was prescribed in monotherapy in 34 (89.5%) patients, and combined with methotrexate in 4 (10.5%) patients. At the time of switching from TCZ-reference product to TCZ-biosimilar, 31 patients were in EULAR remission, the median (IQR) prednisone dose was 0 [0-5] mg/day, and the median ESR and CRP were 3 [2-8] mm/1st hour, and 0.4 [0.1-0.4] mg/dL, respectively. After a mean follow-up of 7.5±3.4 months from switching to TCZ biosimilar, there were no significant differences in EULAR remission, daily prednisone dose and CRP and ESR values **(Figure)**. Due to GCA remission TCZ administration interval was increased in 4 (10.5%) patients and discontinue in other. One patient developed herpes zoster one month after switching fromTCZ-reference product to TCZ-biosimilar

Conclusion: Our results suggest that TCZ-biosimilar is an effective and safe treatment for GCA patients when they were switched from the TCZ-reference product.

References

1. Calderón-Goercke M, et al. Clin Exp Rheumatol. 2020. PMID: 32441643
2. Loricera J et al. Clin Exp Rheumatol. 2014. PMID: 24854377
3. Prieto Peña D, et al. Clin Exp Rheumatol. 2021. PMID: 33253103
4. Loricera J, et al. Ther Adv Musculoskelet Dis. 2022. PMID: 35898567
5. Dejaco C, Kerschbaumer A, Aletaha D, Bond M, Hysa E, Camellino D, et al. Treat-to-target recommendations in giant cell arteritis and polymyalgia rheumatica. *Ann Rheum Dis* 2024. PMID: 36828585

Disclosure: A. Martin-Gutierrez: None; **F. Lopez Gutierrez**: Roche, Galápagos, Novartis, UCB Pharma, MSD, Celgene, Astra Zeneca, Grünenthal, Janssen, Abbvie, Lilly, Pfizer, 12, support for attending meetings and/or travel; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **J. Molina-Collada**: None; **J. Nieto**: None; **M. Sánchez-Lucas**: None; **M. silva**: None; **P. Moya Albarado**: None; **E. Labrador-Sanchez**: None; **I. Ferraz Amaro**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1614

A Systematic Literature Review to Inform the EULAR Recommendations for the Management of Polymyalgia Rheumatica and Large Vessel Vasculitis: Focus on Referral and Diagnosis

Alice Bartoletti[1], Georgina Ducker[2], Mrinalini Dey[3], Durga Prasanna Misra[4], Sara Monti[5], Bernhard Hellmich[6], Chetan Mukhtyar[7], Paul Studenic[8], Elena Nikiphorou[9] and EULAR taskforce for the 2025 EULAR recommendations for the management of PMR and LVV, [1]Department of Rheumatology, ASST Gaetano Pini CTO, Milan, Italy, Milan, Lombardia, Italy, [2]Department of Rheumatology, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK, Norwich, England, United Kingdom, [3]Department of Rheumatology, King's College Hospital NHS Foundation Trust, London, UK, London, England, United Kingdom, [4]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, Lucknow, Uttar Pradesh, India, [5]University of Pavia, Pavia, Pavia, Italy, [6]Department of Internal Medicine, Rheumatology, Pulmonology, Nephrology and Diabetology, Medius Kliniken Kirchheim/Teck, University Tübingen, Tübingen, Germany, Kirchheim-Teck, Germany, [7]Norfolk and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

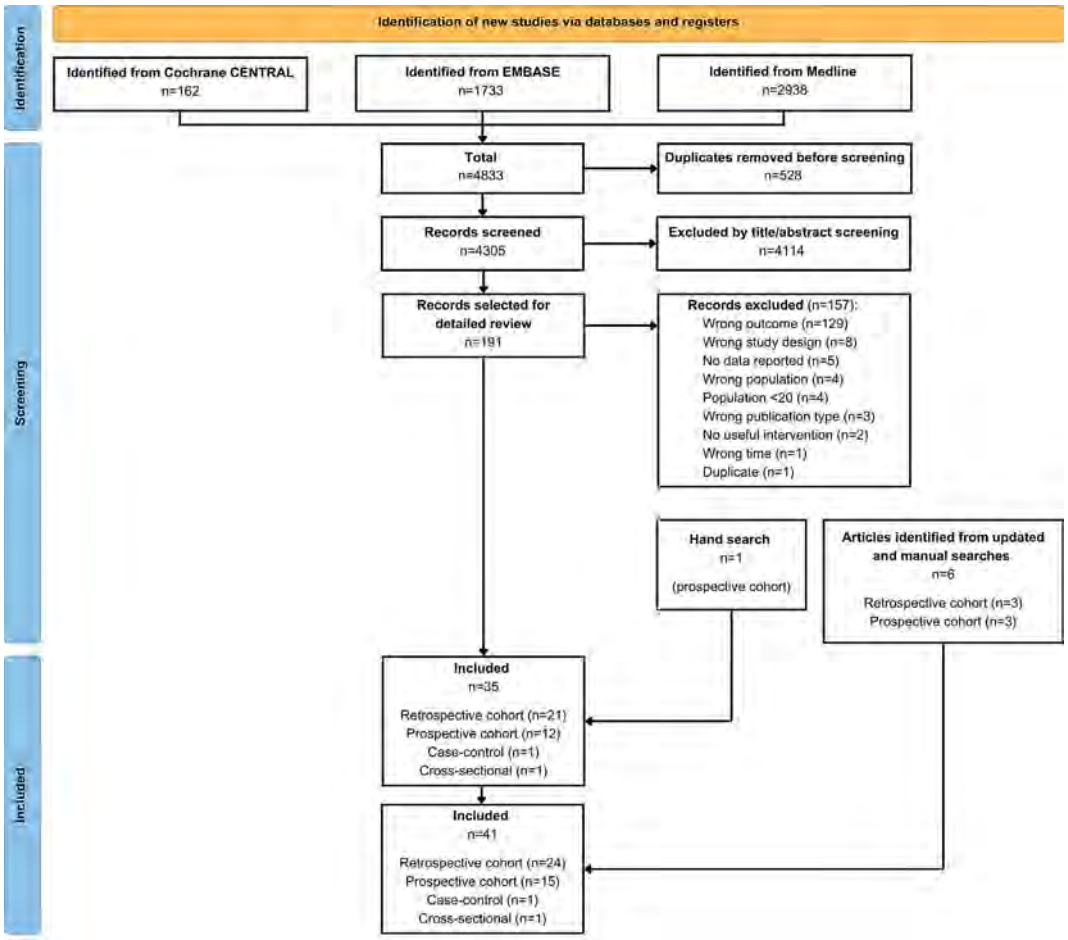


Figure 1. PRISMA flowchart.

Table 1. Outcomes of subclinical LVV vs isolated PMR. DMARD disease-modifying antirheumatic drug, GC glucocorticoid, LVV large vessel vasculitis; MPDN, methylprednisolone; PDN, prednisone; PMR polymyalgia rheumatica.

Disease, Population	Author Year	Intervention (n) Comparator (n)	Outcome	Results	Conclusion
Subclinical LVV in PMR	Moreel 2024	PMR+LVV (31) Isolated PMR (306)	GC starting dose (MPDN equivalents)	24.3 mg/day PMR+LVV 14.6 mg/day isolated PMR p<0.001	PMR+LVV had higher GC doses in the first year of treatment. No relapse differences between PMR+LVV and isolated PMR
			GC dose during follow-up	Higher in PMR+LVV in the first year p<0.001	
			Need for DMARD	3 (10%) PMR+LVV 31 (10%) isolated PMR p=1	
			Relapse	HR 0.82 95% CI 0.50-1.36 p=0.4	
	De Miguel 2024	PMR+LVV (50) Isolated PMR (100)	GC starting dose (PDN equivalents)	36.6±14.3 mg/day PMR+LVV 19.5±7.4 mg/day isolated PMR p=0.001	Higher number of relapses in PMR+LVV compared to isolated PMR. Rapid GC tapering in the first 3 months is a risk factor for relapse.
			GC dose at 12 months (PDN equivalents)	7.5±13.5 mg/day PMR+LVV 2.4±3.4 mg/day isolated PMR p=0.02	
			csDMARD	25 (50%) PMR+LVV 13 (13%) isolated PMR p=0.001	
			bDMARD or tsDMARD	14 (28%) PMR+LVV 2 (2%) isolated PMR p=0.001	
			Relapse	31 (62%) PMR+LVV 16 (16%) isolated PMR p<0.001 OR 6.99 95% CI 2.30-21.74 p<0.001	
			Impact of fast GC tapering on relapse	Relapsing PMR+LVV patients had a faster GC tapering: 13.4±7.1 mg/day vs 18.8±7.5 mg/day at 3 months p=0.02	
	Arévalo-Ruales 2019	PMR+LVV (11) Isolated PMR (12)	Need for DMARD	8 (73*%) PMR+LVV 3 (25%) isolated PMR	LVV patients are more often started a DMARD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Norwich University Hospital, Norwich, England, United Kingdom, [8]Internal Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, Vienna, Austria, [9]King's College London, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: European Alliance of Associations for Rheumatology (EULAR) recommendations for the management of Polymyalgia Rheumatica (PMR) and Large Vessel Vasculitis (LVV) date back to 2015 and 2020 respectively. Novel evidence about their management has emerged since then.

This study aims to systematically review the recent literature on the referral and diagnosis of PMR and LVV to inform the related EULAR recommendations.

Methods: A systematic review (PROSPERO CRD42024560403) focused on PMR, giant cell arteritis (GCA) and Takayasu arteritis (TAK) referral and diagnosis, was conducted across MEDLINE, Embase, and Cochrane databases with publications dating from May 2014 for PMR, and January 2018 for LVV, up to December 2024. No language restriction was applied. Age was limited to adults above 18 years. Randomised trials, observational studies (cohort, case-control, cross-sectional), systematic reviews and meta-analyses were included. Studies of single imaging modalities were outside the remit of the project. EULAR 2024 and American College of Rheumatology 2024 congress abstracts were additionally screened to identify relevant studies published after the end date of the search.

Relevant risk of bias tools were used to assess study quality.

Results: Forty-one studies (all observational) met the inclusion criteria (Figure 1).

Fast-track clinics (FTC) for suspected GCA (3 studies, n=682) reduced the risk of blindness from 19–27% to 12–13% and shortened the time to diagnosis from a median of 62 days to 33 days (p=0.04). FTC for suspected PMR (3 studies, n=662) reduced the diagnostic latency (7–53 days FTC vs 12–80 days controls, p=0.001) and the hospitalisation rate (3.5% FTC vs 20.4% controls, p=0.001).

Ten studies investigating the presence of subclinical LVV in patients with a PMR-like presentation have been retrieved (n=1229). The clinical presentation of isolated PMR and subclinical LVV was similar. However, subclinical LVV had a higher risk of relapse and greater need for immunosuppression (Table 1).

Ten studies (n=1047) confirmed similar or superior performance of imaging, namely temporal and axillary artery ultrasound (US) or positron emission tomography (PET) compared to temporal artery biopsy (TAB) alone for the diagnosis of GCA in terms of sensitivity and rapidity of diagnosis. Moreover, multimodal diagnostic pathways (9 studies, n=2470) integrating pre-test probability scores, imaging and/or TAB increased the accuracy of GCA diagnosis. A pathway based on US, followed by PET, and ultimately an expert clinician's opinion was more sensitive than TAB (92% vs 39%) and decreased the diagnostic delay (1.1 days US, 1.9 days PET, 10.8 days TAB).

Glucocorticoids (GC) rapidly reduced the sensitivity of TAB (5 studies): 23–74% GC < 1 week vs 20–52% GC > 1 week – OR 0.36, 95% CI 0.13–0.96 (p=0.04).

No new high-quality evidence emerged concerning the referral and diagnosis of TAK.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This systematic review provides new insights into the referral and diagnosis of PMR and LVV, including the value of multimodal FTC pathways, the use of US in the workup of PMR and LVV, and subclinical LVV in patients presenting with PMR-like symptoms. This evidence will inform the 2025 EULAR recommendations for the management of PMR and LVV.

Disclosure: A. Bartoletti: None; **G. Ducker**: None; **M. Dey**: None; **D. Misra**: None; **S. Monti**: None; **B. Hellmich**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, CSL Vifor, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Novartis, 1, 6, Pfizer, 6; **C. Mukhtyar**: None; **P. Studenic**: None; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

Abstract Number: 1615

Prevalence of Clinical and Laboratory Manifestations of Patients with Deficiency of Adenosine Deaminase 2 (DADA2): A Systematic Review and Meta-Analysis

Athanasios Vassilopoulos[1], Stephanos Vassilopoulos[1], Anushri Nimbvikar[1], Eleftherios Mylonakis[2] and Anthony M. Reginato[3], [1]Division of Internal Medicine, Warren Alpert Medical School of Brown University, Rhode Island Hospital, Providence, Rhode Island, Providence, [2]Department of Medicine, Houston Methodist Hospital, Houston, [3]Brown University, Providence, RI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Deficiency of adenosine deaminase 2 (DADA2) is a rare autosomal recessive autoinflammatory disorder first identified in 2014. Four major disease phenotypes have been described: vasculitic, hematologic, immunodeficient, asymptomatic. The mainstay treatment is TNF inhibitors (TNFi), especially in patients with the vasculitic phenotype. The prevalence of its various clinical and laboratory manifestations has not been previously reported in a meta-analysis.

We aimed to calculate the prevalence of the following clinical and laboratory manifestations: cutaneous involvement, polyarteritis nodosa (PAN)-like presentation, stroke (ischemic or hemorrhagic), ocular involvement, cytopenias, recurrent infections, hemophagocytic lymphohistiocytosis (HLH), fever and hepatosplenomegaly.

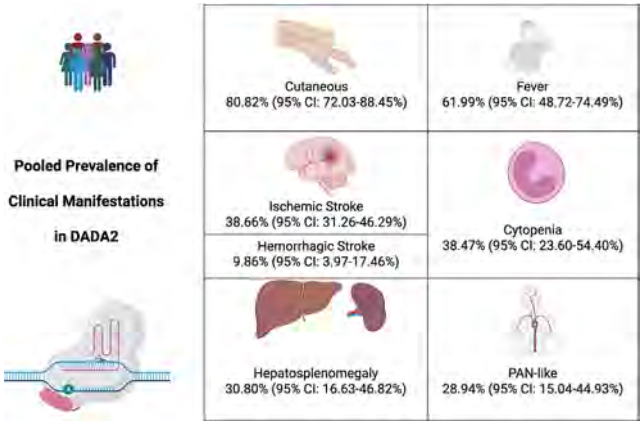


Figure 1. Pooled Prevalence of Clinical Manifestations Among Patients with DADA2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics and treatment options. AZA: azathioprine, CYC: cyclophosphamide, IL1i: Interleukin 1 inhibitor, MMF: mycophenolate mofetil, MTX: methotrexate, RTX: rituximab, TNFi: tumor necrosis alpha factor inhibitor

Study	Year	Type	Country	Patients	% Female	TNFi	CYC	AZA	MTX	MMF	IL1i	RTX
Andriessen et al.	2023	retrospective	Netherlands	29	41.4	19	0	0	3	0	0	0
Ayan et al.	2024	retrospective	Turkey	32	34.4	27	6	10	3	4	0	0
Barron et al.	2022	prospective	USA	58	57	7	9	7	0	6	11	4
Bulte et al.	2025	retrospective	Italy	18	66.6	17	0	0	0	0	1	0
Caorsi et al.	2016	retrospective	Italy	15	33.3	10	5	5	3	4	1	0
Nihira et al.	2021	retrospective	Japan	8	50	8	2	0	0	0	0	1
Rama et al.	2018	retrospective	France	13	53.8	5	3	2	2	0	0	1
Sahin et al.	2017	retrospective	Turkey	8	25	6	3	3	0	1	1	0
Schepp et al.	2017	retrospective	Germany	11	36.4	3	0	0	1	0	0	0
Sharma et al.	2021	retrospective	India	33	31.3	25	13	8	6	7	0	4

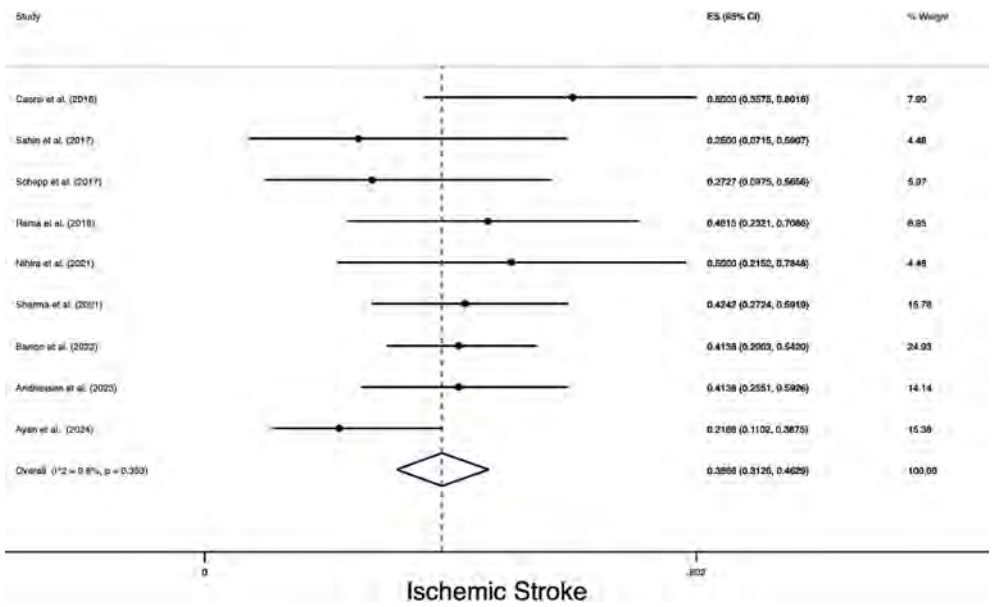


Figure 2. Pooled Prevalence of Ischemic Stroke with 95% Confidence Intervals. ES: Effect Size (Prevalence)

Methods: We searched PubMed and EMBASE for cohorts of patients with DADA2. In order to be considered eligible for our inclusion criteria, studies should have met the following criteria: (1) DADA2 diagnosis confirmed with genetic analysis, (2) reporting of clinical manifestations in both children and adults.

Results: Ten studies, 9 retrospective and 1 prospective, published between 2016 and 2025 provided data on 225 patients with DADA2. Cutaneous findings were the most common clinical manifestations with a prevalence of 80.82% (95% CI: 72.03-88.45%), while biopsy confirmed PAN was present in 28.94% (95% CI: 15.04-44.93%) of patients. Ischemic stroke was the manifestation with the lowest heterogeneity among included studies and yielded a prevalence of 38.66% (95% CI: 31.26-46.29%), while the prevalence of hemorrhagic stroke was lower at 9.86% (95% CI: 3.97-17.46%). Other common manifestations included fever 61.99% (95% CI: 48.72-74.49%), cytopenias 38.47% (95% CI: 23.60-54.40%), recurrent infections 35.72% (95% CI: 9.00-67.75%), hepatosplenomegaly 30.80% (95% CI: 16.63-46.82%), ocular involvement 13.85% (95% CI: 8.02-20.71%) and HLH 6.92% (95% CI: 1.69-14.50%). Finally, the majority (n=127, 56.4%) received TNFi; etanercept (79 patients) and adalimumab (31 patients) were the most commonly used.

Conclusion: In this meta-analysis of 225 patients with DADA2, cutaneous involvement, fever and ischemic stroke were the most common manifestations. Closer monitoring for cytopenia is needed to reduce the risk of recurrent infections. Both outcomes occurred in one third of patients included in this study. More than half of patients are receiving TNFi, leading to

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

prolongation of life-expectancy. Therefore, adult rheumatologists are expected to encounter patients with DADA2 more frequently and increased awareness of the disease and its manifestations is warranted for optimized patient care.

Disclosure: A. Vassilopoulos: None; **S. Vassilopoulos**: None; **A. Nimbvikar**: None; **E. Mylonakis**: Chemic Labs/KODA Therapeutics, 5, Lumen, 12, DSMB, NIH/NIAID, 5, SciClone Pharmaceuticals, 5, Shionogi, 1, Synexis, 12, Clinical Trial; **A. Reginato**: None.

Abstract Number: 1616

Short-Course Prednisone and Methotrexate in Polymyalgia Rheumatica: A Potential Therapeutic Approach

Edoardo Conticini[1], Silvia Grazzini[1], Raffaele Truscelli[2], Paolo Falsetti[3], Luca Cantarini[4] and Bruno Frediani[4], [1]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Italy, Siena, Italy, [2]University of Siena, Siena, Italy, [3]Siena University Hospital, Siena, Italy, [4]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University Hospital of Siena, Siena, Italy, Siena, Italy

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite being considered an easy-to-diagnose and easy-to-treat condition, the optimal treatment of PMR is far from being fully elucidated. Three recently published trials have evidenced efficacy and safety of anti-IL6R agents, but their cost, as well as the high incidence and prevalence of PMR, make them unsuitable for extensive use as a first line treatment. At the same time, only a few, poorly designed, trials explored the role of cDMARDs. In addition, none of these studies adequately ruled out the presence of subclinical GCA, which, accounting for more than 20% of cases, may justify the poor response to MTX. In this regard, the aim of this prospective study was to assess whether the precocious administration of MTX, in association with a short course of GC, could be safe and effective in patients with recently diagnosed PMR, upon exclusion of subclinical GCA.

Methods: In this single arm, open label, prospective study, all patients with a recent diagnosis of PMR (< 4 weeks), fulfilling ACR/EULAR criteria with US were included. Patients with Southend pre-test score > 12 and OGUS > 1 were excluded beforehand. As a control group, an age and sex matched historical cohort of PMR treated with a monotherapy of GCs for at least 3 months from diagnosis was included.

At baseline, all patients were treated with 25 mg of PDN and 0,2 mg/kg/weekly MTX; PDN was gradually tapered to 0 within 20 weeks and, in case of flare, re-increased to the minimum effective dosage.

The primary endpoint of the study was PDN-free remission at 24 weeks. Secondary endpoints were sustained remission at 52 weeks (defined as clinical remission, absence of flares, CRP normalization), number of flares, PDN dosage, CRP and ESR at 24 and 52 weeks compared to historical cohort.

Results: Forty-one patients were prospectively included, while 63, age and sex matched, were included in the retrospective cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Baseline	6 months	12 months	p value 0-6 months	P value 0-12 months	P value 6-12 months
CRP (mg/dl)	6.28 ± 4.97	0.9 ± 0.47	1.13± 2.46	<0.001	<0.001	1.000
ESR (mm/h)	67.7 ± 26.7	18.13 ± 11.37	28.85± 30.91	<0.001	0.097	0.041
PDN dosage (mg/day)	25	3.42 ± 3.3	0.45± 0.11	<0.001	<0.001	<0.001
Patients in PDN-free remission (N/%)		24 (58%)	19 (59%)			
Patients dropping out for adverse events (N/%)		4 (9,7%)	2 (6,25%)			
Patients with flare (N/%)		7 (17%)	5 (15,3%)			

Legend: CRP: C-reactive protein; ESR: erythron sedimentation rate; PDN: prednisone. Values are expressed as mean

Values at baseline and during follow-up

In the MTX-cohort, at 6-months, 58% of patients were in steroid-free remission and therefore met the primary endpoint of the study. Eight, yet without any sign or symptom of PMR, were still taking a mean daily dosage of 3,88 mg of PDN.

Overall, a significant reduction of both CRP and ESR was observed. Similarly, mean daily PDN dosage dropped to 3,42 ± 3,3 mg. Seven patients (17,5%) suffered from disease flares, requiring a temporary increase of PDN dosage.

Thirty-two patients, upon the exclusion of those who dropped out due to the discontinuation of MTX and/or due to the administration of biological DMARDs, reached 52-weeks phase of the study and 59% of them maintained GCs-free remission.

A significantly higher number of relapses were reported within the first 12 months in the retrospective cohort (p = 0,036), in which up to 49 patients (77,8%) were still taking PDN, (4 > 7,5 mg).

Conclusion: In conclusion, upon a subclinical GCA is excluded, MTX, administered at adequate dosages, is a suitable option for the treatment of PMR, allowing a precocious discontinuation of oral GCs. The superiority of our findings can be explained by a higher dosage of MTX employed and by the exclusion of subclinical GCA, which is known to be associated with a higher relapse ratio. In this case, precocious administration of anti-IL6R agents should be warranted.

Disclosure: E. Conticini: GlaxoSmithKlein(GSK), 2, 6; **S. Grazzini**: None; **R. Truscelli**: None; **P. Falsetti**: None; **L. Cantarini**: None; **B. Frediani**: None.

Abstract Number: 1617

Evaluating Familiarity and Knowledge Gaps in Polymyalgia Rheumatica Among Public Health Professionals

Erik Stone[1], Shilpa Venkatachalam[2], angela Degrassi[3], Laura Stradford[1], Ambika Vartak[4] and Shelley Fritz[5], [1]Global Healthy Living Foundation, Nyack, NY, [2]Global Healthy Living Foundation, New York, NY, [3]Global Healthy Living Foundation, Upper Nyack, NY, [4]Global Healthy Living Foundation, Meriden, [5]Global Healthy Living Foundation, Kalaheo, HI

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

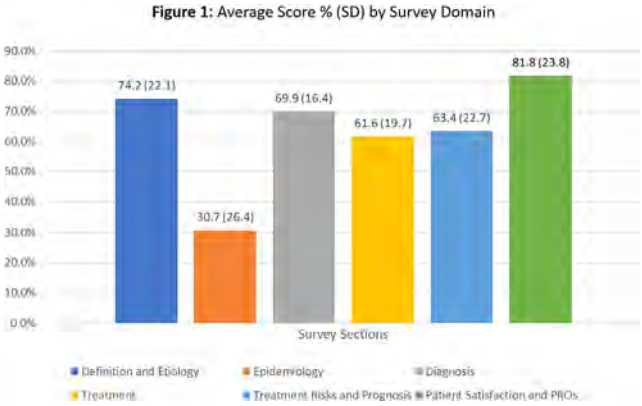


Figure 1: Average Score % (SD) by Survey Domain

Table 1: PMR Familiarity and Knowledge Assessment Participation Overview

Familiarity Category	n	% (of total respondents)
Total respondents asked about PMR	920	100%
Reported awareness of PMR	289	31.4%
Not aware or unsure about PMR	631	68.6%
...of whom recognized a condition with PMR-like symptoms	276	30.0%
Total invited to complete knowledge assessment	**565**	**61.4%**
Total completed knowledge assessment	**417**	**45.3%**

Background/Purpose: Polymyalgia rheumatica (PMR) is a commonly occurring inflammatory condition affecting older adults, primarily presenting with bilateral shoulder and hip stiffness. Despite its high prevalence in individuals over 50, there is a lack of evidence characterizing awareness or understanding of PMR among public health professionals (PHPs), defined as individuals working in disease diagnosis and treatment, health promotion, disease prevention, and health policy. This study assessed PHPs' familiarity with PMR and their knowledge across key clinical domains.

Methods: A cross-sectional knowledge assessment was administered to PHPs using convenience sampling via social media platforms and targeted outreach via the American Public Health Association email list. Participants were screened for prior familiarity of polymyalgia rheumatica (PMR) or familiarity with the hallmark symptoms of PMR. Those reporting familiarity were directed to complete a 31-item multiple-choice knowledge assessment across six domains: definition and etiology, epidemiology, diagnosis, treatment, treatment risks and prognosis, and patient satisfaction and reported outcomes. Those with no familiarity were excluded from the assessment to prevent bias but were included in descriptive reporting of awareness levels. Survey items were developed from a systematic literature review and validated by subject matter experts. Descriptive statistics were used to calculate mean scores and domain specific accuracy rates (**Figure 1**). Only fully completed responses from self-identified PHPs were analyzed. Duplicate entries were removed based on IP address, timestamps, and demographic data.

Results: Of 920 respondents asked about PMR, 289 (31.4%) reported prior awareness, while 631 (68.6%) had not heard of it or were unsure (**Table 1**). Among those not aware or unsure, 276 (43.7%) recognized a condition with symptoms consistent with PMR. In total, 565 participants familiar with PMR or its symptoms were invited to complete the full knowledge assessment; 417 provided complete responses and were included in the analysis. The average knowledge score was 64.7% (SD: 13.1%), with only 12.2% scoring 80% or higher. The largest knowledge gaps were in epidemiology, which had the lowest average score (30.7%); only 18.2% correctly identified estimated PMR prevalence, and 12.7% knew its estimated annual incidence. In the treatment domain, the mean score was 61.6% with 57.5% not knowing the proportion of patients who continue to experience symptoms with treatment, 50.9% not knowing appropriate visit frequency, and only 44.4% of respondents correctly identifying the first-line treatment for PMR.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Fewer than 40% of PHPs were familiar with PMR by name, and those with prior awareness showed notable gaps in epidemiology and treatment knowledge. Limited understanding of PMR's prevalence, diagnosis, and management among PHPs may contribute to under-recognition and delayed diagnosis. These findings underscore the need for targeted education to support earlier diagnosis, effective treatment, and better patient outcomes.

Disclosure: E. Stone: None; **S. Venkatachalam**: None; **a. Degrassi**: None; **L. Stradford**: None; **A. Vartak**: None; **S. Fritz**: None.

Abstract Number: 1618

Use of JAK inhibitors in patients with refractory Takayasu arteritis: A worldwide retrospective study

Fatma Alibaz-Oner[1], İbrahim yahya Çakır[2], Alessandro Tomelleri[3], Aysegul Avcu[4], Kaitlin Quinn[5], Durga Prasanna Misra[6], Matthew Koster[7], Peter Grayson[8], Alojzija Hocevar[9], Kenan Aksu[10], Duygu Kerim[11], Ertugrul Cağrı Bolek[12], Elena Baldissera[13], Corrado Campochiaro[14], Lorenzo Dagna[15], Sema Kaymaz-Tahra[16] and Haner Direskeneli[4], [1]MARMARA UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF INTERNAL MEDICINE, DIVISION OF RHEUMATOLOGY, Istanbul, Turkey, [2]Gazi University, Ankara, [3]IRCCS San Raffaele Hospital, Milan, Italy, Milano, Italy, [4]Marmara University, Istanbul, Turkey, [5]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [6]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, Lucknow, Uttar Pradesh, India, [7]Mayo Clinic, Rochester, MN, [8]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD, [9]University Medical Center Ljubljana, LJUBLJANA, Slovenia, [10]Ege Uni. Tip Fak., Istanbul, Turkey, [11]Ege University, Izmir, [12]Gazi University, Rheumatology, Ankara, [13]IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy, Milan, [14]IRCCS San Raffaele Hospital. Vita-Salute San Raffaele University, Milan, Milan, Italy, [15]Ospedale San Raffaele, Milano, Italy, [16]Bahcesehir University Faculty of Medicine Department of Internal Medicine Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Glucocorticoids(GCs) are the mainstay of treatment in Takayasu arteritis (TAK). Conventional DMARDs(cDMARDs) and biologic DMARDS(bDMARDs) are often used as steroid sparing agents in TAK. Janus kinase inhibitors (JAKi), recently shown to be effective in giant-cell arteritis may be effective to treat TAK,but evidence to date has been limited to small, single-center studies.In this worldwide multi-center study, we aimed to assess the efficacy and safety of JAKi in patients with TAK.

Methods: Patients fullfilling the 1990 ACR Classification Criteria for TAK were eligible to participate in a retrospective observational cohort study. Each patient must have been treated with a JAKi at any point in the disease course. A standardized case report form was completed by investigators at each participating tertiary referral center. Physician global assessment (PGA) was used as the gold standard definition of active disease, and the Kerr et al(NIH definition) was also used, if available. Complete remission was defined as no new signs and symptoms of vascular disease assessed by a physician, normalized acute phase reactants (APR) and reduction of GC dose under 10 mg/d of prednisolone or its equivalent at the third month of treatment. Partial response was defined as at least 50% decrease in PGA score,APR and at least 50% reduction of initial GC dose at the third month.

Results: Data was collected from 25 patients with TAK (mean age:34.5±11 years; female/male: 24/1;mean disease duration: 8.1±6 years) from 8 centers. All patients were refractory to both cDMARDs and bDMARDs, except 2 patients who were refractory only to cDMARDs and given JAKi prior to a trial of bDMARDs. Before switching to JAKi (19 tofacitinib,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1:Demographic and clinical features of patients with Takayasu arteritis at baseline

Table 1:Demographic and clinical features of patients with Takayasu arteritis at baseline

Age current, years	34.5±11.6
Age symptom onset, years	23.2±8.1
Age diagnosis, years	23.9±8.5
Gender, female, n (%)	24 (96)
Hata angiographic classification, type 5, n (%)	13 (52)
Goel et al, angiographic cluster, cluster 2, n (%)	8 (32)
Number of previous cDMARDs	2 (1-4)
Number of previous bDMARDs	2 (0-5)
Combined DMARDs, present, n (%)	4 (16)
Baseline disease activity	
PGA, active, n (%)	24 (96)
Kerr, active, n (%)	22 (88)
ITAS2010	3.4±2.5

Table 2. Follow- up data under JAK inhibitors

Table 2. Follow- up data under JAK inhibitors

	Baseline visit	3rd month of treatment (%)	6th month of treatment (%)	Last visit (%)
Complete Remission, n (%)	-	6/17 (35)	3/13 (23)	6/22 (27)
Partial Response, n(%)	-	2/17 (12)	3/13 (23)	4/22 (18)
PGA remission, n (%)	1 (4)	6/15 (40)	6/11 (54)	8/13 (62)
Kerr remission, n (%)	1 (4)	6/17 (35)	4/13 (30)	6/16 (38)
CRP, mg/L	24.6 (1-326)	3.1 (1.6-37.8)	8.1 (1.0-75.0)	6.1 (1.0-49.3)
GC dose, mg/d	15 (0-60)	8 (0-30)	7.5 (0-16)	4 (0-15)
VDI	3 (1-12)	-	-	3 (1-12)
Radiographic progression, n(%)	-	0/13 (0)	2/9 (22)	4 (19)

PGA: Physician global assessment, CRP: C reactive protein, GC: glucocorticoid, VDI: Vasculitis Damage Index

6 upadacitinib), patients had received a median of 2 cDMARDs (range 1-4). Additionally, 23 (92%) patients received TNF inhibitors, 12(48%) tocilizumab, 3 (12%) secukinumab, 2 (8%) ustekinumab and 1 (4%) rituximab. The median duration of treatment with JAKi was 15.5(2-87) months. Remission was achieved in 13 (52%) patients in a median of 4(1-16) months, according to PGA.. At the 3rd month of the JAKi treatment, 6 (35%) of the patients were in complete remission while a partial response was observed in 2 (12%) patients. A significant decrease in the GC dose was also observed (GC baseline vs 3rd month:15 (0-60) vs 8 (0-30), p=0.002) At the end of the follow-up, GC dose was ≤ 4 mg in 16% (3/19) of patients. GC dose

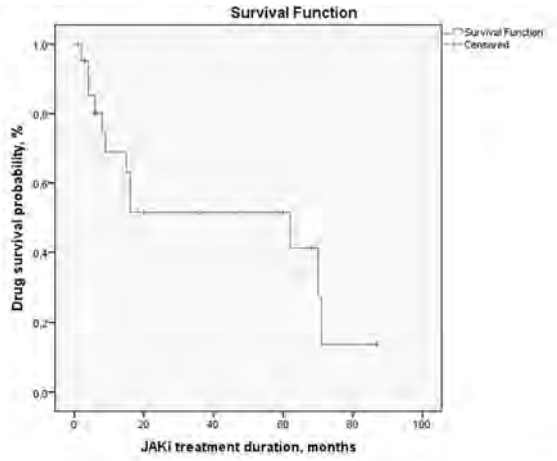


Figure 1. Drug survival of JAK inhibitors in patients with Takayasu arteritis.

Figure 1. Drug survival of JAK inhibitors in patients with Takayasu arteritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

was increased in 1 patient (from 8 mg/d to 15 mg/d). GC was stopped in 3 (19%) patients. During follow-up 22%(4/18) of the patients experienced a relapse. Nine(36%) of the patients had a sustained remission.JAKi was discontinued in 11/23 (48%) patients.The main reason for discontinuation was disease activity in 7, infections in 2,unknown in 2 patients.Radiographic progression was observed in 4/21 (19%) patients during the follow-up.(Figure 1).

Conclusion: This study showed that JAKi achieved clinical remission in about half of patients with TAK refractory to DMARDs within a median 4 months of treatment. Complete remission was also achieved in 35% of the patients with a significant decrease in glucocorticoid dose in the 3rd month.Our results suggest that JAKi may be effective options for the treatment of patients with refractory TAK.

Disclosure: F. Alibaz-Oner: None; **İ. Çakır**: None; **A. Tomelleri**: AbbVie/Abbott, 6; **A. Avcu**: None; **K. Quinn**: None; **D. Misra**: None; **M. Koster**: Amgen, 2; **P. Grayson**: None; **A. Hocevar**: None; **K. Aksu**: None; **D. Kerim**: None; **E. Bolek**: None; **E. Baldissera**: None; **C. Campochiaro**: Boehringer-Ingelheim, 6, Janssen, 6, Novartis, 6; **L. Dagna**: None; **S. Kaymaz-Tahra**: None; **H. Direskeneli**: None.

Abstract Number: 1619

Systemic Immune-Inflammation Index Is Superior to Neutrophil-to-Lymphocyte Ratio for Assessing Disease Activity in Polymyalgia Rheumatica and Giant Cell Arteritis

Gaston Ariel Ghio[1], Maria Gabriela Paz Machado[2], Evelin Encalada[2], Imma Perez Nadales[2], Georgina Salvador Alarcón[2], Elena Riera Alonso[2], manel pujol[2], Marta Pujol Teixidor[2] and Silvia Martinez Pardo[2], [1]Hospital Universitari Mùtua Terrassa, Terrassa, Catalonia, Spain, [2]Hospital Universitari Mùtua Terrassa, Terrassa, Spain

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

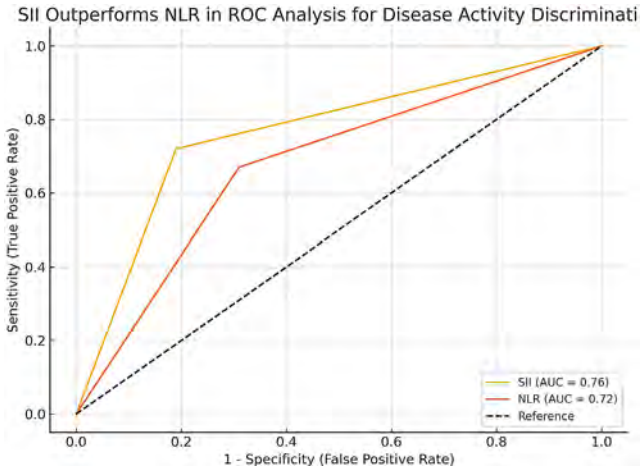
Background/Purpose: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are chronic inflammatory disorders predominantly affecting patients over 50. Despite unclear etiopathogenesis, both conditions share central immunopathogenic pathways. Recent evidence indicates they might constitute a continuum of a single disease with diverse clinical manifestations, highlighting the importance of identifying reliable inflammatory biomarkers. Both disorders drive systemic inflammation, impair patient functionality, and potentially lead to severe complications like ischemic optic neuropathy or aneurysms from vascular involvement. Thus, accessible and cost-effective biomarkers for monitoring disease activity remain critical. This study evaluates the neutrophil-to-lymphocyte ratio (NLR) and the systemic immune-inflammation index (SII) as novel hematological indices for assessing inflammatory activity in PMR and GCA.

BASELINE CHARACTERISTICS OF THE STUDY POPULATION

VARIABLE	VALUE
PCR, MG/L (MEDIANA[IQR])	3,3 [0,9–14,8]
VSG, MM/H (MEDIANA [IQR])	19 [7–31]
HEMOGLOBINA, G/DL (MEDIA ± DE)	13,4 ± 1,4
NEUTRÓFILOS, $\times 10^3/\mu L$ (MEDIA ± DE)	5,0 ± 2,1
LINFOCITOS, $\times 10^3/\mu L$ (MEDIA ± DE)	2,1 ± 0,7
PLAQUETAS, $\times 10^9/L$ (MEDIA ± DE)	249 ± 73
NLR (MEDIA ± DE)	**2,75 ± 1,78**
SII (MEDIA ± DE)	**682 ± 478**
GLUCOCORTICOIDES, N (%)	44 (65)
METOTREXATO, N (%)	14 (21)
TOCILIZUMAB, N (%)	8 (12)

BASELINE CHARACTERISTICS OF THE STUDY POPULATION *NLR (neutrophil-to-lymphocyte rati) SII (systemic immune-inflammation index)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



SII Outperforms NLR in ROC Analysis for Disease Activity Discrimination

Methods: We conducted a cross-sectional observational study including consecutive PMR and/or GCA patients fulfilling ACR-EULAR classification criteria. Patient demographics, clinical data (symptomatic systemic activity, treatment status), and laboratory parameters, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), NLR (neutrophils/lymphocytes), and SII (platelets × neutrophils/lymphocytes), were collected during a single assessment. Correlation analyses were performed using Spearman's test. Receiver operating characteristic (ROC) curves and Youden's index identified optimal diagnostic cut-offs. Sensitivity, specificity, positive (LR+) and negative (LR–) likelihood ratios, and odds ratios (OR) were calculated.

Results: A total of 68 patients were analyzed (mean age 76 ± 7 years; 53% female; PMR 85%, cranial GCA 19%, extracranial GCA 9%). Active systemic symptoms were present in 36 (53%) patients. Both NLR and SII were significantly higher in active compared to inactive patients (median NLR 2.63 vs. 1.84, $p = 0.002$; median SII 701 vs. 460, $p < 0.001$). Each index correlated moderately with CRP (NLR $\rho = 0.55$, SII $\rho = 0.62$; $p < 0.001$) but did not correlate significantly with ESR ($\rho \leq 0.19$; $p > 0.10$), nor were they affected by glucocorticoid therapy. ROC analysis showed SII had superior discriminatory power compared to NLR (AUC 0.76 vs. 0.72; $p < 0.05$). The optimal SII cut-off (≥560) demonstrated a sensitivity of 72%, specificity of 84%, LR+ of 4.6, LR– of 0.34, and OR of 14.0, significantly outperforming NLR ≥ 2.2 (sensitivity 67%, specificity 69%, LR + 2.1). Each 100-unit increase in SII was associated with a 28% increased odds of activity (OR 1.28, 95% CI 1.13–1.45), while each unit increase in NLR raised odds 1.6-fold (OR 1.63, 95% CI 1.11–2.39).

Conclusion: The SII emerges as a superior, glucocorticoid-independent marker of systemic disease activity in PMR/GCA compared to the NLR, providing additional clinical utility beyond ESR and complementing CRP. Its simple calculation from routine complete blood counts positions SII as an accessible and promising biomarker warranting prospective validation in longitudinal monitoring studies

Disclosure: G. Ghio: None; **M. Paz Machado**: None; **E. Encalada**: None; **I. Perez Nadales**: None; **G. Salvador Alarcón**: None; **E. Riera Alonso**: None; **m. pujol**: None; **M. Pujol Teixidor**: None; **S. Martinez Pardo**: None.

Abstract Number: 1620

Correlation Between Histopathological Findings and PET-CT Results in Patients With Inflammatory Aortitis

Guillem Verdaguer Faja[1], rafeal Benito-Melero[2], Ignasi Espadaler Fabregó[1], Laura López Vilaró[1], Mónica Velasco Nuño[1], Antonio José Barros Membrilla[1], Susana Fernández Sánchez[3], Jaime-Félix Dilmé Muñóz[1], Ivan Castellvi[4], Berta Magallares[5], Hye Sang Park[1], Asier García-Alija[6], Albert Casals Urquiza[3], Ana Laiz[3], Cesar Diaz-Torne[1], Jose Luis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Tandaipan[7], Luis Sainz Comas[1], Helena Codes Mendez[3], Júlia Bernardez Moreno[8], Carla Marco-Pascual[1], Concepción Pitarch[3], Andrea Garcia[3], Núria Fernández[3], Lorena Úbeda[3] and Hector Corominas[8], [1]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [2]MD, barcelona, Spain, [3]Sant Pau Hospital, Barcelona, Spain, [4]Hospital Universitari de la Santa Creu i Sant Pau, Sant Just Desvern, Spain, [5]Hospital de Sant Pau, Bareclona, [6]Sant Pau Hospital, Barcelona, Catalonia, Spain, [7]Hospital de la Santa Creu i Sant Pau, Terrassa, Spain, [8]Hospital de Sant Pau, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory aortitis is an uncommon condition that can be associated with rheumatologic, neoplastic, or infectious diseases. GCA and isolated aortitis are the most common causes.

Although diagnosis is typically based on a combination of clinical, laboratory, and imaging findings—with PET-CT being a key tool in evaluating active inflammatory processes—it is often underdiagnosed prior to surgery, and the diagnosis of aortitis is frequently made only after pathological confirmation.

Current literature includes few studies that specifically examine the relationship between preoperative PET-CT results and histopathological findings in patients with inflammatory aortitis.

Objective

To analyze the relationship between histopathological findings and preoperative PET-CT results in patients with biopsy-confirmed inflammatory aortitis or those under rheumatology follow-up.

Methods: Between 2020 and 2023, a total of 188 surgical procedures for aortic pathology were performed at our hospital. Cases were selected if they met at least one of the following criteria: (1) identification of an inflammatory pattern based on the standards of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology, or (2) active follow-up for a diagnosis of aortitis by the Rheumatology Department.

A total of 37 cases met the inclusion criteria. From this cohort, we selected patients who had undergone PET-CT prior to surgery and tissue sampling.

Table 1. Clinical and Demographic Characteristics

Age (years)	64.2 ± 10.2
Female/Male	3/2
Aortic aneurysm diameter (mm)	64.4 ± 12.8
Clinical presentation	
- Acute aortic syndrome	2 (40%)
- Aortic insufficiency	1 (20%)
- Incidental finding	2 (40%)
Time between PET-CT and surgery (months)	6 ± 6
Glucocorticoid treatment during PET-CT and surgery	0 (0%)
Immunosuppressive treatment during PET-CT and surgery	1 (20%) *
CRP levels prior to PET-CT	58.3 ± 97.7
CRP levels prior to surgery	28.3 ± 27.9
Reason for PET-CT request	
- Aortic aneurysm evaluation	3 (60%)
- Suspected neoplastic process	2 (40%)
PET-CT with signs suggestive of vasculitis	0 (0%)
Histology with inflammatory infiltrate	4 (80%)
- Granulomatous pattern	1 (20%)
- Lymphoplasmacytic pattern	2 (40%)
- - Suppurative pattern	1 (20%)
Rheumatology follow-up before histological confirmation of aortitis	1 (20%)

*Ustekinumab for Psoriasis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

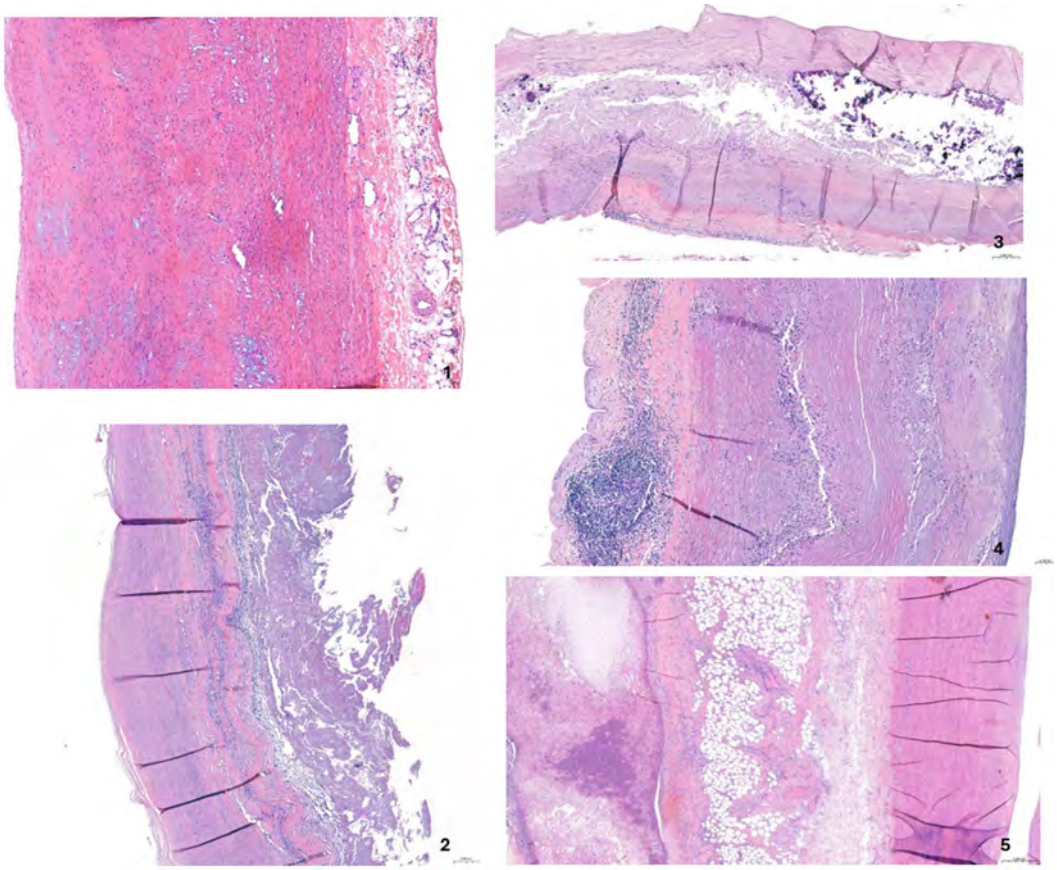
Table 2. Correlation Between PET-CT Findings, Histology, and Rheumatologic Diagnosis

Patient	Increased Vascular Metabolism on PET-CT	Biopsy Histology	Rheumatologic Clinical Diagnosis	Image-Histology Correlation
1	No	Degenerative non-inflammatory	Peripheral spondyloarthropathy	Yes
2	No	Lymphoplasmacytic periaortitis associated with fibrosis	Isolated aortitis	No
3	No	Lymphoplasmacytic periaortitis associated with severe atherosclerosis	Inflammatory atherosclerotic aneurysm	No
4	No	Granulomatous aortitis with multinucleated giant cells	Giant cell arteritis	No
5	No	Acute aortitis with fibrino-leukocytic material and positive culture for *P. acnes*	Infectious aortitis	No

Results: Five patients with a confirmed diagnosis were included: one with GCA, one with peripheral SpA, one with isolated aortitis, one with inflammatory atherosclerotic aneurysm, and one with infectious aortitis. Clinical and demographic characteristics are shown in Table 1.

Two patients underwent emergency surgery for acute aortic syndrome. In one case, a PET-CT performed 4 months prior showed aortomegaly without inflammatory signs, and the biopsy confirmed a non-inflammatory degenerative process, despite elevated CRP at the time of both procedures. In the other case, PET-CT performed the day before surgery revealed

Histopathological sections corresponding to the patients in Table 2. (1) Non-inflammatory medial degeneration with diffuse extracellular mucinous matrix. (2) Lymphoplasmacytic infiltrate and stromal fibrosis in adventitia. (3) Severe calcified arteriosclerosis with chronic lymphoid infiltrate. (4) Non-necrotizing granulomatous inflammation with multinucleated giant cells. (5) Acute neutrophilic infiltrate with adventitial necrosis.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

an aortic aneurysm without signs of vasculitis, while histological analysis showed a lymphoplasmacytic inflammatory infiltrate with associated fibrosis; this patient also had elevated CRP levels.

The remaining 3 patients underwent elective surgery for aortic aneurysm. In these cases, PET-CT also showed no signs of inflammation; however, histopathological analysis revealed inflammatory infiltrates in all specimens (Table 2 and Image).

In summary, among the cases analyzed, concordance between PET-CT and histopathological findings was observed in only 1 of 5 patients. In 4 patients, PET-CT results were negative, while biopsies demonstrated characteristic inflammatory patterns.

Conclusion: In this sample, a weak correlation was observed between PET-CT findings and histopathology. Some patients with negative PET-CT scans, showing no evidence of increased metabolic activity, exhibited inflammatory patterns on histological analysis. These findings suggest that a significant proportion of patients with negative PET-CT results may still have an underlying vasculitic process.

Disclosure: G. Verdaguer Faja: None; **r. Benito-Melero**: AbbVie/Abbott, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6; **I. Espadaler Fabregó**: None; **L. López Vilaró**: None; **M. Velasco Nuño**: None; **A. Barros Membrilla**: None; **S. Fernández Sánchez**: None; **J. Dilmé Muñóz**: None; **I. Castellvi**: None; **B. Magallares**: None; **H. Park**: None; **A. García-Alija**: None; **A. Casals Urquiza**: None; **A. Laiz**: None; **C. Diaz-Torne**: None; **J. Tandaipan**: None; **L. Sainz Comas**: None; **H. Codes Mendez**: None; **J. Bernardez Moreno**: None; **C. Marco-Pascual**: None; **C. Pitarch**: None; **A. Garcia**: None; **N. Fernández**: None; **L. Úbeda**: None; **H. Corominas**: None.

Abstract Number: 1621

Temporal Association Between Viral Positivity Rates and Kawasaki Disease Incidence at a Large Tertiary Center

Jessica Nguyen[1], Duc Nguyen[1], Ankona Banerjee[2], Kenneth Nobleza[2], Denver Niles[2] and Marietta De Guzman[1], [1]Baylor College of Medicine, Houston, TX, [2]Baylor College of Medicine, Houston

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Kawasaki disease (KD) is a systemic vasculitis associated with the development of coronary artery aneurysms predominantly affecting children less than 5 years of age. Prompt and accurate diagnosis remains challenging due to the unknown cause of this condition and the overlap of its clinical findings with other febrile illnesses in children. Viral infections have been proposed as a potential trigger for KD, particularly given the observed seasonal peaks in winter and spring across the continental United States. Previous studies have also suggested temporal associations between viral activity and KD incidence at certain centers. This study aims to characterize the seasonal distribution of KD and assess the temporal relationship between hospital viral positivity rates and KD incidence at a large tertiary center.

Methods: With IRB approval, we retrospectively reviewed patients diagnosed with KD at our institution from 2012 to 2019. We collected admission dates and demographic data. We obtained monthly viral positivity rates in hospitalized patients for 18 viruses (influenza A/B, respiratory syncytial virus, adenovirus, human metapneumovirus, rhinovirus, parainfluenza viruses

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Total (N=858)	2012 (n =85)	2013 (n =126)	2014 (n =111)	2015 (n =116)	2016 (n =109)	2017 (n =118)	2018 (n =104)	2019 (n =89)	Overall p-value
Patient age (years), median (IQR)	2.6 (1.2, 4.5)	2.6 (1.4, 4.6)	2.9 (1.4, 4.7)	2.3 (1.1, 4.3)	3.1 (1.3, 6.0)	2.7 (1.2, 4.6)	2.6 (1.2, 4.1)	2.8 (1.2, 4.8)	2.0 (1.2, 3.7)	0.32
Age (years)										0.26
0-5	676 (78.8)	66 (77.6)	100 (79.4)	90 (81.1)	80 (69.0)	88 (80.7)	97 (82.2)	79 (76.0)	76 (85.4)	
6-12	170 (19.8)	19 (22.4)	24 (19.0)	19 (17.1)	32 (27.6)	20 (18.3)	19 (16.1)	25 (24.0)	12 (13.5)	
13-17	12 (1.4)	0 (0.0)	2 (1.6)	2 (1.8)	4 (3.4)	1 (0.9)	2 (1.7)	0 (0.0)	1 (1.1)	
Legal sex										0.15
Female	324 (37.8)	34 (40.0)	50 (39.7)	35 (31.5)	55 (47.4)	46 (42.2)	40 (33.9)	37 (35.6)	27 (30.3)	
Male	534 (62.2)	51 (60.0)	76 (60.3)	76 (68.5)	61 (52.6)	63 (57.8)	78 (66.1)	67 (64.4)	62 (69.7)	
Race/Ethnicity										0.02
NH White	335 (39.0)	27 (31.8)	62 (49.2)	40 (36.0)	45 (38.8)	40 (36.7)	43 (36.4)	43 (41.3)	35 (39.3)	
NH Black	13 (1.5)	1 (1.2)	3 (2.4)	1 (0.9)	1 (0.9)	2 (1.8)	0 (0.0)	4 (3.8)	1 (1.1)	
Hispanic	490 (57.1)	54 (63.5)	61 (48.4)	68 (61.3)	66 (56.9)	66 (60.6)	72 (61.0)	51 (49.0)	52 (58.4)	
NH Asian	5 (0.6)	2 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	1 (0.8)	1 (1.0)	0 (0.0)	
NH Other	5 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.6)	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)	
Unknown	10 (1.2)	1 (1.2)	0 (0.0)	2 (1.8)	1 (0.9)	0 (0.0)	0 (0.0)	5 (4.8)	1 (1.1)	
Insurance										0.27
Self-pay	10 (1.2)	1 (1.2)	2 (1.6)	1 (0.9)	2 (1.7)	0 (0.0)	0 (0.0)	3 (2.9)	1 (1.1)	
Government	421 (49.1)	41 (48.2)	72 (57.1)	50 (45.0)	45 (38.8)	51 (46.8)	62 (52.5)	55 (52.9)	45 (50.6)	
Private	427 (49.8)	43 (50.6)	52 (41.3)	60 (54.1)	69 (59.5)	58 (53.2)	56 (47.5)	46 (44.2)	43 (48.3)	

Figure 1: Characteristics of patients with Kawasaki disease, by year of diagnosis

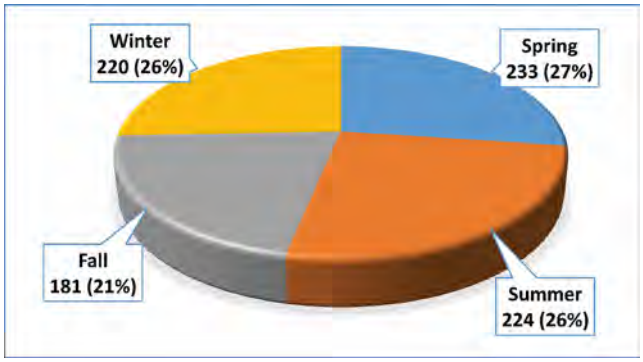


Figure 2: Number of Kawasaki disease cases, by season

1-4, norovirus, sapovirus, rotavirus, adenovirus (including types F40/41), astrovirus, herpes simplex virus (cutaneous, CSF and blood), enterovirus (CSF and blood), and varicella-zoster virus (cutaneous)) from institutional epidemiology reports. Negative binomial regression models were used to assess associations between viral activity and KD incidence: (1) a univariable

	Univariable		Multivariable models including individual viral infection*		Multivariable model including all viral infections*	
	IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
Influenza A	1.01 (0.97, 1.05)	0.69	1.01 (0.97, 1.05)	0.66	1.00 (0.95, 1.05)	0.99
Influenza B	1.01 (0.92, 1.11)	0.85	1.00 (0.90, 1.11)	0.99	0.94 (0.81, 1.10)	0.46
RSV	1.00 (0.98, 1.03)	0.70	1.01 (0.98, 1.03)	0.53	1.02 (0.98, 1.05)	0.39
Adenovirus	1.02 (0.91, 1.14)	0.72	1.02 (0.90, 1.14)	0.80	1.05 (0.91, 1.21)	0.53
hMPV	1.01 (0.97, 1.06)	0.62	1.01 (0.95, 1.07)	0.76	0.99 (0.91, 1.07)	0.74
Rhinovirus	1.00 (0.99, 1.01)	0.94	1.00 (0.99, 1.02)	0.84	1.00 (0.98, 1.02)	0.98
Para1	0.97 (0.88, 1.07)	0.54	0.97 (0.88, 1.08)	0.62	0.93 (0.81, 1.07)	0.33
Para2	0.98 (0.86, 1.12)	0.81	0.99 (0.86, 1.15)	0.93	0.93 (0.76, 1.15)	0.51
Para3	1.01 (0.95, 1.07)	0.71	1.01 (0.94, 1.08)	0.83	1.03 (0.94, 1.13)	0.56
Para4	1.05 (0.69, 1.60)	0.82	1.09 (0.70, 1.70)	0.71	--	--
Norovirus	1.03 (0.82, 1.28)	0.82	1.04 (0.83, 1.32)	0.71	0.95 (0.52, 1.75)	0.88
Sapovirus	1.03 (0.76, 1.41)	0.83	1.06 (0.77, 1.47)	0.72	1.18 (0.47, 2.95)	0.72
Rotavirus	1.27 (0.16, 10.28)	0.83	1.52 (0.17, 13.85)	0.71	--	--
Adenovirus (includes F40/41)	1.04 (0.76, 1.41)	0.82	1.06 (0.77, 1.48)	0.71	--	--
Astrovirus	1.03 (0.74, 1.44)	0.84	1.06 (0.75, 1.51)	0.73	--	--
HSV (cutaneous)	1.01 (0.95, 1.07)	0.86	1.01 (0.95, 1.08)	0.75	--	--
HSV (CSF + blood)	1.00 (0.89, 1.11)	0.94	1.00 (0.89, 1.11)	0.93	1.00 (0.89, 1.13)	0.96
Enterovirus (CSF)	0.99 (0.95, 1.02)	0.44	0.98 (0.94, 1.03)	0.44	0.98 (0.93, 1.04)	0.56
Enterovirus (CSF/blood)	0.99 (0.96, 1.02)	0.48	0.99 (0.96, 1.02)	0.51	0.99 (0.94, 1.04)	0.68
VZV cutaneous	1.03 (0.80, 1.32)	0.82	1.05 (0.81, 1.37)	0.71	--	--

RSV, respiratory syncytial virus
hMPV, human metapneumovirus
Para, parainfluenza
HSV, herpes simplex virus
VZV, varicella-zoster virus
IRR, incidence rate ratio - obtained from the negative binomial regression models.
***Multivariable model were adjusted for month and year of Kawasaki disease diagnosis**
"--" removed from the model due to collinearity

Figure 3: Association of viral infections and numbers of Kawasaki disease cases diagnosed, negative binomial regression models

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

analysis assessing each virus independently; (2) a multivariable model for individual viral infection adjusting for month and year; and (3) a fully adjusted model including all viruses while controlling for month and year.

Results: From 2012-2019, 858 patients were diagnosed with KD at our institution. The median age was 2.6 years (IQR 1.2–4.5), with no significant difference in male-to-female ratio across the study period. A statistically significant difference in racial/ethnic distribution was observed in 2013 compared to 2012, 2014, 2015, and 2017 (Figure 1). KD cases were evenly distributed across winter (26%), spring (27%), and summer (26%) (Figure 2). For all regression models, no significant temporal association was found between viral positivity rates and KD incidence (Figure 3).

Conclusion: At our institution, KD cases were evenly distributed across winter, spring, and summer, a pattern that contrasts with prior studies reporting seasonal peaks. Additionally, we found no significant temporal associations between viral positivity rates and KD incidence. These negative findings suggest that common viruses may not be the primary triggers of KD and underscore the need for broader investigative approaches. Ongoing research is critical to elucidate the underlying causes of KD and to enhance timely diagnosis and treatment in young children.

Disclosure: J. Nguyen: None; **D. Nguyen**: None; **A. Banerjee**: None; **K. Nobleza**: None; **D. Niles**: None; **M. De Guzman**: None.

Abstract Number: 1622

Defective CD4+ regulatory T cells in active Takayasu arteritis patients can be improved by efficiency treatment of tofacitinib

Jing Luo[1] and Lan He[2], [1]the first affiliated hospital of xi'an jiaotong university, xi'an, China (People's Republic), [2]The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China (People's Republic)

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: To investigate the efficacy of tofacitinib (TOF) in patients with active TAK, explore the effect on CD4+ regulatory T cells (Tregs) homeostasis and relationship with clinical outcomes.

Methods: This was a prospective, open-label cohort study. Thirty-four active TAK patients and 28 healthy controls (HCs) of comparable sex and age were recruited. All the patients were treated with glucocorticoids (GCs) and TOF. Complete response (CR) was assessed at the 6th month and relapse was recorded after CR, inflammatory parameter, GCs dose, vascular imaging, frequency and cytokine production of CD4+ regulatory T cells were evaluated for 24month follow-up. SPSS 22.0(SPSS, USA) was employed for data analysis. $P< 0.05$ indicated statistical significance.

Results: 1. CR was reached in 26/34 (76.47%) patients at 6th month. In responders group, the mean dosage of steroids and acute-phase reactants significantly decreased after 6 months TOF therapy.

2. In active TAK, the frequence of CD4+CD25+Foxp3+ Tregs and the percentage of Foxp3+ in CD4+CD25high T cells decreased, but IFN-γ+ and IL-17+ Tregs increased. Inflammatory Tregs correlated with disease activity parameters positively.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3.After 6months TOF efficiency therapy, the percentage of IFN-γ+ and IL-17+Tregs decreased, but the frequence of CD4+-CD25+Foxp3+ Tregs and the percentage of Foxp3+ in CD4+CD25high T cells increased in CR group, and the alterations existed during 24 months follow up.

Conclusion: Decreased CD4+Tregs displaying reduced expression of FOXP3, increased expression of IFN-γ and IL-17 have been implicated in the pathogenesis of TAK.TOF therapy can be a promising treatment for active TAK patients and improving the Tregs defects.

Disclosure: j. luo: None; **L. He**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GSK, 5, 6, Novartis, 6, Qilu Pharmaceutical, 6.

Abstract Number: 1623

The Association of Calprotectin with Vascular Injury and Remodeling in Clinically-Isolated Aortitis

Katarina Kmetova[1], Gavin Poppei[2], Kavya Sugur[3], Julia Ford[4], Wenying Liang[4], Emily Chong[4], Srilakshmi Yalavarthi[4], NaveenKumar Somanathapura[4], Nataliya Milman[5], Peter Merkel[6], Ora Singer[7] and Yu (Ray) Zuo[4], [1]Division of Rheumatology, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor, MI, [2]University of Michigan, Ann arbor, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Ann Arbor, MI, [4]University of Michigan, Ann Arbor, MI, [5]the Ottawa Hospital, Ottawa, ON, Canada, [6]University of Pennsylvania, Philadelphia, PA, [7]University of Michigan, Huntington Woods, MI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinically-isolated aortitis (CIA), defined as inflammation of the aortic wall in the absence of extra-aortic arterial involvement, systemic vasculitis, or other associated autoimmune disease, is often discovered incidentally on surgical pathology after resection of an aortic aneurysm. The pathogenesis of CIA remains largely unknown, complicating both diagnosis and management. Neutrophil extracellular traps (NETs) have been implicated in the pathophysiology of various forms of vasculitis and vascular injury. Calprotectin, a circulating marker of NET formation, is a promising mechanistic biomarker in various NET-driven diseases. This study aimed to investigate the role of calprotectin in CIA pathogenesis, focusing on endothelial activation, vascular remodeling, and calcification (**Fig. 1A**).

Methods: A multicenter CIA cohort (n=28) with pathology- or imaging-confirmed cases was assembled, along with healthy controls (n=34) without systemic autoimmune disease. Plasma calprotectin and endothelial activation markers (ICAM-1, VCAM-1) were measured. In vitro, plasma-derived and recombinant calprotectin were tested on human aortic endothelial (HAOEC) and smooth muscle cells (HASMC) to assess activation, proliferation, migration, endothelial-to-mesenchymal transition (EndoMT), and calcification.

Results: Circulating calprotectin levels were significantly higher in CIA patients compared to controls (**Fig. 1B**). Using a threshold defined by the 99th percentile of control values, 68% of patients with CIA were classified as calprotectin-positive. Among 14 patients with longitudinal imaging, 3 had progression of aortic disease (i.e., worsening aortic dilatation or new aneurysm), 2 of whom were previously calprotectin-positive. Patients with CIA showed higher levels of ICAM-1 and VCAM-1 (**Fig. 1C-D**). Calprotectin levels correlated with CRP ($r=0.63$, $p< 0.001$). Mechanistic studies revealed that plasma from calprotectin-high CIA patients activated HAOECs, significantly increasing surface expression of ICAM-1 ($p< 0.01$) and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

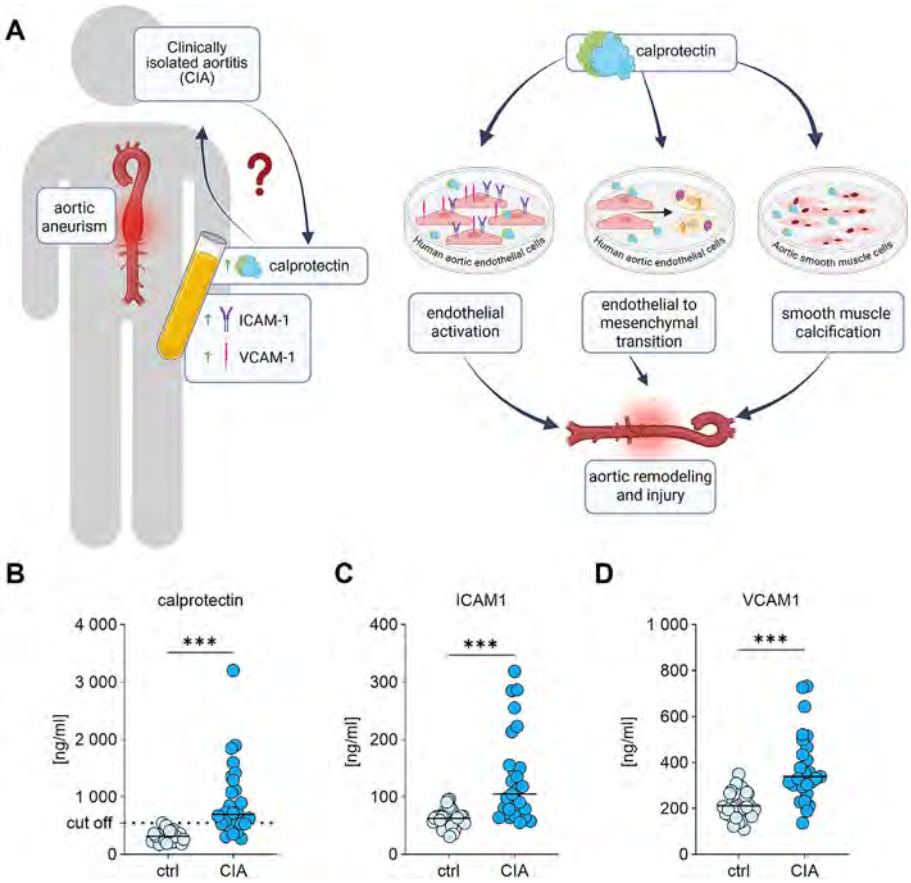


Figure 1: Circulating calprotectin and endothelial activation in patients with clinically-isolated aortitis. (A) Study design. Plasma samples were obtained from 28 patients with clinically-isolated aortitis and 34 healthy controls. Circulating levels of (B) calprotectin, (C) ICAM-1, and (D) VCAM-1 were quantified by ELISA. Data presented with median value. Statistical comparisons were performed using the Kruskal-Wallis test. *** - p<0.001;

VCAM-1 ($p < 0.05$). Similarly, exposure to recombinant calprotectin upregulated expression of ICAM-1 and VCAM-1 transcripts ($p < 0.05$ for both). Calprotectin exposure resulted in i) increased expression of mesenchymal markers, including α-SMA and Transgelin (**Fig. 2A–E**), consistent with the induction of EndoMT and ii) promotion of endothelial cell proliferation and migration (**Fig. 2F–I**). In HASMCs, the addition of recombinant calprotectin significantly increased intracellular calcium deposition (**Fig. 3**), suggesting a role in promoting microcalcification and vascular stiffening.

Conclusion: Calprotectin is elevated in most patients with CIA and may contribute to disease pathogenesis by activating aortic endothelial cells, triggering proliferation, migration, and EndoMT, while also driving microcalcification in smooth muscle cells. Together, these changes suggest a role for calprotectin in vascular remodeling. Our findings suggest a neutrophil-driven pathway of aortic injury in CIA, supporting further investigation of calprotectin as a potential biomarker and therapeutic target.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

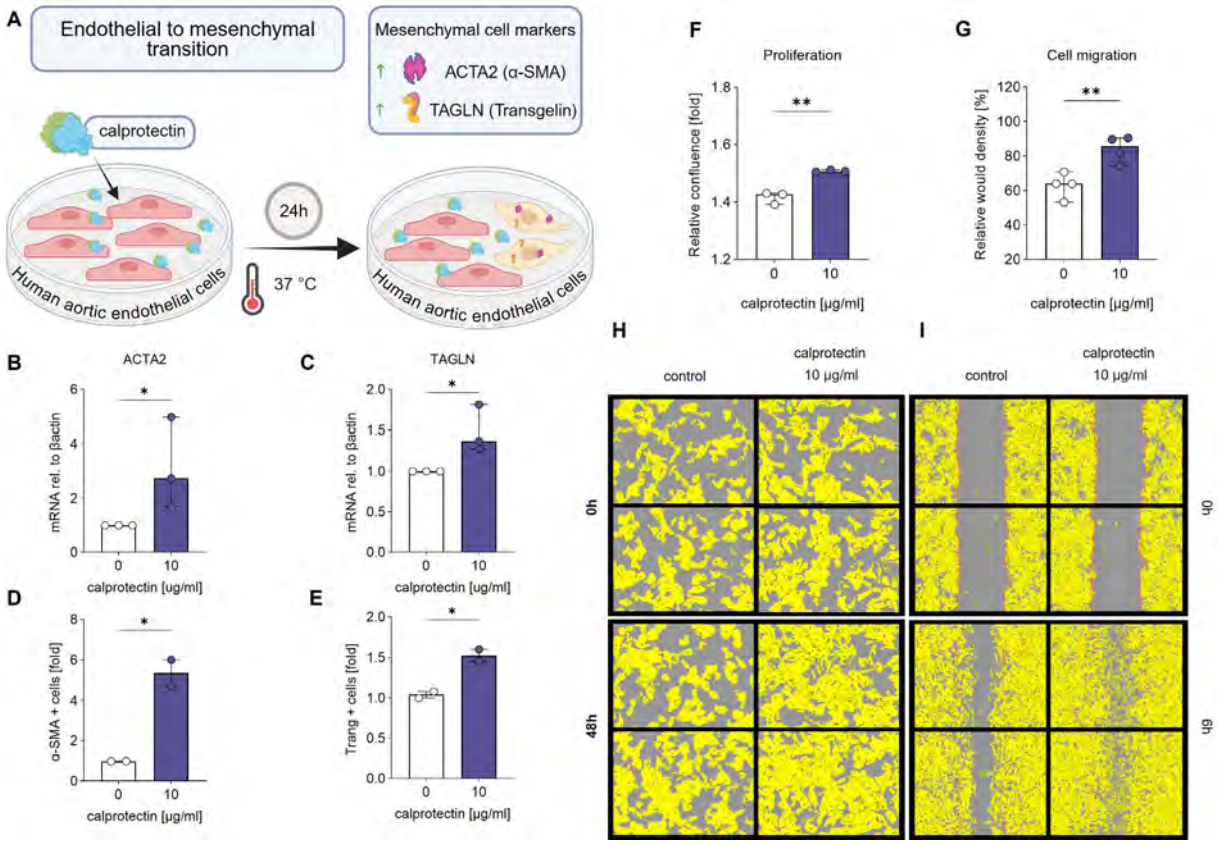


Figure 2: Calprotectin triggers endothelial-to-mesenchymal transition (EndoMT) in human aortic endothelial cells (HAOECs). (A) HAOECs were cultured with 10 µg/mL recombinant calprotectin for 24 h. (B, C) Calprotectin-treated cells showed an increased expression of markers of EndoMT: ACTA2 and TAGLN (D, E) further validated by flow cytometry. Calprotectin also altered behavior of HAOECs, promoting (F, H) proliferation and (G, I) migration. Images were captured and analyzed using the Incucyte® Live-Cell Analysis System. Data presented with median ± 95% CI. Statistical analysis was performed using the Kruskal-Wallis test. * - p<0.05; ** - p<0.01

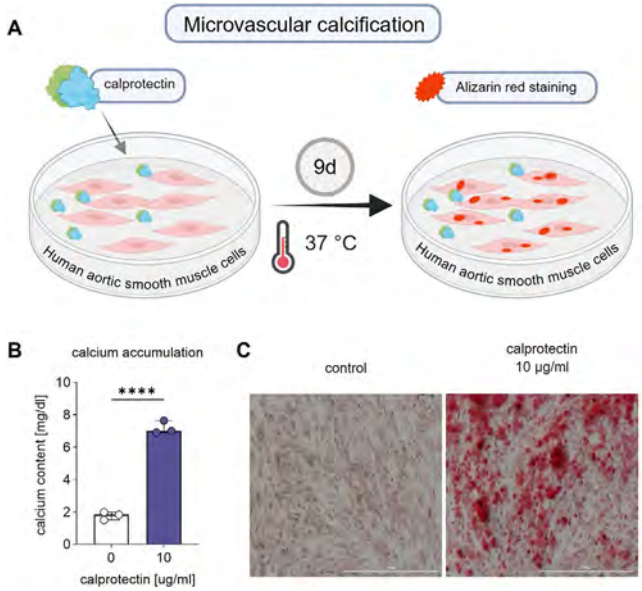


Figure 3: Calprotectin-induced microvascular Ca2+ accumulation in human aortic smooth muscle cells (HASMC). (A) HASMCs were treated with 10 µg/mL calprotectin for 9 days. (B) Following treatment, cells were washed and incubated with 1 M HCl to dissolve intracellular calcium. Calcium content was quantified using the QuantiChrom™ Calcium Assay Kit. (C) Calcium accumulation was visualized by staining with 1% Alizarin Red for 45 min, with calcified areas appearing as red deposits. Data presented with median ± 95% CI. Statistical analysis was performed using the Kruskal-Wallis test. **** - p<0.0001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Kmetova: None; **G. Poppei**: None; **K. Sugur**: None; **J. Ford**: None; **W. Liang**: None; **E. Chong**: None; **S. Yalavarthi**: None; **N. Somanathapura**: None; **N. Milman**: Abbvie, 1, Boehringer Ingelheim, 1, 6, Fresenium-Kabi, 1, 6, Gilead, 1, GlaxoSmithKlein(GSK), 6, Novartis, 1, Otsuka, 1, Sandoz, 1, TEVA, 1; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **O. Singer**: None; **Y. Zuo**: None.

Abstract Number: 1624

Disease activity status in Takayasu's arteritis influences the angiogenic potential of patient-derived endothelial cells

Luciana Yamamoto de Almeida[1], Kaitlin Quinn[2], James Simone[2], Lily Dai[2], Benjamin Turturice[2], Urvashi Kaundal[2], Chloe Palmer[2], Karyssa Stonick[3], davide Randazzo[4], Carmelo Carmona-Rivera[5] and Peter Grayson[6], [1]National Institutes of Health, Bethesda, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [3]National Insitute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [4]Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, [5]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, MD, [6]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Takayasu's arteritis (TAK) is a rare, systemic, chronic large vessel vasculitis of unknown etiology primarily affecting the aorta and its branches. Arterial damage, with stenosis or occlusion of the large arteries, may occur as a result of vascular inflammation. In response, collateral circulation is known to develop in some patients and helps overcome vascular damage by providing alternative blood flow to areas where major vessels are blocked or narrowed. Therapeutic targeting of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) can lead to clinical improvement in subsets of patients with TAK. However, it remains unclear which components are more likely to be effective targets for the treatment of TAK and whether they may impact collateral vessel formation. The aim of this study is to investigate whether and how inflammation affects angiogenic outcomes in the context of TAK.

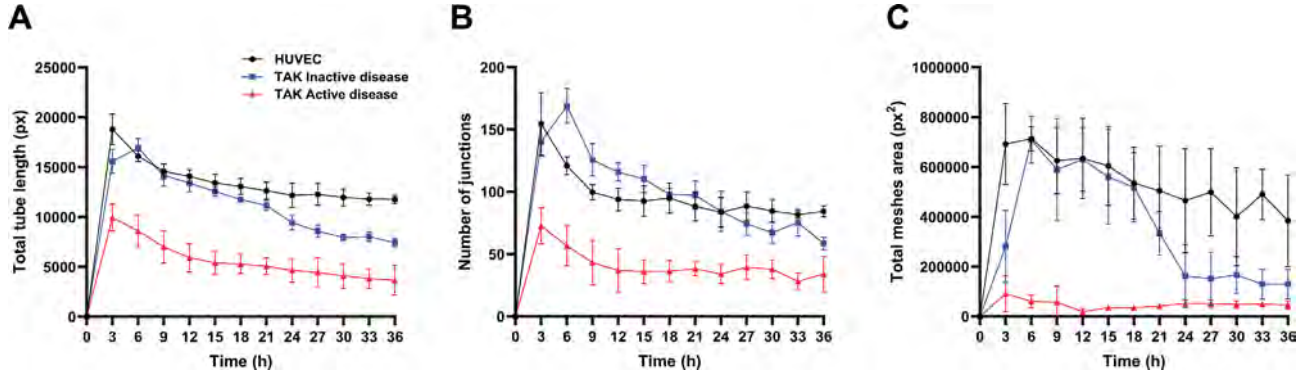


Figure 1: Matrigel tube formation assay in an Incucyte® Live-Cell Analysis System. TAK-derived CECs from active and inactive disease states, as well as HUVECs, were cultured in endothelial growth media (EGM-2) for 36 h in 96-well plates coated with a semi-solid Matrigel. The total tube lengths (A), number of junctions (B), and total meshes area (C) formed in the assay were measured. Data are presented as the mean ± standard error of the mean.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: To understand the molecular players involved in TAK disease activity and blood vessel formation, we utilized flow cytometry to analyze the frequency of peripheral blood-derived circulating endothelial progenitor (EPCs) and $CD31^+$ terminally differentiated endothelial cells (CECs), Luminex assays to measure plasma-derived cytokines and growth factors, and live cell imaging of Matrigel-based tube formation assays to test the angiogenic potential of CECs and endothelial cell lines *in vitro* (Figure 1). As TNF-α and IL-6 have an important role in driving TAK-related inflammation, we investigated their effect on angiogenesis.

Results: Neither the frequency of EPCs nor CECs among TAK patients was significantly correlated with disease activity in our cohort TAK patients (n = 9). Additionally, there were no striking differences in the overall profile of plasma-derived cytokines and growth factors in these patients (n= 64). However, CECs isolated from TAK patients in remission exhibited a robust angiogenic potential that was similar to that of endothelial cell lines, while those from TAK patients with active disease showed diminished capacity to form tubular structures. Finally, TNF-α but not IL-6 or the IL6/sIL6R complex showed an apparent anti-angiogenic effect *in vitro*.

Conclusion: We established an efficient *in vitro* assay capable of confirming that chronic inflammation in TAK can lead to endothelial dysfunction, since the disease activity state influences the angiogenic capabilities of patient-derived CECs. In addition, we identified TNF-α as a dominant cytokine that contributes to vascular pathology. Overall, our experimental framework provides useful insights into the basic mechanisms of TAK pathogenesis. Future research integrating clinical response with effective therapy to reduce inflammation and promote collateral vessel formation may be potentially beneficial for patients with TAK.

Disclosure: L. Yamamoto de Almeida: None; **K. Quinn**: None; **J. Simone**: None; **L. Dai**: None; **B. Turturice**: None; **U. Kaundal**: None; **C. Palmer**: None; **K. Stonick**: None; **d. Randazzo**: None; **C. Carmona-Rivera**: None; **P. Grayson**: None.

Abstract Number: 1625

Factor VIII as a Potential Biomarker of Disease Activity in Relapsing Polychondritis

Ashika Ajitumar[1], Eric Robbins[2], Yusuf Mastoor[2] and **Marcela ferrada**[3], [1]University of Maryland, baltimore, MD, [2]University of Maryland, baltimore, [3]University of Maryland, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Relapsing polychondritis (RP) is a rare autoimmune disease marked by episodic inflammation of cartilaginous tissues. A major challenge in its clinical management is the absence of reliable biomarkers to track disease activity. Conventional inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) often fail to correlate with clinical disease flares. As part of a prospective cohort study of patients with relapsing polychondritis we evaluated the utility of Factor VIII levels as a potential biomarker for disease activity in patients with RP.

Methods: Patients older than 18 years old with a confirm diagnosis of RP were included in this study. All patients were evaluated prospectively as part of a dedicated relapsing polychondritis cohort at the University of Maryland. Each patient underwent standardized assessment for disease activity and organ damage using clinical evaluations at the time of laboratory

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

testing. Serum levels of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and Factor VIII were measured in all participants. Statistical analysis was performed using t-tests for categorical variables to evaluate associations between biomarkers and disease activity.

Results: Of the 50 patients included, the majority were female (87%). Factor VIII levels ranged from 70% to 400%, with a median value of 172%. Laboratory values were collected at the time of clinical evaluation. Elevated Factor VIII was identified in 27 patients; of these, 22 (81%) had clinically active disease, a statistically significant association ($p = 0.02$). In contrast, ESR was elevated in only 2 patients and CRP in just 1, demonstrating poor correlation with disease activity. LDH, measured in a subset, also correlated with both elevated Factor VIII and clinical activity.

Conclusion: Factor VIII appears to be a promising biomarker for disease activity in relapsing polychondritis, showing a statistically significant correlation with active disease. In contrast, traditional inflammatory markers like ESR and CRP were elevated in very few patients and did not reflect disease status. These findings support the need for further investigation of Factor VIII as a more reliable tool for monitoring RP, and highlight the limitations of relying solely on ESR and CRP in clinical assessment

Disclosure: A. Ajitumar: None; **E. Robbins**: None; **Y. Mastoor**: None; **M. ferrada**: UpToDate, 9.

Abstract Number: 1626

A Delphi Exercise Informing the Development of Criteria to Measure Response to Treatment in Giant Cell Arteritis

Medha Soowamber[1], Milena Bond[2], Catalina Sanchez Alvarez[3], Carol Langford[4], Sibel Aydin[5], FRANK BUTTGEREIT[6], Dario Camellino[7], Maria Cid[8], Peter Grayson[9], Bernhard Hellmich[10], Tanaz Kermani[11], Nader Khalidi[12], Sarah Mackie[13], Alfred Mahr[14], Eric L Matteson[3], Mehrdad Maz[15], Peter Merkel[16], Paul Monach[17], Lorna Neill[18], Cristina Ponte[19], Carlo Salvarani[20], Wolfgang Schmidt[21], Peter Villiger[22], Kenneth Warrington[23], Christian Dejaco[24], Sofia Ramiro[25] and Zahi Touma[26], [1]Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, [2]South Tyrol Health Trust and Teaching Hospital of the Paracelsus Medical University, Brunico, Italy, [3]Mayo Clinic College of Medicine and Science, Rochester, MN, [4]Cleveland Clinic, Moreland Hills, OH, [5]Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [6]Charité University Medicine Berlin, Berlin, Berlin, Germany, [7]"La Colletta" hospital, Azienda Sanitaria Locale 3 Genovese, Arenzano, Italy, [8]Department of Autoimmune Diseases (member of European Reference Network RITA), Hospital Clinic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain, [9]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD, [10]Department of Internal Medicine, Rheumatology, Pulmonology, Nephrology and Diabetology, Medius Kliniken Kirchheim/Teck, University Tübingen, Tübingen, Germany, Kirchheim-Teck, Germany, [11]David Geffen School of Medicine, University of California, Los Angeles, CA, [12]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Canada, [13]University of Leeds, Leeds, United Kingdom, [14]Klinik für Rheumatologie, Kantonspital St Gallen, St Gallen, Switzerland, [15]The University of Kansas Medical Center, Kansas City, KS, [16]University of Pennsylvania, Philadelphia, PA, [17]VA Boston Healthcare System, Boston, MA, [18]Patient Charity Polymyalgia Rheumatica and Giant Cell Arteritis Scotland, Nethy Bridge, United Kingdom, [19]Unidade Local de Saúde de Santa Maria, Lisbon, Portugal, [20]Unit of Rheumatology, Azienda USL - IRCCS di Reggio Emilia, and University of Modena and Reggio Emilia, Reggio Emilia, Italy, [21]Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch; Waldfriede Hospital, Rheumatology, Berlin, Germany, [22]Medical Center Monbijou, Rheumatology and Clinical Immunology, Bern, Switzerland, [23]Mayo Clinic, ROCHESTER, MN, [24]Medical University of Graz, Graz, Austria, [25]Leiden University Medical Center, Bunde, Netherlands, [26]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

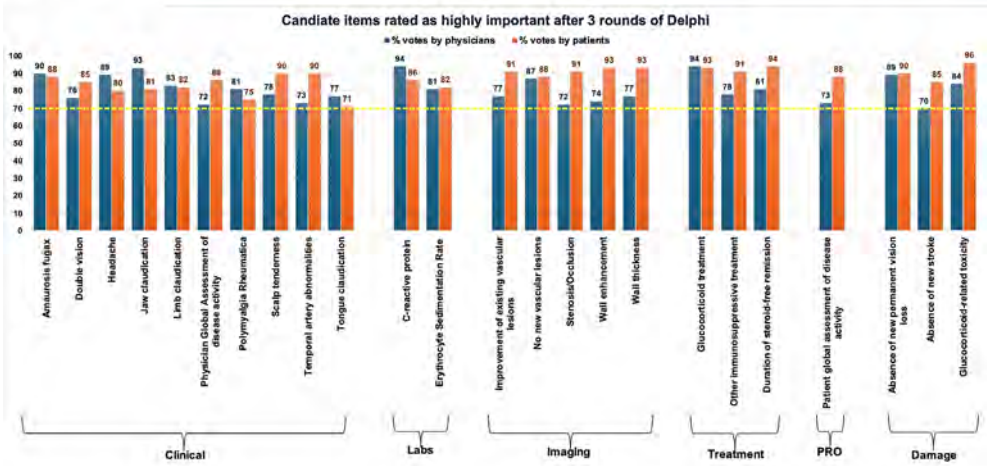
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Twenty-four items regarding response to treatment in giant cell arteritis that reached consensus after 3 Delphi rounds



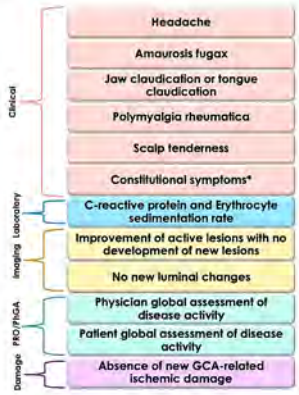
Legend: Labs: laboratory parameters; PRO: patient-reported outcome; yellow dotted line: cut-off for consensus (consensus: Items obtaining a score 7-9 by at least 70% of physicians and 70% of patients); Items shown here reached consensus in the last round each item was included.

Background/Purpose: The therapeutic landscape of giant cell arteritis (GCA) is growing rapidly but there are currently no internationally standardized criteria for assessing response to treatment in GCA. To address this issue, there is an ongoing project to develop response criteria for GCA, supported by European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR). Following a systematic literature review (SLR), a Delphi exercise was conducted to determine items that might be included in the future response criteria.

The goal of this Delphi exercise was to identify the most important and relevant items to consider when developing criteria to measure response to treatment in GCA.

Methods: A four-round web-based Delphi exercise was conducted. Participants from 38 countries included patients with GCA and physicians with expertise in GCA. They rated the importance (1=lowest, 9=highest) of 51 items from a prior SLR, grouped into six domains, and suggested additional items. Items obtaining a score of 7-9 by at least 70% of physicians

Figure 2. The 12 items selected for the next step in developing criteria for response in giant cell arteritis: preliminary criteria and item weighting



Legend: PRO: patient-reported outcome; PhGA: physician global assessment of disease activity; Colors are reflective of the categories of items selected.

*Items selected by the task force, despite not reaching consensus in the Delphi exercise.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and 70% of patients were considered critically important and to have reached consensus for inclusion. Items which scored 1-3 by 70% of physicians and patients were considered not important and excluded from subsequent rounds. In a 4th round of the Delphi (ranking round), participants selected and ranked the 10 most relevant items from those deemed most important in the previous three rounds. A task force (n=32 members) meeting followed to review the Delphi results, discuss rankings, and finalize the selection of items.

Results: A total of 187 physicians and 85 patients participated in the Delphi exercise. Thirteen new items were proposed in round 1. Twenty-four items were rated as critically important (18 in round 1, 5 in round 2, 1 in round 3) by ≥70% of patients and ≥70% of physicians **(Figure 1)**. These items covered the six domains of the Delphi **(Figure 1)**: 10 for clinical, 2 for laboratory, 5 for imaging, 3 for treatment, 1 for patient-reported outcomes and 3 for damage. No items were excluded during any round, and consensus was not reached for 40 items.

The top three highest-rated items by both patients and physicians were headache (ranked highest by 52% of patients and physicians), amaurosis fugax (ranked highest by 10%), and jaw claudication (ranked highest by 7%).

Of the task force members, 24/32 (75%) participated in the virtual task force meeting. Among the items discussed by the task force **(Figure 1)**, glucocorticoid-related parameters were excluded as they were considered indirect indicators of response to treatment. Constitutional symptoms were added by the task force as they are important constellation of symptoms seen in GCA. The task force also decided to cluster items with similar constructs to capture the spectrum of the disease more concisely. 12 items were selected for the next phase of the project **(Figure 2)**.

Conclusion: This Delphi exercise identified a set of 12 items within 6 domains as being relevant towards measuring response in GCA. These 12 items will be used in a subsequent group conjoint analysis to further prioritize and weigh potential items for inclusion in a draft set of criteria to measure treatment response in GCA.

Disclosure: M. Soowamber: AbbVie/Abbott, 6; **M. Bond**: AbbVie/Abbott, 6; **C. Sanchez Alvarez**: None; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6; **D. Camellino**: AstraZeneca, 6, Boehringer-Ingelheim, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6; **M. Cid**: AbbVie, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL-Vifor, 2, 6, GSK, 2, 6, Kiniksa Pharmaceuticals, 5, UpToDate, 9; **P. Grayson**: None; **B. Hellmich**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, CSL Vifor, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Novartis, 1, 6, Pfizer, 6; **T. Kermani**: None; **N. Khalidi**: AbbVie/Abbott, 2, 5, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 5, GlaxoSmithKlein(GSK), 2, 6, Mallinckrodt, 2, NS Pharma, 5, Otsuka, 2, 6, Roche, 2, 6, Sanofi, 2, 5; **S. Mackie**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, Fresenius Kabi, 6, Novartis, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, UCB, 6, Vifor, 6; **A. Mahr**: None; **E. Matteson**: Amgen, 4, Boehringer-Ingelheim, 2, 6, HorizonTherapeutics, 4; **M. Maz**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **P. Monach**: Boehringer-Ingelheim, 2; **L. Neill**: None; **C. Ponte**: AbbVie/Abbott, 2, 4, 6, CSL Vifor, 2, 4, 6, GlaxoSmithKlein(GSK), 2, 6, Novartis, 5, 6, Pfizer, 6; **C. Salvarani**: None; **W. Schmidt**: AbbVie, 1, 5, 6, Alfasigma, 6, Amgen, 6, Boehringer-Ingelheim, 1, Chugai, 6, Eli Lilly, 6, Fresenius Kabi, 1, GlaxoSmithKline, 6, Medac, 6, Novartis, 1, 5, 6, Pfizer, 6, UCB, 6; **P. Villiger**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **C. Dejaco**: AbbVie/

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abbott, 2, 5, 6, Eli Lilly and Company, 2, 6, Janssen Pharmaceuticals Inc, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Sparrow Pharmaceuticals, 2, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2.

Abstract Number: 1627

A Systematic Literature Review to Inform the 2025 EULAR Recommendations for Management of Polymyalgia Rheumatica and Large Vessel Vasculitis: Management of Disease Including Relapse and Complications

Mrinalini Dey[1], Durga Prasanna Misra[2], Alice Bartoletti[3], Georgina Ducker[4], Sara Monti[5], Bernhard Hellmich[6], Chetan Mukhtyar[7], Paul Studenic[8], Elena Nikiphorou[9] and The EULAR taskforce for the 2025 EULAR recommendations for PMR and LVV, [1]Centre for Rheumatic Diseases, King's College London, London, United Kingdom, [2]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, Lucknow, Uttar Pradesh, India, [3]ASST Gaetano Pini CTO, Cremona, Italy, [4]Department of Rheumatology, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK, Norwich, England, United Kingdom, [5]University of Pavia, Pavia, Pavia, Italy, [6]Department of Internal Medicine, Rheumatology, Pulmonology, Nephrology and Diabetology, Medius Kliniken Kirchheim/Teck, University Tübingen, Tübingen, Germany, Kirchheim-Teck, Germany, [7]Norfolk and Norwich University Hospital, Norwich, England, United Kingdom, [8]Internal Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, Vienna, Austria, [9]King's College London, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

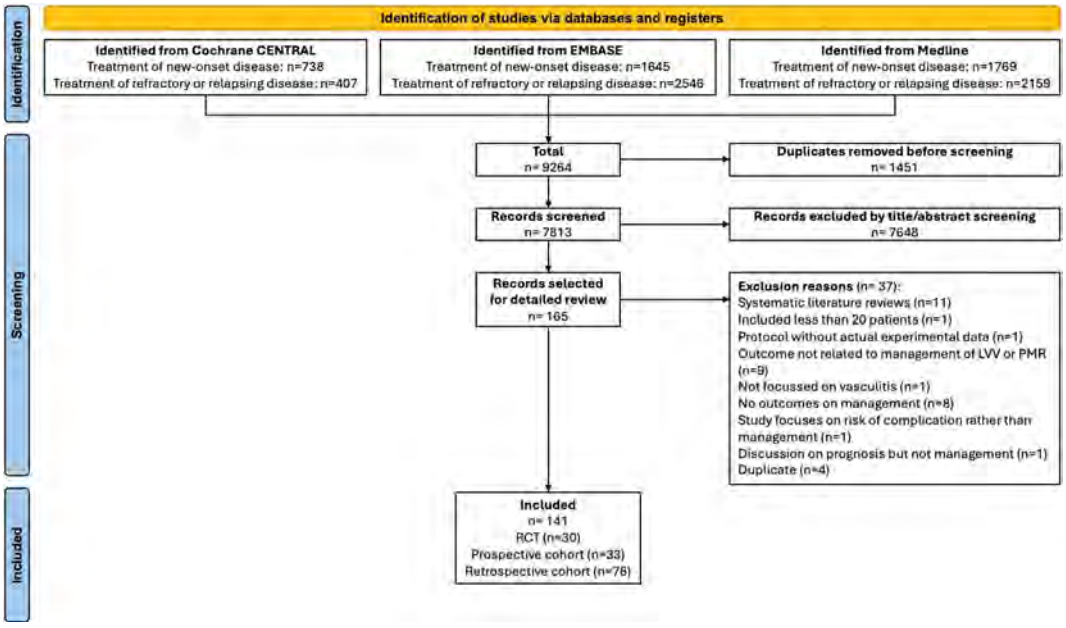


Figure 1: PRISMA flowchart

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Low Risk of Bias RCTs of patients with GCA or PMR

Disease, Population (treatment-naïve/ relapsing)	Author/ Year	Intervention (n) Comparator (n)	Primary outcome	Results	Conclusion
GCA: treatment-naive and relapsing	Cid 2022	MAV (n=42) PBO(n=28)	Time to flare (ITT)	HR 0.38 (0.15-0.92)	MAV superior to PBO
	Venhoff 2023	SEC(n=27) PBO (n=25)	Sustained remission (28w, ITT)	RD 0.50 (0.29 - 0.67) RR 3.43 (2.10 - 5.87)	SEC superior to PBO
	Blockmans 2025	UPA 15 mg (n=209) UPA 7.5 mg (n=107) PBO (n=112)	Sustained remission from week 12 to 52w	UPA 15: 37.1% (30.5 – 43.7) UPA 7.5: 26.2% (17.8 – 34.5) PBO: 16.1% (9.3 – 22.9)	UPA 15 superior to UPA 7.5 or PBO
PMR: treatment-naive	Cutolo 2017	MR PRED (n=32) IR PRED (n=30)	Complete response rate (4w, PP)	RD 12.22 (95%CI -15.82% to 40.25%) did not met non-inferiority criteria (-15%).	MR PRED similar to IR PRED.
	Bonelli 2022	TOC (n=19) PBO (n=17)	GC-free remission (16w)	OR 12.9 (2.2-73.6)	TOC superior to PBO
	Saraux 2024	BARI (n=18) PBO (n=16)	CRP PMR-AS≤10 without GC (ITT) at 12w	RR 5.8 (3.2 – 10.6)	BARI superior to PBO
PMR: treatment-naive and relapsing	Marsman 2021	RTX Single dose 1000 mg (n=23) PBO (n=24)	GC-free remission (21w)	RD (one sided 95%CI): 27 (4) % RR: 2.3 (1.1)	RTX superior to PBO
	Devauchelle-Pensec 2022	TOC (n=49) PBO (n=51)	CRP PMR AS <10 with PRED≤5 mg/day/ reduction in PRED dose ≥10 mg/day (w24, ITT)	RR 2.3 (1.5-3.6)	TOC superior to PBO
PMR: relapsing	Spiera 2023	SAR (n=59) PBO (n=58)	Sustained remission (52w)	SAR 28%, PBO 10%	SAR superior to PBO

BARI – Baricitinib, CRP -C-reactive protein, GC – Glucocorticoid, HR – Hazard ratio, IR – Immediate release, ITT – Intention to treat, MAV – Mavrilimumab, OR – Odds ratio, PBO – Placebo, PP – Per protocol, PRED – Prednisone, MPRED – Methylprednisolone, MR – Modified release, PMR-AS - PMR activity score, RD - Risk difference, RR – Risk ratio, RTX – Rituximab, SAR – Sarilumab, SEC – Secukinumab, TOC – Tocilizumab, UPA – Upadacitinib, w - weeks
*Studies published since 1st April 2014 (for PMR) or 31st December 2017 (for GCA)

Background/Purpose: EULAR recommendations informing the management of Polymyalgia Rheumatica (PMR) and Large Vessel Vasculitis (LVV) were previously published separately in 2015 [1] and 2020 [2] respectively. Newly-emerging evidence has necessitated a comprehensive update. We aimed to conduct a systematic literature review (SLR) to inform the 2025 EULAR recommendations for PMR and LVV.

Methods: An SLR (PROSPERO registration: CRD42024560403), performed on 31st December 2024 on MEDLINE, EMBASE and CENTRAL searched for literature on adult patients with PMR, Giant Cell Arteritis (GCA) or Takayasu arteritis (TAK), using MeSH terms for pharmacological and non-pharmacological management. Eligible studies included randomized controlled trials (RCTs) and observational studies, published since 1st April 2014 (for PMR) or 31st December 2017 (for LVV), without language limitations. Abstracts presented at EULAR 2024 and ACR 2024 were additionally hand-searched. Studies were assessed for their quality using relevant Risk of Bias (RoB) tools for RCTs/observational studies (Cochrane Risk of Bias 2/Newcastle Ottawa Scale).

Results: After deduplication and full-text screening, 141 articles were included (30 RCTs) (Figure 1). RCTs of GCA (low RoB) reported superiority of secukinumab (Phase-2, n=1), mavrilimumab (Phase-2, n=1) and upadacitinib (Phase-3, n=1) vs placebo; Phase-2 trials of sarilumab (n=1) and sirukumab (n=1) were prematurely terminated (high RoB). The two RCTs of sariliumab and sirukumab in GCA were at high risk of bias due to their premature termination due to which no inferences could be drawn about their effectiveness. Secondary analyses from the GiACTA trial reported similar efficacy of tocilizumab versus placebo in those with cranial symptoms, PMR symptoms, or both cranial & PMR symptoms, and better improvements in SF-36 and fatigue scores with tocilizumab than placebo. RCTs of TAK reported similar effectiveness of methotrexate or mycophenolate (unclear RoB), and superiority of adalimumab vs tocilizumab (high RoB). Phase-3 RCTs in PMR revealed superiority of tocilizumab and sarilumab (low RoB) vs. placebo while smaller phase-2 studies provided initial evidence for efficacy of rituximab (low RoB) and abatacept (unclear RoB) vs placebo (Table 1). A RCT showed similar efficacy of tofacitinib or glucocorticoids in PMR although this study was at high risk of bias.

Conclusion: The SLR identified several new Phase-2 and Phase-3 RCTs about the efficacy and safety of IL-6i, IL-17i, Janus kinase inhibitors and B-cell depletion therapies in GCA and PMR. High quality adequately sized RCTs in TAK are still lacking. This evidence was used to inform the 2025 EULAR recommendations for management of Polymyalgia Rheumatica and Large Vessel Vasculitis.

References

1. Dejaco C, et al. Ann Rheum Dis. 2015 Oct;74(10):1799-807.
2. Hellmich B, et al. Ann Rheum Dis. 2020 Jan;79(1):19-30.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Dey: None; **D. Misra**: None; **A. Bartoletti**: None; **G. Ducker**: None; **S. Monti**: None; **B. Hellmich**: AbbVie/Abbott, 1, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 1, 6, CSL Vifor, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Novartis, 1, 6, Pfizer, 6; **C. Mukhtyar**: None; **P. Studenic**: None; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

Abstract Number: 1628

Characterization of non-GCA, non-Takayasu Aortitis in a Single Health System Cohort

Nuzhat Batool[1], Zuha Anwar[1], Sharika Hasan[2], Miltiadis Tembelis[2], Jason Hoffmann[1], Nihan Gencerliler[2], justeena Joseph[3], Steven Carsons[4] and Elise Belilos[1], [1]NYU Grossman LI School of Medicine, Queens, NY, [2]NYU Grossman LI School of Medicine, Queens, [3]Long Island Community Hospital, Long Island, NY, [4]NYU Long Island School of Medicine, Mineola, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Advances in imaging modalities has led to increased diagnosis of aortitis. While aortitis occurring in the setting of giant cell arteritis (GCA) and Takayasu arteritis (TAK) is well characterized, other forms of aortitis are less well characterized and can be associated with a variety of other etiologies or may be idiopathic. We sought to identify the demographic, clinical and imaging characteristics of non-GCA/TAK aortitis.

Methods: In this retrospective cross-sectional study, the study population was identified using ICD 10 codes for aortitis from 1/1/12-12/31/22, across NYU Health system. Eligibility criteria were age between 18-90 years and a diagnosis of aortitis. 300 subjects were identified by using EMR diagnoses of aortitis, GCA, TAK. All charts were reviewed by rheumatology and radiology teams. 52 cases met the inclusion criteria. For data analysis used Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical variables. A p-value of < 0.05 was considered statistically significant. All analyses were performed using R (R Core Team) version 4.4.0.

Table 1

Characteristic	N	Overall, N=52	GCA/TAK aortitis (N=16)	Other Aortitis Cases (N=36)	P Value
Aortitis	52				<0.001
GCA		7 (13%)	7 (44%)	0 (0%)	
Takayasu		9 (17%)	9 (56%)	0 (0%)	
Non-GCA/Non-TAK		36 (69%)	0 (0%)	36 (100%)	
Age	52	66 (50,75)	45 (40,66)	69 (63,76)	0.002
Sex	52				0.006
F		30 (58%)	14 (88%)	16 (44%)	
M		22 (42%)	2 (13%)	20 (56%)	
Ethnicity	51				0.005
Asian		9 (18%)	7 (44%)	2 (5.7%)	
Black		4 (7.8%)	0 (0%)	4 (11%)	
Hispanic		11 (22%)	4 (25%)	7 (20%)	
White		27 (53%)	5 (31%)	22 (63%)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2

Characteristics	N	Overall N=52	GCA/TAK Aortitis N=16	Other Aortitis Cases N=36	P value
Clinical presentation	44				0.05
Abdominal		14(32%)	1(7.7%)	13(42%)	
Constitutional		9(20%)	4(31%)	5(16%)	
Cranial		4(9.1%)	3(23%)	1(3.2%)	
Renal		1(2.3%)	0(0%)	1(3.2%)	
thoracic		16(36%)	5(38%)	11(35%)	
Back pain	52	13(25%)	1 (6.3%)	12 (33%)	0.04
Abdominal pain	52	18 (35%)	3 (19%)	15(42%)	0.13
Signs of Claudication	37	2 (5.4%)	2 (22%)	0 (0%)	0.05
ESR	46	60 (36,110)	75 (38,110)	57(37,110)	0.8
Initial imaging study concerning for aortitis	46	28 (61%)	12 (92%)	16 (48%)	0.007
Aortic wall thickening	46	31 (67%)	10 (77%)	21 (64%)	0.5
Aortic wall enhancement	40	17 (43%)	7 (54%)	10 (37%)	0.5
Aortic stenosis	52	5 (9.6%)	4 (25%)	1 (2.8%)	0.03
Aortic aneurysm	52	11 (21%)	2 (13%)	9 (25%)	0.5
Periaortic fat stranding and inflammatory changes	46	24 (52%)	7 (54%)	17 (52%)	>0.9

Results:

36 cases of non-GCA/TAK aortitis and 16 cases of TAK/GCA aortitis were identified. Of the TAK/GCA group, 44% were identified as GCA and 56% were identified as TAK. Of the non-GCA/TAK aortitis cases, 25% were associated with other autoimmune diseases such as ANCA-related disease, Bechet's, RA, Sarcoid and SPA. In addition, 39% of the non-GCA/TAK cases were associated with infection and 36% were idiopathic.

The median age for the non-GCA/TAK and GCA/TAK groups was 69 years and 45 years, respectively (p=0.002). 45% of aortitis cases were incidental findings. When patients did present with symptoms, 42% of non-GCA/TAK patients presented with abdominal pain and 33% with back pain (p=0.05).

CTA/ CT was the most frequently utilized imaging modality in both groups. MRA/ MRI was utilized in 48% of cases for follow up purposes. Common imaging findings associated with aortitis included periaortic fat stranding and inflammatory changes which were seen in more than 54% of GCA/TAK aortitis and 52% of non-GCA/TAK aortitis cases (p=NS). Aortic wall thickening, which was seen in 77% of GCA/TAK aortitis cases and 64% of non-GCA/TAK aortitis p=NS. Aortic wall enhancement was seen in 54% of GCA/TAK aortitis cases vs 37% of non-GCA/TAK cases p=NS. Aortic stenosis was seen in 25% in GCA/TAK patients vs 2.8% non-GCA/TAK patients p=0.03.

70% of study participants received medical treatment for aortitis (85% of GCA/TAK cases and 69% of non-GCA/TAK cases). Steroids were used to treat over 66% of study participants; 87% in the GCA/TAK group and 55% in the non-GCA/TAK group (p=0.054).

Table 3

Characteristic	N	Overall N=52	GCA/TAK Aortitis N=16	Other Aortitis Cases N=36	P value
Did the patient receive treatment?	46	3 (70%)	11 (85%)	21 (64%)	0.3
Steroids used for treatment	44				0.05
IV		10 (23%)	3 (20%)	7 (24%)	
PO		18 (41%)	9 (60%)	9 (31%)	
Pulse		1 (2.3%)	1 (6.7%)	0 (0%)	
No Steroids Used		15 (34%)	2 (13%)	13 (45%)	
Immunosuppressive therapy used	36	14 (39%)	5 (56%)	9 (33%)	0.3
Aspirin	36	17 (47%)	8 (73%)	9 (36%)	0.07
Plavix	35	7 (20%)	4 (40%)	3 (12%)	0.2

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In our health system cohort of aortitis cases, 45% were incidental findings. In non-GCA/TAK aortitis, 39% were attributed to infection, 25% to autoimmune conditions and 36% were idiopathic. Steroids, when employed for treatment of aortitis, were more commonly used in GCA/TAK aortitis vs non-GCA/ TAK aortitis. The difference may reflect caution regarding steroids use in cases of infectious aortitis as well some uncertainty regarding approach to treatment for non-GCA/TAK aortitis.

Disclosure: N. Batool: None; **Z. Anwar**: None; **S. Hasan**: None; **M. Tembelis**: None; **J. Hoffmann**: None; **N. Gencerliler**: None; **j. Joseph**: None; **S. Carsons**: None; **E. Belilos**: None.

Abstract Number: 1629

Real-World Effectiveness of Interleukin-6 Receptor Inhibitors Compared to Methotrexate in Steroid-Refractory Frail Patients with Polymyalgia Rheumatica

Sebastian E Sattui[1], Christian Dejaco[2], Kerri Ford[3], **Stefano Fiore**[4], Sebastian H Unizony[5], Fenglong Xie[6] and Jeffrey Curtis[7], [1]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, [2]Medical University of Graz, Department of Rheumatology, Graz, Austria; Department of Rheumatology, Hospital of Brunico (SABES-ASDAA), Brunico, Italy, [3]Sanofi, Cambridge, MA, [4]Sanofi, Morristown, NJ, [5]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [6]The University of Alabama at Birmingham, Birmingham, AL, [7]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: A previous post hoc analysis of frail (defined by claims-based frailty index [CFI] ≥0.2) patients with PMR on second line (2L) and 3L treatment showed that those on IL-6 receptor inhibitors (IL-6Ri) were more than twice (HR 2.32) as likely to discontinue GC vs. those on conventional synthetic immunomodulators (csIM: methotrexate [MTX], azathioprine, and leflunomide), nearly 2 times the effect size in overall PMR cohort (HR 1.28). This study builds on prior analysis by comparing IL-6Ri to MTX as 2L treatment, with frailty as inclusion criteria and level of frailty as PS match covariate. Frailty was defined as CFI ≥0.25 (validated threshold in the general population), minimizing inclusion of patients with pre-frailty. This study compared effectiveness of IL-6Ri to MTX in GC-refractory frail patients with PMR.

Methods: This observational retrospective comparative cohort study compared effectiveness of IL-6Ri to MTX using US Medicare claims data (10/2016-12/2022). Inclusion criteria were age ≥50 years, ≥1 inpatient or ≥2 outpatient PMR diagnosis codes ≥30 days apart, ≤25 mg prednisone equivalent dose (PED), CFI ≥0.25, initiation of IL-6Ri or MTX (index date) with no prior IL-6Ri/csIM and continuous enrollment 180 days prior (baseline) to 1 day. Patients initiating IL-6Ri and csIM on same day and patients with seropositive RA, other systemic rheumatic disease (except giant cell arteritis), organ transplant, multiple sclerosis or active malignancy treatment during baseline were excluded. MTX initiators were direct matched on select characteristics and then PS matched on demographic, treatment and clinical characteristics. Primary and key secondary outcomes were time to GC discontinuation (>60-day gap) and time to minimal (≤2 mg/day PED) or no GC, respectively.

Results: Overall, 29% and 18.3% of patients in IL-6Ri and MTX groups, respectively, had CFI ≥0.25. Of these, 86 matched pairs receiving 2L treatment with no prior IL-6Ri were identified. Patient characteristics were generally balanced, though the mean time from first PMR diagnosis to index date (1025 vs. 799 days) and occurrence of seronegative RA (32.6%

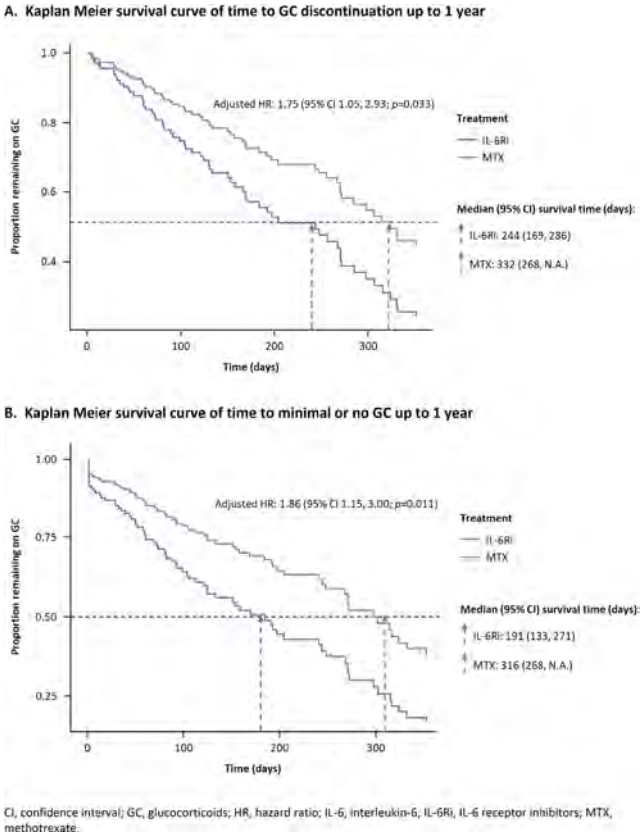
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Post propensity score match patient characteristics.

Characteristics[a]	Match covariate: Yes (Y) / No (N)	IL-6Ri[b] (N=86)	MTX[b] (N=86)	SMD	*p* value
Age at index date, years	Y[d]	79.0 (6.0)	78.4 (5.6)	0.10	0.395[e]
Gender, female	Y[d]	71 (82.6%)	67 (77.9%)	0.12	0.444[f]
Race	Y			0.20	0.505[g]
White		77 (89.5%)	76 (88.4%)		
Black		<11	<11		
Other		<11	<11		
Region	Y			0.17	0.989[g]
West		25 (29.1%)	25 (29.1%)		
Midwest		Redacted	Redacted		
Northeast		23 (26.7%)	23 (26.7%)		
South		24 (27.9%)	23 (26.7%)		
Unknown		<11	<11		
Original reason eligible for Medicare	Y			0.00	>0.999[h]
Age 65 or older		72 (83.7%)	72 (83.7%)		
Disabled		14 (16.3%)	14 (16.3%)		
Baseline prednisone equivalent dose (mg/day)	N	8.9 (6.1)	8.8 (6.1)	0.02	0.901[e]
Baseline prednisone equivalent dose category (mg/day)	Y[d]			0.15	0.995[g]
<2.5		<11	<11		
2.5–<5		14 (16.3%)	15 (17.4%)		
5–<10		35 (40.7%)	36 (41.9%)		
10–<15		19 (22.1%)	21 (24.4%)		
15–<20		<11	<11		
20–25		<11	<11		
>25		<11	<11		
Index day prednisone equivalent dose (mg)	N	12.1 (6.2)	11.5 (5.9)	0.09	0.526[e]
Index day prednisone equivalent dose category (mg)	Y[d]			0.35	0.404[g]
<2.5		<11	<11		
2.5–<5		<11	<11		
5–<10		27 (31.4%)	34 (39.5%)		
10–<15		17 (19.8%)	23 (26.7%)		
15–<20		21 (24.4%)	13 (15.1%)		
20–25		16 (18.6%)	13 (15.1%)		
Charlson Comorbidity Index	N	4.0 (2.5)	3.6 (2.7)	0.14	0.259[e]
Time from first PMR diagnosis to index date	Y	1,024.9 (1,047.0)	799.0 (886.0)	0.23	0.183[e]
Frailty	Y			0.14	0.371[f]
Mildly frail (CFI: 0.25–0.34)		68 (79.1%)	63 (73.3%)		
Moderately-severely frail (CFI: ≥0.35)		18 (20.9%)	23 (26.7%)		
GCA (any history)	Y[d]	43 (50.0%)	43 (50.0%)	0.00	>0.999[h]
Baseline period comorbidities	Y				
Asthma		13 (15.1%)	16 (18.6%)	-0.09	0.541[f]
Atopic dermatitis		<11	<11	-0.15	>0.999[f]
COPD		21 (24.4%)	13 (15.1%)	0.24	0.126[f]
Crohn's disease		<11	<11	0.15	>0.999[g]
Psoriasis		<11	<11	-0.15	0.621[g]
Seronegative RA		28 (32.6%)	19 (22.1%)	0.24	0.124[h]
Ulcerative colitis		<11	<11	0.15	>0.999[g]
Inpatient days	Y	3.2 (7.1)	1.8 (4.1)	0.23	0.345[e]
Emergency department visits number	Y	1.0 (1.8)	1.0 (1.3)	0.03	0.450[e]
Outpatient office visits number	Y	13.4 (6.3)	13.3 (6.9)	0.01	0.772[e]
Calendar year of index date	Y			0.50	0.120[h]
2016		<11	13 (15.1%)		
2017		<11	14 (16.3%)		
2018		11 (12.8%)	15 (17.4%)		
2019		21 (24.4%)	15 (17.4%)		
2020		12 (14.0%)	15 (17.4%)		
2021		20 (23.3%)	<11		
2022		<11	<11		

Index date was the date IL-6Ri or MTX was initiated. Baseline was defined as the 180 days prior to index date.
[a]Unless otherwise stated, continuous variables are reported as Mean (SD) and categorical as n (%); [b]To protect patient privacy and avoid potential identification of patients only results with ≥11 patients are reported, and data are redacted when there are >11 patients when such results would allow derivation of the number of patients when <11 are reported; [d]Covariates used both for direct and PS match. [e]Wilcoxon rank sum test; [f]Pearson's Chi-squared test; [g]Fisher's exact test.
CFI, claims-based frailty index; COPD, chronic obstructive pulmonary disease; GCA, giant cell arteritis; IL-6Ri, IL-6 receptor inhibitors; MTX, methotrexate; PMR, polymyalgia rheumatica; PS, propensity score; RA, rheumatoid arthritis; SMD, standardized mean difference; SD, standard deviation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CI, confidence interval; GC, glucocorticoids; HR, hazard ratio; IL-6, interleukin-6; IL-6Ri, IL-6 receptor inhibitors; MTX, methotrexate.

Figure 1.

vs. 22.1%) were higher in IL-6Ri vs. MTX groups. About 1/4th of the patients were moderately-severely frail (CFI ≥0.35, 20.9% vs. 26.7%) **(Table 1)**. Time to GC discontinuation **(Figure 1A)** and time to minimal or no GC **(Figure 1B)** up to 1 year were significantly shorter for IL-6Ri vs. MTX-treated patients (HR [95% CI] 1.75 [1.05, 2.93]; p=0.033) and (HR [95% CI] 1.86 [1.15, 3.00]; p=0.011), respectively.

Conclusion: IL-6Ri therapy led to a more rapid GC discontinuation or to achieving minimal GC dose in frail patients with PMR, suggesting that this vulnerable population may benefit more from IL-6Ri vs. MTX.

Original abstract at EULAR 2025.

Disclosure: S. Sattui: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2; **C. Dejaco**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Sparrow, 2, 6; **K. Ford**: Sanofi, 3, 11; **S. Fiore**: Sanofi, 3, 11; **S. Unizony**: Harvard Pilgrim Healthcare, 2, IQVIA, 2, Sanofi, 2; **F. Xie**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1630

Validation of the classification algorithm using the modified 2022 ACR/EULAR giant cell arteritis classification criteria and Japanese Takayasu arteritis diagnostic criteria

Takahiko Sugihara[1], Masayoshi Harigai[2], Haruhito Uchida[3], Yasuhiro Maejima[4], Hajime Yoshifuji[5], Yoshiko Watanabe[6], Yasuhiro Onishi[3], Shunsuke Furuta[7], Tomonori Ishii[8], Tsuyoshi Shirai[9], Taio Naniwa[10], Noriyoshi Ogawa[11], Yuko Kaneko[12], Hiroaki Dobashi[13], Koichi Amano[14], Jun Ishizaki[15], Takako Miyamae[16], Shuichi Ito[17], Yoshinori Komagata[18], Naoto Tamura[19] and Yoshikazu Nakaoka[20], [1]Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine, Tokyo, Japan, [2]Department of Rheumatology, International University of Health and Welfare, Tokyo, Japan, [3]Department of Chronic Kidney Disease and Cardiovascular Disease, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, [4]Department of Cardiovascular Medicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan, [5]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [6]Department of General Medicine, Kawasaki Medical School, Kurashiki,, Japan, [7]Department of Allergy and Clinical Immunology, Chiba University Hospital, Chiba, Japan, [8]Division of Hematology and Rheumatology, Tohoku Medical and Pharmaceutical University, Sendai, Japan, [9]Department of Rheumatology, Tohoku University Hospital, Sendai, Miyagi, Japan, [10]Division of Rheumatology, Department of Internal Medicine, Nagoya City University Hospital, Nagoya, Japan, [11]Department of Internal Medicine 3, Hamamatsu University School of Medicine, Hamamatsu, Japan, [12]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [13]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa, Japan, [14]Department of rheumatology and clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan, [15]Department of Hematology, Clinical Immunology and Infectious Diseases, Ehime University Graduate School of Medicine, Ehime, Japan, [16]Department of Pediatric Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University Hospital, Tokyo, Japan, [17]Department of Pediatrics, Yokohama City University School of Medicine, Yokohama, Japan, [18]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan, [19]Juntendo University School of Medicine, Tokyo, Japan, [20]Department of Vascular Physiology, National Cerebral and Cardiovascular Center Research Institute,, Suita, Japan

SESSION INFORMATION

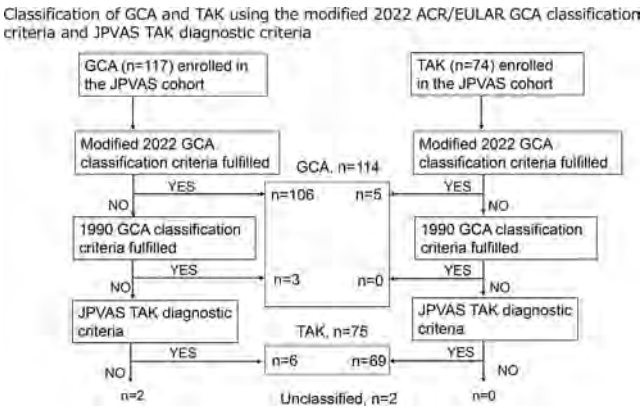
Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: Given the increasing number of patients with giant cell arteritis (GCA) in Japan and the higher incidence of Takayasu arteritis (TAK) compared to Europe and the U.S., our aim is to validate the discriminability of the modified 2022 ACR/EULAR GCA classification criteria for TAK and GCA and to compare the clinical profiles of GCA and TAK reclassified by the classification criteria for large-vessel vasculitis (LVV).



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Clinical features of GCA and TAK after classification according to the algorithm*

	GCA (n=114)	TAK (n=75)	*P*-value
Age at onset, mean (SD)	72.7 (8.2)	37.5 (20.3)	<0.001
50 years old and more, %	99.1	29.3	<0.001
Female, %	68.4	70.7	0.743
New headache, %	63.2	6.7	<0.001
Scalp tenderness, %	28.1	0	<0.001
Abnormal examination of the temporal artery, %	58.8	0	<0.001
Visual disturbance, %	14.9	2.7	0.004
Sudden visual loss, %	2.6	0	0.217
Jaw claudication, %	33.3	9.3	<0.001
Polymyalgia rheumatica, %	37.7	0.0	<0.001
Arthralgia/arthritis/myalgia, %	49.1	21.3	<0.001
Definitive vasculitis on temporal artery biopsy, %	83.3 (70 / 84)	0	–
Large-vessel involvement, %	65.8	100	–

* We applied the modified 2022 ACR/EULAR GCA classification criteria (1) first to our cohort, followed by the 1990 ACR GCA classification criteria and the JPVAS diagnostic criteria for TAK (2). According to the JPVAS diagnostic criteria for TAK, patients are diagnosed with TAK if they exhibit at least one clinical symptom along with diffuse or multiple arterial lesions including wall thickening, while GCA is excluded.

1. Sugihara T, et al. Arthritis Res Ther. 2025;27:19.

2. Isobe M, et al. Circ J. 2020;84:299-359.

Table 2 Imaging findings of LV-GCA and TAK after classification according to the algorithm

	LV-GCA (n=76)	TAK (n=75)	*P*-value
50 years old and more, %	100	29.3	<0.001
Claudication of upper legs, %	17.1	24.0	0.294
Pulse loss of arteries, %	11.8	30.7	0.005
Systolic blood pressure difference, %	11.8	29.3	0.008
Left axially artery lesion, %	22.4	12.0	0.092
Stenosis of left axially artery, %	6.6	9.3	0.532
Right axially artery lesion, %	22.4	6.7	0.006
Stenosis of right axially artery, %	5.3	2.7	0.347
Bilateral axillary artery lesions, %	21.1	4.0	0.002
Left subclavian artery lesion, %	56.6	52.0	0.572
Stenosis of left subclavian artery, %	10.5	21.3	0.069
Right subclavian artery lesion, %	47.4	36.0	0.157
Stenosis of right subclavian artery, %	6.6	12.0	0.251
Left carotid artery lesion, %	40.8	68.0	<0.001
Stenosis of left carotid artery, %	1.3	18.7	<0.001
Right carotid artery lesion, %	36.8	58.7	0.007
Stenosis of right carotid artery, %	1.3	17.3	0.001
Vertebral artery lesion, %	17.1	12.0	0.374
Brachiocephalic lesion, %	75.9	60.0	0.690
Pulmonary artery lesion, %	0.0	9.3	0.006
Ascending aorta lesion, %	47.4	48.0	0.938
Aneurysm of ascending aorta, %	0.0	8.0	0.014
Aortic arch lesion, %	57.9	65.3	0.347
Descending thoracic aorta lesion, %	65.8	50.7	0.060
Abdominal aorta lesion, %	67.1	40.0	0.001
Descending thoracic aorta-abdominal aorta lesions, %	57.9	33.3	0.002
Stenosis of mesenteric artery, %	1.3	6.7	0.102
Renal artery lesion, %	11.8	6.7	0.273
Stenosis of renal arteries, %	3.9	5.3	0.493

LV-GCA: large-vessel GCA with or without cranial lesions

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis (JPVAS) prospective study included 117 incidental GCA and 74 TAK diagnosed by attending physicians at participating JPVAS facilities from 2015 to 2019. In the modified 2022 ACR/EULAR GCA classification criteria, shoulder or neck stiffness was changed to polymyalgia rheumatica (PMR), and fluorodeoxyglucose (FDG)-positron emission tomography (PET) activity to wall thickening, stenosis, or aneurysm of the descending thoracic to abdominal aorta. We applied the GCA criteria first to our cohort, followed by the JPVAS diagnostic criteria for TAK, in which patients are classified as TAK if they exhibit at least one clinical symptom along with diffuse or multiple arterial lesions including wall thickening.

Results: The modified GCA classification criteria had sensitivities of 91.5% for overall GCA, 90.9% for large-vessel GCA (LV-GCA), and 36.3% for isolated LV-GCA without cranial lesions. The specificity was 93.2%. Discrimination between GCA and TAK using the modified criteria excluding age was high, with a C statistic of 0.945 (95% CI: 0.916–0.975). Combining PMR, bilateral axillary arteries, descending thoracic to abdominal aortic lesions, and inflammatory markers (i.e., using only these four items out of original 11 items) yielded a C statistic of 0.730 (95% CI: 0.661–0.799). Excluding PMR from this combination resulted in poor discrimination of 0.598 (95% CI: 0.530–0.667); adding age 50 years or older improved the discrimination to 0.898 (95% CI: 0.847–0.949).

Out of 117 GCA and 74 TAK patients enrolled in the JPVAS, 106 and five were classified as GCA based on the modified 2022 GCA classification criteria, followed by the 1990 ACR classification criteria and the JPVAS criteria, and overall, 114, 75, and two were classified as GCA, TAK, and unclassified, respectively (Figure 1). A comparison of GCA and TAK after the classification revealed notable differences in age and clinical features (Table 1). Bilateral axillary artery and descending thoracic to abdominal aorta were more common lesions in LV-GCA than in TAK. Arterial stenosis was significantly more prevalent in TAK than in LV-GCA (Table 2). Among the five patients with TAK classified as GCA, two were under 60, one had carotid artery tenderness, three had bilateral axillary artery lesions, and two were HLA-B52 positive.

Conclusion: The discriminability of the modified 2022 ACR/EULAR GCA classification criteria for TAK and GCA was good, and the classification utilizing the modified GCA criteria and the JPVAS TAK criteria was seen as beneficial. However, the 1990 ACR classification criteria was needed for a few cases, and classification of late-onset TAK and LV-GCA was difficult in some cases.

Disclosure: T. Sugihara: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas Pharma, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, Janssen, 6, Kissei, 6, Mitsubishi-Tanabe, 6, Ono, 6, Pfizer, 6, Taisho, 6; **M. Harigai**: None; **H. Uchida**: AstraZeneca, 6, Boehringer-Ingelheim, 5, 6, Daiichi Sankyo, 6, Kowa, 6, Mochida Pharma., 6, Olba Healthcare Holdings, 5, Terumo, 5; **Y. Maejima**: None; **H. Yoshifuji**: AbbVie/Abbott, 6, Chugai, 6, Janssen, 6; **Y. Watanabe**: None; **Y. Onishi**: Astellas pharma, 6, AstraZeneca, 6, Boehringer-Ingelheim, 6, Daiichi Sankyo, 6, Kowa, 6, Kyowa Kirin, 6, Mitsubishi Tanabe,, 6, Otsuka, 6, Torii Pharma, 6, Vantive, 6; **S. Furuta**: Asahi Kasei, 6, AstraZeneca, 2, 6, Daiichi Sankyo, 6, Eisai, 6, GlaxoSmithKlein(GSK), 6, Kissei, 6, Novartis, 2, Pfizer, 6; **T. Ishii**: AbbVie, 2, Asahi Kasei Pharma, 2, Astellas, 2, Ayumi Pharmaceutical, 2, BMS, 2, Chugai Pharmaceutical, 2, Daiichi-Sankyo, 2, Eisai, 2, Janssen, 2, Mitsubishi Tanabe, 2, Ono Pharmaceutical, 2, Pfizer, 2, Sanofi, 2; **T. Shirai**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Chugai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 6, Pfizer, 6, Sanofi, 6; **T. Naniwa**: AbbVie/Abbott, 6, Argenx, 6, Asahi Kasei, 6, AstraZeneca, 6, Ayumi, 6, Boehringer-Ingelheim, 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 6, Mitsubishi-Tanabe, 6, Novartis, 6, Otsuka, 6, Pfizer, 6, Sanofi, 6, Taisho, 6, UCB, 6; **N. Ogawa**: Chugai, 6, Eisai, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Kissei, 6, Tanabe-Mitsubishi, 6, Towa, 6; **Y. Kaneko**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Chugai, 5, 6; **H. Dobashi**: None; **K. Amano**: AbbVie/Abbott, 6, Asahi Kasei, 5, AstraZeneca, 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **J. Ishizaki**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 6, Mitsubishi Tanabe, 6, Pfizer, 6, Taisho, 6; **T. Miyamae**: None; **S. Ito**: None; **Y. Komagata**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eli Lilly, 6, Takeda, 6; **N. Tamura**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, AstraZeneca, 6, Ayumi, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, 6, Cell Exosome Therapeutics Co., Ltd., 5, Chugai, 5, 6, Daiichi Sankyo, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Kissei, 6, Novartis, 6, Taisho, 5, UCB, 6; **Y. Nakaoka**: AbbVie/Abbott, 5, 6, Asahi Kasei, 6, Chugai, 5, 6, Janssen, 5, JSR, 5, JT, 5, Kaneka, 5, Nippon Shinyaku, 6.

Abstract Number: 1631

New Arterial Damage in Takayasu's Arteritis

Tanaz Kermani[1], Sema Kaymaz-Tahra[2], Aysegul Avcu[3], Fatma Alibaz-Oner[4], Haner Direskeneli[3], Peter Merkel[5] and Vasculitis Clinical Research Consortium, [1]University of California Los Angeles, Santa Monica, CA, [2]Bahcesehir University Faculty of Medicine Department of Internal Medicine Division of Rheumatology, Istanbul, Turkey, [3]Marmara University, Istanbul, Turkey, [4]MARMARA UNIVERSITY, SCHOOL OF MEDICINE, DEPARTMENT OF INTERNAL MEDICINE, DIVISION OF RHEUMATOLOGY, Istanbul, Turkey, [5]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session B
Session Time: 10:30AM–12:30PM

Background/Purpose: Damage is one of the consequences of disease and is often considered irreversible. This study aimed to evaluate new arterial damage in Takayasu's arteritis (TAK).

Methods: Patients with TAK were included in this analysis if they were enrolled in a multicenter, prospective, observational cohort from North America, or seen at a single-center in Turkey, and had available data on vascular imaging. Baseline imaging and imaging at last visit were compared to identify new lesions (stenosis, occlusions, aneurysms) in previously unaffected territories. Variables associated with new arterial damage were evaluated.

Results: The study included 305 patients with TAK: 92% female; mean±SD age 40.9 (13.5) years; median (25^{th}, 75^{th} percentile) disease duration from diagnosis 1.2 (0, 4.9) years; median (25^{th}, 75^{th} percentile) time from symptom onset to diagnosis 54.1 (16.6, 178.2) weeks; median duration of follow-up 5.8 (2.0, 9.4) years. 128 patients (42%) were enrolled ≤ 180 days from time of diagnosis (the "recently diagnosed" group).

Table 1: Frequency and type of vascular lesions in 305 patients with Takayasu's arteritis

	Entire cohort, N = 305			Recently diagnosed, N = 128		
Vessel	Stenosis	Occlusion	Aneurysm	Stenosis	Occlusion	Aneurysm
Ascending aorta	2	1	16	0	1	4
Aortic arch	7	1	6	1	1	2
Descending aorta	22	1	11	3	1	3
Abdominal aorta	40	1	7	16	5	1
Innominate	12	6	3	4	4	0
Left carotid	83	25	2	33	15	0
Right carotid	66	15	6	28	10	3
Left vertebral	35	11	0	15	4	0
Right vertebral	37	5	0	13	4	0
Left subclavian	129	66	4	50	34	2
Right subclavian	77	49	1	36	25	2
Left axillary	32	6	1	12	3	0
Right axillary	17	3	0	10	3	0
Celiac	43	6	4	12	4	0
Superior mesenteric	35	14	1	15	5	0
Inferior mesenteric	11	2	0	5	1	0
Left renal	41	3	1	22	2	0
Right renal	42	4	1	22	2	0
Left iliac	20	3	0	9	2	0
Right iliac	22	4	0	12	2	0
Left femoral	4	3	0	3	1	0
Right femoral	5	2	0	3	2	0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: New arterial lesions in previously unaffected vascular regions in 204 patients with Takayasu's arteritis

Vessel	Stenosis	Occlusion	Aneurysm
Ascending aorta	0	0	2
Aortic arch	1	0	4
Descending aorta	4	0	0
Abdominal aorta	12	0	0
Innominate	3	0	1
Left carotid	19	3	1
Right carotid	8	2	1
Left vertebral	7	2	0
Right vertebral	5	1	0
Left subclavian	5	6	1
Right subclavian	5	2	1
Left axillary	1	4	0
Right axillary	1	1	0
Celiac	6	4	2
Superior mesenteric	10	0	0
Inferior mesenteric	2	2	0
Left renal	8	0	0
Right renal	8	0	0
Left iliac	3	0	2
Right iliac	5	0	0
Left femoral	1	0	0
Right femoral	1	1	0

Table 3: New arterial lesions in previously unaffected arterial regions in 204 patients with Takayasu's arteritis

Variable	New lesion N=72	No new lesion N=132	p-value
Mean age, years (SD)	40.6 (13.4)	41.5 (13.4)	0.64
Female sex, N (%)	65 (90)	123 (93)	0.59
Mean disease duration, years (SD)	3.3 (4.4)	2.7 (4.5)	0.36
Recently diagnosed, N (%)	31 (43)	64 (49)	0.47
Mean time between first and last imaging, years (SD)	4.9 (4.5)	6.5 (5.5)	0.04
Glucocorticoid ever, N (%)	69 (96)	121 (92)	0.39
DMARDs ever, N (%)	64 (89)	121 (92)	0.62
Biologic drugs ever, N (%)	29 (40)	40 (30)	0.17

SD: standard deviation; % = percentage, DMARDs: non-biologic disease-modifying anti-rheumatic drugs

The lesions on imaging at first visit in all 305 patients are outlined in **Table 1**. Aneurysmal disease was more frequently observed in the ascending aorta and aortic arch, while stenotic disease was more frequent in the abdominal aorta.

204 patients (67%) had at least 1 follow-up imaging study. Median (25^{th}, 75^{th} percentile) time from first available imaging study to last available imaging study was 4.1 (1.6, 8.4) years. 72 patients (35%) had at least 1 new arterial lesion in a previously unaffected territory. Among 95 patients recently diagnosed, 31 patients (32%) had new arterial lesions. The distribution of new vascular lesions is outlined in **Table 2**. The majority of new lesions were stenoses and occurred in the left carotid artery, abdominal aorta, and superior mesenteric artery. Of the 72 patients with new lesions, 36 patients (50%) had ≥ 2 new lesions (range 2-9).

When characteristics were compared between patients with and without new arterial lesions (**Table 3**), no differences were found in age, sex, time between imaging studies, recent diagnosis, or treatment.

Conclusion: Nearly one-third of patients with TAK develop *new*, often multiple, arterial lesions during follow-up, indicating significant burden of disease despite treatment. The majority of the new lesions are stenotic or occlusive. Given the frequency of new lesions, serial imaging remains important in the monitoring of TAK. To better capture the longitudinal arterial damage that occurs in this disease, indices of damage in TAK should include data derived from vascular imaging.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Kermani: None; **S. Kaymaz-Tahra**: None; **A. Avcu**: None; **F. Alibaz-Oner**: None; **H. Direskeneli**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2.

Abstract Number: 1632

PET/CT-Based Distribution of Arterial Involvement and Its Association With Clinical Outcomes in Takayasu Arteritis

Tokio Katakura[1], Tsuyoshi Shirai[2], Kentaro Mori[1], Mikihiro Takahashi[1], Yuito Tanno[3], Soshi Okazaki[3], So Itoi[3], Yosuke Hoshi[3], Tomoaki Machiyama[3], Yusho Ishii[3], Hiroko Sato[3] and Hiroshi Fujii[3], [1]Department of Rheumatology, Tohoku University Hospital, Sendai, Japan, [2]Department of Rheumatology, Tohoku University Hospital, Sendai, Miyagi, Japan, [3]Department of Rheumatology, Tohoku University Hospital, Sendai

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: (1612–1632) Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session B

Session Time: 10:30AM–12:30PM

Background/Purpose: PET/CT enables assessment of active vascular inflammation in Takayasu arteritis (TAK), which is often difficult to evaluate with conventional imaging. Although the distribution of affected arteries has been classified into patterns by both conventional imaging and PET/CT, its relationship with clinical outcomes remains unclear. This study aimed to evaluate the significance of PET/CT-based arterial involvement in treatment-naïve TAK and its association with relapse and cardiovascular events.

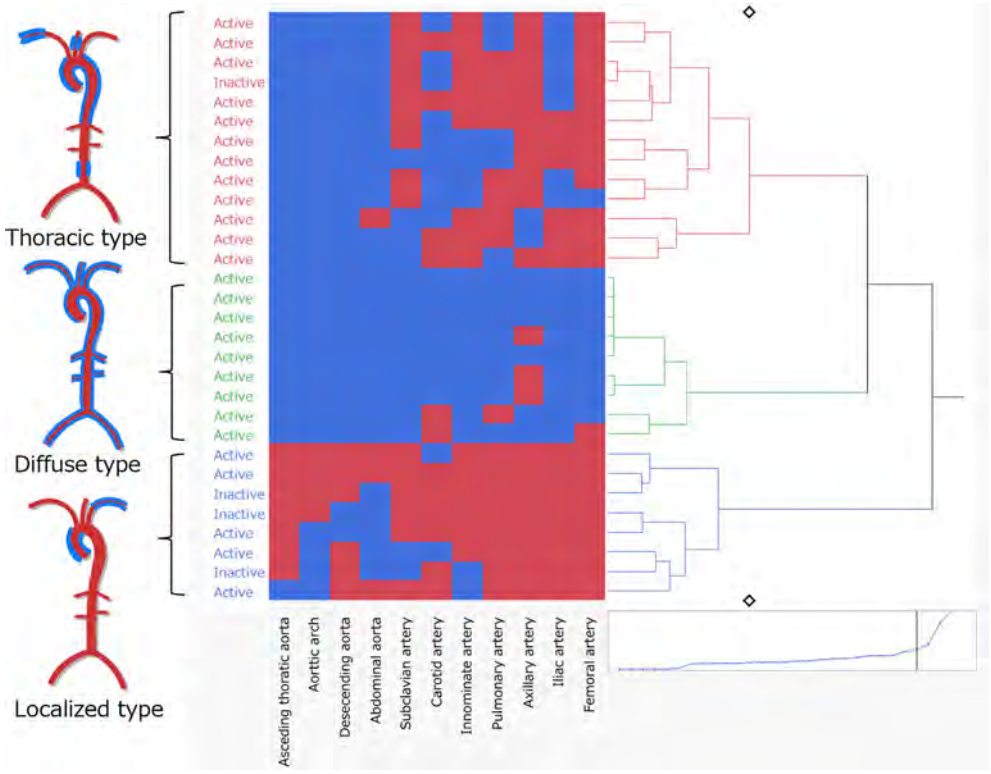


Figure 1. Hierarchical clustering based on the distribution of affected arteries revealed three distinct patterns.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

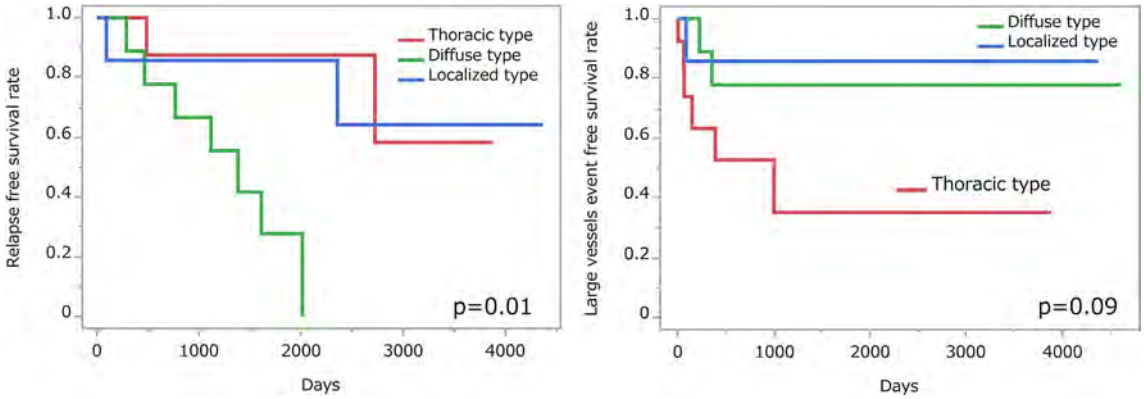


Figure 2. Survival curve analysis showed higher relapse rates in the diffuse type and a trend toward more large vessel events in the thoracic type.

Methods: We conducted a retrospective study of patients with TAK who underwent PET/CT before treatment between 2010 and 2024. Hierarchical clustering was performed based on the distribution of affected arteries, with 18F-fluorodeoxyglucose uptake assessed by a four-grade visual scale; the score ≥1 was considered positive. Clinical characteristics and outcomes were compared across clusters. Relapse and large vessel events were defined according to the 2018 EULAR recommendations and analyzed using survival analysis. Longitudinal changes in PET/CT and clinical activity were evaluated in patients with post-treatment PET/CT. Continuous variables were expressed as medians with interquartile ranges.

Results: Thirty patients were included, with a follow-up of 4.8 years (1.4–9.9), age at diagnosis of 48 years (28–58), and 90% female. All met Japanese diagnostic criteria; 80% met the 2022 ACR/EULAR criteria. Numano's classification based on CT was as follows; I, 2; II, 10; III, 3; V, 15. Relapse occurred in 12 patients (40%) with one major relapse; and large vessel events in nine patients (30%); aortic regurgitation, 2; aortic aneurysm, 5; aortic stenosis. 4; cardiovascular death, 1. Hierarchical clustering revealed three distinct patterns: (A) thoracic type (mainly thoracic aorta with less frequent branch involvement; 43%), (B) diffuse type (extensive involvement of the aorta and its branches; 30%), and (C) localized type (mainly branch lesions; 27%) (Figure 1). The proportion of type V was 78% in A, 38% in B, and 38% in C (p=0.35), indicating inconsistency between PET/CT and angiographic classifications. PET vascular activity scores were significantly different among clusters: 9 (7–13) in A, 15 (12–21) in B, and 3 (1–5) in C (p< 0.01). CRP levels were as follows; 3.1 (1.7–3.8), 3.4 (1.4–5.6), and 0.7 (0.1–7.1) mg/dL (p=0.28). Relapse rates were the highest in B (23%, 78%, and 25%, p=0.04), whereas large vessel events tended to occur more in A (46%, 22%, and 13%; p=0.09) (Figure 2). Numano's classification was not associated with relapse or large vessel events. Among 17 patients with repeated scans, PET/CT activity was observed despite clinical inactivity, indicating a risk of relapse in such patients. Meanwhile, a relapse was also observed in a patient whose PET/CT activity had normalized (Figure 3).

Conclusion: PET/CT-based arterial pattern in TAK was classified into three clusters with distinct prognostic profiles. Diffuse type was associated with higher relapse, whereas thoracic type tended to present vascular complications. Conventional angiographic classification failed to predict these outcomes, and thus PET/CT would provide superior risk stratification in TAK.

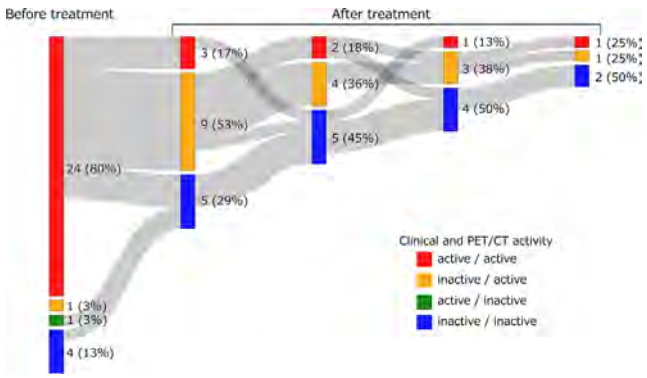


Figure 3. Sankey diagram illustrating temporal changes in clinical and PET/CT disease activity.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Katakura: None; **T. Shirai**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Chugai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 6, Pfizer, 6, Sanofi, 6; **K. Mori**: None; **M. Takahashi**: None; **Y. Tanno**: None; **S. Okazaki**: None; **S. Itoi**: None; **Y. Hoshi**: None; **T. Machiyama**: None; **Y. Ishii**: None; **H. Sato**: None; **H. Fujii**: None.

Abstract Number: 1650

Malondialdehyde-Acetaldehyde and Citrulline Modified Proteins are Overexpressed in Cardiac Tissues in Rheumatoid Arthritis-Associated Heart Failure and Mediate Endothelial Cell Dysfunction

Hannah Johnson[1], Wenxian Zhou[2], Michael Duryee[1], Engle Sharp[1], Kimberley Sinanan[1], Carlos Hunter[1], Tate Johnson[1], Mabruka Alfaidi[1], Daniel Anderson[3], Geoffrey Thiele[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Medical Center, Bellevue, NE, [3]0587964, Durham, NC

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Cytokines & Cell Trafficking (1650–1655)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Previous reports show that malondialdehyde-acetaldehyde (MAA) adducts are overexpressed in RA, especially in joint/lung tissues, and that they colocalize with citrulline (CIT). This is relevant as MAA and CIT act synergistically through p38- and NF-κB-dependent pathways to activate macrophages, producing proinflammatory and profibrotic effects mediated through crosstalk with tissue resident cells. Heart failure (HF) is a highly overrepresented cause of death

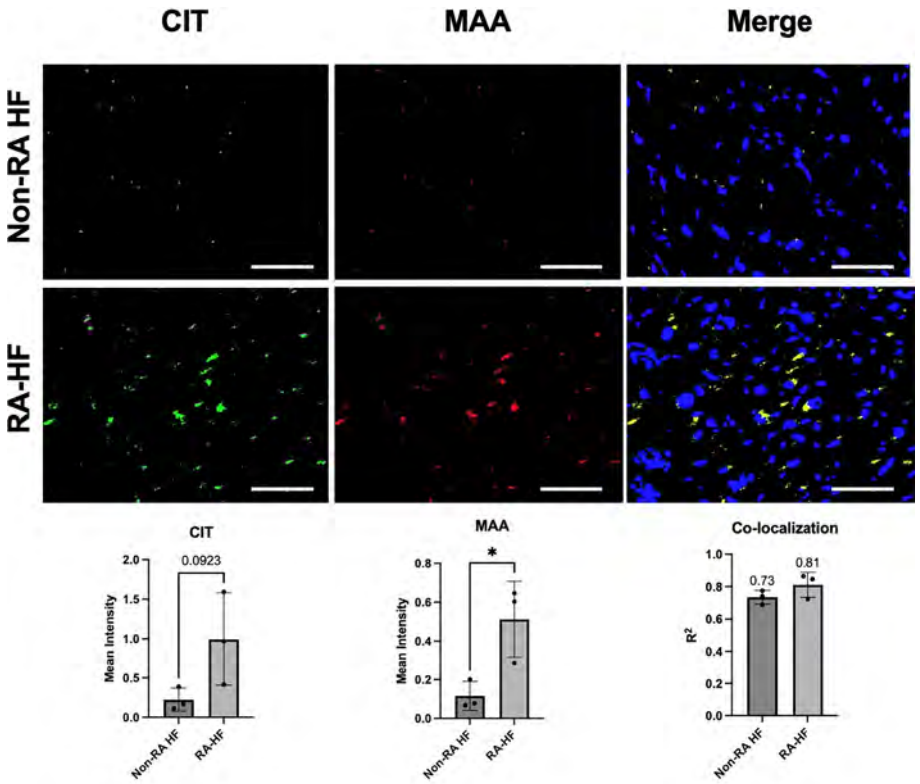


Figure 1. Immunohistochemistry Reveals CIT and MAA Expression and Colocalization in the Heart of RA-HF Patients. Representative image of 20X frame at apex of left ventricle is shown. White scale bar = 200 μm. Data shown on graphs are mean ± standard deviation. Student's T test was performed and the statistical differences between groups are shown in *: * p<0.05.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

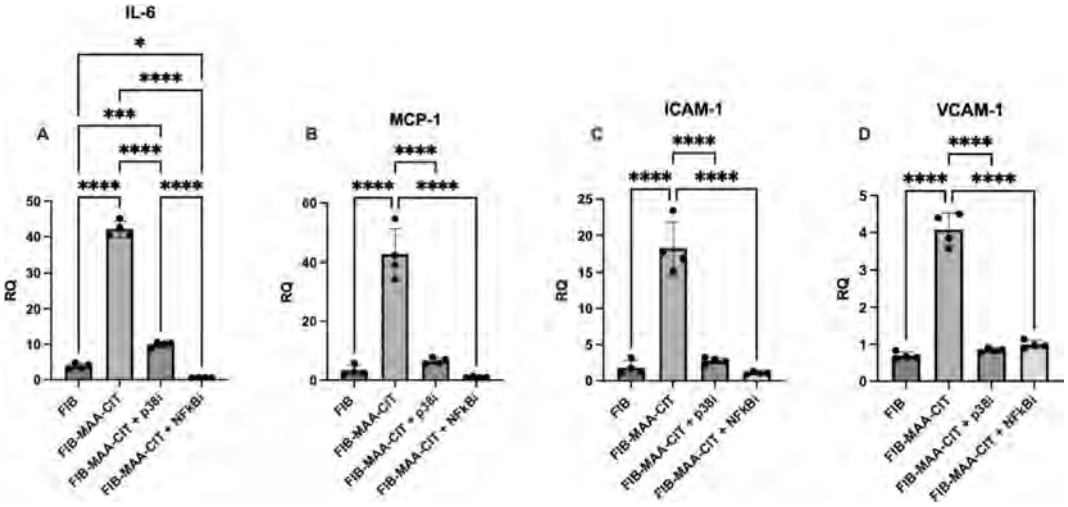


Figure 2. RT-PCR Demonstrating Attenuated HCAEC Inflammatory Gene Expression Following Incubation with Supernatants from Macrophages Stimulated with FIB-MAA-CIT in the Presence or Absence of p38 and NF-κB Inhibitors. 24-hr mRNA expression was measured for; A) IL-6, B) MCP-1, C) ICAM-1, and D) VCAM-1. Relative quotient (RQ) compared to media-cultured negative control cells were calculated and shown in the y-axis. One-way ANOVA was performed and the statistical differences between groups are shown in *: * p<0.05; *** p<0.001; **** p<0.0001.

in RA patients, characterized by tissue inflammation, fibrosis, and vascular endothelial dysfunction. Herein, we sought to examine whether MAA has increased expression and colocalization with CIT in heart tissues from patients with RA-HF. We also examined whether inhibition of macrophage signaling pathways limits endothelial cell (EC) activation and inflammation mediated by MAA-CIT stimulation.

Methods: Left ventricular (LV) apex tissue from RA-HF patients and age/sex matched non-RA HF controls were examined (n=3/group). LV tissues were stained with anti-CIT and anti-MAA antibodies. Quantification and co-localization were done using ImageJ and FIJI Coloc2. Separately, human U-937 macrophages were pre-incubated with either media, 1 μM of BIRB-796 (p38 inhibitor), or 50 μM of BAY-11-7085 (NF-κB inhibitor) for 1-hr before stimulation with unmodified fibrinogen (FIB) or FIB co-modified with MAA+CIT (FIB-MAA-CIT) for 48-hrs. To assess the crosstalk between macrophages and ECs, macrophage supernatants were collected and used to indirectly stimulate human coronary artery endothelial cells (HCAECs) for 24-hrs. HCAEC supernatants were then analyzed for IL-6, MCP-1, ICAM-1, and VCAM-1 by ELISA, while RNA was analyzed by RT-PCR. Analyses were performed using a Student's T test or one-way ANOVA with Tukey's post hoc test.

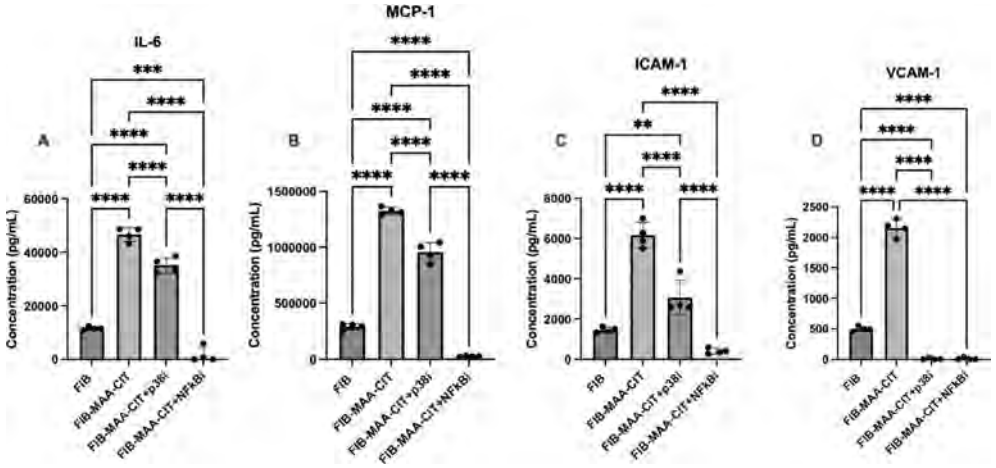


Figure 3. ELISA Demonstrating Attenuated HCAEC Inflammatory Protein Release Following Incubation with Supernatants from Macrophages Stimulated with FIB-MAA-CIT in the Presence or Absence of p38 and NF-κB Inhibitors. 24-hr cytokine concentrations in supernatants were measured for; A) IL-6, B) MCP-1, C) ICAM-1, and D) VCAM-1. One-way ANOVA was performed and the statistical differences between inhibitory groups are shown in *: ** p<0.01; *** p<0.001; **** p<0.0001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: LV tissues from RA-HF patients demonstrated trends towards increased CIT deposition (p=0.09) and significantly increased MAA deposition (p< 0.05) vs. non-RA HF controls, with strong co-localization (R2=0.81) (Fig 1). HCAECs stimulated with supernatants from macrophages treated with FIB-MAA-CIT showed significantly increased expression of IL-6, MCP-1, ICAM-1, and VCAM-1 compared to FIB control, validating prior observations. Interestingly, direct stimulation of HCAECs with FIB-MAA-CIT yielded diminished effects (not shown). HCAECs stimulated with supernatants from macrophages pre-treated with p38 or NF-κB inhibitors and FIB-MAA-CIT showed significantly attenuated mRNA expression and soluble cytokine/chemokine production (Figs 2,3).

Conclusion: This study is the first to demonstrate increased MAA expression and MAA-CIT co-localization in cardiac tissues of RA-HF patients compared to non-RA HF patients. We also demonstrated that macrophages activated with FIB-MAA-CIT mediate coronary EC inflammation through their supernatants, an effect that is attenuated following inhibition of p38 and NF-κB. Further research will validate these findings using patient-derived monocytes and explore whether agents targeting MAA, CIT, or downstream signaling pathways have the potential to attenuate cardiac dysfunction that occurs in mouse models of RA.

Disclosure: H. Johnson: None; **W. Zhou**: None; **M. Duryee**: None; **E. Sharp**: None; **K. Sinanan**: None; **C. Hunter**: None; **T. Johnson**: None; **M. Alfaidi**: None; **D. Anderson**: None; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

Abstract Number: 1651

Compound Heterozygosity for the Ile692del and Val726Ala Pathogenic *MEFV* Variants and Elevated IL-18 (CHIVE-18 syndrome) Is Distinct from Familial Mediterranean Fever (FMF) and Includes a Pronounced Response to Interferon Stimulation in Myeloid Cell Populations

Mary Maclean[1], Sabrina Helmold Hait[2], Cindy Phung[3], Deborah Stone[4], Sophie georgin-Lavialle[5], Scott Canna[6], Carl Esperanzate[7], Amanda Ombrello[8], Daniel Kastner[9], Ivona Aksentijevich[10] and Massimo Gadina[11], [1]NIH-NIAMS, Rockville, MD, [2]NIAMS/NIH, Bethesda, MD, [3]National Institute of Arthritis, Musculoskeletal, and Skin Diseases (NIAMS), Bethesda, MD, [4]NIH, Bethesda, MD, [5]Sorbonne university, Tenon hospital, DMU3ID, CEREMAIA, ERN RITA, Paris, France, [6]Children's Hospital of Philadelphia, Philadelphia, PA, [7]National Human Genome research Institute (NHGRI), National Institutes of Health (NIH), Bethesda, MD, [8]National Institutes of Health, Rockville, MD, [9]National Human Genome Research Institute, Bethesda, MD, [10]100, Bethesda, MD, [11]National Institute of Arthritis Musculoskeletal and Skin diseases, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Cytokines & Cell Trafficking (1650–1655)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Familial Mediterranean fever (FMF) is an autoinflammatory disease associated with biallelic pathogenic variants in the *MEFV* gene encoding the myeloid-restricted inflammasome sensor pyrin. The majority of FMF-associated missense variants reside in exon 10 of *MEFV within the B30.2/SPRY domain*, with M680I, M694V, and V726A being the most common disease-associated variants in Eastern Mediterranean populations. The Ile692del (rs104895093) variant has been reported in Arab patients with recessively inherited FMF, Patients who are compound heterozygous for the I692del and V726A variants presented with a severe inflammatory phenotype including transfusion-dependent anemia and neutrophilic dermatoses. Several patients had a history of cytokine storm, which is not reported in patients with classical FMF. To study the impact of the Ile692del variant, we analyzed the clinical histories, biomarker testing, and response to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

therapy of 53 individuals who have at least one copy of the Ile692del variant. We then examined the inflammatory signature associated with this phenotype in the primary cells of patients who are compound heterozygotes for I692del/Val726Ala. We have designated this condition as CHIVE-18 syndrome.

Methods: We designed analogous panels to measure the response to cytokine stimulation in whole blood and cryopreserved PBMCs. Phospho-STAT staining was carried out on whole blood (n=2) or frozen PBMCs (n=2) of compound heterozygotes for I692del/Val726Ala with controls. Samples were stained with fluorochrome-conjugated antibodies for myeloid and lymphoid markers, stimulated with IFN-a, IFN-g, or IL-10 and then stained with intracellular antibodies for pSTAT1 and pSTAT3. Stained cells were acquired on a 5-laser Cytek® Aurora Spectral Cytometer.

Results: All patients with CHIVE-18 had significantly elevated levels of serum total IL-18, IL-18 BP, and free IL-18. Given high serum levels of the IL-18 cytokine, a known inducer of IFN-g, we measured phosphorylation of STAT1 and STAT3 in stimulated patients' cells. CHIVE-18 patients had enhanced STAT1 phosphorylation after stimulation with IFN-g compared to age-matched controls, while pSTAT3 was not higher. Interferon-induced STAT1 phosphorylation was more pronounced in cellular populations from the myeloid lineage, confirming the role of these cells in mediating FMF pathology.

Conclusion: CHIVE-18 syndrome is a severe inflammatory disease distinct from classic FMF. Our data show that IFN-induced pSTAT1 was more pronounced in cellular populations from the myeloid lineage, consistent with observations in patients with pyogenic arthritis, pyoderma gangrenosum and acne (PAPA) syndrome, another pyrin-related autoinflammatory disease, and confirms the role of these cells in mediating FMF pathology. Although IFN-γ is not a major driver of a pyrin-mediated inflammatory disease, it is a contributing factor to disease pathophysiology and could make patients with high-impact mutations prone to episodes of cytokine storm. Such hyperinflammatory episodes increase mortality risk and should be treated aggressively. Affected patients usually require treatment with high-dose of IL-1 inhibitors or with combination of cytokine inhibitors.

Disclosure: M. Maclean: None; **S. Helmold Hait**: None; **C. Phung**: None; **D. Stone**: None; **S. georgin-Lavialle**: Novartis, 2, Sobi, 2; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **C. Esperanzate**: None; **A. Ombrello**: None; **D. Kastner**: In Vitro Diagnostics, 12, NIH Licensing Agreement; **I. Aksentijevich**: In Vitro Diagnostics, 9; **M. Gadina**: None.

Abstract Number: 1652

The Hidden Impact of Hyperuricemia on Immune Cell Dysfunction

Isabella Yi, Henry Ping and **Qian Wang**, iLab Research Institute, Mountain View, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Cytokines & Cell Trafficking (1650–1655)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Background: Hyperuricemia, characterized by elevated serum uric acid levels, is often asymptomatic yet poses serious health risks. This study investigates how soluble monosodium urate (MSU) influences immune cell dynamics, uncovering potential immunological consequences of high uric acid levels.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Methods: Leukocyte Reduction System (LRS) cells were cultured with or without soluble MSU at 100 μg/mL for 24 hours. Single-cell and bulk RNA sequencing was conducted to assess changes in immune cell populations, and enzyme-linked immunosorbent assays (ELISA) were utilized to measure cytokine production.

Results: Results: MSU exposure led to significant alterations in immune cell profiles, decreasing CD8+ T cells including CD8+ TCM (T central memory), CD8+ TEM (T effector memory), and effective CD8+ T cells, monocytes and dendritic cells while increasing CD4+ T cells, Tregs, macrophages, mast cells. Importantly, MSU markedly elevated proinflammatory cytokines, including TNF-α, IL-1β. Additionally, upregulation of inhibitory immune checkpoint molecules such as CD274, PDCD1LG2, CD276, PDCD1, and ELISA showed the increased protein levels CD274 and CD276. These results indicated a shift toward an immunosuppressive state.

Conclusion: Conclusions: These findings reveal that MSU profoundly alters immune cell behavior, driving inflammation and activating immunosuppressive pathways. Asymptomatic hyperuricemia may compromise immune function, potentially diminishing cancer surveillance or inducing autoimmune conditions such as lupus. Proactive management of elevated uric acid levels is crucial for maintaining immune balance. Moreover, LRS cells serve as a valuable model for investigating immune interactions under stress, paving the way for future research into the health impacts of hyperuricemia.

Disclosure: I. Yi: None; **H. Ping**: None; **Q. Wang**: None.

Abstract Number: 1653

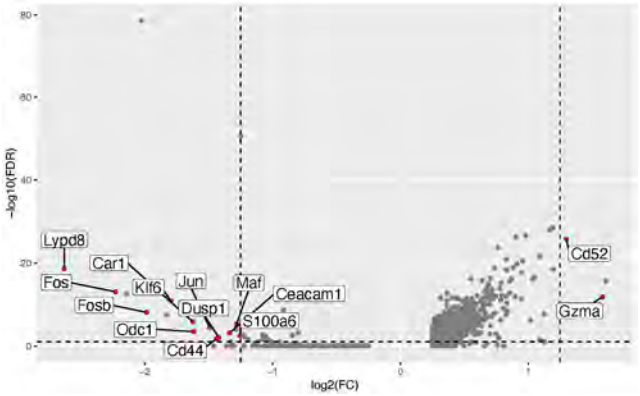
Gut-joint lymphocyte trafficking functions to regulate systemic immunity

Sarah Danielson[1], Sucai Liu[2] and Kristine Kuhn[3], [1]University of Colorado Anschutz Medical Campus, Aurora, [2]University of Colorado School of Medicine, Aurora, CO, [3]2022 - 2023 / Adult/ University of Colorado, Aurora, CO

SESSION INFORMATION

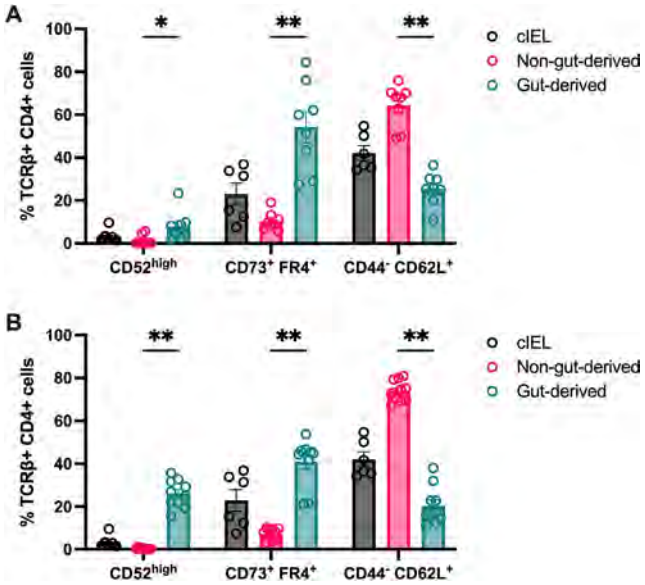
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Cytokines & Cell Trafficking (1650–1655)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: The gut-joint and mucosal origins hypotheses postulate that immune alterations in mucosal sites may precede and impact the development of rheumatoid arthritis and spondyloarthritis. However, the mechanisms behind these connections remain unknown. Our prior work using KikGR transgenic mice, in which we performed colonoscopy-



Volcano plot of differentially expressed genes in gut-derived CD4+ splenocytes after RNA sequencing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



cIELs and cells from spleen (A) or joint-draining lymph nodes (B) were isolated from colonoscopy-guided photoconverted KikGR mice and expression of the indicated markers was evaluated CD4+ TCRαβ+ T cells from each tissue by flow cytometry. Non-gut-derived and gut-derived cells were compared using multiple Wilcoxon tests. *, p<0.05; **, p<0.01.

guided green-to-red photoconversion, demonstrated that colon intraepithelial lymphocytes (cIELs) constitutively traffic. The trafficking cIELs, referred to as gut-derived T cells, were characterized as TCRαβ^{+} CD4^{+} and found in extraintestinal tissues including the spleen, liver, lungs, and joints. In this study, we aimed to further elucidate the functions of gut-derived T cells and the intestinal signals that influence their systemic function.

Methods: Using colonoscopy-guided photoconverted KikGR mice, we performed single cell RNA sequencing of sorted KikGreen^{+} (non-gut-derived) and KikRed^{+} (gut-derived) splenocytes, then validated results by flow cytometry. We used an MHCII tetramer containing the flagellin peptide Cbir1, a common T cell antigenic target, to evaluate broad commensal reactivity. We then generated KikGR^{+} I-Ab$^{fl/fl}$ Villin-Cre (MHCII$^{\Delta IEC}$) mice, which lack expression of MHCII on intestinal epithelial cells, and performed single cell ATAC sequencing on cIELs from MHCII$^{\Delta IEC}$ and MHCII^{WT} mice followed by flow cytometry on trafficking cells.

Results: Differential gene expression analysis of our RNA sequencing data revealed increased transcription of *Cd52*, a marker of regulatory function, and decreased transcription of the AP-1 transcription factor family members *Fos*, *Jun*, and *Maf* in gut-derived CD4^{+} T cells, suggesting either antigen inexperience or anergy. Flow cytometry of lamina propria, spleen, mesenteric lymph nodes, and joint-draining lymph nodes confirmed significantly higher numbers of gut-derived regulatory CD52^{high} and anergic CD73^{+} FR4^{+} CD4^{+} T cells and significantly lower numbers of gut-derived naïve CD62L^{+} CD44^{-} T cells. Cbir1-reactive CD4^{+} T cells, representative of microbiome reactivity, were more frequent in gut-derived than non-gut-derived cells, and gut-derived Cbir1-reactive T cells expressed more CD73 and FR4 as well as CD52 than non-gut-derived Cbir1-reactive cells. We then hypothesized that epithelial antigen presentation to commensal-reactive cIELs induced anergy. Single cell ATAC sequencing of MHCII$^{\Delta IEC}$ cIELs revealed modest decreases in accessibility of NFAT binding sites compared to cIELs from littermate controls. However, we did not see significant differences in expression of regulatory markers (Foxp3, CD73 and FR4, CD52) or antigen experience markers (CD62L, CD44) by flow cytometry.

Conclusion: Our analysis of gut-derived CD4^{+} T cells suggest that these cells are commensal-reactive and may play a role in peripheral tolerance through induction of anergy or expression of the regulatory marker CD52. These data are in line with our previous work demonstrating that gut-derived T cells help resolve joint inflammation. Ongoing studies will now assess the role of intestinal inflammation on gut-derived T cell function as well as interrogate how these cells gain their function.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Danielson: None; **S. Liu**: None; **K. Kuhn**: Solarea, 2.

Abstract Number: 1654

A Dual Inhibitor of TAK1 and MAP4K2, NG25, Suppresses Cytokine-driven Inflammation in Juvenile Idiopathic Arthritis Synovial Fibroblasts

Meena Afroze Shanta[1] and Salahuddin Ahmed[2], [1]College of Pharmacy and Pharmaceutical Science, Washington State University, Spokane, WA, [2]Washington State University, Spokane, WA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Cytokines & Cell Trafficking (1650–1655)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Chronic synovitis is a hallmark of juvenile idiopathic arthritis (JIA), and synovial fibroblasts are major perpetrators of inflammation and tissue destruction. Thus, we tested the efficacy of NG25, a dual TAK1 and MAP4K2 inhibitor, on IL-1β- or cytokine cocktail-activated JIA synovial fibroblasts (JIASFs) *in vitro*.

Methods: JIASFs were isolated from the synovial fluid aspirated from the knees of de-identified JIA patients. JIASFs (n=3-4) were pretreated with NG25 (0.01–1 μM) followed by IL-1β (10 ng/ml) stimulation for 15 minutes to study the impact on signaling pathways or 24 hours to account for inflammatory or invasive proteins or gene expression. To study the involvement of TAK1 in inducing JIASF aggressive and inflammatory phenotype, the expression of COX-2, podoplanin, IL-6, IL-8, CXCL5, and CCL5 following NG25 treatment was determined by ELISA or Western blotting. The inhibitory potential of NG25 against IL-1β activation was further extended to cytokine cocktail [IL-1β (1 ng/ml), TNF-α (5 ng/ml), and IFN-γ (10 ng/ml)] driven activation of JIASFs. The efficacy of NG25 was further compared with different TAK1 inhibitors (5Z-7-oxozeaenol (5Z), takinib, or HS-276). The statistical value of $p< 0.05$ was considered statistically significant.

Results: NG25 (0.01–1 μM) dose-dependently inhibited IL-1β-induced p-TAK1 at $Thr^{184/187}$ in JIASFs with IC_{50} of 531 nM (n=3, $p< 0.01$), which resulted in downstream inhibition of p-JNK, p-p38, and p-NF-kBp65, but no effect on p-ERK. Western blot analysis showed that NG25 selectively inhibits IL-1β-induced COX-2 expression in a dose-dependent manner (n=4; $p< 0.001$), with no effect on the markers of cell adhesion and invasion (ICAM-1, VCAM-1, and Podoplanin). Evaluation of the conditioned media by ELISA showed a significant and selective inhibitory effect of NG25 on CXC chemokines (ENA-78 and IL-8), IL-6, and MMP-3 production (n=4; $p< 0.001$ at 250 nM). In a wash-out experiment where fresh low-serum media was replaced after 24 h of IL-1β +/- NG25 (1 μM) treatment, the inhibitory actions of NG25 on IL-6, IL-8, and MMP-3 production were sustained for up to 7 days in JIASFs and were superior compared to 5Z (0.25 μM), takinib (10 μM) or HS-276 (10 μM) (n=3; $p< 0.01$). Furthermore, NG25 inhibited the cytokine cocktail (TNFα/IL-1β/IFN-γ)-induced IL-6 (85%), IL-8 (86%), ENA-78 (100%), and MMP-3 (100%) production in JIASFs more efficiently when compared to the other TAK1 inhibitors (5Z, takinib, and HS-276) (n=3-4; $p< 0.01$-0.001). Similarly, NG25 was most effective in the selective inhibition of COX-2 expression, without affecting the expression of VCAM-1, Cadherin-11, or Podoplanin in cytokine cocktail-activated JIASFs *in vitro* (n=4; $p< 0.05$).

Conclusion: Our preliminary findings delineate NG25's potential anti-inflammatory and anti-chemotactic activities in JIASFs. These findings lay a foundation for testing the efficacy of NG25 in animal models of JIA.

Disclosure: M. Shanta: None; **S. Ahmed**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1655

Aberrant Noncoding RNAs Are Enriched in Extracellular Vesicles and Implicated in Interferon Activation

Sandra Williams[1], Soyeong Sim[2] and Sandra Wolin[2], [1]National Institute of Arthritis, Musculoskeletal and Skin Diseases; National Cancer Institute, Bethesda, MD, [2]National Cancer Institute, Frederick, MD

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Cytokines & Cell Trafficking (1650–1655)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Extracellular vesicles (EVs) are small structures that enclose a variety of nucleic acids. While much of the published work on EV RNA has focused on the role of mRNAs and microRNAs in intercellular communication, these RNAs are a small fraction of the RNA cargoes of EVs (1). RNA surveillance pathways eliminate defective RNAs and are also implicated in maintaining immunological tolerance to host RNA (2). We hypothesized that EVs package defective noncoding RNAs (ncRNAs) as part of a novel RNA surveillance pathway, which may prevent these RNAs from being recognized as foreign and activating an interferon response.

Methods: We generated mouse macrophage RAW 264.7 cell lines that stably express doxycycline-inducible shRNAs against Dis3l2 as well as control nonsilencing shRNAs. Dis3l2 is a ribonuclease that degrades aberrant structured ncRNAs in cytosol. We purified EVs from these cell lines and used a thermostable group II intron reverse transcriptase to make cDNA libraries and sequence RNA from whole cells and EVs, which allowed us to characterize highly structured RNAs that are missed by conventional RNA-Seq.

We also performed conventional RNA-Seq on Dis3l2-depleted cells. To determine effects of preventing exosome packaging, we treated RAW 264.7 cells with pharmacological EV inhibitors and performed Northern blots and qPCR on cellular RNA after drug treatment.

Results: Across multiple classes of RNAs, including small ncRNAs, repeat RNAs, mRNAs, and microRNAs, EVs are enriched for aberrant transcripts. Many aberrant transcripts are further enriched in EVs purified from cells depleted of Dis3l2. We confirmed our sequencing results with Northern blots.

Transcriptomic analysis of Dis3l2-depleted RAW 264.7 cells show a striking Type I interferon signature. Treating cells with an EV inhibitor was associated with cellular accumulation of some of the aberrant RNAs found in EVs, as well as upregulation of interferon-stimulated genes.

Conclusion: Our data implicate EVs in a novel RNA surveillance pathway that competes with other surveillance pathways to purge cells of RNAs that may otherwise activate an interferon response. Thus, EVs may be involved in protecting cells from aberrant activation of innate immune sensors. Such pathways may be important for diseases like systemic lupus erythematosus, where aberrant nucleic acid sensing and an interferon response are implicated in pathogenesis.

1. Shurtleff MJ, Yao J, Qin Y, Nottingham RM, Temoche-Diaz MM, Schekman R, et al. Broad role for YBX1 in defining the small noncoding RNA composition of exosomes. Proc Natl Acad Sci U S A. 2017;114(43):E8987-E95.

2. Wolin SL, Maquat LE. Cellular RNA surveillance in health and disease. Science. 2019;366(6467):822-7.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Williams: None; **S. Sim**: None; **S. Wolin**: None.

Abstract Number: 1656

Risk of Serious Infection associated with non-TNF biologic initiation after Anti-TNF Use in Older Adults with Rheumatoid Arthritis

Jiha Lee[1], Sofia Pedro[2] and Kaleb Michaud[3], [1]University of Michigan, Ann Arbor, [2]Forward, The National Databank for Rheumatic Diseases, Wichita, KS, [3]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Health Services Research (1656–1661)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: In older adults with rheumatoid arthritis (RA), anti-TNF therapies are typically used as first-line biologic treatment. However, many patients require a switch to non-TNF biologics due to inadequate response or adverse effects. While the infection risk associated with initial anti-TNF therapy is well-established, less is known about the safety of non-TNF therapies initiated after anti-TNF exposure in this population. This uncertainty is particularly relevant for late-onset RA (LORA), where age-related immune changes and distinct disease characteristics may increase infection risk. This study examines the risk of serious infection (SI) associated with initiating non-TNF biologics after anti-TNF therapy in older adults with RA, comparing outcomes between those with LORA and younger-onset RA (YORA).

Methods: Using data from FORWARD—The National Databank for Rheumatic Diseases (2001–2019), we identified RA patients aged ≥60 years who initiated a non–TNF b/tsDMARD (anakinra, abatacept, JAK inhibitors, tocilizumab, rituximab) following anti-TNF therapy. Patients were categorized as LORA or YORA based on RA diagnosis age (≥60 vs < 60) and propensity score–matched on age at treatment, sex, race/ethnicity, and comorbidities. Those with other rheumatic diseases, cancer, or HIV before the first SI event were excluded. The index date was the first report of subsequent treatment after anti-TNF use. SI was defined as infection requiring IV antibiotics, hospitalization, or resulting in death within 12 months of

Table 1: Baseline characteristics of propensity-score matched older adults with RA and anti-NTNF initiation following anti-TNF therapy use by age of RA diagnosis

	LORA (N=198)	YORA (N=675)	P-value
Age at anti-TNF initiation	74.3 (5.6)	74.2 (6.3)	0.837
Female, %	80.3	79.8	0.900
Non-Hispanic White race/ethnicity, %	96.0	98.5	0.127
Medicare coverage, %	93.9	87.9	0.036
Educational level, years	13.4 (2.3)	14.0 (2.3)	0.011
Annual income, US$1,000	45.8 (29.2)	43.6 (29.2)	0.479
Urban community, %	27.9	20.8	0.100
Disease duration, years	8.9 (4.5)	27.9 (13.0)	<0.01
Past Smoking habits	45.5	50.5	0.3112
RDCI (0-9)	2.0 (1.5)	2.0 (1.5)	1.000
HAQ (0-3)	1.3 (0.7)	1.3 (0.7)	0.780
Pain VAS (0-10)	4.7 (2.4)	4.8 (2.7)	0.673
Global seventy VAS (0-10)	4.7 (2.4)	4.2 (2.4)	0.053
PAS (0-10)	4.4 (2.2)	4.6 (2.1)	0.469
Prior serious infections, %	14.6	25.8	0.006
Ever glucocorticoid use, %	87.4	85.9	0.659
Current glucocorticoid use, %	42.6	39.4	0.513
Long-term GC use pre-index, %	25.8	30.3	0.252
Concurrent methotrexate use, %	60.1	48.5	0.020

Note: Each LORA patient was matched to YORA patients based on age at NTNF initiation, sex, race/ethnicity, and comorbidity burden
*The values are presented as mean (SD) unless indicated otherwise.
Abbreviations: NTNF = non-TNF biologic or targeted synthetic DMARD, LORA = Late Onset Rheumatoid Arthritis; YORA = Young Onset Rheumatoid Arthritis; RDCI = Rheumatic Disease Comorbidity Index, HAQ = Health Assessment Questionnaire; VAS = Visual Analog Scale; PAS = Patient Activity Scale

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Adjusted HR for risk of serious infection related to subsequent non-TNF b/tsDMARD use after exposure to anti-TNF in older adults with RA

Variable	Adjusted HR	95% (CI)	
LORA	1.26	0.44	3.60
Age group at non-TNF therapy initiation			
60-70	Reference		
70-80	2.11	0.68	6.54
80+	3.83	1.01	14.4
Prior Infections	3.24	1.19	8.85
HAQ disability	6.24	2.45	15.9
Concurrent MTX use	1.17	0.48	2.84
Long-term GC use (time-varying)*	2.62	1.04	6.62
Other NTNF vs ABA	1.33	0.48	3.72

GC = glucocorticoid, NTNF = non-TNF therapy, ABA = Abatacept
*long-term GC use (time-varying) defined as at least 5mg/day prednisone equivalent for 90 consecutive days prior to SI

the index date and was attributed to subsequent therapy if it occurred during treatment or within three months of discontinuation (extended to 12 months for rituximab). SI risk differences were estimated using kernel-weighted, propensity score–adjusted survival models, stratified by RA onset group.

Results: 198 LORA patients were matched to 675 weighted YORA patients. Baseline characteristics after kernel propensity-score matching are summarized in Table 1. Abatacept was the most commonly used non-TNF b/tsDMARD in both groups (49.1% in YORA, 47.7% in LORA), followed by rituximab (22.6% in YORA, 22.2% in LORA). A greater proportion of LORA patients initiated subsequent therapy after only one prior anti-TNF agent compared to YORA (81.5% vs. 68.2%). The crude incidence of SI was 1.4 per 1,000 patient-years in YORA and 2.0 per 1,000 patient-years in LORA. In Cox regression models, the risk of SI was higher with older age groups at non-TNF therapy initiation, prior infection, higher HAQ disability score, and recent long-term GC use (Table 2). The risk of SI did not differ significantly between abatacept and other non-TNF therapies.

Conclusion: Among older adults with RA who initiated a non-TNF b/tsDMARD after anti-TNF therapy, the risk of SI did not differ by RA onset age or by specific treatment regimen (abatacept vs. other non-TNF therapies). However, prior SI, recent long-term GC use, and higher HAQ disability scores were independently associated with increased SI risk. These findings highlight the importance of individualized infection risk assessment when selecting second-line therapies in older adults.

Disclosure: J. Lee: None; **S. Pedro**: None; **K. Michaud**: None.

Abstract Number: 1657

Extracting TNF Inhibitor Switching Reasons and Trajectories From Real-World Data Using Large Language Models

Brenda Miao[1], Marie Binvignat[2], **Augusto Garcia-Agundez**[3], Maxim Bravo[4], Christopher Williams[5], Claire Miao[4], Ahmed Alaa[6], Vivek Rudrapatna[5], gabriela Schmajuk[7] and Jinoos Yazdany[3], [1]UCSF, Fremont, CA, [2]Sorbonne University, Paris, France, [3]UCSF, San Francisco, CA, [4]UC Berkeley, San Francisco, [5]UCSF, San Francisco, [6]UC Berkeley, Berkeley, [7]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Health Services Research (1656–1661)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics and TNF inhibitor (TNFi) switch counts, n=2112	
Mean age, First TNFi (SD)	36.3 (18.4)
Mean follow-up time, years (SD)	7.1 (5.6)
Female (%)	1275 (60.5)
First documented TNFi (%)	
Etanercept	671 (31.8)
Adalimumab	668 (31.6)
Infliximab- biooriginator	530 (25.1)
Infliximab -biosimilar	140 (6.6)
Certolizumab	67 (3.2)
Golimumab	36 (1.7)
Number of switches between TNFi drugs (%)	
1	1,481 (70.1)
2	418 (19.8)
>2	150 (7.1)

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) are cornerstones of autoimmune-disease therapy, yet many patients switch agents because of loss of effectiveness, adverse events, or insurance barriers. Unstructured clinical notes contain the rationale for switching but are costly to review manually. Our objective was to determine whether large language models (LLMs) can automatically identify TNFi-to-TNFi switching and the reasons for switching in real-world practice.

Methods: We conducted a retrospective observational study of de-identified electronic health records (2012-2023) from a single academic center. We defined TNFi-to-TNFi switching as a change from one TNFi to a different TNFi at consecutive encounters and include patients with a TNFi-to-TNFi switch and ≥6 months follow-up. Using a zero-shot prompt, GPT-4-turbo-128k and eight open-source LLMs extracted (1) TNFi stopped, (2) TNFi started, and (3) reason category between: adverse event, anti-drug antibodies, insurance/cost, lack of effectiveness, patient preference, other, or unknown. Performance was assessed on a subset of manually expert-annotated notes with micro-F1 scores.

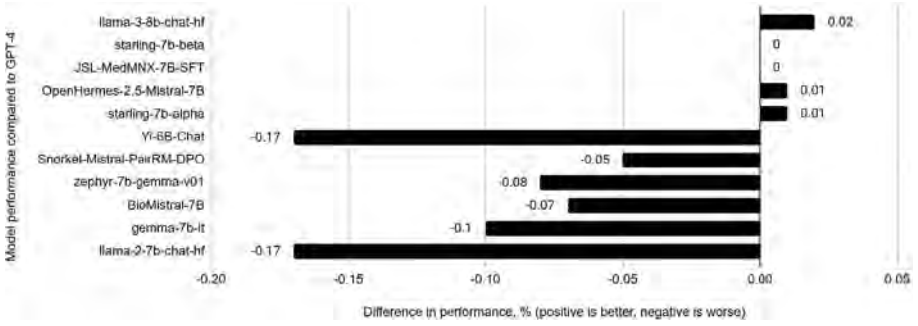


Figure 1. Average win minus loss percentage rates of open-source large language models compared to GPT-4 in identifying started and stopped medication on the manually reviewed note subset. Positive numbers indicate the model is superior to GPT-4 (the model correctly identified a started or stopped medication where GPT-4 did not), negative numbers indicate the contrary.

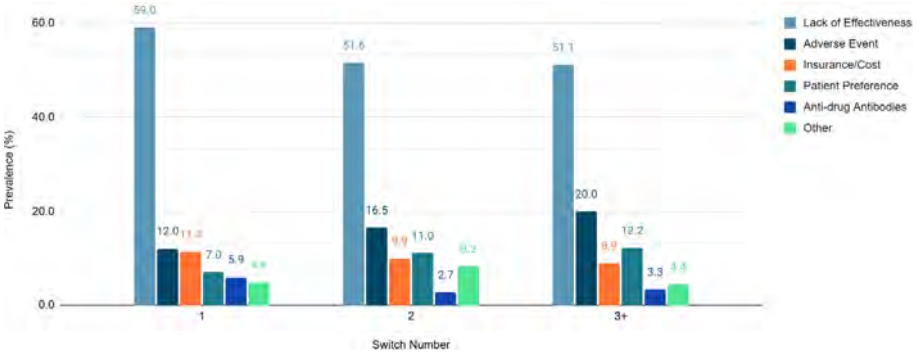


Figure 2. Percentage of identified reasons for switching.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 2,112 patients met inclusion criteria (Table 1). On the manually annotated subset (n=146), GPT-4 achieved micro-F1 scores of 0.75 for stopped TNFi, 0.80 for started TNFi, and 0.83 for reason extraction. The best open-source models approached GPT-4 for medication identification: Starling-7B-beta (0.88 stopped, 0.79 started) and Llama-3-8B-Instruct (0.82 stopped, 0.75 started). Only Llama-3-8B-Instruct matched GPT-4 for reason identification with F1=0.83. Figure 1 depicts a direct comparison between models. In the first switch, the leading reasons were lack of effectiveness (59%), adverse events (12%), and insurance/cost issues (11%). Subsequent switches showed a higher share of adverse events and patient preference and fewer effectiveness and cost-driven changes (Figure 2).

Conclusion: GPT-4 can extract complex TNFi switching patterns from clinical notes with high accuracy, substantially reducing the need for manual chart review. Several local models offer comparable performance. This capability enables scalable pharmacoepidemiologic studies of treatment lines and could power point-of-care tools that summarize medication histories for clinicians. Further work should evaluate generalizability to other biologic classes and multi-institution datasets.

Disclosure: B. Miao: Quality Health, 12, Co-Founder; **M. Binvignat**: None; **A. Garcia-Agundez**: None; **M. Bravo**: None; **C. Williams**: None; **C. Miao**: None; **A. Alaa**: None; **V. Rudrapatna**: Dataunite, ZebraMD, AcucareAI, 1, Genentech, BeOne, Merck, Janssen, Takeda, Blueprint Medicines, Mitsubishi Tanabe, Stryker, 5, Ironwood, Natera, 2; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5.

Abstract Number: 1658

Cardiovascular Disease Risk and Risk Calculator Performance in Rheumatoid Arthritis-Associated Interstitial Lung Disease

Omair Khan[1], Halie Frideres[2], Punyasha Roul[3], Grant Cannon[4], Gary Kunkel[5], Brian Sauer[6], Joshua Baker[7], Ted Mikuls[1], Bryant England[1] and Tate Johnson[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]UNMC Department of Rheumatology, Omaha, NE, [3]UNMC, Omaha, NE, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [6]Salt Lake City VA/University of Utah, Salt Lake City, UT, [7]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Health Services Research (1656–1661)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Existing cardiovascular disease (CVD) risk stratification strategies underperform in RA. Lung disease is an established CVD risk factor, and RA-interstitial lung disease (RA-ILD) clinically affects 1 in 10 RA patients. As RA-ILD is not captured by current CVD risk calculators, we evaluated RA-ILD as a risk factor for major adverse cardiovascular events (MACE) and heart failure (HF) in RA, and assessed the performance of the Predicting Risk of cardiovascular disease EVENTs (PREVENT) calculator in RA-ILD.

Methods: We performed a retrospective cohort study of patients with RA and RA-ILD using national Veterans Administration (VA) data (2000-2021). RA patients were identified using ≥2 diagnostic codes, a rheumatologist diagnosis, plus a positive autoantibody or DMARD dispense. RA-ILD was defined at baseline and in follow up, using a validated RA-ILD administrative algorithm (PPV >80%). Cohort entry was the date the RA algorithm was fulfilled or the date of RA-ILD diagnosis (if ILD developed in follow up). Overall CVD, MACE (myocardial infarction, stroke), and HF were identified in VA, Medicare, and National Death Index data. Those with pre-existing MACE or HF were excluded. Cox regression was used to estimate the risk of CVD related to RA-ILD status, adjusted for age, sex, race, BMI, smoking status, CVD risk factors, rurality, and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Association of RA-ILD with CVD risk in patients with RA

	Incidence rate per 100 PY (95% CI)			
	RA (N=66,295)	RA-ILD (N=3,620)	HR (95% CI)	aHR (95% CI)*
Overall CVD**	2.96 (2.92-3.01)	6.09 (5.73-6.48)	1.93 (1.81-2.07)	1.19 (1.11-1.28)
MACE	2.12 (2.09-2.16)	3.36 (3.10-3.65)	1.49 (1.37-1.63)	0.98 (0.90-1.07)
HF	1.33 (1.30-1.36)	3.48 (3.21-3.77)	2.46 (2.26-2.68)	1.44 (1.31-1.58)

*Adjusted hazard ratios (aHR) estimated in Cox regression models adjusted for age, sex, race, BMI, smoking status, hypertension, hyperlipidemia, diabetes, renal function, health care utilization, rurality.

**Overall CVD = composite of MACE and HF outcomes

Abbreviations: RA, rheumatoid arthritis; RA-ILD, rheumatoid arthritis associated interstitial lung disease; PY, person years; IR, incidence rate; CI, confidence interval; aHR, adjusted hazard ratio; CVD, cardiovascular disease; MACE, major adverse cardiovascular events; HF, heart failure

Table 2. Baseline 10-year CVD risk in RA and RA-ILD according to Predicting Risk of cardiovascular EVENTs (PREVENT) calculator

	RA (N=66,295)	RA-ILD (N=3,620)	p-value
Overall CVD			
Low/Borderline risk (<7.5%)	18,352 (34.3%)	525 (22.2%)	
Intermediate risk (7.5-20%)	24,998 (46.7%)	984 (41.5%)	
High risk (≥20 %)	1,0209 (19.1%)	860 (36.3%)	<0.001
MACE			
Low/Borderline risk (<7.5%)	31,536 (58.9%)	1,045 (44.3%)	
Intermediate risk (7.5-20%)	20,225 (37.8%)	1,047 (44.4%)	
High risk (≥20 %)	1,798 (3.4%)	268 (11.4%)	<0.001
Heart Failure			
Low/Borderline risk (<7.5%)	33,736 (63.0%)	1,060 (44.7%)	
Intermediate risk (7.5-20%)	16,915 (31.6%)	968 (40.9%)	
High risk (≥20 %)	2,908 (5.4%)	341 (14.4%)	<0.001

Abbreviations: RA, rheumatoid arthritis; RA-ILD, rheumatoid arthritis associated interstitial lung disease; CVD, cardiovascular disease; MACE, major adverse cardiovascular events

healthcare utilization. PREVENT variables were queried in the 12 months prior to cohort entry. Estimated 10-year risk of overall CVD, MACE and HF was calculated and PREVENT categories (low/borderline, intermediate, high risk) were described. Calibration (standardized incidence ratios [SIR = observed:predicted event rate]) and discrimination (Harrell's C statistic, sensitivity using cutoff of 7.5%) of PREVENT were compared between those with and without RA-ILD.

Results: We studied 69,915 RA patients (mean age 63, 87% male). Patients with RA-ILD (N=3,620) were more frequently smokers, seropositive, with more traditional CVD risk factors and healthcare utilization. Over 613,200 person-years, 17,713 overall CVD events occurred. The incidence of all CVD outcomes was higher in RA-ILD, as were unadjusted hazards for overall CVD (HR 1.93 [1.81-2.07]), MACE (1.49 [1.37-1.63]), and HF (2.46 [2.26-2.68], **Table 1)**. In adjusted models, the risk of overall CVD (aHR 1.19 [1.11, 1.28]) and HF (1.44 [1.31, 1.58]) persisted, while MACE risk was null in RA-ILD vs. RA without ILD (0.98 [0.90, 1.07], **Table 1)**. A greater percentage of patients with RA-ILD were categorized as high risk (overall

Table 3. Performance of the PREVENT CVD risk calculator in RA-ILD vs. RA without ILD

Table 3. Performance of the PREVENT CVD risk calculator in RA-ILD vs. RA without ILD *

	RA (N=66,295)	RA-ILD (N=3,620)
Overall CVD **		
SIR (95% CI)	2.07 (2.04-2.11)	1.49 (1.37-1.61)
Sensitivity	82.61%	93.09%
Harrel's C statistic	0.64	0.64
MACE		
SIR (95% CI)	2.60 (2.55-2.65)	1.50 (1.35-1.66)
Sensitivity	60.00%	75.88%
Harrel's C statistic	0.62	0.62
Heart Failure		
SIR (95% CI)	1.61 (1.57-1.65)	1.41 (1.27-1.56)
Sensitivity	59.93%	73.24%
Harrel's C statistic	0.67	0.67

*Standardized incidence ratios (SIR) calculated as observed to expected CVD events, based on estimated CVD risk in the PREVENT calculator (SIR > 1 reflecting an underestimation of CVD risk). Measures of discrimination (sensitivity and Harrel's C) calculated using an estimated risk cutoff of 7.5%.

**Overall CVD = Composite of MACE and HF

Abbreviations: RA, rheumatoid arthritis; RA-ILD, rheumatoid arthritis associated interstitial lung disease; SIR, Standardized incidence rate; CI, confidence interval; CVD, cardiovascular disease; MACE, major adverse cardiovascular events; HF, heart failure

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

CVD: 36.3% vs 19.1%; **Table 2**) using PREVENT, which demonstrated improved calibration (overall CVD SIR 1.49 vs. 2.07) and sensitivity (93.1 vs. 82.6%) in RA-ILD vs. RA without ILD (**Table 3**). Harrel's C was similar regardless of RA-ILD.

Conclusion: RA-ILD was associated with higher CVD risk in RA, driven by increased HF risk, possibly due to the effect of pulmonary hypertension and chronic hypoxia on cardiac function. Reflecting a high comorbidity burden, RA-ILD patients were more frequently categorized as high risk by PREVENT, which may in turn improve calibration of PREVENT in RA-ILD. Whether early identification and management of RA-ILD may help mitigate the elevated HF risk observed in RA requires continued research.

Disclosure: O. Khan: None; **H. Frideres**: None; **P. Roul**: None; **G. Cannon**: None; **G. Kunkel**: None; **B. Sauer**: None; **J. Baker**: Amgen, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Johnson**: None.

Abstract Number: 1659

Prevalence and Progression of Multimorbidity in Rheumatoid Arthritis-Associated Interstitial Lung Disease

James Fagerland[1], Yangyuna Yang[1], Punyasha Roul[2], Tate Johnson[1], Scott Matson[3], Grant Cannon[4], Brian Sauer[5], Jeffrey Curtis[6], Joshua Baker[7], Ted Mikuls[1] and Bryant England[1], [1]University of Nebraska Medical Center, OMAHA, NE, [2]UNMC, Omaha, NE, [3]University of Kansas, Kansas City, MO, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]Salt Lake City VA/University of Utah, Salt Lake City, UT, [6]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [7]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Health Services Research (1656–1661)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Multimorbidity, the presence of multiple chronic conditions, is common in RA, and the progression of multimorbidity in RA is associated with poor long-term outcomes. However, the burden and progression of multimorbidity in high-risk RA populations, such as those with the extra-articular manifestation of RA-associated interstitial lung disease (RA-ILD), is not well understood. Thus, we evaluated the prevalence and progression of multimorbidity in RA-ILD within the Veterans Health Administration (VA).

Methods: We performed a cohort study of RA-ILD patients using national VA data between 1999 and 2021. RA-ILD patients were identified with validated RA and ILD administrative algorithms (>80% PPV), then followed from the date the RA-ILD algorithm was fulfilled (index date) until death or end of study period. Multimorbidity burden was quantified as the number of conditions present among 43 chronic conditions (based on prior published multimorbidity studies in RA), using diagnostic codes from inpatient and outpatient encounters prior to the index date and throughout follow-up. The prevalence of individual morbidities at baseline and newly developing annually through the end of follow-up was descriptively summarized. Group based trajectory modeling was utilized to derive unique longitudinal trajectories of multimorbidity burden, stratified by tertile of baseline multimorbidity burden (low, moderate, and high). Multimorbidity trajectory group membership was then used to predict respiratory-related hospitalizations (respiratory-related discharge diagnosis in primary position from VA administrative data) in Cox regression models that adjusted for age, sex, race, smoking status, baseline multimorbidity burden, and calendar year.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Multimorbidity at baseline and over follow-up among patients with RA-ILD

Morbidity*	Baseline N (%)	Baseline + Follow-up N (%)	Change in prevalence (%)
Hypertension	4326 (69.4)	5107 (82.0)	12.6
Hyperlipidemia	3848 (61.8)	4552 (73.0)	11.2
Severe vision reduction	3482 (56.0)	4652 (74.7)	18.7
Osteoarthritis	2951 (47.5)	3757 (60.3)	12.8
Chronic back disorders	2824 (45.3)	3799 (61.0)	15.7
COPD	2574 (41.3)	3279 (52.6)	11.3
GERD	2562 (41.1)	3506 (56.3)	15.2
Depression	2338 (37.5)	2908 (46.7)	9.2
Coronary artery disease	2159 (34.6)	2960 (47.5)	12.9
Diabetes	1992 (32.0)	2589 (41.5)	9.5
Hearing loss	1944 (31.2)	2711 (43.5)	12.3
Anemia	1819 (29.2)	3055 (49.0)	19.8
Prostatic hyperplasia	1668 (26.8)	2451 (39.3)	12.5
Neuropathy	1611 (25.9)	2253 (36.2)	10.3
Obesity	1595 (25.6)	2034 (32.6)	7.0
Sleep disorder	1486 (23.8)	2094 (33.6)	9.8
Cardiac arrhythmias	1422 (22.8)	2551 (40.9)	18.1
Heart failure	1079 (17.3)	2134 (34.2)	16.9
Inflammatory skin diseases	1055 (16.9)	1536 (24.7)	7.8
Cancer	969 (15.6)	1699 (27.3)	11.7
PTSD	939 (15.1)	1151 (18.5)	3.4
Osteoporosis	935 (15.0)	1547 (24.8)	9.8
Anxiety	931 (14.9)	1370 (22.0)	7.1
Peripheral vascular disease	902 (14.5)	1507 (24.2)	9.7
Hypothyroid	846 (13.6)	1203 (19.3)	5.7
Cerebrovascular disease	747 (12.0)	1222 (19.6)	7.6
Renal disease	734 (11.8)	1456 (23.4)	11.6
Chronic headache	632 (10.1)	925 (14.8)	4.7
Diverticular disease	615 (9.9)	1022 (16.4)	6.5
Alcohol abuse	571 (9.2)	723 (11.6)	2.4
Asthma	540 (8.7)	764 (12.3)	3.6
Valvular heart disease	459 (7.4)	907 (14.6)	7.2
Gout	451 (7.2)	648 (10.4)	3.2
Pulmonary circulation disorder	420 (6.7)	1174 (18.8)	12.1

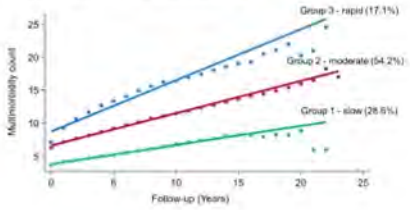
*Morbidities from England BR et al. Burden and trajectory of multimorbidity in rheumatoid arthritis: a matched cohort study from 2006 to 2015. *Ann Rheum Dis*. 2021 Mar;80(3):286-292. Morbidities sorted by prevalence at baseline. Morbidities with <10% prevalence at baseline + follow-up not listed.

Abbreviations: COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; PTSD, post-traumatic stress disorder

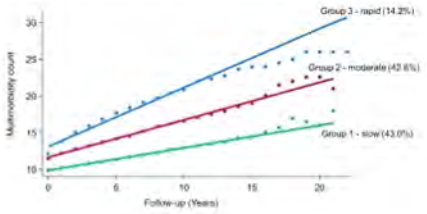
Multimorbidity at baseline and over follow-up among patients with RA-ILD

Figure 1: Multimorbidity trajectory groups in RA-ILD stratified by baseline multimorbidity burden tertile.

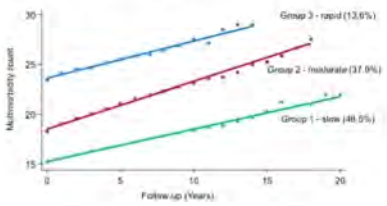
A: Tertile 1 - low baseline multimorbidity



B: Tertile 2 – moderate baseline multimorbidity



C: Tertile 3 – high baseline multimorbidity



Multimorbidity trajectory groups in RA-ILD stratified by baseline multimorbidity burden tertile.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Adjusted hazard ratios for respiratory-related hospitalization among RA-ILD patients by multimorbidity trajectory groups.

Model	aHR (95% CI)
Tertile 1 – low baseline multimorbidity	
Group 3. Rapid multimorbidity progression	1.24 (0.98, 1.57)
Group 2. Moderate multimorbidity progression	1.23 (1.03, 1.48)
Group 1. Slow multimorbidity progression	1 (referent)
Tertile 2 – moderate baseline multimorbidity	
Group 3. Rapid multimorbidity progression	1.60 (1.29, 1.98)
Group 2. Moderate multimorbidity progression	1.30 (1.11, 1.52)
Group 1. Slow multimorbidity progression	1 (referent)
Tertile 3 – high baseline multimorbidity	
Group 3. Rapid multimorbidity progression	1.58 (1.12, 2.24)
Group 2. Moderate multimorbidity progression	1.27 (1.07, 1.51)
Group 1. Slow multimorbidity progression	1 (referent)

Values adjusted hazard ratio and 95% confidence interval from Cox model adjusting for age, sex, race, smoking status, baseline multimorbidity burden, and calendar year. Base rate of respiratory hospitalizations in the slow multimorbidity progression groups were: 10.4/100PY in Tertile 1, 11.8/100PY in Tertile 2, and 16.1/100PY in Tertile 3.

Group numbering corresponds to numbering in **Figure 1**.

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval

Adjusted hazard ratios for respiratory-related hospitalization among RA-ILD patients by multimorbidity trajectory groups.

Results: We studied 6,232 RA-ILD patients (92.6% male, mean age 69 years) with a mean (SD) of 11.2 (5.3) morbidities at baseline that increased to 13.5 (5.5) over a median follow-up of 5 years. Cardiometabolic, respiratory, and musculoskeletal morbidities were the most frequent and present in most RA-ILD patients by the end of follow-up (**Table 1**). All morbidities increased in prevalence over follow-up, with cardiometabolic and cancer morbidities among those with the greatest increase in prevalence. Trajectory modeling identified 3 multimorbidity trajectories within each tertile of baseline multimorbidity burden representing slow, moderate, and rapid multimorbidity progression during follow-up (**Figure 1**). Within each baseline multimorbidity burden tertile, the rapid (group 3; aHR range 1.24 to 1.60) and moderate (group 2; aHR range 1.23 to 1.30) multimorbidity progression trajectory groups were associated with a higher risk of respiratory-related hospitalization compared to the slow progression group (group 1) (**Table 2**).

Conclusion: Multimorbidity was highly prevalent and progressive throughout the RA-ILD disease course in this national VA RA-ILD cohort. More rapidly progressive multimorbidity trajectories predicted higher risk of respiratory-related hospitalization independent of baseline multimorbidity burden. Together, these findings emphasize the need to monitor and manage multimorbidity in RA-ILD patients to optimize long-term outcomes.

Disclosure: J. Fagerland: None; **Y. Yang**: None; **P. Roul**: None; **T. Johnson**: None; **S. Matson**: None; **G. Cannon**: None; **B. Sauer**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **J. Baker**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 1660

Digital Psychological Support for Inflammatory Rheumatic Diseases: A Randomized Clinical Trial

Johannes Knitza[1], Julia Kraus[2], Martin Krusche[3], Isabell Haase[3], Philipp Klemm[4], Axel Hueber[5], Pfeil Alexander[6], Ulrich Drott[7], Sebastian Kuhn[8] and Jan Philipp Klein[9], [1]Institute for Digital Medicine, University Hospital Gießen-Marburg, Philipps University, Marburg, Germany, [2]Vila Health, Berlin, Germany, [3]Division of Rheumatology and Systemic Inflammatory Diseases, III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [4]Department of Rheumatology and Clinical Immunology Center, JLU Giessen, Campus Kerckhoff, Bad Nauheim, Germany, Bad Nauheim, Germany, [5]Klinikum Nuernberg, Nuernberg, Germany, [6]Department of Internal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medicine III, Jena University Hospital - Friedrich Schiller University Jena, Jena, Germany, [7]Deutsches Endokrinologisches Versorgungszentrum, Frankfurt, Germany, [8]Institute for Digital Medicine, University Hospital of Giessen and Marburg, Philipps University Marburg, Marburg, Germany, [9]Department of Psychiatry, Psychosomatics and Psychotherapy, University of Lübeck, Lübeck, Germany

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Health Services Research (1656–1661)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Patients with inflammatory rheumatic diseases (IRDs) frequently experience psychological distress, however access to psychological support remains limited. The aim of this trial (DRKS identifier: DRKS00032862) was to investigate the effectiveness of a digital psychological intervention for individuals with IRDs.

Methods: Participants aged 18 years or older were recruited across Germany between February 22, 2024 and June 4, 2024 if they had been diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or systemic lupus erythematosus (SLE) and reported psychological distress and reduced quality of life. Participants were randomized to either a self-guided digital psychological intervention or a treatment as usual control condition. The primary outcomes were change in psychological distress (Hospital Anxiety and Depression Scale [HADS]) and quality of life (Assessment of Quality of Life [AQoL-8D]) from baseline to three months. Secondary outcomes included changes in self-efficacy, health literacy, perceived stress, functional impairment, depression and anxiety.

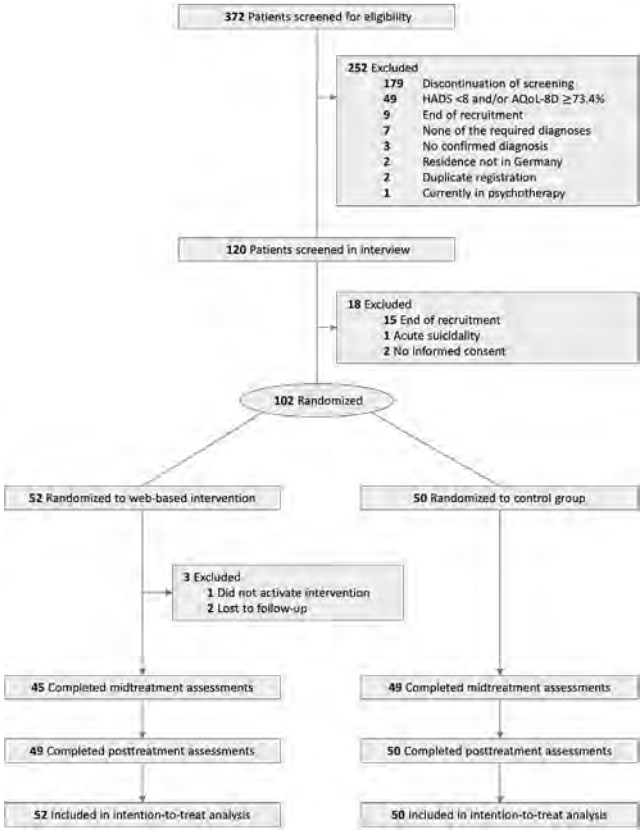


Figure 1. Trial Participant Flow Diagram

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

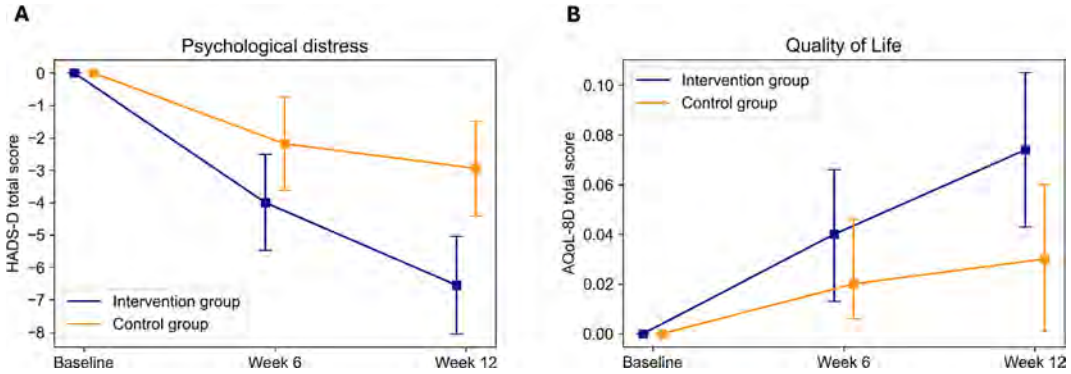


Figure 2. Least-squares Mean Changes of Primary Outcome Measures

Results: A total of 102 participants (mean [SD] age, 47.2 [12.9] years; 92 [90.2%] female; see Table 1) were randomized to the intervention group (n = 52) and the control group (n = 50) (Fig.1). The intervention group showed a significantly greater reduction in psychological distress at the 3-month follow-up (least squares mean difference, −3.60; 95% CI, −5.73 to −1.47; $P < .001$; Cohen's d = -0.71), and a greater improvement of quality of life (least squares mean difference, 0.04; 95% CI, 0.00 to 0.09; $P = .047$; Cohen's $d = 0.49$) (Fig.2). A significantly greater proportion of participants in the intervention group experienced a clinically meaningful improvement in psychological distress (59.2% vs. 34.0%, $P = .016$) and quality of life (55.1% vs 32.0%, $P = .026$) compared to the control group. Secondary outcomes measures showed a similar pattern of improvement, except for functional impairment. No adverse events related to the intervention were reported.

Table 1. Baseline Characteristics (Intention-to-Treat Sample)

Characteristic	Participants, No. (%)		
	Total (N = 102)	Intervention group (n = 52)	Control group (n = 50)
Age, mean (SD), y	47.2 (12.9)	52.4 (12.5)	41.8 (11.2)
Gender			
Female	92 (90.2)	47 (90.4)	45 (90.0)
Male	10 (9.8)	5 (9.6)	5 (10.0)
Rheumatic disease			
Psoriatic arthritis	33 (32.4)	18 (34.6)	15 (30.0)
Rheumatoid arthritis	37 (36.3)	23 (44.2)	14 (28.0)
Systemic lupus erythematosus	32 (31.4)	11 (21.2)	21 (42.0)
Rheumatic disease duration, mean (SD), y	8.4 (9.0)	9.4 (9.8)	7.4 (8.0)
PhGA	4.0 (1.9)	4.3 (2.1)	3.7 (1.5)
Educational level			
High school diploma	64 (62.7)	33 (63.5)	31 (62.0)
Secondary school diploma	34 (33.3)	16 (30.8)	18 (36.0)
Other	4 (3.9)	3 (5.8)	1 (2.0)
Occupation status			
Employed	60 (58.8)	25 (48.1)	35 (70.0)
Unemployed	1 (1.0)	0	1 (2.0)
Civil servant	2 (2.0)	1 (1.9)	1 (2.0)
Retired	17 (16.7)	14 (26.9)	3 (6.0)
Student	5 (4.9)	1 (1.9)	4 (8.0)
Self-employed	7 (6.9)	4 (7.7)	3 (6.0)
Other	10 (9.8)	7 (13.5)	3 (6.0)
Marital status			
Living alone	23 (22.6)	13 (25.0)	10 (20.0)
In a partnership or married	65 (63.7)	32 (61.5)	33 (66.0)
Divorced	11 (10.8)	5 (9.6)	6 (12.0)
Widowed	3 (2.9)	2 (3.8)	1 (2.0)

Abbreviations: PhGA, Physician's global assessment of disease activity.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This randomized clinical trial supports the effectiveness and safety of a digital psychological intervention in individuals with IRDs. These findings suggest that such digital interventions could be a valuable, scalable approach to addressing mental health needs in rheumatology.

Disclosure: J. Knitza: GAIA, 2, Vila Health, 12,, 2; **J. Kraus**: Vila Health, 3; **M. Krusche**: None; **I. Haase**: None; **P. Klemm**: None; **A. Hueber**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos/Alfasigma, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Alexander**: None; **U. Drott**: None; **S. Kuhn**: None; **J. Klein**: all about me, 2, Boehringer-Ingelheim, 2, Ethypharma, 2, GAIA, 2, 6, medac, 2, Oberberg, 6, Servier, 6, Stillachhaus, 6, sympatient, 2.

Abstract Number: 1661

Artificial Intelligence Applied to Patient Reported Outcomes and Passive Physiologic Sensor Data Can Accurately Classify Low Disease Activity in Rheumatoid Arthritis Patients

Jeffrey Curtis[1], Yujie Su[2], sam Barskiy[3], Emily Holladay[3], Shilpa Venkatachalam[4], David Curtis[5], Tapan Mehta[3] and Fenglong Xie[6], [1]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [2]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Global Healthy Living Foundation, New York, NY, [5]Global Healthy Living Foundation, Meriden, [6]The University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Health Services Research (1656–1661)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Remote therapeutic monitoring (RTM) and remote physiologic monitoring (RPM) programs have the potential to capture data between clinical visits and provide information back to providers about the health status of their patients. We evaluated the ability of patient reported outcome (PRO) data coupled with passive biosensor data streams to classify RA low disease activity (LDA).

Methods: We recruited 150 RA patients to a prospective study that captured PRO data and among a subgroup (n=96), wear a Fitbit Versa2 device for approximately 3-4 months at the time that they initiated adalimumab or upadacitinib. Clinical Disease Activity Index (CDAI) was collected at baseline and follow-up. A variety of PROs and passive biosensor activity data were captured at various frequencies.

Various machine learning methods (Distributed RandomForests [DRF], Gradiant Boosting, Generalized Linear Models, Ensemble) were used to classify LDA using only the baseline clinical data plus longitudinal PROs and biosensor data. Models were trained on a random split sample (training/testing) in a 2/3:1/3 ratio. Model building prioritized parsimonious models that minimized the number of PROs that patients were asked to provide (allowing for 3 PROs, at most), de-prioritizing more frequently collected PROs (e.g. daily) and favoring less frequently collected PROs (e.g. weekly, monthly). A scenario that simulated PRO data collection with at half the frequency was modeled to evaluate ML model performance under these conditions, intended to reduce participant burden. The best models were selected based on the F1 statistic (harmonic mean of sensitivity and positive predictive value), and separately, the F1 statistic, requiring a PPV of ≥80%. Confidence intervals were estimated using 1000 bootstrap samples.

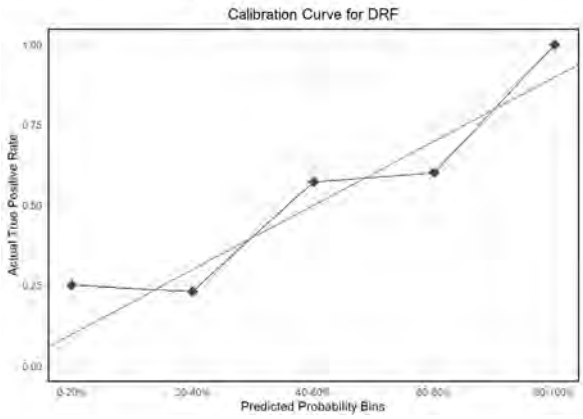
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 : Baseline Characteristics of the Rheumatoid Arthritis Cohort

	Overall	with Fitbit	without Fitbit
	N = 150	N = 96	N = 54
Demographic			
Age	52.1 (12.0)	51.1 (12.7)	54.1 (10.4)
Sex			
Female	119 (79.3%)	77 (80.2%)	42 (77.8%)
Male	31 (20.7%)	19 (19.8%)	12 (22.2%)
Race			
Asian	3 (2.0%)	2 (2.1%)	1 (1.9%)
Black or African American	11 (7.3%)	9 (9.4%)	2 (3.7%)
White	124 (82.7%)	75 (78.1%)	49 (90.7%)
American Indian or Alaska Native	1 (0.7%)	1 (1.0%)	0 (0.0%)
Multiple Race	5 (3.3%)	3 (3.1%)	2 (3.7%)
Refuse to Answer	6 (4.0%)	6 (6.3%)	0 (0.0%)
Hispanic			
Yes	36 (24.0%)	21 (21.9%)	15 (27.8%)
No	112 (74.7%)	73 (76.0%)	39 (72.2%)
Unknown	2 (1.3%)	2 (2.1%)	0 (0.0%)
BMI	31.5 (7.7)	31.9 (8.1)	30.9 (7.1)
smoking			
Current Smoker	27 (18.0%)	16 (16.7%)	11 (20.4%)
Former Smoker	34 (22.7%)	21 (21.9%)	13 (24.1%)
Never Smoker	89 (59.3%)	59 (61.5%)	30 (55.6%)
Years Since RA Diagnosis			
<2	56 (37.3%)	33 (34.4%)	23 (42.6%)
2-5	36 (24.0%)	28 (29.2%)	8 (14.8%)
6-10	12 (8.0%)	7 (7.3%)	5 (9.3%)
>10	46 (30.7%)	28 (29.2%)	18 (33.3%)
RA Disease Activity			
Physician Global Assessment	5.4 (2.2)	5.2 (2.2)	5.7 (2.2)
Patient Global Assessment	5.7 (2.4)	5.6 (2.4)	6.0 (2.4)
Tender Joint Count	6.8 (6.5)	6.9 (6.9)	6.6 (5.7)
Swollen Joint Count	12.5 (9.0)	12.3 (9.0)	12.9 (9.0)
Clinical Disease Activity Index (CDAI)	29.9 (16.4)	29.6 (16.9)	30.4 (15.6)
Lab Results			
Rheumatoid Factor Positive	89 (59.3%)	57 (59.4%)	32 (59.3%)
CCP Antibody Positive	68 (45.3%)	44 (45.8%)	24 (44.4%)
CCP or RF Positive	97 (64.7%)	62 (64.6%)	35 (64.8%)
Condition			
Osteoarthritis	23 (15.3%)	15 (15.6%)	8 (14.8%)
Fibromyalgia	16 (10.7%)	7 (7.3%)	9 (16.7%)
Other Rheumatic or Musculoskeletal Condition	119 (79.3%)	77 (80.2%)	42 (77.8%)
Anxiety	40 (26.7%)	19 (19.8%)	21 (38.9%)
Depression	45 (30.0%)	22 (22.9%)	23 (42.6%)
Diabetes	22 (14.7%)	15 (15.6%)	7 (13.0%)
COPD/CPD	9 (6.0%)	4 (4.2%)	5 (9.3%)
Heart Failure	1 (0.7%)	0 (0.0%)	1 (1.9%)
Sleep Apnea or Other Sleep Disorders	15 (10.0%)	11 (11.5%)	4 (7.4%)
PRO measures			
PROMIS Pain Interference	62.2 (6.1)	61.5 (5.5)	63.5 (7.0)
PROMIS Physical Function	38.9 (7.2)	39.8 (6.7)	37.4 (8.0)
PROMIS Fatigue	60.5 (7.8)	60.0 (7.3)	61.5 (8.6)
PROMIS Sleep Disturbance	57.2 (7.9)	56.4 (7.0)	58.7 (9.2)
PROMIS Social Activities	44.1 (7.1)	45.0 (6.9)	42.3 (7.4)
Patient Global Assessment	5.6 (2.1)	5.6 (2.2)	5.5 (2.1)
RADAI-5	6.2 (2.1)	6.2 (1.9)	6.3 (2.3)
PROMIS Anxiety	57.5 (8.8)	56.3 (9.1)	59.8 (7.7)
Pain (0~10 NRS)	5.2 (2.5)	5.1 (2.5)	5.5 (2.5)
Fatigue (0~10 NRS)	5.8 (2.7)	5.7 (2.6)	6.0 (2.8)

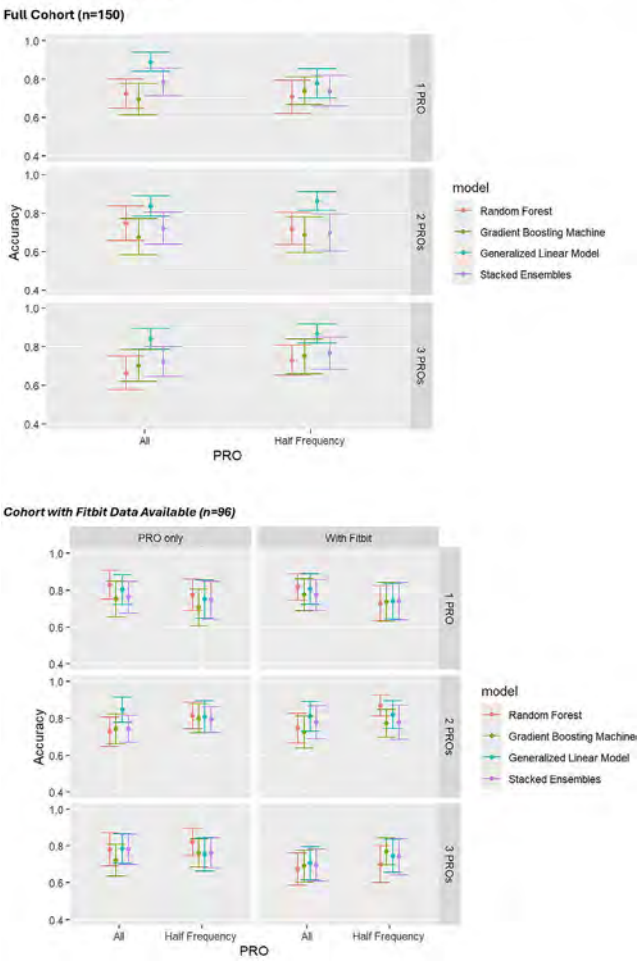
Mean (SD); n (%)

Figure 1: Model Calibration Showing Predicted Likelihood of Low Disease Activity or Remission (CDAI <=10) at Month 3-4 among RA Patients Initiating Upadatacinib and Adalimumab (results shown from testing sample) from Distributed RandomForests machine learning model



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Model Performance to Classify RA Low Disease Activity or Remission at 3 months following Adalimumab or Upadacitinib, Varying the Machine Learning Method, Number of PROs, and Use of Biosensor Data



Results: Characteristics of the RA cohort (Table 1) were: mean (SD) age 52.1(12.0) years, 79.3% female, mean (SD) BMI 31.5 (7.7), mean (SD) baseline CDAI 29.9 (16.4), 64.7% seropositive. Concomitant therapies included NSAIDs (40.7%), glucocorticoids (32.7%), opioids (24.7%) opioids. Prior treatment history: 36.7% were biologic naïve, and 27.3% used exactly 1 biologic. Mean (SD) step count was 6299 (3815) steps and mean (SD) sleep was 6.5 (2.9) hours of sleep.

The most important longitudinal PRO variables included weekly PROMIS Fatigue, PROMIS Pain Interference, and RADAI5. Model accuracy (predicted vs. observed LDA) is shown (Figure 1) and indicated that model calibration was reasonable. Model accuracy exceeded 80% with 1, 2, or 3 PROs, with or without Fitbit biosensor data (Figure 2). Using only half-frequency PRO data capture (e.g. every 2 weeks) did not substantially impair model accuracy. Performance was modestly better if daily PROs plus Fitbit data were used (not shown), albeit at the expense of greater participant burden.

Conclusion: Machine learning can accurately identify RA patients in LDA or remission measured 3-4 months after starting adalimumab or upadacitinib using as few as 1 longitudinal PRO measures collected as infrequently as every 2 weeks. Only small increases in performance were observed when actigraphy biosensor data was added.

Disclosure: J. Curtis: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **Y. Su**: None; **s. Barskiy**: None; **E. Holladay**: None; **S. Venkatachalam**: None; **D. Curtis**: None; **T. Mehta**: Heart Rhythm Clinical Research Solutions., 2; **F. Xie**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1662

Efficacy and Safety of Nerandomilast in Patients with Autoimmune Disease-Related Progressive Pulmonary Fibrosis: Subgroup Analysis of the FIBRONEER-ILD trial

Anna-Maria Hoffmann-Vold[1], Shervin Assassi[2], Vincent Cottin[3], Michael Kreuter[4], Claudia Valenzuela[5], Marlies S Wijsenbeek[6], Hui Gu[7], Ivana Ritter[8], Susanne Stowasser[8], Gerrit Weimann[8], Toby M Maher[9] and FIBRONEER-ILD investigators, [1]Oslo University Hospital, Oslo, Norway, [2]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [3]National Reference Center for Rare Pulmonary Diseases, Louis Pradel Hospital, Hospices Civils de Lyon, Claude Bernard University Lyon 1, UMR 754, ERN-LUNG, Lyon, France, Lyon, France, [4]Center for Pulmonary Medicine, Department of Pneumology, Mainz University Medical Center and Pulmonary, Critical Care & Sleep Medicine, Marienhaus Clinic Mainz, Mainz, Germany, Heidelberg, Germany, [5]Pulmonology Department, Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain, Madrid, Spain, [6]Center of Expertise for Interstitial Lung Diseases, Department of Respiratory Medicine, Erasmus MC, University Medical Centre, Rotterdam, The Netherlands, Rotterdam, Netherlands, [7]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA, Ridgefield, [8]Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany, Ingelheim am Rhein, Germany, [9]Department of Pulmonary, Critical Care and Sleep Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA and Section of Inflammation, Repair and Development, National Heart and Lung Institute, Imperial College London, London, UK, Los Angeles

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms (1662–1667)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Nerandomilast is a preferential inhibitor of phosphodiesterase 4B with antifibrotic and immunomodulatory properties. The Phase III FIBRONEER-ILD trial in patients with progressive pulmonary fibrosis (PPF) showed that nerandomilast significantly reduced the decline in forced vital capacity (FVC) and had an acceptable safety profile. We explored the efficacy and safety of nerandomilast in the subgroup of patients with autoimmune disease-related interstitial lung diseases (ILDs) (autoimmune ILDs) in the FIBRONEER-ILD trial.

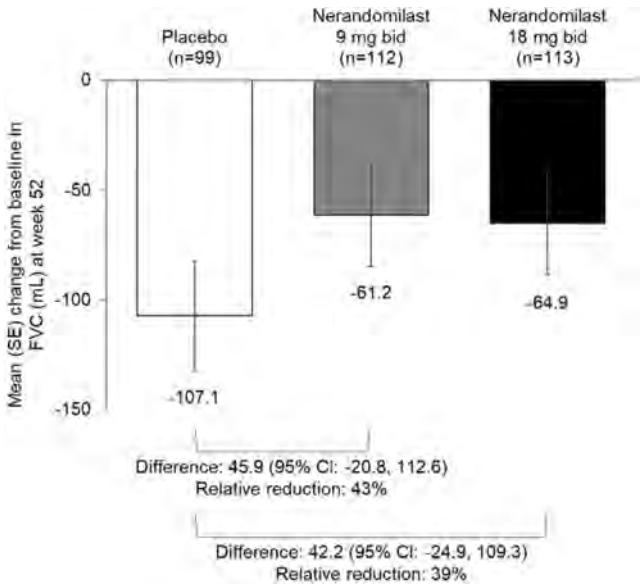


Figure. Change from baseline in FVC (mL) at week 52 among patients with autoimmune ILDs in the FIBRONEER-ILD trial.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Adverse events up to week 52 in patients with autoimmune ILDs in the FIBRONEER-ILD trial.

	Placebo (n=100)	Nerandomilast 9 mg bid (n=112)	Nerandomilast 18 mg bid (n=113)
Most frequent adverse event(s)*			
Diarrhea	22 (22.0)	29 (25.9)	35 (31.0)
Upper respiratory tract infection	17 (17.0)	11 (9.8)	19 (16.8)
Cough	11 (11.0)	14 (12.5)	14 (12.4)
Anxiety	9 (9.0)	11 (9.8)	15 (13.3)
Depression	10 (10.0)	9 (8.0)	14 (12.4)
Nasopharyngitis	7 (7.0)	15 (13.4)	11 (9.7)
COVID-19	11 (11.0)	8 (7.1)	12 (10.6)
Pneumonia	12 (12.0)	8 (7.1)	9 (8.0)
Condition aggravated	14 (14.0)	6 (5.4)	8 (7.1)
Weight decreased	4 (4.0)	8 (7.1)	15 (13.3)
Decreased appetite	6 (6.0)	4 (3.6)	13 (11.5)
Nausea	4 (4.0)	5 (4.5)	12 (10.6)
Serious adverse event(s)	31 (31.0)	27 (24.1)	41 (36.3)
Adverse event(s) leading to treatment discontinuation	8 (8.0)	5 (4.5)	11 (9.7)

Data are n (%) of patients with ≥1 such adverse event reported over 52-week treatment period or until 7 days after the last dose in patients who discontinued treatment before week 52. *Adverse events (coded based on preferred terms in the Medical Dictionary for Regulatory Activities) reported in >10% of patients in any treatment group in patients with autoimmune ILDs.

Methods: Patients with PPF (excluding idiopathic pulmonary fibrosis) were randomized 1:1:1 to receive nerandomilast 9 mg bid, nerandomilast 18 mg bid, or placebo. PPF was defined using the same criteria as in the INBUILD trial (Flaherty KR et al. N Engl J Med 2019;381:1718-27). Patients taking nintedanib (at a stable dose for ≥12 weeks) or not taking nintedanib (for ≥8 weeks) were eligible to participate. Cyclophosphamide, tocilizumab, mycophenolate, or rituximab were not permitted at enrolment but could be initiated after 6 months to manage worsening systemic disease. Prednisone >15 mg/day (or equivalent) was not permitted at enrolment but could be prescribed during the trial for acute exacerbation of ILD or after 6 months to manage worsening systemic disease. In the subgroup with autoimmune ILDs, we evaluated absolute change from baseline in FVC (mL) at week 52 and adverse events up to week 52. Analyses were pre-specified.

Results: Among 1176 treated patients, 325 (27.6%) had autoimmune ILDs (100 placebo, 112 nerandomilast 9 mg bid, 113 nerandomilast 18 mg bid). At baseline, among patients with autoimmune ILDs, 212 (65.2%) were female, mean (SD) age was 63.4 (11.2) years, FVC was 71.5 (15.0) % predicted, diffusing capacity for carbon monoxide (DLco) was 51.5 (16.8) % predicted; 111 (34.2%) patients were taking nintedanib. The most frequent autoimmune disease diagnoses were rheumatoid arthritis (118 patients [36.3%]), systemic sclerosis (75 [23.1%]), and mixed connective tissue disease (47 [14.5%]). Among patients with autoimmune ILDs, adjusted mean changes in FVC (mL) at week 52 were -107.1 (95% CI: -156.1, -58.0) in the placebo group, -61.2 (-106.9, -15.5) in the nerandomilast 9 mg bid group (difference vs placebo: 45.9 [95% CI: -20.8, 112.6]), and -64.9 (-111.0, -18.7) in the nerandomilast 18 mg bid group (difference vs placebo: 42.2 [-24.9, 109.3]) (Figure). The most frequent adverse event was diarrhea (Table). Adverse events leading to treatment discontinuation were similar across treatment groups.

Conclusion: In the FIBRONEER-ILD trial, the efficacy of nerandomilast on slowing decline in FVC in patients with autoimmune ILDs was consistent with that observed in the overall trial population. Nerandomilast had an acceptable safety and tolerability profile.

Disclosure: A. Hoffmann-Vold: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **V. Cottin**: AbbVie, 2, AstraZeneca, 2, Avalyn, 2, Boehringer Ingelheim, 2, 6, 12, Support for attending meetings and medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb/Celgene, 2, CSL (Behring/Vifor), 2, Ferrer/United Therapeutics, 2, 6, FibroGen, 12, Adjudication committee, GlaxoSmithKleine, 1, 2, Gossamer, 2, Liquidia, 2, Molecure, 1, Pliant, 2, PureTech, 2, Roche, 2, 6, Roivant, 2, Sanofi, 2, 6, 12, Support for attending meetings, Shionogi, 2; **M. Kreuter**: AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Deutsche Gesellschaft für Pneumologiex, 12, Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, European Respiratory Society, 12, Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, GlaxoSmithKleine, 2, Roche, 2, 5, 6; **C. Valenzuela**: Boehringer-Ingelheim, 1, 2, 6, 12, Support for attending meetings and medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb, 2, Ferrer, 2, 6, 12, Support for attending meetings, Pliant, 1, 3; **M. Wijsenbeek**: AstraZeneca, 2, AstraZeneca/Daiichi, 5, Avalyn Pharma, 2, 6, 12, Support for attending meetings, Boehringer Ingelheim, 2, 5, 6, 12, Support for attending meetings and Marlies Wijsenbeek served as a member of the SC for the FIBRONEER trials which are funded by Boehringer Ingelheim, Bristol-Myers Squibb, 2, CSL Behring, 2, 6, Erasmus MC, 5, Galapagos, 2, Galecto, 2, GlaxoSmithKleine, 2, 12, Support for attending meetings, Hoffmann-La Roche, 2, 5, Horizon Therapeutics, 2, Kinevant Sciences, 2, Molecure, 2, NeRRe Therapeutics, 2, Novartis, 2, PureTech Health, 2, Respivant Science, 2, Sanofi, 2, Sarcoidosis.nl, 5, The Dutch Lung Foundation, 5, The Dutch Pulmonary Fibrosis Patients Association, 5, The Netherlands Organization for Health Research and Development, 5, The Thorax Foundation, 5, Trevi, 2, Vicore, 2; **H. Gu**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **I. Ritter**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **S. Stowasser**: Boehringer Ingelheim, 3, 12, Medical writing support provided by Fleishman Hillard; **G. Weimann**: Boehringer Ingelheim, 3; **T. Maher**: AbbVie, 2, Amgen, 2, AstraZeneca, 2, 5, Bayer, 2, Biogen Idec, 2, Blade Therapeutics, 2, Boehringer Ingelheim, 2, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb, 2, Endeavor BioMedicines, 2, Galapagos NV, 2, Galecto Pharma, 2, GlaxoSmithKline, 2, 5, Gossamer Bio, 2, Merck, 2, Pfizer, 2, Pliant, 2, Redx Pharma, 2, Roche, 2, 6, Three Lakes Partners, 2, Trevi, 2, UCB, 2, 5, United Therapeutics, 2, Vicore Pharma, 2.

Abstract Number: 1663

Tocilizumab for acute exacerbation of rheumatic disease-related interstitial lung disease: A prospective real-world study

Wenwen Xu[1], Yiyangzi Ma[2], Shuang Ye[3] and Qiong Fu[2], [1]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [2]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, Shanghai, China (People's Republic), [3]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms (1662–1667)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Acute exacerbation (AE) of rheumatic disease-related interstitial lung disease (RD-ILD) is a severe and potentially life-threatening condition, while there remains no clear consensus of evidence-based therapy guidelines. Conventional treatments rely on high-dose corticosteroids and broad immunosuppressants, which carry significant toxicity and variable efficacy. This study aims to evaluate the effectiveness and safety of the interleukin-6 (IL-6) receptor inhibitor tocilizumab in managing AE-RD-ILD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This prospective observational study enrolled hospitalized AE-RD-ILD patients treated with tocilizumab between January 2023 and May 2024. Retrospective controls were selected from the same institution and period, receiving corticosteroids with or without conventional immunosuppressants (e.g., cyclophosphamide, mycophenolate mofetil). All patients met diagnostic criteria for AE-RD-ILD, including: acute worsening of respiratory distress requiring additional oxygen supply within 1-month, High-resolution computed tomography (HRCT) demonstrating new bilateral ground-glass opacities and/or consolidations superimposed on pre-existing ILD patterns, and confirmed underlying rheumatic disease by clinical and serological criteria. Exclusion criteria included active infections, severe comorbidities (e.g., heart failure), or recent use of interleukin-6 inhibitors. Primary outcome was complete response (CR) at 24 weeks, defined by resolution of dyspnea, radiographic improvement, steroid reduction (≤15 mg/day prednisone equivalent), and survival without severe adverse events or lung transplantation.

Results: A total of 45 patients were included in the analysis (tocilizumab group: n=26; control group: n=19). Baseline characteristics were comparable with no significant differences in median age (62 vs. 63 years, P=0.918) or ILD duration (16 vs. 15 months, P=0.991). Among enrolled patients, 39 (86.6%) met American College of Rheumatology (ACR) classification criteria for defined rheumatic diseases (dermatomyositis: 33, rheumatoid arthritis: 3, systemic sclerosis: 2, ANCA associated vasculitis: 1), while the remaining 6 (13.3%) were diagnosed as undifferentiated connective tissue disease. The tocilizumab group achieved a significantly higher 24-week CR rate of 80.8% (21/26) compared to 10.5% (2/19) in the control group (P< 0.001), with 26% lower cumulative prednisone use (3955 vs. 5375 mg, P=0.017), reduced maintenance doses by 50% (10 vs. 20 mg/day, P< 0.001), fewer new acute exacerbations (3 vs. 8 events, P=0.045), and higher oxygen discontinuation rates (76.9% vs. 5.3%, P< 0.001). Safety outcomes favored tocilizumab, with significantly fewer infections (7 vs. 21 events, P< 0.001) and lower composite mortality/lung transplantation rates (3.8% vs. 31.6%, P=0.034). Subgroup analyses showed consistent benefits across demographics (P for interaction >0.05).

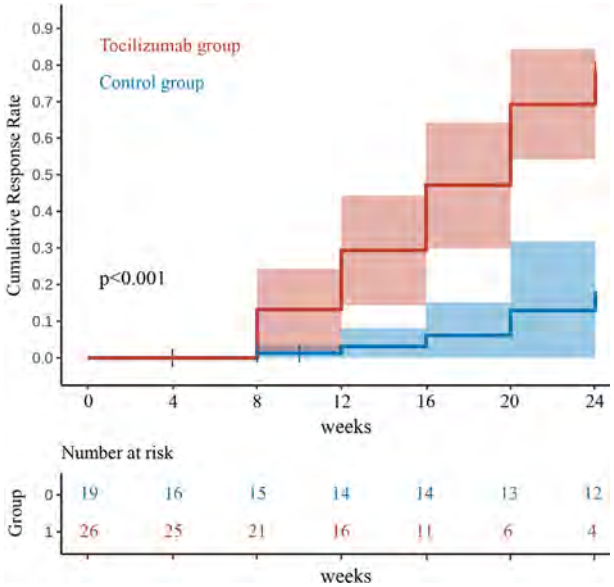


Figure 1. Cumulative response curve for the tocilizumab and control groups within 24 weeks. Direct Standardization adjusted by variables of sex, age, course, PaO2/FiO2, forced vital capacity predicted, baseline immunosuppressive therapy, the maximum daily dose of steroids after AE, anti-fibrotic drugs, B cells, and ILD field. One death and five deaths were censored in the tocilizumab group and control group respectively. The complete response rate was 80.8% (21/26) compared to 10.5% (2/19) (p<0.001). The difference between the response rates for two groups after 8, 12, 16, 20 and 24 weeks were 11.9% (95% CI 0.6-23.3), 26.2% (10.4-42.0), 41.0% (21.5-60.5), 56.3% (32.2-80.5) and 60.3% (31.1-89.5), all P<0.05.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

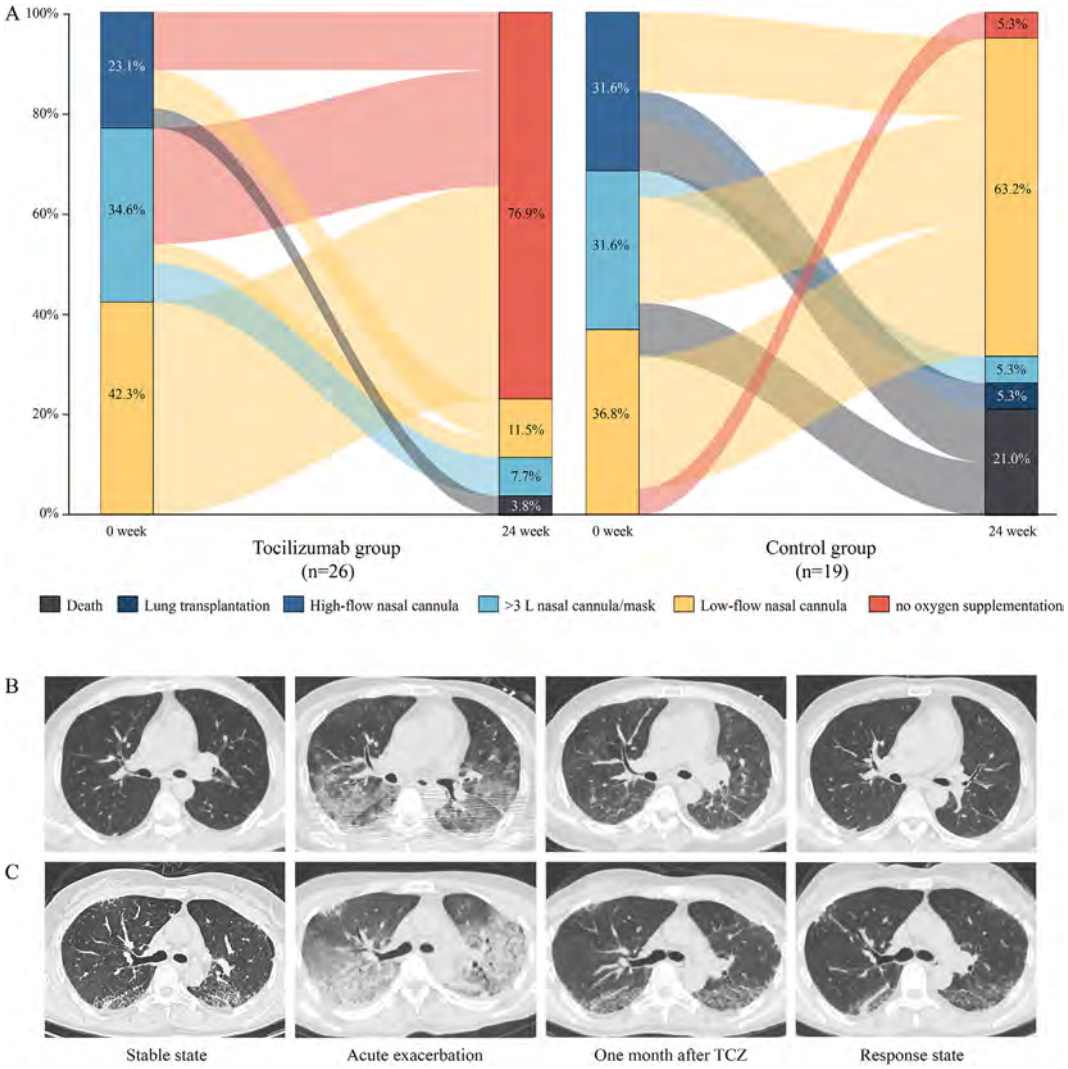


Figure 2. Respiratory Support Parameters & CT Images: Pre-Post Treatment Comparison. B: A 45-year-old male with anti-Jo-1 syndrome ILD. Baseline HRCT showed non-specific interstitial pneumonia (NSIP) pattern with homogeneous ground-glass opacities and spared subpleural parenchyma. After 6 months, acute exacerbation led to respiratory failure with increased ground-glass opacities and diffuse lung involvement without volume loss. After high-dose prednisone and tocilizumab treatment, significant absorption and improvement of pulmonary lesions were observed. C: A 41-year-old female with anti-synthetase syndrome ILD. Baseline HRCT showed NSIP pattern. After 5 months, acute respiratory failure occurred with diffuse ground-glass opacities, consolidation, increased subpleural reticulation, and traction bronchiectasis severity, with volume loss. One-month post-treatment, pulmonary lesions improved.

Conclusion: AE-RD-ILD patients treated with the tocilizumab demonstrated higher CR rate at 24 weeks, reduced steroid requirement, with a favorable safety profile, which support the potential for tocilizumab to addresses the critical unmet need in managing AE-RD-ILD.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

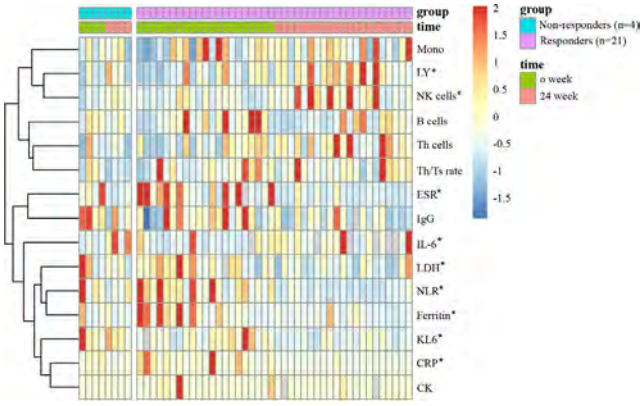


Figure 3. Comparison of baseline and post-treatment laboratory parameters between Tocilizumab responders (n=21) and non-responders (n=4). Heatmaps were used to display data before and after treatment in tocilizumab group, with each variable standardized; standardized values >2 was displayed as 2, and those less than -2 as -2, with statistically significant between-group differences (P<0.05) indicated by an asterisk (*). Mono: monocytes; LY: lymphocytes; NK: natural killer; Th: T helper cells; Ts: T suppressor cells; ESR: erythrocyte sedimentation rate; IgG: immunoglobulin G; IL: interleukin; LDH: lactate dehydrogenase; NLR: neutrophil-to-lymphocyte ratio; KL6: Krebs von den Lungen-6; CRP: C-reactive protein; CK: creatine kinase.

Disclosure: W. Xu: None; **Y. Ma**: None; **S. Ye**: None; **Q. Fu**: None.

Abstract Number: 1664

Cardiac Sarcoidosis Response to Steroid-Sparing Immunosuppression

Alexia Zagouras[1], Sammy Pickell[1], Yuhan Liu[1], Ronald Witteles[1] and **Matthew Charles Baker**[2], [1]Stanford University, Stanford, CA, [2]Stanford University, Menlo Park, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms (1662–1667)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: There are no FDA-approved therapies for cardiac sarcoidosis (CS), a disease associated with high morbidity and mortality. Treatment typically consists of glucocorticoids and off-label use of steroid-sparing immunosuppressive therapies. For over a decade, we have implemented a consistent treatment approach for patients with CS at our institution. Here we report the treatment outcomes of this approach and explore disease-related characteristics associated with first-line treatment failure.

Methods: This retrospective cohort study was conducted utilizing a registry of adult cardiac sarcoidosis patients seen in the Stanford University Cardiology and Rheumatology clinics between 1/1/2011 and 12/31/2024. All patients met the Heart Rhythm Society diagnostic criteria for CS or the Japanese Circulation Society criteria for isolated CS and were treated with a standard protocol (**Figure 1**), consisting of prednisone (20mg-60mg daily) and methotrexate (up to 25mg weekly), followed by the addition of a tumor necrosis factor (TNF) inhibitor for patients who did not have complete resolution of ^{18}F-fluorodeoxyglucose (FDG) uptake on cardiac FDG-positron emission tomography/computed tomography (FDG-PET/CT) on methotrexate alone. Patients were excluded if they did not have at least one follow-up cardiac FDG-PET/CT after treatment initiation. Through manual chart review, we extracted demographics and clinical variables and determined treatment response. Comparisons between methotrexate responders and non-responders were made using Fisher's exact test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

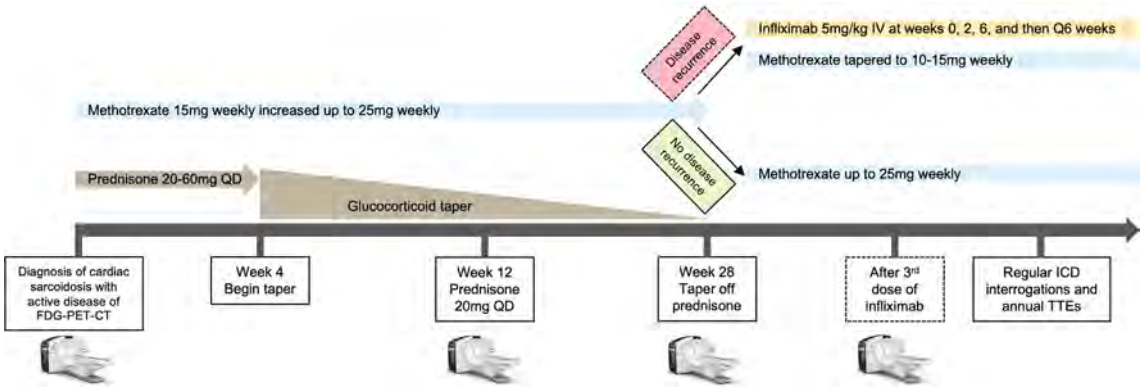


Figure 1. Cardiac sarcoidosis treatment and monitoring approach.

Table 1. Demographics and baseline characteristics of cardiac sarcoidosis patients.

Characteristic	Total Cohort (*n* = 57)	Methotrexate Responders (*n* = 18)	Methotrexate Non-Responders (*n* = 39)
Age, mean (SD), y	63.1 (9.7)	65.7 (9.6)	61.9 (9.6)
Age at diagnosis, mean (SD), y	57.0 (9.9)	59.6 (10.0)	55.6 (9.7)
Sex, n (%)			
Female	18 (31.6)	8 (44.4)	10 (25.6)
Male	39 (68.4)	10 (55.6)	29 (74.4)
Race, n (%)			
Asian	6 (10.5)	3 (16.7)	3 (7.7)
Black	3 (5.3)	1 (5.6)	2 (5.1)
Hispanic	1 (1.8)	0 (0.0)	1 (2.6)
White	46 (80.7)	14 (77.8)	32 (82.1)
Other	1 (1.8%)	0 (0.0)	1 (2.6)
Body mass index, mean (SD), kg/m^2	29.0 (5.2)	29.2 (4.9)	28.9 (5.4)
Other organ involvement, n (%)			
Lungs	25 (43.9)	7 (38.9)	18 (46.2)
Lymph nodes	36 (63.2)	8 (44.4)	28 (71.8)
Eyes	5 (8.8)	2 (11.1)	3 (7.7)
Skin	3 (5.3)	0 (0.0)	3 (7.7)
Liver	7 (12.3)	1 (5.6)	6 (15.4)
Neurological	1 (1.8)	0 (0.0)	1 (2.6)
Other	16 (28.1)	3 (16.7)	13 (33.3)
Number of organs involved, mean (SD)	2.7 (1.5)	2.2 (1.2)	2.9 (1.6)
Baseline LVEF, %			
Mean (SD)	45.4 (14.6)	39.9 (15.9)	47.9 (13.4)
Median [Min, Max]	45.0 [20.0, 70.0]	33.0 [20.0, 70.0]	50.0 [20.0, 70.0]
Baseline PET/CT pattern, n (%)			
Diffuse	4 (7.0)	1 (5.6)	3 (7.7)
Focal	45 (78.9)	17 (94.4)	28 (71.8)
Focal on diffuse	8 (14.0)	0 (0.0)	8 (20.5)
Area of FDG uptake			
Septum	41 (71.9)	13 (72.2)	28 (71.8)
Right ventricle	14 (24.6)	1 (5.6)	13 (33.3)

SD = standard deviation, y = year, kg = kilogram, m = meter, LVEF = left ventricular ejection fraction.

Table 2. Cardiac sarcoidosis treatment characteristics and outcomes.

	Total Cohort (*n* = 57)	Methotrexate Non-Responders (*n* = 39)
Prednisone max dose, mean (SD), mg	42.2 (14.4)	-
Prednisone duration, mean (SD), y	1.4 (3.7)	-
Methotrexate max dose, mean (SD), mg	23.5 (3.0)	-
Methotrexate duration before PET/CT, mean (SD), y	0.6 (0.9)	-
Methotrexate responders, n (%)	18 (31.6)	-
TNF inhibitor, n (%)	-	37 (94.9)
Infliximab	-	28 (71.8)
Adalimumab	-	9 (23.1)
Lost to follow-up	-	2 (5.1)
TNF inhibitor duration before PET/CT, mean (SD), y	-	0.5 (0.7)
TNF inhibitor responders, n (%)	-	36 (97.3)

SD = standard deviation, mg = milligrams, y = year, PET/CT = positron emission tomography/computed tomography, TNF = tumor necrosis factor.

Results: Fifty-seven CS patients were followed for a mean (standard deviation [SD]) of 3.8 (3.0) years. After stopping prednisone, 18 patients (31.6%) on methotrexate monotherapy had complete resolution of FDG uptake on cardiac FDG-PET/CT, and 39 patients (68.4%) had ongoing disease activity. Methotrexate responders were older (66 years vs 62 years), more likely to be female (44% vs 26%), had fewer organs involved by their sarcoidosis (2.2 vs 2.9), and had a lower baseline left ventricular ejection fraction (40% vs 48%) (**Table 1**). Right ventricular involvement was present in only 1 of 18 (5%) methotrexate responders vs 13 of 39 (33%) methotrexate non-responders (p = 0.037). Of the methotrexate non-responders, 37 (95%) were treated with a TNF inhibitor, and all but one patient had a complete response to therapy (**Table 2**).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Treating cardiac sarcoidosis with upfront initiation of methotrexate and a relatively rapid prednisone taper over 28 weeks resulted in complete resolution of FDG uptake in roughly one-third of patients, with two-thirds requiring the addition of a TNF inhibitor; RV involvement was associated with more difficult to treat disease. Our results support the use of methotrexate as a first-line steroid-sparing medication for the treatment of CS, demonstrate the efficacy of TNF inhibitors in methotrexate non-responders, and highlight the need for future studies to further define risk factors for inadequate response to methotrexate.

Disclosure: A. Zagouras: None; **S. Pickell**: None; **Y. Liu**: None; **R. Witteles**: None; **M. Baker**: Amgen, 2, Sanofi, 2, Zenas BioPharma, 2.

Abstract Number: 1665

Comparative Effectiveness of Biologic Versus Conventional Therapy in Uveitis with Systemic Rheumatic Diseases: Real-World Evidence from a Propensity-Matched Cohort

Hanieh Akbari[1] and shahrzad Abdollahi[2], [1]Jefferson Einstein Montgomery Medical Center, Norristown, PA, [2]Jefferson Einstein Philadelpha, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms (1662–1667)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Uveitis is a vision-threatening manifestation of systemic rheumatic diseases. While conventional immunosuppressants are typically first-line, biologics are often reserved for refractory cases. Long-term real-world data comparing these approaches remain limited.

Methods: We performed a retrospective cohort study using TriNetX, a global database of de-identified electronic health records from 146 healthcare organizations. Adults with non-infectious uveitis and a systemic rheumatic disease were identified using ICD-10-CM codes. Patients were grouped into:

Table 1. Baseline Demographic, Clinical, and Treatment Characteristics of Patients with Rheumatic Disease–Associated Uveitis Before and After Propensity Score Matching

Characteristic	Conventional (Pre-match)	Biologic (Pre-match)	Conventional (Post-match)	Biologic (Post-match)	p-value (Post-match)
Age, mean ± SD	50.1 ± 16.0	48.3 ± 15.6	49.7 ± 15.9	49.7 ± 15.9	0.98
Female, %	60.5%	57.8%	59.3%	59.3%	0.99
White	58.1%	56.0%	57.2%	57.2%	0.94
Black	21.3%	23.5%	22.2%	22.2%	0.97
Asian	6.1%	6.3%	6.2%	6.2%	0.99
Hispanic/Latino	5.2%	6.1%	5.6%	5.6%	0.88
Diabetes Mellitus	14.7%	12.2%	13.5%	13.5%	0.96
Hypertension	32.9%	29.4%	31.1%	31.1%	0.98
Chronic Kidney Disease	7.8%	6.9%	7.3%	7.3%	0.97
Hyperlipidemia	26.3%	24.2%	25.3%	25.3%	0.94
Coronary Artery Disease	5.4%	4.8%	5.1%	5.1%	0.93
Heart Failure	4.3%	3.1%	3.7%	3.7%	0.91
Stroke	3.1%	2.4%	2.8%	2.8%	0.96
Smoking History	22.7%	21.4%	22.0%	22.0%	0.99
Baseline corticosteroid use	84.2%	79.1%	81.6%	81.6%	0.98
Immunosuppressant (non-biologic) us	100%	27.4%	71.5%	71.5%	0.99
Biologic use	0%	100%	50.0%	50.0%	1.00

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparative Ocular, Procedural, Systemic, and Cardiovascular Outcomes at 1 and 5 Years in Patients with Rheumatic Disease–Associated Uveitis Treated with Biologic versus Conventional Therapy After Propensity Score Matching

Outcome	Conventional (n=2,985)	Biologic (n=2,985)	Risk Ratio (95% CI)	p-value
1-Year Outcomes				
Blindness	2.0%	0.8%	2.57 (1.57–4.20)	<0.001
5-Year Ocular Outcomes				
Blindness	3.8%	2.0%	1.85 (1.39–2.47)	<0.001
Glaucoma	8.3%	4.2%	1.96 (1.58–2.43)	<0.001
Cataracts	8.2%	5.3%	1.53 (1.26–1.86)	<0.001
Macular Edema	3.0%	0.9%	3.46 (2.27–5.27)	<0.001
Uveitis Flares	5.2%	4.1%	0.78 (0.58–1.06)	0.47
5-Year Procedural Outcomes				
Optical Coherence Tomography (OCT)	11.0%	7.2%	1.54 (1.30–1.83)	<0.001
Intravitreal Injection	3.1%	0.9%	3.69 (2.40–5.69)	<0.001
5-Year Systemic Outcomes				
Sepsis	4.1%	1.6%	2.63 (1.84–3.75)	<0.001
Pneumonia	5.5%	3.5%	1.55 (1.20–2.01)	<0.001
Heart Failure	4.3%	1.8%	2.34 (1.66–3.31)	<0.001
Myocardial Infarction	1.8%	1.0%	1.84 (1.17–2.89)	0.008
Major Adverse Cardiovascular Events (MACE)	14.6%	12.3%	1.19 (1.02–1.39)	0.031
All-Cause Mortality	5.8%	2.4%	2.40 (1.84–3.13)	<0.001

Table 3. Subgroup Comparison of Major Adverse Cardiovascular Events and Other Clinical Outcomes Between TNF and JAK Inhibitors in Biologic-Treated Patients with Rheumatic Disease–Associated Uveitis

Outcome	TNF Inhibitors (n=317)	JAK Inhibitors (n=317)	Risk Ratio (95% CI)	p-value
Major Adverse Cardiovascular Events (MAC	3.1%	9.0%	0.34 (0.13–0.86)	0.017
All-Cause Mortality	1.9%	2.5%	0.76 (0.26–2.21)	0.61
Sepsis	1.3%	2.2%	0.59 (0.17–2.05)	0.41
Pneumonia	3.8%	4.4%	0.86 (0.40–1.87)	0.71
Blindness	2.2%	2.8%	0.78 (0.29–2.11)	0.63

(1) a conventional therapy cohort (corticosteroids plus methotrexate, azathioprine, or mycophenolate), and

(2) a biologic therapy cohort (TNF, IL-17/23, or JAK inhibitors).

Patients with infectious uveitis or concurrent use of both therapies were excluded. Among 11,432 eligible patients (6,661 in the conventional cohort; 4,771 in the biologic cohort), 2,985 from each group were matched 1:1 using propensity scores based on demographics, comorbidities, and baseline corticosteroid use. Outcomes were assessed at 1 and 5 years following the index treatment. Primary endpoints included ocular complications, ophthalmic procedures, systemic infections, cardiovascular events, and all-cause mortality. Risk ratios (RRs), 95% confidence intervals (CIs), and p-values were reported. A subgroup analysis compared TNF vs. JAK inhibitors.

Results: The matched cohort had a mean age of 49.7 ± 15.9 years; 59.3% were female. Racial distribution included White (57.2%), Black (22.2%), Asian (6.2%), and Hispanic/Latino (5.6%).

At 1 year, biologics were associated with reduced blindness (0.8% vs. 2.0%; RR 2.57, 95% CI 1.57–4.20; $p< 0.001$), with similar uveitis flare rates (3.2% vs. 2.5%; $p=0.19$).

At 5 years, biologics significantly reduced glaucoma (4.2% vs. 8.3%; RR 1.96), cataracts (5.3% vs. 8.2%; RR 1.53), macular edema (0.9% vs. 3.0%; RR 3.46), and blindness (2.0% vs. 3.8%; RR 1.85) ($p< 0.001$ for all). Procedural use was also lower: optical coherence tomography (7.2% vs. 11.0%; RR 1.54) and intravitreal injections (0.9% vs. 3.1%; RR 3.69) ($p< 0.001$).

Systemic complications favored biologics, including sepsis (1.6% vs. 4.1%; RR 2.63), pneumonia (3.5% vs. 5.5%; RR 1.55), heart failure (1.8% vs. 4.3%; RR 2.34), and all-cause mortality (2.4% vs. 5.8%; RR 2.40) ($p< 0.001$ for all). Cardiovascular

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

events were also reduced: myocardial infarction (1.0% vs. 1.8%; RR 1.84; p=0.008) and major adverse cardiovascular events (MACE) (12.3% vs. 14.6%; RR 1.19; p=0.031).

In a matched subgroup analysis (n=317 per group), TNF inhibitors were associated with fewer MACE events than JAK inhibitors (3.1% vs. 9.0%; RR 0.34, 95% CI 0.13–0.86; p=0.017).

Conclusion: Biologic therapy was associated with significantly improved ocular, systemic, cardiovascular, and survival outcomes in patients with rheumatic disease–associated uveitis, without compromising inflammatory control. These findings support earlier use of biologics in this population. Future prospective studies are needed to validate these associations, refine treatment strategies, and identify subgroups most likely to benefit from targeted biologic therapy.

Disclosure: H. Akbari: None; **s. Abdollahi**: None.

Abstract Number: 1666

Treatment with Rilzabrutinib was associated with Rapid and Sustained Reduction in Disease Activity in Patients with IgG4-RD Previously Treated or Naïve to B cell Depletion

John Stone[1], Mollie Carruthers[2], Alireza Meysami[3], Matthew Charles Baker[4], Daniela Ghetie[5], Lindsay Lally[6], Fernando Martinez-Valle[7], Lorenzo Dagna[8], nicolas schleinitz[9], Jeea Choi[10], Leda Mannent[11] and Owen Hagino[10], [1]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [2]Vancouver General Hospital, Vancouver, BC, Canada, [3]Henry Ford Health, Detroit, MI, [4]Stanford University, Menlo Park, CA, [5]Oregon Health and Science University, Portland, OR, [6]Hospital for Special Surgery, NEW YORK, NY, [7]Vall d'Hebron Hospital, Barcelona, Spain, [8]IIRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, [9]Aix Marseille university, AP-HM, Marseille, France, [10]Sanofi, Morristown, NJ, [11]Sanofi, Gentilly, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms (1662–1667)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: IgG4-RD is a progressive, immune-mediated fibrotic disease with limited treatment options. Rilzabrutinib is a reversible, orally available inhibitor of Bruton's tyrosine kinase (BTKi). Here, we conducted an open label proof-of-concept safety and efficacy study of rilzabrutinib in adult patients with IgG4-RD, stratified by prior rituximab treatment history.

Methods: The study (NCT04520451) included patients with active IgG4-RD whose last dose of rituximab was >6 months prior to screening (or with evidence of B cell reconstitution)[rituximab-experienced] or naïve to rituximab [rituximab-naïve]. During the 4-week screening period, prednisone (20 mg/day to 40 mg/day) was prescribed according to the investigator's assessment of organ(s) involved and level of disease activity . Over the first 4 weeks of rilzabrutinib treatment, prednisone was tapered off and rilzabrutinib continued for up to 52 weeks. Disease activity was tracked with the IgG4-RD Responder Index (RI). Efficacy endpoints included proportion of participants without disease flare (defined as an increase in RI >2 or initiation of rescue treatment with glucocorticoid or immunomodulator), RI Total Activity score (observed and change from baseline) at each visit, and proportion of participants with a reduction in RI Total Activity score ≥2 at each visit.

Results: A total of 27 participants (15 rituximab-experienced, 12 rituximab-naïve) were enrolled. At baseline, 10/15 (67%) rituximab-experienced participants had a history of flaring on treatment, 1 (7%) without response to rituximab, 3 (20%) with adverse reaction to rituximab, and 1 (7%) with prior response to rituximab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The proportion of participants on rilzabrutinib monotherapy without a disease flare at the end of treatment was 19/27 (70%), and was similar in both the rituximab-experienced subgroup (73%) and the rituximab-naïve subgroup (67%). Rituximab-naïve participants had a higher total activity score at baseline vs rituximab-experienced participants (mean±SD: 15.7±7.6 vs. 10.1±5.7), By Week 12 the total activity scores were 3.0±2.0 (77% reduction from baseline) and 4.3±3.4 (52% reduction from baseline) in the rituximab-naïve and rituximab-experienced groups, respectively. At Week 52, the total activity score (mean±SD) in the rituximab-naïve subgroup was 1.7±1.5 (an 88% reduction from baseline) and 3.1±3.7 (71% reduction from baseline) in rituximab-experienced group. At Week 52, all participants in the rituximab naïve-subgroup and 88% in the rituximab-experienced subgroup had a reduction of >2 points in IgG4-RD RI Total Activity score.

Conclusion: Following withdrawal of oral prednisone, disease activity as measured by the RI Total Activity score declined rapidly, substantially, and was sustained during the 52-week treatment period. Although comparisons are limited by the small sample size, and differences in disease characteristics at baseline, the proportions without flare or rescue and reductions in disease activity were substantial in both the participants who were previously treated with rituximab (including those refractory to rituximab) and naïve to rituximab.

Disclosure: J. Stone: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **M. Carruthers**: AbbVie, 2, Amgen, 2, Janssen, 2, Pfizer, 2, Roche, 2, Sanofi, 2, UCB, 2, Zenas, 2; **A. Meysami**: Amgen, 1, 2, 6, AstraZeneca, 1, GlaxoSmithKlein(GSK), 1, Janssen, 1, Zenas, 1; **M. Baker**: Amgen, 2, Sanofi, 2, Zenas BioPharma, 2; **D. Ghetie**: None; **L. Lally**: AbbVie, 2, Amgen, 2; **F. Martinez-Valle**: Amgen, 1; **L. Dagna**: AbbVie, 2, Alfasigma, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, Eli Lilly, 2, Galapagos, 2, GlaxoSmithKlein(-GSK), 2, Johnson & Johnson, 2, Kiniksa Pharmaceuticals, 2, Merck/MSD, 2, Novartis, 2, Sanofi, 2, SOBI, 2, UCB, 2, vifor, 2; **n. schleinitz**: Amgen, 1, 2; **J. Choi**: Sanofi, 3; **L. Mannent**: Sanofi, 3; **O. Hagino**: Sanofi, 3.

Abstract Number: 1667

Recurrent or Incident Pericarditis With Concurrent Autoimmune Disease: Stable Control With Rilonacept Interleukin-1 Pathway Inhibition

Zachary Daniel[1], Summia Afridi[1], Michael Allen[2] and Khoa Ngo[1], [1]Albany Medical College, Albany, NY, [2]Albany Med, Albany, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases II: Models and Mechanisms (1662–1667)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Up to 30% of patients with incident pericarditis will develop recurrent pericarditis (RP), with severe impact on quality of life. More than 20% of these patients have concurrent autoimmune disease, and this subgroup is at particularly high risk for recurrence. RHAPSODY established that IL-1 pathway inhibition with rilonacept is highly effective in preventing episodes of RP for idiopathic or post-pericardiotomy etiologies. This study aimed to investigate the efficacy and safety of rilonacept in the autoimmune RP subgroup.

Methods: This is a single-center retrospective case series of consecutive patients with incident or RP and underlying autoimmune disease who initiated rilonacept at any time between 7/2022 to 1/2024 at an academic tertiary referral center. Patients were included if they met ESC criteria for recurrent, incessant, or incident pericarditis at the time of rilonacept initiation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Characteristics at Rilonacept Initiation

Characteristic	Value
Total number of patients	16
Incessant/incident, n (%)	4 (25.0)
Recurrent, n (%)	12 (75.0)
Demographics	
Age, years old, mean +/-SD	49.6 +/-18.4
Gender	
Females, n (%)	9 (56.3)
Males, n (%)	7 (43.8)
ESC Pericarditis Diagnostic Criteria	
Chest pain, n (%)	16 (100)
Friction rub, n (%)	1 (6.3)
TTE w/ pericardial effusion, n (%)	14 (87.5)
EKG findings, n (% of pts with EKG obtained)	9/12 (75.0)
Cardiac MRI findings, n (% of pts with Cardiac MRI obtained)	1/2 (50.0)
Elevated CRP prior, n (%)	16 (100)
Medications Prescribed	
Aspirin, n (%)	1 (6.3)
NSAIDs, n (%)	7 (43.8)
Colchicine, n (%)	13 (81.3)
Corticosteroids, n (%)	12 (75.0)
Dose in prednisone equiv. (mg/d)	28.2 +/- 24.6
Hydroxychloroquine, n (%)	5 (31.3)
Mycophenolate, n (%)	2 (12.5)

Results: A total of 16 patients were followed for 1.6 (IQR 1.2-2.2) years after rilonacept initiation. Time elapsed from first pericarditis episode to rilonacept initiation was 8.8 (IQR 0.1-19.5) months, with 2.5 (IQR 1-4) prior flares. Sjogren's syndrome was diagnosed in 14 patients, SLE in 2, and sarcoidosis/Sjogren's in 1. Out of 16 patients, 4 had preceding autoimmune disease, diagnosed a median 15 months prior to their first pericarditis episode.

During the RP episode that led to rilonacept initiation, CRP was elevated in 100% of patients to a mean 173.8 +/- 120.4 mg/L. Corticosteroids were used for RP in 12 (75%), and 13 (81%) were treated with colchicine. Additional patient characteristics are described in Table 1. Both patients with SLE were prescribed HCQ and mycophenolate throughout the follow-up period.

The duration of rilonacept treatment was 1.5 (IQR 0.8-2.2) years. No recurrences were observed in patients while on treatment. There were no adverse events related to rilonacept reported to providers during the follow-up period. All 12 patients treated previously with corticosteroids for RP were able to taper entirely off.

A total of 2 patients withdrew from rilonacept prior to data cutoff, one with SLE and one with Sjogren's (range 8.3-9.0 months post-initiation), both due to patient preference. These patients remained recurrence free over a mean 1.2 years of follow-up after discontinuation of rilonacept.

Conclusion: IL-1 pathway inhibition with rilonacept in the autoimmune RP subgroup was associated with complete abrogation of RP episodes. Further research should establish the optimum duration of treatment in the high-risk autoimmune RP cohort, evaluate the safety profile of rilonacept with concomitant DMARD therapy, and assess the efficacy of treatment in a broader spectrum of autoimmune conditions.

Disclosure: Z. Daniel: None; **S. Afridi**: None; **M. Allen**: Kiniksa Pharmaceuticals, 2; **K. Ngo**: Kiniksa, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1668

A Clinically Validated Assay for Rapid Determination of Type I and Type II Interferon Activity in Pediatric Inflammatory Diseases

Evan Hsu[1], Courtney Leson[2], Amrita Basu[3], Michael Lam[4], Jian Yue[4], Casey Rimland[5], Rachel Weng[4], Lauren Henderson[6], Joyce Chang[2], Mary Beth Son[4], Fatma Dedeoglu[4], roshini Abraham[3] and **Pui Lee[1]**, [1]Boston Children's Hospital, Newton, MA, [2]Boston Children's Hospital, Boston, [3]Nationwide Children's Hospital, Columbus, OH, [4]Boston Children's Hospital, Boston, MA, [5]Brigham and Women's Hospital, Boston, [6]Boston Children's Hospital, Watertown, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Pediatric Rheumatology – Clinical I (1668–1673)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Type I interferons (IFN-I) and type II interferon (IFN-g) are essential to host defense but dysregulated production of these cytokines is increasingly recognized in inflammatory diseases. Aberrant IFN-I production is associated with autoimmunity and excess IFN-g is linked to cytokine storm syndromes with T lymphocyte activation. Assays to measure IFN-I and IFN-g are not available in most institutions. We aimed to develop a clinical flow cytometry assay that rapidly captures the activity of IFN-I and IFN-g.

Methods: We compared bulk RNA sequencing data from healthy controls and patients with macrophage activation syndrome (MAS), multisystem inflammatory syndrome in children (MIS-C), and systemic lupus erythematosus (SLE) to identify biomarkers of IFN-I and IFN-g signaling. We developed a flow cytometry assay to measure IFN-inducible markers on

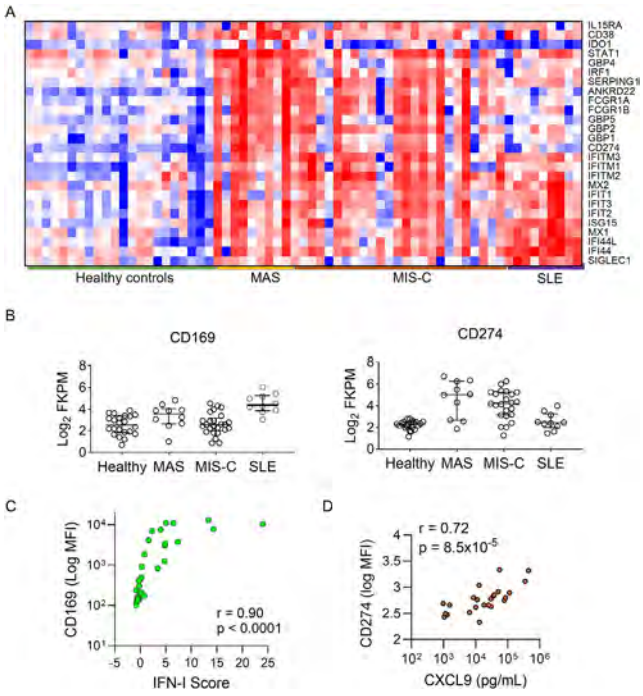


Figure 1. Bulk RNA sequencing data of peripheral blood mononuclear cells from healthy controls and patients with MAS, MIS-C, or SLE. A) Heat map comparing the expression of genes preferentially induced by IFN- (top half) and by IFN-I (bottom half). B) Comparison of CD169 (SIGLEC-1) and CD274 (PD-L1) expression among healthy controls and patient groups. C) Spearman's correlation between CD169 expression and the 28-gene composite IFN-I score in healthy controls and patients with SLE. D) Spearman's correlation between CD274 expression and plasma CXCL9 levels in patients with MAS.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

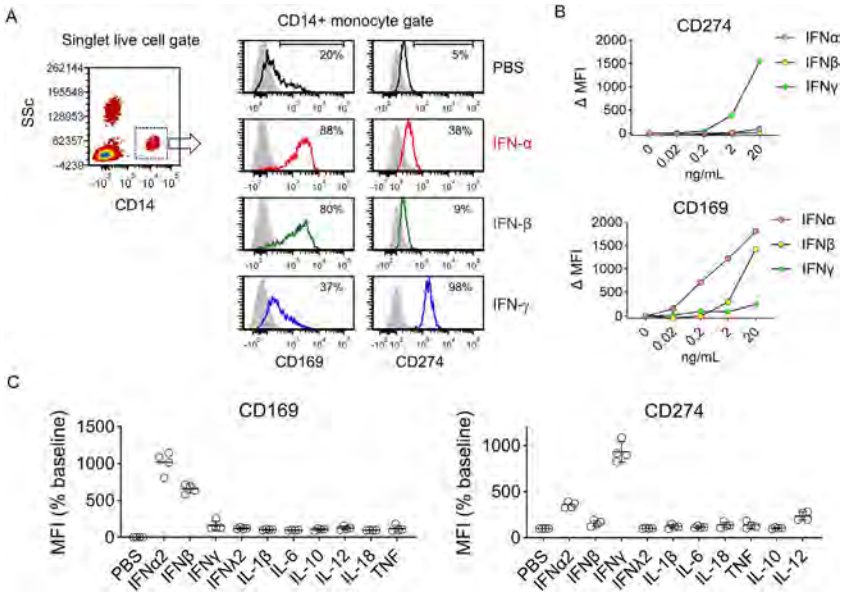
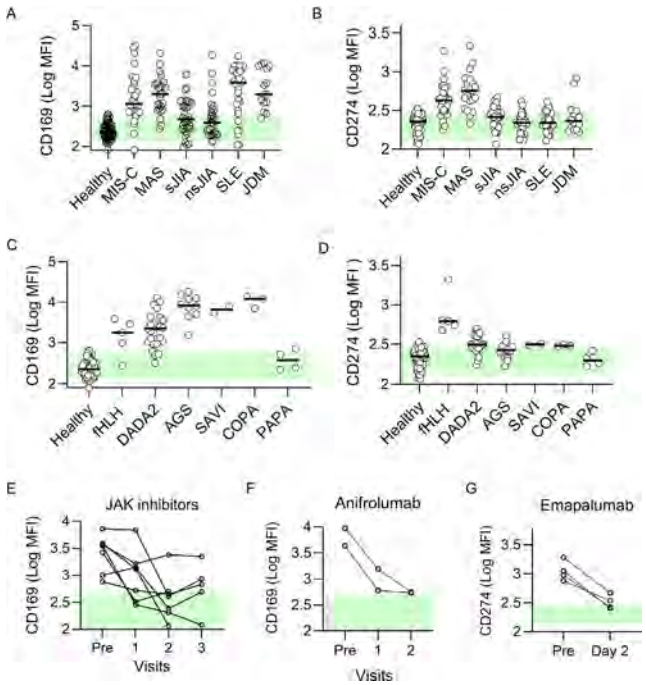


Figure 2. Development of a flow cytometry assay to evaluate IFN activation. A) Gating strategy and representative histograms for evaluation of CD169 and CD274 expression in peripheral blood CD14+ monocytes from a healthy donor with and without IFN stimulation. B) Change in mean fluorescence intensity of CD274 and CD169 expression in response to IFN stimulation at different concentrations. C) Changes in CD169 and CD274 expression on CD14+ monocytes from 4 healthy donors in response to stimulation by different cytokines.

peripheral blood monocytes and acquired data across different pediatric inflammatory diseases. The findings were verified by a clinical laboratory that independently developed and validated this assay for clinical use.



Quantifying IFN-I and IFN- activity in pediatric inflammatory diseases. A) CD169 and B) CD274 expression in healthy controls compared to patients with different inflammatory diseases. C) CD169 and D) CD274 expression in healthy controls compared to patients with familial hemophagocytic lymphohistiocytosis and monogenic autoinflammatory diseases. E) Changes in CD169 expression in patients with Aicardi-Goutières syndrome after treatment with JAK inhibitors. F) Changes in CD169 expression in a patient with SLE and a patient with Singleton-Merten syndrome after anifrolumab treatment. G) Changes in CD274 expression in patients with MAS after initiation of emapalumab. Green area indicates normal range (mean +/- 2 standard deviations) established by the healthy control group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Consistent with previous studies, RNA sequencing data from peripheral blood mononuclear cells identified a strong IFN-I signature in patients with SLE and a strong IFN-g signature in patients with MAS and MIS-C. We found that CD169 (SIGLEC-1) transcript levels positively correlated with the IFN-I signature while CD274 (PD-L1) expression reflected the IFN-g signature (Figure 1). Flow cytometry confirmed that surface expression of CD169 and CD274 on $CD14^+$ monocytes are specific readouts of IFN-I and IFN-g activity, respectively (Figure 2). Based on these findings, we developed a flow cytometry assay to capture CD169 and CD274 expression, which requires 50 μL of whole blood and 30 minutes of hands-on time. We demonstrated the utility of this method for rapid screening of IFN dysregulation in >200 patients with a variety of pediatric inflammatory diseases including MAS, MIS-C, SLE, juvenile idiopathic arthritis, juvenile dermatomyositis, and monogenic autoinflammatory diseases (Figure 3A-D). We further illustrated the use of this test for therapeutic monitoring of recently approved medications that target the IFN pathways including Janus kinase inhibitors, emapalumab (anti-IFN-g), and anifrolumab (anti-IFN α/β receptor; Figure 3E-G). Finally, we outlined the steps of validating this assay for clinical use and summarize the findings during test validation and post-clinical implementation.

Conclusion: We developed a clinically validated flow cytometry test to rapidly assess type I IFN and IFN-g activity. This test is useful for evaluation and monitoring of pediatric inflammatory diseases and can be readily implemented in clinical laboratories.

Disclosure: E. Hsu: None; **C. Leson**: None; **A. Basu**: None; **M. Lam**: None; **J. Yue**: None; **C. Rimland**: None; **R. Weng**: None; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2; **J. Chang**: Century Therapeutics, 2; **M. Son**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **r. Abraham**: Amgen, 5; **P. Lee**: Pfizer, 2.

Abstract Number: 1669

Development and Validation of Minimal Disease Activity and Disease Flare for Children with Chronic Nonbacterial Osteomyelitis Using a Consensus and Data-Driven Approach

Farzana Nuruzzaman[1], Natalie Rossenwasser[2], Xing Wang[3], Ava Klein[3], Ian Muse[4], Erin Balay-Dustrude[5], Megan Nguyen[6], Emily Deng[3], Jonathan Akikusa[7], Matthew Basiaga[8], Lindsey Bergstrom[9], Fatma Dedeoglu[10], Bin Huang[11], Jenna King[12], Sivia Lapidus[13], Tzielan Lee[14], Aleksander Lenert[15], Cassandra Levesque[16], Lillian Lim[17], Kimberly Martin[18], Elizabeth Murray[19], Melissa Oliver[20], Karen Onel[21], Seza zen[22], Lauren Potts[23], Sara M. Stern[24], Robin Villaverda[25], Eveline Wu[26], Ronald laxer[27], Polly Ferguson[28], Daniel Lovell[29] and Yongdong (Dan) Zhao[30], on behalf of CHOIR network and CARRA CNO workgroup, [1]Stony Brook Children's Hospital, Stony Brook, NY, [2]Seattle Children's Hospital, Seattle, WA, [3]Seattle Children's Hospital, Seattle, [4]University of Washington, Department of Pediatrics, Seattle Children's Hospital, Seattle, [5]University of Washington, Seattle, WA, [6]Seattle Children's Research Institute, Seattle, [7]The Royal Children's Hospital, Parkville, Victoria, Australia, [8]Mayo Clinic, Rochester, MN, [9]Patient/parent research partner, Harpswell, ME, [10]Boston Children's Hospital, Boston, MA, [11]Cincinnati Children's Hospital, Cinciannati, OH, [12]Patient/parent Research Partner, Planation, FL, [13]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Montclair, NJ, [14]Stanford University School of Medicine, Palo Alto, CA, [15]Iowa Carver College of Medicine, Iowa City, IA, [16]Patient/parent research partners, DC district, DC, [17]University of Alberta, Edmonton, AB, Canada, [18]Patient/parent research partners, Houston, TX, [19]Patient/parent research partners, Lynnwood, WA, [20]Indiana University, Indianapolis, IN, [21]HSS, New York, NY, [22]Hacettepe University Medical Faculty, Ankara, Turkey, [23]Patient/parent research partners, Santa Cruiz, CA, [24]University of Utah, Salt Lake City, UT, [25]Patient/parent research partners, Thorton, CO, [26]UNC Chapel Hill, Chapel Hill, NC, [27]The Hospital for Sick Children, Toronto, ON, Canada, [28]University of Iowa Carver College of Medicine, Iowa City, IA, [29]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [30]Seattle Children's Research Institute, Redmond, WA

SESSION INFORMATION

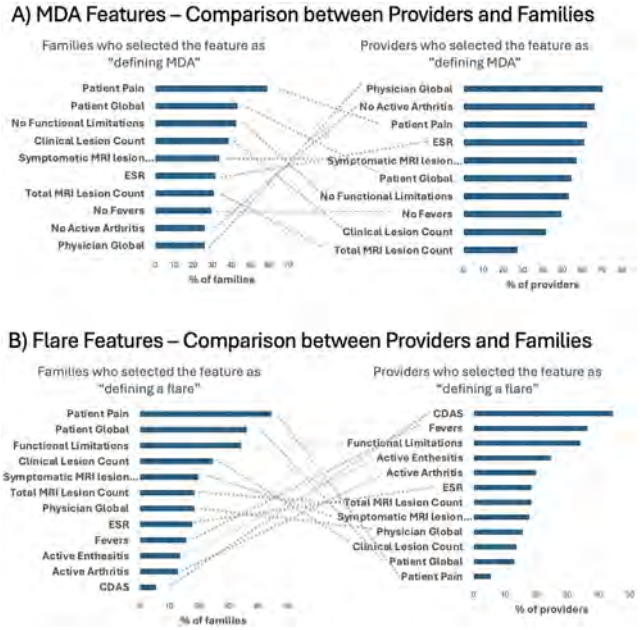
Session Date: Monday, October 27, 2025

Session Title: Abstracts: Pediatric Rheumatology – Clinical I (1668–1673)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Provider and Patient/Caregiver Family Priorities in Defining Minimal Disease Activity and Flare in CNO Delphi Survey Results

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is an inflammatory bone disease that can result in bone destruction/deformity, persistent bone pain and pathological fractures. Due to the lack of randomized control trials, treatment is empirical and based on physician experience. Clinical studies to compare treatments require validated definitions of minimal disease activity (MDA) and disease flare. This study aims to develop and validate definitions of MDA and flare in patients with CNO.

Methods: A Delphi survey on priorities for defining MDA and flare was sent to CNO patient/caregivers and CARRA's CNO Workgroup. Based on responses, key parameters from our multisite prospective registry (CHronic nonbacterial Osteomyelitis International Registry, CHOIR) were extracted to create 2 cohorts to define MDA and flare (Table 1). Missing variables

Table 1. Characteristics of Cohorts Used to Develop Definitions of Minimal Disease Activity and Flare in CNO

	MDA Cohort (n=600)	Flare Cohort (n=573)
Age: in years, median [IQR]	12.7 [10.2, 15.1]	12.8 [10.3, 15.1]
Sex (n, %)	Female: 320 (55) Male: 261 (45)	Female: 309 (56) Male: 248 (45)
Extracted Parameters		
Pain Level (0-10): median [IQR]	1 [0, 4]	1 [0, 4]
Patient global assessment (PAGA) (0-10): median [IQR]	2 [0, 5]	2 [0, 5]
Physician global assessment (PHGA) (0-10): median [IQR]	1 [0, 2]	1 [0, 2]
CNO clinical lesion count: median [IQR]	0 [0, 1]	0 [0, 1]
MRI type: n (%)	Whole Body MRI: 531 (89) Regional with Spine: 12 (2) Regional without Spine: 57 (10)	Whole Body MRI: 504 (88) Regional with Spine: 12 (2) Regional without Spine: 57 (10)
Total MRI lesion count: median [IQR]	3 [2, 4]	3 [2, 4]
Active spinal lesion on MRI: n (%)	No: 532 (89) Yes: 68 (11)	No: 505 (88) Yes: 68 (12)
Active sacroiliitis on MRI: n (%)	No: 571 (95) Yes: 29 (5)	No: 544 (95) Yes: 29 (5)
Erythrocyte Sedimentation Rate (ESR): n (%)	Abnormal: 105 (18) Normal: 495 (83)	Abnormal: 104 (18) Normal: 469 (82)
C-Reactive Protein (CRP): n (%)	Abnormal: 68 (11) Normal: 532 (89)	Abnormal: 67 (12) Normal: 506 (88)
CNO Disease Activity Score (CDAS)*: median [IQR]	4 [1, 10]	5 [1,10]
*CDAS: Sum of patient pain score (0-10), PAGA (0-10), and total number of clinically active CNO lesions defined as focal tenderness, and/or swelling, and/or warmth		

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

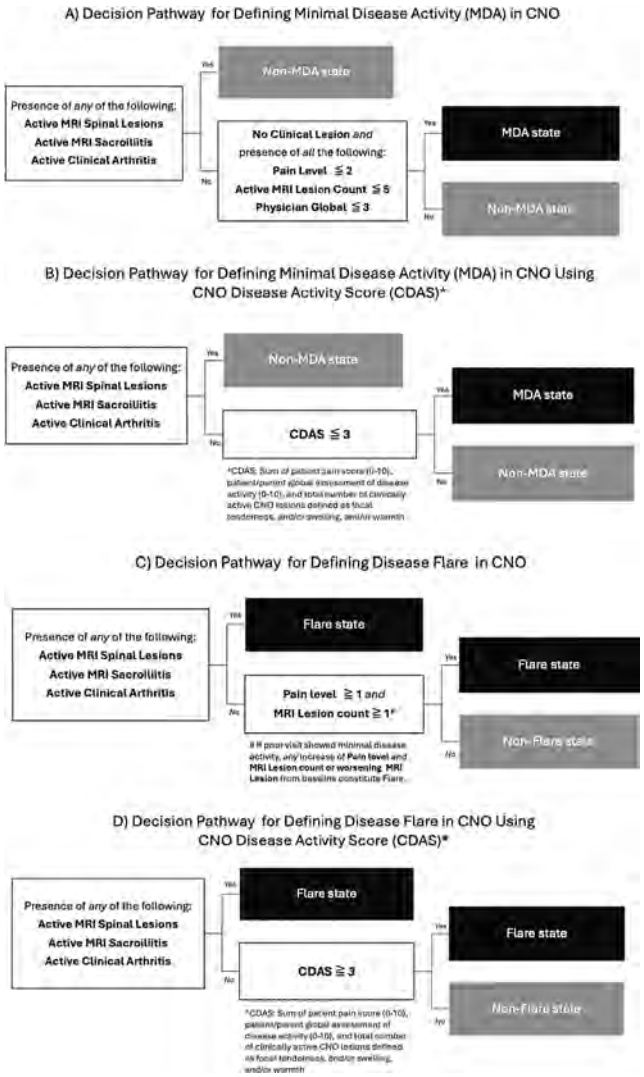


Figure 2. Decision Pathways for Defining Minimal Disease Activity and Disease Flare in CNO

were imputed. A global expert panel of 13 pediatric rheumatologists and 7 patient/caregivers voted on whether a clinical scenario was considered MDA (a single time point assessment) or flare (worsening disease compared to prior visit). Consensus was defined as ≥80% agreement using nominal group technique. A decision tree or ROC analysis were used to determine the cutoff points. The model was validated using 10-fold cross-validation to ensure generalizability.

Results: Results: A total of 252 participants (172 patients/caregivers and 80 providers) completed the survey from 5 continents. Most providers (90%) had >5 years of experience treating children with CNO with ≥5 patients/year. Among patients, 91% were diagnosed within 10 years, 98% had taken medications for CNO and 85% had experienced a flare. Discrepancy was noted among items deemed important for MDA and flare between the 2 groups (Figure 1). Of the MDA cohort, 253 cases were classified by consensus as MDA, 324 as non-MDA, and 23 as inconclusive. Pain level ($p< 0.001$), physician global ($p=0.012$), patient global ($p=0.005$), clinical lesion count ($p=0.001$) and MRI lesion count (< 0.001) were significantly associated with MDA classification. Of the flare cohort, 404 were classified by consensus as flare, 159 as non-flare and 10 were inconclusive. Pain level ($p< 0.001$) and MRI lesion count ($p=0.049$) were associated with flare designation. Cases with presence of either sacroiliitis or spinal lesions on MRI or active clinical arthritis were consistently voted as flare and as non-MDA ($p< 0.001$). The median [IQR] clinical disease activity score (CDAS) was 0 [0,2] in cases with MDA compared to 10 [6, 12] in those without MDA ($p< 0.001$) with a threshold CDAS ≤ 3 for being categorized as MDA. The accuracy of the MDA model without CDAS and with CDAS was 0.77 and 0.89, respectively. The median [IQR] CDAS was 8 [4, 12] in cases

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

with flare, compared to 0 [0, 2] in those without flare (p< 0.001) with a threshold CDAS ≥3 for being categorized as flare.The accuracy of the flare model without CDAS and with CDAS was 0.78 and 0.87 respectively. Decision pathways were developed (Figure 2).

Conclusion: Through Delphi survey and formal consensus techniques, we developed definitions and decision pathways of MDA and flare in patients with CNO proposed as useful targets for future clinical trials.

Disclosure: F. Nuruzzaman: None; **N. Rossenwasser**: None; **X. Wang**: None; **A. Klein**: None; **I. Muse**: None; **E. Balay-Dustrude**: None; **M. Nguyen**: None; **E. Deng**: None; **J. Akikusa**: None; **M. Basiaga**: None; **L. Bergstrom**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **B. Huang**: None; **J. King**: None; **S. Lapidus**: None; **T. Lee**: None; **A. Lenert**: None; **C. Levesque**: None; **L. Lim**: None; **K. Martin**: None; **E. Murray**: None; **M. Oliver**: None; **K. Onel**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **L. Potts**: None; **S. Stern**: None; **R. Villaverda**: None; **E. Wu**: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **R. Iaxer**: Akros pharma, 2, Eli Lilly Canada, 2, Novartis, 2, Sanofi, 2; **P. Ferguson**: None; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **Y. Zhao**: american board of pediatrics, 4, Bristol-Myers Squibb(BMS), 5, UpToDate, 9.

Abstract Number: 1670

Large Retrospective Cohort Study Of Chronic Recurrent Multifocal Osteomyelitis: Disease Presentation, Clinical, And Laboratory Features

Shima Yasin[1], Shima Yasin[2] and Polly Ferguson[3], [1]King Abdullah Specialized Children's Hospital,Ministry of National Guard Health Affairs, Jeddah, Saudi Arabia, [2]Univeristy of Iowa, Iowa City, [3]University of Iowa Carver College of Medicine, Iowa City, IA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical I (1668–1673)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Chronic recurrent multifocal osteomyelitis (CRMO) is an autoinflammatory bone disease that affects children and adolescents. The disease typically presents with bone pain with or without systemic features. Treatment options for CRMO include non-steroidal anti-inflammatory drugs (NSAIDs), methotrexate, bisphosphonates and TNF inhibitors. To date all presented cohorts were of very small numbers and lack generalizability. We are presenting one of the largest CRMO cohorts, aiming to provide more detailed and generalizable clinical and laboratory features.

Methods: This study was approved by Institutional Review Board. Using retrospective chart review we identified more than 200 subjects with confirmed CRMO seen at our center. Descriptive statistics were used for clinical and laboratory features and chi^2 test for comparison of subgroups.

Results: This cohort consisted of 204 patients, of those 141 (69%) were females, and 63 (31%) were males. Age at onset of symptoms ranged from 3 to 17 years of age. Mean age at onset of symptoms was 8 years and 10 years at diagnosis. This demographic and clinical characteristics of the whole cohort is shown in Table (1). The clinical history of the subjects in this study varied between individuals but many of the characteristic symptoms for CRMO were very similar. All patients presented with bone pain at onset. The average number of sites of bone pain was three, and pain was bilateral in 39%. Pain at night was evident in 43% of patients, and 46% of patients had objective swelling at onset. In total, there were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographics and Clinical Characteristics of Study Population

	Total Cohort (n= 204)	Males (n=63)	Females (n=141)	Male vs Female Chi2 p-value
Mean age at onset yr	8.3	8.38	8.2	
Mean age at diagnosis (yr)	10.1	10.27	10.0	
Mean time between onset and diagnosis (months)	21.79	22.52	21.79	
Race/Ethnicity				
Asian	8(4%)	4(6%)	4(3%)	
Black	3(2%)	0	3(2%)	
Hispanic	11(5%)	2(3%)	9(6%)	
Native American/Pacific Islander	2(1%)	1(2%)	1(<1%)	
Multi-Racial	7(3%)	3(5%)	4(3%)	
White	168 (82%)	51(81%)	117(83%)	
Decline to Answer	5(3%)	2(3%)	2(1%)	
Disease Location				
Spinal Disease	59(29%)	14(22%)	45(32%)	0.6022
Mandibular Disease	22(11%)	3(5%)	19(13.4%)	0.280
Clavicular Disease	27(13%)	6(10%)	21(15%)	0.6403
Sacroiliac Disease	41(20%)	16(25%)	25(18%)	0.0795
Upper Body Long Bones	38(18.6%)	11(17.5%)	27(19.1%)	
Lower Body Long Bones	171(83.3%)	54(85.7%.)	117(82.9%)	
CRMO Symptom at Onset				
Back Pain	53(26%)	13(21%)	40(28%)	0.3007
Pain at Night	88(43%)	30(48%)	58(41%)	0.2173
Sleep Disturbance	77(38%)	26(41%)	51(36%)	0.2679
Fever	55(26%)	17(27%)	38(27%)	0.7317
Joint Swelling	94(46%)	23(36%)	71(50%)	0.4417
Fractures	28(14%)	8(13%)	20(14%)	0.8298
Skin Rashes	61(30%)	14(22%)	47(33%)	0.3934
Hospitalizations at onset	49(24%)	15(8%)	34(24%)	

Table 1: Demographics and Clinical Characteristics of Study Population-Continued

	Total Cohort (n=204)	Male (n=63)	Female (n=141)
Associated Autoimmune Diseases			
Acne	14(7%)	8(13%)	6(4%)
JIA	20(10%)	4(6%)	17(12%)
Psoriasis	30(15%)	7(10%)	23(16%)
IBD	13(6%)	4(6%)	9(6%)
PPP	8(4%)	2(3%)	6(10%)
Oral Ulcers	40(20%)	12(19%)	28(20%)
Family History of Autoimmune Disease			
CRMO	8(4%)		
Acne	1(0.50%)		
Psoriasis	65(31.8%)		
Ankylosing Spondylitis	6(3%)		
RA	52(25.5%)		
IBD	45(22.1%)		
PPP	2(1%)		
Thyroid Disease	54(26.5%)		
Laboratory Values			
ESR Elevated	112(58.6%)		
CRP Elevated	82(51%)		
ANA Positive	29(56.8%)		
HLA-B27 Positive	3(10.7%)		
Medication Prescription			
NSAID	103		
DMARD	43		
TNF	52		
Bisphosphonates	29		
Corticosteroid	14		

89(43.6%) patients with at least one co-morbid inflammatory disease, with psoriasis in 14.7%. Also, 32% of CRMO patients in the study had either a first or second degree relative with psoriasis. ESR wand CRP were elevated in more than half of the patients. The most common drugs prescribed to patients were NSAIDS with just over 50% of patients being prescribed a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

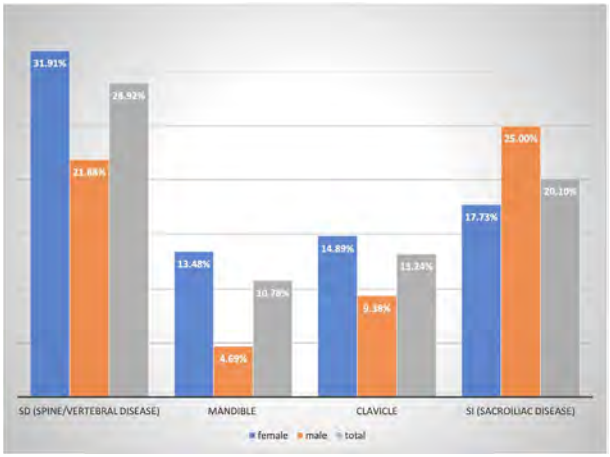


Figure 1: Chronic Recurrent Multifocal Osteomyelitis site of involvement in the total cohort and in male and female subgroups.

type of NSAID at some point in their treatment. Most patients were prescribed approximately two medications during their treatment regimen. Each of the medications prescribed for CRMO were divided into groups based on drug class and reported in (Table1).

When assessing location, 170 patients (84%) had evidence of CRMO in the lower body long bones, 29% of patients had spine disease, and 21% had sacroiliac (SI) disease (Figure 1). When comparing males and females, there was not statistically significant difference between males and females in clinical features or site/location (Table 1). Females had a higher percentage of spine, mandible, and clavicle lesions, compared to the males. In contrast, SI disease was more common in males and the difference approached significance at p=0.08, when compared to females (Tabel 1).

Conclusion: CRMO is more likely to be present in females than males and the average age of diagnosis is at approximately 10 years of age. In our study population, lower body CRMO involvement was the most common, and least common in the mandible. Males had higher percentage of sacroiliac disease. There was no significant difference between females and males in demographics or clinical features. Substantial number of patients in the study who had a milder form of CRMO were able to mitigate symptoms with the use of NSAIDs only.

Disclosure: S. Yasin: None; **S. Yasin**: None; **P. Ferguson**: None.

Abstract Number: 1671

Emapalumab Treatment for Patients with Differing Presentations of Macrophage Activation Syndrome (MAS) Secondary to Still's Disease: Results from a Pooled Analysis of Two Prospective Trials

Alexiei GROM[1], Sebastiaan Vastert[2], Jordi anton[3], Pierre Quartier[4], Bruno Fautrel[5], Paul Brogan[6], Edward Behrens[7], Melissa Elder[8], Francesca Minoia[9], Pavla Dolezalova[10], Robert Biesen[11], Masaki Shimizu[12], Uwe Ullmann[13], Adnan Mahmood[14], Andrew Danquah[13], Elena Burillo[13], Marco Petrimpol[13], Steve Mallett[15], Brian Jamieson[16] and Fabrizio De Benedetti[17], [1]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [2]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [3]Hospital Sant Joan de Déu. Universitat de Barcelona, Barcelona, Spain, [4]Hôpital Necker-Enfants Malades, Paris, France, [5]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [6]Great Ormond Street Hospital for Children NHS Foundation Trust and University College London Great Ormond Street Institute of Child Health, London, United Kingdom, [7]CHOP, West Chester, PA, [8]College of Medicine and Division of Pediatric Allergy, Immunology, and Rheumatology, Department of Pediatrics, University of Florida, GAINESVILLE, FL, [9]Pediatric Immuno-Rheumatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, [10]Paediatric Rheumatology and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Autoinflammatory Diseases Unit, General University Hospital, Prague, Czech Republic, [11]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Germany, [12]Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan, [13]Sobi, Basel, Switzerland, [14]Sobi, Stockholm, Sweden, [15]Sobi, Stock, Sweden, [16]Sobi Inc., Morrisville, NC, [17]Bambino Gesu Children's Hospital, Rome, Rome, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Pediatric Rheumatology – Clinical I (1668–1673)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: MAS is a life-threatening complication of Still's disease characterized by systemic IFNg-driven hyperinflammation. Patients with Still's disease may present with MAS at any disease stage, including at the time of initial diagnosis. MAS episodes may also recur. Emapalumab, an anti-IFNg antibody, achieved sustained control of MAS and facilitated rapid tapering of glucocorticoids (GCs) in a phase 2 pilot study (NCT03311854). This analysis presents data by MAS presentation from an expanded population of patients treated with emapalumab for MAS in Still's disease.

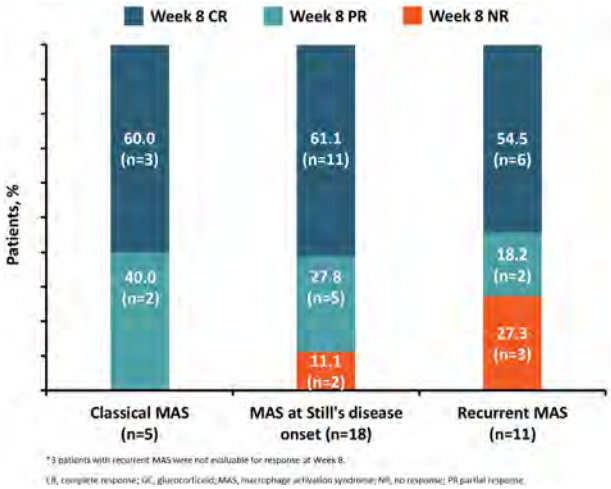


Figure 1. Week 8 responder status* by presentation subgroup amongst patients with MAS in Still's disease with an inadequate response to high-dose GCs

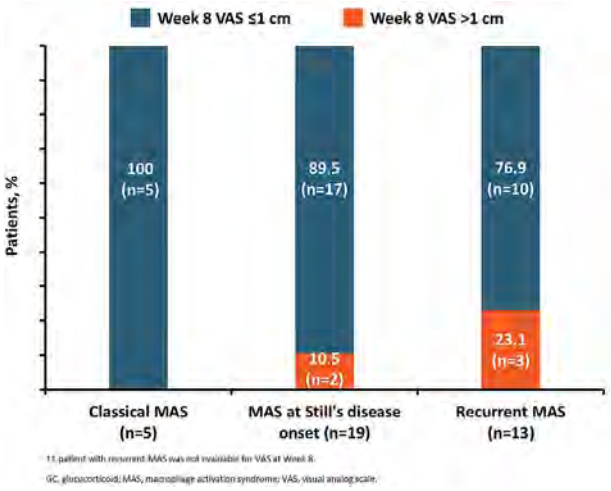


Figure 2. Prevalence of VAS ≤1 cm† at Week 8 by presentation subgroup amongst patients with MAS in Still's disease with an inadequate response to high-dose GCs

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

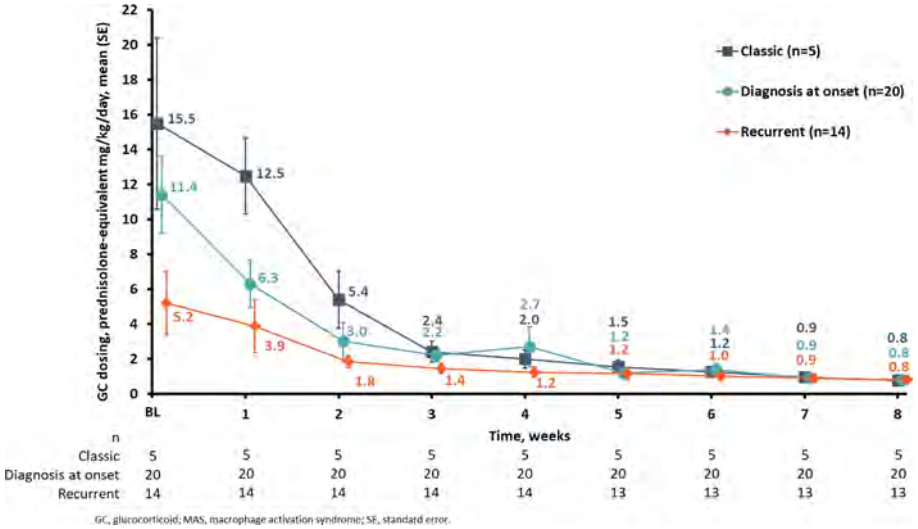


Figure 3. Change in GC dosing over time in patients treated with emapalumab from different MAS subgroups who had an inadequate response to high-dose GCs

Methods: Data were pooled from 2 open-label, single-arm interventional studies (NI-0501-06 [NCT03311854] and NI-0501-14 [EMERALD; NCT05001737]) in patients with MAS in Still's disease who had an inadequate response to high-dose GCs or investigator-assessed rapid worsening of clinical condition and/or laboratory parameters. All patients were administered a loading dose of emapalumab 6 mg/kg via intravenous infusion on Day 1; emapalumab 3 mg/kg was then administered every 3 days from Days 4–16 and twice weekly from Days 17–28 (or longer for insufficient clinical response). The primary efficacy endpoint was complete response (CR) at Week 8 (MAS clinical activity score measured on a 10 cm visual analog scale [VAS] ≤1/10 cm) and normalization of 7 MAS-related laboratory parameters. Partial response (PR) was defined as VAS < 4 cm and normalization of ≥3 abnormal baseline laboratory parameters included in the composite primary endpoint. MAS was classified as classic (first MAS diagnosis secondary to an earlier Still's diagnosis), diagnosed at onset of Still's disease or recurrent. MAS subgroup data was collected prospectively in EMERALD and retrospectively using patient narratives for NCT03311854.

Results: 39 patients were enrolled (31 [79.5%] females), with a median age of 12 years (range, 9 months–64 years). 84.6% of patients received concomitant biologics alone or in combination, mainly anti-interleukin-1 (66.6%) and cyclosporine A (43.6%). Twenty patients (51.3%) had MAS at Still's disease onset, 5 (12.8%) patients had classical MAS, and 14 (35.9%) had recurrent MAS. A higher proportion of patients in EMERALD had recurrent MAS compared with NI-0501-06 (10/25 [40.0%] vs 4/14 [28.7%]) and a lesser proportion had classical MAS (2/25 [8.0%] vs 3/14 [21.4%]). CR (54.5–60.0%) and VAS ≤1 cm (76.9–100%) rates were similar across groups (**Figures 1 and 2**). While the recurrent group had the highest rates of non-responders at Week 8, overall response (OR) rates were still high with 8/11 patients (72.7%) achieving an OR at Week 8 and 10/13 (76.9%) achieving VAS ≤1 cm at Week 8. Changes in GC dosing from baseline to Week 8 were similar across MAS subgroups (**Figure 3**). Emapalumab was well tolerated. One patient with MAS at diagnosis of Still's disease and one patient with recurrent MAS died during the study.

Conclusion: Emapalumab treatment was associated with consistent CR rates of approximately 55–60% among patients with different MAS presentations, who had an inadequate response to high-dose GCs, including patients with recurrent disease. Patients achieving VAS ≤1 cm, changes in GC dosing and safety were also similar across MAS subgroups.

Disclosure: A. GROM: National Institutes of Health, 5, Novartis, 2, 5, sJIA Foundation, 5, Sobi, 2, 5, Up-To-Date, 9; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **J. anton**: Sobi, 1, 5, 6; **P. Quartier**: AbbVie, 2, 6, Chugai-Roche, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 1, 2, Sobi, 2, 6; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **P. Brogan**: Sobi, 6; **E. Behrens**: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9; **M. Elder**: None; **F. Minoia**: Novartis, 2, 6, Sobi, 2, 6; **P. Dolezalova**: Medac, 6, Novartis, 6, Pfizer, 6, Sobi, 6; **R. Biesen**: None; **M. Shimizu**: Medical and Biological Laboratories Co. Ltd, 5; **U. Ullmann**: Sobi, 2; **A. Mahmood**: Sobi, 2; **A. Danquah**: Sobi, 3; **E. Burillo**: Sobi, 3; **M. Petrimpol**: Sobi, 3; **S. Mallett**: Sobi, 2; **B. Jamieson**: Sobi Inc, 3; **F. De Benedetti**: AbbVie, 2, 5, Apollo, 2, 5, Elixiron, 2, 5, Kiniksa, 2, 5, Novartis, 2, 5, Sanofi, 2, 5, Sobi, 2, 5.

Abstract Number: 1672

Classification criteria, disease phenotypes and long-term outcomes of childhood Sjögren's Disease into adulthood

Coziana Ciurtin[1], Ruby Gotch[2], Hannah Peckham[1], Robert Wilson[2], Muthana AlObaidi[3] and Elizabeth C Jury[1], [1]University College London, London, United Kingdom, [2]University College London Hospital NHS Trust, London, United Kingdom, [3]Great Ormond Street Hospital, London, United Kingdom

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical I (1668–1673)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Childhood Sjögren Disease (cSjD) is a rare clinical phenotype lacking research on long-term outcomes and impact on the quality of life of young people (YP). This study aimed to characterise the natural history of cSjD into adulthood mapped onto the available classification criteria, the adult SjD clinical phenotypes (1) and the Florida Scoring System (FSS)-derived classification for cSjD (2).

Methods: Detailed patient and disease characteristics were collected retrospectively from a single centre, including assessment of disease activity, symptoms severity and damage using validated scores (ESSDAI, ESSPRI and SSDDI). Two paediatric diagnosis criteria, Bartunkova et al.,1999 (3) and Tomiita et al., 2019 (4), as well as the 2016 ACR/EULAR adult classification criteria (5) were tested at disease onset vs. last assessment.

Results: We identified 30 YP with cSjD (F:M=14:1, 60% White), aged 25.8+/-5.2 years, with symptoms onset at age 12.7+/-3.3 years, follow-up 1-25 years (mean 10.5+/-5.4 years), and diagnosis delay of 3 weeks-5 years (**Table**). Manifestations at cSjD onset included: fatigue (73.3%), arthralgia (70%), dryness (56.6%), glandular swelling (33.6%), and skin rashes (30%). All 9 patients with >3 years diagnostic delay had dryness (100% vs. 38% of the ones diagnosed within 3 years, $p< 0.001$). All by one were ANA positive, while 83.3%, 40% and 43.3% were anti-Ro, anti-La and rheumatoid factor positive, respectively. All YP had ultrasound features of sialadenitis at diagnosis and 40% had salivary/lachrymal gland diagnostic biopsies. Three patients were diagnosed with lymphoma (10%), all within 3 years from diagnosis. All patients were treated with hydroxychloroquine, 19 with various cDMARDs, 7 with rituximab, one with belimumab and 3 with cyclophosphamide. At the last assessment, the median ESSDAI was 2 (IQR 2-8), median ESSPRI was 5.33 (IQR 3-7); 17 (56.6%) cSjD patients had damage due to decreased saliva/tear secretion, and 3 (10%) experienced teeth loss. At the time of diagnosis compared to last assessment, 12(40%) vs. 20(66.6%) fulfilled the ACR/EULAR criteria, 9(29%) vs. 14(46.6%) fulfilled the paediatric Bartunkova criteria and 12(40%) vs. 19(61.2%) had at least a 'probable' diagnosis of cSjD based on Tomiita criteria. At the last assessment, 36.6% had 'high' vs. 30% 'low symptoms burden', while 26.6% had 'dominant pain' and 6.66% 'dominant dryness with fatigue' symptoms. At presentation, 56.6% patients could not be mapped onto any of the FSS-derived clusters as they presented with either 'high' or 'low symptoms and positive tests', reflecting their longer diagnosis delay compared to the cSjD cohort used for the FSS classification.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Cohort characteristics

Individuals with cSjD N(%)	At diagnosis N=30	At last assessment N=30 (all adults)
Age (years, mean +/-SD) F:M =14:1 60% White 23.33% Black African 16.6% Asian	12.7+/- 3.3	25.8+/-5.2
Duration of symptoms	median 1 year, IQR = 1-3 (interval 3 weeks - 5 years)	10.5+/-5.4 years (interval 1-25 years)
Treatment N (%)	NSAIDs -22 (73.3) Short course steroids - 8 (26.6) HCQ -11 (36.6)	Short course steroids – 4 (13.3) HCQ – 25 (83.3) AZT – 5 (16,6) MTX – 7 (23.3) MMF – 4 (13.3) Belimumab + MMF – 1 (3.3)
Diagnostic and classification criteria fulfilled N (%)		
2016 ACR/EULAR criteria	12 (40%)	20 (66.6%)
Paediatric diagnostic criteria (Bartunkova, 1999)	9 (29%)	14 (46.6%)
'Definite' or 'Probable' diagnosis (Tomlits algorithm, 2021)	12 (40%)	19 (61.2%)
Mapping onto the paediatric FSS-derived categories at diagnosis N (%)		
Dryness with positive tests	8 (26.6%)	Not applicable
High symptoms with negative tests	5 (16.6%)	
Low symptoms with negative tests	1 (3.33%)	
Unclassifiable as presented with either 'high' or 'low symptoms', but found with 'positive tests'	17 (56.6%)	
Mapping onto the NSST-derived adult clinical phenotypes N (%)		
High symptom burden	Data not available at diagnosis	11 (36.6%)
Low symptom burden		9 (30%)
Pain dominant with fatigue		8 (26.6%)
Dryness dominant with fatigue		2 (6.66%)

Legend: ACR – American College of Rheumatology; AZT – azathioprine; cSjD – Childhood onset Sjögren Disease; EULAR – European Alliance of Associations for Rheumatology; F – females; FSS – Florida Scoring System; H – hydroxychloroquine; M – males; MMF – mycophenolate mofetil; MTX – methotrexate; N – number; NSST – Newcastle Sjögren Stratification Tool.

Conclusion: This unique longitudinal cohort analysis revealed differences between cSjD and adult SjD clinical phenotypes, and poor performance of the FSS for cSjD classification at presentation. Almost 2/3 patients could not be initially classified/diagnosed by any of the available criteria, and 1/3 still could not be classified even after 10 years of follow-up. These findings highlight the critical need for adequate classification/research in cSjD, characterised by early damage accrual and 10% risk of lymphoma in this unique adult cohort.

Disclosure: C. Ciurtin: None; **R. Gotch**: None; **H. Peckham**: None; **R. Wilson**: None; **M. AlObaidi**: None; **E. C Jury**: None.

Abstract Number: 1673

Is Transient Synovitis of the Hip preclinical Juvenile SpA ? A follow-up study

Anirudh Bandu[1], Michal Cidon[2] and Michael Weisman[3], [1]CHLA, Los Angeles, NJ, [2]Children's Hospital of Los Angeles, Los Angeles, CA, [3]Cedars-Sinai Medical Center, LOS ANGELES, CA

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical I (1668–1673)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Transient synovitis (TS) of the hip is considered a common, self-limited condition in the pediatric population. However, recurrences can occur; these may signal an early manifestation of enthesitis-related arthritis (ERA) or

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Juvenile Spondylarthritis (SpA). We conducted a retrospective chart review study that identified the initial visit of all coded transient synovitis cases from 2002 to 2022 and attempted to contact these patients by telephone. The study goal was to determine, through direct interview, whether these patients had recurrent disease and subsequent clinical features indicative of early juvenile spondylarthritis (SpA) or enthesitis-related arthritis (ERA).

Methods: Data collected from the initial chart review included demographics and details from the initial ED visit. A follow-up by telephone interview obtained data on the recurrence of transient synovitis, chronic back pain (lasting > 6 weeks), joint pain, and physician diagnoses such as Enthesitis Related Arthritis, Juvenile SpA, or related conditions after obtaining consent.

Results: A Total of 184 charts were analyzed after review to determine the accurate diagnosis of transient synovitis; 74 patients (40%) were successfully contacted. The demographics and clinical features of the 74 contacted were no different from those of the 110 who were unable to be contacted. [Refer to Figure 1] One third of the contacted patients reported recurrent transient synovitis; these subjects exhibited significantly higher rates of musculoskeletal pain compared to those with non-recurrent transient synovitis. Chronic back pain was reported in 41.7% of the recurrent transient synovitis group vs. 0% of the non-recurrent group ($p < 0.001$). Chronic peripheral pain was present in 66.7% in the recurrent group vs. 8.0% in the non-recurrent group (OR 21.6, 95% CI: 5.3–113.0, $p < 0.001$). Combined chronic peripheral and back pain was present in 75.0% in the recurrent group vs. 8.0% in the non-recurrent group (OR 31.8, 95% CI: 7.5–176.9, $p < 0.01$). Pain localized to hips, knees, and ankles was significantly more common in recurrent cases ($p < 0.005$). Absence of pain was strongly associated with the non-recurrent group (92.0% vs. 33.3%, $p < 0.001$). [Refer to Figure 2]

Conclusion: Recurrent transient synovitis may be an early indicator of Juvenile SpA or Enthesitis Related Arthritis. In our retrospective cohort, one-third of transient synovitis cases reported recurrence of transient synovitis. Of those who reported

Table 1: Contacted versus Unable to contact

	Unable to contact	Contacted	Test
	110 (59.8%)	74 (40.2%)	
Age at ED visit	4.72 (2.76)	4.54 (2.40)	0.879
Sex at birth			
Female	34 (30.9%)	28 (37.8%)	0.344
Male	76 (69.1%)	46 (62.2%)	
Race			
White/Caucasian	15 (15.0%)	14 (20.9%)	0.713
Black/African American	5 (5.0%)	2 (3.0%)	
Asian	8 (8.0%)	6 (9.0%)	
Other	72 (72.0%)	45 (67.2%)	
Ethnicity			
Non-Hispanic	34 (34.7%)	21 (33.3%)	1.000
Hispanic	64 (65.3%)	42 (66.7%)	
Length of hip symptoms (days) before ED presentation	2.22 (2.98)	2.68 (4.08)	0.552
Fever at presentation			
No	104 (94.5%)	67 (90.5%)	0.381
Yes	6 (5.5%)	7 (9.5%)	
ESR	13.51 (11.21)	19.05 (19.18)	0.281
CRP	1.67 (3.77)	1.24 (1.35)	0.698
Imaging done (US)			
No	49 (44.5%)	31 (41.9%)	0.763
Yes	61 (55.5%)	43 (58.1%)	
Imaging done(MRI)			
No	108 (98.2%)	69 (93.2%)	0.119
Yes	2 (1.8%)	5 (6.8%)	
Imaging done (XR)			
No	52 (47.3%)	45 (60.8%)	0.097
Yes	58 (52.7%)	29 (39.2%)	
US results (Synovial thickening)			
No	95 (86.4%)	64 (86.5%)	1.000
Yes	15 (13.6%)	10 (13.5%)	
US results (Effusion)			
No	55 (50.0%)	39 (52.7%)	0.765
Yes	55 (50.0%)	35 (47.3%)	
US results (Normal)			
No	104 (94.5%)	66 (89.2%)	0.256
Yes	6 (5.5%)	8 (10.8%)	
Has the transient synovitis recurred ?			
No	0 (0.0%)	50 (67.6%)	<0.001
Yes	10 (100.0%)	24 (32.4%)	
Location of recurrence			
Peripheral Enthesis	1 (12.5%)	3 (12.5%)	1.000
Hip	7 (87.5%)	21 (87.5%)	

Mean (Standard Deviation): p-value from a Kruskal-Wallis test.
Frequency (Percent%): p-value from Fisher's exact test.

Demographic comparison of Contacted vs Unable to Contacted

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: No TS Recurrence versus TS Recurrence

	No	Yes	Test
	50 (67.6%)	24 (32.4%)	
Experiencing chronic (>6 weeks of constant) back pain			
No	50 (100.0%)	14 (58.3%)	<0.001
Yes	0 (0.0%)	10 (41.7%)	
Peripheral Pain (>6 weeks)			
No	46 (92.0%)	8 (33.3%)	<0.001
Yes	4 (8.0%)	16 (66.7%)	
Combined Chronic Pain			
No	46 (92.0%)	6 (25.0%)	<0.001
Yes	4 (8.0%)	18 (75.0%)	
Pain in Ankles			
No	49 (98.0%)	18 (75.0%)	0.004
Yes	1 (2.0%)	6 (25.0%)	
Pain in Hips			
No	49 (98.0%)	15 (62.5%)	<0.001
Yes	1 (2.0%)	9 (37.5%)	
Pain in Lower Back			
No	50 (100.0%)	22 (91.7%)	0.102
Yes	0 (0.0%)	2 (8.3%)	
Pain in Knees			
No	48 (96.0%)	16 (66.7%)	0.001
Yes	2 (4.0%)	8 (33.3%)	

Mean (Standard Deviation): p-value from a Kruskal-Wallis test.
Frequency (Percent%): p-value from Fisher's exact test.

No TS Recurrence versus TS Recurrence

recurrences, a substantial number of participants also indicated additional symptoms that are concerning for a developing enthesitis related arthritis or Juvenile SpA such as chronic back pain and lower extremity pain. Recurrent transient synovitis may signify an important precursor to Juvenile SpA or enthesitis related arthritis and potentially be considered a risk factor. These findings support the need for ongoing follow-up with pediatric rheumatology. A future prospective study would be necessary to establish a diagnosis of Enthesitis Related Arthritis or Juvenile SpA in individuals who experienced recurrent transient synovitis.

Disclosure: A. Bandu: None; **M. Cidon**: None; **M. Weisman**: Spyre Therapeutics, 1, 2.

Abstract Number: 1674

A Phase 2, Randomized, Placebo-controlled Trial of Hydroxychloroquine in Individuals At-risk for Future Rheumatoid Arthritis

Kevin Deane[1], Christopher Striebich[2], Marie Feser[3], James O'Dell[4], Judith James[5], Jeffrey Sparks[6], John Davis[7], Jonathan Graf[8], Maureen McMahon[9], Elizabeth Solow[10], Lindsy Forbess[11], Athan Tiliakos[12], Elena Schiopu[13], David Fox[14], Maria I. (\"Maio\") Danila[15], Diane Horowitz[16], Jonathan Kay[17], Colin Strickland[3], Joel Guthridge[5], Cristina Arriens[5], Jennifer Grossman[18], Kristen Demoruelle[19], Elizabeth Bemis[3], Ashley Frazer-Abel[3], Chelsie Fleischer[20], Ted Mikuls[4], Melissa Greenleaf[21], Kate York[22], Sarah Walker[23], Lynette Keyes-Elstein[23], Margie Byron[23], Janel Fedler[24], Ellen Goldmuntz[25] and V. Michael Holers[26], [1]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [2]University of Colorado, Aurora, CO, [3]University of Colorado Anschutz Medical Campus, Aurora, CO, [4]University of Nebraska Medical Center, Omaha, NE, [5]Oklahoma Medical Research Foundation, Oklahoma City, OK, [6]Brigham and Women's Hospital, Boston, MA, [7]Mayo Clinic, Rochester, MN, [8]UCSF, San Francisco, CA, [9]UCLA David Geffen School of Medicine, Los Angeles, CA, [10]UT Southwestern Medical Center, Dallas, TX, [11]Cedars-Sinai Medical Center, Los Angeles, CA, [12]Emory University, Roswell, GA, [13]Medical College of Georgia at Augusta University, Martinez, GA, [14]University of Michigan, Dexter, MI, [15]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [16]Northwell Health, Jericho, NY, [17]UMass Chan Medical School, Worcester, MA, [18]UCLA, Sherman Oaks, CA, [19]University of Colorado Anschutz Medical Campus, Golden, CO, [20]University of Colorado Denver, Aurora, CO, [21]National Institutes of Health, Rockville, MD, [22]Rho, Inc, Durham, NC, [23]Rho, Inc., Durham, NC, [24]Rho, Inc., Salem, IA, [25]NIAID/ NIH, Washington, DC, [26]University of Colorado, Denver, CO

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments (1674–1679)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Individuals with elevations of serum anti-cyclic citrullinated peptide (anti-CCP) antibodies are at-risk for rheumatoid arthritis (RA). Identification of interventions to prevent RA in anti-CCP-positive individuals is a current priority. Hydroxychloroquine (HCQ) has been used in such individuals without supporting clinical trial data. We conducted a phase 2, randomized, double-masked, placebo-controlled, parallel group trial to evaluate the efficacy and safety of a 12-month course of HCQ to prevent clinically apparent RA (clinical RA) by 36 months. We previously reported results from interim analyses (ACR Convergence abstract 1604); this current report presents the final clinical trial results.

Methods: Individuals at-risk for RA with anti-CCP3 ≥2 times the upper limit of normal (ULN) were assigned to receive HCQ or placebo for 12 months, with up to 24 months of post-drug follow-up. The primary outcome was the development of clinical RA at 36 months. Clinical RA was defined using the 2010 ACR/EULAR RA Classification Criteria with a score of ≥6, or a joint examination with RA-like synovitis with ≥1 erosion identified via x-ray imaging of the hands, wrists, and feet. Evaluation for clinical RA was triggered by the presence on physical examination of ≥1 joint with RA-like synovitis. Secondary outcomes included safety, development of inflammatory arthritis (IA)(≥1 joint with RA-like synovitis), and participant-reported joint symptoms.

Results: Of 144 randomized participants, 71 were assigned to HCQ and 73 to placebo (Table 1). In the modified intent-to-treat population, clinical RA occurred in 21 of 69 (30.4%) participants in the HCQ group and 24 of 73 (32.9%) in the

Table 1. Characteristics of StopRA trial participants

Table 1. Characteristics of StopRA trial participants			
	HCQ (N=71)	Placebo (N=73)	Total (N=144)
Age at Screening - yr, mean (SD)	51.7 (12.31)	49.3 (14.39)	50.5 (13.41)
Female sex - no. (%)	57 (80.3)	58 (79.5)	115 (79.9)
Race - no. (%)			
White	56 (78.9)	58 (79.5)	114 (79.2)
Black	8 (11.3)	7 (9.6)	15 (10.4)
Asian	1 (1.4)	3 (4.1)	4 (2.8)
American Indian or Alaska Native	2 (2.8)	3 (4.1)	5 (3.5)
Other/Unknown	4 (5.6)	2 (2.7)	6 (4.2)
Hispanic ethnicity - no. (%)			
Hispanic	15 (21.1)	8 (11.0)	23 (16.0)
Not Hispanic	55 (77.5)	64 (87.7)	119 (82.6)
Unknown	1 (1.4)	1 (1.4)	2 (1.4)
Body Mass Index (BMI) - kg/m2, mean (SD)	30.59 (6.719)	28.72 (6.811)	29.64 (6.807)
Recruitment method - no. (%)			
First Degree Relative (FDR)	7 (9.9)	3 (4.1)	10 (6.9)
Clinic Patient	45 (63.4)	48 (65.8)	93 (64.6)
General Population	19 (26.8)	22 (30.1)	41 (28.5)
First degree relative with RA - no. (%) [1]			
Yes	26 (36.6)	18 (24.7)	44 (30.6)
No	32 (45.1)	42 (57.5)	74 (51.4)
Unknown	13 (18.3)	13 (17.8)	26 (18.1)
Smoking status - no. (%) [2]			
Current Smoker	4 (5.6)	7 (9.6)	11 (7.6)
Former Smoker	19 (26.8)	18 (24.7)	37 (25.7)
Never smoker	48 (67.6)	48 (65.8)	96 (66.7)
Anti-CCP3 positivity at Screening - no. (%)			
Medium Positive (40 to <60 units)	9 (12.7)	14 (19.2)	23 (16.0)
High Positive (≥60 units)	62 (87.3)	59 (80.8)	121 (84.0)
RF-IgM positive (>6.7 IU/mL) - no. (%)	47 (66.2)	35 (48.6)	82 (57.3)
Missing - no.	0	1	1
hs-CRP positive (>3.0 mg/L) - no. (%)	31 (43.7)	36 (50.7)	67 (47.2)
Missing - no.	0	2	2

StopRA=Strategy to Prevent the Onset of Clinically Apparent Rheumatoid Arthritis; Anti-CCP3= Anti-cyclic Citrullinated Peptide 3; HCQ=Hydroxychloroquine; hs-CRP= High Sensitivity C-reactive Protein; max=Maximum; min=Minimum; RA=Rheumatoid Arthritis; RF-IgM= Rheumatoid Factor Immunoglobulin M; SD=Standard Deviation

[1] Participant self-report of having a first-degree relative (FDR) with RA. Individuals reporting an FDR with RA may not have been recruited for the StopRA study via that pathway.

[2] Smoking status was collected at the baseline visit (Week 0) via the epidemiologic questionnaire.

Table 2. Participant-reported joint symptoms over time

Table 2. Participant-reported joint symptoms over time						
	42 Joints [1]			32 Joints [2]		
	HCQ N=69	Placebo (N=73)	Difference (95% CI) [3]	HCQ N=69	Placebo (N=73)	Difference (95% CI) [2]
No. of participant-reported painful joints						
Baseline/Week 0						
n	68	73		68	73	
Median (min, max)	2.0 (0, 39)	1.0 (0, 40)	1.0 (-1.00, 3.00)	0.0 (0, 31)	0.0 (0, 32)	0.0 (-1.00, 1.00)
No. of joints >0						
no. (%)	47 (69.1)	43 (58.9)		31 (45.6)	31 (42.5)	
Median (min, max)	4.0 (1, 39)	3.0 (1, 40)	1.0 (-0.75, 3.00)	4.0 (1, 31)	3.0 (1, 32)	1.0 (-2.00, 3.00)
Week 52						
n	54	57		54	57	
Median (min, max)	1.0 (0, 23)	1.0 (0, 38)	0.0 (-1.00, 2.00)	0.0 (0, 21)	0.0 (0, 32)	0.0 (0.00, 1.00)
No. of joints >0						
no. (%)	31 (57.4)	31 (54.4)		23 (42.6)	21 (36.8)	
Median (min, max)	3.0 (1, 23)	3.0 (1, 38)	0.0 (-3.00, 3.00)	2.0 (1, 21)	3.0 (1, 32)	-1.0 (-6.00, 1.50)
Month 36						
n	38	39		38	39	
Median (min, max)	1.0 (0, 13)	2.0 (0, 36)	-1.0 (-3.00, 0.50)	0.0 (0, 11)	0.0 (0, 30)	0.0 (-1.50, 0.00)
No. of joints >0						
no. (%)	20 (52.6)	25 (64.1)		13 (34.2)	18 (46.2)	
Median (min, max)	2.5 (1, 13)	4.0 (1, 36)	-1.5 (-8.00, 1.00)	2.0 (1, 11)	4.0 (1, 30)	-2.0 (-8.00, 2.00)
No. of participant-reported stiff joints						
Baseline/Week 0						
n	68	73		68	73	
Median (min, max)	1.0 (0, 40)	0.0 (0, 40)	1.0 (0.00, 2.00)	0.0 (0, 32)	0.0 (0, 32)	0.0 (0.00, 0.00)
No. of joints >0						
no. (%)	40 (58.8)	33 (45.2)		22 (32.4)	22 (30.1)	
Median (min, max)	3.5 (1, 40)	4.0 (1, 40)	-0.5 (-3.00, 2.50)	4.5 (1, 32)	4.5 (1, 32)	0.0 (-4.50, 6.00)
Week 52						
n	54	57		54	57	
Median (min, max)	1.0 (0, 32)	1.0 (0, 42)	0.0 (-1.00, 1.00)	0.0 (0, 22)	0.0 (0, 32)	0.0 (0.00, 1.00)
No. of joints >0						
no. (%)	28 (51.9)	31 (54.4)		20 (37.0)	17 (29.8)	
Median (min, max)	4.0 (1, 32)	3.0 (1, 42)	1.0 (-2.00, 4.50)	3.5 (1, 22)	10.0 (1, 32)	-6.5 (-11.00, 6.00)
Month 36						
n	38	39		38	39	
Median (min, max)	0.0 (0, 32)	1.0 (0, 20)	-1.0 (-2.00, 1.00)	0.0 (0, 22)	0.0 (0, 20)	0.0 (0.00, 0.00)
No. of joints >0						
no. (%)	17 (44.7)	20 (51.3)		9 (23.7)	12 (30.8)	
Median (min, max)	3.0 (1, 32)	4.0 (1, 20)	-1.0 (-6.25, 5.00)	8.0 (1, 22)	4.0 (1, 20)	4.0 (-4.00, 8.00)
No. of participant-reported swollen joints						
Baseline/Week 0						
n	68	73		68	73	
Median (min, max)	0.0 (0, 19)	0.0 (0, 24)	0.0 (0.00, 0.00)	0.0 (0, 19)	0.0 (0, 20)	0.0 (0.00, 0.00)
No. of joints >0						
no. (%)	22 (32.4)	23 (31.5)		14 (20.6)	13 (17.8)	
Median (min, max)	2.5 (1, 19)	2.0 (1, 24)	0.5 (-1.00, 2.00)	3.0 (1, 19)	2.0 (1, 20)	1.0 (-6.00, 3.00)
Week 52						
n	54	57		54	57	
Median (min, max)	0.0 (0, 8)	0.0 (0, 25)	0.0 (0.00, 0.00)	0.0 (0, 8)	0.0 (0, 21)	0.0 (0.00, 0.00)
No. of joints >0						
no. (%)	15 (27.8)	18 (31.6)		11 (20.4)	9 (15.8)	
Median (min, max)	2.0 (1, 8)	2.0 (1, 23)	0.0 (-1.00, 2.00)	2.0 (1, 8)	1.0 (1, 21)	1.0 (-12.00, 2.50)
Month 36						
n	38	39		38	39	
Median (min, max)	0.0 (0, 3)	0.0 (0, 24)	0.0 (0.00, 0.00)	0.0 (0, 3)	0.0 (0, 22)	0.0 (0.00, 0.00)
No. of joints >0						
no. (%)	10 (26.3)	13 (33.3)		5 (13.2)	10 (25.6)	
Median (min, max)	2.0 (1, 3)	4.0 (1, 24)	-2.0 (-9.00, 1.00)	2.0 (1, 3)	2.5 (1, 22)	-0.5 (-10.50, 2.00)

CI=Confidence Interval; HCQ=Hydroxychloroquine; max=Maximum; min=Minimum

Note: Percentages are based on the number of participants with evaluable data

[1] Participant-reported joints assessed were hand (proximal interphalangeal joints and metacarpal phalangeal joints), wrist, elbow, shoulder, hip, knee, ankle (including subtalar joint and calcaneonavicular joint) and foot (metatarsal phalangeal joints) joints on both sides

[2] Participant-reported joints assessed were hand (proximal interphalangeal joints and metacarpal phalangeal joints), wrist and foot (metatarsal phalangeal joints) joints on both sides.

[3] Difference in medians is calculated as HCQ - Placebo. Confidence intervals (CIs) for the differences in medians were calculated using bootstrap resampling.

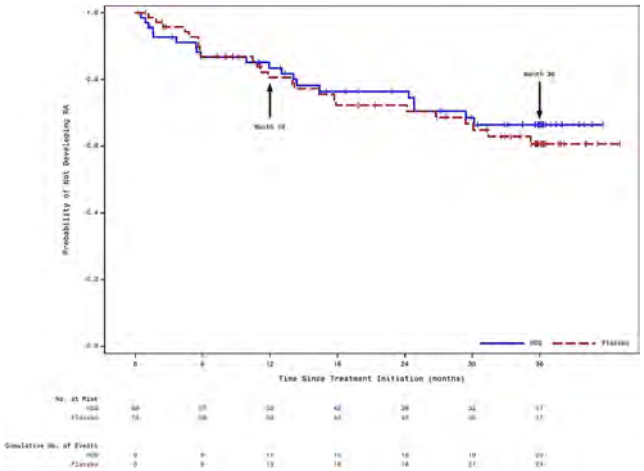


Figure. Development of clinical rheumatoid arthritis. Shown is the Kaplan-Meier based survival estimates of not developing clinical rheumatoid arthritis (clinical RA) in the modified intention-to-treat population. Tick marks indicate censored data. The number of participants at risk for development of clinical RA and the cumulative number of events in each group at each time point is given below the graph. Arrows indicate Month 12 and Month 36. In the modified intent-to-treat population, clinical RA occurred in 21 of 69 (30.4%) participants in the HCQ group and 24 of 73 (32.9%) in the placebo group. The Kaplan-Meier derived risk of clinical RA at 36 months was 0.336 with HCQ and 0.394 with placebo (difference -0.058; 95% confidence interval -0.336 to 0.220; P=0.52).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

placebo group. The Kaplan-Meier derived risk of clinical RA at 36 months was 0.336 with HCQ and 0.394 with placebo (difference -0.058; 95% confidence interval -0.336 to 0.220; P=0.52) (Figure). Results for IA were similar. The occurrence and severity of joint symptoms were not observed to differ between groups (Table 2). Adverse event incidence was similar between groups.

Conclusion: In this randomized, placebo-controlled trial involving individuals with anti-CCP3 levels ≥2 times the ULN, a 12-month course of HCQ was not effective in reducing rates of clinical RA at 36 months. No differences were observed between groups in the development of IA or symptoms. These findings demonstrate that this duration of HCQ is not beneficial to prevent clinical RA in similar populations. Moreover, given that there are costs and potential toxicities of HCQ the findings of this trial should inform the care of similar populations. Funded by the National Institute of Allergy and Infectious Diseases; ClinicalTrials.gov NCT02603146.

Disclosure: K. Deane: Inova Diagnostics, 1; **C. Striebich**: None; **M. Feser**: None; **J. O'Dell**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **J. Graf**: None; **M. McMahon**: Artiva, 2, AstraZeneca, 2, 6, Aurinia, 6, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 1, 5, 6, Novartis, 5, Roche, 1; **E. Solow**: None; **L. Forbess**: Novartis, 5; **A. Tiliakos**: None; **E. Schiopu**: None; **D. Fox**: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5; **D. Horowitz**: None; **J. Kay**: Biogen, 5, Celltrion, Inc., 2, Gate Bioscience, 2, Immunitas Therapeutics, 2, Immunovant, Inc., 2, Istesso, Ltd, 2, Kolon TissueGeje, Inc, 1, Organon, LLC, 2, Sana Biotechnology, Inc., 2, Santa Ana Bio, Inc., 2, Spyre Therapeutics, 2, Wolters Kluwer NV, 9; **C. Strickland**: None; **J. Guthridge**: None; **C. Arriens**: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **J. Grossman**: artiva, 5, exact sciences, 11, illumina, 11, iqvia, 11, Merck/MSD, 11, Novartis, 5; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5; **E. Bemis**: None; **A. Frazer-Abel**: None; **C. Fleischer**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **M. Greenleaf**: None; **K. York**: None; **S. Walker**: None; **L. Keyes-Elstein**: None; **M. Byron**: None; **J. Fedler**: None; **E. Goldmuntz**: None; **V. Holers**: None.

Abstract Number: 1675

Neuroimmune modulation in patients with active rheumatoid arthritis with an inadequate response to TNF inhibitors (TNFi)

Guillermo Valenzuela[1], Jane Box[2], Angela Crowley[3], Joshua June[4], Pendleton Wickersham[5], Jeff Peterson[6], Michael Thakor[7], Susan Kim[8], Tina Shah[9], David Chernoff[10] and John Tesser[11], [1]Integral Rheumatology & Immunology Specialists, Plantation, FL, [2]DJL Clinical Research, PLLC, Charlotte, NC, [3]Illinois Bone and Joint Institute - Hinsdale Orthopaedics, Hinsdale, IL, [4]Great Lakes Center of Rheumatology, Lansing, MI, [5]Arthritis Associates PA, San Antonio, TX, [6]Western Washington Arthritis Clinic, Seattle, WA, [7]arthritis and rheumatology, Fort Collins, CO, [8]Lehigh Valley Hospital Network, Allentown, PA, [9]Kansas City Physician Partners, Kansas City, MO, [10]SetPoint Medical, Sausalito, CA, [11]Arizona Arthritis & Rheumatology Associates, Phoenix, AZ

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments (1674–1679)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: A substantial number of patients with rheumatoid arthritis (RA) experience treatment failure, incomplete response, or intolerance to TNFis (TNFi-IR). Neuroimmune modulation using an implantable neurostimulator device to

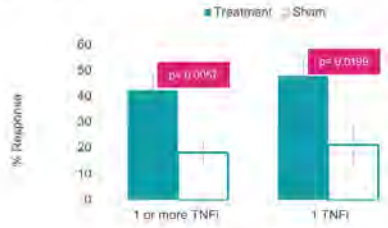
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

electrically stimulate the left cervical vagus nerve is an emerging therapeutic approach for such patients. We present a TNFi-IR subgroup analysis from the RESET-RA study (ClinicalTrials.gov, NCT04539964).

Methods: RESET-RA is a randomized, double-blind, sham-controlled study that enrolled 242 patients at 41 sites in the U.S. with moderate to severe RA, and an inadequate response or intolerance to at least 1 prior biological or targeted-synthetic DMARD. All patients were implanted with an integrated neurostimulator device and randomized 1:1 to receive either active stimulation (treatment) or sham. The primary endpoint of ACR20 response was assessed at 3 months. After 3 months, all patients crossed over to receive active stimulation during an open-label follow-up period, with results reported through 12 months. A subgroup analysis for patients only having prior exposure to TNFi therapies was performed to assess efficacy outcomes, including ACR20/50/70 response, improvement in disease activity, and adjunctive drug use in combination with stimulation.

Results: 124 patients (67 treatment; 57 sham) had exposure solely to TNFi therapies prior to enrolling. 83 (67%) had inadequate response or intolerance to 1 prior TNFi, 31 (25%) to 2 prior TNFis, and 10 (8%) to ≥3 prior TNFis. Baseline characteristics were well-balanced with mean age 55.5 years, 85.5% female, RA duration 11.7 years, 14.4 tender joints, 9.9 swollen joints (28 joint count), 5.3 DAS28-CRP, and 36.5 CDAI. ACR20 response at 3 months showed a statistically significant difference between treatment 42.4% (28/66) vs. sham 18.2% (10/55) (p=0.0057). ACR20 response at 3 months for patients with prior exposure to just 1 TNFi was even higher, with treatment 48.0% and sham 21.2% (p=0.0199) (**Figure 1**). ACR responses improved further through 12 months (**Table 1**). Other endpoints such as mean change in tender and swollen joint counts, DAS28-CRP and CDAI LDA/remission rates also favored the treatment group at 3 months and further improved through 12 months (**Figure 2**). Augmentation of therapy with a b/tsDMARD in combination with stimulation was allowed without restriction following the 3-month, controlled portion of participation. Therapy augmentation with a b/tsDMARD occurred in 7%, 11%, and 13% of all patients at months 6, 9, and 12, respectively. For treatment patients only receiving

Figure 1: ACR20 Response Rates at Month 3



ACR20 response rates for treatment and sham groups for patients exposed to 1 or more TNFi therapies (left) and exposure to 1 TNFi therapy (right) at 3 months. Patients were imputed as non-responders if missing or rescued with high-dose steroids or b/tsDMARDs.

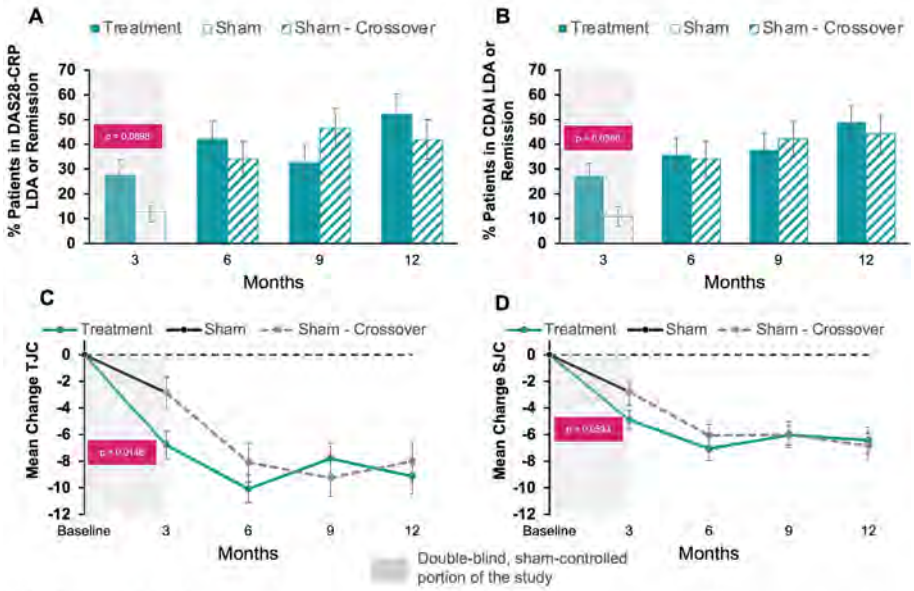
Table 1: ACR Response Rates from 3-12 Months

	Month 3		Month 6			Month 9			Month 12		
	Treatment	Sham	Treatment	Sham - Crossover	All	Treatment	Sham - Crossover	All	Treatment	Sham - Crossover	All
ACR20	42.4% (28/66)	18.2% (10/55)	54.7% (29/53)	50.0% (25/50)	52.4% (54/103)	51.9% (28/54)	60.0% (27/45)	55.6% (55/99)	60.0% (27/45)	51.2% (22/43)	56.7% (49/88)
ACR50	16.7% (11/66)	7.3% (4/55)	28.3% (15/53)	24.0% (12/50)	26.2% (27/103)	27.8% (15/54)	28.9% (13/45)	28.3% (28/99)	37.8% (17/45)	34.9% (15/43)	36.4% (32/88)
ACR70	6.0% (4/66)	1.8% (1/55)	17.0% (9/53)	6.0% (3/50)	11.7% (12/103)	13.0% (7/54)	13.3% (6/45)	13.1% (13/99)	15.6% (7/45)	14.0% (6/43)	14.8% (13/88)

ACR response rates for treatment group for patients exposed to 1 or more TNFi therapies at 3, 6, 9, and 12 months. Patients were imputed as non-responders if missing or rescued with high-dose steroids or b/tsDMARDs up to 3 months. Month 6, 9, and 12 results exclude patients that augmented stimulation therapy with high-dose steroids or b/tsDMARD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Disease Activity and Mean Change in Joint Counts through Month 12



DAS28-CRP LDA/remission rates (A), CDAI LDA/remission rates (B), mean change in the number of tender joints (C), and mean change in the number of swollen joints (D) shown at 3, 6, 9, and 12 months. Patients imputed as non-responders if missing or rescued with high-dose steroids or b/tsDMARDs up to 3 months. Month 6, 9, and 12 results exclude patients that augmented stimulation therapy with high-dose steroid or b/tsDMARD.

stimulation (i.e., non-augmented), ACR20/50/70 response rates at 12 months were 60%, 38% and 16% respectively, with 52% and 49% achieving LDA or remission per DAS28-CRP and CDAI scores, respectively.

Conclusion: In a population of RA patients previously treated with only TNFi therapies, neuroimmune modulation using an implantable device to stimulate the left vagus nerve had statistically significant and clinically meaningful improvements in efficacy at 3 months, with durable improvements through 12 months. Neuroimmune modulation provides a differentiated, non-pharmaceutical treatment option for RA in patients with inadequate response to TNFi therapy.

Disclosure: G. Valenzuela: AbbVie, 1, 2, 2, 6, 6, Alexion, 1, 2, Amgen, 1, 2, 6, Artiva Biotherapeutics, 2, 5, AstraZeneca, 6, Boehringer-Ingelheim, 1, 2, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 1, 2, 6, Centocor, 6, Eli Lilly, 1, 2, 6, Esaote, 1, Exagen, 1, 2, Genentech, 1, 2, 6, Gilead, 1, 2, Global Healthy Living Foundation, 1, 2, Horizon, 1, 2, 6, Image Analysis Group, 1, Janssen, 1, 2, 6, Mallinckrodt, 5, 6, Merck, 1, 2, Novartis, 1, 2, 6, Pfizer, 1, 2, 6, Pharmacia, 1, 2, 6, Radius, 6, Regeneron, 1, 2, 6, Sandoz, 1, 2, Sanofi, 1, 2, 6, Takeda, 6, Theramex, 6, UCB, 1, 2, 6, Vividion therapeutics, 1, 2; **J. Box**: Setpoint, 5; **A. Crowley**: None; **J. June**: Janssen, 2, SetPoint Medical, 2, 5; **P. Wickersham**: AbbVie/Abbott, 1, 5, 6, 7, Amgen, 6, AstraZeneca, 1, 2, 6, 7, Eli Lilly, 5, 6, Janssen, 1, 6, Novartis, 6, UCB, 1; **J. Peterson**: Amgen, 1, 2, 5, 6, 10, Arthrosi, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 1, 2, 5, 6, Johnson and Johnson, 6, Novartis, 2, SOBI, 2, UCB, 1, 6; **M. Thakor**: None; **S. Kim**: SetPoint Medical, 2; **T. Shah**: AbbVie/Abbott, 2, 5, 11, Amgen, 5, Johnson and Johnson, 5, 6, 11, Merch, 5, Novartis, 5, Tukeda, 5, UCB, 5; **D. Chernoff**: SetPoint Medical, 12,, 3, 8, 10, 11; **J. Tesser**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, 6, Celgene, 5, Eli Lilly, 2, 5, 6, Genentech, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, 6, IGM Biosciences, 5, Janssen, 2, 5, 6, Merck/MSD, 5, Novartis, 2, 5, Pfizer, 5, 6, Roche, 5, SetPoint Medical, 2, UCB, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1676

Long-Term Safety and Efficacy of Upadacitinib or Adalimumab in Patients With Rheumatoid Arthritis: 7-Year Data From the SELECT-COMPARE Study

Roy Fleischmann[1], Jerzy Swierkot[2], Patrick Durez[3], Louis Bessette[4], Xianwei Bu[5], Irina Fish[5], Andrew Gara[5], Diane Caballero[5], Charles Peterfy, MD, PhD[6], Yoshiya Tanaka[7] and Eduardo Mysler[5], [1]Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, [2]Wroclaw Medical University, Department of Rheumatology and Internal Medicine, Wroclaw, Poland, [3]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium, [4]Centre de l'Ostéoporose et de Rhumatologie de Québec, Quebec, QC, Canada, [5]AbbVie Inc., North Chicago, [6]Spire Sciences, Inc., Boca Raton, FL, [7]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments (1674–1679)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: We assessed the safety and efficacy of UPA versus ADA from SELECT-COMPARE through 7-years.

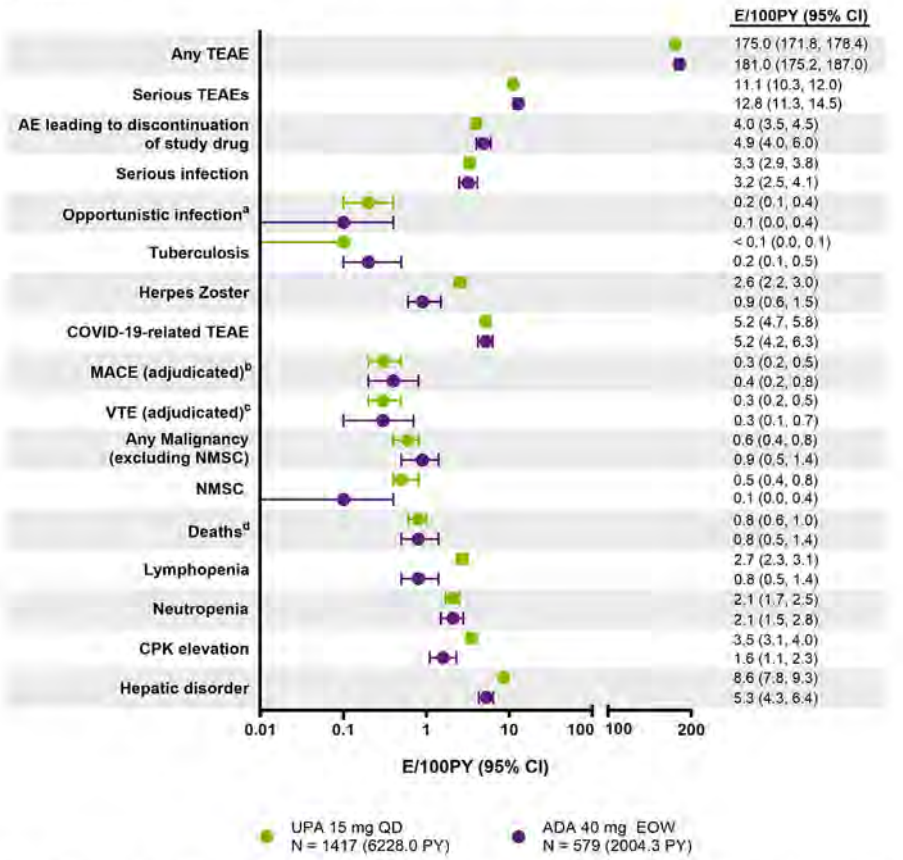
Methods: Patients with RA and an inadequate response to MTX were randomized 2:2:1 to UPA 15 mg once daily, placebo(PBO), or ADA 40 mg every other week, with patients receiving background MTX. For < 20% improvement in tender or swollen joint counts at weeks 14, 18, or 22, or failure to achieve CDAI low disease activity (LDA) by week 26, patients were switched from PBO or ADA to UPA, or from UPA to ADA. All remaining on PBO switched to UPA at week 26. Safety was evaluated by exposure-adjusted event rates of treatment-emergent adverse events (TEAEs) per 100 patient-years up to 7 years (cutoff: September 19, 2024) for all patients receiving ≥1 dose of UPA or ADA. Efficacy through ∼7 years was evaluated based on as observed data by treatment sequence on achievement of low disease activity (CDAI≤10) and remission (CDAI≤2.8), and DAS28(CRP) ≤3.2 and < 2.6.

Results: 1,629 patients (PBO, N=651;UPA, N=651; ADA, N=327) were randomized and treated. At 7 years, 820 patients remained on UPA or ADA (continuous UPA,n=216; PBO to UPA,n=338; continuous ADA, n=82; ADA to UPA, n=80;UPA toADA, n=104). UPA was generally well tolerated, displaying similar rates of overall TEAEs and most adverse events of special interest when compared to ADA (Figure 1). Most adverse events of special interest, such as MACE, VTE, and malignancies excluding nonmelanoma skin cancer (NMSC) occurred at similar rates for both treatments; UPA showed numerically higher rates of herpes zoster, creatine phosphokinase elevation, NMSC, lymphopenia, and hepatic disorders than ADA. Disease activity targets showed consistent achievement over 7 years, with >88% of patients receiving continuous UPA or ADA achieving CDAI LDA and/or DAS28(CRP) ≤ 3.2 at week 372. Generally similar proportions of patients receiving continuous UPA vs continuous ADA achieved CDAI remission and DAS28(CRP) < 2.6 over time. Numerically greater proportions of patients who switched from ADA to UPA after inadequate initial response achieved CDAI and DAS28(CRP) targets compared to those who switched from UPA to ADA. Evaluating efficacy responses by NRI, recognizing the limitation of applying NRI over long-term, randomized UPA showed greater efficacy than ADA at week 372 with higher rates of CDAI LDA (31.2% vs 23.5%), CDAI remission (21.8% vs 13.1%), DAS28(CRP) ≤ 3.2 (28.7% vs 20.8%), and DAS28(CRP) < 2.6 (26.4% vs 16.8%) (all comparisons, nominal P < .05).

Conclusion: The UPA safety profile at 7 years remained consistent to previous findings with no new safety concerns. Treatment with continuous UPA and ADA resulted in stable maintenance of disease activity targets over 7 years. In patients with an early insufficient response to their original treatment who switched to the alternate therapy, those who were switched from ADA to UPA showed numerically greater efficacy than those who switched from UPA to ADA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Exposure-Adjusted Event Rates of Treatment-Emergent Adverse Events Through 7 Years in SELECT-COMPARE



Data are for all patients receiving UPA or ADA, including exposure to rescue treatment after switching, with assignment based on drug exposure at the time of event.

[a]Excludes tuberculosis and herpes zoster.

[b]Includes cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.

[c]Defined as deep vein thrombosis and pulmonary embolism (fatal and non-fatal).

[d]Includes treatment-emergent deaths (occurring ≤ 30 days after last dose of UPA or ≤ 70 days after last dose of ADA) and non-treatment-emergent deaths (occurring > 30 days after last dose of UPA or > 70 days after last dose of ADA).

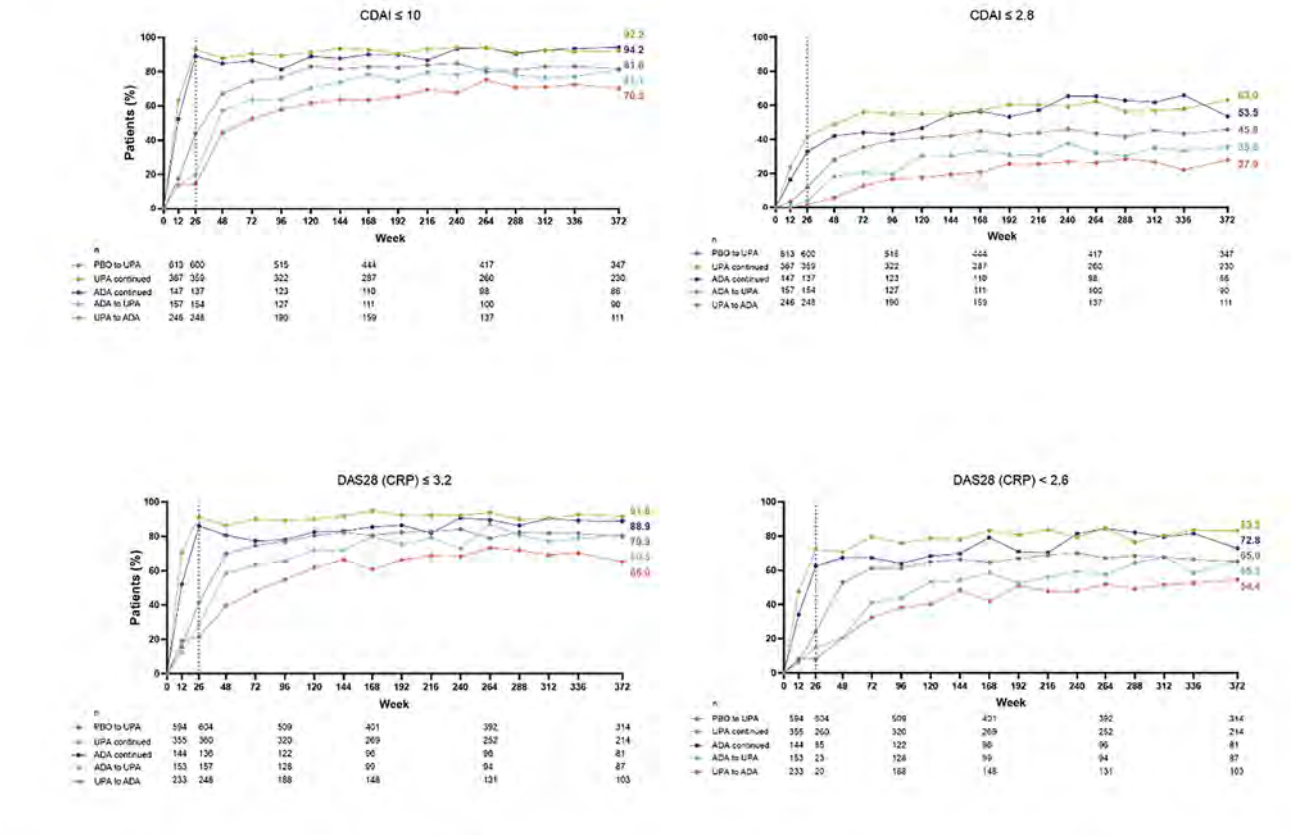
ADA, adalimumab; AE, adverse event; CPK, creatine phosphokinase; E, event; EOW, every other week; HZ, herpes zoster; NMSC, nonmelanoma skin cancer; PY, patient-year; QD, once daily; TB, tuberculosis; TEAE, treatment-emergent adverse event; UPA, upadacitinib.

1. Conaghan P, et al. Rheumatol Ther. 2022;9:191-206.
2. Fleischmann R, et al. RMD Open. 2024;10:e004007.
3. Burmester GR, et al. RMD Open. 2023;9:e002735.

Disclosure: R. Fleischmann: AbbVie/Abbott, 2, Almirall, 2, Artiva Biotherapeutics, 2, Atomwise, 2, Biohaven Pharmaceuticals, 2, Bristol-Myers Squibb(BMS), 2, Cyoxone, 2, Deep Cure, 2, Dren Bio, 2, ECOR, 2, Eli Lilly, 2, Galvani, 2, Gates Bio, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Halia, 2, ImmuneMed, 2, Immunovant, 2, InventisBio, 2, Istesso, 2, Janssen, 2, Janux, 2, Monte Rosa, 2, Novartis, 2, Overland, 2, Pfizer, 2, Synact, 2, TPG, 2, UCB, 2, Vyne, 2, Xencor, 2; **J. Swierkot**: AbbVie/Abbott, 2, 5, 6, Accord, 2, 5, 6, BMS, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sandoz, 2, 5, 6, UCB, 2, 5, 6; **P. Durez**: AbbVie/Abbott, 6, Galapagos, 6, Lilly, 6, Nordimed, 6, Thermofischer, 6; **L. Bessette**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, 5, 6, Fresenius Kabi, 2, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, TEVA, 2, 6, UCB, 2, 5, 6; **X. Bu**: AbbVie, 3, 11; **I. Fish**: AbbVie, 3, 11; **A. Gara**: AbbVie, 3, 11; **D. Caballero**: AbbVie, 3, 11; **C. Peterfy, MD, PhD**: Abbisko, 2, AbbVie/Abbott, 2, Daiichi-Sankyo, 2, Deciphera, 2, Eli Lilly, 2, Genascense, 2, Hutchmed, 2, Istesso, 2, Labcorps, 2, Nimbus, 2, Orthotrophix, 2, Paradigm, 2, Samsung Bioepois, 2, Sarepta,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Achievement of CDAI and DAS28(CRP) Disease Activity Targets Through 7 Years in SELECT-COMPARE (As Observed)



Proportions of patients attaining disease activity states through 372 weeks. Groups are by treatment sequence as observed, without imputation for missing data. All patients in the PBO group who were not previously rescued were switched to UPA at week 26.

Sample sizes (n) are shown below each graph.

ADA, adalimumab; PBO, placebo; UPA, upadacitinib.

2, SetPoint, 2, Sonoma, 2, SynOx, 2; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **E. Mysler**: AbbVie, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, AZ, 1, 2, 5, 6, BMS, 1, 2, 5, 6, Janssen, 1, 2, 5, 6, Lilly, 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Roche, 1, 2, 5, 6, SanAlpine Immunology and HI Bio, 1, 2, 5, 6, Sandoz, 1, 2, 5, 6.

Abstract Number: 1677

First line anti-TNF therapy in early rheumatoid arthritis is associated with a lower frequency of difficult-to-treat disease at five years and better long-term outcomes compared with usual care

Task Toyoda[1], Kerem Abacar[1], Farag Shuweihdi[2], Megan Sheridan[3], Jacqueline Nam[3], Ai Lyn Tan[4], Lesley-Anne Bissell[3], Paul Emery[5] and Kulveer Mankia[5], [1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, England, United Kingdom, [2]Dental Translational and Clinical Research Unit, School of Medicine, University of Leeds, Leeds, England, United Kingdom, [3]Leeds Teaching Hospitals NHS Trust, Leeds, England, United Kingdom, [4]NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds; Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, England, United Kingdom, [5]University of Leeds, Leeds, England, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments (1674–1679)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose:

While conventional synthetic DMARDs (csDMARDs) remain first line therapy in early RA, most patients do not achieve sustained remission, and a subgroup develop difficult-to-treat RA (D2TRA). More effective remission induction is achieved with first line biologic DMARDs (bDMARDs), which have a comparable safety profile to csDMARDs in clinical trials. Falling treatment costs through biosimilar use further support the health economic argument for first line bDMARD, particularly for anti-TNF drugs. Beyond early remission induction, it is important to assess whether first-line bDMARDs improve long-term outcomes compared with csDMARD treat-to-target approach.

Methods:

An Inflammatory Arthritis cohort was used to identify DMARD-naive early RA patients treated with an anti-TNF as first-line induction therapy for 12 months as part of a clinical trial. Early RA patients who received usual care with treat-to-target csDMARDs were used as controls. All patients had ≥5 years follow-up. Outcomes at 5 and 10 years were categorized as: 1) drug free remission, 2) csDMARDs only, 3) single bDMARD, 4) failure of bDMARD class or 5) failure of ≥2 mechanisms of actions (MoA) of b/tsDMARDs (EULAR D2TRA criterion #1 [1]). Rates of sustained remission (DAS28 or clinician-documented remission for ≥6 months) and time to first bDMARD were evaluated. Analyses used multinomial and binary logistic regression and Wilcoxon rank-sum test.

Results: 114 anti-TNF induction patients and 228 matched controls with RA, diagnosed between 2007-2015, were included. Baseline characteristics were similar between groups (Table 1). All cases that satisfied "failure of ≥2 MoA b/tsDMARDs" also fulfilled all three criteria of the EULAR definition for D2TRA. At 5 years, only 0.9% were D2T in the anti-TNF group compared to 7% in the controls (OR 0.11, p=0.033) (Table 2). Rates of drug free remission were also significantly higher in the anti-TNF group compared to the controls at 5 years (13.2% vs 6.1%, OR 2.25, p=0.049). Eighty-eight percent of all patients had 10-year follow-up data available. The differences in rates of D2TRA and drug free remission at 10 years were no longer apparent. However, a significantly higher proportion of patients who received anti-TNF induction therapy were on single bDMARD at 10 years compared to the csDMARD controls (27.7% vs 12.5%, OR 2.64, p=0.006). Sustained remission was more frequent in the anti-TNF group compared with controls at 10 years (62% vs 45%, adjusted OR 1.91, p=0.014). The median adjusted time to require escalation to biologic therapy was 52.5 months in the anti-TNF group compared to 39.3 months in the control group (p=0.019).

Table 1. Baseline characteristics

	csDMARD (n=228)	Anti-TNF (n=114)	p-value
Female n (%)	176 (77%)	78 (68%)	0.106
Age (years) Median (IQR)	51.0 (44.0-63.0)	50.0 (40.2-62.0)	0.073
Seropositivity* n (%)	180 (79%)	86 (75%)	0.550
Symptom Duration (months) Median (IQR)	6.0 (5.0-9.0)	6.0 (4.0-8.0)	0.103
Baseline DAS28-ESR Median (IQR)	4.48 (3.77-5.25)	4.52 (4.01-5.50)	0.221

csDMARD: conventional synthetic disease modifying anti-rheumatic drug, TNF: tumour necrosis factor, IQR: interquartile range, DAS28-ESR: disease activity score in 28 joints using erythrocyte sedimentation rate
*Anti-cyclic citrullinated peptide antibody and/or rheumatoid factor positive

Table 2. Clinical outcomes at 5 and 10 years

	5 Years				10 Years			
Clinical Outcome	csDMARD n=228 % (n)	Anti-TNF n=114 % (n)	OR (95% CI)	p-value	csDMARD n=208 % (n)	Anti-TNF n=94 % (n)	OR (95% CI)	p-value
Drug Free	6.1% (14)	13.2% (15)	2.25 (1.00–5.07)	***0.049***	10.1% (21)	12.8% (12)	1.39 (0.60–3.21)	0.441
csDMARD only	66.2% (151)	57.9% (66)	-	-	52.9% (110)	43.6% (41)	-	-
Single bDMARD	15.4% (35)	22.8% (26)	1.73 (0.94–3.18)	0.080	12.5% (26)	27.7% (26)	2.64 (1.33–5.24)	***0.006***
Failure of single bDMARD	5.3% (12)	5.3% (6)	1.08 (0.38–3.07)	0.885	13.9% (29)	9.6% (9)	0.68 (0.28–1.62)	0.381
Difficult to treat RA	7% (16)	0.9% (1)	0.11 (0.01–0.84)	***0.033***	10.6% (22)	6.4% (6)	0.72 (0.27–1.97)	0.527
Sustained Remission	54.4% (124)	64.0% (73)	1.54 (0.96-2.50)	0.079	45.2% (94)	61.7% (58)	1.91 (1.15-3.22)	***0.014***

csDMARD; conventional synthetic disease modifying anti-rheumatic drug, TNF; tumour necrosis factor, OR; odds ratio, CI; confidence interval, bDMARD; biological disease modifying anti-rheumatic drug, RA; rheumatoid arthritis

Conclusion: These data suggest first line anti-TNF induction therapy in RA is associated with better long-term outcomes compared with treat-to-target csDMARD approach with favourable health economic data. Fewer than 1% of anti-TNF treated patients were D2T at 5 years. Furthermore, fewer anti-TNF treated patients required ≥2 bDMARDs at 10 years and a higher proportion achieved sustained remission. This real-world study further highlights the potential benefits, including costs, to be realised from adopting routine first line bDMARD use in early RA.

Disclosure: T. Toyoda: None; **K. Abacar**: None; **F. Shuweihdi**: None; **M. Sheridan**: None; **J. Nam**: None; **A. Tan**: UCB, 6; **L. Bissell**: None; **P. Emery**: Abbvie, 1, Activa, 1, Anaptysbio, 1, Astra-Zeneca, 1, BMS, 1, Boehringer Ingelheim, 1, Galapagos, 1, Gedeon Richter, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, Novartis, 1; **K. Mankia**: AbbVie, 2, 6, ALLin Bio, 2, 6, AstraZeneca, 2, 5, 6, Bristol-Myers Squibb(BMS), 5, Deepcure, 2, 5, 6, Galapagos, 2, 5, Gilead, 5, Lilly, 2, 5, 6, Serac Healthcare, 2, 5, 6, UCB, 2, 6, Zura Bio, 2, 6.

Abstract Number: 1678

Abatacept in Individuals at Risk of Developing Rheumatoid Arthritis: Results from the Arthritis Prevention in the Pre-clinical Phase of RA with Abatacept Long Term Outcomes (ALTO) Study

Andrew Cope[1], Joana Vasconcelos[1], Marianna Jasenecova[2], Andrew Filer[3], Karim Raza[4], Sumera Qureshi[1], Maria Antonietta D'Agostino[5], Iain McInnes[6], Stefan Siebert[6], John Isaacs[7], Arthur Pratt[8], Benjamin A. Fisher[9], Christopher Buckley[10], Paul Emery[11], Kulveer Mankia[11], Pauline Ho[12], MAYA BUCH[13], Coziana Ciurtin[14], Dirkjan van Schaardenburg[15], Tom Huizinga[16], René Toes[16], Caroline Murphy[1], A. Toby Prevost[1] and The ALTO study investigators, [1]King's College London, London, United Kingdom, [2]King's College London, London, [3]The University of Birmingham, Birmingham, United Kingdom, [4]University of Birmingham, Birmingham, United Kingdom, [5]Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [6]University of Glasgow, Glasgow, United Kingdom, [7]Newcastle University, Newcastle upon Tyne, United Kingdom, [8]University of Newcastle, Newcastle, United Kingdom, [9]King's College London, London, UK; Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK, Birmingham, United Kingdom, [10]University of Oxford, Oxford, United Kingdom, [11]University of Leeds, Leeds, England, United Kingdom, [12]The Kellgren Centre for Rheumatology, Manchester Royal Infirmary, Manchester, United Kingdom, [13]UNIVERSITY OF MANCHESTER, MANCHESTER, United Kingdom, [14]University College London, London, [15]Amsterdam UMC, Amsterdam, Netherlands, [16]Leiden University Medical Center, Leiden, Netherlands

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments (1674–1679)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Clinical trials aimed at delaying or preventing rheumatoid arthritis (RA) in individuals at risk have been published with variable results. In the APIPPRA study, 52 weeks of treatment with abatacept reduced rates of progression to RA, effects sustained beyond the treatment period. The aim of this study was to capture long term outcomes in the ALTO study to establish whether one year of abatacept treatment prevents or delays the onset of RA in subsequent years.

Methods: APIPPRA was a phase IIB randomised, controlled trial recruiting 213 ACPA+$^{-}$ individuals with inflammatory arthralgia but no clinical synovitis. Participants were randomised to receive 52 weekly subcutaneous injections of placebo (n=103) or 125mg abatacept (n=110) and followed up for a further 52 weeks. All study participants deemed eligible and randomised to the APIPPRA study were invited to participate in the follow up study. The primary endpoint was the time to development of either clinical synovitis in ^{3} 3 joints, RA according to ACR/EULAR 2010 criteria, or time to first treatment with disease modifying anti-rheumatic drugs, whichever was met first. Primary endpoints were evaluated after stratifying for serum autoantibodies defined at the APIPPRA baseline visit. Secondary endpoints included multiple disease activity assessments. Severe adverse events and events of special interest were recorded.

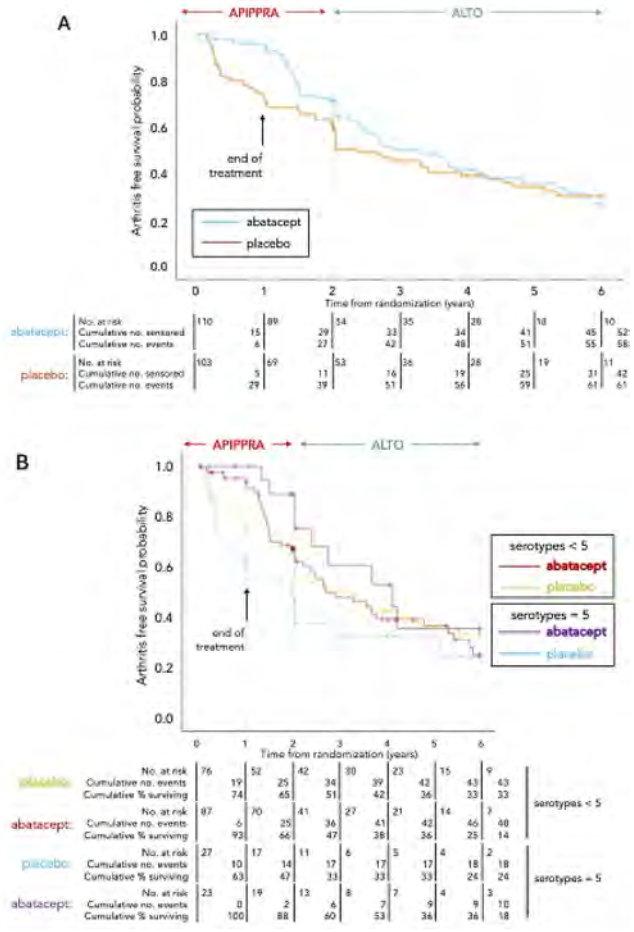


Figure 1: Kaplan-Meier arthritis-free survival curves by study arm for the combined APIPPRA and ALTO study periods for the intention to treat population (A) and stratified by baseline autoantibody status (B).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Between 26th April 2021 and 31st January 2023, 143 enrolled in ALTO; 71 randomised to abatacept and 72 to placebo. Median follow up time was 66 months (Q25-Q75: 54 – 78). At the end of follow up, there were 119 primary outcome events. By the end of the first year after randomisation, the cumulative Kaplan-Meier proportion with arthritis was 29% in the placebo arm and 6% in the abatacept arm. At the end of 2 years these were 40% and 30%, and at the end of the third and fourth years, differences between arms were 4% and 2% respectively (Figure 1A). Differences in restricted mean arthritis-free survival time up to 2 years were 3.3 months (95% CI 1.4 – 5.3; p=0.001), up to 3 years 4.4 months (95% CI 1.1 – 7.8; p=0.008), and up to 4 years 5.0 months (95% CI 0.38 – 9.8; p=0.039). Differences were no longer sustained at 5 years. Stratifying by baseline IgG ACPA levels the cumulative proportion with arthritis after 2 years was 49% in the placebo arm compared to 27% in the abatacept arm in those with levels □ 340 IU/ml; by 4 years it was 67% and 59% for placebo and abatacept, respectively. For those with an extended serotype (IgG and IgA ACPA, anti-carbamylated protein antibodies, anti-acetylated protein antibodies and RF, designated 5 serotypes), the cumulative proportion with arthritis was 53% for placebo and 12% for abatacept after 2 years, and 67% and 47% by the end of 4 years of follow up, differences sustained to 6 years (Figure 1B). There were 5 SAEs in those randomised to the abatacept arm and one in the placebo arm; none were deemed related to study drug.

Conclusion: Interception with abatacept for one year delays progression to RA for up to 4 years. Those at highest risk of progression have a more mature autoantibody response and are sensitive to T cell co-stimulation modulation. RA interception with abatacept is well tolerated, with no new safety signals emerging during follow up.

Disclosure: A. Cope: Bristol-Myers Squibb(BMS), 2, 5, 6; **J. Vasconcelos**: None; **M. Jasenecova**: Bristol-Myers Squibb(BMS), 5; **A. Filer**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 2, 5, Synact, 5; **K. Raza**: Bristol-Myers Squibb(BMS), 5; **S. Qureshi**: Bristol-Myers Squibb(BMS), 5; **M. D'Agostino**: Bristol-Myers Squibb(BMS), 5; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **S. Siebert**: AbbVie, 6, Amgen, 6, AstraZeneca, 6, BMS, 5, Boehringer-Ingelheim, 5, Eli Lilly, 5, GlaxoSmithKlein, 5, Johnson & Johnson, 5, 6, Novartis, 6, Pfizer, 6, Syncona, 6, Teijin Pharma, 6, UCB, 5, 6; **J. Isaacs**: Bristol-Myers Squibb(BMS), 5; **A. Pratt**: Bristol-Myers Squibb(BMS), 5; **B. Fisher**: Bristol-Myers Squibb(BMS), 2, Galapagos, 5, Janssen, 2, 5, Novartis, 2, Servier, 2, 5; **C. Buckley**: Bristol-Myers Squibb(BMS), 5, Mestag, 11; **P. Emery**: Abbvie, 1, Activa, 1, Anaptysbio, 1, Astra-Zeneca, 1, BMS, 1, Boehringer Ingelheim, 1, Galapagos, 1, Gedeon Richter, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, Novartis, 1; **K. Mankia**: AbbVie, 2, 6, ALLin Bio, 2, 6, AstraZeneca, 2, 5, 6, Bristol-Myers Squibb(BMS), 5, Deepcure, 2, 5, 6, Galapagos, 2, 5, Gilead, 5, Lilly, 2, 5, 6, Serac Healthcare, 2, 5, 6, UCB, 2, 6, Zura Bio, 2, 6; **P. Ho**: Bristol-Myers Squibb(BMS), 5; **M. BUCH**: Bristol-Myers Squibb(BMS), 5; **C. Ciurtin**: Bristol-Myers Squibb(BMS), 5; **D. van Schaardenburg**: Bristol-Myers Squibb(BMS), 5; **T. Huizinga**: None; **R. Toes**: Bristol-Myers Squibb(BMS), 5; **C. Murphy**: None; **A. Prevost**: None.

Abstract Number: 1679

Does First-Line b- or tsDMARDs Choice Influence Progression to Difficult-to-Treat Rhumatoid arthritis? Insights from our longitudinal RA UCLouvain Brussels cohort

Cécile VAN MULLEM[1], Francesco NATALUCCI[1], Stéphanie DIERCKX[1], Aleksandra AVRAMOVSKA[1], Tatiana SOKOLOVA[2] and Patrick Durez[1], [1]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium, [2]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Brussels Hoofdstedelijk Gewest, Belgium

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment I: Preventative and Novel Treatments (1674–1679)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: The management of Rheumatoid Arthritis (RA) has markedly advanced, enabling the achievement of disease control and remission. Nevertheless, a proportion of patients remains refractory to multiple therapies. These individuals have recently been included in the newly proposed Difficult-to-Treat (D2T) RA classification. As this concept gains traction, ongoing research is increasingly aimed at identifying the determinants of treatment resistance across bDMARDs mechanisms of action, including patient characteristics and treatment trajectories. In this study, we aimed to estimate the probability of progressing to D2T RA within our RA UCLouvain cohort and assess whether the initial choice of b- or ts-DMARDs influences this risk.

Methods: Retrospective analysis recording clinical, laboratory, radiologic, and treatment data from the first consultation available through all b/tsDMARD treatments until the last and at becoming D2T visit. Kaplan-Meier analyses and subgroup comparisons were performed based on diagnosis era and treatment strategies.

Table 1A-B. A) Comparisons of Demographic and Clinical Characteristics Between D2T and Non-D2T RA Groups B) Comparison of Clinical Characteristics in D2T RA Patients Diagnosed Before and After 2000 Legend: Values are presented as mean ± SD or % (n), unless otherwise indicated. Abbreviations: ACPA, anti-citrullinated protein antibody; RF, rheumatoid factor; DAS28, 28-joint Disease Activity Score; HAQ, Health Assessment Questionnaire; D2T RA, difficult-to-treat rheumatoid arthritis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; b/tsDMARD, biological or targeted synthetic DMARD; SD, standard deviation; ns, non specified.

	Table 1A				Table 1B		
Variable	Total (N=675)	D2T RA (n=126)	Non-D2T RA (n=549)	p-value	Before 2000 (N=39)	After 2000 (N=87)	p-value
Demographics							
Age at diagnosis, years	41.8 ± 13.5	39.5 ± 12.8	42.3 ± 14.9	**0.032**	35.8 ± 1.7	42.3 ± 1.3	**0.006**
Female, (n) %	(517) 76.6	77.0	76.5	ns	79.5%	75.9%	ns
Follow-up							
Follow-up duration, months	217.1 ± 9.8	243.1 ± 10.7	211.2 ± 5.6	**0.013**	377.4 ± 15.4	182.9 ± 7.6	ns
Time to D2T, months	na	158.1 ± 10.3	na	ns	264.9 ± 19.3	109.8 ± 7.7	**<0.001**
Serology							
ACPA positive, (n) %	(454) 70.3	74.8	69.3	ns	79.4%	72.9%	ns
RF positive, (n) %	(468) 70.2	76.0	68.8	ns	79.5%	74.4%	ns
Clinical Features							
Bone erosion at baseline, (n) %	(376) 57.3	63.9	55.8	ns	77.8%	58.1%	**0.042**
Smoker, (n) %	(152) 26.0	26.8	25.8	ns	27.0%	26.7%	ns
Disease Activity and Function							
DAS28-CRP at 1st b/tsDMARD	4.74 ± 0.05	4.97 ± 0.16	4.69 ± 0.05	ns	5.05 ± 0.34	4.95 ± 0.18	ns
HAQ at 1st b/tsDMARD	1.34 ± 0.04	1.60 ± 0.12	1.30 ± 0.04	**0.004**	1.53 ± 0.57	1.61 ± 1.05	ns
Treatment History							
Time to 1st csDMARD, months	23.4 ± 2.4	23.2 ± 5.4	23.5 ± 2.7	ns	63.1 ± 15.4	5.7 ± 2.2	**<0.001**
Time to 1st b/tsDMARD, months	135.4 ± 57.3	70.5 ± 7.8	150.1 ± 70.2	ns	155.9 ± 16.3	32.3 ± 4.5	**<0.001**
Corticosteroid before b/tsDMARD, (n) %	(432) 67.2	82.8	63.8	**<0.001**	89.7%	79.2%	ns
Methotrexate before b/tsDMARD, (n) %	(432) 67.2	85.4	88.4	ns	94.9%	81.0%	0.054

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

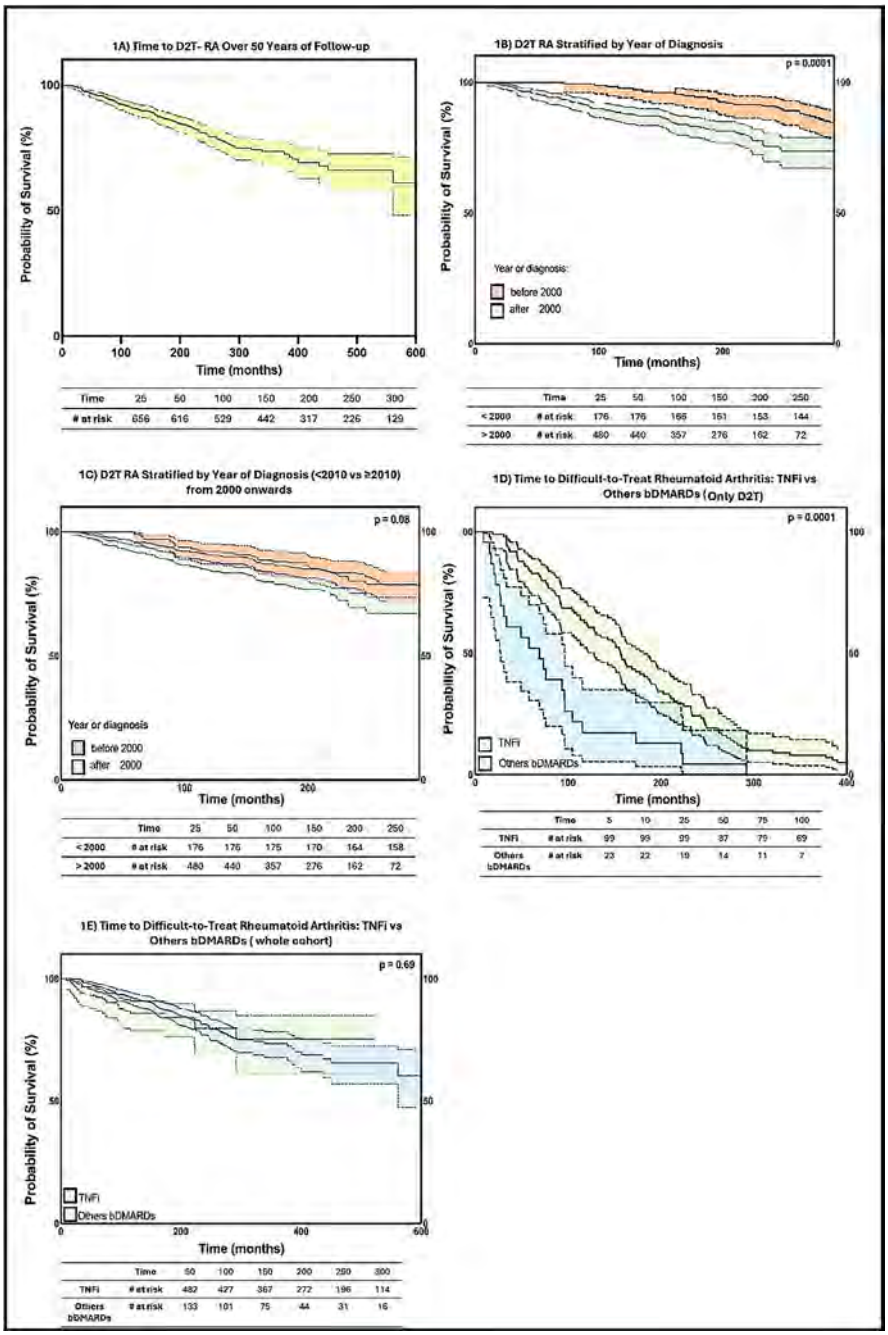


Figure 1. Progression to D2T Rheumatoid Arthritis Over Time (Kaplan–Meier Curve) Legend: Keplen – Meier curve analysis (Outcome = Becoming D2T) for: 1A) Whole cohort up to 50 years of follow up; B) Whole cohort stratified for years of diagnosis (before or after 2000); C) Whole cohort stratified for years of diagnosis (before or after 2000) without considering medical history before year 2000; D) Time to difficult to treat stratified for first line of therapy only including D2T patients; E) Time to difficult to treat stratified for first line of therapy (whole cohort).

Results: We included 675 RA patients [M/F, 158/517], with a median duration of follow-up of 217.1 ±9.8. months. 126 (18.7%) RA patients fulfilled the D2T RA definition. As shown in Table 1A, compared to non-D2T patients, the D2T group was diagnosed at a younger age (p=0.032) and had higher functional impairment (HAQ: 1.60 ± 0.12 vs. 1.30 ± 0.04; p = 0.004), and were more frequently exposed to corticosteroids before b or tsDMARD initiation (82.8% vs. 63.8% ;p< 0.001). Kaplan-Meier curves (Figure 1A-E) showed a progressive decline in D2T-free survival. Patients diagnosed after 2000 had earlier access to b or tsDMARDs (p < 0.001) (Table 1B), but D2T rates remained similar, suggesting that earlier treatment did not fully mitigate risk (Figure 1C). Treatment pathway (Figure 2A) revealed frequent transitions between mechanisms of action, particularly from anti-TNF to IL-6 and JAK inhibitors, reflecting a pattern of therapeutic escalation typical of D2T RA. A heatmap

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

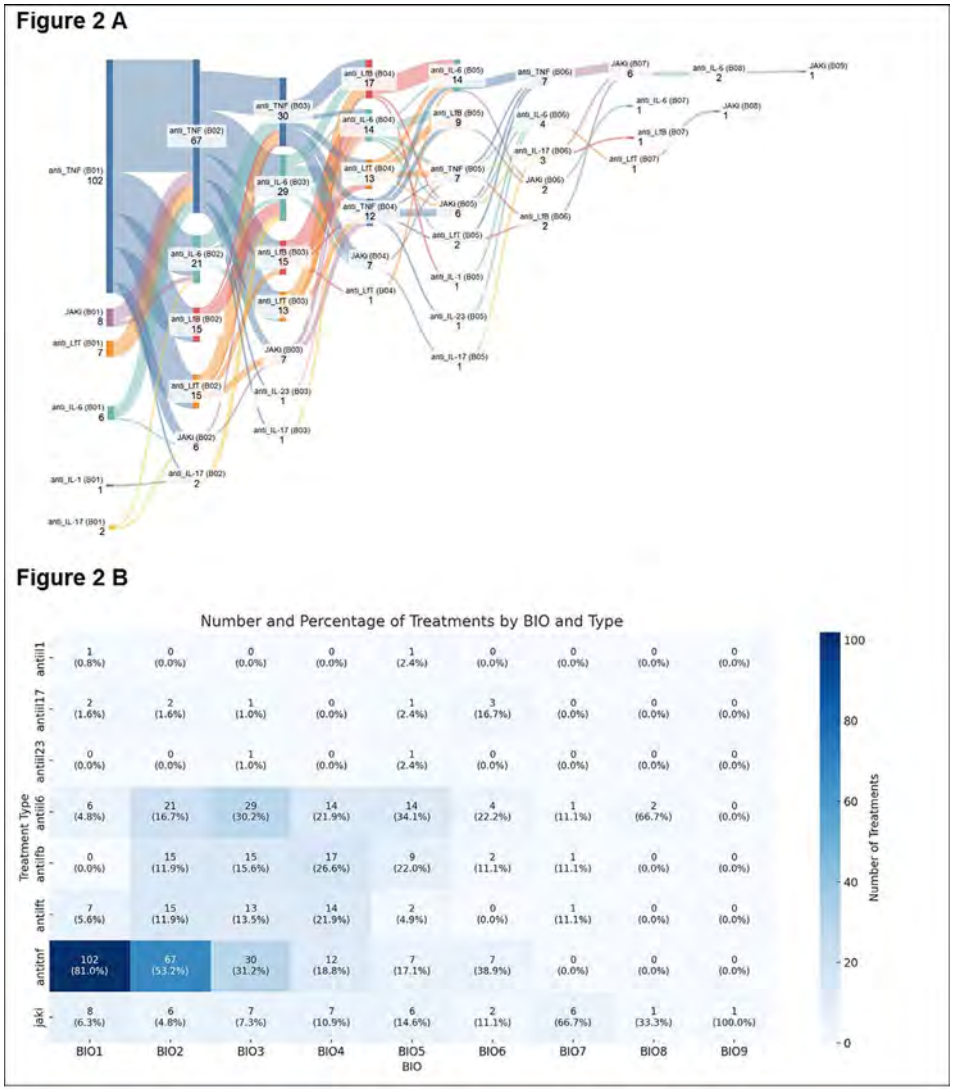


Figure 2 A-B. A) Sankey diagram of biologic transitions in D2T RA patients B) Heatmap of treatment classes by biologic line (BIO1-BIO9) Legend: A) Sankey-Plot showing b/tsDMARDs progression from the first (BIO1) to the ninth (BIO9) line of therapy. B) Heatmap for b/ts DMARDs prescription. Each cell represents the absolute (and relative, %) number of prescriptions for each treatment line

(Figure 2B) confirmed that while anti-TNFs dominated the first biologic line (81%), their use dropped markedly in later lines treatments. Analysis of reasons for treatment discontinuation showed that from the third biologic line, inefficacy—either primary or secondary—was by far the most common driver of therapeutic switches (over 80%), outweighing adverse events or other causes, underscoring the refractory nature of the disease in these patients. Importantly, D2T-free survival did not differ significantly based on the class of initial b/tsDMARD (Figure 1D-E) or whether csDMARDs were used in combination.

Conclusion: In this large cohort of 675 RA patients with a longterm follow-up, 127 RA patients developed D2T RA (18.8%). D2T patients are younger and have more functional impairment. Corticosteroid use prior to the first bDMARD was more frequent in the D2T group We did not identify a difference in the outcome (D2T) when comparing different treatment strategies comparing TNFi or other as the first line. Disease severity and persistent inflammation appears to be the primary drivers of D2T progression, rather than specific treatment strategies. Further analyses are ongoing to better define the concept of D2T RA.

Disclosure: C. VAN MULLEM: None; **F. NATALUCCI**: None; **S. DIERCKX**: None; **A. AVRAMOVSKA**: None; **T. SOKOLOVA**: None; **P. Durez**: AbbVie/Abbott, 6, Galapagos, 6, Lilly, 6, Nordimed, 6, Thermofischer, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1680

Major salivary gland ultrasonographic features of lymphoma and high lymphoproliferative risk lesions in Sjögren's Disease: a systematic review

Alen Zabotti[1], **Valeria Manfrè**[1], Maria Teresa Rizzo[1], Alessia Nano[1], Garifallia Sakellariou[2] and Luca Quartuccio[1], [1]Division of Rheumatology, Department of Medicine (DMED), Academic Hospital "Santa Maria della Misericordia", ASUFC, University of Udine, Udine, Italy, Udine, Italy, [2]Department of Internal Medicine and Therapeutics, Università Di Pavia, Pavia, Italy; Istituti Clinici Scientifici Maugeri IRCCS Pavia, Pavia, Italy

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Sjögren's Disease – Basic & Clinical Science (1680–1685)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Table 1 LYMPHOMA IN SJD

Specific ultrasonographic features of focal lesions evaluated

Main elementary feature	***Subclassification***	***Authors, year***	***n/N***
Echogenicity	Hypoechoic	Lorenzon et al., 2021	1/9
	Very hypoechoic	Lorenzon et al., 2021	8/9
Inner appearance/homogeneity	Inhomogeneous	Lorenzon et al., 2021	2/9
	Homogeneous	Lorenzon et al., 2021	7/9
Shape	Oval	Lorenzon et al., 2021	8/9
	Lobulated	Lorenzon et al., 2021	1/9
Margins	Well defined	Lorenzon et al., 2021	9/9
Presence of septa	Yes	Lorenzon et al., 2021	8/9
		Governato et al., 2022	NOS
		Fulvio et al., 2022	NOS
	No	Lorenzon et al., 2021	1/9
Hypervascularization	Yes	Lorenzon et al., 2021	8/9
Anarchic intralesional vascularization	Yes	Governato et al., 2022	NOS
High peri/intralesional doppler	Yes	Fulvio et al., 2022	NOS
Posterior acoustic features	Enhancement	Lorenzon et al., 2021	9/9
		Fulvio et al., 2022	NOS
		Governato et al., 2022	NOS
Dimension	>20 mm	Badarinza et al., 2020	8/8
Other morphological descriptions of focal lesions reported		***Authors, year***	***n/N***
Hypoechoic nodule with sonographic features of hypertrophic lymphoid structure		Zabotti et al., 2021	5/10
Limited hypoechoic area larger and/or more confluent than the remaining parenchyma		Zabotti et al., 2021	5/10
Grouped hypoechoic lesions		Baer et al., 2021	2/4
Solid cystic mass		Baer et al., 2021	1/4
Multilobulated solid mass		Baer et al., 2021	1/4
Bilateral parotid mass 17x10x17 mm and 20x7x6 mm		Feld et al., 1999	1/1
Focal hypoechoic lesions		Hüper et al., 2025	NOS
Abnormal lymph nodes		Hüper et al., 2025	NOS
Ill-defined hypoechoic area with cobblestone pattern		Makula et al., 2000	1/2
Hypoechoic macroareas		Governato et al., 2022	NOS
		Fulvio et al., 2022	NOS
SGUS scores in cases of focal lesions		***Authors, year***	***n/N***
OMERACT	≥2	Giovannini et al., 2021	10/10
OMERACT	2	Lorenzon et al., 2021	2/9
OMERACT	3	Lorenzon et al., 2021	7/9
PIH[a]	3	Makula et al., 2000	1/1
SGUS scores in cases of diffuse involvement		***Authors, year***	***n/N***
OMERACT	≥2	Giovannini et al., 2021	4/4
	2	Lorenzon et al., 2021	1/5
	3	Giovannini et al., 2024	17/17
		Lorenzon et al., 2021	4/5
Simplified Hočevar	3	Theander and Mandl, 2014	4/6
Cases of lymphoma in normal parenchyma, without any focal or diffuse involvement		***Authors, year***	***n/N***
Simplified Hočevar	0	Theander and Mandl, 2014	2/6
Adjunctive ultrasonographic features of glandular parenchyma associated with lymphoma		***Authors, year***	***% of glands***
Presence of hyperechoic bands	>50%	Badarinza et al., 2020	68,75%
Parotid surface area	>5 cm^2	Badarinza et al., 2020	100%
Shear wave elastography	>11.2 kPa	Badarinza et al., 2020	68.75%
Other examples of association between SGUS scores and lymphoma		***Authors, year***	
Regression model on OMERACT and Hočevar scores		Giovannini et al., 2024	
Simplified USS ≥ 4[b] as threshold of higher risk, no cases quantified		Jazzar et al., 2019	
Jousse Joulin core items > 13 as threshold of higher risk, quantified on 68.75 % of glands		Badarinza et al., 2020	
OMERACT expressed on total lymphomatous biopsied glands, not on lymphoma cases: 2/18 grade 2; 16/18 grade 3		Governato et al., 2022	
		Fulvio et al., 2022	

Data presented derive from studies reporting quantitative and/or qualitative measures for the question of analysis. n/N = quantitatively reported cases/ total number of focal or diffuse patterns considered in the cited studies. SJD: Sjögren's disease. NOS=Not otherwise specified. SGUS: salivary gland ultrasonography. PIH: parenchymal inhomogeneity. USS: Ultrasound scoring system

[a]De Vita et al., Clin Exp Rheumatol 1992; 10:351-6; Makula et al., Br J Rheumatol 1996;35:572-7

[b]Brown, J et al. Oral Dis 2010; 16(6), 503–504; Hočevar, et al. Rheumatology 2005; 44(6), 768–772.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Sjögren's disease (SjD) is burdened by significant lymphoproliferative risk. Up to date there is no established consensus on the salivary gland ultrasonographic (SGUS) features of lymphoma or of high lymphoproliferative risk (HLR) lesions (e.g., LELs, GCs, MESA/LESA). The aim is to systematically review existing literature on SGUS features of SjD patients complicated by SG Lymphoma or HLR lesions.

Methods: A systematic review of existing literature (SLR) (January 1988 – January 2025) was conducted according to PRISMA 2020 guidelines (Prospero registration: CRD420251008467).

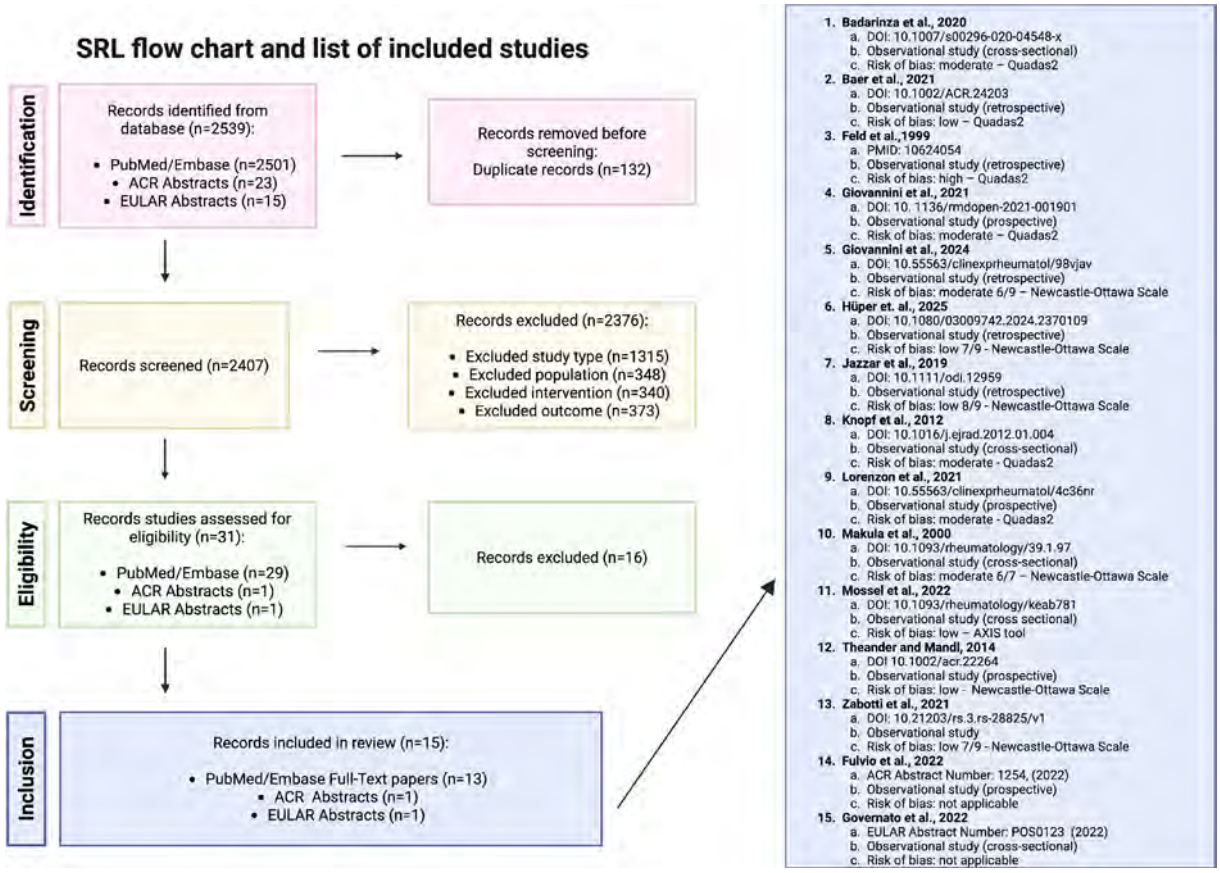
Results: 15 studies (13 full text articles, 2 international conference abstracts) were included, with a predominantly moderate-low risk of bias (Figure 1). 13/15 described SGUS features of lymphoma, considering 121 total cases. 11/13 described the presence of focal lesions in lymphomas (8/11 quantitatively), identifying 45 focal lesions on 117 cases. These lesions were described with variable features, but commonly presented as a dominant glandular hypo- to anechoic mass on SGUS (Table 1). In 3/11 studies, the parenchyma surrounding the focal lesion was also assessed, with quantitative or inferable SGUS scores indicating moderate to severe involvement in all cases (Table 1). 10/13 studies described a diffuse glandular involvement (presence of SGUS abnormalities) in lymphoma cases (7/10 quantitatively), identifying 32 cases on 105 lymphomas. 4/10 studies quantitatively reported SGUS scores, with moderate-severe involvement in most cases (Table 2). 9/15 studies described HLR lesions, with a total of 161 quantifiable cases. In 4/9 a focal lesion in HLR cases was described, resulting in 11 focal lesions on 16 HLR cases considered, with descriptions and features as heterogeneous as lymphomas. Only 1/4 studies addressed SGUS features of the surrounding parenchyma, reporting a severe grade (Tab.2). 5/9 studies

Table 2 HIGH LYMPHOPROLIFERATIVE RISK LESIONS IN SJD

Specific ultrasonographic features of focal lesions evaluated			
Main elementary feature	***Subclassification***	***Authors, year***	***n/N***
Echostructure	Very hypoechoic	Lorenzon et al., 2021	1/1
	Hypoechoic	Feld et al., 1999	1/1
		Knopf et al., 2012	6/6
Echo free area	>71%	Knopf et al., 2012	6/6
Inner appearance	Homogeneous	Lorenzon et al., 2021	1/1
Shape	Lobulated	Lorenzon et al., 2021	1/1
		Feld et al., 1999	1/1
	Oval	Knopf et al., 2012	4/6
	Round	Knopf et al., 2012	2/6
Margins	Well defined	Lorenzon et al., 2021	1/1
		Knopf et al., 2012	5/6
	Poorly defined	Knopf et al., 2012	1/6
Presence of septa	Yes	Lorenzon et al., 2021	1/1
Hypervascularization	Yes	Lorenzon et al., 2021	1/1
Capsule vascularization	Slight	Knopf et al., 2012	4/6
	Strong	Knopf et al., 2012	2/6
Posterior acoustic features	Presence of enhancement	Lorenzon et al., 2021	1/1
	Absence of enhancement	Knopf et al., 2012	6/6
Dimension	19x11x7 mm	Feld et al., 1999	1/1
	Mean area 0,67 cm2	Knopf et al., 2012	6/6
Presence of echogenic ilum		Feld et al., 1999	1/1
Other morphological descriptions of focal lesions reported		***Authors, year***	***n/N***
Grouped hypoechoic lesions		Baer et al., 2021	1/3
Solid cystic mass		Baer et al., 2021	1/3
Abnormal lymph node		Baer et al., 2021	1/3
Monolateral parotid mass		Feld et al., 1999	1/1
SGUS scores in cases of HLR lesion presenting with focality		***Authors, year***	***n/N***
OMERACT	2	Lorenzon et al., 2021	1/1
SGUS scores in cases of HLR lesions presenting with diffuse involvement		***Authors, year***	n/N
OMERACT	1	Lorenzon et al., 2021	2/3
	3	Lorenzon et al., 2021	1/3
Simplified Hočevar	1	Theander and Mandl, 2014	22/72
	2	Theander and Mandl, 2014	25/72
	3	Theander and Mandl, 2014	25/72
Cases of HRH lesions in normal parenchyma, without any focal or diffuse involvement		***Authors, year***	***n/N***
Simplified Hočevar	0	Theander and Mandl, 2014	27/99
Other examples of association between SGUS score and HLR lesions		***Authors, year***	
Regression models on OMERACT and Hočevar scores		Giovannini et al., 2024	
PGUS total score and subscore (PGUS hypo)[a] stattistical association with presence/absence of histopathological parameters		Mossel et al., 2022	

Data presented derive from studies reporting quantitative and/or qualitative measures for the question of analysis. n/N = quantitatively reported cases/ total number of focal or diffuse patterns considered in the cited studies. SJD: Sjögren's disease. NOS=Not Otherwise specified. HLR: high lymphoproliferative risk. SGUS: salivary gland ultrasonography. PGUS: parotid gland ultrasonography.
[a]Mossel E, et al. Ann Rheum Dis 2018;77: 556–62.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



reported a diffuse involvement in the absence of mention of focal lesions in HLR lesions (only 3 quantitatively), identifying 77 cases on 149 HLR lesions. 2/5 of these studies address SGUS scores reporting quantitative measures, more frequently a moderate-severe involvement (Table 2). No prospective studies define SGUS's role in detecting or predicting lymphoproliferative evolution.

Conclusion: The SLR confirms that both major salivary gland lymphoma and HLR lesions in SjD can appear as a dominant focal lesion (mostly hypo-anechoic lesion/mass), or as a diffuse involvement (mostly moderate-severe SGUS scores). SGUS features are described with highly heterogenous methodology and terminology, thus highlighting the necessity of a standardization in the reporting measures.

Disclosure: A. Zabotti: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, UCB, 2, 5; **V. Manfrè**: None; **M. Rizzo**: None; **A. Nano**: None; **G. Sakellariou**: None; **L. Quartuccio**: None.

Abstract Number: 1681

Lymphoma and Other Malignancies in Sjögren's Disease: Incidence, Predictive Factors, and Mortality Outcomes.

Olga Rusinovich[1], Zulema Plaza[2], Monica Fernandez Castro[3], Jose Rosas Gómez de Salazar[4], Victor Martinez-Taboada[5], Alex Olive[6], Belén Serrano-Benavente[7], Judit Font-Urgelles[8], Angel Garcia-Aparicio[9], Sara Manrique-Arija[10], Jesús Alberto Garcia Vadillo[11], Ruth Lopez-Gonzalez[12], Javier Narváez[13], Maria Beatriz Rodriguez[14], Carlos Galisteo[15], Jorge Juan Gonzalez Martin[16], Paloma Vela Casasempere[17], Rabadán Elena[18], Antonio Naranjo[19], Beatriz Paredes-Romero[20],

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Leyre Riancho-Zarrabeitia[21], Sheila Melchor Diaz[22], Irene Altabás-González[23], Sergi Heredia Martin[24], Clara Moriano[25], Mª Angeles Blazquez Cañamero[26], Paula Estrada-Alarcón[27], Enrique Judez[28], Nerea Alcorta Lorenzo[29], Javier Loricera[30], Rosalía Martínez Pérez[31], Fernando Sánchez-Alonso[32] and Jose Luis Andreu[33] On behalf SJÖGRENSER PROS Group, part of the Spanish Society of Rheumatology Systemic Autoimmune Diseases Study Group (EASSER), [1]Puerta de Hierro University Hospital, Boadilla del Monte, Spain, [2]Research Unit, Spanish Society of Rheumatology, Madrid, Spain, Madrid, Spain, [3]PUERTA DE HIERRO HOSPITAL, Madrid, Spain, [4]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [5]Facultad de Medicina. Universidad de Cantabria, Santander, Spain, [6]Solo practice, Barcelona, Spain, [7]Hospital Gregorio Marañon, Madrid, Spain, [8]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [9]Hospital Universitario de Toledo, Toledo, Spain, [10]Hospital Regional Universitario Mlaga, Malaga, Spain, [11]Hospital Universitario La Princesa, Madrid, Spain, [12]Zamora Health Complex, Salamanca, Spain, [13]Hospital Universitario de Bellvitge, Barcelona, Spain, [14]Canarias University Hospital, La Laguna- Tenerife, Spain, [15]Hospital Parc Taulí, Sabadel, Sabadel, Spain, [16]HM Sanchinarro Univeristary Hospital, Madrid, Spain, [17]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [18]Hospital Universitario Príncipe de Asturias, Alcala de Henares, Spain, [19]Hospital Dr Negrin, PALMAS DE GRAN CANARIA (LAS), Spain, [20]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, San Sebastian de los Reyes, Spain, [21]Rheumatology Department. Hospital Sierrallana, Torrelavega, Spain, [22]12 de Octubre University Hospital, Madrid, Spain, [23]Complejo Hospitalario de Vigo, Vigo, Spain, [24]Complex Hospitalari Moisès Broggi, Barcelona, Spain, [25]Hospital Len, LEON, Castilla y Leon, Spain, [26]Hospital Ramon y Cajal, Madrid, Spain, [27]Complex Universitari Hospital Moisès Broggi, Barcelona, Spain, [28]Albacete University Hospital, Albacete, Spain, [29]University Hospital Donostia, san sebastian, Spain, [30]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [31]Hospital Universitario Virgen de Valme, Servicio de Reumatología, Seville, Spain, [32]Sociedad Española de Reumatología, Madrid, Spain, [33]Hospital Universitario Puerta de Hierro, Majadahonda, Spain

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Sjögren's Disease – Basic & Clinical Science (1680–1685)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: The association between Sjögren's disease (SjD) and non-Hodgkin lymphoma (NHL) is well established, although reported standardized incidence ratios (SIRs) vary considerably across studies. In contrast, the risk of solid tumors in SjD remains controversial, with conflicting evidence in the literature. This study aimed to determine the SIRs for lymphoma and other malignancies (both hematologic and solid tumors) in patients with SjD, identify independent predictors of cancer development, and assess the impact of malignancies on overall mortality.

Methods: We conducted a prospective, multicenter observational study including 314 patients with SjD who met the 2002 American-European Consensus Group criteria. Clinical, demographic, and serological data, as well as malignancy incidence and survival outcomes, were prospectively collected over a median follow-up of 9.5 years [IQR 9.2–9.9]. SIRs were calculated using data from the GLOBOCAN project. Independent predictors of lymphoma and other malignancies were identified through multivariate Cox regression analysis. Cancer-related mortality and its impact on overall survival were assessed using relative risk (RR) estimates.

Results: Among the 314 patients, 22 incident malignancies (7.01%) were identified: 11 hematologic (all NHL) and 11 solid tumors. The overall cancer risk was elevated (SIR: 1.68; 95% CI: 1.68–1.69). A markedly increased risk was observed for NHL (SIR: 15.36; 95% CI: 15.32–15.40) and hematologic malignancies overall (SIR: 3.55; 95% CI: 3.54–3.56), while a modest increase was seen for solid tumors (SIR: 1.54; 95% CI: 1.53–1.55). Multivariate analysis identified older age (HR: 1.06; 95% CI: 1.01–1.11), smoking (HR: 3.56; 95% CI: 1.24–10.24), lymphadenopathy (HR: 3.34; 95% CI: 1.33–8.37), splenomegaly (HR: 14.04; 95% CI: 1.36–144.51), and cryoglobulinemia (HR: 9.12; 95% CI: 1.93–43.07) as independent predictors of malignancy. Cryoglobulinemia emerged as the strongest predictor of lymphoma (HR: 11.07; 95% CI: 1.18–103.75). A prior history of cancer significantly differentiated hematologic malignancies from solid tumors (HR: 26.97; 95% CI: 1.26–418.46). Malignancies accounted for 23.8% of all deaths in the cohort (RR: 2.21; 95% CI: 1.18–4.12).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Patients with Sjögren's disease are at increased risk of developing hematologic malignancies—particularly non-Hodgkin lymphoma—and, to a lesser extent, solid tumors. Cryoglobulinemia emerged as the strongest independent predictor of lymphoma. Malignancies significantly contribute to mortality, highlighting the need for targeted surveillance and timely intervention in high-risk patients. Further research is needed to validate findings and guide personalized approaches to improve outcomes.

Disclosure: O. Rusinovich: None; **Z. Plaza**: None; **M. Fernandez Castro**: None; **J. Rosas Gómez de Salazar**: None; **V. Martinez-Taboada**: None; **A. Olive**: None; **B. Serrano-Benavente**: None; **J. Font-Urgelles**: None; **A. Garcia-Aparicio**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 1, 2, 6, UCB, 6; **S. Manrique-Arija**: None; **J. Garcia Vadillo**: None; **R. Lopez-Gonzalez**: None; **J. Narváez**: None; **M. Rodriguez**: None; **C. Galisteo**: None; **J. Gonzalez Martin**: None; **P. Vela Casasempere**: None; **R. Elena**: None; **A. Naranjo**: None; **B. Paredes-Romero**: None; **L. Riancho-Zarrabeitia**: None; **S. Melchor Diaz**: None; **I. Altabás-González**: None; **S. Heredia Martin**: None; **C. Moriano**: None; **M. Blazquez Cañamero**: Astrazeneca, 12, conference registrations, Gsk, 6, Novartis, 12, conference registrations, Rubio, 12, conference registrations; **P. Estrada-Alarcón**: None; **E. Judez**: None; **N. Alcorta Lorenzo**: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **R. Martínez Pérez**: None; **F. Sánchez-Alonso**: None; **J. Andreu**: None.

Abstract Number: 1682

Sjögren's Disease Salivary Gland Fibroblast Subsets are Proinflammatory and Aberrantly Promote Pain

Sara McCoy[1], Rachael Bogle[2], michele larsen[3], Li Chen[4], thomas pranzatelli[5], Paola Perez[6], john chiorini[7], Alan Baer[8], A. Darise Farris[9], Christopher Lessard[9], Astrid Rasmussen[9], Caroline Shiboski[10], Stephen Shiboski[10], Alexander Mikesell[3], Zachary Campbell[3], Alex Tsoi[2], Johann Gudjonsson[11] and Blake M. Warner[12], [1]University of Wisconsin–Madison, Madison, WI, [2]University of Michigan, Holland, OH, [3]University of Wisconsin, Madison, [4]University of Michigan, Ann Arbor, [5]NIH, Bethesda, [6]NIDCR, Bethesda, MD, [7]NIH, bethesda, MD, [8]Johns Hopkins University School of Medicine, Baltimore, MD, [9]Oklahoma Medical Research Foundation, Oklahoma City, OK, [10]University of California San Francisco, San Francisco, CA, [11]University of Michigan, Ann Arbor, MI, [12]National Institutes of Health, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Sjögren's Disease – Basic & Clinical Science (1680–1685)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Fibroblasts (fb) are increasingly recognized as dynamic signaling hubs in rheumatic disease, yet their contribution to Sjögren Disease (SjD) remains poorly defined. We dissect fb subpopulations, uncovering pathways by which fbs orchestrate the immunopathology of SjD.

Methods: We analyzed 3'-scRNAseq from freshly dissociated salivary gland (SG) biopsies of SjD^{SSA+} (n=15; 60,873 cells) and nonSjD^{SSA-} control subjects (n=19; 36,467 cells), using informatic approaches to predict cellular interactions (Fig 1a-b). We used 5000 plex spatial transcriptomics to corroborate the SjD enriched cell subsets and signaling hubs in a representative SjD^{SSA+} SG (FS:3). We used immunofluorescence microscopy of human SGs, murine dorsal root ganglion sensory neurons, and a pre-clinical model to quantitatively assess tactile allodynia.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

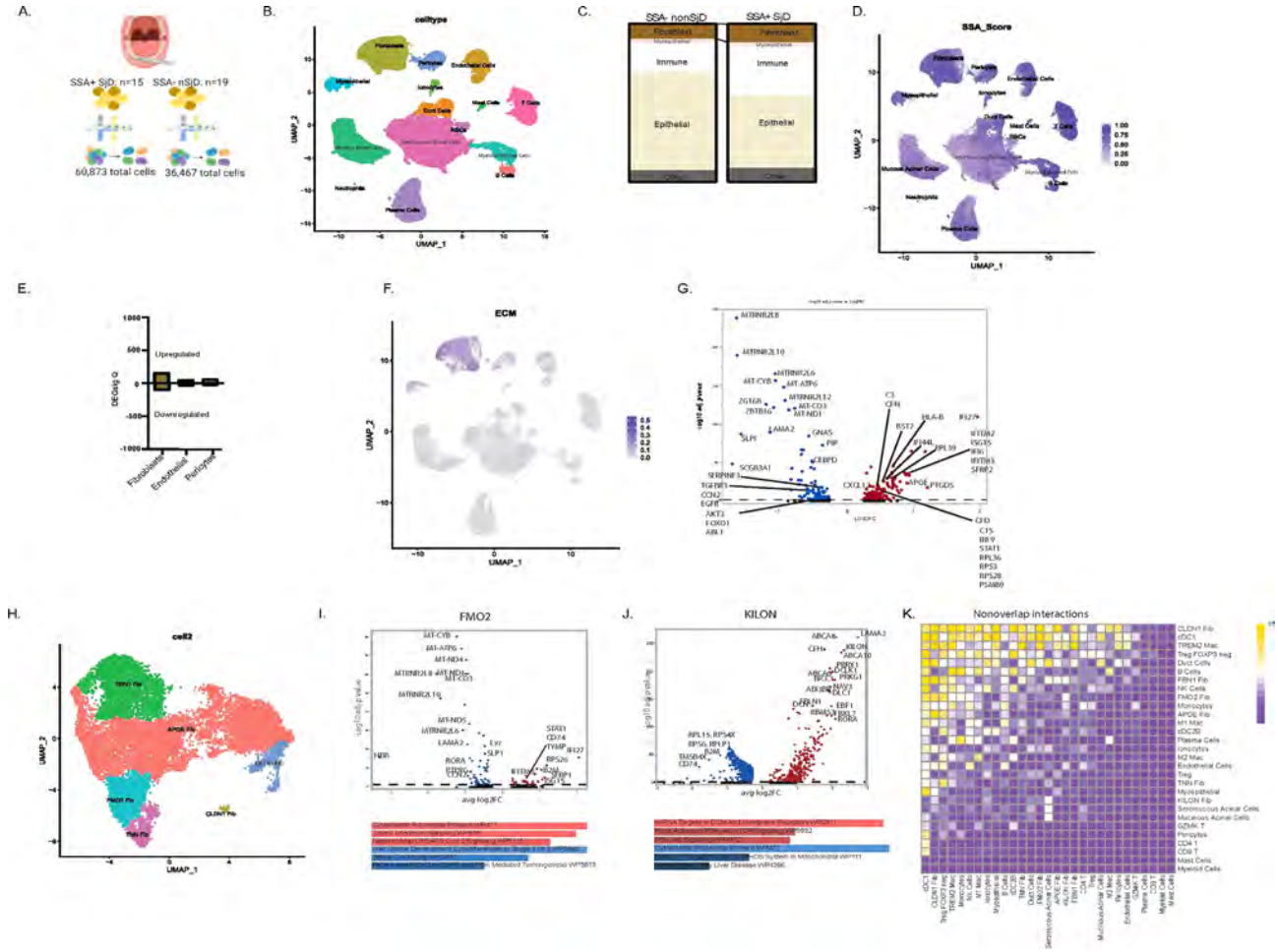


Figure 1. SSA+ SjD salivary glands fb populations with aberrant transcriptional signaling and cellular interactions. A) Schematic of our single cell analysis pipeline; B) UMAP plot of 97,340 cells colored by cell type; C) Number of cells in each population comparing SSA+ SjD to nonSjD controls; D) UMAP plot of differentially expressed transcripts in each cell subset between SSA+ SjD and nonSjD controls; E) Number of differentially expressed transcripts between SSA+ SjD and non SjD control participants by stromal cell populations (q-value ≤0.05); F) UMAP plot of differentially expressed ECM-related transcripts of each cell subset; G) Volcano plot showing top up and down regulated transcripts in SSA+ SjD fbs compared to control fbs subsets; H) Sub clustering identified six fb subsets: 1) APOE+; 2) CLDN1+; 3) FBN1+; 4) FMO2+; 5) KILON+; and 6) TNN+. I) FMO2+ fbs display greater ribosomal proteins, Type-II IFN response, and viral infection-related pathways; J) KILON+ fbs express transcripts related to axon and nerve growth and have pathways related to miRNA targets in the ECM/membrane receptors and PI3K Akt mTOR signaling. Top five upregulated (red) and downregulated (blue) pathways shown wikipathways darker and longer=more significant, corrected for sex. Pathways were selected from transcripts with q value <= 0.05; K) Based on ligand-receptor (L-R) signaling, FMO2+ fbs are predicted to signal with dendritic cells, Treg cells, monocytes, and TREM2+ macrophages more in SjD. KILON+ fbs exclusively interact with seromucous acinar more in SjD – key target cells in SjD.

Results: SG fbs are numerically expanded (Fig. 1c) in SjD^{SSA+} and exhibit more differentially expressed genes (DEGs) than control fbs (Fig. 1d–e). SjD^{SSA+} fbs upregulate extracellular matrix related transcripts (i.e., fibrosis; Fig. 1f), with pathways enriched in ribosomal proteins and interferon (IFN) signatures (Fig. 1g). Given these aberrant transcriptional profiles, we hypothesized that distinct fb subsets drive these changes. We identify six fb subsets: 1) *APOE*$^{+}$; 2) *CLDN1*$^{+}$; 3) *FBN1*$^{+}$; 4) *FMO2*$^{+}$; 5) *KILON*$^{+}$; and 6) *TNN*$^{+}$ (Fig 1h). We focus on the *FMO2*$^{+}$ fbs, with a strong IFN signature (Fig 1i), and *KILON*$^{+}$ fbs, with multiple nerve/axon related transcripts (Fig 1j). Ligand-receptor analysis predict SjD interactions between *FMO2*$^{+}$ fbs and dendritic cells, Treg cells, and macrophages/monocytes (Fig 1k), while *KILON1*$^{+}$ fbs engage with seromucous acinar cells (Fig 1k). Upstream regulator analysis of *FMO2*$^{+}$ fbs includes IFN regulatory factors and STAT1 (Fig. 2a) and signaling with *TREM2*$^{+}$ macrophages via predicted interactions such as CSF1–CSF1R (Fig. 2b). Spatial transcriptomics confirms

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

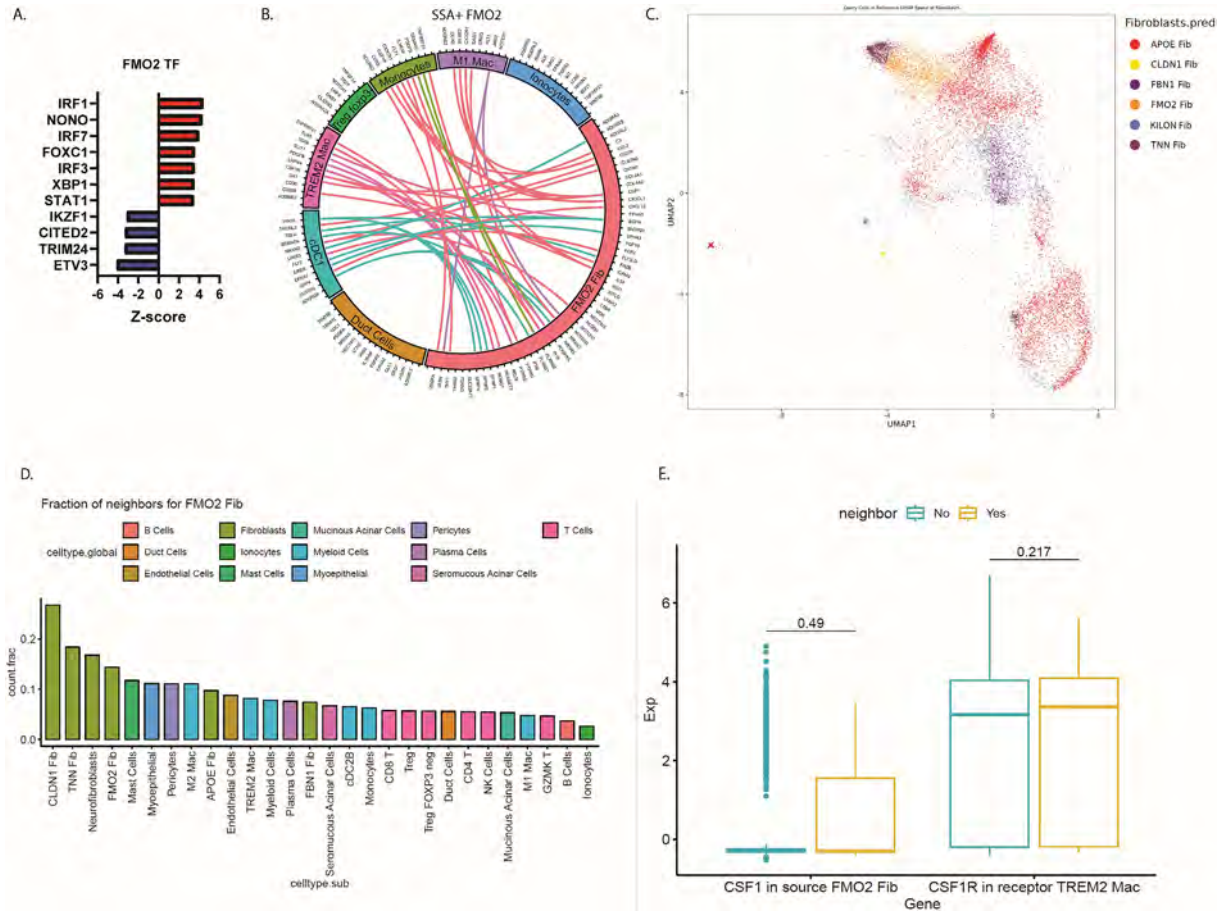


Figure 2. FMO2+ fb clusters are regulated by interferon-related transcription factors and interact with monocytes through unique ligand-receptor interactions. A) Upstream transcription factors of FMO2+ fbs involve interferon regulatory factors (IRF) and STAT1; B) FMO2+ fb interactions with TREM2 macrophages that uniquely occur in SSA+ SjD include CSF1R/CSF1; C) UMAP of fb clusters identified in a SSA+ SjD salivary gland using xenium spatial transcriptomics; D) Using xenium spatial transcriptomics, we showed that FMO2+ fb co-localize with TREM2 macrophages; E) FMO2+ fbs that co-localize with TREM2 macrophages trend toward expressing more CSF1R/CSF1.

FMO2^{+} Fbs and *TREM2*$^{+}$ macrophages colocalize in SjD SGs (Fig. 2c–d), with a trend of CSF1–CSF1R enrichment (Fig. 2e). In contrast, *KILON*$^{+}$ fbs are transcriptionally regulated by MLXIPL and MYC (Fig. 3a) and are increased in SjD^{SSA+}. Injection of recombinant human KILON increases the depolarization of mouse dorsal root ganglia neurons (Fig. 3b–e) and induces mechanical allodynia (Fig. 3f–g).

Conclusion: We characterize fb heterogeneity in SjD^{SSA+} and uncover disease-associated subsets with divergent functionality. *FMO2*$^{+}$ fbs align with previously described "immune-fbs," exhibiting IFN signaling and predicted crosstalk with *TREM2*$^{+}$ macrophages via CSF1–CSF1R, supporting macrophage survival, migration, and expansion. We identify a novel *KILON*$^{+}$ fb subset enriched for neuron/axon guidance transcripts, that causes allodynia *in vivo*. We propose two hypotheses: *KILON*$^{+}$ fbs innervate functional epithelium or contribute to neuroimmune dysregulation driving glandular dysfunction. We expand paradigms of fb function beyond structural support, positioning fbs as drivers of immune modulation and maladaptive transformation of SGs innervated by the primary afferents of sensory neurons. These findings suggest a potential molecular mechanism that underlies pain amplification in SjD patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

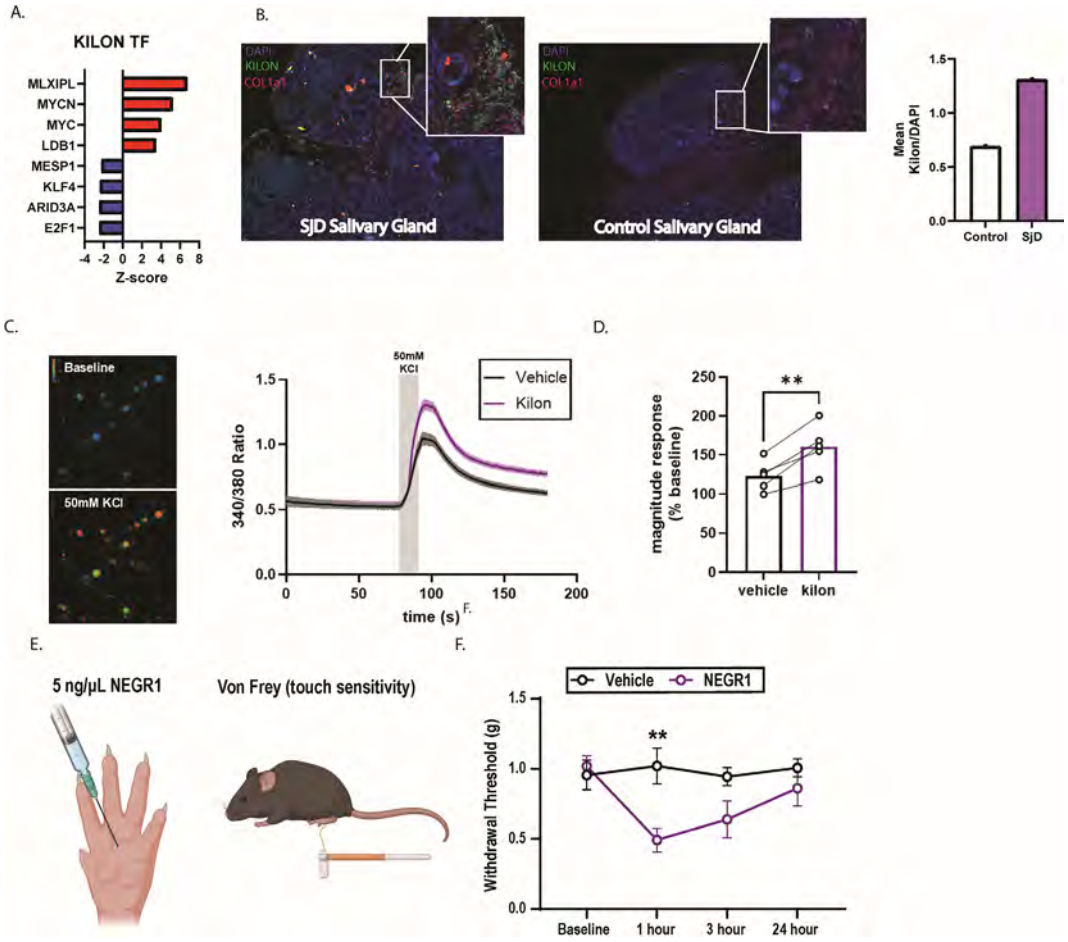


Figure 3. KILON+ fb clusters are uniquely regulated and enriched in SjD, and KILON increases pain sensitization in mice. A) Upstream transcription factors of KILON+ fbs involve and MLXIPL and MYC; B) SSA+ SjD (n=3) and control salivary glands (n=3) were stained with KILON, COL1A1 (fbs) and DAPI (nuclei). KILON was significantly higher in SjD fbs (*= p-value <0.05, determined by student's t-test); C) Dorsal root ganglion from mice were stimulated with KCl in the presence or absence of human recombinant KILON. Mouse dorsal root ganglion (cells from n=3 mice combined for analyses) were cultured in the presence of 200 ng/mL of human recombinant KILON or vehicle for two hours before proceeding to Fura Calcium imaging. Blue shows low calcium influx compared to high red calcium influx. Treatment with recombinant human KILON increases calcium influx in neurons; D) The average response of cells to depolarization increases in each animal treated with KILON (p-value determined using paired t-test); E) Representative figure of intraplantar injection of 5 ng/µL KILON and the von Frey pain test; F) Mice (n=9 animals per group; n=6 male and n=3 female) were injected with recombinant human KILON or with vehicle into the paw. At one hour, mice treated with KILON had a significantly lower withdrawal threshold than mice treated with vehicle (p-value **= ≤0.01 as determined by the repeated measures two-way ANOVA).

Disclosure: S. McCoy: Amgen, 2, Aurinia, 2, iCell, 2, Kiniksa, 2, Novartis, 2, Otsuka, 2, TearSolutions, 2, Visterra, 2; **R. Bogle**: None; **m. larsen**: None; **L. Chen**: None; **t. pranzatelli**: None; **P. Perez**: None; **j. chiorini**: None; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **A. Farris**: Johnson & Johnson Innovative Medicine, 5; **C. Lessard**: Janssen Global Services, 2, Johnson & Johnson Innovative Medicine, 2, 5; **A. Rasmussen**: Clinical Outcomes Solutions, 2, Immunovant Corporation, 2; **C. Shiboski**: None; **S. Shiboski**: None; **A. Mikesell**: None; **Z. Campbell**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **J. Gudjonsson**: None; **B. Warner**: Mitobridge, subsidiary of Astellas Bio, 5, Pfizer, Inc., 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1683

Serum APRIL Is Associated With B-Cell Activation Markers, Disease Activity, and Lymphoma Risk in Sjögren Disease (SD): Data From the prospective ASSESS Cohort

Pierre-Marie Duret[1], Pascal Schneider[2], Ludivine Robin[3], Marine Vierling[4], Nicolas Meyer[5], Valerie Devauchelle[6], Divi Cornec[7], Alain SARAUX[8], Jean Sibilia[9], Raphaele Seror[10], Yann Nguyen[11], Gaetane Nocturne[12], Laurent Mauvieux[13], Laurent Miguet[14], Xavier Mariette[15] and Jacques-eric GOTTENBERG[16], [1]Colmar General Hospital; Strasbourg University Hospital, Strasbourg, France, [2]Université de Lausanne,Département de biochimie, Lausanne, Switzerland, [3]Strasbourg University Hospital, Department of pathology, 4CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire (IBMC), Strasbourg, France Strasbourg, France;, Strasbourg, Alsace, France, [4]Strasbourg University Hospital, Department of Public Health, GMRC, Strasbourg, France,, Strasbourg, Alsace, France, [5]Strasbourg University Hospital, Department of Public Health, GMRC, Strasbourg, France, Strasbourg, Alsace, France, [6]UBO, Brest, France, [7]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, Bretagne, France, [8]CHU Brest, Brest, France, [9]Rheumatology Department, National Center for Rare autoimmune disease RESO,Strasbourg University Hospital, Strasbourg, Alsace, France, [10]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [11]Department of Internal Medicine, Beaujon Hospital, AP-HP Nord, Université Paris Cité, Clichy, France, Clichy, France, [12]University Paris Saclay, Le Kremlin Bicetre, Ile-de-France, France, [13]Strasbourg University Hospital, Laboratory hematology, Strasbourg, France,CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire (IBMC), Strasbourg, France, Strasbourg, Alsace, France, [14]Strasbourg University Hospital, Laboratory hematology, Strasbourg, France, CNRS, Immunopathologie et Chimie Thérapeutique/Laboratory of Excellence Medalis, Institut de Biologie Moléculaire et Cellulaire (IBMC), Strasbourg, France, Strasbourg, Alsace, France, [15]Université Paris-Saclay, Le Kremlin Bicetre, France, [16]Hautepierre Hospital, STRASBOURG, Alsace, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Sjögren's Disease – Basic & Clinical Science (1680–1685)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Sjögren disease (SD) is a B cell driven systemic auto-immune disease, with a need for biomarkers to better assess disease activity, risk of lymphoma and finding new therapeutic targets. While BAFF, a key B cell survival cytokine involved in precoce steps of B cell ontogeny, has been previously associated with systemic manifestations and lymphomagenesis in SD, data on a proliferation-inducing ligand (APRIL), another B cell cytokine acting in later stages of B cell ontogeny (e.g., plasmablasts and plasma cells via BCMA and TACI receptors), remain limited. This study aimed to investigate associations between APRIL, B cell biomarkers, disease activity and risk of lymphoma in SD.

Methods: Serum APRIL levels (ELISA, Invitrogen°) were assessed in 337 patients with SD from the French ASSESS cohort (17-year follow-up) and 40 healthy donors (HD). All patients met 2016 ACR/EULAR classification criteria. Patients were stratified according to the validated clustering of the ASSESS cohort: (C1) biologically active without systemic manifestations; (C2) systemic manifestations; (C3) low activity/high symptom burden; and SD-related lymphoma (incident n=9, prevalent n=16). The association between SD-related lymphoma, APRIL and lymphoma predictors at enrollment (clinESSDAI, ESSDAI, lymphocytopenia < 0.5 G/L, CD4/CD8 T cell ratio≤0.8, RF positivity, cryoglobulinemia, monoclonal component, and low C4) and other potential biomarkers (IgG levels, total gammaglobulins, immune-complexes, beta2microglobulin, kappa and lambda free light chains, quantitative [q] anti- SSA/SSB autoantibodies, digital interferon [IFN] alpha, s-FLT3, CXCL10, CCL19, CXCL13, BAFF), were analyzed in univariate and multivariate models. Multivariate analyses took into account APRIL and variables significantly associated with lymphoma in univariate analyses selected by a stepwise procedure. Estimation of incident lymphoma risk was assessed in a separate multivariate model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: APRIL levels increased across subgroups: HD (0.36 ng/mL), cluster 3 (0.34), cluster 1 (0.97), cluster 2 (1.2), lymphoma (2.33), with highest levels in incident lymphoma (2.8; p< 0.0001). In multivariate analysis, including only markers significantly associated with lymphoma in univariate analyses, APRIL expression at enrollment remained significantly associated with lymphoma (OR 1.1; 95% CI [1- 1.17] p=0.045), along with BAFF levels (mean [SD]: 1085.1 pg/ml [742.4]; per 1000 BAFF units, OR 1.75; 95% CI [1.11-2.71]; p=0.0012), CD4/CD8 ratio ≤ 0.8 (OR 4.7 95% CI [1.13-18.03]; p=0.027), low C4 (OR 5.38 95% CI [1.89-16.04]; p=0.002), lymphopenia < 0.5 G/L (OR 51.02 95% CI [4.65-611.01]; p=0.001), glandular (OR 4.95 95% CI [1.49-15.97]; p=0.007), and adenopathy (OR 6.43 95% CI [1.1-31.8]; p=0.027) domains of the ESSDAI. In a separate multivariate model, APRIL (OR 1.1 95% CI [1.01-1.21]; p=0.02) and CXCL13 (OR 1.0 95% CI [1.0-1.0]; p=0.01) were found independently associated with the risk of developing incident lymphoma.

Conclusion: These results suggest the interest of APRIL, a B-cell cytokine easily measurable in patients' sera, as a potential biomarker of SD-related lymphoma, and as a potentially relevant therapeutic target in SD.

Disclosure: P. Duret: None; **P. Schneider**: None; **L. Robin**: None; **M. Vierling**: None; **N. Meyer**: None; **V. Devauchelle**: None; **D. Cornec**: None; **A. SARAUX**: Novartis, 6; **J. Sibilia**: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **Y. Nguyen**: None; **G. Nocturne**: None; **L. Mauvieux**: None; **L. Miguet**: None; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6.

Abstract Number: 1684

Integration of Multiple Spatial Transcriptomics Reveals Novel Insights into Sjogren Disease Salivary Gland Fibroblast by Peripheral Serostatus

Zhou Fang[1], Ahmet Coskun[1] and **Sara McCoy**[2], [1]Georgia Tech, Atlanta, [2]University of Wisconsin–Madison, Madison, WI

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Sjögren's Disease – Basic & Clinical Science (1680–1685)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Anti-SSA antibody positive (SSA+ [Ro52 or Ro60]) and negative (SSA-) Sjögren disease (SjD) have differing clinical phenotypes and prognostic features; however, the pathogenesis driving these two endotypes remains unclear. We define a novel pathogenic SjD cell, fibroblasts (fbs), and shed new light on traditional pathogenic processes (Ro52/60) using integrated spatial sequencing techniques. Our objective is to define the salivary gland (SG) fibroblasts (fb) cellular neighborhoods and interactions driving pathology in SSA+ compared to SSA- SjD with a focus on Ro52/60

Methods: We performed spatial analyses with Xenium and CosMx of human SG tissue derived from 2 SSA+ and 2 SSA- patients fulfilling 2016 ACR/EULAR criteria for SjD. After data integration, we labeled cell types and proceeded to neighborhood analyses using graph attention neural networks. We performed immunofluorescence for Ro52 and Ro60 in SSA+ and SSA- SjD SG (n=9).

Results: Our data integration and analyses using Xenium and CosMX yielded nine major cell types. Next, we performed neighborhood analyses, comparing SSA+ and SSA- SjD neighborhoods and found SSA+ fbs interact most with ductal epithelial and T cells. In contrast, SSA- fbs interact with ductal epithelial cells alone. We compared neighborhoods that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

predominate in SSA+ or SSA- SjD SGs and that had similar cell subset composition. For example, neighborhood clusters 1 and 7 show plasma cells and seromucous acini neighboring with fbs; yet cluster 1 is found nearly exclusively in SSA+ samples and cluster 7 is found in SSA- SjD SGs, respectively. In the SSA+ predominant cluster 1, fb transcripts include JAK1, IRF4, and STAT6, whereas the SSA- cluster 7 fbs have important transcripts that include CXCL12/14 and IFITM3. Analyses of top differential transcripts show SSA+ fbs expressed CSF1R and CD40, whereas SSA- fbs express CCL28, IL10, and IFI6.

We used seqFISH to orthogonally identify 12 cell subsets in SSA+ and SSA- SjD SGs. We labeled our glands with Ro52 and Ro60. Ro52 expression is lower in SSA- compared to SSA+ SjD cell subsets except in T-cells, ki67 high B-cells, and follicular dendritic cells. In contrast, Ro60 expression is lower in SSA- compared to SSA+ SjD cell subsets except for basal and luminal ductal cells. Both Ro52 and Ro60 are most differentially expressed by serostatus in myoepithelial cells. SSA+ non-lymphocytes express more Ro52 than lymphocytes. This pattern is reversed in SSA- SGs. Akin to Ro52, SSA+ non-lymphocytes express more Ro60 than lymphocytes. In contrast to Ro52, SSA- non-lymphocytes express more Ro60 than lymphocytes.

Conclusion: By integrating multiple spatial profiling techniques, we identify unique fb subsets driving cellular interactions in SSA+ and SSA- SjD. Ro52/Ro60 have long been hypothesized to be central to SjD pathogenesis. For the first time, we determine cell-specific Ro52/60 expression in SSA+ compared to SSA- SGs. Ro52/Ro60 expression differs by cell subsets in SSA+ and SSA- SjD, with myoepithelial cells showing the most divergent Ro52/Ro60 expression by serostatus, a potential nidus for autoantibody formation. These findings provide new pathogenic insight into SjD fb by serostatus and gain new perspectives on Ro52 and Ro60 in a cell-specific manner.

Disclosure: Z. Fang: None; **A. Coskun**: None; **S. McCoy**: Amgen, 2, Aurinia, 2, iCell, 2, Kiniksa, 2, Novartis, 2, Otsuka, 2, TearSolutions, 2, Visterra, 2.

Abstract Number: 1685

The Sjögren's Tool for Assessing Response (STAR) demonstrates its ability to accurately detect treatment efficacy in 11 recent RCTs in Sjögren's disease

Raphaele Seror[1], Gabriel Baron[2], Elodie Perrodeau[3], Alena Piatrova[4], Hendrika Bootsma[5], Simon Bowman[6], Jacques-eric GOTTENBERG[7], Divi Cornec[8], michele Bombardieri[9], Suzanne Arends[10], Benjamin A. Fisher[11], Wolfgang Hueber[12], Antoine Sreih[13], Antonia Christodoulou[14], Andre van Maurik[15], Joel van Roon[16], Valerie Devauchelle[17], Peter Gergely[18], Xavier Mariette[19], Raphael Porcher[20] the NECESSITY WP5- STAR working group, [1]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [2]Hôtel-Dieu, Université Paris Cité, Paris, France, [3]Université Paris Descartes Sorbonne Paris Cité, Paris, France, [4]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., Paris, Ile-de-France, France, [5]UMCG, Groningen, Netherlands, [6]University Hospitals Birmingham, Birmingham, United Kingdom, [7]Hautepierre Hospital, STRASBOURG, Alsace, France, [8]Departement of Rhumatology, CHU Brest, Université de Brest, INSERM UMR1227: LBAI, Brest, France, Brest, France, [9]Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, UK, London, United Kingdom, [10]University Medical Center Groningen, Groningen, Netherlands, [11]King's College London, London, UK; Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK, Birmingham, United Kingdom, [12]Novartis Pharmaceuticals, Basel, Switzerland, [13]Cullinan Therapeutics, New York, NY, [14]BMS, Princeton, NJ, [15]GlaxoSmithKline, Stevenage, United Kingdom, [16]Center of Translational Immunology, Department of Immunology and Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht University, Utrecht PO BOX 85500, 3508 GA, Netherlands, Utrecht, Netherlands, [17]UBO, Brest, France, [18]Novartis Biomedical Research, Basel, Switzerland,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[19]Universit Paris-Saclay, Le Kremlin Bicetre, France, [20]Université Paris Cité and Université Sorbonne Paris Nord, INSERM, INRAE, Center for Research in Epidemiology and StatisticS (CRESS), Paris, France, Paris, France

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: Sjögren's Disease – Basic & Clinical Science (1680–1685)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Performance of the recently developed composite responder index STAR is highly awaited.

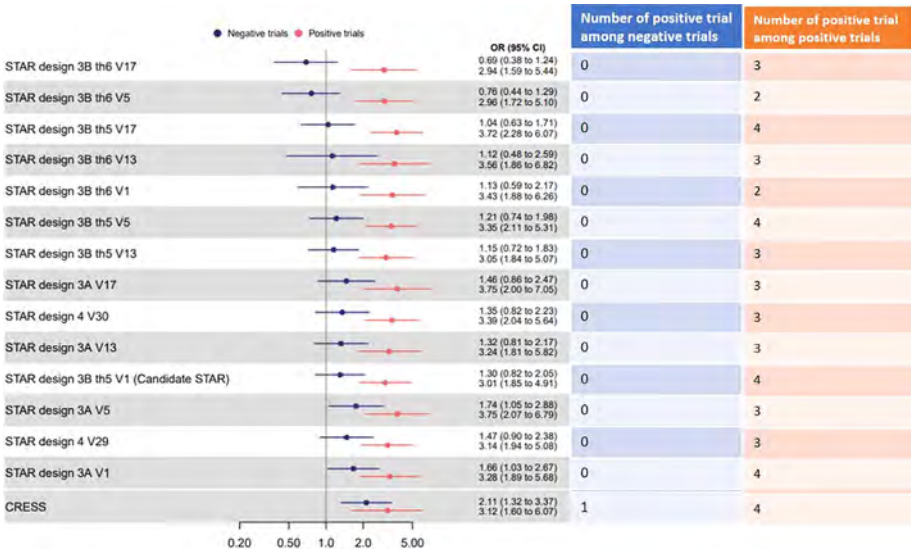
We conduscted this study to evaluate the performance of STAR in previously completed clinical trials shared within the NECESSITY consortium.

Methods: Data from 9 trials used for STAR development (Abatacept (ASAP-III), leflunomide+hydroxychloroquine (REPURP-SS) and rituximab (TEARS and TRACTISS), the iscalimab and ianalumab phase 2 trials, Baminercept, hydroxychloroquine (JOQUER), tocilizumab (ETAP)) and two other independent clinical trials (GSK (NCT02631538), Belimumab + Rituximab, Belimumab, Rituximab versus placebo and BMS Abatacept (NCT02915159). Trials were classified, by an expert panel, as positive, negative or "in between", in regards to primary and key secondary endpoints.

The STAR candidate, and its 14 alternate binary option (including the recently developed CRESS) responses were calculated retrospectively at the timing of the primary endpoint of the corresponding trial.

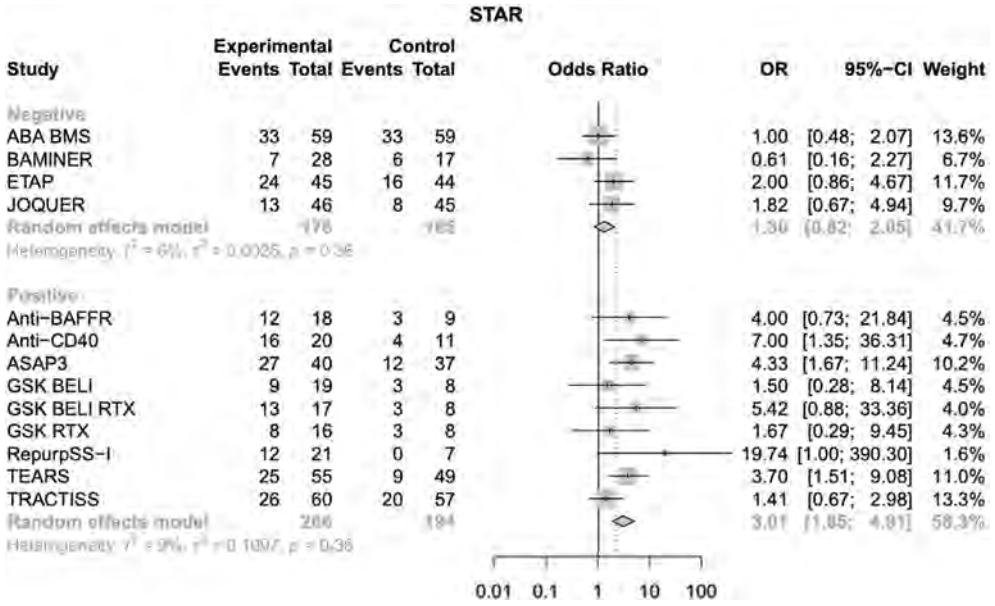
To better appraise sensitivity to change of the STAR options, meta-analyses of the 11 RCTs were run for each option, separately for positive and "in between" trials together, where positive results were expected, and negative trials, where no difference between groups was expected.

Meta-analyses were run using the Mantel-Haenszel method with Paule-Mandel estimator for τ2, Q-profile method for confidence interval of τ2and τ and continuity correction of 0.5 in studies with zero cell frequencies. Treatment effect was expressed as an odds ratio (OR): 1 or below indicates the absence of any effect, above 1 favors the experimental treatment. Consequently, a STAR option that is sensitive and specific to change should have a treatment effect close to the null effect for the negative trials, and as far from the null effect for the positive trials.



Summary of results of the meta-analyses of negative and positive trials, using as endpoint, the STAR candidate and alternate binary options

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Meta-analyses of the 4 negative and 7 positive trials using the STAR candidate as endpoint

Results: Of the 11 trials, 7 were classified as positive by the expert panel. Among these positive trials, when using STAR candidate and the 14 alternate binary options, OR ranged from 2.85 to 3.75, and the number of trials actually positive (ie, having significant between arm difference with the STAR option) ranged from 2 to 4 (figure 1 in red).

Among the 4 negative trials, when using the STAR candidate and the 14 alternate binary options, OR ranged from 0.69 to 2.11. OR was statistically significant (in favor of an effect of the treatment) in 3 STAR alternate option, which wrongly detect a difference in trial were no efficacy was observed (figure 1 in blue).

The STAR candidate displays an OR of 3.01 (1.85 - 4.91) in positive trials and 1.30 (0.82 – 2.05) in negative trials and detects significant differences in 4 of the 7 positive trials (figure 2). The CRESS displays an OR of 3.12 (1.60 – 6.07) in positive trials and 2.11 (1.32 – 3.37) in negative trials and detects significant differences in 4 of the 7 positive trials, and one of the negative trials.

Conclusion: In this analysis based on 11 trials, the STAR appears to detect treatment response accurately, with a high sensitivity to change for treatments showing a beneficial effect. Additionally, it exhibits specificity to change by not falsely detecting improvement in negative trials.

Disclosure: R. Seror: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **G. Baron**: None; **E. Perrodeau**: None; **A. Piatrova**: None; **H. Bootsma**: Bristol-Myers Squibb(BMS), 2, 5, Medimmune, 2, Novartis, 2, Roche, 2, 5, Union Chimique Belge, 2; **S. Bowman**: AbbVie/Abbott, 2, 4, Aera, 2, 4, Amgen, 2, 4, Argenx, 2, 4, AstraZeneca, 2, Aurinia, 2, 4, Bain, 2, Birmingham NIHR Biomedical Research Centre, 3, Bristol-Myers Squibb(BMS), 2, 4, EcoR1, 2, Galapagos, 2, IQVIA, 2, 4, Johnson and Johnson, 2, 4, Kiniksa, 2, 4, Novartis, 2, Royal College of Physicians (Medical Charity) and related entities, 4, Scitaris, 2; **J. GOTTENBERG**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 5, 6, CSL Behring, 6, Eli Lilly, 6, Galapagos, 6, Genzyme, 6, Gilead, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6; **D. Cornec**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Pfizer, 2, Roche, 2; **m. Bombardieri**: Amgen, 5, 12, Personal fees, GlaxoSmithKlein(GSK), 5, 12, Personal fees, Janssen, 5, 12, Personal fees, Ono Pharmaceuticals Co. Ltd, 1, 2, UCB, 12, Personal fees; **S. Arends**: argenx, 2, BMS, 2, Novartis, 2; **B. Fisher**: Bristol-Myers Squibb(BMS), 2, Galapagos, 5, Janssen, 2, 5, Novartis, 2, Servier, 2, 5; **W. Hueber**: Novartis, 3, 11; **A. Sreih**: Bristol-Myers Squibb(BMS),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3, 11; **A. Christodoulou**: Bristol-Myers Squibb, 3, 11; **A. van Maurik**: GlaxoSmithKlein(GSK), 3, 11; **J. van Roon**: None; **V. Devauchelle**: None; **P. Gergely**: Novartis, 3, 11; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **R. Porcher**: None.

Abstract Number: 1686

The Prevalence of Depressive Symptoms and Persistent Depression among Older Adults with Systemic Lupus Erythematosus (SLE)

Patti Katz[1], Sofia Pedro[2] and Kaleb Michaud[3], [1]UCSF, San Rafael, CA, [2]Forward, The National Databank for Rheumatic Diseases, Wichita, KS, [3]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: ARP I: Multidimensional Influences on Health in SLE (1686–1691)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Depression is reported to be common in SLE, but little is known about depressive symptoms among older adults with SLE. While the burden of comorbid conditions and the cumulative effects of SLE may be heightened in this group,[1] odds of depression are higher in younger age groups in the general population.[2] Screening for depression appears to be uncommon in rheumatology settings. We compared depressive symptom levels and the self-reported awareness of depression among older adults with SLE to those with RA and OA.

Methods: Data were from FORWARD, The National Databank for Rheumatic Diseases, a longitudinal observational cohort. Data are collected semiannually. Individuals with diagnosed SLE, rheumatoid arthritis (RA), and osteoarthritis (OA) were included in analyses; those with concurrent fibromyalgia were excluded. Depressive symptoms were assessed with the Patient Heath Questionnaire (PHQ)-8 over 4 survey periods. PHQ-8 scores were classified as ≥mild (≥5) or ≥moderate (≥10) levels of depressive symptoms. Persistent depression was defined as mild/moderate symptoms at ≥2 time points. Generalized estimating equation (GEE) regression analyses (unadjusted and adjusted for age, sex, education, disease duration, physical function, and pain) compared scores among the 3 groups. The proportion of individuals with notable levels of depressive symptoms who did not self-report with depression was examined.

Results: Data from 3770 participants (12,896 observations) were included (SLE n=179, obs=663; RA n=2088, obs=7792; OA n=1503, obs=4441). Mean age was 69±8 years (Table 1). Across years, with only one exception, older adults with SLE had higher PHQ-8 scores and higher frequencies of scores ≥5, and ≥10. Any occurrence of PHQ-8 scores ≥10 was seen in 21.0%, 18.2%, and 11.0% of those with SLE, RA, and OA, respectively. Persistent PHQ-8 scores ≥10 were found in 11.4%, 11.6%, and 8.2% of those with SLE, RA, and OA. GEE analyses (unadjusted and adjusted) showed significantly higher PHQ-8 scores and significantly higher prevalence of mild depressive symptoms in SLE compared to RA and OA (Table 2). Prevalence of moderate symptoms were significantly higher in SLE compared to OA in unadjusted analyses, but differences were attenuated after adjustment. In each year, at least 2/3 of those with ≥mild and about half of those with ≥moderate depressive symptoms did not self-report having depression (Table 3).

Conclusion:

Older adults with SLE appear to carry a greater burden of depressive symptoms than individuals of similar age with RA or OA, and large portions of individuals seem to be unaware of having depressive symptoms. Given this lack of awareness,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Sample characteristics by diagnosis group

	Total sample	SLE	RA	OA	
N participants	3770	179	2088	1503	
N observations	12,896	663	7792	4441	P*
Characteristics at first questionnaire in analysis					
Age, years	69.9 ± 8.0	69.3 ± 7.6	70.8 ± 8.0	68.7 ± 7.8	<0.0001
Female, %	76.2 (2874)	94.4 (169)	82.3 (1719)	65.6 (986)	0.0001
Education, years	14.8 ± 2.4	14.7 ± 2.1	14.7 ± 2.2	14.8 ± 2.6	0.66
Rheumatic Disease Comorbidity Index	1.90 ± 1.64	2.48 ± 1.69	2.04 ± 1.65	1.64 ± 1.60	<0.0001
BMI	27.9 ± 6.3	28.2 ± 7.3	28.4 ± 6.5	27.1 ± 5.9	<0.0001
Disease duration, years	22.3 ± 14.0	32.7 ± 14.4	25.5 ± 13.1	16.6 ± 13.1	<0.0001
Fatigue rating (0 – 10)	3.8 ± 3.0	4.5 ± 3.0	4.2 ± 3.0	3.2 ± 2.9	<0.0001
Pain rating (0 – 10)	3.0 ± 2.7	3.7 ± 2.8	3.5 ± 2.7	2.3 ± 2.6	<0.0001
SF-36 Physical Function subscale	42.6 ± 12.3	39.8 ± 12.2	39.2 ± 12.1	47.3 ± 11.0	<0.0001
Depressive symptoms					
PHQ-8 score, mean ± SD					
Time 1	3.9 ± 42	4.8 ± 4.3	4.3 ± 4.3	3.3 ± 4.0	<0.0001
Time 2	4.0 ± 4.1	4.9 ± 4.2	4.0 ± 3.9	3.0 ± 4.0	<0.0001
Time 3	4.0 ± 4.2	4.4 ± 4.0	4.0 ± 4.0	3.0 ± 3.7	<0.0001
Time 4	4.2 ± 4.1	4.5 ± 3.5	3.9 ± 4.0	3.3 ± 3.3	0.0032
Mild or greater depressive symptoms (PHQ-8 ≥5), % (n)					
Time 1	33.2 (1201)	41.7 (70)	36.7 (733)	27.3 (398)	<0.0001
Time 2	31.3 (758)	50.4 (65)	34.0 (508)	23.2 (185)	<0.0001
Time 3	32.1 (813)	42.9 (59)	34.5 (557)	25.3 (199)	<0.0001
Time 4	32.4 (578)	39.3 (44)	33.6 (451)	25.2 (83)	0.004
At any time	44.6 (1674)	61.4 (108)	50.4 (1041)	34.1 (508)	<0.0001
Persistent	35.0 (1306)	46.0 (81)	39.1 (807)	28.1 (418)	<0.0001
Moderate or greater depressive symptoms (PHQ-8 ≥10), % (n)					
Time 1	10.5 (380)	15.5 (26)	11.4 (228)	8.7 (127)	0.0036
Time 2	8.8 (212)	11.6 (15)	9.7 (145)	6.5 (52)	0.0177
Time 3	8.4	8.3 (11)	9.6 (155)	5.8 (46)	0.0077
Time 4	8.6 (154)	12.5 (14)	9.2 (124)	4.9 (16)	0.0131
At any time	15.7 (589)	21.0 (37)	18.2 (375)	11.0 (164)	<0.0001
Persistent	10.2 (381)	11.4 (20)	11.6 (239)	8.2 (122)	0.004

PHQ-8 = Patient Health Questionnaire-8
BMI = body mass index
SLE = Systemic lupus erythematosus, RA = rheumatoid arthritis, OA = osteoarthritis
*p-values from chi-square analyses or analyses of variance

the reported low levels of screening, and the significant impact of depression on health and well-being, results support greater attention to mental health in clinical encounters, particularly among older adults with SLE.

[1] Leiber S et al. J Rheumatol 2025; 52:145-150.

[2] Hasin D et al. JAMA Psychiatry 2018; 75:336-346

Table 2. Comparison of PHQ scores among disease group

	Unadjusted analyses		Adjusted analyses	
	LS mean from GEE	p-value	LS mean from GEE	p-value
Mean PHQ-8 score				
RA	4.35	0.02	3.88	0.03
OA	3.30	<0.0001	3.82	0.02
SLE	5.17	(reference)	4.39	(reference)
Mild or greater depressive symptoms (PHQ-8 ≥ 5)				
RA	37.3%	0.002	32.8%	0.0035
OA	27.4%	<0.0001	32.7%	0.0054
SLE	47.3%	(reference)	40.2%	(reference)
Moderate or greater depressive symptoms (PHQ-8 ≥ 10)				
RA	11.8%	0.10	9.5%	0.03
OA	7.7%	0.001	10.0%	0.13
SLE	15.7%	(reference)	13.1%	(reference)

Results from GEE analyses with SLE as the reference group.
Adjusted analyses controlled for age, sex, education, disease duration, pain, and physical function

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Proportion of individuals with at least mild/moderate depressive symptoms who do not self-report depression

	Time 1	Time 2	Time 3	Time 4
PHQ-8 ≥5				
Total	68.3% (824 / 1207)*	66.3% (510 / 769)	67.8% (559 / 825)	73.0% (430 / 589)
PHQ-8 ≥10				
Total	52.0% (204 / 392)	50.9% (108 / 220)	47.0% (103 / 219)	54.0% (88 / 163)

* Numerator = number of individuals with PHQ-8 ≥5/≥10 who do not self-report having depression.
Denominator = total number of individuals with PHQ-8 ≥5/≥10.

Disclosure: P. Katz: None; **S. Pedro**: None; **K. Michaud**: None.

Abstract Number: 1687

Body Esteem and Sexual Function in Women with Systemic Lupus Erythematosus

Hector Alejandro Martinez-Espinosa[1], Jorge Antonio Esquivel Valerio[2], Arantza Michelle Núñez-Elizondo[3], Regina Esdeyne Rivera-Villafuerte[2], Maria Eugenia Corral-Trujillo[3], Gisela Garcia-Arellano[2], Rosa Arvizu-Rivera[4], Griselda Serna-Peña[2], Dionicio A. Galarza-Delgado[5] and Jesus Alberto Cardenas-de la Garza[6], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [2]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., MONTERREY, Mexico, [3]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., Monterrey, Nuevo Leon, Mexico, [4]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico, [5]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [6]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: ARP I: Multidimensional Influences on Health in SLE (1686–1691)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: SLE predominantly affects women and is often accompanied by physical changes and psychological distress. Although both body image dissatisfaction and sexual dysfunction are reported in SLE, their relationship remains

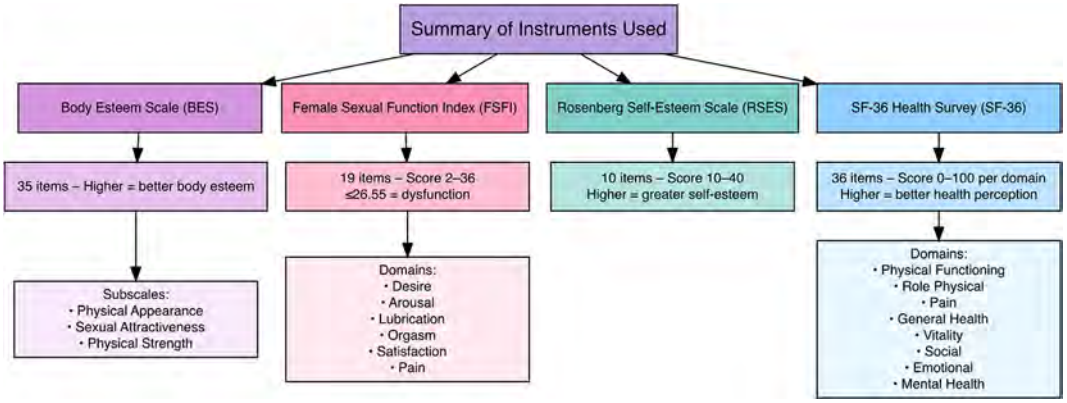


Figure 1: Flowchart detailing the instruments used (BES, FSFI, RSES, SF-36), including the number of items, score interpretation, and corresponding domains assessed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

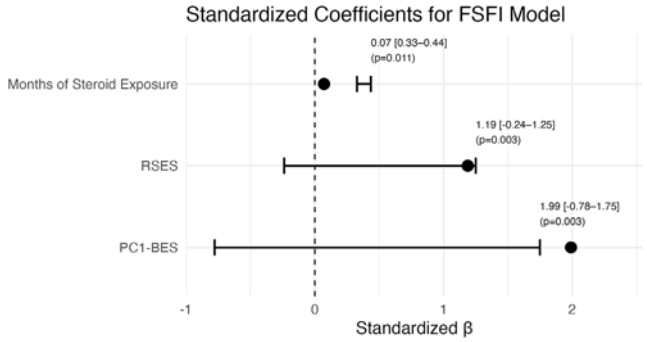


Figure 2: Forest plot of standardized regression coefficients (β) ± 95% confidence intervals for PC1-BES, RSES, and months of steroid exposure in the multivariable model predicting FSFI total score.

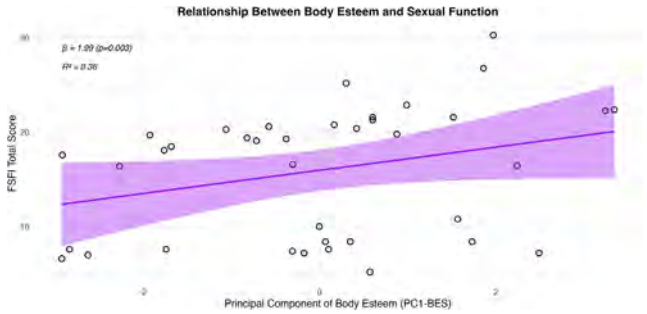


Figure 3: Scatterplot of PC1-BES versus FSFI total score with fitted regression line (β = 1.99, p = 0.003) and 95% confidence ribbon (R^2 = 0.36).

unclear. We sought to determine whether body esteem is independently associated with overall sexual function in women with SLE.

Methods: In this cross-sectional observational study, we analyzed data from 38 adult women who all met the 2019 EULAR/ACR classification criteria for SLE. Participants completed the Body Esteem Scale (BES), the Rosenberg Self-Esteem Scale (RSES), the Female Sexual Function Index (FSFI), and the SF-36 v2 questionnaire (Figure 1). Steroid exposure was measured as the total number of months the patient had received steroid treatment, from initiation to the most recent use. Principal component analysis summarized the three BES subscales into a single component: PC1-BES. We used linear regression to predict the FSFI total score and assessed interactions, nonlinearity, outliers, and subdomain effects. Statistical significance was set at α = 0.05.

Results: The mean±SD age was 35.8±12.6 years, disease duration was 7.5±6.8 years, and months of steroid exposure were 29.3±36.5 months. In the adjusted model, greater body esteem (PC1-BES) was significantly associated with higher FSFI scores (β = 1.990; 95% CI, 0.730 to 3.250; p = 0.003), independent of self-esteem (RSES; β = 1.190; 95% CI, 0.440 to 1.930; p = 0.003) and months of steroid exposure (β = 0.070; 95% CI, 0.020 to 0.130; p = 0.011). The model explained 27% of the variance in sexual function (R^2 = 0.270), with overall fit significant (F(3,34) = 6.470; p = 0.001) (Figures 2 and 3).

The interaction and non-linearity tests did not yield significant findings. Subdomain analyses revealed consistent positive associations between PC1-BES and FSFI domains of arousal, lubrication, orgasm, satisfaction, and pain (all p < 0.05). Adding the eight SF-36 subscales did not improve model performance.

Conclusion: Among 38 women with SLE, higher body esteem is independently and positively associated with overall sexual function (FSFI), independent of self-esteem (RSES) and steroid exposure. This relationship was consistent across the FSFI subdomains. Addressing concerns about body image should be considered in comprehensive SLE care to improve sexual health and quality of life. Interventions targeting body image, such as cognitive-behavioral therapy, may improve sexual health. The independent positive link observed with months of steroid exposure warrants longitudinal investigation to clarify its role.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Martinez-Espinosa: None; **J. Esquivel Valerio**: None; **A. Núñez-Elizondo**: None; **R. Rivera-Villafuerte**: None; **M. Corral-Trujillo**: None; **G. Garcia-Arellano**: None; **R. Arvizu-Rivera**: None; **G. Serna-Peña**: None; **D. Galarza-Delgado**: None; **J. Cardenas-de la Garza**: None.

Abstract Number: 1688

Impact of Stress, Anxiety, and Depression on Fatigue as moderated by Resilience and Exposure to Trauma in Rheumatology Patients

Akhila Veeravalli[1], Sankeerthana gajjala[2] and Sarath Chandra Mouli Veeravalli[3], [1]Department of Rheumatology, KIMS Hospitals, Secuderabad, India, Hyderabad, Telangana, India, [2]KIMS Hospitals, Secunderabad, India, Hyderabad, Telangana, India, [3]Dept. of Rheumatology and Clinical Immunology, KIMS Hospitals, Secunderabad, India, Hyderabad, Telangana, India

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: ARP I: Multidimensional Influences on Health in SLE (1686–1691)

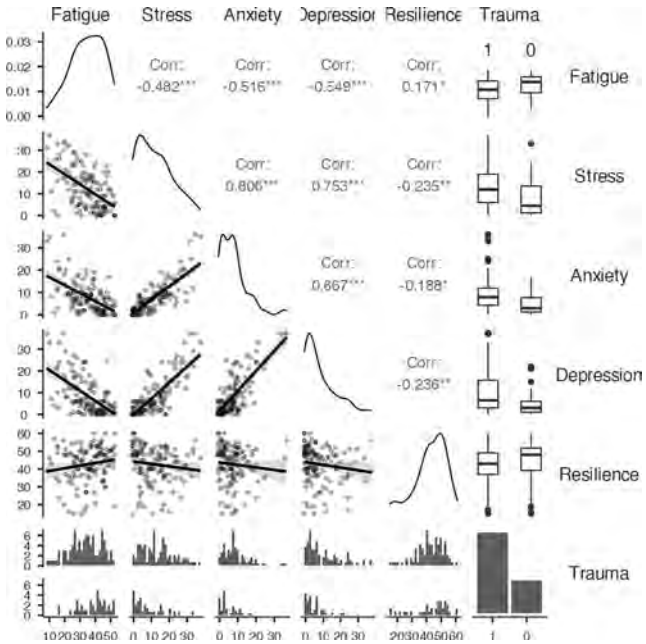
Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose:

This study aimed to examine the impact of psychological distress—specifically stress, anxiety, and depression—on fatigue in rheumatology patients, and explored how this relationship is moderated by trauma exposure and resilience. Understanding these dynamics is essential for developing holistic psychosocial interventions for individuals with chronic autoimmune disorders.

Methods: A quantitative, non-experimental comparative design with a between-groups approach was employed using convenience sampling. The sample comprised 132 participants recruited from the outpatient departments of KIMS Hospitals, Secunderabad, and HRC Hospital, Begumpet. Participants included 95 females and 37 males, aged 19 to 78 years



Spearman's Correlation Matrix among the variables.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Defined Parameters

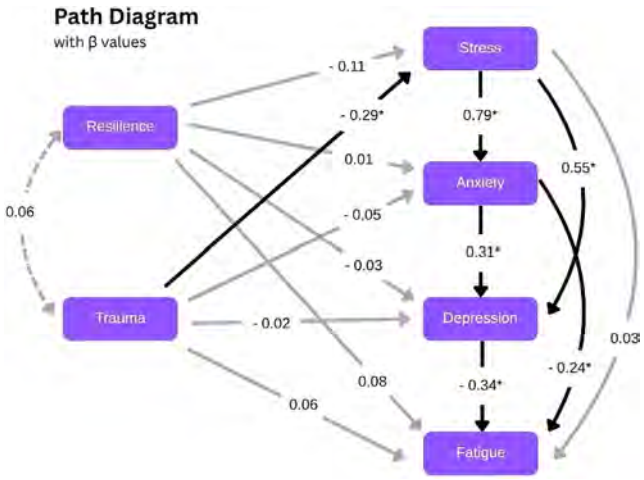
Label	Description	Parameter	Estimate	SE	95% Confidence Intervals		β	z	p
					Lower	Upper			
IE1	Stress ⇒ Anxiety ⇒ Fatigue	p8*p2	−0.210	0.110	−0.425	0.006	−0.189	−1.908	0.056
IE2	Stress ⇒ Anxiety ⇒ Depression ⇒ Fatigue	p8*p13*p3	−0.093	0.042	−0.176	−0.010	−0.084	−2.192	0.028
IE3	Stress ⇒ Depression ⇒ Fatigue	p12*p3	−0.206	0.081	−0.366	−0.047	−0.186	−2.534	0.011
IE4	Anxiety ⇒ Depression ⇒ Fatigue	p13*p3	−0.155	0.070	−0.292	−0.018	−0.106	−2.216	0.027
IE5	Resilience ⇒ Stress ⇒ Fatigue	p6*p1	0.004	0.016	−0.028	0.036	0.004	0.250	0.803
IE6	Resilience ⇒ Stress ⇒ Anxiety ⇒ Fatigue	p6*p8*p2	0.022	0.020	−0.017	0.061	0.022	1.117	0.264
IE7	Resilience ⇒ Stress ⇒ Anxiety ⇒ Depression ⇒ Fatigue	p6*p8*p13*p3	0.010	0.008	−0.007	0.026	0.010	1.166	0.244
IE8	Resilience ⇒ Stress ⇒ Depression ⇒ Fatigue	p6*p12*p3	0.022	0.018	−0.013	0.057	0.021	1.210	0.226
IE9	Resilience ⇒ Anxiety ⇒ Fatigue	p9*p2	−0.002	0.013	−0.026	0.023	−0.001	−0.120	0.904
IE10	Resilience ⇒ Anxiety ⇒ Depression ⇒ Fatigue	p9*p13*p3	−0.001	0.006	−0.012	0.010	−0.001	−0.121	0.904
IE11	Resilience ⇒ Depression ⇒ Fatigue	p11*p3	0.012	0.018	−0.023	0.047	0.012	0.683	0.494
IE12	Trauma1 ⇒ Stress ⇒ Fatigue	p7*p1	0.226	0.892	−1.523	1.974	0.010	0.253	0.800
IE13	Trauma1 ⇒ Stress ⇒ Anxiety ⇒ Fatigue	p7*p8*p2	1.234	0.737	−0.212	2.679	0.054	1.673	0.094
IE14	Trauma1 ⇒ Stress ⇒ Anxiety ⇒ Depression ⇒ Fatigue	p7*p8*p13*p3	0.547	0.295	−0.031	1.125	0.024	1.854	0.064
IE15	Trauma1 ⇒ Stress ⇒ Depression ⇒ Fatigue	p7*p12*p3	1.213	0.592	0.052	2.374	0.053	2.048	0.041
IE16	Trauma1 ⇒ Anxiety ⇒ Fatigue	p10*p2	0.271	0.322	−0.359	0.902	0.012	0.844	0.399
IE17	Trauma1 ⇒ Anxiety ⇒ Depression ⇒ Fatigue	p10*p13*p3	0.120	0.139	−0.152	0.393	0.005	0.865	0.387
IE18	Trauma1 ⇒ Depression ⇒ Fatigue	p14*p3	0.140	0.397	−0.637	0.918	0.006	0.354	0.724

Mediation Analysis (indirect effects) of the hypothesied Path Model

(M = 42.7), diagnosed with Rheumatoid Arthritis (n = 36), Spondyloarthritis (n = 32), Psoriatic Arthritis (n = 26), or Systemic Lupus Erythematosus (n = 38). A General Information Schedule was used to collect demographic data. Disease activity was assessed using DAS-28, ASDAS, cDAPSA, or SLEDAI as appropriate. Fatigue was measured using the FACIT-Fatigue Scale (Version 4). Depression, Anxiety, and Stress were assessed using the DASS-42. Trauma exposure was measured using the Brief Trauma Questionnaire (BTQ), which included items on emotional abuse, familial illness, and pregnancy-related issues. Resilience was assessed using the abbreviated Nicholson McBride Resilience Questionnaire.

Data were analyzed using JAMOVI. Descriptive statistics were calculated, and normality tested with the Shapiro-Wilk test. Inferential analyses included the Mann-Whitney U test, Kruskal-Wallis test, Spearman's correlation matrix, and path analysis using the SEMLj module.

Results: While no significant group differences were found, Spearman's correlation revealed that higher psychological distress is linked to greater fatigue, while resilience showed a protective effect, implying complex, non-linear relationships, supporting the use of structural equation modeling to clarify how resilience may buffer the impact of trauma-related distress on fatigue. The path model demonstrated excellent fit (CFI = 1.000; RMSEA = 0.000). Depression was the strongest direct predictor of fatigue (β = -0.34, p = 0.006); anxiety had a marginal effect; stress influenced fatigue only indirectly. Resilience did



The Hypothesized Path Model showing the direct and indirect effects of the studied variables

23652203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

not significantly mediate or moderate these paths, potentially due to the small, non-normally distributed sample, which may have limited power to detect subtle effects.

Conclusion: The findings underscore the critical role of psychological factors—particularly stress, anxiety, and depression—in the experience of fatigue among patients with rheumatological conditions. Trauma exerts an indirect effect, while resilience showed no significant buffering, possibly due to sample size and distribution limitations. Results support the need for integrated care. Interventions could be two-pronged: one path reducing psychological distress, the other bolstering resilience, thereby addressing fatigue from two converging angles. Future research will expand the sample and test the effectiveness of such interventions.

Disclosure: A. Veeravalli: None; **S. gajjala**: None; **S. Veeravalli**: None.

Abstract Number: 1689

Addressing Perceived Discrimination in Lupus Care: Enhancing Patient Empowerment and Health Equity Through Education and Support

Kimberly Cabrera[1], Priscilla Calvache[2], Lillian Mendez[3], Giselle Morales[4] and Jillian Rose-Smith[2], [1]Hospital for Special Surgery, New York, [2]Hospital for Special Surgery, New York, NY, [3]Patient Advocate, Carteret, NJ, [4]Hospital for Special Surgery, Glendale, NY

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: ARP I: Multidimensional Influences on Health in SLE (1686–1691)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: SLE is a life-threatening autoimmune disease that disproportionately affects African American (AA), Hispanic/Latino, & Asian populations. These communities experience serious health disparities, including more severe illness & poorer health outcomes. Research highlights that perceived racial discrimination in healthcare is a major concern among SLE patients, particularly among AA patients, contributes to lower trust in physicians, treatment adherence, & worsened health outcomes. A hospital-based support & education program conducted a survey to identify lupus patients' self-reported experiences with perceived discrimination & healthcare navigation.

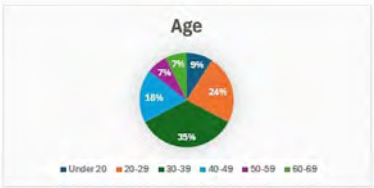
Figure 1

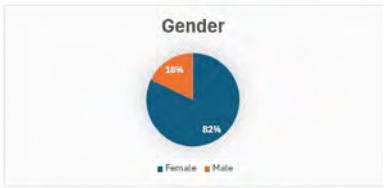
Age	Pre-Test	Post-Test	Total
Under 20	3	2	5
20-29	8	5	13
30-39	12	7	19
40-49	5	5	10
50-59	4	0	4
60-69	3	1	4

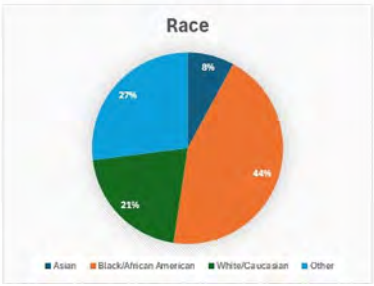
Gender	Pre-Test	Post-Test	Total
Female	29	17	46
Male	6	4	10

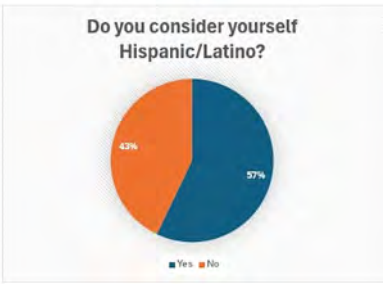
Race	Pre-Test	Post-Test	Total
Asian	3	2	5
Black/African American	17	11	28
White/Caucasian	10	3	13
Other	11	6	17

Do you consider yourself Hispanic/Latino?	Pre-Test	Post-Test	Total
Yes	20	12	32
No	15	9	24









23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2 Everyday Discrimination Scale

Pre-Test

Please think about all the times in your life when you have gotten health care. When getting health care, how often have any of the following things happened to you because of your race, ethnicity, or color?	Never	Once in a while	Sometimes	A lot	Most of the time	Almost all of the time
You are treated with less courtesy than other people	9	13	12	0	1	0
You are treated with less respect than other people	15	12	8	0	0	0
You receive poorer service than other people	14	16	5	0	0	0
A doctor or nurse acts as if he or she thinks you are not smart	19	8	5	1	2	0
A doctor or nurse acts as if he or she is afraid of you	30	2	2	0	1	0
A doctor or nurse acts as if he or she is better than you	20	8	7	0	0	0
You feel like a doctor or nurse is not listening to what you were saying	18	6	8	3	0	0

Post-Test

Please think about all the times in your life when you have gotten health care. When getting health care, how often have any of the following things happened to you because of your race, ethnicity, or color?	Never	Once in a while	Sometimes	A lot	Most of the time	Almost all of the time
You are treated with less courtesy than other people	11	6	4	0	1	0
You are treated with less respect than other people	12	6	3	1	0	0
You receive poorer service than other people	11	7	3	0	1	0
A doctor or nurse acts as if he or she thinks you are not smart	11	4	4	2	0	1
A doctor or nurse acts as if he or she is afraid of you	18	1	2	1	0	0
A doctor or nurse acts as if he or she is better than you	14	3	3	1	0	1
You feel like a doctor or nurse is not listening to what you were saying	10	6	2	2	1	1

Calculate % Reporting Discrimination

Please think about all the times in your life when you have gotten health care. When getting health care, how often have any of the following things happened to you because of your race, ethnicity, or color?	Pre-Test (35)	Post-Test (22)	% Pre	% Post	Change (%)
You are treated with less courtesy than other people	26	11	74.3%	50.0%	-24.3%
You are treated with less respect than other people	20	10	57.1%	45.5%	-11.6%
You receive poorer service than other people	21	11	60.0%	50.0%	-10.0%
A doctor or nurse acts as if he or she thinks you are not smart	16	11	45.7%	50.0%	4.3%
A doctor or nurse acts as if he or she is afraid of you	5	4	14.3%	18.2%	3.9%
A doctor or nurse acts as if he or she is better than you	15	8	42.9%	36.4%	-6.5%
You feel like a doctor or nurse is not listening to what you were saying	17	12	48.6%	54.5%	5.9%

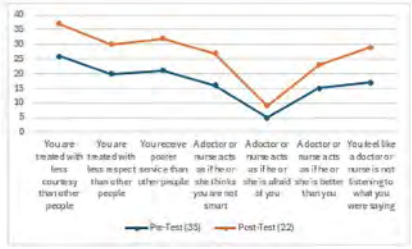


Figure 2

Methods: A pre/post-test survey, including validated scales such as the Everyday Discrimination Scale (EDS) was disseminated online to lupus patients participating in monthly support group sessions. The survey assessed key areas, including disease activity, experiences of discrimination, & patient-provider communication. A pre-test was administered at the beginning of the year, followed by 6 virtual support group meetings that provided education on recognizing & intervening when discrimination occurs in healthcare settings.

Results: A total of 37 participants completed the pre-test, and 23 completed the post-test (n=56). Most respondents (82%) identified as female. The racial breakdown included 44% Black/AA, 21% White, 57% identifying as Hispanic/Latino, 27% identifying as other races, and 8% Asian. There was a notable concentration of respondents aged 30–39 (35%). (See Figure 1)

Using the criteria that responses other than "Never" indicate a discriminatory experience, analysis of the EDS revealed a decrease () in reported discrimination experiences from pre-test to post-test. Participants who reported being treated with less courtesy by 24.3%, while reports of being treated with less respect by 11.6%. Perceived poorer service by 10% and reports of feeling that a doctor or nurse acted superior by 6.5%.

However, some areas saw slight increase (): participants reporting that a doctor or nurse did not listen by 5.9%, and those perceiving that a healthcare provider believed they were not smart by 4.3%. (See figure 2)

Conclusion: Despite limitations, this study affirms that tailored education & peer support can meaningfully reduce perceived discrimination and strengthen patient empowerment in lupus. Participants reported greater awareness, improved communication with providers, & enhanced healthcare navigation skills. These findings highlight the benefit of incorporating equity-driven, patient-centered programs into clinical & community settings to build trust, promote self-advocacy, & advance health equity for individuals living with SLE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Cabrera: None; **P. Calvache**: None; **L. Mendez**: None; **G. Morales**: None; **J. Rose-Smith**: None.

Abstract Number: 1690

Environmental Heat Exposure and Risk of Systemic Lupus Erythematosus

Jennifer Woo[1], Kaitlyn Lawrence[2] and Dale Sandler[1], [1]National Institute of Environmental Health Sciences, Durham, NC, [2]DLH, Corp., Durham, NC

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: ARP I: Multidimensional Influences on Health in SLE (1686–1691)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Environmental heat exposures have been linked to increased morbidity and mortality. Individuals with systemic lupus erythematous (SLE) often have heat- and photo- sensitivity, which may make them particularly vulnerable to environmental heat exposure. While exposure to heat has been associated with disease flares and hospitalization among individuals with SLE, it is unknown whether exposure to extreme heat is associated with incident SLE and how socioeconomic factors may impact the association.

Methods: We use data from 48,934 eligible participants in the Sister Study, a prospective breast cancer cohort in the US aged 35 to 74 (enrollment: 2003-2009). Eligible participants had no prior history of SLE and had heat exposure data linked to their residential address at enrollment. Incident SLE was self-reported during follow-up through October 2022. PRISM weather data were obtained at 4km resolution and linked to participant baseline residence to estimate single year and 3-year average estimates of average daily maximum apparent temperature (i.e., heat index) and the total number of hot days where the apparent temperature exceeded 85 degrees Fahrenheit (F). Hazard ratios (HR) and 95% confidence intervals (CI) for SLE associated with quartile differences in heat measures were estimated using Cox proportional hazards regression. Models were adjusted for age, enrollment year, race and ethnicity, age at menarche, smoking status, alcohol status, and body mass index. We explored effect measure modification, stratifying by educational attainment—a proxy for resource availability to potentially mitigate heat exposure.

Results: Over follow-up (672,477 person years), 395 participants reported incident SLE after enrollment (mean age at diagnosis: 61±10 years) with an average time to diagnosis of 6.4 years. Increasing quartiles of environmental residential heat were associated with greater SLE. Individuals living in areas of the highest quartile of 3-year average daily apparent temperature had 1.35 (CI:1.00, 1.82) times greater SLE hazard than those living in the lowest quartile. Similarly, SLE hazard was also elevated for individuals living in areas in the highest quartile of 3-year average number of annual days over 85F compared to participants living in the lowest quartile (HR:1.40; CI:1.04, 1.89). Single year associations were similar in magnitude and trend. When stratified by educational attainment, participants who reported less than a bachelor's degree and lived in areas in the highest quartile of 3-year average annual days over 85F had 1.47(CI:1.00, 2.16) times greater SLE hazard compared to those in the lowest quartile. SLE hazard was slightly lower for participants who attained a bachelor's degree or higher (HR:1.24; CI:0.78, 1.97) and lived in the hottest areas.

Conclusion: Environmental heat exposure was associated with increased hazard of SLE. Associations were slightly modified by educational attainment, a proxy for potential availability of socioeconomic resources to mitigate heat exposure. Environmental heat exposure should be further assessed as a potential risk factor for SLE.

Disclosure: J. Woo: None; **K. Lawrence**: None; **D. Sandler**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1691

Standardizing DXA Screening in Childhood-Onset Systemic Lupus Erythematosus at A Single Center: A Quality Improvement Initiative Using a Decision-Tree Algorithm

Andrea Gutierrez[1], Stephanie Armendariz[2], Muniza Mogri[3] and Kristina Ciaglia[4], [1]UT Southwestern Medical Center, Dallas, TX, [2]Texas Scottish Rite Hospital, Dallas, TX, [3]UT Southwestern Medical Center / Children's Health Dallas, Dallas, TX, [4]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX

SESSION INFORMATION

Session Date: Monday, October 27, 2025

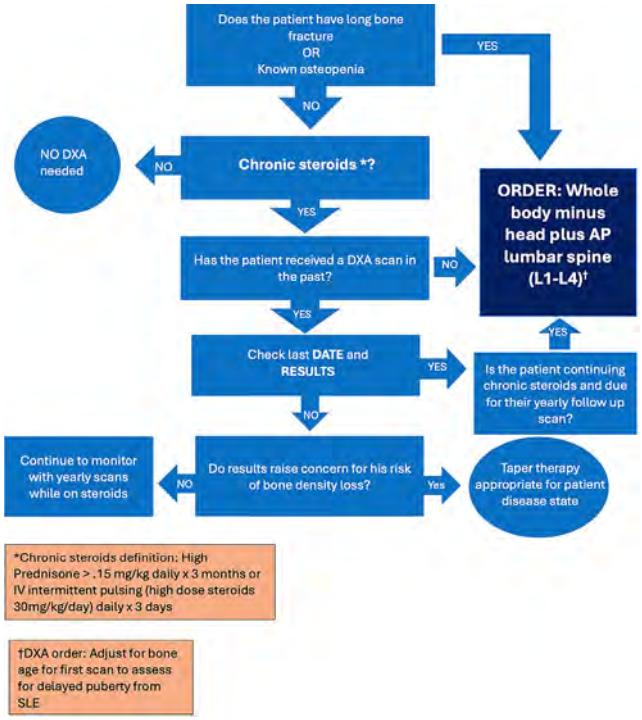
Session Title: Abstracts: ARP I: Multidimensional Influences on Health in SLE (1686–1691)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

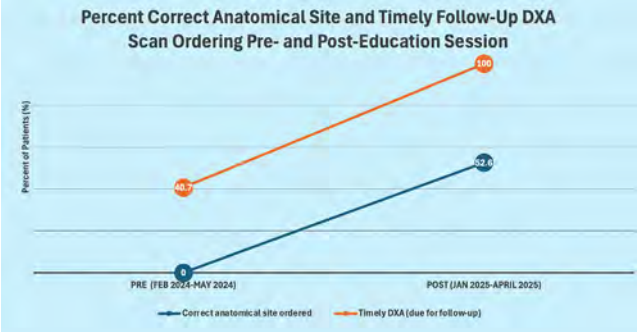
Background/Purpose: Patients with childhood-onset systemic lupus erythematosus (cSLE) are at increased risk of low bone mineral density, with studies showing a 40% frequency of osteopenia (Lilleby, 2007). Guidelines for adults with SLE recommend yearly screening for patients on chronic steroids with dual X-ray absorptiometry (DXA). However, pediatric-specific protocols are lacking, leading to inconsistencies in care. The aim of this project was to assess current DXA screening practices at a pediatric rheumatology outpatient clinic and evaluate the early impact of a decision-tree algorithm on screening consistency.

Methods: A retrospective chart review of 70 cSLE patients seen from February 2024-May 2024 was performed to assess baseline screening practices and barriers. Quality improvement tools, including root cause analysis and a driver diagram with provider input, prompted the development of a decision-tree algorithm, based on current guidelines and expert input. This

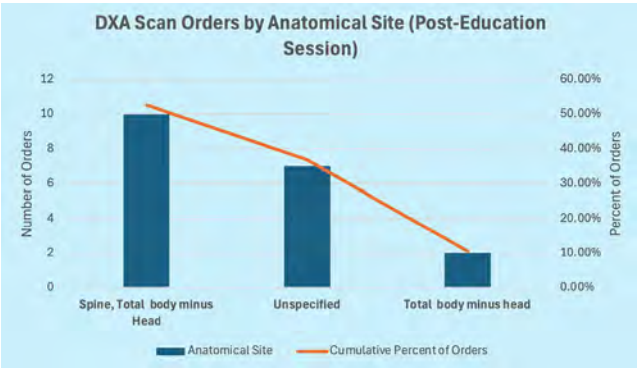


Decision-tree algorithm guiding DXA screening for childhood-onset SLE patients to standardize patient selection, timing, and site selection at a pediatric rheumatology outpatient clinic.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Line chart illustrating improvements in timely follow-up DXA orders (40.7% to 100%) and correct anatomical site selection (0% to 52.6%) among pediatric SLE patients from baseline (January-May 2024) to post-intervention ((January-April 2025) after introduction of the DXA screening algorithm and guidelines in an education session.



Pareto chart illustrating the frequency of anatomical sites ordered for DXA scans among pediatric SLE patients after introduction of the DXA screening algorithm and guidelines in an education session (January-April 2025), highlighting that 52.6% of provider orders adhered to recommended pediatric DXA guidelines.

algorithm specified DXA eligibility (chronic steroids), frequency (yearly), and recommended sites (total body less head and lumbar spine). The algorithm was introduced to providers during an educational session in September 2024. DXA screening practices were then compared before and after the intervention.

Results: At baseline, screening rates varied by insurance status, with commercial insurance patients at 78.6%, government-insured at 66.7%, and uninsured at just 12.5%. Despite relatively high screening rates among the insured, 59.3% of eligible patients did not receive timely follow-up DXA scans and most DXA results were not accessible in the EMR. Additionally, there was significant inconsistency in anatomical site selection for DXA scans.

Following the educational intervention, chart review of 87 cSLE patients seen from January to April 2025 showed a marked improvement in correct anatomical site ordering, increasing from 0% to 52.6%. Appropriate, timely DXA ordering for patients due for follow up also increased from 40.7% to 100%. Overall, if a DXA was due, whether for an initial visit or follow-up visit, it was ordered 84% of the time, and the correct decision regarding DXA ordering was made 94.1% of the time. An informal, oral survey revealed ongoing difficulty among providers in instantly recalling the correct anatomical site, suggesting more sustainable interventions will help maintain consistent improvement.

Conclusion: These findings highlight a knowledge gap among providers of who, when, and where to DXA screen pediatric SLE patients. Early assessment of this intervention suggests a decision-tree algorithm can help address this gap by improving clarity, guiding providers to appropriate decisions, and standardizing DXA screening for optimal care. Ongoing efforts are focusing on sustainable implementation, including posting the algorithm in clinic workspaces and integrating a default DXA order set into the EMR, with future steps to address access disparities. Enhancing screening consistency

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

may lead to earlier identification of bone density loss, enabling timely therapeutic adjustments and interventions to reduce fracture risk and long-term bone complications in this high-risk pediatric population.

Disclosure: A. Gutierrez: None; **S. Armendariz**: None; **M. Mogri**: None; **K. Ciaglia**: None.

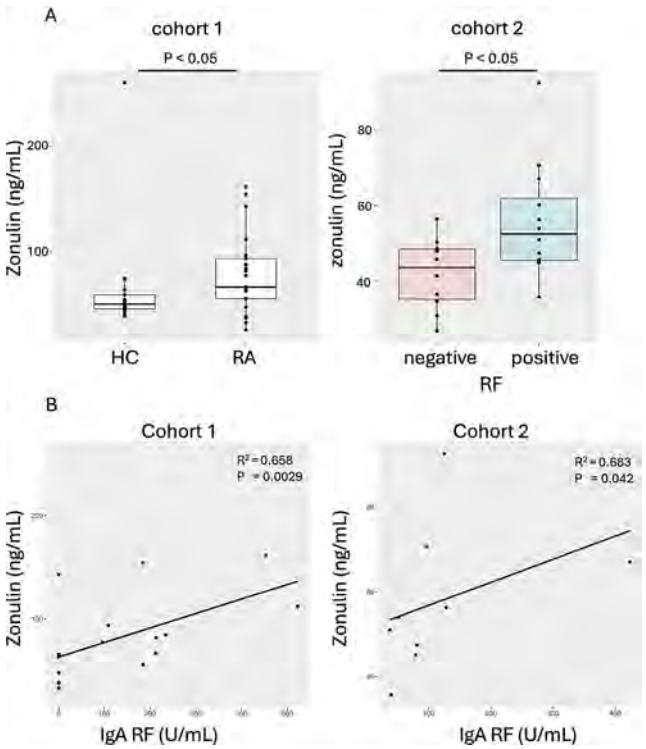
Abstract Number: 1692

Rheumatoid factor is associated with increased gut permeability and migration of B cells to the joint via CXCR3 in rheumatoid arthritis

Ken Yasaka[1], Nida Pellett[2], Daria Krenitsky[1] and Jennifer Anolik[2], [1]University of Rochester, Rochester, NY, [2]University of Rochester Medical center, Rochester, NY

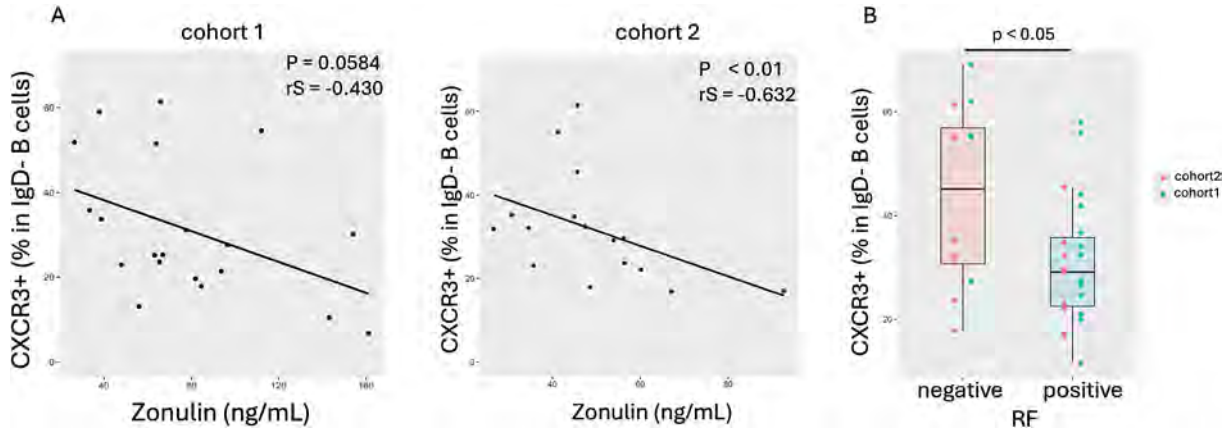
SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1692–1697)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: It has been proposed that the mucosal environment is associated with the pathogenesis of rheumatoid arthritis (RA). In addition to gut dysbiosis, intestinal barrier dysfunction has been reported prior to disease onset and may potentiate immune activation but has not been well-studied in relation to B cell dysregulation. Here we examined serum zonulin as a read-out of gut permeability and its relationship with autoantibodies and B cell subsets in RA to decipher the impact of increased gut permeability on autoimmunity.



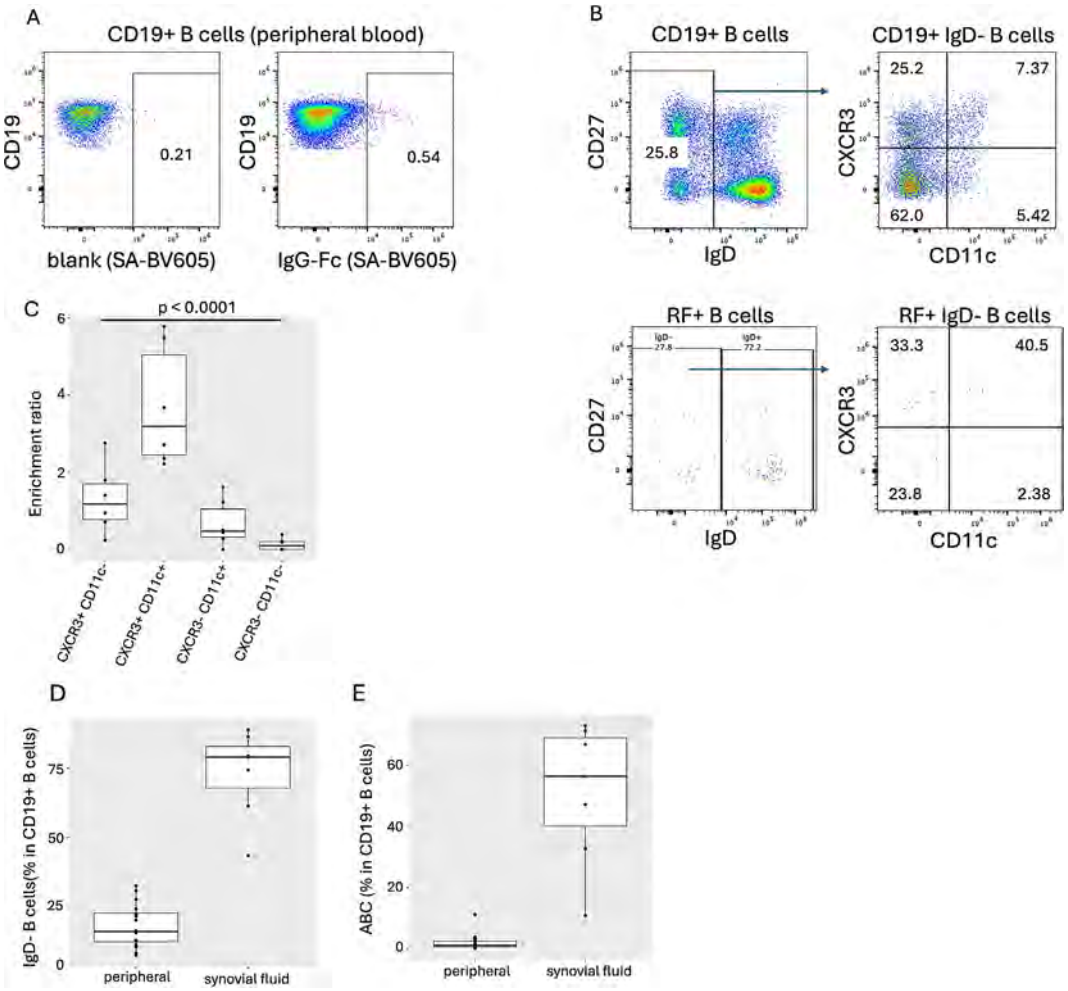
A. Serum zonulin levels. The Mann-Whitney U test was done in both cohorts. B. The correlation analysis between serum zonulin and IgA-RF titer. The Spearman's correlation test was done.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A. Correlation between serum zonulin levels and expression of CXCR3 in IgD- B cells in both cohort 1 and 2. The Spearman's correlation test was done. B. Comparison of the expression of CXCR3 in IgD- B cells between RF- RA (n=12) vs RF+ RA (n=23). The Mann-Whiney U test was done.

Methods: Cohort 1 were composed of 20 RA patients (85% positive for either rheumatoid factor (RF) or anti-CCP antibodies (CCP)) and 16 age-matched healthy controls (HC). Cohort 2 comprised 22 RA patients with a higher seronegative fraction (40%) in order to examine the impact of autoantibody status. Serum zonulin levels were measured by zonulin ELISA kit (Immundiagnostik AG), serum IgA-RF titer was measured by ELISA kit (Abonova), and flow cytometry was conducted to



A. The gating of RF+ B cells using blank control (only SA-BV605 was added). B. The distribution of RF+ B cells in terms of CD11c and CXCR3 expression. C. The analysis of enrichment of RF+ B cells in each subset in RA (n=6). Enrichment ratio = (% in RF+ IgD- B cells / % in CD19+ IgD- B cells). Kruskal-Wallis test was done. D and E Comparison of each subset between unpaired peripheral and synovial samples.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

characterize B cell subsets. In CD19+ IgD- antigen-experienced B cells, Age-associated B cells (ABCs) were defined as CD11c+ and CXCR5-, and the expression of CXCR3 was determined using isotype control. RF+ B cells were detected using biotinylated IgG-Fc fragment followed by streptavidin – BV605 in peripheral blood samples (n=6). Flow cytometry was also conducted on synovial fluid samples from RA patients (n = 7) to characterize ABCs.

Results: Serum zonulin levels were significantly elevated in RA compared to HC (cohort 1) and higher in RF+ RA patients (cohort 2) (Figure 1A), while there was no statistically significant difference between CCP+ and CCP- patients. Moreover, both IgM and IgA-RF titers were significantly correlated with zonulin levels (Figure 1B). In IgD- B cells, CXCR3 was more highly expressed in ABCs than other B cells. CXCR3 expression in IgD- B cells was inversely correlated with zonulin levels in both cohorts (Figure 2A). Moreover, CXCR3 expression in IgD- B cells was significantly lower in RF+ patients (Figure 2B). Of note, there was no significant difference of the frequencies of ABC between HC and RA, and the frequencies of ABC were associated with neither RF positivity nor zonulin.

RF+ B cells were detected in the peripheral samples (Figure 3A). In IgD- B cells, RF+ B cells were enriched in the CXCR3+ CD11c+ subset (Figure 3B and C). Out of two synovial fluid samples on which RF+ B cells were investigated, RF+ B cells were detected (0.56% in total B cells) in one sample. In this sample, RF+ B cells were also enriched in CD11c+ CXCR3+ subset. Overall, in the synovial samples, majority of B cells were IgD-, and ABCs were more expanded than peripheral blood (Figure 3D and E).

Conclusion: Increased gut permeability was associated with the presence of RF. Serum zonulin was inversely correlated with circulating CXCR3+ B cells, and RF+ B cells were enriched in CXCR3+ CD11c+ B cells. We hypothesize that pathological B cells including ABCs may migrate to the joint via a CXCR3 – CXCL9/10 axis in the setting of increased gut permeability resulting in the decrease in CXCR3+ B cells in the circulation. Our ongoing research investigates how the migratory process of B cells is influenced by gut factors as well as how this affects the clinical outcome.

Disclosure: K. Yasaka: None; **N. Pellett**: None; **D. Krenitsky**: None; **J. Anolik**: None.

Abstract Number: 1693

Characterizing ANCA-specific B Cells in ANCA-associated Vasculitis

Laura van Dam[1], Mengrui Zhang[1], Shima Parsafar[2], Audra Horomanski[3], Sajede Rasouli[2], Orr Sharpe[2], Jolijn van Leeuwen[4], Tobias Lanz[2], Cees van Kooten[4], Onno Teng[5] and William H. Robinson[3], [1]Stanford University, Stanford, CA, [2]Stanford University, Stanford, [3]Stanford University, Palo Alto, CA, [4]Leiden University Medical Center, Leiden, Netherlands, [5]Leiden University Medical Center, Leiderdorp, Netherlands

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1692–1697)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) is a severe autoimmune disease, characterized by ANCAs targeting myeloperoxidase (MPO) or proteinase-3 (PR3). ANCA-specific B cells have a central role in AAV pathophysiology, but current knowledge of their markers and pathways is limited. Rituximab is an effective treatment, but relapses remain challenging. Therefore, there is an unmet need for treatments that achieve durable remission. Aim of this study is to characterize ANCA-specific B cells in AAV patients to gain pathophysiologic insight and identify novel treatment targets.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

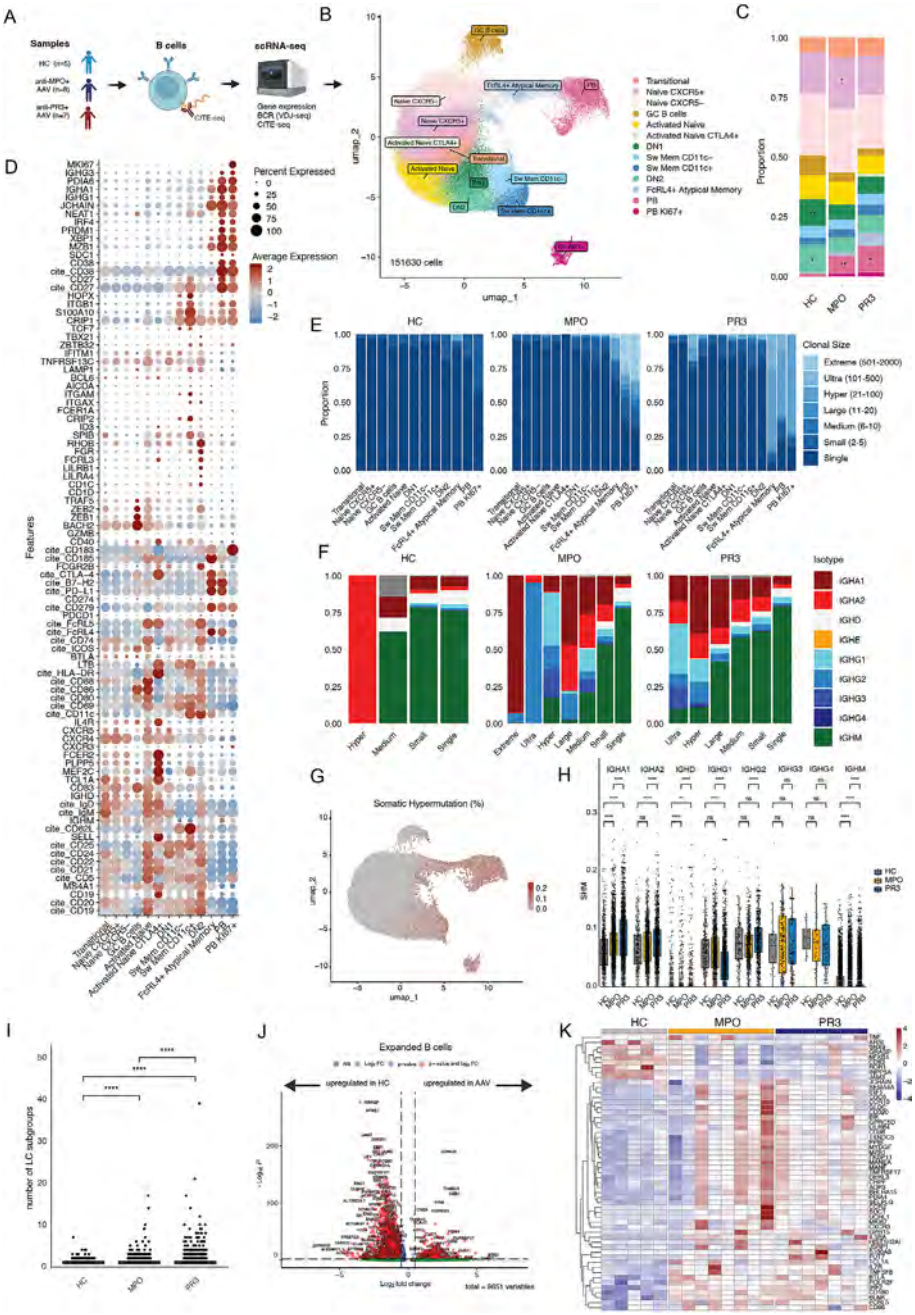


Figure 1. Overview of single cell RNA sequencing of B cells and B cell receptor (BCR) repertoires in ANCA-associated vasculitis patients (n=15) and healthy controls (n=5). A) Whole transcriptome and BCRs of B cells from 8 anti-MPO and 7 anti-PR3 AAV and 5 HC were analyzed with single cell RNA sequencing combined with CITE-seq. B) Thirteen distinct B cell subsets were identified after unsupervised clustering and annotated based upon gene and CITE-seq expression, visualized in a UMAP plot (n=151630 cells). C) Proportions of different B cell clusters for HC, anti-MPO, anti-PR3 AAV patients. *p<0.05, **p<0.01. D) Dotplot of gene and CITE-seq expression of B cell markers which was used to annotate the different B cell clusters. E) Clonal family size of B cells in the different B cell clusters in HC, anti-MPO and anti-PR3 AAV patients. F) Isotypes within the different clonal family size groups for HC, anti-MPO and anti-PR3 AAV patients. G) Umap plot with somatic hypermutation frequency displayed. H) Somatic hypermutation per isotype in different patient subgroups. I) Number of light chain rearrangements within each clonal family based on heavy chain. J) Differential gene expression analysis of expanded B cells, comparing AAV versus HC. K) Heatmap of normalized pseudobulk expression of genes which are significantly differently expressed in expanded B cells comparing AAV versus HC.

Methods: B cell receptor repertoires and whole transcriptomes of B cells were analyzed with single cell RNA sequencing combined with CITE-seq in 15 AAV patients and 5 healthy controls (HCs) (Fig 1A). 184 monoclonal antibodies (mAbs) and 25 germlines were expressed of highly expanded and/or mutated B cells. Their target antigens were screened with ELISAs and affinity (Kd) was measured with bio-layer interferometry (Fig 2A). Neutrophils of HCs were isolated, fixed with ethanol and stained with mAbs to study ANCA staining patterns.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

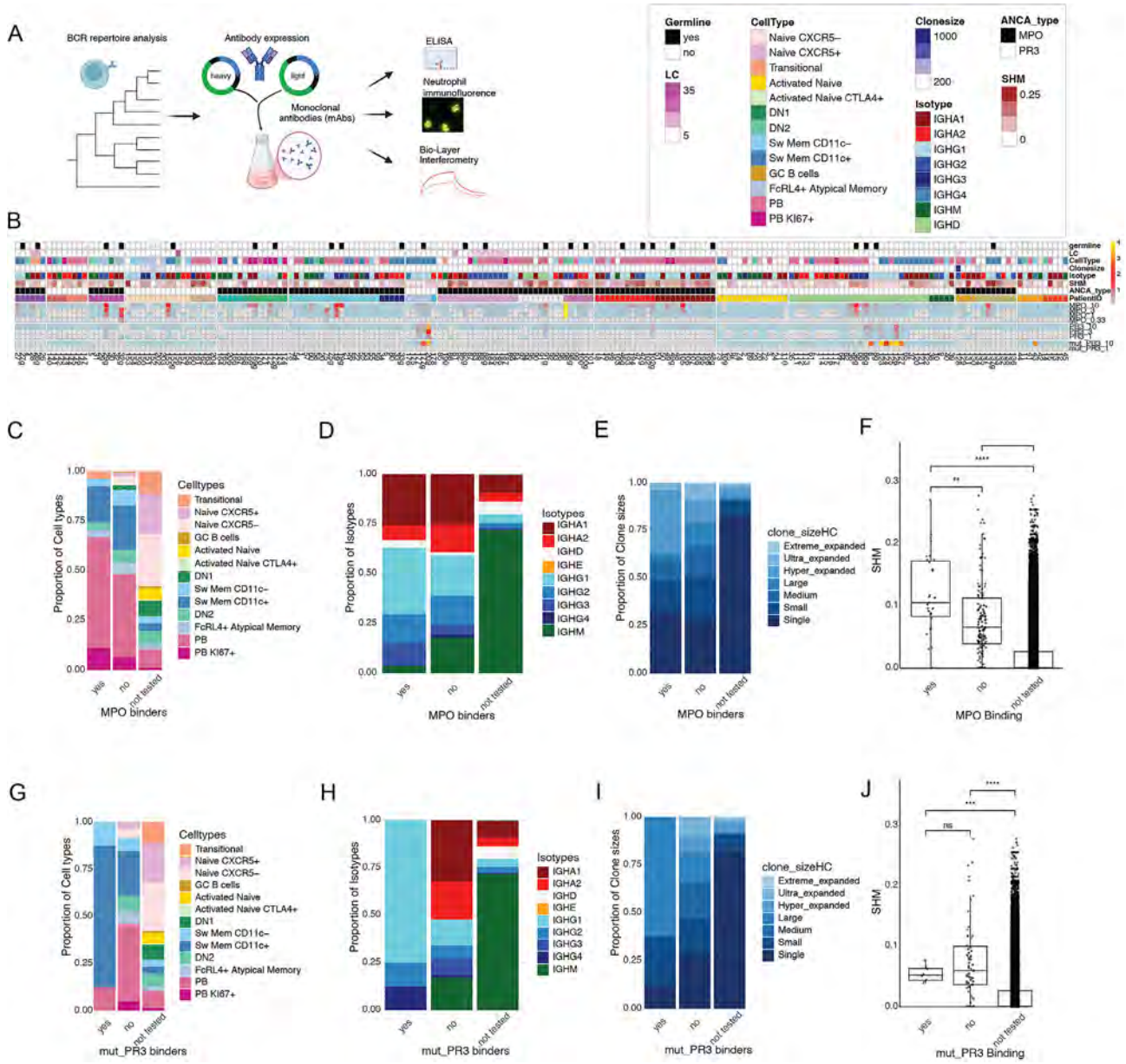


Figure 2. B cell receptor repertoire studies. A) Simplified methods overview of the expression of monoclonal antibodies. Sequences from highly expanded and/or mutated BCR repertoires were selected and expressed as monoclonal antibodies for downstream analyses. B) Heatmap of ELISA binding of monoclonal antibodies (n=184) and germline antibodies (n=25) from 12 AAV patients. mAbs were titrated (10, 3, 1, 0.33 ug/ml) on MPO, PR3 and mutated PR3 ELISAs. Mutated PR3 has a point mutation at S176A, resulting in lack of enzyme activity, and lack the N-terminal propeptide, resulting in mature PR3 (as published previously Specks et al. 2000 Arthritis Res.). C-F) Characteristics of MPO-specific B cells including C) Cell types, D) Isotypes, E) Clonal expansions, F) Somatic hypermutation. G-J) Characteristics of PR3-specific B cells incuding G) Cell types, H) Isotypes, I) Clonal expansions, J) Somatic hypermutation. ** p<0.01, *** p<0.001, **** P<0.0001.

Results: Both anti-MPO$^+$ and anti-PR3$^+$ AAV patients had significantly increased proportion of plasmablasts (PBs) and decreased DN1 and DN2 B cells as compared to HCs (Fig 1B-D). Additionally, PBs exhibited large clonal expansions in AAV (Fig 1E), which were mostly IgA and IgG isotypes (Fig 1F). Somatic hypermutation (SHM) was significantly higher in IgA1$^+$ and IgA2$^+$ and lower in IgD$^+$ and IgM$^+$ B cells in AAV (Fig 1G-H). AAV patients had increased light chain rearrangements per clonal family (Fig 1I). Overall, the lambda usage was significantly higher and increased with larger clonal families (data not shown). Differential gene expression analysis of expanded B cell clones identified several significant up- and down-regulated genes in AAV as compared to HC, including *TNFRSF17*, *SDC1* and *JCHAIN* (Fig 1H-I), involved in B cell activation, survival, migration and antibody production.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

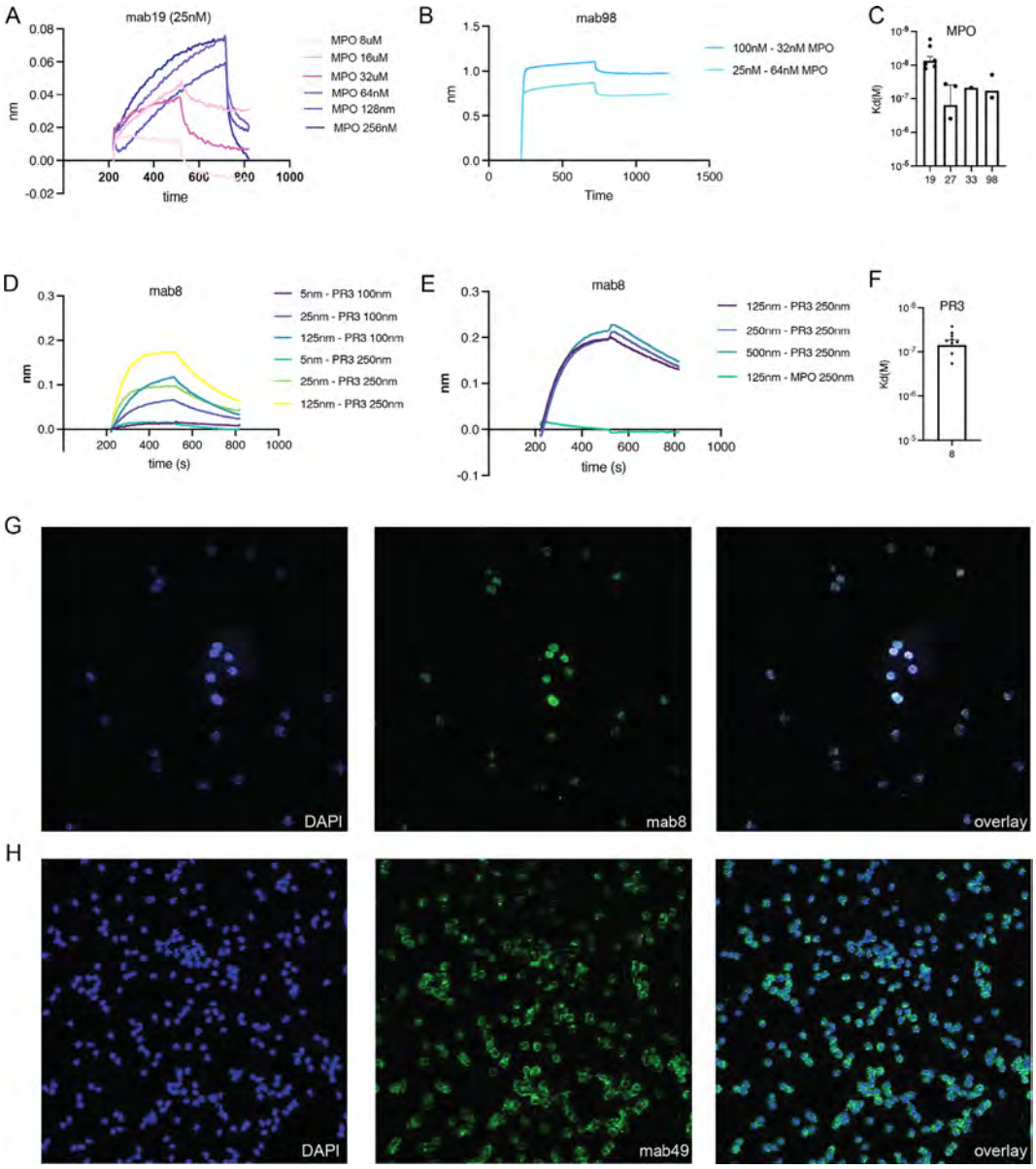


Figure 3. The binding affinity (Kd) of several mAbs with MPO or PR3 was measured with bio-layer interferometry. A) 25nM mab19 binding affinity curves with different molarities of MPO. B) 25nM and 100nM mab98 binding affinity curves with different molarities of MPO. C) Binding affinity Kd values of several mAbs for MPO. D-E) Titration of mAb 8 binding affinity curves with different molarities of PR3. F) Binding Affinity Kd values of mab 8 for PR3. G-H) Neutrophils were isolated and fixed with ethanol on ibidi slides, afterwards stained with 1ug/ml mab8 (G) or 1ug/ml mab49 (H), secondary anti-human IgG-Alexa488, DAPI and visualized with fluorescence microscopy.

We identified 28 mAbs targeting MPO (7 anti-MPO$^+$ and 2 anti-PR3$^+$ patients) and 9 targeting PR3 (3 anti-PR3$^+$ patients)(Fig 2B). The majority of MPO-specific B cells were IgA$^+$/IgG$^+$ PB or switched memory B cells (Fig 2C-D), clonally expanded and had increased SHMs (Fig 2E-F). PR3-specific B cells were clonally expanded IgG1-2-4 switched memory B cells (Fig 2G-J). Bio-layer interferometry demonstrated that the affinity (Kd) of several mAbs was 10^{-7}–10^{-8} nM for the ANCA antigens (Fig 3A-F). Neutrophil stainings confirmed c-ANCA and p-ANCA pattern for respectively PR3- and MPO-specific mAbs (Fig 3G-H).

Conclusion: Our single cell RNA-seq analysis of B cells in AAV patients reveals significant alterations in B cell populations and their functional characteristics. AAV patients exhibit increased clonal expansions, somatic hypermutation in IgA$^+$ B cells and light chain rearrangements. Our findings suggest a potential ongoing mucosal immune activation in these AAV patients. Our characterization of ANCA-specific B cells and their dysregulated activation provides insight into the pathogenic

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

mechanisms underlying AAV and underscores the potential for future therapeutic applications and biomarker development.

Disclosure: L. van Dam: None; **M. Zhang**: None; **S. Parsafar**: None; **A. Horomanski**: Gilead, 5, VielaBio, 5, Zenas, 5; **S. Rasouli**: None; **O. Sharpe**: None; **J. van Leeuwen**: None; **T. Lanz**: None; **C. van Kooten**: None; **O. Teng**: GlaxoSmithKlein(GSK), 5, Vifor, 5; **W. Robinson**: None.

Abstract Number: 1694

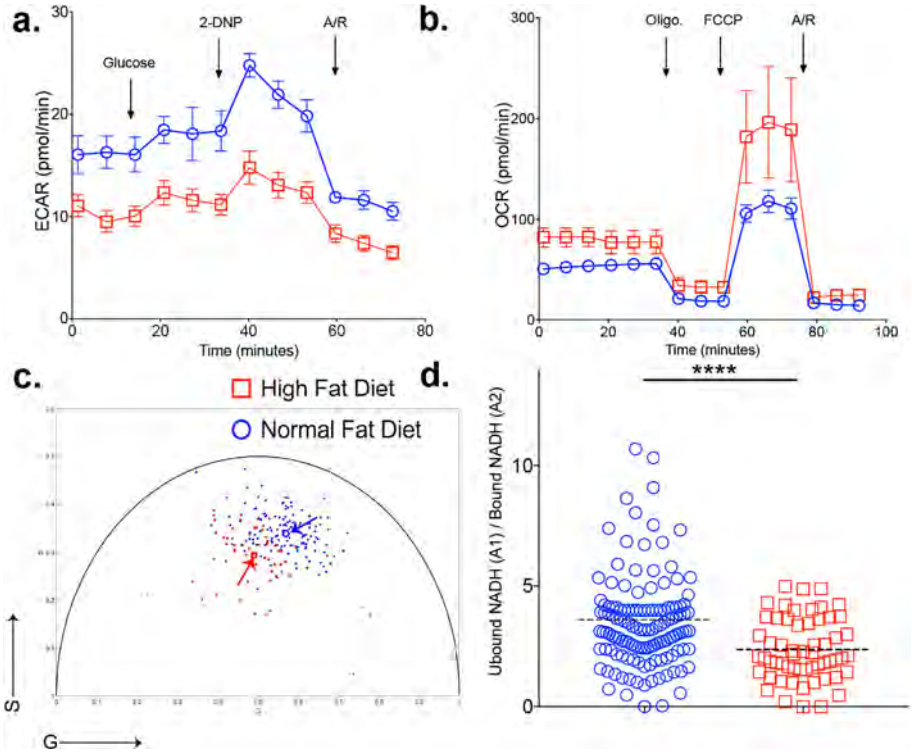
Obesity Exacerbates Autoimmunity by Dysregulating B Cell Behavior

Munir Akkaya, Sohret Gokcek, Billur Akkaya and Wael Jarjour, The Ohio State University, Columbus, OH

SESSION INFORMATION

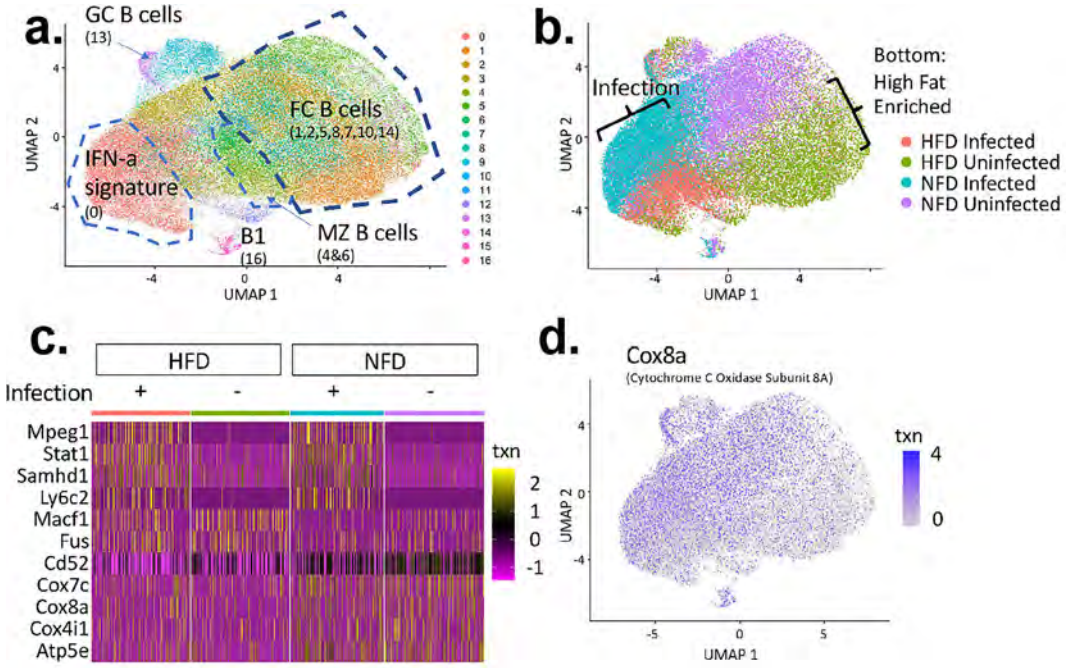
Session Date: Monday, October 27, 2025
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1692–1697)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Obesity is a major public health concern in the United States, affecting over 100 million individuals. While its detrimental effects on multiple organ systems are well documented, the impact of obesity on immune responses remains incompletely understood. In this study, we address this knowledge gap by identifying obesity-driven B cell dysfunction that exacerbates autoimmunity in a diet-induced obesity mouse model.

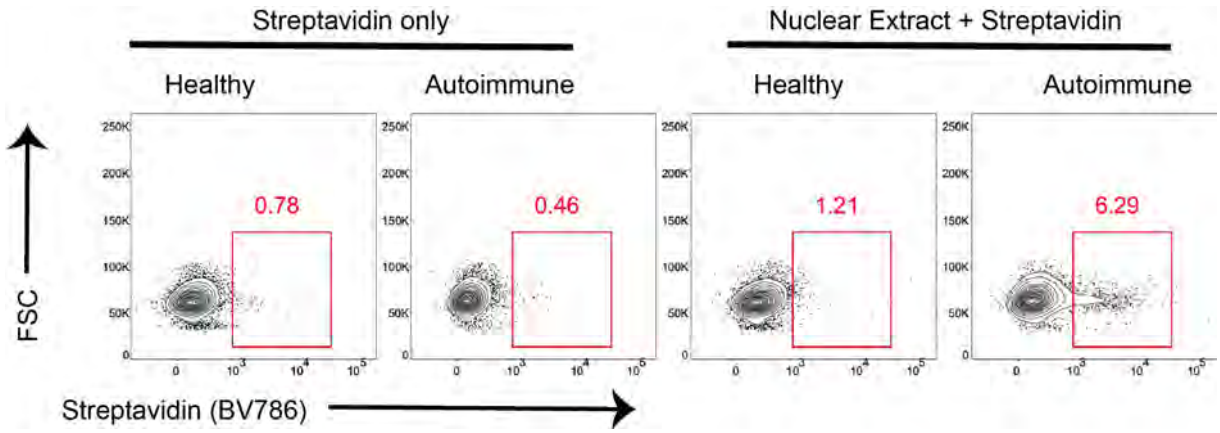


B cells in obese mice has higher tendency towards oxidative phosphorylation and lower tendency towards glycolysis as compared to their lean counterparts. a,b) Seahorse extracellular flux assay, c,d) Fluorescence life time imaging microscopy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



B cells in obese mice have distinct transcriptional remodeling as compared to B cells in lean mice both at rest and upon infection.



Novel strategy to detect nuclear antigen specific (self reactive) B cell clones

Methods: We developed a diet-induced obesity model in C57BL/6 mice and monitored B cell development and differentiation under both steady-state conditions and following immune challenges, including LCMV and *Plasmodium* infections, NP-CGG immunizations, and topical imiquimod (a TLR7 ligand) application to induce a lupus-like autoimmune setting. We assessed:

1. changes in B cell activation markers;
2. alterations in cellular metabolism using state-of-the-art fluorescence lifetime imaging microscopy and extracellular flux assays;
3. the frequency of self-reactive B cell clones using our novel nuclear antigen staining strategy coupled with flow cytometry; and
4. transcriptional changes via single-cell RNA sequencing.

Additionally, we conducted a thorough clinical comparison between obese and lean mice in both TLR7-induced and genetic (NZM) lupus models.

Results: . Int

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Interestingly, obese mice developed spontaneous germinal centers (GCs), yet paradoxically exhibited reduced responsiveness to NP-CGG immunization and infection, indicating disrupted B cell development and differentiation. Using our novel nuclear antigen staining strategy, we found that these spontaneous GCs in obese animals were predominantly composed of nuclear antigen-specific clones, suggesting a heightened propensity for autoimmunity.

Adoptive transfer experiments demonstrated that obesity-induced B cell dysregulation is cell-intrinsic, as the dysfunction persisted even after transferring B cells from obese donors into lean recipients. Further cellular and metabolic analyses revealed extensive remodeling in B cells from obese mice, including altered surface marker expression, a metabolic shift toward increased fatty acid utilization, and enhanced sensitivity to leptin receptor signaling. Single-cell RNA sequencing uncovered distinct transcriptional profiles in B cells from obese mice, both at baseline and following infection.

In lupus-like autoimmune models, obese mice exhibited a more severe and rapidly progressing disease course, characterized by skewed antibody responses, an increased frequency of autoreactive B cell clones, and accelerated mortality.

Conclusion: Collectively, these findings provide novel mechanistic insights into how obesity alters humoral immune responses and establish a direct link between obesity and heightened autoimmune risk.

Disclosure: M. Akkaya: None; **S. Gokcek**: None; **B. Akkaya**: None; **W. Jarjour**: None.

Abstract Number: 1695

The B Cell Compartment Exhibits a Pro-Inflammatory Skewing During Progression to Rheumatoid Arthritis

Ziyuan He[1], **Marla Glass**[1], Mark Gillespie[1], Elisabeth Dornisch[1], Pravina Venkatesan[2], Troy Torgerson[3], Kevin Deane[4], Gary Firestein[5], Adam Savage[1], Xiaojun Li[1], V. Michael Holers[6], Fan Zhang[7], David Boyle[8], Christy Bennett[1], Kristine Kuhn[9], Kristen Demoruelle[10], Peter Skene[11] and Ananda Goldrath[11], [1]Allen Institute for Immunology, Seattle, WA, [2]Allen Insitute, Seattle, WA, [3]Allen Institute for Immunology, Enumclaw, WA, [4]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [5]University of California, San Diego, San Diego, CA, [6]University of Colorado, Denver, CO, [7]The University of Colorado, Aurora, CO, [8]UCSD, La Jolla, CA, [9]2022 - 2023 / Adult/ University of Colorado, Aurora, CO, [10]University of Colorado Anschutz Medical Campus, Golden, CO, [11]Allen Institute for Immunology, Seattle

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1692–1697)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by joint inflammation and bone destruction. RA is preceded by a subclinical phase defined by elevated levels of RA-associated autoantibodies, most preeminently anti-citrullinated protein antibodies (ACPA). Nonetheless, we have an incomplete understanding of the changes in the B cell compartment that contribute to the breaking of tolerance that underlies risk of RA development. Here, we performed a multi-omics study of peripheral B cells from ACPA+ at-risk individuals (ARI) and longitudinally studied those ARI that progressed to clinical RA, referred to as disease 'converters'.

Methods: We applied single-cell RNA sequencing (scRNA-seq) and flow cytometry to peripheral blood from 45 ACPA+ ARI. For converters, we profiled blood samples over a period of 2 years prior to the onset of clinical RA (n=13). The productive immunoglobulin heavy chain (IgH) isotype of B cell subsets was determined from scRNA-seq data. We applied spectral flow cytometry to characterize cytokine profiles of activated peripheral B cells from age-matched ACPA- control and ACPA+ ARI after TLR9 ligand and CD40 stimulation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Upon productive IgH isotype labeling, IGHG3 sterile IgH expression by unswitched naive B cells was significantly increased among ARI (FDR=0.1). This suggests a greater likelihood that naïve B cells of ARI will class-switch to the IgG3+ isotype upon activation. A subset of naïve B cells also expanded in RA converters (FDR=0.02), a feature previously reported to correlate with activation in ACPA+ individuals (Inamo et al. 2023, JCI). Pathway analysis showed increased activation and antigen presentation activity compared to controls. Upon in vitro stimulation, naive B cells from ARI had higher frequencies of IL-6+ and RANKL+ cells compared to controls (FDR< 0.05) and trended toward elevated TNFα+ cells (FDR=0.19), suggesting they are primed for proinflammatory cytokine and RANKL secretion. Further, we identified a subset of CD27- ITGAX/CD11c+ effector memory B cells that increase in abundance during progression to clinical RA (FDR=0.11). This population has transcriptional features of chronic BCR engagement, including elevated class-switched cells as compared to the non-expanding effector memory subset, and a gene program associated with long-lived humoral immunity. Together these data show broad activation across naive and memory ARI B cell populations with evidence of a naive B cell primed state in ACPA+ ARI.

Conclusion: Our results indicate proinflammatory-skewed naive and memory B cell subsets among ARI, coinciding with systemic inflammation. An increased activation signature and *IGHG3* GLT suggest that naive B cells from ARI may be in a functionally "primed" state. Further, a subset of CD27- atypical or effector memory B cells with an activated transcriptional profile are found in converters as clinical RA approaches. Collectively, these data suggest that in addition to ACPA production, ongoing B cell activation is a feature of progression to clinical RA.

Disclosure: Z. He: None; **M. Glass**: None; **M. Gillespie**: Novo Nordisk, 11, Omeros, 11; **E. Dornisch**: None; **P. Venkatesan**: None; **T. Torgerson**: Eli Lilly, 2, Pharming Healthcare, 2, Takeda, 2; **K. Deane**: Inova Diagnostics, 1; **G. Firestein**: Eli Lilly, 5; **A. Savage**: None; **X. Li**: Eli Lilly, 5; **V. Holers**: None; **F. Zhang**: None; **D. Boyle**: None; **C. Bennett**: Adaptive Biotechnologies, 11, Eli Lilly, 5; **K. Kuhn**: Solarea, 2; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5; **P. Skene**: None; **A. Goldrath**: Arsenal Bio, 1, Foundery Innovations, 1.

Abstract Number: 1696

A Multi-omics Resource of B Cell Activation Reveals Genetic Mechanisms for Autoimmune Diseases

Vitor Aguiar[1], Marcella Franco[1], Nada Abdel Aziz[1], Daniela Fernandez-Salinas[2], Marcos Chinas[1], Mariasilvia Colantuoni[2], Qian Xiao[1], Nicolaj Hackert[1], Yifei Liao[3], Rodrigo Cervantes-Diaz[1], Marc Todd[1], Brian Wauford[1], Alex Wactor[1], Vaishali Prahalad[1], Raquel Laza-Briviesca[1], Roxane Darbousset[1], Qiang Wang[1], Scott Jenks[4], Kevin Cashman[4], Esther Zumaquero[4], Zhu Zhu[1], Junning Case[3], Paloma Cejas[5], Miguel Munoz-Gomez[5], Hannah Ainsworth[6], Miranda Marion[7], Mehdi Benamar[1], Pui Lee[8], Lauren Henderson[9], Margaret Chang[2], Kevin Wei[10], Henry Long[5], Carl Langefeld[11], Benjamin Gewurz[3], Ignacio Sanz[4], Jeffrey Sparks[12], Esra Meidan[13], Peter Nigrovic[2] and **Maria Gutierrez-Arcelus**[2], [1]Boston Children's Hospital, Boston, [2]Boston Children's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, [4]Emory University, Atlanta, [5]Dana Farber Cancer Institute, Boston, [6]Wake Forest University, Winston-Salem, NC, [7]Wake Forest, Winston-Salem, [8]Boston Children's Hospital, Newton, MA, [9]Boston Children's Hospital, Watertown, MA, [10]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [11]Wake Forest University School of Medicine, Winston Salem, NC, [12]Brigham and Women's Hospital, Boston, MA, [13]Boston Children's Hospital, Somerville, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1692–1697)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

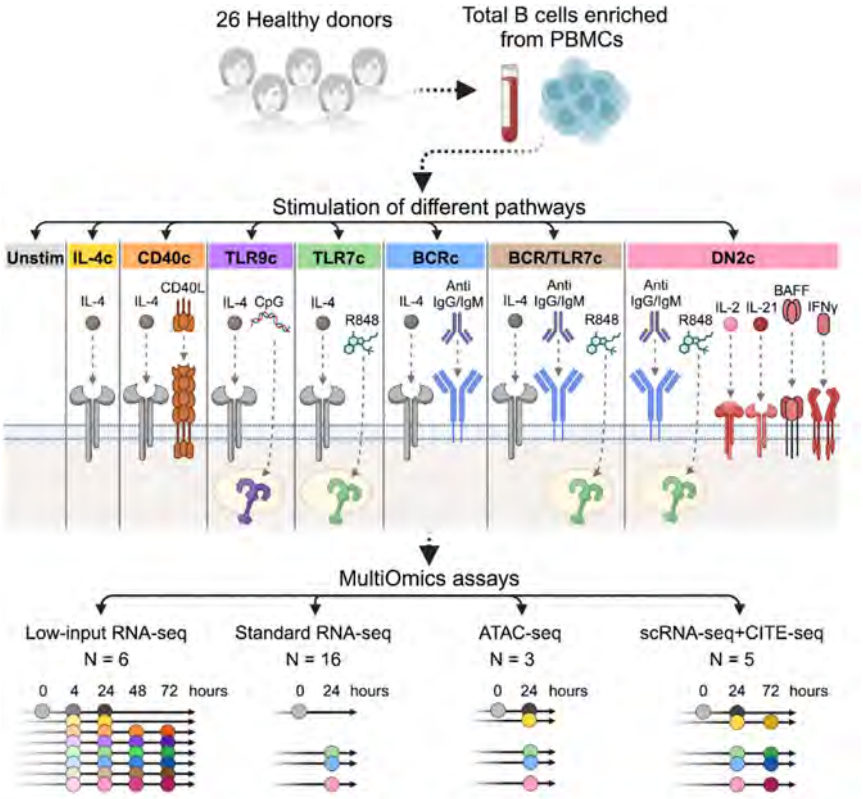


Figure 1. B cell activation resource. Illustration of experimental design, activation conditions used, and assays performed. Created with Biorender.

Background/Purpose: Most genetic variants that confer risk of complex autoimmune diseases affect gene regulation in specific cell types. Their target genes and focus cell types are often unknown, partially because some effects are hidden in untested cell states. B cells play important roles in autoimmune diseases, including systemic lupus erythematosus (SLE), rheumatoid arthritis, and multiple sclerosis. However, despite this established importance, B cell activation states are underrepresented in functional genomics studies.

Methods: In this study, we obtained B cells from 26 healthy female donors. We stimulated B cells *in vitro* with six activation conditions targeting key pathways: the B cell receptor (BCR), Toll-like receptor 7 (TLR7), TLR9, CD40, and a cocktail that promotes differentiation into double negative 2 (DN2) IgD^{-} $CD27^{-}$ $CD11c^{+}$ $CD21^{-}$ B cells, a likely pathogenic B cell subset for autoimmunity (**Fig. 1**). We profiled up to 24 human B cell activation states and up to 5 control conditions using RNA-seq, single-cell RNA-seq coupled with surface protein markers (CITE-seq), and ATAC-seq.

Results: We provide an in-depth characterization of how autoimmune disease-associated genes respond to stimuli and group into modules with distinct functions (**Fig. 2a-c**). Using high-depth RNA-seq data, we find pervasive splicing effects during B cell activation. Using single-cell data, we describe stimulus-dependent B cell fates (**Fig. 2d-g**). Chromatin data reveal the transcription factors likely involved in stimulus-dependent B cell activation. These open chromatin regions capture a significant proportion of the genetic risk of multiple autoimmune diseases and elucidate autoimmune disease genetic risk variants with previously unknown function.

To validate the utility of our findings, we performed fine-mapping for an SLE risk locus and identified a candidate causal variant (**Fig. 3a**) that overlaps an open chromatin region specific for B cells activated with the DN2-cocktail (**Fig. 3b**). This intergenic open chromatin peak is 15kb away from *TNFSF4*, which codes for OX40L and mediates interaction with activated T

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

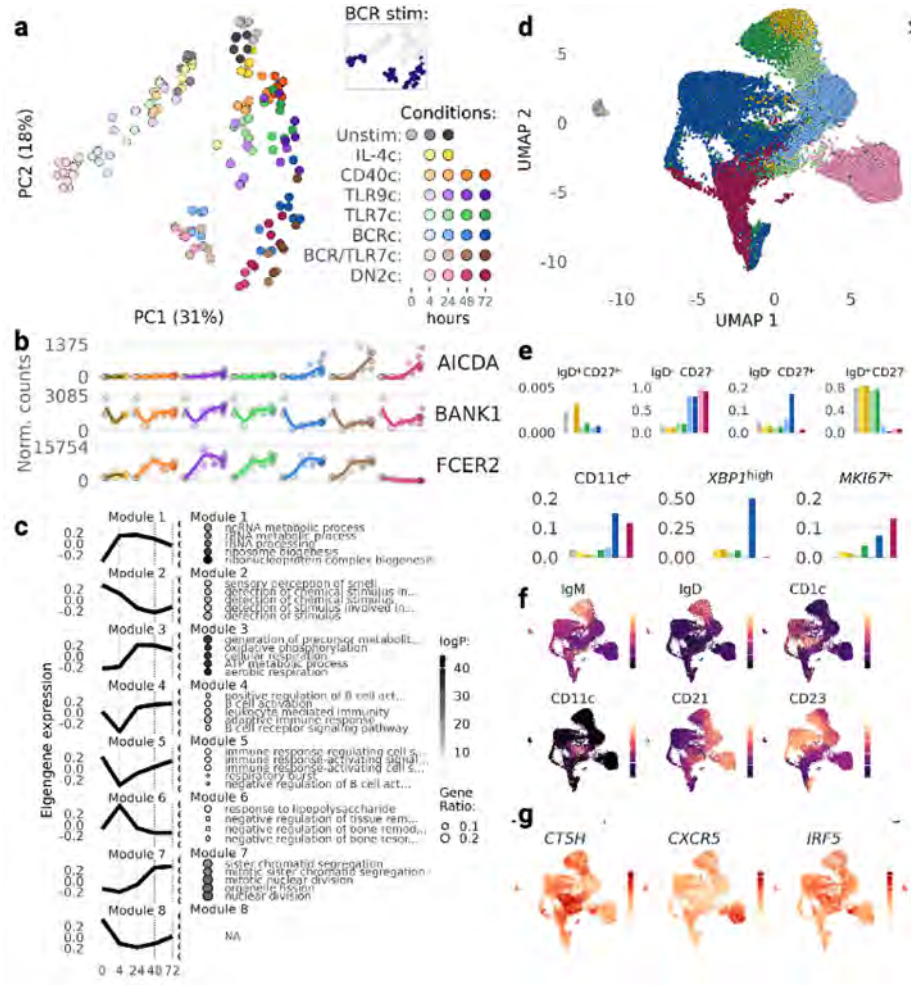


Figure 2. Dynamic gene expression in activated B cells over time and pathway-dependent B cell fates. **a**, Principal component analysis (PCA) with the top 2,000 most variable genes shows separation of conditions and time points. Inset: PCA plot highlighting conditions that include BCR stimulation. **b**, Expression levels of selected B cell activation genes. **c**, Modules of gene expression identified by Weighted Gene Correlation Network Analysis (WGCNA). X-axis: time in hours. On the right, enrichment of Gene Ontology (GO) biological processes for modules. **d**, Uniform Manifold Approximation and Projection (UMAP) based on gene expression after Harmony correction. **e**, Proportion of B cell subsets defined by expression of marker protein/genes (genes in italic) for each condition and time point (colors as in (d)). **f**, UMAP as in (d) colored by protein expression levels of key markers. **g**, UMAP as in (d) colored by gene expression levels of autoimmunity-associated genes.

cells. *TNFSF4* gets upregulated with DN2-cocktail activation at 48 and 72 hours (**Fig. 3c**). We used CRISPR inactivation in a B cell line to silence the putative enhancer where the SLE risk variant is located, which demonstrated that its target gene is *TNFSF4* (**Fig. 3d**).

We have made our multiomics resource available via an interactive browser that can be used to query the dynamics of gene regulation and B cell differentiation during activation by different stimuli, enhancing further investigation of B cells and their role in autoimmune diseases.

Conclusion: Our B cell activation multi-omics resource reveals how B cells are transcriptionally and epigenetically wired to respond to distinct stimuli, highlighting pathway-specific activation programs. It also offers mechanistic insights into the genetic basis of autoimmune diseases, including functional validation of a lupus-associated risk locus.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

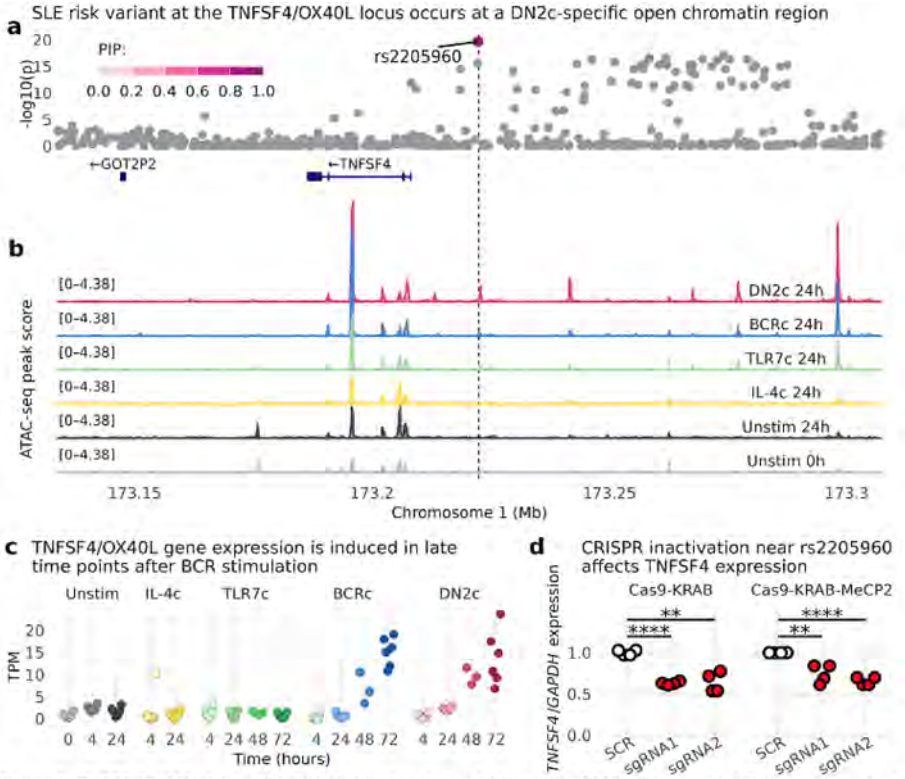


Figure 3. *TNFSF4*/OX40L locus. (a) GWAS data from Langefeld et al.[40] rs2205960 is the most likely causal variant. PIP: posterior inclusion probability from SuSiE.[67] **(b)** Chromatin peaks at the genomic region in (a). **(c)** *TNFSF4* gene expression in the same conditions shown in (b). TPM: transcripts per million. **(d)** CRISPRi shows that inhibiting the region containing the putative causal variant leads to *TNFSF4* downregulation.

Disclosure: V. Aguiar: None; **M. Franco**: None; **N. Abdel Aziz**: None; **D. Fernandez-Salinas**: None; **M. Chinas**: None; **M. Colantuoni**: None; **Q. Xiao**: None; **N. Hackert**: None; **Y. Liao**: None; **R. Cervantes-Diaz**: None; **M. Todd**: None; **B. Wauford**: None; **A. Wactor**: None; **V. Prahalad**: None; **R. Laza-Briviesca**: None; **R. Darbousset**: None; **Q. Wang**: None; **S. Jenks**: None; **K. Cashman**: None; **E. Zumaquero**: None; **Z. Zhu**: None; **J. Case**: None; **P. Cejas**: None; **M. Munoz-Gomez**: None; **H. Ainsworth**: None; **M. Marion**: None; **M. Benamar**: None; **P. Lee**: Pfizer, 2; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2; **M. Chang**: None; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **H. Long**: None; **C. Langefeld**: None; **B. Gewurz**: None; **I. Sanz**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **E. Meidan**: None; **P. Nigrovic**: None; **M. Gutierrez-Arcelus**: None.

Abstract Number: 1697

Dynamic Effects of T cell Engager Therapy on B and T cells in Autoimmune Disease.

Laura Bucci[1], Tobias Rothe[2], Ann-Kathrin Goetz[3], Kirill Anoshkin[1], Danae-Mona Nöthling[1], Melanie Hagen[1], Sebastian Böltz[1], Andreas Wirsching[1], Georg Schett[4] and Ricardo Grieshaber-Bouyer[5], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlagen, Germany, [3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, [4]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [5]University Hospital Erlangen, Erlangen, Germany

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Monday, October 27, 2025
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1692–1697)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Treatment of autoimmune disease with T cell engagers (TCEs) leads to profound peripheral B cell depletion, followed by their reconstitution. However, the dynamics of B cell depletion as well as concomitant T cell activation, are poorly understood.

Methods: 14 patients with RA were treated with the CD19xCD3 TCE blinatumomab, 10 patients with SSc, IIM, IgG4-RD and GD were treated with the BCMAxCD3 TCE teclistamab. All patients had active, multi-drug-resistant AID. Longitudinal high dimensional flow cytometry was performed on peripheral blood mononuclear cells (PBMCs). 1-year follow-up was available for 8/14 patients treated with blinatumomab. 6-months follow-up was available for 8/10 patients treated with teclistamab.

Results: TCE therapy led to a rapid B cell depletion (Fig. 1A-B). 11/14 RA patients had circulating B cells at baseline (median 114/nl), and 3/14 patients had no B cells because of recent rituximab therapy. Complete B cell depletion was reached in 8/11 RA patients (in 2 patients after the first cycle, in 4 patients after the second cycle and in 2 patients after a third cycle).

Teclistamab led to complete B cell depletion in all patients (in 4/10 patients after the first dose and in 6/10 patients after the third dose). A significant decrease of serum immunoglobulins and free light chains indicated effective depletion of the plasma cell compartment via teclistamab, in contrast to blinatumomab.

B cells reconstituted after a median of 61 days after blinatumomab and a median of 157 days after teclistamab (Fig. 1C). Reconstituted B cells were mostly of a naive phenotype. Correspondingly, $CD19^+$ $CD27^+$ memory B cells decreased substantially (blinatumomab: average 16% to 7%; teclistamab: average 8% to 2%). One year after blinatumomab treatment

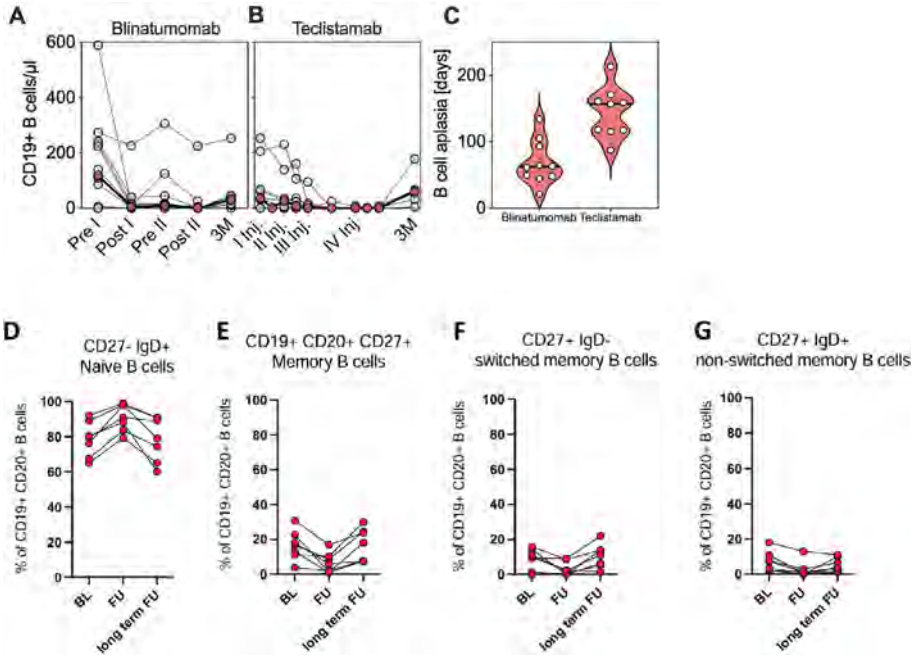


Fig. 1: A-B. Quantification of B cells during therapy with A. blinatumomab and B. teclistamab. C. B cell aplasia after treatment with TCEs, D-G. Frequencies of D. Naive, E. Memory, F. switched memory, and G. non switched memory B cells at short term follow-up (FU) and at 1-year follow-up (long term FU) after Blinatumomab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

initiation (6/14 patients), both CD27^{+}IgD^{+} non-switched and CD27^{+} IgD^{-} switched memory B cells re-emerged, while CD20^{+}CD27^{-} naive B cells slightly decreased (Fig. 1D-G). Plasmablasts were depleted after both therapies and stayed depleted at long-term follow up.

Circulating T cells transiently decreased during TCE therapy (Fig. 2A-B). A relative shift towards CD8^{+} cells during teclistamab indicated a stronger activation and expansion of cytotoxic T cells (Fig. 2C-D). TCE therapy led to a noticeable increase in exhaustion related T cell phenotypes. PD1+ CD8^{+} T cells accumulated after the first cycle (blinatumomab: from 11.2 to 20.7%; teclistamab: from 6.9 to 24.3%). CD8^{+} CD62L^{-} CD45RA^{-} CD8^{+} effector memory (EM) and CD62L^{-} CD8^{+} effector memory re-expressing CD45RA (EMRA) T cells expressed more PD-1 compared to the other CD8^{+} subpopulations, suggesting increased exhaustion (Fig. 2E-F).

Teclistamab led to an increase in CD8^{+} TEM and TEMRA, which also expressed more PD-1 compared to the other CD8^{+} subpopulations. CD4^{+} T cells were less influenced in both therapies, a slight increase of CD4+ CD62L^{+} CD45RA^{-} central memory (CM) T cells was observed during both treatments.

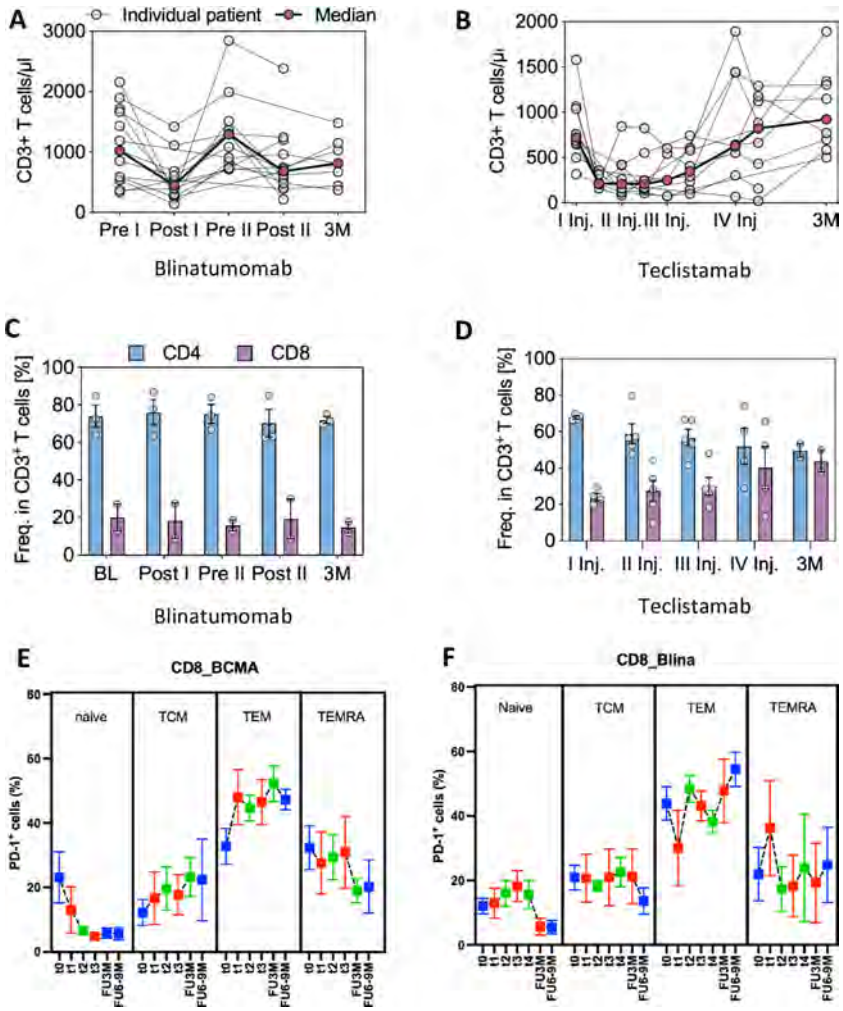


Fig. 2: A-B. Quantification of CD3+ T cells during therapy with A. blinatumomab and B. teclistamab. C-D. T CD4+/CD8+ cell ratio during treatment with TCEs, E. expression of PD-1 in T cell subpopulations during treatment with teclistamab at baseline (t0), after the 3rd injection (t1), at 14-days (t2) and 1-month follow up (t3) and at 3-months follow up (FU3M), F. expression of PD-1 in T cell subpopulations during treatment with blinatumomab at baseline (t0), during the first infusion (t1), between the first and second infusion (t2), during the second infusion (t3), after the second infusion (t4), at 3-months follow-up and at 6-9-months follow-up.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Together, these data demonstrate the dynamic impact of TCEs on B cell depletion and reconstitution in AIDs. Furthermore, strong effects on the T cell compartment are observed, raising the intriguing possibility that their mechanism of action is not limited to the B cell depletion alone.

Disclosure: L. Bucci: None; **T. Rothe**: None; **A. Goetz**: None; **K. Anoshkin**: None; **D. Nöthling**: None; **M. Hagen**: None; **S. Böltz**: None; **A. Wirsching**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6.

Abstract Number: 1698

X Chromosome DNA Methylation Changes Suggest Epigenetic Contributions to Immune Dysregulation in Male Lupus

Desire Casares Marfil[1], Gülşah Kavrul Kayaalp[2], Vafa Guliyeva[2], Özlem Akgün[2], Şeyma Türkmen[3], Elif Kilic Konte[4], Sezgin Sahin[4], Ozgur Kasapcopur[5], Betul Sozeri[6], Selçuk Sözer Tokdemir[7], Nuray Aktay Ayaz[8] and Amr Sawalha[1], [1]University of Pittsburgh, Pittsburgh, PA, [2]Istanbul University Faculty of Medicine, Istanbul, Turkey, [3]University of Health Sciences, Umraniye Research and Training Hospital, Istanbul, Turkey, [4]Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [5]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey, [6]Health sciences university, Istanbul, Turkey, [7]Istanbul University, Istanbul, Turkey, [8]Istanbul University Medical School, Istanbul, Turkey

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Genetics, Genomics & Proteomics (1698–1703)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: DNA methylation plays a critical role in the pathogenesis of lupus. Although most epigenetic studies have focused on autosomal regions, the X chromosome remains underexplored. In this study, we investigate X chromosome DNA methylation patterns in male patients with lupus. Studying male individuals allows us to circumvent the analytical complexities posed by random X-inactivation in female patients with two X chromosomes, enabling a clearer view of epigenetic changes that may contribute to disease mechanisms.

Methods: A total of 16 male patients with childhood-onset lupus and 14 healthy male controls were included. DNA from peripheral blood mononuclear cells (PBMCs) was isolated to assess DNA methylation patterns using the Infinium MethylationEPIC v2.0 array (Illumina). Data processing and statistical analyses were conducted using the *minfi* and *limma* R packages. Group differences in methylation patterns were tested via linear regression, adjusting for age and estimated cell-type proportions. Gene ontology enrichment analysis was performed with Metascape.

Results: A total of 23,364 DNA methylation sites (CpGs) on the X chromosome were analyzed. Differential methylation analysis between cases and controls identified 1,120 CpG sites with suggestive associations ($p < 0.05$), mapping to 593 genes. Approximately half of these sites were hypomethylated in patients compared to controls, with several CpGs located in immune-related genes. Notably, several hypomethylated CpGs were found in genes involved in the toll-like receptor (TLR) signaling pathway, including *TLR7*, *TASL*, and *BTK*, which are key components of innate immune signaling pathways that drive the expression of pro-inflammatory cytokines. Pathway enrichment analysis of the top 100 most significant differentially methylated CpGs revealed overrepresentation of immune and regulatory pathways, such as positive regulation of type I interferon production, response to interleukin-1, and regulation of cellular response to growth factor stimulus, suggesting epigenetic remodeling of critical processes in disease pathogenesis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: These findings highlight previously underrecognized X chromosome DNA methylation changes in lupus, particularly in immune-related genes and pathways. Our results suggest that epigenetic dysregulation on the X chromosome may contribute to immune activation and disease pathogenesis, underscoring the importance of including sex chromosomes in lupus epigenetic studies.

Disclosure: D. Casares Marfil: None; **G. Kavrul Kayaalp**: None; **V. Guliyeva**: None; **Ö. Akgün**: None; **Ş. Türkmen**: None; **E. Kilic Konte**: None; **S. Sahin**: None; **O. Kasapcopur**: None; **B. Sozeri**: None; **S. Sözer Tokdemir**: None; **N. Aktay Ayaz**: None; **A. Sawalha**: None.

Abstract Number: 1699

Protein-coding Somatic Genetic Variation in Lymphocytes in Systemic Lupus Erythematosus

Siva Kasinathan[1], Minh Pham[2] and Ansuman Satpathy[2], [1]Stanford University School of Medicine, Palo Alto, CA, [2]Stanford University School of Medicine, Stanford, CA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Genetics, Genomics & Proteomics (1698–1703)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: The genetic and environmental factors underlying pathogenesis of systemic lupus erythematosus (SLE) are incompletely resolved. While inherited genetic variation has been extensively queried in lupus, post-zygotically acquired somatic mutations remain largely unexplored. Somatic lesions are continually generated in all cells by physiologic processes and exogenous exposures, rendering every human a genetic mosaic. Lymphocytes are especially prone to mutagenesis in part due to programmed genomic instability during antigen receptor maturation. We therefore sought to survey somatic single nucleotide variants (sSNVs) in lymphocytes towards testing the hypothesis that mosaicism contributes to impaired self-tolerance in autoimmunity.

Methods: Subjects aged 6 – 21 years who met 2019 ACR/EULAR SLE classification criteria (n = 22) and unaffected controls (JIA, n = 6; low-titer ANA positive without disease, n = 4) were recruited from Stanford Pediatric Rheumatology clinics between August 2023 and October 2024. Peripheral blood mononuclear cells were obtained from controls at one timepoint and from SLE cases during active (n = 14, SLEDAI >4) and/or quiescent disease (n = 14). B cells, CD4 and CD8 T cells, and monocytes were isolated via fluorescence-activated cell sorting and sSNVs were detected via deep cell type-specific exome sequencing (~300X coverage).

Results: We discovered 9,650 candidate sSNVs with median variant allele frequency (VAF) of 3.4% (range 1.9 – 20.1%) across 112 exome datasets representing 4 cell types and 38 samples from 32 subjects. Based on sequencing synthetic mixtures of well-characterized cell lines, our workflow recovered SNVs with VAF ≥1.5% with precision >95% and recall >60%. B cells in active SLE were enriched for non-synonymous sSNVs relative to quiescent lupus and controls (median 62 vs. 40 – 52, p = 0.028, Mann-Whitney U test). Similarly, CD8 T cells in active SLE carried more sSNVs than in quiescent disease or in controls (median 65 vs. 40 – 41, p = 0.004, Mann-Whitney U test). Differences in age-stratified sSNV burden and cell type-specific VAFs were not significant. Genes harboring sSNVs in SLE lymphocytes included *JAK1*, *STAT3*, and *RELB*. Pooled analysis of non-synonymous sSNVs in SLE lymphocytes identified enrichment of survival signaling pathway genes ($p < 0.001$, hypergeometric test, Bonferroni corrected).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Interim analysis of immunogenetic mosaicism identified frequent protein-coding candidate sSNVs in peripheral B and T cells in clinically active SLE. Together with ongoing validation of sSNVs, sequencing of additional pediatric and adult subjects, and longitudinal analyses, we expect that future mechanistic studies will clarify the role of somatic variation in lupus pathogenesis and heterogeneity.

Disclosure: S. Kasinathan: None; **M. Pham**: None; **A. Satpathy**: 10x Genomics, 2, Astellas, 5, Cartography Biosciences, 12,, Immunai, 12,, Prox Biosciences, 12,, Santa Ana Bio, 12,, Wing Venture Capital, 2.

Abstract Number: 1700

Altered Gene Expression in Male SLE Is Mapped to a Male-specific Y Chromosome Locus Associated with Microdeletions

Mikhail Olferiev[1], Kyriakos Kirou[1], Emily Wu[2], Dina Greenman[1] and Mary Crow[3], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Union City, NJ, [3]Hospital for Special Surgery, New York

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Genetics, Genomics & Proteomics (1698–1703)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: SLE occurs more frequently in females than males, with relative prevalence 9-10:1. While the impact of hormones on immune function may contribute to the female predominance of SLE, recent interest has focused on the immune functions conferred by the two X chromosomes in women. To identify unique mechanisms that may result in SLE in males, we generated RNA transcript data from male and female subjects with SLE or from healthy individuals.

Methods: Female and male SLE patients were characterized in detail based on demographic, clinical and laboratory features. Multiple correspondence analysis of 95 parameters was used to optimally match 15 female and 15 male SLE patients, along with healthy donors. A PBMC sample for RNAseq analysis was selected for each patient at the time of their lowest level of disease activity. RNA sequencing was performed and data analyzed using principal component analysis (PCA) and determination of differentially expressed gene transcripts.

Results: PCA distribution of RNAseq data showed male SLE patients distinct from healthy males and female SLE patients. As observed for the overall SLE population, type I interferon-stimulated genes dominate transcripts differentially expressed between SLE males and healthy males, with SLE males also showing higher expression of NFkB pathway genes and pro-inflammatory cytokines/chemokines compared with healthy males. Among the differentially expressed genes, 4 Y chromosome-encoded transcripts (*TXLNGY, ENSG00000267793*, *BCORP1* and *KDM5D*) were significantly decreased in SLE males compared with healthy males and 1 Y chromosome-encoded gene (*EIF1AY*) was increased in SLE males. Of those, *KDM5D*, also called *SMCY*, encoding lysine demethylase 5D, is of particular interest as it mediates the removal of methyl groups from histone lysine residues at the K4 position and regulates both promoters and enhancers throughout the genome. Remarkably, review of the Y chromosome location of those differentially expressed genes revealed that all 5 genes share a portion of a genomic locus (termed AZFb) in the male-specific region of Y that is associated with microdeletions and male infertility.

Conclusion: Males with SLE demonstrate altered expression of several genes occupying a common Y chromosome locus, along with increased expression of NFkB and pro-inflammatory cytokine genes. Among the Y chromosome-encoded transcripts decreased in male SLE, *KDM5D*, a histone demethylase, warrants further investigation. *KDM5D* is expressed in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

multiple cell types and may contribute to impaired epigenetic regulation and activation of inflammation-related pathways throughout the genome. Our data suggest that males with SLE may be enriched in genomic Y chromosome variants that contribute to altered immune function.

Disclosure: M. Olferiev: None; **K. Kirou**: AMPEL Biosolutions, 5, Bristol-Myers Squibb(BMS), 5, Novartis, 5; **E. Wu**: None; **D. Greenman**: None; **M. Crow**: Abelzeta, 1, Aboleris, 1, AMPEL Biosolutions, 1, AstraZeneca, 1, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Gilead, 5, GlaxoSmithKlein(GSK), 1, Novartis, 1, Palleon, 1.

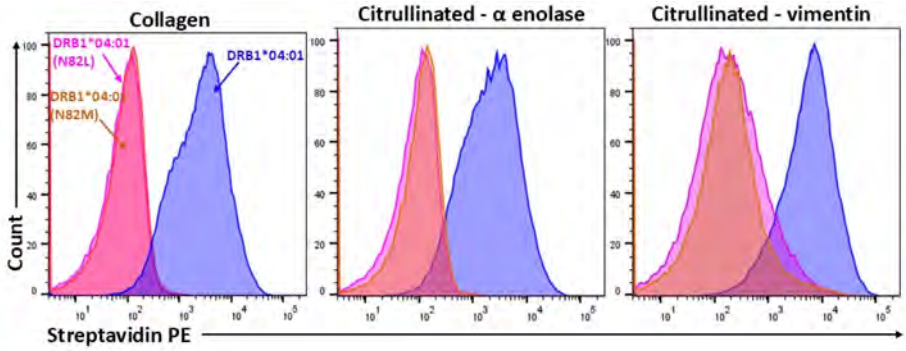
Abstract Number: 1701

Gene Editing of HLA-Class II DRB1*04:01 at Position 82 Abrogates Binding of Citrullinated Arthritogenic Peptides and Collagen

Vibha Jha[1], Brian Freed[2], Niyun Jin[1], Manjula Miglani[1] and Christina Roark[2], [1]University of Colorado, Aurora, CO, [2]Clinimmune Labs Immunology, School of Medicine, Aurora, CO

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Genetics, Genomics & Proteomics (1698–1703)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease with a strong genetic association to Class II HLA-DRB1*04:01. Presentation of arthritogenic peptides bound to DRB1*04:01 results in activation of autoreactive T cells which then mediate arthritic inflammation. Our previous work has demonstrated that a single amino acid change from lysine (K) to glutamic acid (E) at position 71 of DRB1*04:01 blocks binding of collagen$^{258\text{-}272}$ and abrogates collagen-specific CD4^{+} T cell activation without inducing alloreactivity (1). However, the K71E edit does not block binding of native or citrullinated vimentin$^{66\text{-}78}$ and α-enolase$^{11\text{-}25}$ peptides. Position 71 is located in pocket 4 of the peptide binding groove. Here we investigate if changing the amino acid in pocket 1 (position 86) or in pocket 2 (position 82) would eliminate binding of citrullinated arthritogenic peptides in addition to the immunodominant collagen peptide.



Mean MFI from three different repeats

HLA-Class II allele	Collagen	Citrullinated α enolase	Citrullinated vimentin
DRB1*04:01	3889	3867	7131
DRB1*04:01(N82L)	77	122	1082
DRB1*04:01(N82M)	71	97	339

Figure 1: Binding of arthritogenic peptides with unedited DRB1*04:01, and edits at position 82

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We edited DRB1*04:01 at position 82, from N to either leucine (L) or methionine (M) and at position 86 from glycine (G) to L. The edited DRB1*04:01^{N82L} (N82L), DRB1*04:01^{N82M} (N82M) and DRB1*04:01^{G86L} (G86L) molecules were expressed in T2 cells. Peptide binding of biotinylated citrullinated and native α-enolase$^{11-25}$, citrullinated and native vimentin$^{66-78}$ and native collagen$^{258-272}$ peptides was detected by streptavidin-PE using flow cytometry.

Results: All three edits blocked binding of the native forms of -enolase, vimentin and collagen. Citrullinated vimentin66-78 binding to DRB1*04:01N82L was reduced 85% and binding to DRB1*04:01N82M was reduced 95%. Similarly, binding of citrullinated α-enolase11-25 to DRB1*04:01N82L and to DRB1*04:01N82M was reduced by 97%. The G86L edit to DRB1*04:01 abrogated binding of citrullinated α-enolase11-25 and collagen258-272 but citrullinated vimentin66-78 could still bind.

Conclusion: Replacing N at position 82 of DRB1*04:01, with either L or M, abrogates peptide binding of citrullinated a-enolase, citrullinated vimentin and collagen. Blocking the binding of citrullinated peptides to edited DRB1*04:01 on APCs would prevent presentation of these autoantigens to autoreactive T cells. Our results demonstrate that introducing mutations at position 82 in DRB1*04:01 blocks binding of all arthritogenic peptides and thus has potential to be used as gene therapy to safely halt progression of RA in patients carrying DRB1*04:01

Disclosure: V. Jha: None; **B. Freed**: None; **N. Jin**: None; **M. Miglani**: None; **C. Roark**: None.

Abstract Number: 1702

Powerful and Accurate Case-Control Analysis of Spatially Resolved Molecular Data in Autoimmune Disease

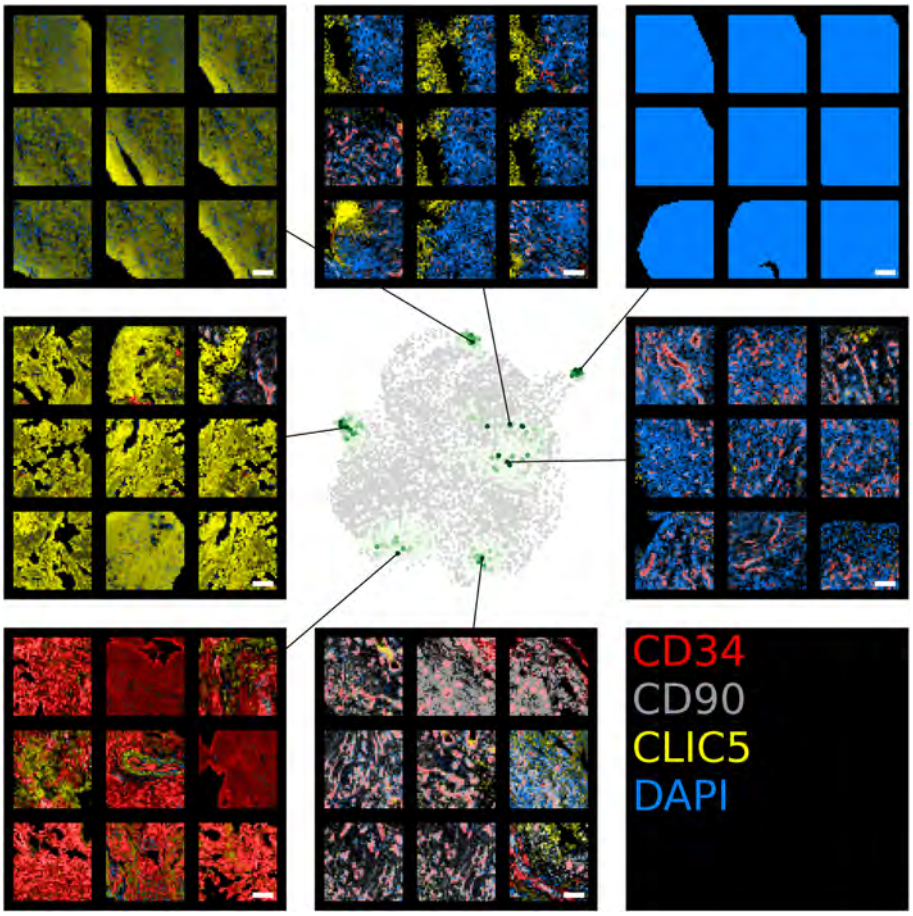
Yakir Reshef[1], Lakshay Sood[1], Michelle Curtis[1], Laurie Rumker[2], DANIEL STEIN[3], Mukta Palshikar[1], Saba Nayar[4], Andrew Filer[5], Anna Helena Jonsson[6], ilya Korsunsky[7], Soumya Raychaudhuri[7] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM), Accelerating Medicines Partnership: RA/SLE Network (AMP RA/SLE), [1]Brigham and Women's Hospital, Boston, [2]Broad Institute, Boston, [3]Harvard University, Boston, [4]University of Birmingham, Birmingham, United Kingdom, [5]The University of Birmingham, Birmingham, United Kingdom, [6]University of Colorado School of Medicine, Aurora, CO, [7]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Genetics, Genomics & Proteomics (1698–1703)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Autoimmune diseases such as rheumatoid arthritis (RA) involve complex spatial organization of immune and stromal cells within inflamed tissues. As spatial molecular profiling methods grow in scale and resolution, there is increasing opportunity to identify clinically and pathophysiologically informative tissue structures through case-control comparisons. Existing approaches to define key pathological structures rely either on bespoke manual scoring systems such as the Krenn inflammation score or on clustering spatial neighborhoods of segmented and typed cells based on cell-type abundances. These approaches are limited by confirmation bias, segmentation error, loss of local spatial relationships among cells, and inability to model spatial overlap of multiple biological processes.

Methods: We developed variational inference-based microniche analysis (VIMA), an artificial intelligence-driven method for case-control analysis of spatial data. VIMA uses AI to learn numerical "fingerprints" of small tissue patches that capture their biological content, groups similar patches into thousands of overlapping "microniches" across samples, and identifies microniches whose abundance differs by condition. VIMA requires no cell segmentation or typing and can be used on any high-resolution spatial modality.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



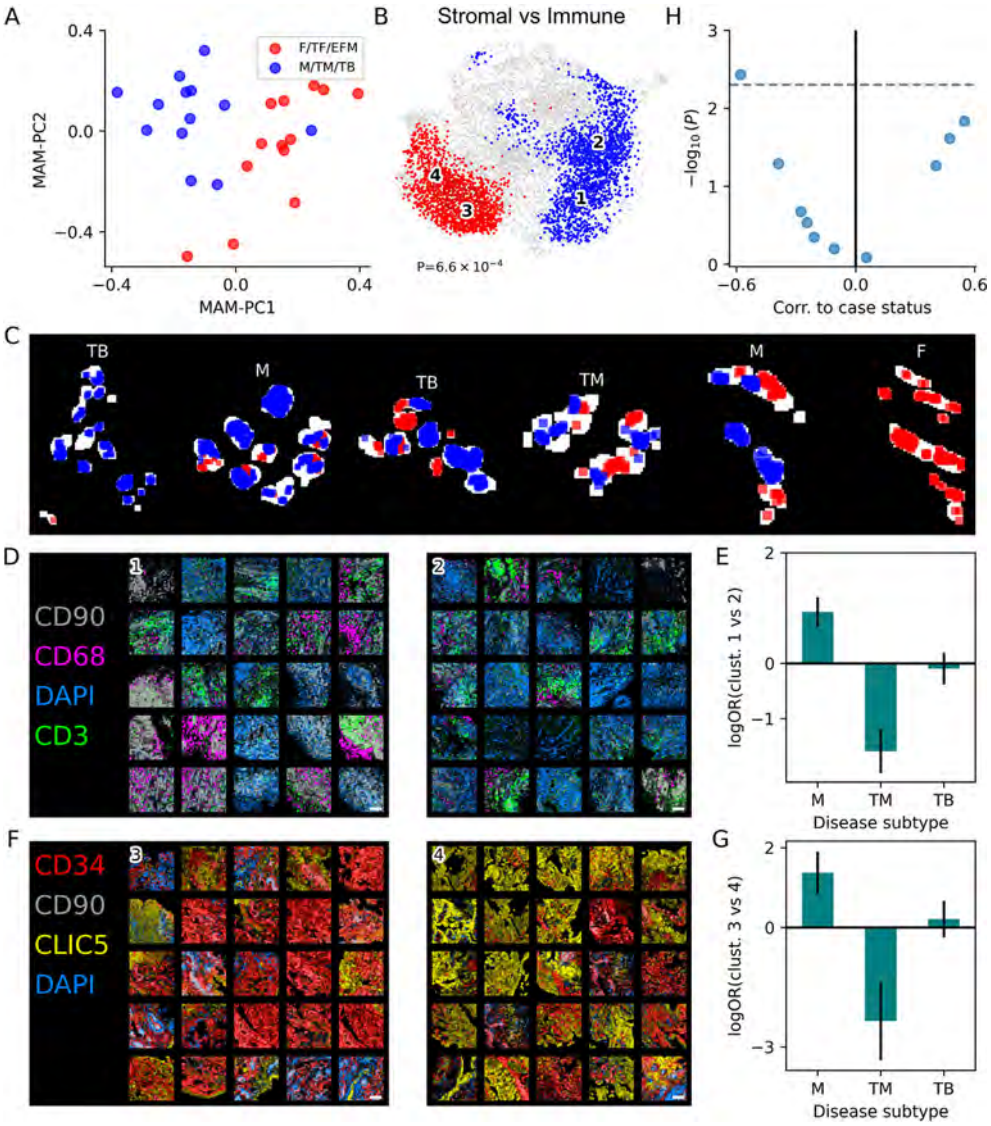
Examples of VIMA's microniches in the RA IHC dataset. We show a UMAP of all the patches in the dataset generated using the patch fingerprints, together with randomly selected patches drawn from 7 example microniches; these microniches are characterized by (clockwise from bottom-left): high CD34 intensity with interspersed CLIC5 signal, high CLIC5 intensity with minimal CD34 signal, high CLIC5 intensity but with a blurrier texture and interspersed DAPI signal, a vertical boundary between CLIC5-high/DAPI-low pixels and CLIC5-low/DAPI-high pixels, a DAPI staining artifact, DAPI-high infiltrate surrounding CD34-high regions that are likely blood vessels, and perivascular CD90-high pixels. All scale bars represent 100um.

Results: We first applied VIMA to a 7-marker N=22 immunohistochemistry (IHC) dataset in RA. Without prior labels, VIMA stratified samples into an "immune" and a "stromal" subtype (P=6.5e-4). The stromal subtype contained swathes of CLIC5+ staining and CD34+ regions; the immune subtype contained perivascular infiltrates and macrophages contacting sublining fibroblasts. These subtypes matched cell-type abundance phenotypes (CTAPs) defined previously in a much larger (N=79) non-spatial single-cell dataset, showing that VIMA can extract information from IHC that previously required state-of-the-art sequencing at large samle sizes to uncover. VIMA also revealed striking within-sample spatial heterogeneity, with many RA samples containing patches from both the stromal and immune subtypes, challenging the notion of one subtype per patient. We confirmed similar heterogeneity in subsequently collected synovial samples profiled with spatial transcriptomics as well.

We also applied VIMA to a 54-marker N=34 CODEX dataset in UC. Here, VIMA was able to powerfully distinguish UC samples from healthy samples (P=6.5e-4), and then to identify a dose-response relationship between duration of TNF inhibition and absence of lymphoid aggregates (P=1.4e-3). VIMA can therefore detect clinically relevant spatial signals -- including signatures of therapeutic immune modulation -- across diseases, technologies, and tissue types.

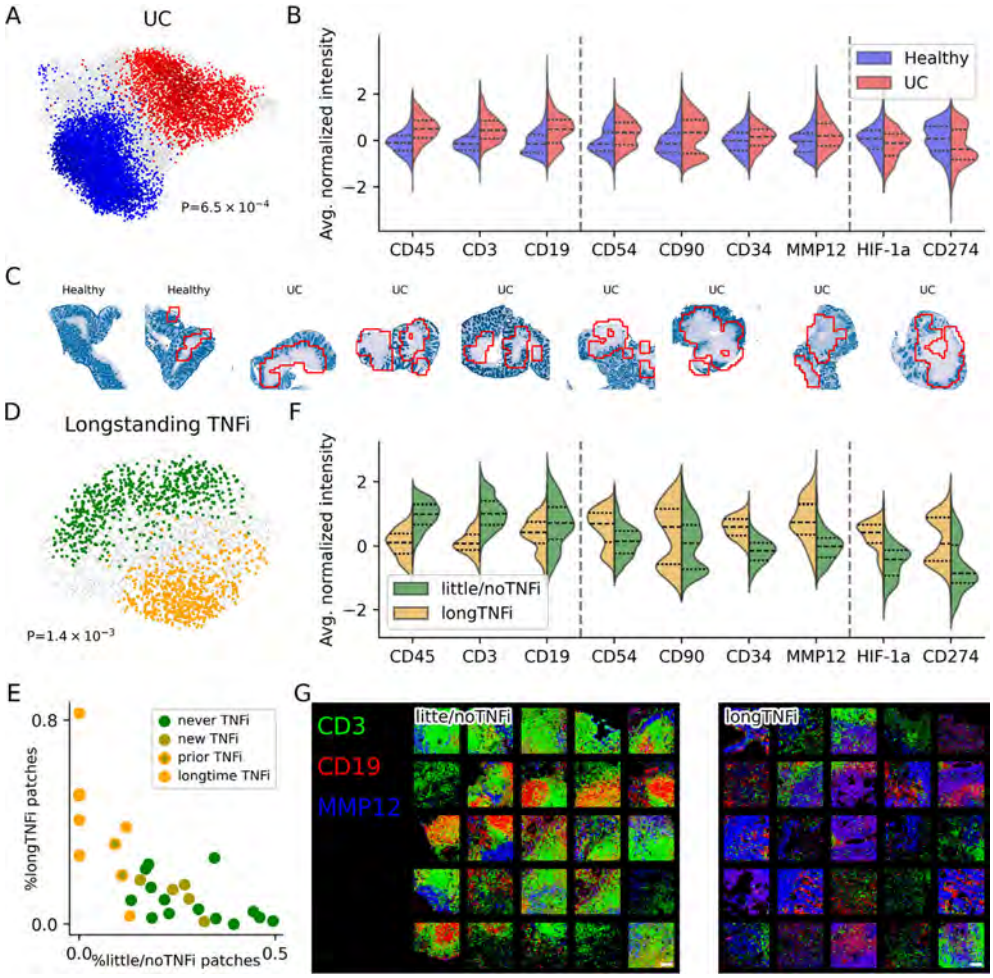
Conclusion: VIMA enables flexible, high-resolution spatial analysis of autoimmune disease. It identifies biologically meaningful signals missed by existing tools and reveals within-sample heterogeneity, demonstrating the promise of AI-based methods for advancing our understanding of autoimmune disease pathogenesis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



VIMA analysis of the RA IHC dataset. A) plot of the first two VIMA-determined principal components, with each dot representing a sample and samples colored by RA subtype (CTAP) as determined using a larger scRNA-seq dataset. F: fibroblast, TF: T-cell/fibroblast, EFM: endothelial/fibroblast/myeloid, M: myeloid, TM: T-cell/myeloid, and TB: T-cell/B-cell. B) Results of VIMA case-control analysis for the "stromal" (F/TF/EFM) versus "immune" (M/TM/TB) subtypes: a UMAP of all the patches in the dataset is generated using the patch fingerprints, and the anchor patches for microniches passing the 10% FDR threshold are colored in proportion to the correlation between the abundance of each microniche and sample-level stromal vs immune status, with red denoting stromal-enriched and blue denoting immune-enriched. The centroids of the two subclusters of each set of patches, respectively, are indicated with numbers. The global P-value for the association test is overlaid. C) A subset of 6 samples from the dataset exemplifying both spatial homogeneity in local stromal vs immune status within a sample (the leftmost and rightmost samples) and spatial heterogeneity in stromal vs immune status within a sample (middle samples), with disease subtype indicated above each sample. Each patch in each sample is colored red if it is stromal-associated by VIMA or blue if it is immune-associated. D) Randomly selected patches from each of the two clusters of immune-associated patches. E) Log-odds ratios among the immune-associated patches for belonging to cluster 1 (positive log-odds) vs cluster 2 (negative log-odds) as a function of disease subtype, with 95% confidence intervals. F) Randomly selected patches from each of the two clusters of stromal-associated patches. G) Log-odds ratios among the stromal-associated patches for belonging to cluster 3 (positive log-odds) vs cluster 4 (negative log-odds) as a function of disease subtype. H) A volcano plot showing that a cluster-based rather than microniche-based case-control analysis using the patch fingerprints learned by VIMA does not identify as robust of a signal. The Bonferroni significance threshold is shown with a dotted line. Scale bars represent 100um throughout.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



VIMA analysis of UC CODEX dataset. A) Results of VIMA case-control analysis for UC versus healthy: a UMAP of all the patches in the dataset is generated using the patch fingerprints, and the anchor patches for microniches passing the 10% FDR threshold are colored in proportion to the correlation between the abundance of each microniche and UC status, with red denoting to positive correlations and blue denoting negative correlations. The global P-value for the association test is overlaid. B) Distributions of average intensity per patch of selected markers among UC-associated and healthy-associated patches. The selected markers are grouped using dotted lines according to the relationship of their directions of effect to those in panel (F). C) Selected samples shown with cytokeratin staining in blue and contiguous areas of UC-associated patches outlined in red. D) Results of VIMA analysis of UC-associated patches only, comparing the samples with longstanding TNF inhibition (longTNFi) to those with no TNF inhibition, prior TNF inhibition only, or recent TNF inhibition only (little/noTNFi), with gold denoting positive correlation to longTNFi status and green denoting negative correlation. The global P-value for the association test is overlaid. E) Comparison of fraction of longTNFi-associated vs little/noTNFi-associated patches in each sample. For each sample, the percent of patches in that sample that anchor microniches significantly associated with longTNFi is plotted against the percent of patches in that sample significantly associated with little/noTNFi. Each sample is then colored by its detailed TNFi status. F) Distributions of average intensity per patch of selected markers among TNFi-associated and non-TNFi-associated patches. The selected markers are grouped using dotted lines as follows: markers that are higher in UC compared to control and in little/noTNFi compared to longTNFi (left), markers that are higher in UC compared to control but lower in little/noTNFi compared to longTNFi (middle), and markers that are lower in UC compared to control and lower in little/noTNFi compared to longTNFi (right). G) Randomly selected patches from the little/noTNFi-associated patches (left) and the longTNFi-associated patches (right).

Disclosure: Y. Reshef: None; **L. Sood**: None; **M. Curtis**: None; **L. Rumker**: None; **D. STEIN**: None; **M. Palshikar**: None; **S. Nayar**: None; **A. Filer**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Janssen, 2, 5, Synact, 5; **A. Jonsson**: Arpelos Biosciences, 2, Ono Pharmaceuticals, 5, Pfizer, 6; **i. Korsunsky**: Mestag therapeutics, 2; **S. Raychaudhuri**: Bonito, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Mestag, 1, 8, Nimbus, 2, Pfizer, 1, Sonoma, 1, 8, Visterra, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1703

Predicting Rheumatoid Arthritis Flare Using Longitudinal Cytokine Trajectories, Machine Learning and Spatial Transcriptomic Imaging

Wittaya Suwakulsiri[1], Lukas Andriessen[2], Coline Fournier[3], Saritha Kodikara[4], Amy Anderson[5], Jasmine Sim[5], Kim-Anh Le Cao[4], Yann Abraham[6], Kevin Wei[7], Kenneth Baker[5], Arthur Pratt[8], Mihir Wechalekar[9], John Isaacs[10] and Ranjeny Thomas[1], [1]Frazer Institute, University of Queensland, Brisbane, Queensland, Australia, [2]Frazer Institute, University of Queensland, Woolloongabba, Queensland, Australia, [3]Melbourne Integrative Genomics & School of Mathematics and Statistics, The University of Melbourne, Melbourne, Australia, [4]Melbourne Integrative Genomics & School of Mathematics and Statistics, The University of Melbourne, Melbourne, Victoria, Australia, [5]Translational and Clinical Research Institute, NIHR Newcastle Biomedical Research Centre, Newcastle University and The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle, United Kingdom, [6]DeepLife, Vernon, France, [7]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [8]University of Newcastle, Newcastle, United Kingdom, [9]Flinders Medical Centre, Adelaide, Australia, [10]Newcastle University, Newcastle upon Tyne, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Genetics, Genomics & Proteomics (1698–1703)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Many patients living with rheumatoid arthritis (RA) can achieve remission with modern treat-to-target disease-modifying anti-rheumatic drugs (DMARDs), albeit with the risks associated with long-term immunosuppression. Some may choose to try reducing or stopping treatment, though this carries a risk of flare which is currently unpredictable. We explored whether high-throughput serial measurement of circulating proteomic biomarkers could predict risk of future arthritis flare after DMARD cessation.

Methods: We analyzed longitudinal expression of 250 soluble factors (NULISA technology) in serum collected from 115 patient with RA in remission at 0, 2, 5, 8, 12 and 24 weeks after stopping conventional synthetic DMARDs (BIO-FLARE study). Additionally, synovial tissue (ST) biopsies from 22 recent-onset untreated disease-active ACPA+ RA patients and 6 healthy individuals were imaged using spatial transcriptomic profiling (5,101 genes, 10x Genomics).

Results: Over 24 weeks, 57 BIOFLARE participants flared and 58 maintained drug-free remission. A linear mixed model identified 68 cytokines with significantly different expression trajectories between flare and remission groups. KEGG Pathways indicate enrichment in inflammatory pathways, including Cytokine-cytokine receptor interaction, Viral protein interaction with cytokine and cytokine receptor, and JAK-STAT signaling pathway, which are associated with RA flare pathology. Addition of a random forest algorithm achieved 88% accuracy in distinguishing flare events. The model identified a subset of cytokines that best predicted flare before it was clinically apparent. Of these, Xenium spatial imaging co-located *CXCL13, TNFSF13C* and *CD83* RNA expression to follicles containing memory B cells, plasma cells and peripheral/follicular helper T cells (Tph/fh). In contrast, *CXCL10* was expressed in small lining-adjacent foci by lining-layer fibroblasts and endothelial cells surrounded by CD8+GZMK+ T cells. Notably, these fibroblasts co-expressed type 1 interferon (IFN)-inducible genes, particularly *GBP1, GBP5, IFIT3* and *IFIT2* that are involved in anti-viral and anti-bacterial defence.

Conclusion: Biomarkers of flare after DMARD withdrawal, identified by integrating cytokine trajectory analysis, machine learning and spatial transcriptomics, reflect chemoattractants and soluble markers of activated memory B cells and Tph/fh to ST. Furthermore, spatial data suggest that pathogen-mediated type I IFN-induced chemoattraction of CD8+GZMK+ T cells contributes to RA disease flares. With validation, these circulating markers may improve monitoring of disease activity and provide opportunity for interception of flare during DMARD withdrawal.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: W. Suwakulsiri: None; **L. Andriessen**: None; **C. Fournier**: None; **S. Kodikara**: None; **A. Anderson**: None; **J. Sim**: None; **K. Le Cao**: None; **Y. Abraham**: DeepLife, 3, Johnson & Johnson, 11; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **K. Baker**: Genentech, 5, Pfizer, 5; **A. Pratt**: Bristol-Myers Squibb(BMS), 5; **M. Wechalekar**: GlaxoSmithKlein(GSK), 5, Janssen, 5; **J. Isaacs**: Bristol-Myers Squibb(BMS), 5; **R. Thomas**: AbbVie/Abbott, 2, CSL, 2.

Abstract Number: 1704

Relationships between Neighborhood Disadvantage, Cumulative Social Disadvantage, and JIA Outcomes: A CARRA Registry Study

William Soulsby[1], John Boscardin[2], Daniel Horton[3], Andrea Knight[4], Karine Toupin-April[5], Emily von Scheven[2] and CARRA Registry Investigators, [1]University of California, San Francisco, San Francisco, CA, [2]UCSF, San Francisco, CA, [3]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [4]Hospital for Sick Children, Toronto, ON, Canada, [5]University of Ottawa, Ottawa, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Healthcare Disparities in Rheumatology (1704–1709)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Social determinants of health (SDOH) operate across individual, family, and community levels. We previously demonstrated that cumulative social disadvantage, comprised of individual and family-level SDOH, was associated with persistent disease activity among children with JIA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. However, the role of community-level SDOH, and their interaction with cumulative social disadvantage, in JIA health disparities is unknown.

Methods: In this cohort study of children with JIA in the CARRA Registry (July 2015-January 2022), a cumulative social disadvantage score was generated (range 0-3) for each subject with a score of 1 for each parameter (1) family income < $50,000/year, 2) guardian education at less than high school level, and 3) public or no insurance). Community-level SDOH

Table 1: Demographic and clinical characteristics of children with JIA in the CARRA Registry by National Area Deprivation Index (ADI) quartile

	National Area Deprivation Index (ADI) Quartiles						
	Q1 (Lowest)*	Q2	Q3	Q4 (Highest)	Missing	Total	p-value
	2,097 (21.8%)	1,990 (20.7%)	1,920 (20.0%)	1,956 (20.3%)	1,649 (17.2%)	9,612 (100.0%)	
Cumulative Social Disadvantage Score:							
0	1,703 (81.2%)	1,336 (67.1%)	1,026 (53.4%)	687 (35.1%)	1,100 (66.7%)	5,852 (60.9%)	<0.001
1	269 (12.8%)	410 (20.6%)	490 (25.5%)	545 (27.9%)	333 (20.2%)	2,047 (21.3%)	
2	102 (4.9%)	183 (9.2%)	313 (16.3%)	482 (24.6%)	164 (9.9%)	1,244 (12.9%)	
3	23 (1.1%)	61 (3.1%)	91 (4.7%)	242 (12.4%)	52 (3.2%)	469 (4.9%)	
Score Components:							
Household income <$50,000/year	129 (6.2%)	266 (13.3%)	409 (21.3%)	749 (38.3%)	282 (17.1%)	1,834 (19.1%)	<0.001
Less than high school education of guardians	138 (6.6%)	249 (12.5%)	384 (20.0%)	560 (28.6%)	247 (15.0%)	1,578 (16.4%)	<0.001
Public insurance or no insurance	275 (13.1%)	445 (22.4%)	596 (31.0%)	926 (47.3%)	288 (17.5%)	2,530 (26.3%)	<0.001
Race and/or ethnicity[a]							
White	1,567 (74.7%)	1,527 (76.7%)	1,498 (78.0%)	1,409 (72.0%)	1,199 (72.7%)	7,200 (74.9%)	<0.001
Hispanic	139 (6.6%)	151 (7.6%)	148 (7.7%)	193 (9.9%)	103 (6.2%)	734 (7.6%)	
More than one race	143 (6.8%)	137 (6.9%)	117 (6.1%)	115 (5.9%)	113 (6.9%)	625 (6.5%)	
Black	45 (2.1%)	51 (2.6%)	68 (3.5%)	163 (8.3%)	51 (3.1%)	378 (3.9%)	
Asian	116 (5.5%)	37 (1.9%)	26 (1.4%)	14 (0.7%)	62 (3.8%)	255 (2.7%)	
Other race	41 (2.0%)	38 (1.9%)	33 (1.7%)	45 (2.3%)	76 (4.6%)	233 (2.4%)	
Refused or Missing	46 (2.2%)	49 (2.5%)	30 (1.6%)	17 (0.9%)	45 (2.7%)	187 (1.9%)	
Median cJADAS-10 score (IQR[b])	3.5 (0.5-9.0)	4.0 (1.0-9.0)	4.0 (1.0-10.0)	4.5 (1.0-10.0)	4.0 (1.0-9.0)	4.0 (1.0-9.0)	<0.001
Active disease by cJADAS-10[c]	1,244 (59.3%)	1,232 (61.9%)	1,198 (62.4%)	1,293 (66.1%)	1,009 (61.2%)	5,976 (62.2%)	<0.001

*Area deprivation index (ADI) quartiles from lowest levels of ADI (Q1) to highest levels (Q4), corresponding to least (Q1) to most (Q4) disadvantaged
[a]Race and ethnicity were self-reported and are mutually exclusive categories.
[b]Interquartile range
[c]Clinical Juvenile Arthritis Disease Activity Score-10 (cJADAS) scores >1.1 for those with oligoarticular JIA and >2.5 for all other subtypes were used to define active disease.

Demographic and clinical characteristics of children with JIA in the CARRA Registry by National Area Deprivation Index (ADI) quartile

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Associations between area deprivation index and cumulative social disadvantage with any active disease[1] throughout Registry follow-up:

	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Area deprivation index		
1 (Lowest)	*Ref*	*Ref*
2	1.15 (1.01-1.30)	1.05 (0.88-1.25)
3	1.22 (1.03-1.45)	1.05 (0.87-1.28)
4 (Highest)	1.43 (1.15-1.76)	1.06 (0.85-1.32)
Cumulative social disadvantage score		
0	*Ref*	*Ref*
1	1.35 (1.18-1.56)	1.30 (1.10-1.54)
2	1.81 (1.53-2.14)	1.94 (1.62-2.32)
3	2.06 (1.59-2.68)	2.22 (1.68-2.93)
Race and/or ethnicity[α]		
White	*Ref*	*Ref*
Black	1.88 (1.50-2.36)	1.30 (1.03-1.64)
Hispanic	1.30 (1.08-1.58)	0.96 (0.78-1.18)
Asian	0.72 (0.60-0.89)	0.81 (0.68-0.96)
Other race	1.14 (0.92-1.41)	0.97 (0.77-1.24)
More than one race	1.36 (1.16-1.59)	1.25 (1.07-1.46)
Refused or Missing	1.27 (0.96-1.68)	1.12 (0.84-1.49)

[1]Defined in subjects with a Clinical Juvenile Arthritis Disease Activity Score-10 (cJADAS-10) >1.1 for oligoarticular JIA and >2.5 in all other JIA categories.
*Adjusted for age at enrollment, time from symptom onset to diagnosis, year of diagnosis, sex, JIA category, presence of secondary rheumatic disease, medication use during follow up (bsDMARD, csDMARD, small molecule), current steroid use, any steroid use during follow-up.
[α]Race and ethnicity were self-reported and are mutually exclusive categories.

Associations between area deprivation index and cumulative social disadvantage with any active disease throughout Registry follow-up

Table 3: The adjusted average proportion of the effect of area deprivation index quartile on disease activity mediated by the cumulative social disadvantage score and its components via causal mediation analysis[1,2] (n=50 cycles):

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Cumulative social disadvantage score	*Ref*	35.0%	74.4%	67.6%
Low income	*Ref*	27.8%	59.6%	80.2%
Underinsured status	*Ref*	14.7%	47.1%	75.2%
Low guardian education level	*Ref*	7.4%	56.9%	27.0%

[1]Causal mediation analysis quantifies the total effect of a predictor (highest ADI quartile as compared to lowest) into its direct effect on an outcome (disease activity by cJADAS-10 score) and indirect effect mediated through a proposed mediator (cumulative social disadvantage score), from which the total proportion of the effect that is mediated can be calculated (proportion mediated).
[2]Note: Age at enrollment, time from symptom onset to diagnosis, year of diagnosis, sex, JIA category, presence of secondary rheumatic disease, medication use during follow up (bsDMARD, csDMARD, small molecule), current steroid use, and any steroid use during follow-up were adjusted for in this analysis.

The adjusted average proportion of the effect of area deprivation index quartile on disease activity mediated by the cumulative social disadvantage score and its components via causal mediation analysis1,2 (n=50 cycles)

was assessed using the national Area Deprivation Index (ADI), a measure of neighborhood-level socioeconomic disadvantage geocoded at the census tract level. Descriptive statistics were performed to summarize demographic and clinical characteristics by ADI quartile. Mixed-effects logistic regression models were generated to investigate the association between ADI quartile and active disease (cJADAS-10 >1.1 for oligoarticular JIA; >2.5 for all other subtypes), adjusting for the cumulative social disadvantage score and other covariates. Multiple imputation (50 cycles) addressed missingness in ADI (17%), income (25%), and education (16%). Causal mediation analysis was used to assess the cumulative social disadvantage score and its components as mediators of the association between ADI and disease activity.

Results: Among 9,612 children with JIA, cumulative social disadvantage was more prevalent in the most disadvantaged neighborhoods (Table 1: ADI Q4: 64.9% with score >0 vs. Q1: 18.8%). While ADI was independently associated with persistent disease activity in unadjusted models (ADI Q4: OR 1.43, 95% CI: 1.15-1.76), this was significantly attenuated (ADI Q4: aOR 1.06, 95% CI: 0.85-1.32) upon adjustment for the cumulative social disadvantage score and covariates (Table 2). Cumulative social disadvantage mediated 67.6% of the relationship between most (ADI Q4) versus least (ADI Q1) neighborhood disadvantage and disease activity (Table 3). Low income and insurance mediated 80.2% and 75.2% of this relationship, respectively, while guardian education only mediated 27.0%.

Conclusion: While neighborhood-level deprivation (ADI) was independently associated with persistent disease activity, this relationship was largely mediated by individual and family-level SDOH, particularly household income and insurance status. Therefore, interventions that can address these individual/family-level factors, such as social work and patient navigator services, may be effective strategies for reducing JIA health disparities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: W. Soulsby: None; **J. Boscardin**: None; **D. Horton**: None; **A. Knight**: Pfizer, 6; **K. Toupin-April**: None; **E. von Scheven**: None.

Abstract Number: 1705

Associations Between Social Risk Factors and Acute Care Use Among Patients with Rheumatic Conditions

Haelynn Gim[1], Leah Santacroce[2], Rebecca Summit[3], Karli Retzel[4], Virginia Bills[4], Nancy Shadick[3], Sara Schoenfeld[5] and Candace Feldman[2], [1]Harvard Medical School, Brookline, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham & Women's Hospital, Boston, MA, [4]Brigham & Women's Hospital, Boston, [5]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Healthcare Disparities in Rheumatology (1704–1709)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Adverse social determinants of health, or social risk factors (e.g., housing instability, food insecurity), contribute to disparities in rheumatic disease care and outcomes. Understanding differences in health care use among individuals with vs. without social risk factors is critical to inform resource allocation, prevention strategies, and outpatient care coordination. We aimed to examine associations between social risk factors and acute care use, including preventable and non-preventable emergency department (ED) visits and hospitalizations, among patients with rheumatic conditions.

Table 1. Patient Characteristics by Presence vs. Absence of Social Risk Factors

Characteristics	≥1 Social Risk Factor (N = 1,614)	No Social Risk Factors (N = 7,976)
Age - Mean (SD)	56 (16)	59 (15)
Gender - N (%)		
Female	1,297 (80)	5,961 (75)
Male	316 (20)	2,015 (25)
Race - N (%)		
White	1,009 (63)	6,818 (85)
Black / African American	215 (13)	333 (4.2)
Asian	69 (4.3)	348 (4.4)
More than One Race	37 (2.3)	54 (0.7)
Other	223 (14)	273 (3.4)
Ethnicity - N (%)		
Non-Hispanic	1,392 (86)	6,976 (87)
Hispanic	84 (5.2)	88 (1.1)
Primary language - N (%)		
English	1,440 (89)	7,774 (97)
Spanish	121 (7.5)	85 (1.1)
Other non-English Language	43 (2.7)	81 (1.0)
Insurance - N (%)		
Commercial	719 (45)	4,916 (62)
Medicare	510 (32)	2,594 (33)
Medicaid	373 (23)	427 (5.4)
Rheumatic Condition - N (%)		
Inflammatory Arthritis	975 (60)	5,094 (64)
Systemic Rheumatic Disease*	456 (28)	1,843 (23)
Osteoarthritis	359 (22)	1,825 (23)
Vasculitis	41 (2.5)	154 (1.9)
Crystalline Arthropathy	55 (3.4)	298 (3.7)

*Includes systemic lupus erythematosus, Behcet's, systemic sclerosis, Sjogren's/sicca syndrome, mixed/unspecified connective tissue disease, dermatomyositis/polymyositis/inclusion body myositis, and sarcoidosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We identified adults ≥18 years with ≥2 ICD-10 codes for a systemic rheumatic condition, inflammatory arthritis, crystalline arthropathy, or osteoarthritis receiving care within a multihospital academic health system, who completed ≥1 social risk factor questionnaire at the time of a rheumatology visit (6/2022-12/2024). We compared the presence vs. absence of social risk factors by demographic factors. Using modified Poisson regression models, we estimated incidence rates (IRs) and incidence rate ratios (IRRs) with 95% confidence intervals for ≥1 ED visit and ≥1 hospitalization following screening among patients reporting ≥1 vs. 0 social risk factor, and by individual social risk factors. We also examined the IR and IRR of preventable ED visits[1] by social risk factor presence. Models were adjusted for age, sex, race, ethnicity, primary language, rheumatic condition, and Charlson-Deyo comorbidity index.

Results: Among 9,590 patients with rheumatic conditions screened for social risk factors, 1,614 (17%) reported ≥1 social risk factor. Patients with ≥1 (vs. 0) social risk factor more frequently identified as Black or Hispanic, were ≤50 years of age, spoke Spanish as their primary language, and were Medicaid beneficiaries (Table 1). Among patients with ≥1 social risk factor, 491 (30%) had ≥1 ED visit and 261 (16%) had ≥1 hospitalization following screening. Among patients without risk factors, 1,532 (19%) had ≥1 ED visit and 802 (10%) had ≥1 hospitalization. In adjusted models, there were higher rates of ED visits (IRR 1.38, 95% CI 1.33-1.43) and hospitalizations (IRR 1.59, 95% CI 1.52-1.67) among patients with vs. without social risk factors, and for all individual risk factors except digital access needs (Table 2). Education and transportation needs were associated with the highest rates of ED visits and hospitalizations, respectively. Among patients with any ED visit, 24 (4.9%) of those with risk factors and 63 (4.1%) of those without had ≥1 preventable visit (IRR 1.08, 95% CI 0.92-1.26).

Conclusion: Among patients with rheumatic conditions, presence vs. absence of social risk factors was strongly associated with higher rates of acute care use. The rate of preventable ED visits, however, did not differ. Limitations include inability to adjust for rheumatic disease severity and to account for health care use outside of the multihospital medical system. Future studies are needed to assess mechanisms behind these associations and to test the impact of interventions that address social needs on acute care use.

Table 2. Adjusted* Incidence Rates (IRs) and Incidence Rate Ratios (IRR) for ≥1 ED Visit and ≥1 Hospitalization by Presence vs. Absence of Social Risk Factors

	≥1 ED Visit		≥1 Hospitalization	
	IR (95% CI)	IRR (95% CI)	IR (95% CI)	IRR (95% CI)
Any Social Risk Factor				
Absent (0 Risk Factors)	0.081 (0.073-0.090)	*Ref.*	0.013 (0.011-0.015)	*Ref.*
Present (≥1 Risk Factor)	0.113 (0.101-0.123)	1.38 (1.33-1.43)	0.021 (0.018-0.025)	1.59 (1.52-1.67)
Transportation Access Needs				
Absent	0.086 (0.078-0.096)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.125 (0.111-0.141)	1.45 (1.36-1.54)	0.030 (0.025-0.035)	1.86 (1.72-2.00)
Food Insecurity				
Absent	0.086 (0.078-0.096)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.125 (0.112-0.141)	1.45 (1.38-1.52)	0.025 (0.021-0.029)	1.55 (1.45-1.66)
Housing Insecurity				
Absent	0.087 (0.078-0.096)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.116 (0.102-0.131)	1.34 (1.24-1.44)	0.025 (0.020-0.030)	1.53 (1.38-1.69)
Medication Access Needs				
Absent	0.088 (0.079-0.097)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.121 (0.107-0.136)	1.38 (1.3-1.46)	0.023 (0.012-0.028)	1.42 (1.32-1.54)
Education Needs				
Absent	0.083 (0.075-0.093)	*Ref.*	0.015 (0.013-0.018)	*Ref.*
Present	0.127 (0.112-0.144)	1.52 (1.42-1.63)	0.025 (0.021-0.030)	1.63 (1.47-1.80)
Utility Bill Needs				
Absent	0.087 (0.079-0.097)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.105 (0.093-0.118)	1.2 (1.13-1.27)	0.022 (0.018-0.026)	1.33 (1.23-1.44)
Unemployment				
Absent	0.084 (0.076-0.093)	*Ref.*	0.016 (0.013-0.018)	*Ref.*
Present	0.120 (0.106-0.136)	1.43 (1.33-1.53)	0.023 (0.019-0.028)	1.47 (1.33-1.63)
Digital Access Needs				
Absent	0.088 (0.079-0.097)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.082 (0.070-0.096)	0.94 (0.83-1.06)	0.014 (0.011-0.017)	0.84 (0.72-0.99)
Caregiving Needs				
Absent	0.086 (0.078-0.096)	*Ref.*	0.016 (0.014-0.019)	*Ref.*
Present	0.114 (0.099-0.132)	1.32 (1.19-1.46)	0.025 (0.020-0.031)	1.57 (1.36-1.80)

*Modified Poisson regression models adjusted for age, sex, race, ethnicity, primary language, rheumatic condition, and Charlson-Deyo comorbidity index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[1] NYU ED Algorithm, https://wagner.nyu.edu/faculty/billings/nyued-background

Disclosure: H. Gim: None; **L. Santacroce**: None; **R. Summit**: None; **K. Retzel**: None; **V. Bills**: None; **N. Shadick**: Bristol-Myers Squibb(BMS), 5, Janssen, 5; **S. Schoenfeld**: None; **C. Feldman**: American College of Rheumatology, 2, Arthritis Foundation, 5, 12, Task Force Member, Bain Capital, 2, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 1, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2.

Abstract Number: 1706

Overcoming Barriers to ANA Testing in Pediatric Populations in Africa

Ekemini Ogbu[1], Angela Migowa[2], Rashmi Sahay[1], Dhriti Sharma[1], Patricia Vega-Fernandez[1], Michael Henrickson[1], Evans Omalla[3], Ayodele Faleye[4], Wafa Hamdi[5] and Hermine Brunner[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Aga Khan University Medical College East Africa, Nairobi, Kenya, [3]Pediatric Society of the African League Against Rheumatism, Nairobi, Kenya, [4]Lagos state university teaching hospital Ikeja, Lagos, Lagos, Nigeria, [5]Kassab Institute, Faculty of Medicine of Tunis UR17SP04, Tunis El Manar Univeristy, MANOUBA, Tunisia

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Healthcare Disparities in Rheumatology (1704–1709)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Timely diagnosis of children, adolescents and young adults with rheumatologic disorders remains a global challenge especially in *lower resource countries and areas (LRCs)*. There are several LRCs on the African continent with limited access to antinuclear antibodies (ANA) testing necessary to support a diagnosis of several pediatric rheumatic disorders (PRD; % of patients with positive ANA) including systemic lupus erythematosus (100%), juvenile dermatomyositis (60-75%), and juvenile idiopathic arthritis (40-60%). As the presence of ANA has near-ubiquitous utility in initially evaluating for a rheumatic condition, we aimed to understand physician perspectives on the barriers to ANA testing in pediatric populations across Africa, and the regional differences in barriers.

Methods: Electronic REDCap surveys were sent to physicians within the Pediatric Society of the African League Against Rheumatism (PAFLAR). Surveys were sent via individual email links from January to March 2025. Dillman's methods for surveys were used to optimize survey response rates. Descriptive analysis was done and comparisons considering geographic region and the World Bank classification of economies based on Gross National Income per capita.

Results: Response rate was 74% (38 of 50). Most respondents were attendings (89%), from Lower Middle-Income Countries (LMIC; 68%), and from North Africa (41%) (Table 1). All physicians had experience in treating PRDs, including 30% of respondents who lacked formal training in rheumatology. ANA testing was needed > 10 times a month (46%). The cost of ANA testing was high at $20 – 60/test (60%). Over 80% of respondents had little to no difficulty collecting and centrifuging venous blood for ANA testing. However, only 31% found it easy to ship samples to a lab within 1 - 2 days of sample collection. There was difficulty in processing ANA testing by ELISA which was worse in the Southern (100%), and West regions (83%) (p=0.03). Over 70% of respondents had difficulty receiving results of ANA testing quickly enough to support patient care which was worse with lower income countries and LMIC compared to others (p = 0.04); and in West and Central/East regions compared to others (p = 0.03). Even with local laboratories available, ANA testing was not readily available in public hospitals and so samples were often sent overseas.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1: Demographic Characteristics of Study Respondents

Respondents	n (%)
Consultants (aka Attendings)	33 (89)
Fellows/Registrars	4 (11)
Primary Specialty	
Pediatric Rheumatology	6 (16)
Adult and Pediatric Rheumatology	12 (32)
Adult Rheumatology	8 (22)
Pediatric Nephrology	1 (3)
General Pediatrics	7 (19)
Internal Medicine	1 (3)
Clinical Immunology	1 (3)
Pediatric Cardiology	1 (3)
Respondent country by income level	
High Income Countries	2 (5)
Low Income Countries	8 (22)
Lower Middle-Income Countries	25 (68)
Upper Middle-Income Countries	2 (5)
Respondent country by region	
Central Africa	2 (5)
East Africa	11 (30)
North Africa	15 (41)
Southern Africa	3 (8)
West Africa	6 (16)
Most common rheumatic disease treated	
Juvenile Idiopathic Arthritis	20 (54)
Lupus	8 (22)
Sjogren's Syndrome	1 (3)
Other rheumatic diseases	8 (22)
Number of pediatric patients with rheumatic disease treated in past year	
1- 20	8 (22)
21 – 40	5 (14)
Over 40	24 (65)

Conclusion: Our results provide highly desired quantitative evidence of the urgent need to improve access to affordable, and robust ANA testing in LRCs in Africa. Specifically, our results highlight critical barriers to ANA testing that will inform successful scaling of testing methods and future research and intervention efforts that would improve early diagnosis of rheumatic conditions in children, adolescents and young adults.

Disclosures: Supported by the Cincinnati Children's Hospital Medical Center Faculty International Research Excellence (FIRE) Award.

Disclosure: E. Ogbu: Cartesian Therapeutics, 2; **A. Migowa**: None; **R. Sahay**: None; **D. Sharma**: None; **P. Vega-Fernandez**: None; **M. Henrickson**: None; **E. Omalla**: None; **A. Faleye**: None; **W. Hamdi**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1707

Racial and Ethnic Disparities in Kidney Transplant Outcomes Among Patients With Systemic Lupus Erythematosus (SLE): A 20-Year Analysis Spanning Before and After the 2014 Kidney Allocation System Revision

Soziema Salia[1], Boniface Mensah[2], Ufuoma Mamoh[1], Gilava Hedayati[1], Terrylyna Baffoe-Bonnie[3], Joan Morny[4] and Christhopher Haas[3], [1]MedStar Health Georgetown University (Baltimore) Internal Medicine Program, Baltimore, MD, [2]MedStar Health Georgetown University (Baltimore) Internal Medicine Program, Baltimore, CA, [3]MedStar Health Georgetown University (Baltimore) Internal Medicine Program, Baltimore, [4]Piedmont Athens Regional Internal Medicine Residency Program, Athens, GA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Healthcare Disparities in Rheumatology (1704–1709)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a leading cause of end-stage kidney disease (ESKD) in young women, particularly among racial and ethnic minorities. Kidney transplantation is the preferred treatment for SLE-related ESKD, yet disparities in transplant access and outcomes persist. In 2014, the Kidney Allocation System (KAS) was revised to improve equity in organ distribution. This study evaluates racial and ethnic disparities in kidney transplant outcomes among SLE patients during the 10 years before and after the 2014 KAS revision.

Table 1: Demographic and Clinical Characteristics of SLE Patients Who Received Kidney Transplants Before and After the 2014 Kidney Allocation System (KAS) Revision

	Pre-Revision N = 4,255	Post-Revision N = 6,292	P - value
Recipient Age, mean (SD)	40.41 (12.04)	41.86 (12.50)	<0.001
Donor Age, mean (SD)	36.50 (14.54)	35.41 (14.43)	<0.001
Sex, n (%)			0.35
Male	791 (18.6%)	1,125 (17.9%)	
Female	3,464 (81.4%)	5,167 (82.1%)	
Race / Ethnicity, n (%)			<0.001
White	1,166 (27.5%)	1,281 (20.5%)	
Black or African American	1,832 (43.3%)	2,795 (44.8%)	
Hispanic	890 (21.0%)	1,600 (25.6%)	
Other	346 (8.2%)	562 (9.0%)	
Dialysis, n (%)			<0.001
Yes	3,299 (77.5%)	5,168 (82.1%)	
No	956 (22.5%)	1,124 (17.9%)	
HLA Mismatch Level, n (%)			<0.001
0 (No mismatch)	384 (9.1%)	321 (5.1%)	
1-2 (Low)	521 (12.3%)	525 (8.4%)	
3-4 (Moderate)	1,619 (38.2%)	2,617 (41.8%)	
5-6 (High)	1,718 (40.5%)	2,794 (44.7%)	
Functional Status (Karnofsky), n (%)			<0.001
10% - 40%	78 (1.9%)	116 (1.9%)	
50% - 70%	1,016 (25.1%)	2,510 (41.7%)	
80% - 100%	2,958 (73.0%)	3,391 (56.4%)	
Insurance Type, n (%)			<0.001
Private	1,397 (32.9%)	1,870 (30.1%)	
Medicaid	258 (6.1%)	542 (8.7%)	
Medicare	2,532 (59.5%)	3,687 (59.3%)	
Veteran's Affairs	13 (0.3%)	43 (0.7%)	
Other	52 (1.2%)	77 (1.2%)	
Days on Waitlist, mean (SD)	815.51 (802.69)	759.76 (873.23)	<0.001
1-Year Graft Failure, n (%)	307 (7.2%)	1,272 (20.2%)	<0.001
1-Year Mortality, n (%)	82 (1.9%)	94 (1.5%)	0.088

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Changes in Kidney Transplant Wait Times and Outcomes in SLE Patients Following the 2014 Kidney Allocation System (KAS) Revision, by Race/Ethnicity

	White	Black	Hispanic	Other
Days on waitlist pre-revision, mean (SD)	629.89 (719.81)	938.84 (825.03)	799.62 (788.57)	829.80 (869.45)
Days on waitlist post-revision, mean (SD)	622.77 (776.45)	795.62 (890.63)	763.49 (886.94)	912.29 (929.75)
Δ Mean Days on Waitlist	-7.12 (p=0.81)	-143.22 (**p<0.001**)	-36.13 (p=0.31)	82.49 (p=0.18)
Δ 1-Year Graft Failure (%)	11.3 (**p<0.001**)	14.7 (**p<0.001**)	13 (**p<0.001**)	6.6 (**p=0.002**)
Δ 1-Year Mortality (%)	-0.2 (p=0.73)	-0.3 (p=0.47)	-0.6 (p=0.086)	-0.3 (p=0.61)
Adjusted OR: 1-Year Graft Failure post-revision	1.00 (ref)	1.46 (1.22 – 1.75), **p<0.001**	1.28 (1.04 – 1.56), **p=0.017**	0.72 (0.54 – 0.97), **p=0.029**
Adjusted OR: 1-Year Mortality post-revision	1.00 (ref)	1.00 (0.60 – 1.66), p=0.99	0.29 (0.12 – 0.69), **p=0.005**	0.55 (0.22 – 1.38), p=0.20

Δ= Post revision (2015-2024) - Pre revision (2005-2014); ORs adjusted for Recipient age, Donor age, Recipient sex, Dialysis status, HLA mismatch level, Functional status, Insurance type
Bolded p-values indicate statistical significance (p<0.05)

Methods: We conducted a retrospective cohort study using the United Network for Organ Sharing (UNOS) Standard Transplant Analysis and Research (STAR) files. Adult patients with SLE who received kidney transplants between 2005-2024 were identified and stratified into two cohorts: Pre-revision (2005–2014) and Post-revision (2015–2024).

We compared demographics, mean waitlist days, 1-year graft failure, and 1-year mortality across cohorts, stratified by race/ethnicity (Black, White, Hispanic, Other).

Multivariable logistic regression estimated the adjusted odds of 1-year graft failure and mortality by race/ethnicity (White as reference), adjusting for age, sex, HLA mismatch level, insurance type, and other clinical covariates.

Results: A total of 10,547 SLE kidney transplant recipients were included (4,255 pre-revision; 6,292 post-revision) (Table 1). Before KAS revision, Black patients had the longest mean waitlist time (938.8 vs 629.9 days for White patients). Post-revision, they had the largest decrease in wait time (–143.2 days; **p< 0.001**), while other groups showed no significant change (Table 2). All groups experienced increased 1-year graft failure post-revision, with the greatest increases among Black (+14.7%) and Hispanic (+13.0%) recipients. No significant changes were observed in 1-year mortality across groups.

In adjusted post-revision models, Black (OR 1.46, 95% CI 1.22–1.75; p< 0.001) and Hispanic (OR 1.28, 95% CI 1.04–1.56; p=0.017) recipients had significantly higher odds of graft failure compared to White recipients (Table 2). "Other" had lower odds (OR 0.72, 95% CI 0.54–0.97; *p=0.029*). Only Hispanic patients had significantly lower odds of 1-year mortality (OR 0.29, 95% CI 0.12–0.69**; p=0.005**).

Conclusion: Although the 2014 KAS revision reduced wait times for Black recipients, it was associated with increased 1-year graft failure across all groups, particularly among Black and Hispanic patients There were no significant corresponding changes in mortality. The reasons for these trends are likely multifactorial and may include changes in immunologic matching, or shifts in perioperative care and follow-up practices. The findings suggest that while the KAS revision may have improved access to transplantation, it may have inadvertently introduced new risks for certain populations. Further investigation is needed to understand the mechanisms driving these outcome disparities and to inform future refinements to transplant policy.

Disclosure: S. Salia: None; **B. Mensah**: None; **U. Mamoh**: None; **G. Hedayati**: None; **T. Baffoe-Bonnie**: None; **J. Morny**: None; **C. Haas**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1708

Assessing Social Determinants of Health Using PRAPARE in a Rheumatology Patient Navigator Program for Underserved Brooklyn Communities

Meenakshi Kurup[1], Jasmine Pak[2], Alyssa Carlson[2], Beylul Negassi[2], Callie Sacks[2], Ettiman Kaur[2], Fanyu Hercules-Tawe[2], Gabriel Cruz[2], Julia Fisher[2], Grace Shadid[2], Hadar Shimshon[2], Maria Botero Pinzon[2], Naureen Kabani[2], Sharon Glick[2] and Ellen Ginzler[3], [1]SUNY Downstate Health Sciences University, Brooklyn, NY, [2]SUNY Downstate Health Sciences University, Brooklyn, [3]SUNY Downstate Health Sciences University, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Healthcare Disparities in Rheumatology (1704–1709)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Social determinants of health (SDoH) contribute significantly to disparities in care but are rarely addressed in subspecialty settings. The PRAPARE (Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences) tool is a validated questionnaire that screens for SDoH across multiple domains, including housing, employment, education, stress, and social support. Scores range from 0 to 22, with higher scores indicating greater social risk. At SUNY Downstate, the PRAPARE tool was implemented within a rheumatology and dermatology patient navigator program, which pairs 22 second-year medical students with 169 high-risk patients, yielding a navigator-to-patient ratio of 1:7.68. Since 2020, patients were recruited from subspecialty clinics based on identified needs such as severe disease manifestations, poor adherence to appointments or medications, and/or language barriers. Patients were randomly assigned to navigators unless a specific language preference was stated. Most participants were publicly insured (72%) and identified as Black or Caribbean (86.6%). The mean age was 48.5 years (SD 18.8), with a male-to-female ratio of 1:5.13. The most common conditions were lupus (53.6%) and hidradenitis suppurativa (52.0%).

Methods: Since program inception, 716 navigator-patient encounters were documented (mean 5.44 per patient; median 4.00), primarily addressing appointment scheduling (40.3%). To assess social risk, 64 of 169 patients (37.9%) completed PRAPARE screening via standardized telephone interviews conducted by navigators in December 2024.

Results: Among 64 individuals enrolled in a rheumatology patient navigator program, the mean PRAPARE social risk score was 5.9 (SD 3.32; range 1–18). The most frequently reported social needs were elevated stress levels (28%), housing instability (18%), limited social integration (16%), safety concerns at home (11%), and material insecurity (8%). Among the 9 patients with scores >8 (defined as a high social risk), 100% reported transportation barriers, 67% reported stress, and 56% reported housing instability. Subgroup analysis revealed that individuals identifying as Hispanic/Latino ($p = 0.0204$) and those with limited English proficiency ($p = 0.0012$) were more likely to have high PRAPARE scores. Spearman correlation analysis demonstrated a strong positive correlation between household size and total PRAPARE score ($\rho = 0.72$), suggesting that larger households may be associated with increased social risk burden.

Conclusion: The program identified a significant burden of unmet social needs among patients. These findings support the integration of routine SDoH screening in rheumatology clinics to better identify at-risk individuals and guide tailored interventions. Further research is needed to evaluate the long-term impact of targeted support measures on health outcomes.

Disclosure: M. Kurup: None; **J. Pak**: None; **A. Carlson**: None; **B. Negassi**: None; **C. Sacks**: None; **E. Kaur**: None; **F. Hercules-Tawe**: None; **G. Cruz**: None; **J. Fisher**: None; **G. Shadid**: None; **H. Shimshon**: None; **M. Botero Pinzon**: None; **N. Kabani**: None; **S. Glick**: None; **E. Ginzler**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1709

Association Between Social Risk Factors and Major Adverse Cardiovascular Events Among Individuals with Rheumatic Conditions

Leah Santacroce[1], Jeong Yee[2], Jing Cui[3], Emily Oakes[1], Hongshu Guan[4] and Karen H. Costenbader[5], [1]Brigham and Women's Hospital, Boston, MA, [2]Sungkyunkwan University, Suwon, MA, South Korea, [3]Brigham Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital/ Harvard Medical School, Boston, [5]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Healthcare Disparities in Rheumatology (1704–1709)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Individuals with rheumatic conditions are at an increased risk of experiencing cardiovascular events. Social risk factors contribute to disparities in comorbidities and adverse outcomes and may confer higher risk of Major Adverse Cardiovascular Events (MACE) in patients with rheumatic conditions. We aimed to understand whether MACE risk differed by exposure to specific social risk factors including poverty, discrimination and food insecurity.

Methods: We used data from the nationwide NIH All of Us Research Program (V8) and included adults age ≥18 years with ≥ 2 diagnosis codes ≥30 days apart for lupus (SLE), rheumatoid arthritis (RA), and osteoarthritis (OA) 2 years pre-enrollment. We required participants to have completed Social Determinants of Health-related questionnaires at enrollment. We examined individual answers to social risk factor questions about economic instability, healthcare access challenges, and neighborhood factors, as well as scores on the previously validated Everyday Discrimination Scale and Ross-Mirowsky Neighborhood Disorder Scale. The primary outcome was MACE (myocardial infarction, stroke, intervention for coronary artery disease). Patients were followed from enrollment until their first MACE-related event or end of study period. We used multivariable Cox proportional hazard models to evaluate associations between each social risk factor and MACE, adjusting for age, sex, race, ethnicity, rheumatic disease and Deyo-Charlson Comorbidity index.

Results: We identified 17,121 individuals in All of Us who met our criteria. The mean (SD) age was 65 (11) years, 69% were female, and 75% were white. There were 1,336 outcome events, and the mean (SD) follow up time was 2.6 (1.8) years. After adjusting for covariates, presence vs. absence of several social risk factors was associated with a higher risk of MACE (Figure 1). Specifically, food insecurity (HR 1.35, 95% CI 1.16 – 1.56), delaying medical care due to cost (HR 1.17, 95% CI

Table 1. Baseline Characteristics of individuals with SLE, RA, and OA in All of Us

Characteristic	N = 17,121
	N (%) or Mean (SD)
Age at Enrollment – Mean (SD)	65 (11)
Race	
Asian	153 (0.9)
Black	1727 (10.1)
Hispanic	1195 (7.0)
More than one race	589 (3.4)
White	12822 (74.9)
Other/Unknown	635 (3.7)
Sex at Birth	
Female	11821 (69.0)
Male	5128 (30.0)
Other/Unknown	172 (1.0)
Deyo-Charlson Comorbidity Index – Mean (SD)	1.65 (2.18)
Rheumatic Condition	
Systemic Lupus Erythematosus	795 (4.6)
Rheumatoid Arthritis	2151 (12.6)
Osteoarthritis	15448 (90.2)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

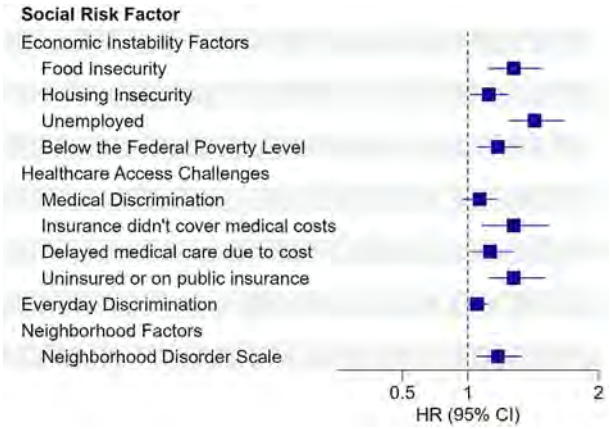


Figure 1. Hazard ratios for the association between several social risk factors and major adverse cardiovascular events adjsuted by age, sex, race, ethnicity, rheumatic condition and comorbidity index

1.02 – 1.35), and living in areas with high neighborhood disorder (HR 1.23, 95% CI 1.07 – 1.41) were all associated with increased risk of MACE.

Conclusion: In this national study, we found that the presence vs. absence of most social risk factors was strongly associated with increased risk of MACE among individuals with SLE, RA, and OA. Further studies should determine whether addressing these risk factors reduces the risk of cardiovascular events.

Disclosure: L. Santacroce: None; **J. Yee**: None; **J. Cui**: None; **E. Oakes**: None; **H. Guan**: None; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 1710

Defining sonographic enthesitis in psoriatic arthritis: Developing a data- and expert-driven definition for inflammatory enthesitis at the single enthesis level

Andre Lucas Ribeiro[1], Sibel Aydin[2], Gurjit Kaeley[3], Fahmeen J. Afgani[4], Catherine Bakewell[5], Marcos Rosemffet[6], Minna Kohler[7], Amir Haddad[8], Maria S. Stoenoiu[9], Ari Polachek[10], josefina marin[11], Arnon Katz[12], Sahil Koppikar[13] and Lihi Eder[14], [1]Hospital de Clínicas de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil, [2]Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [3]UF COM-J, Ponte Vedra Beach, FL, [4]Women's College Hospital, Toronto, Canada, [5]Intermountain Healthcare, Salt Lake City, UT, [6]Instituto de Rehabilitación Psicofísica, Capital Federal, Argentina, [7]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [8]Carmel Medical Centre, Haifa, Israel, [9]Cliniques Universitaires Saint-Luc, Brussels, Belgium, [10]Rheumatology Institute of Beilinson Hospital, Petah Tikva, Israel, [11]Hospital Universitario Rey Juan Carlos, Madrid, Spain, [12]GRAPPA, Seattle, [13]Women's College Hospital & University of Toronto, Markham, ON, Canada, [14]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease (1710–1715)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. New definition of inflammatory enthesitis at the single-enthesis level.

Inflammatory Enthesitis Definition
"The presence of a power Doppler signal grade ≥2 near the bone cortex, in the presence of hypoechogenicity and/or thickening of the entheseal structure, and within the appropriate clinical context*." **This excludes cases where findings are better explained by mechanical stress or trauma.*

Background/Purpose: Enthesitis affects 30–40% of PsA patients but remains difficult to diagnose due to overlap with non-specific entheseal pain. While OMERACT has standardized ultrasound (US) elementary lesions, no validated definition of inflammatory enthesitis (IE) exists at the single-enthesis level. This limits diagnostic specificity and contributes to misclassification and overtreatment. We aimed to develop an expert- and data-driven definition of sonographic IE at the single-enthesis level in PsA, with the goal of improving diagnostic accuracy and patient selection for clinical research.

Methods: Ten expert sonographers from the DUET (Diagnostic Ultrasound Enthesitis Tool)[1] study independently reviewed 90 US video scans of PsA patients at six entheseal sites. Each scan was score from –10 ("Definite not IE") to +10 ("Definite IE"), and those with ≥70% agreement and scores of +7 were labeled "Definite IE." Experts annotated key sonographic features influencing their assessments. Quantitative analysis included group comparison of elementary lesion distribution using the DUET consensus scoring for descriptive statistics and chi-square tests. Thematic analysis was performed on free-text annotations. This data was used to inform a proposed definition of IE, which was subsequently approved through a Delphi vote.

Results: Of 90 scans, 29 (32.2%) were "Definite IE", 21 (23.3%) "Definite not IE", and 40 (44.5%) "Uncertain". Most "Definite IE" had ≥4 elementary lesions, while "Uncertain" scans commonly had 2 to 4 lesions (**Figure 1A**). The absence of elementary lesions or presence of isolated findings characterized the "Definite not IE" group.

Power Doppler (PD) grade ≥ 2 near the bone cortex was present in 97% of the "Definite IE" group and in 55% of "Uncertain" scans (**Figure 1B, Figure 2F**). Importantly, grades 2-3 PD were almost exclusively found in these two groups, with grade 3 almost only found in the "Definite IE" group. Thematic analysis revealed that lesion combinations, cortical location of PD, and contextual interpretation were critical for classification. Isolated findings (e.g., small enthesophytes) lacked diagnostic

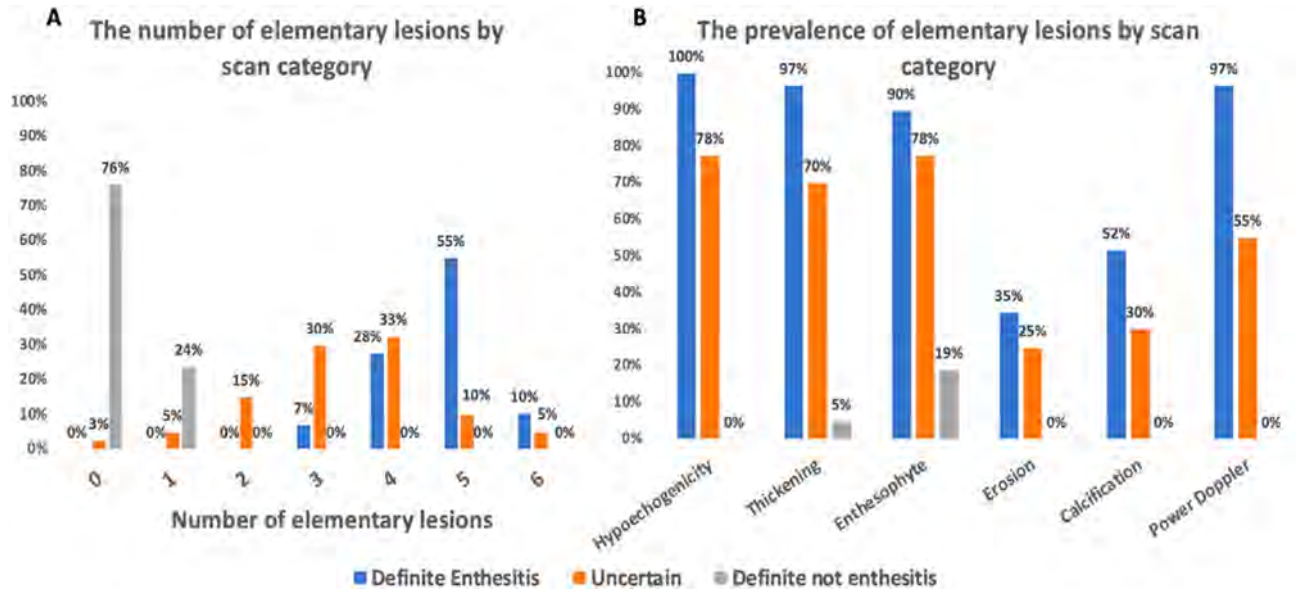


Figure 1A . Number of elementary lesions identified in each category; 1B. Distribution of sonographic elementary lesions by category.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

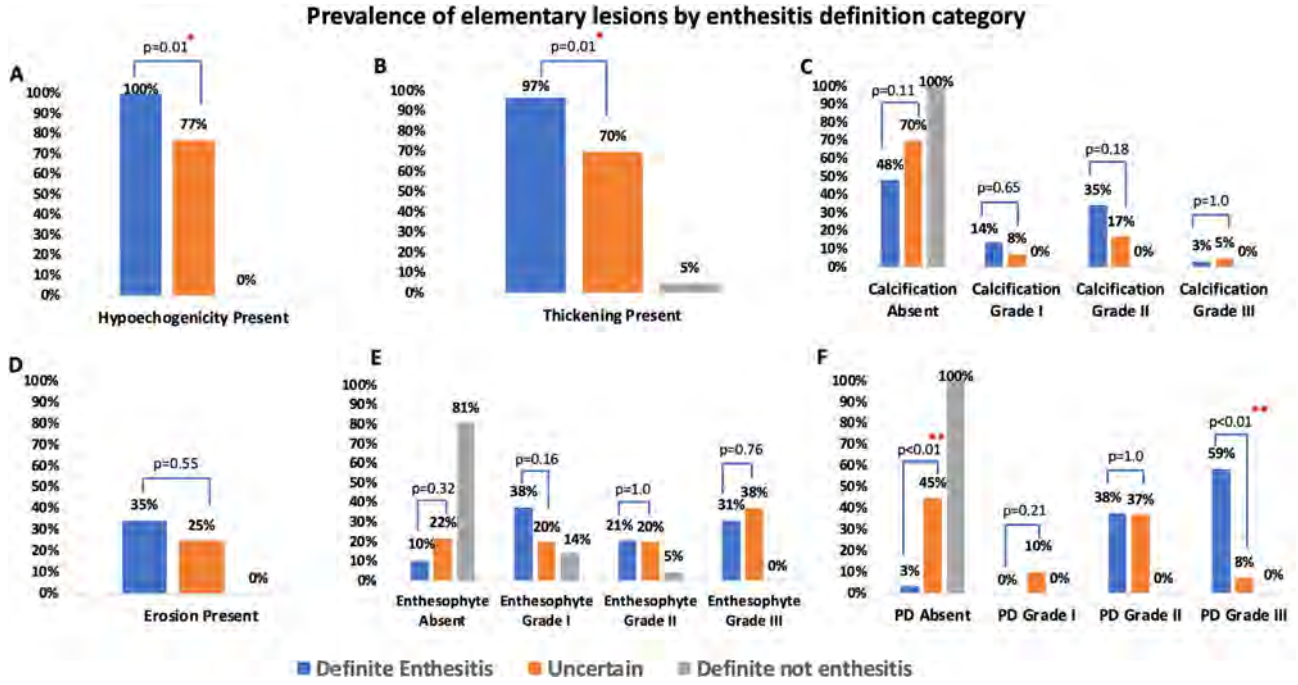


Figure 2. The prevalence of elementary lesions by enthesitis definition category. 1A. Hypoechogenicity (score 0-1); 1B. Enthesophyte (score 0-3); 1C. Thickening (score 0-1); 1D Calcification (Score 0-3); 1E. Erosion (score 0-1); 1F. Power Doppler (score 0-3). Chi-square test was performed to compare the "definite enthesitis" and "uncertain" groups, with p-value < 0.05 marked with an asterisk (*) and a p-value < 0.01 marked with two asterisks.

value unless part of a broader inflammatory pattern. Structural lesions (e.g., cortical irregularities, erosions) were interpreted as signs of prior inflammatory process.

Based on these findings the proposed definition for IE is "**"The presence of a power Doppler signal grade ≥2 near the bone cortex, in the presence of hypoechogenicity and/or thickening of the entheseal structure, and within the appropriate clinical context*."** This excludes cases where findings are better explained by mechanical stress or trauma." (**Table 1**). This definition achieved consensus in the Delphi exercise (10 out of 10 voted to approve).

Conclusion: The new proposed definition for sonographic IE in the context of PsA should facilitate the development of standardized diagnostic criteria for IE in PsA, and improve patient enrollment specificity in clinical research.

Reference: Eder L, Aydin S, Kaeley G, et al. Arthritis Rheumatol. 2020;72(Suppl 10). Abstract.

Disclosure: A. Lucas Ribeiro: AbbVie/Abbott, 2, 6, Eli Lilly, 6, Janssen, 2, 6, Novartis, 6, UCB, 5, 6; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **G. Kaeley**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Janssen, 5, Novartis, 5; **F. Afgani**: None; **C. Bakewell**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 2, 6, UCB, 2, 6; **M. Rosemffet**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **A. Haddad**: AbbVie/Abbott, 6, AstraZeneca, 6, Janssen, 6, Novartis, 6; **M. Stoenoiu**: AbbVie/Abbott, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 5, 6, UCB, 5, 6; **A. Polachek**: None; **j. marin**: None; **A. Katz**: None; **S. Koppikar**: AbbVie/Abbott, 1, 2, 5, 6, Novartis, 2, 6, Pfizer, 12, Unrestricted educational grant for Northern Ontario Clinic, UCB, 2, 6; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1711

Dysfunctional Neurobiology Of The Insula Characterizes Fatigue In Psoriatic Arthritis

Andrew McGucken[1], Flavia Sunzini[2], Kristian Stefanov[1], Joel Parkinson[1], Salim Al-Wasity[1], John McLean[1], Gordon Waiter[3], Stefan Siebert[1] and Neil Basu[4], [1]University of Glasgow, Glasgow, United Kingdom, [2]Glasgow University, Glasgow, United Kingdom, [3]University of Aberdeen, Aberdeen, United Kingdom, [4]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease (1710–1715)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Fatigue is a pervasive and burdensome symptom for people with psoriatic arthritis (PsA). The mechanisms underlying PsA related fatigue are unknown. In other clinical populations, the brain's insula region, a key integration hub between peripheral signals of pain/inflammation and central signals such as mood, has emerged as a key component of the fatigue network[1]. Moreover, excess levels of brain glutamate has been implicated with this symptom[2]. To date, no studies have specifically examined the potential role of brain connectivity and glutamate in PsA fatigue.

Methods: Patients with active PsA who fulfilled the CASPAR criteria were evaluated. Fatigue was measured using a fatigue numeric rating scale averaged over the prior week (7-day fatigue NRS). Subjects then undertook functional MRI and single voxel MRI spectroscopy brain scans. Images were acquired using 3 Tesla Siemens PRISMA with 32-channel phased array head coil using a T2*-weighted gradient-echo echo-planar imaging pulse sequence. Functional MRI data was analyzed using functional connectivity CONN toolbox employing a right posterior insula seed. The functional connectivity of this region of interest to the whole brain was estimated, followed by group level multiple linear regression to 7-day fatigue NRS corrected for age, sex and multiple comparisons (FDR< 0.05). Right posterior insula spectroscopy data was analyzed using LCModel. Individual glutamate/glutamine concentrations were calculated and corrected for levels of brain creatine (Glx/Cr). Glx/Cr correlation with fatigue scores and insula seed functional connectivity was assessed.

Results: 38 enrolled patients completed both functional MRI and MRI spectroscopy (mean age 46.7 ± 9.9; 47% female; mean BMI 29.2 ± 4.6; mean 7-day fatigue NRS 6.4 ± 2.8; mean DAPSA 38 ± 15.8). Higher fatigue scores correlated with higher functional connectivity from the right posterior insula to cerebellum (R=0.694, p< 0.022FDR) and anti-correlated with functional connectivity to the superior frontal gyrus, which covers the medial prefrontal cortex (R=-0.7029, p=0.0008FDR) (Figure A). PsA patients with higher fatigue scores also trended towards increased Glx/Cr (R=0.3, p=0.07) in the right posterior insula and these levels significantly correlated with fatigue associated functional connectivity of this region (cerebellum: R=0.49, p=0.003 and superior frontal gyrus: R=-0.4, p=0.016) (Figure B).

Conclusion: We demonstrate for the first time that the brain may have a role in PsA fatigue. Specifically, the multifaceted role of the insula is highlighted. Altered functional connectivity between the posterior insula to brain regions involved in movement, motivation, and peripheral sensations (cerebellum); and executive decision making/emotions (superior frontal gyrus) appears to characterize fatigue severity in PsA. Excess of the excitatory neurotransmitter glutamate within the posterior insula may mediate this neural dysfunction but further research is warranted to understand it's functional role and clarify its potential as a future therapeutic target for PsA fatigue.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

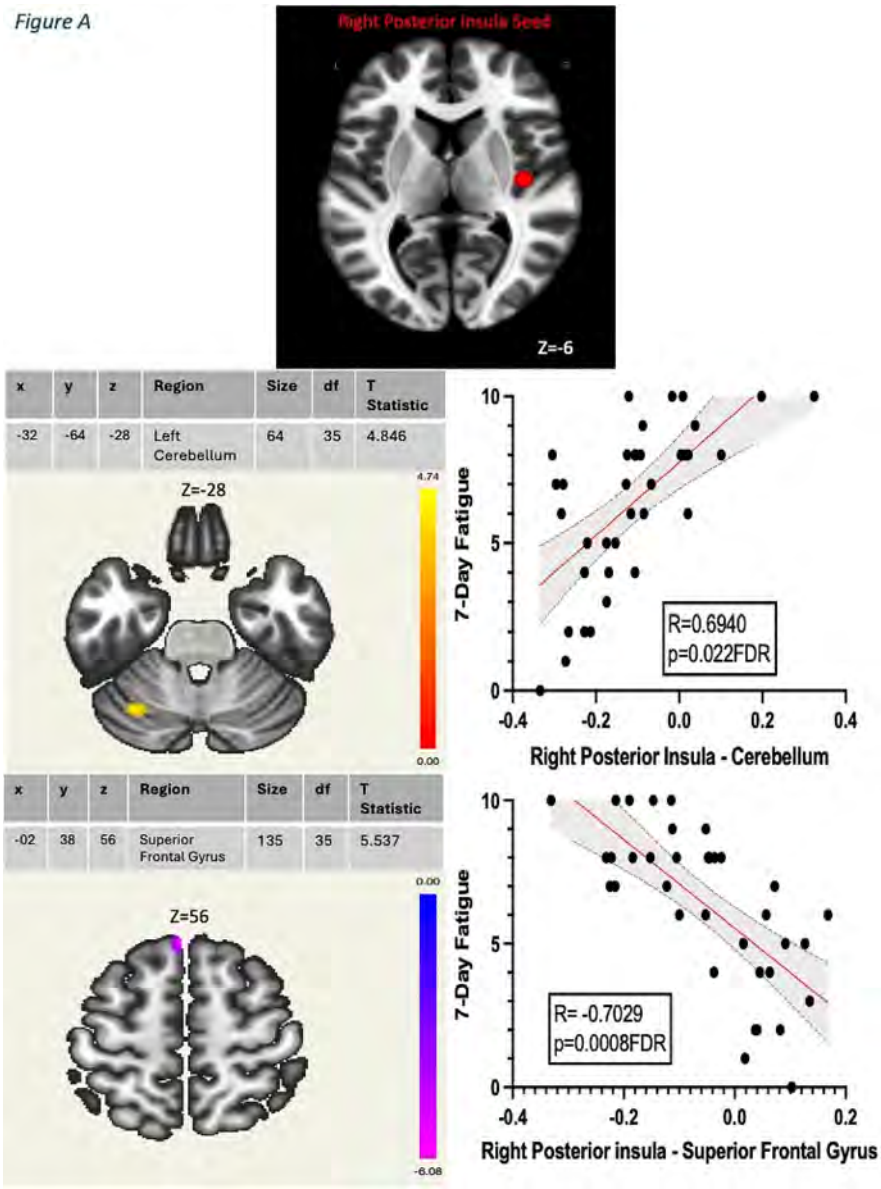


Figure A shows significant altered functional connectivity that correlates with fatigue scores. The top panel demonstrates the insula seed used for the seed-to-voxel analysis. The images show the voxel positions (colored area on brain slice) with slice number (Z) at the top of each image. The scatterplots visualize the correlation of functional connectivity (Fischer z-transformed r values) between two brain regions and fatigue scores, Pearsons R, and p values after false discovery rate for multiple comparisons (FDR). The tables demonstrate results from multi-linear modelling (correcting for age and sex), degrees of freedom (df), peak voxel co-ordinates in MNI space (x,y,z), and cluster size.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

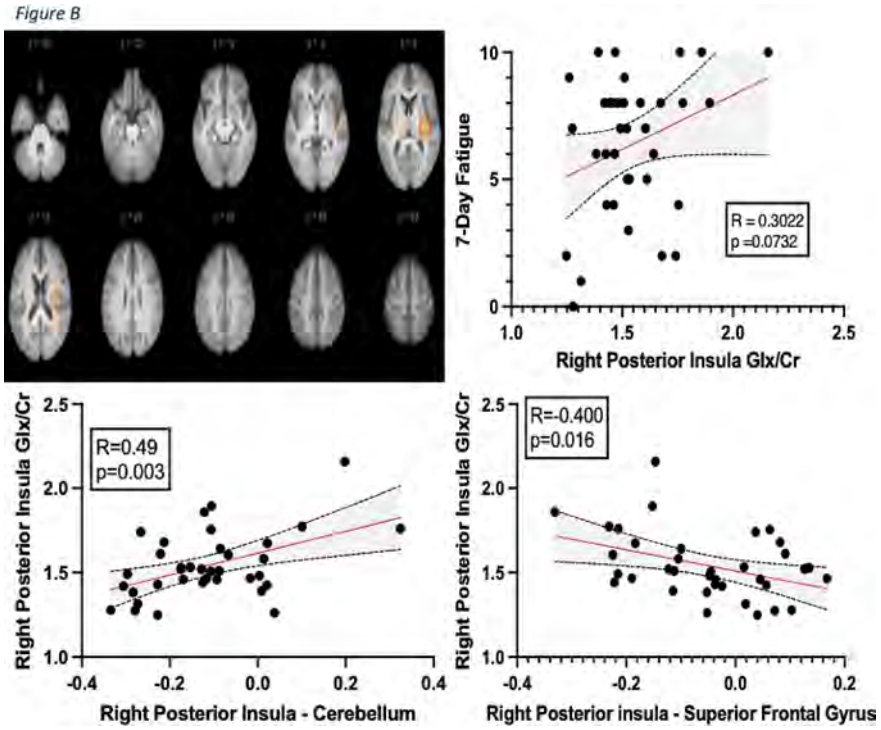


Figure B shows (top left) the average position across all participants of 20x20x20mm voxel for the right posterior insula used in this analysis. The top right figure demonstrates right posterior insula glutamate/glutamine levels correlation of creatine (Glx/Cr) with 7-day fatigue scores. Bottom scatterplots illustrate right posterior insula functional connectivity correlating with right posterior insula Glx/Cr levels.

Disclosure: A. McGucken: None; **F. Sunzini**: None; **K. Stefanov**: None; **J. Parkinson**: None; **S. Al-Wasity**: None; **J. McLean**: None; **G. Waiter**: None; **S. Siebert**: AbbVie, 6, Amgen, 6, AstraZeneca, 6, BMS, 5, Boehringer-Ingelheim, 5, Eli Lilly, 5, GlaxoSmithKlein, 5, Johnson & Johnson, 5, 6, Novartis, 6, Pfizer, 6, Syncona, 6, Teijin Pharma, 6, UCB, 5, 6; **N. Basu**: AbbVie, 6, AstraZeneca, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, GSK, 2, 5, MSD, 2, Nesos, 5, Pfizer, 5, 6, Roche, 2, 6, Vifor, 2, 5, 6.

Abstract Number: 1712

Reduced Cardiometabolic Burden and Inflammation in Patients with Psoriatic Arthritis Cared for in a Multi-Disciplinary, Combined Psoriasis-Psoriatic Arthritis Center

Rebecca Haberman[1], Nicolas Coudray[2], Xu Han[2], Morgan Grams[2], Eric Oermann[2], Aristotelis Tsirigos[2] and Jose Scher[3], [1]NYU Langone Health, New York, NY, [2]NYU Grossman School of Medicine, New York, [3]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease (1710–1715)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease that affects both the skin and musculoskeletal system and is frequently associated with a heightened burden of cardiometabolic comorbidities, including hypertension (HTN), obesity, and type 2 diabetes (DM2). These conditions contribute to elevated morbidity and mortality.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

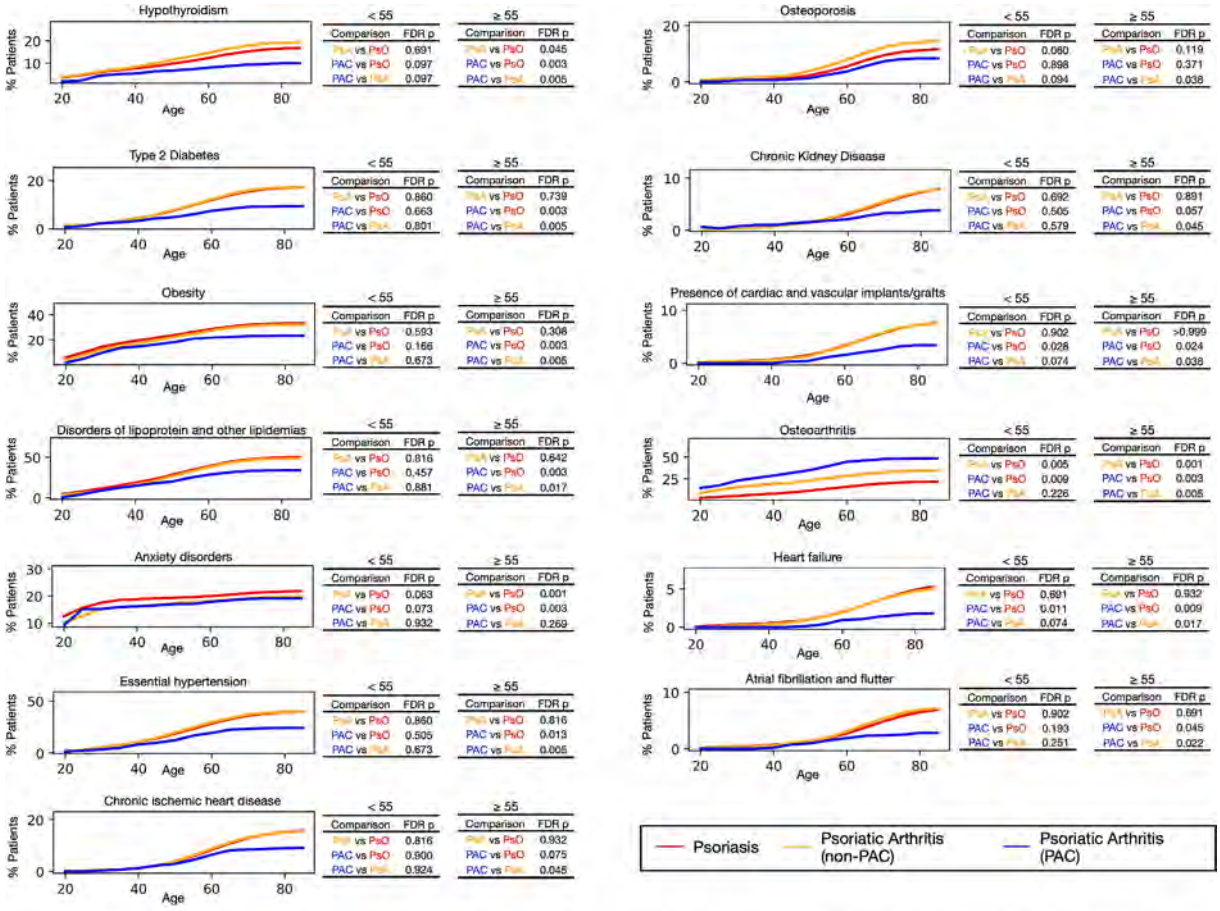


Figure 1. Comorbidities in patients with psoriasis, psoriatic arthritis (PsA), and PsA seen in the Psoriatic Arthritis Center (PAC). All p-values adjusted for false discovery rate (FDR) given multiple comparisons.

Despite growing awareness, management of systemic inflammation and comorbid risk factors remains suboptimal in routine care. Multi-disciplinary, integrated centers that co-locate rheumatology, dermatology, cardiology and allied specialties offer a promising approach to comprehensive, disease-targeted care. However, real-world data supporting their effectiveness in mitigating systemic burden remain limited. We aimed to evaluate whether patients with PsA seen under optimized care—the NYU Psoriatic Arthritis Center (PAC)—demonstrate improved health profiles compared to those receiving standard specialty care at the same institution.

Methods: Using the electronic medical record (EMR) system at NYU Langone Health (Epic), we identified patients with ICD-10 codes for psoriasis or PsA from 2012 to 2024. Patients with both diagnoses were classified as PsA. PsA patients were further categorized into those seen at the NYU PAC (PAC group) versus those seen exclusively outside the PAC (non-PAC group). For all groups, comorbidities were extracted using ICD-10 codes, and laboratory markers of systemic inflammation (CRP, ESR) were obtained. Comparisons of comorbidity prevalence and laboratory values were performed using Mann-Whitney U tests and mixed linear regression, adjusting for age. False discovery rate (FDR) correction was applied using the Benjamini-Hochberg method.

Results: 890 PAC patients, 12,079 non-PAC PsA patients, and 28,393 patients with only skin psoriasis were identified. PAC and non-PAC patients had similar rates of comorbidities prior to the age of 55 (**Figure 1**). Among those ≥55 years old, PAC patients had significantly lower rates of key cardiometabolic conditions compared to non-PAC PsA patients, including DM2, obesity, HTN, ischemic heart disease, atrial fibrillation, and chronic kidney disease (all FDR-adjusted p<

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

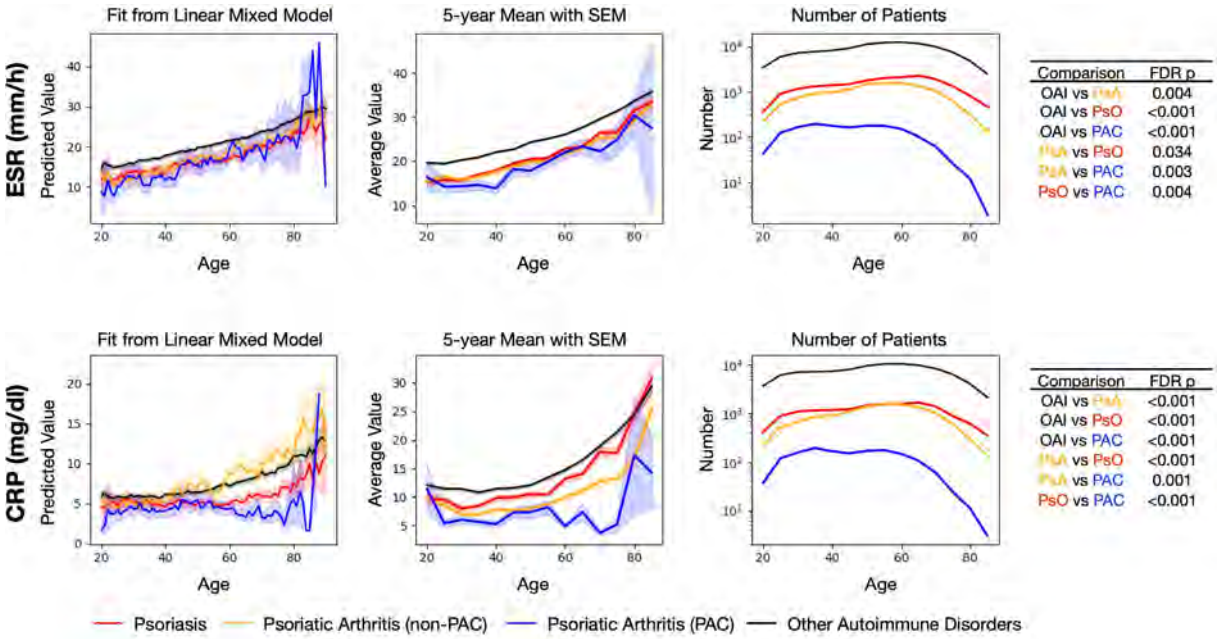


Figure 2. Systemic markers of inflammation in patients with psoriasis, psoriatic arthritis (PsA), PsA seen in the Psoriatic Arthritis Center (PAC), and other autoimmune disorders. ESR denotes erythrocyte sedimentation rate, CRP denotes C-reactive protein, FDR false discovery rate, SEM standard error of the mean. Other autoimmune disorders include celiac disease, Sjogrens Syndrome, Hashimoto's thyroiditis, ulcerative colitis, Crohn's disease, type 1 diabetes, multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis.

0.05). Inflammatory markers were also significantly lower in PAC patients (ESR p< 0.001; CRP p=0.026, **Figure 2**). Rates of osteoarthritis were higher in PAC patients (p=0.005), possibly reflecting more active musculoskeletal screening. Of interest, both PAC and non-PAC PsA patients had lower anxiety and systemic inflammation compared to patients with psoriasis alone or other autoimmune diseases.

Conclusion: In this large EMR-based study, patients with PsA receiving care at a dedicated, multi-disciplinary, specialized center had a significantly reduced burden of cardiometabolic comorbidities and inflammation, particularly in older adults. While validation of these observations is warranted in other combined clinics (i.e., PPACMAN dual-care facilities), our findings highlight the potential of integrated psoriatic disease care models to modify systemic disease expression, decrease the deleterious effects of metabolic and cardiovascular comorbidities and improve overall long-term outcomes in PsA.

Disclosure: R. Haberman: Johnson and Johnson, 1, 5, Novartis, 1; **N. Coudray**: Imagenomix, 1; **X. Han**: None; **M. Grams**: None; **E. Oermann**: Merck, 2, Mirati Therapeutics, 2, Sofinnova Partners, 2; **A. Tsirigos**: Imagenomix, 12, Co-founder; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2.

Abstract Number: 1713

Diagnostic Delay in Psoriatic Arthritis and its Impact on Radiological Outcomes: A Systematic Review and Meta-analysis of 23,894 Patients

Mohamed Abdelsalam[1], Menat Alla Ayman Ali Mahdy[2], Maryam Lasheen[3], Hadeer Hafez[4], Nourhan Abouelella[5], Abdelhfeez Moshrif[6] and Mohamed Reda Awad[7], [1]Misr University For Science and Technology, 6 october, Al Jizah, Egypt, [2]Misr University For Science and Technology, Nasr City, Al Qahirah, Egypt, [3]Misr University For Science and Technology,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Helwan, Al Qahirah, Egypt, [4]6th October University, 6 october, Al Jizah, Egypt, [5]Faculty of Medicine, Misr University for Science and Technology, 6 october, Al Jizah, Egypt, [6]Al Azhar University, Asyut, Egypt, assyut, Asyut, Egypt, [7]Al Azhar University, Cairo, Egypt, Giza, Al Jizah, Egypt

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease (1710–1715)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Psoriatic arthritis (PsA) remains widely underdiagnosed and misdiagnosed worldwide, leading to delays in appropriate management and increased disease burden. While diagnostic delay has been extensively studied in axial spondyloarthritis (axSpA), there remains a significant research gap in understanding delays specific to PsA. This study aims to examine the extent and consequences of diagnostic and referral delays in PsA and their impact on radiographic outcomes.

Methods: We systematically searched PubMed, Web of Science, and Scopus from inception until March 16, 2025, following PRISMA guidelines (Fig.1) to identify observational studies reporting diagnostic delay in PsA. Studies were included if they diagnosed PsA patients based on the CASPAR classification criteria, confirmed diagnosis by a rheumatologist or self-reported physician diagnosis. Diagnostic and referral delays were extracted if reported as mean (SD) or median (IQR).

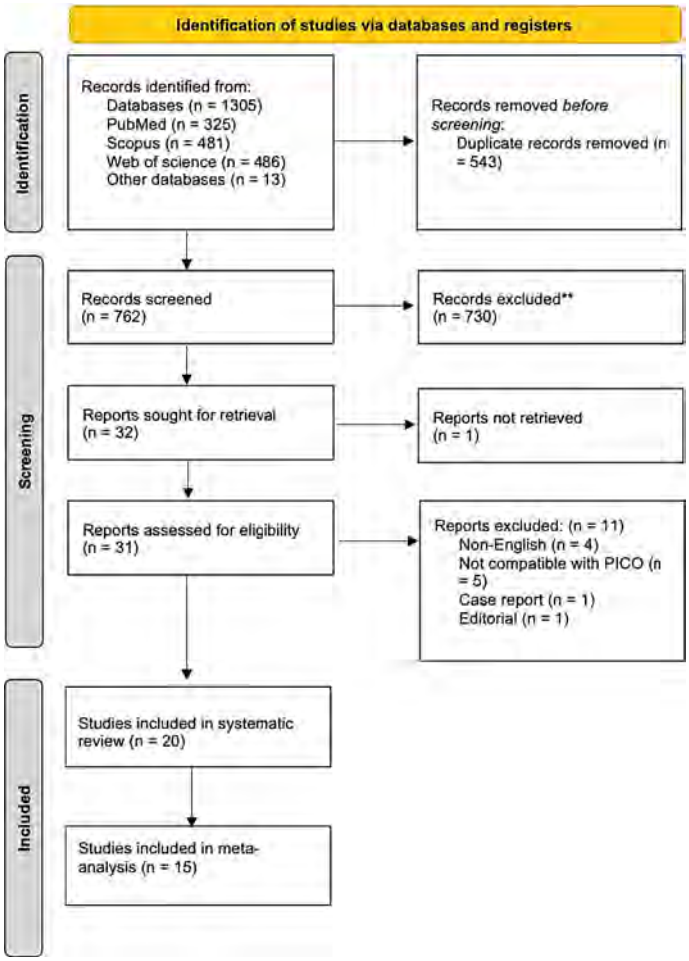


Fig (1) PRISMA Flow Chart Illustrating Search Strategy and Selection of Included Studies

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Meta-analysis was conducted using Review Manager software 5.4 (RevMan), employing random- and fixed-effects models using the inverse variance method. Heterogeneity was assessed using I^2 statistics following Cochrane guidelines.

Results: A total of 20 observational studies were included encompassing 23,894 participants, with 15 contributing to the meta-analysis encompassing 22,749 participants. The pooled mean diagnostic delay was 31.24 months (95% CI: 22.48, 40.00) using a random-effects model, with considerable heterogeneity (I^2 = 100%) (Fig. 2). The mean referral delay was analyzed using both fixed- and random-effects models, with the random-effects model yielding a pooled mean referral delay of 21.69 months (95% CI: 15.02, 28.35) and the fixed-effects model yielding 15.32 months (95% CI: 13.98, 16.67), with considerable heterogeneity (I^2 = 92%) (Fig. 2). Patients with prolonged diagnostic delay had significantly increased odds of radiographic damage. The fixed-effects model yielded a pooled OR of 2.80 (95% CI: 2.31, 3.39), while the random-effects model showed an OR of 2.54 (95% CI: 1.58, 4.09). Heterogeneity for both was moderate (I^2 = 49%) (Fig. 2). Studies indicated substantial geographic variation in diagnostic delay, with reports ranging from 6.55 months in India to over 62.4 months in Italy (Fig. 3).

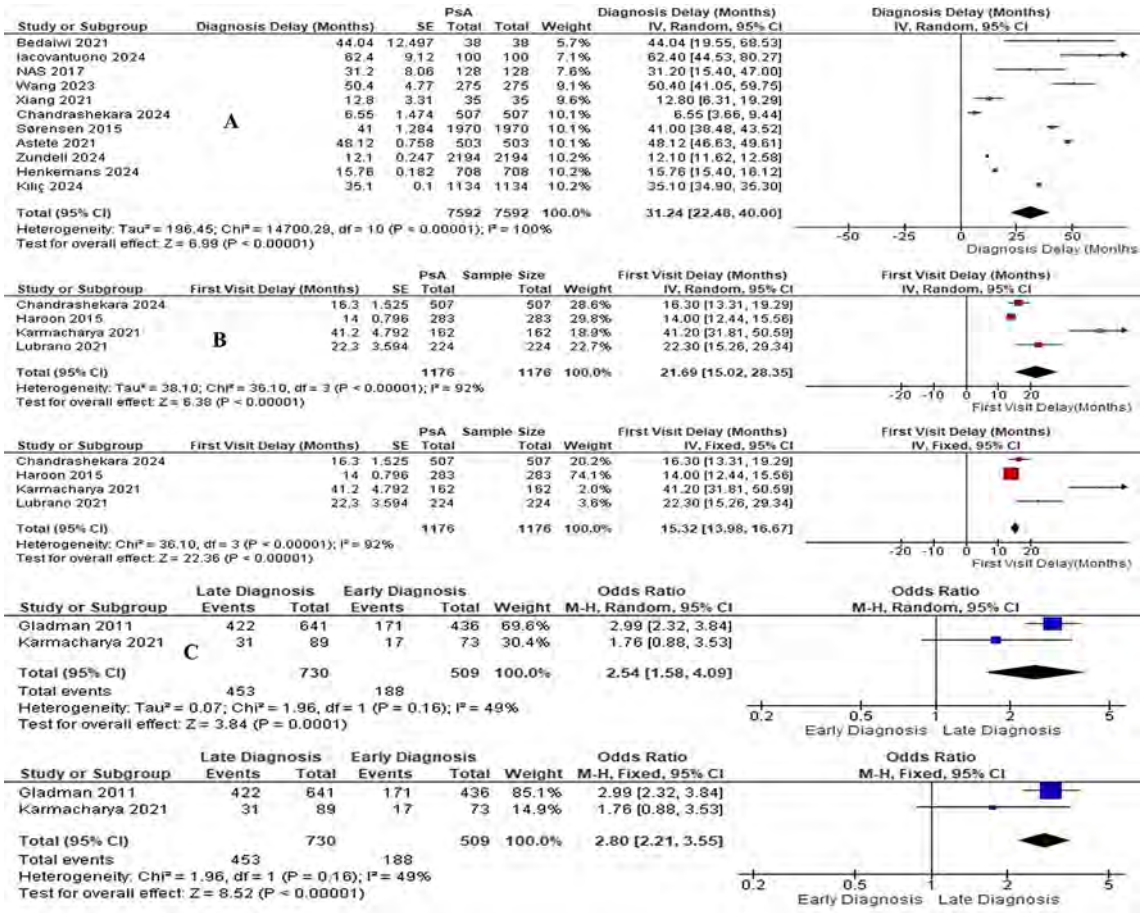
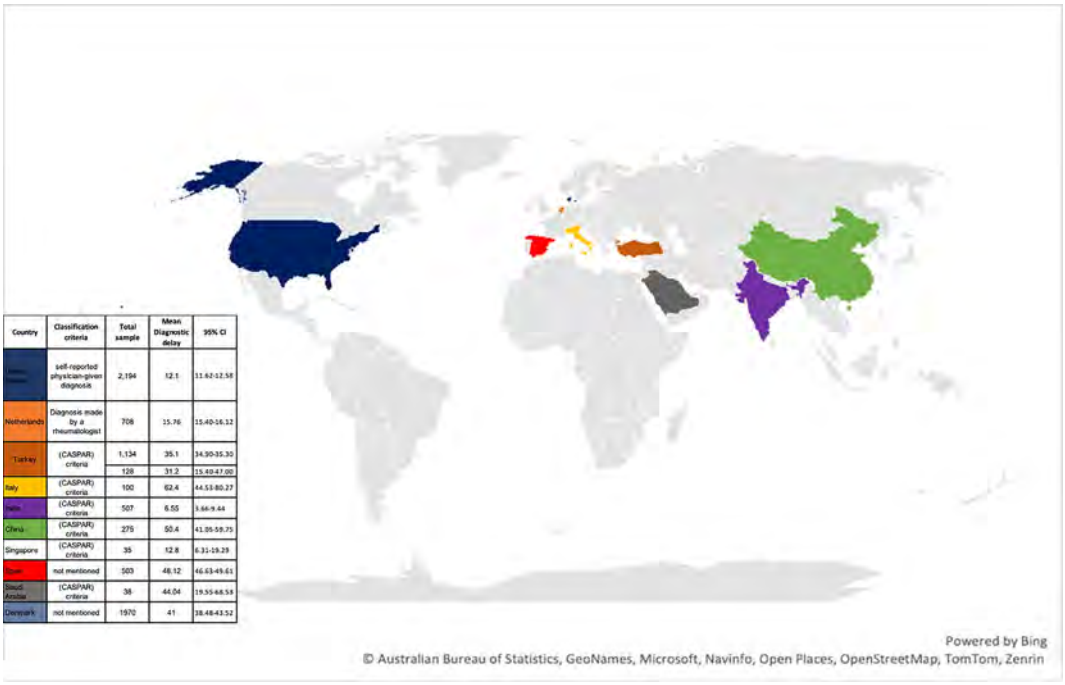


Fig 2. (A) Forest Plot of PsA Diagnosis Delay (Months): Forest plot of PsA diagnosis delay (months). Studies included: Bedaiwi 2021, Iacovantuno 2024, NAS 2017, Wang 2023, Xiang 2021, Chandrashekara 2024, Sørensen 2015, Astete 2021, Zundell 2024, Henkemans 2024, Kilic 2024. The plot shows the mean diagnosis delay for each study and the overall pooled mean delay of 31.24 months (95% CI: 22.48 to 40.00), with considerable heterogeneity (I^2=100%). (B) Forest plot of PsA first visit delay (months) (Random and Fixed effects model). Studies included: Chandrashekara 2024, Haroon 2015, Karmacharya 2021, Lubrano 2021. The plot shows the mean first visit delay for each study and the overall pooled mean delay of 15.32 months (95% CI: 13.98 to 16.67), with considerable heterogeneity (I^2=92%). (C) Forest Plot of Odds Ratio Comparing Late Diagnosis to Early Diagnosis in PsA Patients (Random and Fixed effects model). Forest plot of odds ratio comparing late diagnosis to early diagnosis in PsA patients. Studies included: Gladman 2011, Karmacharya 2021. The overall pooled odds ratio was 2.80 (95% CI: 2.21 to 3.55), indicating a significant association (P<0.00001), with moderate heterogeneity (I^2=49%). CI, confidence interval; df, degrees of freedom; IV, inverse variance; SD, standard deviation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Country	Classification criteria	Total sample	Mean Diagnostic delay	95% CI
[redacted]	self-reported physician-given diagnosis	2,194	12.1	11.62-12.58
Netherlands	Diagnosis made by a rheumatologist	708	15.76	15.40-16.12
Turkey	(CASPAR) criteria	1,134	35.1	34.90-35.30
		128	31.2	15.40-47.00
Italy	(CASPAR) criteria	100	62.4	44.53-80.27
[redacted]	(CASPAR) criteria	507	6.55	3.66-9.44
China	(CASPAR) criteria	275	50.4	41.05-59.75
Singapore	(CASPAR) criteria	35	12.8	6.31-19.29
Spain	not mentioned	503	48.12	46.63-49.61
Saudi Arabia	(CASPAR) criteria	36	44.04	19.55-68.53
Denmark	not mentioned	1970	41	38.48-43.52

Fig 3. Map of Mean Diagnostic Delay in Years for PsA by Country. Countries included: United States, Netherlands, Turkey, Italy, India, China, Singapore, Spain, Saudi Arabia, Denmark. The accompanying table provides classification criteria, sample size, mean delay, and 95% CI for each country. Map powered by Bing.

Conclusion: This is the first systematic review and meta-analysis that explores diagnostic and referral delays in PsA, and their relationship to radiographic joint damage. This meta-analysis confirmed that both diagnostic and referral delays in psoriatic arthritis are statistically and clinically significant, with longer delays linked to an increased risk of radiographic joint damage. These delays reflect gaps in disease recognition and care coordination. Improving early detection, particularly in primary care and dermatology settings, and streamlining referral pathways to rheumatology are essential in reducing structural damage and improving patient outcomes.

Disclosure: M. Abdelsalam: None; **M. Mahdy**: None; **M. Lasheen**: None; **H. Hafez**: None; **N. Abouelella**: None; **A. Moshrif**: None; **M. Awad**: None.

Abstract Number: 1714

The perimenopause period is associated with increased levels of disease activity in psoriatic arthritis

Lihi Eder[1], Xianwei Li[2], Sahil Koppikar[3], Iliana Lega[4], Dafna D. Gladman[5], Vinod Chandran[1] and Richard Cook[6], [1]University of Toronto, Toronto, ON, Canada, [2]Department of Statistics and Actuarial Science, University of Waterloo, Waterloo, Canada, [3]Women's College Hospital & University of Toronto, Markham, ON, Canada, [4]University of Toronto and Women's College Hospital, Toronto, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Waterloo, Waterloo, Canada

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease (1710–1715)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

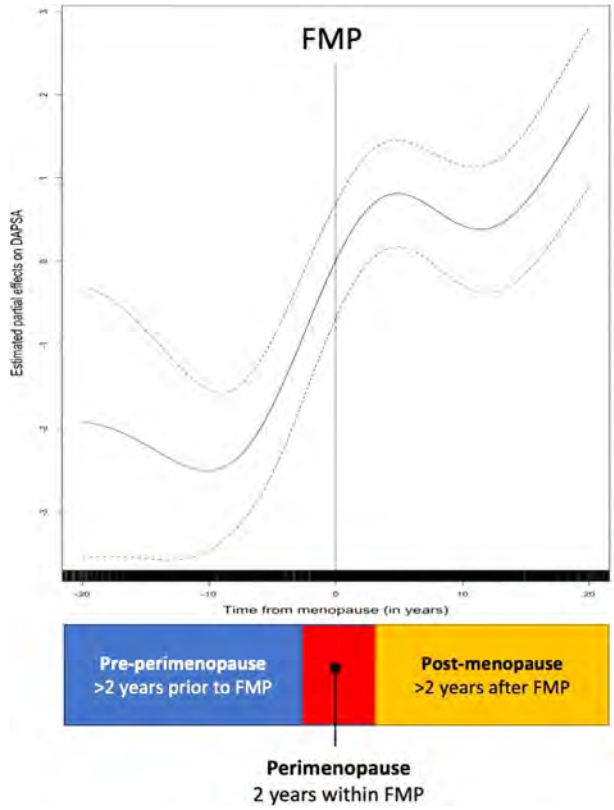


Figure 1: Time from final menstrual period (FMP) estimated partial effect on the individual mean DAPSA score by Generalized Additive Model adjusted for age, disease duration and medication use

Background/Purpose: Perimenopause is associated with a wide spectrum of symptoms, including mood changes, sleep disturbances, and joint pains. Limited information exists on the effect of perimenopause on psoriatic arthritis (PsA). We assessed whether PsA disease activity worsens during perimenopause compared to the pre- and post-menopause stages.

Methods: We analyzed data on female patients with PsA followed in a prospective cohort from 1978 to 2024. Data on PsA disease activity, medications, co-morbidities, and age at menopause were collected using standard protocols. Pre-perimenopausal and post-menopausal stages were defined as >2 years before and after the final menstrual period (FMP), respectively, while the perimenopause stage was within two years (before or after) of the FMP. PsA disease activity was assessed at each visit using Disease Activity in PsA (DAPSA), tender and swollen joint counts, PASI, CRP, and FACIT-

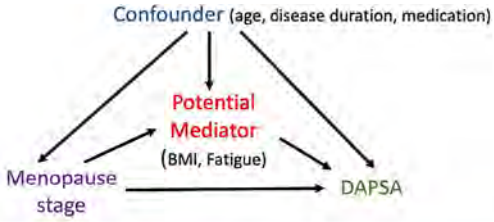
Table 1 - Estimated fixed effects on change in PsA disease activity measures for perimenopause stage using linear mixed effects models

Table 1 - Estimated fixed effects on change in PsA disease activity measures for perimenopause stage using linear mixed effects models (N=477 patients, 8381 visits)

	Peri- vs. Pre-perimenopause			Peri- vs. Post-menopause		
	Adjusted β coefficient*	95% CI	P value	Adjusted β coefficient*	95% CI	P value
DAPSA	**1.92**	**0.87, 2.97**	**<0.001**	**1.56**	**0.66, 2.47**	**0.001**
Tender joint count (0-68)	**1.04**	**0.42, 1.67**	**0.001**	**0.77**	**0.22, 1.32**	**0.006**
Swollen joint count (0-66)	**0.60**	**0.29, 0.90**	**<0.001**	**0.54**	**0.27, 0.81**	**<0.001**
HAQ-DI (0-3)	0.03	-0.02, 0.08	0.24	**-0.05**	**-0.10, -0.01**	**0.02**
FACIT-Fatigue (0-52)	**-1.41**	**-2.81, -0.02**	**0.05**	-0.58	-1.67, 0.51	0.29
C-Reactive Protein (mg/L)	0.50	-0.93, 1.94	0.49	0.76	-0.95, 2.46	0.36
PASI (0-72)	0.13	-0.31, 0.56	0.57	**0.57**	**0.18, 0.95**	**0.004**
Pain score (0-10)	0.15	-0.11, 0.41	0.25	0.12	-0.09, 0.34	0.26

*Each model is adjusted for age, PsA duration, csDMARD, b/tsDMARD and corticosteroid use.
CI – confidence interval; DAPSA – Disease activity in psoriatic arthritis; FACIT - Functional Assessment of Chronic Illness Therapy; Health Assessment Questionnaire Disability Index; PASI – Psoriasis Area and Severity Index

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Model 1: Mediator ~ Menopause stage + age + disease duration + medications
Model 2: DAPSA ~ Mediator + Menopause stage + age + disease duration + medications
Model 3: DAPSA ~ Menopause stage + age + disease duration + medications

Effect of menopause stage on the potential mediator (Model 1)*					Model estimates for menopause stage effect on DAPSA with the mediator (Model 2) and without it (Model 3)*			
Menopause stage	BMI		FACIT-Fatigue		BMI		FACIT-Fatigue	
	Adjusted β coefficient	P value	Adjusted β coefficient	P value	Without BMI in model	With BMI in model	Without FACIT in model	With FACIT in model
Peri- vs. Pre-perimenopause	0.33	0.30	-1.41	0.05	1.92	1.88	1.92	1.57
Peri- vs. Post-menopause	0.18	0.53	-0.58	0.29	1.56	1.53	1.56	1.37

*All models reports the β coefficient for menopause stage adjusted for age, PsA duration, csDMARD, ts/bDMARD and corticosteroid use

Figure 2: Assessment of the mediating effect of BMI and fatigue on DAPSA change during peri-menopause.
First we assessed the overall effect of perimenopause on the potential mediator (**Model 1**). No significant effect of peri-menopause on BMI while an increase in fatigue levels (reduction in FACIT) was seen vs. pre-perimenopause. We then assessed the effect perimenopause on DAPSA with and without including the potential mediator in the regression model (**Model 2** and **3**). FACIT-fatigue is a partial mediator of the DAPSA increase during peri-menopause, as its inclusion in the model resulted in a 18.2% attenuation in the β coefficient (1.92 to 1.57) for peri- vs. pre-perimenopause and in a 12% reduction in the β coefficient (1.88 to 1.53) for peri- vs. post-menopause.

Figure 2: Assessment of the mediating effect of BMI and fatigue on DAPSA change during peri-menopause.

fatigue. Disease activity during the perimenopause stage was compared to the pre-perimenopause and post-menopause visits.

The association between menopausal stages and PsA disease activity measures was assessed with a Generalized Additive Model with splines (considering time from FMP as continuous variable) and with linear mixed-effects models (considering menopausal stages as categorical variables). Each model was adjusted for age, disease duration, and medication use, and accounted for repeated observations via a subject-specific random effect.

We assessed the mediating effects of BMI and fatigue on the increase in DAPSA during perimenopause.

Results: A total of 477 female patients provided data for 8,381 visits over a mean follow-up of 12.1 years. Mean age at first visit was 44.9±13.9 years, and mean age at menopause was 48.7 years. Hormone replacement therapy had been used by only 1.5% of patients at any time point. A rise in DAPSA scores was found during perimenopause years, followed by a slight drop post-menopause (Figure 1).

Linear mixed models found an association between being in perimenopause and higher DAPSA compared to the pre-perimenopause ($\beta = 1.92$, $p < 0.001$) and post-menopause stages ($\beta = 1.56$, $p=0.001$, Table 1). Significantly higher tender and swollen joint counts were found in perimenopause compared to both pre- and post-menopause. Higher PASI scores were found in perimenopause compared to the post-menopause stage (Table 1).

An increase in fatigue levels during perimenopause only partially mediated the increase in DAPSA during perimenopause, explaining 12% to 18% of this change (Figure 2). BMI did not have a mediating effect on DAPSA change during perimenopause.

Conclusion: Perimenopause is associated with an increase in PsA disease activity, which includes both patient-reported outcomes and objective measures of activity. These findings highlight the need to study the effect of hormone replacement therapy in perimenopausal PsA patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **X. Li**: None; **S. Koppikar**: AbbVie/Abbott, 1, 2, 5, 6, Novartis, 2, 6, Pfizer, 12, Unrestricted educational grant for Northern Ontario Clinic, UCB, 2, 6; **I. Lega**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **R. Cook**: None.

Abstract Number: 1715

Spondyloarthritis and Psoriatic Arthritis Patients Under Immunosuppressive Conventional and Biologic DMARDs: Favorable Disease Safety and Attenuated Immunogenicity Following Recombinant Herpes Zoster Vaccination

Carla Saad[1], Eduardo Borba[2], Fernanda Chaer[3], Ana C Medeiros-Ribeiro[1], Sandra G Pasoto[1], Nadia Emi Aikawa[4], Luisa Correia[5], Percival Sampaio-Barros[6], Julio Moraes[7], Murillo Dorio[1], Claudia Goldenstein-Schainberg[1], Clovis Artur Silva[8] and Eloisa Bonfa[2], [1]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [2]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Santos, Brazil, [4]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, [6]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [7]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Jundiai, Brazil, [8]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Advances in Psoriatic Disease (1710–1715)

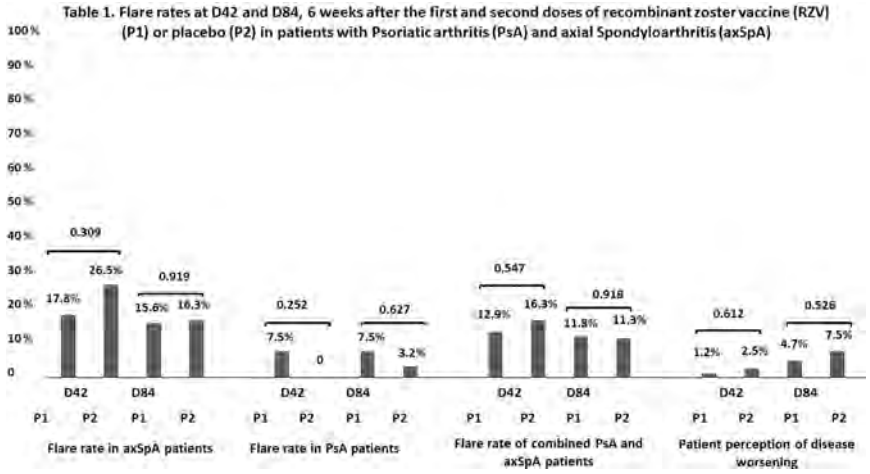
Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) patients are at increased risk for herpes zoster(HZ) due to impaired cell-mediated immunity associated with the underlying disease and therapies. Although the adjuvanted recombinant zoster vaccine (RZV, Shingrix®) has shown high efficacy and a favorable safety profile in immunocompetent individuals, its performance in PsA and axSpA patients under immunosuppressive treatment has not been evaluated and may hamper vaccination recommendations for these patients. The present study evaluates the humoral immunogenicity and safety of RZV in immunosuppressed PsA and axSpA patients compared to healthy controls (CG) and to investigate the possible impact of immunosuppressive conventional and/or biologic disease-modifying antirheumatic drugs (DMARDs) and disease activity on vaccine response.

Methods: This was a prospective, randomized, placebo-controlled clinical trial enrolled adult PsA and axSpA. Patients were randomized 1:1 to receive RZV (P1) and placebo(P2). A CG was included at a 2:1 (ARD:CG) ratio. Both CG and P1 groups received two intramuscular dose of the recombinant zoster vaccine (RZV) administered 6 weeks apart (Day 0 and Day 42) while P2 received placebo. After unblinding at Day 84, P2 participants received two doses of the vaccine. A positive humoral response was defined as an anti-gE antibody concentrations at least four times above the assay's lower detection at baseline and 6 weeks after second dose. Geometric mean titres (GMTs) and factor increase (FI) were calculated. Safety was evaluated using standardized one-week diary and disease flares was assessed by the rheumatologist in each visit using validated disease indices/scores: BASDAI, ASDAS, PASI, DAPSA and MDA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



For safety analyses, all patients who adhered to protocol were included (n=165): 71 axSpA patients (40 in P1 and 31 in P2) and 94 PsA patients (45 in P1 and 49 in P2). Results are expressed in n (%) and compared with the chi-square or Fisher's exact test, as appropriate, as two-sided analyses; Flare rate in axSpA patients was defined as an increase > 0.9 in ASDAS-CRP. Flare rate in PsA patients was defined as worsening in DAPSA category. ASDAS-CRP, DAPSA classification and patient perception of disease worsening at D42 and D84 were compared to baseline status (D0)

Results: A total of 185 SpA patients and 92 controls with similar sex distribution (37.8% vs. 38.0% female, p=0.974) and age (54.7±13.0 vs. 58.3±8.6 years, p=0.071) were enrolled. At D84 after vaccination, seroconversion (93.9% vs. 98.9%,p=0.037) and GMT [(8.9(7.6-10.4) vs. 13.5(11.6-15.7), p=0.001)] were significantly reduced in patients compared to CG. FI-GMT was similar between groups [(43.3(33.9-55.3) vs. 59.0(44.1-78.8), p=0.083)]. No factor was identified to contribute to decreased seroconversion in SpA patients (p >0.05). Disease safety evaluation revealed no increase in disease flares among patients who received P1 in comparison to patients who received P2 at D84 (11.8% vs. 11.3%,p=0.918) in the whole group or among patients with axSpA according to ASDAS-CRP (7.5% vs. 3.2%,p=0.627) or PsA according to the DAPSA (15.6% vs 16.3%,p=0.919) (Figure 1). RZV was well-tolerated, with adverse events being mild and self-limited.

Conclusion: In this first prospective controlled study, RZV demonstrated favorable safety and high rates of immunogenicity in PsA and axSpA patients under immunosuppressive treatment. However, the lower frequency of seroconversion and reduced antibody titers compared to CG raise concerns about vaccine-induced protection. These findings support the use of RZV in high-risk patients and highlights the need for long-term monitoring of vaccine efficacy. (ClinicalTrials NCT05879419).

Disclosure: C. Saad: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **F. Chaer**: None; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **N. Aikawa**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Correia**: None; **P. Sampaio-Barros**: None; **J. Moraes**: None; **M. Dorio**: None; **C. Goldenstein-Schainberg**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1716

The frequency and impact of cardiovascular disease in systemic lupus erythematosus: a Nationwide, matched case-control study.

Jessica Fairley[1], **Laura Ross**[1], Elizabeth Paratz[2], Penelope McKelvie[3], Simin Daneshvar[3], Shereen Oon[4], Dylan Hansen[3], Wendy Stevens[1], Andre La Gerche[2] and Mandana Nikpour[5], [1]The University of Melbourne, Melbourne, Victoria, Australia, [2]St Vincent's Institute of Medical Research, Melbourne, Victoria, Australia, [3]St Vincent's Hospital Melbourne, Melbourne, Victoria, Australia, [4]St Vincent's Hospital Melbourne, Melbourne, Victoria, Australia, [5]University of Sydney School of Public Health and Department of Rheumatology, Royal Prince Alfred Hospital, Sydney, Victoria, Australia

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality (1716–1721)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Cardiovascular disease is the leading cause of death in systemic lupus erythematosus (SLE).[1] Whilst histopathology remains the gold standard for establishing the pathogenesis of cardiac disease, endomyocardial biopsy is invasive and subject to sampling error. We aimed to examine the frequency of cardiovascular disease in SLE compared with the general population, and associations of specific findings with patient outcomes.

Methods: A case-control study was performed using data from the Australian National Coronial Information System, a database of deaths referred for forensic investigation. SLE cases were identified via keyword/ICD-10 code search. Age- and sex-matched controls were selected from victims of motor vehicle accidents. Demographic data and autopsy findings (macroscopic and histopathological) were extracted. Cardiomegaly was defined as heart weight >95th centile for body weight/sex. Odds ratios (OR) were calculated with 95% confidence intervals (CI).

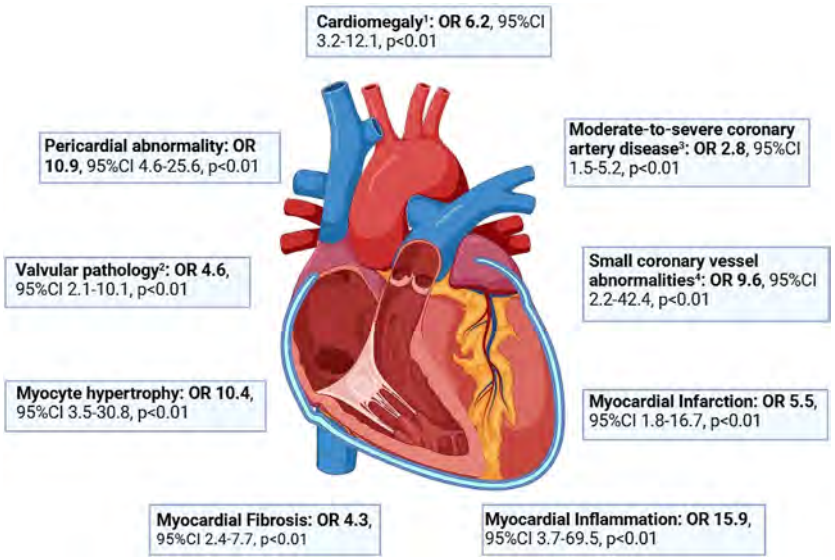


Figure 1: Odds of cardiovascular disease in SLE compared to controls using logistic regression, adjusted for age and sex. Abbreviations: CI (confidence interval), OR (odds ratio), SLE (systemic lupus erythematosus). 1Cardiomegaly defined as heart weight >95th centile for body weight. 2Valvular pathology defined as at least moderate aortic stenosis, aortic regurgitation, mitral stenosis or mitral regurgitation. 3Coronary artery disease defined as moderate to severe when stenosis >50% vessel occlusion, or qualitative description of "moderate", "severe" or "critical". 4Small vessel coronary abnormalities defined as thickening, vasculitis or other abnormality within the small intramural coronary arteries.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Logistic regression analysis describing the association between cardiovascular abnormalities and both any cardiovascular death and sudden cardiac death in SLE cases only, adjusted for age and sex. Abbreviations: CI (confidence interval), OR (odds ratio), SLE (systemic lupus erythematosus). 1Cardiomegaly defined as heart weight >95th centile for body weight. 2Coronary artery disease defined as moderate to severe when stenosis >50% vessel occlusion, or qualitative description of "moderate", "severe" or "critical". 3Valvular pathology defined as at least moderate aortic stenosis, aortic regurgitation, mitral stenosis or mitral regurgitation.

Outcome	Number	OR	95%CI	p-value
Association with cardiovascular death				
Cardiomegaly[1]	117	3.6	1.6-7.9	<0.01
Myocardial fibrosis	113	2.6	1.1-5.9	0.02
Myocardial Inflammation	111	1.3	0.5-3.3	0.60
Pericardial abnormalities	120	1.7	0.8-3.7	0.16
Moderate to severe coronary artery disease[2]	121	4.0	1.8-9.2	<0.01
Myocyte hypertrophy	113	1.1	0.5-2.7	0.76
Vegetations	123	5.7	0.6-49.7	0.12
Valvular pathology[3]	123	2.8	1.2-6.7	0.02
Association with sudden cardiac death				
Cardiomegaly[1]	113	3.4	1.5-7.5	<0.01
Myocardial fibrosis	110	1.4	0.7-3.2	0.36
Myocardial Inflammation	108	0.8	0.3-2.0	0.65
Pericardial abnormalities	115	1.0	0.4-2.1	0.90
Moderate to severe coronary artery disease[2]	116	2.5	1.1-5.7	0.03
Myocyte hypertrophy	110	0.6	0.3-1.5	0.27
Valvular vegetations	118	2.9	0.5-16.0	0.22
Valvular pathology[3]	118	1.1	0.5-2.6	0.80

Results: 123 SLE cases and 123 controls were included. Both groups were predominantly female (85%) and of similar age (median SLE 53 (IQR 40-65) years vs. control 54 (41-65) years, p=0.90).

After adjusting for age and sex, myocardial fibrosis (OR 3.4, 95%CI 1.8-6.5, p< 0.01), myocardial inflammatory infiltrates (OR 15.5, 95%CI 3.5-68.5, p< 0.01) and pericardial abnormalities (OR 8.9, 95%CI 3.7-21.3, p< 0.01) were significantly more common in SLE (Figure 1). SLE cases were 6.2-times more likely to have cardiomegaly (95% CI 3.2-12.1, p< 0.01). Moderate-to-severe epicardial coronary artery disease (CAD; OR 2.8, 95% CI 1.5-5.2, p< 0.01), myocardial infarction (OR 5.5, 95% CI 1.8-16.7, p< 0.01) and abnormalities of the small intramural coronary vessels (OR 9.6, 95% CI 2.2-42.4, p< 0.01) were more common in SLE after age and sex adjustment. These associations persisted after adjustment for age, sex and moderate to severe CAD (cardiomegaly OR 4.9, 95% CI 2.5-9.7, p< 0.01; myocardial fibrosis OR 3.4, 95%CI 1.8-6.5, p< 0.01; myocyte hypertrophy OR 8.2, 95%CI 2.7-24.8, p< 0.01; small intramural coronary vessel abnormalities OR 9.9, 95%CI 2.2-45.0, p< 0.01). Coronary vasculitis was exclusively identified in 8% of SLE cases. Valvular pathology was more common in SLE (OR 4.9, 95% CI 2.2-10.8, p< 0.01), with vegetations observed in 6% of cases.

Cardiovascular death was more common in SLE cases with myocardial fibrosis (OR 2.6, 95% CI 1.1-5.9, p=0.02), moderate-to-severe CAD (OR 4.0, 95% CI 1.8-9.2, p< 0.01) and cardiomegaly (OR 3.6, 95% CI 1.6-7.9, p< 0.01), after adjusting for age and sex (Table 1). Sudden cardiac death was more common in those with cardiomegaly (OR 3.4, 95% CI 1.5-7.5, p< 0.01) and moderate-to-severe CAD (OR 2.5, 95%CI 1.1-5.7, p=0.03), after age and sex adjustment.

Conclusion: SLE is associated with a significant excess of atherosclerotic vascular, inflammatory and fibrotic cardiac lesions. These data highlight the scope of cardiovascular abnormalities occurring in SLE, and their association with cardiovascular causes of death.

References

1. Taylor T, Anastasiou C, Ja C, et al. Causes of Death Among Individuals With Systemic Lupus Erythematosus by Race and Ethnicity: A Population-Based Study. *Arthritis Care Res (Hoboken)* 2023; **75**(1): 61-8.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Fairley: Boehringer-Ingelheim, 6, Pfizer, 12, Support for ACR Registration 2021; **L. Ross**: None; **E. Paratz**: Bristol-Myers Squibb(BMS), 6, Pfizer, 12, Conference Sponsorship; **P. McKelvie**: None; **S. Daneshvar**: None; **S. Oon**: None; **D. Hansen**: None; **W. Stevens**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Merck/MSD, 2; **A. La Gerche**: None; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer Ingelheim, 2, 5, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6.

Abstract Number: 1717

The Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) Predicts Mortality In Systemic Lupus Erythematosus (SLE) Patients: Data From The Almenara Lupus Cohort

Benny Rashuamán-Conche[1], Rocío Gamboa-Cárdenas[2], Victor Pimentel-Quiroz[3], Anubhav Singh[4], Cristina Reategui-Sokolova[5], Claudia Elera-Fitzcarrald[5], Samira Garcia-Hirsh[6], Cesar Pastor-Asurza[7], Zoila Rodriguez-Bellido[8], Risto Perich-Campos[9], Graciela Alarcón[10] and Manuel Ugarte-Gil[11], [1]Hospital Guillermo Almenara Irigoyen, Lima, Lima, Peru, [2]Universidad Científica del Sur, Lima, Peru, [3]Universidad Científica del Sur, San Isidro, Peru, [4]Baptist hospital of southeast Texas, Beaumont, TX, [5]Hospital Guillermo Almenara Irigoyen, Lima, Peru, [6]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Peru, [7]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Pakistan, [8]Universidad Nacional Mayor de San Marcos, Lima, Peru, [9]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [10]The University of Alabama at Birmingham, Oakland, CA, [11]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality (1716–1721)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Frailty has been shown to predict damage accrual in patients with SLE, including those from Latin America. However, the impact of frailty on mortality has been scarcely evaluated, particularly in the Latin American population. The aim of this study was to evaluate frailty as a predictor of mortality in Latin American SLE patients.

Methods: The Almenara Lupus Cohort is a longitudinal study which was started in January 2012. The present study includes all patients in this cohort from its inception until the end of follow-up in March 2025. All patients met the ACR 1997 or the SLICC 2012 criteria set and were older than 18 years of age at baseline. Patients who had a diagnosis of other autoimmune disease except for Sjögren's and the antiphospholipid syndromes were excluded. Mortality was defined as the vital status according to the official information from the Peruvian Department of Health. Frailty was ascertained using the SLICC-FI as a continuous variable. Univariable and multivariable Cox regression models were done to estimate the impact of the SLICC-FI on mortality. Multivariable model was adjusted for possible confounders (age at diagnosis, gender, socioeconomic status, years of education, ethnic group, tobacco use, disease duration, SLEDAI-2K, SLICC/ACR damage index,

Table 1. Association between SLICC-FI and mortality risk. Unadjusted and adjusted analyses* * Cox regression multivariable model was adjusted for age at diagnosis, gender, socioeconomic status, ethnic group, tobacco use, disease duration, SLEDAI-2K, SLICC/ACR damage index, prednisone daily dose, antimalarial and immunosuppressive drugs use. SLICC-FI: Systemic Lupus International Collaborating Clinics Frailty Index; HR: Hazard ratio

	Unadjusted			Adjusted		
Variable	HR	(95% IC)	*p* value	HR	(95% IC)	*p* value
SLICC-FI per 0.05 increase	1.888	(1.466-2.432)	<0.001	1.540	(1.108-2.138)	0.010

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

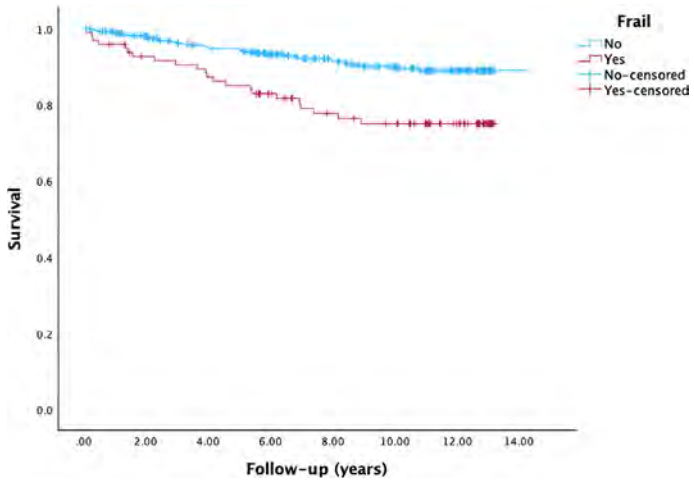


Image 1. Survival by frail status

prednisone daily dose, antimalarial and immunosuppressive drugs use). Additionally, a Kaplan-Meier curve was calculated by frail status (frail: SLICC-FI > 0.21 and non-frail: SLICC-FI ≤ 0.21).

Results: Five-hundred and nine patients were included, 470 (92.3%) were women and 96 (18.9%) were frail. Their mean (SD) age at diagnosis was 35.0 (14.0) years, their disease duration at baseline was 6.7 (6.1) years and their mean follow-up time was 8.5 (4.1) years. Fifty-seven (11.2%) patients died during the follow-up. The SLICC-FI predicted mortality in the unadjusted and adjusted models, which are depicted in Table 1. The corresponding Kaplan-Meier curve is depicted in Figure 1 (log-rank: $p < 0.001$).

Conclusion: Frailty, as ascertained with the SLICC-FI, predicted mortality, even after adjustment by possible confounders, in a Latin American cohort of SLE patients. Additional research is needed to evaluate this association and its impact as a clinical outcome in SLE in different settings. Further strategies to improve frailty should be developed.

Disclosure: B. Rashuamán-Conche: None; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **A. Singh**: None; **C. Reategui-Sokolova**: None; **C. Elera-Fitzcarrald**: None; **S. Garcia-Hirsh**: Adium, 3; **C. Pastor-Asurza**: None; **Z. Rodriguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcón**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6.

Abstract Number: 1718

Mortality and Hematological Adverse Events in Patients with Cancer Receiving Immune Checkpoint Inhibitors: Impact of Pre-existing Systemic Lupus Erythematosus

Kevin Sheng-Kai Ma[1], Dominique Feterman Jimenez[2], You Wu[3], Jenna Thomason[3], Jean Liew[4] and Namrata Singh[5], [1]Center for Global Health, Perelman School of Medicine, Philadelphia, PA, [2]University of Washington, Seattle, [3]University of Washington, Seattle, WA, [4]Boston University, Boston, MA, [5]University of Washington, Bellevue, WA

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality (1716–1721)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

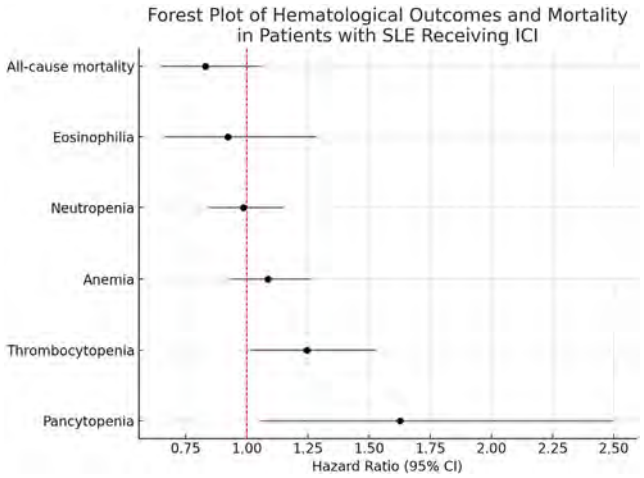


Figure 1: Forest plot of adjusted hazard ratios and 95% confidence intervals for hematological outcomes and all-cause mortality in cancer patients with pre-existing SLE treated with ICIs.

Background/Purpose: Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment, but their safety profile in patients with pre-existing autoimmune diseases, such as systemic lupus erythematosus (SLE), is not well characterized. Hematologic abnormalities are common in patients with SLE. Given the potential for ICIs to exacerbate immune-mediated adverse events, this study evaluated the risk of mortality and hematological adverse events in patients with cancer and pre-existing SLE treated with ICIs compared to matched patients without SLE.

Methods: We conducted a propensity score-matched cohort study using electronic health records from 101 U.S. healthcare organizations. Patients diagnosed with SLE (identified using International Classification of Diseases 10 codes) prior to cancer treatment and subsequently treated with ICIs (anti-PD-1/PD-L1 or CTLA-4) were matched 1:1 with non-SLE comparators based on demographics, comorbidities, cancer types, metastatic status, and prior cancer treatments. Outcomes of interest were a) hematologic abnormalities that were determined using laboratory measurements (i.e., defined by the presence of an abnormal lab value recorded after ICI initiation) and included pancytopenia, thrombocytopenia, anemia, neutropenia, and eosinophilia; and b) all-cause mortality. Cox proportional hazards models estimated the risk of hematological adverse events and all-cause mortality adjusting for above confounders.

Results: The analysis included 403 SLE patients and 403 matched non-SLE patients receiving ICIs. Mean age was 63.1 years; 77.8% were female and 68.7% White. Patients with pre-existing SLE demonstrated a significantly higher risk of developing pancytopenia (13.2% vs. 8.4%; HR=1.63, 95% CI: 1.06–2.5) and thrombocytopenia (50.9% vs. 42.4%; HR=1.25, 95% CI: 1.02–1.53). Risks of anemia, neutropenia, and eosinophilia did not differ significantly between groups. All-cause mortality was not significantly increased in patients with SLE compared to non-SLE controls (29.8% vs. 35.5%; HR=0.83, 95% CI: 0.65–1.06).

Conclusion: Cancer patients with pre-existing SLE receiving ICIs exhibit an increased risk of hematological adverse events, notably pancytopenia and thrombocytopenia, compared to matched controls without SLE. However, overall survival was comparable between both groups. These findings highlight the importance of vigilant hematological monitoring in this patient population and suggest the need for tailored management strategies when initiating ICI therapy in patients with SLE.

Disclosure: K. Ma: None; **D. Feterman Jimenez**: None; **Y. Wu**: None; **J. Thomason**: None; **J. Liew**: None; **N. Singh**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1719

Impact of SGLT2 Inhibitors on Cardiovascular Events, Mortality, and Lupus Nephritis in Patients with Systemic Lupus Erythematosus and Diabetes: Retrospective Cohort Study

Rusudan Tskitishvili[1], Abdallah Hussein[2], Nanuka Tsibadze[3], Shatha Shahwan[4] and Priju Varghese[2], [1]Virtua Health, Camden, NJ, [2]Virtua Health, Camden, [3]Jefferson Health - Einstein, Philadelphia, PA, [4]Jordan University of Science and Technology, Jordan

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality (1716–1721)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with increased risks of cardiovascular events, renal complications, and premature mortality. Sodium-glucose co-transporter-2 (SGLT2) inhibitors have shown cardiorenal benefits in diabetic populations, but their impact among patients with both SLE and diabetes remains unclear.

Methods: This retrospective cohort study utilized data from the global TriNetX Collaborative Network and included adult patients (aged ≥18 years) diagnosed with systemic lupus erythematosus (SLE) and diabetes, with or without exposure to sodium-glucose co-transporter-2 (SGLT2) inhibitors, between January 1, 2015, and December 31, 2023. Patients were grouped based on receipt of SGLT2 inhibitors. The primary outcome was all-cause mortality, while secondary outcomes included major adverse cardiovascular events (MACE) and incidence of lupus nephritis over one year. Propensity score matching was employed to balance baseline characteristics between the SGLT2 and non-SGLT2 groups. Risk ratios and 95% confidence intervals (CIs) were calculated for univariable comparisons of outcomes after matching.

Results: After propensity score matching, 1,024 patients were included in each group. The overall cohort's mean ± SD age was 58.4 ± 12.4 years, with 80% female and the majority identifying as White (approximately 36%). Matching achieved balance across cohorts (standardized differences < 0.1 for key demographics). The incidence of major adverse cardiovascular events (MACE) was lower in the SGLT2 group compared to the non-SGLT2 group (4.3% vs. 6.1%; risk ratio [RR], 0.71; 95% CI, 0.487–1.034; p = 0.0726), though not statistically significant. All-cause mortality was significantly lower in the SGLT2 group (4.7% vs. 7.8%; RR, 0.60; 95% CI, 0.424–0.849; p = 0.0035). However, the incidence of lupus nephritis was significantly higher in the SGLT2 group compared to the non-SGLT2 group (11.3% vs. 5.0%; RR, 2.28; 95% CI, 1.655–3.125; p < 0.0001).

Conclusion: Among patients with SLE and diabetes, treatment with SGLT2 inhibitors was associated with a significant reduction in all-cause mortality but an increased risk of lupus nephritis. Although a trend toward fewer cardiovascular events was observed, it did not reach statistical significance. These findings highlight the need for careful benefit-risk assessment when prescribing SGLT2 inhibitors in this population and underscore the importance of further prospective studies.

Disclosure: R. Tskitishvili: None; **A. Hussein**: None; **N. Tsibadze**: None; **S. Shahwan**: None; **P. Varghese**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1720

Comparison of Mortality Trends in Adults with Systemic Lupus Erythematosus and Cutaneous Lupus Erythematosus: A 21-Year Analysis Using CDC WONDER DATABASE.

Khadija Mohib[1], Rameez Qasim[2], Zaiya Waseem[3], Shaheer Ahmad[4] and Ahmad Ali Hussain[5], [1]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, [2]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [3]AtlantiCare Regional Medical Center, New Jersey, [4]Allama Iqbal Medical College, Lahore, Pakistan, [5]Allama Iqbal Medical College Lahore, Lahore

SESSION INFORMATION

Session Date: Monday, October 27, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality (1716–1721)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

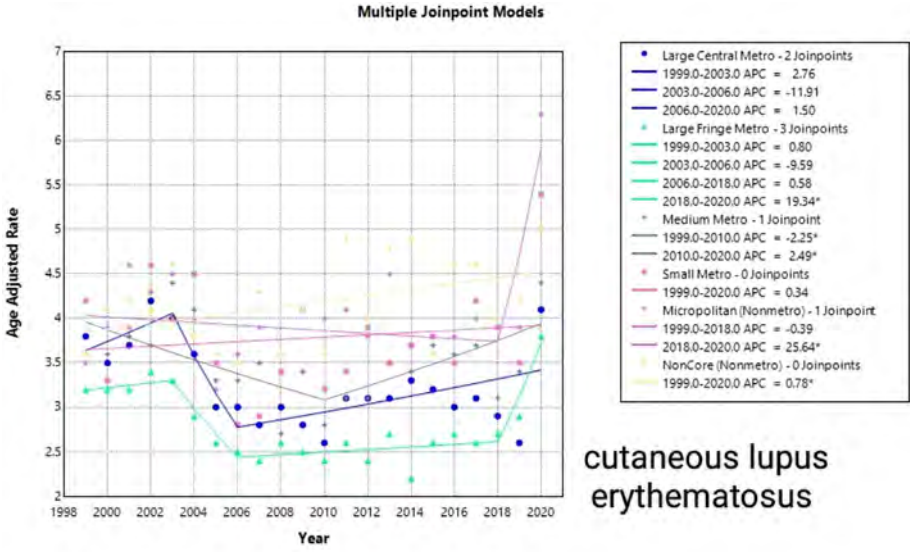
Background/Purpose: Systemic Lupus Erythematosus (SLE) and Cutaneous Lupus Erythematosus (CLE) are chronic autoimmune diseases with significant morbidity and mortality, collectively accounting for approximately 5,000 deaths annually in the United States. Understanding long-term mortality trends can inform clinical management strategies and public health policies aimed at reducing mortality and addressing disparities across populations. This study analyzes national mortality data from 1999 to 2020 to compare demographic and geographic disparities in deaths associated with SLE and CLE. The goal is to identify at-risk populations and inform future interventions to improve outcomes and reduce preventable deaths.

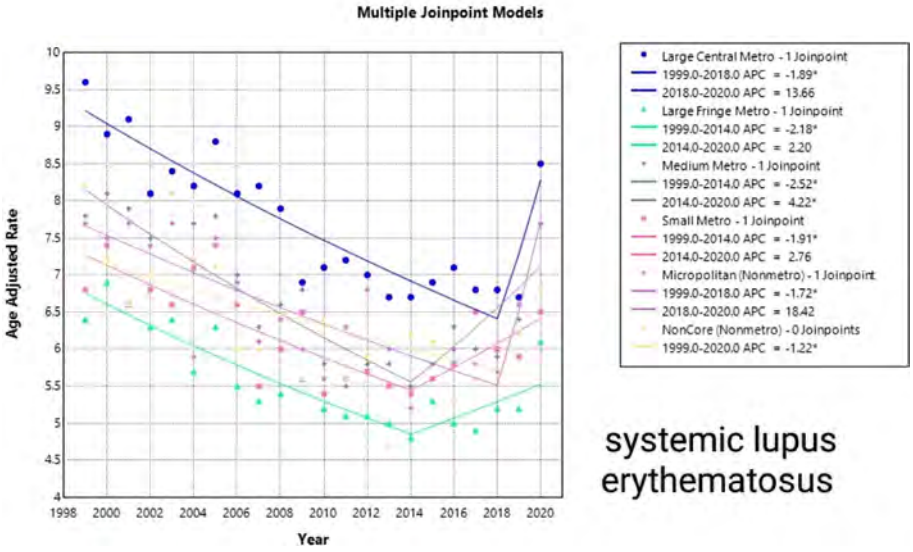
Methods: Age-adjusted mortality rates (AAMRs) per 1,000,000 adults were calculated using CDC WONDER data. Deaths attributed to SLE were identified using ICD-10 code M32, while CLE-related deaths included codes L93.0 (discoid lupus), L93.1 (subacute cutaneous lupus), and L93.2 (other local lupus). Age-stratified trends were examined in 10-year intervals. Joinpoint regression analysis was used to estimate annual percent change (APC) and average annual percent change (AAPC) in mortality from 1999 to 2020.

Results: From 1999 to 2020, mortality rates for both systemic lupus erythematosus (SLE) and cutaneous lupus erythematosus (CLE) declined overall. However, deaths from SLE remained consistently higher than those from CLE. During this period, there were 47,337 recorded deaths due to SLE and 24,563 due to CLE. The average age-adjusted mortality rate (AAMR) for SLE was 6.6 per million, compared to 3.4 per million for CLE. Mortality rates were higher in females for both conditions, with a particularly large gap in SLE—10.7 in females versus 2.2 in males. Racial disparities were evident as well: non-Hispanic Black individuals had the highest mortality for both SLE (17.4) and CLE (7.4), followed by Native Americans. Urban areas saw slightly higher SLE mortality (6.6) than rural areas (6.4), while the opposite was true for CLE, with rural areas showing a higher rate (4.1 vs. 3.3). Regionally, SLE mortality was highest in the West and lowest in the Northeast, whereas CLE mortality peaked in the South and was lowest in the Northeast. Among states, Oklahoma reported the highest SLE mortality (10.8), while Arkansas had the highest for CLE (6.9).

Conclusion: Although overall mortality rates for SLE and CLE have declined over the past two decades, marked disparities persist by sex, race, and geography. SLE disproportionately affects females, NH Black individuals, urban populations, and those residing in the Western U.S. Conversely, CLE mortality is highest among females, NH Blacks, rural populations, and those in the Southern U.S.

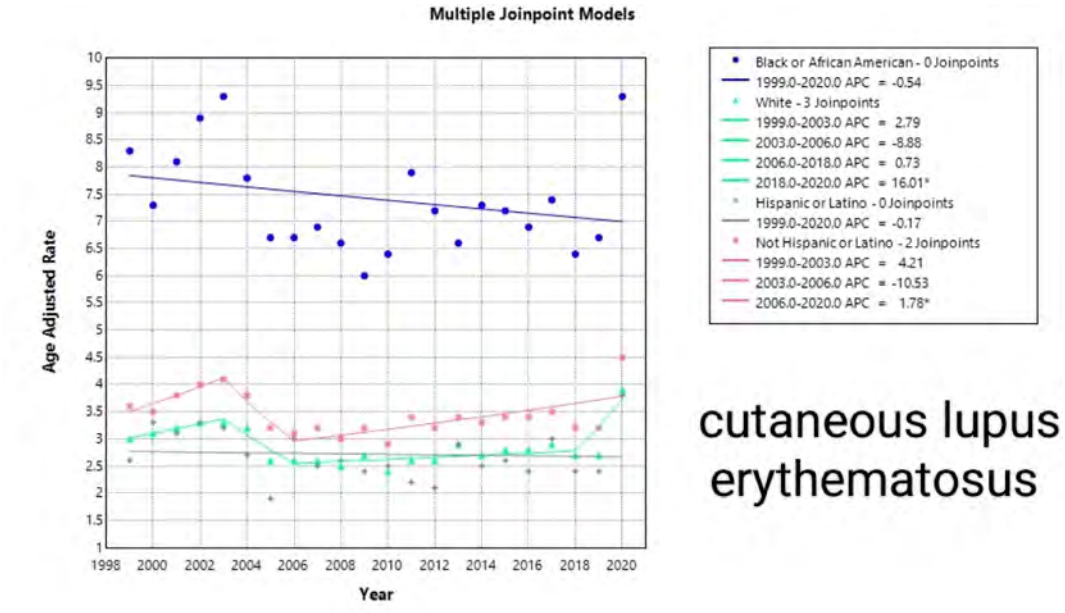
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

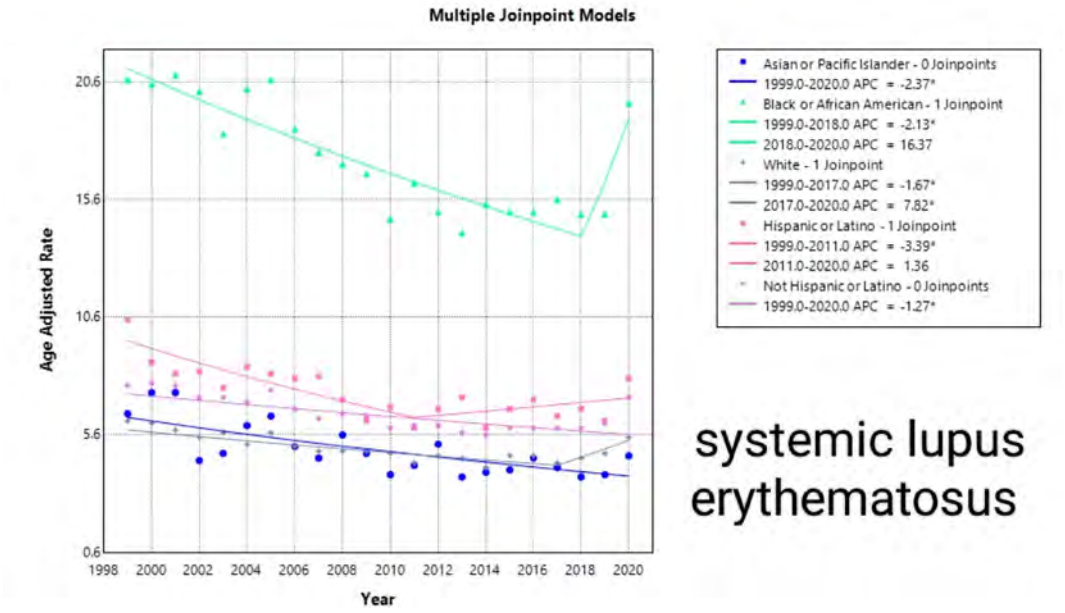




These findings underscore the need for state-specific interventions, improved access to rheumatologic care, and targeted public health strategies. Enhanced screening, early diagnosis, and equitable healthcare access are essential for reducing disease burden and closing existing mortality gaps. Future research should explore the underlying causes of these disparities and evaluate the impact of proposed interventions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





Disclosure: K. Mohib: None; **R. Qasim**: None; **Z. Waseem**: None; **S. Ahmad**: None; **A. Hussain**: None.

Abstract Number: 1721

Excess Mortality in SLE Is Concentrated in Lupus Nephritis and aPL-Positive Subsets: A population-based inception cohort study

Mario Bautista-Vargas[1], Erika Navarro-Mendoza[1], Jaime Flores-Gouyonnet[1], Ali Ardekani[1], Maria Cuellar-Gutierrez[1], Gabriel Figueroa-Parra[2], Mariana Gonzalez-Treviño[3], Jose Antonio Meade-Aguilar[4], Alain Sanchez-Rodriguez[5], Andrew C. Hanson[1], Cassondra Hulshizer[6], Cynthia Crowson[7] and Ali Duarte-Garcia[1], [1]Mayo Clinic, Rochester, MN, [2]Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico, [3]Vanderbilt University Medical Center, Nashville, TN,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[4]Boston University/Boston Medical Center, Boston, MA, [5]ABC Medical Center, Ciudad de México, Federal District, Mexico, [6]Mayo Clinic, Rochester, [7]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION
Session Date: Monday, October 27, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes II: Morbidity & Mortality (1716–1721)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Five-year survival in SLE has plateaued since the 1990s. Most epidemiologic studies pool all SLE phenotypes; It is possible that the excess mortality observed in SLE occurs and is driven predominantly in subgroups of patients. We examined whether excess mortality is confined to LN and/or antiphospholipid-antibody (aPL)–positive subsets.

Methods: We identified incident SLE cases diagnosed between 1976 and 2018 in a 27-county region of the US Midwest. Each case was matched 1:2 to non-SLE comparators on age, sex, race/ethnicity, and county of residence. SLE onset was defined by the first date fulfilling the 2019 EULAR/ACR criteria. A time-dependent lupus state exposure model was applied. All SLE patients initially contributed person-time to a non-renal, aPL-negative state (**SLE state**). Transition to an **aPL-positive state** occurred upon detection of lupus anticoagulant or IgG anticardiolipin/β2-glycoprotein I antibodies (≥40 GPL); transition to the **LN state** occurred at the first biopsy-confirmed nephritis or proteinuria ≥500 mg/24h. Patients fulfilling both criteria were classified in the LN state. Follow-up continued until death, emigration, or June 30, 2023. All-cause mortality was assessed using time-updated Cox proportional hazards models adjusted for age, sex, race/ethnicity, smoking status, and index date. Restricted mean survival time was used to estimate years of life lost compared to comparators.

Table 1. Baseline Characteristics of Systemic Lupus Erythematosus (SLE) Cases and Matched comparators*

	Comparator(N=752)	*SLE Case (N=376)*
Age at index	45 (32, 60)	45 (32, 60)
Female Sex, *n* (%)	606 (80.6%)	303 (80.6%)
Race/ethnicity, *n* (%)		
Black	28 (3.7%)	14 (3.7%)
Asian	54 (7.2%)	27 (7.2%)
American Indian	2 (0.3%)	1 (0.3%)
Other/Mixed	10 (1.3%)	5 (1.3%)
Non-Hispanic White	618 (82.2%)	309 (82.2%)
Hispanic	34 (4.5%)	17 (4.5%)
Unknown	6 (0.8%)	3 (0.8%)
SLEDAI score , n=370	NA	6 (4, 9)
SDI score		
0	NA	202 (53.7%)
1-2	NA	119 (31.6%)
3-4	NA	32 (8.5%)
5+	NA	23 (6.1%)
Years of follow-up	10 (7, 15)	9 (7, 14)
Immunosuppressants Use, *n*	0	346
Lupus Nephritis†, *n*	0	105
Positive aPL‡, *n*	0	69
Deaths, *n*	100	97
Smoking status		
Never	383 (50.9%)	166 (44.1%)
Quit/former	179 (23.8%)	141 (37.5%)
Current	133 (17.7%)	65 (17.3%)
Unknown	57 (7.6%)	4 (1.1%)

*Values are presented as median, IQR for continuous variables and n (%) for categorical variables. The index date refers to the date at which SLE cases met the EULAR/ACR classification criteria. † Lupus nephritis was defined by biopsy-confirmed nephritis or proteinuria >0.5g/day without other causes. ‡ Antiphospholipid Test included patients with at least one aPL positive (either anti-B2GPI IgG or aCL IgG antibodies or LAC) confirmed between 12 weeks apart and maximum 3 years Abbreviations: AcL, Anticardiolipin antibodies aPL; Anti-B2GP1, Anti-Beta-2 glycoprotein-1 antibodies; Antiphospholipid antibodies; LAC, Lupus anticoagulant; SLE, systemic lupus erythematosus; SLEDAI, SLE Disease Activity Index; SDI, SLICC/ACR Damage Index; BMI, body mass index; NA, not applicable; IQR: interquartile range.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Association of Systemic Lupus Erythematosus (SLE), aPL (Antiphospholipid Antibodies positive), and lupus nephritis (LN) with mortality risk.

Mortality Risk		
States	**HR (95% CI)**	**p value**
SLE	1.72 (1.24 – 2.39)	0.001
aPL+	3.51 (1.80 – 6.84)	<.001
LN	4.65 (2.98 – 7.26)	<.001

Abbreviations: HR, Hazard ratios; CI, Confidence intervals.

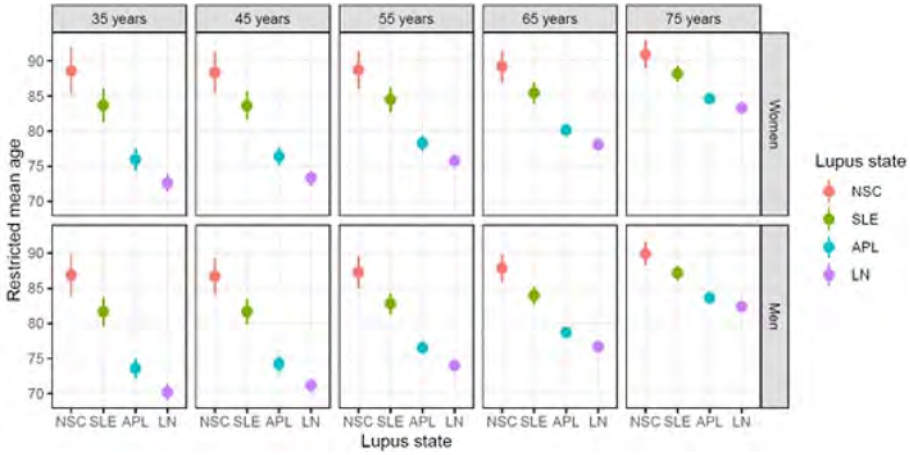


Figure. Restricted Mean Survival Age by Lupus Status, Sex, and Baseline Age. Each panel represents the restricted mean survival age for individuals categorized by baseline age (35, 45, 55, 65, and 75 years) and stratified by sex (women: top row, men: bottom row). Groups include non-SLE comparators (NSC), systemic lupus erythematosus (SLE), positive aPL (aPL), and lupus nephritis (LN). Error bars indicate confidence intervals.

Results: Among 1,128 participants (376 SLE, 752 comparators; median age 45 y; 80.6 % women), median follow-up was 9 years (IQR 7-14). There were 97 deaths among SLE patients and 100 among comparators, corresponding to crude mortality rates of 22 and 10 per 1,000 person-years, respectively. Among SLE patients, 105 developed LN, 69 became aPL-positive, and 227 remained free of both conditions. Twenty-five fulfilled criteria for both LN and aPL and were analyzed within the LN state (**Table 1**).

While patients remained in the SLE state, mortality was 72 % higher than in matched controls (HR 1.72, 95 % CI 1.24–2.39; $p = 0.001$). Risk rose sharply after transition to high-risk phenotypes—365 % higher with LN (HR 4.65, 95 % CI 2.98–7.26; $p < 0.001$) and 251 % higher after aPL seroconversion (HR 3.51, 95 % CI 1.80–6.84; $p < 0.001$) (**Table 2**). Restricted-mean survival showed life-expectancy deficits of 5 years for the SLE state, 16 years with LN and 13 years with aPL positivity (**Figure**).

Conclusion: Excess mortality in SLE was largely attributable to renal and aPL-positive disease. These findings support phenotype-based risk stratification and targeted interventions for high-risk subgroups, while offering a more reassuring prognosis for patients who remain free of nephritis and aPL seroconversion.

Disclosure: M. Bautista-Vargas: None; **E. Navarro-Mendoza**: None; **J. Flores-Gouyonnet**: None; **A. Ardekani**: None; **M. Cuellar-Gutierrez**: None; **G. Figueroa-Parra**: None; **M. Gonzalez-Treviño**: None; **J. Meade-Aguilar**: None; **A. Sanchez-Rodriguez**: None; **A. Hanson**: None; **C. Hulshizer**: None; **C. Crowson**: None; **A. Duarte-Garcia**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1722

Defining Safe Hydroxychloroquine Blood Levels: Time to Switch to Precision Monitoring for Optimized Lupus Care

Shivani Garg[1], Benoit Blanchet[2], Yann Nguyen[3], Fauzia Hollnagel[4], Ada Clarke[5], Michelle Petri[6], Murray Urowitz[7], John Hanly[8], Caroline Gordon[9], Sang-Cheol Bae[10], Juanita Romero-Diaz[11], Jorge Sanchez-Guerrero[12], Ann Clarke[13], Sasha Bernatsky[14], Daniel Wallace[15], David A. Isenberg[16], Anisur Rahman[16], Joan Merrill[17], Paul Fortin[18], Dafna D. Gladman[19], Ian Bruce[20], Ellen Ginzler[21], Mary Anne Dooley[22], Rosalind Ramsey-Goldman[23], Susan Manzi[24], Andreas Jönsen[25], Graciela Alarcón[26], Ronald van Vollenhoven[27], Cynthia Aranow[28], Murat Inanc[29], Meghan mackay[30], Guillermo Ruiz-Irastorza[31], S. Sam Lim[32], Murat Inac[33], Kenneth Kalunian[34], Søren Jacobsen[35], Christine Peschken[11], Diane Kamen[36], Anca Askanase[37], Jill Buyon[38], Julie Chezel[5], Alicja Puszkiel[39] and Nathalie Costedoat-Chalumeau[40], [1]University of Madison, School of Medicine and Public Health, Madison, WI, [2]National Referral Centre for Rare Autoimmune and Systemic Diseases, Hôpital Cochin, Paris, France, [3]Department of Internal Medicine, Beaujon Hospital, AP-HP Nord, Université Paris Cité, Clichy, France, Clichy, France, [4]University of Wisconsin, School of Medicine and Public Health, Madison, Madison, WI, [5]Cochin Hospital, Paris, France, [6]Johns Hopkins University School of Medicine, Timonium, MD, [7]University of Toronto, Toronto, ON, Canada, [8]Dalhousie University, Halifax, NS, Canada, Halifax, NS, Canada, [9]Department of Inflammation and Ageing, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom, [10]Hanyang University Medical Center, Seoul, South Korea, [11]University of Manitoba, Winnipeg, MB, Canada, [12]Mount Sinai Hospital and University Health Network, Toronto, Canada, [13]Division of Rheumatology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [14]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [15]Cedars Sinai Medical Center, Studio City, CA, [16]University College London, London, United Kingdom, [17]Oklahoma Medical Research Foundation, Oklahoma, [18]Centre ARThrite - CHU de Québec - Université Laval, Quebec, QC, Canada, [19]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [20]Centre for Public Health, Faculty of Medicine, Health and Life Sciences, Queen's University Belfast, Belfast, United Kingdom, [21]SUNY Downstate Health Sciences University, New York, NY, [22]UNC physician network, Chapel Hill, NC, [23]Northwestern University Feinberg School of Medicine, Chicago, IL, [24]Lupus Center of Excellence, Autoimmunity Institute, Allegheny Health Network, Pittsburgh, PA, [25]Department of Clinical Sciences, Lund University, Lund, Sweden, [26]The University of Alabama at Birmingham, Oakland, CA, [27]Department of Rheumatology, Amsterdam University Medical Centre, Amsterdam, Netherlands, [28]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [29]Istanbul University, Istanbul, Turkey, [30]Feinstein Institutes for Medical Research, Manhasset, NY, [31]Biobizkaia Health Research Institute, Barakaldo, Spain, [32]Emory University School of Medicine, Atlanta, GA, [33]Istanbul University, Istanbul, [34]UC San Diego, La Jolla, CA, [35]Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, [36]Medical University of South Carolina, Johns Island, SC, [37]Columbia University Medical Center, New York, NY, [38]NYU Grossman School of Medicine, New York, NY, [39]Cochin Hospital, Paris, [40]Inserm DR Paris 5, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Plenary III (1722–1727)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Current guidelines recommend using hydroxychloroquine (HCQ) dose ≤5.0 mg/kg for managing SLE. However, 6-fold higher SLE flares, including those requiring hospitalizations, are noted with HCQ dose of ≤5mg/kg vs. >5mg/kg (Jorge, 2022). Moreover, clear guidance on adjusting HCQ dose in chronic kidney disease (CKD) is lacking. HCQ blood level monitoring could better guide precise HCQ dosing based on patient risk factors. Leveraging data from diverse SLE cohorts, we aimed to study the upper threshold to define a therapeutic range for HCQ blood levels to support clinical use and inform dose adjustments.

Methods: Data were pooled from the SLICC Inception Cohort (n=660, 33 centers in 11 countries in North America, Europe, Asia), one longitudinal prevalent SLE registry (n=269, Wisconsin, USA), and three previously published studies of HCQ levels in SLE (n=1081, centralized in Paris, France). HCQ levels (T0) at first visit for the registry/cohort were measured in whole blood or serum; HCQ serum levels were converted to HCQ whole blood equivalent using the validated conversion factor of dividing by 0.53. The primary outcome was HCQ-related systemic toxicity (cardiac, retinal, muscle) at the last follow-up

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

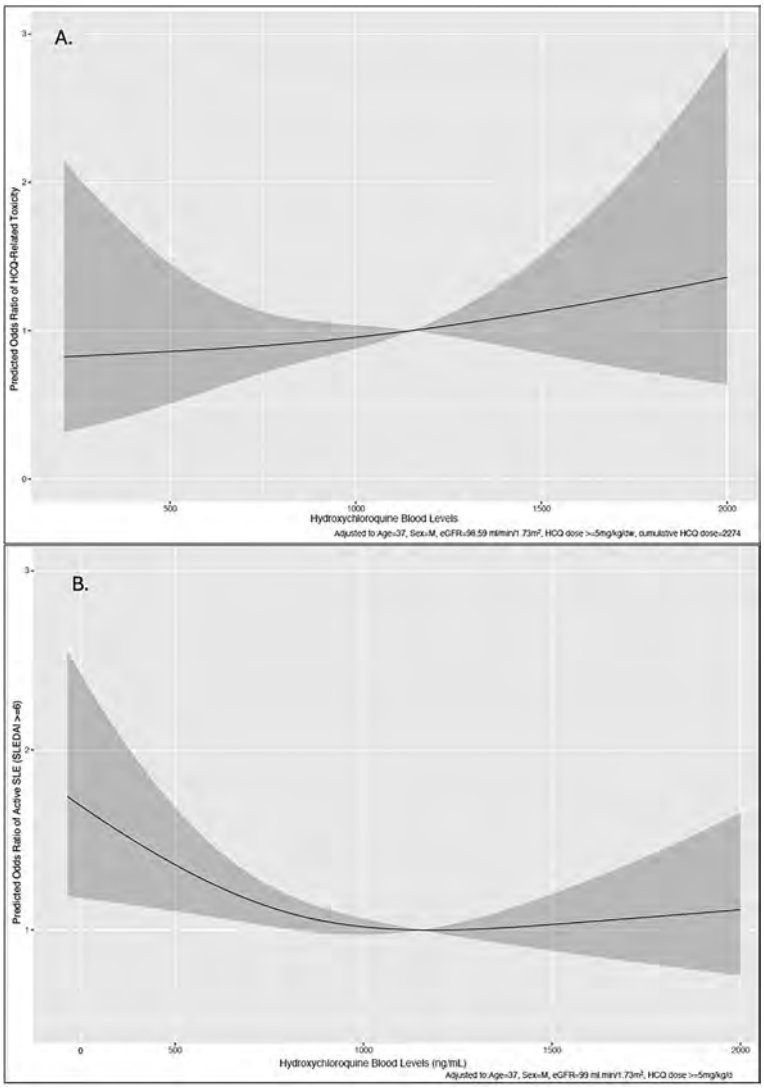


Fig. 1. Adjusted restricted cubic splines to show associations between: HCQ blood levels and toxicity (panel A), and HCQ blood levels and active lupus (SLEDAI ≥6) (panel B) using data from 1842 patients

(T last visit), identified from clinical reports. SLE Disease Activity Index (SLEDAI-2K) at T0 was abstracted to identify active SLE defined as SLEDAI-2K ≥6 (Secondary outcome). Using mixed regression analysis, we first identified a HCQ blood level (T0) predictive of higher HCQ toxicity (T last visit). Next, we tested if this upper threshold was supratherapeutic (no further risk reduction for active SLE). Finally, we examined associations between CKD stage ≥3 and supratherapeutic/toxic HCQ blood levels at T0.

Results: Among 1842 patients, 4.4% had toxicity (85% retinopathy, 9% cardiomyopathy, 6% myopathy). Odds of toxicity were 1.9-fold higher with blood levels >1150 ng/mL (Fig. 1A, Table 1A), and 1.04-fold higher with cumulative HCQ dose per 100g increase (Table 1A).

Using 750-1150 ng/ml as a reference range, levels < 750 ng/mL were associated with 1.4 fold higher odds of active SLE (Table 1B), while levels >1150 ng/mL were associated with a saturation in therapeutic effect, indicating supratherapeutic levels (Fig. 1B, Table 1B).

Patients on HCQ dose < 5mg/kg had 1.9-fold higher odds of active SLE (Table 1B); 52% of patients on ≤5mg/kg dose had subtherapeutic levels (< 750 ng/ml), and 18% supratherapeutic levels (>1150 ng/mL).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1A. Multivariable logistic regression analysis showing factors (T0) associated with HCQ toxicity (T last visit) of HCQ using data from different populations (n=1842); Table 1B. Multivariable logistic regression analysis showing factors (T0) associated with clinical response (active SLE defined as SLEDAI ≥6) at T0 with HCQ use using data from different populations (n=1842)

Table 1A. Multivariable logistic regression analysis showing factors (T0) associated with HCQ toxicity (T last visit) of HCQ using data from different populations (n=1842)

Variables	Adjusted OR[1] (95% CIs)	p-value
Age per 10 years increase	**1.03 (1.01-1.05)**	**0.0002**
Female	0.74 (0.38-1.58)	0.39
Weight based HCQ dose, >5mg/kg/day	1.35 (0.76-2.46)	0.31
Cumulative HCQ dose per 100 g increase	**1.04 (1.02-1.07)**	**0.007**
eGFR per 10 mL/min/1.73m² increase	0.96 (0.89-1.03)	0.24
HCQ Blood levels >1150 ng/mL	**1.86 (1.16-2.95)**	**0.009**

Abbreviations: HCQ=Hydroxychloroquine; eGFR=estimated glomerular filtration rate.
[1]Adjusted for age (continuous at T0), sex (patient-reported at T0), weight-based HCQ dose (>5 vs. ≤5 (reference group) mg/kg/day, at T0), cumulative HCQ dose (continuous and measured until last visit or day of HCQ toxicity, Tlast visit), eGFR (continuous and measured on the day of HCQ blood levels T0), and using HCQ blood level categories (>1150 vs. ≤1150 (reference group) ng/mL, measured at T0).
Statistically significant p-values (<0.05) shown in bold font. [+]Trend towards significance.

Table 1B. Multivariable logistic regression analysis showing factors (T0) associated with clinical response (active SLE defined as SLEDAI ≥6) at T0 with HCQ use using data from different populations (n=1842)

Variables	Adjusted OR[1] (95% CIs)	p-value
Age in 10-year increments	**0.98 (0.98-0.99)**	**<0.0001**
Female	1.40 (0.99-2.04)	0.07[+]
Weight-based HCQ dose, ≤5mg/kg/day	**1.86 (1.50-2.30)**	**<0.0001**
eGFR in 10-unit increments	**1.04 (1.01-1.07)**	**0.02**
HCQ Whole Blood levels 750-1150ng/mL[2]	ref	
HCQ Whole Blood levels <750 ng/mL	**1.36 (1.07-1.72)**	**0.0126**
HCQ Whole Blood levels >1150 ng/mL	0.95 (0.72-1.24)	0.69

Abbreviations: HCQ=Hydroxychloroquine; eGFR=estimated glomerular filtration rate.
[1]Adjusted for age (continuous, T0), sex (patient-reported, T0), weight-based HCQ dose (>5 vs. ≤5 (reference group) mg/kg/day at T0), eGFR (continuous at T0), and HCQ whole blood level categories (<750 (reference group) vs. 750-1150 vs. >1150 ng/mL at T0). SLEDAI-2K scores at T0 categorized as ≥6 to identify active SLE.
[2]Model uses HCQ Whole Blood levels 750-1150 ng/mL as reference category to demonstrate the ceiling or saturation effect in clinical response with levels >1150 ng/mL.
Statistically significant p-values (<0.05) shown in bold font. [+]Trend towards significance.

Table 2A. Multivariable logistic regression analysis showing factors (T0) associated with supratherapeutic (or toxic) whole blood levels, >1150 ng/mL, at T0 across all patients (n=1842); Table 2B. Multivariable subgroup analysis showing factors (T0) associated with supratherapeutic (or toxic) whole blood levels, >1150 ng/mL, at T0 including only patients on dose ≤5mg/kg (n=781)

Table 2A. Multivariable logistic regression analysis showing factors (T0) associated with supratherapeutic (or toxic) whole blood levels, >1150 ng/mL, at T0 across all patients (n=1842)

Variables	Adjusted OR[1] (95% CIs)	p-value
Age in 10-year increment	1.01 (1.00-1.01)	0.10
Female	1.42 (0.96-2.16)	0.09[+]
Weight based HCQ dose, >5mg/kg/day	**2.38 (1.83-3.13)**	**<0.0001**
Weight in 1-kg increment	1.00 (0.99-1.01)	0.68
Chronic Kidney Disease Stage ≥3 (eGFR <60 mL/min/1.73m²)	**2.27 (1.45-3.53)**	**0.0003**

Abbreviations: HCQ=Hydroxychloroquine; eGFR=estimated glomerular filtration rate.
[1]Adjusted for age (continuous), sex (patient-reported), weight in kg (continuous), weight-based HCQ dose (>5 vs. ≤5 (reference group) mg/kg/day), eGFR categorized as CKD stage ≥3 (<60) vs. <3 (≥60 mL/min/1.73m²; reference group).
Statistically significant p-values (<0.05) shown in bold font. [+]Trend towards significance.

Table 2B. Multivariable subgroup analysis showing factors (T0) associated with supratherapeutic (or toxic) whole blood levels, >1150 ng/mL, at T0 including only patients on dose ≤5mg/kg (n=781)

Variables	Adjusted OR[1] (95% CIs)	p-value
Age in 10-year increment	**1.01 (1.00-1.013)**	**0.025**
Female	1.62 (0.91-3.06)	0.12
Weight in 1-kg increment	1.01 (1.00-1.02)	0.12
Chronic Kidney Disease Stage ≥3 (eGFR <60 mL/min/1.73m²)	**1.94 (1.05-3.48)**	**0.029**

Abbreviations: HCQ=Hydroxychloroquine; eGFR=estimated glomerular filtration rate.
[1]Adjusted for age (continuous), sex (patient-reported), weight in kg (continuous), eGFR categorized as CKD stage ≥3 (<60) vs. <3 (≥60 mL/min/1.73m²; reference group).
Statistically significant p-values (<0.05) shown in bold font.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patients with CKD stage ≥3 had 2.3-fold higher odds of having supratherapeutic/toxic levels (>1150 ng/mL) (Table 2A). These associations remained significant even in patients on HCQ dose ≤5mg/kg (OR=1.94; Table 2B).

Conclusion: HCQ whole blood levels >1150 ng/mL predicted 2-fold higher risk of HCQ-related toxicity (confirming findings in Petri et al 2020), while levels < 750 ng/mL were associated with 1.4-fold higher active SLE risk. Even with HCQ dose ≤5mg/kg, 52% had subtherapeutic vs. 18% had supratherapeutic levels risking active SLE vs. toxicity, while those with CKD stage ≥3 had supratherapeutic/toxic levels (>1150 ng/mL). These findings establish the clinical significance of HCQ blood level monitoring to guide precise and optimal HCQ use to balance safety and efficacy in SLE.

Disclosure: S. Garg: None; **B. Blanchet**: None; **Y. Nguyen**: None; **F. Hollnagel**: None; **A. Clarke**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **M. Urowitz**: AstraZeneca, 6, GSK, 2, Merck/MSD, 2; **J. Hanly**: None; **C. Gordon**: Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB, 2; **S. Bae**: None; **J. Romero-Diaz**: None; **J. Sanchez-Guerrero**: None; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, Novartis, 2, Roche, 2; **S. Bernatsky**: None; **D. Wallace**: PPD, 2; **D. A. Isenberg**: None; **A. Rahman**: None; **J. Merrill**: None; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **I. Bruce**: AstraZeneca, 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Merck/MSD, 2, Novartis, 5, Otsuka, 5, UCB, 2; **E. Ginzler**: None; **M. Dooley**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **S. Manzi**: AstraZeneca, 2, CAQH, 1, Cartesian, 1, 2, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, Lily, 2, Lupus Foundation of America, 4, UCB Advisory Board, 2; **A. Jönsen**: None; **G. Alarcón**: None; **R. van Vollenhoven**: AbbVie, 2, 6, Alfasigma, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 5, 6, Galapagos, 2, 5, 6, GSK, 2, 6, Janssen, 2, 6, MSD, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, 6, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **M. Inanc**: None; **M. mackay**: None; **G. Ruiz-Irastorza**: None; **S. Lim**: Accordant, 2, AstraZeneca, 2, Biogen, 5, BMS, 5, Genentech, 2, Gilead, 5, GSK, 2, Novartis, 5, UCB, 5; **M. Inac**: None; **K. Kalunian**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Genentech, 1, GlaxoSmithKlein(GSK), 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, Roche, 1; **S. Jacobsen**: None; **C. Peschken**: None; **D. Kamen**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **J. Chezel**: None; **A. Puszkiel**: None; **N. Costedoat-Chalumeau**: Bristol-Myers Squibb(BMS), 6, Roche, 5, UCB Pharma France, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1723

Impaired Maintenance of X-Chromosome Inactivation in B Cells, But Not T Cells, Exacerbates Interferon-Driven Systemic Autoimmunity

Nikhil Jiwrajka[1], Claudia Lovell[1], Zowie Searcy[1], Katherine Forsyth[1], Emma Welter[1], Natalie Toothacre[2], Nuriban Valero-Pacheco[1], Katherine Premo[1] and Montserrat Anguera[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Plenary III (1722–1727)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Many systemic autoimmune diseases associated with chronic type 1 interferon (IFN) signaling, including SLE, SjD, and SSc, preferentially afflict females. The biological basis of this female sex bias and its role in chronic IFN signaling are not well understood. Emerging data have implicated the X chromosome as a key contributor to female-biased autoimmunity. In XX individuals, X chromosome dosage is balanced with that of XY individuals via X-Chromosome Inactivation (XCI), an epigenetic mechanism that transcriptionally silences supernumerary X chromosomes via the long non-coding RNA, XIST. Strikingly, T and B cells from females with SLE exhibit epigenetic features of impaired XCI maintenance (XCIm). However, it is unclear from these data whether impaired XCIm in T or B cells directly contributes to IFN-mediated disease. Given the many immunomodulatory X-linked genes with roles in lymphocyte function and IFN signaling, we investigated whether impaired XCIm in female lymphocytes modifies the development of IFN-driven systemic autoimmunity.

Methods: We generated female C57BL/6 mice with either a B-cell-specific deletion of *Xist* (Mb1cre$^{+/-}$Xist$^{fl/fl}$, "Xist BcKO") or a T cell-specific deletion of *Xist* (Cd4cre^{+}Xist$^{fl/fl}$, "Xist TcKO"). Female Xist BcKO mice and littermate controls ("WT") or female Xist TcKO mice and littermate controls ("WT") were treated thrice weekly with topical imiquimod (IMQ), a Tlr7 agonist, for 12 weeks (**Fig. 1A**). Serum, spleens, cervical lymph nodes, kidneys, and other tissues were harvested upon euthanasia and processed for autoantibody quantification, flow cytometry, and histology.

Results: IMQ-treated Xist BcKO mice exhibited markedly increased spleen mass, increased anti-dsDNA and anti-U1RNP/Smith autoantibody production, and more severe glomerular disease compared to WT mice (**Fig. 1B-C**). In contrast, IMQ-treated Xist TcKO mice did not exhibit significant differences in spleen mass, autoantibody levels, or glomerular pathology compared to IMQ-treated WT mice (**Fig. 1D**). Unlike IMQ-treated Xist TcKO mice, IMQ-treated Xist BcKO mice exhibited greater proportions of antibody-secreting and activated T and B cell subsets, including germinal center (GC) and age-associated B cells (ABCs), across the spleen, lymph nodes, and peripheral blood. Anti-U1RNP/Smith autoantibody levels were strongly correlated with the proportion of ABCs across all tissues; both rely on Tlr7 signaling (**Fig. 2A-B**). Activated B cell subsets from IMQ-treated Xist BcKO mice exhibited higher median fluorescence intensities of X-linked proteins, including Tlr7 and Cxcr3, suggesting their aberrant overexpression in the setting of *Xist* deletion (**Fig. 2C**).

Conclusion: These data demonstrate that impaired XCIm via *Xist* deletion has cell-type-specific effects on IFN-driven autoimmunity. They also demonstrate that impaired XCIm in B cells, but not T cells, amplifies humoral, cellular, and histopathological features of IFN-driven disease, and results in the overexpression of X-linked proteins likely derived from the inactive X chromosome. These findings support a novel mechanism of female-biased autoimmunity wherein impaired XCIm in B cells enhances susceptibility to IFN-mediated autoimmunity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

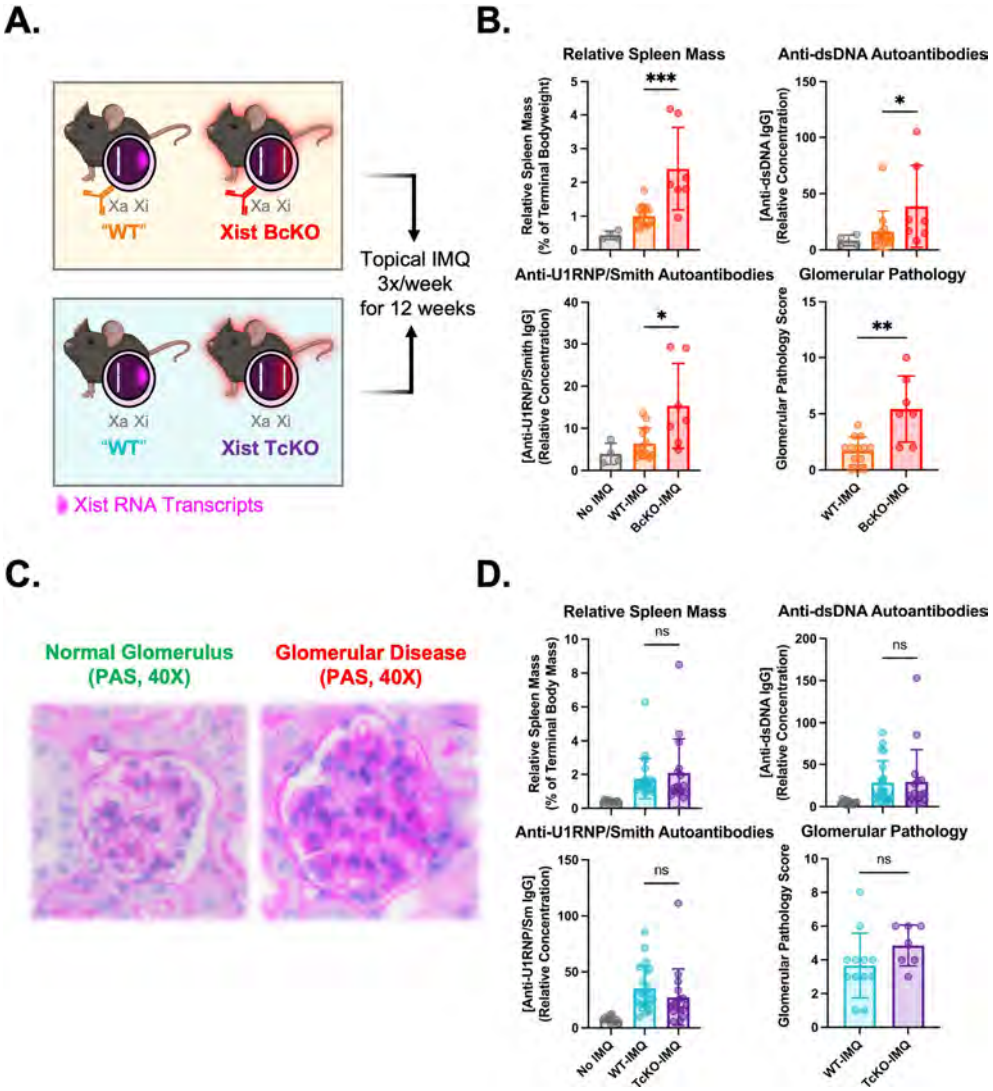


Figure 1. Xist Deletion in B Cells, But Not T Cells, Exacerbates Humoral and Histopathological Features of IMQ-Induced Disease. A. Schematic of the experimental approach. B. Quantification of relative spleen mass, autoantibody concentration, and glomerular pathology in IMQ-treated Xist BcKO mice (n=7) versus IMQ-treated WT mice (n= 13). The "Glomerular Pathology Score" represents the sum of subscores (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe) for key histopathologic features specific to the glomerulus; 10-50% of glomeruli were affected in most mice. C. Images of an unaffected and a diseased glomerulus (40X; same image scale), stained with periodic acid-Schiff (PAS). D. Quantification of relative spleen mass, autoantibody concentration, and glomerular pathology in IMQ-treated Xist TcKO mice (n=16) versus IMQ-treated WT mice (n=21). WT mice that were not treated with IMQ are included for both experiments to serve as a reference (n=4 for Xist BcKO experiments; n=12 for Xist TcKO experiments). Data are depicted as mean +/- SD. *, **, *** = $p < 0.05$, 0.01, 0.001 via pairwise Mann-Whitney U test (IMQ-cKO vs. IMQ-WT). ns = not statistically significant; Xa = active X chromosome; Xi = inactive X chromosome.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

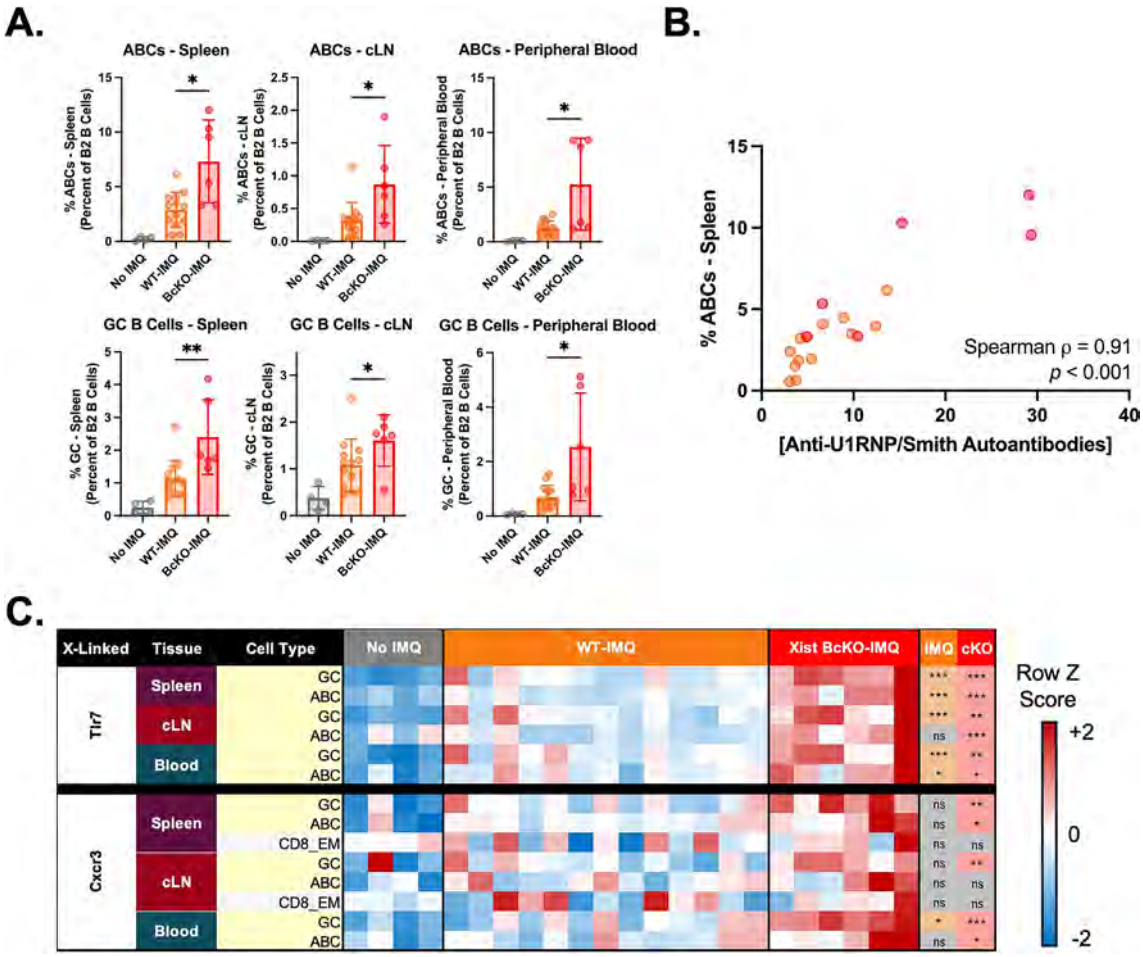


Figure 2. IMQ-treated Xist BcKO Mice Exhibit Increased Proportions of Activated B Cell Subsets in the Setting of Increased Tlr7 Protein Levels. A. Proportions of activated B cell subsets across the spleen, cervical lymph nodes, and peripheral blood in untreated WT, IMQ-treated WT, and IMQ-treated Xist BcKO mice, quantified via flow cytometry‡. Data are depicted as mean +/- SD. *, ** = p < 0.05, and 0.01, respectively, via pairwise Mann-Whitney U test (BcKO-IMQ vs. WT-IMQ). B. Scatterplot and Spearman correlation of anti-U1RNP/Smith antibody concentration versus the percent of splenic age-associated B cells among IMQ-treated mice. Data are colored by experimental group. C. Heatmap depicting the row-normalized median fluorescence intensities of Tlr7 and Cxcr3 across B cell subsets, tissue types, and experimental groups. Each column represents a unique biological sample. The results of the pairwise Mann-Whitney U tests are depicted in the columns "IMQ" and "cKO". "IMQ" refers to the pairwise comparison between "WT-IMQ" and "No IMQ". "CKO" refers to the pairwise comparison between "BcKO-IMQ" and "WT-IMQ". *, **, *** = p < 0.05, 0.01, and 0.001, respectively. ABCs = age-associated B cells (Cd21/35-Cd23-Cd11c+Tlr7+); CD8_EM = CD8+ Effector

Disclosure: N. Jiwrajka: None; **C. Lovell**: None; **Z. Searcy**: None; **K. Forsyth**: None; **E. Welter**: None; **N. Toothacre**: None; **N. Valero-Pacheco**: None; **K. Premo**: None; **M. Anguera**: None.

Abstract Number: 1724

Pathogenic role of Mucosal-Associated Invariant T cells in Rheumatoid Arthritis.

Manon LESTURGIE-TALAREK[1], Virginie Gonzalez[2], Anne Cauvet[2], Lucie Beaudoin[3], Fiona Oudart[4], Adrien Schvartz[5], Francesco Carbone[5], Mickael Menager[5], Noémie Sénot[3], Francoise Tilotta[6], Yannick Allanore[7], Agnes Lehuen[8] and Jérôme AVOUAC[9], [1]Paris University, Paris, France, [2]INSERMU1016, Paris, France, [3]Institut Cochin, Paris, [4]APHP - Cochin hospital, Paris, France, [5]Institut Imagine, Paris, [6]Université Paris Cité, Montrouge, France, [7]Université Paris Cité, Paris, France, [8]Hôpital Cochin, Paris, France, [9]Rheumatology department, Cochin hospital, Paris, France

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Plenary III (1722–1727)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Mucosal-associated invariant T (MAIT) cells are innate-like lymphocytes that produce cytokines and cytotoxic molecules. Reduced frequencies and altered phenotypes of MAIT cells have been described in autoimmune diseases. Their ability to interact with microbiota and accumulate in inflamed tissues suggests a role in RA pathogenesis.

The objective was to explore the phenotypic, functional, and transcriptomic alterations of MAIT cells in blood and synovial fluid (SF) in RA and assess their impact on inflammation and joint damage using in vitro and in vivo models.

Methods: MAIT cells were analyzed by flow cytometry in peripheral blood from 75 RA patients and 42 healthy donors (HD). SF MAIT cells were studied in 19 RA patients. Single-cell RNA sequencing (scRNA-seq) was performed on paired blood and SF samples from 6 RA patients and 4 HDs. MAIT–fibroblast-like synoviocyte (FLS) interactions were assessed in co-culture. To study their in vivo role, MAIT cells were modulated in two arthritis mouse models—mBSA (methylated bovin serum albumin)-induced and TNF-transgenic—using MR1 knockout mice and Ac-6-FP, a pharmacological inhibitor of MAIT cell activation.

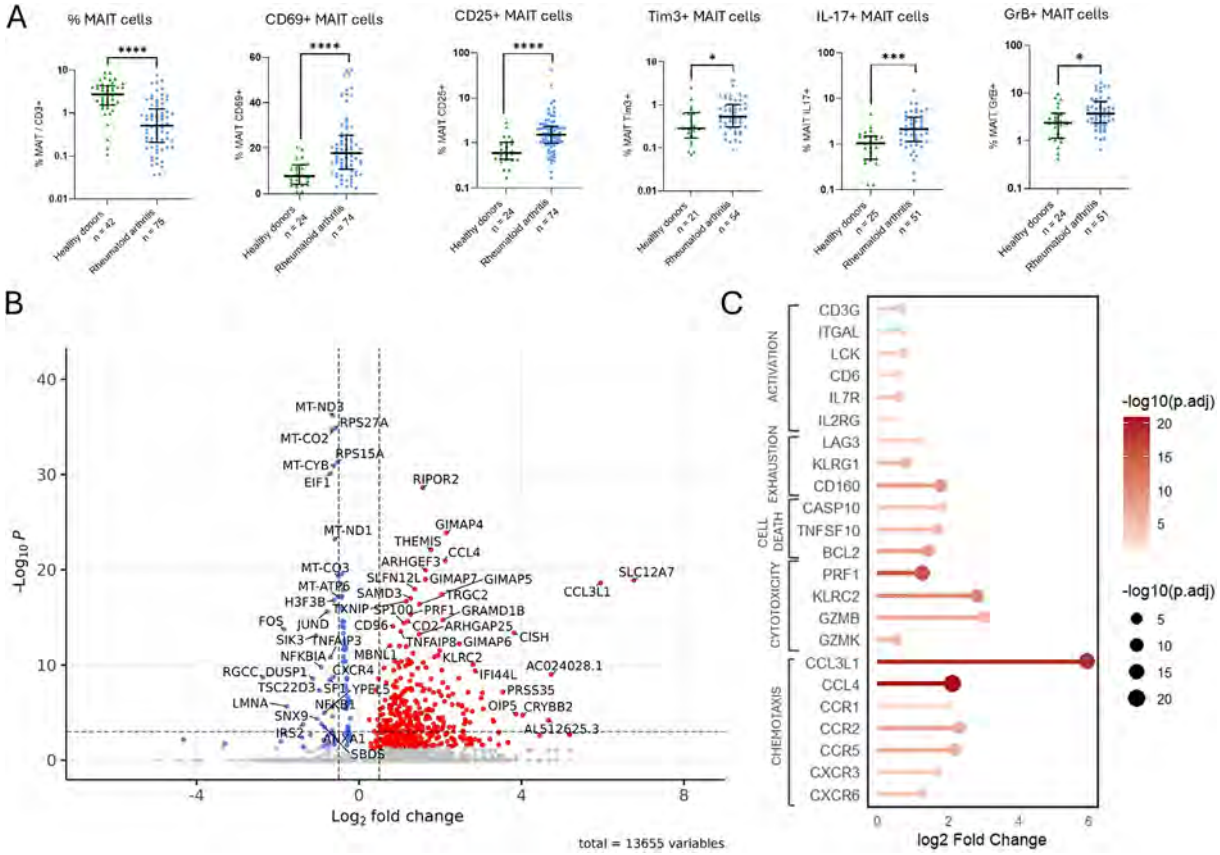


Figure 1. Phenotypic and transcriptomic alterations of circulating MAIT cells in RA. (A) Frequency and functional profile of circulating MAIT cells in RA patients compared to healthy donors (HD), including expression of CD69, CD25, Tim-3, IL-17, and granzyme B after stimulation. (B) Volcano plot showing differentially expressed genes in RA MAIT cells versus HD, based on single-cell RNA sequencing (scRNA-seq). (C) Lollipop plot summarizing selected upregulated genes in RA MAIT cells, categorized into functional groups: activation, exhaustion, apoptosis, cytotoxicity, and chemotaxis. Statistical comparisons were performed using Mann–Whitney test. MAIT: mucosal-associated invariant T cell; RA: rheumatoid arthritis; HD: healthy donor; scRNA-seq: single-cell RNA sequencing.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

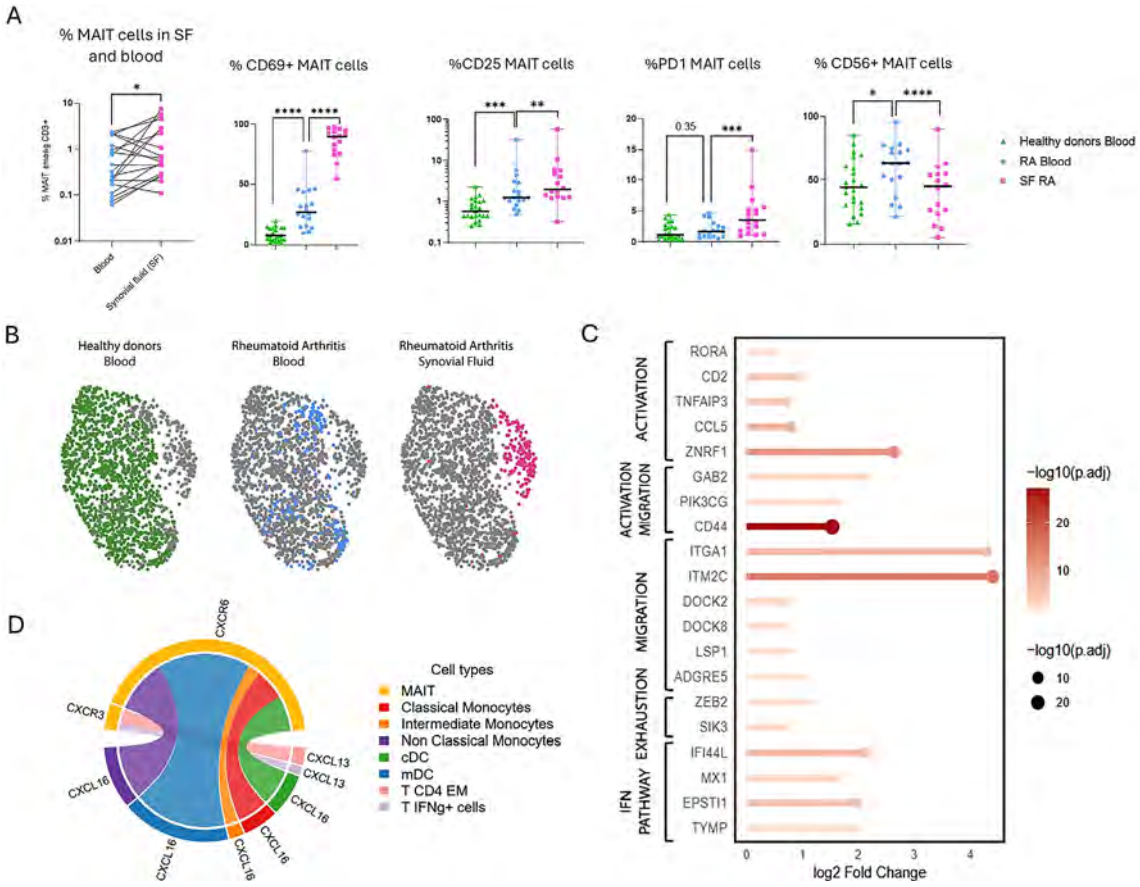


Figure 2. Phenotypic and transcriptomic profile of MAIT cells in synovial fluid. (A) Frequency and surface marker expression of MAIT cells from synovial fluid (SF) of RA patients compared to paired peripheral blood MAIT cells and blood MAIT cells from healthy donors (HD), including CD69, CD25, PD-1, and CD56. (B) UMAP projection of all MAIT cells analyzed by single-cell RNA sequencing (scRNA-seq), colored by sample origin: HD blood, RA blood, and RA SF. (C) Lollipop plot showing selected differentially expressed genes in RA SF MAIT cells compared to RA blood MAIT cells, grouped by function: activation, activation/migration, migration, exhaustion, and interferon (IFN) pathway. (D) Circos plot illustrating CellChat-predicted interactions between chemokine receptors expressed by circulating MAIT cells (e.g., CXCR3, CXCR6) and their ligands expressed by synovial immune cell subsets. Statistical comparisons were performed using Wilcoxon Test. MAIT: mucosal-associated invariant T cell; RA: rheumatoid arthritis; SF: synovial fluid; HD: healthy donor; scRNA-seq: single-cell RNA sequencing; IFN: interferon.

Results: Circulating MAIT cells were reduced in RA compared to HD (0.51% vs 2.7%, p< 0.001), with an activated/exhausted phenotype (↑CD69, CD25, Tim-3) and increase production of IL-17 and granzyme B. scRNA-seq showed upregulation of genes linked to activation, exhaustion, apoptosis, cytotoxicity (GZMB, PRF1), and chemokines receptors (CCR1, CXCR6). Despite their depletion in blood, MAIT cells were enriched in SF (0.65% vs 0.32%, p=0.048), especially in early arthritis. SF MAIT cells were more activated (↑CD69, CD25), exhausted (↑PD-1, ↓CD127), and had lower CCR6 and CD56 expression. scRNA-seq confirmed this profile, and revealed type I IFN pathway engagement, as well as chemokine-driven migration signature. CellChat analysis implicated pDCs and monocytes in generating a chemokine gradient recruiting MAIT cells into joint. SF MAIT cells also showed increased IL-10, suggesting combined inflammatory and regulatory roles.

Activated MAIT cells enhanced FLS activation in co-culture, increasing ICAM1 and PDPN expression, and secretion of IL-1β, IL-6, IL-8, and MCP-1. Bulk RNA-seq of FLS exposed to activated MAIT cells showed upregulation of inflammatory cytokines, chemokines, IFN-stimulated genes, and matrix-degrading enzymes.

In vivo, MR1 KO mice showed reduced arthritis severity and joint damage in both models. Ac-6-FP treatment also improved clinical and histological outcomes in mBSA arthritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

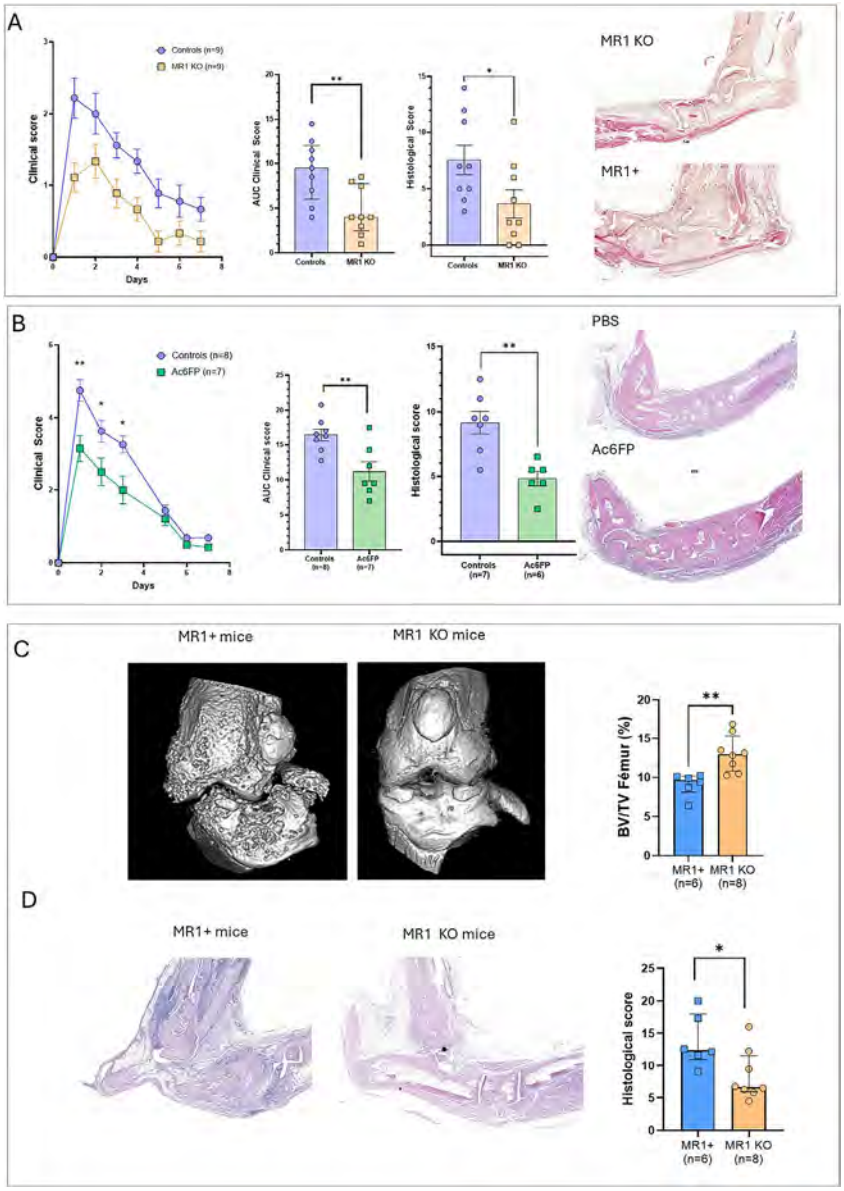


Figure 3. In vivo modulation of MAIT cells in two murine models of arthritis. (A) Clinical arthritis score and histological inflammation score in the mBSA-induced arthritis model, comparing MR1 knockout (KO) mice (MAIT cell-deficient) to wild-type controls. (B) Effect of pharmacological MAIT cell inhibition using Ac-6-FP versus PBS control in the mBSA model: clinical score and histological inflammation score. TNF arthritis in MR1 KO mice compared to controls : (C) Micro-computed tomography (microCT) assessment of bone erosions showing increased bone volume fraction (BV/TV) in MR1 KO mice compared to controls. (D) Histological inflammation score in TNF-transgenic MR1 KO and control mice. Statistical comparisons were performed using Student T test. MAIT: mucosal-associated invariant T cell; MR1 KO: MR1 knockout; mBSA: methylated bovine serum albumin; BV/TV: bone volume/total volume; PBS: phosphate-buffered saline.

Conclusion: MAIT cells are reduced in blood but accumulate in RA synovial fluid, where they are highly activated and exhausted, likely shaped by local inflammation. Their migration from blood to the joint may be driven by a synovial chemokine gradient. In the joint, they promote inflammation through cytotoxicity, cytokine production, and FLS activation. Notably, their IL-10 expression suggests additional immunoregulatory functions. Modulating MAIT cells reduces arthritis in murine models, supporting their therapeutic potential in RA.

Disclosure: M. LESTURGIE-TALAREK: None; **V. Gonzalez**: None; **A. Cauvet**: None; **L. Beaudoin**: None; **F. Oudart**: None; **A. Schvartz**: None; **F. Carbone**: None; **M. Menager**: None; **N. Sénot**: None; **F. Tilotta**: None; **Y. Allanore**: None; **A. Lehuen**: None; **J. AVOUAC**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1725

Functional NOTCH4 Variants Drive Vasculopathy and Fibrosis in Systemic Sclerosis.

Urvashi Kaundal[1], Pei-Suen Tsou[2], Mousumi Sahu[3], Mengqi Huang[4], Steven Boyden[5], Curtis Woodford[6], Daniel Shriner[7], Emilee Stenson[41], Sarah Safran[8], Yuechen Zhou[9], Taylor Talley[42], Kaavya Gudapati[43], Xuetao Zhang[6], Yosuke Kunishita[10], Janet Wang[44], Ami Shah[11], Maureen Mayes[12], Ayo Doumatey[13], Amy Bentley[7]Janet, Robyn Domsic[4], Thomas Medsger, Jr[14], Paula Ramos[15], Richard Silver[16], Virginia Steen[17], John Varga[2], Vivien Hsu[18], Lesley Ann Saketkoo[19], Elena Schiopu[20], Jessica Gordon[21], Lindsey Criswell[22], Heather Gladue[23], Chris Derk[24], Elana Bernstein[25], S. Louis Bridges[21], Victoria Shanmugam[26], Lorinda Chung[27], Suzanne Kafaja[28], Reem Jan[45], Marcin TROJANOWSKI[29], Avram Goldberg[46], Benjamin Korman[30], James Mullikin[31], James Thomas[31], Stefania Dell'orso[32], davide Randazzo[33], Adebowale Adeyemo[7], Elaine Remmers[34], Pamela Schwartzberg[35], Ivona Aksentijevich[36], Charles Rotimi[7], Fredrick Wigley[37], Rong Wang[6], Francesco Boin[38], Dinesh Khanna[2], Robert Lafyatis[4], Daniel Kastner[39], Pravitt Gourh[40], [1]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD, [2]University of Michigan, Ann Arbor, MI, [3]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [4]University of Pittsburgh, Pittsburgh, PA, [5]Utah Center for Genetic Discovery, Department of Human Genetics, University of Utah, Salt Lake City, UT, Bethesda, MD, [6]Laboratory for Accelerated Vascular Research, Department of Surgery, University of California, San Francisco, San Francisco, CA, san francisco, CA, [7]Center for Research on Genomics and Global Health, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, bethesda, MD, [8]National Institute of Arthritis and Musculoskeletal and Skin Diseases, New York, NY, [9]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, Pittsburg, PA, [10]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Rockville, MD, [11]Johns Hopkins Rheumatology, Baltimore, MD, [12]UT Health Houston Division of Rheumatology, Houston, TX, [13]Center for Research on Genomics and Global Health, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, bethedsa, MD, [14]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, Verona, PA, [15]Emory University School of Medicine, Atlanta, GA, [16]Medical University of South Carolina, Charleston, SC, [17]Georgetown University School of Medicine, Washington, DC, [18]Rutgers- RWJ Medical School, South Plainfield, NJ, [19]University Medical Center - Comprehensive Pulmonary Hypertension Center and ILD Clinic Programs // New Orleans Scleroderma and Sarcoidosis Patient Care & Research Centeris, New Orleans, LA, [20]Division of Rheumatology, Medical College of Georgia at Augusta University, Augusta, GA, Augusta, GA, [21]Hospital for Special Surgery, New York, NY, [22]NIH/NHGRI, Bethesda, MD, [23]Arthritis & Osteoporosis Consultants of the Carolinas, Charlotte, NC, [24]University of Pennsylvania, Philadelphia, PA, [25]Columbia University Irving Medical Center, New York, NY, [26]Office of Autoimmune Disease Research, Office of Research on Women's Health, Office of the Director, National Institutes of Health, Bethesda, MD, bethesda, MD, [27]Stanford University, Stanford, CA, [28]UCLA Department of Medicine, Division of Rheumatology, Los Angeles, CA, [29]BOSTON UNIVERSITY SCHOOL OF MEDICINE, BOSTON, MA, [30]University of Rochester, Rochester, NY, [31]NIH Intramural Sequencing Center, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, bethesda, MD, [32]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [33]Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, [34]Medical Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, bethesda, MD, [35]Cell Signaling and Immunity Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, Bethesda, MD, [36]100, Bethesda, MD, [37]Johns Hopkins University, Baltimore, MD, [38]Cedars-Sinai Medical Center, Beverly Hills, CA, [39]National Human Genome Research Institute, Bethesda, MD, [40]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD,[41]NIH, Bethesda, MD, [42]Spelman College and post-bac National Institutes of Health, Bethesda, MD, [43]Georgia Institute of Technology, Alpharetta, GA, [44]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Beachwood, OH, [45]University of Chicago, Chicago, IL, [46]NYU Langone Health - NYU Hospital for Joint Diseases, Lake Success, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Plenary III (1722–1727)

Session Type: Plenary Session

Session Time: 8:00AM–9:30AM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

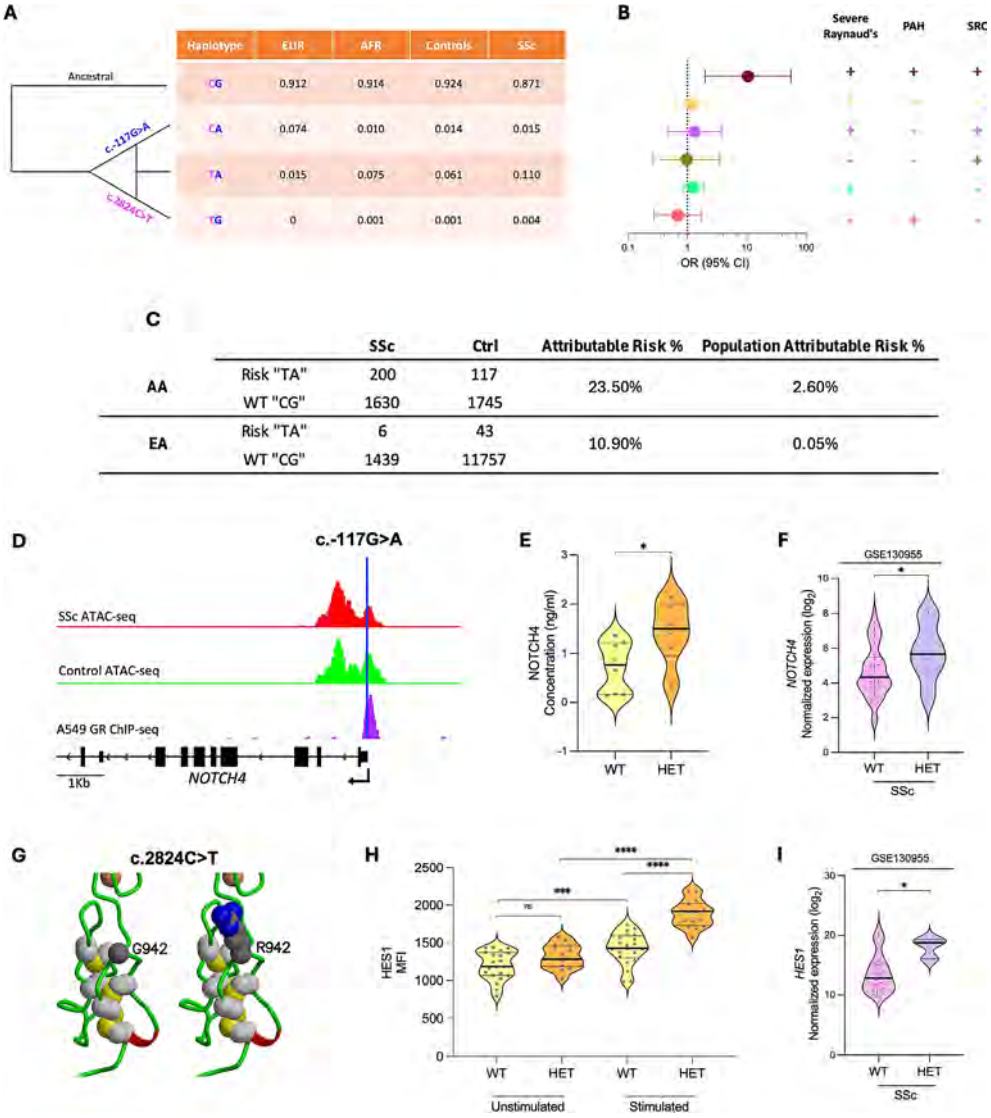


Fig. 1. A. Frequencies of c.2824C>T and c.-117G>A haplotypes in SSc cases, controls and reference European (EUR) (n=136) and African (AFR) (n=471) ancestral populations. B. Odds ratios for the risk "TA" haplotype vs. wildtype "CG" across SSc vascular phenotypes. C. Population Attributable risk for the NOTCH4 haplotype in African Americans (AA) and European Americans (EA). D-F show c.-117G>A data. G-I show c.2824C>T data. D. ATAC-seq signal at the NOTCH4 locus in primary endothelial cells from SSc patients and healthy controls (GSE163199) and the GR-a ChIP-seq in A549 cells with c.-117G>A marked in blue. E. NOTCH4 ELISA data in unstimulated LCLs wild type (WT) or Heterozygous (HET) for c.-117G>A. F. NOTCH4 expression in SSc skin, stratified by the c.-117G>A variant (GSE130955). G. c.2824C>T alters glycine to arginine at position 942. H. Flow cytometry data for HES1 before and after stimulation of NOTCH4 with DLL4 ligand, in LCLs WT or HET for the c.2824C>T variant. I. HES1 expression in SSc skin, stratified by the c.2824C>T variant (GSE130955).

Background/Purpose: Systemic sclerosis (SSc) is characterized by vasculopathy, progressive fibrosis of skin and internal organs, and autoimmunity. Notably, African American (AA) patients with SSc exhibit a more severe vascular phenotype and poorer outcomes than European Americans. We hypothesized that common variants in SSc tag gene regions enriched for rare, functional variants cause increased disease burden in AAs with SSc.

Methods: Exome and targeted sequencing were performed in discovery and replication cohorts comprising 969 AA SSc patients and 771 AA controls, focusing on 32 SSc-associated genes. Two *NOTCH4* variants were examined in lymphoblastoid cell lines (LCL) using RT-PCR, ELISA, and flow cytometry. SSc skin single-cell RNA-Seq and publicly available bulk gene expression datasets were analyzed. Endothelial cell (EC) lines and variant-carrying ECs from SSc patients (pECs) were used

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

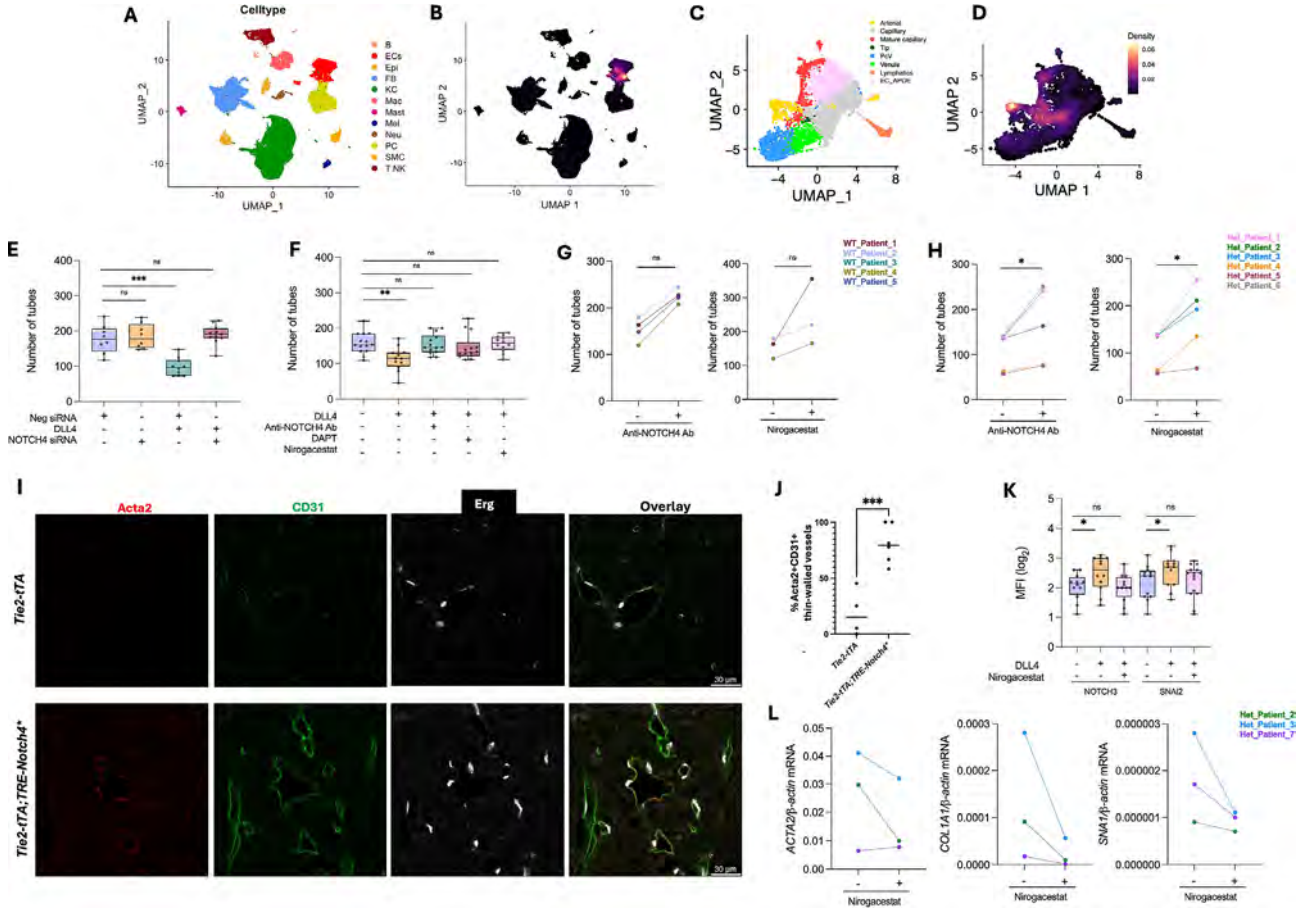


Fig. 2. A. UMAP plot of subclustered skin cells of SSc and control subjects with colors denoting different subpopulation. B. Density plot for NOTCH4 expression, primarily in endothelial cells, with lighter color indicating higher expression. C. UMAP plot of reclustered endothelial cells in SSc and control subject. D. Density plot for NOTCH4 expression, primarily in arterial, mature capillary and tip endothelial cell cluster, with lighter color indicating higher expression. E. Decreased tube formation upon NOTCH4 activation by its ligand DLL4 in endothelial cell line, unaffected by prior NOTCH4 knockdown. F. Restoration of normal tube formation after inhibition of NOTCH4 signaling using anti-NOTCH4 antibody, DAPT, or Nirogacestat prior to DLL4 stimulation. G-H. Rescued tube formation in SSc primary endothelial cells (WT and HET for c.-117G>A variant) after blocking NOTCH4 signaling with anti-NOTCH4 antibody or Nirogacestat. I. Co-staining of Acta2 (red), CD31 (green) and Erg (white) in thin-walled vessels of constitutively Notch4* expressing brain endothelial cells in Tie2-tTA;TRE-Notch4* mutant mice and Tie2-tTA littermate control mice. J. Quantification of thin-walled vessels co-stained for Acta2 (EndoMT marker) and CD31 in constitutively Notch4* expressing brain endothelial cells in Tie2-tTA;TRE-Notch4* mutant mice and Tie2-tTA littermate control mice. K. Increase in EndoMT markers NOTCH3 and SNAI2 following DLL4-induced NOTCH4 stimulation; restored to baseline levels with Nirogacestat. L. Decrease in ACTA2, COL1A1, and SNAI1 expression in primary endothelial cells from SSc patients (Het for c.-117G>A) after Nirogacestat treatment.

to assess angiogenesis using tube formation assays and to study endothelial-to-mesenchymal transition (EndoMT) following NOTCH4 stimulation or inhibition. A Tie2-tTA;TRE-Notch4* mouse model with inducible, EC-specific expression of active Notch4 was used to study EndoMT.

Results: Gene-based testing identified *NOTCH4* association with SSc (P=1.6x10^{-7}) particularly in AAs with severe vasculopathy (P=3.5x10^{-7}). The risk haplotype "TA", defined by the missense (c.2824C >T) and promoter (c.-117G >A) variants, was enriched in AAs with SSc (11%) and increased the risk of having severe Raynaud's, scleroderma renal crisis (SRC), and pulmonary arterial hypertension (PAH) (OR=10.6, 95% CI 2-56) (Fig. 1A-B). The population attributable risk due to this haplotype in AAs with SSc was 2.6%, 52-fold higher than in European Americans (Fig. 1C). The c.-117A allele bound glucocorticoid receptor and increased NOTCH4 protein expression (Fig. 1D-E). SSc skin samples with c.-117G >A variant had a higher *NOTCH4* expression than those with the G allele (Fig. 1F). The c.2824T allele upregulated NOTCH4 signaling in LCLs (Fig. 1G-H), confirmed in vivo by elevated *HES1* transcripts in c.2824T **vs. c.2824C** SSc samples (Fig. 1I). scRNA-Seq data for SSc skin revealed that *NOTCH4* is predominantly expressed by ECs (Fig. 2 A-B) especially arterial, mature capillary and

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

tip cells (Fig 2 C-D). NOTCH4 stimulation in the EC line and c.-117A allele-carrying pECs led to decreased tube formation (an angiogenesis indicator) (Fig. 2E-H) and increased EndoMT (Fig. 2K-L). NOTCH4 overexpression in *Tie2-tTA;TRE-Notch4** mutant mice also increased Acta2 (EndoMT marker) expression in ECs (Fig. 2I-J). Nailfold capillary abnormalities, decreased angiogenesis, and fibrosis of the vascular lumen are commonly seen in SSc. Inhibition of NOTCH4 using genetic knockdown, blocking antibody, or the FDA-approved drug Nirogacestat restored angiogenesis (Fig. 2 E-H) and normalized EndoMT in ECs (Fig. 2 K-L).

Conclusion: Functional variants in *NOTCH4* gene are associated with SSc pathogenesis and vasculopathy and may explain the higher disease burden of SSc in AAs. Blocking NOTCH4 signaling restored angiogenesis and EndoMT, highlighting its potential as a therapeutic target in restoring angiogenesis in SSc and connective tissue diseases.

Disclosure: U. Kaundal: None; **P. Tsou**: None; **M. Sahu**: None; **M. Huang**: None; **S. Boyden**: None; **C. Woodford**: None; **D. Shriner**: None; **S. Safran**: None; **Y. Zhou**: None; **X. Zhang**: None; **Y. Kunishita**: None; **A. Shah**: None; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **A. Doumatey**: None; **A. Bentley**: None; **R. Domsic**: None; **T. Medsger, Jr**: None; **P. Ramos**: None; **R. Silver**: None; **V. Steen**: None; **J. Varga**: None; **V. Hsu**: None; **L. Saketkoo**: Abbvie, 6, Argenx, 1, 2, 5, aTyr Pharmaceuticals, 12,, 1, 5, Boehringer-Ingelheim, 2, 5, 6, CSL Behring, 5, EMD Serono, 2, 5, Horizon, 5, Johnson & Johnson, 6, Kadmon, 5, Kinevant, 12,, 2, 5, Mallinckrodt, 1, 2, 5, Novartis, 1, 2, 5, Priovant, 5; **E. Schiopu**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **L. Criswell**: None; **H. Gladue**: None; **C. Derk**: None; **E. Bernstein**: AstraZeneca, 5, aTYR, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **S. Bridges**: None; **V. Shanmugam**: None; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **S. Kafaja**: None; **M. TROJANOWSKI**: None; **B. Korman**: None; **J. Thomas**: None; **S. Dell'orso**: None; **d. Randazzo**: None; **A. Adeyemo**: None; **E. Remmers**: None; **P. Schwartzberg**: None; **I. Aksentijevich**: In Vitro Diagnostics, 9; **C. Rotimi**: None; **F. Wigley**: None; **R. Wang**: None; **F. Boin**: Adicet Bio, 2, Boehringer Ingelheim, 1, Janssen Pharmaceuticals, 6; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **R. Lafyatis**: AbbVie/Abbott, 2, Advarra/GSK, 12, Independent Data Safety Monitoring Committees, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, EMD Sereno, 2, Formation, 2, 5, Genentech, 12, Independent Data Safety Monitoring Committees, Genentech/Roche, 2, Mediar, 2, Merck/MSD, 2, Moderna, 5, Modumac Therapeutics Inc., 12, President and holds stock, Morphic, 2, Pfizer, 5, Regeneron, 5, Sanofi, 2, Third Rock Ventures, 2, Thirona Bio, 2, Zag Bio, 2; **D. Kastner**: In Vitro Diagnostics, 12, NIH Licensing Agreement; **P. Gourh**: None; **E. Stenson**: None; **T. Talley**: None; **K. Gudapati**: None; **J. Wong**: None; **R. Jan**: None; **A. Goldberg**: None; **J. Mullikin**: None.

Abstract Number: 1726

Inflammatory arthritis immune related adverse events represent a unique autoimmune disease entity primarily driven by T cells, but likely not autoantibodies

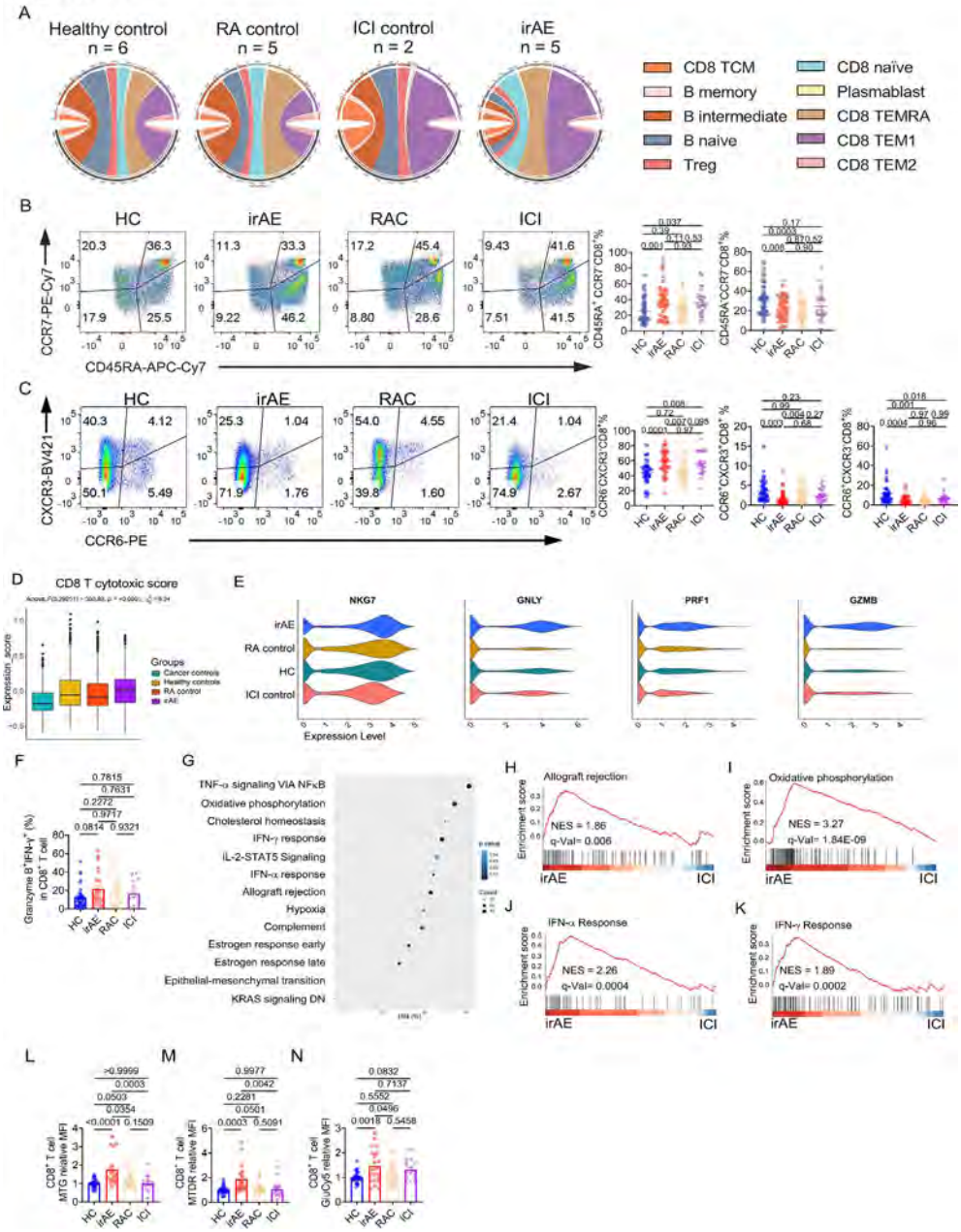
Xingxing Zhu[1], yue Yu[1], Yangfen Li[1], Panwen wang[2], ying li[2], Chantal McCabe[2], shiju chen[2], Brenna Sharp[2], Amber Wolzen[2], Hannah Langenfeld[1], Andrew C. Hanson[1], Cynthia Crowson[3], svetomir Markovic[2], John Davis[1], Haidong Dong[2], Uma Thanarajasingam[1] and **Hu Zeng**[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, [3]Mayo Clinic, Stewartvillle, MN

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Plenary III (1722–1727)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Figure 1

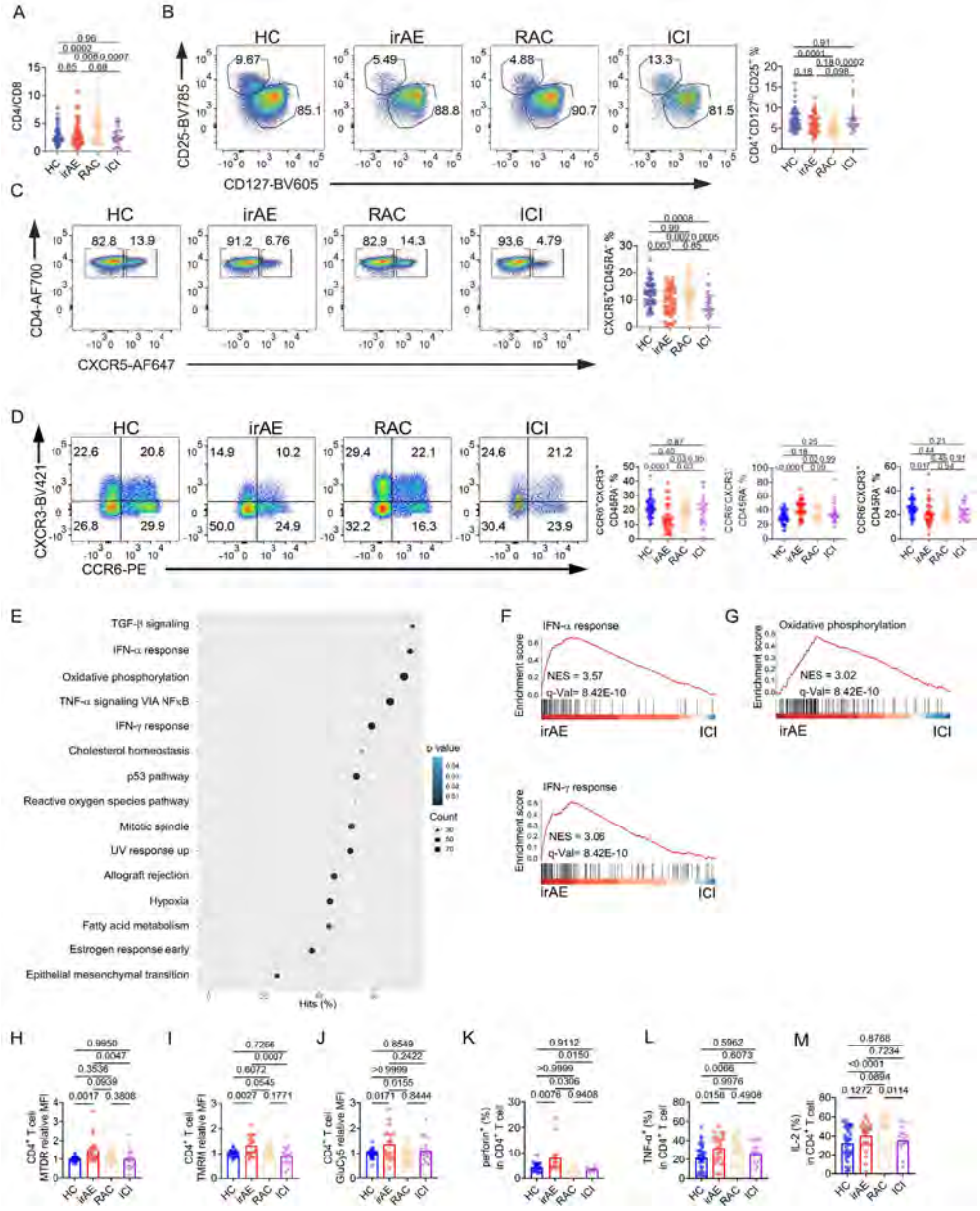


(A) Circos plots show the percentage of different subsets of CD8+ T cells and B cells. (B) Representative flow cytometry plot of CD45RA and CCR7 expression on CD8+ T cells from HC, ICI, RAC or irAE. Right, summaries of the percentage of CD45RA+CCR7–CD8+ T cells and CD45RA–CCR7–CD8+ T cells. (C) Representative flow cytometry plot of CXCR3 and CCR6 expression on CD8+ T cells. Right, summaries of CXCR3–CCR6–CD8+, CXCR3+CCR6+CD8+, and CCR6+CXCR3–CD8+ T cells. (D) The cytotoxic score was evaluated on CD8+ T cells using the gene list identified in the paper (78) . (E) Specific cytotoxic or effector function–related genes were evaluated on the CD8+ T cells. (F) Fresh PBMCs from different groups were stimulated with PMA/Ionomycin/Monensin for 5 h, Granzyme B+IFN–g+CD8+ T cells were evaluated. (G–K) GSEA was performed on the CD8+ T cells between irAE and ICI. (G) Pathways that were significantly enriched in the comparison. GESA plot of the allograft rejection (H), oxidative phosphorylation (I), IFN–a response (J), and IFN–g response (K). (L–N) PBMCs from different groups were stimulated with 10 μg/mL plate–coated anti–CD3 and anti–CD28 for 5 days, dyes including mitochondria green (MTG) (L), mitochondria deep red (MTDR) (M), or GlucoseCy5 (GluCy5) (N) were examined on CD8+ T cells, and the expression was normalized to the HC in each experiment. Data in graphs represent mean ± SEM, Significance was tested by one-way ANOVA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

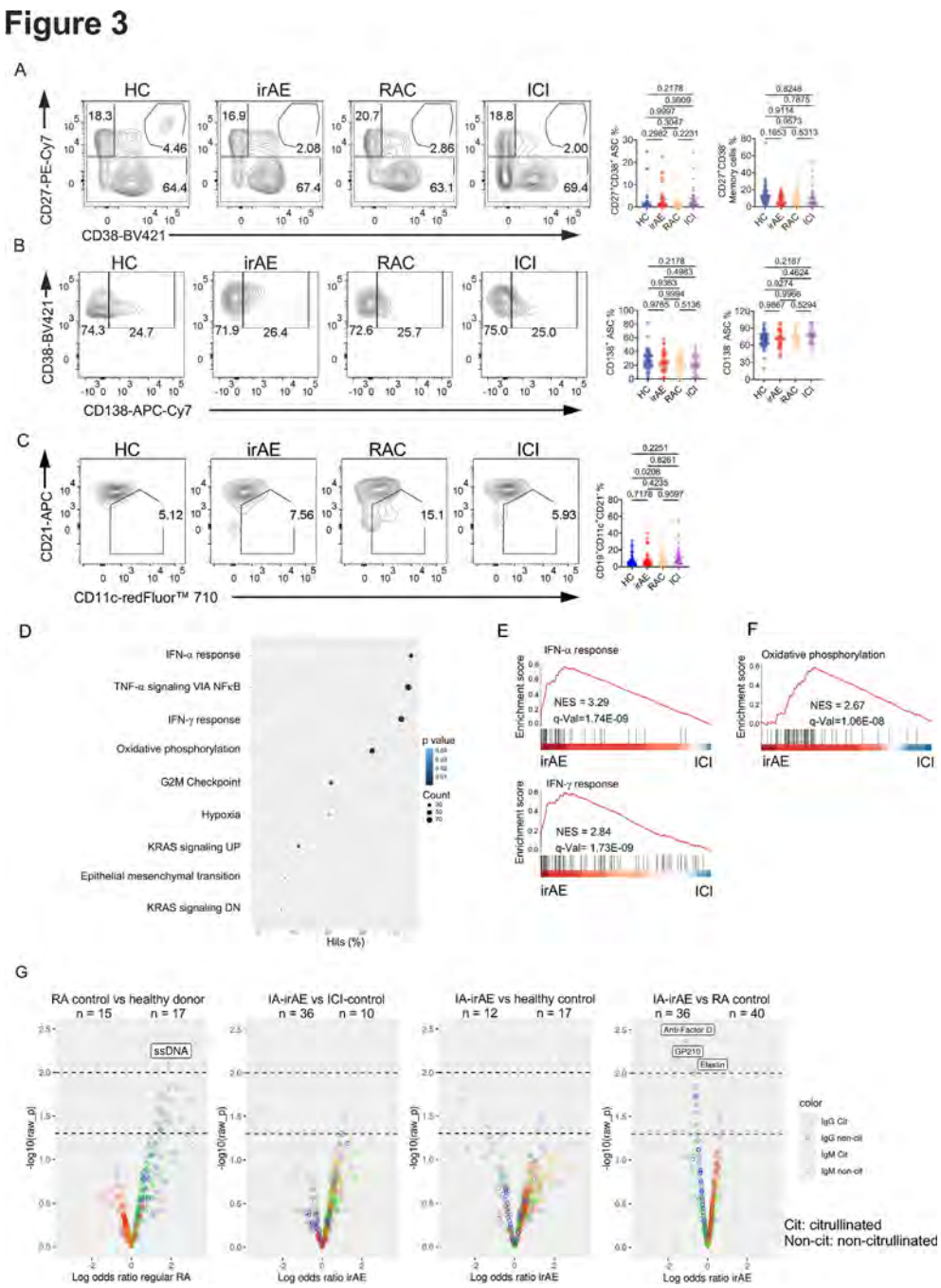
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2



(A) The ratio of CD4 to CD8 in the PBMCs was calculated. (B) Representative flow cytometry plot of CD25 and CD127 expression on CD4+ T cells. Right, a summary of the percentage of CD25+CD127lo regulatory T cells in CD4+ T cells from different groups. (C) Representative flow cytometry plot of CXCR5 and CD4 expression on the CD45RA–CD4+ T cells. Right, a summary of the percentage of CXCR5+CD45RA–CD4+ T cells. (D) Representative flow cytometry plot of CCR6 and CXCR3 expression on CD45RA–CD4+ T cells. Right, summaries of the percentage of CXCR3+CCR6–CD45RA–, CXCR3+CCR6+CD45RA–, CXCR3–CCR6–CD45RA– CD4+ T cells. (E–G) GSEA was performed on the CD4+ T cells between irAE and ICI. (E) Significantly enriched pathways in CD4+ T cells from irAE and ICI. GSEA plots of IFN–a and IFN–g response (F), and oxidative phosphorylation (G). (H–M) PBMCs from different groups were stimulated with 10 μg/mL plate–coated anti–CD3 and anti–CD28 for 5 days, dyes including MTDR (H), TMRM (I), or GluCy5 (J) were measured on CD4+ T cells, and the expression was normalized to the HC in each experiment. (K-M) Fresh PBMCs from different groups were stimulated with PMA/Ionomycin/Monensin for 5 h, and perforin+ (K), TNF–a+ (L) and IL–2+ CD4+ T cells were examined. Data in graphs represent mean ± SEM, Significance was tested by one-way ANOVA.

Background/Purpose: The immunological basis of inflammatory arthritis (IA) immune related adverse event (irAE) following anti-PD-1/PD-L1 immune checkpoint inhibition (ICI) therapy is incompletely understood. The relationship between IA irAE and rheumatoid arthritis (RA) remain unclear. Furthermore, while both autoreactive T and B cells critically contribute to



(A) Representative flow cytometry plot of CD27 and CD38 expression on the PBMCs. Right, summaries of the percentage of CD27hiCD38hi antibody–secreting cells (ASCs) and CD27+CD38– memory B cells. (B) Representative flow cytometry plot of CD138 in CD27hiCD38hi ASCs. Right, summaries of the percentage of CD138+ ASCs and CD138– ASCs. (C) Representative flow cytometry plot of CD11c and CD21 expression on IgD–CD27– B cells and summary of the percentage of CD11c+CD21–IgD–CD27– B cells. (D–F) GSEA was performed on the B cells between irAE and ICI. (D) Significantly enriched pathways in B cells from irAE and ICI. GSEA plots of IFN–a and IFN–g response (E), and Oxidative phosphorylation (F). (G) The volcano plot of the citrullinated or non–citrullinated relative IgG or IgM–isotype autoantigen levels comparing RA and HC, irAE and ICI, irAE and HC, or irAE and RA. The autoantigens were labeled when $p < 0.01$. Data in graphs represent mean ± SEM, Significance was tested by one-way ANOVA.

immunopathology in most RA patients, the existence of antibody independent arthritis has been suggested, but remains contentious. We aim to investigate the distinguishing immunological phenotypes between anti-PD-1/PD-L1 treated patients with IA irAE and those without irAE, and the relationship between IA irAE and serologically matched RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We analyzed a cohort of 163 patients, including 34 rheumatic irAE patients (all with inflammatory arthritis), 26 ICI control patients (cancer patients receiving anti-PD-1/PD-L1 treatment without developing irAE), 47 RA control (age, sex and serologically matching rheumatic irAE patients) and 56 healthy controls. Flow cytometry was employed to analyze immune cell subsets, metabolic states, and response to soluble factors. Single cell RNA sequencing was performed on a small group of patients to profile gene expression. Beads based multiplex assay was carried out to measure plasma concentrations of major cytokines and chemokines. Autoantigen array was used to assess plasma autoantibody levels. T and B cells were purified and cultured in vitro to assess their functions in the presence of various cytokines and blocking antibodies.

Results: $CD8^+$ T cells from irAE and ICI control patients exhibited elevated expression of effector molecules, but irAE $CD8^+$ T cells, but not ICI control $CD8^+$ T cells, had the highest level of cytotoxic molecule expression. RA control patients, but not irAE patients, had increased CD4/CD8 ratio and reduced regulatory T cell (Treg) frequency. IrAE $CD4^+$ T cells had significantly increased $CXCR3^-CCR6^-$ subset and reduced $CXCR3^+CCR6^+$subset compared to other control groups. Both $CD4^+$ and $CD8^+$ T cells from irAE patients exhibited increased metabolic activities. RA control patients, but not irAE patients, had increased frequency of $CD11c^+CD21^-$atypical B cells and increased level of autoantibodies. IrAE patients showed increased plasma levels of IL-6, IL-12 and enhanced expression of type I interferon (IFN) signatures. Combination of IL-6, IL-12 and IFNα promotes T cell cytotoxic gene expression, whereas blockade of IL-6 receptor, IL-12 and IFNA receptor reduces cytotoxic and metabolic phenotypes of irAE T cells.

Conclusion: Inflammatory arthritis irAE is immunologically distinct from conventional RA, distinguished by high level of cytotoxic gene expression in $CD8^+$ T cells, reduced CXCR3 and CCR6 expression in $CD4^+$ T cells and increased metabolic activity in both $CD4^+$ and $CD8^+$ T cells. It is likely driven primarily by autoreactive T cells following anti-PD-1/PD-L1 inhibition, but potentially independent of autoantibodies. Some of the immunological abnormalities may be driven by increased IL-6, IL-12 and type I IFN.

Disclosure: X. Zhu: None; **y. Yu**: None; **Y. Li**: None; **P. wang**: None; **y. li**: None; **C. McCabe**: None; **s. chen**: None; **B. Sharp**: None; **A. Wolzen**: None; **H. Langenfeld**: None; **A. Hanson**: None; **C. Crowson**: None; **s. Markovic**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **H. Dong**: None; **U. Thanarajasingam**: None; **H. Zeng**: None.

Abstract Number: 1727

Distribution of Fracture Risk Status and Osteoporosis Treatment Use Among Postmenopausal Women with Osteoporosis in the United States

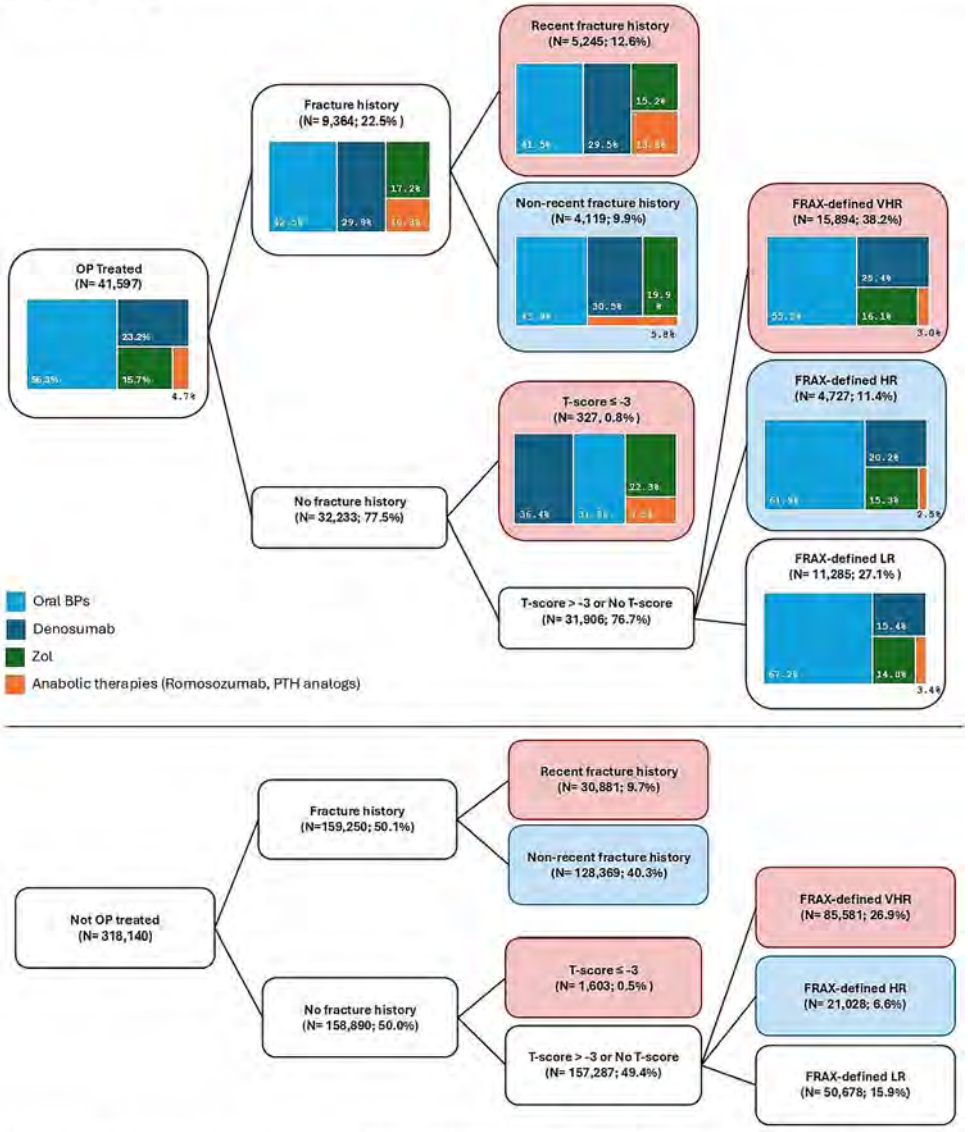
Hsu-Chih Chien, Min Kim, Michele McDermott, Mary Oates, Xiaodong Li and **Lara Yoon**, Amgen Inc, Thousand Oaks, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Plenary III (1722–1727)
Session Type: Plenary Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Current guidelines recommend treating women with postmenopausal osteoporosis (PMO) based on fracture risk. Anabolic therapy (AT), the RANKL inhibitor denosumab (Dmab), and intravenous zoledronic acid (ZOL) are recommended as initial therapy for patients at very high risk (VHR) for fracture. This study described the proportion of PMO women at VHR or high risk (HR) of fracture by treatment status in a commercially insured population in the US.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Distribution of Fracture Risk Characteristics and OP Treatments Among Postmenopausal Women with Osteoporosis



Red-shaded boxes refer to very high risk (VHR) of fracture and includes those with fracture in the past 12 months, without fracture history but with a BMD T-score ≤ -3.0, or without fracture history, a BMT T-score > 3.0 or no BMD T-score, or a BMI-based FRAX score for major osteoporotic fracture of > 30% or hip fracture > 4.5%. Blue shaded boxes refer to high risk (HR) of fracture and includes those with no fracture history, a BMD T-score > 3.0 or no BMD T-score, and a major osteoporotic fracture risk of 20-30% or hip fracture of 3-4.5%.
Acronyms: Ats, anabolic therapies; BMD, bone mineral density; BPs, bisphosphonates; HR, high risk; LR, low risk; OP, osteoporosis; PTH, parathyroid; VHR, very high risk; Zol, zotendronic acid.

Methods: This retrospective cohort study used Optum® Market Clarity Bone Data. Women ≥55 years with a diagnosis of osteoporosis (OP), fracture, or OP medication use, ≥455 days of continuous enrollment, a valid BMI and race, and no history of Paget's disease or metastatic cancer were included. Women who newly initiated an OP treatment from April 1, 2016 – September 30, 2023 were included in the treated cohort; date of treatment initiation was the index date. Women with no history of OP treatment in the 15-months prior to January 1, 2023 (index date) were included in the untreated cohort. Cohorts were not mutually exclusive. OP medications included oral bisphosphonates (BPs; alendronate, risedronate, ibandronate), Dmab, ZOL, and AT (romosozumab, parathyroid hormone analogues [teriparatide, abaloparatide]). HR and VHR were defined based on AACE guidelines for the treatment of PMO women and assessed over 15-months before index.

Results: Of the 41,597 treated PMO women identified (mean age=73 y), 51.6% met the VHR criteria, including 5,245 women with recent (≤12 months) fracture (12.6%), 327 with a BMD T-score ≤ -3.0 (0.8%), and 15,894 with a FRAX score indicating VHR (38.2%). Approximately 21.3% were HR; 27.1%, low risk (LR). The most frequent OP treatments overall

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and among fracture risk subgroups were oral BPs (56.3%) followed by Dmab (23.2%) and ZOL (15.7%). Only 4.7% of treated PMO women overall and 5.7% of treated VHR PMO women were using AT. Among the 318,140 untreated PMO women identified (mean age=74 y), 118,065 (37.1%) met the criteria for VHR; 149,397 (47.0%), HR; 50,678 (15.9%), LR.

Conclusion: More than 1/3 of untreated PMO women are at VHR for fracture and eligible for ATs, Dmab, or ZOL in accordance with treatment guidelines. Among treated VHR PMO women, over half were treated with oral BP in contradiction with current treatment guidelines. Only a small percentage were treated with ATs, which clinical studies have shown are the most effective initial therapy for PMO women at VHR for fracture.

Disclosure: H. Chien: Amgen, 3, 11; **M. Kim**: Amgen, 3, 11; **M. McDermott**: Amgen, 3, 11; **M. Oates**: Amgen, 3, 11; **X. Li**: Amgen, 3, 11; **L. Yoon**: Amgen, 3, 11.

Abstract Number: 1728

Longitudinal Proteomic Signatures for Prediction of Immune-Related Adverse Events during Immune Checkpoint Inhibitors therapy: A Machine Learning-Guided Prospective Biomarker Discovery Study

Jiana Chen[1], Jiaqi Xu[1], Ziyue Zhou[2], Xu Jiang[1] and **Huaxia Yang**[1], [1]Department of Rheumatology and Clinical Immunology, National Clinical Research Center for Dermatologic and Immunologic Diseases, the Ministry of Education Key Laboratory, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 100730, Beijing, China, Beijing, China (People's Republic), [2]peiking meidical, beijing

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Immunological Complications of Medical Therapy (1728–1733)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Immune checkpoint inhibitors (ICIs), while revolutionary in cancer treatment, may induce severe or even fatal immune-related adverse event (irAE). The mechanisms underlying irAE development remain unclear, and early identification of predictive biomarkers for irAE is urgently needed to improve risk stratification and clinical management. However, most current studies on irAE-related potential biomarkers predominantly conduct cross-sectional analyses at a single time point, leaving a critical cap in tracking dynamic changes predicting irAE onset.

Methods: This prospective study enrolled 60 lung cancer patients receiving ICIs therapy at Peking Union Medical College Hospital from January 2022 to September 2024. Additionally, 23 irAE patients with various cancers were included at the time of irAE onset as an observational cohort. Serum samples collected longitudinally at baseline (pre-treatment), 1-3 weeks, 3-6 months post-treatment and the onset of irAE after starting ICIs were analyzed by Olink proximity extension assay technology. Advanced analytical approaches included time-series clustering, linear mixed-effects models, and differential expression analysis across multiple time points. Predictive performance of candidate biomarkers was assessed using receiver operating characteristic (ROC) analysis and support vector machine (SVM) classifiers integrating temporal features.

Results: In the prospective cohort, 26 out of 60 patients (43.3%) developed irAE within 6 months after ICIs initiation. Longitudinal proteomic analysis revealed distinct temporal profiles between irAE and non-irAE groups, with six proteins (IL10, NT-3, CCL23, FGF-19, LIF-R and uPA) exhibiting significantly different trajectories **(Fig.1)**. At baseline, 10 serum proteins (e.g., CXCL1, CXCL6, CXCL11, IL6 and HGF) were significantly depressed in irAE patients, with moderate predictive accuracy for irAE occurrence (AUC > 0.6). Besides, patients with new-onset irAE exhibited significantly elevated CCL25, IL4, IL10

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

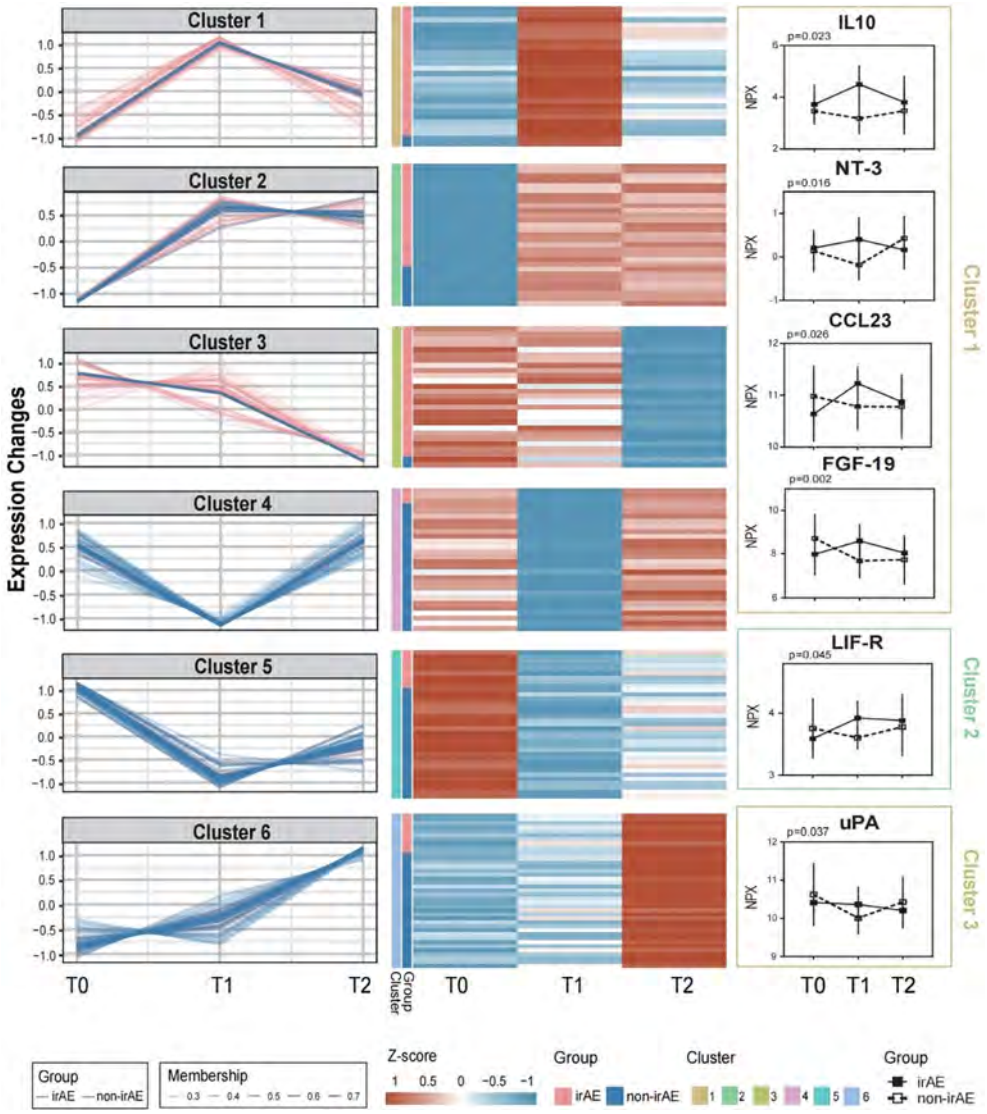


Fig.1. Longitudinal serum proteomic clustering analysis in irAE and non-irAE patients. Mfuzz analysis of differential proteins expression between irAE and non-irAE groups and heatmap of Z-score–normalized expression profiles across three time points (T0, T1, T2) for proteins grouped in each cluster. Linear mixed-effects regression analysis of 6 significant proteins for the three time points in two groups. irAE, immune-related adverse event; NPX, normalized protein expression; T0, before the initiation of ICIs treatment; T1, 1-3 weeks after treatment; T2, 3-6 months after treatment. The y axis represents the Olink assay value (NPX). P-values were calculated using linear mixed-effects models.

and IL20, and decreased IL-15RA and CD8A l compared to non-irAE patients. Longitudinal fold-change analyses from baseline to irAE onset further identified 24 significantly differential proteins, with CXCL9, IL33, IL-18R1, FGF-19 and FGF-23 showing strong predictive power (AUC > 0.8). Furthermore, machine learning models based on SVM integrating temporal features achieved high accuracy in predicting irAE development (AUC > 0.9) **(Fig.2)**, suggesting that these protein-based models provide robust predictive power for irAE occurrence.

Conclusion: Our study provides valuable insights into the dynamic temporal immunological patterns associated with the development of irAE. The identification of temporally regulated biomarkers and the development of predictive models based on machine learning offer promising tools for early risk prediction, diagnostic stratification, and longitudinal monitoring of therapeutic response. These findings advance our understanding of irAE pathogenesis and may inform future biomarker-driven approaches to individualized patient management and targeted therapeutic interventions.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

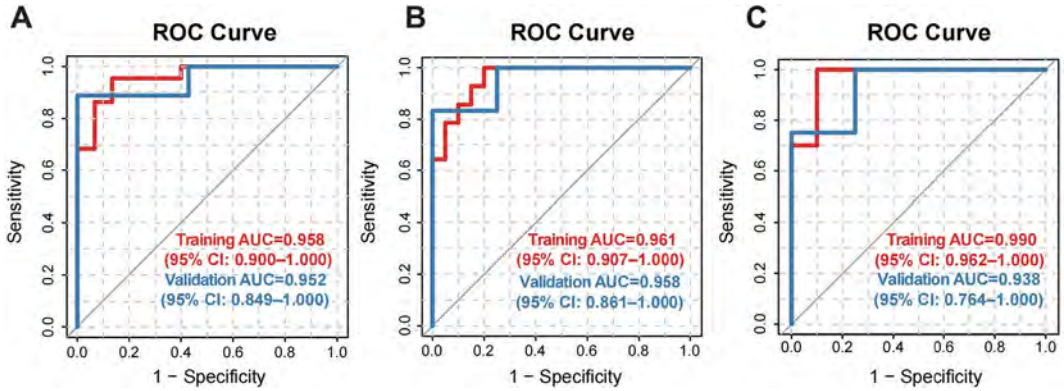


Fig.2. The composite biomarkers performance for predicting irAE in train and valid set. ROC analysis showed the composite model performance of ten differentially expressed proteins at baseline (A), six differentially expressed proteins at irAE onset (B) and top six differentially expressed proteins at the onset of irAE compare to at baseline (C) in train and test set. irAE, immune-related adverse event; ROC, Receiver operating characteristic; AUC, area under the curve.

Disclosure: J. Chen: None; **J. Xu**: None; **Z. Zhou**: None; **X. Jiang**: None; **H. Yang**: None.

Abstract Number: 1729

The ERIN Registry: Real-World Data on Rheumatic Immune-Related Adverse Events from Immune Checkpoint Inhibitor Therapy

Didzis Gailis[1], Fabian T.H. Ullrich[1], Sophia Dombret[1], Rebecca Hasseli-Fräbel[2], Marc Schmalzing[3], Torsten Witte[4], Mara Oleszowsky[5], Marcel Müller[6], Karolina Gente[7], Uta Kiltz[8], Christof Specker[9], Alla Skapenko[10] and Hendrik Schulze-Koops[10], [1]Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, LMU University Hospital, Münich, Bayern, Germany, [2]Section of Rheumatology and Clinical Immunology, University Hospital Munster, Münster, Nordrhein-Westfalen, Germany, [3]Department of Medicine II, Rheumatology/ Immunology,University Hospital of Wuerzburg, Wuerzburg, Bayern, Germany, [4]Dept of Rheumatology and Immunology, Hannover, Niedersachsen, Germany, [5]Private Rheumatology Practice, Köln, Nordrhein-Westfalen, Germany, [6]The Institute for Medical Information Processing, Biometry, and Epidemiology, LMU University Hospital, München, Bayern, Germany, [7]Department of Internal Medicine V - Hematology, Oncology and Rheumatology, University Hospital Heidelberg, Heidelberg, Baden-Wurttemberg, Germany, [8]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [9]Department of Rheumatology and Clinical Immunology, Kliniken Essen-Mitte, Düsseldorf, Nordrhein-Westfalen, Germany, [10]LMU Hospital, Division for Rheumatology and Clinical Immunology, Munich, Bayern, Germany

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Immunological Complications of Medical Therapy (1728–1733)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are a mainstay of cancer immunotherapy. However, their increasing use has led to more immune-related adverse events (irAEs), including rheumatic irAEs (rh-irAEs). These often have delayed onset, may require extended immunomodulatory therapy beyond CS, and were previosly underreported in ICI registration trials due to limited awareness and clinical heterogeneity.

To address this, the ERIN registry (Evaluation of Rheumatologic Immune-related Adverse Events) was launched in May 2024 at LMU University Hospital. As the national, multicenter, first practice-based online registry focused on rh-irAEs, ERIN complements existing initiatives by enabling real-time data collection embedded in routine care. This collaborative effort aims to improve understanding and support evidence-based management of rh-irAEs.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of the ERIN Cohort (n = 40)

General	Total patients, n	40
	Male sex, n (%)	23 (57.5%)
	Median age, years (IQR)	65 (58–73)
	Median age of axSpA patients (IQR)	46 (44–49.75)
Cancer types, n (%)	Malignant melanoma	18 (45.0%)
	NSCLC	6 (15.0%)
	Urothelial carcinoma	5 (12.5%)
	Breast cancer	4 (10.0%)
	Squamous cell carcinoma	3 (7.5%)
	Renal cell carcinoma	2 (5.0%)
	Pleural mesothelioma	1 (2.5%)
	Diffuse B-cell lymphoma	1 (2.5%)
ICI therapies, n (%)	Nivolumab	14 (35.0%)
	Pembrolizumab	14 (35.0%)
	Nivolumab/Ipilimumab	6 (15.0%)
	Ipilimumab	2 (5.0%)
	Durvalumab	1 (2.5%)
	Atezolizumab	1 (2.5%)
	Cemiplimab	1 (2.5%)
	Relatlimab	1 (2.5%)
	Avelumab	1 (2.5%)
Most frequent rh-irAEs, n (%)	RA-like polyarthritis	21 (52.5%)
	Peripheral SpA-like syndrome	6 (15.0%)
	PMR-like syndrome	5 (12.5%)
	axSpA-like syndrome	4 (9.1%)
	Monoarthritis	2 (5.0%)
	Myositis	1 (2.5%)
	Sarcoidosis-like syndrome	1 (2.5%)
History / Comorbidities, n (%)	Pre-existing RD flare, n (%)	2 (5.0%)
rh-irAE grading, n (%)	Mild (Grade I)	2 (5.0%)
	Moderatee (Grade II)	22 (55.0%)
	Severe (Grade III)	14 (35.0%)
	Life threating (Grade IV)	2 (5.0%)
Treatment outcome, n (%)	ICI interruption, n (%)	7 (17.5%)
	ICI discontinuation, n (%)	11 (27.5%)
	Complete remission, n (%)	12 (30.0%)
	Improvement only, n (%)	28 (70.0%)

Abbreviations: IQR = interquartile range; NSCLC= Non-small cell lung cancer; ICI = immune checkpoint inhibitor; rh-irAE = rheumatic immune-related adverse event; RA = rheumatoid arthritis; SpA = spondyloarthritis; PMR = polymyalgia rheumatica; axSpA = axial SpA; RD = rheumatic disease; csDMARD = conventional synthetic disease-modifying antirheumatic drug; bDMARD = biologic DMARD;

Methods: ERIN is open to healthcare professionals and includes adult patients (≥18 years) with rh-irAEs under ICI therapy. It supports prospective and retrospective, longitudinal and cross-sectional data collection on comprehensive demographic, rheumatic and oncologic characteristics, diagnosis, treatment and outcomes. Complete remission was defined as symptom absence. Ethics and data protection approvals were obtained. As of early 2025, 9 German centers contribute with increasing numbers. A scientific advisory board was formed in January 2025.

Results: As of May 2025, 40 patients were enrolled (23/40 males, 57.5%; median age 65, IQR: 58–73). The most common malignancy was melanoma (18/40, 45.0%), followed by non-small cell lung cancer (6/40, 15.0%). Nivolumab and pembrolizumab were each used as monotherapy in 14 patients (35.0%). RA-like polyarthritis was the leading rh-irAE (21/40, 52.5%), followed by peripheral spondyloarthritis (SpA)-like rh-irAE (6/40, 15.0%), PMR-like (5/40, 12.5%), and axial SpA (axSpA)-like syndromes (4/40, 9.1%). AxSpA patients were younger (median age 46, IQR: 44–49.75). A flare of pre-existing rheumatic disease occurred in 2/40 (5.0%). rh-irAEs were moderate (grade II) in 22/40 (55.0%) and severe (grade III) in 14/40 (35.0%) per Common Terminology Criteria for Adverse Events. ICIs were interrupted in 7/40 (17.5%) and discontinued in 11/40 (27.5%). Systemic CS was initiated in 32/40 (80.0%). Complete remission occurred in 12/40 (30.0%), improvement in 28/40 (70.0%). Among those in remission, conventional synthetic (cs) DMARDs were used in 6 cases (50.0%); others received biological DMARDs (n=2), intra-articular CS (n=2), or systemic CS (n=2).

Conclusion: ERIN provides real-world insight into rh-irAEs under ICIs. RA-like polyarthritis was the most common rh-irAE, while axSpA-like manifestations occurred more often in younger patients, suggesting age-related immune patterns. Systemic CS were initiated in most cases, underlining their key role in early management. Frequent csDMARD use in patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

achieving remission highlights their therapeutic value. These findings emphasize rh-irAE heterogeneity and the need for personalized care. Developing evidence-based guidelines and collaborating with other irAE-focused initiatives like MalheuR and SERIO are key to improving care and understanding of rh-irAEs.

Disclosure: D. Gailis: None; **F. Ullrich**: None; **S. Dombret**: None; **R. Hasseli-Fräbel**: None; **M. Schmalzing**: None; **T. Witte**: None; **M. Oleszowsky**: None; **M. Müller**: None; **K. Gente**: None; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **C. Specker**: None; **A. Skapenko**: None; **H. Schulze-Koops**: AbbVie, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Amgen, 12, Research support and principal investigator (clinical trials funds to institution), Biogen Idec, 12, Research support and principal investigator (clinical trials funds to institution), Boehringer Ingelheim, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Bristol Myers Squibb, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Eli Lilly, 6, 12, Research support and principal investigator (clinical trials funds to institution), Galapagos, 2, GSK, 12, Research support and principal investigator (clinical trials funds to institution), Janssen, 6, Janssen-Cilag, 12, Research support and principal investigator (clinical trials funds to institution), Merck Sharp & Dohme, 6, 12, Research support and principal investigator (clinical trials funds to institution), Novartis, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Pfizer, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Roche, 12, Research support and principal investigator (clinical trials funds to institution), Sandoz-Hexal, 6, 12, Research support and principal investigator (clinical trials funds to institution), Sanofi, 6, 12, Research support and principal investigator (clinical trials funds to institution), UCB, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution).

Abstract Number: 1730

Oral glucocorticoid treatment for checkpoint inhibitor associated inflammatory arthritis do not affect progression free survival: a RADIOS Registry cohort study

Deanna Jannat-Khah[1], Pankti Reid[2], Maria Suarez-Almazor[3], Noha Abdel-Wahab[4], Jeffrey Sparks[5], Tawnie Braaten[6], Cassandra Calabrese[7], Alexa Meara[8], Minerva Nong[9], Kyle Ge[10], Laura Cappelli[11], Ami Shah[12], Clifton Bingham[13] and Anne R. Bass[1], [1]Hospital For Special Surgery, New York, NY, [2]University of Chicago Medical Center, Chicago, IL, [3]MD Anderson Cancer Center, Houston, TX, [4]University of Texas MD Anderson Cancer Center, houston, TX, [5]Brigham and Women's Hospital, Boston, MA, [6]UNIVERSITY OF UTAH, Salt Lake City, UT, [7]Cleveland Clinic Foundation, Cleveland Heights, OH, [8]The Ohio State University Wexner Medical Center, COLUMBUS, OH, [9]Columbia University, New York, [10]Hospital for Special Surgery, New York, [11]Johns Hopkins School of Medicine, Baltimore, MD, [12]Johns Hopkins Rheumatology, Baltimore, MD, [13]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Immunological Complications of Medical Therapy (1728–1733)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: As immune checkpoint inhibitor (ICI) usage increases for various cancers the prevalence of rheumatologic immune related adverse events (irAEs) also grows. Glucocorticoids are first line treatment, but standardization in dosing, tapering, and duration is lacking. There are mixed results on the effect of oral glucocorticoids on progression-free survival (PFS) among ICI-treated patients. We investigated oral glucocorticoid use and its association with PFS among ICI-treated cancer patients with ICI-inflamatory arthritis (ICI-IA).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table1. Demographic and Cancer Characteristics of N=206 RADIOS patients

Table 1 Demographic and Cancer Characteristics (N=206)	
Age, mean (SD)	65.41(12.36)
Female*	100 (48.5%)
White Race	177 (85.9%)
Hispanic	10 (4.9%)
Baseline irAE grade 3 or 4*	22 (10.7%)
Melanoma	67 (32.5%)
Non Small Cell Lung Cancer	24 (11.7%)
Renal Cell Cancer	38 (18.4%)
Baseline Cancer Stage 3 or 4*	175 (85%)
ICI combination	76 (36.9%)
Time to glucocorticoid initiation from arthritis onset in days, median (IQR)	24.5 (3, 63)
Time to glucocorticoid initiation from ICI initiation in days, median (IQR)	210 (86.5, 442)
Cancer Progression	46 (22.3%)
Time to cancer progression if progressed from ICI initiation in days, median (IQR)	487 (255, 881)
Time to cancer progression if progressed from steroid initiation in days, median (IQR)	82.5 (-70, 283)
Has ICI been held for rheumatic irAE at any point since ICI start?	71 (34.5%)
ICI duration from ICI initiation in days, median (IQR)	188 (77, 397)
irAE=immune related adverse events ; ICI= immune checkpoint inhibitor ; IQR= interquartile range ; *Missing data : N=1 for female ; N= 40 for baseline irAE grade ; N=17 baseline cancer stage.	

Methods: Data from the RADIOS registry, a prospective U.S. multi-center rheumatic irAE cohort was used. Patients enrolled since February 2023 who were treated with an ICI for cancer and who developed ICI-IA, which we defined as inflammatory arthritis, arthralgia, or PMR, and were treated with glucocorticoids for ICI-IA were included. Patients were excluded if they had pre-existing autoimmune disease or were being treated with glucocorticoids for another irAE. Demographics, cancer and cancer treatment, DMARD and glucocorticoid treatment were collected. Glucocorticoid dosage was converted to prednisone equivalents. Cumulative glucocorticoid exposure and the average daily prednisone dose was calculated at 1-2 weeks, 2-4 weeks, month 2, and months 3,4,5 and displayed in a box plot. Descriptive statistics were calculated. Thirty-day landmark Kaplan Meier plots assessed glucocorticoid exposure and its association with PFS, measured from

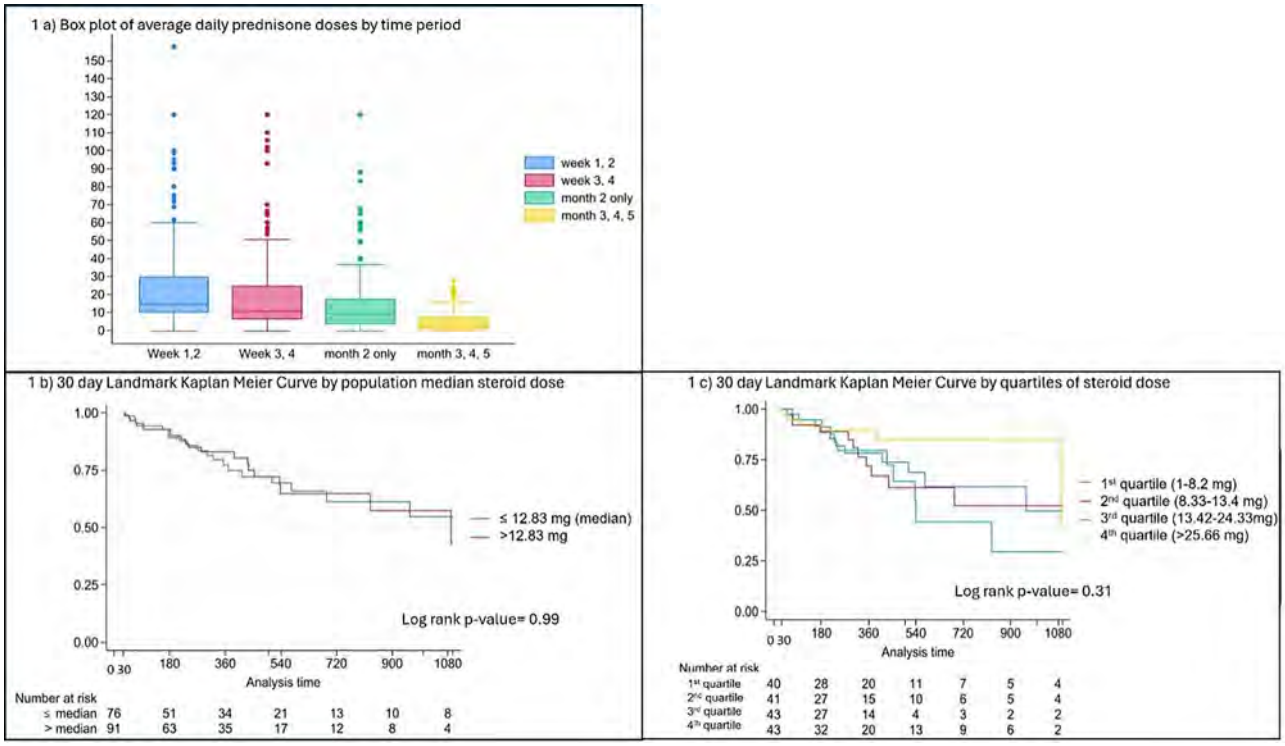


Figure 1. A) Box plot of average daily prednisone doses by time period. B) 30 Day Landmark Kaplan Meier Curve by population median steroid dose C) 30 day Landmark Kaplan Meier Curve by quartiles of steroid dose

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

glucocorticoid initiation to radiographic cancer progression or death. Adjusted cox proportional models with a time varying covariant (time from ICI initiation to glucocorticoid treatment) were performed. Models were adjusted for age, irAE grade at baseline, cancer type (melanoma, non-small cell lung cancer [NSCLC], renal cell cancer [RCC]), cancer stage, ICI combination therapy.

Results: The analytic cohort consisted of 206 patients with a mean age of 65 (SD 12.36), 48.5% were female and 85.9% were White (**Table 1**). Most patients had melanoma (32.5%), RCC (18.4%), or NSCLC (11.7%), and were Stage 3 (26.7%) or 4 (58.3%). The median time from ICI-IA diagnosis to glucocorticoid initiation was 24.5 days (IQR 3, 63). Cancer progression occurred in 46 patients (22.3%), and the median time from glucocorticoid initiation to cancer progression was 82.5 days (IQR -70, 283).

Figure 1a displays the median and interquartile ranges of the average daily prednisone dose, which was highest in the first month of treatment and decreased over time. The first month median glucocorticoid dose was not associated with PFS in a landmark Kaplan Meier curve (log-rank p-value 0.99, Figure 1b). Additionally, there was no difference between quartiles of glucocorticoid dose and PFS (log rank p-value 0.31, Figure 1c). None of the adjusted Cox models were significant for glucocorticoid dose and PFS.

Conclusion: In this cohort, there was not a dose-dependent effect of glucocorticoids on PFS in patients with ICI-IA. Rheumatologists typically use a lower dose than oncology guidelines suggest, and these findings suggest that glucocorticoid treatment of ICI-IA may not have a substantial impact on cancer outcomes.

Disclosure: D. Jannat-Khah: AstraZeneca, 11, CytoDyn, 11; **P. Reid**: AbbVie/Abbott, 1, Amgen, 6, Mustang Bio, 1, UCB, 1; **M. Suarez-Almazor**: Novartis, 5, SetPoint Medical, 2, Syneos Health, 2; **N. Abdel-Wahab**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **T. Braaten**: None; **C. Calabrese**: Eli Lilly, 2, Invivyd, 2, 6, sanofi, 2, 6; **A. Meara**: AbbVie/Abbott, 1, 2, Amgen, 1, 2, AstraZeneca, 1, 2, sanofi, 1, 2; **M. Nong**: None; **K. Ge**: None; **L. Cappelli**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, 5, Sanofi, 2, Uniquity Bio, 2; **A. Shah**: None; **C. Bingham**: Bristol-Myers Squibb(BMS), 5, Eli Lilly and Company, 1, 2, Janssen, 2, NIH, 5, Pfizer, 2, Sanofi, 2, UpToDate, 9; **A. Bass**: None.

Abstract Number: 1731

A Post-marketing Analysis of Autoimmune Toxicities Following Chimeric Antigen Receptor T-cell Therapy Using the FDA Adverse Event Reporting System

Malvika Gupta[1], Christopher Graham[2] and Supriya Gupta[3], [1]Mayo Clinic, Rochester MN, Rochester, MN, [2]University of Minnesota, Minneapoils, MN, [3]University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Immunological Complications of Medical Therapy (1728–1733)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Chimeric Antigen Receptor (CAR-T) therapy has transformed the management of hematologic cancers, with multiple products approved by the U.S. Food and Drug Administration (FDA). While immune-mediated toxicities such as cytokine release syndrome and neurotoxicity are well described, the spectrum of autoimmune adverse events

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of Patients with Immune-Mediated Adverse Reactions Reported to the FDA Adverse Event Reporting System (FAERS)		
CAR-T Product	**Number of Adverse Reactions on FAERS (N=16267)**	**Number of Immune-Mediated Reactions with CAR-T (N=207)**
Axicabtagene ciloleucel	7342 (45.13%)	74 (35.74%)
Tisagenlecleucel	3450 (21.2%)	52 (25.12%)
Ciltacabtagene autoleucel	2605 (16%)	59 (28.5%)
Brexucabtagene autoleucel	1473 (9.05%)	8 (3.86%)
Idecabtagene vicleucel	900 (5.53%)	10 (4.83%)
Lisocabtagene maraleucel	497 (3.05%)	4 (1.93%)
Indication for CAR-T Therapy	**Number of Adverse Reactions on FAERS (N=16267)**	**Number of Immune-Mediated Reactions with CAR-T (N=207)**
Non-Hodgkin's B-Cell Lymphomas	10159 (62.45%)	114 (55%)
Large B-cell Lymphomas	5347 (32.87%)	70 (33.8%)
Diffuse Large B-Cell Lymphoma	5084 (31.25%)	58 (28%)
High-Grade B-Cell Lymphoma	96 (0.59%)	4 (1.93%)
Primary Mediastinal Large B-Cell Lymphoma	167 (1.02%)	8 (3.86%)
Mantle Cell Lymphoma	672 (4.13%)	4 (1.93%)
Indolent B-cell Lymphomas	416 (2.55%)	10 (4.83%)
Follicular Lymphoma	385 (2.36%)	9 (4.34%)
Marginal Zone Lymphoma	31 (0.19%)	1 (0.48%)
Other Non-Hodgkin's Lymphoma or unavailable	3724 (22.9%)	30 (14.5%)
Multiple Myeloma	3505 (21.5%)	69 (33.82%)
B-Cell Acute Lymphoblastic Leukemia	1573 (9.66%)	18 (8.69%)
Unavailable	1030	6
Gender	**Number of Adverse Reactions on FAERS (N=16267)**	**Number of Immune-Mediated Reactions with CAR-T (N=207)**
Male	7809 (48%)	94 (45.41%)
Female	4743 (29.15%)	87 (42%)
Unavailable	3715	26
Age (Years)	**Number of Adverse Reactions on FAERS (N=16267)**	**Number of Immune-Mediated Reactions with CAR-T (N=207)**
<18	595 (3.65%)	6 (2.89%)
18-64	4874 (29.96%)	80 (38.64%)
>65	3921 (24.1%)	66 (31.88%)
Unavailable	6877	55

Characteristics of Patients with Immune-Mediated Adverse Reactions Reported to the FDA Adverse Event Reporting System (FAERS)

(AEs) remain poorly defined. Emerging case reports and small series suggest a potential link between CAR-T and new-onset autoimmune conditions. As the use of CAR-T expands to rheumatologic conditions, understanding the autoimmune safety profile is critical.

Methods: We conducted a pharmacovigilance analysis of autoimmune AEs reported to the FDA Adverse Event Reporting System (FAERS) for each FDA-approved CAR-T product through March 2025. All individual case safety reports listing any of the CAR-T therapies—tisagenlecleucel (tisacel), axicabtagene ciloleucel (axicel), lisocabtagene maraleucel (lisocel), brexucabtagene autoleucel (brexucel), idecabtagene vicleucel (idecel), and ciltacabtagene autoleucel (ciltacel)—as the suspected drug were included. Autoimmune AEs were identified using standardized MedDRA terms. The patient characteristics including malignancy, CAR-T products and AEs were summarized. Disproportionality analysis was performed using Reported Odds Ratio (ROR).

Results: There were 207 immune-mediated AEs with CAR-T reported in the FAERS database (Table 1 and 2). Compared to other products, Idecel was associated with development of sarcoidosis (ROR 17.15, CI 4.28-68.67, $p< 0.0001$). Ciltacel was associated with Guillain-Barre syndrome (ROR 7.31, CI 3.57-14.93, $p< 0.0001$) and immune effector cell associated enterocolitis (IEC-EC) (ROR 58.42, CI 17.90-190.62, $p< 0.0001$). Axicel was associated with dermal autoimmune AEs (Table 2) (ROR 3.65, CI 1.18-11.33, $p=0.024$). Tisacel was associated with myocarditis (ROR 6.20, CI 1.48-25.95,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Immune-Mediated Adverse Events Following CAR-T Therapy	
Immune-Mediated Adverse Events with CAR-T Therapy	**Number of Reactions (N=207)**
Musculoskeletal	**19 (9.2%)**
Myositis	7 (3.4%)
Lupus / Lupus like Reaction	4 (1.9%)
Systemic Sclerosis	4 (1.9%)
Rheumatoid Arthritis	1 (0.5%)
Sacroiliac Joint Dysfunction	1 (0.5%)
Bursitis	1 (0.5%)
Tendonitis	1 (0.5%)
Neurological	**62 (30%)**
Guillain Barre Syndrome	31 (15%)
Immune Mediated Encephalopathy other than ICANS	12 (5.8%)
Transverse Myelitis	10 (4.8%)
Multiple Sclerosis	3 (1.5%)
Myasthenia Gravis	3 (1.5%)
Autoimmune Neuropathy	2 (1%)
Chronic Inflammatory Demyelinating Polyneuropathy	1 (0.5%)
Gastrointestinal	**47 (22.7%)**
Immune Effector Cell Associated Enterocolitis	36 (17.4%)
Inflammatory Bowel Disease	5 (2.4%)
Non-Infectious Sialadenitis	2 (1%)
Sclerosing Cholangitis	2 (1%)
Celiac Disease	1 (0.5%)
Immune Mediated Esophagitis	1 (0.5%)
Pulmonary	**21 (10.1%)**
Interstitial Lung Disease	12 (5.8%)
Sarcoidosis	8 (3.9%)
Immune-Mediated Lung Injury	1 (0.5%)
Dermatological	**16 (7.7%)**
Bullous Dermatitis	5 (2.4%)
Psoriasis	3 (1.5%)
Eosinophilic Cellulitis	3 (1.5%)
Purpura Fulminans	3 (1.5%)
Alopecia Areata	1 (0.5%)
Dermatitis Herpetiformis	1 (0.5%)
Cardiovascular	**15 (7.2%)**
Myocarditis	8 (3.9%)
Vasculitis	7 (3.4%)
Ophthalmologic	**9 (4.3%)**
Optic Neuritis	7 (3.4%)
Uveitis	2 (1%)
Hematologic	**12 (5.8%)**
Immune Thrombocytopenia	6 (2.9%)
Autoimmune Hemolytic Anemia	4 (1.9%)
Thrombotic Thrombocytopenic Purpura	2 (1%)
Endocrine	**6 (2.9%)**
Thyroiditis	5 (2.4%)
Type 1 Diabetes Mellitus	1 (0.5%)

Immune-Mediated Adverse Events Following CAR-T Therapy

p=0.012) and vasculitis (ROR 4.96, CI 1.11-22.16, p=0.036). Compared to other malignancies with CAR-T approval, indolent B-cell lymphoma was associated with myocarditis (ROR 10.72, CI 2.07-55.40, p=0.004) and musculoskeletal autoimmune AEs (Table 2) (ROR 8.05, CI 2.21-29.37, p=0.001) - in particular, myositis (ROR 10.72, CI 2.07-55.40, p=0.004) and lupus/lupus-like reaction (ROR 13.37, CI 1.21-147.72, p=0.034). Follicular lymphoma in particular was associated with vasculitis (ROR 9.66, CI 1.002-93.06, p=0.049). Higher odd of developing optic neuritis was seen in patients age < 18 years (ROR 7.41, CI 1.35-40.55, p=0.02), acute B-cell lymphoblastic leukemia (ROR 21.78, CI 4.22-112.37, p=0.0002), and Tisacel (ROR 22.33, CI 2.69-185.53, p=0.004). Female sex and age >65 were more likely to develop IEC-EC (ROR 1.90, CI 0.90-4.0, p=0.089; ROR 2.04, CI 1.01-4.14, p=0.047).

Conclusion: This post-marketing pharmacovigilance analysis highlights product- and disease-specific patterns of autoimmune AEs following CAR-T therapy. While limited by FAERS reporting bias, these findings support the need for monitoring strategies and emphasize the importance of prospective studies to validate these associations. Integrating pharmacogenomic and immunologic correlates may further elucidate underlying mechanisms.

Disclosure: M. Gupta: None; **C. Graham**: None; **S. Gupta**: Atara Biotherapeutics, INC., 5, Imugene, INC., 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1732

Incidence of Flares in Pre-existing Rheumatologic Diseases Among Patients with Solid Tumors Undergoing Cancer Immunotherapy: A Systematic Review and Meta-analysis

Takemichi Matsui[1], Kenji Yamada[2], Toshiaki Takahashi[3], Yoshito Nishimura[4] and Yu Fujiwara[5], [1]Department of Medicine, Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, [2]Department of Allergy and Rheumatology, Kameda Medical Center, Chiba, Japan, [3]Department of Medicine, John A. Burns School of Medicine, University of Hawaii, Honolulu, HI, [4]Division of Hematology/Oncology, Mayo Clinic, Rochester, MN, [5]Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Immunological Complications of Medical Therapy (1728–1733)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have become essential in cancer treatment, offering significant survival benefits across various malignancies. However, ICIs can cause immune-related Adverse Events (irAEs) and potentially exacerbate pre-existing autoimmune diseases. Rheumatologic diseases (RDs) are frequently excluded from clinical trials of ICIs due to these concerns. Understanding flare incidence is crucial for optimizing cancer management and ensuring safety in patients with co-existing autoimmune RDs. Thus, we investigated the incidence and severity of disease flares of pre-existing RDs, with a focus on rheumatoid arthritis (RA), in patients with solid tumors treated with ICIs.

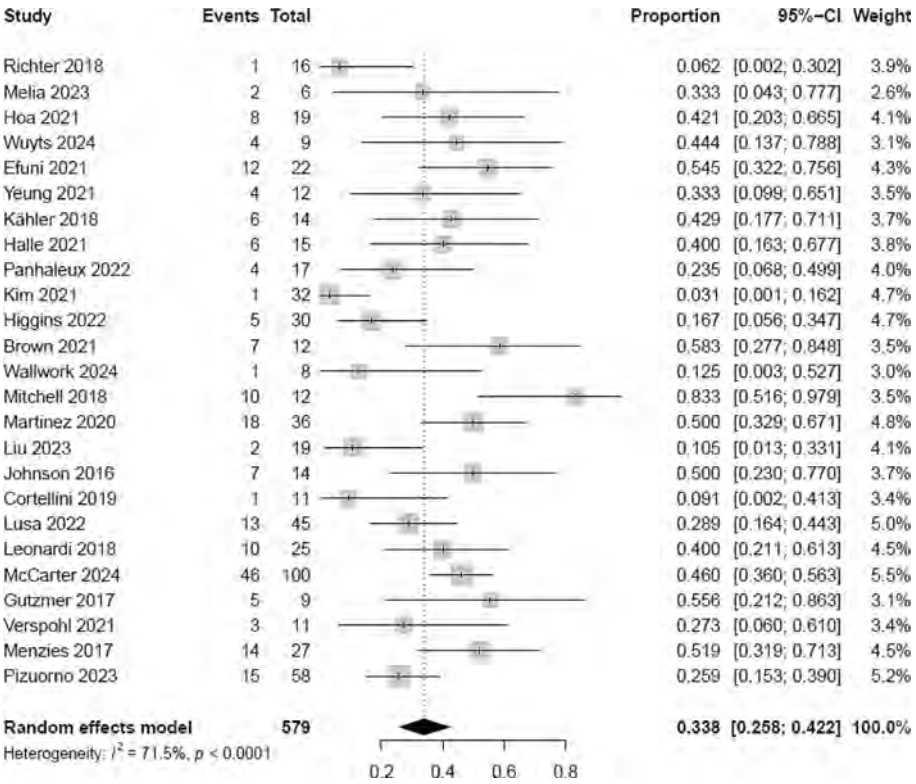


Figure 1: Incidence of flares in patients with pre-existing RDs

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

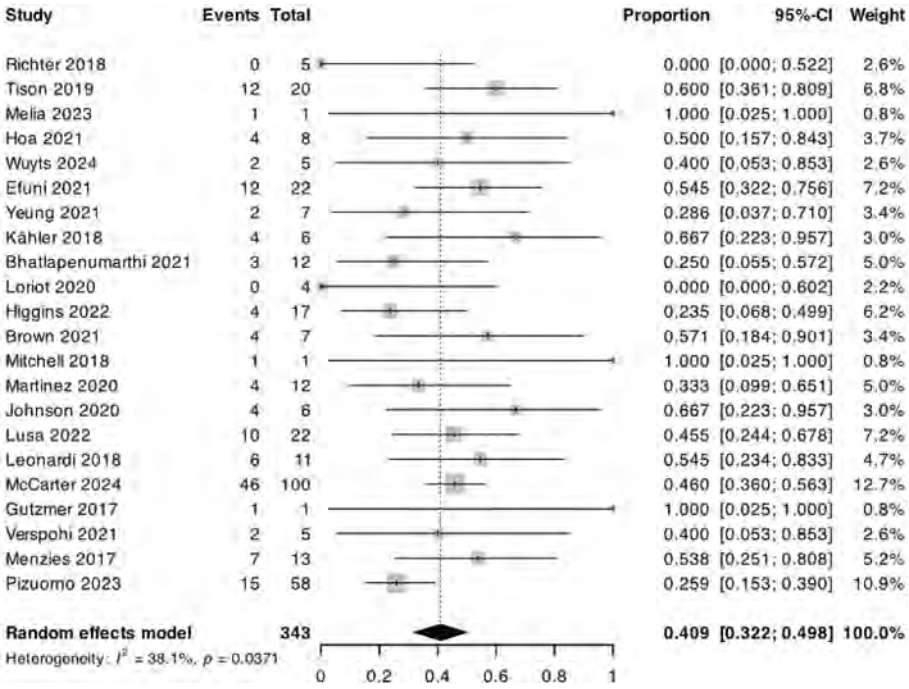


Figure 2: Incidence of flares in patients with pre-existing RA

Methods: A systematic review was conducted in PubMed/MEDLINE and Embase for all peer-reviewed articles from inception to May 16, 2024. Eligible studies were cohort studies and case series (>5 cases) involving patients with solid tumors and concomitant RD treated with ICI therapy. A proportional meta-analysis with a random-effects model was conducted to pool the incidence of grade 1-5 flares and grade 3-5 severe flares in RDs and RA based on Common Terminology Criteria for Adverse Events (CTCAE) across the included studies.

Results: Among 2599 studies, 247 articles were eligible for full-text review, and 31 studies were included in the analysis. In total, 579 patients with RA, systemic lupus erythematosus, Sjögren's syndrome, systemic sclerosis, sarcoidosis, spondyloarthritis, myositis, Behçet's disease, vasculitis, polymyalgia rheumatica were included. Three studies evaluated PD-1/PD-L1 inhibitor monotherapy, two studies evaluated CTLA-4 inhibitor monotherapy, and 12 studies evaluated dual ICIs (ICI subtype unclear in 14 studies). Among all the RDs, the pooled incidence of flares was 33.8% (95% CI, 25.8–42.2; Figure 1). The median time to the first flare after initiating ICIs was 38.5 days (interquartile range: 30.0 – 52.6 days). The incidence of severe flares among overall RDs was 4.2% (95% CI, 0.6-9.6). Patients with RA were included in 22 studies with 343 patients. The pooled incidence of flares in patients with RA was 40.9% (95% CI, 32.2–49.8; Figure 2). Among patients with RA who developed flares, the incidence of severe flares was 8.3% (95% CI, 4.3–15.4).

Conclusion: Our study revealed that more than 30% of cases with RDs and RA develop flare with ICI therapy. These findings would be informative upon risk and benefit discussion before the initiation of ICI therapy for patients with solid tumors and concurrent RDs. Future studies are warranted to explore risk factors of flare and preventative strategies to mitigate the risk of flare development.

Disclosure: T. Matsui: None; **K. Yamada**: None; **T. Takahashi**: None; **Y. Nishimura**: None; **Y. Fujiwara**: Conquer Cancer, the ASCO Foundation, 5, Johnson & Johnson, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1733

Risk factors for the development of immune checkpoint inhibitor-related adverse events, including rheumatology-related presentations

Adela Francis-Malave[1], Terri Laufer[2], Joshua Baker[3], Kyra Sacksith[4], Melissa Batson[4] and Sokratis Apostolidis[3], [1]University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA, [2]University of Pennsylvania, Bala Cynwyd, PA, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Pennsylvania, Philadelphia

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Immunological Complications of Medical Therapy (1728–1733)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: While immune-related adverse events (irAEs) are a commonly reported complication of immune checkpoint inhibitor (ICI) therapy, factors associated with their development remain poorly defined. In this unique prospective cohort study, we explored lab data and patient-reported outcomes (PROs) associated with the probability of developing irAEs, focusing on those that could prompt a rheumatology consult. We aimed to identify high-risk patients who would potentially benefit from closer monitoring and early referral.

Methods: We enrolled cancer patients who were initiating ICI therapy. Demographics, PROs, and lab data were collected during routine clinical visits. irAEs were defined by health providers during routine practice. Rheumatologic-related irAEs included arthritis, myositis, myocarditis, rash, and dry mouth/eyes. Analysis was performed using chi-square or t-tests to compare the pre-treatment characteristics of patients who developed at least one irAE vs those who did not. Logistic regression models were used to evaluate if factors such as age, sex, treatment type (monotherapy with PD-1/PD-L1 inhibitors vs. combination therapy including CTLA-4 inhibitors), as well as baseline lab values (e.g., lymphocyte count, neutrophil-to-lymphocyte ratio, liver function tests), and PROs increased the odds of developing any irAE or rheumatologic irAEs. Cox regression models were used to assess whether time-varying assessments of these characteristics could identify those at more immediate risk.

Table 1. Baseline comparison of cancer patients on immune checkpoint inhibitors who developed at least one irAE vs those who did not develop an irAE

Demographics and lab values	No irAE	At least one irAE	p-value
Age, years	64.0 (10.5)	64.7 (11.1)	0.64
Male Sex (%)	34 (26.0%)	40 (32.0%)	0.29
ICI therapy modality, N (%)			
Monotherapy	116 (88.5%)	103 (82.4%)	0.16
Polytherapy (at one time point)	15 (11.5%)	22 (17.6%)	
Laboratory			
Creatinine	0.99 (0.44)	0.99 (0.32)	0.97
ALT	33.7 (56.7)	23.8 (19.4)	0.07
AST	40.4 (73.1)	25.8 (24.1)	**0.04**
Lymphocytes	15.5 (8.14)	17.9 (9.18)	**0.03**
Neutrophils	71.7 (10.0)	69.6 (10.2)	0.09
Neutrophils/Lymphocytes Ratio	6.98 (6.26)	5.78 (5.32)	0.10
WBCs	7.64 (3.15)	7.78 (3.36)	0.74
Patient Reported Outcomes			
Physical Activity Level	2.23 (1.04)	1.99 (0.91)	0.06
Frequency of Joint pain	1.55 (0.98)	1.81 (1.16)	0.07
Swelling interfering with daily life	1.40 (1.02)	1.10 (1.01)	**0.02**
Data presented as mean (SD) unless otherwise noted			

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Associations between baseline demographics, laboratory values, and patient-reported outcomes with the odds of developing an irAE

Variables	Any irAE		Rheum irAE	
Demographics and lab values	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**
Age, years	1.01(0.98, 1.03)	0.63	1.01 (0.99, 1.04)	0.29
Female Sex	1.34 (0.78, 2.31)	0.29	0.95 (0.52, 1.74)	0.87
Autoimmune Disease	1.71 (0.64, 4.56)	0.28	1.73 (0.64, 4.66)	0.28
ICI therapy modality	1.65 (0.81, 3.35)	0.17	2.27 (1.11, 4.66)	**0.03**
Laboratory				
Creatinine	1.01 (0.53, 1.92)	0.97	1.23 (0.62, 2.44)	0.56
ALT	0.99 (0.98, 1.0)	0.08	1.0 (0.99, 1.01)	0.64
AST	0.99 (0.98, 1.0)	**0.03**	1 (0.99, 1.0)	0.45
Lymphocytes	1.03 (1.0, 1.1)	**0.03**	1.03 (1.0, 1.06)	0.09
Neutrophils	0.98 (0.96, 1.0)	0.10	0.98 (0.96, 1.01)	0.17
Neutrophils/Lymphocytes Ratio	0.96 (0.92, 1.01)	0.11	0.97 (0.92, 1.03)	0.30
WBCs	1.01 (0.94, 1.09)	0.74	1.01 (0.93, 1.10)	0.83
Patient Reported Outcomes				
Joint pain interfering with daily life	1.06 (0.82, 1.37)	0.66	1.01 (0.76, 1.34)	0.06
Frequency of joint pain	1.25 (0.98, 1.58)	0.07	1.18 (0.92, 1.51)	0.195
Joint pain severity	0.93 (0.65, 1.33)	0.69	0.98 (0.66, 1.45)	0.92
Activity level	0.78 (0.60, 1.01)	0.06	0.82 (0.61, 1.10)	0.19
Fatigue interfering with daily life	0.91 (0.74, 1.12)	0.38	0.84 (0.66, 1.06)	0.14
Severity of fatigue	1.01 (0.80, 1.27)	0.93	1.01 (0.78, 1.31)	0.92
Quality of life	0.99 (0.77, 1.27)	0.95	0.86 (0.65, 1.14)	0.30
Frequency of muscle pain	1.04 (0.83, 1.32)	0.72	0.83 (0.63, 1.10)	0.19
Severity of muscle pain	0.75 (0.52, 1.07)	0.11	0.74 (0.50, 1.11)	0.15
Muscle pain interfering with daily life	0.88 (0.68, 1.14)	0.33	0.87 (0.66, 1.16)	0.35
Frequency of heart palpitations	1.10 (0.73, 1.65)	0.64	0.90 (0.57, 1.44)	0.67
Severity of heart palpitations	0.72 (0.51, 1.03)	0.07	0.81 (0.55, 1.18)	0.27
Frequency of nausea	0.81 (0.59, 1.09)	0.16	0.76 (0.52, 1.10)	0.15
Depression interfering with daily life	0.85 (0.63, 1.15)	0.30	0.83 (0.58, 1.18)	0.30
Frequency of swelling	0.91 (0.73, 1.15)	0.44	0.90 (0.69, 1.18)	0.46
Swelling interfering with daily life	0.74 (0.57, 0.96)	**0.02**	0.76 (0.57, 1.01)	0.06
Severity of swelling	0.94 (0.69, 1.27)	0.67	0.97 (0.69, 1.36)	0.86
Severity of itching	1.17 (0.83, 1.67)	0.37	1.0 (0.68, 1.47)	0.99

Results: Among 256 patients, 71.1% were male (n=182). Non-small lung cancer was the most common malignancy (23.1%), and the most common ICI was Pembrolizumab (40.9%). The incidence rate for any irAE was 11.3% (events/person-month) while it was 3.6% for rheumatologic irAEs. Notably, 50% of patients on ICIs had developed an irAE within 3.5 months, with 25% experiencing their first adverse event in the first month. At baseline, those who had irAEs had similar age, sex, rates of combination therapy with ICIs and PROs compared to those who did not. Patients who developed at least one irAE had higher lymphocyte counts (p=0.03) and a lower AST (p=0.04) (Table 1). Higher lymphocyte count (OR: 1.03; 95% CI: 1.0, 1.1; p=0.03) and lower AST (OR: 0.99; 95% CI: 0.98, 1.0; p=0.03) were associated with higher odds of developing an irAE, while use of combination immunotherapy (OR: 2.27; 95% CI: 1.11, 4.66; p=0.03) was associated with a higher odds of developing a rheumatologic irAE (Table 2). Most evaluated factors were unrelated to the immediate risk of developing irAEs.

Conclusion: In this large cohort study, PROs assessed at baseline and over time were poor predictors of irAE onset, including irAEs that would likely result in rheumatology referral. Consistent with prior literature, use of combination immune checkpoint inhibitor (ICI) therapy was associated with increased odds of irAEs, including rheumatologic irAEs. Higher baseline lymphocytes and lower AST levels were associated with an increased odds of irAE, and the neutrophil-to-lymphocyte ratio tended to be associated with irAEs, as has been observed in prior studies. Future studies should evaluate whether recent changes in lab values or PROs can predict the onset of irAEs.

Disclosure: A. Francis-Malave: None; **T. Laufer**: None; **J. Baker**: Amgen, 5; **K. Sacksith**: None; **M. Batson**: None; **S. Apostolidis**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1734

Intra-articular Liraglutide Halts Osteoarthritis Progression, Surpassing Dexamethasone in Synovial and Cartilage Protection

Coralie Meurot[1], Celine Martin[1], Margot Vieubled[2], Indira Toillon[3], Claire Deldycke[1], Valentine Cheron[1], Soline Trombetta[1], William Sibran[1], Revital Rattenbach[1] and **Francis BERENBAUM**[4], [1]4P Pharma, Lille, France, [2]4P Pharma, Lille, [3]Sorbonne University, Paris, France, [4]Sorbonne University/Inserm/AP-HP/4Moving Biotech, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (1734–1739)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Osteoarthritis (OA) is an age-related joint disease that cause chronic pain and reduced mobility. Current treatments mainly relieve pain and inflammation, often with corticosteroid injections. However, no therapy modifies disease progression, highlighting the need for new strategies. Our team is investigating intra-articular GLP-1 analogs for their anti-inflammatory and protective properties. This study evaluates liraglutide, a GLP-1 analogue, in a rat model of OA, focusing on its effects on synovial membrane and cartilage structure.

Methods: The effects of one, two, or eight intra-articular (IA) injections of liraglutide or vehicle were evaluated in a rat OA model induced by ACLT/pMMx surgery, compared to eight injections of dexamethasone. Sham-operated animals were used as controls. Body weight was monitored. Synovial membrane (Krenn [0–9] and Obeidat scores) and cartilage (OARSI [0–26]) were blindly assessed per joint quadrant (MTP, MFC, LTP, LFC) by two independent investigators. The Krenn score evaluates the inner synovial layer, cell density, and inflammation; the Obeidat score evaluates hyperplasia, cellularity, and fibrosis; the OARSI score quantifies the depth and extension of of cartilage lesions.

Table 1: Krenn, Obeidat and OARSI score in ACLT/pMMx rat model Mean ± SD, Statistical analyses: Mann-Whitney test: * p<0.05, **p<0.01, *** p<0.001 and **** p<0.0001 vs 3M - ACLT/pMMx/vehicle (2IA) group; *p<0.05, vs 5M - ACLT/pMMx/ Liraglutide 60 µg (1IA) group; $ p<0.05, $ $p<0.01, $$$ p<0.001 and $$$$ p<0.0001 vs 4M - ACLT/pMMx/vehicle (8IA) group. $ p<0.05, $$p<0.01, $$$ p<0.001 vs 8M - ACLT/pMMx/ Dexamethasone 120 µg (8IA) group. N=5-6 for Sham groups (1M-2M) and 11-12 for ACLT/pMMx groups (3M to 8M).

	Krenn score				Obeidat score						OARSI score		
					Hyperplasia		Cellularity		Fibrosis		MFC	LFC	Global severity index (%)
	Cell layer	Density	Inflammation	Total	MFC / MTP	LFC / LTP	MFC / MTP	MTP / LTP	LTP / MTP	LFC / LTP	MTP	LTP	
Sham/ Vehicle (2IA)	0.17±0.20 ***	0.03±0.07 ***	0.07±0.09 ***	0.27±0.25 ***	0.65±0.30 ***	0.29±0.32 ***	0.17±0.12 ***	0.51±0.30**	0.00±0.00 **	0.00±0.00***	2.64±2.90 **	2.34±2.96 **	17.3±10.9 **
					0.21±0.23 ***	0.10±0.15 ***	0.10±0.09 ***	0.17±0.20***	0.00±0.00**	0.00±0.00***	6.63±6.36 **	6.08±6.53 *	
Sham/ Vehicle (8IA)	0.65±0.24 $$$	0.73±0.42 $$$	0.45±0.26 $$$	1.84±0.85 $$$	0.77±0.22$$$	0.60±0.35$$$	0.48±0.26$$$	0.80±0.55$$$	0.00±0.00	0.27±0.25$$$	4.88±4.75 $$	3.40±1.97 $$$	25.8±18.5 $$
					0.50±0.12$$$	0.57±0.43$$$	0.43±0.37$$$	0.55±0.37$$$	0.08±0.12$	0.17±0.24$$	9.56±8.79 $	10.25±8.35 $$	
ACLT/pMMx/ Vehicle (2IA)	1.85±0.34	2.51±0.48	1.35±0.23	5.72±0.66	1.69±0.38	1.59±0.40	2.35±0.60	2.44±0.47	0.64±0.34	0.81±0.28	9.48±5.64	9.39±5.77	48.0±19.1
					1.53±0.33	1.39±0.47	1.95±0.52	1.94±0.55	0.70±0.31	0.78±0.28	16.49±6.59	14.44±6.50	
ACLT/pMMx/ Vehicle (8IA)	2.06±0.37	2.41±0.56	1.40±0.15	5.88±0.77	1.83±0.42	1.96±0.45	1.83±0.75	2.54±0.44	0.70±0.32	0.92±0.16	11.85±7.14	10.55±6.25	54.3±19.9
					1.76±0.38	1.74±0.47	1.78±0.62	2.14±0.58	0.69±0.37	0.85±0.31	17.61±5.01	19.07±5.75	
ACLT/pMMx/ Liraglutide 60 µg (1IA)	0.91±0.31 ****	1.28±0.69 ***	0.82±0.37 ***	3.00±1.00 ***	1.00±0.41 **	0.82±0.34 ***	0.87±0.40 ****	1.24±0.49 **	0.23±0.26 **	0.45±0.40 *	5.38±4.03 *	4.60±3.32 *	32.0±19.8 *
					0.71±0.50 ***	0.74±0.48 **	0.60±0.38 ****	1.12±0.55 **	0.08±0.12 ***	0.45±0.38 *	10.92±6.48 *	10.91±6.77	
ACLT/pMMx/ Liraglutide 60 µg (2IA)	0.76±0.35 ****	0.80±0.29 ****	0.55±0.25 ****	2.11±0.47 ****/*	0.91±0.44 ***	0.71±0.48 ***	0.76±0.41 ****	0.70±0.31 ***/*	0.17±0.17 **	0.36±0.30 **	4.44±3.42 **	3.56±2.73 **	21.6±11.3 **
					0.84±0.46 ***	0.62±0.56 **	0.58±0.42 ****	0.98±0.36 ***	0.14±0.18 ***	0.53±0.29	8.74±4.87 **	6.98±3.71 ***	
ACLT/pMMx/ Liraglutide 60 µg (8IA)	0.85±0.16 $$$$/$$	0.89±0.33 $$$$/$	0.50±0.33 $$$$/$$	2.23±0.47 $$$$/$$	0.82±0.35 $$$$/$	0.62±0.41 $$$$/$$	0.56±0.38 $$$$/$$$	0.84±0.42 $$$$/$$	0.15±0.22 $$$/$$	0.35±030 $$$$/$$$	6.03±4.25 $$	5.69±4.66 $$	32.1±13.5 $$
					0.62±0.69 $$$/$$	0.68±0.38 $$$$/$	0.55±0.30 $$$$/$$$	0.97±0.55 $$$/$	0.14±0.26 $$/$$$	0.38±0.37 $$/$	13.43±5.89 $	9.05±6.33 $$$	
ACLT/pMMx/ Dexamethasone 120 µg (8IA)	1.17±0.35 $$$$	1.49±0.76 $$	1.00±0.38 $$	3.66±1.27 $$$$	1.27±0.47 $$	1.32±0.43 $$	1.17±0.81	1.89±0.73 $	0.55±0.42	0.74±0.34	9.05±6.67	8.4±6.91	45.1±22.1
					1.29±0.42 $$	1.04±0.38 $$	1.39±0.62	1.66±0.42 $$	0.51±0.34	0.78±0.29	15.73±7.75	14.55±8.37	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

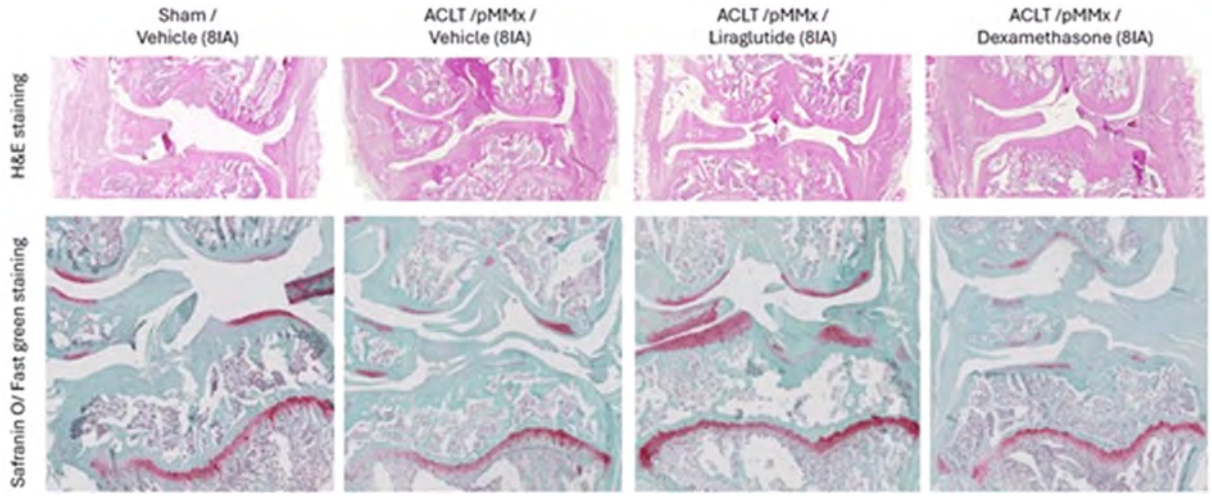


Figure 1: Representative picture of Hematoxylin eosin and Safranin O/Fast green staining to determine the Krenn, Obeidat and OARSI score

Results: The total synovitis score using Krenn methods showed a significant increase in synovial inflammation in ACLT/pMMx/vehicle groups vs. respective sham controls ($p< 0.001$), while treatment significantly reduced this score by ±48–63% for liraglutide and 38% for dexamethasone ($p< 0.001$ and $p< 0.0001$ for liraglutide groups, $p< 0.0001$ for dexamethasone). Liraglutide 60 μg significantly improved all synovitis parameters compared to vehicle, with superior effects to dexamethasone ($p< 0.05$ for density, $p< 0.01$ for layer, inflammatory, and total synovitis scores). These results suggest that liraglutide reduces the severity of synovitis, with 2 or 8 injections showing the greatest improvement. Obeidat scores showed increased hyperplasia, cellularity, and fibrosis across all quadrants (MTP, MFC, LTP, LFC) in the vehicle versus sham groups. Both treatments significantly reduced these scores compared to vehicle, with liraglutide showing broader effects. In particular, liraglutide 60 μg was more effective than dexamethasone in reducing medial cellularity and fibrosis. OARSI scores showed significantly increased cartilage degradation in the vehicle groups compared to sham ($p< 0.01$). Liraglutide reduced degradation by 34–55%, while dexamethasone had no significant effect (17%). The global severity index confirmed these findings: liraglutide improved cartilage integrity ($p< 0.05$, $p< 0.001$, $p< 0.01$ for 1, 2, 8 injections vs. vehicle), while dexamethasone showed no benefit (Figure 1, Table 1).

Conclusion: These results show that intra-articular liraglutide effectively reduces synovial inflammation and protects joint structure. It outperforms dexamethasone by preserving both synovial tissue and cartilage, highlighting its potential as a superior OA treatment offering symptomatic relief and structural preservation, unlike dexamethasone, which lacks cartilage protection and may be harmful in the long-term.

Disclosure: C. Meurot: 4P Pharma, 3; **C. Martin**: 4P Pharma, 3; **M. Vieubled**: 4P Pharma, 3; **I. Toillon**: None; **C. Deldycke**: 4P Pharma, 3; **V. Cheron**: 4P Pharma, 3; **S. Trombetta**: 4P Pharma, 3; **W. Sibran**: 4P Pharma, 3; **R. Rattenbach**: 4P Pharma, 3, 8, 10; **F. BERENBAUM**: 4Moving Biotech, 2, 8, 10.

Abstract Number: 1735

Endocrine Disruptors Exacerbates Osteoarthritis Pain and Inflammation

Elise Herardot[1], Nadine Soliman[1], Audrey Pigenet[1], Ilana Slotine[1], Anni Herranan[2], Samia Bahieddine[1], Jean-Baptiste Fini[2], Olivier Tabary[1], Adeline Cambon[3], Xavier HOUARD[4], Francis BERENBAUM[5], SELLAM JEREMIE[6] and Alice Courties[7], [1]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, F-75012 Paris, France, Paris, France, [2]UMR 7221, Phyma, CNRS–Muséum National d'Histoire Naturelle, Sorbonne Université, 75005 Paris, France, Paris, France, [3]Department of Orthopedic, Trauma and Hand Surgery, Hôpital Saint-Antoine, Sorbonne University, 184 Rue du Faubourg Saint-Antoine, 75012, Paris, France, Paris, France, [4]Centre de Recherche Saint-Antoine, UMR_S938 INSERM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

/Sorbonne Université, Paris, France, PARIS, France, [5]Sorbonne University/Inserm/AP-HP/4Moving Biotech, Paris, France, [6]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, F-75012 Paris, France, /Rheumatology Department, AP-HP Saint-Antoine Hospital, 184, rue du Faubourg Saint-Antoine, 75012, Paris, France., Paris, France, [7]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, F-75012, Paris, France / Rheumatology Department, AP-HP Saint-Antoine Hospital, 184, rue du Faubourg Saint-Antoine, 75012, Paris, France, Paris, France

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (1734–1739)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Osteoarthritis (OA) affects over 590 million individuals globally. Epidemiological data suggest that exposure to environmental pollutants, particularly endocrine-disrupting chemicals (EDCs) such as phthalates, PFAS, and heavy metals, may contribute to increased OA risk and severity (1). Chronic exposure to these compounds begins as early as in utero and continues throughout life via environmental and household sources with at least 14 EDCs ubiquitously present in daily life (2). Several have also been identified in the synovial fluid of OA patients, indicating both systemic and local joint exposure. Yet, their functional role in pain modulation and joint inflammation remains insufficiently understood **This study aimed to determine whether local and/or systemic low-dose exposure to a mixture of 14 EDCs modulates OA severity and pain**, and to explore potential effects on sensory neuron.

Methods: Male and female 12-week-old C57BL/6 mice were exposed either locally by intra-articular (IA) injections of an EDCs mix (e.g., Perfluorooctanoic acid [PFOA]=10^{-7}M) or vehicle, one week before and after OA induction by IA injection of monoiodoacetate. An additional cohort was systemically (via lifelong administration through drinking water) exposed to the EDCs mix from in utero through 15 weeks. Pain-related behaviour, locomotor activity, and body weight were monitored over 21 days. Histological and molecular analyses were performed on knee joints and dorsal root ganglia (DRG). In vitro, primary DRG neurons from male mice were treated with the EDCs mix (e.g., [PFOA]=10^{-8}M or 10^{-9}M), and calcium responses to capsaicin (TRPV1 agonist) were recorded.

Results: In male mice, local IA EDCs exposure significantly increase OA-related pain over the 21-day period ($p< 0.001$) and reduce the physical activity (day 21: mean [SEM] 13.2m [4.7] vs. 17.4m [2.3] in controls, $p< 0.05$). Histological analysis revealed more severe synovitis (Krenn score) (5.1 [1.55] vs. 4.3 [1.5], $p< 0.05$) and OARSI cartilage damage (3 [0.75] vs. 2.5 [2.94], $p=0.03$). Enhanced macrophage infiltration and elevated Bdnf gene expression in the DRG were also observed. In contrast, female mice with IA EDCs exposure did not display significant mechanical hypersensitivity, although they exhibited reduced physical activity (day 21: 13.5m [1.4] vs 19.5m [2.3] in controls, $p< 0.05$) along with upregulation of Bdnf expression in DRGs.

Male mice exposed systemically to EDCs via drinking water developed persistent OA pain-related behaviours ($p=0.001$) and unexpectedly showed increased physical activity (16.9m [181.0] vs. 13.6m [127.8], $p< 0.05$), potentially reflecting EDCs-induced anxiety. No significant effects were observed in female mice. In vitro, EDCs-treated sensory neurons displayed altered calcium dynamics with prolonged depolarization following capsaicin stimulation.

Conclusion: This study reveals that low-dose exposure to EDCs can amplify OA-related pain and inflammatory responses in a sex-specific manner. This study supports the role of EDCs in modulating neuroimmune interactions and sensory neuron excitability in OA pathophysiology.

(1) Deprouw C, RMD Open. 2022
(2) Woodruff, Environmental health perspectives. 2011

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Herardot: Ffizer, 5, Fondation pour la recherhce médicale, 5; **N. Soliman**: La société Française de Rhumatologie, 5; **A. Pigenet**: None; **I. Slotine**: None; **A. Herranan**: None; **S. Bahieddine**: None; **J. Fini**: None; **O. Tabary**: None; **A. Cambon**: None; **X. HOUARD**: None; **F. BERENBAUM**: 4Moving Biotech, 2, 8, 10; **S. JEREMIE**: None; **A. Courties**: Dreamer, 5, Sorbonne Université, 5.

Abstract Number: 1736

Multi-Model Evaluation of the Impact of CD14 on Synovial Inflammation and Pain During PTOA.

Kevin Burt[1], Sanique South[2], Natalie Adamczyk[3], Shingo Ishihara[3], Vu Nguyen[4], Robert Mauck[4], Anne-Marie Malfait[5], Timothy Griffin[6], Rachel Miller[7] and Carla Scanzello[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Oregon, Eugene, [3]Rush University, Chicago, [4]University of Pennsylvania, Philadelphia, [5]Rush University, Oak Park, IL, [6]Oklahoma Medical Research Foundation, Oklahoma City, [7]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (1734–1739)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Soluble CD14, a co-receptor of inflammatory toll-like receptor signaling that is produced primarily by monocytes/macrophages, is present in synovial fluid in patients with OA and positively associates with joint space narrowing and pain. **Utilizing both global genetic deletion of CD14 and intra-articular CD14 blockade across mild to severe models of murine PTOA, we aimed to test the hypothesis that CD14 inhibition can attenuate synovial inflammation and associated pain during disease progression**.

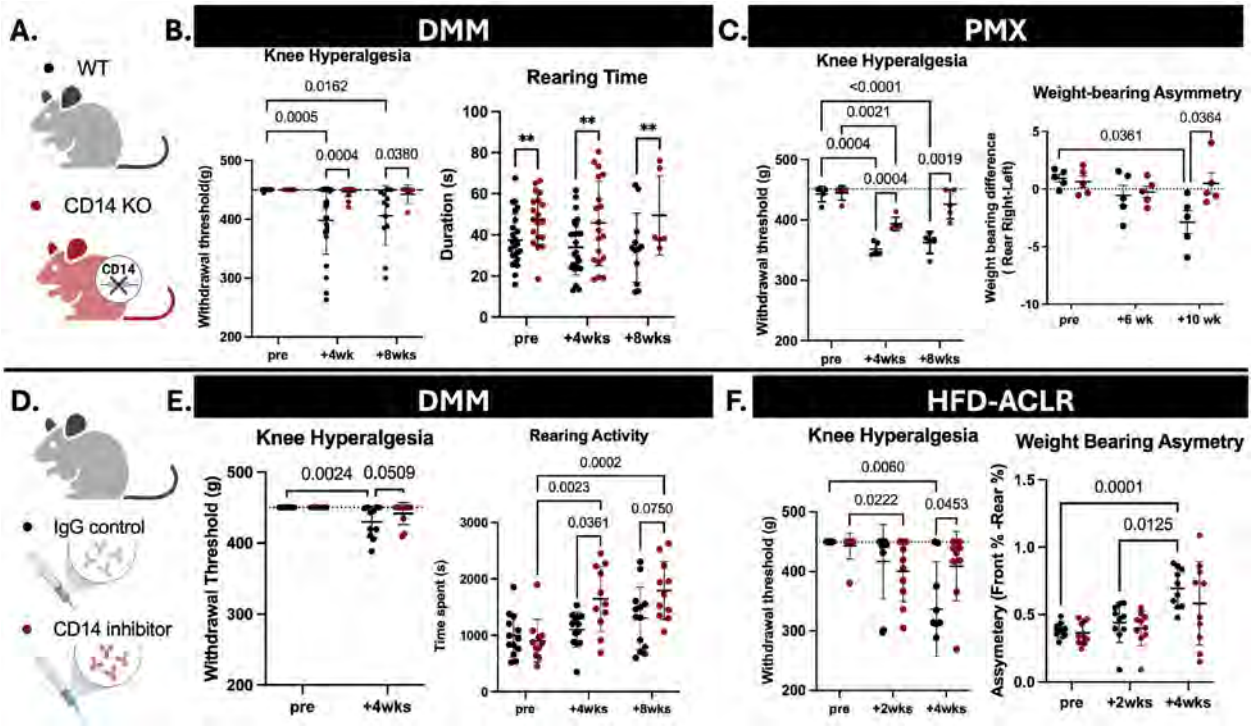


Figure 1: (A,D) Study schematic. (B,C,E,F) Knee hyperalgesia measured via withdrawal threshold (g). (B,E) Time spent rearing (sec). (C) Weight bearing asymmetry measured as (C) the difference between rear right (DMM) to rear left paw (unoperated) weight (g) or (F) as front to rear paw weight bearing ratio (%/%).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

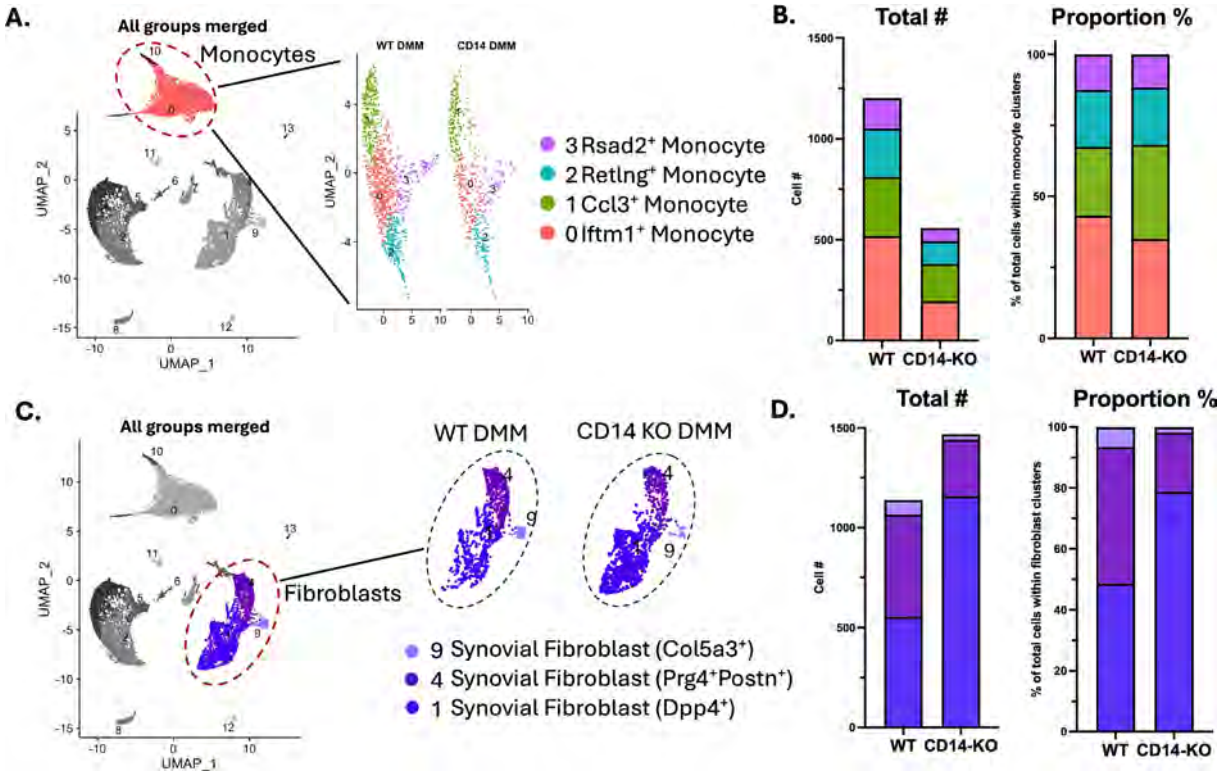


Figure 2: (A) UMAP of cell clusters within WT and CD14 KO synovium harvested 4-wks post injury with re-clustered monocyte populations delineated. (B) Monocyte specific cell cluster breakdown represented as the number and percentage of total cells within monocyte clusters. (C) UMAP of re-clustered monocyte populations. (C) UMAP of cell clusters within WT and CD14 KO synovium harvested 4-wks post injury with fibroblast clusters (Clusters 1, 4, & 9) delineated. (D) Fibroblast cell cluster breakdown represented as the number and percentage of total cells within fibroblast clusters. (pooled n=15/group).

Methods: *DMM:* Destabilization of the medial meniscus (DMM) surgery was performed in 12-wk old male C57BL/6 mice. *2) PMX:* Partial meniscectomy (PMX) surgery was performed in 12-wk old male mice. *3) HFD-ACLR:* Nonsurgical anterior cruciate ligament rupture (ACLR) was performed via overloading in 36-wk old female mice fed a high fat diet (HFD). *CD14 knockout:* A global genetic knockout of CD14 was utilized and evaluated in the DMM and PMX models. *Drug intervention:* WT mice were treated intra-articularly (IA) with either an anti-CD14 monoclonal antibody or an IgG2a control (0.5mg/kg). Mice received 3 weekly injections beginning 48 hours post DMM or ACLR injuries. *Evoked pain:* Knee hyperalgesia was measured using a pressure application measurement (PAM) device. *Spontaneous pain behavioral:* Spontaneous cage behavior was evaluated using the Laboratory Animal Behavior Observation Registration and Analysis System™. Paw weight bearing distribution and rearing behavior was measured using the Advanced Dynamic Weight Bearing system or a static incapacitance meter system. *Single-cell sequencing (scRNA-seq) (n=15):* Synovial cells were isolated from DMM- and sham- operated knee joints 4-wks post-surgery. scRNA-seq data was processed using Seurat.

Results: Global deletion of CD14 mitigated knee hyperalgesia in both DMM and PMX models of PTOA, with a significant increase in withdrawal threshold in CD14-KO mice compared to WT post-injury (**Fig. 1A-C**). Further, delivery of a CD14 blocking antibody mitigated knee hyperalgesia in both DMM and HFD-ACLR models of PTOA (**Fig. 1D-F**). Spontaneous pain behavior analysis revealed that genetic deletion of CD14 increased mobility (rearing time) in the DMM model, comparing to WT. Further, a protection from weight bearing asymmetry was observed following PMX injury in CD14-KO mice compared to WT (**Fig. 1A-C**). IA delivery of anti-CD14 increased rearing activity following DMM and protected from weight bearing asymmetry following ACLR injury, both compared to the IgG control (**Fig. 1D-F**). Mild attenuation of OA histopathology was observed across models. Lastly, synovial scRNA-seq analysis at 4-wks post DMM revealed clear decreases across multiple monocyte populations, as well as a differential modulation of multiple fibroblast populations within the CD14-KO synovium compared to WT (**Fig. 2**).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The consistent attenuation of pain behavior in both mild and severe models of PTOA strongly supports the potential of targeting CD14 to treat painful OA. Our scRNA-seq results suggest that the protective effects may be mediated in part by decreased inflammatory signaling within the synovium, which influenced both the myeloid and fibroblast populations that emerge after injury.

Disclosure: K. Burt: None; **S. South**: None; **N. Adamczyk**: None; **S. Ishihara**: None; **V. Nguyen**: None; **R. Mauck**: None; **A. Malfait**: Eli Lilly, 5, Merck, 2, Novartis, 2, Orion, 5, Roivant, 2; **T. Griffin**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10, Novo Nordisk, 2; **R. Miller**: None; **C. Scanzello**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10.

Abstract Number: 1737

CR10049, the first intra-articular Src family kinase inhibitor as a long-acting symptom- and disease-modifying drug for the inflammatory OA phenotype

Luigino Giancotti, Tiziana Piepoli, Roberto Artusi, Matteo Ghirri, Michela Visintin, Gianfranco Caselli and Lucio Rovati, Rottapharm Biotech, Monza, Italy

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (1734–1739)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: The inflammatory osteoarthritis (OA) phenotype is characterized by the presence of synovial membrane inflammation, pain and pathological changes in joint structure leading to rapid disease progression and debilitating chronic conditions. Efforts to develop effective OA therapies against a single target failed. Therefore, we designed a small molecule, CR10049, which preferentially inhibits the pro-inflammatory Src family kinases members, along with kinases that have a major role in OA development and maintenance such as members of the Ephrin receptor, Trk and the VEGFR family.

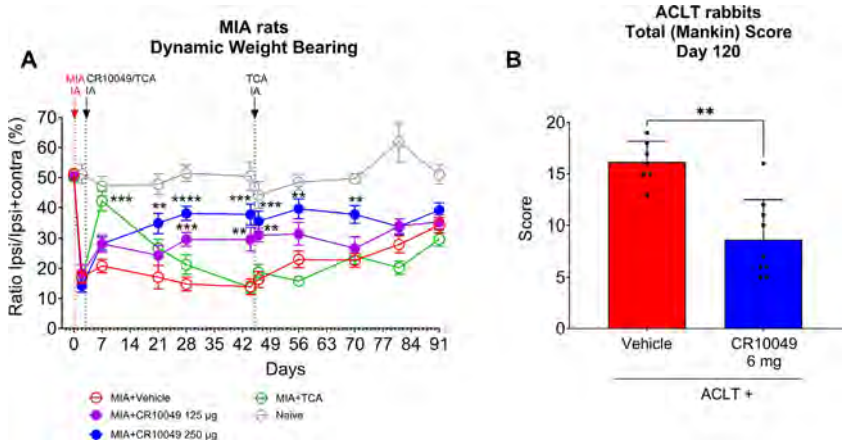


Figure 1. Representative data of the weight-bearing imbalance (A) and Mankin score (B) of CR10049-treated animals. Results are expressed as mean ± SEM (A) or SD (B) for n=11/group-n=6/naïve (A) or n=7/9 (B) animals and analyzed by two-way ANOVA with Dunnett (A) or Mann-Whitney t-test (B) comparisons. ** p<0.01, ***p<0.001, **** p<0.0001 vs Vehicle.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The aim of this study was to characterize the pharmacological activity of CR10049 in vitro and in long-lasting small (rats) and large (rabbits) animal models of OA. Moreover, preliminary acute toxicology studies were employed to support the next development for human clinical trials.

Methods: A panel assay of 159 kinases was used to evaluate the binding affinity of CR10049. In vivo, OA was induced by injecting 2 mg of MIA into the knee of Sprague Dawley rats. On day 3 (D3) after MIA injection, animals received CR10049 (125 and 250 μg) or vehicle intraarticularly (IA, 30 μl). On D3 and D45 an additional control group received IA triamcinolone acetonide (TCA, 60 μg). Pain was blindly evaluated by electronic Von Frey testing and dynamic weight bearing for 91 days, at variance with the 28 days of the conventional MIA OA model. In another experiment, New Zealand rabbits that underwent ACL transection (ACLT), were administered IA with CR10049 (6 mg in 600 μl) or vehicle on D7, D20 and D40. At sacrifice (D120), explanted joints were processed for blinded histology evaluation. For toxicology studies in Wistar rats, CR10049 was injected intravenously (IV) at doses up to 60 mg/kg and IA up to 5 mg.

Results: CR10049 inhibited, in a nanomolar range (IC_{50} < 25 nM), the Src family member cSrc, Lck, Fyn, Fgr, Frk and Yes as well as other kinases including VEGFR1/2, FGFR1, EPHA3, EPHA5, TrkB and TrkC that have a major role in synovial inflammation and fibrosis, cartilage degradation, bone remodeling and pain status.

In the long MIA rat paradigm, CR10049 significantly reduced weight-bearing imbalance for long period (Fig.1A) in a dose-dependent fashion; these effects were confirmed by mechanical allodynia and were significant up to D91. TCA exerted the known acute benefit that was rapidly lost and not replicated with a second injection (Fig.1A). In ACLT rabbits, CR10049 significantly preserved cartilage tidemark integrity and reduced GAG degradation, cartilage and cell damage, osteophytes formation and subchondral bone thickening for 3 months after the last IA injection (as summarized by total score in the fig.1B). In preliminary rat toxicology studies, CR10049 did not induce toxicological effects when injected systemically (IV) up to 60mg/kg and locally (IA) up to 5 mg, i.e. a 20x higher dose than the maximum effective dose.

Conclusion: We identified the first intra-articular drug, CR10049, with a long-acting effect on pain reduction and joint structure improvement in the experimental inflammatory OA setting. Its unique characteristics of selectively targeting kinases with a major role in OA, makes CR10049 a good candidate for the treatment of the OA inflammatory phenotype.

Disclosure: L. Giancotti: Rottapharm Biotech, 3; **T. Piepoli**: Rottapharm Biotech, 3; **R. Artusi**: Rottapharm Biotech, 3; **M. Ghirri**: Rottapharm Biotech, 3; **M. Visintin**: Rottapharm Biotech, 3; **G. Caselli**: Rottapharm Biotech, 3; **L. Rovati**: Rottapharm Biotech, 4, 8, 10.

Abstract Number: 1738

Coexpression and Infiltration of Endoplasmic Reticulum Stress Proteins Together With CD34+ Fibroblast-like Synoviocytes In Human Inflamed Synovial Membranes

Zoe Gendebien[1], Pauline Salpetier[2], Celine Deroyer[2], Genevieve Paulissen[2], Alexandre Hego[2], Gaetan Lefevre[2], Christophe Poulet[2], Sophie Neuville[2], Patrick Durez[3], Patrice Hemon[4], Nadege Marec[5], Elettra Bianchi[2], Philippe Delvenne[2], Clio ribbens[2] and Dominique de Seny[2], [1]ULiege, Liège, Belgium, [2]ULiege, Liege, Belgium, [3]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatologie, Brussels, Brussels Hoofdstedelijk Gewest, Belgium, [4]Brest, Brest, Belgium, [5]Brest, Brest, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

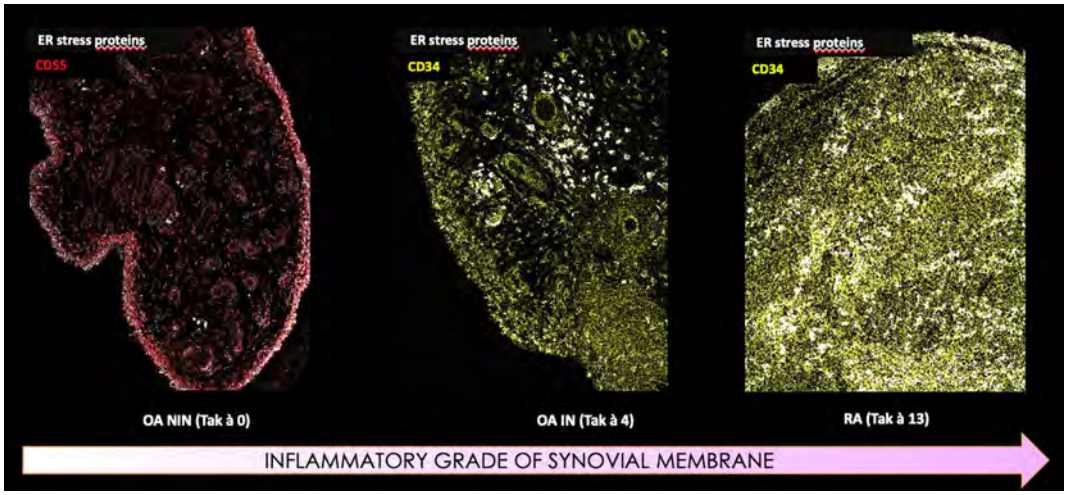
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (1734–1739)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: A strong crosstalk exists between endoplasmic reticulum (ER) stress and synovitis. Several ER chaperone proteins, besides their function in protein folding, can play a role in cell survival enhancing inflammation and immunogenicity once ER stress occurs in pathological conditions. This research aims at localizing and quantifying ER stress proteins (BiP, HYOU1, MANF, PDIA4, GANAB, HSP90B1, TXNDC5, DNAJB11, LMAN1, ERP29 and CALR) in inflamed and non-inflamed synovial membranes, as well as assessing their cellular localization. It also investigates the modulation of these ER protein expressions in fibroblast-like synoviocytes (FLS) under ER stress, profibrotic and proinflammatory conditions.

Methods: Immunohistochemistry was performed on formalin-fixed paraffin-embedded synovial tissues from patients with osteoarthritis (OA; n=9), chronic pyrophosphate arthropathy (n=7), and rheumatoid arthritis (n=8), exhibiting continuous degree of inflammation. These results were confirmed using the collagenase-induced osteoarthritis (CIOA) mouse models. Protein localization and semi-quantification were done using QuPath. Imaging mass cytometry (IMC) was performed on the biopsies but were conjugated with metal antibodies recognizing synovial cells (FLS, immune cells, ...) and the 11 ER stress proteins, followed by laser desorption and time-of-flight mass spectrometry to detect and quantify the spatial distribution of multiple proteins simultaneously. FLS were isolated from OA patient synovium post-surgery and stimulated in vitro with tunicamycin (0.1–10 µg/mL, 1–7 days) to induce ER stress. TNF-α and TGF-β were used to mimic inflammatory or fibrotic conditions. Protein expression and secretion were assessed by western blot on cell lysates and supernatants. Fibroblasts markers (CD55 and CD34) expression was also evaluated by immunofluorescence.

Results: ER stress proteins were mostly restricted to the lining layer in mildly inflamed synovium and infiltrated the whole sCollynovium when the inflammation was severe. Their differential expression was confirmed in a CIOA mice model. This spatial distribution mirrors the fibroblast phenotype shift, with $CD55^+$ (lining) fibroblasts predominating in non-inflamed OA and declining with inflammation, while $CD34^+$ (sublining) fibroblasts, enriched in inflamed OA and RA, become prominent in the sublining. IMC confirmed the co-expression of ER stress proteins with $CD55^+$ fibroblasts in the lining layer of non-inflamed OA, and with $CD34^+$ fibroblasts in the sublining layer of inflamed OA. ER stress proteins do not co-express with lymphocytes markers. In vitro, these proteins were observed under basal conditions in FLS, which expressed CD55 and CD34. ER stress induction increased their intracellular levels and, for some, their secretion. Inflammatory (TNF-α) and profibrotic (TGF-β) stimuli further enhanced their expression.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: These findings suggest that fibroblasts infiltrating the synovial membrane—particularly CD34$^+$ cells—may play a central role in the pathogenesis of synovial inflammation, acting as secretory cells of the chaperone proteins which may exhibit pro-inflammatory and pro-fibrotic properties.

Disclosure: Z. Gendebien: None; **P. Salpetier**: None; **C. Deroyer**: None; **G. Paulissen**: None; **A. Hego**: None; **G. Lefevre**: None; **C. Poulet**: None; **S. Neuville**: None; **P. Durez**: None; **P. Hemon**: None; **N. Marec**: None; **E. Bianchi**: None; **P. Delvenne**: None; **C. ribbens**: None; **D. de Seny**: None.

Abstract Number: 1739

Acute Transcriptomic Response of Synovium and Dorsal Root Ganglia to Joint Injury

Michael Newton[1], Lai Wang[2], Anne-Marie Malfait[3], Rachel Miller[2] and Tristan Maerz[4], [1]University of Michigan, South Lyon, MI, [2]Rush University Medical Center, Chicago, IL, [3]Rush University, Oak Park, IL, [4]University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (1734–1739)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: In arthritic synovium, emerging clinical evidence suggests crosstalk between synovial cells and dorsal root ganglion (DRG) neurons drives nerve sprouting and pain sensitization [Bai+ 2024, Nanus+ 2021]. Similarly, preclinical post-traumatic osteoarthritis (PTOA) models demonstrate progressive knee hyperalgesia and rapid nociceptor sprouting post-injury [Bergman+ 2023, Obeidat+2024]. To elucidate the synovium-nerve signaling underpinning injury-induced nociceptor sprouting, we used bulk RNA sequencing to characterize the acute response of paired synovium and DRG to ACL rupture (ACLR).

Methods: Under IACUC approval, 12-week-old male C57Bl/6 mice underwent ACLR or sham procedure (n=6). At 1, 3, or 7 days post-injury, total RNA was isolated from ipsilateral synovium and L3-L5 DRGs for bulk RNA sequencing. Quality control confirmed high RNA and sequencing quality and high DRG neuronal enrichment (Fig 1A,B). Data were analyzed for differentially-expressed genes (DEGs) via weighted Limma-Voom, and pathway enrichment via gene set enrichment analysis (GSEA). A published DRG interactome database [Wangzhou+ 2021] was utilized to identify putative interactions between ACLR-upregulated synovial ligands and DRG-neuron receptors. Reference single cell RNA sequencing (scRNAseq) data of murine synovium and DRG was used to assess cell-specific ligand/receptor expression.

Results: The synovium exhibited a marked, gradually-evolving response to ACLR (Fig 1C,D). Most injury-induced DEGs (>60%) were conserved across timepoints (Fig 1E), with >10% shared between adjacent timepoints (Fig 1E). Angio- and neurogenic synovial signaling was detectable at 1d and progressive out to 7d (Fig 1D,E). Inflammatory signaling was most enriched at 1d but sustained throughout (Fig 1D). Neuroinflammatory leading edge genes suggested multifaceted neuroimmune signaling (e.g. complement (C5ar1), toll-like receptor (Tlr7), and cytokine (Tnfrsf1b) pathways, Fig 1E). Progressive fibroblast-associated matrix changes denoted initiation of progressive fibrosis, hyperplasia, and ossification known to present at later timepoints in this model (Fig 1D). DRG response to ACLR was comparatively subtler (Fig 2A-C), but GSEA revealed significant enrichment of several neuron sprouting pathways (Fig 2D,E) across timepoints, with different facets preferentially enriched at 1, 3, and 7 days post-ACLR (Fig 2D), suggesting a rapid, evolving post-injury response. Interactome analysis (Fig 3A) implicated pathways including NGF, semaphorin-plexin, FGF and integrin signaling as putative mediators

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

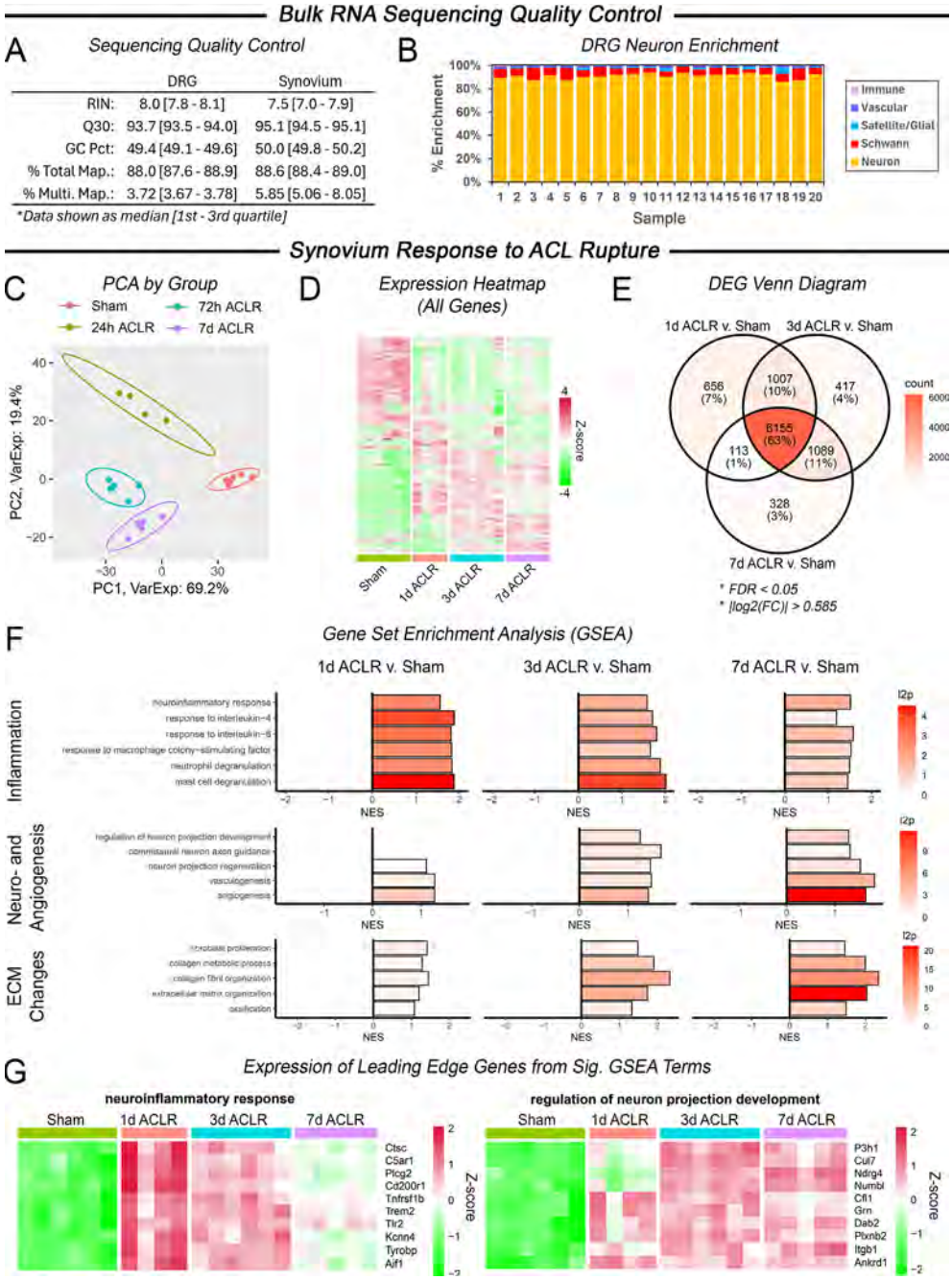


Figure 1. (A) Bulk RNA sequencing quality control metrics for DRG and synovium. (B) DRG neuron enrichment, calculated via bulk seq. deconvolution. Synovium response to ACL rupture: (C) PCA plot. (D) Heatmap of all genes. (E) Venn diagram of DEG overlap between timepoints. (F) Significant GSEA terms related to inflammation, neuroangiogenesis, and ECM. (G) Expression of leading-edge genes from significant GSEA terms.

of time-dependent (Fig 3C), injury-induced synovium-nerve crosstalk. scRNAseq demonstrated synovial ligand secretion primarily by fibroblasts, Schwann cells, and pericytes (Fig 3B), with receptor expression by various neuronal subsets (Fig 3D).

Conclusion: These data reveal a rapid, injury-induced neuroinflammatory synovial response concomitant with transcriptional programs indicative of neuronal plasticity in the DRG. Putative synovium-DRG interactome analysis implicated pathways such as NGF and sema-plex as potential axes of synovium-DRG crosstalk underlying injury-induced nociceptor sprouting.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

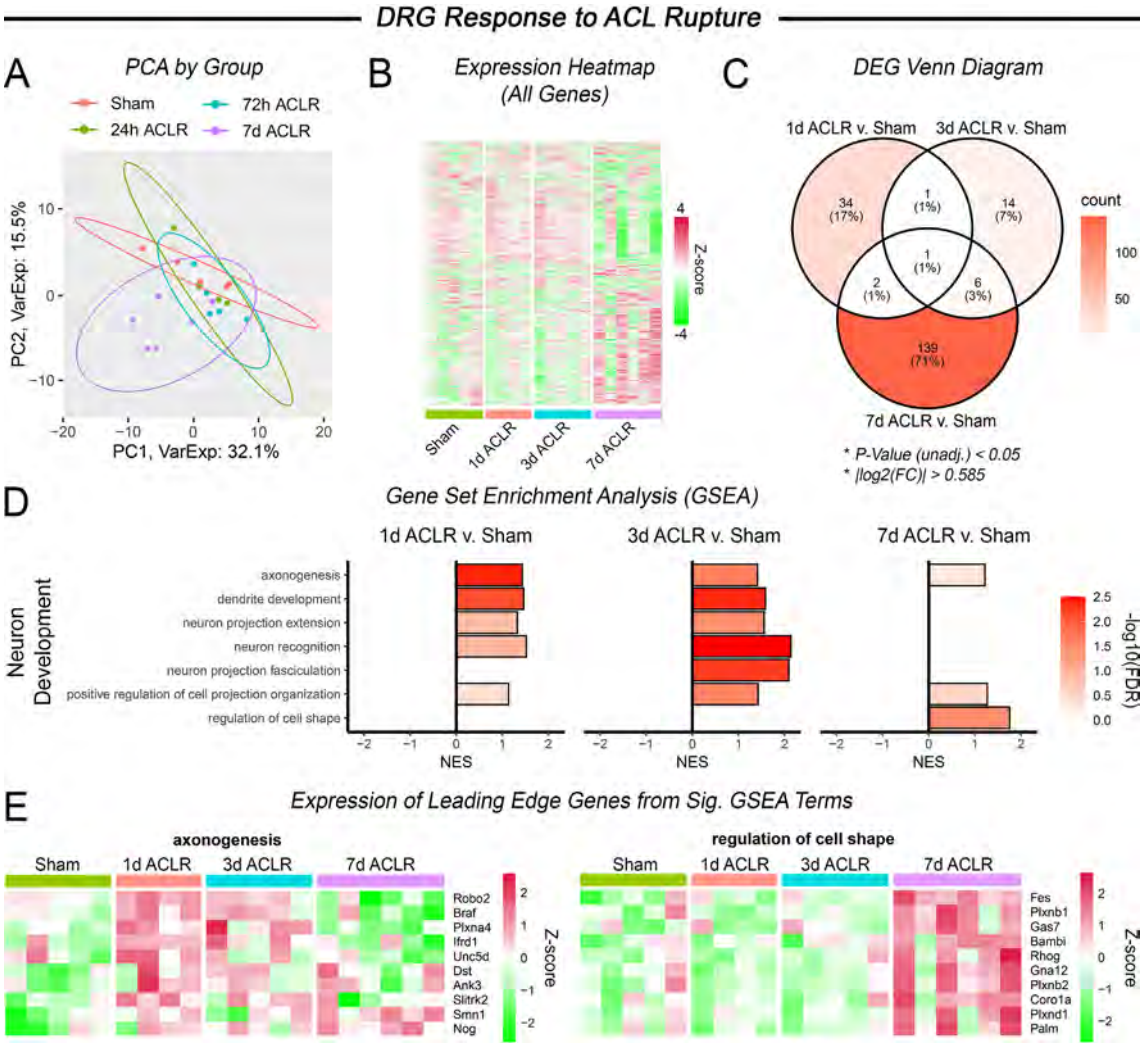


Figure 2. DRG response to ACL rupture (A) PCA plot. (B) Heatmap of expression across all genes. (C) Venn diagram of DEG overlap between time-points. (D) Significant GSEA terms related to neuron sprouting and synapse regulation (E) Expression of leading-edge genes from significant GSEA terms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

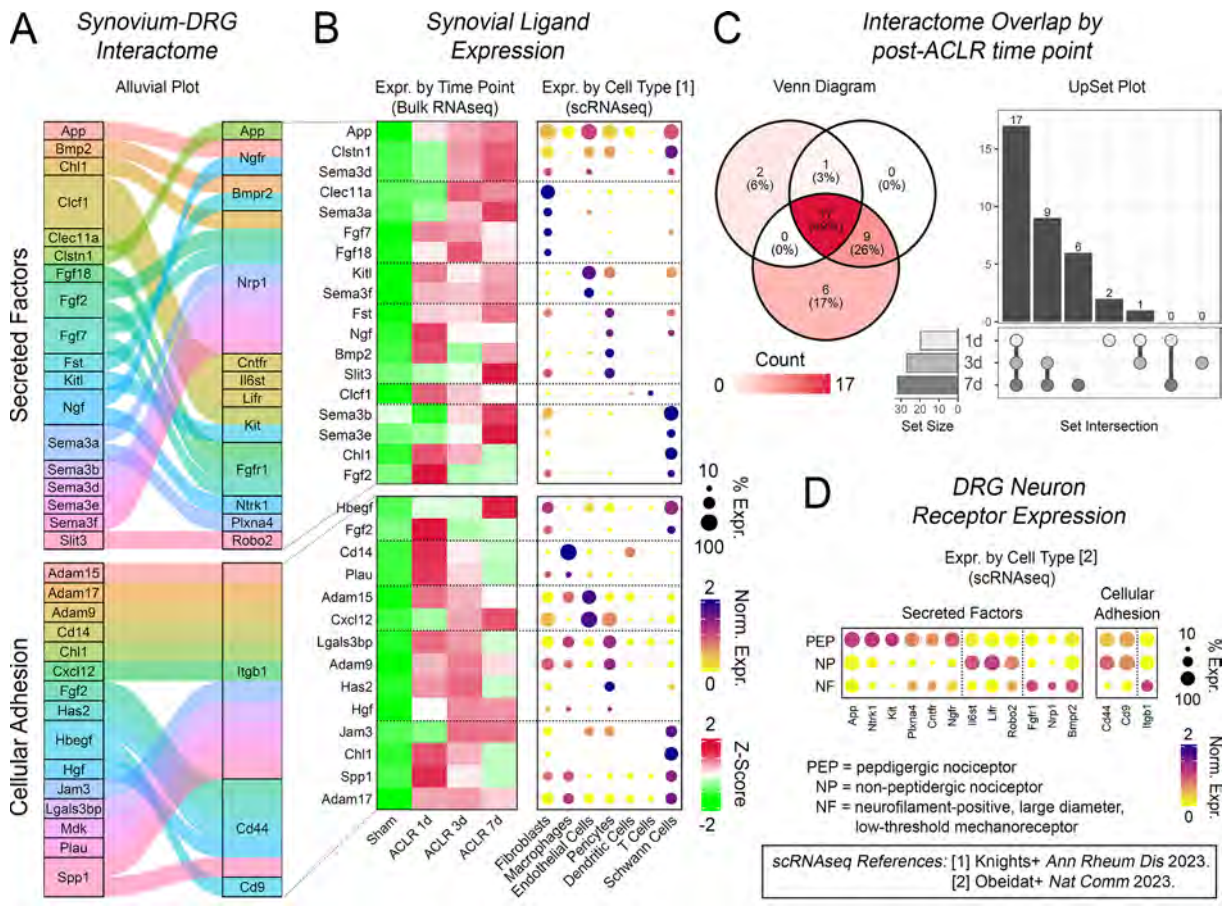


Figure 3. Synovium-DRG interactome. (A) Alluvial plots showing potential interactions between significantly injury-upregulated, secreted synovial ligands and membrane-bound, DRG neuron-derived receptors. (B) Synovial ligand expression by post-injury time point and cell type, generated using a reference scRNAseq dataset of murine synovium. (C) Overlap in interactions by post-injury timepoint. (D) DRG neuron expression by neuron subset, generated using a reference scRNAseq dataset of murine DRG.

Disclosure: M. Newton: None; **L. Wang**: None; **A. Malfait**: Eli Lilly, 5, Merck, 2, Novartis, 2, Orion, 5, Roivant, 2; **R. Miller**: None; **T. Maerz**: None.

Abstract Number: 1740

A New Link Between Calprotectin, Cholesterol Efflux Dysfunction, and Premature Atherosclerosis in Juvenile Dermatomyositis

Emily Chong[1], Kavya Sugur[2], Sophia Matossian[1], Katarina Kmetova[3], Christine Goudsmit[4], Jessica Turnier[5] and Yu (Ray) Zuo[1], [1]University of Michigan, Ann Arbor, MI, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Ann Arbor, MI, [3]Division of Rheumatology, University of Michigan, Ann Arbor, Michigan, USA, Ann Arbor, MI, [4]University of Michigan, Ann Arbor, [5]University of Michigan, Saline, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Pediatric Rheumatology – Clinical II (1740–1745)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Adults with dermatomyositis face a well-established 2–3-fold increased risk of major adverse cardiovascular events, driven by systemic inflammation, endothelial dysfunction, and treatment-related metabolic complications. In contrast, cardiovascular risk in juvenile dermatomyositis (**JDM**) remains poorly defined, despite a higher prevalence of clinical vasculopathy in children and emerging evidence that early, severe vasculopathic skin involvement is linked to cardiovascular dysfunction. Our previous work identified circulating calprotectin—a marker of neutrophil activation and NET formation—as a predictor of future cardiovascular disease (**CVD**) and a correlate of impaired HDL function in the general population. Notably, many JDM patients have elevated calprotectin levels. This study aimed to evaluate HDL function and early atherosclerotic risk in JDM and to investigate their potential association with calprotectin.

Methods: We assessed cholesterol efflux capacity (**CEC**, a measure of HDL function) in HDL-rich (apoB-depleted) plasma from 51 JDM patients and 24 pediatric controls without systemic autoimmune disease (**Fig. 1A**). We also measured plasma paraoxonase-1 (**PON1**) activity, an indicator of oxidative stress and HDL dysfunction linked to future CVD risk, and conducted a foam cell formation assay to evaluate plasma-driven fatty acid uptake, where greater uptake reflects a more pro-atherogenic profile.

Results: Compared to pediatric controls, JDM patients exhibited significantly impaired CEC and reduced PON1 activity (**Fig. 1B–C**), consistent with dysfunctional HDL. CEC was inversely correlated with fatty acid uptake in a foam cell assay ($r = -0.39$, $p = 0.0045$), indicating a shift toward a more pro-atherogenic state marked by increased lipid accumulation in macrophages. Among JDM patients, those with elevated circulating calprotectin had significantly lower CEC and PON1 activity (**Fig. 2A–B**), linking neutrophil activation and NET-associated inflammation to HDL dysfunction. Reduced CEC also correlated with clinical markers of disease activity, including elevated muscle enzymes such as creatine phosphokinase (CPK; $r = -0.35$, $p = 0.012$) and aspartate aminotransferase (AST; $r = -0.28$, $p = 0.046$), suggesting an association between active myositis and impaired vascular protection. Notably, JDM patients receiving immunomodulatory therapy

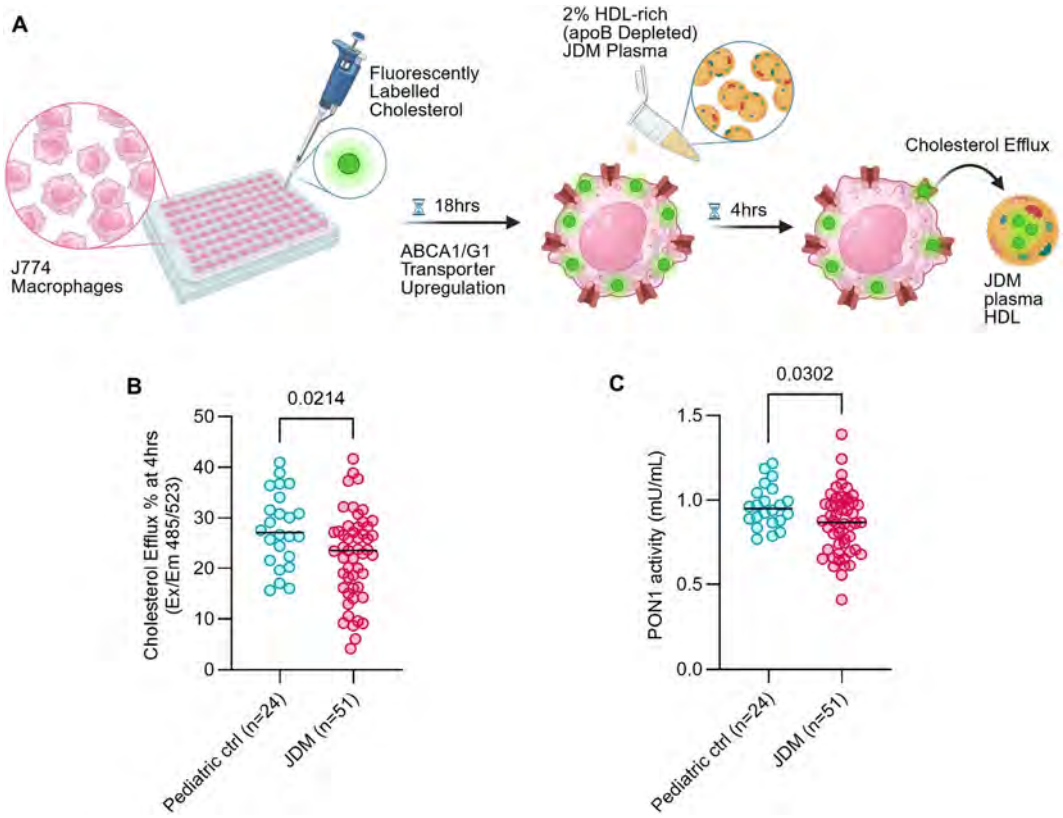


Figure 1: Impaired cholesterol efflux capacity (CEC) and reduced PON1 activity among JDM patients. A, Schematics of CEC assay. B, % CEC in JDM patients versus pediatric controls. C, Plasma PON1 Activity (mU/mL) in JDM patients compared to pediatric controls.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

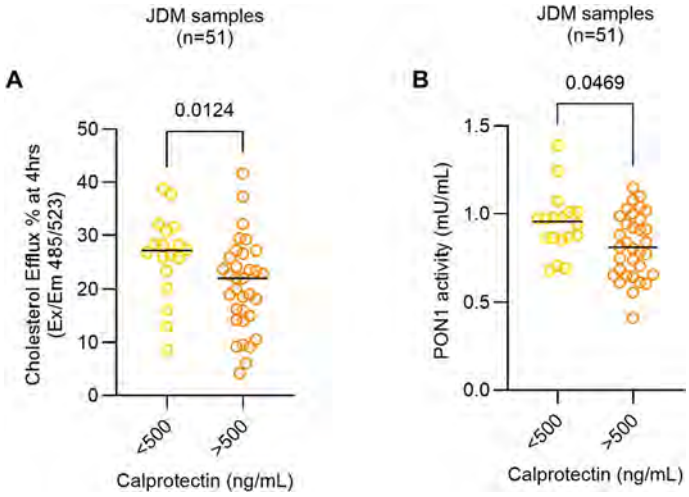


Figure 2: JDM patients with elevated calprotectin levels exhibit impaired cholesterol efflux capacity and decreased PON1 activity. A, % CEC and B, Plasma PON1 Activity (mU/mL) in JDM patients with high calprotectin levels (>500 ng/mL) compared to those with low calprotectin levels (<500 ng/mL).

(e.g., methotrexate) had significantly higher CEC than untreated patients ($p = 0.04$), raising the possibility that such treatments may help preserve or restore HDL function and vascular health beyond their anti-inflammatory effects.

Conclusion: JDM patients demonstrate marked HDL dysfunction that correlates with both heightened calprotectin levels and disease activity, underscoring a link between inflammation and early atherogenic risk. These findings support the importance of early cardiovascular surveillance and proactive management strategies in JDM patients, also highlighting the critical need to develop biomarkers of vascular health in children with JDM.

Disclosure: E. Chong: None; **K. Sugur**: None; **S. Matossian**: None; **K. Kmetova**: None; **C. Goudsmit**: None; **J. Turnier**: Cabaletta Bio, 2; **Y. Zuo**: None.

Abstract Number: 1741

Chronic JDM Plasma Proteomic Signature Reflects Inflammation from Immune and Tissue-resident Muscle and Skin

Marianne Kerski[1], Celine Berthier[1], Benjamin Klein[1], Li Chen[2], Christine Goudsmit[2], Sophia Matossian[1], Qinmengge Li[3], Chioma Madubata[4], Jessica Neely[5], J. Michelle Kahlenberg[1] and Jessica Turnier[6], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, [3]University of Michigan, Ypsilanti, MI, [4]UCSF, SF, CA, [5]UCSF, San Francisco, CA, [6]University of Michigan, Saline, MI

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical II (1740–1745)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Juvenile dermatomyositis (JDM) and childhood-onset SLE (cSLE) are systemic autoimmune diseases characterized by overlapping yet distinct clinical manifestations and treatment responses. In this study, we evaluate unique signatures in JDM using multi-omic approaches of plasma proteomics and single cell resolution tissue transcriptomics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

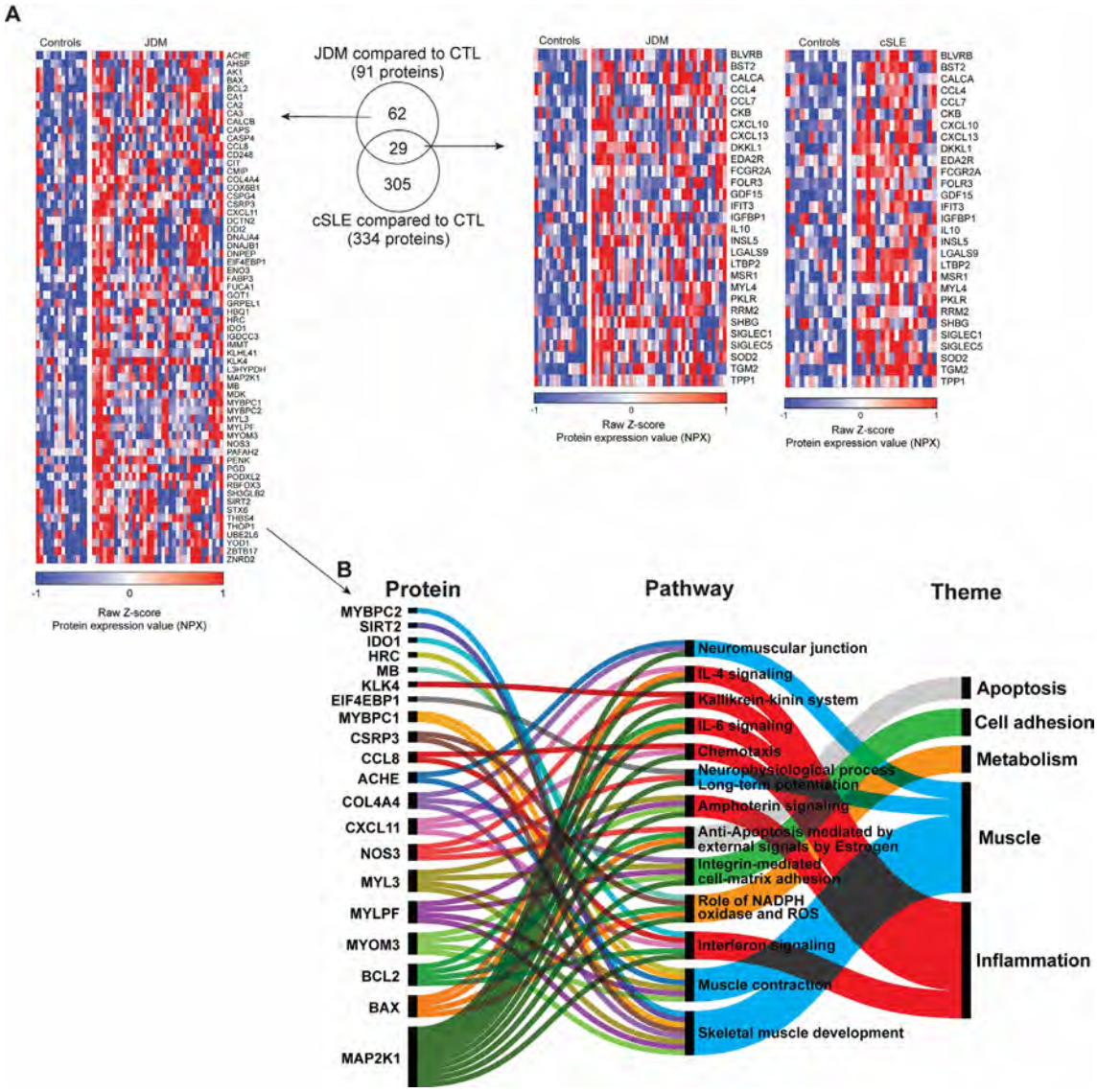


Figure 1. Comparison of plasma proteomic signature in JDM vs. cSLE highlights altered muscle signaling in JDM and shared interferon and innate immune signature with cSLE. A.) Venn Diagram highlighting number of differentially regulated proteins (DRPs) in each JDM (n=36) and cSLE (n=18) relative to CTL (n=14), with heatmap on left demonstrating 62 DRPs unique to JDM vs. CTL comparison and heatmap on right highlighting 29 DRPs in common between each JDM and cSLE relative to CTL. In the heatmaps, each column represents an individual patient sample while each row represents a DRP, with color indicating NPX z-score expression of each protein. B.) Alluvial plot showing biological pathways and associated proteins regulated in JDM.

Methods: Plasma protein levels were measured using the Olink® Explore 3072 panel in 36 JDM, 18 cSLE and 14 controls (CTL). All JDM and cSLE met EULAR/ACR classification criteria. Differential expression analysis identified differentially regulated proteins (DRPs) (false discovery rate (FDR)< 0.10) in (1) all JDM, (2) all cSLE and (3) treatment naïve (TN) JDM (n=6) relative to CTL. Regulated pathways were assessed using MetaCore™ (FDR< 0.10). Pearson correlation evaluated association of DRPs with global and organ-specific JDM disease activity measures (p< 0.05). We further evaluated candidate disease activity-associated DRPs by analyzing cell-type specific RNA expression of genes encoding the DRPs in a JDM single-nucleus transcriptomic dataset from muscle (n=6) and single-cell transcriptomic datasets from skin (n=12) and blood (n=5).

Results: We identified 91 DRPs in JDM and 334 in cSLE, of which 29 DRPs overlapped in JDM and cSLE **(Fig 1A)**. 62 DRPs were unique to JDM, representing five biological pathway themes, including skeletal muscle development and contraction, inflammation, apoptosis, metabolism and cell adhesion **(Fig 1B)**. In TN JDM vs. CTL, 962 DRPs were identified, with

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

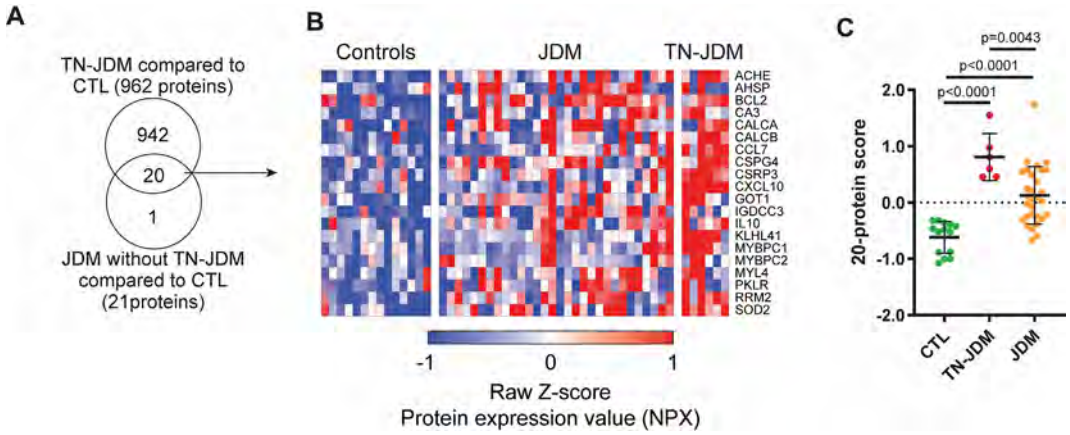


Fig 2. Identification of 20 common differentially regulated proteins (DRPs) in both treatment naïve (TN) and chronic JDM. A.) Venn diagram displaying number of DRPs in each TN JDM (n=6) and chronic JDM (n=30) relative to CTL (n=14). B.) Heat map demonstrating NPX z-score expression of the 20 common DRPs in each TN and chronic JDM samples. C.) Protein expression score of the 20 common DRPs in TN JDM, chronic JDM and CTL samples. Protein expression score is higher in both TN and chronic JDM compared to CTL.

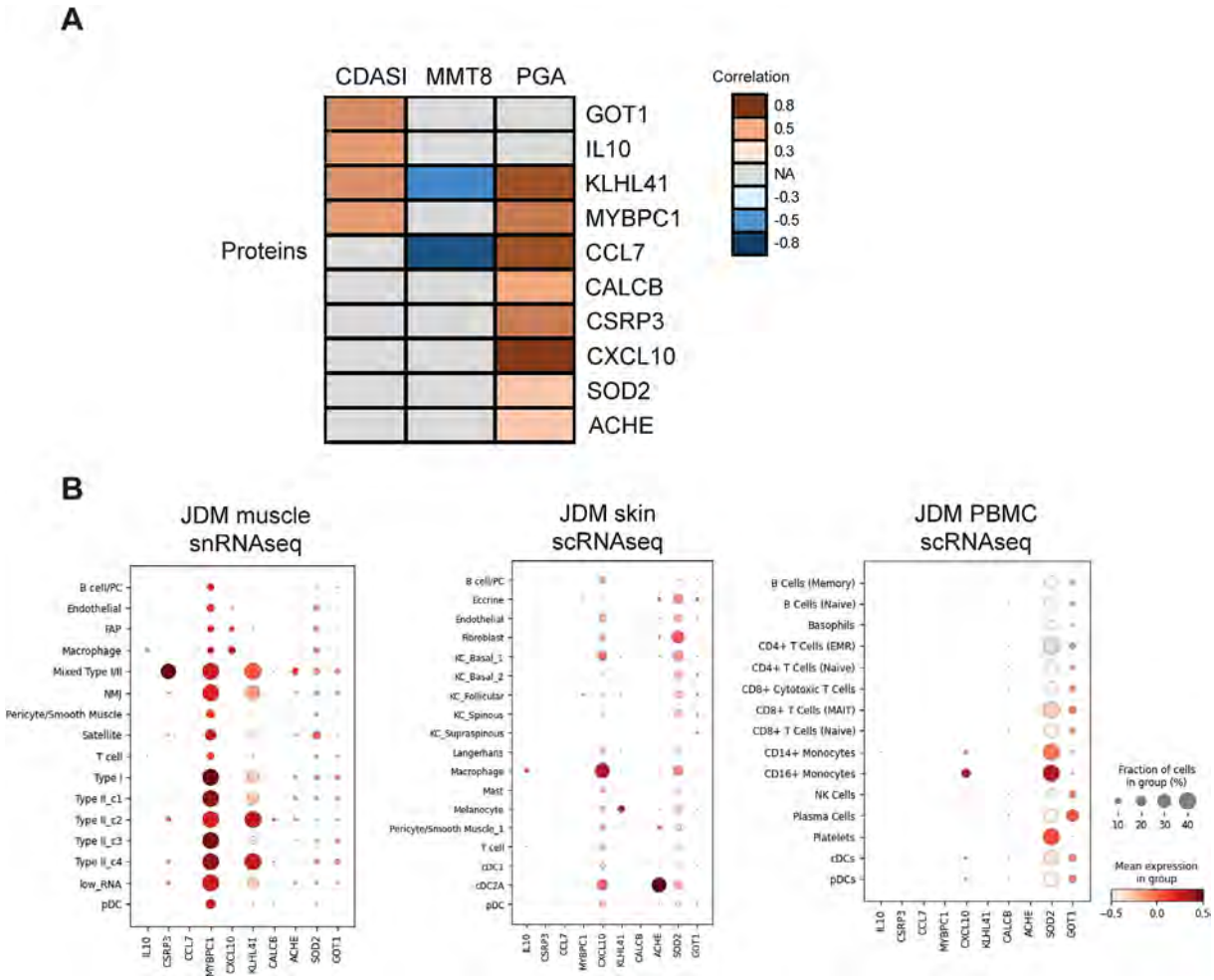


Fig 3. Ten differentially regulated proteins in chronic JDM also display association with JDM disease activity measures. A.) Pearson correlation of ten DRPs from chronic JDM with JDM disease activity measures for skin (Cutaneous Dermatomyositis Disease Area and Severity Index; CDASI activity score), muscle (Manual Muscle Testing; MMT-8 scores) and global (Physician's Global Activity Assessment; PGA scores) disease activity ($p<0.05$). B.) Dot plots displaying normalized and scaled gene expression (indicated by color) and percent of cells (indicated by size of dot) expressing the ten candidate markers in three additional datasets: single-nuclei RNA-sequencing data from muscle (n=6 JDM), single-cell RNA-sequencing data from skin (n=12 JDM) and treatment naïve peripheral blood mononuclear cells (PBMCs) (n=5 JDM).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

neutrophil degranulation, IL-10 and death receptor signaling representing top biological pathways. To identify a chronic JDM signature, we analyzed DRPs in non-TN JDM, which resulted in 21 DRPs **(Fig 2A,B)**, including both immune signaling (IL-10, CCL7, CXCL10) and muscle and metabolism-associated (CSRP3, MYBPC1, KLHL41, CALCB, ACHE, SOD2, GOT1). A protein expression score incorporating the 20 overlapping proteins from chronic and TN JDM was higher in JDM versus CTL ($p< 0.05$) **(Fig 2C)**. Ten of these chronically elevated DRPs correlated with JDM disease activity measures **(Fig 3A)**. Upon evaluation of cell-type specific, single-cell expression of these ten markers, we identified a predominant tissue-based origin, with only CXCL10, SOD2 and GOT1 exhibiting expression in circulating immune cells (**Fig 3B**). Interestingly, IL-10 displayed specific expression only in skin and muscle tissue macrophages, while CXCL10 exhibited widespread expression, including circulating CD14 and CD16+ monocytes and resident muscle and skin populations (FAPS, ECs, basal keratinocytes, fibroblasts) **(Fig 3B)**.

Conclusion: JDM as compared to cSLE demonstrated increased expression of proteins associated with myogenesis and metabolism. We identified a chronic disease signature in JDM, which included DRPs associated with metabolism (GOT1, SOD2), myogenesis/muscle structure (KHL41, CSRP3, MYBPC1), and immune dysregulation (CXCL10, IL10, CCL7). The majority of chronic DRPs in JDM, including DRPs specific to immune cells, exhibited higher gene expression in tissue, highlighting the need for further tissue-based studies in JDM to identify targeted therapies and biomarkers.

Disclosure: M. Kerski: None; **C. Berthier**: None; **B. Klein**: None; **L. Chen**: None; **C. Goudsmit**: None; **S. Matossian**: None; **Q. Li**: None; **C. Madubata**: None; **J. Neely**: None; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5; **J. Turnier**: Cabaletta Bio, 2.

Abstract Number: 1742

S100B in Childhood-onset Systemic Lupus Erythematosus: Associations with Disease Features, Interferon Levels, and Cognitive Functioning

Ganesh Ramanathan[1], Justine Ledochowski[2], Oscar Mwizerwa[3], Tala El Tal[4], Lawrence Ng[5], Asha Jeyanathan[6], Adrienne Davis[6], Ann Yeh[6], Linda Hiraki[2], Deborah Levy[2], Zahi Touma[7], Joan Wither[8], Busisiwe Zapparoli[9], Ashley Danguecan[10] and Andrea Knight[10], [1]The Hospital for Sick Children, Brampton, ON, Canada, [2]The Hospital for Sick Children, Toronto, ON, Canada, [3]University of Toronto, The Hospital for Sick Children, Toronto, ON, Canada, [4]Children's Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada, [5]The Hospital for Sick Children, Toronto, Canada, Toronto, ON, Canada, [6]The Hospital for Sick Children, Toronto, Canada, [7]University of Toronto, Toronto, ON, Canada, [8]University Health Network, Toronto, ON, Canada, [9]The Hospital for Sick Children, Etobicoke, ON, Canada, [10]Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical II (1740–1745)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Cognitive impairment is common in childhood-onset systemic lupus erythematosus (cSLE), particularly in domains like executive function and attention. However, attributing cognitive difficulties to brain inflammation—such as interferon (IFN)-mediated processes in cSLE—remains challenging. Neuroglial proteins are potential biomarkers of brain injury and cognitive impairment in cSLE. S100B is a calcium-binding signaling protein produced by astrocytes that reflects acute brain injury. Elevated levels of S100B and related S100 proteins have been reported in patients with neuropsychiatric lupus (NPSLE) and cognitive impairment but remain understudied in pediatric populations. We compared serum S100B

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

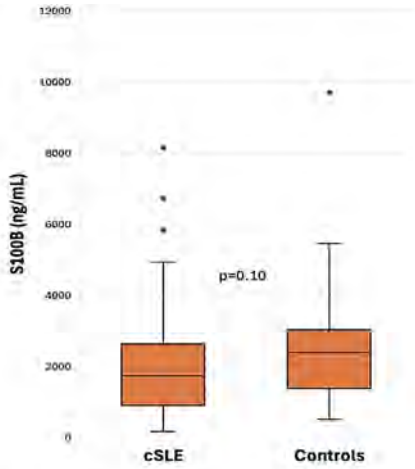


Figure 1: Boxplot showing group differences in serum S100B level between cSLE and controls. Boxes represent median and IQR; whiskers extend to 1.5×IQR below Q1 and above Q3. Using Wilcoxon Rank Sum Test, no significant differences were observed.

Figure 1: Boxplot showing comparison of serum S100B level between cSLE and controls.

Table 1: Relationship between S100B, Disease Characteristics, and Interferons in cSLE (n=49)

Table 1: Relationship between S100B, Disease Characteristics, and Interferons in cSLE (n=49)

	SLEDAI-2K at Study Visit	SDI	Current GC Dose	Cumulative GC Exposure	IFN-α	IFN-γ
S100B	r = -0.10 p = 0.514	r = 0.22 p = 0.124	r = 0.20 p = 0.168	r = -0.07 p = 0.617	r = -0.30 **p = 0.039**	r = -0.35 **p = 0.014**

Shown are Spearman correlations analyzing relationships between S100B, cSLE disease features, and serum-IFN levels. Statistically significant correlations are bolded ($p<0.05$).

Table 2: Correlations between S100B and Cognitive Measures in cSLE (n=49)

Table 2: Correlations between S100B and Cognitive Measures in cSLE (n=49)

	Inhibition	Inhibition Switching	Digit Span	Omissions	Commissions	Hit Reaction Time
S100B	r = 0.07 p = 0.643	r = 0.02 p = 0.904	r = -0.07 p = 0.639	r = 0.12 p = 0.423	r = 0.13 p = 0.377	r = 0.09 p = 0.545

Shown are Spearman correlations analyzing relationships between S100B and cognitive measures in cSLE. The cognitive domains tested include cognitive inhibition and mental flexibility using Delis-Kaplan Executive Function System Color Word Interference Test (inhibition, inhibition/switching scaled scores), working memory using Wechsler Adult Intelligence Scale IV or Wechsler Intelligence Scale for Children V (digit span scaled score), and attention using Conners Continuous Performance Test 3 (omissions, commissions, hit reaction time t-scores).

levels between children with cSLE and controls, and investigated its relationship with cSLE disease features, serum-IFN levels, and cognitive functioning.

Methods: Cross-sectional data were prospectively collected from cSLE participants (ages 12-17 years) meeting ACR classification criteria for SLE, recruited from the Lupus Clinic at a Canadian tertiary children's hospital from Jan 2020–Dec 2023 and age-, sex-matched healthy controls. S100B, IFN-α and IFN-γ serum levels were quantified using their respective Simoa assays (Quanterix, Billerca, MA, USA). Disease features included disease activity (SLEDAI-2K), damage (SLICC damage index, SDI >0), glucocorticoid (GC) dose at study visit, and cumulative GC exposure (prednisone-equivalent). Assessment of cognitive function domains included: cognitive inhibition and mental flexibility using Delis-Kaplan Executive Function System Color Word Interference Test (inhibition, inhibition/switching), working memory using Digit Span from the Wechsler Adult Intelligence Scale IV/Wechsler Intelligence Scale for Children V, and attention using Conners Continuous Performance Test

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3 (omissions, commissions, hit reaction time). Wilcoxon rank sum test compared S100B levels; Spearman correlations tested associations.

Results: 49 cSLE participants (mean age=15.2±1.8 years, 90% female) and 40 controls (mean age=15.3±1.7 years, 80% female) were included. For cSLE, median disease duration was 25.1 months (IQR 13.3-46.2), median SLEDAI-2K was 2.0 (IQR 2.0-4.0), 10% had disease damage, 41% were using glucocorticoids at study visit, and median cumulative GC exposure was 2.3 grams (IQR 0.6-7.0). One patient had a NPSLE diagnosis. There were no group differences in serum S100B levels between cSLE and controls (median 1714.9 vs 2369.4 ng/mL; Figure 1). In cSLE, S100B showed positive but non-significant correlations with SDI and current GC dose (Table 1). Significant inverse associations were observed between S100B and both IFN-α and IFN-γ (Table 1). No correlations were found between S100B and cognitive test performance (Table 2).

Conclusion: In cSLE, serum S100B was not associated with cognitive functioning and did not differ from controls, contrasting prior findings in adult SLE. Inverse associations with type I and II IFNs suggest a potential downregulation of this protein in IFN-driven inflammation, perhaps during the early stages of brain inflammation. Future studies will examine these relationships longitudinally in larger cSLE cohorts.

Disclosure: G. Ramanathan: None; **J. Ledochowski**: None; **O. Mwizerwa**: None; **T. El Tal**: None; **L. Ng**: None; **A. Jeyanathan**: None; **A. Davis**: None; **A. Yeh**: Alexion, 5, Novartis, 5, Pfizer, 2, Roche, 1, 5, WIRB-Copernicus Group, 12, DSMB; **L. Hiraki**: Janssen, 2, 5; **D. Levy**: AbbVie/Abbott, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Roche, 5; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **J. Wither**: None; **B. Zapparoli**: None; **A. Danguecan**: None; **A. Knight**: Pfizer, 6.

Abstract Number: 1743

Comparative assessment of cardiovascular risk and its predictors in a large cohort of young adults with juvenile systemic lupus erythematosus and juvenile dermatomyositis

Jiangning Li, Shreya Doddi, Tharuni Mailoo and **Coziana Ciurtin**, University College London, London, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical II (1740–1745)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Juvenile systemic lupus erythematosus (JSLE) and juvenile dermatomyositis (JDM) are associated with chronic inflammation that can accelerate atherosclerosis. There is no specific guidance regarding the best way to stratify adolescents/young adults (AYA) based on cardiovascular disease (CVD)-risk for personalised management.

Objective: To evaluate the performance of validated CVD-risk scores in JSLE/JDM, comparing risk prediction with long term atherosclerotic burden indicators.

Methods: A retrospective cohort analysis of 155 AYA with JSLE (n=76) and JDM (n=79) using descriptive statistics/regression analysis was conducted. CVD-risk was assessed at last follow-up using validated adult scores: Framingham Risk Score (FRS), Atherosclerotic Cardiovascular Disease (ASCVD) and QRISK3, and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) score (validated from age 14).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: AYA with JSLE vs. JDM were 84% vs.72% females (P=0.08), 60% vs. 29% Non-White (P < 0.001), with age at last follow-up of 22.3±5.4 vs.18.3±5.5 years (P < 0.001), and median age at disease onset 13.0 (11-16) and 7.5 (5-10) years (P < 0.001). At last assessment, AYA with JSLE had more hypertension (13% vs. 3%, P=0.02), and higher total cholesterol (P=0.01) and LDL-cholesterol (P=0.02) levels compared to JDM, while there were no differences in BMI, smoking or diabetes prevalence. The cumulative dose of steroids was higher in JSLE vs. JDM (P < 0.001).

The PDAY score was the only one with adequate performance, stratifying 43.5% and 32.8% of JSLE patients as 'high' and 'very high' risk, respectively, while only 15% of AYA with JDM were classified as 'high' risk (P < 0.001). PDAY scores remained significantly higher in JSLE vs. JDM after adjusting for age/disease duration (P < 0.001). PDAY did not correlate with FRS, ASCVD or QRISK3 scores in either cohort.

When last visit was dichotomized by any major flare, AYA with active JSLE or damage (PedSDI >1) had higher PDAY score (mean 11 vs. 7, P=0.004, and mean 10 vs. 6, P=0.02, respectively). In a multivariable logistic model, four independent predictors of high CVD-risk were identified in JSLE: older age (OR ∼1.5 per 5-year increase, P=0.03), longer disease duration (OR ∼1.4 per 5-year increase, P=0.04), higher LDL level (OR ∼2.0 per 1 mmol/L increase, P=0.02), and presence of active JSLE (OR ∼3.3 for any BILAG A vs. no BILAG A flare at last visit, P=0.01). Too few AYA with JDM had 'high' CVD-risk based on PDAY score for robust modeling; all were males (N=12), one was an ex-smoker and N=9 had low HDL-cholesterol during active disease. None of the typical JDM features (muscle enzyme levels, MMT8 score or CDASI skin disease score) showed an association with PDAY, supporting that traditional factors drove the high CVD-risk observed in JDM.

Conclusion: Traditional 10-year CVD-risk assessments validated in adults consistently classified all AYA with JSLE and JDM as low risk, while PDAY score was the only one useful for risk stratification in AYA with JSLE/JDM. This study is the first to highlight higher CVD-risk in JSLE vs. JDM in young adulthood, after adjustment for age/disease duration, as well as disease-related factors driving high CVD-risk in JSLE compared to traditional ones in JDM in young adulthood.

Disclosure: J. Li: None; **S. Doddi**: None; **T. Mailoo**: None; **C. Ciurtin**: None.

Abstract Number: 1744

Preceding Mental Health Diagnosis Does Predict Eventual Neuropsychiatric Disease in Childhood-Onset Systemic Lupus Erythematosus

Ekemini Ogbu[1], Clare Treutel[1], Angela Merritt[2], Michael Wagner[1] and Hermine Brunner[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Childrens Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical II (1740–1745)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Childhood-onset Systemic Lupus Erythematosus (cSLE) affects approximately 1 in 10,000 children in the United States, with the estimated prevalence of childhood neuropsychiatric SLE (NPSLE) at 43 - 95%. Risk factors of NPSLE are poorly understood though NPSLE could severely impact cognitive development and long-term neurologic outcomes. Thus, identification of accurate predictors of increased NPSLE risk are greatly needed. The objective of our study

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1: Demographics of Study Population

	Unmatched Cohort			Matched Cohort		
	Total cohort (N = 8504) (n (%))	cSLE without NPSLE (N = 2624) (n (%))	cSLE with NPSLE (N = 5880) (n (%))	Total Cohort (N = 4626) (n (%))	cSLE without NPSLE (N = 2313) (n (%))	cSLE with NPSLE (N = 2313) (n (%))
Age at cSLE diagnosis in years (mean (SD))	13.69 (4.85)	13.2 (4.81)	13.9 (3.65)	13.45 (4.314)	13.1 (4.81)	13.8 (3.72)
Sex						
Female	5930 (69.73)	1920 (81.46)	4010 (83.86)	3781 (81.73)	1888 (81.63)	1893 (81.84)
Male	1188 (13.97)	432 (18.33)	756 (15.98)	835 (18.05)	420 (18.16)	415 (17.94)
Race						
White	2766 (32.53)	905 (38.40)	1861 (38.92)	1807 (39.06)	905 (39.13)	902 (39.00)
Black or African American	1671 (19.65)	414 (17.57)	1257 (26.29)	833 (18.01)	414 (17.90)	419 (18.12)
Asian	852 (10.02)	336 (14.26)	516 (10.79)	673 (14.55)	334 (14.44)	339 (14.66)
Other	696 (8.18)	248 (8.99)	448 (9.36)	447 (9.66)	221 (9.42)	226 (9.62)
Unknown	1167 (13.72)	467 (20.78)	700 (14.64)	872 (18.85)	442 (19.11)	430 (18.60)
Ethnicity						
Hispanic	1510 (17.76)	390 (16.55)	1120 (23.42)	777 (16.80)	390 (16.86)	387 (16.73)
Not Hispanic	4230 (49.74)	1332 (56.51)	2898 (60.60)	2664 (57.59)	1332 (57.59)	1332 (57.59)
Ethnicity	1399 (16.45)	635 (26.94)	764 (15.98)	1185 (25.62)	591 (25.55)	594 (25.68)

Abbreviations: cSLE = Childhood-onset Systemic Lupus Erythematosus, NPSLE = Neuropsychiatric Lupus

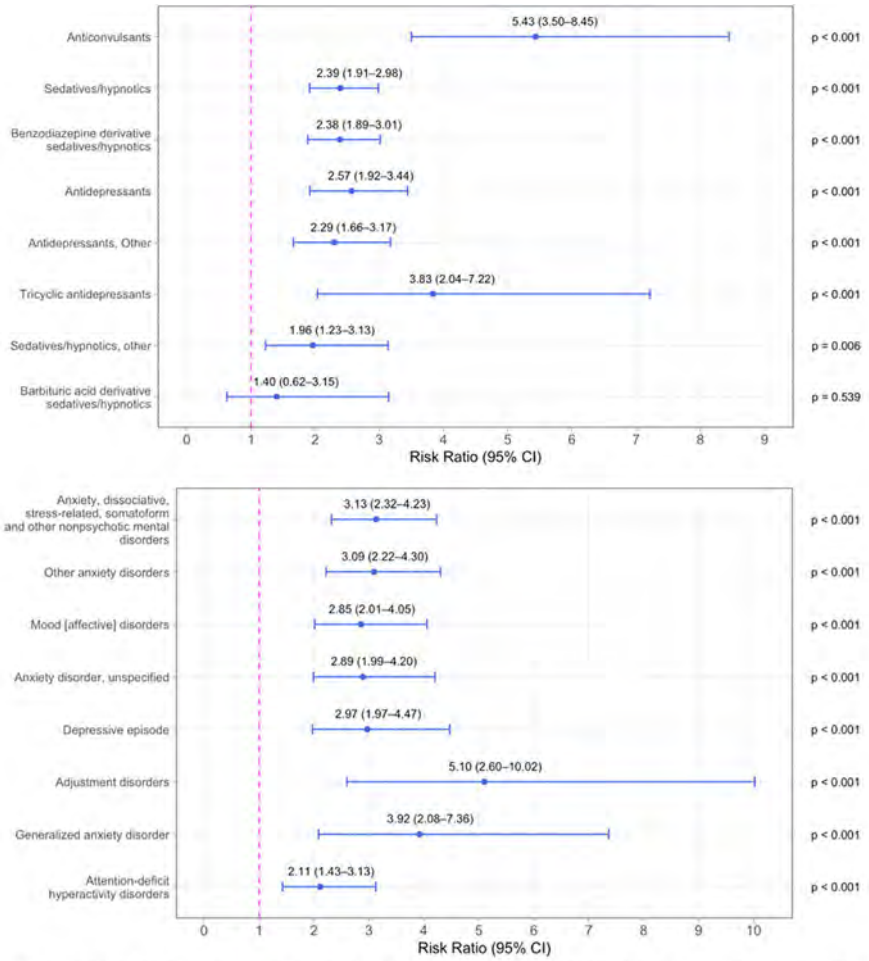


Figure 1: Risk of NPSLE occurrence in relation to premorbid mental health diagnosis or prescription any time prior to cSLE diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

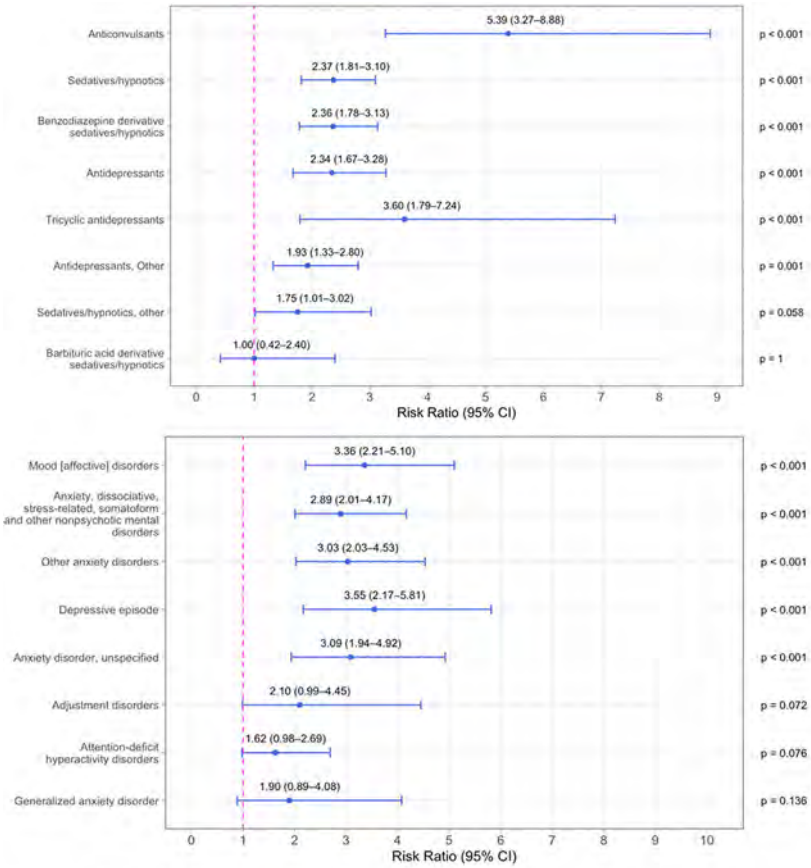


Figure 2: Risk of NPSLE occurrence in relation to premorbid mental health diagnosis or prescription within 18 months prior to cSLE diagnosis.

Figure 2: Risk of NPSLE occurrence in relation to premorbid mental health diagnosis or prescription within 18 months prior to cSLE diagnosis.

was to understand whether premorbid mental health history predicted neuropsychiatric disease in cSLE. We hypothesized that mental health diagnoses and prescriptions occurring before cSLE diagnosis are predictive of future NPSLE.

Methods: Retrospective case-control study using a federated patient database (TriNetX Research network). We included patients aged ≤18 years at first SLE diagnosis between January 2014 and April 2025. We defined NPSLE using the 19 American College of Rheumatology classified neuropsychiatric syndromes with corresponding ICD-10 codes. Premorbid mental health diagnosis was defined as a neuropsychiatric diagnosis any time up to one day before initial SLE diagnosis using specific ICD-10 codes [(i.e. mood disorders (F30 - 39), depression (F32), anxiety disorders (F40 – 48; F41, F41.1, F41.9), adjustment disorders (F43.2) and attention deficit hyperactivity disorder (F90)]; and prescriptions using Veterans Affairs National Drug File (VA NDF) codes (CN300, CN301, CN302, CN309, CN400, CN600, CN601, CN609). The risk of NPSLE occurrence in relation to premorbid mental health diagnosis or prescription was analyzed over 2 time periods: (a)18-months and (b) total observation period, prior to SLE diagnosis. Propensity score matching was based on patient sex and race, and regression analyses conducted for the risk of NPSLE compared between cases and controls.

Results: The total TriNetX population queried included approximately 140 million patients from 102 healthcare organizations . A total of 8504 cSLE patients (5,880 cSLE patients with NPSLE and 2,624 without NPSLE) were identified. After propensity matching by sex, ethnicity, and race, 2,313 patients were included in each cohort (Table 1). Premorbid diagnosis of mood disorders, depression and anxiety disorders within 18 months prior to cSLE diagnosis were associated with > 2-fold risk of subsequent NPSLE (RR: 3.4, 3.6, 3.0; all $p < 0.05$. Similarly, the risk of developing NPSLE was increased with a diagnosis of mood disorders, depression, anxiety and attention-deficit hyperactivity disorder at

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

any time point prior to cSLE diagnosis (RR: 2.9, 3.0, 3.0,2.1; all $p < 0.05$). History of use of anticonvulsant, antidepressants and sedatives within 18 months or at any time prior to cSLE diagnosis was also associated with increased risk of subsequent NPSLE. (Figures 1 & 2).

Conclusion: Preceding mental health diagnoses predict future neuropsychiatric disease in cSLE. Further research is needed to understand earlier clinical, laboratory and neuroimaging indicators of NPSLE development to delineate surveillance measures and interventions.

Disclosure: E. Ogbu: Cartesian Therapeutics, 2; **C. Treutel**: None; **A. Merritt**: None; **M. Wagner**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2.

Abstract Number: 1745

High Emotional Distress Predicts Suboptimal Cardiovascular Health Among Patients with Juvenile-Onset Lupus and Dermatomyositis: Longitudinal Analysis of the Lupus Erythematosus and Dermatomyositis Stress and Cardiovascular Health Cohort Study

Kaveh Ardalan[1], Angel Davalos[1], Hwanhee Hong[1], Bryce Reeve[1], Christoph Hornik[1], M. Anthony Moody[1], Donald Lloyd-Jones[2], Eveline Wu[3], Audrey Ward[4], Simisola Gbadegesin[5], Rebecca Sadun[6], Jeffrey Dvergsten[7], Lauren Covert[1], Ann Reed[1], Mark Connelly[8] and Laura Schanberg[9], [1]Duke University School of Medicine, Durham, NC, [2]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, [3]UNC Chapel Hill, Chapel Hill, NC, [4]Children's National Hospital, Washington, DC, [5]Wake Forest University School of Medicine, Winston-Salem, NC, [6]Duke University, Durham, NC, [7]Duke University Hospital, Hillsborough, NC, [8]Children's Mercy Kansas City/University of Missouri-Kansas City School of Medicine, Kansas City, MO, [9]Duke University Medical Center, DURHAM, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Pediatric Rheumatology – Clinical II (1740–1745)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Juvenile lupus & dermatomyositis (JSLE/JDM) patients experience high emotional distress and premature loss of cardiovascular health (CVH), defined as protective factors against cardiovascular disease (CVD). Although general pediatric studies show emotional distress is associated with worse CVH, the contribution of emotional distress to suboptimal CVH in JSLE/JDM has not been studied. We present longitudinal analyses from the Lupus Erythematosus & Dermatomyositis Stress & Cardiovascular Health (LEADS-CV) cohort, the first multicenter biopsychosocial study assessing emotional distress and CVH in JSLE/JDM.

Methods: Of 83 LEADS-CV participants (5-22yo), 72 with non-missing data on study measures at ≥1 study visit (baseline, 6 & 12 months) were included for analysis. Emotional distress measures included PROMIS® Pediatric Psychological Stress Experiences, Depressive Symptoms, and Anxiety (self-report in ≥8yo, parent-report in 5-7yo). CVH Behaviors (diet quality screener, self-report ≥12yo, parent-report < 12yo; PROMIS Pediatric Physical Activity self-report ≥8yo, parent-report 5-7yo) and CVH Factors (body mass index, blood pressure, non-HDL cholesterol, HbA1c) were assessed. CVH Summary (CVH-S, all 6 indicators), Behaviors (CVH-B), and Factors (CVH-F) scores were determined using AHA guidelines (0 = very poor, 100 = ideal). Linear mixed-effects models (LMMs) assessed associations of emotional distress and CVH-S/-B/-F,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of Baseline Visit Participant Characteristics for LEADS-CV Full Cohort Versus Analytic Sample

Table 1: Comparison of Baseline Visit Participant Characteristics for LEADS-CV Full Cohort Versus Analytic Sample

	n (%), Median (IQR)	
	LEADS-CV Full Cohort (n = 83)	**Analytic Sample (n = 72)**
Age (years)	16 (12-18)	16 (12-18.2)
Race & Ethnicity		
Non-Hispanic White	26 (31.3%)	25 (34.7%)
Any US Minority	57 (68.7%)	47 (65.3%)
Gender		
Female	66 (79.5%)	56 (77.8%)
Male	17 (20.5%)	16 (22.2%)
Diagnosis		
JSLE	48 (57.8%)	39 (54.2%)
JDM	35 (42.2%)	33 (45.8%)
Disease Activity		
Minimal (PGA < 1.5)	52 (62.7%)	47 (65.3%)
Active (PGA ≥ 1.5)	31 (37.3%)	25 (34.7%)
Steroid Dosage (mg/kg/day prednisone equivalent)		
Off steroids (0mg/kg/day)	45 (54.2%)	40 (55.6%)
Low dose steroids (≤0.15mg/kg/day)	15 (18.1%)	11 (15.3%)
Medium to high dose steroids (>0.15mg/kg/day)	23 (27.7%)	21 (29.2%)
Emotional Distress Measures		
PROMIS Psychological Stress Experiences	57.8 (50.7-64)	57.8 (50.7-64.3)
PROMIS Depressive Symptoms	54.9 (47-62.9)	55.3 (47.1-62.5)
PROMIS Anxiety	53.7 (46-61.4)	53.5 (46-61.5)
Cardiovascular Health Scores		
Cardiovascular Health Summary Score (CVH-S)	58.8 (60-76.9)	70 (60-77.5)
Cardiovascular Health Behavior Subscore (CVH-B)	45 (30-55)	45 (31.9-55)
Cardiovascular Health Factors Subscore (CVH-F)	81.2 (68.8-93.8)	85 (72.5-94.4)

Table 2: Linear Mixed-Effects Models (LMM) (n = 72 with 171 observations)

Table 2: Linear Mixed-Effects Models (LMM) (n = 72 with 171 observations)

	PROMIS Psychological Stress Experiences			PROMIS Depressive Symptoms			PROMIS Anxiety		
Predictors^	**CVH-S**	**CHV-B**	**CVH-F**	**CVH-S**	**CVH-B**	**CVH-F**	**CVH-S**	**CVH-B**	**CVH-F**
(Intercept)	**71.68 (62.32, 81.04)**	**58.34 (43.43, 73.24)**	**79.29 (66.83, 91.76)**	**71.94 (62.71, 81.18)**	**58.92 (44.27, 73.56)**	**79.56 (67.19, 91.93)**	**73.02 (63.72, 82.32)**	**58.34 (43.32 – 73.37)**	**81.26 (68.85, 93.66)**
PROMIS emotional distress measure T-score*	-0.09 (-0.28, 0.11)	-0.15 (-0.48, 0.18)	-0.09 (-0.35, 0.18)	-0.15 (-0.33, 0.03)	-0.25 (-0.56, 0.05)	-0.14 (-0.38, 0.09)	**-0.19 (-0.36, -0.02)**	-0.11 (-0.40, 0.18)	**-0.25 (-0.47, -0.02)**
6 mo	0.29 (-2.4, 2.97)	1.07 (-3.62, 5.75)	0.08 (-3.48, 3.64)	0.49 (-2.18, 3.16)	1.42 (-3.27, 6.16)	0.27 (-3.27, 3.82)	0.26 (-2.39, 2.9)	1.11 (-3.58, 5.80)	0.02 (-3.48, 3.52)
12 mo	**3.12 (0.38, 5.85)**	1.01 (-3.74, 5.77)	3.6 (-0.03, 7.23)	**3.14 (0.42, 5.86)**	1.06 (-3.67, 5.80)	**3.62 (0.01, 7.23)**	**2.74 (0.02-5.47)**	0.87 (-3.93, 5.66)	3.11 (-0.5, 6.71)
Active Disease (PGA ≥ 1.5)	**-4.85 (-8.25, -1.45)**	-3.33 (-9.12, 2.46)	**-4.73 (-9.24, -0.22)**	**-4.96 (-8.31, -1.61)**	-3.54 (-9.26, 2.18)	**-4.83 (-9.29, -0.37)**	**-4.74 (-8.08, -1.4)**	-3.47 (-9.25, 2.30)	**-4.52 (-8.95, -0.1)**
Current Steroid Use	-2.91 (-6.79, 0.97)	1.27 (-5.28, 7.81)	**-5.87 (-11.02, -0.72)**	-2.54 (-6.4, 1.33)	1.86 (-4.67, 8.38)	**-5.51 (-10.65, -0.36)**	-2.85 (-6.67, 0.98)	1.32 (-5.23, 7.87)	**-5.81 (-10.98, -0.74)**
Age**	-0.22 (-0.87, 0.43)	**-1.04 (-2.07, -0.01)**	0.24 (-0.82, 1.1)	-0.22 (-0.87, 0.42)	**-1.05 (-2.07, -0.03)**	0.24 (-0.82, 1.1)	-0.23 (-0.87, 0.41)	**-1.07 (-2.10, -0.04)**	0.23 (-0.82, 1.09)
Any US Minority Race and/or Ethnicity	-1.15 (-6.65, 4.35)	-7.55 (-16.25, 1.15)	1.92 (-5.41, 9.25)	-0.8 (-6.29, 4.68)	-6.92 (-15.56, 1.71)	2.25 (-5.1, 9.6)	-1.19 (-6.61, 4.24)	-7.76 (-16.46, 0.91)	1.94 (-5.31, 9.19)
Female Gender	1.46 (-4.92, 7.85)	1.45 (-8.68, 11.58)	0.47 (-8.04, 8.98)	1.5 (-4.74, 7.74)	1.58 (-8.26, 11.42)	0.52 (-7.85, 8.89)	1.5 (-4.88, 7.48)	0.71 (-9.19, 10.62)	0.48 (-7.78, 8.74)
Diagnosis - JDM	**6.13 (0.2, 12.06)**	0.61 (-8.78, 10.00)	**8.94 (1.03, 16.84)**	**6.25 (0.36, 12.14)**	0.77 (-8.50, 10.05)	**9.05 (1.16, 16.94)**	**6.17 (0.3, 12.04)**	0.69 (-8.71, 10.08)	**8.97 (1.13, 16.81)**

*PROMIS T-scores covariates are centered at 40
**Age (years) centered at 7y.o.
^Reference groups for binary predictors are as follows: 6 mo vs baseline visit reference group; 12 mo vs baseline visit reference group; Active Disease (PGA ≥ 1.5) vs Minimal/Inactive Disease (PGA < 1.5) reference group; Current Steroid Use vs Off Steroids reference group; Any US Minority Race and/or Ethnicity vs Non-Hispanic White reference group; Female Gender vs Male Gender reference group; Diagnosis JDM vs JSLE reference group

adjusted for gender, race/ethnicity, diagnosis, disease activity, steroid use, and time. Growth mixture models (GMMs) identified latent trajectories of emotional distress and CVH-S/-B/-F. Proportions of patients in CVH-S/-B/-F latent trajectories were compared across emotional distress latent trajectories.

Results: LMM results (Table 2) show JSLE and active disease are associated with lower CVH-S and CVH-F scores across all models. Higher PROMIS Anxiety is associated with lower CVH-S and CVH-F. Increasing age is associated with lower CVH-B . Across models, slightly higher CVH-S was estimated at the 12-month visit compared with baseline. Among patients with maximal (79.8) vs minimal (38.8) PROMIS Anxiety scores, estimated CVH-S and CVH-F scores were lower (-7.79 and -10.25, respectively). GMMs identified latent trajectories of CVH and emotional distress with clinically distinct

Table 3: Latent Trajectory Classes of Emotional Distress and Cardiovascular Health in LEADS-CV Participants

Table 3: Latent Trajectory Classes of Emotional Distress and Cardiovascular Health in LEADS-CV Participants

				Emotional Distress Trajectory Classes						
				PROMIS Psychological Stress Experiences			PROMIS Depressive Symptoms		PROMIS Anxiety	
				Low	Moderate	High	Low	High	Low	High
			median (IQR)	37.6 (37-42.3)	55.4 (52.1-58.3)	85.2 (82.3-88.9)	40.8 (39.9-48.1)	60.5 (55.9-64.7)	45.1 (39-50)	60.2 (55.5-62.2)
CVH Trajectory Classes*	CVH-S	High	76.7 (70.8-81.7)	8 (80%)	29 (74.4%)	12 (52.2%)	21 (77.8%)	28 (62.2%)	21 (77.8%)	28 (62.2%)
		Moderate	56.1 (50-62.3)	2 (20%)	10 (25.6%)	11 (47.8%)	6 (22.2%)	17 (37.8%)	6 (22.2%)	17 (37.8%)
	CHV-B	Moderate	65 (52.5-70)	6 (60%)	17 (43.6%)	5 (21.7%)	14 (51.9%)	14 (31.1%)	14 (51.9%)	14 (31.1%)
		Low	32.5 (22.5-42.5)	4 (40%)	22 (56.4%)	18 (78.3%)	13 (48.1%)	31 (68.9%)	13 (48.1%)	31 (68.9%)
	CHV-F	High	93.8 (87.5-100)	7 (70%)	26 (66.7%)	13 (56.5%)	19 (70.4%)	27 (60%)	19 (70.4%)	27 (60%)
		Moderate	72.5 (63.8-78.8)	2 (20%)	10 (25.6%)	9 (39.1%)	5 (18.5%)	18 (36.8%)	5 (18.5%)	18 (35.8%)
		Low	55 (37.8-55)	1 (10%)	3 (7.7%)	1 (4.3%)	3 (11.1%)	2 (4.4%)	3 (11.1%)	2 (4.4%)

*CVH trajectory classes are named based on correspondence to published score ranges: High (approximately 80-100), Moderate (approximately 50-79), and Low (< 50)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

score distributions; worse CVH-S/-B/-F was more common in higher emotional distress latent trajectory classes, with 69-78% of patients in higher emotional distress latent trajectory classes having poor CVH-B (Table 3).

Conclusion: Higher emotional distress is associated with worse CVH in JSLE/JDM. Severe anxiety is associated with sufficiently large decreases in CVH-S/-F that higher mid-life risk of CVD events would be expected. Low CVH-B is present in most JSLE/JDM patients following high emotional distress latent trajectories. Interventions are needed to address dual risks of emotional distress and suboptimal CVH in JSLE/JDM. Our ongoing work will identify mediators by which emotional distress worsens CVH and child/parent targets for stress reduction and CVH promotion interventions in JSLE/JDM.

Disclosure: K. Ardalan: Cabaletta Bio, 1, 2, SingHealth, 12, honorarium paid directly to institution (not investigator) for grant pre-review program participation; **A. Davalos**: None; **H. Hong**: None; **B. Reeve**: None; **C. Hornik**: Cytokinetics, 1, Emmes Corporation, 12, DSMB, Tellus, 2; **M. Moody**: Grid Therapeutics, LLC., 12,; **D. Lloyd-Jones**: None; **E. Wu**: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **A. Ward**: None; **S. Gbadegesin**: None; **R. Sadun**: The Expert Institute, 12,; **J. Dvergsten**: None; **L. Covert**: None; **A. Reed**: None; **M. Connelly**: None; **L. Schanberg**: Bristol-Myers Squibb(BMS), 5, Sanofi, 12, DSMB, UCB, 12, DSMB.

Abstract Number: 1746

Inflammatory- and Fibrosis-Related Biomarkers and Rheumatoid Arthritis-Associated Interstitial Lung Disease Risk

Bryant England[1], Tate Johnson[1], Michael Duryee[1], Halie Frideres[2], Katherine Wysham[3], Grant Cannon[4], Gary Kunkel[5], Dana Ascherman[6], John Richards[7], Paul Monach[8], Gail Kerr[9], Andreas Reimold[10], Joshua Baker[11], Geoffrey Thiele[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]UNMC Department of Rheumatology, Omaha, NE, [3]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [6]University of Pittsburgh, Pittsburgh, PA, [7]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [8]VA Boston Healthcare System, Boston, MA, [9]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [10]Dallas VA Medical Center, Dallas, TX, [11]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary) (1746–1751)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: There exists a need to identify informative peripheral blood biomarkers for RA-interstitial lung disease (RA-ILD) and elucidate the pathophysiological processes driving RA-ILD onset. Several inflammatory- and fibrosis-related mediators have been identified in diseases characterized by tissue fibrosis such as idiopathic pulmonary fibrosis (IPF) and heart failure, but few have been evaluated specifically in RA-ILD. We investigated the association of inflammatory- and fibrosis-related biomarkers with RA-ILD risk in a large, prospective RA cohort.

Methods: Using a multicenter, prospective cohort of U.S. Veterans with RA, we performed a cross-sectional study of prevalent RA-ILD and cohort study of incident RA-ILD. Inflammatory- and fibrosis-related biomarkers discovered in IPF and heart failure: growth differentiation factor-15 (GDF-15), interleukin-18, interferon-gamma inducible protein-10, interferon-inducible T-cell alpha chemoattractant, monokine induced by gamma interferon, pentraxin-3, and soluble vascular cell adhesion molecule, were measured from serum at enrollment using the MesoScale Discovery platform. Biomarker concentrations were log-transformed and standardized, as well as categorized into quartiles to assess non-linear associations. RA-ILD was identified through informatics-based screening and validation by a board-certified rheumatologist requiring a clinical diagnosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Associations of selected inflammatory- and fibrosis-related mediators with prevalent and incident RA-ILD.

Table 1. Associations of selected inflammatory- and fibrosis-related mediators with prevalent and incident RA-ILD.

Analyte	aOR/aHR (95% CI) per SD
Prevalent RA-ILD (aOR)	
Growth differentiation factor-15 (GDF-15)	1.42 (1.08, 1.87)
Interleukin-18	0.97 (0.80, 1.17)
Interferon-gamma inducible protein-10 / CXCL10	0.93 (0.76, 1.14)
Interferon-inducible T-cell alpha chemoattractant / CXCL11	0.97 (0.80, 1.17)
Monokine Induced by Gamma Interferon / CXCL9	0.81 (0.66, 1.00)
Pentraxin-3	1.30 (1.07, 1.58)
Soluble vascular cell adhesion molecule	0.95 (0.79, 1.16)
Incident RA-ILD (aHR)	
Growth differentiation factor-15 (GDF15)	1.20 (0.99, 1.46)
Interleukin-18	1.15 (0.99, 1.35)
Interferon-gamma inducible protein 10 / CXCL10	1.10 (0.94, 1.28)
Interferon-inducible T-cell alpha chemoattractant / CXCL11	1.10 (0.94, 1.29)
Monokine Induced by Gamma Interferon / CXCL9	1.03 (0.86, 1.23)
Pentraxin-3	1.17 (0.99, 1.38)
Soluble vascular cell adhesion molecule	1.07 (0.91, 1.26)

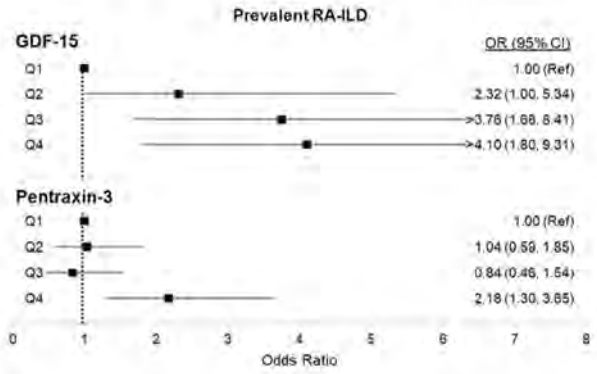
Models adjusted for age, sex, race, smoking status, BMI category, anti-CCP antibody positivity, DAS28, Rheumatic Disease Comorbidity Index score. Analytes assessed in separate models.

Abbreviations: aHR, adjusted hazard ratio; aOR, adjusted odds ratio; CI, confidence interval; RA, rheumatoid arthritis; RA-ILD, rheumatoid arthritis-associated interstitial lung disease; SD, standard deviation

plus imaging or biopsy findings. The associations of candidate biomarkers with RA-ILD were assessed separately in multivariable logistic (prevalent RA-ILD) and Cox (incident RA-ILD) regression models adjusted for age, sex, race, smoking status, body mass index category, anti-CCP antibody positivity, DAS28, and comorbidity burden.

Results: Cross-sectional analyses were conducted among 2,737 RA participants (87% male, mean age 64 years), with 124 having prevalent RA-ILD. Higher concentrations of GDF-15 (per 1 SD aOR 1.42 [1.08, 1.87]) and pentraxin-3 (aOR 1.30 [1.07, 1.58]) were significantly associated with prevalent RA-ILD (**Table 1**). Referent to the lowest quartile, higher

Figure 1. Associations of Growth Differentiation Factor-15 and Pentraxin-3 quartiles with prevalent RA-ILD.



Models adjusted for age, sex, race, smoking status, BMI category, anti-CCP positivity, DAS28, and Rheumatic Disease Comorbidity Index Score. Analytes assessed in separate models.

Q4 = highest quartile
Q1 = lowest quartile (referent)

Abbreviations: OR, odds ratio; CI, confidence interval

Figure 1. Associations of Growth Differentiation Factor-15 and Pentraxin-3 quartiles with prevalent RA-ILD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

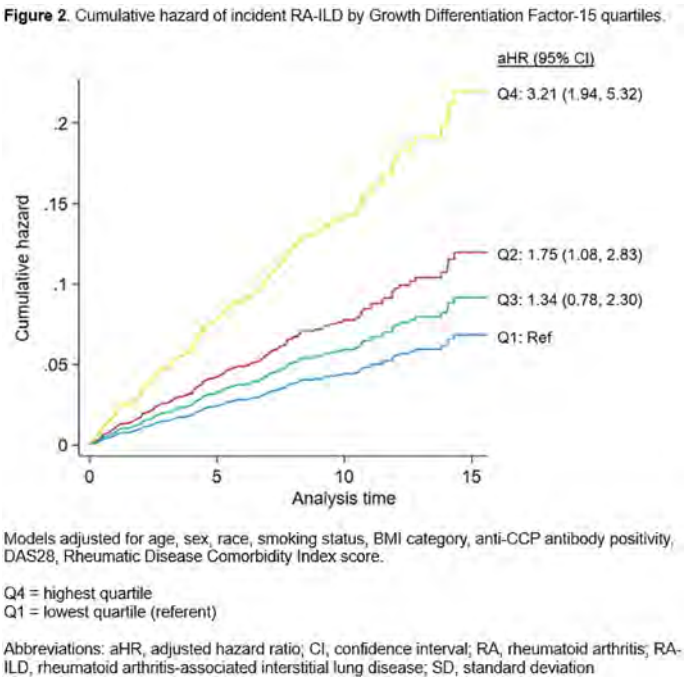


Figure 2. Cumulative hazard of incident RA-ILD by Growth Differentiation Factor-15 quartiles.

quartiles of GDF-15 (Q3 aOR 3.76 [1.68, 8.41]; Q4 4.10 [1.80, 9.31]) and the highest quartile of Pentraxin-3 (aOR 2.18 [1.30, 3.65]) were associated with prevalent ILD (**Figure 1**). Concentrations of other biomarkers were not associated with prevalent RA-ILD. After excluding those with prevalent RA-ILD, 174 participants developed incident RA-ILD over 20,957 patient-years of follow-up. None of the analyte concentrations were significantly associated with incident RA-ILD risk (**Table 1**). However, the highest quartile of GDF-15 was associated with a >3-fold higher risk of incident RA-ILD (adjusted HR 3.21 [1.94, 5.32]) (**Figure 2**).

Conclusion: GDF-15, a member of the transforming growth factor-β family, was independently associated with both prevalent and incident RA-ILD in a large RA cohort. Other inflammatory- and fibrosis-related mediators seen in other fibrotic diseases, such as IPF and heart failure, were not associated with RA-ILD risk, suggesting there may be unique disease specific inflammatory and fibrotic pathophysiologic pathways in RA-ILD.

Disclosure: B. England: Boehringer-Ingelheim, 2, 5; **T. Johnson**: None; **M. Duryee**: None; **H. Frideres**: None; **K. Wysham**: None; **G. Cannon**: None; **G. Kunkel**: None; **D. Ascherman**: None; **J. Richards**: None; **P. Monach**: Boehringer-Ingelheim, 2; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **A. Reimold**: None; **J. Baker**: None; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

Abstract Number: 1747

Risk of serious infection in patients with rheumatoid arthritis-associated interstitial lung disease or bronchiectasis: A matched cohort study

QIANRU ZHANG[1], Ying Qi[2], Xiaosong Wang[3], Gregory McDermott[4], Sung Hae Chang[5], Mark Chaballa[6], Vadim Khaychuk[7], Misti Paudel[8] and Jeffrey Sparks[9], [1]Brigham and Women's Hospital/Beijing Tsinghua Changgung Hospital, Cambridge, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, Natick, MA, [4]Brigham and Women's Hospital, Brookline, MA, [5]Soonchunhyang University College of Medicine, Cheonan, MA, South Korea, [6]Bristol

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Myers Squibb, Princeton, NJ, [7]Bristol Myers Squibb, Pennington, NJ, [8]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [9]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

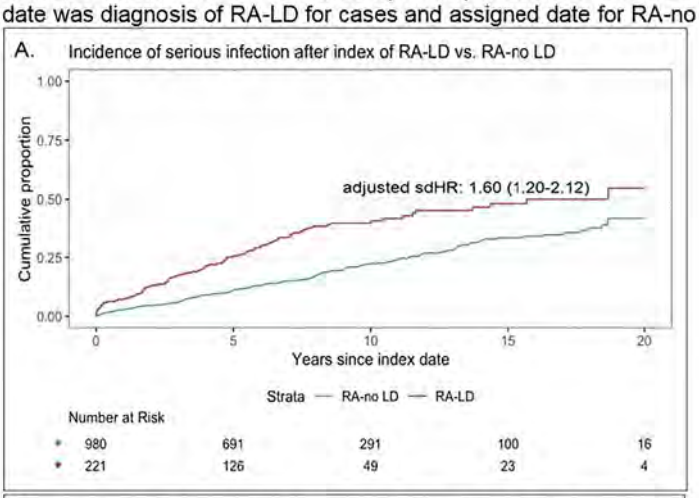
Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary) (1746–1751)

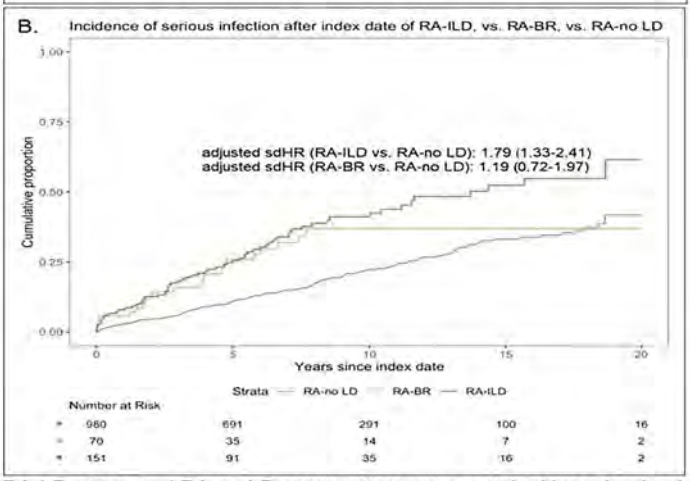
Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: RA-associated lung disease (RA-LD), including RA-associated interstitial lung disease (RA-ILD) and RA-associated bronchiectasis (RA-BR), contributes significantly to morbidity and mortality in RA patients. RA is associated with a 2-fold increased risk of serious infection compared to the general population. However, the association of RA-LD and the risk of serious infection is unclear.

Figure 1. A. Cumulative incidence of first serious infection, comparing rheumatoid arthritis-associated lung disease (RA-LD) cases and RA-no LD comparators. B. Cumulative incidence of first serious infection, comparing RA-associated interstitial lung disease (RA-ILD) cases, RA-associated bronchiectasis (RA-BR) cases, and RA-no LD comparators. The index date was diagnosis of RA-LD for cases and assigned date for RA-no LD comparators.





RA-LD cases and RA-no LD comparators were matched by calendar date, age, sex, and RA duration at index date of RA-LD diagnosis.
Additionally adjusted for propensity score that included smoking status, pack-years, Charlson Comorbidity Index score, serostatus, glucocorticoids, csDMARDs, bDMARDs, previous serious infection, and health care utilization.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Anatomic site and care setting of infection after index date, comparing RA-LD cases and RA-no LD comparators. The index date was diagnosis of RA-LD for cases and assigned date for RA-no LD comparators.

Outcomes	RA-LD cases (n=221)	RA-no LD comparators (n=980)	p-value
Any infections	166 (75)	583 (59)	**<0.001**
Inpatient	85 (38)	204 (21)	**<0.001**
Pulmonary infections	119 (54)	232 (24)	**<0.001**
Inpatient	68 (31)	102 (10)	**<0.001**
Skin and soft tissue infections	85 (38)	332 (34)	0.20
Inpatient	28 (13)	69 (7)	**0.006**
ENT infections	85 (38)	268 (27)	**0.001**
Inpatient	15 (7)	23 (2)	**0.002**
Urinary tract infections	66 (30)	229 (23)	**0.04**
Inpatient	25 (11)	78 (8)	0.11
Musculoskeletal infections	18 (8)	49 (5)	0.07
Inpatient	11 (5)	28 (3)	0.14
GI infections	14 (6)	56 (6)	0.72
Inpatient	9 (4)	26 (3)	0.27
Other infections*	42 (19)	144 (15)	0.11
Inpatient	30 (14)	77 (8)	**0.007**

*Other infections included infections of the eye, nervous system, prosthetic devices, implants, and grafts, sepsis, SIRS of infectious origin, and septic shock

ENT, ear, nose, and throat; GI, gastrointestinal; RA-LD, rheumatoid arthritis-associated lung disease; RA-no LD, rheumatoid arthritis without lung disease; SIRS, systemic inflammatory response syndrome

Table 2. Specific pathogens and care setting of infection after index date, comparing RA-ILD cases, RA-BR cases, and RA-no LD comparators. The index date was diagnosis of RA-LD for cases and assigned date for RA-no LD comparators.

Outcomes	RA-no LD comparators (n=980)	RA-ILD (n=151)	p-value (RA-ILD vs. RA-no ILD)	RA-BR (n=70)	p-value (RA-BR vs. RA-no LD)
Viral infections					
SARS-CoV-2	264 (27)	44 (29)	0.57	15 (21)	0.31
Inpatient	38 (4)	12 (8)	**0.02**	2 (3)	0.67
Influenza virus	47 (5)	13 (9)	0.05	5 (7)	0.38
Inpatient	15 (2)	7 (5)	**0.02**	5 (7)	**0.008**
Respiratory syncytial virus	8 (0.8)	4 (3)	0.06	2 (3)	0.14
Inpatient	7 (0.7)	3 (2)	0.14	0 (0)	1.00
Cytomegalovirus	5 (0.5)	5 (3)	**0.006**	1 (1)	0.34
Inpatient	1 (0.1)	5 (3)	**<0.001**	1 (1)	0.13
Parainfluenza	0 (0)	3 (2)	**0.002**	0 (0)	-
Inpatient	0 (0)	2 (1)	**0.02**	0 (0)	-
Bacterial infections					
Staphylococcus	57 (6)	16 (11)	**0.03**	10 (14)	**0.005**
Inpatient	46 (5)	15 (10)	**0.008**	9 (13)	**0.003**
Escherichia coli	22 (2)	13 (9)	**<0.001**	2 (3)	0.67
Inpatient	20 (2)	13 (9)	**<0.001**	2 (3)	0.65
Pseudomonas	14 (1)	8 (5)	**0.005**	7 (10)	**<0.001**
Inpatient	13 (1)	6 (4)	**0.03**	5 (7)	**0.005**
Klebsiella pneumoniae	8 (0.8)	5 (3)	**0.02**	0 (0)	1.00
Inpatient	8 (0.8)	4 (3)	0.06	0 (0)	1.00
Mycobacterial infections					
Nontuberculous mycobacteria	7 (0.7)	3 (2)	0.14	8 (11)	**<0.001**
Inpatient	0 (0)	1 (0.7)	0.13	3 (4)	**<0.001**
Fungal infections					
Candida albicans	83 (8)	34 (23)	**<0.001**	15 (21)	**<0.001**
Inpatient	27 (3)	14 (9)	**<0.001**	5 (7)	0.056
Aspergillus	3 (0.3)	8 (5)	**<0.001**	2 (3)	**0.04**
Inpatient	2 (0.2)	5 (3)	**<0.001**	2 (3)	**0.02**
Pneumocystosis	2 (0.2)	7 (5)	**<0.001**	0 (0)	1.00
Inpatient	2 (0.2)	5 (3)	**<0.001**	0 (0)	1.00

RA-BR, rheumatoid arthritis-associated bronchiectasis; RA-ILD, rheumatoid arthritis-associated interstitial lung disease; RA-no LD, rheumatoid arthritis without lung disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective matched cohort study of patients enrolled in the biobank of a large U.S. health care system, comparing RA-LD cases to RA patients without lung disease (RA-no LD), matched by calendar date, age, sex, and RA duration at the index date of RA-LD diagnosis. Patients with RA met the 2010 ACR/EULAR classification criteria. RA-LD cases were verified by medical record review and chest imaging for clinically-apparent RA-ILD and/or RA-BR. The primary outcome was serious infection, defined as infections requiring hospitalization. Secondary outcomes included any infection, infections by anatomic site, pathogen type, and specific pathogens. Incidence rates and propensity score-adjusted subdistribution hazard ratios (sdHR) using Fine and Gray models to account for competing risk of death were calculated for RA-LD vs. RA-no LD as well as RA-ILD or RA-BR vs. RA-no LD.

Results: We analyzed 221 RA-LD cases (151 RA-ILD and 70 RA-BR) and 980 RA-no LD matched comparators. After propensity score adjustment, RA-LD cases had a significantly higher risk of serious infections compared to RA-no LD comparators (55.8 vs. 25.8 per 1,000 person-years, adjusted sdHR 1.60, 95%CI 1.20-2.12, **Figure 1**). The increased risk remained significant for RA-ILD cases (adjusted sdHR 1.79, 95%CI 1.33-2.41), but not for RA-BR cases (adjusted sdHR 1.19, 95%CI 0.72-1.97). Anatomic sites of infection that were more common in RA-LD cases vs. RA-no LD comparators, including pulmonary (31% vs. 10%, p< 0.001), skin and soft tissue (13% vs. 7%, p=0.006), and ear, nose and throat (7% vs. 2%, p=0.002, **Table 1**). RA-LD was associated with pathogen types: viral (16% vs. 8%, p< 0.001), bacterial (19% vs. 9%, p< 0.001), fungal (10% vs. 3%, p< 0.001), and mycobacterial infections (2% vs. 0.1%, p=0.001). Specific pathogens with higher frequency in RA-LD cases vs. RA-no LD comparators, particularly among RA-BR cases, included influenza virus (7% vs. 2%, p=0.008), respiratory syncytial virus (3% vs. 0.3%, p=0.04), *Staphylococcus* (14% vs. 6%, p=0.005), *Pseudomonas* (10% vs. 1%, p< 0.001), and nontuberculous mycobacteria (11% vs. 0.7%, p< 0.001, **Table 2**).

Conclusion: RA-LD, particularly RA-ILD, was associated with higher risk of serious infection across anatomic sites and diverse pathogen types. While RA-BR was not associated with serious infection, it was associated with higher risk of pulmonary infection and nontuberculous mycobacterial infection. Findings may be explained by lung damage and/or more intense immunosuppression, so tailored infection prevention strategies, including vaccination, are essential for this vulnerable population.

Disclosure: Q. ZHANG: None; **Y. Qi**: None; **X. Wang**: None; **G. McDermott**: None; **S. Chang**: None; **M. Chaballa**: Bristol-Myers Squibb(BMS), 3, 11; **V. Khaychuk**: Bristol-Myers Squibb(BMS), 3, 11; **M. Paudel**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 1748

Effect of Air Pollution on Disease Activity in Patients with Rheumatoid Arthritis

Sung Cheol Jung[1], Jeffrey Curtis[2], Seojin Yang[3], Min Hyuk Lim[4], Saram Lee[5], Sung Ik Cho[6], Jin Kyun Park[7] and Eun Bong Lee[6], [1]Seoul National University College of Medicine, Seoul, Republic of Korea, [2]University of Alabama at Birmingham, Birmingham, AL, [3]Seoul National University, Seoul, Republic of Korea, [4]Ulsan National Institute of Science and Technology (UNIST), Ulsan, Republic of Korea, [5]Seoul National University Hospital, Seoul, Republic of Korea, [6]Seoul National University Hospital, Seoul, South Korea, [7]Seoul National University College of Medicine, Jongno-gu, Seoul, South Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary) (1746–1751)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

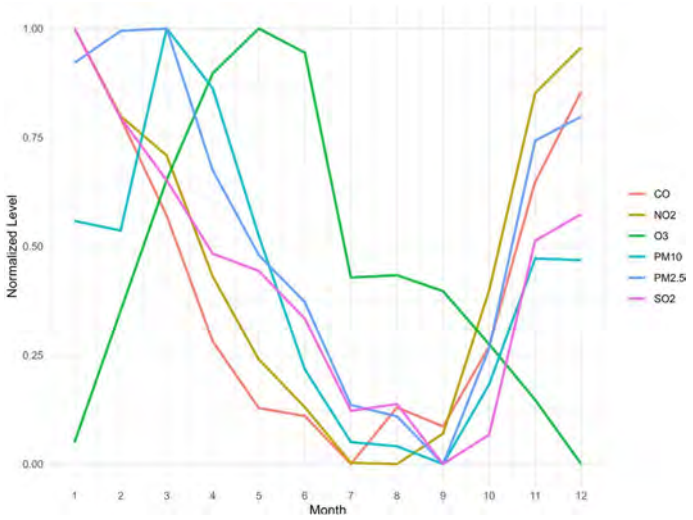


Figure 1. Longitudinal trends of monthly Air Pollutant concentrations

Table 1. Effects of Air Pollution on Flare occurrence in RA

		FLARE[a]			
		univariable		multivariable[b]	
		Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
GAS	SO_2[c]	1.037 (0.983, 1.093)	0.180	1.027 (0.971, 1.086)	0.350
	NO_2[c]	1.047 (0.991, 1.106)	0.101	0.999 (0.912, 1.094)	0.984
	O_3[c]	0.963 (0.914, 1.013)	0.147	1.035 (0.961, 1.115)	0.366
	CO[c]	1.044 (0.990, 1.100)	0.109	0.966 (0.886, 1.052)	0.422
Particle	PM_{10}[c]	1.085 (1.031, 1.143)	0.002*	1.079 (1.006, 1.157)	0.033*
	$PM_{2.5}$[c]	1.094 (1.039, 1.152)	0.001*	1.095 (1.009, 1.188)	0.029*

[a]Flare was defined as an increased in DAS28 ESR > 1.2, or > 0.6 if the DAS28 ESR ≥ 3.2.
[b]Adjusted for age, sex, smoking status, serologic status, dose of concomitant glucocorticoids, type of DMARDs, and climate variables (temperature and humidity)
[c]Concentrations of air pollutants were standardized to have a mean of 0 and a standard deviation of 1.
*p-value < 0.05

Table 2. Effects of Air Pollution on Disease Activity in RA

		TJC28				SJC28				CDAI			
		univariable		multivariable[a]		univariable		multivariable[a]		univariable		multivariable[a]	
		β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value
GAS	SO_2[b]	0.016 (-0.030, 0.063)	0.488	-0.002 (-0.057, 0.053)	0.930	0.022 (-0.012, 0.057)	0.208	0.027 (-0.015, 0.069)	0.206	0.012 (-0.096, 0.122)	0.831	0.007 (-0.125, 0.139)	0.915
	NO_2[b]	0.018 (-0.016, 0.051)	0.301	0.039 (-0.073, 0.151)	0.497	-0.005 (-0.028, 0.019)	0.687	0.035 (-0.047, 0.118)	0.397	-0.008 (-0.086, 0.070)	0.847	0.129 (-0.135, 0.394)	0.338
	O_3[b]	0.011 (-0.017, 0.039)	0.447	0.037 (-0.018, 0.092)	0.187	0.029 (0.007, 0.050)	0.009*	0.055 (0.012, 0.099)	0.012*	0.084 (-0.003, 0.130)	0.060	0.156 (0.021, 0.290)	0.023*
	CO[b]	0.004 (-0.026, 0.034)	0.786	-0.016 (-0.088, 0.056)	0.661	-0.008 (-0.030, 0.013)	0.458	0.011 (-0.045, 0.067)	0.704	-0.026 (-0.098, 0.045)	0.470	-0.003 (-0.178, 0.172)	0.972
Particle	PM_{10}[b]	0.036 (0.007, 0.065)	0.016*	0.049 (-0.003, 0.101)	0.064	0.017 (-0.004, 0.038)	0.105	0.035 (-0.003, 0.072)	0.068	0.030 (-0.039, 0.099)	0.398	0.083 (-0.037, 0.204)	0.177
	$PM_{2.5}$[b]	0.041 (0.011, 0.070)	0.007*	0.078 (0.020, 0.136)	0.008*	0.020 (-0.000, 0.041)	0.056	0.068 (0.023, 0.112)	0.003*	0.060 (-0.010, 0.130)	0.091	0.211 (0.069, 0.353)	0.004*

		DAS28 CRP				DAS28 ESR			
		univariable		multivariable[a]		univariable		multivariable[a]	
		β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value	β coefficient (95% CI)	p-value
GAS	SO_2[b]	-0.003 (-0.022, 0.016)	0.753	-0.004 (-0.026, 0.019)	0.780	0.019 (-0.001, 0.040)	0.064	-0.008 (-0.032, 0.016)	0.516
	NO_2[b]	0.001 (-0.013, 0.015)	0.866	0.028 (-0.014, 0.071)	0.186	0.036 (0.021, 0.051)	< 0.001*	0.016 (-0.025, 0.052)	0.408
	O_3[b]	0.006 (-0.006, 0.018)	0.299	0.022 (-0.002, 0.045)	0.071	-0.012 (-0.025, 0.000)	0.057	0.023 (-0.002, 0.048)	0.073
	CO[b]	-0.005 (-0.018, 0.008)	0.453	-0.011 (-0.041, 0.018)	0.461	0.023 (0.009, 0.036)	0.001*	-0.023 (-0.054, 0.008)	0.142
Particle	PM_{10}[b]	0.008 (-0.004, 0.020)	0.204	0.024 (0.005, 0.044)	0.016*	0.031 (0.018, 0.044)	< 0.001*	0.025 (0.004, 0.046)	0.018*
	$PM_{2.5}$[b]	0.011 (-0.001, 0.024)	0.074	0.040 (0.017, 0.064)	0.001*	0.038 (0.025, 0.052)	< 0.001*	0.037 (0.013, 0.061)	0.003*

TJC28 = Tender Joint Count based on 28 joints, SJC28 = Swelling Joint Count based on 28 joints, CDAI = Clinical Disease Activity Index, DAS28 = Disease Activity Score based on 28 joints, CRP = C-reactive protein, ESR = Erythrocyte Sedimentation Rate
[a]Adjusted for age, sex, smoking status, serologic status, dose of concomitant glucocorticoids, type of DMARDs, and climate variables (temperature and humidity)
[b]Concentrations of air pollutants were standardized to have a mean of 0 and a standard deviation of 1.
*p-value < 0.05

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: While air pollution has been implicated in the pathogenesis of rheumatoid arthritis (RA), its association with RA disease activity remains insufficiently investigated (1, 2). We aimed to evaluate the effect of air pollution on disease activity and flare occurrence in patients with RA.

Methods: This prospective study included patients with RA who visited a tertiary medical center in South Korea between January 2021 and October 2024, with at least 6 months of follow-up. Air pollution levels were assessed using monthly mean concentrations of six air pollutants (SO_2, NO_2, O_3, CO, PM_{10}, and $PM_{2.5}$) obtained from the Korean National Institute of Environmental. RA disease activity was evaluated using the tender joint count, swollen joint count based on 28 joints (TJC28, SJC28), clinical disease activity Index (CDAI), and disease activity score based on 28 joints (DAS28). Flare events were defined based increases in DAS28 scores. Associations between air pollution and RA disease activity or flare occurrence were analyzed using linear and logistic generalized estimating equations (GEE), accounting for repeated measures within the study population and adjusting for prespecified covariates including age, sex, smoking status, serologic status, dose of concomitant glucocorticoids, type of disease-modifying anti-rheumatic drugs (DMARDs), and climate variables (temperature and humidity).

Results: A total of 1,056 RA patients were included, with a mean (SD) age of 61.2 (12.7) years, and 907 (85.9%) were female. Patients contributed data for a median (IQR) of 11.0 (8.0, 13.0) visits. There were 1,724 flare events during the observation period, with an incidence rate of 56.3 per 100 person-years (95% CI: 53.7 to 59.1). Air pollution concentrations were high in winter and spring and low in summer (Figure 1). Increases in PM_{10}, and $PM_{2.5}$ levels were associated with flare occurrence (Table 1). Among individual pollutants, O_3 was associated with SJC28 and CDAI, and PM_{10} was associated with both DAS28 CRP and DAS28 ESR. In particular, higher $PM_{2.5}$ levels showed the strongest association with increased RA disease activity, with β coefficients (95% CIs) of 0.078 (0.020 to 0.136) for TJC28, 0.068 (0.023 to 0.112) for SJC28, 0.211 (0.069 to 0.353) for CDAI, 0.040 (0.017 to 0.064) for DAS28 CRP, 0.037 (0.013 to 0.061) for DAS28 ESR when six air pollutants were standardized to a mean of 0 and standard deviation of 1 (Table 2).

Conclusion: Elevated air pollution levels, especially PM 2.5, are associated with increased RA disease activity and flare occurrence in patients of RA.

References

1. Zhang RD, Chen C, Wang P, Fang Y, Jiang LQ, Fang X, et al. Air pollution exposure and auto-inflammatory and autoimmune diseases of the musculoskeletal system: a review of epidemiologic and mechanistic evidence. Environ Geochem Health. 2023;45(7):4087-105.
2. Ingegnoli F, Ubiali T, Schioppo T, Longo V, Murgo A, De Lucia O, et al. Potential Short-Term Air Pollution Effects on Rheumatoid Arthritis Activity in Metropolitan Areas in the North of Italy: A Cross-Sectional Study. Int J Environ Res Public Health. 2021;18(16).

Disclosure: S. Jung: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **S. Yang**: None; **M. Lim**: None; **S. Lee**: None; **S. Cho**: None; **J. Park**: None; **E. Lee**: None.

Abstract Number: 1749

External validation of a combined clinical and genetic risk score for the identification of interstitial lung disease in rheumatoid arthritis

Mikael Brink[1], **Austin Wheeler**[2], Bryant England[2] and Solbritt Rantapaa-Dahlqvist[3], [1]Umeå Universitet, Umeå, Sweden, [2]University of Nebraska Medical Center, Omaha, NE, [3]Umeå University, Umea, Sweden

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary) (1746–1751)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: RA-associated interstitial lung disease (RA-ILD) causes substantial morbidity and mortality in RA. Despite this, a limited number of clinical and genetic risk factors have been identified. Recently, a combined clinical-genetic risk score (VARA-ILD Combined Risk Score) has been shown to enhance identification of ILD among RA patients (Wheeler et al., *Rheumatology* 2024). We performed external validation of that combined risk score in a cohort of early RA patients from northern Sweden.

Methods: Participants were enrolled in an inception RA cohort from northern Sweden who were diagnosed with RA between 1996-2016. Clinical data including age, sex, smoking history, and disease activity score with 28-joint count (DAS28) were collected routinely by treating rheumatologists. RF and anti-CCP were assessed at baseline using standard lab methods. ILD screening was performed per clinical indication, with ILD diagnosis based on consistent chest x-ray and/or high-resolution chest CT findings. Genotyping was performed on DNA collected at baseline using the Illumina Global Screening Array, and single nucleotide polymorphisms (SNPs) included in the VARA-ILD Genetic Risk Score (GRS) were extracted. The VARA-ILD Combined Risk score was calculated for each participant and evaluated via multivariable regression. Overall model performance was assessed using the area under the receiver operating characteristic curve (AUC). Sensitivity and specificity were calculated at the recommended cut-point value (0.05) and at the cut-point that optimized Youden's index in this cohort.

Results: We studied 1,118 RA participants (70% female), with ILD present in 60 (5.4% prevalence). RA-ILD participants were older, had more RF positivity, and had higher disease activity (**Table 1**). Among SNPs included in the VARA-ILD GRS, *MUC5B* rs35705950 (OR 3.70, 95% CI 2.18-6.32) and *FAM13A* rs2609255 (OR 1.91, 95% CI 1.13-3.25) were individually associated with RA-ILD (**Table 2**). Within the VARA-ILD combined risk score regression model, the largest effects were seen with the VARA-ILD GRS (OR 2.36, 95% CI 1.24-4.48) and RF positivity (OR 2.96, 95% CI 1.14-7.70). The VARA-ILD Combined Risk Score enhanced discrimination of ILD (AUC 0.75, 95% CI 0.69-0.81) over the GRS alone (AUC 0.62, 95% CI 0.54-0.69; **Figure 1**). At the recommended cut-point of 0.05, the VARA-ILD Combined Risk Score yielded 93% sensitivity and would eliminate 36% of the cohort from undergoing additional testing for ILD. We also calculated an optimal cut-point of 0.08 within this cohort which would yield a sensitivity of 79% and specificity of 95%.

Conclusion: The VARA-ILD GRS and VARA-ILD Combined Risk Score were externally validated in a cohort of early RA patients in northern Sweden. Given the differences in study population between this cohort and the VARA-ILD derivation cohort, our findings demonstrate the generalizability and potential clinical utility of these risk stratification tools for RA-ILD.

Table 1. Characteristics of participants in the northern Sweden early RA cohort. Values shown as mean (standard deviation) unless specified. *DAS28 averaged from prior 24 months. Abbreviations: rheumatoid arthritis without interstitial lung disease (RA-noILD), rheumatoid arthritis-associated interstitial lung disease (RA-ILD), rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), disease activity score with 28 joint count (DAS28)

	RA-noILD (n=1058)	RA-ILD (n=60)	p-value
Age at inclusion	57.50 (14.19)	65.10 (10.29)	<0.001
Female sex, n (%)	747 (70.6)	37 (61.7)	0.185
Cigarette smoking (ever), n(%)	644 (60.9)	42 (70.0)	0.167
RF positive, n (%)	770 (72.8)	53 (88.3)	0.012
Anti-CCP positive, n (%)	712 (67.3)	47 (78.3)	0.101
Mean DAS28*	3.55 (0.87)	3.82 (0.72)	0.020

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Genotype frequencies and OR of the effect allele for each single nucleotide polymorphism included in the VARA-ILD genetic risk score. Abbreviations: rheumatoid arthritis without interstitial lung disease (RA-noILD), rheumatoid arthritis-associated interstitial lung disease (RA-ILD), odds ratio (OR), confidence interval (CI)

		RA-noILD (n=1058)	RA-ILD (n=60)	OR (95%CI)	p-value
***MUC5B* rs35705950 (G>T) (%)**	GG	780 (96.8)	26 (3.2)		
	GT, TT	276 (89.0)	34 (11.0)	**3.70 (2.18 - 6.32)**	**<0.001**
***DSP* rs2076295 (T>G) (%)**	TT	342 (95.0)	18 (5.0)		
	GT, GG	715 (94.5)	42 (5.5)	1.12 (0.64 - 2.01)	0.704
***LRRC34* rs6793295 (T>C) (%)**	TT	497 (94.7)	28 (5.3)		
	TC, CC	560 (94.6)	32 (5.4)	1.01 (0.60 - 1.72)	0.957
***OBFC1* rs11191865 (A>G) (%)**	AA	299 (93.7)	20 (6.3)		
	AG, GG	758 (95.0)	40 (5.0)	0.79 (0.46 - 1.40)	0.401
***FAM13A* rs2609255 (T>G) (%)**	TT	627 (96.0)	26 (4.0)		
	GT, GG	430 (92.7)	34 (7.3)	**1.91 (1.13 - 3.25)**	**0.016**

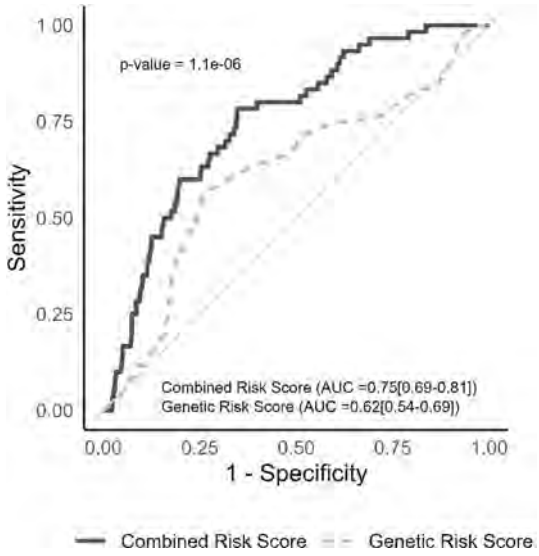


Figure 1. Comparison of receiver operating characteristic curves for the VARA-ILD Combined Risk Score and GRS alone. Abbreviations: area under the receiver operating characteristic curve (AUC)

Disclosure: M. Brink: None; **A. Wheeler**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **S. Rantapaa-Dahlqvist**: None.

Abstract Number: 1750

Urinary Proteomic Signature Identifies Rheumatoid Arthritis Patients at Risk for Interstitial Lung Disease

Jia Shi[1], Xueting Yuan[2], Yafang Deng[3], Chen Yu[4], Nan Jiang[5], Zhengguang Guo[6], Christian Lood[7], Mengtao Li[5], Wei Sun[6], Qian Wang[5] and Xinping Tian[5], [1]University of Washington, Seattle, WA, [2]Peking Union Medical College Hospital (CAMS), Beijing, China (People's Republic), [3]Peking Union Medical College Hospital. Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, Beijing, China (People's Republic), [4]Peking Union Medical College Hospital, Dong Cheng Qu, Beijing, China (People's Republic), [5]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [6]Peking Union Medical College, Beijing, China (People's Republic), [7]University of Washington, Division of Rheumatology, Seattle

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary) (1746–1751)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Interstitial lung disease (ILD) is a serious pulmonary complication of rheumatoid arthritis (RA), contributing significantly to morbidity and mortality. Non-invasive tools for identifying ILD risk in RA patients remain limited. As a stable and accessible biofluid, urine represents a promising source of biomarkers. We aimed to identify ILD-associated urinary proteomic signatures and evaluate their potential utility for risk stratification and clinical assessment.

Methods: We analyzed the urine proteome of 78 RA patients (14 with ILD and 64 without ILD) using data-independent acquisition (DIA) liquid chromatography-tandem mass spectrometry (LC-MS). ILD-associated proteins were identified through differential expression analysis and LASSO regression, supported by 1000 bootstrap iterations. Candidate markers were evaluated using logistic regression, ROC analysis, and correlation with pulmonary function.

Results: A total of 2,482 urinary proteins were quantified. Differential expression analysis, LASSO regression, and 1,000 bootstrap iterations (Figure 1) jointly identified two robust ILD-associated proteins: SPOCK1 and PGRMC1, both significantly upregulated in RA-ILD patients ($p < 0.001$). A composite Urine_ILD_Score was constructed based on their expression levels. The score was significantly elevated in ILD patients ($p < 0.001$; Figure 2A) and associated with pulmonary impairment.

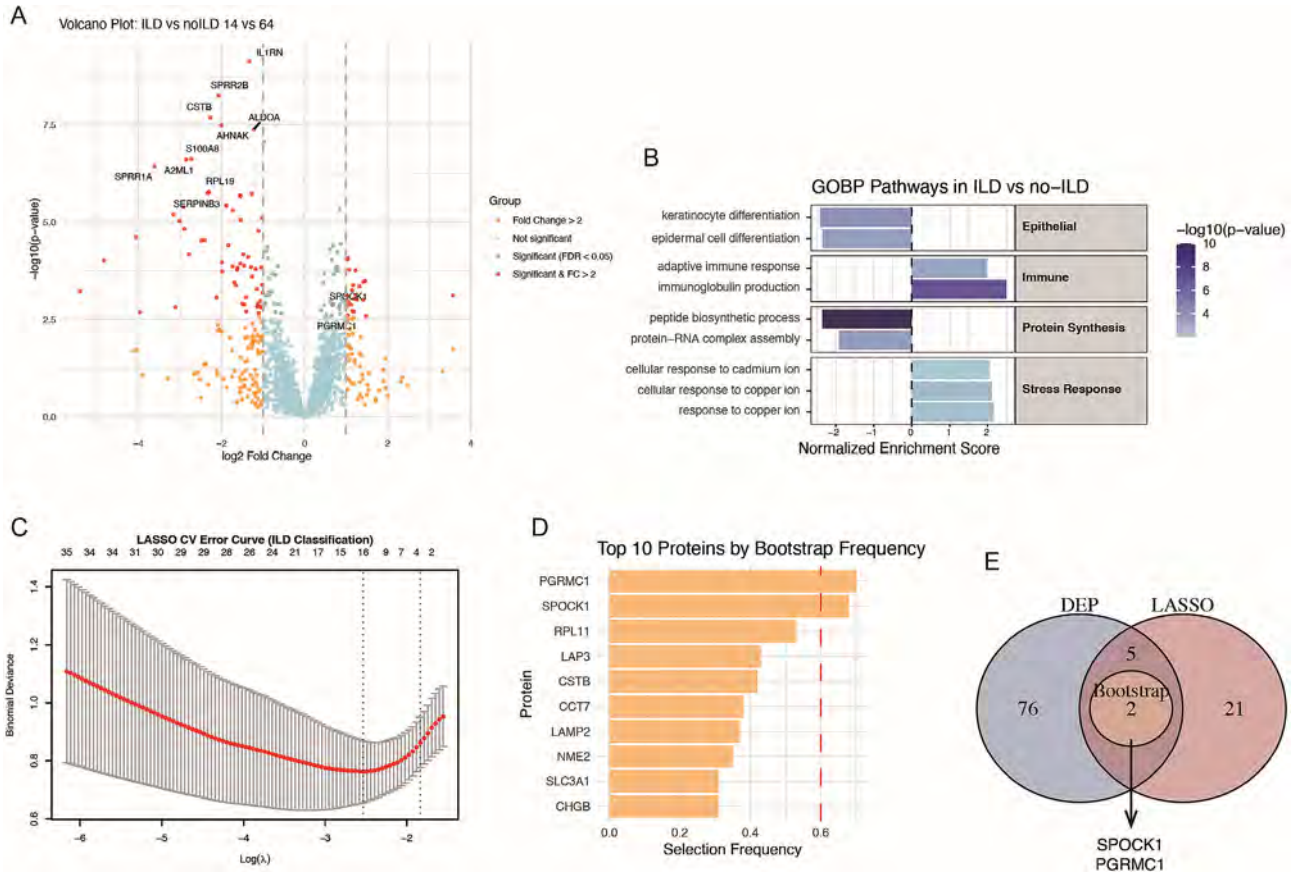


Figure 1. Identification of ILD-associated urinary proteins in RA patients. (A)Volcano plot of differentially expressed urinary proteins between RA patients with ILD (n = 14) and without ILD (n = 64). (B) Gene set enrichment analysis (GSEA) of Gene Ontology Biological Processes based on ranked protein expression between ILD and no-ILD RA patients. (C) LASSO regression with 10-fold cross-validation for ILD classification. (D) Top 10 proteins ranked by bootstrap selection frequency across 1,000 iterations. (E) Venn diagram showing overlap of differentially expressed proteins, LASSO-selected features, and proteins consistently selected by bootstrap.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

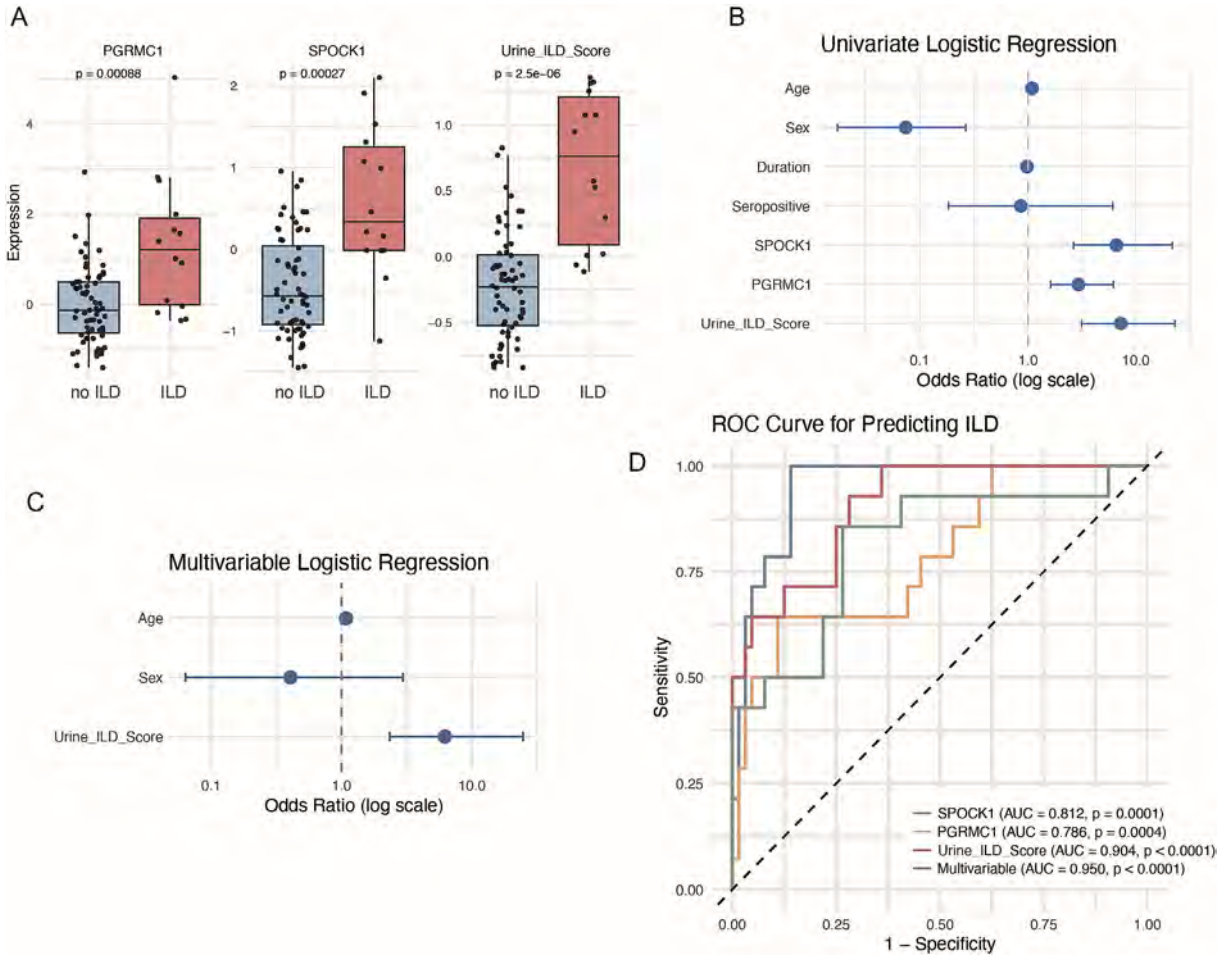


Figure 2. Urine-based protein biomarkers and composite score predict ILD in RA patients. (A)Expression levels of SPOCK1, PGRMC1, and the composite Urine_ILD_Score in RA patients with and without ILD. (B) Forest plot of univariable logistic regression assessing the association of clinical and proteomic variables with ILD status. (C) Forest plot of multivariable logistic regression including age and sex as covariates. (D) ROC analysis comparing the discriminatory performance of SPOCK1, PGRMC1, the composite score, and a full multivariable model (including clinical covariates).

In ROC analysis, the score demonstrated high discriminatory ability (AUC = 0.904, $p < 0.0001$), outperforming either protein alone (SPOCK1: AUC = 0.812; PGRMC1: AUC = 0.786; Figure 2D). In multivariable logistic regression adjusting for age and sex, the Urine_ILD_Score remained independently associated with ILD (OR = 6.19, 95% CI [2.34–24.64], $p = 0.002$; Figure 2C). A combined multivariable model incorporating clinical covariates further improved classification performance (AUC = 0.950; Figure 2D). Importantly, PGRMC1 levels correlated positively with KL-6 ($r = 0.79$, $p = 0.028$) and negatively with total lung capacity (TLC%) ($r = –0.79$, $p = 0.048$), suggesting potential relevance to ILD pathogenesis and severity.

Conclusion: Urinary proteomic profiling can identify RA patients at increased risk for ILD. A composite score based on SPOCK1 and PGRMC1 provides a promising, non-invasive biomarker for ILD risk stratification in RA and may support clinical decision-making and patient monitoring.

Disclosure: J. Shi: None; **X. Yuan**: None; **Y. Deng**: None; **C. Yu**: None; **N. Jiang**: None; **Z. Guo**: None; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11; **M. Li**: None; **W. Sun**: None; **Q. Wang**: None; **X. Tian**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1751

Disease activity, inflammation, and older age are associated with quantitative interstitial abnormalities in early RA: Results from a multicenter, prospective cohort study

Gregory McDermott[1], Xiaosong Wang[2], Misti Paudel[3], Ying Qi[4], Emily Kowalski[5], Grace Qian[6], Liya Sisay Getachew[5], Kevin Mueller[6], Alene Saavedra[6], Lauren O'Keeffe[6], Natalie Davis[1], Alison Puri[7], Kathleen Vanni[6], Caleb Bolden[8], Tina Mahajan[9], Erica Mulcaire-Jones[10], Neda Kortam[11], Pierre Antoine Juge[12], Tracy J. Doyle[13], Marcy Bolster[14], Kevin Deane[15], Dinesh Khanna[10], Bryant England[9], Raul San Jose Estepar[6], George Washko[6] and Jeffrey Sparks[5], [1]Brigham and Women's Hospital, Brookline, MA, [2]Brigham and Women's Hospital, Natick, MA, [3]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [4]Brigham and Women's Hospital, Boston, [5]Brigham and Women's Hospital, Boston, MA, [6]Brigham and Women's Hospital, Boston, [7]Boston University, Brookline, MA, [8]Massachusetts General Hospital, Boston, [9]University of Nebraska Medical Center, Omaha, NE, [10]University of Michigan, Ann Arbor, MI, [11]University of Michigan, Ann Arbor, [12]Hopital Bichat, APHP, Paris, France, [13]Brigham and Women's Hospital, West Roxbury, MA, [14]Massachusetts General Hospital, Concord, MA, [15]University of Colorado Denver Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes I: Breathe (ILD/Pulmonary) (1746–1751)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Quantitative computed tomography (QCT) methods using machine learning have been developed to automatically quantify parenchymal lung features on chest CT imaging. QCT can detect subtle or early abnormalities, and abnormal QCT findings have been associated with symptoms, progressive lung disease, and mortality in general population studies. Based on prior studies linking RA disease activity to interstitial lung disease (ILD) in patients with established RA, we hypothesized that higher RA disease activity would be associated with increased interstitial changes on QCT in early RA.

Methods: We performed a cross-sectional study of participants in SAIL-RA (Study of Inflammatory Arthritis and ILD in Early RA), an ongoing prospective, multicenter longitudinal study of patients recently diagnosed with RA at five U.S. sites between 2017 and 2025. All participants had early RA (diagnosed < 2 years prior to enrollment) and were assessed with physical examination, chest high-resolution CT imaging, pulmonary function tests (PFTs), and peripheral blood testing. QCT was performed using a *k*-nearest neighbor machine learning classifier that categorizes regions of interest into normal lung, interstitial changes, or emphysema based on the local tissue density and distance from the pleural surface. Interstitial changes on QCT may represent features of ILD or other abnormalities such as scarring after infection. We examined the correlation of QCT interstitial changes with PFTs, RA disease activity, and erythrocyte sedimentation rate (ESR) using Spearman correlation coefficients. We tested the association between baseline age, sex, smoking status, RF, anti-CCP, and RA disease activity with QCT interstitial features using multivariable linear regression.

Results: We performed chest QCT analysis on 200 participants with early RA (median RA duration 0.72 years, mean age 55.7 years, 75% female, 85% seropositive) (**Table 1**). On QCT, early RA patients had mean normal lung percentage of 88.0% (SD 7.8). The mean percentage of interstitial changes and emphysema was 5.6% (SD 6.8) and 1.2% (SD 1.7), respectively. Interstitial changes on QCT were correlated with higher DAS28-ESR (rho=0.26, p=0.0003) and ESR (rho=0.30, p< 0.0001), as well as lower FVC% (rho=-0.23, p=0.002) and DLCO% (rho=0.42, p< 0.0001) (**Figure 1**). In a multivariable linear regression model, older age (b=+0.14 per year, 95%CI 0.07-0.21, p< 0.0001) and DAS28-ESR (b=0.64 per point, 95%CI 0.01-1.26, p=0.046) were independently associated with percentage of interstitial changes (**Table 2**). The b

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

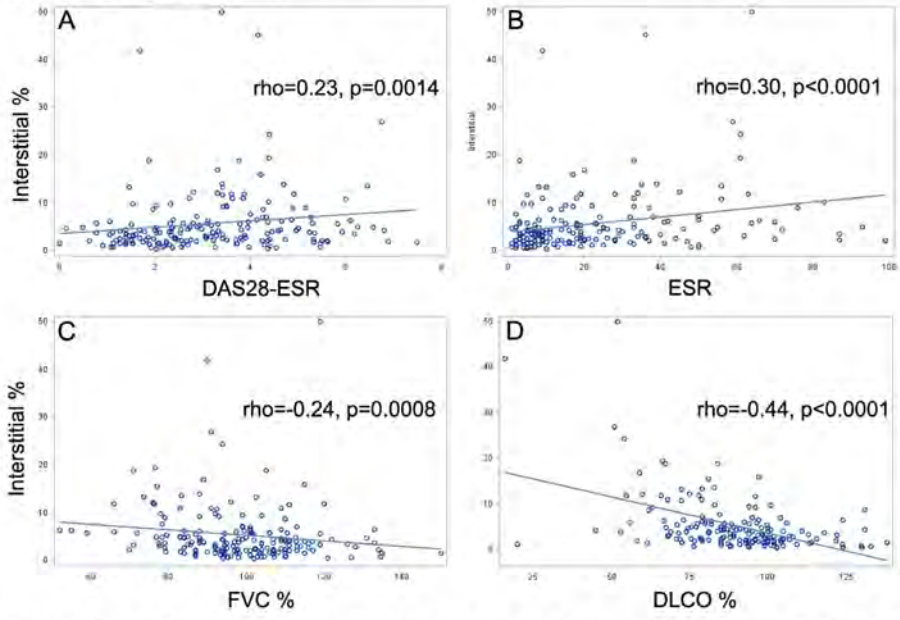
Table 1: Baseline characteristics of early RA participants in SAIL-RA, a multicenter, prospective longitudinal cohort study with QCT data (n=200)

Characteristic	Early RA patients with QCT data (n=200)
Demographics and Lifestyle	
Age, years (mean, SD)	55.7 (13.9)
Female sex at birth	149 (74.5%)
Race	
Asian	8 (4.0%)
Black	10 (5.0%)
White	170 (85.0%)
Other	12 (6.0%)
Smoking status	
Never	125 (62.5%)
Past	64 (32.0%)
Current	11 (5.5%)
BMI, kg/m², median (IQR)	27.8 (24.3, 32.8)
RA characteristics	
RA diagnosis duration, years (median, IQR)	0.72 (0.36, 1.62)
DAS28-ESR (median, IQR)	3.1 (2.0, 4.3)
TJC28 (median, IQR)	1 (0, 4)
SJC28 (median, IQR)	1 (0, 3)
PtGA (median, IQR)	20 (10, 50)
ESR (median, IQR)	16 (7, 33)
Disease activity	
Remission/low	100/189 (52.9%)
Moderate/high	89/189 (47.1%)
Seropositive for anti-CCP and/or RF	167/196 (85.2%)
Current medications	
Glucocorticoids	58 (29.0%)
Methotrexate	141 (70.5%)
Other csDMARDs	71 (35.5%)
TNFi	38 (19.0%)
Non-TNFi b/tsDMARDs	11 (5.5%)
Pulmonary function tests	
FEV_1/FVC (median, IQR)	0.79 (0.73, 0.82)
FEV_1% (median, IQR)	97 (85, 108)
FVC% (median, IQR)	98 (88, 109)
DLCO% (median, IQR)	89 (77.3, 100)
FVC% <80%	25/187 (13.4%)
FEV_1/FVC <70%	28/188 (14.9%)
DLCO% <75%	35/164 (21.3%)

Index date = date of baseline visit with high-resolution CT chest imaging performed

Anti-CCP = anti-cyclic citrullinated peptide antibody, b/tsDMARD = biologic or targeted synthetic disease modifying antirheumatic drug, csDMARD = conventional synthetic disease modifying antirheumatic drug, DAS28-ESR = disease activity score of 28 joints with erythrocyte sedimentation rate, DLCO = diffusion capacity of carbon monoxide, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, HRCT = high resolution computed tomography, IQR = interquartile range, RF = rheumatoid factor, SD = standard deviation, SJC = swollen joint count, TJC = tender joint count, TNFi = tumor necrosis factor inhibitor

Figure 1: Correlation of quantitative CT interstitial changes with (A) DAS28-ESR disease activity, (B) erythrocyte sedimentation rate, (C) forced vital capacity, and (D) diffusion capacity of carbon monoxide



DAS28-ESR = disease activity score with 28 joints and with ESR, DLCO = diffusion capacity of carbon monoxide, ESR = erythrocyte sedimentation rate, FVC = forced vital capacity

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Associations of baseline factors with percentage of interstitial changes on QCT in early RA patients (n=200)

Characteristic	Unadjusted β	95%CI	p-value	Multivariable* β	95%CI	p-value
Demographics						
Age at RA (per year)	0.16	(0.10, 0.23)	**<0.0001**	0.14	(0.07, 0.21)	**0.0001**
Age at RA, categorical						
<60 years	Ref	Ref	Ref			
≥60 years	3.76	(1.90, 5.62)	**<0.0001**			
Male (vs. female)	1.03	(-1.16, 3.22)	0.36	0.88	(-1.34, 3.09)	0.44
Lifestyle						
Smoking status						
Never	Ref	Ref	Ref	Ref	Ref	Ref
Past	2.20	(0.15, 4.26)	**0.036**	0.57	(-1.50, 2.64)	0.59
Current	-0.43	(-4.64, 3.78)	0.84	-2.76	(-6.99, 1.46)	0.20
Smoking pack-years (per unit)	-0.003	(-0.03, 0.02)	0.81			
BMI (per unit)	0.06	(-0.08, 0.20)	0.43			
RA characteristics						
DAS28-ESR (per unit)	0.67	(0.04, 1.29)	**0.037**	0.64	(0.01, 1.26)	**0.046**
TJC28 (per unit)	0.02	(-0.18, 0.23)	0.82			
SJC28 (per unit)	0.03	(-0.22, 0.29)	0.81			
PtGA (per unit)	0.02	(-0.02, 0.05)	0.34			
ESR (per unit)	0.08	(0.03, 0.12)	**0.0006**			
Moderate/high DAS28-ESR (vs. remission/low)	3.09	(1.20, 4.98)	**0.002**			
Seropositive (vs. seronegative)	0.85	(-1.86, 3.57)	0.54			
Anti-CCP positive (vs. anti-CCP negative)	0.71	(-1.55, 2.96)	0.54			
RF positive (vs. RF negative)	2.22	(0.001, 4.43)	**0.049**	1.78	(-0.40, 3.95)	0.11
Current medications						
Glucocorticoids (vs. not)	2.05	(-0.03, 4.14)	0.054			
Methotrexate (vs. not)	0.58	(-1.51, 2.66)	0.58			
TNF inhibitors (vs. not)	-1.50	(-3.93, 0.92)	0.22			
PFTs						
FEV_1/FVC (per unit)	-0.13	(-0.52, 0.27)	0.53			
FEV_1% (per unit)	-0.01	(-0.06, 0.03)	0.55			
FVC% (per unit)	-0.06	(-0.11, -0.001)	**0.045**			
DLCO% (per unit)	-0.16	(-0.20, -0.11)	**<0.0001**			

* = multivariable linear regression adjusted for age at RA diagnosis, sex, smoking status, RF status, and DAS28-ESR

Anti-CCP = anti-cyclic citrullinated peptide antibody, csDMARD = conventional synthetic disease modifying antirheumatic drug, DAS28-ESR = disease activity score of 28 joints with erythrocyte sedimentation rate, DLCO = diffusion capacity of carbon monoxide, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, HRCT = high resolution computed tomography, IQR = interquartile range, MRC = modified research council, RF = rheumatoid factor, SD = standard deviation, SJC = swollen joint count, TJC = tender joint count, TNFI = tumor necrosis factor inhibitor

from the linear regression model can be interpreted as a percentage increase in interstitial changes per unit increase in the predictor (increase of 0.70% per point of DAS28-ESR).

Conclusion: In this prospective, multicenter study of 200 patients with early RA analyzed using machine learning QCT methods, older age and higher RA disease activity were associated with more QCT interstitial changes. QCT interstitial changes were correlated with lower FVC and DLCO. These findings emphasize the role of inflammation in RA-ILD pathogenesis early in the RA disease course and demonstrate the potential of QCT for RA-ILD screening and monitoring.

Disclosure: G. McDermott: None; **X. Wang**: None; **M. Paudel**: None; **Y. Qi**: None; **E. Kowalski**: None; **G. Qian**: None; **L. Getachew**: None; **K. Mueller**: None; **A. Saavedra**: None; **L. O'Keeffe**: None; **N. Davis**: None; **A. Puri**: None; **K. Vanni**: None; **C. Bolden**: None; **T. Mahajan**: None; **E. Mulcaire-Jones**: Caribou Pharmaceuticals, 2; **N. Kortam**: AstraZeneca, 5; **P. Juge**: None; **T. Doyle**: Bayer, 5, Sanofi, 3; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **K. Deane**: Inova Diagnostics, 1; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **B. England**: Boehringer-Ingelheim, 2, 5; **R. Estepar**: Boehringer-Ingelheim, 5, Gossamer Bio, 5, Lung Biotechnology, 7, Quantitative Imaging Solutions, 12,; **G. Washko**: Apogee, 2, AstraZeneca, 2, Boehringer-Ingelheim, 5, Intellia Therapeutics, 2, Pieris Therapeutics, 2, Quantitative Imaging Solutions, 12,, Regeneron, 2, Sanofi, 2, Verona, 1, 2; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1752

Prg4+ Ligament Cells Are Involved in Ligament Ossification in Ankylosing Spondylitis

Kunhai Tang[1], Lilu Zu[1], Chenyuan Wu[1], Jiucun Wang[1] and Jing Liu[2], [1]Fudan University, shanghai, China (People's Republic), [2]Fudan University, Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science (1752–1757)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Ankylosing spondylitis(AS) is a chronic inflammatory disease with clinical symptoms characterized by inflammatory low back pain and spinal ankylosis due to ligament ossification. Enthesitis is considered an important manifestation of ankylosing spondylitis and is involved in ligament ossification in AS. However, the exact mechanism of ligament

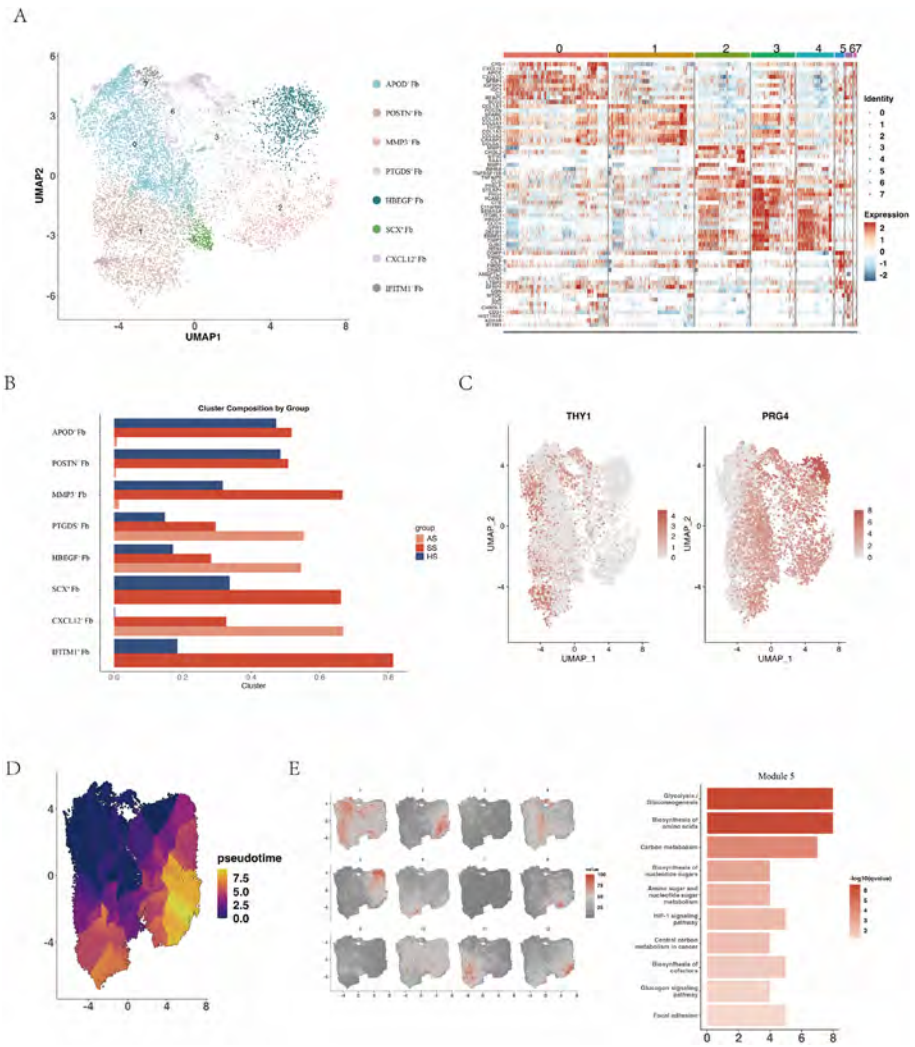


Figure 1 A) Single-cell UMAP plot and cluster marker gene heatmaps of spinal ligament fibroblasts from healthy subjects, AS patients, and patients with degenerative spinal stenosis. B) Cluster composition map between three groups. C) Distribution of PRG4 and THY1 in different clusters. D) Pseudotime analysis of different modules. E) Gene pathway enrichment analysis (KEGG) of module 5 between healthy controls and AS patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

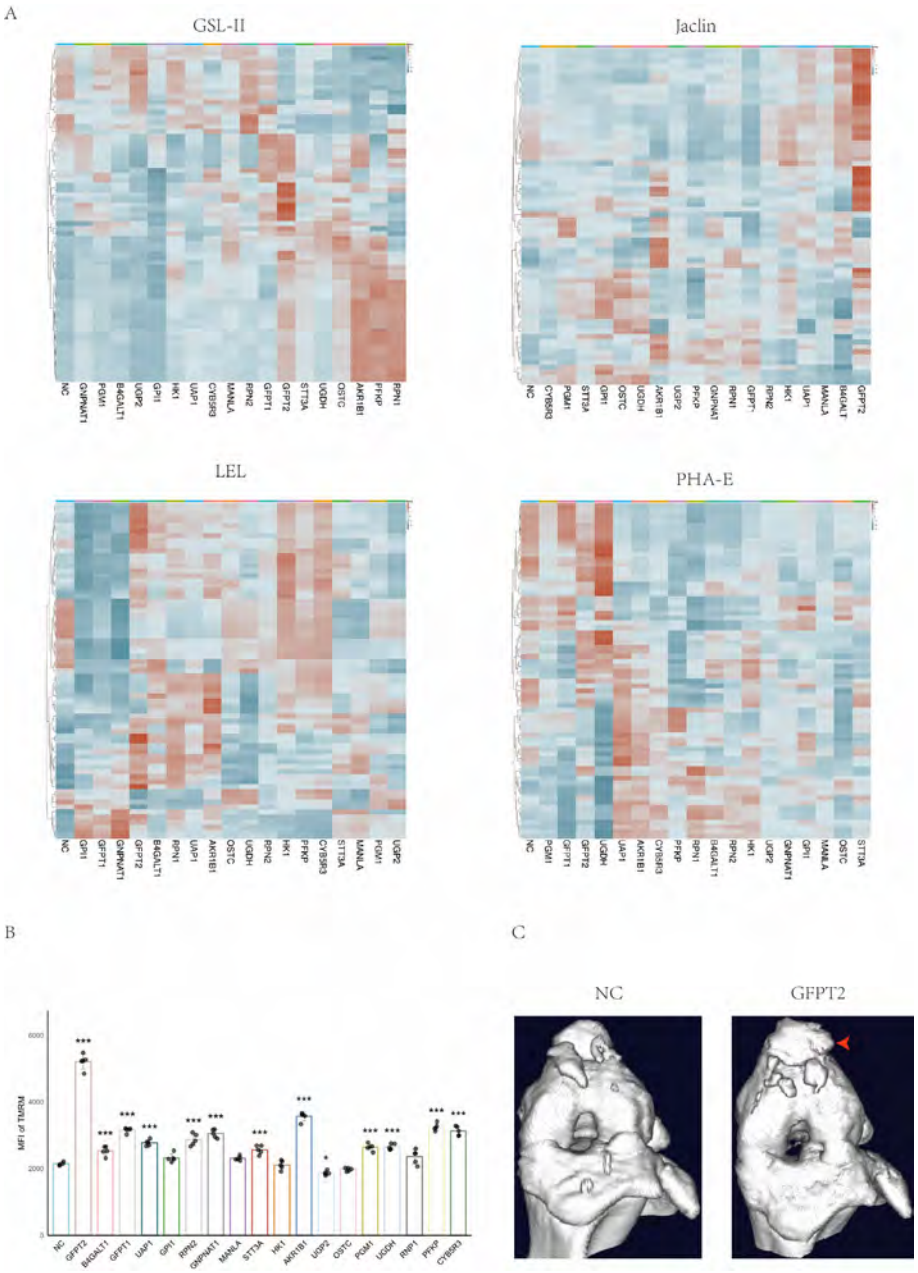


Figure 2 A) Detection of glycosylation levels in cells overexpressing different genes by high content imaging system using four different lectins. Mapping of heatmaps using high content parameters. B) Mitochondrial membrane potential (MPP) was detected by flow cytometry in cells overexpressing different genes. C) MicroCT assay of mice transplanted with different TT-D6 cell sheets after patellar ligament resection modeling. Red arrows indicate abnormal ossification at the enthesis.

ossification is still poorly understood. The aim of this study was to systematically investigate the mechanisms of AS ligament ossification through combination of multiple methods.

Methods: Single-cell sequencing of spinal ligament samples from AS patients (ligament ossification) and healthy controls. Pathway enrichment analysis (KEGG) and gene set enrichment analysis (GSEA) was conducted on the differential cell populations between the two groups. Eighteen-key differential genes (up-regulated in AS) identified by single cell sequencing were separately overexpressed in TT-D6 (mouse tendon cell line) using the CRISPR-Cas9 system. Intracellular glycosylation levels and mitochondrial membrane potential were detected by using a high-content cell imaging system and flow cytometry respectively. Effect of key gene overexpression on ligament ossification in vivo verified by tendon cell sheet transplantation experiments.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Through single-cell transcriptome analysis, we identified a population of fibroblasts (ligament cells) with Prg4 as a marker gene whose proportion was significantly upregulated in ligament ossification AS patients (**Figure 1A-C**). Gene pathway enrichment analysis (KEGG) showed significant activation of glycolysis and nucleotide biosynthesis pathways in this subpopulation of cells in AS patients (**Figure 1D**). GFPT2 (Glutamine-Fructose-6-Phosphate Transaminse 2) as identified as a possible key gene involved in AS ligament ossification by a CRISPR-Cas9 gene screen combined with high content cell imaging system and flow cytometry (**Figure 2A and 2B**). In vivo transplantation experiments show that GFPT2 enhances abnormal ossification at the enthesis after patellar ligament resection modeling in mice (**Figure 2C**).

Conclusion: GFPT2 is a key gene for ligament ossification in AS, and targeting GFPT2 may serve as a novel approach to treating ankylosing spondylitis.

Disclosure: K. Tang: None; **L. Zu**: None; **C. Wu**: None; **J. Wang**: None; **J. Liu**: None.

Abstract Number: 1753

Axial Psoriatic Arthritis is Phenocopied in a Humanized Mouse Model

Christopher Ritchlin[1], Javier Rangel-Moreno[2], Angel Rangel-Garcia[3], Marissa Krantz[4], Madison Brien[2], Thiloginy Sathilaseenlan[2], Jeffrey Fox[5], Ronald Wood[2] and **Maria de la Luz Garcia-Hernandez**[3], [1]University of Rochester Medical Center, Canandaigua, NY, [2]University of Rochester, Rochester, NY, [3]University of Rochester, West Henrietta, NY, [4]University of Rochester, Bethesda, MD, [5]University od Rochester, Rochester, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science (1752–1757)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Psoriatic arthritis (PsA) is a complex and heterogeneous inflammatory disorder involving the axial skeleton in approximately 30% of patients. The mechanisms that underlie psoriatic axial inflammation (AxPsA) are not well understood and longitudinal studies to examine the immune mechanisms involved in disease pathogenesis and progression

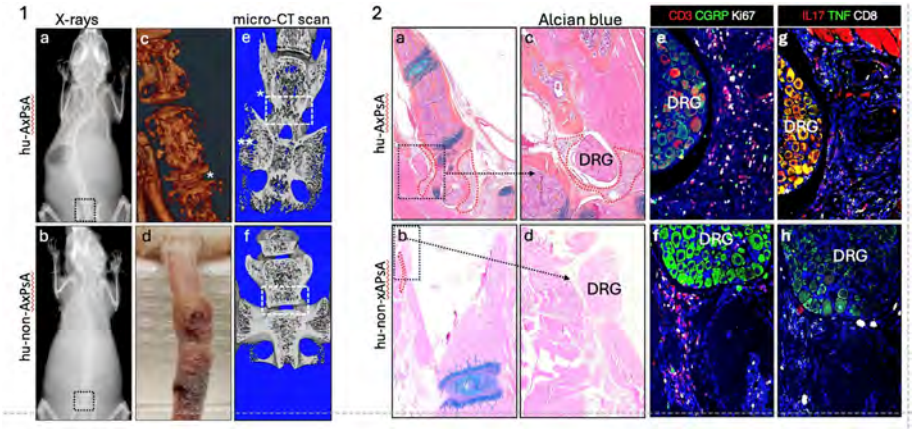


Figure 1. Humanized NSG-SGM3 mice generated with sera and PBMC from AxPsA and non-AxPA patients. 1) Hu-AxPsA mice demonstrated (a), cervical and thoracic kyphosis not seen in controls (b) (c), spinal fusion and erosion in the lumbar spine (c, * fusion and erosion below), (d) tail inflammation and necrosis and (e) L5, S1 fusion * and bone resorption ** not observed in controls (f). Figure 2. Alcian blue staining of the spine shows abundant infiltrating immune cells (dotted red line) around the dorsal root ganglion (DRG) (a,c) and low infiltration in the spine of hu-non-AxPsA mice (b,d). Immunofluorescence staining shows more proliferating CD3 (red and white) and IL-17+ (red) TNF + (green) CD8+ (white) and Il-17+ TNF+ cells in the DRG of hu-AxPsA (e, g) compared to hu-non-AxpSA mice (f,h).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

using human cells in an animal model have not been performed. In previous analyses, we demonstrated that human PsA phenotypes in the peripheral skeleton, entheses and skin are recapitulated in the NSG-GM3 humanized mouse model. Herein, we examined if axial disease is phenocopied in this mouse model.

Methods: Two groups of NSG-SGM3 mice were injected with serum and peripheral blood mononuclear cells (PBMC) collected from three biologic naive PsA patients with inflammatory back pain and radiographic or MRI documented sacroiliitis (AxPsA) and controls (PsA patients without axial disease). At day 30, mice were anesthetized, and their spines were dissected for radiographic and micro-CT scan analysis. Tissue sections from decalcified spines were stained with anti CD45, CD14, CD8, Ki67, TNF and Il-17 antibodies.

Results: NSG-SGM3 mice injected with serum and engrafted with PBMC from patients with AxPsA exhibited pronounced spinal deformities. Radiographic imaging revealed marked cervical and thoracic kyphosis, bone erosion and osteoproliferation in the tail and micro-computed tomography (micro-CT) scans identified both bone resorption and pathological bone fusion in the sacroiliac joint and lumbar spine. In contrast, mice injected with PBMC and sera from non-AxPsA controls did not demonstrate significant inflammation or structural alterations. Histological analysis in the spine of mice injected with AxSpA PBMC and sera revealed accumulation of lymphocytes in and around the dorsal root ganglion (DRG) and in the surrounding muscle. Inflammatory cell infiltrates were characterized by proliferating CD3 T and CD8 T cells that expressed both TNF and IL-17. TNF and IL-17 expression were elevated most notably in the DRG.

Conclusion: Injection of PBMC and sera from AxPsA patients recapitulated axial clinical features in hu PsA mice. HuAxPsA mice developed kyphosis in the distal cervical and thoracic spine and structural damage in the lower lumbar and sacroiliac region and tail, including bone loss and new bone formation. Proliferating $CD3^+$ T and $CD8^+$ T cells expressing TNF and IL-17 were noted near the DRG and in surrounding tissues and paravertebral muscles. This model will accelerate investigation of immune mechanisms in AxPsA.

Disclosure: C. Ritchlin: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **J. Rangel-Moreno**: None; **A. Rangel-Garcia**: None; **M. Krantz**: None; **M. Brien**: None; **T. Sathilaseenlan**: None; **J. Fox**: None; **R. Wood**: None; **M. Garcia-Hernandez**: None.

Abstract Number: 1754

B3GNT2 Regulates Integrin β3 Glycosylation and Th17/Treg Imbalance in Axial Spondyloarthritis Pathogenesis

Chengchun Geng[1], Dachun Zhuo[1], Jiucun Wang[2] and **Jing Liu[1]**, [1]Fudan University, Shanghai, Shanghai, China (People's Republic), [2]Fudan University, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science (1752–1757)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: The rs6759298 variant near *B3GNT2* is associated with Axial Spondyloarthritis (AS); however, its pathogenic mechanisms remain unknown. In this study, we explored the role of B3GNT2 in glycosylation modifications and their impact on Th17/Treg imbalance, contributing to AS development.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

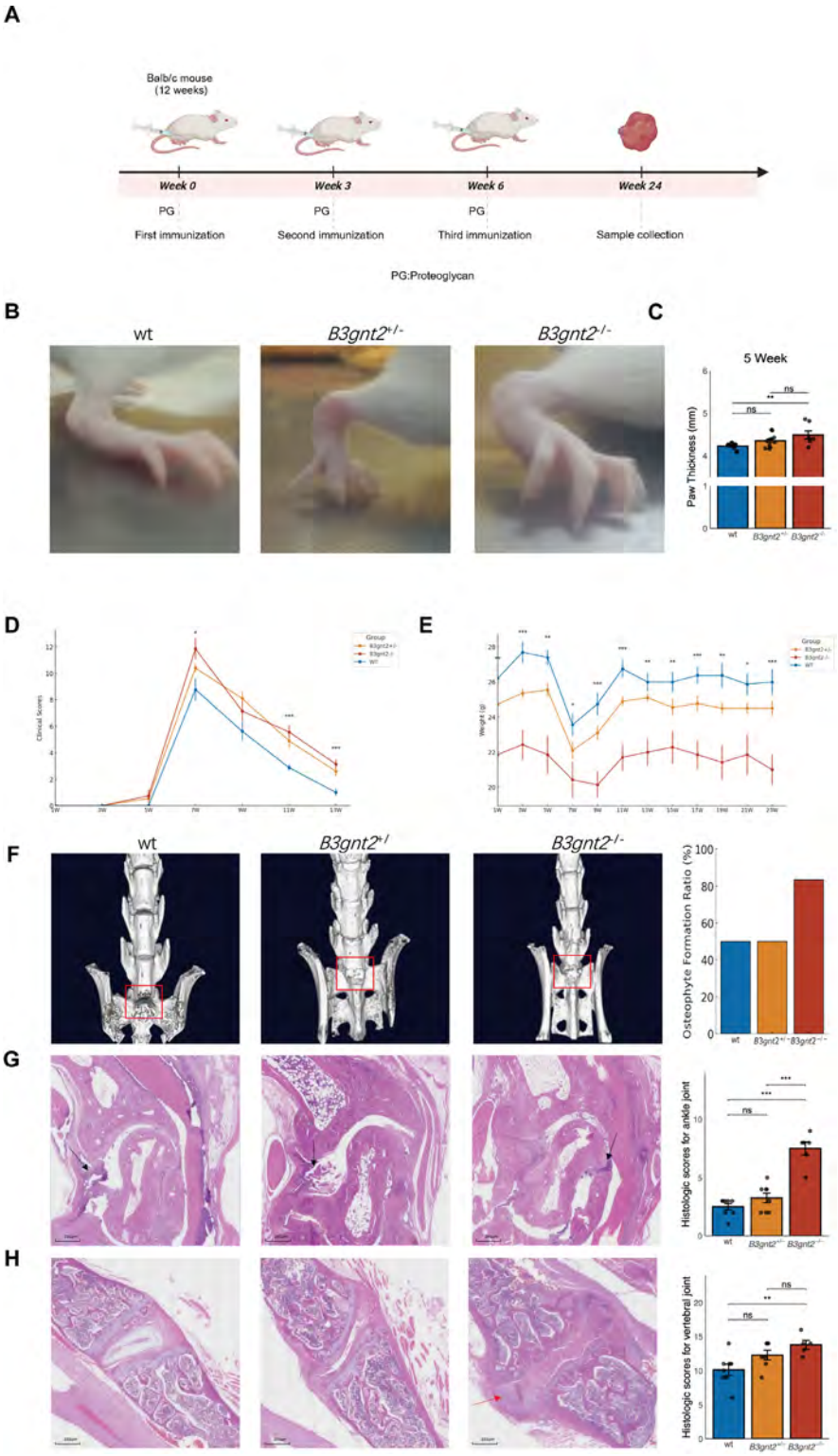


Figure 1. B3gnt2 Knockout Promotes inflammation and exacerbated osteophyte formation in Proteoglycan-induced arthritis Mice. (A) Schematic diagram for study design. Created in BioRender. (B) Representative pictures of the paw in three groups of mice at week 5. (C)Thickness of ankle joint in three groups of mice at week 5. (D) Degree of paw swelling in three groups of mice (n = 10). (E) Body weight monitoring in model mice. (F) Representative pictures of Micro-CT of the sacroiliac joint in three groups of mice at the end of week 24 and Statistics of osteophyte formation rate. Osteophyte formation (red square). (G) Representative pictures of ankle joint sections in three groups of mice (HE staining, scale bar = 250 μm) and histologic scores for ankle joint sections. Inflammatory cell infiltration in the synovium of the joint capsule (black arrow). (H) Representative pictures of vertebral joint sections in three groups of mice (HE staining, scale bar = 250 μm) and histologic scores of vertebral joint sections. New cartilage (red arrow). *P<0.05, **P<0.01, ***P<0.001; ns, Not Significant.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

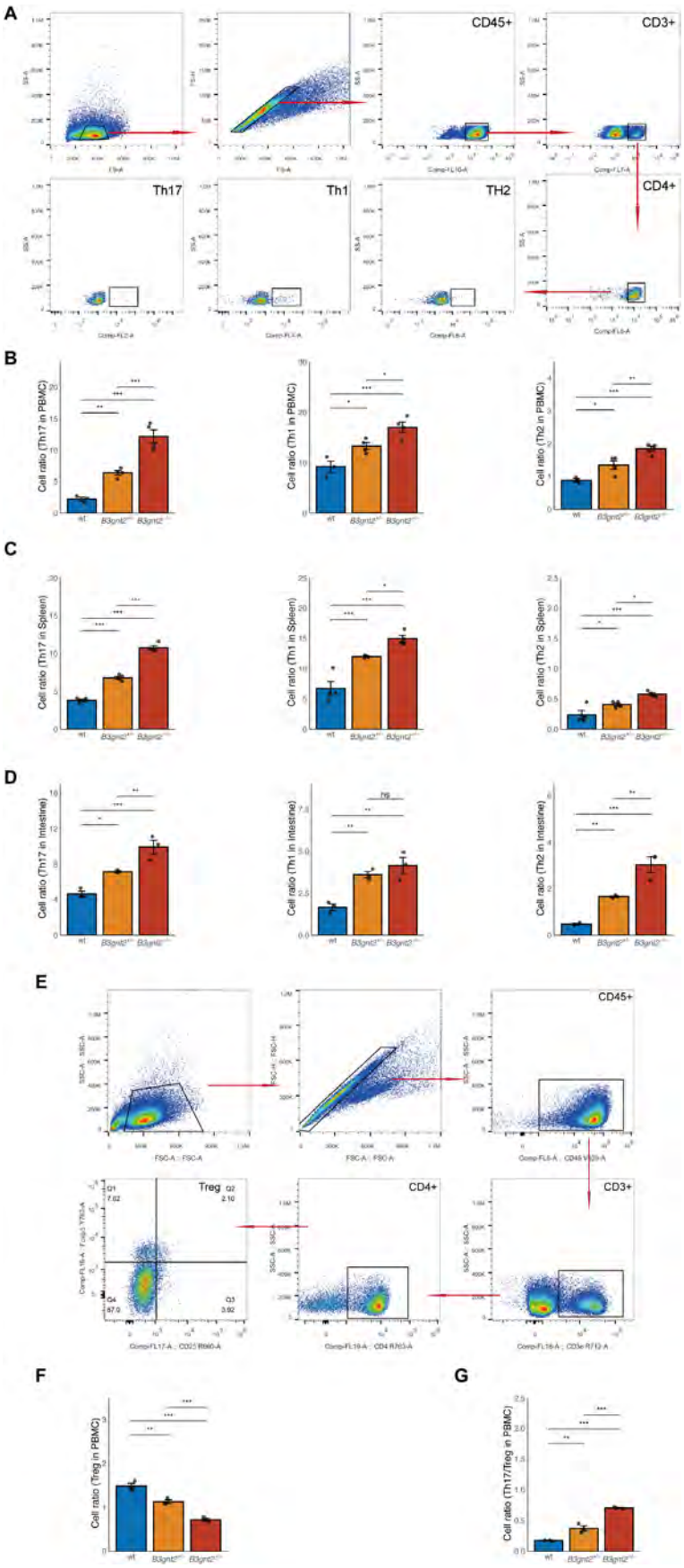


Figure 2. B3gnt2 knockout resulted in Th17/Treg imbalance. (A) Gating strategy used for analysis of Th cells. Arrows indicate that Th cells were sequentially gated from single cells, CD45+ cells, CD3+ cells and CD4+ cells. Gated CD4+ cells were analyzed for expression of IL-17A, IFN-γ, and IL-4. (B) Percentage of IL-17A+ cells or IFN-γ+ cells or IL-4+cells among CD4+ T cells in PBMC. (C) Cell ratio in spleen. (D) Cell ratio in Intestine. (E) Gating strategy used for analysis of Treg cells. Arrows indicate that Treg cells were sequentially gated from single cells, CD45+ cells, CD3+ cells and CD4+ cells. Gated CD4+ cells were analyzed for expression of CD25 and FoxP3. (F) Percentage of CD25+ FoxP3+ cells among CD4+ T cells in PBMC. (G) Cell ratio (Th17/Treg in PBMC). *P<0.05, **P<0.01, ***P<0.001; ns, Not Significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

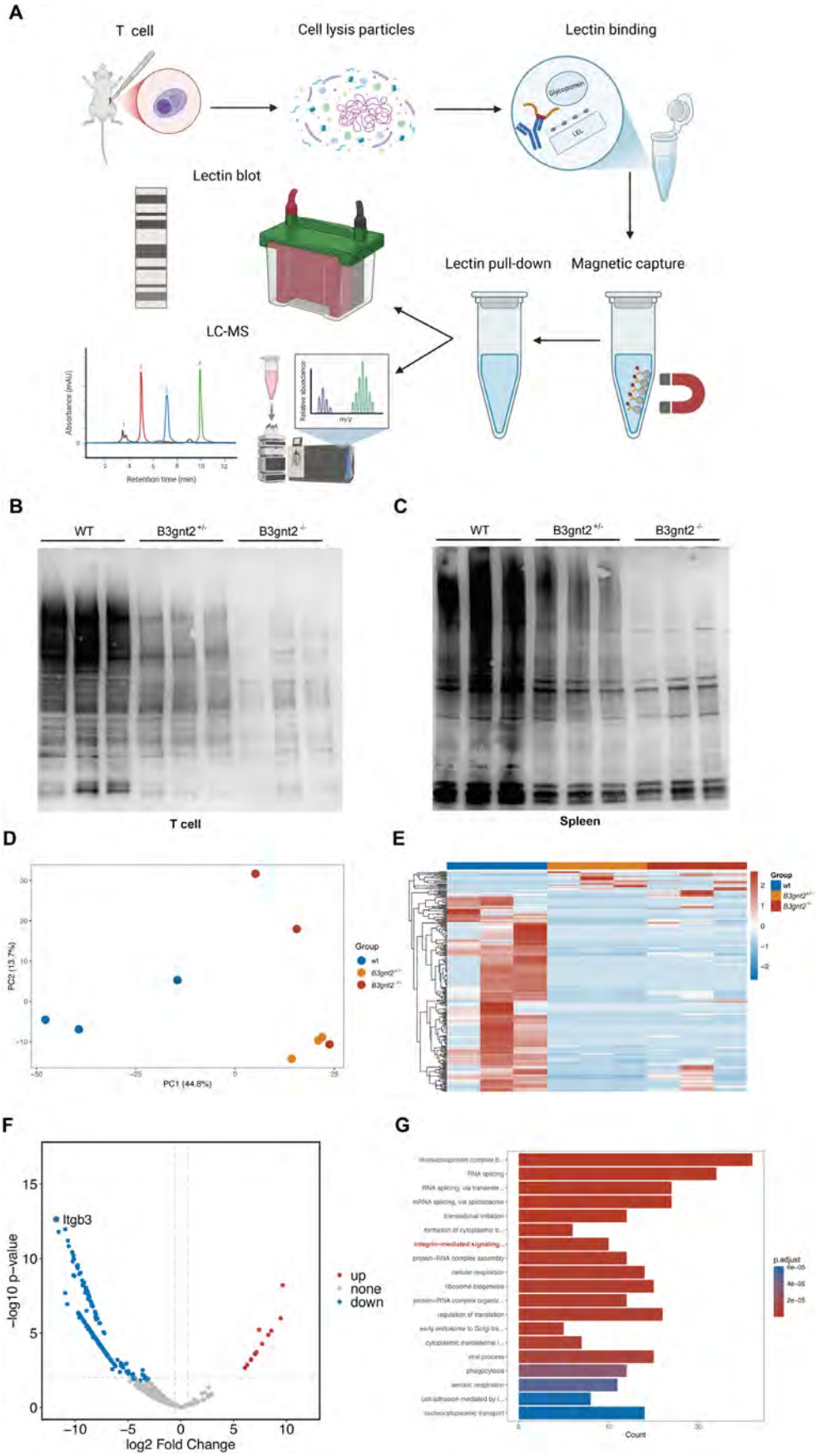


Figure 3. B3GNT2 Targets ITGB3 as a Key Glycosylation Substrate. (A) Schematic diagram for study design. Created in BioRender. (B) Lysates of T cells were incubated overnight and subjected to LEL blots for polylactosamine. (C) Lysates of Spleen cells were incubated overnight and subjected to LEL blots for polylactosamine. (D) Principal component analysis of protein across three groups (n=3/group). (E) Heatmap visualization of differentially expressed proteins with hierarchical clustering. (F) Volcano plot of differentially expressed proteins in B3gnt2-/- vs WT. (G) Gene Ontology enrichment of downregulated proteins in B3gnt2-/- vs WT.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted SNP genotyping and RNA-seq analysis on blood samples from 39 AS patients. Additionally, we generated *B3gnt2*-deficient mice (*B3gnt2*$^{+/-}$ and *B3gnt2*$^{-/-}$) to investigate the role of B3GNT2 in AS using a proteoglycan-induced arthritis (PGIA) model. The mechanism of B3GNT2 in AS was further explored through flow cytometry, RNA-seq, lectin blotting and mass spectrometry analysis.

Results: The rs6759298 mutant genotype (G/G) significantly downregulated *B3GNT2* expression in AS patients. In the PGIA model, *B3gnt2*-deficient mice exhibited an earlier onset of arthritis, higher arthritis severity scores, and prolonged inflammation. Functionally, we found a disrupted Th17/Treg balance in *B3gnt2*-deficient mice. Lectin blotting analysis revealed a marker reduction in poly-lactosamine expression on T cells from *B3gnt2*-deficient mice. Mass spectrometry identified integrin β3 (ITGB3) as a key glycoprotein differentially modified by B3GNT2. Furthermore, treatment of SKG mice with Cilengitide, an ITGB3 antagonist, effectively delayed disease onset.

Conclusion: This study demonstrates that rs6759298 reduces *B3GNT2* gene expression, thereby altering the glycosylation of ITGB3 and promoting the progression of AS. These findings offer new insights into the immune mechanisms underlying AS.

Disclosure: C. Geng: None; **D. Zhuo**: None; **J. Wang**: None; **J. Liu**: None.

Abstract Number: 1755

Multi-Omic Profiling Of CD8+ T Cells In Axial Spondyloarthritis (axSpA) And Reactive Arthritis (ReA) Implicates Common Pathways

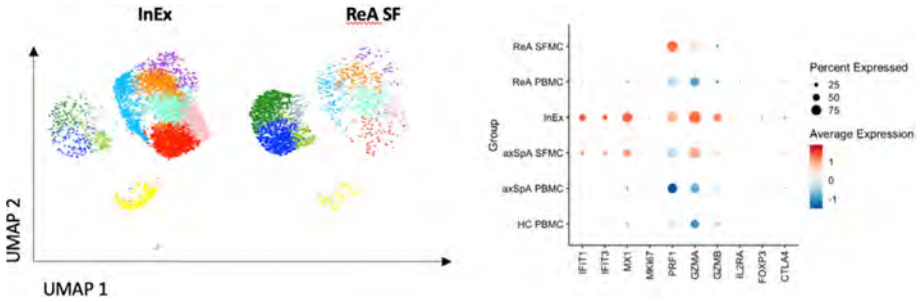
Zoya Qaiyum[1], Michael Tang[2], Shirin Soleimani[3], Addison Pacheco[2], Melissa Lim[4], Fataneh Tavasolian[4], Trevor Pugh[3] and Robert Inman[2], [1]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [2]University Health Network, Toronto, ON, Canada, [3]Princess Margaret Cancer Centre, University Health Network, Toronto, Canada, [4]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science (1752–1757)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

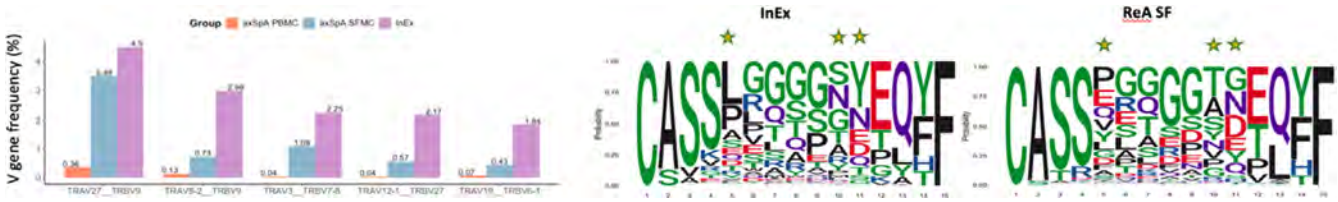
Background/Purpose: The strong clinical and genetic associations between axial spondyloarthritis (axSpA) and inflammatory bowel disease (IBD) underscore the pathogenic role of the gut-joint axis. We previously identified a subpopulation of pathogenic mature CD8+ T cells in the axSpA synovial fluid (SF), expressing CD103+ and CD49a+ integrins (InEx cells). The expression of integrins on InEx cells implicates their role in aberrant migration between the gut-joint axis. Whether InEx cells recognize an arthritogenic peptide remains unclear. We hypothesize that InEx cells may incite and perpetuate chronic inflammation in axSpA. To this end, we characterized their T-cell receptor (TCR) repertoire and gene expression profile.

Methods: Patients fulfilling the ASAS classification for axSpA were recruited (n=4). Active joint effusion from these patients is reflective of active joint inflammation which coincided with high disease activity (BASDAI >4). We isolated peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs), followed by FACS-sorting of mature CD8+ T cells and InEx cells. Subsequently, single-cell TCR (paired ab chains) and RNA sequencing were performed on these cell types. An HLA-B27+ reactive arthritis (ReA) sample were used as a comparison. These were all compared to HLA-B27+ healthy controls (n=4). Additionally, we used the GLIPH2 computational tool to assess TCR sequence convergence based on shared motifs to infer antigen-specific TCR groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Left panel displaying transcriptome profile of InEx vs mature CD8+ ReA SFMCs on UMAP plots. Genetic profile of InEx cells cluster differently to ReA SF. Right panel displaying notable gene expression across all groups, particularly in InEx and ReA SFMC. UMAP = Uniform Manifold Approximation and Projection, SF = synovial fluid, HC = healthy controls.



Left panel displaying the V gene frequency (% total cells in the group) of paired TRAV_TRBV genes expanded in InEx cells vs axSpA PBMC. Right panel displaying the CDR3b sequence logo plots between InEx and ReA SF mature CD8 T cells. Yellow stars highlight the amino acids that differ between the two groups.

Results: 12 distinct clusters of mature CD8+ T cells from all samples were observed, exhibiting gene expression consistent with TRM-like, cytotoxic and interferon-stimulated gene (ISG) potential. axSpA InEx cells showed a preferential expression of clusters associated with ISG expression and proliferation vs ReA mature CD8+ T cells, as judged by high *IFIT1*, *IFIT3*, *MX1*, and *MKI67* transcripts. Increased cytotoxic potential, based on elevated *GZMA* and *GZMB*, with some suppressive capacity, based on elevated *IL2RA*, *FOXP3*, and *CTLA4*, was also observed in axSpA InEx cells. The axSpA InEx TCR repertoire was less diverse, clonally expanded, and demonstrated specific TRBV9_TRAV27, TRBV9_TRAV8-2, and TRBV7-8_TRAV3 gene usage vs mature CD8+ T cells from either axSpA PB or SF. However, axSpA InEx cells demonstrated similarities with ReA mature CD8+ T cells, based on TCR gene usage (TRBV20-1_TRAV1-2, TRBV6-1_TRAV1-2, and TRBV6-2_TRAV1-2) and CDR3b motifs.

Conclusion: These observations suggest that InEx cells may incite inflammation similarly to ReA due to potential recognition of similar peptides, ultimately driving the selection of specific T cell clones. However, InEx cells represent a hybrid tissue resident memory-like population, likely primed by chronic type I interferon exposure. This may underlie the functional capacity of their clonal expansion and their ability to perpetuate inflammation which is distinct from ReA. This has important implications for therapeutic designs attempting to target integrin blockade in axSpA.

Disclosure: Z. Qaiyum: None; **M. Tang**: None; **S. Soleimani**: None; **A. Pacheco**: None; **M. Lim**: None; **F. Tavasolian**: None; **T. Pugh**: AstraZeneca, 2, 5, Chrysalis Biomedical Advisors, 2, Dynacare, 10, Merck, 2, Roche/Genentech, 2, 5; **R. Inman**: AbbVie/Abbott, 2, Janssen, 2, Novartis, 2, 5, UCB, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1756

Exosomal Cargo and Surface Markers: Informative Signals in Axial Spondyloarthritis

Fataneh Tavasolian[1], star lively[2], chiara Pastrello[3], Melissa Lim[1], Addison Pacheco[4], Zoya Qaiyum[5], Michael Tang[4], Zeynep Baskurt[3], Igor Jurisica[6], Mohit Kapoor[5] and Robert Inman[4], [1]University of Toronto, Toronto, ON, Canada, [2]University Healklth Network, Toronto, [3]University Health Network, Toronto, [4]University Health Network, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [6]University Health Network, Toronto, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science (1752–1757)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Exosomes are small extracellular vesicles carrying surface molecules and molecular cargo, including microRNAs (miRNAs), that mediate intercellular communication. Both the exosomal cargo and surface markers are increasingly recognized as key players in immune modulation and potential biomarkers in autoimmune diseases. In ankylosing spondylitis (AS), their role remains underexplored. We conducted an integrated investigation of exosomal surface markers, miRNA profiles, and their functional impact on regulatory T cells (Tregs) and purinergic signaling, aiming to identify new diagnostic and therapeutic avenues.

Methods: Plasma-derived exosomes were isolated from AS patients and healthy controls (HC). Exosomal surface markers were analyzed using flow cytometry, and miRNA sequencing was performed to profile cargo signatures. Functional effects were assessed in CD4+ T cells and Tregs by evaluating FOXP3+IRF4+ and FOXP3+IRF4+CTLA4+ subsets, proliferation assays, and CD39/CD73 enzymatic activity. DNA methylation of FOXP3, IL2R, and IRF4 was analyzed in four groups: HC Tregs, AS Tregs, HC Tregs exposed to AS exosomes, and CD4+CD25– controls. Gene expression profiling in sorted Tregs was used to assess key immune regulatory and apoptotic genes.

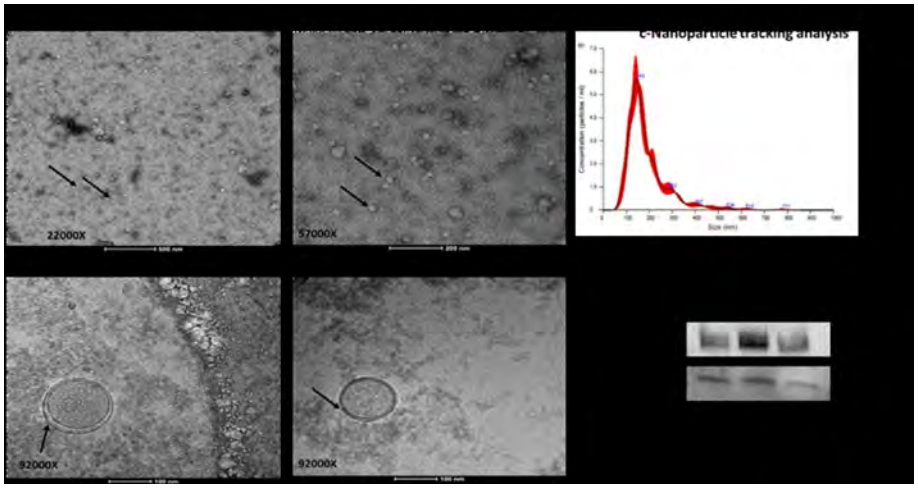


Figure 1- Exosome Isolation and Validation : (a) Exosome characteristics with morphology, size and markers. Exosomes display a round-shaped morphology in negative transmission electron microscopy (TEM). It is at 22 000× magnification, demonstrating the density of isolated exosomes in plasma (b) and are bilayer and spherical by cryo-TEM imaging. (c) Exosome sizes can be determined using nanoparticle tracking. Nanoparticle tracking analysis was used to examine the exosome size and concentration, and the results showed that the exosomes had an average size of 147 nm. (d) Expression of the exosomal markers CD63 and CD9 was confirmed with western blot.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

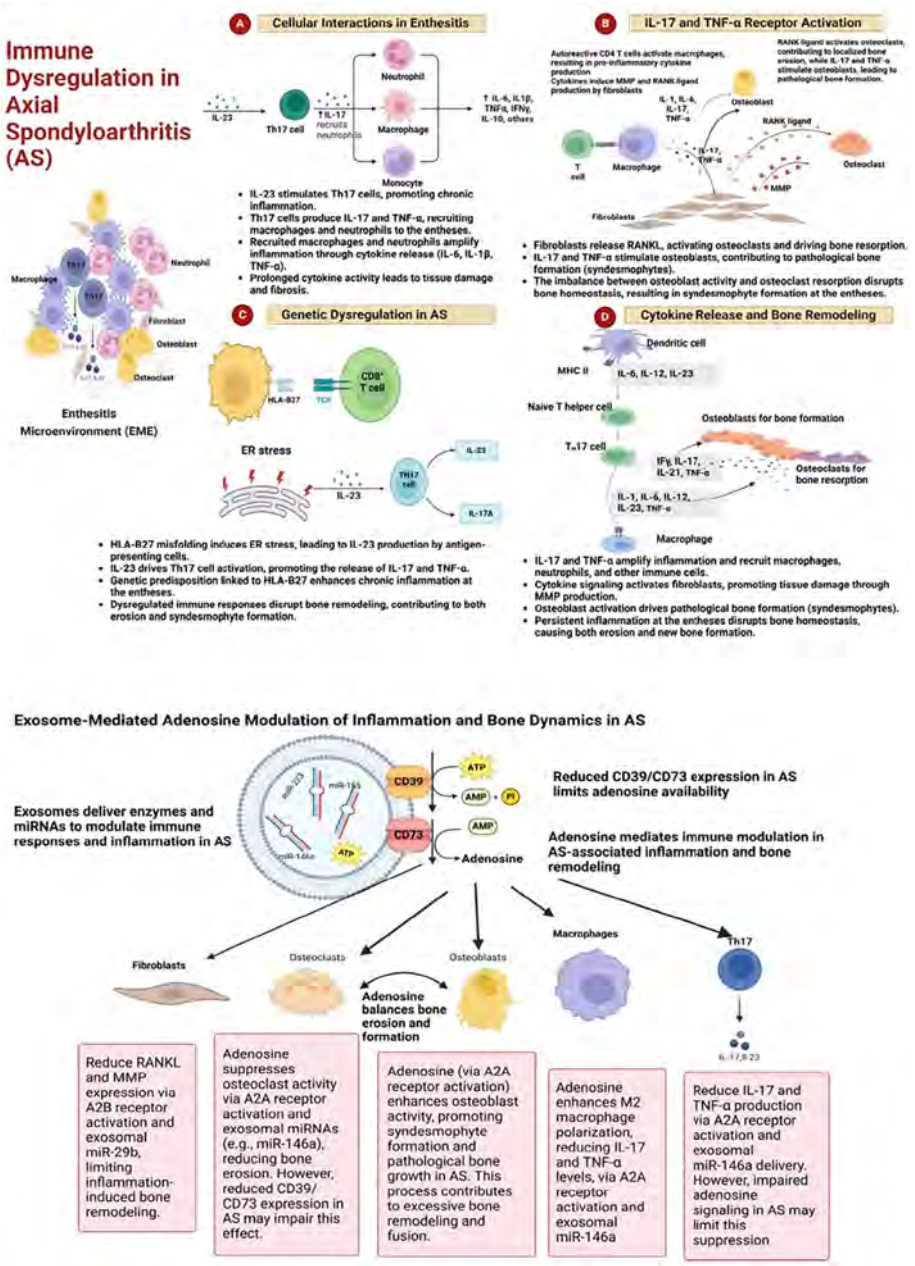


Figure 2: Immune Dysregulation and Exosome-Mediated Adenosine Modulation in axial spondyloarthritis (AS) (A) Immune Dysregulation in AS: The enthesitis microenvironment (EME) in AS is characterized by cellular interactions that drive inflammation and pathological bone remodeling. Panel A depicts cellular interactions where IL-23 stimulates Th17 cells to produce IL-17 and TNF-α, recruiting macrophages and neutrophils to the entheses. The cytokine release amplifies inflammation, leading to tissue damage and fibrosis. Panel B illustrates the roles of fibroblasts, macrophages, and T cells in the dysregulated cytokine signaling cascade. IL-17 and TNF-α receptor activation stimulate fibroblasts to release RANKL and MMP, driving osteoclast activity and disrupting bone homeostasis. Concurrently, osteoblast activation leads to pathological bone formation (syndesmophytes), highlighting the imbalance in bone remodeling. Panel C demonstrates genetic dysregulation in AS, with HLA-B27 misfolding inducing ER stress, promoting IL-23 production, and driving Th17-mediated inflammation. Panel D emphasizes cytokine-driven bone remodeling, showing osteoclast-mediated bone resorption and osteoblast-driven syndesmophyte formation under persistent inflammation. (B) Exosome-Mediated Adenosine Modulation of Inflammation and Bone Dynamics in AS: Exosomes released from immune and stromal cells deliver enzymes (CD39/CD73) and miRNAs (e.g., miR-146a, miR-29b) to modulate immune responses and bone remodeling in AS. CD39/CD73-mediated adenosine production suppresses osteoclast activity and enhances osteoblast activity via A2A receptor signaling. While adenosine reduces RANKL and MMP expression in fibroblasts and promotes M2 macrophage polarization, the reduced CD39/CD73 expression observed in AS limits adenosine availability, impairing its anti-inflammatory and bone-regulating effects. The balance between osteoclast-mediated bone erosion and osteoblast-mediated syndesmophyte formation is critical to AS pathology. Arrows indicate cellular interactions and regulatory pathways modulated by adenosine and exosomal components.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Gene expression profiling of sorted Tregs from AS patients revealed downregulation of IKZF2/Helios, TNFα, CD95/FAS, BCLXL, and CD45RO, alongside upregulation of IGF1R, indicating disrupted transcriptional networks important for Treg survival and stability. DNA methylation analysis demonstrated hypermethylation of FOXP3, IL2R, and IRF4 in AS Tregs, with similar patterns observed in HC Tregs exposed to AS exosomes, highlighting the epigenetic reprogramming potential of exosomes. miRNA sequencing of AS plasma-derived exosomes identified upregulation of miR-30c-5p, a regulator targeting IRF4, directly linking exosomal cargo to impaired Treg function. Functionally, AS exosomes carrying miR-30c-5p led to decreased proliferation of CD4+ T cells and a marked reduction in FOXP3+IRF4+ and FOXP3+IRF4+CTLA4+ Treg subsets. In parallel, AS exosomes induced reduced CD39/CD73 surface expression and impaired ATPase activity, indicating defective extracellular adenosine production and weakened immunosuppressive signaling. Collectively, these results demonstrate that AS exosomes orchestrate immune dysregulation through parallel effects on Treg stability and purinergic signaling.

Conclusion: Our integrated study demonstrates that AS plasma-derived exosomes drive immune dysregulation through miRNA-mediated gene regulation, epigenetic remodeling, and impaired purinergic signaling, culminating in Treg instability and loss of immune tolerance. These findings highlight exosomal signatures as promising biomarkers and therapeutic targets to restore immune balance in AS.

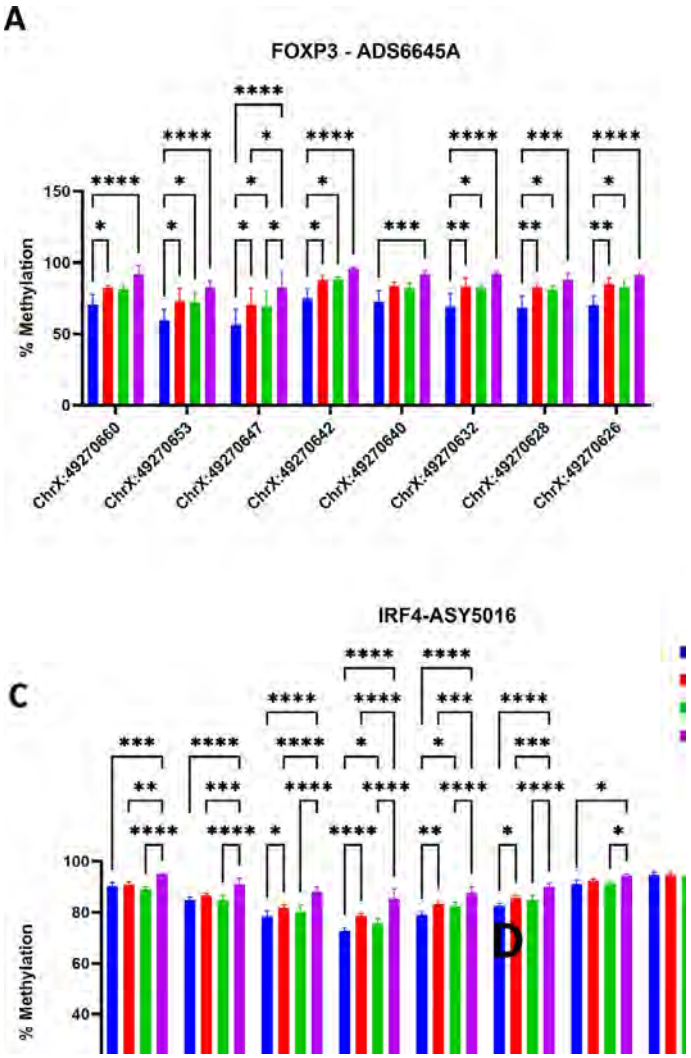


Figure 3. DNA Methylation Analysis. A: Hypermethylation of FOXP3 in AS Treg cells compared to HC. B: Hypermethylation of IL2R in AS Treg cells, contrasting with the typical demethylation observed in Tregs. C & D: Hypermethylation of IRF4 in Treg cells may impair their function in AS. This alteration may impact Treg function. HC Treg cells exposed to AS exosomes exhibited similar methylation patterns to AS Treg cells in all figures, highlighting the role of AS exosomes in Treg dysfunction.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: F. Tavasolian: None; **s. lively**: None; **c. Pastrello**: None; **M. Lim**: None; **A. Pacheco**: None; **Z. Qaiyum**: None; **M. Tang**: None; **Z. Baskurt**: None; **I. Jurisica**: None; **M. Kapoor**: None; **R. Inman**: AbbVie/Abbott, 2, Janssen, 2, Novartis, 2, 5, UCB, 2, 5.

Abstract Number: 1757

Skin-to-Joint Immune Cell Migration and Synovial Reprogramming in Psoriatic Arthritis Onset

Maria Gabriella Raimondo[1], Hashem Mohammadian[2], Mario Angeli[2], Vladyslav Fedorchenko[2], Kaiyue Huang[3], Yi-Nan Li[4], Raphael Micheroli[5], Jörg Distler[6], Ursula Fearon[7], Juergen Rech[2], Francesco Ciccia[8], Juan Cañete[9], Adam Croft[10], Mariola Kurowska-Stolarska[11], Stefano Alivernini[12], Maria Antonietta D'Agostino[13], Georg Schett[2], Simon Rauber[14] and Andreas Ramming[15], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [3]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, [4]University Hospital of Dösseldorf, Dösseldorf, Germany, [5]University Hospital Zurich, Zurich, Switzerland, [6]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [7]Trinity College Dublin, Dublin, Dublin, Ireland, [8]Rheumatology Section, University of Campania L. Vanvitelli, Naples, Italy, Naples, Italy, [9]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [10]University of Birmingham, Hagley, Stourbridge, United Kingdom, [11]University of Glasgow, Glasgow, [12]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [13]Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [14]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Bayern, Germany, [15]Department of Internal Medicine 3, Rheumatology & Immunology, Friedrich-Alexander-University (FAU) & Universitätsklinikum Erlangen, Erlangen, Germany

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Basic Science (1752–1757)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Psoriatic arthritis (PsA) develops in about 30% of individuals with psoriasis (PsO), highlighting a critical connection between skin and joint inflammation. However, the mechanisms driving the transition from skin-limited disease to joint involvement remain unclear. This study investigates the skin-joint axis in PsA pathogenesis using a preclinical model, with translational validation in human samples.

Methods: We employed the IL-23 overexpression (IL-23OE) mouse model in KAEDE mice, which facilitate the tracking of skin-derived immune cell migration via photo-conversion. Psoriatic skin lesions were converted to KAEDE-RED through UV irradiation, allowing for detailed analysis using light sheet fluorescence microscopy (LSFM) and flow cytometry. Immune cell populations were characterized through imaging flow cytometry, while single-cell RNA sequencing (scRNA-seq) offered insights into their phenotypic profiles. To corroborate these findings, we analyzed human samples from individuals with established PsO and early PsA, utilizing scRNA-seq and imaging mass cytometry. Cell trafficking in human was further examined by sequencing mitochondrial DNA (mtDNA-seq) from paired skin and synovial tissue samples of early PsA patients to identify shared lineages between skin- and joint-derived myeloid cells.

Results: The IL-23OE model successfully induced psoriatic skin lesions and enabled the migration of immune cells from inflamed skin to the synovial compartments. However, the presence of these skin-derived immune cells did not consistently correlate with the development of arthritis. Notably, although $CD2^{+}MHCII^{+}$ myeloid progenitors trafficked into the synovial membrane, some mice remained resistant to inflammation. Comparative analysis revealed no intrinsic differences in the myeloid progenitors between resistant and susceptible animals; rather, once within the synovium, these cells differentiated

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

into pro-inflammatory macrophages in PsA-susceptible mice, whereas in resistant mice, they adopted an M2-like anti-inflammatory phenotype. $CD200^{+}$ synovial fibroblasts emerged as key modulators of macrophage fate, promoting protective immune responses that mitigated arthritis development. In parallel, human scRNA-seq confirmed the presence of the corresponding myeloid precursors in psoriatic skin and in synovial tissue of both PsO and earla PsA patients, with flow cytometry detecting them in circulation. Imaging mass cytometry localized these precursors within synovial niches, showing an increase of CD200+ fibroblasts in the non-arthritic tissues. Finally, mtDNA sequencing further validated the skin origin of these myeloid precursors within the synovial tissue of early PsA patients.

Conclusion: This study identifies a key role for synovial fibroblasts in shaping macrophage differentiation and joint inflammation outcomes. Crucially, it provides the first direct evidence of a functional skin-joint axis in humans, showing that immune cells originating in the skin can contribute to joint pathology. These insights may inform early PsA diagnosis, risk stratification, and precision therapeutic strategies in PsO patients.

Disclosure: M. Raimondo: UCB, 6; **H. Mohammadian**: None; **M. Angeli**: None; **V. Fedorchenko**: None; **K. Huang**: None; **Y. Li**: None; **R. Micheroli**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **U. Fearon**: Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Quotient, 2; **J. Rech**: AbbVie, 6, 12, Received consulting fees, Biogen, 6, 12, Received consulting fees, Bristol-Myers Squibb(BMS), 6, 12, Received consulting fees, Chugai, 6, 12, Received consulting fees, Eli Lilly, 6, 12, Received consulting fees, GlaxoSmithKlein(GSK), 6, 12, Received consulting fees, Janssen, 6, 12, Received consulting fees, MSD, 6, 12, Consulting fees, Novartis, Sobi, 1, 2, 5, 6, Roche, 6, 12, Received consulting fees, Sanofi, 6, 12, Received consulting fees, Sobi, 6, 12, Received consulting fees, UCB, 6, 12, Received consulting fees; **F. Ciccia**: None; **J. Cañete**: None; **A. Croft**: None; **M. Kurowska-Stolarska**: None; **S. Alivernini**: None; **M. D'Agostino**: Bristol-Myers Squibb(BMS), 5; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **S. Rauber**: None; **A. Ramming**: Boehringer-Ingelheim, 2, Johnson & Johnson, 2, MoonLake Immunotherapeutics AG, 2, 5, Novartis Pharma GmbH, 2, UCB, 2.

Abstract Number: 1758

Treg need a MAIT: Investigating the contribution of MAIT cells to impaired UV-induced Treg expansion in lupus photosensitive reactions

Grace Crossland[1], Lindsay Mendyka[1], Vianey Chavez[1], Kaitlyn Dowling[1], Michael Constantinides[2] and Sladjana Skopelja-Gardner[1], [1]Dartmouth College, Lebanon, NH, [2]Scripps, La Jolla

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Animal Models (1758–1763)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Most systemic lupus erythematosus (SLE) patients experience sensitivity to ultraviolet (UV) light, which can trigger disfiguring skin lesions or systemic flares. In healthy skin, UV light promotes a robust immunosuppressive response, driven in part by the expansion of regulatory T cells (Treg). In contrast, UV light instead elicits an inflammatory response in SLE skin. The cellular mediators that drive Treg response in healthy skin and the mechanisms by which this

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

response fails in SLE remain incompletely understood. Here, we present new findings that implicate mucosal-associated invariant T cells (MAITs) in the (dys)regulation of skin response to UV light in healthy and lupus skin.

Methods: 8-week-old female B6, MAIT-deficient (*Mr1-/-*), and SLE (MRL/lpr or imiquimod, TLR7/8 agonist) mice were exposed to chronic low-dose UVB (50mJ/cm^2 daily, 2 or 6 doses). Skin MAITs were expanded by topical application of MAIT antigen, 5-OP-RU (1mM, every 48hr x 4). Skin inflammatory responses, including MAIT detection by 5-OP-RU-loaded MR1 tetramer, were quantified by scRNAseq and flow cytometry.

Results: In healthy (B6) skin, UV light stimulated ~5-fold expansion of both MAIT cells and Treg. MAITs were required for UV-induced T_{reg} expansion, as no increase in skin Treg proportion or number was seen in MAIT-deficient (*Mr1-/-*) mice following UVB. Moreover, Treg in MAIT-deficient skin did not proliferate (no change in %Ki67+ vs. >10% increase in Ki67+ in B6 skin) and exhibited a fragile phenotype early after UVB (only 2 doses): Neuropilin-1^{low}GITR^{low}ICOS^{low} but PD1^{high}CD69-^{high}. Consistent with a potential tolerogenic role of myeloid cells in the skin, Langerhans cells (LCs), monocyte-derived dendritic cells (moDCs), and type 2 dendritic cells (cDC2s) expanded only in B6 but not *Mr1-/-* skin after two doses of UV light. Like in *Mr1-/-* skin, Treg did not proliferate or expand in response to UV in SLE-prone (MRL/lpr) skin, which is low in MAITs (~2% of TCRb+ T cells vs. ~12% in B6 skin). In the absence of Treg expansion, CD8+ T cells increased ~10-20-fold in MRL/lpr skin, leading to a marked reduction in the Treg:CD8 ratio. The same reduction in the Treg:CD8 ratio following UV was observed in the TLR7/8 model of SLE in *Mr1-/-* but not B6 skin. The CD8s that expanded in SLE-like skin expressed high Ki67, CD69, PD1, and CXCR6. Exposing SLE-like skin to UV after first topically expanding MAITs restored the Treg:CD8 ratio, and the CD8 T cells in MAIT-expanded UV-exposed skin expressed lower levels of Ki67, CD69, PD1, and CXCR6, compared to UV-exposed skin without prior MAIT expansion.

Conclusion: In healthy skin, UV-induced proliferation and immunosuppressive phenotype of Treg are dependent on MAIT cells and may require the contribution of a subset of myeloid cells, such as LCs, moDCs, or cDC2s. SLE-like skin fails to mount the Treg response to UV light, which enables proliferation and activation of CD8 T cells, known contributors to SLE skin pathology. The failure of the UV-induced MAIT-Treg axis in SLE skin can be reversed by topically expanding MAIT cells prior to UV exposure, revealing a novel therapeutic strategy to mitigate photosensitive skin reactions in lupus.

Disclosure: G. Crossland: None; **L. Mendyka**: None; **V. Chavez**: None; **K. Dowling**: None; **M. Constantinides**: None; **S. Skopelja-Gardner**: None.

Abstract Number: 1759

Role of a pathogenic bacterial factor produced by a human gut pathobiont in inducing platelet activation and thrombo-inflammation.

Abhimanyu Amarnani[1], Cristobal F. Rivera[2], Susan RS Gottesman[3], Zakia Azad[1], Mingyang Yi[4], Joshua Prasad[4], Cynthia Loomis[4], Andy Lee[4], Nimat Ullah[4], Bhama Ramkhelawon[5] and Gregg J. Silverman[1], [1]New York University Grossman School of Medicine, New York, NY, [2]New York University Grossman Department of Surgery, New York, [3]SUNY Downstate Health Sciences University, New York, [4]New York University Grossman School of Medicine, New York, [5]New York University Department of Surgery, New York

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Animal Models (1758–1763)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: SLE is an autoimmune disease that causes progressive multi-organ damage, leading to renal injury, or lupus nephritis (LN), in half of patients. Despite treatment, 20% progress to renal failure within 15 years (1). Recent studies show that about 40% of LN flares are linked to intestinal expansions of the human pathobiont *Ruminococcus gnavus* (RG), which produces an immunogenic pro-inflammatory cell wall lipoglycan (LG) (2). LN patients with gut dysbiosis may represent a distinct endotype, where increased gut permeability and microbial factors contribute to pathogenesis. In murine studies, we have demonstrated gut colonization of mice with human RG strains (3,4). Notably, in Sle1.Sle2.Sle3 B6 congenic lupus-prone mice, colonization with an LG+ strain accelerated disease progression (4). To investigate pathogenic mechanisms, we here used a different lupus-prone murine model to elucidate the pathways connecting RG-driven platelet activation to worsening renal disease progression.

Methods: Using whole-blood transcriptomics, we recently demonstrated that RG intestinal colonization induced platelet and myeloid cell activation (manuscript submitted). Here, lupus-prone FcgRIIb$^{-/-}$ B6 congenic mice were either sham-treated or colonized with RG strains, including isogenic paired strains that differ only in LG production. Colonization was confirmed by fecal qPCR. Splenic megakaryocytes were quantified by CD41+ immunofluorescence. Renal histology was evaluated by H&E.

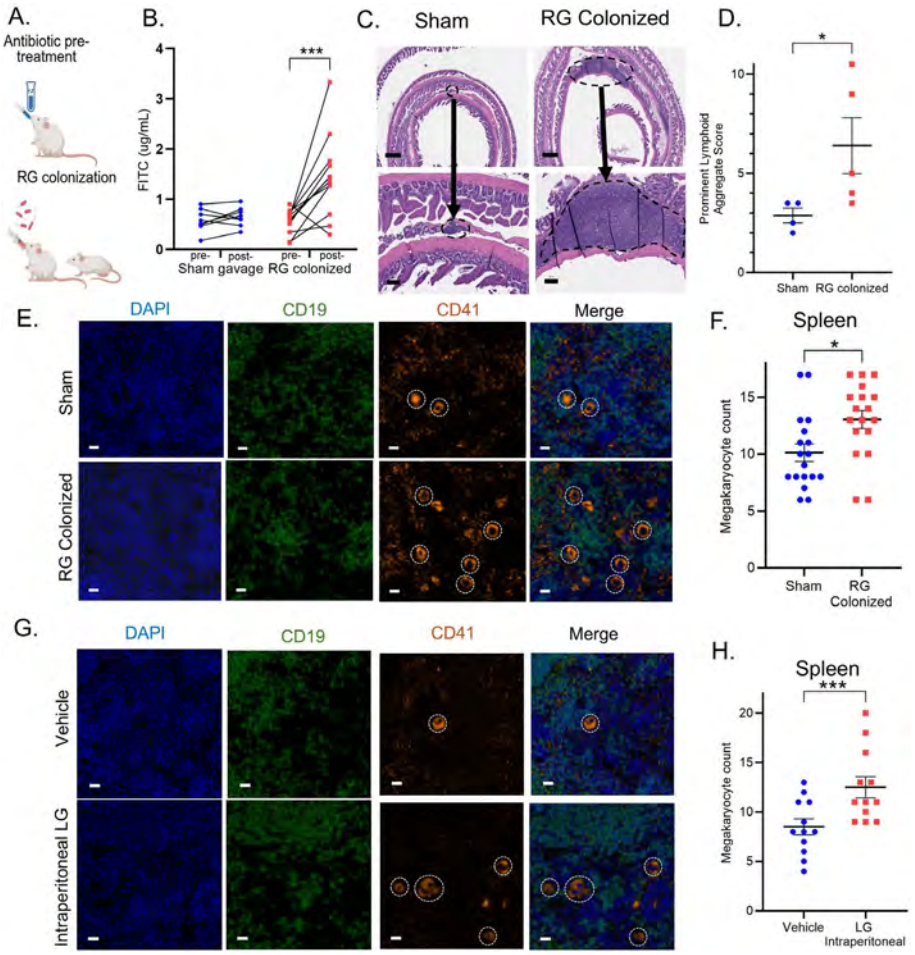


Figure 1. Effect of R. gnavus gavage and RG-immunodominant lipoglycan on the intestine and spleen. (A) Mice were orally treated with antibiotics, then subsequently orally gavaged with RG culture or sham (B). Serum FITC-dextran levels were determined pre- and post-oral gavage of sham vs. RG-treated (RG colonized B6) mice. (C) Lymphoid aggregates were observed in sham (left) vs. RG-colonized (right) B6 mice at the terminal ileum. (D) Quantification of total prominent lymphoid aggregates, which were scored in the equivalent total length of the distal small intestine in Swiss rolls. Scoring was based on the number of lymphoid cells per aggregate; +0.5 represents 25-55 lymphocytes/aggregate, +1: 56-149/ aggregate, +2: 150–299/ aggregate, +3:300+ /aggregate, and +1:GC identified. (E,F) Immunofluorescence of splenic megakaryocyte in B6 mice after RG gavage as identified by CD41+. In 3-4 months old, female. (G,H) IF megakaryocyte quantification in the spleens of 5-8 month old lupus-prone, female FcgRIIb-/- mice at six days after a single LG intraperitoneal injection (2ug/g). (E-H) Cell count per high-powered field, in at least three mice per group. *p<0.05. ***p<0.01.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

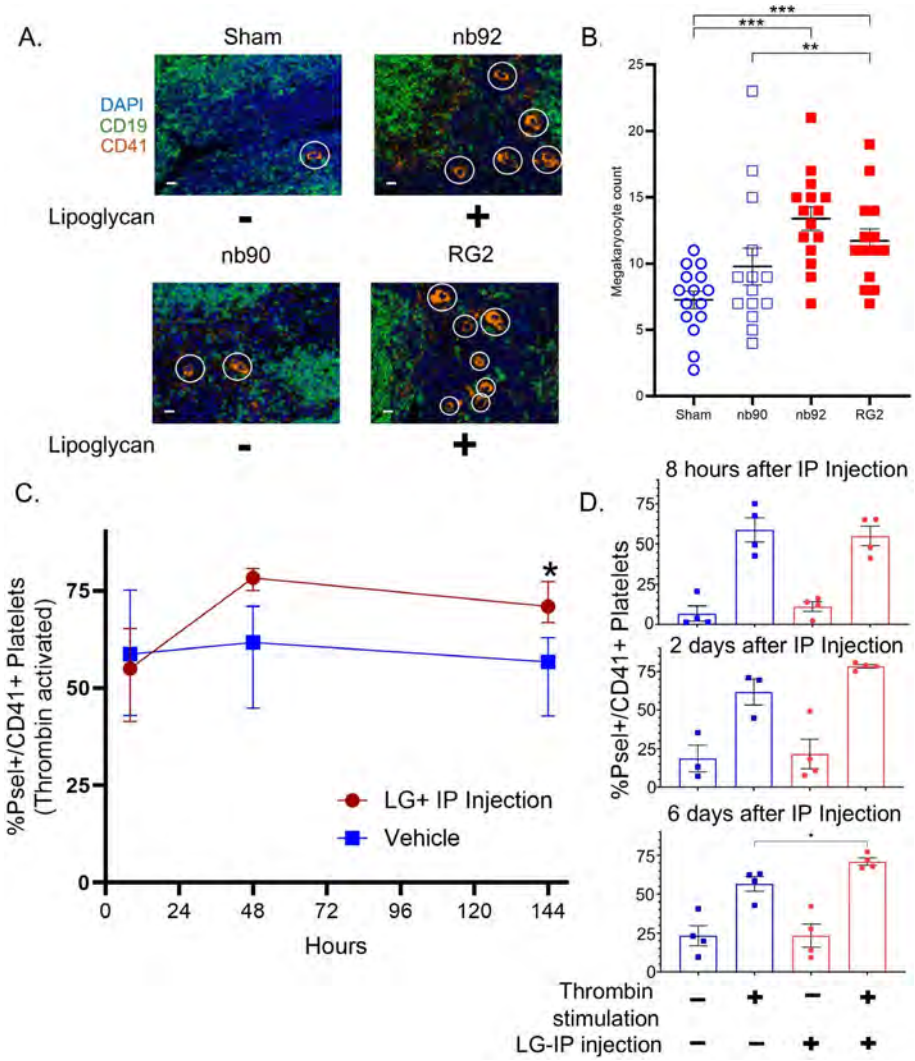


Figure 2. Pathogenic R. gnavus strains that produce lipoglycan, but not strains without lipoglycan, drive increases in splenic megakaryocytes. (A) Immunofluorescence of splenic megakaryocyte in FCGRIIb-/- mice as defined by CD41+ after RG gavage with lipoglycan-positive strains (nb92, RG2) versus strains without lipoglycan (nb90). 12 months old, female. (B) Cell count per high-powered field, at least three mice per group.**p<0.02, ***p<0.01 (C, D) Platelet activation induced by a single intraperitoneal injection of lipoglycan in FCGRIIb-/- mice was evaluated by flow cytometric monitoring of the percentage of surface P-selectin expressing cells after thrombin stimulation at 8 hours, 2 days (48 hours), and 6 days (144 hours) after administering 1.5 μg/g of lipoglycan. *p<0.05. (C) shows mean with range.

Results: Colonization with LG+ RG resulted in increased intestinal permeability, as quantified by serum detection of orally administered fluorochrome-labeled dextran (FITC-dextran, Fig. 1B). Increased gut leakiness correlated with prominent lymphoid follicles in the small intestine (Fig. 1C,D). RG colonization with LG-producing strains induced persistent platelet activation (Fig 2C), as well as extramedullary expansions of platelet progenitors (megakaryocytes), in the spleen (Fig 1E & 2A). Renal injury was induced as documented by increased tubulointerstitial lymphoid infiltrates (Fig. 3). To assess the direct pathogenic effects of purified LG, mice were given an intraperitoneal LG injection, which also induced persistent splenic megakaryocytosis that was detected after 6 days (Fig. 1G).

Conclusion: To understand how the RG pathobiont induces systemic platelet activation and neutrophil death extracellular trap release (i.e. NETosis) in a subset of active LN patients, we have here elucidated distinct pathogenic pathways of this newly identified endotype of proliferative LN. In murine models, we have documented that RG strains that produce an immunostimulatory lipoglycan cause the expansion of splenic megakaryocytes and renal disease exacerbation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

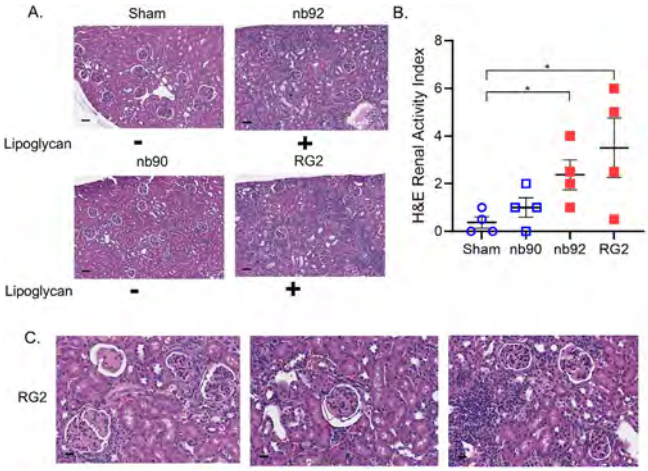


Figure 3. R. gnavus gut colonization causes increased renal cellular infiltration in lupus-prone mice. (A) Representative kidney sections (H&E) after FcgRIIb-/- colonization with lipoglycan-positive R. gnavus strains (nb92, RG2), and lipoglycan-non-producing isogenic (nb90) strains. (B) Quantification of the renal activity index is scored based on a blinded review for the presence (scored from 0-3) of mononuclear cells in the tubulointerstitium, glomerular leukocyte infiltration, and deposition of hyaline thrombi, closed capillary loops, or early crescent formation/fibrotic ring. *p<0.05.(C) 40x magnification example glomeruli of RG2 (LG producing strain) colonized FcgRIIB-/- lupus-prone mice, showing hyalinization (left, middle), and mononuclear interstitial cellular infiltrations (right).

References

1. Anders HJ et al. NatRevDzPrimers 2020; 6(1):7
2. Azzouz DA et al. ARD 2023; 0:1-13
3. Silverman GJ et al. Front Immun 2022; Vol 13
4. Ma L et al. ACR Open 2025;7.5;e70033

Disclosure: A. Amarnani: None; **C. Rivera**: None; **S. Gottesman**: None; **Z. Azad**: None; **M. Yi**: None; **J. Prasad**: None; **C. Loomis**: None; **A. Lee**: None; **N. Ullah**: None; **B. Ramkhelawon**: None; **G. Silverman**: New York University, 10, Sanofi, 5.

Abstract Number: 1760

Targeting the Female-biased Factor VGLL3 in Cutaneous and Systemic Lupus

Vincent van Drongelen[1], Joanna Rew[1], Emma Griffin[2], Kelly Young[2], Olesya Plazyo[1], Mehrnaz Gharaee-Kermani[1], Li-Jyun Syu[2], Stefan Stoll[2], Jiliang Zhou[3], Nicole Ward[4], J. Michelle Kahlenberg[1], Lam Tsoi[1], Andrzej A Dlugosz[2], Johann Gudjonsson[1] and Allison C Billi[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, [3]Augusta University, Augusta, [4]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Animal Models (1758–1763)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Approximately 90% of patients with systemic lupus erythematosus are women, and skin is one of the most frequently affected organs. We previously found that the transcription coregulator VGLL3 is enriched in the keratinocytes of healthy women, where it promotes expression of inflammatory genes. We subsequently showed that mice with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

epidermal overexpression of VGLL3 develop cutaneous and systemic lupus-like autoimmune disease. However, the value of VGLL3 as a therapeutic target in lupus remains unknown.

Methods: We have combined mouse modeling and investigations in human skin to explore VGLL3 as a potential therapeutic target in lupus. To gain insight into VGLL3-related disease mechanisms, we developed several novel transgenic mouse models that enable us to reverse epidermal VGLL3 overexpression, test VGLL3 necessity for cofactor binding, and robustly induce VGLL3 in adulthood. Furthermore, we used in vitro IP-mass spectrometry (IP-MS) as well as proximity ligation assay to identify VGLL3 binding partners in human keratinocytes and skin from discoid lupus erythematosus (DLE) patients, respectively.

Results: We determined that normalization of epidermal VGLL3 activity ameliorates skin and select systemic manifestations of VGLL3-induced murine lupus. Through *in vitro* IP-MS, we identified TEAD1 and TEAD3 as major binding partners of VGLL3 in human keratinocytes, while our proximity ligation assay data showed nuclear colocalization of VGLL3 and TEAD transcription factors in the epidermis of healthy human individuals and in patients with DLE, with increased detection in the latter. Exploiting our novel transgenic mouse models, we determined that TEAD binding capacity is required for epidermal VGLL3 to cause murine lupus-like disease. Mutations in the binding site where VGLL3 interacts with TEADs abrogated disease development in mice that overexpress VGLL3 in the epidermis. Furthermore, induction of epidermal VGLL3 overexpression in adulthood resulted in rapid onset of murine lupus that was attenuated by simultaneous epidermal deletion of *Tead1*, resulting in significantly improved survival. Similarly, pharmacologic inhibition of VGLL3-TEAD binding improved survival of mice with epidermal VGLL3 overexpression. Currently, we are testing additional drugs that are predicted to target TEAD interaction with transcription coregulators for therapeutic effect utilizing both our innovative lupus mouse models and human patient skin explants.

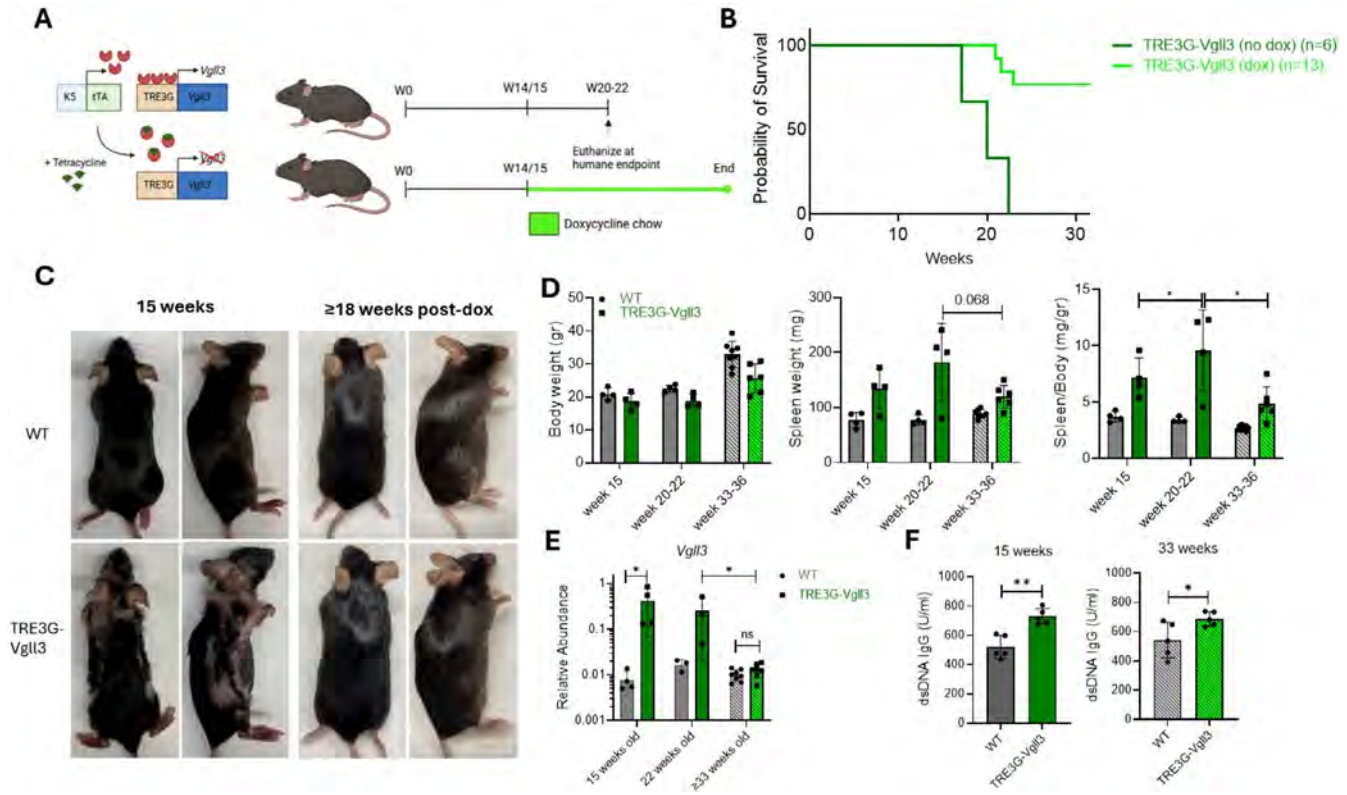


Figure 1: Normalization of epidermal VGLL3 activity ameliorates skin disease and select systemic manifestations. A. Schematic overview of K5-tTAxTRE3G-Vgll3 mouse model and experimental approach. B. Survival curve of mice on and off Doxycycline (dox) chow regimen. C. Gross images of mice at 15 weeks (before dox) and after ≥18 weeks of dox chow. D. Body weights, spleen weights, and spleen/body ratios of mice at 15 and 22 weeks (without dox, solid) and at ≥33 weeks (with dox, dashed). E. RNA expression levels in the same groups. F. Serum anti-dsDNA IgG at 15 weeks and 33 weeks.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The results of this work show the relevance of VGLL3-TEAD interaction in murine lupus-like disease development and are anticipated to provide vital preclinical data supporting the approach of VGLL3-TEAD inhibition in lupus patients with skin involvement.

Disclosure: V. van Drongelen: None; **J. Rew**: None; **E. Griffin**: None; **K. Young**: None; **O. Plazyo**: None; **M. Gharaee-Kermani**: None; **L. Syu**: None; **S. Stoll**: None; **J. Zhou**: None; **N. Ward**: AbbVie/Abbott, 1, Leo Foundation, 1, Sun Pharma, 12, Investigator Initiated Sponsored Project; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5; **L. Tsoi**: Galderma, 5, Janssen, 5; **A. Dlugosz**: None; **J. Gudjonsson**: None; **A. Billi**: None.

Abstract Number: 1761

The Application of SLE Patient-derived PBMC-induced Mouse Model in Preclinical Pharmacological Studies

Juan Liang[1], Yinlian Zhang[2], Feng Li[2], Yingfeng Huang[3], Ruixia Zhang[3] and Ruixue Dai[3], [1]Gempharmatech, Nanjing, Jiangsu, China, [2]GemPharmatech, Nanjing, China (People's Republic), [3]CytoCares, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Animal Models (1758–1763)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder characterized by the production of autoantibodies targeting nuclear antigens, immune complex deposition, and chronic inflammation of organs such as the skin, joints, and kidneys. Despite advancements in diagnosis and therapeutic strategies, SLE continues to impose a significant clinical challenge, underscoring the urgent need for novel therapies. While indispensable for elucidating disease mechanisms and evaluating treatments, conventional animal models are limited by interspecies differences in immune systems that hinder translational relevance. To overcome this, we developed a humanized SLE model by engrafting immunodeficient mice with peripheral blood mononuclear cells (PBMCs) derived from SLE patients. This model successfully mimics key pathological features, including elevated autoantibody levels (e.g., anti-dsDNA) and renal immune complex deposition, making it a valuable platform for evaluating B cell-targeted antibody therapies and cell-based interventions.

Methods: SLE model was generated by intraperitoneal injection of SLE patient-derived PBMC. Three therapeutic evaluation cases were conducted:

Case 1: Three T cell engagers (TCEs) were administered intraperitoneally once weekly for four weeks, starting on day of PBMC engraftment. Peripheral blood was collected on days 7, 14, 21, and 28 days for flow cytometry analysis of hCD20+ B cells. Plasma was analyzed for human anti-dsDNA antibodies and total IgG.

Case 2: T cell engager and Blincyto were administered intravenously 7 days post-PBMC engraftment, twice a week for three consecutive weeks. Peripheral blood was collected 14 and 28 days for flow cytometry analysis of plasma B cells. Plasma was analyzed human anti-dsDNA antibodies and total IgG. Kidneys was collected and freshly embedded for Immunofluorescence staining of human IgG.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Case 3: CAR-T cells were administered intravenously on day 6 post- engraftment. Plasma was collected 3 weeks after PBMC inoculation for ELISA test of human total IgG.

Results: Following PBMC engraftment, SLE-PBMC-NCG humanized mice demonstrated elevated levels of total human IgG and anti-dsDNA antibodies.

Case 1: Treatment with TCEs reduces auto-antibody levels and the number of peripheral hCD20+B cells in SLE PBMC-NCG mice.

Case 2: T cell engager and Blincyto treatment both led to reduction in plasma B cell and anti-dsDNA antibody levels. IgG deposition in the kidneys was also considerably reduced 3 weeks post-treatment.

Case 3: CAR-T treatment led to a decrease in total human IgG levels two weeks post-infusion.

Conclusion: The SLE patient-derived PBMC-NCG model effectively reproduces key pathogenic features of SLE and responds to multiple therapeutic modalities, including TCEs and CAR-T. This model offers a translationally relevant platform for preclinical evaluation of B-cell targeted therapies, supporting biomarker identification, dosing optimization, and acceleration of SLE drug development.

Disclosure: J. Liang: None; **Y. Zhang**: None; **F. Li**: None; **Y. Huang**: None; **R. Zhang**: None; **R. Dai**: None.

Abstract Number: 1763

Spatial Organization and Function of Disease-Associated Macrophages in Lupus Nephritis: Insights from Cross-Species Analyses

Paul Hoover[1], Chirag Raparia[2], Rollin Leavitt[3], Nir Hacohen[4], Arnon Arazi[5] and Anne Davidson[2], [1]Brigham and Women's Hospital, Boston, MA, [2]Feinstein Institutes for Medical Research, Manhasset, NY, [3]Broad Institute, Boston, MA, [4]Broad Institute, Cambridge, MA, [5]The Feinstein Institutes for Medical Research, Manhasset

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Animal Models (1758–1763)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Myeloid cells are linked to kidney injury in lupus nephritis (LN) but lack targeted therapies, underscoring the need to better understand myeloid biology in LN. While LN mouse models provide biological systems to develop new therapies, identifying shared molecular features relevant to human disease is essential to fully optimize the effectiveness of these models. We recently compared kidney myeloid single-cell datasets from four LN mouse strains with different pathogenic backgrounds and 155 patients across various disease stages and histologic subtypes (Fig. 1). This revealed similar intrarenal myeloid subsets, including Disease-Associated Macrophages (D-Macs), which correlated with clinical disease in both species (Fig. 1C, F). In this follow-up study, we examined two aspects of myeloid biology in mouse and human LN: 1) the in situ distribution of D-Macs and myeloid subsets to evaluate whether analogous cells could interact similarly with their tissue microenvironment, and 2) functional characteristics of murine D-Macs relevant to LN pathogenesis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

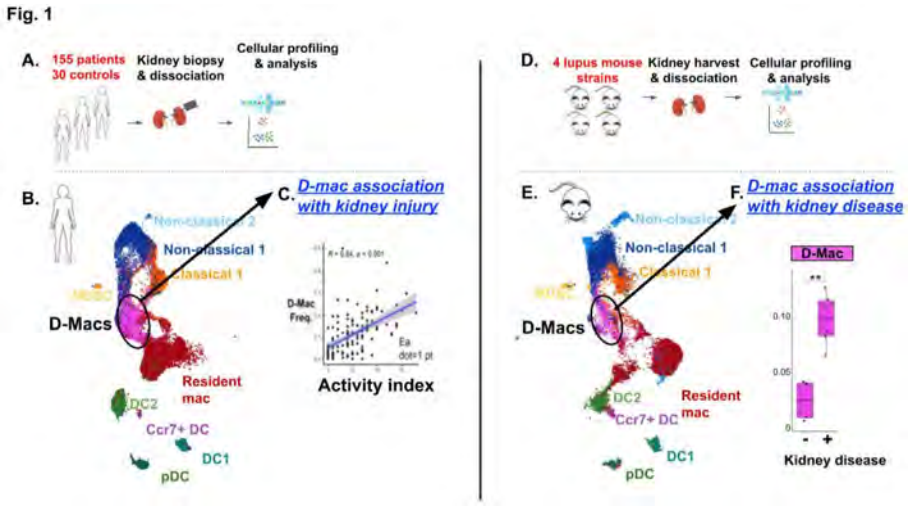


Fig. 1. Integrated landscape of myeloid cells in kidneys from mice and patients with lupus nephritis. (A) Kidney myeloid cells from 155 LN patients and 30 control biopsies were collected and processed for single-cell RNA seq with the AMP RA/SLE Network. (B) UMAP of human myeloid cells and cluster names. (C) Frequency of D-Mac (vs. all myeloid cells) is associated with activity index. A dot=1 pt. (D) Kidney myeloid cells from 4 lupus mouse strains were processed similarly and integrated with human data set. (E) UMAP of lupus murine myeloid cells and cluster names. (F) Frequency of D-Mac (vs. all myeloid cells) is associated with nephritis in all mouse models. A dot=1 mouse. Results in mice were confirmed by flow cytometry (not shown).

Methods: To map myeloid localization, we used Xenium spatial transcriptomics on FFPE kidney sections from 2 mouse strains and human patients (n=6 LN pts. with proliferative or mixed histologic classes; mean ISN/RPS activity = 13.5; S.D = 5.8) and 2 controls, employing custom probes based on scRNA-seq and the multi-tissue panel. For functional assays, we performed ex vivo phagocytosis and metabolic tests on single-cell suspensions from myeloid cells isolated by flow from dissociated murine kidneys (pre- and post-nephritis), using fluorescent immune complexes (ICs) and ATP substrates to evaluate phagocytic capacity and metabolism—particularly of D-Macs—via flow cytometry.

Results: In situ mapping findings (Fig. 2): (1) In nephritic mice, D-Macs resided within glomeruli and periglomerular infiltrates, with strain-specific differences. In humans, D-Macs were most abundant within nephritic glomeruli. (2) Resident macrophages in both species localized mainly in the tubulointerstitium, with murine RMs forming rings around glomeruli. (3) Non-classical myeloid subsets were primarily restricted to glomeruli, with minimal presence in the interstitium. (4) Murine dendritic cells localized to parenchymal areas and aggregates, while human dendritic cells were mainly in the tubulointerstitium.

Murine D-Mac functions (Fig. 3): Compared to other monocyte subsets enriched in nephritic glomeruli (C1, NC1, NC2), D-Macs showed increased uptake of immune complexes and higher membrane potential and ATP levels, suggesting an alternatively activated state.

Conclusion: Across species, D-Macs, along with classical and non-classical monocytes, were positioned near injured glomeruli—within glomeruli in humans—while resident macrophages and dendritic cells mainly localize to the tubulointerstitium and periglomerular zones. Mouse studies further indicate D-Macs adopt an alternatively activated phenotype, potentially contributing to immune complex uptake that emerges in nephritic glomeruli that may modulate inflammation. These studies advance our understanding of D-Macs in LN and support the use of mouse models to study human-derived hypotheses.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

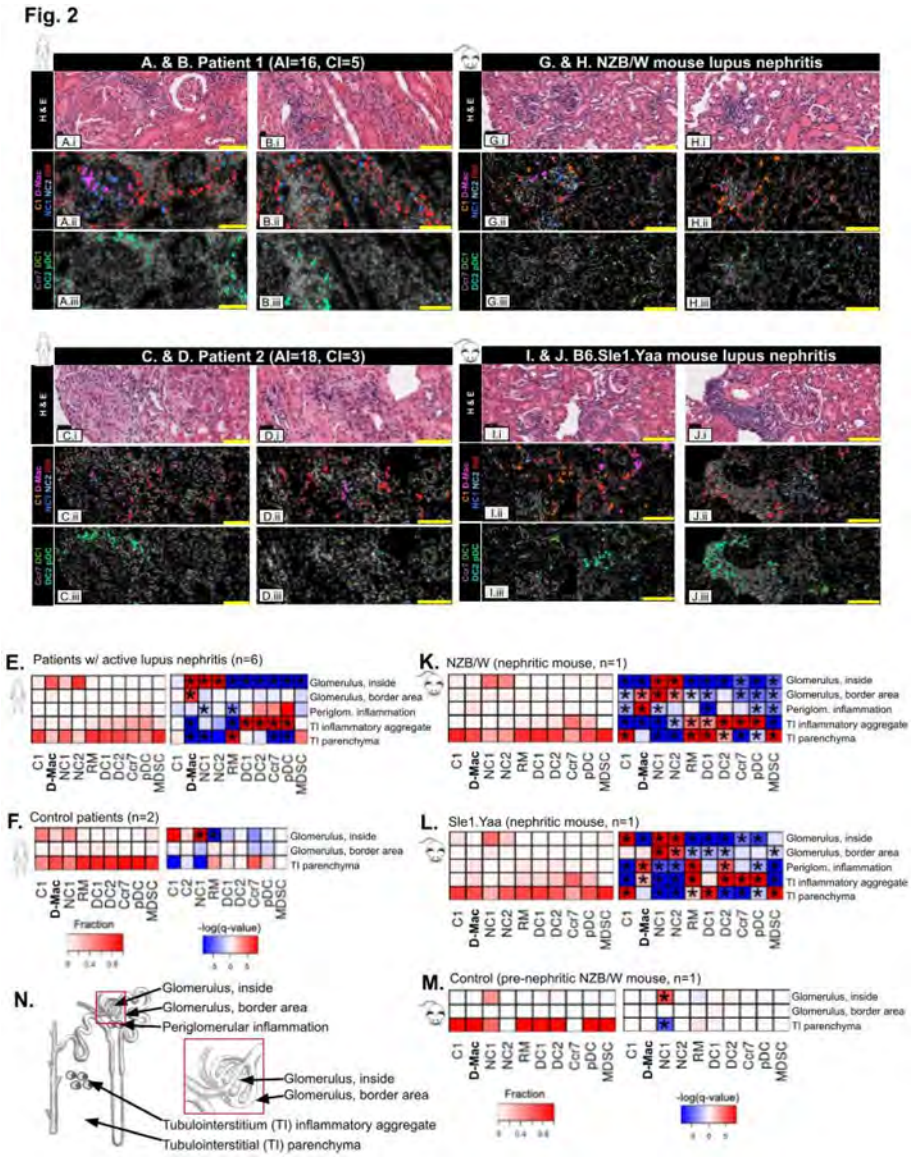


Fig. 2. In situ localization of analogous myeloid states in human and mouse kidney sections. (A-J) This series presents images of kidney sections and myeloid states within renal compartments from patients (A-D) and mice (G-J) with lupus nephritis. All panels are stained with hematoxylin and eosin (H&E), highlighting various subsets of monocytes and macrophages (D-Mac, C1, NC1, NC2, RM) as well as dendritic cells (Ccr7, DC1, DC2, pDC). The Activity Index (AI) and Chronicity Index (CI) are noted. Scale bars indicate measurements of 100 microns. (E-M) These panels quantify myeloid subsets by compartment in humans with lupus nephritis (E) and human control kidneys (F), as well as in lupus nephritis mouse models (K. NZB/W; L. Sle1.Yaa) and pre-nephritic mice (M. NZB/W). The left side of each panel displays the proportion of each indicated cell type within renal compartments across all samples. The right side presents the -log of the q-value, which indicates either depletion (blue) or enrichment (red) of the respective cell type for each renal compartment. Asterisks mark q-value <0.05. (N) Areas of renal compartments that were analyzed in the spatial assessment. Abbreviations: TI = tubulointerstitial; Periglom. = Periglomerular. Definitions: Glomerulus, inside = area within annotated glomerular border. Glomerulus, border = area that includes -/+ 20 microns from annotated border; Periglomerular inflammation = area adjacent to at least 25% of annotated glomerular border containing >50% immune cells. Tubulointerstitial inflammatory aggregate = non-adjacent area outside of glomerular border with >10 contiguous immune cells.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

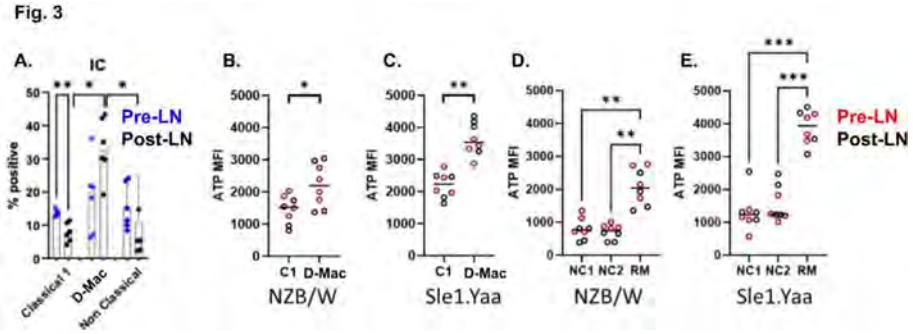


Fig. 3. Selected functional assays of murine D-Macs and related subsets. A) Phagocytosis of APC-labeled ova-anti-ova immune complexes. * p <0.05; ** p<0.01 (non-parametric t-test for 2-group comparisons or Kruskal-Wallis ANOVA with Dunn's correction for 3-group comparisons). B. Metabolic profile of murine renal myeloid subsets demonstrated by indicated macrophages or monocytes from pre-disease or nephritic NZB/W and Sle1.Yaa mice. Cells were stained with ATP biosensor (B-E) showing increased ATP in D-Macs and RMs that was not accounted for my differences in mitochondrial abundance or membrane potential (not shown). Pre-disease (black) and nephritis (red) samples are shown together as there was no difference between them.

Disclosure: P. Hoover: None; **C. Raparia**: None; **R. Leavitt**: None; **N. Hacohen**: None; **A. Arazi**: None; **A. Davidson**: None.

Abstract Number: 1764

Development and Validation of a Simulation Model for Induction of Remission in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis

Naomi Patel[1], Aaron Wu[2], Eli Miloslavsky[3], Peter Merkel[4], John Stone[5], Hyon K. Choi[6], Zachary Wallace[3] and Emily Hyle[2], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Massachusetts General Hospital, Newton, MA, [4]University of Pennsylvania, Philadelphia, PA, [5]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [6]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Vasculitis – ANCA-Associated (1764–1769)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: Evaluating the effectiveness and safety profile of treatment strategies for the induction of remission of individuals with newly diagnosed AAV is important for guiding care. We expanded AAV-Sim, a previously developed and validated microsimulation model of ANCA-Associated Vasculitis (AAV). Thus far, the model has simulated strategies to maintain remission in AAV. We expanded the model to project clinical outcomes in the setting of induction of remission in individuals with newly-diagnosed AAV receiving rituximab along with a reduced-dose glucocorticoid (GC) taper.

Methods: We expanded AAV-Sim, a C++-based microsimulation model with a monthly timestep that simulates clinical events among individuals with AAV undergoing treatment, to incorporate outcomes during induction of remission among those with newly-diagnosed disease (**Figure**). At model start, all simulated individuals are newly-diagnosed with active disease and are at risk of severe infection, end-stage renal disease (ESRD), diabetes mellitus, and death. The model assumes all individuals receive rituximab as remission induction therapy. Remission within 6 months is based on a probability of entering remission during each month. Once an individual enters remission, there is a monthly probability of minor or major relapse. Inputs were derived from outcomes observed in clinical trials (RAVE or LoVAS, depending on outcome of interest) (**Table 1**) or from an observational cohort of individuals with AAV seen in a large academic center. We also included

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

multipliers for certain parameters (e.g., risk of ESRD among those with vs. without baseline renal involvement from AAV) from observational data. We performed validation by using the mean average percent error (MAPE), a measure of the accuracy of predictions in forecasting methods, to compare the predicted outcomes in AAV-Sim with observed outcomes. MAPE results less than 10% are considered to be highly accurate and 11-20% are considered very good. We projected model outcomes over 6 months for: time to remission, minor and major relapse, severe infection, incident diabetes mellitus, ESRD, and death.

Results: Using the expanded AAV-Sim model, we projected outcomes similar to observed outcomes in clinical trials and observational data, including: *time to remission* (2.44 months in AAV-Sim vs. mean of 2.37 months in RAVE, MAPE 3.0%), *minor relapse* (2.39% in AAV-Sim vs. 2.90% in LoVAS, MAPE 17.6%), *major relapse* (1.32% in AAV-Sim vs. 1.45% in LoVAS, MAPE 9.0%), *≥1 severe infection* (6.66% in AAV-Sim vs. 7.24% in LoVAS, MAPE 8.0%), *incident diabetes* (11.54% in AAV-Sim vs. 13.04% in LoVAS, MAPE 11.5%), *incident ESRD* (0.40% in AAV-Sim vs. 0.51% in MGB AAV cohort, MAPE 21.6%), and *death* (2.71% in AAV-Sim vs. 2.90% in LoVAS, MAPE 6.6%) (**Table 2**).

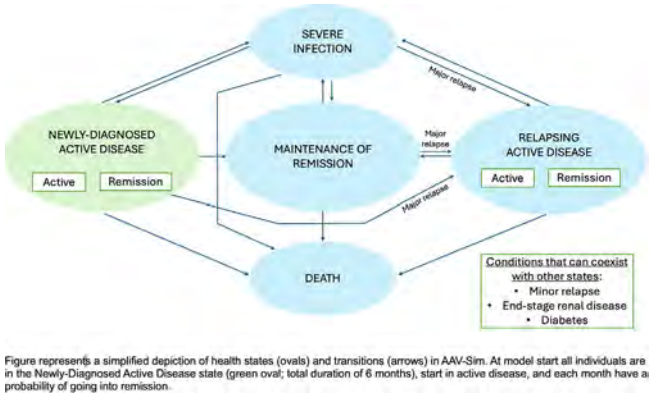


Figure represents a simplified depiction of health states (ovals) and transitions (arrows) in AAV-Sim. At model start all individuals are in the Newly-Diagnosed Active Disease state (green oval; total duration of 6 months), start in active disease, and each month have a probability of going into remission.

Figure. Schematic of Health States and Transitions in the Expanded AAV-Sim Model that Incorporates Induction of Remission in People with Newly-Diagnosed Active ANCA-Associated Vasculitis

Table 1. Selected Input Parameters for the Expanded AAV-Sim Model that Includes Induction of Remission in People with Newly-Diagnosed ANCA-Associated Vasculitis

Input Parameter	Base Case Value		Source
Demographics			
Age, years, mean (SD)	73.0 (9.1)		LoVAS
Male, %	42		LoVAS
MPO-ANCA(+), %	87		LoVAS
Renal involvement, %	69		LoVAS
Time from newly-diagnosed active disease to remission, months, mean (SD)	2.4 (1.7)		RAVE
	Base Case Monthly Transition Probability		
Remission to minor relapse	PR3(+)/MPO(+)	0.01476/0.00741	LoVAS
Remission to major relapse	PR3(+)/MPO(+)	0.00735/0.00368	LoVAS
Severe infection among people with:			
No diabetes or ESRD	0.01493		LoVAS
Diabetes	0.02964		LoVAS and observational data*
ESRD	0.02217		LoVAS and observational data*
Incident diabetes	0.02301		LoVAS
Incident ESRD[#]	0.00085		Real-world AAV cohort and observational data*
Death[§]	0.00243		LoVAS

ANCA, anti-neutrophil cytoplasmic antibody; AAV, ANCA-associated vasculitis; PR3, proteinase 3; MPO, myeloperoxidase; ESRD, end-stage renal disease; LoVAS, reduced-dose vs. high-dose glucocorticoids in AAV trial (*JAMA* 2021;325(21):2178); RAVE, rituximab in AAV trial (*NEJM* 2010;363:221)

*Data for multiplier for severe infection with diabetes from *Clin Infect Dis* 2016;63(4):501: data for multiplier for severe infection with ESRD from 2021 USRDS Annual Data Report, National Institutes of Health. Data for multiplier for ESRD risk with active renal disease from *Rheumatol* 2019;58(1):103

[#]Based on a 73-year-old with renal involvement from AAV at baseline

[§]Based on a 73-year-old male with active disease and no end-stage renal disease

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Model-Projected Outcomes versus Observed Outcomes over 6 months during Induction of Remission in Newly Diagnosed Disease Using the Expanded AAV-Sim Model

Outcome	AAV-Sim Projections	Observed Data Estimates	MAPE, %
Time to remission, months, mean	2.44	2.37	3.0
Minor relapse, %	2.39	2.90	17.6
Major relapse, %	1.32	1.45	9.0
1 or more severe infection, %	6.66	7.24	8.0
Incident diabetes, %	11.54	13.04	11.5
Incident ESRD, %	0.40	0.51	21.6
Death, %	2.71	2.90	6.6

ESRD, end-stage renal disease; MAPE, mean average percent error

Conclusion: We expanded and validated a model to simulate induction of remission in AAV. The expanded AAV-Sim model can be used to project clinical outcomes after induction of remission. These results can be used and further expanded upon to address important clinical questions in AAV in research studies and in clinical trial design. Further expansion of the model will evaluate outcomes between those receiving different GC regimens.

Disclosure: N. Patel: Amgen, 5; **A. Wu**: None; **E. Miloslavsky**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **Z. Wallace**: Amgen, 3; **E. Hyle**: None.

Abstract Number: 1765

Maintenance of remission with rituximab versus azathioprine in newly diagnosed or relapsing eosinophilic granulomatosis with polyangiitis. A prospective, randomized, controlled, double-blind trial

Xavier Puéchal[1], Grégory Pugnet[2], Elisabeth Diot[3], Claire de Moreuil[4], Stéphane Jouneau[5], Thomas Quemeneur[6], Gabriel Baron[7], Perrine Smets[8], Antoine Néel[9], Thomas Le Gallou[10], Nicolas Noël[11], Yurdagül Uzunhan[12], Cloé Comarmond[13], Geoffrey Urbanski[14], Ygal Benhamou[15], Alice Bérezné[16], Arsène Mekinian[17], Mohamed Hamidou[9], Julien Campagne[18], Noemie Abisror[19], Benjamin Torreau[3], Pascal Cohen[20], Loic Guillevin[20], Philippe Ravaud[7], Benjamin Terrier[21] and French Vasculitis Study Group, [1]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [2]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France, [3]Internal Medicine and Immunology, CHU Tours, Tours, France, [4]CHU DE BREST, BREST, France, [5]Respiratory Medicine, Université de Rennes 1, CHU Pontchaillou, Rennes, France, [6]Nephrology and Internal Medicine, CH Valenciennes, Valenciennes, France, [7]Hôtel-Dieu, Université Paris Cité,, Paris, France, [8]Internal Medicine, CHU Gabriel-Montpied, Clermont-Ferrand, France, [9]Internal Medicine, CHU Hôtel-Dieu, Nantes, France, [10]Internal Medicine and Clinical Immunology, CHU Rennes Sud, Rennes, [11]Internal Medicine and Clinical Immunology, CHU Bicêtre, Bicêtre, [12]Respiratory Medicine, Hôpital Avicenne, Bobigny, France, [13]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, INSERM U942, Paris, France, [14]Internal Medicine and Clinical Immunology, CHU Angers, Angers, France, [15]Internal Medicine, CHU Rouen, Rouen, France, [16]Internal Medicine, CH, Annecy, Annecy, France, [17]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [18]Internal Medicine, CH Robert Schuman, Metz, France, [19]Internal Medicine, CHU Saint-Antoine,, Paris, France, [20]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [21]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Vasculitis – ANCA-Associated (1764–1769)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The eosinophilic granulomatosis with polyangiitis (EGPA) guidelines recommend considering maintenance therapy after remission to reduce the risk of relapse and toxicity, but data on maintenance therapy is limited. The primary objective of this randomized, double-blind trial was to compare rituximab (RTX) and azathioprine (AZA) maintenance therapy on the duration of remission in EPGA patients who had recently achieved vasculitis remission after standard therapy, including tapering/withdrawal of glucocorticoids (GCs).

Methods: Patients with newly diagnosed or relapsing EGPA within 30-360 days of achieving vasculitis remission were randomized to receive maintenance AZA (2 mg/kg/d, 24 months) plus placebo RTX infusions or 500 mg RTX every 6 months for 18 months (4 infusions) plus placebo AZA for 24 months. The primary endpoint was total remission duration over the 28-month study period, defined as the accrued number of weeks a patient remained in remission (BVAS=0) and prednisone ≤7.5 mg/d. Secondary endpoints included the proportion of participants who remained in remission (i) with prednisone ≤7.5 mg/d during the 28-month study period; (ii) regardless of GC dose; (iii) with prednisone ≤4 mg/d at month 18 and month 28; percentage of patients with ≥1 vasculitis flare; of those with ≥1 clinically significant asthma/rhinosinusitis exacerbations; cumulative GC dose; adverse events; damage, disability and quality of life.

Results: 98 patients were enrolled from 36 centers between March 2018 and June 2022, 49 per arm: newly diagnosed (75%), MPO-ANCA+ (49%), five-factor score (FFS) ≥1 (46%), remission achieved with GCs only (29%). The mean number of weeks in remission with prednisone ≤7.5 mg/d was 96.0 vs 91.1 in the AZA and RTX arms, respectively (mean difference 5.0; 95% CI [-6.2 to 16.1]). The percentage of patients who remained in remission during the 28-month study period (i) with prednisone ≤7.5 mg/d was 11/49 (22.5%) vs 17/49 (34.7%) (RR 0.66 [0.37 to 1.20]) and (ii) regardless of GC dose was 31/49 (63.3%) vs 41/49 (83.7%) (RR 0.76 [0.60 to 0.94]) in the AZA and RTX arms, respectively. The percentage of patients in remission with prednisone ≤4 mg/d was (i) 25/49 (51.0%) vs 34/49 (69.4%) at month 18 (RR 0.79 [0.60 to 1.02]) and (ii) 23/49 (46.9%) vs 37/49 (75.5%) at month 28 (RR 0.62 [0.48 to 0.80]) in the AZA and RTX arms, respectively. The relapse rate for vasculitis was 22.2% vs 14.4%, and the rate of clinically significant exacerbations of asthma and/or rhinosinusitis was 40.5% vs 32.7% in the AZA vs RTX arms, respectively. No differences were found in the cumulative GC, damage, disability, or quality of life. One patient in the AZA group died of SARS-CoV2 infection before the vaccine was developed. No difference in serious adverse events was observed.

Conclusion: Following remission within the previous year after a new EGPA diagnosis or vasculitis relapse, RTX did not show overall superiority to AZA in maintaining vasculitis remission, reducing asthma/rhinosinusitis exacerbations or sparing GC. However, RTX was superior to AZA in maintaining remission with prednisone ≤4 mg/d at month 28. It remains to be determined whether RTX can reduce vasculitis relapse rates in ANCA-positive patients, who are at a higher risk of relapse.

Disclosure: X. Puéchal: Roche, 5; **G. Pugnet**: None; **E. Diot**: Roche, 5; **C. de Moreuil**: Roche, 5; **S. Jouneau**: Roche, 5; **T. Quemeneur**: Roche, 5; **G. Baron**: None; **P. Smets**: Roche, 5; **A. Néel**: Roche, 5; **T. Le Gallou**: Roche, 5; **N. Noël**: Roche, 5; **Y. Uzunhan**: Roche, 5; **C. Comarmond**: Roche, 5; **G. Urbanski**: Roche, 5; **Y. Benhamou**: None; **A. Bérezné**: Roche, 5; **A. Mekinian**: Roche, 5; **M. Hamidou**: Roche, 5; **J. Campagne**: Roche, 5; **N. Abisror**: Roche, 5; **B. Torreau**: None; **P. Cohen**: Roche, 5; **L. Guillevin**: Roche, 5; **P. Ravaud**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1766

Clinical Impact of Incomplete B-cell Depletion in ANCA-Associated Vasculitis Patients Receiving Maintenance Rituximab Therapy: a Retrospective Study

caterina ricordi[1], Maxime Beydon[2], Johanne Liberatore[3], Pascal Cohen[4], bertrand Dunogue[5], Camille Mettler[6], Benjamin Torreau[7], Luc Mouthon[5], Xavier Puéchal[8] and Benjamin Terrier[9], [1]Unit of Rheumatology, Azienda USL - IRCCS di Reggio Emilia, and University of Modena and Reggio Emilia, Reggio Emilia, Italy, [2]Sorbonne University, INSERM, Institut Pierre Louis of Epidemiology and Public Health, Equipe PEPITES, Pitié Salpêtrière Hospital, Service of Public Health, Centre of Pharmacoepidemiology (Cephepi), Paris, France, [3]Department of Internal Medicine, Centre Hospitalier d'Angouleme, Angouleme, France, [4]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [5]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [6]Department of Internal Medicine, Hôpital Bichat - Claude-Bernard, Paris, France, [7]Internal Medicine and Immunology, CHU Tours, Tours, France, [8]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [9]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Vasculitis – ANCA-Associated (1764–1769)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Rituximab (RTX) is the standard of care for both induction and maintenance in ANCA-associated vasculitides (AAVs). While CD19 B-cell monitoring is used to evaluate the duration and magnitude of the biological effect of RTX, its prognostic value in predicting relapse remains controversial. We aimed to determine the significance of incomplete B-cell depletion during maintenance therapy in AAV patients and its subsequent risk of relapse.

Methods: This is a retrospective, single-center cohort study on AAV patients including patients with the following inclusion criteria: i) newly diagnosed or relapsing granulomatosis with polyangiitis or microscopic polyangiitis, ii) induction therapy with either cyclophosphamide (CYC) or RTX, iii) standard maintenance therapy with RTX 500 mg fixed dose every 6 months. Follow-up started from the first maintenance treatment (month 0) until the earliest occurrence of flare, last follow-up, or death. CD19 levels were measured at each RTX infusion and analyzed as a time-dependent variable. We analyzed the risk of relapse separately in 2 phases: during RTX maintenance treatment (from the first RTX infusion until 6 months after the last infusion), and after RTX discontinuation (from 6 months after the last RTX infusion until last follow-up).

Results: 199 patients were included. The median duration of RTX maintenance was 19 (IQR 18-40) months. A total of 21 relapses were observed during maintenance, and 30 after discontinuation of RTX. At month 0, incomplete B-cell depletion, either defined for CD19 >1/mm3 or >5/mm3 were observed in 29% and 18.1% of patients, respectively, and remained stable during maintenance treatment.

Variables that were associated with the magnitude of B-cell depletion during RTX maintenance therapy, evaluated by the area under the curve (AUC) of CD19+ B cells, were the age at diagnosis (β = -0.05; 95% CI: -0.11 to 0.00) and serum creatinine level (β = 0.01; 95% CI: 0.00 to 0.02).

During maintenance therapy, age was the only variable associated with the risk of relapse (OR 0.97, 95%CI 0.94-1.00, p=0.019), while B cell count, whatever the definition used, was not associated with relapse during maintenance. In multivariate analysis, age remained associated with the risk of relapse (HR 0.97, 95%CI 0.94-1.00, p=0.019).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

After RTX discontinuation, variables that was associated with the risk of relapse were absolute CD19+ B cell count (HR 1.01, 95%CI 1.00-1.01, p=0.024), CD19+ B cell ≤5/mm3 (HR 0.44, 95%CI 0.21-0.95, p=0.036) at last RTX infusion, and the AUC of CD19+ B cells during maintenance (HR 1.01, 95%CI 1.00-1.03, p=0.040). In multivariate analysis, all these variables related to B-cell depletion remained associated with the subsequent risk of relapse.

Conclusion: Incomplete B-cell depletion during RTX maintenance, which occurs in one third of patients, is not associated with an increased risk of relapse while RTX is continued. In contrast, after discontinuation of RTX, the B-cell count at the last RTX infusion or the AUC of CD19+ B cells during maintenance were associated with subsequent relapse risk, suggesting that achieving complete B-cell depletion may be a goal to reduce the risk of subsequent relapse.

Disclosure: c. ricordi: None; **M. Beydon**: None; **J. Liberatore**: None; **P. Cohen**: Roche, 5; **b. Dunogue**: None; **C. Mettler**: None; **B. Torreau**: None; **L. Mouthon**: None; **X. Puéchal**: Roche, 5; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 1767

Identification of C3 complement fragments in lesional tissues in ANCA-associated vasculitis

Claire Galand[1], Fei Liu[2], Katherine Vernon[2], Ravi Vats[2], Christine Lian[3], V. Michael Holers[4], H. Terence Cook[5], David Cuthbertson[6], Nader Khalidi[7], Curry Koening[8], Carol Langford[9], Carol McAlear[10], Paul Monach[11], Christian Pagnoux[12], Jason Campagna[2], Shelia Violette[2] and **Peter Merkel**[10], [1]Q32 Bio Inc,, Waltham, MA, [2]Q32 Bio Inc, Waltham, MA, [3]Department of Pathology, Brigham & Women's Hospital/Harvard Medical School, Boston, MA, [4]University of Colorado Anschutz Medical Campus, Aurora, [5]Department of Immunology and Inflammation, Imperial College London, London, United Kingdom, [6]University of South Florida, Tampa, [7]McMaster University, Hamilton, ON, Canada, [8]University of Texas Dell Medical School, Austin, TX, [9]Cleveland Clinic, Moreland Hills, OH, [10]University of Pennsylvania, Philadelphia, PA, [11]VA Boston Healthcare System, Boston, MA, [12]Mount Sinai Hospital, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Vasculitis – ANCA-Associated (1764–1769)
Session Type: Abstract Session
Session Time: 10:00AM–11:30AM

Background/Purpose: One proposed mechanism of tissue damage in ANCA-associated vasculitis (AAV) is the formation of neutrophil extracellular traps (NETs) during extravasation of neutrophils into and through blood vessel walls. NETs carry antimicrobial peptides, myeloperoxidase, proteinase 3, and alternative pathway (AP) complement protein split products. AAV is typically described as pauci-immune, with renal and other tissues often reported as C3 negative.

This study aimed to characterize complement activation in affected tissue in AAV using novel techniques to identify active complement as compared to C3d deposition. C3d is a covalently membrane-bound biomarker generated by C3 cleavage that demonstrates extended tissue half-life.

Methods: Immunofluorescence (IF) staining was performed using an anti-C3c polyclonal antibody (Dako) and a novel anti-C3d monoclonal antibody (mAb, 3d8b mouse IgG1). IF was conducted on renal biopsy samples from patients with AAV (n=32), IgA nephropathy (IgAN, n=29), C3 glomerulonephritis (C3G, n=9), and class III lupus nephritis (LN, n=30), and skin biopsy samples from patients with leukocytoclastic vasculitis (LCV, n=37), and skin lesions in AAV (n=4). Immunohistochemistry (IHC) staining of C3d was performed on biopsy samples of kidney (n=8), skin (n=3), lung (n=5), and sinus (n=2) from patients with AAV. Immunostainings (IF and IHC) were semi-quantitatively scored. Renal biopsy IF intensity was further evaluated for digital quantification using image analysis software.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: IF staining detected active complement (anti-C3c) and C3d deposition (anti-C3d) in the glomeruli of AAV, IgAN, C3G, and LN) (Figure 1). Both semi-quantitative scoring and digital quantification revealed a moderate glomerular IF intensity in AAV and IgAN, and a higher intensity in C3G and LN. A distinct glomerular staining pattern with C3c/C3d was seen in AAV and IgAN with deposition more in mesangium than capillaries, as compared to C3G and LN in which C3c/C3d deposited equally in mesangium and capillaries. IHC staining of AAV renal tissue confirmed C3d deposition in glomeruli and revealed extra-glomerular small vessels (Figure 2); 3/6 of these same biopsies tested negative for C3 by routine diagnostic immunostaining.

IF staining detected active complement and C3d deposition on superficial dermal vasculature in LCV. Semi-quantitative scoring demonstrated higher anti-C3c staining than anti-C3d IF intensity in four AAV-LCV samples, as compared to non AAV-LCV samples (Figure 3). IHC staining of FFPE tissue also detected C3d deposition in skin, lung, and sinus biopsies from AAV patients.

Conclusion: Immunostaining for complement AP fragments, particularly C3d, reveals evidence of complement activation in AAV in kidney, skin, lung, and sinus, including biopsies deemed negative by routine C3 staining. These data demonstrate that glomerulonephritis in AAV is less "pauci-immune" than previously considered. These findings also suggest that the complement AP contributes to the pathogenesis of AAV and that treatment using an anti-C3d tissue targeted AP inhibitor approach could mitigate inflammation-related damage in AAV.

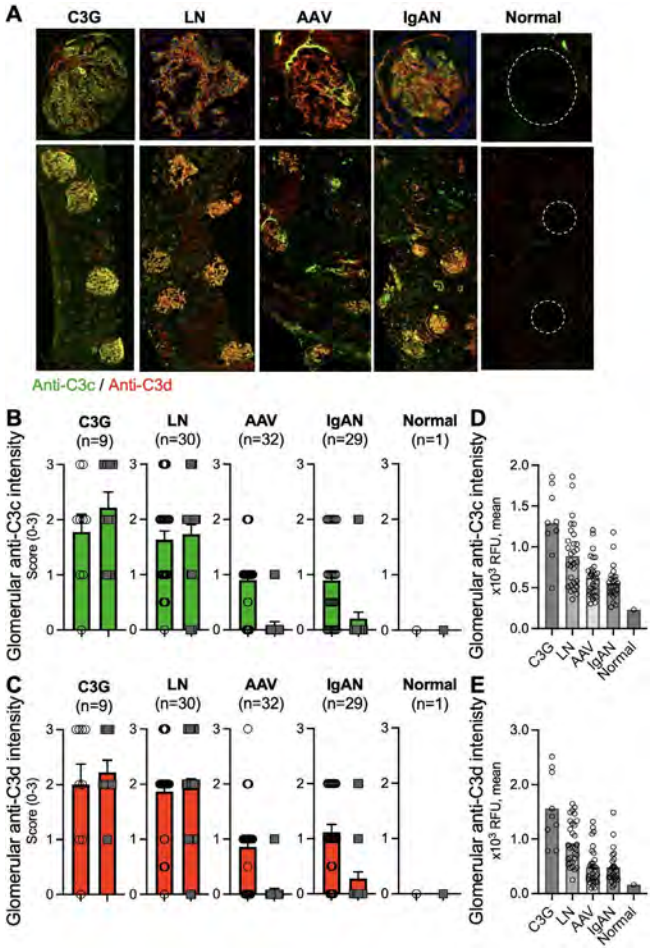


Figure 1. Immunofluorescent staining developed to capture complement fragments demonstrates glomerular complement activation in frozen kidney biopsies from patients with ANCA-associated vasculitis, in comparison to other glomerulonephritides and normal tissue. Anti-C3c and anti-C3d stainings (A, representative images) were semi-quantitatively scored (B-C) and evaluated for digital quantification (D-E).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

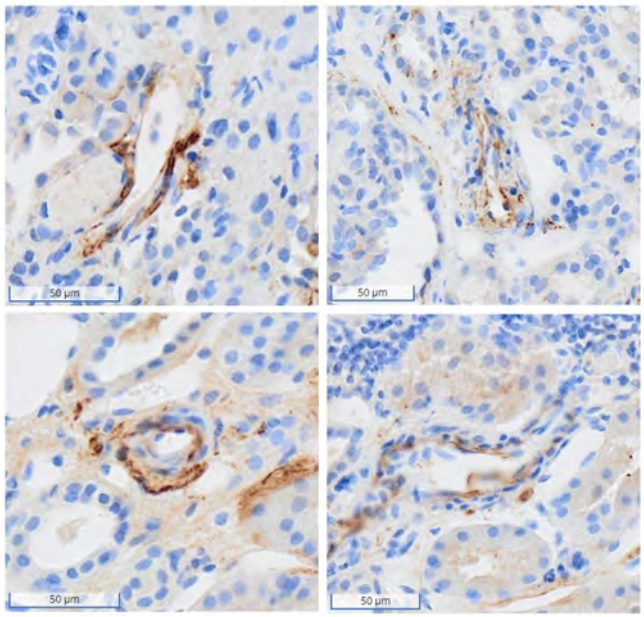


Figure 2. Histochemistry staining reveals the presence of C3d deposition in extra-glomerular kidney small vessels, in formalin-fixed-paraffin-preserved kidney biopsies from patients with ANCA-associated vasculitis.

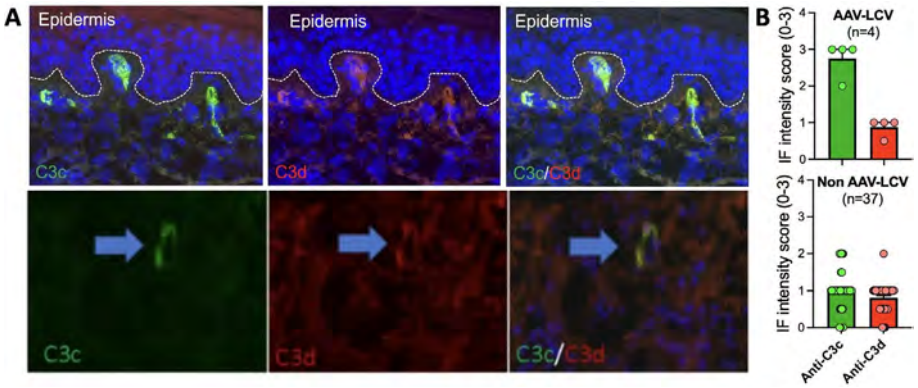


Figure 3. Immunofluorescent staining in lesional skin biopsies (A, representative images) reveals a higher level of complement activation in biopsy specimens of leukocytoclastic vasculitis from patients with ANCA-associated vasculitis (AAV-LCV) compared to samples from patients without AAV (Non AAV-LCV) (B).

Disclosure: C. Galand: Q32 Bio, 3; **F. Liu**: Q32 Bio, 12,, 3; **K. Vernon**: Q32 Bio, Inc., 11; **R. Vats**: None; **C. Lian**: None; **V. Holers**: Q32 Bio, 12,, 2; **H. Cook**: Novartis, 2, Q32Bio, 2, Sobi, 1; **D. Cuthbertson**: None; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 6, Mallinckrodt, 6, NS Pharma, 5, Otsuka, 6, Roche, 2, Sanofi, 5; **C. Koening**: Amgen, 1, Boehringer-Ingelheim, 1; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **C. McAlear**: None; **P. Monach**: Boehringer-Ingelheim, 2; **C. Pagnoux**: AstraZeneca, 1, ChemoCentryx, 1, GlaxoSmithKlein(GSK), 1, 5, InflaRx GmbH, 1, otsuka, 1, 5, Pfizer, 1, 5, Roche, 1, 5; **J. Campagna**: None; **S. Violette**: Mediar Therapeutics, 12,, 1, Q32 Bio, 12,, 3, 8, 10, Triveni, 12,, 1; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1768

TREM-1 and TREM-2 Define Inflammatory and Protective Axes in ANCA-Associated Glomerulonephritis

Lea Dionet[1], Alexandre Lanau[2], Paul Breillat[3], Quentin Delcros[4], Federica Pallotti[5], Margot Poux[6], Pierre Isnard[1], Arthur Lavigne[4], Xavier Puéchal[7], alexandre karras[8], Jean-Paul Duong[9], Olivia Lenoir[10], Pierre-Louis Tharaux[11] and Benjamin Terrier[12], [1]INSERM, Paris, France, [2]Institut Curie, Paris, France, [3]INSERM, PARIS 17, Ile-de-France, France, [4]AP-HP, Paris, France, [5]Internal Medicine and Clinical Immunology, Rennes, France, [6]Universitä de Paris, PARIS 04EME, France, [7]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [8]HEGP - assistance publique hopitaux de paris, paris, France, [9]INSERM, Paris, [10]Paris Cardiovascular Research Center, Université Paris Cité, INSERM U970, Paris, France, PARIS, Ile-de-France, France, [11]Paris Cardiovascular Research Center, Université Paris Cité, INSERM U970, Paris, France, PARIS, France, [12]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Vasculitis – ANCA-Associated (1764–1769)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: ANCA-associated vasculitis (AAV) is a small-vessel vasculitis that can lead to life-threatening renal injury. Neutrophils, monocytes and macrophages play a pivotal role not only in sustaining inflammation and promoting fibrosis, but also in mediating tissue repair. In this study, we investigated the role of TREM-1 and TREM-2, two key receptors expressed on myeloid cells, in regulating myeloid cells activation and their contribution to AAV-induced kidney injury.

Methods: We analyzed blood and renal biopsy samples from patients with AAV and controls, as well as publicly available transcriptomic datasets. Surface expression of TREM-1 and TREM-2 on circulating leukocytes was assessed by flow cytometry, while serum concentrations of soluble TREM-1 (sTREM-1) and sTREM-2 were measured by ELISA. To investigate the role of TREM-1 and TREM-2 *in vivo*, we used a murine model of MPO-ANCA-induced glomerulonephritis. Disease was induced in wild-type, *Trem1-/-* or *Trem2-/-* mice, *via* passive transfer of anti-MPO antibodies. Renal inflammation and tissue injury were assessed by histological scoring.

Results: Publicly available transcriptomic datasets from microdissected renal biopsies of AAV patients revealed significant upregulation of *TREM1* and *TREM2* in glomerular compartments, whereas only *TREM2* was upregulated in the tubulointerstitial region. Single-cell RNA sequencing of renal $CD45^+$ immune cells showed a strong enrichment of $TREM1^+$ neutrophils in AAV samples, while *TREM2* was restricted to two macrophage subsets distinguished by *FOLR2* expression.

In peripheral blood, surface expression of TREM-1 and TREM-2 on circulating neutrophils and monocytes was similar between AAV patients and controls, except for higher mean TREM-1 fluorescence intensity on neutrophils in AAV. Serum levels of sTREM-1 and sTREM-2 were significantly elevated in AAV patients (both GPA and MPA) compared to controls (sTREM-1: 608.9 ± 386.2 vs. 209.2 ± 87.2 pg/mL, $p< 0.0001$; sTREM-2: 996.7 ± 788.7 vs. 253.8 ± 105.0 pg/mL, $p< 0.0001$), and both were significantly higher in AAV patients with renal involvement compared to those without. Furthermore, sTREM-1 positively correlated with CRP ($r=0.30$, $p=0.045$), serum creatinine ($r=0.61$, $p< 0.0001$) and BVAS ($r=0.48$, $p< 0.001$), and sTREM-2 correlated with serum creatinine ($r=0.61$, $p=0.009$) and BVAS ($r=0.39$, $p=0.01$).

To investigate the role of TREM-1 and TREM-2 *in vivo*, we induced MPO-ANCA glomerulonephritis in wild-type, *Trem1-/-*, and *Trem2-/-* mice. *Trem1-/-* mice showed milder kidney injury, with fewer crescentic and necrotic glomeruli and increased normal glomeruli. Neutrophil infiltration was significantly reduced in the kidneys of *Trem1-/-* mice. In contrast, *Trem2-/-* mice developed more severe disease and showed reduced survival compared to wild-type mice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: TREM-1 and TREM-2 are differentially involved in AAV-associated glomerulonephritis. Their circulating levels correlate with disease activity, and mouse models show opposing roles in renal injury: TREM-1 promotes inflammation, whereas TREM-2 is protective. These findings identify TREM pathways as promising therapeutic targets in AAV.

Disclosure: L. Dionet: None; **A. Lanau**: None; **P. Breillat**: None; **Q. Delcros**: None; **F. Pallotti**: None; **M. Poux**: None; **P. Isnard**: None; **A. Lavigne**: None; **X. Puéchal**: Roche, 5; **a. karras**: None; **J. Duong**: None; **O. Lenoir**: None; **P. Tharaux**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 1769

Classification of Relapses of Eosinophilic Granulomatosis with Polyangiitis After Two-Years of Treatment with Anti-Interleukin-5/ Receptor Therapy

Christian Pagnoux[1], Arnaud Bourdin[2], Bernhard Hellmich[3], Nader Khalidi[4], David Jackson[5], David Jayne[6], Parameswaran Nair[7], Ulrich Specks[8], Benjamin Terrier[9], Lena Börjesson Sjö[10], Priya Jain[11], Aadarsh Lal[12], Sofia Necander[13], Claire Walton[14], Michael Wechsler[15] and Peter Merkel[16], [1]Mount Sinai Hospital, University Health Network, Toronto, and Canadian Vasculitis Research Network (CanVasc), Toronto, ON, Canada, [2]Department of Respiratory Diseases, Montpellier University Hospitals, Arnaud de Villeneuve Hospital, Montpellier, France, [3]Klinik für Innere Medizin, Rheumatologie, Pneumologie, Nephrologie und Diabetologie, Medius Kliniken, Akademisches Lehrkrankenhaus der Universität Tübingen, Kirchheim unter Teck, Germany, [4]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Canada, [5]Guy's Severe Asthma Centre, Guy's and St Thomas' NHS Trust, London, and School of Immunology and Microbial Sciences, King's College London, London, United Kingdom, [6]University of Cambridge, Cambridge, United Kingdom, [7]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, ON, Canada, [8]Mayo Clinic, Rochester, MN, [9]Cochin Hospital, Paris, France, [10]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca,, Gothenburg, Sweden, [11]BioPharmaceuticals Medical, AstraZeneca, Cambridge, United Kingdom, [12]Respiratory & Immunology, AstraZeneca, Bengaluru, Karnataka, India, [13]Late-stage Respiratory & Immunology, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [14]Late-Stage Respiratory and Immunology, BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom, [15]Department of Medicine, National Jewish Health, Denver, [16]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Vasculitis – ANCA-Associated (1764–1769)

Session Type: Abstract Session

Session Time: 10:00AM–11:30AM

Background/Purpose: Results from the ongoing open-label extension (OLE) of the MANDARA trial (NCT04157348) have demonstrated the efficacy of two years of anti-interleukin-5/receptor (anti-IL-5/R) therapies in inducing and maintaining remission in more than half of patients with eosinophilic granulomatosis with polyangiitis (EGPA). This analysis describes the types of relapses occurring in patients during the combined double-blind (DB) period and first year of the OLE.

Methods: 140 patients were randomized to receive either benralizumab (n=70) or mepolizumab (n=70) in the DB period of the MANDARA trial. After completing the 52-week DB period, 128 patients entered an OLE where they continued benralizumab (benra/benra; n=66) or switched from mepolizumab to benralizumab (mepo/benra; n=62) along with oral glucocorticoid (OGC) therapy, which could be tapered based on disease status. Relapse was defined as the presence of 1) active vasculitis (Birmingham Vasculitis Activity Score [BVAS] >0); OR asthma; OR sinonasal disease, leading to 2) an increase in OGC dose to >4 mg/day; OR initiation or increase in other immunosuppressive therapy; OR hospitalization for worsening EGPA. In this analysis, relapses were classified as asthma-related, sinonasal-related, 'other' (i.e., not asthma or sinonasal-related), or a combination of these three types for a total of seven types of relapses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: During the DB period, 21 (30%) in each treatment group experienced a relapse. Among the 128 patients who entered the OLE, 15 (22.7%) patients in the benra/benra group and 20 (32.3%) patients in the mepo/benra group experienced a relapse. During the study, there were 127 relapse events reported during the DB (n=64) and first year of the OLE (n=63). Of these, 60 relapses occurred in the benralizumab (during the DB) or benra/benra group, and 67 in the mepolizumab (during the DB) or mepo/benra group (**Figure 1**). Over the two-year period, 103 (81.1%) of relapses involved asthma and/or sinonasal disease: 40 (31.5%) asthma, 27 (21.3%) sinonasal, 16 (12.6%) asthma-sinonasal, and 8 (6.3%) asthma-sinonasal-other. There were 24 (18.9%) exclusively 'other' types of relapses. The most common disease manifestations associated with the 'other' category of relapse were arthralgia/arthritis, myalgia, and sensory peripheral neuropathy (**Figure 2**).

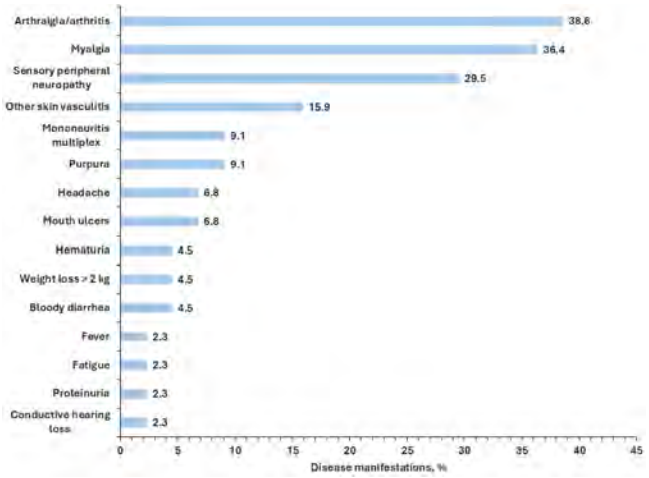


Figure 1. Subtypes of relapses in patients with eosinophilic granulomatosis with polyangiitis treated with anti-IL-5/R therapies

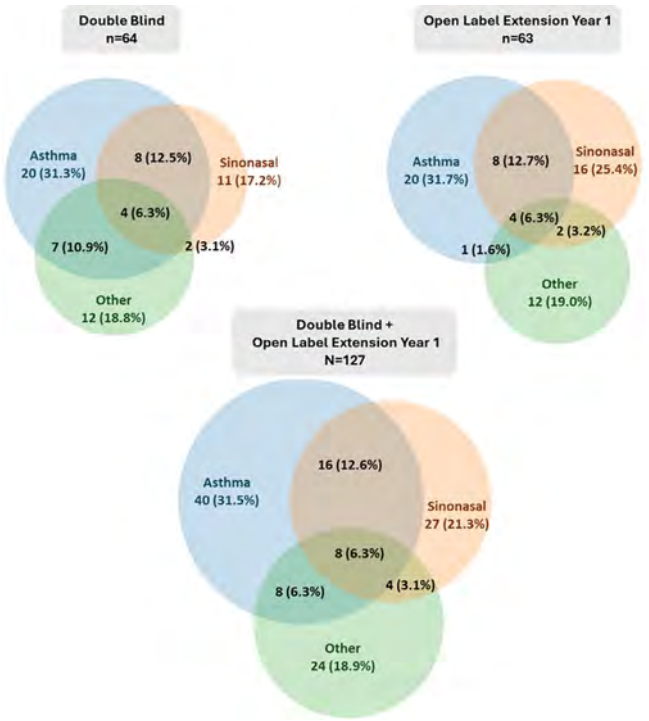


Figure 2. Disease manifestations of relapses of eosinophilic granulomatosis with polyangiitis involving non-airway manifestations among patients treated with anti-IL-5/R therapies during the one-year double-blind period and the first year of the open-label extension periods in MANDARA. Relapses may be associated with more than one disease manifestation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Among patients with EGPA treated with anti-IL-5/R therapies, the majority of relapses are airway-related, including asthma and/or sinonasal relapses. Arthralgia/arthritis, myalgia, and sensory peripheral neuropathy are the most common manifestations of non-airway relapses.

Disclosure: C. Pagnoux: amgen, 1, 2, 6, Astra zeneca, 1, 6, csl vifor, 1, 2, 6, gsk, 1, 2, 6, Novartis, 2, ns pharma, 1, otsuka, 1, 2, 5, 6, Pfizer, 2, 6; **A. Bourdin**: Amgen, 2, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Chiesi, 2, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Novartis, 2, 6, Sanofi Regeneron, 2, 6; **B. Hellmich**: AbbVie, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Chugai, 2, 6, CSL Vifor, 2, 6, GlaxoSmithKlein(GSK), 2, 6, InflaRx, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Phadia, 2, 6, Roche, 2, 6; **N. Khalidi**: AbbVie/Abbott, 2, 5, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 5, GlaxoSmithKlein(GSK), 2, 6, Mallinckrodt, 2, NS Pharma, 5, Otsuka, 2, 6, Roche, 2, 6, Sanofi, 2, 5; **D. Jackson**: AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 6, Chiesi, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Sanofi Regeneron, 2, 6; **D. Jayne**: Alentis, 2, 11, Amgen, 2, 6, AstraZeneca, 1, 2, 6, Aurinia, 1, 11, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, ChemoCentryx, 2, 6, Chinook, 1, Chugai, 2, 6, CSL Vifor, 2, 6, Fate, 2, GlaxoSmithKlein(GSK), 2, 6, GSK, 1, Hansa, 1, Novartis, 1, 2, 6, Otsuka, 2, Roche, 2, 6, Takeda, 1, 2, 6; **P. Nair**: Arrowhead Pharmaceuticals, 6, AstraZeneca, 5, 6, CSL Behring, 6, Cyclomedica, 5, Equillium, 5, Foresee, 5, Genentech, 5, GlaxoSmithKlein(GSK), 6, Sanofi, 5, 6, Teva, 5; **U. Specks**: Amgen, 1, 2, 5, Argenx, 2, AstraZeneca, 1, 5, Boehringer-Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 5, CSL Vifor, 1, Genentech, 5, GlaxoSmithKlein(GSK), 5, Mayo Foundation for Education and Research, 9, Melodia Therapeutics, 2, NorthStar Medical Radioisotopes, 5, Novartis, 1, 2, 5, NS Pharma, 5, UpToDate, 9; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **L. Börjesson Sjö**: AstraZeneca, 3, 11; **P. Jain**: AstraZeneca, 3, 11; **A. Lal**: AstraZeneca, 3, 11; **S. Necander**: AstraZeneca, 3, 11; **C. Walton**: AstraZeneca, 3, 11; **M. Wechsler**: allakos, 1, 2, 6, Amgen, 1, 2, 6, Areteia Therapeutics, 1, 2, 6, Arrowhead Pharmaceuticals, 1, 2, 6, AstraZeneca, 1, 2, 6, Avalo Therapeutics, 1, 2, 6, Celldex, 1, 2, 6, Connect Biopharma, 1, 2, 6, Eli Lilly, 1, 2, 6, Equillium, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Incyte, 1, 2, 6, Kinaset, 1, 2, 6, Kymera, 1, 2, 6, Merck, 1, 2, 6, Phylaxis, 1, 2, 6, Pulmatrix, 1, 2, 6, Rapt Therapeutics, 1, 2, 6, Recludix Pharma, 1, 2, 6, Regeneron Pharmaceuticals, 1, 2, 6, Roche/Genentech, 1, 2, 6, Sanofi/Genzyme, 1, 2, 6, Sentien, 1, 2, 6, Sound Biologics, 1, 2, 6, Tetherex Pharmaceuticals, 1, 2, 6, Uniquity Bio, 1, 2, 6, Upstream Bio, 1, 2, 6, Verona Pharma, 1, 2, 6, Zurabio, 1, 2, 6; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2.

Abstract Number: 1770

Brepocitinib Inhibits Key Pathogenic Cytokine Signaling in Dermatomyositis Patients

Christina Charles-Schoeman[1], Yessar Hussain[2] and Brendan Johnson[3], [1]UCLA Medical Center, Santa Monica, CA, [2]Austin Neuromuscular Center, Austin, TX, [3]Priovant Therapeutics, Durham, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Dermatomyositis (DM) is a rare autoimmune disease of the skin and muscles with significant unmet need and limited treatment options. Brepocitinib is an oral, selective inhibitor of TYK2/JAK1 that suppresses signaling of multiple pathogenic cytokines that have been implicated in the pathogenesis of DM disease activity including Type I and II interferons (IFN) and IL-6. Previous data has suggested that brepocitinib 30 mg may demonstrate superior inhibition of DM-relevant cytokine signaling *in vitro* compared to tofacitinib, a JAK1/JAK3 inhibitor.[1] The purpose of this study was to evaluate the ability of brepocitinib to inhibit pathogenic cytokine signaling *ex vivo* in peripheral blood mononuclear cells (PBMCs) from patients with DM and healthy donors.

Methods: PBMCs were isolated from whole blood from six participants with a diagnosis of DM according to the 2017 EULAR/ACR Classification Criteria for Idiopathic Inflammatory Myopathies and screened for baseline responsiveness to cytokine stimulation. PBMCs from responsive DM patients (n=5) and healthy donors (n=3) were separately pooled, pretreated with brepocitinib [0.0192 to 1500 nM] for 2 hours, and then stimulated with IFNα, IFNβ, or IL-6. IC_{50} curves for both groups were generated for inhibition of downstream STAT1 and STAT3 phosphorylation from each cytokine using flow cytometry.

Results: Brepocitinib potently inhibited STAT1 and STAT3 phosphorylation following IFNα, IFNβ, or IL-6 stimulation. All IC_{50}s were ≤ 30 nM in pooled PBMCs from 5 DM patients, with IC_{50} values of 4 nM and 2 nM for IFNα- and IFNβ-induced STAT1 and STAT3 phosphorylation, respectively. Brepocitinib demonstrated greater potency in inhibiting signaling in

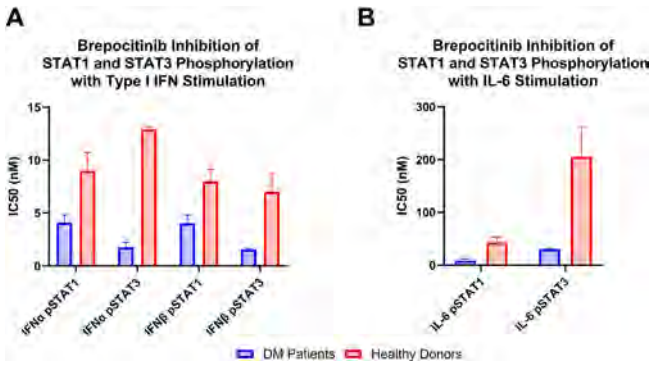


Figure 1: IC50 Values for Brepocitinib Inhibition of (A) Type I IFN Signaling and (B) IL-6 Signaling. N = 5 donors, 2 replicates for DM patients. N = 3 donors, 3 replicates for healthy donors. Error bars represent SEM

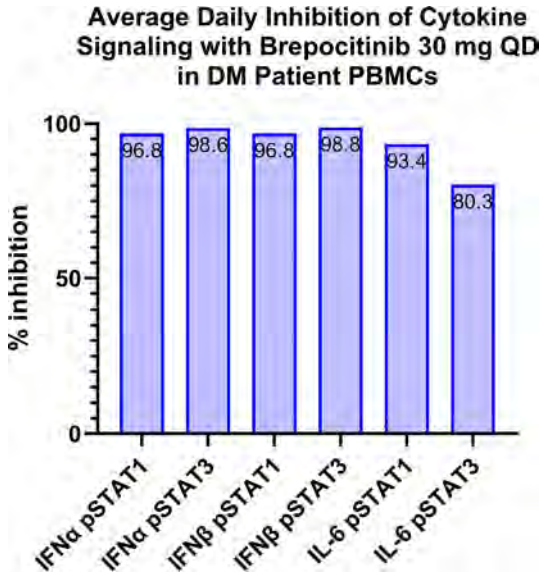


Figure 2: Percent Inhibition of Cytokine Signaling in DM Patient PBMCs. The average daily percent inhibition was calculated using: (free Cavg × 100) / (free Cavg + IC50).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

PBMCs from DM patients compared to healthy donors (Figure 1). Daily average unbound plasma concentrations (free C_{avg}, 123 nM) after administration of 30 mg once daily exceed these IC_{50}s by ≥ 4-fold, resulting in > 96% inhibition of IFNα and IFNβ signaling and > 80% inhibition of IL-6 signaling over a 24-hour dosing interval in the pooled DM patient PBMCs (Figure 2).

Conclusion: Brepocitinib demonstrated potent inhibition of proinflammatory cytokine signaling in PBMCs at exposures achieved with brepocitinib 30 mg QD. This inhibition was more potent in samples from patients with DM than healthy donors, which may reflect pathologic overactivation of JAK-STAT signaling in DM. These results confirm findings from previous work and strongly support the therapeutic rationale for TYK2/JAK1 inhibition with brepocitinib in DM. Results of a global, Phase 3, randomized, placebo-controlled trial are expected in late 2025 (VALOR; NCT05437263).

References:

Pa1. Paiik JJ, et al. Clin Exp Rheumatol. 2025 Feb;43(2):354-363.

Disclosure: C. Charles-Schoeman: AbbVie/Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Immunovant, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2, Sana Biotechnology, 2; **Y. Hussain**: None; **B. Johnson**: Priovant Therapeutics Inc, 3.

Abstract Number: 1771

Interferon- α, Anti-Interferon-Alpha Antibodies and Disease Activity in Systemic Lupus Erythematosus

Gollakota Nandita[1], Kambhampati Sreelekha[2], Kaushik Puranam[3], Phani Kumar D[4], Meghna Gavali[5] and Liza rajasekhar[6], [1]NIMS, Hyderabad, Hyderabad, Telangana, India, [2]Nizams institute of medical sciences, hyderabad, Andhra Pradesh, India, [3]Nizams Institute Of Medical Sciences , Hyderabad, hyderabad, Telangana, India, [4]NIMS, Hyderabad, Telangana, India, [5]nizam's institute of medical sciences ,Hyderabad, Hyderabad, Telangana, India, [6]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease, partly driven by Interferon-alpha (IFN-α). Studies suggest that anti-IFN-α antibodies (AIAA) may neutralize IFN-α, potentially reducing disease activity, promoting clinical quiescence despite serologic activity, and increasing the risk of infections.

Methods: SLE patients meeting the revised 1997 ACR/EULAR criteria who attended rheumatology services at a tertiary care center in India between July 2024 and February 2025, along with healthy controls, were enrolled. Exclusion criteria included active infections, juvenile SLE, pregnancy, and lactation. Data collected included baseline demographics, disease characteristics and activity, steroid dose at the time of sampling, and history of infections.

Disease activity was assessed using SLEDAI (with HDA defined as ≥10 and LDA as ≤4) and numerical BILAG scores, with BILAG scores prioritized in case of conflict. LDA patients were further classified as either serologically active (SACQ) or serologically and clinically quiescent (SQCQ).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Serum IFN-α and AIAA levels were measured using ELISA (GENLISA kits, Krishgen Biosystems); detection ranges were 7.82–500 pg/mL for IFN-α and 16–256 pg/mL for AIAA. Levels were compared between patients and controls and correlated with disease duration, clinical features, anti-dsDNA, complement levels, ESR, steroid dose, and disease activity.ROC curve analysis was performed to evaluate and compare the sensitivity and specificity of various markers in predicting disease activity. A p-value < 0.05 was considered statistically significant. Written informed consent was obtained from all participants.

Results: A total of 117 lupus patients (112 females) and 30 healthy controls (24 females) were included. Baseline characteristics are shown in Table 1. IFN-α levels were significantly higher in patients [median(IQR): 15.989(8.18-22.370)]compared to healthy controls (median: 0). They were undetectable in 29 cases and all controls with a p-value < 0.0001. Surprisingly, AIAA levels were significantly higher in healthy controls [median(IQR): 146.74(21.29-45.4)) than in patients [median(IQR): 31.34 (32.06-303.31)], p-value < 0.0001.

IFN-α positively correlated with ESR, c-SLEDAI, and BILAG scores. AIAA showed no correlation with any parameter. No significant differences in IFN-α or AIAA levels were seen between disease activity groups (LDA, HDA, SACQ, SQCQ) or clinical features or prior infections. Steroid dose showed no correlation with either IFN-α or AIAA (Table 2).

Upon comparison of IFN-α and AIAA with traditional markers such as ESR, dsDNA, C3, and C4, the conventional markers demonstrated superior performance in predicting disease activity.

Conclusion: IFN-α levels correlated with higher disease activity, as measured by BILAG scores. Established markers anti-dsDNA, C3, C4, and ESR performed better than interferon as a biomarker of disease activity.AIAA levels were not predictive of disease status or clinical phenotype. AIAA presence was not associated with infections or disease flares. If reproducible , the higher AIAA levels in healthy controls may suggest a protective role against autoimmunity.

Table 1- Baseline Demographics and Clinical Manifestations

Demographics & Laboratory Parameters

Variable	Median (IQR)
Age (years)	27 (23.0 – 33.2)
BILAG Score at Sampling	12 (1 – 25)
C3 (mg/dL)	75 (45.75 – 106)
C4 (mg/dL)	10 (5 – 19)
Steroid Dose (mg)	20 (5 – 40)
Anti-dsDNA (IU/mL)	80 (20 – 234.5)
ESR (mm/hr)	37 (17.5 – 52.5)
AIAA (pgm/l)	31.34 (21.29 – 45.5)
IFN-α (pg/mL)	15.98 (0.33 – 52.6)
SLEDAI	7 (2 – 14)

Clinical Manifestations

Manifestation	n (%)
Mucocutaneous	34 (29.1%)
Musculoskeletal	32 (27.4%)
Cardiovascular	20 (17.1%)
Gastrointestinal	12 (10.3%)
Haematological	53 (45.3%)
Constitutional	19 (16.2%)
Nephritis	49 (41.9%)
Neuropsychiatric Lupus	9 (7.7%)
Ophthalmological	1 (0.9%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2-Baseline Disease Activity status, Biomarkers and Infection history

Disease Activity Status

Category	n (%)
High Disease Activity (HDA)	54 (46.2%)
Low Disease Activity (LDA)	40 (34.2%)
Serologically Active Clinical Quiescence (SACQ)	15 (13%)
Serologically and Clinically Quiescent (SQCQ)	27 (23%)
BILAG A	54 (46.2%)
BILAG B	56 (47.9%)
BILAG A and/or B	76 (65%)

Biomarkers and Infection History

Marker	n (%)
Anti-dsDNA Positivity	56 (47.9%)
Hypocomplementemia	73 (63.2%)
History of Infections	29 (24.8%)

Table 3- Correlation coefficients (r) between IFN-α, AIAA and various clinical/laboratory variables. * indicates statistical significance.

Variable	IFN-α (r)	AIAA (r)
C3	-0.110	0.036
C4	-0.115	0.038
Steroid Dose	0.067	0.005
dsDNA	0.075	0.079
ESR	0.212*	-0.079
IFN-α	-	0.033
AIAA	0.033	-
SLEDAI	0.101	0.018
c-SLEDAI	0.248*	0.082
BILAG Score at sampling	0.193*	0.001

Disclosure: G. Nandita: None; **K. Sreelekha**: None; **K. Puranam**: None; **P. D**: None; **M. Gavali**: None; **L. rajasekhar**: None.

Abstract Number: 1772

Correlation between Soluble Checkpoint Molecules and Disease Activity in Autoimmune Diseases

Kosaku Murakami[1], Akiko Yoshida[2], Hitoshi Uga[3], Shuji Sumitomo[4], Koichiro Ohmura[5], Ryosuke Hiwa[6], Tomohiro Kozuki[7], Mao Kuroishi[3], Chihiro Suminaka[3], Mirei Shirakashi[6], Hideaki Tsuji[8], Shuji Akizuki[6], Ran Nakashima[6], Hajime Yoshifuji[6], Akira Onishi[9], Masao Tanaka[9], Akio Morinobu[10], Kenji Chamoto[7] and Tasuku Honjo[7], [1]Division of Clinical Immunology and Cancer Immunotherapy, Center for Cancer Immunotherapy and Immunobiology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [2]Division of Clinical Immunology and Cancer Immunotherapy, Center for Cancer Immunotherapy and Immunobiology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [3]Central Research Laboratories, Sysmex corporation, Kobe, Hyogo, Japan, [4]Kobe City Medical Center General Hospital, Kobe city, Hyogo, Japan, [5]Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan, [6]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [7]Department of Immunology and Genomic Medicine, Center for Cancer Immunotherapy and Immunobiology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [8]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [9]Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [10]Kyoto University, Kyoto, Kyoto, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Soluble checkpoint molecules (sCM) may be involved in the pathophysiology of autoimmune diseases by inhibiting the suppressive signals of immune cell activation through binding to membrane-bound checkpoint molecules. The serum levels of soluble programmed death-1 (sPD-1) and soluble programmed death ligand 1 (sPD-L1) have been reported to correlate with disease activity in systemic lupus erythematosus (SLE) , but their dynamics in other autoimmune diseases remain unclear.

Methods: Plasma from healthy controls (HC) and patients was used. The plasma concentrations of sPD-1, sPD-L1, and soluble cytotoxic T-lymphocyte-associated protein 4 (sCTLA-4) were measured (pg/ml) by a fully automated immunoassay (HISCL system). If possible, samples at multiple timepoint were collected from the same patient with different disease states. Disease activity was assessed using Simplified Disease Activity Index (SDAI) for RA, SLE Disease Activity Index (SLEDAI) for SLE, Birmingham Vasculitis Activity Score (BVAS) for AAV and Myositis Intention To Treat Activity Index (MITAX) for Idiopathic inflammatory myopathies (IIM). Other clinical evaluation items, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), were also compared.A patent application has been filed related to the methodology described in this study.

Results: There were 29 HC (44% female, median age 35 years), 30 RA patients (59 samples, 81% female, median age 66 years), 42 SLE patients (84 samples, 94% female, median age 43 years), 20 AAV patients (41 samples, 70% female, median age 75 years), and 21 IIM patients (49 samples, 59% female, median age 58 years). In the present patient cohort,

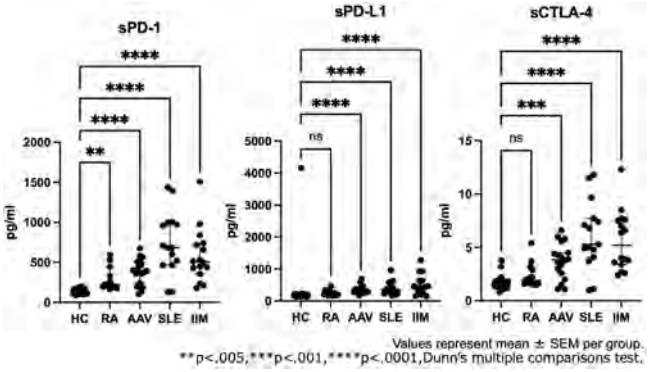


Figure1. Plasma sCM in healthy individuals and autoimmune disease patients before treatment.

All IIM samples (n=49)		
valuables	Spearman rho	p value
sCTLA-4	0.81	<.0001
sPD-1	0.76	<.0001
sPD-L1	0.75	<.0001
CK†	0.48	0.0009
ESR	0.47	0.0015
CRP	0.36	0.0092

† Analysis was performed using only the 43 samples from patients who presented with muscle symptoms at their initial visit.

Anti-ARS antibody positive (n=17)		
valuables	Spearman rho	p value
sCTLA-4	0.87	<.0001
sPD-L1	0.82	<.0001
sPD-1	0.80	<.0001

Anti-MDA5 antibody positive (n=16)		
valuables	Spearman rho	p value
sCTLA-4	0.89	<.0001
sPD-1	0.87	<.0001
sPD-L1	0.82	<.0001
Anti-MDA5 Ab	0.64	0.0098
Ferritin	0.36	0.163

Figure 2. The correlation of each assessment parameter with MITAX.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

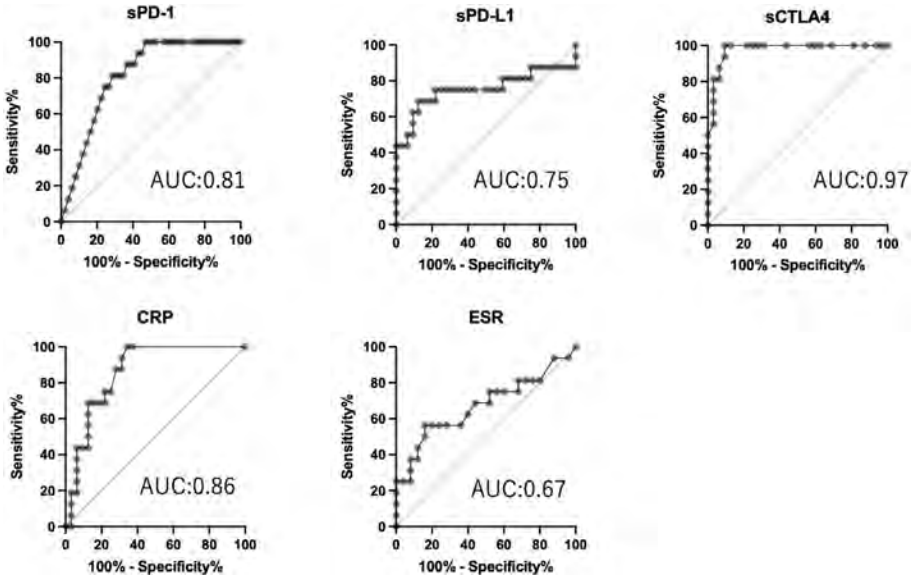


Figure 3. Receiver Operating Characteristic Curve (ROC) of plasma sCM in IIM patients before and after treatment.

untreated patients generally showed higher levels of sCM compared to HC. The SDAI had no correlation with sCM. SLEDAI and BVAS showed mild correlations with sCM (rs=0.48-0.55; p< 0.001). MITAX showed high correlations with sCM (sPD-1, sPD-L1, sCTLA-4; rs=0.76, 0.75, 0.81; p< 0.0001), In particular, sCM showed a stronger correlation with MITAX (rs > 0.8) in cases of anti-ARS antibody or anti-MDA5 antibody positive. And when calculating the AUC using ROC curves, sCTLA-4 (0.97) were able to distinguish between pre- and post-treatment more effectively than CRP (0.86) and ESR (0.67) in IIM patients. Even after performing multivariate analysis with age, sex, sPD-L1, and sCTLA4, sCTLA-4 and sPD-L1 remained independent factors associated with MITAX, regardless of age and sex.

Conclusion: The correlation between disease activity and sCM varied among autoimmune diseases. sCM may be useful as evaluation parameters, especially in IIM patients.

Disclosure: K. Murakami: None; **A. Yoshida**: None; **H. Uga**: None; **S. Sumitomo**: AbbVie/Abbott, 6, Asahi-kasei, 6, Astellas, 6, AstraZeneca, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **K. Ohmura**: Asahi-kasei, 6, AstraZeneca, 6, Chugai, 6, Eisai, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Mitsubishi-Tanabe, 6; **R. Hiwa**: None; **T. Kozuki**: None; **M. Kuroishi**: None; **C. Suminaka**: None; **M. Shirakashi**: None; **H. Tsuji**: None; **S. Akizuki**: None; **R. Nakashima**: None; **H. Yoshifuji**: AbbVie/Abbott, 6, Chugai, 6, Janssen, 6; **A. Onishi**: None; **M. Tanaka**: None; **A. Morinobu**: None; **K. Chamoto**: None; **T. Honjo**: None.

Abstract Number: 1773

Redefining disease activity assessment in IgG4-Related Disease: The role of classical and novel biomarkers

Marta López[1], rafeal Benito-Melero[2], Laura Martinez-Martinez[3], Hye Sang-Park[4], sara Calleja[3], Helena Codes Mendez[5], Mar Concepción Martín[3], Berta Magallares[3], Ivan Castellví[6], Ana Laiz[5], Cesar Diaz[3] and Hector Corominas[7], [1]Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain, [2]MD, barcelona, Spain, [3]Hospital Santa Creu i Sant Pau, Barcelona, Spain, [4]Hospital Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [5]Sant Pau Hospital, Barcelona, Spain, [6]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, barcelona, Spain, [7]Hospital de Sant Pau, Barcelona, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory disorder characterized by elevated serum IgG4 levels and tissue infiltration by IgG4-positive plasma cells. Despite advances in understanding this entity, there is a lack of reliable biomarkers for assessing disease activity and improving follow-up.

The aim is to evaluate the role of novel biomarkers, including plasmablasts and the cytokines IL-1β, IL-4, IL-5, IL-10, IL-13, IL-21, and IFN-gamma as well as their respective ratios, in monitoring disease activity. Additionally, to compare them with classical biomarkers used to date.

Methods: An ambispective cohort of patients with IgG4-RD was recruited at a single tertiary care hospital. Inclusion required fulfilling at least one of the established diagnostic criteria: Umehara, Okazaki, or the 2019 ACR/EULAR classification criteria. Clinical variables were collected, including demographic data and initial disease manifestations. Disease activity was assessed using the IgG4-RD Responder Index, blood tests, and physician-determined activity, all evaluated at the same time point upon study inclusion. In patients with an available PET-CT at that time, this was also included as an additional variable.

Table 1. Baseline demographic characteristics

	N=35	p-value
Gender (men)	27 (77,14%)	0,6855
Okazaki criteria	23 (65,71%)	1
Umehara criteria		0,71
· Possible	20 (57,14%)	
· Probable	2 (5,71%)	
· Definitive	10 (28,57%)	
ACR/EULAR criteria	23 (65,71%)	0,002
Responder index	6,09 (SD 4,41)	0,1
Increased organ size	33 (94,29%)	0,5
Glandular involvement		0,08
· >1	3 (8,82%)	
· >2	3 (8,82%)	
Thorax involvement		0,72
· Peribronchovascular and septal thickening	5 (14,29%)	
· Soft tissue resembling a paravertebral band in the thorax	2 (5,71%)	
Pancreas involvement		0,36
· Involvement of the pancreas and biliary tract	7 (20,00%)	
· Diffuse pancreatic enlargement with capsule-like rim of low density.	2 (5,71%)	
· Diffuse pancreatic enlargement (loss of lobulation)	1 (2,86%)	
Renal involvement		0,05
· Bilateral low-density areas in the renal cortex	10 (28,57%)	
· Hypocomplementemia	4 (11,43%)	
· Thickening of the renal pelvis/soft tissue	3 (8,57%)	
Retroperitoneal involvement		0,006
· Peripheral or anterolateral soft tissue around the infrarenal aorta or iliac arteries	12 (34,29%)	
· Diffuse thickening of the abdominal aortic wall	8 (22,86%)	
Fever	5 (14,29%)	0,63
Toxic syndrome	7 (20,00%)	0,65
Low back pain	8 (22,86%)	0,68
Hydronephrosis	5 (14,29%)	0,29
Aneurism	13 (37,14%)	0,47
Hypophysitis	1 (2,86%)	1
Pachymeningitis	1 (2,86%)	0,31
Orbital pseudotumor	0 (0%)	-
Uveal involvement	0 (0%)	-
Wallace subtype classification:		0,29
· Retroperitoneum and aorta	21 (60,00%)	
· Pancreato-biliary	8 (22,86%)	
· Systemic Mikulicz	5 (14,29%)	
· Head and neck	1 (2,86%)	
Clinically assessed disease activity	12 (34,29%)	0,12
Responder index	4,83 (SD 3,97)	0,013
RI >4	19 (54,29%)	0,03
Damage control index	3,09 (SD 1,51)	
Activity based on PET	8 (28,57%)	0,65
CT	14 (40,00%)	0,4
· Aorta involvement	3 (21,43%)	1
· Retroperitoneum involvement	3 (21,43%)	1
Histological involvement	11 (31,43%)	1
· Plasmatic cells	10 (90,91%)	
· Lymphocytic infiltration	10 (90,91%)	
· Phlebitis	3 (27,27%)	
· Fibrosis	4 (36,36%)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Comparative Analysis of Classical and Novel Biomarkers According to PET Findings, Clinical Assessment, and IgG4-RD Responder Index

	PET			Clinical activity based in medical judgement			Responder Index		
	Positive (n=8) mean (SD)	Negative (n=20) mean (SD)	p-value	Clinical activity (n=12) mean (SD)	No clinical activity (n=23) mean (SD)	p-value	>4 (n=19) mean (SD)	<4 (n=16) mean (SD)	p-value
Plasmoblastos	1417,62 (1460,60)	731,95 (1001,53)	0,22	832,50 (1133,89)	1308,43 (2121,22)	0,7	568,68 (616,01)	1829,94 (2506,96)	0,14
INF-gamma	9,09 (8,45)	5,95 (5,24)	0,19	7,66 (7,86)	6,04 (4,52)	0,63	7,34 (6,77)	5,72 (4,49)	0,45
IL-10	19,86 (39,44)	12,42 (21,23)	0,27	14,09 (32,03)	10,98 (20,57)	0,43	12,46 (26,54)	11,56 (23,07)	0,98
IL-13	9,35 (24,31)	12,71 (23,94)	0,16	11,64 (21,55)	8,68 (21,86)	0,87	10,84 (20,26)	8,34 (23,45)	0,2
IL-1 beta	0,88 (0,86)	0,73 (0,86)	0,51	0,89 (0,98)	0,66 (0,65)	0,53	0,83 (0,82)	0,63 (0,72)	0,33
IL-21	0,29 (0,22)	0,42 (0,51)	0,97	0,49 (0,65)	0,29 (0,16)	1	0,43 (0,52)	0,27 (0,15)	0,57
IL-4	18,95 (45,38)	44,69 (86,90)	0,16	26,61 (47,78)	33,38 (80,32)	0,88	31,28 (59,47)	30,80 (83,17)	0,54
IL-5	2,48 (3,52)	2,07 (2,30)	1	2,49 (2,89)	1,63 (2,16)	0,15	2,27 (2,38)	1,51 (2,49)	0,03
C3	130,25 (25,89)	125,27 (32,24)	0,71	135,17 (26,60)	118,07 (28,30)	0,12	129,93 (27,34)	120,55 (30,09)	0,41
C4	26,10 (11,32)	26,61 (6,29)	0,88	28,12 (8,70)	25,36 (6,90)	0,37	27,36 (8,17)	25,65 (7,41)	0,58
Eosinophiles	0,90 (1,87)	0,15 (0,10)	0,03	0,90 (1,87)	0,15 (0,10)	0,8	0,16 (0,11)	0,56 (1,34)	0,17
PCR	10,86 (22,75)	15,61 (43,22)	0,77	18,91 (55,51)	8,03 (15,51)	0,95	15,58 (44,42)	7,23 (16,33)	0,80
VSG	19,75 (30,34)	16,89 (15,77)	0,59	9,55 (7,13)	19,32 (23,30)	0,64	13,72 (15,52)	18,87 (24,35)	0,84
Hemoglobina	83,86 (58,35)	57,74 (61,71)	0,43	92,42 (59,14)	51,98 (58,53)	0,06	64,67 (61,95)	67,25 (61,97)	0,69
IgG	1538,75 (651,38)	1688,50 (2527,09)	0,3	2459,75 (3148,47)	1126,00 (321,46)	0,01	1986,79 (2547,64)	1104,12 (341,32)	0,02
IgG4	110,62 (95,89)	102,20 (88,13)	0,74	137,50 (105,83)	95,52 (84,80)	0,20	145,53 (107,72)	67,62 (47,44)	0,01
INF-gamma/IL-10	4,80 (4,79)	1,75 (2,01)	0,13	4,39 (4,08)	2,96 (5,46)	0,26	3,40 (3,60)	3,36 (6,42)	0,46
IL-13/INF-gamma	0,49 (0,93)	2,73 (5,01)	0,04	1,70 (4,23)	1,74 (3,89)	0,82	1,70 (3,85)	1,76 (4,19)	0,44
INF-gamma/IL-1 beta	11,53 (6,82)	17,06 (16,84)	0,81	11,71 (9,47)	14,36 (13,98)	0,52	11,93 (8,53)	15,26 (16,20)	0,71
IL-21/INF-gamma	0,04 (0,05)	0,08 (0,05)	0,02	0,06 (0,04)	0,07 (0,05)	0,47	0,06 (0,04)	0,08 (0,06)	0,45
INF-gamma/IL-4 pg/mL	3,15 (2,33)	0,95 (0,77)	0,00	1,86 (1,79)	1,60 (1,89)	0,66	1,50 (1,51)	1,91 (2,18)	0,78
INF-gamma/IL-5 pg/mL	7,66 (8,63)	8,83 (20,78)	0,38	4,24 (3,06)	11,36 (20,16)	0,66	4,42 (3,72)	14,25 (23,60)	0,16
IL-13/IL-10 pg/mL	0,41 (0,46)	0,65 (0,60)	0,39	0,63 (0,51)	0,65 (0,65)	0,79	0,76 (0,67)	0,51 (0,48)	0,22
IL-10/IL-1beta pg/mL	16,12 (24,10)	24,33 (35,42)	0,24	14,99 (27,08)	19,79 (31,70)	0,21	15,40 (23,38)	21,40 (36,70)	0,44
IL-21/IL-10 pg/mL	0,21 (0,27)	0,12 (0,14)	0,94	0,20 (0,22)	0,14 (0,16)	0,48	0,18 (0,21)	0,15 (0,15)	0,93
IL-10/IL-4 pg/mL	1,92 (2,76)	0,90 (1,20)	0,50	0,56 (0,40)	1,28 (1,96)	0,58	0,63 (0,54)	1,51 (2,28)	0,45
IL-10/IL-5 pg/mL	8,32 (12,70)	8,97 (12,80)	0,36	3,40 (3,93)	9,71 (13,48)	0,08	5,80 (3,71)	12,01 (15,60)	0,05
IL-13/IL-1beta pg/mL	6,75 (14,59)	22,91 (48,88)	0,14	14,25 (31,47)	15,47 (42,08)	0,64	13,35 (26,44)	17,07 (49,78)	0,54
IL-13/IL-21 pg/mL	17,56 (40,93)	44,38 (86,08)	0,17	37,82 (82,65)	27,31 (64,47)	1	31,34 (66,82)	30,00 (75,12)	0,17
IL-13/IL-4 pg/mL	0,21 (0,22)	0,29 (0,31)	0,42	0,31 (0,35)	0,26 (0,22)	0,79	0,34 (0,33)	0,20 (0,14)	0,32
IL-13/IL-5 pg/mL	1,20 (2,16)	3,57 (4,51)	0,07	2,56 (3,61)	2,69 (3,83)	0,62	2,78 (3,71)	2,49 (3,80)	0,79
IL-21/IL-1beta pg/mL	0,57 (0,42)	0,73 (0,30)	0,26	0,56 (0,30)	0,70 (0,33)	0,20	0,58 (0,29)	0,74 (0,34)	0,14
IL-1beta/IL-4 pg/mL	0,35 (0,44)	0,09 (0,07)	0,06	0,25 (0,37)	0,12 (0,12)	0,38	0,19 (0,30)	0,13 (0,13)	1
IL-1beta/IL-5	0,68 (0,82)	0,70 (1,04)	0,74	0,55 (0,49)	0,82 (1,03)	0,66	0,53 (0,48)	0,96 (1,17)	0,29
IL-21/IL-4	0,08 (0,07)	0,07 (0,05)	0,55	0,08 (0,06)	0,07 (0,05)	0,78	0,07 (0,06)	0,08 (0,05)	0,66
IL-21/IL-5	0,20 (0,17)	0,44 (0,53)	0,43	0,27 (0,27)	0,45 (0,49)	0,24	0,25 (0,23)	0,55 (0,56)	0,05
IL-4/IL-5	3,86 (3,70)	15,12 (16,64)	0,07	7,33 (10,40)	12,80 (15,05)	0,38	9,60 (13,86)	12,49 (13,85)	0,24
Plasmoblastos/IgG4	168,93 (452,67)	12,23 (21,85)	0,31	111,15 (370,96)	18,28 (24,53)	0,63	6,57 (14,37)	101,84 (317,53)	0,07
IgG4/IgG	0,06 (0,04)	0,08 (0,07)	0,56	0,08 (0,08)	0,08 (0,06)	0,74	0,10 (0,08)	0,06 (0,03)	0,21

Biomarkers used to assess activity included classical parameters: CRP, ESR, serum IgG4 and total IgG levels (and their ratio), C3, C4, hemoglobin, and eosinophil count. Novel biomarkers included plasmablasts and the cytokines IL-1β (proinflammatory), IL-10 (anti-inflammatory), IL-13 (profibrotic), IFN-gamma (Th1 phenotype), IL-5 (Th2), IL-4 and IL-21 (follicular Th phenotype), as well as their respective ratios.

Results: The study included 35 patients with IgG4-RD, predominantly male (77.14%), with a mean Responder Index of 6.09 (CI 4.63–7.55) (Tabla 1). PET-CT evaluation showed statistically significant correlations with eosinophil count (p=0.03) and the ratios IL-13/IFN-γ (p=0.04), IL-21/IFN-γ (p=0.02), and IFN-γ/IL-4 (p=0.00), highlighting the role of these interleukins in inflammatory processes. Physician-based activity assessment showed a statistically significant correlation only with IgG levels (p=0.01).

The Responder Index correlated significantly with IgG (p=0.02), IgG4 (p=0.01), and IL-5 levels (p=0.03), as well as with the IL-10/IL-5 (p=0.05) and IL-21/IL-5 (p=0.05) ratios. Neither CRP nor ESR showed statistically significant associations (Table 2)

Conclusion: This study demonstrates the utility of novel biomarkers in monitoring IgG4-RD activity. The correlation between PET-CT findings and cytokine ratios (IL-13/IFN-γ, IL-21/IFN-γ, IFN-γ/IL-4) supports their role in inflammatory assessment. IgG and IgG4 remain relevant markers correlated with the Responder Index, whereas CRP and ESR showed limited utility. IL-5 stands out as key, especially through its ratios with IL-10 and IL-21, showing significant correlations with disease activity. These findings support an integrative approach combining classical and novel biomarkers (particularly cytokine ratios) to improve disease activity monitoring in IgG4-RD.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. López: None; **r. Benito-Melero**: AbbVie/Abbott, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Merck/MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6; **L. Martinez-Martinez**: None; **H. Sang-Park**: None; **s. Calleja**: None; **H. Codes Mendez**: None; **M. Martín**: None; **B. Magallares**: None; **I. Castellví**: Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 6, Gebro, 6, GlaxoSmithKlein(GSK), 2, Innovarderm, 2, Janssen, 2, 6, Kern Pharma, 2, 6, Novartis, 2, Roche, 6, Sanofi-Genzyme, 6; **A. Laiz**: None; **C. Diaz**: None; **H. Corominas**: None.

Abstract Number: 1774

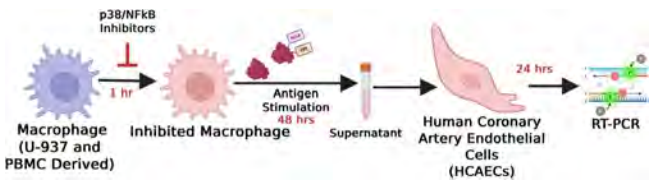
Citrullinated and Malondialdehyde-Acetaldehyde Co-Modified Fibrinogen Activates Macrophages and Induces Pro-Fibrotic shift in Coronary Endothelium Phenotype

Nozima Aripova[1], Wenxian Zhou[2], Hannah Johnson[1], Michael Duryee[1], Kimberley Sinanan[1], Carlos Hunter[1], Tate Johnson[1], Mabruka Alfaidi[1], Daniel Anderson[3], Kishore Bidasee[1], Geoffrey Thiele[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Medical Center, Bellevue, NE, [3]0587964, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

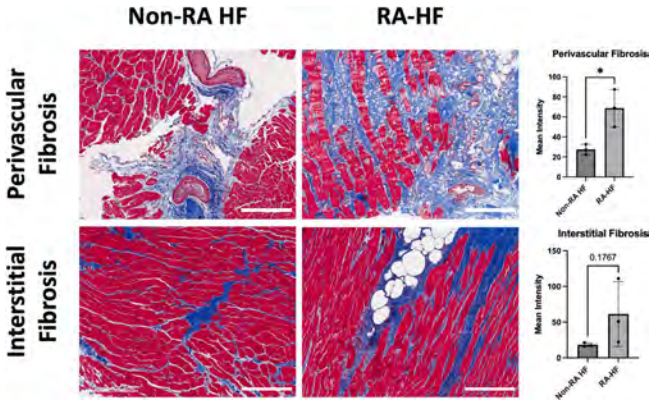
Background/Purpose: Rheumatoid arthritis (RA) patients are at increased risk for developing heart failure with preserved ejection fraction (HFpEF), which is characterized by impaired left ventricular relaxation. The mechanisms underlying RA-associated HFpEF remain unclear, but pro-fibrotic pathways are well-characterized. Citrulline (CIT) and malondialdehyde-acetaldehyde (MAA) are post-translational modifications (PTMs) that serve as autoantigens in RA. These mediators synergistically activate macrophages via NFkB and p38 signaling, leading to pro-inflammatory and pro-fibrotic responses *in vitro*. Our laboratory recently demonstrated that PTMs are over-expressed and co-localized in the cardiac tissues of RA-HF compared to non-RA HF patients. The objective of this study is to investigate whether cardiac fibrosis is also increased in RA-HF patients and to identify whether PTMs induce a pro-fibrotic responses in human coronary artery endothelial cells (HCAECs).

Methods: Left ventricular (LV) apex tissues from RA-HF patients (n=3) and age- and sex-matched non-RA HF controls (n=3) were stained with Masson's trichrome. Cardiac fibrosis was measured by quantifying collagen deposition using ImageJ and analyzed using Student's t test. In separate experiments, human U-937 monocytes (source) were differentiated into macrophages (**Fig. 1**). Macrophages were pre-incubated for 1 hr with either 1 μM BIRB-796 (p38 inhibitor), 50 μM BAY-11-7085 (NF-κB inhibitor), or media control. After that, macrophages were stimulated with 25 μg/mL of either unmodified fibrinogen (FIB) or PTM co-modified fibrinogen (FIB-MAA-CIT) for 48 hours. After stimulation, supernatants were collected and applied to HCAECs for 24 hours. HCAEC mRNA was isolated, and expression of fibrotic mediators (SMAD3, ACTA2, PDGF) was quantified by qRT-PCR. Fibrotic mediator expression was then compared using one-way ANOVA followed by Tukey's post hoc test.

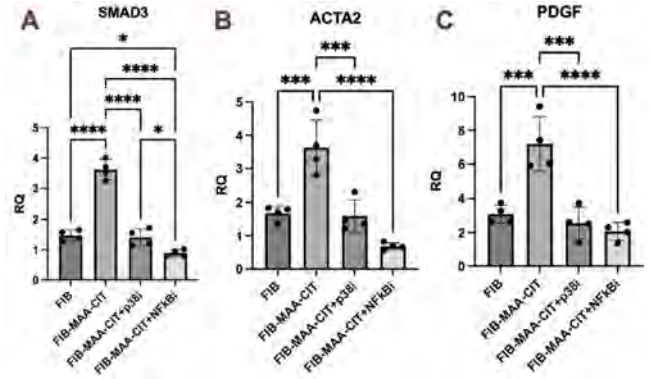


Methods set up.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Trichrome stain measuring collagen deposition in human heart tissues. Cardiac tissues from non-RA controls (non-RA HF controls) and RA patients (RA-HF) with Heart Failure (n=3/group). Collagen deposition (blue) were quantified using with Fiji plug-in and mean values from 3 images/patient calculated. Images were taken around blood vessels (perivascular fibrosis) and between cardiomyocytes (interstitial fibrosis). Representative image of 20X frame at left ventricle apex was shown. Data shown on graphs are mean ± standard deviation. Student's t test was performed, and statistical differences were shown in *: * p<0.05.



PCR measuring pro-fibrotic markers in HCAEC cells following stimulation with macrophage supernatants. Macrophage supernatants were collected post antigen stimulation (FIB or FIB-MAA-CIT) in the presence or absence of inhibitors (p38i or NFkBi). HCAEC gene expression was measured post 24-hour incubation for A) SMAD3, B) ACTA2, and C) PDGF. One-way ANOVA was performed and the statistical differences were shown in *: * p<0.05; *** p<0.001; **** p<0.0001.

Results: Patients with RA-HF exhibited significantly increased perivascular fibrosis (p< 0.05) and a non-significant trend toward increased interstitial fibrosis (p=0.18) compared to non-RA HF controls (**Fig. 2**). Supernatants from FIB-MAA-CIT–stimulated macrophages significantly upregulated mRNA expressions of *SMAD3*, *ACTA2*, and *PDGFB* in HCAECs compared to FIB (p< 0.001). Pre-treatment with p38 or NF-κB inhibitors brought pro-fibrotic gene expression back to baseline levels (**Fig. 3**).

Conclusion: Our findings suggest that PTM–activated macrophages secrete soluble factors that induce marked pro-fibrotic responses in HCAECs. Those soluble factors are potentially contributing to increased collagen deposition, suggested by perivascular fibrosis observed in RA-HF cardiac tissues. Macrophage activation via p38 and NF-κB pathways appears critical in this process. Targeting PTMs or their downstream signaling pathways may represent a novel therapeutic strategy to attenuate HF burden in RA.

Disclosure: N. Aripova: None; **W. Zhou**: None; **H. Johnson**: None; **M. Duryee**: None; **K. Sinanan**: None; **C. Hunter**: None; **T. Johnson**: None; **M. Alfaidi**: None; **D. Anderson**: None; **K. Bidasee**: None; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1775

Study Of Type -1 Interferon Gene Signature Markers In Muscle Biopsy Samples Of Patients With IIM

pradeep sosigowda[1], Phani Kumar D[1], Megha Uppin[1] and Liza rajasekhar[2], [1]NIMS, Hyderabad, Telangana, India, [2]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune diseases primarily affecting skeletal muscle, with potential involvement of other organs. They are classified into five distinct subsets: dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), immune-mediated necrotizing myopathy (IMNM), and anti-synthetase syndrome (ASyS). Diagnosing IIMs remains challenging due to overlapping clinical features and limitations in current diagnostic modalities. Emerging evidence implicates Type 1 interferons (IFNs), particularly in the pathogenesis of DM. Identifying IFN-related markers in muscle biopsies may enhance diagnostic precision and guide targeted therapy.

Methods: A cross-sectional observational study was conducted involving patients who met the 2017 EULAR/ACR classification criteria or the Bohan and Peter criteria for IIMs. Muscle biopsy samples were analyzed via immunohistochemistry for the expression of Type 1 IFN-inducible genes—Myxovirus resistance protein A (MxA), Interferon-stimulated gene 15 (ISG15), and Retinoic acid-inducible gene I (RIG-I). The expression patterns of these markers were compared between DM and non-DM IIM subgroups.

Results: The study included 50 patients: 25 with DM and 25 with non-DM IIMs (18 IMNM, 4 ASyS, 2 IBM, and 1 PM). A distinct differential expression of all three Type 1 IFN markers was observed, with significantly higher expression in the DM group.

- In DM patients, MxA expression was predominantly perifascicular, while ISG15 and RIG-I showed focal or scattered sarcoplasmic distribution.
- Thirteen DM patients were myositis-specific antibody (MSA) negative; a majority of these exhibited significant expression of Type 1 IFN markers.
- MHC Class I upregulation was observed in all DM cases and in 84% of non-DM cases.
- Among seven DM patients negative for perifascicular atrophy (PFA), six showed positive expression of at least one Type 1 IFN marker.
- Of the four ASyS patients, all were PFA-positive, but only one exhibited Type 1 IFN expression.

These findings highlight the pathological relevance of Type 1 IFN markers, suggesting they may offer superior specificity for DM diagnosis compared to traditional histopathological features like PFA.

Table 1- IFN -1 Expression in muscle biopsy specimens of DM versus non DM

	DM	Non DM	P value
MxA	19/25(76%)	3/25(12%)	0.001
RIG-I	15/25(60%)	6/25(24%)	0.03
ISG-15	12/25(48%)	4/25(16%)	0.015

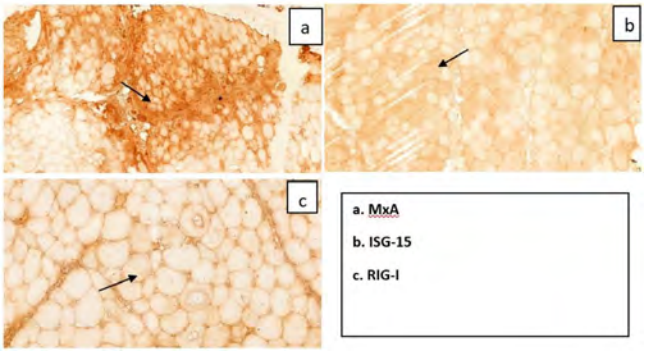
Expression in muscle biopsy specimens of DM and Non DM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2- INF -1 Expression in MSA negative subset of DM

MSA Negative	DM(n=13)	NON-DM(n=15)	P value
MxA Positive	9	2	0.0029
ISG 15 positive	6	2	0.057
RIG Positive	6	3	0.149

IFN-1 expression in MSA negative subset of DM



Histopathological images showing all 3 IFN-1 markers

Conclusion: This study underscores the diagnostic utility of Type 1 IFN markers—MxA, ISG15, and RIG-I—in distinguishing DM from other IIMs. Among these, MxA showed the most pronounced differential expression and demonstrated sensitivity and specificity comparable to PFA. Notably, MxA was positive in 72% of MSA-negative DM cases. While PFA remains a hallmark of DM, our findings suggest that IFN markers, particularly MxA, may serve as valuable adjuncts or alternatives in diagnostic evaluation. These insights support the incorporation of IFN markers into routine histopathological assessment and highlight their potential role in advancing precision medicine for DM.

Disclosure: p. sosigowda: None; **P. D**: None; **M. Uppin**: None; **L. rajasekhar**: None.

Abstract Number: 1776

Preclinical Development of a Novel TL1A-Targeting Antibody with Extended Half-life and Low Immunogenicity Risk for the Treatment of Inflammatory Diseases

Yali Zhou[1], Huilin Li[1], Hang Su[1], Mingjun Zhao[1], Haiying Wang[1], Qiong Wang[1], Xiaojin Zhang[2], Yanliu Fan[1], Lulu Li[1], Miaomiao Wang[1], Jinglu Xia[1], Wenyue Zong[1], Jingjing Li[1], Simin Yi[1], Bing Zou[1], Zhen Lu[1], Yali Wang[1], Yupeng Zhu[1], Lingjian Yang[1], Zenglin Pei[1], Barry Duplantis[3], Yuhao Wang[3], Yi Li[1] and **Quan Yu**[1], [1]Ailux, Shanghai, China (People's Republic), [2]XtalPi, Shanghai, China (People's Republic), [3]Ailux, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune and inflammatory diseases such as inflammatory bowel disease (IBD) and psoriasis are driven by dysregulated cytokine networks. TL1A, a member of the TNF superfamily, plays a key role in modulating inflammation and fibrosis through interaction with its cognate receptor, DR3. While anti-TL1A antibodies have shown promising efficacy in clinical trials, there remains a significant need for next-generation therapeutics with improved efficacy and safety,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and more convenient dosing. Here, we describe the development and characterization of a humanized anti-TL1A antibody engineered for extended serum half-life and reduced immunogenicity risk. On this basis, a bispecific antibody targeting both TL1A and an orthogonal pathway such as IL-23 may offer synergistic benefits in alleviating IBD pathogenesis.

Methods: Humanized anti-human TL1A antibodies were derived from immune repertoire mining and optimized for pH-sensitive TL1A binding and FcRn-mediated IgG recycling. Binding to TL1A or related TNF superfamily members was assessed using surface plasmon resonance and ELISA, respectively. The formation of antibody-TL1A immune complexes was analyzed by negative-stain electron microscopy. Functional inhibition of TL1A signaling was evaluated using TF-1 cell apoptosis assay and human whole blood-based IFN-γ secretion assay. In vivo efficacy was assessed in a 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis model using human TL1A transgenic mice. Immunogenicity was evaluated by monitoring anti-drug antibody (ADA) responses in animal models. Serum half-life was examined in non-human primates following single-dose administration.

Results: The anti-TL1A antibody demonstrated epitope-specific pH-sensitive binding with human TL1A and cross-reactivity with cynomolgus TL1A, with no detectable binding to TNF-α or TRAIL. The antibody did not form large immune complexes when incubated with TL1A trimers in vitro, nor did it elicit ADA responses in animal models. It selectively inhibited TL1A/DR3 interaction while sparing TL1A/DcR3 binding, and effectively suppressed TL1A-induced TF-1 cell apoptosis and IFN-γ secretion in vitro. In the TNBS-induced mouse colitis model, the antibody exhibited a strong anti-inflammatory effect and alleviated disease symptoms. In non-human primates, the antibody showed an extended serum half-life compared to clinical-stage antibodies.

Conclusion: The humanized anti-TL1A antibody demonstrates high binding specificity and potent anti-inflammatory activity both in vitro and in vivo. The multi-objective antibody engineering confers extended half-life and low immunogenicity risk, supporting the potential for infrequent subcutaneous administration and improved safety. Further preclinical studies and development of a novel bispecific antibody targeting TL1A and an orthogonal inflammatory pathway are warranted.

Disclosure: Y. Zhou: None; **H. Li**: None; **H. Su**: None; **M. Zhao**: None; **H. Wang**: None; **Q. Wang**: None; **X. Zhang**: None; **Y. Fan**: None; **L. Li**: None; **M. Wang**: None; **J. Xia**: None; **W. Zong**: None; **J. Li**: None; **S. Yi**: None; **B. Zou**: None; **Z. Lu**: None; **Y. Wang**: None; **Y. Zhu**: None; **L. Yang**: None; **Z. Pei**: None; **B. Duplantis**: None; **Y. Wang**: None; **Y. Li**: None; **Q. Yu**: None.

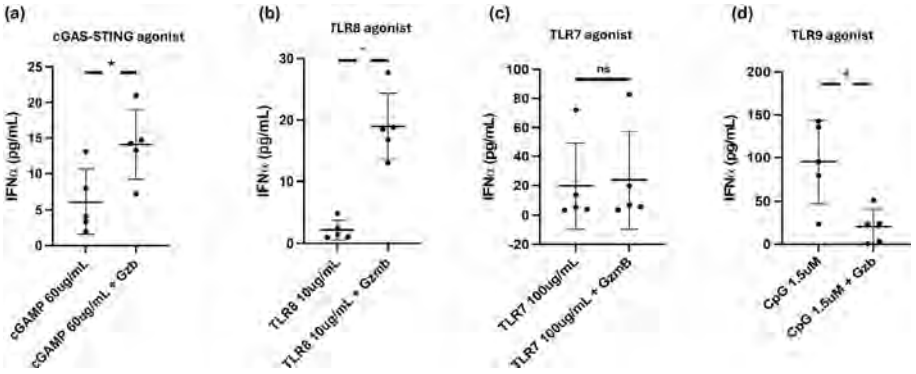
Abstract Number: 1777

Granzyme B as a regulator of interferon alpha production in cutaneous lupus erythematosus

Touraj Khosravi[1], Ahmed Eldaboush[2], Darae Kang[3] and Victoria Werth[2], [1]Department of Dermatology, Perelman Shool of Medicine, University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]University of Pennsylvania, Potomac, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Background/Purpose: Recent studies have shown that monocytes, macrophages, and conventional DCs, but not plasmacytoid dendritic cells (pDC), are major sources of IFNα in cutaneous lupus erythematosus (CLE). However, novel medications targeting pDCs reduce IFNα levels and improve CLE. Granzyme B is a proteolytic enzyme that induces apoptosis, and large concentrations are produced by pDCs in CLE, yet its role in modulating signaling pathways, including IFNα release, has not been elucidated.

Methods: Peripheral blood mononuclear cells (PBMCs) were obtained from 25 CLE patients. PBMCs were co-incubated for 20 hours with 500U of recombinant human granzyme B alone or with either 100ug/mL C307 (TLR7 agonist), 10ug/mL TL8-506 (TLR8 agonist), 1.5uM CpG (TLR9 agonist) or 60ug/mL cGAMP (STING agonist). Positive controls were PBMCs stimulated separately with only C307, TL8-506, CpG or cGAMP. Supernatants were then analyzed for IFNα production via ELISA.

Results: PBMCs incubated with granzyme B alone did not produce any IFNα (n=5). PBMCs co-incubated with granzyme B and C307 (n=5) did not result in any significant change in IFNα production compared to PBMCs incubated with C307 alone (mean IFNα 20.0±13.3 vs. 22.7±15.3 pg/mL respectively, p=0.11). PBMCs co-incubated with granzyme B and CpG (n=5) significantly reduced IFNα production compared to PBMCs incubated with CpG alone (mean IFNα 20.6±9.1 vs. 95.2 ±21.5 pg/mL respectively, p< 0.01). However, PBMCs co-incubated with granzyme B with either TL8-506 (n=5) or cGAMP (n=5) produced significantly increased IFNα compared to PBMCs incubated with either TL8-506 or cGAMP alone (for TL8-506, mean IFNα 18.9±2.4 vs. 2.2±0.7 pg/mL respectively, p< 0.01; for cGAMP, mean IFNα 14.1±2.2 vs 6.1±2.0 pg/mL respectively, p< 0.01).

Conclusion: CpG stimulates the TLR9 pathway primarily on pDCs and granzyme B may have a negative feedback effect in suppressing TLR9-induced IFNα release from pDCs, as suggested by recent studies. Granzyme B may not affect the TLR7 pathway which is also highly expressed on pDCs. However, monocytes and macrophages primarily use the TLR8 and STING pathways for IFNα production. Granzyme B which is produced in large numbers by pDCs may potentiate IFNα release by enhancing the TLR8 or STING pathways on macrophages and monocytes in CLE. Outside of its role in inducing apoptosis, granzyme B may be a bridge between pDCs and other immune cells by modulating signaling pathways, in particular that of type-1 IFN in CLE.

Disclosure: T. Khosravi: Pfizer, 1; **A. Eldaboush**: None; **D. Kang**: None; **V. Werth**: AbbVie/Abbott, 2, Alpine Immune Sciences, 2, Amgen, 2, 5, AnaptysBio, 2, argenx, 2, AstraZeneca, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Calyx, 2, Caribou, 2, CESAS Medical, 6, Corbus Pharmaceuticals, 5, Crisalis, 2, CSL Behring, 2, 5, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 2, 5, Immunovant, 2, Innovaderm, 2, Janssen, 2, Kyowa Kirin, 2, MAPI Trust, 9, Merck KGaA, Darmstadt, Germany, 2, N/A, 12, The

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

University of Pennsylvania owns the copyright for the CLASI., Nektar, 2, Nuvig Pharmaceuticals, 2, Pfizer, 2, 5, Priovant, 5, Regeneron, 2, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Takeda, 2, UCB, 2, Ventus, 2, 5, Viela Bio, 2, 5, Xencor, 2.

Abstract Number: 1778

Towards an Earlier and Accurate Diagnosis of Connective Tissue Disease-related Interstitial Lung Disease: TGFB Isoform Genes as Upcoming Biomarkers

Verónica Pulito Cueto[1], Joao Carlos Batista-Liz[1], Rebeca Nieto-Nieto[2], Clara Vaquera-Illescas[2], Diego San Emeterio-Villar[2], Daniel Vicente-Mínguez[2], María Sebastián Mora-Gil[2], Belén Atienza-mateo[3], Ana Serrano-Combarro[4], David Iturbe-Fernández[5], Victor M. Mora-Cuesta[5], Carolina Aguirre-Portilla[4], Jose M Cifrián[5], Ricardo Blanco[4] and Raquel Lopez Mejias[1], [1]IDIVAL, Santander, Spain, [2]Immunopathology Group, IDIVAL, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, PALMA DE MALLORCA/BALEARES, Spain, [4]Immunopathology Group, IDIVAL and Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [5]Immunopathology Group, IDIVAL and Division of Pneumology, Hospital Universitario Marqués de Valdecilla, Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is one of the leading cause of mortality in patients with connective tissue diseases (CTDs) [1]. The onset of CTD-ILD is insidious, and the clinical symptoms are atypical and not obvious, therefore ILD is often diagnosed in later stages with severe consequences [1]. Moreover, a confident diagnosis of CTD-ILD can be difficult due to certain similarities with idiopathic pulmonary fibrosis (IPF), the most severe ILD with different prognosis and therapies [2]. Early and accurate diagnosis is crucial to delay fibrosis progression in CTD-ILD, but the limitations of current clinical

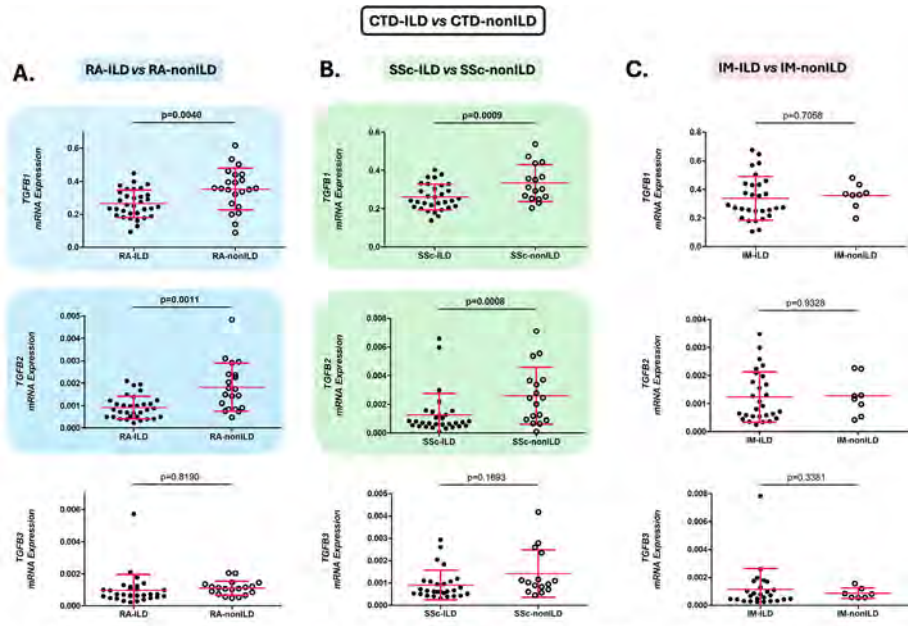


Figure 1. Role of TGFB isoforms mRNA expression as biomarkers for the early diagnosis of CTD-ILD. A. Differences in TGFB1, TGFB2, and TGFB3 mRNA expression between patients with RA-ILD and those with RA-nonILD; B. Differences in TGFB1, TGFB2 and TGFB3 mRNA expression between patients with SSc-ILD and those with SSc-nonILD; C. Differences in TGFB1, TGFB2 and TGFB3 mRNA expression between patients with IM-ILD and those with RA-nonILD. CTD: connective tissue disease; ILD: interstitial lung disease; RA: rheumatoid arthritis; SSc: systemic sclerosis; IM: inflammatory myopathies. Significant results are highlighted in ***bold****.*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

tools highlight the need to complement them with accessible and non-invasive methods. Transforming growth factor-β (TGF-β) is the main profibrogenic agent involved in different lung pathologic conditions [3]. Therefore, it is plausible to think that the *TGFB* expression is differentially altered in CTD-ILD patients. Accordingly, we focused on evaluating the role of *TGFB* isoforms as new biomarkers with clinical value for the early and accurate diagnosis of ILD in the most affected CTDs for this devastating disease, systemic sclerosis (SSc), rheumatoid arthritis (RA), and inflammatory myopathies (IM).

Methods: Peripheral blood was collected from 93 CTD-ILD patients: 33 RA-ILD, 31 SSc-ILD, and 29 IM-ILD; 48 CTD-nonILD patients: 22 RA-nonILD, 18 SSc-nonILD, and 8 IM-nonILD; and 148 IPF patients. The relative *TGFB1*, *TGFB2*, and *TGFB3* mRNA expression was quantified by qPCR.

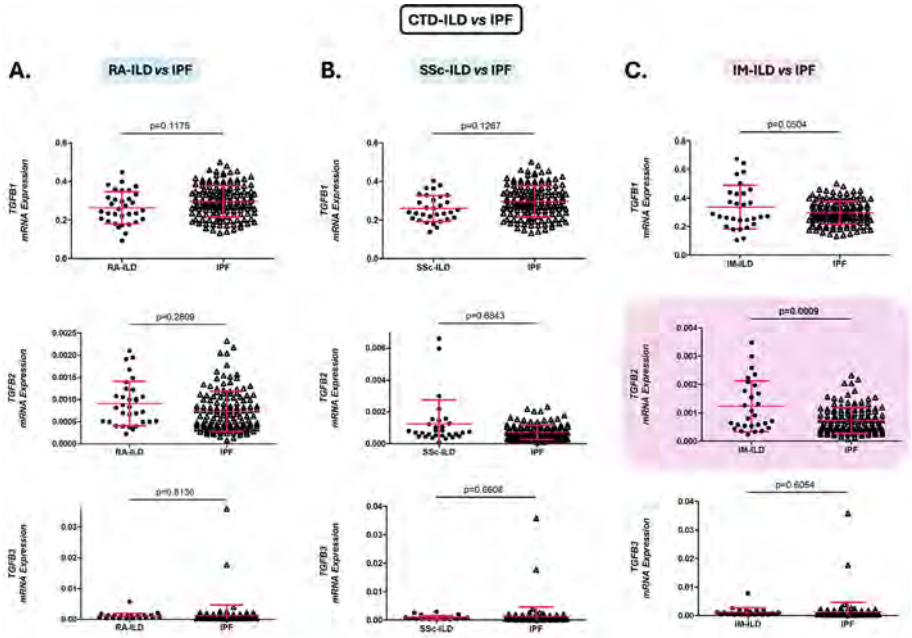


Figure 2. Role of TGFB isoforms mRNA expression as biomarkers for the accurate diagnosis of CTD-ILD. A. *Differences in TGFB1, TGFB2, and TGFB3 mRNA expression between patients with RA-ILD and IPF;* ***B.*** *Differences in TGFB1, TGFB2 and TGFB3 mRNA expression between patients with SSc-ILD and IPF;* ***C.*** *Differences in TGFB1, TGFB2 and TGFB3 mRNA expression between patients with IM-ILD and IPF. CTD: connective tissue disease; ILD: interstitial lung disease; RA: rheumatoid arthritis; SSc: systemic sclerosis; IM: inflammatory myopathies; IPF: idiopathic pulmonary fibrosis. Significant results are highlighted in* ***bold****.*

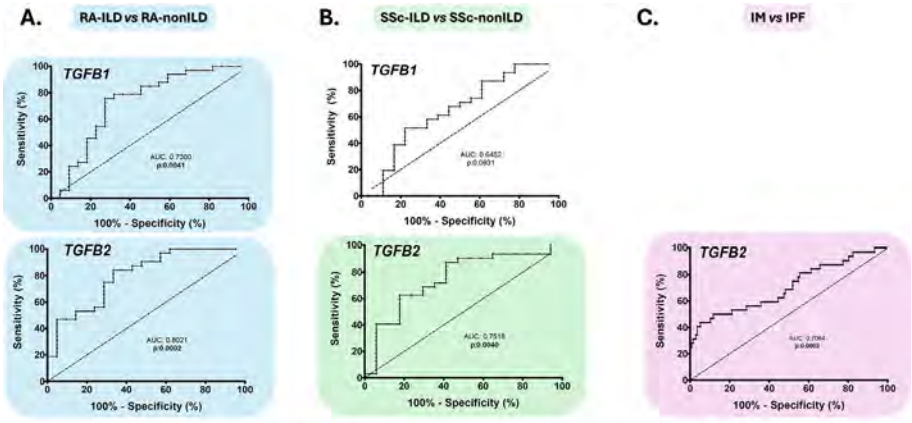


Figure 3. Utility of TGFB isoforms as biomarkers for the early and accurate diagnosis of CTD-ILD. A. ROC curve analysis to evaluate the ability of TGFB1 and TGFB2 to discriminate RA-ILD from RA-nonILD (A), SSc-ILD from SSc-nonILD (B) and IM-ILD from IPF (C). *CTD: connective tissue disease; ILD: interstitial lung disease; RA: rheumatoid arthritis; SSc: systemic sclerosis; IM: inflammatory myopathies; IPF: idiopathic pulmonary fibrosis. Significant results are highlighted in* ***bold****.*

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A significant decrease in *TGFB1* and *TGFB2* expression was observed in RA-ILD and SSc-ILD patients compared to those with RA-nonILD and SSc-nonILD, respectively (*TGFB1*: p=0.0040, **Figure 1A** and p=0.0009, **Figure 1B**, respectively; and *TGFB2:* p=0.0011, **Figure 1A** and p=0.0008, **Figure 1B**, respectively). Interestingly, IM-ILD patients showed an increased *TGFB2* expression compared to IPF patients (p=0.0009, respectively, **Figure 2C**),

In a further step, ROC curve analysis confirmed the capacity of *TGFB1* and *TGFB2* expression to differentiate RA-ILD from RA-nonILD, acting as biomarkers for the early detection of RA-ILD (p=0.0041 and p=0.0002, respectively, **Figure 3A**) with < 0.3185 for *TGFB1* and < 0.001410 for *TGFB2* as optimal cut-off values. Furthermore, *TGFB2* expression levels also revealed an ability to discriminate SSc-ILD and SSc-nonILD patients, representing an early diagnostic biomarker of SSc-ILD (p=0.0040, **Figure 3B**) with < 0.001795 as optimal cut-off value. Meanwhile, differences in *TGFB2* gene expression were sufficient to differentiate between patients with IM-ILD and those with IPF, acting as a biomarker for the accurate diagnosis of IM-ILD (p=0.0003, **Figure 3C**) with >0.001547 as optimal cut-off value.

Conclusion: *TGFB1* and *TGFB2* constitute biomarkers with clinical value for the early detection of ILD in RA and SSc, and the accurate diagnosis of IM-ILD versus IPF, representing promising screening tools for CTD-ILD in clinical practice.

References:[1]Autoimmun Rev.2024;23(6):103582.; [2]Respir Investig. 2024;62(3):465-480; [3]J Exp Med. 2020;217 (3):e20190103

Funding:BoehringerIngelheim;VP-C:NVAL23/02,INNVAL24/10;JCB-L:FI22/00020;RL-:CPII21/00004.

Disclosure: V. Pulito Cueto: None; **J. Batista-Liz**: None; **R. Nieto-Nieto**: None; **C. Vaquera-Illescas**: None; **D. San Emeterio-Villar**: None; **D. Vicente-Mínguez**: None; **M. Sebastián Mora-Gil**: None; **B. Atienza-mateo**: None; **A. Serrano-Combarro**: None; **D. Iturbe-Fernández**: None; **V. Mora-Cuesta**: None; **C. Aguirre-Portilla**: None; **J. Cifrián**: None; **R. Blanco**: AbbVie, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Galapagos, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6; **R. Lopez Mejias**: None.

Abstract Number: 1779

Citrullinated and Malondialdehyde-Acetaldehyde Modified Fibrinogen Activates Macrophages and Induces Inflammatory Responses in Coronary Endothelium

Wenxian Zhou[1], Hannah Johnson[2], Michael Duryee[2], Engle Sharp[2], Carlos Hunter[2], Tate Johnson[2], Mabruka Alfaidi[2], Daniel Anderson[3], Kishore Bidasee[2], Geoffrey Thiele[2] and Ted Mikuls[2], [1]University of Nebraska Medical Center, Bellevue, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]0587964, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1770–1779) Cytokines & Cell Trafficking Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Endothelial cell (EC) dysfunction is a key driver of cardiovascular (CV) complications in rheumatoid arthritis (RA), yet mechanisms underlying EC dysfunction in RA are not fully understood. Citrulline (CIT) and malondialdehyde-acetaldehyde (MAA) are post-translational modifications (PTMs) that are increasingly expressed and co-localized in RA tissues. These PTMs synergistically activate macrophages, leading to pro-inflammatory and pro-fibrotic responses *in vitro*. Our lab recently demonstrated increased expression and co-localization of CIT and MAA in heart tissues

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of mice with collagen-induced arthritis (CIA) that precedes fibrosis, suggesting a role of these PTMs in promoting local CV inflammation. However, their effects on EC function has not been examined. This study aims to examine whether CIT and MAA induce inflammatory responses in human coronary artery endothelial cells (HCAECs).

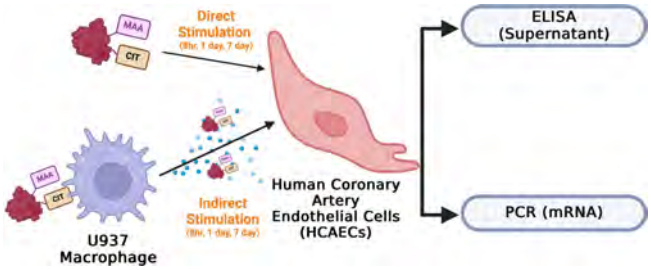


Fig 1. Study schema. HCAECs were either directly stimulated with CIT- and/or MAA-modified FIB or indirectly stimulated with supernatants from antigen-stimulated U-937 macrophages for 8 hours, 1 day, and 7 days. After stimulation, HCAEC supernatants were collected for ELISA, and mRNA was extracted for PCR.

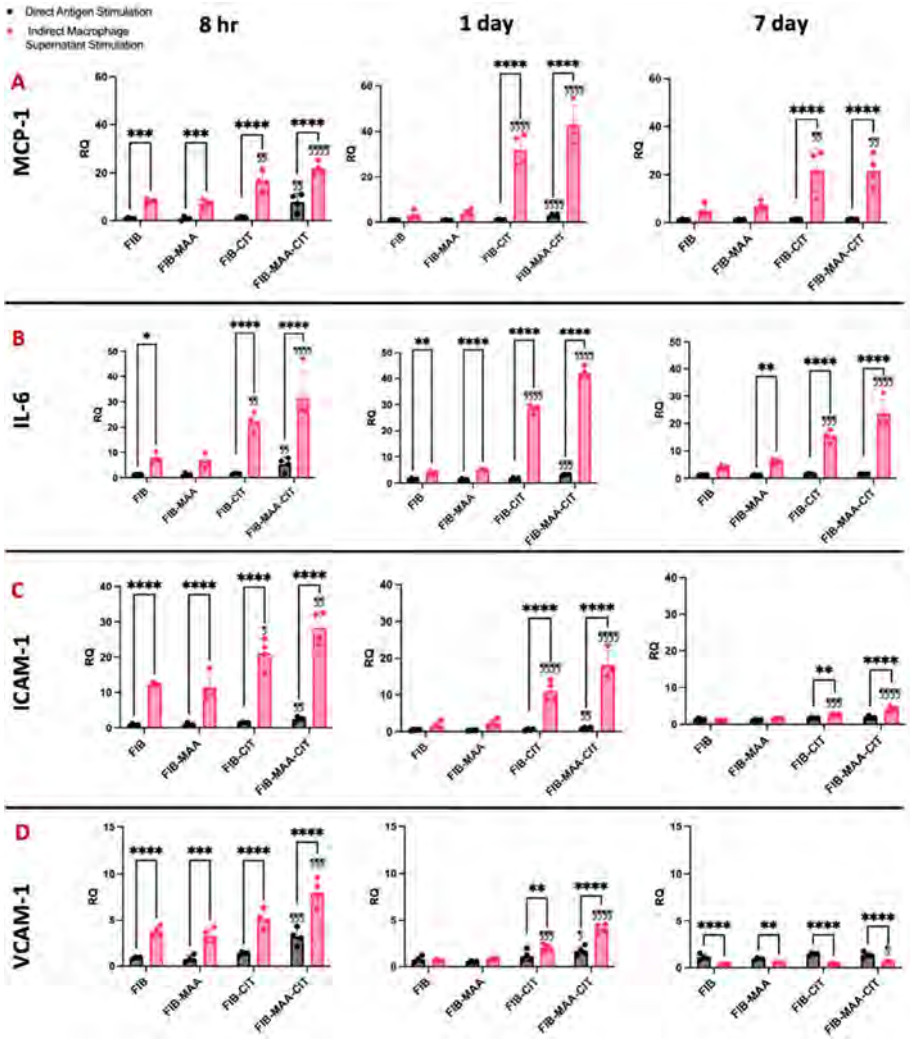


Fig. 2. PCR Demonstrating Changes in HCAEC Gene Expression Following Direct Antigen Stimulation and Indirect Stimulation with Macrophage Supernatants. 8hr, 1 day, and 7 day mRNA expression was measured for A) MCP-1, B) IL-6, C) ICAM-1, and D) VCAM-1. Relative quotient (RQ) compared to media-cultured negative control cells were calculated and shown in y-axis. Two-way ANOVA was performed and the statistical differences between direct and indirect stimulation were shown in *: * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001. Statistical differences between CIT- and/or MAA-modified FIB compared with unmodified FIB were shown in ¶: ¶ p<0.05; ¶¶ p<0.01; ¶¶¶ p<0.001; ¶¶¶¶ p<0.0001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Human U-937 monocytes were differentiated into macrophages (M0 cells) and stimulated for 48 hrs with 25 ng/mL of fibrinogen that was unmodified (FIB) or modified with MAA (FIB-MAA), CIT (FIB-CIT), or MAA and CIT (FIB-MAA-CIT) (**Fig. 1**). To assess crosstalk, macrophage supernatants were collected, and HCAECs were **indirectly** stimulated with these supernatants using 25% of total well volume for 8 hrs, 1 day, or 7 days. Concurrently, HCAECs were **directly** stimulated with FIB, FIB-MAA, FIB-CIT, or FIB-MAA-CIT. After stimulation, HCAEC supernatants were analyzed by ELISA and mRNA measured by qRT-PCR. Statistical analyses were performed using GraphPad Prism and statistical significance was achieved when $p < 0.05$ and data comparision was conducted by a two-way ANOVA and Tukey's post hoc test.

Results: Direct EC stimulation with FIB-MAA-CIT resulted in significantly higher levels of mRNA expressions of proinflammatory mediators, including MCP-1, IL-6, ICAM-1, VCAM1 (**Fig. 2**) and protein secretion (**Fig. 3**) vs. direct stimulation with FIB-MAA, FIB-CIT, or FIB alone. Interestingly, indirect stimulation of HCAECs with macrophage supernatants showed a similar pattern of inflammatory responses as direct stimulation, but the magnitude of the response was remarkably higher with indirect stimulation compared to direct antigen stimulation, suggesting an additional souble mediator secreted by macrophages

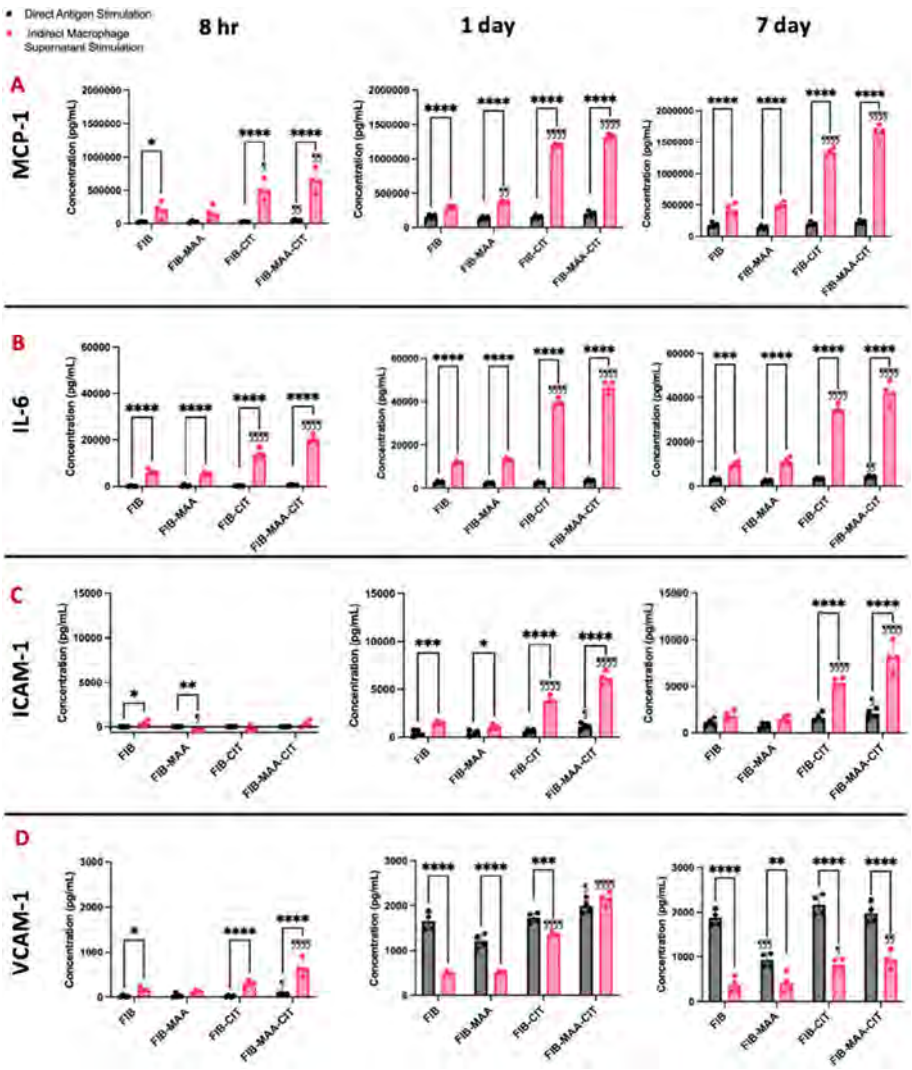


Fig. 3. ELISA Demonstrating Changes in HCAEC Protein Secretion Following Direct Antigen Stimulation and Indirect Stimulation with Macrophage Supernatants. 8hr, 1 day, and 7 day protein concentrations in supernatants were measured for A) MCP-1, B) IL-6, C) ICAM-1, and D) VCAM-1. Two-way ANOVA was performed and the statistical differences between direct and indirect stimulation were shown in *: * $p<0.05$; ** $p<0.01$; *** $p<0.001$; **** $p<0.0001$. Statistical differences between CIT- and/or MAA-modified FIB compared with unmodified FIB were shown in ¶: ¶ $p<0.05$; ¶¶ $p<0.01$; ¶¶¶ $p<0.001$; ¶¶¶¶ $p<0.0001$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

contributing to EC activation. Additionally, we observed an earlier activation at mRNA and protein levels for adhesion molecules than peaks for cytokines, confirming cellular cross communications in response to MAA and CIT.

Conclusion: This research provides novel insights into the mechanistic crosstalk between inflammatory cells and coronary EC activation in RA. The data suggest that proteins co-modified with MAA and CIT (enriched in RA tissues) act synergistically to induce inflammatory responses in HCAECs. These inflammatory responses in HCAECs are amplified through macrophage activation and secretion of soluble mediators. In addition to identifying these mediators, further research is needed to examine whether inhibition of MAA, CIT, or downstream signaling pathways attenuates HCAEC activation and reduces CV complications in RA.

Disclosure: W. Zhou: None; **H. Johnson**: None; **M. Duryee**: None; **E. Sharp**: None; **C. Hunter**: None; **T. Johnson**: None; **M. Alfaidi**: None; **D. Anderson**: None; **K. Bidasee**: None; **G. Thiele**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

Abstract Number: 1780

Modeling Osteoarthritis Knee Joint in a Compartmentalized Microfluidic System using IPSC-derived Sensory Neurons and human Synovial Fibroblasts

Abdelhak Belmadani[1], Dongjun Ren[1], Daniel Hoffman[2], Nirupa Jayraj[1], Paola Pacifico[1], Vince Truong[3], Patrick Walsh[3], Daniela Menichella[1], Anna Rapp[4], Carla Scanzello[5], Rachel Miller[6], Richard Miller[7] and Anne-Marie Malfait[8], [1]Northwestern University Chicago, Chicago, IL, [2]Rush University, Chicago, IL, [3]Anatomic Inc, Minneapolis, MN, [4]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [5]University of Pennsylvania, Philadelphia, [6]Rush University Medical Center, Chicago, IL, [7]Northwestern University, Chicago, [8]Rush University Medical Center, Chicago

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Joint pain is one of the most significant clinical hallmarks of knee osteoarthritis (OA). Knee OA is a chronic degenerative disease of the joints characterized by the breakdown of articular cartilage, changes in the subchondral bone (sclerosis) and synovium (synovitis). Uncovering the mechanisms and circuits underlying pain in knee OA remains a major challenge to finding effective and disease-modifying therapy. The synovium is heavily innervated by sensory nerve terminals potentially enabling communication between synovial fibroblasts (sFBs), the predominant cells of the synovium and knee afferents. The aim of this study is to explore mechanisms by which sFBs communicate with knee afferents and how this communication impacts sensory neuron sensitivity in OA knee joints using a microfluidic coculture system.

Methods: In a pilot and feasibility studies, we pioneered a compartmentalized microfluidic system, in which we integrated human iPSCs-derived sensory neurons (SNs) and human sFBs and tested the effects of various stimuli, known to be released by FBs on neurite outgrowth, activity and pain signaling pathways.

Results: Using a two-compartment microfluidic device, we found that hiPSCs–SNs were able to grow neurites towards sFBs within 7 days, where they form extensive connections with cocultured hsFBs. Real time monitoring of the changes in intracellular calcium levels in hiPSC-SNs cocultured with sFBs revealed a dynamic interplay between neuronal activity and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

sFBs. For example, we have used this system for targeting specific signaling pathways or receptors such as NGF and MRGPRD and study the effects on neurite growth and sensitivity. Similarly, calcium imaging studies in hsFBs from OA patients revealed that the number of FBs with higher baseline signal was significantly increased compared to sFBs from heathy individuals, indicating altered calcium homeostasis, which can impact various cellular processes, including the release of various factors that can activate nociceptors.

Conclusion: This human relevant platform with hiPSCs and hsFBs can be used to explore mechanisms and accelerate the identification of targets for analgesic therapy in joint pain in various health conditions such as in OA.

Disclosure: A. Belmadani: None; **D. Ren**: None; **D. Hoffman**: None; **N. Jayraj**: None; **P. Pacifico**: None; **V. Truong**: None; **P. Walsh**: None; **D. Menichella**: None; **A. Rapp**: None; **C. Scanzello**: None; **R. Miller**: None; **R. Miller**: None; **A. Malfait**: Asahi Kasei Pharma Corporation, 23andMe, Orion, 2.

Abstract Number: 1781

Specific gut microbiome remodeling occurs after induction of OA via DMM surgery compared to sham surgery

Aleksander Szymczak[1], Cindy Miranda Brawner[2], Nicholas Hanebutt[2], Gabriella Dyson[2], Montana Barrett[2], Anna Rapp[3], Carla Scanzello[4] and Matlock Jeffries[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, [3]University of Pennsylavnia, Philadelphia, [4]University of Pennsylvania, Philadelphia

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The destabilization of the medial meniscus (DMM) model is widely used in murine OA research due to its reproducibility and ability to recapitulate key features of human disease, particularly in the central weight-bearing regions of the medial tibial plateau and femoral condyle. While the role of the gut microbiome in OA pathogenesis is increasingly recognized, with mounting evidence linking gut dysbiosis to musculoskeletal outcomes, the impact of DMM-induced OA on the gut microbiota-and whether similar shifts occur following sham surgery-remains insufficiently characterized. This study addresses this gap by systematically evaluating gut microbiome changes following DMM and sham interventions in mice.

Methods: Male (N = 59) and female (N = 14) B6 mice underwent either DMM or sham surgery (skin, fascia, and joint capsule opened but no meniscus transection) at 12 weeks of age. Biological samples in the form of cecal contents were collected at 4 weeks, 8 weeks, and 12 weeks after surgical intervention. Bacterial DNA was isolated from these samples and subjected to 16S rRNA gene sequencing using an Illumina MiSeq sequencer. The obtained data were analyzed using the Qiime2 workflow. Group comparisons were determined using LEfSe analysis, with a 95% confidence interval after taxonomic assignment by alignment to the Greengenes2 dataset. Differences among bacterial groups were assessed using the Mann-Whitney U test.

Results: In a comparison between DMM and Sham samples, data reveals shift in microbiota composition. Specifically, the Sham group exhibited significant enrichments ($p < 0.005$) in Clostridia_258483 (Christensenellales, CAG_552), Oscillospirales ($p < 0.002$) including Acutalibacteraceae, Oscillospiraceae_88309, and Ruminococcaceae, as well as TANB77

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

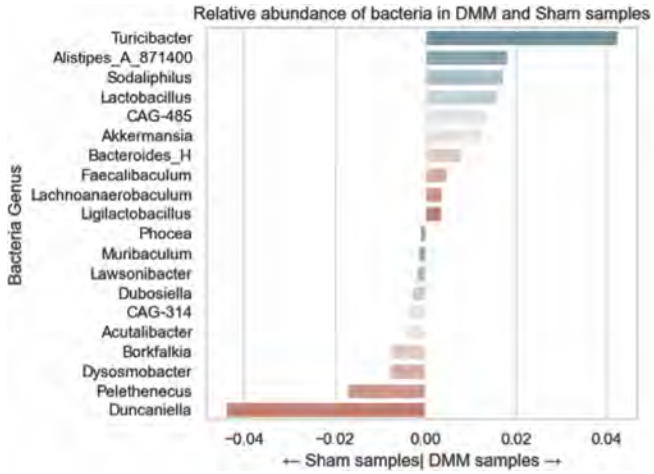


Figure 1: Differential microbiome clades between DMM and sham surgery

(CAG_508) and Bacilli (RF39, Turicibacter). Conversely, the DMM group showed significant enrichments in Oscillospirales ($p< 0.002$) including Oscillospiraceae_88309 and Ruminococcaceae, TANB77 ($p< 0.05$) including CAG_508, and Bacilli ($p< 0.05$) including RF39 and UBA660. Additional comparisons revealed that DMM vs Control groups showed significant increases in Bacteroidota ($p< 0.002$) including Bacteroidia, Rikenellaceae, and Muribaculaceae, Oscillospirales ($p< 0.002$) including Acutalibacteraceae, and Bacilli ($p< 0.05$) (Erysipelotrichales and Coprobacillaceae), while no significant differences were observed between Sham and Control mice.

Conclusion: Our data underscore a modulatory role for the gut microbiota in OA progression while confirming that brief surgical trauma alone does not perturb the intestinal microbial community. Mapping these gut–joint interactions may unveil novel microbiome-targeted strategies for OA treatment. Ongoing and future work to dissect the mechanistic links and long-term effects of dysbiosis will be critical to advancing our understanding of OA pathogenesis and guiding precision therapies.

Disclosure: A. Szymczak: None; **C. Miranda Brawner**: None; **N. Hanebutt**: None; **G. Dyson**: None; **M. Barrett**: None; **A. Rapp**: None; **C. Scanzello**: None; **M. Jeffries**: Being Inc., 1.

Abstract Number: 1782

Mapping The Synovial Innervation Of The Human Knee Joint

alia obeidat[1], Jun Li[1], Spencer Fullam[2], Roderick Carter[2], Merissa Olmer[3], Bella Mehta[4], Miguel Otero[5], Daniel Ramirez[6], Richard Miller[7], Dana Orange[8], Martin Lotz[9], Rachel Miller[10] and Anne-Marie Malfait[2], [1]Rush University Medical Center, Chicago, [2]rush university, CHICAGO, IL, [3]Scripps Research Institute, La Jolla, CA, [4]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ, [5]Hospital For Special Surgery, New York, [6]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [7]Northwestern University, Chicago, [8]Rockefeller University, New York, [9]Scripps Research, La Jolla, CA, [10]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

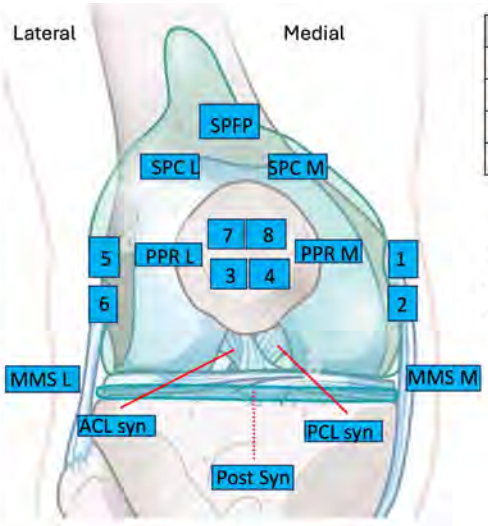
Background/Purpose: Knee joints are densely innervated by sensory neurons, predominantly nociceptors. Knowledge about innervation of healthy human synovium and the changes that accompany osteoarthritis (OA) is limited. Very few studies described innervation changes in select areas of synovium collected at total knee arthroplasty (1-3). Here, we sought to perform a comprehensive analysis of the sensory innervation of the synovium of healthy human knees.

Methods: Leveraging the availability of non-OA *postmortem* knee samples from human donors of different ages, we collected synovia from 4 males, ages 23, 42, 52 and 81, all from knees where cartilage was scored as grade 1-1.5 on the Modified Outerbridge classification. For each donor, a total of 18 tissue blocks were collected from 18 distinct synovial locations in the knee **Fig. 1**. These areas are medial (area 1,2) and lateral (area 5,6) femoral gutters, medial and lateral perimeniscal synovium (MMS M, MMS L) and anterior synovium (areas 3,4,7,8), the synovium covering the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL), medial and lateral suprapatellar compartments (SPC M, SPC L), medial and lateral parapatellar recess (PPR M, PPR L), posterior synovium (Post syn), and suprapatellar fat pad (SPFP). Tissues were formalin fixed, paraffin embedded and shipped from Scripps to Rush. Five-mm sections were stained with hematoxylin and eosin (H&E) and sent to the Hospital for Special Surgery for synovial scoring. Adjacent sections were used for immunohistochemical staining with the pan-neuronal marker, PGP9.5 (Abcam ab27053, 1:200), endothelial cell markers (CD31, Abcam Ab28364, 1:50), calcitonin gene related peptide (CGRP, immunostar 24112,1:500) or isotype control (Rabbit IgG, Abcam Ab172730, 1μg/ml). Proteinase K was used for antigen retrieval. Sections were incubated with primary antibody at 4°C overnight, stained with biotin-streptavidin/HRP and DAB chromogen, and counterstained with methyl green. PGP9.5+ and CGRP+ signal was quantified in adipose and fibrous areas of synovium using Qupath by 2 blinded observers.

Results: In all 18 regions, PGP9.5+ innervation was denser in the adipose rich areas compared to the fibrous areas. PGP9.5+ nerve signal was abundant in the synovium of medial and lateral femoral gutters, medial and lateral suprapatellar compartment, anterior synovium and synovium of the suprapatellar fat pad. PGP9.5+ nerves were more abundant in the medial synovium of the 81yr-old compared to younger donors **Fig. 2**. PGP9.5 innervation of SPFP and anterior and lateral perimeniscal synovium declined with age but increased in the lateral femoral gutters. Further characterization of the synovial samples, including CD31 staining for blood vessels is ongoing.

Conclusion: PGP9.5+ nerve fibers were abundant in medial, lateral and anterior synovium of non-OA male donors aged 23 to 81, but a marked heterogeneity was observed across the 18 regions. Adipose rich synovium showed more innervation compared to fibrous synovium. These findings are the foundation for future studies on describing the innervation changes in the OA synovium.

18 synovial blocks/donor	Acronyms
Medial synovium	Syn 1,2
Lateral synovium	Syn 5,6
Inferior anterior synovium	Syn 3,4
Superior anterior synovium	Syn 7,8
Supraparapatellar compartment	SPC M
	SPC L
Parapatellar Recess	PPR M
	PPR L
Suprapatellar Fat Pad:	SPFP
Intercondylar: adjacent to PCL	ACL Syn
Intercondylar: adjacent to ACL	PCL Syn
Perimeniscal synovium	MMS M MMS L
Posterior mid region synovium	Post Syn



Age	Sex	Grade	BMI
23yrs	M	1	29.43
52yrs	M	1	31.13
42yrs	M	1	39.68
81yrs	M	1.5	28.29

Figure 1. Synovial areas collected per donor and donor's demographic.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

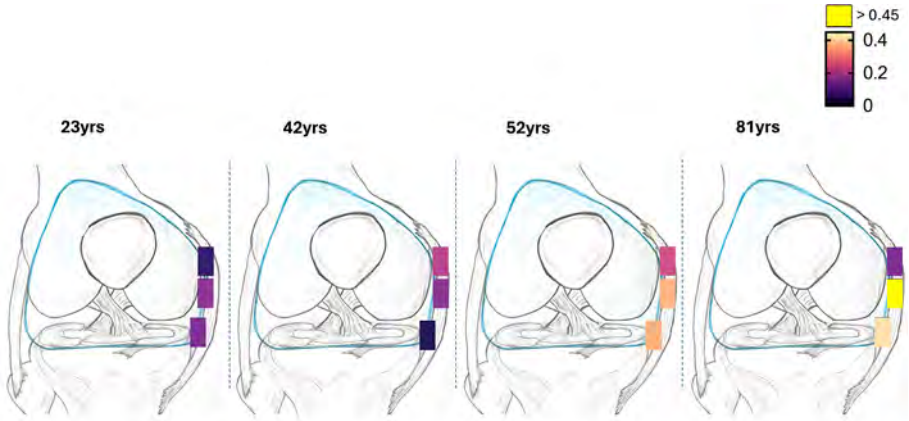


Fig. 2: Heatmaps of PGP9.5+ signal in the 4 donors showing the PGP9.5+ nerves being more abundant in the medial femoral synovial gutters and perimeniscal areas of 81yr-old compared to younger donors (increased with age)

1. Saito T *et al*., Clin Orthop. 2000.
2. Eitner *et al*., OAC. 2013.
3. Eitner A *et al*., Front Endocrinol. 2024.

Disclosure: a. obeidat: None; **J. Li**: None; **S. Fullam**: None; **R. Carter**: None; **M. Olmer**: None; **B. Mehta**: Amgen, 1, Horizon, 1; **M. Otero**: Jannu Therapeutic, 1; **D. Ramirez**: None; **R. Miller**: None; **D. Orange**: None; **M. Lotz**: Blackbird, 2; **R. Miller**: None; **A. Malfait**: None.

Abstract Number: 1783

Nerve Growth Factor Causes Sensitization, Nociceptor Sprouting, Synovitis, And Osteophyte Formation In Naïve Murine Joints

alia obeidat[1], michael Newton[2], Jun Li[1], Baofeng Hu[3], Shingo Ishihara[4], Lindsey Lammlin[2], Lucas Junginger[2], Easton Farrell[2], Frank Ko[1], Richard Miller[5], Carla Scanzello[6], Tristan Maerz[7], Rachel Miller[8] and Anne-Marie Malfait[9], [1]Rush University Medical Center, Chicago, [2]University Of Michigan, Ann Arbor, [3]University of Pennsylvania, Wynnewood, PA, [4]Rush University, Chicago, [5]Northwestern University, Chicago, [6]University of Pennsylvania, Philadelphia, [7]University of Michigan, Ann Arbor, MI, [8]Rush University Medical Center, Chicago, IL, [9]rush university, CHICAGO, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The neurotrophin, nerve growth factor (NGF), a key mediator of pain and inflammation, is increased in joints with osteoarthritis (OA). Neutralizing NGF with monoclonal antibodies has shown promising analgesic effects in painful knee OA, but clinical development was stopped owing to ill-understood side effects in the joints[1]. Knowledge about the biological effects of long-term exposure of healthy joint tissues to NGF is limited. Therefore, we aimed to explore the effects of repeated intra-articular (IA) injections of NGF into the knee joints of healthy mice on sensitization and pain, as well as joint innervation and structure.

Methods: All animal experiments were IACUC approved. Five experiments were conducted, all using 12-week old naïve male mice. In Experiment 1, NGF (50 ng or 500 ng in 5 uL, n=5 mice/group) or vehicle control (0.1% BSA in PBS, n=5 mice) was injected IA into the right knee joint of wildtype (WT) C57BL/6 mice, twice a week for 4 weeks. We assessed knee

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

swelling and knee hyperalgesia as described[2], as well as joint histopathology. Synovial changes including hyperplasia, cellularity and fibrosis were assessed by four different scorers blinded to treatment groups[3]. In Experiment 2, mice were injected with NGF (500ng) or vehicle, twice a week for 4 weeks and microCT of the knee was performed. In Experiment 3, $Na_V1.8$-tdTomato reporter mice were injected with NGF (500ng) or vehicle, twice a week for 4 weeks, and joint innervation was assessed[4]. In Experiment 4, WT mice received 500ng NGF or vehicle twice a week for 4 weeks and were used for single cell RNA sequencing (scRNAseq) of the synovium. In Experiment 5, L3-L5 DRGs were collected from mice that received 3 IA injections of 500ng NGF or vehicle twice a week for 10 days and processed for bulk RNA sequencing.

Results: Repeated bi-weekly IA injections of both doses of NGF caused knee hyperalgesia in naïve mice **(Fig. 1A)**. NGF caused dose-dependent knee swelling **(Fig. 1B)**, synovial pathology **(Fig. 1C)**, increased bone mineral density and trabecular bone thickness in the medial subchondral bone. NGF also caused osteophyte growth in the medial compartment, but no cartilage degeneration **(Fig. 1D)**. NGF injection caused sprouting of $Na_V1.8$+ neurons in the medial but not the lateral synovium **(Fig. 1E)**. ScRNAseq of the synovium revealed upregulated genes related to neuronal sprouting, synovial fibrosis and ossification, confirming histopathological findings **(Fig. 2)**. Bulk RNA seq of DRG showed upregulated pathways related to axonal growth **(Fig. 3)**.

Conclusion: In healthy mouse knees, NGF induced mechanical sensitization, synovitis, neoinnervation in the medial synovium, and subchondral bone changes and osteophyte growth in the medial compartment, thus capturing many pathological changes observed in OA, except cartilage damage. It will be critical to describe in great depth the distribution of NGF and its receptors in all joint tissues, and how they change with age and disease. Such insights are

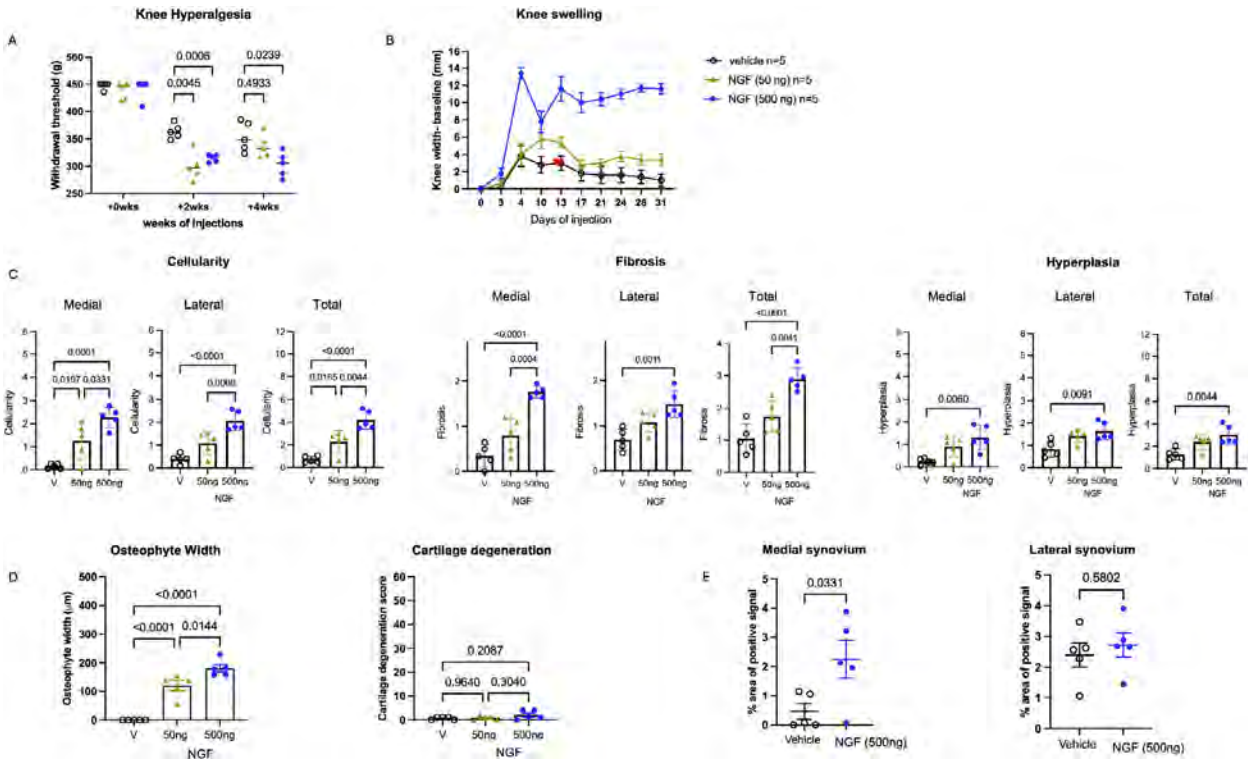


Figure 1: (A) Knee hyperalgesia was assessed for mice given repeated intra-articular injections of recombinant murine NGF (i.a. 50 ng or 500 ng, 5 µL, 2x/week) or vehicle (5 µL, 2x/week) for 4 weeks at 0-, 2, and 4-week (B) Knee swelling was assessed in wild-type mice given NGF (50 ng or 500 ng) or vehicle. Red arrowhead indicates the first injection. (C) Synovial cellularity, fibrosis and hyperplasia were evaluated in wild-type mice that received NGF at 50 ng or 500 ng or vehicle. (D) Osteophyte width measured in µm and cartilage degeneration scores. (E) Quantification of neuronal signal in the medial and lateral synovium of NaV1.8-tdTomato mice injected with vehicle or NGF. (A) Two-way ANOVA with Dunnett's post-test. (C-D) Two-way ANOVA with Sidak's post-test. (E) Unpaired two-tailed t test.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

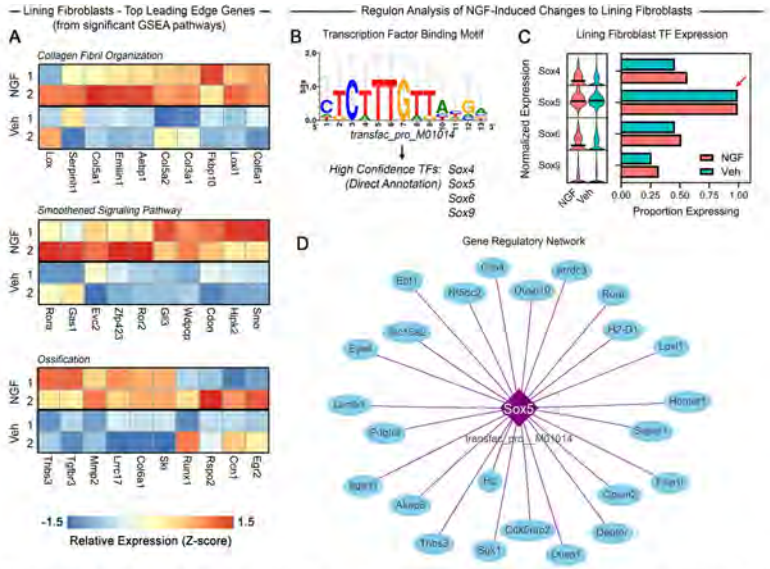


Figure 2: NGF-induced changed in lining fibroblast transcriptome. (A) Heatmap of top gene set enrichment analysis-derived leading-edge genes, demonstrating coordinated upregulation of genes related to collagen fibril organization, smoothened signaling, and ossification. (B) Transcription factor binding motif analysis (RcisTarget) of lining fibroblasts in NGF v. Veh revealed significantly enriched motif transfac_pre_M01014 for the Sox family of transcription factors, predicted by direct annotation. (C) Expression of predicted transcription factors by lining fibroblasts in Veh and NGF groups, demonstrating highest expression of Sox5 (red arrow). (D) Gene regulatory network plot for Sox5 in lining fibroblasts.

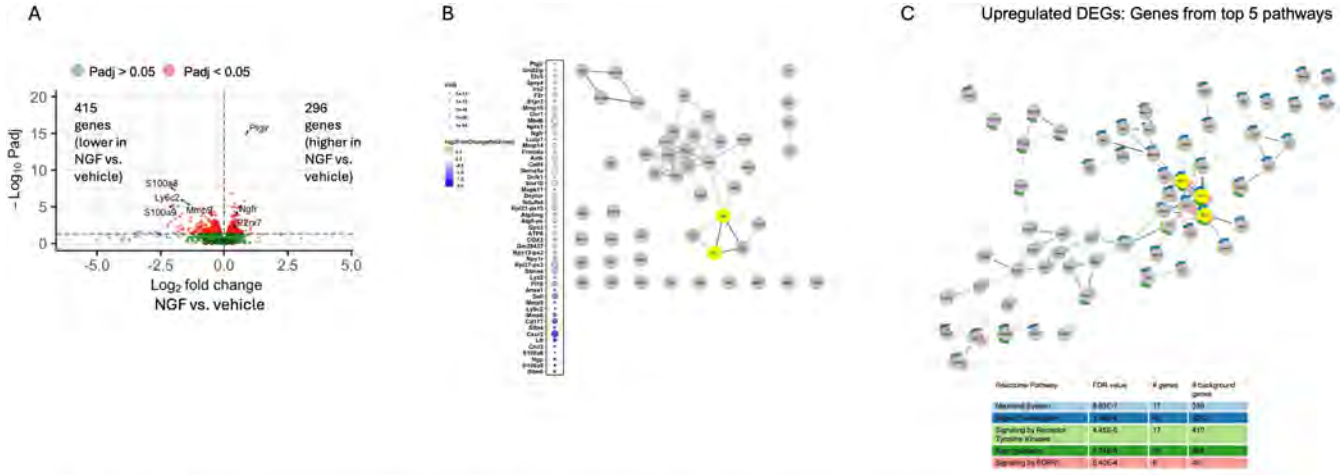


Figure 3: Differential gene expression analysis on bulk RNAseq conducted on DRGs collected after 3 injections of NGF or vehicle. (A) Volcano plot showing all genes that were not filtered out by DESeq2 (15,664). Red indicates genes that met the Padj cut-off < 0.05. No fold change cutoff was applied. Genes of interest are labeled. (B) Top 50 genes by padj, ordered by log2 fold change with the size of the bubble mapped to the adjusted p-value. String network showing known relationships to Ngf and to Ntrk1 (highlighted in yellow). (C) Functional enrichment was performed on the upregulated DEG list using Cytoscape String Enrichment; Interacting genes contributing to the top 5 Reactome pathways are shown using a redundancy cutoff of 0.5. Hub genes are highlighted in yellow.

especially important, as they may enable the modulation of NGF signaling to selectively target pain pathways while maintaining its protective functions.

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1. Hochberg, OAC, 2015.
2. Miller, JCI Insight, 2018.
3. Obeidat, OAC, 2024.
4. Obeidat, OAC, 2019.

Disclosure: a. obeidat: None; **m. Newton**: None; **J. Li**: None; **B. Hu**: None; **S. Ishihara**: None; **L. Lammlin**: None; **L. Junginger**: None; **E. Farrell**: None; **F. Ko**: None; **R. Miller**: None; **C. Scanzello**: None; **T. Maerz**: None; **R. Miller**: None; **A. Malfait**: None.

Abstract Number: 1784

Multimodal Preclinical Screening Of Glucocorticoid-Induced Disruption Of Bone Remodeling In Rat

Anik Tuladhar, Caitlyn Carter, Erin Vaughan, martin j.voorbach, Sabyasachi Biswas, Timothy Brayman, Pankaj Kumar, anastasia marinopoulos, Xin Huang, Sjoerd J. Finnema, Romy Christmann, Terry vanVleet, Brian Enright, Magali Guffroy and Stacey Fossey, AbbVie, North Chicago, IL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Bone toxicity during drug development can arise from intended pharmacologic mechanisms or off-target effects. Standard histopathological evaluation often fails to detect early skeletal alterations, especially in short-term studies. Early detection is crucial for mitigating risks in compounds affecting skeletal remodeling, growth, or maintenance.

Methods: Data was compiled from naïve Sprague-Dawley rats typically used in early exploratory and chronic toxicity studies. Naïve male Sprague-Dawley rats were treated with prednisolone (7.5 mg/kg/day) for 14 or 28 days. Bone mineral density (BMD) was measured using dual-energy X-ray absorptiometry (DXA), and microCT analysis assessed trabecular microarchitecture. Serum biomarkers related to bone turnover were also evaluated.

Results: Prednisolone treatment significantly reduced femoral BMD in the 28-day group, with a decreasing trend in the 14-day group. MicroCT showed compromised trabecular microarchitecture with decreased thickness and increased separation. Histology revealed thinning of the physis, indicating impaired growth. Serum biomarkers such as P1NP, osteocalcin, and CTX-1 showed reduced bone formation and resorption.

Conclusion: Integrating serum biomarkers and imaging assays with routine histopathology improves detection and characterization of skeletal toxicity. This multimodal approach enhances nonclinical safety assessments' sensitivity and supports including bone-specific endpoints in early toxicology studies.

Disclosure: A. Tuladhar: None; **C. Carter**: None; **E. Vaughan**: None; **m. j.voorbach**: None; **S. Biswas**: None; **T. Brayman**: None; **P. Kumar**: None; **a. marinopoulos**: None; **X. Huang**: None; **S. J. Finnema**: None; **R. Christmann**: None; **T. vanVleet**: None; **B. Enright**: None; **M. Guffroy**: None; **S. Fossey**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1785

Soluble CD14 Amplifies Chondrocyte Inflammatory Responses to Lipopolysaccharide and Is Targetable by Anti-CD14 Therapy

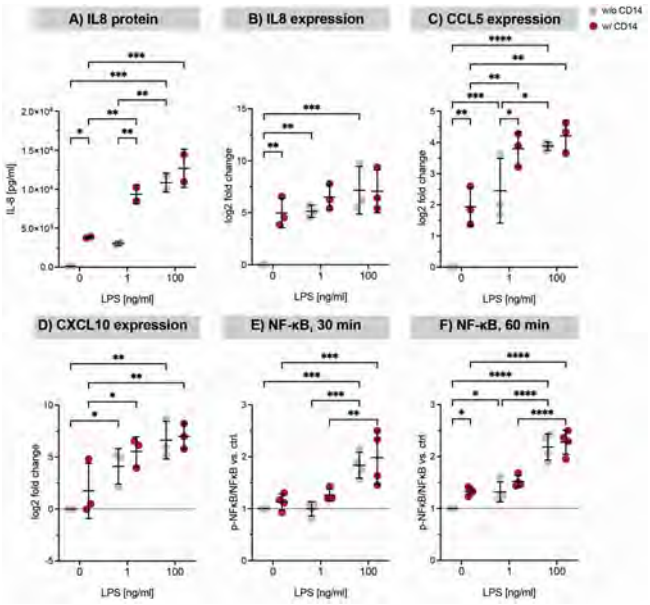
Anna Rapp[1], Kate Sharp[1], Baofeng Hu[2] and Carla Scanzello[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Wynnewood, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

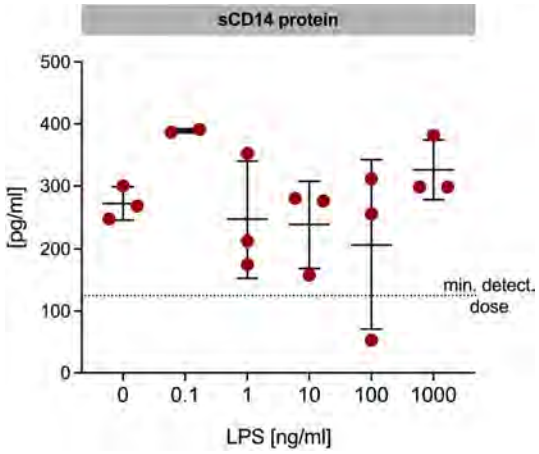
Background/Purpose: Osteoarthritis (OA) is characterized by a pro-inflammatory joint microenvironment, including elevated levels of endogenous pattern recognition receptor ligands in synovial fluid. Notably, both lipopolysaccharide (LPS) and its soluble co-receptor, soluble CD14 (sCD14), are increased in OA synovial fluid, and sCD14 levels correlate with disease severity. sCD14 facilitates LPS transfer to Toll-like receptor 4 (TLR4), potentiating immune responses to otherwise sub-threshold ligand levels. Although this mechanism has been demonstrated in myeloid cells and synovial fibroblasts, whether sCD14 can enhance LPS-driven inflammatory activation of human chondrocytes, at the low levels found in OA joints, remains unclear.

Methods: Primary human articular chondrocytes (hACs) were isolated from non-arthritic knee cartilage (obtained through the National Disease Research Interchange) and treated with LPS at OA-relevant (1 ng/mL) or supraphysiologic (100 ng/mL) concentrations, with or without sCD14 (2 μg/mL). NF-κB activation was assessed via Western blot, inflammatory gene expression by qPCR, and IL-8 and sCD14 secretion by ELISA (n=2–4). To assess CD14 dependency of the responses, C28/I2 chondrocytes (Merck) were treated with anti-CD14 antibody in parallel experiments.

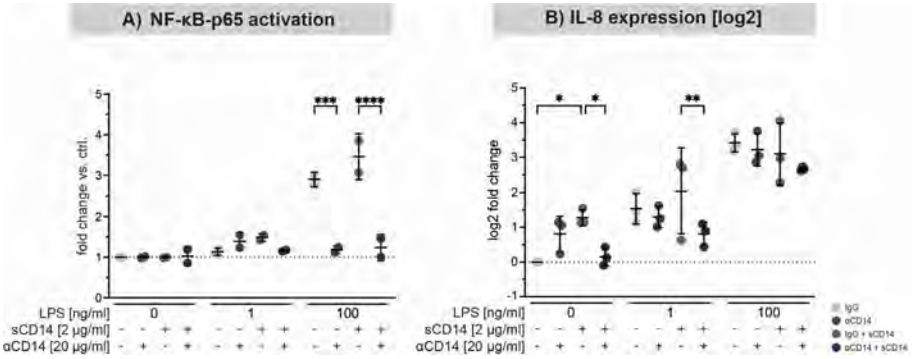


hAC were stimulated with 1 and 100 ng/ml LPS with and without 2 μg/ml sCD14. A) IL-8 secretion was determined by ELISA. Expression of B) IL-8, D) CCL5, and E) CXCL10 were determined by qPCR. Activation of NFkB-p65 was measured by western blot after E) 30 and F) 60 min. n= 2-4 donors, mean±SD. 2-way ANOVA and Tukey's post hoc.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



sCD14 was determined in supernatants form hAC stimulated with increasing LPS concentrations. n = 2-3 donors, mean±SD.



C28/I2 cells were stimulated with 1 and 100 ng/ml LPS±sCD14, with and without anti-CD14 (αCD14, clone 18D11). Anti-CD14 prevented A) NFκB activation by high-dose LPS independent of sCD14 (1h) and reduced the sCD14-dependent increase in B) IL-8 expression after low-dose LPS+sCD14 (24h). n= 2-3, mean±SD. 2-way ANOVA and Dunnett's multiple comparisons test.

Results: Disease-relevant concentrations of LPS (1 ng/mL) alone did not increase IL-8 secretion by hAC; however, co-treatment with sCD14 significantly elevated IL-8 protein levels compared to either condition alone (Fig. 1A). Expression of IL-8, CCL5, and CXCL10 was moderately increased with 1 ng/ml LPS, with trends toward enhancement by sCD14. In contrast, supraphysiologic LPS (100 ng/mL) induced robust inflammatory gene expression that was not further enhanced by sCD14, indicating a threshold effect (Fig. 1B-D). NF-κB activation was modestly affected by sCD14, suggesting involvement of additional signaling pathways (Fig. 1E, F). We further observed that chondrocytes did not secrete sCD14 under basal or LPS-stimulated conditions, supporting an exogenous origin of sCD14 (Fig. 2). Notably, sCD14 alone induced low-level inflammatory gene expression, suggesting it may function as a damage-associated molecular pattern in chondrocytes.

In a therapeutic approach, CD14 blockade abrogated NF-κB activation induced by high-dose LPS, regardless of sCD14 presence, but had no effect on IL-8 expression. Importantly, at the OA-relevant concentration of 1 ng/mL LPS, CD14 inhibition reversed the sCD14-mediated increase in IL-8, effectively dampening inflammation (Fig. 3A, B).

Conclusion: sCD14 enhances chondrocyte sensitivity to disease-relevant concentrations of LPS, promoting inflammatory activation in a CD14-dependent manner. These findings identify sCD14 as a potential amplifier of chondrocyte-inflammatory responses in OA and support the potential of CD14 blockade to mitigate low-grade inflammation in cartilage.

Disclosure: A. Rapp: None; **K. Sharp**: None; **B. Hu**: None; **C. Scanzello**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1786

SEV-101, A Regenerative Exosome Therapeutic for the Treatment of Osteoarthritis

Beth Lindborg[1], Amanda Vegoe[2], Michael Williams[1], Parthasarathy Rangarajan[3], Marc Tompkins[4], Sabarinathan Ramachandran[5] and Timothy O'Brien[6], [1]Sarcio, Inc., St. Paul, [2]Department of Veterinary Population Medicine and Stem Cell Institute, University of Minnesota, Sarcio, Inc, St. Paul, [3]Schulze Diabetes Institute, Department of Surgery, University of Minnesota, Minneapolis, [4]Department of Orthopedic Surgery, University of Minnesota, Sarcio, Inc., Minneapolis, [5]Schulze Diabetes Institute, Department of Surgery, University of Minnesota, Minneapolis, MN, [6]Department of Veterinary Population Medicine and Stem Cell Institute, University of Minnesota, Sarcio, Inc, Minneapolis

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is a chronic, debilitating joint disease affecting 595 million people worldwide, including over 32 million in the United States. It is characterized by progressive degeneration of articular cartilage, most commonly in the knees, hips, and hands. Risk increases with age, joint overuse, and obesity. Despite an annual economic burden of $550 billion in the US, no FDA approved disease-modifying osteoarthritis drugs (DMOADs) are currently available. In this study, we evaluate the therapeutic potential of SEV-101, a novel exosome-based treatment, to promote hyaline cartilage regeneration in weight-bearing regions of the knee in a rat model of OA.

Methods: SEV-101 is a novel exosome therapeutic isolated from induced pluripotent stem cell (iPSC)-derived cartilage tissue. To evaluate the efficacy of SEV-101 in regenerating hyaline cartilage, the rat monosodium iodoacetate (MIA) model of OA was utilized. On Day 1, animals received a unilateral intra-articular injection of MIA in the knee (femorotibial) joint.

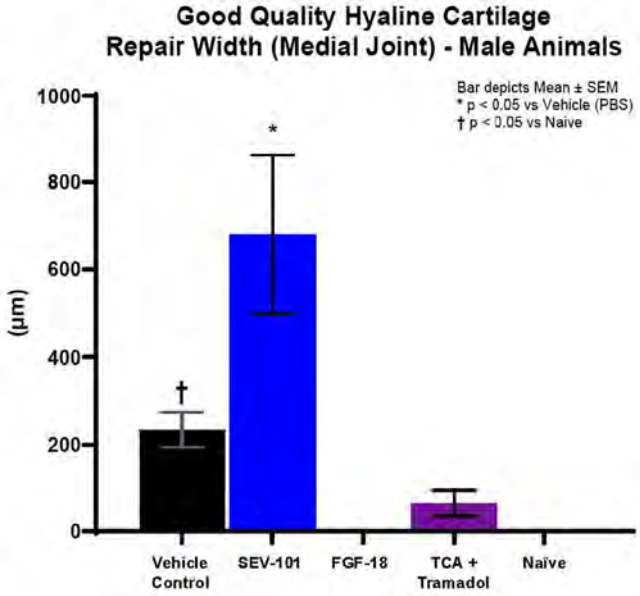


Figure 1. Good Quality Hyaline Cartilage Repair Width in the Medial (weight bearing) Knee Joint. Toluidine Blue Stained Histological sections of knee joints in male animals were assessed using the following criteria to ensure that regeneration, and not preservation was being measured: 1) the tidemark and corresponding bone/calcified cartilage had evidence of resorption, 2) the presence of proteoglycan (any degree of blue pigment) and/or chondrocytes within the intact pre-existing cartilage matrix, 3) had evidence of normal chondrocyte arrangement/maturation (does not have obvious features of fibrocartilage, such as elongate cellular morphology or streaming).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

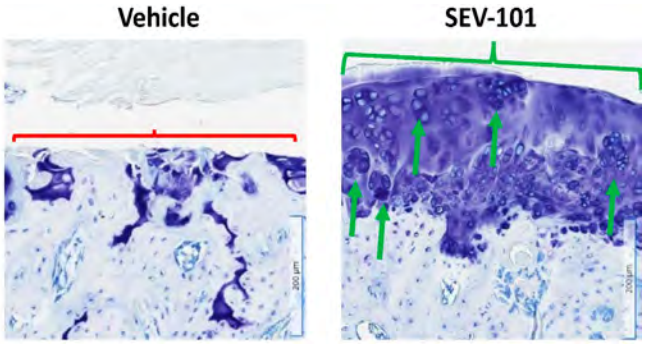


Figure 2. Histopathology of the medial compartment of male right stifle (knee) joints stained with toluidine blue. Vehicle control animals showed extensive loss of articular cartilage (red bracket delineates affected areas) with minimal regeneration of articular cartilage evident. SEV-101 treated animals showed prominent regions of articular hyaline cartilage regeneration (green bracket delineates this region and green arrows indicate chondrogenic clusters forming hyaline cartilage).

Treatment began on Day 4 and was administered once per week for 10 weeks. Animals were randomized into four treatment groups (7 males, 7 females per group) and one naïve control group (5 males, 5 females). SEV-101 was dosed at 2.2 × 10^{11} exosomes. Phosphate-buffered saline served as a vehicle control. FGF-18 was used as a positive control as it has been shown to promote cartilage regeneration. A standard-of-care positive control for pain included intra-articular triamcinolone and oral tramadol. In-life assessments included safety monitoring and Dynamic Weight Bearing (DWB) analysis. Animals were sacrificed on Day 72, and joints underwent histological evaluation, including quantitative analysis of hyaline cartilage regeneration in the medial joint compartment. Rigorous criteria included presence of tidemark and bone resorption, in addition to other measurements that ensured that the cartilage being measured was new, good quality hyaline cartilage.

Results: No safety signals were observed in SEV-101 treated rats. SEV-101 treated male rats showed a statistically significant increase in regeneration of hyaline articular cartilage in weight-bearing regions of the knee joint (designated as "good quality hyaline cartilage") compared to all other treatment groups. In addition, SEV-101 treated male rats showed more intact meniscus structure and more Type 2 Collagen immunohistochemical staining compared to vehicle controls. There was no significant difference in DWB vehicle controls and SEV-101 treated animals.

Conclusion: SEV-101 promoted the regeneration of new hyaline cartilage rather than merely preserving existing cartilage. Additionally, SEV-101-treated animals exhibited improved meniscal integrity and increased Type II Collagen staining relative to vehicle controls. These findings support SEV-101's capacity to regenerate cartilage in weight-bearing regions of the joint and to confer structural protection, reducing the risk of further degeneration. Collectively, these data strongly support the continued development of SEV-101 as a DMOAD.

Disclosure: B. Lindborg: Sarcio, Inc., 12,, 4, 8, 10, 11; **A. Vegoe**: Sarcio, Inc., 12,, 4, 8, 10, 11; **M. Williams**: Sarcio, Inc., 12,, 4, 8, 11; **P. Rangarajan**: Sarcio, Inc., 5; **M. Tompkins**: Sarcio, Inc., 12,, 4, 11; **S. Ramachandran**: Sarcio Inc, 5; **T. O'Brien**: Sarcio, Inc., 12,, 4, 8, 10, 11.

Abstract Number: 1787

Spatial and Quantitative Semiautomated Image Analysis of Synovial Biopsies Studied Using a Novel High-Plex Immunofluorescence Platform

Estefania Quesada-Masachs[1], Luis Peñaranda Bolaño[1], Aakriti Arora[2], Jessica Murillo-Saich[3], Edward Lo[4], Tad George[4], Daniel Tanoeihusada[4], Sara McArdle[5] and Monica Guma[6], [1]University of Miami, Miami, FL, [2]University of Miami / Jackson Memorial Hospital, Miami, FL, [3]University of California, San Diego, San Diego, CA, [4]RareCyte, Seattle, WA, [5]La Jolla Institute for Immunology, La Jolla, CA, [6]University of California San Diego, San Diego, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Although not part of the formal ACR criteria for RA, PsA, or OA, synovial pathology can be a helpful tool in clinical practice. Histopathologic evaluation in RA has led to the development of a synovitis score and a joint pathology algorithm. Three synovial pathotypes—lympho-myeloid, diffuse-myeloid, and pauci-immune—have been described, but are based on a limited number of markers and currently provide limited clinical information. Recent advances allow for minimally invasive synovial biopsies and multiplex microscopy to provide mechanistic insights into tissue pathology. This is especially relevant as targeted therapies for OA are still lacking. Artificial intelligence (AI) enables detailed image analysis, preserving spatial context, allowing for single-cell quantification and identification of cellular interactions that may inform therapy and predict response. Our objective was to apply a novel high-plex IF platform coupled with a semi-automated image analysis approach using machine learning algorithms to characterize synovial inflammatory infiltrates in patients with PsA, RA, and OA

Methods: FFPE synovial tissue biopsies from nine patients from patients with RA (n=5), OA (n=2), and PsA (n=2) were stained with a 17-marker IF panel targeting nuclei, CD31, CD68, CD163, CD20, CD4, CD8a, CD45RO, PD-L1, CD3e, Ki-67, PD-1, FOXP3, CD45, Pan-CK, vimentin, and SMA. Some RA and PsA samples had prior classification (lymphoid or lympho-myeloid) based on conventional IF/IHC staining. Whole sections were scanned at 20x using the Orion platform.A semi-automated AI pipeline originally developed for pancreatic tissue was adapted to synovial tissue. Regions of interest (ROIs, lining and sublining) were selected. Cell classification was based on fluorescence intensity and morphology. Spatial context and cellular neighborhoods were also analyzed using unsupervised clustering algorithms

Results: Nine synovial biopsies from five male and five female (mean age 59.1 years, SD10.1) with a total of 105,364 cells across 130 ROIs were analyzed over 23.7 mm^2 of tissue. Cellular density was higher in the lining (mean 10,461 cells/mm^2) than in the sublining (mean 5,017 cells/mm^2). As expected, OA showed fewer immune cells, fibroblasts, and vessels than RA and PsA. Macrophage and fibroblast predominance was observed across all samples, especially in immune-mediated arthritis. In RA, T cell infiltration was more abundant in the sublining, and proportions of T cell subsets were similar across knees and wrists. Distinct cellular clusters were identified in the unsupervised analysis, differentiating between diseases

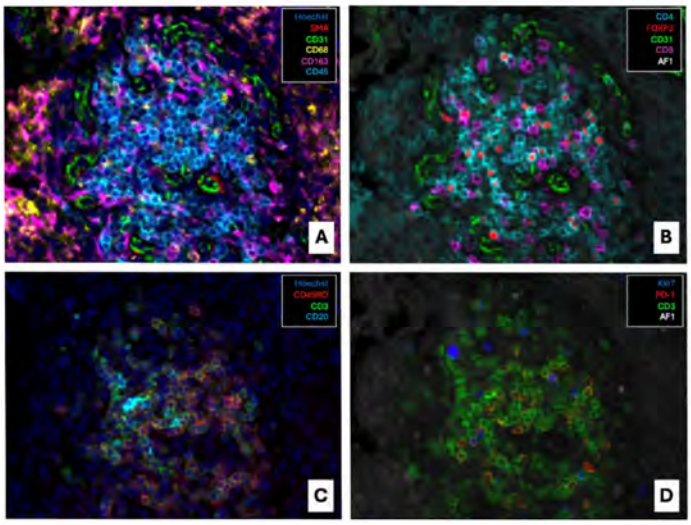


Figure 1: Synovial tissue biopsy from knee of a patient with PsA. A, B, C, D show different combinations of markers to visualize different immune infiltrates within the same tissue region. A high level of definition for different immune cell types is displayed in the images acquired at 20x with Orion slide scanner. **A.** Macrophages (magenta & yellow) surround a lymphocyte cluster (cyan), CD31 highlights endothelium (green) surrounded by SMA (red). **B.** Nuclear FOXP3 (Treg, red) is expressed by a subset of CD4+ T cells. **C.** A subset of T cells display memory phenotype (CD45RO (red) is visualized in yellow/orange after combining with CD3 (green)), B cells (cyan) present in lymphoid cluster. **D.** A subset of T cells co-express PD-1 (red), proliferating cells (Ki67+, blue nuclei)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: These preliminary findings support the suitability of this new high-plex microscopy technology and AI-driven image analysis in assessing synovial inflammation. Despite limited tissue, we achieved robust, high-resolution profiling of thousands of cells. We envision that this type of data may help create algorithms in joint pathology to further aid in patient management. Novel platforms currently restricted to research can be incorporated into the clinical arena to serve as a diagnostic tool as well as a personalized treatment tool based on a patient's specific histological characteristics

Disclosure: E. Quesada-Masachs: None; **L. Peñaranda Bolaño**: None; **A. Arora**: None; **J. Murillo-Saich**: None; **E. Lo**: Rarecyte, 3; **T. George**: RareCyte, 3; **D. Tanoeihusada**: RareCyte, 3; **S. McArdle**: None; **M. Guma**: AbbVie, 5, Sonoma, 5.

Abstract Number: 1788

Manganese-associated Single-nucleotide Polymorphisms are Associated with Radiographic Knee Osteoarthritis: The Johnston County Osteoarthritis Project

Griffin Sonaty[1], Carolina Alvarez[2], Liubov Arbeeva[3], Joanne Jordan[1], Brian Diekman[4], Doug Phanstiel[1], Richard Loeser[5] and Amanda Nelson[1], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]University of North Carolina, Chapel Hill, Carrboro, NC, [4]Univesity of North Carolina at Chapel Hill, Chapel Hill, NC, [5]University of North Carolina, Chapel Hill, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Trace elements may be differentially associated with osteoarthritis (OA) risk. Single-nucleotide polymorphisms (SNPs) have been found to correlate to cumulative exposure level, free of temporal effects. The purpose of this study was to identify whether SNPs known to be associated with the body concentration of certain trace elements were associated with OA development in a prospective cohort and then explore functional consequences (Figure 1).

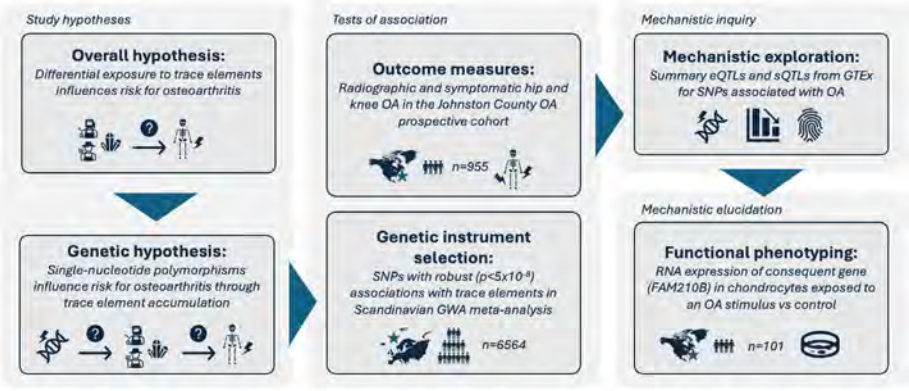


Figure 1. Study overview from conception to mechanistic elucidation in four stages: hypothesis generation, tests of association with primary outcome and genetic instruments, exploration of genetic consequences (expression and splicing quantitative trait loci, eQTL and sQTL, respectively) from a large database (Adult Genotype Tissue Expression Project, GTEx), and functional outcomes on consequent genes in an OA chondrocyte model. GWA, genome-wide association; OA, osteoarthritis; SNP, single-nucleotide polymorphism.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This was a cross-sectional analysis from the second follow-up visit (2006-11) of the Johnston County Osteoarthritis Project, a prospective population-based cohort designed to evaluate risk factors for development of OA. This analysis was limited to White participants with toenail metals data, as exposure SNPs were selected from those with robust ($p < 5x10^{-8}$) associations with trace element body concentration in a Scandinavian population (PMID: 38594418). Radiographic knee (rKOA) and hip (rHOA) OA were defined by Kellgren-Lawrence (K/L) grade ≥ 2 on bilateral posteroanterior knee or hip radiograph, respectively, at any point throughout follow-up. Symptomatic OA (sOA) consisted of radiographic OA with pain in the same joint. Linear regression of each SNP variant with natural log-transformed toenail metal concentrations was assessed before performing logistic regression for OA outcomes and each SNP, metal, and their interaction as predictors, providing odds ratio [OR]; 95% confidence interval [CI]) if interaction p-value< 0.1. Each model was adjusted for age, sex, body mass index (BMI), smoking, and alcohol use. A functional study was then conducted for a novel impacted gene (FAM210B) in a previously described chondrocyte OA model (PMID: 33248223).

Results: Among 955 White adults (mean age 66 ± 11, mean BMI 30 ± 6 kg/m^2, 38% male), 42% had rKOA and 30% had rHOA. There were no associations between toenail metal concentrations of selenium, mercury, chromium, scandium, zinc, iron, or cadmium with selected SNPs. However, SNPs previously linked to decreased manganese concentration including *rs6099115* and *rs855791* were associated with rOA, but not sOA. In multivariable regression, both heterozygous and

Table 1. Adjusted associations, odds ratio (95% CI), between SNPs and OA outcomes.

	Outcome			
SNPs	*Knee rOA*	*Hip rOA*	*Knee SOA*	*Hip SOA*
rs6099115				
homozygous unaffected	1 (reference)	1 (reference)	1 (reference)	1 (reference)
heterozygous	**2.66 (1.01, 7.05)**	0.96 (0.40, 2.29)	1.28 (0.43, 3.77)	1.04 (0.29, 3.77)
homozygous affected	**3.05 (1.18, 7.90)**	0.95 (0.41, 2.20)	1.61 (0.63, 5.18)	1.11 (0.32, 3.87)
rs855791				
homozygous unaffected	1 (reference)	1 (reference)	1 (reference)	1 (reference)
heterozygous	0.72 (0.49, 1.05)	1.01 (0.69, 1.49)	0.71 (0.47, 1.07)	0.70 (0.40, 1.22)
homozygous affected	0.73 (0.48, 1.10)	1.27 (0.83, 1.92)	0.87 (0.56, 1.35)	1.21 (0.68, 2.13)

Logistic regression modeling log odds of OA outcome and its association with each SNP variant and toenail metal. Shown **BOLD** when significant at 0.05 level. Each model includes covariables for age, sex, BMI, past/current smoking, alcohol use, and SNP variant. rOA, radiographic osteoarthritis; SOA, symptomatic osteoarthritis; SNP, single-nucleotide polymorphism.

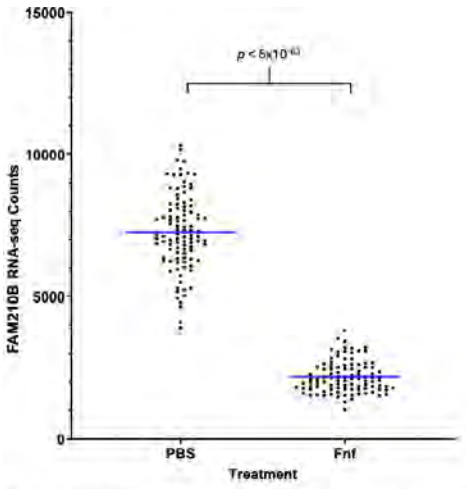


Figure 2. FAM210B expression is significantly decreased in chondrocytes responding to an OA stimulus. RNA-sequence counts of FAM210B in paired donor chondrocytes treated with fibronectin fragments (Fnf) [OA model] vs phosphate-buffered saline (PBS) [control].

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

homozygous variants of *rs6099115* were associated with increased odds of rKOA (OR 2.66; 95% CI 1.01, 7.05 and 3.05; 1.18, 7.90, respectively, Table 1). Homozygous affected variant *rs855791* was associated with increased odds of rKOA only when toenail levels of chromium or iron were increased (OR 1.62; 1.13, 2.31, and 1.53; 1.07, 2.18, respectively). Variants in *rs855791* result in missense mutations in transmembrane protease serine 6 (TMPRSS6), involved in extracellular matrix degradation and hepcidin regulation. Variants in *rs6099115* result in missense mutations of FAM210B, a mitochondrial membrane transporter involved in cellular response to iron, estradiol, and cell differentiation. In a chondrocyte OA model, FAM210B expression was decreased by 69.2%, $p < 5x10^{-63}$ (Figure 2).

Conclusion: Two novel associations were identified, linking risk of rOA with SNPs known to be associated with decreased manganese concentrations, with functional consequences in FAM210B. Further investigation in the roles of FAM210B and TMPRSS6 in the pathogenesis of OA is needed.

Disclosure: G. Sonaty: None; **C. Alvarez**: None; **L. Arbeeva**: None; **J. Jordan**: None; **B. Diekman**: None; **D. Phanstiel**: None; **R. Loeser**: None; **A. Nelson**: Novo Nordisk, 1.

Abstract Number: 1789

Spatial Analysis of Advanced Osteoarthritis Synovial Tissue

jacob Dickman[1], Stephanie Ruzicka[1], Holub Meaghan[2], Jutras Brandon[3], Adam Edelstein[3] and Robert Lochhead[4], [1]Medical College of Wisconsin, Milwaukee, WI, [2]Central Michigan University College of Medicine, Mount Pleasant, MI, [3]Northwestern University, Chicago, IL, [4]Medical College of Wisconsin, GERMANTOWN, WI

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is a joint pathology involving joint cartilage destruction and synovial inflammation. Severe knee OA is often surgically treated with total knee arthroplasty (TKA) joint replacement. Approximately 20% of patients experience continued pain and dysfunction postoperatively, but no predictors of outcome are known. We previously reported that bacterial peptidoglycan (PG) is associated with increased synovitis and elevated IL-6. However, PG did not correlate with patient reported outcomes (PRO) post-TKA, indicating other immune mediators may be contributing to surgical outcome. We therefore used highly multiplexed cell imaging to identify cell-cell interactions associated with incomplete responses to surgery and other disease features.

Table 1: Patient Data.

Patient Diagnosis (sample n)	Median Age (min – max)	Median BMI	KOOS JR Pre-operative Average (St. Dev)	KOOS JR 12 months post-TKA Average (St. Dev)
Osteoarthritis (OA) (20)	67 (52-85)	31.8	39.9 (15.6)	79.5 (13.0)
Inflammatory Arthritis (2)	29 (29-48)	22.9	41.9 (15.0)	75.0 (35.3)
Revision due to Infection (1)	NA	NA	NA	NA
All Patients (23)	66 (29-85)	31.6	40.1 (15.2)	79.0 (15.1)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Discarded synovial tissue (ST) were collected from 23 patients undergoing primary TKA, 20 (87%) of which met ACR criteria for knee OA (Table 1). Knee Osteoarthritis Outcome Score – Joint Replacement (KOOS JR) PRO were collected at pre-operative and 3-, 6-, and 12-month post-operative time points. Multiplexed immunofluorescence microscopy (Akoya Biosciences) was used to identify T cells (CD3, CD4, CD8), antigen presenting cells (HLA-DR, CD11c), endothelial cells (CD31), plasma cells (CD138), and stromal cells (CD90, CD34) in synovial tissue. Cell-cell distance was calculated to infer cell interaction using the Scimap Python package. For the patients with advanced knee OA, associations between spatial

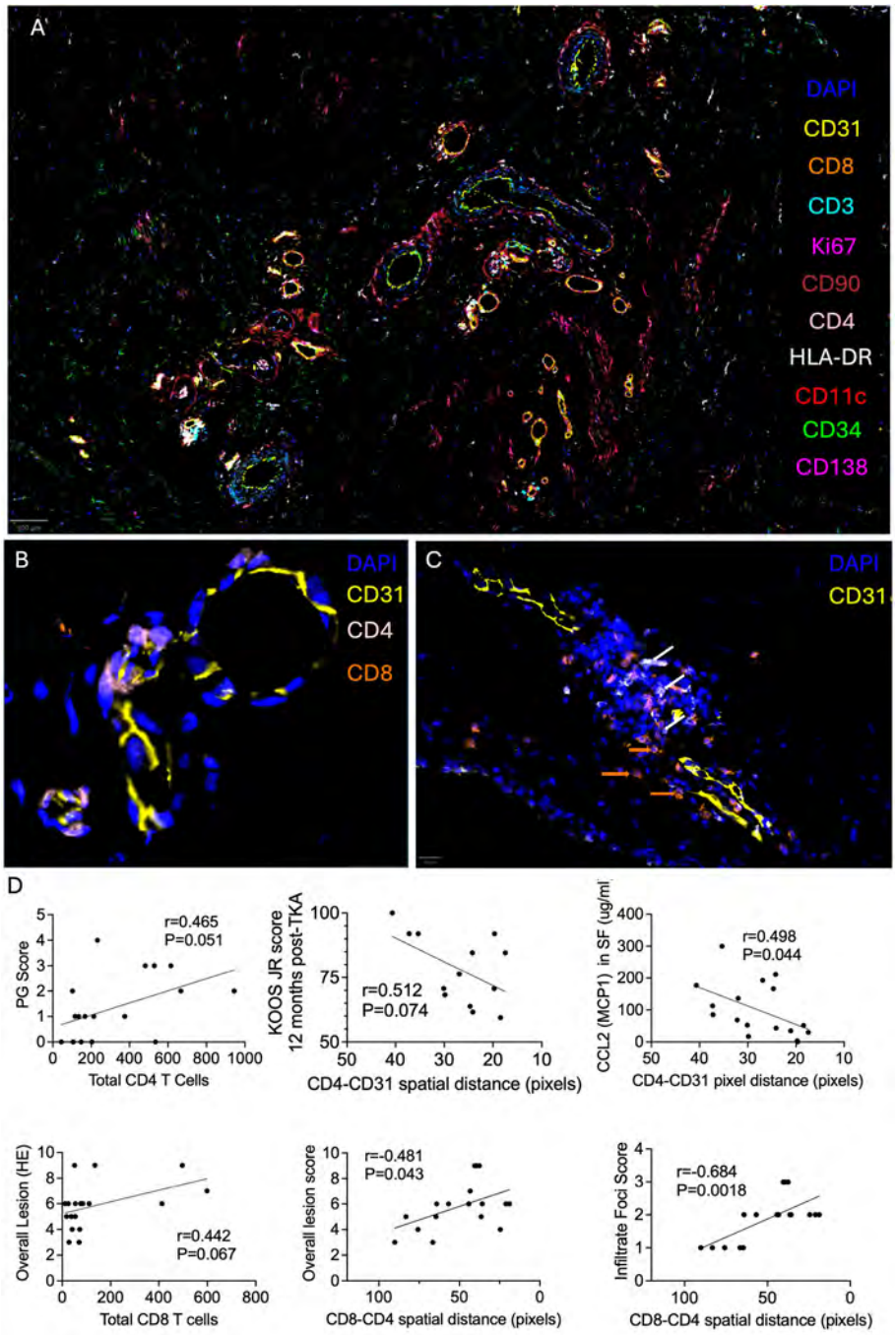


Figure 1. Spatial imaging analysis of advanced OA synovial tissue. (A) Representative images are shown of OA synovial tissue is shown using cell markers indicated in figure; (B) a representative image of CD4 T cells in close proximity to CD31+ endothelial cells; (C) and a representative image of typical inflammatory foci containing CD4 and CD8 T cells. (D) Associations between total T cell numbers and cell-cell spatial distances with disease features. Pearson's R and P values are indicated in figure. For spatial distance analyses, only OA synovial tissue were included, and spatial distance is shown in pixels (1 pixel≅2 μm).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

imaging data and disease features, including PRO scores, were determined by calculating Pearson's r correlation coefficients using Prism software (v.10).

Results: Patient synovitis was highly variable, consisting of infiltrate-rich inflammatory foci and/or regions of vascular inflammation and fibrosis (Fig 1A). Vascular lesions typically contained CD4+ T cells near CD31+ endothelial cells (Fig 1B). Inflammatory foci were enriched in both CD4+ T cells and CD8+ T cells (Fig 1C). Total CD4+ T cells correlated with PG in tissue, whereas total CD8+ T cells correlated with overall synovial lesion score (Fig 1D). CD4-CD31 spatial distance tended to be shortest in patients with low/variable PRO score 12 months post-TKA (Pearson's r=0.512, P=0.074), whereas CD8-CD4 spatial distance was associated with inflammatory synovitis.

Conclusion: Spatial imaging of advanced OA ST revealed an important role in T cells in contributing to synovitis. In our cohort, average distances between CD4+ T-helper cells and CD31+ endothelial cells in ST at time of surgery correlated with low 12-month PRO score, suggesting that vascular inflammation in OA synovitis may contribute to poor or variable long-term outcome post-TKA.

Disclosure: j. Dickman: None; **S. Ruzicka**: None; **H. Meaghan**: None; **J. Brandon**: None; **A. Edelstein**: None; **R. Lochhead**: None.

Abstract Number: 1790

Targeted Ablation of Knee-innervating Nociceptors Attenuates Pain and Cartilage Degeneration in Experimental Osteoarthritis

Lai Wang[1], alia obeidat[2], Shingo Ishihara[3], Jun Li[2], Frank Ko[2], Terese Geraghty[2], Natalie Adamczyk[3], Sarah Soorya[2], Richard Miller[4], Rachel Miller[1] and Anne-Marie Malfait[2], [1]Rush University Medical Center, Chicago, IL, [2]Rush University Medical Center, Chicago, [3]Rush University, Chicago, [4]Northwestern University, Chicago

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Nociceptors abundantly innervate the knee joint. In experimental osteoarthritis (OA), nociceptors sprout in the medial synovium and in subchondral bone channels. We aimed to determine the effect of selective ablation of knee-innervating nociceptors in murine OA.

Methods: Adeno-associated virus AAV.PHP.S carrying diphtheria toxin A (dtA) (AAV-dtA) or control AAV (AAV-Ctrl) was injected intra-articularly (i.a.) into the knee cavity of 7-week old male $Na_V1.8$-Cre mice. Destabilization of the medial meniscus (DMM) or sham surgery were performed 3 weeks later. Pain-related behaviors (weight bearing and knee hyperalgesia) were assessed up to 16 weeks after surgery. Knee joints were collected for histology, microCT, innervation analysis, and protein antibody array. Lumbar dorsal root ganglia (DRG) were collected for immunofluorescence staining or qPCR analysis.

Results: Injection of AAV-dtA effectively ablated joint nociceptors. This had no effect on knee hyperalgesia but attenuated weight bearing deficits (Fig. 1A-B), with decreased *Ccl2* in DRG (Fig. 1C). AAV-dtA administration suppressed nociceptor sprouting in subchondral bone channels (Fig. 1D), but not in the medial synovium (Fig. 1E). Marked cartilage damage observed in AAV-Ctrl injected joints was attenuated in AAV-dtA injected mice (Fig. 2A), while synovitis, osteophytes, and microCT of the subchondral bone were similar in both groups. Knee joint lysates showed lower levels of calcitonin gene-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

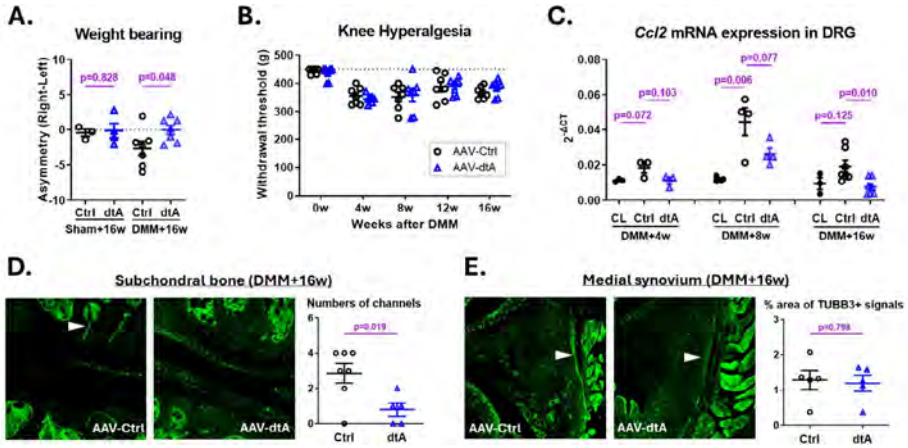


Fig. 1. Pain behavioral tests and knee joint innervation analysis in DMM mice with IA NaV1.8+ neuron ablation. (A) Weight bearing tests. (B) Knee hyperalgesia tests. (C) Expression of pro-algesic Ccl2 mRNA in ipsilateral L3-L5 DRG. (D, E) Nerve sprouting in subchondral bone (D) and medial synovium (E) was analyzed with IF staining of a pan-neuronal marker TUBB3.

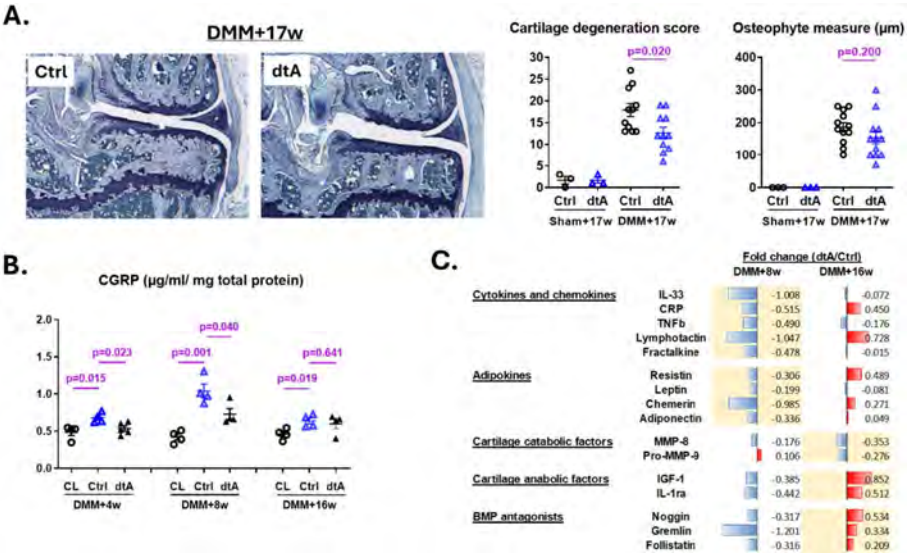


Fig. 2. Knee joint histopathological analysis and joint lysate protein analysis of DMM mice with intra-articular NaV1.8+ neuron ablation. (A) Representative images of medial compartments of mouse knee sections stained with toluidine blue. Cartilage degeneration and osteophyte formation were evaluated using a modified OARSI scoring system. (B) ELISA assay of CGRP protein in DMM knee joint lysates. (C) Antibody arrays of DMM knee joint lysates (Quantibody® Mouse Cytokine Antibody Array, RayBiotech).

related peptide (CGRP) 4 and 8 weeks after DMM in AAV-dtA injected mice (Fig. 2B), as well as decreased pro-inflammatory factors 8 weeks after DMM and increased levels of cartilage-anabolic markers 16 weeks after DMM (Fig. 2C). CGRP+ neurons were also decreased in ipsilateral lumbar DRGs, along with reduced $Na_V1.8$+ neurons after ablation.

Conclusion: Knee-innervating nociceptor ablation before DMM attenuated weight bearing asymmetry, subchondral bone nerve sprouting, and cartilage degeneration. Cartilage anabolic factors were increased in the joints, while CGRP levels were decreased. The neurogenic contribution to OA may result from the neuropeptides released from nerve endings in early stages of OA.

Disclosure: L. Wang: None; **a. obeidat**: None; **S. Ishihara**: None; **J. Li**: None; **F. Ko**: None; **T. Geraghty**: None; **N. Adamczyk**: None; **S. Soorya**: None; **R. Miller**: None; **R. Miller**: None; **A. Malfait**: Asahi Kasei Pharma Corporation, 23andMe, Orion, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1791

Determining the Effect of CD14 Deficiency on Osteoblastogenesis and Subchondral Bone Remodeling In Mice

Kate Sharp[1], **Lance Murphy**[2], Vu Nguyen[3], Baofeng Hu[4] and Carla Scanzello[5], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, [3]University of Pennsylvania, Phildealphia, [4]University of Pennsylvania, Wynnewood, PA, [5]University of Pennsylvania, Philadelphia

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is a debilitating disease affecting ~54% of US adults 75 and older. Toll-like receptor 4 (TLR4), and its co-receptor CD14, have been implicated in disease severity and progression. CD14 sensitizes TLR4 to low concentrations of its ligands, including ligand lipopolysaccharide (LPS). Osteoblasts (OB) from the mesenchymal cell (MSC) lineage are not known to express significant levels of CD14 but do express TLR4. As a result, the role of CD14 on OB differentiation has not been fully elucidated. However, the response of OB to LPS has been reported to be multi-faceted and dependent on LPS concentration; the effect may be stimulatory at low concentrations and inhibitory at high concentrations. **With this, we aimed to identify the effect of CD14 deficiency on bone remodeling in a murine model of OA in vivo and characterize the effect of low-level, OA-relevant LPS stimulation in vitro**.

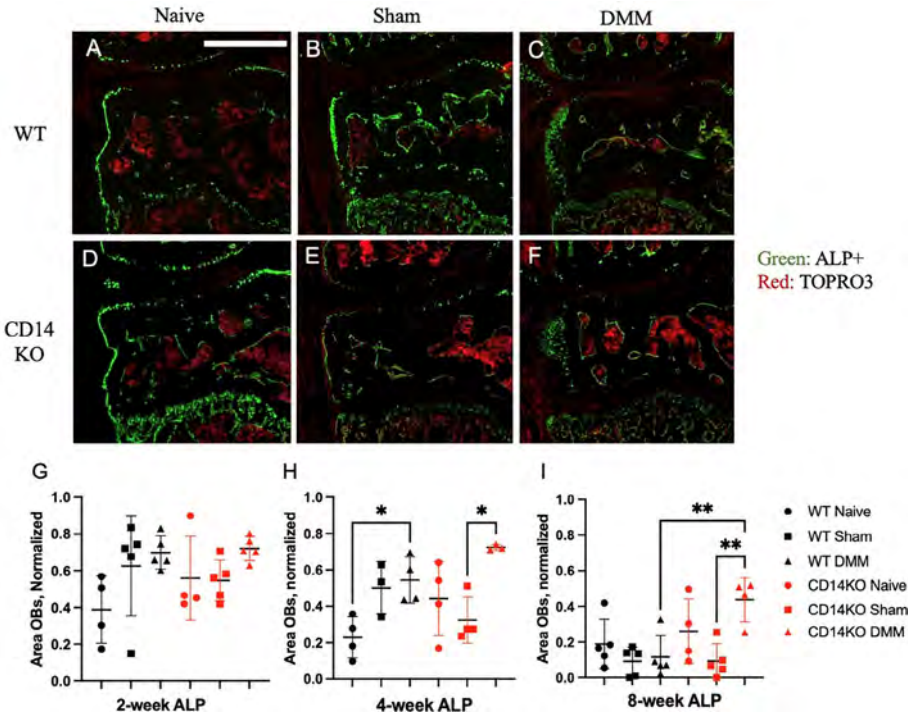


Figure 1: (A-F) Representative images of in vivo ALP activity 4-wks post-surgery. (A) WT Naïve, (B) WT Sham, (C) WT DMM, (D) CD14KO Naïve, (E) CD14KO Sham, (F) CD14KO DMM. (G, H, I) 2, 4, and 8-wk quantification of OB area in the medial subchondral bone region normalized to trabecular area. *p<0.05, scale bar = 500 μm.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

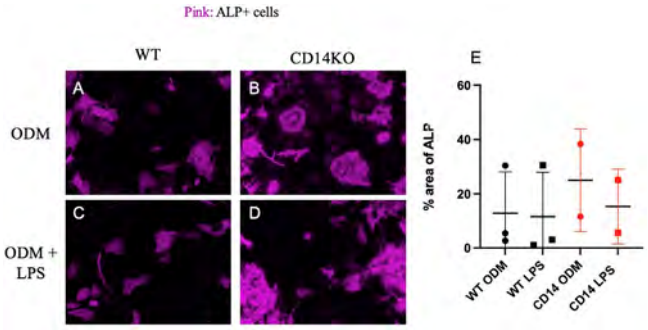


Figure 2: (A-D) Representative images of in vitro ALP activity after 14 days in cell culture imaged in the Cy5 fluorescent channel at 10x. (A) WT MSCs cultured with ODM. (B) CD14KO MSCs cultured with ODM. (C) WT MSCs treated with ODM + 1 ng/mL of LPS. (D) CD14KO MSCs treated with ODM + LPS. (E) Quantification of % area of ALP normalized by total area.

Methods: We first performed destabilization of the medial meniscus (DMM) or sham surgery on 4-5 C57BL/6 (WT) and CD14KO male mice at 12 wks of age. After 2-, 4-, and 8-wks post-surgery, the knees were processed and stained for alkaline phosphatase (ALP) using ELF 97 fluorescent substrate followed by TOPRO3 nuclear counterstaining. Area of ALP+ staining in the medial tibial subchondral area was quantified and normalized to overall trabecular area. *In vitro*, MSCs were harvested from 5-7 WT and CD14KO male mice at 12 wks of age. Upon confluency, cells were passaged and cultured for 14d with osteogenic differentiation media (ODM □ MEM + 10% FBS + ascorbic acid + □-glycerophosphate) with or without 1 ng/mL of LPS. After 14d, the cells were stained for ALP and imaged at 10x. Percent area of ALP (+) staining was quantified via Cell Profiler.

Results: Fig. 1A-F depicts representative sections from naïve, sham, and DMM-operated WT and CD14KO mice stained for ALP. At 2wks ALP activity seemed to be increased in the surgical groups of both strains,but no significance differences were observed (**Fig. 1G**) At 4wks, the area of ALP was increased in both the WT and CD14KO DMM groups compared to either naïve (WT) or sham (CD14KO) controls (**Fig 1H**). By 8 wks, there was no difference between WT DMM and WT control groups (**Fig 1I**). However, ALP+ area remained elevated in the CD14KO DMM group compared to both sham controls, and the WT DMM group (**Fig 1I**). *In vitro* staining for ALP revealed no significant difference between strains, with or without LPS both qualitatively (**Fig. 2A-D**) and quantitatively (**Fig 2E**).

Conclusion: In conclusion, our findings suggest OB density is increased in the remodeling subchondral bone post-DMM injury, and the response of WT and CD14KO mice is similar up to 4 wks. However, by 8 wks, ALP activity in WT DMM mice decreased back to baseline, but remained elevated in the DMM-injured CD14KO mice, suggesting prolonged or delayed OB-genesis in response to DMM in CD14KO mice. Thus far, our *in vitro* experiments did not reveal an inherent defect in osteoblast differentiation evaluated by ALP staining between strains, either in the presence or absence of low concentrations of LPS. Future experiments will more fully characterize the effects of LPS dosage and of related gene expression to determine whether OB differentiation or activity is altered on WT and CD14KO mice.

Disclosure: K. Sharp: None; **L. Murphy**: None; **V. Nguyen**: None; **B. Hu**: None; **C. Scanzello**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1792

OA protection in African spiny (*Acomys*) mice is partially mediated by the gut microbiome and is transferrable to wild-type mice via microbiome transplantation

Gabriella Dyson[1], Montana Barrett[1], Nicholas Hanebutt[1], Aleksander Szymczak[2], Cindy Miranda Brawner[1], Pratibha Dube[3], Padmaja Mehta-d'Souza[1], Ashley Siefert[4] and **Matlock Jeffries**[2], [1]Oklahoma Medical Research Foundation, Oklahoma City, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Oklahoma Medical Research Foundation, Edmond, OK, [4]University of Kentucky, Lexington, KY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Mounting evidence suggests that gut microbiome shifts may be associated with knee osteoarthritis (OA) development. We have previously shown that gut microbiome transplantation from OA-resistant MRL/MpJ mice into OA-susceptible B6 mice results in robust protection against OA development. In the present study, we evaluated genus *Acomys* (African spiny mice), also previously shown to be resistant to OA.

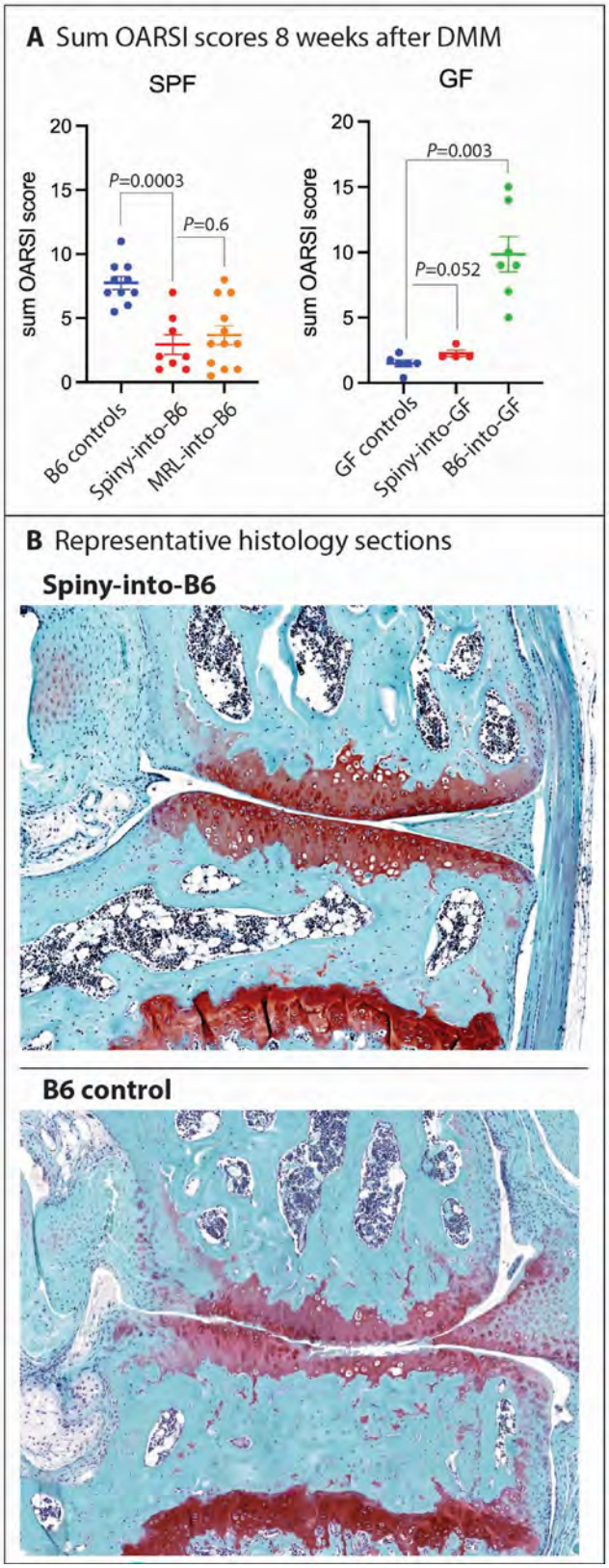
Methods: Fresh frozen cecal content from 7 adult male spiny mice was obtained from the University of Kentucky colony (Dr. Seifert). Under sterile conditions, cecal content was diluted in 200uL of 50:50 sterile glycerol and PBS then transplanted via oral gavage into n=8 11-week-old B6 non-Germ-free (SPF) male mice and n=4 11-week-old C57BL6 (B6) Germ-free (GF) male mice in the OMRF gnotobiotic facility. One week later, unilateral destabilization of the medial meniscus (DMM) surgery was performed. Control groups included n=7 B6-SPF-microbiota-into-male GF mice, n=10 male B6-SPF mice, and n=6 male B6-GF mice. Mice were euthanized 8 weeks after DMM and submitted for OARSI histopathologic scoring. For microbiome analysis, cecal DNA was extracted, 16S rRNA gene amplification done, initial analysis performed via QIIME2 amplicon v.2024-10, aligned to the GreenGenes2 reference tree, and differential microbiome analysis performed using Maaslin2 (v.1.16.0). We also analyzed similarities to our previous histologic and microbiome studies of the OA-protected MRL/MpJ mouse strain (n=5 SPF MRL-into-B6 GF, n=12 SPF MRL-into-B6).

Results: Gut microbiome transplantation from spiny mice to SPF B6 mice prior to DMM surgery resulted in substantial protection from histologic OA development (spiny-into-B6 2.9±0.8 vs. B6 control 7.8±0.5, mean summed OARSI score±SEM, P=0.0003, **Figure 1A, 1B**). We then confirmed this finding by transplanting gut microbial content from spiny mice to GF B6 mice (ordinarily OA protected), where spiny transplantation induced mild OA susceptibility, whereas wild-type B6 cecal transplant did induce OA susceptibility (spiny-into-GF 2.3±0.3, GF control 1.5±0.3, B6-into-GF 11.2±0.9, P=0.053 spiny-into-GF vs. GF control, P=0.003 spiny-into-GF vs. B6-into-GF). In microbiome analysis, substantial differences were present between spiny mice and B6 mice (n=75 differences, q≤0.05). These differences were substantially similar to our previously published MRL-into-B6 transplantation experiments (n=29 in current reanalysis), **Figure 2**. Indeed, 13 of these microbiome clades were shared in both comparisons, and 11 were similar in direction and magnitude of change (increased in MRL were all increased in spiny and vice-versa).

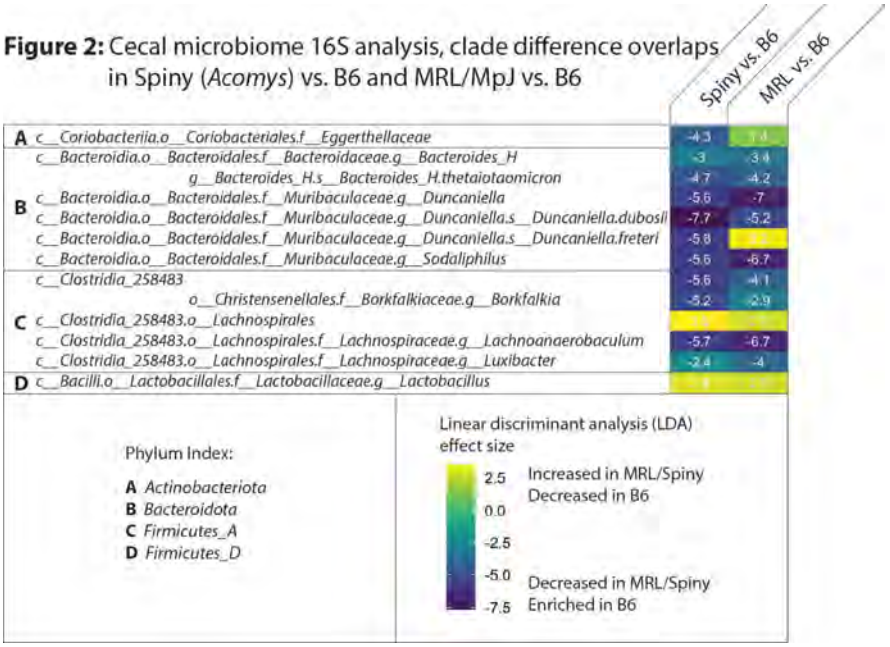
Conclusion: The gut microbiome of OA-protected spiny mice confers OA protection in wild-type mice following microbiome transplantation. Microbiome differences in spiny mice are largely similar to previous studies of another OA protected strain, MRL/MpJ. Future work should evaluate whether spiny mouse microbiome transplantation also confers OA pain/behavioral protection and the degree to which individual microbiome species contribute to these findings.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Histologic OA outcomes following microbiome transplantation and DMM



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: G. Dyson: None; **M. Barrett**: None; **N. Hanebutt**: None; **A. Szymczak**: None; **C. Miranda Brawner**: None; **P. Dube**: None; **P. Mehta-d'Souza**: None; **A. Siefert**: None; **M. Jeffries**: Being Inc., 1.

Abstract Number: 1793

Sex-associated changes to synovial macrophages in the aging joint

Matthew Dapas[1], Erica De Jong[2], Yidan Wang[3], Cally Mills[3], Samuel Dowling[4], Tyler Therron[5], Carla Marie Cuda[3], Dawn Bowdish[6] and Deborah Rachelle Winter[7], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]McMaster Immunology Research Centre, Hamilton, ON, Canada, [3]Northwestern University, Chicago, IL, [4]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [5]Northwestern Feinberg School of Medicine, Chicago, IL, [6]McMaster University, Hamilton, ON, Canada, [7]Northwestern University, Skokie, IL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Macrophages are found in nearly every tissue of the body where they maintain homeostasis and drive healthy immune response. However, macrophages are dysregulated with age and have been found to play a role in many age-associated diseases, such as arthritis. We hypothesized that macrophage dysregulation in aging stems from an increased contribution of infiltrating monocytes that have been reprogrammed by the aging environment of the bone marrow in a manner that prevents them from fully recapitulating the tissue-resident macrophage phenotype. To test this hypothesis, we are investigating aging macrophages in the murine joint synovium using functional genomic approaches.

Methods: We compared synovial macrophage composition and transcriptional profiles in young vs. aged joints from male and female mice using single-cell RNA sequencing with cell-surface protein detection (CITE-seq).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We identified both conserved age-related changes and those that differed between sexes. Among synovial macrophages, we observed significant ($p < 0.0001$) expansion of infiltrating Ly6C+ monocytes/macrophages in both males and females (8.0% vs. 2.1%, and 9.5% vs. 2.3%, respectively) and significant reductions in the proportion of CXCR1+ lining macrophages (35.6% vs. 29.8%, and 32.4% vs. 24.9%, respectively). In females, there were significantly more MHCII+ macrophages in aged mice (17.3% vs. 12.9%) and no statistical difference in osteoclast precursors (5.8% vs. 5.3%), but in males there were significantly fewer MHCII+ macrophages in aged mice (11.3% vs. 14.7%) and significantly more osteoclast precursors (7.6% vs. 4.6%). Pseudotime analysis revealed four diverging trajectories of differentiation from infiltrating Ly6C+ monocytes/macrophages to CXCR1+ lining macrophages, AQP1+ interstitial macrophages, RELM-α+ interstitial macrophages, and osteoclast precursors, respectively, with fewer early-stage interstitial cells observed in aged mice. Total inter-macrophage heterogeneity was significantly greater in aged vs. young mice in females ($p < 0.0001$), but not statistically different in males. Overall, age-associated gene expression changes were not highly correlated between sexes, with mean fold-change correlations ranging from r=-0.065 in MHCII+ macrophages to r=0.23 in interstitial macrophages. Significantly enriched pathways included upregulated electron transport chain signaling in interstitial macrophages in both sexes and downregulated EGFR signaling in osteoclast precursors in females.

Conclusion: We find that monocyte-derived synovial macrophages are increased in the aging joint and synovial macrophages exhibit decreased expression of homeostatic genes. Our results provide insights on how macrophage programming changes with age and the impact on tissue health. This study will inform efforts to boost immune system function in aging.

Disclosure: M. Dapas: None; **E. De Jong**: None; **Y. Wang**: None; **C. Mills**: None; **S. Dowling**: None; **T. Therron**: None; **C. Cuda**: None; **D. Bowdish**: None; **D. Winter**: None.

Abstract Number: 1794

OA-associated pain sensitivity is reduced in OA-protected MRL/MpJ mice, partially mediated by the gut microbiome, and transferable via microbiome transplantation

Gabriella Dyson[1], **Montana Barrett**[1], Nicholas Hanebutt[1], Aleksander Szymczak[2], Cindy Miranda Brawner[1], Pratibha Dube[3], Ausitn Lopez[1], Padmaja Mehta-d'Souza[1] and Matlock Jeffries[2], [1]Oklahoma Medical Research Foundation, Oklahoma City, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Oklahoma Medical Research Foundation, Edmond, OK

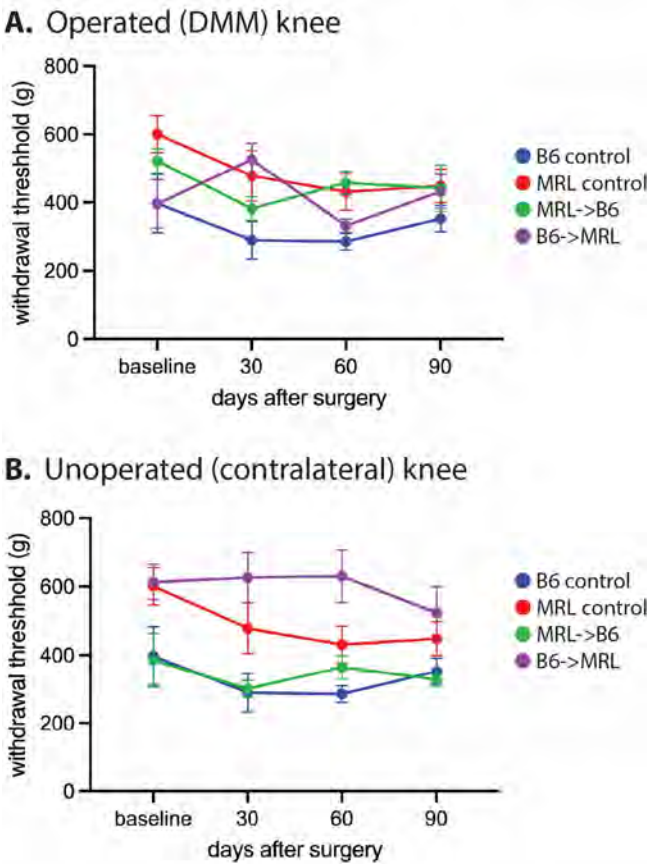
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: MRL/MpJ (MRL) mice are protected from developing post-traumatic osteoarthritis (OA) histologic changes. We have previously shown the gut microbiome to play a key role in mediating this OA protection, wherein microbiome transplantation from MRL mice to B6 mice can prevent OA. The goal of the present study was to examine the effects of microbiome manipulation on OA-associated pain in MRL and wild-type C57BL/6 (B6) mice.

Methods: Young adult male B6 or MRL mice (11 weeks of age) underwent one-time microbiome transplantation via oral gavage of 200uL of diluted cecal contents from adult reciprocal-strain animals (n=6 MRL-into-B6, n=6 B6-into-MRL), or 200uL control solution (n=6 MRL, n=6 B6). One week later, unilateral destabilization of the medial meniscus (DMM) surgery

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Pain sensitivity (withdrawal) thresholds by microbiome transpl. group



was used to induce OA. Pain sensitivity thresholds were measured via small animal algometry of the operated and contralateral knees prior to intervention (10 weeks of age). Algometry data were collected every 4 weeks until euthanasia 12 weeks after DMM.

Results: There were no differences at baseline in pain sensitivity, although there was a trend towards lower pain sensitivity in MRL animals at all timepoints (P=0.073 at baseline, P=0.069 at 4 weeks, P=0.033 at 8 weeks, P=0.16 at 12 weeks). At 4 weeks after DMM, MRL-into-B6 transplanted mice had substantially reduced pain sensitivity compared to B6 controls (P=0.0090), which was lost at later timepoints (P=0.17 at 8 weeks, P=0.23 at 12 weeks, **Figure 1**). B6-into-MRL transplantation did not alter pain sensitivity in MRL recipient mice at any timepoint. In the contralateral (unoperated) knee, we found MRL mice to have reduced pain sensitivity at all timepoints. MRL-into-B6 transplantation reduced pain sensitivity at 4 weeks (P=0.015) and 12 weeks (P=0.032). B6-into-MRL transplantation increased pain sensitivity at 4 weeks (P=0.012). Correlation of gut microbiome changes with pain sensitivity is ongoing.

Conclusion: Knee pain sensitivity is reduced in OA-protected MRL mice compared to wild-type B6 mice and is partially mediated by the gut microbiome, although the effects of a single timepoint microbiome manipulation are lost at timepoints beyond 4 weeks post-DMM. Future studies should investigate whether sustained changes in pain sensitivity could be seen with repeated microbiome manipulation, and whether OA-associated behavioral changes are similarly mitigated with microbiome manipulation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Dyson: None; **M. Barrett**: None; **N. Hanebutt**: None; **A. Szymczak**: None; **C. Miranda Brawner**: None; **P. Dube**: None; **A. Lopez**: None; **P. Mehta-d'Souza**: None; **M. Jeffries**: Being Inc., 1.

Abstract Number: 1795

Trends and Disparities in Osteoarthritis-Related Mortality in the United States: A 21-Year Analysis (1999-2020)

muzamil Khan[1], Swetha Balaji[2], Ayesha Cheema[3], Wajdan Ahmad[3], Dhruv gandhi[4] and Steven Golombek[5], [1]George Washington University School of Medicine and Health Sciences, Washington D.C, [2]New York Medical College at St. Mary's General Hospital and St. Clare's Health, Parsippany-Troy Hills, NJ, [3]Al Tibri Medical College, Karachi, Pakistan, [4]St. Francis Medical Center, Monroe, [5]NYMC at St. Mary's General Hospital and St. Clare's Health, Dover

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis/arthrosis is an aging-related disease which is associated with significant morbidity in the United States. However, epidemiological data regarding osteoarthritis-associated mortality in the United States (US) remains scarce. The aim of this study is to determine trends and disparities in osteoarthritis-related mortality in the US between 1999 and 2020.

Methods: A retrospective analysis was conducted using the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research database. The age-adjusted mortality rates (AAMR) and crude death rates per 100,000 persons were determined. The average annual percentage change (AAPC) was calculated through Joinpoint regression analysis. The results were compared to determine temporal trends in sex, race, geographical distribution and patient age-related mortality in osteoarthritis patients.

Results: Between 1999 and 2020, 277,211 deaths occurred in osteoarthritis patients aged 45 years and above. Majority of the patients had died within nursing homes/long-term care facilities (47.38%). The AAMR reduced from 15.5 in 1999 to 6.52 in 2020 with an AAPC of -4.52% (p< 0.0001). Females were disproportionately affected with higher AAMR (12.04) compared to males (8.27), although their AAPCs were nearly similar (-4.36% vs. -4.39%, respectively). Racial differences persisted with non-Hispanic (NH) White having the highest AAMR (11.43) followed by NH Black/African American (9.52), NH American Indian/Alaskan Native (7.53), Hispanic/Latino (5.73) and NH Asian/Pacific Islander (4.24). Between 1999-2020, Hispanic/Latino showed the greater overall decline in osteoarthritis-related mortality (AAPC of -5.16%; p< 0.0001) while

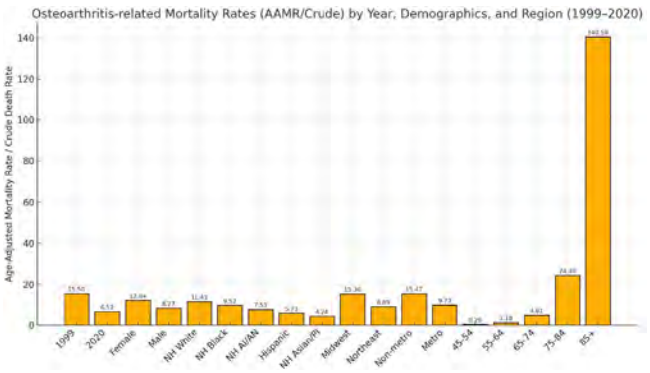


Image 1: Osteoarthritis related Age-Adjusted Mortality Rate (AAMR)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

American Indian/Alaskan Natives showed the least decline (AAPC of -3.88%; p< 0.0001). Geographically, the Midwest had the highest AAMR (15.36) while the Northeast had the lowest (8.89). The decline in osteoarthritis-related mortality was nearly similar between the various census regions (AAPC: -4.25% to -4.34%). States with the highest AAMRs included Nebraska, Ohio, West Virginia, Vermont, and South Dakota. Residents of non-metropolitan areas showed a higher AAMR (15.47) compared to metropolitan areas (9.73). Age-stratification into 10-year age groups showed a consistent increase in the crude death rate with age (from 0.29 in 45-54 years to 140.58 in those older than 85 years). The decline in osteoarthritis-related mortality between 1999-2020 was seen in all age-groups with the greatest overall decline seen in the 75-84 years age group (AAPC:-4.56%; p< 0.0001) followed closely by the 85+ age group (AAPC:-4.45%; p< 0.0001).

Conclusion: Over the past two decades, osteoarthritis-related mortality in the US has significantly declined, with notable disparities across sex, race, geographic location, and age. Females, non-Hispanic Whites, residents of the Midwest, and those in non-metropolitan areas had higher mortality rates. These findings emphasize the need for targeted interventions to address disparities and further reduce mortality.

Disclosure: m. Khan: None; **S. Balaji**: None; **A. Cheema**: None; **W. Ahmad**: None; **D. gandhi**: None; **S. Golombek**: None.

Abstract Number: 1796

Multi-Tissue Molecular and Histopathological Profiling of Facet Joints and Intervertebral Discs

Nashrah Ahmad[1], Lisa Janssen[1], Hannah Swahn[2], Rachel Miller[3], Anne-Marie Malfait[4], Merissa Olmer[5] and Martin Lotz[6], [1]Scripps Research, San Diego, CA, [2]Scripps Research Institute, Carlsbad, CA, [3]Rush University Medical Center, Chicago, IL, [4]Rush University, Oak Park, IL, [5]Scripps Research Institute, La Jolla, CA, [6]Scripps Research, La Jolla, CA

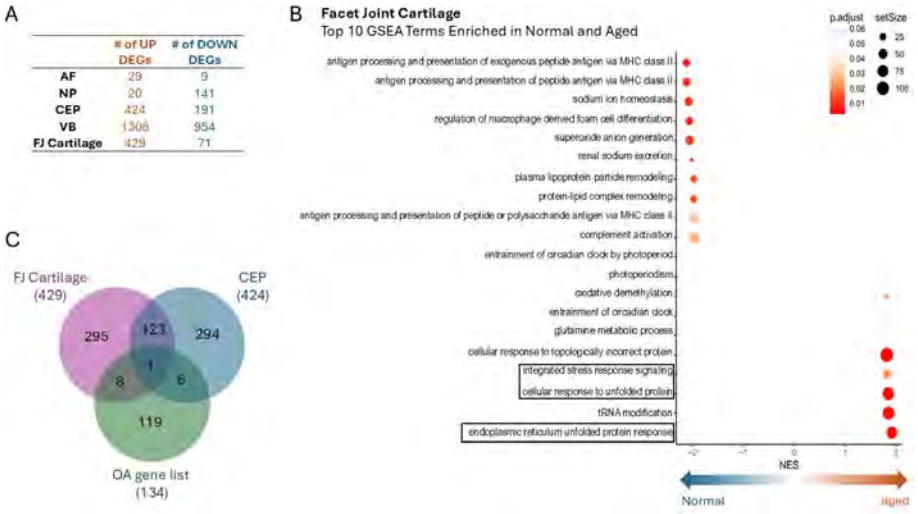
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Intervertebral disc (IVD) degeneration and facet joint (FJ) osteoarthritis (OA) often co-exist, and both are major contributors to lower back pain (LBP). Despite their clinical relevance, the shared mechanisms of tissue damage in these anatomically and functionally linked tissues remain poorly understood. The objective of this study was to perform histological analyses and omics profiling of FJs and IVDs from the same young and aged human donors. Data were analyzed for molecular and cellular alterations linked to tissue damage and LBP.

Methods: IVDs and FJs were harvested from the L3/L4 of 5 young, healthy (aged 23-37) and 10 aged (aged 67–81) donors. IVD and FJ sections were stained with Safranin O and histologically graded using the Thompson system for nucleus pulposus (NP), annulus fibrosus (AF), vertebral body (VB), and cartilaginous end plate (CEP) and OARSI systems for FJ sections. Bulk RNA sequencing was performed on all tissues using SMARTseq.

Results: Histological grading revealed significantly higher overall scores in IVDs from aged donors as compared to normal donors. Sub-compartment scores of VB, NP, AF, and CEP were also elevated in the aged group. Similarly, OARSI scores were significantly higher in FJ cartilage from aged donors compared to young healthy. Transcriptomic analysis identified 38, 161, 615, 2262, and 500 differentially expressed genes (DEGs) in AF, NP, CEP, VB, and FJ, respectively **(A)**. Gene Set Enrichment Analysis (GSEA) revealed upregulation of cartilage and bone development pathways, along with extracellular

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



(A) Differentially expressed genes (DEGs) identified as upregulated or downregulated in nucleus pulposus (NP), annulus fibrosus (AF), vertebral body (VB), cartilage endplate (CEP), and facet joint (FJ) cartilage. (B) Gene set enrichment analysis (GSEA) highlighting the top 10 enriched pathways in normal versus aged FJ cartilage. (C) Venn diagram illustrating the overlap of DEGs among CEP, FJ cartilage, and a curated osteoarthritis (OA) gene set.

matrix (ECM) remodeling in aged AF. In aged NP, ER-associated degradation (ERAD) and unfolded protein response (UPR) pathways were prominently enriched. GSEA in degenerated CEP highlighted enrichment of stress responses and hypoxia-related pathways. In VB, pathways related to oxygen transport, adipogenesis, and neurovascular regulation were enriched. In FJ cartilage, GSEA revealed upregulation of UPR, integrated stress response, and circadian rhythm pathways **(B)**. Notably, stress responses and UPR pathways were consistently upregulated across degenerated NP, CEP, and FJ (highlighted in **B**). Additionally, we investigated the molecular overlap between knee OA pathways and spine degeneration by assessing whether OA-associated genes identified in knee articular cartilage were upregulated in the cartilaginous components of the spine specifically, the CEP and FJ cartilage **(C)**. While transcriptomic profiles of CEP and FJ cartilage showed considerable similarity to each other, overlap with the knee OA gene set was limited, with only 6–8 of the 134 OA-associated genes commonly upregulated. KCNN4, upregulated across CEP, FJ, and OA gene sets, is linked to cartilage homeostasis and mechanotransduction.

Conclusion: The strong correlation between IVD and FJ degeneration, along with shared upregulation of stress-related pathways particularly the UPR and integrated stress response suggests common molecular mechanisms driving IVD and FJ degeneration. These findings highlight the importance of targeting cellular stress response and UPR pathways to develop more effective, system-level therapeutic strategies to address structural damage to IVD and FJ and associated LBP.

Disclosure: N. Ahmad: None; **L. Janssen**: None; **H. Swahn**: None; **R. Miller**: None; **A. Malfait**: Eli Lilly, 5, Merck, 2, Novartis, 2, Orion, 5, Roivant, 2; **M. Olmer**: None; **M. Lotz**: Blackbird, 2.

Abstract Number: 1797

SEV 101 Exosomes Isolated from Induced Pluripotent Stem Cell Derived Hyaline Cartilage Tissue Characterization of Immunomodulatory and Chondroproliferative Effects In Vitro

Parthasarathy Rangarajan[1], Beth Lindborg[2], Amanda Vegoe[3], Yi Wen Chai[4], Anna Tran[1], Magie Steinhoff[1], Bernhard Hering[1], Timothy O'Brien[5] and Sabarinathan Ramachandran[6], [1]Schulze Diabetes Institute, Department of Surgery, University of Minnesota, Minneapolis, [2]Sarcio, Inc., St. Paul, [3]Department of Veterinary Population Medicine and Stem

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cell Institute, University of Minnesota, Sarcio, Inc, St. Paul, [4]Stem Cell Institute, University of Minnesota, Minneapolis, [5]Department of Veterinary Population Medicine and Stem Cell Institute, University of Minnesota, Sarcio, Inc, Minneapolis, [6]Schulze Diabetes Institute, Department of Surgery, University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: SEV-101 are exosomes that are isolated from cultures of Induced Pluripotent Stem Cell (iPSC)-derived hyaline cartilage tissue. Gene expression profiles of the tissue are consistent with early hyaline cartilage development. Given that the biological effects of exosomes tend to parallel those of the cells from which they were derived, we hypothesize that SEV-101 which is secreted from iPSC-derived hyaline cartilage tissue, could deliver effective regenerative cues for cartilage regeneration in addition to factors that promote anti-inflammatory activities.

Methods: Exosomes in iPSC-derived hyaline cartilage tissue culture medium were isolated through a series of centrifugation steps followed by ultracentrifugation. Particle concentration and size distribution was characterized utilizing Nanosight. Mixed Lymphocyte Reaction (MLR) cultures of human Peripheral Blood Mononuclear Cells (PBMCs) were performed in the presence of SEV-101 from multiple batches, and the results were analyzed using multiparametric flow cytometry to asses regulatory T cell populations, including Tregs and Tr1cells. Additionally, activation markers such as CD69 were evaluated to quantify activated Tregs and Tr1 cells. Proliferation of chondrocytes in the presence of SEV-101 were detected via Ki-67 based assays and colony formation assays. Preliminary proteomics was performed by mass spectrometry.

Results: SEV-101 contained high levels of anti-inflammatory molecules such as CD9 and CD81 compared to the exosomes isolated from undifferentiated iPSC culture medium. SEV-101 effectively reversed TNFa-induced inflammation in PBMCs. Treatment with SEV-101 increased the frequency of $CD4^+FoxP3^+$ regulatory T cells (Tregs) by 1.3- to 2.03-fold and $CD49b^+LAG\text{-}3^+$ Tr1 cells by 1.33- to 3.34-fold. Furthermore, the proportion of $CD69^+$ T cells, including $CD69^+$ Tregs and $CD69^+$ Tr1 cells-was significantly elevated in human MLR cultures treated with SEV-101. CD69+ T cells can induce indoleamine 2,3-dioxygenase in OA models and down-regulate inflammatory immune responses. Ki-67-based proliferation and colony formation assays demonstrated that SEV-101 induces chondrocyte proliferation by 82.18 to 96.29 fold. Preliminary proteomics showed the presence of pro-regenerative and anti-inflammatory proteins.

Conclusion: SEV-101 exhibits potent anti-inflammatory and chondro-regenerative properties in vitro, indicating its potential as a disease-modifying agent for the treatment of osteoarthritis.

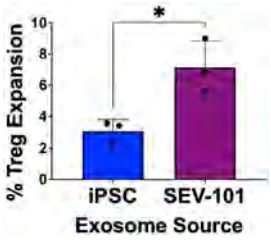


Figure 1. SEV-101 increase proliferation of Treg cells. Flow cytometric analysis of peripheral blood mononuclear cells treated with 100 μg of SEV-101 exosomes showed a significant ($P<0.0196$) increase in the expansion of CD4+ CD25+ FoxP3+ Tregs compared to iPSC exosome treated controls. Each data point represents the mean ± SD of three independent experiments and were analyzed with a student's t-test (*$P<0.05$).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

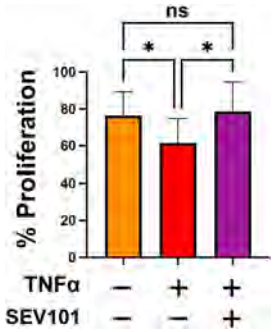


Figure 2. SEV-101 exosomes increase proliferation of chondrocytes. Treatment with 50μg SEV-101 results in significant reversal of TNF- mediated inhibition in the proliferation of chondrocytes when compared to untreated controls. Each data point represents the mean ± SD of 4 independent experiments and were analyzed with a student's t-test (*P<0.05, nsP>0.05)

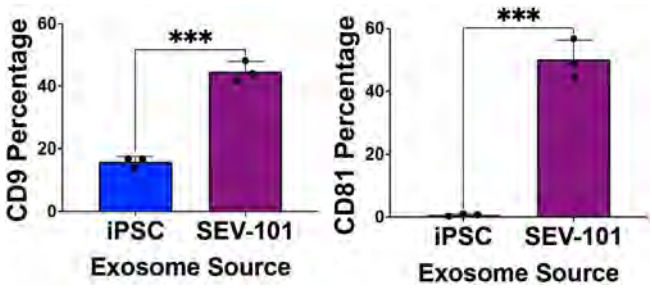


Figure 3. Immunoinhibitory receptors in SEV-301 exosomes. SEV-101 shows a significant level of expression of anti-inflammatory markers CD9 and CD81 when compared to the exosomes from iPSC culture media. Each data point represents the mean ± SD of 3 independent experiments and were analyzed with a student's t-test (***P<0.001).

Disclosure: P. Rangarajan: Sarcio, Inc., 5; **B. Lindborg**: Sarcio, Inc., 12,, 4, 8, 10, 11; **A. Vegoe**: Sarcio, Inc., 12,, 4, 8, 10, 11; **Y. Chai**: Sarcio, Inc., 11; **A. Tran**: None; **M. Steinhoff**: None; **B. Hering**: None; **T. O'Brien**: Sarcio, Inc., 12,, 4, 8, 10, 11; **S. Ramachandran**: Sarcio Inc, 5.

Abstract Number: 1798

Proteomic Profiling of Chondrogenic Gene Therapy in Human MSCs Reveals Distinct Regenerative Pathways for Articular Cartilage Repair

Patricia Quaranta[1], Jagadeesh K Venkatesan[2], Valentina Calamia[3], Patricia Fernández-Puente[4], francisco J Blanco[5], Magali Cucchiarini[2] and Cristina Ruiz-Romero[6], [1]Instituto de Investigacion Biomedica de A Coruna (INIBIC), coruna, Spain, [2]Center of Experimental Orthopaedics, Saarland University and Saarland University Medical Center, Homburg, Germany, [3]INIBIC, A Coruña, Spain, [4]Instituto de Investigacion Biomedica de A Coruna (INIBIC), coruña, Spain, [5]INIBIC-University of A Coruña, A Coruña, Galicia, Spain, [6]Department of Rheumatology, Rheumatology Research Group (GIR) Biomedical Re-search Institute (INIBIC),, A Coruña, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatic diseases are characterized by pain and a progressive loss of joint function. Classical treatments alleviate pain symptoms but fail to fully repair sites of articular cartilage damage. Gene therapy for rheumatic diseases aims to deliver gene-based treatments into the joint space, resulting in a localized, controlled, and long-term

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

therapeutic effect to protect and regenerate damaged cartilage. Recombinant adeno-associated viral (rAAV) vectors are the only class of vectors currently available that allow for both an effective, direct, and prolonged gene transfer to articular cartilage *in vivo*. This study aims to characterize the proteomic changes induced by gene therapy on human mesenchymal stromal cells (MSCs) derived from patients with osteoarthritis (OA). The goal is to gain insights into the underlying pathways and mechanisms involved, and to explore their potential roles in cartilage regeneration

Methods: Different chondrogenic factors (IGF-I, FGF-2, TGF-β, SOX9, and reporter *lacZ* as the control) were delivered using rAAV vectors for hMSC-based gene therapy. hMSC cultures were transduced with the rAAV and maintained for 21 days in a defined chondrogenic medium. Proteomic profiling of the micromasses was performed using high resolution mass spectrometry (TimsTOF-Pro, Bruker). Differential expression analysis was conducted using protein-wise linear models combined with empirical Bayes statistics (adjusted p-value < 0.05 and log2 fold change ≥0.5)

Results: Proteomic analysis was performed on 25 micromass samples (five samples for each chondrogenic factor and control). A total of 3,565 proteins (with >1 unique peptides) were identified in the micromass proteome (Fig. 1). Subsequent data analysis revealed 139, 100, 150, and 230 proteins that were significantly differentially expressed under IGF-I, FGF-2, TGF-β, and SOX9 conditions, respectively. The growth factors IGF-I, FGF-2, and TGF-β shared 16 significant proteins related to metabolic processes and intracellular protein transport (Fig. 2). IGF-I and TGF-β shared 25 proteins related to RHO GTPase effectors and asparagine N-linked glycosylation. IGF-I and FGF-2 shared 22 proteins related to carbohydrate catabolism and translation, while FGF-2 and TGF-β shared 12 proteins involved in membrane trafficking. SOX9 exhibited minimal overlap with the other factors and had 219 uniquely significant proteins associated with ossification, neutrophil degranulation, and extracellular matrix (ECM) components such as glycoproteins, collagens, and proteoglycans. TGF-β modulated

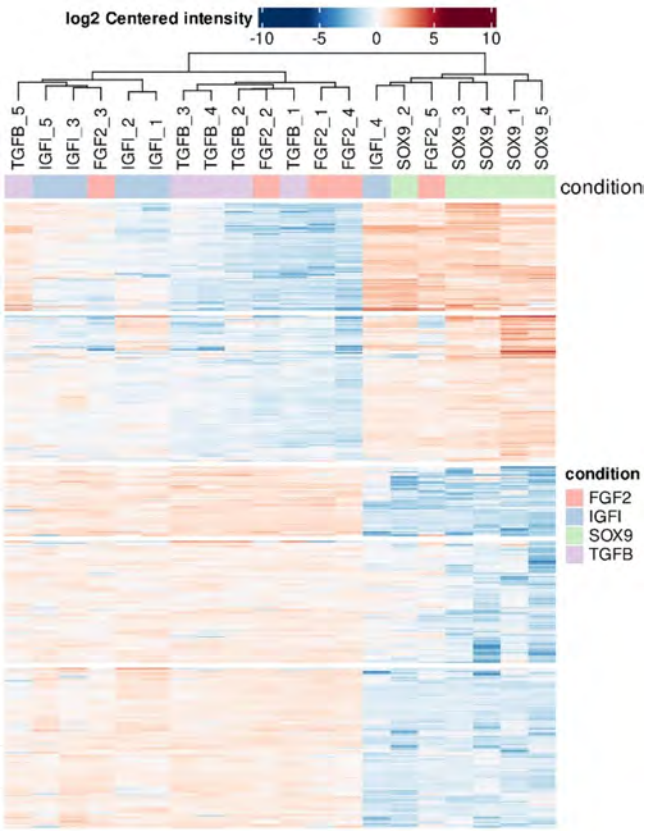


Figure 1. Heatmap showing the differential proteomic profiles induced in hMSCs following gene therapy treatment with various chondrogenic factors. Five independent experiments are displayed, with lacZ used as the control.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

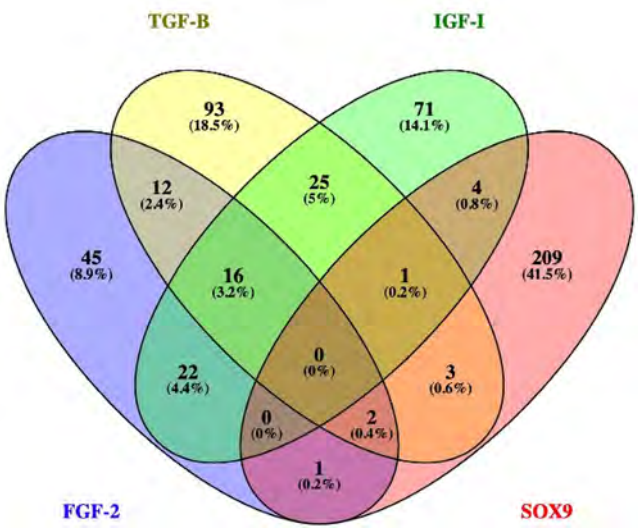


Figure 2. Venn diagram of significant proteins, illustrating the number of unique and shared proteins altered in response to each chondrogenic factor.

93 exclusive proteins linked to VEGFA-VEGFR2 signalling and proteolysis. IGF-I uniquely affected 71 proteins involved in intracellular EGF-EGFR signalling and metabolism. Finally, FGF-2 was characterized by 45 unique proteins associated with ECM glycoproteins and lipid metabolism

Conclusion: This study provides valuable data supporting the use of gene therapy with chondrogenic factors as a promising strategy for cartilage regeneration. The identification of key proteins involved in cartilage repair and regeneration pathways highlights the therapeutic potential of this approach for the treatment of articular cartilage diseases

Disclosure: P. Quaranta: None; **J. Venkatesan**: None; **V. Calamia**: None; **P. Fernández-Puente**: None; **f. Blanco**: None; **M. Cucchiarini**: None; **C. Ruiz-Romero**: None.

Abstract Number: 1799

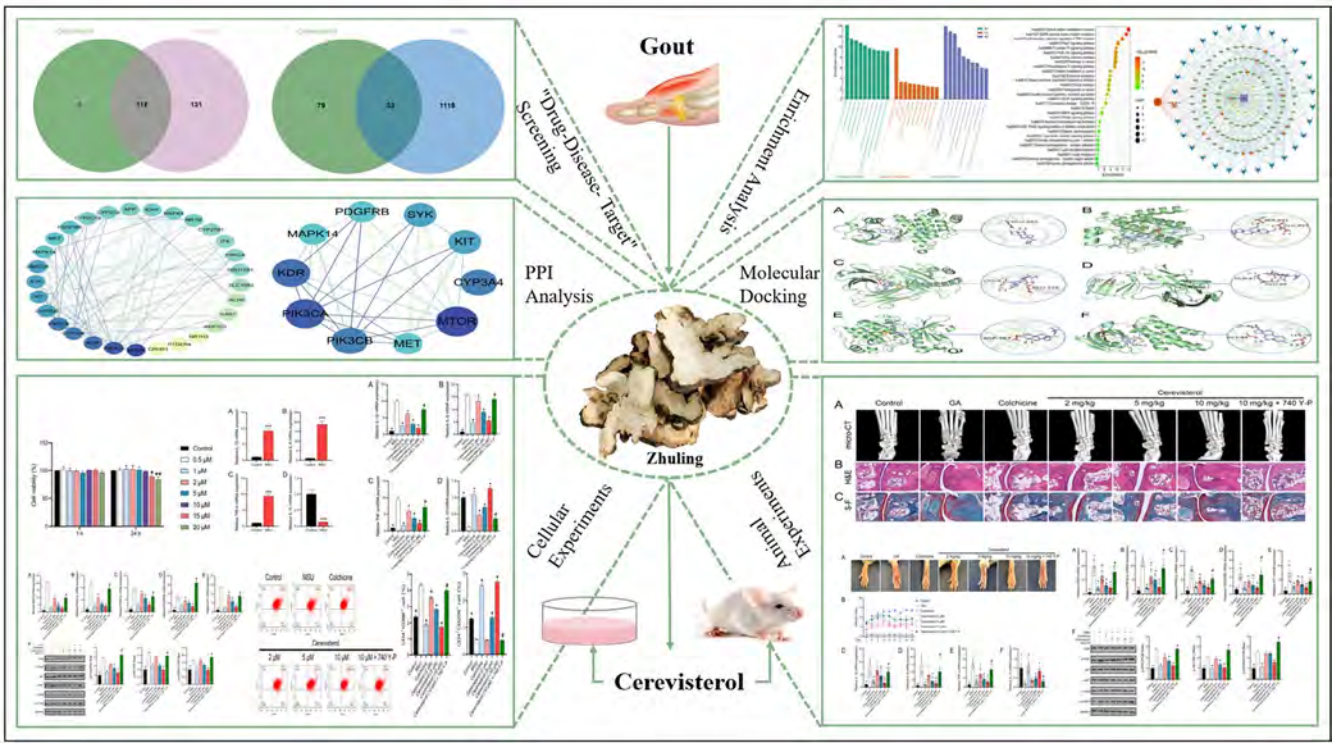
Validating the Gouty Arthritis Alleviating Effects of Cerevisterol through Integrated In Silico, In Vitro, and In Vivo Studies

Xiao-Na Ma[1], Mei-Feng Shi[1], Qian Chen[1], Fang-Shu Zou[1], Wei Feng[1], Qing-Ping Liu[1], Chang-Song Lin[1], Nan Li[2], Xiao-Bao Liu[1] and **Qiang Xu**[1], [1]Guangzhou University of Traditional Chinese Medicine, Guangzhou, China (People's Republic), [2]School of Traditional Chinese Medicine, Jinan University, Guangzhou, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Zhuling has traditionally been utilized in the treatment of gouty arthritis (GA). Although its therapeutic benefits are recognized, the molecular mechanisms underlying Zhuling's action and those of its principal component are still largely uncharted. The purpose of this study was to clarify the molecular mechanisms responsible for the therapeutic benefits of Cerevisterol, a principal component of Zhuling, in the treatment of gout. This was achieved through an integrated approach that combined network pharmacology with in vitro and ex vivo experimental methods.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Graphical Abstract

Methods: We employed the TCMSP database, the Uniprot platform, and SwissTargetPrediction to identify the targets of Zhuling and Cerevisterol. Gout-associated targets were sourced from DrugBank, GeneCards, OMIM, and DisGeNET. Utilizing Cytoscape, we constructed a protein-protein interaction (PPI) network to pinpoint core targets. Pathway enrichment analysis was conducted using Metascape and the Microbiotics platform. Subsequently, we focused on the potential targets and related pathways of Cerevisterol, followed by molecular docking simulations using AutoDockTools and PyMOL. To validate our in silico findings, we established an monosodium urate (MSU)-induced GA cell model using mouse bone marrow-derived macrophages (BMDMs) and evaluated the expression of inflammatory factors, pivotal pathway proteins, and macrophage polarization via RT-qPCR, Western blot, and flow cytometry. We also developed GA mouse models to assess ankle swelling and joint dysfunction indices, and quantified serum inflammatory factors using RT-qPCR. Pathological changes in mouse joints were examined using Micro-CT, H&E staining, and S-F staining, while the impact of Cerevisterol on key pathway proteins was investigated using Western blot.

Results: Network pharmacology and bioinformatics analyses revealed 243 potential targets for Zhuling in gout treatment, among which 112 were potential targets for the treatment of gout by its principal active component, Cerevisterol. Cerevisterol was found to modulate the expression of pro-inflammatory factors such as IL-1β, IL-6, and TNF-α, while upregulating the anti-inflammatory factor IL-10 in MSU-induced GA cells and mouse models. Additionally, Cerevisterol facilitated macrophage polarization towards the M2 phenotype by targeting key molecules like KDR, PIK3CA, PRKCA, PDGFRB, and KIT, Cerevisterol exerted its therapeutic effects by regulating the PI3K/AKT/mTOR signaling pathway and the expression of critical proteins, thereby ameliorating the inflammatory response and pathological changes in GA models.

Conclusion: Our findings suggest that Cerevisterol, a pivotal active ingredient in Zhuling, may exert its therapeutic effects on gout through a multi-target and multi-pathway mechanism. In vitro and in vivo studies corroborate that Cerevisterol can mitigate joint inflammation and pathological alterations in gout by influencing macrophage polarization and the expression of inflammatory mediators through the PI3K/AKT/mTOR pathway. These insights offer a promising avenue for the clinical management of gout.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: X. Ma: None; **M. Shi**: None; **Q. Chen**: None; **F. Zou**: None; **W. Feng**: None; **Q. Liu**: None; **C. Lin**: None; **N. Li**: None; **X. Liu**: None; **Q. Xu**: None.

Abstract Number: 1800

The Role of Nociceptor-Expressed Piezo2 in Nervous System Immune Cell Infiltration in a Mouse Model of Osteoarthritis

Natalie Adamczyk[1], Terese Geraghty[2], Shingo Ishihara[3], alia obeidat[2], Jun Li[2], Anne-Marie Malfait[2] and **Rachel Miller**[1], [1]Rush University Medical Center, Chicago, IL, [2]Rush University Medical Center, Chicago, [3]Rush University, Chicago

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis is one of the leading causes of chronic pain and disability worldwide with 500 million people affected. We have previously reported that nociceptor-conditional Piezo2 knock-out mice ($Na_V1.8$cre-Piezo2fl/fl; Piezo2cko), were protected from pain-related behaviors associated with a surgical model of OA along with spontaneous OA with aging, while joint damage was not affected. Persistent pain development is associated with molecular and cellular changes in the dorsal root ganglia (DRG), which contain the cell bodies of nociceptors as well as various types of non-neuronal cells. Previously, in wild-type mice, we have reported elevated levels of immune cells such as macrophages in the knee-innervating DRG in mouse models of OA, but the link between stimuli sensed by nociceptors in the knee joint and the recruitment of these cells in the DRG is not yet fully elucidated. The objective of the present study was to investigate whether the ion channel Piezo2, expressed by nociceptors, plays a role in these changes within the dorsal root ganglia in a mouse model of osteoarthritis (OA).

Methods: Twelve-week-old WT and Piezo2cko mice of both sexes underwent PMX or sham surgery (n=9-10). Mice were behaviorally assessed pre-operatively and every 4 weeks thereafter for knee hyperalgesia and weight bearing asymmetry. At 13 weeks *post* operatively knees were used for OA scoring by H&E and Safranin-O. Spinal cords were used for immunofluorescent staining for IBA1+ microglia and GFAP+ astrocytes. Separate cohorts of mice were used to perform flow cytometry or bulk RNAseq on L3-L5 DRG.

Results: Piezo2cko mice of both sexes were protected throughout the time course from knee hyperalgesia and from weight bearing asymmetry development, however Piezo2cko mice developed OA pathology at the same level as WT PMX mice. Piezo2cko PMX mice were protected from innate immune cell influx of NK1.1+ and F4/80+ cells compared to WT PMX mice, which was supported by DRG bulk RNAseq findings. Neuroimmune protection seen at the DRG extends to the CNS as Piezo2cko PMX mice had less activated IBA1+ microglia. In addition, male WT PMX mice displayed an increase in the number of GFAP+ astrocytes compared to Piezo2cko PMX mice. No differences in GFAP+ astrocytes were observed in female mice across the conditions.

Conclusion: Piezo2cko from nociceptors was protective against pain-related behaviors and neuroimmune changes associated with OA in the PMX model in both sexes. However, conditional knockout did not protect from OA joint pathology. Targeting Piezo2 could prove to be a valuable target for inhibiting chronic pain in patients.

Disclosure: N. Adamczyk: None; **T. Geraghty**: NS Pharma, 3; **S. Ishihara**: None; **a. obeidat**: None; **J. Li**: None; **A. Malfait**: Asahi Kasei Pharma Corporation, 23andMe, Orion, 2; **R. Miller**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1801

Matrikine Activation of Synovial Fibroblasts Promotes Monocyte Migration and Stimulates an OA Chondrocyte Phenotype

Richard Loeser[1], Jorge Fernandez Davila[1], Philip Coryell[2], Susan Chubinskaya[3] and Doug Phanstiel[4], [1]University of North Carolina, Chapel Hill, NC, [2]University of North Carolina-Chapel Hill, Chapel Hill, NC, [3]University of Texas Medical Branch, Galveston, TX, [4]University of North Carolina at Chapel Hill, Chapel Hill, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Protease cleavage of matrix proteins generates matrix fragments including fibronectin fragments (FN-f) found in OA cartilage and synovial fluid. Matrix fragments or "matrikines" activate signaling to increase production of OA mediators promoting a feed-forward loop of matrix destruction. Stimulation of chondrocytes with an Fn-f (FN7-10) that binds the α5β1 integrin has been shown to model the OA chondrocyte phenotype. Synovial fibroblasts contribute to OA by producing factors that promote synovitis and cartilage destruction. The **purpose of this study** was to determine if FN7-10 activates synovial fibroblasts to produce factors that promote monocyte migration, differentiation, and an OA chondrocyte phenotype.

Methods: OA synovial fibroblasts (SFs) were isolated from tissue obtained during knee replacement and chondrocytes from normal cartilage were from tissue donors. RNA and serum-free conditioned media were collected after 18 hours of stimulation of SFs with FN7-10 or PBS as control and used for RNAseq, cytokine/chemokine protein arrays for 80 proteins and Luminex assays designed to measure 18 OA mediators. To evaluate the effects of activated SFs on the OA microenvironment, a 4-hour FN7-10 stimulation was performed, followed by a transition to serum-free medium and overnight incubation. The conditioned media was harvested and assessed for its chemotactic effects on THP1 monocytes, and its impact on the expression of inflammatory mediators in THP1 monocytes and chondrocytes.

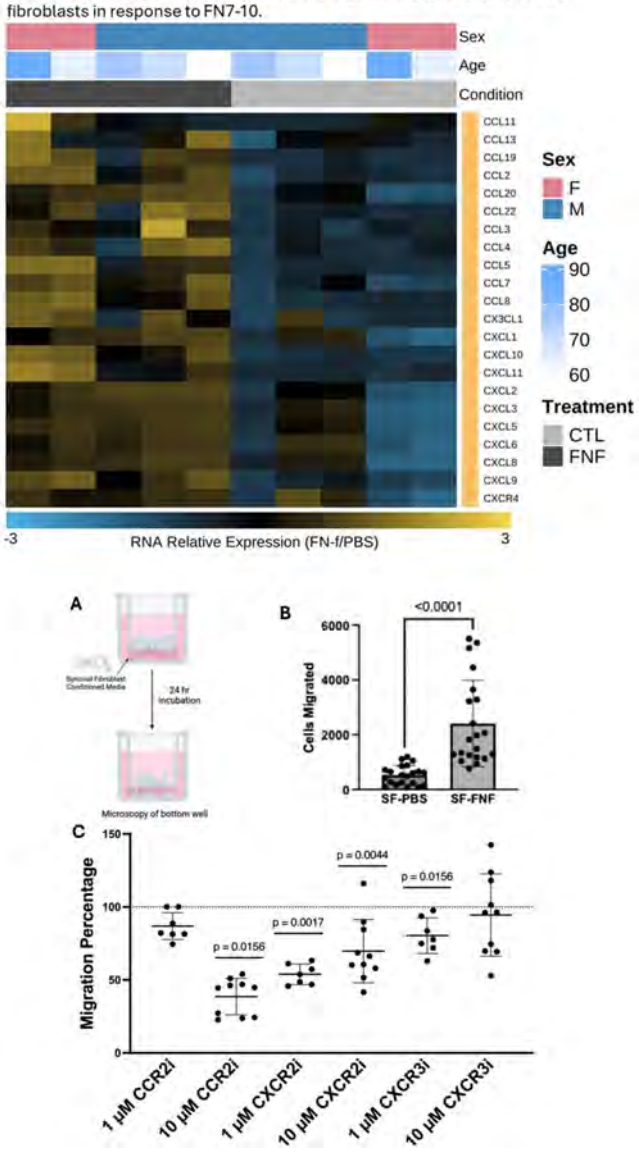
Results: SF RNAseq revealed 1487 differentially expressed (DE) genes (772 up and 715 down) in response to FN7-10 vs PBS control (DESeq2, adjusted p value < 0.05, absolute differences of log2 fold-change >1). Upregulated genes were enriched for KEGG pathways including TNF and IL-17 signaling, cytokine-cytokine receptor interaction, and NOD-like,Toll-like receptor, and NFκB signaling. There were 22 upregulated chemokine genes (**Fig.1**) many of which also exhibited increased protein levels (greater than 2-fold) as detected by cytokine/chemokine protein arrays and/or Luminex including IL-6, CXCL5, CCL5, MCP1-3, CXCL10, CXCL20, LIF, FGF-2, MMP-3, MMP-13 and TNFα. Conditioned media from SFs stimulated by FN7-10 induced monocyte migration, which was blocked by CCR2 and CXCR2 chemokine receptor inhibitors (**Fig. 2**), and induced macrophage differentiation. Chondrocytes incubated with SF FN7-10 conditioned media demonstrated significant increases in expression of OA mediators and a downregulation of aggrecan (*ACAN*) and *COL2A1* (**Table 1**).

Conclusion: OA SFs produce proinflammatory cytokines, chemokines, and MMPs when exposed to a matrikine (FN7-10) produced by cartilage degradation. Chemokines released from activated SFs induce monocyte migration and promotion of a macrophage phenotype which could contribute to synovitis. SF factors also stimulated chondrocytes to produce key OA mediators, down regulate anabolic genes and increase expression of the OA biomarker CRTAC1. These findings demonstrate a mechanism for cross-talk between the synovium and cartilage mediated by cartilage matrix damage that could promote OA progression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig. 1 Clustering and heatmap of chemokine genes expressed by synovial fibroblasts in response to FN7-10.



Monocyte migration in response to synovial fibroblast conditioned media after FN7-10 stimulation. A). Serum-free conditioned media collected from OA synovial fibroblasts after treatment with FN7-10 or PBS as control was incubated with THP-1 cells in transwells. B). After 24hrs cells that had migrated out of the transwell to the well with conditioned media were

Table 1. Effects of synovial fibroblast conditioned media on chondrocyte gene expression

Gene	Mean fold change ± SD	P value
ACAN	0.60 ± 0.4	8.55E-04
COL2A1	0.59 ± 0.9	9.02E-04
IL1B	9.73 ± 9.2	1.10E-05
IL6	16.9 ± 10.4	5.09E-11
TNFA	5.45 ± 4.1	1.06E-06
CXCL5	38.3 ± 25.0	4.45E-09
CXCL10	8.53 ± 9.3	5.38E-07
CRTAC1	1.95 ± 0.8	9.40E-05
MMP1	5.64 ± 1.8	1.39E-11
MMP13	3.56 ± 2.2	4.31E-06

counted (n=21 samples). C). THP-1 cells were pre-incubated with inhibitors to CCR2, CXCR2 or CXCR3 prior to placement in the transwells and treatment with the synovial fibroblast conditioned media. % migration was compared to cells without the receptor inhibitors set as 100%.

RNA was isolated from chondrocytes treated for 24hrs with synovial fibroblast (SF) conditioned media (CM) obtained from SFs treated for 24hrs with FN7-10 or PBS control. n=5 chondrocyte donor samples treated with n=3 samples of SF conditioned media. p value = FN7-10 CM vs PBS CM on Delta Ct values, 2 tailed, paired t test

Disclosure: R. Loeser: None; **J. Fernandez Davila**: None; **P. Coryell**: None; **S. Chubinskaya**: None; **D. Phanstiel**: None.

Abstract Number: 1802

Clearance Kinetics and Cartilage Retention of MM-II, a Dispersion of Large Empty Liposomes, in Rat Knees

Roni Wechsler and Rany Rotem, Moebius Medical, Tel Aviv, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: MM-II is a dispersion of large, empty multilamellar liposomes for intraarticular (IA) injection that reduced knee pain in osteoarthritic patients for up to 26 weeks in a global clinical study (NCT04506463). Previous studies showed these liposomes coat cartilage and menisci under compression, providing lubrication and reducing wear. After injection, most liposomes are absorbed and metabolized by joint tissues, while some adhere to knee

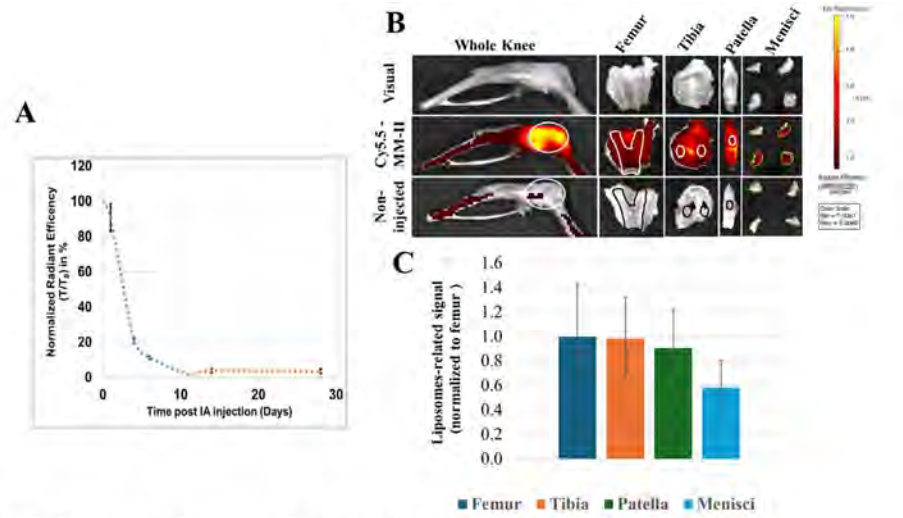


Figure 1. Clearance profile of intraarticularly injected MM-II and its retention in articular cartilage and menisci .
A = In vivo clearance profile of IA-injected sulfo-Cy5.5-MM-II (N=8 rats for days 0-14 and N=4 rats for day 28). Background in each time point was determined each day using average of both knees from one non-injected rat and subtracted from the corresponding values. Blue dotted line indicates initial exponential phase and orange dotted line indicates the second phase; **B** = Representative images of whole knees and knee components that were scanned on day 28 to quantitate cartilage-retained MM-II. The ROIs in cartilaginous areas were selected while being blinded to fluorescence signal to avoid bias; **C** = Relative MM-II associated signal at day 28 in cartilage of femur, tibia and patella as well as in menisci. Data is normalized to average signal found in femurs. Background in each time point was subtracted for each knee region using non-injected corresponding region. The presented data are mean values with standard error of the means.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

surfaces to maintain lubrication. This study aimed to characterize MM-II clearance and its association with knee components in healthy rats.

Methods: Sulfo-Cyanin 5.5–labelled MM-II (Cy5.5-MM-II) liposomes were produced from dipalmitoylphosphatidylcholine (DPPC), dimyristoylphosphatidylcholine (DMPC), and Sulfo-Cy5.5-phosphatidylethanolamine at a molar ratio of 0.5445:0.4550:0.0005. Male Wistar rats (N=8) received bilateral IA injections of Cy5.5-MM-II (3.2 mg per knee) on day 0 and were imaged with an IVIS Lumina LT on days 0, 1, 4, 6, 14, and 28 to measure radiant efficiency, with a non-injected rat as a background control. On day 28, knees from N=3 Cy5.5-MM-II injected rats were excised, soft tissues removed, and components (femur head, tibia plateau, patella, menisci) isolated for scanning. Regions of interest (ROIs) were defined in cartilage areas to normalize fluorescence signals. Additional knees were decalcified, stained with DAPI, cryosectioned, and analyzed via fluorescent microscopy.

Results: MM-II clearance showed an initial exponential phase (half-life ~3 days) for 11 days, followed by a terminal phase where approximately 3% of the dose remained through day 28 (Figure 1A). Ex vivo imaging and histology at day 28 (Figure 1B, C) confirmed similar liposome distribution in femur, tibia, and patella cartilage, with retention also observed in the menisci.

Conclusion: IA injection in rat knees led to most MM-II liposomes clearing within 1–2 weeks, while a fraction persisted on cartilage and menisci for at least 28 days, supporting clinical findings of prolonged knee pain relief.

Disclosure: R. Wechsler: Moebius Medical, 3, 11; **R. Rotem**: Moebius Medical, 3.

Abstract Number: 1803

Patching of Damaged Meniscus and Cartilage of Osteoarthritic Animals by MM-II, a Dispersion of Empty Large Multilamellar Liposomes

Roni Wechsler and Rany Rotem, Moebius Medical, Tel Aviv, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Cartilage wear in knee osteoarthritis (KOA) is linked to reduced boundary lubrication. Occasionally, the meniscus also wears out in KOA, potentially accelerating the disease. MM-II is a dispersion of empty, large multilamellar liposomes for intraarticular (IA) injection. A single injection of MM-II has reduced knee pain for up to 26 weeks in a global clinical study (NCT04506463). MM-II was shown to coat cartilage and menisci and to reduce cartilage degeneration in surgically induced KOA models. The current study aimed to assess interaction of MM-II with cartilage and menisci in monosodium-iodoacetate KOA rat model in which cartilage pathology is reminiscent of human KOA.

Methods: Osteoarthritis was induced by 0.6mg monoiodoacetate (MIA) IA injection in rats. At 14 days post MIA injection, fluorescently labelled MM-II liposomes were bilaterally IA injected. Knees were harvested at 1-week post-injection, fixed, decalcified in EDTA, frozen, cryosectioned, stained with DAPI and visualized by fluorescent microscopy. Animal procedures were approved by the local ethics committee and relevant authorities.

Results: In MIA-treated knees, accumulation of MM-II was seen one week post administration specifically in regions with extensive cell death in both cartilage and meniscus. In contrast, in flanking regions with live cells or in healthy knees, MM-II was shown to coat cartilage and meniscus with fine layer as seen previously in surgically induced KOA models.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Pending on the KOA model, MM-II liposomes coat or patch OA cartilage and menisci. These observations, together with previous ones showing lubrication by MM-II, suggest a novel mechanism that may underlies MM-II clinical benefit in KOA.

Disclosure: R. Wechsler: Moebius Medical, 3, 11; **R. Rotem**: Moebius Medical, 3.

Abstract Number: 1804

Pharmacology of LEVI-04, a novel treatment for OA

Simon Westbrook[1] and Kerry af Forselles[2], [1]Levicept Ltd, Sandwich, United Kingdom, [2]Levicept, Sandwich, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: LEVI-04 is a novel fusion protein comprising the extracellular domain of p75 neurotrophin receptor (p75NTR) coupled to IgG1 Fc, being developed for the treatment of osteoarthritis (OA) symptoms and disease progression. Results from a phase II study showed a significant reduction of WOMAC pain, function and stiffness vs placebo, supporting its clinical potential[1]

Methods: Binding affinities of LEVI-04 to neurotrophins (NTs) were determined using surface plasmon resonance assays. Functional potency was assessed in cell-based assays measuring inhibition of NT-induced activation of Trk and p75NTR/Trk receptors. Analgesia (weight-bearing) and disease modification (histopathology) were assessed in a monosodium iodoacetate (MIA) induced OA model in the rat.

Results: LEVI-04 bound to all NTs, with highest affinity for NT-3 (Table 1). However, while dissociation from NT-3, BDNF, and NT-4 was slow, such that rate measurement was challenging, dissociation from NGF was rapid. LEVI-04 inhibited the activation of Trk receptors by all NTs. However, while LEVI-04 completely inhibited NT-3-induced activity, inhibition of NGF, BDNF, and NT-4 was not complete (Figure 1), especially when Trk receptors were co-expressed with p75NTR. LEVI-04 had highest potency for inhibition of NT-3 at TrkC receptors and TrkC receptors co-expressed with p75NTR (Table 1).

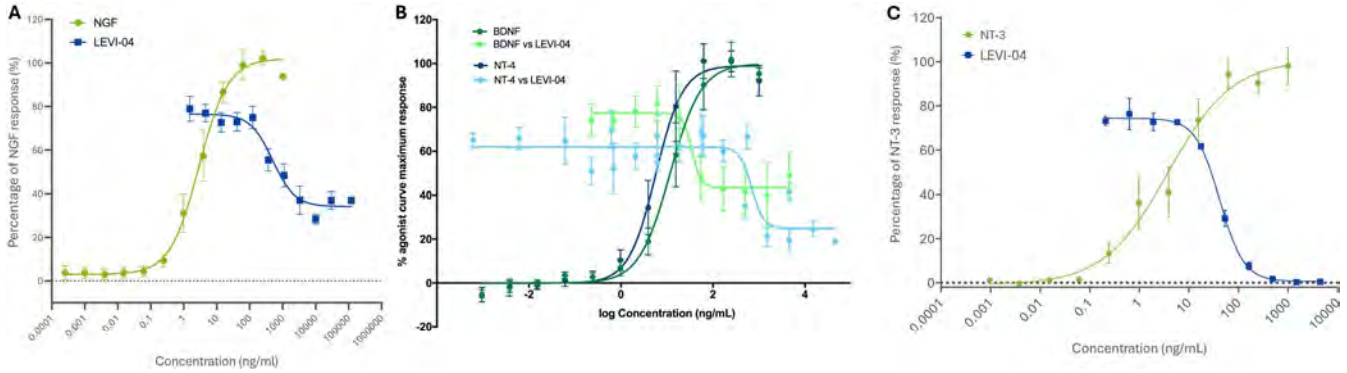
In the MIA model of OA, analgesia was seen with therapeutic LEVI-04 treatment (0.03–3 mg/kg SC) initiated following establishment of pain (determined by imbalance of weight distribution). LEVI-04 returned the MIA-induced imbalance in weight distribution to normal. MIA injection caused chondrocyte death, reduced cartilage thickness and reactive joint and bone

	NT-3	BDNF	NT-4	NGF
Binding				
Association rate, 1/Ms*	4.10e+04	5.29e+06	5.86e+04	2.03e+06
Dissociation rate, 1/s*	3.49e-08	1.86e-05	8.51e-05	2.2e-03
Binding affinity, nM (CI)†	0.014 (0.002-0.02)	0.042 (0.004-0.049)	0.18 (0.008-0.77)	0.88 (0.43-0.95)
Functional Potency: Schild analysis				
TrkA KB, nM	-	-	-	7.1
TrkA/p75NTR KB, nM	-	-	-	25
TrkC KB, nM	1.4	-	-	-
TrkC/p75NTR KB, nM	0.3	-	-	-

*Values from study with one batch of LEVI-04 using 1:1 model. †Affinity values are mean values across batches. -, not tested in Schild assay format

In vitro pharmacology of LEVI-04

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Inhibition of NT-induced activity by LEVI-04 in U20S cells expressing (A) TrkA and p75NTR, (B) TrkB and (C) TrkC receptors

pathology. LEVI-04 treatment resulted in chondroprotection, with reduced bone pathology and osteolysis-mediated bone erosion compared with IgG control. In MIA-injected joints in the LEVI-04-treated groups there was reduction in osteolysis, thus limiting myeloid cell activation, and osteoblast pool expansion thereby augmenting the mesenchyme cell pool, leading to repair and reduction in MIA-induced histopathology.

Conclusion: LEVI-04 supplements endogenous soluble p75NTR. Like soluble p75NTR, LEVI-04 interacts with all NTs but inhibits NT-3. Of note, NGF-, BDNF- and NT-4-induced Trk receptor activity cannot be fully inhibited by LEVI-04. In the MIA model of OA, LEVI-04 provided analgesia and reduced histopathology. Phase 3 trials to assess the effect of chronic LEVI-04 treatment on OA symptoms and disease progression are planned.

Reference: 1. Conaghan P, et al. Arthritis Rheumatol. 2024;76 (suppl 9).

Disclosure: S. Westbrook: Levicept Ltd, 3; **K. af Forselles**: Levicept Ltd, 2.

Abstract Number: 1805

Human meniscus histopathological and transcriptomic changes at early and advanced stages of knee osteoarthritis

Takuya Sakamoto[1], Merissa Olmer[1], chelsea Kenvisay[1], Rachel Miller[2], Anne-Marie Malfait[3], Darryl D'Lima[4], William Bugbee[5], Hannah Swahn[6] and Martin Lotz[7], [1]Scripps Research Institute, La Jolla, CA, [2]Rush University Medical Center, Chicago, IL, [3]Rush University, Oak Park, IL, [4]Scripps Clinic, San Diego, CA, [5]Scripps Clinic, La Jolla, CA, [6]Scripps Research Institute, Carlsbad, CA, [7]Scripps Research, La Jolla, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

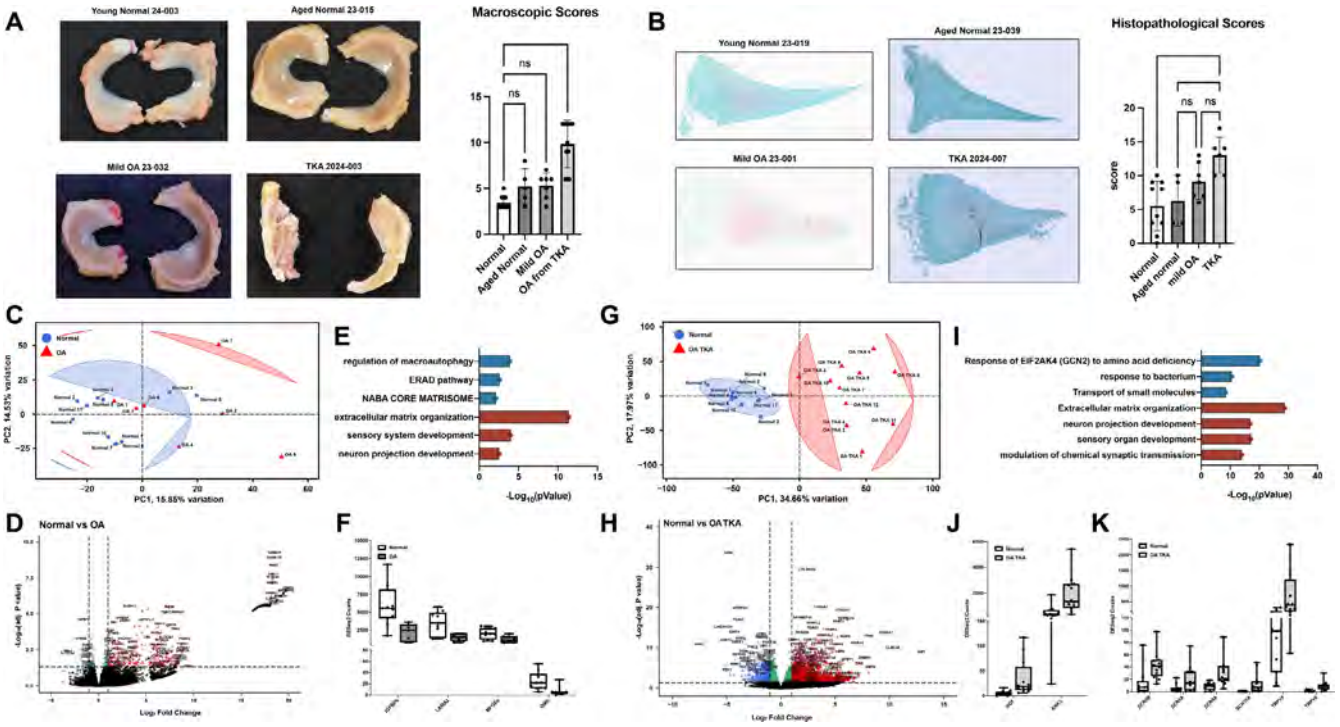
Background/Purpose: The knee menisci are essential in joint biomechanics while meniscus damage is a driver of knee osteoarthritis (OA) and an important source of knee pain. As early molecular and cellular changes mediating the onset of tissue damage and mechanisms of progression are poorly understood, there are no approaches to prevent, delay or stop progression of meniscus destruction. The goal of this study is to discover genes and mechanisms of meniscus aging and OA at early and late stages.

Methods: This study used human knees from organ donors, including young healthy donors and aged donors with macroscopically normal knee cartilage and menisci, aged donors with cartilage damage indicative of mild OA and patients with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

severe OA undergoing total knee arthroplasty (TKA) (**A**). The menisci were scored for histopathological changes (**B**). Bulk RNA-sequencing (RNA-seq) and single nuclei multiome were performed.

Results: Meniscus histopathology scores were normal in the young donor group (5.18±3.6) but also in the aged group (6.00 ±3.3) (**B**). The meniscus scores of the aged mild OA group were (9.14±2.7) and of the TKA group were 13.0±2.7 (**B**). RNA-seq detected only three DEGs in the menisci from aged normal donors as compared to the young normal. The aged OA group showed some separation from the young normal group on a principal component analysis (PCA) plot (**C**) and had 84 downregulated genes (DRGs) and 413 upregulated genes (URGs) (**D**). Metascape analysis revealed biological processes (BPs) regulated by the DRGs including macroautophagy, Endoplasmic-reticulum-associated protein degradation (ERAD), protein folding and NABA core matrisome (**E, F**). The URGs were also enriched for BPs related to extracellular matrix (ECM) and sensory system remodeling (**E**). The TKA group showed clear separation from the young normal group on PCA plot (**G**) and had 577 DRGs and 2680 URGs (**H**). The DRGs were enriched for metabolic pathways and protective BPs related to response to amino acid deficiency and antimicrobial defense (**I**). The URGs were strongly enriched for matrisome and ECM and for neuronal system, synaptic transmission and sensory organ development (**I**). Among the URGs were genes related to pain, including *NGF* and *ANK3* (**J**), and genes encoding voltage-gated sodium channels and transient receptor potential cation channels (**K**). In multiome analysis, several cell populations were significantly enriched in TKA compared to normal (clusters 0, 10 and 16). Cluster 10 had 1554 differentially expressed genes with enrichment for the OA-promoting genes, pathways related to calcium signaling, ECM, chondrocyte/bone differentiation and mitochondrial dysfunction. NFATC2 and NFATC1 were differentially expressed in cluster 10 in TKA compared to normal and had enhanced regulon activity.



(A) Representative macroscopic images (left) and quantification of macroscopic scores (right) for young normal, aged normal, mild OA and TKA menisci. (B) Representative histologic images (left) and quantification of histological scores (right) for young normal, aged normal, mild OA and TKA menisci. (C) PCA plot showing separation between young normal and mild OA groups. (D) Volcano plot showing the differentially expressed genes (adj $p < 0.05$ and baseMean > 1). (E) Metascape functional enrichment analysis showing enrichment of biological processes in young normal (blue) and mild OA (red). (F) Box plots showing DESeq2 counts of several differentially expressed genes between young normal and mild OA menisci. (G) PCA plot showing separation between young normal and TKA groups. (H) Volcano plot showing the differentially expressed genes (adj $p < 0.05$ and log2FC > |1|) . (I) Metascape functional enrichment analysis showing enrichment of biological processes in young normal (blue) and TKA (red). (J, K) Box plots showing DESeq2 counts of several differentially expressed genes between young normal and TKA menisci.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Early or mild stages of OA are primarily characterized by disruption of cellular homeostasis and defense mechanisms and a relatively low level of ECM process activation. These processes are more enriched in late-stage OA which also has a marked enhancement of processes related to neuronal remodeling and pain. A pathogenic cell population that is expanded in OA and is a promising new therapeutic target.

Disclosure: T. Sakamoto: None; **M. Olmer**: None; **c. Kenvisay**: None; **R. Miller**: None; **A. Malfait**: Eli Lilly, 5, Merck, 2, Novartis, 2, Orion, 5, Roivant, 2; **D. D'Lima**: None; **W. Bugbee**: None; **H. Swahn**: None; **M. Lotz**: Blackbird, 2.

Abstract Number: 1806

Sex differences in knee joint microbial DNA of C57BL/6 mice and the effect of cross-sex microbiome transplantation

Veera Durga Vaishnavi Kurra[1], Ausitn Lopez[2], Aleksander Szymczak[3], Gabriella Dyson[3], Pratibha Dube[4], Padmaja Mehta-d'Souza[2] and Matlock Jeffries[3], [1]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]Oklahoma Medical Research Foundation, Edmond, OK

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Recent studies have suggested an association between the gut microbiome and osteoarthritis. We have previously shown that the joint microbiome is derived at least in part from the gut microbiome. However, there is little information on the role of the joint microbiome in OA development or progression, or on the differences in the joint microbiome based on biological sex. The goal of the present study was to examine sex differences in knee joint microbial DNA and the impact of opposite sex transplantation on the joint microbiome with and without PTOA using paraffin-embedded tissue sections of the knee joint.

Methods: Diluted cecal microbiome samples (200uL or vehicle control) was transplanted via single-timepoint oral gavage at 11 weeks of age. One week later, OA was induced in the right knee via destabilization of the medial meniscus (DMM) surgery. Mice were euthanized 8 weeks after DMM and knee joints were processed into formalin-fixed paraffin-embedded (FFPE) blocks. Eight 6μm sections per knee were then subjected to DNA extraction from both knees in each animal (DMM'd and unoperated) in four groups of mice (male and female controls and transplanted F- >M, transplanted M- >F).

Table 1

Table 1: Sex differences in knee joint microbial DNA

Comparison	Clade	Enriched Group	LDA coefficient	*P* value
All – M vs F	*Clostridiaceae*	F	1.44	0.022
All – M vs F	*Alistipes*	F	0.62	0.080
All – M vs F	*Bifidobacterium*	F	0.18	0.12
All – M vs F	*Neisseriaceae*	M	1.05	0.14
All – M vs F	*Blautia*	M	0.62	0.14
DMM – M vs F	*Clostridiaceae*	F	1.27	0.043
DMM – M vs F	*Alistipes*	F	1.35	0.057
DMM – M vs F	*Duncaniella*	F	0.47	0.11
DMM – M vs F	*Clostridium_T*	F	0.68	0.14
DMM – M vs F	*Geobacillus*	F	0.89	0.14
noDMM – M vs F	*Muribaculaceae*	F	1.92	0.056
noDMM – M vs F	*Sphingomonadaceae*	F	1.60	0.083
noDMM – M vs F	*Staphylococcus*	M	1.31	0.149

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2

Table 2: Linear correlations between gut microbiome clades and sex / cross-sex microbiome transplantation group (Male, Female->Male, Male->Female, Female)

Clade	LDA coefficient	Std. error	*P* value
Clostridiaceae	0.66	0.29	0.024
Alistipes	0.38	0.19	0.054
Coprocola	-0.056	0.031	0.076
Bacteroides	-0.071	0.041	0.090
Blautia	-0.26	0.16	0.11
Neisseriaceae	-0.35	0.23	0.13
Dysosombacter	-0.24	0.15	0.14
Staphylococcus	-0.23	0.16	0.15

Table 3

Table 3: DMM-induced OA differences in knee joint microbial DNA pattern

Clade	Enriched Group	LDA coefficient	*P* value
Clostridiaceae	Non-DMM	1.3	0.043
Alistipes	Non-DMM	1.3	0.057
Duncaniella	Non-DMM	0.470.47	0.11
Clostridium_T	Non-DMM	0.66	0.14
Geobacillus	Non-DMM	0.89	0.14

DNA was extracted using a QIAamp FFPE Tissue Kit, quantified using Qubit dsDNA HS Assay, and 16S libraries were generated by real-time quantitative PCR, using unique primer indexes. The pooled library was sequenced on an iSeq sequencer and the taxonomic profiles determined. 16S data were analyzed using a custom QIIME2-based pipeline, Maaslin2 was used for group and correlation analyses.

Results: When considering both DMM and control mice, 5 microbiome clades were discordant or trended towards discordance according to sex (cutoff $P \leq 0.15$), 5 were discordant when only OA knees were tested, and 3 when only non-OA knees were tested (**Table 1**). Next, we included specimens from cross-sex microbiome transplants and performed linear correlation analysis across the sex spectrum (male, female-into-male, male-into-female, female). Eight clades were correlated in this analysis (**Table 2**). We also evaluated the effect of OA by comparing DMM to non-DMM knees and found 5 clades discordant (**Table 3**). All of these were seen in our sex analysis and were enriched in female mice.

Conclusion: Although our study was underpowered, we nonetheless detected several statistically significant or suggestive differences in the mouse joint microbial DNA pattern according to sex, and these differences can be transferred to the other sex via gut microbiome transplantation. Intriguingly, all 5 of the DMM-associated microbial differences were concordant (all were reduced with DMM and enriched in female animals, which have a lower histologic severity following DMM). Although a larger confirmation study is indicated, our findings nonetheless suggest that sex-associated microbiome differences may be present in joint tissues and may correlate with OA propensity, underscoring the role of non-genetic factors in sex-specific OA susceptibility.

Disclosure: V. Kurra: None; **A. Lopez**: None; **A. Szymczak**: None; **G. Dyson**: None; **P. Dube**: None; **P. Mehta-d'Souza**: None; **M. Jeffries**: Being Inc., 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1808

Lightsheet imaging with 3D analysis for wholistic assessment of synovial lymphatic vasculature within joints of murine models of arthritis

Xi Lin[1], Edward Schwarz[2] and Lianping Xing[3], [1]University of Rochester, Rochester, NY, [2]University of Rochester, Rochester, NY, USA, Rochester, NY, [3]University of Rochester, Webster, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1780–1808) Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The synovial lymphatic system (SLS) maintains joint homeostasis. Post-traumatic osteoarthritis (PTOA) has increased lymphatic vessels (LVs), but decreased SLS drainage. LVs are routinely studied by immunostaining of Lymphatic Vessel Endothelial Hyaluronan Receptor 1 (LYVE1) on tissue sections, but it cannot address the discrepancy between increased LV #s and decreased SLS function in PTOA joints. Lightsheet microscopy allows observation of the full depth of a 600-700mm mouse joint, compared to 4-10mm in 2D imaging. Here we describe the first lightsheet microscopy study of healthy vs. PTOA mouse knees for distribution and alteration of synovial LVs. We hypothesize that lightsheet 3D imaging is superior to traditional immunohistochemistry for comprehensive LV network analyses of mouse knee joints in full depth, which provides new information of SLS.

Methods: Knee joints of 5-m-old C57 male mice receiving sham or PTOA surgery (n=3/group) were stained for synovial LVs with anti-LYVE1. Samples were subjected to lightsheet microscopy and a total of 550-650 consecutive 1mm slices were collected for volumetric/branching analysis in Imaris 10.2 software.

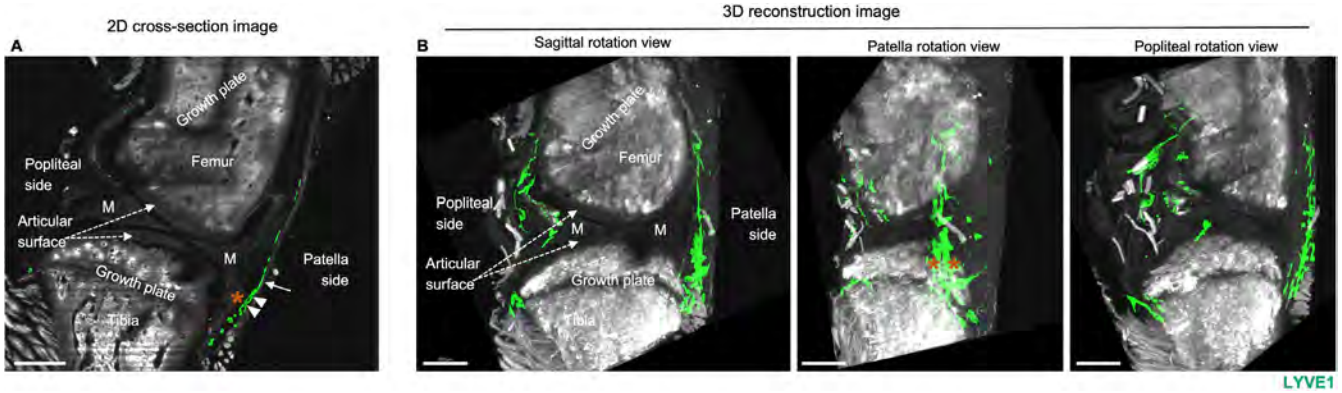


Fig 1. 3D reconstruction of the synovial lymphatic vessels from light sheet images reveals much more extensive lymphatic network than those from a 2D image. Knee joints of 5-m-old C57Bl/6 male mice were processed for the lightsheet microscopy. The synovial LVs were labeled with anti-LYVE1/AlexaFluor647 antibody. Joints were mounted in a sagittal position, and a series of 550-650 consecutive images (=slices) were collected from the medial side of the joint with a step size of 1mm. Fluorescence signal were collected in the AlexaFluor647 channel to visualize the LYVE1+ LVs (green) and GPF channel to visualize the anatomic structure of the joint using the GPF autofluorescence of the bone. (A) A 2D cross-section of 1 mm from the series of 622 slices collected for this joint. The autofluorescence signal shows the histology landmarks, including the distal end of femur and the proximal end of tibia with articular cartilage, subchondral bone, growth plates, and menisci (M). Arrow: most LYVE1+ signals are located on the anterior (patellar) side as unbranched vessel-like structures. Arrowheads: a possible lymphatic vessel branch point. Star: two circular LYVE1+ structures near the tibial growth plate. Note that since this is a 2D cross-section, whether they are two branching vessels perpendicular to the observation plane or two vessels parallel to the tibia axis is unclear. (B) 3D reconstruction of the synovial LVs of the joint (622mm), including sagittal, patella, and popliteal views. Anatomical structures of the joint can be observed. Note that in contrast to the 2D image, both the patella side and popliteal side have initial LVs with extensive branching. *Note in the patella rotation view, at the level of the tibial growth plates, two LVs are parallel to the tibial axis, which as represented as the two circular structures in the 2D cross-section image. Scale bar= 500mm

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

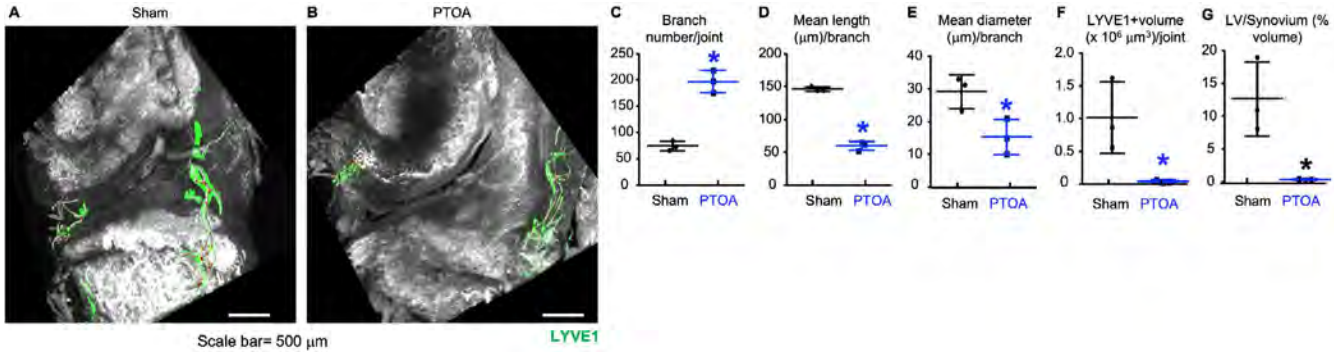


Fig 2. Synovial lymphatic vessels in PTOA joints have increased branches, but shorter length, thinner diameter and smaller volume. 3D reconstruction showing LYVE1+ LVs (green) in the sham and PTOA joints. Branch analysis was performed using the "filament" module in Imaris10.2 (Oxford), which identifies branches (grey) and branch points (red). (A&B) Initial LVs in the PTOA joint visibly differs from sham. (C) Branch number/joint. (D) The mean length of all individual branches recognized by Amira in one joint. (E) The mean diameter of all individual branches recognized by Amira in one joint. (F) The total volume of LYVE1+signal of one joint. (G) LYVE1+LV volume/the volume of the synovial tissues. Student t-test were used to assess the statistical difference between sham and PTOA group.

Results: 1. 3D reconstruction of LVs reveals extensive LV network compared to a 2D image in the normal joint (Fig.1). One 1μm thick image of lightsheet 2D data resembled a typical LYVE1 immunohistochemistry of the knee, where the LYVE1+ signals were located in the synovium on the patella side, forming long unbranched vessel-like structures. Few LYVE1+ signals were on the popliteal side (1A). 3D reconstruction of 622μm in depth revealed LYVE1+ signals on both side of the joint, forming extensive LV structure with complex branching (1B). To visualize the LV branching structure, the 3D reconstructed image was rotated towards the patella (1B middle) and popliteal side (1B right). Notably, the star shows 2 circular LYVE1+ structures at the tibial growth plate level in the 2D (1A) were 2 LVs along the tibial axis in 3D (1B middle).

2. Synovial LVs in PTOA joints have increased branches with shorter length, thinner diameter, and smaller volume (Fig.2). We performed quantitative branching analysis, recognizing LV structures in grey lines, and branching points in red balls. PTOA joints had increased branching that were smaller and shorter (2A-B): increased branch # (197±22 vs. 74±9 in sham, p=0.0008) (2C), decreased mean branch length (59±7 vs. 146±3μm in sham, p< 0.0001) (2D), diameter (15±5 vs. 29 ±5μm in sham, p=0.03) (2E), and smaller LVYE1+ volume (0.36±0.11 vs. 12±4% in sham, p=0.03) (2G).

Conclusion: PTOA induces local lymphangiogenesis with impaired function. We found decreased LV volume (3D) despite increased LV branching #s (2D) in PTOA joints. Possible explanations for the difference between 2D and 3D analysis are: 1) 2D area underestimates the diameter changes; and 2) histology sections (4-10μm) underrepresents the fewer LV branches with ~30μm-diameter. Thus, impaired SLS draining function in PTOA joints are likely due to decreased LV volume. In conclusion, lightsheet imaging/3D analysis is an advantaged tool for studying SLS than the conventional immunostaining, allowing the observation of LV network in full depth of joints.

Disclosure: X. Lin: None; **E. Schwarz**: None; **L. Xing**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1809

Mass Spectrometry-Based N-Terminomics Uncovers Proteolytic Signatures and Pathways in Juvenile Idiopathic Arthritis Synovial Fluid

Andrew Zeft[1], Sirada Panupattanapong[2], Laura Nedorezov[3], Sumit Bhutada[3] and Suneel Apte[3], [1]Cleveland Clinic, Cleveland, OH, [2]Cleveland Clinic Foundation, Cleveland, OH, [3]Cleveland Clinic, Cleveland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile idiopathic arthritis (JIA) is a chronic disease marked by persistent synovial inflammation, often leading to structural joint damage. While numerous proteases produced by synovial cells, chondrocytes, macrophages, and polymorphonuclear cells were implicated in joint damage in rheumatoid arthritis, few studies explored similar mechanisms in JIA. Targeting proteolysis represents a promising disease-modifying strategy and may yield novel biomarkers for JIA, but this approach requires a comprehensive understanding of proteolytic activity. The study objective was to utilize N-terminomics to define the proteolytic landscape of JIA joints.

Methods: Synovial fluid samples (n=5) were collected from JIA patients under an approved IRB protocol. Proteins were labeled at their N-termini using reductive dimethylation. Samples underwent trypsin digestion, followed by enrichment of N-terminally labeled or modified peptides using HPG-ALD polymer. Peptides were further separated by high-pH off-line fractionation and analyzed on a Bruker TimsTOF Pro mass spectrometer. High-confidence peptides were identified using a stringent false discovery rate and mapped to full-length protein sequences to determine cleavage sites. Proteases present in the samples were also identified.

Results: This analysis of JIA synovial fluid identified 13,268 proteolytically cleaved peptides from 854 proteins. Of these, 5,805 peptides (44%) originated from secreted proteins, reflecting the prevalence of circulating proteins in synovial fluid. Notably, 2,732 peptides (19.2%) were detected in all five samples. Comparison with the previously characterized osteoarthritis (OA) synovial fluid degradome showed 6,978 cleavage sites (32.9%) from 325 proteins to be unique in JIA synovial fluid. Ingenuity Pathway Analysis of peptides unique to JIA identified neutrophil degranulation as the most significant pathway. In total, 95 proteases were detected in JIA synovial fluid, including neutrophil-derived proteases and others distinct from OA synovial fluid.

Conclusion: Our findings demonstrate a vast proteolytic landscape of JIA synovial fluid, providing an unprecedented expansion of proteolytic events and identifying potentially causative proteases. Implication of neutrophil activity in protein and joint breakdown highlights the relatively neglected role of innate immunity in JIA and identifies numerous potential biomarkers of their impact. Continued degradome analysis of larger JIA cohorts and stratification by clinical variables will be crucial for elucidating affected pathways and advancing both diagnostic and therapeutic strategies for JIA.

Disclosure: A. Zeft: GE Healthcare, 12,, Merck/MSD, 12,, Opko, 12,, Sobi, 1, Teva, 12,; **S. Panupattanapong**: None; **L. Nedorezov**: None; **S. Bhutada**: None; **S. Apte**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1810

Destabilized Treg Cells Predominant in Severe Forms of Juvenile Idiopathic Arthritis

Ki Pui Lam[1], Claudia Harris[2], Jennifer Cheng[3], Lwiza AitDowd[4], Maryam Ashoor[5], Ahmad Bakhsh[3], Carrie Bryant[3], Siobhan Case[6], Mia Chandler[3], Joyce Chang[3], Ezra Cohen[7], Fatma Dedeoglu[3], Olha Halyabar[8], Jonathan Hausmann[9], Melissa Hazen[3], Sonia Iosim[10], Liyoung Kim[11], Jeffrey Lo[3], Mindy Lo[3], Emma Materne[3], Esra Meidan[12], Megan Perron[13], Helene Powers[10], Mary Beth Son[3], Holly Wobma[3], Margaret Chang[3], Pui Lee[14], Peter Nigrovic[11] and Lauren Henderson[15], [1]Division of Immunology, Boston Childrens Hospital, Harvard Medical School, Boston, MA, [2]Division of Immunology, Boston Childrens Hospital, Boston, MA, [3]Boston Children's Hospital, Boston, MA, [4]Boston Children's Hospital, Harvard Medical School, Boston, MA, [5]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Brookline, MA, [6]UpToDate, Brigham and Women's Hospital, Boston Children's Hospital, Boston, MA, [7]Bmc, NEEDHAM, MA, [8]Children's Hospital/Boston Medical Center, Newton, MA, [9]Boston Children's Hospital / Massachusetts General Hospital, Cambridge, MA, [10]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, [11]Boston Children's Hospital, Brookline, MA, [12]Boston Children's Hospital, Somerville, MA, [13]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Natick, MA, [14]Boston Children's Hospital, Newton, MA, [15]Boston Children's Hospital, Watertown, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: T peripheral helper (Tph) cells stimulate excessive B cell responses in the joints of patients with autoantibody-positive arthritis, including seropositive RA in adults and ANA-positive oligoarticular (oligo) JIA in children. Despite this potentially shared disease pathogenesis, a substantial proportion of children with oligo JIA enter long-term remission while this is rare in seropositive arthritis. To better understand these divergent outcomes, we studied the ability of regulatory T (Treg) cells to restrain Tph-B cell interactions in oligo and seropositive polyarticular (poly) JIA.

Table 1. Clinical Characteristics of Study Participants.

	JIA (N=22)	Adult Controls (N=10)
Age at disease onset (median years, IQR)	6.5 (8.7)	-
Age at sampling (median years, IQR)	16.0 (9.0)	24.0 (6.0)
Sex (n, % female)	17, 77%	8, 80%
Self-Reported Race (n, %)		-
-American Indian/Alaska Native	0, 0%	
-Asian	2, 9%	
-Black	0, 0%	
-Native Hawaiian/Other Pacific Islander	0, 0%	
-Other	2, 9%	
-Undisclosed	8, 36%	
-White	10, 45%	
Ethnicity (n, %)		-
Hispanic	2, 9%	
Non-Hispanic	0, 0%	
Undisclosed	20, 91%	
JIA disease course at sampling (n, %)		-
New Onset Oligo*	7, 32%	
Persistent Oligo	5, 23%	
Extended Oligo	5, 23%	
RF+ Poly JIA	5, 23%	
Active joints at sampling (median joints, IQR)	2, 3	-
Medications at sampling (n, %)		-
Methotrexate/leflunomide	9, 41%	
TNF Inhibitor	5, 23%	
NSAIDs	5, 23%	
Others	1, 5%	
None	5, 23%	

*Disease course not yet determined
JIA, juvenile idiopathic arthritis; oligo JIA, oligoarticular juvenile idiopathic arthritis; poly, polyarticular; RF, rheumatoid factor; NSAIDs, non-steroidal anti-inflammatory drugs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

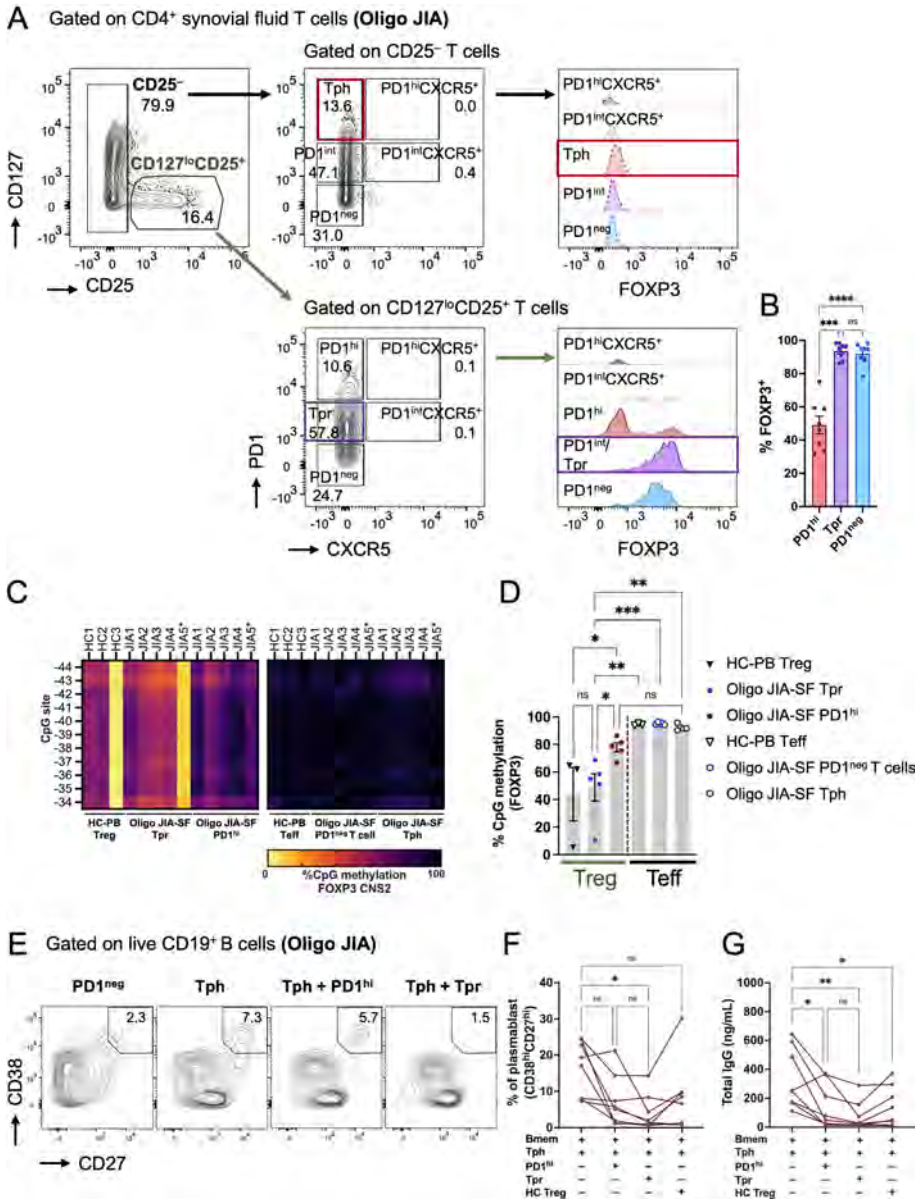


Figure 1. Tpr cells in synovial fluid from oligo JIA patients display features of stable Treg cells. A) Representative flow staining of T cells from the SF of oligo JIA patients. Histogram overlay showing the mean florescence intensity (MFI) of FOXP3 expression in the T cell subsets as indicated. B) Bar chart showing the % of FOXP3+ cells of the given Treg subsets in oligo JIA SF (n=8). CXCR5-expressing Treg subsets were excluded due to the insufficient cell number for analysis. C) Heatmap showing the % of methylation at 11 CpG sites in CNS2 of the FOXP3 locus in the sorted T cell populations. D) Bar charts showing the % of methylation in CpG sites of FOXP3 in the given T cell populations. For C-D) the following were studied: HC-PB Treg (CD4+CD127loCD25+) (n=3), oligo JIA-SF Tpr (CD4+CD127loCD25+PD1intCXCR5–) (n=5), oligo JIA-SF PD1hi T cells (CD4+CD127loCD25+PD1hiCXCR5–) (n=5), HC-PB Teff cells (CD4+CD25–) (n=3), oligo JIA-SF PD1neg T cells (CD4+CD25–PD1negCXCR5–) (n=5), oligo JIA-SF Tph cells (CD4+CD25–PD1hiCXCR5–) (n=5). An asterisk after the sample ID indicates male subjects. E) Representative flow staining showing % of plasmablast (CD38hiCD27+) of alive CD19+ B cells after co-culture of the given T cell populations with Bmem cells from the PB of a third party. Scatter plots showing F) the % of plasmablast and G) the level of total human IgG after co-culture SF Tph cells and an indicated Treg cell population from seroneg JIA-SF (n=8). Mean ± SEM is shown. Statistical analysis: One-way ANOVA with Holm-Šidák 's correction for multiple comparisons. P-value: ns, >0.05; *, ≤0.05; **, ≤0.01; ***, ≤ 0.001; ****, ≤ 0.0001. HC, healthy control; oligo JIA, oligoarticular juvenile idiopathic arthritis; poly, polyarticular; RF, rheumatoid factor; PB, peripheral blood; SF, synovial fluid; CpG, cytosine guanine dinucleotide; CNS2, conserved noncoding sequence 2; Bmem, memory B cells; Tph, T peripheral helper; Tpr, T peripheral regulatory cells; Teff, effector T; Treg, regulatory T.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

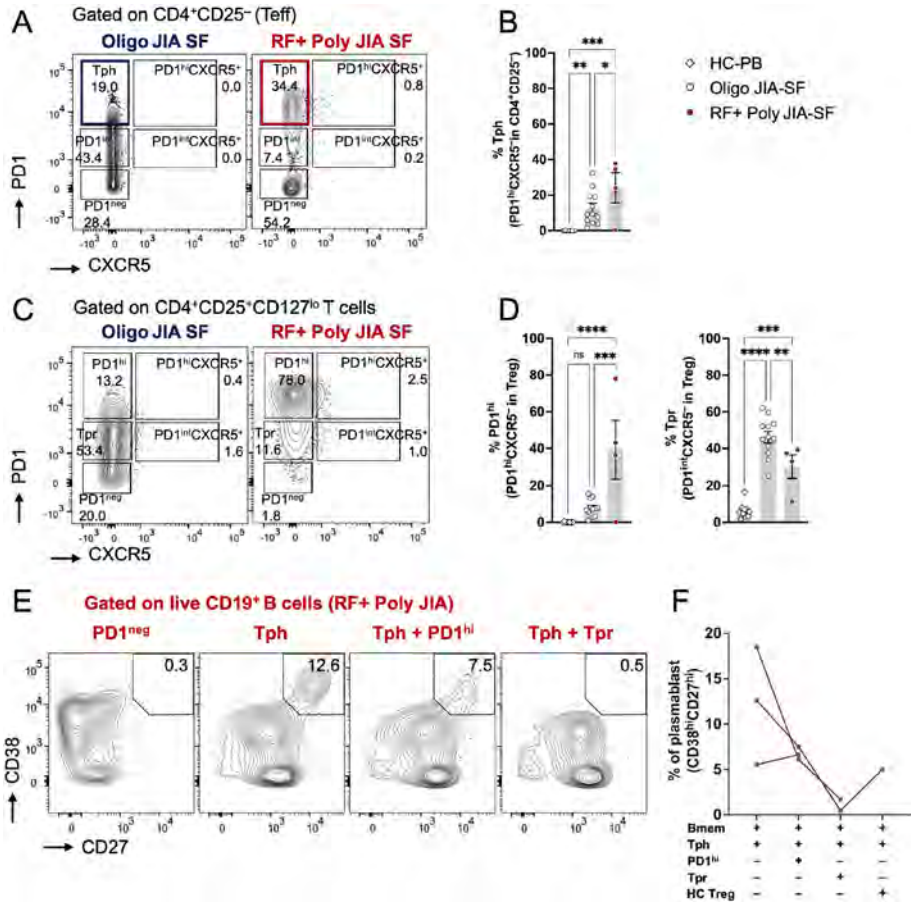


Figure 2. Synovial fluid Treg compartment of RF+ poly JIA patients display features of destabilized Treg cells. A) Representative flow staining showing Tph cells (CD4+CD25–PD1hiCXCR5–) from the oligo JIA-SF and RF+ poly JIA-SF. B) Bar chart showing the % of Tph cells from oligo JIA-SF (n=12) and RF+ poly JIA-SF (n=4) compared to HC-PB (n=10). C) Representative flow staining showing Tpr (PD1intCXCR5–) and PD1hi T cells (PD1intCXCR5–) from the oligo JIA-SF and RF+ poly JIA-SF. D) Bar charts showing % of PD1hi and Tpr cells in SF from oligo JIA-SF (n=12) and RF+ poly JIA-SF (n=4) compared to HC-PB (n=10). E) Representative flow staining showing % of plasmablast (CD38hiCD27+) of alive CD19+ B cells after co-culture of the given T cell populations from a RF+ poly JIA patient with Bmem cells from the PB of a third party. F) Scatter plot showing the % of plasmablast after co-culture SF Tph cells and an indicated Treg cell population from RF+ poly JIA-SF (n=3) with Bmem from PB of a third party. Mean ± SEM is shown. Statistical analysis: One-way ANOVA with Holm-Šidák 's correction for multiple comparisons. P-value: ns, >0.05; *, ≤0.05; **, ≤0.01; ***, ≤ 0.001; ****, ≤ 0.0001. HC, healthy control; oligo JIA, oligoarticular juvenile idiopathic arthritis; poly, polyarticular; RF, rheumatoid factor; PB, peripheral blood; SF, synovial fluid; Bmem, memory B cells; Tph, T peripheral helper cells; Tpr, T peripheral regulatory cells; Teff, effector T cells; Treg, regulatory T cells.

Methods: Synovial fluid (SF) from children with oligo and RF+ poly JIA (ILAR criteria) and peripheral blood (PB) from healthy controls were studied. Mononuclear cells were stained for surface markers, fixed/permeabilized for FOXP3 staining, and evaluated by flow cytometry. Bisulfite conversion pyrosequencing was done for methylation analysis of cytosine guanine dinucleotide (CpG) sites in the conserved noncoding sequence 2 (CNS2) region of *FOXP3* (EpigenDx). SF Tph cells were co-cultured in the presence of SEB for 5 days with memory B cells (Bmem) obtained from controls with/without a given Treg population at a ratio of 1:10:1. The percentage of plasmablasts measured by flow cytometry and total IgG level measured by ELISA served as co-culture readouts.

Results: Table 1 summarizes the study participants. FOXP3, the lineage defining transcription factor for Treg cells, was measured in Treg and T effector (Teff) cells oligo JIA SF. We identified a population of SF Tregs that co-expressed Treg ($CD4^+CD25^+CD127^{lo}FOXP3^+$) and B cell help ($PD1^{int}$) markers, which we termed T peripheral regulatory (Tpr) cells (Fig 1A-B). By contrast, T cells in the Treg gate that were $PD1^{hi}$ expressed low levels of FOXP3. Similar to PB Tregs, Tpr cells maintained a Treg-specific methylation pattern while $PD1^{hi}$ T cells did not (Fig 1C-D). Confirming their suppressive capacity, the addition of Tpr cells to Tph-Bmem co-cultures reduced plasmablast differentiation and IgG production (Fig 1E-G). Next,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

we compared RF+ poly vs. oligo JIA and found that SF Tph cells were significantly more frequent in seropositive patients (Fig 2A-B). In the SF Treg compartment, PD1^{hi} T cells predominated in RF+ poly JIA patients while PD1^{int} Tpr cells were more plentiful in oligo JIA patients (Fig 2C-D). While not statistically significant, there was a trend towards reduced plasmablast differentiation in Tph-B cell co-cultures with PD1^{int}Tpr cells compared to PD1^{hi} T cells from RF+ poly JIA patients (Fig 2E-F).

Conclusion: Tpr cells expressing intermediate levels of PD1 were enriched in the joints of oligo vs. RF+ poly JIA patients and displayed features of stable Treg cells, including robust FOXP3 expression, Treg-specific methylation patterns, and intact suppressive capacity. By contrast, the Treg compartment of seropositive JIA patients was characterized by PD1^{hi} cells that had low FOXP3 expression, lack the Treg epigenic signature, and may be less suppressive. These findings suggest that Treg fitness and ability to suppress Tph-B cell interactions may play a role in disease course.

Disclosure: K. Lam: None; **C. Harris**: None; **J. Cheng**: None; **L. AitDowd**: None; **M. Ashoor**: None; **A. Bakhsh**: None; **C. Bryant**: None; **S. Case**: None; **M. Chandler**: None; **J. Chang**: Century Therapeutics, 2; **E. Cohen**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **O. Halyabar**: None; **J. Hausmann**: None; **M. Hazen**: None; **S. Iosim**: None; **L. Kim**: None; **J. Lo**: None; **M. Lo**: None; **E. Materne**: None; **E. Meidan**: None; **M. Perron**: None; **H. Powers**: None; **M. Son**: None; **H. Wobma**: None; **M. Chang**: None; **P. Lee**: Pfizer, 2; **P. Nigrovic**: Alkermes, 2, Apollo, 2, Bristol-Myers Squibb(BMS), 5, Century, 2, Edelweiss Therapeutics, 11, Merck, 2, Monte Rosa, 2, Novartis, 2, Pfizer, 2, 5; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2.

Abstract Number: 1811

Pharmacogenomic analysis of prediction of IL-1 Inhibitor treatment response in the CARRA First-line Options for Systemic Juvenile Idiopathic Arthritis Treatment (FROST) Study

Mariana Correia Marques[1], Michael Matt[2], Sophia Chou[3], Peter Burbelo[4], Zuoming Deng[5], George Tomlinson[6], Yukiko Kimura[7], Grant Schulert[2], Michael Ombrello[8] and CARRA FROST Investigators, For the CARRA Registry investigators, [1]Translational Genetics and Genomics Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, Rockville, MD, [4]Adeno-Associated Virus Biology Section, National Institute of Dental and Craniofacial Research (NIDCR), Bethesda, [5]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [6]University of Toronto, Toronto, ON, Canada, [7]Hackensack Meridian School of Medicine, New York, NY, [8]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), North Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin (IL)-1 inhibitors are now regarded as the first line treatment option for systemic juvenile idiopathic arthritis (sJIA), however in up to half of cases there may be an incomplete response. Our objective was to evaluate the use of candidate biomarkers to predict responsiveness to IL-1 inhibition in a real-world cohort of new-onset sJIA patients who were enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry FROST study.

Methods: FROST patients who received IL-1 inhibitors and had available DNA, RNA or plasma were included. Response was defined as cJADAS10 inactive disease (≤ 2.5, without fever or steroids) at 6 months while on IL-1 monotherapy. Whole

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

genome sequencing was used to determine class II HLA alleles and *IL1RN* single nucleotide polymorphisms (SNPs) associated with poor response to IL-1 therapy (PMID: 29609200). Expression of candidate genes associated with response and non-response (PMID: 33452871) and 28 interferon stimulated gene panel (ISG-28) were measured with custom NanoString assays. IL1RA autoantibodies were measured using Luciferase Immunoprecipitation System.

Results: 17/31 (54%) patients responded to IL-1 inhibition. We found no significant differences in expression of IL-1 response genes or in ISG-28 scores; however, *STAB1*, *CD163* and *VCAN* expression were significantly higher at baseline in non-responders compared to responders. A composite geomean score of these three genes >545 yielded 78% sensitivity and 93% specificity for non-response to IL-1 inhibitors. Non-responders trended toward lower neutrophil counts at baseline (p=0.0944). 6/29 (20%) patients were positive for HLA-DRB*15. There was no difference in response rate based on homozygosity for high-expressing IL1RN SNPs, presence of HLA-DRB1*15 or HLA-DRB1*11. No patients presented with autoantibodies to IL1RA at disease onset, but 2 patients developed them at 6 months. Both patients had been exposed to anakinra and achieved clinical response, which was maintained through 18 months. 3 patients had adverse events reported which may be suggestive of a possible drug hypersensitivity reaction (2 severe injection site reactions, one hepatitis). None of these patients were positive for HLA-DRB1*15 and 2 were positive for HLA-DRB1*11. There was no significant difference in the median ISG-28 scores between baseline and follow up of patients with paired samples (329.5 vs 509.0, p = 0.42), suggesting stability of the signature.

Conclusion: In this real-world cohort of new onset sJIA patients, we confirmed that *STAB1*, *CD163* and *VCAN* expression at baseline correlated with poor response to IL1 inhibition, suggesting a different immunologic phenotype that might benefit from alternative therapy. 2 patients who responded to IL-1 inhibitors developed anti-IL1RA antibodies at follow up. We identified that IL-1 inhibitors do not significantly increase type I interferon signatures in sJIA patients. *IL1RN* SNPs and HLA-DRB1*15 were not different between responders and non-responders in this cohort. It is possible that biomarkers have less predictive effect on treatment response in new onset patients, which might include monophasic patients who will improve independently of therapy.

Disclosure: M. Correia Marques: None; **M. Matt**: None; **S. Chou**: None; **P. Burbelo**: None; **Z. Deng**: None; **G. Tomlinson**: None; **Y. Kimura**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **M. Ombrello**: None.

Abstract Number: 1812

Inflammasome and UPR activation in monocytes of HLA B27 positive children with Enthesitis related arthritis category of JIA

Shivika Guleria[1] and Amita Aggarwal[2], [1]SGPGIMS, Lucknow, Lucknow, Uttar Pradesh, India, [2]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Enthesitis related arthritis (ERA) is a chronic immune-inflammatory disease with unknown etiology. HLA-B27 is the strongest risk factor predisposing to ERA like Spondyloarthritis (SpA). In adult SpA, HLA-B27 has been associated with unfolded protein response (UPR) and inflammasome activation in monocytes. However, no data is available in ERA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table1. Clinical Characteristics and demographic details of the JIA-ERA patients

Parameter	HLA B27 Positive ERA	HLA B27 Negative ERA	p-value
Number	12	6	
Male/ Female	12/0	6/0	
Median age (years)	15 (12.25-17.5)	20.5(14.5-22.75)	**0.0497**
Median duration of illness (months)	25 (10-54)	72 (21-102)	
Arthritis	10 (83%)	3 (50%)	**<0.0001**
Enthesitis	8(66%)	0 (0%)	**<0.0001**
Sacroiliitis	8 (66%)	2 (33%)	**<0.0001**
Uveitis	0 (0%)	0 (0%)	
IBP	6 (50%)	3 (50%)	
ESR (mm/h)	48 (40-110)	23 (15.5-64)	
Family History	3 (25%)	1 (16%)	
Disease activity (JSpADa score)	4.75 (2.25-5)	1.75 (0.75-3.375)	**0.0196**

Methods: Patients with ERA and healthy controls (HC) were enrolled after informed consent. Monocytes from ERA patients and HC were separated from PBMCs/SFMCs using MACS columns. Purity and viability were checked by flow cytometry. Monocytes were stimulated with LPS (100ng/ml) and mRNA levels of TLR4, NLRP3, IL-1β, IL-18, BiP, sXBP1, CHOP, IRE1α and IL-23R were measured by qPCR. Protein levels of IL-1β and IL-18 in the culture supernatant were measured by ELISA. The caspase-1 activity was measured by flow cytometry using the Caspase 1 Kit.

Results: 12 HLA B27 positive, 6 HLA B27 negative ERA patients and 6 HLA B27 negative HC were included. Clinical features such as arthritis, enthesitis and sacroiliitis were more common in HLA-B27 positive ERA patients than in B27 negative patients (**Table1**). HLA B27 positive patients had higher disease activity compared with HLA B27 negative patients.

Monocytes of HLA-B27 positive ERA patients had more than 1.5-fold increase in mRNA expression of IL-1β, NLRP3, and TLR4 than HC. On the other hand, monocytes from HLA-B27 positive ERA patients also had more than 1.5-fold increase in mRNA expression of IL-18, NLRP3, and TLR4 as compared to monocytes from HLA-B27 negative patients. Monocytes from HLA B27 positive ERA patients produce more IL-1β than HLA B27 negative HC ($p< 0.01$). After LPS stimulation, there was further increase in mRNA expression of all the 4 genes and IL-1β production ($p< 0.001$). In comparison to HLA-B27 negative HC ($p< 0.05$) and HLA -B27 negative ERA patients ($p< 0.05$), the caspase expression was greater in HLA B27 positive ERA patients (**Figure1**). Expression of mRNA related to UPR activation (BiP and sXBP1, IRE1α) were similar in all 3 groups.

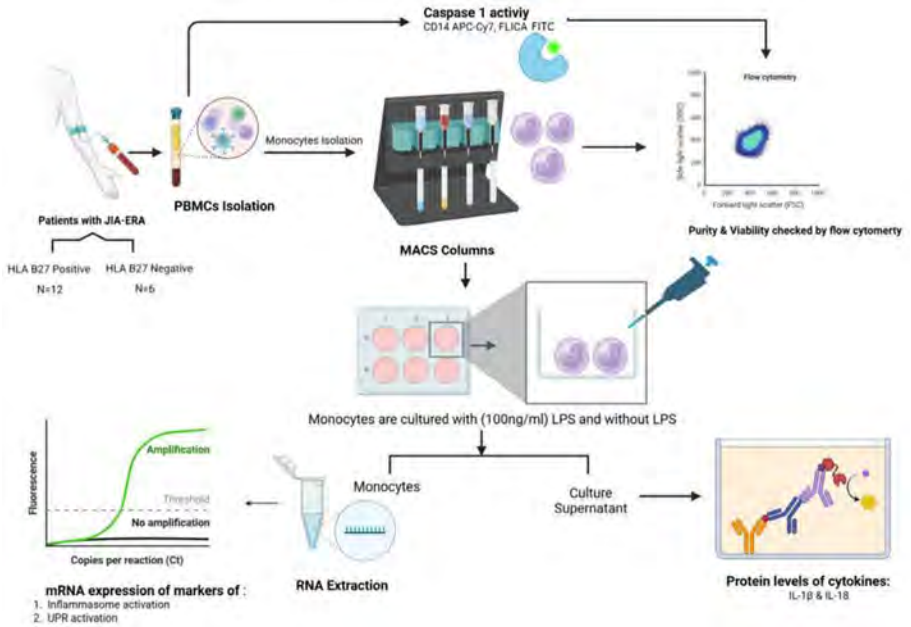


Figure1. Workflow of experiments

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

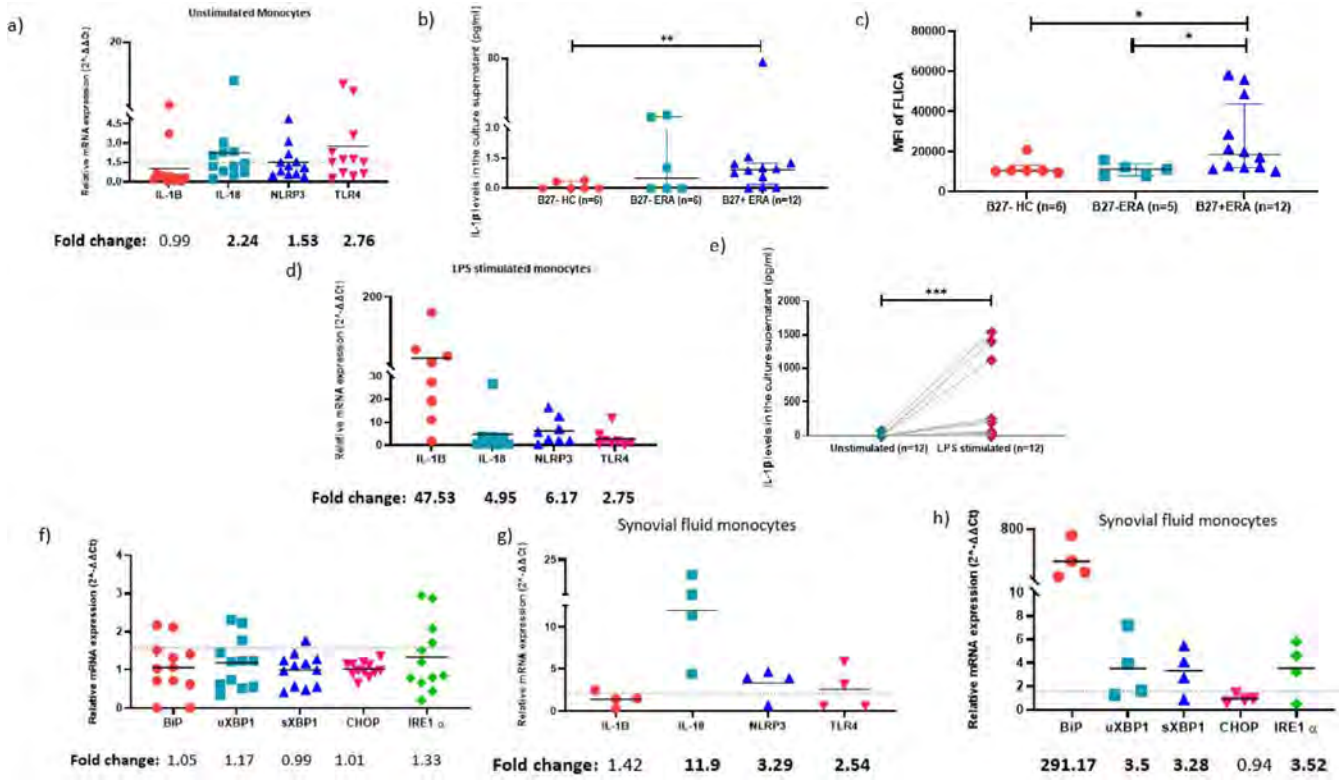


Figure2. a) Relative mRNA expression of inflammasome markers in the monocytes isolated from HLA B27 positive ERA patients compared to HLA B27 negative patients at baseline b) IL-1β levels in the culture supernatant of unstimulated monocytes of HLA B27 negative HC, HLA B27 negative patients, and HLA B27 positive ERA patients c) Mean Fluorescence Intensity (MFI) of FLICA FITC in HLA B27 negative HC, HLA B27 negative patients, and HLA B27 positive ERA patients d) Relative mRNA expression of inflammasome markers in the monocytes isolated from HLA B27 positive ERA patients after LPS stimulation e) IL-1β levels in the culture supernatant of LPS stimulated monocytes of HLA B27 positive ERA patients f) Relative mRNA expression of UPR activation markers in the monocytes isolated from HLA B27 positive ERA patients compared to HLA B27 negative patients g) Relative mRNA expression of inflammasome markers in monocytes from SFMCs compared to monocytes from PBMCs of HLA B27 positive ERA patients h) Relative mRNA expression of UPR activation markers in monocytes from SFMCs compared to monocytes from PBMCs of HLA B27 positive ERA patients

Paired analysis of monocytes from SFMCs of HLA B27 positive patients revealed 1.5-fold higher expression of IL-18, NLRP3, TLR4, BiP, sXBP 1, and IRE1α as compared to PBMCs. IL23R mRNA expression was only present in the monocytes isolated from SFMCs.

Conclusion: Activation of inflammasome pathway in the circulating monocytes and activation of both ER stress and inflammasome pathway at local site may contribute to higher inflammation burden and more severe disease in HLA-B27 positive ERA patients.

Disclosure: S. Guleria: None; **A. Aggarwal**: None.

Abstract Number: 1813

Frequency of Tissue-Specific Activated CD8+ T Cells is Correlated To Disease Severity in Juvenile Idiopathic Arthritis

Abigail Thielbar[1], Tracy Ting[2], Lexi Auld[3], Kelly Rogers[4], Megan Quinlan-Waters[5], Sheila Angeles-Han[4], Ekemini Ogbu[2], Daniel Lovell[2], Jennifer Huggins[6], Grant Schulert[2], Yuriy Baglaenko[4] and Patricia Vega-Fernandez[2], [1]Cincinnati Children's Hospital, Cincinnati, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Cincinnati Children's Hospital

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medical Center, Division of Rheumatology, Cincinnati, OH, [4]Cincinnati Children's Hospital, Cincinnati, OH, [5]Cincinnati Children's Hospital Medical Center, CCHMC, [6]Cincinnati Children's Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is characterized by joint pain and inflammation. Persistent oligoarticular JIA(oligoJIA) is defined by the involvement of up to 4 joints throughout disease course. OligoJIA can progress to an extended form of arthritis (extended-oligoJIA), involving 5 or more joints after the first 6 months of disease. Polyarticular JIA is defined as affecting 5 or more joints in the first 6 months of disease. Over 30% of children with extended-oligoJIA experience uncontrolled disease requiring the use of several immunosuppressive medications even after 8-year follow-up. Moreover, even with current treatment options, 50-60% of children with extended-oligoJIA continue to experience pain, functional disability, disease activity, and impaired quality of life extending into adulthood. There is limited understanding of the cellular composition of inflammatory tissues in JIA, particularly in the affected synovium, which is a major barrier for the identification of disease biomarkers, diagnosis, and therapeutic targeting. The purpose of this study was to identify cell subsets associated with disease progression and severity in the synovium of children with JIA.

Methods: Fourteen synovial tissue biopsies of children with oligoJIA or polyarticular JIA, were collected by ultrasound guided biopsy. Cryopreserved synovial tissue was thawed and enzymatically digested in Liberase and DNAse I, prior to staining with a comprehensive antibody panel encompassing all major immune and non-immune cell types. Matching PBMC samples were also stained for flow analysis from 5 of the individuals. Synovial fluid biomarkers were measured by Luminex.

Results: Flow cytometry analysis revealed significant differences in the cellular composition of B cells, fibroblasts, and T-cell subtypes between PBMC and synovium samples from patients with JIA. Interestingly, we note a significant difference in tissue-specific HLA-DR+ CD8+ activated T cells in polyarticular JIA when compared to oligoJIA. Extending this analysis, we discovered significant correlations of activated and regulatory CD8+ T cell states with Juvenile Arthritis Disease Activity Scores (JADAS). Synovial fluid biomarkers such as IL-18, CD25, IL-6, and IL-23 were similarly correlated to disease activity and the frequency of tissue-specific activated T cells (PD-1+ CD-8+), T peripheral helper cells (HLA-DR+ CD4+), and HLA-DR+ fibroblasts.

Conclusion: With comprehensive flow cytometry analysis, we characterized the heterogenous cellular composition of JIA in both PBMC and disaggregated synovium. We observed increased frequencies of activated T cells specifically within the synovium correlated to disease severity and synovial fluid biomarkers.

Disclosure: A. Thielbar: None; **T. Ting**: None; **L. Auld**: None; **K. Rogers**: None; **M. Quinlan-Waters**: None; **S. Angeles-Han**: None; **E. Ogbu**: Cartesian Therapeutics, 2; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **J. Huggins**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **Y. Baglaenko**: None; **P. Vega-Fernandez**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1814

Trapped in the NET: Impaired DNase function and targeted antibodies in the pathogenesis of pediatric lupus nephritis

Sohei Makita[1], Joyce Hui-Yuen[2], **Bharati Matta**[3], Betsy Barnes[4], Jenna Battaglia[5], Tatiana Borja[6], Boris Reizis[7], Lydia Thomas[8] and Kim Simpfendorfer[9], [1]NYU, New York, [2]North Shore LIJ Health System, Great Neck, NY, [3]The Feinstein Institutes for Medical Research, Manhasset, NY, [4]Northwell Health, Manhasset, NY, [5]Northwell Health, Manhasset, [6]Northwell Health- Cohen Children's Medical Center, Elmhurst, NY, [7]New York University Grossman School of Medicine, New York, NY, [8]Northwell Health - Cohen Children's Medical Center, Lake Success, NY, [9]Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Up to 80% of patients with pediatric systemic lupus erythematosus (pSLE) can present with renal abnormalities. Treatment of pSLE is often difficult and includes broad immunosuppression, which can lead to further damage, necessitating the discovery of new targets for therapy. In adult SLE (aSLE), neutrophil extracellular traps (NETs) have been shown to play a role in the development of lupus nephritis (LN). Further, loss-of-function mutations in the genes encoding for *DNASE1* and *DNASE1L3* are associated with aSLE and *DNASE1L3* mutations have been implicated in early onset monogenic lupus. Anti-NET protective antibodies have been also shown to be present in aSLE serum, thus protecting the NETs from DNASE digestion. In a cohort of treatment naïve pSLE patients with and without LN, we detected a significant increase in both blood and urinary NETs. The purpose of this study was to determine the mechanisms driving spontaneous NETosis in these patients, pre- and post-treatment, and evaluate whether NET levels may be used as an indicator of treatment response.

Methods: Plasma was obtained from 21 pSLE treatment-naïve patients, 13 post-treatment patients and 12 age- and sex-matched healthy children (pHC). Lupus disease activity was measured using SELENA-SLEDAI scoring, dsDNA antibody levels, and urine protein/creatine ratios. ELISA and smear assay were used to detect NETs in plasma and urine samples. DNase1L3 concentration was measured by ELISA, DNase enzymatic activity was determined via targeted assay (Dnase1 versus DNase1L3), NET degradation was determined with patient plasma, and blocking assays were used to assess autoantibody functionality. Targeted and whole exome sequencing was performed to identify genetic mutations. Immunofluorescence in renal biopsies was performed to evaluate NETs at end organ.

Results: Accumulation of NETs was observed with significant inhibition of DNase1 and DNase1L3 activities pre-treatment. Notably, NET levels remained high post-treatment. No known loss-of-function variants in *DNASE1L3* or *DNASE1* were found. Finally, we found higher anti-DNASE1 and anti-DNASE1L3 antibodies selectively playing role in inhibition of DNASE1L3 activity. Moreover, higher anti-NET protective antibodies were found in pLN plasma pre- and post-treatment.

Conclusion: Our data show that defective functional DNase1/1L3 activity and increased anti-NET protective antibodies drive delayed clearance and accumulation of NETs in pLN. Taken together, our results suggest NETs and the mechanisms driving spontaneous NETosis as novel non-invasive biomarkers of pLN and potential novel targets for therapy.

Disclosure: S. Makita: None; **J. Hui-Yuen**: None; **B. Matta**: None; **B. Barnes**: None; **J. Battaglia**: None; **T. Borja**: None; **B. Reizis**: None; **L. Thomas**: None; **K. Simpfendorfer**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1815

New-Onset Juvenile Spondyloarthritis is Characterized by Bone Metabolism Disturbances with Biomarker Potential

Brittney Newby[1], Timothy Brandon[1], Pamela Weiss[2] and E. John Wherry[3], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Childrens Hospital of Philadelphia, Philadelphia, PA, [3]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile spondyloarthritis (JSpA) management is hindered by the lack of reliable biomarkers to predict which patients will develop progressive structural changes, such as erosions and ankylosis. Chronic inflammation, driven by cytokines like IL-17 and TNFα, disrupts bone homeostasis by enhancing osteoclast-mediated resorption and compensatory osteoblast-driven deposition, ultimately resulting in bone damage. Bone turnover proteins may serve as potential biomarkers for disease activity and progression in JSpA. In this study, plasma levels of key regulators of bone resorption-including osteopontin (OPN), acid phosphatase 5 (ACP5), and dickkopf-1 (DKK-1)-as well as bone formation markers, such as platelet-derived growth factor-BB (PDGF-BB), and alkaline phosphatase (ALPL), were compared between JSpA patients and healthy controls.

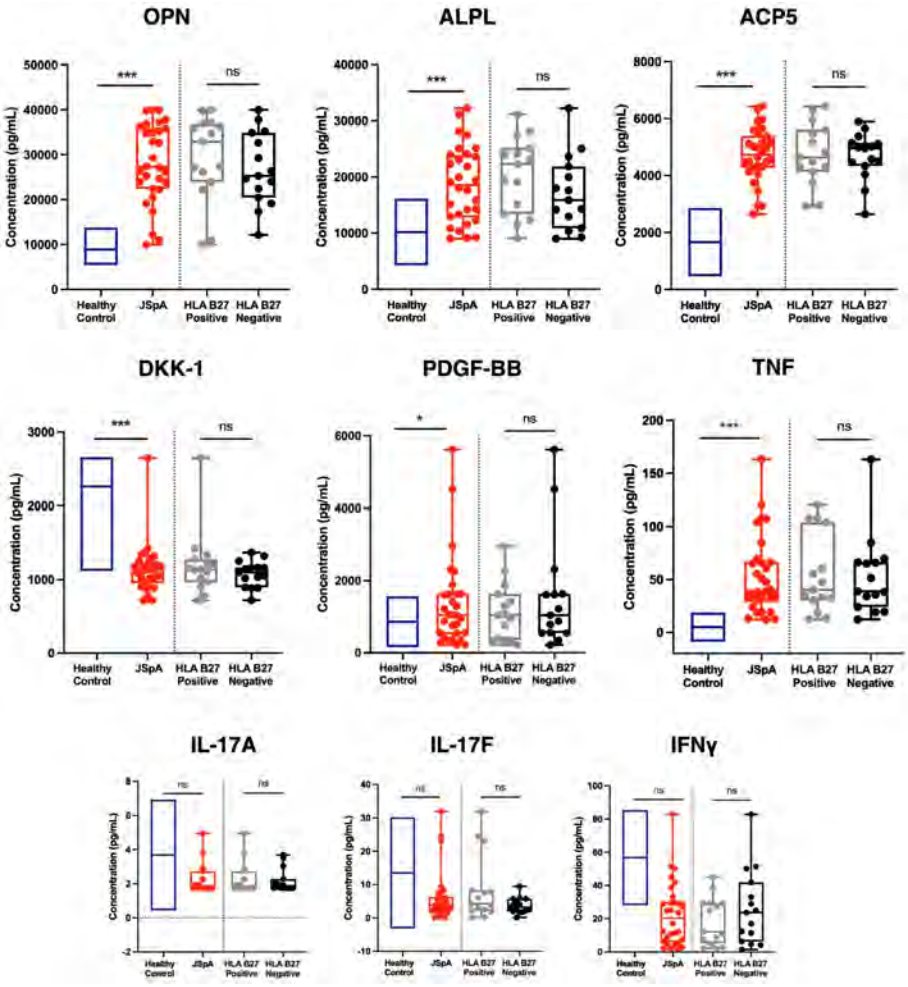
Methods: This cross-sectional, single-center study analyzed plasma samples from 30 systemic medication-naïve JSpA patients who met at least one of the following criteria: (1) International League of Associations for Rheumatology (ILAR) enthesitis-related arthritis (ERA) criteria, or (2) inflammatory sacroiliitis on MRI. Plasma concentrations of 13 bone metabolism–related proteins, along with IL-17, IFN-γ, and TNFα, were measured using the LEGENDPlex multiplex bead-based immunoassay. These levels were compared to previously published reference ranges from healthy controls using the Mann-Whitney test. Plasma concentrations were correlated with other analytes and clinical metadata using Spearman's Rank Correlation.

Results: Table 1 summarizes the demographic data and plasma protein concentrations. Compared to healthy controls, subjects with JSpA had significantly higher levels of OPN ($P < 0.0001$), ACP5 ($P < 0.0001$), and ALPL ($P < 0.0001$). In contrast, DKK-1 ($P < 0.001$) and PDGF-BB ($P = 0.004$) levels were significantly lower in JSpA patients. TNFα was significantly

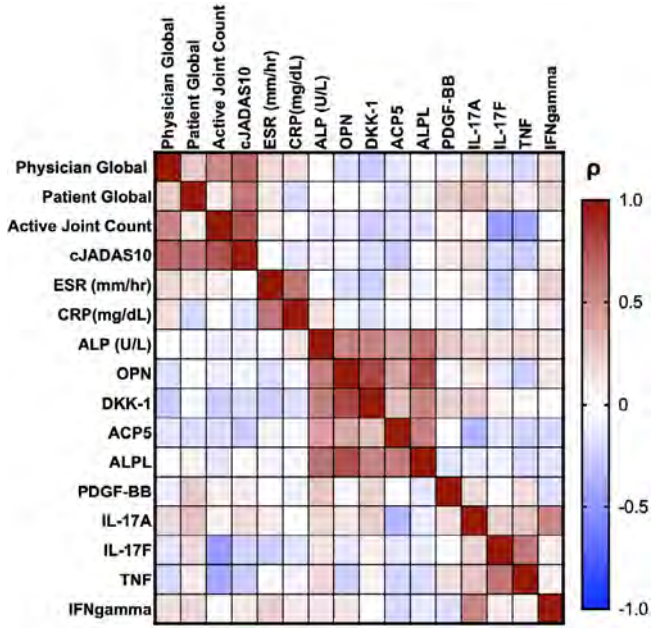
Patient Characteristics	Ref Range	JSpA	P Value
N		30	
Age (years, mean ± SD	2-19*	13.3 ± 1.9	**<0.0001**
Sex (N, % Female)		11(36.7%)	**0.0005**
HLA B27 Positive		50%	
*Age differed across studies used for establishing healthy reference ranges. Age range of the included participants are listed here.			
Plasma Protein Concentrations (pg/mL)			
Osteopontin (OPG)	10654±5172	28117 ± 8795	**<0.0001**
Dikkopf-1 (DKK-1)	2373 ± 691	1139 ±339	**<0.0001**
Acid Phosphatase 5 (ACP5)	1667 ± 613	4714 ± 957.7	**<0.0001**
Alkaline Phosphatase (ALPL)	10190 ± 3032	18688 ± 6788	**<0.0001**
Platelet Derived Growth Factor (PDGF-BB)	870 ± 360	1322±1232	**0.004**
Tumor Necrosis Factor (TNF)	5.04 ± 7.09	70.1 ± 67.0	**<0.0001**
Interleukin-17A (IL-17A)	5.25 ± 6.17	2.22 ± 0.81	0.9928
Interleukin-17F (IL-17F)	7.79 ± 11.08	6.10 ± 7.42	0.7234
Interferon gamma (IFNγ)	43.9 ± 61.7	22.4 ±19.0	0.9875
All comparisons between groups were performed using a non-parametric t-test with the Mann-Whitney test. Mean ± Standard Deviations listed throughout table			

Patient Characteristics and Comparison of Plasma Protein Concentrations in Juvenile Spondyloarthritis Patients versus Healthy Reference

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Juvenile Spondyloarthritis Patients reveal an altered bone metabolism profile



Spearman Rank Correlation Analysis of Bone Metabolism Proteins with Clinical Metadata

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

elevated in patients, whereas no significant differences were observed in IL-17 or IFN-γ. Sub analysis reveals no difference between HLA B27 positive and negative subjects. These findings are graphically represented in Figure 1. These proteins had low correlation with clinical Juvenile Arthritis Disease Activity Score (cJADAS10) and inflammatory markers (ESR and CRP), with all r between -0.25 and < 0.25 (Figure 2). OPN, ACP5, ALPL, and DKK-1 had strong, positive correlations with alkaline phosphatase activity

Conclusion: Significant differences in bone metabolism proteins were observed between JSpA patients and healthy controls, suggesting a shift toward bone resorption driven by increased osteoclast activity and disrupted bone homeostasis. Further, the low correlations observed between disease activity measures and inflammatory markers highlight the need for a multimodal approach to assessing activity in axJSpA. Further validation is needed to determine whether bone metabolism proteins could serve as biomarkers of disease progression and potential therapeutic targets.

Disclosure: B. Newby: None; **T. Brandon**: None; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1; **E. Wherry**: None.

Abstract Number: 1816

Single-Cell RNA-Transcriptomics of JDM Skin Identifies JDM-Associated Immune Cell Populations and Dysregulated Interferon Signaling in Immune and Endothelial Cells

Chioma Madubata[1], Jessica Neely[2], Christine Goudsmit[3], Celine Berthier[4], Zilan Zheng[5], Sophia Matossian[4], Jeffrey Dvergsten[6], Andrew Heaton[7], J. Michelle Kahlenberg[4], Gabrielle Fragiadakis[8] and Jessica Turnier[9], [1]UCSF, SF, CA, [2]UCSF, San Francisco, CA, [3]University of Michigan, Ann Arbor, [4]University of Michigan, Ann Arbor, MI, [5]University of California, San Francisco, San Francisco, CA, [6]Duke University Hospital, Hillsborough, NC, [7]Cure JM Foundation, Anthony, FL, [8]UCSF, San Francisco, [9]University of Michigan, Saline, MI

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy in children. JDM often presents with rash, and skin inflammation is more refractory to treatment compared to muscle inflammation. Treatments are limited due to incomplete understanding of disease pathogenesis, including under-explored analysis of the cellular composition of lesional skin, exacerbated by a lack of access to pediatric tissue. Therefore, we assembled a cohort of archival JDM skin biopsies and performed single-nuclei RNA-sequencing for an unbiased analysis of skin-specific cellular and transcriptomic drivers of JDM.

Methods: Single nuclei RNA was isolated from formalin-fixed paraffin-embedded (FFPE) skin biopsies using the 10X Genomics Flex platform; the cohort included patients with JDM (n=12) and controls (CTL, n=4). All JDM patients met 2017 EULAR/ACR classification criteria, and 11/12 were treatment-naïve at sampling. We used SoupX to remove ambient RNA, and DoubletFinder to remove doublets. We performed UMAP dimensionality reduction and Louvain clustering with Seurat. Cell clusters were annotated using published cell type-specific marker genes. Analysis of differentially expressed genes (DEG) was performed using Model-based Analysis of Single-cell Transcriptomics. Cell type abundance between JDM and CTL was analyzed with Milo and the Wilcoxon rank sum test. Gene set scores were calculated using the Seurat AddModuleScore() function. Given clinical differences between skin and muscle inflammation in JDM, we compared our skin data to a single-nuclear RNA-sequencing dataset from JDM (n=6) and control (n=7) muscle biopsy samples.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

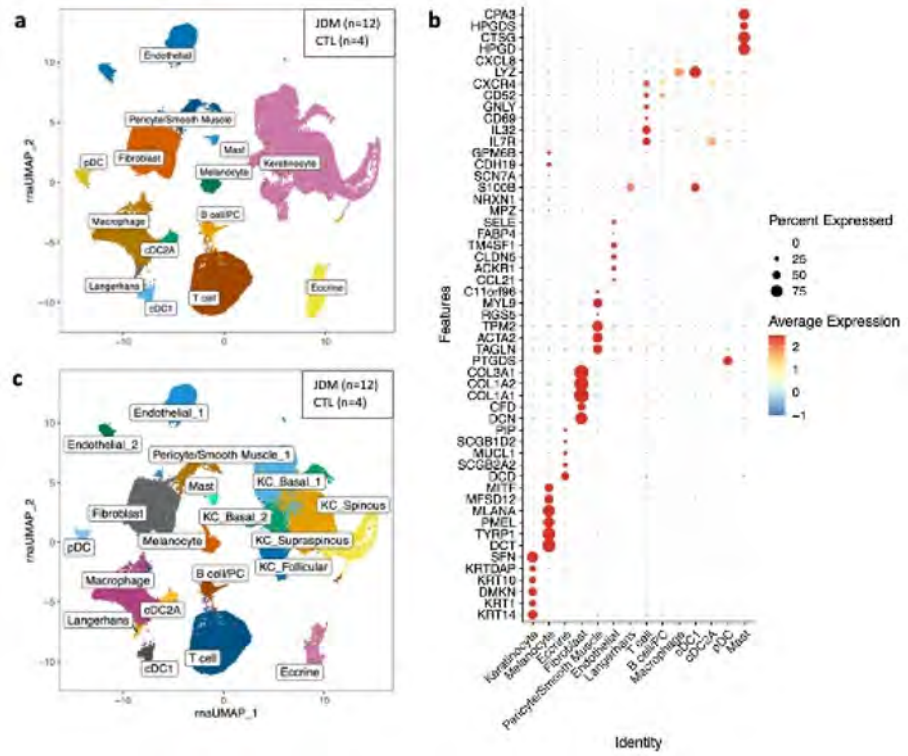


Fig 1. Single cell transcriptomics of JDM skin identifies keratinocyte, endothelial, and immune cell populations. a) UMAP plot colored by cell type. b) UMAP plot colored by cell cluster fine annotation. c) Dot plot of expression for cell type marker genes.

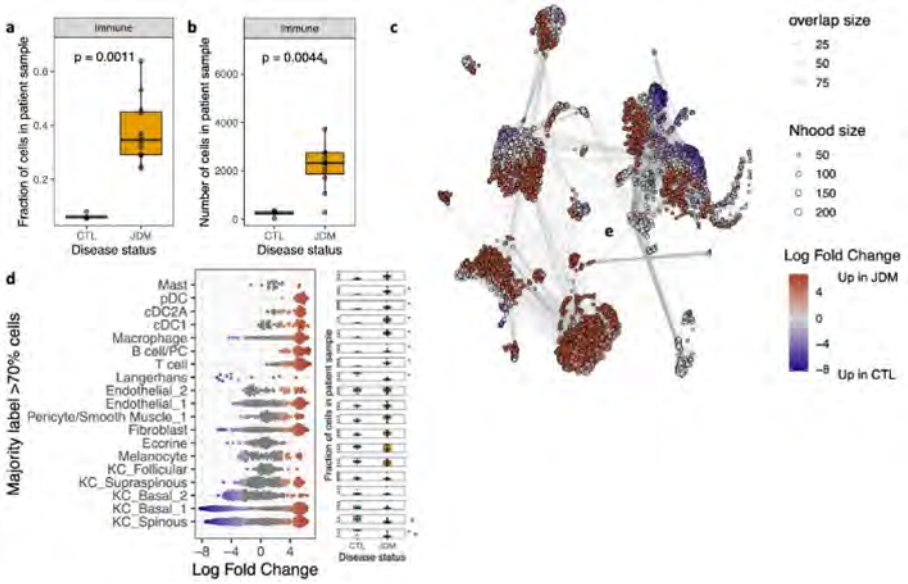


Fig 2. Immune cell clusters and neighborhoods show high abundance of cells from JDM samples. a,b) Boxplots representing the fraction (a) and number (b) of cells that come from immune cell types among all JDM or CTL cells; p-value from Wilcoxon rank-sum test. c) Neighborhood graph from Milo showing log2(fold change) of cell abundance of JDM vs CTL within a neighborhood of cells. Each node is a neighborhood of cells, with edges indicating cells in common between two neighborhoods. Graph layout reflects the position of each neighborhood's index cell within the UMAP embedding in 1a. d) Right panel) Beeswarm Milo plots showing distribution of log2(fold change) of cell abundance in neighborhoods, grouped by the majority cell type within a neighborhood (>70% of cells). Left panel) Boxplots representing the fraction of cells that come from each cell type among all JDM or CTL cells; + indicates p-value < 0.05 from Wilcoxon rank-sum test, * indicates FDR < 0.05 after Benjamini-Hochberg.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

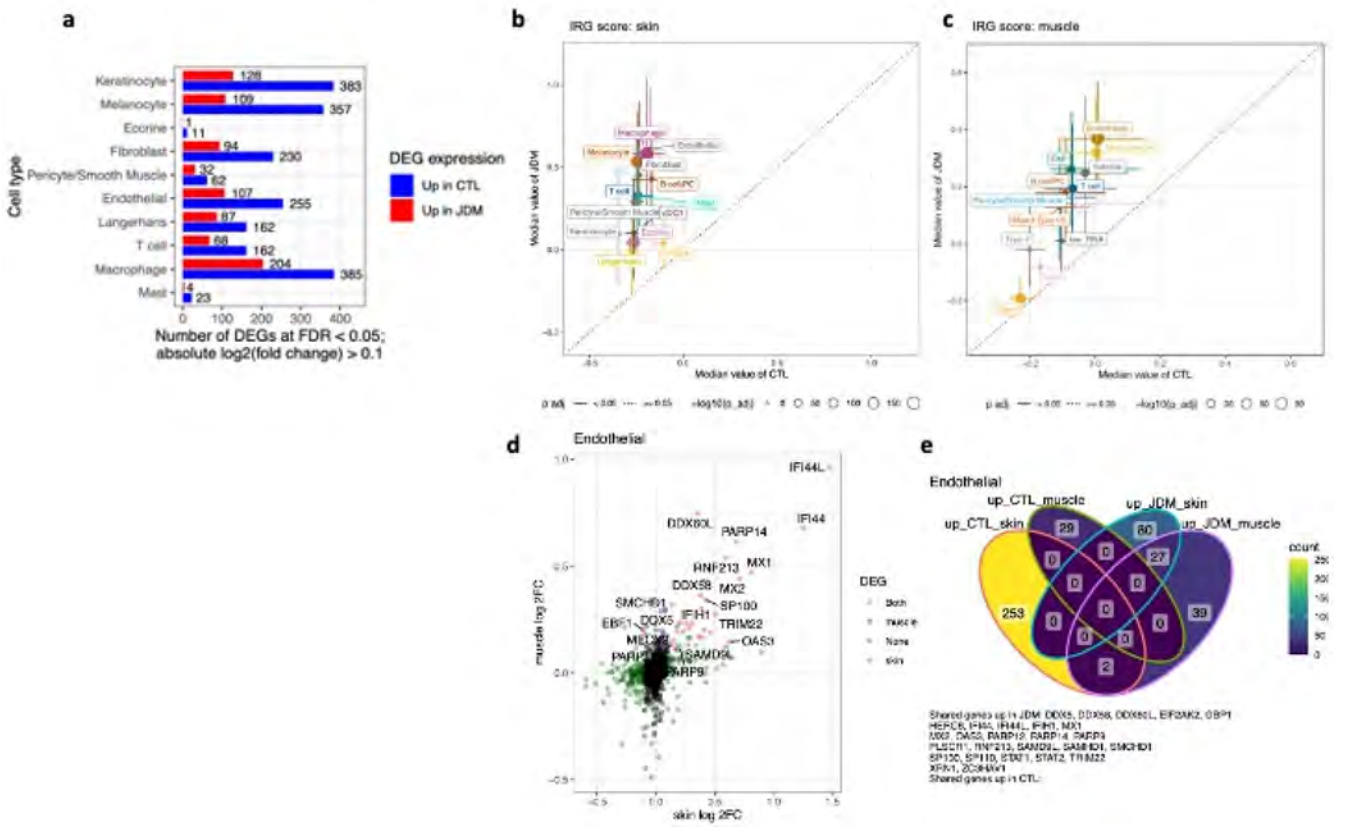


Fig 3. Endothelial cells exhibit high differential expression of IFN-response genes in both muscle and skin JDM samples. a) Number of differentially expressed genes (DEG) in each cell type that show increased expression in JDM or CTL. b,c) IRG score for b) skin samples and c) an outside muscle biopsy single-nuclei RNA-seq dataset. Scores are calculated using 28 IRG from Kim et al 2018. Dots indicate the median IRG score across all cells in a cell type from CTL samples (X-axis) and JDM samples (Y-axis); lines indicate interquartile range. d) Scatterplot comparing the log2(fold change) values of DEG analysis in muscle (X-axis) and skin (Y-axis); DEG criteria is FDR < 0.05, absolute(log2(fold change)) >0.1. e) Venn diagram comparing DEG in outside muscle data set and skin JDM atlas.

Results: From the 91,216 cells analyzed, we identified 14 major cell types (Fig 1a,b) and 20 unique cell clusters (Fig 1c). JDM samples showed increased abundance of immune cells compared to CTL (Fig 2a,b). Analysis of cellular neighborhoods also identified subsets of neighborhoods with consistently higher abundance of JDM in immune cell types (Fig 2c,d). Keratinocytes, melanocytes, endothelial cells, and macrophages showed the highest number of differentially expressed genes (Fig 3a). In all skin cell types, JDM samples had higher average expression of Interferon (IFN)-response genes (IRG) compared to CTL (Fig 3b). Endothelial cells showed the highest median IRG set expression in both JDM skin (Fib 3b) and muscle (Fig 3c), with many IRG demonstrating differential expression in both skin and muscle endothelial cells (Fig 3d,e).

Conclusion: Single cell skin transcriptomics in JDM highlights dysregulated immune and endothelial cell populations contributing to disease pathogenesis. Altered IFN is a hallmark of JDM skin tissue, with macrophages, melanocytes, and endothelial cells exhibiting the highest levels of IRG expression. While all cell types show high IRG expression in JDM, endothelial cells exhibit the highest median IRG expression in both muscle and skin. This unique single-cell atlas of JDM skin will generate critical hypotheses for investigating cellular mechanisms of JDM rash and vasculopathy and for identifying targeted therapies.

Disclosure: C. Madubata: None; **J. Neely**: None; **C. Goudsmit**: None; **C. Berthier**: None; **Z. Zheng**: None; **S. Matossian**: None; **J. Dvergsten**: None; **A. Heaton**: None; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5; **G. Fragiadakis**: None; **J. Turnier**: Cabaletta Bio, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1817

Sex-specific mechanisms associated with female childhood-onset systemic lupus erythematosus revealed by transcriptomic analysis of transgender adolescents undergoing gender-affirming sex hormone therapy.

Heather Cross[1], Hannah Peckham[1], Gary Butler[2], Elizabeth Rosser[3], Elizabeth C Jury[1], George Robinson[1] and **Coziana Ciurtin**[1], [1]University College London, London, United Kingdom, [2]University College London Hospital NHS Trust, London, England, United Kingdom, [3]University College London, London, England, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sex determinants may play a role in the immunological sexual dimorphism of childhood-onset systemic lupus erythematosus (cSLE). This study aimed to investigate the impact of sex determinants on immune transcriptomic changes and their association with cSLE.

Methods: We performed PBMC RNAseq analysis on post-pubertal cis-female adolescents with cSLE (n=74) and healthy controls (HCs, n=20), as well as transgender adolescents (trans-male, XX TM; trans-female, XY TF, n=32 samples) undergoing gender-affirming hormone therapy (GAHT) across 3 timepoints; pre-treatment, on gonadotrophin-releasing hormone agonist (GnRHa, puberty blocker) and on GAHT, TM on testosterone (T) and TF on oestradiol (E). Rstudio was used to

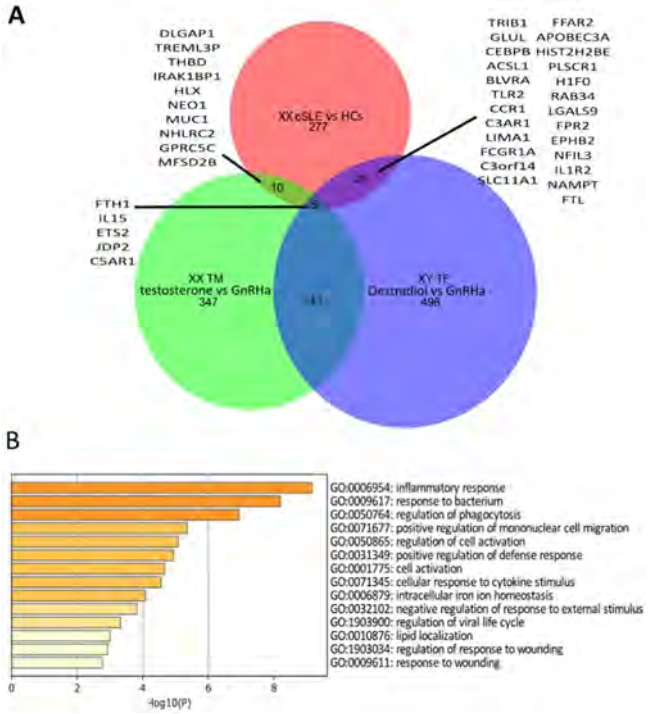


Figure 1. A. Venn diagram showing DEGs shared between cSLE cohort vs. age matched healthy controls (HCs) and transgender cohort for each distinct sex chromosomal background, comparing the effect of GAHT (XX TM receiving testosterone vs. VY TF receiving estrogen) vs. GnRHa ($P<0.05$). B. Pathway enriching analysis of the overlapping 40 DEGs between the cSLE cohort vs. HCs vs. transgender cohort, indicating the inflammatory response as being the most enriched.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

identify the significantly differentially expressed genes (DEGs, DEseq2). Pathway enrichment analysis (PEA), clustering and normalised gene count analysis were conducted with compatible software.

Results: We identified 40 DEGs (fold change >1.5, P< 0.05) in the cis-female cSLE cohort vs. HCs (defining a post-pubertal cSLE signature) that overlapped with the transgender cohort (on GAHT) **(Figure 1A**). Specifically, in the XY TF group (on E vs. GnRHa), there were 24 upregulated/1 downregulated DEGs, including TLR2 (upregulated, p= 0.0077), and IL1R2 (upregulated, p=0.018), which overlapped with the cSLE signature. Similarly, in the XX TM group (on T vs. GnRHa), there were 6 upregulated/4 downregulated overlapping DEGs, including IL15 (upregulated, p= 0.019). PEA revealed DEGs linked to the inflammatory response processes, cell migration/activation and lipid regulation (**Figure 1B**). Additionally, we discovered 63 X-linked DEGs (P < 0.05) in the GAHT vs. GnRHa groups across both XX and XY backgrounds, however, these did not overlap with the cSLE signature, suggesting a lesser impact of sex hormones on X-linked transcripts related to cSLE susceptibility. However, the X-linked non-coding RNA X-inactive specific transcript (XIST) and the XIST antisense non-coding RNA TSIX, were both significantly increased in cSLE vs. HCs (p=0.018 and 0.0007). XIST correlated negatively with cSLE interferon scores (P=0.0010, r=-0.38) and X-linked TLR7 expression (P=0.0004, r=-0.40), but TSIX did not, supporting a role for X chromosome inactivation in controlling the pathogenic mechanisms associated with cSLE in females.

Conclusion: This analysis demonstrated unique inflammatory transcriptomic changes (DEGs) induced by GAHT in transgender adolescents, which overlapped with cis-female cSLE adolescents, as well as sex hormone-independent associations between XIST expression and inflammatory cSLE pathogenic mechanisms. To our knowledge, this is the first exploration of the impact of sex hormones disaggregated from their corresponding sex chromosomal background in driving transcriptomic changes potentially relevant for understanding female cSLE pathogenesis.

Disclosure: H. Cross: None; **H. Peckham**: None; **G. Butler**: None; **E. Rosser**: None; **E. C Jury**: None; **G. Robinson**: None; **C. Ciurtin**: None.

Abstract Number: 1818

Epigenetic Profiling of Childhood-onset Lupus Reveals Distinct Epigenetic Clusters and Suggests Epigenetic Drivers of Disease Activity

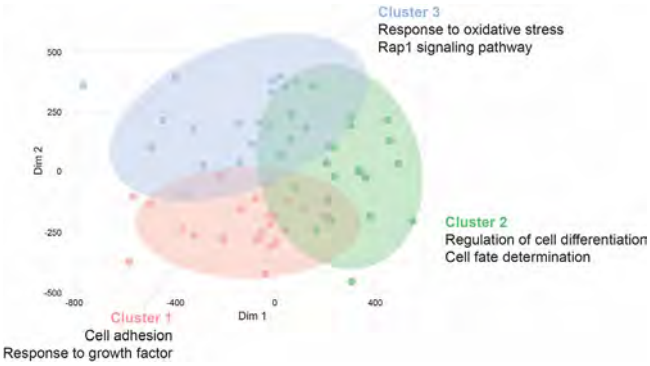
Desire Casares Marfil[1], Gülşah Kavrul Kayaalp[2], Vafa Guliyeva[2], Özlem Akgün[2], Şeyma Türkmen[3], Elif Kilic Konte[4], Seher Şener[5], Sezgin Sahin[4], Ozgur Kasapcopur[6], Betul Sozeri[7], Selçuk Sözer Tokdemir[8], Seza Kzen[9], Nuray Aktay Ayaz[2] and Amr Sawalha[1], [1]University of Pittsburgh, Pittsburgh, PA, [2]Istanbul University Faculty of Medicine, Istanbul, Turkey, [3]University of Health Sciences, Umraniye Research and Training Hospital, Istanbul, Turkey, [4]Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [5]Hacettepe University Faculty of Medicine, Ankara, Turkey, [6]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey, [7]Health sciences university, Istanbul, Turkey, [8]Istanbul University, Istanbul, Turkey, [9]Hacettepe University Medical Faculty, Ankara, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Childhood-onset lupus is generally associated with a more severe disease course than adult-onset lupus. DNA methylation alterations are known to play a key role in lupus pathogenesis. While we previously showed that childhood-onset lupus is linked to a higher genetic risk burden compared to adult-onset disease, the epigenetic landscape of childhood-onset lupus remains largely unexplored. This study aimed to characterize DNA methylation changes in childhood-onset lupus.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



K-means clustering of patients with childhood-onset lupus based on DNA methylation profiles. Hypomethylated CpG sites characteristic of each cluster were analyzed for functional enrichment, revealing significant overrepresentation in Gene Ontology (GO) biological processes and KEGG pathways.

Methods: A total of 64 patients with childhood-onset lupus and 47 healthy controls were included in this study, along with an independent validation cohort of 38 additional patients. DNA was isolated from PBMCs in the study cohort and from whole blood in the validation cohort to assess DNA methylation using the Infinium MethylationEPIC v2.0 array (Illumina). Quality controls and statistical analyses were performed using *minfi* and *limma* R packages. Methylation differences among groups were tested through linear regression, adjusting for age, sex, medication use, and cell subset compositions. Differences in clinical manifestations were assessed using Fisher's exact tests. Gene ontology enrichment analyses were performed with Metascape and GREAT.

Results: Case-control differential DNA methylation analysis revealed significant hypomethylation in interferon-regulated genes in lupus, such as *DTX3L*, *PARP9*, *IFI44L*, and *MX1*. The enrichment analysis confirmed the presence of type I interferon signature-related biological processes, consistent with adult-onset lupus. Hypomethylation in genes related to B cell activation and cellular senescence was correlated with more active disease, as measured by SLEDAI scores. K-means clustering analysis of patients based on DNA methylation patterns identified 3 distinct lupus clusters. Cluster 1 was characterized by the enrichment of hypomethylated genes involved in cell adhesion and response to growth factor pathways; Cluster 2 exhibited hypomethylation in genes related to regulation of cell differentiation and cell fate determination; and Cluster 3 was enriched in response to oxidative stress and Rap1 signaling pathway in hypomethylated genes. Sex-based analysis revealed hypomethylation in males at sites enriched in immune response pathways, with over 80% of differentially methylated positions in male individuals with childhood-onset lupus validated in the replication cohort.

Conclusion: Childhood-onset lupus is marked by significant hypomethylation in interferon-regulated genes, with DNA methylation changes correlating with disease activity and revealing distinct epigenetic molecular subgroups. Sex-specific patterns further suggest epigenetic contributions to sex-based disease heterogeneity in lupus.

Disclosure: D. Casares Marfil: None; **G. Kavrul Kayaalp**: None; **V. Guliyeva**: None; **Ö. Akgün**: None; **Ş. Türkmen**: None; **E. Kilic Konte**: None; **S. Şener**: None; **S. Sahin**: None; **O. Kasapcopur**: None; **B. Sozeri**: None; **S. Sözer Tokdemir**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **N. Aktay Ayaz**: None; **A. Sawalha**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1819

Spatial Transcriptomic Profiling Reveals Interferon Activation and CD8$^+$ T Cell Dominance in Systemic Juvenile Idiopathic Arthritis-Macrophage Activation Syndrome Liver Inflammation

Esraa Eloseily[1], Taskin Sabit[2], Lara Berklite[3], Grant Schulert[4] and Alexei Grom[4], [1]UT Southwestern Children's Medical Center, Dallas, TX, [2]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [3]Cincinnati Children's Hospital, Cincinnati, OH, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA) with macrophage activation syndrome (MAS) involves severe systemic inflammation and hepatocellular injury. Our prior histopathology studies showed increased CD8$^+$ T cell and CD163$^+$ macrophages in SJIA-MAS compared to SJIA without MAS (1). However, distinguishing SJIA-MAS liver involvement from autoimmune hepatitis (AIH), familial hemophagocytic lymphohistiocytosis (FHLH), and steatohepatitis (SH) remains challenging. We aimed to define spatial immune signatures across SJIA-MAS, AIH, FHLH, SH, and healthy controls (HC) using spatial transcriptomics with the ultimate goal to develop diagnostic biomarkers for clinical practice.

Methods: Formalin-fixed, paraffin-embedded liver tissues from SJIA-MAS (n=6), SJIA without MAS (n=1), AIH (n=7), FHLH (n=6), SH (n=5), and HC (n=6) were analyzed using the NanoString GeoMx DSP® platform. Immunofluorescent staining for CD18, CD68, CDE, and nuclear DNA was used to select regions of interest (ROIs) enriched for (1) hepatocytes; (2) macrophages, and (3) lymphocytes. Spatially resolved gene expression was Q3 normalized. In the initial analysis, levels of expression of the IFN-induced signature genes (ISG) as well as markers specific for CD4+ T cells, cytotoxic T cells (CD8, GZMb, PRF) and macrophages (CD163) were compared between the clinical groups in macrophage- and T cell-enriched compartments.

Results: SJIA-MAS samples showed strong interferon-stimulated gene (ISG) activation (STAT1, EPSTI1, CXCL9) in both macrophage and T lymphocyte enriched ROIs and higher expression of cytotoxic markers (GZMB), particularly in T cell–enriched areas, compared to mild ISG activation in SJIA without MAS (figure 1). AIH samples exhibited heterogeneous

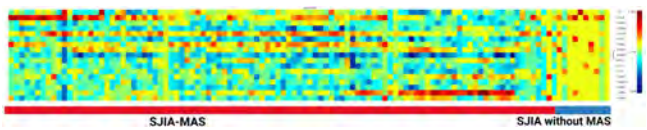


Figure 1 Heatmap showing differential expression of interferon-stimulated genes and genes and T cell markers between SJIA-MAS and SJIA without MAS

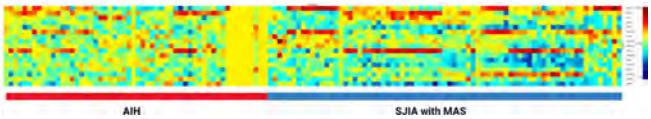


Figure 2 Heatmap showing differential expression of interferon-stimulated genes and genes and T cell markers between autoimmune hepatitis and SJIA-MAS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Spatial expression of immune markers across SJIA-MAS, SJIA without MAS, AIH, and FHLH. SJIA-MAS shows high ISG and cytotoxic signatures; other groups display lower or variable expression

Feature / Marker	SJIA-MAS	SJIA without MAS	AIH	FHLH
STAT1 / CXCL9 / EPSTI1	High (consistent across cell types)	Moderate	mild to moderate	Low to moderate
GZMB (cytotoxic markers)	High	Mild	Low	Low
CD8A (CD8+ T cell infiltration)	High	Mild	Low	Low
CD4 (CD4+ T cells)	Low	Moderate	Moderate	Low to moderate
LY6E	Low to moderate	Mild	Low to mild	Moderate to High (in macrophages)
Overall ISG intensity	Strong and widespread	Mild to moderate	Weak and inconsistent	Low to moderate, Patchy

immune profiles with variable but modest $CD4^+$ T cell expression with less prominent ISG (figure 2). FHLH shared partial interferon signatures but had lower overall ISG expression. LY6E was selectively elevated in FHLH macrophages (table 1).

Conclusion: SJIA-MAS is defined by activation and expansion of $CD8^+$ T cells in addition to strong type I/II interferon responses, distinct from SJIA without MAS, AIH, and FHLH. Particularly high expression of CXCL9 distinguished SJIA-MAS. This suggests that serum CXCL9 may help distinguish MAS-related liver injury from other SJIA-associated pathologies. Global gene expression analysis in the same samples is ongoing.

Disclosure: E. Eloseily: None; **T. Sabit**: None; **L. Berklite**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9.

Abstract Number: 1820

Cytokine profiling in refractory systemic juvenile idiopathic arthritis reveals distinct signatures for macrophage activation syndrome and lung disease.

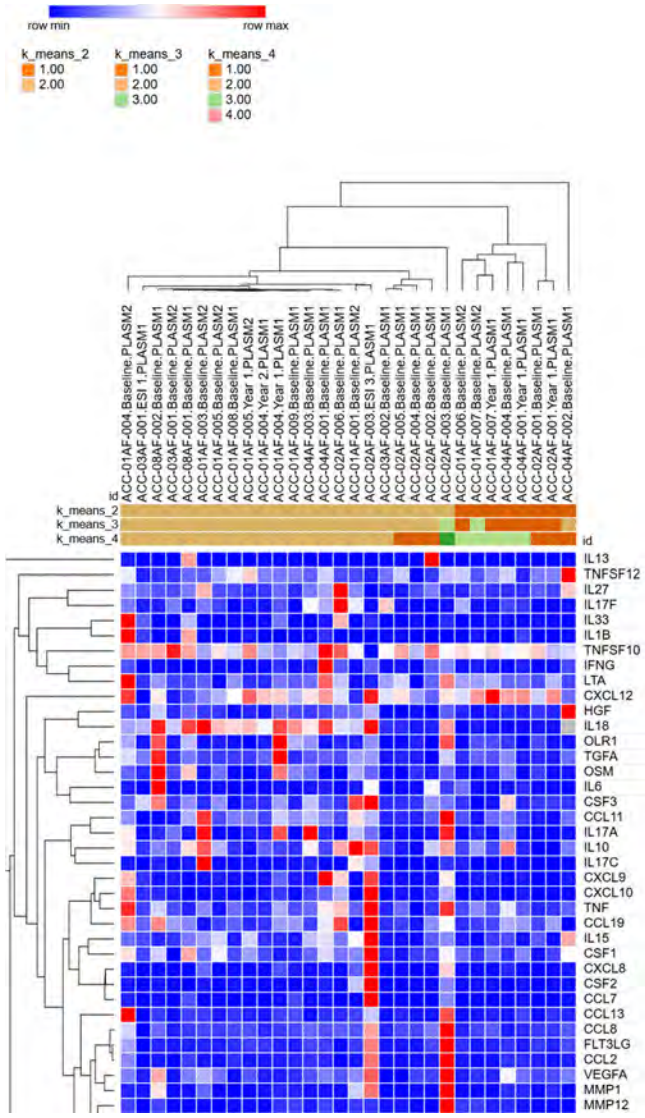
Taskin Sabit[1], Minyi Yu[2], Joy Baker[1], Sanjeev Dhakal[3], Sam Chiang[4], Scott Canna[5], Randy Cron[6], Lauren Henderson[7], Karen Onel[8], Mona Riskalla[9], Tiphanie Vogel[10], Pui Lee[11], **Grant Schulert**[2] and Alexei Grom[2], [1]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Cincinnati Children hospital, Cincinnati, OH, [4]Cincinnati Children's Hospital Medical Center, Cincinnnati, OH, [5]Children's Hospital of Philadelphia, Philadelphia, PA, [6]University of Alabama at Birmingham, Birmingham, AL, [7]Boston Children's Hospital, Watertown, MA, [8]HSS, New York, NY, [9]University of Minnesota Masonic Children's Hospital, Minneapolis, MN, [10]Baylor College of Medicine, Houston, TX, [11]Boston Children's Hospital, Newton, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (SJIA) is a severe inflammatory disorder that affects the joints as well as other organ systems, with complications including Macrophage Activation Syndrome (MAS) and Lung Disease (LD). Identification of biomarkers and cytokines remains crucial for prognosis and for defining therapeutic targets for SJIA with and without MAS and LD. In this study, we investigated plasma cytokine profiles in a large, multicenter cohort of refractory SJIA cases.

Methods: 22 SJIA patients were enrolled from 5 centers along with 6 healthy sibling controls. 11 had MAS at the onset of SJIA diagnosis, 8 had been diagnosed with LD, 4 have 1-year follow-up, 1 has 2-year follow-up. Based on clinical history, the samples were subdivided into groups as SJIA with/without MAS or LD. Plasma cytokine profiling of 37 cytokines,

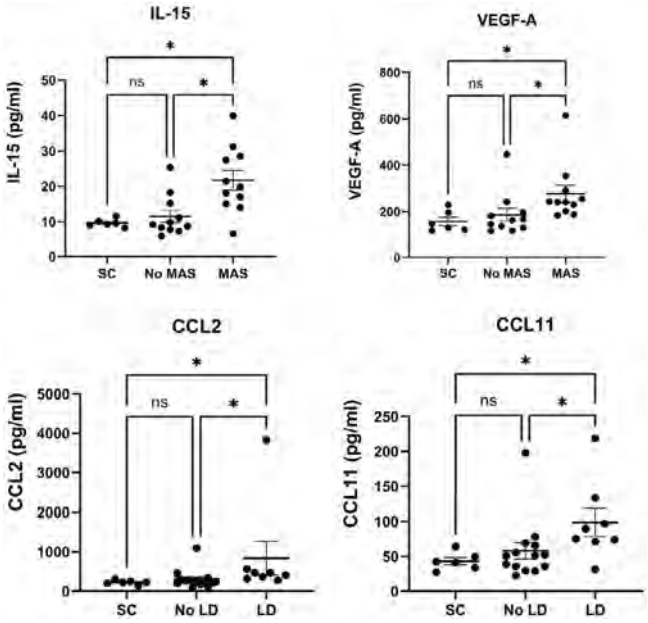
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



chemokines and immune-related signaling proteins were measured using the Target 48 Olink cytokine panel. Interferon transcriptional scores were determined using a custom Nanostring panel.

Results: Plasma levels of several cytokines—including IL-2, IL-1β, HGF, IL-7, IL-18, IFN-γ, CXCL8, CSF3, CCL7 and IL-17A—were significantly elevated in SJIA patients compared with sibling controls. Hierarchical clustering of the cytokine profiles showed that healthy controls clustered with a subset of patients samples, but were segregated from patients with SJIA and elevated IL-18. K-means clustering of patients revealed 3 distinct groups (Figure). SJIA with MAS (n=11) at onset showed an upregulation in IL-15 and Vascular Endothelial Growth Factor-A (VEGF-A) compared to the SJIA without MAS group (n=11). While CCL2 and CCL11 showed similar levels in SJIA patients without lung disease (no LD group, n=14) and sibling controls (SC group, n=6), these chemokines were significantly elevated in SJIA patients with lung disease (LD group, n=8). Of the 13 SJIA patients who underwent Interferon transcriptional score test, only one was newly diagnosed and treatment-naive, while the remaining patients had previously been diagnosed with SJIA and had already received treatment. Interferon transcriptional scores were normal in most patients, but were elevated at 3 patient visits and in one control. One patient had an elevated type I IFN score (120.5, normal range < 57) with various scratched bug bites and dry skin on shins and salves at time of sample collection. Another patient with a highly elevated type I IFN score (563.2) had a history

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



of acute illnesses at the time of sample collection (cough and congestion). Another patient, triggered by disease flare and had MAS at the time of sample collection exhibited an elevated type I IFN score of 238.5.

Conclusion: This represents a multisite, longitudinal cohort of refractory SJIA patients. Our analysis reveals a distinct biomarker signature for SJIA complications, suggesting differential immunopathogenic mechanisms. Interestingly, most patients did not have an elevated interferon score at visit 1 for the study cohort. Further work will examine how inflammatory signatures change during treatment of refractory SJIA.

Disclosure: T. Sabit: None; **M. Yu**: None; **J. Baker**: None; **S. Dhakal**: None; **S. Chiang**: None; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **R. Cron**: AbbVie/Abbott, 12, MAS Adjudication committee, American Board of Pediatrics, 12, Question writer for pediatric rheumatology boards, AS2 Biotherapeutics, 2, 12, Data Safety monitoring board, CareerPhysician, 1, 2, Neurogene, 2, Pfizer, 12, MAS Adjudication committee, Sobi, 1, 2, 5, Springer, 9, VIDA Ventures, 2; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2; **K. Onel**: None; **M. Riskalla**: SOBI, 2; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6; **P. Lee**: Pfizer, 2; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9.

Abstract Number: 1821

Transcriptiomics of tear RNA from children with active and inactive chronic anterior uveitis

Donna Do[1], Brandon Michalidas[2], Mariia Pavlenko[3], Alexandra Duell[2], Sheila Angeles-Han[4] and **Grant Schulert**[2], [1]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Cincinnati Children`s Hospital Medical Center, Cincinnati, OH, [4]Cincinnati Children's Hospital, Cincinnati, OH

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic anterior uveitis (CAU) is a potentially sight-limiting complication of pediatric rheumatic diseases, including juvenile idiopathic arthritis. However, the underlying inflammatory biology of CAU in the eye is poorly understood, and there is a critical need for improved biomarkers for CAU development, progression, and damage. Here, we developed methods for RNA collection and transcriptional profiling from tear fluid of children with CAU.

Methods: Tear fluid was collected using Schirmer strips. CAU was graded as active (anterior chamber [AC] cell ≥0.5+) or inactive (AC=0) by Standardization of Uveitis Nomenclature (SUN) criteria. RNA was extracted from fresh or frozen absorbed Schirmer strips using three methods. MagMAX-96 Total RNA Isolation Kit was used after incubating with either 140uL of Lysis/Binding, or with 500uL Phosphate Buffered Saline (PBS). Alternatively, 500uL of TRIzol Reagent (ThermoFisher) was added to each tear strip, followed by RNA extraction. Samples with RNA Integrity Number (RIN) > 4 were selected for transcriptional profiling using the Ampliseq Transcriptome Panel on the Ion Torrent sequencing system. Sequencing data was processed and aligned using Ion Torrent, and differential gene expression for genes with mean reads per million > 5 was determined using AltAnalyze ($p < 0.05$, fold change >2). Pathway analysis was performed using GO-Elite.

Results: For both RNA extraction methods using the MagMAX-96 Total RNA Isolation kit, the concentration of RNA was low and of poor quality. In contrast, for 32 samples that were extracted via TRIzol, RNA concentrations ranged from 6.9ng/uL – 69.8ng/uL with RIN numbers 1.0 – 7.8. We then performed Ampliseq Transcriptome profiling on 6 tear RNA samples from 4 patients with active CAU and 7 samples from 5 patients with inactive CAU (Table 1). One patient with active CAU was excluded after sequencing for low read quality. The remaining samples were sequenced to a mean depth of 6.4 million reads (range 4.0-9.9 million) and we identified 11,595 genes with mean expression >5 RPM. Comparing active to inactive CAU, we found 113 significantly upregulated and 35 significantly downregulated genes (Figure 1). Among the most enriched gene pathways of upregulated genes in active CAU were laminin complex (z-score 13.3, adjusted p=0.026), extracellular matrix (z-score 7.6, adjusted p=0.003), and regulation of cell migration (z-score 5.1, adjusted p=0.09). The most significantly enriched gene pathway of downregulated genes in active CAU was immune system processes (z-score 6.2, adjusted p=0.0001), including *IL7R*, *IRF5*, *NAIP*, and *NCF1*. Among the marker genes for patients with inactive CAU was MAPILC3A, which encodes LCA3, expressed in the retinal pigment epithelium, which has a key role in blood-retinal barrier and retinal immune regulation.

Table 1: Clinical and demographic features of uveitis patients in the study, as well as RNA concentration, quality, and sequencing depth.

Sample ID	Sex	Age	Diagnosis	OD/OS?	Uveitis Activity	SUN Grade	RNA concentration (ng/uL)	RIN	Sequence depth
0HHU0	F	15	Oligo JIA	OS	Inactive	0	25.4	4	4,154,389
0HHU1	F	15	Oligo JIA	OD	Inactive	0	11.7	4.1	4,039,293
0EKES	F	14	Sarcoid	OD	Active	0.5+	17.8	5.9	9,686,382
0EKFF	F	14	Sarcoid	OS	Active	0.5+	34.6	4.4	5,535,275
0EKF6	M	18	CAU	OS	Active	2+	69.6	4.4	4,762,362
0FTF7	M	18	CAU	OD	Active	2+	24.8	5.8	6,361,012
0EMZE	F	19	Psoriatic JIA	OS	Inactive	0	27.6	6.9	8,329,319
0FUHT	M	15	CAU	OD	Inactive	0	20	4.1	9,902,675
0EKF9	F	5	CAU	OS	Active	1+	15.6	3.9	4,610,757
0HHXH	M	20	CAU	OS	Inactive	0	47.9	4.5	6,482,942
0EN0A	F	19	Psoriatic JIA	OD	Inactive	0	12.7	7.8	9,391,735
0HWMX	F	10	Oligo JIA	OD	Inactive	0	9.2	5.1	9,230,240

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

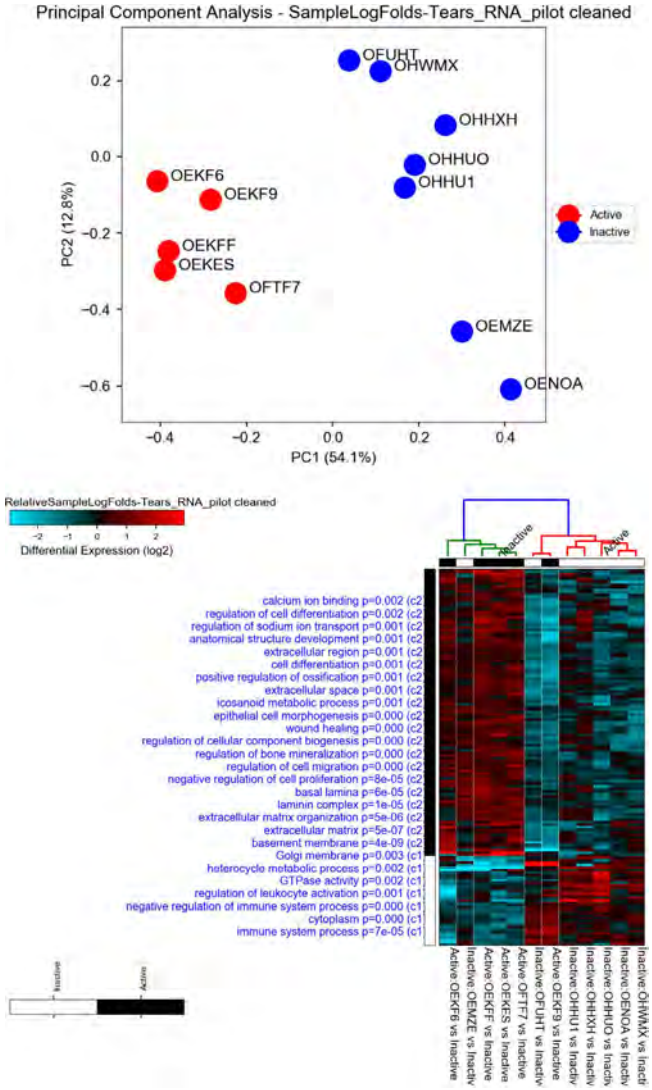


Figure 1: Transcriptomic profiling of tear RNA from chronic anterior uveitis. Top: principal component analysis of differentially expressed genes. Red= active uveitis, blue= inactive uveitis. Bottom: hierarchical clustering of differentially expressed genes between active and inactive uveitis.

Conclusion: This pilot work demonstrates our ability to obtain high-quality RNA suitable for transcriptomics from tear fluid of children with CAU. We also find that active CAU is associated with transcriptional activation in pathways associated with eye injury and blood-retinal barrier, including laminin complex, extracellular matrix, and cellular migration, as well as downregulation of inflammatory response genes.

Disclosure: D. Do: None; **B. Michalidas**: None; **M. Pavlenko**: None; **A. Duell**: None; **S. Angeles-Han**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1822

The Circulating Immune Profile of Systemic JIA Patients with HLA-DRB1*15 alleles, Eosinophilia, and Lung Disease

Jennifer Cheng[1], Alexandra Pommier[2], Ki Pui Lam[3], Evan Hsu[4], Courtney Leson[5], Kyle McBrearty[1], Itohan Aigbekaen[1], Maryam Ashoor[6], Ahmad Bakhsh[1], Carrie Bryant[1], Siobhan Case[7], Mia Chandler[1], Margaret Chang[1], Ezra Cohen[8], Fatma Dedeoglu[1], Olha Halyabar[9], Jonathan Hausmann[10], Melissa Hazen[1], Sonia Iosim[1], Liyoung Kim[6], Jeffrey Lo[1], Mindy Lo[1], Emma Materne[1], Esra Meidan[11], Megan Perron[12], Helene Powers[13], Mary Beth Son[1], Holly Wobma[1], Peter Nigrovic[6], Alicia Casey[1], Joyce Chang[1], Pui Lee[4] and Lauren Henderson[14], [1]Boston Children's Hospital, Boston, MA, [2]Harvard Medical School, Boston, MA, [3]Division of Immunology, Boston Childrens Hospital, Harvard Medical School, Boston, MA, [4]Boston Children's Hospital, Newton, MA, [5]Boston Children's Hospital, Boston, [6]Boston Children's Hospital, Brookline, MA, [7]UpToDate, Brigham and Women's Hospital, Boston Children's Hospital, Boston, MA, [8]Bmc, NEEDHAM, MA, [9]Children's Hospital/Boston Medical Center, Newton, MA, [10]Boston Children's Hospital / Massachusetts General Hospital, Cambridge, MA, [11]Boston Children's Hospital, Somerville, MA, [12]Boston Children's Hospital, Natick, MA, [13]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, [14]Boston Children's Hospital, Watertown, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: We aimed to explore the association between HLA-DRB1*15 alleles, eosinophilia, and lung disease (LD) in patients with systemic juvenile idiopathic arthritis (sJIA) through proteomic profiling of circulating immune proteins.

Table 1. Clinical Characteristics of the Study Participants

	sJIA (N=26)	Healthy Controls (N=51)*
Age at sampling (median years, IQR)	4, 8.4	5, 10
Sex (% female)	50%	55%
Self-Reported Race (n, %)		
-American Indian/Alaska Native	0, 0%	-
-Asian	2, 8%	-
-Black	3, 12%	-
-Native Hawaiian/Pacific Islander	0, 0%	-
-Other	2, 8%	-
-Undisclosed	5, 19%	-
-White	14, 53%	-
Ethnicity (n, %)		
Hispanic	4, 15%	-
Non-Hispanic	19, 73%	-
Undisclosed	3, 12%	-
HLA-DRB1*15:01 (n, %)		
Yes	8, 31%	-
No	10, 38%	-
Unknown	8, 31%	-
History of MAS (n, %)Δ		
Yes	13, 50%	-
No	13, 50%	-
Unknown	0, 0%	-
Eosinophilia @ sampling (n, %)◊		
Yes	9, 35%	-
No	17, 65%	-
Diagnosis of sJIA-LD (n, %)		
Yes	4, 15%	-
No	22, 85%	-

*Healthy controls were deidentified and only information on sex and age were available. No demographic information was available for 2/51 controls.

ΔMAS defined by the 2016 Classification Criteria for MAS in sJIA

◊Eosinophilia defined as AEC >500/μL by clinical CBC on the day the research sample was collected.

sJIA, systemic juvenile idiopathic arthritis; MAS, macrophage activation syndrome; LD, lung disease

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

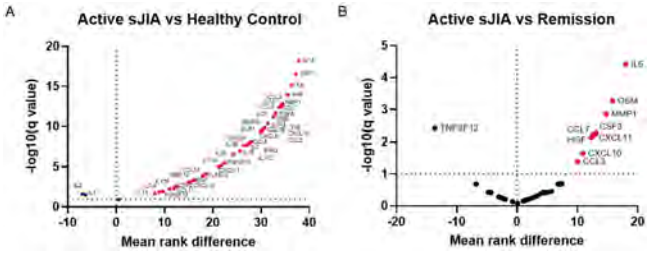


Figure 1. Differential expression of circulating immune proteins in study participants. Volcano plot of immune proteins from plasma in patients with A) active sJIA (n=25) vs. healthy controls (n=51), and B) active sJIA vs. sJIA patients in remission (n=21). Dots in red are significantly higher in patients with active sJIA than the comparison group, with dots in blue representing significantly lower levels. Statistics: Mann-Whitney U tests corrected for an FDR of 0.1. sJIA, systemic juvenile idiopathic arthritis; CCL, C-C motif chemokine; CSF, colony stimulating factor; CXCL, C-X-C motif chemokine; EGF, pro-epidermal growth factor; FLT3LG, fms-related tyrosine kinase 3 ligand; HGF, hepatocyte growth factor; IFNG, interferon gamma; IL, interleukin; LTA, lymphotoxin-alpha; MMP, matrix metallopeptidase; OLR, oxidized low-density lipoprotein receptor; OSM, oncostatin-M; TGFA, transforming growth factor alpha; TNF, tumor necrosis factor; TNFSF, tumor necrosis factor ligand superfamily; TSLP, thymic stromal lymphopoietin; VEGFA, vascular endothelial growth factor A.

Methods: Peripheral blood (PB) was obtained from children with sJIA (PRINTO criteria) and healthy controls evaluated at our center. Disease status (active/remission) was defined by the treating clinician and confirmed through chart review based on the presence/absence of fever, rash, arthritis, serositis, hepatosplenomegaly, and/or elevated inflammatory markers. Eosinophilia was defined as an absolute eosinophil count (AEC) > 500/μl. A pulmonologist adjudicated the diagnosis of sJIA-LD. HLA typing was done on a clinical basis or through research testing of samples in our institutional biorepository. A proximity extension assay (PEA, Olink Proteomics) was used to profile 45 immune proteins in plasma. Mann-Whitney U tests corrected for an FDR of 0.1 for our discovery analysis were used to compare groups. Volcano plots were generated with GraphPad Prism while PCA plots were created with Clustvis Web Tool.

Results: Table 1 summarizes study participants. Most sJIA patients treated with IL-1 inhibitors at the time of sampling. As expected, broad differences in protein expression were found between active sJIA patients and controls (Fig1A). Previously reported sJIA biomarkers, CCL7, CXCL10, CXCL11, HGF, IL-6, MMP1, and OSM, were confirmed to be significantly elevated in patients with active disease compared to those in remission (Fig1B). We also identified novel proteins differentially expressed in this comparison, including CCL3, CSF3, and TNFSF12/TWEAK (Fig1B). Next, we evaluated sJIA patients with or without eosinophilia at the time of sampling, stratified by disease activity. By univariate testing, IL-33 was elevated in sJIA

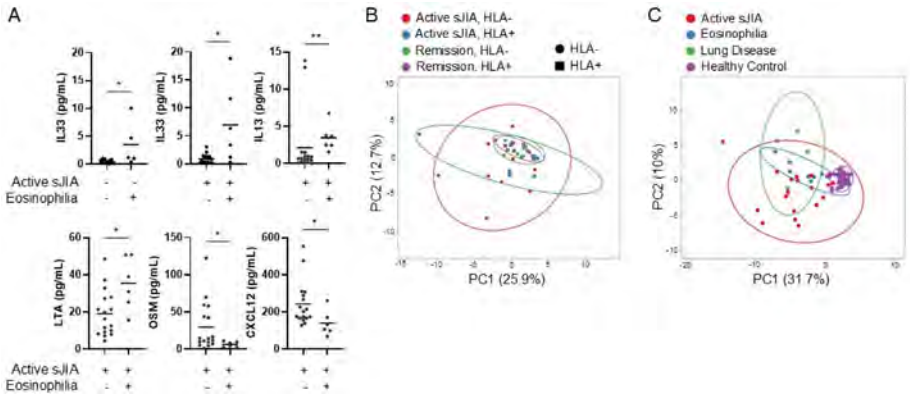


Figure 2. Immune profile of patients with sJIA and eosinophilia. A) Expression level of the given immune protein found in the plasma of patients with sJIA in remission with (n=5) and without eosinophilia (n=12) or during active disease with (n=6) and without eosinophilia (n=17). Eosinophilia was defined as AEC >500/μL by clinical CBC on the day the research sample was collected. Only the immune proteins that were significantly different based on Mann-Whitney U tests are reported. P value, ns, >0.05; *, ≤ 0.05; **, ≤ 0.01. No significance was found after correction for multiple comparison. B-C) PCA plots using z-scores for all 45 proteins in the PEA were included. 95% confidence level was used for ellipses. B) Groupings of patients during active sJIA with (n=8) and without HLA-DRB1*15:01 alleles (n=11), and patients in remission with (n=7) and without HLA-DRB1*15:01 alleles (n=9) are shown in their respective colors. C) Groupings of patients with active sJIA (n=19), healthy controls (n=51), patients with eosinophilia (n=8), and patients with sJIA-LD (n=4) are shown in their respective colors. sJIA, systemic juvenile idiopathic arthritis; AEC, absolute eosinophil count; PEA, proximity extension assay; CXCL, C-X-C motif chemokine; IL, interleukin; LTA, lymphotoxin-alpha; OSM, oncostatin-M

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients with vs. without eosinophilia, regardless of disease status (Fig2A). In patients with active sJIA, IL-13 and LTA were increased while CXCL12 and OSM were decreased in those with vs. without eosinophilia (univariate testing) (Fig 2A). Levels of circulating immune proteins were not significantly different in patients with and without HLA-DRB1*15:01 alleles when stratified by disease activity and PCA confirmed this finding (Fig2B). Finally, PCA showed that samples obtained from sJIA patients during an episode of eosinophilia closely associated with samples from patients with sJIA-LD who did not have eosinophilia at the time of testing (Fig 2C).

Conclusion: We identified a network of immune proteins in sJIA linked with eosinophilia and type 2-related cytokines. This includes OSM, an IL-6 family member that induces eotaxin-1 release, in sJIA patients with active disease. The IL-1 cytokine family member IL-33, which induces innate lymphoid 2 cells (ILC2s) to produce IL-4, -5, and -13, was associated with eosinophilia in sJIA patients. HLA status did not significantly impact the profile of circulating immune proteins in this cohort. Our studies suggest that the sJIA cytokine milieu may promote type-2 immunity and these responses are likely important in patients who develop eosinophilia and lung disease.

Disclosure: J. Cheng: None; **A. Pommier**: None; **K. Lam**: None; **E. Hsu**: None; **C. Leson**: None; **K. McBrearty**: None; **I. Aigbekaen**: None; **M. Ashoor**: None; **A. Bakhsh**: None; **C. Bryant**: None; **S. Case**: None; **M. Chandler**: None; **M. Chang**: None; **E. Cohen**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **O. Halyabar**: None; **J. Hausmann**: None; **M. Hazen**: None; **S. Iosim**: None; **L. Kim**: None; **J. Lo**: None; **M. Lo**: None; **E. Materne**: None; **E. Meidan**: None; **M. Perron**: None; **H. Powers**: None; **M. Son**: None; **H. Wobma**: None; **P. Nigrovic**: Alkermes, 2, Apollo, 2, Bristol-Myers Squibb(BMS), 5, Century, 2, Edelweiss Therapeutics, 11, Merck, 2, Monte Rosa, 2, Novartis, 2, Pfizer, 2, 5; **A. Casey**: None; **J. Chang**: Century Therapeutics, 2; **P. Lee**: Pfizer, 2; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2.

Abstract Number: 1823

Genome-Wide DNA Methylation Analysis in Familial Mediterranean Fever

Kader Cetin Gedik[1], Desire Casares Marfil[2], Busra Baser Taskin[3], Elif Kilic Konte[4], Sezgin Sahin[4], Mckenna Bowes[2], Ferhat Guzel[5], Micol Romano[6], Ozgur Kasapcopur[7], Nuray Aktay Ayaz[3], Erkan Demirkaya[6] and Amr Sawalha[2], [1]UPMC Children's Hospital of Pittsburgh/University of Pittsburgh, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, PA, [3]Istanbul University Medical School, Istanbul, Turkey, [4]Istanbul University Cerrahpasa Medical School, Istanbul, Turkey, [5]Department of Research and Development, Ant Biotechnology, Istanbul, Turkey, [6]University of Western Ontario, London, ON, Canada, [7]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, istanbul, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Familial Mediterranean fever (FMF) is an autoinflammatory disease most commonly associated with biallelic mutations in the *MEFV* gene. Patients carrying the same pathogenic variant in *MEFV* can exhibit a broad spectrum of clinical phenotypes. Identifying factors contributing to this clinical variability is essential for understanding disease mechanisms. DNA methylation has been proposed as a potential modifier of *MEFV* mutations and clinical presentation. However, prior studies exploring this hypothesis included heterogeneous cohorts, lacked genome-wide methylation analyses, and yielded inconsistent findings. We aimed to investigate the role of DNA methylation in FMF using a genome-wide DNA methylation approach.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a cross-sectional, genome-wide DNA methylation analysis using whole blood samples from pediatric FMF patients and age- and ethnicity-matched healthy controls (2:1 ratio), all recruited from Istanbul University Medical School. To minimize confounding, we included only patients homozygous for the M694V mutation and from the same geographical region. DNA methylation profiling was performed using the Illumina Infinium MethylationEPIC v2.0 BeadChip array, covering over 930,000 CpG sites. Data analysis was conducted in R (v4.4.0), adjusting for age, sex, and cell composition.

Results: We identified 22 differentially methylated CpG sites in 32 FMF patients compared with 16 healthy controls. Of these, 18 were hypomethylated—including a CpG site within the *MEFV* gene—and four were hypermethylated. Notably, several differentially methylated CpGs were located in genes encoding zinc finger proteins, a family of transcriptional regulators. Of the 22 CpGs, 13 were found on chromosome 16, where *MEFV* is located. Three hypomethylated CpGs were within 1.1 kb of the *MEFV* transcription start site, two of which overlapped with enhancer regions, suggesting a potential regulatory role. Cell-type–specific analysis revealed significant differential methylation in NK cells, $CD8^+$ T cells, and $CD4^+$ T cells in FMF patients compared with controls.

Conclusion: Our findings suggest that DNA methylation changes may contribute to the pathogenesis of FMF. The enrichment of differentially methylated sites near *MEFV* on chromosome 16 and in immune cell subsets supports a role for epigenetic regulation in disease expression. These results highlight DNA methylation as a potential modifier of FMF and a promising target for future biomarker development and personalized therapeutic strategies.

Disclosure: K. Cetin Gedik: None; **D. Casares Marfil**: None; **B. Baser Taskin**: None; **E. Kilic Konte**: None; **S. Sahin**: None; **M. Bowes**: None; **F. Guzel**: None; **M. Romano**: None; **O. Kasapcopur**: None; **N. Aktay Ayaz**: None; **E. Demirkaya**: None; **A. Sawalha**: None.

Abstract Number: 1824

Tissue-Resident Natural Killer Cells May Drive Monocyte Differentiation And Macrophage Accumulation In The Inflamed Joints Of Pediatric Juvenile Idiopathic Arthritis Patients

Roselyn Fierkens[1], Jun Inamo[2], Clara Lin[3], Nathan Rogers[4], Kari Hayes[1], Heather Leach[3] and Kentaro Yomogida[1], [1]University of Colorado, Aurora, CO, [2]University of Colorado School of Medicine, Aurora, CO, [3]Children's Hospital Colorado, Aurora, [4]Children's Hospital Colorado, Aurora, CO

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Natural Killer (NK) cells are the most abundant innate lymphoid cells, accounting for 10–40% of total lymphocytes in peripheral blood. They adapt to diverse tissue microenvironments and exert tissue-specific functions. Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis of childhood, with oligoarticular/polyarticular (oligo/poly JIA) subtypes comprising about 80% of cases. Although JIA research has primarily focused on T cells, the role of NK cells remains underexplored despite their abundance and potent immunomodulatory functions.

Methods: Peripheral blood, synovial fluid, and synovial tissue biopsies were obtained from children diagnosed with oligoarticular JIA or RF-negative polyarticular JIA, meeting the ACR criteria for JIA. Lymphocytes were isolated using density

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

gradient centrifugation. Cells were analyzed for comprehensive profiling and stimulated to evaluate cytokine production. Synovial tissue biopsy was fixed and assayed for spatial transcriptomics using 10x genomics protocol. Cell types were evaluated for colocalization within the inflamed tissue.

Results: NK cells were classified into two subsets based on CD56 expression: cytotoxic $CD56^{dim}$ and immunomodulatory $CD56^{bright}$. We discovered that the immunomodulatory $CD56^{bright}$ subset was predominant in JIA synovial fluid, whereas the cytotoxic $CD56^{dim}$ subset made up the majority of peripheral NK cells. These synovial NK cells expressed tissue-residency markers such as CD49a, CD103, and CD69. Functionally, synovial NK cells produced abundant cytokines, including IFN-γ and TNF-α. Although previous reports have identified T cells as the primary producers of GM-CSF in inflammatory arthritis, our data showed that synovial NK cells were one of the main producers of GM-CSF alongside T cells. With GM-CSF being an established stimulant of monocyte differentiation, we analyzed spatial transcriptomic data obtained from synovial tissue biopsy. Here, NK cells were found to be consistently in close proximity with macrophages.

Conclusion: Our data suggests that tissue-resident synovial NK cells may drive monocyte differentiation and macrophage accumulation through elevated GM-CSF secretion, acting as a mechanism to exacerbate inflammation in juvenile arthritis. Our findings reveal novel immunoregulatory functions of synovial NK cells, highlighting their significance in understanding JIA disease pathogenesis and treatment.

Disclosure: R. Fierkens: None; **J. Inamo**: None; **C. Lin**: None; **N. Rogers**: None; **K. Hayes**: None; **H. Leach**: None; **K. Yomogida**: None.

Abstract Number: 1825

Serum proteomic and single cell RNA sequencing analysis reveals macrophage activation syndrome physiology and widespread complement dysregulation are associated with severe dengue infection in a pediatric cohort

Sarah McCuaig[1], Molly Gallagher[1], Yentli E. Soto Albrecht[2], Francia Acosta[3], Shanti Turbi-Cornielle[4], Reyna Soriano[4], Eugenia Gonzalez-Diaz[4], Vincenta Sanchez[5], Elsa Herrera[6], Aide Cornielle[4], Anabel Fernandez[1], Adriana LaMonte[1], Sarah E Henrickson[1], Laura Vella[1], Andrew P Steenhoff[7] and Edward Behrens[8], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [3]Ninos Primeros en Salud Program, Consuelo, Dominican Republic, [4]Universidad Central del Este, San Pedro de Macorís, Dominican Republic, [5]Robert Reid Cabral Children's Hospital, Santo Domingo, Dominican Republic, [6]Dr. Antonio Musa Regional Hospital, San Pedro de Macorís, Dominican Republic, [7]Children's Hospital of Philadelphia, Philadelphia, [8]CHOP, West Chester, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Dengue virus (DENV) is a global public health threat that is increasing in incidence and endogenous DENV infections are expected to dramatically rise in the US. DENV has four serotypes (DENV1-4) and infection with any serotype can cause two main syndromes: 1) mild disease characterized by non-specific symptoms including fever, rash, and musculoskeletal pain, and 2) severe disease/hemorrhagic fever that can rapidly lead to multi-organ failure and death. However, the immunologic drivers of severe disease remain poorly understood. Using serum proteomics and peripheral

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

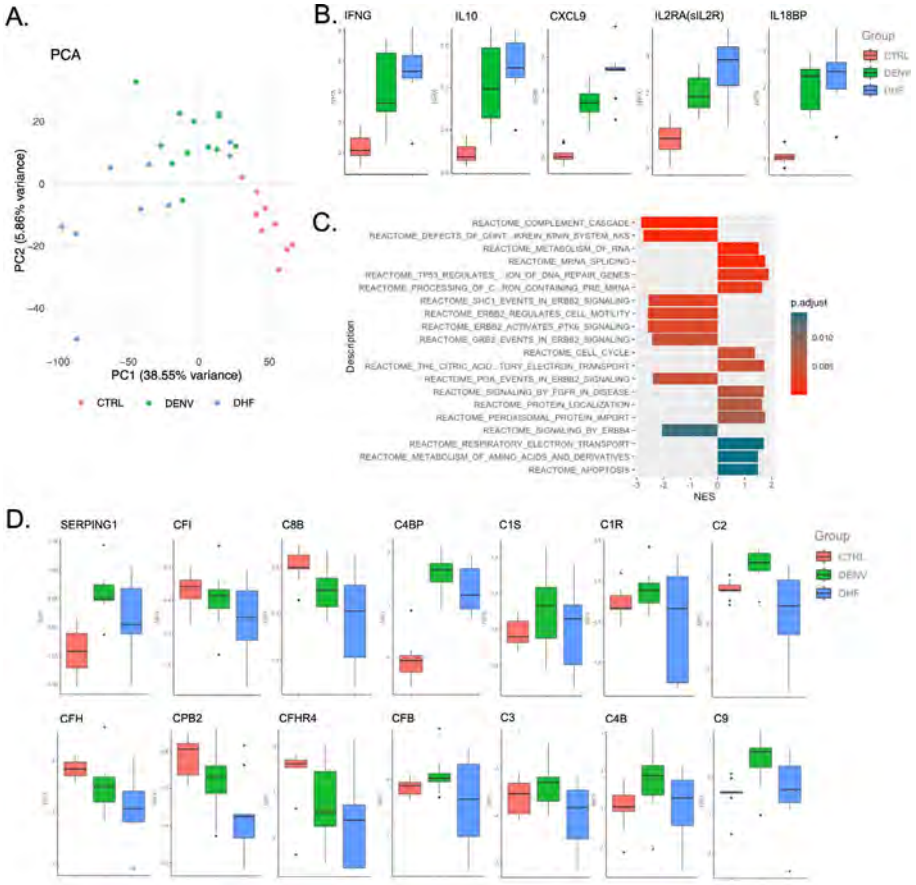


Figure 1 – Serum proteomic analysis reveals upregulation of MAS biomarkers and complement dysregulation are features of severe dengue. (A) Principal component analysis of serum proteomic data from pediatric control (CTRL, N=9), mild dengue infection (DENV, N=12), and severe dengue/dengue hemorrhagic fever (DHF, N=9). (B) Box and whisker plots showing expression of the MAS associated proteins IFNG, IL10, CXCL9, IL2RA (sIL2R), IL18BP. (C) Reactome pathway analysis of significantly differentially expressed proteins comparing DHF to DENV. (D) Box and whisker plots of expression of the individual proteins that make up the Reactome Complement Cascade pathway. NPX = O-link's Normalized Protein Expression.

blood mononuclear cell (PBMC) single cell RNA sequencing (scRNAseq) from pediatric patients with mild and severe dengue infection we interrogated immunologic factors associated with severe disease.

Methods: In this cross-sectional study, sera and PBMCs were collected from pediatric patients with mild dengue (DENV) (N=12) and severe dengue/hemorrhagic fever (DHF) (N=9) at the Robert Reid Cabral Children's and Antonio Musa District Hospitals, Dominican Republic and from age-matched healthy controls (N=9) at the Children's Hospital of Philadelphia. Serum proteomics was performed using the O-link Explore HT platform. 5' scRNAseq was performed using the 10X Genomics platform. Data analysis was performed in R.

Results: Principal component analysis of ~5000 serum proteins revealed 3 distinct clusters that separate DHF, DENV, and healthy controls (Figure 1A). DHF patients showed upregulation of multiple biomarkers consistent with Macrophage Activation Syndrome (MAS) physiology (Figure 1B). Additionally, pathway analysis performed on the significantly differentially expressed proteins (DEPs) comparing DHF to DENV demonstrated complement activation was the most significantly altered pathway (Figure 1C). Examination of the specific proteins that drive this difference showed widespread consumption of complement proteins across the complement cascade (Figure 1D). scRNAseq analysis showed increased *IFNG* transcription in *IFNG*-positive cells in DHF compared to DENV, consistent with the serum protein MAS markers (Figure 2A,B). Furthermore, the monocyte cluster is altered in DHF compared to DENV and healthy controls (Figure 2B). Re-clustering of the monocytes showed an increase in 4 monocyte subclusters in DHF (Figure 2C). Differential expression analysis to identify

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

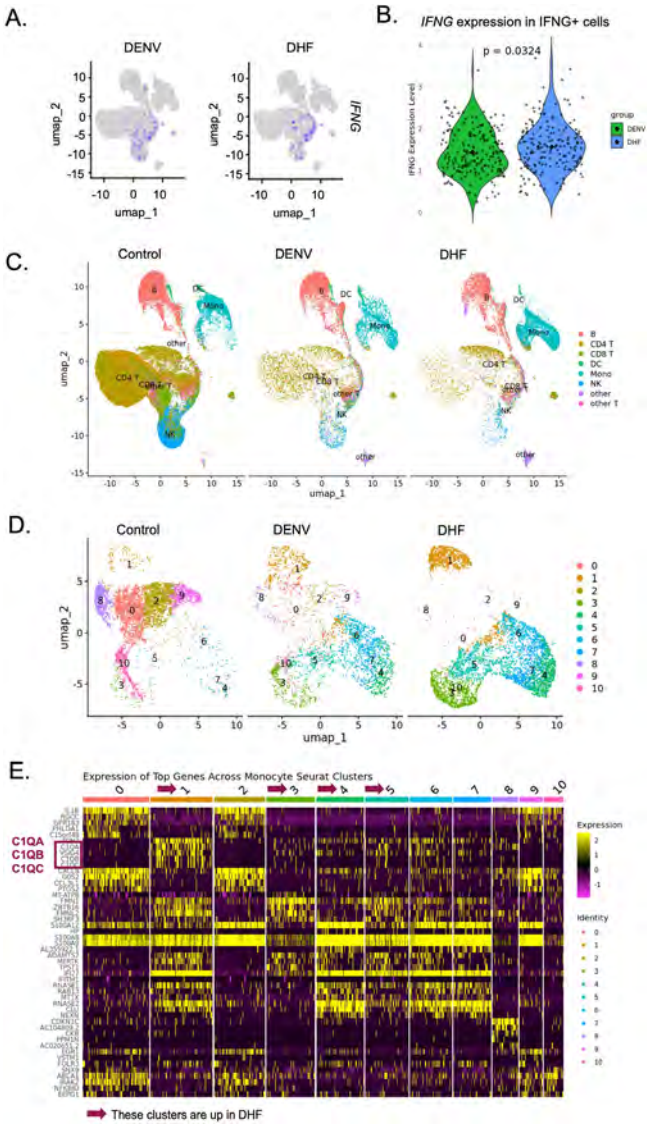


Figure 2 – scRNAseq of PBMCs from patients with dengue infection shows increased IFNG expression and an altered monocyte compartment with overrepresentation of a subpopulation expressing early complement genes in severe dengue. (A) UMAP projection overlayed with IFNG transcription in mild dengue infection (DENV, N=9) and severe dengue/dengue hemorrhagic fever (DHF, N=6). (B) Violin plot of IFNG expression among all IFNG positive cells in DENV (N=9) and DHF (N=6). P value determined by unpaired T-test. (C) UMAP projection showing Azimuth l1 annotated cell types stratified by disease state; pediatric control (control, N=5), DENV (N=9), DHF (N=6). (D) UMAP projection showing Seurat clusters following re-clustering of the Monocyte population, stratified by disease state; control (N=5), DENV (N=9), DHF (N=6). (E) Heatmap of top differentially expressed genes that define each of the Monocyte Seurat Clusters. Clusters 1,3,4,5 are overrepresented in DHF (marked by red arrows). The red box highlights the genes that are uniquely upregulated in Cluster 1, which are composed of the genes for the C1q complement complex.

the top genes that define each cluster revealed that one of these clusters was characterized by early complement gene expression (*C1QA, C1QB, C1QC*) (Figure 2D).

Conclusion: We have identified MAS and complement dysregulation as unique features of severe dengue. Serum proteomics showed elevated IFNg and CXCL9 as well as consumption of complement proteins and loss of complement regulatory proteins that typically constrain complement activation. *IFNG* was also increased at the transcriptional level. Moreover, monocytes expressing early complement components are overrepresented in severe dengue patients. These findings may unveil factors that predispose to risk of developing severe dengue and support precision immunomodulation with either MAS directed or complement inhibiting therapies in severe dengue.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. McCuaig: None; **M. Gallagher**: None; **Y. Soto Albrecht**: None; **F. Acosta**: None; **S. Turbi-Cornielle**: None; **R. Soriano**: None; **E. Gonzalez-Diaz**: None; **V. Sanchez**: None; **E. Herrera**: None; **A. Cornielle**: None; **A. Fernandez**: None; **A. LaMonte**: None; **S. Henrickson**: None; **L. Vella**: None; **A. Steenhoff**: None; **E. Behrens**: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9.

Abstract Number: 1826

Single Nuclei Multiome of JDM Muscle Biopsies Reveals Novel Upregulation of Inflammatory and Vascular Pathways

Shannon O'Connor, Casey Swoboda, Matthew Weirauch, Alexander Zygmunt, Douglas Millay and Leah Kottyan, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is a multisystem vasculopathy and inflammatory myopathy characterized by proximal muscle weakness, distinct rash, and risk of long-term complications such as calcinosis, skin ulceration, and chronic disease. Although Type I and Type II Interferon signatures are well established, this alone does not explain the full pattern of disease; the basic biology of JDM remains poorly defined. Heterogeneity in outcomes necessitates a more fundamental understanding of disease mechanisms.

Our objective is to understand genome-scale gene dysregulation in JDM through a multiomic study of single nuclei from treatment naïve muscle biopsies. We hypothesize that JDM etiology is mediated by molecular and cellular changes in the muscle and associated small blood vessels.

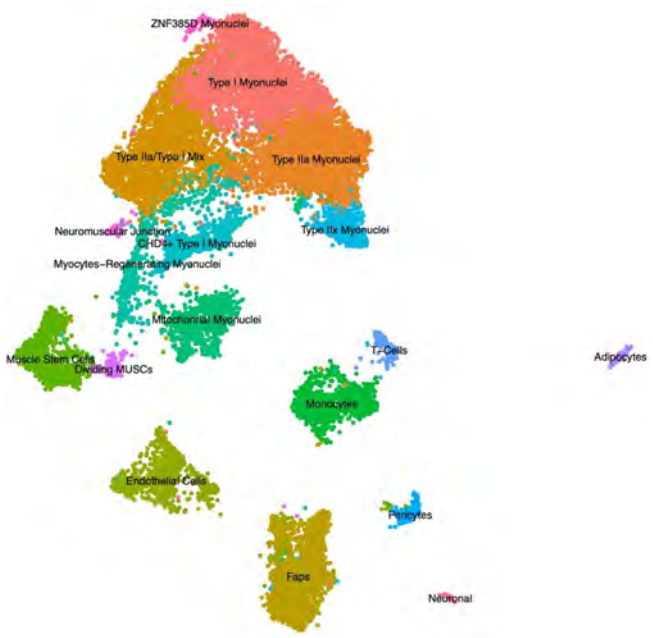


Figure 1. Uniform Manifold Approximation and Projection (UMAP) visualization represents sixteen color-coded nuclei clusters identified by tandem single nuclei RNA-sequencing and ATAC-sequencing. Data were generated from treatment naïve muscle biopsies from patients with juvenile dermatomyositis and congenital myopathy. FAPs = fibro-adipogenic precursors. MT = mitochondrial. NK = natural killer.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

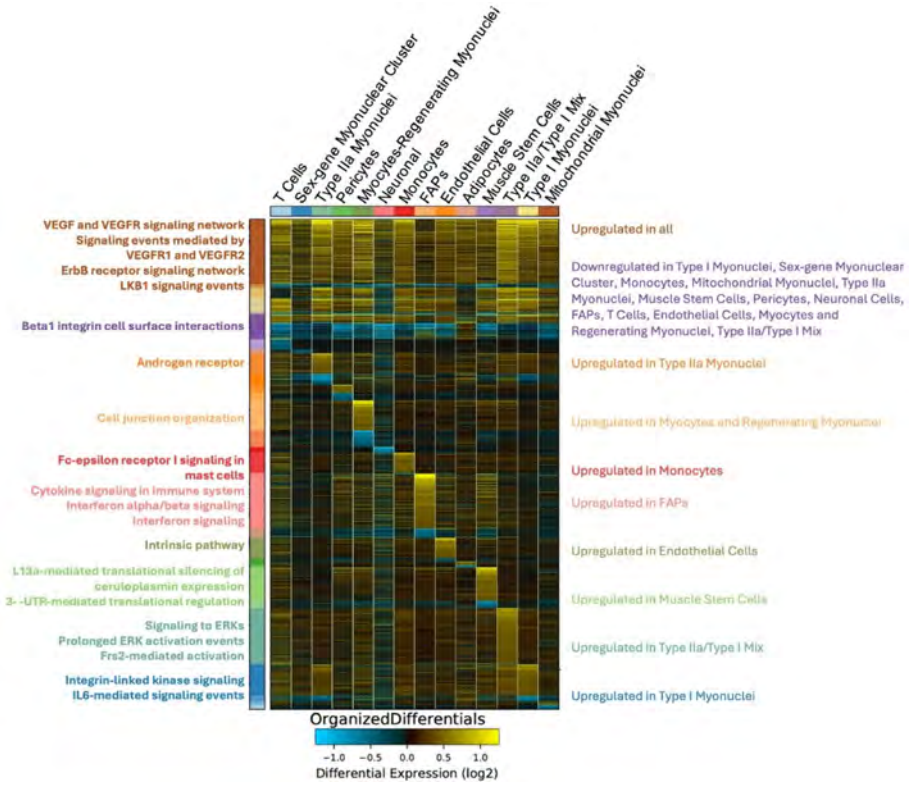


Figure 2. Heatmap of differentially expressed genes by cell type (columns) highlighting significant changes in expression profiles across specific pathways (left side). Data generated by tandem single nuclei RNA-sequencing and ATAC-sequencing from treatment naïve muscle biopsies from patients with juvenile dermatomyositis and congenital myopathy. FAPs = fibro-adipogenic precursors.

Methods: Muscle biopsies were collected from treatment naïve patients with JDM and congenital myopathy (CM). Biopsies were flash-frozen in liquid nitrogen and stored at -80°C (Cincinnati Children's Hospital Medical Center (CCHMC) Pathology Core). Single nuclei isolation was performed (10x Genomics protocol with optimization performed on murine samples), followed by Chromium Next GEM Single Cell Multiome ATAC+ Gene Expression processing (CCHMC Single Cell Genomics Core).

Sequencing data were analyzed through DNA and RNA read alignment and quantification using CellRanger. Ambient mRNA was removed, doublets identified, and low-quality nuclei removed using CellBender. Data were visualized in a two-dimensional space using dimensionality reduction and cluster identification using Seurat. Additional discovery of molecular pathway signatures was performed using CellHarmony.

Results: Single nuclei clustering revealed typical cell types consistent with previously demonstrated normal muscle tissue (Figure 1). Differentially expressed genes within individual cell types highlighted the known interferon signatures in multiple cell types. We also identified molecular signals consistent with dysfunction of vascular signaling pathways, especially between muscle and endothelial cells. There was marked upregulation of several inflammatory pathways that have not previously been described in JDM but have been identified in other inflammatory conditions (Figure 2).

Conclusion: We conducted a multiome study of single nuclei from treatment naïve muscle biopsies in JDM patients with a comparator group of congenital myopathy patients. While typical cell types of muscle are maintained, several pathways, in addition to a known interferon signature, demonstrate dysregulation, opening doors for further studies into the molecular dysfunction driving JDM pathology.

Disclosure: S. O'Connor: None; **C. Swoboda**: None; **M. Weirauch**: None; **A. Zygmunt**: None; **D. Millay**: None; **L. Kottyan**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1827

Transcriptomics and Machine Learning Unraveling the Molecular Drivers of PFAPA Flares

Sivia Lapidus[1], Tresa Ambooken[2], Ellen Hakim[3], Tara Lozy[4], Elahe Golalipour[3], Sohail Adonimohammed[5], Jennifer Weiss[6], Suzanne Li[6], Amanda Nowakowski[7], Aryeh Lejtman[8], Aaron Sebbag[3], Ariel Aptekmann[9] and Jigar Desai[9], [1]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Montclair, NJ, [2]Food and Drug Administration, Floral Park, NY, [3]Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ, [4]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Nutley, [5]Hackensack Meridian School of Medicine, Nutley, NJ, [6]Joseph M. Sanzari Children's Hospital and Hackensack Meridian School of Medicine, Hackensack, NJ, [7]Joseph M. Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, NJ, [8]Joseph M. Sanzari Children's Hospital and Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ, [9]Center for Discovery and Innovation and Hackensack Meridian School of Medicine, Hackensack Meridian Health, Nutley, NJ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis (PFAPA) is the most common periodic fever presenting with frequent episodes of pain and impaired function. While its etiology remains unknown, evidence suggests a genetic component and dysregulation of innate immunity. Our objective is to develop transcriptomic insights into the molecular pathways predicting PFAPA flares.

Methods: Ten PFAPA patients, fulfilling consensus patient characteristics, had blood samples collected during flare and non-flare times. Differences between groups were analyzed with the paired t-test. Differentially Expressed Genes (DEGs) were analyzed with standard RNA sequencing pipelines, including quality control, alignment to the reference genome (hg39), and quantification of transcript levels (STAR). Genes with significant differential expression were identified (DESeq2) and analyzed for pathway enrichment (gseapy). We trained a random forest (RF) classifier on gene expression counts to distinguish between flare and non-flare states, obtaining a final model with area under the ROC curve of 1. Top-ranked features' biological relevance to understand key pathways driving disease flares were evaluated.

Results: The PFAPA cohort's age of onset was 32 (IQR; 12-78) months, maximum temperature of 104.9 (IQR 103.4-105.2) degrees Fahrenheit, fever duration of ~4 (IQR:3-4.25) days and an 8 out of 10 in severity (IQR: 6-8,9) with how an episode feels and affects function. During flares, 100% of patients had pharyngitis, 80% cervical lymphadenopathy, and 50% oral

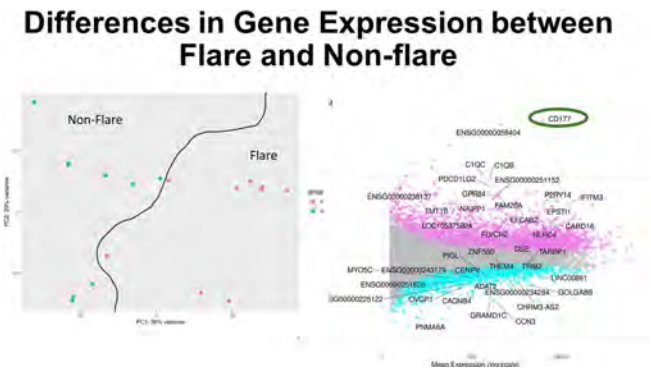


Figure 1: (Left) Principal Component Analysis Showing a Clear Separation and (Right) MA Plot of Log Fold Change Between PFAPA Flare and Non-Flare Plotted Against Mean Gene Expression. Significantly altered genes at p value < 0.05 are marked in color .

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

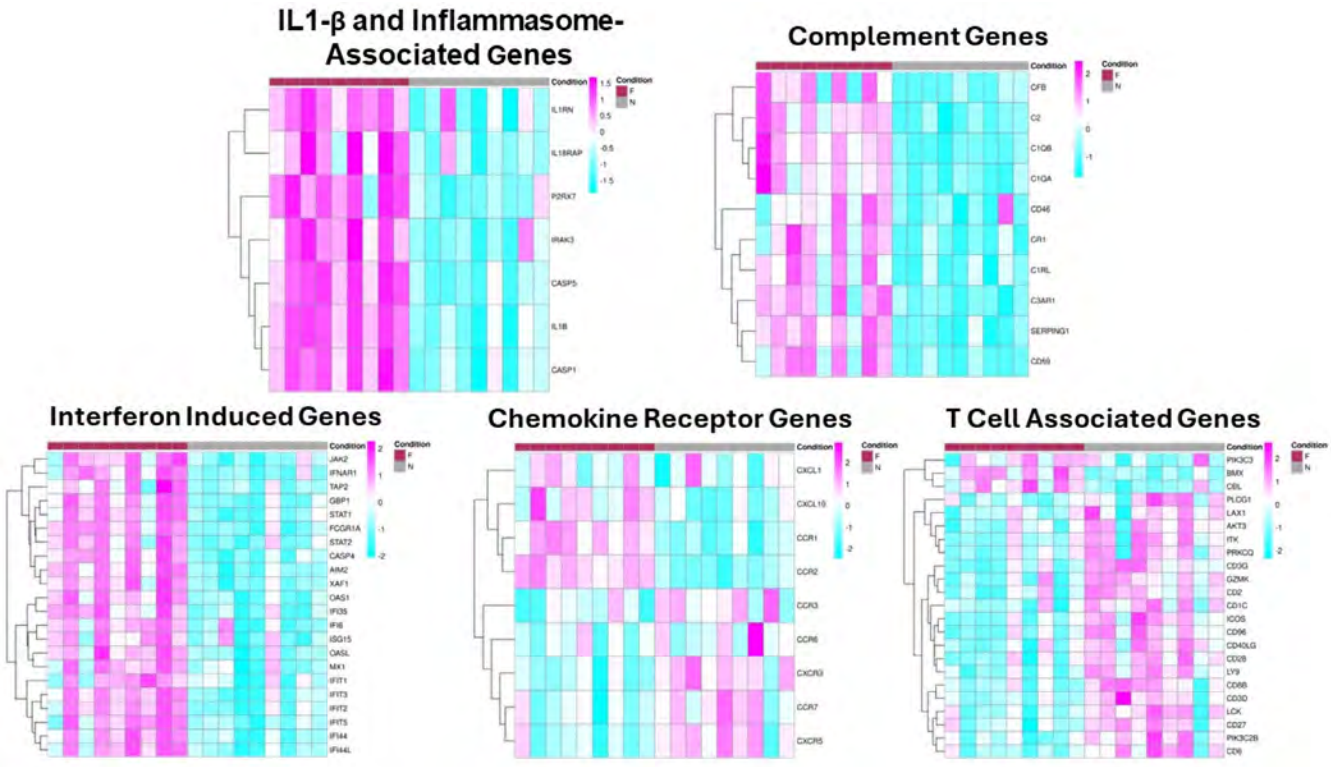


Figure 2: Gene Expression Signatures between PFAPA Flare and Non-Flare for Gene Ontologies Associated with Inflammation

aphthae. Lab abnormalities with flare included leukocytosis, neutrophilia, monocytosis, lymphopenia, and increased CRP ($P < 0.01$). A clear distinction between flare and non-flare gene expression was identified by RNA-sequencing Principal Component Analysis with multiple DEGs (Fig. 1). The top 50 DEGs by adjusted p-value included upstream regulators of immune pathways (*CD177*, *GPR84, C1QC*, and *CARD17P*). Gene Set Enrichment Analysis identified neutrophilic, interferon, response to organism and protein processing as key inflammatory pathways. Differentially regulated pathway signatures are depicted in Fig. 2. The top 20 features from the RF of flare versus non-flare were related to cell cycle arrest and microtubule polymerization. The highest-ranking feature was microRNA 5195 (downstream effectors Fig. 3), which at low levels was most predictive of flare.

Conclusion: We identified distinct gene expression profiles between PFAPA states demonstrating a transcriptomic signature of immune dysregulation associated with flares. The flare state reflects neutrophilic activation (modulated by corticosteroids aborting fever), interferon signaling, innate immune dysregulation and heightened cellular activity manifesting as cell cycle arrest as well as microtubule polymerization (modulated by colchicine). The MicroRNA 5195 gene was identified as the highest-

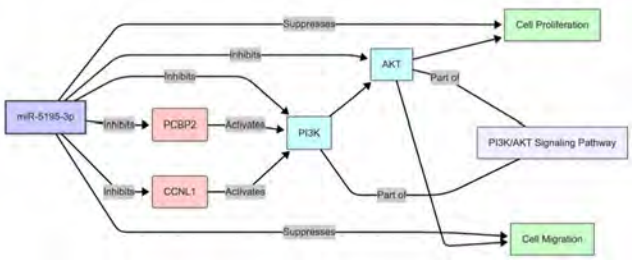


Figure 3: Network Motif of MICRO-RNA 5195: Downstream Effectors

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ranking predictive feature of PFAPA flares. Future work incorporating machine learning models in prioritizing biologically relevant markers in comparison to other cohorts will enable future development of a unique potential PFAPA biomarker.

Disclosure: S. Lapidus: None; **T. Ambooken**: None; **E. Hakim**: None; **T. Lozy**: Eli Lilly & Company, 11; **E. Golalipour**: None; **S. Adonimohammed**: None; **J. Weiss**: None; **S. Li**: Boehringer-Ingelheim, 2, Merck/MSD, 12, Spouse was an employee and receiving pension from them; **A. Nowakowski**: None; **A. Lejtman**: None; **A. Sebbag**: None; **A. Aptekmann**: None; **J. Desai**: None.

Abstract Number: 1828

CD14+CXCL10+Monocytes Remodel the Peripheral Immune Network in sJIA via UBE2D1-Driven Inflammatory Programming

Xuemei Tang[1], Qiang Luo[2], Jun Yang[3], Haiguo Yu[4], Xinglin Wu[1], Xiwen Luo[5], Xi Yang[5], Zhiyong Zhang[5], Yunfei An[5], Xiaodong Zhao[1] and Hongmei Song[6], [1]Department of Rheumatology and Immunology, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity, Chongqing, China, Chongqing, China (People's Republic), [2]Department of Rheumatology and Immunology, Children's Hospital of Chongqing Medical University, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Children's Hospital of Chongqing Medical University, Chongqing, China (People's Republic), [3]Rheumatology and Immunology Department of Shenzhen Children's Hospital, Shenzhen, 518100, China., Shenzhen, China (People's Republic), [4]Department of Rheumatology and Immunology, Nanjing Children's Hospital, Nanjing, 210000, China., Nanjing, China (People's Republic), [5]Department of Rheumatology & Immunology, Children's Hospital of Chongqing Medical University, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, National Clinical Research Center for Child Health and Disorders (Chongqing), Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Infection and Immunity, Chongqing, China., Chongqing, China (People's Republic), [6]Pediatric Department of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, 100000, China., Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is an autoinflammatory disorder characterized by systemic immune dysregulation. However, reliable biomarkers to predict its unpredictable disease course are still lacking. Identifying immune cell subsets and molecular drivers of disease progression is crucial for improving prognosis and developing targeted therapies.

Methods: We performed comprehensive immunophenotypic profiling of PBMCs from sJIA patients across five clinical centers. Deconvolution analysis combined with clinical follow-up in the Chongqing cohort was used to assess the prognostic value of key subpopulations. In vivo validation was performed using UBE2D1 knockout mice. A cross-disease single-cell reference was developed to compare sJIA-associated immune subsets with those found in other inflammatory diseases.

Results: We identified a novel CD14+CXCL10+monocyte subset distinguished by a unique transcriptomic signature enriched in immune regulatory genes. Notably, flow cytometry revealed that this subset was significantly elevated during the active phase of sJIA and decreased during remission, demonstrating a strong correlation with disease activity. In vitro inflammatory stimulation promoted the differentiation of monocytes into the CXCL10+phenotype. But, this process was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

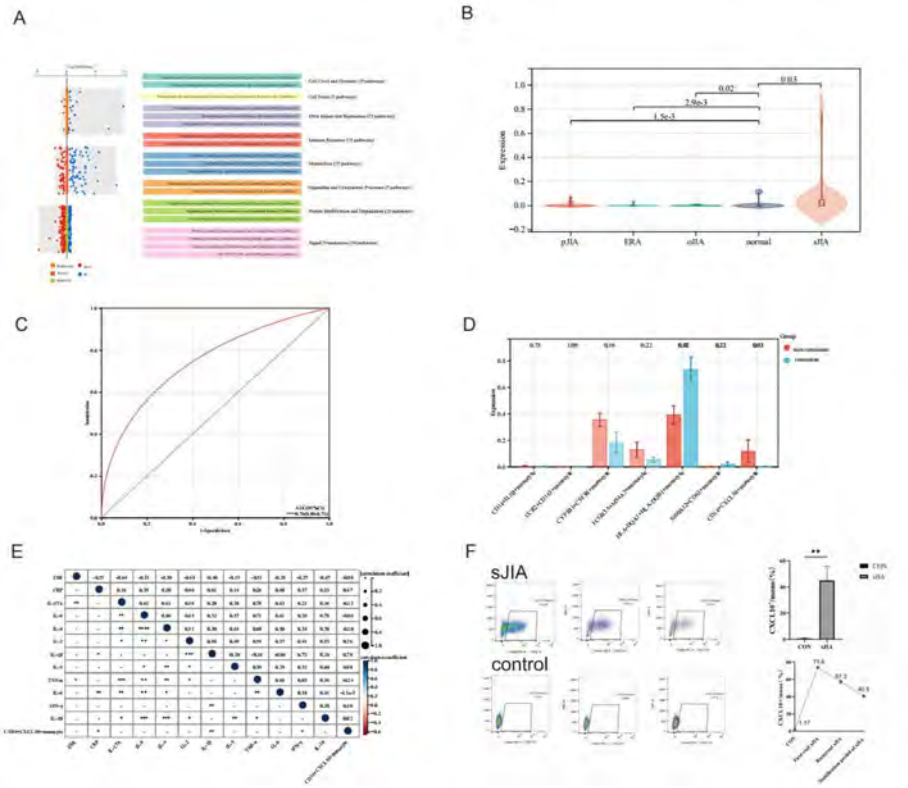


Figure 1: Exploration of CD14+CXCL10+Monocyte Function (A)Exploration of Biological Functions of CD14+CXCL10+Monocyte. (B) Violin plot showing CD14+CXCL10+monocyte levels across pJIA, ERA, oJIA, controls, and sJIA. (C) ROC curve illustrating the diagnostic performance of CD14+CXCL10+monocyte for distinguishing sJIA. (D) Differential expression of monocyte subpopulations in sJIA patients with and without remission. (E) Dot plot showing the Spearman's correlations of CD14+CXCL10+monocyte and clinical features across the Chongqing Clinical Dataset (*p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001). (F) Flow cytometry analysis of CD14+CXCL10+monocyte in peripheral blood of sJIA patients and controls. Left: Representative flow cytometry plots showing the percentage of CD14+CXCL10+monocyte in PBMCs from sJIA patients (top row) and controls (bottom row). Top right: Quantification shows that the proportion between sJIA and controls. Bottom right: Longitudinal analysis in the progression of sJIA disease.

markedly impaired in UBE2D1-deficient mice, which exhibited lower expression of CXCL10 mediators, underscoring the pivotal role of UBE2D1 as a central driver of this inflammatory program. Finally, by comparing this subset with other JIA subtypes and inflammation-related diseases, we found that it exhibits a distinct expression pattern in sJIA.

Conclusion: Our findings suggest that UBE2D1-driven CD14+CXCL10+monocyte play a key role in sJIA pathogenesis and may serve as both a biomarker and therapeutic target for disease monitoring and intervention.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

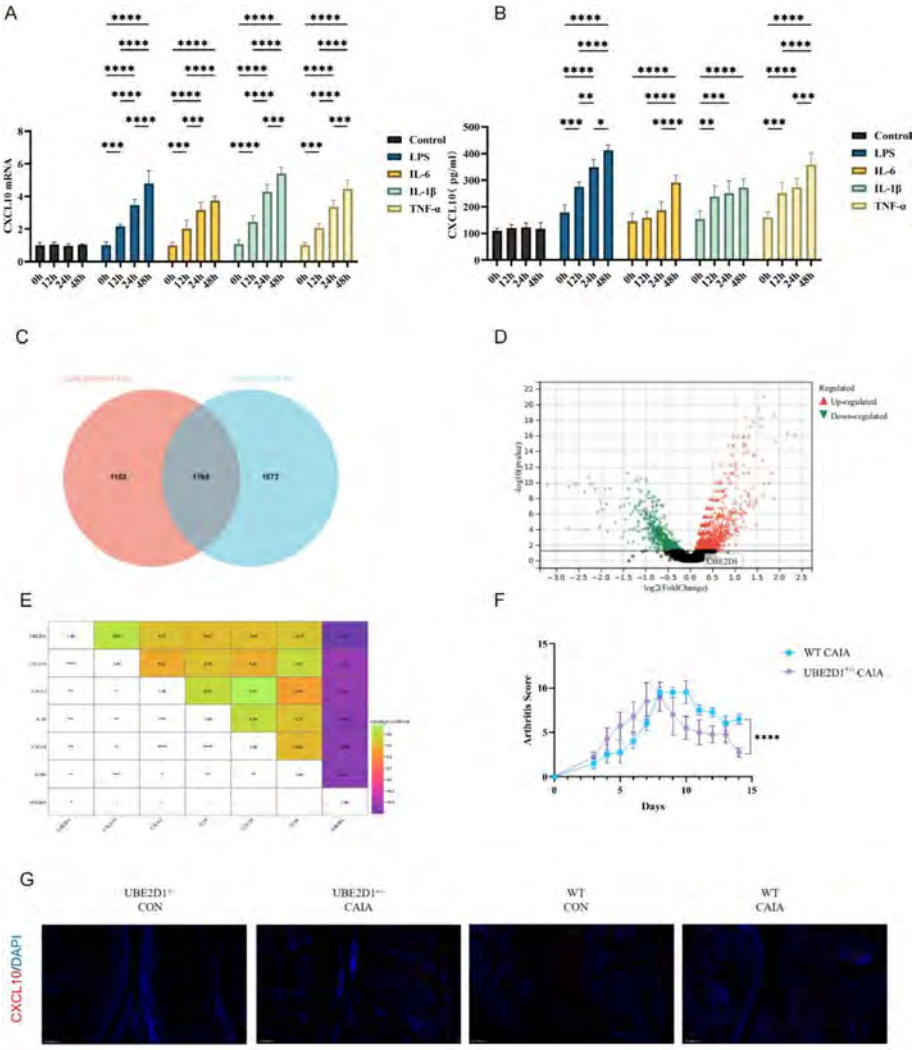


Figure 2: Exploration of CD14+CXCL10+Monocyte Core Network (A-B) Expression of CXCL10 gene and protein in THP-1 cells under different inflammatory stimuli in vitro. (C) Overlapping DEG genes between sJIA internal and external datasets. (D) DEG analysis in post-treatment sJIA and control. (E) Dot plot showing the Spearman's correlations of UBE2D1 and feature genes (*p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001). (F) Time-course plot showing arthritis scores over 15 days: UBE2D1$^{+/-}$ CAIA mice and WT CAIA mice (****p < 0.0001). (G) Representative multiplex immunofluorescence staining images of joint tissues from four experimental groups: UBE2D1$^{+/-}$ CON, UBE2D1$^{+/-}$ CAIA, WT CON, and WT CAIA.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

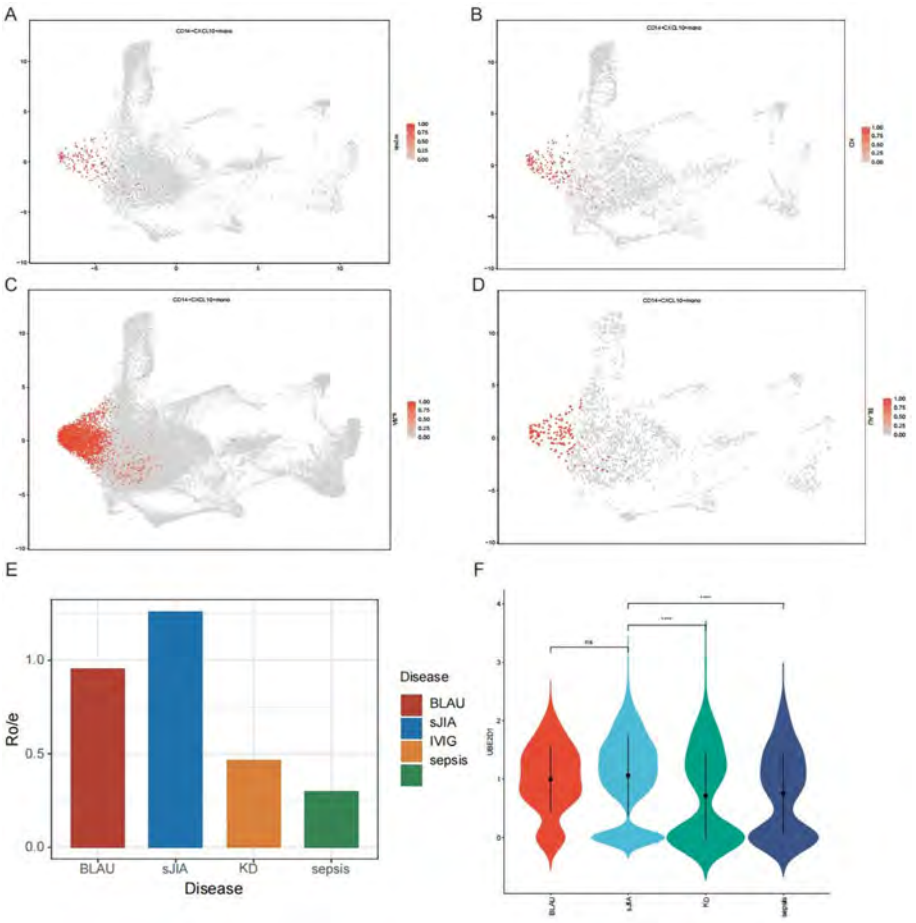


Figure 3: CD14+CXCL10+ monocyte Show Disease-Specific in Kawasaki Disease, BLAU, sepsis, and sJIA (A) CD14+CXCL10+ monocyte enriched in sepsis samples. (B) CD14+CXCL10+ monocyte enriched in Kawasaki Disease (KD samples. (C) CD14+CXCL10+ monocyte enriched in BLAU samples. (D) CD14+CXCL10+ monocyte enriched in BLAU samples. (E) Ratio of observed to expected proportions of CD14+CXCL10+ monocyte across four disease. (F) Violin plots displaying UBE2D1 expression levels in CD14+CXCL10+ monocyte from each disease cohort.

Disclosure: X. Tang: None; **Q. Luo**: None; **J. Yang**: Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties, 5; **H. Yu**: None; **X. Wu**: None; **X. Luo**: None; **X. Yang**: None; **Z. Zhang**: None; **Y. An**: None; **X. Zhao**: None; **H. Song**: None.

Abstract Number: 1829

Multiomic Investigation of Juvenile Idiopathic Arthritis Synovium Reveals Immune Cell Heterogeneity

Abigail Thielbar[1], Tracy Ting[2], Lexi Auld[3], Kelly Rogers[4], Megan Quinlan-Waters[5], Sheila Angeles-Han[4], Ekemini Ogbu[2], Daniel Lovell[2], Jennifer Huggins[6], Grant Schulert[2], Patricia Vega-Fernandez[2] and **Yuriy Baglaenko**[4], [1]Cincinnati Children's Hospital, Cincinnati, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [4]Cincinnati Children's Hospital, Cincinnati, OH, [5]Cincinnati Children's Hospital Medical Center, CCHMC, [6]Cincinnati Children's Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1809–1829) Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease of childhood, affecting 1:1,000 children worldwide. The hallmark of JIA is immune-mediated chronic inflammation in the synovium – clinically reflected by the presence of arthritis or a combination of joint pain, swelling, or limitation of joint movement. If inadequately treated, JIA can lead to profound lifelong joint deformity and disability. Thus, early diagnosis and treatment initiation is essential in the management of patients with JIA. Histological examination of synovium, although limited in scope, has identified immune cell infiltration of lymphocytes, plasma cells, macrophages as well as proliferation of fibroblast- and macrophage-like synoviocytes. To date, no comprehensive studies of JIA synovium have been performed as current best-practices do not routinely collect tissue biopsies for diagnosis or analysis. Recent single cell methodologies that assay open chromatin and transcriptome have made great strides in bridging this gap in adult rheumatic conditions by directly examining the synovium. The objective of this study is to leverage novel multiomic single cell strategies to characterize cell heterogeneity in the synovium of children with JIA.

Methods: Ultrasound guided synovial biopsies were performed in two children to isolate synovium. Tissue was enzymatically digested, sorted for viability, nuclei isolated, and single cell libraries generated with the 10X multiome (RNA + ATAC) pipeline. A PBMC sample from a JIA patient was also included to define tissue enrichment. Data was aligned with cellranger and processed with custom analysis pipelines.

Results: We obtain high quality data from three samples for single cell RNA and ATAC sequencing with a median of 1350 genes and 6233 ATAC peaks from 5771 cells. Integration of gene expression and open chromatin data, harmonization by donor, and clustering identifies 11 broad populations including T, B and fibroblasts cells. Comparison between tissue and blood sample identifies an enrichment of activated/memory CD4 and CD8 T cells and a decrease in monocytes populations specific to the synovium. Pathogenic HLA-DR+ fibroblasts are exclusively identified in synovium. Fine-grained analysis of T cells with our recently developed T cell annotation program (TCAT) identifies evidence of proliferation in Tfh/Tph and T regulatory cells.

Conclusion: To our knowledge, this is the first multiomic single cell study of JIA synovium that simultaneously captures gene expression and open chromatin. We implement a high-quality processing pipeline and identify cell heterogeneity specific to the synovium. In particular, we find evidence of immune cell activation and proliferation in Tfh/Tph and T regulatory cells from synovium.

Disclosure: A. Thielbar: None; **T. Ting**: None; **L. Auld**: None; **K. Rogers**: None; **M. Quinlan-Waters**: None; **S. Angeles-Han**: None; **E. Ogbu**: Cartesian Therapeutics, 2; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **J. Huggins**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **P. Vega-Fernandez**: None; **Y. Baglaenko**: None.

Abstract Number: 1830

Single-Cell and Spatial Profiling Reveal Proinflammatory and Profibrotic Fibroblast-Macrophage Niches in Lupus Nephritis

Chirag Raparia[1], Paul Hoover[2], Nir Hacohen[3], Arnon Arazi[4], Anne Davidson[1] and Accelerating Medicines Partnership: RA/SLE Network (AMP RA/SLE), AMP-SLE Working Group, [1]Feinstein Institutes for Medical Research, Manhasset, NY, [2]Brigham and Women's Hospital, Boston, MA, [3]Broad Institute of MIT Harvard, Cambridge, MA, [4]Feinstein Institutes for Medical Research, Acton, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

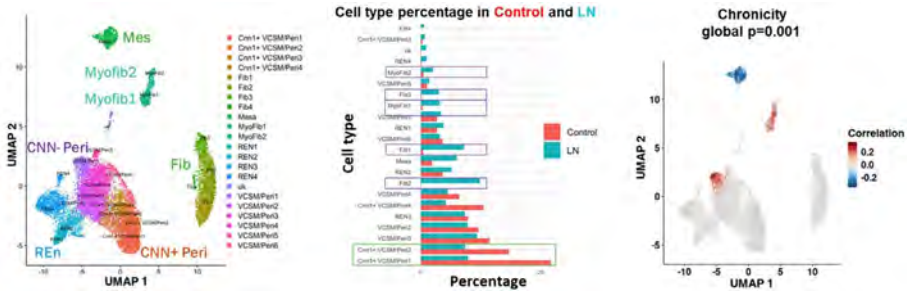


Figure 1: Fibroblast-like PDGFRB+ cell landscape in Lupus Nephritis. A. UMAP of 6 PDGFRB+ subsets, each containing unique subclusters from single-cell RNA-sequencing of stromal cells from 156 LN patients and 30 live donor controls. B. A bar graph of each subcluster as a percentage of total PDGRB+ stromal cells in LN patients (Blue) and controls (red), highlighting subclusters that increased in frequency during LN (Purple box; Fib1-3, Myofib 1-2) and subclusters that decreased (Green box; CNN1+ VSCM/Per1-2). C. Covarying Neighborhood Analysis (CNA) on LN patients projecting onto the PDGFRB+ stromal cells showing association with chronicity. Red indicates a significant positive clinical correlation with the cell subset, while blue indicates a significant negative correlation. The false detection rate is less than 0.1.

Background/Purpose: Lupus nephritis (LN) is a severe complication of SLE that can progress to chronic kidney disease, renal fibrosis, and eventual renal failure. Fibroblasts activated by pro-inflammatory cytokines and damage signals adopt a heterogeneous pro-inflammatory or profibrotic phenotype, which contribute to pathological fibrosis; however, the fibroblast landscape in autoimmune kidney disease remains poorly understood. Here, using renal biopsies collected through the AMP-SLE, we define and localize fibroblast heterogeneity in LN through single-cell and spatial transcriptomics.

Methods: Single-cell RNA-sequencing was used to profile dissociated kidney biopsies collected from 156 LN patients and 30 controls. High-resolution clustering was performed to identify both tissue and immune cell subsets. 16,187 PDGFRB+ stromal cells were used for further subclustering. Covarying Neighborhood Analysis (CNA) was performed to identify statistically significant Pearson's correlations between the frequencies of cell subsets and the ISN chronicity and activity indices. Spatial transcriptomics was performed using the 10x Genomics Xenium platform, with a gene panel customized to allow the identification of high-resolution myeloid populations.

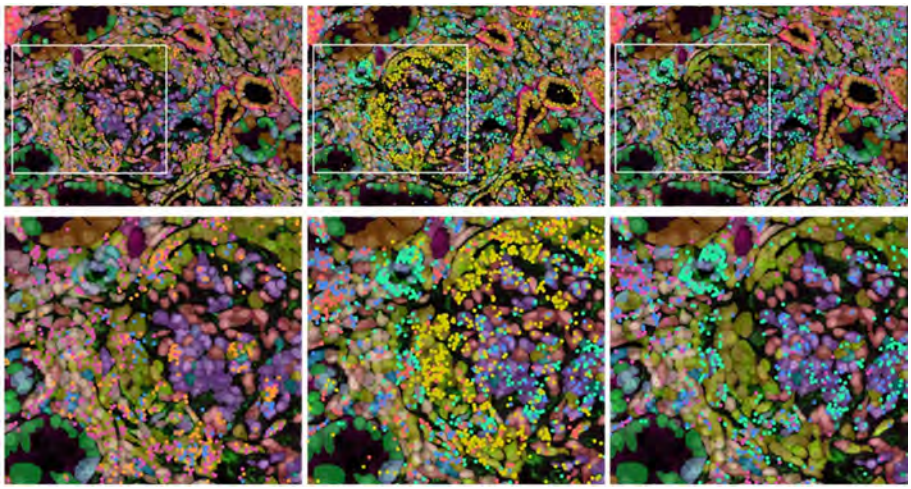


Figure 2: Spatial transcriptomic representation of a glomerulus from a LN patient renal biopsy. A. An overview of the area of interest (Top) with damage-associated macrophage transcripts GPNMP, FABP5, and CSF1R are highlighted. Magnification of the boxed area (bottom) shows GPNMP+ and FABP5+ macrophages localizing in the glomeruli and peri-glomeruli areas (white arrows) compared to macrophages expressing CSF1R alone in the interstitium B. Image of the same area (Top) with Myofib2 transcripts ACTA2, ITGA3, and VCAN highlighted. Magnification of the boxed area (bottom) shows Myofib2, located in the glomerulus and in the crescent (C) (white arrows). V indicates an Acta2+ blood vessel. C. Image of the same area (Top) with Myofib1 transcripts PDFGRA and C7 highlighted. Magnification of the boxed area (bottom) details Myofib1, which are predominantly located in the interstitium (white arrows), separate from Myofib2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We identified fibroblasts, myofibroblasts, CNN1+ vascular smooth muscle cells/pericytes (VSMC/peri), mesangial cells and renal endothelial cells, with relative expansion of fibroblasts, myofibroblasts, and mesangial cells occurring during LN together with relative contraction of CNN1- VSMC/peri (Fig.1A, B). Fine clustering of myofibroblasts revealed two transcriptionally distinct myofibroblast-like populations with increased collagen scores compared to other fibroblast-like subsets: proinflammatory myofibroblasts (Myofib1) and profibrotic myofibroblasts (Myofib2). CNA revealed that both clusters of myofibroblasts and the VCSM/Peri1 subset were positively correlated with chronicity (Fig. 1C), but not with the activity index. Gene expression and pathway enrichment analyses highlighted MyoFib2 as a matrix-producing, contractile population, while MyoFib1 was enriched for immune signaling and complement pathways. PDGFRA+, ACTA2+ C7+ ITGA3- Myofib1 myofibroblasts were located preferentially in the interstitium adjacent to CSF1R+ resident macrophages, whereas PDGFRA, ACTA2+, ITGA3+ VCAN+ Myofib2 myofibroblasts were located in sclerotic areas of the glomeruli and fibrous crescents adjacent to GPNMB+ FABP5+ damage-associated infiltrating macrophages (Fig. 2A-C). Vascular mural cells also showed heterogeneity: VCSM/Peri1 was enriched for immune-related genes and expressed a detachment profile, whereas VCSM/Peri2–6 retained a contractile phenotype.

Conclusion: Our findings reveal the diversity of PDGFRB+ populations in LN kidneys and the presence of both proinflammatory and profibrotic myofibroblasts in various renal compartments associated with LN chronicity. Previously described LN associated resident and infiltrating macrophages co-localize with proinflammatory and profibrotic fibroblasts respectively creating unique renal niches that promote tissue damage.

Disclosure: C. Raparia: None; **P. Hoover**: None; **N. Hacohen**: Calico Biosciences, 5, Cytoreason, 1, 11, Danger Bio, 1, 11, Moderna, 5, Repertoire Immune Medicines, 1, 11, Takeda, 5; **A. Arazi**: None; **A. Davidson**: None.

Abstract Number: 1831

Distinct Proteomic Signature Predicts Post-MMF Withdrawal Flares in Systemic Lupus Erythematosus Patients

Christian Wright[1], Miles Smith[2], Rufei Lu[2], Catriona Wagner[3], Aleksandra Bylinska[2], Carla Guthridge[2], Nicholas Domingez[2], Susan Macwana[2], Wade DeJager[4], Marci Beel[5], Joan Merrill[6], Eliza Chakravarty[2], Ellen Goldmuntz[7], Study Team ALE06 Clinical[8], Judith James[2] and Joel Guthridge[2], [1]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma city, OK, [3]Oklahoma Medical Research Foundation, Santa Cruz, CA, [4]Oklahoma Medical Research Foundation, Oklahoma City, [5]Oklahoma Medical Research Foun, Oklahoma City, OK, [6]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [7]NIAID/ NIH, Washington, DC, [8]Autoimmunity Center of Excellence, Oklahoma City, OK

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: : Systemic Lupus Erythematosus (SLE) follows a characteristic relapsing-remitting course with unpredictable flares interspersed with periods of relative quiescence. Mycophenolate mofetil (MMF) has emerged as a cornerstone immunosuppressive therapy in SLE management, the challenges of balancing effective disease control against medication-associated toxicities remain significant. Our recent clinical trial (Chakravarty, et al. Lancet Rheum 2024) suggests that MMF discontinuation in clinically quiescent patients may allow remission rates similar to continuous therapy in select patients. However, an integrated set of clinically and biologically relevant biomarkers capable of identifying patients at the highest risk of disease flare following MMF withdrawal is needed to optimize clinical outcomes and guide clinical care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) flares were tracked for 60 weeks post-MMF withdrawal. Serum (baseline) samples from SLE patients (n=50) with clinically quiescent disease (physician defined and SLEDAI< 4) on long-term MMF from the "Randomized MMF Withdrawal in Systemic Lupus Erythematosus (SLE) (ALE06)" trial (Chakravarty, et al. Lancet Rheum. 2024) with available samples and appropriate follow-up were collected prior to and after MMF taper. Soluble serum proteins were profiled using Olink Explore HT and an iterative machine learning approach (ML) used to elucidate soluble protein signatures that predict disease flare post-MMF withdrawal.

Results: In total, 31 SLE patients experienced a SELENA-SLEDAI flare within 60 weeks of MMF withdrawal, compared to 19 who did not. Using 283 known secreted protein levels predictive ML modeling was able to identify disease flares post-MMF withdrawal with 70.3% accuracy and an AUC of 88.4 ± 9 using 34 proteins (**Fig 1A**). Among the top predictors, TGF-β2, a less recognized immune modulatory isoform of TGF-B that can directly regulate T cell functions, was lower in patients who flared (**Fig 1B**). Of note, T cells are one of the cell lineages directly affected by MMF usage. Protein set enrichment analysis of ML model proteins show elevations of ERK1/2 signaling proteins, B cell proteins such as FcγR2b a moderator of B Cell activity with known deficiencies in lupus, and phagocytosis-associated proteins in patients who flared post MMF withdrawal (**Fig 1C**). Together, these findings suggest that immunologic pathway dysregulation is present in clinically quiescent patients at the highest risk of disease flares after MMF withdrawal.

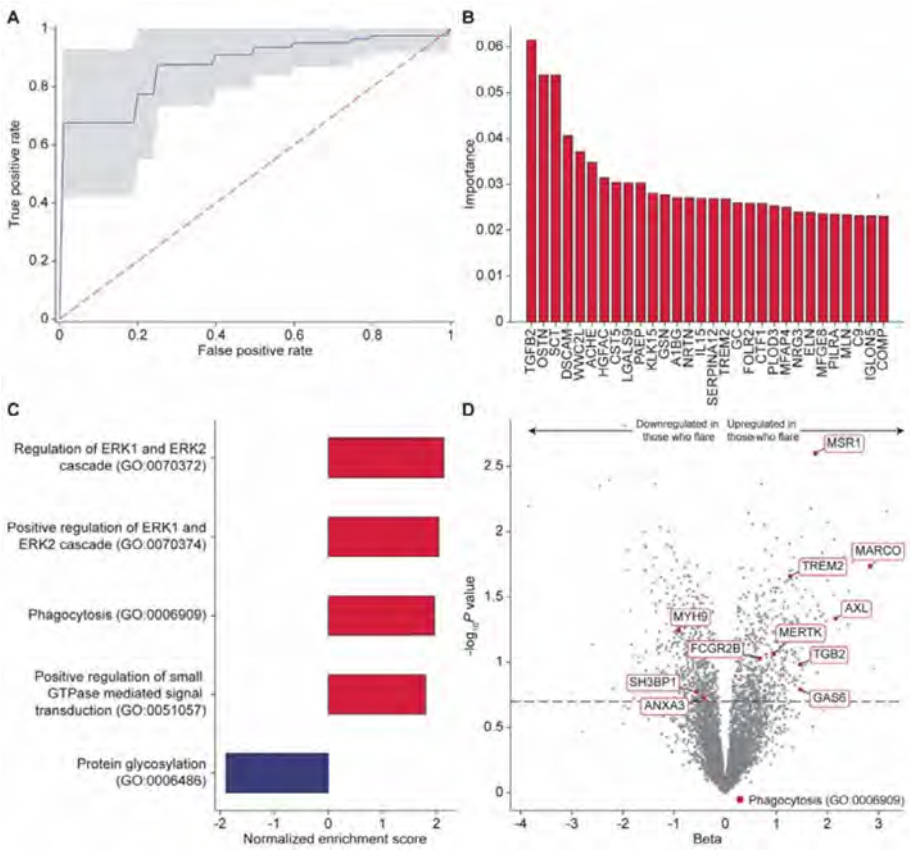


Fig. 1: Proteomic biomarkers are associated with subsequent disease flare following MMF withdrawal in SLE patients. (A) Random forest model using baseline serum levels of secreted proteins (identified via the Human Protein Atlas) predicts SELENA-SLEDAI flare within 60 weeks of MMF discontinuation. (B) Ranked importance of the top secreted protein predictors for disease flare following MMF withdrawal, as determined by the random forest model. (C) Pathways with significant enrichment in patients with disease flare following MMF withdrawal. (D) Volcano plot of phagocytosis-related proteins showing differential abundance between patients who experienced a disease flare compared to those who did not following MMF withdrawal.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our findings demonstrate that a secreted protein-based proteomic signature can robustly predict imminent SLE flares following MMF withdrawal, with TGF-β2 and FcγR2b emerging as key biomarkers associated with flare risk. These results also highlight the value of proteomic profiling for risk stratification and provide new insights into the mechanisms underlying disease reactivation after immunosuppressant withdrawal.

Disclosure: C. Wright: None; **M. Smith**: None; **R. Lu**: None; **C. Wagner**: None; **A. Bylinska**: None; **C. Guthridge**: None; **N. Domingez**: None; **S. Macwana**: None; **W. DeJager**: None; **M. Beel**: None; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **E. Chakravarty**: None; **E. Goldmuntz**: None; **S. ALE06 Clinical**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Guthridge**: None.

Abstract Number: 1832

Time-to-Event Analysis of Statin Use and Thrombotic Risk in Patients with Systemic Lupus Erythematosus: A Single-Center Retrospective Study

Christine Lenchur[1], Niurka Liranzo Tejera[1], Adal Abonamah[1], Takemichi Matsui[1], Emily Cosentino[1], Priscilla Abate Namnum[2], Olga Marushchak[1], Melissa Akselrad[1], Martin John[3], Sophia Lutgen[4], Celestine He[5], Boluwatito Oladeinde[3], Harleen Sidhu[6], Emilia Bagiella[5], Ian Wright[5] and Chrisanna Dobrowolski[5], [1]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, [2]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York, [3]Icahn School of Medicine at Mount Sinai, New York, [4]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York City, NY, [5]Icahn School of Medicine at Mount Sinai, New York, NY, [6]Icahn School of Medicine at Mount Sinai/NYC H+H- Elmhurst, Queens, NY, Rego Park, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) face elevated risk of thrombotic events (TEs) due to traditional cardiovascular factors and chronic inflammation. Statins may offer anti-inflammatory effects beyond lipid lowering, making them potentially valuable in this population. This retrospective cohort study examines the association between statin use and TEs in SLE patients, aiming to clarify inconsistent findings in prior research and optimize further management strategies.

Methods: We conducted a retrospective cohort study using the Mount Sinai Health System's Epic-linked electronic medical record to identify patients >18 years old diagnosed with SLE via ICD-10 codes between January 2000 and March 2024. Patients not meeting the 2019 ACR/EULAR classification criteria for SLE were excluded. The primary outcome of the study was the occurrence of a TE (arterial or venous), assessed using time to event analysis from the time of SLE diagnosis to the TE event or last follow-up. Patients free of a TE by the time of the last follow-up were censored. Statin use was the primary predictor variable. Univariate extended Cox models were utilized to explore the role of seven independent variables, including the primary exposure of interest as a time-dependent variable, on the risk of thrombotic events. P-values < 0.05 were considered statistically significant.

Results: A total of 376 patients with SLE were included in the study. Patient demographics, hydroxychloroquine use, as well as concomitant comorbidities of smoking, hypertension, diabetes mellitus, secondary antiphospholipid syndrome (APS) and lupus nephritis are detailed in Table 1. Of the 376 patients, 6.4% experienced thrombotic events during follow-up; 35.6% of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient clinical characteristics and co-morbidities.

Characteristic	Number (%)
Female	348 (92.6%)
Mean Age of Diagnosis (SD)	40.4 (±17.4) years
Race	
White	153 (40.7%)
African American	116 (30.9%)
Other/Unknown	88 (23.4%)
Asian	19 (5.1%)
Ethnicity	
Non-Hispanic	203 (53.9%)
Hispanic	93 (24.7%)
Other/Unknown	80 (21.2%)
Antiphospholipid Syndrome	36 (9.6%)
Lupus Nephritis	52 (13.8%)
Use of Hydroxychloroquine	258 (68.6%)
Hypertension	152 (40.4%)
Diabetes Mellitus	36 (9.6%)
Smoker	94 (25.0%)
Thrombotic Event	24 (6.4%)
Statin Use	65 (17.3%)

Table 2. Univariate extended Cox models of thrombotic risk by demographics, comorbidities, and treatment variables.

Parameter	Comparison	Estimate	Std Error	Chi Sq	P-value	Hazard Ratio	95% CI
Statin Use	Yes vs No	1.89	0.51	13.80	**< 0.01**	6.62	[2.44, 17.93]
Sex	Male vs Female	0.43	1.04	0.17	0.677	1.54	[0.20, 11.90]
APS Diagnosis	Yes vs No	3.86	0.78	24.65	**<0.01**	47.34	[10.33, 217.00]
APS Diagnosis	Unconfirmed vs No	4.17	0.85	24.29	**<0.01**	64.52	[12.30, 338.40]
Hydroxychloroquine	Yes vs No	-0.13	0.51	0.07	0.79	0.88	[0.32, 2.37]
Hypertension	Yes vs No	0.11	0.49	0.05	0.83	1.11	[0.43, 2.91]
Diabetes mellitus	Yes vs No	-15.31	1169	0.00	0.99	0.00	[0.00, 0.00]
Smoking	Yes vs No	-0.51	0.64	0.64	0.42	0.60	[0.17, 2.10]

Table 3. Final extended Cox model assessing the association between time-dependent statin use and thrombotic events.

Parameter	DF	Parameter Estimate	Standard Error	Chi Square	P-value	Hazard Ratio	95% CI
Statin Use	1	1.89	0.51	13.80	**< 0.01**	6.62	[2.44, 17.93]

these patients had a diagnosis of secondary APS. In univariate analyses, statin use, and secondary antiphospholipid syndrome (APS) showed significant associations with TEs. However, due to sparse data and wide confidence intervals, particularly among patients without APS, APS variable was excluded from the final model. Statin exposure was unexpectedly associated with an increased hazard of thrombotic events (HR 6.62; 95% CI: 2.44–17.93; $p < 0.001$; Table 2, Table 3).

Conclusion: While these results were statistically significant, the wide confidence interval suggests variability in the estimate, likely reflecting the limited number of events among non-statin users and heterogeneous exposure timing. These findings should be interpreted in the context of an exploratory analysis and warrant further investigation in a larger study. Results likely also reflect residual confounding, such as the preferential use of statins in higher-risk patients. Similar findings have been reported in other chronic inflammatory conditions, suggesting that statins alone do not sufficiently address thrombotic risk in people living with SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Lenchur: None; **N. Liranzo Tejera**: None; **A. Abonamah**: None; **T. Matsui**: None; **E. Cosentino**: None; **P. Abate Namnum**: None; **O. Marushchak**: None; **M. Akselrad**: None; **M. John**: None; **S. Lutgen**: None; **C. He**: None; **B. Oladeinde**: None; **H. Sidhu**: None; **E. Bagiella**: None; **I. Wright**: None; **C. Dobrowolski**: Novartis, 1.

Abstract Number: 1833

DM618: A Novel Anti-IL12p35 Antibody Specifically Inhibiting IL-12 with Therapeutic Potential in a Set of Autoimmune Diseases

Dong ZHANG, Guangan Hu, Xiaodong Jiang, Quanju Zhao, Tainfei Hou, Zhengwang Sun, Mousheng Xu and Nan Bing, D2M Biotherapeutic, Inc, NATICK, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IL-12, via its p35 subunit, drives Th1-mediated pathology in autoimmune diseases. Genome-wide association studies (GWAS) suggested that *IL12A* encoding IL12p35 is associated with systemic lupus erythematosus (SLE), systemic sclerosis (SSc), primary biliary cholangitis (PBC), and Sjögren's syndrome (SS), but *IL12B* and *IL23R* are not. Antibodies targeting *IL12B* and *IL23A* have been developed in the clinic but no proven effects were shown for the above-mentioned immune diseases. DM618, a monoclonal antibody selectively targeting IL12p35, was designed to inhibit IL-12 signaling without affecting IL-23. Preclinical efficacy was evaluated using a surrogate anti-mouse IL12p35 antibody.

Methods: Colocalization analyses of gene expression/protein quantitative trait loci (eQTLs/pQTLs) with autoimmune disease GWAS data were performed. Anti-IL12p35 antibody was generated in RenMab mice. Affinity was measured using Biacore, and IL-12 neutralization was assessed in reporter and primary cells. *In vivo* evaluation employed murine models: DNFB-induced skin inflammation, streptozotocin-induced SS, and IMQ-NZBWF1 lupus nephritis. Pharmacokinetics were evaluated in human FcRn transgenic mice.

Results: The eQTLs/pQTLs of IL-12 pathway genes *IL12A* and *IL12RB2* colocalized with SLE, SSc, PBC, and SS, but not with other autoimmune diseases such as psoriasis (Pso), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC), or inflammatory bowel disease (IBD). In contrast, *IL12B* and *IL23R* eQTLs colocalized with Pso, AS, CD, UC, and IBD, but not SLE, SSc, PBC, or SS. DM618, the lead candidate, exhibited high Biacore affinity (KD = 6.49×10^{-11} M) and superior IL-12 neutralization (EC_{50}: 0.0059 μg/mL) compared to ustekinumab (anti-IL12p40; EC_{50}: 1.3 μg/mL) in IL-12 reporter cells. DM618 suppressed both exogenous and endogenous IL-12-induced IFN-γ secretion in primary cell-based assays, outperforming ustekinumab. Critically, DM618 did not inhibit IL-23 signaling. Due to its lack of cross-reactivity with mouse IL-12, preclinical validation was conducted using a surrogate anti-mouse IL12p35 antibody in murine models. The surrogate antibody significantly reduced ear thickness ($P = 0.0026$) in a subchronic DNFB-induced skin inflammation model, alleviated salivary gland inflammation in an SS model, and decreased albuminuria in a lupus nephritis model (10-fold reduction vs. controls). Importantly, the human genetic association data have informed the clinical development pathway for DM618.

Conclusion: DM618, a first-in-class anti-IL12p35 antibody, selectively inhibits IL-12 and demonstrates potential to address Th1-driven autoimmune pathology. Supported by human genetic evidence and preclinical validation using a surrogate antibody, DM618's specificity preserves IL-23-mediated immunity, aligning with the distinct roles of IL-12 and IL-23 in their

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

respective disease pathways. The preclinical efficacy of surrogate anti-mouse IL12p35 in lupus nephritis, SSc, and SS models provides proof of concept for selective IL-12 targeting and supports clinical development for these high-unmet-need diseases.

Disclosure: D. ZHANG: D2M Biotherapeutics, Inc., 3, 4, 8; **G. Hu**: D2M Biotherapeutics, Inc., 3; **X. Jiang**: D2M Biotherapeutics, Inc., 3; **Q. Zhao**: D2M Biotherapeutics, Inc., 3; **T. Hou**: D2M Biotherapeutics, Inc., 3; **Z. Sun**: D2M Biotherapeutics, Inc., 3; **M. Xu**: D2M Biotherapeutics, Inc., 3; **N. Bing**: D2M Biotherapeutics, Inc., 4, 8.

Abstract Number: 1834

Integrative Bioinformatics Analysis Reveals Key Genes and Immune Profiles Associated with Preeclampsia in Lupus Pregnancy

Rodolfo Martinez-Canales[1], **Eva Abigaid Galindo-Calvillo**[2], Andres M. Ortiz-Rios[2], Braulio R. Avalos-Garcia[2], Lorena Perez-Barbosa[2], Dionicio A. Galarza-Delgado[3], Cassandra Michele Skinner-Taylor[2], Mario Cesar Salinas-Carmona[1] and Noe Macias-Segura[1], [1]Immunology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Preeclampsia (PE) is a serious complication of pregnancy associated with significant maternal and fetal outcomes. Systemic lupus erythematosus (SLE) significantly increases the risk of PE, which is not explained by traditional risk factors. A dysregulated immune response, with altered gene expression and aberrant immune cell activation play a critical role in the development of PE in patients with SLE. We conducted an integrative bioinformatics analysis to identify candidate genes and pathways implicated in PE among patients with SLE. By leveraging publicly available transcriptomic datasets, we aimed to uncover potential early biomarkers and explore their association with immune cell populations in peripheral blood, providing insights into the immunopathogenesis of PE in SLE.

Methods: We selected the next datasets from the Gene Expression Omnibus database: GSE177029, GSE185047, and GSE48424 (Table 1). We filtered differentially expressed genes (DEGs) using the R-based tool GEO2R, with a false-discovery rate (FDR) value of < 0.05 and a log2foldchange >1 for upregulated genes. A Venn diagram was drawn to visualize shared DEGs across datasets. Enrichment analysis was performed to retrieve gene ontology (GO) biologic processes (BP) and KEGG pathways using ShinyGO. Protein-protein interactions (PPIs) were analyzed with the Cytoscape software, and key hub genes (HGs) were identified with the Cytohubba plugin using the maximal clique centrality algorithm. The Cibersort online tool was utilized to characterize the immune cell population from peripheral blood in dataset GSE48424. A two-way ANOVA test was done to compare immune cell proportions. The two-stage step up method was applied as a post-hoc test to control the FDR. Mean fluorescence intensity (MFIs) values were retrieved, and a Spearman correlation test was performed to assess the relationship between the HG expression and immune cell populations.

Results: 40 DEGs were shared in at least two different datasets (Figure 1A), and whose functional enrichment was notable for BPs related to regulation of viral genome replication and response to type I interferon (Figure 1C). Such terms were then supported by KEGG pathways related to viral infections such as pertussis, measles and influenza A (Figure 1D). PPI analysis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

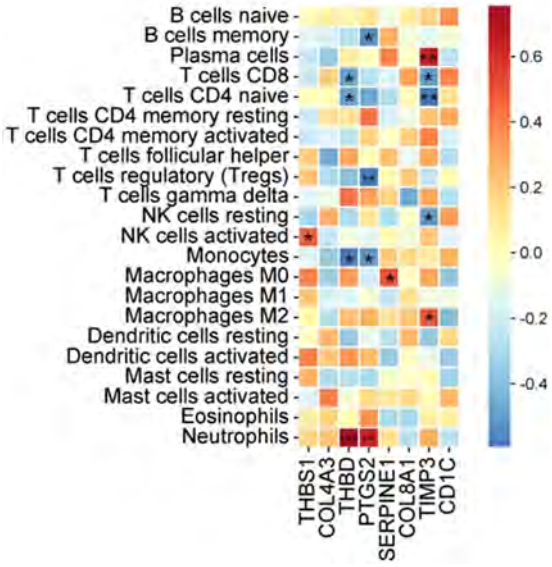


Figure 1. Correlation heatmap between candidate hub genes and immune cell populations in peripheral blood of pregnant women with systemic lupus erythematosus (SLE). Spearman correlation coefficients are represented by color scale, with red indicating positive and blue indicating negative correlations. Significant correlations are marked with asterisks (*p < 0.05, **p < 0.01). Genes along the x-axis correspond to top hub genes identified through PPI analysis (e.g., THBS1, COL4A3, THBD), and immune cell subsets along the y-axis were estimated using CIBERSORT. Notable associations include negative correlations between THBD and neutrophils, and positive correlations between THBD and regulatory T cells (Tregs), suggesting immune regulatory involvement in preeclampsia pathogenesis in SLE.

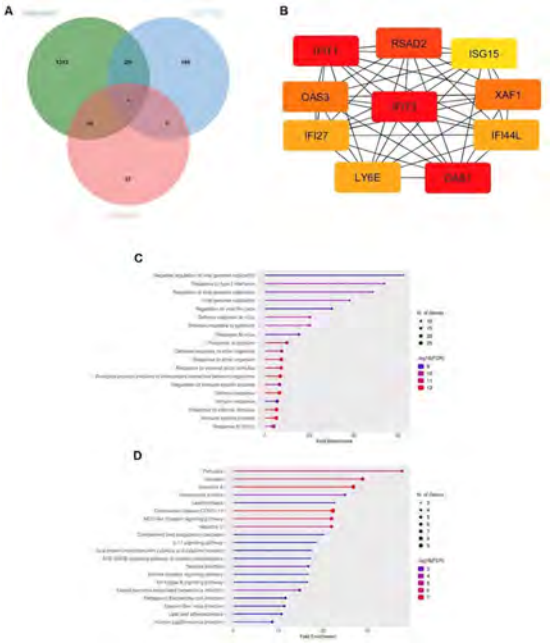


Figure 2. Transcriptomic analysis of shared differentially expressed genes (DEGs) in preeclampsia among pregnant women with systemic lupus erythematosus (SLE). (A) Venn diagram showing overlapping DEGs among three GEO datasets: GSE177029, GSE185047, and GSE48424. A total of 40 genes were shared by at least two datasets. (B) Protein-protein interaction (PPI) network of the top hub genes identified via CytoHubba's MCC algorithm in Cytoscape. Key interferon-stimulated genes such as IFIT1, OAS3, ISG15, and IFI44L were prominent. (C) Gene ontology (GO) enrichment analysis (biological processes) revealed significant overrepresentation of terms related to type I interferon signaling, viral genome replication, and immune response regulation. (D) KEGG pathway enrichment analysis identified key pathways involving infectious and inflammatory responses, including pertussis, measles, COVID-19, complement and coagulation cascades, and IL-17 signaling, highlighting immune activation as a central mechanism in SLE-associated preeclampsia.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of GEO datasets

Dataset ID	Platform	Disease	Sample	Subjects
GSE185047	GPL570	SLE	Peripheral Blood	10 HC, 87 SLE
GSE177029	GPL24676	SLE	Placenta	8 HC, 8 SLE
GSE48424	GPL6480	PE	Peripheral Blood	18 HC, 18 PE

Abbreviations: SLE = systemic lupus erythematosus; PE = preeclampsia; HC = healthy controls.

successfully depicted 40 nodes and 172 edges. The MCC algorithm identified the top 10 HGs (Figure 1B) Regarding immune cell populations in peripheral blood, significant differences were observed in CD8+ T cells and neutrophils proportions. Finally, IFIT1, OAS3, IFI27, LY6E, OAS1, IFI44L, XAF1, and ISG15 were observed to have significant correlations with different immune cells (Figure 2).

Conclusion: This study aimed to identify candidate early biomarkers for preeclampsia in pregnant patients with SLE with novel approach. Ten candidate genes were identified and showed to be significantly correlated with immune cell populations in peripheral blood in patients with preeclampsia. These results provide a molecular framework for the study of preeclampsia in pregnant patients with SLE, which warrant further validation in a longitudinal cohort of patients.

Disclosure: R. Martinez-Canales: None; **E. Galindo-Calvillo**: None; **A. Ortiz-Rios**: None; **B. Avalos-Garcia**: None; **L. Perez-Barbosa**: None; **D. Galarza-Delgado**: None; **C. Skinner-Taylor**: None; **M. Salinas-Carmona**: None; **N. Macias-Segura**: None.

Abstract Number: 1835

Serum Zonulin As A Biomarker Of Renal Involvement In Systemic Lupus Erythematosus: Shedding Light On The Gut-Kidney Axis

Alessandra Milone[1], **Giulio Forte**[2], Alessia Salzillo[2], Barbara De Marino[2], Rosa Giacca[2], Francesco Ciccia[3] and Daniele Mauro[4], [1]University of Campania L. Vanvitelli, Naples, [2]University of Campania L. Vanvitelli, Naples, Italy, [3]Rheumatology Section, University of Campania L. Vanvitelli, Naples, Italy, Naples, Italy, [4]University of Campania, Italy, Naples, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease in which lupus nephritis (LN) remains a major cause of morbidity and mortality. Zonulin, a modulator of intestinal permeability via tight junction regulation, has been implicated in the pathogenesis of several inflammatory diseases. Elevated zonulin levels are associated with systemic inflammation and have been linked to gut-organ axes, such as the gut-joint axis in spondyloarthritis and the gut-brain axis in neuropsychiatric disorders. However, its role in SLE and renal involvement remains largely unexplored.

This study aimed to investigate the potential role of zonulin in SLE pathogenesis, with a specific focus on its association with LN.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

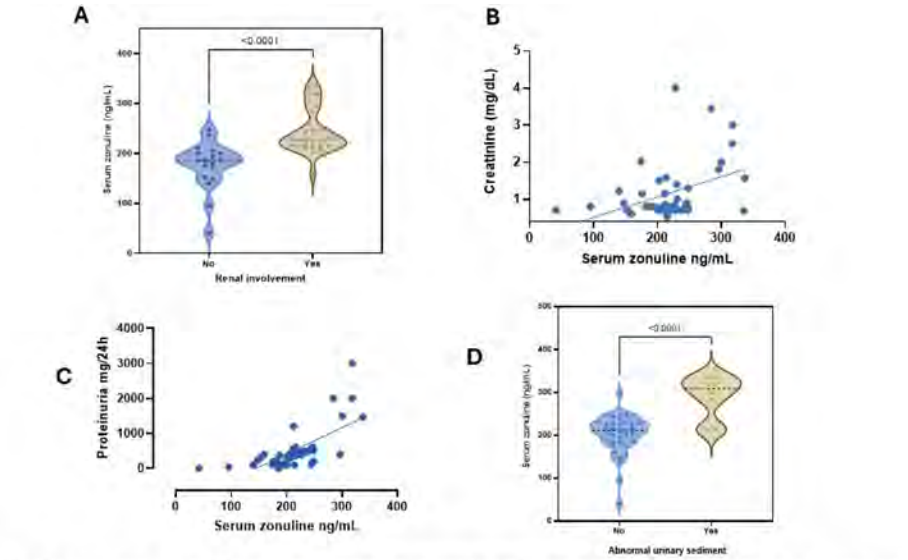


Fig.1 **A:** Correlation ($p < 0.0001$) observed between serum zonulin levels and renal involvement, suggesting a potential link between zonulin and kidney dysfunction.**B:** Correlation ($p < 0.005$; $r = 0.16$) is found between serum zonulin and plasma creatinine in SLE patients (n=46), indicating a limited association with kidney function.**C:** Correlation ($p < 0.0001$; $r = 0.349$) observed between serum zonulin and proteinuria in SLE patients (n=46), suggesting zonulin could be a useful marker for proteinuria.**D:** Correlation ($p < 0.0001$) observed between serum zonulin and abnormal urinary sediment, reflecting potential kidney damage.

Methods: Serum zonulin levels were measured in 46 patients with SLE (2019 ACR/EULAR criteria) and 41 healthy controls using an enzyme-linked immunosorbent assay (ELISA) in a cross-sectional study. Comprehensive demographic, clinical, laboratory, and clinimetric data were collected. Associations between zonulin levels and renal involvement, urinary sediment, serum creatinine, and urinary protein were analyzed. Zonulin expression in LN kidney biopsies was assessed by immunohistochemistry and immunofluorescence.

Results: Analysis of serum zonulin levels revealed a significant increase in SLE patients compared to healthy controls (mean 217.37 ± 56.96 vs. 120.63 ± 83.37; $p < 0.0001$). To determine whether zonulin levels differ between SLE patients with and without lupus nephritis (LN), we analyzed serum zonulin levels according to renal involvement. Interestingly, a substantial increase in zonulin levels was observed in patients with LN compared to those without LN (mean 244.19 ± 44.61 vs. 175.6 ± 48.67; $p < 0.0001$). To investigate whether serum zonulin levels might be associated with renal disease activity or damage, we analyzed zonulin levels in relation to urinary sediment abnormalities, serum creatinine levels, and urinary protein levels. Zonulin levels were significantly higher in patients with abnormal urinary sediment compared to those with normal sediment (mean 289.8 ± 50.25 vs. 202.1 ± 45.6; $p < 0.0001$). Additionally, serum zonulin levels showed a positive correlation with serum creatinine levels ($p < 0.005$; $r = 0.16$) and urinary protein levels ($p < 0.0001$; $r = 0.349$) (Fig. 1).

IHC staining revealed local presence of zonulin in glomeruli and tubules, with higher expression in the latter, suggesting either local production or binding of circulating zonulin, and supporting a direct role in modulating glomerular and tubular function.

Conclusion: Elevated circulating zonulin is associated with renal involvement in SLE, suggesting a previously unexplored gut-kidney axis and a novel biological function of zonulin in regulating glomerular permeability.

Disclosure: A. Milone: None; **G. Forte**: None; **A. Salzillo**: None; **B. De Marino**: None; **R. Giacca**: None; **F. Ciccia**: None; **D. Mauro**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1836

Emerging Role of B Cell Subtype-Specific Intracytoplasmic Toll-Like Receptor Expression and Serum Eotaxin as Biomarkers in Lupus Nephritis

Jennifer Tiaré Balderas Miranda[1], Yatzil Reyna Juarez[2], Beatriz Alcalá-Carmona[3], Nancy R Mejía Domínguez[4], María José Ostos Prado[3], José Luis Maravillas-Montero[5], Fabiola Cassiano-Quezada[6], Guillermo Juárez Vega[4], karina santana[7], Jiram Torres Ruiz[8] and Diana Gómez-Martín[9], [1]Universidad Nacional Autónoma de México, Coyoacán, Federal District, Mexico, [2]Instituto Politècnico Nacional, Tultitán de Mariano Escobedo, Mexico State, Mexico, [3]Instituto Nacional De Ciencias Médicas Y Nutrición Salvador Zubirán, Mexico City, Distrito Federal, Mexico, [4]Universidad Nacional Autónoma de México, Mexico City, Distrito Federal, Mexico, [5]Red de Apoyo a la Investigación, Universidad Nacional Autónoma de México, Tlalpan, Distrito Federal, Mexico, [6]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Ciudad de México, Mexico, [7]INCMNSZ, Ciudad de México, Federal District, Mexico, [8]INCMNSZ, Mexico, Federal District, Mexico, [9]INCMNSZ, Mexico city, Federal District, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: B cells play an essential role in lupus nephritis (LN) pathogenesis. However, abnormalities in specific subtypes like age-associated B cells (ABCs) and double negative (DN) cells have been associated with this clinical manifestation. These cell populations share an increased response to intracytoplasmic TLR (iTLR) stimulation, leading to increased autoantibody production. Besides, diverse cytokines/chemokines have shown to play a role in LN. Nonetheless, the association between B cell subtype-specific expression of iTLRs and the serum levels of diverse cytokines/chemokines with lupus nephritis has not been fully addressed, which is the aim of the present study.

Methods: We carried a cross-sectional study including 54 lupus patients that fulfilled the 2019 EULAR/ACR classification criteria for SLE. 28 with LN according to laboratory and/or histopathological findings and 26 with extrarenal activity (NLN) with SLEDAI-2K ≥6. From each subject we collected clinical, and laboratory data related to disease activity and isolated

Table 1. Demographic, activity and treatment data by study group. LN, lupus nephritis group ; NNL, active non-lupus nephritis ; IQR, interquartile range.

	LN Median (IQR)	NNL Median (IQR)	*p*
Female, n (%)	24 (85.7)	24 (92.3)	0.441
Age (years)	30 (24-39)	38 (27-48)	0.246
Evolution time (months)	66 (19.5-96)	84 (6.25-175.5)	0.472
SLEDAI-2k (points)	**14 (11-16)**	**10 (6.25-12)**	**0.007**
Leukocytes (cells/mm^3)	6150 (4925-7775)	5300 (3800-6375)	0.053
Lymphocytes (cells/mm^3)	1060 (662.5-1630)	1010 (755-1202)	0.478
B cells (%)	18.45% (14.8-40)	16.45 (7.2-31.9)	0.697
B cells (cells/mm^3)	256.56 (87.9-390)	135.5 (85-301)	0.604
C3 (mg/dL)	82 (47.75-114.25)	82 (49.75-103.75)	0.628
C4 (mg/dL)	12 (8-30.25)	8 (8-15)	0.218
Anti-dsDNA (UI/mL)	18.7 (7.72-248.3)	44.5 (6.4-283.9)	0.802
Treatment			
Steroid, n (%)	24 (85.7)	23 (88.5)	0.76
Hydroxychloroquine, n (%)	15 (53.6)	12 (46.2)	0.58
Methotrexate, n (%)	1 (3.6)	2 (7.7)	0.5
Azathioprine, n (%)	**0**	**4 (15.4)**	**0.01**
Mycophenolate, n (%)	**17 (60.7)**	**8 (30.8)**	**0.02**
Cyclophosphamide, n (%)	2 (7.1)	1 (3.8)	0.59
Tacrolimus, n (%)	2 (7.1)	0	0.1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

PBMCs for flow cytometry analysis of TLR7 and TLR9 expression (percentage and absolute number of positive cells and median fluorescence intensity (MFI)) in these B cells subtypes ($CD19^+$): transitional ($CD27^-$ $CD24^{hi}$ $CD38^{hi}$), naïve ($CD27^-$ $CD24^-$ IgD^+), classical ($CD27^+$) and non-classical memory ($CD27^-$ $CD24^+$ $CD38^{-/lo}$), ABCs ($CD21^-$ $CD11c^+$ T-bet^+), DN ($CD24^+$ $CD27^-$ IgD^-) and plasmablasts ($CD27^{hi}$ $CD38^{hi}$). Additionally, serum cytokines were measured by luminometry in a multiplexed assay , including: IL-1α, IL-1β, IL-1ra, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-12 (p70), IL-13, IL-15, IL-17ª, IP-10, MCP-1, MIP-1α, MIP-1β, TNF-α, TNF-β, VEGF and eotaxin. Demographic variables were compared with the Mann-Whitney U test, potential confounder variables were assessed with the G test and associations with mixed logistic regression.

Results: Demographic, laboratory and treatment data are shown in Table 1. Mycophenolate and azathioprine were the only confounding variables. Therefore, we analysed the association of immunological variables adjusted by treatment. As shown in Table 2, a higher expression of MyD88 was constantly associated with LN, from early stages like transitional and naïve B cells to late ones like memory and DN cells. We found that TLR7 associates with LN when expressed in naïve and DN1 cells, and only through transitional cells, TLR9 is associated with LN. All significant variables competed to create a multivariate predictive model. One was selected according to Akaike information criteria, which resulted from the mixed effect of TLR9 MFI in transitional cells (OR 1.006, CI 95% 1.001-1.01, p 0.013) and serum eotaxin (OR 1.018, CI 95% 1.003-1.03, p 0.017), Figure 1.

Conclusion: Our data shows that TLR7/9 and MyD88 expression in B cells and their relation with LN are subtype-specific. However, further studies are needed to delimitate the functional effects of TLRs signaling by cell subset and their relationship to renal affection. As for eotaxin, its potential as a LN biomarker in serum and urine has been previously reported. Nonetheless, the source and specific cell effect induced by this chemokine in LN context remains to be explored.

Table 2. TLR7, 9 and MyD88 expression by B cell subtype associated with LN. Results obtained by mixed logistic regression adjusted by treatment. OR, Odd ratio; CI, confidence interval; MFI, median fluorescence intensity; AU, arbitrary units.

B cell subtype	OR (CI 95%)	p
B cells MyD88⁺ (%)	1.029 (1.008-1.05)	0.007
Transitional		
Transitional cells MyD88⁺ (%)	1.02 (1.005-1.04)	0.016
Transitional 1 cells MyD88+ (%)	1.02 (1.005-1.04)	0.013
MyD88 MFI in transitional 1 cells (AU)	1.001 (1-1.003)	0.043
TLR9 MFI in transitional cells (AU)	1.008 (1.002-1.013)	0.004
Naïve		
Naïve cells TLR7⁺ (%)	1.02 (1.005-1.04)	0.015
Resting naïve cells TLR7⁺ (%)	1.02 (1.003-1.04)	0.02
Activated naïve cells TLR7⁺ (%)	1.01 (1.002-1.03)	0.028
Resting naïve cells MyD88⁺ (%)	1.02 (1.006-1.04)	0.011
Memory		
Classic memory cells MyD88⁺ (%)	1.02 (1.004-1.04)	0.022
Unswitched non-classical memory cells MyD88⁺ (%)	1.02 (1.008-1.04)	0.006
Double negative		
TLR7 MFI in DN1(AU)	1.003 (1-1.006)	0.04
DN2 MyD88⁺ (%)	1.02 (1.003-1.03)	0.02
DN2 MyD88⁺ (cells/mm³)	37.5 (2.44-576.89)	0.01
MyD88 MFI in DN4 (AU)	1.002 (1-1.003)	0.03
Cytokines		
Eotaxin (pg/mL)	1.02 (1.006-1.03)	0.006

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

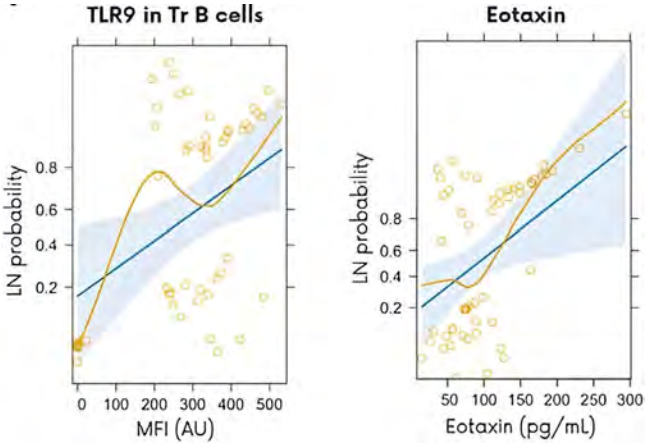


Figure 1. LN predictive model

Disclosure: J. Balderas Miranda: None; **Y. Reyna Juarez**: None; **B. Alcalá-Carmona**: None; **N. Mejía Domínguez**: None; **M. Ostos Prado**: None; **J. Maravillas-Montero**: None; **F. Cassiano-Quezada**: None; **G. Juárez Vega**: None; **k. santana**: None; **J. Torres Ruiz**: None; **D. Gómez-Martín**: None.

Abstract Number: 1837

Enhanced Mitochondrial Activity in B cells from Females Is Required to Drive Increased T-bet Induction by TLR7 in Lupus

John D. Mountz[1], Kathryn Sullivan[2], Shanrun Liu[2], Cynthia Liu[2], Min Gao[2], Walter Winn Chatham[3], Tanecia Mitchell[2] and Hui-Chen Hsu[2], [1]University Alabama Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Nevada, Las Vegas, Las Vegas, NV

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a predominantly female autoimmune disease, with a 9:1 female-to-male ratio. Our previous studies indicated that increased T-bet$^+$ age-related B cells (ABCs) was associated with elevated circulating type I interferon (IFN) and autoantibody development in female, but not male, lupus prone BXD2 mice. While dysregulated type I IFN signaling and Toll-like receptor 7 (TLR7) activation are established contributors to SLE, the molecular mechanisms underlying sex-specific immune responses in mice and humans are not fully understood.

Methods: The transcriptomic profiles of naïve B cells (*IGHM+IGHD+IGHG-*) from 11 female (5 SLE patients and 6 healthy) and 11 male donors (4 autoimmune inflammatory disease patients [AID] and 7 healthy) were analyzed by single cell-RNA sequencing analysis. B-cell response induced by R848 (TLR7 agonist) plus IFNβ *in vitro* was analyzed for early activation of CD69 at 4h and T-bet at 24h, respectively, using B cells derived from female and male BXD2 mice. Real-time PCR was used to determine if R848 plus IFNβ impacts the expression of mitochondrial electron transport chain (ETC) complex I genes, *Ndufa1* and *Ndufa3*. Mitochondrial oxidative phosphorylation (OxPhos) was measured using the Mitochondrial Stress Test and Seahorse Analyzer at 48 and 72h. Flow cytometry was used to evaluate the impact of the complex I inhibitor IM-156 on R848 plus IFNβ-induced T-bet and GL7 upregulation at 72h.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Increased IFN-stimulated genes was the primary transcriptomic signature in female SLE patient B cells. B cells from females, regardless of health status and ethnicity, exhibited elevated expression of mitochondrial ETC genes, including complex I genes compared to males. Regarding mice, there was similar early activation of CD69 at 4h and T-bet expression at 24h in B cells from both sexes. However, B cells from female mice exhibited significantly higher expression of *Ndufa1* and *Ndufa3* at 24h and 72h. There was a significant increase in basal and maximal respiration, ATP production, and reserve capacity in B cells from female mice at 48h and 72h. This was associated with significantly increased development of T-bet^{+}GL7^{+} B cells in female mice at 72h. *In vitro* pharmacologic inhibition of complex I with IM-156 significantly attenuated T-bet upregulation in B cells of female mice.

Conclusion: These findings suggest that the development of T-bet^{+} B cells in female BXD2 mice is strongly dependent on increased mitochondrial OxPhos. Sex-biased differences in OxPhos may therefore act as an intrinsic factor, making it more likely for precursor B cells to reach the energy thresholds needed for differentiation into ABCs under TLR7 and type I IFN stimulation in females with lupus.

Disclosure: J. Mountz: None; **K. Sullivan**: None; **S. Liu**: None; **C. Liu**: None; **M. Gao**: None; **W. Chatham**: Sobi, 2; **T. Mitchell**: None; **H. Hsu**: None.

Abstract Number: 1838

Differential Expression Of Activation Markers On dsDNA-reactive B-cells Between Healthy Subjects And SLE Patients Reveals Unconventional Extrafollicular Activation In SLE

Lars Van Vliet, Annemarie Dorjée, René Toes and **Jolien Suurmond**, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-dsDNA IgG antibodies are a hallmark of systemic lupus erythematosus (SLE), an autoimmune disease characterized by chronic inflammation and multi-organ damage. Evidence suggests that anti-dsDNA antibodies contribute to a range of end-organ injuries, particularly lupus nephritis. Although the overall expansion of plasma cells is well established in SLE, surprisingly little is known about the phenotype of antigen-specific, dsDNA-reactive B cells and the mechanisms underlying tolerance break towards dsDNA. As insights into these mechanisms are important to understand the emergence of autoantibody responses hallmarking SLE, we aimed to disentangle the cellular phenotype and B cell differentiation pathways involved in the production of anti-dsDNA antibodies.

Methods: PBMCs were isolated from healthy subjects and SLE patients. A novel flow cytometry staining for dsDNA was developed using fluorescent dsDNA tetramers and validated using supernatants of single-cell sorted dsDNA-reactive B cells. Phenotyping of dsDNA-reactive B cells was performed using spectral flow cytometry on PBMCs from healthy subjects (n=10), and anti-dsDNA+ (n=10) and anti-dsDNA- (n=11) SLE patients. Anti-dsDNA positivity in serum and culture supernatants was determined using ELISA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: By index sorting and single cell culture we show that naïve dsDNA-reactive B cells are present in both healthy donors and SLE patients. Spectral flow cytometry revealed that dsDNA-reactive B cells are expanded and activated in anti-dsDNA+ SLE patients only, as compared to negative patients and healthy subjects. The largest expansion was observed in the activated CD21-CXCR5- B cell subsets, pointing to activation through the extrafollicular pathway. While comprising only 2.3% ± 0.2% of the dsDNA-reactive B cells in healthy controls, class-switched CD21-CXCR5- B cells accounted for 21% ± 1.5% of the dsDNA-reactive cells in anti-dsDNA+ SLE patients. These findings indicate a direct relationship between immunological activity of dsDNA-reactive B cells and serological anti-dsDNA positivity, which was further confirmed by the observation that dsDNA-reactive B cells in anti-dsDNA+ versus anti-dsDNA- subjects exhibit increased expression of CD11c, CD95, CD69, Ki67, and BST2, and decreased expression of CXCR5, CD23, and CD72. Interestingly, whereas most CD11c+ cells in the total B cell compartment co-expressed T-bet, CD11c+ dsDNA-reactive B cells largely lacked T-bet expression.

Conclusion: We conclude that dsDNA-reactive B-cells are present within resting naïve B cells in healthy subjects and anti-dsDNA IgG-negative SLE, pointing to defective elimination of dsDNA-reactivity in the human naïve B cell repertoire. In anti-dsDNA+ SLE patients, these cells display markers typifying an extrafollicular pathway maturation and are hallmarked by CD11c expression in the absence of T-bet. These findings identify a novel, unconventional, pathway of CD11c+ B cell differentiation, indicate that human dsDNA-IgG responses in SLE have been licensed to differentiate through an extrafollicular pathway, and offer potential targets for selectively inhibiting these cells in SLE.

Disclosure: L. Van Vliet: None; **A. Dorjée**: None; **R. Toes**: Bristol-Myers Squibb(BMS), 5; **J. Suurmond**: None.

Abstract Number: 1839

Transcriptional Profiling of Whole Blood and Kidney Biopsy Samples from Lupus Nephritis and IgA Nephropathy Patients Suggests Different Disease Pathways

Christopher Sisk[1], **Loqmane Seridi**[2], Alan Perlman[3], Matthew Loza[2], Sheng Gao[2], Thomas Parker[4], Daniel Levine[4], Thangamani Muthukumar[5], Yonatan Bardash[6], Benjamin Horowitz[7], Surya Seshan[5] and James Chevalier[3], [1]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, CA, [2]Johnson & Johnson, Spring House, PA, [3]The Rogosin Institute, New York, NY, [4]The Rogosin Institute, Weill Cornell Medical College, New York, NY, [5]Weill Cornell Medical College, New York, NY, [6]Hackensack Meridian Health, Hackensack, NJ, [7]Columbia University Medical Center, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE), associated with significant morbidity and mortality. IgA nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide, characterized by IgA deposition in the glomeruli and subsequent renal damage. Although LN and IgAN share some clinical and immunological similarities, their underlying pathogenic pathways are likely distinct, necessitating further research into their molecular profiles. While the transcriptomic profiles of whole blood samples from SLE patients have been investigated in different cohorts and pointed to the dysregulations of key immune pathways, the differences have not been closely examined in the kidney for LN and IgAN. This study evaluated and compared the transcriptomic profiles of whole blood and kidney biopsy samples from the LN and IgAN patients, as well as the matching healthy controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Samples from 52 patients (34 with LN and 18 with IgAN) were included in this study. Whole blood samples (33 LN and 18 IgAN) were collected in PAXGene tubes. Kidney biopsy samples (24 LN and 16 IgAN) were collected following standard clinical practice, with residual samples preserved for transcriptomic analysis. Healthy control samples including whole blood (n=30) and kidney tissue (n=7) were obtained independently. RNA was extracted from whole blood and kidney samples and used for standard RNA sequencing analysis. In this analysis, statistical significance for differentially expressed genes (DEGs) was defined as a fold change > 2 and FDR < 0.05. Interferon (IFN) gene signature enrichment was quantified using gene set variation analysis (GSVA).

Results: In comparison to healthy controls, there were 2151 differentially expressed genes (DEGs) identified in whole blood of LN patients and 200 DEGs in IgAN patients, respectively. The LN vs IgAN comparison revealed 1054 DEGs. LN DEGs were enriched in Reactome pathways related to "innate immune" and "neutrophil activation", while IgAN DEGs were enriched in "B cell" and "Fc receptor signaling" pathways. Both LN and IgAN kidney samples exhibited over 3000 DEGs compared to controls and shared similar enriched pathways, with IFN pathway further enriched in LN. The kidney IFN gene signature score correlated with serum creatinine levels and eGFR in both diseases.

Conclusion: Transcriptomic analysis highlighted similar and distinct dysregulated pathways in LN and IgAN whole blood and kidney. Greater differences were observed in whole blood transcriptomics, indicating a greater extent of systemic immunological dysregulation between LN and IgAN. Renal IFN pathway activation was prominent in LN and correlated with the severity of kidney dysfunction in both diseases.

Disclosure: C. Sisk: Johnson & Johnson, 3, 11; **L. Seridi**: Johnson & Johnson, 3, 11; **A. Perlman**: Travere, 1; **M. Loza**: Johnson & Johnson, 3, 11; **S. Gao**: Johnson & Johnson, 3, 11; **T. Parker**: None; **D. Levine**: None; **T. Muthukumar**: None; **Y. Bardash**: None; **B. Horowitz**: None; **S. Seshan**: None; **J. Chevalier**: None.

Abstract Number: 1840

Breathomics in Systemic Lupus Erythematosus: uncovering non-invasive markers of disease activity

Lorenzo Beretta[1], Martina Iacubino[2], Lorenzo Rocco[3], Alexandre Voskuijl[4], Marta Alarcon-Riquelme[5], Guillermo Barturen[6], Llam Grimmett[7], Matt Kerr[7], Chiara Bellocchi[3], Barbara Vigone[8], Alessandro Santaniello[8] and Ioannis Parodis[9], [1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Milan, Italy, [2]UNIMI, Milano, Milan, Italy, [3]University of Milan, Milan, Italy, [4]Amsterdam University Medical Center, Amsterdam, Netherlands, [5]Fundación Progreso y Salud, Andalusian Government, Granada, Spain, [6]Center for Genomics and Oncological Research (GENYO), Andalusia, Spain, [7]Owlstone Medical, Cambridge, United Kingdom, [8]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy, [9]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: 3TR (taxonomy, treatment, targets and remission) aims to provide insights into the mechanisms of response and non-response to treatment in systemic autoimmune diseases, including SLE. The lupus arm of 3TR focuses on identifying biomarkers of disease activity. Volatile organic compounds (VOCs) can be generated by metabolic processes in the body. VOCs can diffuse from their point of origin into the blood and be emitted through breath, providing a potential non-invasive method to assess whole-body metabolism and pathophysiological associations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Thirty SLE patients and 29 age- and sex-matched healthy controls were recruited to a single-site, case-control observational study. Breath VOC sampling was performed using the ReCIVA® breath sampler, linked to a clean air supply (CASPER®). Samples were collected on sorbent tubes and analyzed by thermal desorption gas chromatography-mass spectrometry (TD-GC-MS) by Owlstone Medical. VOCs were chemically identified in alignment with the Metabolomics Standards Initiative (MSI) criteria, with blank air samples analyzed to discern VOCs genuinely present in patients' breath. Associations with disease activity (SLEDAI-2K, BILAG-2004, PGA, PhGA), LLDAS, DORIS remission, and fatigue measures were assessed using robust covariate-adjusted models.

Variable	SLE (n = 30)	Controls (n = 29)	p
Age	46.3 ± 13.8	46.7 ± 14.7	NS
Females, n (%)	25 (83.3%)	24 (82.8%)	NS
BMI	23.5 ± 4.7	23.9 ± 3.6	NS
Time since last meal, hours	7.1 ± 5.6	7.7 ± 5.3	NS
Time since last drink, hours	4.3 ± 4.4	3.7 ± 4.2	NS
Time since brushing teeth, hours	3.8 ± 2.1	4.1 ± 2.5	NS
Disease duration, years	14 ± 10.4	-	-
SLEDAI-2K	2.5 (1.25 – 5.75)	-	-
BILAG-2004	5 (1 - 10)	-	-
PhGA (0 - 3)	0.3 (0.232 - 0.825)	-	-
PGA (0 - 100)	40 (2.5 - 70)	-	-
Hypocomplementemia, n (%)	18 (60%)	-	-
Increased anti-dsDNA binding, n (%)	14 (46.7%)	-	-
Steroid use, n (%)	18 (60%)	-	-
Steroid dose, mg/day	2.6 ± 2.7	-	-
Hydroxycloroquine use, n (%)	21 (70%)	-	-
Immunosuppressant use, n (%)	13 (43.3%)	-	-
LLDAS, n (%)	20 (66.6%)	-	-
DORIS remission, n (%)	13 (43.3%)	-	-
FACIT-Fatigue	41.5 (31.5 - 47.5)	48 (44 - 51)	$2.2*10^{-16}$
Fatigue (0 – 100)	50 (0 - 80)	0 (0 – 10)	$3.2*10^{-4}$
LupusQoL fatigue (0 – 100)	81.25 (51.6 - 93.7)	-	-

Demographic and clinical characteristics

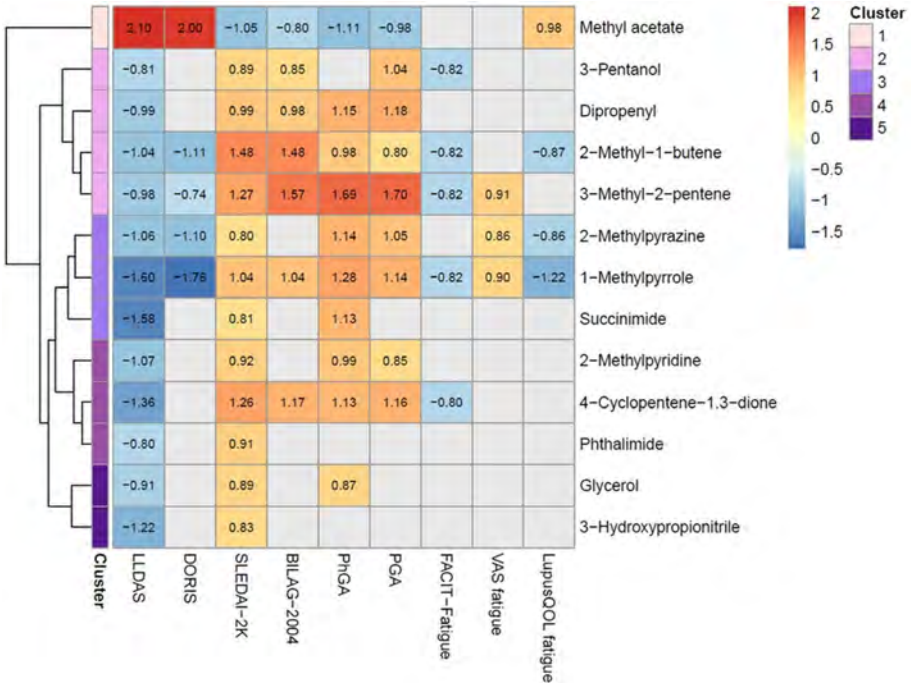


Figure 1 – Strength of associations with selected compounds (robust Cohen's d)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

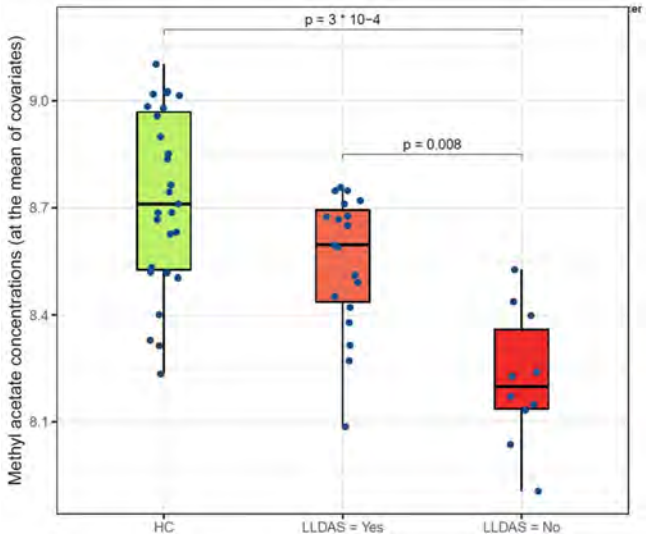


Figure 2 – Concentrations of methyl acetate in HC and in relation to LLDAS status

Results: Demographic and clinical characteristics of patients and controls are summarized in the Table. Among 1,433 detected VOCs, 539 exceeded background levels. Focusing on high-confidence annotations (MSI tier 1 or 2), several significant correlations emerged with clinical parameters, as depicted in Figure 2. Based on compound correlations, five distinct VOC clusters were identified: 1) The anti-inflammatory compound methyl acetate stood apart as the only compound negatively associated with disease activity indices and failure to achieve LLDAS or DORIS remission; consistently, its levels in healthy controls were higher and comparable to those in non-active SLE patients (figure 3); 2) A cluster of four VOCs containing by-products of lipid peroxidation showed a coherent pattern of association with disease activity, lack of remission, and fatigue; 3) A cluster, composed of nitrogen-containing heterocycles of exogenous origin and suggestive of gut barrier disruption, showed moderate associations with disease activity; 4) A cluster, whose main representative a member of the Cyclopentenediones family with pro-inflammatory prostaglandin properties, related with disease activity and fatigue measures; 5) A small heterogeneous group with weak associations with SLEDAI-2K and LLDAS.

Conclusion: These data demonstrate the potential of breath-based VOC analysis in detecting non-invasively pathophysiological changes in SLE. Our findings highlight the intricate role of unresolved inflammation, oxidative stress, and gut barrier dysfunction in driving disease activity, as well as in influencing the patient's perception of fatigue and overall disease severity. Future work should focus on validating these markers and exploring their associations with additional inflammatory indicators as well as assessing their potential for monitoring changes, therapy response, and prognostication.

Disclosure: L. Beretta: None; **M. Iacubino**: None; **L. Rocco**: None; **A. Voskuijl**: None; **M. Alarcon-Riquelme**: None; **G. Barturen**: None; **L. Grimmett**: Owlstone Medical ltd, 3; **M. Kerr**: Owlstone Medical ltd, 3; **C. Bellocchi**: None; **B. Vigone**: None; **A. Santaniello**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1841

Differential metabolomic signatures along lupus nephritis spectrum

Mariana Jiménez Tirado[1], karina santana[2], Jiram Torres Ruiz[3], Jennifer Tiaré Balderas Miranda[4], Diana Gómez-Martín[5], José Carlos Páez Franco[6], Nancy R Mejía Domínguez[7], Hilda Sánchez Vidal[6] and Imelda Cecilia Zarzoza Mendoza[8], [1]Instituto Nacional de Nutrición Salvador Zubirán, Mexico City, Distrito Federal, Mexico, [2]INCMNSZ, Ciudad de México, Federal District, Mexico, [3]INCMNSZ, Mexico, Federal District, Mexico, [4]Universidad Nacional Autónoma de México, Coyoacán, Federal District, Mexico, [5]INCMNSZ, Mexico city, Federal District, Mexico, [6]Red de Apoyo a la Investigación, Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City, Distrito Federal, Mexico, [7]Universidad Nacional Autónoma de México, Mexico City, Distrito Federal, Mexico, [8]Red de Apoyo a la Investigación, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán and Universidad Nacional Autónoma de México, Mexico City, Distrito Federal, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is a common feature in systemic lupus erythematosus (SLE) affecting up to 50% of the individuals with this disease. The gold standard for diagnosis is renal biopsy, nonetheless this procedure can entail complications due to its invasive nature. Metabolomic profile seems to be a promising alternative as a noninvasive diagnostic tool, as it has demonstrated to be useful distinguishing between active LN, SLE without renal involvement and healthy controls. However, scarce information exists about metabolomic profile differences in LN active patients, patients achieving renal response and patients with sustained response. The aim of this study is to characterize the metabolomic profile of three distinct groups of patients representing a broad spectrum of LN, from activity to sustained response.

Methods: Adult patients that met the 2019 ACR/EULAR criteria for SLE were eligible for inclusion and assigned into groups according to LN activity and treatment response. Group 1 included patients with active LN diagnosed by renal biopsy and/or 24-hour urinary protein-creatinine ratio greater than 0.5, active urinary sediment and creatinine increase of 0.3 mg/dl from baseline. Group 2 encompassed patients with either complete or partial renal response after 6 months of starting induction therapy. Group 3 encompassed patients with sustained response defined as a period greater than 2 years since achieving complete response to induction therapy without relapse. Urine metabolomic analysis was performed using a non-targeted method based on liquid chromatography tandem mass spectrometry.

Results: Urine metabolomic profile was obtained from 21, 21 and 20 patients in groups 1, 2 and 3 respectively. The population included adults with a median age of 36 years out of which 90% were female. Among 37 identified metabolites, 10 differential metabolites were detected, of which 7 were increased in group 1. Most of these correspond to sugar acids such as threonic acid (median concentration of 125 in group 1 vs. 89 and 82 in group 2 and 3 respectively, $p < 0.001$), as reported in previous literature reports, has been shown to differentiate between SLE with renal involvement from non-renal involvement. Amino acids were also increased in group 1, such as vanillylmandelic acid (median concentration 5.4 vs 4.6 and 4.1 group 2 and 3 respectively, $p= 0.010$) and norvaline (5.5 vs 4.8 and 4.4, group 2 and 3 respectively, $p= 0.025$), which differs from previous data. Citrate was diminished in active LN, but increased in group 2 and 3 patients (9 vs. 27 and 53 respectively, $p=0.008$). This observation has been related to a dampened oxidative phosphorylation in activated immune cells which normalize after treatment.

Conclusion: Urine metabolomic profile differentiates active LN patients from individuals that have achieved and maintained response to treatment and may serve as a noninvasive diagnostic tool for LN. Active LN is characterized by increased sugar acids and lower citrate levels. These findings give insight into the metabolomic shifts underlying renal activity in SLE and may resolve once response to therapy has been achieved.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Jiménez Tirado: None; **k. santana**: None; **J. Torres Ruiz**: None; **J. Balderas Miranda**: None; **D. Gómez-Martín**: None; **J. Páez Franco**: None; **N. Mejía Domínguez**: None; **H. Sánchez Vidal**: None; **I. Zarzoza Mendoza**: None.

Abstract Number: 1842

Social Vulnerability Index, Type 2 Lupus Symptoms, and Select Dysregulated Immune Features Identify Stage 2 (Pre-classification) SLE in the Lupus Autoimmunity in Relatives (LAUREL) Follow-up Cohort

Melissa Munroe[1], Zoe Reed[2], Joel Guthridge[2], Diane Kamen[3], Timothy Niewold[4], Kendra Young[5], Angel Weng[5], Emma Wu[5], Gary Gilkeson[6], Michael Weisman[7], Mariko Ishimori[7], Daniel Wallace[8], John Harley[9], David Karp[10], Jill Norris[11] and Judith James[2], [1]Oklahoma Medical Research Foundation; Progentec Diagnostics, Inc., Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Medical University of South Carolina, Johns Island, SC, [4]Hospital for Special Surgery, New York, New York, [5]Colorado School of Public Health, Aurora, CO, [6]Medical University of South Carolina, Charleston, SC, [7]Cedars-Sinai Medical Center, LOS ANGELES, CA, [8]Cedars Sinai Medical Center, Studio City, CA, [9]US Department of Veterans Affairs Medical Center, Cincinnati, OH, [10]UT Southwestern Medical Center, Dallas, TX, [11]Colorado School of Public Health, Denver, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Socioeconomic environmental factors are associated with SLE disease activity and early mortality and may contribute to disease progression in at-risk populations. Blood relatives (BRs) of lupus patients have an increased risk of SLE; identification of those at greatest risk of disease transition is essential for early intervention strategies and prevention trial enrollment. The goal of this study is to determine factors associated with the Social Vulnerability Index (SVI; Flanagan et al. 2011. JHSEM. 8[1]: Article 3) that distinguish previously healthy BRs who progress to SLE compared to those who remain stable.

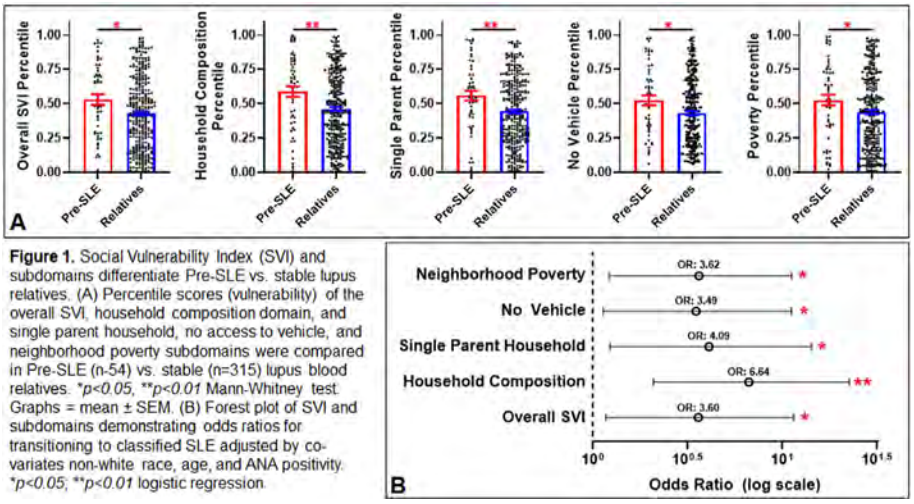


Figure 1. Social Vulnerability Index (SVI) and subdomains differentiate Pre-SLE vs. stable lupus relatives. (A) Percentile scores (vulnerability) of the overall SVI, household composition domain, and single parent household, no access to vehicle, and neighborhood poverty subdomains were compared in Pre-SLE (n-54) vs. stable (n=315) lupus blood relatives. *$p<0.05$, **$p<0.01$ Mann-Whitney test. Graphs = mean ± SEM. (B) Forest plot of SVI and subdomains demonstrating odds ratios for transitioning to classified SLE adjusted by covariates non-white race, age, and ANA positivity. *$p<0.05$; **$p<0.01$ logistic regression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We evaluated domains/sub-domains of the census-tract informed SVI in follow-up Pre-SLE (n=54) vs. stable (n=315) BRs of SLE patients with available geographical location data who previously enrolled in a genetics study (mean time to follow-up = 6.3 yrs) and did not meet SLE classification (≥4 ACR criteria) at baseline (BL). ACR classification criteria were determined by medical record review. BRs completed the connective tissue disease questionnaire (CSQ), type 2 symptom questions, and provided demographic and geographic information. Census-tract based percentile rankings of the overall SVI and its domains/subdomains were calculated. BL sample data included serum ANA and SLE-associated autoantibody specificities, as well as 52 plasma immune mediators (xMAP and ELISA assay available for 54 Pre-SLE vs.137 matched stable BRs).

Results: The overall SVI, as well as household composition domain and single parent household, no vehicle, and neighborhood poverty subdomains differentiated Pre-SLE from stable relatives ($p< 0.05$, **Fig. 1A**) with increased vulnerability (percentile) in Pre-SLE BRs, even after adjusting for race, age, and ANA positivity (**Fig. 1B**). Type 2 symptoms, including anxiety, depression, and chronic fatigue, as well as < 7 hours of sleep/night were consistently associated with SVI/domains ($p< 0.05$; representative features shown in **Fig. 2**) and specifically affected Pre-SLE vs. stable BRs to varying degree (**Fig. 2**).

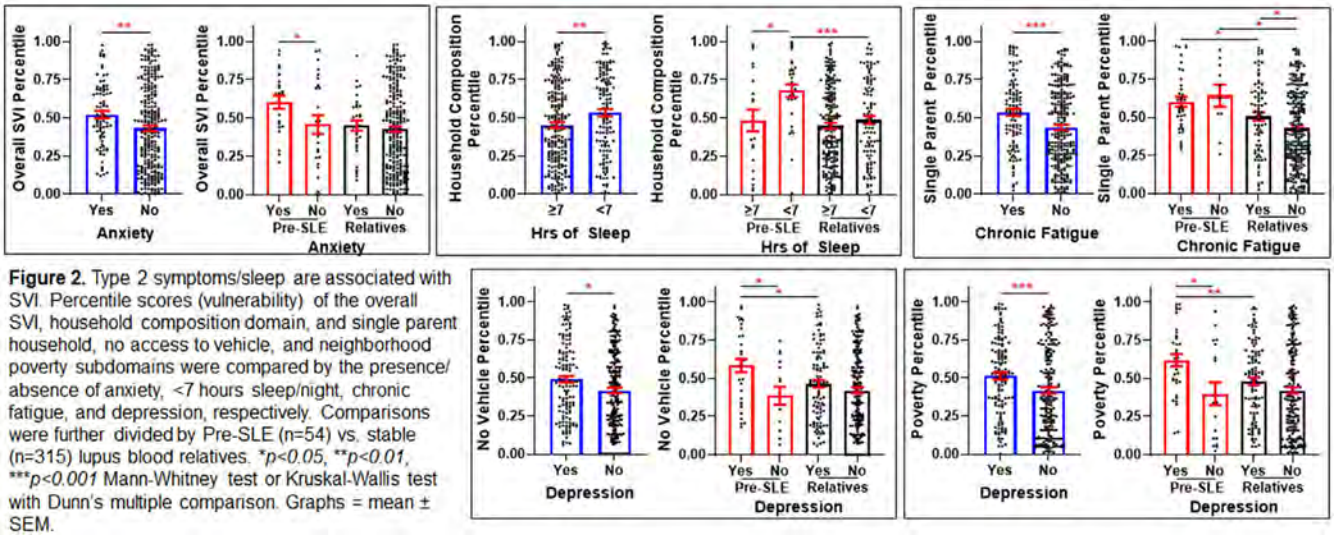


Figure 2. Type 2 symptoms/sleep are associated with SVI. Percentile scores (vulnerability) of the overall SVI, household composition domain, and single parent household, no access to vehicle, and neighborhood poverty subdomains were compared by the presence/absence of anxiety, <7 hours sleep/night, chronic fatigue, and depression, respectively. Comparisons were further divided by Pre-SLE (n=54) vs. stable (n=315) lupus blood relatives. *$p<0.05$, **$p<0.01$, ***$p<0.001$ Mann-Whitney test or Kruskal-Wallis test with Dunn's multiple comparison. Graphs = mean ± SEM.

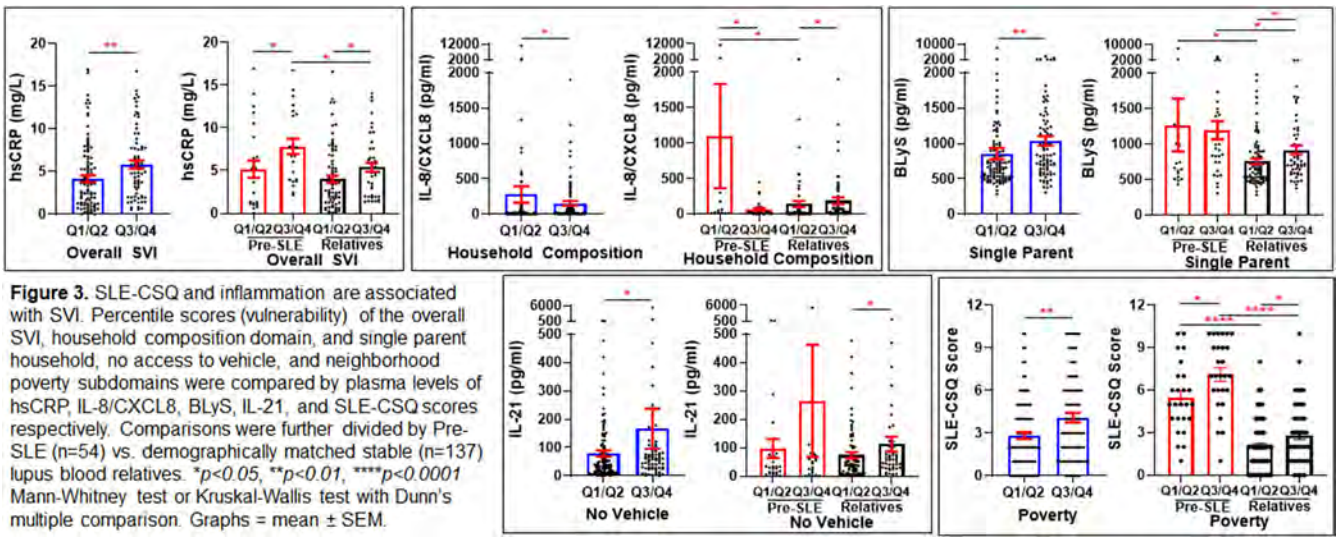


Figure 3. SLE-CSQ and inflammation are associated with SVI. Percentile scores (vulnerability) of the overall SVI, household composition domain, and single parent household, no access to vehicle, and neighborhood poverty subdomains were compared by plasma levels of hsCRP, IL-8/CXCL8, BLyS, IL-21, and SLE-CSQ scores respectively. Comparisons were further divided by Pre-SLE (n=54) vs. demographically matched stable (n=137) lupus blood relatives. *$p<0.05$, **$p<0.01$, ****$p<0.0001$ Mann-Whitney test or Kruskal-Wallis test with Dunn's multiple comparison. Graphs = mean ± SEM.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In addition to BMI and its associated immune mediator leptin (Spearman r >0.2, $p< 0.01$), the SLE-CSQ and associated inflammatory factors CRP, BLyS, IL-8/CXCL8, and IL-21 consistently correlated (Spearman r >0.2, $p< 0.01$) and associated with SVI/domain percentiles/quartiles and specifically affected Pre-SLE vs. stable BRs to varying degree, with IL-8/CXL8 increased with less vulnerability, while other inflammatory and symptomatic factors, including CRP, BLyS, IL-21 and SLE-CSQ scores being increased with greater vulnerability ($p< 0.05$, representative characteristics shown in **Fig. 3**).

Conclusion: The SVI was associated with type 2 and inflammatory features, distinguishing BRs at risk of SLE disease transition vs. BRs who remained stable. Addressing aspects of socioeconomic vulnerability, including poverty, single parent households, and access to vehicle transportation, may be required to advance early intervention strategies and prevention trial participation to decrease chronic inflammation and type 2 symptoms associated with SLE in at-risk populations.

Disclosure: M. Munroe: Progentec Diagnostics, Inc., 3, 4, 5, 10; **Z. Reed**: None; **J. Guthridge**: None; **D. Kamen**: None; **T. Niewold**: AstraZeneca, 2, Pioneering Medicines, 2, Progentec, 2, 4, Zenas, 5; **K. Young**: None; **A. Weng**: None; **E. Wu**: None; **G. Gilkeson**: None; **M. Weisman**: Spyre Therapeutics, 1, 2; **M. Ishimori**: None; **D. Wallace**: PPD, 2; **J. Harley**: None; **D. Karp**: Ampel Biosciences, 2, Biogen, 5, Bristol-Myers Squibb(BMS), 5, Caribou, 1, Eli Lilly, 5, Novartis, 5, Sanofi, 1, UCB, 5, Zura, 1; **J. Norris**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5.

Abstract Number: 1843

Tissue Neutrophils in The Pathogenesis of Lupus Nephritis

Norio Hanata[1], Carmelo Carmona-Rivera[1], Victoria Hoffman[2], Kan Jiang[3], davide Randazzo[4], Meryl Waldman[5], Sarfaraz Hasni[6] and Mariana Kaplan[1], [1]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, MD, [2]Diagnostic and Research Services Branch, Division of Veterinary Resources, Office of Research Services, National Institutes of Health, Bethesda, MD, Bethesda, [3]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, [4]Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, [5]Kidney Disease Section, Kidney Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, Bethesda, PA, [6]National Institutes of Health, Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multiorgan autoimmune disease that frequently affects the kidneys, with lupus nephritis (LN) being a major contributor to morbidity and mortality. A neutrophil gene signature in peripheral blood has been associated with LN, and neutrophil infiltration has been detected in the lupus kidney parenchyma. A putative pathogenic contribution of neutrophils to SLE is the externalization of modified autoantigens and proteins that are detrimental to the host, through dysregulated neutrophil death by the formation of neutrophil extracellular traps (NETs). However, the specific pathogenic impact of neutrophils/NETs in LN has not been systematically studied.

Methods: Lupus-prone NZB/W F_1 and control C57BL/6 (B6) mice were analyzed. The number and maturity of neutrophils were assessed in PBS-perfused kidneys by flow cytometry. The morphology and localization of neutrophils were evaluated by different light microscopy approaches such as, brightfield, namely, hematoxylin-eosin and immunohistochemical (IHC) staining, as well as by immunofluorescence (IF) staining. Kidney biopsies from patients with LN were also analyzed by IHC and IF to corroborate findings obtained from mice. Furthermore, human mesangial cells were stimulated with NETs, and their interactions were assessed by IF and RNA sequencing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: NZB/W F_1 mice exhibited increased renal neutrophil infiltration in comparison to the control B6 mice, particularly following the onset of proteinuria, which correlated with its severity. Kidney-infiltrating neutrophils exhibited a predominantly mature phenotype and localized primarily in the glomerular region. Fragmented neutrophil remnants, suggesting cell death and enhanced debris deposition, accumulated in mesangial areas post-proteinuria onset and in association with mesangial matrix damage score. IF analysis confirmed that NETs deposited in the mesangial regions. Similar findings were observed in biopsies from SLE patients with a diagnosis of LN. *In vitro*, human mesangial cells internalized NETs via endocytosis and phagocytosis, leading to phenotypic changes detectable by RNA sequencing and functional studies.

Conclusion: These results suggest that neutrophils contribute to the pathogenesis of LN through infiltration, NET formation, and interaction with mesangial cells. These observations further implicate aberrant neutrophils in the pathogenesis of lupus-associated organ damage.

Disclosure: N. Hanata: None; **C. Carmona-Rivera**: None; **V. Hoffman**: None; **K. Jiang**: None; **d. Randazzo**: None; **M. Waldman**: None; **S. Hasni**: None; **M. Kaplan**: None.

Abstract Number: 1844

Disease-Associated Macrophages Express an Injury-Associated Gene Program and Localize to Distinct Compartments in Proliferative and Mixed Histologic Classes of Lupus Nephritis

Paul Hoover[1], Rollin Leavitt[2], Jill Buyon[3], Jennifer Anolik[4], Jennifer Barnas[5], Judith James[6], Joel Guthridge[6], Michelle Petri[7], Betty Diamond[8], Soumya Raychaudhuri[1], Nir Hacohen[9], Anne Davidson[10], Arnon Arazi[11] and Accelerating Medicines Partnership: RA/SLE Network, [1]Brigham and Women's Hospital, Boston, MA, [2]Broad Institute, Boston, MA, [3]NYU Grossman School of Medicine, New York, NY, [4]University of Rochester Medical Center, Rochester, NY, [5]University of Rochester, Rochester, NY, [6]Oklahoma Medical Research Foundation, Oklahoma City, OK, [7]Johns Hopkins University School of Medicine, Timonium, MD, [8]The Feinstein Institutes for Medical Research, Manhasset, NY, [9]Broad Institute, Cambridge, MA, [10]Feinstein Institutes for Medical Research, Manhasset, NY, [11]The Feinstein Institutes for Medical Research, Manhasset

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: In collaboration with the AMP-RA/SLE network, we identified disease-associated macrophages (D-Macs) in kidney biopsies from 155 patients with active lupus nephritis (LN) and 30 controls, using single-cell RNA sequencing of ~25,000 myeloid cells (Fig. 1A, B). D-Macs comprised several macrophage subsets and expressed an injury-associated gene program, including TREM2, CD63, CTSD, APOE, SPP1, GPNMB, CD9, and FABP5 (Fig. 1C), which are conserved across monocytes and macrophages in other injured tissues. D-Macs showed positive correlation with the ISN/RPS activity index and were more prevalent in proliferative and mixed histological classes (III/IV±V) compared to the pure membranous class (V) or healthy individuals (not shown). In this follow-up study, we explored the origins and significance of D-Macs in proliferative/mixed LN.

Methods: We analyzed kidney biopsies from LN patients and controls using single-cell RNA sequencing to identify distinct cell populations. Spatial transcriptomics was performed with a custom gene panel to map myeloid subtypes in FFPE kidney samples. We also examined transcriptomic responses to putative nephritic glomerular factors plus M-CSF in healthy CD14 monocytes using flow cytometry and RNA sequencing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Bioinformatic analysis suggested that D-Macs likely differentiate in situ from infiltrating monocytes or resident macrophages, indicating a process of "convergent differentiation" where blood and tissue myeloid cells adopt similar transcriptional profiles in response to factors from diseased kidneys (Fig. 1D-G). To gain further insight into D-Mac differentiation and function, we mapped each D-Mac subset alongside other myeloid populations across renal compartments and in relation to lesions in FFPE sections from 6 LN patients with proliferative or mixed histologic classes (mean ISN/RPS activity = 13.5; S.D = 5.8) and 2 controls. Certain D-Mac subsets were statistically enriched in glomeruli with proliferative lesions (Glomerular D-Macs), while others were mainly found in the tubulointerstitium (Tubulointerstitial D-Macs) (Fig. 2), suggesting that distinct D-Mac subsets may differentiate from different precursors in a compartment-specific manner.

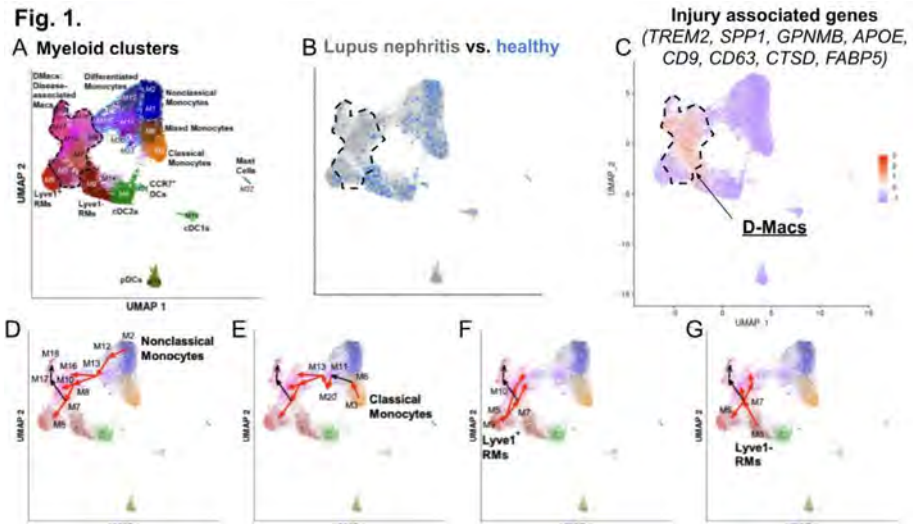


Fig. 1. (A-C) UMAP of single-cell analysis of myeloid cells labeled by clusters (A), case vs. controls (B), or average expression of injury associated genes. Black dotted line outlines the D-Mac clusters. (D-G) Assessing the feasibility of differentiation of monocytes and RMs into DMac clusters. The shortest paths from each putative origin into each DMac cluster is shown based on the results of trajectory analysis using partition based graph abstraction (PAGA) (PMID 30890159). Edges colored in red area also supported by the colocalization analysis presented below in Fig. 3. Paths originating from (D) CD16+ nonclassical monocytes (cluster M2); (E) CD14+ classical monocytes (cluster M3); (F) Lyve1+ RMs (cluster M9); (G) Lyve1- RMs (cluster M0).

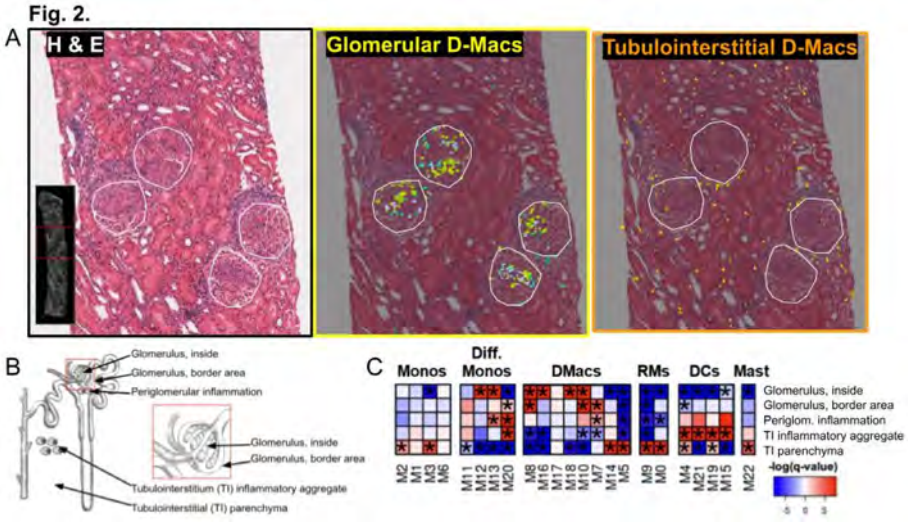


Fig. 2. Specific D-Mac subsets localize to glomeruli or tubulointerstitial regions of tissue. (A) Top panel shows example biopsy from patient with cass IV+V, activity 16/24 and chronicity 5/12. Bottom panel shows (B) areas of kidney in our analysis and (C) quantification of enrichment (red), depletion (blue), and statistical significance (asteriks) across indicated areas from 6 patients and 2 controls.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

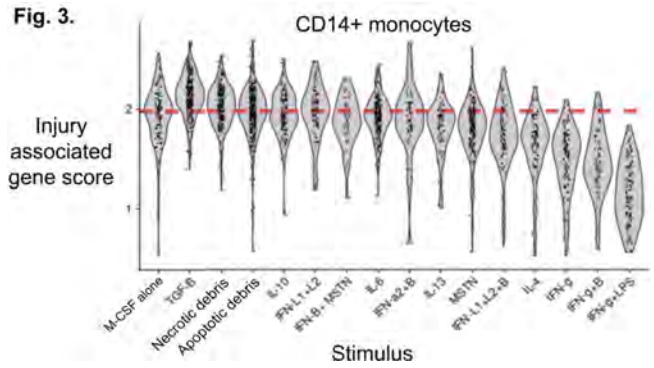


Fig. 3. CD14 monocytes were stimulated with M-CSF alone or with the indicated factors and subject to single cell RNA-seq to measure the average expression of the injury associated score (genes in Fig. 1C).

To determine whether factors from nephritic glomeruli drive D-Mac differentiation from infiltrating CD14+ or CD16+ monocytes, we screened 40 inflammatory mediators identified through single-cell data, spatial transcriptomics, histology, and literature review. Results showed that several glomerular factors—such as immune complexes with resiquimod, cell debris, and TGF-β—promoted the induction of D-Mac-like states, including an injury-associated gene program similar to that observed in patients, from both CD14+ (Fig. 3) and CD16+ (not shown) monocyte precursors.

Conclusion: Our findings highlight key glomerular mediators in proliferative lupus nephritis that may promote D-Mac differentiation from infiltrating monocytes. They support the idea that distinct monocyte states respond similarly to nephritic factors, converging on a shared cellular phenotype. Ongoing studies are focused on elucidating the functional roles of these cells.

Disclosure: P. Hoover: None; **R. Leavitt**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **J. Anolik**: None; **J. Barnas**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Guthridge**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **B. Diamond**: None; **S. Raychaudhuri**: Bonito, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Mestag, 1, 8, Nimbus, 2, Pfizer, 1, Sonoma, 1, 8, Visterra, 6; **N. Hacohen**: None; **A. Davidson**: None; **A. Arazi**: None.

Abstract Number: 1845

Immune Cell Profiles and Transcriptomic Signatures of Atherosclerosis in Systemic Lupus Erythemathosus

Rodolfo Martinez-Canales[1], Andres M. Ortiz-Rios[2], Braulio R. Avalos-Garcia[2], Eva Abigaid Galindo-Calvillo[2], Mario Cesar Salinas-Carmona[1], Noe Macias-Segura[1], Lorena Perez-Barbosa[2], Dionicio A. Galarza-Delgado[3] and Cassandra Michele Skinner-Taylor[2], [1]Immunology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) significantly increases the risk of premature atherosclerosis, contributing to long-term morbidity and mortality. Traditional cardiovascular risk factors do not fully explain this phenomenon. Immunologically driven endothelial injury is proposed as a key mechanism. This study integrates transcriptomic and immune cell profiling data to identify molecular and cellular signatures associated with subclinical atherosclerosis in SLE.

Methods: Transcriptomic datasets GSE154851 and GSE110174 were obtained from the Gene Expression Omnibus. GSE154851 includes patients with increased carotid intima-media thickness (CIMT), while GSE110174 includes SLE patients without CIMT and healthy controls. Gene set enrichment analysis (GSEA) was conducted to identify genes linked to coronary atherosclerosis. Protein-protein interaction (PPI) networks were analyzed using Cytoscape, with hub genes (HGs) identified through five centrality algorithms. Immune cell fractions (22 types) were estimated via CIBERSORTx. A two-way ANOVA with FDR correction was used to compare cell populations across groups, and logistic regression assessed associations with CIMT status.

Results: Nineteen genes were significantly enriched in the atherosclerosis phenotype, including ACTA2, ABCA1, MYH11, APOB, PCSK9, PPARG, TGFBR1, and SMAD3. Immune cell profiling revealed significant differences in CD8+ T cells, CD4+ naïve and memory subsets, NK cells, monocytes, M0 macrophages, and neutrophils. CD8+ T cells, CD4+ naïve T cells, and resting NK cells were negatively associated with CIMT, whereas CD4+ memory resting T cells, monocytes, and

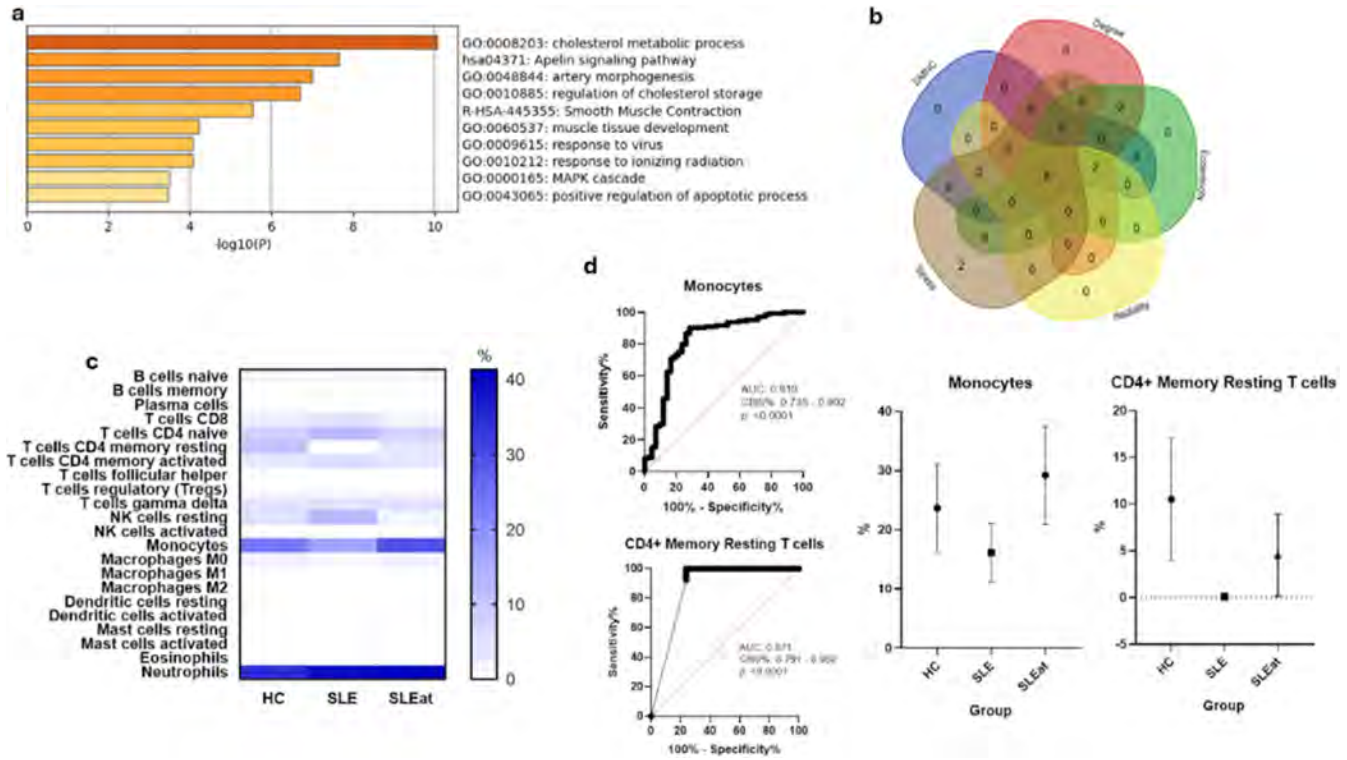


Figure 1. Immune profiling and diagnostic relevance of hub genes in SLE-related atherosclerosis. (a) Gene set enrichment analysis of transcripts linked to coronary atherosclerosis in individuals with systemic lupus erythematosus (SLE). (b) Common hub genes determined by the intersection of five centrality-based algorithms. (c) Relative abundance of 22 immune cell subsets in healthy controls (HC), SLE patients without carotid intima-media thickening (CIMT), and SLE patients with increased CIMT (SLEat). (d) Receiver operating characteristic (ROC) curves showing the predictive performance of monocyte counts and resting CD4+ memory T cells for identifying subclinical atherosclerosis in the SLE cohort.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Logistic Regression Analysis of Immune Cell Types Associated with SLE-Related Atherosclerosis

Cell Type	OR	CI 95%	p
CD8+ T cells	0.72	0.62 – 0.85	<0.001
CD4+ Naïve T cells	0.81	0.74 – 0.89	<0.001
CD4+ Memory Resting T cells	4.81	2.48 – 9.35	<0.001
CD4+ Memory Activated T cells	0.36	0.25 – 0.51	<0.001
Resting Natural Killer cells	0.27	0.14 – 0.50	<0.001
Monocytes	1.41	1.26 – 1.58	<0.001
Macrophages M0	2.71	1.87 – 3.91	<0.001

Note: Odds ratios (OR), confidence intervals (CI95%), and p-values indicate the strength of association between immune cell subsets and the presence of increased carotid intima-media thickness (CIMT) in SLE patients, relative to those without CIMT.

M0 macrophages showed positive associations (all $p < 0.001$). Diagnostic accuracy was supported by ROC curve analysis, highlighting monocytes and CD4+ memory T cells as potential biomarkers.

Conclusion: This study uncovers specific immune cell subsets and gene networks linked to atherosclerosis in SLE. The findings emphasize the contribution of innate and adaptive immune dysregulation in vascular pathology and support further exploration of immune-based biomarkers to stratify cardiovascular risk in lupus.

Disclosure: R. Martinez-Canales: None; **A. Ortiz-Rios**: None; **B. Avalos-Garcia**: None; **E. Galindo-Calvillo**: None; **M. Salinas-Carmona**: None; **N. Macias-Segura**: None; **L. Perez-Barbosa**: None; **D. Galarza-Delgado**: None; **C. Skinner-Taylor**: None.

Abstract Number: 1846

Integrated spatial and single-cell profiling of treatment-naïve lupus nephritis biopsies

Roopa Madhu[1], Rachael Bogle[2], DANIEL STEIN[3], JIngyi Cao[4], Alex Tsoi[2], Caleb Marlin[5], Thomas Eisenhaure[6], Peter Izmirly[7], Mala Masson[8], Kevin Wei[9], Victoria Werth[10], Jennifer Barnas[11], Michael Brenner[12], Judith James[5], Johann Gudjonsson[13], Joel Guthridge[5], Nir Hacohen[14], Kelly Ruggles[15], Soumya Raychaudhuri[16], Jill Buyon[17], Michelle Petri[18], Brad Rovin[19], Andrea Fava[20], ilya Korsunsky[16] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network,Accelerating Medicines Partnership: RA/SLE Network, [1]Brigham and Women's Hospital, Brookline, MA, [2]University of Michigan, Holland, OH, [3]Harvard University, Boston, [4]BWH, Boston, [5]Oklahoma Medical Research Foundation, Oklahoma City, OK, [6]Broad Institute, Cambridge, MA, [7]New York University Grossman School of Medicine, New York, NY, [8]NYU Langone Health, New York, [9]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [10]University of Pennsylvania, Wynnewood, PA, [11]University of Rochester, Rochester, NY, [12]Brigham and Women's Hospital, Harvard Medical School, Newton, MA, [13]University of Michigan, Ann Arbor, MI, [14]Broad Institute of MIT Harvard, Cambridge, MA, [15]NYU Grossman School of Medicine, Brooklyn, NY, [16]Brigham and Women's Hospital, Boston, MA, [17]NYU Grossman School of Medicine, New York, NY, [18]Johns Hopkins University School of Medicine, Timonium, MD, [19]The Ohio State University, Columbus, OH, [20]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Lupus nephritis (LN) is characterized by kidney inflammation and leads to loss of kidney function. Depending on race/ethnicity, up to 60% of Systemic Lupus Erythematosus (SLE) patients develop LN early in their disease. However, the cellular pathways driving disease onset and progression remain poorly defined. Because these pathways involve cell interactions at different spatial scales, spatial mapping of kidney biopsies can provide critical insights. This study aimed to spatially profile kidney biopsies from early LN patients to identify key cellular states, interactions, and regions associated with disease progression and to construct a spatial atlas of early LN pathology.

Methods: We analyzed Formalin-Fixed Paraffin-Embedded (FFPE) kidney biopsies from patients with LN and UPCR between .250 and .499 (n = 8), non-LN SLE (no LN; n = 3), and healthy controls (n = 4). Serial sections were profiled using Xenium (5 μm; 5101 genes) and single-cell FFPE RNA seq (23 μm; whole transcriptome). Xenium transcripts were quality filtered and segmented into cells using a transcript density-based segmentation method (Baysor). Custom pipelines were used to process and integrate Xenium and scFFPE data. After QC, we obtained ∼400,000 cells from Xenium and ∼100,000 cells from scFFPE.

Results: Integration of scFFPE and Xenium data revealed 8 major cell lineages based on marker expression (Fig. 1A, B). LN and non-LN samples showed enrichment of lymphocytes compared to controls (Fig. 1C). Cell projections (Xenium)

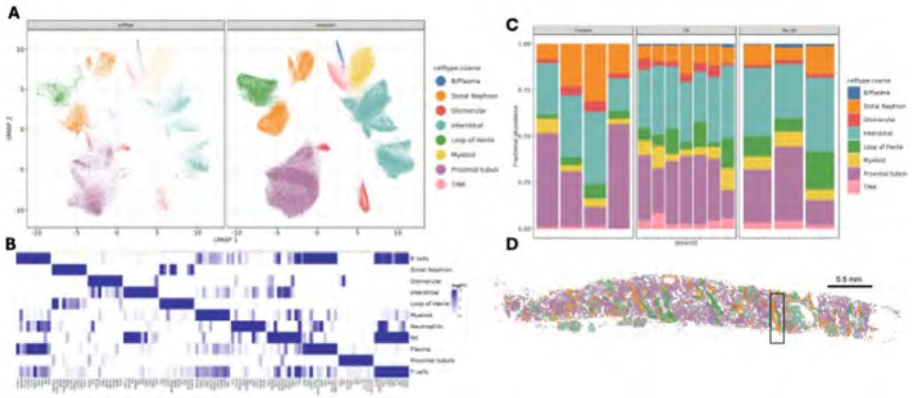


Figure1: (A) UMAP projection of cells from scFFPE RNA sequencing and Xenium datasets. Cells are colored by their major cell types. (B) Heat map of logFC of top 15 marker genes for every cell type. (C) Relative abundance of cell type populations in each sample. Relative abundance is the ratio of number of cells of each type to the total number of cells in the sample. (D) Spatial projection of the cell types in (A) onto tissue space. Insert highlights the distal tubule.

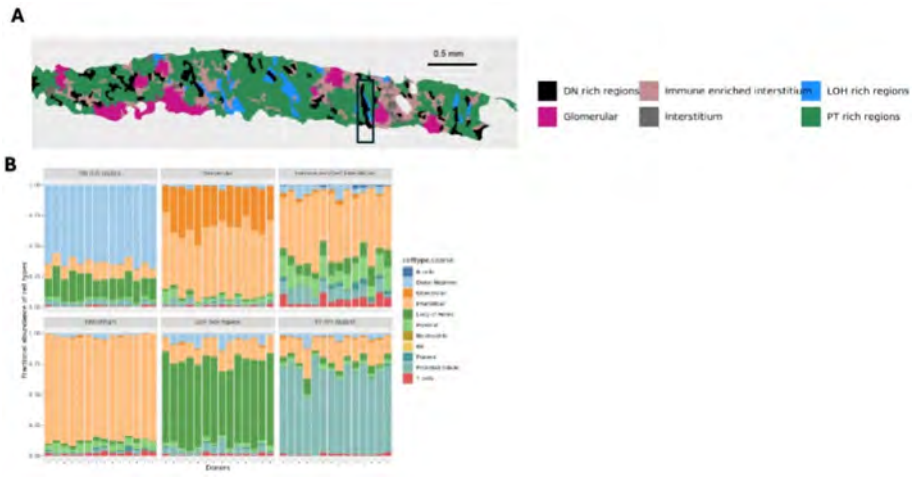


Figure2: (A) Spatial segmentation of the tissue shown in 1D. Regions are colored by their type. Insert highlights the distal tubule in 1D, which is now detected and annotated as a DT rich region. (B) Relative abundance of cell types in each region in each sample in the dataset. Regions are annotated based on their cell composition.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

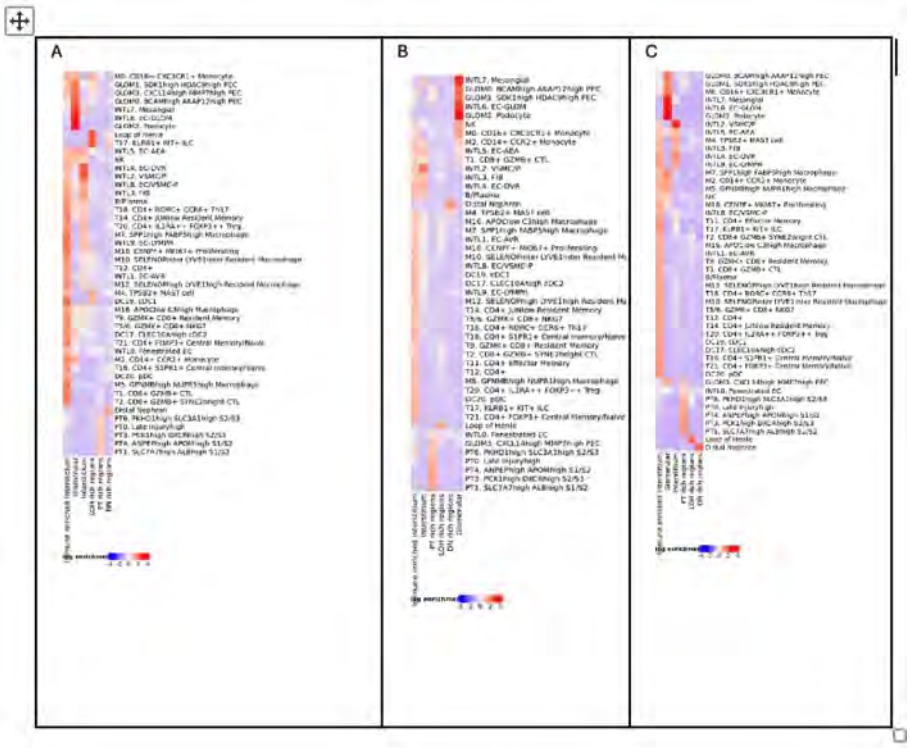


Figure3: (A-C): Log enrichment of cell states within each spatial region: (A) in control samples, (B) No LN samples, (C) LN samples.

confirmed that profiled cells localized to expected anatomical regions (Fig. 1D). Using the public AMP SLE reference and in house pipelines, we annotated 43 cell states across the 8 cell lineages and mapped in tissue space. Transcript-based tissue segmentation with Tessera identified six regions: 3 tubular, 1 glomerular, and two interstitial (Fig. 2A, B).

We next quantified cell state enrichment in each region across groups (Fig. 3). In controls, cell states localized to expected regions. In LN, macrophage subsets M5 (GPNMB high NUPR high) and M7 (SPP1 high FABP5 high) were enriched in glomerular regions, compared to interstitial enrichment in controls and non-LN SLE. Colocalization analyses revealed that M5 and M7 colocalized in the glomerular regions in LN samples, suggesting recruitment to inflamed regions during early disease.

Conclusion: We generated a comprehensive kidney spatial atlas of early LN, non-LN SLE, and healthy controls, integrating scFFPE RNA sequencing and Xenium spatial transcriptomics. In this initial study of patients with early-stage LN, we have started to characterize distinct cell states that may be involved in the development of LN in patients with SLE. We found that patients with SLE and no LN accumulated lymphocytes, suggesting that even in the absence of frank LN, the kidneys of lupus patients may be affected. We also found that resident macrophages tend to move from the interstitium to the glomerular region in patients with early LN. These macrophages may be involved in initiating glomerular injury in LN.

Disclosure: R. Madhu: None; **R. Bogle**: None; **D. STEIN**: None; **J. Cao**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **C. Marlin**: None; **T. Eisenhaure**: None; **P. Izmirly**: Hansoh Bio, 2; **M. Masson**: None; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **V. Werth**: AbbVie/Abbott, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta Bio, 2, Calyx, 2, CSL Behring, 5, Cugene, 2, Eli Lilly, 2, EMD Serona, 2, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 5, Immunovant, 2, Janssen, 2, Kwoya Kirin, 2, Merck/MSD, 2, Novartis, 2, Nuvig, 2, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, Rome Pharmaceuticals, 5, Sanofi, 2, Takeda, 2, UCB, 2, 2, Ventus, 2, Viela, 5; **J. Barnas**: None; **M. Brenner**: AbbVie/Abbott, 2, Johnson & Johnson, 5, Mestag Therapeutics, 2, 8, Moderna, 2, Ono Pharma, 5, Simcere, 2; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Gudjonsson**: None;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

J. Guthridge: None; **N. Hacohen**: Calico Biosciences, 5, Cytoreason, 1, 11, Danger Bio, 1, 11, Moderna, 5, Repertoire Immune Medicines, 1, 11, Takeda, 5; **K. Ruggles**: None; **S. Raychaudhuri**: Bonito, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Mestag, 1, 8, Nimbus, 2, Pfizer, 1, Sonoma, 1, 8, Visterra, 6; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **i. Korsunsky**: Mestag therapeutics, 2.

Abstract Number: 1847

Spatial transcriptomics reveals a complex microanatomic patterning of complement mediated inflammation and fibrosis in Class III pediatric lupus nephritis associated with local histologic injury

Sarah McCuaig[1], Julia Rood[1], Em Elliott[1], Portia Kreiger[1] and Edward Behrens[2], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]CHOP, West Chester, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) occurs in over 50% of patients with pediatric systemic lupus erythematosus (pSLE) and results in significant morbidity due to suboptimal kidney remission rates and the sequelae of prolonged intensive immunosuppressive therapy. LN is often patchy, with some glomeruli severely damaged while others remain histologically unaffected in the same kidney. However, the local factors that drive this patchy tissue injury remain unclear. Using novel spatial transcriptomic technology, we interrogated microanatomic transcriptional differences between histologically damaged and unaffected glomeruli and adjacent tubules in pSLE LN to understand local drivers of renal injury.

Methods: Archived pre-treatment FFPE pediatric renal biopsies were stained with H&E. Using the Visium 10x platform, spatially barcoded gene expression libraries mapped to 55μM diameter spots were sequenced. A pediatric pathologist identified histologically damaged and unaffected glomeruli based on H&E staining. Loupe Browser (10X Genomics) was used to annotate damaged versus unaffected glomeruli (Figure 1A) and adjacent tubules (Figure 2A) and their associated barcoded spots. Differential gene expression analysis of spots was performed in R. 3 cases of pSLE Class III LN, 3 cases of pSLE Class V LN, and 3 "healthy control" kidneys resected for non-immune pathology were assessed. Immunofluorescence staining was used to assess cellular localization of specific transcriptional changes at the protein level.

Results: Differential gene expression analysis revealed a unique transcriptional signature in histologically damaged compared to unaffected Class III LN glomeruli (Figure 1B). While interferon-stimulated genes were unchanged (Figure 1C), damaged Class

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

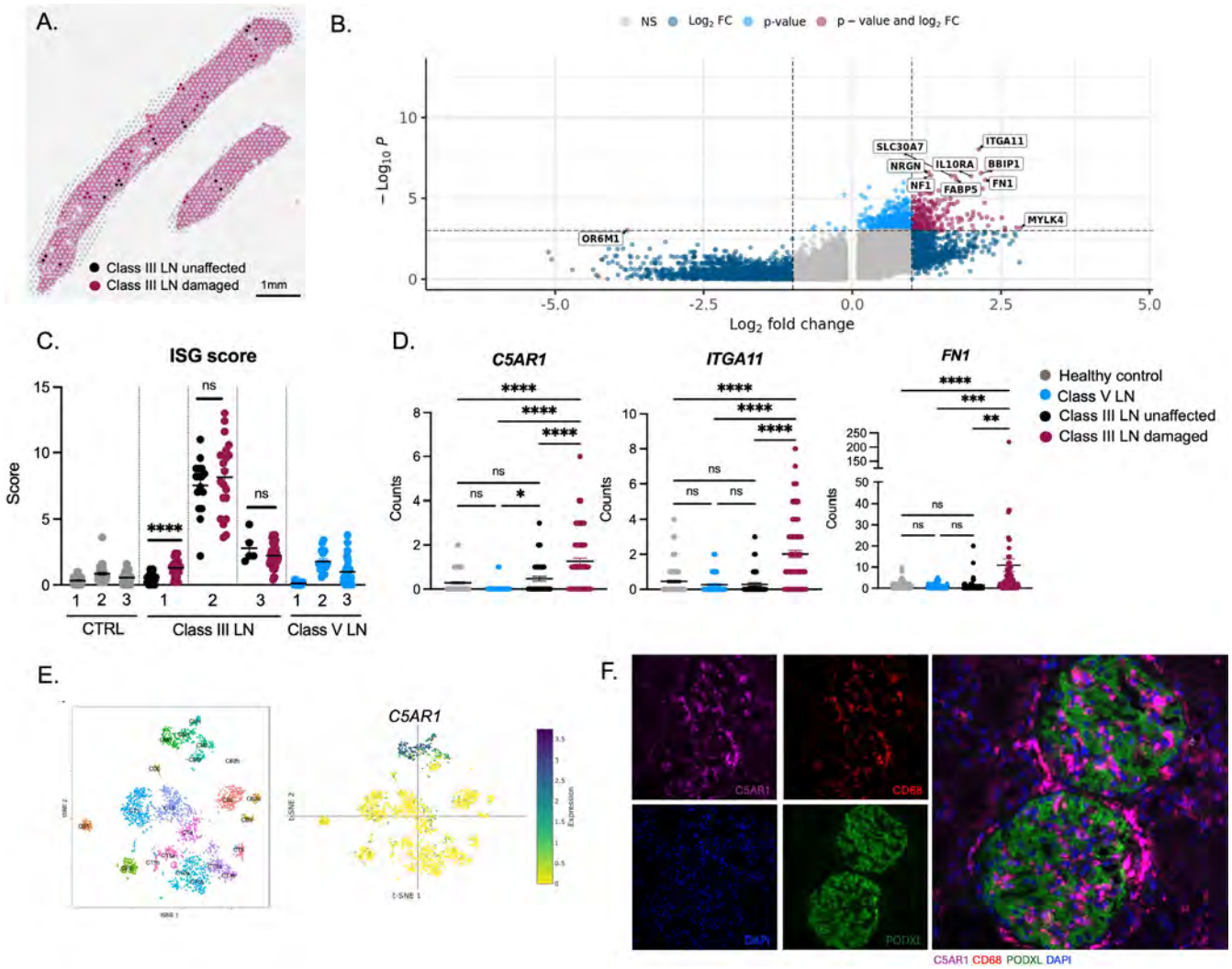


Figure 1 – Damaged Class III LN glomeruli show upregulation of C5AR1 and genes linked to fibrosis. Spatial transcriptomics using the Visium 10x platform was performed on FFPE renal biopsies from pediatric patients with Class III LN (N=3), Class V LN (N=3), and "healthy" controls (N=3). (A) Representative H&E section from Class III LN biopsy with overlay of 55uM spots showing pathologist annotation of histologically damaged (pink) and unaffected (black) glomeruli. (B) Enhanced volcano plot showing differentially expressed genes comparing histologically damaged to unaffected glomeruli Class III LN glomeruli. Positive log2 fold changes are genes with increased expression in damaged compared to unaffected glomeruli. (C) ISG score computed as the average of the expression of IFI44, IFI44L, MX1, IFIT1, HERC6. Each dot is expression from a 55uM spot. X axis numbers represent individual patients in each disease subset. **** p< 0.0001 unpaired T-test for comparison between damaged and unaffected Class III LN glomeruli. (D) C5AR1, ITGA11, FN1 expression. Each dot is expression from a 55uM spot. N=3 healthy control. N=3 Class III LN. N=3 Class V LN. ****p<0.0001, ***p<0.001, **p<0.01, one way ANOVA with Tukey's post-test for multiple comparisons. (E) Publicly available single cell sequencing data from LN biopsies from the Accelerating Medicines Partnership (AMP) showing C5AR1 expression is highest in the macrophage clusters. (F) Immunofluorescence staining of C5AR1, CD68 (marks myeloid cells), PODXL (marks podocytes) in a representative Class III LN biopsy.

III LN glomeruli showed increased expression of *C5AR1* and both *ITGA11* and *FN1* compared to unaffected Class III LN glomeruli (Figure 1D) implicating complement component 5a activity and fibrosis respectively. *C5AR1* expression is likely driven by myeloid cells based on analysis of single cell RNA sequencing data from the Accelerating Medicines Partnership (Figure 1E) and immunofluorescence staining (Figure 1F). Periglomerular tubules next to damaged Class III LN glomeruli show increased early complement gene expression and expression of the fibrosis inducing gene *POSTN* compared to those next to unaffected Class III LN glomeruli and those far from glomeruli (Figure 2B,C). All changes remain significant even after correcting for patient level differences. *POSTN* expression correlates with other fibrosis-related genes including *LGALS1* (Figure 2D).

Conclusion: LN is characterized by a specific microanatomic patterning of inflammation and fibrosis. Damaged glomeruli and adjacent tubules in Class III LN are marked by local complement gene and *C5AR1* expression and fibrosis-related

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

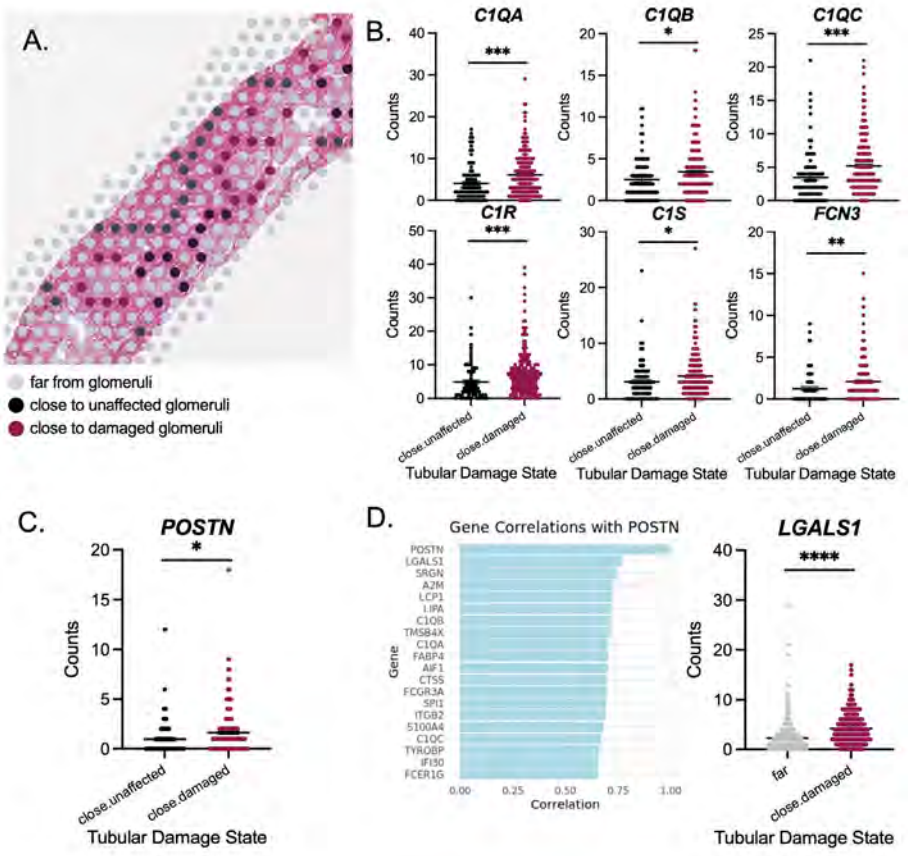


Figure 2 – Transcriptional differences between periglomerular tubules close to damaged and unaffected glomeruli in Class III pSLE GN. (A) Representative H&E section from Class III LN biopsy with overlay of 55uM spots showing annotation of tubules that are periglomerular (black = close to unaffected glomeruli, pink = close to damaged glomeruli) or far from glomeruli (grey). (B) Complement gene expression in periglomerular tubules close to damaged and unaffected glomeruli. C) POSTN expression in periglomerular tubules. (D) Pearson correlation analysis showing top genes correlated with POSTN. LGALS1 expression in tubules close to damaged glomeruli and far from damaged glomeruli. Each dot represents expression from a 55uM spot. N=3 pSLE Class III LN patients. P values are unpaired T-tests. ****p<0.0001, ***p<0.001, **p<0.01, *p<0.05.

genes. These results suggest novel useful biomarkers and potential therapeutic targets for LN (eg. avacopan to target C5aR and early targeting of fibrosis-related pathways). These data will inform mechanistic studies using animal models, and translational clinical studies of these novel targets.

Disclosure: S. McCuaig: None; **J. Rood**: None; **E. Elliott**: None; **P. Kreiger**: None; **E. Behrens**: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9.

Abstract Number: 1848

DS-7011a, An Anti-TLR7 Antagonistic Monoclonal Antibody, Suppresses Human Immune Cells and Multiple Cytokines/Chemokines Related to the Pathogenesis of SLE

Nanako NIshiyama[1], Atsushi Manno[1], Tomohiro Honda[2], **Shigeko Uryu**[1], Yuichiro Imamura[2], Ryutaro Fukui[3], Yusuke Murakami[4], Kensuke Miyake[5] and Yoshiaki Tomimori[6], [1]Daiichi Sankyo Co., Ltd., Tokyo, Tokyo, Japan, [2]Daiichi Sankyo Co., Ltd., Tokyo, Japan, [3]Chiba University, Tokyo, Japan, [4]Musashino University, Tokyo, Japan, [5]Chiba University, Chiba, Japan, [6]Daiichi Sankyo, Inc., Basking Ridge, NJ

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Toll-like receptor (TLR) 7 is a pattern recognition receptor that recognizes nucleic acids and is implicated in the pathogenesis of systemic lupus erythematosus (SLE). We have previously shown that DS-7011a, an anti-TLR7 monoclonal antibody, inhibits IFNα and IL-6 release from TLR7 agonist-stimulated human peripheral blood mononuclear cells (PBMCs). As TLR7 is expressed in human plasmacytoid dendritic cells (pDCs), B cells and monocytes, in this study, we aim to investigate the inhibitory effects of DS-7011a on TLR7-mediated activation of pDCs, B cells and monocytes related to the pathogenesis of SLE. Additionally, we also aim to evaluate the inhibitory effects of DS-7011a on the production of multiple cytokines/chemokines implicated in the pathogenesis of SLE in human PBMCs.

Methods: Human PBMCs were isolated from fresh whole blood of healthy donors and frozen purified human pDCs, B cells and monocytes were purchased. These cells were stimulated with TLR7 agonists in the presence of DS-7011a to evaluate its inhibitory effects on TLR7-mediated activation *in vitro*. The production of cytokines/chemokines after stimulation was measured by Multiplex assay or AlphaLISA. The production of IgG from B cells was measured by cell-based ELISA,

Results: The production of IFNα, IL-6 and IgG stimulated with TLR7 agonists in human pDCs, monocytes and B cells respectively, was suppressed by DS-7011a dose dependently. Additionally, stimulation with a TLR7 agonist led to the production of several cytokines/chemokines implicated in the pathogenesis of SLE, including IL-6, monocyte chemoattractant protein (MCP) -1, MCP-3, monocyte inflammatory protein (MIP) -1α, MIP-1β, IL-12 (p40), and TNF-α in human PBMCs. All of these cytokine productions were also inhibited by DS-7011a in a dose-dependent manner.

Conclusion: DS-7011a demonstrated inhibitory effects on TLR7-mediated activation of immune cells and suppressed the production of IgG and pro-inflammatory cytokines/chemokines implicated in the pathogenesis of SLE. Since autoantibodies and pro-inflammatory cytokines/chemokines are known as therapeutic targets individually, DS-7011a has shown potential as a novel therapeutic agent for SLE by inhibiting these multiple mechanisms.

Disclosure: N. NIshiyama: Daiichi Sankyo Co., Ltd., 3; **A. Manno**: Daiichi Sankyo Co., Ltd., 3; **T. Honda**: Daiichi Sankyo Co., Ltd., 3; **S. Uryu**: Daiichi Sankyo Co., Ltd., 3; **Y. Imamura**: Daiichi Sankyo Co., Ltd., 3; **R. Fukui**: Daiichi Sankyo Co., Ltd., 5, 10; **Y. Murakami**: Daiichi Sankyo Co., Ltd., 5, 10; **K. Miyake**: Daiichi Sankyo Co., Ltd., 5, 10; **Y. Tomimori**: Daiichi Sankyo, Inc., 3.

Abstract Number: 1849

Time-course RNA sequencing analysis of longitudinal peripheral blood samples to elucidate the factors determining treatment resistance in systemic lupus erythematosus

Shuji Sumitomo[1], Hideki Oka[2], Takeshi Iwasaki[3] and Koichiro Ohmura[4], [1]Kobe City Medical Center General Hospital, Kobe city, Hyogo, Japan, [2]Kobe City Medical Center General Hospital, Kobe, Japan, [3]Kyoto University, Kyoto, Japan, [4]Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) encompasses a subset of patients who exhibit resistance to standard treatments, posing a significant challenge to achieving remission. Our study aimed to elucidate the molecular mechanisms underlying treatment resistance in clinical practice. To address this, we conducted RNA sequencing analysis using longitudinal peripheral blood samples.

Methods: 42 peripheral blood samples from naïve or flare 14 SLE patients were collected before treatment and 4 and 12 weeks after treatment who received standard induction therapy except for belimumab, anifrolumab, and rituximab. Patients were divided into two groups based on their response to treatment. 1) Treatment responder group; those who achieved a SLEDAI-2K score of less than 4 after 12 weeks, and 2) Treatment-resistant group; those who did not achieve less than 4.

RNA sequencing was performed using NovaSeq 6000 (Illumina) with a paired-end read of 100 base pairs. FASTQ format data were mapped to the UCSC human genome 38 as the reference sequence. Sequence read count data was analyzed using R (4.3.2). Basic analysis were performed using edgeR. Time-course expression analysis was performed using maSigPro. We identified differentially expressed genes (DEGs) by comparing samples obtained before treatment and at 12 weeks post-treatment.

Results: Patients with a SLEDAI score of 4 or less at 12 weeks were classified as responders (n=8), and those with a score of more than 4 were classified as the resistant group (n=6). In PCA plot of RNA-seq of peripheral blood, there was no clear distinction between responders and resistant. No clear group discrimination was found after treatment.

In DEG analysis, 19 DEGs were detected in responder comparing 0w and 12 weeks after treatment, and 85 in resistant. Enrichment analysis showed that adequately suppressed immune response in resistant group. We thought that information of the time series sample of the same person was not utilized, and planned to take advantage of the sequential sampling information.

We performed time-course analysis using samples before treatment and 4 and 12 weeks after treatment to identify critical factors that are involved in treatment resistance over time. maSigPro is a software to identify genes that show different gene expression profiles across analytical groups in time-course experiments. maSigPro can also perform time-series clustering to identify genes with significant intergroup differential expression.

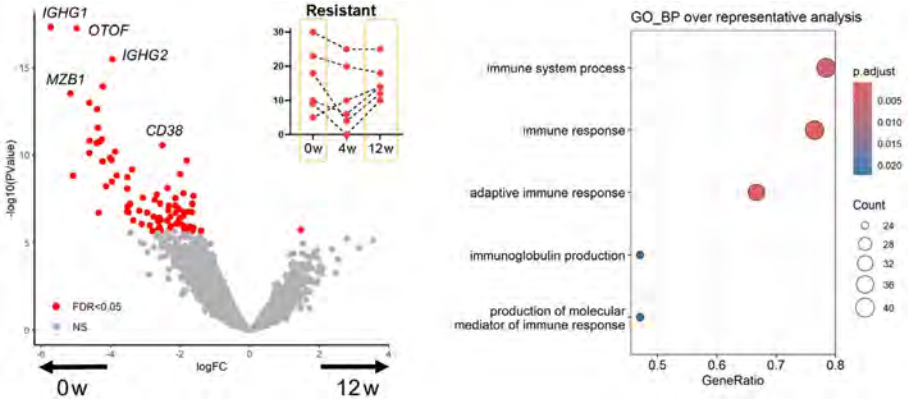


Figure 1. DEG-based analysis; 85 DEGs were detected in treatment-resistant group comparing 0w and 12 weeks after treatment (left, volcano plot). Enrichment analysis (right) showed that immune response process is suppressed in treatment-resistant group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

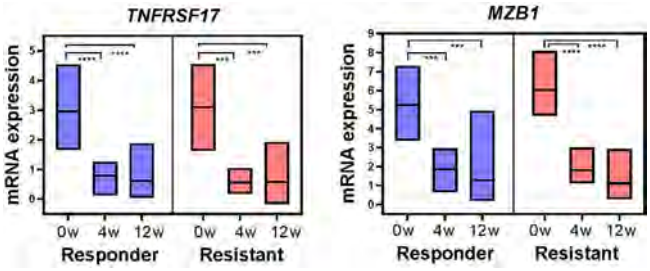


Figure 2. Time course expression of TNFRSF17 and MZB1; The time course expression patterns of TNFRSF17 and MZB1, being sufficiently suppressed from the week 4 and further decreasing at week 12. ***: p <0.001, ****: p <0.0001.

The responder and resistant group were compared, and the differentially expressed genes in the time series were extracted. *TNFRSF17* ($P = 1.144 \times 10^{-21}$) and *MZB1* ($P = 3.547 \times 10^{-16}$) were identified in addition to immunoglobulin-related genes. *TNFRSF17* (BCMA), a receptor for BAFF/BLyS, has been investigated as a therapeutic target for SLE. MZB1 is a B-cell-specific endoplasmic reticulum chaperone complex that plays a key role in antibody secretion and is increased in SLE lymph nodes. These molecules are supposed to be critical for treatment resistance.

Conclusion: Time-course analysis using longitudinal peripheral blood samples of SLE suggested that the expression levels and trends of *TNFRSF17* and *MZB1* are important for treatment resistance in SLE.

Disclosure: S. Sumitomo: AbbVie/Abbott, 6, Asahi-kasei, 6, Astellas, 6, AstraZeneca, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **H. Oka**: None; **T. Iwasaki**: None; **K. Ohmura**: Asahi-kasei, 6, AstraZeneca, 6, Chugai, 6, Eisai, 6, Gilead, 6, GlaxoSmithKlein(GSK), 6, Mitsubishi-Tanabe, 6.

Abstract Number: 1850

First American SLE patients demonstrate enhanced lipid metabolism and B cell activation by high-content proteomic analyses

Rufei Lu[1], **Tayte Stephens**[2], Carla Guthridge[1], Miles Smith[1], Joseph Kheir[1], Cristina Arriens[1], Joan Merrill[3], Marci Beel[4], Susan Macwana[1], Wade DeJager[5], Nicholas Domingez[1], Teresa Aberle[1], Joel Guthridge[1] and Judith James[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Oklahoma Health Science Center, Oklahoma City, OK, [3]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [4]Oklahoma Medical Research Foun, Oklahoma City, OK, [5]Oklahoma Medical Research Foundation, Oklahoma City

SESSION INFORMATION

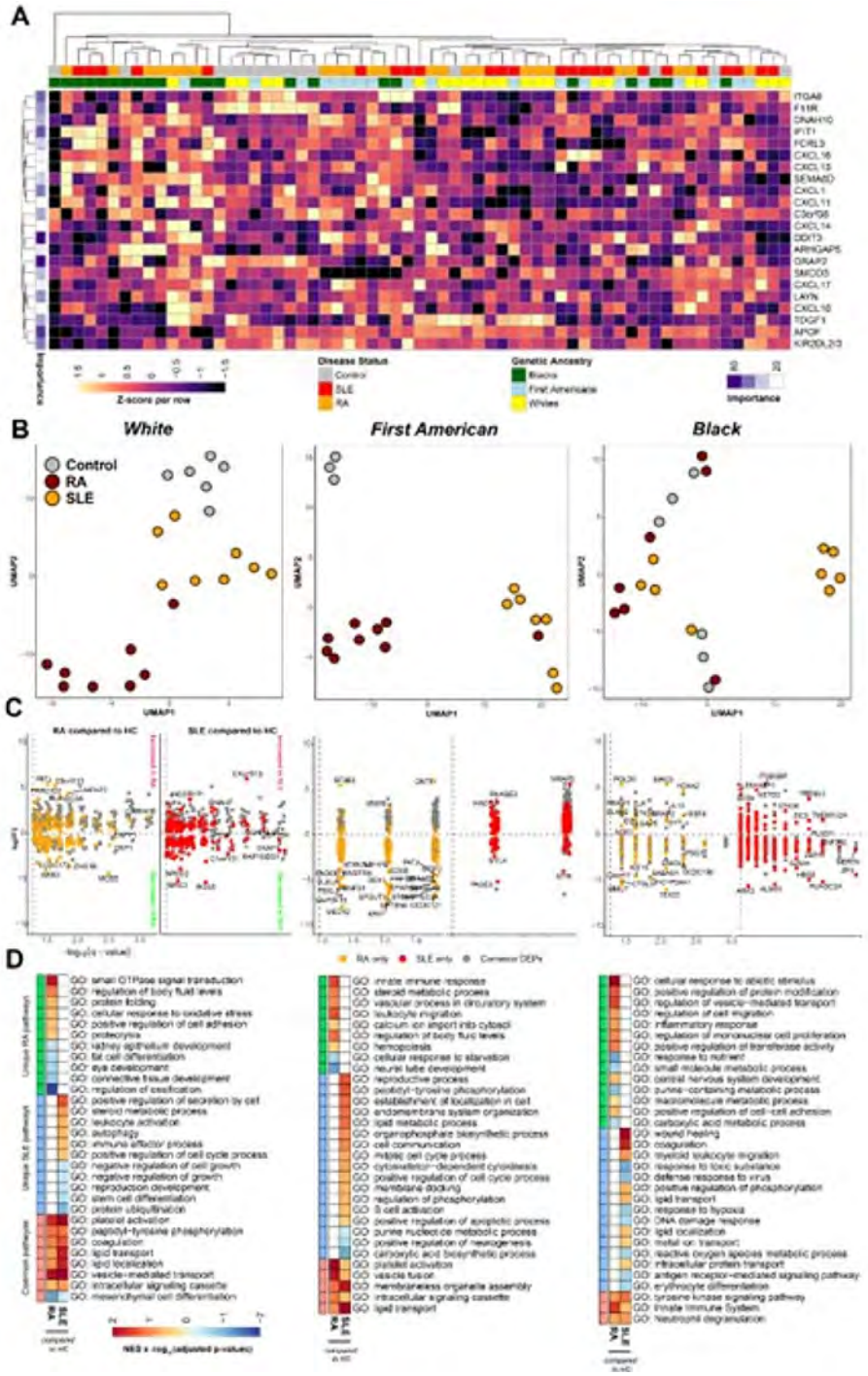
Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are autoimmune diseases with overlapping yet distinct immunopathologies. Proteomic profiling of soluble plasma factors can reveal disease- and ancestry-specific immune dysregulation. Using RA as a disease control, we investigated ancestry-specific plasma proteomic signatures in SLE to elucidate unique pathways contributing to disease pathogenesis.

Methods: Serum samples from 90 female participants (SLE=30, RA=30, healthy controls=30) stratified by ancestry-Black, First American, and White were analyzed using the Olink Explore HT assay, quantifying over 5,000 proteins. Differential expression and pathway enrichment analyses were performed with false discovery rate correction (FDR< 0.05) to identify ancestry- and disease-specific proteomic alterations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Proteomic profiles distinctly separated SLE, RA, and healthy controls, with notable ancestry-associated differences (Figure). In SLE, all ancestries demonstrated increased lipid and vesicle-mediated transport pathways; however, First American patients uniquely exhibited lipid metabolic dysfunction. Black patients showed increased myeloid activity, including neutrophil degranulation and migration pathways. White patients displayed dysregulated protein degradation and nucleotide modification pathways, particularly involving nuclear proteins and SUMOylation. Notably, First American SLE patients had



A, Heatmap of top predictors revealing distinct soluble proteomic profiles among different ancestries between rheumatic disease and healthy controls. B, UMAPs based on Olink Explore HT Assay highlighting distinct soluble proteomics between two rheumatic diseases (RA and SLE) and healthy controls. C, Volcano plots showing the differentially detected proteins (DEP) between RA and SLE and healthy controls in different ancestries. D, Heatmaps of gene set enrichment analyses based on DEPs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

significantly elevated B-cell activation pathways, consistent with heightened interferon hypersensitivity and cellular frequency data. Using RA as a disease control, we observed that Black RA patients had pronounced upregulation of vesicle-mediated transport pathways compared to SLE. Additionally, White RA patients showed downregulation of connective tissue-related pathways and First American RA patients exhibited neuronal and vascular system pathway alterations. Across diseases, Black patients demonstrated predominant dysregulation of innate immune pathways, whereas White and First American patients showed more adaptive immune system involvement.

Conclusion: Ancestry shapes plasma proteomic landscapes in SLE and RA, with distinct immune and metabolic pathways differences. The use of RA as a disease control underscores unique SLE-specific proteomic signatures, particularly in lipid metabolism and B-cell activation among First American patients and myeloid-driven inflammation in Black patients. These results emphasize the importance of integrating ancestry and disease context in proteomic analyses to inform personalized therapeutic strategies in autoimmune diseases.

Disclosure: R. Lu: None; **T. Stephens**: None; **C. Guthridge**: None; **M. Smith**: None; **J. Kheir**: None; **C. Arriens**: Astra-Zeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **M. Beel**: None; **S. Macwana**: None; **W. DeJager**: None; **N. Domingez**: None; **T. Aberle**: None; **J. Guthridge**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5.

Abstract Number: 1851

Endotype Discovery in Systemic Lupus Erythematosus Using Multi-Omic Approaches: Toward Precision Insights into Cardiovascular and Renal Damage

Chary López pedrera[1], Laurel Woodridge[2], Sagrario Corrales[3], Juan Rafael Muñoz-Castañeda[4], Ana Isabel Torralbo[4], Anisur Rahman[5], Filipa Farinha[2], Rafaela Ortega-Castro[6], Pedro Seguí-Azpilcueta[7], Ismael Sanchez-Pareja[3], Laura muñoz-Barrera[3], Christian Merlo-Ruiz[8], Desiree Ruiz-Vilchez[9], M Carmen Abalos-Aguilera[8], Pilar Font[10], Nuria Barbarroja[11], Marta Alarcon-Riquelme[12], Alejandro Escudero Contreras[13], MARIA ANGELES AGUIRRE ZAMORANO[3], Carlos Pérez Sánchez[14], Elizabeth C Jury[5], **Tomás Cerdó**[3] and PRECISESADS Clinical Consortium, [1]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [2]Centre for Rheumatology Research, Division of Medicine, University College London, London, United Kingdom, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Crdoba, Spain, [4]IMIBIC/Hospital Reina Sofía/ University of Córdoba, Córdoba, Spain, [5]University College London, London, United Kingdom, [6]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [7]Radiology Service, Reina Sofia Hospital/Maimonides Institute for Research in Biomedicine of Cordoba/University of Cordoba, Spain, Córdoba, United Kingdom, [8]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [9]Department of Rheumatology, Reina Sofía University Hospital / Maimonides Institute for Biomedical Research of Córdoba (IMIBIC) / Department of Medical and Surgical Sciences, Faculty of Medicine, University of Córdoba, Spain, Cordoba, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, SpainBiomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [11]Rheumatology service/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [12]Fundacin Progreso y Salud, Andalusian Government, Granada, Spain, [13]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [14]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder characterized by marked clinical variability, which complicates both diagnosis and treatment. Among its most severe manifestations are cardiovascular (CV) complications and lupus nephritis (LN), both of which are associated with increased morbidity and mortality. Conventional biomarkers often fall short in capturing the molecular intricacies of these conditions, highlighting the need for integrative multi-omic strategies.

Methods: In this study, proteomic and metabolomic analyses were combined to uncover molecular signatures linked to CV risk and LN. Serum samples from 199 SLE patients were examined using proximity extension assays for proteomic profiling and nuclear magnetic resonance (NMR) spectroscopy for metabolomic analysis. In vitro assays were performed by treating HUVECs and HK2 cells with serum from SLE patients to assess endothelial and renal proteomic responses. Ex vivo experiments involved culturing rat kidney slices with the same sera to evaluate inflammatory signalling through p65 immunofluorescence.

Results: Unsupervised clustering based on proteomic data identified two patient subgroups: one with high disease severity (HDS) and another with low disease severity (LDS). The HDS group showed increased levels of inflammatory proteins (e.g., IL6, CD40, CXCL9) and metabolites (e.g., creatinine, citrate), which were associated with CV risk and renal involvement. Using machine learning, patients were accurately classified into HDS and LDS groups (AUC = 0.77), with biomarkers such as citrate and LDL subclasses playing a key role.

These results were validated in an independent patient cohort, confirming the robustness of the identified molecular patterns. In vitro assays revealed that serum from HDS patients induced endothelial dysfunction in HUVECs and triggered inflammatory responses in HK2 kidney cells, including the upregulation of proteins involved in tissue damage and immune activation. Furthermore, ex vivo experiments using rat kidney slices demonstrated NF-κB pathway activation in tissues exposed to HDS serum.

Conclusion: Overall, this study provides compelling evidence that CVS risk and LN in SLE are associated with distinct proteomic-metabolomic signatures that reflect underlying disease mechanisms. The integration of omics data with functional assays offers valuable insights into the molecular drivers of organ-specific damage in SLE. These findings might pave the way for biomarker-driven diagnostic tools and personalized therapeutic strategies based on patient stratification, aiming to mitigate disease-related complications.

Supported by ISCIII (PI24/00959, CD21/00187 and RICOR-24/0007/0019), co-financed by European Union, and MINECO (RYC2021-033828-I/PID2022-141500OA-I00).

Disclosure: C. López pedrera: None; **L. Woodridge**: None; **S. Corrales**: None; **J. Muñoz-Castañeda**: None; **A. Torralbo**: None; **A. Rahman**: None; **F. Farinha**: None; **R. Ortega-Castro**: None; **P. Seguí-Azpilcueta**: None; **I. Sanchez-Pareja**: None; **L. muñoz-Barrera**: None; **C. Merlo-Ruiz**: None; **D. Ruiz-Vilchez**: None; **M. Abalos-Aguilera**: None; **P. Font**: None; **N. Barbarroja**: None; **M. Alarcon-Riquelme**: None; **A. Escudero Contreras**: None; **M. AGUIRRE ZAMORANO**: None; **C. Pérez Sánchez**: None; **E. C Jury**: None; **T. Cerdó**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1852

Cellular Landscape of Cutaneous Lupus Erythematosus Revealed by Single-Cell RNA Sequencing and Spatial Transcriptomics in the Lupus Accelerating Medicine Partnership Cohort

Victoria Werth[1], Jun Kang[2], Lais Lopes Almeida Gomes[3], Christopher Richardson[4], Benjamin Chong[5], J. Michelle Kahlenberg[6], Joel Guthridge[7], Wade DeJager[8], Susan Macwana[7], Caleb Marlin[7], Judith James[7], Rachael Bogle[9], Alex Tsoi[9], Johann Gudjonsson[6] and Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network, [1]University of Pennsylvania, Wynnewood, PA, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Rochester Medical Center, Rochester, NY, [5]University of Texas Southwestern Medical Center, Dallas, TX, [6]University of Michigan, Ann Arbor, MI, [7]Oklahoma Medical Research Foundation, Oklahoma City, OK, [8]Oklahoma Medical Research Foundation, Oklahoma City, [9]University of Michigan, Holland, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is a chronic inflammatory skin disease associated with systemic lupus erythematosus (SLE) and characterized by a prominent type I interferon response. Although the mechanisms that trigger cutaneous lupus lesions remain unclear, recent therapeutic developments have highlighted a pivotal role for plasmacytoid dendritic cells (pDCs) in its disease pathogenesis.

Methods: As part of the NIH AMP-AIM-supported Lupus Omics Cutaneous Kidney Investigation Team (LOCKIT), we performed advanced multi-omics profiling using single-cell and spatial transcriptomics on paired lesional and non-lesional skin samples from 12 patients with CLE, including 11 with discoid lupus erythematosus (DLE) and 1 with subacute CLE (SCLE). CLE patients were treatment-naïve or on treatment with hydroxychloroquine only.

Results: Biopsies were obtained from scalp (n=10) and back (n=2) from 12 patients (5 Black, 7 White, 80% female). For scRNA-seq, we generated 537 million reads from over 130,000 cells. Our analysis identified two distinct pDC populations, pDC1 and pDC2 (pDC-like cells), based on expression of *LILRA4* (ILT7), *CLEC4C* (BDC2A), *LTK*, GZMB, *SIGLEC6*, and *IRF7*. Both pDCs predominantly enriched in lesional skin (>74%), with pDC1 comprised 0.06% to 4.66% of total cells and pDC2 ranged from 0% to 0.31%, while both were markedly reduced (∼0.16%) in non-lesional skin. pDC1 (891 cells) expressed classical pDC markers such as *GZMB*, *C12orf75*, *IRF7*, *SOX4*, and *LDLRAD4*. In contrast, pDC2 (68 cells) showed lower *GZMB* and higher expression of *PPP1R14A*, *LTK*, and *KCNK17*, and clustered with the rest of the myeloid cells, suggesting a transitional myeloid state (**Figure 1**). Among the differentially expressed genes, *CLEC4C* (BDCA2) was significantly higher in pDC1 (adjusted $p = 7.09 \times 10^{-19}$, $\log_2$FC = 2.48) compared to pDC2. While both *LILRA4* (ILT7) and CLEC4C (BDCA2) were found prominently on pDCs and pDC-like cells, lower intensity of *CLEC4C* was seen on a larger percentage of cDC1 cells, while *ILT7* was present on a small number of cDC1 cells. Macrophages and other cell types did not express these genes (**Figure 2**). Using the Xenium platform with a 5,000-gene core and 100 custom genes, we spatially profiled 28 skin samples. Cell type annotations derived from scRNA-seq confirmed the presence and distribution of both pDC subsets. Neighborhood analysis revealed that pDC1s were proximity to B and T cells, whereas, conversely, pDC2s were localized near pDC1s and conventional dendritic cells (cDCs) (**Figure 3**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

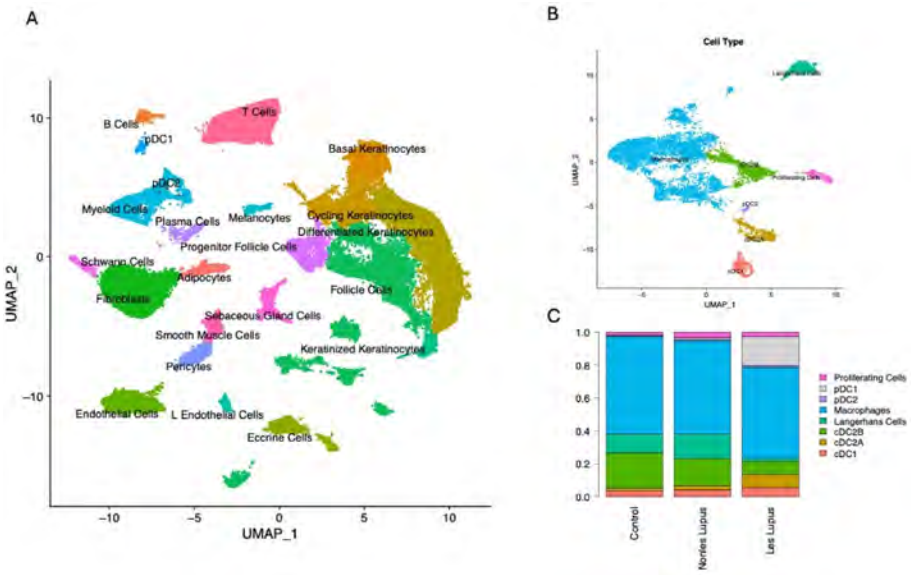


Figure 1: UMAP visualization of single-cell RNA-seq data in major- (A) and sub- (B) types. The distribution highlights transcriptionally distinct myeloid subsets and a pDC-like (pDC2) population relevant to autoimmune pathogenesis. Histogram illustrates proportions of each cell populations in different skin types (C).

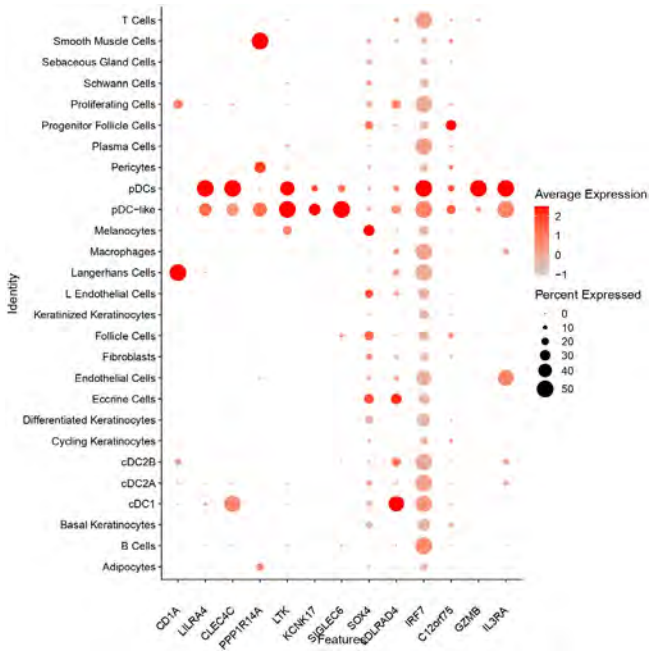


Figure 2: Dot plot showing expression of selected genes across annotated skin and immune cell types. Dot size represents the percentage of cells expressing each gene, while color intensity reflects average expression. pDC and pDC-like populations show enriched expression of LILRA4, CLEC4C, IRF7, and GZMB, consistent with their transcriptional identity.

Conclusion: This study provides new insights into early disease mechanisms in cutaneous lupus and identifies two transcriptionally distinct pDC populations associated with specific cellular niches and immune interactions in the skin, suggesting complex cellular hierarchy in driving inflammation and type I interferon responsesD in CLE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

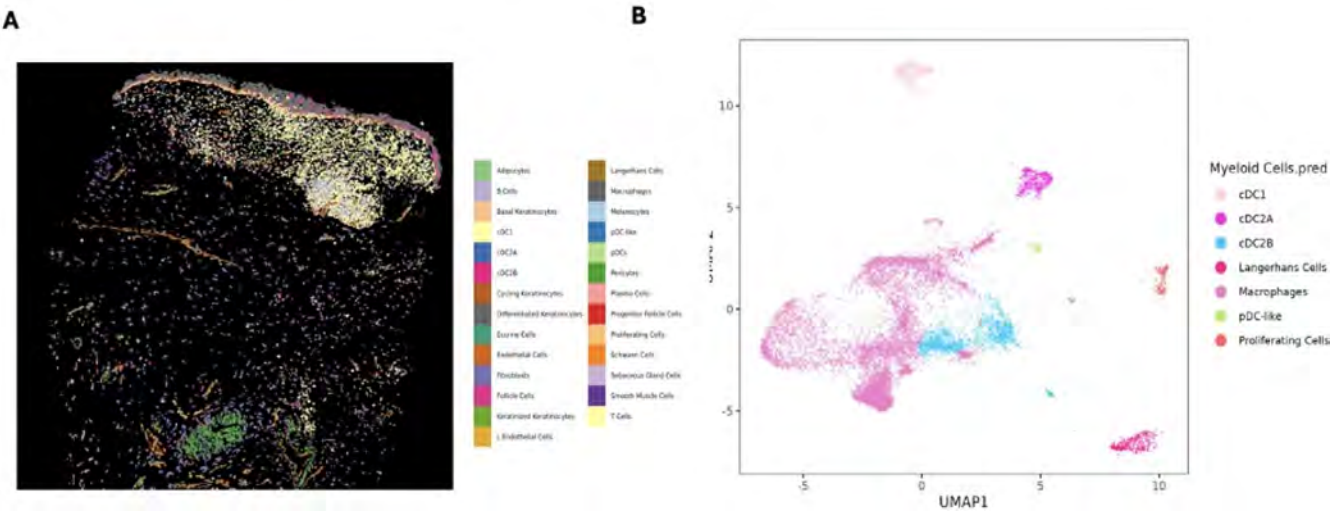


Figure 3: Spatial transcriptomic map of human skin biopsies (A). Cell identities of the spatial data were projected on scRNA-seq-derived annotations. Myeloid cell projection of the spatial data also confirms the pDC2 (pDC-like) population.

Disclosure: V. Werth: AbbVie/Abbott, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta Bio, 2, Calyx, 2, CSL Behring, 5, Cugene, 2, Eli Lilly, 2, EMD Serona, 2, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 5, Immunovant, 2, Janssen, 2, Kwoya Kirin, 2, Merck/MSD, 2, Novartis, 2, Nuvig, 2, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, Rome Pharmaceuticals, 5, Sanofi, 2, Takeda, 2, UCB, 2, 2, Ventus, 2, Viela, 5; **J. Kang**: AstraZeneca, 12,, 5; **L. Lopes Almeida Gomes**: None; **C. Richardson**: AstraZeneca, 5, Biogen, 1, Immunovant, 2, Incyte, 5, Merck/MSD, 2, Ribon, 5; **B. Chong**: Amgen, 2, 6, AstraZeneca, 2, Biogen Incorporated, 12,, 2, Bristol-Myers Squibb(BMS), 2, Cesas Medical, 6, EMD Serono, 12,, 2, Lupus Research Alliance, 2, MAPI Research Trust, 9; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5; **J. Guthridge**: None; **W. DeJager**: None; **S. Macwana**: None; **C. Marlin**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **R. Bogle**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **J. Gudjonsson**: None.

Abstract Number: 1853

SAP Expression in SLE T Cells is Associated with Differentiation Towards Pro-Inflammatory Effector Subsets.

Yevgeniya Gartshteyn[1], Daniel Portnoy[2], Matthieu Paiola[3], Anca Askanase[2] and Adam Mor[4], [1]Columbia University Medical Center, Glen Rock, NJ, [2]Columbia University Medical Center, New York, NY, [3]Columbia University Irving Medical Center, New York, NY, [4]Columbia University, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: SAP is an adaptor protein that mediates signaling downstream of SLAMF T cell receptors. SAP deficiency results in X-linked Lymphoproliferative immunodeficiency characterized by impaired TCR-mediated induction of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

GATA-3 and IL4 production, absence of mature germinal centers and loss of T cell-dependent B cell maturation. mature germinal centers, and loss of T cell-dependent B cell maturation. Our earlier research revealed elevated SAP levels in lupus and established a link between the proliferation of SAP-expressing T helper cells and lupus nephritis (LN). In this abstract, we reveal the mechanistic role of these SAP+ T cells in driving the inflammatory response associated with LN.

Methods: We enrolled lupus patients who had not previously been analyzed for SAP expression. We performed extra- and intra-cellular immunophenotyping of PBMCs using a CYTEK Aurora 35-color flow cytometry panel. PBMCs were isolated and stored in liquid nitrogen. All samples were analyzed at the same time to minimize batch effect bias. Data was analyzed in GraphPad Prism 8.4.3.

Results: 13 patients with SLE (mean age 36±13, 85% female, median SLEDAI-2K score 6 [IQR 2-7]) and 4 age and gender matched controls (age 35±7, 75% female) were included. Figure 1A shows a higher frequency of SAP+ T cells in SLE patients with a SLEDAI of ≥6 compared to controls (44% vs 27%, Mann-Whitney U test, p=0.042). SAP expression differentiates T cell maturation subsets, especially in CD4+ T cells, where SAP+ cells were more likely to be central and effector memory subsets and less likely to be naïve (Fig. 1C, 2-way ANOVA p< 0.001). Figure 2A (top panel) shows that in CD4 T cells, SAP expression is associated with polarization away from T regulatory (Treg) (CD127^{low}CD25^{hi}) and T follicular helper (TFH) (CXCR5+) lineages and instead associates with increased TH2 differentiation (*CCR4*+CCR6-CD161-CXCR3-). A smaller but still significant increase in TH1 (CCR4-CCR6-CD161-*CXCR3*+) and TH17 (CD161+) subsets was also seen among the SAP+ vs. SAP- CD4 T cells. Figure 2A (bottom panel) shows increased GATA3 transcription factor expression in SAP+ CD4 T cells, further supporting predisposition to TH2 differentiation in these cells. On the other hand, Figure 2B shows that in CD8 T cells, SAP expression is associated with an increase in CCR4-CXCR+ subset and T-Bet transcription factor expression, consistent with a Th1-like CD8 T cell (TC1). Increased HLADR and granzyme B expression in SAP+ CD8 T cells suggests an activated, cytotoxic effector phenotype.

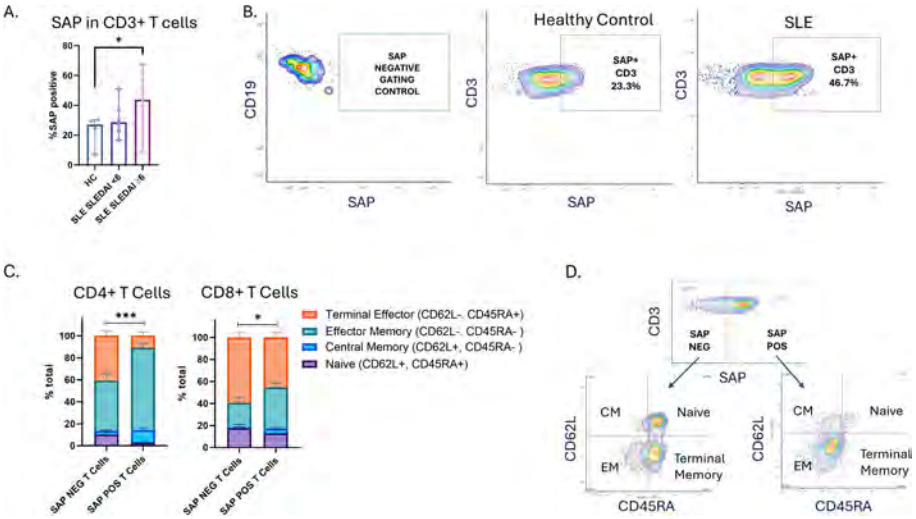


Figure 1. SAP expression is increased in effector T cells isolated from SLE patients. A. PBMCs from 13 patients with SLE (SLEDAI-2K <6 in N=6, SLEDAI-2K≥6 in N=7) and healthy controls (HC, N=4), were analyzed by flow cytometry. The frequency of SAP positive T cells is shown. B) An example of differential SAP expression between a healthy control and a patient with SLE. Gate selection was based on B cells, which do not express SAP. C) T cell maturation subsets were defined by cell surface expression of CD62L and CD45RA. In CD4 T cells (left) and CD8 T cells (right) the association of SAP expression with the distribution of maturation subsets was assessed. The stacked bars represent total population of SAP negative (SAP NEG) vs. SAP positive (SAP POS) cells from 13 patients with SLE, with the proportion of maturation subsets shown as purple (naïve cells), blue (central memory, CM), turquoise (effector memory, EM) and orange (terminal effectors). A 2-way ANOVA was used to compare subset distributions between SAP negative vs. SAP positive cells. (D) An example of T cell subset distribution comparing SAP negative to SAP positive T cells isolated from the same patient.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

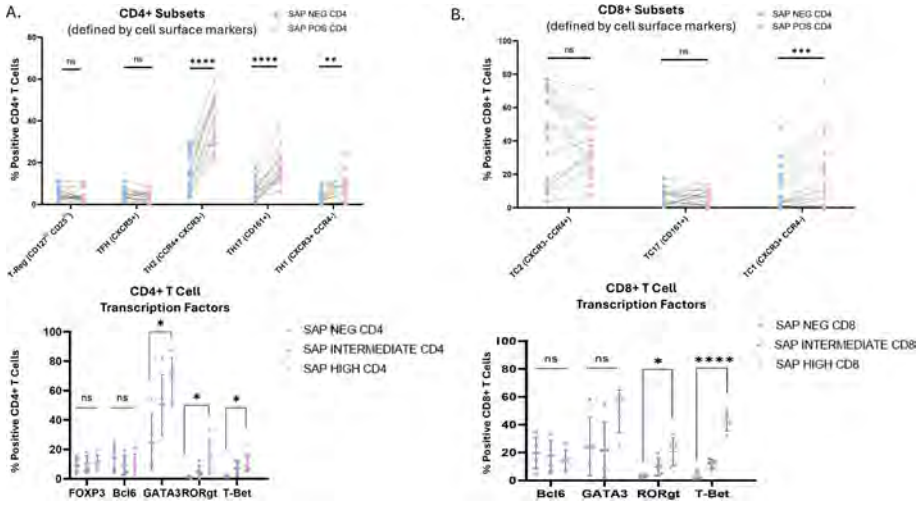


Figure 2. SAP Positive T Cells are polarized towards differentiated TH2, TH1 and TH17 subsets. A. (Top Panel) CD4+ T cell subsets were defined based on cell surface expression markers and further stratified by SAP expression (POS vs. NEG). Every paired line is a unique patient sample. (Bottom Panel) Expression of transcription factors was quantified using intracellular flow cytometry and stratified by SAP expression (negative, intermediate, high). Mean ± S.D is shown. B. (Top and Bottom Panels) CD8+ T cells subsets were defined using the same method as in 2A. A t-test with p-value adjusted using the Benjamini and Hochberg correction for multiple comparisons was used. * p<0.05, ** p<0.01, **** p<0.0001.

Conclusion: T cell SAP levels are elevated in SLE and are linked to disease severity. Mechanistically, we demonstrate that SAP expression correlates with T cell maturation and differentiation into pro-inflammatory effector subsets. This is significant because a better understanding of signaling downstream of SAP activation can reveal novel targetable pathways in SLE pathogenesis.

Disclosure: Y. Gartshteyn: None; **D. Portnoy**: None; **M. Paiola**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **A. Mor**: None.

Abstract Number: 1854

Resting-State Functional Magnetic Resonance Imaging Analysis Revealed Altered Functional Connectivity Associated with Fatigue in Systemic Lupus Erythematosus

Yujie Song[1], Nobuya Abe[1], Yuichiro Fujieda[2], Kodai Sakiyama[1], Yuta Inoue[1], Kenichi Miyamoto[1], Kazuro Kamada[1], Yotaro Oki[1], Maria Tada[1], Shuhei Takeyama[1], Ryo Hisada[2], Michihito Kono[2] and Tatsuya Atsumi[2], [1]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, [2]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1830–1854) Systemic Lupus Erythematosus – Etiology and Pathogenesis Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Fatigue is one of the most frequent constitutional symptoms in systemic lupus erythematosus (SLE), usually accompanied with impaired quality of life. Resting-state functional magnetic resonance imaging (rs-fMRI) has emerged as a powerful technique for mapping extensive neural networks in the human brain through blood-oxygen-level-dependent (BOLD) signal. The temporal synchronization between separate brain regions of interest (ROI) can be termed as functional connectivity (FC). Although several altered FCs have been confirmed to be associated with fatigue severity in diseases such as multiple sclerosis and chronic fatigue syndrome, specific FCs associated with fatigue in SLE remain unclear. In this study, we aim to identify the specific FCs linked to fatigue in patients with SLE.

Methods: Totally 16 patients with SLE and 16 healthy controls (HCs) were enrolled in this study. Rs-fMRI data from 32 subjects were acquired. The patients' fatigue severity and psychiatric status were estimated by 11-item Chalder Fatigue Scale and Hospital Anxiety and Depression (HAD) Scale respectively, in addition to Visual Analogue Scale to rate pain (pain-VAS). The scores were collected at the same date of conducting fMRI. Demographic and clinical data were collected from medical records. We used functional connectivity multivariate pattern analysis (fc-MVPA) to identify the clusters distinguishing SLE patients from HCs, adjusted for age and sex. And seed-based connectivity (SBC) analysis was conducted to identify the FCs associated with fatigue severity. Finally, we used simple linear regression to calculate the correlations.

Results: A total of 16 SLE patients (93.75% female; median age: 46.5 years, IQR: 31.75–56.75) and 16 HCs (56.25% female; median age: 41 years, IQR: 33–45.75) were enrolled. In patients with SLE, the median Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score was 4 (IQR: 2–8), the median prednisolone (PSL) dose was 6.0 mg/day (IQR: 2.875–13.75), and the median Chalder fatigue scale score was 18.5 (IQR:11.25–24). The fatigue severity showed no significant correlation with age (p=0.81), SLEDAI (p=0.3) or PSL dose (p=0.89), while it was positively correlated with HAD scores (p< 0.0001). We identified an alteration of FCs between the MVPA-identifying ROI centering on left superior frontal gyrus and SBC-identifying ROI containing atlas ROIs of left inferior lateral occipital cortex and left temporooccipital middle temporal gyrus. In patients of SLE, the FCs were significantly correlated with fatigue severity (p< 0.0001, R^2=0.80), and separately, correlated with physical symptom scores (p< 0.0001, R^2=0.70) and mental symptom scores (p< 0.0001, R^2=0.75). Besides, these FCs were also significantly correlated with HAD scores (p=0.0006, R^2=0.58). There was no significant correlation between FCs and SLEDAI or pain-VAS scores.

Conclusion: Altered connectivity involving the left inferior lateral occipital cortex and left temporooccipital middle temporal gyrus were associated with fatigue severity, reflecting the influence of anxiety and depression.

Disclosure: Y. Song: None; **N. Abe**: None; **Y. Fujieda**: None; **K. Sakiyama**: None; **Y. Inoue**: None; **K. Miyamoto**: None; **K. Kamada**: None; **Y. Oki**: None; **M. Tada**: None; **S. Takeyama**: None; **R. Hisada**: None; **M. Kono**: None; **T. Atsumi**: None.

Abstract Number: 1855

Small Bowel Microbial Dysbiosis and Impaired Intestinal Absorptive Function in Systemic Sclerosis- A Single Center Prospective Study

Adam Edwinson[1], Elvira Lesmana[2], Thomas Guedens[3], Ruben Mars[3], Margaret Breen-Lyles[4], Stephen Johnson[3], Jun Chen[3], Madhusudan Grover[4] and Ashima Makol[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, USA, Rochester, MN, [3]Mayo Clinic, Rochester, [4]Mayo Clinic, Rochester, Rochester, MN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic sclerosis (SSc) is characterized by peripheral vasculopathy and widespread fibrosis of skin and internal organs. Up to 90% of SSc patients report gastrointestinal (GI) symptoms of varying severity. Small intestinal bacterial overgrowth by quantitative cultures and breath testing have been well described in SSc. However, no studies to date have assessed small intestinal microbial composition in SSc. We aimed to characterize the small bowel microbiome composition and *in vivo* intestinal absorption in SSc patients with and without GI symptom burden.

Methods: SSc patients meeting ACR/EULAR 2013 criteria were prospectively recruited. The UCLA GIT 2.0 questionnaire was used to evaluate GI symptom severity. Non-SSc healthy volunteers (HV) without any GI symptoms matched for age, sex and BMI were used as controls. Upper endoscopies were performed on SSc and healthy volunteers to collect duodenal aspirates, from which DNA was extracted and underwent 16S sequencing. Reads were processed via nf-core AmpliSeq pipeline (v.2.12) and Silva (v138) database for taxonomy assignment. Alpha diversity was calculated using R phyloseq package with beta diversity measured using the R GUniFrac and tested via PERMANOVA. Lactulose and ^{13}C mannitol tracer-based testing was used to evaluate small intestinal (SI) permeability and absorptive capacity, respectively.

Results: 94 SSc participants (79 females; mean age ± SD: 58.0 ± 12.2 years) were enrolled, and a subset of these underwent SI microbiome analysis (n=28) and permeability testing (n=26). The average UCLA GIT 2.0 score for SSc participants was 0.6±0.4, indicating moderate GI disease severity. Compared to healthy volunteers (n=38), there is decrease in α-diversity in SSc (Observed, FDR< 0.001) suggesting decreased species richness and evenness as well as compositional changes in the microbiota structure as described by β-diversity measures (UniFrac FDR< 0.001). On taxonomic analysis, these differences were observed at all phylogenetic levels. Twelve differentially abundant bacterial species were identified (FDR< 0.01), with 9 in greater abundance in SSc patients. Of note, two species of *Fusobacterium* were in greater abundance in SSc, a genus previously identified to correlate with severity of GI symptoms in SSc. Firmicutes, which constitute a major phylum of the duodenal microbiome of healthy populations by providing a homeostatic role and aiding in absorption, were decreased in SSc individuals. SSc participants, compared to HV (n=29), had a lower cumulative 0–2-hour ^{13}C mannitol excretion (6.7±4.6 vs 11.4±3.3 mg, P < 0.001), suggestive of decreased SI absorptive function.

Conclusion: This is the first and only study to our knowledge that has explored the SI microbiome composition in SSc. Impaired SI absorptive capacity coupled with a loss of microbiota diversity was observed in SSc patients. Expansion of pathobionts like *Fusobacterium* and depletion of *Firmicutes* colonizing the SI may contribute to fibrosis and worse GI function. Future work investigating the mechanisms of SI absorptive properties and the specific role of intestinal microbiota will be critical in addressing GI dysfunction in SSc.

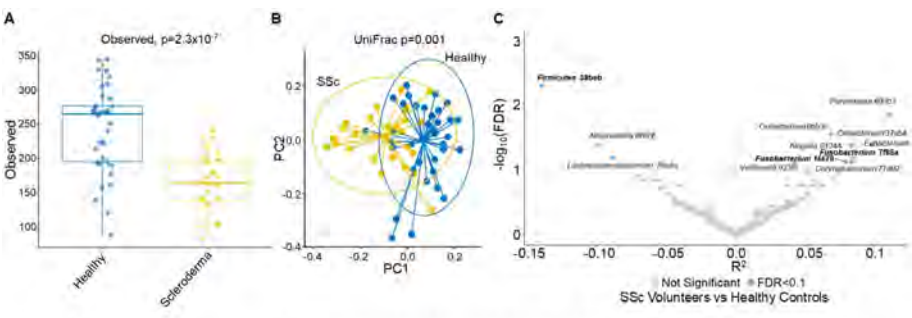


Figure1. Systemic sclerosis patients are characterized by reduced microbial diversity and compositional changes in small intestinal microbiota. A. Observed alpha diversity between healthy and scleroderma (SSc) volunteers (p=2x10^{-7}, Observed, n= 38 healthy, 28 SSc). Observed alpha diversity refers to average species diversity within a single sample, considering the number of different species observed. **B.** PCoA plot of UniFrac β-diversity metric with describes differences in SI microbiota composition between healthy and SSc volunteers. Compositionally, SSc volunteers are distinctly different from healthy participants (p=0.001, UniFrac, PERMANOVA, n= 38 healthy, 28 SSc). **C.** Volcano plot highlighting species level differences between healthy and SSc (n= 38 healthy, 28 SSc). 12 species were differentially abundant between the groups, with 9 in greater abundance in SSc. PC= Principal Coordinate, FDR= False Detection Rate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Edwinson: None; **E. Lesmana**: None; **T. Guedens**: None; **R. Mars**: None; **M. Breen-Lyles**: None; **S. Johnson**: None; **J. Chen**: None; **M. Grover**: Alfa-Sigma, 5, Takeda, 5; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial.

Abstract Number: 1856

Spatial Proteomic-based Phenotyping of Fibroblast Populations and their Microenvironment in Systemic Sclerosis Primary Heart Involvement

Ayla Nadja Stuetz[1], Giacomo de Luca[2], Alexandru-Emil Matei[3], Yi-Nan Li[4], Veronica Batani[2], Tim Filla[5], Aleix Rius Rigau[6], Bilgesu Safak Tümerdem[1], Cosimo Bruni[7], Maike Büttner-Herold[8], Stefania Rizzo[9], Monica De Gaspari[9], Markus Eckstein[10], Georg Schett[11], Cristina Basso[9], Jörg Distler[12], Marco Matucci-Cerinic[13] and **Andrea-Hermina Györfi**[14], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Nordrhein-Westfalen, Germany, [2]Vita-Salute San Raffaele University. Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Hospital, Milan, Italy, [3]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, and Fraunhofer Cluster of Excellence for Immune Mediated Diseases CIMD, Frankfurt am Main, Germany, Düsseldorf, Germany, [4]University Hospital of Dösseldorf, Dösseldorf, Germany, [5]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [6]Department of Internal Medicine 3, Rheumatology and Clinical Immunology, Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen. Deutsches Zentrum Immuntherapie (DZI), Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [7]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [8]Department of Nephropathology, University Hospital Erlangen, Erlangen, Germany, [9]Cardiovascular Pathology Unit, Department of Cardiac, Thoracic and Vascular Sciences, University and Hospital of Padua, Padua, Italy, [10]Institute of Pathology and Comprehensive Cancer Center EMN, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [11]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [12]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [13]University San Raffaele Milano, Milano, Milan, Italy, [14]Department of Rheumatology, University Hospital Dösseldorf, Medical Faculty of Heinrich Heine University., Dösseldorf, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Primary heart involvement (pHI) is one of the leading causes of death in systemic sclerosis (SSc). However, the cellular and molecular pathomechanisms of SSc-pHI are largely unknown (1, 2). Compared with other forms of autoimmune or non-immune-related myocarditis associated with fibrotic remodeling, SSc-myocarditis presents a higher degree of myocardial fibrosis, which is associated with increased mortality (3). Imaging mass cytometry (IMC) is a spatial proteomic technique with cellular resolution. We aimed to characterize the fibroblast populations and their microenvironment in SSc-pHI and compare it to other forms of virus-negative, autoimmune-related myocarditis (aVNM) and isolated VNM (iVNM)) using IMC.

Methods: Endomyocardial biopsies (EMB) were obtained from the right ventricle of ten SSc-pHI-, nine iVNM, and seven aVNM patients. We designed and validated a panel of 40 metal-labeled antibodies for the identification of fibroblast populations and other types of stromal cells, as well as immune cell subsets. Data analysis was performed as described previously (4-7).

Results: We detected a total of 17985 fibroblasts and 6444 immune cells. We identified seven distinct fibroblast populations: PI16^{-}/POSTN^{high}, PI16^{high}/POSTN^{high}, FAP^{high}/POSTN^{+}, TCF21^{+}, CD90^{+}/ADAM12^{+}/FSP1^{+}, and SOX9^{+} fibroblasts,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and myofibroblasts. We observed a significant upregulation of SOX9^{+} and CD90^{+}/ADAM12^{+}/FSP1^{+} fibroblasts in SSc-pHI compared with the other forms of myocarditis. PI16^{-}/POSTN^{high} and PI16^{high}/POSTN^{high} fibroblasts were associated with both SSc-pHI and aVNM. The expression of FAP^{high}/POSTN^{+} fibroblasts was increased in aVNM and iVNM, compared with SSc-pHI. CD163^{high}/HLA-DR^{+} macrophages and HLA-DR^{high} monocytes were significantly upregulated in SSc-pHI compared with aVNM and iVNM. Activated helper and cytotoxic T cells and CD20^{+} B cells were less frequent in SSc-pHI than in aVNM. The microenvironment of PI16^{-}/POSTN^{high} fibroblasts was enriched in helper T cells and FAP^{high}/POSTN^{+} fibroblasts, while the PI16^{high}/POSTN^{high} fibroblast niche was enriched in TCF21^{+} fibroblasts, CD163^{+}/HLA-DR^{-} macrophages, HLA-DR^{high} monocytes, and CD20^{+} B cells. The microenvironment of SOX9^{+} fibroblasts was enriched in several subsets of immune cells and FAP^{high}/POSTN^{+} fibroblasts. The SOX9^{+} fibroblast, CD34^{+} stromal cell, and pericyte niches were upregulated in SSc-pHI compared to aVNM and iVNM. We detected two myofibroblast niches, which were enriched in CD163^{high}/HLA-DR^{+} macrophages, or CD90^{+}/ADAM12^{+}/FSP1^{+} fibroblasts and CD68^{+} mast cells, respectively. These cellular changes were associated with profound differences in the cellular interaction network of the fibroblast subsets in SSc-pHI compared to aVNM and iVNM.

Conclusion: We identify seven distinct fibroblast populations in SSc-pHI, as well as profound changes in their frequencies, their microenvironment and cellular interactions compared with other forms of myocarditis. Our findings provide new insights into the pathophysiology of SSc-pHI and may offer a rationale for specific targeting of individual fibroblast populations in cardiac fibrosis.

Disclosure: A. Stuetz: None; **G. de Luca**: None; **A. Matei**: None; **Y. Li**: None; **V. Batani**: None; **T. Filla**: None; **A. Rius Rigau**: None; **B. Tümerdem**: None; **C. Bruni**: Boehringer Ingelheim, 2, EMDO Foundation, 5, Iten-Kohaut Foundation, 5, Scleroderma Clinical Trials Consortium (SCTC), 5, Scleroderma Research Foundation (SRF), 2; **M. Büttner-Herold**: None; **S. Rizzo**: None; **M. De Gaspari**: None; **M. Eckstein**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **C. Basso**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **M. Matucci-Cerinic**: None; **A. Györfi**: AbbVie, 6, Boehringer-Ingelheim, 6.

Abstract Number: 1857

Role of autoantigen-specific reactivity in the pathogenesis of murine interstitial lung disease model with anti-MDA5 antibody mouse model

Atsubumi Ogawa[1], Ran Nakashima[2], Tsuneyasu Yoshida[3], Keisuke Hirobe[1], Yasuhiro Nohda[1], Tsuneo Sasai[1], Mirei Shirakashi[2], Ryosuke Hiwa[1], Hideaki Tsuji[1], Shuji Akizuki[2], Hajime Yoshifuji[2], Kosaku Murakami[4], Norimichi Nomura[5], Atsuyasu Sato[6], Motomu Hashimoto[7] and Akio Morinobu[8], [1]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [2]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [3]Division of Clinical Immunology and Cancer Immunotherapy, Center for Cancer Immunotherapy and Immunobiology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [4]Division of Clinical Immunology and Cancer Immunotherapy, Center for Cancer Immunotherapy and Immunobiology, Graduate School of Medicine, Kyoto University, Kyoto, Kyoto, Japan, [5]Department of Cell Biology, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [6]Department of Respiratory Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan, [7]Department of Clinical Immunology, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Sakyo-ku, Japan, [8]Kyoto University, Kyoto, Kyoto, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Anti-Melanoma differentiation-associated gene 5-positive dermatomyositis (MDA5-DM) is often complicated by rapidly progressive interstitial lung disease (RP-ILD) and has a poor prognosis. Although there has been one report on this disease mouse model, the role of autoantigen-specific reactivity, especially anti-MDA5 antibody itself, on the pathogenesis of the disease has never been elucidated. In this study, we established a new mouse model of MDA5-DM-ILD and investigated the meanings of autoreactivity to MDA5 in the pathogenesis of the disease.

Methods: C57BL/6J wild-type mice were immunized with complete Freund's adjuvant (CFA) and recombinant human MDA5 protein purified from baculovirus-insect cell system 6 times once a week, and polyinosinic-polycytidylic acid (poly I:C) was administered intratracheally 16 times over a 4-week period, starting from the 3rd week. The production of anti-mouse MDA5 antibodies was confirmed by immunoprecipitation. The area of cell infiltration in lung was quantitatively evaluated using an all-in-one fluorescence microscope (BZ-X810), the cell ratio was evaluated by flow cytometry, and interferon-stimulated gene (ISG) was evaluated by RT-PCR. In addition, we observed whether the lung infiltrating cells were reacted with MDA5 protein and releasing cytokines and granzyme B. After then, CD4(+) T cells and B cells were sorted and co-cultured, and IFN-γ production was confirmed by adding MDA5 protein. Furthermore, anti-human MDA5 monoclonal mouse antibodies were transferred intraperitoneally to C57BL/6J wild-type mice 5 times once a week, and poly I:C was administered intratracheally 16 times over a 4-week period, and the area of cell infiltration in lung tissue was quantitatively evaluated.

Results: We confirmed the production of anti-mouse MDA5 antibodies in immunized mice. The MDA5-immunized/poly I:C mice showed larger cellular infiltration area of the lungs ($p< 0.01$, Figure1) and lower survival ($p< 0.05$) compared to CFA only immunized/poly I:C mice. ISG15 expression in lung tissue was increased. In vitro cytokine releasing assay using MDA5 protein revealed that lung-infiltrating cells of MDA5-immunized/poly I:C mice produced significantly more IFN-γ, IL-15, and granzyme B than control mice ($p< 0.05$, Figure2), which can be observed even after purification of infiltrating B cells and CD4(+) Tcells.

The area of pneumonia in the mice injected with the monoclonal antibody was different from that in the mice injected with normal IgG, with dominant cellular infiltration just below the pleura, which was similar to the initial development of ILD in MDA5-DM patients (Figure3).

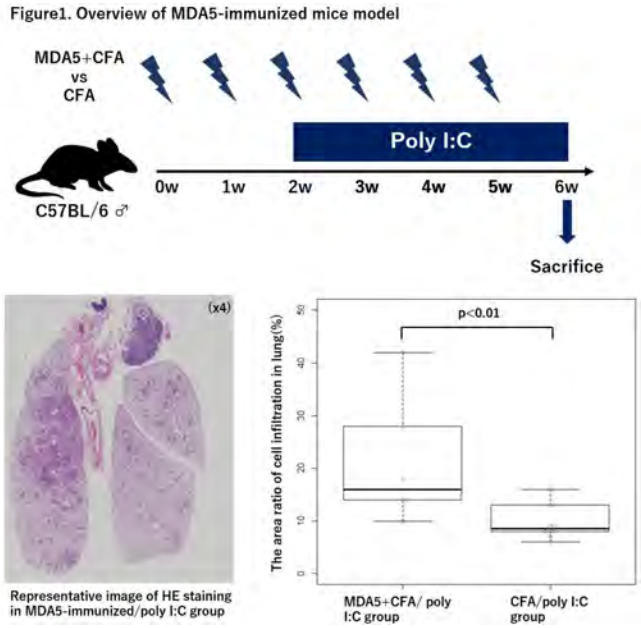


Figure 1. Overview of MDA5-immunized mice model

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

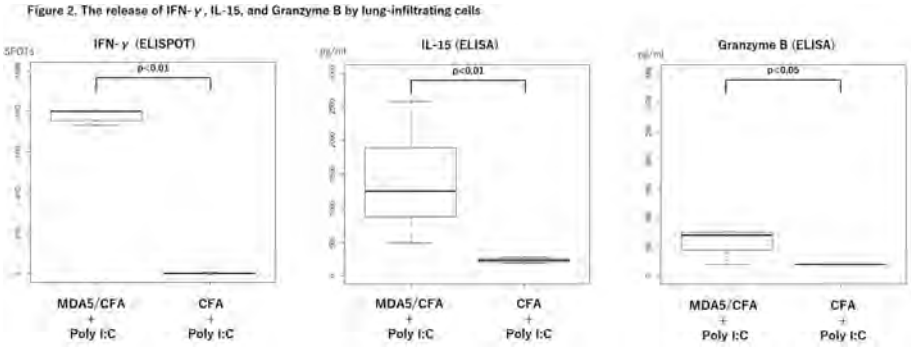


Figure 2. The release of IFN-γ, IL-15, and Granzyme B by lung-infiltrating cells

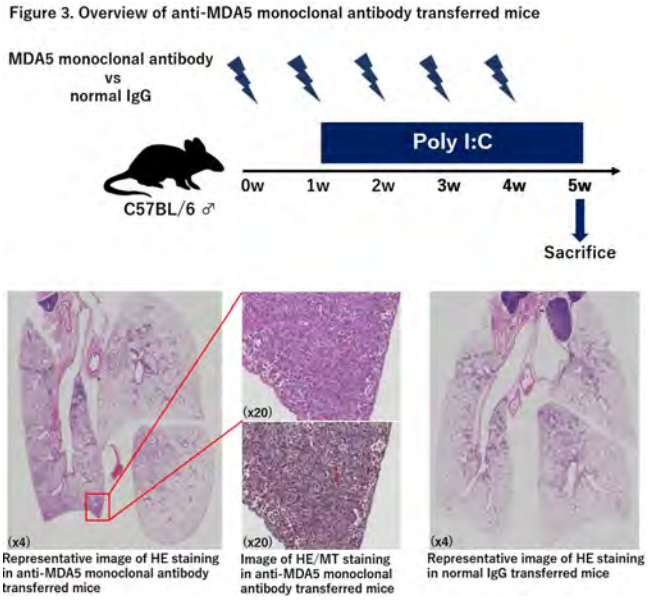


Figure 3. Overview of anti-MDA5 monoclonal antibody transferred mice

Conclusion: Infiltration of MDA5-specific T/B cells in the lungs as well as anti-MDA5 antibody itself may play a pivotal role for lung injury in MDA5-DM.

Disclosure: A. Ogawa: None; **R. Nakashima**: None; **T. Yoshida**: None; **K. Hirobe**: TAISHO PHARMACEUTICAL HOLDINGS CO., LTD., 6; **Y. Nohda**: None; **T. Sasai**: None; **M. Shirakashi**: None; **R. Hiwa**: None; **H. Tsuji**: None; **S. Akizuki**: None; **H. Yoshifuji**: AbbVie/Abbott, 6, Chugai, 6, Janssen, 6; **K. Murakami**: None; **N. Nomura**: None; **A. Sato**: None; **M. Hashimoto**: None; **A. Morinobu**: None.

Abstract Number: 1858

Antinuclear Antibodies from Systemic Sclerosis Patients Enter Cells *via* a Clathrin Endocytosis Mechanism and Interact with Their Intracellular Antigen

Aurélien Chepy[1], Marie-Elise Martel[1], Solange Vivier[1], Meryem Tardivel[2], Antonino Bongiovanni[2], Marie Mistretta[1], Maxime Secq[1], Lucile Guilbert[3], Eric HACHULLA[4], Sylvain Dubucquoi[5], David Launay[1] and Vincent Sobanski[1], [1]Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE - Institut de Recherche Translationnelle en Inflammation, Lille, France., Lille, France, [2]Univ. Lille, BioImaging Center Lille-Nord de France (BICeL), Lille, France., Lille, France, [3]CHU Lille, Institut d'Immunologie,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lille, France., Lille, France, [4]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-Immunes et Auto-Inflammatoires Rares du Nord, Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille, France, Lille, France, [5]Univ. Lille, Inserm, CHU Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, Lille, France ; CHU Lille, Institut d'Immunologie, Lille, France, Lille, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Antinuclear autoantibodies (ANA) are robust biomarkers for the diagnosis and prognosis of systemic sclerosis (SSc), but their role in pathogenesis is still uncertain. Recent evidence showed that purified IgG from SSc patients alter the molecular signatures of key effector cells (fibroblasts [FB] and endothelial cells [EC]) in a serotype-dependent manner, and that ANA might interact with intracellular antigens. This study aims to evaluate ANA's ability to penetrate cells, understand the internalization mechanisms and determine intracellular interactions.

Methods: We employed a panel of antibodies (Ab) comprising total purified IgG from anti-topoisomerase I positive (IgG-ATA$^+$) and anti-centromere positive (IgG-ACA$^+$) patients, alongside IgG from healthy controls (IgG-HC). In addition, we utilized polyclonal SSc ATA (poly-ATA, TopoGEN®) and fluorochrome-conjugated poly-ATA antibodies (fluo-poly-ATA). Following a 72-hour culture and 24-hour serum deprivation, FB and EC were incubated with the aforementioned antibodies

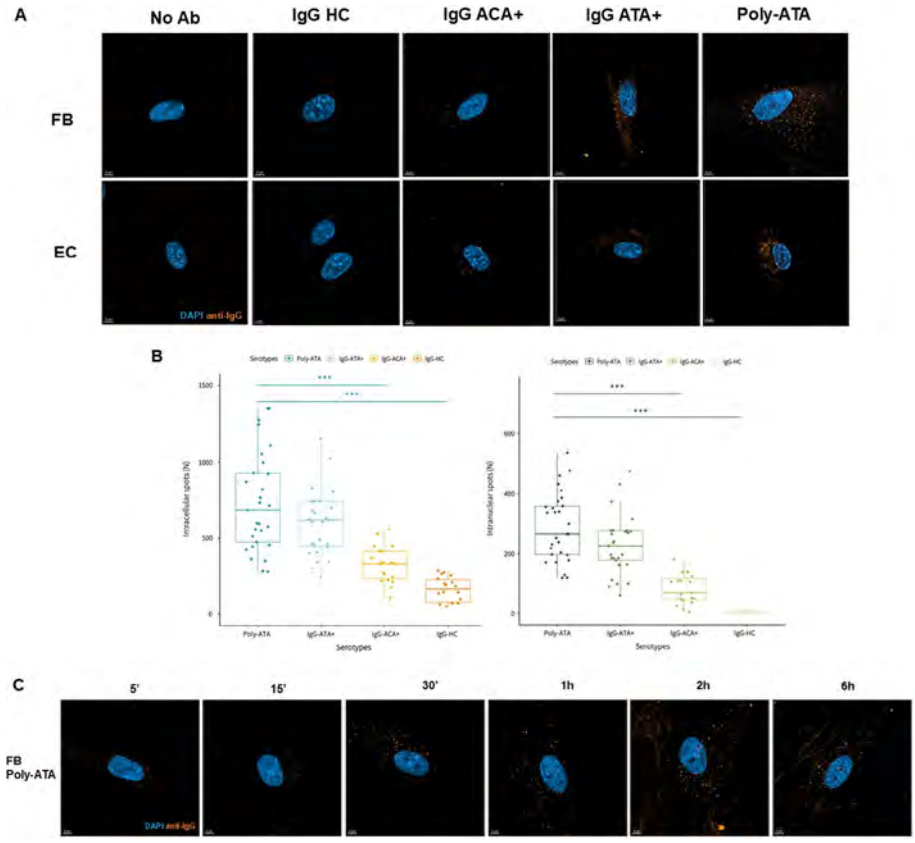


Figure 1. A. Representative image of FB and EC following 1-hour incubation with IgG-HC, IgG-ACA+, IgG-ATA+ and poly-ATA (number of patients for each total IgG condition=5). B. Quantification of fluorescently labeled antibodies in FB and EC following 1-hour incubation with distinct IgG serotypes. Ab spot counts were quantified using Imaris in both cytoplasmic and nuclear compartments. A total of 30 cells per condition were analyzed across two to three independent experiments, depending on the serotype. Data are presented as median ± interquartile range (IQR). Statistical significance was assessed using the Kruskal–Wallis test followed by Dunn's post hoc test; ***$p < 0.001$. C. Kinetic of fluorescence patterns in FB incubated with poly-ATA for durations ranging from 5 minutes to 6 hours.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

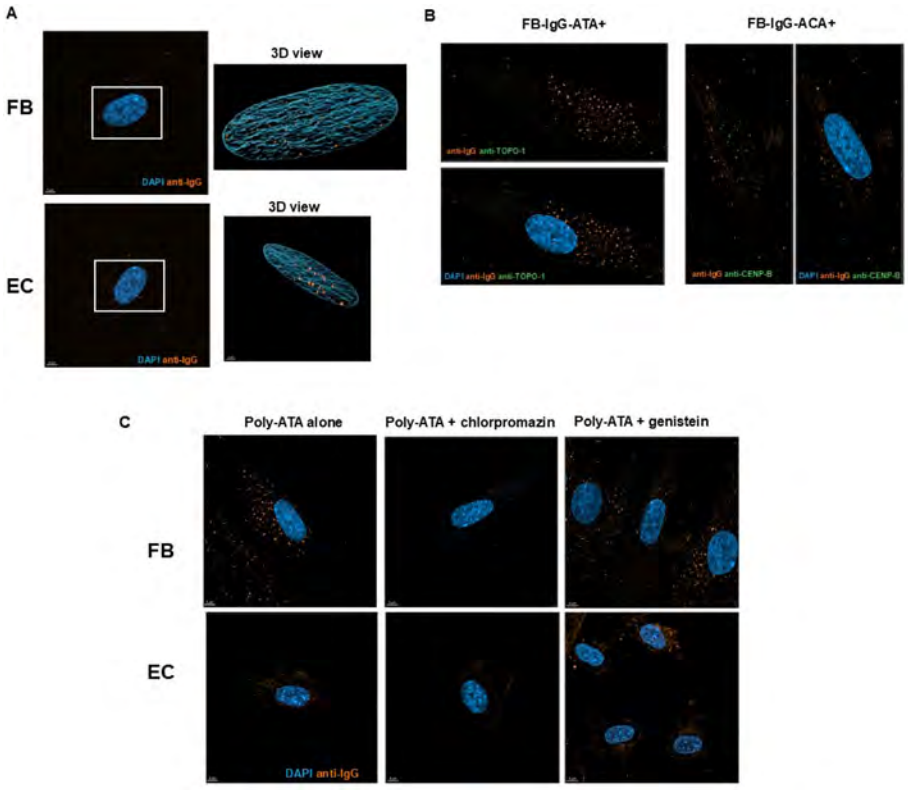


Figure 2. A. Three-dimensional FB and EC incubated 1 hour with poly-ATA generated from Z-stack confocal imaging (0.2 μm optical sections). B. FB topoisomerase-I protein co-staining after 1-hour incubation of IgG-ATA+ and FB CENP-B protein co-staining after 1-hour incubation of IgG-ACA+. C. FB and EC after 1 hour with poly-ATA alone, poly-ATA + clathrin endocytosis pathway blockage pretreatment (chlorpromazine) and poly-ATA + caveolin endocytosis pathway blockage pretreatment (genistein).

for 5 minutes to 6 hours. For fixed-cell imaging, cells were washed post-incubation, fixed, permeabilized, and stained using anti-human IgG antibodies. For live-cell imaging, fluo-poly-ATA was added to the cultures, and time-lapse experiments were performed using confocal microscope. Confocal images were obtained using a LSM 980 Airyscan 2 confocal microscope (Zeiss) and analyzed with Imaris 10.2 software (Oxford Instruments).

Results: Following 1-hour of Ab incubation, intracellular fluorescent spots were detected in cytoplasmic and nuclear compartments of FB and EC exposed to total IgG from SSc patients and poly-ATA. These spots were more numerous in cells treated with IgG-ATA$^+$ and poly-ATA compared to IgG-ACA$^+$. In contrast, while some fluorescence was detected in cells incubated with IgG-HC, nuclear localization was minimal to absent under this condition (**Figure 1A and B**). Using poly-ATA, fluorescent signal appeared as early as 5 minutes post-incubation and increased progressively up to 6h (**Figure 1C**). Live-cell microscopy confirmed the rapid cellular uptake and nuclear penetration of fluo-poly-ATA. To verify nuclear localization of ANA, Z-stack confocal imaging was performed with 0.2 μm optical sections to generate three-dimensional cell reconstructions. These analyses confirmed nuclear localization of poly-ATA and fluo-poly-ATA both in FB and EC (**-Figure 2A**). Co-immunostaining with topoisomerase-1 revealed 28% and 31% colocalization with IgG-ATA$^+$ and poly-ATA, respectively, while CENP-B protein exhibited 22% colocalization with IgG-ACA$^+$ (**Figure 2B**). To investigate the mechanism of internalization, endocytic pathway inhibition assays were conducted. Pretreatment of FB with a clathrin-mediated endocytosis inhibitor significantly reduced intracellular fluorescence, whereas caveolin pathway inhibitor had no observable effect (**Figure 2C**).

Conclusion: SSc ANA can penetrate cells and reach their target antigen *in vitro*. A clathrin-mediated endocytosis mechanism for ANA internalization is suggested. Further mechanistic and *in vivo* studies are needed to assess ANA pathogenicity in SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Chepy: None; **M. Martel**: None; **S. Vivier**: None; **M. Tardivel**: None; **A. Bongiovanni**: None; **M. Mistretta**: None; **M. Secq**: None; **L. Guilbert**: None; **E. HACHULLA**: None; **S. Dubucquoi**: None; **D. Launay**: None; **V. Sobanski**: None.

Abstract Number: 1859

Unraveling Disparities in Systemic Lupus Erythematosus-Related Mortality Among U.S. Adults (≥25 Years) with Malignancy: A Longitudinal Analysis of Gender, Race, and Geographic Inequities Using CDC WONDER (1999–2020)"

Asma Chaudhary[1], Aizaz Anwar Khalid[2] and **Ayesha Khan**[3], [1]Fazaia Medical College, Islamabad, Pakistan, [2]peshawar medical college, Pesahwar, North-West Frontier, Pakistan, [3]Dow medical college, Karachi, Pakistan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that increases vulnerability to malignancy and premature mortality. Understanding long-term trends and disparities in SLE-related cancer deaths is essential for guiding equitable public health strategies.

Methods: A retrospective population-based analysis was performed utilizing the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database. Age-adjusted mortality rates (AAMR) per 1,000,000 individuals were extracted and calculated the annual percentage change (APC) through Joinpoint regression The data were stratified to evaluate temporal trends and disparities based on sex, race, and geographic region in systemic lupus erythematosus (SLE)-related cancer mortality among adults.

Results: From 1999 to 2020, a total of 2,642 cancer-related deaths among adults aged ≥25 years with SLE were recorded in the United States. The overall AAMR for SLE-associated cancer mortality rose from 0.58 [95% CI: 0.46–0.69] in 1999 to 0.69 [95% CI: 0.59–0.79] in 2020. A period of stability was observed between 1999 and 2016 (APC: -1.00; 95% CI: -2.09–0.09; p=0.07), followed by a significant increase from 2016 to 2020 (APC: 10.71; 95% CI: 1.91–20.27; p=0.02). Sex-based disparities were evident, with females exhibiting a markedly higher AAMR [0.83; 95% CI: 0.79–0.87] compared to males [0.22; 95% CI: 0.20–0.24]. Racial disparities were also pronounced, with non-Hispanic (NH) Black or African American individuals experiencing double the AAMR [1.03] of NH White individuals [0.49]. Regionally, the Western United States reported the highest AAMR [0.59; 95% CI: 0.54–0.64], while the Northeast had the lowest [0.43; 95% CI: 0.39–0.47]. Additionally, nonmetropolitan areas demonstrated higher mortality rates [0.59; 95% CI: 0.53–0.64] compared to large metropolitan areas [0.54; 95% CI: 0.52–0.56].

Conclusion: Emerging data highlight a rising trend in SLE-associated cancer mortality, particularly in recent years, alongside marked disparities by sex, race, and geography. These findings underscore the urgent need for tailored, population-level interventions to mitigate inequities and improve outcomes in vulnerable populations.

Disclosure: A. Chaudhary: None; **A. Khalid**: N/A, 12, N/A, Roche, 2; **A. Khan**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1860

GLUT and FAPα as molecular imaging markers for interstitial lung disease in systemic sclerosis

Bo Broens[1], Conny van der Laken[1], Teodora Radonic[1], Douwe Mulder[2], esther Nossent[1], Yehya Al-Adwi[2], Tji Gan[2], Wim Timens[2], Alexandre Voskuijl[3] and Jan Willem Duitman[1], [1]Amsterdam UMC, Amsterdam, Netherlands, [2]UMCG Groningen, Groningen, Netherlands, [3]Amsterdam University Medical Center, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The clinical management of systemic sclerosis-associated interstitial lung disease (SSc-ILD) is challenging due to its heterogeneous progression. While recent studies have shown that pulmonary uptake of ^{18}F-FDG and ^{68}Ga-FAPI on positron emission tomography (PET) may indicate ILD activity, the spatial distribution of their molecular targets—GLUT1, GLUT3, and FAPα—in SSc-ILD lung tissue is largely unexplored. Here, we investigate the expression patterns of these markers across varying fibrosis stages in lung tissue of SSc-ILD patients and controls to improve PET interpretation.

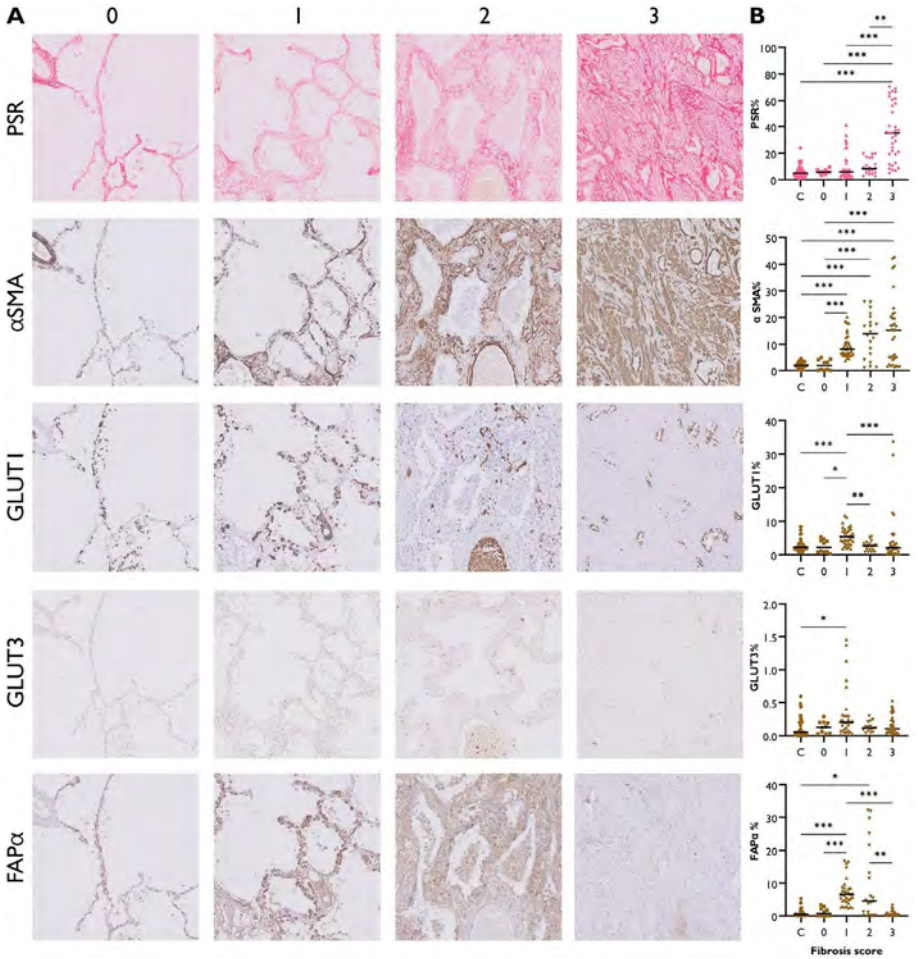


Figure 1. Expression of GLUT1, GLUT3 and FAPα varies between areas with different stages of fibrosis (0-3) in systemic sclerosis-associated interstitial lung disease.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Immunohistochemistry for GLUT1, GLUT3, and FAPα was performed on lung tissue from SSc-ILD patients (n=9) and controls (n=8). Fibrosis stage and cell-type-specific expression of these markers were analyzed by 2 experienced ILD pathologists, and quantitative staining was assessed using QuPath software. Marker expression was analyzed in and compared between areas with varying fibrosis stages.

Results: GLUT1 positive cells were primarily erythrocytes, GLUT3 positive cells were mainly myeloid cells and FAPα positive cells were predominantly fibroblasts, endothelial cells, epithelial cells, and macrophages. All cells positive for these markers were significantly more present in SSc-ILD compared to controls, with GLUT1 and FAPα positive cells showing highest prevalence in areas with early signs of fibrosis (Figure 1).

Conclusion: The prevalence of cells expressing GLUT1 and FAPα is increased in areas with early signs of fibrosis and the expression of GLUT1, GLUT3 and FAPα is observed in different cell types suggesting that ^{18}F-FDG and ^{68}Ga-FAPI PET each may be useful to visualize different aspects of ILD activity.

Disclosure: B. Broens: None; **C. van der Laken**: None; **T. Radonic**: None; **D. Mulder**: None; **e. Nossent**: None; **Y. Al-Adwi**: None; **T. Gan**: None; **W. Timens**: None; **A. Voskuijl**: None; **J. Duitman**: None.

Abstract Number: 1861

Accelerated and Gene-specific Patterns of Clonal Hematopoiesis Distinguish Subtypes of Systemic Sclerosis

Brecca Miller[1], Shervin Assassi[2], Maureen Mayes[3], alejandro Molina[4], Kelly Ruggles[5], David Beck[6] and Meng Zhang[7], [1]Center for Human Genetics and Genomics, NYU Grossman School of Medicine, Brooklyn, NY, [2]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [3]UT Health Houston Division of Rheumatology, Houston, TX, [4]Georgia Institute of Technology, Atlanta, GA, [5]NYU Grossman School of Medicine, Brooklyn, NY, [6]Center for Human Genetics and Genomics, NYU Grossman School of Medicine. Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine. Department of Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, New York, NY, USA, New York, NY, [7]UTHealth Houston Division of Rheumatology, Houston

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by widespread fibrosis, vasculopathy, autoantibody presence, and high mortality in its diffuse subtype with limited effective therapies. Genome-wide association studies (GWAS) have identified candidate genes that contribute to SSc development, but do not fully explain the drivers of heterogeneity between subtypes. Preliminary evidence suggests somatic (acquired) mutations contribute to SSc, and that there is elevated age-related clonal hematopoiesis (ARCH) variant burden in SSc versus healthy individuals. We hypothesized that immune dysregulation of ARCH contributes to the pathogenesis of the increased inflammatory phenotype of diffuse SSc.

Methods: Our cohort consists of limited cutaneous SSc (lcSSc) (n = 1611, mean = 55.9 ± 13 years, non-White = 6.82%, Female = 90.2%), diffuse cutaneous SSc (dcSSc) (n = 1240, mean = 50.47±13 years, non-White = 18.1%, Female =

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

82.3%), and healthy control (HC) (n= 984, mean = 46.7 ± 15.4 years, non-White = 5.7%, Female = 54.9%) whole blood exome sequences (WES) (median depth = 39X). We performed somatic variant calling with Mutect2 and a panel of normals generated from a subset of our HC sequences. We filtered germline and technical artifacts and annotated variants with ANNOVAR. We adhered to best practices of sequence-based filtering (DP >20, minAD ≥ 3, F2R1 ≥ 1, variant allele fraction (VAF) > 2%) and curated ARCH variants for all samples against a list of 74 CH driver genes. Logistic regression and Fisher's exact test were used to compare CH between sample groups and clinical features when suitable and linear regression was used for inspection of CH rate increases.

Results: We observe a significantly higher likelihood of ARCH in dcSSc compared to lcSSc after adjusting for age and sex, with confirmation in the UK Biobank (n=454,787). Additionally, the rate of CH with age rises faster in dcSSc than lcSSc or HC (R^2 values = 0.86, 0.65, 0.85 respectively). The most frequently mutated genes are *DNMT3A*, *TET2*, and *ASXL1* and the median VAF of all ARCH variants is 12.3%. *PPM1D* variants are elevated in dcSSc and occur in younger patients (n= 7, mean = 55.3 years) compared to lcSSc (n= 2, mean = 76.0 years). *PPM1D* variants are also associated with shorter disease duration in dcSSc patients (mean = 4.12 years, total mean of dcSSc ARCH variants = 9.17 years). We observe modest odds of anti-RNA polymerase III autoantibody presence and ARCH in dcSSc (OR = 1.20), and moderate association between ARCH and an impaired lung function threshold of % predicted diffusing capacity of the lung for carbon monoxide (DLCO) < 40 (p = 0.1, OR = 2.02 adjusted for disease duration). However, larger clone ARCH variants with VAF > 10% confer significant likelihood of having % predicted DLCO < 40 within dcSSc subtype (p = 0.0495, OR = 1.53 adjusted for disease duration).

Conclusion: Higher prevalence of ARCH in dcSSc versus lcSSc and gene-specific patterns of ARCH variant occurrence in dcSSc suggest a biological mechanism driving clonal selection between subtypes and possibly influencing fibrotic progression patterns. Understanding the timing and gene-specific nature of these mutations provides insight into selective pressures underlying SSc subtype heterogeneity.

Disclosure: B. Miller: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **a. Molina**: None; **K. Ruggles**: None; **D. Beck**: Alexion, 2, Genesis Therapeutics, 2, GSK, 2, Novartis, 2, Sobi, 2; **M. Zhang**: None.

Abstract Number: 1862

Comprehensive analysis of the major histocompatibility complex in systemic sclerosis-associated interstitial lung disease identifies novel associated loci and potential progression biomarkers

Carlos de la Rosa Báez[1], Carlos Rangel Peláez[1], Inmaculada Rodríguez Martín[1], Martin Kerick[1], Alfredo guillen-del-castillo[2], Carmen Pilar Simeon[3], Jose Luis Callejas[4], Alexandre Voskuijl[5], Alexander Kreuter[6], Oliver Distler[7], Susanna Proudman[8], Mandana Nikpour[9], Nicolas Hunzelmann[10], Jeska de Vries-Bouwstra[11], Ariane Herrick[12], Yannick Allanore[13], Lorenzo Beretta[14], Maureen Mayes[15], Christopher Denton[16], Shervin Assassi[17], Javier Martin[1], Marialbert Acosta-Herrera[1] and International SSc Group and Australian Scleroderma Interest Group (ASIG), [1]Department of Cell Biology and Immunology, Institute of Parasitology and Biomedicine López-Neyra, CSIC, Granada, Spain, [2]Unit of Autoimmune Diseases, Department of Internal Medicine, Hospital Universitario Vall d'Hebron, Barcelona, Spain, [3]Department of Internal Medicine, Hospital Universitario Vall d'Hebron, Barcelona, Spain, [4]Department of Internal Medicine, Hospital San Cecilio, Granada, Spain, [5]Amsterdam University Medical Center, Amsterdam, Netherlands, [6]Department of Dermatology, Venereology, and Allergology, Helios St. Elisabeth Klinik Oberhausen, University Witten-Herdecke,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Oberhausen, Germany, [7]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [8]Royal Adelaide Hospital and University of Adelaide, Medindie, South Australia, Australia, [9]University of Sydney School of Public Health and Department of Rheumatology, Royal Prince Alfred Hospital, Sydney, Victoria, Australia, [10]Department of Dermatology and Venereology, University Hospital Cologne, Cologne, Germany, [11]Leiden University Medical Center, Leiden, Netherlands, [12]The University of Manchester, UK, Aberdeen, United Kingdom, [13]Department of Rheumatology, Université Paris Cité UFR de Médecine, Paris, France, [14]Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy, [15]UT Health Houston Division of Rheumatology, Houston, TX, [16]University College London, UK, London, United Kingdom, [17]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The main causes of death in systemic sclerosis (SSc) are pulmonary complications such as SSc-associated interstitial lung disease (SSc-ILD). SSc-ILD is highly heterogeneous and difficult to manage. Although several studies have proven the crucial role of genetics in SSc susceptibility, especially in the major histocompatibility complex (MHC) region, genetic research focusing on SSc-ILD patients is scarce, with limited sample size and statistical power. Considering this, we aimed to conduct a comprehensive MHC genetic scan in the largest cohort of SSc-ILD to date, encompassing a total of 2,363 SSc-ILD patients, 3,526 SSc patients without ILD, and 15,026 controls from 10 international cohorts of European ancestry.

Methods: After genotypic quality controls, the MHC region was imputed using the human leukocyte antigen (HLA) imputation tool from the Michigan Imputation Server. Variants with imputation quality > 0.3 and minor allele frequency > 0.01 were considered for association analyses. Logistic regressions were performed adjusting for the first five principal components and sex, considering two comparisons: SSc-ILD vs SSc patients without ILD, and SSc-ILD vs controls. Finally, inverse variance weighted meta-analyses were performed. To identify jointly significant variants, conditional stepwise analyses were carried out separately for HLA classical alleles, polymorphic amino acid positions (AAs), and single nucleotide polymorphisms (SNPs).

Results: Results from the meta-analyses identified 2,966 significant variants associated with SSc-ILD when compared to SSc patients without ILD, and 5,610 variants when compared to controls. After conditional analysis, the most significant associations mapped in class II HLA genes, such as *HLA-DQA1*01:01:01:01* (odds ratio [OR] = 0.54 and 95% confidence interval [95%CI] [0.48 – 0.61] p-value = 3.41×10^{-21}) and, interestingly, we also found novel associated variants implicating class I HLA genes as *HLA-B*35:02:01:01* (OR = 2.44 [1.81 – 3.29], p-value = 5.64×10^{-9}), *HLA-C*07:01:01:01* (OR = 1.30 [1.19 – 1.42], p-value = 1.54×10^{-9}), and the serine substitution in position 24 of *HLA-B* (OR = 1.28 [1.18 – 1.39], p-value = 4.44×10^{-9}).

Conclusion: In this study, we identify for the first time class I HLA associated with SSc-ILD. These results emphasize the potential role for $CD8^+$ T cell mediated cytotoxicity in the pathogenesis of this clinical manifestation. Risk variants in class I HLA region may contribute to the unpaired immune response and tissue injury in the lungs, leading to inflammation and fibrosis. These findings could have significant clinical implications, with potential role as progression biomarkers in SSc patients with lung involvement.

Disclosure: C. de la Rosa Báez: None; **C. Rangel Peláez**: None; **I. Rodríguez Martín**: None; **M. Kerick**: None; **A. guillen-del-castillo**: None; **C. Simeon**: None; **J. Callejas**: None; **A. Voskuijl**: None; **A. Kreuter**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **S. Proudman**: Boehringer-Ingelheim, 5, 6, Janssen, 5, 6, Merck/MSD, 1; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer Ingelheim, 2, 5, 6, GSK, 2, 6, Janssen Pharmaceuticals, 2, 5, 6; **N. Hunzelmann**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **A. Herrick**: Abbvie, 2, Boehringer-Ingelheim, 2, Janssen, 2, 6, Zura Bio, 2; **Y. Allanore**: None; **L. Beretta**: None; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **J. Martin**: None; **M. Acosta-Herrera**: None.

Abstract Number: 1863

bag3 in Systemic Sclerosis: Possible Therapeutic Target and Biomarker for Pulmonary Fibrosis

Claudia Iannone[1], Margot De Marco[2], Antonina Minniti[3], Giuseppe Armentaro[4], Antonia Falco[2], Angela D'Ardia[2], paola Manzo[2], Liberato Marzullo[5], Anna Basile[2], Alessandra Rosati[2], Maria Caterina Turco[2], Roberto Caporali[6] and Nicoletta Del Papa[7], [1]University of Milan, Gaetano Pini CTO, Milano, Milan, Italy, [2]Department of Medicine, Surgery and Dentistry "Schola Medica Salernitana", University of Salerno, Baronissi, Italy, Baronissi, Campania, Italy, [3]ASST Gaetano Pini, milano, Milan, Italy, [4]ASST Pini-CTO, Clinical Rheumatology Unit, Milano, Italy, [5]Department of Medicine, Surgery and Dentistry "Schola Medica Salernitana", University of Salerno, Baronissi, Italy, Baronissi, Italy, [6]University of Milan and ASST Gaetano Pini-CTO, Milano, Italy, [7]ASST Pini CTO, Milano, Milan, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: BAG3 (Bcl2-associated athanogene 3) regulates cellular pathways including apoptosis and autophagy, and induces fibroblast-to-myofibroblast transformation. In systemic sclerosis (SSc), myofibroblasts drive fibrosis of skin and internal organs, with interstitial lung disease (ILD) affecting ~50% of patients and being the leading cause of mortality. Recent evidence shows BAG3 serum levels correlate with nintedanib treatment response in SSc-ILD. This study aimed to investigate the role of BAG3 in SSc pathophysiology using complementary in vitro, ex vivo, and in vivo approaches

Methods: Immunohistochemistry of BAG3 expression was performed on lung tissue from SSc patients (N=3) and healthy controls (N=5). For in vivo studies, pulmonary fibrosis was induced in mice (N=23) using bleomycin, followed by treatment with either vehicle (N=11) or anti-BAG3 mAb (20mg/kg twice weekly, N=12) after 7 days until day 28. Lungs were collected for proteomic analysis using label-free shotgun proteomics following the SP3 protocol, with protein expression analyzed using Proteome Discoverer 2.4 software. Skin-derived fibroblasts of 10 SSc patients and 7 healthy controls (HC) were evaluated for BAG3 expression and its receptor. We tested nintedanib's (50nM) influence on BAG3 release in HC fibroblasts before and after TGFβ stimulation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Our study revealed a clear pattern of BAG3 dysregulation in SSc. Western blotting demonstrated significantly higher BAG3 expression in SSc skin fibroblasts versus HC, both in whole cell lysates and supernatants (Fig 1A), while flow cytometry showed corresponding upregulation of the BAG3 receptor IFITM-2 in SSc fibroblasts (70% positive cells vs 40% in HC, p=0.0016), with increased mean fluorescence intensity (p=0.007) indicating higher receptor density (Fig 1B). To understand the regulation of this pathway, we assesed that TGF-β1, a key profibrotic cytokine, significantly induced BAG3 expression in HC fibroblasts in a dose-dependent manner (75 pg/ml at 10 ng/ml and 40 pg/ml at 5 ng/ml TGFβ, $p < 0.01$). Importantly, nintedanib treatment effectively suppressed this TGF-β-induced BAG3 expression to near-baseline levels (Fig 2), suggesting a mechanism for its antifibrotic effects. Extending these findings to tissue level, immunohistochemistry confirmed significant BAG3 overexpression in SSc lung specimens compared to controls, particularly in areas with inflammatory infiltrates and fibrotic changes. To establish causality, we employed a bleomycin-induced pulmonary fibrosis model where anti-BAG3 mAb treatment (N=12) markedly reduced fibrotic areas compared to PBS-treated controls (N=11). Proteomic analysis of lung tissue from both experimental groups revealed that BAG3 inhibition downregulated key pathological processes including apoptosis, fibrosis, and inflammation while activating cell survival pathways, providing mechanistic insights into BAG3's role in fibrosis pathogenesis.

Conclusion: This study establishes BAG3 as a central player in SSc-associated fibrosis. These findings identify BAG3 as both a potential therapeutic target and biomarker for monitoring treatment response in SSc-ILD, warranting further investigation in larger cohorts.

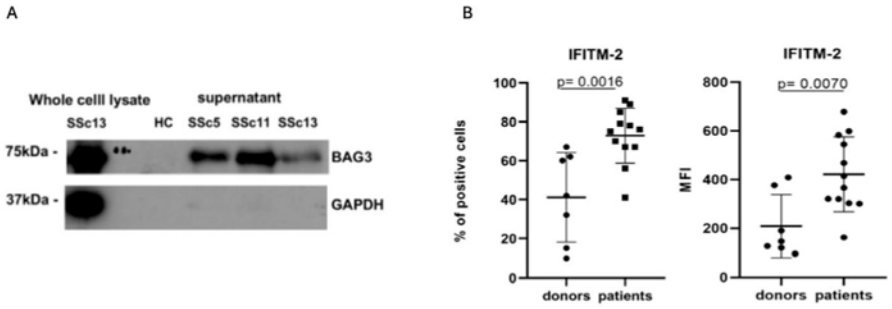


Figure 1. Expression of BAG3 and its receptor IFITM-2 in SSc and healthy control fibroblasts. (A) Western blot analysis showing BAG3 protein expression in whole cell lysates and supernatants from SSc patients (SSc5, SSc11, SSc13) and healthy control (HC) fibroblasts. GAPDH was used as loading control. (B) Flow cytometric analysis of IFITM-2 (BAG3 receptor) expression in SSc patients and healthy donors (HD) fibroblasts. Left panel shows the percentage of IFITM-2-positive cells ; right panel shows mean fluorescence intensity (MFI) of IFITM-2 expression. Data are presented as mean ± SD.

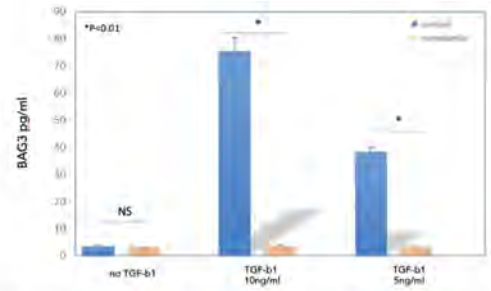


Figure 2. Effect of nintedanib on TGF-β1-induced BAG3 secretion in healthy control fibroblasts. BAG3 levels were measured in supernatants of healthy control fibroblasts treated with TGF-β1 (5 ng/ml and 10 ng/ml) in the presence or absence of nintedanib. Data are presented as mean ± SEM of three independent experiments.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Iannone: None; **M. De Marco**: None; **A. Minniti**: None; **G. Armentaro**: None; **A. Falco**: None; **A. D'Ardia**: None; **p. Manzo**: None; **L. Marzullo**: None; **A. Basile**: None; **A. Rosati**: None; **M. Turco**: None; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Eli Lilly & Co., 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **N. Del Papa**: None.

Abstract Number: 1864

Mitochondrial Dysfunction Drives cGAS-STING–Mediated Type I Interferon Production and Fibrosis in Systemic Sclerosis

Giulio Forte[1], Vasiliki Liakouli[1], Alessia Salzillo[2], Mario Angeli[3], Daniele Mauro[1], Antonio Ciancio[1], Barbara De Marino[2], Iacopo Panarese[1], Mario Faenza[1], roberto giacomelli[4], Andreas Ramming[5] and Francesco Ciccia[6], [1]Università della Campania Luigi Vanvitelli, Naples, Italy, [2]University of Campania L. Vanvitelli, Naples, Italy, [3]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [4]Università Campus Bio-Medico, Roma, Italy, [5]Department of Internal Medicine 3, Rheumatology & Immunology, Friedrich-Alexander-University (FAU) & Universitätsklinikum Erlangen, Erlangen, Germany, [6]Rheumatology Section, University of Campania L. Vanvitelli, Naples, Italy, Naples, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by type I interferon (IFN-I) production and mitochondrial dysfunction. Emerging evidence suggests that activation of the stimulator of interferon genes (STING) pathway in SSc is triggered by cytosolic mitochondrial DNA (mtDNA) released during mitochondrial stress. This link is further supported by the similarities between SSc and SAVI (STING-associated vasculopathy with onset in infancy) syndrome, a condition caused by a gain-of-function mutation in TMEM173 (which encodes STING) that phenocopies many key features of SSc. Nevertheless, the role of mitochondrial damage in activating cGAS-STING and driving IFN-I production in SSc remains poorly understood.

This study aims to investigate whether mitochondrial dysfunction activates the cGAS-STING pathway and drives IFN-I production and fibrosis in SSc.

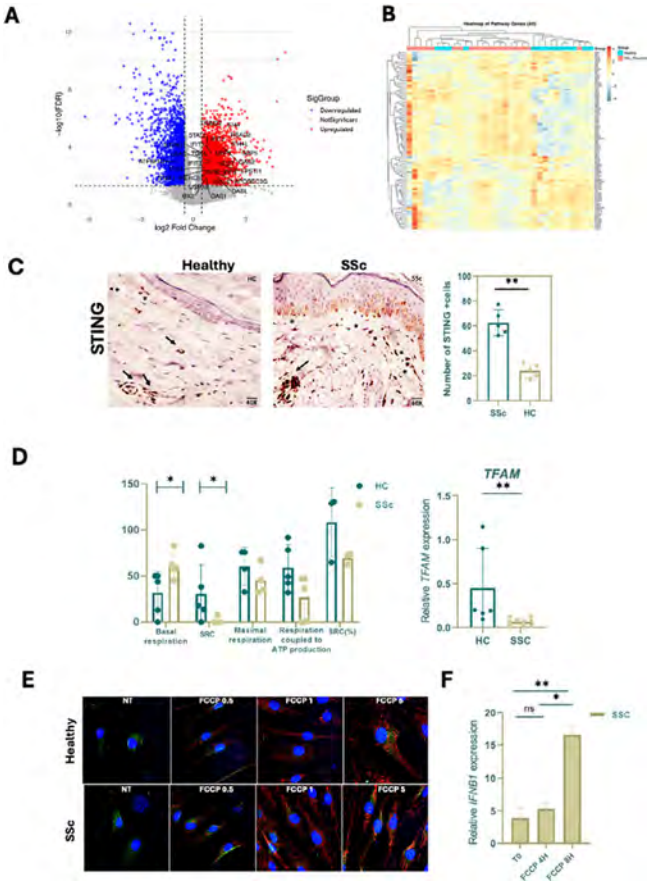
Methods: Transcriptomic analysis was performed on RNA-seq data (GSE231692, FaSScinate trial) to assess mitochondrial, cGAS-STING, and interferon-related gene expression. Skin biopsies from SSc patients and healthy controls (n=10 per group) were analyzed by RT-PCR and immunohistochemistry (IHC) for cGAS, STING, IRF3, and IFN-I. Mitochondrial dysfunction was evaluated through TFAM and MTND1 expression, Seahorse metabolic profiling, and ATP quantification in fibroblasts. To examine STING activation, fibroblasts were treated with the mitochondrial uncoupler FCCP, followed by confocal microscopy and IFNB1 quantification. In vivo relevance was tested in bleomycin-induced fibrosis (BIF) mice, with or without treatment with the selective STING inhibitor H-151.

Results: SSc skin exhibited upregulation of STING1, cGAS, TBK1, IFI16, and STAT1 compared to controls, with overexpression of STING, cGAS, and IFNB1 confirmed by RT-PCR ($p < 0.01$) and IHC. Mitochondrial dysfunction was evident in SSc fibroblasts, with significantly reduced TFAM expression ($p < 0.01$), impaired oxidative phosphorylation, decreased ATP levels, and increased glycolytic activity. FCCP-induced mitochondrial stress promoted STING nuclear translocation and IFNB1 induction, more pronounced in SSc than in control fibroblasts supporting the idea of a direct link between

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

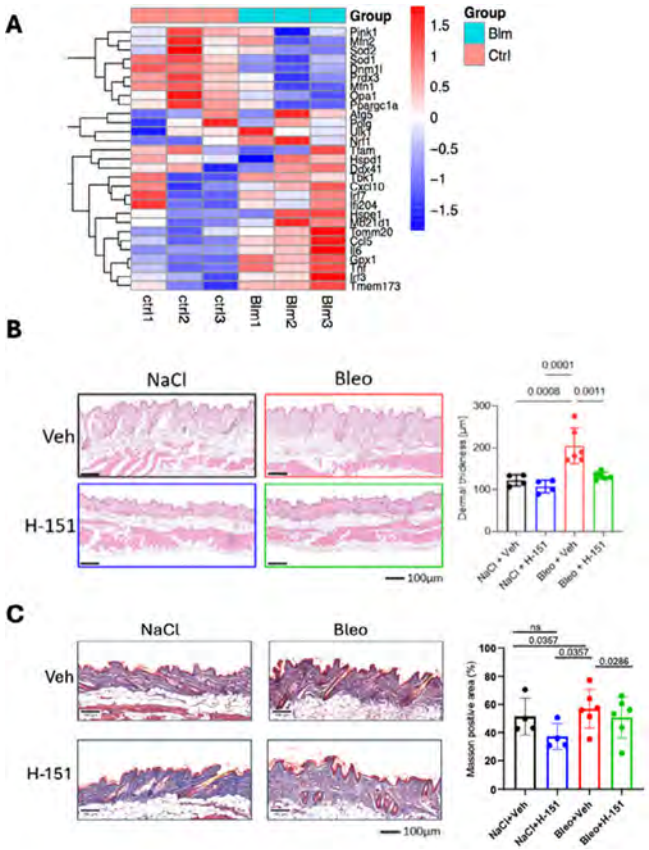
mitochondrial dysfunction, STING activation, and IFNβ production. Bleomycin-treated mouse models mirrored these findings, with STING-related genes (Irf3, Tmem173) being upregulated, and antioxidant defenses (Sod1, Prdx3) diminished. Treatment with H-151 significantly reduced dermal thickness and collagen deposition, underscoring the role of STING in fibrosis and the possible therapeutic potential of targeting the STING pathway in SSc.

Conclusion: Mitochondrial dysfunction in SSc promotes activation of the cGAS-STING pathway and IFN-I production, contributing to fibrotic remodeling. Pharmacologic inhibition of STING attenuates skin fibrosis in vivo, supporting STING as a novel therapeutic target in systemic sclerosis.



A. Volcano plot illustrating upregulated and downregulated gene in RNAseq of SSc skin vs HCs. B. Heatmap of the expression of mitochondrial, cGAS-STING and Interferon-associated genes across SSc vs HCs skin. C. Representative immunohistochemistry image of skin tissue showing overexpression of Sting in SSc compared to HC. D. On the left, mitostress analysis showing increased mean basal respiration and reduced spare respiratory capacity (SRC) of five control and five paired lesional SSc fibroblast cultures; on the right, rtPCR result showing TFAM downregulation in SSc skin compared to HC. E. Representative immunofluorescence image showing nuclear Sting translocation at 1 and 5 umol FCCP concentration compared to HC. F. The graph shows significant upregulation of Interferon Beta 1 gene in scleroderma fibroblasts 4 and 8 hours after FCCP stimulation, linking mitochondrial damage to interferon induction."Error bars indicate standard deviation. Asterisks denote statistically significant differences (*P<0.05; **P<0.005).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A. Heatmap from a public-available dataset showing downregulation of different mitochondrial-related genes and upregulation of Sting and Interferon type I related genes in bleomycin-treated mice compared to controls. B. Quantification in H&E staining of dermal thickness in bleomycin-treated mice compared to control mice as indicated (n = 6 per group) showing dramatic improvement of dermal thickness following Sting inhibitor H-151 administration. C. Masson Trichrome staining showing increased collagen (blue) in both control and Bleomycin-treated mice with a reduction in collagen following administration of H151. Error bars indicate standard deviation. Asterisks denote statistically significant differences (*P<0.05; **P<0.005).

Disclosure: G. Forte: None; **V. Liakouli**: None; **A. Salzillo**: None; **M. Angeli**: None; **D. Mauro**: None; **A. Ciancio**: None; **B. De Marino**: None; **I. Panarese**: None; **M. Faenza**: None; **r. giacomelli**: None; **A. Ramming**: Boehringer-Ingelheim, 2, Johnson & Johnson, 2, MoonLake Immunotherapeutics AG, 2, 5, Novartis Pharma GmbH, 2, UCB, 2; **F. Ciccia**: None.

Abstract Number: 1865

Shared and unique molecular signatures across different autoantibody groups in systemic sclerosis: a multi-omics analysis

Hanlin Yin[1], Wanyi Lin[2], Zhangyi zhao[1], Chenhan Jia[1] and Liangjing Lu[1], [1]Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, Shanghai, Shanghai, China (People's Republic), [2]Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Antinuclear antibodies (ANA) are detected in over 95% of systemic sclerosis (SSc) patients. Compared to cutaneous subtype classification, autoantibody-based stratification more accurately predicts survival, disease progression, and organ involvement. The distinct clinical features associated with each SSc-specific autoantibody suggest underlying molecular phenotypic differences. Recent studies have revealed distinct

molecular signatures between SSc patients with anti-centromere (ACA) and anti-topoisomerase antibodies (ATA). However, the molecular features of those less frequent autoantibody groups have not been studied.

Methods: This study aims to investigate the shared and unique molecular signatures among SSc patients with different SSc-associated autoantibody group (ACA, ATA, anti-RNA polymerase III antibodies (ARA), anti-U3RNP, anti-U1RNP, anti-Th/To, and anti-Ku antibodies) through a multi-omics analysis including plasma proteomics, PBMC transcriptomics, and immune cell phenotyping.

Results: 166 Asian SSc patients were included in this study and grouped by different SSc-associated antibody status: 55 patients with ACA, 58 with ATA, 24 with ARA, 12 with anti-U1RNP, 8 with anti-U3RNP, 4 with anti-Ku, and 5 with anti-Th/To antibodies. Plasma proteomic profiling identified 1,159 proteins, with 846 remaining after stringent filtering. Differential expression analysis revealed 86 consistently upregulated proteins across all antibody subgroups compared to healthy controls (HCs). These proteins were closely associated with endothelial injury, cell-cell adhesion, extracellular matrix deposition, and growth factor binding, reflecting shared pathogenic mechanisms in SSc. Gene Set Enrichment Analysis (GSEA) further identified antibody-specific pathway activation patterns, correlating with distinct clinical manifestations, including calcinosis, renal involvement, cancer, myopathy, and cardiomyopathy. PBMC RNA-seq analysis demonstrated that common upregulated pathways across autoantibody groups (vs. HCs) were associated with immune activation, the ubiquitin-proteasome system, and cytoskeletal regulation. Additionally, GSEA highlighted unique metabolic and immune activation pathways that varied among autoantibody subgroups. Immune cell phenotyping revealed broadly consistent alterations across SSc subgroups, including increased neutrophils and monocytes, decreased lymphocytes and regulatory B (Breg) cells, and elevated activated T cells. However, the magnitude of these changes differed significantly among autoantibody-defined subgroups, indicating heterogeneous immune dysregulation in SSc.

Conclusion: This study provides the first multi-omics characterization of both common and rare SSc-associated autoantibody groups, revealing shared and distinct molecular signatures that correlate with clinical features. Our findings highlight the potential for autoantibody-based stratification to guide precision management of SSc. Future studies should validate these molecular profiles in larger cohorts and explore their therapeutic implications, paving the way for biomarker-driven approaches in SSc care.

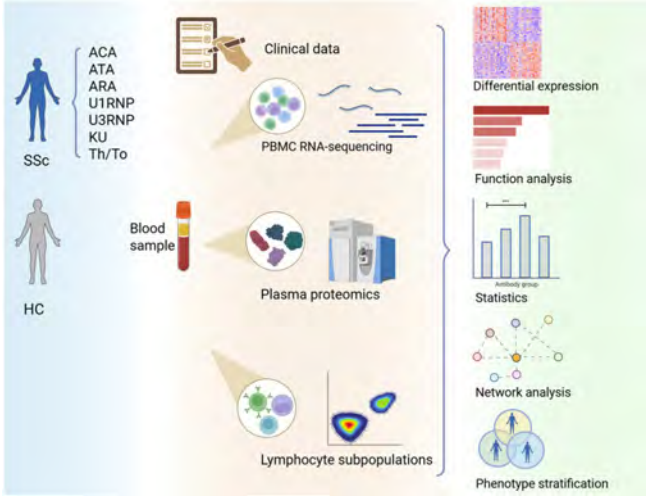


Figure 1. Study design

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

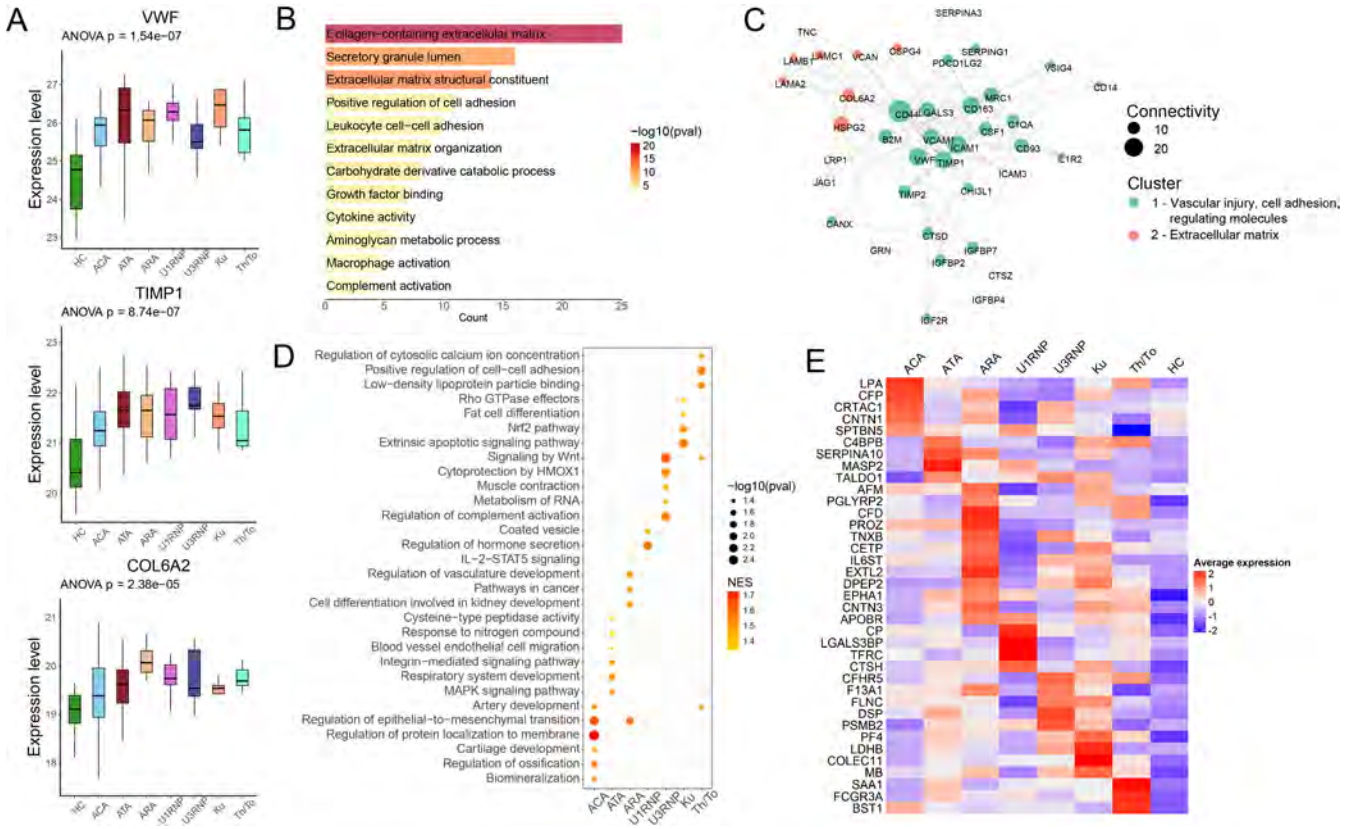


Figure 2. Plasma proteomic profiles of different antibody groups compared with HC. (A) Box plots showing log-transformed expression of functionally important shared DEPs. (B) GO enrichment analysis of shared upregulated proteins across antibody groups. (C) Interaction network of shared upregulated proteins with connectivity ≥ 4. The size of the circle represented the degree of each node and the color represented different Louvain clusters. (D) Bubble plot showing uniquely upregulated pathways in different antibody groups identified with GSEA analysis. Pathways with FDR<0.1 were visualized. The size and the color of the dot denote log-transformed FDR and NES of the corresponding pathways, respectively. (E) Heatmap displaying scaled expression of uniquely upregulated proteins in different antibody groups.

Disclosure: H. Yin: None; **W. Lin**: None; **Z. zhao**: None; **C. Jia**: None; **L. Lu**: None.

Abstract Number: 1866

Elucidating gastric pathology in systemic sclerosis using single-cell RNA sequencing

kristina clark[1], Moustafa Attar[2], Matthias Friedrich[3], Charles Murray[4], Alexander Clarke[2] and Christopher Denton[5], [1]Kennedy Institute of Rheumatology, University of Oxford, London, United Kingdom, [2]Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom, [3]Translational Gastroenterology Unit, University of Oxford, Oxford, United Kingdom, [4]Royal Free Hospital NHS Trust, London, United Kingdom, [5]University College London, UK, London, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Gastrointestinal (GI) involvement in systemic sclerosis (SSc) affects over 90% of patients and represents a large clinical burden and unmet need. Unlike the skin and lung, GI disease does not respond to immunosuppression and generally worsens with time despite treatment. Postmortem studies describe smooth muscle atrophy, fibrosis, and increased immune cells within the wall of the GI tract, but the cellular pathogenesis remains poorly understood. Here we investigate the single-cell composition of biopsies taken from SSc patients, particularly fibroblast subsets which may contribute to disease pathogenesis.

Methods: Gastric biopsies were obtained from four SSc patients, and four healthy controls (HC). Single-cell RNA sequencing (scRNAseq) was performed on whole biopsies using 10X Genomics Chromium workflow. Data were analysed using scanpy, scvi-tools, pertpy and pydeseq2.

Results: After filtering we analyzed 30,872 cells. There was a significant expansion of T cells proportions in SSc compared to HC, and a significant reduction in fibroblast, plasma cell, and epithelial cell cluster frequencies (FDR < 0.2) (Figure 1).

Within the stomal cell compartment, we identified several fibroblast clusters with similar gene expression to skin fibroblast subsets. Myofibroblasts and pericytes showed a trend to increased abundance in SSc compared to HC. Fibroblasts with similar gene expression to mesenchymal fibroblasts were most abundant across all samples, with no difference between SSc and HC. There was a significant reduction of *SFRP1*+ *CXCL12*+ and *EGR1*+ *POSTN*+ fibroblasts (FDR< 0.05) in SSc compared to HC. These have similar gene expression to secretory/papillary fibroblasts and proinflammatory skin fibroblasts. Pseudobulk differential gene expression analysis (Figure 2) across all fibroblasts revealed downregulation of *KLF2*, *TNFSF10*, and *C3*, whilst *AREG, STC1*, and *FAM155A* were upregulated in SSc compared to HC.

Gene Set Enrichment analysis between SSc and HC of each fibroblast cluster (using Reactome and Hallmark pathways) revealed upregulation of the mTOR pathway in the mesenchymal-like fibroblasts in SSc. Within the EGR1+POSTN+ fibroblasts there was significant downregulation of interferon signalling and complement cascade pathways in SSc compared to HC (FDR < 0.05).

There was significant expansion of CD8 T cells in SSc compared to HC (FDR< 0.05), with reduction in IgA plasma cells, SELL + CD4 cells, and memory B cells (FDR< 0.2) (Figure 3).

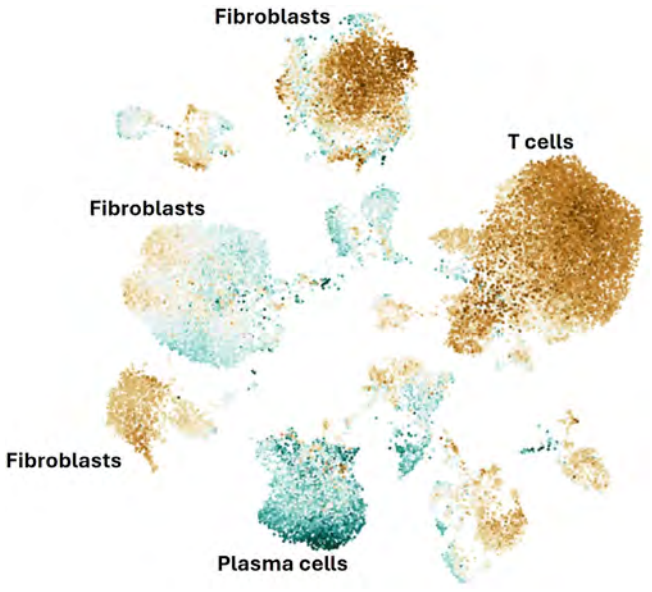


Figure 1: UMAP displaying differential abundance of all cells in the stomach, highlighting increased T cells, reduced plasma cells and perturbed fibroblast populations (Brown = increased, blue = reduced)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

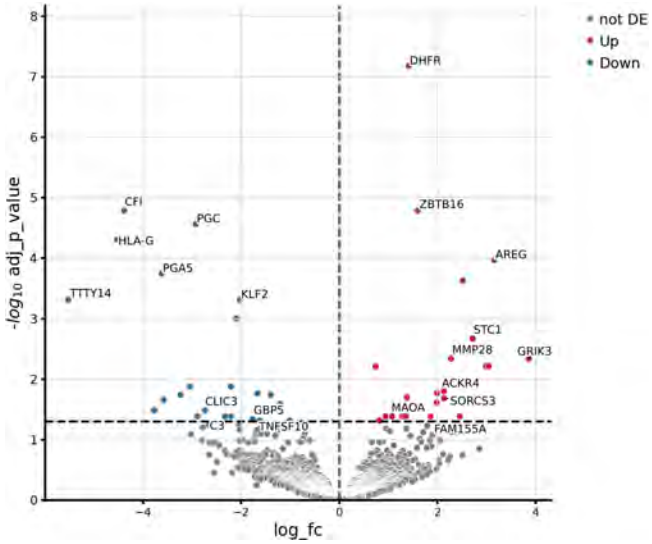


Figure 2: Pseudobulk analysis of differential gene expression across the whole fibroblast compartment, comparing differentially expressed genes between SSc and HC

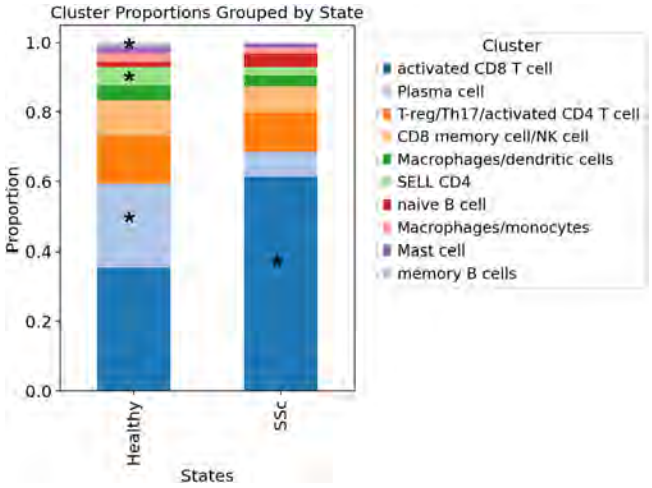


Figure 3: differential abundance within the immune cell compartment comparing SSc and HC. Activated CD8 T cells, plasma cells, SELL+CD4 T Cells and memory B cells all showed significant difference between SSc and HC (indicated by *).

Conclusion: Utilising scRNAseq on gastric tissue biopsies, we have identifed marked differences in immune cells, including increased abundance of cytotoxic CD8 T cells, and reduction in plasma cells in SSc compared to HC. Within the stromal compartment, there was a proportional increase in pericytes and myofibroblasts. Fibroblast gene expression analysis confirmed similarities to SSc skin (e.g. downregulation of KLF2), but also some notable differences including reduction in PTGDS, TNFSF10 and C3, and Interferon signaling. These represent a distinct population of gastric fibroblasts not present in SSc skin. Our findings may help to explain differences in natural history and treatment response between gut and other organs in SSc.

Disclosure: k. clark: None; **M. Attar**: None; **M. Friedrich**: None; **C. Murray**: None; **A. Clarke**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1867

Deciphering the Molecular Landscape of the Small Intestine in Early and Late SSc Using High-Definition Spatial Transcriptomics

Laura Much[1], Elena Pachera[2], Havard Fretheim[3], Knut EA Lundin[4], Lumeng Li[5], Astrid Hofman[6], Pietro Bearzi[5], Philip Stauffer[1], Michael Scharl[7], Oyvind Molberg[8], Oliver Distler[9] and Anna-Maria Hoffmann-Vold[3], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [2]University Hospital Zurich, Zurich, Switzerland, [3]Oslo University Hospital, Oslo, Norway, [4]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway, [5]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [6]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [7]Department of Gastroenterology and Hepatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [8]Oslo University Hospital, Oslo, Nepal, [9]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: SSc frequently results in serious gastrointestinal (GI) complications that contribute to increased morbidity and mortality. Understanding the molecular changes across different disease stages is crucial for elucidating the pathophysiology. Our study employs high-definition spatial transcriptomics to decipher the molecular and cellular landscape of the GI, assessing distinct alterations in the lamina propria associated with early and late disease stages.

Methods: We studied gastroduodenal biopsies from SSc patients enrolled in the ReSScue trial (n=10, 2013 ACR/EULAR classification criteria). Patients presented moderate to severe lower GI symptoms assessed by the UCLA GIT score. Formalin-fixed paraffin-embedded (FFPE) samples were processed for spatial transcriptomics using the Visium HD Spatial Gene Expression Reagent kit v1. Libraries were sequenced on the Illumina NovaSeq X platform and alignment was performed with Space Ranger 3.1.3. The data was analyzed using the packages *Seurat* v5 and *Banksy* for cell typing. *Speckle* was used for compositional analysis between SSc patients with early (symptom onset < 3.5 years) and late stage disease (symptom onset > 13.5 years). Differentially expressed genes (DEG) were identified between early and late patients using *MAST* (adjusted p-value < 0.05, |log2 FC| ≥ 0.2) and the *clusterProfiler* package was used for pathway over-representation analysis (ORA) and gene set enrichment analysis (GSEA) with the Gene Ontology (GO) database.

	All	Early SSc	Late SSc	p-value
	n = 10	*n* = 5 (50%)	*n* = 5 (50%)	
Age, mean years (SD)	59.4 (9.3)	56 (5.3)	63 (2.4)	0.3
Female sex, *n* (%)	10 (100%)	5 (100%)	5 (100%)	
Disease duration, mean years (SD)	10.3 (9.2)	1.9 (0.3)	18.6 (1.8)	< 0.001
lcSSc, *n* (%)	10 (100%)	5 (100%)	5 (100%)	
Anti-centromere antibody, *n* (%)	10 (100%)	5 (100%)	5 (100%)	
Distension, *n* (%) *	6 (60%)	2 (40%)	4 (80%)	0.52
Diarrhoea, *n* (%) *	4 (40%)	3 (60%)	1 (20%)	0.52
mRSS, mean (SD)	2.5 (2.6)	1.4 (0.6)	3.6 (1.5)	0.22
ILD, *n* (%)	0 (0%)	0 (0%)	0 (0%)	
Arthritis, *n* (%)	0 (0%)	0 (0%)	0 (0%)	
Digital ulcers, *n* (%)	2 (25%)	1 (20%)	1 (33.3%)	1
Immunosuppressants, *n* (%)	0 (0%)	0 (0%)	0 (0%)	

Fig. 1: Characteristics and clinical data for SSc patients with early and late disease. mRSS = modified Rodnan skin score, ILD = Interstitial lung disease. * symptoms assessed by the UCLA GIT score.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We included 5 SSc patients with early and 5 with late stage, with mean disease durations of 1.9 years and 18.6 years, respectively. The two groups did not differ in other clinical parameters (Fig. 1). Six tissue domains were annotated: Epithelium (villi), crypts, lamina propria, Brunner's glands, muscularis mucosae and isolated lymphoid follicles (ILF; Fig. 2A-B). Compositional analysis between early and late disease showed no significant differences in the tissue regions (Fig. 2C). DEG of the lamina propria revealed 61 significantly upregulated genes and 2,355 significantly downregulated genes in early compared to late disease (Fig. 3A). ORA showed upregulated pathways related to pathogen defense (*GBP3*, *GBP5*, *LYZ*, *CHGA*) in early compared to late disease (Fig. 3B). In contrast, several pathways associated with extracellular matrix (ECM) organization, including *ADAM19* and various collagen types, were significantly downregulated in early compared to late disease (Fig. 3C). Also, both ORA and GSEA showed downregulation in early SSc of immune response pathways, including JAK-STAT signaling and interferon responses (e.g., *JAK1*, *STAT2*, *IRF8*, *IRF4*), and pathways related to actin cytoskeleton organization and angiogenesis (e.g. *CAPZA2*, *GSN*, *VEGFA*, *VEGFB*; Fig. 3C).

Conclusion: This is a first report investigating the molecular landscape in GI tissue of SSc patients using high-definition spatial transcriptomics across different disease stages. Our findings could allude to the importance of exogenous agents in early disease stages, with an upregulation of pathogen defense pathways in early SSc. In addition, our results show an upregulation of fibrosis pathways and ongoing inflammatory processes in late SSc.

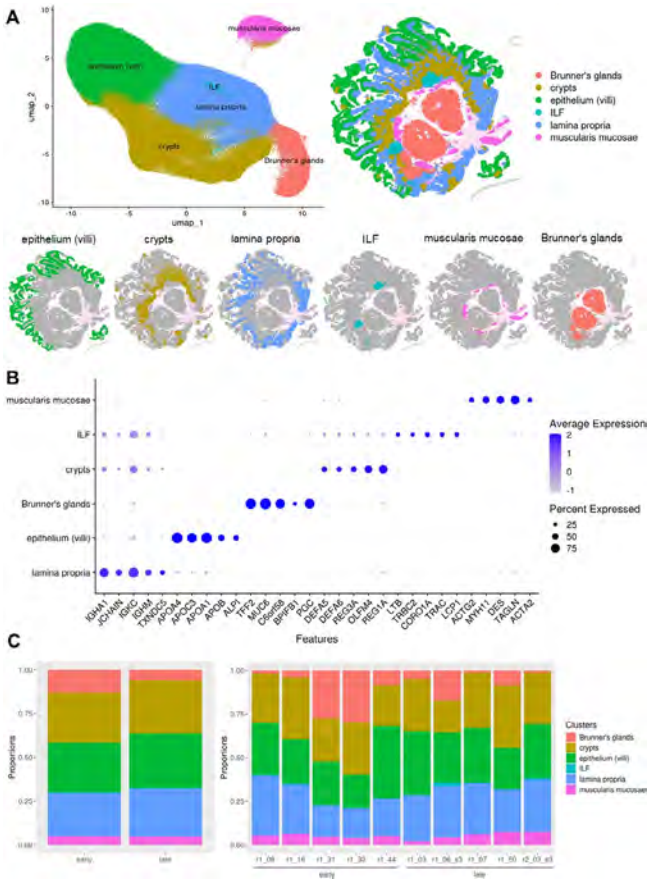


Fig. 2: Spatial transcriptomic analysis reveals 6 distinct tissue regions in the duodenum of SSc patients. A) UMAP of all 10 samples (908,423 8x8µm bins) and representative spatial plots of 1 sample show 6 distinct tissue regions. B) A dotplot of the 6 identified tissue regions shows the top 5 expressed marker genes in each cluster, which were used for manual annotation. C) Compositional analysis shows no significant differences in the proportions of the tissue regions between early and late SSc patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

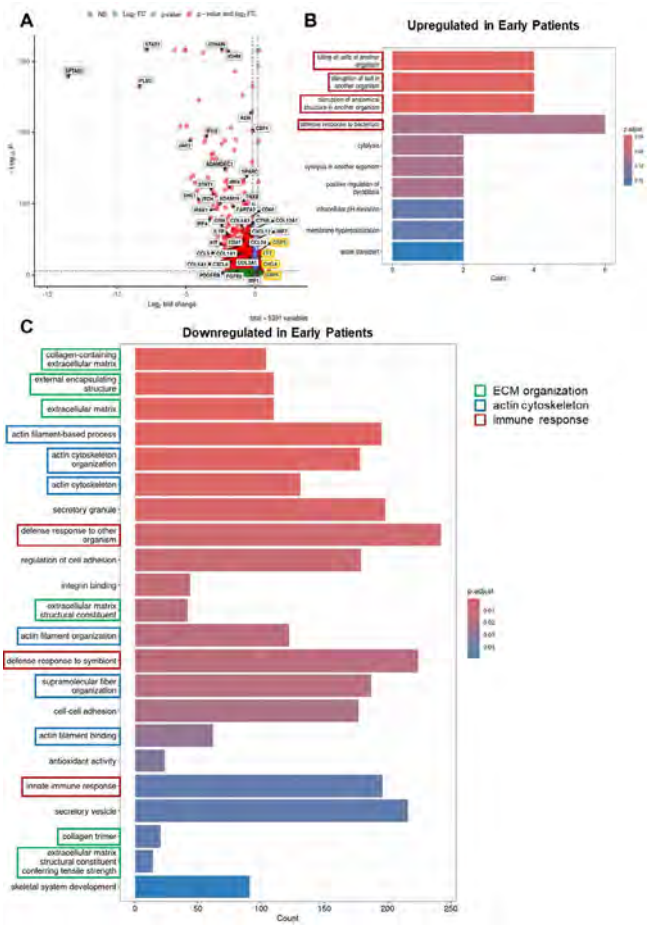


Fig. 3: DEG of the lamina propria show downregulated genes and pathways related to immune response and ECM in early compared to late patients. A) Volcano plot of 61 significantly upregulated and 2,355 significantly downregulated genes in early compared to late SSc, highlighting genes related to the pathways identified by GO. Upregulated genes are marked in yellow. B) ORA with the GO database shows upregulated pathways related to pathogen defense in early SSc (red boxes). C) ORA with the GO database shows downregulated pathways related to immune response (red boxes), ECM organization (green boxes) and actin cytoskeleton organization (blue boxes) in early compared to late SSc.

Disclosure: L. Much: None; **E. Pachera**: None; **H. Fretheim**: Boehringer-Ingelheim, 6; **K. Lundin**: None; **L. Li**: None; **A. Hofman**: None; **P. Bearzi**: None; **P. Stauffer**: None; **M. Scharl**: None; **O. Molberg**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1868

Global Downregulation of Fli1 in Mice Induces Cardiac Dysfunction via Enhanced β-fatty acid Oxidation and Collagen Deposition

Knowledge Mudhibadhi Moyo[1], Fatima-Ezzahrae El Adili[2], Maria Trojanowska[1] and Andreea Bujor[1], [1]Boston University, Boston, MA, [2]Boston University School of Medicine, Revere, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Primary cardiac involvement is a common complication of Systemic sclerosis (SSc), characterized by fibrosis and diastolic dysfunction, presumably due to microvascular dysfunction and repeated ischemia reperfusion injury. Downregulation of transcription factor Fli1 in SSc contributes to vasculopathy and skin fibrosis, but its potential role in cardiac disease is unclear. Using mice with heterozygous deletion of Fli1 (*Fli1*$^{+/-}$), we aim to uncover the effects of Fli1 downregulation on cardiac dysfunction in SSc through cardiac phenotypic studies and single-cell analyses.

Methods: Cardiac function was evaluated at 10-12 weeks in wild type and *Fli1*$^{+/-}$ mice using echocardiography. Sirius red staining followed by Image J analysis was used to assess cardiac collagen content. Cardiac apex tissue underwent mechanical and enzymatic dissociation for single-nuclei isolation using the 10X Genomics Nuclei Isolation Kit. The nuclei were barcoded using the 10X Chromium Single-Cell Platform, followed by cDNA library preparation. FASTQ files were generated and analyzed using BioTuring Single-Cell Analysis Software to identify distinct cellular clusters and transcriptional changes.

Results: *Fli1*$^{+/-}$ mice exhibited diastolic dysfunction, with elevated *E/e'* and prolonged isovolumic relaxation time, as well as reduced systolic function indicated by decreased ejection fraction and fractional shortening (Fig. 1A). Sirius red staining confirmed increased collagen deposition in *Fli1*$^{+/-}$ hearts (Fig. 1B). Single-cell transcriptomic analysis identified 13 major cell types (Figure 2A). Cardiomyocyte cluster analysis revealed a transcriptional shift, with appearance of a novel, mutant specific cluster, and loss of a wild type cluster (Figure 2B). Differential gene expression analysis between these two

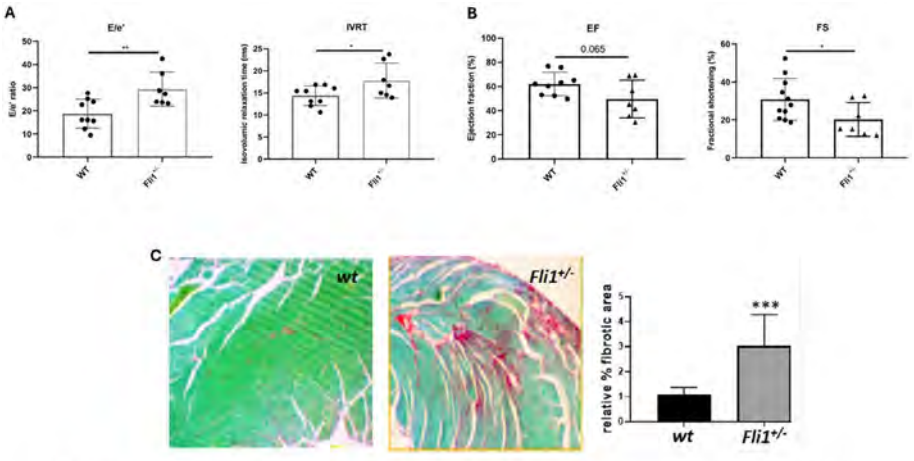


Figure 1. Fli1 downregulation resulted in diastolic and systolic dysfunction, and increased collagen accumulation in cardiac tissue

Fli1 downregulation resulted in diastolic and systolic dysfunction, and increased collagen accumulation in cardiac tissue

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

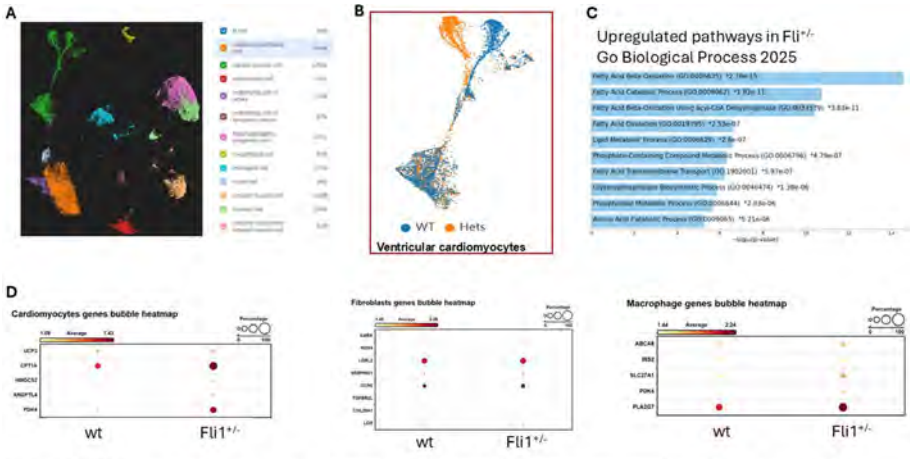


Figure 2. UMAP of cardiac tissue cells, upregulated pathways and differentially expressed genes in cardiomyocytes, fibroblasts and macrophages.

UMAP of cardiac tissue cells, upregulated pathways and differentially expressed genes in cardiomyocytes, fibroblasts and macrophages

clusters revealed several upregulated genes including *PDK4 (log2FC=3.3 FDR=1.36e-23)*, and *ANGPTL (log2FC=2.18 FDR=7.54 e-64)*. Analysis of the enriched pathways revealed upregulation of β-fatty acid oxidation in Fli1$^{+/-}$ cardiomyocytes (2.78e-15), a metabolic shift previously linked to impaired cardiomyocyte proliferation following ischemia-reperfusion injury. Additionally, macrophages from *Fli1*$^{+/-}$ mice showed increased expression of *PLA2G7*, a gene linked to inflammatory remodeling and fatty acid metabolism in cardiac macrophages. Supporting a role in cardiac fibrosis, *Fli1+/-* fibroblasts displayed elevated expression of fibrosis related genes including *LOX, COL20A1, TGFBR3L, CCN2, SERPINE1, LOXL2, NOX4*, and *IL6RA*.

Conclusion: Fli1 haploinsufficiency drives cardiac dysfunction and fibrosis via metabolic reprogramming in cardiomyocytes and macrophages with enhanced fatty acid oxidation and profibrotic activation of fibroblasts through TGF-β/LOX pathways. This suggest that Fli1 deficiency may be a contributor to primary cardiac involvement in SSc.

Disclosure: K. Moyo: None; **F. El Adili**: None; **M. Trojanowska**: None; **A. Bujor**: None.

Abstract Number: 1869

A Mirna Signature Consisting of High let7i-5p, High mir-483-5p, Low mir-223- 3p Characterizes Connective Tissue Diseases with Interstitial Lung Disease

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with interstitial lung disease associated to a connective tissue disease (CTD-ILD) are a heterogeneous population both concerning mechanisms and trajectories. In an RNA Seq approach we have previously identified differentially expressed miRNA in patients with CTD-ILD. The current study was conducted to confirm the association of 7 miRNA with CTD-ILD and with disease subgroups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The selected miRNA were analysed with qPCR techniques. The study population comprised 110 patients (89% women) and 10 healthy controls (90% women) from the NEREA register of CTD-ILD. Demographics and process-related data were extracted from RedCap files where the register is hosted. Results are shown as mean (SEM) or n (%). Associations were assessed with cross-sectional variables and with 18 month follow-up outcomes. Functional deterioration was defined by a 10% fall in forced vital capacity (FVC). Statistics were done with t test and Spearman's correlation. Target prediction analysis was carried out with miRPath v4.0 tools.

Results: Age was 64.9 (1.1) in the CTD-ILD group and 62.1 (1.2) yrs in healthy controls (ns). Process related variables are shown at the **Table**. At baseline, disease duration was 4.1 (0.5) yrs. Survival at endpoints was 91%, while functional decline was observed in 24%.

As compared to healthy controls, patients with CTD-ILD were identified by higher **Let7i-5p** (p 0.001) and **miR-483-5p** (p 0.018), accompanied by lower **miR-223-3p** (p 0.025).

Within the patient cohort, the presence of SSc-related antibodies associated with higher **miR-142-5p** (p 0.013) and lower **miR185-5p** (p 0.039). An increase in miR-142-5p levels was also shown in relationship with NVC alterations (p 0.04). Patients with RA had lower levels of **miR-320d** (p 0.03), while patients with SS had higher **Let7i-5p** (p 0.043), lower **miR-142-5p** (p 0.016) and higher **miR-185-5p** (p 0.025). No specific miRNA profiles differentiated between radiographic patterns, whereas fibrotic disease associated with lower **miR-142-5p** (p 0.004) and this miRNA levels also dropped in correlation with disease duration (p 0.047).

Patients requiring oxygen therapy had lower levels of **miR-483-5p** (p 0.016), while functional deterioration over time was associated with lower **Let7i-5p** (p 0.019). Fatal outcomes were marginally associated to lower baseline levels of miR-320d (p 0.065) and of miR-483-5p (p 0.095). Principal differentially regulated molecules in each subgroup and pathways involved are shown in the **Figure**.

Conclusion: A 3 miRNA signature consisting of high Let7i-5p, high miR-483-5p, low miR-223- 3p defined the CTD-ILD population. According to our data, the up-regulation of Let7i-5p and miR-483-5p might drive an adaptive response to lung injury, whose loss parallels functional deterioration. On the other hand, patients with vasculopathy showed a distinc profile characterized by an increase in miR-142-5p. The latter miRNA could also have a regulatory role, since its levels descended in fibrotic disease and in advanced stages.

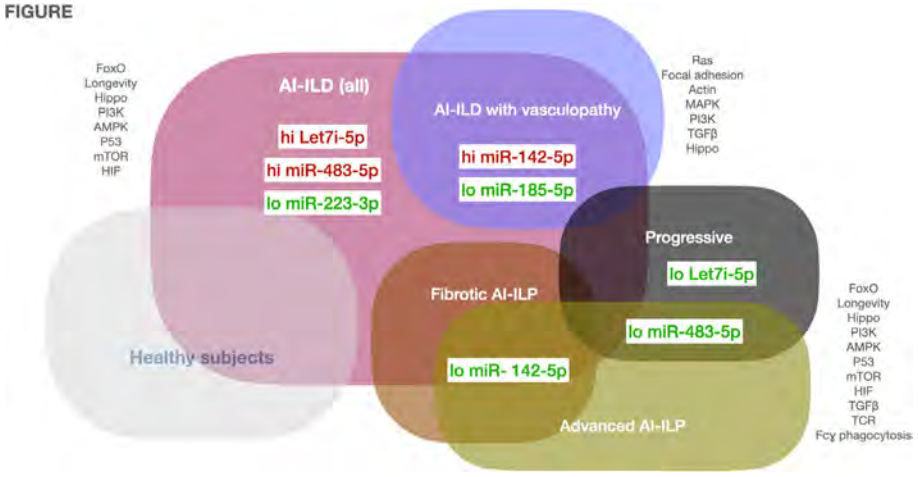
TABLE

CTD-ILD cohort: process related variables

Clinical diagnoses		Radiographic patterns		Autoantibodies		Nailfold capillaroscopy		Functional status	
SSc/related conditions	24p (21.8%)	NSIP	48p 843.6%)	RF	36p (35%)	Major alterations	41p (54.6%)	FVC (% predicted values)	78.6 (3.4)
RA and RA-overlapping diseases	15p (13.6%)	UIP	36p (32.7%)	ARS	11p (11.3%)				
IIM and ARS syndromes	9. (8.2%)	Undetermined	9p (8.2%)	Ro 52kDa	23p (24%)			DLco (% predicted values)	61.1 (4.1)
SS	9p (8.2%)	OP/OP-NSIP	9p (8.2)	SSc-specific	22p (22.7%)				
IPAF	39p (35.5%)	LIP	4p (3.6%)	U1RNP	6p (5.4%)			home oxygen	15p (13.6%)
miscellaneous	12p (10.9%)	Others	4p (3.6%)	RNP70kDA	5p (4.5%)				

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

FIGURE



On the whole, our results unveil both process-dependent and shared mechanisms in CTD-ILD processes of interest in the design of therapeutic strategies.

Disclosure: O. Sanchez Pernaute: None; **M. Rodriguez-Nieto**: None; **C. Vadillo Font**: None; **M. Nieto**: None; **L. Cebrian**: None; **B. Lopez Muñiz**: None; **H. Godoy Tundidor**: None; **R. Laporta**: None; **J. Loarce Martos**: None; **J. A Rigual**: None; **f. Romero-Bueno**: None; **I. Llorente Cubas**: None; **C. Valenzuela**: None; **G. Bonilla**: None; **L. Gomez Carrera**: None; **R. Garcia Vicuña**: None; **A. Jaureguizar**: None; **J. Morell Hita**: None; **I. Abasolo Alcazar**: None.

Abstract Number: 1870

Paracrine WNT Signaling Modulates Profibrotic Macrophage Metabolic Activation in Systemic Sclerosis

emily Morris[1], Helen Jarnagin[1], Chen-Yu Wang[1], Michael Whitfield[2] and **Patricia Pioli**[3], [1]Dartmouth College, Lebanon, NH, [2]Geisel School of Medicine, Lebanon, NH, [3]Geisel School of Medicine at Dartmouth, Lebanon, NH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: An immune fibrotic axis consisting of activated macrophages (MØs) and fibroblasts has been identified in autoimmune systemic sclerosis (SSc) that drives disease across affected tissue types. In prior work, we have shown that SSc fibroblasts and MØs, which co-localize in lesional SSc skin, participate in reciprocal paracrine signaling mediated by SSc fibroblast-derived exosomes. The goal of this study was to identify the specific cargo carried by SSc fibroblast exosomes that mediates profibrotic MØ activation, and to elucidate the molecular mechanism responsible for this activation. Because MØ activation is intrinsically dependent on ATP availability, we hypothesized that SSc fibroblast-derived paracrine signals may induce profibrotic MØ activation in part by driving functional changes in MØ bioenergetics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: To identify candidate regulators responsible for inducing dermal SSc MØ activation, publicly available single cell RNAseq (scRNA-seq) data from SSc patient and non-SSc control skin were interrogated. Because MØ activation is driven by metabolic utilization, exosome-mediated effects on MØ bioenergetics were ability investigated using Single Cell ENergetIc metabolism by profilng Translation inhibition (SCENITH). Protein content of exosomes was analyzed by immunoblot. Inhibitor studies were performed to assess the contribution of noncanonical WNT signaling to exosome-mediated profibrotic MØ activation, and co-cultures were employed to determine the requirement for WNT signaling in the ability of SSc fibroblast exosome-stimulated MØs to induce reciprocal fibroblast activation.

Results: scRNA-seq analyses of SSc and control skin demonstrated that pathways related to lipid metabolism, nutrient sensing, and oxidative phosphorylation (OXPHOS) were significantly enriched in SSc dermal MØs. Using SCENITH, we demonstrated that stimulation of MØs with SSc fibroblast-derived exosomes resulted in enhanced OXPHOS reliance, consistent with scRNA-seq results, while healthy fibroblast-derived exosomes failed to increase OXPHOS utilization. Furthermore, intact OXPHOS was required for profibrotic activation of human MØs by SSc fibroblast-derived exosomes. WNT5A, a known regulator of myeloid metabolism, was overexpressed in SS fibroblast exosomes, and studies with the WNT5A inhibitor Box5 demonstrated that blockade of WNT5A signaling abrogates OXPHOS upregulation and significantly attenuates the ability of SSc fibroblast exosome-stimulated MØs to elicit SSc fibroblast activation.

Conclusion: Collectively, our data indicate that SSc fibroblast-derived paracrine signals promote profibrotic MØ activation by altering MØ bioenergetics through noncanonical WNT-mediated signaling. These findings suggest that MØs meet the increased energy demand of the SSc dermal fibrotic niche by upregulating both mitochondrial dependency and mitochondrial content, and that blocking either OXPHOS or the WNT5A receptor, FZD5, is sufficient to inhibit profibrotic SSc MØ activation. Thus, MØ-specific metabolism and/or WNT5A signaling may represent novel therapeutic targets in SSc.

Disclosure: e. Morris: None; **H. Jarnagin**: None; **C. Wang**: None; **M. Whitfield**: Boehringer Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 2, Celdara Medical LLC, 2, 5, 10, 12, Scientific Founder; **P. Pioli**: None.

Abstract Number: 1871

Examining the Impact of ETV2 on altered endothelial phenotype in systemic sclerosis

Elio Carmona[1], Alyssa Rosek[2], Neha Khanna[2], Dinesh Khanna[3], Amr Sawalha[4] and **Pei-Suen Tsou**[3], [1]Division of Pediatric Rheumatology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA, Pittsburgh, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [3]University of Michigan, Ann Arbor, MI, [4]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Our prior research demonstrated that epigenetic modifications are central to the pathogenesis of scleroderma (SSc)[1]. Using ATAC-seq, we found that chromatin accessibility was significantly reduced in diffuse cutaneous (dc) SSc dermal endothelial cells (ECs) compared to those from healthy individuals. We also observed an increase in the chromatin binding of ETV2, a key transcription factor in the ETS family, within dcSSc ECs. ETV2 is crucial for both

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hematopoietic and EC function and has been implicated in reprogramming non-ECs to an endothelial phenotype. Its deficiency results in developmental failure of blood vessels in embryos. Here, we explore the impact of ETV2 dysregulation on EC dysfunction in SSc.

Methods: ECs were isolated from skin biopsies of healthy subjects and dcSSc patients. We evaluated ETV2 expression using qPCR, Western blot, and immunofluorescence. ETV2 was overexpressed in ECs via viral transduction, and its expression was also profiled in scRNA-seq data from 18 healthy individuals and 23 dcSSc patients. We assessed functional outcomes like proliferation and angiogenesis. To pinpoint genes influenced by ETV2 in dcSSc ECs, CUT&RUN-seq and bulk RNA-seq were utilized. Statistical significance was set at $P< 0.05$.

Results: Despite low baseline levels, ETV2 was markedly upregulated in dcSSc ECs compared to controls. scRNA-seq analysis showed increased ETV2 expression in capillary and venular ECs in SSc skin. ETV2 overexpression in dcSSc ECs significantly boosted EC proliferation (n=4 patient lines, $p< 0.01$) and angiogenic activity, evidenced by increased tube and node formation on Matrigel (n=4 patient lines, $p< 0.05$). Relative to healthy ECs, dcSSc ECs showed decreased *CDH5* and increased *COL1A1* and *CDKN1A* expression, indicative of an endothelial-to-mesenchymal transition phenotype and elevated cellular senescence. ETV2 overexpression elevated EC marker *CDH5* (1.385 ± 0.17, $p< 0.05$ vs. control, fold change) and diminished fibrotic marker *COL1A1* (0.680 ± 0.147, $p< 0.05$ vs. control, fold change) and senescence marker *CDKN1A* (0.719 ± 0.175, $p< 0.05$ vs. control, fold change). Through CUT&RUN-seq and bulk RNA-seq, we identified specific genes and pathways significantly regulated by ETV2 in dcSSc ECs.

Conclusion: This study highlights the significant impact of ETV2 in modifying EC function in dcSSc. Upregulation of ETV2 is associated with increased cell proliferation and angiogenesis, which may contribute to disease progression. Changes in gene expression following ETV2 overexpression suggest its potential to reverse endothelial-to-mesenchymal transition and reduce senescence. Further investigation into ETV2-regulated pathways could provide valuable insights into SSc vasculopathy.

1. Tsou et al. Genome-Wide Reduction in Chromatin Accessibility and Unique Transcription Factor Footprints in Endothelial Cells and Fibroblasts in Scleroderma Skin. Arthritis Rheumatol. 2021 Aug;73(8):1501-1513.

Disclosure: E. Carmona: None; **A. Rosek**: None; **N. Khanna**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **A. Sawalha**: None; **P. Tsou**: None.

Abstract Number: 1872

High-throughput Screening Uncovers Distinct Molecular Signatures Linked with HRCT Patterns in SARD-ILD

Philip Stauffer[1], Vyacheslav Palchevskiy[2], Laura Much[3], Phuong Diep[4], Magdalena Abel[4], Natasha Moe[4], Thomas Gaisl[5], Carolin Steinack[5], Shahrzad Lari[2], Elena Pachera[6], Øyvind Molberg[7], Oliver Distler[8], S. Samuel Weigt[2], John A. Belperio[2] and Anna-Maria Hoffmann-Vold[4], [1]University of Zurich Hospital, Schlieren, Switzerland, [2]UCLA, Los Angeles, [3]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [4]Oslo University Hospital, Oslo, Norway, [5]USZ, Zürich, Switzerland, [6]University Hospital Zurich, Zurich, Switzerland, [7]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [8]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: High-Resolution Computed Tomography (HRCT) is crucial for diagnosing and managing interstitial lung disease associated with systemic autoimmune rheumatic diseases (SARD-ILD), as it reveals characteristic patterns that inform treatment and prognosis in clinical practice. However, molecular expression patterns linked to HRCT findings remain underexplored. Since lung sampling is invasive and rare clinically, identifying alternative biological materials that reflect lung processes is essential. The united airway disease hypothesis posits that similar molecular pathways exist between the upper and lower respiratory tracts. Therefore, the objective of this study was to investigate the association between HRCT patterns and molecular expression profiles in SARD-ILD using transcriptomics.

Figure 1: Underlying SARD segregated by the HRCT pattern groups.

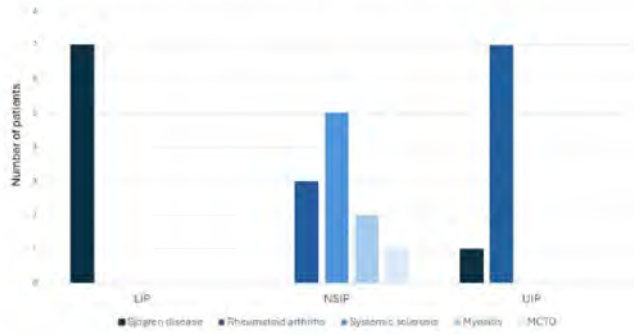
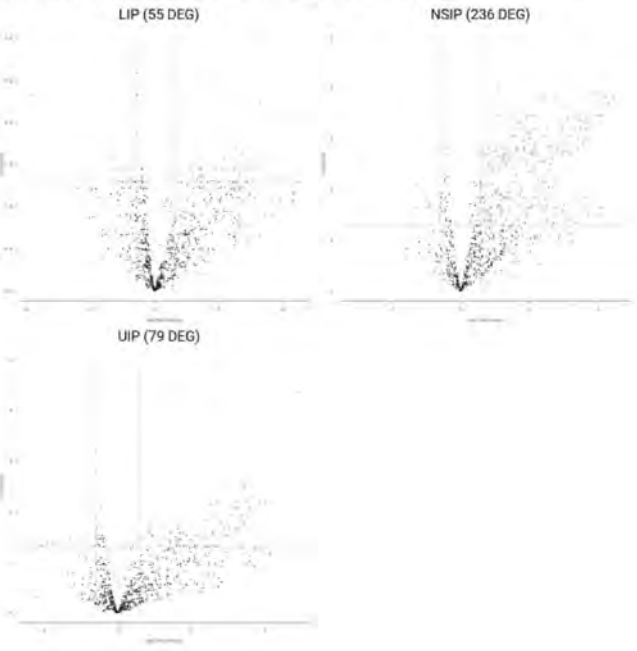


Figure 2: Volcano plots of LIP, NSIP, and UIP differentially expressed genes (DEG) compared to healthy control (|log2FC| ≥ 0.58 (up-regulated) or ≤ -0.58 (down-regulated), corresponding to fold change of 1.5, and adjusted p-value < 0.05).



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Nasal mucosa samples were collected via Copan Flocked Swab (Copan Diagnostics 56380CS01) from SARD-ILD patients at Oslo University Hospital and healthy controls from UCLA and Oslo. HRCT patterns and clinical data were collected simultaneously. We assessed nasal mucosa transcriptomes to identify molecular expression profiles of SARD-ILD with lymphocytic interstitial pneumonia (LIP), nonspecific interstitial pneumonitis (NSIP) and usual interstitial pneumonia (UIP) compared to healthy controls. Transcriptomes were determined by NanoString technology, using the Autoimmune Profiling panel. Gene expression and pathway analyses were conducted using ROSALIND software (https://www.rosalind.bio/). To confirm lung-level findings, lung tissue samples were collected at the University Hospital Zurich from eight SARD-ILD and two healthy controls. Gene expression patterns were assayed using the 10x VisiumHD spatial transcriptomics platform.

Results: We included nasal mucosa samples from 7 LIP, 11 NSIP, 8 UIP patients, and 10 healthy controls (Fig. 1). We identified 55, 236, and 79 significant differentially expressed genes for LIP, NSIP, and UIP, respectively, compared to controls (Fig. 2). LIP was enriched mainly for IFN-type I, MHC class I antigen presentation, epigenetic and transcriptional regulation, and IFN-type II; NSIP for IFN-type I, Treg and TH2 differentiation, and IFN-type II; UIP for TH2 differentiation, complement system, IL activation, inflammasomes, Treg, and TH17 differentiation (Fig. 3). Visium HD data from lung biopsies are being processed to spatially resolve whole transcriptomes and further examine these pathways in the lung.

Conclusion: The molecular fingerprints of LIP, NSIP, and UIP provide critical insights into their distinct pathophysiological mechanisms. While LIP is characterized by significant inflammation driven by lymphocytes, NSIP shows a mixed inflammatory response with some regulatory T cell involvement. In contrast, UIP is associated with a complex interplay of immune pathways that drive chronic inflammation and tissue remodeling. Understanding these molecular profiles is essential for

Figure 3: NanoString Gene Set Analysis annotations of upregulated genes.

LIP

Term	Significance Score
Type I Interferon Signaling	2.5743
MHC Class I Antigen Presentation	2.1929
Epigenetics and Transcriptional Regulation	2.1239
Type II Interferon Signaling	2.0586
TGF-beta Signaling	1.9895
Inflammasomes	1.8852
Treg Differentiation	1.8543
Lymphocyte Trafficking	1.852
NF-kB Signaling	1.8455
Complement System	1.8298

NSIP

Term	Significance Score
Type I Interferon Signaling	3.3792
Treg Differentiation	3.0831
Th2 Differentiation	3.0666
Type II Interferon Signaling	3.0485
MHC Class I Antigen Presentation	2.9201
Inflammasomes	2.8795
Th17 differentiation	2.7562
Other Interleukin Signaling	2.7104
NLR Signaling	2.676
NF-kB Signaling	2.6522

UIP

Term	Significance Score
Th2 Differentiation	2.2209
Complement System	2.2194
Other Interleukin Signaling	2.2174
Inflammasomes	2.1964
Treg Differentiation	2.1317
Th17 differentiation	2.0309
MHC Class I Antigen Presentation	1.9995
NF-kB Signaling	1.9709
TGF-beta Signaling	1.9609
Chemokine Signaling	1.9348

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

tailoring treatment strategies and improving outcomes in patients with SARD-ILD. Our Visium HD results will further validate and characterize this preliminary molecular fingerprint by generating spatially resolved and unbiased lung transcriptome data.

Disclosure: P. Stauffer: None; **V. Palchevskiy**: None; **L. Much**: None; **P. Diep**: Boehringer-Ingelheim, 6, NordicInfu Care AB, 1; **M. Abel**: None; **N. Moe**: Boehringer-Ingelheim, 6; **T. Gaisl**: None; **C. Steinack**: None; **S. Lari**: None; **E. Pachera**: None; **Ø. Molberg**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **S. Weigt**: None; **J. Belperio**: None; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2.

Abstract Number: 1873

TGF-β-Driven Mitochondrial Stress Activates cGAS-STING Signalling via Impaired Mitophagy in Systemic Sclerosis Endothelial Cells

Stefano Di Donato[1], Ceclie Bordes[2], Claude Lalou[2], agathe Depaire[2], John Tchen[2], Charlene Lhuissier[2], damien Brisou[2], Vanja Sisirak[2], Johan Garaude[2], Christopher Wasson[3], Rebecca Ross[4], Francesco Del Galdo[3] and Marie-Elise Truchetet[5], [1]University of Leeds, Canosa Sannita, Chieti, Italy, [2]University of Bordeaux, Bordeaux, France, [3]University of Leeds, Leeds, United Kingdom, [4]Medicine and Health, University of Leeds, Leeds, United Kingdom, [5]Bordeaux University Hospital, Bordeaux, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Emerging evidence implicates mitochondrial dysfunction as a contributor to tissue fibrosis in systemic sclerosis (SSc) (1). Endothelial cells, which are a key player in vascular injury and immune activation, are increasingly recognized as one of the main drivers of both fibrotic and type I interferon responses in SSc tissues (2). Since increased TGF-β stimulation is a hallmark of SSc pathogenesis, we hypothesized that it drives mitochondrial stress and impairs mitophagy in SSc endothelial cells, leading to cytosolic mitochondrial DNA (mtDNA) accumulation and subsequent activation of the cGAS-STING pathway that ultimately promote disease progression.

Methods: Primary dermal microvascular endothelial cells (MVECs) and fibroblasts from healthy donors (HD) and SSc patients were treated with TGF-β (10 ng/mL), IL-4 (5 ng/mL, negative control) or CCCP (positive control for mitophagy). Mitochondrial fission and stress-related transcripts were assessed by RT-qPCR. Oxygen Consumption Rate (OCR) was measured via Seahorse assays. Mitochondrial morphology and content were analysed via Immunofluorescence using MitoTracker Deep Red. Immunoblots were used to evaluate cGAS-STING pathway activation (P-STING, P-IRF3). The presence of mtDNA release in the supernatant was assessed by qPCR. Conditioned media from stimulated cells were tested in THP-1 dual luciferase reporter cells for ISRE/IRF3-driven transcription.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: At steady-state, MVECs from SSc patients exhibited an elevated expression of mitochondrial fission genes and a reduction in mitochondrial content compared to HD MVEC, suggesting defective mitochondrial quality control in SSc MVECS. Fibroblasts and MVECs from HD exposed to TGF-β upregulated multiple mitochondrial fission and mitophagy-related genes (DRP1, RALA, SPIRE1, HDN1) after 24 hours.

Long-term TGF-β exposure (7 days) in HD MVECs led to a 2.5-fold reduction in baseline and maximal OCR as assessed by Seahorse analysis. Concordantly, Seahorse assays revealed a marked decrease in basal and maximal respiration in SSc MVECs compared to HD MVECs at baseline.

Short-term TGF-β treatment (6h) of MVECs induced cGAS-STING activation, as evidenced by increased P-STING and P-IRF3. Conditioned media from TGF-β-treated MVECs triggered time-dependent IRF3-driven luciferase activity in THP-1 reporter cells, correlating with duration of TGF-β exposure, suggesting the hypothesis of a paracrine transmission of mtDNA or other interferon stimulating mediators.

Conclusion: Long-term TGF-β exposure induces mitochondrial fragmentation, stress, and dysfunctional mitophagy in HD MVECs. This leads to cytosolic accumulation and extracellular release of mtDNA and induces a *low-respiration* phenotype similar to SSc primary MVECs. This process triggers intracellular and paracrine activation of the cGAS-STING axis. Our findings uncover a novel mechanistic link between TGF-β signalling, mitochondrial dysfunction, and innate immune activation in SSc endothelium, identifying mitochondrial quality control as a potential therapeutic target

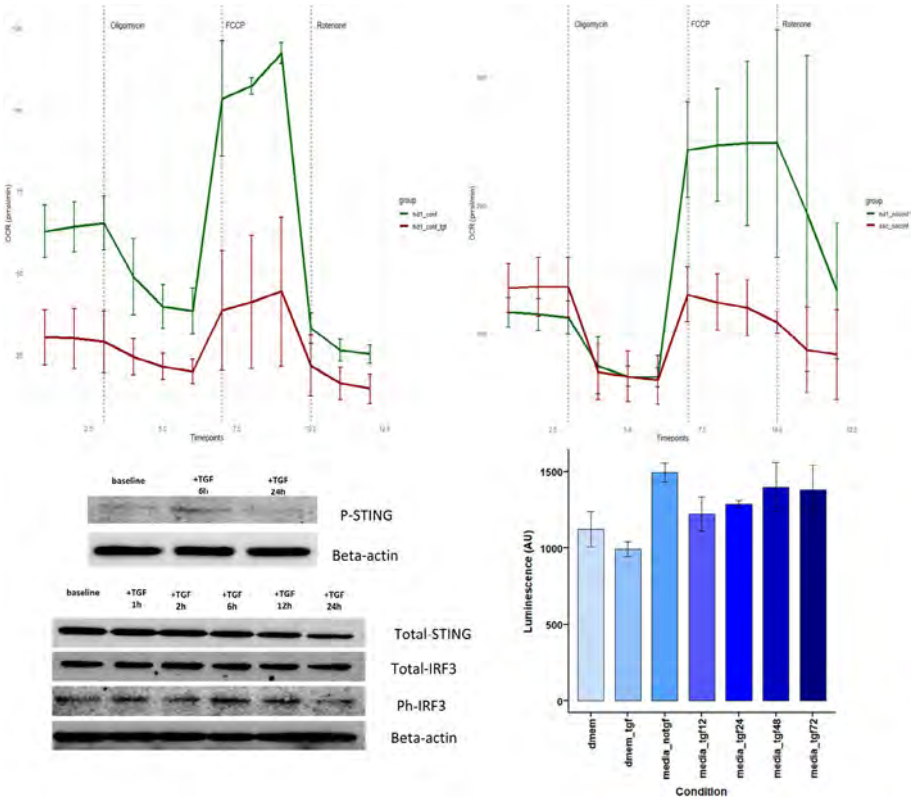


Figure 1. Mitochondrial dysfunction and STING pathway activation in endothelial cells treated with TGF-β. Top: Seahorse OCR traces showing reduced mitochondrial respiration in TGF-β treated endothelial cells (left: healthy untreated vs healthy treated with TGF; right: healthy untreated vs Systemic Sclerosis untreated). Dotted lines indicate the addition of oligomycin, FCCP, and rotenone. Data are presented as mean ± SEM. Bottom left: Western blot showing P-STING, total STING, total IRF3, and phosphorylated IRF3 (Ph-IRF3) in endothelial cells at baseline and after TGF-β stimulation. Beta-actin was used as a loading control. Bottom right: Luminescence assay quantifying cGAS-STING pathway activation at different time points following TGF-β treatment, confirming sustained activation at 12-72h.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Di Donato: None; **C. Bordes**: None; **C. Lalou**: None; **a. Depaire**: None; **J. Tchen**: None; **C. Lhuissier**: None; **d. Brisou**: None; **V. Sisirak**: None; **J. Garaude**: None; **C. Wasson**: None; **R. Ross**: None; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2.

Abstract Number: 1874

Neutrophil Extracellular Trap-Rich Systemic Sclerosis Plasma Promotes Microvascular Endothelial Cell Proliferation and Migration: Implications for Aberrant Angiogenesis

Wenying Liang[1], James St. Clair[1], Pei-Suen Tsou[2], John Varga[2], Jason S. Knight[2], Dinesh Khanna[2] and Ramadan Ali[3], [1]University of Michigan, Ann arbor, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan, Ann Arobr, MI

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (**SSc**, also known as scleroderma) is a systemic disease characterized by fibrosis, autoimmunity, and vasculopathy. Neutrophil extracellular traps (**NETs**) are web-like chromatin structures released by activated neutrophils. They contribute to the vascular pathology in multiple diseases, but their role in SSc remains poorly understood. We recently demonstrated elevated plasma NET levels in SSc patients with vascular complications compared to those without vascular complications. Here, we sought to determine the direct effects of NET-rich SSc plasma on microvascular endothelial cells (**MVECs**).

Methods: Human dermal MVECs were cultured in the presence of 2% pooled plasma from SSc patients with vascular complications exhibiting high circulating NET remnants (n=5), 2% pooled plasma from matched SSc patients without vascular complication exhibiting low circulating NET remnants (n=5), 2% pooled plasma from matched healthy controls (n=5), or purified NETs (0.1-0.5 μg/ml). Proliferation was quantified over 24 hours and calculated as the relative confluence change. Migration was evaluated via a scratch-wound assay over 24 hours and quantified by wound confluence (%).

Results: We first stimulated MVECs with different concentrations of purified NETs (0.1 μg/ml versus 0.5 μg/ml) for 24 hours. Compared with vehicle control, NETs (0.5 μg/ml) increased MVEC proliferation (1.4-fold change, P=0.0001) and migration (mean 52% vs. 23% wound confluence, P=0.0001) at 24 hours in a concentration-dependent manner (**Figure 1**). Next, we stimulated MVECs with 2% NET-rich SSc plasma compared with 2% NET-poor SSc plasma or 2% healthy control plasma. We found that NET-rich SSc plasma promoted MVECs proliferation (P=0.0003) and migration (P=0.0001) over 24 hours. In contrast, the effects of NET-poor SSc plasma on proliferation (P=0.986) and migration (P=0.729) were comparable to healthy control plasma (**Figure 2**). Notably, NET-targeting agents, such as anti-histone 4 and a neutrophil elastase inhibitor, significantly reduced MVEC proliferation and migration induced by NET-rich SSc plasma.

Conclusion: Our study demonstrates that SSc plasma containing high levels of NETs robustly stimulates MVEC proliferation and migration in vitro, and that NET-targeting agents can reverse these effects significantly. These data preliminarily identify NETs as mediators of abnormal angiogenesis contributing to the aberrant and dysfunctional characteristics of the SSc

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

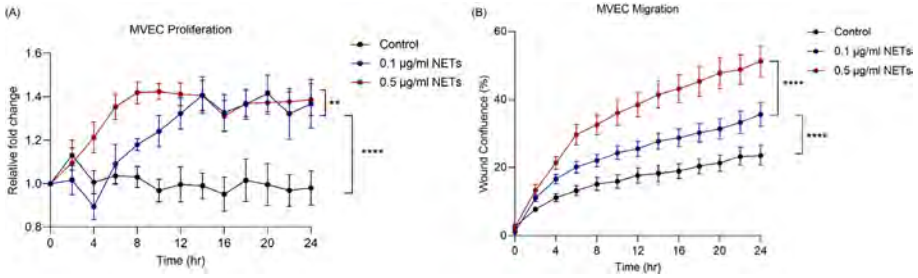


Figure 1: NETs increased MVECs proliferation and migration. MVECs were stimulated with NETs (0.1 or 0.5 μg/ml) or basic medium as a control for 24 hours. IncuCyte software was used to quantify (A) cell proliferation as the relative confluence change compared to time 0 hour and (B) cell migration by wound confluence (%). Data were represented as means ± sem. Two-way ANOVA test was applied; (**p < 0.01, ****p < 0.0001).

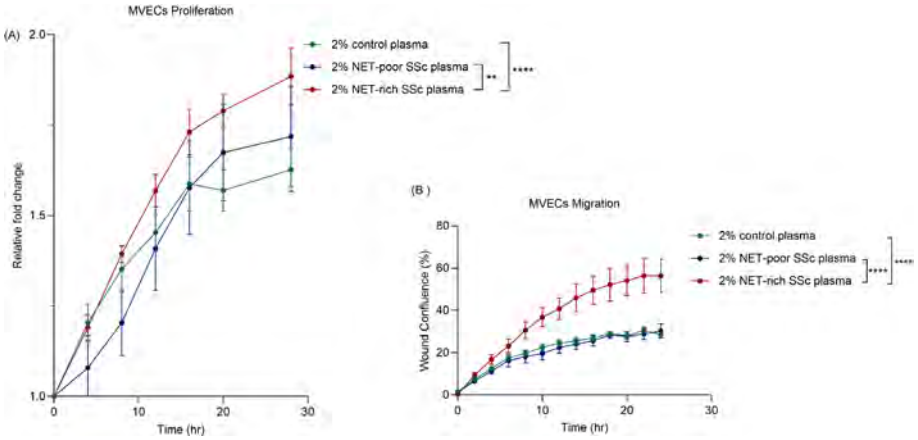


Figure 2: NET-rich SSc plasma increased MVECs proliferation and migration. MVECs were stimulated with 2% NET-rich SSc plasma, 2% NET-poor SSc plasma, 2% healthy control plasma for 24 hours. IncuCyte software was used to quantify (A) cell proliferation as the relative confluence change compared to time 0 hour and (B) cell migration by wound confluence (%). Data were represented as means ± sem with n=3 independent experiments. Two-way ANOVA test was applied; (**p < 0.01, ****p < 0.0001).

microvasculature. Targeting NET formation may represent a novel therapeutic avenue to restore vascular homeostasis and ameliorate microvascular complications in SSc.

Disclosure: W. Liang: None; **J. St. Clair**: None; **P. Tsou**: None; **J. Varga**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **R. Ali**: None.

Abstract Number: 1875

Fcγ-receptor activation by circulating immune complexes in autoimmunity and CD19.CAR-T cell therapy

Merle Freitag[1], Maren Claus[2], Philippe Kolb[3], Valeria Falcone[4], Ivana Andreeva[1], Norbert Blank[5], Hanns-Martin Lorenz[6], Georg Schett[7] and **Wolfgang Merkt**[8], [1]Uniklinik Heidelberg, Heidelberg, Germany, [2]IfADo, Leibniz Institute Dortmund, Dortmund, Germany, [3]INSTITUTE OF VIROLOGY Medical Center, Freiburg, Freiburg, Germany, [4]University Medical Center, Freiburg, Freiburg, Germany, [5]University Hospital Heidelberg, Heidelberg, Germany, [6]Universitätsklinikum Heidelberg, Heidelberg, Germany, [7]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [8]University Hospital Dösseldorf, Dösseldorf, Germany

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

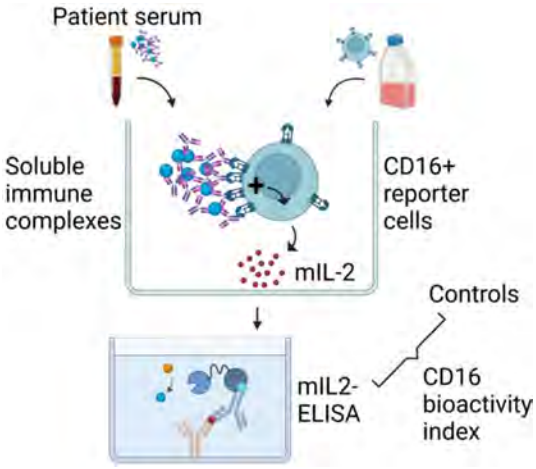
Session Date: Tuesday, October 28, 2025
Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The role of autoantibodies in systemic autoimmunity, such as connective tissue diseases (CTD), has been recently highlighted by the successful treatment with CD19-targeting CAR-T cells. Although many downstream effects of autoantibodies require immune complex formation as to activate low-affinity IgG/Fcγ-receptors (FcγRs), circulating immune complexes (cICs) have experienced far less attention in the last decade. In fact, clinical testing of cICs, and thus thorough investigation of this potential chain link between adaptive and innate immune mechanisms, was impeded by lacking reliable detection methods. We have recently overcome methodological limitations by introducing a novel reporter cell assay that directly measures the presence of cICs in untreated serum with high sensitivity via their functional engagement to single FcγRs.

Methods: Here, we used a comprehensive reporter cell panel to assess the presence of cICs in autoantibody-positive CTD patients (cross-section analysis) and in eight patients treated with CD19.CAR-T cells (longitudinal analysis).

Results: The bioactivity of cICs in the CTD cohort was highly significantly elevated compared to healthy individuals and patients with autoantibody-negative psoriatic arthritis. Analyses of individual diseases indicated that cICs were present in sera from all CTD, including systemic sclerosis (SSc) and primary Sjögren's syndrome (SjS). FcγR-activation of cICs was heterogeneous within disease entities and correlated with the extent of cutaneous and lung manifestations in SSc, indicating pronounced cIC-bioactivity in the more systemic disease forms. In patients treated with CD19.CAR-T cells, the bioactivity of cICs was significantly reduced.

Conclusion: In summary, our study closes a knowledge gap by proving the presence of FcγR-engaging cICs that can be associated with clinical parameters and treatment in systemic autoimmune diseases.



Graphical overview of the reporter cell model used to determine the bioactivity of circulating immune complexes in patient sera at Fc-receptors such as CD16. Sera are diluted in assay medium without other processing steps.

Disclosure: M. Freitag: None; **M. Claus**: None; **P. Kolb**: None; **V. Falcone**: None; **I. Andreeva**: None; **N. Blank**: None; **H. Lorenz**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **W. Merkt**: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, Evotec, 5, Glapagos, 12, support for congress travel, Kyverna, 6, Lilly, 12, support for congress travel.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1876

Targeting the NK cell checkpoint NKG2A promotes lung fibrosis resolution by enhancing immune clearance of senescent myofibroblasts

Wolfgang Merkt[1], Lea Rodon[2], Franca Sophie Deicher[3], Maren Claus[4], Rachel Lister[5], Hongwei Han[5], Yan Zhou[5], Zhengwang Sun[5], Arik Horne[6], Ayla Nadja Stuetz[7], Michael Kreuter[8], nicolas kahn[9], Marc Schneider[9], Simon Haas[10], Norbert Blank[11], Hanns-Martin Lorenz[12], Carsten Watzl[4], Daniel Hübschmann[13] and David Lagares[5], [1]University Hospital Dösseldorf, Dösseldorf, Germany, [2]University Hospital Heidelberg, Heidelberg, Hungary, [3]Uniklinik Düsseldorf, Düsseldorf, Germany, [4]IfADo, Leibniz Institute Dortmund, Dortmund, Germany, [5]Massachusetts General Hospital and Harvard Medical School, Boston, [6]Charite, Berlin, Berlin, [7]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University, Düsseldorf, Nordrhein-Westfalen, Germany, [8]Universitätsmedizin Mainz, Mainz, [9]Thoraxklinik, Heidelberg University, Heidelberg, Germany, [10]Charite, Berlin, Berlin, Germany, [11]University Hospital Heidelberg, Heidelberg, Germany, [12]Universitätsklinikum Heidelberg, Heidelberg, Germany, [13]Heidelberg University, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1855–1876) Systemic Sclerosis & Related Disorders – Basic Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: A key event driving pulmonary fibrosis in interstitial lung disease (ILD) is the accumulation of pathologic senescent myofibroblasts, thought to be promoted by insufficient clearance by exhausted NK cells. The aim of this study was to identify mechanisms of NK cell inhibition in pulmonary fibrosis with a focus on checkpoint receptors, which may represent novel targets for the treatment of age-related fibrotic disorders.

Methods: Transcriptomic datasets and spectral flow cytometry were applied to characterize pulmonary NK cells. The bleomycin-induced lung fibrosis model and in vitro cultures were used to investigate the effect of NKG2A-inhibition on lung fibrosis and the elimination of senescent primary human lung fibroblasts.

Results: Proteomics and transcriptomics analyses revealed that NKG2A exhibits the highest and most selective expression among NK checkpoints in human ILD. In preclinical models, blockade of NKG2A promoted resolution of established pulmonary fibrosis, as demonstrated by reduced collagen content and decreased number of senescent myofibroblasts. Importantly, we showed translational potential of this therapeutic approach to human disease by showing that NKG2A blockade with the checkpoint inhibitor monalizumab unleashed patient-derived NK cell activity and significantly increased lysis of

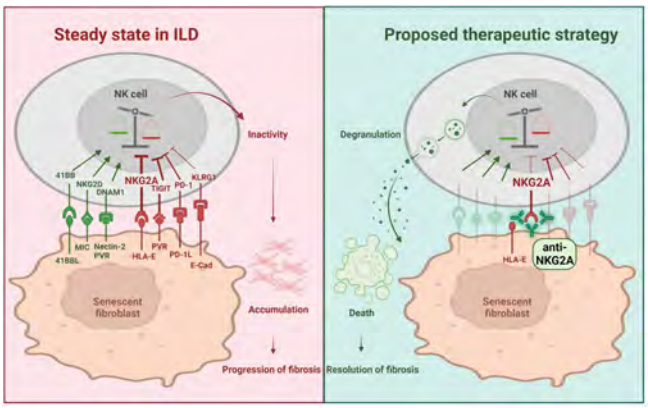


Image 1: graphical abstract

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

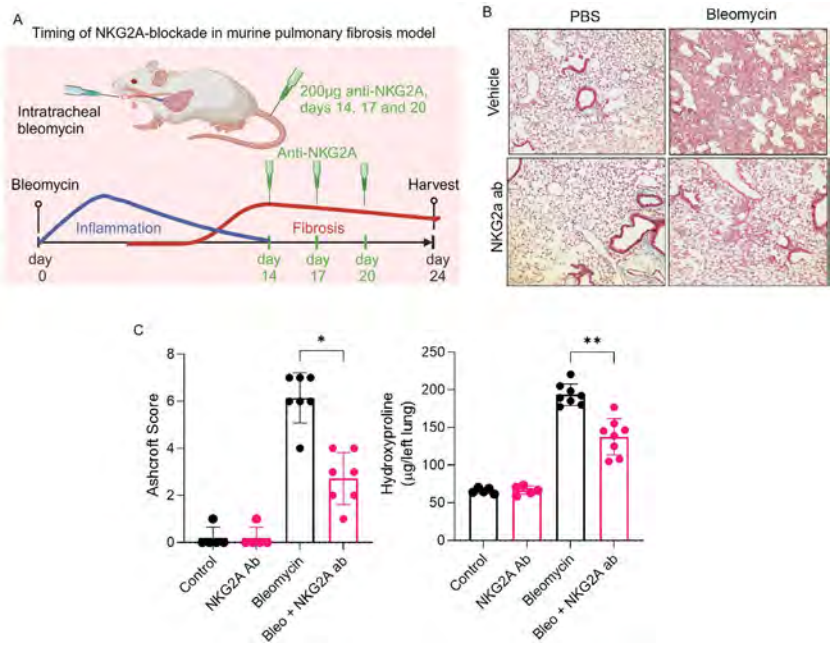


Image 2: NKG2A blockade reduces lung fibrosis. A Schematic representation of the bleomycin mouse model and the timing of anti-NKG2A dosing. B Example results from histological analysis. C statistical summary of the experimental series; Ashcroft score (left) and hydroxyproline content were used as proxies of pulmonary fibrosis.

human senescent myofibroblasts in vitro. Of note, monalizumab did not activate NK cells in absence of senescent myofibroblasts, ensuring selective killing and lowering the risk of unwanted generalized NK cell activation.

Conclusion: In summary, NKG2A checkpoint blockade selectively enhances elimination of senescent myofibroblasts by NK cells and promotes the resolution of fibrosis in preclinical models.

Disclosure: W. Merkt: Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 5, Evotec, 5, Glapagos, 12, support for congress travel, Kyverna, 6, Lilly, 12, support for congress travel; **L. Rodon**: None; **F. Deicher**: None; **M. Claus**: None; **R. Lister**: None; **H. Han**: None; **Y. Zhou**: None; **Z. Sun**: None; **A. Horne**: None; **A. Stuetz**: None; **M. Kreuter**: None; **n. kahn**: None; **M. Schneider**: None; **S. Haas**: None; **N. Blank**: None; **H. Lorenz**: None; **C. Watzl**: None; **D. Hübschmann**: None; **D. Lagares**: Mediar Therapeutics, 1, 3, 8, 10, Zenon Biotech, 1, 3, 8.

Abstract Number: 1877

Demographics and trends of Inflammatory Arthritis-Related Mortality in the United States, 1999–2019

Aishwarya Sudheer[1], Ishan Jani[2], Sarath Lal Mannumbeth Renjithlal[2] and Qi Wang[3], [1]Saint Vincent Hospital, Worcester, MA, [2]Rochester General Hospital, Rochester, NY, [3]Metrohealth System/Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1877–1913) Epidemiology & Public Health Poster III

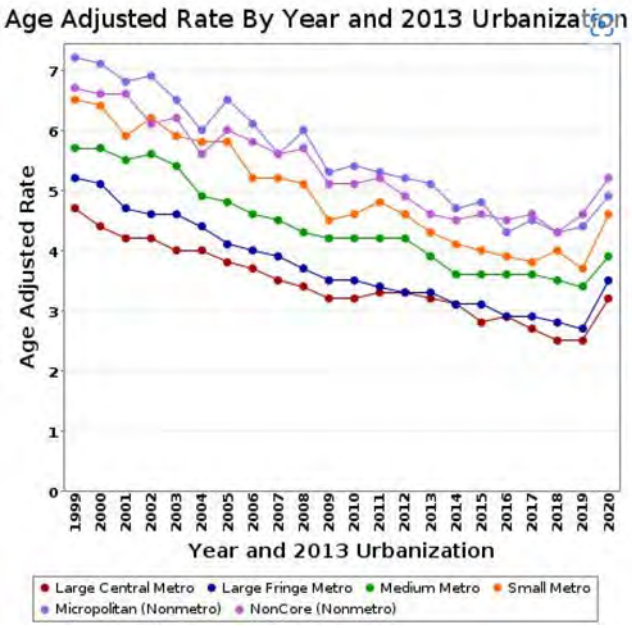
Session Type: Poster Session C

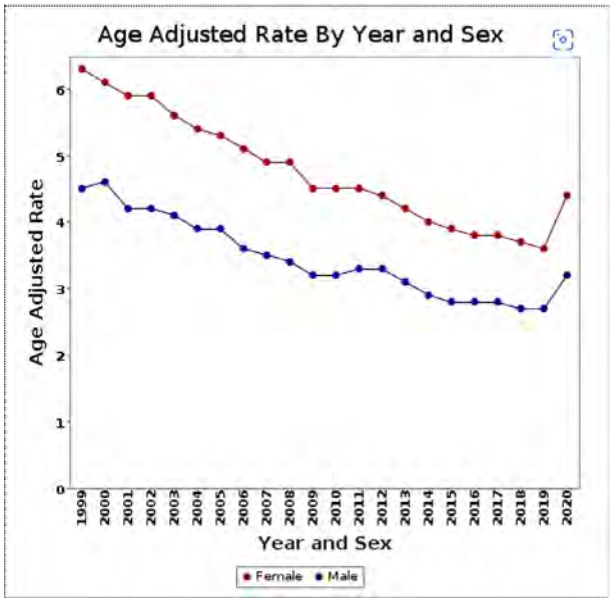
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

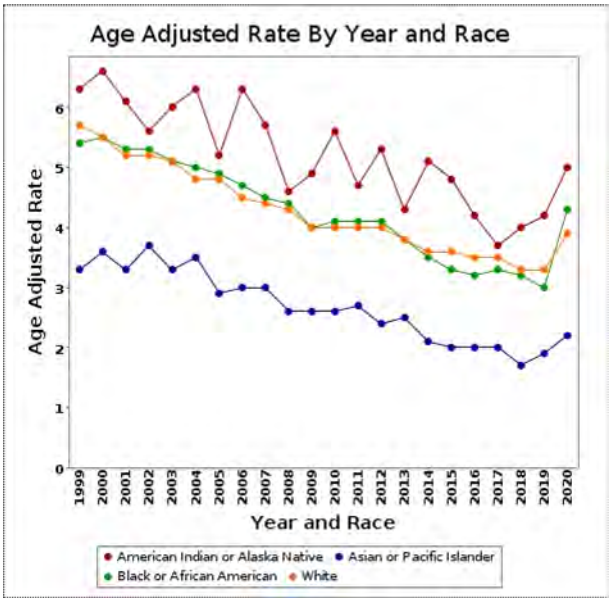
Background/Purpose: The study aims to evaluate the racial, sex-related and urbanization-related trends of deaths in patients with inflammatory polyarthropathies in the United States between 1999 and 2019

Methods: A retrospective analysis was conducted using the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC-WONDER) database. Deaths attributed to inflammatory polyarthritis were identified using ICD-10 codes M05–M13. Age-adjusted mortality rates (AAMRs) per 1,000,000 individuals were calculated, and temporal trends were analyzed using Joinpoint regression to estimate annual percentage changes (APCs) and 95% confidence intervals (CIs). Mortality trends were stratified by sex, race/ethnicity, and urbanization level.





23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Results: Between 1999 and 2019, a total of 288,661 deaths were associated with inflammatory polyarthropathies. The overall AAMR declined from 5.6 (95% CI: 5.4–5.6) in 1999 to 3.2 (95% CI: 3.2–3.3) in 2019. Women had consistently higher AAMRs than men throughout the study period. Among females, the AAMR decreased from 6.3 (95% CI: 6.2–6.4) to 3.6 (95% CI: 3.5–3.7), with an overall rate of 4.7 (95% CI: 4.7–4.7). In comparison, the AAMR in males declined from 4.5 (95% CI: 4.4–4.7) to 2.7 (95% CI: 2.6–2.8), with an overall rate of 3.3 (95% CI: 3.3–3.4).

Racial disparities were evident, with the highest AAMR observed among American Indian/Alaska Native populations at 5.0 (95% CI: 4.7–5.2), followed by White individuals at 4.2 (95% CI: 4.2–4.2), and Black individuals at 4.1 (95% CI: 4.1–4.2).

Stratification by urbanization revealed higher mortality rates in rural non-metro areas (AAMR 5.3, 95% CI: 5.3–5.4) compared to large metropolitan areas (AAMR 3.4, 95% CI: 3.4–3.4).

Conclusion: In the United States, there has been a general reduction in mortality associated with inflammatory polyarthritis over the last two decades. Early diagnosis and improvement in treatment modalities could be the reason for this trend. Further studies to evaluate role of access to rheumatology care needs to be investigated as a cause for worse mortality rates in rural areas and specific ethnicities.

Disclosure: A. Sudheer: None; **I. Jani**: None; **S. Mannumbeth Renjithlal**: None; **Q. Wang**: None.

Abstract Number: 1878

Customized Therapy for SLE: How Disease Severity Influences the Use of Corticosteroids and Biologics in Patients with SLE in the Lupus Federated Data Network (LupusNet) and a US Claims Database

Ashley Orillion[1], Federico Zazzetti[2], Anna Sheahan[3], Clair Blacketer[1], Michel van Speybroeck[4], Sarah Gasman[1], Reyhan Sonmez[5], Erika Noss[1], Manuel Ugarte-Gil[6], Rocío Gamboa-Cárdenas[7], Víctor Pimentel-Quiroz[8], Kaleb Michaud[9], Patti Katz[10], Rangi Kandane-Rathnayake[11], Eric Morand[12], Worawit Louthrenoo[13], Alberta Hoi[14], Yi-Hsing Chen[15], Jiacai Cho[16], Laniyati Hamijoyo[17], Shue Fen Luo[18], Sandra Navarra[19], Mandana Nikpour[20], José María Pego-Reigosa[21], Iñigo

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rúa-Figueroa[22], Zulema Plaza[23], María Galindo-Izquierdo[24], Julia Martínez Barrio[25], Jaime Calvo[26], Antonio Fernández-Nebro[27], Raúl Menor Almagro[28], EVA GLORIA TOMERO MURIEL[29], Javier Narváez[30] and Chetan S. Karyekar[31], [1]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [2]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [3]Johnson & Johnson, Horsham, PA, USA, Horhsam, PA, [4]Johnson & Johnson, Beerse, Belgium, Beerse, Belgium, [5]Capgemini Consulting, Zurich, Switzerland, Zurich, Switzerland, [6]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [7]Universidad Científica del Sur, Lima, Peru, [8]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Perú; Rheumatology Department, Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Perú, Lima, Peru, [9]University of Nebraska Medical Center, Omaha, NE, [10]UCSF, San Rafael, CA, [11]Center for Inflammatory Diseases, Monash University, Clayton, Victoria, Australia, [12]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [13]Chiang Mai University Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai, Thailand, Chiang Mai, Thailand, [14]Centre for Inflammatory Diseases, Monash University and Department of Rheumatology, Monash Health, Clayton, Victoria, Australia, [15]Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Taichung, Taiwan, Taichung, Taiwan (Republic of China), [16]National University Hospital, Rheumatology Division, Department of Medicine, Singapore, Singapore, Singapore, Singapore, [17]Padjadjaran University/Hasan Sadikin General Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Bandung, Indonesia, Badung, Indonesia, [18]Chang Gung Memorial Hospital, Chang Gung University, Department of Rheumatology, Allergy and Immunology, Taipei, Taiwan, Taoyuan, Taiwan (Republic of China), [19]University of Santo Tomas, Manila, Philippines, [20]University of Sydney, School of Public Health, Faculty of Medicine and Health, Sydney, New South Wales, Australia; St Vincent's Hospital Melbourne, Department of Rheumatology, Fitzroy, Victoria, Australia, Melbourne, Victoria, Australia, [21]Department of Rheumatology, University Hospital of Vigo, Vigo, Spain; IRIDIS Group (Investigation in Rheumatology and Immune-Diseases), Galicia Sur Health Research Institute, Vigo, Spain, [22]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [23]Research Unit, Spanish Society of Rheumatology, Madrid, Spain, Madrid, Spain, [24]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Madrid, Spain, [25]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [26]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain, [27]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [28]Department of Rheumatology, Hospital de Jerez, Spain, Puerto De Santa María, Spain, [29]Hospital Universitario de la Princesa, Madrid, Spain, [30]Hospital Universitario de Bellvitge, Barcelona, Spain, [31]Johnson & Johnson, Spring House, PA, USA, Spring House

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The management of SLE varies worldwide. Current SLE treatment goals focus on preventing flares, controlling disease activity, and preventing organ damage accrual. LupusNet is the largest federated data network in SLE that combines and harmonizes data from 5 existing registries to enable greater data consistency and enhance understanding of global clinical presentations and outcomes of SLE. This study assessed treatment patterns for patients with SLE, categorized by disease severity, from LupusNet and a US claims database.

Methods: Data from 3 of 5 SLE registries in LupusNet, APLC (Asia Pacific), RELESSER (Europe), and Almenara (South America), were analyzed from 2012 to 2024, using a privacy-preserving federated data network approach where only aggregated results were shared. Additionally, data from the US Merative MarketScan® Commercial Claims and Encounters (CCAE) Database from 2019 to 2024 were included in the analysis. In LupusNet, data from patients with ≥3 years of follow-up and ≥3 follow-up visits were collected and stratified into mild, moderate, or severe disease based on a SLEDAI score at year 3 follow-up visit (**Table 1**). In the US claims database, data from patients who were diagnosed with SLE were stratified by mild, moderate, or severe disease based on documented symptoms and clinical features (**Table 1**). Treatment exposures (ie, glucocorticoids, antimalarials, immunosuppressants, biologic therapies, and other immunosuppressants/immunomodulators) were assessed over follow-up.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: LupusNet included 3857 eligible patients: 3070 with mild disease, 637 with moderate disease, and 150 with severe disease. US claims data included 49,350 eligible patients: 23,461 with mild disease, 16,172 with moderate disease, and 9717 with severe disease. Glucocorticoid use was widespread across all disease severity levels: 63%-65% of patients with mild disease, 76%-84% with moderate disease, and 89%-95% with severe disease received glucocorticoids in both

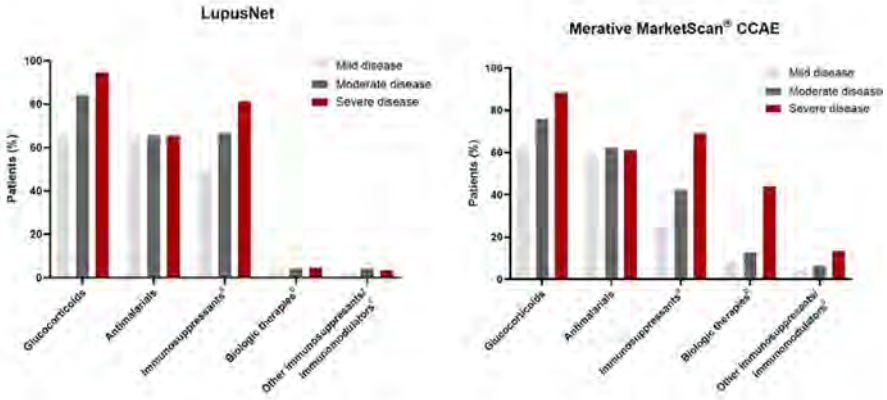
Table 1. Classification of disease severity in patients with SLE from LupusNet and the Merative MarketScan® CCAE Database

Definition	LupusNet Classification	Merative MarketScan® CCAE Database Classification[1]
Mild disease	SLEDAI score <6 at year 3 follow-up visit	Absence of moderate and severe SLE symptoms, and no record of rituximab or cyclophosphamide treatment
Moderate disease	SLEDAI score from 6 to <11 at year 3 follow-up visit	Record of scleritis, hemolytic anemia, myelopathy, avascular necrosis, demyelinating disease, pancreatitis, polyradiculoneuropathy, chorioretinitis, myocarditis, pleural effusion, pleurisy, retinal vasculitis, seizure, uveitis, mononeuropathy, episcleritis, and/or nephritis
Severe disease	SLEDAI score ≥11 at year 3 follow-up visit	Record of psychosis, aortitis, end-stage renal disease, stroke, optic neuritis, pulmonary hemorrhage, intestinal obstruction, delirium, thrombosis, and/or cranial neuropathy

CCAE, Commercial Claims and Encounters; LupusNet, Lupus federated data Network.

1. Garris C, et al. *J Med Econ.* 2013;16(3):667-77.

Figure 1. Distribution of Treatment Use by Disease Severity from LupusNet and Merative MarketScan® CCAE Database.



[a]Immunosuppressants include azathioprine, chlorambucil, cyclophosphamide, cyclosporine, leflunomide, methotrexate, mycophenolate, mycophenolate mofetil, mycophenolic acid, and voclosporin.
[b]Biologic therapies include anifrolumab, belimumab, and rituximab.
[c]Other immunosuppressants/immunomodulators include penicillamine, sulfasalazines, and tacrolimus.

CCAE, Commercial Claims and Encounters; LupusNet, Lupus federated data Network.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

LupusNet and US claims data (**Figure 1**). Antimalarials were also frequently prescribed in 58%-66% of patients, regardless of disease severity. In contrast, use of immunosuppressants varied with disease severity: 25%-50% of patients with mild disease, 43%-67% with moderate disease, and 69%-81% with severe disease received immunosuppressants. Biologic therapies and other immunosuppressants/immunomodulators were utilized less frequently across all disease severity levels in LupusNet (4% and 2%-4%, respectively), while the use of these therapies increased with disease severity in US claims data (8%-44% and 4%-13%, respectively).

Conclusion: This analysis of patient data from LupusNet registries and the US claims database revealed that a considerable number of patients with active, severe SLE across geographic locations were not receiving immunosuppressants or biologic therapies. This suggests a heavy dependence on glucocorticoids to control disease activity and a potential underutilization of steroid-sparing therapies. Additional research is needed to explore long-term treatment trends and barriers to accessing treatments in patients with SLE.

Disclosure: A. Orillion: Johnson & Johnson, 3, 11; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Sheahan**: Johnson & Johnson, 3, 12, may hold stock options; **C. Blacketer**: Johnson & Johnson, 3, 12, may hold stock options; **M. van Speybroeck**: Johnson & Johnson, 3, 12, may hold stock options; **S. Gasman**: Johnson & Johnson, 3, 12, may hold stock options; **R. Sonmez**: Johnson & Johnson, 2, 12, may hold stock options; **E. Noss**: Johnson & Johnson, 3, 12, may hold stock options; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: None; **K. Michaud**: None; **P. Katz**: None; **R. Kandane-Rathnayake**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKline (GSK), 5, Novartis, 5; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **W. Louthrenoo**: None; **A. Hoi**: AstraZeneca, 1, 5, 12, contract research, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, GlaxoSmithKline (GSK), 1, Johnson & Johnson, 1, Merck/MSD, 12, contract research, UCB, 5; **Y. Chen**: Abbvie, 12,, 2, 6, Agnitio Science Technology, 2, 6, Astellas, 12,, 2, 6, AstraZeneca, 12,, 2, 6, Biogen, 12,, BMS, 12,, 2, 6, Boehringer-Ingelheim, 12,, Celldex, 12,, CSL Behring, 2, 6, Eisai, 2, 6, Gilead, 12,, 2, 6, GSK, 12,, 2, 6, Guigai, 12,, 2, 6, Inova Diagnostics, 2, 5, Johnson & Johnson, 12,, 2, 6, Lilly, 2, 6, Medigen Vaccine Biologics, 12,, MSD, 12,, 2, 6, Novartis, 2, 6, Pfizer, 12,, 2, 6, Roche, 12,, Sanofi, 12,, 2, 6, Taichung Veterans General Hospital, 12,, Taiwan Department of Health, 12,, Taiwan Ministry of Science and Technology, 12,, Thermo Fisher, 2, 6, UCB, 12,, 2, 6, United Biopharma, 2, 6; **J. Cho**: None; **L. Hamijoyo**: None; **S. Luo**: None; **S. Navarra**: Astellas, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Biogen, 2, 12, Independent Data Monitoring Committee, Viatris (Idorsia), 2, 6; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 2, 6; **J. Pego-Reigosa**: AstraZeneca, 1, 5, 6, GlaxoSmithKline (GSK), 1, 5, 6, Otsuka, 1, 6; **I. Rúa-Figueroa**: None; **Z. Plaza**: None; **M. Galindo-Izquierdo**: None; **J. Martínez Barrio**: None; **J. Calvo**: None; **A. Fernández-Nebro**: Argenx, 5, AstraZeneca, 2, 5, 6, Chemo, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Gebro Pharma, 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 5, Merck Serono, 5, MSD, 5, Novartis, 2, 5, 6, Takeda, 5, UCB, 5; **R. Menor Almagro**: None; **E. TOMERO MURIEL**: None; **J. Narváez**: None; **C. Karyekar**: Johnson & Johnson, 12, Former employee and may hold stock options.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1879

Infections in Hospitalized Patients With and Without Psoriatic Arthritis (2016–2021): A National Inpatient Sample Study

Ayema Haque, Ana Salas, Bruna Diniz, Harshank Patel and Philip Kroth, Western Michigan University School of Medicine, Kalamazoo, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic, immune-mediated inflammatory disorder affecting up to 30% of psoriasis patients and is associated with increased infection risk. This study evaluates the incidence, trends, and outcomes of common infections during PsA hospitalizations, including healthcare utilization and inpatient mortality.

Methods: Discharge data from the 2016–2021 National Inpatient Sample (NIS), an all-payer database representing a 20% stratified sample of U.S. hospitalizations, were analyzed. Hospitalizations with predefined clinical infections were identified and categorized by the presence (cohort 1) or absence of PsA (cohort 2). Descriptive statistics included counts and percentages for categorical variables, and medians with interquartile ranges for numerical variables. Trends were assessed using Cochran-Armitage tests. Rao-Scott chi-square tests evaluated associations, with odds ratios (95% confidence intervals) reported. Statistical significance was set at $p< 0.05$, with Bonferroni correction applied when appropriate. Analyses followed NIS guidelines and were conducted using SAS version 9.4.

Results: From 2016 to 2021, there were 8,598,744 (99.8%) hospitalizations with infections identified without PsA (cohort 1) and 14,683 (0.17%) with PsA (cohort 2). Cohort 2 was younger (median age 63.9 vs 67.6 years) and more likely to be female (OR 1.28; 95% CI 1.24-1.33; $p < 0.0001$), and Caucasian (OR 5.96; 95% CI 5.39-6.58; $p < 0.0001$). From 2016 to 2021, opportunistic infections (OIs) and urinary tract infections (UTIs) decreased significantly in cohort 1 ($p < 0.0001$), while skin and soft tissue infections (SSTIs), pneumonia, and sepsis increased significantly ($p < 0.0001$) (see figure 1). In cohort 2, OIs decreased significantly ($p < 0.0001$), pneumonia and sepsis increased significantly ($p < 0.0001$), and no significant changes were observed for SSTIs ($p = 0.7$) or UTIs ($p = 0.07$) (see figure 2). Cohort 2 had significantly increased odds of developing OI (OR 1.60; 95% CI, 1.50–1.70; $p < 0.0001$), SSTI (OR 1.4; 95% CI, 1.3–1.4; $p < 0.0001$), and sepsis (OR 1.1; 95% CI, 1.1–1.2; $p < 0.0001$), while having significantly lower odds of UTI (OR 0.8; 95% CI, 0.7–0.8; $p < 0.0001$)

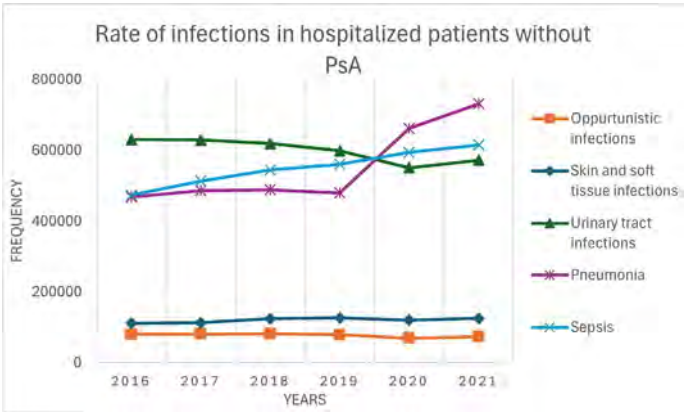


Figure 1: Rate of infections in hospitalized patients without PsA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

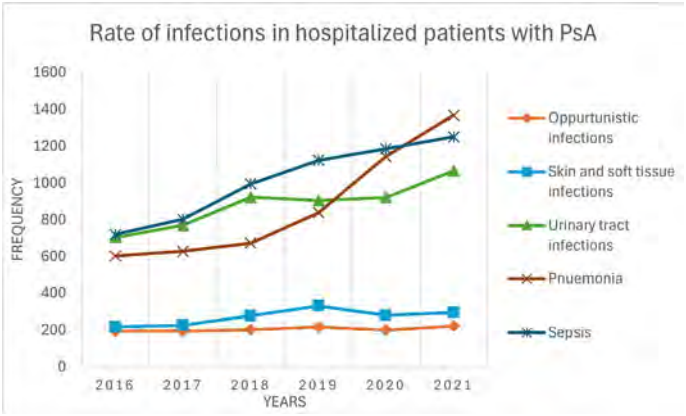


Figure 2: Rate of infections in hospitalized patients with PsA

and pneumonia (OR 0.8; 95% CI, 0.8–0.9; $p < 0.0001$). No significant associations were found between cohort 2 and alcohol abuse, drug abuse, and diabetes ($p > 0.05$). In cohort 2, severe renal failure was less common (OR 0.58; 95% CI, 0.54–0.63; $p < 0.0001$), while both mild (OR 1.60; 95% CI, 1.51–1.68) and severe liver disease (OR 1.38; 95% CI, 1.25–1.51) were more prevalent ($p < 0.0001$). Inpatient mortality was lower in cohort 2 (OR 0.66; 95% CI, 0.60–0.70; $p < 0.0001$). There was no significant difference in hospital charges (median charges $42407 vs $42410) and length of stay (median 4.25 vs 4.27) between the cohorts ($p > 0.05$).

Conclusion: Hospitalized PsA patients had higher odds of opportunistic infections, SSTIs, and sepsis, but lower odds of pneumonia and UTIs compared to those without PsA. Despite these differences, length of stay and hospital charges were similar, while inpatient mortality was lower in the PsA group. These findings highlight a distinct infection profile in PsA and emphasize the need for targeted infection management.

Disclosure: A. Haque: None; **A. Salas**: None; **B. Diniz**: None; **H. Patel**: None; **P. Kroth**: None.

Abstract Number: 1880

Rheumatoid Arthritis Mortality in the U.S. (1999–2020): A Decline in Rates, But Not in Disparities

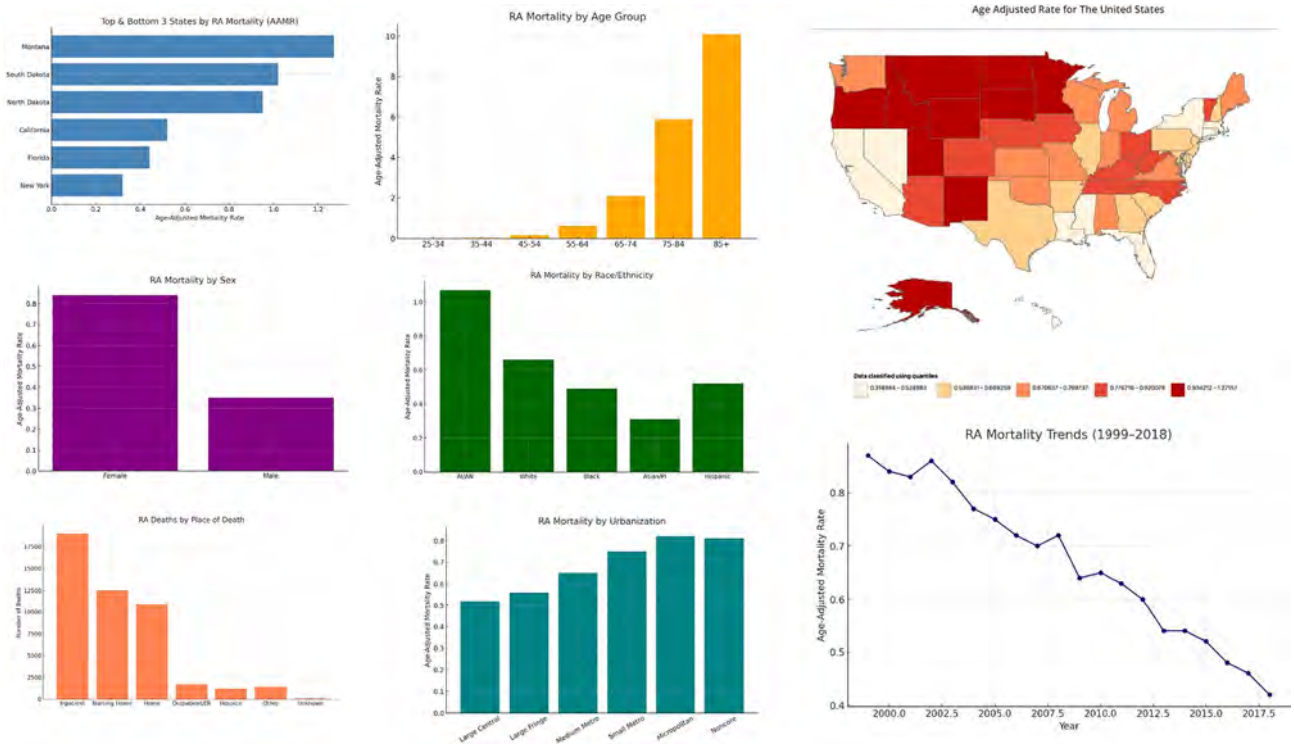
Aziz-ur-Rahman Khalid[1], Ghassan Makhoul[2], Hasan Munshi[2], Islam Rajab[2], Emmanuel Olumuyide[3], MD Walid Akram Hussain[2], Aqsa Sorathia[2], Elvira Assaf[2], Amer Al Badawy[2], John Salama[2] and Robert Lahita[4], [1]St. Joseph's University Medical Center, wayne, [2]St. Josephs University Medical Center, Paterson, [3]Advocate Illinois Masonic Medical Center, Chicago, [4]St. Josephs University Medical Center, Wayne, NJ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease associated with increased morbidity and mortality. While treatments have evolved, national trends and sociodemographic disparities in RA-related mortality are poorly characterized. This study evaluates patterns in RA mortality over two decades, focusing on age, sex, race, geography, and place of death.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Graphs showing state, demographic, gender, race, age groups, place of death, and yearly mortality from Rheumatoid Arthritis

Methods: Mortality data for RA (ICD-10 code M06.9) from 1999–2020 were obtained from the CDC WONDER database. Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated using census-adjusted estimates. Data were stratified by year, state, age group (10-year intervals), sex, race/ethnicity, Hispanic origin, urbanization level (2013 classification), and place of death.

Results: Between 1999 and 2020, there were 47,075 deaths related to rheumatoid arthritis (RA) in the United States. The age-adjusted mortality rate (AAMR) declined significantly from 0.87 per 100,000 in 1999 to 0.42 in 2020, representing a 51.7% decrease. Women experienced 2.4 times higher mortality than men, with an AAMR of 0.84 compared to 0.35. Mortality increased steeply with age, peaking at 10.1 per 100,000 among those aged 85 and older. By race and ethnicity, American Indian/Alaska Native individuals had the highest AAMR (1.07), followed by White (0.66), Black (0.49), and Asian/Pacific Islander (0.31); Hispanic individuals had an AAMR of 0.52. Urbanization patterns revealed the lowest AAMR in large central metro areas (0.52) and the highest in noncore rural areas (0.81). Geographic variation showed state AAMRs ranging from 0.52 in California to 1.27 in Montana, with elevated rates in older, less urbanized states. In terms of place of death, most occurred in inpatient settings (40.4%) or nursing homes (26.6%), followed by the decedent's home (23.2%), hospice facilities (2.6%), outpatient/ER (3.6%), and other locations.

Conclusion: RA-related mortality in the U.S. declined significantly from 1999 to 2020. However, persistent disparities by age, sex, race, urbanization, and place of death underscore the need for targeted public health and clinical strategies to improve equity in RA outcomes and end-of-life care.

Disclosure: A. Khalid: None; **G. Makhoul**: None; **H. Munshi**: None; **I. Rajab**: None; **E. Olumuyide**: None; **M. Hussain**: None; **A. Sorathia**: None; **E. Assaf**: None; **A. Al Badawy**: None; **J. Salama**: None; **R. Lahita**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1881

Silent Impact: Two Decades of Sjögren's Syndrome Mortality in the United States

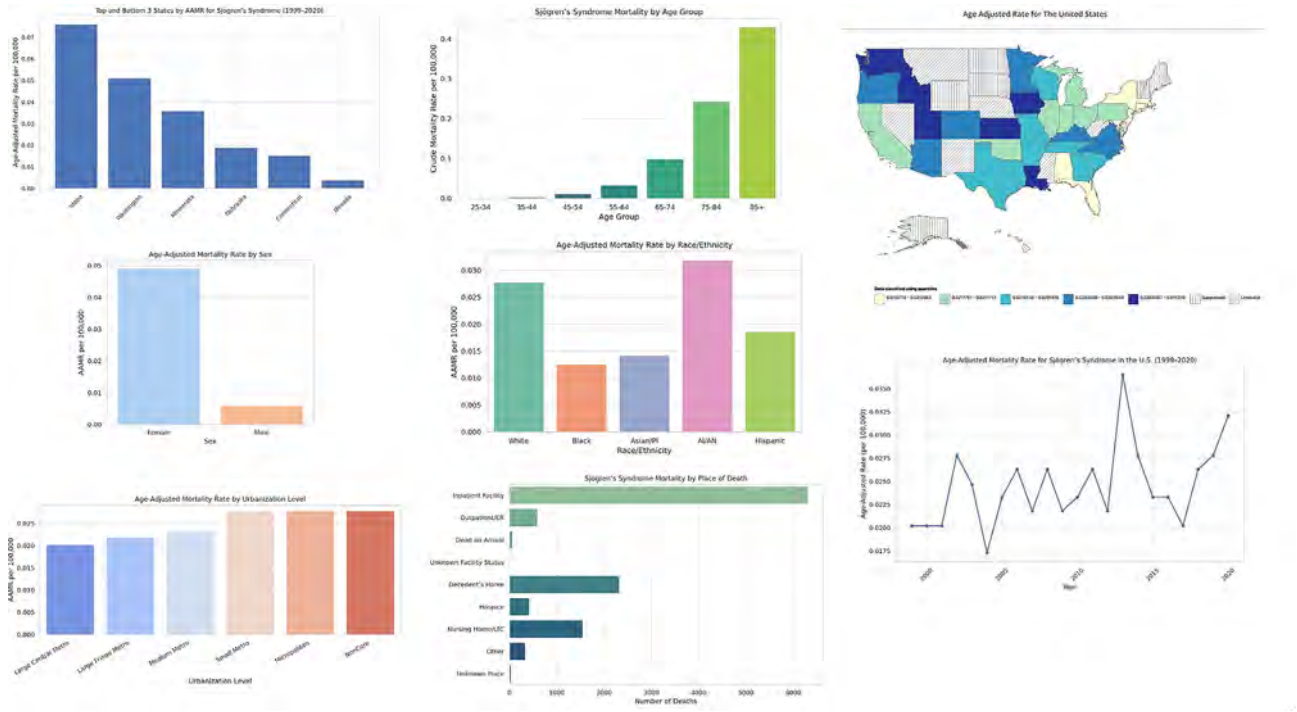
Aziz-ur-Rahman Khalid[1], Ghassan Makhoul[2], Hasan Munshi[2], Islam Rajab[2], MD Walid Akram Hussain[2], Reshma John[2], Elvira Assaf[2], Amer Al Badawy[2], Barbare Khatiashvili[2], Rouba Isshak[2], John Salama[2], Ibrahim Sabah[2] and Robert Lahita[3], [1]St. Joseph's University Medical Center, wayne, [2]St. Josephs University Medical Center, Paterson, [3]St. Josephs University Medical Center, Wayne, NJ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's syndrome is a chronic autoimmune disease characterized by lymphocytic infiltration of exocrine glands with potential systemic involvement. Despite its known complications, population-level mortality trends in Sjögren's syndrome remain poorly characterized. This study evaluates national mortality trends and sociodemographic disparities in Sjögren's syndrome-related deaths in the United States from 1999 to 2020.

Methods: We used the CDC WONDER Multiple Cause of Death database to identify decedents with ICD-10 code M35.0 (Sjögren's syndrome) listed as a cause of death from 1999 to 2020. Age-adjusted mortality rates (AAMRs) were calculated per 100,000 population using the direct method and the 2000 U.S. standard population. Mortality trends were analyzed over time and stratified by sex, age, race/ethnicity, urbanization, place of death, and U.S. state of residence.



Graphs showing state, urbanization, gender, race, place of death, age and year.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 2,149 Sjögren's syndrome-related deaths occurred during the study period. The AAMR increased by 57.5%, from 0.0202 in 1999 to 0.0321 in 2020. Females accounted for 88.2% of deaths and had an AAMR over eight times higher than males (0.049 vs. 0.006). Mortality increased markedly with age, from 0.01 per 100,000 in adults aged 45–54 to 0.43 in those aged ≥85 years. By race/ethnicity, White individuals had the highest AAMR (0.028), followed by American Indian/Alaska Native (0.032), Black (0.013), Asian/Pacific Islander (0.014), and Hispanic individuals (0.019). AAMRs rose with increasing rurality, ranging from 0.0202 in large central metro areas to 0.0278 in noncore rural regions. State-level AAMRs varied widely, from 0.015 in Connecticut to 0.051 in Washington. The majority of deaths occurred in inpatient hospital settings (42.3%) and nursing homes or long-term care facilities (26.6%), followed by the decedent's home (23.9%), hospice facilities (1.9%), and emergency/outpatient departments (2.6%).

Conclusion: Mortality from Sjögren's syndrome in the United States has increased over the past two decades, with a disproportionate burden among elderly women, rural populations, and White individuals. These findings underscore the need for improved disease recognition, timely systemic management, and targeted interventions to address healthcare disparities in Sjögren's syndrome.

Disclosure: A. Khalid: None; **G. Makhoul**: None; **H. Munshi**: None; **I. Rajab**: None; **M. Hussain**: None; **R. John**: None; **E. Assaf**: None; **A. Al Badawy**: None; **B. Khatiashvili**: None; **R. Isshak**: None; **J. Salama**: None; **I. Sabah**: None; **R. Lahita**: None.

Abstract Number: 1882

Vessels Under Fire: National Mortality Trends in Systemic Vasculitides in the United States, 1999–2020

Aziz-ur-Rahman Khalid[1], Ghassan Makhoul[2], Hasan Munshi[2], Islam Rajab[2], Emmanuel Olumuyide[3], MD Walid Akram Hussain[2], Ahmed Huzien[2] and Robert Lahita[4], [1]St. Joseph's University Medical Center, wayne, [2]St. Josephs University Medical Center, Paterson, [3]Advocate Illinois Masonic Medical Center, Chicago, [4]St. Josephs University Medical Center, Wayne, NJ

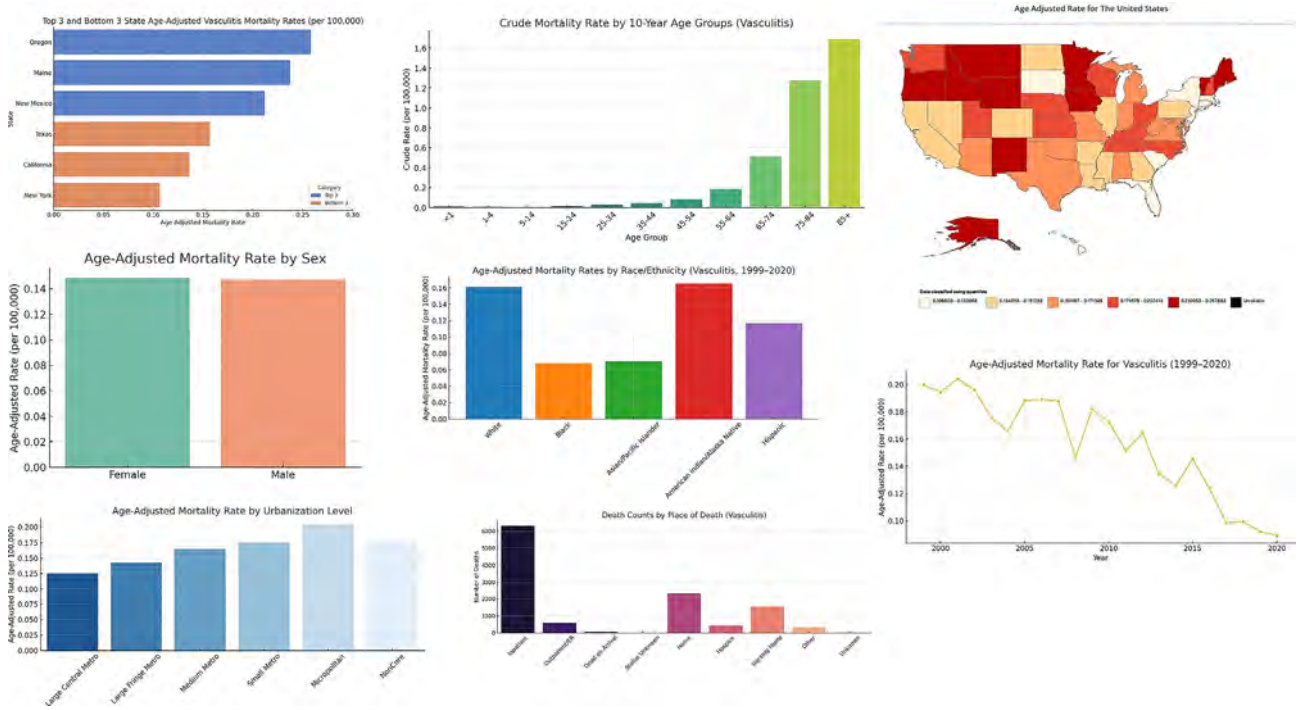
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic vasculitides are rare but potentially life-threatening inflammatory disorders affecting blood vessels. Despite therapeutic advances, national mortality trends across vasculitis subtypes remain poorly defined. We analyzed U.S. mortality trends from 1999–2020 using CDC WONDER, focusing on 10 vasculitis-related ICD-10 codes.

Methods: CDC WONDER Multiple Cause of Death data (1999–2020) were queried using ICD-10 codes: D69.0 (Allergic purpura), M30.0 (Polyarteritis nodosa), M30.1 (Churg-Strauss), M30.3 (Kawasaki disease), M31.3 (Wegener granulomatosis), M31.4 (Takayasu arteritis), M31.5 (Giant cell arteritis with polymyalgia rheumatica), M31.6 (Other giant cell arteritis), M31.7 (Microscopic polyangiitis), and M35.2 (Behçet disease). Age-adjusted mortality rates (AAMRs) were calculated using the 2000 U.S. standard population. Analyses were stratified by age, sex, race/ethnicity, urbanization, state, and place of death.

Results: A total of **11,602 vasculitis-related deaths** occurred from 1999–2020. The **overall AAMR was 0.15 per 100,000**, declining from **0.20 in 1999 to 0.09 in 2020**. The **highest age-specific mortality** occurred in adults ≥85 years (**AAMR: 1.69**), with the **lowest** in children 5–14 years (**AAMR: 0.004**). Females accounted for **56% of deaths**, with AAMRs

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Graphs showing state, urbanization, gender, race, age, and year mortality from Vasculitis

nearly equal between sexes (**0.149 vs. 0.147**). By race, **American Indian/Alaska Native (0.165)** and **White (0.161)** individuals had the highest AAMRs, while **Black (0.068)** and **Asian/Pacific Islander (0.070)** individuals had the lowest. **Hispanic individuals** had an AAMR of **0.117**. The highest mortality occurred in **micropolitan** (0.205) and **noncore rural areas** (0.178). Regarding place of death, **54.3% occurred in inpatient medical facilities**, followed by **20.0% at home** and **13.3% in nursing homes**.

Conclusion: Vasculitis-related mortality in the U.S. has declined substantially since 1999. However, disparities persist among older adults, rural populations, and American Indian/Alaska Native individuals. These findings highlight the need for improved access to rheumatologic care and early detection strategies in high-risk populations.

Disclosure: A. Khalid: None; **G. Makhoul**: None; **H. Munshi**: None; **I. Rajab**: None; **E. Olumuyide**: None; **M. Hussain**: None; **A. Huzien**: None; **R. Lahita**: None.

Abstract Number: 1883

Temporal Patterns of Cardiometabolic Comorbidities Before and After Psoriatic Arthritis Diagnosis: A Nationwide Retrospective Study from Poland.

Batko Bogdan[1], Mateusz Szeląg[2], Krzysztof Batko[3], Magdalena Krajewska-Włodarczyk[4], Zbigniew Żuber[5], Marcin Stajszczyk[6], Brygida Kwiatkowska[7] and Tomasz Guzik[8], [1]Department of Rheumatology and Immunology, Faculty of Medicine and Health Sciences, Andrzej Frycz Modrzewski University, Krakow, Poland, Kraków, Poland, [2]Ministry of Health, Warsaw, Poland, [3]Department of Dermatology, University Hospital in Krakow, Poland, Krakow, Poland, [4]University of Warmia & Mazury, Olsztyn, Poland, [5]Department of Pediatrics, Faculty of Medicine and Health Sciences, Andrzej Frycz Modrzewski University, Krakow, Poland, Krakow, Poland, [6]Department of Rheumatology and Autoimmune Diseases, Silesian Center for Rheumatology, Orthopedics and Rehabilitation, Ustroń, Poland, Ustron,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

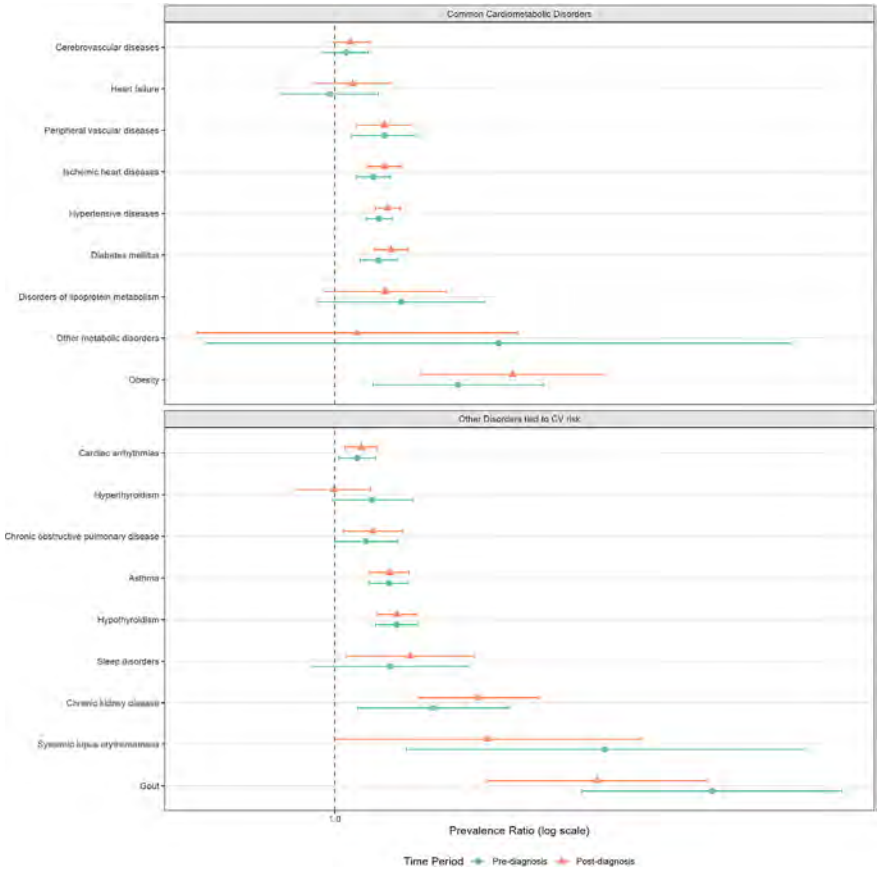
Poland, [7]Clinic of Early Arthritis, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland, Warsaw, Poland, [8]BHF Centre for Research Excellence, Centre for Cardiovascular Sciences, The University of Edin-burgh, Edinburgh, UK, Edinburgh, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: While the association between psoriatic arthritis (PsA) and cardiometabolic disorders is established, the temporal sequence and progression of these comorbidities remain poorly characterized. To examine the temporal relationship between psoriatic arthritis (PsA) and cardiometabolic disorders by comparing their prevalence patterns before and after PsA diagnosis.

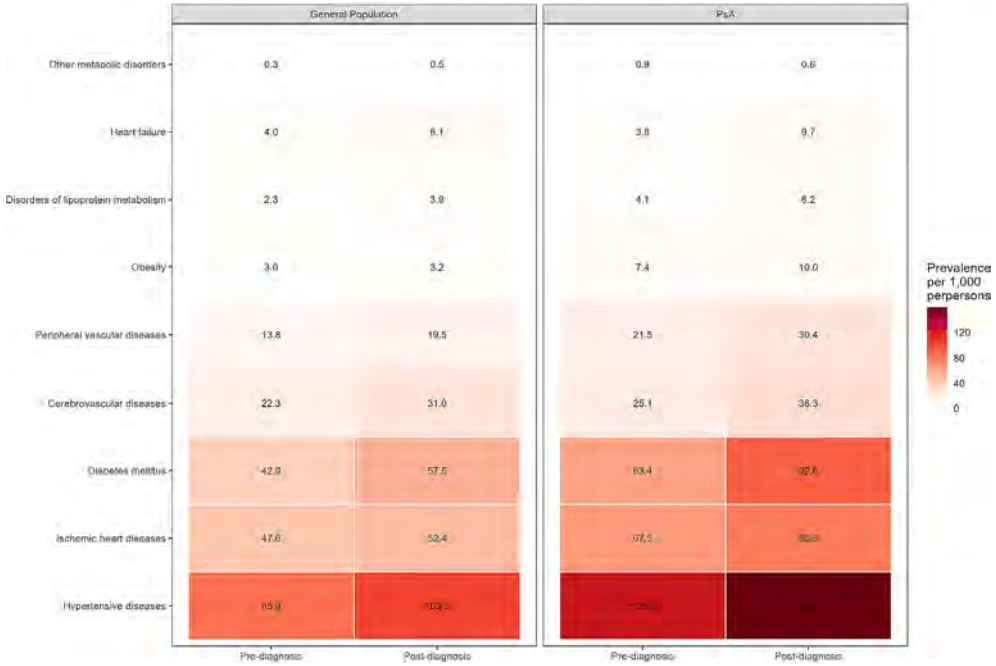
Methods: This nationwide retrospective case-control study analyzed Polish National Health Fund claims data (2011–2021). We identified 3,391 incident PsA patients diagnosed in 2016 using a definition requiring either: ICD-10 codes (M07.0-M07.3, L40.5) plus DMARD prescriptions, or ≥3 encounters with these codes in rheumatology settings. Cases were matched 1:10 to population controls by age, sex, and region. Cardiometabolic conditions (including hypertension, diabetes, ischemic heart disease, and metabolic disorders) were assessed based on ≥2 recorded diagnoses during five-year periods before and after PsA diagnosis.



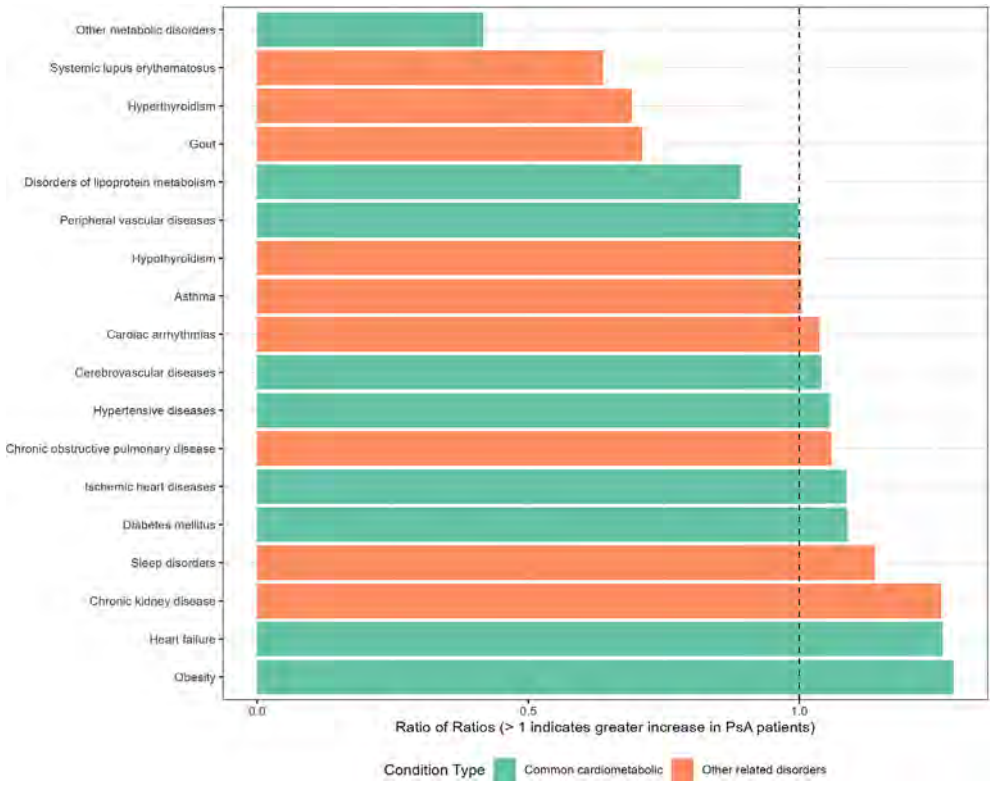
Temporal risk of various cardiometabolic disorders in patients with incident psoriatic arthritis as compared to the general population

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: PsA patients demonstrated significantly elevated cardiometabolic risk both before and after diagnosis. Prevalence ratios (PR) were consistently higher across multiple conditions, with slight increases observed following diagnosis: hypertensive diseases (pre-PR 1.05 [95% CI 1.03–1.06] to post-PR 1.06 [1.04–1.07]), diabetes mellitus (pre-PR 1.05 [1.03–1.07] to



Heatmap for the overall burden of common cardiometabolic disorders in incident psoriatic arthritis patients and the general population



Temporal change in the burden of various cardiometabolic disorders in the five years after psoriatic arthritis diagnosis, as compared to the general population.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

post-PR 1.06 [1.04–1.08]), and ischemic heart diseases (pre-PR 1.04 [1.02–1.06] to post-PR 1.05 [1.03–1.07]). Notably, obesity showed the highest relative risk (pre-PR 1.13 [1.04–1.24] to post-PR 1.20 [1.09–1.32]). The mean cardiometabolic burden per patient increased by 34% following PsA diagnosis (from 0.32 to 0.43 conditions), with marked increases in heart failure (154%), lipoprotein disorders (50%), and diabetes (46%).

Conclusion: Temporal patterns in comorbidity of cardiovascular significance support the concept of shared inflammatory and metabolic pathways underlying these associations, highlighting the need for early cardiometabolic risk assessment and intervention in PsA management.

Disclosure: B. Bogdan: AbbVie/Abbott, 2, 6, Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 1, 6, Celgene, 1, 6, Eli Lilly, 1, 4, 5, GlaxoSmithKlein(GSK), 1, 6, Janssen, 1, 6, Novartis, 1, 5, 6, Roche, 1, 6, UCB, 1, 6; **M. Szeląg**: None; **K. Batko**: None; **M. Krajewska-Włodarczyk**: AbbVie/Abbott, 6, Eli Lilly, 6, Pfizer, 6, Roche, 6, UCB, 6; **Z. Żuber**: AbbVie/Abbott, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **M. Stajszczyk**: AbbVie/Abbott, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **B. Kwiatkowska**: AbbVie/Abbott, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **T. Guzik**: AbbVie/Abbott, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6.

Abstract Number: 1884

The Importance of Adherence to Dietary Recommendations for Rheumatoid Arthritis Risk May Be Greater in Younger Individuals – Results from a Nested Case-Control Study

Rebecka Bäcklund[1], Ulf Bergström[1], Michele Compagno[1], Linnea arvidsson[2], Emil Rydell[3], Emily Sonestedt[1] and **Carl Turesson**[3], [1]Lund University, Malmö, Sweden, [2]Lund University, Malmö, [3]Lund University, Malmö, Sweden

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Healthy eating habits might prevent the development of rheumatoid arthritis (RA). The impact of such lifestyle factors on the risk of RA may differ across age groups. We previously reported a reduced risk of RA among individuals who adhere to dietary recommendations, particularly regarding higher intake of vegetables and fruit and reduced consumption of red/processed meat. In a post hoc analysis, we investigated the relation between adherence to dietary recommendations and the risk of RA in models stratified by age.

Methods: A nested case-control study was conducted within a population-based survey performed in 1991-1996. Incident cases of RA were identified through linkage with patient registers up to December 2016, and the diagnoses were validated according to established criteria. Four controls for each case, matched for sex, year of birth, and year of inclusion, were included. The controls were alive and free of RA when the index person was diagnosed with RA. Diet was assessed using a modified diet history method comprising of a seven-day menu book, a diet history questionnaire, and a complementary diet history interview. The cutoff values for the recommendations in the Swedish Dietary Guidelines (SDG) from 2015 are based on the Nordic Nutrition Recommendations from 2012 and the WHO guidelines from 2015. Logistic regression analysis, taking into account the matched design of the study, was applied to investigate the relation with future RA for fibers, vegetables and fruit, fish, added sugar and red/processed meat as dichotomous (compliant with recommendation or not) and continuous variables per standard deviation. Furthermore, we assessed the impact of the SDG score (SDGS; 1 point

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1. SDGS, its components and the risk of developing RA (logistic regression), stratified by median age at screening (55.8 years). Adjusted for total energy intake, smoking, alcohol (sex-specific quintiles), leisure time physical activity (quintiles)*

		Age ≤ 55.8 years		Age > 55.8 years	
		OR	95% CI	OR	95% CI
SDGS components	Recommendation				
Compliant with recommendation					
Fiber (g/MJ)	≥2.4	**0.41**	**0.20 – 0.85**	0.92	0.54 – 1.59
Vegetables and fruits (g/day)	≥ 400	**0.53**	**0.30 – 0.95**	0.70	0.41 – 1.18
Fish and shellfish (g/week)	≥ 300	1.13	0.63 – 2.06	**2.07**	**1.24 – 3.46**
Added sugar (E%)	≤ 10	0.74	0.42 – 1.30	0.68	0.42 – 1.10
Red and processed meat (g/week)	< 500	**0.40**	**0.17 – 0.95**	0.67	0.37 – 1.20
SDGS					
0–1		1.00	(Ref)	1.00	(Ref)
2–3		0.64	0.35 – 1.17	0.96	0.56 – 1.66
4-5		**0.26**	**0.09 – 0.78**	0.88	0.41 – 1.86
Per additional score		**0.72**	**0.57 – 0.92**	0.95	0.79 – 1.14
Reported intake, per SD**					
Fiber		**0.68**	**0.48 – 0.98**	0.85	0.64 – 1.13
Vegetables and fruits		**0.62**	**0.45 – 0.86**	0.75	0.55 – 1.01
Fish and shellfish		0.93	0.71 – 1.22	1.22	0.96 – 1.56
Added sugar		**1.42**	**1.05 – 1.93**	1.08	0.86 – 1.37
Red and processed meat		**1.47**	**1.09 – 1.98**	1.20	0.92 – 1.56

Odds ratio (OR), Swedish Dietary Guidelines Score (SDGS), Rheumatoid arthritis (RA), Standard deviation [SD], Percent of total energy intake (E%), Confidence interval (CI), Reference (Ref)
* All potential energy misreporters excluded
** SD for fiber 0.64; vegetables and fruits 185.60; fish and shellfish 229.58; added sugar 4.28; Red and processed meat 406.01

for adherence to each recommendation, total 0-5) on the risk of RA. Analyses were adjusted for factors that have been associated with both diet and RA (smoking, alcohol and leisure time physical activity). All models were adjusted for reported total energy intake, and stratified by age at inclusion in the health survey (above vs below the median). Misreporters of total energy intake were excluded.

Results: A total of 305 incident cases of RA were identified (76% women, mean time from screening to diagnosis 12 years). A high adherence (SDGS 4-5 vs 0-1) was associated with a reduced risk of future development of RA (odds ratio 0.26; 95% confidence interval 0.09-0.78) among survey participants aged ≤55.8 years, whereas there was no such association among older individuals (Table 1). Younger individuals who were adherent to recommendations on fiber, vegetables and fruit, and red/processed meat, had a lower risk of RA. There were corresponding associations with quantified intakes of each of these diet components in the younger group, but not in the older age group (Table 1).

Conclusion: Adherence to dietary recommendations, including high intakes of fiber and vegetables and fruit, and limited consumption of red/processed meat, may reduce the risk of RA in younger individuals. These findings suggest that the impact of lifestyle factors such as diet on future RA development may vary by age, potentially reflecting distinct early disease mechanisms.

Disclosure: R. Bäcklund: None; **U. Bergström**: None; **M. Compagno**: None; **L. arvidsson**: None; **E. Rydell**: None; **E. Sonestedt**: None; **C. Turesson**: AbbVie/Abbott, 1, 6, Nordic Drugs, 2, 6, Novartis, 1, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1885

Sex-specific Associations of Anthropometrics, Smoking and Eduction with the Risk of Rheumatoid Athritis: A Nested Case-Control Study

Carl Turesson[1], Linnea arvidsson[2], Emil Rydell[1] and Ulf Bergström[3], [1]Lund University, Malmö, Sweden, [2]Lund University, Malmö, [3]Lund University, Malmö, Sweden

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Smoking is an established risk factor for rheumatoid arthritis (RA), and there is also evidence for an association with socioeconomic factors. As RA is more common in women compared to men, most studies of disease predictors have mainly included women, and data on risk factors in men are limited. Some studies indicate an increased risk of RA in women with high body mass index (BMI), whereas a negative association between BMI and future RA development in men has been reported. The purpose of this study was to investigate BMI, other anthropometric factors, smoking and level of formal education as potential predictors of RA in middle-aged men and women.

Methods: A nested case-control study was performed including participants in a population-based survey performed in 1991-1996. Cases diagnosed with RA from inclusion until December 2016 were identified through register linkage and validated in a structured process. Four controls for each case, matched for sex, year of birth, and year of inclusion, were included. Height and weight were measured as part of the health survey, and BMI was calculated as weight (in kg)/height (in m)^2. Waist was measured as the circumference (cm) between the lowest rib and the iliac crest. Hip circumference (cm) was measured as the largest circumference between waist and thighs. Waist/hip ratio (WHR) was defined as the waist circumference divided by the hip circumference. Information on lifestyle habits and socioeconomics was collected using a self-administered questionnaire. Logistic regression analysis, taking into account the matched design of the study, was applied to investigate the relation between these exposures and risk of RA diagnosis during the follow-up.

Results: There were 305 incident cases of RA (232 women, 73 men), with a mean time from screening to diagnosis of 12 years. The mean age at inclusion in the survey for those diagnosed with RA during the follow-up was 56.8 years, and similar in women and men (Table 1). These cases were compared to 1220 matched controls (Table 1).

Table 1.

Table 1. Baseline characteristics at inclusion in the health survey of pre-RA cases and controls; by sex

	Women		Men	
	Pre-RA cases	Controls	Pre-RA cases	Controls
n	232	928	73	292
Age (years); mean (SD)	56.7 (7.2)	56.3 (7.2)	57.4 (6.6)	57.0 (6.6)
BMI (kg/m^2); mean (SD)	25.7 (4.8)	25.6 (4.3)	25.5 (3.1)	26.6 (3.6)
Waist (cm); mean (SD)	79.0 (12.3)	78.3 (10.7)	92.1 (8.4)	94.3 (10.6)
Hip (cm); mean (SD)	99.1 (10.6)	98.1 (9.8)	98.8 (6.0)	99.3 (7.0)
Waist/hip ratio; mean (SD)	0.80 (0.06)	0.80 (0.05)	0.93 (0.05)	0.95 (0.06)
Current smoking; n (%)	70 (31.8)	187 (21.5)	16 (25.4)	62 (23.2)
Low level of formal education*; n (%)	99 (45.0)	339 (39.1)	26 (41.9)	112 (38.4)

*≤8 years of school

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2.

Table 2. Relation between baseline factors and subsequent development of rheumatoid arthritis, by sex. Logistic regression. Odds ratios with 95% confidence intervals

	Women	Men
BMI (per SD)	1.03 (0.88-1.22)	**0.63 (0.46-0.87)**
Waist (per SD)	1.09 (0.93-1.28)	0.75 (0.55-1.01)
Hip (per SD)	1.13 (0.96-1.33)	0.92 (0.68-1.22)
Waist/hip ratio (per SD)	0.97 (0.82-1.14)	**0.68 (0.51-0.93)**
Current smoking	**1.99 (1.34-2.95)**	1.11 (0.52-2.37)
Low level of formal education*	**3.08 (1.69-5.63)**	1.09 (0.42-2.84)

*<8 years of school compared to university degree
SD, Standard deviation: BMI men 3.5 kg/m^2, women 4.4 kg/m^2; Waist men 10.3 cm, women 11.1 cm; Hip men 6.8 cm, women 10.0 cm; Waist/hip ratio men 0.06, women 0.05.

In men, higher BMI was associated with a reduced risk of RA (odds ratio [OR] 0.63 per standard deviation [SD]; 95% confidence interval [CI] 0.46-0.87). There was also a trend towards a lower waist circumference among men who subsequently developed RA (Table 2), and a significant negative association with the WHR (OR 0.68 per SD; 95% CI 0.51-0.93). No associations between anthropometric measures and RA risk were found in women (Table 2). However, smoking and a low level of formal education were predictive of RA in women, but not in men (Table 2).

Conclusion: Anthropometric measures seem to have differential effects on the risk of RA in women and men. The inverse association between BMI and RA risk in men is supported by a similar relation with WHR. This suggests distinct underlying mechanisms related to abdominal obesity in men and women. Female smokers and women with limited education had an increased risk of RA, whereas no similar associations were observed in the smaller subset of men in this study.

Disclosure: C. Turesson: AbbVie/Abbott, 1, 6, Nordic Drugs, 2, 6, Novartis, 1, 6; **L. arvidsson**: None; **E. Rydell**: None; **U. Bergström**: None.

Abstract Number: 1886

Thirty Percent of Older Adults with Rheumatic Disease Receive High-Risk Medication

Christine Anastasiou[1], Eric Roberts[2], gabriela Schmajuk[3] and Jinoos Yazdany[4], [1]Stanford University, Pleasanton, CA, [2]University of California, San Francisco, SF, CA, [3]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [4]UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: High-risk medications (HRMs) may increase the risk of adverse events such as falls and fractures, hospitalizations, hospital length of stay, and death in older adults. We hypothesized that older adults with rheumatic disease, especially those with multiple comorbidities, had significant use of HRMs. We aimed to characterize HRM use, sources of prescription, and predictors of HRM exposure in older adults in a large national registry of older adults with rheumatic conditions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We analyzed 2021 data from practices enrolled in the Rheumatology Informatics System for Effectiveness (RISE) registry linked to Medicare parts A, B, D. Patients ≥65 years old with ≥2 RISE visits, continuous Medicare enrollment, and a qualifying rheumatic diagnosis were included (SLE, RA, PsA, axSpA, SS, SSc, Gout, OA). HRM exposure was defined according to the Merit-Based Incentive Payment System Clinical Quality Measure #238 "Use of High-Risk Medications in Older Adults". We determined prescriber specialty using National Provider Identifiers (NPI) and a list of provider specialties

Table 1

10 Most Commonly Prescribed HRM

		Full Sample (N=49210)	Among patients with any HRM (N=15035)
Drug	N	%	%
Cyclobenzaprine	3261	6.63	21.69
Zolpidem	1981	4.03	13.18
Estradiol	1711	3.48	11.38
Meclizine	1613	3.28	10.73
Dicyclomine	1534	3.12	10.2
Amitriptyline	1516	3.08	10.08
Hydroxyzine	1251	2.54	8.32
Ketorolac	1031	2.1	6.86
Methocarbamol	917	1.86	6.1
Paroxetine	834	1.69	5.55

Table 2

	Odds of One or More High Risk Med Prescription N= 49210			
Variable	**Unadjusted Bivariable Model**		**Fully Adjusted Model**	
Primary rheumatic diagnosis	**Odds ratio**	**95% CI**	**Odds ratio**	**95% CI**
RA	ref	ref	ref	ref
OA	1.28	(1.16 - 1.41)	1.29	(1.20 - 1.40)
PMR	0.86	(0.78 - 0.95)	0.98	(0.88 - 1.09)
axSpA	1.35	(1.18 - 1.56)	1.42	(1.24 - 1.62)
Gout	0.94	(0.81 - 1.08)	1.16	(1.00 - 1.34)
PsA	1.15	(1.04 - 1.28)	1.23	(1.11 - 1.36)
SS	1.78	(1.37 - 2.31)	1.48	(1.12 - 1.95)
SLE	1.5	(1.34 - 1.68)	1.25	(1.12 - 1.40)
SSc	1.25	(1.01 - 1.55)	1.12	(0.90 - 1.38)
Age (years)	0.97	(0.97 - 0.97)	0.97	(0.97 - 0.98)
Sex (ref = female)				
Male	0.56	(0.53 - 0.59)	0.62	(0.59 - 0.66)
Area Deprivation Index				
First Quartile (lowest dep)	ref	ref	ref	ref
Second	1.03	(0.96 - 1.10)	0.93	(0.88 - 0.99)
Third	1.09	(1.01 - 1.19)	0.94	(0.87 - 1.01)
Fourth (highest deprivation)	1.17	(1.08 - 1.27)	0.96	(0.89 - 1.04)
Missing	1.19	(1.05 - 1.35)	1	(0.91 - 1.09)
Comorbidities				
Fibromyalgia	2.74	(2.52 - 2.98)	2.06	(1.90 - 2.23)
Mood disorder	1.99	(1.89 - 2.10)	1.44	(1.35 - 1.53)
Anxiety	2.05	(1.94 - 2.16)	1.54	(1.45 - 1.63)
Osteoporosis	1.06	(1.01 - 1.11)	0.97	(0.93 - 1.02)
Charlson Comorbidity Index				
0	ref	ref	ref	ref
1	0.87	(0.79 - 0.96)	1.02	(0.93 - 1.11)
3	1.02	(0.92 - 1.12)	1.2	(1.10 - 1.32)
4+	1.17	(1.06 - 1.29)	1.43	(1.31 - 1.57)

Covariates not shown in table: Race/ethnicity; Geographic Division; Rural-Urban Commuting Area

The data presented here was supported by the American College of Rheumatology's RISE Registry. However, the views expressed represent those of the author(s) and do not necessary represent the views of the American College of Rheumatology. Funding for this project was provided by the Rheumatology Research Foundation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

from the Centers for Medicare & Medicaid Services to categorize prescribers as rheumatologist, non-rheumatologist MD, a rheumatology affiliated NP or PA, or a NP or PA not affiliated with a rheumatology practice. We reported the frequency and percent of patients exposed to the top 10 most common high-risk medications by primary rheumatic diagnosis. We constructed a series of logit linear models predicting exposure to any high-risk medication using generalized estimating equations to adjust for patients nested within practices.

Results: Out of the 49,210 patients (mean age 76±6.5, 75.4% women, 87.7% non-Hispanic white) meeting inclusion criteria, 30.6% received ≥1 HRM in 2021; 7.6% received ≥2 HRMs. The top most-used high-risk medications included cyclobenzaprine (6.6% of full sample; 21.7% among patients with any HRMs) and zolpidem (4.0% of full sample; 13.2% among patients with any HRMs), among others (Table 1). Four of the ten most common prescriptions were for psychotropic medications. Prescriptions primarily originated from non-rheumatology physicians (67.1%) or non-rheumatology affiliated NP or PA (9.9%). In adjusted models, patients with SS and axSpA had the highest odds of receiving a HRM when compared with RA (OR 1.48, 95% CI 1.2 – 1.4 and OR 1.42, 95% CI 1.24 – 1.62); (Table 2). Patients with fibromyalgia, mood disorder or anxiety disorder, and patients with higher Charlson Comorbidity Index (3-4+) also had higher odds of receiving a HRM (Table 2).

Conclusion: Thirty percent of older adults with rheumatic diseases received at least one high-risk medication. The most common medications prescribed were cyclobenzaprine and zolpidem, suggesting that this population has significant pain and sleep dysfunction prompting use of HRMs. Further research is warranted to identify optimal strategies and medications to balance symptom relief with patient safety, ensuring that pain, mood, and insomnia in older adults with rheumatic disease are effectively managed without incurring undue harm in this vulnerable population.

Disclosure: C. Anastasiou: Priovant, 12, VALOR Study. Served as Co-PI at UCSF Site.; **E. Roberts**: None; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2.

Abstract Number: 1887

Incidence, Prevalence and Mortality of Systemic Lupus Erythematosus – A 20-year territory-wide analysis of electronic health records in Hong Kong

Danting zhang[1], jiaxin S. Wu[1] and Desmond Yat-Hin Yap[2], [1]The University of Hong Kong, Hong Kong, Hong Kong, [2]Department of Medicine, The University of Hong Kong, Hong Kong SAR, Hong Kong

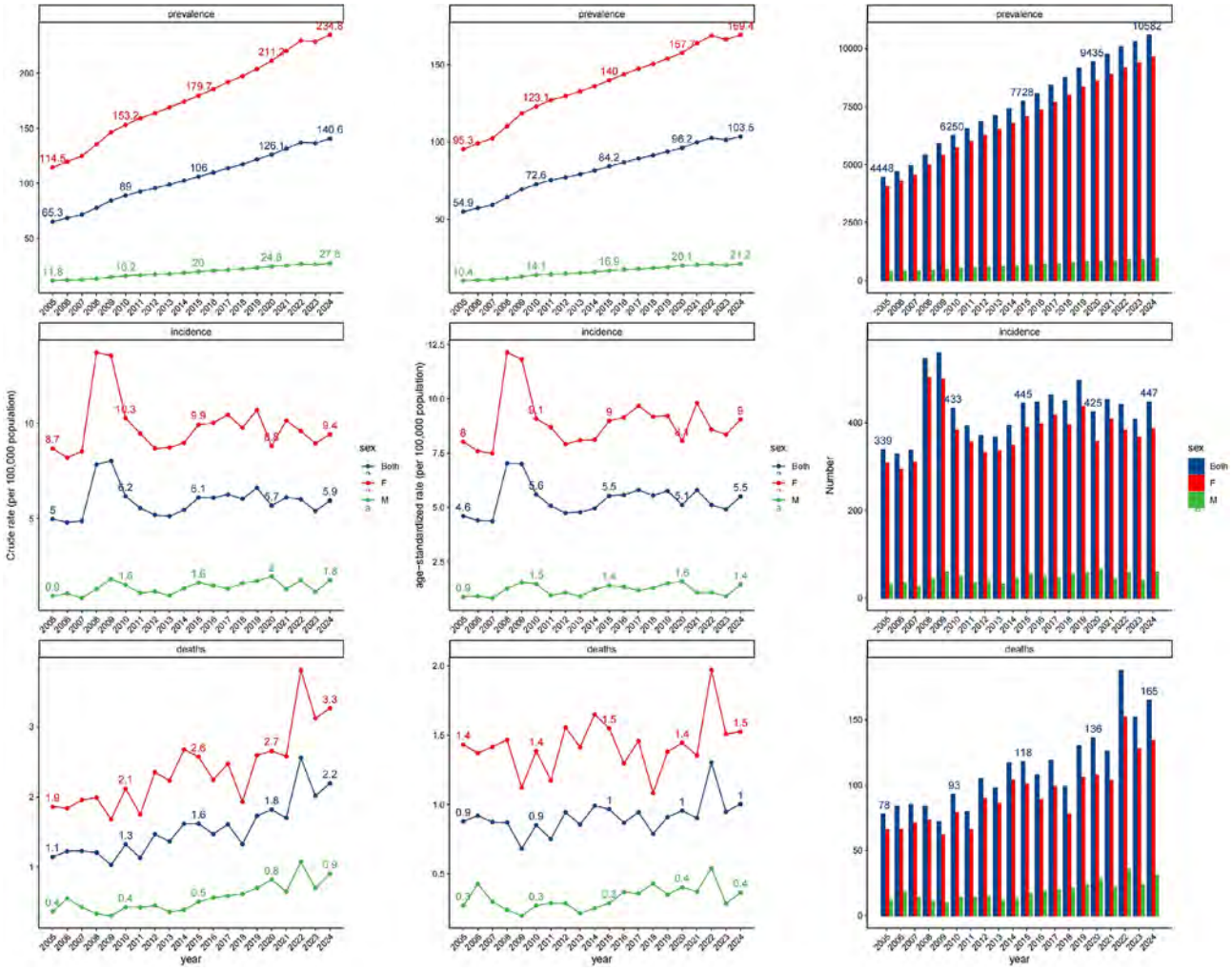
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

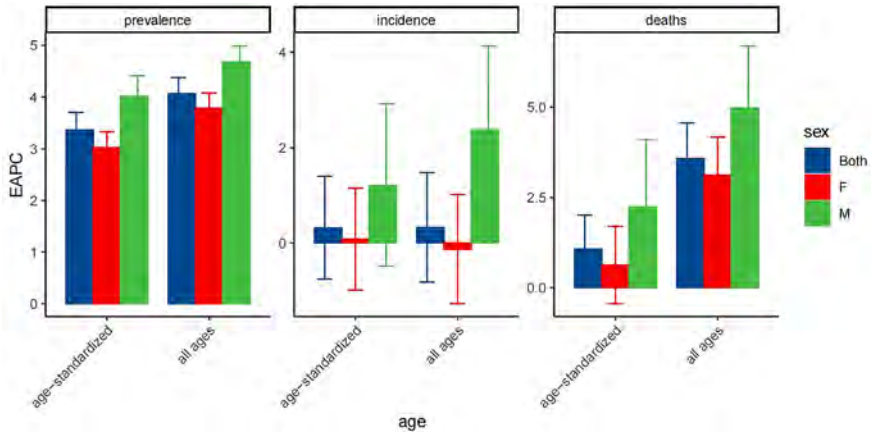
Background/Purpose: Advancements in immunosuppressive treatments and general medical care in the past two decades have influenced the disease burden and outcomes of patients with systemic lupus erythematosus (SLE). This study aimed to provide an up-to-date analysis on the prevalence, incidence, and mortality in the present era of SLE management.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We established a large retrospective cohort of SLE patients using the Clinical Data Analysis and Reporting System (CDARS, an territory-wide electronic health records system managed by the Hospital Authority of Hong Kong) between 1995 to 2024. The incidence, prevalence and all-cause mortality were evaluated between 2005 and 2024, and age-



The trends in crude and age-standardized rates of prevalence, incidence and death in SLE between 2005 and 2024



Estimated annual percentage change (EAPC) for crude and age-standardized rates of prevalence, incidence and death in SLE between 2005 and 2024

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

standardization was based on the WHO 2000–2025 standard population (SEER datasets). The change of trends was assessed by the estimated annual percentage change (EAPC).

Results: 8,545 incident cases were observed between 2005 and 2024, with a prevalence of 10,582 in 2024. Crude prevalence (per 100,000 persons) of SLE increased from 65.3 to 140.6 [EAPC: 4.1 (3.8 to 4.4)], and prevalence rates for female and male were 234.8 and 27.6 respectively by the end of 2024. Crude incidence (per 100,000 persons) remained largely unchanged over the years [5.0 vs. 5.9 (EAPC: 0.3 (-0.8 to 1.5)], but the crude mortality (per 100,000 persons) increased from 1.1 to 2.2 [EAPC: 3.1 (2.1 to 4.2)]. The life-expentacy for female and male SLE patients were 77 and 73.8 years, respectively. While the age-standardized death rate for male showed a significant increase [EAPC 2.2 (0.4 to 4.1)], the rate for female has remained unchanged [EAPC 0.6 (-0.4 to 1.7)]. The female to male rate ratio for age-standardised prevalence, incidence and death rate were 8, 6 and 4, respectively, in 2024. Disparity in trends was also observed among different age groups.

Conclusion: The evolution of SLE management has led to increased disease prevalence. Such change in disease burden may be related to better immunosuppressive therapies and general medical care that has led to reduced early mortality.

Disclosure: D. zhang: None; **j. Wu**: None; **D. Yap**: None.

Abstract Number: 1888

Developing Machine Learning Algorithm in Electronic Health Record to Accurately Identify Psoriasis Patients

Dilli Poudel[1], Leslie Crofford[2], Avery Fortier[3], Lee Wheless[4], Georgina Sellyn[4], Gyaljin Sherpa[5], Alexis Ogdie[6] and Paras Karmacharya[7], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Melbourne, AR, [3]Vanderbilt University, Lexington, MA, [4]Vanderbilt University, Nashville, TN, [5]Mercy Health - St. Elizabeth Youngstown Hospital, Newyork, NY, [6]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [7]Vanderbilt University, Nashville, TN, Hermitage, TN

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Accurate identification of patients with psoriasis from large electronic health record (EHR) databases is crucial for conducting robust real-world research. While EHRs offer an efficient resource, traditional identification methods are often laborious. Machine learning (ML) can present a promising high throughput approach with accuracy. The objective of this study was to develop and validate machine learning algorithms using EHR data to identify patients with psoriasis.

Methods: We used data from Vanderbilt University Medical Center's de-identified EHR database, the Synthetic Derivative (SD), which contains longitudinal clinical data from approximately 3.5 million subjects. Adult patients (≥18 years) were initially screened based on potential psoriasis indicators like International Classification of Diseases (ICD) codes or keywords. Non-overlapping random samples formed the training (N=200) and validation (N=300) sets. A true psoriasis case was defined through manual chart review as documented confirmatory or probable diagnosis by a dermatologist or rheumatologist, or a positive skin biopsy. Potential machine learning features included ICD-9/10 codes for psoriasis and related conditions, provider specialty associated with codes (dermatology, rheumatology), problem list keywords, and use of relevant medications (e.g., topical treatments, systemic therapies, biologics). Three ML models (logistic regression, random forest, XGBoost)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

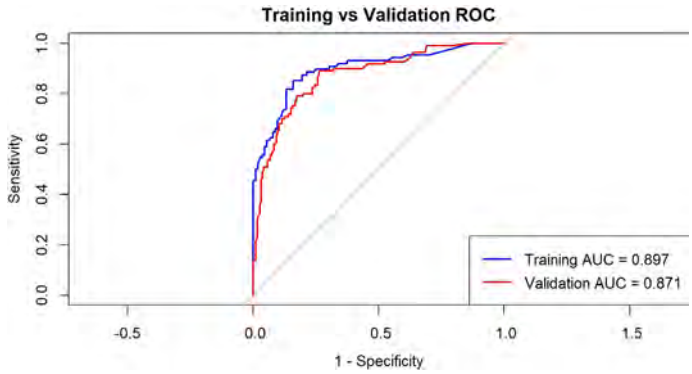
were developed on the training set, with the random forest model undergoing hyperparameter tuning via repeated 10-fold cross-validation. Models were tested on the independent validation set, assessing performance using F1-score, sensitivity, positive predictive value (PPV), area under the receiver operating characteristic curve (AUC), and accuracy.

Results: All three ML models demonstrated strong performance identifying psoriasis patients in the validation set. Tuned random forest model achieved the highest F1-score (0.757), with an AUC of 0.871, sensitivity of 0.791, and PPV of 0.725 (**Table 1, Figure 1**). Feature importance analysis confirmed that ICD codes related to psoriasis diagnoses documented by dermatologists and rheumatologists, overall psoriasis visit codes, and specific medication usage patterns were among the most significant predictors of a true psoriasis diagnosis (**Figure 2**).

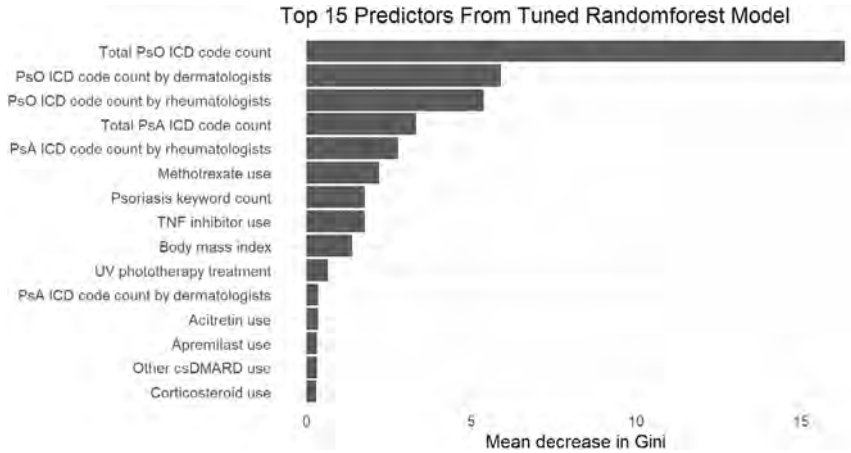
Conclusion: Machine learning algorithms, particularly tuned random forest models, leveraging readily available EHR data could provide an accurate and efficient method for identifying psoriasis patients comparable to true diagnosis made by dermatologist or rheumatologist or with skin biopsy. Such validated algorithms represent valuable tools for researchers seeking to assemble large, real-world cohorts of patients with psoriasis enabling studies on disease epidemiology, treatment effectiveness, and patient outcomes.

Model	F1-score	Sensitivity	PPV	AUC	Accuracy
Logistic Regression	0.726	0.739	0.713	0.856	0.7867
Random Forest	**0.757**	0.791	0.725	0.873	0.8133
XGBoost	0.75	0.736	0.764	0.88	0.8233

Comparison of Performances Among Three Different Machine Learning Models



Receiver Operating Curves with Area Under Curve for Random Forest Model in Training and Validation Sets



Top 15 Predictors of a True Psoriasis Diagnosis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: D. Poudel: None; **L. Crofford**: Argenyx, 5, Evergreen, 5, Kezar, 1, Otsaka, 1, UCB, 1; **A. Fortier**: None; **L. Wheless**: None; **G. Sellyn**: None; **G. Sherpa**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **P. Karmacharya**: None.

Abstract Number: 1889

Navigating Diagnostic Challenges: Insights into the Patient Journey and Delays in Diagnosing Dermatomyositis from a Real-world Survey in the United States and Europe

Esther Yi[1], Jason Xenakis[1], Chris Blazos[2], Jade Garratt-Wheeldon[2], James Piercy[2], Peter Anderson[2] and Rohit Aggarwal[3], [1]Pfizer Inc., New York, United States of America, New York, [2]Adelphi Real World, Bollington, United Kingdom, Bollington, United Kingdom, [3]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are a heterogenous group of rare autoimmune inflammatory rheumatic diseases, including dermatomyositis (DM).

Methods: Data were drawn from the Adelphi Real World IIMs Disease Specific Programme™, a cross-sectional survey, including retrospective data collection, of rheumatologists, dermatologists, neurologists, and internists in Europe (France, Germany, the United Kingdom) and the United States (US) from September 2023–July 2024. Physicians reported demographics, consultation history, tests, and diagnoses, for up to 10 consecutively consulting adult patients with a physician-confirmed diagnosis of DM. Analyses were descriptive, and missing data were not imputed.

Results: Overall, 222 physicians provided data on 513 DM patients (n=381 Europe, n=132 US). Physician reported patient demographics at survey are reported in **Table 1**. Mean (standard deviation [SD]) patient age was 49.5 (12.8) years, 73% were female, and 87% were White. Mean [SD] time since DM diagnosis was 2.7 (2.9) years. Family history of an autoimmune disease was confirmed for 38% of patients and 67% had a confirmed comorbidity.

Signs/symptoms present at onset included fatigue (63%; Europe 66%, US 53%), heliotrope rash (45%; Europe 46%, US 41%), Gottron's papules (46%; Europe 48%, US 41%), erythematous rashes (without secondary changes) (40%; Europe 39%, US 42%), and myalgia 29%; Europe 29%, US 29%).

Diagnostic characteristics are reported in **Table 2**. Mean (SD) time from symptom onset to diagnosis was 24.3 (32.4) weeks, and 13.1 (27.2) weeks from first consultation to diagnosis. Following DM symptom onset, 47% of patients initially consulted a general practitioner (GP)/ primary care physician (PCP), 22% consulted a dermatologist, and 14% consulted a rheumatologist. For patients who initially consulted a GP/PCP, dermatologist, or rheumatologist, the mean (SD) durations from first consultation to DM diagnosis were 12.4 (21.1), 8.1 (11.6), and 16.7 (33.4) weeks, respectively.

Creatine kinase (CK) testing was conducted to aid diagnosis for 84% of patients and myositis specific/associated antibody testing for 74%.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Physician reported patient demographics at time of survey, across Europe and the United States

	All patients	Europe	US
Patient age, years	***n=513***	***n=381***	***n=132***
Mean (SD)	49.5 (12.7)	48.3 (12.5)	52.8 (12.9)
Patient ethnicity, n (%)	***n=375***	***n=243***	***n=132***
White	325 (87%)	216 (89%)	109 (83%)
Black	27 (7%)	11 (5%)	16 (12%)
South Asian (Indian subcontinent)	15 (4%)	11 (5%)	4 (3%)
East or Southeast Asian	4 (1%)	3 (1%)	1 (1%)
Middle Eastern or North African	4 (1%)	3 (1%)	1 (1%)
Other	2 (1%)	0 (0%)	2 (2%)
Patient sex, n (%)	***n=513***	***n=381***	***n=132***
Male	139 (27%)	107 (28%)	32 (24%)
Female	374 (73%)	274 (72%)	100 (76%)
Time since Dermatomyositis diagnosis, days	***n=484***	***n=359***	***n=125***
Mean (SD)	979.8 (1044.9)	953.1 (1062.8)	1056.6 (991.9)
Top 5 most frequently reported autoimmune conditions with confirmed family history, n (%)	***n=181***	***n=146***	***n=35***
Thyroid-related disease (e.g., Grave's disease, Hashimoto's thyroiditis)	52 (29%)	41 (28%)	11 (31%)
Rheumatologic disease	49 (27%)	42 (29%)	7 (20%)
Inflammatory bowel disease	31 (17%)	25 (17%)	6 (17%)
Multiple sclerosis	20 (11%)	15 (10%)	5 (14%)
Sjogren's syndrome	19 (10%)	15 (10%)	4 (11%)
Top 10 most frequently reported comorbidities, n (%)	***n=344***	***n=245***	***n=99***
Hypertension	128 (37%)	77 (31%)	51 (52%)
Anxiety	104 (30%)	69 (28%)	35 (35%)
Dyslipidemia	95 (28%)	66 (27%)	29 (29%)
Depression	81 (24%)	58 (24%)	23 (23%)
Thyroid-related disease (e.g., Grave's disease, Hashimoto's thyroiditis)	45 (13%)	29 (12%)	16 (16%)
Diabetes without chronic complications	40 (12%)	21 (9%)	19 (19%)
Any malignancy, including and lymphoma	26 (8%)	16 (7%)	10 (10%)
Rheumatologic disease	22 (6%)	17 (7%)	5 (5%)
Arrythmia	19 (6%)	14 (6%)	5 (5%)
Mild liver disease	19 (6%)	16 (7%)	3 (3%)

Overall, 34% of patients were initially diagnosed with a different condition, which was later identified as DM. Among these patients, initial diagnoses included 21% fibromyalgia, 20% systematic lupus erythematosus, and 16% rheumatoid arthritis (**Table 2**). Figure 3 shows the rate of initial diagnoses by physician types that conducted the first consultation. For patients that had been given an initial diagnosis, mean (SD) duration from first consultation to DM diagnosis was 18.2 (34.8) weeks (Europe 17.3 [27.4], US 19.7 [44.8]).

Conclusion: While almost half of patients first consulted a PCP, DM diagnosis was invariably made by a specialist. Despite significant levels of testing to aid diagnosis, other than CK, testing practice varies between patients but more generally between the US and Europe. Further research is needed to confirm the consequences of delay in terms of clinical and patient-reported outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Diagnostic characteristics for dermatomyositis patients across Europe and the United States

	All patients	Europe	US
Duration from symptom onset to diagnosis, weeks	***n=411***	***n=304***	***n=107***
Mean (SD)	24.3 (32.4)	21.0 (25.8)	33.6 (45.3)
Duration from first visit with a healthcare professional to diagnosis, weeks	***n=416***	***n=308***	***n=108***
Mean (SD)	13.1 (27.2)	10.7 (18.9)	19.9 (42.2)
First consulting healthcare professional, n (%)	***n=513***	***n=381***	***n=132***
General practitioner/ primary care physician	241 (47%)	205 (54%)	36 (27%)
Dermatologist	112 (22%)	79 (21%)	33 (25%)
Rheumatologist	74 (14%)	51 (13%)	23 (17%)
Internist	41 (8%)	21 (6%)	20 (15%)
Neurologist	23 (4%)	9 (2%)	14 (11%)
Diagnosing healthcare professional, n (%)	***n=513***	***n=381***	***n=132***
Dermatologist	194 (38%)	162 (43%)	32 (24%)
Rheumatologist	178 (35%)	129 (34%)	49 (37%)
Neurologist	65 (13%)	26 (7%)	39 (30%)
Internist	54 (11%)	51 (13%)	3 (2%)
General practitioner/ primary care physician	14 (3%)	8 (2%)	6 (5%)
Was the patient previously diagnosed with a condition that was later attributed to dermatomyositis?, n (%)	***n=513***	***n=381***	***n=132***
Yes	338 (66%)	270 (71%)	68 (52%)
No	175 (34%)	111 (29%)	64 (48%)
Prior diagnosed that were later attributed to dermatomyositis, n (%)	***n=175***	***n=111***	***n=64***
Fibromyalgia	37 (21%)	20 (18%)	17 (27%)
Systematic lupus erythematosus	35 (20%)	17 (15%)	18 (28%)
Rheumatoid arthritis	28 (16%)	13 (12%)	15 (23%)
Polymyositis	26 (15%)	16 (14%)	10 (16%)
Sjogren's syndrome	20 (11%)	11 (10%)	9 (14%)
Top 10 most frequently reported tests used to aid diagnosis, n (%)	***n=489***	***n=361***	***n=128***
Physical examination	421 (86%)	308 (85%)	113 (88%)
Creatine kinase test	409 (84%)	315 (87%)	94 (73%)
Medication/ medical history review	404 (83%)	290 (80%)	114 (89%)
Myositis-specific/associated antibody test	361 (74%)	290 (80%)	71 (55%)
Complete blood count	349 (71%)	270 (75%)	79 (62%)
Review of social and family history	330 (67%)	231 (64%)	99 (77%)
C-reactive protein test	322 (66%)	249 (69%)	73 (57%)
Muscle biopsy	314 (64%)	251 (70%)	63 (49%)
Skin biopsy	300 (61%)	239 (66%)	61 (48%)
Blood pressure	268 (55%)	198 (55%)	70 (55%)
Number of tests used to aid diagnosis	***n=513***	***n=381***	***n=132***
Mean (SD)	15.8 (9.7)	16.5 (10.2)	13.6 (7.5)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

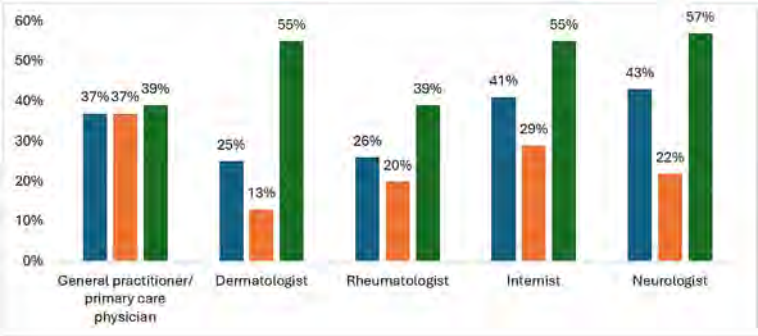


Figure 1: Proportion of patients who were initially diagnosed with a different condition, which was later identified as dermatomyositis, split by the first consulting physician type, across Europe and the United States

Disclosure: E. Yi: Pfizer, Inc., 3, 11; **J. Xenakis**: Pfizer, Inc., 3, 11; **C. Blazos**: Adelphi Real World, 3; **J. Garratt-Wheeldon**: Adelphi Real World, 3; **J. Piercy**: Adelphi Real World, 3; **P. Anderson**: Adelphi Real World, 3; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

Abstract Number: 1890

Quantifying the Inflammatory Toll: Smoking-Attributable Rheumatoid Arthritis Burden Across the Globe, 1990–2021

Eva Kalra[1], Shreyaa Rajpal[2], Twisha Parikh[3], Drumadala Gajbhiye[4], Chethan Raj Gundoji[5], Sagar Patel[6], Jay Patel[7], Neelima Sinha[8], Nikhil Rayarakula[9], Dhwani Vaghani[10] and Hardik Dineshbhai Desai[11], [1]Trident Medical Center, North Charleston, SC, [2]Osmania Medical College, Hyderabad, Telangana, India-500095, Hyderabad, India, [3]GMERS Medical College and Hospital, Gotri, Vadodara, India 390021, Vadodara, India, [4]Government medical college Akola Maharashtra India 444001, Akola, India, [5]Internal Medicine, Government Medical College Nizamabad, Nizamabad, Telangana, India, 503001, Nizamabad, India, [6]Internal medicine -Ward Wizard Medicare Pvt Ltd, Nadiad, Gujarat, India, 387002, Nadiad, India, [7]MGM Medical College, Aurangabad, Maharashtra, India-431003, Aurangabad, India, [8]Department of Medicine, Kurji Holy Family Hospital, Patna, Bihar, India, 800010, Patna, India, [9]College of Public Health, Kent State University, Kent,Ohio, USA, 44242., Kent, OH, [10]Internal Medicine, MGM Medical College, Aurangabad, Maharashtra, India,431003, Aurangabad, India, [11]Ahmedabad, Gujarat, India, 382350, Ahmedabad, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1877–1913) Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA), a chronic systemic inflammatory disorder, imposes a significant global health burden. Smoking is a well-established modifiable risk factor implicated in both the onset and progression of RA. However, comprehensive estimates of the global burden of RA attributable to smoking over time remain limited. This study aims to quantify the burden of RA attributable to smoking across 204 countries and territories over a 32-year period, disaggregated by age, sex, and location.

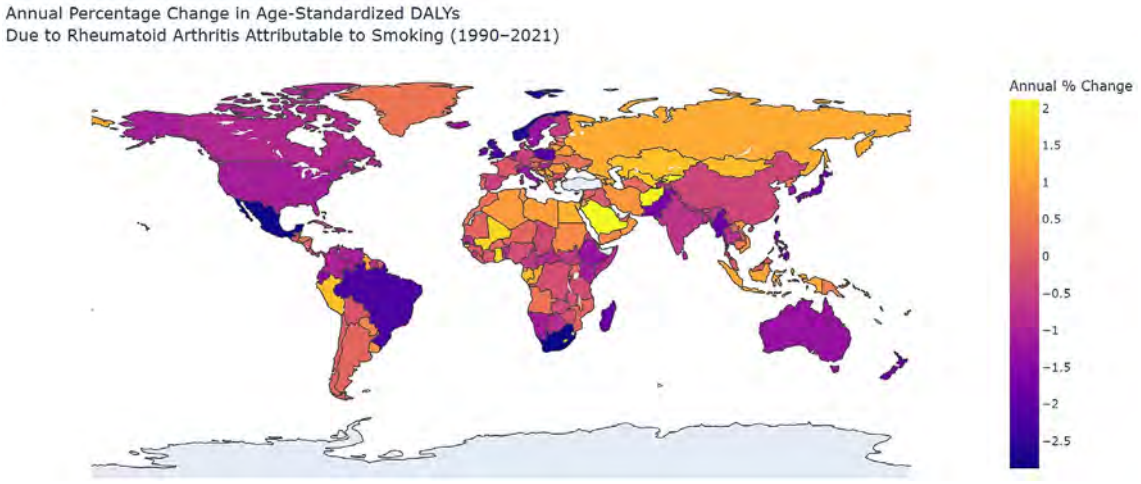
Methods: We estimated deaths, DALYs, and YLDs attributable to smoking-related RA from 1990 to 2021 across 204 countries and territories using a standardized global burden of disease study 2021 risk attribution framework. Burden estimates were stratified by age, sex, year, and geography. Counterfactual analysis assuming zero smoking exposure was applied to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

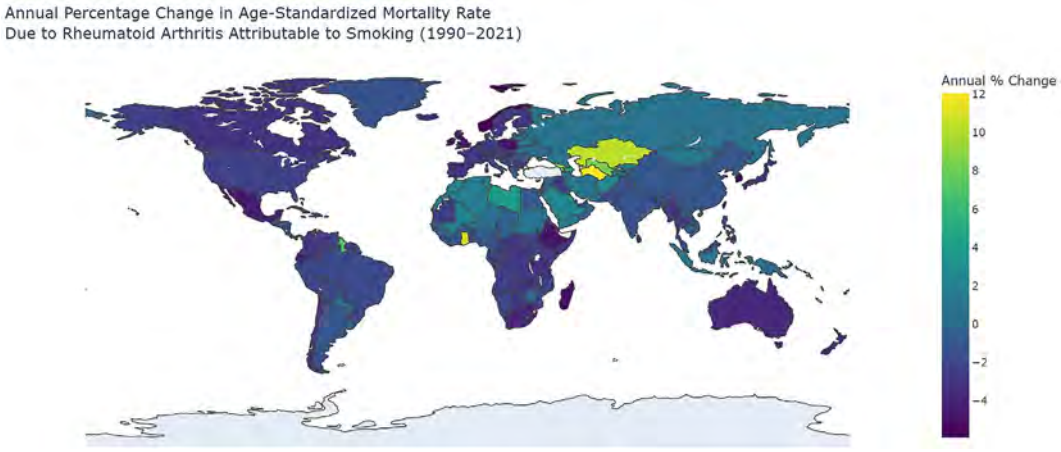
compute attributable fractions, and temporal trends were assessed using annual percentage change in age-standardized rates and absolute counts.

Results: Between 1990 and 2021, the total number of deaths due to RA attributable to smoking increased from 1,791 (95% UI: 1,323–2,227) to 2,263 (1,509–2,911). During the same period, DALYs rose from 145,727 (102,543–200,899) to 215,779 (147,152–300,761), and YLDs increased from 102,310 (65,671–151,392) to 166,709 (107,433–247,042). From 1990 to 2021, smoking-attributable deaths due to RA declined in High SDI regions (APC: –1.04%) and High-income settings (–0.99%), while increasing in High-middle SDI regions (APC: +1.91%). In contrast, DALYs rose substantially in High-middle SDI regions (APC: +2.48%) and to a lesser extent in Central and Eastern Europe (+0.79%) and High-income regions (+0.18%), reflecting a shifting burden from mortality to chronic disability. By 2021, individuals aged 50–54 years recorded the highest burden with 21,342 DALYs and 16,213 YLDs, showing consistent increases since 1990 (APC: +0.84% and +0.96%, respectively). In 2021, females accounted for 57% of total DALYs and 61% of YLDs, with a slower decline in mortality rates compared to males (APC: –0.88% vs –1.15%).

Conclusion: In the last 3 decades, the global burden of RA attributable to smoking revealed a complex epidemiological shift—mortality declined in several high-income regions, while DALYs and YLDs rose markedly in Eastern Europe, Central Asia, and Southern Latin America. The disproportionate rise among midlife adults and females highlights a growing chronic

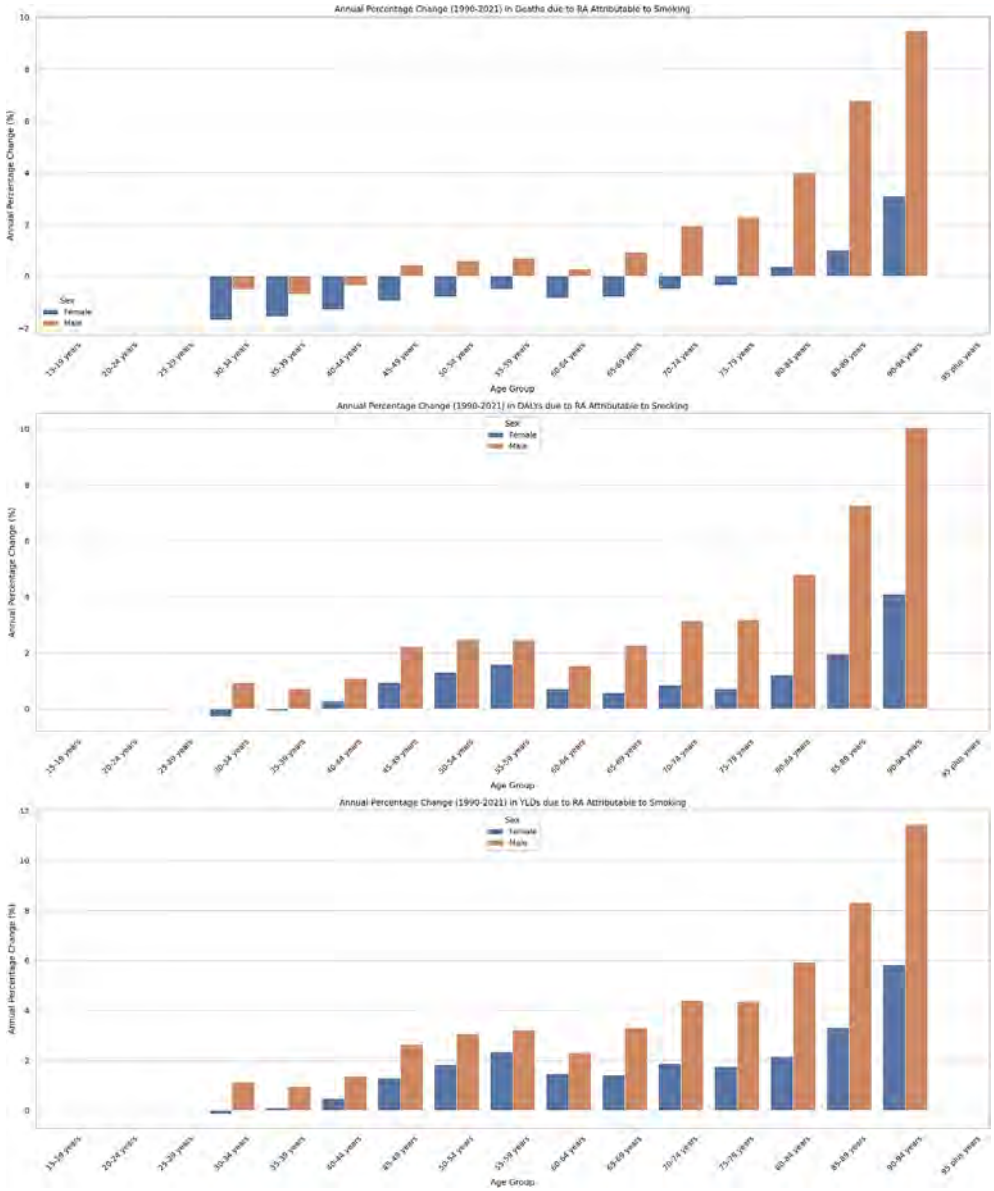


Global Burden of Rheumatoid Arthritis attributable to Smoking in 204 Countries and Territories from 1990-2021, Annual Percentage of change, Age-standardized DALYs rate per 100,000, Both Sexes



Global Burden of Rheumatoid Arthritis attributable to Smoking in 204 Countries and Territories from 1990-2021, Annual Percentage of change, Age-standardized Deaths rate per 100,000, Both Sexes

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Age-Sex wise Burden of Rheumatoid Arthritis attributable to Smoking in 204 Countries and Territories from 1990-2021, Annual Percentage of change, absolute counts-Deaths, DALYs, and YLDs.

disability gap. These findings emphasize the need for integrated, region-specific strategies that extend beyond tobacco cessation to address the long-term inflammatory consequences of smoking.

Disclosure: E. Kalra: None; **S. Rajpal**: None; **T. Parikh**: None; **D. Gajbhiye**: None; **C. Gundoji**: None; **S. Patel**: None; **J. Patel**: None; **N. Sinha**: None; **N. Rayarakula**: None; **D. Vaghani**: None; **H. Desai**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1891

Geographic Trends in the Burden of Gout in the United States from 1990 to 2021: A State-Level Analysis of Prevalence, Incidence, and Disability

Eva Kalra[1], Drumadala Gajbhiye[2], Chandana Tummala[3] and Hardik Dineshbhai Desai[4], [1]Trident Medical Center, North Charleston, SC, [2]Government medical college Akola Maharashtra India 444001, Akola, India, [3]Internal Medicine, Vydehi Institute Of Medical Sciences and Research Centre, Whitefield-560066, Bangalore, Karnataka, India, Banglore, India, [4]Ahmedabad, Gujarat, India, 382350, Ahmedabad, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1877–1913) Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

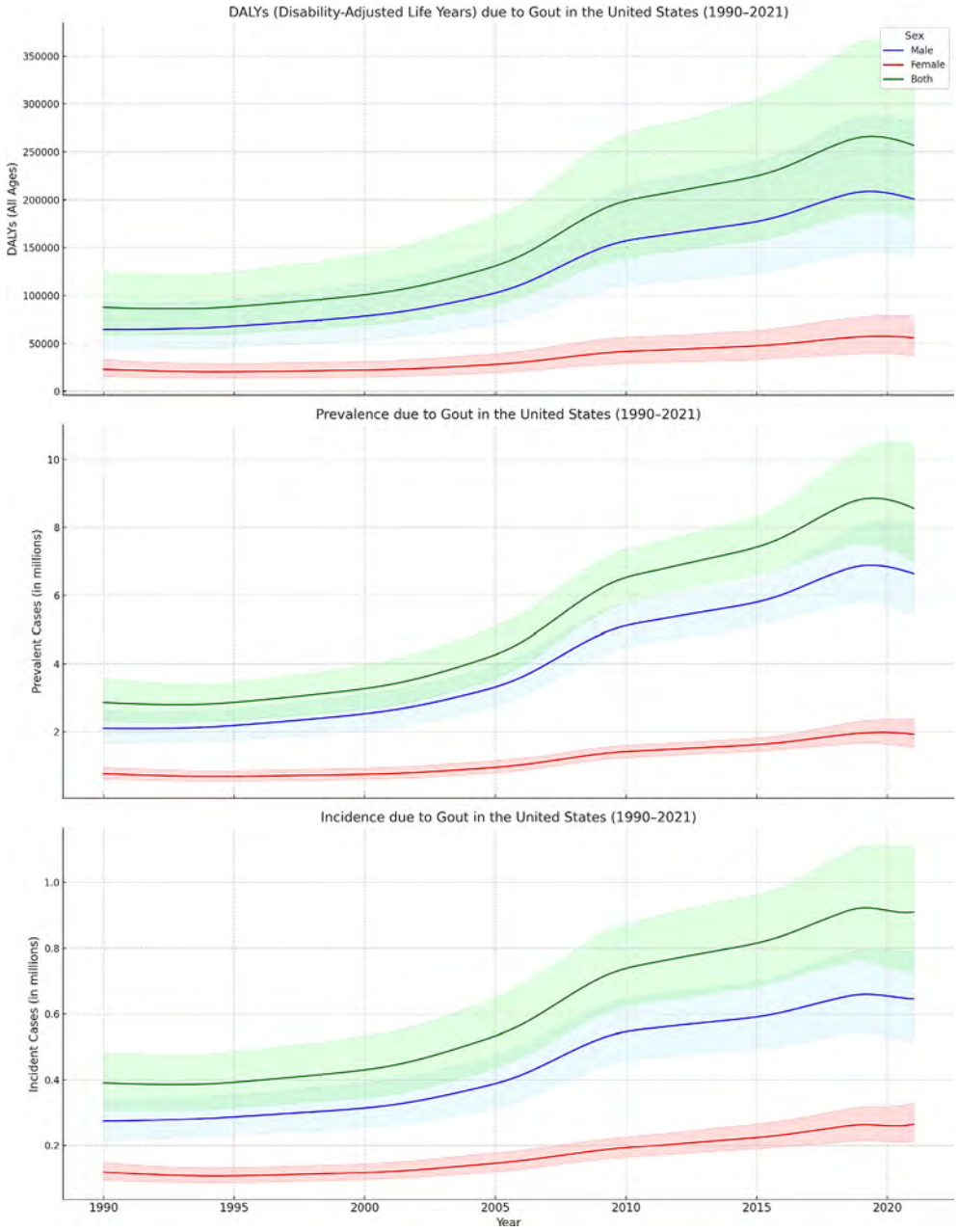
Background/Purpose: Gout, a chronic inflammatory arthritis driven by hyperuricemia, has become an increasingly significant cause of disability in the United States. Despite therapeutic advances, its rising burden and geographic disparities remain poorly understood. This study quantifies the long-term trends in gout-related prevalence, incidence, and years lived with disability (YLDs) across all 50 U.S. states from 1990 to 2021.

Methods: We utilized the Global Burden of Disease (GBD) 2021 study framework to estimate gout-related prevalence, incidence, and years lived with disability (YLDs) across all U.S. states from 1990 to 2021. Data were stratified by sex and analyzed at the state level. To assess temporal trends, we calculated the annualized percentage change (APC).

Results: Nationally, from 1990 to 2021, the age-standardized prevalence rate of gout increased from 1,036 to 1,723 per 100,000, incidence rose from 140 to 230 per 100,000, and YLDs grew from 31.8 to 56.4 per 100,000. The corresponding national APCs were 1.61% for prevalence, 1.45% for incidence, and 1.87% for YLDs. State-level analysis revealed the highest APC in YLDs occurred in Mississippi (2.12%), Georgia (2.10%), and Hawaii (2.09%), while the lowest was observed in Minnesota (1.50%). For prevalence, Mississippi (2.17%) and Georgia (2.12%) again led, whereas Minnesota (1.55%) and Maine (1.58%) showed the slowest rise. Incidence rates saw the steepest increase in Wyoming (1.40%) and Mississippi (1.38%), with the smallest change in Minnesota (0.89%). Sex-specific analysis showed consistently higher rates and steeper increases in males compared to females across all measures.

Conclusion: The burden of gout has risen substantially across the U.S. over the past three decades, with marked geographic heterogeneity. Southern states like Mississippi and Georgia experienced the fastest growth across all indicators. These findings underscore the urgent need for targeted public health interventions and equitable access to preventive and therapeutic gout care in high-burden regions.

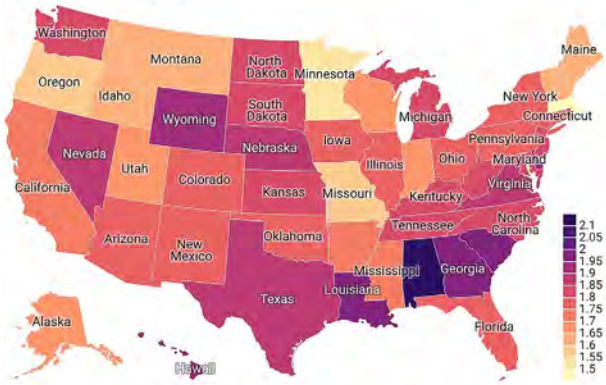
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

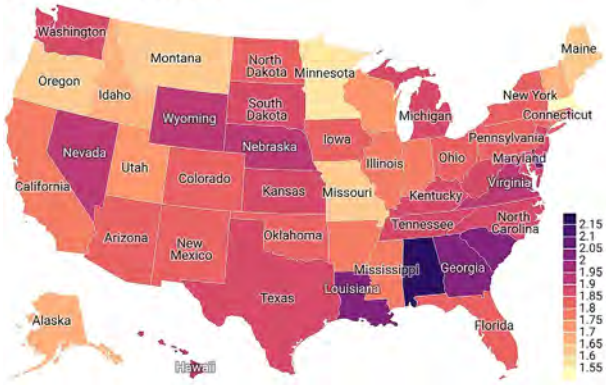
Annual Percentage of Change, YLDs Rate, Gout, USA from 1990-2021

Age-standardized Rate per 100,000



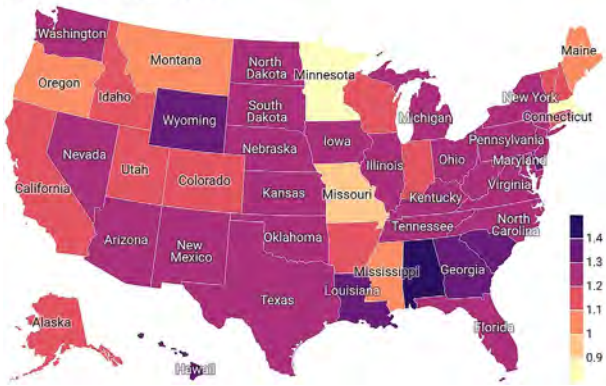
Annual Percentage of Change, Prevalence Rate, Gout, USA from 1990-2021

Age-standardized Rate per 100,000

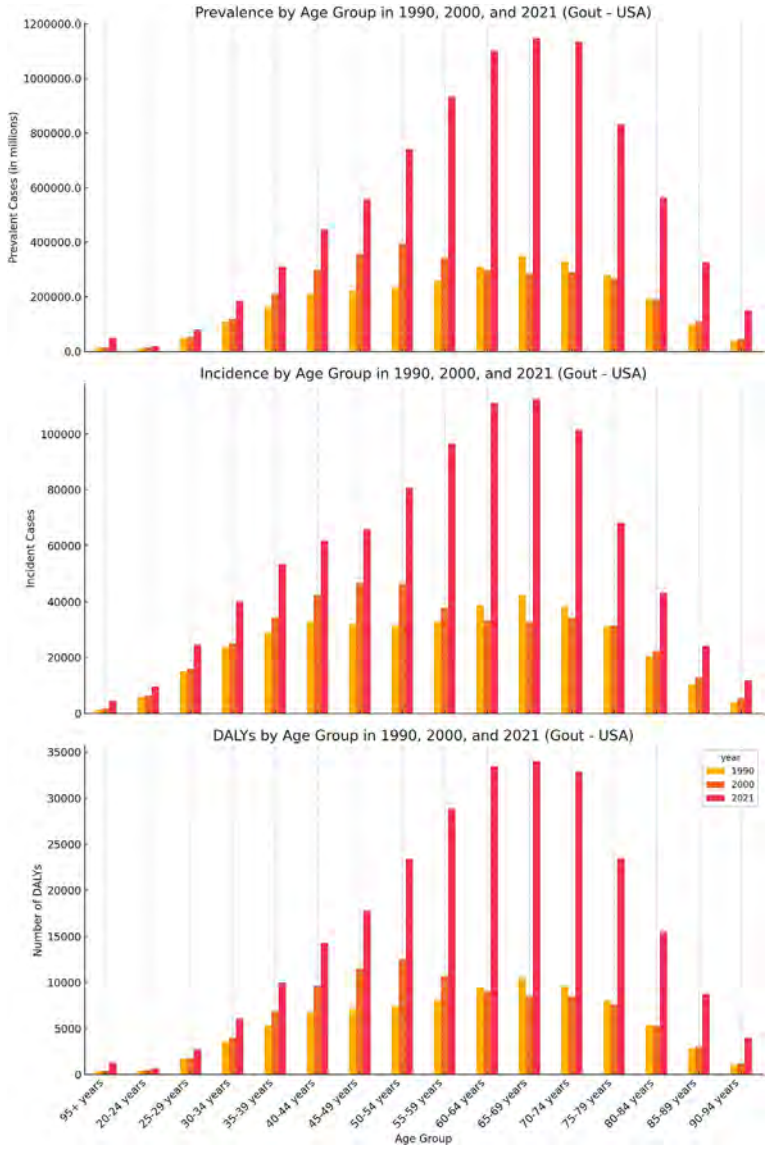


Annual Percentage of Change, Incidence Rate, Gout, USA from 1990-2021

Age-standardized Rate per 100,000



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: E. Kalra: None; **D. Gajbhiye**: None; **C. Tummala**: None; **H. Desai**: None.

Abstract Number: 1892

Impact of Systemic Lupus Erythematosus on In-Hospital Outcomes Following Percutaneous Coronary Intervention: Insights from a 7 year Nationwide Analysis

siddharth Agrawal[1], **Freya Shah**[1], Ritu Tated[2], Radhe Shah[3] and Mahir Modi[4], [1]landmark medical center, cumberland, RI, [2]New York Medical College, Vallaha, [3]Beth Israel Deaconess Medical Center, Boston, [4]GCS Medical College, hospital and Research Centre, Ahmedabad, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1877–1913) Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with systemic inflammation and heightened cardiovascular risk. However, the impact of SLE on outcomes following percutaneous coronary intervention (PCI) remains understudied. We aimed to evaluate in-hospital outcomes in SLE patients undergoing PCI.

Methods: We performed a retrospective analysis of the National Inpatient Sample from 2016 to 2022, identifying adult patients who underwent PCI. Patients were stratified based on the presence or absence of SLE. Multivariate logistic regression models adjusted for demographics, comorbidities, and hospital characteristics were used to assess outcomes. The primary outcome was in-hospital mortality; secondary outcomes included stroke, atrial fibrillation, heart failure, and bleeding complications.

Results: Of 3,132,560 PCI hospitalizations, 12,765 (0.4%) involved patients with SLE. Compared with non-SLE patients, SLE patients were younger, more likely to be female (78.7% vs 32.5%), and more often Black (23.5% vs 9.6%) (all p< 0.001). SLE patients had a higher prevalence of hypertension, anemia, chronic kidney disease, peripheral arterial disease,

Table 1. Baseline Characteristics of Patients Undergoing PCI, Stratified by SLE Status

Variable	No SLE (n=3,119,795)	SLE (n=12,765)	P-value
Age			<0.001
18–34 years	0.60%	2.32%	
35–49 years	9.57%	15.54%	
50–64 years	35.60%	41.90%	
65–79 years	39.78%	32.81%	
≥80 years	14.45%	7.38%	
Sex			<0.001
Male	67.48%	21.27%	
Female	32.52%	78.73%	
Race			<0.001
White	75.10%	61.19%	
Black	9.59%	23.47%	
Hispanic	8.39%	9.69%	
Asian/Pacific Islander	2.88%	2.28%	
Native American	0.59%	0.85%	
Other	3.44%	2.51%	
Comorbidities			
Hypertension	82.86%	84.69%	<0.001
Diabetes Mellitus	51.41%	45.21%	<0.001
Hyperlipidemia	67.48%	60.71%	<0.001
Anemia	14.00%	26.37%	<0.001
COPD	14.10%	17.70%	<0.001
Peripheral Arterial Disease	7.57%	12.87%	<0.001
CKD (Stage 4+)	17.27%	20.49%	<0.001
ESRD	4.00%	9.77%	<0.001
Coagulation Disorders	6.48%	10.00%	<0.001
Obesity	24.00%	25.24%	0.001
OSA	9.57%	9.89%	0.001
Tobacco Use	26.00%	23.67%	<0.001
Drug Use	26.10%	26.65%	0.334
Prior PCI	31.00%	31.83%	0.04
Prior Heart Surgery	27.69%	28.41%	0.06
Family History of CAD	15.62%	14.91%	0.02
Hospital Characteristics			
Medicare/Medicaid	63.55%	70.49%	<0.001
Private Insurance	28.23%	24.80%	
Self-pay/Other	8.22%	4.71%	
Teaching Hospital	74.57%	77.79%	<0.001
Length of Stay (days)	4.0 ± 5.1	4.4 ± 4.6	<0.001
Total Charges (USD)	1,25,716.74	1,27,578.16	<0.001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adjusted In-Hospital Outcomes for SLE vs Non-SLE Patients Undergoing PCI

Outcome	Adjusted Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Death	0.954	0.856–1.063	0.3905
Stroke	1.407	1.348–1.474	<0.001
Atrial Fibrillation	1.078	1.022–1.136	0.005
Heart Failure	1.023	0.983–1.066	0.281
Bleeding Complication	1.147	1.051–1.253	0.002

and coagulation disorders. There was no significant difference in adjusted in-hospital mortality between groups (OR 0.954, 95% CI 0.856–1.063, p=0.391). However, SLE was associated with higher odds of stroke (OR 1.407, 95% CI 1.348–1.474, p< 0.001), atrial fibrillation (OR 1.078, 95% CI 1.022–1.136, p=0.005), and bleeding complications (OR 1.147, 95% CI 1.051–1.253, p=0.002). No significant difference was observed in the incidence of heart failure.

Conclusion: Among patients undergoing PCI, SLE is associated with increased risks of stroke, atrial fibrillation, and bleeding, but similar in-hospital mortality compared to non-SLE patients. Focused risk mitigation strategies may improve outcomes in this high-risk population.

Disclosure: s. Agrawal: None; **F. Shah**: None; **R. Tated**: None; **R. Shah**: None; **M. Modi**: None.

Abstract Number: 1893

Increased Atrial Fibrillation Risk in Rheumatoid Arthritis: Greater in Seropositive Than Seronegative Patients

Hyungjin Kim[1], Seonyoung Kang[2], Kyungdo Han[3], Jinhyung Jung[4], Seulkee Lee[5], Hoon-Suk Cha[5], Jaejoon Lee[6], Seonghye Kim[5] and Se Yun Kim[7], [1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, [2]Samsung Medical Center, Sungkyunkwan University School of Medicine, Gangnam-gu, Seoul, Republic of Korea, [3]Soongsil University, Seoul, Republic of Korea, [4]Sungkyunkwan University School of Medicine, Suwon, Republic of Korea, [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [6]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [7]Sungkyunkwan University, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The association between rheumatoid arthritis (RA) and cardiovascular disease (CVD) is well-established, with systemic inflammation as a potential mechanism. Although atrial fibrillation (AF) is the most common arrhythmia, the link between RA and AF has received less attention compared to other CVD traits like myocardial infarction and stroke.

This study aimed to examine the association between RA and incident AF in Republic of Korea, considering serostatus (seropositive RA [SPRA], seronegative RA [SNRA]) and the use of biologic or targeted synthetic DMARDs (b/tsDMARDs).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This retrospective cohort study used the National Health Insurance Service database to include participants (aged ≥40 years) who were first diagnosed with RA between 2010 and 2017, had no previous AF, and who had a health checkup within 2 years before the index date (to collect covariate information). Matched non-RA controls were selected at a 1:3 ratio by age, sex, and index date. Participants were followed from 1 year after the index date until December 31, 2020, to mitigate surveillance bias.

Results: Totals of 48,885 RA patients (34,699 SPRA, 14,186 SNRA) and 146,655 matched controls were included. Patients with RA had a significantly higher risk of AF than did controls (adjusted hazard ratio [aHR] 1.55, 95% confidence interval [95% CI] 1.46-1.65). Both patients with SPRA (aHR 1.63, 95% CI 1.52-1.74) and SNRA (aHR 1.37, 95% CI 1.23-1.53) had a higher AF risk than did those without RA. Patients with SPRA had a higher risk compared to those with SNRA (aHR 1.19, 95% CI 1.02-6.34). The use of bDMARDs was associated with a slightly higher risk of AF, while tsDMARD use led to risk reduction but, non-statistical significant.

Conclusion: This study shows that both patients with SPRA and SNRA are at a significantly greater risk for AF compared to those without RA, with SPRA patients at the highest risk. The use of b/tsDMARDs might be associated with RA-related AF, but further studies are warranted to confirm this association and understand the underlying mechanisms.

Disclosure: H. Kim: None; **S. Kang**: None; **K. Han**: None; **J. Jung**: None; **S. Lee**: None; **H. Cha**: None; **J. Lee**: Samsung Bioepis, 5; **S. Kim**: None; **S. Kim**: None.

Abstract Number: 1894

Opioid Use Disorder Among Patients with Rheumatic Conditions in the *All of Us* Research Program: A Descriptive Analysis

Jacob Riegler[1], Leah Santacroce[2], Karen H. Costenbader[3] and Candace Feldman[4], [1]Cambridge Health Alliance, Harvard Medical School, Somerville, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital/ Harvard Medical School, Boston

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Opioid use disorder (OUD) is associated with high morbidity and mortality and in the U.S. in 2022, resulted in over 81,000 overdose deaths.[1] However, little is known about the prevalence of OUD in patients with rheumatic disease (RMD). Medications for OUD (MOUD; buprenorphine, methadone, naltrexone) are known to reduce mortality in OUD, yet no study has examined the use of MOUD in patients with RMD. This study had two primary objectives: to describe the population of patients with RMD with and without OUD and to assess use of MOUD in this population.

Methods: The data source used in this study was the All of Us Research Program (version 8), a national cohort consisting of electronic medical records for > 393,000 enrolled U.S. adults. We identified those with ≥2 ICD-9/10 or SNOMED codes for RA, SLE, spondyloarthritis (SpA), or osteoarthritis ≤ 2 years pre-enrollment. Patients with OUD were identified with ≥1 ICD 9/10 or SNOMED code for opioid dependence or abuse that occurred after the first code for RMD. Demographic characteristics (race, age at enrollment, sex at birth, insurance type), prevalent psychiatric disorders (bipolar disorder, schizophrenia, schizoaffective disorder, borderline personality disorder, depression, anxiety, and post-traumatic stress disorder),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with RMD in the All of Us Research Program (version 8) by the presence of opioid use disorder

	Without Opioid Use Disorder (n=35,780)	With Opioid use Disorder (n=1,502)	*p* value*
Age at enrollment, mean years (SD)	63.7 (12.4)	57.5 (11.6)	<0.001
Sex at birth, N (%)			0.037
Female	24,345 (68.0)	993 (66.1)	
Male	10,985 (30.7)	480 (32.0)	
Other/Prefer not to answer/skipped	450 (1.3)	29 (1.9)	
Self-reported Race and Ethnicity [a], N (%)			<0.001
Black	6,222 (17.4)	374 (24.9)	
Hispanic	4,065 (11.4)	180 (12.0)	
White	22,133 (61.9)	761 (50.7)	
Other/Missing	2,008 (5.6)	88 (5.9)	
> 1	1,352 (3.8)	99 (6.6)	
Insurance category, N (%)			<0.001
Commercial	10,358 (32.4)	183 (14.6)	
Medicaid	7,304 (22.9)	635 (50.7)	
Medicare	11,198 (35.1)	327 (26.1)	
Other/Missing	3,068 (9.6)	107 (8.5)	
Rheumatic Disease, N (%)			<0.001
Osteoarthritis	29,033 (81.1)	1,119 (74.5)	
Rheumatoid Arthritis	4,136 (11.6)	216 (14.4)	
Systemic lupus erythematosus	2,023 (5.7)	137 (9.1)	
Spondyloarthritis	588 (1.6)	30 (2.0)	
Psychiatric diagnoses [a,b], N (%)			<0.001
Bipolar disorder	2,007 (5.6)	285 (19.0)	
Schizophrenia	232 (0.6)	33 (2.2)	
Schizoaffective disorder	213 (0.6)	29 (1.9)	
Borderline personality disorder	138 (0.4)	28 (1.9)	
Depression	3,460 (9.7)	297 (19.8)	
Anxiety	7,875 (22.0)	739 (49.2)	
PTSD	1,544 (4.3)	165 (11.)	
Charlson comorbidity index [b], mean (SD)	1.9 (2.4)	3.1 (2.9)	<0.001
ER visits and inpatient admissions [b], mean (SD)	3.6 (9.3)	7.3 (14.5)	<0.001

*Chi square tests calculated for categorical variables and t tests calculated for continuous variables
[a] Cell sizes <20 suppressed per All of Us reporting requirements. Asian race was collapsed into the other category and obsessive-compulsive disorder was not shown here due to reporting guidelines.
[b] Catalogued ≤ 1 year prior to first opioid use disorder code

Charleson comorbidity index (CCI), and acute care utilization (emergency department [ED] visits, hospitalizations) ≤ 1 year prior to first OUD code were compared between patients with RMD with and without OUD. We identified a subset of patients with OUD codes and no prior MOUD use at any point prior to the first OUD code and examined differences in patient characteristics between those who received MOUD vs. did not in the subsequent period.

Results: Among 37,282 patients with RMD, we identified 1,502 (4%) with OUD billing codes (Table 1). Patients with vs. without OUD were younger, had more comorbidities, had higher acute care utilization, were more likely to have Medicaid insurance, and had a higher prevalence of psychiatric diagnoses, including psychotic and mood disorders. Patients with vs. without OUD were more likely to have RA, SLE, and SpA diagnoses. MOUD was initiated in 163/1121 (14.5%) patients. Patients who received vs did not receive MOUD were younger (mean (SD) age 55.6 (12.3) $p = 0.003$), had fewer comorbidities (CCI (SD) 2.6 (2.6) vs 3.3 (3.1) $p = 0.001$) more likely to be male (42.9% vs 27.7% $p < 0.001$), and were more likely to have PTSD (14.1% vs 8.7% $p = 0.04$).

Conclusion: In this nationwide population with RMD, we found demographic, clinical and psychiatric differences among patients with RMD with vs. without OUD. General population estimates of MOUD are around 25%, which is higher than in this RMD population.[1] Future research is needed to understand the barriers that exist for patients with RMD and OUD to receiving MOUD, the influence of social risk factors on development and treatment of OUD, and the role of increased screening for psychiatric disorders with comorbid OUD and RMD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

1. Dowell D, Brown S, Gyawali S, et al. Treatment for Opioid Use Disorder: Population Estimates — United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2024;73(25):567-574. doi:10.15585/mmwr.mm7325a1

Disclosure: J. Riegler: None; **L. Santacroce**: None; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **C. Feldman**: American College of Rheumatology, 2, 12, Committee Member/Interim Chair, Arthritis Foundation, 5, 12, Task Force Member, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 2, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2.

Abstract Number: 1895

Assessing the Validity of Self-reported Medication Data Through Metabolite Analysis: Data from the Osteoarthritis Initiative

Kate Lapane[1], Anne Hume[2], **Jeffrey Driban**[3], Shao-Hsien Liu[1], Timothy McAlington[4], Charles Eaton[5], Shike Xu[6] and Bing Lu[7], [1]UMass Chan Medical School, Worcester, MA, [2]College of Pharmacy, University of Rhode Island, Kingston, RI, [3]University of Massachusetts Chan Medical School, Marlborough, NH, [4]UMass Chan School of Medicine, Arlington, MA, [5]Brown University, Pawtucket, RI, [6]University of Connecticut Health Center, Farmington, CT, [7]UConn Health Center, Newton, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Pharmacotherapy, including non-steroidal anti-inflammatory agents (NSAIDs), is commonly used to alleviate symptoms of osteoarthritis (OA); however, these medications may increase the risk of adverse effects and drug interactions, especially in older adults taking multiple medications for other comorbid conditions. Accurate documentation of medication use in OA research is important and is often based on self-report. While self-reported medication use provides insights into real-world patterns of medication use, its validity in research studies remains largely unknown. In this study, we evaluated the validity of the Osteoarthritis Initiative's (OAI) medication inventory form by comparing self-reported use with metabolites or active ingredients measured in plasma.

Methods: The OAI had a structured protocol to collect detailed information on prescription medications. Participants were told to bring all medications used in the 30 days before each study visit. The study staff then recorded all the prescription medications. If a participant forgot to bring their medications, the interviewer relied on a medication list or conducted a follow-up call to complete the medication inventory form. Although drug metabolites and active ingredients were not routinely measured in the OAI, a case-cohort sub-study that included 465 participants had plasma assayed using liquid chromatography-tandem mass spectrometry. We calculated sensitivity, specificity, and kappa statistics for the most commonly reported medications with metabolite or active ingredient plasma levels.

Results: Among the 465 participants, 301 (65%) were females, 197 (42%) had frequent knee pain, and the mean age was 60 years (SD=9) with a mean body mass index of 27.8 kg/m^2 (SD=4.6). Table 1 shows strong agreement between self-report and presence of metabolites for antihypertensive medications (e.g., hydrochlorothiazide κ=0.71) and anti-diabetic medications (e.g., metformin κ=0.97), with sensitivity exceeding 85% and specificity exceeding 90%. For NSAIDs, we found strong agreement for celecoxib (κ=0.94), but not naproxen (κ=0.42) or ibuprofen (κ=0.23). While specificity was high for celecoxib, naproxen, and ibuprofen (>97%), sensitivity was high only for celecoxib.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Sensitivity, Specificity, and Kappa Agreement of Self-reported Medication Use and Detectable Presence of Metabolite/Active Ingredients

Table. Sensitivity, Specificity, and Kappa Agreement of Self-reported Medication Use and Detectable Presence of Metabolite/Active Ingredients

	Self-reported	Detectable Presence of Metabolite/Active Ingredient Yes	No	Prevalence of self-reported use	Sensitivity	Specificity	Kappa (95% CI)
					Percentages		
Hydrochlorothiazide	Yes	62	31	20.0	87.3	92.1	0.71 (0.62-0.79)
	No	9	363				
Atenolol	Yes	30	2	6.9	100.0	99.5	0.97 (0.92-1.00)
	No	0	433				
Metformin	Yes	20	0	4.3	95.2	100	0.97 (0.92-1.00)
	No	1	444				
Celecoxib	Yes	24	3	5.8	100.0	99.3	0.94 (0.87-1.00)
	No	0	438				
Naproxen	Yes	17	2	4.1	30.9	99.5	0.42 (0.28-0.57)
	No	38	408				
Ibuprofen	Yes	6	11	3.7	19.4	97.5	0.23 (0.11-0.36)
	No	25	423				
Omeprazole	Yes	12	5	3.7	40.0	98.9	0.49 (0.31-0.67)
	No	18	430				

Note. 95% CI = 95% confidence interval

Conclusion: The validity of self-reported medication use in the OAI varied by medication. Sensitivity and agreement were high for some medications but lower for others. The three medications with low sensitivity were the only ones we examined that were available over the counter at the baseline visit (2004-2006). Specificity was high across all medications. These findings highlight the need to consider potential misclassification for specific drug classes when using the data from the OAI medication inventory, as some classes offer more reliable and higher accuracy of self-reported medication use than others.

Disclosure: K. Lapane: None; **A. Hume**: None; **J. Driban**: None; **S. Liu**: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **C. Eaton**: None; **S. Xu**: None; **B. Lu**: None.

Abstract Number: 1896

Electronic Cigarette Use in Association with Risks of Developing Rheumatoid Arthritis or Systemic Lupus Erythematosus in the All of Us Research Program

Jeong Yee[1], Emily Oakes[2], Candace Feldman[3] and Karen H. Costenbader[4], [1]Sungkyunkwan University, Suwon, MA, South Korea, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital/ Harvard Medical School, Boston, [4]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Electronic cigarettes, or e-cigarettes, are inhalable aerosol nicotine-delivery devices increasingly used in addition or in place of cigarettes. Cigarette smoking is strongly associated with an at least ~1.5-fold increased risk of both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). The association of e-cigarettes with RA and SLE risk has not been well studied, however. We investigated e-cigarette use and risks of developing RA or SLE in a nationwide US cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We used data from the All of Us Research Program (version 8), comprised of >393,000 U.S. adults with linked electronic health records. Using a matched cohort design, we identified participants with baseline self-reported ever use of e-cigarettes, including electronic nicotine products such as vape pens and hookah pens. We created a cohort matched on age, sex at birth, race/ethnicity, enrollment year, and cigarette smoking status, without any e-cigarette use. The primary outcome was RA or SLE, identified by ≥ 2 ICD9, ICD10, or SNOMED codes. After excluding those with RA or SLE pre-enrollment, individuals were followed from enrollment until 1st occurrence of RA or SLE, death, end of study period (October 1, 2023), or up to 5 years, whichever occurred first. We estimated incidence rates (IRs) and an incidence rate ratio (IRR) and plotted the cumulative incidence curves. Stratified and interaction analyses by cigarette smoking status were performed.

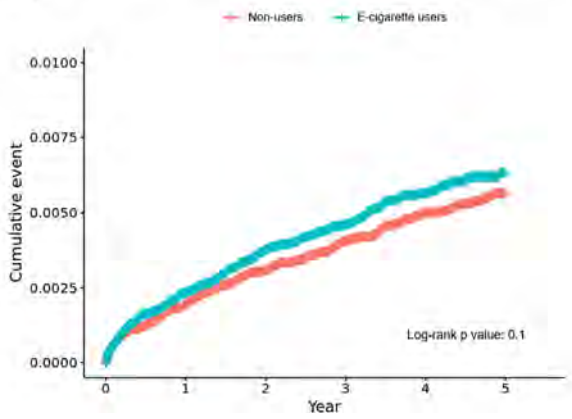
Results: We identified 60,285 e-cigarette users and 60,285 matched non-users (**Table 1**). The mean age was 40 (SD 14) years and 40% were male; 65% were ever smokers. A total of 271 cases developed among e-cigarette users in 182,978 person-years (IR 1.48 [95% CI 1.31-1.67]) vs 239 incident cases among matched non-users in 186,127 person-years (IR 1.28, 95% CI 1.13-1.46; IRR 1.15 [95% CI: 0.97-1.37]). E-cigarette users had a not statistically significant higher risk of RA or SLE (p 0.1, **Figure 1**). In analyses stratified by smoking status, a similar trend was observed among smokers, while

Table 1. Baseline Characteristics of Study Population in the All of Us Research Program (version 8) by Baseline Self-Report of E-Cigarette Use

	E-Cigarette User Cohort (n=60,285)	Matched E-Cigarette Non-user Cohort (n=60,285)
***Age**, mean years (SD)	39.9 (14.5)	40.9 (14.4)
***Male at birth**, N (%)	24,347 (40.4)	23,687 (39.3)
***Self-reported Race/Ethnicity**, N (%)		
Black	8,853 (14.7)	10,708 (17.8)
Hispanic	11,561 (19.2)	12,037 (20.0)
White	31,762 (52.7)	29,459 (48.9)
Others	8,109 (13.5)	8,081 (13.4)
≤ High school education, N (%)	19,389 (32.7)	20,609 (34.9)
Annual household income <$35,000, N (%)	26,502 (51.6)	21,859 (45.0)
U.S. region of residence, N (%)		
Northeast	14,619 (24.3)	15,324 (25.4)
South	10,857 (18.0)	11,255 (18.7)
Midwest	13,468 (22.4)	15,292 (25.4)
West	21,296 (35.4)	18,358 (30.5)
***Self-reported ever smoking**, N (%)	40,606 (67.4)	39,221 (65.1)
Follow-up, years (mean, SD)	3.04 (1.74)	3.09 (1.72)

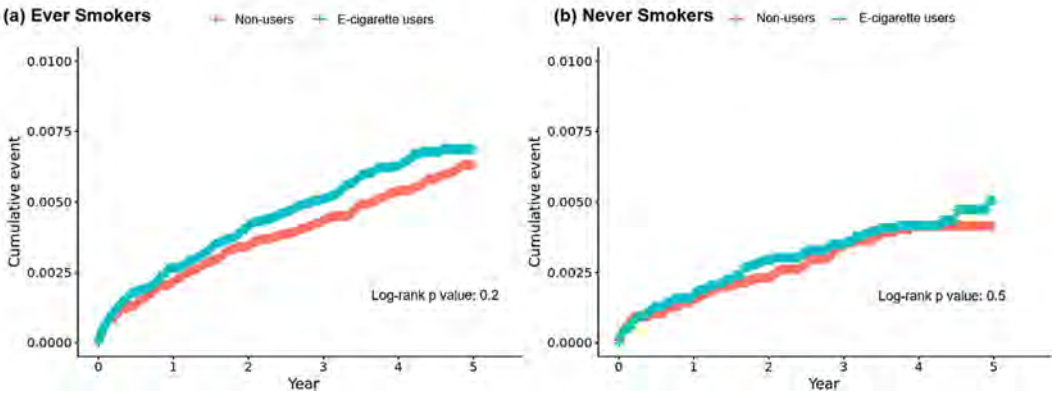
Missing data: education level in 2,138 participants, income in 20,624 participants, region of residence in 101 participants.
* matching factors

Figure 1. Cumulative incidence curves for the time to rheumatoid arthritis or systemic lupus erythematosus comparing e-cigarette users and non-users at baseline within the All of Us Research Program (version 8).



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Cumulative incidence curves for the time to rheumatoid arthritis or systemic lupus erythematosus between e-cigarette users and non-users within the All of Us Research Program (version 8), stratified by smoking status. (a) Smokers. (b) Non-smokers.



the risk of RA or SLE was comparable between e-cigarette users and non-users among non-smokers (**Figure 2**). No statistically significant interaction according to smoking status was observed on either the additive or multiplicative scale.

Conclusion: Our findings suggest that e-cigarette users may have a slightly higher risk of developing RA or SLE vs. non-users, especially in smokers. Key considerations in interpreting these results include that a substantial proportion of e-cigarette users were smokers, a known risk factors for RA and SLE itself and the intensity of smoking and e-cigarette use were not well captured by the survey. E-cigarette users were also younger, although we matched by age to limit age-related bias. Further studies are warranted, particularly those assessing the amount, frequency, or duration of e-cigarette use.

Disclosure: J. Yee: None; **E. Oakes**: None; **C. Feldman**: American College of Rheumatology, 2, 12, Committee Member/Interim Chair, Arthritis Foundation, 5, 12, Task Force Member, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 2, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 1897

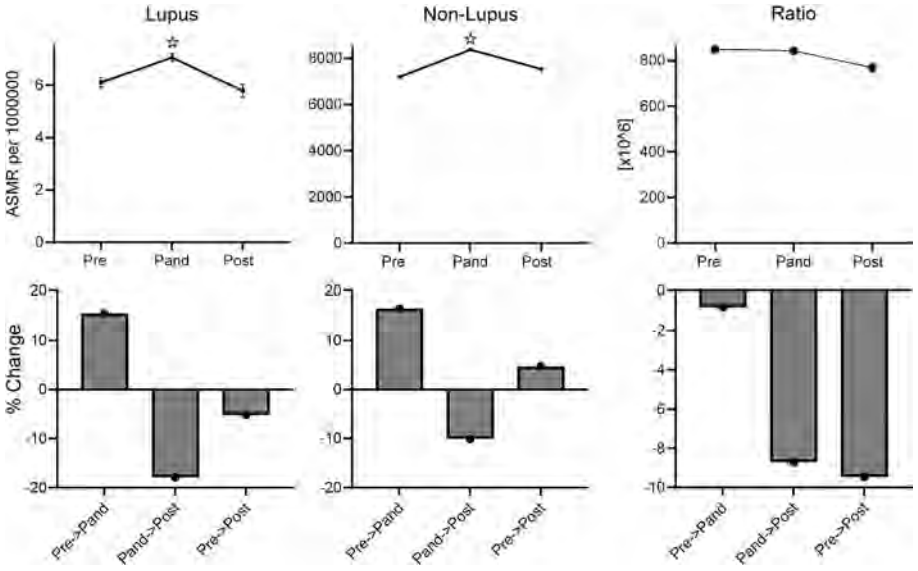
Changes in SLE Mortality During and After the COVID-19 Pandemic

Laura Hernandez[1] and Ram Singh[2], [1]University of California, Los Angeles, Murrieta, CA, [2]UCLA David Geffen School of Medicine, Los Angeles, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are vulnerable to infections due to both underlying immune dysfunction and the use of immunosuppressive therapies. Hence, it was assumed that patients with SLE would experience disproportionately poor outcomes during the COVID-19 pandemic. We aimed to evaluate changes in SLE mortality in relation to the COVID-19 pandemic: before (2018–2019), during (2020–2022), and after (2023); and to assess whether these trends differed from all-cause mortality.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Age standardized mortality rates for SLE before (2018-2019), during (2020-2022), and after (2023) the COVID-19 pandemic.

Methods: We retrieved mortality data for SLE from the CDC national mortality database, and calculated age-standardized mortality rates (ASMRs) per million population with 95% confidence intervals (CI), overall and by race/ethnicity, age group (≤44, 45–64, ≥65 years), sex, and U.S. census region (Northeast, Midwest, South, West) across three time periods: pre-pandemic (2018–2019), during the pandemic (2020–2022), and post-pandemic (2023). We repeated these analyses for all-cause deaths other than SLE (non-SLE). We then computed ratios of SLE ASMR to non-SLE ASMR to contextualize lupus mortality within overall general population mortality trends. We performed percent change calculations between the three periods.

Results: SLE-ASMR increased from 6.1 per million (95% CI, 5.9–6.3) pre-pandemic to 7.1 (95% CI: 6.9–7.2) during the pandemic, before declining to 5.8 (95% CI: 5.5–6.0) post-pandemic. Non-SLE ASMR followed a similar trend, however, non-SLE ASMR remained significantly elevated post-pandemic compared to pre-pandemic levels. Consequently, the ratio of SLE-ASMR to non-SLE-ASMR continued to decline from the pre-pandemic to pandemic years (by 0.83%) and from the pandemic to post-pandemic years (by 8.71%). This trend was seen in all subpopulations by race/ethnicity, age, sex, and geographic region, except in individuals aged ≥65 years and those living in the South census region of the U.S. that experienced increases in the ratio.

Conclusion: This nationwide analysis shows that SLE mortality did not increase disproportionately during the COVID-19 pandemic, and that it declined more than the all-cause mortality after the pandemic. However, certain subgroups including older individuals and people in the South, experienced relatively higher SLE mortality during the pandemic. Further analyses of reasons underlying these trends, including the precise identification of subpopulations in the South that had the highest SLE mortality during the pandemic, would have implications for managing these at-risk subpopulations during future viral outbreaks and medical emergencies.

Disclosure: L. Hernandez: None; **R. Singh**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1898

Assessing Representation in a Nation-wide Psoriasis Registry: A Single-institution Comparison

Evelyn Fagan[1], Joseph McGrath[1], Calla Sullivan[1], **Mackenzie Kilton**[1], Kaeli Samson[2], Kaleb Michaud[3] and Sarah Lonowski[1], [1]University of Nebraska Medical Center Department of Dermatology, Omaha, NE, [2]University of Nebraska Medical Center Department of Biostatistics, Omaha, NE, [3]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Ensuring that data registries include a representative sample is crucial for obtaining findings that can be generalized to the larger population. This comparative observational study sought to determine whether participants with psoriasis and psoriatic arthritis, enrolled in the FORWARD Psoriasis Registry, reflect the broader invited population at a single institution.

Table 1. Demographic Characteristics and Comorbidities in Enrolled and Invited Psoriasis FORWARD Registry Groups

	Enrolled (n=113)	Invited (n=804)	P-value
Age			0.004[1]
Mean (SD)	48.8 (15.7)	53.5 (16.3)	
Median (IQR)	48.0 (36.0, 61.0)	54.0 (41.0, 67.0)	
Sex, n (%)			0.400[2]
Male	41/113 (36.3%)	325/804 (40.4%)	
Female	72/113 (63.7%)	479/804 (59.6%)	
Race, n (%)			0.801[2]
White	103/112 (92.0%)	722/791 (91.3%)	
Non-white	9/112 (8.0%%)	69/791 (8.7%)	
Ethnicity, n (%)			0.413[2]
Non-Hispanic	105/112 (93.8%)	764/800 (95.5%)	
Hispanic	7/112 (6.3%)	36/800 (4.5%)	
Rurality, n (%)			0.589[2]
Urban	104/113 (92.9%)	750/803 (93.4%)	
Rural	9/113 (8.0%)	53/803 (6.6%)	
Insurance			0.013[2]
Medicare	23/113 (20.4%)	262/781 (33.5%)	
Medicaid	9/113 (8.0%)	39/781 (5.0%)	
Private	81/113 (71.7%)	480/781 (61.5%)	
Smoking status, n (%)			0.168[2]
Non-Smoker	64/113 (56.6%)	423/800 (52.9%)	
Current	7/113 (6.2%)	98/800 (12.3%)	
Former	42/113 (37.2%)	279/800 (34.9%)	
Comorbidities			
Obesity, n (%)	59/113 (52.2%)	398/798 (49.9%)	0.642[2]
Hypertension, n (%)	51/113 (45.1%)	374/804 (46.5%)	0.782[2]
Hyperlipidemia, n (%)	43/113 (38.1)	358/804 (44.5%)	0.194[2]
Thromboembolic event, n (%)	9/113 (8.0%)	82/804 (10.2%)	0.457[2]
Diabetes, n (%)	18/113 (15.9%)	167/804 (20.8%)	0.230[2]
Psoriatic arthritis, n (%)	30/113 (26.5%)	136/804 (16.9%)	0.013[2]

[1]Equal variance two sample t-test p-value; [2]Chi-Square p-value

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The FORWARD Psoriasis Registry is a multi-institutional, prospective U.S. study collecting patient-reported outcomes via online questionnaires.1 Patients with "psoriasis" documented in their medical record were invited to the registry via email. Enrollment status was tracked, and medical records were reviewed for demographics, comorbidities, dermatology visits, and current and past psoriasis therapies. Patients without a confirmed psoriasis diagnosis were excluded. Chi-squared, Fisher's Exact, Wilcoxon rank sum, and equal variance t-tests were used to compare enrolled and non-enrolled groups.

Results: Of 917 patients invited, 113 enrolled (12%) and 804 (88%) did not. Enrollees were younger than non-enrollees (mean age 48.8 vs. 53.5; p=0.004), and insurance type varied significantly between groups (p=0.013). Enrollees had a higher proportion of private insurance while non-enrollees were more likely to have Medicare. Enrollees and non-enrollees did not differ across other demographic variables. Rates of obesity, hypertension, hyperlipidemia, thromboembolic events, and diabetes were not significantly different between groups. However, psoriatic arthritis was more common among enrollees (26.5% vs. 16.9%; p=0.013) (Table 1). Plaque psoriasis was the most common psoriasis phenotype among both enrollees and non-enrollees, and the proportion of those with plaque psoriasis did not vary between groups (p=0.455). The use of topical and biologic therapy did not differ between groups, though there was a significantly greater proportion of enrollees who utilized non-biologic systemic therapy in the past (34.5% vs. 24.9%; p=0.029) (Table 2).

Table 2. Psoriasis Phenotype and Therapy Usage in Enrolled vs. Invited Psoriasis FORWARD Registry Groups

	Enrolled (n=113)	Invited (n=804)	P-value
Phenotype			0.455[1]
Plaque psoriasis	88/107 (82.2%)	622/786 (79.1%)	
All other types	19/107 (17.8%)	164/786 (20.9%)	
Guttate	3/107 (2.8%)	26/786 (3.3%)	
Pustular	6/107 (5.6%)	14/786 (1.8%)	
Inverse	1/107 (0.9%)	31/786 (3.9%)	
Sebopsoriasis	2/107 (1.9%)	60/786 (7.6%)	
Erythrodermic	0/107 (0.0%)	1/786 (0.1%)	
Isolated nail psoriasis	0/107 (0.0%)	4/786 (0.5%)	
Multiple	7/107 (6.5%)	28/786 (3.6%)	
Therapy			
Current use of topicals	101/113 (89.4%)	684/796 (85.9%)	0.317[1]
Previous use of topicals	2/111 (1.8%)	756/793 (95.3%)	0.215[2]
Current use of biologics	38/113 (33.6%)	202/797 (25.3%)	0.061[1]
Previous use of biologics	43/112 (38.4%)	250/795 (31.4%)	0.141[1]
Current use of non-biologic systemics	19/113 (16.8%)	89/796 (11.2%)	0.082[1]
Previous use of non-biologic systemics	39/113 (34.5%)	200/796 (25.1%)	0.029[1]
Total # of biologics			0.081[3]
Mean (SD)	2.2 (1.48)	1.9 (1.29)	
Median (IQR)	2.0 (1.0, 3.0)	1.0 (1.0, 2.0)	
Total # of non-biologic systemics			0.029[3]
Mean (SD)	1.7 (0.98)	1.3 (0.63)	
Median (IQR)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	
Number of UNMC/NM dermatology visits			0.638[3]
Mean (SD)	4.5 (3.68)	4.5 (3.61)	
Median (IQR)	4.0 (2.0, 6.0)	4.0 (2.0, 6.0)	
Days since last dermatology visit			0.039[3]
Mean (SD)	266.3 (233.26)	309.8 (240.62)	
Median (IQR)	205.0 (108.0, 341.5)	226.0 (125.0, 423.5)	

[1]Chi-Square p-value; [2]Fisher Exact p-value; [3]Wilcoxon rank sum p-value

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Enrollees were broadly representative of those who were invited across demographic and cardiometabolic variables, though they were younger, had a higher prevalence of psoriatic arthritis, and were more likely to have tried non-biologic systemic therapy previously. This bias may reflect higher levels of participation among patients who are more comfortable with the registry's online format and may indicate that patients with multisystem (i.e. skin and joint) disease are more motivated to participate in research registries. Overall, the study suggests findings from this institution's FORWARD psoriasis registry can be generalized to the broader psoriasis population if these important differences are taken into account in future research.

References:

1. Song WB, Michaud K, Lonowski SL, et al. The forward psoriasis registry: patient-reported outcomes in a novel psoriasis registry. J Psoriasis Psoriatic Arthritis. 2024 Nov 20. doi:10.1177/24755303241303089.

Disclosure: E. Fagan: None; **J. McGrath**: None; **C. Sullivan**: None; **M. Kilton**: None; **K. Samson**: None; **K. Michaud**: None; **S. Lonowski**: AstraZeneca, 12,, 5, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 12,, 5.

Abstract Number: 1899

Regional Variability in SLE Damage Accumulation by Disease Activity Across the Lupus Federated Data Network (LupusNet)

Manuel Ugarte-Gil[1], Sarah Gasman[2], Federico Zazzetti[3], Ashley Orillion[2], Anna Sheahan[4], Clair Blacketer[2], Michel van Speybroeck[5], Reyhan Sonmez[6], Erika Noss[2], Rocío Gamboa-Cárdenas[7], Víctor Pimentel-Quiroz[8], Kaleb Michaud[9], Patti Katz[10], Rangi Kandane-Rathnayake[11], Eric Morand[12], Worawit Louthrenoo[13], Alberta Hoi[14], Yi-Hsing Chen[15], Jiacai Cho[16], Laniyati Hamijoyo[17], Shue Fen Luo[18], Sandra Navarra[19], Mandana Nikpour[20], José María Pego-Reigosa[21], Iñigo Rúa-Figueroa[22], Zulema Plaza[23], Maria Galindo-Izquierdo[24], Julia Martínez Barrio[25], Jaime Calvo[26], Antonio Fernández-Nebro[27], Raúl Menor Almagro[28], EVA GLORIA TOMERO MURIEL[29], Javier Narváez[30] and Chetan S. Karyekar[31], [1]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru, [2]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [3]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [4]Johnson & Johnson, Horsham, PA, USA, Horhsam, PA, [5]Johnson & Johnson, Beerse, Belgium, Beerse, Belgium, [6]Capgemini Consulting, Zurich, Switzerland, Zurich, Switzerland, [7]Universidad Científica del Sur, Lima, Peru, [8]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Perú; Rheumatology Department, Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Perú, Lima, Peru, [9]University of Nebraska Medical Center, Omaha, NE, [10]UCSF, San Rafael, CA, [11]Center for Inflammatory Diseases, Monash University, Clayton, Victoria, Australia, [12]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [13]Chiang Mai University Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai, Thailand, Chiang Mai, Thailand, [14]Centre for Inflammatory Diseases, Monash University and Department of Rheumatology, Monash Health, Clayton, Victoria, Australia, [15]Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Taichung, Taiwan, Taichung, Taiwan (Republic of China), [16]National University Hospital, Rheumatology Division, Department of Medicine, Singapore, Singapore, Singapore, Singapore, [17]Padjadjaran University/Hasan Sadikin General Hospital, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Bandung, Indonesia, Badung, Indonesia, [18]Chang Gung Memorial Hospital, Chang Gung University, Department of Rheumatology, Allergy and Immunology, Taipei, Taiwan, Taoyuan, Taiwan (Republic of China), [19]University of Santo Tomas, Manila, Philippines, [20]University of Sydney, School of Public Health, Faculty of Medicine and Health, Sydney, New South Wales, Australia; St Vincent's Hospital Melbourne, Department of Rheumatology, Fitzroy, Victoria, Australia, Melbourne, Victoria, Australia, [21]Department of Rheumatology, University Hospital of Vigo, Vigo, Spain; IRIDIS Group (Investigation in Rheumatology and Immune-Diseases), Galicia Sur Health Research Institute, Vigo, Spain, [22]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [23]Research Unit, Spanish Society of Rheumatology, Madrid, Spain, Madrid, Spain, [24]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Spain, [25]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [26]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain, [27]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [28]Department of Rheumatology, Hospital de Jerez, Spain, Puerto De Santa María, Spain, [29]Hospital Universitario de la Princesa, Madrid, Spain, [30]Hospital Universitario de Bellvitge, Barcelona, Spain, [31]Johnson & Johnson, Spring House, PA, USA, Spring House

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

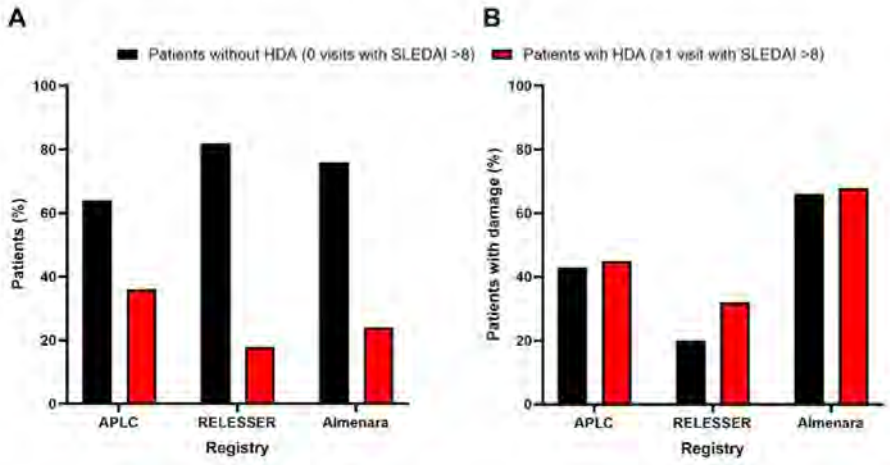
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: SLE is characterized by heterogeneous clinical presentation and periods of flare and remission, with variation in management globally. A goal for SLE management is to achieve and maintain remission or low disease activity to minimize long-term accrual of organ damage. This goal of this study is to assess the frequency, severity, and accrual of damage in patients with SLE as a function of disease activity using LupusNet, the largest existing federated data network in SLE. LupusNet combines and harmonizes data from 5 existing SLE registries, which enables data consistency and enhances understanding of global clinical presentations and outcomes of SLE.

Methods: Data from patients with ≥3 years of follow-up and ≥3 follow-up visits in 3 of 5 LupusNet registries, APLC (Asia Pacific), RELESSER (Europe), and Almenara (South America), were analyzed using a privacy-preserving federated data network approach where only aggregated results were shared. Disease activity was assessed using SLEDAI (recorded at least once a year) and organ damage was measured using SLICC Damage Index (SDI score >0). High disease activity (HDA) was defined as a SLEDAI score >8 at ≥1 visit. The proportion of patients experiencing HDA over the 3-year observation period and the presence of organ damage were reported.

Results: A total of 5019 patients from LupusNet were included. At baseline, 34%, 41%, and 48% of patients had damage in APLC, RELESSER, and Almenara, respectively. At any time over the 3-year follow up, 36% of patients in APLC, 18% in RELESSER, and 24% in Almenara experienced HDA; after 3 years, damage occurred in 44% of patients in APLC, 23% in RELESSER, and 66% in Almenara, and was similar between patients with HDA (32%-68%) and without HDA (20%-66%) across cohorts (**Figure 1**). However, renal, ocular, and skin damage were more prevalent in patients who experienced HDA compared to those without HDA (**Figure 2**). Regional variations were evident in the types of organ damage observed, with renal and musculoskeletal damage being consistently prominent across regions. Notably, ocular damage was more prevalent in RELESSER, while gastrointestinal damage was more prevalent in Almenara. The prevalence of most types of

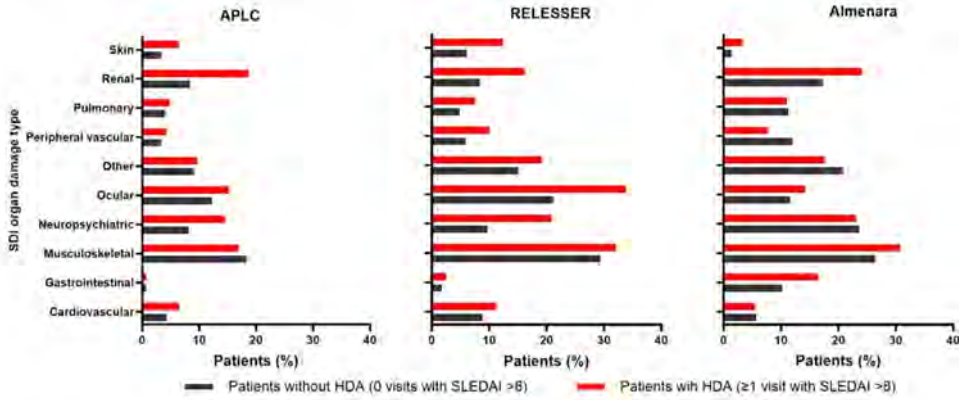
Figure 1. Proportion of Patients (A) with HDA and without HDA and (B) Presence of Damage (SDI score >0) by HDA over 3 Years of Follow-up.



Almenara, Almenara Lupus Cohort; APLC, Asia Pacific Lupus Collaboration; HDA, high disease activity; RELESSER, Lupus Register of the Spanish Society of Rheumatology; SDI, SLICC Damage Index.

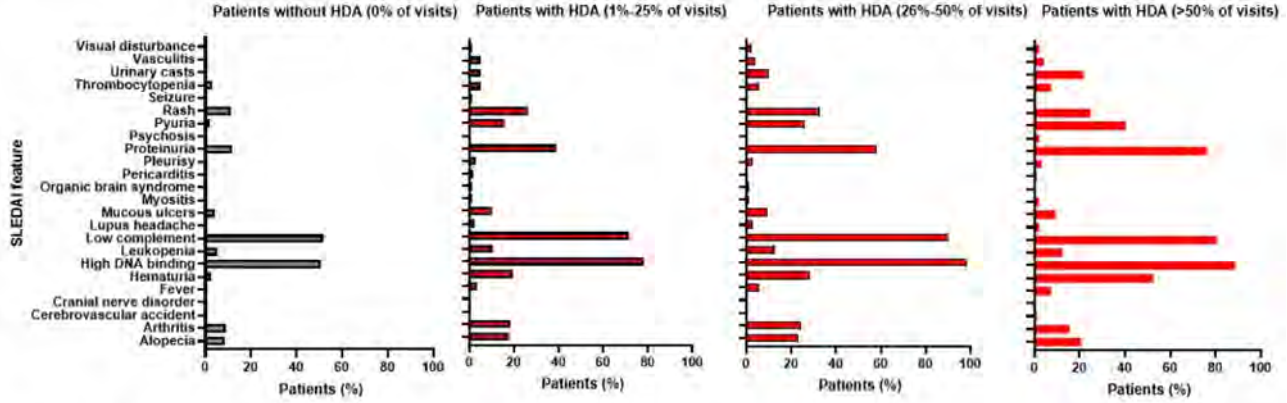
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Proportion of Patients with SDI Organ Damage by Disease Activity Over Follow Up.



Almenara, Almenara Lupus Cohort; APLC, Asia Pacific Lupus Collaboration; HDA, high disease activity; RELESSER, Lupus Register of the Spanish Society of Rheumatology; SDI, SLICC Damage Index.

Figure 3. Proportion of Patients with SLEDAI Features by Disease Activity Over Follow-up.



HDA, high disease activity.

organ damage was lower in APLC compared to Almenara and RELESSER. When analyzed by the proportion of visits with HDA, patients who had SLEDAI >8 at more visits exhibited higher rates of proteinuria, haematuria, urinary casts, and pyuria compared to patients without visits with SLEDAI >8. Low complement and high DNA binding were commonly observed irrespective of disease activity (**Figure 3**).

Conclusion: Despite the well-known link between disease activity and damage accrual, this analysis revealed similar overall rates of damage between patients with and without HDA. However, renal, ocular, and skin damage were more prevalent in patients with HDA. Moreover, regional variations in damage types underscore the complexity of SLE. These findings provide further insights into damage accrual as a function of disease activity in patients with SLE, highlighting the impact of disease activity on certain types of damage and the need for further research to identify factors driving these disparities.

Disclosure: M. Ugarte-Gil: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6; **S. Gasman**: Johnson & Johnson, 3, 12, may hold stock options; **F. Zazzetti**: Johnson & Johnson, 3, 11; **A. Orillion**: Johnson & Johnson, 3, 11; **A. Sheahan**: Johnson & Johnson, 3, 12, may hold stock options;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

C. Blacketer: Johnson & Johnson, 3, 12, may hold stock options; **M. van Speybroeck**: Johnson & Johnson, 3, 12, may hold stock options; **R. Sonmez**: Johnson & Johnson, 2, 12, may hold stock options; **E. Noss**: Johnson & Johnson, 3, 12, may hold stock options; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: None; **K. Michaud**: None; **P. Katz**: None; **R. Kandane-Rathnayake**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKline (GSK), 5, Novartis, 5; **E. Morand**: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **W. Louthrenoo**: None; **A. Hoi**: AstraZeneca, 1, 5, 12, contract research, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, GlaxoSmithKline (GSK), 1, Johnson & Johnson, 1, Merck/MSD, 12, contract research, UCB, 5; **Y. Chen**: Abbvie, 12,, 2, 6, Agnitio Science Technology, 2, 6, Astellas, 12,, 2, 6, AstraZeneca, 12,, 2, 6, Biogen, 12,, BMS, 12,, 2, 6, Boehringer-Ingelheim, 12,, Celldex, 12,, CSL Behring, 2, 6, Eisai, 2, 6, Gilead, 12,, 2, 6, GSK, 12,, 2, 6, Guigai, 12,, 2, 6, Inova Diagnostics, 2, 5, Johnson & Johnson, 12,, 2, 6, Lilly, 2, 6, Medigen Vaccine Biologics, 12,, MSD, 12,, 2, 6, Novartis, 2, 6, Pfizer, 12,, 2, 6, Roche, 12,, Sanofi, 12,, 2, 6, Taichung Veterans General Hospital, 12,, Taiwan Department of Health, 12,, Taiwan Ministry of Science and Technology, 12,, Thermo Fisher, 2, 6, UCB, 12,, 2, 6, United Biopharma, 2, 6; **J. Cho**: None; **L. Hamijoyo**: None; **S. Luo**: None; **S. Navarra**: Astellas, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Biogen, 2, 12, Independent Data Monitoring Committee, Viatris (Idorsia), 2, 6; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 2, 6; **J. Pego-Reigosa**: AstraZeneca, 1, 5, 6, GlaxoSmithKline (GSK), 1, 5, 6, Otsuka, 1, 6; **I. Rúa-Figueroa**: None; **Z. Plaza**: None; **M. Galindo-Izquierdo**: None; **J. Martínez Barrio**: None; **J. Calvo**: None; **A. Fernández-Nebro**: Argenx, 5, AstraZeneca, 2, 5, 6, Chemo, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Gebro Pharma, 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 5, Merck Serono, 5, MSD, 5, Novartis, 2, 5, 6, Takeda, 5, UCB, 5; **R. Menor Almagro**: None; **E. TOMERO MURIEL**: None; **J. Narváez**: None; **C. Karyekar**: Johnson & Johnson, 12, Former employee and may hold stock options.

Abstract Number: 1900

Capturing Patient Cohorts: A Temporal Arteritis Classifier

Megan Sullivan[1], Joseph Rosen[1], Christopher Grilli[1], Kenneth Warrington[2] and Victor E Ortega[1], [1]Mayo Clinic Arizona, Scottsdale, AZ, [2]Mayo Clinic, ROCHESTER, MN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA) is a granulomatous vasculitis affecting cranial and large arteries in individuals over 50 years of age. Its relative rarity poses challenges for large-scale study. Institutional electronic medical record (EMR) datasets offer opportunities to examine GCA at scale but are often hindered by unstructured data formats. To address this, we developed a natural language processing (NLP) pipeline to classify temporal artery biopsy reports as positive or negative for arteritis.

Methods: Patients seen within our tri-site single-center institution with an ICD code consistent with GCA or polymyalgia rheumatica were identified. Temporal artery biopsy impression statements authored by pathologists were extracted and preprocessed using a custom regular expression script to remove Rich Text Formatting, standardize punctuation, and convert text to lowercase. These statements were then tokenized and input into a fine-tuned ClinicalBERT model[1] (MedicalAI, Hugging Face). The dataset was split 80:20 into training and testing sets, with further subdivision of the training set for validation. The dataset used to train the model consisted of 349 negative and 137 positive samples. "Healed arteritis" in the report was considered a negative biopsy result. Data augmentation was implemented following initial training with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

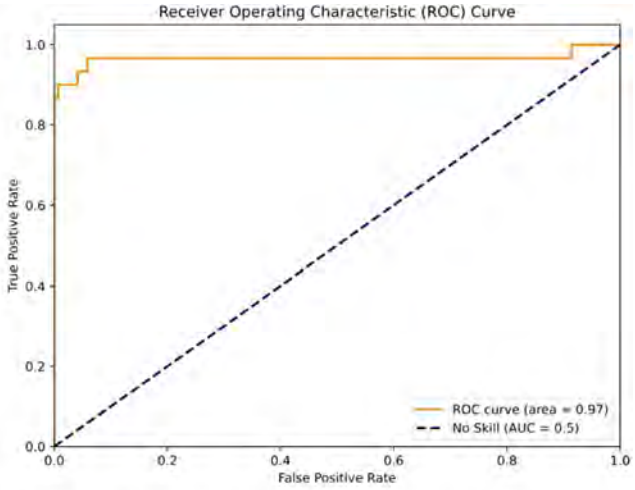


Figure 1 - Discrimination performance of the model in a receiver operating characteristic curve

Table 1 - Model Prediction Metrics

Metrics	Estimate
Total Validation Cohort	320
Total Correct Predictions	315
True Positives	26
False Positives	1
True Negatives	289
False Negatives	4
Performance	
Accuracy	0.98
Precision	0.96
Recall	0.87
F1	0.91

5 augmented impression reports added to the training dataset to enhance model performance. Discrimination performance was assessed using the area under the receiver operating characteristic curve (AUC).

Results: The validation cohort, consisting of 320 patient records (30 positive entries and 290 negatives), was able to provide significant discrimination of positive temporal artery biopsies with an area under the curve of 0.97 **(Figure 1)**, accuracy of 98%, precision of 96%, and recall of 87%. Of the predictions, 315/320 (98.4%) were correct. This amounted to 5 misclassifications within the dataset, which included 1 false positive and 4 false negatives (**Table 1)**.

Conclusion: Fine-tuned language models trained on clinical text can accurately classify pathology reports, offering a scalable approach to identifying specific diagnoses within large EMR datasets. This method improves the accuracy and utility of cohort identification for rare conditions such as GCA, supporting future research efforts.

References:

1. 1. K. Huang, J. Altosaar, R. Ranganath, ClinicalBERT: Modeling Clinical Notes and Predicting Hospital Readmission, in: CHIL '20 Workshop: ACM Conference on Health, Inference, and Learning 2020, Toronto, 2020.

Disclosure: M. Sullivan: None; **J. Rosen**: None; **C. Grilli**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **V. Ortega**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1901

Epidemiology of Adult-Onset Still's Disease in South Korea: A Nationwide Study Using Health Insurance Claims Data

Mihye Kwon[1], Younghee Jung[2], Chung-il Joung[1] and Jeeyoung Hong[1], [1]Konyang University Hospital, Daejeon, Republic of Korea, [2]Chungnam National University Hospital, Daejeon, Republic of Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1877–1913) Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Adult-onset Still's disease (AOSD) is a rare systemic autoinflammatory disorder characterised by heterogeneity in clinical course and long-term outcomes. Despite its rarity being recognised globally, population-based epidemiologic studies estimating the incidence, prevalence, and mortality of AOSD remain extremely limited. This study aimed to estimate the national incidence, prevalence, and mortality of AOSD and to describe the demographic and clinical characteristics of affected individuals in South Korea.

Methods: We identified AOSD patients using the Korean National Health Insurance Service (NHIS) database from 2002 to 2022, applying the ICD-10 diagnostic code in conjunction with characteristic patterns of hospital utilisation and medication prescription. To improve diagnostic specificity, individuals with coexisting autoimmune diseases or malignancies diagnosed within three months before or after the first AOSD claim were excluded. Age- and sex-adjusted incidence and prevalence rates per 100,000 population were calculated annually, and temporal trends were assessed. Using operational definitions, disease courses were categorised into monocyclic, polycyclic, and chronic patterns.

Table 1. Baseline demographic and clinical characteristics of South Korean AOSD patients (2003-2020) using 3 year-incidence

Characteristics	Total	2003-2005	2006-2008	2009-2011	2012-2014	2015-2017	2018-2020
Number of incident patients	4,207	437	680	689	804	788	809
Female, n (%)	3,023 (71.9)	330 (75.5)	486 (71.5)	517 (75.0)	602 (74.9)	594 (70.3)	534 (66.0)
Age at diagnosis (mean ± SD)	45.5(16.7)	38.8 (14.8)	44.6 (16.0)	44.4 (16.0)	47.9 (17.0)	47.8 (16.9)	47.8 (17.3)
Type of insurance, n (%)							
Health insurance	3,783 (89.9)	374 (85.6)	594 (87.4)	619 (89.8)	737 (91.7)	719 (91.2)	740 (91.5)
Medical aid	424 (10.1)	63 (14.4)	86 (12.6)	70 (10.2)	67 (8.3)	69 (8.8)	69 (8.5)
Disability status							
*Use of medications, n (%)							
Any csDMARDs	2,905 (69.1%)	318 (72.8%)	437 (64.3%)	492 (71.4%)	558 (69.4%)	547 (69.4%)	553 (68.4%)
Methotrexate	2,407 (57.2%)	253 (57.9%)	344 (50.6%)	404 (58.6%)	457 (56.8%)	485 (61.5%)	484 (59.8%)
Sulfasalazine	435 (10.1%)	79 (18.1%)	70 (10.3%)	74 (10.7%)	85 (10.6%)	67 (8.5%)	50 (6.2%)
Hydroxychloroquine	1,497 (35.6%)	246 (56.3%)	280 (41.2%)	277 (40.2%)	310 (38.6%)	217 (27.5%)	167 (20.6%)
Leflunomide	564 (13.2%)	67 (15.3%)	91 (13.4%)	101 (14.7%)	113 (14.1%)	80 (10.2%)	102 (12.6%)
Any immunosuppressants	1,229 (29.2%)	106 (24.3%)	156 (22.9%)	192 (27.9%)	250 (31.7%)	247 (31.3%)	273 (33.7%)
Azathioprine	436 (10.4%)	44 (10.1%)	63 (9.3%)	80 (11.6%)	92 (11.4%)	91 (10.3%)	76 (9.4%)
Cyclosporine	768 (18.3%)	75 (16.7%)	103 (15.1%)	115 (16.7%)	161 (20.0%)	149 (18.9%)	167 (20.6%)
Tacrolimus	333 (7.9%)	9 (2.1%)	29 (4.3%)	39 (5.6%)	66 (8.2%)	98 (10.9%)	84 (10.4%)
Any bDMARDs	257 (6.1%)	5 (1.1%)	11 (1.6%)	29 (4.2%)	35 (4.4%)	84 (8.1%)	113 (14.0%)
Adalimumab	20 (0.5%)	0 (0.0%)	0 (0.0%)	5 (0.7%)	2 (0.2%)	7 (0.9%)	6 (0.7%)
Infliximab	44 (1.0%)	4 (0.9%)	9 (1.3%)	17 (2.5%)	6 (0.7%)	5 (0.6%)	3 (0.4%)
Golimumab	2 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	1 (0.1%)
Tocilizumab	189 (4.5%)	0 (0.0%)	0 (0.0%)	10 (1.5%)	26 (3.2%)	52 (6.6%)	101 (12.5%)
Anakinra	2 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	1 (0.1%)
Abatacept	1 (0.1%)	1 (0.1%)	1 (0.1%)	1 (0.1%)	1 (0.1%)	1 (0.1%)	1 (0.1%)
Rituximab	7 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	3 (0.4%)	3 (0.4%)
Any tsDMARDs	13 (0.3%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	4 (0.5%)	3 (0.4%)	4 (0.5%)
Tofacitinib	7 (0.2%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	4 (0.5%)	1 (0.1%)	0 (0.0%)
Baricitinib	6 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	4 (0.5%)
Upadacitinib	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Any NSAIDs	4,104 (97.6%)	434 (99.3%)	669 (98.4%)	686 (99.6%)	796 (99.0%)	756 (95.9%)	763 (94.3%)
Any Corticosteroids	4,112 (97.7%)	433 (99.1%)	668 (98.2%)	682 (99.0%)	798 (99.3%)	764 (97.0%)	767 (94.8%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

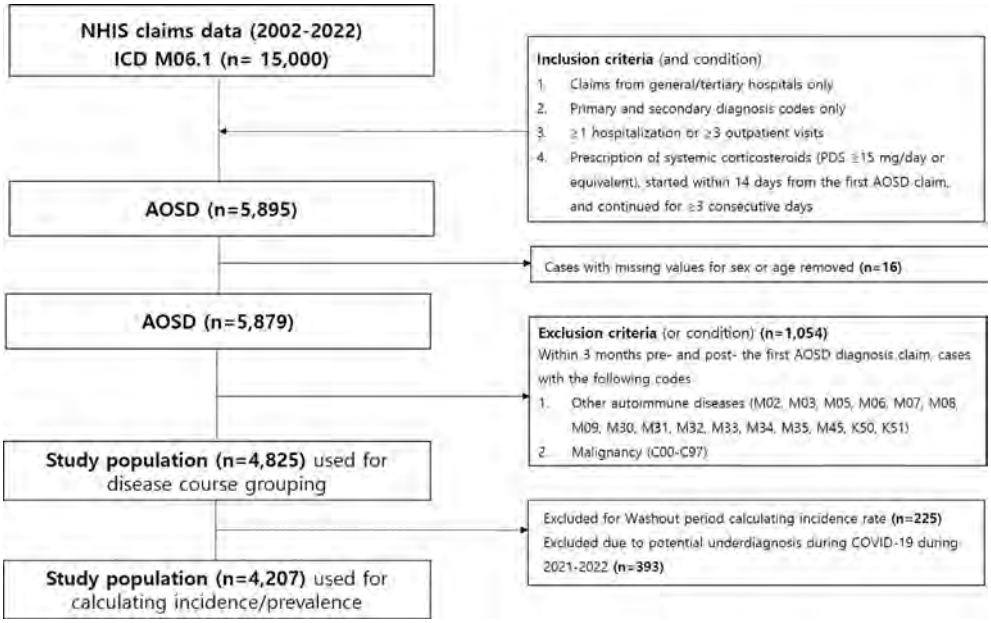


Figure 1. A flow chart for defining study population.

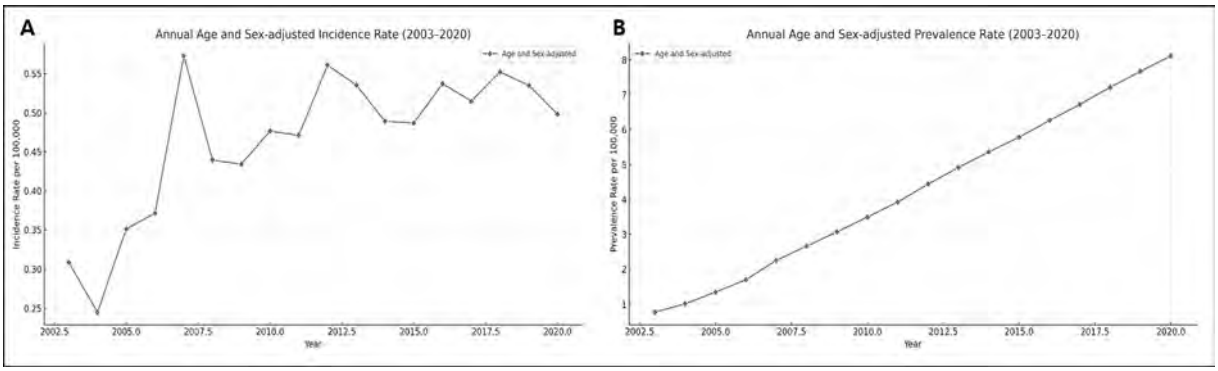


Figure 2. Annual age-, sex- adjusted incidence and prevalence of AOSD in South Korea 2003-2020

Results: A total of 4,825 patients met the criteria for AOSD, and 4,207 patients diagnosed between 2003 and 2020 were included in the final analysis. The overall age- and sex-adjusted incidence and prevalence rates across the study period were 0.49 and 4.25 per 100,000 population, respectively. Annual incidence rates showed a gradually increasing trend from 0.32 in 2003 to 0.50 in 2020, with slight fluctuations across years. The female-to-male ratio was 2.56, and the mean age at diagnosis was 45.5 ± 16.7 years. Based on disease course classification, 1,867 patients (38.7%) had a monocyclic course, 1,197 (24.8%) polycyclic, and 1,761 (36.5%) chronic. During the observation period, 376 patients died, among whom 8 deaths were attributed to macrophage activation syndrome (MAS), the most severe complication of AOSD.

Conclusion: Leveraging 21 years of longitudinal, nationwide claims data, this study provides the first comprehensive national estimates of the incidence, prevalence, and mortality of AOSD in South Korea. Our findings confirm that AOSD remains a rare disease with persistently low incidence and increasing prevalence, mirroring international observations. These data underscore the value of long-term epidemiologic surveillance and may inform future research and health policy planning related to rare systemic autoinflammatory disorders.

Disclosure: M. Kwon: None; **Y. Jung**: None; **C. Joung**: None; **J. Hong**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1902

Investigating Factors Associated With Respiratory Syncytial Virus Vaccination and Breakthrough Infection Among Patients With Systemic Autoimmune Rheumatic Diseases

Natalie Davis[1], Jiaqi Wang[2], Xiaosong Wang[3], Liya Sisay Getachew[4], Lauren O'Keeffe[5], Grace Qian[5], Kevin Mueller[5], Madison Negron[6], Alene Saavedra[5], Naomi Patel[7] and Jeffrey Sparks[4], [1]Brigham and Women's Hospital, Brookline, MA, [2]Massachusetts General Hospital, BOston, [3]Brigham and Women's Hospital, Natick, MA, [4]Brigham and Women's Hospital, Boston, MA, [5]Brigham and Women's Hospital, Boston, [6]Harvard Extension School, Medford, MA, [7]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1877–1913) Epidemiology & Public Health Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Respiratory syncytial virus (RSV) vaccines were approved starting in May 2023 and are recommended by the US CDC to adults aged 60 years or older at increased risk for poor outcomes, including immunocompromising conditions or medications. We previously showed that RSV is associated with poor outcomes and high rates of hospitalization in people with systemic autoimmune rheumatic diseases (SARDs), but less is known about RSV vaccine uptake among individuals with SARDs. Therefore, we described the prevalence, associations, and breakthrough infection of RSV vaccination among people with SARDs.

Methods: We performed a retrospective, cross-sectional study in a US tertiary healthcare system. We identified patients with 2 or more SARD codes and who were prescribed a DMARD or oral glucocorticoid as of February 2025 (positive predictive value 95%). We excluded patients who had died or whose last encounter was on or before May 2023 and those less than 60 years of age on the last day of observation or at time of RSV vaccination. The primary outcome was RSV vaccination documented in the electronic health record. We evaluated factors associated with RSV vaccination and used multivariable logistic regression to assess for associations. We then described breakthrough infections with positive testing after RSV vaccination.

Results: We analyzed 10,587 SARD patients aged 60 years or older at the time of RSV vaccination or the date of last observation (median age 71.7 years, 72.4% female, and 88.0% White; **Table 1**). The most common SARD type was RA (56.8%), and the most common medications were conventional synthetic DMARDs (40.8%). We identified 1,075 people with SARDs (10.2%) who received the RSV vaccine. There was no association of any SARD type with RSV vaccination after adjusting for general population factors that included demographics, comorbidities, area-level income, serious infection, and other vaccine receipt (**Table 2**). Influenza vaccine receipt in the previous year had the strongest association with RSV vaccination (no vs. yes OR 0.021, 95%CI 0.018 to 0.026). No DMARD class was significantly associated with RSV vaccination. CD20 inhibitor use had an OR for RSV vaccination of 0.78 (95%CI 0.45 to 1.36) compared to antimalarial monotherapy. Glucocorticoid users were less likely (OR 0.33, 95%CI 0.23 to 0.49) and interstitial lung disease was more likely (OR 1.53, 95%CI 1.14 to 2.04) to receive RSV vaccination. We identified 9 cases of breakthrough RSV infections, occurring a median of 301 days after vaccination (**Table 3**).

Conclusion: Among patients with SARDs aged 60 years or older, 10.2% were documented to receive RSV vaccination. After accounting for general population factors, glucocorticoid users were less likely to receive RSV vaccination. Neither SARD type nor DMARD class, including CD20 inhibitors, were associated with RSV vaccination. Only 2 of 9 documented

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with SARDs at date of RSV vaccine receipt or last observation. Covariates were assessed within a 12-month period prior to date of vaccination or last documented encounter.

Table 1. Characteristics of patients with SARDs at date of RSV vaccine receipt or last observation. Covariates were assessed within a 12-month period prior to date of vaccination or last documented encounter.

	Overall sample (n=10,587)	Received RSV vaccine (n=1,075)	Did not receive RSV vaccine (n=9,512)
Demographics			
Median age, years (IQR)	71.7 (65.9, 78.1)	74.0 (68.3, 78.9)	71.4 (65.7, 78.0)
Female sex	7664 (72.4)	790 (73.5)	6874 (72.3)
Race			
-American Indian	15 (0.1)	2 (0.2)	13 (0.1)
-Asian	278 (2.7)	25 (2.4)	253 (2.7)
-Black or African American	524 (5.1)	43 (4.1)	481 (5.2)
-Other	428 (4.1)	27 (2.6)	401 (4.3)
-White	9126 (88.0)	963 (90.9)	8163 (87.7)
Hispanic ethnicity	163 (1.7)	7 (0.7)	156 (1.8)
Median census-tract household income, $USD (IQR)	84,883 (65,476, 105,645)	91,596 (73,948, 113,509)	84,847 (65,476, 105,029)
Comorbidities			
Median Charlson Comorbidity Index, (IQR)	9 (9, 11)	10 (9, 12)	9 (9, 11)
-Hypertension	4920 (46.5)	711 (66.1)	4209 (44.3)
-Cancer	3106 (29.3)	537 (50.0)	2569 (27.0)
-CAD	1947 (18.4)	221 (20.6)	1726 (18.2)
-Diabetes	1770 (16.7)	196 (18.2)	1574 (16.6)
-Heart failure	1195 (11.3)	122 (11.4)	1073 (11.3)
-Asthma	1134 (10.7)	197 (18.3)	937 (9.9)
-Chronic kidney disease	1677 (15.8)	189 (17.6)	1488 (15.6)
-Interstitial lung disease	937 (8.9)	146 (13.6)	791 (8.3)
-COPD	732 (6.9)	109 (10.1)	623 (6.6)
SARD type			
-Rheumatoid arthritis	5918 (55.9)	547 (50.9)	5371 (56.5)
-GCA and/or PMR	1206 (11.4)	138 (12.8)	1068 (11.2)
-Other inflammatory arthritis	834 (7.9)	88 (8.2)	746 (7.8)
-SLE	660 (6.2)	70 (6.51)	590 (6.2)
-AAV and other vasculitis	252 (2.4)	21 (2.0)	231 (2.4)
-Multiple	1273 (12.0)	154 (14.3)	1119 (11.8)
-Other	444 (4.2)	57 (5.3)	387 (4.1)
Current DMARD use by hierarchy			
Antimalarial monotherapy	1812 (17.1)	204 (19.0)	1608 (16.9)
CsDMARD only	4323 (40.8)	468 (43.5)	3855 (40.5)
TNFi	2051 (19.4)	174 (16.2)	1877 (19.7)
IL-6	786 (7.42)	68 (6.33)	718 (7.6)
JAKi	410 (3.9)	30 (2.8)	380 (4.0)
CD20i	355 (3.4)	38 (3.5)	317 (3.3)
IL-12/23, IL-17A, and IL-23 inhibitors	208 (2.0)	25 (2.3)	183 (1.9)
Other bDMARDs	448 (4.2)	41 (3.8)	407 (4.3)
Glucocorticoid use	982 (9.3)	67 (6.2)	915 (9.6)
Healthcare in last 12 months			
Hospitalized	2017 (19.1)	195 (18.1)	1822 (19.2)
Serious infection	2859 (27.0)	394 (36.7)	2465 (25.9)
Pulmonary infection	1006 (9.5)	134 (12.5)	872 (9.2)
Vaccine Receipt			
Influenza vaccine	1315 (12.42)	793 (73.8)	522 (5.5)
COVID-19 vaccine	801 (7.6)	249 (23.2)	552 (5.8)

Index date= date of RSV vaccination or date of last encounter
AAV= ANCA-associated vasculitis, bDMARD= biologic DMARD, CAD= coronary artery disease, CD20i= CD20 inhibitor, COPD= chronic obstructive pulmonary disease, csDMARD= conventional synthetic DMARD, GCA= giant cell arthritis, IL-6, IL-12/23, IL-17A= interleukin inhibitors, JAKi= Janus kinase inhibitor, PMR= polymyalgia rheumatica, SLE= systemic lupus erythematosus, TNFi= tumor necrosis factor inhibitor

cases of breakthrough RSV infections were hospitalized and there were no deaths. While our study is limited to a single geographic area and may under-capture RSV vaccinations and breakthrough infections, further research on effectiveness and vaccine-induced SARD flares is needed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Odds ratios for documented RSV vaccine receipt among SARD patients (n=10,587).

Table 2. Odds ratios for documented RSV vaccine receipt among SARD patients (n=10,587).

Characteristics	Unadjusted OR (95%CI)	Multivariable* OR (95% CI)
Female sex (vs. male)	1.06 (0.92, 1.23)	1.15 (0.93, 1.42)
Race		
-American Indian	1.30 (0.29, 5.79)	0.29 (0.02, 4.95)
-Asian	0.84 (0.55, 1.27)	0.76 (0.42, 1.35)
-Black or African American	**0.76 (0.55, 1.04)**	**0.64 (0.42, 0.98)**
-Other	**0.57 (0.38, 0.85)**	**0.49 (0.29, 0.85)**
-White	1.0 (Ref)	1.0 (Ref)
Hispanic (vs. not)	**0.38 (0.18, 0.82)**	0.43 (0.15, 1.23)
Median census-tract household income (per $1K USD)	**1.008 (1.006, 1.010)**	**1.008 (1.005, 1.011)**
Comorbidities		
Diabetes (vs. not)	1.13 (0.95, 1.33)	0.96 (0.74, 1.23)
CAD (vs. not)	**1.17 (1.00, 1.37)**	0.83 (0.64, 1.06)
Heart failure (vs. not)	1.01 (0.83, 1.23)	**0.64 (0.47, 0.88)**
Cancer (vs. not)	**2.70 (2.37, 3.07)**	**1.84 (1.51, 2.23)**
Hypertension (vs. not)	**2.46 (2.16, 2.81)**	**1.80 (1.45, 2.22)**
Asthma (vs. not)	**2.05 (1.74, 2.43)**	**1.90 (1.47, 2.46)**
Chronic kidney disease (vs. not)	1.15 (0.97, 1.36)	0.88 (0.67, 1.14)
Chronic obstructive pulmonary disease (vs. not)	**1.61 (1.30, 1.99)**	1.18 (0.84, 1.65)
Interstitial lung disease (vs. not)	**1.73 (1.43, 2.09)**	**1.53 (1.14, 2.04)**
SARD type		
-Rheumatoid arthritis	1.0 (Ref)	1.0 (Ref)
-Other inflammatory arthritis	1.16 (0.91, 1.47)	1.26 (0.88, 1.82)
-GCA and/or PMR	**1.27 (1.04, 1.55)**	1.07 (0.77, 1.47)
-SLE	1.17 (0.90, 1.52)	1.11 (0.75, 1.64)
-AAV and other vasculitis	0.89 (0.57, 1.41)	1.13 (0.59, 2.18)
-Other	**1.45 (1.08, 1.94)**	1.23 (0.80, 1.88)
-Multiple	**1.35 (1.12, 1.63)**	1.16 (0.86, 1.54)
Current DMARD use (hierarchical)		
-Antimalarial monotherapy	1.0 (Ref)	1.0 (Ref)
-Other csDMARDs only	0.93 (0.76, 1.12)	0.82 (0.62, 1.09)
-TNFi	**0.73 (0.59, 0.90)**	0.88 (0.64, 1.21)
-IL-6i	0.75 (0.56, 1.00)	0.83 (0.54, 1.27)
-CD20i	0.95 (0.66, 1.36)	0.78 (0.45, 1.36)
-IL-12/23, IL-17A, and IL-23 inhibitors	1.08 (0.69, 1.68)	1.12 (0.58, 2.16)
-JAK inhibitors	**0.62 (0.42, 0.93)**	1.11 (0.63, 1.93)
-Other bDMARDs	0.79 (0.56, 1.13)	1.09 (0.66, 1.82)
-No DMARD	1.03 (0.84, 1.25)	0.88 (0.66, 1.19)
Glucocorticoid use (vs. not)	**0.63 (0.48, 0.81)**	**0.33 (0.23, 0.49)**
Vaccine receipt in last 12 months		
No influenza vaccine (vs. yes)	**0.021 (0.018, 0.024)**	**0.021 (0.018, 0.026)**
No COVID-19 vaccine (vs. yes)	**0.20 (0.17, 0.24)**	**0.39 (0.30, 0.49)**

Bolded values are statistically significant (p<0.05).

*Adjusted for all factors listed as well as age, frailty, previous serious infection, and number of outpatient visits.

Index date= date of RSV vaccination or date of last encounter

AAV=ANCA-associated vasculitis, bDMARD=biologic DMARD, CAD=coronary artery disease, CD20i=CD20 inhibitor, COPD=chronic obstructive pulmonary disease, csDMARD=conventional synthetic DMARD, GCA=giant cell arthritis, IL=interleukin; JAKi=Janus kinase inhibitor, PMR=polymyalgia rheumatica, SLE=systemic lupus erythematosus, TNFi=tumor necrosis factor inhibitor

Table 3. Documented breakthrough infections in SARD patients after RSV vaccination (9 cases out of 1,075 receiving vaccinations).

Table 3. Documented breakthrough infections in SARD patients after RSV vaccination (9 cases out of 1,075 receiving vaccinations).

Case	Age range	Sex	Days from RSV vaccine to infection	SARD type	DMARD at RSV infection onset	Glucocorticoid use and dose at RSV infection onset	Comorbidities	Highest care setting	Highest supplemental O2 use
1	70-79	Male	370	RA	Tacrolimus, MMF	Prednisone 5 mg	Lung transplant, ILD, CAD, diabetes, HTN, CKD	Hospitalized for 7 days	5L nasal cannula (home dose)
2	70-79	Female	388	PsA	Adalimumab	Prednisone 4 mg	Hypopituitarism	Hospitalized for 4 days	None
3	70-79	Female	56	RA	Infliximab	None	HTN, CKD	Emergency department	None
4	70-79	Female	90	SSc	Ruxolitinib, MMF, belumosudil	Prednisone 7.5 mg	Lymphoma, MDS, s/p stem cell transplant, GVHD	Emergency department	None
5	60-69	Male	415	AAV	None	None	CKD, HTN, COPD, CAD, ILD	Emergency department	2L nasal cannula
6	80-89	Male	111	RA	Apremilast, colchicine, tofacitinib	None	COPD	Urgent care	None
7	80-89	Male	416	RA	MTX, SSZ, HCQ	None	HTN	Urgent care	None
8	70-79	Female	429	GCA	Tocilizumab	None	Asthma	Clinic	None
9	70-79	Male	431	RA	IVIG and chemotherapy	Dexamethasone 20 mg	Multiple myeloma, HTN	Home hospice	None

AAV=ANCA-associated vasculitis, CAD=coronary artery disease, COPD=chronic obstructive pulmonary disease, CKD=chronic kidney disease, GCA=giant cell arthritis, GVHD=graft-versus-host-disease, HCQ=hydroxychloroquine, HTN=hypertension, ILD=interstitial lung disease, MDS=myelodysplastic syndromes, IVIG=intravenous immunoglobin, MMF=mycophenolate mofetil, MTX=methotrexate, PsA=psoriatic arthritis, RA=rheumatoid arthritis, SSZ=sulfasalazine, SSc=systemic sclerosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Davis: None; **J. Wang**: None; **X. Wang**: None; **L. Getachew**: None; **L. O'Keeffe**: None; **G. Qian**: None; **K. Mueller**: None; **M. Negron**: None; **A. Saavedra**: None; **N. Patel**: Amgen, 5; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 1903

Seasonal and Racial/Ethnic Variation in Achieving Target Uric Acid Levels in Gout Patients on Urate Lowering Therapy in US Veterans in Central California

Nidaa Rasheed[1] and Candice Reyes[2], [1]UCSF Fresno, Fresno, CA, [2]VACCHCS, Fresno, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is a chronic, inflammatory arthritis driven by monosodium urate (MSU) crystal deposition and elevated serum uric acid (SUA) levels, increasing the risk for cardiometabolic comorbidities and premature mortality. While gout and hyperuricemia result from complex gene-environment interactions, emerging evidence suggests that disparities in gout outcomes across racial/ethnic groups are more strongly influenced by social determinants of health than genetic factors. While prior studies have largely focused on differences in gout diagnosis and initiation of urate-lowering therapy (ULT), there is limited data on factors influencing long-term disease control. This project examined racial/ethnic and seasonal differences in maintaining target SUA (< 6 mg/dL) among patients on ULT to better understand non-genetic drivers of disease progression.

Methods: We analyzed data from the San Francisco Quality Enrichment Research Initiative, comprising 747 U.S. veterans in Central California with physician-diagnosed gout on ULT from 1999 to 2023. We excluded patients who declined to report race/ethnicity, were of mixed origin, or lacked recent SUA testing. Seasonal variation was assessed using the subset of patients with ULT and SUA measurements in 2023.

Results: Of the 386 self-identified Caucasian patients, 103 (27%) achieved target SUA, compared to 348 patients identifying as persons of color (POC) (African American, Hispanic/Latinx, Asian, American Indian, Native Hawaiian), of whom only 76 (22%) were at target SUA. African American patients were particularly affected, with just 30% achieving target levels. Overall, POC patients were significantly less likely to reach target SUA despite appropriate ULT [Odds ratio 0.61, 95% CI 0.412-0.899, P = 0.0063].

Figure 1. Weekly average proportion (%) of patients on ULT with uric acid labs at target (UCL = upper collection limit and LCL = lower collection limit) in the 2023 year

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Seasonal analysis revealed a notable decline in target SUA achievement in the spring and early summer, with only 38% of patients reaching goal, compared to other times of the year [Figure 2]. This seasonal effect highlights the potential impact of environmental factors like heat, dehydration, and air pollution, particularly in regions like the Central Valley, known for severe particulate and ozone pollution.

Conclusion: Our findings emphasize the need to move beyond one-size-fits-all gout management and consider the complex interplay of racial/ethnic and environmental factors that influence disease control. Providers should account for the broader social and environmental contexts, including housing location, humidity, seasonal changes, and air quality, as they may contribute to elevated SUA and increased flare risk. Addressing these factors could improve outcomes for historically marginalized groups and reduce the overall burden of gout.

Disclosure: N. Rasheed: None; **C. Reyes**: None.

Abstract Number: 1904

Mapping CTD-ILD in a Spanish Cohort – the NIRRVANA Registry

Paula García-Escudero[1], Marta López-Maraver[2], Tetyana Lozinska-Lozinska[2], Carlos Maria Lizasoain Alustiza[3], César Antonio Egües Dubuc[4], Leire Suárez Zorrilla[5], Mayra Nathali Rivas Zavaleta[5], Elena Garmendia Sánchez[5], Nuria Vegas Revenga[6], Myriam Aburto Barreneche[7], Guillén Sada Urmeneta[8], Elena Abad Plou[9], Maria Luz Garcia Vivar[10], Inmaculada Paniagua Zudaire[11], Marta Inchausti Iguiñiz[12], Iñaki Salegi Etxebeste[12] and Jaime Calvo[13], [1]Hospital Universitario Álava, Bilbao, Spain, [2]Hospital Universitario Araba, Vitoria, Spain, [3]Donostia University Hospital, San Sebastian, Pais Vasco, Spain, [4]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [5]Hospital Universitario Cruces, Barakaldo, Spain, [6]Galdakao- Usansolo University Hospital, Galdakao, Spain, [7]Hospital Galdakao-Usansolo, Galdakao, Spain, [8]Hospital Reina Sofía de Tudela, Tudela, Spain, [9]Hospital Universitario Basurto, Bilbao, Spain, [10]Basurto Hospital, Bilbao, Spain, [11]Hospital Universitario de Navarra, Pamplona, Spain, [12]Hospital Universitario Donosti, Donosti, Spain, [13]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a prevalent feature among patients suffering from connective tissue diseases (CTD), associated with considerable morbi-mortality. Nonetheless, this complication is still poorly defined in our field.

The purpose of this work is to assess the main characteristics of CTD-ILD in our area.

Methods: An ambispective regional registry (NIRRVANA Registry: Neumopatía Intersticial en Reumatología Registro VAsco-NAvarro) of CTD-ILD was conducted in the Basque Country and Navarre, Spain. Adult patients with ILD associated with aPLS, IIM, MCTD, RA, sarcoidosis, SjS, SLE, SSc, UCTD and vasculitis (classification criteria or clinician's judgment) were included, as well as patients meeting criteria for IPAF.

Data on demographics, clinical, radiological and anatomo-pathological features, laboratory results, and outcomes were collected.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Statistical analyses were conducted using standardized tests.

Results: One hundred and thirty-one patients were indentified (87 female, 44 male), with a median disease duration of 6.66 (2.72-13.49) years for CTDs.

RA (26.7%), followed by IIM (16.8%) and SSc (16.8) were the most frequent CTDs, while NSIP and IUP, for ILDs, were evident in equal proportion (29.8%) in this sample. Patients with NSIP were more frequent in the SSc and UCTD groups. UIP and OP were more common in the RA and IIM (specifically, ASS) groups, respectively. LIP was identified in only one case of SjS.

Table 1: Main characteristics of CTD-ILD patients identified in the NIRRVANA Registry.

Characteristics of the patients								n=131
Gender, *n* (%)				Female				87 (66.4)
				Male				44 (33.6)
Age at diagnosis, years[a]				CTD				57.6 (±15.52)
				ILD				60.88 (±12.82)
Main comorbidities, *n* (%)				Dyslipidemia				84 (64.1)
				HBP				42 (32.1)
				Solid tumor history				19 (14.5)
				COPD				4 (3)
Smoking status, *n* (%)				Current smoker				6 (4.5)
				Former smoker				54 (41.2)
				Never smoker				71 (54.2)
					ILD *n* (%)			
			NSIP 39 (29.8)	UIP 39 (29.8)	OP 12 (9.2)	LIP 1 (0.1)	ND ILD 20 (15.3)	Other 20 (15.3)
CTD *n* (%)	RA	35 (26.7)	4	16	2	-	7	6
	IIM	22 (16.8)	6	4	8	-	1	3
	• ASS	17 (13)	6	4	5	-	-	2
	• DM	3 (2.3)	-	-	2	-	-	1
	• MDA5	2 (1.5)	-	-	1	-	1	-
	SSc	22 (16.8)	10	5	-	-	6	1
	IPAF	11 (8.4)	5	3	2	-	1	-
	MCTD	9 (6.9)	5	2	-	-	-	2
	UCTD	8 (6.1)	7	1	-	-	-	-
	SjS	7 (5.3)	-	4	-	1	1	1
	SLE	6 (4.5)	1	3	-	-	2	-
	Sarcoidosis	5 (3.8)	-	-	-	-	1	4
	aPLS	3 (2.3)	1	-	-	-	-	2
	Vasculitis	3 (2.3)	-	1	-	-	1	1

Clinical features, *n* (%)		Laboratory results[b]	
Dyspnoea	89 (70)	Haemoglobin[c] gr/dL	13.9 (±1.46)
Arthritis	74 (56.5)	Leukocytes[c] /mm3	7709 (±2684)
Cough	61 (46.6)	Platelets[c] /mm3	258371 (±90128)
Raynaud's phenomenon	45 (34.3)	CRP[c] mg/L	5 (2-15.6)
Constitutional syndrome	27 (20.6)	ESR[c] mm/h	18 (7.75-38.5)
Expectoration	25 (19.1)	Autoimmunity[c], *n* positive	
Sicca syndrome	25 (19.1)	ANA	86
Cutaneous sclerosis	21 (16)	RF	47
Fever	17 (13)	SSc antibodies	32
Mechanic's hands	15 (11.4)	Anti-Ro52	31
Digital ulcers	14 (10.7)	ACPA	30
Serositis	9 (6.9)	MSA	24
Anatomo-pathological studies, *n* performed		Anti-Ro60	17
Lung biopsy	11	Anti-RNP	7
Muscle biopsy	4		
DLCO at ILD diagnosis, % of patients		6MWT at ILD diagnosis, % of patients	
≤70%	61.3	<250 meters	6.8
FVC at ILD diagnosis, % of patients		Initial O2 saturation ≤92%	8.2
≤80%	39.2	Final O2 saturation ≤92%	16.4

[a]mean (standard deviation), [b]median (Q1-Q3)

[c]at CTD diagnosis, [d]most relevant autoantibodies found in the cohort

6MWT: 6-minute walking test; ACPA: anti-citrullinated protein antibodies; ANA: antinuclear antibodies; aPLS: anti-phospholipids syndrome; ASS: antisynthetase syndrome; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; CTD: connective tissue disease; DLCO: diffusing capacity for carbon monoxide; DM: dermatomyositis; ESR: erythrocyte sedimentation rate; FVC: forced vital capacity; HBP: high blood pressure; IIM: idiopathic inflammatory myopathies; ILD: interstitial lung disease; IPAF: interstitial pneumonia with autoimmune features; LIP: lymphoid interstitial pneumonia; MCTD: mixed connective tissue disease; MSA: myositis specific antibodies; ND ILD: non-defined interstitial lung disease; NSIP: nonspecific interstitial pneumonia; OP: organizing pneumonia; RF: rheumatoid factor; SjS: Sjögren's syndrome; SLE: systemic lupus erythematosus; SSc: systemic sclerosis; RA: rheumatoid arthritis; UCTD: undifferentiated connective tissue disease; UIP: usual interstitial pneumonia

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Treatments used among CTD-ILD patients in the NIRRVANA Registry.

Treatments, %			
GC	84.1	ABA	14.2
MMF	35.9	Nintedanib	13.7
MTX	29.6	TAC	11.9
RTX	20.5	antiTNF	10.3
LEF	18.4	iJAK	7.1
HCQ	16	iIL6	6.2
AZA	15.1	CsA	5
CFM	14.2	IVIg	4

ABA: abatacept; AZA: azatyoprine; CFM: cyclophosphamide; CsA: ciclosporine;
HCQ: Hydroxicloroquine; IL6: interleucine 6 inhibitors; iJAK: JAK kinase inhibitors; IVIg: intravenous immunoglobuline; LEF: leflunomide; RTX: rituximab; TAC: tacrolimus

Fifty-six (42.7%) patients were diagnosed with CTD prior to ILD, 44 (33.6%) patients had CTD and ILD diagnoses concurrently, and 31 (23.7%) patients were diagnosed with ILD prior to CTD.

Details on both CTD and ILD identified, as well as demographic and clinical features, and main complementary studies performed, are collected in "*Table 1*".

Glucocorticoids (GC) were used in 84.1% of the patients (mean initial oral dose 21.3mg per day, mean actual oral dose 2.3mg per day; 38.9% reached complete withdrawal of GC). Mycophenolate (MMF) and methotrexate (MTX) were the most commonly used immunosuppressants (IS). 48.4% of the patients needed ≥2 IS. Antifibrotics were needed in 13.7% of the patients. Regarding other treatments used in the NIRRVANA Registry, these are summarized in "*Table 2*".

After 4.48 (2.2-9) years of median ILD duration, 16.8% patients showed improvement, with total resolution of ILD in 2 cases; stabilization was observed in 50.6% and progression in the remaining 32.6% cases. Of this latter group, 3 patients underwent pulmonary transplant, after a mean follow-up of 5.3 years, and 1 of them died in the context of acute respiratory failure and anasarca.

Conclusion: ILD is a common but yet misunderstood complication of CTDs. The NIRRVANA Registry aims to deepen our understanding of the primary characteristics of these complications within a specific Spanish region, which will hopefully lead to improved management in the future. Ending of cross-sectional phase, a longitudinal follow-up of this registry, which is currently in progress, will provide with additional and relevant data towards achieving such goal.

Disclosure: P. García-Escudero: None; **M. López-Maraver**: None; **T. Lozinska-Lozinska**: None; **C. Lizasoain Alustiza**: None; **C. Egües Dubuc**: None; **L. Suárez Zorrilla**: None; **M. Rivas Zavaleta**: None; **E. Garmendia Sánchez**: None; **N. Vegas Revenga**: None; **M. Aburto Barreneche**: None; **G. Sada Urmeneta**: None; **E. Abad Plou**: None; **M. Garcia Vivar**: None; **I. Paniagua Zudaire**: None; **M. Inchausti Iguiñiz**: None; **I. Salegi Etxebeste**: None; **J. Calvo**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1905

Exploring the Association Between Environmental Quality Index and Rheumatoid Arthritis Mortality in the United States

Rohan Sharma[1], Eric Yen[2] and Ram Singh[3], [1]UCLA, Bakersfield, CA, [2]UCLA, Los Angeles, CA, [3]UCLA David Geffen School of Medicine, Los Angeles, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Environmental factors such as smoking, pollutants, diet, and geography as well as sex, race/ethnicity, and genetics have been linked with rheumatoid arthritis (RA) pathogenesis and outcomes. However, most studies assess individual exposures. The U.S. Environmental Protection Agency's Environmental Quality Index (EQI) provides a multi-domain composite county-level measure of environmental quality by combining 219 variables across five domains: air, water, land, built, and socio-demographic. This offers a unique opportunity to evaluate these cumulative environmental risks on RA mortality. Using this tool, we aimed to investigate the association between EQI domains and the odds of RA-related death versus all-cause mortality, adjusting for urbanization, race/ethnicity, sex, and age.

Methods: We analyzed the individual U.S. death certificate data from 2011 to 2015 using the CDC Multiple Cause of Death dataset. RA deaths were identified using ICD-10 codes for seropositive and seronegative RA. EQI scores for 2006-2010 were linked to decedents' counties using FIPS (Federal Information Processing Standard) codes. Two multivariable logistic regression models were constructed: one assessing total EQI, and another examining individual EQI domains. Both models adjusted for Rural-Urban Continuum Codes (RUCC), race/ethnicity, sex, and age. Interaction terms evaluated effect modification, and stratified analyses were conducted by race/ethnicity and RUCC.

Results: Among 12,970,917 total deaths, 43,757 were attributed to RA. Total EQI was not significantly associated with RA mortality. However, individual domains showed significant associations with RA death odds: increased odds: poorer water (OR 1.13; 95% CI, 1.12–1.14), land (1.05; 95% CI, 1.04–1.06), and socio-demographic (1.05; 95% CI, 1.04–1.06) quality; decreased odds: poorer air (0.95; 95% CI, 0.94–0.96) and built environment (0.91; 95% CI, 0.90–0.92) quality (all $p < 0.001$). Additionally, RA mortality was higher in nonmetro-urbanized areas (OR 1.09; 95% CI, 1.05–1.13) compared to metro areas. Significant interactions were found between the five EQI domains and race/ethnicity and RUCC. Stratified analyses

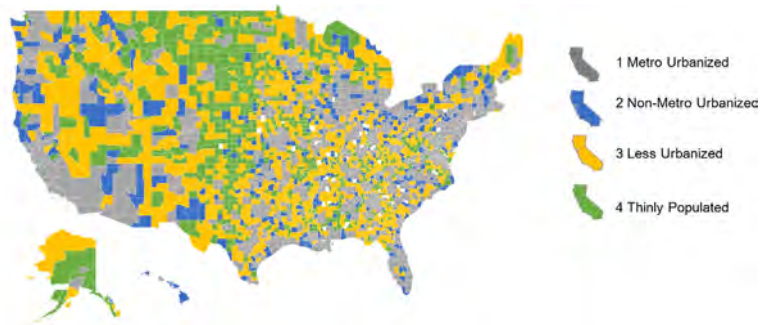


Figure 1. Rural-Urban Continuum Codes (RUCC) by County Counties were grouped into four urbanization categories following EPA methodology. This map illustrates the spatial distribution of RUCC designations across the U.S., providing geographic context for environmental quality and RA mortality patterns.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

revealed differential associations across racial/ethnic groups and urbanization levels. For example, poor water quality was significantly associated with RA death in Hispanic individuals in metro and less-urbanized areas but not in others.

Conclusion: Environmental quality domains independently associate with RA mortality, with variable effects across urbanization and racial/ethnic groups. These findings highlight the importance of addressing environmental and healthcare access disparities to reduce RA-related mortality in vulnerable populations.

Disclosure: R. Sharma: None; **E. Yen**: None; **R. Singh**: None.

Abstract Number: 1906

The incidence and mortality of connective tissue diseases in England: a population-level cohort study from 2012 to 2023

Samir Patel[1], Mark Russell[1], Katie Bechman[1], Maryam Adas[1], Zijing Yang[1], Edward Alveyn[1], Chris Wincup[2], Alexandru Dregan[1], Kate Bramham[1], Sam Norton[1], James Galloway[1] and Patrick Gordon[1], [1]King's College London, London, United Kingdom, [2]King's College Hospital, London, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The reported incidence and mortality of connective tissue diseases (CTDs) in England has been inconsistent in the literature. Our objective was to describe current trends in the incidence and mortality of systemic lupus erythematous (SLE), Sjogren's syndrome (SjS), systemic sclerosis (SSc), idiopathic inflammatory myopathies (IIM) and mixed connective tissue disease (MCTD).

Methods: We conducted a retrospective population-level study using primary care records in England via the Clinical Practice Research Datalink (CPRD). We included individuals ≥18 years old with new CTD diagnoses between 2012 and 2023. Our outcomes were incidence and all-cause mortality, which included age-standardized mortality rates (ASMRs), standardized mortality ratios and risk of death over time using flexible parametric models.

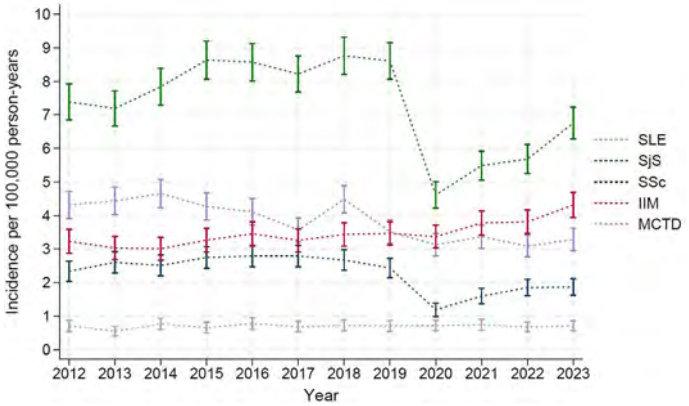


Figure 1. Age and sex standardized incidence rates (ASIRs) by year, 2012-2023, with 95% confidence intervals (95% CI).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Number and characteristics of deaths associated within each incident CTD cohort. Crude and age and sex-standardised mortality rates (AMSRs) are given with 95% confidence intervals (95% CI). Individuals with more than one CTD diagnosis contributed to each relevant group. Counts less than eight were redacted (*).

	SLE	SjS	SSc	IIM	MCTD
	N=385	N=730	N=531	N=755	N=67
Age at death in years: Median (IQR)	72.0 (63.0-80.0)	77.0 (69.0-84.0)	75.0 (66.0-82.0)	74.0 (65.0-81.0)	72.0 (60.0-78.0)
Gender: N (%)					
Male	94 (24.4%)	128 (17.5%)	113 (21.3%)	395 (52.3%)	16 (23.9%)
Female	291 (75.6%)	602 (82.5%)	418 (78.7%)	360 (47.7%)	51 (76.1%)
Ethnicity: N (%)					
White	204 (53.0%)	361 (49.5%)	250 (47.1%)	360 (47.7%)	31 (46.3%)
Black	24 (6.2%)	13 (1.8%)	17 (3.2%)	36 (4.8%)	9 (13.4%)
Asian	18 (4.7%)	45 (6.2%)	26 (4.9%)	48 (6.4%)	10 (14.9%)
Mixed and Other	89 (23.1%)	203 (27.8%)	142 (26.7%)	179 (23.7%)	*
Missing	50 (13.0%)	108 (14.8%)	96 (18.1%)	132 (17.5%)	*
Crude mortality rate per 1,000 person-years	15.46 (13.92 - 17.01)	14.82 (13.74 - 15.89)	37.30 (34.13 - 40.48)	40.89 (37.97 - 43.80)	15.38 (11.70 - 19.06)
ASMR per 1,000 person-years	16.74 (15.03 - 18.46)	9.70 (8.75 - 10.65)	24.43 (22.13 - 26.72)	27.83 (25.63 - 30.03)	16.27 (12.11 - 20.42)

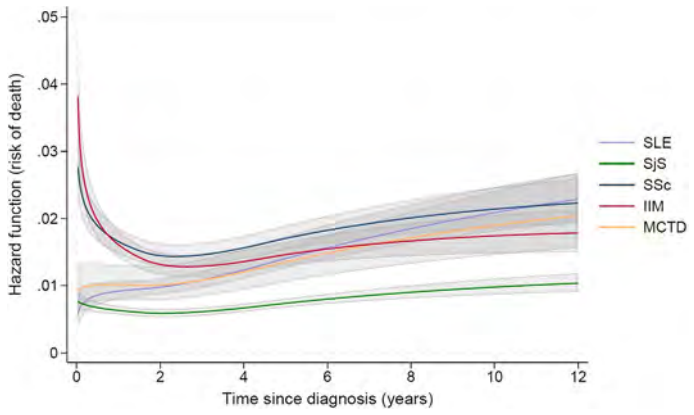


Figure 2. Risk of death in relation to time from each CTD diagnosis with 95% confidence intervals (shaded area).

Results: There were a total of 22,829 incident CTD diagnoses (81.1% female, median age 57). The age and sex-standardised incidence of SLE and SSc fell over the study period 2012 to 2023 (SLE: 4.32 to 3.29 per 100,000 person years (py) and SSc: 2.33 to 1.86 per 100,000 py), whereas SjS and MCTD incidence remained relatively stable (Figure 1). In contrast, IIM diagnoses rose from 3.23 to 4.31 per 100,000 py. ASMRs across the study period were highest for IIM (27.83 per 1,000 py), followed by SSc (24.43), SLE (16.74), MCTD (16.27) and lowest for SjS (9.70) (Table 1). Compared to the general population, mortality was higher in incident SSc, IIM, MCTD and SLE groups (SMRs of 1.74, 1.56, 1.50, and 1.30 respectively). Among all CTDs, the risk of death from time of diagnosis was highest in those diagnosed with IIM or SSc (Figure 2).

Conclusion: Our findings revealed a falling incidence of SLE, a simultaneous rise in IIM incidence and overall high all-cause mortality within IIM and SSc cohorts. Our findings acknowledge the changing landscape of CTDs in England and will aid healthcare resource planning for this vulnerable population.

Disclosure: S. Patel: None; **M. Russell**: AbbVie/Abbott, 6, Biogen, 1, Eli Lilly, 6, 12, support for attending educational meetings, Galapagos, 6, Janssen, 12, support for attending educational meetings, Menarini, 6, Pfizer, 12, support for attending educational meetings, Sandoz, 5, UCB, 6, 12, support for attending educational meetings, Viforpharma, 6; **K. Bechman**: None; **M. Adas**: None; **Z. Yang**: None; **E. Alveyn**: None; **C. Wincup**: None; **A. Dregan**: None; **K. Bramham**: None; **S. Norton**: None; **J. Galloway**: AbbVie, 2, 6, Alfasigma S.p.A., 2, Eli Lilly, 2, 6, Gilead, 2, Janssen-Cilag, 2, 5, 6, Novartis, 6, Pfizer, 2, 5, 6, Takeda, 2, UCB, 6; **P. Gordon**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1907

Twenty-Year Trends in the U.S. Burden of Gout: A State-Level Analysis of Disability and Prevalence from 2001 to 2021

Shiza sarfraz, Hassam Ali and debargha basuli, East Carolina University Brody School of Medicine, Greenville, NC

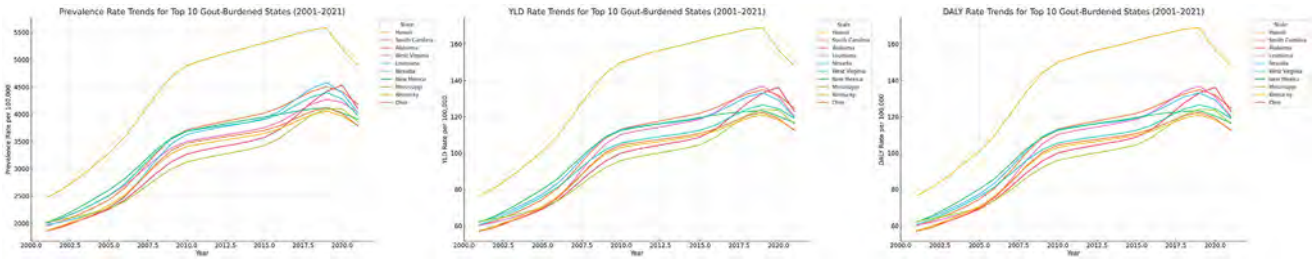
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is the most common inflammatory arthritis and an important driver of chronic disability. However, long-term trends in gout burden across U.S. states are not well-characterized. Using nationally representative data, we aimed to quantify changes in age-standardized gout-related disability-adjusted life years (DALYs), years lived with disability (YLDs), and prevalence rates between 2001 and 2021, with a focus on regional disparities.

Methods: We extracted age-standardized DALY, YLD, and prevalence rates for gout from the Global Burden of Disease 2021 dataset for adult patients. Annual rates per 100,000 population were obtained for all 50 U.S. states and the national average from 2001 to 2021. We calculated national trends with 95% confidence intervals (CIs) and computed percent change in burden over time for each state. The ten states with the highest burden in 2021 were identified.

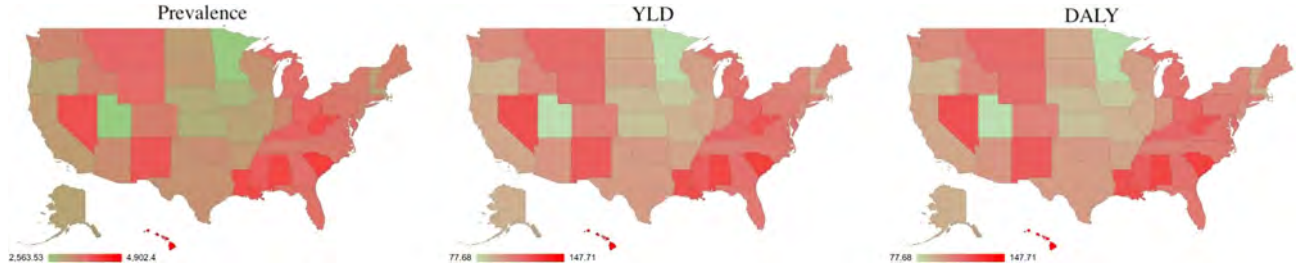
Results: Between 2001 and 2021, the national average DALY rate for gout increased from 53.1 (95% CI: 51.4–54.8) to 102.9 (95% CI: 99.4–106.4) per 100,000—a 93.7% increase. The YLD rate mirrored this trend, rising from 53.1 (95% CI: 51.4–54.8) to 102.9 (95% CI: 99.4–106.4). The prevalence rate more than doubled, from 1,677.2 to 3,408.9 per 100,000 (+103.2%). In 2021, the states with the highest DALY and YLD rates included Hawaii (147.7, +93.3%), South Carolina (124.7, +107.4%), Alabama (123.0, +114.0%), and Louisiana (120.4, +99.6%). Prevalence rates followed a similar pattern, with Hawaii (4,902.4, +98.6%), South Carolina (4,185.0, +114.0%), and Alabama (4,104.9, +118.2%) ranking among the highest. All ten highest-burden states demonstrated steep upward trajectories over the two-decade period (Figure 1). Regional clustering was evident, with the Southeast disproportionately represented (Figure 2).

Conclusion: The prevalence and disability burden of gout in the United States have more than doubled over the past 20 years. DALY and YLD rates show that the impact of gout extends beyond symptoms, contributing significantly to long-term health loss. Southern and Western states carry the highest burden, emphasizing the need for targeted public health strategies.



Trends in gout burden among the top 10 most affected U.S. states, 2001–2021.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Geographic variation in gout burden across U.S. states in 2021.

Disclosure: S. sarfraz: None; **H. Ali**: None; **d. basuli**: None.

Abstract Number: 1908

Clinical and Imaging Features of Haemochromatosis Arthropathy - a Systematic Literature Review and Meta- Analysis

Svenja Engelhardt[1], Sabine Buroh[2], Guido Schwarzer[3], Andreas Kerschbaumer[4], Axel Braner[5], Mathilde Herber[6], Pedro Machado[7], Patrick Kiely[8] and **Stephanie Finzel**[9], [1]University of Freiburg, Freiburg im Breisgau, Germany, [2]Library of the Medical Center - University of Freiburg, Faculty of Medicine, Library of the Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, Freiburg, Germany, [3]University of Freiburg, Freiburg, Germany, Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center - University of Freiburg, Freiburg, Germany, Freiburg, Germany, Freiburg, Germany, [4]Stanford University / Medical University of Vienna, Stanford, CA, [5]MVZ Aschaffenburg, Aschaffenburg, Germany, Frankfurt, Germany, [6]Strasbourg Centre University, Strasbourg, France, Department of Internal Medicine, Strasbourg, France, Strasbourg, France, [7]Department of Rheumatology, University College London, and Department of Rheumatology, Northwick Park Hospital, London North West University Healthcare NHS Trust, Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [8]St George's University Hospitals NHS Foundation Trust, London, United Kingdom, [9]Department of Rheumatology and Clinical Immunology, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Haemochromatosis arthropathy (HA) has been little researched to date. Arthropathy frequently is amongst the

first clinical manifestations of haemochromatosis, but might be overlooked or misdiagnosed as being of different origin, which impacts significantly on the patient's joint function and health due to delayed diagnose and therapy initiation. This SLR aimed to summarise the imaging and clinical features of haemochromatosis arthropathy to inform the development of EULAR classification criteria for HA.

Methods: We performed a systematic literature review by searching Medline (PubMed, Ovid), the Cochrane Library and

Embase, as well as conference abstract databases. Only original articles describing clinical and/or imaging features of HA (without language restriction or year of publication) were eligible for inclusion. After article and abstract screening, we assessed articles in detail for eligibility based on study quality and adequate reporting of outcomes. Random intercept logistic regression was utilised (using R, version 4.2.1) to calculate individual probabilities of outcomes assessed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 595 articles initially screened, 52 were analysed in detail and 36 studies were found appropriate for final analysis (Figure 1). The most common ineligibility reasons during detailed article review were poor study quality and insufficient reporting of outcomes. The most prevalent clinical characteristics were focussed on the MCP2 and MCP3 joints, with limited range of motion (pooled proportion: 62%, Figure 2 A+B), bony enlargement (48%) and pain (41%). With regards to imaging characteristics, MCP joints 2/3 showed the highest frequency of subchondral cysts (MCP2 and MCP3 52%, respectively), joint space narrowing (MCP2: 62% and MCP3 62%, respectively, Figure 2 C+D), and osteophytes (MCP2: 49%; MCP3:

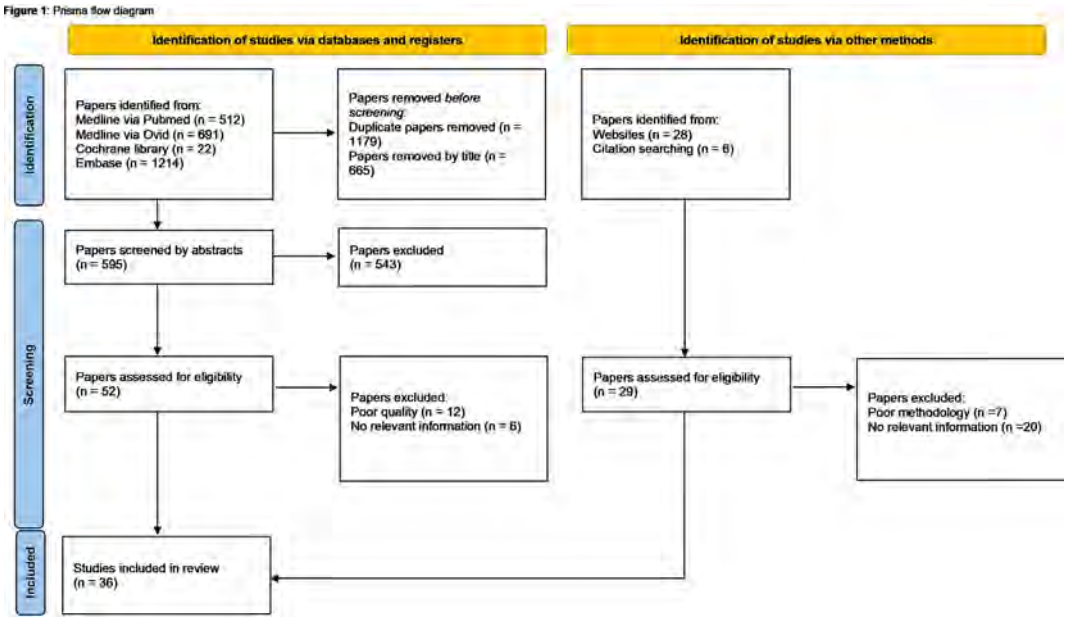
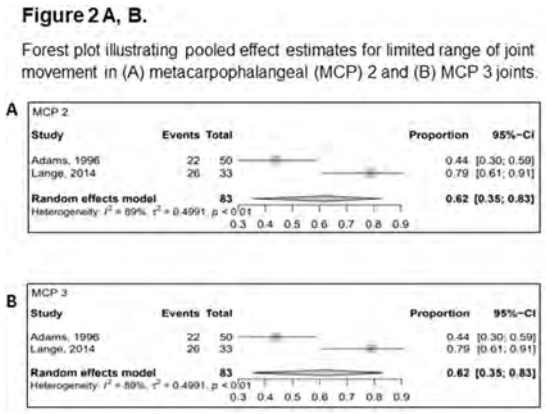


Figure 1: Prisma flow diagram



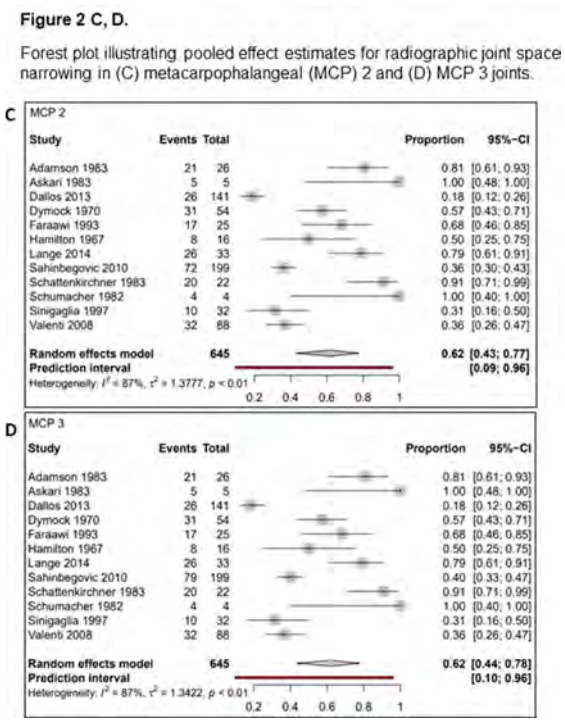


Figure 2 A, B: Forest plot illustrating pooled effect estimates for limited rang of joint movement in (A) metacarpophalangeal (MCP) 2 and (B) MCP 3 joints. Figure 2 C, D: Forest plot illustrating pooled effect estimates for radiographic joint space narrowing in (A) metacarpophalangeal (MCP) 2 and (B) MCP 3 joints.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Detailed results of clinical and imaging findings showing the pooled proportions derived from random intercept logistic regression analyses on reported outcomes.

Table 1: Detailed results of clinical and imaging findings showing the pooled proportions derived from random intercept logistic regression analyses on reported outcomes.

Characteristic	Joint(s)	Pooled proportion	95 % CI	I^2 (%)
Clinical findings				
Limited range of motion	MCP 2/3 (pooled)	0.62	0.35 – 0.83	89
Bony enlargement		0.48	0.09 – 0.90	24
Pain		0.41	0.22 – 0.63	90
Imaging findings				
Subchondral cysts	MCP 2	0.52	0.37 – 0.66	84
	MCP 3	0.52	0.37 – 0.66	84
Joint-space narrowing	MCP 2	0.62	0.43 – 0.77	87
	MCP 3	0.62	0.44 – 0.78	87
Osteophytes	MCP 2	0.49	0.30 – 0.68	85
	MCP 3	0.52	0.33 – 0.71	86
Chondrocalcinosis	Knee	0.29	0.17 – 0.45	87
Subchondral sclerosis	Hip	0.61	0.03 – 0.99	65

52%). Chondrocalcinosis prevailed in the knee (29%), and subchondral sclerosis in the hip in 61%. Considerable heterogeneity (I^2) across most meta-regressions was identified ($p< 0.01$ for all analyses except for bony enlargement in MCP2/3 and subchondral sclerosis of the hip). Table 1 summarizes the detailed results and estimates of the meta-regression analyses.

Conclusion: Our SLR identified the most commonly reported clinical characteristics and imaging patterns of HA joint involvement. As expected for this rare disease, only a limited number of articles were identified and most studies described small numbers of patients, with significant variability of outcomes, also leading to high heterogeneity in our analyses. This SLR summarizes the current evidence on clinical and imaging features important in HA, demonstrating the unmet need of developing classification criteria in patients with HA.

Disclosure: S. Engelhardt: None; **S. Buroh**: None; **G. Schwarzer**: None; **A. Kerschbaumer**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 12, Travel, Eli Lilly, 12, Travel, Janssen, 2, 6, Pfizer, 6, Stada, 6, UCB, 2, 6, 12, Travel; **A. Braner**: None; **M. Herber**: None; **P. Machado**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **P. Kiely**: Alfasigma, 6, Eli Lilly, 12, Sponsorship to attend educational meetings; **S. Finzel**: AbbVie/Abbott, 6, Alfasigma/Galapagos, 6, 12, meeting or travel grant, AstraZeneca, 2, Biotest, 6, 12, meeting or travel grant, Celltrion, 6, Chugai, 6, Eli Lilly, 12, meeting or travel grant, GlaxoSmithKlein(GSK), 2, 6, Johnson&Johnson, 2, 6, 12, meeting or travel grant, Novartis, 2, 6, 12, meeting or travel grant, NovoNordisk, 2, Sobi, 12, meeting or travel grant, UCB, 2, 6, 12, meeting or travel grant.

Abstract Number: 1909

Trends of venous thromboembolism after total joint replacement in the United Kingdom after the introduction of NICE guidelines.

Subhashisa Swain[1], Nadja Leith[2], Sarah Brown[2], Cynthia Wright Drakesmith[2], Jonathan Rees[3], Clare Bankhead[4] and John Powell[4], [1]Keele University, University of Oxford, Keele, United Kingdom, [2]University of Oxford, Oxford, United Kingdom, [3]NDORMS, University of Oxford, Oxford, United Kingdom, [4]NDPCHS, University of Oxford, Oxford, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

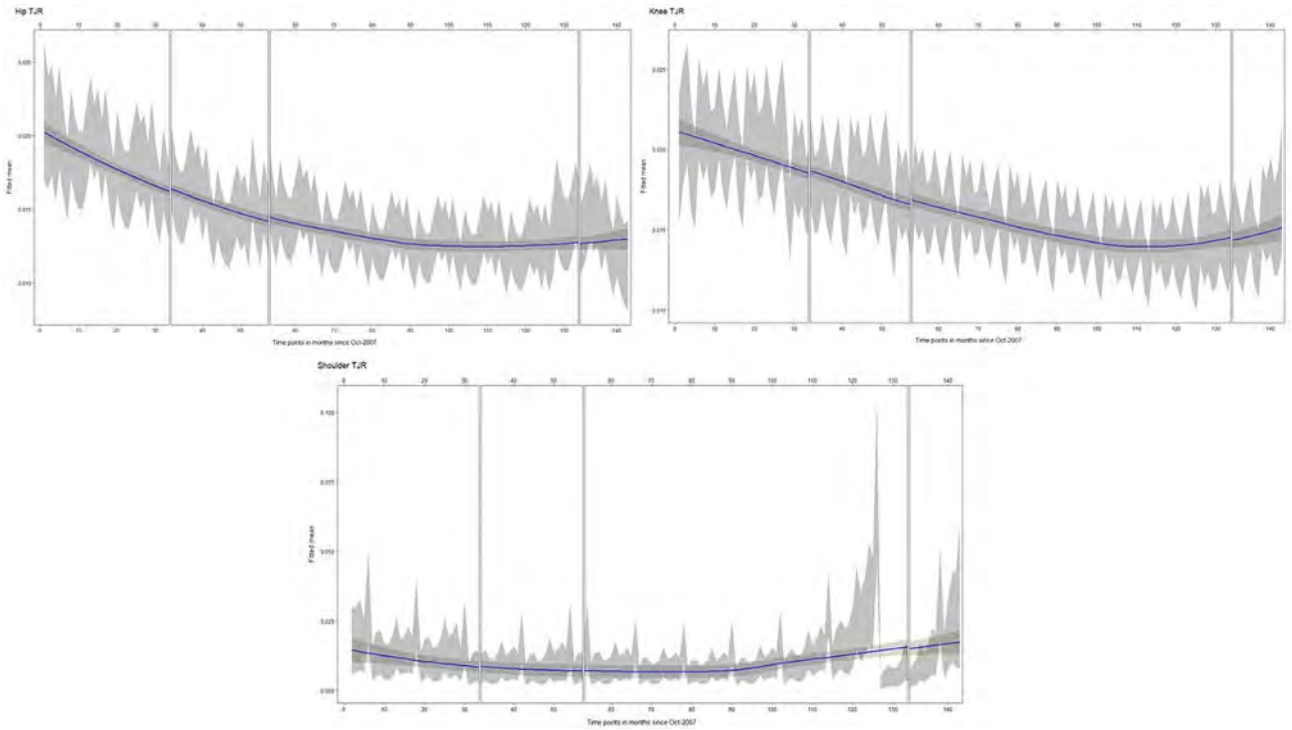
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Joint replacement (JR) surgery is one of the preferred management for end-stage arthritis. Venous Thromboembolism (VTE) is one of the major post-surgical complications after JR. However, trends of the VTE after JR in the UK and whether the guideline updates resulted in a shift in VTE rates has not been studied yet.

The aim of the study was to explore if and how rates of VTE after JR have changed in the UK over the last 12 years since the year 2007.

Methods: We used routinely collected primary care data Clinical Practice Research Datalink (CPRD AURUM) and linked hospital episode statistics (HES) and Office of National Statistics (ONS) for the study(1). We included all adult patients who had primary knee, hip or shoulder replacement surgery between October 2007 and September 2019. The outcome for the study was the recording of VTE within 6 months of JR date (index date). The outcome was reported as overall and separately for hip, knee, and shoulder joints. VTE rate estimated during the study period was compared with respect to different intervention introduced by National Health Services (NHS) in the year 2010(2), 2012(3), and 2018(4). Trends of the VTE rates for all the joints and examined using the Cox-Stuart trend test, and the seasonality and impact of the interventions (NHS guidelines) was examined using logistic regression with a polynomial function.

Results: A total of 476,620 joint replacement records were found to be eligible for the study during the study period 1st Oct 2007 and 30th Sep 2019 (both dates inclusive). Nearly 1.5% of total population had recording of VTE within 6 months from



Fugre 1 Polynomial regression plots with fitted mean for the trends of VTE incidence in the UK. Blue line represents the fitted mean trends and the shadow represents the confidence interval. Grey shadow in the background shows the actual distribution with confidence interval against time (in months). Vertical splits represents the three months after the NICE guideline for VTE prevention was introduced (March 2010, March 2012, and June 2018).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the date of the procedure. The prevalence was higher for knee joints (1.6%) followed by hip (1.4%) and shoulder (1%). The incidence rate of VTE after 6 months was 16.85 per 1000 person-6months for knee, 14.81 per 1000 person-6months, and 10.35 per 1000 person-6months. A decline in overall VTE incidence rate was seen until end of the year 2016, followed by a rise in the trend (p trend = 0.02). A significant decline in VTE was reported within 6 months for hip (p = 0.04) and knee joints (p trend = 0.008). The trend test of VTE for shoulder joint was not statistically significant. (Figure 1)

Adjusted logistic regression with a fifth degree orthogonal polynomial showed the seasonal pattern for the VTE in three joints separately. The three months after effect of three interventions (CG92 in January 2010; TA245 in January 2012; NG89 in March 2018) was examined in the polynomial model after adjusting for the seasonality and regions. No significant step change was seen because of the intervention in the trends of VTE for any joints other than Shoulder joint.

Conclusion: here was no significant change in the rate of VTE after the NICE guidelines introduced. Further study is needed to explore the economic benefits of the change in NICE guidelines.

Disclosure: S. Swain: None; **N. Leith**: None; **S. Brown**: None; **C. Wright Drakesmith**: None; **J. Rees**: None; **C. Bankhead**: None; **J. Powell**: None.

Abstract Number: 1910

Clinical profile and healthcare resource utilization of patients diagnosed with giant cell arteritis or polymyalgia rheumatica in the US: a real-world cohort study using a large database of administrative health claims

Julie Mouchet[1], Tim Nguyen[2], **Valeria Jordan M.**[3], G S Ramakrishna[4], Linda Grinnell-Merrick[2], Andrew Heaney[5], Anushka Mitra Das[5], Pooja Shah[6] and Evi Zhuleku[7], [1]Novartis Pharma AG, Basel, Switzerland, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]Novartis Pharmaceuticals Corporation, Tenafly, NJ, [4]Novartis Healthcare Private Limited, Hyderabad, India, [5]Novartis Ireland Ltd, Dublin, Ireland, [6]Cytel Inc, Cambridge, ON, Canada, [7]Cytel Inc, Berlin, Germany

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are systemic inflammatory conditions which predominantly affect individuals over the age of 50 years. The conditions share overlapping clinical features[1,2] and can significantly impact patients' quality of life. The main symptoms of PMR include pain and stiffness in the shoulder, neck, and hips[1]; whereas patients with GCA present with headache, scalp tenderness, fever, jaw claudication, as well as aortic aneurysm, aortitis and visual disturbances[2,3]. Both conditions are associated with significant disease burden, including cardiovascular, cerebrovascular and malignancies for PMR and detrimental effects on vision for GCA[1,2]. This real-world cohort study aims to understand the clinical profile and healthcare resource utilization (HCRU) of patients with PMR and GCA in the US.

Methods: Adult patients with a first diagnosis (index date) of PMR or GCA aged ≥50 years during Jan 2017- May 2023 and with at least 1 year of database continuous enrolment pre- and post-index were identified from Optum® Clinformatics Data Mart (CDM) claims. To increase the specificity of the diagnosis, at least two ICD-10 CM codes (PMR: M35.3 - GCA: M31.6) recorded 7-30 days apart were required. Patients were also required to have ≥2 outpatient prescriptions of oral glucocorticoids within six months post-index. The total number of patients, and the distribution by age, sex, comorbidities, as well as

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

HCRU during follow-up were reported. Patients were followed from index to earliest of death, end of insurance or study period (5/31/2024).

Results: A total of 13,786 patients newly diagnosed with PMR and 1,520 patients with GCA were included in the study population (Table 1). Mean age (SD) was 74.8 (7.8) years for PMR and 75.0 (8.0) years for GCA. Women represented 57.7% and 68.5% of the PMR and GCA patients, respectively. The mean Charlson Comorbidity Index was slightly higher for GCA (1.7) vs. PMR (1.3). Prevalence of the top 10 comorbidities at baseline ranged from 22 to 68% (Figure 1). On average, patients with PMR and GCA were followed 3.5 (1.7) and 3.3 (1.7) years, respectively. Inpatient and ER visits were reported for 44.0% and 64.3% of patients with PMR. Higher proportions were observed for GCA patients with 66.3% and 80.1% for inpatient and ER visits, respectively.

Conclusion: In the US, both PMR and GCA predominantly affect elderly female patients. The clinical profile of these patients indicates a considerable burden related to highly prevalent comorbidities including cardiovascular, endocrine and musculoskeletal disorders. This impacts HRCU substantially, highlighting the need for better management strategies to reduce clinical and economic burden among patients with GCA and PMR.

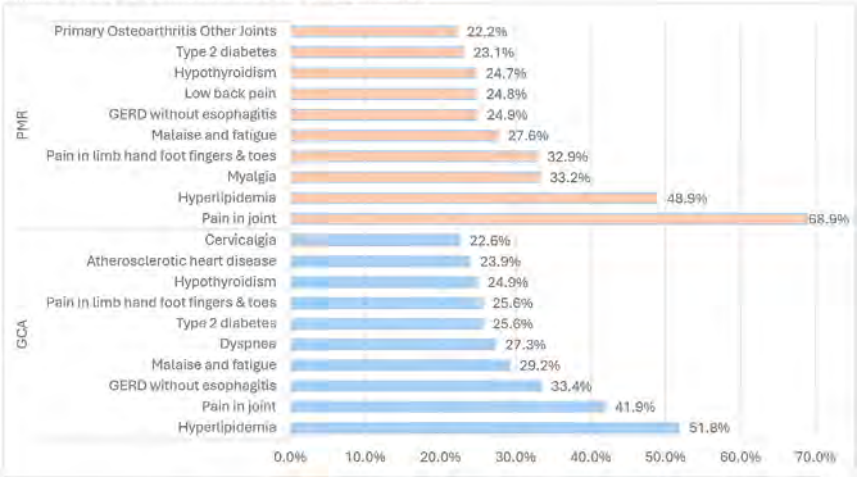
1 Gazitt T, Zisman D, Gardner G. Polymyalgia Rheumatica: a Common Disease in Seniors. *Curr Rheumatol Rep*. 2020;22(8):40. doi:10.1007/s11926-020-00919-2
2 Mohammad AJ, Englund M, Turesson C, Tomasson G, Merkel PA. Rate of Comorbidities in Giant Cell Arteritis: A Population based Study. *J Rheumatol*. 2017;44(1):84-90. doi:10.3899/jrheum.160249

Table 1: Total number and baseline characteristics of the study population

		N	PMR 13786	GCA 1520
Age	Mean (SD)		74.8 (7.8)	75 (8.0)
	Median		75.0	75.0
	Min-Max		70-89	70-89
Gender (%)	Female		57.7	68.5
Race (%)	Caucasian		64.1%	62.2%
	African American		4.9%	9.3%
	Asian		1.3%	1.3%
	Not reported		29.8%	27.2%
Ethnicity (%)	Hispanic		5.8%	6.8%
	Non Hispanic		65.8%	64.8%
	Not reported		28.5%	28.4%
Charlson Comorbidity Index (1 year pre-index)*	Mean (SD)		1.3 (1.8)	1.7 (2.0)
	Median		1.0	1.0

** The Charlson Comorbidity Index (CCI) assesses comorbidity level by taking into account both the number and severity of 19 pre-defined comorbid conditions.*

Figure 1: Top 10 comorbidities for GCA and PMR



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3 Mahr A, Hachulla E, de Boysson H, et al. Presentation and Real World Management of Giant Cell Arteritis. *Front Med*. 2021;8. doi:10.3389/fmed.2021.732934

Disclosure: J. Mouchet: Novartis, 3, 11; **T. Nguyen**: Novartis, 3, 11; **V. Jordan M.**: Novartis, 3, 12, Shareholder; **G. Ramakrishna**: Novartis, 3; **L. Grinnell-Merrick**: Novartis, 3, 11; **A. Heaney**: Novartis, 3, 11; **A. Mitra Das**: Novartis, 3, 11; **P. Shah**: None; **E. Zhuleku**: None.

Abstract Number: 1911

Characterizing Psoriasis Patients at Risk for Transition to Psoriatic Arthritis: Early Insights from the STOP PsA At-Risk Cohort

Victoria Konzett[1], Eva Manger[2], Simon Reider[2], Johannes Griss[3], Constanze Jonak[3], Kastriot Kastrati[4], Peter Mandl[4], Gudrun Ratzinger[5], Christina Duftner[2], Thomas Karonitsch[4], Daniel Aletaha[6] and the STOP PsA study group, [1]Department of Medicine III, Division of Rheumatology, Medical University of Vienna, Vienna, Austria, [2]Department of Internal Medicine, Clinical Division of Internal Medicine II, Medical University of Innsbruck, Innsbruck, Austria, [3]Department of Dermatology, Medical University of Vienna, Austria, Vienna, Austria, [4]Department of Medicine III, Division of Rheumatology, Medical University Vienna, Vienna, Austria, [5]Department of Dermatology, Venereology and Allergology, Medical University of Innsbruck, Austria, Innsbruck, Austria, [6]Medical University Vienna, Wien, Austria

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) develops predominantly in patients with psoriasis (Pso). Although key drivers and predictors of disease progression have been identified in recent years, prospective studies and a detailed understanding of the pathogenetic mechanisms underlying disease transition remain limited.

Methods: The Susceptibility of Transition from Psoriasis to Psoriatic arthritis (STOP PsA) study is a prospective, longitudinal, multicenter cohort study of Pso patients at risk of developing PsA. Comprehensive clinical assessments, including detailed joint counts, patient-reported outcomes (PROs), cardiovascular risk evaluation, and joint sonography, together with transcriptomic and epigenetic analyses of peripheral blood mononuclear cells (PBMC) and skin biopsies, as well as microbiome

Table 1. Baseline characteristics; data are given as N (%) or mean (standard deviation)

	228 patients
Female (%)	108 (47.4%)
Age (years)	44.6 (13.6)
Body Mass Index (kg/m²)	27.8 (6.1)
Caucasian (%)	206 (90.4%)
Psoriasis Duration (years)	17.1 (13.4)
Psoriasis Area and Severity Index (PASI)	4.1 (5.0)
C-reactive protein (mg/dl)	0.3 (0.4)
Tender Joint Count (68 joints)	2.0 (4.5)
Patient Pain Assessment (0-10)	2.0 (2.6)
Patient Global Disease Assessment (0-10)	2.6 (2.6)
Maastricht Ankylosing Spondylitis Enthesitis Score (MASES; 0-13)	0.6 (1.4)
Leeds Enthesitis Index (LEI; 0-6)	0.5 (1.0)
Bath Ankylosing Spondylitis Metrology Index (BASMI; 0-10)	2.0 (1.0)
Dermatological Life Quality Index (DLQI; 0-30)	5.8 (6.2)
Psoriatic Arthritis Impact of Disease (PSAID; 0-10)	2.3 (2.2)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

profiling of skin and gut samples, will generate a broad, multi-dimensional dataset to enable in-depth investigation of disease transition and risk stratification. We included patients with Pso but without clinical arthritis, synovitis or enthesitis. This abstract provides first insights into the baseline characteristics of this patient population in the ongoing study.

Results: After prescreening, a total of 253 patients were assessed in a baseline visit, of whom 228 were finally included. At baseline, ten patients were diagnosed with PsA, and two patients with axial spondyloarthritis (SpA), indicating a 4.7% prevalence of incipient PsA/SpA in this at-risk population. Other reasons for exclusion were patients' decline to participate (n=6), revision of dermatological diagnosis (n=2), and previous diagnosis of arthritis missed at pre-screening (n=5). Included patients had a mean age of 44.6 ± 13.6 years, and a mean Pso duration of 17.1 ± 13.4 years. 108 (47.4%) were female, and 195 (85.5%) had a psoriasis vulgaris subtype. 91 patients (39.9%) had at least one tender joint at screening, and the mean tender joint count of 68 joints was 1.96 ± 4.54. A detailed list of baseline characteristics is shown in Table 1.

106 (46.5%) of patients were DMARD naïve, and 107 (46.9%) received DMARD therapy at screening. Figure 1 displays the distribution of compounds (Panel A) and mechanisms of action (Panel B) among treated patients.

Conclusion: Approximately 40% of Pso patients in this study reported arthralgia, and several early PsA/SpA cases were identified during the screening period. Future analyses from this ongoing study aim to deepen our understanding of disease transition, identify early biomarkers and explore potential therapeutic targets for arthritis prevention.

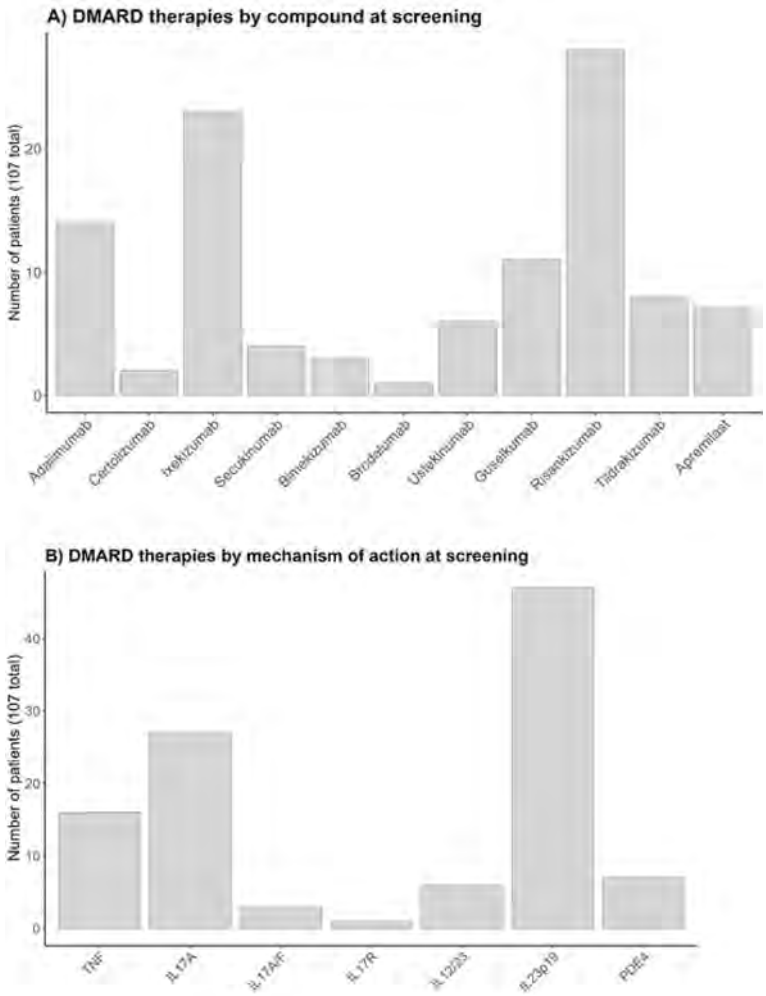


Figure 1. Distribution of disease-modifying anti-rheumatic drug (DMARD) therapies by compound (Panel A) and mechanism of action (Panel B) among the 107 patients receiving therapy at screening.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Konzett: AbbVie/Abbott, 1, AstraZeneca, 6, Eli Lilly, 6; **E. Manger**: None; **S. Reider**: AbbVie, 6; **J. Griss**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Novartis, 6, Pfizer, 6; **C. Jonak**: None; **K. Kastrati**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Eli Lilly, 6, Novartis, 6; **P. Mandl**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Janssen, 6, Novartis, 5, 6, UCB, 5; **G. Ratzinger**: Eli Lilly, 1, 6; **C. Duftner**: None; **T. Karonitsch**: None; **D. Aletaha**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sanofi, 6.

Abstract Number: 1912

Cutaneous manifestations of vasculitis: A cross-sectional analysis from an international cohort

Robert Micheletti[1], **William Song**[1], Brian Chu[2], Lynne Allen-Taylor[3], Joel Gelfand[3], Peter Grayson[4], Cristina Ponte[5], Joanna Robson[6], Ravi Suppiah[7], Raashid Luqmani[8], Richard Watts[9] and Peter Merkel[10], [1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [2]Brown University Health, Providence, RI, [3]University of Pennsylvania, Philadelphia, [4]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD, [5]Unidade Local de Saúde de Santa Maria, Lisbon, Portugal, [6]University of the West of England Bristol, Bristol, United Kingdom, [7]Health New Zealand - Te Toka Tumai, Auckland, New Zealand, [8]University of Oxford, Oxford, United Kingdom, [9]University of East Anglia, Norwich, United Kingdom, [10]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Vasculitis is a group of rare, multisystem diseases which may involve the skin. Characterization of the frequency, type, and significance of cutaneous manifestations in various vasculitides is incomplete.

Methods: This study analyzed cross-sectional data collected through the Diagnostic and Classification Criteria in Vasculitis (DCVAS) (NCT01066208) study, a large, multinational, collaborative effort involving 136 clinical sites in 32 countries from 2011 to 2017, collecting comprehensive clinical data on patients with several forms of vasculitis from disease onset to 6 months after initial presentation. Summary statistics were used to describe cutaneous manifestations of each included type of vasculitis, and logistic regression analysis was used to calculate the odds ratio for severe systemic manifestations of vasculitis based on presence of skin findings.

Results: Data from 4,468 adults diagnosed with vasculitis were analyzed, including 270 with IgA vasculitis (IgAV), 201 with Behçet's disease (BD), 57 with cryoglobulinemic vasculitis (CV), 1,023 with granulomatosis with polyangiitis (GPA), 505 with microscopic polyangiitis (MPA), 382 with eosinophilic granulomatosis with polyangiitis (EGPA), 194 with polyarteritis nodosa (PAN), 1,206 with giant cell arteritis (GCA), and 630 with Takayasu arteritis (TAK). Participants in the DCVAS study were from Europe (59%), North America (21%), Asia (17%), Oceania (2%), and Africa (1%).

Cutaneous manifestations were common at the time of presentation for all types of vasculitis except large-vessel vasculitis (GCA and TAK), ranging from 20% of patients with MPA to 97% of patients with IgAV (Table 1). The frequency of specific cutaneous manifestations encountered in each type of vasculitis varied considerably, although petechiae/purpura was the most common skin finding in all types of small-vessel vasculitis (IgAV, CV, GPA, MPA, and EGPA).

Skin biopsy was utilized to varying degrees, performed in 22-82% of those with small- or medium-vessel vasculitis. When performed, skin biopsy was diagnostic in the majority of cases, including 95% (205/216) of IgAV, 73% (16/22) of CV, 73% (67/92) of GPA, 73% (16/22) of MPA, 67% (49/73) of EGPA, and 70% (52/74) of PAN. Skin biopsy was less often useful for diagnosis of BD (35%; 7/20), GCA (0%; 0/1), and TAK (33%; 2/6).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Univariable logistic regression demonstrated that patients with cutaneous manifestations had significantly greater odds of severe systemic manifestations of GPA (OR 1.8, 95% CI 1.3, 2.6) and EGPA (OR 1.8, 95% CI 1.1, 2.9); those with cutaneous manifestations had lower odds of severe systemic manifestations of PAN (OR 0.5, 95% CI 0.3, 0.99) (Table 2).

Conclusion: These findings characterize the cutaneous manifestations of vasculitis at the time of diagnosis and highlight the potential diagnostic and prognostic importance of the skin in these multisystem diseases. For patients presenting with small-

Table 1. Type and frequency of cutaneous manifestations in different types of vasculitis.

	IgAV	BD	CV	GPA	MPA	EGPA	PAN	GCA	TAK
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Participants, *N*	270	201	57	1023	505	382	194	1206	630
Any skin findings at time of presentation	262 (97%)	118 (59%)	50 (88%)	299 (29%)	102 (20%)	168 (44%)	111 (57%)	34 (3%)	37 (6%)
Petechiae or purpura	243 (90%)	2 (<1%)	38 (67%)	152 (15%)	48 (10%)	78 (20%)	23 (12%)	3 (<1%)	3 (<1%)
Livedo reticularis or racemose	0 (0%)	0 (0%)	1 (2%)	4 (<1%)	7 (1%)	1 (<1%)	10 (5%)	0 (0%)	1 (<1%)
Painful skin lesions	89 (33%)	65 (32%)	15 (26%)	95 (9%)	23 (5%)	40 (11%)	50 (26%)	8 (<1%)	12 (2%)
Maculopapular rash	29 (11%)	44 (22%)	6 (11%)	71 (7%)	25 (5%)	59 (16%)	30 (16%)	7 (<1%)	3 (<1%)
Pruritus	33 (12%)	6 (3%)	5 (9%)	31 (3%)	16 (3%)	44 (12%)	13 (7%)	12 (<1%)	3 (<1%)
Urticaria	2 (<1%)	1 (<1%)	1 (2%)	7 (<1%)	3 (<1%)	30 (8%)	3 (2%)	4 (<1%)	2 (<1%)
Splinter hemorrhage	1 (<1%)	0 (0%)	0 (0%)	17 (2%)	2 (<1%)	7 (2%)	2 (1%)	0 (0%)	2 (<1%)
Cutaneous ulcers	43 (16%)	43 (21%)	12 (21%)	41 (4%)	9 (2%)	14 (4%)	30 (16%)	3 (<1%)	6 (<1%)
Mouth ulcers	11 (4%)	171 (85%)	1 (2%)	66 (7%)	18 (4%)	11 (3%)	9 (5%)	7 (<1%)	12 (2%)
Genital ulcers	0 (0%)	152 (76%)	0 (0%)	2 (<1%)	0 (0%)	0 (0%)	3 (2%)	2 (<1%)	0 (0%)
Gangrene	12 (4%)	2 (<1%)	5 (9%)	22 (2%)	6 (1%)	7 (2%)	22 (11%)	1 (<1%)	7 (1%)
Cutaneous infarct	38 (14%)	1 (<1%)	3 (5%)	16 (2%)	1 (<1%)	5 (1%)	8 (4%)	2 (<1%)	1 (<1%)
Tender skin nodules	3 (1%)	41 (20%)	1 (2%)	22 (2%)	6 (1%)	7 (2%)	27 (14%)	3 (<1%)	8 (1%)
Non-tender skin nodules	2 (<1%)	5 (3%)	1 (2%)	13 (1%)	5 (<1%)	7 (2%)	11 (6%)	3 (<1%)	3 (<1%)
Two or more different skin findings at time of presentation	144 (53%)	66 (33%)	23 (40%)	132 (13%)	31 (6%)	85 (22%)	63 (33%)	9 (<1%)	11 (2%)
Average number of different skin findings at time of presentation, *mean (standard deviation)*	1.8 (1.0)	1.0 (1.1)	1.5 (1.1)	0.5 (0.9)	0.3 (0.7)	0.8 (1.1)	1.2 (1.4)	0.04 (0.3)	0.1 (0.4)

Abbreviations: IgA vasculitis, IgAV; Behçet's disease, BD; cryoglobulinemic vasculitis, CV; granulomatosis with polyangiitis, GPA; microscopic polyangiitis, MPA; eosinophilic granulomatosis with polyangiitis, EGPA; polyarteritis nodosa, PAN; Takayasu arteritis, TAK; giant cell arteritis, GCA

Table 2. Crude Odds of severe systemic manifestations of vasculitis based on presence of cutaneous manifestations*

	Odds ratio (95% confidence interval)	p-value
IgA vasculitis	1.3 (0.3, 6.8)	0.726
Behçet's disease	1.0 (0.5, 2.3)	0.938
Cryoglobulinemic vasculitis	1.5 (0.2, 9)	0.684
Granulomatosis with polyangiitis	1.8 (1.3, 2.6)	<0.001
Microscopic polyangiitis	0.9 (0.4, 1.7)	0.666
Eosinophilic granulomatosis with polyangiitis	1.8 (1.1, 2.9)	0.019
Polyarteritis nodosa	0.5 (0.3, 0.99)	0.046

* Severe systemic manifestations of vasculitis were defined based on components of the Birmingham Vasculitis Activity Score (BVAS) and include: scleritis, sensorineural deafness, mesenteric ischemia, alveolar hemorrhage, respiratory failure, red blood cell casts in urine, rise in serum creatinine >30% or fall in creatinine clearance >25%, meningitis, spinal cord lesion, stroke, cranial nerve palsy, sensory peripheral neuropathy, or mononeuritis multiplex. Analysis was limited to vasculitis types with >10% prevalence of cutaneous manifestations.

Severe systemic manifestations of vasculitis were defined based on components of the Birmingham Vasculitis Activity Score (BVAS) and include: scleritis, sensorineural deafness, mesenteric ischemia, alveolar hemorrhage, respiratory failure, red blood cell casts in urine, rise in serum creatinine >30% or fall in creatinine clearance >25%, meningitis, spinal cord lesion, stroke, cranial nerve palsy, sensory peripheral neuropathy, or mononeuritis multiplex. Analysis was limited to vasculitis types with >10% prevalence of cutaneous manifestations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and medium-vessel vasculitis, early recognition of cutaneous manifestations, combined with the high diagnostic yield of skin biopsy, may help accelerate accurate diagnosis, preclude unnecessary testing, and shorten time to initiation of disease-specific therapy.

Disclosure: R. Micheletti: Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Cabaletta Bio, 2, 5, 6, InflaRx, 2, 5, 6, Vertex, 2, 5, 6; **W. Song**: None; **B. Chu**: None; **L. Allen-Taylor**: None; **J. Gelfand**: AbbVie/Abbott, 2, Amgen, 5, Artax, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, Celldex, 2, Eli Lilly, 2, FIDE, 2, GlaxoSmithKlein(GSK), 2, Inmagene, 2, Janssen Biologics, 2, Leo, 2, Moonlake, 2, Neuroderm, 2, Novartis Corp, 2, Oruka, 2, Pfizer, 5, UCB, 2; **P. Grayson**: None; **C. Ponte**: AbbVie/Abbott, 2, 4, 6, CSL Vifor, 2, 4, 6, GlaxoSmithKlein(GSK), 2, 6, Novartis, 5, 6, Pfizer, 6; **J. Robson**: None; **R. Suppiah**: AbbVie/Abbott, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Novartis Corp, 2, 5, 6, Pfizer, 2, 5, 6; **R. Luqmani**: None; **R. Watts**: None; **P. Merkel**: AbbVie/Abbott, 2, 5, 6, Alpine, 2, 5, 6, Amgen, 2, 5, 6, ArGenx, 2, 5, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CSL Behring, 2, 5, 6, Eicos, 2, 5, 6, Electra, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, iCell, 2, 5, 6, Interius, 2, 5, 6, Kinevant, 2, 5, 6, Kyverna, 2, 5, 6, Lifordi, 2, 5, 6, Metagenomia, 2, 5, 6, Neutrolis, 2, 5, 6, Novartis Corp, 2, 5, 6, NS Pharma, 2, 5, 6, Q32, 2, 5, 6, Quell, 2, 5, 6, Regeneron, 2, 5, 6, Sanofi, 2, 5, 6, Sparrow, 2, 5, 6, Takeda, 2, 5, 6, Vistera, 2, 5, 6.

Abstract Number: 1913

Do We Screen For and Do We Miss Antimalarial-Induced Cardiomyopathy (AMIC)? Risk Profiles according to Hydroxychloroquine Exposure Duration

Youngmin Kim[1], Robert Padera[2], Brittany Weber[3] and Karen H. Costenbader[4], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, DEDHAM, MA, [4]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1877–1913) Epidemiology & Public Health Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is widely used for autoimmune diseases but carries a risk of antimalarial-induced cardiomyopathy (AMIC) that increases with long-term use and is often diagnosed after irreversible heart damage. Endomyocardial biopsy with electron microscopy is the gold standard for diagnosis but is rarely conducted as it is invasive. Screening guidelines, including cardiac biomarkers, ECGs, and imaging, have been proposed to detect early AMIC, but it is not known if they are followed (Tselios et al., 2018; Desmarais et al., 2021; DiGregorio et al., 2025). We aimed to evaluate demographic and clinical features, cardiac biomarkers and cardiac test utilization for patients taking HCQ, according to cumulative HCQ duration, to inform potential risk-based screening approaches.

Methods: We identified patients with ≥10 HCQ prescriptions in the electronic health records (EHR) of our large academic medical center. We extracted patient demographics, rheumatologic diagnoses, HCQ prescription dates, cardiac biomarker testing and results (troponin-I, troponin-T, hsCRP, CK-MB, NT-proBNP), and cardiac testing (ECG, echocardiography [ECHO], cardiac MRI, endomyocardial biopsy). Patients were stratified into 3 groups by HCQ exposure duration: ≤5 years, 5–10 years, and >10 years. Group comparisons were conducted using ANOVA for continuous and Chi-square tests for categorical variables. Cardiac biopsy reports were reviewed to identify AMIC.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 13,266 patients (mean age 62.1 [SD 16.9]; 82.9% female), 56.9% had ≤5 years, 22.4% had 5–10 years, and 20.7% had >10 years of HCQ use. While cardiac testing was more common in longer-duration groups, only 70% had ECGs, 41% echocardiograms, and 4.6% cardiac MRI. Importantly, biomarker testing was performed in only a fraction of the total cohort (e.g., troponin-I in 13.3%, CK-MB in 21.6%). Troponin-I abnormalities did increase in prevalence with longer exposure (8.1% in ≤5 years vs 12.4% in >10 years, p=0.02) among those tested. Of 35 patients who underwent biopsy (0.3%), 11 (31.4%) had biopsy-confirmed AMIC.

Conclusion: Despite known risks, cardiac biomarker and imaging tests are underutilized in long-term HCQ users, and biopsy remains rare. Many patients with potential AMIC risk never had testing, limiting recognition of the true disease burden. Our findings highlight a need to develop and implement standardized, non-invasive screening protocols for AMIC to improve early detection and quantify incidence more accurately in high-risk populations.

Table 1. Demographics and Clinical Characteristics of Patients with ≥10 Prescriptions of Hydroxychloroquine in a Large Academic Hospital Electronic Health Record Database (n=13,266)

Demographics	
Age (mean, SD)	62.1 (16.9)
Females (*n*, %)	11,001 (82.9)
Whites (*n*, %)	10,264 (77.4)
Deceased (*n*, %)	1,914 (14.4)
Hydroxychloroquine Duration	
Mean years of use, (SD)	6.00 (6.02)
Less than 5 years (*n*, %)	7,554 (56.9)
5-10 years (*n*, %)	2,967 (22.4)
More than 10 years (*n*, %)	2,745 (20.7)
Rheumatologic Diagnoses	
Systemic Lupus Erythematosus (*n*, %)	3,670 (37.5)
Rheumatoid Arthritis (*n*, %)	4,200 (42.9)
Sjogren's Syndrome (*n*, %)	382 (3.9)
Other Rheumatologic Diseases (*n*, %)	1,540 (15.7)
Biomarker Abnormalities	
High Troponin-I among n=1,759 tested (*n*, %)	181 (10.3)
High Troponin-T among n=3,071 tested (*n*, %)	671 (21.8)
High CKMB among n=2,859 tested (*n*, %)	795 (27.8)
High NT-BNP among n=3,710 tested (*n*, %)	1,524 (41.1)
High hs-CRP among n=6,121 tested (*n*, %)	3,226 (52.7)
Cardiac Tests Performed Among All Patients	
Electrocardiography (*n*, %)	9,292 (70.0)
Echocardiography (*n*, %)	5443 (41.0)
Cardiac MRI (*n*, %)	604 (4.6)
Cardiac Biopsy (*n*, %)	35 (0.3)

Values are presented as mean (standard deviation) for continuous variables and number (percentage) for categorical variables. p-values were calculated using Fisher's exact test for categorical variables and Student's t-test for continuous variables.

Abbreviations: CKMB, creatine kinase myocardial band; NT-BNP, N-terminal pro B-type natriuretic peptide; hs-CRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging.

Table 2. Demographics and Clinical Characteristics of Patients of <5, 5-10, and >10 years of Hydroxychloroquine Duration in a Large Academic Hospital Electronic Health Record Database (n=13,266)

	0-5 yrs (*n* = 7,554)	5-10 yrs (*n* = 2,967)	>10 yrs (*n* = 2,745)	*p**
Demographics				
Age (mean, SD)	61.8 (17.7)	61.5 (16.9)	63.6 (14.6)	< 0.001
Females (*n*, %)	6,028 (79.8)	2,534 (85.4)	2,439 (88.9)	< 0.001
Whites (*n*, %)	5,899 (78.1)	2,296 (77.4)	2,069 (75.4)	0.02
Deceased (*n*, %)	1,175 (15.6)	365 (12.3)	374 (13.6)	< 0.001
Rheumatologic Diagnoses				
Systemic Lupus Erythematosus (*n*, %)	1,532 (20.3)	857 (28.9)	1,281 (46.7)	< 0.001
Rheumatoid Arthritis (*n*, %)	2,296 (30.4)	1,025 (34.5)	879 (32.0)	< 0.001
Sjogren's Syndrome (*n*, %)	148 (2.0)	101 (3.4)	133 (4.8)	< 0.001
Other Rheumatologic Diseases** (n, %)	782 (10.4)	439 (14.8)	319 (11.6)	< 0.001
Biomarker Abnormalities				
High Troponin-I (*n*, % of tested)	65/807 (8.1)	43/364 (11.8)	73/588 (12.4)	0.02
High Troponin-T (*n*, % of tested)	368/1,578 (23.3)	144/676 (21.3)	159/817 (19.5)	0.09
High CKMB (*n*, % of tested)	400/1,400 (28.6)	165/611 (27.0)	230/848 (27.1)	0.67
High NT-BNP (*n*, % of tested)	824/1,975 (41.7)	308/786 (39.2)	392/949 (41.3)	0.47
High hs-CRP (*n*, % of tested)	1,520/2,851 (53.3)	776/1,542 (50.3)	930/1728 (53.8)	0.09
Cardiac Tests				
Electrocardiography (*n*, %)	5,142 (68.1)	2,016 (67.9)	2,134 (77.7)	< 0.001
Echocardiography (*n*, %)	,2823 (37.4)	1,221 (41.2)	1,399 (51.0)	< 0.001
Cardiac MRI (*n*, %)	303 (4.0)	125 (4.2)	176 (6.4)	< 0.001
Cardiac Biopsy (*n*, %)	20 (0.26)	4 (0.13)	11 (0.40)	0.15
Biopsy Confirmed AMIC (*n*, % of tested)	4 (0.20)	2 (0.50)	5 (0.45)	0.24

* ANOVA for continuous and Chi-square tests for categorical variables
** most common was undifferentiated connective tissue disease

Abbreviations: CKMB, creatine kinase myocardial band; NT-BNP, N-terminal pro B-type natriuretic peptide; hs-CRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging, AMIC: antimalarial-induced cardiomyopathy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Y. Kim: None; **R. Padera**: None; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

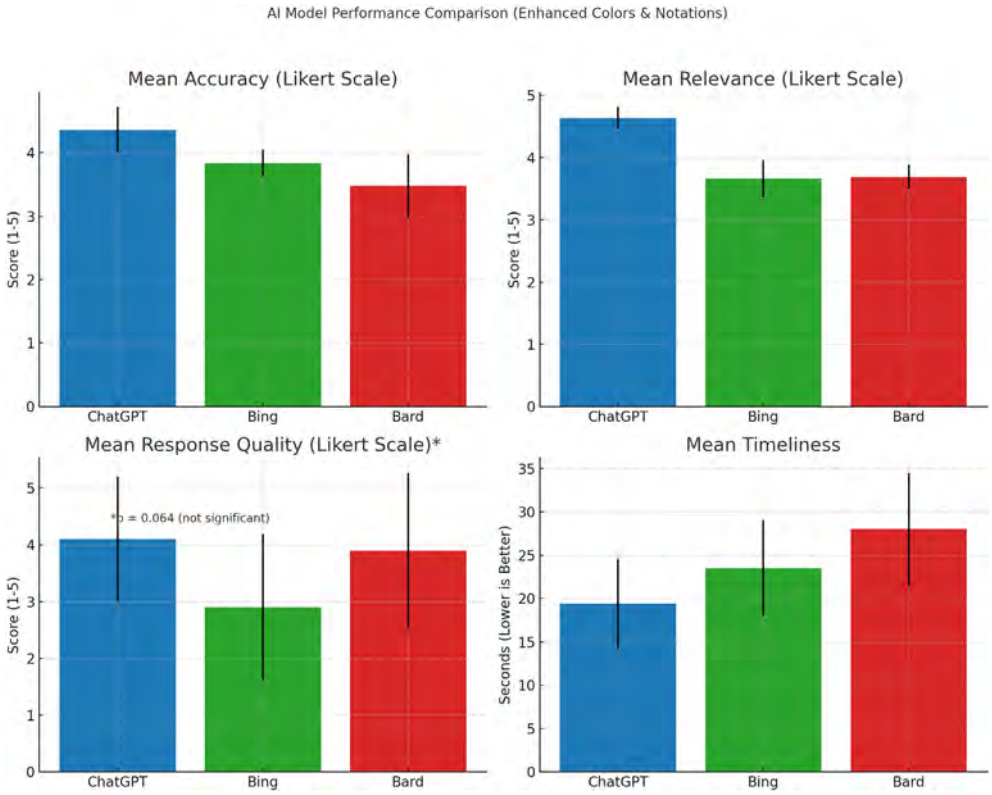
Abstract Number: 1914

Performance Comparison of Artificial Intelligence tools ChatGPT, Bing AI, and Google Bard for Clinical Rheumatology Decision Support: When AI Talks Rheumatology

Aakanksha Pitliya[1], Hema Latha Anam[2], Richard Oletsky[2], Alexandra Georgiana Boc[2], Dipabali Chaudhuri[2] and Rajesh Thirumaran[2], [1]Mercy Catholic Medical Center, Darby, PA, Clifton Heights, PA, [2]Mercy Catholic Medical Center, Darby, PA

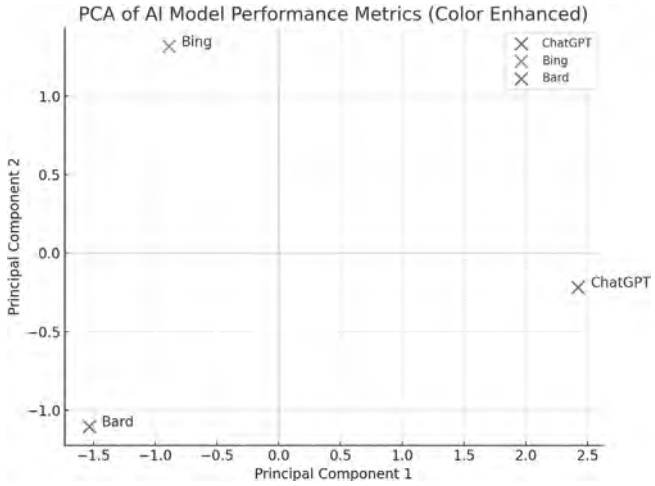
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Artificial intelligence (AI) has shown promise as a tool to assist in clinical decision-making. Given the complex nature of autoimmune pathologies and the critical need for guideline-based precision in management, the relative efficiency of AI tools in answering specific rheumatology questions remains undetermined. This study aimed to evaluate the performance of three leading AI language models: ChatGPT (OpenAI), Bing AI (Microsoft), and Google Bard in responding to clinical questions in rheumatology, focusing on key domains of accuracy, relevance, response quality, and timeliness.



Comparison of AI Model Performance on Clinical Rheumatology Questions Using Likert Scale Metrics.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Principal Component Analysis visualization of the AI models based on their multidimensional performance across accuracy, relevance, response quality, and timeliness.

Metric	ChatGPT (Mean ± SD)	Bing (Mean ± SD)	Bard (Mean ± SD)	ANOVA *p*-value
Accuracy	4.36 ± 0.36	3.84 ± 0.21	3.48 ± 0.50	0.000076
Relevance	4.64 ± 0.17	3.66 ± 0.30	3.69 ± 0.20	1.32×10^{-7}
Response Quality	4.10 ± 1.10	2.90 ± 1.29	3.90 ± 1.37	0.064
Timeliness (s)	19.4 ± 5.19	23.5 ± 5.54	28.0 ± 6.50	1.09×10^{-11}

Likert scale metrics are scored on a 1–5 scale.

Methods: Physician reviewers structured a panel of 50 clinical questions with a rheumatology focus. Each question was submitted independently in plain text to Google Bard, Bing AI, and ChatGPT. Responses were anonymized and rated on a 5-point Likert scale for quality (clarity, completeness, and educational value), accuracy (clinical correctness and factual precision), and relevance (appropriateness and applicability to the question asked) by blinded Internal Medicine Residents to avoid bias. Response latency (in seconds) was recorded for each model via stopwatch timing from prompt submission to completion of response. Descriptive statistics were calculated, and one-way ANOVA was performed to detect significant differences across the models. Principal Component Analysis (PCA) was used for multivariate clustering to explore underlying patterns and potential clustering of model responses. All statistical analyses were conducted using R (v4.3.2). A p-value < 0.05 was considered statistically significant.

Results: ChatGPT scored highest in accuracy (mean ± SD: 4.36 ± 0.36) and relevance (4.64 ± 0.17), with statistically significant differences compared to Bing and Bard (ANOVA $p < 0.001$ for both). While ChatGPT also led in response quality (4.10 ± 1.10), the difference was not statistically significant($p = 0.064$)*. Timeliness varied significantly among models, with ChatGPT responding fastest (19.4 ± 5.19s), followed by Bing (23.5 ± 5.54s) and Bard (28.0 ± 6.50s). PCA demonstrated that ChatGPT exhibited unique multidimensional performance by clustering independently.

Conclusion: Among the three AI systems evaluated, ChatGPT performed most proficiently in answering clinical rheumatology questions, with considerable improvements in accuracy, relevance, and timeliness. According to our research, generative AI models may be used as a supplement to clinical judgment in rheumatology, particularly in instances when quick and accurate synthesis of complicated data is essential.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Pitliya: None; **H. Anam**: None; **R. Oletsky**: None; **A. Boc**: None; **D. Chaudhuri**: None; **R. Thirumaran**: None.

Abstract Number: 1916

Adherence to Cervical Cancer Screening Programs in Women with Systemic Lupus Erythematosus

Carmen Lasa Teja[1], Carolina Aguirre-Portilla[2], Virginia Portilla González[3], Carmen Bejerano-Herreria[2], Alfonso Corrales-Martínez[4] and Ricardo Blanco[5], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, [4]Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, Santander, Spain, [5]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1914–1935) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Women with Systemic Lupus Erythematosus (SLE) are at a higher risk of persistent HPV infection and developing premalignant cervical lesions and cervical cancer. High-risk oncogenic HPV genotypes, particularly types 16 and 18, are the primary causal agents in most cases. Cervical cancer screening using HPV testing and cytology enables early detection of precursive lesions, preventing their progression to invasive cancer. The study aimed to evaluate adherence to the cervical cancer screening program in women with Systemic Lupus Erythematosus of reproductive age. Additionally, it sought to identify the most prevalent high-risk HPV genotypes within this population.

Table 1. Epidemiological characteristics and results of women with SLE (n=128)

Variable	Mean ± SD	n (%)	Adherence CQR≥80 (n, %)	p - value
Age (years)	53,35 ± 14,27			
LES duration (years)	14,27 ± 14			
Overall adherence			67 (58,26)	
Sex				0,0278
Women		105 (91,30)	77 (73,33)	
Men		10 (8,70)	7 (60,0)	
Study level				0,0439
No formal studies		1 (0,87)	0 (0)	
Elementary school studies		18 (15,65)	9 (50,0)	
Secondary school studies		69 (60,0)	44 (63,77)	
University studies		27 (23,48)	22 (81,48)	
Marital status				0,0944
Single		30 (26,09)	16 (53,33)	
Married		69 (60,0)	52 (75,36)	
Divorced		12 (10,43)	6 (50,0)	
Widowed		4 (3,48)	1 (25,0)	
Employment status				0,0316
Employed		55 (47,83)	44 (80,0)	
Unemployed - Retired		60 (52,17)	39 (65,0)	
Comorbidities				0,0402
With comorbidities		99 (86,09)	70 (70,71)	
Without comorbidities		16 (13,91)	13 (81,25)	
Number of oral medications for LES				0,2959
1		73 (63,48)	55 (75,34)	
2		28 (24,35)	20 (71,43)	
3		13 (11,30)	8 (61,54)	
4		1 (0,87)	0 (0)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

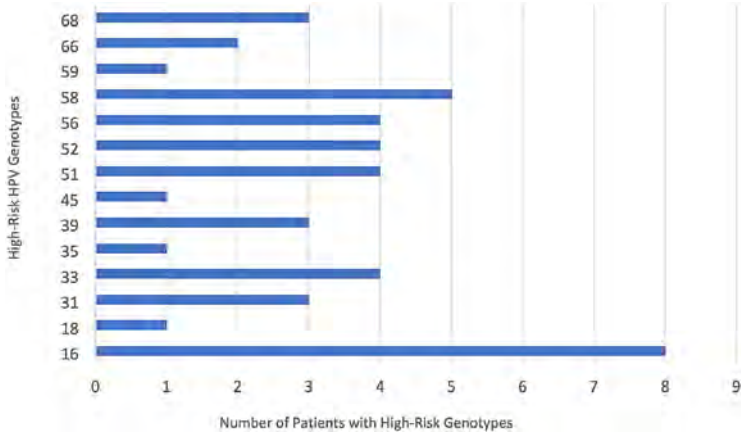


Figure 1. Identified high-risk (HR) HPV genotypes. N= 22 patients

Methods: A retrospective observational study was carried out in a cohort of 128 women with SLE aged 20-50 years, followed in the outpatient rheumatology clinic of a tertiary care hospital in northern Spain.

Results: A total of 128 women were included, with a mean age of 39.11 ± 7.91 years and a mean disease duration of 11.16 ± 7.53 years (Table 1). Among them, 19.53% had never undergone cytology or HPV testing. Among the 80.46% who participated in screening, only 34.37% adhered to the recommended intervals (every three years or less), while the remainder were screened sporadically or outside the established periodicity. A total of 22.65% underwent screening at least once, and 23.43% were screened two or more times without following the recommended intervals. Regarding HPV infections, 18.75% tested positive, predominantly for high-risk genotypes (17.18%), with 8.59% showing coinfection with low-risk genotypes. Genotype 16 was the most frequently identified among high-risk infections (Figure 1). Cervical lesions related to HPV were detected in 14.06% of the women, with 9.37% presenting high-grade lesions (HSIL) and 4.68% presenting low-grade lesions (LSIL). Cervical cancer was diagnosed in 7.03% of the cases, with two patients presenting associated intraepithelial neoplasia of the vagina and vulva. Regarding smoking habits, 21.09% of the women were active smokers, 26.56% were former smokers, and 52.34% had never smoked. No statistically significant association was found between tobacco use and cervical cancer in this cohort ($p = 0.0735$).

Conclusion: The findings reveal a high prevalence of high-risk HPV infections in women with SLE, associated with a considerable risk of progression to premalignant lesions and cervical cancer. However, low adherence to the screening program was observed, highlighting the need for strategies to promote greater participation in such programs.

Disclosure: C. Lasa Teja: None; **C. Aguirre-Portilla**: None; **V. Portilla González**: None; **C. Bejerano-Herreria**: None; **A. Corrales-Martínez**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 1917

Characterizing the Frequency and Timing of Changes in Patient-Reported Social Risk Factors among Rheumatology Outpatients

Daphne Lew[1], Lauren Seidler[2], Patrice Odom[3], Amy McQueen[3], Jessica Williams[4], Seth Eisen[5] and Alfred Kim[4], [1]Washington University in St. Louis School of Medicine, Saint Louis, MO, [2]Washington University School of Medicine, Saint Louis, [3]Washington University School of Medicine, Saint Louis, MO, [4]Washington University School of Medicine, St. Louis, MO, [5]Washington University School of Medicine, St Louis, MO

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Social risk factors (SRFs) are associated with health outcomes, and patients with chronic conditions often report disproportionately higher rates of SRFs, complicating their disease management.[1,2] Although SRFs change over time, the period over which these changes occur is not well-understood.[3] Further, while routine screenings for SRFs are being incorporated in clinical settings, there are no data-driven guidelines for how often screenings should be conducted. Thus, this study aimed to evaluate the timing of SRF changes in a rheumatology outpatient population.

1. Walker et al. *Endocrine*, 2014. doi: 10.1007/s12020-014-0195-0
2. Heller et al. *Prev Med*, 2021. doi: 10.1016/j.ypmed.2021.106752
3. Xu et al. *Med Care*, 2021. doi: 10.1097/MLR.0000000000001441

Methods: Patients seen in Washington University School of Medicine's Division of Rheumatology outpatient clinics were screened for SRFs between 1/1/2023 and 1/31/2025. Patients completed a standardized SRF screening questionnaire via mobile phones before their visit or iPads upon checking in, with responses automatically uploaded to the Epic electronic health record. Four core (financial resource strain, food insecurity, housing instability, and transportation instability) and four supplemental (physical activity risk, social isolation, stress, and depression) SRF domains were assessed and scored as "at risk" or "not at risk" based on existing Epic criteria. For patients with multiple visits during the study period, SRF data from all

Table 1. Descriptive characteristics of the rheumatology outpatient population, stratified by number of total screenings, 2023-2025.x

	1 screening (N=670)	2 or more screenings (N=322)
Age Categories		
18-39 years	178 (26.6%)	81 (25.2%)
40-64 years	334 (49.9%)	164 (50.9%)
65+ years	158 (23.6%)	77 (23.9%)
Sex		
Female	547 (81.6%)	257 (79.8%)
Male	123 (18.4%)	65 (20.2%)
Race		
White	437 (65.2%)	191 (59.3%)
Black	194 (29.0%)	117 (36.3%)
Asian	13 (1.9%)	4 (1.2%)
Pacific Islander	4 (0.6%)	5 (1.6%)
American Indian or Alaska Native	4 (0.6%)	2 (0.6%)
Unknown/Missing	18 (2.7%)	3 (0.9%)
Ethnicity		
Not Hispanic	631 (94.2%)	309 (96.0%)
Hispanic	16 (2.4%)	9 (2.8%)
Unknown/Missing	23 (3.4%)	4 (1.2%)
Marital Status		
Married/committed relationship	362 (54.0%)	183 (56.8%)
Divorced, separated, or widowed	156 (23.3%)	69 (21.4%)
Never married	131 (19.6%)	58 (18.0%)
Unknown/Missing	21 (3.1%)	12 (3.7%)
Insurance		
Government	298 (44.5%)	151 (46.9%)
Private	351 (52.4%)	163 (50.6%)
Other	15 (2.2%)	7 (2.2%)
Unknown/Missing	6 (0.9%)	1 (0.3%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Prevalence of SRFs over time, proportion with any changes over time, and median time to event for change in SRF status

	Prevalence			% with Any Changes over Time	Median Time to Change (days)
	Visit 1	Visit 2	Visit 3		
Core Domains					
Financial Strain	32% (298/921)	32% (99/305)	36% (40/111)	16% (47/290)	200
Housing Instability	21% (170/803)	15% (43/288)	21% (22/109)	13% (32/253)	201.5
Transportation Needs	10% (97/966)	12% (38/319)	16% (18/114)	12% (37/310)	231
Food Insecurity	24% (218/904)	23% (68/298)	29% (32/111)	10% (28/269)	192
Supplemental Domains					
Stress	51% (489/960)	47% (147/316)	51% (58/114)	31% (95/310)	183
Physical Inactivity	73% (711/977)	74% (231/314)	75% (86/114)	21% (64/310)	170.5
Social Isolation	56% (470/833)	56% (157/279)	61% (60/98)	19% (47/251)	182
Depression	17% (159/937)	16% (50/315)	19% (22/116)	16% (48/300)	186

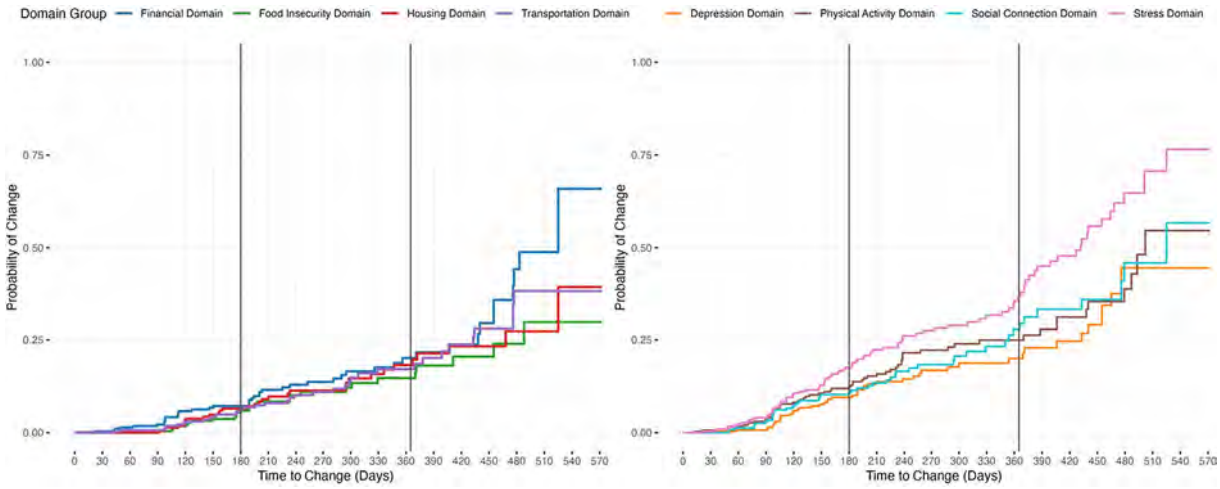


Figure 1. Change curves for all social risk factor domains

relevant visits were used. Descriptive statistics were used to summarize patient characteristics and SRF prevalence. Kaplan-Meier time-to-event analyses and change curves assessed time to changes in risk status for individuals with 2 or more screenings. Events were defined as any change in SRF status from "at risk" to "not at risk," or vice versa. If no change was reported, patients were censored on their last SRF screening date during the study period.

Results: 992 patients (50% 40-64 years, 81% female, 31% Black) were screened for SRFs, with 322 (33%) screened more than once. Characteristics of patients with 2+ screenings were similar to those with only one, except for race (36% vs. 29% Black, respectively; Table 1). The prevalence of SRFs across visits remained fairly stable, with physical inactivity most prevalent (73%-75%) and transportation needs least prevalent (10%-16%) at all visits (Table 2). Only 10% of patients changed risk status for food insecurity compared to 31% for stress, and the median time to change ranged from 170.5 days for physical inactivity to 231.0 days for transportation needs (Table 2). Change curves (Figure 1) showed that stress was most likely to change over time, while the core SRF domains showed low probability of changes.

Conclusion: SRFs among rheumatology outpatients remained stable over time, with most patients reporting consistent SRF status for 6 months or more. Stress exhibits greater variability over time, while less than 25% of patients report changes in core SRF domains over 1 year. This work provides insight into how frequently SRFs should be screened and highlights the importance of incorporating interventions to address SRFs as part of clinical care.

Disclosure: D. Lew: None; **L. Seidler**: None; **P. Odom**: None; **A. McQueen**: None; **J. Williams**: CVS Pharmacy, Inc, 2, Lupus Research Alliance, 1, 5; **S. Eisen**: None; **A. Kim**: Abbvie, 2, AstraZeneca, 2, 5, Atara Bio, 2, Bristol Myers Squibb, 5, Cargo Therapeutics, 2, CRISPR Therapeutics, 1, 5, Exagen Diagnostics, 2, 6, Genentech/Roche, 2, GlaxoSmithKline, 2, 6, Hinge Bio, 2, Invivyd, 2, Kypha, Inc., 2, 10, Novartis, 5, Zenas BioPharma, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1918

Vigorous Physical Activity in Patients with SLE Was Not Associated with Disease Activity or Socioeconomic and Social Factors

Heather Gold[1], Yi Li[1], Isabella Giunta[1], Jill Buyon[1], Peter Izmirly[2], Mala Masson[3], Amit Saxena[1], H Michael Belmont[4], Chung-E Tseng[5] and Rebecca Anthopolos[1], [1]NYU Grossman School of Medicine, New York, NY, [2]New York University Grossman School of Medicine, New York, NY, [3]NYU Langone Health, New York, [4]NYU School of Medicine, New York, NY, [5]New York University Grossman School of Medicine, Flushing, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1914–1935) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Physical activity can mitigate cardiovascular disease and depression risk and improve fatigue, physical function, and quality of life in patients with SLE. To facilitate physical activity in a diverse patient population with SLE, it is critical to understand whether and how it is associated with socioeconomic, social, demographic, or clinical factors.

Methods: Cross-sectional analysis of patients with SLE from a large, urban city (n=189) who completed the International Physical Activity Questionnaire (IPAQ) based on the past 7-days recall of vigorous physical activity, moderate activity, or walking. Examples of vigorous physical activity include heavy lifting, digging, aerobics, or fast bicycling; moderate activity would include carrying light loads, bicycling at a regular pace, or doubles tennis, but not walking. Variables considered were financial insecurity, Everyday Discrimination Scale, education, age, sex, race, ethnicity, lupus-specific disease activity (any of cutaneous, nephritis, or arthritis), immunosuppressive medication, and Area Deprivation Index. Statistical tests of associations were 2-sided: chi-squared for categorical and Spearman rank correlation for continuous variables. Multivariable analyses applied a quasi-Poisson model due to overdispersion.

Results: The majority of patients (n=120/189, 64%) reported zero days of vigorous physical activity, whereas 42% reported no moderate activity (n=79) and only 4% reported no walking (n=7). Bivariate analyses showed that vigorous physical activity was associated only with lower disease activity (median=0, IQR=0-2 for no vigorous activity vs. median=0, IQR=0-1 for any vigorous activity; p=0.047). Multivariable analysis indicated that the count of vigorous activity days was modestly and negatively associated with disease activity, where a 1-unit increase in disease activity was associated with a 46% decrease in

Table. Multivariable analysis of days of vigorous physical activity in the past week.

	Coefficient	Standard Error	Percentage change*	p-value
Any financial insecurity	0.17	0.27	0.19	0.5
Everyday Discrimination Scale	-0.07	0.09	-0.07	0.5
Disease activity	-0.62	0.34	-0.46	0.068
College degree or more	0.42	0.47	0.51	0.4
Age	-0.01	0.01	-0.01	0.3
Male sex	-0.06	0.39	-0.05	0.9
Asian	-0.74	0.41	-0.52	0.07
Black	-0.38	0.33	-0.32	0.3
Other race	-0.23	0.36	-0.21	0.5
Hispanic ethnicity	-0.13	0.33	-0.12	0.7
unknown ethnicity	-0.54	0.66	-0.42	0.4
Immunosuppressive medications	0.21	0.24	0.24	0.4
Area Deprivation Index	0.0004	0.008	0	1.0
Intercept	0.35	0.72	0.42	0.6

*percentage change in vigorous activity days

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

physical activity (p=0.068). Results suggest there is insufficient evidence of significant associations with most covariates in our sample.(Table) Outcomes of total physical activity, moderate activity, and walking in multivariable models showed no significant associations with covariates, leaving only vigorous activity reported here.

Conclusion: The null findings are illuminating and suggest that disease activity and socioeconomic and social factors did not keep patients from engaging in vigorous activity. Future longitudinal analysis will aid in understanding patterns of physical activity related to clinical factors and patient-reported outcome measures of pain, fatigue, depression, and more.

Disclosure: H. Gold: None; **Y. Li**: None; **I. Giunta**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **P. Izmirly**: Hansoh Bio, 2; **M. Masson**: None; **A. Saxena**: AbbVie/Abbott, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, 6, Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 5, Synthekine, 1, 2, UCB, 1, 6; **H. Belmont**: None; **C. Tseng**: None; **R. Anthopolos**: None.

Abstract Number: 1919

Financial insecurity and discrimination are associated with patient-reported quality of life in patients with SLE

Heather Gold[1], Yi Li[1], Peter Izmirly[2], Jill Buyon[1], Mala Masson[3], Amit Saxena[1], H Michael Belmont[4], Chung-E Tseng[5] and Rebecca Anthopolos[1], [1]NYU Grossman School of Medicine, New York, NY, [2]New York University Grossman School of Medicine, New York, NY, [3]NYU Langone Health, New York, [4]NYU School of Medicine, New York, NY, [5]New York University Grossman School of Medicine, Flushing, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Manifestations of SLE are known to affect patient-reported outcome measures (PROs) such as physical function, fatigue, and pain. Other work has suggested economic insecurity is associated with worse PRO scores, and discrimination can have a chronic effect on health status. This study focused on the association of PROs with individual and structural socioeconomic factors and SLE-related clinical variables.

Methods: A cohort of patients (n=272) diagnosed with SLE according to standard classification criteria (ACR revised classification, European Alliance of Association for Rheumatology/ACR classification, or SLICC classification) were surveyed using measures from the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) for physical function, cognitive function, pain interference, fatigue, anxiety, sleep disturbance, and depression. Analyses included demographics, financial/material insecurity such as in housing, finances, healthcare, or job status, and clinical data on disease activity (any of cutaneous, nephritis or arthritis) and immunosuppressive medication use. Everyday Discrimination Scale was captured to quantify the potential impact of discrimination and its associated chronic stress on health (coded as never vs ever experienced 9 discrimination types and summed across types). Multivariable linear regression models of PROs included clinical and socioeconomic factors.

Results: The cohort was 90% female, 28% African American/Black, 17% Asian, 39% white, and 16% other/unknown, with an average age of 40 years. Average SLEDAI was 3.17 (SD=3.52) and SLICC damage score 1.12 (SD=1.53). Multivariable models showed that experiencing financial insecurity was associated with significantly worse scores on all PROs, from 4-7

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Multivariable linear regression analysis of patient-reported outcome measures (coefficient & significance level), n=272

PROMIS measure	financial insecurity		Disease activity (any of cutaneous, arthritis, nephritis)		Immunosuppressive medications		Everyday Discrimination Scale	
Physical Function	-5.17	***	-4.24	*	-0.50		-1.33	**
Cognitive Function	-6.10	**	-1.10		-1.35		-1.22	*
Pain Interference	7.39	***	2.71		0.97		1.59	**
Fatigue	5.76	***	2.69		0.17		2.02	**
Sleep Disturbance	3.80	*	3.37	*	-2.87	*	1.38	*
Depression	4.82	***	4.14	***	-0.26		1.43	**
Anxiety	3.53	*	2.25	*	-0.48		1.53	**

***p<0.0001; **p<0.001; *p<=0.04
Models adjusted for age, sex, race, ethnicity, Area Deprivation Index.
Note: PROs for function are better when higher, whereas PROs for symptoms are better when lower.

points worse (p< 0.01). Each additional point on the Everyday Discrimination Scale was associated significantly with 1 point worse on physical and cognitive function score, 1 point higher sleep disturbance, depression, and anxiety, and 2 points higher on fatigue on average (p< 0.05). Finally, experiencing disease activity was significantly associated with lower physical function and higher sleep disturbance, depression, and anxiety (p< 0.05). (Table)

Conclusion: Experiencing financial insecurity was associated with clinically important negative impacts in function and symptom PROs; everyday discrimination consistently significantly negatively affected PRO scores; and disease activity was negatively associated with 4 of the 7 measures. Understanding the full experience of patients with SLE, beyond their clinical manifestations, may help identify approaches to support patients for improved function and reduced symtpoms.

Disclosure: H. Gold: None; **Y. Li**: None; **P. Izmirly**: Hansoh Bio, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Masson**: None; **A. Saxena**: AbbVie/Abbott, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, 6, Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 5, Synthekine, 1, 2, UCB, 1, 6; **H. Belmont**: None; **C. Tseng**: None; **R. Anthopolos**: None.

Abstract Number: 1921

Re-escalation of Treatment in Older Adults with Rheumatoid Arthritis After Anti-TNF Therapy De-escalation

Jiha Lee[1], Jonathan Martindale[2], Una Makris[3] and Julie Bynum[2], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, [3]UT Southwestern Medical Center and Dallas VA, Dallas, TX

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Older adults with rheumatoid arthritis (RA) treated with biologic disease-modifying antirheumatic drugs (bDMARDs), including anti-TNFs, are at an increased risk of adverse effects. Current guidelines recommend de-escalating DMARDs for patients with low disease activity or remission to optimize the benefit-harm ratio of treatment. We previously found that 20% of older adults with RA de-escalated anti-TNFs. In this follow-up study, we investigated the frequency and factors associated with re-escalation of treatment after de-escalation of anti-TNFs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We used 20% Medicare data from 2009-2022 to identify RA patients ≥66 years of age on Part D self-injectable anti-TNF therapy (i.e. Adalimumab, Etanercept, Certolizumab, and Golimumab) with de-escalation by cessation (> 90-day gap) or by taper (>50% effective dose reduction), and at least one rheumatologist visit pre- post-de-escalation (i.e. index date). The outcome of interest was re-escalation, defined as restarting the same anti-TNF or another bDMARD after at least a 90-day gap or increasing the effective dose of anti-TNF by >50% after the index date. Information on baseline patient characteristics, concomitant use of conventional synthetic DMARDs (csDMARDs), and changes in average glucocorticoids (GC) dose were collected. The Cox proportional hazard model was used to identify factors associated with re-escalation.

Results: We identified 949 Medicare beneficiaries who met the inclusion criteria. Three in five (61.6%) re-escalated treatment with a median time of 164 (IQR 113-301) days since the index date (Figure 1). Older adults who re-escalate treatment, compared to those with sustained de-escalation, were less frequently non-Hispanic white (72.6% vs 81.3%, p=0.002) and had fewer comorbidities (mean Elixhauser index 2.9 [2.1] vs 3.3 [2.4], p=0.003) (Table 1). The two groups, re-escalators vs. sustained de-escalators, were similar in their age distribution (mean age 74.9 [5.8] vs 75.4 [SD 5.9], p=0.172), female predominance (83.2% vs 81.3%, p=0.447), low-income subsidy (LIS) status (43.9% vs 38.7%, p=0.115), and concomitant use of csDMARDs at index (62.7% vs 61.0%, p=0.590). The change in average daily dose of glucocorticoids pre- and post-index was not significantly different between the two groups (mean 0.6mg/day [4.0] vs 0.5 [SD 3.7], p=0.334). In Cox analyses, re-escalation was more likely in blacks, Hispanics/others, and those with lower comorbidity burdens (Table 2).

Table 1: Baseline characteristics of older adults with RA who had de-escalation of primary anti-TNF use and in fee-for-service Medicare, between 2009-2022

Variables	All RA patients N=949	Pattern of Primary Anti-TNF use after de-escalation		P*value
		Sustained de-escalation N=364	Re-escalation N=585	
Sociodemographic				
Age at index date				0.172
mean (SD)	75.1 (5.8)	75.4 (5.9)	74.9 (5.8)	
median (IQR)	74 (70-79)	75 (70-79)	74 (70-79)	
Female n (%)	783 (82.5)	296 (81.3)	487 (83.2)	0.447
Race/Ethnicity n (%)				0.002
White	724 (76.3)	299 (82.1)	425 (72.6)	
Black	77 (8.1)	19 (5.2)	58 (9.9)	
Hispanic/Other	148 (15.6)	46 (12.6)	102 (17.4)	
Low-Income Subsidy, n (%)	398 (41.9)	141 (38.7)	257 (43.9)	0.115
Comorbidities				0.003
mean (SD)	3.1 (2.2)	3.3 (2.4)	2.9 (2.1)	
median (IQR)	3 (1-4)	3 (2-5)	2 (1-4)	
Number of Rheumatologist visits				0.051
mean (SD)	4.5 (4.1)	4.7 (4.4)	4.3 (4.0)	
median (IQR)	4 (2-5)	4 (2-5)	3 (2-5)	
Concomitant medication use (pre-index, unless specified otherwise)				
csDMARD use (any), n (%)	589 (62.1)	222 (61.0)	367 (62.7)	0.590
Number of unique csDMARDs				0.013
0	360 (37.9)	142 (39.0)	218 (37.3)	
1	495 (52.2)	174 (47.8)	321 (54. 9)	
≥2	94 (9.9)	48 (13.2)	46 (7.9)	
Methotrexate use, n (%)	441 (46.5)	159 (43.7)	282 (48.2)	0.174
Average daily GC dose (mg/day)				0.048
mean (SD)	1.7 (2.9)	1.9 (3.1)	1.6 (2.8)	
median (IQR)	0.3 (0.0-2.5)	0.3 (0.0- 3.0)	0.0 (0.0-2.1)	
Change in average daily GC dose pre- to post-index (mg/day)				
mean (SD)	0.5 (3.9)	0.5 (3.7)	0.6 (4.0)	0.334
median (IQR)	0.0 (-0.3-1.0)	0.0 (-0.3-1.1)	0.0 (-0.2-0.9)	

*Wilcoxon rank sum test for continuous and Chi-square test of independence for categorical variables were used to compare de-escalation and continuation groups.

**Index date = final day of primary anti-TNF use before de-escalation occurred

***GC dose calculated in prednisone equivalent mg/day

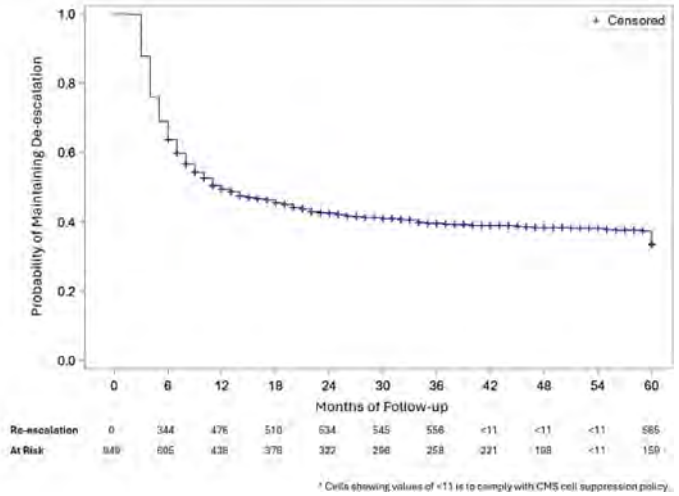
Abbreviations: SD=standard deviation, IQR=interquartile range, csDMARD=conventional synthetic disease-modifying antirheumatic drug, GC=glucocorticoid

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Hazard ratio of re-escalation of treatment in older adults after de-escalation of anti-TNFs

Covariates	Hazard Ratio (95% CI)	
	Unadjusted	Adjusted
Mode of De-escalation		
Cessation	1.00 (reference)	1.00 (reference)
Taper	0.78 (0.52, 1.17)	0.75 (0.49, 1.14)
Age at index date	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)
Female	1.03 (0.83, 1.28)	0.94 (0.75, 1.18)
Race/Ethnicity n (%)		
White	1.00 (reference)	1.00 (reference)
Black	1.62 (1.23, 2.13)	**1.60 (1.19, 2.15)**
Hispanic/other	1.38 (1.11, 1.71)	**1.31 (1.05, 1.65)**
Low-Income Subsidy	1.25 (1.07, 1.48)	1.18 (0.93, 1.43)
Comorbidities, Elixhauser		
<3 conditions	1.00 (reference)	1.00 (reference)
3-5 conditions	0.86 (0.72, 1.02)	**0.80 (0.67, 0.96)**
>5 conditions	0.79 (0.60, 1.02)	**0.70 (0.53, 0.92)**
Concomitant csDMARD use	1.05 (0.89, 1.25)	1.08 (0.91, 1.28)
Increase in average dose steroids pre- to post-index, (mg/day)	1.01 (0.98, 1.03)	1.01 (0.99, 1.03)
Index Year	Not significant	Not significant

Figure 1: Kaplan-Meier curve for time to re-escalation of treatment in older adults with RA after de-escalation of anti-TNFs



[1] Cells showing values of <11 is to comply with CMS cell suppression policy.

Conclusion: Nearly two-thirds of older adults re-escalate treatment within a year of de-escalating anti-TNF therapy, displaying a frequency comparable to that observed in the younger population. These findings suggest that continued exposure to anti-TNF for most older RA patients. In our prior study, de-escalation was associated with a greater comorbidity burden. In this follow-up study, re-escalators had fewer comorbidities, possibly due to concerns for more adverse effects with anti-TNF or other bDMARD therapy. Additional research is needed to identify and understand the subset of older RA patients able to maintain drug-free RA control.

Disclosure: J. Lee: None; **J. Martindale**: None; **U. Makris**: None; **J. Bynum**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1923

A Real-World Survey on Physicians Perspectives of Uncontrolled Gout and Gout Management Practices

John Botson[1], Menaka Bhor[2], Nathan Meyer[2], Molly Edwards[3], Emily Goddard[3], Victoria Barton[4] and Jeff Peterson[5], [1]Orthopedic Physicians of Alaska, Anchorage, AK, [2]Sobi Inc, Waltham, MA, [3]Adelphi Real World, Bollington, United Kingdom, [4]Adelphi Real World, Macclesfield, United Kingdom, [5]Western Washington Arthritis Clinic, Bothell, WA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

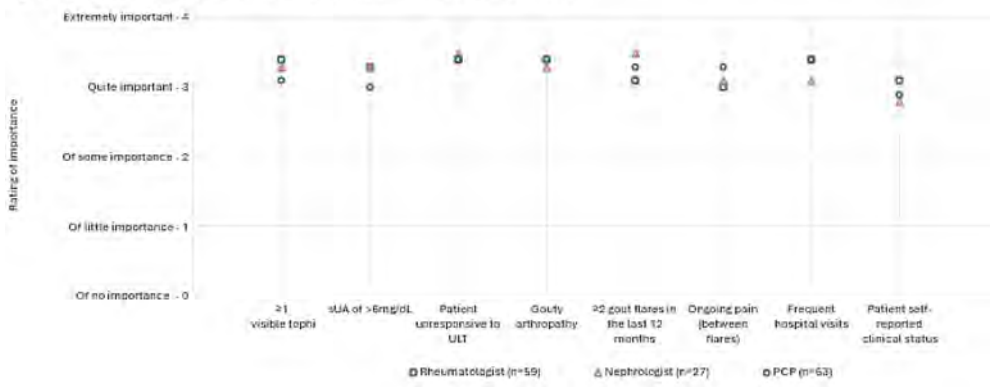
Background/Purpose: Managing uncontrolled gout (UG) can involve a multi-disciplinary approach involving physicians of different specialities, all of whom may have differing perspectives or approaches for management of the condition due to the complex clinical manifestations and comorbidities. An understanding of physician perspectives of gout management across different physician specialties may help to improve education and patient care. This study evaluated physicians' perspectives of UG and gout management practices.

Methods: Data was extracted from the Adelphi Real World Gout Disease Specific Programme (DSP)™, a cross-sectional survey (with retrospective data collection) from rheumatologists, nephrologists and PCPs in the United States from August 2023 - March 2024. Physicians who participated in this study managed ≥ 8 patients with gout in a month with urate lowering therapy (ULT). Physicians' perspectives obtained on UG included importance of different attributes in defining UG (where 0 was of no importance and 4 was extremely important); factors contributing to UG development; management of gout (including UG): use of treat to target (T2T), diagnostic and monitoring tests; and remission. Analyses were descriptive.

Results: Overall, 59 rheumatologists, 27 nephrologists and 63 PCPs participated in the study.

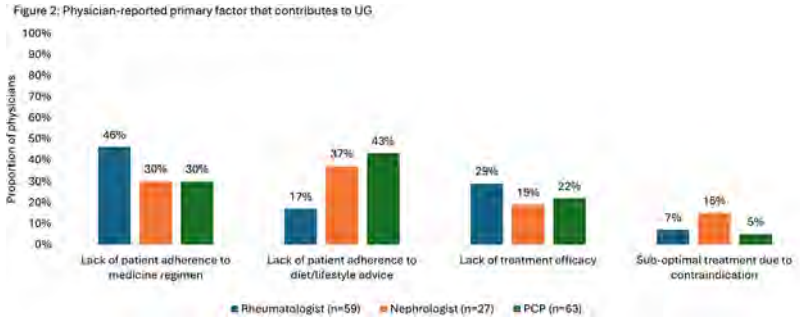
Physicians across specialities rated most attributes associated with UG with an importance of 3-3.5 out of 4 (Figure 1). Overall, non-response to ULT and presence of gouty arthropathy were rated the most important (with an overall mean score of 3.4 across all physicians).

Figure 1. Physician-rated Importance Of Attributes Associated With Uncontrolled Gout



Frequent hospital visits: >2 annually. Gouty arthropathy: defined clinically or radiographically as joint damage due to gout. sUA: serum uric acid, PCP: primary care physician, UG: uncontrolled gout, ULT: urate lowering therapy.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



PCP: primary care physician, UG: uncontrolled gout

The top factor contributing to UG reported by rheumatologists was lack of patient adherence to medicine regimen (46%), whereas adherence to diet/lifestyle advice was the top reason reported by nephrologists (37%) and PCPs (43%) (Figure 2).

To monitor clinical manifestations of their UG patients, test use varied across physician types. Tophi size measurement was used by 56% of rheumatologists, 37% of nephrologists and 48% of PCPs. C-reactive protein tests were used by 53%, 37%, 35% and synovial fluid aspiration by 15%, 11% and 5% respectively, whilst sUA levels were monitored by >80% physicians regardless of speciality.

When looking at treatment response, T2T was reported to be used in all patients with gout by 59% of rheumatologists, 41% of nephrologists and 40% of PCPs.

With regard to possibility of remission of gout and UG, 42% of rheumatologists reported that remission was possible in all patients with gout, as opposed to 26% of nephrologists and 35% of PCPs.

Conclusion: There was variation in perceptions of UG and gout management practices amongst physician specialties, which may come from differences in training and experience with managing patients with uncontrolled gout. Future research initiatives which focus on education, adherence to guidelines, intensive management (T2T), monitoring, and remission as a goal may standardize care among specialties and may improve patient outcomes.

Disclosure: J. Botson: AbbVie/Abbott, 6, Amgen, 2, 5, 6, 10, ANI, 6, Arthrosi, 5, Eli Lilly, 6, Novartis, 2, Olatec, 5, Shanton Pharma, 1; **M. Bhor**: Sobi, 3; **N. Meyer**: Sobi, Inc., 3; **M. Edwards**: AbbVie, 2, Adelphi Real World, 3; **E. Goddard**: Adelphi Real World, 3; **V. Barton**: Adelphi Real World, 3; **J. Peterson**: Amgen, 1, 2, 5, 6, 10, Eli Lilly, 1, 6, Johnson and Johnson, 6, Novartis, 2, SOBI, 1, 2.

Abstract Number: 1924

Real-World Treatment Patterns of Patients with Systemic Autoimmune Rheumatic Disease-associated Interstitial Lung Disease After Progression in The United States

Joseph Yang[1], Katy Sadowski[1], Akshay Kharat[1], Ann Chauffe[1] and Tejaswini Kulkarni[2], [1]Boehringer Ingelheim, Ridgefield, CT, [2]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic autoimmune rheumatic diseases (SARDs) are a group of autoimmune diseases that affect multiple organ systems, including the lungs. The development of interstitial lung disease (ILD) in the context of SARD (SARD-ILD) is a significant clinical concern due to its high prevalence, progressive nature, and its associated morbidity and mortality. There is limited published evidence describing how SARD-ILD patients with disease progression are being managed in the United States. This study aims to bridge the knowledge gap by describing the treatment patterns of patients with SARD-ILD following ILD progression.

Methods: This retrospective cohort study used Optum Clinformatics® administrative claims database from 01 January 2017 to 31 March 2024. The study cohort included adult patients diagnosed with SARD-ILD on or after 01 Jan 2018 and with evidence of ILD progression. Disease progression was identified using previously published claims-based proxies, which included health care utilization related to the management of ILD progression The earliest date of ILD progression was defined as the index date, with a requirement for a minimum of 12-month continuous enrollment before (baseline period) and after the index date (follow-up period). The proportion of patients receiving pharmacologic and non-pharmacologic treatments related to SARD-ILD following ILD progression was descriptively assessed for the overall SARD-ILD cohort. Pharmacologic treatments include antifibrotics, biologic and non-biologic disease modifying antirheumatic drugs (DMARDs), immunomodulators, oral corticosteroids, and other ILD-related treatments. Non-pharmacologic treatments included lung transplant, pulmonary rehabilitation and supplemental oxygen therapy.

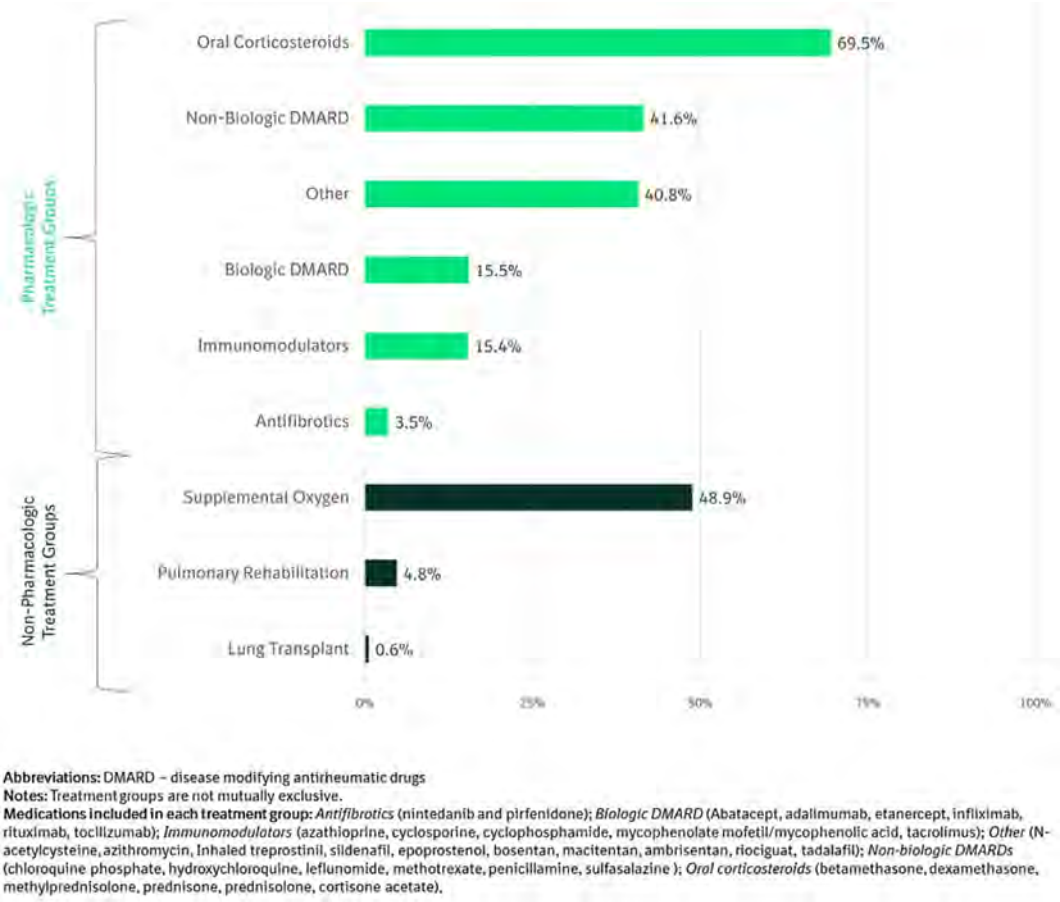
Results: The study included a total of 6,431 patients. The mean (standard deviation [SD]) age of the overall cohort was 71.2 (11.1) years and 75.3% were female (Table 1). Rheumatoid arthritis was the most prevalent underlying SARD type (52.6%). The mean (SD) follow-up duration was 936 (467) days. While 83% of patients received any pharmacologic treatment group during the follow-up, only 55% have received disease modifying treatments (i.e., biologic and non-biologic DMARDs, immunomodulators, and antifibrotics). Oral corticosteroids and non-biologic DMARDs were the most frequently prescribed pharmacologic treatment groups (Figure 1). Among immunomodulators, mycophenolate (10.6%), azathioprine (5.5%), and

Table 1. Baseline demographics and clinical characteristics

	Progressive SARD-ILD (n=6,431)
Age on index, mean (SD)	71.2 (11.1)
Gender, n (%)	
Female	4,843 (75.3)
Race, n (%)	
White	4,428 (68.9)
Black	818 (12.7)
Asian	148 (2.3)
Unknown	1,037 (16.1)
Ethnicity, n (%)	
Hispanic	911 (14.2)
Not Hispanic	3,272 (50.9)
Unknown	2,248 (35.0)
Insurance type, n (%)	
Commercial only	865 (13.5)
Medicare only	5,538 (86.1)
Multiple known types	28 (0.4)
Nicotine exposure, n (%)	
Exposed	2,762 (43.0)
Quan-Charlson Comorbidity Index Score, mean (SD)	4.5 (2.5)
Underlying SARD types	
Rheumatoid Arthritis	3,385 (52.6)
Systemic Sclerosis	218 (3.4)
Mixed Connective Tissue Disease	124 (1.9)
Dermatomyositis/Polymyositis	71 (1.1)
Systemic Lupus Erythematosus	277 (4.3)
ANCA vasculitis	112 (1.7)
Sjogren's syndrome	353 (5.5)
Multiple SARD types[1]	1,891 (29.4)

Notes:
[1] Multiple SARD types include those who meet ≥1 of the listed underlying SARD types

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Abbreviations: DMARD – disease modifying antirheumatic drugs
Notes: Treatment groups are not mutually exclusive.
Medications included in each treatment group: *Antifibrotics* (nintedanib and pirfenidone); *Biologic DMARD* (Abatacept, adalimumab, etanercept, infliximab, rituximab, tocilizumab); *Immunomodulators* (azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil/mycophenolic acid, tacrolimus); *Other* (N-acetylcysteine, azithromycin, Inhaled treprostinil, sildenafil, epoprostenol, bosentan, macitentan, ambrisentan, riociguat, tadalafil); *Non-biologic DMARDs* (chloroquine phosphate, hydroxychloroquine, leflunomide, methotrexate, penicillamine, sulfasalazine); *Oral corticosteroids* (betamethasone, dexamethasone, methylprednisolone, prednisone, prednisolone, cortisone acetate).

Figure 1. Proportion of patients receiving ILD-related treatments after ILD progression during follow-up, among all patients with SARD-ILD

tacrolimus (0.8%) were the most commonly prescribed medications. While only 3.5% of patients received antifibrotics after progression, we observed increasing trend in the use of antifibrotics across the study period. Supplemental oxygen therapy was the most commonly used non-pharmacologic treatment (Figure 1).

Conclusion: The study provides real-world insights into the treatment patterns of patients with SARD-ILD after ILD progression. The study findings suggest unmet needs and gaps in current treatment strategies remain. The limited use of disease modifying pharmacotherapies post-progression underscores a gap between real-world practice and evidence-based recommendations, potentially leading to suboptimal disease management.

Disclosure: J. Yang: Boehringer Ingelheim, 3; **K. Sadowski**: Boehringer Ingelheim, 3; **A. Kharat**: Boehringer-Ingelheim, 3; **A. Chauffe**: Boehringer Ingelheim, 3; **T. Kulkarni**: Boehringer-Ingelheim, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1925

Associations Between representation And quality in Clinical Trials for Systemic Lupus Erythematosus

Joshua Skydel[1], Anna Leland[2], Reshma Ramachandran[3], Fotios Koumpouras[3] and Joshua Wallach[2], [1]Yale-New Haven Hospital, New Haven, CT, [2]Rollins School of Public Health, Atlanta, GA, [3]Yale School of Medicine, New Haven, CT

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1914–1935) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Drug development in SLE is informed by US Food and Drug Administration recommendations for study design, enrollment, and efficacy endpoints. However, persistent challenges to conducting high-quality randomized clinical trials (RCTs) have been noted, including variation in endpoint assessment, predominantly urban enrollment, and underrepresentation of minoritized populations. RCT quality contributes to the perceived strength of research findings, yet little is known about heterogeneity in trial design, including potential associations between representation and the quality of RCTs in SLE.

Table 1: Enrollment characteristics of registered and published SLE clinical trials

Table 1: Enrollment characteristics of registered and published SLE clinical trials

		Clinical trials, No.	US sites in small or non-metropolitan areas, No. (%)[b]		US sites in MUAs, No. (%)[c]		Enrollment, Median (IQR)	PPR, Median (IQR)[d]				
			Less than 5%	Greater than or equal to 5%	Yes	No		AIAN	Asian	Black	White	Hispanic[e]
All trials		55	27 (49)	28 (51)	35 (64)	20 (36)	298 (130-449)	0.7 (0.1-1.3)	2.1 (0.8-3.4)	0.4 (0.2-0.6)	1.0 (0.7-1.2)	1.3 (0.8-1.7)
Year of study start	Prior to 2010	15	10 (67)	5 (33)	4 (27)	11 (73)	238 (112-334)	0.1 (0-0.2)	1.1 (0.7-3.4)	0.6 (0.4-0.9)	0.9 (0.7-1.1)	0.9 (0.5-1.4)
	2010-2014	16	4 (25)	12 (75)	13 (81)	3 (19)	439 (245-753)	1.0 (0.6-2.0)	2.6 (1.6-4.3)	0.3 (0.2-0.4)	1.0 (0.7-1.1)	1.4 (1.0-1.9)
	2015-2020	24	13 (54)	11 (46)	18 (75)	6 (25)	290 (124-379)	0.8 (0.3-1.3)	2.3 (0.8-3.3)	0.3 (0.2-0.4)	1.1 (0.9-1.1)	1.4 (0.9-1.7)
Study indication	SLE	41	17 (41)	24 (59)	28 (68)	13 (32)	314 (183-469)	0.8 (0.2-1.4)	1.9 (0.8-2.9)	0.4 (0.3-0.5)	1.1 (1.0-1.2)	1.2 (0.8-1.7)
	LN	14	10 (71)	4 (29)	7 (50)	7 (50)	140 (62-298)	0.3 (0-0.9)	4.1 (1.1-7.0)	0.3 (0.2-0.7)	0.7 (0.6-0.8)	1.6 (0.8-1.8)
Therapeutic type	Small molecule	17	11 (65)	6 (35)	10 (59)	7 (41)	314 (100-370)	0.9 (0-1.3)	2.1 (1.1-3.6)	0.4 (0.3-1.0)	1.0 (0.7-1.1)	1.0 (0.3-1.7)
	Biologic	38	16 (42)	22 (58)	25 (66)	13 (34)	295 (137-455)	0.7 (0.2-2.2)	2.1 (0.8-3.4)	0.3 (0.2-0.5)	1.0 (0.8-1.2)	1.3 (0.9-1.8)
Enrollment sites	US only	7	7 (100)	0 (0)	2 (29)	5 (71)	47 (29-82)	0 (0-0.3)	0.5 (0.1-1.4)	1.6 (1.3-1.9)	0.7 (0.5-0.8)	0.4 (0.3-0.7)
	Multinational	48	20 (42)	28 (58)	33 (69)	15 (31)	310 (184-458)	0.9 (0.3-1.8)	2.4 (1.1-3.6)	0.3 (0.2-0.4)	1.1 (0.8-1.2)	1.5 (0.9-1.9)
Approved for lupus indication[a]	Yes	12	4 (33)	8 (67)	11 (92)	1 (8)	404 (302-451)	0.7 (0.4-0.9)	3.1 (1.5-4.9)	0.4 (0.4-0.5)	1.0 (0.7-1.1)	1.3 (0.9-1.5)
	No	43	23 (53)	20 (47)	24 (56)	19 (44)	257 (103-429)	0.8 (0.1-1.3)	2.0 (0.7-3.3)	0.3 (0.2-0.6)	1.0 (0.8-1.1)	1.3 (0.6-1.8)

Abbreviations: SLE, systemic lupus erythematosus; LN, lupus nephritis; US, United States; MUA, Medically Underserved Area; IQR, interquartile range; PPR, Participation-to-Prevalence Ratio; AIAN, American Indian/Alaska Native.

[a] Includes trial evaluating anifrolumab, belimumab, or voclosporin for use in SLE or LN.

[b] Based on National Center for Health Statistics Urban-Rural Classification, updated 2023.

[c] Based on Health Resources and Services Administration designation of US counties lacking access to primary care services, updated December 2024.

[d] Based on US Census Bureau nomenclature. Enrollment data was not available for all trials (see Table 2 footnotes).

[e] Includes 5 trials for which "Hispanic" was reported as a race, and 38 trials for which "Hispanic" was reported as an ethnicity (i.e., independent of race).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We identified RCTs of small molecules and biologics for SLE registered on ClinicalTrials.gov and published in peer-reviewed journals as of January 2025. Eligible RCTs evaluated a primary efficacy endpoint and included 1+ US enrollment site. US enrollment sites for RCTs were classified using the National Center for Health Statistics Urban-Rural Classification Scheme; medically underserved areas were identified. For each RCT, enrollment by sex, race, and ethnicity was identified from publications and compared to the demographics of US Centers for Disease Control and Prevention SLE registries using participation-to-prevalence ratios (PPRs). PPRs greater than 0.8 indicated adequate representation. RCT quality was assessed using the Cochrane Risk of Bias 2 tool. Associations between RCT enrollment and quality were evaluated using Fisher's exact tests, with significance set at .05.

Results: There were publications for 54 RCTs and 1 pooled analysis of 2 RCTs. Median enrollment among 55 unique RCT reports was 298 (interquartile range, 130-449) (**Table 1**). Half of RCTs enrolled in at least one small metropolitan or non-metropolitan area in the US; however, most US sites (1392/1845, 75%) were in large metropolitan areas. Representation across RCTs was adequate for female (median PPR 1.0), Hispanic (median PPR 1.3), Asian (median PPR 2.1) and White (median PPR 1.0) participants, while American Indian/Alaska Native (AIAN, median PPR 0.7) and Black (median PPR 0.4) participants were underrepresented. Enrollment was similar regardless of whether therapeutics are approved for use in SLE. Among 55 RCTs, there were similar numbers with low risk (19, 34%), some concerns (19, 34%), or high risk (17, 30%) of bias (**Table 2)**. There were no significant differences in RCT quality by geographic enrollment features. A significantly higher proportion of RCTs at high risk of bias was observed among those inadequately enrolling AIAN (*P*=.04) or White (*P*=.02) participants.

Conclusion: This study suggests that although numerous therapies have been investigated for use in SLE, US enrollment remains limited outside of large metropolitan areas, and enrollment overall underrepresents minoritized populations at risk of severe disease. Although RCT quality was not associated with geographic enrollment features, high risk of bias was less

Table 2: Cochrane Risk of Bias 2 analyses for SLE clinical trials

Table 2: Cochrane Risk of Bias 2 analyses for SLE clinical trials

		Clinical trials, No. (%)[c]	Overall risk of bias assessment, No. (%)			*p*-value
			Low risk	Some concerns	High risk	
All trials		55	19 (34)	19 (34)	17 (30)	-
US sites in small or non-metropolitan areas[a]	Less than 5%	27	8 (30)	9 (33)	10 (37)	.63
	Greater than or equal to 5%	28	11 (39)	10 (36)	7 (25)	
US enrollment site(s) in MUAs[b]	Yes	35	15 (43)	11 (31)	9 (26)	.26
	No	20	4 (20)	8 (40)	8 (40)	
PPR, AIAN[c]	Inadequate	22	8 (36)	3 (14)	11 (50)	.04
	Adequate	20	9 (45)	8 (40)	3 (15)	
PPR, Asian	Inadequate	13	5 (38)	5 (38)	3 (23)	.78
	Adequate	39	13 (33)	12 (31)	14 (36)	
PPR, Black	Inadequate	44	17 (39)	16 (36)	11 (25)	.21
	Adequate	11	2 (18)	3 (27)	6 (55)	
PPR, White	Inadequate	17	4 (24)	3 (18)	10 (59)	.02
	Adequate	37	14 (38)	16 (43)	7 (19)	
PPR, Hispanic[d]	Inadequate	11	4 (36)	1 (9)	6 (55)	.05[f]
	Adequate	32	11 (34)	14 (44)	7 (22)	

Abbreviations: US, United States; MUA, Medically Underserved Area; PPR, Participation-to-Prevalence Ratio; AIAN, American Indian/Alaska Native.

[a] Based on National Center for Health Statistics Urban-Rural Classification, updated 2023.

[b] Based on Health Resources and Services Administration designation of US counties lacking access to primary care services, updated December 2024.

[c] For all PPRs, values below 0.8 were considered to represent "inadequate" representation, and 0.8 or above "adequate" representation.

[d] Includes 5 trials for which "Hispanic" was reported as a race, and 38 trials for which "Hispanic" was reported as an ethnicity (i.e., independent of race).

[e] Variable demographic reporting between clinical trials (e.g., use of "Other" categorical) resulted in differences in the number of trials reporting enrollment for each demographic subgroup. All trials are included for which enrollment was identifiable or calculable from data provided in trial publications and/or registrations. Pooled enrollment was reported for 2 trials, which were considered a single clinical trial for the purpose of analyses.

[f] Non-significant *p*-value rounded to .05.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

frequently observed among RCTs with adequate enrollment of AIAN and White participants. Variation in RCT quality is notable and may limit the generalizability of findings to real-world patients, contributing to uneven update and lack of clarity over the optimal use of promising therapies.

Disclosure: J. Skydel: None; **A. Leland**: None; **R. Ramachandran**: None; **F. Koumpouras**: AbbVie/Abbott, 5, Adicet Bio, 2, AstraZeneca, 1, 2, 5, 6, Atara Bio, 2, Bristol-Myers Squibb(BMS), 5, 12, Clinical Trial, Cabaletta Bio, 2, Gilead, 12, Clinical Trial, GlaxoSmithKlein(GSK), 2, 5, ITN, 12, Clinical Trial, LRA/LuCIN, 5, Miltenyi Bio, 2, NIH, 5, Novartis, 2, RRF, 5, UCB, 12, Clinical Trial; **J. Wallach**: Janssen, 5.

Abstract Number: 1926

Real World Rate of Efficacy of Adalimumab Biosimilars Following a Mandated Switch in an Academic Medical Center

Katharine McCarthy, viktoriya avlasevich and Darren Tabechian, URMC, Rochester, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The proliferation of similar biotherapeutic products (biosimilars) has helped to reduce the cost burden of biologic therapies for health care systems[1]. Multiple studies have demonstrated biosimilars to be equally effective based on head-to-head trials of various adalimumab biosimilars in inflammatory autoimmune diseases[2]. Switching from adalimumab to a biosimilar in patients with stable and controlled diseases generally results in 1-year retention rates of 90% from real world experience outside the U.S.[3]. Due to the dynamic changes of insurance plans and formularies within the United States healthcare system, there is minimal data on retention rates and persistence of efficacy in real-world U.S. patients. It was our intention to survey the rate of continuation of adalimumab biosimilars in patients switched from adalimumab for inflammatory indications in a single academic medical center.

Methods: All patients 2 years of age and older who had received adalimumab or a biosimilar dispensed by the University of Rochester Specialty Pharmacy between 7/1/2023 and 12/31/2024 were included in the study. Patients were categorized into two cohorts, including those continuing adalimumab exclusively compared to patients who switched to a biosimilar agent(s). Patients were followed until 3/31/2025. The URMC IRB approved the study as exempt with data collected from Epic electronic medical record and Willow Ambulatory Pharmacy dispensing databases.

Results: 1,006 patients were identified and included in the study with an average age of 44 years old (range 2 – 88) and majority (60.2%) female. Rheumatoid arthritis was the most common diagnosis (32.1%) Across the 18-month time period, 97 patients (9.6%) were switched to a biosimilar with adalimumab-adaz and adalimumab-bwwd most common. 15 of 97 (15.5%) did not continue the biosimilar

Conclusion: Real world experience following mandated switch from adalimumab to a biosimilar showed a marginally higher rate of discontinuation than comparable cohorts from outside the United States. The cost of medication saved by switching to biosimilar medications may justify this rate of unanticipated mediation interruption.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. McCarthy: None; **v. avlasevich**: None; **D. Tabechian**: None.

Abstract Number: 1928

Oral Health in Patients with Rheumatic Diseases: A Pilot Quality Improvement Program

Margarita Isabel Alarcon-Jarquin[1], Fernanda M. Garcia-Garcia[2], Vanessa L. Lopez-Flores[1], Aleydis Gonzalez-Melendez[3], Gabriel Figueroa-Parra[3], Dionicio A. Galarza-Delgado[2] and Janett C. Riega-Torres[4], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Mexico, [4]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatic diseases commonly experience oral health issues such as dental caries, xerostomia, and periodontal disease. These complications are linked to both the disease itself and immunosuppressive treatments, often leading to reduced quality of life and poor systemic inflammatory control. Despite this, oral health remains insufficiently addressed in rheumatologic care.

This study presents the experience of an interdisciplinary rheumatology-dentistry clinic. It evaluates the impact of collaborative care on early oral risk detection, health promotion, and oral health-related quality of life in patients with rheumatic diseases.

Methods: A structured interdisciplinary care model was established in 2017 to link rheumatologists with dental professionals. Its aim was to prevent oral health deterioration in patients with rheumatic diseases. During routine evaluations, rheumatologists screened for oral risk factors and referred patients to dentists trained in rheumatologic oral conditions.

Dentists conducted comprehensive evaluations including physical exams, salivary tests, ICDAS (International Caries Detection and Assessment System), and GOHAI (Geriatric Oral Health Assessment Index) scoring. Individualized prevention plans were developed addressing hygiene, diet, salivary stimulation, and fluoride use. Referrals to dental specialists were made as necessary. The model ensured continuous monitoring of clinical and patient-reported outcomes, creating a feedback loop to promote adherence and sustained care integration (Figure 1).

Results: A total of 415 patients with rheumatic diseases were included. The mean age was 52.27 ± 14.17 years; 91.1% were female, and 6.3% were pregnant. Diagnoses included rheumatoid arthritis (57.1%), systemic lupus erythematosus (17.1%), primary Sjögren's syndrome (14.2%), and other conditions (11.6%).

All patients attended the initial dental consultation; 90% were referred to other dental specialties. Prevalence of oral conditions included dental caries in 60.7%, reduced unstimulated salivary flow in 46.7%, and missing teeth in 10.3%. All received personalized oral health recommendations from trained dental professionals.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Integrated Oral Health Workflow in Rheumatology Care

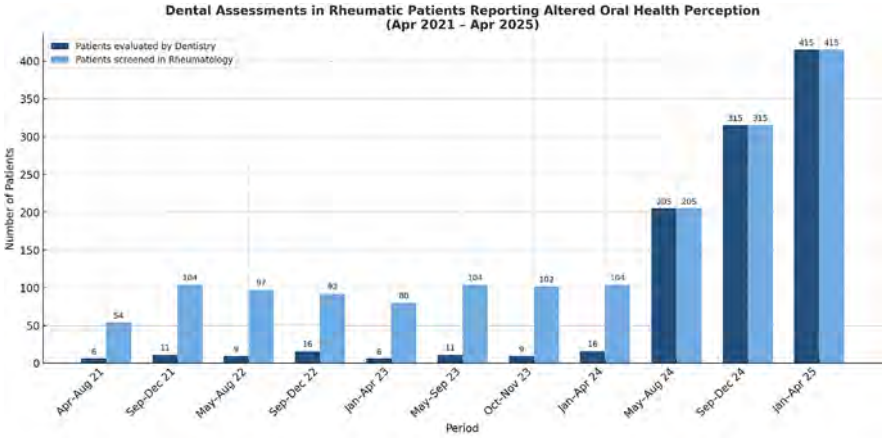


Figure 2. Rheumatologic and *dental assessments over time in patients with rheumatic diseases reporting altered oral health perception (April 2021 – April 2025).*

Initially launched in collaboration with the dentistry department, the program expanded in 2024 due to increasing demand. That year, dental services were fully integrated within the rheumatology clinic's physical space, significantly increasing dental consultations and improving referral pathways and specialized care access (Figure 2).

Conclusion: Integrating dental evaluations into rheumatology care improved detection and management of oral health issues in patients with rheumatic diseases. The increase in referrals and enhanced interdisciplinary collaboration demonstrates the feasibility and value of coordinated care. Immediate referrals and universal oral health guidance highlight the success of this patient-centered, integrated model.

Disclosure: M. Alarcon-Jarquin: None; **F. Garcia-Garcia**: None; **V. Lopez-Flores**: None; **A. Gonzalez-Melendez**: None; **G. Figueroa-Parra**: None; **D. Galarza-Delgado**: None; **J. Riega-Torres**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1929

Economic Burden of Macrophage Activation Syndrome (MAS) in Patients with Still's Disease (Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult-onset Still's Disease (AOSD)): Analysis of a US National Administrative Claims Database

Michael Marrone[1], Christopher McPherson[2] and Abiola Oladapo[3], [1]Sobi Inc., Mt Pleasant, SC, [2]Sobi, University City, MO, [3]Sobi INC, Waltham, MA

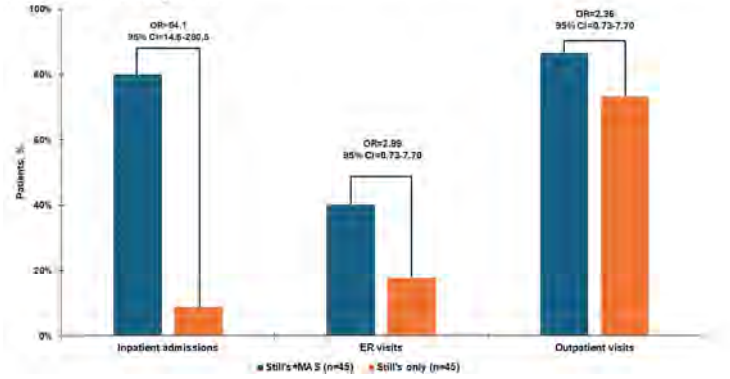
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Macrophage activation syndrome (MAS) is a severe, life-threatening complication of rheumatologic disease. MAS is a form of secondary hemophagocytic lymphohistiocytosis which occurs most frequently in patients with Still's disease (i.e., systemic juvenile idiopathic arthritis (sJIA) or adult-onset Still's disease (AOSD)). MAS, if not properly treated, may progress to multiple organ failure and mortality. Treatment is aimed at achieving clinical stability and symptom resolution. However, there is currently no FDA approved therapy for MAS and corticosteroids remain the mainstay of treatment. Further, limited information exists regarding the economic burden (i.e., healthcare resource utilization (HCRU) and costs) of MAS in patients with Still's disease in the United States.

Methods: A retrospective analysis of administrative claims (IQVIA PharMetrics Plus) from 2019 to 2024 was used to identify: Patients diagnosed with Still's disease [(ICD-10:M082) including AOSD (ICD-10:M061) and sJIA (ICD-10:M08)] with ≥6 months of continuous enrolment prior to Still's diagnosis (index date) and ≥12 months of continuous enrolment post-index without a MAS diagnosis (ICD-10:D76.1); and patients with Still's disease with ≥6 months of continuous enrolment prior to earliest MAS diagnosis observed in the study period and ≥12 months of continuous enrolment post-MAS diagnosis. A propensity score was used to match patients (1:1) with Still's disease with and without MAS. All-cause HCRU (inpatient [IP] admission, emergency room [ER] visits, and outpatient [OP] visits) and costs (all-cause and rheumatologic; adjusted to

Figure 1. All-cause HCRU (i.e. proportion of patients by visit type) during the post-index period



HCRU was measured during the observation period, defined as the 12-month post-index period. ORs were evaluated for binary variables (ie, at least one visit) using logistic regression. Models were controlled for age at Still's diagnosis, underlying Still's diagnosis (AOSD, sJIA), sex, and ECI during the baseline period. ORs >1 indicate higher odds for patients with Still's and MAS compared with propensity score matched patients with Still's without MAS. ECI= Elixhauser Comorbidity Index; CI=Confidence interval; ER= Emergency room; HCRU=Healthcare resource utilization; MAS=Macrophage Activation Syndrome; OR= Odds ratio.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. All -cause HCRU (i.e. number of visits per patient by visit type) during the post-index period

	Still's + MAS (n=45)	Still's only (n=45)	Mean difference (95% CI)	p-value*
In-patient admissions				
Mean (SD)	1.51 (1.46)	0.09 (0.29)	1.42 (1.05-1.79)	<0.001
In-patient length of stay†				
Mean (SD), mos	9.53 (7.5)	4.75 (3.86)	4.78 (2.42-7.15)	<0.001
ER visits				
Mean (SD)	0.78 (1.24)	0.22 (0.56)	0.56 (0.26-0.85)	<0.001
Outpatient visits				
Mean (SD)	26.62 (31.32)	4.91 (6.94)	21.71 (20.07-23.35)	<0.001

* Results remained robust when adjusted for age at Still's diagnosis, underlying Still's diagnosis (i.e., AOSD, sJIA), sex, and ECI †Limited to patients with at least 1 in-patient admission AOSD= Adult-onset Still's disease (AOSD); CI= confidence interval; ECI= Elixhauser Comorbidity Index; ER=Emergency room; MAS= macrophage activation syndrome; MOS= Months; sJIA= Systemic juvenile idiopathic arthritis

Table 2. All-causes healthcare cost ($US) during the post-index period

	Still's + MAS (n=45)	Still's only (n=45)	Mean difference (95% CI)	p-value*
Total all-cause cost (Medical and Pharmacy)				
Mean (SD)	318,828 (930,736)	19,233 (33,689)	299,595 (76,681 – 522,509)	0.008
In-patient cost†				
Mean (SD)	135,951 (387,983)	1,570 (6,291)	134,381 (-3,782 – 273,544)	0.06
ER cost				
Mean (SD)	547 (1,420)	293 (1,411)	254.27 (-448 – 956)	0.5
Outpatient cost				
Mean (SD)	3,627 (5,200)	910 (2,186)	3,455.76 (824 – 6,097)	0.01
Pharmacy cost				
Mean (SD)	30,857 (58,592)	9,533 (26,624.45)	21,224.10 (-1210 – 43,658)	0.06
Rheumatologic-related cost (Medical and Pharmacy)				
Mean (SD)	163,099 (575,457)	1,930 (4,063)	161,169 (22,714 – 299,623)	0.02

* Results remained robust when adjusted for age at Still's diagnosis, underlying Still's diagnosis (i.e., AOSD, sJIA), sex, and ECI †Limited to patients with at least 1 in-patient admission AOSD= Adult-onset Still's disease (AOSD); CI=Confidence interval; ECI= Elixhauser Comorbidity Index; ER=Emergency room; MAS= macrophage activation syndrome; sJIA= Systemic juvenile idiopathic arthritis

2024 US dollars using the medical component of the Consumer Price Index) were ascertained in the post-index period. Differences in HCRU and costs were estimated using both unadjusted and adjusted analysis.

Results: After propensity score matching, 45 patients with Still's and 45 patients with Still's and MAS were included (mean [SD] age, 26.8 [15.1] and 26.8 [16.0] years at Still's diagnosis, respectively; female, 55.6% and 60.0%, respectively). Mean (SD) Elixhauser Comorbidity Index was 1.6 (1.5) and 2.1 (2.8), respectively. The most common comorbidities were rheumatoid arthritis (48.9% and 42.2%) and cardiac arrythmia (13.3% and 22.2%) in patients with Still's with and without MAS, respectively.

Patients with MAS were significantly more likely to have an ER visit (P=0.04) and/or IP admission (P< 0.001) than patients without MAS in the 12-month post-index period (Figure 1). They also had significantly more frequent IP admissions (P< 0.001), ER visits (P< 0.001), OP visits (P=< 0.001), and longer IP stays (P< 0.001) than patients without MAS (Table 1). In addition, patients with MAS incurred significantly (P=0.008) higher total all-cause ($318,828 vs $19,233) and rheumatologic-related ($163,099 vs $1,930) healthcare costs (P=0.02) than patients without MAS (Table 2).

Conclusion: Patients with Still's and MAS incurred significantly higher HCRU and associated costs compared with similar patients without MAS. Availability of novel therapies targeted to treat MAS may reduce the overall burden of disease to patients and the healthcare system.

Disclosure: M. Marrone: Sobi Inc., 3; **C. McPherson**: Sobi, 3; **A. Oladapo**: Sobi Inc, 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1930

Can a Multinational Awareness Campaign Improve Referral Rates and Reduce Diagnostic Delays in Patients with Chronic Inflammatory Rheumatic Diseases? The Impact of a Prospective Interventional Study

Nelly Ziade[1], Karen Mechleb[2], Fatima Alnaimat[3], Sherif Gamal[4], Avin Maroof[5], Bassel Elzorkany[6], Manal Mashaleh[7], Manal El Rakawi[8], Mahmoud Adly[9], Lina Elkibbi[10], ERRAOUI Mariam[11], Krystel Aouad[12], Chafika Haouichat[13], Nizar Abdullateef[14], ASAL ADNAN RIDHA[15], Fatemah Baron[16], Ihsane Hmamouchi[17] and ARCH group, [1]Department of Rheumatology, Saint-Joseph University and Hotel-Dieu de France, Beirut, Lebanon, [2]Saint Joseph University Beirut, Beirut, Lebanon, [3]The University of Jordan, amman, Jordan, [4]Cairo University, Cairo, Egypt, [5]University of Kurdistan Hawler, Erbil, Iraq, [6]Private (BZRC), Cairo, Egypt, [7]Al Saudi Hospital, Amman, Jordan, [8]Djillali Bounaama University Hospital, Algiers, Algeria, Algiers, Algeria, [9]Ministry of Health, Kuwait, Kuwait, Saad Elabdulla, Kuwait, [10]Specialized Medical Center, Riyadh, Saudi Arabia, Riyadh, Saudi Arabia, [11]CHU Agadir, Agadir, Morocco, [12]Department of Rheumatology, Saint George Hospital University Medical Center, Beirut, Lebanon, [13]Djillali Bounaama University Hospital, Algiers, Algeria, [14]Baghdad College of Medicine, Baghdad, Iraq, [15]Baghdad Teaching Hospital, Baghdad, Iraq, [16]Al-Jahra Hospital, Kuwait, Kuwait, Kuwait, Kuwait, [17]Health Sciences Research Center (CReSS).Faculty of Medicine, International University of Rabat, Rabat, Morocco

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1914–1935) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Delayed diagnosis and treatment in chronic inflammatory rheumatic diseases (CIRDs), including rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), and psoriatic arthritis (PsA), is associated with poorer clinical outcomes. Although referral algorithms exist, there is limited evidence on the real-world effectiveness of awareness campaigns in improving referral practices to rheumatology.

The objective of this study was to assess the impact of a multinational awareness campaign on referral trends and diagnostic delays for CIRDs across Arab countries.

Methods: This prospective pre-post interventional study was conducted in eight Arab countries between November 2023 and November 2024. Baseline data on referral patterns and diagnostic delays were collected in November 2023. Diagnostic delay was defined as the interval from symptom onset to confirmed diagnosis in newly diagnosed CIRD patients. From December 2023 to October 2024, a structured awareness campaign targeted primary care physicians and non-rheumatology specialists.

Table 1. Change in the proportion of new patients referred to 14 high-volume rheumatology clinics in 8 countries, before and after the multinational awareness campaign

	2023 (pre-campaign)	2024 (post-campaign)	Absolute difference in %	p-value
N	2490	3616		
New patients, N (%*)	746 (29.96%)	1031 (28.51%)	-1.45%	
New patients with CIRDs, N (%**)	234 (31.37%)	383 (37.15%)	**+5.78%**	<0.001
New patients with RA, N (%**)	124 (16.62%)	184 (17.85%)	+1.23%	<0.001
New patients with axSpA, N (%**)	94 (12.60%)	136 (13.19%)	+0.59%	<0.001
New patients with PsA, N (%**)	16 (2.14%)	63 (6.11%)	+3.97%	<0.001

*Percentages from all patients (in columns)

**Percentages from new patients (in columns)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

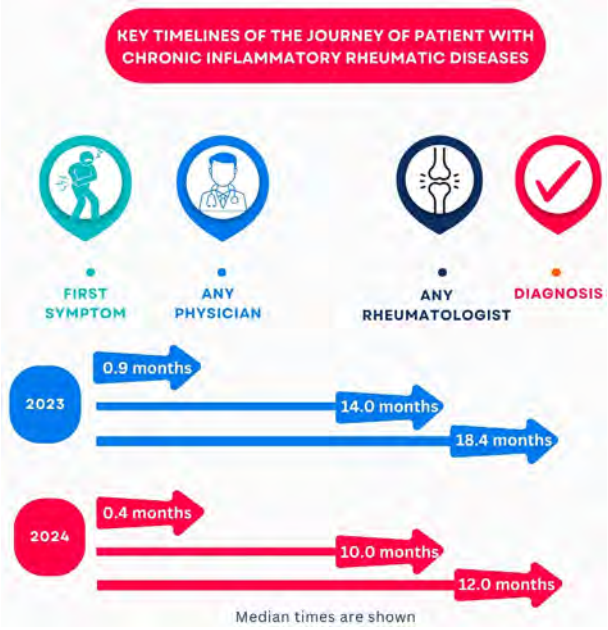


Figure 1. Key timelines in the referral of new patients with CIRDs to rheumatology, before and after the multinational awareness campaign

The campaign featured live webinars (n=9), social media dissemination via the Arab League of Associations for Rheumatology (ArLAR) channels, and in-person workshops held in September–October 2024 (n=22), using a previously validated referral algorithm. The primary outcome was the change in the proportion of newly referred RA, axSpA, and PsA patients (collectively referred to as CIRDs) across 14 high-volume rheumatology centers. Secondary outcomes included time intervals from symptom onset to first physician contact and to rheumatologic diagnosis. Descriptive statistics were presented using medians and interquartile ranges (IQRs). Multivariable linear regression was used to identify factors associated with diagnostic delays.

Results: In November 2024, 3616 patients were seen across the 14 clinics, including 1031 (28.5%) new patients, of whom 383 (37.1%) were newly diagnosed with CIRDs (RA: n=184; axSpA: n=136; PsA: n=63). Compared to baseline, the proportion of newly referred CIRD cases increased by 5.8% (from 31.4% to 37.1%, $p< 0.001$). Subgroup increases were observed in RA (from 16.6% to 17.8%), axSpA (12.6% to 13.2%), and PsA (2.1% to 6.1%) (Table 1). Among 365 newly diagnosed CIRD patients (mean age 42.6±15.2 years; 62.7% female), the median time from symptom onset to diagnosis decreased from 18.4 months (IQR 5.8–48.7) to 12.0 months (IQR 4.0–36.0). Reductions were also observed by disease subtype: RA (12.2 to 9.0 months), axSpA (36.5 to 27.5 months), and PsA (24.3 to 12.0 months) (Figure 1). Multivariable analysis identified longer disease duration (B=4.969, $p< 0.001$), lower educational attainment (B=10.589, $p=0.015$), and longer time to rheumatologist consultation (B=0.727, $p< 0.001$) as independent predictors of diagnostic delay.

Conclusion: This multinational intervention was associated with increased rheumatology referrals and significantly reduced diagnostic delays for patients with CIRDs. While causality cannot be definitively established, the findings support the value of targeted awareness strategies in improving early access to rheumatologic care. Further longitudinal studies are recommended to evaluate sustained impact.

Disclosure: N. Ziade: None; **K. Mechleb**: None; **F. Alnaimat**: None; **S. Gamal**: None; **A. Maroof**: None; **B. Elzorkany**: None; **M. Mashaleh**: None; **M. El Rakawi**: None; **M. Adly**: None; **L. Elkibbi**: None; **E. Mariam**: None; **K. Aouad**: None; **C. Haouichat**: None; **N. Abdullateef**: None; **A. RIDHA**: None; **F. Baron**: None; **I. Hmamouchi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1931

COSMOS Prevalence of aTTP in SLE

Nisha Sapkota[1], Yevheniia Andriushchenko[2], Saadia Malik[2], Sarang Choi[2] and Sima Terebelo[2], [1]Interfaith Medical Center, One Broolyn Health, Brooklyn, NY, [2]Brookdale Hospital Medical Center, One Brooklyn Health, Brooklyn

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with diverse manifestations, including thrombotic thrombocytopenic purpura (TTP), a life-threatening hematologic disorder. The pathogenesis of acquired TTP (aTTP) in SLE is believed to involve formation of autoantibodies against ADAMTS13, which inhibit this matrix metalloproteinase activity, thus inhibiting the cleavage of von Willebrand factor multimers and ultimately promoting platelet aggregation and leading to microvascular thrombosis. The clinical overlap between SLE flares and aTTP poses significant diagnostic and therapeutic challenges. This study aims to assess the prevalence, clinical characteristics, and management of aTTP in SLE patients.

Methods: We conducted a retrospective cohort study using the Cosmos Cohort, an integrated database with nearly 296 million patient encounters from multiple US healthcare systems. We searched all encounters from March 31, 2015 to March 5, 2025 for aTTP cases using the grouper name "thrombotic microangiopathy" and included all subsets. We then identified SLE patients using the grouper name "systemic lupus erythematosus" and included all subsets. We then combined both datasets to analyze population characteristics. To compare with local data, we extracted SLE and aTTP cases from our institutional dataset using Epic SlicerDicer and performed a comparative analysis of prevalence, demographics, and treatment patterns.

Results: Among 751,633 SLE patients in the Cosmos Cohort, 1,610 (0.21%) were diagnosed with aTTP, with a female predominance (1,346 females, 264 males; 83.6% female). In our institutional dataset of 1,397 SLE patients, the prevalence was

Table 1 compares number of SLE and aTTP cases from COSMOS and our institutional dataset by age, sex, treatment, and complications.

	OBH Epic	Cosmos
SLE cases	1397	751633
TTP cases	95	15903
TTP in SLE	4	1610
Age (years)	Age: 50 to 84 Average = 60 Median =54	Age: 5 to 101 Average 47y Median 46 y
Sex	Female: 2 Male: 2	Female: 1346 Male: 264
Kidney biopsy	0	525
Treatment		
• Rituximab	3	460
• Cyclophosphamide	0	225
• MMF	0	764
Other Complications		
• M32.11 Endocarditis in SLE	0	70
• M32.12, pericarditis in SLE	0	127
• M32.13 lung involvement in SLE	0	143
• M32.14 Glomerular disease in SLE,	1	847
• M32.15 Tubulointerstitial nephropathy in SLE,	0	129
• M32.19 other organ or system involvement in SLE (includes cerebritis)	1	653

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

slightly higher at 0.29% (4 patients: 2 females, 2 males). The mean age was 46 years in the Cosmos Cohort and 60 years in our dataset. SLE activity showed Kidney involvement in 60.6% (976 patients, lung involvement in 9% (143 patients), pericarditis in 7.9% (127 cases) and other organ or system involvement in 41% (653 patients). There was a history of renal biopsy in 525 patients. Treatments in the Cosmos Cohort included rituximab (28.6%, 460 patients), mycophenolate mofetil (47.5%, 764 patients), and cyclophosphamide (14%, 225 patients).12 patients received plasma exchange (PLEX) therapy. In our dataset, 3 of 4 patients (75%) received rituximab, while the treatment for the remaining patient was unknown. A total of 397 patients in the Cosmos cohort are currently deceased, however the cause of death and relationship to aTTP and SLE are unknown.

Conclusion: SLE-associated aTTP is a rare yet severe complication requiring early detection and aggressive treatment. Our study describes its prevalence in the modern era of immunosuppression, highlights differences in prevalence and treatment approaches across datasets, and emphasizes the need for standardized guidelines. Further research, including multi-center prospective studies, would be beneficial to establish a more comprehensive understanding of aTTP prevalence in SLE patients across different populations and settings and investigate effectiveness of treatment approaches.

Disclosure: N. Sapkota: None; **Y. Andriushchenko**: None; **S. Malik**: None; **S. Choi**: None; **S. Terebelo**: None.

Abstract Number: 1932

Evaluating a Potential Cause of Excess Lung Cancer Mortality in RA: An Analysis of Chest CT Imaging Frequency in RA

Rebecca Brooks[1], Sara Achenbach[2], Vanessa Kronzer[1], Bryant England[3], Emily Leasure[1], Elena myasoedova[1], John Davis[1] and Cynthia Crowson[4], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, [3]University of Nebraska Medical Center, Omaha, NE, [4]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Recent studies have demonstrated that patients with RA are at an increased risk for the development of lung cancer and lung cancer related death. However, the cause for the increased risks has not been established. Although previous studies have investigated the delay of other age recommended cancer screenings, few studies have investigated lung cancer screening in RA patients with a smoking history. Therefore, we evaluated the cumulative incidence of chest CT imaging in RA patients with either a current or former smoking history between 50-80 years old.

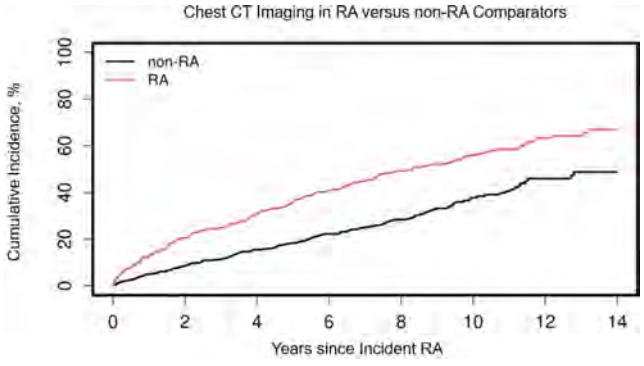


Figure 1. Cumulative Incidence of Chest CT Imaging in RA versus non-RA comparators

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We performed a retrospective cohort study of patients with incident RA in a geographically defined area who fulfilled either the 1987 ACR or 2010 ACR/EULAR classification criteria between 2010 and 2019. Non-RA comparators of similar age, sex and county were randomly selected. The analyses included RA and non-RA patients who were between the ages of 50 and 80 years old and were either former or current smokers. Patients with a prior history of lung cancer were excluded from analyses. Chest CT imaging was defined as completed if it was performed by the end of the study period, emigration out of the geographical area, or death. Aalen-Johansen methods determined the cumulative incidence of chest CT imaging in both cohorts, accounting for the competing risk of death. Cox proportional hazard models adjusted for age, sex, index year, and education were utilized to compare the rates of chest CT imaging.

Results: This study included 407 patients with RA and 360 non-RA comparators. The patients with RA had a mean age of 63 years, 57% being female, and 52% having education beyond high school. During follow-up, >50% of the RA patients had chest CT imaging (55.8% [50.7-61.5]) compared to the non-RA cohort with < 40% (37.8% [32.3-44.2]) (Figure 1). After adjusting for age, sex, index year, and education, the patients with RA were 90% more likely to have chest CT imaging compared to the non-RA cohort (aHR 1.90 [1.51-2.39]. The increased likelihood of chest CT imaging persisted when examining former (aHR 1.95 [1.48-2.57]) and current (aHR 1.88 [1.23-2.89]) smokers separately.

Conclusion: RA was associated with an >85% increase in chest CT imaging after adjusting for potential confounders in this analysis of former and current smokers. These findings suggest that the increased risk of lung cancer related death in RA patients is not due to a decrease in chest CT imaging leading to a delay in the diagnosis of lung cancer. The increased incidence of chest CT imaging in the RA cohort could partially be explained by the increased risk of interstitial lung disease in those with RA, prompting more frequent evaluation of respiratory symptoms with chest CT imaging. Therefore, further studies investigating adherence to lung cancer screening guidelines, the effect of changes in lung cancer screening guidelines, and the impact of pack years are necessary to fully understand the impact of lung cancer screening on the RA population.

Disclosure: R. Brooks: None; **S. Achenbach**: None; **V. Kronzer**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **E. Leasure**: None; **E. myasoedova**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **C. Crowson**: None.

Abstract Number: 1934

Analysis of the Determinants of Vaccine Acceptance and Hesitancy in Germany: A Mixed-methods Approach Incorporating Health Insurance Data and Qualitative Interviews with Patients and Physicians

Maria Zacharopoulou[1], thomas Grüter[2], Heike van de Sand[3], Romy Lauer[4], Marianne Tokic[5], Jale Basten[5], Robin Denz[5], Anastasia Suslow[6], Andreas Stallmach[7], Anika Franz[7], Theresa Oganowski[2], Ina Otte[6], Ingo Meyer[3], Horst Christian Vollmar[6], Nina Timmesfeld[5], Ursula Marschall[8], Joachim Saam[8], Kerstin Hellwig[2], **Uta Kiltz**[9] and VAC-MAC consortium, [1]Rheumazentrum Ruhrgebiet, Herne, Germany, [2]St. Josef Hospital, Ruhr University Bochum, Germany, Bochum, Germany, [3]PMV research group, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany, Cologne, Germany, [4]Institute of General Practice and Family Medicine, Ruhr-University Bochum, Bochum, Germany, [5]Department of Medical Informatics, Biometry, and Epidemiology, Ruhr University Bochum, Germany, Bochum, Germany, [6]Institute of General Practice and Family Medicine (AM RUB), Medical Faculty, Ruhr University Bochum, Germany, Bochum, Germany, [7]University Hospital Jena, Germany, Jena, Germany, [8]BARMER Institute for Health System Research, Department Medicine and Health Services Research, Wuppertal, Germany, Wuppertal, Germany, [9]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1914–1935) Health Services Research Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Adequate immunization is essential for patients with inflammatory rheumatic and musculoskeletal diseases (iRMD). Autoimmunity itself and immunotherapy increase the risk of infection independent of each other. In Germany, the Standing Committee on Vaccination recommends influenza and pneumococcal vaccine for all patients above the age of 60 and for all iRMD patients above the age of 50. However, many data suggest that this vulnerable group is not sufficiently vaccinated. To explore barriers and facilitators to influenza and pneumococcal vaccine uptake in immunosuppressed adults with iRMDs.

Methods: Using claims data of a German statutory health insurance, the "VAC-MAC" - VACcination of MS/Arthritis/Colitis Patients´ project analysed vaccine uptake in patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and systemic lupus erythematous (SLE). Quantitative analyses were based on approximately 9 million individuals in Germany insured from 2013-2021. Determinants of vaccine uptake were analyzed based on insurance data of 2019 with univariate and multivariate logistic regression analysis. The analysis includes both the overall patient cohort and a subset of newly vaccinated iRMD patients, defined as those who were unvaccinated for three or more consecutive seasons and received the influenza vaccine between Q3 2019 and Q2 2020. Additionally, semi-structured interviews with trained qualitative researcher were performed in 2023 with in total 30 patients, rheumatologist, and primary care physicians.

Results: We identified 229.913 patients (73% female, mean age 66±15 years) in 2019. The rate of influenza vaccination with 31% was moderate for the total iRMD group but higher with 41,.6% in the group ≥ 50 years of age and substantially higher with 47% in the group ≥ 60 years of age. The rate of pneumococcal vaccine was low with 6.0% in the total iRMD group with an insignificant increase to 6.8% in the group ≥ 50 years of age and to 8.2% in the group ≥ 60 years of age. Older age, more frequent physicians´ visits, higher number of comorbidities, health care provided by vaccination-oriented physicians and residence in the former East German states, were associated with a higher vaccination rate (figure 1).

The following barriers to vaccination were identified in the qualitative survey: 1) concerns about side effects including experience of flares, 2) negative vaccination experiences, 3) insufficient medical information and proactive discussion about the need for vaccination, 4) too little or complicated information material, 5) gaps in knowledge about immunomodulation and vaccination recommendations for patients with autoimmune diseases, and 6) unclear roles and too little communication between treating rheumatologist and general practitioners.

Conclusion: Although influenza vaccination is recommended of all iRMD patients, a German health insurance dataset shows an influenza vaccination rate of only 37% of all iRMD patients in 2019. There is a substantial gap in quality of care in vaccination against pneumococci. Physicians and patient factors as well as fears and concerns about side effect of patients and physicians can serve as modifiable factors to improve quality of care for iRMD patients.

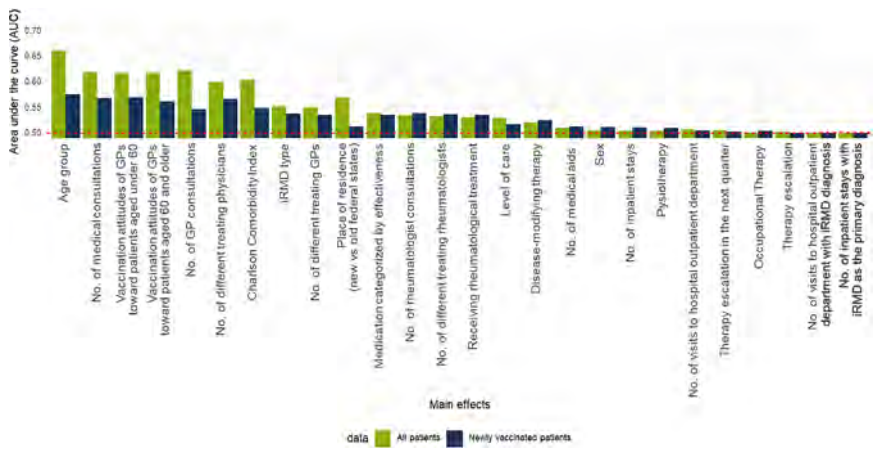


Figure 1: Area under the curve (AUC) of univariate models assessing factors influencing influenza vaccination coverage in patients with iRMD

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Zacharopoulou: None; **t. Grüter**: None; **H. van de Sand**: None; **R. Lauer**: None; **M. Tokic**: None; **J. Basten**: None; **R. Denz**: None; **A. Suslow**: None; **A. Stallmach**: None; **A. Franz**: None; **T. Oganowski**: None; **I. Otte**: None; **I. Meyer**: None; **H. Vollmar**: None; **N. Timmesfeld**: None; **U. Marschall**: None; **J. Saam**: None; **K. Hellwig**: None; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5, Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5.

Abstract Number: 1935

Sex-associated disparities in industry payments to US authors in high-impact rheumatology journals correlate with author impact

William Stohl[1], Krishan Parikh[1], Anuj Parikh[2] and Sheldon Stohl[3], [1]University of Southern California, Los Angeles, CA, [2]Cerritos High School, Cerritos, CA, [3]Hadassah Medical Center, Jerusalem, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1914–1935) Health Services Research Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: To assess sex-associated disparities in industry payments to US physician-authors in high-impact rheumatology journals and their correlation with author impact.

Methods: US authors of publications in four high-impact rheumatology journals (January-June 2023 issues of *Lancet Rheumatol*, *Nat Rev Rheum*, *Ann Rheum Dis*, *Arthritis Rheumatol*) were vetted on Open Payments Database (OPD) for industry payments (2017-2021). The *h*-index (an accepted metric of author impact) and dollar amounts were recorded. Differences in the percentages of male vs female US authors with or without OPD entries, in research-associated and non-research-associated payments, and in *h*-indexes were determined. Two hematology, two surgery, and two obstetrics/gynecology (ob/gyn) high-impact journals were similarly vetted.

Results: We vetted 296 publications in the rheumatology journals. Of the 712 (356M + 356F) discrete US physician-authors, 150 (42.1%) men and 112 (31.5%) women received ≥1 industry payment ($p = 0.003$). Total, non-research-associated, and research-associated industry payments to the 150 men than to the 112 women ($p \leq 0.022$). Male US physician-authors of publications in hematology, surgery, and ob/gyn journals also received greater payments than did corresponding female US physician-authors (Table I), with the disparities being numerically greater for rheumatology than for the other disciplines (Fig 1A).

The *h*-indexes of the men in each journal-discipline were also greater than those of the corresponding women ($p < 0.001$; Fig 1B). Plots of industry payments vs *h*-index revealed the regression lines for the women to be lower than those for the men at low *h*-indexes but to catch up and overtake at higher *h*-indexes (Fig 2A). Of note, at the female *h*-index 90th percentiles for the individual journal-disciplines, total, non-research-associated, and research-associated payments were all numerically greater to the women than to the men only in rheumatology. In contrast, the respective payments in hematology and surgery remained numerically greater to the men than to the women, with the payments to the men and women being similar in ob/gyn (Fig 2B). This suggests that, especially in rheumatology, author impact is an important contributory factor to the magnitude of industry payments.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table I

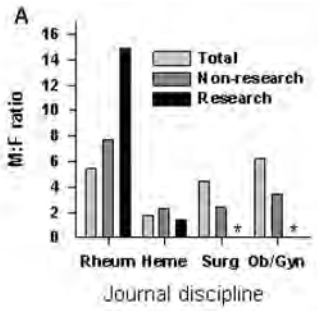
Table I. Industry payments to US physician-authors of publications in the vetted journals.

Journal discipline	Category	Sex/Gender	Median	25% percentile	75% percentile	Maximum	P value
Rheumatology (150M + 112F)	Total	Male	$107,853	$4,284	$948,192	$20,407,159	<0.001
		Female	$19,774	$646	$324,972	$5,473,919	
	Non-research	Male	$15,702	$868	$104,280	$1,825,932	<0.001
		Female	$2,038	$178	$24,068	$873,069	
	Research	Male	$55,740	$0	$616,148	$20,329,307	0.022
		Female	$3,756	$0	$262,102	$4,600,851	
Hematology (432M + 214F)	Total	Male	$209,445	$6,522	$1,379,625	$99,003,346	0.091
		Female	$117,081	$1,421	$1,096,739	$149,476,816	
	Non-research	Male	$11,056	$566	$66,959	$1,466,214	0.002
		Female	$4,732	$241	$31,684	$671,046	
	Research	Male	$149,837	$0	$1,213,598	$98,136,786	0.311
		Female	$104,252	$0	$992,111	$149,452,759	
Surgery (369M + 200F)	Total	Male	$5,282	$312	$69,588	$10,862,686	<0.001
		Female	$1,195	$144	$18,186	$30,003,962	
	Non-research	Male	$2,002	$204	$15,475	$6,344,435	<0.001
		Female	$837	$123	$5,658	$680,228	
	Research	Male	$0	$0	$8,358	$10,786,531	0.008
		Female	$0	$0	$0	29,941,815	
Ob/Gyn (181M + 257F)	Total	Male	$5,350	$251	$104,098	$9,803,592	<0.001
		Female	$852	$116	$14,838	$17,914,107	
	Non-research	Male	$1,077	$100	$12,632	$527,233	0.004
		Female	$311	$91	$3,098	$226,802	
	Research	Male	$0	$0	$51,804	$9,781,100	0.001
		Female	$0	$0	$2,650	$17,914,107	

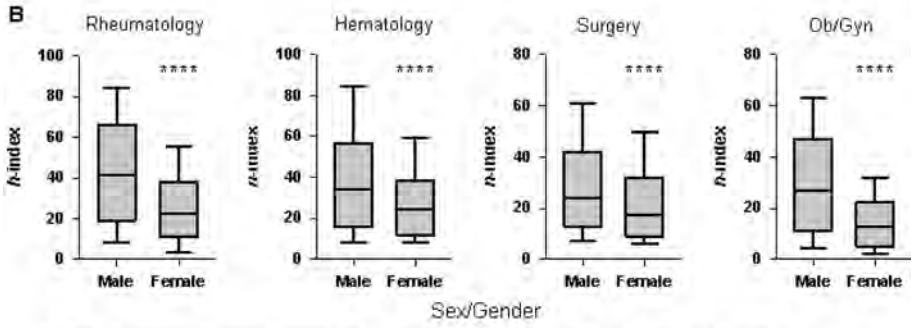
Results are presented as industry payments rounded to the nearest dollar.
"Ob/Gyn" denotes obstetrics/gynecology.

Conclusion: Significant differences exist in industry payments and *h*-indexes between male and female US physician-authors of publications in high-impact journals, especially high-impact rheumatology journals. The correlation between industry payments and *h*-index suggests that the greater payments to men than to women are not a conscious preference by the pharmaceutical industry for men *per se* but rather reflects industry's preference for physicians, male or female, with "stature" (high author impact). Nonetheless, differential industry payments to male vs female authors may have unknown ramifications for the types of studies executed and the experimental approaches taken. Additional studies are warranted to elucidate the root causes for the differences in author impact between men and women and how they lead to differential industry payments to men vs women.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

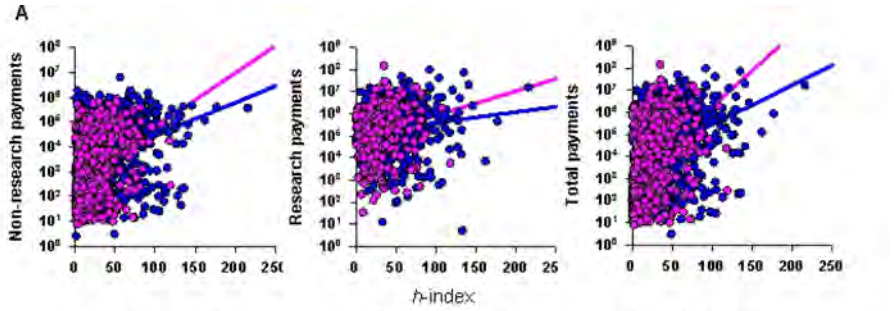


The ratios of the median dollar payments to males to the median dollar payments to females (M:F) are plotted as bars for total payments (light gray), non-research-associated payments (dark gray), and research-associated payments (black) for the indicated journal-disciplines for all US physician-authors who received ≥1 industry payment.

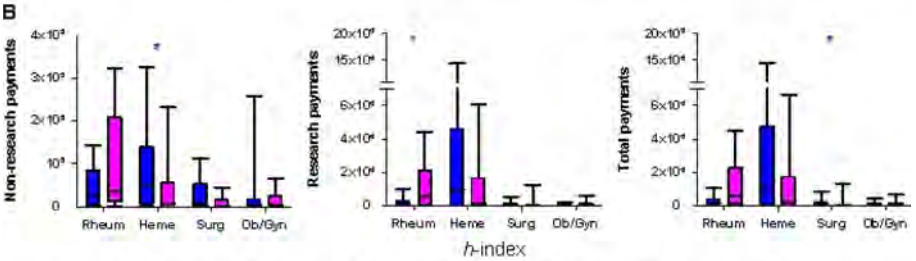


The *h*-indexes of the vetted male and female US physician-authors of publications in the indicated journal-disciplines are plotted as box plots. In each panel, the lines inside the boxes indicate the medians, the outer borders of the boxes indicate the 25th and 75th percentiles, and the bars extending from the boxes indicate the 10th and 90th percentiles. "****" denotes $p \leq 0.001$.

Figure 1



The scatter plots indicate non-research-associated industry payments, research-associated industry payments, and total industry payments vs *h*-index. The blue circles represent the individual male authors, and the pink circles represent the female authors. The blue and pink solid lines indicate the respective linear regression lines.



Results are presented as box plots for non-research-associated (left), research-associated (middle), and total (right) industry payments to the male (blue bars) and female (pink bars) US physician-authors at the female *h*-index 90th percentiles for the individual journal-disciplines. Blue asterisk indicates male value significantly greater than female value, and pink asterisk indicates female value significantly greater than male value ($p < 0.05$).

Figure 2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: W. Stohl: None; **K. Parikh**: None; **A. Parikh**: None; **S. Stohl**: None.

Abstract Number: 1936

A Fully Automated Method for Measuring Minimum Tibiofemoral Joint Space Width in Knee Osteoarthritis Assessment: Data from the FNIH Cohort

Ahmad Almhdie-Imjabbar[1], Yousra TOUZANI[2], Hechmi Toumi[2] and Eric Lespessailles[3], [1]University Hospital Center of Orleans, Orleans, France, [2]PRIMMO- University Hospital Center of Orleans, Orleans, France, [3]CHU Orléans, Orléans, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis is one of the most prevalent chronic diseases worldwide, with knee osteoarthritis (KOA) being a particularly painful and debilitating form. The minimum tibiofemoral joint space width (mJSW) is a key criterion for assessing KOA progression. This study aims to evaluate a fully automated method for measuring mJSW in a reproducible and reliable manner, accounting for structural changes in knee anatomy.

Methods: This study included 599 patients from the Foundation for the National Institutes of Health (FNIH) cohort, in which measurements of the Medial Compartment mJSW were reported. Our method consists of two main steps. First, we use a machine learning-based tool to automatically detect the tibiofemoral contour of the knee. Second, we compute mJSW as perpendicular distance from each point on the femoral side to the line connecting the two closest points on the tibial side, Figure 1. Statistical analyses were performed to compare our measurements with those obtained by the FNIH team. Reliability was assessed using the Intraclass Correlation Coefficient (ICC) and the Bland–Altman analysis.

Results: The ICC demonstrated excellent agreement (0.906, 95% CI: 0.891 – 0.919) across all patients. The Bland–Altman analysis revealed a bias of -0.202 mm (limits of agreement: -1.095 mm to +0.691 mm), Figure 2. The observed bias is systematic and does not depend on the width of the joint space.

Conclusion: The proposed method enables fully automated, reliable, and reproducible measurement of mJSW. While our method slightly underestimates mJSW compared to the reference measurements from the FNIH team, it remains a robust and consistent approach for assessing KOA progression.

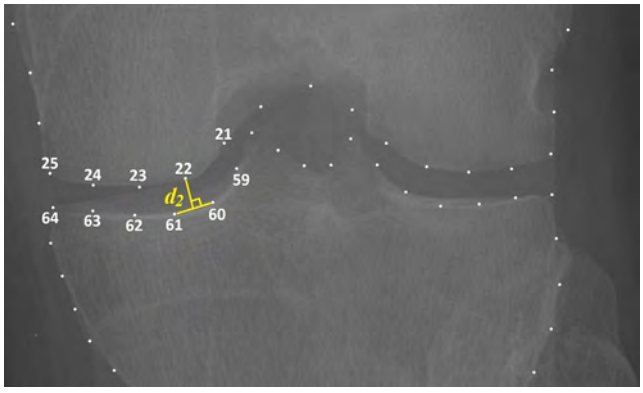


Figure 1: Calculating the minimum tibiofemoral joint space

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

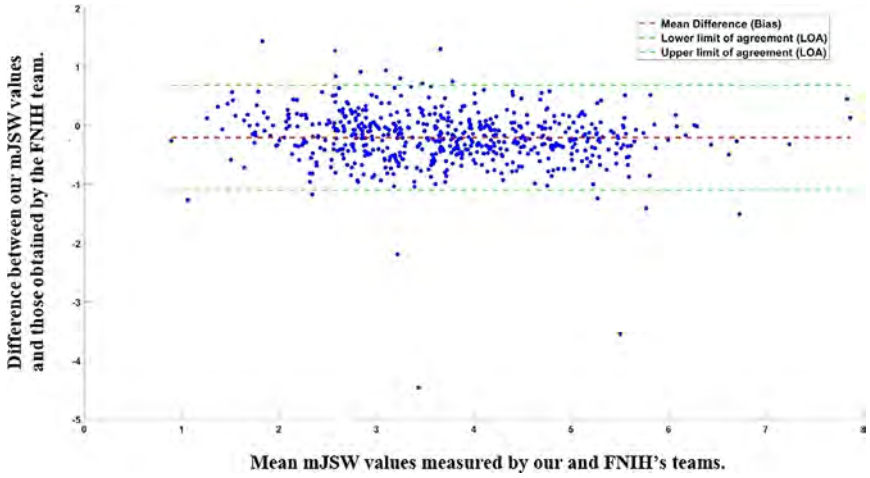


Figure 2: Bland-Altman plot illustrating the agreement between mJSW values measured by our and FNIH's teams

Disclosure: A. Almhdie-Imjabbar: None; **Y. TOUZANI**: None; **H. Toumi**: None; **E. Lespessailles**: None.

Abstract Number: 1937

Does Combining Standard MRI-Based Scores with Radiographic Trabecular Bone Texture Biomarkers Improve Predictive Performance for Radiographic Knee Osteoarthritis Progression?

Ahmad Almhdie-Imjabbar[1], Saida Daroussi[2], Daniela Herrera[3], Hechmi Toumi[2] and Eric Lespessailles[4], [1]University Hospital Center of Orleans, Orleans, France, [2]PRIMMO- University Hospital Center of Orleans, Orleans, France, [3]PRIMMO- University Hospital Center of Orleans, Olreans, France, [4]CHU Orléans, Orléans, France

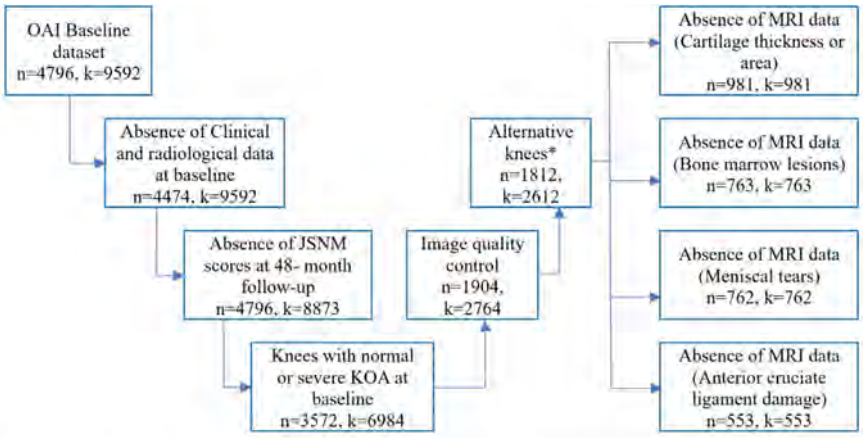
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Knee osteoarthritis (KOA) is a major cause of disability worldwide, particularly impacting the elderly and obese population. Radiographic trabecular bone texture (TBT) is demonstrated as a promising biomarker for predicting KOA progression. However, integrating MRI biomarkers with TBT from the Osteoarthritis Initiative (OAI) cohort remains underexplored. Our study aimed to assess whether associating MRI biomarkers with TBT biomarkers could enhance the predictive performance of models for KOA progression

Methods: From the OAI database, 1812 patients were selected, meeting predefined criteria (outlined in Figure 1), including knees with Kellgren-Lawrence (KL) scores of 2 or 3, availability of baseline and 48-month follow-up medial joint space narrowing (JSNM) scores, and availability of baseline clinical and MRI parameters. Clinical parameters included sex, age, body mass index, pain, and race. MRI parameters investigated included quantitative measures such as cartilage thickness (CartTh) and area (CartA), as well as semi-quantitative assessments such as meniscal tears (MTs), bone marrow lesions (BMLs) and anterior cruciate ligament (ACL) damage. Cases were defined as those with increased JSNM within 48 months. A prediction model using TBT biomarkers associated with the aforementioned clinical covariates and other radiological scores (KL and JSNM) served as a reference model. Other prediction models were created by incorporating combinations of the aforementioned MRI biomarkers. Performance analyses employed logistic regression with 10-fold cross-validation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



* Alternative knees refer to the knees opposite to the targeted knees for patients with two knees available at this corresponding stage, in order to keep one knee per patient in our study.

Figure 1: Diagram of the data selection process followed in the study.

Table 1: Characteristics of the dataset included in the study.

Dataset	Biomarkers		Size	Females	Age	BMI	KL=2	KL=3
1	Cartilage thickness and area	Progressors	279	145	62.6±8.7	30.4±4.7	114	165
		Non progressors	702	440	61.7±9.0	29.8±4.8	468	234
		All	981	585	62.0±8.9	30.0±4.8	582	399
2	Bone marrow lesions	Progressors	250	1235	63.1±8.6	30.5±4.8	114	136
		Non progressors	513	326	62.4±8.9	29.8±4.8	347	166
		All	763	461	62.5±4.8	30.1±4.8	461	302
3	Meniscal tears	Progressors	250	135	63.1±8.6	30.5±4.8	114	136
		Non progressors	512	325	62.4±8.9	29.8±4.8	346	166
		All	762	460	62.6±8.8	30.1±4.8	460	302
4	Anterior cruciate ligament	Progressors	211	112	63.3±8.7	30.7±4.8	89	122
		Non progressors	342	218	61.5±8.8	30.5±4.7	222	120
		All	553	330	62.2±8.8	30.6±4.8	311	242

Values of age and Body Mass Index (BMI) are represented as mean ± standard deviation

Table 2: Performance results of the prediction models evaluated in the study.

Data size	Model	BACC	PPV	NPV	AUC (95%CI)	p-value
981	TBT← CLIN+KL+JSNM*	0.60	0.53	0.77	0.74 (0.71 - 0.77)	-
	TBT	0.55	0.52	0.74	0.66 (0.63 - 0.70)	0.000
	CartTh	0.54	0.58	0.73	0.57 (0.53 - 0.62)	0.000
	TBT ← CLIN+KL+JSNM+ CartTh	0.62	0.54	0.77	0.75 (0.72 - 0.78)	0.280
	CartArea	0.53	0.61	0.73	0.70 (0.66 - 0.75)	0.221
	TBT ← CLIN+KL+JSNM+ CartA	0.60	0.53	0.76	0.73 (0.69 - 0.76)	0.115
763	TBT← CLIN+KL+JSNM*	0.62	0.56	0.74	0.72 (0.68 - 0.76)	-
	TBT	0.56	0.50	0.71	0.65 (0.61 - 0.69)	0.000
	BMLs	0.60	0.66	0.73	0.66 (0.62 - 0.70)	0.011
	TBT ← CLIN+KL+JSNM+ BMLs	0.64	0.58	0.75	0.73 (0.69 - 0.77)	0.156
762	TBT← CLIN+KL+JSNM*	0.62	0.55	0.74	0.72 (0.68 - 0.75)	-
	TBT	0.56	0.50	0.71	0.65 (0.62 - 0.69)	0.000
	MTs	0.52	0.45	0.68	0.61 (0.57 - 0.65)	0.000
	TBT ← CLIN+KL+JSNM+MTs	0.62	0.56	0.74	0.72 (0.68 - 0.75)	0.911
553	TBT← CLIN+KL+JSNM*	0.64	0.59	0.71	0.70 (0.66 - 0.75)	-
	TBT	0.58	0.56	0.67	0.65 (0.60 - 0.69)	0.001
	ACL	0.52	0.58	0.63	0.74 (0.69 - 0.78)	0.319
	TBT ← CLIN+KL+JSNM+ACL	0.63	0.58	0.71	0.70 (0.66 - 0.74)	0.421
	TBT← 5MRIs	0.62	0.59	0.69	0.66 (0.62 - 0.71)	0.150
	TBT ← CLIN+KL+JSNM+5MRIs	0.64	0.57	0.72	0.71 (0.67 - 0.75)	0.745

TBT refers to trabecular bone texture; CLIN refers to clinical covariates (sex, age, BMI, race); KL refers to Kellgren-Lawrance grades; JSNM refers to medical joint space narrowing scores; CartTh refers to cartilage thickness; CartA refers to cartilage area; BMLs refers to bone marrow lesions; MTs refers to meniscal tears; ACL refers to anterior cruciate ligament; 5MRIs refers to the five MRI parameters evaluated (CartTh, CartA, BMLs, MTs and ACL).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

repeated 300 times. The area under the ROC curve (AUC) served as the primary metric, and balanced accuracy (BACC), positive predictive value (PPV) and negative predictive value (NPV) as secondary metrics.

Results: Among the analyzed knees, 981, 763, 762 and 553 had CartTh and CartArea, BMLs, MTs, and ACL data, respectively. The characteristics of these datasets are presented in Table 1. Performance results, as shown in Table 2, demonstrated slightly higher AUC scores, but not statistically significant, when adding one or a combination of MRI parameters to the reference model. For example, when adding all 5 MRI biomarkers, the model slightly improved (AUC=0.71, p-value=0.7), compared to the reference model (AUC=0.70). Comparable results were observed for secondary metrics.

Conclusion: Integrating certain MRI-based biomarkers (CartTh, CartA, MTs, BMLs and ACL data) into a reference XR-based model using TBT biomarkers associated with clinical and radiographic biomarkers did not show evidence of improving the performance in predicting radiographic KOA progression.

Disclosure: A. Almhdie-Imjabbar: None; **S. Daroussi**: None; **D. Herrera**: None; **H. Toumi**: None; **E. Lespessailles**: None.

Abstract Number: 1938

Optimizing Patient Outcomes: The Experience of a Multidisciplinary Rheumatology and Hand Surgery Clinic with Point-of-Care Musculoskeletal Ultrasound Integration

Aidan pye[1], Samuel Chan[2], Gary Xu[3] and Mohammad Bardi[4], [1]University of British Columbia, VANCOUVER, BC, Canada, [2]UBC, Vancouver, [3]UBC, Vancouver, Canada, [4]UBC, Vancouver, BC, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: In the last decade, rheumatologists have employed musculoskeletal Ultrasound (MSUS) as a highly sensitive and accurate clinical assessment tool at the bedside. By integrating complementary specialties, interdisciplinary clinics aim to enhance patient outcomes. Here, we introduce a novel Rheumatology and Hand Surgery interdisciplinary clinic and examine the patient outcomes when MSUS is used for assessment of active joint disease.

Methods: We conducted a retrospective chart review of 218 patients seen at a Rheumatology-Plastic Surgery interdisciplinary hand clinic from January 2018 to May 2024. Demographics data, use of MSUS diagnostically, frequency of modifying disease-modifying antirheumatic drugs (DMARDSs) escalation/surgery, and out data were compared and analysed.

Results: With MSUS implementation, subclinical synovitis was detected in 31% of patients (whereas clinical synovitis was only detected in 12% of patients on physical exam only). As patients with active synovitis are recommended escalation of DMARDs rather than surgical management, there was a 25.8% absolute reduction in surgery recommendation (from 60% to 34%), and a 26.2% absolute increase in DMARD escalation recommendation (from 5% to 31%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

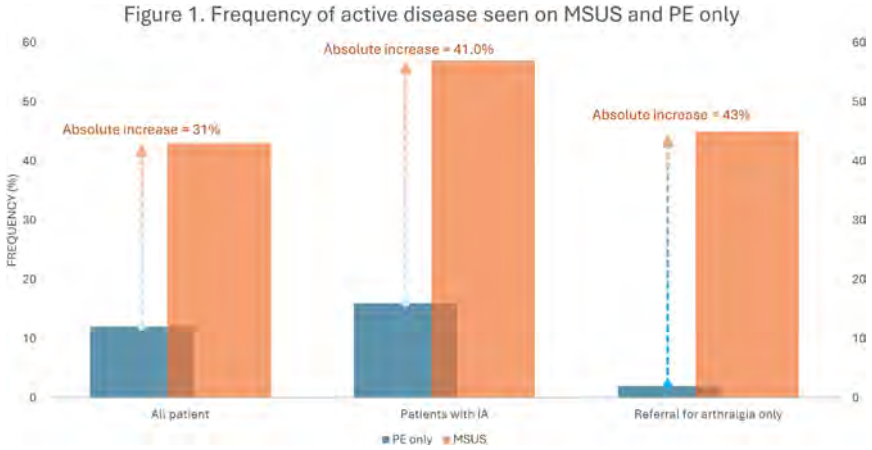


Figure 1 shows how commonly active inflammatory hand disease was found on assessment with physical exam alone as compared to with MSUS. It shows the comparison for all patients who attended the clinic, as well as two subgroups: patients referred with confirmed inflammatory arthritis and patients referred for pain as their main concern.

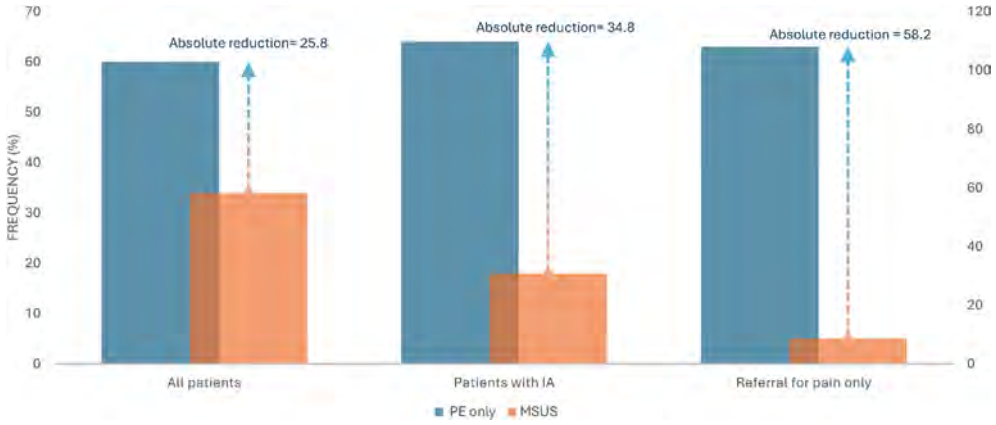


Figure 2 shows how commonly surgery was recommended with physical exam alone as compared to with MSUS. It shows the comparison for all patients who attended the clinic, as well as two subgroups: patients referred with confirmed inflammatory arthritis and patients referred for pain as their main concern.

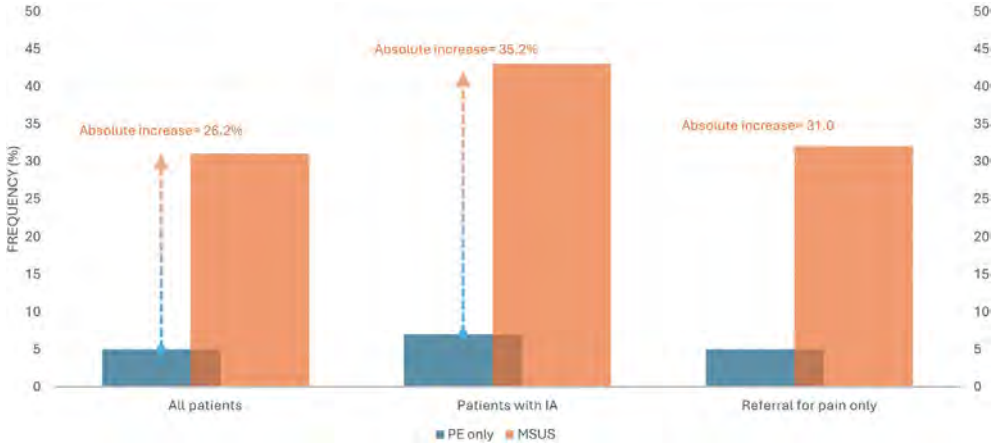


Figure 3 shows how commonly DMARD escalation was recommended with physical exam alone as compared to with MSUS. It shows the comparison for all patients who attended the clinic, as well as two subgroups: patients referred with confirmed inflammatory arthritis and patients referred for pain as their main concern.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The use of MSUS significantly improves the detection of active inflammatory arthritis in referred patients, resulting in increased DMARD escalation and decreased surgery recommendations. These data suggest that it may be beneficial to incorporate MSUS into standard care. The use of MSUS may aid in identifying patients with active disease, such that these patients may be medically optimized with DMARDSs and potentially avoid surgical intervention.

Disclosure: A. pye: None; **S. Chan**: None; **G. Xu**: None; **M. Bardi**: None.

Abstract Number: 1939

Salivary Gland Ultrasounds Can Be Read by General Radiologists: A Review Of 4 Years of Reports from an Urban Academic Radiology Department

Ali Dhanaliwala and Dana DiRenzo, University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Salivary gland ultrasound (SGUS) has the potential to inform diagnosis and progression of Sjogren's disease, a systemic autoimmune disease which results in progressive inflammation and loss of exocrine gland function. SGUS has primarily been performed and read by rheumatologists in Europe. Despite its potential benefit, SGUS is not widely performed in the United States. Radiology departments have the resources to perform SGUS, however there remains little referral. To assess the feasibility of radiology performed SGUS in the United States, we sought to review the implementation and outcomes of a standardized SGUS protocol at a large urban academic radiology department in the United States which includes a large number of radiologists with diverse experience.

Methods: A standardized SGUS protocol was developed by the radiology department in consultation with rheumatology. SGUS were performed and read by two groups, a general radiology practice, and an academic practice. A retrospective analysis of these studies was performed. SGUS between August 2021, when the protocol was instituted, and February 2025 were identified within the radiology information system stored within a web-based data lake. Meta data within the image DICOM header was used to calculate study metrics such as time to complete study, number of images within study, and storage size of study. A large language model (LLM) was used to evaluate the consistency of the reports with the standardized template and to extract OMERACT score and gland size from the reports. Outcomes for patients with suspected lymphoma were reviewed.

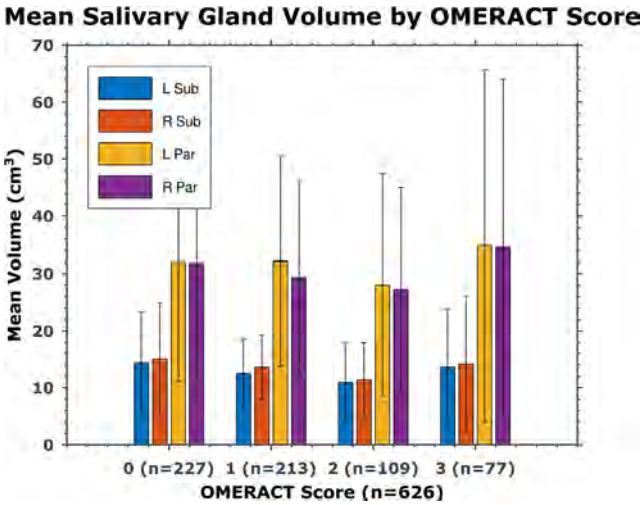
Results: A total of 811 SGUS were performed over the 41-month period. The mean age of the patients was 54 ± 15 years with 89% (721/811) female. The study was ordered by 58 different departments with 78% (632/811) of the orders coming from a Rheumatology practice. Studies were read by 53 different radiologists, 55% of which were in the academic group. The academic group read 56% (458/811) of the studies. Exams took a median of 15 minutes (IQR = 12 min) to complete. Each exam contained an average of 11.8 cines and 84 still images and a median size of 274 MB (IQR = 223 MB).

Analysis of the report text by the LLM demonstrated 64% (519/811) to be consistent with the template. Of the inconsistent reports, 35% (99/292) were from the academic group. Incomplete scoring of all the glands (at least one gland not given an OMERACT score) was found in 13% (103/811) of the reports of which 71% (73/103) were from the academic group.

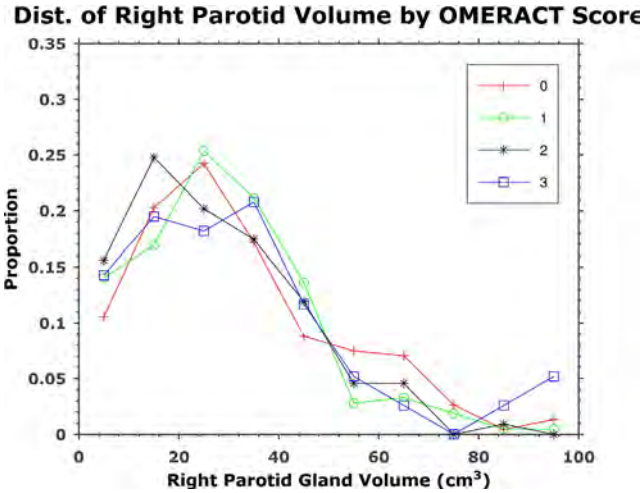
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

		SGUS with OMERACT scoring (n = 811)	P value
Age, mean (SD)		54 (15)	
Gender			
	Male	90 (11 %)	p=0.9
	Female	721 (89 %)	
Top Ordering Depts			
	Rheum	631 (78 %)	
	IM	24 (3 %)	
	Surgery	11 (1 %)	
Max OMERACT		Mean right parotid volume (cm^3)	ANOVA
	0	16.7 ± 10.5	p = 0.1
	1	15.4 ± 8.8	
	2	14.3 ± 9.3	
	3	18.1 ± 15.4	

Salivary gland ultrasound study characteristics. Differences in mean right parotid volume according to maximum OMERACT score calculated via ANOVA. SGUS: salivary gland ultrasound.



Mean salivary gland volume by OMERACT score. No significant difference identified.



Distribution of right parotid volume by OMERACT score. No significant difference identified.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Incomplete measurements of the glands (at least one dimension not reported) were found in 23% (188/811) of which 79% (149/188) were from the academic group.

No association was found between salivary gland volume and OMERACT score. Only 0.5% (4/811) of studies had a recommendation for a gland biopsy due to concern for lymphoma. Of these four, only one was positive for lymphoma, and was likely a recurrence as the patient had a prior history of lymphoma.

Conclusion: SGUS can be reasonably implemented by both general and academic radiologists with minimal time and storage burden. Radiologists create consistent reports which can be used for subsequent cohort analysis.

Disclosure: A. Dhanaliwala: None; **D. DiRenzo**: Amgen, 2, Novartis, 2, Sjogren's Foundation, 5.

Abstract Number: 1940

Correlation of Hand and Lymphatic Function Post Exercise Intervention in Rheumatoid Arthritis

Allen Anandarajah[1], Ronald Wood[2], Edward Schwarz[3], Ram Haddas[2] and Homaira Rahimi[2], [1]University of Rochester Medical Center, Rochester, NY, [2]University of Rochester, ROCHESTER, NY, [3]University of Rochester, Rochester, NY, USA, Rochester, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease which often leads to deformities and loss of function of hands. Despite the availability of new treatments for RA, patients can have persistent and refractory disease. Thus, optimal management requires a holistic personalized medicine approach and exercise programs are now broadly acknowledged to be a high priority in rheumatology. We have previously demonstrated that lymphatic drainage is dysfunctional in the hands of RA patients with active disease (Bell RD, et al. 2020 Arthritis Rheumatol 72:1447). In this pilot study, we aim to determine the correlation between hand strength as assessed by Manugraphy and lymphatic flow and study the effects of standardized hand exercises on these outcome measures.

Methods: Five subjects with RA of less than 6 years disease duration were recruited with four completing Manugraphy studies. Three subjects completed both hand strength assessments and lymphatic studies. Hand grip and strength measures were completed using a Jamar Dynamometer and Manugraphy device followed a day later by lymphatic flow measurements. Lymphatic function was assessed using a novel near-infrared indocyanine green (NIR-ICG) method as previously published. Briefly, 0.1mL ICG dye was injected into the webspaces of each hand and ICG flow was recorded for 10 minutes to calculate lymphatic contraction rate. One week later, hands were again measured to quantify clearance. Patients were educated on standardized hand exercises by an occupational therapist. Subjects were provided calendars to document compliance of exercises over the next 6 weeks. Hand strength and lymphatic function assessments were then repeated.

Results: Preliminary baseline results of the right hand of a subject are shown in Figure 1. Lymphatic function at baseline confirms the presence of contracting lymphatic vessels from each webspace and clearance was measured at 5373 fluorescence units. Parameters were quantified for each digit per hand to be correlated with lymphatic data. Peak pressure was measured for the 1st digit and found to be 120.6 +/- 8.2 kPa. Additional Manugraphy parameters measured include

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

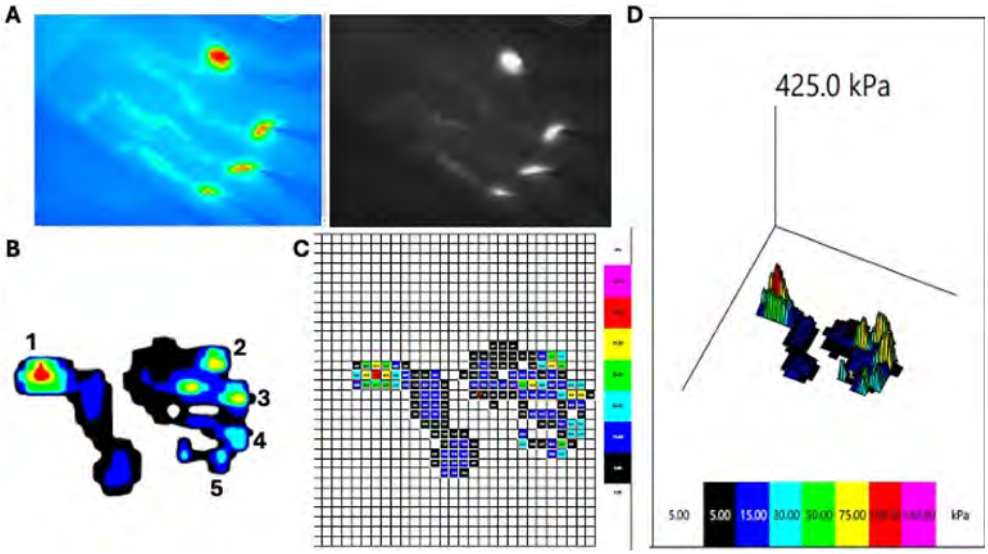


Fig 1: (A) Representative NIR-ICG images of active lymphatic flow after webspace injections and 1 week later. (B) Hand measurements via Manugraphy captures pictorial representation of digits (labeled 1-5) and further quantified via (C) "heat map". (D) Pressure measurements analysis delineates specific pressures at each area of the hand with peak pressure (in red) of 120.6+/-8.2 kPa identified at 1st digit.

maximum force (49.3 N), force-time integral 125.4 (N*s), force for the mean value picture (MVP) (41.7N), contact area for MVP (11.17 cm2), and contact area for the maximum pressure picture (12.17 cm2).

Conclusion: We initiated a novel study to correlate lymphatic function with hand function measures in patients with RA. Preliminary baseline measures show altered lymphatic function consistent with prior data and confirm ability to measure hand function using Manugraphy. Post-exercise intervention studies will be completed to determine if active hand mobility and lymphatic function can be altered in subjects with RA.

Disclosure: A. Anandarajah: None; **R. Wood**: None; **E. Schwarz**: None; **R. Haddas**: Medtronic Inc., 2, 5; **H. Rahimi**: None.

Abstract Number: 1941

How Calculating Consensus Change Scores Can Go Wrong: Lessons from Multi-reader Imaging Assessments in Axial Spondyloarthritis

Ana Bento da Silva[1], Sofia Ramiro[2], Floris A. van Gaalen[1], Robert Landewé[3], Miranda van Lunteren[1], Liese de Bruin[1], Gizem Ayan[4], Xenofon Baraliakos[5], Monique Reijnierse[6], Jürgen Braun[7], Désirée Van Der Heijde[1] and Manouk de Hooge[8], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Leiden University Medical Center, Bunde, Netherlands, [3]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [4]Ankara Research and Training Hospital, Ankara, Turkey, [5]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [6]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [7]Ruhr-University, Bochum, Germany; and Rheumatologische Versorgungszentrum (RVZ) Steglitz, Berlin, Germany, [8]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: In research, imaging findings are often assessed by multiple readers and individual readers' scores are combined into aggregate scores to determine the presence of lesions. In longitudinal studies, the focus shifts to change in lesions. Diverse strategies for aggregating change scores are at hand, but may yield different results. We aimed to establish a methodological framework for aggregating change scores, using the example of syndesmophyte progression in axial spondyloarthritis (axSpA).

Methods: Data from the Sensitive Imaging in Ankylosing Spondylitis cohort were used, including patients with axSpA and established spinal damage. Syndesmophytes were assessed on vertebral corners (hereafter 'level') on conventional radiography (CR) and low-dose computed tomography (ldCT) of the spine at baseline and 2 years. CR were scored by 3 central readers and ldCT by 2, blinded for time order. Consensus was determined by majority reader agreement. New syndesmophytes (change score) were assessed by 2 strategies. Strategy 1 calculates change score per reader, then determines consensus on the change per level. Strategy 2 derives consensus change scores from consensus status scores (syndesmophyte present/absent) (Box 1). The means and standard deviations (SD) of the different aggregate change scores were compared. For analyses at the patient level, the total number of new syndesmophytes was averaged across readers, only if patients had ≤25% scores missing per spinal segment at both timepoints.

Results: Complete data from 52 patients were used. In example 3 (Figure 1a), the two strategies yielded different results. When consensus change scores are derived from change scores of individual readers (strategy 1), because only reader C detected a new syndesmophyte, there is no new syndesmophyte in the aggregated score. In contrast, when consensus status scores are determined first (strategy 2), indicating no syndesmophyte at baseline but one at 2 years, the consensus change score suggests a new syndesmophyte.

Strategy	Description	Key steps
1	Consensus change score is based on the agreement of individual readers' change scores	1. Assess delta (progression) of a lesion per level for each reader 2. Calculate consensus change score by assessing the majority reader agreement on change score per level
2	Consensus change score is based on the change of consensus status scores	1. Calculate consensus status scores by assessing the majority reader agreement on lesion presence at each timepoint per level 2. Calculate change scores based on delta from consensus status scores per level

Box 1. Explanation of two strategies for defining a consensus change score in multi-reader imaging assessments

1a. Examples of calculating new syndesmophytes based on scores per level of three readers according to two strategies

	Reader A	Reader B	Reader C	Consensus status score	Strategy 1: Consensus change score based on individual readers' change scores	Strategy 2: Consensus change score based on change of consensus status scores	Average of total new syndesmophytes across readers (patient level)
Example 1							
Syndesmophyte at baseline	0	0	0	0			
Syndesmophyte at 2 years	0	1	0	0			
New syndesmophyte	0	1	0		0	0	
Example 2							
Syndesmophyte at baseline	0	0	0	0			
Syndesmophyte at 2 years	1	1	0	1			
New syndesmophyte	1	1	0		1	1	
Example 3							
Syndesmophyte at baseline	0	1	0	0			
Syndesmophyte at 2 years	0	1	1	1			
New syndesmophyte	0	0	1		0	1	
Total new syndesmophytes	**1**	**2**	**1**		**1**	**2**	**1.33**

1b. Total number of new syndesmophytes at the level and at the patient level in the SIAS cohort calculated according to two strategies

Strategy	Imaging modality	Number of patients	Number of vertebral corners	Total new syndesmophytes: agreement at the level Mean (SD)	Range	Total new syndesmophytes: average across readers at the patient level Mean (SD), n*
1	CR	51	1035	0.69 (0.95)	0 – 4	0.66 (1.10), n=36
2				0.86 (1.00)	0 – 4	
1	ldCT	52	9035	2.35 (4.44)	0 – 18	5.55 (6.65), n=48
2				7.23 (7.46)	0 – 41	

* To calculate the total number of new syndesmophytes at the patient level, only patients with ≤25% scores missing per spinal segment (on ldCT, the cervical and thoracic spine were considered together) at both timepoints were included (with the remaining missing scores considered 'no (new) syndesmophyte').
0: absence of a (new) syndesmophyte; **1:** presence of a (new) syndesmophyte; **CR:** conventional radiography; **ldCT:** low-dose computed tomography; **SIAS:** Sensitive Imaging in Ankylosing Spondylitis cohort.

Figure 1. Comparison of strategies for assessing new syndesmophytes in patients with axial spondyloarthritis after 2 years, illustrating a broad imaging framework for consensus change scores

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Strategy 2 is more sensitive, identifying 1.2 times more new syndesmophytes on CR (mean [SD]: 0.86 [1.00] *vs* 0.69 [0.95]) and 3.1 times more on ldCT (7.23 [7.46] *vs* 2.35 [4.44]). However, this is accompanied with higher variability (Figure 1b). Only strategy 1 represents "true consensus" among readers, but requires site-level agreement, which compromises sensitivity to change at the patient level. At the patient level, the total number of new syndesmophytes should be calculated as the average of the total number across all readers (CR: 0.66 [1.10]; ldCT: 5.55 [6.65]).

Conclusion: Consensus change scores should be derived from individual readers' change scores. Strategy 1 approaches true change best, while strategy 2 artificially inflates change. At the patient level, the average total number of new syndesmophytes across readers should be reported. While we focus on syndesmophyte progression in axSpA, this framework is broadly applicable to imaging findings across multiple diseases. Advanced statistical analyses beyond descriptive purposes should preferably be performed on individual readers' scores, using multilevel models that properly account for variability in reader assessment.

Disclosure: A. Bento da Silva: None; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **M. van Lunteren**: None; **L. de Bruin**: None; **G. Ayan**: None; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **M. Reijnierse**: None; **J. Braun**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, GreyWolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **M. de Hooge**: UCB pharma, 2.

Abstract Number: 1942

An Agnostic Evaluation of Serum Proteins Discriminates the Severity of Ultrasound Arthritis in SLE Patients

Robert Clancy[1], Philip Carlucci[2], Alberto Nordmann-Gomes[3], Leila Khalili[4], Wei Tang[5], Giovanna Rosas Chavez[4], Stephen Suh[6], Laura Geraldino-Pardilla[1], Yevgeniya Gartshteyn[7], Joel Guthridge[8], Judith James[8] and **Anca Askanase**[4], [1]Columbia University, New York, NY, [2]New York University School of Medicine, New York, NY, [3]Columbia University Irving Medical Center, New York, NY, [4]Columbia University Medical Center, New York, NY, [5]Westchester Medical Center, Valhalla, NY, [6]Columbia University Irving Medical Center, New York City, NY, [7]Columbia University Medical Center, Glen Rock, NJ, [8]Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of the lupus arthritis patients of interest.

Table 1. Demographic and clinical characteristics of the lupus arthritis patients of interest.

	Total (N=15)	Cluster A (n = 5)	Cluster B (n = 10)
Sex			
Female, n (%)	13 (87)	4 (80)	9 (90)
Male, n (%)	2 (13)	1 (20)	1 (10)
Age, mean years (SD)	43.4 (14.9)	47.0 (16.3)	41.6 (14.7)
Race			
White, n (%)	4 (27)	2 (40)	2 (20)
Black, n (%)	2 (13)	0 (0)	2 (20)
Asian, n (%)	1 (7)	0 (0)	1 (10)
Other, n (%)	8 (53)	3 (60)	5 (50)
Ethnicity			
Hispanic, n (%)	9 (60)	3 (60)	6 (60)
Not Hispanic, n (%)	6 (40)	2 (40)	4 (40)
SLE disease duration, mean years (SD)	10 (4.8)	6.8 (5.5)	11.6 (3.8)
Treatment at the time of evaluation			
Hydroxychloroquine, n (%)	14 (93)	5 (100)	9 (90)
Prednisone, n (%)	4 (27)	1 (20)	5 (50)
Immunosuppressants, n (%)	9 (60)	1 (20)	7 (70)
Biologics, n (%)	3 (20)	2 (40)	1 (10)
Ultrasound combined PDGS			
mean score (SD)	1.5 (0.9)	2.0 (0.9)	1.2 (0.9)*
Amount of PIP joints with grade 0 score, n (%)	17 (16)	1 (2)	17 (27)
Amount of PIP joints with grade 1 score, n (%)	32 (31)	11 (28)	21 (33)
Amount of PIP joints with grade 2 score, n (%)	36 (35)	14 (35)	21 (33)
Amount of PIP joints with grade 3 score, n (%)	19 (18)	14 (35)	5 (7)
Total combined tender joint count	159	50	109
Total combined swollen joint count	215	94	121

*p=0.05

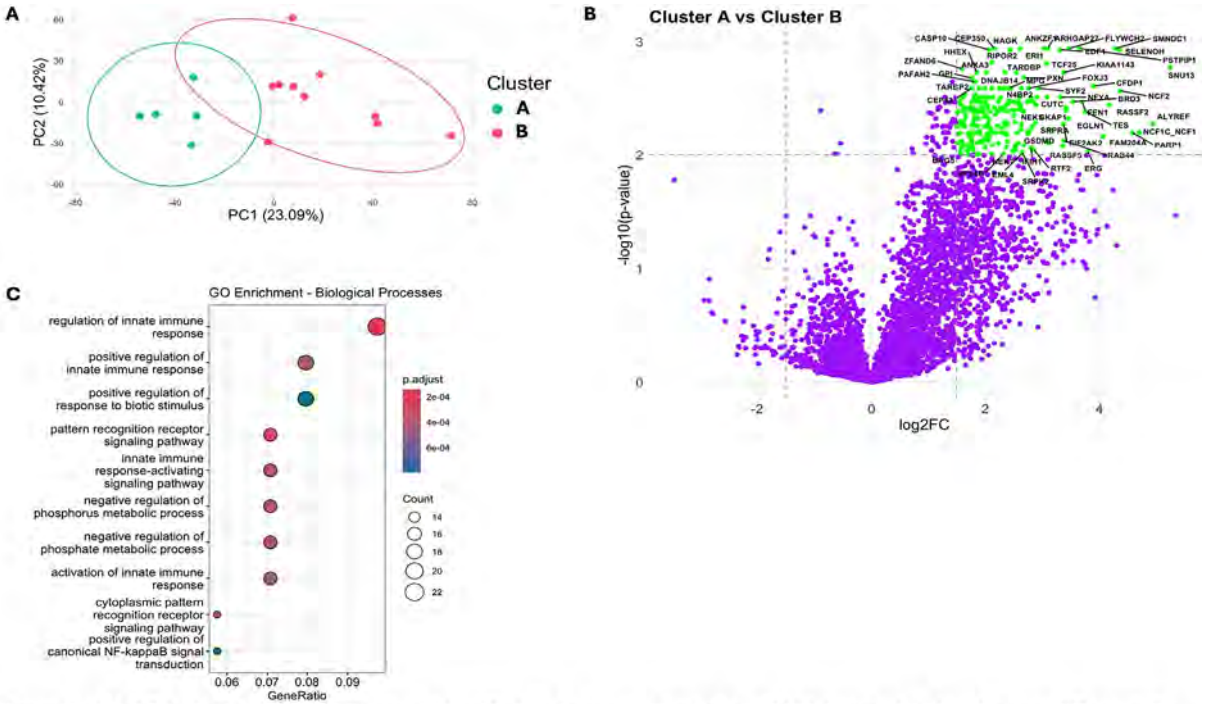


Figure 1: (A) PCA showing the two clusters identified by k-means clustering. (B) Volcano plot showing the differentially abundant proteins between cluster A and cluster B with adjusted p-value <0.01 and log2FC |1.5|. (C) Gene ontology pathway enrichment analysis of the 238 proteins that were significantly higher in cluster A compared to cluster B.

Figure 1: (A) PCA showing the two clusters identified by k-means clustering. (B) Volcano plot showing the differentially abundant proteins between cluster A and cluster B with adjusted p-value <0.01 and log2FC |1.5|. (C) Gene ontology pathway enrichment analysis of the 238 proteins that were significantly higher in cluster A compared to cluster B.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Inflammatory arthritis occurs in up to 90% of patients and is a main cause of SLE work-related disability. SLE arthritis is difficult to evaluate because of the evanescent nature of the symptoms and limitations of physical exams and imaging. Although advanced imaging modalities have been used to characterize SLE arthritis insights into the pathophysiology and predictive biomarkers to address optimal surveillance, and clinical trial design are lacking. We leveraged serum collected at the time of arthritis evaluations to agnostically survey potential soluble mediators of arthritis in SLE patients using the Olink platform.

Methods: Sera from 15 subjects with clinical lupus arthritis were evaluated. All samples were collected in proximity to clinical and imaging evaluations. Swollen and tender joint counts were performed, MSK US used multiplanar grey-scale (GS) to evaluate synovitis/effusion and power Doppler (PD) for synovial hypertrophy/inflammation, and was scored by OMERACT definitions to generate a composite PDGS score on a scale of 0-3 (2-3 representing moderate/severe arthritis) at bilateral PIP joints. Serum proteins were assessed by the Olink Explore HT assay to evaluate >5400 proteins. All included samples passed standard Olink quality control metrics. K-means clustering agnostically defined groups of interest. Principal component analysis (PCA) was used for data visualization and a t-test was employed to compare clusters with candidate proteins considered at adjusted p-value by Benjamin-Hochberg method < 0.01 and log2fc |1.5|.

Results: Clinical and imaging variables for the 15 patients are described in Table 1. Olink data identified 2 clusters of interest, cluster A (5 subjects) and cluster B (10 subjects) (Fig 1A). Differential protein expression revealed 238 proteins significantly higher in cluster A vs cluster B (Fig 1B). Gene ontology (GO) analysis showed significant enrichment of pathways related to innate immune signaling in cluster A (Figure 1C). The top 10 proteins higher in cluster A compared to cluster B are shown in Figure 2. Clinically, patients in cluster A had significantly higher levels of active synovitis measured by GS compared to those in cluster B (PDGS >/=2) (p=0.05) (Table 1) despite having similar tender/swollen joint counts on physical exam (Table 1).

Conclusion: In this serum proteomic evaluation, an unsupervised machine learning algorithm was able to agnostically identify patients with more severe arthritis as measured by MSK US but not physical exam. These data suggest significant aberrations in the serum proteome likely contribute to arthritis severity in SLE.

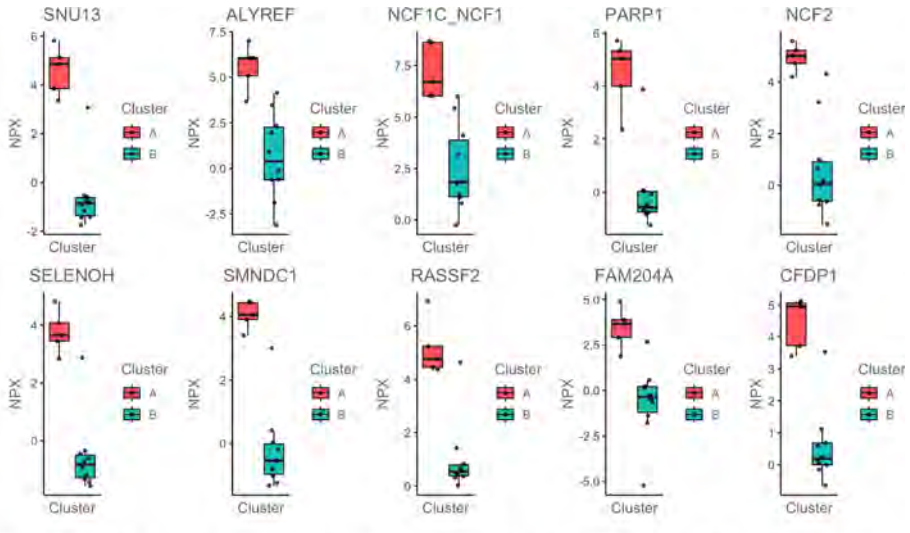


Figure 2: Boxplots showing the top 10 differentially expressed proteins by log2FC, all met adjusted pvalues <0.01.

Figure 2: Boxplots showing the top 10 differentially expressed proteins by log2FC, all met adjusted pvalues <0.01.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Clancy: None; **P. Carlucci**: None; **A. Nordmann-Gomes**: None; **L. Khalili**: None; **W. Tang**: None; **G. Rosas Chavez**: None; **S. Suh**: None; **L. Geraldino-Pardilla**: Aurinia, 2, 6, Bristol-Myers Squibb(BMS), 1, 2, 6; **Y. Gartshteyn**: None; **J. Guthridge**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5.

Abstract Number: 1943

Searching for subclinical synovitis and erosions in seropositive palindromic rheumatism: the added value of the ultrasonographic study of feet

Andrés Ponce[1], Cynthia Vanesa del Valle Rojas[2], nuria Sapena[3], Georgina Novell[3], anastasia Motcritcaia[3], Beatriz Frade Sosa[4], Juan Camilo Sarmiento-Monroy[5], Vicenç Torrente-Segarra[6], Julio Ramirez[7], Virginia Ruiz-Esquide[8], ana Belen Azuaga[3], Francisco Vilchez[3], Sandra Farietta[3], Patricia Corzo[9], Juan Cañete[10], José Gomez-Puerta[11] and Raimon Sanmartí[8], [1]Hospital Clinic, Barcelona, Spain, [2]Consorci Sanitari Alt Penedès-Garraf, Barcelona, Catalonia, Spain, [3]Hospital Clinic, Barcelona, Catalonia, Spain, [4]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [5]Hospital Clinic Barcelona, Barcelona, Spain, [6]Hospital Comarcal Alt Penedés Garraf, Vilafranca del Penedés, Spain, [7]Clinic Barcelona Hospital Universitari, Barcelona, Catalonia, Spain, [8]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [9]Rheumatology Department, Hospital Clínic, Barcelona, Barcelona, Spain, [10]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [11]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Palindromic rheumatism (PR) is characterized by intermittent episodes of arthritis or periarthritis, and it can progress to rheumatoid arthritis (RA), particularly in patients with positive autoantibodies (RF and/or ACPA). Few studies have used ultrasonography (US) to assess joints during symptom-free periods, and most have found no evidence of subclinical synovitis. [1,2]. However, none of these studies have included the feet, specifically the metatarsophalangeal (MTP) joints, which are commonly affected in RA.

To assess the presence of subclinical synovitis and erosions by ultrasound (US) during the intercritical phase of seropositive PR and to evaluate the added value of including the feet in the assessment.

Methods: 39 seropositive PR patients (76% female, mean age 54.4 years), 67% received csDMARDs (mainly hydroxychloroquine). Table1.

Ultrasound assessment of 1,404 joints revealed synovial hypertrophy (SH ≥2) in 1.7% of joints and 28% of patients; power Doppler signal (PD ≥1) in 1.28% of joints and 23% of patients. US-active synovitis (SH ≥2 plus PD ≥1) was found in 23% of patients. Subchondral bone erosions were detected by US in 0.85% of joints (18% of patients), mostly grade 1. Only two erosions were visible on X-rays.

When comparing patients with and without US-active subclinical synovitis, a significantly higher frequency of US-detected bone erosions and use of hydroxychloroquine was observed in the former group (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 39 patients (76% female) with seropositive PR were included. The mean age was 54.4 years (±12.6), and the mean disease duration was 9.2 years (±8.5). RF was positive in 23 patients (59%), and ACPA in 32 patients (82%). A total of 26 patients (67%) were treated with csDMARDs, mainly hydroxychloroquine (51%).

A total of 1,404 joints (858 in the hands and 546 in the feet) were assessed by US in the 39 patients. Synovial hypertrophy (SH) ≥2 (gray scale) was observed in 24 joints (1.7%)-9 in the hands and 15 in the feet-and in 28% of patients. Power Doppler (PD) ≥1 was observed in 18 joints (1.28%)-9 in the hands and 9 in the feet-and in 9 patients (23%). US-active synovitis, as previously defined (SH ≥2 plus PD ≥1), was observed in 15 joints (8 in the hands and 7 in the feet) and in 9 patients (23.1%).

Subchondral bone erosions detected by US were observed in 12 joints (0.85%)-5 in the hands and 7 in the feet (MTP)-corresponding to 7 patients (18%). All US-detected erosions were grade 1 (< 2 mm), except for one case of grade 2 (>2 mm). Erosions were also observed on X-rays in only two of these cases.

When comparing patients with and without US-active subclinical synovitis, a significantly higher frequency of US-detected bone erosions and use of hydroxychloroquine was observed in the former group (Table 2).

	US Subclinical Active Synovitis (n=9)	No US Subclinical Active Synovitis (n=30)	p-value
Age, years, mean ± SD	57.1 ± 11.1	54.8 ± 12.7	N/S
Sex (male/female), n (%)	2 (22.2) / 7 (77.8)	7 (23.3) / 23 (76.7)	N/S
Disease duration, years, mean ± SD	9.2 ± 6.2	10 ± 8.9	N/S
Frequency of attacks, last 12 months, mean	2.62	2.68	N/S
Current smoker, n (%)	5 (55.6)	17 (56.6)	N/S
RF+, mean titer ± SD	103 ± 103	96.9 ± 176.5	N/S
ACPA, mean titer ± SD	650.9 ± 840.7	824 ± 1762.5	N/S
CRP, mean ± SD	0.83 ± 0.7	0.72 ± 0.6	N/S
ESR, mean ± SD	16.7 ± 14.7	15 ± 13.4	N/S
Calprotectin, mean ± SD	0.69 ± 0.5	0.57 ± 0.5	N/S
Hydroxychloroquine, n (%)	8 (88.9)	12 (40.0)	**P < 0.05**
Methotrexate, n (%)	3 (33.3)	3 (10.0)	N/S
Other treatments, n (%)	2 (22.2)	5 (16.6)	N/S
US Bone erosions, n (%)	4 (44.4)	3 (10.0)	**P = 0.018**
X-ray Bone erosions, n (%)	2 (22.2)	0	N/S

Demographic, clinical, serological, therapeutic and different US findings

	Total		Hands		Feet	
	Joints (n=1404)	Patients (n=39)	Joints (n=858)	Patients (n=39)	Joints (n=546)	Patients (n=39)
SH ≥2	24 (1.7%)	11 (28%)	9 (1.0%)	6 (15.4%)	15 (2.7%)	5 (12.8%)
PD ≥1	18 (1.3%)	9 (23%)	9 (1.0%)	7 (18%)	9 (1.6%)	2 (5.1%)
SH ≥2 plus PD ≥1	15 (1.1%)	9 (23%)	8 (0.9%)	7 (18%)	7 (1.3%)	2 (5.1%)
US Bone erosions	12 (0.9%)	7 (18%)	5 (0.6%)	5 (13%)	7 (1.3%)	5 (12.8%)

Prevalence of US findings in RP patients

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In patients with longstanding seropositive PR, significant subclinical active synovitis in at least one joint was observed in 23% of patients during the intercritical period, and US-detected bone erosions were found in 18% of patients, especially in the feet (metatarsophalangeal joints). These findings support that subclinical synovitis and even erosions may be present in patients with PR in the absence of a history of persistent clinical arthritis.

Disclosure: A. Ponce: None; **C. Rojas**: None; **n. Sapena**: None; **G. Novell**: None; **a. Motcritcaia**: None; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **J. Sarmiento-Monroy**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6; **V. Torrente-Segarra**: None; **J. Ramirez**: Janssen, 2; **V. Ruiz-Esquide**: None; **a. Azuaga**: None; **F. Vilchez**: None; **S. Farietta**: None; **P. Corzo**: GlaxoSmithKlein(GSK), 6; **J. Cañete**: None; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **R. Sanmartí**: AbbVie/Abbott, 5, 6, Bristol-Myers Squibb(BMS), 5, 6, Eli Lilly, 5, 6, Merck/MSD, 5, 6, Pfizer, 5, 6, Roche, 5, 6.

Abstract Number: 1944

Musculoskeletal Ultrasound Clinic Referral Patterns and Joint Findings in a Tertiary Care Center amongst Patients with Elevated BMI and Inflammatory Arthritis

Anna Lichtiger[1], Ying Jin[2], Caroline Rourke[1], Kiera Brennan[3], Hillary Weisleder[4], Melissa Fazzari[5] and Melissa Band[6], [1]Montefiore Medical Center, The Bronx, NY, [2]Albert Einstein College of Medicine, Bronx, NY, [3]Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, [4]Montefiore Einstein, New York, NY, [5]Department of Epidemiology & Population Health, Albert Einstein College of Medicine,, Bronx, NY, [6]Montefiore Medical Center, New York, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal ultrasound (MSUS) has been well known to aid in both early diagnosis and monitoring of inflammatory arthritis. Patients with an elevated BMI have an increased prevalence of inflammatory joint disease, pose a more challenging clinical exam, and traditional disease activity scores may overestimate tender joint counts[1]. This study aims to assess differences in reasons for referral to the rheumatology MSUS Clinic and in joint findings among patients with elevated BMI compared to those with a normal BMI.

Methods: A retrospective analysis of 203 patients that attended the MSUS Clinic at Montefiore Medical Center, a tertiary academic center, was performed from March 2022 to September 2023. Electronic health record data was extracted to assess demographics, referral questions, joint findings, and underlying rheumatologic diseases. Differences in these domains between patients with normal BMI, overweight, and obese BMI were assessed with bivariate analyses using Pearson's Chi-squared tests and Fischer's exact test as appropriate. Patients were divided into three groups: normal weight (BMI 18.5-24.99), overweight (BMI 25-29.99), and obese (BMI ≥30).

Results: There were no significant differences seen in the reason for referral to the MSUS clinic between the three groups. Normal weight patients were referred more frequently for monitoring and evaluation of inflammatory joint disease, while patients with obesity were more frequently referred for procedures, however this was not statistically significant (figure 2). Patients with a normal BMI were significantly more likely to have active inflammatory arthritis on ultrasound (38% vs. 22% in overweight patients and 13% in obese patients $p < 0.01$) (figure 3). Joint findings between the groups were otherwise not statistically significant, however, there was a trend towards increased chronic inflammatory arthritis in patients with obesity (figure 3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: MSUS has an important role in identifying inflammatory arthritis. Among our patient population, overweight and obese patients were less likely to have active inflammatory arthritis, which is concordant with previous research demonstrating patients with elevated BMI have less hyperemia on ultrasound[1]. However, in our cohort, there was a non-significant trend

Table 1. Patient Characteristics by BMI Category

		BMI Category			
	Overall, N=203[1]	Normal, N=29[1]	Overweight, N=60[1]	Obese, N=114[1]	p-value[2,3]
Age	57 [49, 64]	54 [47, 64]	57 [51, 64]	57 [48, 64]	0.89
Gender					0.16
Female	175 (86%)	22 (76%)	51 (85%)	102 (89%)	
Male	28 (14%)	7 (24%)	9 (15%)	12 (11%)	
Race					0.028*
African American	61 (30%)	4 (14%)	12 (20%)	45 (39%)	
Caucasian	39 (19%)	8 (28%)	14 (23%)	17 (15%)	
Declined	21 (10%)	2 (6.9%)	9 (15%)	10 (8.8%)	
Other	82 (40%)	15 (52%)	25 (42%)	42 (37%)	
Ethnicity					0.62
Hispanic	101 (50%)	17 (59%)	32 (53%)	52 (46%)	
Not Hispanic	86 (42%)	10 (34%)	22 (37%)	54 (47%)	
Declined	12 (5.9%)	1 (3.4%)	5 (8.3%)	6 (5.3%)	
Other	4 (2.0%)	1 (3.4%)	1 (1.7%)	2 (1.8%)	
Referring Provider					0.002**
Rheumatogist	192 (95%)	25 (86%)	54 (90%)	113 (99%)	
Non-rheumatologist	11 (5.4%)	4 (14%)	6 (10%)	1 (0.9%)	
Rheumatologic Disease					
Rheumatoid arthritis	69 (34%)	10 (34%)	20 (33%)	39 (34%)	>0.99
Mixed Connective Tissue Disease/Undifferentiated Connective Tissue Disease	5 (2.5%)	2 (6.9%)	1 (1.7%)	2 (1.8%)	0.27
Undiffentiated Inflammatory Arthritis	8 (3.9%)	2 (6.9%)	3 (5.0%)	3 (2.6%)	0.35
Osteoarthritis	62 (31%)	10 (34%)	15 (25%)	37 (32%)	0.53
Fibromyalgia	33 (16%)	3 (10%)	11 (18%)	19 (17%)	0.67
Crystalline Arthropathy	16 (7.9%)	3 (10%)	4 (6.7%)	9 (7.9%)	0.87
Spondyloarthropathy	5 (2.5%)	2 (6.9%)	2 (3.3%)	1 (0.9%)	0.084
Sjogren's Syndrome	5 (2.5%)	0 (0%)	2 (3.3%)	3 (2.6%)	>0.99
Systemic Lupus Erythematosus	7 (3.4%)	2 (6.9%)	4 (6.7%)	1 (0.9%)	0.035*
Psoriatic Arthritis	7 (3.4%)	1 (3.4%)	1 (1.7%)	5 (4.4%)	0.76
Noninflammatory Musculoskeletal Disease	43 (21%)	2 (6.9%)	15 (25%)	26 (23%)	0.12

1. Median [IQR] was reported for age, and frequency (%) was reported for all categorical variables
2. *p<0.05; **p<0.01; ***p<0.001
3. Pearson's Chi-squared test was used for English as preferred language, osteoarthritis, rheumatoid arthritis, and noninflammatory musculoskeletal disease, Fisher's exact tests were used for other categorical variables, and Kruskal-Wallis rank sum test was used for age

Table 2. Referral Reasons to the MSUS Clinic by BMI Category

		BMI Category			
	Overall (N=203)[1]	Normal (N=29)[1]	Overweight (N=60)[1]	Obese (N=114)[1]	p-value[2,3]
Active inflammatory arthritis	39 (19%)	11 (38%)	13 (22%)	15 (13%)	0.009**
Chronic inflammatory arthritis	20 (9.9%)	2 (6.9%)	4 (6.7%)	14 (12%)	0.51
Noninflammatory conditions	90 (44%)	12 (41%)	28 (47%)	50 (44%)	0.88
Procedures	62 (31%)	7 (24%)	17 (28%)	38 (33%)	0.57
Other	51 (25%)	5 (17%)	13 (22%)	33 (29%)	0.33

1. Frequency (%) is reported for all categorical variables.
2. *p<0.05; **p<0.01; ***p<0.001
3. Fisher's exact test was used for chronic inflammation, while Pearson's Chi-squared tests were used for all other conditions.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. MSUS Joint Findings by BMI Category

	Overall (N=203)[1]	BMI Category			p-value[2,3]
		Normal (N=29)[1]	Overweight (N=60)[1]	Obese (N=114)[1]	
Active inflammatory arthritis	39 (19%)	11 (38%)	13 (22%)	15 (13%)	0.009**
Chronic inflammatory arthritis	20 (9.9%)	2 (6.9%)	4 (6.7%)	14 (12%)	0.51
Noninflammatory conditions	90 (44%)	12 (41%)	28 (47%)	50 (44%)	0.88
Procedures	62 (31%)	7 (24%)	17 (28%)	38 (33%)	0.57
Other	51 (25%)	5 (17%)	13 (22%)	33 (29%)	0.33

1. Frequency (%) is reported for all categorical variables.
2. *p<0.05; **p<0.01; ***p<0.001
3. Fisher's exact test was used for chronic inflammation, while Pearson's Chi-squared tests were used for all other conditions.

toward more chronic inflammatory arthritis. This differs from previous ultrasound studies showing less radiographic joint damage in patients with obesity based on the proposed theories of decreased bone remodeling in obesity and protective effects of adipocytes on the synovium[1]. These results highlight the need for more consistent MSUS in elevated BMI patients with inflammatory arthritis as the length to the initial diagnosis of inflammatory arthritis in this cohort may be contributing to this trend. Patients with elevated BMI were referred more often for procedural accuracy rather than evaluation and monitoring of inflammatory arthritis, which also highlights the need for more referrals for evaluation and monitoring in this cohort.

1. Bauer EM, et al. Joint-specific assessment of swelling and power Doppler in obese rheumatoid arthritis patients. *BMC Musculoskelet Disord*. (2017)

Disclosure: A. Lichtiger: None; **Y. Jin**: None; **C. Rourke**: None; **K. Brennan**: None; **H. Weisleder**: None; **M. Fazzari**: None; **M. Band**: None.

Abstract Number: 1945

Significance of Finger Joint Tenderness With or Without Swelling in Relation to MRI, Ultrasound, and X-Ray Findings in Psoriatic Arthritis_Final results

Victoria Furer[1], iris Eshed[2], Moshe Iluz[1], Ori Elkayam[3] and **Ari Polachek**[4], [1]Tel-Aviv Medical Center, Tel-Aviv, Israel, [2]Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer affiliated with School of Medicine, Tel Aviv University, Tel Aviv, Israel, [3]Tel Aviv medical center, Tel Aviv, Israel, [4]Rheumatology Institute of Beilinson Hospital, Petah Tikva, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal involvement in psoriatic arthritis (PsA) affects both articular and extra-articular structures, presenting as inflammatory and structural lesions. The relationship between tender and/or swollen joints and these lesions on imaging is not fully defined.

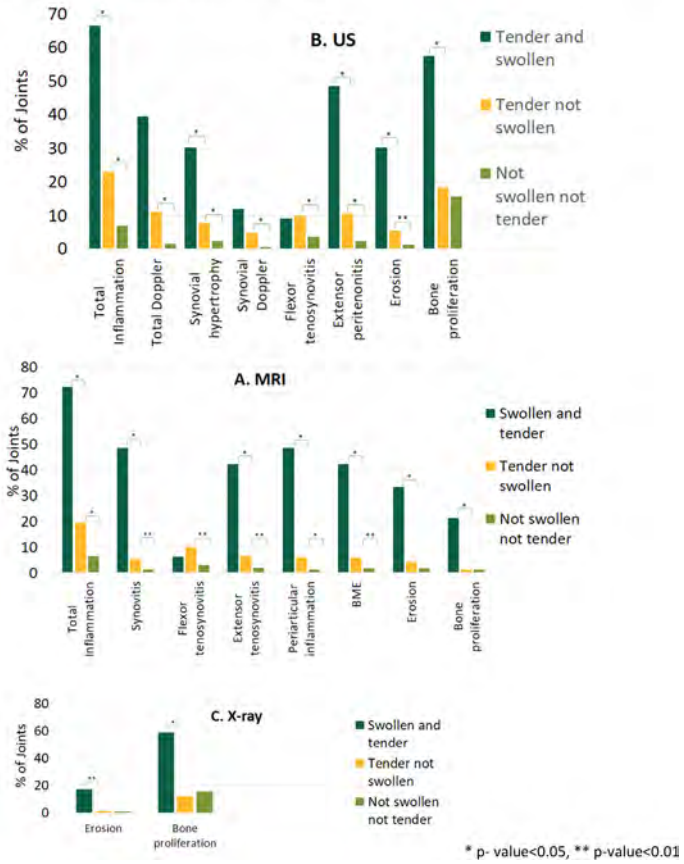
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Purpose: To assess the clinical significance of tender-only (TJ+/SJ–) finger joints in PsA, compared to tender and swollen joints (TJ+/SJ+), in relation to inflammatory and structural lesions on MRI, ultrasound (US), and X-ray, and to evaluate the added diagnostic value of imaging.

Methods: This prospective study included 100 consecutive PsA patients (CASPAR criteria) with finger joint involvement. Physical exam categories were: tender and swollen joints (TJ+/SJ+), tender only (TJ+/SJ–), and normal joints (TJ–/SJ–). Swollen-only joints (TJ–/SJ+) were excluded due to small numbers (n=3). On the day of clinical evaluation, all patients underwent US (gray scale and Doppler) of 14 finger joints on the symptomatic hand (MCP I–V, IP, PIP II–V, DIP I–V), assessing synovitis, flexor tenosynovitis, extensor peritenonitis, erosions, and bone proliferation per EULAR-OMERACT. Within 3 days, MRI of the hand was performed, assessing the same lesions plus bone marrow edema (BME) and periarticular inflammation using PsAMRIS. Seventy patients completed hand X-rays within 1 month, scored by PsA Ratingen Score. Imaging assessors were blinded to clinical findings.

Results: Mean age was 51.2±12.6 years, 59% were female, and mean PsA duration was 10.3±11.2 years. TJ+/SJ+ joints had the highest prevalence of inflammatory and structural lesions across all modalities. However, 28% (MRI) and 33% (US) of joints in this category showed no inflammatory lesions. TJ+/SJ– joints had a lower prevalence of findings but were more involved than TJ–/SJ– joints. Subclinical inflammation (in TJ–/SJ–) was rare. Agreement between TJ+/SJ+ and imaging findings ranged from slight to moderate (kappa 0.42–0.01), with highest values for synovitis. TJ+/SJ– showed lower

Figure 1: Prevalence of inflammatory and structural lesions (dichotomized) in MRI, US and X-ray according to Tender and/or swelling joints



A) MRI, (B) Ultrasound (US), and (C) X-ray findings showing the percentage of joints with dichotomized inflammatory and structural lesions, stratified by physical examination: tender and swollen (TJ+/SJ+), tender only (TJ+/SJ–), and non-tender/non-swollen (TJ–/SJ–). TJ+/SJ+ joints had the highest prevalence of imaging-detected abnormalities across modalities. TJ+/SJ– joints showed intermediate frequencies, while TJ–/SJ– joints had low prevalence, indicating minimal subclinical inflammation. Asterisks indicate statistically significant differences between groups (*p<0.05, **p<0.01).

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Diagnostic Agreement, Sensitivity, and Specificity of Physical Exam Joint Categories Compared to MRI and Ultrasound Findings

	TJ + SJ			TJ not SJ			TJ or SJ		
	Kappa	Sensit	Specif	Kappa	Sensit	Specif	Kappa	Sensit	Specif
MRI									
Synovitis	0.42	0.48	0.98	0.02	0.19	0.97	0.16	0.12	0.98
Flex. Teno	0.01	0.06	0.96	0.05	0.1	0.97	0.05	0.09	0.97
Ext. Teno	0.32	0.42	0.97	0.04	0.06	0.97	0.15	0.13	0.98
BME	0.34	0.42	0.97	0.04	0.06	0.97	0.25	0.12	0.98
Periartic	0.43	0.48	0.98	0.05	0.06	0.98	0.17	0.13	0.98
Tot Inf	0.26	0.73	0.92	0.12	0.19	0.92	0.26	0.28	0.94
US									
Synovitis	0.27	0.63	0.89	0.08	0.19	0.90	0.17	0.26	0.91
Syn. Hyp	0.22	0.30	0.97	0.07	0.08	0.97	0.13	0.11	0.98
Syn. Dopp	0.15	0.36	0.98	0.07	0.06	0.98	0.09	0.11	0.99
Flex. Teno	0.03	0.00	0.98	0.09	0.04	0.96	0.08	0.03	0.99
Ext. Teno	0.13	0.09	0.99	0.05	0.04	0.99	0.08	0.04	0.99
Tot. Dopp	0.3	0.40	0.97	0.13	0.11	0.97	0.21	0.16	0.99
Tot. Inf	0.26	0.66	0.91	0.15	0.23	0.91	0.26	0.30	0.93

Agreement (κ), sensitivity, and specificity of physical examination categories—tender and swollen (TJ+/SJ+), tender only (TJ+/SJ–), and either tender or swollen (TJ or SJ)—for detecting inflammatory lesions on MRI and ultrasound (US). TJ+/SJ+ joints demonstrated higher sensitivity but only slight to moderate agreement, while TJ+/SJ– joints showed low sensitivity and agreement. Specificity was consistently high across all categories. Tot. Inf = Total inflammation; Syn. Hyp = Synovial hypertrophy; Syn. Dopp = Synovial Doppler; Flex./Ext. Teno = Flexor/Extensor tenosynovitis; BME = Bone marrow edema; Periartic = Periarticular inflammation.

agreement. Sensitivity and positive predictive value (PPV) of TJ+/SJ+ ranged from low (tenosynovitis) to moderate (synovitis), while specificity and negative predictive value (NPV) were high. TJ+/SJ– had low sensitivity and PPV but high specificity and NPV. MCP, PIP, and DIP joint-level analyses showed similar trends.

Conclusion: Tender and swollen joints (TJ+/SJ+) were associated with the highest prevalence of imaging-detected inflammatory lesions. However, a considerable proportion of these joints did not show active inflammation on MRI or US, highlighting the limited positive predictive value of physical examination. Tender-only joints (TJ+/SJ–) demonstrated fewer imaging abnormalities but still had a higher prevalence of lesions than clinically inactive joints (TJ–/SJ–), indicating their intermediate diagnostic relevance. Importantly, subclinical inflammation in non-tender, non-swollen joints (TJ–/SJ–) was rare, reinforcing the utility of physical examination in ruling out active disease. These findings underscore the limitations of physical examination alone and support the integration of imaging into routine PsA assessment.

Disclosure: V. Furer: None; **i. Eshed**: None; **M. Iluz**: None; **O. Elkayam**: AbbVie/Abbott, 6, Janssen, 6; **A. Polachek**: None.

Abstract Number: 1946

Quantitative Imaging Analysis of Chest Computed Tomography in Rheumatoid Arthritis-Associated Interstitial Lung Disease

Emily Anthone[1], Emily Wan[2], Aimee Schreiner[1], Katherine Wysham[3], Gary Kunkel[4], Grant Cannon[5], Andreas Reimold[6], John Richards[7], Dana Ascherman[8], Gail Kerr[9], Paul Monach[10], Halie Frideres[11], Punyasha Roul[12], Scott Matson[13], Joshua Baker[14], Ted Mikuls[1] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]VA Boston, Omaha, NE, [3]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [4]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [5]University of Utah and Salt Lake City VA, Salt Lake City, UT, [6]Dallas VA Medical Center, Dallas, TX, [7]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [8]University of Pittsburgh, Pittsburgh, PA, [9]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [10]VA Boston Healthcare System, Boston, MA, [11]UNMC Department of Rheumatology, Omaha, NE, [12]UNMC, Omaha, NE, [13]University of Kansas, Kansas City, MO, [14]University of Pennsylvania, Philadelphia, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) frequently complicates the disease course in RA. While forced vital capacity (FVC) from pulmonary function tests (PFTs) is the most common measure used to monitor RA-ILD, quantitative imaging analysis of chest computed tomography (qCT) represents an alternative, and increasingly feasible, approach. We evaluated the role of qCT in RA-ILD by comparing to PFTs, respiratory patient-reported outcomes (PROs), and evaluating its prognostic value for survival.

Methods: We performed cross-sectional and cohort analyses using a multicenter, prospective cohort of patients with RA-ILD. Patients fulfilling ACR criteria for RA who were diagnosed with ILD by their treating clinician and had supporting imaging findings were enrolled between 1/2021 and 2/2025. qCT analysis was performed on baseline non-contrast chest CT as part of routine clinical care using the 3D SLICER Chest Imaging Platform. High attenuation areas between -600 and -250 Hounsfield units were quantified by the percentage of lung voxels in six lung regions to assess ILD (%HAA), with higher values indicating a greater degree of lung involvement. Additional assessments completed among participants included PFTs (FVC, diffusion capacity [DLCO]) and respiratory PROs (University of California San Diego Shortness of Breath Questionnaire [UCSD SOBQ] and Leicester Cough Questionnaire [LCQ]). Participants' vital status was reported by site investigators. We assessed the correlations of chest CT %HAA with PFTs and respiratory PROs using Pearson correlations, as well as associations with survival using Cox regression adjusting for age and sex.

Results: We studied 113 participants with RA-ILD from 9 sites in this prospective cohort. The cohort had a mean (SD) age of 70.4 (8.0) years, was primarily male (78.8%), had frequent smoking history (69.9%), a mean RA duration of 20.5 (14.2) years, and a mean ILD duration of 6.7 (8.0) years. Mean (SD) FVC % predicted was 87.7 (22.1), and DLCO % predicted was 58.3 (19.9). Mean total lung %HAA was 6.2, with higher values in the lower lung regions (9.2 and 9.9) compared with the upper

Table 1. Correlations of Chest Computed Tomography High Attenuation Areas with Pulmonary Function Tests and Respiratory Patient-Reported Outcomes.

	FVC % pred	DLCO % pred	UCSD SOBQ	LCQ
% HAA on chest CT				
Total lung	-0.33*	-0.35*	0.17	-0.11
Max lung region	-0.33*	-0.34*	0.20*	-0.16
Left lung total	-0.36*	-0.33*	0.14	-0.09
Left upper	-0.32*	-0.24*	0.13	-0.11
Left middle	-0.37*	-0.28*	0.10	-0.05
Left lower	-0.29*	-0.32*	0.13	-0.07
Right lung total	-0.28*	-0.33*	0.18	-0.13
Right upper	-0.22*	-0.22*	0.17	-0.15
Right middle	-0.26*	-0.32*	0.17	-0.11
Right lower	-0.28*	-0.36*	0.18	-0.13
Pulmonary function test				
FVC % pred	-	0.36*	-0.39*	0.19

*Denotes p value < 0.05
Values Pearson correlation coefficients
Shading denotes direction (green positive, orange negative) and strength of association (dark shade >0.3, light shade <0.3) for correlations with p < 0.05.

Abbreviations: DLCO, diffusion capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; LCQ, Leicester Cough Questionnaire; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

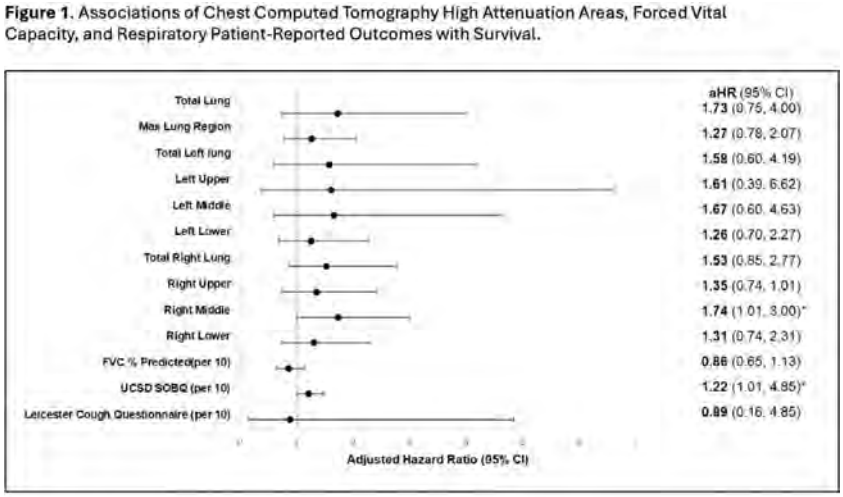


Figure 1. Associations of Chest Computed Tomography High Attenuation Areas, Forced Vital Capacity, and Respiratory Patient-Reported Outcomes with Survival.

regions (4.3 and 3.5). qCT %HAA parameters were weakly to moderately negatively correlated with FVC (range *r* -0.22 to -0.37; p< 0.05) and DLCO (range *r* -0.22 to -0.35; p< 0.05) (**Table 1**). Lung %HAA was not associated with respiratory PROs. Over 169 patient-years of follow-up, 17 deaths occurred. Patients with higher %HAA tended to have poorer survival (range aHR 1.26 to 1.74 per 10 %HAA; **Figure 1**), though findings did not reach statistical significance. While FVC was similarly not significantly associated with survival, higher UCSD SOBQ scores, but not LCQ scores, were associated with poorer survival (per 10 units, aHR 1.22 [1.01, 1.48]).

Conclusion: In this study, qCT %HAA was weakly to moderately correlated with FVC and DLCO percent predicted in a multicenter, prospective RA-ILD cohort. Over an initial follow-up period with a limited number of deaths, qCT %HAA appeared to provide similar prognostic information on survival as FVC % predicted. These findings highlight a potential role for chest CT quantitative analysis to characterize and monitor RA-ILD.

Disclosure: E. Anthone: None; **E. Wan**: None; **A. Schreiner**: None; **K. Wysham**: None; **G. Kunkel**: None; **G. Cannon**: None; **A. Reimold**: None; **J. Richards**: None; **D. Ascherman**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **P. Monach**: Boehringer-Ingelheim, 2; **H. Frideres**: None; **P. Roul**: None; **S. Matson**: None; **J. Baker**: Amgen, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 1947

Coronary computed tomography incidental findings in rheumatoid arthritis.

Emmanuel Tapia López[1], Jessica Roldan Ortega[2], Evelyn Aranda Cano[3], Itzel Palafox Sosa[4], Luz Viruel[5], Luis H Silveira[6], Laura Aline Martinez-Martinez[7] and Francisco Castillo-Castellon[8], [1]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Naucalpan de Juarez, Estado de México, Mexico, [2]INSTITUTO NACIONAL DE CARDIOLOGIA, Ciudad de México, Federal District, Mexico, [3]Departament of rheumatology Instituto Nacional de Cardiología Ignacio Chávez,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ciudad de Mexico, Federal District, Mexico, [4]Escuela Superior de Medicina-Instituto Politècnico Nacional, ciudad de mexico, Federal District, Mexico, [5]Universidad Autónoma del Estado de Hidalgo, Tula de Allende, Hidalgo, Mexico, [6]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [7]Rheumatology Department at National Institute of Cardiology Ignacio Chávez, Mexico City, Federal District, Mexico, [8]Instituto Nacional de Cardiología Ignacio Chavez, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) have a greater cardiovascular risk than does the general population. The coronary calcium score is a measure used to determine subclinical coronary disease in patients with low or intermediate cardiovascular risk. (Pearson GJ, et al. Can J Cardiol. 2021;37:1129–50). Incidental findings in cardiac computer tomography scans (CT) in the general population have been described in up to 28% of patients, and 3–39% are of clinical relevance (Bendix K, et al. Eur J Radiol. 2011;80:109–114). However, although there is information about cardiovascular risk measured by coronary calcium scores in patients with RA, incidental findings have not been systematically described. The objective of this subanalysis is to describe the incidental CT findings of coronary calcium studies in patients with RA.

Methods: CT studies of patients with RA who attended the rheumatology outpatient clinic of a national reference center for cardiovascular diseases were included. The patients included were of indistinct sex, seropositive for RA, and 18 years of age or older. Cardiovascular risk was classified according to the Canadian Society of Cardiology. Incidental CT findings were classified according to the anatomy of their location, system, and clinical significance. The records of all the participants were reviewed, and they provided their informed consent for the CT procedure. Informed consent was signed for this protocol.

Descriptive statistics were performed, and the data are expressed according to the distribution of the data based on normality analysis. A value of $p< 0.05$ was considered statistically significant.

Results: Fifty-four patients were analyzed, 87% of whom were women. The mean age was 57 years (+/-10), with a median RA evolution of 11.5 years (IQR 5-16), 67% were in remission and the rest (33%) had some degree of activity measured by the DAS-28PCR at the time of the study. A total of 74% of the patients were under treatment with methotrexate, 31% with sulfasalazine, 21% with leflunomide, 34% with hydroxychloroquine, and 5% with biological DMARDs. Fifty-four CT scans were analyzed, revealing a minimum coronary calcium score of 0 in 61% of the patients and a maximum of 4,530 in the group with increased cardiovascular risk.

The frequency of incidental findings was 96%, of which 30% were clinically significant; 18% required some type of medical follow-up. The most prominent findings were pulmonary nodules (41%) and atelectasis (31%), cardiovascular findings, atherosclerosis (11%), pericardial effusion (9%), and osteodegenerative changes (60%).

Conclusion: The percentage of incidental findings found in the measurement of coronary calcium in patients with RA in a reference center for cardiovascular diseases is high, with the most frequent findings being osteodegenerative, pulmonary, and cardiovascular findings. Interestingly, more than 10% of cases are clinically relevant and require some type of follow-up. To date, this is the first study to report incidental findings in patients with RA in whom coronary calcium was measured. However, larger studies are needed to confirm these results.

Disclosure: E. Tapia López: None; **J. Roldan Ortega**: None; **E. Aranda Cano**: None; **I. Palafox Sosa**: None; **L. Viruel**: None; **L. Silveira**: None; **L. Martinez-Martinez**: None; **F. Castillo-Castellon**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1948

Enhanced Prediction of Knee Osteoarthritis Progression through Deep Learning-Based Multimodal Data Fusion

Daniela Herrera[1], Ahmad Almhdie-Imjabbar[2], Hechmi Toumi[3] and **Eric Lespessailles**[4], [1]PRIMMO- University Hospital Center of Orleans, Olreans, France, [2]University Hospital Center of Orleans, Orleans, France, [3]PRIMMO- University Hospital Center of Orleans, Orleans, France, [4]CHU Orléans, Orléans, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Effective diagnosis and management of knee osteoarthritis (KOA) increasingly rely on integrating diverse data sources, including imaging and clinical information. The practice of combining data from several modalities to extract more comprehensive and complementary information for machine learning models that perform better than those that only use one data modality is known as data fusion. Data fusion in machine learning is expected to enhance predictive power for decision-making in health, leading to more reliable outcomes in poor validity conditions. This study aimed to evaluate the use of multimodal deep learning models assisted by transfer learning (TL) to enhance the prediction of KOA progression. The Development and application of a two-step transfer learning strategy utilizing the OAI and MOST datasets were also evaluated

Methods: From the Osteoarthritis Initiative (OAI) and the Multicenter Osteoarthritis Study (MOST) cohorts, the MRI and X-ray images of 973 and 741 knees were selected, respectively as shown in Figure 1. Two primary encoders were used as the backbone for the fusion of features extracted from MRI and X-ray images: Resnet 34 and DenseNet 201. TL strategies included one-step transfer using ImageNet pretrained weights and two-step transfer initially pretraining on one KOA cohort and then fine-tuning and validating on an external KOA cohort.

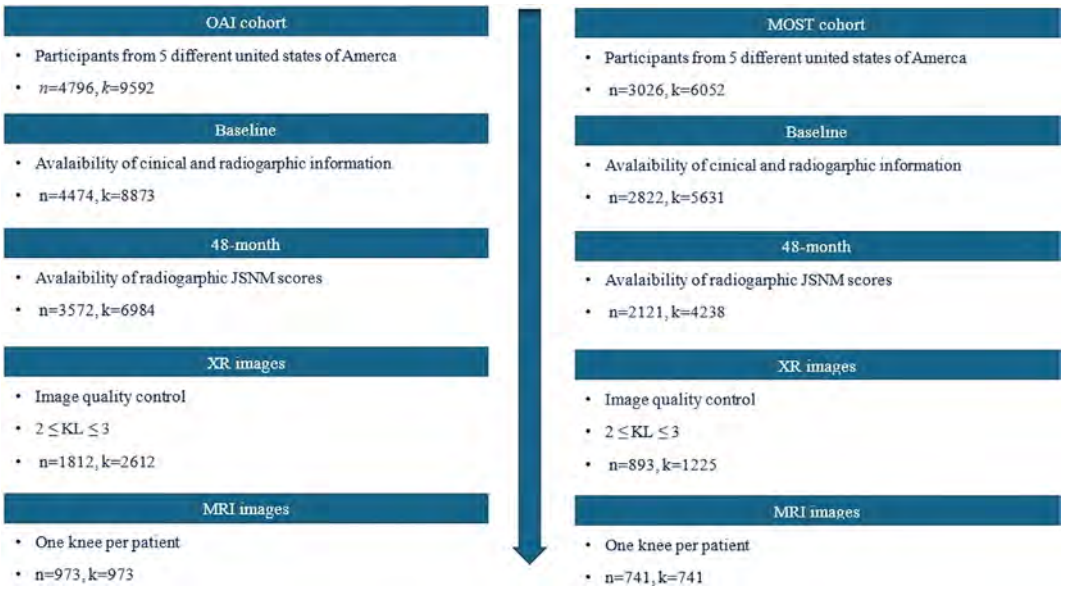


Figure 1: The CONSORT diagram of the subject selection process showing the number of patients (n) and number of knees (k) at each selection stage.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. AUC results for testing different fusion combinations without transfer learning in a) OAI and b) MOST cohorts. Results presented as mean AUC (± standard deviation)

	a) OAI		b) MOST	
	Resnet 34	**DenseNet 201**	**Resnet 34**	**DenseNet 201**
Single modality: *X-ray*	0.643 (± 0.035)	0.694 (±0.010)	0.653 (±0.023)	**0.719 (±0.036)**
Single modality: *MRI*	0.629 (± 0.038)	**0.708 (±0.051)**	0.630 (±0.039)	0.659 (±0.036)
Dual modality: *X-ray + Radio-Clinical data*	0.598 (± 0.023)	0.683 (± 0.036)	0.650 (± 0.029)	**0.735 (±0.018)**
Dual modality: *MRI + Radio-clinical Clinical data*	0.671 (± 0.041)	0.674 (±0.041)	0.680 (±0.05)	0.670 (±0.06)
Dual modality: *X-ray + MRI*	0.652 (± 0.035)	0.686 (± 0.03)	0.589 (± 0.010)	**0.719 (±0.024)**
Multimodality: *X-ray + MRI + Radio-clinical Clinical data*	0.646 (± 0.031)	0.678 (± 0.027)	0.662 (±0.020)	**0.713 (±0.04)**

AUC values greater than 0.7 are highlighted in bold, indicating models that met the threshold for acceptable predictive performance

Table 2. AUC results for testing different fusion combinations with transfer learning in a) OAI and b) MOST cohorts. Results presented as mean AUC (± standard deviation)

	a) OAI		b) MOST	
	Resnet34	**DenseNet 201**	**Resnet34**	**DenseNet 201**
Single modality: *X-ray*	0.721 (± 0.019)	0.733 (±0.043)	0.769 (±0.031)	0.786 (±0.035)
Dual modality: *X-ray + Radio-Clinical data*	0.739 (± 0.015)	0.662 (±0.034)	0.776 (±0.021)	0.786 (±0.028)
Dual modality: *X-ray + MRI*	0.739 (± 0.017)	**0.741 (±0.032)**	**0.783* (±0.031)**	0.776 (±0.03)
Multimodality: *X-ray + MRI + Radio-clinical Clinical data*	**0.749* (± 0.012)**	0.739 (±0.032)	0.774 (±0.033)	**0.787 (±0.038)**

The best AUC values in each category are highlighted in bold, representing the top-performing models across cohorts. An asterisk (*) denotes statistically significant differences compared to the values achieved by the single-modality X-ray model.

Results: Results demonstrated that ImageNet-based TL significantly improved the predictive performance of X-ray models, with AUC scores exceeding 0.7 in both the OAI and MOST cohorts (Tables 1 and 2). For MRI-based models, the lack of large-scale pretrained weights limited the performance benefit of TL. Multimodal configurations offered no clear advantage over unimodal or dual-modality models (Table 2). Without TL, DenseNet almost outperformed ResNet (Table 1). However, with TL, neither encoder demonstrated a clear advantage. The two-step TL did not show a significant benefit over one-step TL, highlighting the need for pretrained weights derived from larger KOA datasets.

Conclusion: These findings underscore the potential of transfer learning in predicting KOA progression and help fill an important gap in the focus on progression prediction

Disclosure: D. Herrera: None; **A. Almhdie-Imjabbar**: None; **H. Toumi**: None; **E. Lespessailles**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1949

Relapsing Polychondritis: Mimicking Asthma while Airways get Damaged

Eric Robbins[1] and Marcela ferrada[2], [1]University of Maryland, baltimore, [2]University of Maryland, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Relapsing polychondritis (RP) is an autoimmune disorder that can present with airway inflammation, leading to dyspnea, cough, and fatigue. These respiratory symptoms are frequently misattributed to difficult-to-control asthma, often resulting in delayed or missed RP diagnoses. In our single-center prospective cohort, we aimed to evaluate the prevalence of prior asthma diagnoses and characterize airway findings on imaging among patients ultimately diagnosed with RP.

Methods: All patients had with confirmed diagnosis of RP based were enrolled in a prospective cohort study. A presumptive diagnosis of asthma was defined as either a chart-documented asthma diagnosis or a prescription for a rescue or maintenance inhaler prior to the RP diagnosis. All patients were evaluated for disease activity and organ damage at the time of clinical assessment. Patients with respiratory symptoms underwent dynamic expiratory CT imaging to evaluate for airway involvement. Statistical analysis was performed using t-tests for categorical variables to assess associations

Results: A total of 40 patients with confirmed relapsing polychondritis (RP) underwent dynamic expiratory CT imaging at our institution. Of these, 15 (38%) had a prior diagnosis of asthma, and 7 (18%) were diagnosed with tracheomalacia (TM). Overall, 6 patients were male; of those, 4 had TM. Males were more likely to have TM in this cohort. All patients were tested for VEXAS, and none of the male patients tested positive.

Air trapping, indicative of small airway involvement, was identified in 13 patients (33%). TM strongly correlated with air trapping: all 7 patients with TM had air trapping, while none of the patients without TM did (100% vs. 19%, $p < 0.001$). Of the 13 patients with air trapping, 7 (54%) had TM.

Despite frequent respiratory symptoms, only 5 patients underwent pulmonary function testing (PFTs), and none demonstrated improvement with bronchodilators. Only 3 patients had been evaluated by a pulmonologist. Most were treated empirically with short-acting beta agonists, without objective testing or confirmation of the underlying cause.

There were no significant differences between patients with and without TM in inflammatory markers, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or Factor VIII. Muscle weakness was also not significantly different between groups

Conclusion: This study demonstrates that patients with relapsing polychondritis often have airway involvement, which is frequently misdiagnosed as asthma. The overlap in symptoms can lead to delayed recognition of RP-related airway disease and inappropriate treatment. These findings highlight an urgent need for better diagnostic tools to identify early airway involvement and prevent long-term damage. Future research should focus on characterizing the full spectrum of RP-related airway disease and developing reliable, noninvasive tests to support early diagnosis and targeted intervention.

Disclosure: E. Robbins: None; **M. ferrada**: UpToDate, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1950

Pericoronary fat enhancement in rheumatoid arthritis differs from controls and associates with coronary atherosclerosis independently of epicardial fat volume

Frederik Enevoldsen[1], Sarah Ormseth[2], Dzenan Masic[1], Matthew Budoff[3], Ellen-Margrethe Hauge[1] and George Karpouzas[3], [1]Aarhus University, Aarhus, Denmark, [2]The Lundquist Institute for Biomedical Innovation, Torrance, CA, [3]Harbor-UCLA Medical Center, Torrance, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Pericoronary adipose tissue attenuation (PCATa) reflects the composition of the fat directly surrounding the coronary arteries and is associated with coronary wall inflammation. In general patients with coronary atherosclerosis, PCATa, particularly around the right coronary artery (RCA), predicted plaque burden, plaque vulnerability, and optimized cardiovascular risk estimates. The volume of epicardial adipose tissue (EATv) contained between the free cardiac surface and the visceral pericardium, which includes PCAT, was linked to coronary atherosclerosis burden and progression in rheumatoid arthritis (RA). We here explore differences in PCATa and PCATa-atherosclerosis associations between RA and controls and whether PCATa relates to coronary plaque burden and composition independently of EATv in RA.

Methods: PCATa around the proximal left anterior descending (LAD), left circumflex (LCx) and RCA, total EATv, and atherosclerosis burden and composition (noncalcified, mixed and calcified) were evaluated with coronary computed tomography angiography (CCTA) in 150 RA patients and 120 age and gender-matched controls without known coronary artery disease. Linear regression evaluated the association between RA and PCATa. Negative binomial regression explored the association of collective (3-artery) and artery-specific PCATa on numbers of plaques (total and plaque subtypes). RA x PCATa interactions evaluated the moderating effect of disease state on plaque outcomes.

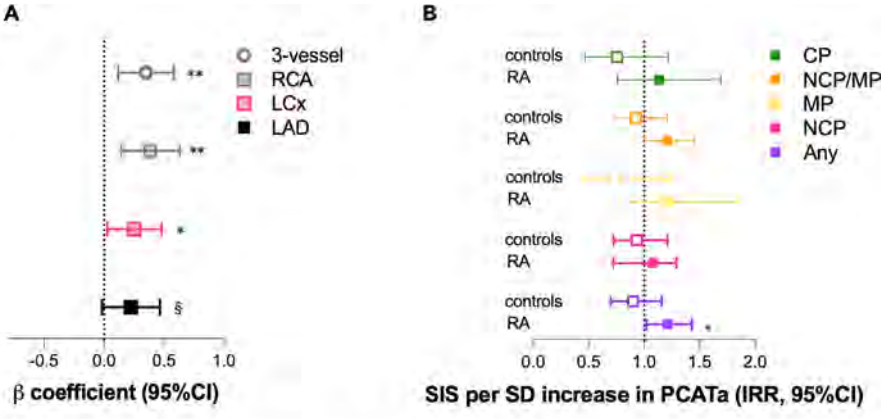


Figure 1 Differences in PCATa and their links to atherosclerotic burden between RA and controls **A.** Collective and artery-specific PCATa is higher in RA compared to controls. **B.** PCATa associates with coronary atherosclerosis burden in RA but not controls (p-for-interaction=0.037). Models adjusted for age, sex, HTN, DM, dyslipidemia, EATv LAD: left anterior descending, LCx: left circumflex, RCA: right coronary artery, NCP: noncalcified, MP: mixed, CP: calcified plaque, β: standardized coefficient, SIS: segment involvement score representing number of plaques per patient, SD: standard deviation, CI: confidence interval, PCATa: pericoronary adipose tissue attenuation. §p=0.070, *p<0.05, **p<0.01

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

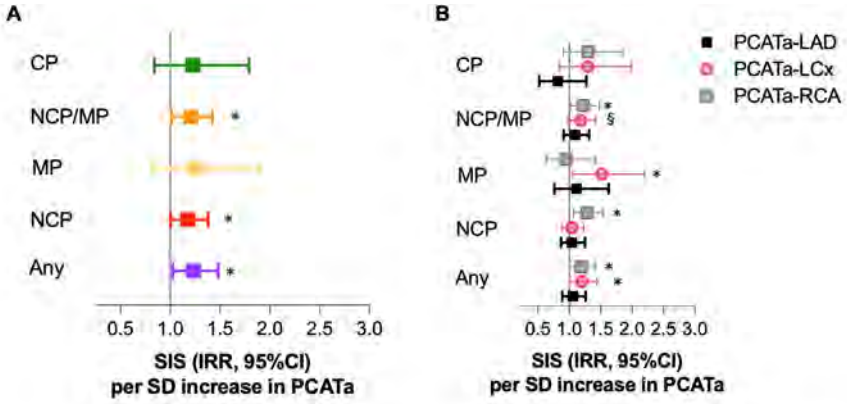


Figure 2 Collective **(A)** and artery-specific **(B)** PCATa associates with atherosclerosis burden and plaque composition in RA. Models adjusted for atherosclerotic cardiovascular risk score (ASCVD), EATv, erythrocyte sedimentation rate (ESR), prednisone and statin use. NCP: noncalcified, MP: mixed, CP: calcified plaque, SIS: segment involvement score representing number of plaques per patient, IRR: incidence rate ratio, SD: standard deviation, CI: confidence interval, PCATa: pericoronary adipose tissue attenuation.
§p=0.077, *p<0.05

Results: Collective PCATa (standardized b-coefficient 0.35, 95% confidence interval 0.12-0.58) and artery-specific PCATa around LCx (b 0.25, 95%CI 0.03-0.48) and RCA (b 0.39, 95%CI 0.14-0.63) was higher in RA compared to controls (Figure 1A) after adjustments for age, sex, hypertension, diabetes, dyslipidemia and EATv. Collective PCATa (per standard deviation increase) associated with 21% more total plaques in RA (incidence rate ratio-IRR 1.21, 95%CI 1.02-1.43) but not in controls (p for interaction=0.037, Figure 1B) after similar adjustments. In patients with RA, collective PCATa (IRR 1.23, 95%CI 1.03-1.48) and artery-specific PCATa around LCx (IRR 1.20, 95%CI 1.01-1.44) and RCA (IRR 1.19, 95%CI 1.00-1.41) associated with more plaques, especially those with soft components (noncalcified or mixed, Figure 2A and B) after adjustment for atherosclerotic cardiovascular risk score, EATv, erythrocyte sedimentation rate, prednisone, and statin use. There was no difference in artery-specific PCATa among matched normal arteries in RA patients with and without atherosclerosis (all p >0.05). In contrast, upon comparing matched arteries with vs. without plaque, PCATa was higher only around atherosclerotic LCx vessels.

Conclusion: Cumulative PCATa is higher and is linked to coronary atherosclerosis burden in RA but not controls. Cumulative and artery-specific PCATa in RA is linked to more total, soft, and vulnerable plaques, and provides additional information over EATv on atherosclerosis burden. The nature of compositional changes in PCAT may vary regionally and reflect the presence of explicit structural changes, such as plaque, in the underlying vessel wall.

Disclosure: F. Enevoldsen: None; **S. Ormseth**: None; **D. Masic**: None; **M. Budoff**: None; **E. Hauge**: None; **G. Karpouzas**: Janssen, 1, Pfizer, 5, Scipher, 2.

Abstract Number: 1951

Quantitative HRCT Analysis in Sjögren's Disease-associated ILD: CALIPER-Derived Imaging Biomarkers for Prognostic Assessment

Gaetano La Rocca[1], Francesco Ferro[2], Vincenzo Uggenti[3], Beatrice Dei[4], Giovanni Fulvio[4], Michele Moretti[4], Marta Mosca[5], Chiara Romei[3] and Chiara Baldini[5], [1]University of Pisa, Rheumatology Unit, Pisa, Pisa, Italy, [2]Clinical and Experimental Medicine Department, Azienda Ospedaliero-Universitaria Pisana, Pisa, Pisa, Italy, [3]University of Pisa, 2nd Radiology Unit, Pisa, Italy, [4]Rheumatology Unit, University of Pisa, Pisa, Toscana, Italy, [5]University of Pisa, Pisa, Pisa, Italy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial Lung Disease (ILD) is a frequent manifestation of Sjögren's Disease (SjD), associated with significant morbidity and mortality. However, data on the prevalence of progressive ILD in SjD remain scarce, and biomarkers for predicting progression are lacking. Computer-Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER) is a validated CT-based software that quantifies ILD patterns such as ground-glass opacities, reticulation, honeycombing, and low attenuation areas. CALIPER-derived parameters correlate with pulmonary function tests (PFT) and outcomes in IPF and other autoimmune ILDs, but their role in SjD-ILD is unexplored.

The aim of this study was to assess the prognostic value of CALIPER-derived parameters in SjD-ILD patients

Methods: SjD patients (2016 ACR/EULAR criteria) with HRCT-confirmed ILD followed from Jan 2018 to Sep 2023 were retrospectively included if ≥1 HRCT was suitable for CALIPER analysis. Clinical, lab, respiratory, and PFT data were collected at baseline and follow-up. Progressive fibrosing ILD (PF-ILD) was defined (ATS criteria) by ≥2 of: worsening symptoms, FVC decline ≥5% or DLCO ≥10%, or radiological progression within 1 year. CALIPER-derived ILD% (sum of ground-glass, reticular, honeycombing) and VRS% (vascular-related structures) were calculated. Visual ILD extent (Warrick score) and ILD pattern were assessed by a thoracic radiologist

Results: Twenty-three patients (F:M=18:5, mean age 66.2±9.5 yrs, mean follow-up 6.1±5 yrs) were enrolled. ILD patterns included NSIP (n=14), UIP (n=6), and NSIP+OP (n=3). Dyspnea and cough occurred in 21 and 19 patients, respectively. Median baseline FVC and DLCO were 83% and 64%. Seventeen patients received immunosuppressants; none received antifibrotics. Seven required long-term oxygen (LTO2) and 7 developed PF-ILD.

Both baseline ILD% and VRS% demonstrated a moderate to strong correlation with FCV% and DLCO%, visual ILD quantification with Warrick score and between them (table 1). VRS%, Reticulation%, and Honeycombing% were significantly higher in UIP (p=.021, .038, and .047, respectively). On univariate regression analysis, VRS% (OR 3.2, 95%CI 1.1-9.1, p=.03) and ILD% (OR 1.13, 95%CI 1.01-1.3, p=.05) were associated with LTO2 necessity. According to ROC analysis, VRS% had an AUC of 0.813 (p=.019) with an optimal cut-off of 3.8%, yielding a sensitivity of 71.4% and a specificity of 87.5% in predicting LTO2 necessity. ILD% had an AUC of 0.777 (p=.038) with a cut-off of 11.6% resulting in a sensitivity of 71.4% and a specificity of 75% in predicting LTO2 necessity.

On univariate regression analysis VRS% (OR 2.8, 95%CI 1-8, p=.05) was associated with a PF-ILD behavior in the next year, with an AUC of 0.85 (p=.023) and an optimal cut-off of 3.8% resulting in a sensitivity of 83.3% and specificity of 80%.

Conclusion: CALIPER-derived parameters correlate strongly with lung function and predict adverse outcomes in SjD-ILD. Automated HRCT analysis offers promising digital biomarkers for disease assessment and risk stratification. Integrating these metrics with clinical and functional data could support early identification of progressive ILD and guide therapy. Further validation in larger cohorts is warranted

	FVC%	DLCO%	Warrick score	ILD%	VRS%
ILD%	r=-0.731 p=0.001	r= -0.658 p=0.008	r= 0.500 p=0.048	r= 1.000	r= 0.927 p=0.000
VRS%	r= -0.716 p=0.002	r= -0.686 p=0.005	r= 0.573 p=0.020	r= 0.927 p=0.000	r= 1.000

Correlation of CALIPER-derived parameters with functional indices and HRCT visual assessment with Warrick score

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. La Rocca: None; **F. Ferro**: None; **V. Uggenti**: None; **B. Dei**: None; **G. Fulvio**: None; **M. Moretti**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **C. Romei**: None; **C. Baldini**: None.

Abstract Number: 1952

Dermatoscopy Limitation and the Critical Role of Capillaroscopy in Systemic Sclerosis and Raynaud's Phenomenon among African American Veterans

Genessis Maldonado[1], Maurizio Cutolo[2], Tracy Frech[1], Mislav Radic[3], Marcus Snow[4] and Vanessa Smith[5], [1]Vanderbilt University Medical Center, Nashville, TN, [2]University of Genova, Genova, Italy, [3]University Hospital Split, Division of Rheumatology and Clinical Immunology, Split, Croatia, Split, Croatia, [4]University of Nebraska Medical Center, Omaha, NE, [5]Ghent University Hospital, Gent, Belgium

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Nailfold capillaroscopy (NFC) is an essential tool for evaluating microvascular abnormalities in patients with Raynaud's phenomenon (RP) in United States (U.S.) Veterans (1). While dermatoscopy is an acceptable and cost-effective screening method for nailfold assessment in systemic sclerosis (SSc), published guidelines highlight the importance of clear image acquisition for appropriate interpretation (2). The objective of this project was assessment of NFC in patients with concern for connective tissue disease (CTD)-related RP to determine whether different intensities of skin pigmentation impacts the interpretability of dermatoscopy screening.

Methods: Patients undergoing evaluation for CTD-related RP were consented for participation in Institutional Review Board approved research at the time of care at the Veterans Affairs (VA) Hospital (No. 1618579-17). Patients were prepared for NFC per published protocols (3). Images were obtained with two devices available at the VA Hospital, a dermatoscope attached to a smart phone (200X magnification, smart phone focus) and Smart G-Scope (250X magnification, USB

Table 1: Demographic data

Table 1	Fitzpatrick Skin Types IV and V	Fitzpatrick Skin Types I, II, and III	P value
Dermatoscope Parameters	**[n=11]**	**[n=27]**	
Blurry	63.63% [7]	37% [10]	**< 0.01**
Unable to interpret	**45.45% [5]**	**37% [10]**	
Abnormal findings	36.36% [4]	44.44% [12]	
Normal findings	18.18% [2]	18.51% [5]	
Presence of Giant Capillaries	**18.18% [2]**	**29.62% [8]**	**< 0.01**
Unable to interpret presence of Giants Capillaries	54.54% [6]	37% [10]	
Presence of Abnormal Shapes	**9.09% [1]**	**25.92% [7]**	**< 0.01**
Unable to interpret presence of Abnormal Shapes	54.54% [6]	37% [10]	
Presence of Hemorrhages	**36.36% [4]**	**51.85% [14]**	**< 0.01**
Unable to interpret presence of Hemorrhages	45.45% [5]	29.62% [8]	
Presence of Decreased Density	**9.09% [1]**	**25.92% [7]**	**< 0.01**
Unable to interpret Decreased Density	54.54% [6]	37% [10]	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Nailfold capillaroscopy characteristics

Table 2

Smart-G Capillaroscopy Parameters	[n=11]	[n=27]
Capillary Density (No. per mm)	5.03 ± 1.72 [2.5-7.2]	6.2±1.6 [1.9-8.3]
Giant capillaries %	10.30%	3.4%
Apical Diameter (um)	21.28 ± 4.17 [16.7-29.5]	23.1±5.4 [15.6-35.3]
Dilated Capillaries	47.06%	17.30%
Tortuous Capillaries (%)	7.38%	1%
Abnormal shapes (%)	1.39%	1%
Hemorrhages (%)	72.72%	63.3%
Microvascular Pattern		
Normal	18.18% [2]	81.3% [13]
Scleroderma (SD)-Pattern	**45.45% [5]**	**59.25% [16]**
Early SD-pattern	9.09% [1]	75% [3]
Active SD-pattern	9.09% [1]	80% [4]
Late SD-pattern	27.27 [3]	57.1% [4]
Non-specific	36.36% [4]	55.6% [5]

Table 3: Capillaroscopy findings in the uninterpretable group.

Table 3

Capillaroscopy in Uninterpretable Dermatoscopy	[n =5]
Capillary Density (No. per mm)	4.56 ± 1.91 [2.5-6.8]
Giant capillaries %	0.82%
Apical Diameter (um)	20.18 ± 3.25 [16.7-24.2]
Dilated Capillaries	19.65%
Tortuous Capillaries (%)	3.90%
Abnormal shapes (%)	1.97%
Hemorrhages (%)	80%
Pattern	
Normal	20% [1]
SD-Pattern	60% [3]
Early SD-pattern	20% [1]
Active SD-pattern	20% [1]
Late SD-pattern	20% [1]
Non-specific	20% [1]

automatic focus). Each image was classified for the clarity of image by two capillaroscopy experts. Microvascular findings for capillary density, apical enlargement, hemorrhages, and abnormal shapes were determined by the capillarscopy.io software application.

Results: A total of 38 U.S. Veterans were assessed for RP by NFC using clinically available two devices. Among these, 28% (n=11) of subjects were classified as African American. As shown in Table 1, dermatoscopy produced blurry images in 63.6% (7/11) of patients with Fitzpatrick skin type IV and V and 37% (10/31) in Fitzpatrick skin type I, II, and III. In 45.5% (5/11) of dermatoscopy exams in Fitzpatrick skin type IV and V skin were deemed uninterpretable compared to 37% (10/31) of Fitzpatrick skin type I, II, and III (kappa statistic >0.9). Smart G-Scope improved interpretability across the cohort of patients (Table 2), especially in Fitzpatrick Skin Types IV and V. A scleroderma (SD)-pattern characteristic of scleroderma microangiopathy was detected by the Smart-G-scope in 3 of those 5 uninterpretable dermatoscope acquired images (Table 3).

Conclusion: In patients with CTD-related RP, particularly among African American Veterans, a dermatoscopy device led to a high rate of uninterpretable examinations. The Smart-G USB device improved diagnosis of abnormal NFC. These results highlight that reliance on dermatoscopy alone as a screening tool may risk underdiagnosing microvascular involvement in SSc.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References:

1. Frech TM et al. BMC Rheumatol. 2021; 15; 5 (1): 42.
2. Radic M et al. Clin Exp Rheumatol. 2020; 38 Suppl 125 (3): 132-136.
3. Smith V et al. Autoimmun Rev. 2020; 9 (3): 102458.

Disclosure: G. Maldonado: None; **M. Cutolo**: None; **T. Frech**: None; **M. Radic**: None; **M. Snow**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6.

Abstract Number: 1953

Machine Learning-Based Classification of Raynaud's Phenomenon and Autoimmune Diseases in Indeterminate Capillaroscopic Patterns

Genessis Maldonado[1], Adela Marin Ballve[2], Luis Sáez Comet[3], Mayka Freire Dapena[4], Miguel Antonio Mesa[5], Miguel Martín Cascón[6], Gema María Lledó Ibáñez[7], Elena Martínez Robles[8], Begoña Marí-Alfonso[9], Alfredo Guillén del Castillo[10], Carmen Pilar Simeón Aznar[10], Borja del Carmelo Gracia Tello[2], Eduardo Ramos ibáñez[11], Tracy Frech[12] and Spanish Systemic Autoimmune Diseases Group (GEAS) and the Multidisciplinary Spanish Society of Systemic Autoimmune Diseases (SEMAIS), [1]Vanderbilt University Medical Center, Nashville, [2]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [3]Hospital Universitario Miguel Servet; Zaragoza, Zaragoza, Spain, [4]Hospital Clínico Universitario de Santiago de Compostela, La Coruña, Spain, [5]Universidad Pontificia Bolivariana, Medellin, Colombia, [6]Hospital General Universitario Morales Meseguer, Murcia, Spain, [7]Hospital Clínic de Barcelona, Barcelona, Spain, [8]Hospital Universitario La Paz, Madrid, Spain, [9]Hospital Universitario Parc Taulí, Barcelona, Spain, [10]Hospital Universitario Vall D´Hebron, Barcelona, Spain, [11]Capillary.io, Zaragoza, Aragon, Spain, [12]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Artificial intelligence (AI) has increasingly been integrated into the analysis of nailfold capillaroscopy (NFC), offering new opportunities to automate image interpretation and enhance diagnostic accuracy in rheumatologic conditions. NFC is a key non-invasive tool for the evaluation of Raynaud's phenomenon (RP), which may be primary (PRP) or secondary to a connective tissue disease (CTD). Differentiating PRP from early or overlapping autoimmune conditions remains a clinical challenge, especially when NFC findings fall within a non-specific pattern -characterized by tortuosity, abnormal shapes, dilated capillaries, and microhemorrhages. The ability to detect subtle morphological differences using machine learning may support early diagnosis, risk stratification, and clinical decision-making. The aim of this study was to differentiate PRP from various autoimmune conditions that may present with secondary Raynaud's or overlapping CTD features.

Methods: We developed a machine learning classifier using quantitative image-based features extracted via the Capillary.io platform[1-2], Images were uploaded by multiple rheumatology centers across Europe. A 50-fold stratified cross-validation approach was employed to ensure robust performance estimation, with 20% of the cases (n=153) serving as the validation set in each fold.

Results: A total of 761 NFC cases were analyzed. All cases were automatically classified as having a non-specific capillaroscopic pattern by the Capi-Detect algorith. Clinical diagnoses were made independently, based on established criteria and without reference to the capillaroscopic findings. Among the cohort, 473 patients were diagnosed with PRP, while others were diagnosed with: inflammatory myopathies (n=49; including dermatomyositis n=38, polymyositis n=4, antisynthetase syndrome n=4, necrotizing myopathy n=2, overlap syndrome n=1), systemic lupus erythematosus (SLE; n=61), limited

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

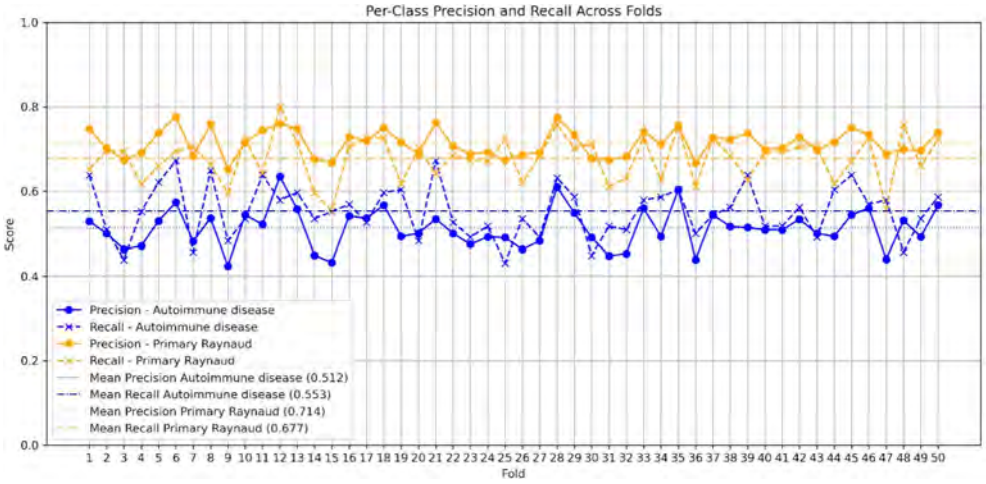


Figure 1: Precision and Recall Across Folds

systemic sclerosis (lSSc; n=54), Sjögren's syndrome (n=34), diffuse systemic sclerosis (dSSc; n=26), very early diagnosis of systemic sclerosis (VEDOSS; n=23), antiphospholipid syndrome (APS; n=9), and ANCA-associated vasculitis (n=3).

The classifier achieved a mean weighted precision of 0.637, recall of 0.630, and F1-score of 0.632 across all folds. Weighted F1-scores ranged from 0.56 to 0.71, indicating performance variability across different data splits. The majority of misclassifications involved autoimmune cases being labeled as PRP (Figure 1), underscoring the morphological overlap that exists within the non-specific capillaroscopic pattern category.

Conclusion: These findings suggest that subtle but quantifiable differences exist between PRP and autoimmune diseases presenting with non-specific capillaroscopic patterns. Machine learning models may aid in identifying these distinctions and improving diagnostic interpretation. Further studies involving larger, more balanced cohorts are warranted to enhance model sensitivity, generalizability, and overall diagnostic performance.

References:

1. Gema M Lledó-Ibáñez et al. Rheumatology, 2025; keaf073.
2. Gracia Tello BC et al. Rheumatology (Oxford). 2024; keae197.

Disclosure: G. Maldonado: None; **A. Marin Ballve**: None; **L. Sáez Comet**: None; **M. Freire Dapena**: None; **M. Mesa**: None; **M. Martín Cascón**: None; **G. Lledó Ibáñez**: None; **E. Martínez Robles**: None; **B. Marí-Alfonso**: None; **A. Guillén del Castillo**: None; **C. Simeón Aznar**: None; **B. Gracia Tello**: None; **E. Ramos ibáñez**: None; **T. Frech**: None.

Abstract Number: 1954

Revolutionizing Microvascular Screening: AI-Powered Dermatoscopy for Efficient Nailfold Capillary Evaluation

Genessis Maldonado[1], Eduardo Ramos ibáñez[2], Borja del Carmelo Gracia Tello[3] and Tracy Frech[4], [1]Vanderbilt University Medical Center, Nashville, [2]Capillary.io, Zaragoza, Aragon, Spain, [3]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [4]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Model performance

Table 1.

Label	Precision	Recall	f1
Abnormal Shapes	0.75	0.5625	0.6429
Giant Capillaries	0.8462	0.5238	0.6471
Hemorrhages	0.7059	0.6	0.6486
Lowered Density	0.7368	0.6087	0.6667
Blurry	0.8157	0.9415	0.8741

Table 2. Sample of images by label.

Table 2.

Label	Number of examples*
Abnormal Shapes	111
Giant Capillaries	108
Hemorrhages	123
Lowered Density	150
Blurry	882

*multi-label: one image may have no label, one label or multiple labels

Background/Purpose: Nailfold capillaroscopy plays a critical role in the diagnosis and management of systemic sclerosis (SSc) and related connective tissue diseases. However, access to capillaroscopy remains limited outside specialized rheumatology centers. Dermatoscopy is a more accessible alternative, but its use for nailfold evaluation lacks standardization. In 2024, we demonstrated preliminary evidence that artificial intelligence (AI) could support dermatoscopic nailfold analysis in rheumatology clinics (Maldonado et al., Arthritis Rheumatol. 2024). Building on that work, we now present a refined and more efficient AI model designed for possible real-world implementation.

Methods: We developed a multi-label image classification model using 1,405 dermatoscopic nailfold images labeled for five key features: abnormal shapes, giant capillaries (replacing the broader "enlarged" category for better dermatoscopic specificity), hemorrhages, low capillary density, and image blurriness. Unlike our 2024 approach, which used separate binary models per feature, this year's model employs a unified architecture to predict all labels simultaneously—enhancing computational efficiency and deployment feasibility. The model was based on ConvNeXt V2 and trained on an 80/20 stratified split, with performance evaluated using standard machine learning metrics. Images were retrieved using a 200x magnification lens adapted for smartphones (value $30).

Results: The model achieved strong performance across all target features (table 1), with F1-scores as follows: abnormal shapes (0.643), giant capillaries (0.647), hemorrhages (0.649), low density (0.667), and image too blurry (0.874), yielding a mean F1-score of 0.696. The multi-label framework significantly reduced inference time and memory usage while maintaining consistent accuracy across folds (table 2). The model also demonstrated robustness despite the lower resolution typical of dermatoscopic images compared to nailfold capillaroscopy.

Conclusion: This AI-driven model shows promising accuracy in detecting microvascular abnormalities from dermatoscopic images and represents a meaningful step toward accessible, point-of-care screening for SSc and related diseases. By leveraging the lightweight ConvNeXt V2 architecture in a multi-label framework, we pave the way for integration into mobile applications using a smartphone camera and dermatoscopy lens. Such a tool could support early detection of microvascular abnormalities in patients with Raynaud's phenomenon, especially in non-specialist or resource-limited settings. However, given the high proportion of low-quality (blurry) images in dermatoscopy and in alignment with current recommendations (Mislav R. et al. Clin Exp Rheumatol. 2020;38 Suppl 125:132–136), nailfold video capillaroscopy should be pursued for comprehensive evaluation when clinically indicated. Prospective validation and clinical integration studies are ongoing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Maldonado: None; **E. Ramos ibáñez**: None; **B. Gracia Tello**: None; **T. Frech**: None.

Abstract Number: 1955

Regional variations in the relationship between pericoronary fat enhancement and atherosclerosis may reflect differences in local vascular inflammation in rheumatoid arthritis

George Karpouzas[1], Frederik Enevoldsen[2], Dzenan Masic[2], Matthew Budoff[1], Ellen-Margrethe Hauge[2] and Sarah Ormseth[3], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]Aarhus University, Aarhus, Denmark, [3]The Lundquist Institute for Biomedical Innovation, Torrance, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The composition of fat around the coronary arteries is evaluated as pericoronary adipose tissue attenuation (PCATa) on coronary CT-angiogram (CCTA). In general patients PCATa was linked to plaque burden and cardiovascular risk independently of epicardial adipose tissue volume (EATv) and is considered to reflect arterial inflammation. In the presence of plaque and an inflamed vessel wall, higher EATv offset inflammation in PCAT and inversely associated with PCATa. Rheumatoid arthritis (RA) therapies attenuated EATv, arterial inflammation, plaque progression and promoted plaque stabilization via fibrosis and calcification. We here explore the relationships between artery-specific PCATa and atherosclerosis burden in the respective arteries, the influence of methotrexate, prednisone and statin use on those relationships and the link between artery-specific PCATa and inflammation in RA.

Methods: PCATa around proximal left anterior descending (LAD), left circumflex (LCx) and right coronary artery (RCA), total EATv, atherosclerosis burden and composition (noncalcified, mixed and calcified) were evaluated with CCTA in 150 RA

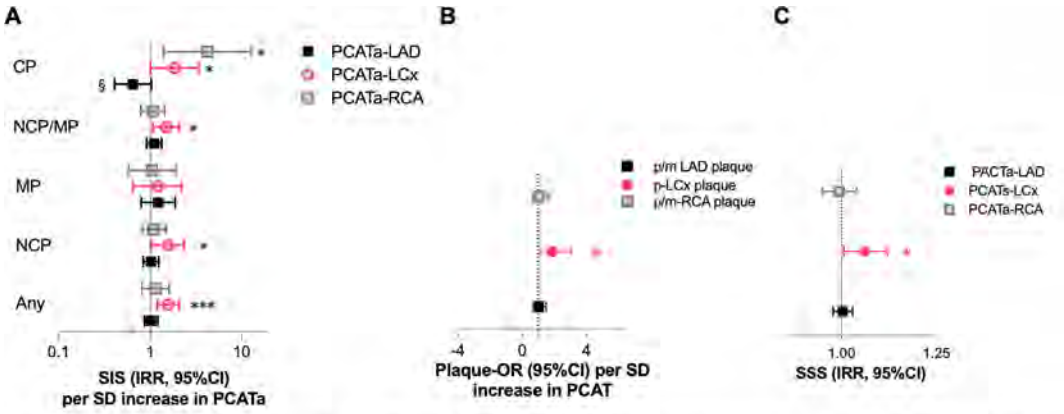


Figure 1 Associations of artery-specific PCATa with **A.** Artery-specific plaque burden and composition, **B.** likelihood of plaque presence in directly underlying segments and **C.** stenotic plaque severity in directly underlying segments. Models in panel A adjusted for adjusted for ASCVD, EATv, ESR and prednisone. LCx models for any plaque and models for CP additionally adjusted for statins. Models in panel B adjusted for ASCVD, bDMARD use, EATv, DAS28-CRP. Models in panel C adjusted for ASCVD and EATv. LAD: left anterior descending, LCx: left circumflex, RCA: right coronary artery, NCP: noncalcified, MP: mixed, CP: calcified plaque, SIS: segment involvement score representing number of plaques per patient, SSS: segment stenosis score, IRR: incidence rate ratio, SD: standard deviation, CI: confidence interval, PCATa: pericoronary adipose tissue attenuation.
§p=0.066, *p<0.05, **p<0.01, ***p<0.001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

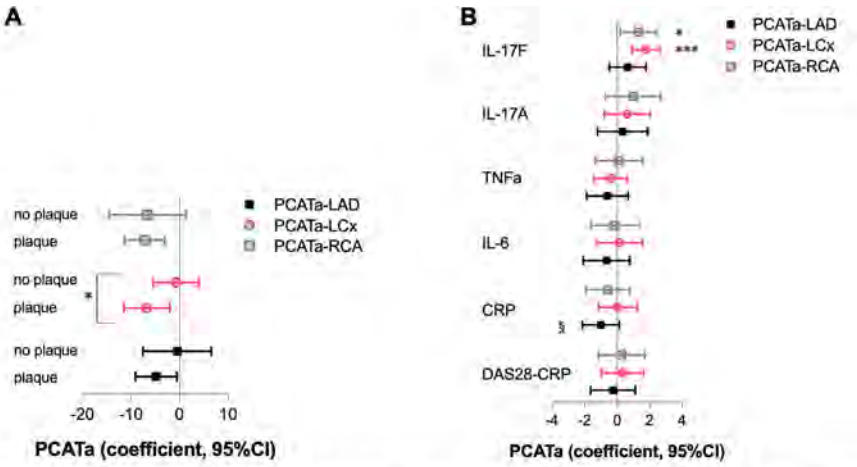


Figure 2 (A) Association between PCATa and EATv across all 3 coronary arteries in the presence or absence of plaque. **(B)** Association of artery-specific PCATa with inflammation. Models in both A and B adjusted for ASCVD score and BMI. CI: confidence interval, PCATa: pericoronary adipose tissue attenuation, EATv: epicardial adipose tissue volume, IL: interleukin, TNFα: tumor necrosis factor α, DAS28-CRP: disease activity score based on 28-joint counts and CRP
§p=0.082, *p<0.05, **p<0.01, ***p<0.001

patients without known coronary artery disease. Serum cytokines were measured with microparticle immunoassay. Negative binomial regression explored associations of artery-specific PCATa and its interactions with methotrexate, prednisone and statin use on plaque numbers (total and subtypes) and stenotic severity in underlying coronary segments. Robust linear regression assessed associations of cytokines with artery-specific PCATa.

Results: Artery-specific PCATa was linked to artery-specific plaque burden and composition exclusively for LCx (all p< 0.05, Figure 1A). Each standard deviation increase in PCATa only around LCx associated with 85% greater likelihood of plaque presence in directly underlying segments (odds ratio-OR 1.85, 95% confidence interval 1.12-3.06) and greater stenotic severity (Figure 1B,C). Plaque presence only in LCx, but not other arteries, influenced the relationship between PCATa and EATv: PCATa around LCx inversely associated with EATv only in the presence of plaque (p for interaction< 0.05, Figure 2A). PCATa around LCx associated with interleukin-17F (figure 2B), and plaque presence exclusively in LCx influenced the relationship between PCATa and IL-17A (p for interaction < 0.01). Likewise, in the presence of mixed plaque exclusively in LCx, PCATa around LCx associated with serum vascular endothelial growth factor (VEGF, p for interaction=0.002). Lastly, PCATa associated with more noncalcified plaques in the absence of methotrexate, prednisone, or statin use (all p-for-interactions< 0.05) exclusively in LCx.

Conclusion: The association of increased PCATa with atherosclerosis burden and composition specifically around LCx may coincide with regional inflammation-dependent compositional changes in PCAT including IL-17A,F-induced adipocyte remodeling and VEGF-induced neovascularization and edema. In contrast, post-inflammatory fibrosis or adaptive remodeling may account for increased PCATa and the lack of association with plaque in LAD and RCA.

Disclosure: G. Karpouzas: Janssen, 1, Pfizer, 5, Scipher, 2; **F. Enevoldsen**: None; **D. Masic**: None; **M. Budoff**: None; **E. Hauge**: None; **S. Ormseth**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1956

68ga-fapi-04 and 18F-FDG PET/ CT in MDA5 Dermatomyositis-associated Interstitial Lung Disease: A Single-center, Pilot Study

Jia Li[1], Weijun Wei[2], Lianghua Li[2], Wenwen Xu[3], Jianjun Liu[2] and Shuang Ye[4], [1]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [2]Department of Nuclear Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200217, China., Shanghai, China (People's Republic), [3]Department of Rheumatology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200217, China., Shanghai, China (People's Republic), [4]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of death in MDA5 dermatomyositis (MDA5-DM). Fibrosis and inflammation are pivotal drivers in the pathogenesis of DM-ILD. This study aims to investigate the imaging characteristics of ^{68}Ga-FAPI-04 and ^{18}F-FDG PET/CT in MDA5 DM ILD, and to evaluate the association between pulmonary metabolic parameters of fibrosis and inflammation and mortality in MDA5 DM-ILD.

Methods: Between August 2022 and November 2024, 20 patients with newly diagnosed (duration ≤6 months) MDA5 DM were enrolled in the study, followed by a 6-month longitudinal observation period.All participants underwent baseline ^{68}Ga-FAPI-04 PET/CT and ^{18}F-FDG PET/CT scanning. Parameters including total lesion volume (TLV), total target-to-background ratio (TBR_total), mean TBR (TBR_mean), and maximum TBR (TBR_max) based on standardized uptake values (SUV) were quantified.Non-parametric Mann-Whitney U tests compared group differences.Spearman's rank correlation analyes parameter associations, and point-biserial correlation coefficients quantified associations with mortality.

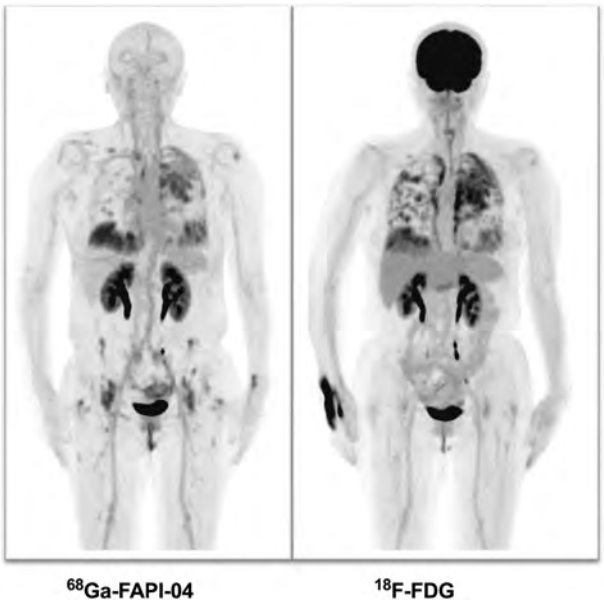


Figure 1 68Ga-FAPI-04 and 18F-FDG PET/CT imaging in a representative patient

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

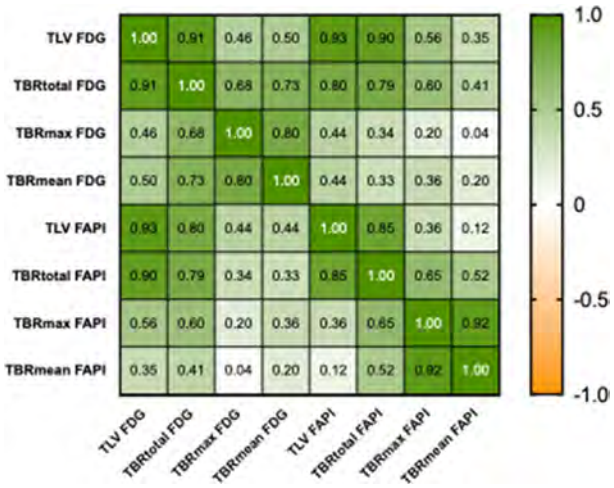


Figure 2 The association between pulmonary metabolic parameters of FAPI and FDG in MDA5 DM-ILD.

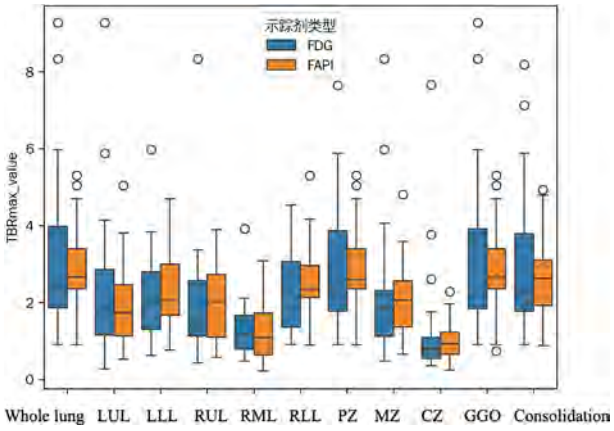


Figure 3 Boxplot of TBRmax for FDG and FAPI Tracers in Different Regions

Results: The study included 20 patients with a mean age of 50.2 ± 13.8 years ,and 60% were male. The median disease duration was 2.0 months (interquartile range [IQR], 1.0–3.0 months). During follow-up , mortality was observed in 3 of the 20 enrolled patients. Lesion volumes quantified by ^{68}Ga-FAPI-04 and ^{18}F-FDG PET/CT exhibited high concordance, with a robust positive correlation (Spearman's ρ = 0.93), indicating spatial colocalization of inflammation and fibroblast activation in the affected regions. TBRmax FAPI and TBRmean also showed a strong positive correlation (Spearman's ρ=0.92). Deceased patients demonstrated significantly elevated ^{18}F-FDG TBRmax values compared to survivors (median: 5.97 vs. 2.04, *P*=0.04), suggesting that inflammatory activity within lung lesions may contribute to the mortality risk of individuals with MDA5 DM.

Conclusion: In MDA5 DM patients, pulmonary lesions were characterized by hypermetabolism and active fibrosis. The ^{18}F-FDG TBRmax emerged as a potential prognostic marker for mortality, reflecting localized hypermetabolism in lung tissue that may indicate aggressive disease progression and correlate with poor clinical outcomes. These findings highlight the complementary roles of inflammation (FDG) and fibrosis (FAPI) imaging in characterizing disease severity. Further studies are warranted to validate the prognostic utility of TBRmax FDG and explore integrated imaging strategies for risk stratification in MDA5 DM-associated interstitial lung disease.

Disclosure: J. Li: None; **W. Wei**: None; **L. Li**: None; **W. Xu**: None; **J. Liu**: None; **S. Ye**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1957

Correlates Between Cardiovascular Risk Scores with Coronary Microvascular Function and Plaque Burden in Rheumatoid Arthritis

Katherine Zhong[1], Lauren rusnak[2], Ying Qi[3], Ilana Usiskin[4], Gregory McDermott[5], Brittany Weber[6], Marcelo DiCarli[5] and **Katherine Liao**[2], [1]Brigham and Women's Hospital, Short Hills, NJ, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, [4]Division of Rheumatology, Inflammation, and Immunity, Department of Medicine, Brigham and Women's Hospital, Boston, [5]Brigham and Women's Hospital, Boston, [6]Brigham and Women's Hospital, DEDHAM, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: A combination of traditional risk factors and chronic inflammation account for the excess cardiovascular risk (CV) observed in rheumatoid arthritis (RA), including atherosclerotic cardiovascular disease (ASCVD) and heart failure (HF). Advanced cardiac imaging methods enable quantitative measurements of CV risk while informing mechanisms for risk such as coronary microvascular disease and plaque burden. The recently published PREVENT equations enable estimates for 10-year risk for ASCVD and HF. The objective of this study was to determine the correlation between the PREVENT estimated ASCVD and HF risk with imaging measurements corresponding to mechanisms of CV risk, specifically coronary microvascular function and plaque volume in patients with RA.

Methods: We studied subjects from the Lipids, Inflammation and Cardiovascular Risk in RA (LiiRA) study (1), which enrolled RA patients, age >35, without a history of CVD, not on a statin and about to initiate a TNFi. All subjects underwent a stress myocardial perfusion PET (cardiac PET) enabling calculation of myocardial flow reserve (MFR) and assessment for coronary microvascular disease (CMD) defined as MFR< 2.5. In a long-term extension study 2+ years post-baseline, a subset of LiiRA subjects with and without MFR< 2.5 had a follow-up cardiac PET and a coronary CT angiogram to quantify plaque volume. ASCVD and HF risk was assessed for all subjects using the PREVENT equations. We tested the baseline cross-sectional correlation between the PREVENT-ASCVD and HF risk with MFR using the Spearman rank correlation test. In the subset of patients with long-term follow-up, we tested the correlation between baseline ASCVD and HF risk with MFR and plaque volume at 2+ years (Figure 1).

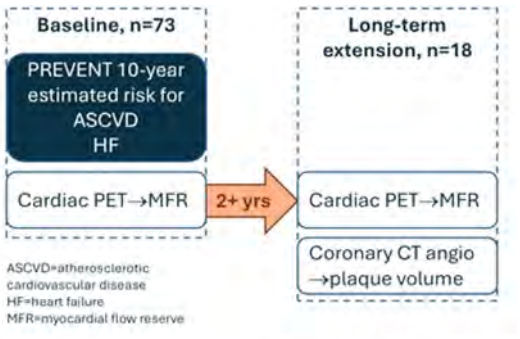


Figure 1. Overview of study design depicting available baseline and follow-up data for analyses.

Figure 1. Overview of study design depicting available baseline and follow-up data for analyses.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline clinical characteristics of the LiiRA cohort n= 73.

Clinical Characteristics	
Age, years mean (SD)	55 (11)
Female, %	82
RA duration, years mean (SD)	7.4 (8.4)
RF or anti-CCP positive, %	68
CV risk factors, %	
Hypertension	24
Known coronary artery disease	0
Diabetes	4
Ever smoker	50
BMI, mean (SD)	30 (7.2)
eGFR, median [IQR]	97 [84 – 107]
PREVENT 10-year estimated CV risk %, median [IQR]	
ASCVD	2.2 [0.95 – 5.3]
HF	2.1 [0.67 – 4.4]

Table 2. Correlation between baseline PREVENT ASCVD and HF risk with (a) MFR and (b) plaque volume at 2+ years (n=18).

(a) Outcome: MFR measured by cardiac PET

PREVENT	r_s	P-value
ASCVD	-0.35	0.152
HF	**-0.54**	**0.022**

(b) Outcome: Plaque burden measured by coronary CT angiogram

PREVENT	Total plaque volume		Total calcified plaque		Total non-calcified plaque	
	r_s	P-value	r_s	P-value	r_s	P-value
ASCVD	0.32	0.191	0.18	0.472	0.32	0.194
HF	**0.61**	**0.008**	0.38	0.124	**0.57**	**0.014**

Results: We studied n=73 subjects, 82% female, 68% seropositive; the overall cohort had low estimated ASCVD and HF risk (Table 1). At baseline a higher HF risk was cross-sectionally correlated with lower MFR (r_s=-0.31, p=0.008); no correlation was observed for the PREVENT ASCVD with MFR. In the long-term extension study, a higher HF risk remained correlated with lower MFR (r= -0.54, p=0.022) as well as higher total and non-calcified plaque volume (Table 2).

Conclusion: RA patients with a higher estimated HF risk at baseline had worse coronary microvascular function, in line with prior studies implicating coronary microvascular disease as a mechanism for HF. After 2+ years, a higher estimated HF risk at baseline correlated with worse coronary microvascular function and a higher plaque burden. These findings suggest that the PREVENT HF equations are a promising approach to identify RA patients should be considered for additional CV screening.

(1)Weber et al., *JAHA* 2024;13(9)

Disclosure: K. Zhong: None; **L. rusnak**: None; **Y. Qi**: None; **I. Usiskin**: None; **G. McDermott**: None; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **M. DiCarli**: Bayer, 2, Gilead, 5, Janssen, 2, Spectrum, 5; **K. Liao**: Merck/MSD, 2, UCB, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1958

Longitudinal analysis on imaging outcomes: should we use the individual scores from multiple readers or rather the consensus or average of readers?

Liese de Bruin[1], Floris A. van Gaalen[1], Manouk de Hooge[2], Miranda van Lunteren[1], Mary Lucy Marques[3], Monique Reijnierse[4], Roberta Ramonda[5], Inger Jorid Berg[6], Carl Turesson[7], Robert Landewé[8], Désirée Van Der Heijde[1] and Sofia Ramiro[9], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [3]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [4]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [5]Rheumatology Unit-DIMED-University of Padova ITALY, Padova, Padua, Italy, [6]6Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Nepal, [7]Lund University, Malmö, Sweden, [8]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [9]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Imaging outcomes are often evaluated using longitudinal analysis based on scores from multiple readers. However, the input into the analysis can vary from the scores of multiple individual readers to using a consensus or average across multiple readers. We assessed if this choice at the analysis stage can result in different estimates of change, we performed longitudinal analyses on different imaging outcomes in patients with early axial SpA (axSpA), using both individual reader scores and consensus scores/averages of readers.

Methods: Patients with chronic back pain (^{3}3 months; ≤2 years; onset < 45 years) from the SPondyloArthritis Caught Early cohort with a rheumatologist's diagnosis of axSpA at the 2-year follow-up were included. MRIs and radiographs of the sacroiliac joints and spine were obtained at baseline, 3 months, 1 and 2 years of follow-up and afterwards scored for inflammatory and structural lesions by 3 central readers, except for the MRI spine (2 readers). Patients included in this analysis had ≥1 score from ≥1 reader at 2-year follow-up. Each outcome was analyzed per reader and also according to the consensus (^{3}2 readers) or average across readers. Change over time was analyzed with generalized estimating equations, with 'time' as explanatory variable. For the analysis per individual reader, a multilevel analysis was performed, taking each individual reader into account. For the analysis of the consensus/average scores, each outcome was modelled according to its consensus/average score across readers.

Results: In total we analyzed 279 patients with axSpA (mean age 31 (SD 8) years; 53% males). As shown in Table 1, change estimates for continuous scores were very similar based on individual reader scores and using average scores across readers. However, larger discrepancies were found when comparing change estimates for dichotomous variables, expressed as yearly percentage change (Table 2).

Overall, the difference between the analytical choices could go in both directions. Spinal change was underestimated using the consensus scores of dichotomous variables, while change scores of the dichotomous variables in SIJ were mostly overestimated, especially of variables including erosions. In dichotomous variables, percentual differences between change scores calculated according to both analytical methods ranged from -35.4 to 37.5%.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The seemingly simple decision of how to incorporate imaging outcomes from multiple readers into a model of change over time can significantly influence the final estimates, especially when dealing with dichotomous outcomes. To minimize the risk of introducing bias at the analytical stage, multilevel analyses that account for individual reader scores are recommended, rather than relying on pre-calculated consensus scores. This analysis also shows the vulnerability of dichotomous outcomes, reinforcing the disposition to use continuous measures as outcomes in analyses.

Table 1. Mean change per year for continuous imaging outcomes over 2-years of follow-up, according to the two different analytical methods, in early axSpA patients (n = 273-278)

	Imaging outcomes	Longitudinal analysis of individual reader scores (multilevel analysis)	Longitudinal analysis of average scores across readers
		Unit change per year (95% CI)	Unit change per year (95% CI)
Sacroiliac joints	**Inflammatory lesions (MRI)**		
	SPARCC SIJ score (0-72)	-1.68 (-2.19; -1.16)	-1.69 (-2.20; -1.17)
	Structural lesions (MRI)		
	No. of fat lesions and/or erosions (0-80)	0.58 (0.38; 0.77)	0.57 (0.38; 0.77)
	No. of erosions (0-40)	0.22 (0.12; 0.31)	0.22 (0.12; 0.31)
	No. of fat lesions (0-40)	0.36 (0.20; 0.52)	0.36 (0.20; 0.52)
	No. of (partial) ankylosis (0-24)	0.04 (0.01; 0,07)	0.04 (0.01; 0.07)
	Total structural lesions (0-144)	0.61 (0.41; 0.82)	0.61 (0.40; 0.81)
	Total structural lesions without sclerosis (0-104)	0.62 (0.42; 0.82)	0.61 (0.41; 0.81)
	Structural lesions (radiograph)		
	mNY continuous grade (0-8)	0.06 (0.03; 0.10)	0.06 (0.03; 0.10)
Spine	**Inflammatory lesions (MRI)**		
	SPARCC spine score (0-414)	-0.45 (-0.76; -0.15)	-0.44 (-0.74; -0.13)
	Structural lesions (MRI)		
	No. of erosions (0-92)	0.02 (-0.01; 0.04)	0.02 (-0.01; 0.04)
	No. of fat lesions (0-92)	0.35 (0.19; 0.50)	0.35 (0.20; 0.50)
	No. of bone spurs (0-92)	0.04 (-0.00; 0.08)	0.04 (0.00; 0.08)
	No. of ankylosis (0-46)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
	Total structural lesions (0-322)	0.41 (0.23; 0.59)	0.42 (0.24; 0.59)
	No. of fat and/or erosions and/or bone spurs (0-276)	0.41 (0.23; 0.59)	0.41 (0.24; 0.59)
	Structural lesions (radiograph)		
	mSASSS (0-72)	0.08 (0.01; 0.16)	0.08 (0.0.; 0.15)

The longitudinal multilevel analysis of individual readers included scores from the individual readers, while the readers were included in the model as a level. The longitudinal analysis of average scores included average scores across readers directly into the analysis, i.e. as the outcome and therefore no further corrections for reader in the model would be possible. The total of structural lesions in the MRI of the sacroiliac joints is a sum of erosions, fat lesions, (partial) ankylosis, and sclerosis. The total of structural lesions in the MRI of the spine is a sum of erosions, fat lesions, bone spurs and ankylosis. AxSpA, axial spondyloarthritis; CI, confidence intervals; mNY, modified New York criteria; MRI, Magnetic resonance imaging; No., number; SIJ, sacroiliac joints; SPARCC, Spondyloarthritis Research Consortium of Canada.

Table 2. Mean percentual change per year for dichotomous imaging outcomes over 2 years of follow-up, according to the two different analytical methods, in early axSpA patients (n = 273-279)

	Imaging outcomes	Longitudinal analysis of individual reader scores (multilevel analysis)	Longitudinal analysis of consensus scores across readers	% difference between change estimates (consensus scores minus individual reader scores)
		% change per year (95% CI)	% change per year (95% CI)	
Sacroiliac joints	**Inflammatory lesions (MRI)**			
	Sacroiliitis (ASAS criteria), no. %	-5.78 (-8.57; -2.99)	-5.57 (-8.78; -2.36)	-3.8
	Structural lesions (radiograph)			
	mNY dichotomous, no. %	0.84 (0.05; 1.63)	1.34 (0.17; 2.52)	37.3
Spine	**Inflammatory lesions (MRI)**			
	MRI-spine positive (ASAS criteria)	-1.29 (-2.85; 0.27)	-0.71 (-2.14; 0.73)	-21.4
	Structural lesions (radiograph)			
	≥1 syndesmophyte, no. %	1.34 (0.07; 2.60)	0.99 (-0.44; 2.42)	-35.4

The longitudinal multilevel analysis of individual readers included scores from the individual readers, while the readers were included in the model as a level. The longitudinal analysis of consensus scores included consensus scores across readers directly into the analysis, i.e. as the outcome and therefore no further corrections for reader in the model would be possible. ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; BME, bone marrow edema; CI, confidence intervals; mNY, modified New York criteria; MRI, Magnetic resonance imaging; No., number; SPARCC, Spondyloarthritis Research Consortium of Canada.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. de Bruin: None; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **M. de Hooge**: UCB pharma, 2; **M. van Lunteren**: None; **M. Marques**: Novartis, 2, 6; **M. Reijnierse**: None; **R. Ramonda**: None; **I. Berg**: None; **C. Turesson**: AbbVie/Abbott, 1, 6, Nordic Drugs, 2, 6, Novartis, 1, 6; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1959

The development and validation of a Diagnostic Ultrasound Enthesitis Score (DUET) for Psoriatic Arthritis

Lihi Eder[1], Ricardo Acayaba de Toledo[2], Catherine Bakewell[3], Philippe Carron[4], Basant Elnady[5], Amir Haddad[6], Arthur Kavanaugh[7], Fahmeen J. Afgani[8], Arnon Katz[9], Minna Kohler[10], josefina marin[11], Nam Nguyen[12], Adrien NZEUSSEU TOUKAP[13], Ari Polachek[14], Ernesto Rodriguez[15], Marcos Rosemffet[16], Abha Singh[17], Maria S. Stoenoiu[18], Agnes Szentpetery[19], Iliara Tinazzi[20], Janeth Yinh[21], Mu Yang[22], Richard Cook[22], Gurjit Kaeley[23] and Sibel Aydin[24], [1]University of Toronto, Toronto, ON, Canada, [2]Centro Integrado de Pesquisas (CIP) do Hospital de Base de São José do Rio Preto, São José do Rio Preto, Brazil, [3]Intermountain Healthcare Medical Group, Salt Lake City, [4]Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [5]Research Centre at Al Hada Armed Forces Hospital, Cairo, Egypt, [6]Carmel Medical Center, Haifa, Israel, [7]University of California, San Diego, School of Medicine, San Diego, CA, [8]Women's College Hospital, Toronto, Canada, [9]GRAPPA, Seattle, [10]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [11]Hospital Universitario Rey Juan Carlos, Madrid, Spain, [12]University of Toronto, Toronto, Canada, [13]Cliniques Universitaires Saint-Luc, St.-Lambrechts-Woluwe, Belgium, [14]Rheumatology Institute of Beilinson Hospital, Petah Tikva, Israel, [15]Florida Medical Clinic, Tampa, [16]Instituto de Rehabilitación Psicofísica, Capital Federal, Argentina, [17]Altman Clinical and Translational Research Institute, University of California San Diego, San Diego, CA, [18]Cliniques Universitaires Saint-Luc, Brussels, Belgium, [19]Uppsala University Hospital, Djursholm, Sweden, [20]Ospedale Sacro Cuore-Don Calabria, Verona, Italy, [21]Massachusetts General Hospital, Boston, MA, [22]University of Waterloo, Waterloo, Canada, [23]UF COM-J, Ponte Vedra Beach, FL, [24]Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Enthesitis is a key lesion in psoriatic arthritis (PsA). The Diagnostic Ultrasound Enthesitis Tool (DUET) study aimed to develop and validate a novel sonographic scoring system for enthesitis to aid PsA diagnosis.

Methods: We prospectively enrolled patients with early PsA, psoriasis alone, and people with non-inflammatory musculoskeletal symptoms as controls, across 17 centers. Participants underwent ultrasound assessment of 16 entheseal sites in the upper and lower extremities, performed by local sonographers. Images were centrally reviewed by 3 readers to derive a consensus score for inflammatory lesions (hypoechogenicity [0–1], thickening [0–1], power Doppler [PD, 0–3]) and structural lesions (calcification [0–3], enthesophyte [0–3], erosion [0–1]).

Using a stepwise approach with logistic regression models stratified by age, we identified optimal combinations of lesions and their weighting, and entheseal sites that maximized the ability to distinguish PsA from controls. Data from the discovery cohort, supplemented by an existing validation dataset, were used to determine cut-off points that optimize sensitivity while

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

maintaining specificity above 70%. We further evaluated the association between the DUET score and PsA disease activity measures.

Results: We analyzed 213 patients with PsA (mean duration 1.9±3.4 yrs), 100 with psoriasis and 106 controls. The mean age was 49.9±14.6 and 53.7% were females. Tenderness at ≥1 entheseal site was observed in 70% of PsA patients, 49% of controls and 33% of psoriasis (SPARCC score: PsA: 3.2, control: 2.5, psoriasis: 1.2). Initial evaluation of 4 inflammatory and 5 structural sub-scores across 16 entheseal sites yielded 48 candidate scores. Stratification by age improved discriminative performance. The best performing score (DUET score), comprising inflammatory (hypoechogenicity + thickening + 2×PD) and structural (enthesophyte + 3×erosion, **Fig. 1**) sub-scores at the Achilles, patellar tendon (patellar insertion), and triceps tendon, achieved an overall AUC of 0.65.

Age-specific cut-offs (age cut off 55) yielded specificity of 73–74% and sensitivity of 47–49% (**Fig. 2**). In the validation cohort (101 PsA, 69 controls), specificity improved to 74–100% with comparable sensitivity (49–52%). Sensitivity increased up to 63% in patients with tender entheseal sites (**Fig. 3**). The mean DUET score was significantly higher in PsA compared with controls and psoriasis (9.07 vs. 5.48 and 6.38, respectively; $p < 0.01$ for both, **Fig. 3**). Scores were elevated among obese patients, those with tender entheses, and those about to escalate PsA therapy.

Conclusion: DUET is a newly developed sonographic tool that may assist in the diagnosis of PsA, particularly among individuals with tender entheseal sites. The findings suggests that large joint enthesitis is not a universal feature of early PsA.

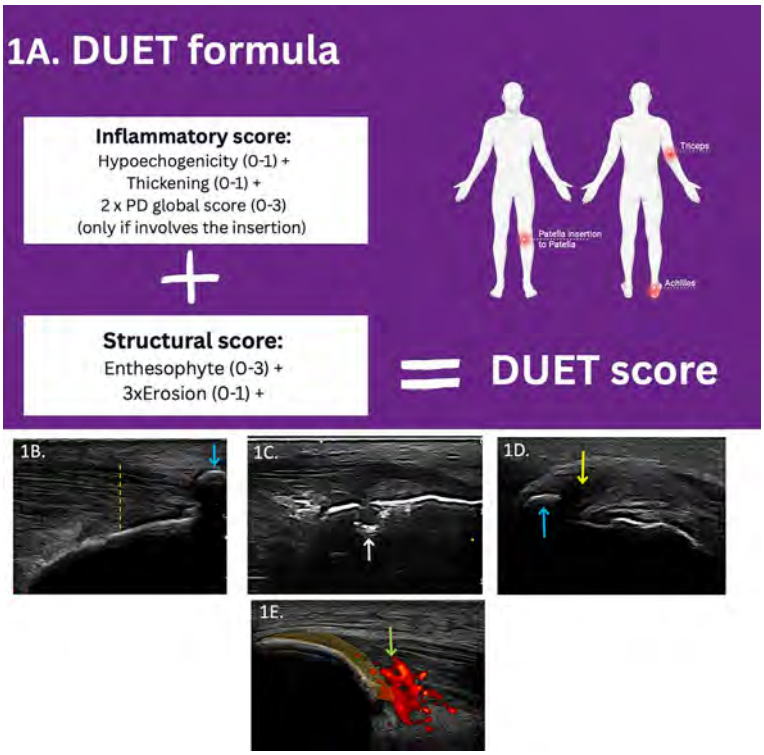


Figure 1: A summary of the DUET score. 1A. The DUET score formula is calculated based on a total of 6 entheseal sites: the Achilles and triceps insertions, and the patellar insertion to the patella. 1B–E. Depiction of selected elementary lesions and their corresponding DUET scores: 1B. Achilles tendon insertion showing thickening (1 point, vertical orange line) and enthesophyte (3 points, blue arrow); 1C. Achilles tendon insertion with erosion (1 point × 3, white arrow); 1D. Triceps tendon insertion with hypoechogenicity (1 point, yellow arrow) and enthesophyte (3 points, blue arrow); 1E. Patellar ligament insertion to the patella showing Doppler signal. The Doppler signal involves the area close to the bone (depicted by the orange marking), but the grading also considers Doppler intensity beyond this marking (3 points × 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

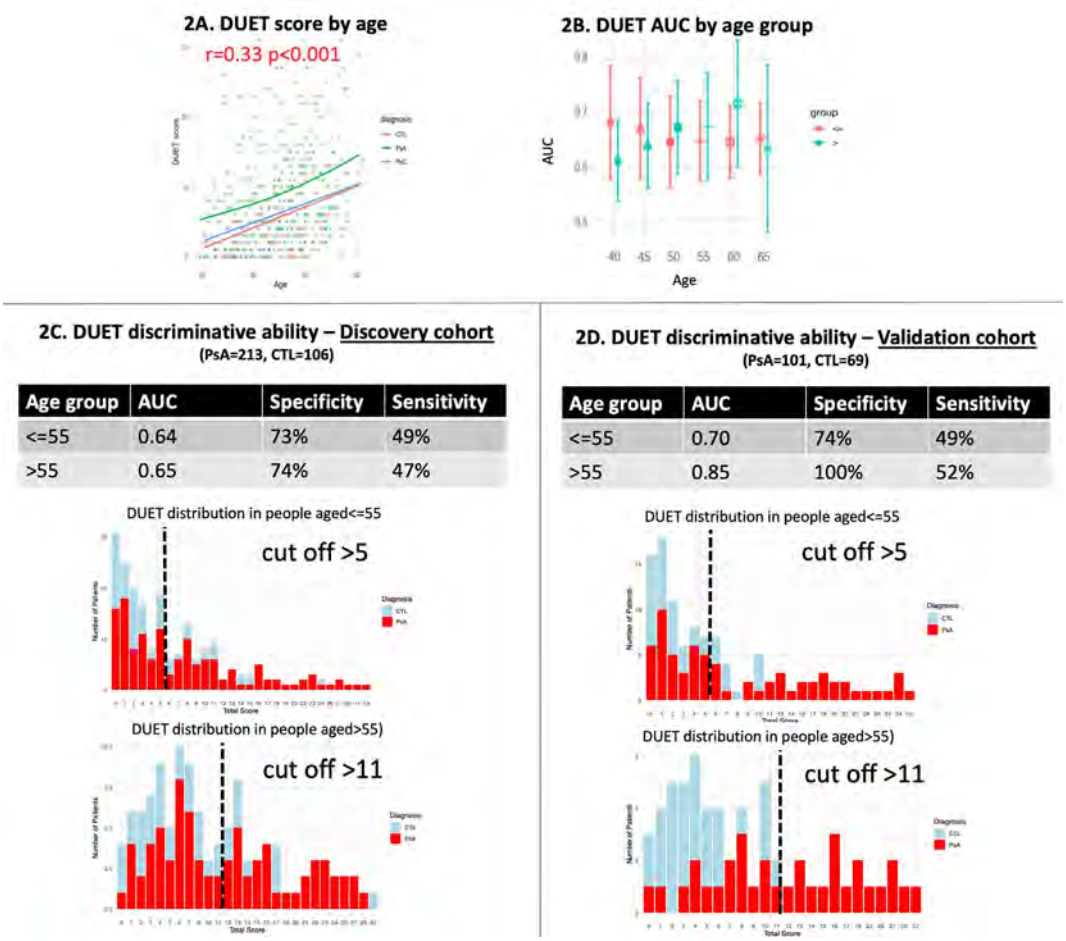


Figure 2: Performance of the DUET score. 2A. Correlation of the DUET score with age across disease groups; 2B. Discriminative ability of the DUET score (by AUC) across various age categories; 2C–2D. Sensitivity, specificity, AUC, and distribution of DUET scores in PsA and controls for the selected cut-off points among individuals aged ≤55 years and >55 years in the discovery (Fig. 2C) and validation (Fig. 2D) cohorts.

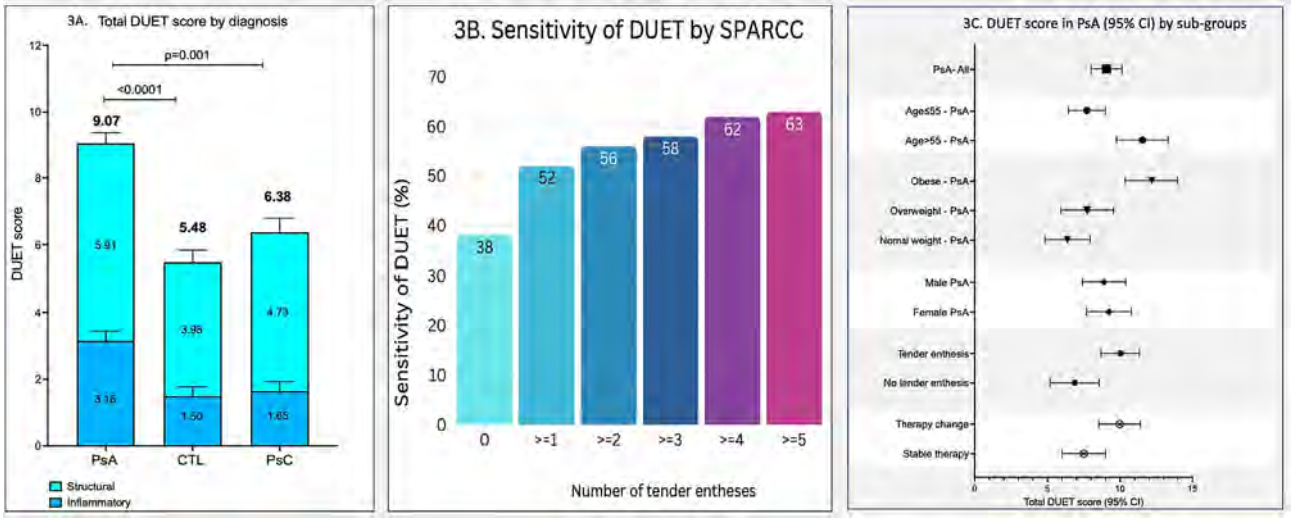


Figure 3: Correlation between the DUET score and clinical measures. 3A. Mean DUET score (by inflammatory and structural sub-scores) is higher in PsA compared to controls and psoriasis; 3B. DUET sensitivity by the number of tender entheses; 3C. DUET sub-score by PsA sub-groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **R. Acayaba de Toledo**: Abbvie, 5, 6, GSK, 6, Johnson & Johnson, 6, Novartis, 6, UCB, 6; **C. Bakewell**: AbbVie/Abbott, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Johnson & Johnson, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **P. Carron**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Johnson & Johnson, 2, 6, Novartis, 2, 6, UCB, 2, 6; **B. Elnady**: None; **A. Haddad**: None; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2; **F. Afgani**: None; **A. Katz**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **j. marin**: None; **N. Nguyen**: None; **A. NZEUSSEU TOUKAP**: Amgen, 5, Eli Lilly, 1, 6, Janssen, 1, 5, 6, Novartis, 6; **A. Polachek**: None; **E. Rodriguez**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Eli Lilly, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6; **M. Rosemffet**: None; **A. Singh**: Sonoma Biotherapeutics, 5; **M. Stoenoiu**: AbbVie/Abbott, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Sanofi, 5, 6, UCB, 5, 6; **A. Szentpetery**: None; **I. Tinazzi**: None; **J. Yinh**: Janssen, 2, Springer, 9; **M. Yang**: None; **R. Cook**: None; **G. Kaeley**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Janssen, 5, Novartis, 5; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6.

Abstract Number: 1960

Item Response Theory to Develop an Ultrasound Composite Score for Knee Osteoarthritis Assessment

Liubov Arbeeva[1], Carolina Alvarez[2], Jonathan Samuels[3], Janice Lin[4], Minna Kohler[5], Catherine Bakewell[6], Todd Schwartz[7] and Amanda Nelson[8], [1]University of North Carolina, Chapel Hill, Carrboro, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]NYU Langone, Rye Brook, NY, [4]Stanford University, Palo Alto, CA, [5]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [6]Intermountain Healthcare, Salt Lake City, UT, [7]University of North Carolina-Chapel Hill, Chapel Hill, NC, [8]University of North Carolina at Chapel Hill, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Semi-quantitative scoring systems have long been used for radiographic findings in osteoarthritis (OA), but limited work has utilized ultrasound (US). The aim of this study was to utilize a rigorous approach based on factor analysis and nonparametric item response theory (IRT) to determine whether a single US summary score is appropriate for knee OA assessment.

Methods: Data were from Johnston County Health Study (JoCoHS) participants who underwent standardized radiography and ultrasonography of bilateral knees (PMID39989271). Symptomatic knee OA (sxKOA) was defined as a Kellgren-Lawrence grade of 2 or more in a knee with self-reported symptoms. A series of iterative procedures, i.e., Principal Components Analysis (PCA), Parallel Analysis (PA), Item Cluster Analysis (ICA), Very Simple Structure analysis (VSS), Confirmatory Factor Analysis (CFA), Mokken Scaling Analysis (MSA), and Classical Test Theory, were used to derive final items and subscales from US features (**Table 1**). In CFA, we considered the comparative fit index (CFI), the Tucker–Lewis index (TLI), and the root mean square error of approximation (RMSEA). MSA examines coefficients of homogeneity for items (H_i) and scale (H) and explores possible dimensionality solutions. Monotonicity, scalability, and invariant ordering of any determined subscales were also assessed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Complete data for 13 US features were available for 824 of 902 JoCoHS participants (91%); 33% were male, 39% had sxKOA, mean age 55 ± 10 years and mean BMI 33 ± 8 kg/m^2. After exclusions based on test diagnostics and outliers, 791 participants and 12 items (all but double contour) remained for analyses. Items with the lowest H_i were removed one by one, and the analyses were repeated until H_i and H were above 0.3. H was 0.356 when all 5 problematic items were excluded (7 items remained, **Table 1**).

Table 1. US features, item inclusion/exclusion and subscale assignment

Subscale	US feature	Reason for item exclusion*
1	Grayscale effusion/synovitis	--
1	Grayscale synovitis	--
1	Grayscale effusion	--
Excl*	Power Doppler for synovitis	Coefficient of homogeneity < 0.3
2	Osteophytes, medial	--
2	Osteophytes, lateral	--
Excl*	Meniscal extrusion, medial	Automatic item selection algorithm
Excl*	Meniscal extrusion, lateral	Coefficient of homogeneity < 0.3
2	Cartilage damage, medial	--
2	Cartilage damage, lateral	--
Excl*	Popliteal cyst	Coefficient of homogeneity < 0.3
Excl*	Calcium crystal deposition	Coefficient of homogeneity < 0.3
Excl*	Double contour sign	>95% responses in a single category (i.e., rare finding)

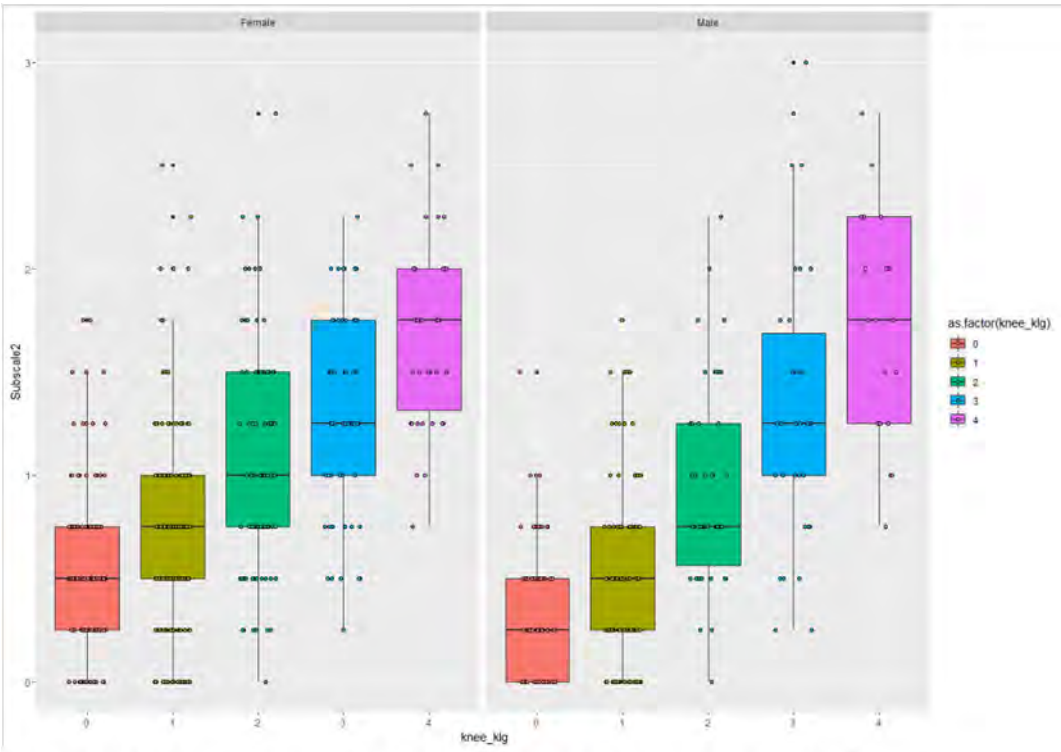


Figure 1. Subscale 2 score by KL score (0-4) at the knee, separately for female (left) and male (right) participants

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The PA, ICA, and VSS analysis on 8 and 7 items suggested 2 factors, but were inconsistent regarding the inclusion of medial meniscal extrusion. As the PCA loadings for this item were low, and its inclusion reduced reliability, we determined that the optimal number of items was 7, and the number of subscales was two (**Table 1**). The 2-factor CFAs of the 7-item model produced CFI and TLI = 0.99; RMSEA = 1.16. The coefficients of homogeneity were 0.747 for Subscale 1 (3 items) and 0.452 for Subscale 2 (4 items).

Since only Subscale 2 met all criteria, a composite score was derived for the second subscale only, demonstrating a linear relationship with KL grade for both females and males (**Figure 1**).

Conclusion: A robust composite score could be applied in clinical and research settings where only US is available or is preferred. The 4 US features in Subscale 2 form a moderate to strong Mokken scale, enabling persons to be ordered using a summary score. Future work will investigate Subscale 1 and the reason for MSA assumptions violation given that the three grayscale US features form a strong Mokken scale (H >=0.5). These results demonstrate that US summary score development and validation can benefit from both CFA and nonparametric IRT. Parametric IRT will be used to diagnose fit further and for scoring algorithm development.

Disclosure: L. Arbeeva: None; **C. Alvarez**: None; **J. Samuels**: None; **J. Lin**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **C. Bakewell**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 2, 6, UCB, 2, 6; **T. Schwartz**: None; **A. Nelson**: Novo Nordisk, 1.

Abstract Number: 1961

Clinical Utility and Patient Experience of Ultrasound-Guided Synovial Biopsy in Refractory Arthritis: A Case Series from a Secondary Care Center

Maria Beatriz Paredes Romero[1], Elisabet Castañeda Estavez[2], Martina Steiner[3], Marco Algarra- San José[3], Ana Valeria Acosta[3], Tatiana Cobo-Ibáñez[4], Isabel De la Cámara[3], Ana Victoria Esteban Vázquez[5], Patricia Richi[3], Maria Liz Romero-Bogado[3], Laura Trives[5], Cristina Vergara-Dangond[4], Jorge palomar-Ramos[3] and Santiago Muñoz[5], [1]Infanta Sofia University Hospital, Madrid, Spain, [2]Hospital Universitario Infanta Sofía, Madrid, Spain, [3]Infanta Sofía University Hospital, Madrid, Spain, [4]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, San Sebastian de Los Reyes, Madrid, Spain, [5]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Diagnosing arthritis remains challenging in a subset of patients despite advances in imaging, serological markers, and clinical scoring systems. Ultrasound-guided synovial biopsy (USG-SB) stands as a potentially valuable tool in clarifying diagnoses and guiding treatment in atypical or refractory joint presentations.

The objective is to evaluate the clinical utility and patient-reported outcomes (PROMs) of USG-SB in patients with refractory arthritis in a real-world, secondary care setting.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Case No.	Age	Sex	Clinical history	Main diagnosis	Pattern	Krenn score	Final diagnosis
1	50	M	Psoriasis, IBD	Undifferentiated arthritis	Oligoarticular	3	Degenerative arthritis
2	45	M	AR (FR 85, ACPAs>320)	RA	Polyarticular	1	Non-active RA
3	45	F	AR (FR 58, ACPAs 7)	RA	Polyarticular	8	Active RA
4	45	F	Psoriasis, PsA	PsA	Oligoarticular	5	Active PsA
5	25	F	None	Undifferentiated arthritis	Oligoarticular	0	Mechanical arthritis
6	55	F	RA (FR-, ACPAs-)	Seronegative RA	Polyarticular	5	Active RA (CD20-)
7	34	M	Psoriasis, PsA	PsA	Polyarticular	5	Active PsA

Figure 1. Clinical and histological features of patients undergoing ultrasound-guided synovial biopsy (SGB). RA: Rheumatoid arthritis; PsA: Psoriatic arthritis; RF: Rheumatoid factor; ACPA: Anti-cyclic citrullinated peptide antibodies

Methods: We conducted a case series of seven patients who underwent knee USG-SB based on clinical indication by the treating rheumatologist. Histological samples were evaluated using the Krenn synovitis score, with scores < 5 indicating non-inflammatory or degenerative pathology, and scores ≥5 suggestive of active rheumatic disease. PROMs were assessed 7–10 days post-procedure via structured questionnaire.

Results: USG-SB provided diagnostic clarification or therapeutic guidance in 5 of 7 cases (71%). Inflammatory histological features (Krenn ≥5) were found in 4 patients and led to treatment adjustments in 3 cases. In one case, CD marker analysis guided selection of a biologic agent. Two patients were reclassified as having non-inflammatory arthritis, avoiding unnecessary immunosuppressive treatment.

PROMs showed that 6 out of 7 patients (86%) reported clear and sufficient pre-procedure information, and 6 out of 7 experienced minimal or no pain during the biopsy, with a median visual analogic score (VAS) of 0. Median VAS in the first 24 hours was 1. No patients reported functional limitations or infection at the puncture site. Most patients (86%) resumed normal activities within 3 days. All patients rated healthcare staff attention as "excellent," and 6 out of 7 (86%) indicated they would repeat the procedure if needed.

Conclusion: USG-SB is a safe, well-tolerated, and clinically useful procedure in patients with refractory arthritis. It contributed to diagnostic clarification and therapeutic decision-making in most cases, with minimal discomfort reported by patients. Its implementation in secondary care centers may help expand access to precision rheumatologic care.

Disclosure: M. Paredes Romero: None; **E. Castañeda Estavez**: None; **M. Steiner**: None; **M. Algarra- San José**: None; **A. Acosta**: None; **T. Cobo-Ibáñez**: None; **I. De la Cámara**: None; **A. Esteban Vázquez**: None; **P. Richi**: None; **M. Romero-Bogado**: None; **L. Trives**: None; **C. Vergara-Dangond**: None; **J. palomar-Ramos**: None; **S. Muñoz**: Janssen, 1, 2, 5, 6, 7.

Abstract Number: 1962

Imaging findings in patients with enteropathic spondyloarthritis

Marika Bodnárová[1], Lucia Ondrejčáková[2], Tomáš Grega[3], Ladislav Šenolt[4], Karel Pavelka[5] and Kristýna Bubová[1], [1]Institute of Rheumatology, Prague, Czech Republic, [2]Institute of Rheumatology, Prague, Hlavni mesto Praha, Czech Republic, [3]Military University Hospital Prague, Prague, [4]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [5]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

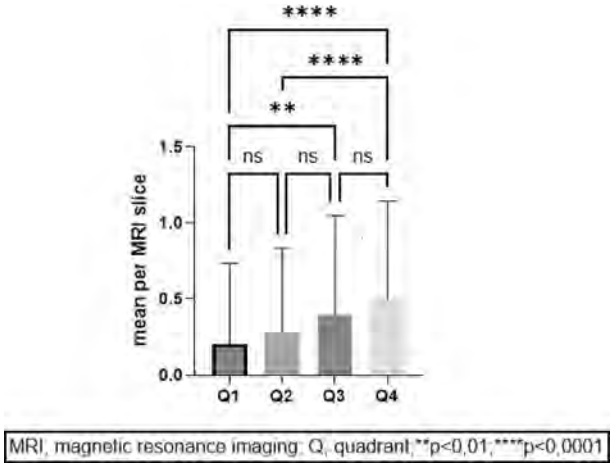
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Enteropathic spondyloarthritis (eSpA) is a subtype of SpA associated with inflammatory bowel disease (IBD). Sacroiliac joints (SIJs) involvement is common in eSpA but often clinically silent, contributing to diagnostic delay. Magnetic resonance imaging (MRI) enables detection of early inflammatory and structural changes, yet lesion patterns specific to eSpA insufficiently characterized. This study aimed to assess active and chronic inflammatory lesions on SIJ MRI.

Methods: We included 107 patients: 46 with IBD and 51 with axSpA with suspected eSpA, plus 10 with previously established eSpA. All underwent SIJ MRI; patients with MRI-confirmed sacroiliitis also underwent SIJs radiographs, scored using Bennett's criteria (stage ≥2 sacroiliitis defined as positive for uni/bilateral involvement). MRI was assessed using the SPARCC scoring system for both active and structural lesions. The distribution of defined lesions were examined in four quadrants (scores ranging from 0-2 per quadrant on each sides of SIJ, expressed as mean (±SD)) and across slices. Two experienced readers, blinded to clinical data, independently scored all images; averaged scores were used. Cohen's kappa showed high inter-reader reliability (BME: 0.8; fat metaplasia: 0.83; erosions: 0.88; backfill: 0.65; ankylosis: 0.84).



Difference in bone marrow edema distribution

Figure 2A: Difference in fat metaplasia distribution

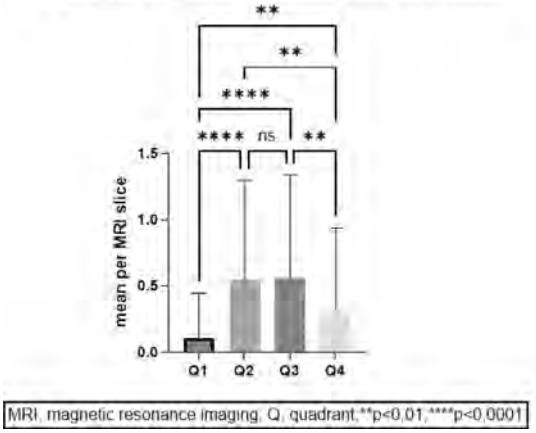
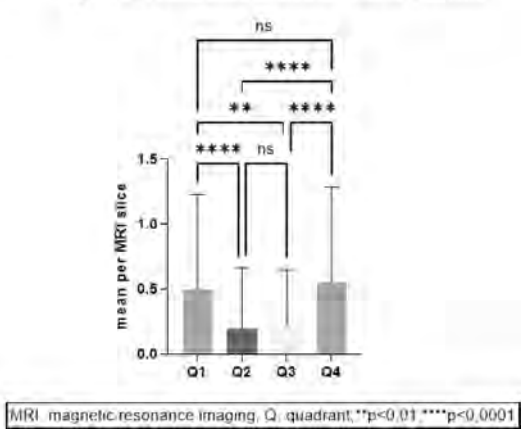
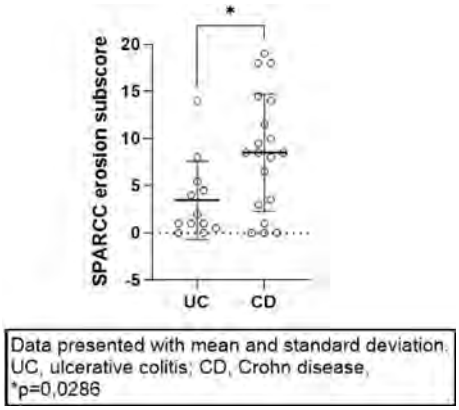


Figure 2B: Difference in distribution of erosions



Difference in fat metaplasia distribution, Difference in distribution of erosions

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Presence of erosions in patients with SpA/IBD: ulcerative colitis vs. Crohn disease

Results: Among 97 evaluated patients, 26 (27%) met classification criteria for eSpA. Including the 10 pre-diagnosed patients, 36 were analyzed: 20 (56%) had radiographic axSpA, 11 (31%) had non-radiographic axSpA, and 5 (14%) had unknown status due to missing x-ray data. Radiographic sacroiliitis was bilateral in 18 (58%), unilateral in 8 (26%), and absent (stage < 2) in 5 (16%). MRI revealed distinct quadrant-level lesion patterns. Bone marrow edema (BME) was significantly more prevalent in Q4 compared to Q1 and Q2 (0.5 (± 0.6) vs. 0.2 (±0.5) and 0.3 (±0.6), p< 0.0001 and < 0.0001, respectively) and in Q3 compared to Q1 (0.4 (±0.7) vs. 0.2 (±0.5), p=0.0023), with no significant difference between Q4 and Q3 (Figure 1). Fat metaplasia was significantly more frequent in Q2 and Q3 compared to Q1 and Q4 (0.5 (±0.8) and 0.6 (±0.8) vs. 0.1 (±0.3) and 0.3 (±0.6) SPARCC SIJ structural score, p< 0.0001, p=0.0051, p< 0.0001, p=0.0033, respectively) and between Q1 and Q4 (0.1 (±0.3) and 0.3 (±0.6), p=0.0043) (Figure 2). Erosions were significantly more frequent in Q1 and Q4 compared to Q2 and Q3 (0.5 (±0.7) and 0.6 (±0.7) vs. 0.2 (±0.5) and 0.2 (±0.4), p< 0.0001, p=0.0030, p< 0.0001, p< 0.0001, respectively) (Figure 2). No significant differences were observed in lesion distribution across MRI slices. Patients with Crohn's disease exhibited significantly more erosions than those with ulcerative colitis (8.5 (±6.2) vs. 3.5 (±4.1), p=0.0286) (Figure 3).

Conclusion: Most patients with eSpA demonstrate bilateral SIJ involvement on radiographs. MRI revealed distinct patterns of inflammatory and structural lesions, with quadrant-specific predilections for BME, fat metaplasia, and erosions. Crohn's disease was associated with a higher burden of erosive changes compared to ulcerative colitis, suggesting phenotypic heterogeneity in musculoskeletal manifestations of eSpA.

Supported by: SVV 260 683, GAUK 310525

Disclosure: M. Bodnárová: None; **L. Ondrejčáková**: None; **T. Grega**: None; **L. Šenolt**: None; **K. Pavelka**: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **K. Bubová**: None.

Abstract Number: 1963

Efficacy of Apremilast in Patients With Psoriatic Arthritis and Pre-existing Dactylitis: Dynamic Contrast-Enhanced MRI Results From the Phase 4 MOSAIC Study

mikael Boesen[1], Philip J. Mease[2], Walter P Maksymowych[3], Robert G. W. Lambert[4], Olga Kubassova[5], John Carrino[6], Kamyar Moradi[7], Michael R. Bubb[8], Guillermo Valenzuela[9], Kurt de Vlam[10], Jyotsna Reddy[11], Siddharth Chaudhari[11], Zhenwei Zhou[11] and Mikkel Ostergaard[12], [1]Copenhagen University Hospital, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Washington, Seattle, WA, [3]Department of Medicine, University of Alberta, Edmonton, AB, Canada, [4]University of Alberta, Department of Radiology & Diagnostic Imaging, Edmonton, AB, Canada, [5]Image Analysis Group, Philadelphia, PA, [6]Department of Radiology and Imaging, Hospital for Special Surgery, New York, NY, [7]Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD, [8]University of Florida, Gainesville, FL, [9]Integral Rheumatology & Immunology Specialists, Plantation, FL, [10]Department of Rheumatology, UZ Leuven, Leuven, Belgium, [11]Amgen Inc., Thousand Oaks, CA, [12]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

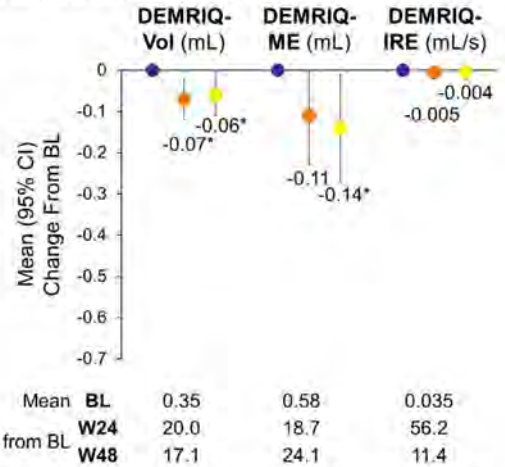
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Primary results from the phase 4 MOSAIC trial demonstrated that apremilast (APR) improved inflammation in patients (pts) with PsA based on PsA MRI scoring of the hand. Pts also underwent optional dynamic contrast-enhanced MRI (DCE-MRI), which evaluated perfusion within soft tissues and bone marrow of the hand to estimate the degree of joint and soft tissue inflammation in dactylitis, a hallmark of PsA characterized by swelling and inflammation of digits. We report the efficacy of APR in pts from the MOSAIC trial with pre-existing dactylitis.

Methods: MOSAIC (NCT03783026) was a multicenter, single-arm, open-label study that evaluated pts with PsA (duration: 3 mo to 5 y; met CASPAR criteria) who received oral APR 30 mg twice daily for up to 48 weeks. Conventional MRIs of pts with clinically reported dactylitis at baseline (BL; digit not specified) were read by an independent radiologist to determine the most affected dactylitic finger. Another 2 independent readers, blinded to time point and clinical information, reviewed DCE-MRI using the Dynamic Contrast-Enhanced MRI Quantification (DEMRIQ) method; the volume of contrast-enhanced voxels in dactylitic fingers and joints were calculated: volume of enhancement (DEMRIQ-Vol), volume of enhancement × mean maximum enhancement (DEMRIQ-ME), and volume of enhancement × mean initial rate of enhancement (DEMRIQ-IRE) within each region of interest around each digit and joint. We report changes in these 3 DCE-MRI outcomes

Figure 1 DCE-MRI outcomes of the MRI-determined most-affected dactylitic finger joint in patients with dactylitis at W24 (n=32) and W48 (n=23)



		DEMRIQ-Vol (mL)	DEMRIQ-ME (mL)	DEMRIQ-IRE (mL/s)
Mean	BL	0.35	0.58	0.035
% Change from BL	W24	20.0	18.7	56.2
	W48	17.1	24.1	11.4

Asterisks indicate statistical significance based on *P* values <0.05. Most-affected joints included distal interphalangeal joints (n=12), proximal interphalangeal joints (n=15), and metacarpophalangeal joints (n=5).
BL, baseline; CI, confidence interval; DCE-MRI, dynamic contrast–enhanced magnetic resonance imaging; DEMRIQ-IRE, DEMRIQ–initial rate of enhancement; DEMRIQ-ME, DEMRIQ–maximum enhancement; DEMRIQ-Vol, DEMRIQ-volume; W, week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

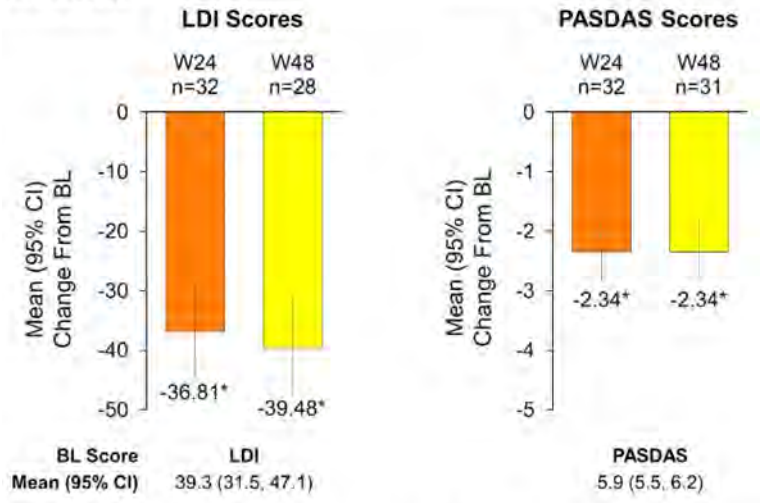
in the MRI-determined most-affected joint of the dactylitic finger, as well as in clinical disease activity measured by the Leeds Dactylitis Index (LDI) and the PsA Disease Activity Score (PASDAS) at Week (W) 24 and W48 (clinical assessments not blinded to time point).

Results: Thirty-two pts in MOSAIC had both BL dactylitis and W24 imaging (mean age: 41.6 y; mean PsA duration: 1.9 y; moderate Clinical Disease Activity Index for PsA [cDAPSA] score [>13 to ≤27]: 46.9%; high cDAPSA score [>27]: 50.0%); 23 had W48 imaging. Statistically significant decreases in DEMRIQ-Vol (W24 and W48) and DEMRIQ-ME (W48) were observed for the MRI-determined most-affected joint ($P< 0.05$; **Figures 1, 2**). DEMRIQ-IRE showed no significant change. Statistically significant decreases in the mean (95% CI) change from BL were observed for clinical outcomes at W24 (LDI: -36.8 [-44.4, -29.2]; PASDAS: -2.3 [-2.8, -1.8]) and W48 (LDI: -39.5 [-47.8, -31.1]; PASDAS: -2.3 [-2.9, -1.8]; **Figure 3**). At W48, 26/28 pts (92.9%) had an LDI of 0, and 13/31 pts (41.9%) had PASDAS < 3.2 (indicating minimal disease activity). Subgroup analyses by BL disease activity will be presented.

Figure 2. Representative images of DCE-MRI of the hand and wrist of a patient with dactylitis at baseline, W24, and W48

This series of images shows MRI scans with superimposed maps of maximum enhancement. The colors indicate the degree of perfusion or inflammation within individual tissues. Those tissues with the highest degree of perfusion as well as blood vessels present in white-yellow colors; tissues with lower degree of perfusion are shown in redder colors, as per the color scale on the left of the image. All colors and measurements are normalized between the 3 exams showing significant reduction in the volume and degree of inflammation.
DCE-MRI, Dynamic Contrast-Enhanced Magnetic Resonance Imaging; W, week.

Figure 3. Mean change from baseline in LDI and PASDAS in patients with dactylitis at W24 and W48



Asterisks indicate statistical significance based on 95% CI. BL, baseline; CI, confidence interval; LDI, Leeds Dactylitis Index; PASDAS, Psoriatic Arthritis Disease Activity Score; W, week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: There were significant reductions in DEMRIQ-ME and DEMRIQ-Vol with APR at W24 and/or W48; DEMRIQ-IRE did not show significant changes. Clinical outcomes significantly improved. DCE-MRI outcomes suggest increased capillary permeability, synovial and joint capsule volume, engorged microvasculature, and delayed contrast washout within dactylitic finger joints in PsA that improve at different rates after APR treatment and highlight the potential of using different DCE-MRI parameters to understand, quantify, and monitor the complex inflammatory load and response to treatment in pts with PsA and dactylitis.

Disclosure: m. Boesen: AbbVie, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Image Analysis Group, 2, 6, 11, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **W. Maksymowych**: AbbVie, 2, 5, 6, 12, Educational grants, Bristol-Myers Squibb(BMS), 2, 5, 6, CARE Arthritis, 12, Chief Medical Officer, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, educational grants, Pfizer, 2, 5, 6, 12, educational grants, UCB Pharma, 2, 5, 6; **R. Lambert**: AbbVie, 2, CARE Arthritis and Image Analysis Group, 2; **O. Kubassova**: AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, Ferring, 2, 5, 6, Image Analysis Group, 3, 11, Medipost, 2, 5, 6, Takeda, 2, 5, 6, Werfen, 2, 5, 6; **J. Carrino**: Arthritis & Rheumatology, 12, Editorial Board, Carestream, 4, Cartilage Imaging, 12, Editorial Board, Covera, 2, Image Analysis Group, 4, Image Biopsy Lab, 4, Radiology, 12, Editorial Board; **K. Moradi**: None; **M. Bubb**: AbbVie/Abbott, 5, Alexion, 5, Amgen Inc., 5, Argenyx, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 5, Priovant, 5, Restem, 5, UCB, 5; **G. Valenzuela**: AbbVie, 1, 2, 2, 6, 6, Alexion, 1, 2, Amgen, 1, 2, 6, Artiva Biotherapeutics, 2, 5, AstraZeneca, 6, Boehringer-Ingelheim, 1, 2, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 1, 2, 6, Centocor, 6, Eli Lilly, 1, 2, 6, Esaote, 1, Exagen, 1, 2, Genentech, 1, 2, 6, Gilead, 1, 2, Global Healthy Living Foundation, 1, 2, Horizon, 1, 2, 6, Image Analysis Group, 1, Janssen, 1, 2, 6, Mallinckrodt, 5, 6, Merck, 1, 2, Novartis, 1, 2, 6, Pfizer, 1, 2, 6, Pharmacia, 1, 2, 6, Radius, 6, Regeneron, 1, 2, 6, Sandoz, 1, 2, Sanofi, 1, 2, 6, Takeda, 6, Theramex, 6, UCB, 1, 2, 6, Vividion therapeutics, 1, 2; **K. de Vlam**: AbbVie, 2, 6, Alphasigma, 2, 6, Amgen, 2, 6, BMS, 2, 6, Galapagos, 2, 6, J&J, 2, 6, Lilly, 2, 6, MoonLake, 2, Novartis, 2, 6, Roche, 2, Sandoz, 2, UCB, 6; **J. Reddy**: Amgen Inc., 3, 11; **S. Chaudhari**: Amgen Inc., 3, 11; **Z. Zhou**: Amgen Inc., 3, 11; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6.

Abstract Number: 1964

Performance of Artificial Intelligence-Based Salivary Gland Ultrasound in Sjögren Syndrome

Otto Olivas[1], Mónica García-Sevilla[2], Lucía Cubero[2], Javier Pascau[2] and Esperanza Naredo[3], [1]Department of Rheumatology and Joint and Bone Research Unit. Fundación Jiménez Díaz University Hospital and Health Research Institute FJD-UAM, Madrid, Spain, Madrid, Madrid, Spain, [2]Department of Bioengineering, Carlos III University of Madrid, Leganes, Madrid, Spain and Health Research Institute Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [3]Department of Rheumatology and Joint and Bone Research Unit. Fundación Jiménez Díaz University Hospital and Health Research Institute FJD-UAM, Madrid, Spain, MADRID, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: To develop a deep learning model for classifying ultrasound images of salivary glands (SG) [parotid (PG) and submandibular (SMG)] based on the Outcome Measures in Rheumatology (OMERACT) 0-3 semiquantitative scoring system for B-mode ultrasound-assessed parenchymal abnormalities in SG in Sjögren syndrome (SjS) (Figure 1)

Methods: For training, we used 3 datasets of SG (PG and SMG) ultrasound images representative of the OMERACT scores: 1) 225 images from 150 suspected or confirmed SjS patients acquired with different ultrasound systems across 4 European centers (https://www.frontiersin.org/articles/10.3389/fmed.2020.581248/full); 2) 80 images from 20 SjS patients provided by a European center; 3) Of 39 SjS patients and 10 controls, 6 images of each acquired by 2 experts with 2 systems (a high-end and a wireless handheld device) in a European center (1176 images). We used a ResNet18 architecture, which was pre-trained on ImageNet and then fine-tuned for this task. The model was trained hierarchically: initially classifying broad categories (scores 0/1 vs. 2/3) and subsequently refining the classification for the specific stages of the disease. 70% of the images were used for training, 15% for validation, and 15% for test. For training, we used a dataset of ultrasound images along with labels indicating the grade of SG involvement. We employed standard deep learning techniques such as data

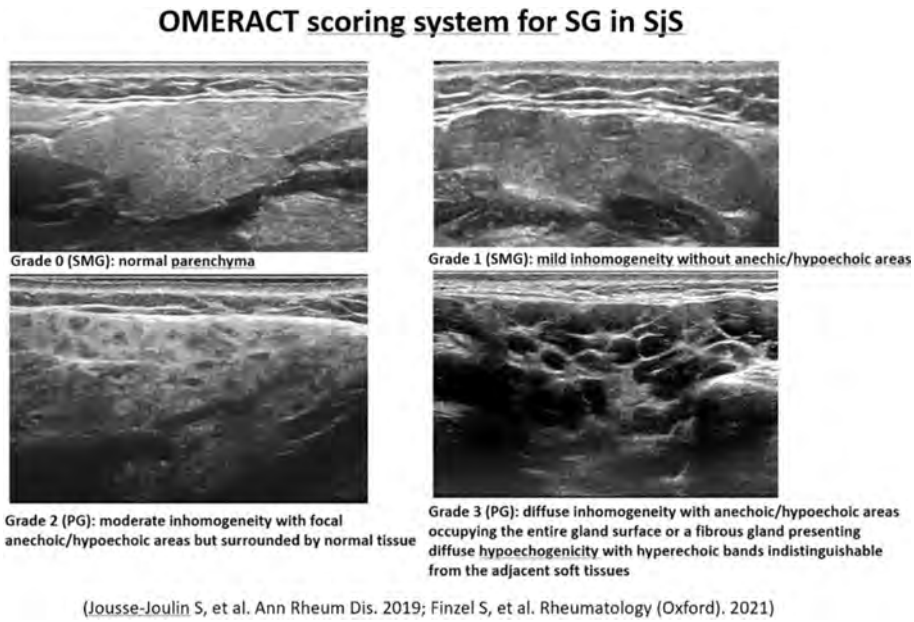


Figure 1

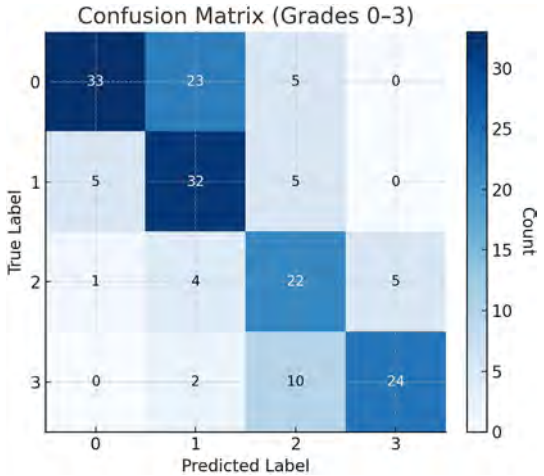


Figure 2

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1.

	Precision	Recall	F1-score
Grade 0	0.85	0.54	0.66
Grade 1	0.52	0.76	0.62
Grade 2	0.52	0.69	0.59
Grade 3	0.83	0.67	0.74

augmentation (e.g., random flipping and brightness adjustments) to increase the model's robustness and generalization capabilities and a step learning rate scheduler to optimize the training process. Precision (correct classifications per predicted class), recall (correct classifications per actual class), and F1-score (harmonic mean of precision and recall) were calculated for each grading class.

Results: The overall performance of the model for grading classes is shown in Table 1. The broad model achieved an accuracy of 90% in distinguishing between 0/1 and 2/3 grades. However, the more specific models, fine-tuned for the 0/1 and 2/3 categories, had lower accuracy (approximately 65% for each). This reflects the increased difficulty of fine-grained classification. The confusion matrix (Figure 2) showed that the model performed well in classifying SG with grade 3 but faced challenges with intermediate categories (class 1 and class 2). The network showed difficulty discriminating between grade 0 and 1; on retrospective review of the ultrasound labels, we noted that this boundary is visually subtle and prone to greater interobserver variability, which likely contributes to the model's confusion between these two lowest scores.

Conclusion: Our results showed the potential of deep learning models, specifically convolutional neural networks, to classify SG ultrasound images based on parenchymal involvement, offering a promising tool for SjS diagnosis. While the broad classification model performed very well, the fine-tuned models, which differentiate between more specific disease stages, still faced challenges. Future work should refine the fine-tuned models with additional data, allowing more complex architecture or domain-specific adjustments.

Disclosure: O. Olivas: None; **M. García-Sevilla**: None; **L. Cubero**: None; **J. Pascau**: None; **E. Naredo**: None.

Abstract Number: 1965

Two-Year Outcomes of Microwave Ablation for Recurrent Monoarthritis with Synovial Hypertrophy Resistant to Medical Treatment: Expanded Cohort and Long-Term Follow-Up Results

Rabia Deniz[1], Tevfik Güzelbey[2], İlhan Nahit Mutlu[2], Kübra Kalkan[3], Özgür Kılıçkesmez[2] and Cemal Bes[4], [1]University of Health Sciences Basaksehir Çam and Sakura City Hospital, Istanbul, Turkey, [2]University of Health Sciences Başakşehir Çam and Sakura City Hospital, Department of Radiology, Istanbul, Turkey, [3]University of Health Sciences Başakşehir Çam and Sakura City Hospital, Department of Rheumatology, Istanbul, Turkey, [4]University of Health Sciences, Basaksehir Çam and Sakura City Hospital, Istanbul, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Recurrent monoarthritis (RM) is a significant therapeutic challenge in rheumatology, often persisting despite NSAIDs, corticosteroids (CS), DMARDs, and biologic therapies. Local interventions like intra-articular aspiration (IAA) and CS injections offer transient relief and are limited by high recurrence rates. Surgical and chemical synovectomy have largely been abandoned due to poor efficacy and high complication rates. Microwave ablation (MWA) is a well-known technique in the treatment of benign or malign lesions of different etiologies. Building upon our initial findings using MWA in RM sucessfully, we present long-term outcomes from a larger cohort of medical treatment-resistant RM, providing real-world data on the efficacy and safety of MWA.

Methods: Patients with RM associated with various inflammatory diseases were included. MWA was performed after measuring the size of synovial hypertrophy (SH) with 15 or 20-watt power and different durations until microbubbles were shown indicating necrosis (Figure 1). Both clinical and radiologic data were recorded baseline and prospectively.

Results: We applied MWA to a total of 43 knee joints in 37 patients (18 female and 19 male) aged between 22 and 71 years. The median number of IAA required in the 6 months prior to MWA was 5 (0–15). Three patients had previously undergone surgical synovectomy. In 3 knees of 2 patients, the number of IAAs in the last 6 months was 0; these patients had persistent synovial effusion and abundant synovial hypertrophy but declined IAA. A 2nd MWA session was required in 5 patients, and 1 patient underwent a 3rd. The median follow-up period was 15 months (5–25). The IAA frequency dropped dramatically from 207 over 258 patient-months (0.81/month) before MWA to just 21 over 624 patient-months post-MWA (0.03/month; $p < 0.001$). Short-term, Lowe dose CS therapy was administered in 14 patients (16 knees) with all anti-inflammatory treatments maintained unchanged during the first 6 months post-procedure.

CS reduction or cessation was achieved in 16 patients. Functional disability and pain scores showed significant improvement, with the median score decreasing from 9 to 1 ($p < 0.0001$ for both, Figure 2). No complications were observed during the procedure or follow-up. While both SH and effusion persisted to varying degrees at the 1st and 3rd months on USG and

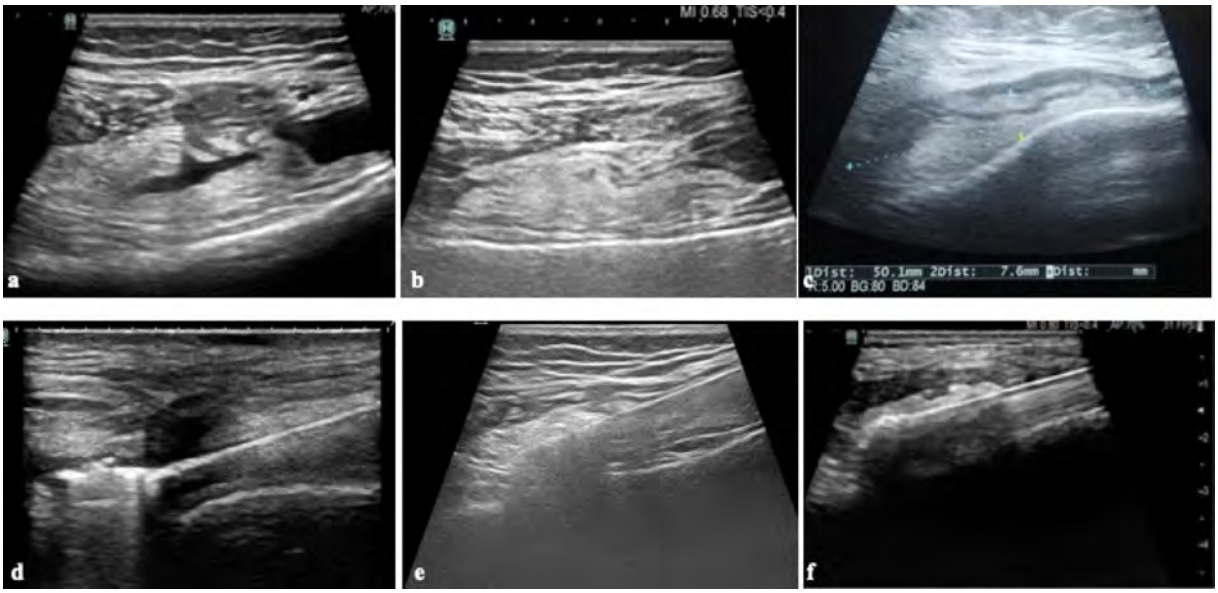


Figure 1. Microwave Ablation Technique. Synovial hypertrophy was assessed using ultrasound (USG), and significant joint effusion, if present, was aspirated. The targeted hypertrophic area is demonstrated in panels 1a and 1b, and the measurement of horizontal and longitudinal dimensions is shown in panel 1c. Following surgical asepsis and local anesthesia, antimicrobial prophylaxis with ampicillin/sulbactam and sedation with midazolam and fentanyl were administered. A monopolar internally cooled MWA probe was inserted through a 2 mm skin incision under USG guidance. Examples of probe placement into hypertrophic synovium are illustrated in panels 1d, 1e, and 1f. Ablation was performed using 15–20 W of energy with the moving-shot technique until microbubbles, indicating effective necrosis, were observed (panels 1d and 1f). For larger hypertrophic areas, multiple ablation zones were treated sequentially. Energy output and ablation duration were recorded.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

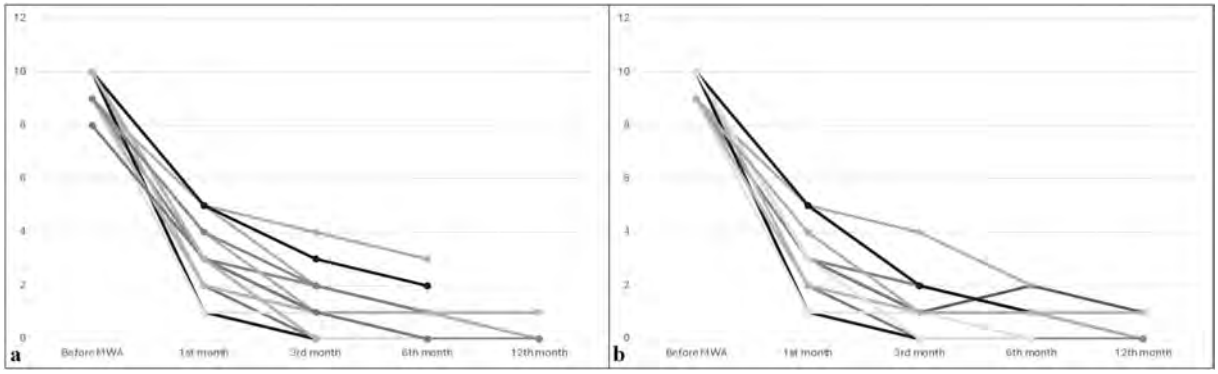


Figure 2: Functional disability and pain scores of patients before MWA procedure and at 1st, 3rd, 6th, and 12th month visits. The figure 2a shows the functional disability score and 2b shows the pain score rated between 0 an 10. 0 means no funcitonal disability or pain, and 10 is the worst possible funcitonal disability or pain, in both.

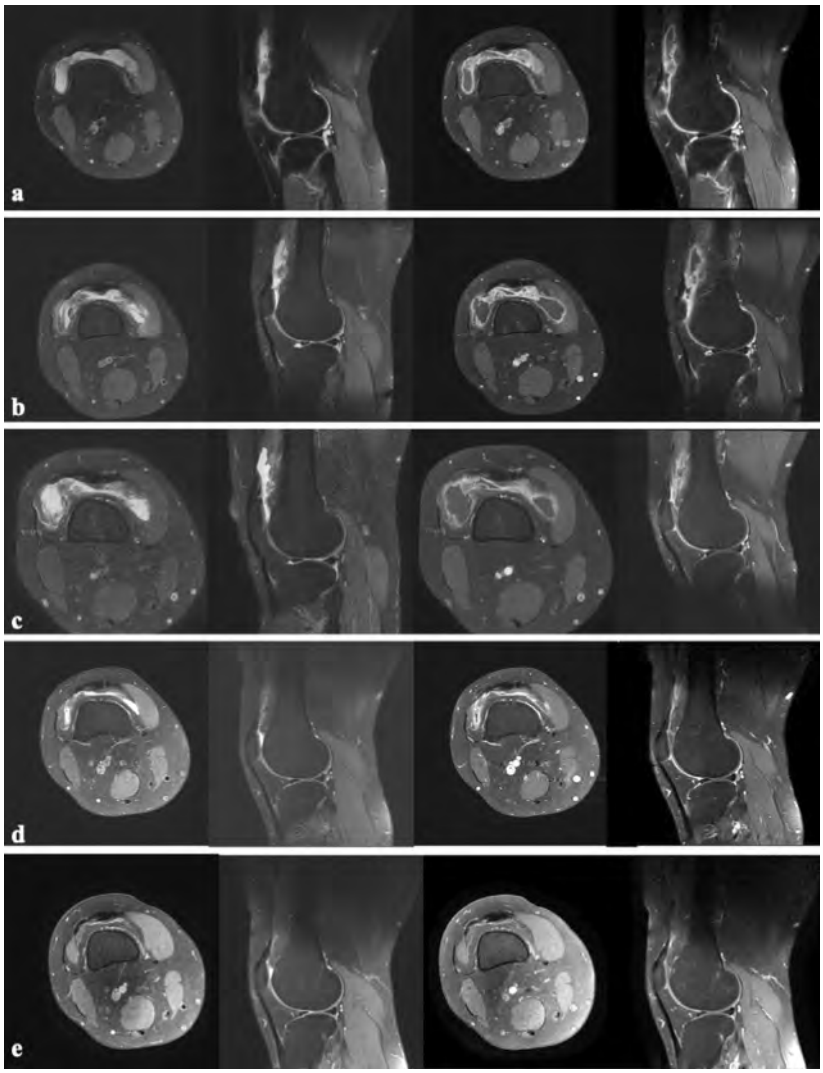


Figure 3: An example of a patient with pre-procedure, and post-procedure 1st, 3rd, 6th, and 12th month MRI images indicating consistent improvement in MRI findings with time. The figure 3a shows pre-procedure, 3b shows post-procedure 1st month, 3c shows post-procedure 3rd month, 3d shows post-procedure 6th month, and 3e shows post-procedure 12th month MR images of the patients. In all rows, the order of images are positron density weighted (PDW) in the axial plane, PDW in the sagittal plane, T1-weighted contrast enhanced in the axial plane, and T1-weighted contrast enhanced in the sagittial plane, from left to right. Synovial hypertrophy and effusion did not show any significant change in the 1st and 3rd months after the procedure, whereas a significant regression was observed starting from the 6th month.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

MRI, IAA was deferred unless symptoms developed. Significant regression in SH was demonstrated on MRI at the 6th month (Figure 3). A discordance between clinical improvement and radiological findings was observed in a small subset of the cohort.

Conclusion: MWA is a safe, effective, and minimally invasive adjunctive option for managing RM with SH. It significantly reduces arthritis flares frequency, CS dependecy, and the need for IAAs while improving functional outcomes and pain. Although early imaging may show persistent effusion and SH, significant regression by six months correlates with sustained clinical improvements. These long-term results support MWA as a promising alternative to surgical interventions in RM resistant to conventional medical therapies.

Disclosure: R. Deniz: None; **T. Güzelbey**: None; **İ. Mutlu**: None; **K. Kalkan**: None; **Ö. Kılıçkesmez**: None; **C. Bes**: None.

Abstract Number: 1966

Assessing the Impact of Cutaneous Melanin on Microvascular Oxygenation Measurement in Systemic Sclerosis Using Multispectral Imaging

Rosie Barnes[1], Joanne Manning[2], Graham Dinsdale[3], Ariane Herrick[4], Mark Dickinson[5] and Andrea Murray[6], [1]University of Manchester, Manchester, England, United Kingdom, [2]Northern Care Alliance NHS Foundation Trust, Salford, United Kingdom, [3]Northern Care Alliance, Salford, United Kingdom, [4]The University of Manchester, UK, Aberdeen, United Kingdom, [5]The University of Manchester, Manchester, [6]University of Manchester, Salford, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Microvascular abnormalities, leading to hypoxia, drive the SSc disease process. Accurate measurement of skin oxygenation, both baseline and during 'stress'/reperfusion (which can be mimicked in the laboratory by occlusion), would not only facilitate studies of pathogenesis but also provide a surrogate outcome measure for clinical trials of vasoactive therapies. But measuring skin oxygen is challenging, especially in darker skin tones. Our aim was to (a) explore the effect of skin tone on skin oxygenation measurements using multispectral imaging (MSI) (which measures oxygen by imaging the skin under white light) and (b) compare skin oxygenation between patients with SSc and healthy controls (HC).

Methods: Fifty patients with SSc (49 fulfilled ACR criteria or were VEDOSS; median age 55.0 (IQR 45.50-63.75) years; F:M 45:5) and 50 healthy controls (55.5, (44.75-64.00) years; F:M 45:5) were recruited. Objective measurements of participants' 'individual typology angle' (ITA) were taken using a colorimeter, to record skin tone. ITA data from recruited participants are given in Table 1. Participants underwent an occlusion of the middle finger on their non-dominant hand to reduce oxygenation and their hands were imaged with MSI before, during, and after occlusion release. From the MSI data an index of oxygenation (Oxy) was calculated. The Oxy index was averaged over a region of interest on the occluded finger. A multiple linear regression model was used to estimate the impact of skin tone and cohort on the change in Oxy (ΔOxy) upon occlusion release.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: The number of participants (healthy controls, patients, and total) recruited in each skin tone group by individual typology angle (ITA).

SKIN TONE GROUP	HEALTHY CONTROLS	PATIENTS	TOTAL
VERY LIGHT (ITA ≥ 55°)	3	1	4
LIGHT (55° > ITA ≥ 41°)	25	15	40
INTERMEDIATE (41° > ITA ≥ °28)	14	20	34
TAN (28° > ITA ≥ 10°)	4	9	13
BROWN (10° > ITA ≥ −30°)	2	4	6
DARK (−30° > ITA)	2	1	3

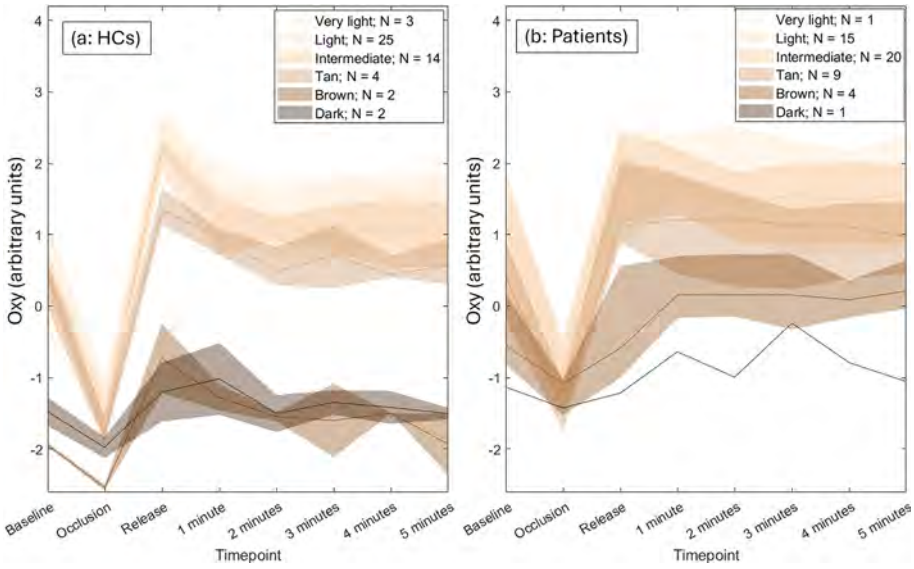


Figure 1: Oxy over time (before, during, and for 5 minutes after occlusion) colour-coded by skin tone group as given in Table 1, showing the median and IQR of each group for (a) healthy controls (HC) and (b) patients. ΔOxy is calculated as the difference in Oxy between release and occlusion.

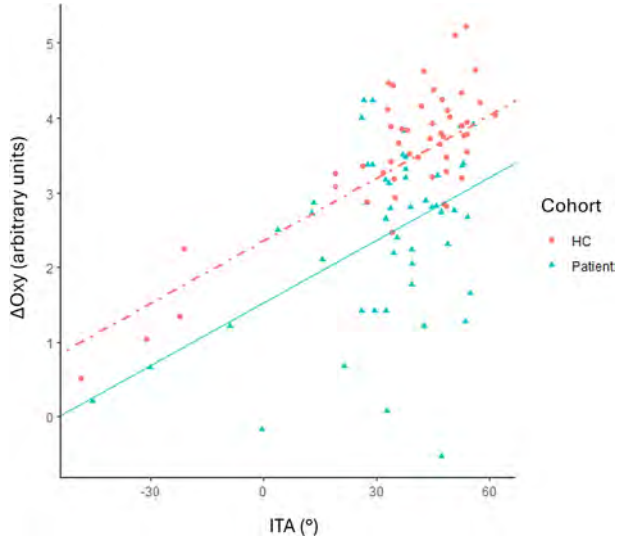


Figure 2: The fitted multiple linear regression model showing the linear effect of individual typology angle (ITA), aka skin tone, on ΔOxy and the difference between cohorts. The red dashed line is the healthy control (HC) fit, while the blue solid line is the patient fit. The model accounts for 47% of variance in the data, with an R^2 of 0.47.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Median and IQR of Oxy over time is shown in Figure 1. The fitted model of ΔOxy, shown in Figure 2, was significant, $F(2,97) = 45.66$, $p < 0.001$, and showed that both cohort, $t(97) = -5.596$, $p < 0.001$, and ITA, $t(97) = 7.041$, $p < 0.001$, had a significant effect on ΔOxy. ΔOxy was reduced for lower ITA, i.e. darker skin tone, and for patients compared with HCs.

Conclusion: (a) Skin tone had a significant effect on Oxy measurements, with lower ΔOxy in darker skin tones. We believe this is due to a lack of sensitivity of the Oxy index to oxygenation in dark skin caused by strong absorption of light by eumelanin (which sits above the vascular network in the skin). This is a problem that is inherent to visible light imaging of the skin and needs to be addressed in MSI and similar optical techniques. This work represents a first step in understanding the effect melanin has on oxygenation measurements; future work is required to further understand and account for this effect and thus ensure equitable techniques for all patients.

(b) ΔOxy was lower in patients, suggesting that patients display a muted response to the occlusion, with less pronounced reactive hyperaemia compared to HCs of a similar age and sex. This clear difference demonstrates the vascular dysfunction in patients, and Oxy could be a promising marker for disease measurement.

Disclosure: R. Barnes: None; **J. Manning**: None; **G. Dinsdale**: None; **A. Herrick**: Abbvie, 2, Boehringer-Ingelheim, 2, Janssen, 2, 6, Zura Bio, 2; **M. Dickinson**: None; **A. Murray**: None.

Abstract Number: 1967

Developing an Algorithm to Quantify Dermatomyositis-associated Calcinosis Using Infrared Imaging

Saahil Sachdeva[1], Briana Cervantes[2], Lisa Rider[3] and Adam Schiffenbauer[4], [1]NIEHS/NIBIB/NIH, Danville, CA, [2]Department of Emergency Medicine, Norfolk, VA, [3]National Institute of Environmental Health Sciences/National Institutes of Health, Environmental Autoimmunity Group, Bethesda, MD, [4]National Institute of Health/National Institute of Dental and Craniofacial Research, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) is a rare autoimmune disease characterized by chronic muscle and skin inflammation. One potential complication of DM is calcinosis, the heterotopic calcification of soft tissue. The differences in depth and densities of these calcifications make early detection difficult by physical exam.

Infrared imaging (IR) is a light-based modality that measures an object's surface temperature. It has been used for other medical applications; however, IR imaging has not previously been employed for assessing DM-associated calcinosis. We proposed an IR algorithm to detect calcinosis in patients with juvenile and adult DM (J/DM) by measuring the value and variability of skin surface temperature. We believe its use will provide clinicians with a supplementary non-ionizing, inexpensive, and easy-to-use imaging modality to quantify DM-associated calcinosis at an early onset.

Methods: Study subjects were recruited from a myositis natural history study conducted at the National Institutes of Health in Bethesda, MD, and enrolled from August 2020 to July 2022. Inclusion criteria for the present study were probable or definite J/DM by Bohan and Peter criteria. Each patient also had suspicion of calcinosis, either self-reported or by documented assessment from a medical professional.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient scans were conducted by an IR camera (ImageIR® 8300, InfraTec, Germany) at the NIH Clinical Center in Bethesda, MD. All scans were done in a temperature-controlled and humidity-monitored room (18-22 °C, 50-60 % humidity). Target scan locations were selected beforehand based on common calcinosis areas in J/DM, including the abdomen, back, arms, and legs. All images were taken as close to perpendicular to the patient as possible.

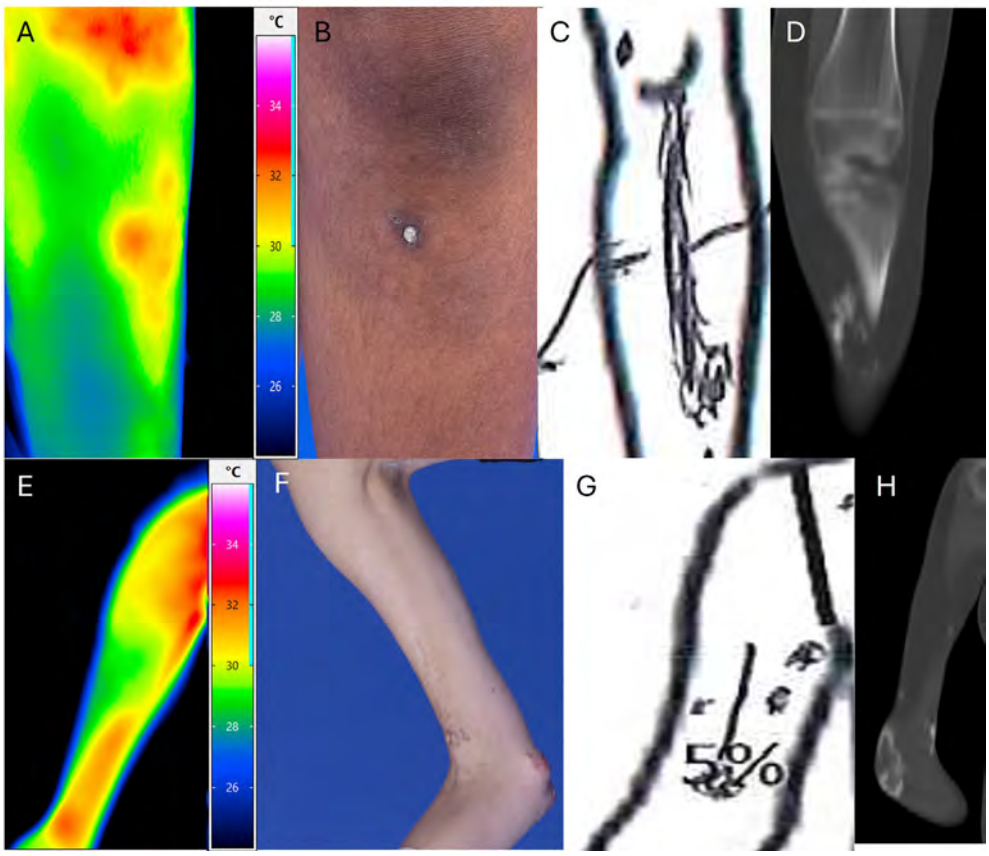
Results: Two hundred fifty-seven IR images from 3 DM and 12 JDM patients (age 9-60) were obtained from 6 body regions consisting of the right/left upper/lower extremities, abdomen, and back. For the population, the mean and range for CDASI activity, damage, and total calcinosis were (10, 2-41; 13, 2-25; 6, 2-11) respectively.

Table: Calcinosis distribution in 15 patients with adult and juvenile dermatomyositis, as determined by an infrared imaging algorithm

Body Region	Average PCA (%)	Standard Deviation of PCA (%)	Minimum PCA (%)	Maximum PCA (%)	Calcinosis Frequency of Each Region
Upper Right Extremities	12.7	4.8	0.1	22.4	12/43 (27.9%)
Upper Left Extremities	12.1	4.3	0.2	24.1	8/43 (18.6%)
Abdomen	11.4	8	0.3	29.8	11/43 (25.6%)
Back	6.4	6.6	0	31.7	3/42 (7.1%)
Lower Right Extremities	11.3	4.4	4.9	24	8/43 (18.6%)
Lower Left Extremities	11.6	5	1.4	24.4	8/43 (18.6%)

Abbreviations: PCA, Percent Calcinosis Area

Figure: Infrared and comparative imaging of calcinosis areas



Patient 1 had calcinosis in their left lower extremity distal to the knee. Image A is the IR image of this area and image B is the traditional photo of the same area. Image C is the physician drawing of the calcinosis from physical exam. Image D is the CT scan of the same area. Patient 2 had calcinosis in their right upper extremity proximal to the elbow. Image E is the IR image of this area and Image F is the traditional photo of the same area. Image G is the physician drawing of the calcinosis from physical exam. Image H is the CT scan of the same area.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The percent calcinosis area (PCA) was calculated as the pixels determined to contain calcinosis by the algorithm divided by the pixels determined to contain body area, multiplied by 100 to express the result as a percent. When PCA exceeded 15% to account for edge effect, the region was defined as positive for calcinosis. The calcinosis frequency of each region was calculated as the number of positive images of the region by its total number of images. The areas most and least frequently identified as positive for calcinosis by IR imaging were the upper right extremities and back, respectively.

The IR algorithm's suspected calcinosis areas ranged from 0.2% to 31.7%, with averages of each region ranging from 6.4 – 12.7% PCA (Table). Left and right extremities were within 0.6% of each other's averages.

Example IR image comparisons with traditional photography, physician exam, and CT are provided in Figure 1 and 2 from patients with calcinosis.

Conclusion: IR detected calcinosis in all body regions examined and demonstrated relative symmetry between left and right extremities. Further evaluation against other standards is required to validate the utility of IR in detecting calcinosis.

Disclosure: S. Sachdeva: None; **B. Cervantes**: None; **L. Rider**: None; **A. Schiffenbauer**: AstraZeneca, 11, Hope Pharmaceuticals, 5.

Abstract Number: 1968

Relationship between ultrasonographic and elastographic findings of the median nerve and disease activity and hand function in patients with rheumatoid arthritis

Gulperi ISAZADE KASIMZADE[1], Ismihan Sunar[2], **Sebnem ATAMAN**[3] and Aysun GENC[1], [1]Ankara University School of Medicine, Physical Medicine and Rehabilitation, Ankara, Turkey, [2]Ankara University School of Medicine, Physical Medicine and Rehabilitation, Rheumatology, Ankara, Turkey, [3]Ankara University School of Medicine, Rheumatology, Turkey, Ankara, Turkey

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune joint disease with systemic involvement which can affect the nerves through either compressive pathology due to intra-articular synovitis and tenosynovitis or vasculitis of the vasa vasorum. Carpal tunnel syndrome (CTS) is a compression neuropathy caused by entrapment of the median nerve within the carpal tunnel. This study aimed to evaluate morphological and elasticity-related changes of the median nerve using B-mode ultrasonography (US) and shear wave elastography (SWE) in RA patients without signs of median nerve involvement and to examine the relationship between these changes, disease activity, and hand functions.

Methods: This cross-sectional study included 55 RA patients without CTS symptoms fulfilling the 2010 ACR/EULAR Classification criteria and 55 age- and sex-matched healthy controls. Exclusion criteria were having diagnosis of CTS, pregnancy, endocrine disorders such as diabetes and hypothyroidism, and trauma or surgery history of the upper limbs. Demographic characteristics, disease activity score (DAS28-CRP), medications, hand grip strength (Jamar dynamometer), lateral pinch strength (pinch meter), and hand function (Duruöz Hand Index) were recorded. An experienced physician blinded to patients' data performed bilateral US evaluations to assess median nerve cross-sectional area (CSA, mm^2) and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

presence of flexor digitorum tenosynovitis by B-mode, inflammatory activity via Power Doppler US, and nerve stiffness using SWE (median and mean velocity values, m/s) using a high frequency linear probe (Siemens S2000 Acuson, Mountain View, CA). The Outcome Measures in Rheumatology (OMERACT) US grading system was used for US evaluations. IBM SPSS Statistics 26 and Python were used for statistical analyses.

Results: The mean age of the RA patients was 58.6 ± 9.1 years and the mean disease duration was 14.3±8.9 years. Sixty nine percent of the cohort was RF positive. RA patients had significantly lower grip strength and worse hand function compared to controls ($p< 0.001$). The mean median nerve CSA (13.79±4.41 mm^2) and the presence of flexor digitorum tenosynovitis and Power Doppler signal were significantly higher in the RA group compared to controls ($p< 0.001$) (Table 1). The mean SWE velocity of the meadian nerve was significantly higher in the RA group (2.58±0.38 m/s vs 1.76±0.45 m/s; $p< 0.001$) and RA patients with flexor tenosynovitis ($p=0.012$). While the median nerve CSA did not show significant relationship with clinical parameters, median nerve SWE velocity showed significant positive correlations with height ($p=0.012$, $r=0.346$) and grip strength ($p=0.018$, r=0,326) and significant negative correlations with CRP and ESR ($p=0.046$, $r=-0.278$; $p=0.001$, $r=-0.460$ respectively).

Conclusion: The median nerve CSA and SWE-measured stiffness were significantly higher in RA patients without CTS symptoms compared to healthy individuals. The association between tenosynovitis and increased SWE values suggests that local subclinical inflammation may affect biomechanical properties of the median nerve. Therefore, SWE appears to be a promising tool for the early detection of subclinical nerve changes in RA.

Table 1. Clinicodemographic characteristics and handgrip strength, hand function, and ultrasonographic parameters in RA and control groups

	RA Group (n=55; wrist=107)	**Control Group (n=55; wrist=109)**	**p**
Gender (% female)	40 (72.7%)	40 (72.7%)	1.000
Age (years), Mean ± SD	58.6 ± 9.1	57.7 ± 10.6	0.630
Disease duration (years), Mean ± SD	14.29±8.90		
Dominant Hand, n (%)	49 (89.1%)	52 (94.5%)	0.297
BMI (kg/m²) Mean ± SD	30.4 ± 6.1	27.9 ± 3.6	**0.024**
Drugs used, n (%)			
No medication	1 (1.8)		
csDMARD	36 (65.5)		
bDMARD	13 (23.6)		
tsDMARD	5 (9.1)		
Steroid use, n (%)			
Yes	7 (12.7)		
No	48 (87.3)		
DAS28-CRP, n (%)			
Remission	24 (43.6)		
Low Disease Activity	9 (16.4)		
Moderate Disease Activity	18 (32.7)		
High Disease Activity	4 (7.3)		
Jamar Dynamometer Grip Strength (kg): Mean ± SD	18±11	26±10	**<0.001**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinicodemographic characteristics and handgrip strength, hand function, and ultrasonographic parameters in RA and control groups

Pinchmeter; Lateral Grip Strength (kg), Mean ± SD	4±2	4±1	0.482
Duruöz Hand Index Score, Mean ± SD	8.16±13.03	1.73±3.78	**<0.001**
Right Hand Synovial Membrane CSA (mm²), Mean ± SD	13.44±4.14	10.46±2.57	**<0.001**
Left Hand Synovial Membrane CSA (mm²), Mean ± SD	14.13±4.67	10.36±2.01	**<0.001**
Synovial Membrane CSA (mm²), Mean ± SD	13.79±4.41	10.41±2.31	**<0.001**
Right Hand FDTT, n (%)	11 (20.4%)	1 (1.9%)	**0.008**
Left Hand FDTT, n (%)	14 (26.4%)	0 (0%)	**<0.001**
Right Hand PDS, n (%)			**0.030**
Mild	9 (16.7%)	1 (1.9%)	
Moderate	1 (1.9%)	0 (0%)	
Severe	1 (1.9%)	0 (0%)	
Left Hand PDS, n (%)			**<0.001**
Mild	11 (20.8%)	0 (0%)	
Moderate	4 (7.5%)	0 (0%)	
Severe	0 (0%)	0 (0%)	
Median nerve SWV (m/s); Mean ± SD	2.58±0.38	1.76±0.45	**<0.001**

FDTT: Flexor Digitorum Tendon Thickness, increased; CSA: Cross-Sectional Area; PDS: Power Doppler Signal; RA: Rheumatoid arthritis: SD: Standard deviation; CRP: C-reactive protein; SWV: shear wave velocity

Disclosure: G. ISAZADE KASIMZADE: None; **I. Sunar**: None; **S. ATAMAN**: None; **A. GENC**: None.

Abstract Number: 1969

Enhancing Objective Evaluation of Raynaud's in Veterans with Scleroderma-related Hand Pain: Integrating Patient Reported Outcomes and Nailfold Capillaroscopy

Genessis Maldonado[1], **Sowmika Rao**[1] and Tracy Frech[2], [1]Vanderbilt University Medical Center, Nashville, [2]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Raynaud's phenomenon (RP) is a painful and disabling feature of systemic sclerosis (SSc) that significantly impairs quality of life. Tools that integrate subjective symptom assessment with objective microvascular evaluation—ideally collected at the point of care—are essential to evaluate therapeutic response. Among U.S. Veterans, RP is highly prevalent, highlighting the importance of early diagnosis and intervention. Nailfold capillaroscopy (NFC) is the gold standard for direct visualization of microvascular changes. The Associated Raynaud Phenomenon (ASRAP) questionnaire is a patient-reported outcome (PRO) that captures the lived experience of RP. This study assessed the combined use of ASRAP and NFC to evaluate short-term therapeutic responses in Veterans with SSc and hand pain.

Methods: This prospective study enrolled Veterans from the SSc Registry (IRB No. 1618579-17) with SSc and RP initiating a single therapeutic intervention for hand pain. Follow-up was conducted 4–8 weeks after baseline. Participants completed the 10-item ASRAP questionnaire[1] and underwent same-day NFC at both visits, using the G-Scope device per standardized protocols. Interventions included the initiation or dosage adjustment of a vasodilator or immunosuppressive agent. Changes in ASRAP scores and NFC parameters—including capillary density, apical diameter, and microhemorrhages—were compared pre- and post-intervention.

Results: Of the total 22 enrolled SSc Registry Veterans, 8 met inclusion criteria between January–April 2025. The majority were male (62%, n=5), with a mean age of 61±12.1 years. Most (75%, n=6) reported military-attributable exposures associated with RP onset. At baseline, all were on a vasodilator; 50% (n=4) were also on immunomodulators (Table 1). The most

Table 1. Demographic and clinical characteristics data

[n=8]	
Male	62 [5]
Age	61±12.08 [41-79]
Intervention for Study	
CCB	12.50% [1]
PDE-5i	62.50% [5]
Hydroxychloroquine	12.50% [1]
Mycophenolate	12.50% [1]
Discontinuation rate	37.50% [3]
Clinical characteristics	
Limited SSc	75% [6]
Diffuse SSc	25% [2]
Exposure to a potentially hazardous substance	75% [6]
Serology	
ANA positive titer not available	75% [6]
Homogeneous	66.66%
Nucleolar	16.66%
Centromere	16.66%
RNA-pol-III	12.50% [1]
Scl-70	37.50% [3]
SSc Disease Features	
Synovitis	0
Pulmonary Arterial Hypertension	12.5% [1]
Interstitial Lung Disease	12.5% [1]
Gastrointestinal Tract Endoscopic Abnormality	25% [2]
Acro-osteolysis	0
Calcinosis	0
Digital Ulcers	0
Scleroderma Renal Crisis	12.5% [1]
Background Therapeutic Management	
CCB	62.50% [5]
PDE5i	50% [4]
MMF	25% [2]
HCQ	25% [2]

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: RP evaluation by ASRAP and NVC

Parameters	Baseline	After Intervention
ASRAP mean	52.25±6.02 [42.17-59.36]	50.76±8.79 [40.58-64.29]
Microvascular evaluation		
Capillary density (um)	6.01±1.37 [3.7-7.8]	5.85±1.66 [3.55-7.5]
Capillary enlargement	51.71%	54.72%
Giant capillaries	7.33%	3.20%
Apical diameter (um)	22.08±6.28 [11.4-31.2]	22.27±6.19 [12.7-32.3]
Tortuous capillaries	7.60%	7.14%
Ramified capillaries	0.87%	4.31%
Hemorrhages	62.50%	75%
Pattern		
Normal	25% [2]	25 [2]
Non-specific	37.5 [3]	37.5 [3]
SD-pattern	**37.5 [3]**	**37.5 [3]**
Early SD-pattern	0	0
Active SD-pattern	25 [2]	12.5 [1]
Late SD-pattern	12.5 [1]	25 [2]

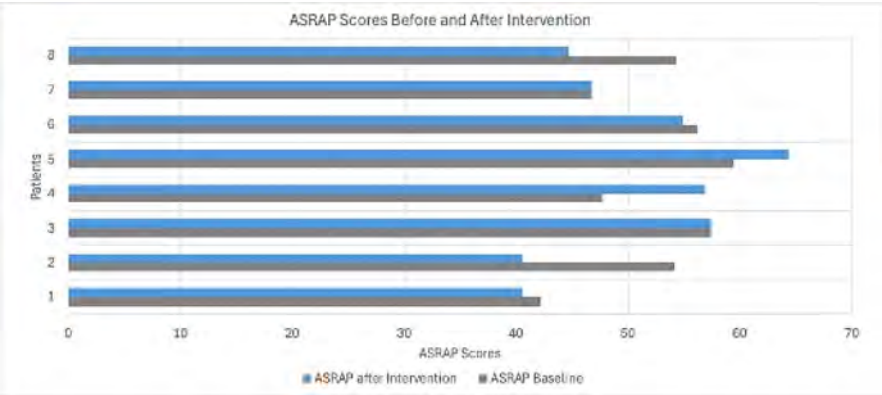


Figure 1: ASRAP scores

frequent intervention was initiation or dose increase of phosphodiesterase-5 inhibitors (PDE5-Is) in five subjects (63%). Three participants (38%) discontinued treatment due to gastrointestinal side effects (two vasodilators, one immunosuppressant). Mean ASRAP scores decreased from 52.25±6.02 to 50.76±8.79 (Figure 1). Capillary density slightly decreased (6.01 ±1.37 μm to 5.85±1.66 μm), apical diameter remained stable (22.08±6.28 μm to 22.27±6.19 μm), and the prevalence of giant capillaries declined (7.33% to 3.20%), while microhemorrhages increased (62.5% to 75%). Two patients had normal NFC throughout (Table 2). One patient who discontinued a vasodilator developed a late scleroderma pattern despite symptom improvement.

Conclusion: Combining ASRAP and NFC provides a multidimensional assessment of RP in Veterans with SSc, particularly in those with military exposure history. Despite short-term improvements in PRO scores, capillaroscopic findings often revealed ongoing or progressive microvascular damage. These findings underscore the need for continued vascular monitoring, early detection of drug intolerance, and proactive strategies for microvascular protection. Larger, longer-term studies are needed to validate these results and optimize RP management in this high-risk population.

References: 1. Yu L et al. Arthritis Care & Research. 2023; 75: 8, 1725-34.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Maldonado: None; **S. Rao**: None; **T. Frech**: None.

Abstract Number: 1970

Comparison of Optical Imaging with Musculoskeletal Ultrasound in Assessment of PIP Joints of Systemic Lupus Erythematosus Patients

Wei Tang[1], Giovanna Rosas Chavez[2], Leila Khalili[2], Alberto Nordmann-Gomes[3], Stephen Suh[4], Alessandro Marone[5], Moegammad Bardien[5], Stephen Kim[5], Laura Geraldino-Pardilla[6], Andreas Hielscher[5] and Anca Askanase[2], [1]Westchester Medical Center, Valhalla, NY, [2]Columbia University Medical Center, New York, NY, [3]Columbia University Irving Medical Center, New York, NY, [4]Columbia University Irving Medical Center, New York City, NY, [5]New York University Tandon School of Engineering, New York, NY, [6]Columbia University, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus arthritis has heterogeneous phenotypes and severity, complicating clinical management and trial endpoints. Advances in musculoskeletal ultrasound (MSK US) and optical imaging have been proposed as objective assessment tools. In a prior study of 20 systemic lupus erythematosus (SLE) patients, we demonstrated that frequency-domain optical imaging (FDOI) and a glove-like optical imaging system (GLOIS) can differentiate inflamed from normal joints by measuring transmitted and reflected lights to assess changes in tissue properties. Here we present extended data comparing FDOI with MSK US in evaluating lupus arthritis, and exploratory findings using GLOIS to monitor arthritis resolution.

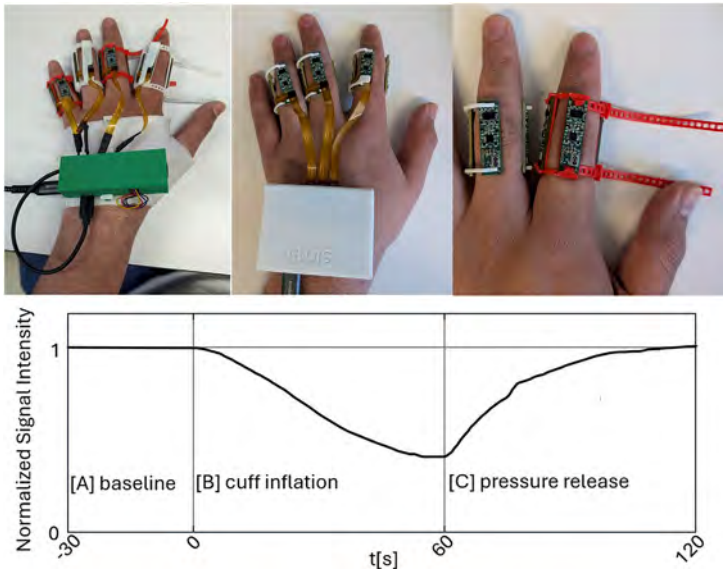


Figure 1. Glove-like optical imaging system (GLOIS) in the Evaluation of Lupus Arthritis The top part of the figure exhibits the glove-like optical imaging system (GLOIS), which comprises a control module, four optical imaging patches, a flexible printed circuit (FPC) connecting band, and an adjustable flexible fixation band. The optical imaging patches deliver light into the affected joint and measure the resulting reflected and transmitted light. Each patch comprises two source-detector modules spaced 10 mm apart, each with three light-emitting diodes (LEDs) (wavelength λ = 880 nm, 660 nm, and 530 nm) and a photodiode. The patches are connected to each other and the control module via the flexible connecting band at 15 mm spacings, allowing the patches to be wrapped around the proximal inter-phalangeal (PIP) joint. The band and patches are fixed to the finger using a 3D-printed flexible fixation band. The bottom part of the figure shows a typical signal trace measured by GLOIS for one source detector, showing significant events, including the baseline measurement (A), the sphygmomanometer cuff inflation (B) to the subject's diastolic blood pressure causing a complete venous occlusion and partial arterial occlusion , and the release of pressure (C) accompanied by 60 more seconds of measurement.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

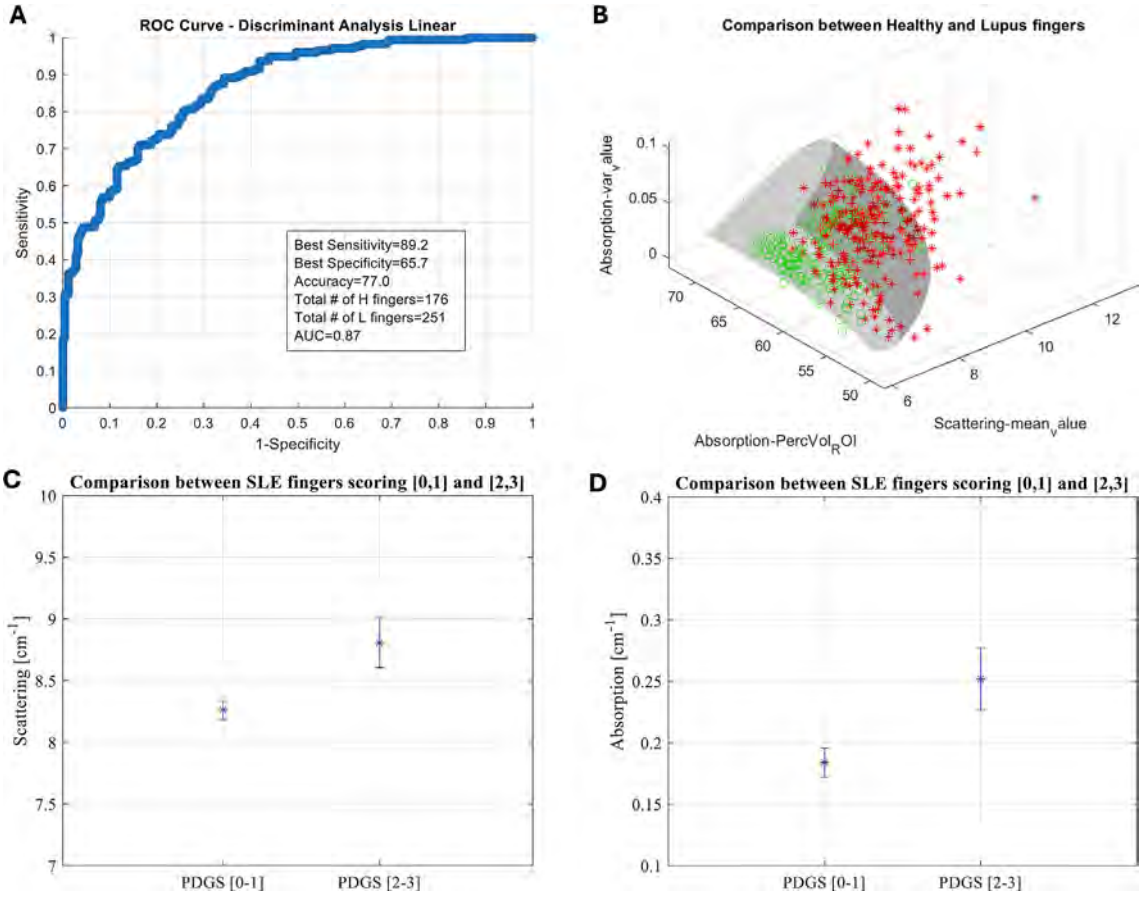


Figure 2. Evaluation of lupus arthritis by frequency domain optical imaging (FDOI) in comparison to musculoskeletal ultrasound (MSK US) ROC curve (A) and discriminant linear analyses (B) of frequency domain optical imaging (FDOI) in comparison to musculoskeletal ultrasound (MSK US) evaluation of lupus arthritis. The three parameters of choice for the discriminant analysis include the mean of the scattering coefficient, variation of the absorption coefficient, and percentage of total finger volume interested. Joints with no/minimal arthritis (PDGS 0 or 1) and moderate/severe arthritis (PDGS 2 or 3) show significantly different mean and standard error of scattering (C) and absorption (D) in reconstructed optical data.

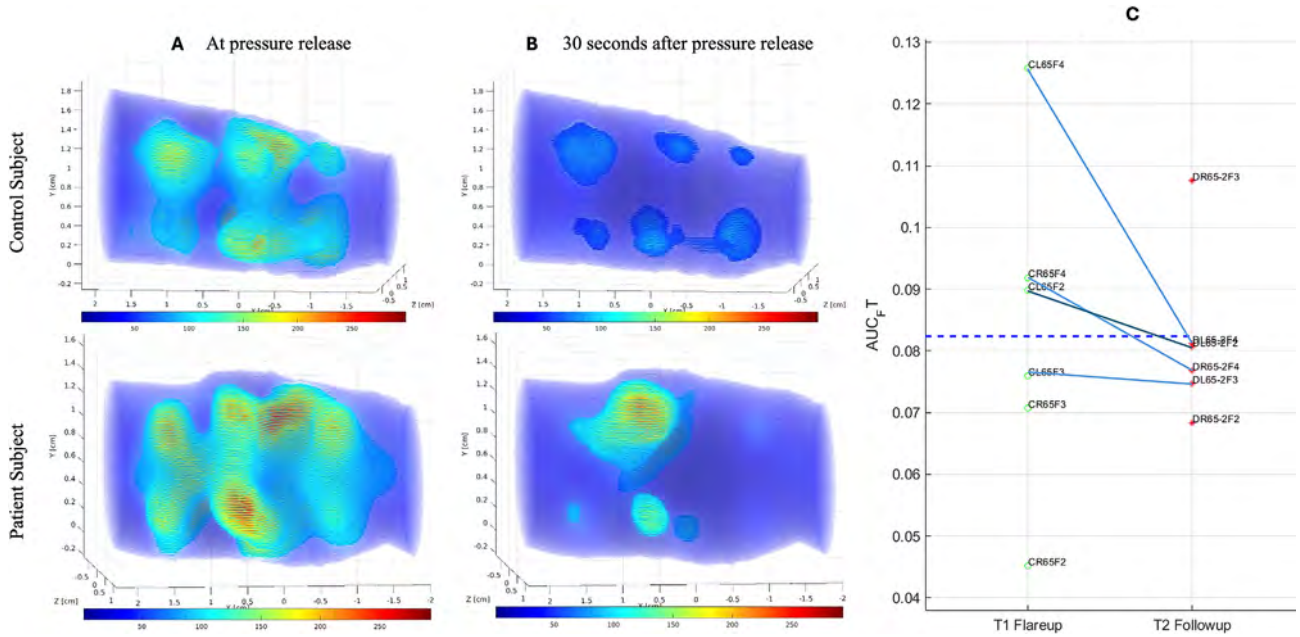


Figure 3. Glove-like optical imaging system (GLOIS) evaluation of joints in patients with lupus and healthy controls 3D Reconstructions of the total hemoglobin (HbT) concentrations in a healthy subject and control subjects at the time of pressure release (A) and 30 seconds after pressure release (B). AUC of Fall Time decreases for 4 of the 6 fingers (C) during and after a lupus arthritis flare.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We evaluated 31 SLE patients and 22 healthy controls via convenience sampling. For each subject, 8 proximal interphalangeal (PIP) joints (bilateral PIPs 2–5) were evaluated by FDOI and MSK US within two hours. MSK US used multiplanar grey-scale (GS) and power Doppler (PD) imaging, scored by OMERACT definitions to generate a composite PDGS score. FDOI employed a 670 nm, 8 mW laser modulated at 300 MHz, and scanned across each PIP to reconstruct three-dimensional (3D) maps of light absorption and scattering. Additionally, 2 SLE patients and 2 healthy controls underwent GLOIS evaluation (Fig 1), and 1 SLE patient was evaluated by GLOIS before and after therapy for an arthritis flare. GLOIS (Fig 1) used flexible bands with 8 optical modules (each with a photodiode and 3 LEDs at 530, 660, and 880 nm). LEDs were sequentially activated; photodiodes captured the transmitted signals. A sphygmomanometer was inflated to the subject's diastolic blood pressure, inducing a complete venous occlusion and partial arterial occlusion, then released after 60 seconds accompanied by 60 more seconds of measurement. Subsequently, the measurements from all the source/detector pairs around the finger joint were used to tomographically reconstruct the distributions of total hemoglobin (HbT) concentrations in the joint.

Results: FDOI data (Fig 2) from 235 PIPs (SLE) and 136 PIPs (controls) produced an AUC of 0.87, with 89% sensitivity and 66% specificity (Fig 2A, 2B). Among 120 joints assessed by MSK US, PDGS scores were 0 (n=47), 1 (n=73), 2 (n=61), and 3 (n=54). Joints with moderate/severe arthritis (PDGS 2–3) had significantly higher scattering (8.8±1.4 vs. 8.3±0.6/cm, $p< 0.01$, Fig 2C) and absorption coefficients (0.25±0.18 vs. 0.18±0.1/cm, $p< 0.01$, Fig 2D) than those with minimal/no inflammation (PDGS 0–1).

3D tomographically reconstructed GLOIS imaging showed higher HbT concentration at pressure release (Fig 3A) and 30 seconds post-release (Fig 3B) in SLE joints (42 μM at both timepoints) with PDGS of 2 compared to controls (29 and 30 μM). In the SLE patient examined at the time of flare (T1) and after symptom resolution (T2), Fall Time AUC decreased in 4 of 6 fingers (Fig 3C), suggesting improvement.

Conclusion: These data support the use of FDOI and GLOIS to reliably detect MSK US-confirmed arthritis in SLE joints and to monitor disease activity. Optical imaging shows promise as a non-invasive, objective tool for lupus arthritis assessment in clinical care and trials. Further development is warranted and ongoing.

Disclosure: W. Tang: None; **G. Rosas Chavez**: None; **L. Khalili**: None; **A. Nordmann-Gomes**: None; **S. Suh**: None; **A. Marone**: None; **M. Bardien**: None; **S. Kim**: None; **L. Geraldino-Pardilla**: Aurinia, 2, 6, Bristol-Myers Squibb(BMS), 1, 2, 6; **A. Hielscher**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5.

Abstract Number: 1971

Intracranial Arterial Stenosis in Antiphospholipid Syndrome: A Neglected Vascular Involvement?

Yuying Fan[1], Jinyi Qian[1], Xiaohan Wei[2], Haoyu Pan[1], Shuyi Yu[1], Zhixia Yang[1], Shiyan Gu[1], Jianzhou Wu[1], Cenyi Wang[1], Tiancheng Zhou[1] and Hui Shi[3], [1]Department of Rheumatology and Immunology, Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [2]Shanghai JiaoTong University, Shanghai, China (People's Republic), [3]Shanghai Jiaotong University Affiliated Ruijin Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1936–1971) Imaging of Rheumatic Diseases Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by thrombotic events and obstetric complications. While macrovascular and microvascular manifestations have been increasingly acknowledged—particularly with the inclusion of microvascular lesions in the 2023 ACR/EULAR classification criteria—arterial stenosis within the central nervous system (CNS) remains insufficiently recognized. This study aimed to systematically evaluate the prevalence, imaging features, and possible pathophysiological mechanisms of intracranial arterial stenosis in patients with APS.

Methods: We prospectively enrolled 123 APS patients meeting the 2023 ACR/EULAR classification criteria. All participants underwent cerebrovascular screening using magnetic resonance angiography (MRA) to detect potential abnormalities. Patients with suspected arterial stenosis on MRA subsequently underwent computed tomography angiography (CTA) for definitive anatomical confirmation. In those with CTA-confirmed intracranial stenosis, high-resolution magnetic resonance vessel wall imaging (HR-VWI) was performed to assess wall morphology, contrast enhancement, and features suggestive of inflammatory vasculopathy (**Fig.1**).

Results: Among the 123 APS patients screened, MRA revealed cerebrovascular abnormalities in 76 patients (61.79%), including 32 patients (26.0%) with confirmed intracranial arterial stenosis with CTA. Other observed MRA findings included suspected stenosis (2.44%), arterial slenderness (18.70%), protrusion shadows potentially indicating aneurysms (7.32%), conical narrowing (1.63%), focal bulging (1.63%), and wall irregularities (4.07%). Among 32 patients with arterial stenosis, the most frequent sites of stenosis were the posterior cerebral artery (PCA) and internal carotid artery (ICA), each observed in 12 patients (37.5%). This was followed by the anterior cerebral artery (ACA) in 9 patients (28.33%), middle cerebral artery (MCA) in 7 patients (21.88%), and vertebral artery (VA) in 5 patients (15.62%) (**Table.1**).HR-VWI in stenosis-confirmed cases

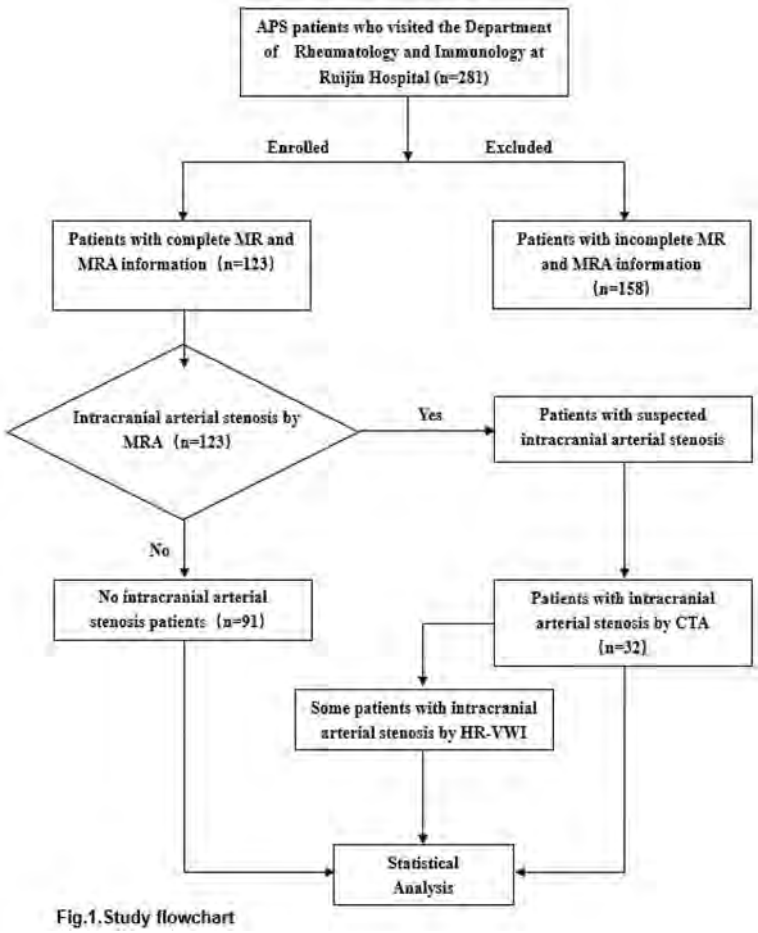


Fig.1.Study flowchart

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table.1. Prevalence and Distribution of Intracranial Vascular Abnormalities in a Cohort of 123 Patients

Table.1. Prevalence and Distribution of Intracranial Vascular Abnormalities in a Cohort of 123 Patients

Intracranial vascular condition	Number(n=123)
cerebrovascular abnormalities	76(61.79%)
Intracranial vascular stenosis	32(26.0%)
ACA	9(28.33%)*
MCA	7(21.88%)*
PCA	12(37.5%)*
ICA	12(37.5%)*
VA	5(15.62%)*
suspected stenosis	3(2.44%)
arterial stenderness	23(18.70%)
protrusion shadows potentially indicating aneurysms	9(7.32%)
conical narrowing	2(1.63%)
focal bulging	2(1.63%)
wall irregularities	5(4.07%)
normal	47(38.2%)

*Percentages for specific arteries are calculated based on total cases with intracranial vascular stenosis (n=32)

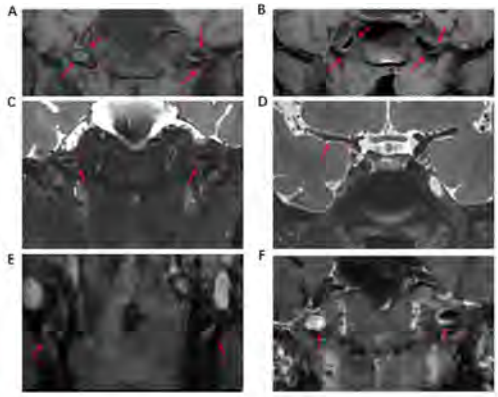


Fig.2. High-Resolution Vessel Wall Imaging (HR-VWI) in a Patient with Intracranial Vascular Stenosis Associated with Antiphospholipid Syndrome (APS). A, B, T1-weighted (T1W) images demonstrate bilateral internal carotid artery (ICA) wall thickening, more pronounced on the right side, with multisegment moderate to severe stenosis in the right ICA. **C, D,** Bilateral ICA wall thickening (predominantly on the right) showing slightly hyperintense signal on T2-weighted (T2W) images. **E, F,** Marked enhancement of the thickened vessel walls (right > left), indicating inflammatory activity and neovascularization within the arterial wall, suggestive of vulnerable plaque formation.

Fig.2. High-Resolution Vessel Wall Imaging (HR-VWI) in a Patient with Intracranial Vascular Stenosis Associated with Antiphospholipid Syndrome (APS).

demonstrated focal vessel wall thickening, contrast enhancement, and vasculitis-like features, suggesting possible immune-mediated endothelial injury (**Fig.2**). Further analysis revealed that stenosis severity was positively correlated with elevated antiphospholipid antibody titers, comorbid valvular heart disease, and cognitive impairment.

Conclusion: This study provides the first systematic evaluation of intracranial arterial stenosis in APS, revealing it to be a relatively common and potentially underrecognized manifestation. Multimodal imaging combining MRA, CTA, and HR-VWI offers a comprehensive strategy for early detection and characterization of CNS vascular involvement. These findings expand the vascular phenotype of APS and underscore the importance of early cerebrovascular surveillance in patients with high-risk clinical or serologic features.

Disclosure: Y. Fan: None; **J. Qian**: None; **X. Wei**: None; **H. Pan**: None; **S. Yu**: None; **Z. Yang**: None; **S. Gu**: None; **J. Wu**: None; **C. Wang**: None; **T. Zhou**: None; **H. Shi**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1972

Enhancing Patient Safety: Improving Contraceptive Counseling for Patients on Teratogenic Medications in the Rheumatology Clinic

Abimbola Fadairo-Azinge[1], jobelle Romulo[2], Daniella Flores[3], jose Giron[2], Joshua Ng[4], Sarah Patterson[5], Jinoos Yazdany[6] and Andrew Gross[6], [1]UCSF, San Francisco, [2]University of California San Francisco, San Francisco, [3]University of California San Francisco, San Francisco, CA, [4]University of California San Francisco, SAN-FRANCISCO, CA, [5]University of California, San Francisco, Pacifica, CA, [6]UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The American College of Rheumatology (ACR) recommends contraceptive counseling for reproductive-age women with rheumatic and musculoskeletal diseases (RMDs), especially those on teratogenic medications. These medications are associated with major birth defects, making it critical to ensure effective contraception counseling for these patients

At the time of the pre-intervention assessment, among 109 patients with rheumatologist diagnoses seen in the UCSF rheumatology clinic who were treated with leflunomide, mycophenolate, or methotrexate, only 41% had contraception use documented and only 35% had documentation of contraception counseling. This project aimed to increase contraceptive counseling documentation to over 70% for all rheumatologic patients on teratogenic medications within the next nine months.

Methods: Eligibility criteria for counseling included patients with any rheumatologic condition who were maintained on methotrexate, mycophenolate, or leflunomide and were being followed at the UCSF Rheumatology Clinic at the Parnassus location, either through in-person or telehealth visits.

The team used the Lean Improvement Methodology to identify the gaps in contraceptive screening and counseling (Figure 1). Most identified gaps led to targeted Interventions which include

- Development of a standardized documentation SmartPhrase in the electronic health record (EHR)
- Collaboration with the complex contraception clinic withing the OB/GYN department to create patient-facing educational materials
- Training of nursing staff to conduct contraceptive counseling
- Workflow redesign to include counseling across visit types (telemedicine and in-person)
- Monthly audits tracked counseling documentation rates among patients prescribed the three targeted teratogenic medications.

Results: Over the course of the project, we reviewed our findings every six weeks by monitoring the in-process metric, which was the percentage of eligible patients missed during each intervention cycle. This was measured to evaluate progress and determine if further changes were necessary. In the first two months, despite implementing targeted interventions, approximately 60% of eligible patients were still missed for contraceptive counseling. This gap was primarily due to challenges in capturing patients seen via telehealth, a limitation of the existing clinic workflow. After identifying this issue, we revised the workflow, enabling nurses with training in contraceptive counseling to proactively identify our target patient

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

sample whether they were receiving care via telehealth and in-person. These changes significantly improved outcomes: documented contraceptive counseling rates rose from 35% (N=109) at baseline to 82% (N=331) (Figure 2), and the proportion of missed eligible patients dropped from 64% in November 2024 to 1.82% in April 2024 (Figure 3). Whenever counseling occurred, contraceptive use was documented in 100% of cases, indicating whether or not the patient was using contraception.

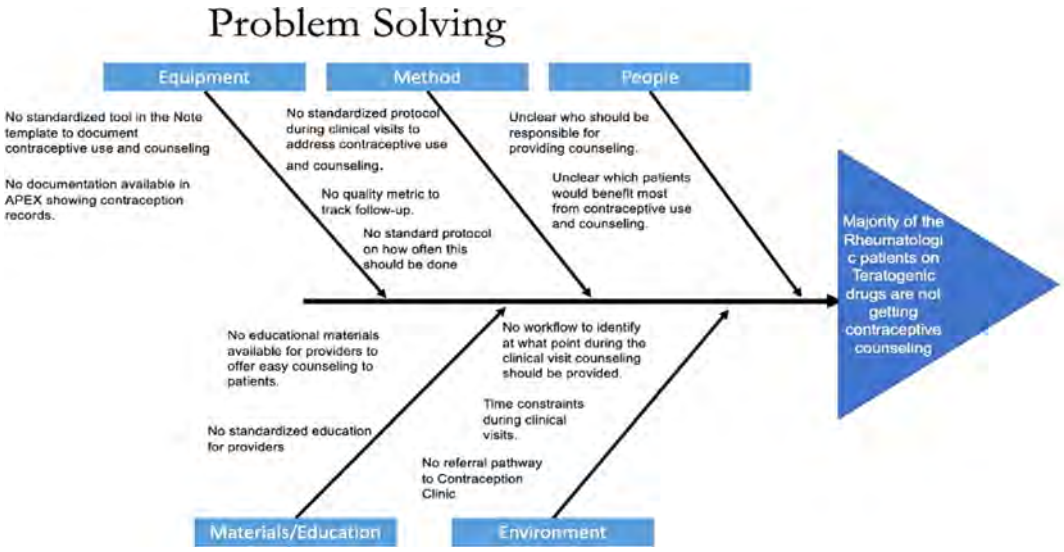


Figure 1. Fishbone Diagram Identifying Barriers to Contraceptive Counseling for Patients on Teratogenic Medications. This diagram outlines the root causes contributing to missed contraceptive counseling opportunities.

Figure 2. A line graph showing the percentage of eligible patients with documented counseling, increasing from 35% at baseline to 82% after the intervention period.

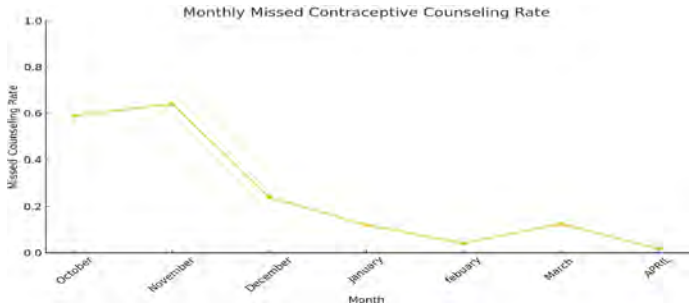


Figure 3. In-process metric showing Reduction in Missed Eligible Patients for Contraceptive Counseling. This is a line graph displaying the decline in missed counseling opportunities, from 64% in November 2024 to 1.82% in April 2025, following workflow revisions and nurse-led interventions.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: A multidisciplinary, systems-based approach led to a substantial improvement in contraceptive counseling rates for patients on teratogenic medications.

Disclosure: A. Fadairo-Azinge: None; **j. Romulo**: None; **D. Flores**: None; **j. Giron**: None; **J. Ng**: None; **S. Patterson**: None; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5; **A. Gross**: None.

Abstract Number: 1973

Evaluating the Impact of Clinical Pharmacist Integration on Patient Care Outcomes in a Private Rheumatology Clinic

Madana Kamineni[1], Janelle Vircks[1], Jessica Lynton[1], Clarisse Purvis[1] and **Brittany Panico**[2], [1]Optum, Gilbert, AZ, [2]Summit Rheumatology, Gilbert, AZ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Existing data demonstrate that clinical pharmacist integration in rheumatology clinics improves provider satisfaction, patient outcomes, medication adherence, and RAPID-3 (Routine Assessment of Patient Index Data 3) scores, yet studies have largely focused on tertiary care settings. This study addresses the gap by evaluating pharmacist integration within a private rheumatology clinic and its impact on patient outcomes, provider satisfaction, and pharmacist-led interventions.

Methods: The study received IRB exemption and was conducted from August 1, 2024, to January 31, 2025. Data were collected manually from the clinic's electronic medical record and analyzed using descriptive statistics. All rheumatology patients referred to the clinical pharmacist during this period were included.

Primary outcomes included changes in RAPID-3 scores at baseline, day 28, 3 months, and 6 months, and documentation of pharmacist interventions such as medication reviews, education, access support, and provider decision-making assistance. These interventions occurred during collaborative visits, phone follow-ups, and real-time consults. Secondary outcomes measured provider satisfaction via a post-study survey.

Results: A total of 302 pharmacist-led consults were conducted. Of these, 224 (74%) involved prior authorization (PA) support, 167 (55%) included patient education, and 120 (40%) addressed side effect management. RAPID-3 assessments were completed for 150 patients (50%). Results showed a statistically significant median RAPID-3 score reduction of 2.65 points ($p<0.0001$), although this did not meet the 3.5-point threshold for minimal clinically important improvement (MCII). Notably, 68 patients (45.3%) achieved clinically meaningful improvement, indicating that nearly half experienced significant benefit from pharmacist involvement.

Provider satisfaction (n=7) was overwhelmingly positive. All respondents agreed or strongly agreed that the pharmacist improved care quality, reduced administrative burden, and supported prior authorization processes. Most strongly agreed that the pharmacist improved medication understanding and was readily accessible. All rated the impact on workflow and prescribing positively, with 71.4% describing it as "very positive." Open-ended comments highlighted enhanced efficiency, decreased workload, and improved patient care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Integration of a clinical pharmacist into a private rheumatology clinic had a meaningful clinical and operational impact. The pharmacist contributed significantly to disease monitoring, medication access, patient education, and treatment side effect management. While the average RAPID-3 improvement did not meet the MCII threshold, nearly half of the patients achieved clinically significant benefit. The high provider satisfaction further supports pharmacist integration as a valuable model for improving quality of care and clinic operations in private practice settings. Further research is warranted to explore long-term outcomes and scalability.

Disclosure: M. Kamineni: None; **J. Vircks**: None; **J. Lynton**: None; **C. Purvis**: None; **B. Panico**: AbbVie/Abbott, 6, Amgen, 1, 2, 6, AstraZeneca, 2, Janssen, 1, Novartis, 2, Sobi, 1, 2, UCB, 6.

Abstract Number: 1974

Serial ferritin as a diagnostic surrogate marker in Hemophagocytic Lymphohistiocytosis (HLH), a retrospective single-center study

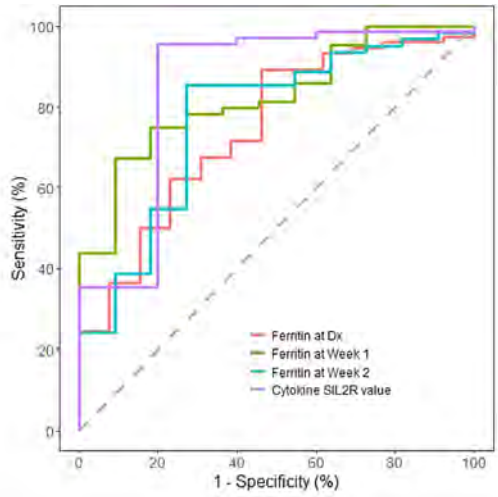
Chen Chao[1], Anna Lichtiger[2], Xianhong Xie[3], Melissa Fazzari[4] and Ayesha Bibi[5], [1]Rheumatology Division, Department of Medicine, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, NY, [2]Internal Medicine, Albert Einstein College of Medicine/Montefiore Medical Center, The Bronx, NY, [3]Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, NY, [4]Department of Epidemiology & Population Health, Albert Einstein College of Medicine,, Bronx, NY, [5]Rheumatology Division, Department of Medicine, Albert Einstein College of Medicine/Montefiore Medical Center, Woodbridge Township, NJ

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hemophagocytic lymphohistiocytosis (HLH) is an immune-mediated disorder characterized by cytokine dysregulation, resulting in multi-organ involvement and high mortality. (1-2) There is a time lag in the consideration of HLH diagnosis and initiation of treatment using HLH-2004 criteria. (1) There is a paucity of current literature to predict the ongoing cytokine storm in these patients, as it necessitates the analysis of soluble interleukin-2 receptor (sIL2r) and bone marrow biopsy, which has a delayed reporting time. Ferritin is a cost-effective and rapidly available biomarker. Our study in a tertiary center highlights the importance of periodic trending of ferritin levels in critically ill patients, which could be used as a surrogate for predicting patients who progress towards HLH and guiding the timely initiation of therapy.

Methods: After Institutional Review Board (IRB) approval, the electronic medical record (EMR) database was queried from 2016 to 2024 to identify patients ≥ 18 years, who were considered to have HLH during their hospital course. Patients were stratified into three groups based on the fulfillment of HLH-2004 criteria: those without HLH (≤ 3/8 criteria), probable HLH (4/8 criteria), and definitive HLH (≥ 5/8 criteria). A Retrospective EMR chart review was conducted. SAS software version 9.4 and R version 4.2.2 were used for the statistical analyses. Two-sample t-tests and Wilcoxon's rank sum tests were used to compare continuous variables depending on whether the variable is normally distributed. Chi-square tests and Fisher's exact tests were used for comparing categorical variables as appropriate. Receiver Operating Characteristic (ROC) curves were drawn, the Youden index was used to choose the best thresholds, and the DeLong method was used to calculate the confidence intervals on the area under the curve (AUC).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Biomarker	AUC (95% CI)	Best threshold	Sensitivity	Specificity
Ferritin at Dx	0.744 (0.598-0.891)	2684	89.2%	53.8%
Ferritin at Week 1	0.824 (0.707-0.941)	4999.5	67.2%	90.9%
Ferritin at Week 2	0.770 (0.608-0.932)	2182.5	85.5%	72.7%

Figure 1: ROC analysis of Ferritin for HLH (probable with definitive HLH) vs without HLH

Table 1: Baseline demographics and HLH-2004 criteria

Baseline demographics	Overall (n=88)	Definitive HLH (n=59)	Probable HLH (n=16)	Without HLH (n=13)
Age at diagnosis (mean)	49.1 (19)	50.5 (18)	48.3 (17)	43.7 (22)
Gender				
Male	56 (64%)	36 (61%)	12 (75%)	8 (62%)
Female	32 (36%)	23 (39%)	4 (25%)	5 (39%)
Ethnicity				
Hispanic or Latino	38 (43%)	26 (44%)	5 (31%)	7 (54%)
Non-Hispanic	41 (47%)	26 (44%)	11 (69%)	4 (31%)
Unknown	9 (10%)	7 (12%)	0 (0%)	2 (15%)
Race				
Black	23 (26%)	13 (22%)	7 (44%)	3 (23%)
Caucasian	9 (10%)	6 (10%)	3 (19%)	0 (0%)
Asian	6 (7%)	5 (9%)	0 (0%)	1 (8%)
Other	50 (57%)	35 (59%)	6 (38%)	9 (69%)
HLH-2004 criteria				
Fever (> 101°F > 48 hours)	73 (83%)	53 (90%)	10 (63%)	10 (77%)
Splenomegaly	56 (64%)	51 (86%)	5 (31%)	0 (0%)
More than 2 Cytopenias (Hb < 9; PLT < 100; Neutrophils < 1000)	43 (48%)	38 (64%)	5 (31%)	0 (0%)
Hypertriglyceridemia	61 (70%)	41 (70%)	10 (63%)	10 (77%)
Hypofibrinogenemia	4 (5%)	3 (5%)	1 (6%)	0 (0%)
Both	15 (17%)	12 (20%)	3 (19%)	0 (0%)
Hyperferritinemia	87 (99%)	59 (100%)	15 (94%)	13 (100%)
Bone marrow biopsy with hemophagocytosis	20 (23%)	18 (31%)	2 (13%)	0 (0%)
Low/absent NK-cell activity	5 (6%)	4 (7%)	1 (6%)	0 (0%)
High soluble IL-2r	70 (80%)	54 (92%)	12 (75%)	4 (31%)

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We identified a total of 88 patients, with a mean age of 49 years, of whom 56 (63%) were males and 38 (43%) were Hispanics. (Table 1) This cohort was critically ill, 53 (60%) requiring intensive care unit, 22 (25%) new replacement kidney therapy and 37 (42%) mechanical ventilation.

Of these 88 patients, 59 were definitive HLH, 16 probable HLH and 13 without HLH. sIL2r is a highly specific marker with a high turnaround time, making its utility low in treatment initiation. Logistic regression analysis of sIL2r showed an odds ratio of 2.09 for in-hospital mortality (1.32-3.30 CI 95%; p-value 0.002). ROC analysis of ferritin levels (Figure 1) achieved a sensitivity of 89% at the time of considering the diagnosis, while a cut-off of 5000 ng/mL was associated with a high specificity of 91% in the first week of suspicion for HLH.

Conclusion: HLH-2004 criteria are not time-sensitive in managing these critically ill patients due to delays in reporting of sIL2r and bone marrow biopsy results. Our study emphasizes that periodically monitoring serial ferritin levels could serve as a valuable, cost-effective surrogate marker to sIL2r for the timely initiation of immunomodulator therapy and avoiding untoward patient outcomes.

References

(1) Hayden A, et al. Hemophagocytic syndromes (HPSs) including HLH in adults. Blood Rev (2016)
(2) Buyse S, et al. Intensive Care Med (2010)

Disclosure: C. Chao: None; **A. Lichtiger**: None; **X. Xie**: None; **M. Fazzari**: None; **A. Bibi**: None.

Abstract Number: 1975

Baseline QTc Screening and Monitoring Among SARD Patients with High Cardiovascular Risks on Hydroxychloroquine Based on 2021 ACR Consensus: A Quality Improvement Project

Cristine Kuzhuppilly Arcilla[1], Gabriel Kirsch[2], Gurjit Kaeley[3] and Myint Thway[4], [1]University of Florida Jacksonville, Jacksonville, FL, [2]University of Florida - Jacksonville, Jacksonville, FL, [3]UF COM-J, Ponte Vedra Beach, FL, [4]UF Jacksonville, ponte vedra, FL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: In 2017, FDA approved warnings regarding fatal cardiac effects such as cardiomyopathy, torsades de pointes, and QTc prolongation related to both acute and chronic Hydroxychloroquine (HCQ) use. QTc >470 ms during HCQ treatment was associated with increased mortality risk[1]. COVID-19 pandemic in 2020 reemerged discussions regarding HCQ's cardiotoxicity as it was experimentally used in the acute setting. In 2021, a white paper on consensus between rheumatologists and cardiologists was released by ACR[2]. While it acknowledged that the foundational benefits of HCQ outweigh the associated cardiac risks in SARD patients, it mentioned utilizing ECG for patients with high-risk cardiovascular (CV) factors. These factors include female, older age (>68 years), recent heart disease, prolonged duration of HCQ use, and >1 QTc-prolonging medications, such as concurrent fibromyalgia and depression/anxiety, prevalent in the SARD population. Hence, this study aims to increase cardiac screening/monitoring through routine ECG, particularly in SARD patients with high CV risks on HCQ.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

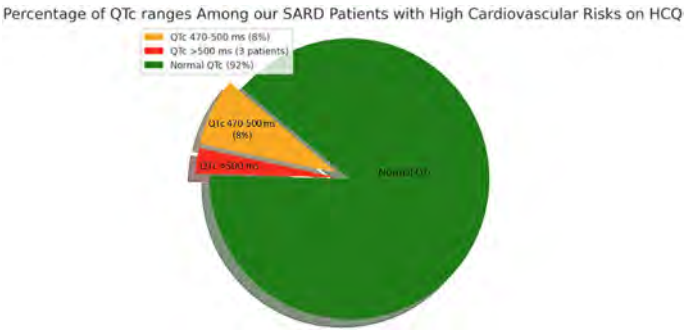
Methods: This quality improvement (QI) project retrospectively analyzed medical records of patients at least 18 years old on HCQ seen at University of Florida rheumatology clinic sites from 06/2023 to 12/2023 and had ECG done within the past year as initial data (pre-intervention phase). Coordination with cardiology and scheduling team allowed same-day walk-in ECG, especially for high-risk patients based on cardiac risk stratification, increasing ECG accessibility. Interventions also included creating flyers and educating medical staff periodically. Documentation of ECG results was facilitated by generating smart phrases into patient's visit note under the specific cardiac risk stratification and diagnosis. Subsequent retrospective chart review of 50 patients was performed after 12 months to analyze impact of interventions.

Results: Initial data showed the need for increasing ECG testing in our high-risk SARD patients (Table 1). All patients were on adequate HCQ dosing. Only 12% had baseline ECG within past year. Post-intervention, this percentage increased to 55%, with more than 2/3 done on same-day rheumatology visits along with electronic documentation of ECG and cardiac risk stratification. Eight percent had QTc 470–500 ms; 3 patients with QTc >500 ms were associated with more acute settings (ESRD, acute admission, and pacemaker) (Figures 1 and 2). Risks vs benefits discussions and decisions on adjusting HCQ dose based on weight and HCQ levels, closer monitoring, and even switching to another DMARD were done accordingly.

Conclusion: This QI project demonstrates routine ECG as simple and inexpensive cardiac screening/monitoring tool for SARD patients with high CV risks on HCQ. We developed interventions (interdepartment collaboration, etc) that facilitated ECG accessibility, identification of cardiac risk stratification, improved documentation and modification, and

Table 1. Patient demographics and clinical characteristics of our SARD patients with high cardiovascular risks on HCQ based on the 2021 ACR Consensus.

Risk factor	% of our SARD patients
Female sex	80
Older age (especially >68 years)	20
Heart disease (including recent history of admissions for cardiac arrhythmias, myocardial infarction, and heart failure) and diabetes mellitus	40
CKD	18
>1 concurrent QTc prolonging drugs	42
More than 5 years HCQ use	42
>1 comorbidities	28
>3 comorbidities	6



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

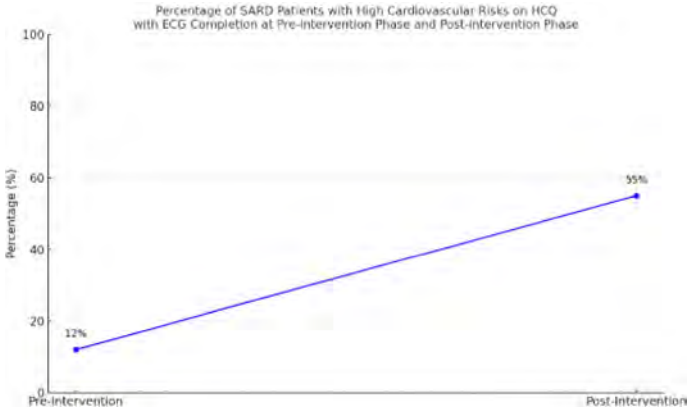


Figure 2. Percentage of SARD patients with High Cardiovascular Risks on HCQ with ECG Completion at the Pre-intervention Phase and Post-intervention Phase.

monitoring of current treatment regimen based on their CV risk factors and disease activity. This study answers ACR's call for addressing the ongoing need for evaluating HCQ's rare but fatal cardiotoxic risks among our SARD patients with high CV risks on HCQ.

Disclosure: C. Kuzhuppilly Arcilla: None; **G. Kirsch**: None; **G. Kaeley**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Janssen, 5, Novartis, 5; **M. Thway**: None.

Abstract Number: 1976

Implementing a Change Package for Depression Screening and Appropriate Response for Children with Rheumatic Disease

Emily Vara[1], Mileka Gilbert[1], Kelly Rouster-Stevens[2], Talia Buitrago-Mogollon[3], Sarah Mabus[3], Justin Moore[4] and Sheetal Vora[5], [1]Medical University of South Carolina, Charleston, SC, [2]Emory University/Children's Healthcare of Atlanta, Peachtree Corners, GA, [3]Atrium Health Levine Children's Center for Advancing Pediatric Excellence, Charlotte, NC, [4]Wake Forest School of Medicine, Winston Salem, NC, [5]Atrium Health Levine Children's Hospital, Charlotte, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Children with rheumatic diseases (RD) are at increased risk for developing mental health (MH) issues, including depression, which can negatively impact disease outcomes. MH disorders are underrecognized in pediatric RD. The ACR recently published MH screening guidelines in pediatric RD (Cunningham et al.). The American Board of Pediatrics' "The Roadmap Project" has a readiness checklist to prepare for outpatient MH screening, which was used to create a depression screening change package with appropriate response documented. An implementation science (IS) framework was applied to gauge the effectiveness of our change package.

Goal: To ensure that our change package can be used across diverse pediatric rheumatology clinics. Aims: 1) Assess IS outcomes of change package feasibility and acceptability to aid depression screening with appropriate response. 2) Determine the impact of implementing the change package on contextual factors of relative advantage and adoptability of depression screening.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Meetings to design the implementation strategy included physicians, psychologists, social workers, parents/patients and an IS scientist. A mixed methods approach using the Health Equity Implementation Framework was designed to implement the change package at 3 pediatric rheumatology clinics to screen patients with RD ≥8 (PROMIS) or ≥12 years old (PHQ-9), using a validated depression tool. Each center revised specific quality improvement tools to address unique barriers to screening and responding to screening results. A health equity fishbone diagram captured root cause delinquencies in depression screening. IS outcome and clinical quality measures, along with effectiveness of each change package component, are currently being assessed by the clinical team/parents/patients via REDCap survey at a regular cadence.

Results: We are 5 months into the 12-month implementation strategy. Survey results are reviewed at local and multi-site team meetings. Identified modifications are implemented. At baseline, the 5 parents/patients team members surveyed all agreed with the importance of screening, approved of routine screening, and MH resource pamphlet value. Table 1 is the first staff survey after change package introduction with all 3 teams' agreement of process feasibility, acceptability and package components' helpfulness. Initially weekly and then monthly random sampling of patients eligible for screening was done to assess clinical quality measures (Figure 1). This sample of patients were 77% female, 60% White, 29% Black, 15% Hispanic, 93% English primary language, 50% with private insurance, and 41% with Medicaid. The most common RD were JIA and SLE, as expected. Appropriate response to screening employed the change package tools and community/clinic resources (Figure 2). No patient required emergent care.

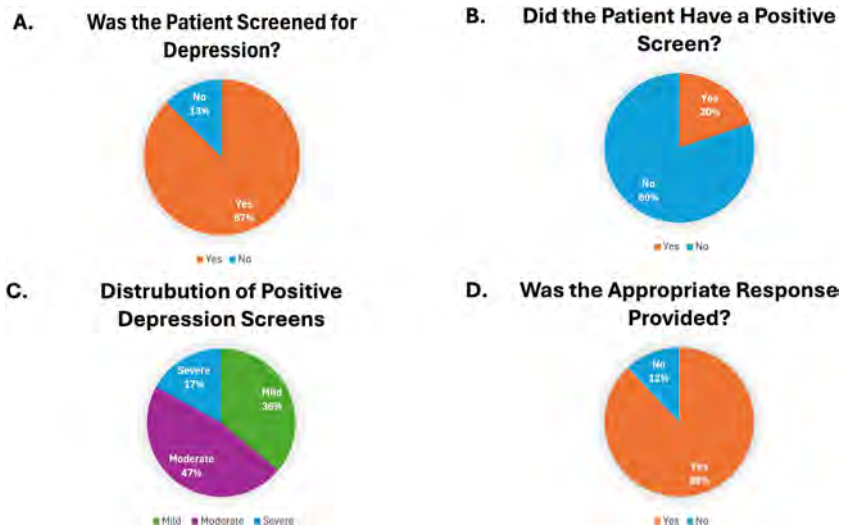


Figure 1. A: 87% of patients were screened for depression. B: 20% of those screened had a positive result. C: for those with a positive depression screen, 36% were mild, 47% moderate, and 17% severe. D: of those with a positive screen, 88% received an appropriate response.

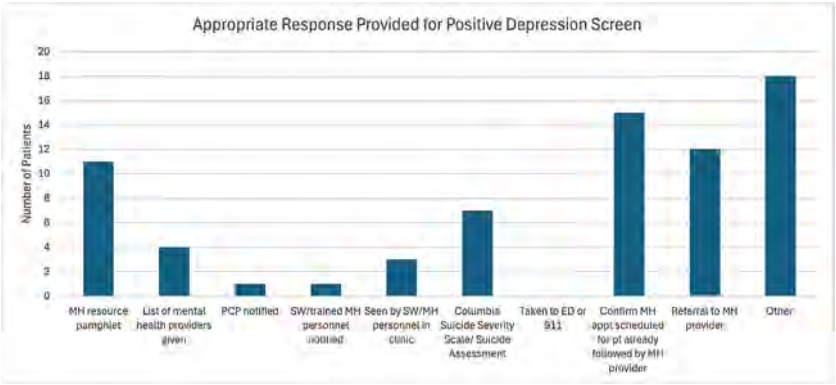


Figure 2. In those with a positive depression screen, 88% received one of the responses noted above. Other included situational stressors reviewed with patient and patient to return to office if symptoms persist or worsen (13 of 18), PCP arranging local therapy referral (1 of 18), and corresponded in EMR with Behavioral/Mental Health provider (1 of 18). Primary Care Provider=PCP, SW=Social Worker, MH=Mental Health

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Clinical Staff Assessment of Change Package

Table. Clinical Staff Assessment of Change Package

Clinical Staff Survey Component	Strongly Agree and Agree Responses			
	AHLC N=8	MUSC N=8	Emory N=9	All sites N=25
Implementation Science Measures				
Acceptability	8/8	8/8	9/9	25/25
Feasibility	8/8	8/8	9/9	25/25
Clinical Flow				
Decreased time for other tasks	3/8	1/8	1/9	5/25
Increased number of meetings	2/8	0/8	0/9	2/25
Increased charting time	6/8	4/8	5/9	15/25
Leadership				
Leadership awareness	6/8	6/8	9/9	21/25
Effectiveness of Change Package				
PPT usefulness	7/8	5/8	7/9	19/25
PPT helpful to the staff to understand importance of mental health screening	7/8	5/8	6/9	18/25
Script provided appropriate explanation to the patient /family	8/8	7/8	9/9	24/25
Patient/Family receptive to screening after hearing the script	8/8	7/8	9/9	24/25
ABP Videos relayed the importance of MH issues to the staff	5/8	7/8	6/9	18/25
ABP Videos helpful to rheumatology provider to introduce MH topic to patient	6/8	5/8	6/9	17/25
MH Resource Pamphlet helpful to family	7/8	7/8	8/9	22/25

AHLC= Atrium Health Levine Childrens, MUSC= Medical College of South Carolina, ABP=American Board of Pediatrics, PPT= PowerPoint, MH=Mental Health

Conclusion: Using IS, our 3 diverse sites have evaluated a change package that to date is feasible and acceptable, providing a systematic approach to fulfill the pediatric rheumatology community's desire to screen and further close the gap in addressing mental health. Patients/parents as equal stakeholders helped to identify areas for adjustment and adoptability.

Disclosure: E. Vara: None; **M. Gilbert**: None; **K. Rouster-Stevens**: Accordant, 2; **T. Buitrago-Mogollon**: None; **S. Mabus**: None; **J. Moore**: None; **S. Vora**: None.

Abstract Number: 1977

The Westergren Sedimentation Rate: To Be or Not to Be! The Westergren Sedimentation Rate is being "Killed" but has not "Died".

John Goldman[1], Michael Goldman[2], Glenn R. Parris[3] and Parris and Associates, [1]Emory University St Josephs Hospital, Atlanta, GA, [2]SENTA Southeastern Ear, Nose, Throat and Allergy, Atlanta, GA, [3]PARRIS & ASSOCIATES, Lilburn, GA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The Westergren Sedimentation Rate (WSR) is a simple, cost-effective laboratory test commonly used by rheumatologists to assess systemic inflammation. This study was initiated to evaluate the current status and availability of the erythrocyte sedimentation rate (ESR) for practicing physicians. Specifically, we aim to compare the accuracy and concordance of the manually performed STAT WSR, processed within two hours of sample collection, with the ESR performed at the central laboratory (CRL), which uses automated capillary photometry. We are particularly interested in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

whether delays in specimen transport to the CRL impact the reliability of ESR results compared to the more immediate manual WSR.

Methods: We reviewed WSR reports for 106 de-identified patients (Table 1) tested in the POL, and for whom a specimen was also sent the same day to a CRL for erythrocyte sedimentation rate (ESR) testing. This dual testing was initiated after observing that ESR results from the CRL were frequently lower than the POL WSR. Notably, no charges for the in-office WSR.

The POL used manual WSR testing. In contrast, the CRL utilized the iSED® system by Alcor, an automated method that directly measures red blood cell aggregation using capillary photometry during rouleaux formation. We also investigated whether the time interval between specimen collection and analysis at the CRL had an impact on ESR comparability.

Results: The ESR measured in the POL was significantly higher than that in the CRL, as demonstrated by both statistical analysis and Passing-Bablok regression (Table 2 and Figure 1). Additionally, we assessed the coefficient of variation (CV) for manual sedimentation rates using three tube comparisons.

Conclusion: This study was conducted to assess the rationale behind requiring WSR specimens to be sent to a CRL and to evaluate how effectively the CRL performs ESR testing. Although the CRL claims its methodology is equivalent to WSR, its ESR testing process is not performed while the specimen is fresh.

Table 1. Patients

Table 1 Patients

Diagnosis	Number of patients
Rheumatoid Arthritis	27
Seronegative Polyarthritis (Some + HLA B27)	11
Fibromyalgia	22
Osteoarthritis	6
Gout + Pseudogout	7
Psoriatic Arthritis	5
Connective Tissue Disease – 10 with SLE, 3 with PSS, 1 with MCTD, 4 with Sjogren's, 1 with Vasculitis, 3 with Raynaud's.	22
Non-inflammatory control 2 with hypermobility syndrome, 1 with miscarriages, 1 myofascial pain	4

Table 2. Statistics

Table 2. Statistics

Physician Office Laboratory Results	Central Reference Laboratory Results	T Statistic	P Value
2 Same 2 mm, 7 mm	2 Same 2 mm, 7 mm		
Higher 92 (1-105 mm)	Higher 10 (1 - 23 mm)		
Mean 36.7 mm	Mean 23.9 mm	-9.55965	3.56301 E – 16

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

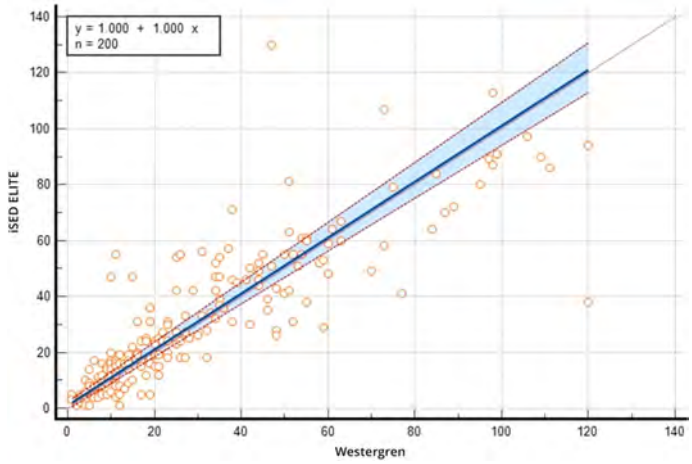


Figure 1. Passing Bablok of the Westergren Sedimentation Rate Compared to the iSED Sedimentation Rate

A WSR must be performed rapidly—ideally within 2 hours of specimen collection—while the blood is still fresh. In the POL it is ordered as a STAT test. Many American patients are covered under insurance plans that either require testing through a CRL or permit POL testing. However, POL testing requires full CLIA certification, which entails substantial administrative overhead, including paperwork, inspections, and associated costs. In-office WSR, by contrast, is a CLIA-waived test, making it a practical option.

The CRL uses automated photocytometry for large-scale ESR testing. However, it remains uncertain whether this automated method provides equivalent clinical value when compared to manual WSR. The core concern is the total turnaround time, from the moment the blood is drawn to when the ESR is actually performed. Some CRLs are located far from the physician's office, in some cases even out of state, necessitating courier or air transport. Often, specimens drawn throughout the day are not shipped until evening. Both resulted in processing delays up to 24 hours or more. This delay could significantly affect clinical decision-making, especially when monitoring conditions such as rheumatoid arthritis using metrics like the DAS28ESR.

Disclosure: J. Goldman: None; **M. Goldman**: None; **G. Parris**: None.

Abstract Number: 1978

Utilizing a Gap to Target Function in the Pediatric Rheumatology Care and Outcomes Improvement Network Registry Dashboard of Quality Measures

Julia Harris[1], Catherine Bingham[2], Sheetal Vora[3], Kerry Ferraro[4], Erik Friedrichsen[5], Cagri Yildirim-Toruner[6], Ted Wimmel[7], Delores Mincarelli[8], Magen Phillips[9] and Esi Morgan[10], for the Pediatric Rheumatology Care and Outcomes Improvement Network, [1]Children's Mercy Kansas City, Overland Park, KS, [2]Penn State Children's Hospital, Hershey, PA, [3]Atrium Health Levine Children's Hospital, Charlotte, NC, [4]Pediatric Rheumatology Care and Outcomes Improvement Network, Cincinnati, [5]Seattle Children's Hospital, Burien, WA, [6]Baylor College of Medicine/ Texas Children's Hospital, Houston, TX, [7]Hive Solutions, LLC, Cincinnati, OH, [8]Hive Solutions, LLC, Newport, KY, [9]Hive Solutions, LLC, Blue Ash, OH, [10]Seattle Children's Hospital, Seattle, WA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is a multi-site learning health network organized to improve outcomes of juvenile idiopathic arthritis (JIA). PR-COIN has a centralized registry that tracks 10 outcome measures, 6 process measures, 3 data quality measures, and 1 balancing measure. A 'gap to target' feature was implemented in the registry for each categorical quality measure (QM). This feature enumerates the count of individual patients (or visits) that would need to meet qualification to pass the QM in order for the performance to reach the established network QM target value. Reporting the performance deficit in individual terms sharpens improvement focus, conveys the order of magnitude to reach the goal, and facilitates interventions to close quality of care gaps for individual patients at the site level.

Methods: The PR-COIN registry captures data from 21 sites with more than 14,500 JIA patients and 96,000 visits since 2011. In 2022, our collaborative switched to a new registry vendor, Hive Solutions, LLC., and developed a new measure dashboard and population management tool. Network performance goals were updated in 2024 based on current network-wide performance, balanced with performance data of specific sites selected based on data completeness for each given measure and representativeness (over 75% of clinic patients enrolled in registry), input of parent/patient partners, and published JIA outcomes. Additional registry functionality was added to include a 'gap to target' feature both at a network and site level.

Results: The 'gap to target' was added to our main measure dashboard page (Figure 1). When viewing network data, the 'gap to target' column identifies the specific number of patients (or visits) needed to be added to a measure numerator (based off the previous month's data) for the network goal to be achieved. Specific sites can also review this data in relation to their own JIA population and the network targets with a separate feature to identify specific patients not yet meeting the measure definition. An additional 'gap to target' page can look at each QM by month (starting in May 2024) to identify the gap to network target by percentage with a quick visual to denote whether that month's performance was better than the target (green check) or lower than the target (orange box), if the desired direction of improvement is up (Figure 2).

Conclusion: Identifying specific gaps to target for QMs will help quantify the scope of effort needed to achieve network goals. This gap analysis can help the PR-COIN sites and the collaborative prioritize efforts to optimize care and outcomes for children with JIA. This registry feature also helps sites stay engaged and encouraged as they can closely track the

Measure Category	Measure Sub-Category	Measure	Network Target	Network Performance Prior Reporting Period	Gap to Target (Prior Month)
Outcome Measure	Disease Activity	Inactive or low disease activity	85.0%	80.8%	86
		Mean disease activity (cJADAS10)	2.50	2.77	
		Inactive/low disease activity by 6 mo	35.0%	62.5%	
		Clinical inactive disease (no ESR/CRP)	65.0%	59.1%	73
		Mean active joint count	0.50	0.75	
		Mean Physician Global Assessment of Disease Activity Score	0.50	0.67	
	Patient-reported outcomes	Mean Patient/Parent Global Assessment	1.30	1.45	
		Patient/Parent Global Assessment <=2	80.0%	76.6%	115
		No or mild pain	83.0%	81.5%	53
		Optimal Physical Function	75.0%	71.3%	69
Process Measure	Routine	Documentation of Physician Global Assessment of Disease Activity score at every visit	95.0%	92.6%	11
		Toxicity labs for synthetic DMARDs	50.0%	57.7%	
		Self Management Support Given	50.0%	28.6%	92
	Treat to Target	Treatment Target Set	50.0%	25.5%	691
		Attest disease activity status for T2T	65.0%	76.8%	
		Care algorithm/clinical decision support	50.0%	59.1%	
Data Quality Measure	Completeness	Critical data recorded	65.0%	53.7%	49
	Timeliness	Patients with Clinic Visit within 120 Days of Initial Diagnosis	35.0%	60.0%	
	Completeness & Timeliness	Active patients with a visit recorded in the last 13 months	60.0%	53.7%	473

Figure 1. PR-COIN network performance dashboard with 'gap to target' feature.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

MeasureName	DenominatorType	Date	Improve Direction	Percent Meeting	Network Target	Gap to Network Target
Toxicity labs for synthetic DMARDs	Patient	2024-May	up	36.59%	50%	13.41%
Toxicity labs for synthetic DMARDs	Patient	2024-Jun	up	39.39%	50%	10.61%
Toxicity labs for synthetic DMARDs	Patient	2024-Dec	up	45.54%	50%	4.46%
Toxicity labs for synthetic DMARDs	Patient	2024-Jul	up	46.15%	50%	3.85%
Toxicity labs for synthetic DMARDs	Patient	2024-Aug	up	47.62%	50%	2.38%
Toxicity labs for synthetic DMARDs	Patient	2025-Jan	up	48.81%	50%	1.19%
Toxicity labs for synthetic DMARDs	Patient	2025-Apr	up	50.00%	50%	0.00%
Toxicity labs for synthetic DMARDs	Patient	2024-Sep	up	52.50%	50%	-2.50%
Toxicity labs for synthetic DMARDs	Patient	2024-Nov	up	52.50%	50%	-2.50%
Toxicity labs for synthetic DMARDs	Patient	2024-Oct	up	53.62%	50%	-3.62%
Toxicity labs for synthetic DMARDs	Patient	2025-Feb	up	54.10%	50%	-4.10%
Toxicity labs for synthetic DMARDs	Patient	2025-Mar	up	57.69%	50%	-7.69%

Figure 2. 'Gap to target' page showing quantitatively and visually if measure performance above or below the network target each month.

number of patients needed to achieve each goal. Network targets will continue to be adjusted based on measure performance.

Disclosure: J. Harris: None; **C. Bingham**: None; **S. Vora**: None; **K. Ferraro**: Abby's Army, 3, 8, 12, President; **E. Friedrichsen**: None; **C. Yildirim-Toruner**: None; **T. Wimmel**: Hive Solutions, LLC, 3; **D. Mincarelli**: Hive Solutions, LLC, 3; **M. Phillips**: Hive Solutions, LLC, 3; **E. Morgan**: None.

Abstract Number: 1979

Utility of ALT/AST and Fibrosis-4 Index (FIB-4) Score in Monitoring Methotrexate Hepatotoxicity in Rheumatologic Disease: A Retrospective Analysis

Julia Wajsberg[1], Dana Nachawati[2], Lenche Kostadinova[3], Donald Anthony[4] and Maya Mattar[3], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]University Hospitals, Cleveland, [3]Louis Stokes Cleveland VA, Cleveland, [4]The MetroHealth System at Case Western Reserve University School of Medicine, Cleveland, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate (MTX) is widely used in rheumatologic disease but carries hepatotoxic risk. Standard monitoring relies on measurement of alanine and aspartate aminotransferase (ALT and AST), though their variability limits specificity. The FIB-4, a composite fibrosis index that combines biochemical values (platelet count, ALT, and AST) and age, may offer a more stable marker of hepatic injury. Our objective was to evaluate the utility of ALT, AST, and FIB-4 in monitoring MTX-related hepatotoxicity and to characterize provider management of transaminitis.

Methods: We retrospectively analyzed 43 patients followed at the Louis Stokes Cleveland Veterans Affairs Medical Center Rheumatology Clinic, treated with MTX for rheumatologic disease, and with AST/ALT >2× upper limit of normal (ULN) during this treatment. Interventions and clinical data—including FIB-4 scores, cumulative MTX exposure, and risk factors (non-alcoholic fatty liver disease (NAFLD), body mass index (BMI) statin use, diabetes, hyperlipidemia, hypertension)—were analyzed. Discriminative performance for MTX dose changes in relation to AST/ALT/Fib4 change was assessed using area under the ROC curve (AUC).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: MTX was held or reduced in 60% of cases (with the median delay between first AST/ALT elevation and MTX dose change: 4.2 months). Responses included early (less than 3 months) repeat of LFTs (37%), liver imaging (12%), and no action (19%). FIB-4 showed modest discrimination for MTX associated change in laboratory parameters (AUC 0.64), slightly outperforming ALT (0.62) and AST (0.57); a composite score incorporating all three yielded a higher AUC of 0.66. None reached statistical significance. Cumulative MTX dose did not differ significantly between patients with persistent vs. non-persistent transaminitis (mean 48,650 mg vs. 55,307 mg; p=0.34). No demographic or clinical variable—including NAFLD, BMI, or statin use—was independently associated with AST, ALT or FIB-4 change.

Conclusion: Provider responses to MTX-induced transaminitis were inconsistent and often delayed beyond 3 months. A composite of FIB-4, ALT, and AST showed the highest discriminative value for guiding MTX modification. Neither traditional metabolic risk factors nor cumulative methotrexate dose were predictive of hepatotoxicity in this cohort. FIB-4 may offer a more consistent signal for MTX hepatotoxicity monitoring compared to AST/ALT, though this requires additional analysis in a larger cohort.

Disclosure: J. Wajsberg: None; **D. Nachawati**: None; **L. Kostadinova**: None; **D. Anthony**: None; **M. Mattar**: None.

Abstract Number: 1980

Improving Vaccination Rates in the Rheumatology Clinic

Kajal Patel[1], Sunita Paudyal[1] and Deborah Hurley[2], [1]Prisma Health, Columbia, [2]Prisma Health Midlands, Columbia

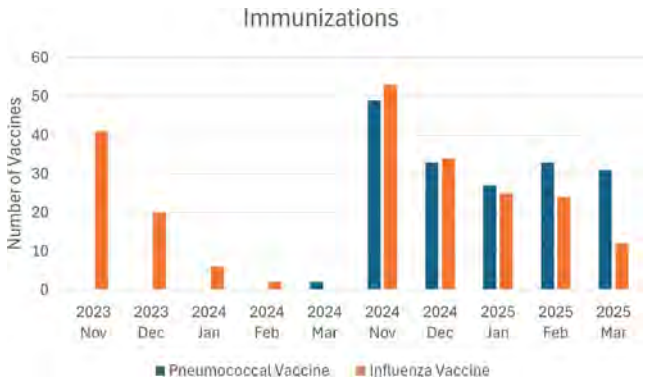
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Influenza and pneumococcal infection can cause mild to severe illness and potentially lead to serious complications or death. Patients with rheumatic diseases have weakened immune defenses due to the disease and immunosuppressive therapy, increasing their risk of infections and complications. The American College of Rheumatology recommends the high-dose or adjuvanted influenza vaccine and the pneumococcal vaccine for patients with rheumatic or musculoskeletal diseases on immunosuppressive therapy. Despite these guidelines, vaccination rates in this population remains suboptimal. Barriers include lack of provider prompts, inconsistent vaccination documentation, and lack of or vaccine misinformation for patients. Our goal is to improve vaccination rates in Rheumatology clinic to protect this vulnerable population.

Methods: Baseline data on influenza and pneumococcal vaccination rates were collected from November 1, 2023 to March 31, 2024 (Period 1). During each visit, patients received a questionnaire to assess vaccine status and interest. Providers and clinic staff attended an educational session outlining the importance of vaccination in immunosuppressed patients, project objectives, and strategies for identifying eligible patients using the questionnaire and electronic medical record care gap alerts. Post-intervention vaccination rates were assessed from November 1, 2024, to March 31, 2025 (Period 2).

Results: Baseline data collected from period 1 revealed administration of 69 influenza vaccines and 2 Pneumococcal (Prevnar 20) vaccines. Following implementation of our intervention, period 2 data demonstrated a marked rise in vaccination rates, with 144 influenza vaccines administered – an 108.9% increase - and 170 Prevnar 20 vaccines administered, reflecting an 8,400% increase. The mean number of influenza vaccines each month was 13.8 and 29.6 in period 1 and 2 respectively with a p-value of 0.144. The mean number of pneumococcal vaccines each month was 0.4 and 34.6 in period 1 and 2 respectively with a p-value of 0.010.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Pneumococcal and Influenza Vaccination Rates from November 1, 2023 to March 31, 2024 and from November 1, 2024 to March 31, 2024.

Conclusion: Vaccinations are crucial in patients with rheumatic and musculoskeletal diseases and receiving immunosuppressive therapy. Baseline data revealed low influenza and pneumococcal vaccine rates, highlighting a critical gap in preventative care. After implementing patient questionnaires and staff education, we observed a marked increase in vaccine uptake—suggesting that targeted interventions with a multidisciplinary team of physicians and ancillary medical staff can effectively improve vaccination rates in high-risk populations. Challenges included inconsistent use of the questionnaire after a few months which was partially mitigated through staff reminders. Furthermore, an area for improvement was ensuring patients receive the high-dose or adjuvanted influenza vaccine when indicated. Limitations included inconsistent access to up-to-date vaccination records and therefore not having denominators for statistical analysis. Moving forward, ongoing education, tracking, and extended outreach are necessary to sustain improvements, ensure administration of indicated vaccines, and further reduce the risk of preventable infections.

Disclosure: K. Patel: None; **S. Paudyal**: None; **D. Hurley**: None.

Abstract Number: 1981

High Patient Satisfaction with a Medication Education Program: Program to Understand Rheumatology Medications with Pharmacist Led Education

Kami Roake[1], Natalie Morlan[1], Stephanie Lim[1], Jennifer Giles[1], Anthony Minjarez[2], Grant Cannon[3], Nadia Grant[4], Vivianne Allsop[5], Miranda Jensen[1], Madeline O'Sullivan[1], Christopher Ching[1], Michael Bessen[1], Javier Rios[6] and Jessica A. Walsh[7], [1]University of Utah, Salt Lake City, UT, [2]Salt Lake City VA, Salt Lake City, UT, [3]University of Utah and Salt Lake City VA, Salt Lake City, UT, [4]University of Utah, Salt Lake City, [5]University of Utah, South Jordan, UT, [6]University of Utah Health, Salt Lake City, UT, [7]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patient education is critical for managing rheumatic diseases. Rheumatology clinic pharmacists are well-positioned to assess and address gaps in patients' understanding of their medications. The objective of this study was to determine patient satisfaction and assess patient understanding of rheumatology medications after a pharmacist-led education (PURPLE) in patients starting new treatment for a rheumatic disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients attending a rheumatology clinic at the University of Utah (UoU) or Salt Lake City Veterans Affairs Health (VA) who were initiating or switching a disease-modifying antirheumatic drug (i.e., conventional synthetic-, biologic-, and targeted synthetic- DMARDs) received initial medication education by the rheumatologist and/or the clinic pharmacist, per standard-of-care practice. Patients were offered a virtual or phone appointment with a rheumatology clinical pharmacist, approximately 2-4 weeks later. The appointments included 1) a structured assessment of the patients' knowledge about their medication and 2) education tailored to each patients' education needs and questions. After the appointment, patients were invited to complete an anonymous survey assessing their satisfaction and knowledge learned during the education appointment.

Results: Among the 62 participants who completed the survey, 49 were from the UoU and 13 from the VA. Patients agreed or strongly agreed the PURPLE education visit was worthwhile (94%), increased their comfort with medication safety (92%), improved their confidence in the medication effectiveness (89%), and provided useful information (95%) (Figure 1). Satisfaction rates were similar between the patient subsets from the UoU and VA (Figure 2). The most frequent categories of information learned during the visit included potential medication related adverse events, what to do if an adverse event occurs, how to administer the medication, and anticipated time to maximum effectiveness (time to onset) (Figure 3).

Conclusion: Patients reported high satisfaction with the PURPLE program. The similarity in outcomes between the clinic sites suggests the program is applicable across different health care systems. These findings underscore the value of personalized, pharmacist-led education for patients receiving treatment for rheumatic diseases.

Figure 1: Patient Satisfaction with the PURPLE Medication Education Program (n=62)

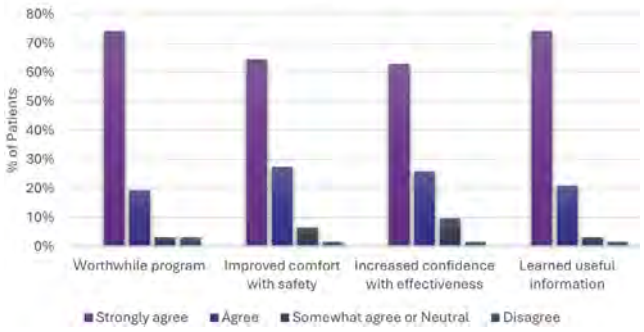
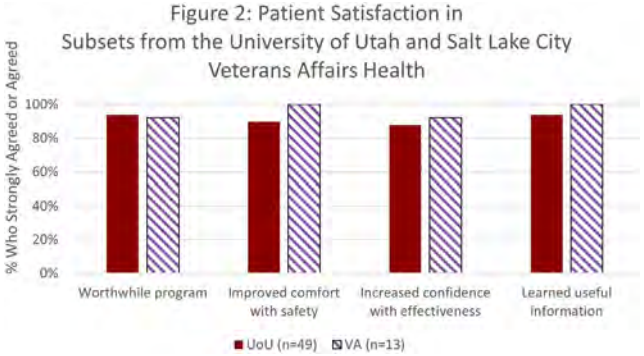
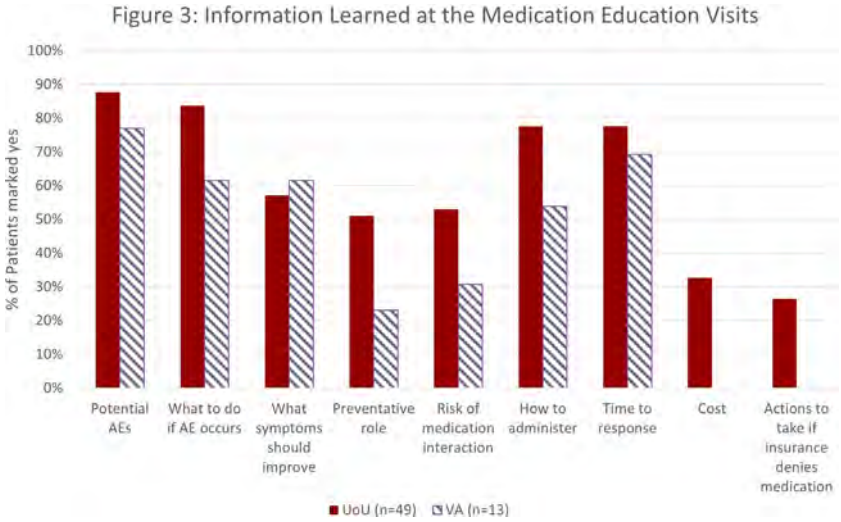


Figure 2: Patient Satisfaction in Subsets from the University of Utah and Salt Lake City Veterans Affairs Health



23265203, 2025, S9, Downloaded from https://accjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: K. Roake: American Pharmacist Association (APhA), 6; **N. Morlan**: None; **S. Lim**: None; **J. Giles**: None; **A. Minjarez**: None; **G. Cannon**: None; **N. Grant**: None; **V. Allsop**: None; **M. Jensen**: None; **M. O'Sullivan**: None; **C. Ching**: None; **M. Bessen**: None; **J. Rios**: None; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5.

Abstract Number: 1982

Bridging the Gap in Underserved Care: A Quality Improvement Initiative to Increase Pneumococcal Vaccination Rates in Immunocompromised Rheumatology Patients

Kuan-Tung Lin[1], Yue Hao[2], Mai Abdelnabi[2] and Wai-Hang Jackie Lam[2], [1]North East Medical Services, San Mateo, CA, [2]North East Medical Services, San Francisco, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatologic conditions who are on immunosuppressive therapy face an elevated risk of pneumococcal infections, particularly those in medically underserved populations. Per ACR and recent CDC guidelines, pneumococcal vaccination is recommended for immunocompromised adults under age 65 and, more recently, for those aged 19–49. However, in busy outpatient settings, vaccination is frequently overlooked. Our goal is to increase pneumococcal vaccination rates among immunocompromised rheumatology patients from a baseline of 33% to 50% in 3 months at North East Medical Services (NEMS), a federally qualified health center (FQHC).

Methods: We focused on patients under 65 years of age diagnosed with RA, PsA, AS, or SLE who were receiving immunosuppressive therapy (excluding hydroxychloroquine and sulfasalazine monotherapy). We used the prior age cutoff (< 65) as the updated CDC guideline for adults under 50 was only released in October 2024 and likely has had limited impact so far. From September 2024 to January 2025, the baseline vaccination rate was identified as 33%. We

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

considered a variety of pneumococcal vaccination sequences valid, including PCV20 or PCV21 alone, PPSV23 followed by PCV20 or PCV21, and PCV13 followed by PCV20 or PCV21.

A root cause analysis (Figure 1) revealed key barriers: patient, physician and other departments (eg, pharmacy, dental). To address these, we introduced a bilingual patient education flyer (English and Mandarin, Figure 2) distributed across all NEMS clinics, simplified the vaccine protocol to PCV20 only, and implemented EMR-based care gap alerts. Additionally, a blast email was sent to all NEMS providers, including PCPs, specialists, and dental staff. The initiative was highlighted during our monthly Medical Quality meeting. At the 2-month mark, we also engaged the pharmacy department to review patients' medication and problem lists during dispensing and offer vaccination if not offered already during clinic visits..

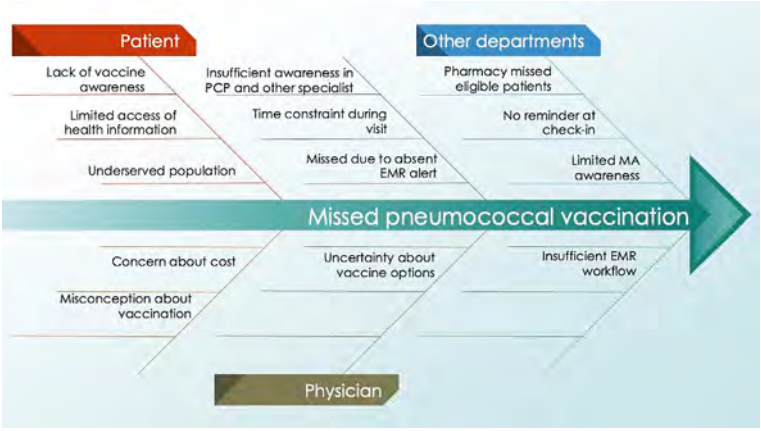


Figure 1: Root cause analysis identified key barriers across three main areas—patients, physicians, and other departments

Figure 2: Patient education flyer (in English and Mandarin) on pneumococcal vaccination for immunocompromised individuals with rheumatologic conditions

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of vaccination rates and patient demographics at baseline and after intervention

	Baseline (Sep/2024-Jan/2025)	Post-QI (Feb-May/2025)
Vaccination rate	33% (36/109)	50% (50/100)
Vaccinated patient	36	50
Gender		
Male	12 (33%)	18 (36%)
Female	24 (67%)	32 (64%)
Race		
Asian	30 (83%)	38 (76%)
African American	0 (0%)	1 (2%)
Caucasian	1 (2.7%)	3 (6%)
Others	5 (13.8%)	8 (16%)
Diseases		
RA	19 (52.7%)	28 (56%)
SLE	11 (30.5%)	10 (20%)
PsA	4 (11.1%)	7 (14%)
AS	2 (5.5%)	5 (10%)
Primary Payer		
Medicare/Medi-Cal	29 (80.5%)	42 (84%)
Private Insurance	7 (19.4%)	8 (16%)

Results: Between September 2024 and January 2025, 109 patients under 65 with RA, PsA, AS, or SLE were seen in the NEMS rheumatology clinic. At baseline, 36 patients (33%) had received a pneumococcal vaccine. By the two-month checkpoint, the rate had increased to 42%, still short of our 50% target. In response, we strengthened collaboration with the pharmacy department, emphasizing their role in reviewing patient records and administering missed vaccinations. This effort led to a continued rise in coverage, and after three months of intervention (February to May 2025), the vaccination rate increased from 33% to 50%, successfully reaching our goal.

Conclusion: Patients with rheumatologic diseases are at increased risk of pneumococcal infection, particularly those in underserved communities. By implementing targeted interventions such as patient education, provider reminders, streamlined EMR alerts, and pharmacy engagement, we successfully reached our vaccination rate goal. With a longer intervention period, we believe coverage could improve even further. This quality improvement model can also be adapted for other types of vaccines and high-risk populations, offering a sustainable strategy to reduce disparities in preventive care.

Disclosure: K. Lin: None; **Y. Hao**: None; **M. Abdelnabi**: None; **W. Lam**: None.

Abstract Number: 1983

Documenting Transition: A Review and Intervention to Increase the Receipt of Transition Summary Letters

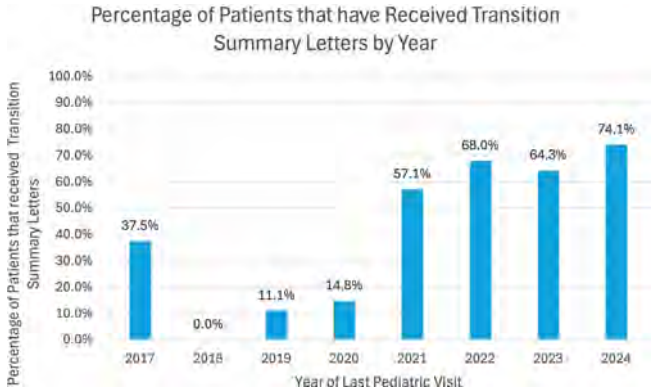
Kyla Blasingame[1], David McDonald[1], Karissa Chesky[1], Jimin Kim[1], charles lee[1], Tiphanie Vogel[1] and Miriah Gillispie-Taylor[2], [1]Baylor College of Medicine, Houston, TX, [2]Baylor College of Medicine/Texas Children's Hospital, Houston, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The transition from pediatric to adult care poses unique challenges for patients with childhood-onset disease, many of whom were young at presentation and do not recall key events surrounding their diagnosis and treatment. This may contribute to knowledge gaps and reduced self-efficacy, increasing the risk for lapses in care and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Bar Chart displaying the percentage of patients that received transition summary letters each year (based on the date of their last pediatric visit). The intervention began in February of 2023.

disease flares during transition. We have developed a pediatric rheumatology transition program and implemented a comprehensive initiative, including a formal transition policy, systematic tracking of patients, use of a structured planning tool, and self-assessment of transition readiness. We have also introduced a formal acknowledgment at the final pediatric visit, including a personalized transition summary letter to support continuity of care and minimize information loss.

Methods: We conducted a retrospective review to assess delivery of transition summary letters to patients with childhood-onset rheumatic disease transitioning to adult care since the start of our program in 2017. We reviewed the electronic medical record of transitioned patients, identified through provider notification or chart review, to determine whether a transition summary letter was provided. In February 2023, we initiated reminder emails to providers—initially biweekly, then weekly—listing all transition-age patients with upcoming visits and reminding providers to discuss transition. Patients aged 17 and older were highlighted due to their impending transfer. Our aim was to increase distribution of summary letters compared to prior years and ensure at least 90% of transitioning patients received a letter post-intervention.

Results: From 2017-2024, 278 patients transitioned to adult rheumatology and had data accessible for analysis. Overall, 149/278 (53.5%) received a transition summary letter. By year, the percentage of patients that received a transition summary letter ranged from 0% in 2018 to a peak of 74% in 2024. Prior to the implementation of our reminder emails in 2023, 66/153 patients received transition summary letters (43%). After implementation of our initiative, 83/125 patients received transition summary letters (66%). Overall, the distribution of transition summary letters trended upward (Figure 1).

Conclusion: Many patients experience information loss as well as lapses in access to care during the transfer from pediatric to adult providers. For this project, we built upon the transition pathway created within pediatric rheumatology to consolidate information for adult providers through a transition summary letter written by the pediatric rheumatology provider. Overall, 53.5% of patients received a transition summary letter, and the distribution to patients has trended upwards over time. Following the institution of a weekly reminder email, 23% more patients received transition summary letters compared to years prior. Our next steps include developing interventions to increase the frequency of transition summary letters toward our goal (>90%) and to longitudinally follow these patients to evaluate the impact of this intervention on successful transfer and continuity of care.

Disclosure: K. Blasingame: None; **D. McDonald**: None; **K. Chesky**: None; **J. Kim**: None; **c. lee**: None; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6; **M. Gillispie-Taylor**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1984

Improving Lipid Screening Rates in Rheumatic Disease Patients: An Academic Fellowship Quality Improvement Project

Mahnoor Javed[1], Deepak Jagannath[2], Lilly Morgan[1], Rishi Patel[1], Eleonora Avenatti[1], Kanika Monga[1] and Kenneth Williams[1], [1]Houston Methodist, Houston, [2]Houston Methodist Hospital, Sugar Land, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune diseases, including rheumatoid arthritis (RA) and spondyloarthritis (SpA)—which encompasses ankylosing spondylitis (AS) and psoriatic arthritis (PsA)—are associated with chronic inflammation and increased cardiovascular morbidity and mortality. Despite guidelines recommending routine lipid testing for these patients, many fail to receive appropriate screening. Obtaining lipid panels helps calculate the Atherosclerotic Cardiovascular Disease (ASCVD) risk score to guide preventive treatment for patients that are deemed high risk. This quality improvement (QI) project at Houston Methodist Hospital (HMH) aimed to increase lipid screening rates among patients with RA and SpA (including AS and PsA) in the rheumatology fellows' continuity clinic.

Methods: Patients seen at HMH in the rheumatology fellows' clinic from July 2024 to February 2025 with ICD codes for RA, AS, or PsA (diagnosed by a rheumatologist) were analyzed for lipid panel screening in the year prior to their visit. This percentage served as a baseline. Two Plan-Do-Study-Act (PDSA) cycles were implemented from March to May 2025. PDSA 1 focused on a house staff education session on lipid screening protocols, creation of an Epic dot phrase and workstation reminder stickers. Lipid panel orders were collected via retrospective chart review. PDSA 2 involved pre-screening patients and pending a lipid panel order in Epic prior to arrival. Upon chart completion of the visit, these orders were signed by the fellows and data was again collected via retrospective chart view.

Results: At baseline, 0% of fellows were ordering lipid panels in their continuity clinics. After PDSA 1, 49 patients with seropositive RA, AS, or PsA were identified over 4 weeks. Of these, 26 (53.1%) had a lipid panel within the prior 12 months. These were ordered by PCPs predominantly. The remaining 23 patients had no recent lipid panel, and 2 new orders were placed by rheumatology fellows, resulting in a post-intervention rate increase of 8.6%. In PDSA 2, 14 patients were identified

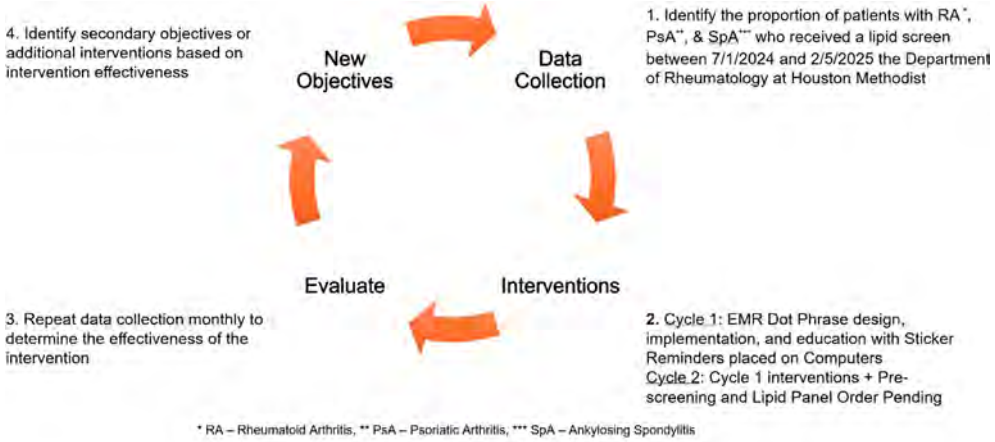


Figure 1. PDSA Cycle 1 and 2

PDSA Cycle 1 and 2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

as lacking appropriate lipid panels within the prior year. After intervention, 13/14 (92.8%) patients received appropriate screening over 4 weeks.

Conclusion: Pre-charting to identify high risk patients and then pre-pending lipid panel orders prior to clinic visits in the fellows' clinic were more effective than educational interventions alone. This agrees with current research that suggests education alone is a low-value improvement intervention. This workflow modification reduced the burden on fellows during busy clinic sessions and led to a higher and more consistent screening rate, suggesting that system-level changes can improve lipid screening. Ongoing data collection and refinement of this QI strategy will help sustain and expand improvements. Future steps will include treatment of patients with elevated ASCVD scores.

Disclosure: M. Javed: None; **D. Jagannath**: None; **L. Morgan**: None; **R. Patel**: None; **E. Avenatti**: None; **K. Monga**: None; **K. Williams**: None.

Abstract Number: 1985

Identifying Gaps in Documented Contraception Counseling and Gynecology Referrals for Women on Teratogenic DMARDs: A Foundation for EMR-Based Quality Improvement

Rachel Galvao, Anokhi Saklecha, Julia Stevenson, Ritche Hao, Eugenia Chock and Abhijeet Danve, Yale University, New Haven, CT

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Teratogenic medications are commonly prescribed to women of reproductive age who have rheumatic conditions. Counseling on teratogenicity and contraception is critical to reducing patients' risk of miscarriage and fetal congenital anomalies. This study assessed the frequency of rheumatologist-documented teratogenic risk counseling, gynecology referrals, and contraceptive methods among women of reproductive age on teratogenic DMARDs in an academic rheumatology clinic. Findings informed the development of a Best Practice Advisory (BPA) in the electronic medical record (EMR) with the goal of improving family planning counseling and documentation.

Methods: Medical records were reviewed for women aged 18–49 who attended at least one rheumatology clinic visit and were prescribed a teratogenic DMARD (methotrexate, mycophenolate, leflunomide, or cyclophosphamide). Descriptive statistics were used to analyze documentation dated between April 1, 2022, and July 31, 2024, including demographic data, clinical notes, referrals, and medication lists.

Results: We reviewed 157 patient charts. Patients had mean age 37 years (SD 8) with lupus as the most common diagnosis (Table 1). Methotrexate was the most frequently prescribed teratogenic DMARD. Over one-quarter of patients (N=41) were not using any contraception, though 45% (N=71) used a highly effective method (sterilization, intra-uterine device, progestin implant) (Figure 1). Documentation of teratogenic risk or contraceptive counseling in rheumatology notes was found in 34% (N=54) and 33% (N=52) of charts, respectively. Contraceptive counseling by Obstetrics/Gynecology (Ob/Gyn) was documented in 41% of cases (N=65). 18% of patients (N=28) had been referred to Ob/Gyn within the study timeframe, of whom 64% (N=18) attended a visit and 14% (N=4) initiated contraception. These findings informed the development of a BPA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Characteristics

Mean age (SD), y	37 (8)
Race, n (%)	
White	82 (52.2)
Black or African American	41 (26.1)
Asian	4 (2.5)
Native American or Alaska Native	2 (1.3)
Native Hawaiian or Pacific Islander	1 (0.6)
Undisclosed	31 (19.7)
Ethnicity, n (%)	
Hispanic or Latina	52 (33.1)
Not Hispanic or Latina	98 (62.4)
Undisclosed	7 (4.5)
Diagnosis, n (%)	
Lupus	54 (34.4)
Rheumatoid arthritis	28 (17.8)
Inflammatory arthritis	24 (15.3)
Scleroderma	16 (10.2)
Psoriatic arthritis/Axial spondyloarthritis	10 (6.4)
Mixed connective tissue disease	9 (5.7)
Sjögren's Syndrome	9 (5.7)
Undifferentiated connective tissue disease	9 (5.7)
Vasculitis	6 (3.8)
Dermatomyositis/polymyositis	6 (3.8)
Other (including interstitial lung disease)	36 (22.9)
Teratogenic medication, n (%)	
Methotrexate	91 (58.0)
Mycophenolate	73 (46.5)
Leflunomide	15 (9.6)
Cyclophosphamide	2 (1.3)
Number of rheumatology visits, mean (SD)	7.5 (4.7)
Number of Ob/Gyn visits, mean (SD)	2.7 (3.1)

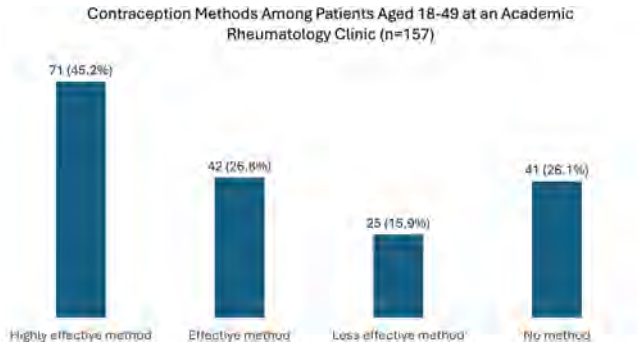


Figure 1. Contraception Methods Among Patients Aged 18-49 at an Academic Rheumatology Clinic. Highly effective method = sterilization (hysterectomy or tubal ligation), intra-uterine device, or progestin implant. Effective method = oral contraceptive pills, depot medroxyprogesterone acetate, transdermal patch, or vaginal ring. Less effective method = condoms. Note: some patients had multiple methods documented.

which will notify rheumatologists of patients' teratogenic medication use, encourage appropriate documentation of counseling, and provide a one-click Ob/Gyn referral pathway with the aim of strengthening quality of care and patient safety (Figure 2).

Conclusion: This study demonstrates substantial gaps in counseling documentation, Ob/Gyn referrals, and contraception for women with rheumatic diseases on teratogenic medications. A BPA was developed in the EMR to improve patient safety and quality of care. We plan to prospectively study the impact of this intervention.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

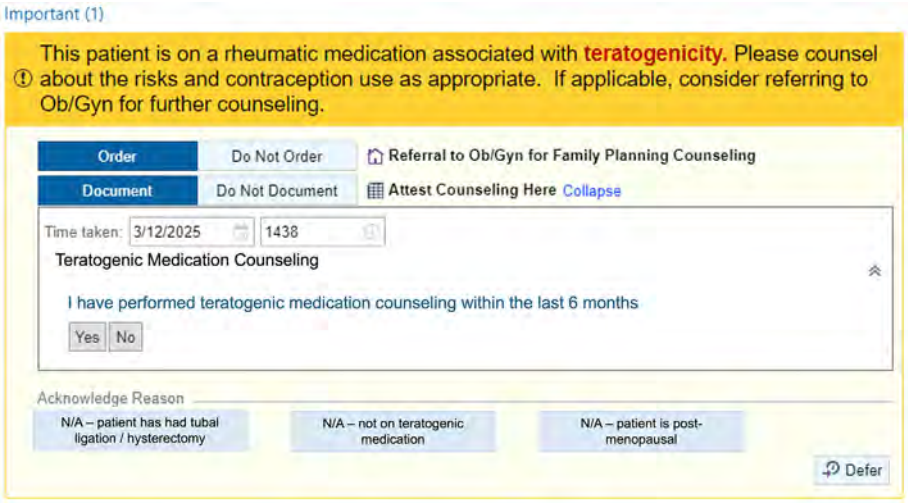


Figure 2. EMR Best Practice Advisory for Teratogenic Medication Counseling. The advisory appears when rheumatologists open an encounter for female patients aged 18-49 with a teratogenic medication on their list or when they prescribe teratogenic medications for patients in this demographic. The advisory provides a one-click order for referral to the academic center's family planning clinic. Documentation is performed directly in the alert and can be viewed in the "Flowsheets" section of the EMR. The alert will not appear if a patient's chart contains history of tubal ligation, hysterectomy, or other surgical sterilization. Once teratogenic medication counseling is documented, the alert will stop appearing for six months, or if the rheumatologist clicks "N/A," the alert will no longer appear.

Disclosure: R. Galvao: None; **A. Saklecha**: None; **J. Stevenson**: None; **R. Hao**: None; **E. Chock**: None; **A. Danve**: Amgen, 6, Eli Lilly, 5, Janssen, 2, 5, 6.

Abstract Number: 1987

Evaluating User Engagement and Real-World Impact of a PMR-Specific Digital Symptom Assessment Tool: A 12-Month Analysis of PainSpot™

Shilpa Venkatachalam[1], Erik Stone[2], Ian Carroll[3], angela Degrassi[3], Shelley Fritz[4] and David Curtis[5], [1]Global Healthy Living Foundation, New York, NY, [2]Global Healthy Living Foundation, Nyack, NY, [3]Global Healthy Living Foundation, Upper Nyack, NY, [4]Global Healthy Living Foundation, Kalaheo, HI, [5]Global Healthy Living Foundation, Meriden

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Polymyalgia rheumatica (PMR) is a systemic inflammatory condition affecting individuals over 50, marked by bilateral shoulder and hip stiffness and pain. Its nonspecific symptoms and overlap with other musculoskeletal disorders often lead to diagnostic delays and misclassification, contributing to avoidable morbidity. Awareness of PMR remains limited, especially outside of rheumatology. Digital tools, such as algorithm-based symptom checkers, offer a scalable approach to identifying PMR-consistent symptom patterns and prompting medical evaluation. To address this gap, the PainSpot™ platform was enhanced with a PMR-specific pathway co-developed by clinicians and patients. This study assessed real-world tool engagement, diagnostic likelihood distribution, and user-reported outcomes.

Methods: PainSpot™ was modified to include a PMR-specific algorithm co-developed by a multi-stakeholder working group including rheumatologists, outcomes researchers, and patients with confirmed PMR diagnoses. Thirteen condition-specific questions were generated and refined through a literature review, clinical input, and patient interviews focusing on

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: PainSpot (TM) PMR Pathway User Engagement Overview

METRIC	VALUE
Total users who completed the PMR assessment	94,454
Users routed to PMR likelihood result	10,545
Average time spent per user	2 minutes and 19 seconds
Total number of follow-up survey respondents	193 (symptom confirmation)

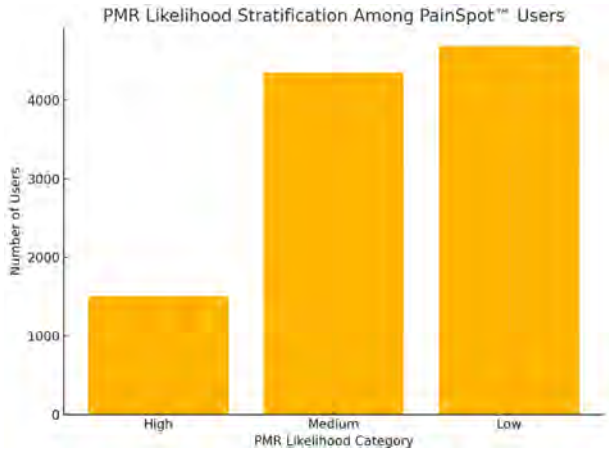


Figure 1: PMR Likelihood Stratification Among PainSpot Users

pre-diagnosis symptom recall. Between March 1, 2024, and February 28, 2025, user-level engagement data were collected and analyzed to evaluate assessment completion rates, PMR likelihood results, and follow-up survey responses.

Results: Of 94,454 users who completed the PainSpot™ assessment between March 2024 and February 2025, a subset were routed to a potential PMR result based on algorithmic analysis of symptom patterns. Among these, 1,509 users (21.0%) were classified as high likelihood of PMR, 4,353 (60.6%) as medium likelihood, and 4,683 (65.2%) as low likelihood. These stratifications were derived from a weighted question algorithm developed through clinician and patient input. Average engagement time across users was 2 minutes and 19 seconds, indicating sustained interaction with the digital interface. Follow-up surveys were administered to users who completed the assessment. Among 111 respondents, 89.2% (n=99) reported discussing their results with a healthcare provider, suggesting potential influence on care-seeking behavior. Additionally, 193 assessment completers (across all diagnostic pathways, not limited to PMR) responded to a separate follow-up question regarding the accuracy of the tool's output; 82.4% (n=159) indicated that the result they received aligned with their symptom experience or was subsequently confirmed.

Conclusion: The PMR-specific pathway within PainSpot™ demonstrated high engagement meaningful stratification of diagnostic likelihood, and strong perceived utility based on user-reported outcomes.. While only a subset of users confirmed seeking medical follow-up, a larger proportion—over 80% of survey respondents—indicated that the tool's output aligned with their symptom experience. These findings support the utility of patient-informed, algorithm-based tools in recognizing symptom patterns consistent with PMR. This work aligns with a four-year CDC-funded initiative aimed at improving national awareness, education, and diagnostic strategies for PMR.

Disclosure: S. Venkatachalam: None; **E. Stone**: None; **I. Carroll**: None; **a. Degrassi**: None; **S. Fritz**: None; **D. Curtis**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1988

Advancing Vascular Assessment: Combining NIRS-VOT and Ultrasound-based Brachial Artery Diameter for Improved Diagnostics in Healthy Controls and APS

Soongho Park[1], Julie Mathew[1], Sharon Osgood[2], Claudia Gomez[1], Eric Leifer[1], Ecem Sevim[1] and Yogendra Kanthi[3], [1]NIH, Bethesda, [2]NHLBI/NIH, Bethesda, [3]National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Near-Infrared Spectroscopy combined with Vascular Occlusion Test (NIRS-VOT) is a non-invasive diagnostic method for assessing microvascular function. However, its diagnostic accuracy is often limited by inter-individual variability, particularly anatomical differences in vascular structure, such as brachial artery diameter (BAD). Since BAD significantly influences blood flow and may affect NIRS-VOT readings, we propose incorporating BAD as a reference parameter to standardize NIRS-VOT results and improve diagnostic reliability. This approach is particularly relevant in diseases like Antiphospholipid Syndrome (APS), a rare autoimmune disorder characterized by vascular dysfunction.

Methods: We applied this combined method to a cohort of 10 healthy controls (HCs) and 9 patients with APS. Brachial artery diameter was measured using ultrasound imaging, and NIRS-VOT was performed to assess tissue oxygen saturation (StO_2) parameters during vascular occlusion and reperfusion. We conducted correlation analyses to evaluate the relationship between BAD and NIRS-VOT parameters and performed logistic regression to examine whether including BAD improved classification between HCs and APS patients. Multiple statistical analyses were used to identify independent predictors of key NIRS-VOT outcomes.

Results: Our results indicate that incorporating BAD into NIRS-VOT significantly improves interpretation of hemodynamic parameters. In HCs, strong correlations were observed between BAD and NIRS-derived parameters (e.g., $r = 0.95$, $p < 0.01$), while correlations in APS patients were notably weaker, suggesting greater variability in vascular response. Both

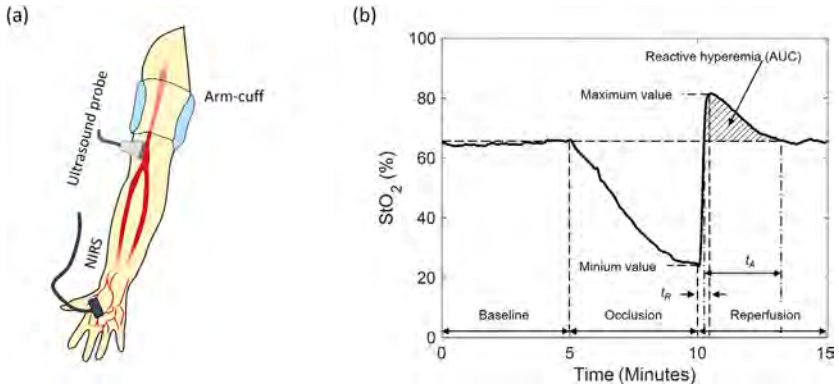


Figure 1. (a) Experimental setup combining a linear ultrasound probe on the upper arm to measure brachial artery diameter and a NIRS probe on the thenar for vascular occlusion testing (VOT). (b) Schematic of NIRS-derived tissue oxygen saturation (StO2) during VOT, including Baseline, Occlusion, and Reperfusion phases. Key parameters analyzed: baseline, minimum, maximum, resaturation time (tR), area under the curve (AUC), and hyperemic recovery time (tA).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

BAD and APS status emerged as significant independent predictors of key NIRS-VOT metrics. Logistic regression analysis showed that the inclusion of BAD improved classification accuracy—by at least 7.14% for baseline and minimum StO_2, and by up to 28.57% for maximum StO_2. Without BAD, the highest classification accuracy for maximum StO_2 was 78.57%, whereas including BAD increased it to 92.86%.

Conclusion: This study demonstrates the feasibility and utility of combining NIRS-VOT with ultrasound-derived BAD measurements for assessing microvascular function. To our knowledge, this is the first study to explore the interplay between conduit artery structure and NIRS-based functional assessments in this way. The integration of BAD into NIRS-VOT significantly enhances diagnostic accuracy, reduces inter-individual variability, and offers a more robust framework for evaluating vascular health. This approach shows promise not only for identifying vascular dysfunction in rare conditions such as APS but may also be applicable to other conduit arteries like the femoral artery, broadening the method's potential clinical applications.

Disclosure: S. Park: None; **J. Mathew**: None; **S. Osgood**: None; **C. Gomez**: None; **E. Leifer**: None; **E. Sevim**: None; **Y. Kanthi**: None.

Abstract Number: 1989

Moving Out of the Kid's Rheum: Transitioning Young Adult Patients from Pediatric to Adult Rheumatology Practices

Victoria Koenigsberger[1], Madeleine Ward[2], Meghan Geary[3] and Ali Yalcindag[4], [1]The Warren Alpert Medical School of Brown University, Providence, RI, [2]The Warren Alpert Medical School of Brown University, Division of Medicine-Pediatrics, Providence, [3]The Warren Alpert Medical School of Brown University, Division of General Internal Medicine, Providence, [4]The Warren Alpert Medical School of Brown University, Division of Rheumatology, Department of Pediatrics, Milton, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1972–1989) Measures & Measurement of Healthcare Quality Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Young adults with childhood-onset rheumatic conditions encounter challenges and barriers to care when transitioning to an adult rheumatologist. At this Pediatric Rheumatology Clinic, patients aged 18 and older were provided with a list of adult providers to call and set up follow-up, however no formal transition process existed. This study aimed to pilot the practice's first program to systematically transition pediatric patients using aspects of the Six Core Elements of Health Care Transition (HCT) from Got Transition.

Methods: One research assistant, two primary care physicians, one pediatric and ten adult rheumatology providers facilitated the program. Patients were eligible if they were 18 years of age or older with confirmed rheumatic disease, and deemed stable to transition by the pediatric rheumatologist. The program structure consisted of four visits, ~three months apart: two appointments with pediatric rheumatology, with ~50% of the time devoted to transition readiness education; a final in-person appointment with pediatric rheumatology, with their chosen adult rheumatologist on video for a warm handoff; and a first appointment with adult rheumatology. Patient-reported transition readiness was assessed at each visit using the Transition Readiness Assessment (TRA) from Got Transition. Patient demographics were assessed via chart review.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Participant Demographics

	N/mean	%/range
Gender		
Male	2	25%
Female	6	75%
Age (recruitment)	19.5	18-23
Race/ethnicity		
Native American/Alaska Native	0	0%
Asian	1	12.5%
Black/African American	0	0%
Hispanic/Latino	1	12.5%
Multiple	1	12.5%
Native Hawaiian or Pacific Islander	0	0%
White/Caucasian	5	62.5%
Rheumatic diagnosis		
Juvenile idiopathic arthritis (oligoarticular, polyarticular, enthesitis-related, or psoriatic JIA)	1	12.5%
Systemic lupus erythematosus (SLE)	2	25%
Discoid lupus	1	12.5%
Gout	1	12.5%
Raynaud's	1	12.5%
Mixed Connective Tissue Disease (MCTD)	1	12.5%
Other	1	12.5%

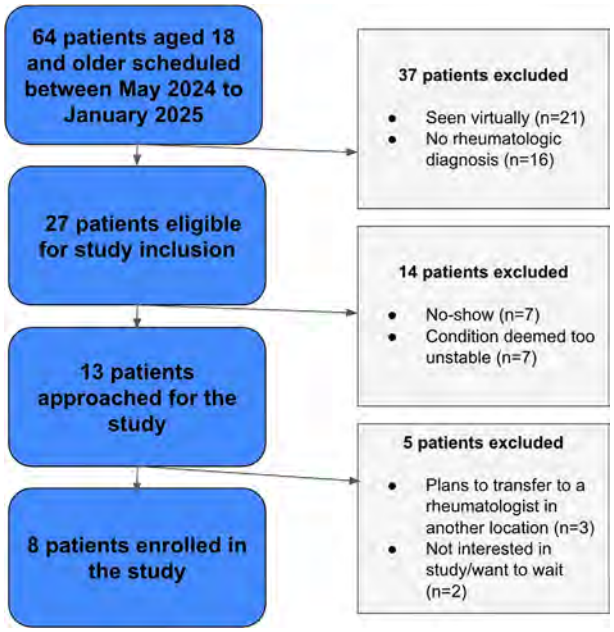
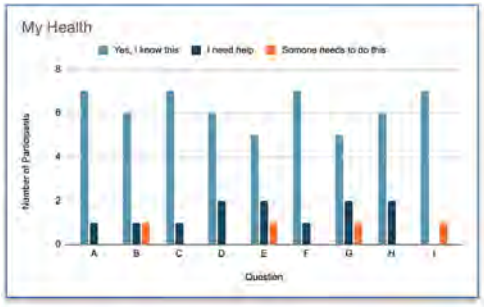
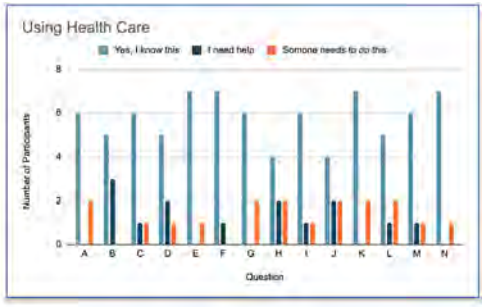


Figure 1: Participant Enrollment

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



TRA responses from initial survey for knowing health (A: I know my medical needs; B: I can explain my medical needs to others; C: I know my symptoms including ones that I quickly need to see a doctor for; D: I know what to do in case I have a medical emergency; E: I know my medicines, what they are for, and when I need to take them; F: I know my allergies to medicines and medicines I should not take; G: I carry my important health information with me every day; H: I understand how health care privacy changes at age 18 when legally an adult; I: I can explain to others how my customs and beliefs affect my health care decisions and medical treatment)



TRA responses from initial survey for using health care (A: I know or I can find my doctor's phone number; B: I make my own doctor appointments; C: Before a visit, I think about questions to ask; D: I have a way to get to my doctor's office; E: I know to show up 15 minutes before the visit to check in; F: I know where to go to get medical care when the doctor's office is closed; G: I have a file at home for my medical information; H: I have a copy of my current plan of care; I: I know how to fill out medical forms; J: I know how to get referrals to other providers; K: I know where my pharmacy is and how to refill my medicines; L: I know where to get blood work or x-rays if my doctor orders them; M: I have a plan so I can keep my health insurance after 18 or older; N: My family and I have discussed my ability to make my own health care decisions at age 18)

Figure 2: Baseline Transition Readiness (TRA) Responses

Results: 64 patients aged 18 and older had scheduled appointments with the Pediatric Rheumatology Clinic from 5/1/24 to 1/31/25. Of these patients, 13 were eligible, determined by diagnosis and disease stability, of which eight (62.5%) chose to enter the pilot (Figure 1). Patient demographics are shown in Table 1.

All participants (100%) completed a baseline TRA. The mean age at enrollment was 19.5 years (range: 18-23). Mean TRA scores for patients' initial self-perceived importance of transition to an adult doctor and confidence in transitioning were 8.13 and 7.13, respectively (out of 0 [not] to 10 [very]). The majority of participants reported knowing their health needs and being able to explain them to others. Knowledge regarding navigating health care, such as getting referrals to other providers, was more mixed (Figure 2). Seven participants (87.5%) have completed at least two transition appointments, and two (25%) have successfully transitioned to adult rheumatology.

Conclusion: Appropriate HCT is crucial to support the health of young adults with childhood-onset chronic illnesses. Initial stages of this transition process have proven acceptable with the majority of patients approached agreeing to participate. It appears that self-perceived importance of transitioning to an adult rheumatologist was greater than confidence in doing so at the initial appointment. It has also proven feasible to complete successful warm video handoff visits with the adult rheumatologists at their final pediatric appointment. Challenges to implementation include time and clinical infrastructure. Next steps involve finalizing remaining adult appointments and assessing the impact of this program on patients with multi-modal data - qualitative and quantitative surveys.

Disclosure: V. Koenigsberger: None; **M. Ward**: None; **M. Geary**: None; **A. Yalcindag**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1990

Pilot Study: Testing the Accuracy of a Capillary Point-of-Care Device Compared to Traditional Venous Analysis for Serum Urate Measurements Among Patients with Gout

Alex Tinianow[1], Saiajay Chigurupati[1], Ethan Carey[1], Jiaqi Wang[2], Sharan Rai[3], Gregory Challener[4], Hyon K. Choi[5], Philip Riches[6], Natalie McCormick[1] and Chio Yokose[7], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, BOston, [3]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [4]MGH, Boston, MA, [5]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [6]NHS Lothian, Edinburgh, UK, Edinburgh, United Kingdom, [7]Massachusetts General Hospital, Waltham, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology guidelines endorse a treat-to-target (TTT) approach targeting serum urate (SU) < 6 mg/dL among patients with gout who qualify for urate-lowering therapy (ULT). However, implementation of TTT remains suboptimal, in part due to frequent laboratory visits required to serially check SU for ULT titration. Prior studies (Kehasse et al., ACR abstract 2023, PMID: 29720236, PMID: 31072349) have investigated the role of capillary point-of-care (POC) SU measuring devices to reduce barriers associated with TTT. However, the results have been inconsistent, with intraclass correlation coefficients (ICC) ranging from 0.75 to 0.90 and Pearson correlation coefficient of 0.96. We sought to investigate the accuracy of a POC device, the BeneCheck Supreme (the same device brand used in a randomized trial of supported self-management in gout (PMID: 38294032) and approved in Europe for home testing), in measuring SU as compared to traditional venous laboratory analysis (TVA) among patients with gout.

Methods: We identified patients with gout who presented in-person to the rheumatology clinic at our academic hospital. Among patients who had a clinical indication to measure SU, we measured SU using both the capillary POC device and TVA on the same day. Written informed consent was required to participate in this Institutional Review Board-approved study. Demographic and clinical information was obtained through retrospective review of the electronic health record. We assessed the correlation between POC and TVA SU values using intraclass correlation coefficients (ICC). A Bland-Altman analysis assessed variability in the difference and limits of agreement between POC with TVA. The performance of POC SU measurements in identifying those with SU >6 mg/dL was analyzed using ROC curve analysis with area under curve (AUC), and was additionally adjusted for the presence of hypertension (HTN), chronic kidney disease (CKD) Stage 3 or greater, and type 2 diabetes mellitus (T2DM).

Table 1. Baseline characteristics of the study population.

	N=27
Mean age (SD)	59.1 (15.3)
Male, n (%)	25 (92.6)
Race, n (%)	
White	20 (74.1)
Asian	4 (14.8)
Black	3 (11.1)
T2DM, n (%)	4 (14.8)
CKD stage 3 or greater, n (%)	5 (18.5)
HTN, n (%)	17 (63.0)
ULT use, n (%)	19 (70.4)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

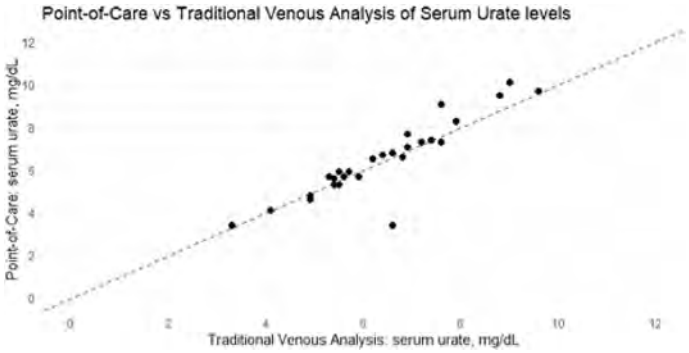


Figure 1. Scatterplot of POC serum urate measurement as compared to TVA measurements, showing ICC of 0.89 (95% CI, 0.77 to 0.95).

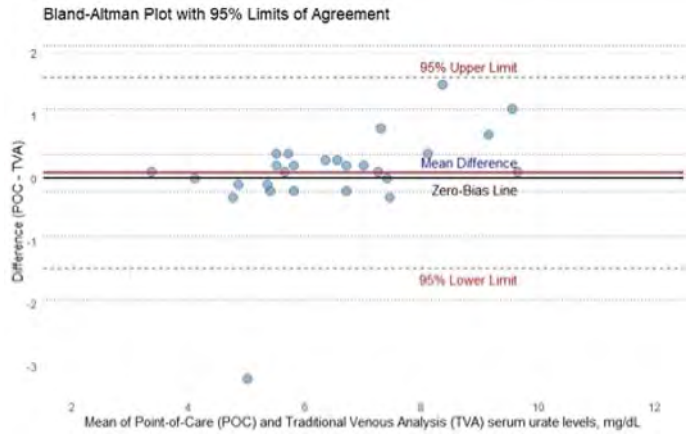


Figure 2. Bland-Altman plot comparing POC to TVA serum urate measurements. Mean difference was 0.09 mg/dL, with limits of agreement of -1.4 to 1.6 mg/dL.

Results: Our study included 27 patients, of whom 25 (92.6%) were male and 20 (74.1%) were White (**Table 1**). Most patients (70.4%) were on ULT. The POC SU measurements ranged from 3.4 to 10.1 mg/dL, with a mean of 6.5 mg/dL. TVA measurements ranged from 3.3 to 9.6 mg/dL, with a mean of 6.4 mg/dL. The ICC between POC and TVA measurements was 0.89 (95% CI, 0.77 to 0.95) (**Figure 1**). In the Bland-Altman analysis, the bias, or mean difference (POC-TVA), was 0.09 mg/dL, with limits of agreement of -1.4 to 1.6 mg/dL (**Figure 2**). For POC detection of SU >6 mg/dL, the unadjusted AUC was 0.94. The results did not differ significantly with inclusion of ULT in the model, but improved nominally to 0.95 with inclusion of HTN, CKD, and T2DM. The sensitivity and specificity of the POC device for detecting SU >6 mg/dL was 0.93 and 1.00, respectively.

Conclusion: In this small pilot study, the POC device and TVA for SU were strongly correlated, with a mean difference of 0.09 mg/dL between the POC and TVA measurements. The POC correctly identified 93% of individuals with SU >6 mg/dL, a clinically meaningful threshold for ULT dose titration. Such POC devices may facilitate real-time implementation of the TTT approach in gout management.

Disclosure: A. Tinianow: None; **S. Chigurupati**: None; **E. Carey**: None; **J. Wang**: None; **S. Rai**: None; **G. Challener**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **P. Riches**: None; **N. McCormick**: None; **C. Yokose**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1991

Co-Use of Mycophenolate Mofetil with Pegloticase Yielded Similar Clinical Outcomes as the Co-Use of Methotrexate

Tingting Zhang[1], Kenneth Saag[2], Yasir Qazi[3], **Bradley Marder**[4] and Brian Lamoreaux[5], [1]Amgen, Inc., Thousand Oaks, [2]The University of Alabama at Birmingham, Birmingham, AL, [3]Keck School of Medicine Renal Transplant Program, University of Southern California, Los Angeles, CA, [4]AMGEN, Inc, Denver, CO, [5]Amgen, Inc., Deerfield, IL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Pegloticase significantly reduces serum uric acid (sUA) values in patients with refractory gout. Co-use of methotrexate (MTX) improves efficacy and safety of pegloticase by reducing the development of anti-drug antibodies[1]. Because MTX is primary excreted through the kidney, there has been concern that MTX use may increase adverse effects in patients with renal impairment. The present study was designed to examine effects of co-using pegloticase with mycophenolate mofetil (MMF), another immunomodulatory (IMM) proven to extend pegloticase efficacy[2].

Methods: This is a longitudinal analysis using the Optum Clinformatics® DataMart®, 2016-2024. The study participants included new users of pegloticase; the first pegloticase infusion defined the index date. Based on the presence of IMM treatment ±90 days from the index date, we defined three exposure groups: MTX co-therapy group, MMF group and pegloticase monotherapy (IMM nonusers). We described pegloticase duration of use, patterns of sUA values and estimated Glomerular Filtration Rate (eGFR). Analyses were stratified by baseline eGFR (60+ vs. < 60 ml/min/1.73m^2).

Results: We identified 903 pegloticase new users who met the inclusion criteria (297 in the MTX co-therapy group, 144 in the MMF group and 462 monotherapy group). The MMF co-therapy group was older, had a high prevalence of comorbid CKD stages 3+ (60%), as well as higher proportions of all-cause hospitalizations and comorbidities than the other two groups (Table 1). By comparison, the MTX group had 23% and the monotherapy group had 37% with advanced CKD. The median number of pegloticase infusions was 11 for the MMF group (IQR: 4-18), 8 for the MTX group (IQR: 3-15) and 6 for the immunomodulator nonusers (IQR: 2-14). The mean sUA levels changed from over 7 mg/dL at baseline, to ~2 mg/dL between 1-6th infusions and ~1mg/dL between 7th infusion and follow-up end (Figure 1). The mean eGFRs were

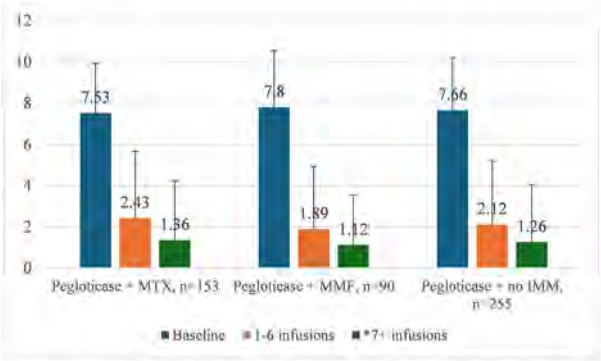
Table 1. Selected patient characteristics at baseline (6 months before the index date)

	Pegloticase + MTX, n=297	Pegloticase + MMF, n=144	Pegloticase + no IMM, n=462
Age, mean (SD)	61 (13)	65 (13)	62 (13)
Males, n (%)	253 (85)	102 (71)	359 (78)
*eGFR, mean (SD)	111 (62)	62 (39)	108 (69)
Presence of comorbidities, n (%)			
CKD stage 3+	69 (23)	87 (60)	169 (37)
Hypertension	94 (32)	56 (39)	144 (31)
Diabetes	93 (31)	57 (40)	150 (33)
Rheumatoid arthritis/Osteoarthritis	53 (18)	19 (13)	57 (12)
Concurrent medication use, n (%)			
oral urate lowering therapies	191 (64)	97 (67)	250 (54)
Colchicine	172 (58)	68 (47)	199 (43)
Health services utilization, n (%)			
All cause ED visits	91 (31)	51 (35)	162 (35)
All cause hospitalizations	41 (14)	28 (19)	66 (14)

*eGRF values were available for 140 patients in the MTX co-therapy group, 87 in the MMF group and 175 monotherapy patients at baseline and the follow-up periods.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Mean and standard deviation of serum uric acid levels at baseline, between 1-6 infusions and 7th infusions onwards



Note: Approximately half of the study participants in each group had sUA values available at baseline and between 1-6 infusions. A total of 103 patients in the MTX group, 62 patients in the MMF group and 173 patients in the immunomodulator nonuser group had sUA value available from 7th infusion to the end of follow-up.

stable [MTX group: 111 (SD: 62) ml/min/1.73m^2 at baseline to 105 (SD: 53) during the follow-up; MMF group: 62 (39) to 60 (34); monotherapy: 108 (69) to 108 (71)]. Stratified analyses produced consistent findings.

Conclusion: 49% of pegloticase patients were treated with immunomodulating co-therapy, among which MMF was 33% of IMM use, with most patients going on MMF having advanced CKD. Pegloticase duration, effectiveness in terms of sUA reduction and eGFR stability in the MMF group were similar to the MTX group. The co-therapy of MMF and pegloticase may be an option for patients with pre-existing renal impairment.

Reference:

[1]Botson et al. Arthritis Rheumatol 2023. [2]Khanna et al. Arthritis Rheumatol 2021.

Disclosure: T. Zhang: Amgen, Inc, 3, 11; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **Y. Qazi**: Travere, CareDx, 6; **B. Marder**: Amgen, Inc, 3, 11; **B. Lamoreaux**: Amgen, 3, 11.

Abstract Number: 1992

Tolerance of Methotrexate Coadministered with Pegloticase in Patients with Uncontrolled Gout: Findings from MIRROR RCT

Vinicius Domingues[1], Alexis Woods[2], Xiaoqing Yang[3], **Brian Lamoreaux**[4] and Michael Weinblatt[5], [1]Rheumatology, Allergy, Asthma & Arthritis Center, Daytona beach, FL, [2]Amgen, Detroit, MI, [3]Amgen, Seattle, WA, [4]Amgen, Inc., Deerfield, IL, [5]Brigham and Women's Hospital/ Harvard Medical School, Waban, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

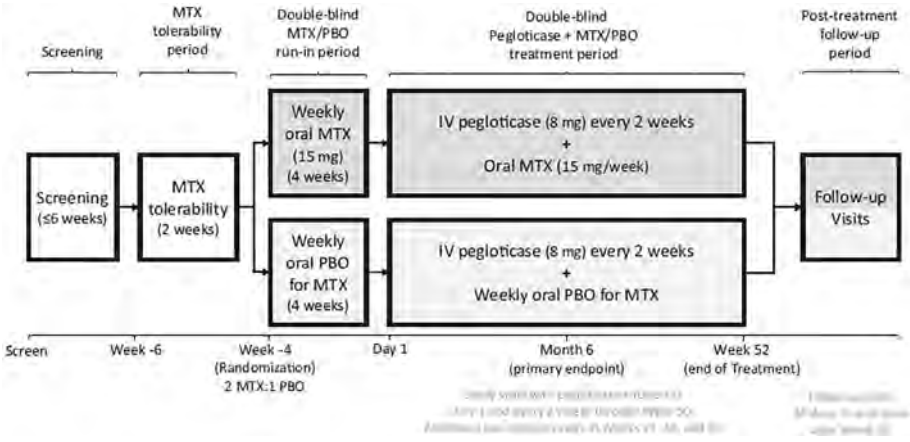
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Methotrexate (MTX) coadministered with pegloticase attenuates anti-drug antibody formation, leading to higher response rates and markedly reduced infusion reaction risk compared with pegloticase + placebo (PBO).[1] Here, we evaluate overall MTX safety data in pts enrolled in the MIRROR RCT.

Methods: Patients (pts; N=152) with uncontrolled gout (SU ≥7 mg/dL, oral ULT failure/intolerance, and tophi, ≥2 flares/yr, and/or gouty arthritis) received up to 52 wks of pegloticase (8 mg infusion Q2W) with either 15 mg oral MTX/wk or PBO and 1 mg folic acid daily; pts with eGFR < 40 ml/min/1.73 m^2 were excluded. First infusion (Day 1) occurred after a 2-wk MTX tolerance period (Wk -6 to Wk -4) and a 4-wk MTX/PBO run-in (Wk -4 to Day 1). Baseline (BL) was prior to MTX exposure (Wk -6). Safety data from on-treatment pts (N=96 MTX and N=49 PBO; ≥1 pegloticase dose) were examined in aggregate (Figure 1).

Results: During the 52-wk tx period, the most common on treatment-emergent adverse event (TEAE) was gout flares (MTX: 66.7%; PBO: 71.4%).[1] MTX-associated AEs (gastrointestinal disorders, skin disorders, infections) were similar between both groups.[1] Pulmonary disorders (9.4% vs 4.1%) occurred more often in the MTX group, but with similar incidence rates **(Table 1)**. More pts in the MTX vs PBO group had transient ALT levels >ULN (13.6% vs 6.3%; no >2 x ULN or above in either group). Pt proportion with AST levels >ULN was similar (6.9% MTX vs 6.3% PBO; >2 x ULN [n=2 vs 0] and >3 x ULN [n=1 vs 0]). However, ALT (+0.6 ± 23.3 vs. +2.5 ± 14.4 U/l), AST (+1.5 ± 22.1 vs. +1.5 ± 11.0 U/l), as well as Fib-4 index, a predictor of hepatic fibrosis progression, did not meaningfully change from BL at Wk 52.[1,2] Occurrence of infections was similar (MTX: 18.8% vs PBO: 18.4%), with COVID-19 being most common (9.4% vs 6.1%; nominal p=0.35). Leukopenia and anemia each occurred in 1 pt in the MTX group (none in the PBO group; **Table 1)**. Permanent MTX and PBO withdrawal due to TEAEs occurred in 11.5% and 16.3% of pts; 2 deaths occurred in the MTX group during the 52-wk tx (cardiac arrest and COVID-19 with multiple comorbidities), deemed unrelated to study tx. Renal function remained stable during tx in both groups.[1] The change in creatinine from BL was -0.08 ± 0.15 and 0.01 ± 0.32 mg/dL. Stomatitis was uncommon (1 event during MTX run-in [1%], with no recurrence). MCV increased by ~4 fL from BL in the MTX group (3.8 ± 3.47]), with no change in the PBO group (0.0 ± 3.51), which is indicative of RBC macrocytosis, a surrogate marker for MTX compliance. Alcohol users (≥3 servings/wk) comprised 3.2% (4/126) of total screening failures. Among alcohol users enrolled (97/159; 61%), liver function did not worsen in the MTX vs PBO groups (ALT increase: 1 pt each [1.7% vs 3.4%]; AST increase: 1 pt [1.7%] vs 0).

Conclusion: MTX safety data from MIRROR RCT demonstrates that MTX in uncontrolled gout pts does not lead to an increased number/frequency of TEAEs vs PBO, including no increase in durable liver function changes and no increase in infections. These findings further underscore the safety of MTX coadministration with pegloticase during the 12 month MIRROR RCT.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Proportion and Incidence Rates (Events/Person-Years) of TEAEs of Interest During Week 52 Treatment Period of MIRROR RCT

TEAEs*	n (%), Total Events/Incidence Rate (Events/PY† of MTX or PBO)	
	Pegloticase+MTX PY of MTX=67.8 N = 96	Pegloticase+PBO PY of PBO=19.5 N = 49
Infections and Infestations‡	**18 (18.8), 26/0.4**	**9 (18.4), 10/0.5**
Abscess Soft Tissue	0	1 (2.0), 1/0.1
Bronchitis	1 (1.0), 1/<0.05	0
Cellulitis	1 (1.0), 1/<0.05	1 (2.0), 1/0.1
COVID-19/Suspected COVID-19	9 (9.4), 9/0.1	3 (6.1), 3/0.2
Ear Infection	1 (1.0), 1/<0.05	0
Folliculitis	1 (1.0), 3/<0.05	0
Fungal Skin Infection/ Fungal Infection	1 (1.0), 1/<0.05	0
Gastroenteritis Viral	0	0
Influenza	1 (1.0), 1/<0.05	0
Localized Infection	0	0
Nasopharyngitis	1 (1.0), 1/<0.05	0
Osteomyelitis	1 (1.0), 1/<0.05	0
Periorbital Cellulitis	1 (1.0), 1/<0.05	0
Pharyngitis	1 (1.0), 1/<0.05	0
Pneumonia	1 (1.0), 1/<0.05	0
Respiratory Tract Infection/Upper Respiratory Tract Infection	1 (1.0), 1/<0.05	1 (2.0), 1/0.1
Sinusitis	1 (1.0), 1/<0.05	1 (2.0), 1/0.1
Tinea Pedis	1 (1.0), 1/<0.05	
Tooth Abscess	0	1 (2.0), 1/0.1
Urinary Tract Infection	1 (1.0), 1/<0.05	1 (2.0), 1/0.1
Viral Upper Respiratory Tract Infection	0	1 (2.0), 1/0.1
Respiratory, Thoracic, and Mediastinal Disorders	**9 (9.4), 10/0.1**	**2 (4.1), 2/0.1**
Cough	1 (1.0), 1/<0.05	0
Dyspnea	1 (1.0), 1/<0.05	1 (2.0), 1/0.1
Hiccups	2 (2.1), 2/<0.05	0
Nasal Congestion	1 (1.0), 1/<0.05	1 (2.0), 1/0.1
Paranasal Sinus Hypersecretion	1 (1.0), 1/<0.05	0
Pneumothorax	1 (1.0), 1/<0.05	0
Pulmonary Embolism	1 (1.0), 1/<0.05	0
Throat Tightness	1 (1.0), 1/<0.05	0
Wheezing	1 (1.0), 1/<0.05	0
Blood and Lymphatic System Disorders	**2 (2.1), 2/<0.05**	**1 (2.0), 1/0.1**
Anemia (Hemoglobin 9.2 g/dL)	1 (1.0), 1/<0.05	0
Leukopenia (WBC count 3.38 × 10^9/L)	1 (1.0), 1/<0.05	0
Lymph Node Pain	0	1 (2.0), 1/0.1

Methotrexate, MTX; person-years, PY; TEAEs, treatment-emergent adverse events.
*TEAEs during the pegloticase + MTX period are defined as events that occur after the start of the first pegloticase infusion through 30 days after the last dose of pegloticase and/or MTX or placebo for MTX (whichever is later). †PYs are limited to exposure in the pegloticase + MTX/PBO period. Total PY = Sum ((last treatment date − first treatment date + 1] / 365.25). Patients who experienced more than one event are counted only once.
‡Serious infection AEs included Covid-19 (n=1 MTX), Covid-19 pneumonia (n=1 MTX and n=1 PBO) and *Pneumonia klebsiella* (n=1 MTX).

References

1. Botson et al. *Arthritis Rheumatol*. 2023;75:293-304.
2. Schlesinger et al. *Arthritis Rheumatol*. 2024; 76 (suppl 9).

Disclosure: V. Domingues: AbbVie, Aurinia pharma, Bristol Mayers, Horizon, Lilly, Novartis, Pfizer, 11, AbbVie, Aurinia, BMY, Exagen, GSK, Horizon, Lilly, and Novartis, 6; **A. Woods**: Amgen, 3, 11; **X. Yang**: Amgen, 3, 11; **B. Lamoreaux**: Amgen, 3, 11; **M. Weinblatt**: aclaris, 2, amgen, 2, anaptysbio, 2, Artiva Bio, 2, Biohaven, 2, Bristol-Myers Squibb(BMS), 2, 5, Canfite, 11, Curie Bio, 2, Deep Cure, 2, Eli Lilly, 2, Gilead, 2, Ignite, 2, Inmedix, 11, Janssen, 5, Janux Therapeutics, 2, Johnson and Johnson, 2, Lifordi, 2, Marvel Bio, 2, Matchpoint, 2, Merck/MSD, 2, Neutrolis, 2, Novartis, 2, Sana, 2, Santa Ana, 2, Sci Rhom, 2, scipher medcine corp, 11, SetPoint Medical, 2, Surf Therapeutics, 2, Thymmune, 2, Xencorp, 2, ZuraBio, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 1993

Risk of Cardiovascular Conditions, Bone Fractures and Mortality in Patients with Uncontrolled Gout in Comparison to Those with Controlled Gout

Tingting Zhang[1], Christian W. Mende[2], Ashraf El-Meanawy[3], Michael Pillinger[4], Kaiding Zhu[5], Bradley Marder[6] and **Brian Lamoreaux**[7], [1]Amgen, Inc., Thousand Oaks, [2]University of California San Diego, San Diego, CA, [3]Medical College of Wisconsin, Milwaukee, WI, [4]New York University Grossman School of Medicine, New York,, NY, [5]Amgen, Inc., San Francisco, CA, [6]AMGEN, Inc, Denver, CO, [7]Amgen, Inc., Deerfield, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Gout may increase the risk of cardiovascular events (CVEs) and bone fractures through urate deposition and chronic inflammation[1,2]. However, the additional effects of uncontrolled gout on these outcomes relative to controlled gout is still unclear. This study was designed to examine the risk of CVEs, fractures and mortality in people with uncontrolled versus controlled gout.

Methods: This retrospective cohort study used Optum Clinformatics DataMart® (2016-2024). Controlled gout was defined by no flares, no visible tophi during the baseline year plus normal baseline serum urate (SU) levels (i.e., pre-index SU < 6 mg/dL for three months). An uncontrolled gout group was defined using a new flare, tophi or gout-related emergency department visit or hospitalization following the use of urate-lowering therapies at baseline, along with pre-index SUs ≥6 mg/dL for three months. Outcomes included 1) a composite outcome of incident stroke/acute myocardial infarction; 2) a composite outcome of incident osteoporosis fractures identified using validated algorithms, and 3) all-cause mortality. Each outcome was analyzed in a separate analysis. We estimated inverse-probability of treatment weights (IPTW) for each comparison group using propensity scores. Poisson regressions were used to estimate incidence rates (IRs) and Cox proportional hazard models were used to generate hazard ratios (HRs). Sensitivity analysis was conducted with exact matching of all covariates.

Results: Study participants included 19,645 patients with uncontrolled (72% males; 63% aged 65+) vs. 13,126 patients with controlled (60% males; 71% aged 65+) gout for the CVE analyses, 21,237 uncontrolled vs. 13,569 controlled gout patients for the fracture analysis, and 21,292 uncontrolled vs. 13,615 controlled patients for the

Table 1. Selected baseline characteristics of study participants for the cardiovascular disease analysis

Baseline characteristics	Uncontrolled gout, n=19,645	Controlled gout, n=13,126
Age, mean (SD) years	66 (14)	69 (12)
Females, %	28	40
Presence of comorbidities, %		
Diabetes	35	28
Chronic kidney disease	32	16
Hypertension	69	43
Hyperlipidemia	58	40
Chronic lung disease	11	7
Obesity	26	12
Alcohol use disorder	3	1
Receipt of medications, %		
Colchicine	16	3
Allopurinol	48	42
Febuxostat	4	4

Note: Patients with coronary artery diseases e.g., stroke, acute myocardial infarction at baseline were excluded from the CVE outcome analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Summary of incidence rates and hazard ratios after inverse probability weighting

Outcome-specific Results	Uncontrolled gout	Controlled gout
Findings from primary analyses		
Stroke/AMI		
Cohort size, n	19,645	13,126
Stroke/AMI events, n (%)	3,381 (17.2)	1,931 (14.7)
Total person-years of follow-up	66,921	83,783
IR of stroke/AMI per 1,000 person years	50.5 (48.8 – 52.2)	23.1 (22.0 – 24.1)
Weighted HR and 95%CIs	2.3 (2.2 – 2.5)	1
Bone fracture		
Cohort size, n	21,237	13,569
Fracture events, n (%)	929 (4.4)	564 (4.2)
Total person-years of follow-up	75,951	90,742
IR of fracture per 1,000 person years	12.2 (11.5 – 13.1)	6.2 (5.7 – 6.7)
Weighted HR and 95%CIs	2.1 (1.9 – 2.4)	1
Mortality		
Cohort size, n	21,292	13,615
Events, n (%)	3,876 (18.2)	1,821 (13.4)
Total person-years of follow-up	79,982	94,960
Mortality per 1,000 person years	59.9 (58.2 – 61.6)	42.2 (40.9 – 43.6)
Weighted HR and 95%CIs	1.5 (1.4 – 1.6)	1

mortality analysis. (Table 1 shows an example of the mortality analysis). All baseline covariates were balanced after IPTW. Following IPTW, uncontrolled gout compared to controlled gout was associated with a higher rate of developing incident stroke/AMI (adjHR 2.3; 95%CI 2.2-2.5; 51 versus 23 events per 1,000 person-years), a higher rate of an incident fracture (adjHR 2.1; 95%CI 1.9-2.4; 12 versus 6 events per 1,000 person-years) and a higher mortality (adjHR 1.5; 95%CI 1.4-1.6; 60 versus 42 events per 1,000 person years, Table 2). Sensitivity analysis yielded consistent findings (Table 2).

Conclusion: Patients with uncontrolled gout experienced increased risk of CVEs, bone fractures and mortality compared to controlled gout. These findings highlight the need for clinician awareness and further research to clarify how better control of gout may improve health outcomes.

References:[1]Clarson et al.2015. [2]Tzeng et al. 2016.

Disclosure: T. Zhang: Amgen, Inc, 3, 11; **C. Mende**: Amgen, Corcept scPharmaceutical, 1, 2, Boehringer Ingelheim , Lilly USA, Novo Nordisk , Bayer, 6; **A. El-Meanawy**: Horizon (now Amgen, Inc.) in 2000, 1; **M. Pillinger**: Amgen, Federation Bio, Fortress Biotech, Scilex, and SOBI, 2, Convergence Bio, 2; **K. Zhu**: Amgen, Inc, 3, 11; **B. Marder**: Amgen, Inc, 3, 11; **B. Lamoreaux**: Amgen, 3, 11.

Abstract Number: 1994

Pharmacokinetics of Ready-to-Use Pegloticase Formulation Compared to Standard Pegloticase Dosing: Data from the AGILE Study

Orrin Troum[1], John Botson[2], Afroz S. Mohammad[3], Xiaoqing Yang[4], Nathan Roe[5], Supra Verma[6] and **Brian Lamoreaux**[7], [1]Providence Health Care/Doctor's of St John's (MDSJ) Santa Monica, CA, Santa Monica, CA, [2]Orthopedic Physicians Alaska, Anchorage, AK, [3]Amgen Inc, Deerfield, [4]Amgen, Seattle, WA, [5]Horizon Therapeutics, Boise, ID, [6]Horizon Therapeutics, Newport Beach, CA, [7]Amgen, Inc., Deerfield, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Pegloticase is approved for uncontrolled gout as 8-mg infusions admixed in 250 cc of normal saline over 120 minutes or more administered every 2 wks with methotrexate (MTX) coadministration. Given the logistical burden of 2-hr infusions every 2 wks and normal saline supply disruptions, the AGILE study evaluated faster 60-minute infusions every two wks with pre-mixed 8 mg pegloticase, in 50 cc ready-to-use (RTU) vials, with MTX co-administration. The overall results of the AGILE study demonstrated a comparable efficacy and safety profile to that of the standard infusion formulation,[1] but the pharmacokinetic (PK) results have not been reported.

Methods: The AGILE study was a phase 4, multicenter, open-label study including patients with uncontrolled gout (oral ULT failure or intolerance, SU ≥6 mg/dL, more than one tophus, more than one flare/yr, or gouty arthritis). Key exclusion criteria were contraindication to MTX, G6PD deficiency, serious bacterial infection, eGFR < 40 mL/min/1.73m^2, or elevated liver function tests. Eligible patients underwent a 4-wk oral MTX run-in of 15 mg weekly with 1 mg daily of folic acid then 24 wks of pegloticase with MTX co-administration. Three cohorts were enrolled receiving 60-, 45-, and 30-minute infusions. Ultimately the 60-minute group was deemed optimal and fully enrolled based on safety reviews. The PK analysis set included all patients who received ≥1 dose of pegloticase and had a post-pegloticase sample evaluable for PK analysis. PK parameters (C_{min}, C_{max}) were analyzed at week 12, including pre- and post-infusion concentrations.

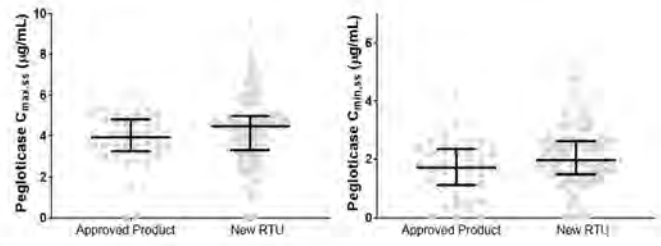
Results: Efficacy and safety of AGILE have been reported among the 60-minute cohort (n = *116)*, showing an infusion reaction rate of 6% (95% CI, 2.5%-12.0%, 7/116) and SU efficacy response rate at month 6 of 67.2% (95% CI, 57.9%-75.7%, 78/116), which were comparable to standard pegloticase with MTX treatment.[1,2] PK analyses included all 3 infusion cohorts and occurred at study week 12, showing a median C_{max} of 4.46 (Q1 of 3.29, Q3 of 4.96, n = 90) for RTU vs 3.92 (Q1 3.24, Q3 4.80, n = 41) for standard pegloticase. The C_{min} followed the same trend, with median C_{min} of 1.96 (Q1 of 1.49, Q3 of

Table 1. Median Peak (Cmax,ss) and Trough (Cmin,ss) Pegloticase Concentrations at Week 12 in Uncontrolled Gout Patients Treated With Approved (Standard) Pegloticase Formulation and New RTU Vial Formulation

Median (Q1, Q3)	Standard Formulation	New RTU Formulation
Observed $C_{max,ss}$ (μg/mL)	3.92 [3.24, 4.80] (n = 41)	4.46 [3.29, 4.96] (n = 90)
Observed $C_{min,ss}$ (μg/mL)	1.70 [1.13, 1.96] (n = 41)	1.96 [1.49, 2.61] (n = 89)

RTU, ready-to-use; Q, quartile; ss, steady-state.
Median concentration is shown with upper and lower error bars representing the first (Q1) and third (Q3) quartiles.

Figure 1. Comparison of Peak (Cmax,ss) and Trough (Cmin,ss) Pegloticase Concentrations at Week 12 in Uncontrolled Gout Patients Treated With Approved (Standard) Pegloticase Formulation and New RTU Vial Formulation



RTU, ready-to-use; Q, quartile; ss, steady-state.

Cmax and Cmin were calculated using pegloticase concentrations observed at Week 12 after reaching steady state. Median concentration is shown with upper and lower error bars representing the first (Q1) and third (Q3) quartiles. 1/41 and 1/91 data point of Cmax were not included in the plot in the approved product and new RTU, respectively, due to abnormally high values. 1 of 89 patients in new RTU group was not included in the plot of Cmin due to abnormally high values.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2.61, n = 89) vs 1.70 (Q1 of 1.13, Q3 of 1.96, n = 41) for standard pegloticase. (**Table 1, Fig. 1)**. These differences were small relative to overall exposure variability and not considered clinically significant. Overall, the RTU formulation showed an 11.7% higher geometric mean simulated exposure compared to standard pegloticase (clinically insignificant). Of note, 5 patients (60-minute cohort [n=1]; 30-minute cohort [n=4]) received standard admixed pegloticase and RTU formulation during the study; the PK parameters and response rates in these patients were comparable to the pegloticase RTU and standard formulations.

Conclusion: Pegloticase given in RTU form of premixed 50 cc with 8 mg of pegloticase coadministered with MTX over 60 minutes showed comparable safety, efficacy, and PK results to standard pegloticase. Among a small number of patients that switched from standard pegloticase to RTU formulation, no change in PK was seen.

References

1. Troum et al. *Arthritis Rheumatol*. 2024; 76 (suppl 9).
2. Botson et al. *Arthritis Rheumatol*. 2023;75:293-304.

Disclosure: O. Troum: AbbVie, Acelyrin, Amgen, Arthrosi, Bristol Myers Squibb, CorEvitas, Eli Lilly, J & J, Moonlake, Novartis, Sanofi-Genzyme, and UCB, 5, AbbVie, Amgen, Eli Lilly, GSK, Pfizer, Sanofi Genzyme, and UCB, 6; **J. Botson**: AbbVie, Amgen, Horizon (now Amgen, Inc.), Lilly, and Novartis,, 2, 6, Horizon (now Amgen, Inc.),, 10, Horizon (now Amgen, Inc.), Allena, Olatec, and Radius Health, 5; **A. Mohammad**: Amgen, 3, 11; **X. Yang**: Amgen, 3, 11; **N. Roe**: Amgen, 3; **S. Verma**: Amgen, 3, 11; **B. Lamoreaux**: Amgen, 3, 11.

Abstract Number: 1995

The Prevalence of Multimorbidity and Polypharmacy Among US Adults with Gout: A General Population-Based Study

Chio Yokose[1], Natalie McCormick[2], Jiaqi Wang[2], Sharan Rai[3], leo lu[4] and Hyon K. Choi[5], [1]Massachusetts General Hospital, Waltham, MA, [2]Massachusetts General Hospital, Boston, [3]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [4]Arthritis Research Canada, Vancouver, BC, Canada, [5]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is an inflammatory-metabolic condition that is associated with a heavy burden of cardiovascular-kidney-metabolic (CKM) comorbidities. Accordingly, multimorbidity and polypharmacy are important considerations which could impact gout management yet have been understudied in this population. We sought to determine the prevalence of multimorbidity and polypharmacy among individuals with gout in the United States.

Methods: We used data from the National Health and Nutrition Examination Survey (NHANES) 2017-18 in which self-reported data on history of gout were ascertained. We examined the national prevalence and population estimates of eight CKM comorbidities, which were defined using a combination of self-reported history, laboratory values, anthropometric measurements, medications, and physical examination data (**Table 1**). Multimorbidity was defined as having two or more CKM conditions. Polypharmacy was defined as having five or more prescription medications. We conducted logistic regression analyses to quantify the magnitude of association between the presence of gout and the presence of comorbidities,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

including sub-group analyses based on sex and age ≥65. All statistical analyses were performed using survey commands of SAS to adjust for clusters and strata of the complex sample design and to incorporate sample weights to generate estimates for the total civilian, non-institutionalized US population.

Results: In the NHANES 2017-18, 5.1% (12.1 million) of the US population reported a history of gout. Multimorbidity was present in 76.7% (9.4 million) of individuals with gout compared to 47.1% of individuals without gout, yielding an age- and sex-adjusted odds ratio (OR) of 1.9 (95% CI, 1.1 to 3.2), which was significantly higher among women with gout compared to men with gout (OR 2.7 versus 1.6, p for interaction 0.006) (**Table 2**). Among those age 65 or greater, individuals with gout were 2.7-fold (1.2 to 6.2) more likely to have multimorbidity compared to those without gout. Individuals with gout were also more likely to experience polypharmacy compared to those without gout, with an age- and sex-adjusted OR of 1.9 (1.1 to 3.4) (**Table 2**). Examining the different CKM conditions, the most prevalent among individuals with gout were hypertension (64.7%; 7.9 million), dyslipidemia (60.9%; 7.4 million), and obesity (57.3%; 6.8 million) (**Table 3**). The prevalences were significantly higher among individuals with gout than those without gout for all conditions except dyslipidemia and MASLD, with highest age- and sex-adjusted OR of 2.7 (1.6 to 4.7) for CKD, followed by 2.3 (1.1 to 4.7) for heart failure (**Table 3**). In our sex-stratified analyses, comorbidities tended to be more frequent among women with gout than men with gout, most notably for hypertension and CHD (**Table 3**).

Conclusion: A significant proportion of US adults with gout experience multimorbidity and polypharmacy. With the emergence of medications with multiple CKM benefits, such as sodium-glucose cotransporter type 2 inhibitors and glucagon-like peptide-1 receptor agonists, additional studies are warranted to determine best practices to streamline gout and CKM comorbidity care.

Table 1. CKM Comorbidities and Their Definitions

Comorbidity	Definition
Obesity	Body mass index ≥30
Hypertension	Self-reported history of hypertension
Type 2 diabetes (T2DM)	Treatment with diabetes medication or self-reported history of diabetes
Dyslipidemia	Hypercholesterolemia (cholesterol >2g/L or treatment with lipid-lowering medications) and/or hypertriglyceridemia (triglycerides >2.5g/L)
Coronary heart disease (CHD)	Self-reported history of angina and/or myocardial infarction
Heart failure	Self-reported history of heart failure
Chronic kidney disease (CKD)	Estimated glomerular filtration rate <60 mL/min/1.73m² using CKD-EPI
Metabolic dysfunction-associated steatotic liver disease (MASLD)	Hepatic steatosis (CAP ≥ 274 dB/m or ≥ 248/302 dB/m) plus one or more cardiometabolic risk factors: overweight/obesity, impaired glucose metabolism, elevated blood pressure, elevated triglycerides, low HDL; excluded individuals with excessive alcohol consumption or other identifiable causes of hepatic steatosis

CAP: controlled attenuation parameter on vibration-controlled transient elastography

Table 2. Prevalence of Multimorbidity and Polypharmacy Among Individuals with and without Gout in the US in 2017-18

	Gout (n =338)		No Gout (n =5222)		OR (95% CI)	P value for Interaction
	Population Estimates (million)	Prevalence, % (95% CI)	Population Estimates (million)	Prevalence, % (95% CI)		
Multimorbidity	9.4	76.7 % (67.3 - 86.1)	106.6	47.1 % (43.7 - 50.6)	1.9 (1.1 - 3.2)	
Men	6.2	75.3 % (65.0 - 85.6)	52.9	49.6 % (45.2 - 53.9)	1.6 (0.9 - 2.8)	0.006
Women	3.2	79.5 % (65.3 - 93.6)	53.7	44.9 % (41.1 - 48.7)	2.7 (1.0 - 7.3)	
≥ 65	4.7	89.0 % (81.1 - 96.8)	32.9	76.0 % (71.8 - 80.2)	2.7 (1.2 - 6.2)	
Polypharmacy	5.1	41.8 % (31.1 - 52.6)	35.6	15.8 % (13.5 - 18.0)	1.9 (1.1 - 3.4)	
Men	3.4	41.4 % (26.6 - 56.2)	15.3	14.4 % (12.2 - 16.6)	2.1 (1.0 - 4.6)	0.56
Women	1.7	42.7 % (28.7 - 56.7)	20.3	17.0 % (14.0 - 20.0)	1.8 (1.0 - 3.2)	
≥ 65	3.1	58.9 % (46.7 - 71.0)	18.4	42.5 % (37.0 - 48.0)	1.9 (1.2 - 3.5)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Prevalence of CKM Comorbidities Among Individuals with and without Gout in the US in 2017-18

	Gout (n =338)		No Gout (n =5222)		OR (95% CI)	P value for Interaction
	Population Estimates (million)	Prevalence, % (95% CI)	Population Estimates (million)	Prevalence, % (95% CI)		
Obesity	6.8	57.3 % (44.2 - 70.3)	93.7	41.9 % (38.6 - 45.2)	1.9 (1.2 - 3.0)	
Men	4.4	54.7 % (39.8 - 69.5)	44.3	42.1 % (36.7 - 47.5)	1.7 (0.9 - 3.0)	0.70
Women	2.4	63.0 % (47.9 - 78.0)	49.4	41.7 % (37.9 - 45.5)	2.4 (1.3 - 4.4)	
Hypertension	7.9	64.7 % (53.2 - 76.2)	69.7	30.9 % (27.7 - 34.0)	2.2 (1.4 - 3.6)	
Men	5.2	62.9 % (51.3 - 74.5)	34.4	32.3 % (28.4 - 36.2)	2.0 (1.2 - 3.5)	0.003
Women	2.8	68.3 % (52.5 - 84.2)	35.4	29.6 % (26.5 - 32.7)	2.8 (1.5 - 5.4)	
Type 2 diabetes	3.5	28.2 % (21.7 - 34.7)	27.3	12.1 % (10.9 - 13.2)	1.6 (1.0 - 2.4)	
Men	2.3	27.7 % (17.8 - 37.7)	13.8	12.9 % (10.7 - 15.1)	1.4 (0.8 - 2.6)	0.13
Women	1.2	29.2 % (11.6 - 46.7)	13.5	11.3 % (9.8 - 12.8)	1.9 (1.0 - 3.8)	
Dyslipidemia	7.4	60.9 % (50.3 - 71.5)	110.3	48.8 % (45.0 - 52.5)	0.7 (0.5 - 1.0)	
Men	4.8	58.7 % (44.2 - 73.1)	51.7	48.5 % (44.0 - 53.0)	0.7 (0.5 - 1.1)	0.30
Women	2.6	65.4 % (54.6 - 76.1)	58.6	49.0 % (44.8 - 53.1)	0.8 (0.5 - 1.3)	
CHD	2.8	22.8 % (15.6 - 30.0)	13.3	5.9 % (4.5 - 7.2)	2.2 (1.4 - 3.5)	
Men	1.9	23.5 % (12.2 - 34.8)	8.4	7.9 % (5.9 - 9.9)	1.8 (0.9 - 3.4)	0.0003
Women	0.9	21.5 % (4.0 - 38.9)	4.9	4.1 % (2.8 - 5.3)	3.6 (1.4 - 9.2)	
Heart failure	1.0	8.4 % (3.3 - 13.5)	4.5	2.0 % (1.4 - 2.6)	2.3 (1.1 - 4.7)	
Men	0.8	9.9 % (4.3 - 15.4)	2.6	2.4 % (1.6 - 3.2)	2.6 (1.2 - 5.9)	0.11
Women	0.2	5.4 % (0.0 - 11.4)	2.0	1.6 % (1.0 - 2.3)	1.5 (0.6 - 4.3)	
CKD	2.5	21.2 % (12.8 - 29.5)	11.0	5.1 % (4.1 - 6.2)	2.7 (1.6 - 4.7)	
Men	1.4	18.1 % (9.7 - 26.4)	4.4	4.3 % (3.1 - 5.6)	2.5 (1.3 - 4.8)	0.60
Women	1.1	27.4 % (11.2 - 43.7)	6.6	5.9 % (4.6 - 7.1)	3.1 (1.5 - 6.4)	
MASLD	2.8	43.2 % (29.5 - 56.9)	44.2	29.4 % (26.4 - 32.3)	1.1 (0.6 - 2.2)	
Men	2.3	47.4 % (30.1 - 64.6)	24.3	32.9 % (28.8 – 37.0)	1.3 (0.6 - 2.7)	0.002
Women	0.5	30.7 % (7.5 – 54.0)	19.9	26.0 % (22.8 - 29.1)	0.8 (0.2 - 3.0)	

Disclosure: C. Yokose: None; **N. McCormick**: None; **J. Wang**: None; **S. Rai**: None; **I. lu**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2.

Abstract Number: 1996

Hospital Burden of Crystal-related Arthritis in Spain: a nationwide dataset of 183,001 inpatients.

Cristina Rodríguez-Alvear[1], Fernando Borrás[2] and Mariano Andrés[3], [1]Virgen de la Peña General Hospital, Fuerteventura, Spain, [2]Miguel Hernández University of Elche, Alicante, Spain, [3]Dr Balmis Alicante General University Hospital-ISABIAL, Alicante, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Gout and calcium pyrophosphate crystal deposition disease (CPPD) are frequent in hospital settings. In Spain, last available data (2005-2015) indicated that 0.48% of hospital discharges had a gout diagnosis, with rising prevalence and mortality (PMID 34168227). Conversely, no population-based studies exist for CPPD. We aimed to analyze prevalence, hospital stays, mortality, and costs of hospitalized patients with gout or CPPD between 2016 and 2022 in Spain.

Methods: We used the Minimum Basic Data Set (MBDS) from the National Health Service to study adult patients with any primary or secondary diagnosis of gout (ICD-10-ES codes M10.X or M1A.X) or CPPD (M11.X) admitted to public or private hospitals between 2016 and 2022.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Prevalence with 95% confidence intervals (CIs) and temporal trends were calculated over annual hospitalization discharges. Differences in age, sex, mean hospital stay, mortality, and costs (measured based on All Patient Refined Diagnosis-Related Groups) were analyzed between patients with gout and CPPD, stratified by being primary or secondary diagnoses. Kruskal-Wallis and chi-square tests were used for comparisons.

Results: After excluding 13,987 for errors in coding, we studied 183,001 patients in the 2016–2022 period. The prevalence of gout was 0.58% (n=167,693/28,861,486; 95%CI 0.58-0.58%), coded as primary diagnosis in 5,314 (3.2%) and secondary in 162,379 (96.8%). Meanwhile, the prevalence of CPPD was 0.05% (n=14,473/28,861,486; 95%CI 0.05-0.05%), mostly as secondary diagnoses (95%, n=13,752). 835 patients had both crystal diagnoses.

Compared to gout, patients with primary or secondary CPPD were older (74.4±14.2 vs 70.8±14.3 years, $p< 0.001$; 79.7 ±10.9 vs 74.8±12.1 years, $p< 0.001$) with a female predominance (52.6% vs 15.8%, $p< 0.001$; 61.4% vs 16.5%, $p< 0.001$). The average age steadily increased up to +2.4 years in gout and +4.8 in CPPD in the study period.

Mean hospital stay was significantly longer in gout than in CPPD (6.5±7 vs 5.6±5.3 days, $p< 0.001$). It decreased only for patients with secondary diagnoses of gout or CPPD (Gout: -0.7 days, $p< 0.001$; CPPD: -0.1 days, $p=0.047$).

Mortality of inpatients with primary diagnosis was 0.7% in gout and 0.1% in CPPD ($p< 0.001$). In secondary diagnoses, respective mortalities were 6.1% and 4.7% ($p< 0.001$). Mortality showed a significant increase in gout (Primary Gout: +0.5%, $p=0.02$; Secondary Gout: +1%, $p< 0.001$), while only in secondary diagnoses of CPPD (+1.1%, $p< 0.001$).

Costs were similar in gout and CPPD-related hospitalizations (3624.6±1794.66 € and 3645.40±1644.52 €), but higher for gout in secondary diagnoses (5318.5±5257.6 € vs 4933.9±4316.3 €, $p< 0.001$). In all cases, mean costs increase progressively.

Conclusion: The updated prevalence of gout in hospitalizations surpasses previous reports. Novel national CPPD data shows it occurs more frequently in older patients and women. Gout results in longer hospital stays and higher mortality. Hospitalizations, age, costs, and mortality rates rose during the study period, indicating a significant burden of crystal-related arthritis in hospitals.

Disclosure: C. RodrÍguez-Alvear: None; **F. Borrás**: None; **M. Andrés**: Grunenthal, 5, Sobi, 1.

Abstract Number: 1997

Bone health in patients with gout using real-world U.S. data

Emily Holladay[1], Alexis Woods[2], Fenglong Xie[3], Jingyi Zhang[1], Angelo Gaffo[4], Jeffrey Curtis[5] and Brian Lamoreaux[6], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Amgen, Detroit, MI, [3]The University of Alabama at Birmingham, Birmingham, AL, [4]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [5]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [6]Amgen, Inc., Deerfield, IL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with gout may be at high risk for developing osteoporosis and fractures, but osteoporosis may be under-recognized and inadequately managed for gout patients. We evaluated fracture rates and features associated with bone health management in patients with gout and comparator groups using data from the American College of Rheumatology's (ACR) Rheumatology Informatics System for Effectiveness (RISE) registry linked to Medicare claims data.

Methods: We performed a retrospective analysis of the RISE registry linked to claims data, 2015-2021. Inclusion criteria: age ≥18 at index (later of qualifying cohort diagnosis date, enrollment start+365 days), ≥1 provider visit after index, and no baseline immunomodulators. Gout and two comparator cohorts (osteoarthritis [OA], soft tissue rheumatism [STR]) were identified using ICD-10-CM codes and medications, and patients were selected via this hierarchy. Gout required ≥2 ICD-9/10 codes and urate-lowering therapy or colchicine. Comparator groups required ≥2 ICD-9/10 codes for OA or STR and no ULT or colchicine. Patients in the gout cohort were matched 1:1 by age (±2 years), sex, race, and Medicare enrollment quarter to patients in the OA cohort and (separately) to the STR cohort. We examined medications, comorbidities,

Table 1: Baseline Demographics of Patients with Gout, Osteoarthritis, and Soft Tissue Rheumatism

Characteristic*	N	Gout 3,350	OA 3,350	SMD	N	Gout 772	STR 772	SMD
Age, years	6,700	72.0 (68.0, 77.0)	72.0 (68.0, 77.0)	0.00	1,544	71.0 (67.0, 76.0)	71.5 (67.0, 76.0)	0.00
Male	6,700	2,151 (64.2%)	2,151 (64.2%)	0.00	1,544	206 (26.7%)	206 (26.7%)	0.00
Race, White	5,894	2,520 (85.5%)	2,520 (85.5%)	0.00	1,372	642 (93.6%)	642 (93.6%)	0.00
Ethnicity, Non-Hispanic	5,056	2,520 (96.4%)	2,317 (94.9%)	0.07	1,074	540 (97.5%)	505 (97.1%)	0.02
BMI kg/m^2	5,596	31.0 (28.0, 36.0)	28.0 (25.0, 32.0)	0.47	1,304	33.0 (28.0, 38.0)	26.0 (23.0, 30.0)	1.0
N		2,827	2,769			644	660	
Baseline RXRISK (excluding gout medications)	6,700	1.0 (0.0, 6.0)	0.0 (0.0, 3.0)		1,544	1.0 (0.0, 6.0)	0.0 (0.0, 2.0)	0.37
N		3,350	3,350			772	772	
ADI≥80	6,258	534 (17.1%)	526 (16.8%)	0.01	1,445	130 (17.8%)	70 (9.8%)	0.23
Region	6,674			0.07	1,535			0.09
Midwest		610 (18.3%)	620 (18.6%)			143 (18.6%)	124 (16.2%)	
Northeast		353 (10.6%)	302 (9.0%)			69 (9.0%)	73 (9.5%)	
South		2,052 (61.6%)	2,144 (64.2%)			493 (64.0%)	487 (63.7%)	
West		318 (9.5%)	275 (8.2%)			65 (8.4%)	81 (10.6%)	
Smoker Ever	5,355	815 (30.0%)	823 (31.2%)	-0.02	1,211	146 (23.9%)	174 (29.0%)	-0.12
GC use at index	6,700	1,538 (45.9%)	1,095 (32.7%)	0.27	1,544	397 (51.4%)	249 (32.3%)	0.40
Oral steroid ≥200mg ***	6,700	1,044 (31.2%)	636 (19.0%)	0.28	1,544	267 (34.6%)	137 (17.7%)	0.39
Medication Use **								
Proton pump inhibitor	6,700	1,184 (35.3%)	1,292 (38.6%)	-0.07	1,544	323 (41.8%)	253 (32.8%)	0.19
Colchicine	6,700	1,604 (47.9%)	0 (0.0%)	1.4	1,544	389 (50.4%)	0 (0.0%)	1.4
NSAID	6,700	1,298 (38.7%)	1,630 (48.7%)	-0.20	1,544	339 (43.9%)	254 (32.9%)	0.23
IMMs	6,700	0 (0.0%)	0 (0.0%)	0.00	1,544	0 (0.0%)	0 (0.0%)	0.00
ULT	6,700	2,999 (89.5%)	0 (0.0%)	4.1	1,544	664 (86.0%)	0 (0.0%)	3.5
Allopurinol	6,700	2,550 (76.1%)	0 (0.0%)	2.5	1,544	583 (75.5%)	0 (0.0%)	2.5
Febuxostat	6,700	593 (17.7%)	0 (0.0%)	0.66	1,544	121 (15.7%)	0 (0.0%)	0.61
Lesinurad	6,700	<11	0 (0.0%)	0.03	1,544	<11	0 (0.0%)	0.05
Probenecid	6,700	84 (2.5%)	0 (0.0%)	0.23	1,544	13 (1.7%)	0 (0.0%)	0.19
Pegloticase	6,700	16 (0.5%)	0 (0.0%)	0.10	1,544	<11	0 (0.0%)	0.05
Any bone protective therapy	6,700	165 (4.9%)	394 (11.8%)	-0.25	1,544	66 (8.5%)	179 (23.2%)	-0.41
Baseline Comorbidities								
Fracture	6,700	47 (1.4%)	88 (2.6%)	-0.09	1,544	15 (1.9%)	26 (3.4%)	-0.09
Osteoporosis	6,700	237 (7.1%)	516 (15.4%)	-0.27	1,544	84 (10.9%)	237 (30.7%)	-0.50
Osteopenia	6,700	131 (3.9%)	233 (7.0%)	-0.13	1,544	54 (7.0%)	88 (11.4%)	-0.15
Hypertension	6,700	2,963 (88.4%)	2,508 (74.9%)	0.36	1,544	717 (92.9%)	477 (61.8%)	0.80
Cardiovascular Disease	6,700	1,169 (34.9%)	926 (27.6%)	0.16	1,544	234 (30.3%)	143 (18.5%)	0.28
Diabetes	6,700	1,357 (40.5%)	937 (28.0%)	0.27	1,544	378 (49.0%)	176 (22.8%)	0.57
Hyperthyroidism	6,700	29 (0.9%)	32 (1.0%)	-0.01	1,544	11 (1.4%)	<11	0.02
COPD	6,700	403 (12.0%)	392 (11.7%)	0.01	1,544	98 (12.7%)	64 (8.3%)	0.14
CPD	6,700	737 (22.0%)	755 (22.5%)	-0.01	1,544	205 (26.6%)	138 (17.9%)	0.21
Tophi	6,700	466 (13.9%)	0 (0.0%)	0.57	1,544	82 (10.6%)	0 (0.0%)	0.49

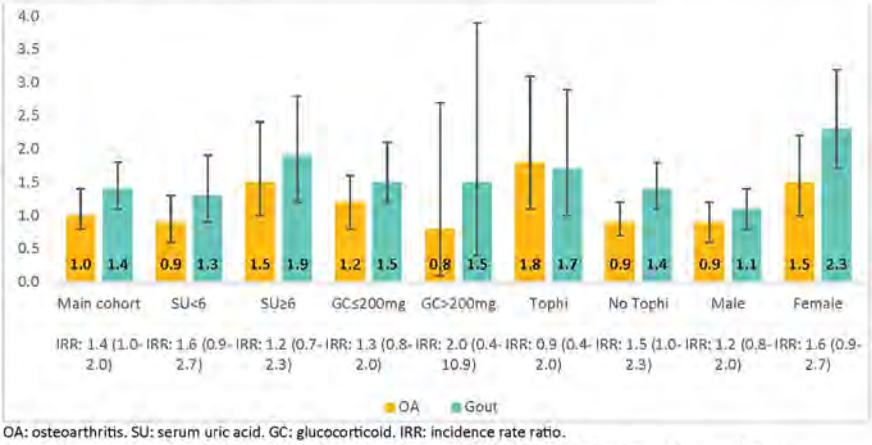
OA: osteoarthritis. STR: soft tissue rheumatism. SMD: standardized mean difference. SD: standard deviation. IQR: Interquartile range. BMI: body mass index. ADI: area deprivation index. GC: glucocorticoid. IMM: immunomodulatory therapy. NSAID: nonsteroidal anti-inflammatory drug. ULT: urate lowering therapy. BP: bisphosphonate. IV: intravenous. COPD: chronic obstructive pulmonary disease. CPD: chronic pulmonary disease.
Note: All baseline characteristics utilized the most recent measurements prior to the index, unless otherwise specified. IMM includes cyclosporine, leflunomide, methotrexate, and sulfasalazine. ULT includes allopurinol, febuxostat, probenecid, lesinurad, pegloticase. Bone protective therapy includes oral/IV bisphosphonate, raloxifene, denosumab, romosozumab, teriparatide, and abaloparatide.
SMDs > 0.10 is a common threshold used to identify factors that may be clinically relevant.
* n(%) or median (IQR)
** on or before index date

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

demographics, and bone protective therapy use and computed crude and adjusted incidence rates (IRs) and incidence rate ratios (IRRs) for fracture (allowing for multiple events) in the gout vs. comparator cohorts.

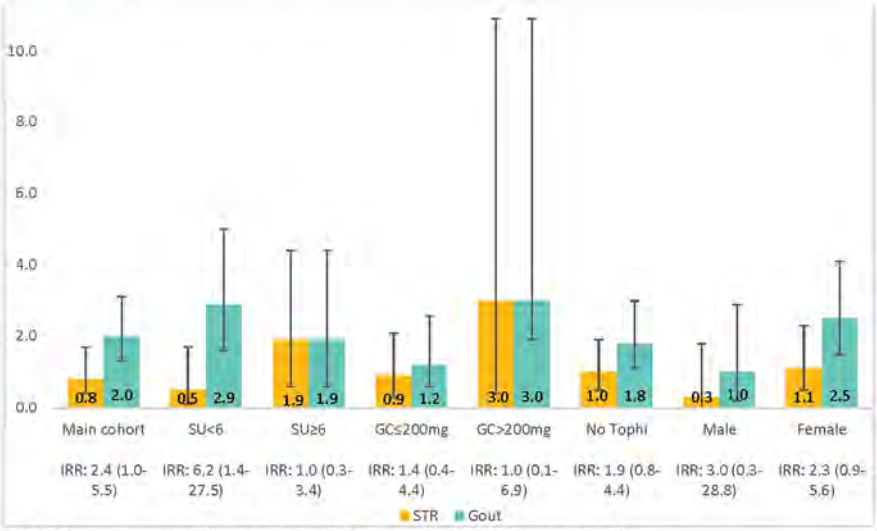
Results: We identified 6700 gout patients and matched them to 6700 OA patients. Most were white (85.5%) and male (64.2%), with median age of 72.0 years (Table 1). Approximately 5% of patients with gout used bone protective therapy at baseline, compared to 11.8% in OA. Baseline fracture and osteoporosis diagnosis prevalence was 1.4% and 7.1% in gout vs. 2.6% and 15.4% in OA patients. The gout and STR cohorts were smaller (n=1544 each) and mostly female (73.3%) with

Figure 1 : Follow-Up Nonvertebral Fracture Incidence Rates per 100 patient-years in Patients with Gout vs. Osteoarthritis*



OA: osteoarthritis. SU: serum uric acid. GC: glucocorticoid. IRR: incidence rate ratio.
*among individuals not using bone protective therapies at baseline. Crude IRs and IRRs for the matched populations.
For the GC ≤200mg subgroup, the patients are in matched pairs, and both patients have GC ≤200mg at baseline. The same applies to the GC >200mg subgroup. For the SU <6 subgroup, the patients are in matched pairs, but the SU condition is restricted only to patients with gout. The same applies to the SU ≥6 subgroup, tophi, and no tophi subgroups.

Figure 2: Nonvertebral Fracture Incidence Rates per 100 patient-years in Patients with Gout vs. Osteoarthritis*



STR: Soft tissue rheumatism. SU: serum uric acid. GC: glucocorticoid. IRR: incidence rate ratio.
*among individuals not using bone protective therapies at baseline. Crude IRs and IRRs for the matched populations.
For the GC ≤200mg subgroup, the patients are in matched pairs, and both patients have GC ≤200mg at baseline. The same applies to the GC >200mg subgroup. For the SU <6 subgroup, the patients are in matched pairs, but the SU condition is restricted only to patients with gout. The same applies to the SU ≥6 subgroup and no tophi subgroups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

demographics otherwise similar to the gout/OA cohorts. Approximately 9.0% of patients with gout used bone protective therapy at baseline, compared to 23.2% in STR. Baseline fracture and osteoporosis diagnosis prevalence was 1.9% vs. 10.9% in gout and 3.4% vs. 30.7% in STR.

Excluding the small number of patients using baseline bone protective medications, higher fracture rates were observed in gout patients compared to OA (IRR: 1.4, 95% CI: 1.0,2.0) and STR (IRR: 2.4, 95% CI: 1.0,5.4) (Figures 1 and 2). The IRRs comparing gout to OA patients were minimally different after adjustment for BMI, NSAIDs, diabetes, and comorbidity, but were higher compared to the STR cohort (aIRR 4.1; 95% CI: 1.4,12.4). New bone protective therapies were infrequently used in all cohorts during follow-up (gout: 2.0% vs. OA: 4.5%; gout: 3.4% vs. STR: 10.3%).

Conclusion: Patients with gout experience greater rates of fracture and more commonly have fracture risk factors (e.g. chronic kidney disease, greater glucocorticoid use) compared to OA and STR patients yet are less likely to receive bone protective therapies. Improved awareness of the risk of fracture and osteoporosis in gout appears warranted, as are strategies to protect bone health in gout patients.

Disclosure: E. Holladay: None; **A. Woods**: Amgen, Inc, 3, 11; **F. Xie**: None; **J. Zhang**: None; **A. Gaffo**: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **B. Lamoreaux**: Amgen, 3, 11.

Abstract Number: 1998

Reduction in Tophi Observed in Patients with Uncontrolled Gout Treated with NASP: Results from Phase 3 DISSOLVE Studies

Herbert Baraf[1], Puja Khanna[2], Frédéric Lioté[3], Rehan Azeem[4], Wesley DeHaan[5], Ben Peace[6], Hugues Santin-Janin[7], Bhavisha Desai[8] and Alan Kivitz[9], [1]The Center for Rheumatology and Bone Research, Rheumatology, Wheaton, Maryland, USA; Division of Rheumatology, The George Washington University, Washington, DC, [2]Division of Rheumatology, University of Michigan, Ann Arbor, MI, [3]Université Paris Cité-Inserm UMR1132 & Rheumatology Department, GH Paris Saint Joseph & Institut Arthur Vernes, Paris, France, [4]Global MACD, Sobi Inc., Waltham, MA, [5]Sobi, Inc, Waltham, MA, [6]Statistical Science, Sobi, Stockholm, Sweden, [7]Sobi, BASEL, Switzerland, [8]Sobi, Glastonbury, CT, [9]Altoona Center for Clinical Research, Duncansville, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients (pts) with uncontrolled gout (UG) and tophi experience joint pain, impaired function and poor quality of life (Schlesinger *et al. Semin Arthritis Rheum* 2020; Dalbeth *et al. Nat Rev Dis Primers* 2019; Dalbeth *et al. Lancet* 2021). With oral urate-lowering therapies, tophus resolution may take several years despite optimal dosing (Laurent *et al. RMD Open* 2023). NASP (formerly SEL-212) is a novel, every 4-week, sequential infusion therapy consisting of targeted immunomodulating, nanoencapsulated sirolimus (NAS; formerly SEL-110) co-administered with a pegylated uricase (formerly SEL-037) designed to reduce serum uric acid (sUA) levels in pts with UG. Here, we report pooled tophus outcomes from the DISSOLVE studies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

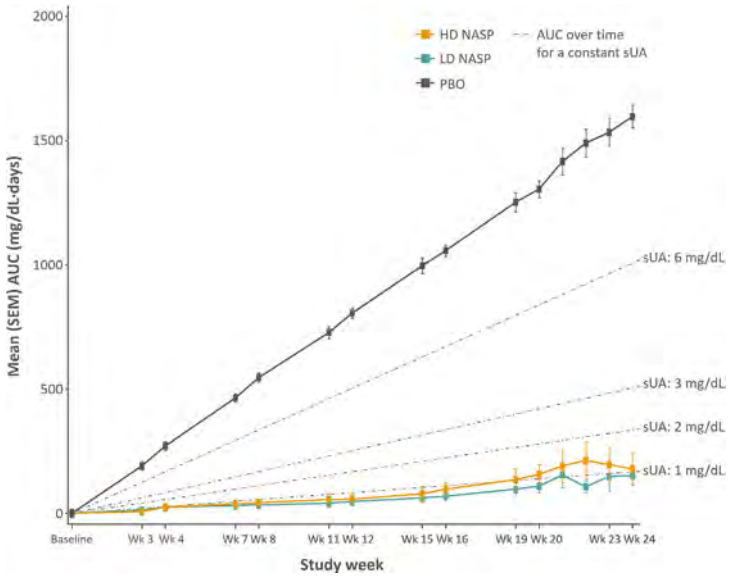


Figure 1. Mean cumulative sUA AUC through week 24 in patients who completed 6 doses of NASP or PBO with tophi at baseline. Cumulative sUA is a measure of the duration and intensity of sUA exposure over time, defined in this study as AUC at each time point (average of the current and previous sUA values multiplied by the time between the current and previous sUA values). The cumulative sUA AUC at each study week in the figure is the total AUC from day 1 up to that week. SUA assessments were performed at the end of each week. Mean (±SEM) is shown for pts with tophi at baseline who completed 6 doses of HD NASP (yellow), LD NASP (teal) or placebo (dark gray). Dashed lines show what the cumulative area under the curve would be at each point in time for a subject that had constant sUA level. AUC, area under the curve; HD NASP, sequential infusions of 0.15 mg/kg nanoencapsulated sirolimus and 0.2 mg/kg pegadricase, LD NASP, sequential infusions of 0.10 mg/kg nanoencapsulated sirolimus and 0.2 mg/kg pegadricase; PBO, placebo; SEM, standard error of mean; sUA, serum uric acid; Wk, week.

Methods: This *post hoc* analysis pooled data from DISSOLVE I II ((NCT04513366, NCT04596540) in the intent-to-treat (ITT) population and in pts who received 6 doses of NASP (high-dose [HD]: sequential infusions of 0.15 mg/kg NAS and 0.2 mg/kg pegadricase; low-dose [LD]: sequential infusions of 0.10 mg/kg NAS and 0.2 mg/kg pegadricase) or placebo (PBO). Tophi response was a predefined secondary endpoint. Percent tophus response included partial response (PR), defined as ≥50% and < 100% reduction in the area of a tophus without enlargement of any existing tophus and no new tophus, and complete response (CR), defined as 100% reduction in area of or complete disappearance of a tophus without enlargement of any existing tophus and no new tophus. A triple read model of tophus evaluation was established after unblinding to improve the quality of measuring tophus size and improve data handling in instances of images with quality issues.

Results: In the ITT population (among pts with tophi at baseline (BL): n=55 [HD]; n=55 [LD]; n=57 [PBO]), tophus response of PR or better was observed in 82% in HD (p=0.0077), 88% in LD (p=0.0016), vs 51% in PBO by week 24. NASP treatment resulted in a clinically relevant response of CR in significantly more patients receiving NASP compared with PBO by week 24: HD, 31% (p=0.0044); LD, 48% (p=0.0001), vs PBO, 5%. In the subset of pts with tophi at BL who received 6 doses of treatment (n=23 [HD]; n=22 [LD]; n=42 [PBO]), a significantly greater proportion of patients on NASP experienced CR by week 24: HD, 49% (p=0.0002); LD, 70% (p< 0.0001), vs PBO, 5%. Consistent with the correlation between tophus reduction and sUA reduction, patients who received 6 doses of HD NASP had 89% lower sUA than PBO-treated patients at Day 168 (end of study) with a similar response for LD NASP (**Figure 1**).

Conclusion: Treatment with NASP resulted in a greater tophus response compared to PBO. In addition, a robust sUA reduction, a key factor in tophus resolution, was observed in NASP-treated pts. These results highlight the effectiveness of NASP in lowering sUA and promoting tophus resolution.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: H. Baraf: Arthrosi, 2, Olatec, 2, Otsuka, 3, Pacira, 2, Selecta Biosciences, 2, Sobi, 2; **P. Khanna**: Arthrosi, 5, Olatec, 5, Selecta Biosciences, 5, Sobi, 2; **F. Lioté**: Amgen, 5, Arthrosi, 5, Bristol-Myers Squibb(BMS), 5, Crystalis, 5, Fresenius Kabi, 5, Horizon, 1, 2, Olatec, 5, 12, Data monitoring committee, Selecta Biosciences, 2, Sobi, 1, 2, 5, 6; **R. Azeem**: Selecta Biosciences, 11, Sobi, 3, 12, Shareholder; **W. DeHaan**: Selecta Biosciences Inc., 11, Sobi, 3; **B. Peace**: Sobi, 7, Veramed, 3; **H. Santin-Janin**: Sobi, 3; **B. Desai**: Sobi, 3, 11; **A. Kivitz**: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2.

Abstract Number: 1999

Characterization of Infusion Reactions Within 1 Hour of Treatment With Nanoencapsulated Sirolimus Plus Pegadricase: Pooled Results From the Phase 3 DISSOLVE I and DISSOLVE II Trials

Herbert Baraf[1], Andrew J. Sulich[2], Guillermo J. Valenzuela[3], Rehan Azeem[4], Ben Peace[5], Bhavisha Desai[6] and Puja Khanna[7], [1]The Center for Rheumatology and Bone Research, Rheumatology, Wheaton, Maryland, USA; Division of Rheumatology, The George Washington University, Washington, DC, [2]Shores Rheumatology, St. Clair Shores, MI, [3]Iris Rheumatology, Plantation, FL, [4]Global MACD, Sobi Inc., Waltham, MA, [5]Statistical Science, Sobi, Stockholm, Sweden, [6]Sobi, Glastonbury, CT, [7]Division of Rheumatology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Uricase-based therapies may profoundly lower serum uric acid (sUA) in patients (pts) with uncontrolled gout (UG) but often lead to anti-drug antibody (ADA) formation, which can predispose pts to infusion reactions (IRs). NASP (formerly SEL-212) is an investigational, novel, every 4-wk (Q4W), sequential 2-component infusion therapy consisting of tolerogenic nanoencapsulated sirolimus (NAS, formerly SEL-110), which mitigates formation of antipegadricase antibodies, and a uricase (pegadricase [P]; formerly SEL-037), which reduces sUA. NASP has shown efficacy and safety in UG (Baraf *et al*. *Rheumatology* 2024). To characterize events that met Rheumatology Common Toxicity Criteria for allergic reaction/hypersensitivity and anaphylaxis (Woodworth *et al*. *J Rheumatol* 2001), we show pt-specific IR details within 1 h of NASP completion from the phase 3 DISSOLVE I and II (NCT04513366, NCT04596540) studies.

Methods: DISSOLVE I and II were replicate, double-blind, placebo (PBO)-controlled trials evaluating 2 NAS doses (0.15 [high-dose; HD] or 0.1 mg/kg [low-dose; LD]) prior to 0.2 mg/kg P in adults with a UG diagnosis per ACR guidelines (Neogi *et al*. *Arthritis Rheumatol* 2015). Eligible pts had a history of symptomatic gout (≥3 gout flares within 18 mo of screening, ≥1 tophus, or current gouty arthritis), lack of sUA normalization and symptom control despite urate-lowering therapies, and sUA ≥7 mg/dL. Pts were randomized 1:1:1 to receive NASP (HD or LD) or PBO Q4W with preinfusion IR prophylaxis (up to six 4-wk treatment periods). Twenty-four–wk safety outcomes included IRs (eg, anaphylaxis, hypersensitivity) within 1 h per NIAID/FAAN criteria (Sampson *et al*. *Ann Emerg Med* 2006).

Results: Overall, 175 pts received HD (n=87) or LD (n=88) NASP; 90 received PBO. Of these, 7 pts (overall: n=7/175, 4.0%; HD NASP: n=3/87, 3.4%; LD NASP: n=4/88, 4.5%; PBO: n=0) had an IR within 1 h of NASP completion (all male; aged 36–63 y). Six IRs occurred shortly after exposure to both NASP components; 1 was during NAS only (pt did not receive P). All IRs were early in the study (first 12 wk). Of the 7 pts with IRs within 1 h, 4 had anaphylactic reactions (2.3% of NASP-treated

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pts overall; 2 in each NASP arm). Common signs/symptoms included rash and shortness of breath. Three of these IRs were grade (G) 3 (2 HD NASP; 1 LD NASP); 1 LD NASP-treated pt had a G4 IR. All pts fully recovered with appropriate medical intervention (mainly steroids and antihistamines) provided at the infusion center; 1 pt received epinephrine for anaphylaxis. One pt each in the HD/LD NASP arms (G3/G4 IRs, respectively) was sent to the emergency room, received observation only, and was discharged the same day. No pts required in-pt hospitalization or intubation. Three pts had hypersensitivity reactions (2 G1; 1 G2); signs/symptoms included flushing (most common) and shortness of breath (G2 only). No pts with hypersensitivity reactions were hospitalized; 1 pt was able to resume NASP after a pause.

Conclusion: The low incidence (4.0%) of pts experiencing IRs, including hypersensitivity reactions, within 1 h of NASP suggests that NAS mitigates ADA formation. No pts required in-patient hospitalization or intubation, and all IRs resolved with standard measures (mainly at the infusion center).

Disclosure: H. Baraf: Arthrosi, 2, Olatec, 2, Otsuka, 3, Pacira, 2, Selecta Biosciences, 2, Sobi, 2; **A. Sulich**: AbbVie, 6, AM, 6, Amgen, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, UCB, 6; **G. Valenzuela**: AbbVie, 2, 6, Alexion, 2, Amgen, 2, 6, Artiva Biotherapeutics, 2, 5, 6, AstraZeneca, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 2, 6, Centocor, 6, Esaote, 2, Exagen, 2, Genentech, 2, 6, Gilead, 2, Global Healthy Living, 2, Horizon, 2, 6, Image Analysis Group, 2, Janssen, 2, 6, Lilly, 2, 6, Mallinckrodt, 5, 6, Merck, 2, Novartis, 2, 6, Pfizer, 2, 6, Pharmacia, 6, Radius, 6, Regeneron, 2, 6, Sandoz, 2, Sanofi, 2, 6, Takeda, 6, Theramex, 6, UCB, 2, 6; **R. Azeem**: Selecta Biosciences, 11, Sobi, 3, 12, Shareholder; **B. Peace**: Sobi, 7, Veramed, 3; **B. Desai**: Sobi, 3, 11; **P. Khanna**: Arthrosi, 5, Olatec, 5, Selecta Biosciences, 5, Sobi, 2.

Abstract Number: 2000

Can Uric Acid Protect Joints? Lower Incidence of Large Joint Replacements Among Individuals with Higher SUA

Janis Timsans[1], Raine Tiihonen[2], Jenni Kauppi[3], Vappu Rantalaiho[4], Anne Kerola[1], Kia Hakkarainen[5], Tiina Lehto[6], Hannu Kautiainen[7] and Markku Kauppi[1], [1]Päijät-Häme Central Hospital, Department of Rheumatology, Lahti, Finland, [2]Päijät-Häme Central Hospital, Department of Orthopedics and Traumatology, Lahti, Finland, [3]Päijät-Häme Central Hospital, Unit of Physiatry and rehabilitation medicine, Lahti, Finland, [4]Tampere University, Faculty of Medicine and Health Technology; Tampere University Hospital, Centre for Rheumatic Diseases, Tampere, Finland, [5]Päijät-Häme Central Hospital, Department of Nephrology, Lahti, Finland, [6]Fimlab Laboratoriot Oy, Department of Clinical Chemistry, Lahti, Finland, [7]Folkhälsan Research Center, Helsinki, Finland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Serum uric acid (SUA) has been linked to various health conditions, including osteoarthritis (OA), though findings have been inconsistent. Data on the relationship between SUA and OA in large joints are particularly limited, and its potential association with the need for large joint replacements (LJRs) has not been previously investigated. This study aimed to examine the association between SUA levels and the incidence of LJRs.

Methods: Data were drawn from the GOAL (**GO**od **A**geing in **L**ahti region) study, a prospective cohort study of individuals aged 52–76 years in Finland's Lahti region. Baseline data included SUA levels, other laboratory parameters, comorbidities, medication use, lifestyle factors, and socioeconomic variables. Information on LJRs was obtained from the National Care Register for Social Welfare and Health Care. After excluding participants with prior LJRs or cancer diagnoses, 2,403

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

individuals (1,115 women and 1,288 men) were included. The incidence of large joint arthroplasty over a 12.7-year follow-up was analyzed in relation to SUA levels, adjusting for age, sex, body mass index (BMI), and Charlson Comorbidity Index (CCI). Hyperuricemia was classified as renal when SUA was ≥420 μmol/L (≈7 mg/dL) and estimated glomerular filtration rate (eGFR) ≤67 ml/min/1.73 m^2 (25^{th} percentile), and as metabolic when SUA was ≥420 μmol/L with eGFR >67 ml/min/1.73 m^2.

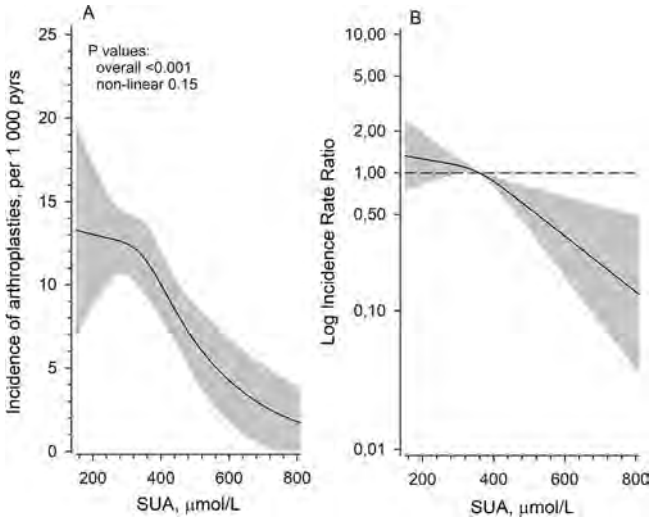


Figure 1. Panel A: Association of serum uric acid (SUA) level and incidence of arthroplasties. Panel B: Log incidence rate ratio of arthroplasties by SUA level. Denominator of IRR is SUA 420 μmol/L. The results are adjusted for age, sex, body mass index and Charlson Comorbidity Index.

Table 1. Incidence and incidence rate ratio (IRR) for incident large joint replacements across different SUA groups. SUA, serum uric acid; LJRs, large joint replacements; pyrs, person-years; IRR, incidence rate ratio

SUA	[Total number of LJRs] Incidence* (95% CI) per 1000 pyrs	IRR (95% CI)*
<300, μmol/L	[88] 13.4 (10.4 to 16.4)	1.00 (Reference)**
300-359, μmol/L	[96] 11,7 (9.4 to 14.1)	0.88 (0.65 to 1.18)
≥360, μmol/L	[69] 11,0 (8.4 to 13.6)	0.82 (0.59 to 1.14)
≥420, μmol/L	[50] 7.1 (5.0 to 9.2)	0.53 (0.36 to 0.78)
		p for linearity 0.006*
Total	[303] 11.2 (10.1 to 12.3)	

*Adjusted for age, sex, body mass index and Charlson Comorbidity Index.
** Denominator of incidence rate ratios

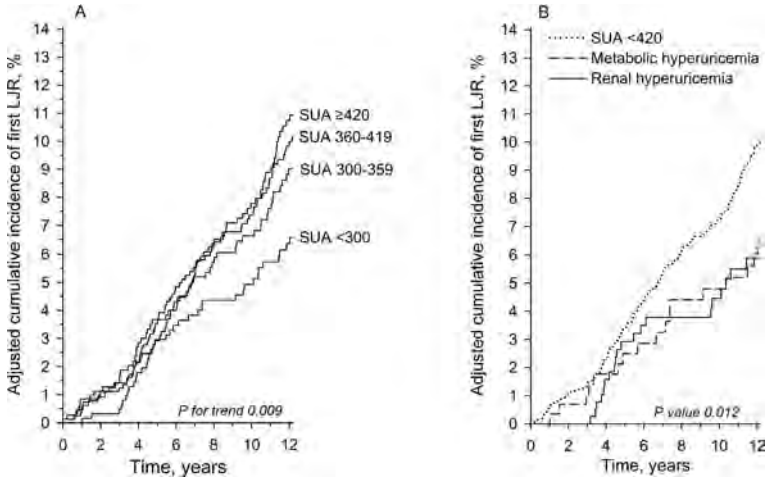


Figure 3. Adjusted cumulative incidence of first LJR. SUA, serum uric acid; LJR, large joint replacement

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Over the 12.7-year follow-up period, a total of 303 LJRs were performed in the study population, including 133 hip replacements, 161 knee replacements, 8 shoulder replacements, and 1 elbow replacement; no ankle replacements were reported. In models adjusted for age, sex, BMI, and CCI, higher SUA levels were associated with a lower incidence of LJRs (Figure 1). When analyzing the incidence rate ratio across SUA categories (< 300 μmol/L, 300–359 μmol/L, 360–419 μmol/L, ≥420 μmol/L), a statistically significant decreasing trend in LJRs with increasing SUA was observed ($p = 0.006$; Table 1). While the adjusted cumulative incidence of first LJR increased with higher SUA, there was no substantial difference between individuals with metabolic versus renal hyperuricemia (Figure 2).

Conclusion: In our study population, individuals with higher SUA levels were less likely to undergo LJR during the 12.7-year follow-up period. This finding has not been previously demonstrated. Future studies are needed to determine whether uric acid has a protective effect on cartilage in large joints, potentially reducing cartilage degradation. Replicating our findings in other studies and further investigating the impact of uric acid on cartilage health are essential.

Disclosure: J. Timsans: None; **R. Tiihonen**: None; **J. Kauppi**: None; **V. Rantalaiho**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 1, Johnson&Johnson, 6, Medac, 6, Novartis, 6, Viatris, 6; **A. Kerola**: None; **K. Hakkarainen**: None; **T. Lehto**: None; **H. Kautiainen**: None; **M. Kauppi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2001

Characteristics of Gout Flares Over Time with Treat-to-Target Urate-Lowering Therapy Use

Jason Yang[1], Ted Mikuls[2], Harlan Sayles[2], Michael Pillinger[3], Jeff Newcomb[2], Bridget Kramer[2], Anne Davis-Karim[4], Mary Brophy[5], Ryan Ferguson[5], Paul Palevsky[6], James O'Dell[2] and Tuhina Neogi[7], [1]Boston Medical Center, Boston, MA, [2]University of Nebraska Medical Center, Omaha, NE, [3]New York University Grossman School of Medicine, New York, NY, [4]VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center, Albuquerque, NM, [5]VA Cooperative Studies Program Coordinating Center, Boston, MA, [6]VA Pittsburgh Healthcare System, Pittsburgh, PA, [7]Boston University School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Gout flares are an important treatment outcome in gout. Although flares are typically assessed by occurrence (yes/no) or a simple count in trials of urate-lowering therapy (ULT), it is possible that certain flare characteristics could also serve as a measure of ULT efficacy. We evaluated gout flare characteristics among trial participants who were started on treat-to-target ULT and assessed the extent to which achievement of serum urate (SU) goal impacted flare characteristics.

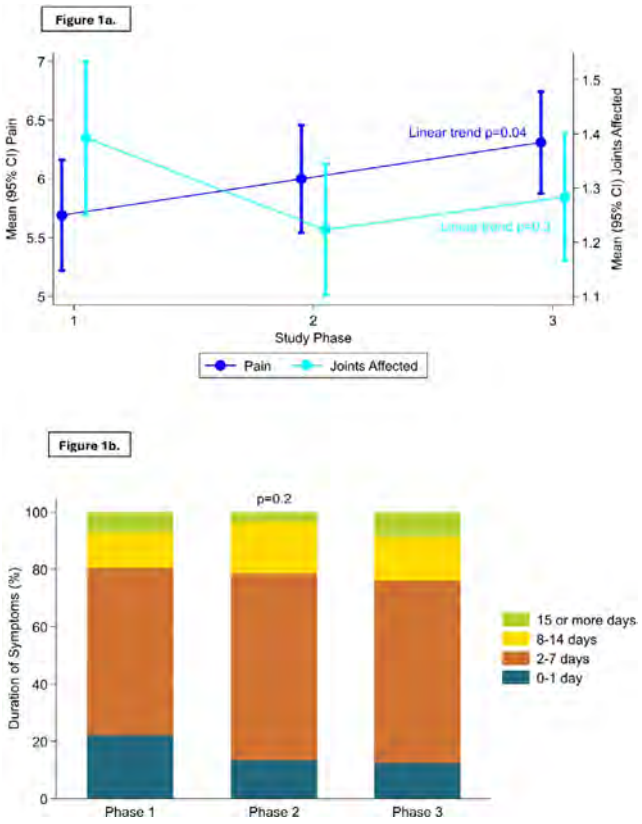


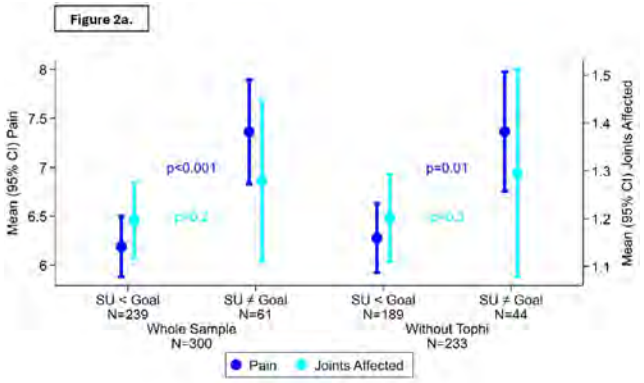
Figure 1a. Mean Pain Intensity and Mean # of Joints Involved for the 1st Flare Within Each Phase in Those who Experienced at least 1 Flare in All Three Phases (n=113). Figure 1b. Duration of Flare Symptoms for the 1st Flare Within Each Phase in Those who Experienced at least 1 Flare in All Three Phases (n=113).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We performed a post-hoc analysis of the STOP Gout trial, a non-inferiority, randomized, double-blind, placebo-controlled trial of allopurinol vs. febuxostat (PMID 35294114). In Phase 1 (0-24 weeks), ULT dose was adjusted to achieve SU goal (i.e., < 6mg/dL or < 5mg/dL with tophi) and prophylaxis was provided (NSAIDs, colchicine, glucocorticoids). In Phase 2 (25-48 weeks), a single ULT dose adjustment was allowed to achieve SU goal. Prophylaxis was discontinued prior to Phase 3 (49-72 weeks). Flares were identified throughout the trial using a modification of validated criteria. Flare characteristics were assessed as pain intensity, number of joints involved, and duration. For those experiencing a flare during all 3 study Phases, characteristics of the first flare in each Phase were compared via generalized linear mixed models with random effects for participants. We next compared characteristics of the first flare in Phase 3 (when participants were off prophylaxis) based upon SU goal achievement at the end of Phase 2. We repeated these analyses limited to those without baseline tophi because the flare criteria may be less sensitive in those with tophi.

Results: Of the 940 STOP Gout participants, 602 (64%) (99% male, mean baseline SU 8.6mg/dL, 19% with tophi) had ≥1 flare during the 72-week study. Flare characteristics were similar across the 3 Phases among the 113 participants with ≥1 flare in each of Phase 1-3 (**Figure 1**); these results did not change after excluding those with tophi (not shown). Of 835 participants with SU measured at the end of Phase 2, 239/648 (37%) who achieved SU goal and 61/187 (33%) who didn't achieve SU goal had ≥1 flare in Phase 3. Flares in those who achieved SU goal had significantly lower mean pain intensity, but similar durations and number of joints involved than in those who did not (**Figure 2**). Among those without baseline tophi, both flare pain intensity and symptom duration were significantly lower with SU goal achievement (vs. not) (**Figure 2**).

Conclusion: In those who experienced ≥1 flare in all three study phases, the flare characteristics did not change meaningfully over time. However, achievement of SU goal was associated with significantly lower pain intensity and shorter symptom duration among those without tophi. With prior reports suggesting that ≥2 years of oral ULT may be required to meaningfully



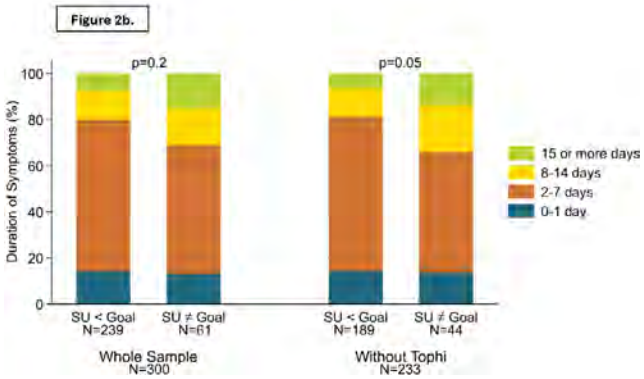


Figure 2a. Comparison of Mean Pain Intensity and Mean # of Joints Affected for the 1st Flare in Phase 3 Based on SU Goal Achievement in the Whole Sample (n=300) and in Those Without Baseline Tophi (n=233). Figure 2b. Comparison of Duration of Flare Symptoms for the 1st Flare in Phase 3 Based on SU Goal Achievement in the Whole Sample (n=300) and in Those Without Baseline Tophi (n=233).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

reduce flares counts, these results suggest that the inclusion of flare characteristics such as pain intensity and symptom duration into trial outcomes could potentially provide insights into efficacy of ULT in a shorter amount of time than conventional studies utilizing flare counts as the outcome.

Disclosure: J. Yang: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **H. Sayles**: None; **M. Pillinger**: Amgen, Federation Bio, Fortress Biotech, Scilex, and SOBI, 2, Convergence Bio, 2; **J. Newcomb**: None; **B. Kramer**: None; **A. Davis-Karim**: None; **M. Brophy**: None; **R. Ferguson**: None; **P. Palevsky**: Chiesi Pharmaceutical, 2; **J. O'Dell**: None; **T. Neogi**: None.

Abstract Number: 2002

Methods to Address Survival Bias and Competing Risks in Estimating the Causal Risks of Gout on Dementia Risk

Joshua Baker[1], Harlan Sayles[2], Chung-Chou Chang[3], Brian Coburn[4], Bryant England[2] and Ted Mikuls[2], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Pittsburgh, Pittsburgh, PA, [4]Hospital of the University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Informative censoring in epidemiologic research studies (the loss of data from the risk set that is related to the exposure and/or outcome) can cause bias in the estimation of causal risks. An example of this bias occurs when there is a competing risk of death for an outcome that occurs in older individuals, such as dementia. Gout and hyperuricemia have been associated with a lower risk of dementia in observational studies, leading to questions about the potential neuroprotective role of hyperuricemia. However, these prior findings may result of this type of bias. In this situation, *gout may appear to lower the risk of dementia because many patients with gout do not live long enough to develop it*. The purpose of this study was to evaluate distinct methods to estimate causal risks of gout on the risk of dementia using data from the Veterans Affairs (VA) health system.

Methods: We studied patients with gout and age- and sex- matched controls from national VA health record data. We defined incident cases of gout based on the presence of an ICD-9 or ICD-10 code from at least two separate encounters at least 30 days apart and matched to controls of similar age, sex, and calendar year. The outcome of dementia was defined using previously validated administrative algorithms. An extensive list of comorbidities, medications, and other covariates were extracted from the medical record and defined using validated algorithms. We tested three approaches to estimating the causal risks of gout: 1) a traditional Cox model, 2) a commonly used competing risks model (Fine & Gray) and 3) a joint frailty model that accounts for informative censoring by considering the propensity for dementia among those that died (Figure 1). Due to large sample sizes and computational requirements, we meta-analyzed up to 30 models for each method run on the same randomly selected samples of 0.1% of the population adjusting for potential confounders identified in the descriptive analysis.

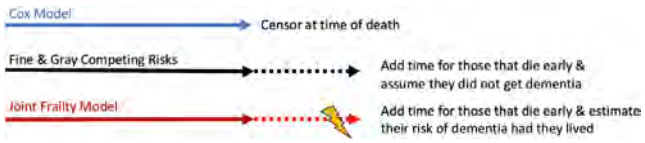


Figure 1: Illustration of modeling approaches to consider the competing risk of death.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

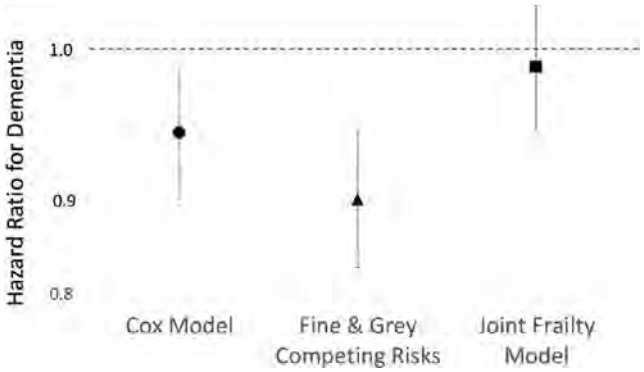


Figure 2: Hazard Ratios for the risk of dementia for patients with gout based on 3 distinct modeling approaches: 1) Cox proportional hazards model (circle), 2) Fine and Gray competing risks model (triangle), and 3) the joint frailty model (square).

Results: There were significant and expected differences in patient characteristics between the 533,465 patients with gout and 4,935,717 matched controls including higher body mass index (BMI) and higher rates of cardiovascular comorbidity (not shown). In the traditional adjusted Cox model that assumes that censoring is uninformative, the risk of dementia among patients with gout was significantly lower than controls [HR: 0.93 (95% CI: 0.87, 0.98)]. The protective effect was larger in Fine & Gray competing risks models [HR 0.90 (95% CI: 0.85, 0.96)]. In contrast, the joint frailty model accounting for informative censoring suggested no significant reduction in dementia risk in gout compared to controls [HR: 0.97 (95% CI: 0.91, 1.03)] (Figure 2).

Conclusion: Estimates of the risk of dementia in patients with gout varied according to the method used to address the competing risk of death. Analyses performed using a method that more comprehensively accounts for informative censoring suggested no reduction in the risk of dementia among patients with gout. These findings call into question the results of multiple prior studies and should help to reassure clinical providers that urate-lowering to manage gout is not likely to increase the long-term risk of dementia.

Disclosure: J. Baker: Amgen, 5; **H. Sayles**: None; **C. Chang**: None; **B. Coburn**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

Abstract Number: 2003

Evaluating Patient Outcomes Pre and Post Pegloticase Initiation among Uncontrolled Gout Patients: Findings from MORE^2 Registry and Medicare Fee-For-Service Claims Data

Julia Buchfuhrer[1], Niranjan Kathe[2], Elizabeth Ibiloye[3], Seth Kuranz[4], Virginia Noxon-Wood[4], Alexis Woods[5] and Laurence Gozalo[4], [1]JB Arthritis and Rheumatology Center, Downey, CA, [2]Amgen Inc, San Diego, CA, [3]Amgen Inc, Thousand Oaks, CA, [4]Inovalon, Bowie, MD, [5]Amgen, Detroit, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Among patients (pts) with chronic refractory gout (CRG), traditional urate lowering therapies are often inadequate, necessitating advanced therapies. Pegloticase, a recombinant uricase enzyme, rapidly lowers serum uric acid, reducing flares and tophi in CRG. However, real-world data on its effectiveness, particularly with methotrexate co-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics for pegloticase initiators in MORE² and Medicare Fee-for-Service databases identified between 2018-2021.

Patient Characteristics	N=203
Age [mean (SD)]	67.1 (13.1)
Sex (n, %)	
Male	155 (76.4%)
Female	48 (23.6%)
Race/ethnicity (n, %)	
White	137 (67.5%)
Black or African American	15 (7.4%)
Other	20 (9.9%)
Unknown	31 (15.3%)
Payer channel (n, %)	
Medicare FFS	153 (75.4%)
Commercial	30 (14.8%)
Other	20 (9.8%)
Geographic region (n, %)	
Northeast	20 (9.9%)
Midwest	47 (23.3%)
South	92 (45.3%)
West	44 (21.7%)
Index year (n, %)	
2018	37 (18.2%)
2019	56 (27.6%)
2020	54 (26.6%)
2021	56 (27.6%)
Elixhauser Comorbidity Index (mean [SD])	9.0 (9.1)
Other Comorbidities of interest (n, %)	
Chronic kidney disease	117 (57.6%)
Depression	29 (14.3%)
Heart failure	51 (25.1%)
Hyperlipidemia	130 (64%)
Hypertension	173 (85.2%)
Osteoarthritis	102 (50.2%)
Type 2 Diabetes	85 (41.9%)
Nephrolithiasis	11 (5.4%)

Includes pegloticase new users with 12 months of baseline and follow-up data and receiving label recommended 12 infusions within 180 days. Patient socio-demographics characteristics were measured on index date, while clinical characteristics were measured at baseline.

treatment, remains limited. This study assessed gout flare outcomes pre and post treatment amongst pts with uncontrolled gout treated with pegloticase.

Methods: The study included adults diagnosed with gout who were newly treated with pegloticase between January 1, 2018, and December 31, 2021 in the MORE2 registry or Medicare Fee-For-Service (FFS) databases. Pts were required to have at least 360 days of baseline and follow-up enrollment from the index date (date of first pegloticase dose) and at least 12 infusions of pegloticase within 180 days from the index date. The primary outcome, gout flare, was identified as follows: 1) having an inpatient visit with a primary diagnosis of gout or 2) having an outpatient or emergency department claim with a diagnosis of gout accompanied by treatment or follow-up visit within a 7-day period, or 3) an outpatient or ED claim with a diagnosis for unspecified joint pain accompanied by a claim for oral/injectable colchicine within 7 days. Gout flare rates as well as secondary outcomes of any glucocorticoid prescription and any opioid prescription were assessed during the following time periods: from 360 days prior to index date to the day prior to the index date (baseline), from end of the first 180 days after index date until the earliest event of death, disenrollment or end of study (12/31/2022) (Follow-up 1), and from date of pegloticase treatment discontinuation to the earliest of death, disenrollment or end of study (12/31/2022): (Post completion). The outcomes were

Table 2. Pegloticase treatment characteristics during the follow-up period

Pegloticase treatment pattern	
Methotrexate combination therapy (n, %)	70 (34.5%)
Number of pegloticase claims (mean [SD])	26.7 (17.9)
Time on pegloticase in days (mean [SD])	376.5 (247.5)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Flare and treatment outcomes pre-post pegloticase

	Baseline[&]	Follow-up 1[#]	Post completion[^]
Gout flare rate per person per years	1.3	0.2*	0.1*
Glucocorticoid prescription (n, %)	171 (84.2%)	111 (54.7%)*	80 (39.4%)*
Opioid prescription (n, %)	169 (83.3%)	127 (62.6%)*	92 (45.3%)*

*p-value<0.001 compared with baseline using generalized estimating equations.
Gout flares were identified as follows: having an inpatient visit with a primary diagnosis of gout or OR having an outpatient or emergency department (ED) claim with a diagnosis of gout accompanied by treatment or follow-up visit within a 7-day period, OR an outpatient or ED claim with a diagnosis for unspecified joint pain accompanied by a claim for oral/injectable colchicine within 7 days.
[&]Baseline period was defined as 360 days prior to index date to the day prior to the index date.
[#]Follow-up 1 was defined as period from the end of the first 180 days after index date till the earliest of death, disenrollment or end of study (12/31/2022).
[^]Post completion was defined as period from the date of pegloticase treatment discontinuation to the earliest of death, disenrollment or end of study.

compared between baseline and Follow-up 1 and between baseline and post completion using generalized estimating equations.

Results: The final cohort included 203 pts initiating pegloticase (mean [SD] age: 67.1[13.1] years; 76.4% male; 67.5% White) with a mean [SD] Elixhauser comorbidity score of 9.0 [9.12] (Table 1). The most prevalent baseline comorbidities were hypertension (85.2%), osteoarthritis (50.2%), chronic kidney disease (57.6%), and type 2 diabetes mellitus (41.87%). The average treatment duration was 376.5 days (SD=247.5), and 70 (34.5%) of the pts had a co-prescription for methotrexate (Table 2). At baseline the cohort experienced a flare rate of 1.3 flares per person years (ppy), which was significantly reduced at Follow-up 1 (0.2 flares ppy) and at post completion period (0.1 flares ppy); (Table 3). Similarly, both proportion of pts with a prescription for glucocorticoids and with a prescription for opioids were lower by at least 20 percentage points during Follow-up 1 compared to baseline and by at least 35 percentage points at post completion compared to baseline.

Conclusion: Pts with CRG, treated with pegloticase in the MORE[2] and Medicare FFS, showed a substantial reduction in the rate of gout flares during the follow-up periods. These data further support the use of pegloticase, as a uric acid debulker, for CRG management, thus decreasing the risk of flareup.

Disclosure: J. Buchfuhrer: AbbVie/Abbott, 1, 6, Amgen, 1, 2, 6, Janssen, 1, 6; **N. Kathe**: Amgen, 3, 11; **E. Ibiloye**: Amgen, 3, 11, AstraZeneca, 3, 11; **S. Kuranz**: Inovalon, 3; **V. Noxon-Wood**: Amgen, 2; **A. Woods**: Amgen, 3, 11; **L. Gozalo**: Amgen, 2.

Abstract Number: 2004

Characteristics and Management of Gout Patients Under Rheumatologist Care from Low-Income and Middle-Income Asia-Pacific Countries: Data from the APLAR Gout Registry

Kanon Jatuworapruk[1], Binit Vaidya[2], ANA MONICA ESTRELLA[3], MA. HANNA MONICA SOLLANO[3], Ronaldo De Vera[4], Ida Ayu Ratih Wulansari Manuaba[5], Rakhma Hellmi[6], Panchalee Satpanich[7], Nittayawadee Aeamsaard[8], MAHABALESHWAR MAMADAPUR[9], Mustafa Alhayali[10], Chang-Nam Son[11], Syahrul Sazliyana Shaharir[12], Galymzhan Togizbayev[13], Jose Paulo Lorenzo[3] and The APLAR Crystal-Induced Arthritis Special Interest Group, [1]Thammasat University, Pathumthani, Thailand, [2]National Center for Rheumatic Diseases, Kathmandu, Nepal, [3]Makati Medical Center, Makati, Philippines, [4]Tricity Medical Center in Pasig City, Pasig, Philippines, [5]Bali International University, Bali, Indonesia, [6]Kariadi Hospital Medical Center, Semarang, Indonesia, [7]Faculty of Medicine Vajira Hospital, bangkok, Thailand, [8]Saraburi Hospital, Saraburi, Thailand, [9]JSS MEDICAL COLLEGE AND HOSPITAL, Mysore, Karnataka, India, [10]Baghdad Teaching Hospital, Baghdad, Iraq, [11]UIJEONGBU EULJI MEDICAL CENTER, EULJI UNIVERSITY, UIJEONGBU, Republic of Korea, [12]Universiti Kebangsaan Malaysia, Selangor, Malaysia, [13]Qazaq College of Rheumatology, Almaty, Kazakhstan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The burden of gout is rising in low-income and middle-income countries in the Asia-Pacific region. However, individuals with gout in this region remain underrepresented in research, resulting in a limited understanding of the unique challenges and pain points shaped by their geographic and cultural context. The Asia Pacific League of Associations for Rheumatology (APLAR) Gout Registry was established to gain a deeper understanding of the characteristics and management of gout among patients in this region.

Methods: This is a longitudinal, multinational, rheumatologist-reported registry that began in August 2023. It includes adults (aged 18 years or older) diagnosed with gout who are under the care of, and being followed by, participating rheumatologists. Gout was defined as having experienced at least one gout flare and receiving a diagnosis of gout by the reporting physician. Data on demographics, comorbidities, gout symptoms, gout treatments, serum urate levels, and flares were collected over a 12-month period from the time of recruitment.

Results: A total of 549 participants from eight countries were recruited, and data from 903 visits were collected by December 2024 (Figure 1). The cohort was predominantly male (512/549, 93%) with a mean age of 53 years. The most common

Figure 1. Participating Asia-Pacific countries

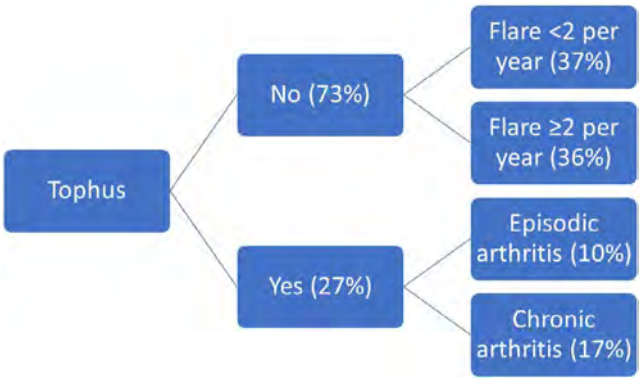


Figure 2. Clinical manifestations at baseline categorized by the presence of tophi and pattern of articular symptoms

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

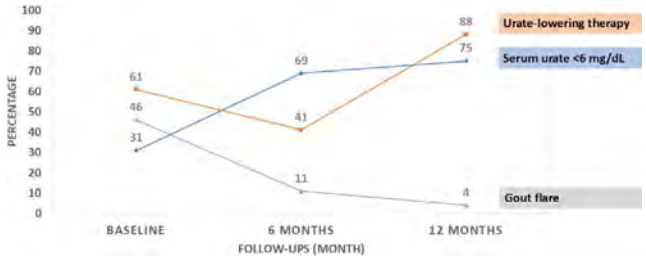


Figure 3. Prevalence of ULT prescription, gout flare and serum urate at target during 12-month period

comorbidities were hypertension (196/549, 36%), followed by hyperlipidemia (123/549, 22%) and chronic kidney disease (103/549, 19%). The mean duration of gout since the first flare was 8.2 years. The first metatarsophalangeal joint was the most commonly affected site (311/549, 57%). Tophaceous gout was present in 144 individuals (27%), and chronic symptoms were reported in 90 individuals (17%) (Figure 2). At baseline, 314 participants (57%) were receiving at least one urate-lowering therapy (ULT); however, only 128 of 498 individuals (30%) had a serum urate level below 6 mg/dL (0.36 mmol/L). Among those not taking ULT at baseline, 17% (40/235) were using colchicine for gout flare prophylaxis. At the 12-month follow-up, 75% (37/49) of individuals had achieved serum urate levels below 6 mg/dL, and 88% (43/49) were prescribed at least one ULT. Gout flares were reported in 46% (152/326) of participants at baseline, decreasing to 4% (2/49) at the 12-month follow-up (Figure 3).

Conclusion: Gout patients in the Asia-Pacific region face multiple challenges, including severe disease manifestations, low rates of ULT prescription, and poor attainment of serum urate targets. These suboptimal outcomes persist even under specialist care, highlighting the urgent need for improved gout management strategies in this population.

Disclosure: K. Jatuworapruk: None; **B. Vaidya**: None; **A. ESTRELLA**: None; **M. SOLLANO**: None; **R. De Vera**: None; **I. Wulansari Manuaba**: None; **R. Hellmi**: None; **P. Satpanich**: None; **N. Aeamsaard**: None; **M. MAMADAPUR**: None; **M. Alhayali**: None; **C. Son**: None; **S. Shaharir**: None; **G. Togizbayev**: None; **J. Lorenzo**: None.

Abstract Number: 2005

Elevated Serum Uric Acid as an Independent Risk Factor for Multiple Stent Placement in Non-Hypertensive, Non-Diabetic Patients with Coronary Artery Disease: A Retrospective Cohort Analysis

qingyan li[1], Jianguo Li[1], Mengwen Niu[1], Tianshu chu[1] and **lemei an**[2], [1]Henan Provincial People's Hospital, zhengzhou, China (People's Republic), [2]Henan Provincial People's Hospital, zhengzhou

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: While the relationship between serum uric acid (SUA) and coronary artery disease (CAD) remains controversial, emerging evidence suggests a particularly significant association in patients lacking traditional cardiovascular risk factors. The specific role of hyperuricemia in determining CAD severity in non-hypertensive, non-diabetic populations warrants further investigation.

Methods: In this retrospective cohort study, we analyzed 716 consecutive CAD patients undergoing percutaneous coronary intervention (PCI), with a focus on 279 individuals without hypertension or diabetes. We employed multivariable logistic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

regression and stratified analyses to assess the independent association between SUA levels and multiple stent implantation (≥2 stents), a robust indicator of CAD complexity and prognosis. Hyperuricemia was defined using gender-specific thresholds (>420 μmol/L for males and postmenopausal females; >360 μmol/L for premenopausal females).

Results: In the overall cohort, multivessel disease (OR=2.27, 95% CI:1.94–3.96, p< 0.001) and diabetes (OR=1.47, 95% CI:1.05–2.07, p=0.027) independently predicted multiple stent placement. Notably, in the non-hypertensive, non-diabetic subgroup, hyperuricemia emerged as a strong independent predictor (OR=4.62, 95% CI:1.93–11.07, p=0.001), exceeding the predictive value of multivessel disease (OR=3.16, 95% CI:1.78–5.55, p< 0.001). No significant association was observed between SUA levels and stent number in the broader cohort.

Conclusion: Elevated serum uric acid independently predicts complex coronary lesions requiring multiple stent placements in non-hypertensive, non-diabetic CAD patients. These findings suggest that uric acid assessment may enhance risk stratification in this specific patient population, warranting further investigation into its clinical implications.

Disclosure: q. li: None; **J. Li**: None; **M. Niu**: None; **T. chu**: None; **l. an**: None.

Abstract Number: 2006

Storytelling and Navigation to Improve Gout Follow-up: A Multicenter, Randomized Controlled Trial

Lesley Jackson[1], Rahima Begum[2], Gary Cutter[2], Hyon K. Choi[3], Brett Faine[4], Nora G. Singer[5], Natalie McCormick[6], hamid shokoohi[7], Blair Parry[7], Oliva Nelson[7], James Booth[1], Zachary Armor[1], John Osborne[1], Kenneth Saag[8] and Maria I. (\"Maio\") Danila[9], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, [3]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [4]University of Iowa, Iowa City, IA, [5]The MetroHealth System at Case Western Reserve University School of Medicine, Cleveland, OH, [6]Massachusetts General Hospital, Boston, [7]Massachusetts General Hospital, Boston, MA, [8]The University of Alabama at Birmingham, Birmingham, AL, [9]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with gout are frequently treated in the emergency department (ED) for flares but may not receive consistent outpatient care. Approaches to mitigate this care pattern are understudied. We tested whether a direct-to-patient multimodal behavioral intervention could improve outpatient follow-up for gout after an ED visit.

Methods: We conducted a multicenter parallel group randomized clinical trial at 4 geographically diverse sites in the U.S. Participants were randomized 2:1 to the intervention or usual care (control) groups. The intervention included: 1) a storytelling video with gout patient testimonials, and 2) patient navigation whereby patients were contacted by phone after their ED visit by lay navigators to encourage outpatient follow up for gout. We assessed outcomes by phone surveys at 3-months. The primary outcome was the proportion of participants with an outpatient visit addressing gout in the 3-months post-ED visit, assessed by self-report and electronic health record (EHR) review. Secondary outcomes included rates of gout medication use, opioid use, and acute care utilization in the 3 months post-ED visit (documented in EHR, and as binary composite outcome including self-report). We performed intent-to-treat (ITT) and per-protocol (PP) analyses (i.e., intervention participants that viewed the storytelling video and 1+ navigator interaction). Differences in proportions were compared using Chi square tests and means using t-tests.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline demographic characteristics of all randomized participants (N=200)

Characteristics	Intervention Group N=135	Control Group N=65	p
Current Age in Yrs., mean (SD)	57.6 (13.6)	58.9 (12.4)	0.5
Sex, N (%)			0.7
Male	101 (74.8)	50 (76.9)	
Female	34 (25.2)	15 (23.1)	
Race /Ethnicity, N (%)			0.1
Black or African American	92 (68.2)	45 (69.2)	
White	35 (25.9)	16 (24.6)	
Asian, Hispanic or Latino, Unknown/other	8 (5.9)	4 (6.2)	
Marital Status, N (%)			0.5
Married	41 (31.1)	23 (35.4)	
Not Married*	91 (68.9)	42 (64.6)	
Health Status, Excellent or Very Good, N (%)	26 (19.6)	15 (23.4)	0.5
Health Literacy, Inadequate, N (%)	39 (29.3)	21 (32.3)	0.7
PROMIS Depression 4a Measure T-score, mean (SD)	46.4 (13.7)	48.3 (10.8)	0.3
Education Level, N (%)			0.9
High School graduate or less	65 (49.2)	30 (46.2)	
Vocational training or some college	44 (33.3)	23 (35.4)	
4-year degree or more completed	23 (17.4)	12 (18.5)	
Employment Status, N (%)			0.1
Full-time work	61 (46.6)	19 (29.2)	
Part-time work or not seeking work**	37 (28.2)	22 (33.9)	
Unemployed	25 (19.1)	16 (24.6)	
Other or choose not to answer	8 (6.1)	8 (12.3)	
Yearly Income, N (%)			0.4
Less than $30,000	42 (33.9)	20 (31.8)	
$30,000 to less than $60,000	13 (10.5)	13 (20.6)	
$60,000 to less than $100,000	14 (11.3)	8 (12.7)	
Greater than $100,000	11 (8.9)	4 (6.4)	
Prefer not to answer	44 (35.5)	18 (28.6)	
Smoking status, N (%)			0.4
Currently smoking every day	17 (12.9)	9 (14.3)	
Currently smoking some days	18 (13.6)	4 (6.4)	
Not smoking at all	97 (73.5)	50 (79.4)	
Alcohol use, N (%)			0.4
2 or more times per week	24 (18.3)	10 (15.4)	
2-4 times per month	53 (40.5)	22 (33.9)	
Never	54 (41.2)	33 (50.8)	

P<0.05 represented in bold. *Not Married includes: divorced, widowed, separated, never married, a member of an unmarried couple. **not seeking work includes student, retired, disabled, unpaid primary care giver. Health status was assessed with the question "In general, how would you rate your health?" and 'good' defined by grouping the following answers: "extremely" or "very good". Health literacy was assessed with the question "How confident are you filling out medical forms by yourself?" and "inadequate" defined by grouping the following answers: "Somewhat", "A little bit", and "Not at all". PROMIS, Patient-Reported Outcomes Measurement Information System, SD, standard deviation. Marital Status missing for 3 individuals; health status missing for 3 individuals; health literacy missing for 2 individuals; education level missing for 3 individuals; employment status missing for 4 individuals; income missing for 13 individuals; smoking status missing for 5 individuals; alcohol use missing for 4 individuals.

Results: From June 2021 to June 2024, 200 individuals (mean age 58 years; 76% men, 69% Black), were enrolled, with 135 randomized to intervention and 65 to control groups. Baseline characteristics are reported in Table 1. In ITT analyses, we found no significant differences between intervention vs control groups in rates of outpatient gout follow-up (47% vs 54%, p=0.4) (**Table 2**). Of gout follow-up visits captured in the EHR, a majority occurred with primary care (60%) followed by internal medicine subspecialties (29%). In the intervention group compared to control, there were no statistically significant differences in self-reported new allopurinol use post-ED (17% vs 11%, p=0.2). Among those who reported past or present allopurinol use, new initiation post-ED visit was more common in the intervention group (23/55 [42%] vs 7/32 [22%], p=0.05). Intervention group participants were less likely to have subsequent ED visits (intervention vs control 32% vs 49%, p=0.02) and there was a non-significant trend for fewer subsequent ED visits documented in the EHR at each site (intervention vs control 0.3 vs 0.6 visits, p=0.09). There were no differences in opioid prescription use or incident

Table 2: Results for primary and secondary outcomes by randomization group, intent-to-treat and per protocol analyses; number (%) represented unless otherwise stated. P<0.05 represented in bold.

	Intent-to-treat			Per Protocol		
	Intervention (N=135)	Control (N=65)	p	Intervention (N=117)	Control (N=64)	p
Primary Outcome						
Presence of gout follow-up, N (%)	64 (47.4)	35 (53.8)	0.4	58 (49.6)	34 (53.1)	0.7
Secondary Outcomes						
Allopurinol use,[a] N (%)	23 (17.0)	7 (10.8)	0.2	23 (19.7)	7 (10.9)	0.1
Opioid use,[β] N (%)	66 (48.9)	34 (52.3)	0.7	59 (50.4)	33 (51.6)	0.9
Subsequent ED visits,[γ] mean (SD)	0.3 (0.6)	0.6 (1.2)	0.09	0.3 (0.6)	0.6 (1.2)	0.09
Subsequent ED visits,[γδ] (yes/no), N (%)	43 (31.9)	32 (49.2)	**0.02**	38 (32.5)	32 (50.0)	**0.02**
Subsequent hospitalizations,[γ] mean (SD)	0.1 (0.4)	0.1 (0.4)	0.8	0.1 (0.4)	0.1 (0.4)	0.8
Subsequent hospitalizations,[γδ] (yes/no), N (%)	14 (10.4)	7 (10.8)	0.9	12 (10.3)	7 (10.9)	0.9

[a]self-reported new prescription medication use following the index ED visit for a gout flare.
[β]composite outcome of self-reported current medication use or electronic health record (EHR) evidence of prescription use of opioids (i.e., hydrocodone-acetaminophen, oxycodone, oxycodone-acetaminophen, tramadol, hydromorphone) in the 3 months after the index ED visit for a gout flare.
[γ]EHR evidence of acute care utilization occurring in the 3 months after the index ED visit for a gout flare.
[δ]composite binary outcome representing presence/absence of 1 or more subsequent visits based on self-report or EHR documentation in respective health systems.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hospitalizations between groups. In PP analyses, trends were similar to ITT analysis with no significant differences between groups.

Conclusion: While our intervention did not lead to a significant improvement in outpatient gout follow-up, we did observe trends in improved uptake of allopurinol initiation and reduction in repeat ED visits. The findings suggest that while patient activation strategies may play a role, achieving improvements in routine gout follow-up care likely requires multifaceted approaches beyond behavioral interventions targeted to patients alone.

Disclosure: L. Jackson: None; **R. Begum**: None; **G. Cutter**: Consulting or Advisory BoardsAlexion, Antisense Therapeutics/Percheron, Avotres, Biogen, Clene Nanomedicine, Clinical Trial Solutions LLC, Endra Lif, 1, 2, Data and Safety Monitoring BoardsApplied Therapeutics, AI therapeutics, AMO Pharma, Argenx, Astra-Zeneca, Avexis Pharmaceuticals, Bristol Meyers Squ, 2, Pythagoras, Inc., 4, 8; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **B. Faine**: None; **N. Singer**: None; **N. McCormick**: None; **h. shokoohi**: None; **B. Parry**: None; **O. Nelson**: None; **J. Booth**: None; **Z. Armor**: None; **J. Osborne**: None; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5.

Abstract Number: 2007

Machine Learning-Based Prediction of Gout Onset in Individuals with Asymptomatic Hyperuricemia Using a Common Data Model

Min Jung Kim[1], Sang Min Lee[2], Jun Seok Kim[2], Borim Ryu[2] and Kichul Shin[3], [1]Seoul Metropolitan Government Boramae Medical center, Dongjak-gu, Seoul, South Korea, [2]Center for Data Science, Biomedical Research Institute, Seoul Metropolitan Government–Seoul National University Hospital Boramae Medical Center, Seoul, Republic of Korea, [3]Seoul National University, Seoul, South Korea

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Long-term hyperuricemia is essential for the development of gout. However, only 9.9% of individuals with asymptomatic hyperuricemia (AHU) develop gout within 10 years. Identifying high-risk individuals with AHU is crucial for implementing timely and targeted interventions to prevent or delay the onset of gout. We aimed to create a machine learning-based risk stratification model to predict the onset of gout in individuals with AHU.

Methods: We conducted a retrospective cohort study utilizing a Common Data Model (CDM) database from a single academic medical center. Subjects (age ≥ 18 years) were identified if they had at least one serum urate level ≥ 7 mg/dL or a diagnosis of AHU (concept ID 4147761) between 2010 and 2022. The index date was defined as the earliest report of a high serum urate level or the first diagnosis of AHU. Subjects were excluded if they had a prior diagnosis of gout or received a prescription for colchicine, allopurinol, febuxostat, or benzbromarone within 365 days before the index date. The outcome measured was the development of gout between 90 and 3650 days after the index date. Machine learning models, including LightGBM, XGBoost, Random Forest, AdaBoost, Decision Tree, and Logistic Regression, were employed to predict the development of gout. Model performance was assessed using the area under the receiver operating characteristic curve (ROC-AUC) and the precision-recall AUC (PR-AUC). We evaluated the contribution of each variable to the model's predictions using feature importance and SHAP values. The Cox proportional hazard model was applied to construct a risk-scoring model with key predictors.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

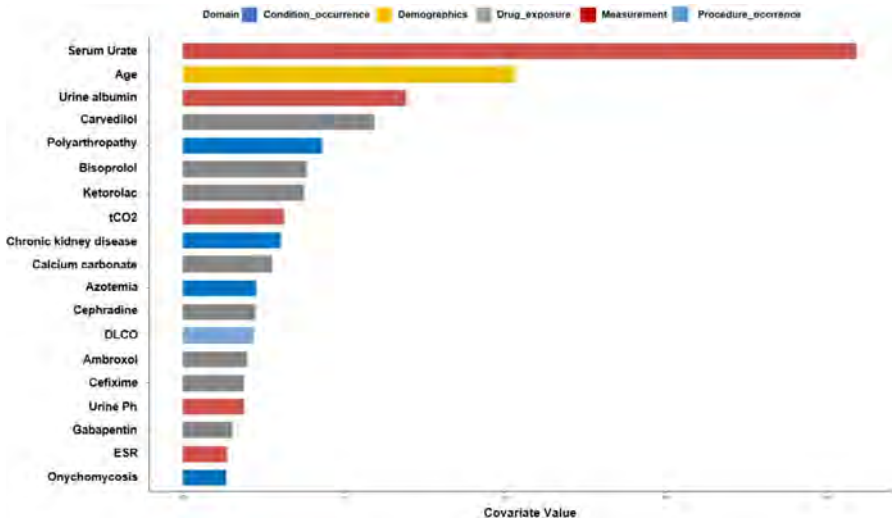


Figure. Top 15 features ranked based on feature importance in the machine learning model

Table. Final risk-scoring model for predicting the onset of gout in individuals with asymptomatic hyperuricemia

	β coefficient	HR (95% CI)	*P* value	Score
Age, years				
<35	0	Ref	Ref	0
≥35, <65	0.345	1.412 (0.909-2.193)	0.124	4
≥65	0.410	1.506 (0.934-2.428)	0.093	5
Chronic kidney disease	2.142	8.516 (1.969-36.843)	0.004	24
Hypertension	0.387	1.473 (0.556-3.901)	0.436	4
tCO2, mmol/L				
≥23	0	Ref	Ref	0
<23	0.616	1.852 (1.391-2.465)	<0.001	7
LDL cholesterol, mg/dL				
<130	0	Ref	Ref	0
≥130	0.413	1.511 (0.879-2.599)	0.135	5
ESR, mm/hr				
<20	0	Ref	Ref	0
≥20	0.299	1.348 (0.839-2.167)	0.217	3
Serum urate, mg/dL				
≥7, <8	0	Ref	Ref	0
≥8, <9	-0.124	0.884 (0.635-1.229)	0.462	-
≥9, <10	0.090	1.094 (0.729-1.642)	0.664	1
≥10	0.452	1.572 (1.063-2.326)	0.024	5

tCO2, total carbon dioxide; ESR, erythrocyte sedimentation rate; LDL, low-density lipoprotein; HR, hazard ratio.

Results: Among 8,139 subjects with AHU, 223 (2.7%) developed gout during the 10-year follow-up period. Eighty-three percent of the patients were male, most between 30 and 40 years of age. LightGBM demonstrated the best performance among the models, achieving an ROC-AUC of 0.812 and a PR-AUC of 0.112. Among the top 15 features identified by feature importance and SHAP values (figure), serum urate level, LDL cholesterol, total carbon dioxide (tCO2), ESR, age, chronic kidney disease, and hypertension were identified as key predictors. In the final risk-scoring model, chronic kidney disease was assigned 24 points, hypertension 4, age 4 to 5, low tCO2 7, high LDL cholesterol 5, high ESR 3, and serum urate level 1 to 5 points (table). The C-index of the model was 0.730.

Conclusion: We developed a machine learning-based risk-scoring model using real-world data to predict the onset of gout in individuals with AHU. This model showed promising results based on routinely collected clinical parameters that may help identify high-risk individuals who would benefit from rigorous lifestyle monitoring or early intervention.

Disclosure: M. Kim: None; **S. Lee**: None; **J. Kim**: None; **B. Ryu**: None; **K. Shin**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2008

Exposure to Anaerobic Antibiotics and Risk of Gout Flares: Target Trial Emulation for the Potential Role of the Gut Microbiome in Gout and Chronic Kidney Disease (CKD)

Natalie McCormick[1], Sharan Rai[2], Chio Yokose[3], leo lu[4], Robert Terkeltaub[5], Lama Nazzal[6], Huilin Li[6], Dylan Dodd[7] and Hyon K. Choi[8], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [3]Massachusetts General Hospital, Waltham, MA, [4]Arthritis Research Canada, Vancouver, BC, Canada, [5]Retired, San Diego, CA, [6]NYU Langone, New York, NY, [7]Stanford University, Palo Alto, CA, [8]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: As reported in *Cell Press* journals,[1,2] intestinal commensal purine-degrading bacteria anaerobically degrade urate to anti-inflammatory short chain fatty acids, including butyrate, and thus may partially compensate for uricase

Table 1: Recurrent gout flare count among patients with no history of gout at baseline, following initiation of Clindamycin versus Trimethoprim/Sulfamethoxazole (T/S), after 1:1 propensity score matching.

3 Months' Follow-Up		
	Clindamycin	**T/S**
Patients with CKD		
Patients, number	6775	6775
Event, number	62	17
IR, per 1000 person-years	37.18	10.31
RR (95% CI)	3.71 (2.17 to 6.34)	1.0 (ref)
Patients without CKD		
Patients, number	298,510	298,510
Event, number	372	251
IR, per 1000 person-years	5.02	3.39
RR (95% CI)	1.61 (1.37 to 1.89)	1.0 (ref)
All patients		
Patients, number	306,058	306,058
Event, number	428	267
IR, per 1000 person-years	5.64	3.52
RR (95% CI)	1.78 (1.52 to 2.07)	1.0 (ref)
12 Months Follow-Up		
	Clindamycin	**T/S**
Patients with CKD		
Patients, number	6775	6775
Event, number	166	92
IR, per 1000 person-years	26.13	14.80
RR (95% CI)	1.78 (1.38 to 2.30)	1.0 (ref)
Patients without CKD		
Patients, number	298,510	298,510
Event, number	1171	981
IR, per 1000 person-years	4.00	3.37
RR (95% CI)	1.28 (1.17 to 1.39)	1.0 (ref)
All patients		
Patients, number	306,058	306,058
Event, number	1308	1054
IR, per 1000 person-years	4.36	3.54
RR (95% CI)	1.34 (1.24 to 1.45)	1.0 (ref)

CKD, chronic kidney disease; IR, incidence rate; RR, rate ratio; 95% CI, 95% confidence interval

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Frequency of gout-primary outpatient encounters among patients with no history of gout at baseline, following initiation of Clindamycin versus Trimethoprim/Sulfamethoxazole (T/S), after 1:1 propensity score matching, 3 months' follow-up.

Table 2: Frequency of gout-primary outpatient encounters among patients with no history of gout at baseline, following initiation of Clindamycin versus Trimethoprim/Sulfamethoxazole (T/S), after 1:1 propensity score matching, 3 months' follow-up.

	Clindamycin	T/S
Patients with CKD		
Patients, number	6775	6775
Event, number	105	43
IR, per 1000 person-years	63.60	26.16
RR (95% CI)	2.45 (1.72 to 3.49)	1.0 (ref)
Patients without CKD		
Patients, number	298,510	298,510
Event, number	628	511
IR, per 1000 person-years	8.49	6.92
RR (95% CI)	1.23 (1.09 to 1.38)	1.0 (ref)
All patients		
Patients, number	306,058	306,058
Event, number	732	550
IR, per 1000 person-years	9.65	7.26
RR (95% CI)	1.33 (1.19 to 1.49)	1.0 (ref)

CKD, chronic kidney disease; IR, incidence rate; RR, rate ratio; 95% CI, 95% confidence interval

absence in humans. This enables homeostatic control over urate levels, particularly in those with chronic kidney disease (CKD) where the role of extrarenal urate elimination increases. Indeed, in severe CKD the gut becomes predominant site of urate disposition.

Since treatment with anaerobe-targeted antibiotics rapidly elevates serum and cecal urate in mice,[1] and has been linked to increased incidence of gout diagnosis in a Stanford University cohort,[1] we hypothesized such treatment in humans with CKD is linked to more frequent gout flares.

We conducted target trial emulations to compare rate of gout flares among patients (stratified by CKD) treated with clindamycin, an antibiotic targeting both aerobic and anaerobic microbes, versus trimethoprim/sulfamethoxazole (T/S), antibiotic with limited anaerobic coverage.

Methods: We included adults aged ≥18 years with dispensed prescriptions for ≥ 5 days of oral clindamycin or T/S, and no diagnosis of gout or receipt of antibiotics in prior 12 months. Randomization was emulated based on pre-exposure prognostic factors including sociodemographics, infections, comorbidities, medications, and healthcare use.

Primary outcome was gout flare counts over 3 months after index date, ascertained by emergency department, hospital, outpatient, and prescription records;[3] We assessed *C. difficile* infection as positive control outcome and osteoarthritis (OA) encounter as negative control outcome. Poisson and Cox models were used to calculate adjusted rate ratios (RR) and hazard ratios (HR) with 95% confidence intervals (95% CI).

Results: After 1:1 matching, we included 306,058 adults initiating clindamycin and 306,058 initiating T/S (43% male, mean age 47). Baseline characteristics were well-balanced between treatment arms (standardized differences < 0.1 for all factors).

Among the 13,550 propensity-matched individuals with CKD, rate of gout flares was higher among those initiating clindamycin vs T/S (37.2 vs 10.3 per 1000 person-years, respectively), with adjusted RR 3.71 (95% CI: 2.17, 6.34) (**Table 1**). Associations were smaller but remained significant among non-CKD, with adjusted RR 1.61 (1.37, 1.89) (**Table 1**) (p-interaction 0.003).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Associations persisted when assessing gout flares for 12 months after index date (**Table 1**) and comparing rates of all gout-primary encounters, regardless of medication dispensing (**Table 2**). Clindamycin initiators showed higher risk of *C. diff*. infection vs T/S (HR 3.14 [2.02, 4.90]), but no altered risk of OA encounter, both as expected.

Conclusion: In this general population study, exposure to an anaerobe-targeted antibiotic was associated with >3-fold higher rate of gout flares versus the non-anaerobe-targeted antibiotic T/S, among those with CKD. These findings support a substantial role of gut purine-degrading bacteria (PDB) in urate disposition, as well as suppression by gut PDB of gouty inflammation, particularly in those with CKD.

1. PMID 37541197
2. PMID 37279756
3. *JAMA* 2024 PMID 38319333

Disclosure: N. McCormick: None; **S. Rai**: None; **C. Yokose**: None; **I. lu**: None; **R. Terkeltaub**: Atom Bioscience, 2, BPG Bio, 2, Crystalys, 2, Novartis, 2, Shanton, 2; **L. Nazzal**: None; **H. Li**: None; **D. Dodd**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2.

Abstract Number: 2009

Value of New PREVENT Calculator in Detecting Cardiovascular Disease in Patients with Gout

Patrick Williamson[1], Rouhin Sen[2] and Angelo Gaffo[3], [1]Tinsley Harrison Internal Medicine Residency, Department of Medicine, University of Alabama at Birmingham, Birmingham, [2]University of Alabama at Birmingham, Department of Medicine, Division of Clinical Immunology & Rheumatology, Birmingham, [3]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Gout is associated with a 50% increased risk of cardiovascular disease (CVD).[1] The current recommendation for evaluating CVD risk in gout is to use prediction tools developed in the general population.[2] Studies have shown that CVD risk assessment tools underestimate CVD in people with gout.[3] The Predicting Risk of cardiovascular disease EVENTs (PREVENT) calculator is a newly developed CVD risk predictor that is the first to combine multiple organ systems and social determinants of health.[4] Whether the PREVENT calculator improves prediction of atherosclerotic CVD in patients with gout is unknown. Our aim is to assess the performance of the PREVENT calculator in detecting coronary plaque in patients with gout, against gold standard coronary artery calcium (CAC) testing, a CT-based technique to detect subclinical coronary atherosclerosis.[5]

Methods: We identified adult patients with gout seen in the University of Alabama at Birmingham clinics from 2016-2024. Patients were excluded if they were missing variables needed to calculate PREVENT or missing CAC score. High CVD risk was defined as having a PREVENT score of $\geq 7.5\%$ 10-year total CVD risk or a CAC score > 0.[4,5] Baseline variables were collected at time of CAC score. To assess the discriminative value of PREVENT in detecting coronary plaque, a 2x2 table was created to match high risk PREVENT scores vs high risk CAC scores. Sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated with their 95% confidence intervals (CI).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Demographics at the Time of the CT Scan

Baseline Demographics	Value
Mean age, years (SD)	61.4 (8.4)
Sex, females (n, %)	18 (26.1%)
Race/Ethnicity (n, %)	
Black or African American	6 (8.7%)
White	59 (85.5%)
Other*	4 (5.8%)
Mean BMI (SD)	29.8 (4.0)
Diabetes, n (%)	10 (14.5%)
Smoker (Former or Current), n (%)	23 (33.3%)
Use of anti-HTN, n (%)	53 (76.8%)
Use of lipid lowering medications, n (%)	34 (49.3%)
Mean LDL, mg/dL (SD)	113.4 (32.0)
Mean HgbA1c, % (SD)	5.8 (0.9)
Average serum uric acid, mg/dL (SD)	6.0 (1.9)

*Declined, Multiple, Hispanic or Latino, American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander

Table 2: Statistical Measures Comparing CAC to PREVENT Scores

Statistic	Value	95% CI
Sensitivity	40.0%	25.7% to 55.7%
Specificity	83.3%	62.6% to 95.3%
Positive Predictive Value	81.8%	63.2% to 92.2%
Negative Predictive Value	42.6%	35.5% to 50.0%
Positive Likelihood Ratio	2.4	0.9 to 6.3
Negative Likelihood Ratio	0.7	0.5 to 1.0

Results: 69 patients with gout were eligible for the study. The mean age was 61.4 years, 18 patients were female, 59 patients were White (see Table 1 for other demographics). 65.2% of patients had a high CAC score; 31.9% of patients had a high PREVENT score. The results (95% CI) for sensitivity, specificity, positive, and negative predictive values were 40.0% (25.7–55.7%), 83.3% (62.6–95.3%), 81.8% (63.2–92.2%), and 42.6% (35.5–50.0%), respectively.

Conclusion: The PREVENT score is an inaccurate tool to predict presence of coronary atherosclerosis in patients with gout, being insensitive at identifying individuals with coronary plaque. Like prior calculators, the absence of inflammatory and disease-specific markers in risk tools may limit their discriminative value. Future studies should continue searching for better predictive tools for CVD risk in patients with gout.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

1. Ferguson LD et al. *Lancet Rheumatol*. 2024;6:e156.
2. Andres M et al. *Ann Rheum Dis*. 2017;76:1263
3. Drosos GC et al.. *Ann Rheum Dis*. 2022;8:768
4. Khan SS et al. *Circulation*. 2024;149:430
5. McBride CB et al. *Curr Cardiovasc Imaging Rep*. 2013;6:211

Disclosure: P. Williamson: None; **R. Sen**: None; **A. Gaffo**: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2.

Abstract Number: 2010

Innate Transcriptional Response and Control of Expression of the Gout-Associated Colony Stimulating Factor-1 (CSF1) and CSF1 Receptor (CSF1R) Genes to Stimuli

Tony Merriman[1], Christopher Hall[2], Annie Chien[2], Richard Reynolds[3], Jeffrey Edberg[3], Pariyaphon Lertprachakwong[3], Hannah Darroch[4], Megan Leask[4], Mumin Ozturk[5], Brenda Kischkel[5], Nicholas Sumpter[5], Leo Joosten[5] and Nils Asmann[5], [1]University of Alabama at Birmingham, Homewood, AL, [2]University of Aucklabd, Auckland, New Zealand, [3]University of Alabama at Birmingham, Birmingham, AL, [4]University of Otago, Dunedin, New Zealand, [5]Radboud University Medical College, Nijmegen, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: *CSF1* and *CSF1R* encode a secreted and membrane-bound cytokine and its receptor controlling differentiation of monocytes into macrophages and inflammatory activity of macrophages. There are genetic associations

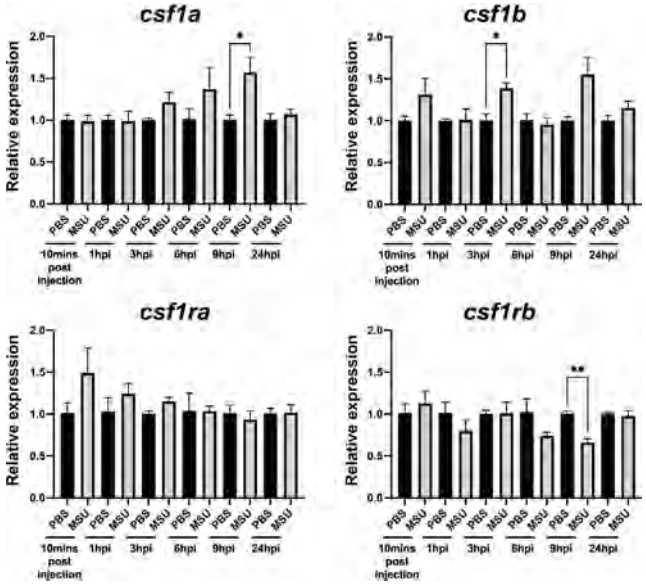


Figure 1. Expression of csf1a, csf1b, csf1ra, csf1rb after injection of MSUc into the hindbrain of 2-day zebrafish larva.

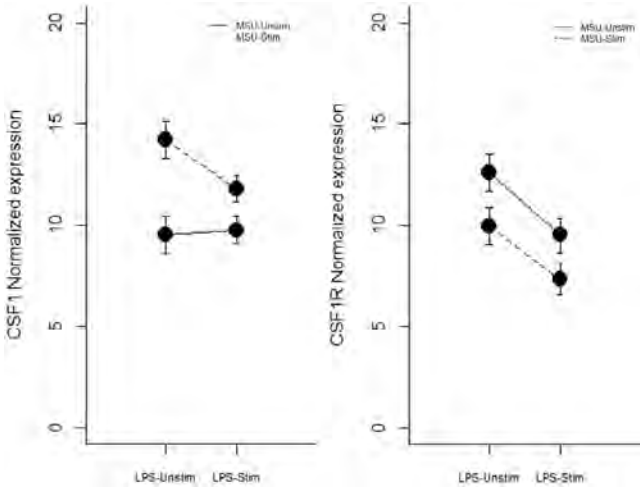


Figure 2. Expression of CSF1 and CSF1R in PBMCs in response to MSU crystal, LPS and their combination at 8-hrs.

with gout in regulatory regions at each locus which connect with the promoter of each gene in stimulated innate immune cells. The *CSF1* locus contains a long noncoding RNA (*LINC01768*) that is more expressed in stimulated innate immune cells and also a putative enhancer RNA. The *CSF1* genetic signal associates with gout but not urate, and CSF1 protein expression is increased in flaring gout patients. We hypothesized that CSF1 has a causal role in gouty inflammation. Our Aim was to gain insights into the molecular control of *CSF1* and *CSF1R* expression.

Methods: MSU crystal (MSUc) was injected into the hindbrain of 2-day larval zebrafish and expression analysis was done by qRT-PCR. For *in vitro* PBMC studies from 20 gout patients, LPS (1ng/mL), MSUc (300ug/mL), and their combination were used to stimulate cells. Total RNA at 8 hrs was sequenced and reads counted and normalized (to cells-only control). A linear mixed model was fit for *CSF1* and *CSF1R* expression (log2 transformed). Fixed effects were tested for main and two-way interactions of MSUc and LPS. THP-1 cells were stimulated with 30 ng/ml PMA up to 96 hrs to upregulate *CSF1* and *CSF1R* expression. For expression analysis of the putative enhancer RNA and *LINC01768*, random hexamers were used for reverse transcription and digital PCR was done. *CSF1* and *CSF1R* mRNA levels were quantified using qPCR.

Results: Zebrafish have two orthologs of each of *CSF1* and *CSF1R* (*csf1a, csf1b, csf1ra, csf1rb*). Injection of MSUc into the hindbrain of zebrafish increased expression of both *csf1a* and *csf1b* up to 1.5-fold within 3-9 hrs (**Fig 1**). However, expression of *CSF1R* orthologs did not change or decreased. In PBMCs, stimulation with MSUc increased expression of *CSF1* with the presence of LPS subduing the increase (**Fig 2**). In contrast, maximal expression of *CSF1R* happened under no stimulation, with LPS and MSUc repressing expression. In THP-1 cells PMA treatment induced expression of *CSF1*, the *LINC01768* IPL and the putative enhancer RNA. Maximal expression of the enhancer RNA and *LINC01768* preceded that of *CSF1*. Maximal expression of *CSF1R* was observed after 48-hours. These *CSF1* and *CSF1R* expression data are

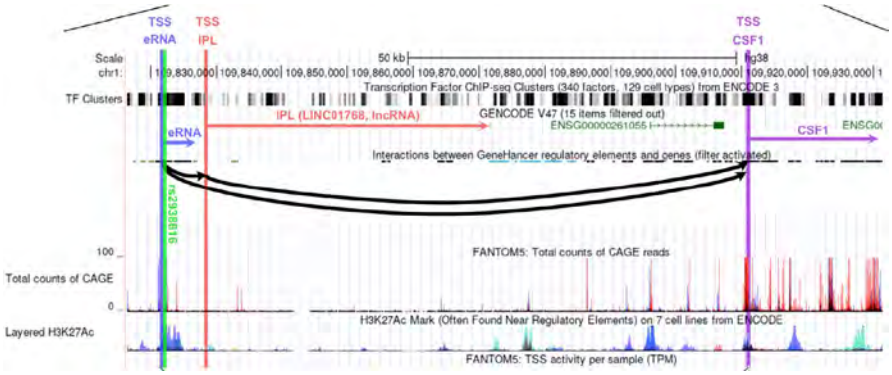


Figure 3. Genomic organization of the CSF1 locus (from the UCSC and Zenbu browsers).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

consistent with previous research. At *CSF1* there were multiple FANTOM5-CAGE multiple transcription start site peaks in monocytes but not in T-cells near the lead SNP (**Fig 3**). Rs2938616 maps within an H3K27Ac transcriptionally active peak, and there are interactions with both *CSF1* and *LINC01768*. FANTOM6-CAGE data provides evidence for selective expression of the transcription start sites upon PMA stimulation of monocytes. Our data are consistent with a model of genomic control where, in response to stimulation, the gout causal genetic variant mediates induction of the enhancer and *LINC01768* RNAs which in turn mediate *CSF1* expression.

Conclusion: In diverse experimental systems MSUc induces *CSF1* expression, and suppresses *CSF1R* expression. With the previous genetic association data our findings directly implicate *CSF1* in the pathogenesis of gout.

Disclosure: T. Merriman: None; **C. Hall**: None; **A. Chien**: None; **R. Reynolds**: None; **J. Edberg**: None; **P. Lertprachakwong**: GE Healthcare, 11, Pfizer, 11; **H. Darroch**: None; **M. Leask**: None; **M. Ozturk**: None; **B. Kischkel**: None; **N. Sumpter**: None; **L. Joosten**: None; **N. Asmann**: None.

Abstract Number: 2011

A Phase 1 Placebo Controlled, Single (SAD) and Multiple Dose Escalation (MAD) Safety and Pharmacokinetic (PK) Study of a Novel Colchicine Analogue ABP-745 in Healthy Volunteers (HV)

ullrich schwertschlag[1], Roy Wu[2], yan yang[3] and William Shi[4], [1]Atom Therapeutics, PALO ALTO, CA, [2]Atom Bioscience, San Francisco, CA, [3]Atom Therapeutics, Suzhou, China (People's Republic), [4]Atom Therapeutics, Newark, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: ABP-745 is a novel colchicine analogue in development as an anti-inflammatory agent for the treatment of acute gout and other chronic inflammatory conditions. In preclinical models, ABP-745 demonstrated comparable biological activity to colchicine with an improved safety profile including no significant drug-drug interactions.

Methods: Subjects were randomized to active drug or placebo in a 6/2 ratio. Subjects were dosed qd or bid in an ascending order (SAD). SAD Cohorts qd or bid of ABP-745 0.5 mg qd, 1.5 mg qd, 4 mg qd , 5 mg qd and 2.0 mg bid, 2.5 mg bid and placebo (N=32). Multiple ascending dose (MAD, 8 days) cohorts were ABP-745 0.5 mg qd; 1.5 mg qd; 4 mg qd; 2.5 mg bid; 2 mg bid (N=41). Single-dose food effect (ABP-745, 4 mg) was also studied (N=8). Safety was monitored until 3 days post last dose by clinical and laboratory methods. PK was followed over 36 hours (single dose) and on Day 1 (24 h) and Day 8 (36 h) of the MAD regimens.

Results: ABP-745 concentrations were detected 10 minutes post dose across all SAD levels. Maximum ABP-745 mean concentrations peaked between 1.50 h and 2.00 h with biphasic decline across all dose levels. Mean ABP-745 concentrations and exposure parameters (Cmax, AUClast, and AUC0-inf) increased over the 0.5 mg to 5 mg dose range. Mean Cmax ranged from 37.7 ng/mL to 216 ng/mL; mean AUClast ranged from 226 h*ng/mL to 1520 h*ng/mL. Mean ABP-745 Cmax, AUClast, and AUC0-inf increased in a less than proportional manner with increases in single ascending ABP-745 doses. MAD: mean ABP-745 concentrations and exposure parameters (Cmax and AUCτ on Day 1; Cmax,ss and AUCs on Day 8) increased with ascending multiple doses of ABP-745 across study days. On Day 8, mean Cmax,ss ranged from 34.0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ng/mL to 175 ng/mL, mean AUCτ ranged from 181 h*ng/mL to 1230 h*ng/mL. Accumulation ratios for Cmax,ss (RCmax) and AUCτ (RAUCτ) indicated no accumulation in ABP-745 exposure occurred during qd and bid 8-day dose regimens. RCmax values ranged from 0.944 to 1.13 for qd treatments and from 1.15 to 1.24 for bid treatments. On Day 8 approximately 20% of the administered oral dose was recovered in the urine. On Day 1 of MAD, maximum and total ABP-745 exposure (Cmax and AUCτ) generally increased in a less than proportional manner with an increase in multiple ascending QD doses. ABP-745 trough concentrations were higher for bid treatments compared to the qd treatment. Steady-state: Day 2 of dosing for both qd and bid dosing regimens. Food effect (fed/fasted) was studied (N=8). Mean ABP-745 Cmax and AUC0-inf were similar after administration of 4 mg ABP-745 under fed and fasted conditions. Median Tmax was delayed by @ 30 minutes under fed conditions (1.50 h vs. 0.988 h, respectively). Four treatment emergent AEs (TEAE) were reported in the SAD in the 5 mg single dose cohort as gastrointestinal symptoms (single events of diarrhea, nausea, abdominal pain, vomiting). In the MAD cohort 11 TEAE were reported in the 2 highest bid dose groups, such as single cases of nausea, constipation, headache, elevated blood lipase and amylase levels.

Conclusion: Safety and pharmacokinetics (PK) of ABP-745 following single, and multiple qd and bid oral doses in healthy volunteers under fasted and fed conditions further supports development of ABP-745 in an acute gout indication.

Disclosure: u. schwertschlag: ATOMBIOSCIENCE, 2; **R. Wu**: ATOMBIOSCIENCE, 2; **y. yang**: ATOMBIOSCIENCE, 3; **W. Shi**: ATOMBIOSCIENCE, 12, 3.

Abstract Number: 2012

A Phase 2a Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Multiple Ascending Doses of ABP-671 in Subjects with Hyperuricemia or Gout in China

ullrich schwertschlag[1], yan yang[2], Jingfei li[3], Roy Wu[4], adam jin[2] and William Shi[5], [1]Atom Therapeutics, PALO ALTO, CA, [2]Atom Therapeutics, Suzhou, China (People's Republic), [3]Atom Therapeutics, Suzhou, Jiangsu, China (People's Republic), [4]Atom Bioscience, San Francisco, CA, [5]Atom Therapeutics, Newark, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: ABP-671 is a novel, selective and potent URAT1 inhibitor in development for the treatment of elevated serum uric acid (sUA) levels and gout.

Methods: Subjects (N=45) ≥18 and ≤ 55 years, without clinically significant kidney abnormalities on renal ultrasound and non-symptomatic hyperuricemia or gout (two separate fasting sUA results of >7 mg/dL and >24 hours apart) were enrolled. Subjects were randomized to 5 multiple ascending oral dose groups including 1, 2, 4, 6, 12 mg of ABP-671 and placebo in a

Table 1: Schedule for dose initiation and target dosing phase

Group	Dose Escalation Period	Target Dose Period
1	d1 - d3: 0.2 mg, QD	d11 - d17: 1 mg, QD
2	d4 - d10: 0.5 mg, QD	d10 - d16: 2 mg, QD
3	d1 - d3: 0.2 mg, QD	d10 - d16: 4 mg, QD
4	d4 - d6: 0.5 mg, QD	d10 - d16: 6 mg, QD
5	d7 - d9: 1 mg, QD	d10 - d16: 12 mg, QD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Response rate (N/%) at selected categories 24 h post dose

24 h post dose	1 mg (n=7)	2 mg (n=7)	4 mg (n=7)	6 mg (n=7)	12 mg (n=7)	Placebo (n=10)
sUA < 6.0 mg/dL	6 (85.7)	7 (100)	7 (100)	7 (100)	7 (100)	0
sUA < 5.0 mg/dL	4 (57.1)	6 (85.7)	6 (85.7)	7 (100)	7 (100)	0
sUA < 4.0 mg/dL	1 (14.3)	1 (14.3)	1 (14.3)	4 (57.1)	7 (100)	0

7/2 ratio. All subjects underwent a dose escalation dosing period starting from 0.2 mg to 1 mg over a 9-day or 10-day period to mitigate any renal uUA overload. A 7-day dosing period of ABP-671 or placebo followed. The groups were enrolled separately and conducted sequentially (Table 1).

TEAEs were reported in 24 (53.3%), including 5 (71.4%), 4 (57.1%), 6 (85.7%), 4 (57.1%), 1 (14.3%), and 4 (40%) in the 1, 2, 4, 6, and 12 mg and placebo groups, respectively. There were no SAEs, grade $\geq$3 TEAEs, or deaths. The incidence of AEs was not found dose dependent.

Results: Serum UA (sUA) levels decreased in a dose dependent manner. The max median decrease of sUA occurred at 3.00-9.00 h post dose. For placebo, 1, 2, 4, 6 and 12mg dose groups, the maximum mean sUA decrease in gout subjects was 17.7%, 56.4%, 58.1%, 69.4%, 77.0%, and 79.2% from baseline, and in hyperuricemia subjects, they were 19.9%, 50.1%, 64.1%, 73.2%, 81.2%, and 82.1%. Subjects (%) with sUA levels lower than 6.0, 5.0, and 4.0 mg/dL 24 h post dose were 85.7%, 57.1%, and 14.3% for 1 mg, 100%, 85.7%, and 14.3% for 2 mg, 100%, 85.7%, and 14.3% for 4 mg, 100%, 100%, and 57.1% for 6 mg, and 100%, 100%, and 100% for 12 mg.

Conclusion: ABP-671 has acceptable safety and tolerability in Chinese subjects with hyperuricemia or gout. ABP-671 reduced the sUA in a dose-dependent manner.

Disclosure: u. schwertschlag: ATOMBIOSCIENCE, 2; **y. yang**: ATOMBIOSCIENCE, 3; **J. li**: Atom Therapeutics, 3; **R. Wu**: ATOMBIOSCIENCE, 2; **a. jin**: Atom Therapeutics, 3; **W. Shi**: ATOMBIOSCIENCE, 12, 3.

Abstract Number: 2013

Efficacy and Safety of Firsekibart in Acute Gouty Arthritis Patients with Limited Treatment Options: A Multicenter, Randomized, Double-Blind, Double-Dummy, Active-Controlled Phase III Trial

Yu Xue[1], Tianshu Chu[2], Jiankang Hu[3], Wei Gou[4], Ning Zhang[5], Juan Li[6], Jing Yu[7], Rongping Li[8], Rongbin Li[9], Long Qian[10], Xinwang Duan[11], Lihua Duan[12] and Hejian Zou[1], [1]Department of Rheumatology,Huashan Hospital, Fudan University, Shanghai, China, shanghai, China (People's Republic), [2]Department of Rheumatology, Henan Provincial People's Hospital, Zhengzhou, China, zhengzhou, China (People's Republic), [3]Department of Rheumatology, Pingxiang People's Hospital, Pingxiang,China,, Pingxiang, China (People's Republic), [4]Department of Rheumatology, Hebei Petro ChinaCentral Hospital, Langfang, China, Langfang, China (People's Republic), [5]Department of Rheumatology, Shengjing Hospital of China Medical University, Shenyang, China, Shengjing, China (People's Republic), [6]The First Affiliated Hospital of Hainan Medical University, Haikou, China (People's Republic), [7]Department of Rheumatology, The FirstAffiliated Hospital of Liaoning University of Traditional Chinese Medicine, Shenyang, China, Shenyang, China (People's Republic), [8]Department of Rheumatology, The First Affiliated Hospital of GannanMedical University, Ganzhou, China, Ganzhou, China (People's Republic), [9]Department ofRheumatology, The First Hospital of Qiqihar, Qiqihar, China, Qiqihar, China (People's Republic), [10]Department of Rheumatology, The Second Hopital of Anhui Medical University, Hefei, China, Hefei, China (People's Republic), [11]The Second Affiliated Hospital of Nanchang University, Nanchang, China (People's Republic), [12]Department of Rheumatology, Jiangxi Provincial People's Hospital, Nanchang, China, Nanchang, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Acute gouty arthritis(GA) is a common and debilitating condition, especially for patients unsuitable for standard therapy. Firsekibart, previously called Genakumab, is a first-in-class fully IgG4/λ anti-human-IL-1β monoclonal antibody, making it a significant option for gout treatment.

Methods: This phase III clinical trial was a multicenter, randomized, double-blind, double-dummy, active-controlled study conducted from Jan. 2023 to Jun. 2024 across 51 centers in China (NCT05983445). Patients aged 18–75 years with GA, contraindicated of, intolerance of, or unresponsiveness to NSAIDs and/or colchicine, with ≥2 episodes during the last 12 months were screened for eligibility.Patients were randomized 1:1 to receive a single subcutaneous dose of Firsekibart (200 mg) or an intramuscular dose of CB 7 mg.The co-primary endpoints were change in pain intensity from baseline to 72 hours in the most affected joint measured on VAS (0–100 mm) and the time to first new episode over 12 weeks. Secondary endpoints included: change in VAS scores at other time points(6h, 24h, 48h, 7 days post-dose), time to reduce 50% pain,proportion of patients experiencing ≥ 1 new flare, the mean flare rate per patient over 12 and 24 weeks, proportion of patients requiring rescue therapy,the dosage of rescue medicine and safety assessments.

Results: The full analysis included 311 patients, with 156 receiving Firsekibart and 155 receiving CB. The median age was 42, 89.4% patients had ≥ 3 flares in the last 12 months. Firsekibart significantly delayed median time to first new flare (Not estimable vs. 45 days) and reduced risk of new flare by 90% (HR0.10; 95% CI: 0.06, 0.17; $p< 0.0001$) over 12 weeks, by 87% (HR 0.13; 95% CI: 0.08, 0.21; $p< 0.0001$) over 24 weeks. Although the reduction of pain intensity and the median time to reduce ≥50% pain were similar Firsekibart showed better pain relief in GA patients from 48 hours to 7 days. Significantly fewer patients treated with Firsekibart experienced ≥ 1 new flare over 12 weeks and 24 weeks (10.9% vs. 65.2%, 14.7% vs. 66.5%, $p < 0.0001$), and the mean number of new flares per patient was lower in Firsekibart group over 12 and 24 weeks (0.2 (0.52) vs. 1.2 (1.27), 0.2 (0.79) vs. 1.6 (1.79)) (mean(SD)). A smaller proportion of patients in the Firsekibart group required rescue therapy (10.9% vs 48.4%). Less mean dosage of rescue medicine was uesd in Firsekibart group (corticosteroid was 69.33 mg vs 202.03 mg).

The overall incidence of treatment-emergent adverse event (TEAE) was comparable, occurring in 111 patients (71.2%; grade ≥3: 12.2%) in the Firsekibart group and 109 patients (69.9%; grade ≥3: 10.9%) in the CB group. The most common TEAE in Firsekibart group was hypertriglyceridaemia(27.6%; grade ≥3: 10.3%), and it may own to the high proportion of patients with dyslipidemia at baseline. Neither extra safety risk for patients with abnormal liver or kidney function nor treatment-related serious adverse events(TRSAE) were reported in Firsekibart group. All 3 TRSAE were reported in CB group.

Conclusion: Firsekibart is effective and well-tolerated for acute gout flares in patients with limited treatment options, demonstrating rapid pain relief and significant superiority in preventing flare compared with CB.

Disclosure: Y. Xue: None; **T. Chu**: None; **J. Hu**: None; **W. Gou**: None; **N. Zhang**: None; **J. Li**: None; **J. Yu**: None; **R. Li**: None; **R. Li**: None; **L. Qian**: None; **X. Duan**: None; **L. Duan**: None; **H. Zou**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2014

Efficacy and Safety of Firsekibart in Acute Gouty Arthritis Patients with eGFR < 60ml/min/1.73m^2:A Post-Hoc Analysis of 24-Week Data

Yu Xue[1], Tianshu Chu[2], Jiankang Hu[3], Wei Gou[4], Ning Zhang[5], Juan Li[6], Jing Yu[7], Rongping Li[8], Rongbin Li[9], Long Qian[10], Xinwang Duan[11], Lihua Duan[12] and Hejian Zou[1], [1]Department of Rheumatology,Huashan Hospital, Fudan University, Shanghai, China, shanghai, China (People's Republic), [2]Department of Rheumatology, Henan Provincial People's Hospital, Zhengzhou, China, zhengzhou, China (People's Republic), [3]Department of Rheumatology, Pingxiang People's Hospital, Pingxiang,China,, Pingxiang, China (People's Republic), [4]Department of Rheumatology, Hebei Petro ChinaCentral Hospital, Langfang, China, Langfang, China (People's Republic), [5]Department of Rheumatology, Shengjing Hospital of China Medical University, Shenyang, China, Shengjing, China (People's Republic), [6]The First Affiliated Hospital of Hainan Medical University, Haikou, China (People's Republic), [7]Department of Rheumatology, The FirstAffiliated Hospital of Liaoning University of Traditional Chinese Medicine, Shenyang, China, Shenyang, China (People's Republic), [8]Department of Rheumatology, The First Affiliated Hospital of GannanMedical University, Ganzhou, China, Ganzhou, China (People's Republic), [9]Department ofRheumatology, The First Hospital of Qiqihar, Qiqihar, China, Qiqihar, China (People's Republic), [10]Department of Rheumatology, The Second Hopital of Anhui Medical University, Hefei, China, Hefei, China (People's Republic), [11]The Second Affiliated Hospital of Nanchang University, Nanchang, China (People's Republic), [12]Department of Rheumatology, Jiangxi Provincial People's Hospital, Nanchang, China, Nanchang, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (1990–2014) Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Approximately 70% of adults with gout have CKD (Chronic Kidney Disease) ≥Stage 3 (i.e estimated glomerular filtration rate (eGFR) < 60ml/min/1.73m^2), significantly restricts treatment options such as colchicine or NSAIDs due to the potential renal toxicity. Firsekibart, previously known as Genakumab, is a novel IgG4/λ anti-human-IL-1β monoclonal antibody eliminated by degradation through intracellular enzymes rather than excretion through the kidney making it a significant option for gout with CKD. Here, we report the efficacy and safety of Firsekibart vs compound betamethasone(CB) in a subgroup of patients with eGFR < 60ml/min/1.73m^2.

Methods: This multicenter, randomized, double-blind, double-dummy, active-controlled phase III clinical trial was conducted across 51 centers in China. (NCT05983445). Patients (aged 18-75) who had acute arthritis of primary gout (GA) and contraindicated of, intolerance of, or unresponsiveness to NSAIDs and/or colchicine, with ≥2 episodes during the previous 12 months were screened for eligibility. Patients were randomized in a 1:1 ratio to either a single subcutaneous dose of Firsekibart (200 mg) or an intramuscular dose of CB 7 mg treatment. The co-primary endpoints were change in pain intensity from baseline to 72 hours in the most affected joint measured on VAS (0–100 mm) with non-inferiority testing and the time to first new episode over 12 weeks with superiority testing. Secondary endpoints included percentage of patients with at least one new flare (12weeks, 24weeks) and the safety evaluation.

Results: Of 313 patients, 42 patients had eGFR< 60ml/min/1.73m^2 at baseline (21 in Firsekibart group and 21 in CB group). 95.24%patients had more than 3 episodes in the preceding 12 months and 50% patients had gouty tophi. Firsekibart demonstrated a competing effect in reducing VAS pain score (58.22 (-67.516, -48.927) mm vs. -58.33 (-67.635, -49.022) mm) (Least Squares Mean(95CI%)). Compared to CB, Firsekibart significantly delayed median time to first new episode (Not estimable vs 21 days) reduced the risk of a new flare by 98% over the 12-week period (HR 0.02; p=0.0002), by 96% over the 24-week period (HR 0.04, p<0.0001). A significantly lower proportion of patients treated with Firsekibart experienced at least one new flare over 12 weeks (4.76% vs. 95.24%) and 24 weeks (9.52% vs. 95.00%).

The treatment emergent adverse events and treatment-related adverse events were 10 (47.6%) and 7 (33.3%) in the Firsekibart-treated group, versus 11 (52.4%) and 6 (28.6%) in the CB-treated group. No serious adverse events were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

reported in Firsekibart-treated group. Besides, neitiher Firsekibart nor CB showed significant damage to kidney function, only one patient in Firsekibart-treated group experienced renal function deterioration over 24 weeks after treatment. (eGFR decreased from 30∼60 to < 30ml/min/1.73m^2).

Conclusion: Compared with a potent long-acting corticosteroid (Compound betamethasone), Firsekibart showed a comparable effect in pain relief and offering significantly better prevention of new flares in GA patients with eGFR < 60ml/min/1.73m^2. The safety profile in this sub population was consistent with that of the overall study population.

Disclosure: Y. Xue: None; **T. Chu**: None; **J. Hu**: None; **W. Gou**: None; **N. Zhang**: None; **J. Li**: None; **J. Yu**: None; **R. Li**: None; **R. Li**: None; **L. Qian**: None; **X. Duan**: None; **L. Duan**: None; **H. Zou**: None.

Abstract Number: 2015

Clinical features of IgG4-related disease - a single centre experience

Alojzija Hocevar[1], Ales Groselj[2], gregor hawlina[2], Matic Kozelj[2], Andrej Skoberne[2], joze Pizem[3] and Vesna Jurcic[3], [1]University Medical Center Ljubljana, LJUBLJANA, Slovenia, [2]UMC Ljubljana, Ljubljana, Slovenia, [3]Medical Faculty, Institute of Pathology, Ljubljana, Slovenia

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related diseases (IgG4-RD) is rare and unique fibroinflammatory disorder. The aim of our study was to study the characteristics of IgG4-RD cohort diagnosed and followed at our secondary/tertiary medical centre.

Methods: This retrospective study covered a period from January 2012 to December 2024. A review of medical records of adult patients diagnosed with IgG4-RD was performed and patient's demographics, comorbidities and IgG4-RD features at presentation were extracted. Data were analysed with descriptive statistical methods.

Results: During a 13-year observation period, 58 patients with IgG4-RD were identified (46 (79.3%) males, median (IQR) age at diagnosis 63.0 (51.3; 68.9) years). Ten patients had a history of diabetes mellitus, 10 of asthma and 5 of atopy. Median (IQR) duration of symptoms attributed to IgG4RD before the diagnosis was 6 (3; 18) months.

Table 1 shows characteristics of our IgG4-RD cohort at diagnosis. The average number of organs and/or regions affected was 2 (ranging from 1 to 7). Thirty-seven (63.8%) patients had predominantly proliferative and 21 (36.2%) predominantly

Table1. Clinical characteristics of IgG4 related disease

Characteristic	No. (%)	Characteristic	No. (%)
Meninges	1 (1.7%)	Aorta	13 (22.4%)
Orbital tissue	8 (13.8%)	Lymph nodes	10 (17.2%)
Lacrimal glands	9 (15.5%)	Joints	1 (1.7%)
Nasal cavity & sinuses	4 (6.9%)		
Salivary glands	13 (22.4%)	Elevated serum IgG4	41/49 (83.7%)
Lungs	6 (10.3%)	Hypergammaglobulinemia	16/40 (40.0%)
Pleura	4 (6.9%)	Hypocomplementemia	2/28 (7.1%)
Hepatobiliary tract	7 (12.1%)	Peripheral eosinophilia	6/43 (14.0%)
Pancreas	12 (20.7%)		
Kidneys	7 (12.1%)	**Biopsy findings**	47 (81.0%)
Omentum, mesenterium	4 (6.9%)	Consistent with IgG4RD	36/47 (76.6%)
Retroperitoneal tissue	16 (27.6%)	Possible IgG4RD	4/47 (8.5%)
		Negative/Non-representative	7/47 (14.9%)
		Fulfilment of 2019 ACR/EULAR IgG4-RD Classification Criteria	40/58 (69.0%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

fibrotic phenotypes. We classified 10 (17.2%) patients as pancreato-hepato-biliary disease, 25 (43.1%) as retroperitoneal fibrosis and/or aortitis, 6 (10.3%) as head and neck limited disease and 15 (25.9%) as Mikulicz syndrome with systemic involvement. In 2 patients the disease could not be classified. Forty-seven patients had an organ biopsy, and histopathological features were consistent with IgG4-RD in 36 (76.6%), and suspicious of IgG4-RD in 4 (8.5%) patients. 2019 ACR-EULAR IgG4RD classification criteria were fulfilled in 40 (69.0%) patients.

A total of 44 patients (75.9%) received systemic therapy: 41 patients were treated with systemic glucocorticoid, 25 with an immunomodulatory medication (3 of them as therapy and 22 concomitantly with glucocorticoids). Nine patients received surgical therapy. Five patients were observed only.

Conclusion: Our IgG4-RD cohort was dominated by middle-aged men with retroperitoneal fibrosis and/or aortitis phenotype.

Disclosure: A. Hocevar: None; **A. Groselj**: None; **g. hawlina**: None; **M. Kozelj**: None; **A. Skoberne**: None; **j. Pizem**: None; **V. Jurcic**: None.

Abstract Number: 2016

Effectiveness of Nintedanib combined with different DMARDs in joint and pulmonary domains of Rheumatoid Arthritis - Interstitial Lung Disease. National multicenter study of 74 patients

Ana Serrano-Combarro[1], Jess Loarce[2], Belén Atienza-mateo[3], Nuria Vegas Revenga[4], Maria Martín López[5], Santos Castañeda[6], Rafael B. Melero-González[7], Natalia Mena Vzquez[8], Carmen Carrasco-Cubero[9], Carolina Diez-Morrondo[10], David Castro-Corredor[11], Tomas Ramon Vazquez Rodriguez[12], Andrea García-Valle[13], Gema Bonilla[14], Marina Rodríguez Lopez[15], Ignacio Braña[16], Pablo Andujar[17], Sara Maria Rojas Herrera[18], Juan Camilo Sarmiento-Monroy[19], Diego Ferrer[20], Ivan Ferraz Amaro[21], Ricardo Blanco[22] and Spanish Collaborative Group of Antifibrotics in Interstitial Lung Disease Associated with Rheumatoid Arthritis, [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [2]Ramn y Cajal University Hospital, Madrid, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, PALMA DE MALLORCA/BALEARES, Spain, [4]Galdakao- Usansolo University Hospital, Galdakao, Spain, [5]Hospital 12 de Octubre, Madrid, Spain, [6]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [7]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [8]Hospital Regional Universitario de Malaga, Malaga, Spain, Mlaga, Spain, [9]Complejo Hospitalario Universitario de Badajoz, Badajoz, Spain, [10]Complejo Asistencial Universitario de León, León, Spain, [11]Hospital General Universitario de Ciudad Real, Ciudad Real, Spain, [12]Complejo Hospitalario Universitario de Ferrol, Ferrol, Spain, [13]Rheumatology. Hospital General Río Carrión, Palencia, Castilla y Leon, Spain, [14]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [15]Complejo Hospitalario Universitario de Santiago, Santiago, Spain, [16]Hospital Universitario Central de Asturias, Oviedo, Spain, [17]Hospital Universitario Doctor Peset, Valencia, Spain, [18]Hospital de Mérida, Rheumatology, Badajoz, Badajoz, Spain, [19]Hospital Clnic Barcelona, Barcelona, Spain, [20]Department of Pulmonology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [21]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [22]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

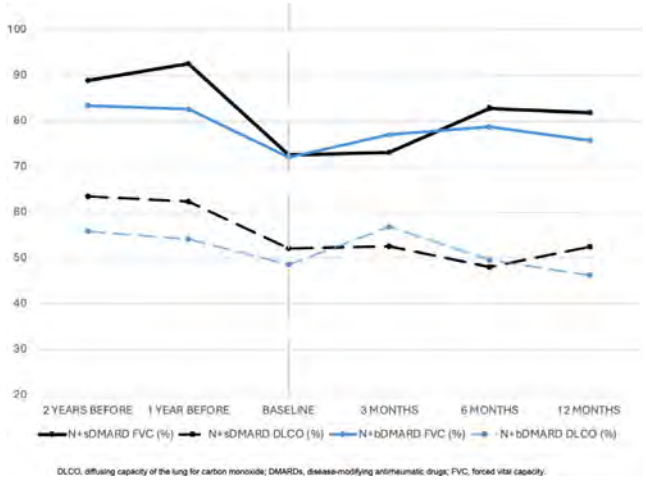
Background/Purpose: Interstitial lung disease (ILD) is a severe complication of rheumatoid arthritis (RA) and its management remains a challenge. Approximately one third of the patients may develop a progressive ILD or show persistent inflammatory joint activity despite of disease-modifying antirheumatic drugs (DMARDs). Favorable results with the antifibrotic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Main general clinical features of RA-ILD patients at nintedanib initiation.

	NINTE (global) n=74	NINTE +only sDMARD n=15	NINTE +only bDMARD n=37	p value
Age, years, mean±SD	69±9	73±8	68±9	0.54
Men, n (%)	43 (74)	10 (67)	22 (60)	0.63
Smoker ever, n (%)	52 (70)	10 (67)	29 (78)	0.38
RF, n (%)	66 (90)	13 (87)	36 (97)	0.13
ACPA, n (%)	63 (85)	11 (73)	34 (92)	0.078
Erosive arthritis, n (%)	24 (33)	2 (14)	14 (38)	0.16
CRP (mg/dL), median [IQR]	2 [0.5-7]	2 [0.4-4]	2 [0.5-7]	0.079
ESR (mm/h), mean±SD	32±29	21±28	31±28	0.36
ILD duration up to antifibrotic initiation, months, median [IQR]	51 [22-78]	30 [14-66]	51 [28-84]	0.76
FVC (% of the predicted), mean±SD	73±23	73±27	72±22	0.962
DLCO (% of the predicted), mean±SD	50±14	52±12	48±15	0.73
HRCT pattern, n (%)				
UIP	46 (66)	9/13	29/37	0.56
NSIP	20 (29)	4/13	7/37	0.59
Other	4 (6)	0/13	1/37	0.59
Concomitant immunosuppressive therapy, n (%)	52 (70)	15 (100)	37 (100)	
sDMARD (LFN/MTX/other)	29(39) [7/8/6/8]/15[2/2/]	15 (100) [5/3/3/2/0/7/47)]	0	
bDMARD (ABA, RTX)	47 (64) [33/45)/10(14)]	0	37 (100) [26/70)/9/24)]	

ACPA, anti-citrullinated protein antibodies; CRP, C-reactive protein; DLCO, diffusing capacity of the lung for carbon monoxide; ESR, erythrocyte sedimentation rate; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; mMRC, modified Medical Research Council; NSIP, non-specific interstitial pneumonia; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia.



DLCO, diffusing capacity of the lung for carbon monoxide; DMARDs, disease-modifying antirheumatic drugs; FVC, forced vital capacity.

Figure. Evolution of pulmonary function in 74 patients with RA-ILD according to the combination of nintedanib with only biologic or only synthetic DMARDs.

nintedanib (NINTE) in RA-ILD patients with pulmonary progressive fibrosis (PPF) in pulmonary function had been reported. However, data on articular response is limited, although NINTE seems to have no efficacy on the articular domain. Therefore, NINTE should be administered combined with DMARDs. Our objective was to assess the evolution of joint and pulmonary outcomes in RA-ILD patients with PPF treated of NINTE and DMARDs in clinical practice.

Methods: National Spanish multicenter study of RA-ILD patients treated with NINTE due to PPF. the main outcome measures were joint activity and forced vital capacity (FVC) evolution of different groups of treatment according to DMARDs category (biological [bDMARDs] or synthetic [sDMARDs]) were the main outcome measures.

Results: A total of 74 patients (43 men/31 women) were collected, mean age of 69±9 years. Median [IQR] ILD duration up to antifibrotic initiation was 51 [22-78] months.

NINTE was used **a)** combined with bDMARDs (n=47, 33 abatacept, 10 rituximab); **b)** combined with sDMARDs (n=29, 7 leflunomide, 6 methotrexate, 4 JAK inhibitor, 8 mycophenolate, 2 hydroxychloroquine, 1 azathioprine and 1 cyclophosphamide); **c)** combined with both bDMARDs and sDMARDs (n=9); and **d)** monotherapy (only glucocorticoids) (n=13).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

To avoid interference, we select only those who are on either biological or synthetic DMARDs. Main baseline characteristics of patients are shown in **Table**. After 12 months of follow-up, joint activity was controlled in 81% of patients (87% in the group of NINTE+ only bDMARDs and 83% in the group of NINTE+ only sDMARDs, p=0.82). In addition, no significant decline in mean FVC or DLCO values was observed, with no statistically significant differences between the 2 groups of treatment (**Figure**).

Conclusion: In our series of RA-ILD patients with PPF treated with NINTE, articular inflammation could be managed either with bDMARDs or sDMARDs, with similar pulmonary function evolution.

Disclosure: A. Serrano-Combarro: None; **J. Loarce**: None; **B. Atienza-mateo**: None; **N. Vegas Revenga**: None; **M. Martín López**: None; **S. Castañeda**: None; **R. Melero-González**: None; **N. Mena Vázquez**: None; **C. Carrasco-Cubero**: None; **C. Diez-Morrondo**: None; **D. Castro-Corredor**: None; **T. Vazquez Rodriguez**: None; **A. García-Valle**: None; **G. Bonilla**: None; **M. Rodríguez Lopez**: None; **I. Braña**: None; **P. Andujar**: None; **S. Rojas Herrera**: None; **J. Sarmiento-Monroy**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6; **D. Ferrer**: None; **I. Ferraz Amaro**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2017

Baseline and 2-year Follow-up of Pulmonary Function Among CTD-ILD Subtypes

Ivana Ilic, **Anchal Sabharwal**, Galina Marder and Sonali Narain, Northwell, Great Neck

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease is a major cause of morbidity and mortality in patients with connective tissue disease (CTD-ILD). Evaluation of ILD severity and progression relies on symptoms along with pulmonary function tests (PFT) and high-resolution computed tomography (HRCT). It has been previously reported that Ro52 antibodies are associated with more severe ILD phenotype. The goal of this study is to evaluate PFT characteristics across CTD-ILDs and whether anti-Ro52 presence determines more severe ILD in scleroderma, Sjogren's, idiopathic inflammatory myopathy (IIM), and Mixed Connective Tissue Disease (MCTD) subgroups.

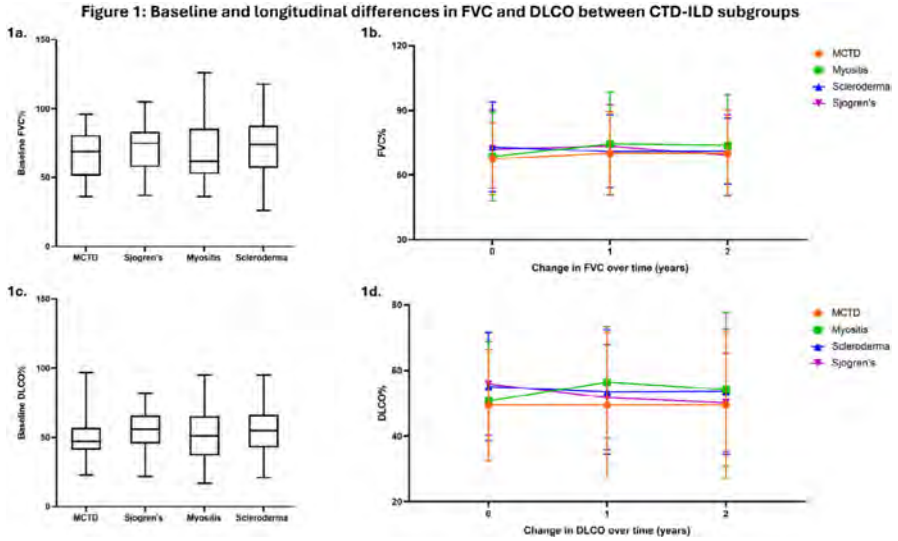
Methods: This is a retrospective analysis of the Northwell CTD-ILD cohort, meeting classification criteria for scleroderma, IIM, Sjogren's, or MCTD. Cases with rheumatoid arthritis ILD and post-transplant were excluded. We combined 22 previously reported cases of IIM-ILD with 101 CTD-ILD patients followed between 2012 – 2024. Longitudinal analysis of PFTs was performed over a 2-year period. HRCT chest were recorded as improved, stable or worsened by radiologist read. Descriptive statistics, Anova (with Geisser-Greenhouse correction, Welch's ANOVA and repeated measures ANOVA) and Mann-Whitney (non-parametric) tests were used.

Results: 123 patients were included in the analysis. Our cohort comprised of 45 IIM, 30 scleroderma, 21 Sjogren's, and 27 MCTD patients. The median age was 58 (22-83) years with a predominantly females (80.5%) with ~5 years follow-up (1-12 years), Table 1. A quarter of patients (26.8%) were Ro-52+ with most distributed between Sjogren's (47.6%) and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Demographics and Characteristics					
	Myositis (n=45)	Scleroderma (n=30)	Sjogren's (n=21)	MCTD (n=27)	All diseases (n=123)
Age - mean year (min-max)	56 (26-83)	57 (31-73)	66 (41-77)	58 (22-80)	58 (22-83)
Female sex (n, %)	39 (86.7%)	23 (76.7%)	15 (71.4%)	22 (81.5%)	99 (80.5%)
Race or ethnic group (n, %)					
Caucasian	12 (26.7%)	16 (53.3%)	9 (42.9%)	7 (26%)	44 (35.8%)
African American	15 (33.3%)	6 (20%)	8 (38.1%)	9 (33.3%)	38 (30.9%)
Asian/Pacific Islander	11 (24.4%)	3 (10%)	2 (9.5%)	5 (18.5%)	21 (17.1%)
Hispanic/Latino	7 (15.6%)	9 (30%)	1 (4.8%)	3 (11.1%)	20 (16.3%)
Other or Multiracial	7 (15.6%)	6 (20%)	2 (9.5%)	4 (14.8%)	19 (15.4%)
Medications (n, %)					
Mycophenolate mofetil	24 (53.3%)	23 (76.7%)	8 (38.1%)	17 (63%)	72 (58.5%)
Methotrexate	6 (13.3%)	0	3 (14.3%)	0	9 (7.3%)
Azathioprine	3 (6.7%)	1 (3.3%)	0	2 (7.4%)	6 (4.9%)
IVIG	2 (4.4%)	0	0	1 (3.7%)	3 (2.4%)
Nintedanib	0	1 (3.3%)	0	0	1 (0.8%)
Tofacitinib	0	0	0	1 (3.7%)	1 (0.8%)
Rituximab	8 (17.8%)	0	4 (19%)	2 (7.4%)	14 (11.4%)
Plaquenil	4 (8.9%)	6 (20%)	5 (23.8%)	10 (37%)	25 (20.3%)
Ro-52 + (n, %)	19 (42.2%)	1 (3.3%)	10 (47.6%)	3 (11.1%)	33 (26.8%)
Baseline PFT parameters (mean, SD)					
FVC % (SD)	68.7 (20.7)	72.6 (21.1)	72.1 (18.3)	69.4 (15.5)	70.1 (19.4)
DLCO % (SD)	50.8 (18.1)	55.1 (16.9)	55.9 (16.1)	52.2 (17.8)	52.4 (17.1)
Baseline HRCT ILD Pattern (n, %)					
NSIP	39 (86.7%)	26 (86.7%)	16 (76.2%)	20 (74.1%)	101 (82.1%)
UIP	2 (4.4%)	0	1 (4.8%)	6 (22.2%)	9 (7.3%)
OP	1 (2.2%)	0	1 (4.8%)	0	2 (1.6%)
OP/NSIP	0	1 (3.3%)	0	0	1 (0.8%)
No ILD	3 (6.7%)	4 (13.3%)	3 (14.3%)	1 (3.7%)	11 (8.9%)

Patient Demographics and Characteristics

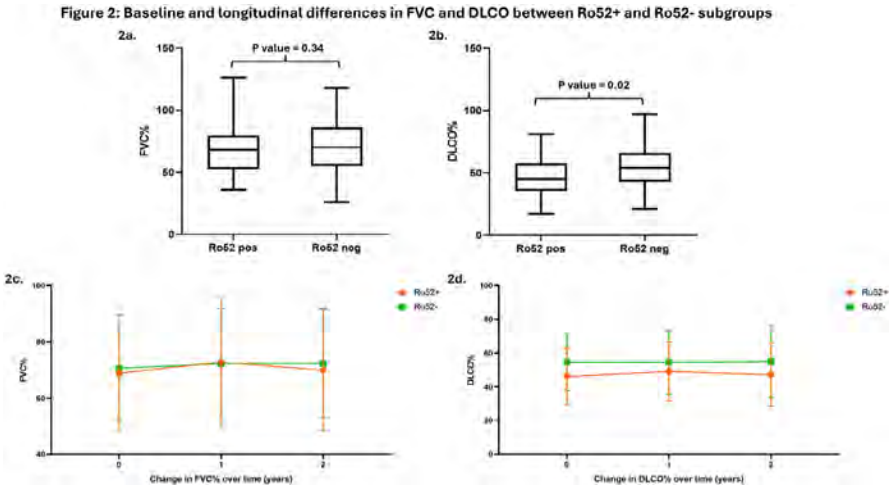


Baseline and Longitudinal Differences in FVC and DLCO Between CTD-ILD Subgroups

IIM (42.2%) subgroups. NSIP was the most common ILD pattern. Most patients in our cohort were on at least 1 immunosuppressive agent, led by mycophenolate mofetil (Cohort: 58.5%; Scleroderma 76.7%, IIM 53.3%, Sjogren's 38.1%, and MCTD 63%).

At baseline, mean FVC % (p=0.67) and DLCO% (p=0.42) were similar across subgroups, Fig1a,c and Ro-52+ patients (all cohort and IIM subgroup) had significantly lower DLCO% compared to Ro52- patients (Cohort: 46.3 vs. 54.8, p=0.02; IIM 43.1 vs. 56.4, p=0.01), while this was not observed for any other subgroups of ILD, Fig 2a,b.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Baseline and Longitudinal Differences in FVC and DLCO Between Ro52+ and Ro52- Subgroups

When we looked at change in disease over time in individual CTD-ILD subgroups, a trend for improvement in both FVC% and DLCO% was noted only in the IIM subgroup (FVC% p=0.05 with baseline to year 1 p=0.02 and to year 2 p=0.04; DLCO% p=0.14 with baseline to year 1 p=0.09 and to year 2 p=0.4, data not shown). When the ILD subgroups were compared to each other, there was no significant change in FVC% or DLCO% over the 2-year period, Fig1b,d.

Similarly, there was no significant change in FVC% or DLCO% between Ro-52+ and negative groups over 2 years (p=0.889). However, Ro52 negative patients consistently maintained higher DLCO% over time (p=0.003) Fig 2c,d. Most patients had stable HRCT over 2-year period in all subgroups.

Conclusion: While all CTD-ILD share similar evolution when compared to each other, myositis-ILD has a higher chance of improvement by PFT parameters. Anti-Ro52 positivity is associated with consistently lower DLCO% over time and may serve as harbinger of more severe ILD across all CTD-ILD subgroups.

Disclosure: I. Ilic: None; **A. Sabharwal**: None; **G. Marder**: None; **S. Narain**: Bristol-Myers Squibb(BMS), 2, Janssen, 2, Novartis, 2.

Abstract Number: 2018

Investigating Epidemiology, Clinical associations, and Outcomes of Uveitis: A Retrospective Cohort Study

Archit Srivastava[1], Jayesh Valecha[2], Sehreen Mumtaz[1], Caroyln Harvey[3], Florentina Berianu[1] and Vikas Majithia[4], [1]Mayo Clinic Florida, Jacksonville, FL, [2]Saint Vincent Hospital, Worchester, FL, [3]Mayo Clinic, Phoenix, AZ, [4]Mayo Clinic Hospital, Jacksonville, FL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Uveitis is a significant cause of visual impairment in the U.S., with a prevalence of 438 per 100,000 persons [1]. It is anatomically classified into anterior, intermediate, posterior, and panuveitis, and is frequently associated

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Combined baseline characteristics, laboratory findings, autoantibody profiles, and HLA typing across uveitis subtypes. Anterior uveitis was the most prevalent (84.5%). Significant differences were observed in age distribution and HLA-B27 positivity (p=0.062, 0.349 respectively). Autoantibodies such as ANA (36.2%) and HLA-B27 (35.0%) were commonly present. Bilateral eye involvement was dominant across all subtypes (75.5%). These findings highlight the clinical heterogeneity and immunological associations in non-infectious uveitis.

Table 1. Combined Patient Characteristics, Labs, Serologies, and HLA

Patient Characteristics						
Characteristic	Anterior Uveitis (N=125)	Intermediate Uveitis (N=6)	Posterior Uveitis (N=8)	Panuveitis (N=9)	Total (N=148)	P-value
Age						0.062[1]
Age, Mean (SD)	51.2 (15.29)	43.3 (16.98)	54.5 (12.04)	62.8 (6.91)	51.7 (15.08)	
Race						0.466[2]
Asian	4 (3.2%)	0 (0.0%)	0 (0.0%)	2 (22.2%)	6 (4.1%)	
White	95 (76.0%)	6 (100.0%)	7 (87.5%)	5 (55.6%)	113 (76.4%)	
Black or African American	23 (18.4%)	0 (0.0%)	1 (12.5%)	2 (22.2%)	26 (17.6%)	
Ethnicity						0.760[2]
Hispanic or Latino	13 (10.4%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	14 (9.5%)	
Not Hispanic or Latino	109 (87.2%)	5 (83.3%)	8 (100.0%)	9 (100.0%)	131 (88.5%)	
Gender						>0.999[2]
Male	29 (23.2%)	1 (16.7%)	2 (25.0%)	2 (22.2%)	34 (23.0%)	
Female	96 (76.8%)	5 (83.3%)	6 (75.0%)	7 (77.8%)	114 (77.0%)	
[1]Kruskal-Wallis p-value; [2]Fisher Exact p-value.						
Labs and Serologies						
Labs	Anterior Uveitis (N=125)	Intermediate Uveitis (N=6)	Posterior Uveitis (N=8)	Panuveitis (N=9)	Total (N=148)	P-value
CRP, n (%)						0.760[1]
Raised	23 (19.8%)	0 (0.0%)	1 (14.3%)	2 (25.0%)	26 (19.0%)	
Normal	93 (80.2%)	6 (100.0%)	6 (85.7%)	6 (75.0%)	111 (81.0%)	
ANA levels, n (%)						0.661[1]
Positive	39 (36.1%)	1 (16.7%)	3 (50.0%)	3 (42.9%)	46 (36.2%)	
Negative	69 (63.9%)	5 (83.3%)	3 (50.0%)	4 (57.1%)	81 (63.8%)	
QuantiFERON test, n (%)						>0.999[1]
Positive	2 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	
Negative	106 (96.4%)	6 (100.0%)	7 (100.0%)	4 (100.0%)	123 (96.9%)	
ENA Panel antibodies						
Anti-Ro/Anti-SSA, n (%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	>0.999[1]
Anti-RNP (Anti-ribonucleoprotein), n (%)	5 (4.5%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	6 (4.5%)	0.635[1]
Anti-Scl70, n (%)	5 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (3.8%)	>0.999[1]
Anti-CCP	5 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (3.8%)	>0.999[1]
Rheumatoid Factor	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.3%)	>0.999[1]
P-ANCA	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	1 (0.8%)	0.152[1]
PR-3	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	>0.999[1]
Anti-Smooth Muscle Ab, n (%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	>0.999[1]
Anti-dsDNA	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	>0.999[1]
No antibodies	93 (83.0%)	6 (100.0%)	6 (100.0%)	6 (75.0%)	111 (84.1%)	0.623[1]
CCP Antibody levels, n (%)						0.637[1]
Positive	6 (6.5%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	7 (6.5%)	
Negative	87 (93.5%)	4 (100.0%)	5 (100.0%)	4 (80.0%)	100 (93.5%)	
RF Antibody levels, n (%)						>0.999[1]
Positive	6 (5.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (5.1%)	
Negative	96 (94.1%)	5 (100.0%)	5 (100.0%)	5 (100.0%)	111 (94.9%)	
P-ANCA antibody presence, n (%)						0.321[1]
Positive	2 (4.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	3 (4.8%)	
Negative	48 (96.0%)	2 (100.0%)	6 (100.0%)	4 (80.0%)	60 (95.2%)	
PR3 Antibody, n (%)						>0.999[1]
Positive	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
Negative	50 (98.0%)	3 (100.0%)	6 (100.0%)	5 (100.0%)	64 (98.5%)	
HLA and Eye Involvement Characteristics						
HLA	Anterior Uveitis (N=125)	Intermediate Uveitis (N=6)	Posterior Uveitis (N=8)	Panuveitis (N=9)	Total (N=148)	P-value
HLA B27, n (%)						0.349[1]
Positive	39 (37.9%)	1 (25.0%)	0 (0.0%)	1 (20.0%)	41 (35.0%)	
Negative	64 (62.1%)	3 (75.0%)	5 (100.0%)	4 (80.0%)	76 (65.0%)	
HLA B51						0.600[1]
Positive	6 (5.8%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	7 (6.0%)	
Negative	97 (94.2%)	4 (100.0%)	4 (80.0%)	5 (100.0%)	110 (94.0%)	
HLA B57						>0.999[1]
Positive	2 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	
Negative	101 (98.1%)	4 (100.0%)	5 (100.0%)	5 (100.0%)	115 (98.3%)	
Eye Involved						0.238[1]
Right	15 (12.1%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	16 (10.9%)	
Left	16 (12.9%)	3 (50.0%)	0 (0.0%)	1 (11.1%)	20 (13.6%)	
Both	93 (75.0%)	3 (50.0%)	7 (87.5%)	8 (88.9%)	111 (75.5%)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

with systemic autoimmune conditions. Management strategies include corticosteroids, immunomodulatory agents, and biologics, tailored to disease severity and underlying etiology [2].

Methods: This retrospective cohort study includes patients ≥18 years diagnosed with uveitis seen at Mayo Clinic Florida Rheumatology Clinic between 10/12/2021 and 10/12/2023. Patients were identified using ICD-10 and location codes. Data include demographics, diagnostic testing, ocular features, serologies, imaging, comorbidities, treatments, morbidity, and mortality. Categorical and continuous variables are analyzed using Fisher's exact and Kruskal-Wallis tests, respectively. Time to remission was assessed using Kaplan-Meier analysis. The primary objective was to investigate the epidemiology,

Table 2. Diagnosis, treatment, complications, and outcomes of uveitis by anatomical subtype. Anterior uveitis was the most common (84.5%), with iritis and iridocyclitis predominating. Cataract and glaucoma were the most frequent complications. Corticosteroids were widely used, but mycophenolate, adalimumab, and methotrexate showed greater association with remission in posterior and panuveitis. Overall remission was achieved in 92.6% of patients, with relapse rates highest in intermediate and panuveitis.

Table 2. Diagnosis, Complications, Treatment, Relapses, and Remission

Uveitis Diagnosis by Intraocular Compartment						
Diagnosis	Anterior Uveitis (N=125)	Intermediate Uveitis (N=6)	Posterior Uveitis (N=8)	Panuveitis (N=9)	Total (N=148)	P-value
Iritis	95 (76.0%)	1 (16.7%)	0 (0.0%)	1 (11.1%)	97 (65.5%)	<.001[1]
Iridocyclitis	31 (24.8%)	2 (33.3%)	0 (0.0%)	1 (11.1%)	34 (23.0%)	0.318[1]
Pars planitis	1 (0.8%)	4 (66.7%)	1 (12.5%)	2 (22.2%)	8 (5.4%)	<.001[1]
Posterior cyclitis	1 (0.8%)	0 (0.0%)	2 (25.0%)	0 (0.0%)	3 (2.0%)	0.013[1]
Complications Due to Uveitis						
Complications	Anterior Uveitis (N=125)	Intermediate Uveitis (N=6)	Posterior Uveitis (N=8)	Panuveitis (N=9)	Total (N=148)	P-value
Cataract	49 (39.2%)	4 (66.7%)	4 (50.0%)	5 (55.6%)	62 (41.9%)	0.400[1]
Posterior Synechiae	10 (8.0%)	0 (0.0%)	0 (0.0%)	3 (33.3%)	13 (8.8%)	0.086[1]
Hypopyon	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	>0.999[1]
None	56 (44.8%)	2 (33.3%)	1 (12.5%)	2 (22.2%)	61 (41.2%)	0.204[1]
Glaucoma	23 (18.4%)	1 (16.7%)	3 (37.5%)	5 (55.6%)	32 (21.6%)	0.035[1]
Keratoconjunctivitis Sicca	3 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.0%)	>0.999[1]
[1]Fisher Exact p-value						
Treatment of Uveitis by Intraocular Compartment						
Treatment	Anterior Uveitis (N=125)	Intermediate Uveitis (N=6)	Posterior Uveitis (N=8)	Panuveitis (N=9)	Total (N=148)	P-value
Corticosteroids	124 (99.2%)	6 (100.0%)	7 (87.5%)	8 (88.9%)	145 (98.0%)	0.063[1]
Cyclophosphamide	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	1 (0.7%)	0.095[1]
Mycophenolate	7 (5.6%)	2 (33.3%)	2 (25.0%)	5 (55.6%)	16 (10.8%)	<.001[1]
Azathioprine	5 (4.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	6 (4.1%)	0.484[1]
Cyclosporine	5 (4.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	6 (4.1%)	0.484[1]
Methotrexate	41 (32.8%)	2 (33.3%)	3 (37.5%)	6 (66.7%)	52 (35.1%)	0.225[1]
Etanercept	5 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (3.4%)	>0.999[1]
Adalimumab	56 (44.8%)	3 (50.0%)	6 (75.0%)	3 (33.3%)	68 (45.9%)	0.336[1]
Infliximab	14 (11.2%)	1 (16.7%)	2 (25.0%)	1 (11.1%)	18 (12.2%)	0.392[1]
Hydroxychloroquine	12 (9.6%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	13 (8.8%)	>0.999[1]
Sulfasalazine	4 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (2.7%)	>0.999[1]
Rituximab	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	>0.999[1]
Tocilizumab	2 (1.6%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	3 (2.0%)	0.268[1]
Number of relapses						0.297[1]
Yes, Mean (SD)	2.2 (2.37)	4.0 (4.00)	2.8 (2.23)	4.1 (3.63)	2.4 (2.53)	
Remission						0.668[2]
Yes, n (%)	115 (92.0%)	6 (100.0%)	7 (87.5%)	9 (100.0%)	137 (92.6%)	
Treatment Leading to Remission						
Corticosteroids, n (%)	104 (83.2%)	4 (66.7%)	4 (50.0%)	7 (77.8%)	119 (80.4%)	0.108[2]
Adalimumab, n (%)	34 (27.2%)	2 (33.3%)	6 (75.0%)	2 (22.2%)	44 (29.7%)	0.037[2]
Mycophenolate, n (%)	5 (4.0%)	1 (16.7%)	1 (12.5%)	4 (44.4%)	11 (7.4%)	<.001[2]
Cyclophosphamide, n (%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	1 (0.7%)	<.001[2]
Tocilizumab, n (%)	0 (0.0%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	1 (0.7%)	<.001[2]
Methotrexate, n (%)	21 (16.8%)	1 (16.7%)	2 (25.0%)	4 (44.4%)	28 (18.9%)	0.221[2]
Infliximab, n (%)	10 (8.0%)	0 (0.0%)	0 (0.0%)	2 (22.2%)	12 (8.1%)	0.303[2]

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

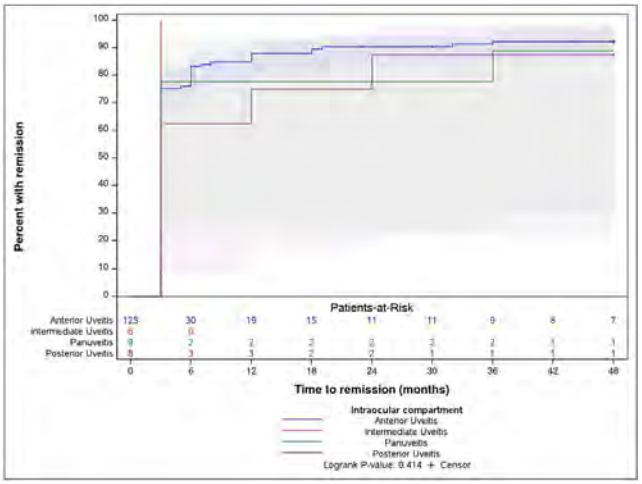


Figure 1: Kaplan-Meier survival analysis showing time to remission among patients with anterior, intermediate, posterior, and panuveitis over a 48-month period. Most patients with anterior uveitis achieved early remission, while posterior and panuveitis cases showed slower remission trends. Shaded areas represent 95% confidence intervals. No statistically significant difference in time to remission was observed between uveitis types (Log-rank test, p = 0.414).

clinical associations, and outcomes of uveitis. Secondary objectives included identifying risk factors, evaluating diagnostic strategies, and determining the most effective treatment regimens. A p-value < 0.05 was considered significant.

Results: A total of 148 adult patients with uveitis were analyzed: anterior (n=125), intermediate (n=6), posterior (n=8), and panuveitis (n=9). The mean age was 51.7 years, and 114 (77%) were female. Most patients were White (76.4%) and non-Hispanic (88.5%). Bilateral involvement was observed in 75.5% of cases (Table 1). Anterior uveitis was most prevalent (84.5%), with iritis being the most common subtype (65.5%). Sarcoidosis was significantly associated with intermediate/posterior uveitis (p=0.029). Visual acuity was preserved in most patients, but those with panuveitis had higher rates of visual impairment. Glaucoma (21.6%) and cataract (41.9%) were notable complications, especially in posterior and panuveitis (p=0.035). Corticosteroids were administered in 98% of cases; topical use predominated, though intraocular delivery was more frequent in posterior/panuveitis (p=0.006). Methotrexate (35.1%) and adalimumab (45.9%) were the most used immunosuppressants. Mycophenolate use varied significantly across types (p< 0.001). Remission was achieved in 92.6% of patients (Figure 1). Adalimumab was associated with higher remission in posterior/panuveitis (p=0.037), and mycophenolate and methotrexate were also linked to remission (Table 2).

Conclusion: This retrospective study demonstrates high remission rates in adult uveitis patients, with 137 (92.6%) achieving remission. Anterior uveitis was the most common subtype, accounting for 115 cases (92.0%). Corticosteroids were widely used, but adalimumab and mycophenolate were significantly effective in posterior/panuveitis. Early diagnosis and targeted therapy are key to improving uveitis outcomes.

References:

[1] Thorne JE, Skup M, Tundia N, et al. *JAMA Ophthalmol*. 2016;134(11):1237–1245.
[2] Nguyen QD, Merrill PT, Jaffe GJ, et al. *Lancet*. 2016;388(10050):1183–1192.

Disclosure: A. Srivastava: None; **J. Valecha**: None; **S. Mumtaz**: None; **C. Harvey**: None; **F. Berianu**: None; **V. Majithia**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2019

Incidence of Coronavirus Disease 2019 in Participants with IgG4-Related Disease Treated with Inebilizumab in the MITIGATE Study

Arezou Khosroshahi[1], Emma Culver[2], Wen Zhang[3], Kazuichi Okazaki[4], Yoshiya Tanaka[5], Matthias Lohr[6], nicolas schleinitz[7], Xinxin Dong[8], Sue Cheng[8], Daniel Cimbora[8] and John Stone[9], [1]Emory University, Atlanta, GA, [2]John Radcliffe Hospital; University of Oxford, Oxford, United Kingdom, [3]Peking Union Medical College Hospital, Dong Cheng Qu, China (People's Republic), [4]Kansai Medical University Kori Hospital, Osaka, Japan, [5]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [6]Karolinska Institutet, Stockholm, Sweden, [7]Aix Marseille university, AP-HM, Marseille, France, [8]Amgen, Thousand Oaks, CA, [9]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The potential of B-cell-depleting therapies to diminish humoral responses is recognized, but whether this leads to an increased risk of Coronavirus Disease 2019 (COVID-19) remains unknown. Inebilizumab (INEB) is a humanized, glycoengineered, CD19-directed, monoclonal antibody that depletes B cells, including plasmablasts and some plasma cells, effectively in a targeted manner. MITIGATE (NCT04540497) is an international, randomized, blinded, placebo (PBO)-controlled Phase 3 trial that evaluates the safety and efficacy of INEB as treatment for IgG4 related disease (IgG4-RD). This ad hoc analysis examined whether INEB treatment is associated with an increased risk of COVID-19 infection in adult participants with IgG4-RD.

Methods: Primary results of the MITIGATE trial have been previously reported (Stone et al, 2024). Eligible participants were randomized 1:1 to inebilizumab or placebo and were treated on day 1, day 15, and week 26 of the 1-year randomized controlled period (RCP). Ad hoc analyses were performed to assess the risk of COVID-19 infections with INEB treatment, as COVID-related endpoints were not prespecified. First participant was enrolled October 26, 2020, after COVID-19 was initially reported (December 2019) and before the first vaccine received approval (December 2020). To determine the relationship between COVID-19 infections and immune response, the lowest recorded values of IgG, IgM, and IgA were measured and compared among participants with COVID-19 infections. Vaccination status, incidence of COVID-19, and safety were evaluated.

Results: In the trial population, 28.4% (n=19/67) of PBO-treated and 29.4% (n=20/68) of INEB-treated participants had received a COVID-19 vaccination. COVID-19 infection was reported in 13 (19.4%) PBO-treated and in 17 (25.0%) INEB-treated participants. Most infections were in participants < 65 years of age (84.6% PBO, 58.9% INEB). The majority of infections were mild [Grade 1; PBO: 7/13 (53.8%); INEB: 11/17 (64.7%)] or moderate [Grade 2; PBO: 6/13 (46.2%); INEB: 5/17 (29.4%)]. Serious COVID-19 occurred in 0 PBO-treated and 2 INEB-treated participants, both requiring hospitalizations, but were not life-threatening (Table 1). Both of these subjects had been vaccinated for COVID-19 prior to COVID-19 infection. There was no significant association between immunoglobulin reductions and occurrence of serious COVID.

Conclusion: Treatment with INEB was not associated with a higher incidence or severity of COVID-19 compared with placebo. Despite B-cell depletion, infections were mostly mild, and serious infections were infrequent. These findings support the safety of INEB in the context of the COVID-19 pandemic.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. COVID-19 in MITIGATE clinical trial (Randomized Control Period)

	Placebo (N = 67)	Inebilizumab (N = 68)
COVID-19 vaccine, n (%)		
Yes[a]	19 (28.4)	20 (29.4)
Before 1st dose	12 (17.9)	7 (10.3)
On/After 1st dose	13 (19.4)	16 (23.5)
Date not reported	1 (1.5)	0
Not reported	48 (71.6)	48 (70.6)
COVID-19 infections,[b] n (%)		
<65 years	11/13 (84.6)	10/17 (58.8)
≥65 years	2/13 (15.4)	7/17 (41.2)
Vaccine status, n (%)		
Yes (ever received)	3/13 (23.1)	6/17 (35.3)
No (never received)	10/13 (76.9)	11/17 (64.7)
Severity,[c] n (%)		
Grade 1	7/13 (53.8)	11/17 (64.7)
Grade 2	6/13 (46.2)	5/17 (29.4))
Grade 3	0	1/13 (5.9)
Grade ≥4	0	0
COVID-19 related hospitalization,[b] n (%)	0	2 (2.9)

[a]'Before 1st dose', 'On/after 1st dose' and 'Date not reported' are not mutually exclusive.
[b]The AE terms included for the Covid-19 infection are: COVID-19 and COVID-19 pneumonia.
[c]If a subject has multiple occurrences; the worst grade will be used.

Disclosure: A. Khosroshahi: Amgen, 1, 2; **E. Culver**: Amgen, 1, 2, Zenus, 2; **W. Zhang**: None; **K. Okazaki**: Amgen, 1; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **M. Lohr**: Amgen, 1; **n. schleinitz**: Amgen, 1, 2; **X. Dong**: Amgen, 3, 11; **S. Cheng**: Amgen, 3, 11; **D. Cimbora**: Amgen, 3, 11; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2.

Abstract Number: 2020

Inebilizumab Efficacy and Safety in Patients with Common, Urgent, and Fibrotic Organ Manifestations of IgG4-RD: Subgroup Analyses from the MITIGATE Trial

Arezou Khosroshahi[1], Emma Culver[2], Wen Zhang[3], Kazuichi Okazaki[4], Yoshiya Tanaka[5], Matthias Lohr[6], nicolas schleinitz[7], Xinxin Dong[8], Sue Cheng[8], Daniel Cimbora[8] and John Stone[9], [1]Emory University, Atlanta, GA, [2]John Radcliffe Hospital; University of Oxford, Oxford, United Kingdom, [3]Peking Union Medical College Hospital, Dong Cheng Qu, China (People's Republic), [4]Kansai Medical University Kori Hospital, Osaka, Japan, [5]University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, [6]Karolinska Institutet, Stockholm, Sweden, [7]Aix Marseille university, AP-HM, Marseille, France, [8]Amgen, Thousand Oaks, CA, [9]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a progressive, systemic, fibroinflammatory disease characterized by unpredictable and recurring flares, leading to organ damage and decreased quality of life. Inebilizumab (INEB) is a humanized, glycoengineered, CD19-directed, monoclonal antibody that depletes CD19+ B cells, including plasmablasts and some plasma cells, effectively in a targeted manner. MITIGATE (NCT04540497) is an international, randomized, blinded, placebo (PBO)-controlled Phase 3 trial that evaluated the safety and efficacy of INEB as treatment for IgG4-RD, and met its primary endpoint (reduction in flare risk, INEB vs. PBO) and all key secondary endpoints.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Here, we evaluate the safety and efficacy of INEB across MITIGATE subgroups defined by baseline organ involvement, with a focus on organs most commonly affected in the study population, organs with potentially urgent manifestations, and organs characteristic of the fibrotic phenotype of IgG4-RD.

Methods: MITIGATE study design and results have been previously reported (Stone et al, NEJM 2024). All participants had experienced a recent flare (prior to screening) that required glucocorticoid (GC) treatment. Post hoc subgroup analyses of efficacy and safety were conducted in participants on the basis of the organs involved in this recent flare. Subgroups were defined by the most common organs (affecting at least 20% of participants), those with urgent or severe manifestations: pancreas, kidney, bile ducts, aorta and large blood vessels, and orbits; and those associated with the fibrotic phenotype of IgG4-RD: retroperitoneum, mediastinum, mesentery, thyroid, and meninges (Lanzillotta et al., 2023).

Results: 135 participants were randomized and received at least one dose of INEB (n=68) or PBO (n=67). The spectrum of organ involvement at baseline was generally well balanced between the 2 treatment groups (Table 1). INEB treatment reduced the risk of flare relative to PBO in all organ subgroups, with HR values similar to that of the overall population (HR 0.13) (Table 2). The greatest treatment effect was observed in participants with pancreatic (HR 0.03), bile duct (HR 0.00), and kidney (HR 0.08) involvement. The orbital and fibrotic organ groups also experienced clear benefit of INEB on flare risk reduction.

Proportions of participants achieving flare-free, corticosteroid-free complete remission at Week 52 were increased by INEB in all organ subgroups with sufficient representation to permit analysis (Table 3). Proportion of subjects requiring on-study

Table 1: Subgroups Defined by Baseline IgG4-RD Organ Involvement

Subgroup	PBO, N=67	INEB, N=68	Overall, N=135
Most Common (≥20%) Organs, n (%)			
Lymph node(s)	26 (38.8)	26 (38.2)	52 (38.5)
Pancreas[a]	24 (35.8)	27 (39.7)	51 (37.8)
Submandibular glands	20 (29.9)	31 (45.6)	51 (37.8)
Lacrimal glands	18 (26.9)	27 (39.7)	45 (33.3)
Kidney[a]	19 (28.4)	21 (30.9)	40 (29.6)
Bile ducts[a]	15 (22.4)	13 (19.1)	28 (20.7)
Parotid glands	10 (14.9)	17 (25.0)	27 (20.0)
Additional Urgent Organs, n (%)			
Aorta and large blood vessels	3 (4.5)	5 (7.4)	8 (5.9)
Orbits	9 (13.4)	7 (10.3)	16 (11.9)
Fibrotic Organs[b], n (%)	8 (11.9)	10 (14.7)	18 (13.3)

[a]Also classified as an urgent organ.
[b]Includes retroperitoneum, mediastinum, mesentery (sclerosing mesenteritis), thyroid, and meninges.

Table 2: Subgroup Analysis of Time to the First Treated and Adjudication Committee-determined IgG4-RD Flare During RCP

Subgroup	PBO, N=67 n (%)	INEB, N=68 n (%)	HR (95% CI)
Most Common (≥20%) Organs, n (%)			
Lymph node(s)	18/26 (69.2)	3/26 (11.5)	0.13 (0.04, 0.44)
Pancreas[a]	17/24 (70.8)	1/27 (3.7)	0.03 (0.00, 0.21)
Submandibular glands	9/20 (45.0)	3/31 (9.7)	0.17 (0.05, 0.63)
Lacrimal glands	10/18 (55.6)	2/27 (7.4)	0.10 (0.02, 0.47)
Kidney[a]	12/19 (63.2)	2/21 (9.5)	0.08 (0.02, 0.36)
Bile ducts[a]	12/15 (80.0)	0/13 (0)	0.00 (0.00, N/A[b])
Parotid glands	6/10 (60.0)	2/17 (11.8)	0.16 (0.03, 0.79)
Additional Urgent Organs, n (%)			
Aorta and large blood vessels	0/3 (0)	0/5 (0)	N/A[b]
Orbits	8/9 (88.9)	1/7 (14.3)	N/A[b]
Fibrotic Organs[c], n (%)	3/8 (37.5)	0/10 (0)	N/A[b]

[a]Classified as an urgent organ.
[b]N/A: Statistical comparisons not calculated due to very low event rates or small subgroup size.
[c]Includes retroperitoneum, mediastinum, mesentery (sclerosing mesenteritis), thyroid, and meninges.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Subgroup Analysis of The Proportion of Subjects Achieving Flare-Free, Corticosteroid-Free Complete Remission[a] at Week 52 (RCP)

Subgroup	PBO, N=67 n (%)	INEB, N=68 n (%)	Odds ratio (95% CI)	Nominal P-value[b]
Most Common (≥20%) Organs, n (%)				
Lymph node(s)	5/26 (19.2)	12/26 (46.2)	3.37 (0.94, 11.98)	.0612
Pancreas[c]	4/24 (16.7)	18/27 (66.7)	10.84 (2.74, 42.90)	.0007
Submandibular glands	6/20 (30.0)	17/31 (54.8)	2.85 (0.85, 9.49)	.0864
Lacrimal glands	4/18 (22.2)	16/27 (59.3)	5.38 (1.35, 21.34)	.0168
Kidney[c]	4/19 (21.1)	12/21 (57.1)	5.08 (1.19, 21.68)	.0281
Bile ducts[c]	2/15 (13.3)	11/13 (84.6)	35.75 (4.30, 297.25)	.0009
Parotid glands	4/10 (40.0)	10/17 (58.8)	2.02 (0.40, 10.19)	.3926
Additional Urgent Organs, n (%)				
Aorta and large blood vessels	1/3 (33.3)	4/5 (80.0)	N/A[d]	N/A[d]
Orbits	1/9 (11.1)	4/7 (57.1)	N/A[d]	N/A[d]
Fibrotic Organs[e], n (%)	2/8 (25.0)	6/10 (60.0)	4.5 (0.59, 34.61)	.1484

[a]Flare-free, corticosteroid-free complete remission is defined as the absence of evident disease activity at week 52; defined as an IgG4-RD Responder Index score of 0 or determination by the investigator that no disease activity is present on the basis of physical, laboratory, pathology, or other evidence), no AC-determined flare during the RCP of the trial, and no corticosteroid treatment for flare or disease control beyond the protocol required prednisone taper.
[b]P-values should be interpreted with caution due to the questionable reliability of the statistical test based on the small sample sizes.
[c]Classified as an urgent organ.
[d]N/A: Statistical comparisons not calculated due to very low event rates or small subgroup size.
[e]Includes retroperitoneum, mediastinum, mesentery (sclerosing mesenteritis), thyroid, and meninges.

GCs for IgG4-RD control and mean daily dose of GCs per subject were substantially reduced with INEB vs. PBO in all organ subgroups with sufficient representation to permit analysis. Safety outcomes will be presented.

Conclusion: The MITIGATE trial demonstrates consistent safety and efficacy of INEB across all IgG4-RD subgroups defined on the basis of organ involvement at study baseline, including the most common organs, urgent organs, and organs characteristic of the fibrotic disease phenotype.

Disclosure: A. Khosroshahi: Amgen, 1, 2; **E. Culver**: Amgen, 1, 2, Zenus, 2; **W. Zhang**: None; **K. Okazaki**: Amgen, 1; **Y. Tanaka**: AbbVie, 6, AstraZeneca, 6, BMS, 6, Boehringer Ingelheim, 6, Chugai, 6, Daiichi Sankyo, 6, Eisai, 6, Eli Lilly & Co., 6, Gilead, 6, GSK, 6, IQVIA, 6, Otsuka, 6, Taisho, 6, UCB, 6; **M. Lohr**: Amgen, 1; **n. schleinitz**: Amgen, 1, 2; **X. Dong**: Amgen, 3, 11; **S. Cheng**: Amgen, 3, 11; **D. Cimbora**: Amgen, 3, 11; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2.

Abstract Number: 2021

Can Colchicine Be a Therapeutic Option for Patients with Ankylosing Spondylitis?

Muhammed Bahaddin Ates[1] and serdal Ugurlu[2], [1]Cerrahpasa Faculty of Medicine, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing Spondylitis (AS) is a subtype of spondyloarthritis (SpA), a group of inflammatory diseases. AS is influenced by a complex interplay of factors arising from both autoimmune and autoinflammatory mechanisms, with key contributors including HLA-B27, alterations in the IL-23 signaling pathway, and mutations in the MEFV gene. Among these factors, MEFV gene mutations are the cause of familial Mediterranean fever (FMF), which is considered one

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1- Patient's clinical scores before and after the treatment

	Before colchicine therapy	After colchicine therapy	P values
Average VAS scores (total back pain), mean±SD	6,69±3,65	5,48±2,65	0,145
Average BASDAI scores, mean±SD	6,17±2,56	5,05±2,26	0,068
Average VAS scores in M694V heterozygous patients, mean±SD	6,88±3,51	5,77±2,72	0,217
Average BASDAI scores in M694V heterozygous patients, mean±SD	5,64±3,16	5,24±2,27	0,47
Average VAS scores in M694V homozygous patients, mean ± SD	8,33±1,96	4,5±2,88	0,011
Average BASDAI scores in M694V homozygous patients, mean±SD	6,68±1,94	4,38±2,38	0,048

of the prototypes of autoinflammatory diseases. In the treatment of FMF, the primary targeted pathways are microtubules and IL-1 pathways, which aim to reduce inflammation through autoinflammatory mechanisms.

In this study, we aimed to investigate whether treating FMF with drugs that inhibit autoinflammatory pathways could also lead to a reduction in the symptoms of AS in patients diagnosed with both FMF and AS.

Methods: In this study, 28 patients were enrolled, all of whom had been diagnosed with both Ankylosing Spondylitis (AS) and Familial Mediterranean Fever (FMF) based on the 1984 Modified New York Criteria and Tel-Hashomer Criteria, respectively. Each patient was contacted and asked about the severity of their AS using the BASDAI and VAS back pain scores before and after colchicine treatment, as well as other IL-1 treatments. Additional information, such as M694V mutations, was obtained from their hospital records.

Results: Twenty-eight patients were included in our study. The mean age of the patients was 44.89 ± 10,9 years. The mean duration of AS and FMF was 12.35±6,95 years and 17.71±7,72 years, respectively.

The impact of colchicine on AS severity was assessed using the BASDAI score before and after treatment. The results were not significant for the BASDAI score (p =0,068). Patients were evaluated using the VAS back pain score before and after colchicine treatment. The results were similarly non-significant (p=0,145)(Table 2).

The BASDAI score improvements before and after treatment for patients using canakinumab and anakinra showed no significant results ($p > 0.05$).

Among the 28 patients, 6 had the M694V homozygous mutation, and 9 had the M694V heterozygous mutation. BASDAI scores before and after colchicine treatment showed a significant difference in M694V homozygous patients (p=0,048). No such improvement in BASDAI scores was observed in patients with M694V heterozygous mutations (p=0,47). VAS back pain scores before and after treatment in M694V homozygous patients also showed significant improvement after colchicine treatment (p=0,011). Similarly to the BASDAI scores, VAS back pain scores remained non-significant in M694V heterozygous patients before and after treatment (p =0,217).

Conclusion: Although colchicine and other IL-1 targeted therapies did not lead to significant clinical improvement in the overall ankylosing spondylitis (AS) patient population, a notable exception was observed in individuals homozygous for the M694V mutation. In this subgroup, colchicine treatment was associated with marked reductions in both BASDAI and VAS back pain scores, suggesting a potential genotype-specific therapeutic response that warrants further investigation.

Disclosure: M. Ates: None; **s. Ugurlu**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2022

Clinical Predictors of Macrophage Activation Syndrome and Treatment Outcomes in Adult-Onset Still's Disease: A 24-Year Single-Center Experience

Oguzhan Omer Kizilkaya[1], **Beste Acar**[1], Berkay Aktas[1], Ozgur Can Kilinc[1] and serdal Ugurlu[2], [1]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Adult-onset Still's disease (AOSD) is a rare autoinflammatory disorder with heterogeneous manifestations. Its most severe complication, macrophage activation syndrome (MAS), occurs in up to 15% of cases and carries high mortality. Early identification of high-risk patients remains challenging and data on long-term outcomes are limited. This study aimed to identify clinical predictors of MAS and assess treatment outcomes and survival in a large AOSD cohort.

Methods: This retrospective study included 93 adults diagnosed with AOSD between 2000 and 2024 at a tertiary university hospital. All fulfilled Yamaguchi criteria and MAS was diagnosed per HLH-2004 and 2016 EULAR/ACR/PRINTO criteria. Demographic, clinical, laboratory and treatment data were included. Pouchot's disease severity scores were calculated based on presenting symptoms. Associations with MAS were evaluated using univariate and multivariate logistic regression.

Table 1. Demographic Features and Clinical Manifestations of Patients

Parameter	Value
Gender (Female)	%64,5 (60/93)
Survival (Alive)	%94,0 (79/84)
Age of onset, mean ± SD, years	33.60 ± 14.42
Diagnostic delay, mean ± SD, years	1.33 ± 2.8
Disease Severity Score, median (IQR, 25-75)	5 (4.0–6.75)
Fever	%93,4 (85/91)
Rash	%65,6 (59/90)
Arthritis	%57,8 (52/90)
Arthralgia	%82,2 (74/90)
Pleuritis	%10,0 (9/90)
Pericarditis	%10,0 (9/90)
Myalgia	%51,7 (46/89)
Pharyngitis	%55,6 (50/90)
Hepatomegaly	%15,6 (14/90)
Splenomegaly	%23,3 (21/90)
Abdominal Pain	17.24% (15/87)
Odynophagia	%40,7 (33/81)
MAS	%14,1 (13/92)
Hypertriglyceridemia	%32,8 (22/67)
Proteinuria	%22,7 (20/88)
LAP	%39,33 (35/89)

LAP: lymphadenopathy, MAS: Macrophage Activation Syndrome, SD: standart deviation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Univariate and Multivariate Logistic Regression Analysis of Risk Factors for MAS

MAS Analysis	Univariate analysis			Multivariate analysis		
	P value	Odds ratio	Confidence interval	P value	Odds ratio	Confidence interval
Ferritin at first visit	0.0209	1.00022	[0.9998, 1.0002]	0.0489	1.0001	[1.0001, 1.0017]
Age	0.0101	0.91	[0.87217, 0.98740]	0 0726	0.7590	[0.5681, 1.0147]
Proteinuria	0.00119	8.27	[7.29359, 9.37712]	0.0888	110.28	[0.491, 24,618]
Anemia	0.017114	6.88	[4.45978, 10.61361]	0.0949	0.094	[0.0058, 1.508]
Disease Severity	0.00058	2.72	[0.48650, 15.20729]	0.0204	3.7	[1.22432, 11.19667]
Phenotype	0.02248	11.4	[4.46345, 29.11647]	0.2458	58.5	[0.06058, 56597.49470]

MAS: Macrophage Activation Syndrome; NA: not available.

Table 3. Treatment choice and response rates of AOSD patients.

	Usage Rate	Response Rate
Stopped Corticosteroids	48.24% (41/85)	-
Methotrexate Use	91.30% (84/92)	66.67% (36/54)
Corticosteroid Use	93.33% (84/90)	NA
Leflunomide Use	10.98% (9/82)	44.44% (4/9)
Anti-TNF	12.50% (11/88)	33.33% (3/9)
Tocilizumab	31.39% (27/86)	58.33% (14/24)
Anakinra	47.19% (42/89)	55.26% (21/38)
Canakinumab	15.91% (14/88)	30.77% (4/13)
HCQ Use	38.89% (35/90)	51.85% (14/27)
JAKi	3.37% (3/89)	100% (3/3)
Lowest GC dosage, median (IQR, 25-75)	0 (0,0-5,0)	-
Highest GC dose, median (IQR, 25-75)	22,0 (10,0-40,0)	-

Anti-TNF: anti-tumor necrosis factor; GC: glucocorticoids HCQ:hydroxychloroquine;IQR: interquartile range; JAKi: janus kinase inhibitors; NA: not available.

Results: The mean age at onset was 33.6 ± 14.4 years and 64.5% of the patients were female. Common symptoms are summarized in Table 1. MAS developed in 14.1% and was associated with younger age at onset (27.7 vs. 34.9 years; p=0.037) and higher baseline ferritin (p=0.0489). Multivariate analysis confirmed elevated ferritin (p=0.0489) and higher Pouchot's scores (p=0.0204) as independent MAS predictors, as detailed in Table 2.

Diagnostic delay averaged 1.33 ± 2.8 (IQR, 25-75:0-1) years and was associated with lower methotrexate response (p=0.0457) and corticosteroid tapering success (p< 0.01). Patients with shorter delays achieved steroid-free remission more frequently (median 4 vs. 8 years; p< 0.01).

Glucocorticoids were prescribed to 93.3% of patients, methotrexate to 91.3% and anakinra to 47.2%. Tocilizumab (31.4%) and canakinumab (15.5%) were also used. JAK inhibitors achieved complete remission in all treated patients (3/3) including one with MAS. Steroid discontinuation was achieved in 37.8% of patients. Treatment responses are shown in Table 3. Overall survival was 94% with MAS accounting for two deaths.

Conclusion: Elevated ferritin and higher Pouchot's scores independently predict MAS, supporting their use in early risk stratification. Diagnostic delay reduces treatment response and remission, highlighting the importance of prompt diagnosis. Although glucocorticoids remain the initial therapy, biologics such as anakinra and tocilizumab combined with JAK inhibitors are effective for remission in refractory cases. Early diagnosis and phenotype-guided treatment, favoring IL-1 inhibitors for systemic manifestations and IL-6 inhibitors for articular involvement, may further improve outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: O. Kizilkaya: None; **B. Acar**: None; **B. Aktas**: None; **O. Kilinc**: None; **s. Ugurlu**: None.

Abstract Number: 2023

Isolated Anti-Ro52 Antibody Positivity Is Associated with Increased Cancer Risk and Distinct Malignancy Patterns: A Retrospective Cohort Study from a Single Tertiary Center

Carmen Secada-Gómez[1], Ligia Gabrie-Rodriguez[2], Hector Ulloa-Alvarado[3], Giuliano Boselli[4], Camilo Veloza-Morales[5], Diana Prieto-Peña[6], juan Irure-Ventura[7], Marcos López-Hoyos[8] and Ricardo Blanco[1], [1]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Servicio Cántabro de Salud, Atención Primaria, Santander, Spain, Santander, Cantabria, Spain, [4]Rheumatology Division, Hospital Universitario Miguel Servet , Zaragoza, Spain, Zaragoza, Aragon, Spain, [5]Rheumatology Division, Hospital Universitario Joan XXIII, Tarragona, Spain, Tarragona, Catalonia, Spain, [6]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [7]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Cantabria, Spain, [8]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-Ro52 antibodies are frequently detected in patients with systemic autoimmune rheumatic diseases (SARDs). Emerging evidence suggests a potential link between isolated anti-Ro52 positivity and increased malignancy risk.

Our aim was to evaluate: a) the association between anti-Ro52 antibody status (negative, isolated, or combined with other autoantibodies) and malignancy risk; b) whether malignancy types differ according to anti-Ro52 status.

Methods: We conducted a retrospective study of 739 patients who underwent immunoblot testing for autoimmune inflammatory myopathies or systemic sclerosis at a university hospital between November 2017 and October 2023. Patients were stratified by anti-Ro52 status: negative, isolated positivity, or combined with other myositis- or sclerosis-related antibodies. Clinical records were reviewed to confirm SARDs diagnoses using established classification criteria and to identify

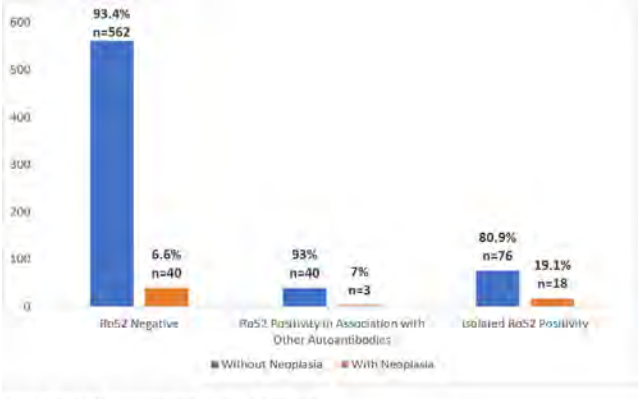


FIGURE. Distribution of Ro52 Positivity and Negativity in Patients With and Without Neoplasia

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Anti-Ro52 Antibodies Status			
		Ro52 Positivity		
	Ro52 Negative n=602	In Association with Other Autoantibodies n=43	Isolated Ro52 n=94	p-value
Age (years), median [IQR]	59 [46-70]	66 [50-75]	62.5 [54.5-72]	.007[a]
Male/female, n (% male)	206 (34)	11 (25)	21 (22)	.046[b]
Autoimmune rheumatic diseases, n (%)	379 (63)	39 (91%)	78 (83%)	.000[b]
Neoplasia, n (%)	40 (6.6)	3 (7)	18 (19.1)	.001[c]
Type of neoplasia, n (%)				.001[c]
Lung Cancer	10 (25)	1 (33.3)	4 (22)	
Hematological Cancer	6 (15)	0	1 (5.6)	
Colorectal Cancer	5 (12.5)	0	1 (5.6)	
Breast Cancer	5 (12.5)	0	1 (5.6)	
Prostate Cancer	3 (7.5)	0	0	
Gastric Cancer	2 (5)	0	0	
Ovarian Cancer	0	0	4 (22)	
Urothelial Cancer	0	0	4 (22)	
Other	7 (17.5)	2 (66.7)	3 (16.7)	

[a]p values according to independent-samples Kruskal-Wallis test. [b]p values according to Pearson Chi-Square test. [c]p values according to Fisher's Exact Test. IQR: interquartile range; n: number.

TABLE. Demographic, Clinical, and Neoplastic Characteristics of Patients Categorized by Anti-Ro52 Antibody Status

malignancies through clinical and/or pathological documentation. Associations were analyzed using logistic regression adjusted for age, sex, and SARDs diagnosis.

Results: Malignancy was identified in 61 of 739 patients (8.25%). Anti-Ro52 status distribution: negative (81.4%, n=602), isolated (12.7%, n=94), and combined positivity (5.8%, n=43). In multivariable analysis, older age and isolated Ro52 positivity were independently associated with increased malignancy risk. Each additional year of age increased risk by 5.3% (OR 1.053; 95% CI 1.031–1.076; p< 0.001). Isolated Ro52 positivity conferred a nearly fourfold increased risk versus seronegative patients (OR 3.968; 95% CI 2.049–7.687; p< 0.001). SARDs diagnosis was inversely associated with malignancy (OR 0.426; 95% CI 0.240–0.759; p=0.004). No significant associations were found for sex (OR 0.693; 95% CI 0.392–1.224; p=0.206) or Ro52 positivity combined with other antibodies (OR 1.063; 95% CI 0.297–3.807; p=0.925).

A secondary analysis revealed significant differences in malignancy types by Ro52 status (p=0.001). Ro52-positive patients showed higher frequencies of ovarian, lung, and urothelial cancers, while the Ro52-negative group exhibited a broader, more heterogeneous profile, including colorectal, gastric, and hematological malignancies.

Conclusion: Isolated anti-Ro52 positivity and advancing age are independent predictors of malignancy. The distinct cancer spectrum among Ro52-positive patients suggests the importance of tailored oncologic surveillance in this subgroup.

Disclosure: C. Secada-Gómez: None; **L. Gabrie-Rodriguez**: None; **H. Ulloa-Alvarado**: None; **G. Boselli**: None; **C. Veloza-Morales**: None; **D. Prieto-Peña**: None; **j. Irure-Ventura**: None; **M. López-Hoyos**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2024

Racial Disparities in Outcomes Among Patients With Neuromyelitis Optica: A Global Population-Based Study

Chukwuemelie Okeke[1], Justin Riley Lam[2], Queeneth Edwards[3] and Ufuoma Mamoh[4], [1]Maimonides Medical Center, Brooklyn, NY, [2]Jefferson Einstein Hospital, Philadelphia, PA, [3]Department of Epidemiology and Biostatistics, Jiann-Ping Hsu College of Public Health, Georgia Southern University, Statesboro, GA, [4]Medstar Health Georgetown University Internal Medicine Residency Program, Baltimore, MD

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Neuromyelitis optica (NMO) is a rare, chronic, immune-mediated, demyelinating disorder predominantly affecting the optic nerve and spinal cord. Despite increasing awareness, racial disparities in NMO outcomes remain poorly characterized.

Methods: This retrospective cohort study used TriNetX, a global federated health research network of 144 healthcare organizations. Two Cohorts were defined: Cohort A (Black or African American with Neuromyelitis Optica; n= 2,101) and Cohort B (Hispanics or Latinos with NMO; n= 1,007). Inclusion criteria required patients to be 18 years or older with at least an NMO diagnosis within the past 20 years. Exclusion criteria included patients younger than 18 or diagnosed more than 20 years ago.

Propensity score matching (1:1) was performed to balance demographics and comorbidities, including age, sex, obesity, dyslipidemia, diabetes, hypertension, kidney disease, and chronic respiratory disease. The final matched sample included 965 patients per group.

Outcomes assessed included all-cause mortality, stroke, and myocardial infarction (MI).

Results: After matching, both cohorts had similar characteristics (mean age 46 years; 76.7% female). Inflammatory markers such as ESR and CRP were higher in Black patients. All-cause mortality was significantly higher among Black patients compared to Hispanic patients (5.0% vs. 2.7%; OR 1.89, 95% CI 1.16–3.07). MI occurred in 4.4% of Black patients vs. 2.8% of Hispanic patients (OR 1.62, 95% CI 0.98–2.66). Stroke occurred in 3.2% of Black patients compared to 1.5% of Hispanic patients, with a statistically significant difference (OR 2.15, 95% CI 1.13–4.09).

Conclusion: This study's findings underscore significant racial disparities in clinical outcomes among patients with Neuromyelitis Optica. Black patients had higher rates of all-cause mortality, myocardial infarction, and stroke compared to their Hispanic counterparts, despite comparable baseline characteristics. The elevated odds of death and cerebrovascular

Table 1. Demographic Comparison of Blacks and Hispanics – Pre- and Post-Propensity Score Matching

Characteristic	Blacks (Pre-Match, N=2,101)	Hispanics (Pre-Match, N=1,007)	Blacks (Post-Match, N=965)	Hispanics (Post-Match, N=965)
Age (Years)	49.2 ± 15.9	45.9 ± 16.0	46.2 ± 15.2	46.2 ± 15.9
Age at Index	42.0 ± 15.6	39.3 ± 15.7	39.5 ± 14.7	39.6 ± 15.7
Female (%)	83.0%	74.9%	76.7%	76.6%
Male (%)	17.0%	25.1%	23.3%	23.4%
Overweight/Obesity (%)	13.5%	12.1%	10.7%	11.7%
Diabetes (%)	9.8%	8.3%	8.1%	8.3%
Metabolic Disorders (%)	21.0%	19.4%	18.4%	19.1%
Hypertension (%)	24.1%	14.9%	15.2%	15.2%
Kidney Disease (%)	5.2%	3.2%	2.7%	3.3%
Chronic Resp. Disease (%)	10.0%	7.0%	6.4%	7.2%
ESR (mean ± SD)	—	—	29.12 ± 28.27	22.36 ± 22.40
CRP (mean ± SD)	—	—	26.52 ± 50.36	23.56 ± 46.89
Aquaporin-4 IgG Result	—	—	14 Positive 40 Negative 16 Unknown	7 Positive 42 Negative 14 Unknown

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical Outcomes

Outcome	Metric	Blacks (n = 965)	Hispanics (n = 965)	Statistical Test	Hazard Ratio (95% CI)	Odds Ratio (95% CI)
All-cause Mortality	Risk	48 / 965 (5.0%)	26 / 965 (2.7%)	Risk Difference: 0.023	1.764 (1.094–2.844)	1.890 (1.163-3.073)
MI (Ischemic Heart Disease)	Risk	41 / 933 (4.4%)	26 / 940 (2.8%)	Risk Difference: 0.016	1.520 (0.930–2.485)	1.616 (0.980-2.664)
Stroke	Risk	29 / 920 (3.2%)	14 / 937 (1.5%)	Risk Difference: 0.017	2.045 (1.080–3.870)	2.146 (1.126-4.088)

events in the Black cohort suggest potential underlying differences in disease progression, access to care, or treatment response. These results highlight the need for tailored interventions and equitable healthcare delivery to mitigate outcome disparities in NMO.

Disclosure: C. Okeke: None; **J. Lam**: None; **Q. Edwards**: None; **U. Mamoh**: None.

Abstract Number: 2025

Spectrum of Autoantibodies in CNS Demyelinating Diseases: Clinical, Laboratory and Imaging Associations

Anna Rapti[1], Dimitris Karathanasis[2], Sylvia Raftopoulou[1], Charalampos Skarlis[1], **Clio Mavragani**[1] and Maria Eleftheria Evangelopoulos[2], [1]Department of Physiology, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece, [2]First Department of Neurology, School of Medicine, Eginition Hospital, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic autoimmune diseases (SADs) may present with CNS demyelination, mimicking multiple sclerosis (MS), though driven by distinct immunopathogenic mechanisms. While ANA and aPL are commonly reported in MS, the role of specific SAD-related autoantibodies (ANA profile) in CNS demyelination remains unclear. The aims of this study were to characterize the distribution of autoantibodies in this context, investigate potential associations with clinical/ radiological/ laboratory features, compare findings with a control group of MS-spectrum patients and assess the efficacy of therapeutic strategies.

Methods: We prospectively enrolled 147 patients with CNS demyelination and ANA profile reactivity (via immunoblot) over a six-year period (CNS-autoimmune group). Patients were classified as SAD or demyelination with autoimmune features (DAF), based on whether they fulfilled criteria or not. A control group of 249 MS-spectrum patients was included. Clinical, laboratory, and imaging assessments were conducted. Univariate and multivariate analyses were performed between groups and treatment outcomes were analyzed using annualized relapse rates (ARRs).

Results: Clinical autoimmune features among CNS-autoimmune patients were generally mild, with the most common being arthralgias and sicca symptoms. Approximately 4% of unselected consecutive patients presenting with CNS demyelination and 21% of ANA profile-positive individuals were eventually diagnosed with SAD, primarily Sjögren's disease and SLE. The remaining 79% of CNS-autoimmune patients constituted the DAF subset.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Multivariate analysis identified arthritis, cerebellar signs, ANA, anti-Ro52/ Ro60 positivity and the absence of typical brain lesions as independent predictors for SAD compared to DAF diagnosis. Compared to MS-spectrum, ANA, aCL IgM and serum monoclonal band positivity, female sex and the presence of atypical brain lesions were more indicative of SAD. However, no robust model effectively discriminated between DAF and MS-spectrum groups.

Among individual antibody reactivities, anti-Ro antibodies were associated with pyramidal and cerebellar manifestations, while anti-dsDNA, anti-nucleosomes, and anti-PM-Scl100 were linked to cortical clinical features. Additionally, anti-Sm, anti-RNP and anti-PMScl100 antibodies were linked to the least purely typical for MS CNS imaging. Conversely, anti-Jo1 and anti-histones were associated with gadolinium enhancement in MRI and high cerebrospinal fluid IgG index, respectively.

Correlation analysis revealed notable antibody associations (e.g., anti-Ro52 with anti-aquaporin-4; AMA-M2 with aPL IgM). In follow-up, anti-CD20 mAbs were linked to zero relapses and the lowest ARR, significantly outperforming MS disease-modifying drugs, immunosuppression, and no treatment ($p < 0.005$).

Conclusion: Distinct autoantibody profiles in patients presenting with CNS demyelination are associated with specific clinical, radiological and laboratory features. MS-like SAD represents a clearly defined subset in contrast to DAF. Anti-CD20 therapies appear most effective in preventing neurological relapses.

Disclosure: A. Rapti: None; **D. Karathanasis**: None; **S. Raftopoulou**: None; **C. Skarlis**: None; **C. Mavragani**: None; **M. Evangelopoulos**: None.

Abstract Number: 2026

Clinical Features and Treatment Outcomes in Aseptic Abscess Syndrome: A Systematic Review of 104 Cases

Eleni Papachristodoulou[1], Loukas Kakoullis[1], Ratnesh Chopra[2], Chris Derk[3] and Konstantinos Parperis[4], [1]Mount Auburn Hospital, Harvard Medical School, Cambridge, MA, [2]UMass Chan Medical School, Worcester, MA, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Cyprus Medical School, Nicosia, Cyprus

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Aseptic abscess syndrome (AAS) is an inflammatory condition of unknown etiology, characterized by the formation of sterile neutrophilic abscesses that frequently respond to immunosuppressive therapy. We conducted a systematic review of all published AAS cases to describe its manifestations and outcomes.

Methods: This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PROSPERO No. CRD42025641038). We searched PubMed/MEDLINE from inception through January 2025 using the terms "aseptic" and "abscess" or "abscesses" (Figure 1). Case reports and case series providing individual-level data were eligible for inclusion.

Results: A total of 73 studies describing 104 patients were included (54% female; median age: 32.5 years). The most frequently associated conditions were Crohn's disease (n = 34, 33%), ulcerative colitis (n = 21, 20%), and Sweet's syndrome

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(n = 8, 8%), which preceded the diagnosis of AAS in 50% of cases (Table 1). Common presenting symptoms included fever (n = 69, 66%), abdominal pain (n = 38, 37%), weight loss (n = 27, 26%), and pyoderma gangrenosum (n = 20, 19%).

The spleen was the most frequent site of abscess development (n = 71, 68%), followed by the liver (n = 38, 37%), skin (n = 38, 37%), and lymph nodes (n = 33, 32%). The median number of organs involved was 2 (IQR: 2–3), with 49 (47%) patients having abscesses in three or more organs. Among those with available data, the median duration of symptoms before diagnosis was 2.3 months (IQR: 0.8–12).

Most patients received corticosteroids (n = 93, 89%), with abscess resolution reported in 59 of 64 (92%) cases with available outcome data. Additional therapies included DMARDs (n = 47, 45%) and biologics (n = 29, 28%). Among the 74 patients with available data, antibiotics were administered in 42 (57%), for a median duration of 14 days (IQR: 7–26.5).

Among 95 patients with follow-up data, 53 (56%) experienced at least one relapse. The median number of relapses was 1 (IQR: 0–2), with the first relapse occurring at a median of 3 months (IQR: 1–12). Relapses were more frequent among patients with splenic abscesses (64% vs. 35%, p = 0.011), lymph node involvement (71% vs. 48%, p = 0.038), and in those with abscesses affecting ≥3 organs (69% vs. 43%, p = 0.010). Notably, among 28 patients who underwent splenectomy, 20 (71%) experienced a relapse despite the procedure. Logistic regression demonstrated that the odds of relapse increased by 70% with each additional organ involved (OR = 1.70, 95% CI: 1.16–2.48, p = 0.007), and nearly tripled among patients with involvement of ≥3 organs (OR = 2.97, 95% CI: 1.28–6.89, p = 0.011). No deaths were reported.

Table 1. Summary of patient characteristics, management, and outcomes.

Table 1. Summary of patient characteristics, management, and outcomes.	
Variable	Patients (n/N, % of available cases)
Demographics	
Female sex	56/104 (54%)
Median age (IQR), years	32.5 (23.3–50.8)
Associated conditions	
Crohn's disease	34/104 (33%)
Ulcerative colitis	21/104 (20%)
Sweet's syndrome	8/104 (8%)
Systemic autoimmune disease*	3/104 (3%)
Behcet's disease	4/104 (4%)
SAPHO syndrome	2/104 (2%)
Condition pre-dating AAS diagnosis	39/78 (50%)
Clinical Manifestations	
Fever	69/104 (66%)
Abdominal pain	38/104 (37%)
Weight loss	27/104 (26%)
Pyoderma gangrenosum	20/104 (19%)
Diarrhea	15/104 (14%)
Erythema nodosum	9/104 (9%)
Arthralgias	6/104 (6%)
Dyspnea	2/104 (2%)
Abscess location	
Spleen	71/104 (68%)
Liver	38/104 (37%)
Skin	38/104 (37%)
Lymph nodes	33/104 (32%)
Soft tissue/muscles	21/104 (20%)
Lung	15/104 (14%)
Joints	9/104 (9%)
Brain	3/104 (3%)
Testicles	2/104 (2%)
Median number of organs involved (IQR)	2 (2–3)
Infectious workup	
Cultures obtained	65/69 (94%)
Cultures negative	65/65 (100%)
Treatment	
Corticosteroids	93/104 (89%)
Response to corticosteroids	59/64 (92%)
Biologics	29/104 (28%)
DMARDs (Azathioprine, Methotrexate, Cyclophosphamide, Hydroxychloroquine and/or Sulfasalazine)	47/104 (45%)
Antibiotics	42/74 (57%)
Splenectomy	28/104 (27%)
Clinical Course	
Experienced a relapse	53/95 (56%)
Median number of relapses (IQR)	1 (0-2)
Relapse despite splenectomy	20/28 (71%)
*Rheumatoid arthritis or systemic lupus erythematosus. Abbreviations: IQR, interquartile range; SAPHO, Synovitis, acne, pustulosis, hyperostosis, and osteitis; AAS, Aseptic abscess syndrome; DMARDs, Disease-Modifying Antirheumatic Drugs.	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

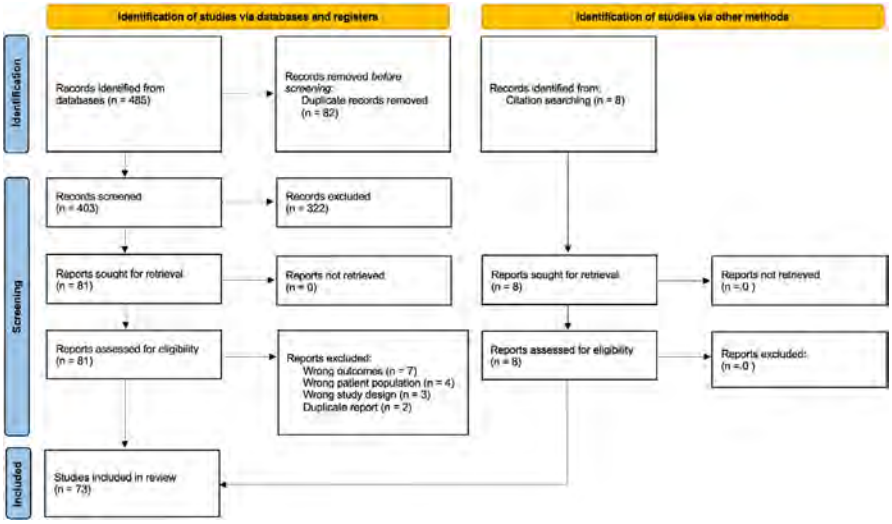


Figure 1. The PRISMA flow diagram for the systematic review

Conclusion: AAS is often associated with underlying inflammatory disorders, particularly inflammatory bowel disease. Fever and splenic abscess are the most common manifestations. Despite high initial response rates to immunosuppressive therapy, relapses are common, particularly in patients with splenic, lymph node involvement, or multi-organ disease, while splenectomy does not appear to prevent recurrence. These findings may inform risk stratification and follow-up strategies in patients with multisystem disease.

Disclosure: E. Papachristodoulou: None; **L. Kakoullis**: None; **R. Chopra**: None; **C. Derk**: None; **K. Parperis**: None.

Abstract Number: 2028

Behçet's Syndrome Beyond Endemic Borders: A 24-Year Longitudinal Analysis of Mortality in a Diverse South American Cohort

Fabio Specian[1], Carolina Ejnisman[2], Rafael Bassara Macedo[1], Pedro Araujo[3], Barbara Bayeh[2], Thiago Freitas[4], Rafael Cordeiro[5] and Henrique Giardini[4], [1]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [3]Universidade de São Paulo, Sao Paulo, São Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's syndrome (BS) is a chronic, relapsing vasculitis that contributes substantially to morbidity and mortality, primarily due to vascular and neurological complications. Most of the available mortality data in BS derive from studies conducted in endemic regions. This study aims to evaluate long-term mortality in a multiethnic South American cohort of BS patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This research is a retrospective analysis of a prospective, single-center and multiethnic cohort of BS patients followed between January 2000 and December 2024. We included BS patients diagnosed according to the International Study Group and/or the International Criteria for Behçet's Disease. Mortality was analyzed according to qualitative and quantitative variables using descriptive statistics. Associations with mortality during follow-up were assessed through bivariate Cox regression, with estimation of unadjusted hazard ratios (HRs) and 95% confidence intervals.

Results: In our cohort of 303 patients, the median follow-up time was 117 months (IQR: 55–184 months); 186(61.6%) were female. Eight (2.6%) patients died during the study period. The mean age at BS diagnosis was 31.5(±10.4) in survivors and 33.4(±8) in non-survivors (p=0.662). The mean age at death among the eight patients was 47.6 years (±14.1), and the mean interval between BS diagnosis and death was 14.6 years (±10.3). Causes of death included three cases of malignancy, one of undetermined cause, and four attributed to disease activity. The presence of pulmonary artery aneurysm (HR=28.4; 95% CI: 3.32–243.53; p=0.002), parenchymal central nervous system involvement (HR=6.81; 95% CI: 1.65-28.06; p=0.008), previous use of cyclophosphamide (HR=20.4; 95% CI: 2.38-175; p=0.006) and infliximab (HR=4.87; 95% CI: 1.16-20.44; p=0.031), type 2 diabetes mellitus (DM2) (HR=6.72; 95% CI: 1.67-27.03; p=0.007) and cancer (HR=8.81; 95% CI: 2.02-38.5; p=0.004) were associated with increased mortality risk. Colchicine use was associated with a significantly reduced risk of mortality (HR=0.08; 95% CI: 0.02-0.36; p=0.001). Given the low mortality, only exploratory (unadjusted) analysis of factors associated with death were performed.

Conclusion: Although mortality was low, the relatively large number of patients for a rare disease, the long-term follow-up, and the inclusion of multiple clinical variables provided meaningful insights into mortality risk factors in our cohort. Consistent with the current literature, pulmonary artery aneurysm and central nervous system involvement were strongly associated with increased mortality. The observed association between cyclophosphamide and infliximab use likely reflects treatment of more severe disease. The apparent protective effect of colchicine may be influenced by indication bias, as this drug is frequently used in milder cases. Nonetheless, its known benefits in cardiovascular prevention raise the hypothesis that colchicine could have a broader impact on mortality reduction in Behçet's syndrome, warranting further investigation.

Disclosure: F. Specian: None; **C. Ejnisman**: None; **R. Bassara Macedo**: None; **P. Araujo**: None; **B. Bayeh**: None; **T. Freitas**: None; **R. Cordeiro**: None; **H. Giardini**: None.

Abstract Number: 2029

Characteristics of a Historical Cohort of Adult Patients with Juvenile Idiopathic Arthritis

Francina salabert-Carreras[1], Raquel Ugena-García[2], Cristina Rocamora-Gisbert[3], Cristina Calomarde-Gómez[2], Clara Churtichaga Domenech[1], Judith Vidal ripoll[1], LOURDES MATEO SORIA[4], Laia Gifre-Sala[1], Maria Aparicio[3], Susana Holgado[5], Águeda Prior Español[1], Anne Riveros frutos[3], Ivette Casafont-Solé[2], Eva Forcadell Pirretas[1], Anna Pujol Manresa[1], Judit Font-Urgelles[2], Melania Martínez-Morillo[1] and Annika Nack[3], [1]Hospital Germans Trias i Pujol, Barcelona, [2]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [3]Hospital Germans Trias i Pujol, Barcelona, Spain, [4]HOSPITAL GERMANS TRIAS I PUJOL, BADALONA, Spain, [5]Hospital Germans Trias i Pujol, Barcelona, Catalonia, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. Up to one-third of patients experience disease flares in adulthood, with significant clinical and therapeutic implications. The introduction of biologic therapies in the year 2000 marked a paradigm shift in managing these patients, leading to better disease control and reduced long-term sequelae. However, limited data are available on how patient characteristics at diagnosis, particularly across different periods, influence disease progression and therapeutic management.

Methods: Retrospective, cross-sectional study including patients diagnosed with JIA between 1960 and 2024 who had at least one follow-up visit in an adult rheumatology clinic at a tertiary care hospital. Sociodemographic, clinical, and laboratory data were collected. Patients with systemic JIA were excluded due to their distinct clinical characteristics.

Results: A total of 46 patients were included (Table 1), predominantly female (71%), with a mean age at diagnosis of 8.9 ± 4.7 years, slightly higher in patients diagnosed after 2000 (9.36 ± 4.5 years). No significant differences were found regarding disease subtypes or autoimmune markers between patients diagnosed in the pre-biologic era (n=21) and post-biologic era (n=25).

The first-line treatment in 58% of cases was NSAIDs, followed by corticosteroids (32%). Among post-2000 patients, 88% required concomitant methotrexate treatment.

Biologic therapy was required at some point in the disease course in 60% of post-biologic era patients, compared to 47% in the pre-biologic group (p=0.401). Disease duration and age at initiation of the first biologic were significantly higher in the pre-biologic group (28.4 ± 12.65 years and 37.4 ± 15.38 years) compared to the post-biologic group (6.4 ± 5.71 years and 16.7 ± 4.77 years) (p < 0.001 for both).

Structural joint damage at baseline and after 10 years of treatment was significantly greater in the pre-biologic group than in the post-biologic group (p = 0.019).

Among all patients who received biologic therapy, 96% were initially treated with anti-TNF agents, with etanercept being the most used (56%).

Table 1: **Clinical and Demographic Characteristics**

Era	TOTAL *n = 46*	Pre-Biologic *n =21*	Post-Biologic *n = 25*	p-value
Female sex, *n (%)*	33 (71.7)	16 (34.78)	17 (36.95)	0.539
Smoker, n (%)	10 (21.7)	8 (17.39)	2 (4.34)	**0.035**
Age at diagnosis (years), *mean (SD)*	8.9 (4.7)	8.4 (5.05)	9.36 (4.5)	0.512
ILAR Subtype				
Oligoarthritis	20 (43.47)	9 (19.56)	11 (23.91)	0.938
Polyarthritis	17 (36.95)	10 (21.79)	7 (15.21)	0.170
Enthesitis-related	5 (10.87)	2 (4.34)	3 (6.52)	1.000
Psoriatic	3 (6.52)	0 (0.00)	3 (6.52)	0.297
Undifferentiated	1 (2.17)	0 (0)	1 (2.17)	1.000
Autoimmunity				
ANA positive, *n (%)*	21 (45.65)	9 (19.56)	12 (26.08)	0.727
RF positive, *n (%)*	10 (21.73)	6 (13.03)	4 (8.69)	0.502
ACPA positive, *n (%)*	7 (15.21)	5 (23.81)	2 (8.00)	0.282
HLA-B27 positive, *n (%)*	7 (15.21)	2 (9.52)	5 (20.00)	0.566
Initial treatment				
NSAIDs, *n (%)*	26 (57.78)	14 (70.00)	12 (48.00)	0.138
Corticosteroids, *n (%)*	15 (32.60)	5 (23.81)	10 (40.00)	0.243
csDMARDs, *n (%)*	5 (10.87)	2 (9.52)	3 (12.00)	0.788
Concomitant csDMARDs, *n (%)*				
Methotrexate, *n (%)*	35 (76.08)	13 (61.90)	22 (88.00)	**0.039**
Leflunomide, *n (%)*	17 (36.95)	8 (38.09)	9 (36.00)	0.883
Biologic use, *n (%)*	25 (54.34)	10 (47.61)	15 (60.00)	0.401
Structural Damage at diagnosis, *n (%)*	13 (28.26)	10 (47.61)	3 (12.00)	**0.019**
Structural Damage 10 years post diagnosis, *n (%)*	19 (41.30)	13 (61.90)	6 (24.00)	**0.009**

ILAR: *International League of Associations for Rheumatology*; ANA: *antinuclear antibodies*; RF: rheumatoid factor; ACPA: Anti-Citrullinated Protein Antibodies; *NSAIDs: Non-Steroidal Anti-Inflammatory Drugs*; *csDMARDs*: conventional synthetic disease-modifying antirheumatic drugs; SD: standard deviation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In our cohort, patients diagnosed with JIA in the pre-biologic era had significantly greater initial structural damage than those diagnosed in the post-biologic era, possibly due to delayed diagnosis. Furthermore, the longer disease duration before initiation of biologic therapy and older age at first biologic use observed in the pre-biologic group may have contributed to increased long-term joint damage, highlighting the potential impact of earlier biologic intervention.

Disclosure: F. salabert-Carreras: None; **R. Ugena-García**: None; **C. Rocamora-Gisbert**: None; **C. Calomarde-Gómez**: None; **C. Churtichaga Domenech**: None; **J. Vidal ripoll**: None; **L. MATEO SORIA**: None; **L. Gifre-Sala**: None; **M. Aparicio**: None; **S. Holgado**: None; **Á. Prior Español**: None; **A. Riveros frutos**: None; **I. Casafont-Solé**: None; **E. Forcadell Pirretas**: None; **A. Pujol Manresa**: None; **J. Font-Urgelles**: None; **M. Martínez-Morillo**: None; **A. Nack**: None.

Abstract Number: 2030

Krebs von den Lungen 6 levels (ΔKL6) is a reliable marker of disease activity and response to therapy in CTD-ILD

fredeswinda Romero-Bueno[1], lydia Abasolo Alcazar[2], Mª Jesus Rodriguez-Nieto[3], Cristina Vadillo Font[4], Maria asuncion Nieto[4], Laura Cebrian[5], Belen Lopez Muñiz[6], Jesus Loarce Martos[7], Juan A Rigual[7], Hilda Godoy Tundidor[8], Rosalia Laporta[9], Irene Llorente Cubas[10], Gema Bonilla[11], Luis Gomez Carrera[12], Rosario Garcia Vicuña[13], Ana Jaureguizar[7], Jose Luis Morell Hita[7], Claudia Valenzuela[10], Olga Sanchez Pernaute[14] and NEREA Study Group, [1]University Hospital Fundacin Jimnez Daz\"\", Madrid, Spain, [2]IdISSC. HCSC, Madrid, Madrid, Spain, [3]Fundacion Jimenez Diaz (IIS-HUFJD), Madrid, Spain, [4]Hospital Clínico S Carlos, Madrid, Spain, [5]Department of Rheumatology, Hospital Universitario Infanta Leonor / Universidad Complutense de Madrid, Madrid, Spain, Madrid, Spain, [6]Hospital Universitario Infanta Leonor, Madrid, Spain, [7]Hospital Ramón y Cajal, Madrid, Spain, [8]Hospital Universitario puerta de hierro, Madrid, Spain, [9]Hospital Puerta de Hierro Majadahonda, Madrid, Spain, [10]Hospital Universitario Princesa, Madrid, Spain, [11]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [12]Hospital Universitario La Paz, Madrid, Spain, [13]Hospital Universitario de la Princesa, Madrid, Spain, [14]Clinica Universidad de Navarra, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Krebs von den Lungen-6 (KL6) is produced by type 2 alveolar epithelial cells. High circulating KL6 levels show a good accuracy in the diagnosis of interstitial lung diseases, including those associated to CTD (CTD-ILD). Increased levels of KL6 have been found to predict mortality in idiopathic pulmonary fibrosis, and also in some cohorts of CTD-ILD patients. Previous data from our prospective CTD-ILD cohort have shown that KL6 changes over time correlate with disease course. Our aim was to evaluate KL-6 sensitivity to change upon different therapeutic interventions

Methods: The study was conducted in CTD-ILD patients included in a multicenter prospective register (NEREA) from Madrid. Demographics and process related variables are recorded and updated with clinical visits (at 6-monthly periods on average). For the aim of the study we selected treatment-naïve incident cases and extracted data regarding underlying disease, date of ILD onset, radiographic patterns, presence of fibrosis at the time of first KL6 determination, FVC (% from reference) and DLco (% from reference). Serum KL-6 concentrations were measured at baseline ($_{bl}$KL-6) and within the following 6 to 24 months ($_{fu}$KL-6). Changes in KL6 levels (ΔKL6%) were also determined. Data are shown as mean ± SD. 95% confident intervals (95CI) were calculated to assess the effect size. Statistical analysis included t test, Wilcoxon rank sum and linear regression. Alpha value was set at 0.05.

Results: The study population comprised 57 subjects (84% women), aged 64.7 ± 10.4 years. There were 25 never smokers (44% of the cohort) and only 3 active smokers. Clinical diagnosis included 24 IPAF cases (42%), 12 patients with SSc or

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

related conditions (21%), 4 with RA (7%), and 4 classified as PM/DM (7%), 3 with SS/lupus (5%) and 10 with other autoimmune conditions (17.5%). Radiographic patterns were classified as NSIP in 18 patients (31%), UIP in 22 (39%), and others in 17 (30%). Signs of fibrotic disease were observed in 34 patients (60%). FVC at baseline was 82±21%, while DLco was 64 ±25%, with 30 patients (53%) showing DLco > 60%. 26 patients (45.6%) remained untreated during the observation period, while 31 patients (54.4%) were put on immunossupressants or/and corticosteroids related to ILD. At baseline, KL-6 levels ($_{bl}$KL-6) were 2029 ± 2118 IU/ml (median 1512 IU/ml). A second KL6 determination ($_{fu}$KL6) was availble at a median of 11.7 (6-12) months of follow-up. Patients treated with immunosuppresants showed a significant reduction in KL6 levels as compared to those remaining untreated ($\Delta KL6_{is}$%: -22.1 ± 38 [95CI: -39.1; -8.2] vs $\Delta KL6_{O}$: 9.0 ± 46.8 [95CI: -9.9; -27.9], p 0.001). After adjustment by age and sex, treatment with immunosupressants resulted in a risk reduction of KL6 increasing over time (+ΔKL6) of 25.9 ± 11.7 [95CI: 2.5; 49.3] vs no treatment (p 0.031). After adjustment for sex and age, treatment initiation was associated with a 22.0 ± 9.7 risk reduction [95CI: 2.7; 41.4] of a +ΔKL6

Conclusion: Our results support the role of KL6 as activity biomarker in CTD-ILD, and underscore its value as surrogate marker of reponse to immunosuppresants both in interventional trials and in clinical practice.

Disclosure: f. Romero-Bueno: None; **I. Abasolo Alcazar**: None; **M. Rodriguez-Nieto**: None; **C. Vadillo Font**: None; **M. Nieto**: None; **L. Cebrian**: None; **B. Lopez Muñiz**: None; **J. Loarce Martos**: None; **J. A Rigual**: None; **H. Godoy Tundidor**: None; **R. Laporta**: None; **I. Llorente Cubas**: None; **G. Bonilla**: None; **L. Gomez Carrera**: None; **R. Garcia Vicuña**: None; **A. Jaureguizar**: None; **J. Morell Hita**: None; **C. Valenzuela**: None; **O. Sanchez Pernaute**: None.

Abstract Number: 2031

Management of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases: A Comparison of Rheumatologist and Pulmonologist Perspectives

Genna Braverman[1], Kerri Aronson[2], Charlene Thomas[2] and Robert Spiera[3], [1]Hospital for Special Surgery, New York, NY, [2]Weill Cornell, New York, NY, [3]Scleroderma, Vasculitis, and Myositis Center, Hospital for Special Surgery, Weill Cornell Medical College, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is common and important feature of systemic autoimmune rheumatic diseases (SARD). Rheumatologists and pulmonologists are central to the care of this complex condition. Specialists have unique training and expertise; whether these differences lead to distinct approaches to SARD-ILD treatment is unknown. We conducted a national, cross-sectional survey of rheumatologists and pulmonologists to assess how subspecialty affects physician management of SARD-ILD.

Methods: Surveys were electronically distributed to United States pulmonologists and rheumatologists identified through professional society memberships and social media. Surveys contained case questions on SARD-ILD management with variations of the underlying disease (mixed connective tissue disease, idiopathic inflammatory myopathy, rheumatoid arthritis, systemic sclerosis and Sjogren's) and ILD severity (asymptomatic, symptomatic, progressive). Surveys also contained

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

items on perceived importance of variables to treatment decisions, as well as opinions on ownership over aspects of management and healthcare maintenance. We analyzed responses submitted 5-9/2024.

We compared specialists' responses via univariate logistic regression, Chi-squared or Fisher's exact tests; we performed multivariable logistic regression of case questions controlling for practice setting, clinical experience and geography.

Results: Analyses included 309 participants (rheumatologists=184, pulmonologists=125) (Table 1). Compared to rheumatologists, pulmonologists were more likely to treat asymptomatic and symptomatic ILD with corticosteroids for all SARD except asymptomatic systemic sclerosis (odds ratios [OR] 2.22-7.69, all $p< 0.05$), and progressive ILD with antifibrotics (OR 3.33-3.84, all $p< 0.05$). Compared to pulmonologists, rheumatologists were more likely to add or modify immunomodulation/immunosuppression for all symptomatic and progressive SARD-ILD (OR 1.82-5.44, all $p< 0.05$) (Figure 1).

There were disciplinary differences in the relative importance of clinical variables to treatment decisions: more rheumatologists than pulmonologists rated as "very important" the extrapulmonary status of a patient's SARD (51.1% vs. 35.0%) and the specific autoantibody (26.7% vs. 19.2%), whereas more pulmonologists rated as "very important" the radiographic

Table 1. Participant Demographics

	Study Cohort (N=309*)	Rheumatologists (N=184*)	Pulmonologists (N=125*)
Practice Setting, N (%)			
Academic medical center	206 (66.9)	117 (63.6)	89 (71.8)
Community medical center	41 (13.3)	22 (12.0)	19 (15.3)
Private practice	46 (15.6)	38 (20.7)	10 (8.1)
Industry	1 (0.3)	1 (0.5)	0 (0.0)
Military	11 (3.6)	6 (3.3)	5 (4.0)
Other	1 (0.3)	0 (0.0)	1 (0.8)
Missing	1	0	1
Years in practice, N (%)			
<5	68 (22.0)	29 (15.8)	39 (31.2)
5-10	62 (20.1)	26 (14.1)	36 (28.8)
11-20	72 (23.3)	49 (26.6)	23 (18.4)
>20	107 (34.6)	80 (43.5)	27 (21.6)
Geographic Location, N (%)			
Northeast	86 (29.6)	55 (31.4)	31 (26.7)
South	88 (30.2)	57 (32.6)	31 (26.7)
Midwest	47 (16.2)	27 (15.4)	20 (17.2)
Mountain / West Coast / Hawaii / Alaska / Puerto Rico	70 (24.1)	36 (20.8)	34 (29.3)
Missing	16	9	9
ILD Panel Representation, N (%)			
Up to 10%			42 (33.6)
Up to 25%			32 (25.6)
Up to 50%			17 (13.6)
>50%			34 (27.2)

*When variable has missing data, denominator used for calculation of percentages is total number of non-missing responses

Table 2. Healthcare Maintenance Responsibility

	Rheumatologists (N=184*)	Pulmonologists (N=125*)	P value**
Pulmonary hypertension screening, N (%)			<0.001
Respondent routinely performs	143 (81.7)	114 (97.4)	
Respondent does not routinely perform	32 (18.3)	3 (2.6)	
Missing	9	8	
Ensuring vaccinations up to date, N (%)			0.2
Respondent routinely performs	110 (62.9)	82 (70.7)	
Respondent does not routinely perform	65 (37.1)	34 (29.3)	
Missing	9	9	
Osteoporosis screening, N (%)			<0.001
Respondent routinely performs	161 (92.0)	19 (16.2)	
Respondent does not routinely perform	14 (8.0)	98 (83.8)	
Missing	9	8	
Osteoporosis treatment, N (%)			<0.001
Respondent routinely performs	151 (86.3)	7 (6.0)	
Respondent does not routinely perform	24 (13.7)	110 (94.0)	
Missing	9	8	
GERD treatment, N (%)			0.014
Respondent routinely performs	123 (70.3)	97 (82.9)	
Respondent does not routinely perform	52 (29.7)	20 (17.1)	
Missing	9	8	
PCP prophylaxis prescribing, N (%)			0.008
Respondent routinely performs	140 (80.0)	107 (91.5)	
Respondent does not routinely perform	35 (20.0)	10 (8.5)	
Missing	9	8	
Reproductive counseling, N (%)			<0.001
Respondent routinely performs	163 (93.7)	59 (50.4)	
Respondent does not routinely perform	11 (6.3)	58 (49.6)	
Missing	10	8	
Ensuring malignancy screening up to date, N (%)			<0.001
Respondent routinely performs	79 (44.9)	29 (24.8)	
Respondent does not routinely perform	97 (55.1)	88 (75.2)	
Missing	8	8	
Smoking cessation medication prescribing, N (%)			<0.001
Respondent routinely performs	29 (16.5)	103 (88.0)	
Respondent does not routinely perform	147 (83.5)	14 (12.0)	
Missing	8	8	

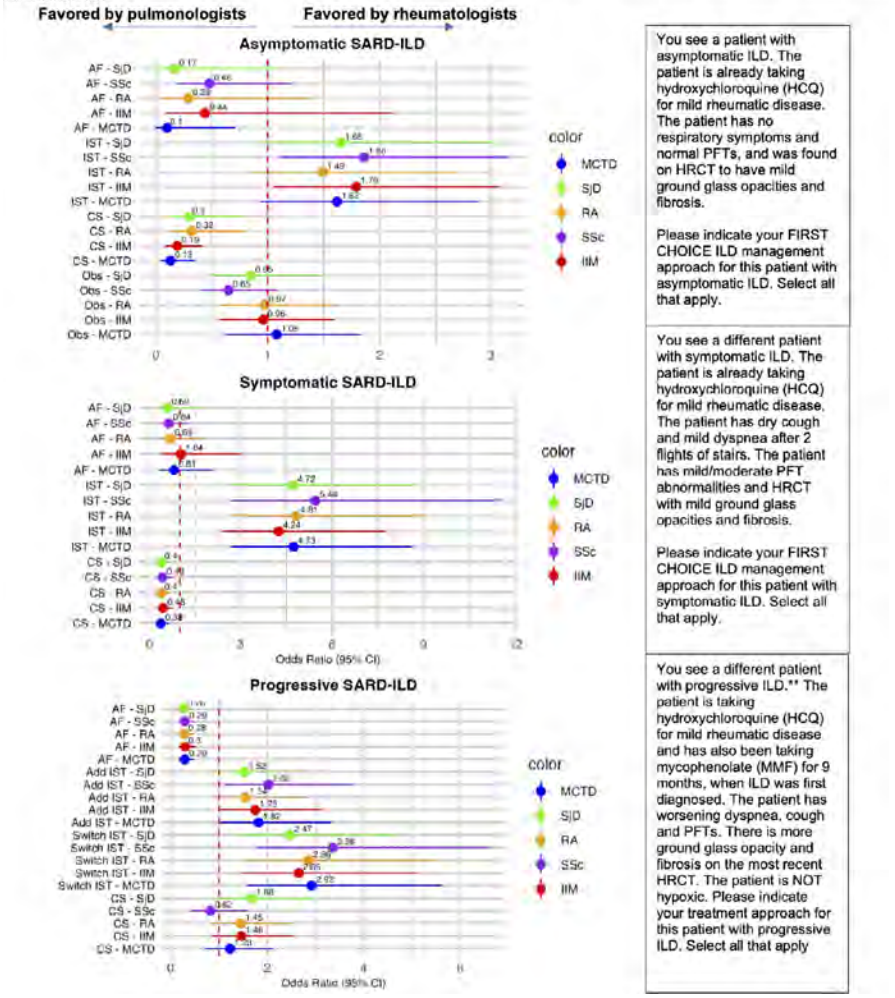
*When variable has missing data, denominator used for calculation of percentages is total number of non-missing responses
**p value reflects results of Pearson's Chi-square test for dichotomous variable

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Case Based Questions – Multivariable Analysis*

"Controlling for region (Northeast, South, Midwest, Mountain/West Coast), practice setting (academic, non-academic), experience (<10, >=10 years)

Respondents selected their first-choice treatment approach, answering each case scenario five times varying the SARD (MCTD, IIM, RA, SSc and SjD). Responses by specialty were compared. Obs=observation; CS=corticosteroid; IST=immunosuppression/immunomodulation; AF=antifibrotic.



pattern of ILD on high-resolution computed tomography (60.0% vs. 39.9%) and the presence of fibrosis (64.7% vs. 46.6%).

Specialists also identified distinct scopes of decision-making responsibility and reported attending to disparate areas of healthcare maintenance. Rheumatologists were significantly more likely to screen for and treat osteoporosis, perform reproductive health counseling and ensure up-to-date cancer screening, whereas pulmonologists were more likely to screen for pulmonary hypertension and provide treatment for GERD, smoking cessation and PCP prophylaxis (all $p < 0.05$) (Table 2).

Conclusion: This national physician survey study suggests distinct specialty approaches to SARD-ILD management, and highlights opportunities to leverage complementary disciplinary expertise as part of a co-management framework.

Disclosure: G. Braverman: None; **K. Aronson**: None; **C. Thomas**: None; **R. Spiera**: Abbvie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Certa, 2, Chemocentryx, 2, 5, Corbus, 5, Cytori, 2, 5, Galderma, 2, GlaxoSmithKlein(GSK), 2, 5, Horizon, 5, Kadmon, 5, Novartis, 2, 5, Principia, 5, Regeneron, 2, Roche-Genentech, 2, 5, Sanofi, 2, Vera Therapeutic, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2032

Validation of systemic Juvenile Arthritis Disease Activity Score 10 (sJADAS 10) in adult patients with Still's Disease

Georgia-Savina Moysidou[1], Spyridon Katechis[2], Stéphane Mitrovic[3] and Bruno Fautrel[4], [1]Sorbonne université, Service de rhumatologie, groupe hospitalier Pitié-Salpêtrière, Assistance publique-Hôpitaux de Paris, Athens, Greece, [2]National and Kapodistrian University of Athens Medical School, Athens, Greece, Athens, Greece, [3]Sorbonne université, Service de rhumatologie, groupe hospitalier Pitié-Salpêtrière, Assistance publique-Hôpitaux de Paris, Paris, France, [4]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Recent EULAR/PReS recommendations have acknowledged the lack of unique and consensual tool to quantify disease activity in Still's disease (SD). The systemic Juvenile Arthritis Disease Activity Score 10 (sJADAS10) (1) is to date the most advanced SD activity outcome measure in terms of construct validity and sensitivity to change with operable threshold already validated in children but not in adults.

The objective of our work was to validate sJADAS10 thresholds in adult patients with SD.

Methods: Post hoc analysis of the cohort of Still's patients from one unique reference center. Adult patients fulfilling Yamaguchi's or Fautrel's classification criteria, and with available clinical and biological data to calculate sJADAS10 score were included in the study.

Disease activity was elicited sJADAS calculation. As a gold standard, patients were categorized into 4 groups according to the 4 qualitative definitions of inactive disease (ID), minimal disease activity (MDA), moderate disease activity (MoDA) and high disease activity (HDA) proposed by Rosina *et al*. (2) (Table 1). The agreement between sJADAS values and disease activity categorization was tested by Cohen's kappa coefficient, to evaluate in what extent sJADAS values in adult patients fits with ID/MDA/MoDA/HDA qualitative categories.

Results: A hundred and twenty-nine visits from 93 patients were included in the study. The visits made by the same patient in a different disease activity state were considered as referring to distinct patients. Most of the patients were women (n= 89) mean aged (SD) of 36 (13) years with a mean (range) disease duration of 6,2 (0-40) years. Median (IQR) sJADAS was 12.8 (4.1-26.2). Forty-two patients were in HDA, 31 MoDA, 29 in MDA and 27 in ID according to their sJADAS-based statuses, respectively, whereas 39 were in HDA, 32 in MoDA, 20 in MDA and 38 in ID according to the qualitative disease assessment, respectively (**Figure 1**). Overall accuracy of sJADAS was 0.77 (95% CI :0.68- 0.84), whereas kappa coefficient was 0.69. Agreement was higher for patients with high disease activity.

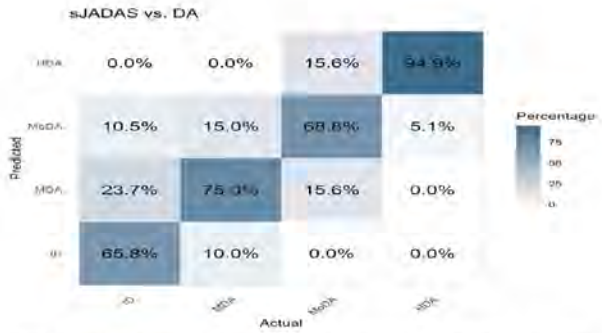
Conclusion: sJADAS thresholds are relevant and validated by our work in adult patients with SD. These results are in favor of the use of sJADAS in both children and adults with SD and could position it as a relevant composite measure for assessing disease activity in SD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Definitions of disease activity based on Rosina et al.

Inactive disease	Minimal disease activity	Moderate disease activity	High disease activity
Absence of fever and of any other systemic or articular manifestations attributable to sJIA. If the patient is still on medications, it may be possible to stop all therapies.	Absence of fever and of other major systemic features. Only mild systemic manifestations (i.e. faint skin rash, residual hepatosplenomegaly) and/or an active joint count of ≤1 can be present. The patient can only be receiving low-dose glucocorticoid therapy (i.e. ≤ 0.1 mg/kg/day), with further dose reduction being possible. If the patient is receiving only therapy with DMARDs or biologics, it might be possible to gradually withdraw it.	Disease activity state in between minimal disease activity and high disease activity. The level of disease activity does not allow any reduction of the ongoing therapy or may require a change or intensification of treatment.	Presence of fever ≥38°C and/or any other major systemic or articular manifestations (i.e., intense rash, severe serositis, active polyarthritis). The start of an aggressive therapy or the intensification of ongoing treatment is definitely required. Typically, a patient in the state of high disease activity is at disease onset or has a disease flare.

Figure 1: Heatmap showing the concordance between patients' status according to sJADAS- based statuses and qualitative disease assessment



sJADAS, systemic Juvenile Arthritis Disease Activity Score; DA, qualitative disease assessment, ID, Inactive Disease; MDA, Minimal Disease Activity; MoDA, Moderate Disease Activity; HDA, High Disease Activity; PPV, Positive Predictive Value; NPV, Negative predictive Value

References

1. Tibaldi J et al. Rheumatology (Oxford) 2020; 59(11): 3505–3514.
2. Rosina S et al. Arthritis Rheumatol. 2024 Sep;76(9):1446-1454.

Disclosure: G. Moysidou: None; **S. Katechis**: None; **S. Mitrovic**: None; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2033

Complement Fragments are Deposited in the Submandibular Glands in IgG4-Related Disease

Guy Katz[1], Judith Ferry[1], Grace McMahon[1], Isha Jha[2], Claire Galand[3], Fei Liu[4], Shelia Violette[4], Jason Campagna[4], Ana Fernandes[1], Cory Perugino[5] and John Stone[6], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Q32 Bio Inc, Waltham, MA, [4]Q32 Bio Inc, Waltham, MA, [5]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [6]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Hypocomplementemia, defined as low serum C3 and/or C4 concentrations, is common in patients with IgG4-related disease (IgG4-RD). While this has historically been linked with renal involvement, recent data have shown that hypocomplementemia is more accurately associated with extent of IgG4-RD across multiple sites rather than individual organ manifestations, suggesting that complement-driven inflammation is central to the disease process. We aimed to assess whether complement is deposited locally in IgG4-RD submandibular gland lesions.

Table 1. Demographics and disease characteristics of eight patients in whom submandibular gland biopsies were stained for complement deposition. Results reported as n (%) unless noted otherwise. §At any point in disease course. *1 patient was treated with methotrexate for comorbid rheumatoid arthritis.

Characteristic	Value
N	8 (100)
Age at time of biopsy, years, mean (SD)	62.72 (10.98)
Female sex	5 (62.5)
Disease duration at time of biopsy, days, median (IQR)	301.5 (221, 1082.5)
Peak serum IgG4 concentration§	
Normal	2 (25)
>1x - ≤2x ULN	4 (50)
>2x - ≤5x ULN	1 (12.5)
>5x ULN	1 (12.5)
Serum C3 and/or C4 below reference range§	3 (37.5)
Organ involvement§	
Lacrimal glands	1 (12.5)
Parotid glands	1 (12.5)
Orbits	0 (0)
Lungs or pleura	2 (25)
Lymph nodes	4 (50)
Large or medium blood vessels	0 (0)
Pancreas	3 (37.5)
Kidneys	1 (12.5)
Retroperitoneum	0 (0)
IgG4-RD Responder Index score at time of biopsy, median (IQR)	6 (4, 6)
Treatment prior to biopsy§	
None	6 (75)
Glucocorticoids (≥20 mg x 4 weeks cumulatively)	1 (12.5)
Conventional synthetic immunosuppressive agents	1 (12.5)*
Rituximab	1 (12.5)

Patient	Lymphoplasmacytic infiltrate	IgG4/IgG ≥40%	Phlebitis	Fibrosis
1	Yes	No	Yes	Yes
2	Yes	No	No	Yes
3	Yes	Yes	Yes	Yes
4	Yes	Yes	No	No
5	Yes	No	No	Yes
6	Yes	Yes	No	No
7	Yes	Yes	No	No
8	Yes	Yes	No	No

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

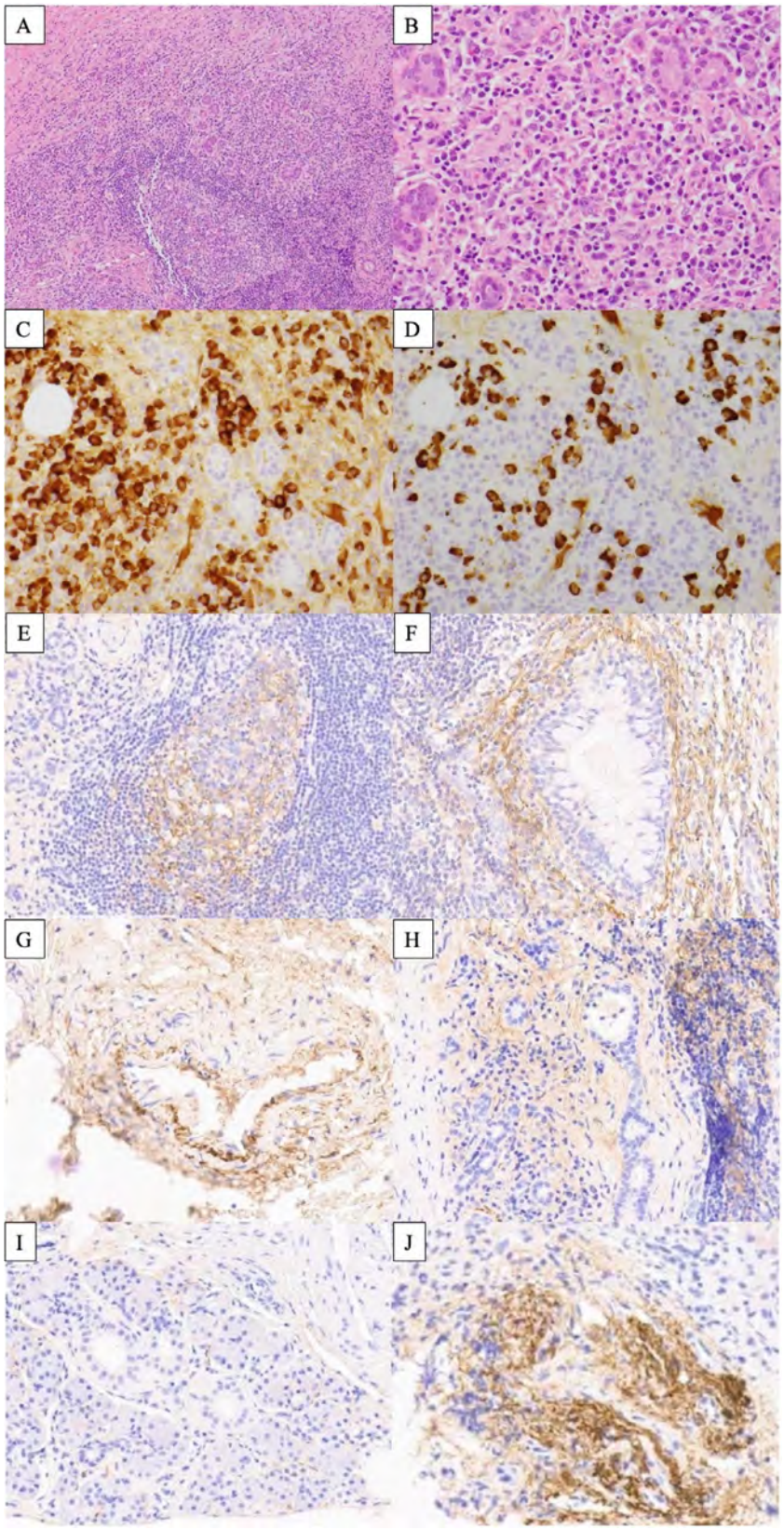


Figure 1. Representative histopathology and immunostaining findings. (A) Low- and (B) high-powered hematoxylin and eosin stain of diseased submandibular glands (SMG) showing dense lymphoplasmacytic infiltrate. (C) IgG and (D) IgG4 stains of diseased SMG showing a large proportion of IgG4+ plasma cells. (E-H) C3d staining of diseased SMG showing C3d staining at sites of inflammation and fibrosis. (I) C3d stain of an uninvolved SMG (negative control) showing absent C3d staining. (J) C3d stain of human liver with primary sclerosing cholangitis (positive control) showing expected pattern of staining.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We obtained submandibular gland tissue from 8 patients who fulfilled the 2019 ACR/EULAR IgG4-RD Classification Criteria and had undergone submandibular gland biopsy for diagnostic purposes. Other disease features, including sites of involvement beyond the submandibular glands and the presence or absence of hypocomplementemia, were not considered when identifying samples to be analyzed. We extracted disease features, laboratory results, demographic data, and treatment status at the time of biopsy from the medical records. All tissues were formalin-fixed and paraffin-embedded prior to sectioning. Immunohistochemistry was performed to stain for C3d, an end product of complement activation that persists in tissue longer than most other complement activation fragments. We similarly stained for C3d in a negative control (uninvolved submandibular gland) and positive control (human liver with primary sclerosing cholangitis).

Results: Demographic and disease characteristics of the 8 IgG4-RD patients studied are shown in **Table 1**. Six of the 8 patients (75%) were treatment-naïve at the time the biopsies were obtained. Five (62.5%) of the patients were female. The median disease duration at the time of biopsy was 301.5 days (IQR: 221, 1082.5). Only 3 patients (37.5%) had hypocomplementemia at any point in the disease course. Histopathologic features of the submandibular glands are shown in **Table 2** and reflect the findings that are typical of submandibular glands involved by IgG4-RD. All samples demonstrated a dense lymphoplasmacytic infiltrate and most (5, 62.5%) demonstrated an IgG4+/IgG+ plasma cell ratio ≥40% (**-Figure 1A-D**). All 8 submandibular gland biopsies showed deposition of C3d at sites of immune infiltration (**Figure 1E-F**), suggesting immune cells may be triggering complement activation. Additionally, C3d was also observed in several sites of fibrosis, suggesting complement may be contributing to fibrosis in IgG4-RD (**Figure 1F-H**). Staining patterns of positive and negative controls were as expected (**Figure 1I-J**).

Conclusion: Evidence of complement deposition was found in 8 of 8 submandibular glands included in this study. Complement activation was evident at this site of disease even in patients who demonstrated no sign of complement consumption in the peripheral blood (i.e., no C3 or C4 hypocomplementemia). These findings raise the possibility that tissue-targeted complement inhibition may be a useful treatment strategy in IgG4-RD and support the notion of complement-mediated inflammation being central to the disease mechanism of IgG4-RD.

Disclosure: G. Katz: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **J. Ferry**: None; **G. McMahon**: None; **I. Jha**: None; **C. Galand**: Q32 Bio, 3; **F. Liu**: Q32 Bio, 12, 3; **S. Violette**: Mediar Therapeutics, 12, 1, Q32 Bio, 12, 3, 8, 10, Triveni, 12, 1; **J. Campagna**: None; **A. Fernandes**: None; **C. Perugino**: Acepodia, 2, Amgen, 1, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Zenas Biopharma, 2; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2.

Abstract Number: 2034

Hidden Burden in Rheumatology: Cross-Sectional Study of Hearing Loss in Systemic Autoimmune Diseases

Ruddy Paola Montoya Rumpf[1], Liliam María Murcia Munévar[1], **Jairo Cajamarca-Baron**[2], Dominique Daniela González Casas[1], María Fernanda González Sánchez[1], Adriana Rojas-Villarraga[3], Henry Leonardo Martínez Bejarano[1], Adriana Isaza[1], Alejandro Escobar[1], Maria Camila Restrepo Guarnizo[1], Nicolás Santiago Rodríguez[1] and Claudia Ibáñez-Antequera[1], [1]Fundacion universitaria de ciencias de la salud, bogota, Distrito Capital de Bogota, Colombia, [2]Fundacion universitaria de ciencia de la Salud, Bogota, Distrito Capital de Bogota, Colombia, [3]Fundacion Universitaria de Ciencias de la salud, Bogotá, Distrito Capital de Bogota, Colombia

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

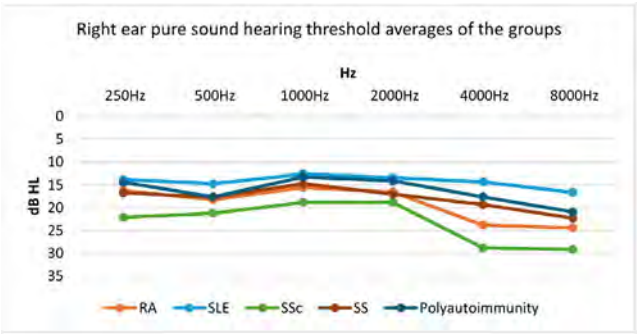
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

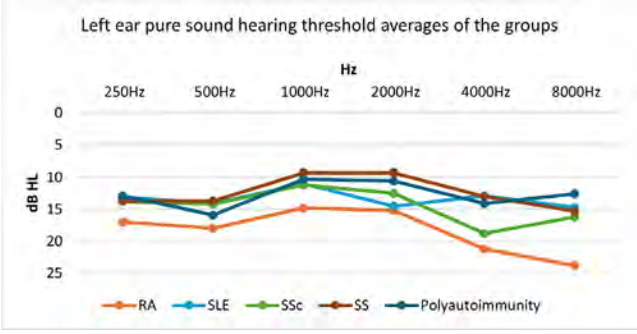
Background/Purpose: Autoimmune inner ear disease is a progressive sensorineural hearing loss of autoimmune origin, often underdiagnosed due to the lack of specific criteria, and requires further research to improve its detection and treatment. To determine the prevalence of hearing loss in adult patients with a confirmed diagnosis of systemic autoimmune rheumatic disease, seen at a Rheumatology Department in Bogotá, Colombia.

Methods: Cross-sectional observational study including 147 patients (18-60 years), selected through non-probabilistic consecutive sampling. Cases of hearing loss attributable to non-autoimmune causes were excluded. Each participant underwent pure tone audiometry (PTA) and a structured clinical interview to assess otovestibular symptoms. Demographic, clinical, audiological, and immunological variables were collected. Statistical analysis was performed using Stata® v17 with descriptive statistics and tests for comparison of proportions and ranks, considering $p < 0.05$ as the significance level.

Results: Only 4.76% (n = 7) of patients had a previously confirmed diagnosis of hearing loss; however, 46.9% (n = 69) were found to have hearing loss confirmed through PTA, of which 91.3% were sensorineural, 81.2% fluctuating, and mostly mild (69.6%) with a descending pattern (87.5%). Hearing loss rates were higher in SSc (75%) and rheumatoid arthritis (RA) (60.6%). Antinuclear antibodies were positive in 70.4% of patients, and 65.9% had received corticosteroids. A significant association was found between hearing loss and systemic sclerosis (SSc) (p = 0.042). When analyzing the pure tone average thresholds in both ears by autoimmune disease (Fig. 1 and 2), it was noted that in RA patients – Left Ear, the curve remained relatively stable between 250–2000 Hz, with a noticeable increase (worsening threshold) from 4000 Hz onward, indicating high-frequency hearing loss. In contrast, in SSc – Right Ear, thresholds were elevated across all frequencies, especially from 4000 Hz onwards, showing a consistently worse hearing profile with marked high-frequency hearing



Right ear pure sound hearing threshold averages of the groups



Left ear pure sound hearing threshold averages of the groups

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

impairment. Anti-Ro antibodies were positive in 46.7% of patients without hearing loss and in 20.4% of those with hearing loss ($p = 0.0078$).

Conclusion: This study reveals a marked underdiagnosis of hearing loss in patients with systemic autoimmune rheumatic diseases, with only 4.76% previously identified versus 46.9% confirmed through audiological assessment during the study. The predominance of sensorineural, mild, and descending-pattern hearing loss—particularly in conditions such as SSc and RA—highlights the need for systematic auditory evaluation in this population. An inverse association was found between Anti-Ro positivity and hearing loss, which may reflect a lower rate of auditory involvement among patients with Sjögren's syndrome within the cohort. As one of the few studies to comprehensively assess hearing loss across a broad spectrum of autoimmune diseases, our findings underscore the importance of increased clinical awareness and early detection strategies in rheumatologic care.

Disclosure: R. Montoya Rumpf: None; **L. Murcia Munévar**: None; **J. Cajamarca-Baron**: None; **D. González Casas**: None; **M. González Sánchez**: None; **A. Rojas-Villarraga**: None; **H. Martínez Bejarano**: None; **A. Isaza**: None; **A. Escobar**: None; **M. Restrepo Guarnizo**: None; **N. Rodríguez**: None; **C. Ibáñez-Antequera**: None.

Abstract Number: 2035

Interim Phase 1 Results for SPY002, a Novel Half-Life Extended Monoclonal Antibody Targeting TL1A, Suggest A Potential for Q3M or Q6M Maintenance Dosing for Rheumatologic Disease

Joshua Friedman[1], JD Lu[2], Bing Wang[2], Kinjal Hew[2], Preeyam Patel[2], Michael Kennedy[2], Mark Rose[2], Curtis Sheldon[2], Rachel McLean[2], Emily Svejnoha[2], MiRa Huyghe[1], Brian Connolly[2] and Deanna Nguyen[2], [1]Spyre Therapeutics, Waltham, MA, [2]Spyre Therapeutics, Waltham

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: TL1A is an inflammatory cytokine and a member of the TNF superfamily. Target cells that express DR3 and respond to TL1A include T cells, B cells, fibroblast-like synoviocytes (FLS), and osteoclasts, each of which is associated with inflammation and joint damage in rheumatoid arthritis (RA), ankylosing spondylarthritis (axSpA), and psoriatic arthritis (PsA). Synovial fluid and serum TL1A levels are highly elevated in RA, axSpA, and PsA, and TL1A promotes FLS activation, chemokine signaling, and MMP production by osteoclasts in vitro. Variants in the TL1A gene are associated with both TL1A levels and the diagnosis of RA, axSpA, and PsA or psoriasis, and multiple animal models demonstrate that TL1A inhibition is therapeutic in arthritis.

SPY002 is an investigational fully human IgG1 monoclonal antibody that specifically binds to TL1A and blocks the interaction of TL1A with its receptor, known as death receptor 3 (DR3). It includes a YTE modification in the Fc domain to increase the binding affinity to FcRn and thereby extend the antibody half-life. A Phase 1, first-in-human study in healthy volunteers is being conducted to characterize the safety, tolerability, PK, and PD properties of SPY002.

Methods: SPY002-101 is a randomized, double-blind, placebo-controlled single ascending dose (SAD) Phase 1 study in healthy volunteers aged 18 to 65. Study participants were randomized to either SPY002 or placebo in a 3:1 ratio as in dose cohorts as follows: 100 mg SC, 300 mg SC, 300 mg IV, 1000 mg IV, or 1500 mg IV. Blood was collected to evaluate safety,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

PK, PD (serum soluble TL1A levels), and ADA assessments at scheduled study visits. Interim safety and bioanalytical data with up to four months of follow-up from the first SAD cohort were analyzed.

Results: Interim PK data from all cohorts demonstrated dose-proportional pharmacokinetics for SPY002. Noncompartmental analysis and population PK modeling suggested a half-life extension of approximately 3-fold relative to typical monoclonal antibodies. PD analysis demonstrated saturating effects on soluble TL1A levels beginning with the lowest dose tested (100 mg SC) that extend to the latest time points assessed thus far. Blinded safety data from all cohorts thus far demonstrated SPY002 to be well tolerated with no serious or severe adverse events, with most adverse events being mild in severity and unrelated to study agent.

Conclusion: Interim PK analysis following single doses of SPY002 demonstrated half-life extension supporting potential maintenance dosing at a frequency of every 3 to 6 months with a single SC injection. SPY002 resulted in saturating changes in soluble TL1A levels. SPY002 was well tolerated, with all adverse events being non-serious and typical of a Phase 1 study in healthy volunteers. These results support advancement of SPY002 into clinical trials in rheumatologic disease and in other potential indications.

Disclosure: J. Friedman: Spyre Therapeutics, 3; **J. Lu**: Spyre Therapeutics, 3; **B. Wang**: Spyre Therapeutics, 2; **K. Hew**: Spyre Therapeutics, 3; **P. Patel**: Spyre Therapeutics, 3; **M. Kennedy**: Spyre Therapeutics, 3; **M. Rose**: Spyre Therapeutics, 3; **C. Sheldon**: Spyre Therapeutics, 3; **R. McLean**: Spyre Therapeutics, 3; **E. Svejnoha**: Spyre Therapeutics, 3; **M. Huyghe**: Spyre Therapeutics, 3; **B. Connolly**: Spyre Therapeutics, 3; **D. Nguyen**: Spyre Therapeutics, 3.

Abstract Number: 2036

JAK1 selective inhibitors versus pan-JAK inhibitors: comparative real-world study of drug retention in chronic inflammatory arthritis

LETICIA LEON[1], Pedro Pablo Bermejo[2], Leonor Laredo[3], José Alberto Peña[4], María Teresa Benítez[5], DALIFER FREITES[6], CLARA DE MIGUEL[3] and lydia Abasolo Alcazar[7], [1]Fundación Investigación Biomédica Hospital Clínico San Carlos, IdISSC; Universidad Camilo Jose Cela, MADRID, Madrid, Spain, [2]Clinical Pharmacology Service, San Carlos Clinical Hospital, MADRID, Madrid, Spain, [3]Hospital Clinico San Carlos, MADRID, Madrid, Spain, [4]Pharmacy Service San Carlos Clinical Hospital, MADRID, Madrid, Spain, [5]San Carlos Clinical Hospital, MADRID, Madrid, Spain, [6]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Madrid, Spain, [7]IdISSC. HCSC, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Janus kinase inhibitors (JAKis) are effective therapeutic agents against chronic inflammatory arthritis (CIA). Tofacitinib and baricitinib were defined as pan-JAK inhibitors, while upadacitinib and filgotinib a JAK1 selective inhibitors. Real world data comparing retention rate across JAKi classes in CIA are limited. The aim of the present study was to compare retention rate between pan-JAK inhibitors and JAK1 selective inhibitors in CIA and to assess the role of JAKi class in the risk of discontinuation and find out other possible predictors of treatment discontinuation.

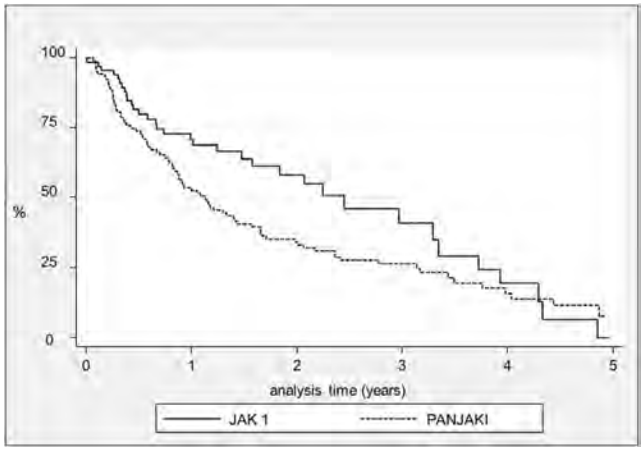
Methods: We retrospectively evaluated patients with CIA [Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), and Spondyloarthritis (SPA)] treated with JAKis from 2017 to 2024. The independent variable was JAKi class (pan-JAK inhibitors/ JAK1 selective inhibitors). Retention rates were assessed by Kaplan–Meier method, and multivariable Cox regression hazards model was run to identified predictors of discontinuation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Causes of JAKis discontinuation; global and stratified

Results: The study comprised 181 patients [83% women, median age 56(49-63)]. 84% had RA, 9% PsA and 7% SpA. Patients received 227 JAKi treatments courses, 96 of JAK1 selective inhibitors y 131 of pan-JAK inhibitors. Overall, 118 courses (52%) were discontinued (55% inefficacy, 42% adverse events, 3% other). The estimated IR of discontinuation was 35.5 [29.6-42.5] and 50% of them discontinued within 1.65 [1.2-2.2] years after JAKI starting. The IR of discontinuation was higher in women, and in those with cardiovascular disease or risk factors, being lower for RA vs other CIAs. Discontinuation rates were lower for JAK1-selective inhibitors (IR: 28.6; 95% CI: 20.5–39.8) vs pan-JAK inhibitors (IR: 39.6; 95% CI: 31.9–49.1). In the multivariate analysis, pan-JAK inhibitors, female gender, PsA, cardiovascular disease, previous b/tsDMARDs courses, cardiovascular risk factors, and leflunomide combined treatment were associated with higher probability of discontinuation.

Conclusion: Pan-JAK inhibitors (baricitinib and tofacitinib) may have higher discontinuation rates than JAK1 selective inhibitors is (upadacitinib and filgotinib) patients with CIAs in real-world settings. Several clinical factors, including diagnosis and comorbidities, influence JAKi retention and should guide treatment selection.



Kaplan-Meier survival estimate curve

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. LEON: None; **P. Bermejo**: None; **L. Laredo**: None; **J. Peña**: None; **M. Benítez**: None; **D. FREITES**: None; **C. DE MIGUEL**: None; **I. Abasolo Alcazar**: None.

Abstract Number: 2037

The Largest International Cohort Study of HA20 Reveals Novel Genetic Architecture and Age-Dependent Phenotypic Evolution

Manuel Carpio Tumba[1], Tingyan He[2], Jun Wang[3], Elizabeth Kairis[1], Kyr Goyette[1], Akuti Kethri[1], Urekha Karri[4], Atif Towheed[1], Jun Yang[5], Qing Zhou[6], Daniella Schwartz[1] and HA20 Working Group, [1]University of Pittsburgh, Pittsburgh, PA, [2]Shenzhen Children's Hospital, Shenzhen, China (People's Republic), [3]Zhejiang University School of Medicine, Zhejiang, China (People's Republic), [4]School of public health, Pittsburgh, PA, [5]Rheumatology and Immunology Department of Shenzhen Children's Hospital, Shenzhen, 518100, China., Shenzhen, China (People's Republic), [6]Zhejiang University School of Medicine, Hangzhou, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Haploinsufficiency of A20 (HA20) is a monogenic autoinflammatory disease caused by loss-of-function (LOF) mutations in *TNFAIP3*. HA20 was initially described as an early-onset form of Behçet's disease (BD)[1]; however, subsequent reports have revealed a broad clinical picture that can also include features of autoimmunity, lymphoproliferation, immunodeficiency, and allergy. The initial clinical descriptions could have led to an inaccurate representation of the natural history due to reporting or ascertainment bias. This study is the first large multicenter cohort study describing the clinical spectrum, genetic landscape, and natural history of patients with HA20.

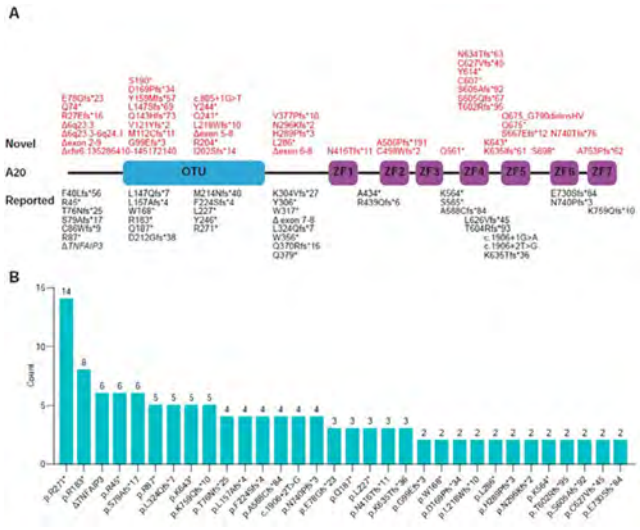
Methods: A retrospective analysis was conducted on HA20 patients referred to the study investigators following genetic testing that revealed a pathogenic or likely pathogenic variant in *TNFAIP3*. All variants were reviewed by study investigators in consultation with geneticists at participating sites. The diagnosis of HA20 was established through the identification of either a heterozygous *TNFAIP3* pathogenic variant (ACMG PVS1) or a heterozygous deletion of 6q23 including *TNFAIP3*. Probands were identified using multigene panels, chromosomal microarrays, or next gen sequencing-based clinical assays. Some family members were diagnosed using single-gene *TNFAIP3* testing after the initial proband diagnosis. Patients were divided into three groups (≤ 6 years, 6-16 years, and ≥ 16 years) for further analysis of the phenotype distribution.

Table 1. Baseline characteristics of patients divided by cohorts and ages

General characteristics	China	US	Total
Male, sex, n (%)	62 (56.4)		
Children, n (%)	81 (73.6)		
Median age at onset (y) (n=93)	3	5	
Median age at diagnosis (y) (n=93)	5.6	21.9	9.3
Median time of follow-up (m) (n=81)	25	39.1	28
Clinical features, n (%)	n = 107	n = 47	n = 154
Short stature	43 (41.2)	8 (17.0)	51 (33.1)
Recurrent fever	55 (51.4)	23 (48.9)	78 (50.6)
Lymphadenopathy	24 (22.4)	21 (44.7)	45 (29.2)
Hepatomegaly	22 (20.6)	9 (19.1)	31 (20.1)
Splenomegaly	16 (15.0)	12 (25.5)	28 (18.2)
Recurrent infection	34 (31.8)	12 (25.5)	46 (29.9)
Mucocutaneous involvement	73 (68.2)	42 (89.4)	115 (74.7)
Gastrointestinal involvement	69 (64.5)	26 (55.3)	95 (61.7)
Hepatic involvement	17 (15.9)	22 (46.8)	39 (25.3)
Hematologic abnormalities	60 (56.1)	40 (85.1)	100 (64.9)
Musculoskeletal system	31 (29.0)	30 (63.8)	61 (39.6)
Thyroid involvement	11 (11.7)*	14 (29.8)	25 (17.7)
Neurologic involvement	13 (12.1)	12 (25.5)	25 (16.2)
Pulmonary involvement	26 (24.3)	11(23.4)	37 (24.0)
Cardiac involvement	4 (3.7)	9 (19.1)	13 (8.4)
Ophthalmologic involvement	1 (0.9)	5 (10.6)	6 (3.9)

If it was clearly labeled, the number of patients in total equalled to the number of Chinese patients in parentheses plus 47 instead of 154.
*From 94 patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Genetic analysis of HA20 patients. A. Genetic analysis of this cohort revealed 85 pathogenic variants in TNFAIP3. Gene variants in red and black font represented novel variants and reported variants, respectively. B. Common variants identified in HA20 patients.

Results: A total of 185 patients with HA20 from 41 rheumatology clinics across 7 countries were included. The median age at onset was 3.3 (range: 0.04-30). Detailed clinical records were available for 169 patients. Among them, 75 (44.4%) presented with an autoinflammation-predominant phenotype, 26 (15.4%) with an autoimmunity-predominant phenotype, and 56 (33.1%) exhibited a mixed autoimmune-autoinflammatory phenotype. Autoinflammation-predominant disease was most common in the youngest age group ($p = 0.029$) and in the Chinese group ($p < 0.0001$). A total of 89 *TNFAIP3* pathogenic mutations were identified, including novel variants resulting in protein truncation or heterozygous deletion. No clear association was found between clinical phenotype and genetic architecture. Anti-TNF and anti-IL-1 agents were effective in most patients (60% and 63.2% respectively), particularly in those with inflammatory arthritis or gastrointestinal ulcers. Two thirds of patients achieved complete remission at their last follow-up visit.

Conclusion: HA20 presents with highly variable phenotypes, including autoinflammation-predominant, autoimmune-predominant, and mixed phenotypes. Autoimmunity may become more common over time and have a lower incidence in individuals with specific ancestries, although these differences could still be related to ascertainment bias in specific age groups and/or countries. No definitive genotype-phenotype correlation was observed. Lastly, this comprehensive and systematic description of a large international cohort may suggest improved precision medicine strategies for the complex care of HA20 patients.

References

Zhou Q, et al. Nat Genet. 2016.

Disclosure: M. Carpio Tumba: None; **T. He**: National Natural Science Foundation of China, 5; **J. Wang**: China Postdoctoral Science Foundation, 5, National Natural Science Foundation of China, 5; **E. Kairis**: None; **K. Goyette**: None; **A. Kethri**: None; **U. Karri**: None; **A. Towheed**: None; **J. Yang**: Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties, 5; **Q. Zhou**: National Natural Science Foundation of China, 5; **D. Schwartz**: Eli Lilly, 5, Jeffrey Modell Foundation, 5, National Institutes of Health, 5, Samuel and Emma Winters Foundation, 5, Sobi, 1, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2038

Real-World Use of Dual Targeted Therapy in Rheumatic Disease: A Single-Center Case Series

Marta Aguilar Zamora[1], Karla Romelia Arévalo Ruales[2], marta Garijo Bufort[2], Maria Isabel Pastor Orduña[1], Celia Aparicio Rubio[3], Silvia Cornejo Uixeda[4] and Joaquín Borrás Blasco[4], [1]Rheumatology Department, Hospital de Sagunto, Spain, Puerto de Sagunto, Comunidad Valenciana, Spain, [2]Rheumatology Department, Hospital de Sagunto, Spain, valencia, Spain, [3]Pharmacy Department, Hospital de Sagunto, Spain, Puerto de Sagunto, [4]Pharmacy Department, Hospital de Sagunto, Spain, Puerto de Sagunto, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Combination therapy with two biologic agents (bDMARDs) or a biologic plus a Janus kinase inhibitor (JAKi) is rarely used in rheumatology due to safety concerns and limited supporting evidence. However, it may be considered for selected patients with refractory disease or those with multiple immune-mediated inflammatory diseases (IMIDs). This case series describes the efficacy and safety of dual targeted therapy in patients with rheumatic conditions, including those requiring treatment for concurrent IMIDs or non-rheumatic comorbidities.

Methods: Patients treated in the Rheumatology Department of a district hospital who received at least two biologic agents or a combination of a bDMARD and a JAKi, dispensed by the hospital pharmacy, were retrospectively reviewed.

Patients were categorized into two groups:

- **Group A:** both agents for IMIDs, (eg., spondyloarthritis [Spa] and inflammatory bowel disease [IBD]).
- **Group B:** one treatment for a rheumatic inflammatory disease and the other for a non-rheumatic condition (eg., migraine, asthma).

Demographics, indications, duration of dual therapy, clinical response (Group A), acute-phase reactants, and adverse events (both groups) were collected. Clinical efficacy was assessed globally ('yes,' 'partial,' 'no') due to population heterogeneity.

Results: 10 patients were included: 6 in Group A and 4 in Group B. One patient in Group A received two different dual therapy regimens over time (both included) and one was in both groups due to triple therapy.

Table 1

Patient Number	Sex (M/F)	Age (years)	Disease Duration (years)	Dual Therapy Exposure Duration (months)	Biologic 1	Biologic 2	Biologic 3	Diseases
1	M	40	9	6	Upadacitinib 45 mg	Risankizumab	Etenimab	Spa, IBD, Psoriasis, Migraine
2	F	46	13	19	Upadacitinib 15 mg	Guselkumab	-	RA, Psoriatic Arthritis
3	M	44	5	16	Tofacitinib 11 mg	Infliximab	-	Spa, IBD
4	F	53	2	5	Tofacitinib 11 mg	Infliximab	-	Spa, IBD
5	F	51	22	12	Upadacitinib 15 mg	Ustekinumab	-	Spa, IBD
6	F	39	12	25	Tofacitinib 11 mg	Ustekinumab	-	Spa, IBD
8	M	39	8	18	Infliximab	Ustekinumab	-	Spa, IBD
7	F	55	9	19	Etenumab	Tocilizumab	-	RA, Migraine
8	F	16	2	17	Benralizumab	Upadacitinib 15 mg	-	Spa, Asthma
9	M	35	10	29	Adalimumab	Benralizumab	-	RA, Asthma
10	F	67	19	6	Clirtolizumab	Dupilumab	-	Spa, Atopic Dermatitis

Spa: spondyloarthritis
IBD: inflammatory bowel disease
RA: Rheumatoid Arthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Among the 10 patients, 4 were male and 6 female, with a mean age of 48.6 ± 18.1 years and a mean disease duration of 8.5 ± 5.4 years.

Therapy characteristics and drug combinations appear in Table 1, with the most frequent being JAK inhibitor plus an IL-23 inhibitor. Mean duration of dual therapy was 17.5 months (range: 5–29).

In Group A, 5/6 patients had Spa + IBD, one had psoriatic arthritis and rheumatoid arthritis. The average number of prior biologic treatments was 3.83 ± 1.47. Among 7 drug combinations, 2 patients showed clinical improvement, 4 partial improvement and 1 failed. One case led to treatment switch, resulting in partial benefit. The mean reduction in CRP was 7.85 ± 2.3 mg/L and in ESR 9.33 ± 15.14 mm/h. No serious adverse events were observed. Two patients experienced mild infections while on tofacitinib combinations, which resolved with dose reduction; treatment continued.

In Group B, non-rheumatic comorbidities included migraine (n=2), asthma (n=2), and atopic dermatitis (n=1). The median duration of treatment was 27 months (range 6–29). Four patients were still receiving treatment at the time of data collection and one patient discontinued due to lack of efficacy for migraine. No major adverse events were reported.

Conclusion: The expanding use of biologic therapies across multiple diseases has led to combination regimens involving biologic and targeted synthetic drugs. In our series the most frequent combination was JAKi with IL-23 inhibitor. Patients needing dual therapy often had Spa and IBD, but others with IMIDs or comorbidities like asthma or migraine also benefited. Despite the clinical complexity of these cases, dual therapy has shown a favorable safety and efficacy profile.

Disclosure: M. Aguilar Zamora: None; **K. Arévalo Ruales**: None; **m. Garijo Bufort**: None; **M. Pastor Orduña**: None; **C. Aparicio Rubio**: None; **S. Cornejo Uixeda**: None; **J. Borrás Blasco**: None.

Abstract Number: 2039

To Hold or Not to Hold: Variability in Management of DMARDs in the Setting of Acute Infections - A Survey of Rheumatologists

Mollie Gellman[1], Medhasweta Sen[2], Ari Schwartz[3], Peter Merkel[4] and Nadine Mbuyi[5], [1]Montefiore Medical Center, Bronx, NY, [2]University of Virginia, Charlottesville, VA, [3]Rheumatology Consultants PC, Brockton, MA, [4]University of Pennsylvania, Philadelphia, PA, [5]George Washington University, Washington, DC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Disease-modifying antirheumatic drugs (DMARDs) vary widely in their immunosuppressive activity. Guidance on managing DMARDs during acute infections is limited, particularly regarding when to hold or resume therapy. This study aimed to investigate clinical practice patterns among rheumatologists concerning management of DMARDs during acute infections, stratified by type of immunosuppression, degree of infection, and disease severity.

Methods: A 27-question survey was distributed to rheumatologists via professional networks and academic listservs; responses were anonymous. Questions assessed clinical decisions on holding/restarting DMARDs during varying severities of acute infection, in patients with either life/organ-threatening or non-life/organ-threatening rheumatic disease. Infections were categorized as: i) outpatient non-serious (unlikely to require hospitalization, may not need treatment), ii) outpatient

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

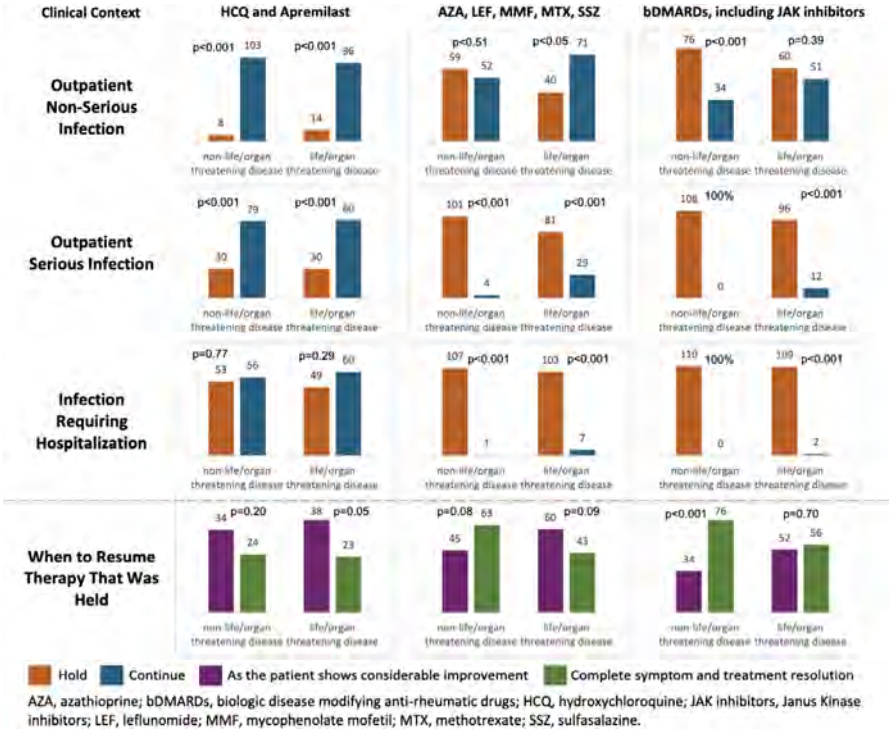


Figure 1. Rheumatologists' Views on Holding DMARDs During Infection

serious (may require hospitalization if not improving), and iii) requires hospitalization. DMARDs were grouped by immunosuppressive risk, from lowest to highest: 1) hydroxychloroquine (HCQ) and apremilast, 2) conventional synthetic DMARDs (csDMARDs: azathioprine, leflunomide, methotrexate, mycophenolate mofetil, sulfasalazine), and 3) biologic DMARDs (bDMARDs) including Janus kinase (JAK) inhibitors. Chi-square tests compared binary responses, with significance defined as $p < 0.05$.

Results: A total of 113 rheumatologists participated: 63% private practice, 34% academic; ages ~30-90 years, from 25 states and D.C. Responses are summarized in **Figure 1**. Depending on scenario, 73-93% of rheumatologists would continue HCQ and apremilast during outpatient infections ($p < 0.001$). Responses were split for infections requiring

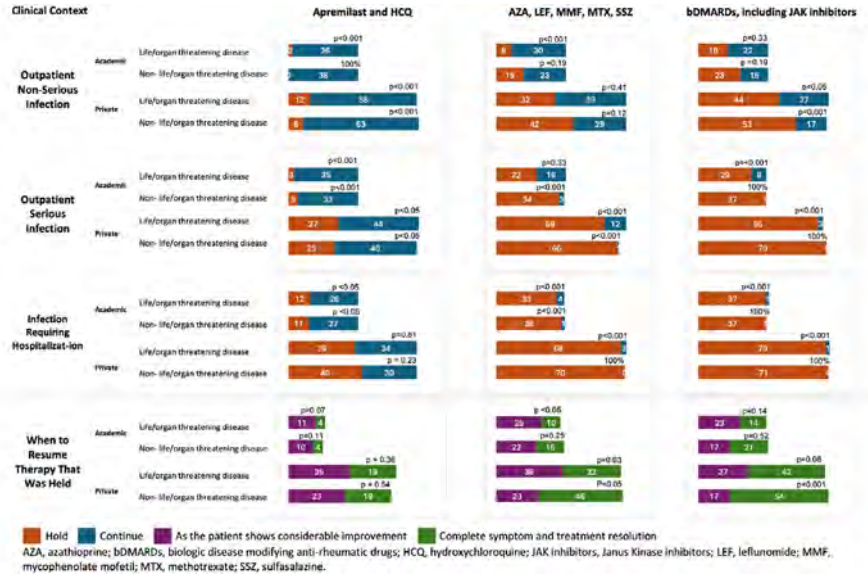


Figure 2. Rheumatologists' Views on Holding DMARDs During Infection, Based on Type of Practice

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hospitalization in both non-life/organ-threatening and life/organ-threatening disease (49%, 51%, and 45%, 55% respectively). 64% would continue csDMARDs for non-serious outpatient infections in patients with severe diseases ($p < 0.05$); responses were split 47% and 53% in less severe disease. 69% would hold bDMARDs and JAK inhibitors in non-serious outpatient infections without severe disease ($p < 0.001$), with divergent responses (54%, 46%) for life/organ-threatening disease. Depending on the context, 74-100% would hold csDMARDs and bDMARDs/JAK inhibitors during serious outpatient infections and infections requiring hospitalization, regardless of disease severity ($p < 0.001$). 77% would restart biologics only after full resolution of symptoms and completion of treatment in non-life/organ-threatening diseases ($p < 0.001$). In all other contexts there was no significant majority regarding when to restart therapy. Academic physicians were more likely than private physicians to continue treatment in milder infections, particularly in more severe rheumatic diseases, and to resume DMARDs earlier (**Figure 2**).

Conclusion: There is substantial variability among US rheumatologists in the management of DMARDs during acute infections. These findings highlight a significant knowledge gap and suggests that development of guidelines on this topic would help inform clinical decision-making and standardize care.

Disclosure: M. Gellman: None; **M. Sen**: None; **A. Schwartz**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **N. Mbuyi**: Sobi, 1.

Abstract Number: 2040

Steroid Psychosis and Neuropsychiatric Symptoms induced by Corticosteroid Injection in Rheumatology Patients

Morvarid Kavosh[1], Virva Walkington[1], Jigisha Rakholiya[1], Krystle Tapia[2], Maheswari Muruganandam[1], N. Suzanne Emil[1], Frank O'Sullivan[3] and Wilmer Sibbitt[1], [1]University of New Mexico, Albuquerque, NM, [2]University of New Mexico Hospital, Albuquerque, NM, [3]University of New Mexico, Albuquerque

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal (MS) corticosteroid (CS) injections are commonly used for joint inflammation with a perceived low risk of systemic toxicity, including hyperglycemia and adrenal suppression. However, rare neuropsychiatric complications, such as acute psychosis, have been reported after MS-CS injection. The exact mechanism is unclear, but systemic absorption and individual vulnerability may play roles. This study examines the incidence and predisposing factors of neuropsychiatric complications following MS-CS injections in rheumatology patients.

Methods: A retrospective analysis was performed on 5487 MS-CS injections at the University of New Mexico Hospital, supervised by one attending. Electronic medical records were reviewed to identify patients with new-onset psychiatric symptoms within seven days post-injection. Psychiatric complaints were confirmed based on provider documentation and mental health evaluations, when applicable. Data collected included the type and dose of corticosteroid, number of injection

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Neuropsychiatric Symptoms after Musculoskeletal Corticosteroid Injection

Table 1. Neuropsychiatric Symptoms after Musculoskeletal Corticosteroid Injection

	Psychiatric Symptoms	No Psychiatric Symptoms		
Number	**24**	**76**	**Confidence Interval** or Odds Ratio *****	**P value**
Age (years)	53.4±13.1	53.5±14.5	CI: -6.5 <-0.1< 6.3	0.98
Women	91.7 % (22/24)	86.8% (66/76)	OR: 1.67 CI: (0.34, 8.2)	0.25
Men	8.3 % *(2/24)*	13.2% (10/76)	OR: 0.6 CI: (0.12, 2.95)	0.25
Inflammatory arthritis	83.3% (20/24)	69.8% (53/76)	OR: 2.17 CI: (0.67, 7.06)	0.09
Dose of Triamcinolone Acetonide	73.3±43.7	76.3±47.3	CI: -24.2 <-3.0< 18.2	0.66
Pre-Existing Depressive Syndrome	83.3% (20/24)	68.4% (52/76)	OR: 2.31 CI: (0.71, 7.49)	0.08
Pre-Existing Anxiety Syndrome	87.5% (21/24)	47.4% (36/76)	OR: 7.78 CI: (2.14, 28.3)	0.001
Bipolar Disorder	12.5% (3/24)	3.9% (3/76)	OR: 3.48 CI: (0.65, 18.5)	0.12
Post-Traumatic Stress Syndrome	12.5% (3/24)	3.9% (3/76)	OR: 7.78 CI: (2.14, 28.3)	0.12
Pre-Existing Psychopharmacologic Therapy Before Injection	91.7% (22/24)	78.9% (60/76)	OR: 3.48 CI: (0.65, 18.5)	0.10

sessions, psychiatric symptom patterns, symptom duration, and whether proactive treatment was implemented during subsequent injections. A comparison was made between patients with and without psychiatric symptoms, focusing on baseline psychiatric history, particularly anxiety disorders.

Results: Of 5487 individual MS-CS injections in 596 individuals, 221 injections (4.02%) resulted in psychiatric complaints that were relayed to a medical provider. These complaints were concentrated in 24 patients, who had recurrent symptoms on reinjection. The mean dose of TA was 73.3±43.7 mg per injection session. The psychiatric symptoms post MS-CS injection in affected patients were vasomotor symptoms (100%), anxiety (100%), paranoia (37.5%), and hallucination (25%), and in certain cases acute medical consultation and/or treatment (29.2%) was required. Preexisting clinical depression (68.4%-83.3%) and anxiety syndromes (47.4%-87.5%) were very common in all rheumatology patients undergoing MS-CS injections (**Table I**). When comparing patients with neuropsychiatric symptoms after MS-CS injection to representative group who did not develop symptoms, a pre-existing anxiety syndrome was markedly increased in the neuropsychiatric group (**-Table 1**). All symptoms typically resolved within 3 days. Because of the recurrent nature of these symptoms in individual patients on reinjection, 11/24 (45.3%) of affected patients requested proactive treatment after an injection, and lorazepam 1 mg every 8 hours after the injection for 2-3 days was prescribed with complete prevention the symptoms.

Conclusion: Preexisting neuropsychiatric disease – especially depression and anxiety syndromes – is present in majority of rheumatology patients undergoing MS-CS injections. MS-CS injections can cause significant psychiatric symptoms in about 4% of cases and typically follows a stereotypic pattern with anxiety most common though psychotic symptoms can also occur. The major predisposing factor appears to be a pre-existing anxiety disorder. For affected patients, short-term benzodiazepine treatment may provide symptomatic relief and prevention.

Disclosure: M. Kavosh: None; **V. Walkington**: None; **J. Rakholiya**: None; **K. Tapia**: None; **M. Muruganandam**: None; **N. Emil**: None; **F. O'Sullivan**: None; **W. Sibbitt**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2041

Evaluating Biologic Effectiveness in Co-Occurring Dermatologic and Rheumatic Disease: A Systematic Review

Nashwah Memon[1], Dylan Wambold[2], Omar Alani[3], Syed Minhaj Rahman[4] and Adel Haque[5], [1]Lake Erie College of Osteopathic Medicine, Miami, [2]Drexel University College of Medicine, Philadelphia, [3]Icahn School of Medicine at Mount Sinai, New York, [4]Department of Medicine, Northwell Health Northern Westchester Hospital, Mount Kisco, [5]Jefferson Health Northeast, Philadelphia

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Clinicians prescribing biologics must be aware of the expanding indications for biologic/systemic therapies across dermatology and rheumatology alike. Given disease-state overlap between these fields, providers should also recognize relevant medical indications beyond their specialty. There is growing evidence supporting biologic off-label use in conditions such as spondyloarthritis and systemic lupus erythematosus (SLE). This systematic review aims to guide clinicians in determining biologic and systemic therapies for patients with co-occurring dermatologic and rheumatologic conditions by summarizing available evidence on overlapping indications.

Methods: A systematic search of PubMed & Scopus databases from inception through March 2025 was conducted using the following format: (((BiologicName treat*[Title/Abstract] OR (BiologicName improve*[Title/Abstract])) NOT (Skin Diseases, Infectious[MeSH Terms])) NOT ("skin and connective tissue diseases"[MeSH Terms])). Biologics included: adalimumab, secukinumab, etanercept, infliximab, ustekinumab, ixekizumab, guselkumab, risankizumab, apremilast, baricitinib, ruxolitinib, brodalumab, dupilumab, and belimumab. Studies describing off-label treatments of patients with rheumatic conditions were included. Data extracted from eligible studies included study design, sample size, biologic dosing and duration, clinical outcomes, and efficacy measures. Studies were then evaluated for their levels of evidence according to the Oxford Centre of Evidence-Based Medicine.

Results: Multiple biologics—including adalimumab, brodalumab, etanercept, infliximab, ixekizumab, risankizumab, ustekinumab, and secukinumab—are indicated for psoriasis. Among these, all except brodalumab are also approved for psoriatic arthritis (PsA), and several are indicated for ankylosing spondylitis (AS). Secukinumab has additional approvals for non-radiographic axial spondyloarthritis and enthesitis-related arthritis, while belimumab is specifically approved for SLE. Adalimumab, etanercept, infliximab, secukinumab are also indicated for rheumatoid arthritis (RA). In a case series of 45 patients, off-label use of TNF inhibitors (infliximab, etanercept, adalimumab) for SAPHO syndrome resulted in 93.3% of patients experiencing musculoskeletal symptom relief and 72.4% showing skin symptom improvement. IL-17/IL-23 inhibitors had moderate efficacy, with ustekinumab improving skin symptoms in 50% of patients and musculoskeletal symptoms in 60%, while secukinumab led to improvements in 57.1% and 37.5%, respectively. In SLE, a randomized controlled trial of ustekinumab showed a 28% greater SRI-4 response compared to placebo. Additionally, in an open-label 28-week trial for AS, off-label ustekinumab use led to reduced symptoms and inflammation by week 24.

Conclusion: This review highlights the expanding role of biologics in the treatment of rheumatologic conditions beyond their primary dermatologic indications. Their interdisciplinary applications present new opportunities for research and clinical practice, underscoring the need for further investigation to optimize their use and broaden their therapeutic scope.

Disclosure: N. Memon: None; **D. Wambold**: None; **O. Alani**: None; **S. Rahman**: None; **A. Haque**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2042

Safety and Effectiveness of the Use of Combined Therapy with bDMARDS and tsDMARDs in Immune-mediated Inflammatory Diseases

Natalia Lopez Juanes[1], Carlota Ureta[1], Marta Novella-Navarro[1], Irene Monjo Henry[1], Diana Peiteado[1], Alejandro Villalba[1], Laura Nuño[2], Victoria Navarro-Compan[3], María Sanz[1], Mª ángeles Gonzalez[1], Cristina Suarez[4], Agustin Remesal[1], Rosa Alcobendas[5], Clara udaondo[1], Elena Sendagorta[5], Alejandro Balsa[1], Eugenio de Miguel[1] and Chamaida Plasencia-Rodríguez[1], [1]Hospital Universitario La Paz, Madrid, Spain, [2]Hospital Universitario Puerta de Hierro, Madrid, Spain, [3]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [4]Hospital Universitario La Paz, Madrid, Madrid, Spain, [5]La Paz University Hospital, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The combination of biological (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) has emerged as a promising approach to improve clinical outcomes in immune-mediated inflammatory diseases (IMIDs), particularly in refractory or complex cases where simultaneous targeting of multiple inflammatory pathways may be beneficial. However, this strategy raises concerns regarding safety, adverse events, and optimal drug selection. The objectives of this

	IMID	Extra-MSK involvement	Gender (age at baseline, years)	Previous DTT	Most recent DTT	DTT indication	DTT exposure (months)	Discontinuation of DTT (reason)	Baseline disease activity	Disease activity at the end of DTT or observational period	Clinical improvement of DTT indication
1	RA	Sicca syndrome	Woman (46.6)	None	TNFi + JAKi	MSK disease	26.3	Yes (infection)	DAS28 6.1	DAS28 2.9	YES
2	RA	Diffuse interstitial lung disease	Woman (68.3)	None	TNFi + JAKi	MSK disease	7.9	Yes (infection)	DAS28 4.5	DAS28 6.9	NO
3	RA	IBD	Woman (54.2)	None	TNFi + anti-IL12 y IL23	IBD	13.8	No	DAS28 1.6	DAS28 2.2	YES
4	1) RA 2) Chronic angioedema	-	Woman (52.7)	TNFi + anti-IgE	Rituximab + anti-IgE	Chronic angioedema	60.3	No	-	-	YES
5	SpA	-	Woman (68.1)	TNFi + JAKi	TNFi + JAKi	MSK disease	15.3	No	ASDAS 4.0	ASDAS 2.93	YES
6	SpA	IBD	Woman (43.8)	1) TNFi + Vedolizumab 2) JAKi + Vedolizumab 3) TNFi + Vedolizumab	TNFi + Vedolizumab	MSK disease	59.4	No	ASDAS 4.7	ASDAS 4.3	YES
7	SpA	IBD Uveitis	Woman (48.5)	None	JAKi + Vedolizumab	MSK disease	17.8	No	ASDAS 3.3	ASDAS 2.2	YES
8	SpA	IBD	Woman (50.6)	1) TNFi + anti-IL23 2) JAKi + anti-IL23	TNFi + anti-IL23	MSK disease	5.9	No	-	-	NO
9	SpA	IBD	Man (51.4)	TNFi + Vedolizumab	TNFi + Vedolizumab	MSK disease + IBD	9.7	Yes (Secondary inefficacy)	ASDAS 3.5	-	NO
10	SpA	IBD	Man (48.7)	TNFi + Vedolizumab	TNFi + Vedolizumab	MSK disease + IBD	4.8	No	-	-	YES
11	1) Spa 2) Chronic urticaria	IBD	Man (56.1)	None	TNFi + anti-IgE	MSK disease	8.5	No	ASDAS 2.3	ASDAS 2.4	NO
12	PsA	Psoriasis	Man (28.5)	None	TNFi + anti-IL23	Skin disease	15.4	No	DAPSA 8.4 ASDAS 1.9	DAPSA 5.0 ASDAS 1.5	YES
13	1) PsA 2) Chronic urticaria	Psoriasis	Woman (67.5)	None	anti-IL23 + anti-IgE	MSK disease	10.3	No	DAPSA 11.7	DAPSA 20.5	NO
14	PsA	Psoriasis	Woman (54.6)	None	TNFi + JAKi	MSK disease	16.5	No	DAPSA 14.1	DAPSA 12.1	YES
15	JIA	Uveitis	Woman (21.2)	None	TNFi + JAKi	MSK disease	25.0	Yes (loss of follow-up)	DAS28 5.7	DAS28 3.1	YES
16	JIA	-	Woman (18.7)	None	JAKi + anti-IL23	MSK disease	14.1	Yes (Inefficacy)	-	-	NO

Clinical characteristics, DTTs used, duration of treatment, reason for discontinuation and disease activity and status at baseline (beginning of most recent DTT) and at discontinuation of treatment or at the end of the study of the included patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

study are to describe the clinical characteristics of IMID patients receiving dual targeted therapy (DTT) with two bDMARDs or a bDMARD plus a tsDMARD, to identify the most commonly used combinations and main adverse events and to evaluate clinical response to DTT.

Methods: We conducted a retrospective observational study including IMID patients treated with bDMARD and/or tsDMARD combinations at Hospital Universitario La Paz from October 2019 to December 2024. We collected clinical data, details of DTT combinations, treatment duration, reasons for discontinuation, and disease activity assessed by DAS28, ASDAS, and DAPSA at baseline and at discontinuation or end of follow-up.

Results: Nineteen patients with 28 DTT cycles were included; 68.4% were women, with a mean age at DTT initiation of 42.9 ±19.4 years. Diagnoses included spondyloarthritis (SpA, 36.8%), rheumatoid arthritis (RA, 21.1%), psoriatic arthritis (PsA, 15.8%), juvenile idiopathic arthritis (JIA, 10.5%), polyarthritis of possible genetic cause (10.5%), and Behçet syndrome (5.3%). A second IMID treated with bDMARD/tsDMARD was associated in 57.9% of patients: 63.3% with bowel disease (IBM), 27.3% with psoriasis, 18.2% with chronic urticaria and 9.1% with chronic angioedema. Extra-musculoskeletal manifestations were present in 21.2%: 1 case of interstitial lung disease, 1 sicca syndrome, 2 uveitis and 1 with neurological involvement. Patients had received a median of five prior DMARDs. Thirteen patients (68.4%) had a single DTT cycle, while six (31.6%) had ≥1 prior DTT cycles. The main indications for DTT initiation were active musculoskeletal disease (63%), active IBD (11.1%), combined active MSK/IBD disease (7.4%), and psoriasis (7.4%). Most frequently used combinations were TNF inhibitor (TNFi)+JAK inhibitor (JAKi, 32.1%), TNFi+vedolizumab (25.0%), and TNFi+anti-IL23 (10.7%). Median DTT duration was 10.3 months (range 0.7–60.3 months). The most common adverse events were infections (25.0%) and hypertransaminasemia (10.7%). Discontinuation occurred in 57.1% of DTT cycles, mainly due to inefficacy (31.1%) and infections (7.1%). At the end of the study, 57.9% of patients maintained TDD and clinical improvement was observed in 52.6%, as assessed by disease activity indices and clinical reports (see Table 1).

Conclusion: DTT appears to be a viable option for refractory IMID patients, achieving clinical improvement in over half of the cases. Nonetheless, the high rate of adverse events and treatment discontinuation underscores the importance of careful patient selection and close monitoring. Further research is needed to refine patient selection, optimize drug combinations, and improve risk management strategies.

Disclosure: N. Lopez Juanes: None; **C. Ureta**: None; **M. Novella-Navarro**: None; **I. Monjo Henry**: None; **D. Peiteado**: None; **A. Villalba**: None; **L. Nuño**: None; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **M. Sanz**: None; **M. Gonzalez**: None; **C. Suarez**: None; **A. Remesal**: None; **R. Alcobendas**: None; **C. udaondo**: None; **E. Sendagorta**: None; **A. Balsa**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6.

Abstract Number: 2043

Renal Outcomes of Long-term Canakinumab in Patients with Adult Familial Mediterranean Fever (FMF) and Biopsy-Confirmed AA Amyloidosis

Büşra Fırlatan Yazgan[1], Gözde Sevgi Kart bayram[1], Buğu Bulat[1], Levent Kılıç[1], Tolga Yildirim[2], Umut Kalyoncu[1], Şule Apraş Bilgen[1], Ali İhsan Ertenli[1], Seref Rahmi Yilmaz[2] and **Omer Karadag**[3], [1]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [2]Division of Nephrology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [3]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Canakinumab, an interleukin-1β inhibitor, has demonstrated efficacy in treating colchicine-resistant/intolerant familial Mediterranean fever (FMF). This study aims to assess the efficacy and safety of long-term canakinumab treatment in AA amyloidosis patients with FMF managed at a tertiary center.

Methods: Adult patients diagnosed with FMF based on the Tel Hashomer criteria and treated with canakinumab, followed at the Rheumatology and Nephrology Clinics of Hacettepe University, were retrospectively evaluated. Biopsy-confirmed AA amyloidosis was identified in 25 of the 107 patients who received canakinumab. One patient who did not come for follow-up after canakinumab was excluded from the study. Data on demographics, age at diagnosis, estimated glomerular filtration rate (eGFR) (≥60 vs < 60 mL/min/1.73 m^2) and proteinuria levels (urine protein/creatinine ratio, mg/g) before and after canakinumab, use of ACE inhibitors or ARBs, presence of diabetes mellitus, history and timing of renal transplantation, colchicine dose at the last visit, canakinumab dose and interval, treatment duration were recorded.

Table 1. Demographic and clinical characteristics of the study cohort

	Study cohort (N:24)	
Gender (F/M)	15/9	
Age (years), median (IQR)	46.5 (39.5-56)	
Age at diagnosis (years), median (IQR)	19 (14.5-37.5)	
Continuation of colchicine (n,%)	22 (91.7)	
Colchicine dose at last visit (mg/day), median (IQR) (n: 22)	1.0 (0.5-1.25)	
Drug survival (months), median (IQR)	69 (30.5-88.5)	
Dose interval (n,%)		
Every 4 weeks (150 mg)	21 (87.5)	
Every 8 weeks (150 mg)	1 (4.2)	
Every 12 weeks (150 mg)	1 (4.2)	
Every 4 weeks (300 mg)	1 (4.2)	
Renal transplantation (n,%)	8 (33.3)	
Before canakinumab	7 (29.2)	
After canakinumab	1 (4.2)	
Use of ACEI/ARB treatment (n,%)	13 (54.2)	
Presence of diabetes mellitus (n,%)	4 (16.7)	
eGFR (mL/min/1.73 m²) (n,%)	**Before CAN**	**After CAN**
≥60	15 (62.5)	10 (41.7)
<60	9 (37.5)	14 (58.3)
Proteinuria	**Before CAN**	**After CAN**
Urine protein/creatinine ratio (mg/g), median (IQR)	2423.2 (454.4–4389)	724.2 (188.9–1975.4)
<3.5 g/day, (n,%)	16 (66.7)	22 (91.7)
≥3.5 g/day, (n,%)	8 (33.3)	2 (8.3)

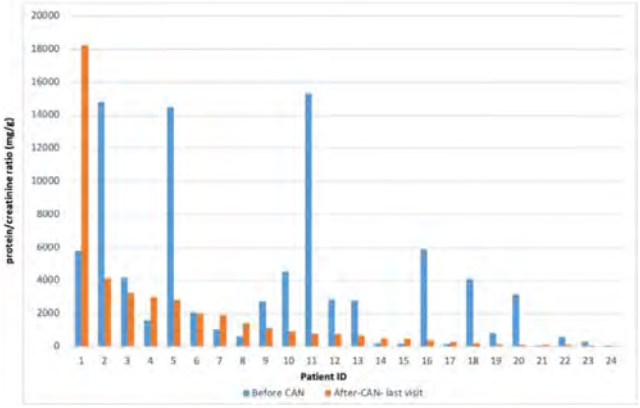


Figure 1. Comparison of baseline and final proteinuria levels in patients receiving canakinumab

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In total 24 patients (15 F, 9 M) were included for final analysis **(Table 1)**. The median age at diagnosis was 19 (14.5-37.5) years, while the median age of the cohort was 46.5 (39.5-56) years. Of eight patients with renal transplantation, only one underwent transplantation after initiation of canakinumab. At the last visit, the median colchicine dose was 1.0 mg/day (0.5–1.25). During a median duration of 69 months (30.5–88.5), canakinumab was administered at 150 mg/4 weeks in 21 patients, every 8 weeks in one patient, and every 12 weeks in another. In one patient, the dose was escalated to 300 mg/4 weeks. The proteinuria level significantly decreased following canakinumab initiation, from 2423.2 mg/g (454.4–4389) to 724.2 mg/g (188.9–1975.4) at the final visit (p=0.034). Nephrotic-range proteinuria (>3.5 g/day) was present in 8 patients before treatment, but persisted in only two patients at the final assessment. A change in eGFR category was observed in only five patients (patients 6, 8, 14, 17, and 18)**(Figure 1)**.

Conclusion: Canakinumab therapy, administered for approximately six years, was well tolerated in patients with FMF and biopsy-proven AA amyloidosis, also patients with renal transplantation. High adherence of colchicine and canakinumab treatment was associated with a significant reduction in proteinuria and stabilization of renal function in the majority of patients.

Disclosure: B. Fırlatan Yazgan: None; **G. Kart bayram**: None; **B. Bulat**: None; **L. Kılıç**: None; **T. Yildirim**: None; **U. Kalyoncu**: None; **Ş. Apraş Bilgen**: None; **A. Ertenli**: None; **S. Yilmaz**: None; **O. Karadag**: None.

Abstract Number: 2044

Infections and Associated Mortality in VEXAS Syndrome: A Systematic Review and Meta-Analysis

Oyku Zeynep Avarbek[1], **Ozlem Arikan**[2], Aysu Tatari[3], Furkan Ak[4], Bengisu Gur[5], Sinem Nursel Duzenci[6], Yasin Taha Tuncar[7], Mustafa Sivri[8], Mustafa Ovayolu[9] and Miray Kurtca[10], [1]Bezmialem Vakif University, Faculty of Medicine, Istanbul, Türkiye, Istanbul, Turkey, [2]Istanbul Aydin University, Faculty of Medicine, Istanbul, Türkiye, Istanbul, Turkey, [3]Pamukkale University, Faculty of Medicine, Denizli, Türkiye, Denizli, Turkey, [4]Sofia University St. Kliment Ohridski, Faculty of Medicine, Sofia, Bulgaria, Sofia, Bulgaria, [5]Istanbul University, Istanbul Faculty of Medicine, Istanbul, Türkiye, Istanbul, Turkey, [6]Balikesir University, Faculty of Medicine, Balikesir, Türkiye, Balikesir, Turkey, [7]Akdeniz University, Faculty of Medicine, Antalya, Türkiye, Istanbul, Turkey, [8]Gazi University, Department of Emergency Medicine, Ankara, Türkiye, Ankara, Turkey, [9]Hacettepe University, Faculty of Medicine, Ankara, Türkiye, Ankara, Turkey, [10]Richmond University Medical Center, Department of Internal Medicine, Staten Island, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome is a late-onset, monogenic autoinflammatory disorder driven by somatic mutations in the UBA1 gene of hematopoietic stem cells. Given that the management of VEXAS syndrome often requires long-term treatment with intense immunosuppressive drugs, the overall susceptibility to infections is elevated in VEXAS patients. This systematic review aims to assess the spectrum of reported infectious pathogens and their associated complications in patients with VEXAS syndrome.

Methods: This study followed the PRISMA 2020 Statement, with its protocol prospectively registered in PROSPERO (CRD42023450442). We screened MEDLINE (via PubMed) and EMBASE from the earliest record until March 25, 2025. Cohort studies that reported infections caused by a confirmed pathogen during the follow-up of patients with VEXAS syndrome were eligible for inclusion. We excluded case reports and patients who lacked confirmation of the VEXAS diagnosis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the included studies bDMARD: biological disease-modifying antirheumatic drugs, cDMARD: conventional disease-modifying antirheumatic drugs, HSV: Herpes simplex virus, JAKi: Janus-kinase inhibitors, PJP: Pneumocystis jiroveci pneumonia, VZV: Varicella zoster virus a: Presented in median (IQR) b: Presented in mean ± SD

Study label	Country	Design	Number of patients, female (n)	Age (median [range])	Glucocorticoid users (n,%)	Glucocorticoid dosage (*mg/day, median [range]*)	Glucocorticoid-sparing medications	Prophylaxis
De Valence 2024	France	Retrospective cohort	124, 4	68 (53-75)[a]	112, 90%	12.5 (10.0–24.8)[a]	csDMARD, bDMARD, JAKi, Azacitidine	Prophylaxis was received by 48% of the infected patients
Johansen 2025	Denmark	Retrospective cohort	16, 0	74 [51-78]	14, 87.5%	0 (n=3) 5-10 (n=7) 25 (n=1) ≥25 (n=4)	bDMARD, Azacitidine	Not reported
Kirino 2024	Japan	Prospective cohort	30, 0	73.5 [55-88]	20, 66.7%	9 (0-40)	csDMARD, bDMARD, JAKi	Not reported
Vitale 2025	Multinational	Retrospective cohort	69, 4	71.8 ± 9[b]	58, 85.5%	Not reported	csDMARD, bDMARD, JAKi	Not reported
Czech 2024	USA	Retrospective cohort	94, 0	64 [40-78]	94, 100%	21 [15–29][a]	csDMARD, bDMARD, JAKi	PJP: 25% risk reduction VZV: 15% risk reduction HSV: no significant reduction

or the infectious etiology. The primary outcome was determined as the frequency distribution of reported infectious agents, stratified by pathogen type, including bacterial, viral, and fungal categories. The secondary outcome was the infection-related mortality risk. A pairwise meta-analysis was conducted to calculate the pooled mortality risk among included patients.

Results: Five cohorts with 333 patients were included. At the time of enrollment, 299 (89.8%) of these patients were receiving glucocorticoids (Table 1). Among the included patients, 110 (33%) were reported to have experienced at least one episode of infection with a confirmed etiologic agent, and multiple infections were observed in 10 (3%). A total of 146 infectious episodes were identified in these patients. Bacterial agents were responsible for 72 (49.3%) of the cases. The most frequently isolated bacterial pathogens were Enterobacteriaceae (22.2%), Legionella pneumophila (19.4%), and non-tuberculous mycobacteria (19.4%). Among viral agents, the highest frequencies were observed for SARS-CoV-2 (41.2%), varicella-zoster virus (21.6%), and herpes simplex virus (15.7%). Pneumocystis jirovecii (73.9%) was the most

Table 2. Distribution of identified pathogens in patients with VEXAS Syndrome

Category	Pathogen	n	Frequency Among All Cases (%)	Frequency Within Category (%)
Bacterial (n =72)				
	Enterobacteriaceae	16	10.96%	22.22%
	Legionella pneumophila	14	9.59%	19.44%
	Non-tuberculous mycobacteria	14	9.59%	19.44%
	Pseudomonas aeruginosa	6	4.11%	8.33%
	Staphylococcus aureus	6	4.11%	8.33%
	Streptococcus spp.	1	0.68%	1.39%
	Listeria monocytogenes	1	0.68%	1.39%
	Actinomyces odontolyticus	1	0.68%	1.39%
	Nocardia spp.	1	0.68%	1.39%
	Coagulase-negative Staphylococci	1	0.68%	1.39%
	Francisella philomiragia	1	0.68%	1.39%
	Achromobacter spp.	1	0.68%	1.39%
	Stenotrophomonas maltophilia	1	0.68%	1.39%
	Campylobacter jejuni	1	0.68%	1.39%
	Acinetobacter johnsonii	1	0.68%	1.39%
	Sphingomonas koreensis	1	0.68%	1.39%
	Mycobacterium tuberculosis	1	0.68%	1.39%
	Clostridioides difficile	1	0.68%	1.39%
	Haemophilus species	1	0.68%	1.39%
Viral (n = 51)				
	SARS-CoV-2	21	14.38%	41.18%
	Varicella-zoster virus	11	7.53%	21.57%
	Herpes simplex virus	8	5.48%	15.69%
	Human metapneumovirus	2	1.37%	3.92%
	Influenza virus	2	1.37%	3.92%
	Cytomegalovirus	2	1.37%	3.92%
	Hepatitis E virus	1	0.68%	1.96%
	Toscana virus	1	0.68%	1.96%
	JC virus	1	0.68%	1.96%
	Parainfluenza virus	1	0.68%	1.96%
Fungal (n = 23)				
	Pneumocystis jirovecii	17	11.64%	73.91%
	Nocardia spp.	2	1.37%	8.70%
	Aspergillus spp.	2	1.37%	8.70%
	Candida albicans	1	0.68%	4.35%
	Cryptococcus neoformans	1	0.68%	4.35%

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

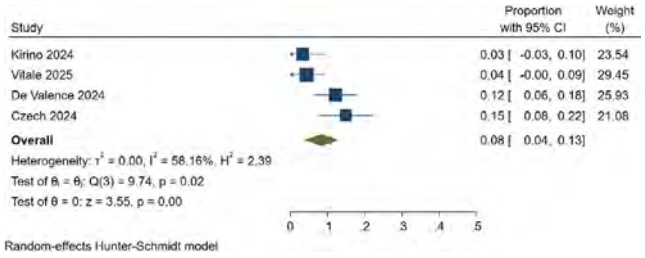


Figure 1. Infection-related mortality in patients with VEXAS syndrome

common cause of fungal infections (Table 2). Most infections were localized to the bronchopulmonary system (64.4%). In the context of glucocorticoid-sparing treatment strategies, 23 (19.3%) infectious episodes occurred during cDMARD therapy, 35 (29.4%) during bDMARD use, 41 (34.4%) during JAK inhibitor treatment, and 20 (16.8%) during azacitidine therapy. According to the meta-analysis outcomes, the overall infection-related mortality risk among included patients was 8% [95% CI (0.04,0.13), Figure 1].

Conclusion: Infections are among the significant causes of morbidity and mortality in patients with VEXAS syndrome. Physicians should closely monitor patients throughout the follow-up period and maintain careful control over immunosuppressive drug dosing. Further studies are needed to evaluate the efficacy of anti-infective prophylaxis in these patients.

Disclosure: O. Avarbek: None; **O. Arikan**: None; **A. Tatari**: None; **F. Ak**: None; **B. Gur**: None; **S. Duzenci**: None; **Y. Tuncar**: None; **M. Sivri**: None; **M. Ovayolu**: None; **M. Kurtca**: None.

Abstract Number: 2045

Malignancy in Behçet's Syndrome: A 24-Year Cohort Study In a Non-Endemicand Multiethnic Country

Pedro Araujo[1], Rafael Bassara Macedo[2], Fabio Specian[2], Carolina Ejnisman[3], Barbara Bayeh[3], Percival Sampaio-Barros[4], Thiago Freitas[4], Rafael Cordeiro[5] and Henrique Giardini[4], [1]Universidade de São Paulo, Sao Paulo, São Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's syndrome (BS) has been associated with an increased risk of malignancy, particularly in studies from endemic regions such as East Asia and the Middle East. Nonetheless, little is known about cancer risk in non-endemic, multiethnic populations. This study aimed to evaluate the frequency and profile of malignancies in a long-term BS cohort from South America.

Methods: We retrospectively conducted a data analysis of a single-center, multiethnic, prospective cohort of patients with BS followed between January 2000 and December 2024. Patients were diagnosed based on the International Study Group and/or the International Criteria for Behçet's Disease. Cancer occurrence was analyzed using descriptive statistics and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

compared across groups with chi-square, Fisher's exact, and unpaired Student's t-tests. Unadjusted odds ratios (OR) (95% CI) were calculated through bivariate logistic regression.

Results: A total of 302 BS patients were included, of whom 14 (4.6%; 95% CI: 2.3%–7.0%) were diagnosed with cancer. The cohort was predominantly female (n=186; 61.6%), with 8 women (57.1%) in the cancer group. The mean follow-up time was 160.3 months (±92.6) in the cancer group and 122.8 months (±80.3) in the non-cancer group. Patients who developed cancer had a mean age of 33.4 years (±8.6) at the time of BS diagnosis, compared to 31.4 years (±10.4) among those without cancer. Cancer was diagnosed 18(±13.1) years after BS diagnosis, at a mean age of 49,4(±17) years. The most common malignancies were endometrial and bladder cancer (2 cases each; 14.3%). Single cases (7.1% each) included cervical intraepithelial neoplasia, breast cancer, undifferentiated soft tissue neoplasm, adenocarcinomas of the lung, colon, prostate, and a metastatic tumor with unknown primary site; chronic myeloid leukemia, large granular lymphocyte leukemia, and central nervous system lymphoma. In univariate analysis, type 2 diabetes mellitus (DM2) was the only variable significantly associated with cancer occurrence ($p = 0.004$), with an OR of 5.8 (95% CI: 1.89–17.74). No statistically significant associations were found with sex, smoking, alcohol use, clinical manifestations, or immunosuppressive therapies, including cyclophosphamide. Due to the presence of only one significant predictor, a multivariate regression model could not be created.

Conclusion: In the present long-term cohort, overall malignancy rate was 4.6%, with hematologic malignancies being the most frequent type, which is consistent with findings from other BS cohorts and raises questions about underlying immunologic mechanisms or exposure to immunosuppressive agents. The average interval between BS diagnosis and cancer onset was 18 years, underscoring the need for long-term vigilance. Notably, DM2 was the only variable significantly associated with cancer, with a nearly sixfold increased risk. This finding reinforces the established link between metabolic comorbidities and carcinogenesis. No associations were found between malignancy and other variables. However, given the relatively small number of cancer cases, the study was underpowered to detect weaker associations.

Disclosure: P. Araujo: None; **R. Bassara Macedo**: None; **F. Specian**: None; **C. Ejnisman**: None; **B. Bayeh**: None; **P. Sampaio-Barros**: None; **T. Freitas**: None; **R. Cordeiro**: None; **H. Giardini**: None.

Abstract Number: 2046

Utilization of the All of Us Research Program to Study the Impact of Genetic Background on Autoinflammatory Diseases

Song Wu[1], Zuoming Deng[2], Peter Gorevic[1] and **Qingping Yao**[1], [1]Stony Brook University, Stony Brook, NY, [2]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: A widely recognized model of disease pathogenesis is the potential interplay of gene x gene x environment. Low penetrance variants in the NOD-like receptor and MEFV genes together may constitute a genetic background and contribute to genetically transitional disease. We utilized the All of Us Research Program (All of Us) to study the impact of genetic backgound in a large cohort of patients with autoinflammatory disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective analysis of adult patients with systemic autoinflammatory diseases (SAIDs). All patients underwent testing for a periodic fever syndrome gene panel designed to capture low penetrance variants of clinical significance. The distribution of gene variants and their frequencies were compared with 128,196 participants of European ancestry from the All of Us control.

Results: In total, 471 patients were genotyped and were divided into genotype-positive and -negative groups. Individual patients with positive genotyping carried variants in one or more SAID genes. SAIDs diagnosed among patients were Yao syndrome, Familial Medeteranean fever, Cryopyrin-associated periodic syndrome, NLRP12-Autoinflammatory disease and Mixed NOD-like receptor associated autoinflamamtory disease among others. For 265 patients who carried digenic or oligogenic variants, various combinations of these SAID genes were computed. We found the following genotype combinations NOD2/NLRP12, NOD2/MEFV, NOD2/NLRP3 and NLRP3/NLRP12, MEFV/NLRP3/NOD2, MEFV/NLRP12/NOD2 in decreasing order of prevalence. The frequencies of digenic and oligogenic variants in our patient population were compared with 128,196 controls in the All of Us dataset. We found that certain combinations of gene variants (e.g., NLRP3 Q705K/NOD2 V955I or NLRP12 F402L/NOD2 IVS8+158, NOD2 V955I/NLRP12 F402L) were significantly more frequent (**-Table to be presented**). These results indicate that digenic or oligogenic variants of low penetrance may constitute a related but divergent genetic backgroud susceptibility for several autoinflammatory diseases.

Conclusion: Comparison of a large cohort of SAID patients seen over a number years in a US referral center with the large All of Us control population underscores the impact of genetic background on disease expression. Genomic testing to search for digenic or oligogenic variants of even low penetrance is likely to significantly aid in disease diagnosis, and guide precision therapy.

Disclosure: S. Wu: None; **Z. Deng**: None; **P. Gorevic**: None; **Q. Yao**: None.

Abstract Number: 2047

Trends in Lung Transplant Listing Outcomes in Connective Tissue Disease associated Interstitial Lung Disease (CTD-ILD) Across Two Decades

Sambhawana Bhandari[1], Derek E. Byers[1] and Deepali Sen[2], [1]Washington University in St. Louis School of Medicine, St. Louis, [2]Washington University in St Louis, Chesterfield, MO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Lung transplantation represents a potential life-extending therapy for patients with advanced CTD-ILD. This study aims to characterize lung transplant listing outcomes among CTD-ILD patients over a 20-year period using the Organ Procurement and Transplantation Network (OPTN) national database.

Methods: Data analyzed from the OPTN between 2003-2023 included adults ≥18 years of age with CTD-ILD listed for lung transplantation. Patients were categorized into six subgroups based on diagnosis: scleroderma, lupus, rheumatoid arthritis (RA), myositis, Sjögren's, and "Other" (including mixed connective tissue disease, CTD, etc.). Trends in listing and outcomes were analyzed in 5-year quartiles and across diagnoses. We analyzed the proportion of patients getting successfully transplanted, wait list times, and death on transplant list.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Shows the number of patients listed for lung transplantation every 5-year intervals, numbers transplanted, percentage transplanted, death on the list (and percentage), and mean time to transplant in days with standard deviation (SD).

Quarter	Listed (N)	Tx (N)	Tx (%)	Death (N)	Death (%)	Mean time to transplant in days (SD)
2003-2008	185	116	62.70%	36	19.50%	233.9 (291.1)
2009-2013	443	317	71.60%	78	12.20%	195 (290.6)
2014-2018	605	459	75.90%	69	7.90%	168 (254.1)
2019-2023	744	607	81.60%	48	5.00%	120.9 (196.4)

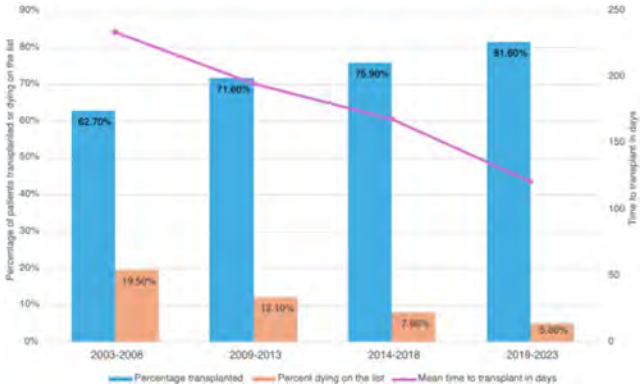


Figure 1: Line graph showing decrease in the time to transplant in days. Bar diagram showing an increase in percentage of transplanted patients and decrease in the percentage of death on the list from 2003-2023.

Results: A total of 1,977 individuals with CTD-ILD were listed for lung transplantation between 2003-2023.

Trends across time: In 5-year intervals numbers of patients listed for transplant increased from 185 in 2003-2007, 443 in 2008-2013, 605 in 2014-2018, and 744 in 2019-2023. The proportion of patients who underwent successful transplantation also steadily increased: from 62.7% in 2003-2008, 71.6% in 2009-2013, 75.9% in 2014-2018, and 81.6% in 2019-2023. The average time from listing to transplant in days decreased significantly, from 233.9 in 2003-2008 to 120.9 in 2019-2023. Death on the waitlist decreased over time: from 19.5% in 2003-2008, 12.2% in 2009-2013, 7.9% in 2014-2018, and 5% in 2019-2023.

Trends across diseases: Of the diagnosis groups listed for transplant, Scleroderma was the most common (47%, n=924) followed by "Other" (16%, n=323), RA (15%, n=293), myositis (11%, n=221), Sjögren's (7%, n=137), and lupus (4%, n=79). Rates of proceeding to transplantation were similar: "Other" (78.32%, n=253), Sjögren's (77.37%, n=106), RA

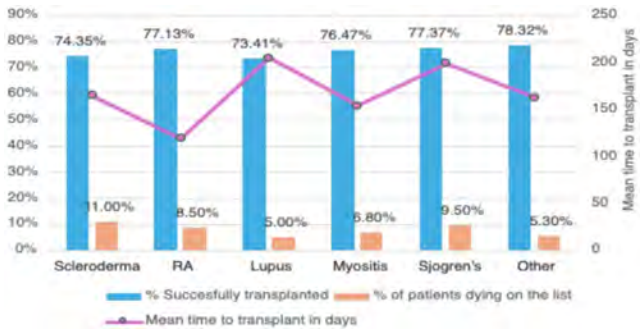


Figure 2: Bar diagram showing percentage of patients successfully transplanted (patients transplanted/patients listed *100), death on the list (%), and mean transplant time in days across various CTD types

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(77.13%, n=226), myositis (76.47%, n=169), scleroderma (74.35%, n=687), and lupus (73.41%, n=58). Mean days from listing to transplant ranged from: lupus (205 days), Sjogren's (199 days), scleroderma (165 days), other (163 days), myositis (154 days), and RA (119 days). Death while awaiting transplant ranged from Scleroderma (11%, n=101), Sjogren's (9.5%, n=13), RA (8.5%, n=25), myositis (6.8%, n=15), other (5.3%, n=17), and lupus (5%, n=4).

Conclusion: Our study suggests positive trends in lung transplant listing outcomes for CTD-ILD as reflected by an increase in the absolute number of listings and improved rates of transplantation. This is matched by shorter wait times and reduced wait list mortality. All CTD diagnoses seem equally likely to get a lung transplant. Some disease specific variability was noted in wait list times. Scleroderma patients exhibit slightly higher waitlist mortality. Limitations in OPTN registry data may impact our results.

Disclosure: S. Bhandari: None; **D. Byers**: None; **D. Sen**: None.

Abstract Number: 2048

DDR2 auto-phosphorylation in patients with Warburg-Cinotti syndrome promotes differentiation of fibroblasts into myofibroblasts and expansion of immature B cells with antibody production.

Sang Jin LEE and Yun Jeong Lee, Kyungpook National University School of Medicine, Daegu, Republic of Korea

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Warburg-Cinotti syndrome (WCS) is a rare connective tissue disorder caused by activating mutations in the DDR2 gene, characterized by progressive corneal neovascularization, keloid-like plaques, and acro-osteolysis. The mechanisms underlying these clinical features remain poorly understood.

Methods: We investigated a family with two WCS patients harboring the DDR2 c.2219A >G (p.Tyr740Cys) variant, a 25-year-old son and his 61-year-old father. Using whole-exome sequencing, single-cell RNA sequencing (scRNA-seq) of skin and peripheral blood mononuclear cells (PBMCs), and protein-level validation, we analyzed the impact of DDR2 activation on fibroblast and immune cells.

Results: Histologic and immunochemical analysis revealed extensive dermal fibrosis and increased smooth muscle actin (SMA)-positive myofibroblasts in WCS skin lesions. scRNA-seq analysis of keloid and normal scar datasets supported the role of DDR2 in promoting fibroblast-to-myofibroblast differentiation. PBMCs analysis from WCS patients showed an expansion of immature/transitional B cells with upregulated *PLCG2, PRKCB*, and *IL7R*, along with enhanced B cell receptor (BCR) signaling (Figures 1 and 2). These expanded immature B cells exhibited increased antibody production but reduced diversity of the antibody repertoire, particularly in the older patient. Serum analysis confirmed elevated IgG and free light chain levels. Immunohistochemistry demonstrated increased infiltration of CD68+ macrophages and CD79A+ B cells, with IgG deposition in WCS skin.

Conclusion: Our findings demonstrate that constitutive DDR2 auto-phosphorylation promotes myofibroblast differentiation and expansion of immature B cells, leading to excessive fibrosis and aberrant antibody production. This study advances the understanding of WCS pathogenesis and suggests potential therapeutic targets for its fibrotic and immune related manifestations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

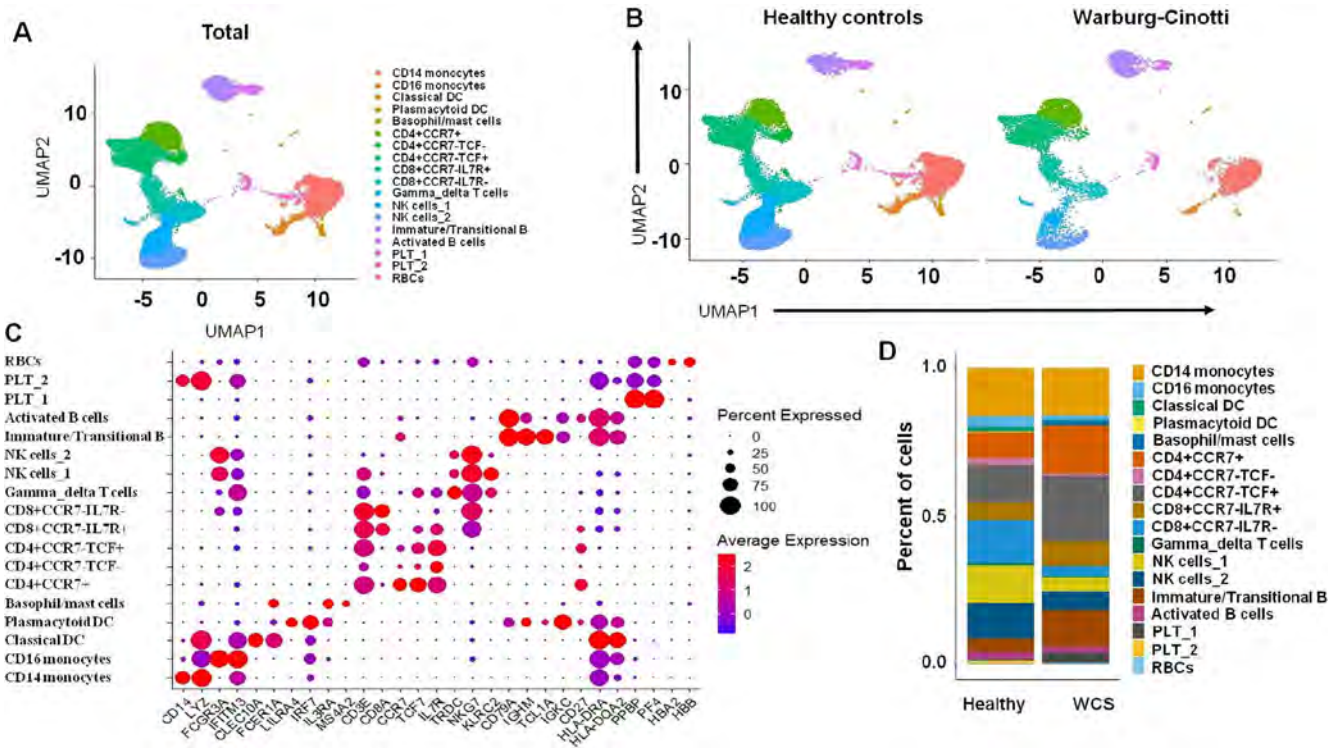


Figure 1

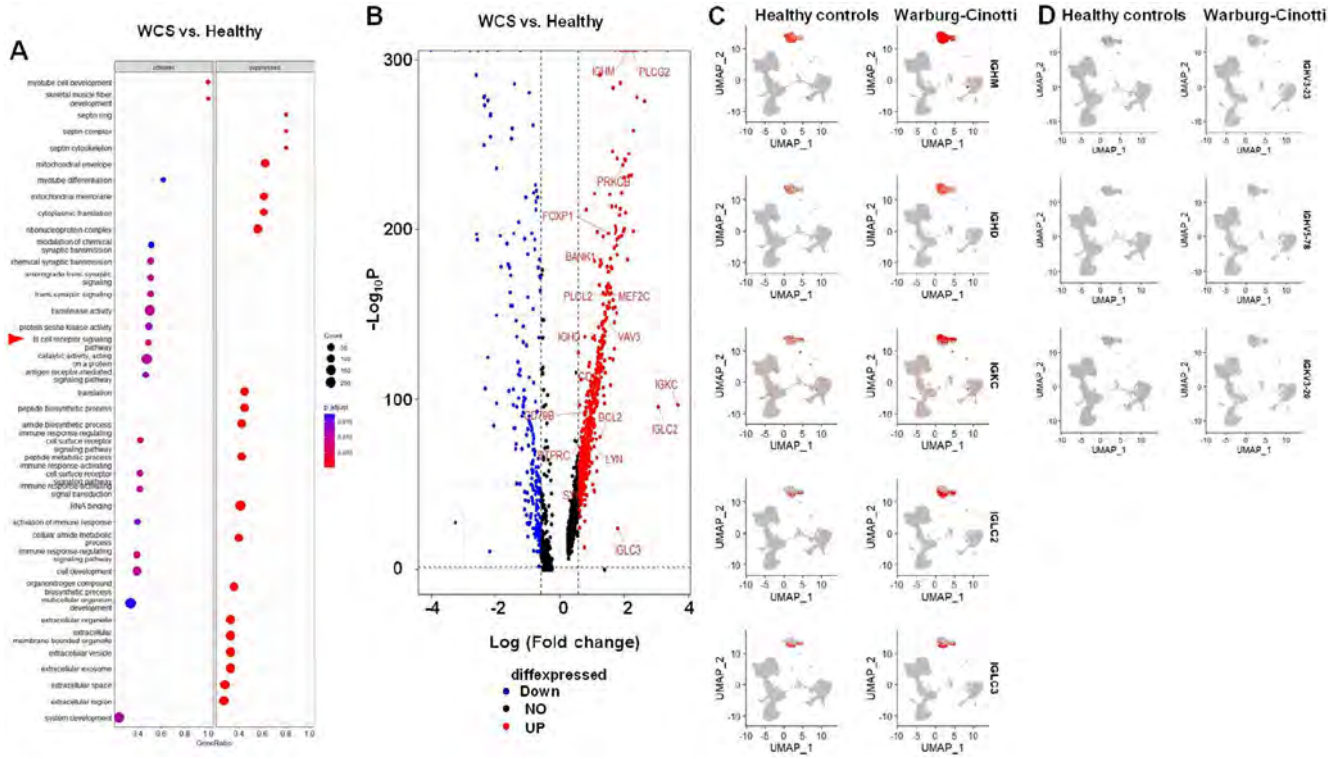


Figure 2

Disclosure: S. LEE: None; **Y. Lee**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2049

Descriptive Analysis of a Cohort of Neurosarcoidosis Mimics

Shivani Rangaswamy[1], Andrea Lopez[1], Megumi Sugita[1], Ethan Eyman[1], Elijah Lackey[1] and Jeffrey Shen[2], [1]Duke University Hospital, Durham, [2]Division of Rheumatology and Immunology, Duke University Department of Medicine, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sarcoidosis is a granulomatous multi-system disease with nervous system involvement in 5-20% of patients. Diagnosis of neurosarcoidosis is challenging due to its broad spectrum of phenotypic and radiographic manifestations. This study leverages a North American registry of patients misdiagnosed as neurosarcoidosis and provides a descriptive analysis of diagnostic tools used to evaluate patients for neurosarcoidosis.

Methods: Two hundred and forty-four patients with a diagnosis code of neurosarcoidosis were identified between 2010 and 2020 at a tertiary care academic institution. Chart review by a neurologist and rheumatologist identified 26 patients who were misdiagnosed as neurosarcoidosis and later found to have an alternative diagnosis. Twenty-three of these charts were reviewed to identify demographic data, relevant laboratory studies, neuroimaging, and pathology. Neuroimaging of a subgroup of 6 neurosarcoidosis mimics and 6 neurosarcoidosis controls were reviewed by 5 neuroimmunology specialists in a blinded survey to obtain additional data regarding radiographic diagnostic certainty of neurosarcoidosis and its mimics.

Results: Over half (52%) of the cohort was diagnosed with another primary CNS process, most commonly multiple sclerosis. Other common mimics included lymphoma (9%), infection (13%), primary ophthalmic conditions (17%), and rheumatoid arthritis (9%). Angiotensin converting enzyme (ACE) was elevated at least once in 40% of the patients. Cerebrospinal fluid (CSF) analysis showed an elevated white blood cell count and protein in approximately 1/3 of the cohort and low glucose in only 1 patient with rheumatoid arthritis. Of the 17 patients who had a biopsy of some tissue for their neurosarcoidosis workup, 12 had granulomas on pathology. Only 1 of 7 patients with a brain biopsy had granulomas on pathology. The majority of patients had MRIs of the brain and/or spine and the most common radiographic patterns were pachymeningeal and parenchymal enhancement.

In a radiographic review survey of 6 neurosarcoidosis mimics and 6 neurosarcoidosis controls, 4 out of 6 mimics and 5 out of 6 controls were correctly identified based on group consensus. The idiopathic hypertrophic pachymeningitis (IHP) case and rheumatoid arthritis case were incorrectly diagnosed as neurosarcoidosis based on group consensus. One neurosarcoidosis control was felt to be most likely IgG4-related disease (IgG4-RD) by 2 reviewers and neurosarcoidosis by 2 reviewers. Pre-existing knowledge of a pulmonary sarcoidosis diagnosis appeared to influence diagnostic certainty of neurosarcoidosis.

Table 1: Serum and CSF Studies

Serum or CSF Study	Lymphoma (n=2)	Infection (n=3)	Rheumatoid Arthritis (n=2)	Primary Ophthalmic Process (n=4)	Primary Central Nervous System Process (n=12)	Total
Elevated Serum Calcium	1/2, 50%	0/3, 0%	1/2, 50%	0/4, 0%	1/12, 8%	3/23, 13%
Elevated Serum ACE	1/1, 100%	0/2, 0%	1/1, 100%	1/3, 33%	3/8, 38%	6/15, 40%
Elevated Serum 1,25 Vitamin D	*	*	0/1, 0%	0/2, 0%	1/5, 20%	1/8, 13%
Elevated CSF White Blood Cells	2/2, 100%	0/2, 0%	1/2 , 50%	1/1, 100%	1/7, 14%	5/14, 36%
Elevated CSF Red Blood Cells	2/2, 100%	1/2, 50%	1/2, 50%	1/1, 100%	4/7, 57%	9/14, 64%
Elevated CSF Protein	2/2, 100%	0/2, 0%	2/2, 100%	0/1, 0%	1/8, 13%	5/15, 33%
Low CSF Glucose	0/2, 0%	0/2, 0%	1/2, 50%	0/1, 0%	0/8, 0%	1/15, 7%

*CSF = cerebrospinal fluid, ACE = angiotensin converting enzyme, n = number of patients, * = no data available*

Serum and CSF Studies

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Pathology and Neuroimaging			
Neursarcoidosis Mimic (n=23)	**Granuloma on any Biopsy**	**Granuloma on CNS Biopsy**	**Most common MRI Radiographic Finding**
Lymphoma (n=2)	0/1, 0%	0/1, 0%	leptomeningeal enhancement, parenchymal enhancement
Infection (n=3)	2/3, 66%	1/2, 50%	parenchymal enhancement
Rheumatoid Arthritis (n=2)	2/2, 100%	0/1, 0%	pachymeningeal enhancement
Primary Ophthalmic Process (n=4)	3/3, 100%	*	optic neuritis
Primary Central Nervous System Process (n=12)	5/8, 63%	0/3, 0%	parenchymal enhancement
*CNS = central nervous system, MRI = magnetic resonance imaging, n = number of patients, * = no data available*			

Pathology and Neuroimaging

Table 3: Neuroimaging Survey Results			
Patients (six neurosarcoidosis controls, six mimics)	**Rate your level of agreement with this statement: These MRI findings are consistent with neurosarcoidosis. [SD]**	**What clinical diagnosis is most consistent with these imaging findings?**	**After knowing whether the patient has been previously diagnosed with pulmonary sarcoidosis, rate your agreement with this statement: These MRI findings are consistent with neurosarcoidosis. [SD]**
Mimic Diffuse Large B cell Lymphoma (n=5)	2.6 [1.71-3.49]	Lymphoma (3/5)	2 [1.29 - 2.71]
Mimic Central Nervous System Lymphoma (n=4)	2 [2-2]	Lymphoma (3/4)	2 [2-2]
Mimic Multiple Sclerosis (n=5)	1.6 [1.05-2.15]	Multiple Sclerosis (5/5)	2.6 [1.71 - 3.49]
Mimic Multiple Sclerosis (n=5)	1.6 [1.05-2.15]	Multiple Sclerosis (4/5)	2.6 [1.08-4.12]
Mimic Idiopathic Hypertrophic Pachymeningitis (n=4)	3.75 [2.49-5.01]	Neurosarcoidosis (3/4)	4 [2.59-5.41]
Mimic Rheumatoid Arthritis (n=4)	3 [1.85-4.15]	Neurosarcoidosis (2/4)	2.6 [1.71-3.49]
Neurosarcoidosis Control 1 (n=5)	4.2 [3.75-4.65]	Neurosarcoidosis (4/5)	3.8 [2.7-4.9]
Neurosarcoidosis Control 2 (n=5)	4 [3.29-4.71]	Neurosarcoidosis (3/5)	3.8 [2.96-4.64]
Neurosarcoidosis Control 3 (n=4)	4.5 [3.92-5.08]	Neurosarcoidosis (4/4)	4.25 [3.75-4.75]
Neurosarcoidosis Control 4 (n=4)	3.5 [2.21-4.79]	Neurosarcoidosis (2/4), IgG4-RD (2/4)	4.25 [3.75-4.75]
Neurosarcoidosis Control 5 (n=3)	4.5 [3.92-5.08]	Neurosarcoidosis (4/4)	4 [3.18-4.82]
Neurosarcoidosis Control 6 (n=4)	5 [5-5]	Neurosarcoidosis (4/4)	4.5 [3.92-5.08]
grey shading = patient has been diagnosed with pulmonary sarcoidosis, white shading = patient has not been diagnosed with pulmonary sarcoidosis, MRI = magnetic resonance imaging IgG4-RD = IgG4 related disease, n = number of reviewers participating, SD = standard deviation			

Neuroimaging Survey Results

Conclusion: Common mimics of neurosarcoidosis include infection, lymphoma, rheumatoid arthritis, another CNS process, and primary ophthalmic processes. Laboratory and CSF studies may not be sensitive for neurosarcoidosis. MRI review by a neurosarcoidosis specialist can help differentiate neurosarcoidosis from mimics with radiographic differences, such as infection or multiple sclerosis, and spare the patient a biopsy. Biopsy may be needed to distinguish neurosarcoidosis from diseases that are radiographically similar, such as IHP or IgG4-RD. Limitations include small sample size and limited follow-up.

Disclosure: S. Rangaswamy: None; **A. Lopez**: None; **M. Sugita**: None; **E. Eyman**: None; **E. Lackey**: Amgen, 1, TG Therapeutics, 1; **J. Shen**: None.

Abstract Number: 2050

Efficacy and Safety of Antifibrotic Therapy in Autoimmune–Associated Interstitial Lung Disease: A Meta-Analysis

Sri Laxmi Priya Sunkara[1], Ravi Medarametla[2], Anjani Mahesh Kumar Cherukuri[3], Rithish Nimmagadda[4], Kaksha Parrikh[5], Punith Chirumamilla[6], Pranathi Bandarupalli[7], Manoja Gullapalli[8] and Naga Alekhya Garikipati[9], [1]White river medical center, batesville, AR, [2]Mamata Medical College, Guntur, Andhra Pradesh, India, [3]Guntur Medical College, Guntur, Andhra Pradesh, India, [4]One Brooklyn Health, New York, NY, [5]Atlanticare regional medical center, New Jersey, [6]Baptist Memorial Hospital North Mississippi, Oxford, MS, [7]Mercy St Vincent Medical Center, Toledo, OH, [8]University of Arkansas for Medical Sciences, Little Rock, AR, [9]Mediciti Institute Of Medical Sciences, Hyderabad, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1a: Annual rate of decline in FVC

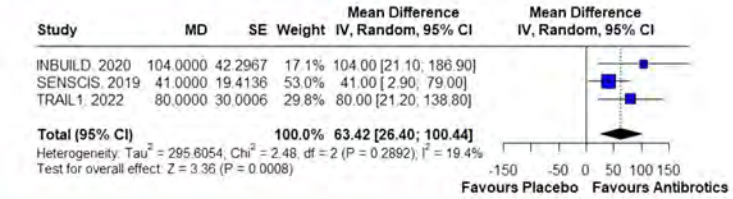
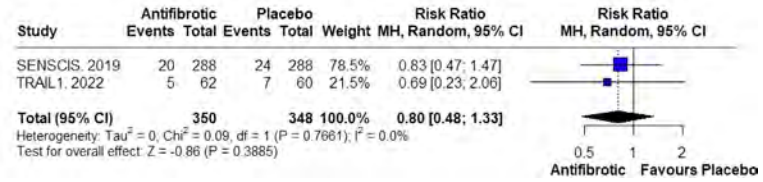


Figure 1b: Patients with an absolute decline from baseline in FVC of >10 percentage points of the predicted value at week 52



Background/Purpose: Autoimmune–associated interstitial lung disease (A-ILD) which includes Rheumatoid arthritis associated interstitial lung disease (RA-ILD), Systemic Sclerosis associated interstitial lung disease (SS-ILD), and others is a progressive fibrosing lung disease, which is associated with substantial morbidity and mortality. Modern treatment strategies rely on immunosuppression but many individuals develop progressive fibrosis. The antifibrotic agents pirfenidone and nintedanib which are approved for use in idiopathic pulmonary fibrosis, now are being studied as possible therapies for inhibiting fibrosis in A-ILD. We performed meta-analysis to evaluate the safety and efficacy of antifibrotic therapy in A-ILD.

Methods: We systematically searched PubMed, Embase, Cochrane for English-language studies involving patients being treated with antifibrotic agents, and reported at least one relevant outcome. Three studies met inclusion criteria. Data were

Figure 2a: Any Adverse Events

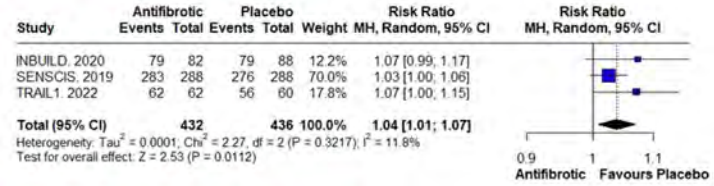


Figure 2b: Serious Adverse Events

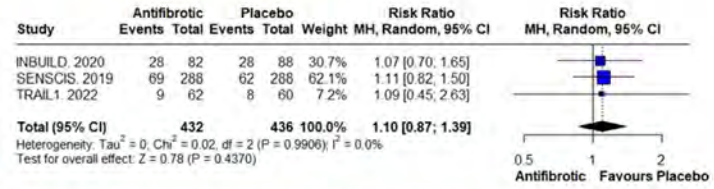
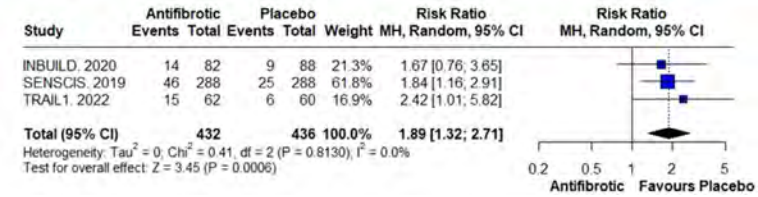


Figure 2c: Adverse event leading to discontinuation of the intervention



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3a: Nausea

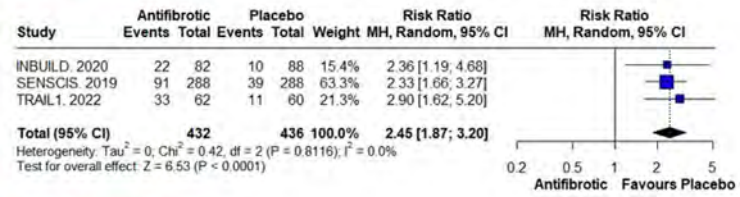


Figure 3b: Vomiting

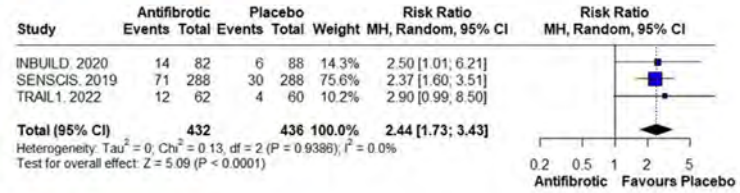
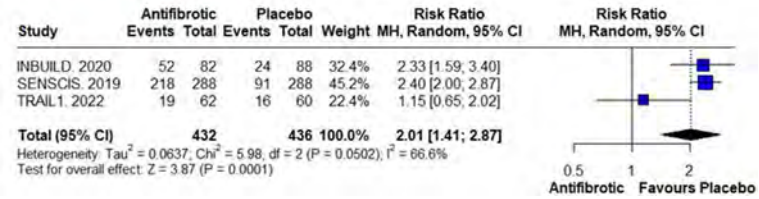


Figure 3c: Diarrhea



pooled using the inverse variance weighting method with a random-effects model in R Studio. Confidence intervals and heterogeneity were assessed, and forest plots were generated to visualise the pooled effect estimates.

Results: Three studies involving 868 patients with A-ILD were included. Analysis of antifibrotic agents demonstrated significant reduction in annual FVC decline rate (MD=63.4 ml/yr, 95% CI: 26.40–100.44, p< 0.01). The risk of experiencing >10% predicted FVC decline at week 52 was lower with antifibrotic therapy, though not statistically significant (RR=0.80, 95% CI: 0.48–1.33, p=0.39). Serious adverse events were comparable between groups (RR=1.10, 95% CI: 0.87–1.39, p=0.44), but antifibrotic therapy showed significantly higher discontinuation rates due to adverse events (RR=1.89, 95% CI: 1.32–2.71, p< 0.01).

Conclusion: Antifibrotic treatment slowed the annual FVC decline in A-ILD patients and had similar rates of serious adverse events compared to placebo. But the treatment discontinuation rates due to adverse events were higher with Antifibrotic agents. This suggests that antifibrotics provide benefit for A-ILD patients, but they have to be monitored closely due to adverse events.

Disclosure: S. Sunkara: None; **R. Medarametla**: None; **A. Cherukuri**: None; **R. Nimmagadda**: None; **K. Parrikh**: None; **P. Chirumamilla**: None; **P. Bandarupalli**: None; **M. Gullapalli**: None; **N. Garikipati**: None.

23265205, 2025, S9, Downloaded from https://accjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2051

Clinical Burden of Illness Among Patients with Immunoglobulin-G4-Related Disease in the United States

Sushmitha Inguva[1], Emma Culver[2], Pallavi Rane[1], Laura Moore-Schiltz[3], melissa rosen[4], Kristina Patterson[4], Donna McMorrow[3], Zulkarnain Pulungan[5], Yasmin Hernandez-Barco[6] and John Stone[7], [1]Amgen Inc., Thousand Oaks, [2]John Radcliffe Hospital; University of Oxford, Oxford, United Kingdom, [3]Inovalon, Bowie, MD, [4]Amgen Inc., Thousand Oaks, CA, [5]Inovalon, Bowie, [6]Massachusetts General Hospital; Harvard Medical School, Boston, MA, [7]Massachusetts General Hospital , Harvard Medical School, Concord, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2015–2051) Miscellaneous Rheumatic & Inflammatory Diseases Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Immunoglobulin G4-related disease (IgG4-RD) is a multi-organ, immune-mediated condition. Timely treatment is critical, as disease flares often result in increased inflammation and organ damage. Glucocorticoids (GCs) are used as standard first-line treatment, followed by GC-sparing therapies including conventional synthetic disease-modifying antirheumatic drugs (DMARDs, such as azathioprine, mycophenolate mofetil etc.), or biologic DMARD (rituximab). This study describes patient characteristics, treatment patterns, and incidence of flares in patients with IgG4-RD using administrative claims databases in the United States.

Methods: A retrospective cohort study was conducted using 100% Medicare Fee-for-Service (FFS) and Inovalon MORE^2 Registry® claims databases. Adults with IgG4-RD were identified using a previously validated algorithm (Wallace et al. *ACR Open Rheumatol*. 2022) from January 1, 2018 through December 31, 2021 (FFS) and June 30, 2023 (MORE^2). Index date was set as the first claim for an algorithm-defined ICD-10 diagnosis code associated with IgG4-RD. Demographics at the index date and comorbidities and medication use in the 12-month pre-index period were assessed. Medication use and claims-based proxy for IgG4-RD flare were evaluated in the ≥12-month post-index follow-up period. Claims-based proxy for flare was defined as: (1) ≥1 claim for an IgG4-RD-associated diagnosis code followed by initiation of IgG4-RD medication,

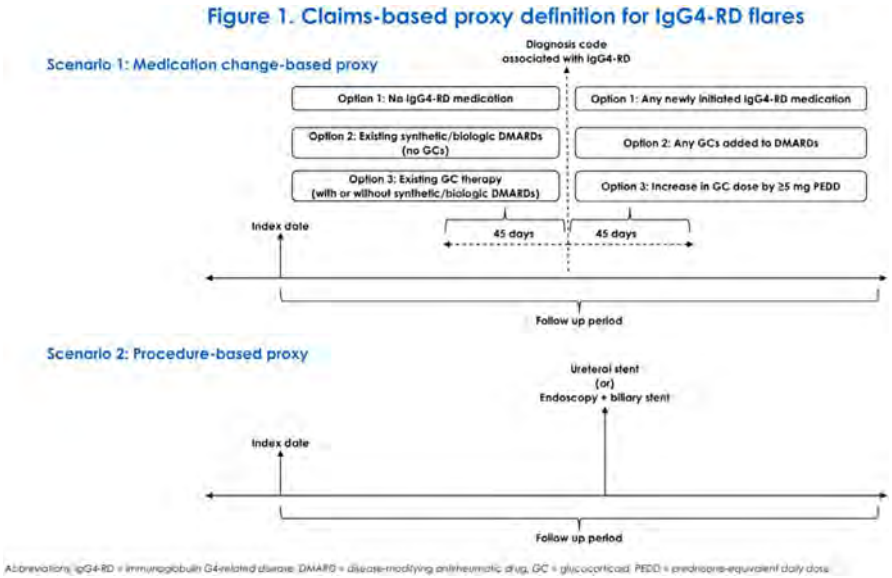


Figure 1. Claims-based proxy definition for IgG4-RD flares

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and baseline clinical characteristics in a national sample of patients with IgG4-RD in the United States

Characteristic	N = 965	
	Mean / N	SD / %
Demographics at index date		
Age at index date (Mean, SD)	65.7	14.2
Sex (N, %)		
Male	571	59.2%
Female	394	40.8%
Race/ethnicity (N, %)		
White	593	61.5%
Asian	74	7.7%
Black	67	6.9%
Hispanic/Latino	49	5.1%
Unknown	182	18.9%
Payer (N, %)		
Medicare Fee-For-Service	625	64.8%
Commercial	201	20.8%
Managed Medicaid	89	9.2%
Medicare Advantage	50	5.2%
Census region (N, %)		
Northeast	269	27.9%
South	251	26.0%
West	248	25.7%
Midwest	197	20.4%
Comorbidity burden during 12-month pre-index period		
Deyo-Charlson Comorbidity Index (Mean, SD)	2.4	2.5
Select comorbid conditions[a] (N, %)		
Hypertension	600	62.2%
Infections	539	55.9%
Hyperlipidemia	532	55.1%
Type 2 diabetes	342	35.4%
Chronic kidney disease	326	33.8%
Gastro-esophageal reflux	321	33.3%
Chronic pulmonary disease	305	31.6%
Medications related to IgG4-RD during 12-month pre-index period		
Patients with ≥1 claim for IV or oral glucocorticoids (N, %)	631	65.4%
Patients with ≥1 claim for oral glucocorticoids (N, %)	474	49.1%
Patients with ≥1 claim for conventional synthetic DMARDs (N, %)	113	11.7%
Patients with ≥1 claim for rituximab (N, %)	82	8.5%
Duration of post-index follow-up period, months (Mean, SD)	45.3	19.5

IgG4-RD = immunoglobulin G4-related disease, SD = standard deviation, IV = intravenous, DMARD = disease-modifying antirheumatic drug.
[a] Comorbidities were identified using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes.

addition of GCs to existing DMARD therapy, or ≥5mg increase in GC prednisone-equivalent daily dose (PEDD); (2) ≥1 claim for ureteral stent; or (3) ≥1 claim for endoscopy and biliary stent (**Figure 1**).

Results: Overall, 965 patients with IgG4-RD were identified: mean (SD) age 65.7 (14.2) years, 59.2% male, 61.5% white (**-Table 1**). Most patients had health insurance coverage through Medicare FFS program (64.8%). In the pre-index period,

Table 2. Treatment patterns and clinical outcomes during ≥12 months of post-index follow-up period in a national sample of patients with IgG4-RD in the United States

Characteristic	N = 965	
	Mean / Median / N	SD / IQR / %
Treatment patterns		
Patients with ≥1 claim for an IV or oral glucocorticoid (N, %)	942	97.6%
Patients with ≥1 claim for a conventional synthetic DMARD (N, %)	324	33.6%
Patients with ≥1 claim for rituximab (N, %)	340	35.2%
Patients with ≥1 claim for an oral glucocorticoid (N, %)	835	86.5%
Total number of days of oral glucocorticoid exposure[a] (Mean, SD)	356.2	433.1
Median, IQR	180.0	418.0
Oral glucocorticoid PEDD[b], mg/day (Mean, SD)	20.8	12.1
Median, IQR	17.9	17.2
PEDD categories[b], mg/day (N, %)		
< 5 mg/day	23	2.8%
5 mg/day - < 7.5	77	9.2%
7.5 mg/day - < 10	70	8.4%
10 mg/day - < 12.5	75	9.0%
12.5 mg/day - < 15	56	6.7%
15 mg/day - < 17.5	72	8.6%
17.5 mg/day - < 20	81	9.7%
≥20 mg/day	381	45.6%
Clinical outcomes		
Claims-based proxy for IgG4-RD flare[c]	873	90.5%

IgG4-RD = immunoglobulin G4-related disease, SD = standard deviation, IQR = interquartile range, IV = intravenous, PEDD = prednisone-equivalent daily dose, DMARD = disease-modifying antirheumatic drug.
[a] Total number of days of oral glucocorticoid exposure was calculated based on the days' supply of medications dispensed as recorded in pharmaceutical claims.
[b] Oral glucocorticoid PEDD was calculated as the total prednisone-equivalent dose across all glucocorticoid fills in the patient's possession divided by the total number of days of oral glucocorticoid exposure.
[c] Claims-based proxy for IgG4-RD flare was defined as: (1) ≥1 claim for an IgG4-RD-associated diagnosis code followed by initiation of IgG4-RD medication, addition of glucocorticoids to existing DMARD therapy, or ≥5mg increase in glucocorticoid PEDD; (2) ≥1 claim for ureteral stent; or (3) ≥1 claim for endoscopy and biliary stent.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hypertension (62.2%), infections (55.9%), and hyperlipidemia (55.1%) were commonly observed. Moreover, 65.4%, 11.7%, and 8.5% received oral or IV GCs, synthetic DMARDs, and rituximab, respectively, during baseline. The mean (SD) duration of the post-index follow-up period was 45.3 (19.5) months. During follow-up, 97.6%, 33.6%, and 35.2% patients received oral or IV GCs, synthetic DMARDs, and rituximab, respectively (**Table 2**). Among patients with oral GCs (N = 835, 86.5%), the mean (SD) PEDD was 20.8 (12.1) mg. Claims-based proxy for flare was observed in 90.5% of patients during follow-up.

Conclusion: Results showed a significant clinical burden among patients with IgG4-RD during follow-up, characterized by elevated GC use which might potentially increase the risk for GC-related toxicity events, as well as a high risk of disease flares. Study findings highlight the need for therapies that better control disease activity and minimize GC exposure in these patients in the long-term.

Disclosure: S. Inguva: Amgen Inc., 3, 11; **E. Culver**: Amgen, 1, 2, Zenus, 2; **P. Rane**: Amgen Inc., 3, 11; **L. Moore-Schiltz**: Amgen, 2, Inovalon, 3; **m. rosen**: Amgen, 3, 11; **K. Patterson**: Amgen, 3, 11; **D. McMorrow**: Amgen, 7, Inovalon, 3; **Z. Pulungan**: Amgen Inc., 2, Inovalon, 3; **Y. Hernandez-Barco**: Amgen, 2, Nestlé Health Science, 1; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2.

Abstract Number: 2052

Prevalence of anti-neutrophil extracellular trap antibodies and their relationship with the clinical characteristics of patients with idiopathic inflammatory myopathies.

Agustin Hernández-López[1], Nancy R Mejía Domínguez[2], Yatzil Reyna Juarez[3], María José Ostos Prado[4], Beatriz Alcalá Carmona[5], Jennifer Tiaré Balderas Miranda[6], Carlos A. Núñez-Álvarez[5], Marta E. Baños-Laredo[7], Álvaro Abiel Sierra-Salazar[5], Johan Camacho-Pérez[5], Marco Aurelio Martínez-Rivera[5], Diana Gómez-Martín[8] and Jiram Torres-Ruiz[9], [1]Instituo Nacional de Ciencias Médicas y Nutricion Salvador Zubirán, Morelia, Michoacan de Ocampo, Mexico, [2]Universidad Nacional Autónoma de México, Mexico City, Distrito Federal, Mexico, [3]Instituto Politècnico Nacional, Tultitán de Mariano Escobedo, Mexico State, Mexico, [4]Instituto Nacional De Ciencias Médicas Y Nutrición Salvador Zubirán, Mexico City, Distrito Federal, Mexico, [5]INCMNSZ, Cdmx, Distrito Federal, Mexico, [6]Universidad Nacional Autónoma de México, Coyoacán, Federal District, Mexico, [7]INCMNSZ, Cdmx, Mexico, [8]INCMNSZ, Mexico city, Federal District, Mexico, [9]INCMNSZ, Ciudad de México, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with idiopathic inflammatory myopathies (IIM) have increased production and decreased clearance of neutrophil extracellular traps (NETs), which may promote the production of anti-NETs antibodies. The aim of this study was to assess the prevalence of anti-NETs antibodies in IIM and their relationship with the clinical features and disease activity.

Methods: For this prospective cohort study, we recruited 157 IIM patients according to the ACR/EULAR or Connors' criteria. We assessed the clinical features, muscle enzymes, disease activity, damage accrual, and the myositis antibodies by Lineblot. IgM, IgG anti-NETs antibodies and NETs remnants (neutrophil elastase-DNA complexes) in serum were measured by ELISA. We determined the cutoff point of the anti-NETs antibodies assay as the 99th percentile of 26 age and sex paired healthy donors (0.183 arbitrary units (AU) for IgG and 0.772 AU for IgM). The positivity for anti-NETs antibodies was corroborated by indirect immunofluorescence (IFI). We assessed the associations between the anti-NETs antibodies, the IIM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

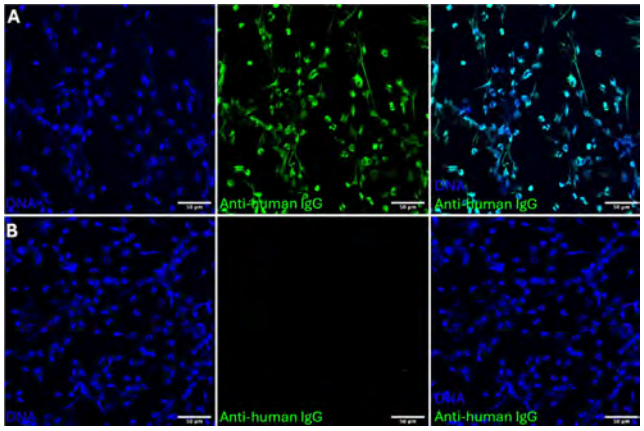


Figure 1. Representative IFI of positive (A) and negative (B) anti-NETs antibodies

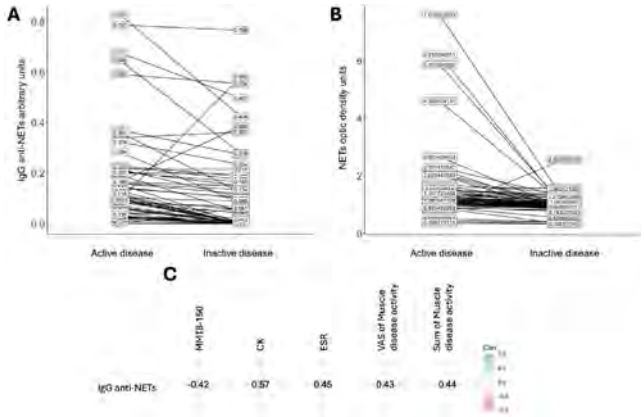


Figure 2. Changes in the concentration of anti-NETs antibodies (A) and NETs remnants (B) in paired samples of active and inactive disease. Correlations between anti-NETs antibodies and the clinical features of patients with AS (C)

phenotypes, and the clinical features using the Chi-2, Mann Whitney U, and Spearman rho. In 68 patients with paired serum samples corresponding to active and inactive disease, we compared the amount of anti-NETs antibodies and NETs remnants using the Wilcoxon test.

Results: 115 (73.2%) were women with a median and interquartile range (IQR) of age at recruitment of 52 years (40-59). The most frequent diagnosis was dermatomyositis (DM) (N=104, 66.2%), followed by anti-synthetase syndrome (AS) (N=24, 15.2%). Thirty-seven patients (23.5%) had positive IgG anti-NETs antibodies, and none were positive for the IgM isotype. Figure 1 shows a representative IFI for positive (1A) and negative (1B) anti-NETs antibodies. The positivity for anti-NETs was closely associated to the AS (Odds Ratio (OR) 6.1 (95% confidence interval 1.5-27.8), P< 0.05), and with positive anti PL12 antibodies (12.1 (95% CI 2.3-91), P< 0.05). As shown in Figure 2, IgG anti-NETs antibodies and NETs remnants decreased when disease becomes inactive (0.09 (0.02-0.19) vs 0.008 (0-0.14), P< 0.0001) (2A), and (1.19 (1.03-1.52) vs 0.95 (0.86-1), P< 0.0001) (2B), respectively. Among participants with AS, patients with anti-NETs antibodies had increased leukocytes/mm3 (7300 (5900-9600) vs 4700 (3900-6300), P=0.04), c-reactive protein (4.2 mg/dL (1.8-8.8) vs 0.7 (0.2-2.4), P=0.04), erythrocyte sedimentation rate (24 mm/hour (8-36.5 vs 5 (2.2-8), P=0.02), visual analog scale (VAS) of cardiovascular (0 (0-10) vs 0 (0-0), P=0.03) and muscular disease activity (4 (0-7) vs 0 (0-3.5), P=0.04), higher damage extension (0.18 (0.07-1) vs 0.06 (0.06-0.09, P=0.03), and VAS of skeletal damage (0 (0-1) vs 0 (0-0), P=0.05). In Figure 2C, we depict the significant correlations between anti-NETs IgG antibodies and the clinical features of patients with AS.

Conclusion: This is the first study to report the prevalence of anti-NETs IgG antibodies in IIM (23.5%). Anti-NETs antibodies were closely associated with the AS and its clinical features. Anti-NETs antibodies and NETs remnants decreased in inactive disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Hernández-López: None; **N. Mejía Domínguez**: None; **Y. Reyna Juarez**: None; **M. Ostos Prado**: None; **B. Alcalá Carmona**: None; **J. Balderas Miranda**: None; **C. Núñez-Álvarez**: None; **M. Baños-Laredo**: None; **Á. Sierra-Salazar**: None; **J. Camacho-Pérez**: None; **M. Martínez-Rivera**: None; **D. Gómez-Martín**: None; **J. Torres-Ruiz**: None.

Abstract Number: 2053

A Prospective Study Unveils Damage Accrual and Myositis Specific Antibodies as Key Risk Factors for Mortality in Myositis

Agustin Hernández-López[1], Nancy R Mejía Domínguez[2], Yatzil Reyna Juarez[3], María José Ostos Prado[4], Beatriz Alcalá Carmona[5], Jennifer Tiaré Balderas Miranda[6], Carlos A. Núñez-Álvarez[5], Marta E. Baños-Laredo[7], Diana Gómez-Martín[8] and Jiram Torres-Ruiz[9], [1]Instituo Nacional de Ciencias Médicas y Nutricion Salvador Zubirán, Morelia, Michoacan de Ocampo, Mexico, [2]Universidad Nacional Autónoma de México, Mexico City, Distrito Federal, Mexico, [3]Instituto Politècnico Nacional, Tultitán de Mariano Escobedo, Mexico State, Mexico, [4]Instituto Nacional De Ciencias Médicas Y Nutrición Salvador Zubirán, Mexico City, Distrito Federal, Mexico, [5]INCMNSZ, Cdmx, Distrito Federal, Mexico, [6]Universidad Nacional Autónoma de México, Coyoacán, Federal District, Mexico, [7]INCMNSZ, Cdmx, Mexico, [8]INCMNSZ, Mexico city, Federal District, Mexico, [9]INCMNSZ, Ciudad de México, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of autoimmune diseases characterized by muscular inflammation that can affect any organ or system. Reported mortality rates are as high as 23–73% due to delayed diagnosis, cardiac and pulmonary involvement, or severe muscle weakness, as well as associated infections and neoplasia. However, the leading causes of mortality vary globally according to the different published cohorts.

Methods: For this prospective cohort study, we recruited 219 IIM patients according to the ACR/EULAR or Connors' criteria. At recruitment (baseline), we assessed the clinical features, muscle enzymes, the myositis disease activity assessment tool (MDAAT), the myositis damage index (MDI), the health assessment questionnaire disability index, the manual muscle test 8 (MMT8), the visual analog scale (VAS) of disease activity by the patient and the physician and the myositis specific and associated antibodies by Lineblot. All patients were followed up prospectively looking for the primary outcome, which was mortality. To assess the independent predictors of mortality, we performed multivariate logistic regression and Cox analyses to calculate the Odds and Hazard ratios with 95% confidence interval.

Results: 164 patients were women (74.8%), the most frequent diagnosis was dermatomyositis (N= 157, 71.6%). After a median follow-up of 62 months, 32 patients (14.6%) died. At baseline, patients who died were older at recruitment (47 (39-52) vs 41(31-52), P=0.04), had more frequently positive anti-SRP (12.5% vs 1.6%, P=0.009), and anti-MDA5 (28.1% vs 11.7%, P=0.024), cancer (15.6% vs 3.7%, P=0.018), lower levels of serum albumin (2.9(2.5-3.6) vs 3.9(3.3-4.2), P< 0.0001), and higher median (min-max) of VAS of gastrointestinal (GI) (0 (0-10) vs 0 (0-7), P=0.0003) and cardiovascular (CV) (0 (0-10) vs 0 (0-6), P=0.04) damage. The independent predictors of mortality were SRP+ (OR 26.24 (95% CI 2.95-283.1), P=0.008), MDA5+ (4.13 (1.23-13.63), P=0.038), malignancy (6.5 (1.20-33.43), P=0.006), albumin (0.26 (0.12-0.51), P< 0.0001), VAS of GI damage (1.41 (1.12-1.81, P=0.006), and VAS of CV damage (2.01 (1.38-3.43), P=0.0001). After Cox analysis, we found the following risk factors for mortality: SRP+ (Hazard Ratio 19.8 (95% CI 5.52-71.0), P< 0.001), MDA5+ (4.92 (1.89-12.8), P=0.001), age at recruitment (1.05 (1.01-1.09), P=0.011), smoking (3.21 (1.35-7.66), P=0.009), physician's VAS of disease activity (1.27 (1.05-1.53), P=0.015), albumin (0.33 (0.17-0.66),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

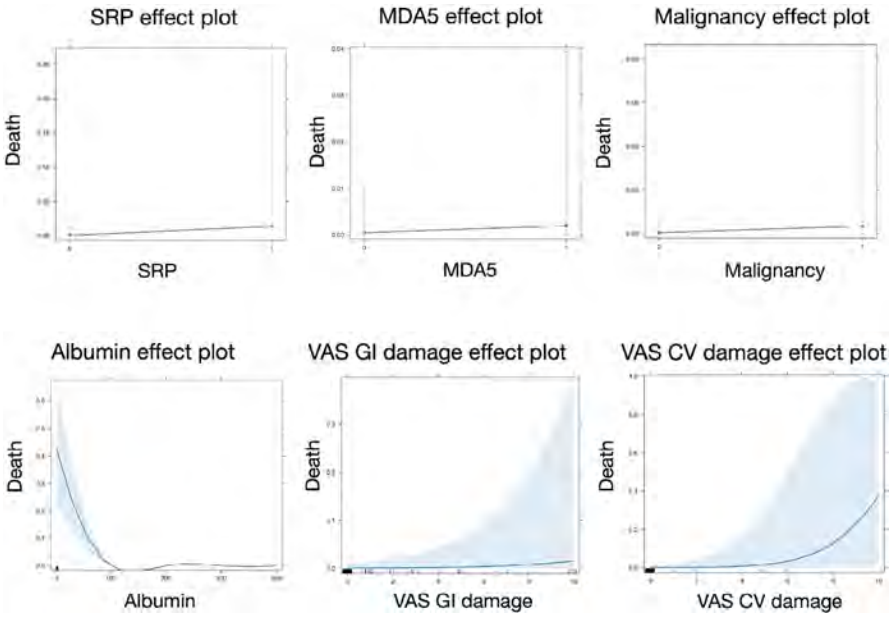


Figure 1. Graphical representation of the effect of each risk factor for mortality in patients with IIM.

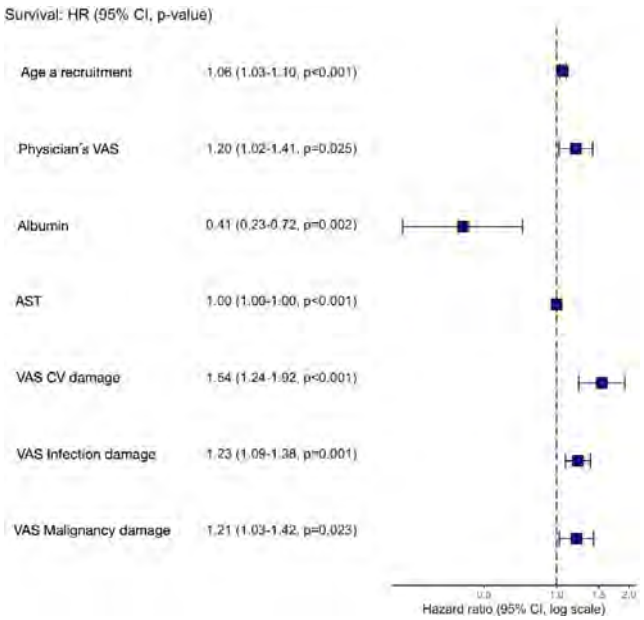


Figure 2. Hazard ratios of each variable independently associated with mortality in patients with IIM.

P=0.002), aspartate aminotransferase (1.00 (1.00-1.00), P< 0.001), VAS of CV damage (1.76 (1.37-2.24), P< 0.001), infectious damage (1.25 (1.09-1.43), P=0.002) and malignancy damage (1.41 (1.17-1.70), P< 0.001). In figure 1, we show a graphical representation of the effect of each risk factor of mortality. In figure 2, we depict the hazard ratios for mortality in patients with IIM.

Conclusion: This prospective study of well characterized IIM patients revealed anti SRP and MDA5 antibodies and the GI, CV, infectious and malignancy damage accrual as key novel risk factors of mortality in this group of diseases.

Disclosure: A. Hernández-López: None; **N. Mejía Domínguez**: None; **Y. Reyna Juarez**: None; **M. Ostos Prado**: None; **B. Alcalá Carmona**: None; **J. Balderas Miranda**: None; **C. Núñez-Álvarez**: None; **M. Baños-Laredo**: None; **D. Gómez-Martín**: None; **J. Torres-Ruiz**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2054

A Changing Paradigm: Reassessing the Role of Muscle Biopsy in Idiopathic Inflammatory Myopathies in a Single-center Cohort

Ami Purohit[1], Najia Shakoor[2], Dmitriy Cherny[1] and Juan Schmukler[1], [1]Rush University Medical Center, Chicago, IL, [2]Rush University, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) encompass a heterogenous group of autoimmune diseases characterized by inflammation of muscle and other target organs. Muscle biopsy was historically the gold standard to characterize these myopathies. With advances in serological, electrophysiological and imaging diagnostics for IIMs, the role of muscle biopsy in the evaluation of contemporary patients with suspected IIM is not clear. Here, we aim to evaluate current practice in the diagnosis of IIMs at an academic medical center with particular focus on characteristics of patients diagnosed with IIMs who underwent muscle biopsy versus those who did not and whether muscle biopsy changed diagnosis.

Table 1: Demographics and Clinical Characteristics - Muscle Biopsy Y/N

	Muscle Biopsy Performed (n=103, 68.7%)	Muscle Biopsy Deferred (n=47, 31.3%)	p values
Age, mean (SD)	58 (±14)	60 (±14)	0.990
Sex, n (%)			0.588
Female	30 (61)	12 (57)	
Male	19 (39)	9 (43)	
Race/Ethnicity, n (%)			0.340
Caucasian	34 (33.0)	14 (29.7)	
African American	45 (43.7)	15 (31.9)	
Hispanic	15 (14.6)	11 (23.4)	
Asian	5 (4.9)	5 (10.6)	
Other	2 (1.9)	1 (2.1)	
Native Hawaiian Pacific Islander	0	1 (2.1)	
CK initial, mean (SD)	5163 (±6216.4)	5732 (±8952)	0.465
Aldolase initial, mean (SD)	38 (±25.4)	33 (±44.0)	0.556
ESR initial, mean (SD)	34 (±29)	33 (±21.8)	0.516
CRP initial, mean (SD)	13 (±20.2)	17 (±12.1)	0.663
AST initial, mean (SD)	173 (±197.2)	158 (±147.0)	0.576
ALT initial, mean (SD)	161 (±166.4)	150 (±156.9)	0.780
Specialist, n (%)			0.232
Rheumatology	52 (50.5)	29 (61.7)	
Neurology	41 (38.8)	12 (25.5)	
Co-Management	10 (9.7)	6 (12.8)	

Table 2: Factors Associated with Biopsy Performance

	Odds Ratio (95% Confidence Intervals)	p-values
Reduced Muscle Strength	0.8 (0.5-1.1)	0.219
Year of Presentation	0.6 (0.4-0.8)	0.002
MSA Positive	0.6 (0.1-2.6)	0.523
HMGCR Ab Positive	0.2 (0.1-0.8)	0.028
Male Gender	0.5 (0.1-1.7)	0.238
Primary Neurology	2.6 (0.7-10.8)	0.157

McFadden pseudo R^2: 0.607

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

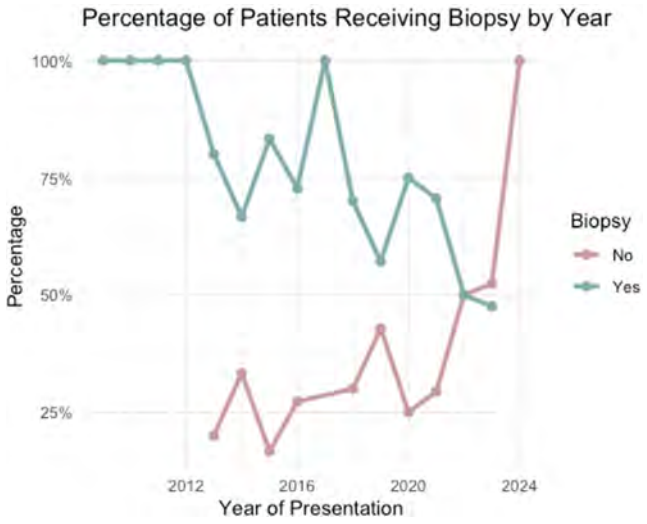


Figure 1: Line Graph Plot of Percentage of Biopsies Over Time

Methods: A retrospective cohort study of adult patients diagnosed with a primary IIM by a rheumatologist or neurologist at a tertiary care medical center was performed. Potential subjects were identified using ICD-10 codes. Demographic, serologic, imaging, histopathologic, and treatment data were collected. Patients were divided into two groups based on whether or not a muscle biopsy was performed. Demographic and clinical characteristics were initially analyzed using chi-squared tests and t-tests; adjusted logistic regression modeling was used to identify factors associated with performing muscle biopsy.

Results: A total of 150 patients with IIM were included, of which 103 patients (68.7%) underwent muscle biopsy and 47 patients (31.3%) who did not (Table 1). There were no significant differences in baseline clinical characteristics between the two groups. Muscle strength, myositis specific antibodies (MSA), gender and primary specialist (neurology vs rheumatology) were not significantly associated with biopsy performance. However, patients with positive HMG-CoA Reductase (HMGCR) antibodies were significantly less likely to have a biopsy (OR 0.2, p=0.02, Table 2). Time was also a significant factor associated with biopsy performance with lower odds of biopsy being performed in more recent years (OR 0.6, p=0.002, Figure 1). With regards to outcomes, the biopsy changed the diagnosis in only 13 cases (12.6%). Results of EMG (performed in over 85% in each group) and MRI (performed in less than 15% in each group) were not significantly associated with biopsy performance.

Conclusion: Our findings suggest a clear trend towards reduced biopsy use over time and whenever HMG-CoA reductase antibodies were present. When biopsies were performed, they infrequently changed the pre-biopsy diagnosis. Given a lack of change in diagnosis in most patients, it may stand to reason that muscle biopsy could be reserved for equivocal or atypical clinical presentations of myositis.

Disclosure: A. Purohit: None; **N. Shakoor**: None; **D. Cherny**: None; **J. Schmukler**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2055

Construct Validity of Total Improvement Score (TIS) as an Endpoint for Clinically Meaningful Improvement in Multiple Patient-Centered Outcome Measures in Dermatomyositis

Anjana Chandrasekhara Pillai[1], Shiri Keret[2], Siamak Moghadam-Kia[3], Chester V. Oddis[4] and Rohit Aggarwal[5], [1]PPCP, Pittsburgh, PA, [2]Bnai Zion Medical Center, Atlit, Israel, [3]University of Pittsburgh Medical Center, Pittsburgh, PA, [4]University of Pittsburgh, Pittsburgh, PA, [5]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Total Improvement Score (TIS), as defined by the ACR/EULAR myositis response criteria, is increasingly employed as a primary endpoint in clinical trials for dermatomyositis (DM). This study aims to assess the construct validity of TIS in a prospective, longitudinal cohort of patients with DM by examining the relationship between TIS improvement categories and Patient-Centered Outcome Measures (PCOMs) and Core Set Measures (CSMs) that assess various domains including fatigue, pain, quality of life, physical activity and physical function.

Methods: Participants met the 2017 EULAR/ACR criteria for probable or definite DM and were enrolled at the University of Pittsburgh Myositis Center between 2016 and 2018. Data collected at baseline, 3 months, and 6 months included manual muscle testing (MMT), physician and patient global activity (MDGA, PtGA), extra-muscular global activity (EMGA), the Health Assessment Questionnaire–Disability Index (HAQ-DI), and muscle enzyme levels. PCOMs included Short Form-36, PROMIS-Physical Function, sit-to-stand (STS), Timed Up-and-Go (TUG), 6-minute walk, pain and fatigue visual analogue scale (VAS), ActiGraph-based physical activity, and hand-held dynamometry. The TIS was calculated according to ACR/EULAR myositis response criteria, with TIS < 20 indicating no improvement and ≥20 indicating at least minimal improvement. Spearman correlation assessed relationships between TIS and outcome changes. Differences between the CSMs and PCOMs amongst patients with and without minimal improvements (TIS ≥20) were evaluated.

Results: Among n=24 participants, the mean age was 47 years; 71% were female and 96% were white. Patient-Reported Outcome Measures (PCOMs), including fatigue, pain, quality of life, muscle strength, disability index, and physical function, demonstrated significantly greater improvement in patients who met minimal improvement criteria by the TIS, compared to those with no improvement. Additionally, most CSMs, including MDGA, EMGA, and MMT, showed significant changes among those with minimal improvement compared to no improvement (Table 1). Among patients with active DM (defined as having active muscle activity at baseline; n=14) , those exhibiting at least minimal improvement on the TIS (≥20) at 6 months demonstrated average improvements across nearly all PCOMs. Correlations between TIS and changes from baseline in PCOMs and CSMs at 6 months revealed that improvement on most measures was associated with TIS. Strong correlations (rho > 0.5) with TIS were observed for physical function measures, handheld dynamometry, Timed Up-and -Go, and some quality of life measures.

Conclusion: The results support the construct validity of TIS and its use as a clinically meaningful endpoint in DM, capturing benefits in disease activity and aspects of pain, fatigue, function, quality of life, and overall well-being.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of myositis core set measures and patient-centered measures (Median, [IQR]) by the ACR-EULAR Myositis Response Criteria Categories of no improvement and improvement at 6 months.

	No improvement (TIS <20) (N=10)	At least minimal improvement (TIS =20) (N=8)	*p* value
Myositis Core Set Measures			
Physician global disease activity (0-10)	0 [0 to 0.38]	-4.2 [-4.62 to 3.25]	0.0005*
Patient global disease activity (0-10)	0 [-1 to 0]	-1.5 [-2.38 to 0.62]	0.47
MMT (0-80)	0 [0 to 0]	7 [3.75 to 9.75]	0.002*
HAQ-DI (0-3)	0 [-0.09 to 0.13]	-0.69 [-1 to -0.22]	0.006*
Extra-muscular disease activity (0-10)	0 [-0.6 to 0]	-2.25 [-3.92 to -1.5]	0.002*
CK IU/L	19.5 [-3.75 to 62.25]	13 [-70 to 15]	0.34
Muscle Disease			
Muscle disease activity (0-10) MDAAT	0 [0 to 0]	-3 [-3.62 to -2.5]	0.0006*
Dynamometry	-6.77 [-38.49 to 8.17]	75.72 [69.18 to 87.78]	0.001*
Physical Function			
Patient-reported outcome measures			
PROMIS PF20	-2 [-4.5 to 0]	17 [6.25 to 21.75]	0.0004*
SF-36 PF10	-7.5 [-18.75 to 0]	15 [5 to 35]	0.008*
Task-oriented tests			
Sit-to-stand	1 [-4.25 to 3]	3.5 [2.5 to 4.25]	0.04
Timed up-and-go	0.78 [-0.31 to 1.05]	-0.5 [-1.53 to 0.27]	0.08
Six-min walk (meters)	-47.5 [-60 to 82.5]	90 [52.5 to 150]	0.12
Physical Activity			
Peak 1-min cadence	-6.33 [-22.11 to 5.55]	5.65 [-6.68 to 20.91]	0.40
Steps per min	-0.79 [-2.39 to 0.22]	0.32 [-0.63 to 2.52]	0.22
Vector magnitude	-75.76 [-174.5 to -0.7]	15.06 [9.11 to 61.16]	0.07
Fatigue			
Fatigue (VAS)	0 [-0.38 to 1]	-2 [-3.5 to -0.38]	0.02*
SF-36 Fatigue/Vitality	-5 [-8.75 to 2.5]	20 [10 to 30]	0.15
Pain			
Pain (VAS)	0 [0 to 0]	-0.5 [-1.62 to -0.12]	0.09
SF-36 Bodily Pain	0 [0 to 0]	45 [35 to 47]	0.002*
HRQoL			
SF-36 Physical Health	0 [-43.75 to 0]	0 [0 to 0]	0.32
SF-36 Emotional Role Limitations	0 [0 to 0]	0 [0 to 67]	0.46
SF-36 Emotional Well-being	-2 [-10 to 3]	12 [-8 to20]	0.22
SF-36 Social Functioning	0 [0 to 0]	25 [25 to 37]	0.004*
SF-36 General Health	0 [-8.75 to 5]	10 [5 to 20]	0.02*
SF-36 Physical Summary Score	-2.06 [-9.57 to 1.31]	5.64 [-0.01 to 14.33]	0.06
SF-36 Mental Summary Score	0.22 [-2.21 to 5.43]	5.84 [-4.63 to 17.3]	0.51

Minimal, moderate and Major categories are combined due to a small number of patients. *p<0.05 considered statistically significant based on Kruskal-Wallis .ACR-EULAR= American College of Rheumatology/European League Against Rheumatism; CK=creatine kinase; HAQ-DI = health assessment questionnaire disability index; MDAAT= Myositis Disease Activity Assessment Tool; MMT = Manual muscle testing; PROMIS PF = Patient Reported Outcome Measurement Information System Physical Functioning; SF-36 = short form 36; VAS = visual analog scale.

Disclosure: A. Chandrasekhara Pillai: None; **S. Keret**: None; **S. Moghadam-Kia**: None; **C. V. Oddis**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2.

Abstract Number: 2056

Systematic Review: Nutritional Interventions in Muscle Diseases

Deepanjali Vedantam[1], Taanya Talreja[2], Pranathi Bandarupalli[3], Sheryl Salis[4], Debra Lupeika[5], Ashley Maclean[6], Karen Cheng[7], Teerin Liewluck[8], Lakshmi Nagendra[9] and Latika Gupta[10], [1]Shasta Regional Medical Centre, Redding, CA, [2]KEM Hospital, Mumbai, Maharashtra, India, [3]Mercy St Vincent Medical Center, Toledo, OH, [4]Nurture Health Solutions, Mumbai, Maharashtra, India, [5]Department of Family Medicine, UC Davis, Redding, [6]Vacaville Ranch Post Acute, Redding, [7]., Basel, Switzerland, [8]Division of Neuromuscular Medicine, Department of Neurology, Mayo clinic-Rochester, Rochester, [9]Department of Endocrinology, JSS Academy of Higher Education and Research, Mysore, Karnataka, India, [10]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Medical nutrition therapy significantly impacts cardiovascular risk and overall health, but effects on muscle diseases remain unclear. This systematic review evaluates nutritional interventions' safety and efficacy on muscle disease outcomes.

Methods: A multidisciplinary team conducted a PRISMA-guided systematic review registered on Prospero. Database searches yielded 107 full-text articles, with 52 meeting inclusion criteria after screening. Four reviewers assessed bias risk, with team review for appropriateness (Figure 1.1).

Results: For inflammatory myopathies, investigations primarily centered on creatine supplementation and branched-chain amino acids (Figure 2). The most notable finding came from a study demonstrating that creatine supplementation combined with exercise significantly improved aggregate functional performance time in patients with polymyositis and dermatomyositis, with a median decrease of 13% compared to only 3% in the placebo group (p = 0.029).

Studies involving congenital muscle disorders and muscular dystrophies examined a wider spectrum of interventions, including various dietary patterns, specific nutrients, supplements, and antioxidants. These studies assessed diverse outcomes from muscle strength and exercise capacity to body composition, functional tests, and quality of life measurements.

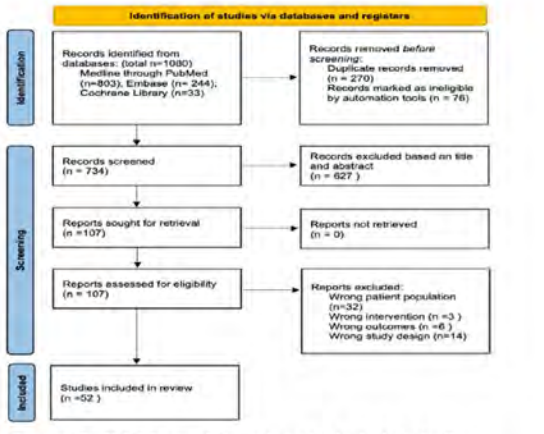


Figure 1.1: PRISMA workflow chart for included studies

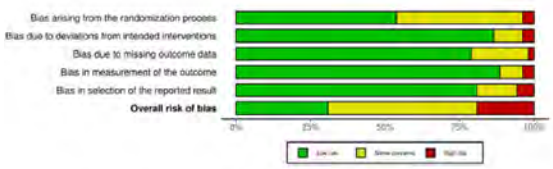


Figure 1.2: Risk of bias of included studies

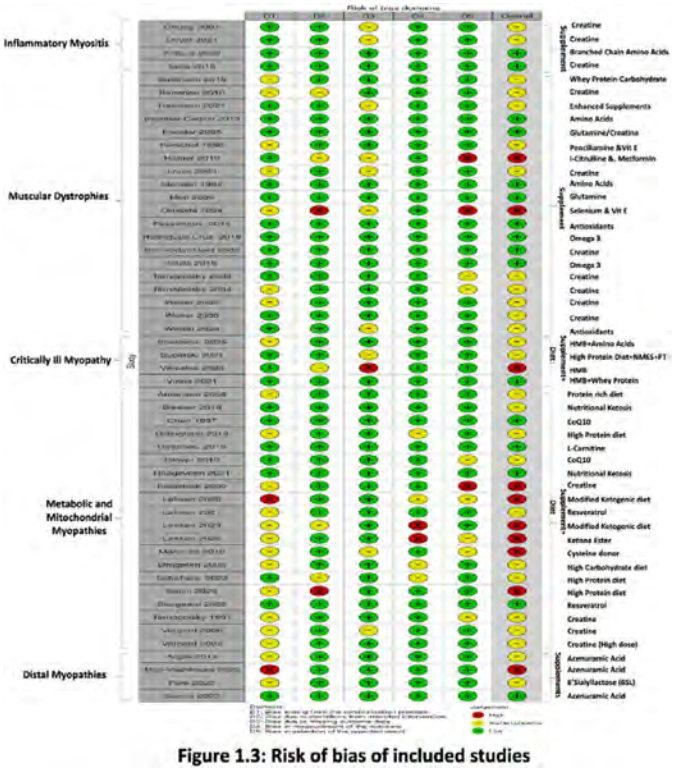


Figure 1.3: Risk of bias of included studies

Figure 1. Workflow chart and Risk of Bias

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

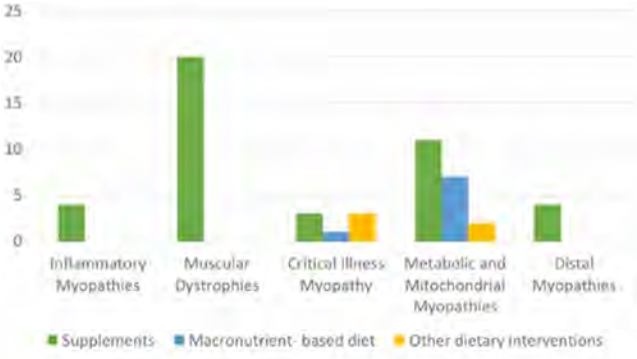


Figure 2.1: Interventions used by disease subtype

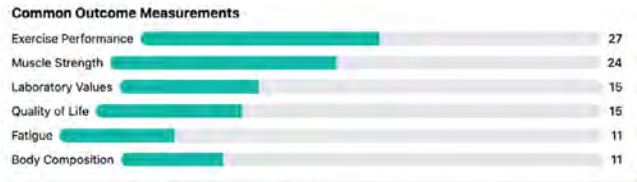


Figure 2.2: Proportion of common outcome measurements

Figure 2. Interventions and common outcome measurements

Several interventions showed promising results, particularly creatine supplementation in Duchenne muscular dystrophy, which increased maximal voluntary contraction by 15% and doubled fatigue resistance ($p < 0.05$). Additionally, ketogenic diets demonstrated improvement in fatty acid oxidation by 60% and increased maximal exercise capacity by approximately 20% in patients with McArdle disease (Table 1).

In critical illness myopathy, research investigating HMB-enriched whey protein supplementation and high-protein dietary interventions generally showed positive trends in outcomes. However, it should be noted that several of these results did not reach statistical significance, highlighting the need for more robust studies in this area.

Quality assessment of the included studies revealed varying levels of methodological rigor, with 32% of studies classified as low risk of bias, 45% raising some concerns, and 22% determined to be at high risk of bias, underscoring the need for more rigorously designed trials in this field (Figure 1.2,1.3).

Conclusion: While nutrition therapy benefits other medical fields, evidence for muscle diseases remains limited. Promising interventions include physiologic creatine, high-protein diets, ketogenic diets, and supplements (CoQ, resveratrol, L-carnitine), which improved endurance/strength in some populations. Methodological concerns highlight the need for larger, better-designed multicenter trials with standardized outcomes. More research exists on non-inflammatory versus inflammatory myopathies. Given these uncertainties, dietary guidance should be tailored to specific disease features and comorbidities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Summary of Nutritional Interventions and Outcomes in Muscle Diseases across included studies

Intervention	Number of RCTs	Disease	Outcome- Improvement	Outcome- No change
A) Inflammatory Myositis				
1. Supplements				
Creatine Supplements	1	Idiopathic inflammatory myopathies (IIMs)	AFPT, Functional Index of Myositis, MMT;	NHP, Short Form McGill Pain Questionnaire, Hospital Anxiety and Depression Scales, and Chalder fatigue scores.
	2	Juvenile Dermatomyositis (JDM)	-	Muscle function, strength & metabolism, aerobic capacity, disease activity, fatigue, physical activity, QoL
Branched Chain Amino Acids	1	Polymyositis and Dermatomyositis	Functional Index (FI) score	MMT, MDACS
B) Muscular Dystrophies				
1. Supplements				
Creatine Supplements	4	Myotonic dystrophy types 1 and 2	Muscle strength, daily activities; refractory muscle pain and subjective muscle performance	MRC, NSS, Lean body mass, Vital capacity, patient's global assessment of improvement, daily activities, hand-held dynamometry
	3	DMD and Becker's dystrophy	Cellular energetics, MMT, Bone mineral density, MVC, resistance to fatigue, FFM, Handgrip strength	Functional scale, Lean body mass, Activities of daily living, CK, PFT
Glutamine supplements	1	DMD	-	Walking speed, 2-minute walk test, work, power, FFM
Glutamine /creatine supplements	1	DMD	Functional timed scores, QMT in both groups	MMT
Enhanced supplements*	1	DMD	6MWD	Body composition, QoL
Antioxidants**	4	DMD, FSHD, Myotonic dystrophy	Muscle and fat volumes, Muscle Strength	Functional grade, timed-functional tests, PFT, CK levels, MMSE, SRB3, Hand grip strength, MVC, Endurance
Omega 3 Fatty Acids	2	DMD, FSHD, LGMD	Proinflammatory markers, Anti-inflammatory markers, safety, tolerability, 6MWD, Serum CK	-
Amino Acid Supplements	3	DMD	Reduction in motor function decline with combination of L-citrulline and Metformin	MMT, Functional evaluation, Joint contractures, timed-
				functional tests, PFTs, serum CK levels
Protein-carbohydrate (Whey protein)	1	FSHD	SF-36	Fitness, walking speed, workload
C) Critical Illness Myopathy				
1. Supplements				
HMB	1	Critical Illness Myopathy	Lean body mass, Global Health assessments	Muscle wasting
HMB+ Whey Protein	1	Critical Illness Myopathy	MMT	Nutritional status, Basal metabolism, Mortality
HMB+ Omega 3 Fatty Acids	1	Mechanically Ventilated Patients (Adult)	-	MMT
2. Macronutrient- based diet				
High Protein Diet With NMES and PT	1	Critical Illness Myopathy	Muscle volume	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

D) Metabolic and Mitochondrial Myopathies				
1. Supplements				
Creatine Supplements	2	Mitochondrial myopathy, cytopathies, CPEO	Handgrip strength, NIDFT, and postexercise lactate	Exercise performance, eye movements, or activities of daily life.
	2	McArdle disease	Muscle complaints, exercise performance during ischemic exercise, surface electromyograms	Worsening of clinical symptoms of exercise intolerance.
Coenzyme Q10	2	Mitochondrial myopathies, encephalomyopathies, cytopathies	Global MRC score, rise in lactate after cycle ergometry (attenuated), VO2/kg lean mass, gray matter choline-containing compounds	Cycle exercise Aerobic capacity, post-exercise lactate, strength, resting lactate
L- carnitine	1	Mitochondrial Myopathy	Limit of tolerance and oxygen consumption (VO2) at constant work rate exercise, inspiratory capacity indicating improved aerobic capacity and exercise tolerance	ICPET
Ketone ester supplementation	1	McArdle disease	-	Exercise capacity, perceived exertion
Cysteine donor supplementation	1	Mitochondrial myopathies and cytopathies	Oxidative stress levels	Lactate concentration, MRC, SF-36
Resveratrol	1	Mitochondrial Myopathy	-	Exercise capacity, perceived exertion, lactate concentrations, SF-36,FSS, mitochondrial biomarkers
				from muscle biopsy
	1	Fatty acid oxidation disorders- CPTII/ VLCAD deficiency	-	HR, rate of fatty acid oxidation, perceived exertion, SF-36, FSS
2. Macronutrient- based diet				
Carbohydrate-rich diet	1	McArdle's Disease	HR, perceived exertion (Borg scale), maximal oxidative work capacity	-
	1	CPT II deficiency	Perceived exertion (Borg scale), Exercise duration, HR	RER and VO2
Protein-rich diet	1	Long-chain fatty acid oxidation disorders	Blood levels of short-chain acylcarnitines, reduced intrahepatic lipid content, and maintained lean body mass	Fasting lipids, FFA, glucose and insulin levels
High protein diet+ exercise	2	Pompe disease	Absolute peak VO2, Muscle strength, core stability, QoL in both children and parents (CHQ), SF-36, FEV-1	6MWT, HR during submaximal CPET, physical activity levels
3. Other Dietary Interventions				
Modified Ketogenic Diet	2	McArdle disease	Symptom relief, SF-36, fatty acid oxidation rates, and maximal exercise capacity	HR
Nutritional Ketosis	1	VLCAD deficiency	Quadriceps glycolytic intermediate levels and in vivo Pi/PCr ratio	-
	1	Glycogen storage disease type IIIa (GSDIIIa)	Quadriceps energetic state by in vivo 31P MR spectra, in subjects with overt myopathy	RER
E) Distal Myopathies				
1. Supplements				
Aceneuramic Acid	3	GNE Myopathy	GNEM-FAS score for Upper Extremity function & mobility; Maintenance of muscle strength in UEC score, Investigator-assessed efficacy rate	LEC Strength , MRI Pathology Scores (fat infiltration), Muscle Sialic Acid levels, INQoL
6'-sialyllactose	1	GNE Myopathy	Proximal limb powers, fat fraction on muscle MRI	GNEM-FAS scores

*Enhanced supplement- protein shake (22 g whey protein), multivitamin capsules, vitamin D capsules (Vitamin D3, 2000 IU) and fish oil capsules followed by enhancement with Standard supplement plus: Creatine monohydrate (5 g), glutamine (0.6 g/kg fat free mass), and HMB (38 mg/kg/day)

**Antioxidants- Selenium, Vitamin E, Penicillamine, Vitamin C, Zinc Gluconate

Abbreviations: AFPT- Aggregate Functional Performance Time; MMT-Manual Muscle Testing; NHP- Nottingham Health Profile; QoL-Quality of Life; MDACS-Myositis Disease Activity Core Set; SF-36 -Short Form Health Survey; MVT -Multi-Vitamin; DMD -Duchenne's Muscular Dystrophy; MVC -Maximal Voluntary Contraction; PFT -Pulmonary Function Testing; FFM -Fat Free Mass; QMT -Quantitative Muscle Testing; MRC -Medical Research Council Scales; NSS -Neuromuscular Symptom Score; 6MWD -6-Minute Walk Distance; CK -Creatine Kinase; PFT -Pulmonary Function Tests; MMSE -Mini-Mental State Examination; SRB3 -Spatial Ability Test; LGMD -Limb Girdle Muscular Dystrophy; HMB- Hydroxymethylbutyrate; NMES- Neuromuscular electrical stimulation; PT- Physical Therapy; RER- Respiratory exchange rate; ICPET- incremental cardiopulmonary exercise test; FFA- Free Fatty Acids; 6MWT- 6 Minute Walk Test; HR- Heart Rate; CPET- Cardiopulmonary Exercise Testing; CHQ- Child Health Questionnaire; FEV-1- Forced Expiratory Volume in 1 second; CPEO- Chronic Progressive External Ophthalmoplegia; NIDFT- nonischemic dorsiflexion torque; FSS- Fatigue Severity Scale; GNEM-FAS -GNE myopathy functional activity scale; UEC- Upper Extremity Composite; LEC- Lower Extremity Composite; INQoL- Individual Neuromuscular Quality of Life Questionnaire; VLCAD- Very Long Chain Acyl-CoA Dehydrogenase; CPT- Carnitine palmitoyltransferase

Disclosure: D. Vedantam: None; **T. Talreja**: None; **P. Bandarupalli**: None; **S. Salis**: None; **D. Lupeika**: None; **A. Maclean**: None; **K. Cheng**: Sobi, 3, 12, Employment projects are unrelated to this abstract.; **T. Liewluck**: Sarepta Therapeutics, Inc, 1; **L. Nagendra**: None; **L. Gupta**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2057

Clinical Associations of Anti-Ro52 Antibodies in Idiopathic Inflammatory Myopathies: A Scoping Review

Emily Sun[1], Huon Wong[2], Robin Sia[3] and Jessica Day[4], [1]Royal Melbourne Hospital, Melbourne, Victoria, Australia, [2]University of Queensland, Brisbane, Australia, [3]Royal Melbourne Hospital, Reservoir, Victoria, Australia, [4]Walter and Eliza Hall Institute, Melbourne, Victoria, Australia

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-Ro52 is a myositis-associated antibody increasingly linked to disease features and outcomes in idiopathic inflammatory myopathies (IIMs). Thorough characterisation of these associations is needed to clarify its clinical relevance and to guide future research. We sought to systematically review the literature on clinical associations of anti-Ro52 in IIMs.

Methods: A systematic search of MEDLINE and EMBASE was conducted from inception until April 2025. Studies reporting clinical associations of anti-Ro52 in adult IIM patients were included (See Figure 1 for PRISMA flow diagram).

Results: Of 1953 studies, 227 full-text articles were assessed for eligibility and 105 met inclusion criteria. All included studies were observational, with majority published since 2021 (69%, n=72) and originating from Asia (67%, n=70). Sample sizes ranged from 11-2085 patients. Considerable heterogeneity was observed in the reported clinical associations for anti-Ro52 within adult IIM cohorts (Figure 2). Anti-Ro52 was commonly associated with higher rates of interstitial lung disease (ILD) (57%, n=29/51 studies), including rapidly progressive interstitial lung disease (RP-ILD) (76%, n=19/25 studies), with nonspecific interstitial pneumonia being the predominant lung pattern among studies reporting radiographic findings (50%, n=4/8). Mechanic's hands (80%, n=8/10 studies) and severe joint involvement (57%, n=8/14 studies) were other commonly reported associations. Among studies examining disease outcomes, anti-Ro52 was frequently associated with increased mortality (65%, n=11/17 studies) and poor prognosis (59%, n=10/17 studies), as indicated by lower cumulative survival or worse functional outcomes. However, anti-Ro52 was rarely linked to malignancy risk (9%, n=1/11 studies). Among 72 studies reporting anti-Ro52 co-positivity with other myositis-specific or myositis-associated antibodies, in a

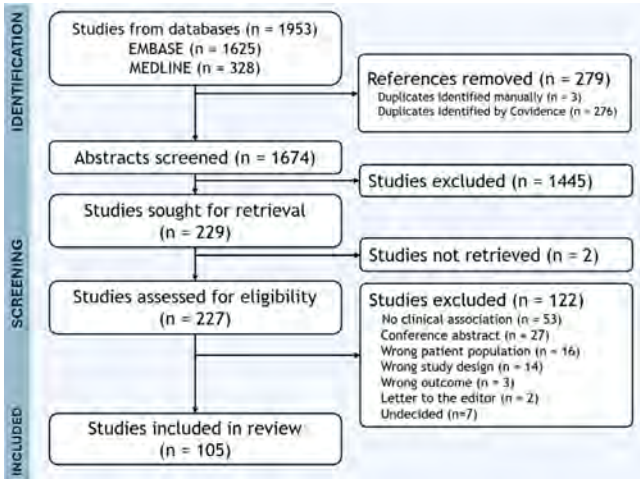


Figure 1. PRISMA flow diagram

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

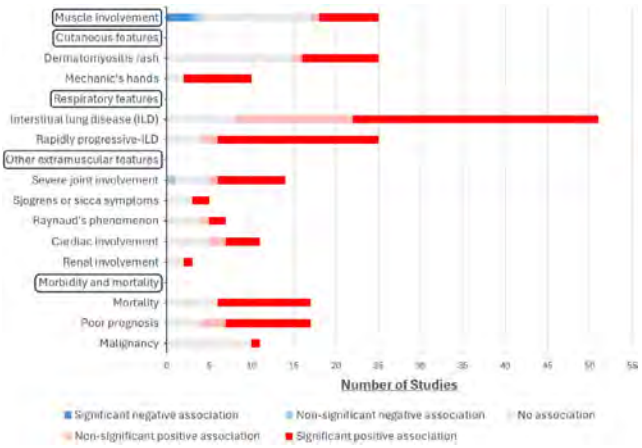


Figure 2. Common clinical associations of anti-Ro52 antibody in adult IIM patients ($p < 0.05$ for significance)

pooled cohort of 4359 patients, the most frequently co-occurring antibodies were anti-MDA5 (55%, n=2393 patients) and anti-aminoacyl-tRNA synthetases (anti-ARS) (35%, n=1537 patients), with the two most common anti-ARS antibodies being anti-Jo1 (15%, n=642 patients) and anti-EJ (5%, n=205 patients) (Figure 3). Antibody co-expression has been linked to a more severe disease phenotype, including RP-ILD, as well as poor treatment response to conventional immunosuppressive therapies, but possibly improved response to rituximab.

Conclusion: Anti-Ro52 is frequently associated with ILD and RP-ILD, poorer prognosis, and increased mortality in adult IIM patients. This review further highlights associations with key extra-muscular manifestations, notably mechanic's hands and severe joint involvement. Antibody co-positivity with anti-Ro52 may predict high-risk clinical phenotype, enabling risk stratification and early targeted therapies that may improve long-term outcomes. Future research should focus on mechanisms

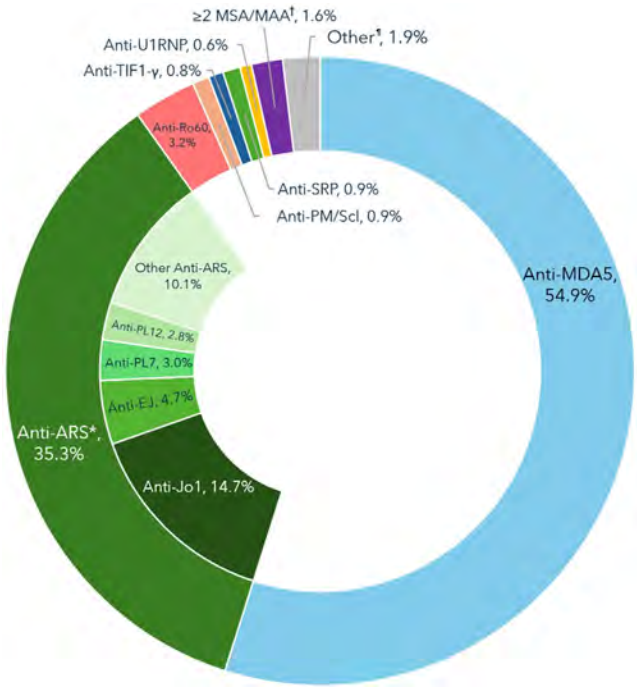


Figure 3. Frequency of myositis-specific antibodies (MSA) and myositis-associated antibodies (MAA) co-positive with anti-Ro52 antibody in adult idiopathic inflammatory myopathies (IIM) patients. * Anti-ARS (anti-aminoacyl-tRNA synthetase) antibodies include anti-Jo1, anti-EJ, anti-OJ, anti-PL7, anti-PL12, anti-KS, and dual anti-ARS antibodies (anti-Jo/anti-PL12, anti-EJ/anti-OJ). Other anti-ARS antibodies include anti-ARS antibodies of lesser frequency and anti-ARS antibody frequency from studies where specific anti-ARS subtypes were not differentiated and the data were reported collectively. † ≥2 MSA/MMA antibodies: the frequency of two or more MSA/MMA antibodies co-positive with anti-Ro52, excluding any dual anti-ARS antibodies. ¶ Other antibodies include anti-HMGCR, anti-SAE1, anti-Scl-70, anti-Sm and anti-U3RNP.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

driving these clinical associations and their implications for disease management, including personalised treatments and risk stratification.

Disclosure: E. Sun: None; **H. Wong**: None; **R. Sia**: None; **J. Day**: CSL Limited, 5.

Abstract Number: 2058

Organ-specific disease activity and serological patterns in idiopathic inflammatory myopathies: A descriptive study in a Hispanic cohort

valeria cantu[1], **Emmanuel Dominguez-Chapa**[2], Rebeca L. Polina-Lugo[1], Ana Cecilia Bardan Inchaustegui[3], fernanda m. garcia-Carrillo[4], Ericka S. Reyna-Hernandez[5], Daniela A. Mejia-Rodriguez[5], Rosa Arvizu-Rivera[6], Jesus Alberto Cardenas-de la Garza[7], Miguel Villarreal-Alarcón[8] and Dionicio A. Galarza-Delgado[9], [1]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [2]Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [3]Universidad Autónoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [4]Hospital Universitario \"Dr. José Eleuterio González\" UANL, Monterrey, Nuevo Leon, Mexico, [5]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [6]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico, [7]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [8]Hospital Universitario UANL, Monterrey, Nuevo León, Mexico, [9]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are rare diseases that involve chronic muscle inflammation, weakness, and pain. Autoantibodies in IIM play a central role in disease pathogenesis and are classified as myositis-specific antibodies (MSA) or myositis-associated antibodies (MAA)[1]. While antibody-related phenotypes may vary by geographic region, data on phenotype stratification by autoantibody profile in Hispanic populations remain scarce. Recognizing distinct clinical phenotypes associated with specific autoantibodies is essential for guiding early diagnosis and individualized therapeutic decisions. We aimed to describe organ-specific disease activity patterns by serological profiles in a Hispanic IIM cohort.

Table 1. Organ involvement and mean MITAX score stratified by autoantibody in idiopathic inflammatory myopathies.

Antibody	Number of patients	Constitutional (%)	Cutaneous (%)	Skeletal (%)	Muscular (%)	Pulmonary (%)	GI (%)	Cardiovascular (%)	MITAX score mean (SD)
Ro52	15	73.3	60	80	93.3	80	33.3	6.6	7.30 (0.97)
TIF1γ	11	81.8	90.9	63.6	90.9	63.6	45.4	0	8.81 (1.45)
MDA5	7	57.1	57.1	57.1	71.4	85.7	42.8	14.2	6.42 (1.74)
Mi2β	7*	60	20	40	60	20	20	0	3.6 (1.6)
SRP	5	60	20	40	40	0	20	0	2.4 (0.67)
PmScl100	5	60	60	20	60	40	0	0	3.6 (0.6)
PmScl75	4	50	25	75	100	75	25	0	5.75 (1.93)
NXP2	4*	66.6	66.6	33.3	100	66.6	33.3	0	8 (2.64)
Ku	3	100	33.3	100	100	33.3	33.3	0	7.33 (2.40)
Jo1	3	100	100	66.6	66.6	100	33.3	0	9.33 (0.66)
PL12	2	100	50	100	100	100	50	50	9.5 (1.5)
OJ	2	100	50	0	50	100	50	0	7.5 (4.5)
EJ	2	100	50	50	100	50	50	0	9 (3)
SAE	1	100	100	0	100	100	100	0	12
PL7	1	0	0	100	100	0	0	0	3

*Mi2β positivity was observed in 7 patients, but organ involvement was assessed in only 5, as 2 patients died and MITAX evaluation could not be performed. *NXP2 was observed in 4 patients, but organ involvement was assessed in 3 patients died and MITAX evaluation could not be performed. GI: gastrointestinal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical and damage characteristics in patients with single and multiple autoantibody positivity

	Single antibody positivity (n=16)	*Multiple antibody positivity (n=22)*	*p-value*
Age, mean (±SD)	47.13 (19.49)	50.95(12.96)	0.471
Sex, woman (%)	15 (93.8)	17 (77.3)	0.217
Time since symptoms onset in months, mean (SD)	8.96 (10.34)	13.72 (20.04)	0.392
Constitutional involvement, n (%)	9 (60)	16 (76.2)	0.298
***Cutaneous involvement*, n (%)**	8 (53.3)	13 (61.9)	0.607
***Skeletal involvement*, n (%)**	8 (53.3)	14 (66.7)	0.418
***Gastrointestinal involvement*, n (%)**	4 (26.7)	7 (33.3)	0.669
***Pulmonary involvement*, n (%)**	6 (40)	15 (71.4)	0.059
***Cardiovascular involvement*, n (%)**	1 (6.7)	1 (4.8)	0.806
***Muscular involvement*, n (%)**	9 (60)	19 (90.5)	**0.03**
MYOACT, mean (±SD)	12.63(13.90)	16.07(8.43)	0.054
MITAX, mean (±SD)	8.17(7.55)	13.43(9.77)	0.551

Methods: We conducted a cross-sectional, retrospective study of Hispanic patients with IIM diagnosis per 2017 ACR/EULAR criteria or clinical judgment. Disease activity was assessed using the MYOACT and MITAX scales. For patients with multiple antibodies, activity scores were attributed to all antibodies detected. Patients were additionally grouped as: monopositive (one autoantibody present), and multipositive (≥2 autoantibodies). Clinical and serological data were compared using Mann-Whitney U and chi-squared or Fisher's exact tests. A p-value ≤ 0.05 was considered statistically significant.

Table 3. Antibody profile patterns

Table 3. Antibody profile patterns	**n=38 patients**
Single antibody positivity	
TIF1γ, n(%)	4 (10.5)
MDA5, n(%)	3 (7.8)
Mi2β, n(%)	3 (7.8)*
Ro52, n(%)	1 (2.6)
PL7, n(%)	1 (2.6)
SRP, n(%)	1 (2.6)
Jo1, n(%)	1 (2.6)
PM Scl100, n(%)	1 (2.6)
NXP2, n(%)	1 (2.6)
Multiple antibody positivity	
Ro52 + MDA5, n(%)	3 (7.8)
Ro52 + TIF1γ, n(%)	2 (5.2)
Ro52 + PL12, n(%)	2 (5.2)
Ro52 + SRP + PM Scl75 + TIF1γ, n(%)	1 (2.6)
Ro52 + PM Scl75 + Mi2beta, n(%)	1 (2.6)
Ro52 + SRP + TIF1γ, n(%)	1 (2.6)
Ro52 + Jo1, n(%)	1 (2.6)
Ro52 + Jo1 + PM Scl75, n(%)	1 (2.6)
Ro52 + NXP2, n(%)	1 (2.6)
Ro52 + PM Scl75 + PM Scl100, n(%)	1 (2.6)
OJ + EJ + SAE1 + NXP2 + TIF1γ, n(%)	1 (2.6)
OJ + SRP + PM Scl100 + MDA5, n(%)	1 (2.6)
Mi2β + SRP + Ku , n(%)	1 (2.6)
Mi2β + NXP2, n(%)	1 (2.6)[a]
Mi2β + PM Scl100, n(%)	1 (2.6)
TIF1γ + PM Scl100, n(%)	1 (2.6)
TIF1γ + Ku, n(%)	1 (2.6)
Ku + EJ, n(%)	1 (2.6)

*Mortality was observed in a patient with this antibody pattern.
[a]Cancer diagnosis and mortality were both reported in a patient with this antibody pattern.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Forty patients were included (mean age 46.8 ± 15.9; 85% women). Disease activity scores and antibody profiles were available in 38 patients; two died during follow-up due to disease activity. Fifteen autoantibodies were identified, most commonly Ro52 (n=15), TIF1γ (n=11), and MDA5 (n=7). Mean MITAX and MYOACT scores were 11.2 (±9.1) and 14.59 (±11.02), respectively. The most frequently affected domains were muscular (73.7%), constitutional (65.8%), and skeletal (57.9%). Stratified by autoantibody positivity, 38 profiles were analyzed (two lacked myositis panel). Pulmonary involvement was most common in MDA5 (85.7%) and Ro52 (80%) positive patients. (Table 1) Cardiovascular involvement was rare, seen only in Ro52, MDA5, and PL12.

Sixteen patients were monopositive (TIF1γ n=4, MDA5 n=3). (Table 2). Although multipositive patients (n=22) showed a trend toward higher damage and activity scores, differences were not statistically significant. However, when stratified by organ domain, muscular involvement was significantly more frequent in this group (90.5% vs. 50%, p=0.03). Antibody profile patterns varied across our cohort (Table 3). Two patients died: one had a diagnosis of renal cancer and both Mi2β and NXP2 positivity; the other had isolated Mi2β.

Conclusion: Disease activity patterns differ by autoantibody profile. MDA5, Ro52, and TIF1y were strongly associated with pulmonary involvement, while patients with anti-synthetase (ARS) antibodies (OJ, EJ, PL12, PL7, and Jo1), Ku, and SAE associated mainly to muscular activity. These findings, though limited by small sample sizes, may support earlier recognition of high-activity phenotypes and organ-specific complications in IIM subgroups, particularly within Hispanic population.

Disclosure: v. cantu: None; **E. Dominguez-Chapa**: None; **R. Polina-Lugo**: None; **A. Bardan Inchaustegui**: None; **f. garcia-Carrillo**: None; **E. Reyna-Hernandez**: None; **D. Mejia-Rodriguez**: None; **R. Arvizu-Rivera**: None; **J. Cardenas-de la Garza**: None; **M. Villarreal-Alarcón**: None; **D. Galarza-Delgado**: None.

Abstract Number: 2059

Autoantibody Patterns in Myositis Immunoblot Testing: A Retrospective Study inInflammatory Myopathies and Connective Tissue Diseases (2017–2023)

Fabricio Benavides Villanueva[1], Ligia Gabrie-Rodriguez[2], Carmen Secada-Gómez[3], Mayra Garcia[4], Hector Ulloa-Alvarado[5], Giuliano Boselli[6], Camilo Veloza-Morales[7], juan Irure-Ventura[8], Marcos López-Hoyos[9], Diana Prieto-Peña[10] and Ricardo Blanco[3], [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Immunopathology Group,Santander, Spain, Santander, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [4]Division of Immunology, Hospital Universitario Marques de Valdecilla, IDIVAL, Immunopathology Group,Santander, Spain, Santander, Cantabria, Spain, [5]Servicio Cántabro de Salud, Atención Primaria, Santander, Spain, Santander, Cantabria, Spain, [6]Rheumatology Division, Hospital Universitario Miguel Servet , Zaragoza, Spain, Zaragoza, Aragon, Spain, [7]Rheumatology Division, Hospital Universitario Joan XXIII, Tarragona, Spain, Tarragona, Catalonia, Spain, [8]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Cantabria, Spain, [9]Division of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [10]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune diseases characterized by muscle inflammation and systemic involvement, often associated with specific autoantibodies. Immunoblot assays provide a simultaneous detection of multiple autoantibodies, yet the clinical implications of their positivity, particularly in the context of inflammatory myopathies and connective tissue diseases (CTD), remain incompletely understood.

Objective: To characterise the clinical and laboratory features of patients who underwent myositis immunoblot testing, with focus on the prevalence and distribution of autoantibody positivity across IIM and other CTDs.

Methods: Retrospective study with all patients who underwent immunoblot testing for myositis-specific and associated autoantibodies using the Autoimmune Inflammatory Myopathies 16 Ag kit (Euroimmun, Lübeck, Germany) between November 2017 and October 2023 at a single hospital in northern Spain. For patients with multiple tests, only the first result was considered. Patients were categorised into three diagnostic groups: no connective tissue disease (No CTD), inflammatory myopathies, and other CTDs, based on established international classification criteria. Data collection encompassed clinical symptoms, laboratory findings, and complementary tests; however, some tests were not performed in all patients. Missing data were excluded from the analysis.

Results: A total of 472 patients (66% female; median age 61 years [IQR: 47–71]) were included, with 181 (38%) testing positive for at least one autoantibody. Among these, 33 patients (7%) exhibited double antibody positivity, most frequently involving anti-Ro52 (26/33). Patients were categorised into three groups: no connective tissue disease (No CTD) (188; 40%), inflammatory myopathies (79; 17%), and other CTDs (205; 43%).

TABLE. Clinical and Serological Characteristics of Patients with Immunoblot Testing Categorised by Diagnostic Groups.

		Connective tissue disease		
	No CTD n=188	Inflammatory myopathy n=79	Other CTD n=205	p-value
Patients age (years), median age [IQR]	59 [46-70]	61 [48-70]	62 [48-71]	.530[a]
Male/female, n (% male)	67 (36)	29 (37)	64 (31)	.552[c]
Autoantibody-Positive Patients[4], n (%)	32[d] (17)	67[e] (85)	82[d] (40)	.000[b]
Antibody specificity, n (%)				
Anti-Ro52	11 (6)	30 (38)	40 (19.5)	.000[b]
Anti-Jo1	3 (1.6)	14 (18)	4 (2)	.000[b]
Anti-PL7	4 (2)	11 (14)	2 (1)	.000[b]
Anti-Mi2	7 (3.7)	7 (9)	7 (3.4)	.148[b]
Anti-PL12	1 (0.5)	6 (8)	1 (0.5)	.000[b]
Anti-PMScl	5 (3)	6 (8)	11 (5)	.143[b]
Anti-Ku	1 (0.5)	3 (4)	18 (9)	.000[b]
Anti-OJ	1 (0.5)	3 (4)	3 (1.5)	.132[b]
Anti-EJ	1 (0.5)	2 (2.5)	0	.035[b]
Anti-NXP2	1 (0.5)	2 (2.5)	0	.037[b]
Anti-TIF-1 gamma	1 (0.5)	2 (2.5)	1 (0.5)	.290[b]
Anti-MDA5	0	1 (1.3)	0	.162[b]
Anti-SAE1	0	1 (1.3)	0	.164[b]
Anti-SRP	1 (0.5)	1 (1.3)	2 (1)	.822[b]
Clinical Features				
Mialgias, n (%)	58 (31)	30 (38)	39 (19)	.002[b]
Patient-reported muscle weakness, n (%)	55 (29)	30 (38)	4 (20.5)	.008[b]
Physician-assessed muscle weakness, n (%)	29 (15)	26 (33)	21 (10)	.000[b]
Raynaud's phenomenon, n (%)	11 (6)	24 (30)	66 (32)	.000[b]
Arthralgias/arthritis, n (%)	35 (18.6)	35 (44)	92 (45)	.000[b]
Cutaneous rash, n (%)	12 (6.4)	26 (33)	24 (12)	.000[b]
Dry eye and mouth symptoms, n (%)	7 (3.7)	7 (9)	23 (11)	.021[b]
Diffuse interstitial lung disease, n (%)	31 (16.5)	37 (47)	63 (31)	.000[b]
Complementary test[f]				
Myopathic electromyography, n (%) Data available for 279 patients (59.0%)	21 (25)	20 (26)	5 (4)	.000[b]
Abnormal muscle MRI, n (%) Data available for 114 patients (24.2%)	15 (33)	22 (73)	8 (21)	.000[b]
Pathological capillaroscopy, n (%) Data available for 130 patients (28.0%)	5 (18.5)	17 (40)	31 (63)	.002[b]
Laboratory Features				
C-reactive protein (mg/dL), median [IQR]	0.4 [0.4-0.6]	0.4 [0.4-1.3]	0.4 [0.4-1.1]	.017[a]
Erythrocyte Sedimentation Rate, median [IQR]	16 [8-29]	28 [13-29]	21 [9-37]	.001[a]
Creatine Kinase (U/L), median [IQR] Data available for 408 patients (86.4)	193 [66-588]	369 [115-2545]	122 [72-274]	.000[a]
Aldolase (U/L), median [IQR] Data available for 225 patients (48%)	7 [5-10]	8 [5-16]	6 [5-9]	.001[a]

[a]p-values according to Kruskal-Wallis test, [b]p-values according to Pearson Chi-Square test, [c] using the Autoimmune Inflammatory Myopathies 16 Ag kit (Euroimmun, Lübeck, Germany), [d]5 patients had double antibody positivity, [e]7 patients had double antibody positivity, [d]21 patients had double antibody positivity, [b]p-values according to Fisher's Exact Test, [f]Not performed in all patients.
CTD, connective tissue disease, IQR, interquartile range, n, number.

TABLE. Clinical and Serological Characteristics of Patients with Immunoblot Testing Categorized by Diagnostic Groups.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Significant differences in autoantibody specificity were observed across the diagnostic groups. Anti-Ro52, anti-Jo1, anti-PL7, anti-EJ, and anti-NXP2 were more frequently detected in patients with inflammatory myopathies, while anti-Ku was predominantly associated with other CTDs ($p< 0.001$).

Muscle-related symptoms, such as myalgia (38%) and muscle weakness (33%), were significantly more prevalent in inflammatory myopathies compared to patients with other CTDs or no CTD ($p< 0.001$). Systemic features were also notably distinct: Raynaud's phenomenon (30%), arthralgia/arthritis (44%), and cutaneous rash (33%) were more common in inflammatory myopathies, while diffuse interstitial lung disease was observed in 47% of these patients ($p< 0.001$). **Table 1** summarizes these findings, along with additional data on complementary tests and laboratory features.

Conclusion: This study underscores the clinical and laboratory differences across diagnostic groups in patients undergoing myositis immunoblot testing. The unexpected prevalence of myopathic findings in patients without CTDs suggests the need for cautious interpretation and potential longitudinal evaluation. Complementary tests remain valuable tools in identifying muscular and vascular abnormalities, supporting a comprehensive diagnostic approach for autoimmune diseases.

Disclosure: F. Benavides Villanueva: None; **L. Gabrie-Rodriguez**: None; **C. Secada-Gómez**: None; **M. Garcia**: None; **H. Ulloa-Alvarado**: None; **G. Boselli**: None; **C. Veloza-Morales**: None; **j. Irure-Ventura**: None; **M. López-Hoyos**: None; **D. Prieto-Peña**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2060

Treatment Patterns And Drug Use In Idiopathic Inflammatory Myopathies. Description Of The First Year After Diagnosis In A Swedish Myositis Cohort.

Irene Peralta-García[1], Naz Haque[2], Dag Leonard[3], Anna Glasin[4], Silva Puksic[5], Balsam Hanna[6], My Axelhed[7], Theodoros Lappas[5], Farbicio Espinosa Ortega[1], Karin Lodin[1], NIls Eckerdal[2], Helene Alexanderson[8], Elizabeth Hsia[9], **Federico Zazzetti**[10], Ingrid Lundberg[11] and Marie Holmqvist[1], [1]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna. Karolinska University Hospital, Medical Unit of Gastroenterology, Dermatology, Rheumatology. Theme Inflammation and Ageing, Stockholm, Sweden, [2]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden, [3]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [4]Rheumatology Department, Linköping Hospital, LInköping, Sweden, [5]Rheumatology Department, Örebro University Hospital, Örebro, Sweden, [6]Rheumatology Department, Sahlgrenska University Hospital, Gothenburg, Sweden, [7]Rheumatology Department, Västmanlands Hospital, Västerås, Sweden, [8]Karolinska University Hospital, Stockholm, Sweden, [9]Johnson & Johnson, Spring House, PA, [10]Johnson & Johnson, Horsham, PA, USA, Ambler, PA, [11]Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Due to the rarity and heterogeneity of idiopathic inflammatory myopathies (IIM), we lack robust randomized trials to guide treatment decisions. Most of current practice is based on case reports or adapted from other diseases. The aims of this study were to investigate the occurrence of IIM subgroups over time and to characterize immunosuppressive treatment during the first year after diagnosis over different calendar periods and subgroups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics according to diagnosis year

	Diagnosed 2008-2013	Diagnosed 2014-2019	Diagnosed 2020-2025
Total, n	136	189	220
Female, n (%)	85 (61.6)	116 (60.7)	115 (52.5)
Age at diagnosis, mean (yr) ± SD	56.9 ± 15.9	57.4 ± 15.7	62.1 ± 14.9
Subtypes, n (%)			
PM	48 (35.3)	38 (20.1)	27 (12.4)
DM	44 (32.4)	60 (31.8)	55 (25.0)
IBM	14 (10.3)	24 (12.7)	27 (12.4)
ASSD	27 (19.8)	52 (27.5)	52 (23.6)
IMNM	3 (2.2)	15 (7.9)	59 (26.9)

Methods: The SweMyoNet is a nationwide Swedish register initiated to study and follow IIM patients. Information is prospectively collected by health care providers and includes details on IIM subtype, disease manifestations, longitudinal disease activity and treatment. For this study, we included IIM patients diagnosed from 31/12/2007 to 15/03/2025, with at least two registered visits in the register, the first within six months of diagnosis. IIM was subgrouped into polymyositis (PM), dermatomyositis (DM), anti-synthetase syndrome (ASSD), immune-mediated necrotizing myopathy (IMNM) and inclusion body myositis (IBM). Unclear diagnoses were excluded. Patients were divided into three calendar periods according to year of diagnosis to compare treatment over time. Continuous variables are described as mean±SD or mean and IQR; categorical as frequencies and percentages.

Results: In total, 545 patients were identified, mostly women (58%) mean age 60 years (±15) at diagnosis. The most frequent IIM subtype was DM (n=159, 29%) followed by ASSD (131, 24%), PM (113, 21%), IMNM (77, 14%) and IBM (65, 12%). The proportion of the different subgroups has changed over time (Table 1), with a rise of ASSD and IMNM (20 and 2% in 2008-2013 to 24 to 27% in 2020-2025, respectively) and a drop in PM (35% in 2008-2013 to 12% in 2020-2025).

Glucocorticoid (GC) treatment was the most used drug the first 12 months after diagnosis (n=379, 82%) (Table 2). Methotrexate (MTX) was the most prescribed immunosuppressant (68% of patients) followed by rituximab (RTX) (23%), cyclophosphamide (CYC) (19%) and mycophenolate mofetil (MMF) (13%). 49 patients received no drug therapy the first

Table 2: Treatment received during the first year after diagnosis according to IIM subtype

	Total (n=545)	DM (n=159)	PM (n=113)	IBM (n=65)	ASSD (n=131)	IMNM (n=77)
Patients without treatment, n (%)	49 (9)	9 (6)	9 (8)	22 (34)	7 (5)	2 (3)
Patients under treatment, n (%)	496 (91)	150 (94)	104 (92)	43 (66)	124 (95)	75 (97)
Drugs, n (% amongst those receiving treatment)						
GC any form	379 (76.4)	131 (87.3)	84 (80.8)	28 (65.1)	100 (80.6)	36 (48.0)
GC oral	367 (73.9)	129 (86.0)	82 (78.8)	28 (65.1)	94 (75.8)	34 (45.3)
GC intravenous	142 (28.6)	56 (35.2)	13 (12.5)	0	60 (48.4)	13 (17.3)
MTX	339 (68.3)	98 (65.3)	65 (62.5)	38 (88.4)	68 (54.8)	70 (93.3)
IVIG	104 (21.0)	36 (24.0)	3 (2.9)	0	7 (5.6)	58 (77.3)
RTX	112 (22.6)	37 (24.7)	16 (15.4)	0	55 (44.4)	4 (5.3)
Azathioprine	60 (12.1)	28 (17.6)	15 (14.4)	3 (7.0)	12 (9.7)	2 (2.7)
Anti-malarial drugs	20 (4.0)	17 (11.3)	2 (1.9)	0	1 (0.8)	0
CYC	96 (19.4)	27 (17.0)	10 (9.6)	0	58 (46.8)	1 (1.3)
MMF	64 (12.9)	17 (11.3)	18 (17.3)	1 (2.3)	28 (22.6)	0
Abatacept	7 (1.4)	3 (2.0)	0	0	0	4 (5.3)
Tacrolimus	10 (2.0)	9 (6.0)	0	0	1 (0.8)	0
JAK inhibitors	4 (0.8)	2 (1.3)	1 (1.0)	0	1 (0.8)	0
Other	13 (2.6)	5 (3.3)	2 (1.8)	3 (7.0)	3 (2.5)	0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Treatment received during the first year after diagnosis according to calendar year of diagnosis

	Diagnosed 2008-2013 (n=136)	Diagnosed 2014-2019 (n=189)	Diagnosed 2020-2025 (n=220)
Patients without treatment, n (%)	20 (15)	17 (9)	12 (5)
Patients under treatment, n (%)	116 (85)	172 (91)	208 (95)
Treatments received, n (% amongst those receiving treatment)			
GC any form	95 (81.9)	144 (83.7)	140 (67.3)
GC oral	94 (81.0)	137 (79.7)	136 (65.7)
GC intravenous	10 (8.5)	60 (34.5)	72 (34.8)
MTX	59 (50.0)	100 (58.1)	180 (86.5)
IVIG	2 (1.7)	20 (11.6)	82 (39.6)
RTX	3 (2.5)	60 (34.5)	49 (23.7)
Azathioprine	29 (25.0)	18 (10.5)	13 (6.3)
Anti-malarial drugs	1 (0.8)	7 (4.0)	12 (5.8)
CYC	22 (18.6)	44 (25.3)	30 (14.5)
MMF	24 (20.3)	40 (23.0)	0
Abatacept	1 (0.8)	3 (1.7)	4 (1.9)
Tacrolimus	0	3 (1.7)	7 (3.4)
JAK inhibitors	0	0	4 (1.9)
Other	3 (2.5)	7 (4.1)	3 (1.4)

12 months after diagnosis. During this same period 87% of all DM, 81% of PM and ASSD, 65% of IBM and 48% of IMNM patients were treated with GC.

Most IMNM patients (93%) received MTX. MTX was also the most frequent immunosuppressant in all other subgroups. 47% of ASSD patients received CYC and 44% RTX. Intravenous immunoglobulin (IVIG) was used in all subtypes except IBM but predominantly in IMNM where 77% received it in the first 12 months. Over time, GC use decreased: 82% patients in the 2008-2013 group received GC in comparison to 67% in the 2020-2025 (Table 3). In contrast, IVIG use increased from 2% of patients in 2008-2013 to almost 40% in 2020-2025. RTX was not widely used in 2008-2013 (3%) but this increased from 2014 onwards (35% and 24% respectively in 2014-2019 and 2020-2025).

Conclusion: In our cohort, ASSD and IMNM occurrence has increased and PM decreased since 2008 and onwards. Over time, drug use has changed with decrease of GC and increase of IVIG. The prescription patterns differed between IIM subtypes but MTX was the most used immunosuppressor in all subgroups of IIM.

Disclosure: I. Peralta-García: Johnson & Johnson, 5; **N. Haque**: None; **D. Leonard**: None; **A. Glasin**: None; **S. Puksic**: None; **B. Hanna**: None; **M. Axelhed**: None; **T. Lappas**: None; **F. Espinosa Ortega**: Johnson & Johnson, 5; **K. Lodin**: Johnson & Johnson, 5; **N. Eckerdal**: None; **H. Alexanderson**: None; **E. Hsia**: Johnson & Johnson, 3; **F. Zazzetti**: Johnson & Johnson, 3, 11; **I. Lundberg**: AstraZeneca, 1, Chugai, 1, Johnson & Johnson, 5, Novartis, 1, 11, Pfizer, 1, Roche, 11; **M. Holmqvist**: Johnson & Johnson, 5.

Abstract Number: 2061

Tryptophan Metabolism Alteration Is Associated With Rapidly Progressive Interstitial Lung Disease Of Anti-MDA5+ Dermatomyositis

Hongjiang liu, Yixue Guo, Xinhua dai, beibei cui, bo chen, changpei li, shuyi liao, Junlong zhang and Qibing Xie, West China Hospital, Sichuan University, Chengdu, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

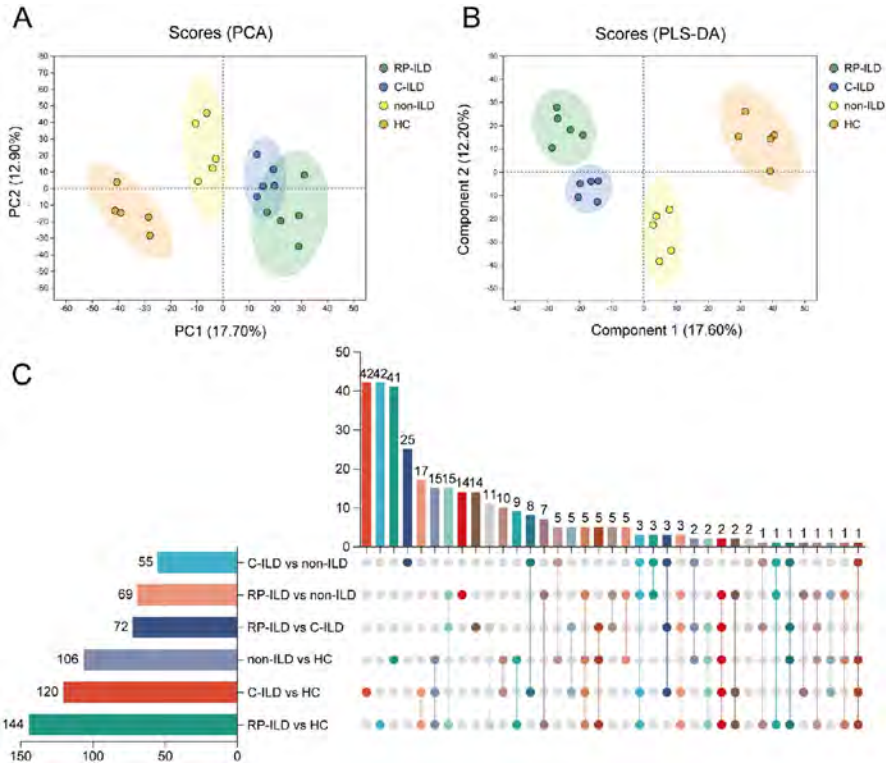


FIG 1. Non-targeted metabolomics profiling analysis of MDA5 positive dermatomyositis (MDA5+ DM) patients with rapidly progressive ILD (RP-ILD, n = 5), chronic ILD (C-ILD, n = 5), non-ILD (n = 5) and healthy controls (HCs, n = 5). (A) Score scatter plot of principal component analysis (PCA) model. (B) Score scatter plot of partial least squares discriminant analysis (PLS-DA) model. (C) Upset plot illustrating overlapping and specific metabolites in various comparison groups.

Background/Purpose: Anti-melanoma differentiation-associated gene 5-positive dermatomyositis (MDA5+ DM) is an autoimmune condition associated with rapidly progressive interstitial lung disease (RP-ILD) and high mortality. Metabolic disturbances have been reported in inflammatory myopathies, including DM. However, whether alterations of metabolomics profiling participate in ILD development in MDA5+ DM remains undetermined.

Methods: Untargeted and targeted metabolomics profiling was performed using liquid chromatography-mass spectrometry (LC-MS) to profile metabolites in distinct subtypes of MDA5+ DM patients (RP-ILD, n = 25, C-ILD, n = 25, non-ILD, n = 24) and healthy controls (HCs, n = 41). Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis was used to identify altered pathways. Pearson correlation analysis was employed to investigate the correlation between metabolites and clinical/laboratory continuous variables.

Results: The metabolic imbalance observed in the plasma of MDA5+ DM patients predominantly affects amino acid metabolism. Compared to MDA5+ DM patients with chronic ILD, non-ILD, and HCs, MDA5+ DM patients with RP-ILD exhibited significant alterations in tryptophan (TRP) and its metabolites (RP-ILD vs C-ILD: $P = 0.0006$, RP-ILD vs non-ILD: $P = 0.0003$, RP-ILD vs HC: $P < 0.0001$). Further analysis revealed that the kynurenine (KYN) pathway may primarily drive abnormal TRP metabolism in MDA5+ DM patients with RP-ILD. In addition, abnormal TRP and KYN pathway metabolites were associated with disease activity indicators in MDA5+ DM patients.

Conclusion: Our results indicated that alterations in the TRP metabolism may play an active role in the pathogenesis of RP-ILD in MDA5+ DM and could be considered as a potential therapeutic approach.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

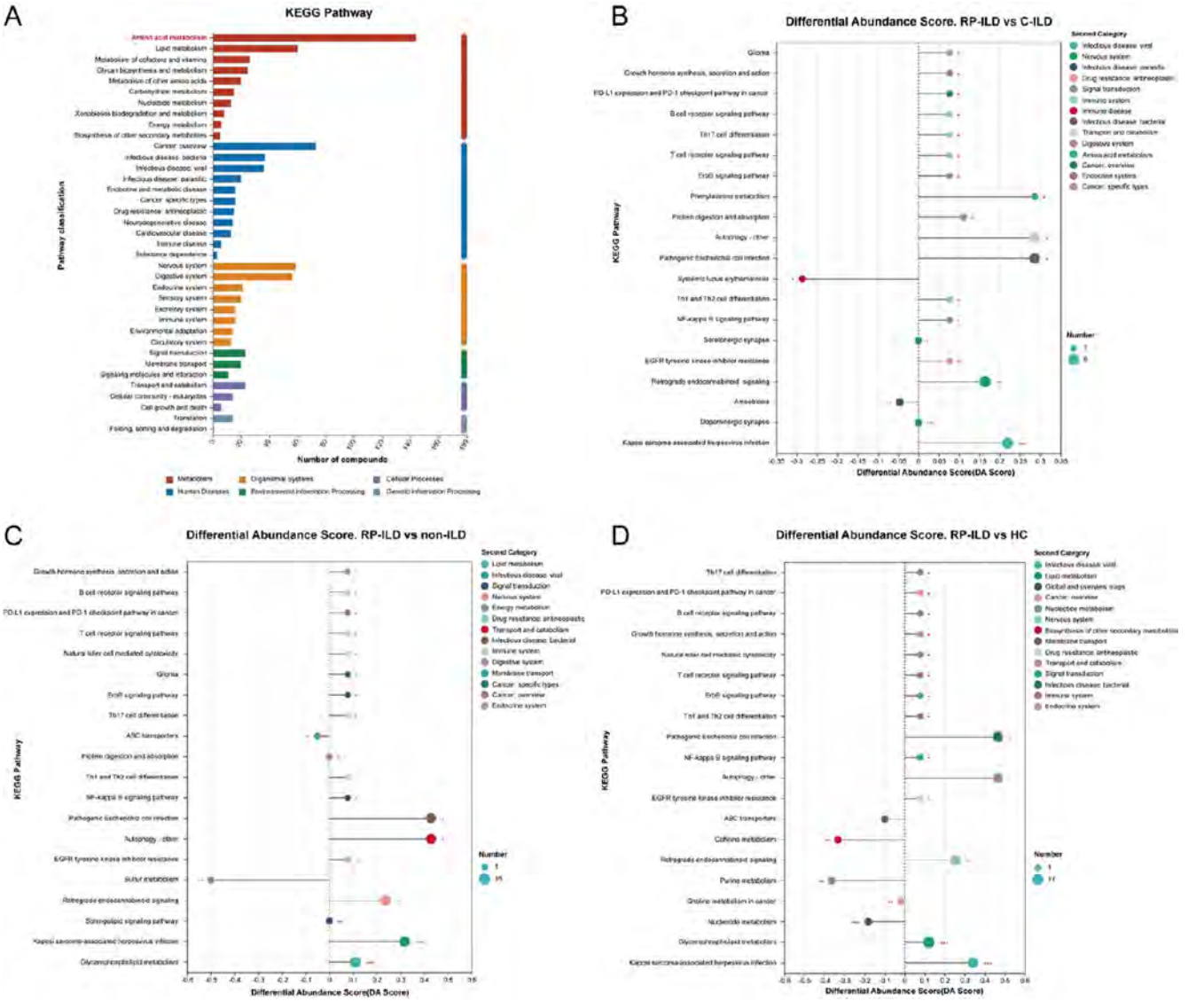


FIG 2. Enrichment of Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways for metabolites. (A) KEGG metabolic pathway classification statistics chart. Y-axis, the secondary classification of the KEGG metabolic pathway. X-axis, the number of compounds annotated under the pathway. (B) Difference abundance score chart of KEGG enrichment between RP-ILD and C-ILD. (C) Difference abundance score chart of KEGG enrichment between RP-ILD and non-ILD. (D) Difference abundance score chart of KEGG enrichment between RP-ILD and HC.

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

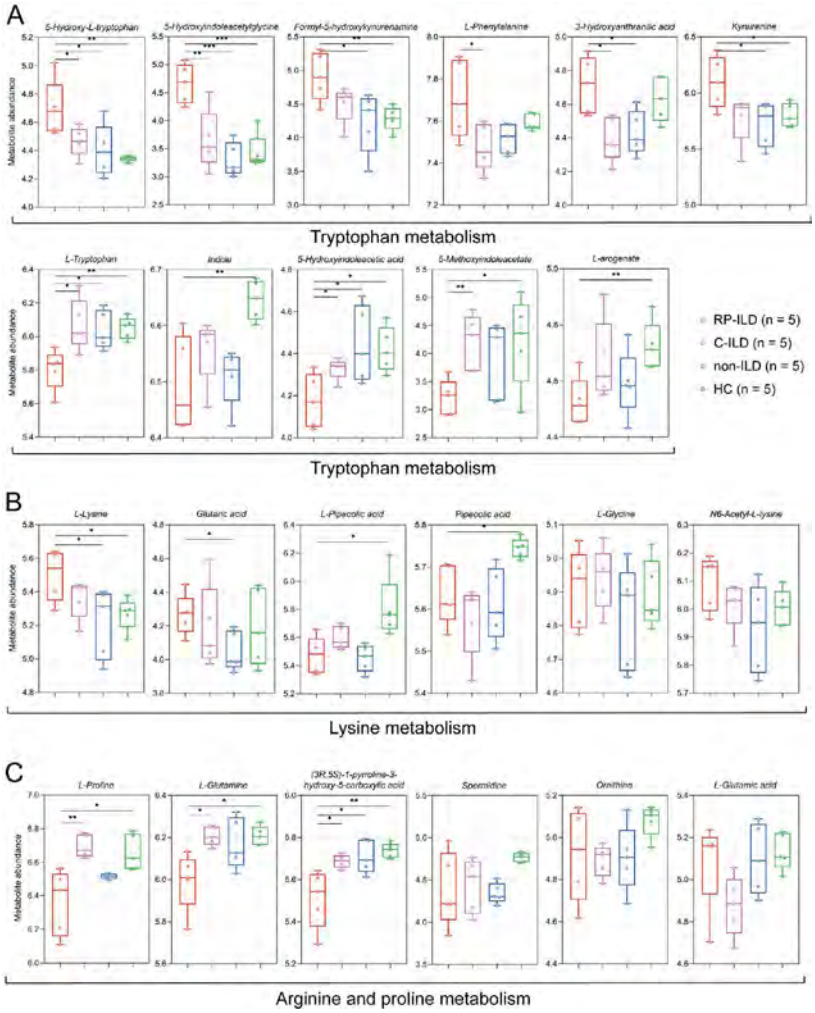


FIG 3. Amino acid pathway-specific metabolite abundance analysis. (A) Box plots showing distribution of metabolite abundance in tryptophan metabolism. (B) Box plots showing distribution of metabolite abundance in lysine metabolism. (C) Box plots showing distribution of metabolite abundance in arginine and proline metabolism. (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

Disclosure: H. liu: None; **Y. Guo**: None; **X. dai**: None; **b. cui**: None; **b. chen**: None; **c. li**: None; **s. liao**: None; **J. zhang**: None; **Q. Xie**: AbbVie, 6, Amgen, 6, Eli Lilly, 6, GSK, 5, 6, Novartis, 6.

Abstract Number: 2062

Immune Cell Signatures Associated with Disease Activity in Dermatomyositis Across Autoantibody Subtypes

Jeffrey Sagun[1], Melissa Leeolou[1], Nicholas Geraci[2], Andrew Bender[3], Fatima Strand[2], David Fiorentino[1] and Kavita Sarin[1], [1]Department of Dermatology, Stanford University Medical Center, Stanford, CA, [2]EMD Serono, Billerica, MA, [3]AbbVie, Worcester, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Dermatomyositis (DM) is a heterogeneous multisystem autoimmune disease characterized by inflammation of the skin, muscle, and lung. Identifying the immune cells that drive disease activity is critical for advancing targeted therapies and improving clinical outcomes. Accordingly, we aimed to define immune cell populations associated with disease activity in DM across autoantibody-defined DM subtypes.

Methods: Bulk RNA sequencing analysis was performed on peripheral blood from 350 comprehensively phenotyped adult DM patients and 92 active DM skin biopsies. Type I (IFN-1) and type II (IFN-2) interferon scores were calculated as previously described. Immune cell proportions were estimated using CIBERSORT deconvolution, and associations with autoantibody subtypes, Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) scores, Manual Muscle Testing (MMT) scores, and IFN scores were evaluated.

Results: Circulating pro-inflammatory M1 macrophage scores were significantly associated with cutaneous disease activity (CDASI; r=0.30, p< 0.001, Spearman's rank correlation coefficient). Concordantly, the M1 macrophage signature was markedly elevated in DM skin compared to healthy controls (18.2 fold increase, p=0.0097, Wilcoxon signed-rank test) and positively correlated with both IFN-1 (r=0.58, p< 0.001, Spearman) and IFN-2 (r=0.69, p< 0.001, Spearman) scores, suggesting a direct role for M1 macrophages in skin inflammation. Notably, the correlation between circulating M1 macrophages and CDASI scores was evident across several autoantibody groups, including anti-TIF1γ (n=105, r=0.41, p< 0.001, Spearman), anti-Mi2 (n=30, r=0.40 p< 0.03, Spearman), and anti-NXP2 (n=20, r=0.48, p< 0.03, Spearman), but was absent in anti-PM/Scl+ or anti-synthetase+ (anti-Jo1, anti-PL7, anti-PL12) DM patients, indicating that distinct immune drivers may underlie disease activity across DM subtypes. In contrast to skin, M1 macrophages were not associated with muscle disease activity in any DM subtype. Instead, increased memory B cell and plasma cell scores were most strongly associated with reduced muscle strength (MMT; memory B cells: r=-0.25, p< 0.01; plasma cells: r=-0.20, p< 0.05; Spearman). Additional immune cell associations were identified with other pathologies.

Conclusion: Our findings implicate circulating M1 macrophages as potentially key contributors to cutaneous disease activity in DM and highlight subtype-specific differences in immune pathogenesis. These results provide new insights into potential cellular therapeutic targets and raise the question of whether organ and autoantibody-specific therapeutic strategies are necessary to effectively manage the heterogeneous clinical presentations of DM.

Disclosure: J. Sagun: None; **M. Leeolou**: None; **N. Geraci**: None; **A. Bender**: None; **F. Strand**: None; **D. Fiorentino**: None; **K. Sarin**: None.

Abstract Number: 2063

Linking PROMIS scores to disease severity and treatment in dermatomyositis: a patient-centered evaluation

Julie Paik[1], Andrea Young[2], Zuzana Bologna[3], Will Kelly[3], Chris Mecoli[4], Jemima Albayda[2] and Lisa Christopher-Stine[2], [1]Johns Hopkins Rheumatology, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University, Baltimore, [4]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Dermatomyositis (DM) is a chronic inflammatory myopathy characterized by muscle weakness and skin rashes, yet its full impact on patient-reported outcomes remains under-explored. We used PROMIS instruments to systematically assess pain, fatigue, and physical function in patients with dermatomyositis, aiming to capture the multidimensional burden of disease from the patient perspective.

Methods: Adult patients with dermatomyositis (DM) fulfilling the 2017 EULAR/ACR Classification Criteria for DM were enrolled at a single center. Inclusion criteria required at least two consecutive visits (baseline and follow-up) with documented PROMIS scores. Demographic data, organ involvement and myositis-specific autoantibody status were obtained. Markers of disease severity included maximum cutaneous dermatomyositis disease area and severity index-activity (CDASI-A), maximum creatine kinase (CK), and lowest Manual Muscle Testing-8 (MMT-8) scores. Medication history of ever taking an immunosuppressant or immunomodulatory agent was also ascertained by chart review. PROMIS domains included PROMIS Short Form Fatigue 7a (v1.0), Pain Interference 6a (v1.1), Physical Function 8b (v2.0) with moderate or worse scores defined as the primary outcome. Logistic regression was performed to evaluate associations between PROMIS scores and clinical covariates, adjusting for baseline PROMIS scores. Covariates included age, race, lowest MMT-8, maximum CDASI-A, CK, medication exposures, and autoantibodies.

Results: A total of 214 patients with DM were identified with PROMIS scores taken at two visits during follow-up. Average age of diagnosis was 51.2 $\pm$ 12.6 years; 167 (76.6%) were female, and 51 (23.4%) were male. 178 (81.7%) were white, 21 (9.6%) were black, and 19 (8.7%) were Asian, Native Hawaiian/Pacific Islander). Mean CDASI-A score was 13.1 + 9.1. Among clinical and demographic variables, race was associated with PROMIS pain and fatigue outcomes. Patients identifying as Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander were less likely to report moderate or worse pain (p=0.023) and fatigue (p=0.075). For fatigue, there was also a trend toward greater impairment with lower MMT-8 scores (p=0.059). Prior treatment with intravenous immunoglobulin (IVIG) was significantly associated with increased odds of reporting moderate or worse fatigue (p=0.001) and impaired physical function (p=0.012).

Conclusion: In this cohort of dermatomyositis patients, patient-reported fatigue and physical function impairments were associated with IVIG use and clinical weakness, while racial differences suggested potential disparities in impairment or reporting. Given the observational nature of this study, associations between treatment exposures and PROMIS outcomes should be interpreted cautiously, as they may reflect underlying disease severity rather than direct treatment effects. These findings highlight the utility of PROMIS measures in capturing patient-centered outcomes and identifying subgroups at risk for higher disease burden.

Disclosure: J. Paik: ArgenX, 12, Priovant, 12,; **A. Young**: None; **Z. Bologna**: None; **W. Kelly**: None; **C. Mecoli**: None; **J. Albayda**: None; **L. Christopher-Stine**: Amgen, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Octapharma, 1, 5, Pfizer, 5, Priovant, 1.

Abstract Number: 2064

Kinematics Underlying IBM-induced Dysphagia

Kevin Renz Ambrocio[1], Vaidehi Kothari[1], Rohit Aggarwal[2], Anna Miles[3], James L. Coyle[1], Eaman Alhassan[4], Sandra Stinnett[1], David Lacomis[1], Lea Sayce[1] and Kendrea (Focht) Garand[1], [1]University of Pittsburgh, Pittsburgh, PA, [2]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA, [3]The University of Auckland, Auckland, New Zealand, [4]University of Pittsburgh Medical Center, Pittsburgh, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Dysphagia remains a key contributor to mortality in IBM due to its connection with aspiration pneumonia and malnutrition (Shelly et al., 2021). Compared to other IIMs, IBM increases the odds of acquiring aspiration pneumonia and non-oral means of nutrition 3-fold (Ma et al., 2023). Yet, dysphagia kinematics in IBM are ill-defined, possibly leading to under-detection, misdiagnosis, and inappropriate dysphagia treatment (Ambrocio et al., 2023). Our study aimed to profile the kinematics underlying dysphagia in IBM using standardized and validated assessment methods and identify clinical predictors of dysphagia severity.

Methods: We conducted a prospective, cross-sectional study involving 15 adults with IBM (9 males) suspected of dysphagia. They had a mean age of 72.7 years (*SD*=5.9) and met the European Neuromuscular Center diagnostic criteria (Lilleker et al., 2024) and ACR classification (Lundberg et al., 2017). Their mean IBM Functional Rating Scale (IBMFRS) score and disease duration were 26.9 (*SD*=5.5) and 8.5 years (*SD*=3.8), respectively. Participants underwent a modified barium swallow study following the Modified Barium Swallow Impairment Profile (MBSImP) protocol, including 12 bolus tasks ranging from thin to highly thick liquids and a solid (Martin-Harris et al., 2008). We analyzed the images using MBSImP ratings, yielding Overall Impression (OI), Oral Total (OT), and Pharyngeal Total (PT) scores across 17 oral, pharyngeal, and esophageal kinematic components. We compared participants' OI, OT, and PT scores with data from age- and sex-matched healthy controls in a normative database (Garand et al., 2022). Mann-Whitney U tests compared OI, OT, and PT scores between groups. We analyzed dysphagia severity using the Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) (Hutcheson et al., 2022). Univariate ordinal logistic regressions estimated the impact of OT and PT scores, age, sex, IBMFRS scores, and disease duration on DIGEST grades.

Results: Compared to controls, the IBM group had significantly higher (worse) OI scores for tongue motion, soft palate elevation, pharyngeal stripping, pharyngoesophageal segment opening, pharyngeal residue, and esophageal clearance, each $p < .05$, with large effects ranging from r=.51-.91 (Table 1). The IBM group had significantly higher (worse) OT (p=.001, r=.62) and PT (p=.013, r=.50) scores than controls, with large effects (Table 2). One participant had a normal DIGEST grade,

Table 1. MBSImP OI Score Summary Between IBM and Healthy Control Groups

Domain	Component	Control Group Score Median (IQR)	IBM Group Score Median (IQR)	*p* value	Effect size (r)
Oral	Lip closure	1 (0)	0 (0)	<.001 (rendered null as scores of 0-1 for this component are normal variants)	-.83
	Tongue control during bolus hold	0 (1)	0 (2)	.30	.22
	Mastication	0 (0)	0 (0)	.74	.12
	Tongue motion	0 (0)	2 (0)	<.001*	.91
	Oral residue	2 (1)	2 (0)	.061	.45
	Pharyngeal swallow initiation	2 (2)	3 (1)	.18	.29
Pharyngeal	Soft palate elevation	0 (0)	1 (1)	.007*	.59
	Laryngeal elevation	1 (1)	1 (1)	.60	.15
	Anterior hyoid excursion	1 (0)	1 (2)	.62	.14
	Epiglottic movement	0 (0)	1 (1)	.12	.36
	Laryngeal vestibular closure	0 (1)	1 (1)	.17	.32
	Pharyngeal stripping	1 (1); Rank sum=152	1 (1); Rank sum=313	.001*	.67
	Pharyngeal contraction	0 (0)	2 (2)	.068	.39
	Pharyngoesophageal segment opening	1 (0); Rank sum=179	1 (1); Rank sum=287	.015*	.53
	Tongue base retraction	2 (1)	2 (0)	.28	.25
	Pharyngeal residue	2 (0); Rank sum=178	2 (1); Rank sum=290	.020*	.51
Esophageal	Esophageal clearance	0 (1)	2 (1)	.006*	.56

n=30 for all tests. * denotes significant values. Higher median scores or rank sum imply worse scores.

Table 2. MBSImP OT and PT Score Summary Between IBM and Healthy Control Groups

Domain		Control Group Score	IBM Group Score	Mean Difference	*p* value	Effect size (*r*)
OT	*M* (*SD*)	5.13 (1.51)	7.8 (2.34)	2.67	.001*	.62
	95% CI	4.30–5.97	6.51–9.09			
	Min, max	2, 8	5, 13			
PT	*M* (*SD*)	7.53 (1.96)	12.73 (5.27)	5.20	.013*	.50
	95% CI	6.45–8.62	9.81–15.65			
	Min, max	5, 11	6, 20			

n=30 for all tests. * denotes significant values. Higher scores imply worse scores.

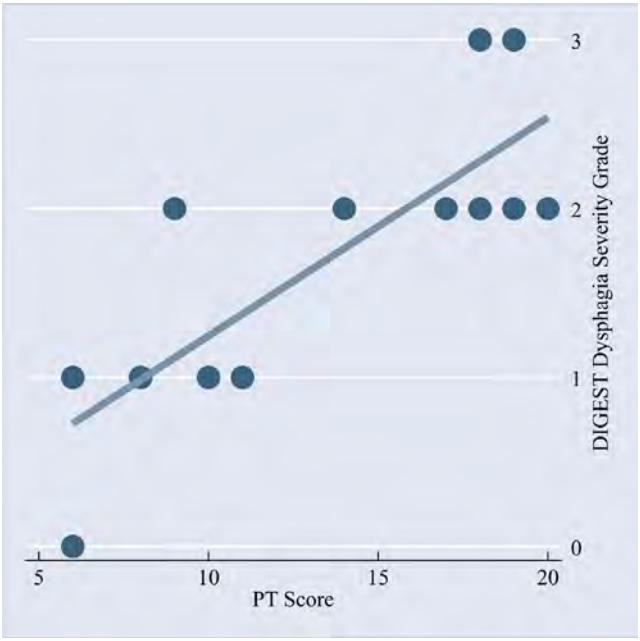


Figure 1. DIGEST Dysphagia Severity Grade Regression. The scatter plot shows the interaction between each participant's PT score and DIGEST dysphagia severity grade, while the line represents the overall trend of the fitted regression model. This trend illustrates that higher (worse) PT scores are generally associated with higher (worse) DIGEST dysphagia severity grades. DIGEST severity grade interpretation: 0=normal, 1=mild, 2=moderate, 3=severe.

but the rest spanned from mild to severe dysphagia. Only PT scores predicted DIGEST grades, with higher PT scores significantly linked to greater dysphagia severity, p=.031, OR=2.16 (Figure 1).

Conclusion: Participants with IBM exhibited kinematic deficits across swallowing phases. Surrogate kinematic markers for pressure generation and bolus propulsion mechanics were most impaired, which may be valuable for predicting dysphagia severity in IBM. Our study demonstrates the use of robust swallowing metrics to quantify and obtain a nuanced phenotypic dysphagia profile for IBM, representing an improvement over prior studies. Such findings facilitate targeted dysphagia treatment, precise symptom monitoring, and early identification of people with IBM at risk of dysphagia.

Disclosure: K. Ambrocio: None; **V. Kothari**: None; **R. Aggarwal**: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2; **A. Miles**: None; **J. Coyle**: None; **E. Alhassan**: None; **S. Stinnett**: None; **D. Lacomis**: UpToDate, 9; **L. Sayce**: None; **K. (Focht) Garand**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2065

Pain in Idiopathic Inflammatory Myopathies: A Global Study of Patient Experience

Lekshmi Minikumari Rahulan[1], Shounak Ghosh[2], Manali Sarkar[3], Didem Saygin[4], Karin Lodin[5], Rima Shrestha[6], Tulika Chatterjee[7], Jessica Day[8], Samuel Shinjo[9], Sreoshy Saha[10], Lorenzo Cavagna[11], Masataka Kuwana[12], Vikas Agarwal[13], Latika Gupta[14] and COVAD study group, [1]Sanjay Gandhi Postgraduate Institute of Medical sciences Lucknow, Lucknow, Uttar Pradesh, India, [2]Department of Rheumatology, The Royal Wolverhampton NHS Trust, Wolverhampton, UK, Wolverhampton, United Kingdom, [3]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India., Mumbai, Maharashtra, India, [4]Rush University Medical Center, Chicago, IL, [5]Department of Gastro, Dermatology and Rheumatology, Karolinska University Hospital, Stockholm, Sweden, Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden, Stockholm, Sweden, [6]Department of Internal Medicine, University of Illinois College of Medicine Peoria, Illinois, United States, Department of Research Services, University of Illinois College of Medicine Peoria, Illinois, United States, Illinois, [7]Department of Internal Medicine, University of Illinois College of Medicine Peoria, Illinois, United States, Illinois, [8]Walter and Eliza Hall Institute, Melbourne, Victoria, Australia, [9]Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [10]Mymensingh Medical College, Mymensingh, Bangladesh, Mymensingh, Bangladesh, [11]Associate Professor in Rheumatology (Internal Medicine and Thepaeutics),University of Pavia, Pavia, Lombardy, Italy, Physician in Chief of Myositis Outpatients Clinic,Fondazione IRCCS Policlinico San Matteo, Pavia, Lombardia,Italy, Lombardia, Italy, [12]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [13]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [14]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Pain remains a significant yet understudied aspect of idiopathic inflammatory myopathies (IIMs), considerably reducing quality of life despite advancements in immunomodulatory therapies. Information obtained from self-reported patients' lived experiences would underscore the crucial information in improving their life quality.

Methods: We analyzed self-reported pain data within a global IIMs dataset that represent 103 countries [1]. This study used patient-experience pain visual analogue scale (VAS) with scores ranging from 0-10 and stratified the participants into mild (VAS ≤3) and moderate-severe (VAS >3) pain groups [2,3]. Socio-demographic characteristics, disease construct (type of IIM, treatment, comorbidities), and psychological construct (mental health comorbidities) were compared between groups-IIMs, RMDs, nRAIDs, and HCs. Basic multimorbidity (BM) was defined as the presence of two or more non-autoimmune comorbidities, while complex multimorbidity (CM) was defined as the presence of three or more such conditions affecting three or more different body systems. Descriptive statistics were calculated; appropriate parametric and non-parametric tests were used for comparison between groups and multivariable logistic regression was used to determine the predictors of moderate-severe pain (R studio version 2024.12.1).

Results: Among 7,847 respondents (4,709 disease controls), 1,045 (13.3%) had IIM: dermatomyositis (26.1%), overlap myositis (OM, 24.3%), inclusion body myositis (IBM, 23.4%), polymyositis (PM, 13.4%), anti-synthetase syndrome (ASyS, 6.8%), and necrotizing myopathies (IMNM, 5.6%) (Figure 1). IIMs exhibited higher pain intensity (median VAS 3.0, 1.0-5.0) than nRAIDs (1.0, 0.0-4.0) and HCs (0.0, 0.0-2.0), $p< 0.01$, but lower than rheumatoid arthritis (4.0, 2.0-6.0), psoriatic arthritis (4.0, 2.0-7.0), and Sjögren's disease (4.0, 2.0-7.0), $p< 0.01$. (Figure 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Characteristics	IIM			RMD (n=3261)	nRAID (n=400)	Healthy controls (n=3138)	Total (n=7847)
	Total IIM (n=1045)	Pain ≤ 3 (n=598)	Pain >3 (n=447)				
Age (years)	58.6±14.3	60.3±14.1	56.4±14.7	48.4±14.4	45.3±14.7	39.9±13.5	46.2±15.3
Female (%)	766 (73.3)	418 (69.9)	348 (77.8)	2783 (85.3)	341 (85.2)	1917 (61.1)	5807 (74.0)
Pain VAS >3 (%)	447 (42.7)	-	447 (100)	1747 (53.6)	112 (28.0)	480 (15.3)	2786 (35.5)
Ethnicity							
Caucasian	808 (77.3)	479 (80.1)	329 (73.6)	1637 (50.2)	226 (56.5)	923 (29.5)	3594 (45.8)
African/African American	55 (5.3)	19 (3.2)	36 (8.1)	231 (7.1)	11 (2.8)	97 (3.1)	394 (5.0)
Hispanic	48 (4.6)	20 (3.3)	28 (6.2)	418 (12.8)	83 (20.8)	898 (28.6)	1447 (18.4)
Asian	91 (8.7)	57 (9.5)	34 (7.6)	555 (17)	48 (12.0)	741 (23.6)	1435 (18.3)
Country of origin							
Low HDI	3 (0.3)	2 (0.3)	1 (0.2)	74 (2.3)	4 (1.0)	119 (3.8)	200 (2.5)
Medium HDI	15 (1.4)	7 (1.1)	5 (1.1)	383 (11.7)	49 (12.2)	799 (25.5)	1246 (15.9)
High HDI	42 (4.0)	15 (2.5)	27 (6.0)	655 (20.1)	96 (24.0)	1181(37.6)	1974 (25.2)
Very high HDI	975 (93.3)	429 (71.7)	404 (90.4)	2094 (64.2)	244 (61)	974 (31)	4287 (54.6)
Myositis subtype							
Dermatomyositis	273 (26.1)	169 (28.3)	104 (23.3)	-	-	-	273 (3.5)
Polymyositis	140 (13.4)	78 (13.0)	62 (13.9)	-	-	-	140 (1.8)
Anti-synthetase syndrome	71 (6.8)	44 (7.4)	27 (6.0)	-	-	-	71 (0.9)
Necrotizing myopathies	58 (5.6)	36 (6.0)	22 (4.9)	-	-	-	58 (0.7)
Inclusion body myositis	245 (23.4)	169 (28.3)	76 (17.0)	-	-	-	245 (3.1)
Overlap myositis	254 (24.3)	101 (16.9)	153 (34.2)	-	-	-	254 (3.2)
Medications							
Current steroids	406 (38.9)	208 (34.8)	163 (36.5)	1043 (32)	30 (7.5)	21 (0.7)	1500 (19.1)
Hydroxychloroquine	163 (15.6)	68 (11.4)	95 (21.2)	984 (30.2)	16 (4.0)	4 (0.1)	1167 (14.9)
Methotrexate	209 (20.0)	110 (18.4)	99 (22.1)	1004 (30.8)	10 (2.5)	6 (0.2)	1229 (15.7)
Mycophenolate	194 (18.6)	114 (19.1)	80 (17.9)	250 (7.7)	8 (2.0)	7 (0.2)	459 (5.8)
Azathioprine	94 (9.0)	45 (7.5)	49 (10.9)	216 (6.6)	8 (2.0)	4 (0.1)	322 (4.1)
IVIG/SCIG	147 (14.1)	78 (13.0)	69 (15.4)	16 (0.5)	5 (1.2)	2 (0.1)	170 (2.2)
Tacrolimus	22 (2.1)	12 (2.0)	10 (2.2)	20 (0.6)	0	4 (0.1)	46 (0.6)
Cyclophosphamide	12 (1.1)	6 (1.0)	6 (1.3)	29 (0.9)	1 (0.2)	3 (0.1)	45 (0.6)
Rituximab	118 (11.3)	61 (10.2)	57 (12.8)	142 (4.4)	5 (1.2)	4 (0.1)	269 (3.4)
JAK inhibitors	12 (1.1)	6 (1.0)	6 (1.3)	67 (2.1)	0	0	79 (1.0)
Comorbidities							
Diabetes mellitus	130 (12.4)	75 (12.5)	55 (12.3)	170 (5.2)	62 (15.5)	128 (4.1)	490 (6.2)
Hypertension	344 (32.9)	184 (30.8)	160 (35.8)	628 (19.3)	57 (14.2)	301 (9.6)	1330 (16.9)
Heart disease	80 (7.7)	47 (7.9)	33 (7.4)	82 (2.5)	4 (1.0)	29 (0.9)	195 (2.5)
Dyslipidemia	262 (25.1)	150 (25.1)	112 (25.1)	405 (12.4)	54 (13.5)	213 (6.8)	934 (11.9)
ILD	202 (19.3)	118 (19.7)	84 (18.8)	116 (3.6)	9 (2.2)	3 (0.1)	330 (4.2)
Others	128 (12.2)	56 (9.3)	72 (16.1)	302 (9.3)	17 (4.2)	63 (2.0)	510 (6.5)
Mental health comorbidities							
Depression	221 (21.1)	94 (15.7)	127 (28.4)	531 (16.3)	60 (15.0)	263 (8.4)	1075 (13.7)
Anxiety	238 (22.8)	102 (17.1)	136 (30.4)	621 (19)	68 (17.0)	388 (12.4)	1315 (16.8)
Insomnia	102 (9.8)	26 (4.3)	13 (2.9)	251 (7.7)	29 (7.2)	84 (2.7)	466 (5.9)
Others	38 (3.6)	13 (2.2)	25 (5.6)	109 (3.3)	23 (5.8)	64 (2.0)	234 (3.0)

Figure 1: Table showing patient characteristics Continuous variables described as mean ± standard deviation, or categories as number (%). Other comorbidities: chronic liver disease, chronic kidney disease, COPD, and stroke. Other mental health comorbidities: bipolar disorder, eating disorders, schizophrenia, attention deficit hyperactivity disorder, post- traumatic stress disorder, and substance use disorder.

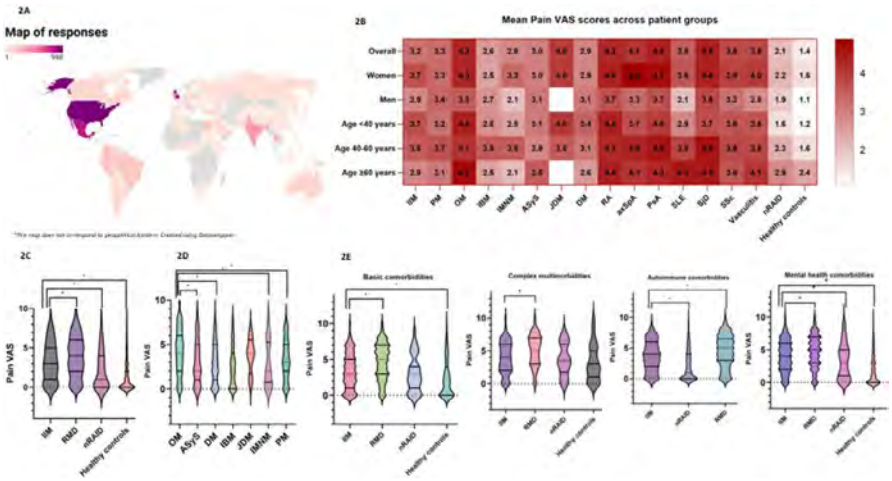


Figure 2. 2A: Map showing participant responses across the world . 2B: Heat map showing pain intensity among different RMDs , IIM subtypes , nRAIDs and healthy controls, stratified by age groups and gender. 2C: Violin plot showing pain intensity across different participant groups. 2D: Violin plot showing pain intensity in different IIM subtypes. 2E: Violin plots showing pain intensity in different patient groups with associated comorbidities. *denotes p<0.05

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

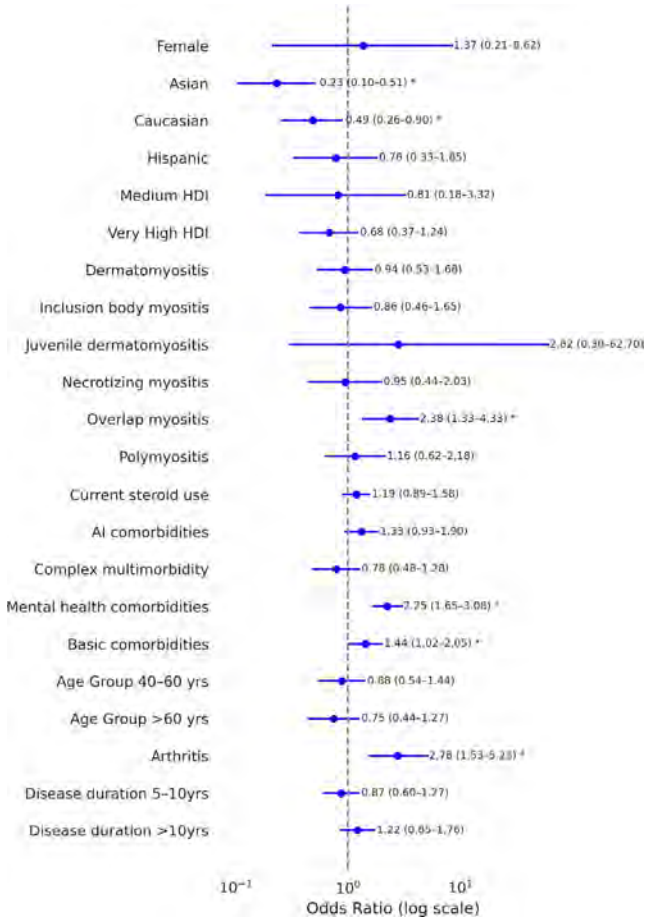


Figure 3: Forest plot showing predictors of moderate to severe pain (Pain VAS>3) in patients with IIM. *denotes p<0.05.

Overlap myositis had the highest pain levels (4.0, 2.0-6.0), while inclusion body myositis had the lowest (2.0, 0.0-4.0). Middle-aged patients (40-60 years) reported more pain than older groups. Pain primarily affected large joints (43%) and leg muscles (36.5%).

Female IIM patients reported higher pain scores than males (3.0, 1.0-5.0 vs. 2.0, 1.0-5.0). Moderate-severe pain (reported by 42.7%) was significantly associated with higher fatigue, worse physical function, and poorer quality of life across all domains (p< 0.001).

Significant predictors of moderate-severe pain included: overlap myositis (odds ratio, OR=2.38), arthritis (OR=2.78), mental health comorbidities (OR=2.25), and basic comorbidities (OR=1.44). Asian (OR=0.23) and Caucasian (OR=0.49) patients had lower odds of severe pain (Figure 3).

Conclusion: Pain represents a substantial burden in IIMs, particularly in overlap myositis. The bimodal distribution in IIM suggests heterogeneous pain mechanisms. Strong associations between pain intensity and reduced quality of life highlight the importance of comprehensive pain management. Multi-faceted interventions addressing identified predictors could significantly improve outcomes in this challenging disease group.

Disclosure: L. Minikumari Rahulan: None; **S. Ghosh**: None; **M. Sarkar**: None; **D. Saygin**: None; **K. Lodin**: None; **R. Shrestha**: None; **T. Chatterjee**: None; **J. Day**: CSL Limited, 5; **S. Shinjo**: None; **S. Saha**: None; **L. Cavagna**: None; **M. Kuwana**: AbbVie, 2, Asahi Kasei Pharma, 6, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, 6, Chugai, 2, 6, GlaxoSmithKlein(GSK), 2, Medical and Biological Laboratories, 5, 9, Mochida, 2, Novartis, 2, Ono Pharmaceuticals, 6; **V. Agarwal**: None; **L. Gupta**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2066

Psychosocial Factors Strongly Influence Subjective Well-being in Patients with Idiopathic Inflammatory Myopathies

Meera Shah[1], Emilia Naseva[2], Tsvetelina Velikova[3], Tamar Rubinstein[4], Manali Sarkar[5], Lavanya Mangla[6], Oliver Distler[7], Ingrid de Groot[8], Lisa Christ[9], Carlo Vinicio Caballero Uribe[10], Ai Lyn Tan[11], Abraham Edgar Gracia Ramos[12], Vincenzo Venerito[13], Vikas Agarwal[14], Latika Gupta[15] and COVAD study group, [1]Indraprastha Apollo Hospital, New Delhi, Mumbai, Maharashtra, India, [2]Faculty of Public Health, Medical University of Sofia, 15 Acad. Ivan Evstratiev Geshov, 1606 Sofia; Medical Faculty, Sofia University St. Kliment Ohridski, Sofia, Bulgaria, [3]Medical Faculty, Sofia University St. Kliment Ohridski, Sofia, Bulgaria, [4]Albert Einstein College of Medicine, White Plains, NY, [5]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India., Mumbai, Maharashtra, India, [6]Maulana Azad Medical College, 2-Bahadurshah Zafar Marg, New Delhi, New Delhi, India, [7]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [8]The Myositis Association, Rotterdam, Netherlands, [9]Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland., Bern, Switzerland, [10]Department of Medicine, Hospital Universidad del Norte, Barranquilla, Atlantico, Colombi, Barranquilla, Colombia, [11]NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds; Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, England, United Kingdom, [12]Department of Internal Medicine, General Hospital, National Medical Center "La Raza", Instituto Mexicano del Seguro Social, Av. Jacaranda S/N, Col. La Raza, Del. Azcapotzalco, C.P. 02990 Mexico City, Mexico., Mexico City, Mexico, [13]Univeristy of Bari \"Aldo Moro\", Italy, Bari, Bari, Italy, [14]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [15]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Traditional clinical measures are well established in idiopathic inflammatory myopathies (IIM), yet exploration of subjective well-being (SWB) remains limited. SWB assessment facilitates holistic patient care and development of targeted interventions. The Satisfaction with Life Scale (SWLS), a validated tool, evaluates the cognitive aspect of well-being, offering valuable insight into patient experience. This study aimed to identify factors associated with SWB in IIM.

Methods: Patient-reported data were collected from a cross-sectional global "Collating the voice of people living with autoimmune diseases" survey covering 111 countries. SWB was assessed using SWLS, categorized as "extremely dissatisfied" (score 5-9) to "extremely satisfied" (score 30-35). We assessed socio-demographic characteristics, disease constructs and psychological constructs [Fig. 1A]. Multivariable regression analysis was performed with SWLS as the dependent variable. Cluster analysis performed using K-means algorithm after proper standardization.

Results: Data from 11,849 participants (IIM=1,252, oRMDs (Other rheumatic and musculoskeletal diseases)=6,653, nrAIDs (non-rheumatic autoimmune diseases)=997, non-autoimmune chronic diseases (CD)=973, healthy population (HC)=1,974) revealed significant differences [Fig.1B] [Table 1] . After adjusting for age, gender, income and education, SWLS scores were lowest in IIM with a median of 17 [Fig 1C,1D] with no significant differences between IIM subtypes.

In multivariable regression, psychological (self-efficacy β=0.15, $p < 0.001$, better mental health β=1.93, $p < 0.001$), and social factors (job satisfaction β=0.50, $p < 0.001$, and family functioning β=0.80, $p < 0.001$) were the strongest positive predictors of SWB. Disease-related factors like damage (β= -0.60, $p < 0.001$), fatigue (β= -0.48, $p = 0.003$), pain (β= -0.45, $p = 0.001$), and depression/anxiety (β= -1.83, $p < 0.05$) were negatively associated. Lower income (β=-3.4 to -8.8, $p < 0.001$) and loneliness (β=-0.99, $p < 0.001$) also predicted lower SWB [Fig. 2A]. Age, disease activity and duration, and comorbidities were not significant in fully adjusted models.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

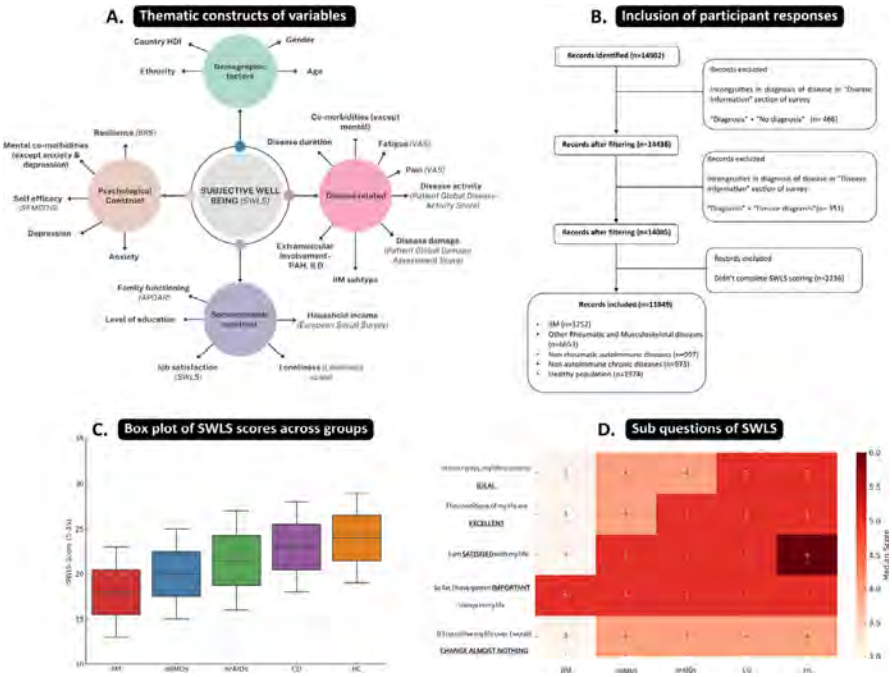


Fig 1: A- Thematic constructs of variables of interest; B- Flowchart depicting inclusion of participant responses; C- Box plot of Satisfaction with life scale (SWLS) score across groups; D- Heat map demonstrating scores for sub questions of SWLS across various groups.

K-means clustering of 851 individuals with myositis identified three distinct SWB profiles: high (24%), moderate (49%), and low (27%). High SWB was associated with better mental health, self-efficacy, and family functioning, alongside lower fatigue, pain, and loneliness, whereas the low SWB cluster exhibited significantly worse scores across these domains [Fig.2B]. Subtype-specific patterns emerged: anti-synthetase syndrome (ASyS) predominantly clustered in moderate SWB,

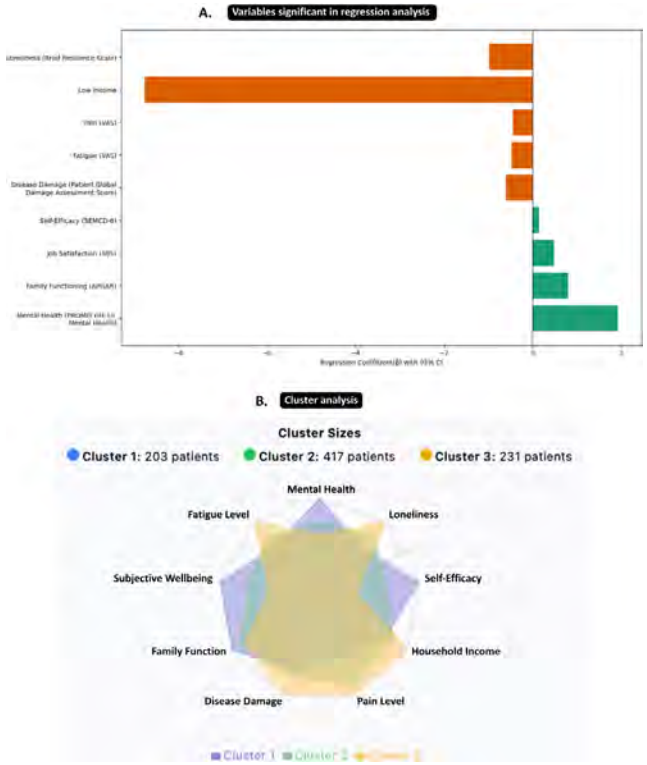


Fig.2: A- Forest plot of variables statistically significant in regression analysis for SWB; B- Radar chart showing various clusters with characteristics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline descriptive data across groups

Table 1: Baseline descriptive data

Characteristics	IIM (n=1252)	oRMD (n = 6653)	nrAID (n = 997)	CD* (n = 973)	HC** (n = 1974)	p-value (IIM vs oRMD)	p-value (IIM vs nrAID)	p-value (IIM vs CD)	p-value (IIM vs HC)
Age (years), median (IQR)	59 (47, 70)	50 (40, 60)	42 (33, 54)	42 (32, 53)	33 (28, 42)	<0.0001	<0.0001	<0.0001	<0.0001
Gender, n (%)						<0.001	<0.001	<0.001	<0.001
Female	740 (69%)	4394 (63%)	671 (81%)	506 (56%)	727 (40%)				
Male	323 (30%)	1323 (23%)	148 (19%)	380 (42%)	1058 (59%)				
Non-binary or transgender	4 (0.4%)	40 (0.7%)	5 (0.6%)	15 (1.7%)	19 (1%)				
Race/Ethnicity, n (%)						<0.001	<0.001	<0.001	<0.001
Caucasian	753 (70%)	2623 (48%)	491 (64%)	303 (36%)	323 (20%)				
Asian	181 (17%)	1348 (25%)	103 (13%)	267 (32%)	837 (52%)				
African	8 (0.8%)	243 (4.5%)	11 (1.4%)	28 (3.3%)	46 (2.9%)				
Arab	12 (1.3%)	191 (3.5%)	6 (0.8%)	36 (4.3%)	68 (4.3%)				
Hispanic	12 (1.3%)	416 (7.6%)	57 (7.4%)	99 (12%)	140 (8.8%)				
Mixed	27 (2.8%)	221 (4%)	34 (4.4%)	53 (6.3%)	80 (5%)				
Others	35 (3.6%)	416 (7.6%)	65 (8.5%)	59 (7%)	103 (6.5%)				
HDI of country of current residence, n (%)						<0.001	<0.001	<0.001	<0.001
Very high	780 (82%)	3414 (60%)	557 (69%)	345 (38%)	484 (27%)				
High	42 (4.4%)	896 (16%)	159 (20%)	196 (22%)	287 (16%)				
Medium	118 (12.5%)	1138 (20%)	86 (11%)	307 (34%)	907 (51%)				
Low	6 (0.6%)	250 (4.4%)	10 (1.2%)	49 (5%)	115 (6%)				
Level of education, n (%)						0.13	<0.001	<0.001	<0.001
Graduate	234 (26%)	1399 (27%)	315 (39%)	341 (40%)	658 (40%)				
Income categories						<0.001	<0.001	<0.001	<0.001
"Living comfortably"	501 (53%)	2583 (46%)	333 (41%)	381 (44%)	887 (51%)				
"Getting by"	298 (32%)	1909 (34%)	320 (40%)	307 (35%)	466 (27%)				
"Finding it difficult"	95 (10%)	786 (14%)	116 (14%)	125 (14%)	286 (16%)				
"Finding it very difficult"	48 (5%)	349 (6.2%)	34 (4%)	61 (7%)	100 (6%)				
Comorbidities***									
Simple	935 (88%)	6537 (78%)	890 (73%)	561 (55%)	93 (3.7%)	<0.001	<0.001	<0.001	<0.001
Basic	739 (70%)	4451 (53%)	872 (72%)	548 (54%)	64 (2.5%)	<0.001	0.3	<0.001	<0.001
Autoimmune	300 (28%)	1556 (18%)	89 (7.3%)	---	---	<0.001	<0.001	---	---
Psychiatric	448 (42%)	2736 (39%)	484 (45%)	402 (40%)	195 (10%)	0.06	0.2	0.2	<0.001
Complex	445 (42%)	1918 (23%)	267 (22%)	157 (15%)	---	<0.001	<0.001	<0.001	---
Disease duration, (years)Median, IQR	8 (3, 16)	10 (4, 19)	9 (4,18)	7 (1, 21)	---	<0.0001	0.008	0.3	---

IIM= Idiopathic inflammatory myopathies; oRMD- other rheumatic and musculoskeletal disease; nRAID: non-rheumatic autoimmune disease; CD: non autoimmune chronic disease; HC: healthy controls
* CD: Non autoimmune chronic disease
**HC: psychiatric conditions were not excluded
***Comorbidity definitions. Simple (>1 diagnosis); Basic (addition of ≥1 non-rheumatic diagnosis); Psychiatric (≥1 psychiatric diagnosis); Complex (comorbidities across ≥ 3 body systems)

polymyositis (PM) in low SWB, and inclusion body myositis (IBM) in both high and low SWB clusters, underscoring heterogeneous psychosocial burden across IIM subtypes.

Conclusion: Our findings show that SWB in IIM is shaped more by psychosocial than clinical factors. Low median SWLS scores highlight the impact of IIM on life satisfaction. Despite similar disease profiles, distinct well-being clusters reveal underlying psychosocial burdens advocating for integrating holistic and person-centered care into rheumatology practice to enhance quality of life.

Disclosure: M. Shah: None; **E. Naseva**: None; **T. Velikova**: None; **T. Rubinstein**: None; **M. Sarkar**: None; **L. Mangla**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **I. de Groot**: None; **L. Christ**: Bristol-Myers Squibb(BMS), 6, Gebauer Foundation Switzerland, 5, Gilead, 5, 11, Novartis, 1, 6, 11, Pfizer, 5, Roche, 5, 11, sanofi, 12, Congress support, Swiss Foundation for Research on Muscle Diseases, 5, Vifor, 6; **C. Uribe**: None; **A. Tan**: UCB, 6; **A. Ramos**: None; **V. Venerito**: None; **V. Agarwal**: None; **L. Gupta**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2067

Patterns of Comorbidity in Idiopathic Inflammatory Myopathies: A Cross-sectional Analysis of Disease Burden and Risk Factors

Ilke Coskun Benlidayi[1], Meghna Lama[2], Oladipo Kunle Afolayan[2], **Meera Shah**[3], Manali Sarkar[4], Tamar Rubinstein[5], Aleksandra Opinc-Rosiak[6], Rada Miskovic[7], Marcin Milchert[8], Dimitri Luz Felipe da Silva[9], Samuel Katsuyuki Shinjo[10], Elena Nikiphorou[11], Ioannis Parodis[12], Vincenzo Venerito[13], Vikas Agarwal[14], Latika Gupta[15] and COVAD Study Group, [1]Cukurova University, Adana, Turkey, [2]The University of Texas Health Science Centre at Houston School of Public Health: Houston, Texas, Houston, [3]Indraprastha Apollo Hospital, New Delhi, Mumbai, Maharashtra, India, [4]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India., Mumbai, Maharashtra, India, [5]Albert Einstein College of Medicine, White Plains, NY, [6]Medical University of Lodz, Zeromskiego 113, 90-549 Lodz, Poland., Lodz, Poland, [7]University of Belgrade; Clinic of Allergy and Immunology, University Clinical Centre of Serbia, Belgrade, Serbia, [8]Pomeranian Medical University in Szczecin, Szczecin, Poland, [9]University Santo Amaro, São Paulo, Brazil, Sao Paulo, Brazil, [10]Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [11]King's College London, London, United Kingdom, [12]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [13]Univeristy of Bari \"Aldo Moro\", Italy, Bari, Bari, Italy, [14]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [15]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Comorbidities contribute to the disease burden in idiopathic inflammatory myopathies (IIMs). Understanding their distribution and predictors across IIM subtypes can guide tailored strategies. This study aimed to evaluate the patterns of comorbidities across IIM subsets, identify predictors of physical and mental comorbidities, and characterize comorbidity clusters.

Methods: This cross-sectional study used data from the Collating the Voices of Patients with Autoimmune Diseases study. Adults with specialist-diagnosed, self-reported IIMs were included. The validated Functional Comorbidities Index (FCI) was used to collect information on comorbidities. Subgroup comparisons were conducted across IIM subtypes. Descriptive statistics were performed and binary logistic regression was used to identify predictors of mental and physical health comorbidities. Hierarchical cluster analysis was applied to derive composite comorbidity clusters using R.

Results: Of 14,902 respondents, 1,209 IIM patients (69.6% female) were included [Fig.1A, 1B], with a median age and disease duration of 60 and 17 years, respectively (Table 1). The most common comorbidities were mental health conditions (32.1%), cardiovascular diseases (32.0%), and musculoskeletal disorders (23.3%). Mental (41.4%) and musculoskeletal (45.2%) comorbidities were most common in overlap myositis (OM). Cardiovascular conditions were most common in inclusion body myositis (IBM) (45.2%) [Fig.1C]. Predictors of mental health comorbidities included older age (OR:0.98; 95% CI=0.96-0.99), high Human Development Index (HDI) (OR:4.35; 95%CI=1.72-1.75), and alcohol intake (2-4 times/month) (OR:0.44; 95%CI=0.24-0.79).

Predictors of physical health comorbidities were older age (OR:1.05; 95%CI=1.02-1.07), high HDI (OR:5.32; 95% CI=1.26-22.39), alcohol intake (2-4 times/month) (OR:0.45; 95%CI=0.23-0.90), and disease damage (OR:1.13; 95% CI=1.01-1.26). Hierarchical cluster analysis identified 3 comorbidity clusters. Cluster 1 was characterized by Hispanic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

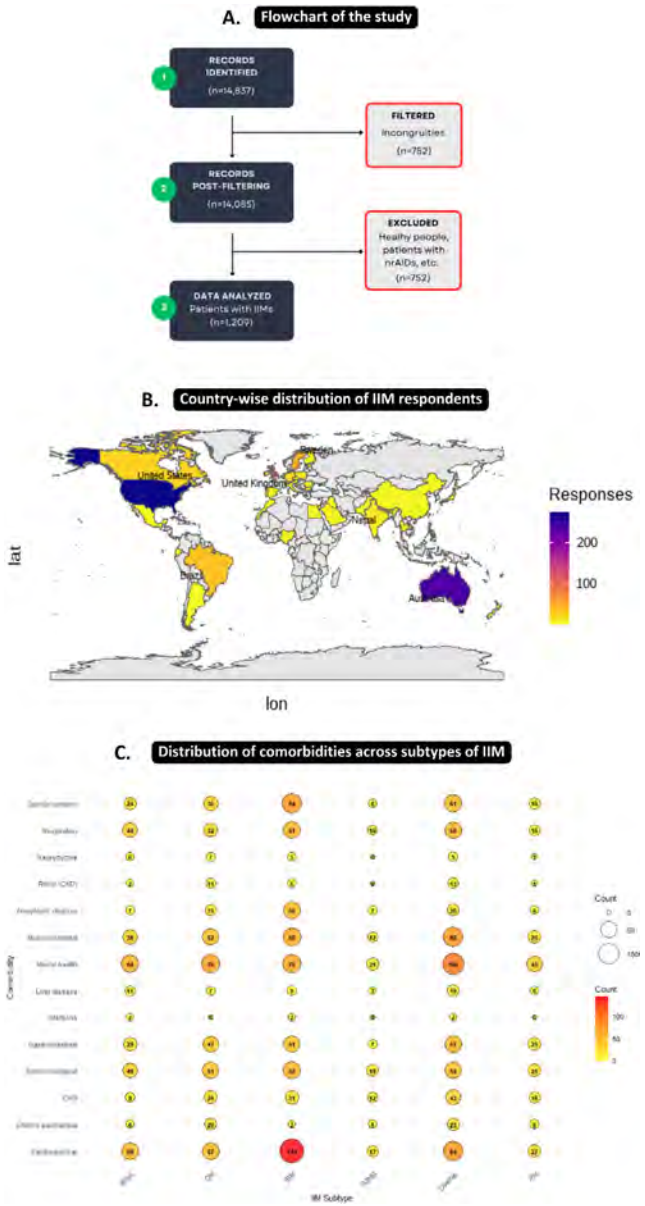


Fig.1: A- Flowchart depicting inclusion of participants; B- World map showing country-wise distribution of IIM respondents; C- Distribution of comorbidities across IIM subtypes

ethnicity, lower HDI, and low multimorbidity, with notable immune-mediated necrotizing myopathies representation but limited variance. Cluster 2 was male-dominated, had very high HDI and moderate mental and physical comorbidity levels, and included the highest proportion of IBM and polymyositis. Cluster 3 showed the highest multimorbidity burden, dominated by dermatomyositis and anti-synthetase syndrome.

Conclusion: Comorbidities vary across IIM subtypes. Older age and high HDI predict both mental and physical health comorbidities, while higher disease damage predicts physical health comorbidity. Comorbidity clusters reveal distinct IIM subtype distributions, highlighting subtype-specific comorbidity patterns that may guide personalized clinical management.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

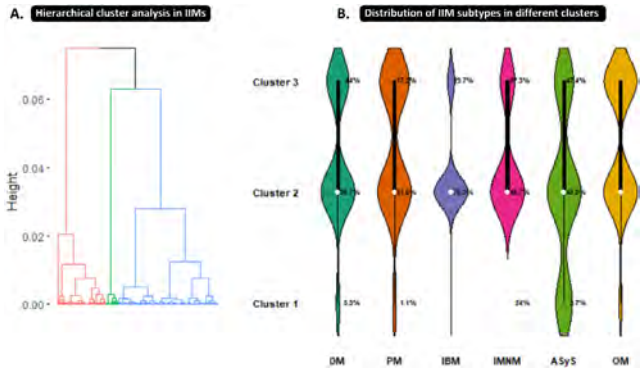


Fig.2: A- Hierarchical cluster analysis in IIMs; B- Distribution of IIM subtypes in different clusters

Table 1: Characteristics of study sample

Table 1. Characteristics of the study sample

Variables	Total (n= 1209)	PM (n=116)	DM (n= 203)	IBM (n= 318)	IMNM (n= 63)	ASyS (n= 253)	Overlap myositis (n= 256)	P-value
Demographic variables								
Age, median (IQR), years	60 (22)	57.5 (20)	54.5 (19)	72 (11)	59 (18)	50 (21.5)	50 (21.5)	<0.001*
Gender, n (%)								
Male	315 (30.45)	14 (15.3)	26 (15.12)	153 (54.45)	9 (16.98)	83 (36.09)	30 (14.42)	<0.001*
Female	720 (69.57)	77 (84.62)	146 (84.88)	128 (45.55)	44 (83.02)	147 (63.91)	178 (85.58)	
Ethnicity, n (%)								
a. African	13 (1.08)	2 (1.72)	0 (0.00)	1 (0.31)	0 (0.00)	3 (1.19)	7 (2.73)	<0.001*
b. Asian	175 (14.47)	13 (11.21)	23 (11.33)	2 (0.63)	3 (4.76)	95 (37.55)	39 (15.23)	
c. Hispanic	13 (1.08)	2 (1.72)	2 (0.99)	3 (0.94)	2 (3.14)	1 (0.40)	3 (1.17)	
d. Caucasian (White)	734 (60.71)	55 (47.41)	135 (68.50)	257 (80.82)	37 (58.73)	117 (46.25)	133 (51.95)	
e. Mixed	28 (2.32)	5 (4.31)	6 (2.95)	7 (2.20)	4 (6.35)	3 (1.19)	3 (1.17)	
f. Others	246 (20.35)	39 (33.62)	37 (18.23)	48 (14.09)	17 (26.98)	34 (13.44)	71 (27.73)	
Socioeconomic variables								
HDI of country of current residence, n (%)								
a. Very high	835 (81.78)	69 (83.13)	149 (86.63)	277 (98.93)	44 (84.6)	128 (55.17)	168 (83.17)	<0.001*
b. High	51 (5.00)	8 (9.64)	10 (5.81)	2 (0.71)	7 (13.46)	12 (5.12)	12 (5.94)	
c. Medium/Low	135 (13.22)	6 (7.23)	13 (7.56)	1 (0.36)	1 (1.92)	92 (39.66)	22 (10.89)	
Smoking (%)								
a. Non-smoker	783 (67.27)	68 (61.31)	146 (75.26)	215 (69.61)	41 (66.13)	139 (55.38)	176 (73.03)	<0.001*
b. Ex-smoker	330 (28.35)	31 (28.20)	43 (22.16)	86 (27.92)	16 (25.81)	104 (41.43)	50 (20.75)	
c. Smoker	51 (4.38)	11 (10.19)	5 (2.58)	7 (2.27)	5 (8.06)	8 (3.19)	15 (6.22)	
Alcohol intake (%)								
a. I do not consume alcohol	467 (41.47)	50 (47.62)	92 (47.82)	95 (35.58)	28 (45.90)	67 (27.13)	125 (54.35)	<0.001*
b. Once a month or less	359 (32.58)	33 (34.43)	51 (26.56)	78 (29.21)	13 (21.31)	123 (49.80)	61 (26.52)	
c. 2-4 times a month	173 (15.70)	16 (15.24)	28 (14.58)	51 (19.10)	13 (21.31)	38 (15.38)	27 (11.74)	
d. 2-3 times a week	113 (10.25)	6 (5.71)	21 (10.94)	43 (16.10)	7 (11.48)	19 (7.69)	17 (7.39)	
Education n (%)								
a. Secondary or less	334 (24.72)	34 (36.96)	50 (30.12)	115 (42.12)	19 (37.25)	57 (31.15)	59 (29.95)	0.006*
b. Undergraduates	376 (49.09)	27 (29.35)	71 (42.77)	85 (31.14)	20 (39.22)	89 (48.63)	84 (42.64)	
c. Graduates	252 (26.20)	31 (33.70)	45 (27.11)	73 (26.74)	12 (23.53)	37 (20.22)	54 (27.41)	
Caring responsibilities, n (%)								
a. No	936 (77.43)	86 (74.14)	153 (75.37)	277 (87.11)	44 (69.84)	182 (71.94)	194 (75.78)	<0.001*
b. Yes	273 (22.58)	30 (26.86)	50 (24.63)	41 (12.89)	19 (30.16)	71 (28.06)	62 (24.22)	
Disease-related variables								
Disease duration, median (IQR)	17 (13)	8 (9)	5 (13)	8 (9)	3 (5)	8 (14)	8 (17.5)	<0.001*
Age at diagnosis, median (IQR)	49 (25)	47.5 (23)	46 (26)	62 (14)	54 (19)	42 (24)	39 (21)	<0.001*
Disease Activity, n (%)								
a. Inactive	832 (77.98)	71 (75.53)	135 (75.84)	260 (87.97)	33 (62.26)	175 (76.17)	154 (70.64)	<0.001*
b. Active	235 (22.02)	23 (24.47)	43 (43.16)	25 (10.03)	20 (37.74)	56 (23.83)	64 (29.36)	
Disease Damage, median (IQR)	6 (3)	7 (4)	5 (3)	7 (2)	6 (4)	5 (2)	6 (3)	<0.001*
VAS-pain mean (SD)	4.36 (2.68)	5.10 (2.90)	4.48 (2.54)	3.48 (2.64)	3.70 (3.05)	4.36 (2.16)	5.23 (2.71)	<0.001*
Medication(s) n (%)								
a. Steroids	473 (39.12)	65 (56.03)	97 (47.78)	43 (13.52)	34 (53.97)	123 (48.62)	111 (43.38)	<0.001*
b. Biologics	80 (6.62)	4 (3.45)	14 (6.90)	29 (9.12)	4 (6.35)	10 (3.95)	19 (7.42)	0.140
c. csDMARDs	583 (48.22)	68 (58.62)	136 (67.00)	68 (21.38)	38 (60.32)	126 (49.80)	147 (57.42)	<0.001*
d. bDMARDs	258 (21.34)	31 (26.72)	45 (22.17)	24 (7.55)	29 (46.03)	70 (27.67)	59 (23.05)	<0.001*
e. tsDMARDs	33 (2.73)	3 (2.59)	9 (4.43)	0 (0.00)	0 (0.00)	9 (3.56)	12 (4.67)	0.004*
f. Immunomodulatory/ Immunosuppressive agents	548 (45.33)	67 (57.76)	134 (66.01)	44 (13.84)	38 (60.32)	123 (47.83)	144 (56.25)	<0.001*
g. Others	80 (6.62)	4 (3.45)	14 (6.90)	29 (9.12)	4 (6.35)	10 (3.95)	19 (7.42)	0.140
Health-related variables								
Subjective well-being n (%)								
a. Satisfied	451 (39.12)	35 (33.02)	80 (41.45)	115 (37.46)	26 (44.07)	99 (39.92)	96 (40.00)	0.669
b. Dissatisfied	702 (60.88)	71 (66.98)	113 (58.55)	192 (62.54)	33 (55.93)	149 (60.08)	144 (60.00)	

Disclosure: I. Coskun Benlidayi: None; **M. Lama**: None; **O. Afolayan**: None; **M. Shah**: None; **M. Sarkar**: None; **T. Rubinstein**: None; **A. Opinc-Rosiak**: None; **R. Miskovic**: None; **M. Milchert**: None; **D. Luz Felipe da Silva**: AbbVie/Abbott, 5, 6, Boehringer-Ingelheim, 5, 6, Eli Lilly, 5, 6, Galderma, 5, 6, Janssen, 5, 6, Leo Pharma, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Sanofi, 5, 6, UCB, 5, 6; **S. Shinjo**: None; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5; **V. Venerito**: None; **V. Agarwal**: None; **L. Gupta**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2068

Comparing characteristics, diagnostics, and treatment in people with different idiopathic inflammatory myopathies using a large representative cohort

Michael George[1], Thomas Riley[1], Ellen Romich[2], Emily Holladay[3], Tim Beukelman[4], Shanette Daigle[5], Amy Mudano[5], Fenglong Xie[6], Xiang Guo[7], Nicole Kulisek[8], Arne Yndestad[9], Ashraf Chaudhary[8] and Jeffrey Curtis[10], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Media, PA, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Foundation for Advancing Science Technology Education and Research, Hoover, AL, [5]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [6]The University of Alabama at Birmingham, Birmingham, AL, [7]Pfizer, Inc, New York, NY, [8]Pfizer, Inc, Collegeville, PA, [9]Pfizer Inc, Oslo, Norway, Oslo, Norway, [10]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

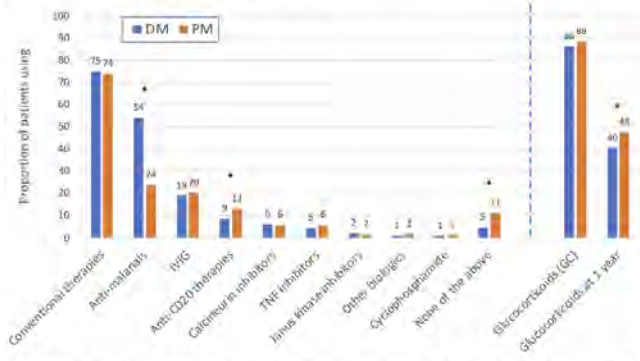
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Studies of idiopathic inflammatory myopathies (IIM) are often based on the analysis of single cohorts at academic centers. We aimed to identify potential gaps in care by comparing testing, treatment, and outcomes of people with IIM diagnosed as dermatomyositis (DM) vs polymyositis (PM) in a nationally representative US cohort.

Methods: This retrospective cohort study used commercial claims (Komodo Healthmap data 1/1/2016-3/31/2024) to identify adults ≥18 with incident IIM, requiring one inpatient diagnosis code for DM (M33.1* or M33.9*) or PM (M33.2*) (positive predictive value 92%) or two outpatient diagnosis codes for DM or PM 7-365 days apart with use of a non-glucocorticoid immunomodulatory therapy (second outpatient diagnosis as the index date). Patients without a 12-month baseline prior to diagnosis #1 or with diagnoses of juvenile DM or inclusion body myositis were excluded. Antisynthetase syndrome and necrotizing myopathy lack specific codes but could be included if DM or PM diagnoses were coded. Standardized differences ≥|0.1| were used to identify differences between those with DM vs PM. Analyses of diagnostic testing and treatment required 12 months of continuous data after index unless limited by death. Time to event analyses for incident hospitalization and major adverse cardiac events (MACE, excluding those with prior MACE) censored at end of follow-up.

Figure 1: Treatments used by people with dermatomyositis (DM) or polymyositis (PM) diagnosis codes, using data from diagnosis #1 through 12 months after the index date



Conventional therapies include methotrexate, azathioprine, mycophenolate, and leflunomide. Anti-malarial includes hydroxychloroquine and chloroquine. Anti-CD20 includes rituximab, obinituzumab, ocrelizumab, ofatumumab, ublituximab. Janus kinase inhibitors include tofacitinib, upadacitinib, baricitinib. Other biologics includes tocilizumab, sarilumab, abatacept, anifrolumab. Glucocorticoid use at 1 year based on ≥ filled oral glucocorticoid prescription 273 to 365 days after index.
IVIG = intra-venous immune globulin; DM = dermatomyositis; PM = polymyositis.
* indicates standardized mean difference ≥0.1 or ≤-0.1, identifying a meaningful difference across groups – anti-malarial SMD 0.65, anti-CD20 SMD -0.14, none of the above SMD -0.24, continued GC use SMD 0.14. In each of these cases $p < 0.001$ by Chi-squared testing.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of baseline characteristics between individuals with idiopathic inflammatory myopathy with dermatomyositis (DM) vs polymyositis (PM) diagnosis codes

Characteristic	Overall N = 9,195[1]	DM N = 5,560[1]	PM N = 3,635[1]	Standardized Difference[2]
Age, years, Mean (SD)	55.4 (14.4)	54.3 (14.5)	57.1 (14.0)	**-0.19**
Female	6,628 (72.1%)	4,274 (76.9%)	2,354 (64.8%)	**0.27**
White, non-Hispanic	4,751 (51.7%)	3,006 (54.1%)	1,745 (48.0%)	**0.29**[1]
Comorbidities				
COPD	1,892 (20.6%)	1,071 (19.3%)	821 (22.6%)	-0.08
Diabetes mellitus	1,962 (21.3%)	991 (17.8%)	971 (26.7%)	**-0.21**
Hypertension	4,528 (49.2%)	2,431 (43.7%)	2,097 (57.7%)	**-0.28**
Hyperlipidemia	3,755 (40.8%)	2,052 (36.9%)	1,703 (46.9%)	**-0.20**
Ischemic heart disease	1,208 (13.1%)	560 (10.1%)	648 (17.8%)	**-0.23**
Heart failure	719 (7.8%)	330 (5.9%)	389 (10.7%)	**-0.17**
Charlson comorbidity index, Mean (SD)	2.5 (2.3)	2.3 (2.2)	2.8 (2.4)	**-0.24**
DM/PM diagnosis from inpatient	1,965 (21.4%)	944 (17.0%)	1,021 (28.1%)	**0.27**
Previous non-IIM autoimmune diagnoses (prior to first PM or DM diagnosis)				
Rheumatoid arthritis	1,218 (13.2%)	606 (10.9%)	612 (16.8%)	**-0.17**
Systemic lupus erythematosus	1,090 (11.9%)	677 (12.2%)	413 (11.4%)	0.03
Sjogren's	603 (6.6%)	343 (6.2%)	260 (7.2%)	-0.04
Psoriasis	524 (5.7%)	389 (7.0%)	135 (3.7%)	**0.15**
Previous non-autoimmune diagnoses (prior to first PM or DM diagnosis)				
Rhabdomyolysis	725 (7.9%)	275 (4.9%)	450 (12.4%)	**-0.27**
Liver test abnormalities	470 (5.1%)	227 (4.1%)	243 (6.7%)	**-0.12**

[1] Standardized Mean Difference, or Standardized Difference in Proportions with values ≥0.1 or ≤-0.1 (bolded) indicating a meaningful difference across groups (*Austin P. Stat Med. 2009*). In all cases with standardized difference ≥0.1 or ≤-0.1, p-values were < 0.001 by Wilcoxon rank sum or Chi-squared testing.
[2] Standardized difference refers to differences across race/ethnicity categories, not fully shown, including 20.8% with unknown race/ethnicity

Table 2: Comparison of treating provider and diagnostic evaluation between individuals with idiopathic inflammatory myopathy with dermatomyositis (DM) vs polymyositis (PM) diagnosis codes using data through 12 months after the index date

	Overall N = 6,490	DM N = 3,989	PM N = 2,501	Standardized Difference[2]
Treating specialists[3]				
Rheumatology	4,662 (71.8%)	2,928 (73.4%)	1,734 (69.3%)	0.09
Dermatology	2,132 (32.9%)	1,721 (43.1%)	411 (16.4%)	**0.61**
Neurology	1,270 (19.6%)	640 (16.0%)	630 (25.2%)	**-0.23**
Pulmonary	1,430 (22.0%)	830 (20.8%)	600 (24.0%)	-0.08
Cardiology	1,464 (22.6%)	784 (19.7%)	680 (27.2%)	**-0.18**
Diagnostic tests performed				
Computed tomography chest (CT)	3,675 (56.6%)	2,358 (59.1%)	1,317 (52.7%)	**0.13**
Pulmonary function tests (PFTs)	2,718 (41.9%)	1,682 (42.2%)	1,036 (41.4%)	0.02
Electromyography (EMG)	1,960 (30.2%)	1,038 (26.0%)	922 (36.9%)	**-0.24**
Muscle magnetic resonance imaging	1,057 (16.3%)	591 (14.8%)	466 (18.6%)	**-0.10**
Muscle biopsy	1,290 (19.9%)	535 (13.4%)	755 (30.2%)	**-0.41**
Skin biopsy	2,253 (34.7%)	1,929 (48.4%)	324 (13.0%)	**0.83**
No CT or PFTs	2,244 (34.6%)	1,307 (32.8%)	937 (37.5%)	**-0.10**
None of any above	1,112 (17.1%)	632 (15.8%)	480 (19.2%)	-0.09
Conditions of special interest				
Interstitial lung disease[4]	1,257 (19.4%)	713 (17.9%)	544 (21.8%)	**-0.10**
Malignancy other than non-melanoma skin cancer[4]	819 (12.6%)	504 (12.6%)	315 (12.6%)	0.00

[1] Standardized Mean Difference, or Standardized Difference in Proportions, with values ≥0.1or ≤-0.1(bolded) indicating a meaningful difference across groups (*Austin P. Stat Med. 2009*). In all cases with standardized difference ≥0.1or ≤-0.1, p-values were < 0.001 by Wilcoxon rank sum or Chi-squared testing.
[2] Defined as an outpatient visit including a diagnosis of DM or PM from diagnosis #1 through 12 months after index
[3] Based on diagnoses on the first diagnosis through 12 months after the index date
[4] Based on diagnosis within 3 years before or 12 months after the index date

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We identified 9,195 people with incident IIM: 5,560 with DM and 3,635 with PM. People with DM were younger, more frequently female, had fewer comorbidities, and were less often diagnosed as inpatients vs PM (**Table 1**). Other rheumatic diagnoses were common in both groups, and those with PM were more likely to have prior diagnoses of rhabdomyolysis or abnormal liver function tests (possibly reflecting muscle injury not identified as IIM). Rheumatologists cared for approximately 70% of those with DM and PM, with dermatologists more frequently involved for DM and neurologists and cardiologists for PM (**Table 2**). Although 19% of patients had a diagnosis of ILD, no pulmonary testing was performed in 35% of patients. Conventional therapies were frequent in both groups, but anti-malarials were used more commonly in those with DM (**Figure 1**). IVIG (19%) and anti-CD20 therapy (10%) use in the first year was not uncommon in DM or PM. Glucocorticoid use was similar in DM and PM, with 87% using glucocorticoids within the first year of diagnosis and median cumulative glucocorticoid exposure among glucocorticoid users 1605mg (IQR 600, 2925). Glucocorticoid use at 1 year, however, was less common in DM (40%) vs PM (48%). During follow-up, incidence of hospitalization (15.1 vs 22.1/100 person-year) and MACE (1.0 vs 1.7/100 person-years) were less common in DM vs PM (both $p < 0.05$).

Conclusion: This large cohort study reveals differences in comorbidity burden and outcomes in people with DM vs PM and highlights differences in the subspecialists caring for these two populations. We found potential gaps in testing, including low rates of ILD screening. The substantial glucocorticoid burden demonstrates the need for more effective treatment.

Disclosure: M. George: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **T. Riley**: None; **E. Romich**: Lungpacer Medical, Inc., 11, Teva Pharmaceuticals, 12, Spouse employment; **E. Holladay**: None; **T. Beukelman**: None; **S. Daigle**: None; **A. Mudano**: None; **F. Xie**: None; **X. Guo**: Pfizer, 3; **N. Kulisek**: Pfizer, 3; **A. Yndestad**: Pfizer, 3, 11; **A. Chaudhary**: Bristol-Myers Squibb(BMS), 3, Pfizer, 3; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 2069

Concordance of low titer positive myositis-specific autoantibodies and myositis-associated autoantibodies on subsequent myositis panel testing.

Nikola Wilk[1], Jocelyn Hui Ching Chow[2], Ian Smith[3], Ronald A. Booth[4], Nancy Maltez[1], Catherine Ivory[1] and Jodi Warman-Chardon[5], [1]Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [2]Department of Medicine, Division of General Internal Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [3]Department of Medicine, Division of Neurology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada., Ottawa, ON, Canada, [4]Department of Pathology and Laboratory Medicine, The Ottawa Hospital, University of Ottawa & Eastern Ontario Regional Laboratory Association, Ottawa, ON, Canada., Ottawa, ON, Canada, [5]Department of Medicine, Division of Neurology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada. Department of Medicine and Cellular and Molecular Medicine, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, ON, Canada., Ottawa, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune connective tissue diseases that commonly affect multiple systems. Myositis-specific autoantibodies (MSA) and myositis-associated autoantibodies (MAA) can be identified in up to 70% of patients with IIM. The clinical significance of multi-specific

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 | Overall concordance among patients with positive titer MSA/MAA

Antibody	Number of patients	Number of tests Total *n* (*n* positive)	Concordance
Anti-Ro	25	57 (17)	30 / 32 (93.8%)
Anti-La	6	16 (0)	6 / 6 (100%)
Anti-Jo-1	25	58 (8)	33 / 33 (100%)
Anti-PL7	25	58 (5)	30 / 33 (90.9%)
Anti-PL12	25	58 (6)	33 / 33 (100%)
Anti-Ku	25	58 (12)	29 / 33 (87.9%)
Anti-EJ	25	58 (0)	33 / 33 (100%)
Anti-OJ	25	58 (2)	32 / 33 (97%)
Anti-SAE	25	58 (8)	30 / 33 (90.9%)
Anti-Mi2-alpha	25	58 (12)	30 / 33 (90.9%)
Anti-Mi2-beta	25	58 (11)	30 / 33 (90.9%)
Anti-MDA5	25	58 (4)	31 / 33 (93.9%)
Anti-HMGCR	25	58 (3)	33 / 33 (100%)
Anti-SRP	25	58 (2)	31 / 33 (93.9%)
Anti-TIF1	25	58 (7)	30 / 33 (90.9%)
Anti-NXP2	25	58 (0)	33 / 33 (100%)
ANti-5NT1A	24	55 (0)	32 / 32 (100%)
Scl100	25	58 (0)	33 / 33 (100%)
Scl75	25	58 (0)	33 / 33 (100%)
Total	**25**	**1056**	**573 / 598 (95.8%)**

immunoassays, especially regarding the clinical relevance of low titer positive MSA/MAA, and their consistency in repeat testing, remains to be determined.

Methods: Using an electronic database, we identified all patients who had a myositis panel assessed through Eastern Ontario Regional Laboratory Association between June 2019 and October 2024. This myositis panel includes 18 autoantibodies detected by a semi-quantitative immunoblot assay, with autoantibodies reported in terms of low, moderate, and high titers (EUROIMMUN Medizinische Labordiagnostika AG, Lübeck Germany). We performed a retrospective chart review on the subset of patients with low positive titers of MSA/MAA and multiple myositis panels performed. Concordance was determined by the stability of the antibody result between sequential testing.

Results: 1478 patients had a myositis panel done, and 166 patients were positive with low-titer MSA or MAA antibodies. A total of 25 patients had two or more myositis panels performed within this timeframe. In these patients with repeat testing, 1056 individual MSA/MAA were measured, and the overall concordance was 95.8% (573/598) [Table 1]. Of the 1056

Table 2 | Concordance of low-titer MSA/MAA

Antibody	Number of patients	Number of tests Total *n* (n^+, n^-)	Concordance (low-titer)
Anti-Ro	7	17 (14, 3)	4 / 6 (67%)
Anti-Jo-1	3	8 (8, 0)	4 / 4 (100%)
Anti-PL7	2	5 (3, 2)	0 / 3 (0%)
Anti-PL12	3	6 (6, 0)	2 / 2 (100%)
Anti-Ku	5	12 (7, 5)	2 / 6 (33%)
Anti-OJ	1	2 (1, 1)	0 / 1 (0%)
Anti-SAE	3	8 (3, 5)	2 / 5 (40%)
Anti-Mi2-alpha	5	12 (8, 4)	4 / 7 (57.1%)
Anti-Mi2-beta	5	11 (7, 4)	3 / 6 (50%)
Anti-MDA5	2	4 (2, 2)	0 / 2 (0%)
Anti-SRP	2	4 (2, 2)	0 / 2 (0%)
Anti-TIF1	5	11 (7, 4)	3 / 6 (50%)
Total	**25**	**102**	**24 / 50 (48%)**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 | Idiopathic inflammatory myopathy diagnosis

Diagnosis	Total
None	17 (68%)
Juvenile Dermatomyositis (JDM)	0
Antisynthetase syndrome	2 (8%)
Immune-mediated necrotizing myopathy	2 (8%)
Overlap/non-specific myositis	0
Polymyositis	0
Dermatomyositis	1 (4%)
Amyopathic dermatomyositis	0
Cancer-associated myositis	0
Inclusion body myositis	1 (4%)
Others	2 (8%)

individual MSA/MAA, 102 were in patients with at least one MSA/MAA positive antibody result. Five patients had concomitant moderate/high positive titer MSA/MAA, though these values were excluded from the primary analysis. Concordance limited to positive low-titer findings on at least one time point was much lower at 48% (24/50) [Table 2]. Among low-titer MSA/MAA, the highest concordance was observed for Ro (4/6, 67%), PL12 (2/2, 100%), and Jo-1 (4/4, 100%), whereas concordance was < 50% for PL7 (0/3, 0%), Ku (2/6, 33%), SAE (2/5, 40%), OJ (0/1, 0%), MDA-5 (0/2, 0%) and SRP (0/2, 0%) antibodies [Table 2]. 68% of the repeat patients (17/25) did not develop any IIM and were deemed to have false positive antibodies on their myositis panel [Table 3].

Conclusion: The concordance of a positive low titer positive MSA and MAA on subsequent myositis panel testing was found to be overall low (48%) within our patient population. Only 3 of 20 patients limited to low-positive titers received an IIM diagnosis, highlighting the high frequency of clinically false positives among low positive titers. Further studies are needed to understand the clinical significance of low positive titers and repeat testing using myositis panels

Disclosure: N. Wilk: None; **J. Chow**: None; **I. Smith**: None; **R. Booth**: None; **N. Maltez**: None; **C. Ivory**: None; **J. Warman-Chardon**: None.

Abstract Number: 2070

Characterization of Hospitalization, Patient Demographics and Impact of Idiopathic Inflammatory Myopathies on Hospitalization Outcomes in Adult Fracture Patients: A National Inpatient Sample Analysis.

Pranathi Bandarupalli[1], Vineeth Potluri[2], Amr Alemairy[2], Harsharn Grewal[2] and Shudipan Chakraborthy[2], [1]Mercy St Vincent Medical Center, Toledo, OH, [2]Mercy Health St. Vincent Medical Center, Toledo, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Idiopathic Inflammatory Myopathies (IIM), including polymyositis and dermatomyositis, are rare systemic autoimmune disorders characterized by chronic muscle inflammation and progressive muscle weakness. Patients with IIM are at an elevated risk of fractures due to a combination of factors, including prolonged corticosteroid use, reduced bone mineral density, impaired mobility, and an increased propensity for falls. Although fracture risk in IIM is well recognized, there is limited understanding of how IIM affects hospitalization outcomes following fractures, including resource utilization, discharge disposition, and mortality. Clarifying these associations is essential to inform clinical management and optimize care strategies for this high-risk patient population. To evaluate the impact of Idiopathic Inflammatory Myopathies (IIM) on hospitalization outcomes among adults admitted with fractures by comparing demographic characteristics, comorbidity burden, resource utilization, and in-hospital mortality between patients with and without IIM using a nationally representative dataset.

Methods: We conducted a retrospective cohort study using the National Inpatient Sample (NIS) data from 2017 to 2022. Adults (≥18 years) hospitalized with a primary diagnosis of fracture were identified and further stratified based on the presence or absence of a secondary diagnosis of IIM which includes polymyositis , dermatomyositis and Inclusion body myositis. using ICD-10 Codes. Patient demographics, comorbidities, fracture types, length of stay (LOS), total hospital charges, discharge disposition, and in-hospital mortality were compared between groups. Multivariable logistic and linear regression models, adjusting for demographic and clinical variables, were used to assess the independent association of IIM with hospitalization outcomes. Adjusted odds ratios (aOR), β coefficients, 95% confidence intervals (CI), and P-values were reported.

Results: Among 5,273,033 fracture hospitalizations, 1,950 (0.04%) had a concurrent diagnosis of IIM. Compared to patients without IIM, those with IIM were older (mean age 72.1 vs. 69.5 years, p< 0.001) and more likely to be female (73.08% vs. 58.13%, p< 0.001). Osteoporosis (24% vs. 11%, p< 0.001) and steroid use (23.27% vs. 1.3%, p< 0.001) were

Table 1. Patient Demographics and Hospitalization Characteristics

Characteristic	Fracture without IIM (n = 5,271,083)	Fracture with IIM (n = 1,950)	P-value
Age, mean (years)	69.5	72.1	<0.001
Female sex (%)	58.13%	73.08%	<0.001
Race: White	80.27%	79.85%	
Race: Black	6.69%	7.46%	
Race: Hispanic	7.99%	4.85%	
Race: Asian/Pacific Islander	2.05%	2.61%	
Race: Native American	0.5%	1.12%	
Race: Other	2.47%	0.41%	0.0154
Insurance: Medicare	66.67%	82.42%	
Insurance: Medicaid	3.76%	1.47%	
Insurance: Private	18.67%	15.75%	
Insurance: Uninsured/Other	8.7%	0.36%	<0.001
Hip Fracture (%)	42.59%	47.69%	
Vertebral Fracture (%)	42.59%	39.74%	
Humerus/Shoulder Fracture (%)	11.2%	12.56%	0.0125
Osteoporosis (%)	11.00%	24.00%	<0.001
Steroid Use (%)	1.3%	23.27%	<0.001
Length of Stay, mean (days)	5.4	6.02	0.002
In-hospital Mortality (%)	1.6%	1.7%	0.77
Mean Total Hospital Charges (US$)	$74,271	581,447	0.02

Patient Demographics and Hospitalization Characteristics

Table 2. Multivariable Regression Analysis for Adjusted Outcomes

Outcome	Adjusted Odds Ratio (aOR) / Beta Coefficient	95% Confidence Interval (CI)	P-value
In-Hospital Mortality	1.29	0.60 - 2.70	0.505
Length of Stay (days)	+0.49 days	0.20 - 0.60	**0.029**
Discharge to Skilled Nursing Facility (SNF)	0.91	0.73 - 1.14	0.408
Total Hospital Charges (US$)	+$4,877	$1,156 - $4,655	**0.037**

Multivariable Regression Analysis for Adjusted Outcomes

significantly more prevalent among IIM patients. After multivariable adjustment, IIM was associated with a significantly longer hospital stay (β = +0.49 days, 95% CI 0.20–0.60, p = 0.029) and higher total hospital charges (β = +$4,877, 95% CI $1,156–$4,655, p = 0.037). No significant differences were observed in in-hospital mortality (aOR 1.29, 95% CI 0.60–2.70, p = 0.505) or discharge to skilled nursing facilities (aOR 0.91, 95% CI 0.73–1.14, p = 0.408).

Conclusion: Among adults hospitalized for fractures, the presence of IIM was associated with longer hospital stays and higher healthcare costs but was not associated with increased in-hospital mortality or skilled nursing facility disposition. These findings underscore the importance of proactive fracture prevention strategies, interdisciplinary peri-fracture management, and early rehabilitation planning in patients with IIM.

Disclosure: P. Bandarupalli: None; **V. Potluri**: None; **A. Alemairy**: None; **H. Grewal**: None; **S. Chakraborthy**: None.

Abstract Number: 2071

Impact of Diagnostic Delay on Disease Activity and Cumulative Damage in Patients with Idiopathic Inflammatory Myopathies in a Third-level Hospital in Mexico

valeria cantu[1], **Rebeca L. Polina-Lugo**[1], Emmanuel Dominguez-Chapa[2], Ana Cecilia Bardan Inchaustegui[3], Fernanda M. Garcia-Carrillo[4], Daniela A. Mejia-Rodriguez[4], Ericka S. Reyna-Hernandez[4], Rosa Arvizu-Rivera[5], Jesus Alberto Cardenas-de la Garza[6] and Miguel Villarreal-Alarcón[7], [1]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [2]Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [3]Universidad Autónoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [4]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [5]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico, [6]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [7]Hospital Universitario UANL, Monterrey, Nuevo León, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a rare and heterogeneous group of autoimmune diseases marked by inflammation of muscle tissue and extramuscular manifestations. Their atypical clinical presentations often lead to diagnostic delays, which hinder timely treatment and contribute to worse outcomes. Early diagnosis is essential to reduce disease activity, prevent long-term damage, and improve quality of life. In juvenile dermatomyositis (JDM), delayed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinicodemographic characteristics and disease activity scales

Characteristics	n=40
Women, n (%)	34 (85)
Men, n (%)	6 (15)
Age, mean (±SD)	46.6 ±16.2
Inflammatory Myopathy	
Dermatomyositis, n (%)	29 (72.5)
Antisynthetase syndrome, n (%)	5 (12.5)
Polymyositis, n (%)	3 (7.5)
Immune-mediated necrotizing myopathy, n (%)	1 (2.5)
Amyopathic dermatomyositis, n (%)	2 (5.0)
Diagnostic delay time, months, median (IQR)	5 (2-11.5)
Disease activity scales	
MDI	
Extent of damage, mean (±SD)	4.8 ± 3.0
Severity of damage, mean (±SD)	14.7 ± 10.8
Extended damage, median (IQR)	1.0 (0-2.0)
MDAAT	
MYOACT, mean (±SD)	14.0 ± 11.0
MITAX, mean (±SD)	11.3 ± 9.1
HAQ, mean (±SD)	0.82 ± 0.7

diagnosis has been linked to greater morbidity and poorer prognosis, with emerging evidence also pointing to disparities based on race. This underscores the need for further research. We aim to examine the correlation between diagnostic delay, disease activity, and cumulative damage in patients with IIM.

Methods: A descriptive, cross-sectional, and comparative study was performed. Patients over 18 years of age diagnosed with IIM according to the 2017 ACR/EULAR classification criteria or the 1975 Bohan and Peter criteria were recruited. A clinical history was obtained, including the duration of symptoms before diagnosis and the disease duration since diagnosis. The cumulative glucocorticoid dose up to the time of recruitment was calculated.

The following scales were assessed:

1. Myositis Damage Index (MDI)
2. Myositis Disease Activity Assessment Tool (MDAAT)
3. Health Assessment Questionnaire (HAQ)
4. Fitzpatrick Scale

Table 2. Comparison of clinical and laboratory characteristics according to diagnostic delay time

	Diagnosis <9 months (n=27)	Diagnosis >9 months (n=13)	p-value
Women, n (%)	22 (81.4)	12 (92.3)	0.36
Age, mean (±SD)	50.8 ± 16.1	37.6 ± 12.8	**0.01**
Dermatomyositis, n (%)	20 (74.0)	9 (69.2)	0.74
Antisynthetase Syndrome, n (%)	4 (14.8)	1 (7.6)	0.52
Polymyositis, n (%)	2 (7.4)	1 (7.6)	0.97
Immune-mediated necrotizing myopathy, n (%)	1 (3.7)	-	0.48
Amyopathic dermatomyositis, n (%)	-	2 (15.3)	**0.03**
Cumulative dose of prednisone, median (IQR)	800 (0–4395)	2715 (1510–9520)	**0.03**
Fitzpatrick			
Type 2-3, n (%)	14 (51.8)	2 (15.3)	**0.03**
Type 4-5, n (%)	12 (44.4)	10 (76.9)	**0.03**
HAQ, mean (±SD)	0.6 ± 0.7	1.2 ± 0.6	**0.01**
MDI			
Extent of damage, mean (±SD)	4.3 ± 2.6	6.0 ± 3.4	0.10
Severity of damage, mean (±SD)	13.1 ± 10.1	17.8 ± 12.1	0.20
Extended damage, median (IQR)	1 (0.0-1.0)	1 (0.0-3.0)	0.74
MDAAT			
MYOACT, mean (±SD)	10.3 ± 9.0	21.0 ± 11.4	**0.003**
MITAX, mean (±SD)	8.9 ± 7.6	15.8 ± 10.3	**0.02**
Laboratories			
CPK, median (IQR)	73 (47.7-100.)	142 (50.0-273.5)	0.13
Aldolase, mean (±SD)	-	3.8 ± 0.4	-
AST, median (IQR)	24.0 (19.0-38.0)	30.5 (20.2-48.0)	0.33
ALT, median (IQR)	28.9 ± 59.5	47.0 ± 59.5	0.90
Albumin, mean (±SD)	3.9 ± 0.4	3.9 ± 0.4	0.93

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

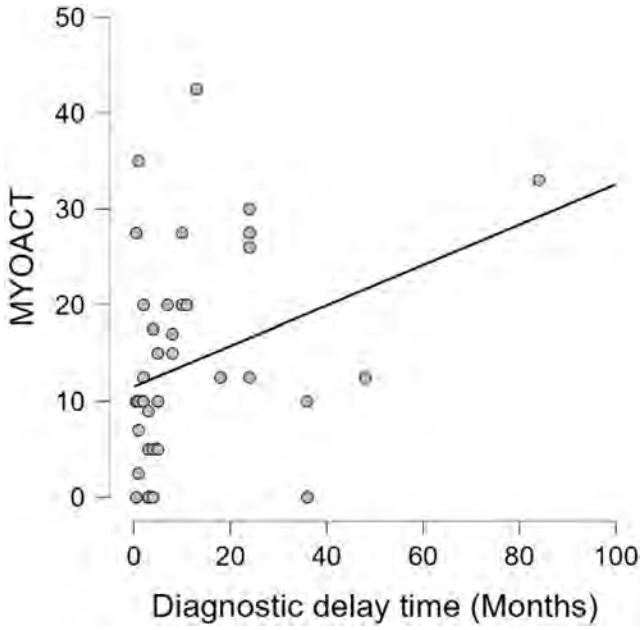


Figure 1. Correlated variables diagnostic delay time and MYOACT scale.

Patients were divided into two groups based on diagnostic delay: ≤9 months and >9 months. The Kolmogorov-Smirnov test, used to assess normality. Group comparisons were made using the Chi-square test, independent samples t-test, or Mann-Whitney U test. Correlations were analyzed using Pearson or Spearman coefficients, depending on data distribution. A p-value of < 0.05 was considered statistically significant.

Results: A total of 40 patients were included, with a mean age of 46.6 years (SD: 16.2). Most patients were female (n=34, 85%). The most frequent IIM was dermatomyositis, observed in 29 patients (72.5%). The median time from symptom onset to diagnosis was 5 months (IQR: 2–11.5). The most prevalent antibodies were anti-Ro52 (37.5%) and anti-TIFy (27.5%). Demographic and clinical characteristics and disease activity scales are shown in Table 1.

Patients with a diagnostic delay greater than 9 months had significantly higher scores on the HAQ, MYOACT, and MITAX scales (p=0.01, p=0.003, and p=0.02, respectively) (Table 2), as well as a younger age (p=0.01). A weak positive correlation was observed between diagnostic delay and MYOACT score (Spearman's $\rho = 0.357$, $p = 0.02$). (Figure 3)

Skin phototype showed differences by diagnostic delay. Among patients with a diagnostic delay ≤ 9 months, 44.4% had Fitzpatrick phototype IV or V, while 51.8% had phototype II or III. In contrast, 76.9% of patients with a delay > 9 months had phototype IV or V, compared to only 15.3% with phototype II or III.

Conclusion: According to our results, IIM is not commonly considered an initial diagnosis in younger patients with phototype IV or V. A diagnostic delay of more than 9 months was associated with higher disease activity, greater cumulative damage, and reduced quality of life, highlighting the need for timely evaluation in patients with these characteristics.

Disclosure: v. cantu: None; **R. Polina-Lugo**: None; **E. Dominguez-Chapa**: None; **A. Bardan Inchaustegui**: None; **F. Garcia-Carrillo**: None; **D. Mejia-Rodriguez**: None; **E. Reyna-Hernandez**: None; **R. Arvizu-Rivera**: None; **J. Cardenas-de la Garza**: None; **M. Villarreal-Alarcón**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2072

Results of an Integrated Program for Early Cancer Detection in Idiopathic Inflammatory Myopathies

valeria cantu[1], **Rebeca L. Polina-Lugo**[1], Emmanuel Dominguez-Chapa[2], Ana Cecilia Bardan Inchaustegui[3], Rosa Arvizu-Rivera[4], fernanda m. garcia-Carrillo[5], Ericka S. Reyna-Hernandez[6], Daniela A. Mejia-Rodriguez[6], Jesus Alberto Cardenas-de la Garza[7] and Miguel Villarreal-Alarcón[8], [1]Division of Rheumatology, University Hospital \"Dr. Jose Eleuterio Gonzalez\", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [2]Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [3]Universidad Autónoma de Nuevo Leon, Monterrey, Nuevo León, Mexico, [4]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico, [5]Hospital Universitario \"Dr. José Eleuterio González\" UANL, Monterrey, Nuevo Leon, Mexico, [6]Rheumatology Service, Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Universidad Autonoma de Nuevo Leon, Monterrey, Nuevo Leon, Mexico, [7]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [8]Hospital Universitario UANL, Monterrey, Nuevo León, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Cancer risk is significantly increased in Idiopathic Inflammatory Myopathies (IIM), particularly within the first 3 to 5 years after diagnosis. Given that cancer represents the leading cause of mortality in IIM, implementing effective screening strategies is crucial for enabling early detection and timely intervention. This underscores the need to establish a comprehensive, multidisciplinary management program that incorporates risk-based cancer screening into routine care. Therefore, we aim to describe the model for the early detection of cancer in patients with IIM in our center's multidisciplinary care program for patients with rheumatic diseases.

Table 1: Screening Coverage and Time to Completion by Sex and Age Category

Table 1: Screening Coverage and Time to Completion by Sex and Age Category

	Women (18-40) (n=20)	Women >40 (n=34)	Men (18-40) (n=4)	Men (>40) (n=5)
Time to complete a single screening procedure, months, median (IQR)	10.0 (2.0-30.0)	12.0 (2-12.0)	4.0 (3.5-9.0)	4.0 (1.0-10.0)
Screening complete according to age and sex, n (%)	7 (35.0)	15 (44.1)	3 (75.0)	3 (60.0)
Screening type				
Colon				
Screening performed, n (%)	8 (40.0)	23 (67.6)	0 (0)	3 (60.0)
Time to complete screening, months, mean±SD	43.9±44.5	18.6±15.4	-	6.7±11.5
Lung				
Screening performed, n (%)	13 (65.0)	25 (73.5)	3 (75.0)	5 (100.0)
Time to complete screening, months, median (IQR)	31.0 (9.0-75.0)	1.0 (1.0-23.0)	4.0 (3.5-11.0)	4.0 (1.0-19.0)
Breast				
Screening performed, n (%)	3 (15.0)	28 (82.3)	NA	NA
Time to complete screening, months, median (IQR)	66.0 (63.0-69.0)	12.0 (1.5-12.0)	NA	NA
Cervix				
Screening performed, n (%)	11 (55.0)	23 (67.6)	NA	NA
Time to complete screening, months, median (IQR)	54.0 (12.0-62.0)	12.0 (2.5-24.0)	NA	NA
Prostate				
Screening performed, n (%)	NA	NA	0 (0)	4 (80.0)
Time to complete screening, months, mean±SD	NA	NA	-	24.0±25.8

IQR, Interquartile Range; SD, Standard Deviation; NA, Not Applicable.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Screening Results of IIM patients.

Table 2: Screening Results of IIM patients.

Screening type	Positive	Negative	Not Screened*
Colon	6 (9.5)	29 (46.0)	21 (33.3)
Lung	4 (6.3)	42 (66.6)	15 (23.8)
Breast†	2 (3.7)	26 (51.6)	12 (22.2)
Cervix†	3 (5.5)	39 (72.2)	10 (18.5)
Prostate†	0 (0)	4 (44.4)	2 (22.2)

*Percentages and frequencies are calculated based on the total number of men and women. †Patients who were not yet due for screening were excluded.

Methods: The Early Cancer Detection Program, initiated on March 1st, 2024, at the Rheumatology Clinic of Dr. Jose Eleuterio González University Hospital (Nuevo Leon, Mexico), targets patients over 18 with IIM. The program has three primary objectives:

a) **Stratify cancer risk** using a digital calculator based on international guidelines, categorizing patients as high, intermediate, or low risk.

b) **Educate patients** on the importance of screening, tailored to individual risk levels, including low-dose CT, FIT, mammography, cervical cytology, and PSA testing.

c) **Identify prevalent cancers** in IIM patients through screening; those with positive results are referred to oncology, while negative results are followed up individually.

Quality indicators include:

1. The proportion of patients screened by age and sex
2. The time from IIM diagnosis to completion of screening
3. The percentage of patients with positive screening results
4. The proportion of patients not screened

Data are presented with descriptive statistics, including frequencies, percentages, mean, standard deviation, median, and interquartile range.

Results: A total of 63 IIM patients were included (54 women, 9 men; mean age 45.9 ± 16.3 years). Most patients were at intermediate cancer risk (47.6%), followed by high risk (41.2%) and low risk (11.1%). All high-risk patients underwent at least one screening, with only five patients not completing any screening. The median time from IIM diagnosis to screening was 10.0 months (IQR: 2.0–12.0).

Men had a higher overall screening rate than women (Table 1). However, 67.6% of colon cancer screenings were performed in women over 40. Lung cancer screening was completed in 100% of men over 40, while 82.3% and 67.6% of women over 40 underwent breast and cervical cancer screenings, respectively.

Regarding screening results (Table 2), lung screening had positive findings in 6.3% of patients, but no neoplasms were diagnosed. One positive breast cancer screening confirmed adenocarcinoma, and one cervical screening found a high-grade squamous intraepithelial lesion.

Conclusion: Our findings reveal that most patients with IIM were classified as high or intermediate cancer risk, underscoring the clinical importance of risk stratification. Despite these insights, gaps in cancer screening highlight the urgent need for targeted education and intervention strategies. Additionally, multidisciplinary efforts and the implementation of personalized management plans are crucial for optimizing cancer prevention strategies.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: v. cantu: None; **R. Polina-Lugo**: None; **E. Dominguez-Chapa**: None; **A. Bardan Inchaustegui**: None; **R. Arvizu-Rivera**: None; **f. garcia-Carrillo**: None; **E. Reyna-Hernandez**: None; **D. Mejia-Rodriguez**: None; **J. Cardenas-de la Garza**: None; **M. Villarreal-Alarcón**: None.

Abstract Number: 2073

Cell-free DNA as a Potential Marker of Muscle Involvement and Treatment Response in Myositis

Sabína Oreská[1], Kristina Svobodová[1], Lucia Vernerová[1], Dana Dlouhá[2], Hana Wunsch[1], Karel Pavelka[1], Jiri Vencovsky[3], Ladislav Šenolt[4], Michal Vrablik[5], Jaroslav Alois Hubáček[2] and Michal Tomcik[1], [1]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, [2]Experimental Medicine Center, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [3]Institute of Rheumatology, Praha 8, Czech Republic, [4]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [5]3rd Department of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are characterized by inflammatory muscle injury. Circulating cell-free DNA (cfDNA), including nuclear (cfnDNA) and mitochondrial (cfmtDNA) DNA, has been shown to increase after exercise primarily due to apoptosis or necrosis and might be a promising biomarker for inflammatory muscle injury in IIM. The aim was to explore the association between cfnDNA and cfmtDNA and muscle damage, strength, and metabolic function.

Methods: 66 patients with IIM were included: 22 male; mean (SD) age 57.6 (13.9); disease duration 2.3 (3.0) years; 21 dermatomyositis (DM)/ 29 polymyositis (PM), both without statin history/ 16 immune-mediated necrotizing myopathystatin-induced (IMNM). Follow-up at 6 months of immunosuppressive therapy included 15 patients (6 DM, 6 PM, 3 IMNM; disease duration 0.9 (1.3) years). Basal laboratory parameters, disease features, current treatment and comorbidities were recorded. Body composition was examined by bioelectric impedance analysis (BIA-2000-M). cfDNA was isolated using the Plasma/ Serum Cell-Free Circulating DNA Purification Mini Kit (Norgen Biotek). qPCR was used to analyze 2 independent markers for cfnDNA (IL6 and CTO), and cfmtDNA (ND5 and CO3). Data are presented as mean (SEM).

Results: There were no significant differences in plasma concentrations of selected cfnDNA and cfmtDNA markers among DM, PM and IMNM (Table 1). Elevated expression of both cfnDNA and cfmtDNA was associated with worse disease damage (MDI), decreased muscle strength (MMT8), higher body fat percentage (BF%), reduced basal metabolic rate (BMR), and decreased capacity for physical activity (higher ECM/BCM and lower phase angle). cfnDNA expression also positively

Table 1: Baseline expression of cfnDNA and cfmtDNA in IIM

Table 1: Baseline expression of cfnDNA (IL6, FTO) and cfmtDNA (ND5, CO3) among IIM subtypes

IIM subtype	IL6 (copies/mL plasma) mean (SEM)	FTO (copies/mL plasma) mean (SEM)	ND5 (copies/mL plasma) mean (SEM)	CO3 (copies/mL plasma) mean (SEM)
DM (n=21)	61,295 (11,757)	65,239 (11,688)	700,286 (106,569)	587,366 (95,370)
PM (n=29)	37,799 (4,221)	38,526 (4,639)	448,894 (52,622)	366,667 (39,524)
IMNM (n=16)	62,707 (23,272)	63,717 (21,297)	857,046 (302,619)	867,834 (374,854)
p-value	0.269	0.177	0.147	0.231

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: associations of cfDNA and markers of muscle and metabolic involvement in IIM

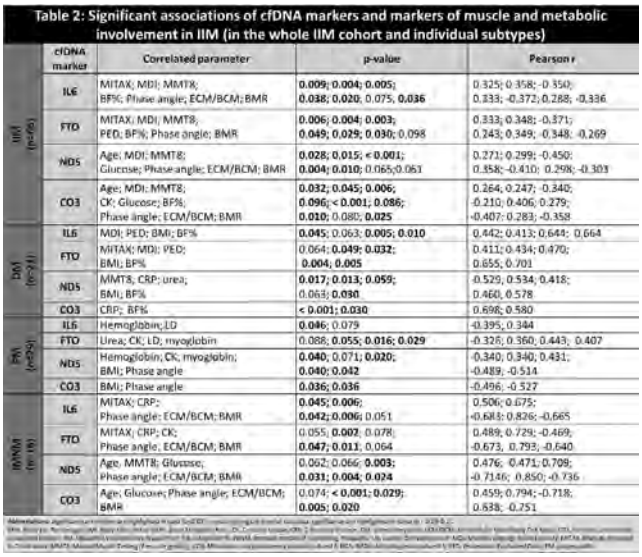


Table 2: Significant associations of cfDNA markers and markers of muscle and metabolic involvement in IIM (in the whole IIM cohort and individual subtypes)				
	cfDNA marker	Correlated parameter	p-value	Pearson r
IIM (n=46)	IL6	MITAX; MDI; MMT8; BF%; Phase angle; ECM/BCM; BMR	**0.009; 0.004; 0.005; 0.038; 0.020**; 0.075; **0.036**	0.325; 0.358; -0.350; 0.333; -0.372; 0.288; -0.336
	FTO	MITAX; MDI; MMT8; PED; BF%; Phase angle; BMR	**0.006; 0.004; 0.003; 0.049; 0.029; 0.030**; 0.098	0.333; 0.348; -0.371; 0.243; 0.349; -0.348; -0.269
	ND5	Age; MDI; MMT8; Glucose; Phase angle; ECM/BCM; BMR	**0.028; 0.015; < 0.001; 0.004; 0.010**; 0.065; 0.063	0.271; 0.299; -0.450; 0.358; -0.410; 0.298; -0.303
	CO3	Age; MDI; MMT8; CK; Glucose; BF%; Phase angle; ECM/BCM; BMR	**0.032; 0.045; 0.006; 0.096; < 0.001; 0.086; 0.010**; 0.080; **0.025**	0.264; 0.247; -0.340; -0.210; 0.406; 0.279; -0.407; 0.283; -0.358
DM1 (n=11)	IL6	MDI; PED; BMI; BF%	**0.045**; 0.063; **0.005; 0.010**	0.442; 0.413; 0.644; 0.664
	FTO	MITAX; MDI; PED; BMI; BF%	0.064; **0.049; 0.032; 0.004; 0.005**	0.411; 0.434; 0.470; 0.655; 0.701
	ND5	MMT8; CRP; urea; BMI; BF%	**0.017; 0.013; 0.059;** 0.063; **0.030**	-0.529; 0.534; 0.418; 0.460; 0.578
	CO3	CRP; BF%	**< 0.001; 0.030**	0.698; 0.580
PM (n=25)	IL6	Hemoglobin; LD	**0.046**; 0.079	-0.395; 0.344
	FTO	Urea; CK; LD; myoglobin	0.088; **0.055; 0.016; 0.029**	-0.328; 0.360; 0.443; 0.407
	ND5	Hemoglobin; CK; myoglobin; BMI; Phase angle	**0.040**; 0.071; **0.020; 0.040; 0.042**	-0.340; 0.340; 0.431; -0.489; -0.514
	CO3	BMI; Phase angle	**0.036; 0.036**	-0.496; -0.527
IMNM (n=10)	IL6	MITAX; CRP; Phase angle; ECM/BCM; BMR	**0.045; 0.006; 0.042; 0.006**; 0.051	0.506; 0.675; -0.683; 0.826; -0.665
	FTO	MITAX; CRP; CK; Phase angle; ECM/BCM; BMR	0.055; **0.007**; 0.078; **0.047; 0.011**; 0.064	0.489; 0.729; -0.469; -0.673; 0.793; -0.640
	ND5	Age; MMT8; Glucose; Phase angle; ECM/BCM; BMR	0.062; 0.066; **0.003; 0.031; 0.004; 0.024**	0.476; 0.471; 0.709; -0.714; 0.850; -0.736
	CO3	Age; Glucose; Phase angle; ECM/BCM; BMR	0.074; **< 0.001; 0.029; 0.005; 0.020**	0.459; 0.794; -0.718; 0.638; -0.751

Table 3: Expression of cfnDNA and cfmtDNA in 15 IIM after 6 months of immunosuppression

Table 3: Expression of cfnDNA (IL6, FTO) and cfmtDNA (ND5, CO3) in 15 patients with early IIM after 6 months of immunosuppressive therapy				
Interval	IL6 mean (SEM)	FTO mean (SEM)	ND5 mean (SEM)	CO3 mean (SEM)
Month 0	33,824 (5,230)	40,158 (8,088)	437,320 (66,502)	394,299 (83,451)
Month 6	31,166 (5,779)	29,628 (5,637)	312,809 (54,498)	293,759 (58,769)
p-value	0.600	0.390	0.107	0.230

correlated with disease activity (MITAX), while cfmtDNA positively correlated with age and glucose plasma levels (Table 2). The analysis of a 6-month follow-up in 15 IIM patients after immunosuppressive treatment initiation showed statistically significant reductions in disease activity, improvement of muscle strength, and decreases in levels of muscle involvement markers (CK, LD, myoglobin) ($p < 0.05$ for all) (Table 3). However, the decrease in both cfnDNA and cfmtDNA expression was not significant. Lower baseline expression of cfnDNA (IL6) predicted a trend to an increase in muscle strength (MMT8) ($p=0.09$).

Conclusion: Expression of nuclear and mitochondrial cfDNA did not vary among the IIM subtypes but was associated with disease activity and damage, muscle weakness, and physical function in patients with IIM. Although there was a significant improvement in muscle impairment (decrease in muscle markers, increase in muscle strength) along with the reduction in glucocorticoid doses observed in only 15 IIM patients after a 6-month initial immunosuppressive therapy, the expression of cfnDNA and cfmtDNA did not change, There was a promising prediction of increased muscle strength by baseline expression of cfnDNA (IL6). Therefore, both cfnDNA and cfmtDNA deserve further studies to elucidate their potential role as a marker of muscle damage, or treatment response in IIM.

Acknowledgments: MH CR 023728, NU21-01-00146, NU21-05-00322, BBMRI.cz-LM2023033, SVV 260638

Disclosure: S. Oreská: None; **K. Svobodová**: None; **L. Vernerová**: None; **D. Dlouhá**: None; **H. Wunsch**: None; **K. Pavelka**: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **J. Vencovsky**: None; **L. Šenolt**: None; **M. Vrablik**: None; **J. Hubáček**: None; **M. Tomcik**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2074

Increased Mortality in Hispanic Males with Lymphopenia: A Descriptive and Statistical Analysis of Anti-Melanoma Differentiation-Associated Protein 5 (MDA-5) Antibody Positive Patients

Sergio Maldonado Chaar[1] and Kelly Corbitt[2], [1]University of Miami/Jackson Health, Miami, FL, [2]University of Miami Miller School of Medicine, El Portal, FL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-melanoma differentiation-associated protein 5 (MDA-5) antibody positivity in dermatomyositis (DM) is often associated with development of interstitial lung disease (ILD), with factors such as advanced age, male sex, lymphopenia, elevated ferritin and elevated lactate dehydrogenase (LDH) increasing mortality risk. Limited studies exist evaluating these risk factors in Hispanic patients. This retrospective study aims to evaluate these risk factors in a predominantly Hispanic population.

Methods: A retrospective cohort analysis was performed using electronic medical record data from 2021 to 2024 including all adult patients with a diagnosis code of either ILD and an abnormal myositis panel or DM. A total of 184 medical record numbers (MRNs) met these criteria. After confirming clinical diagnosis and filtering for positive anti-MDA5-antibodies, 17 MRNs were included. Lymphopenia was defined as an absolute lymphocyte count (ALC) less than 1000 cells/microliter. Advanced age was defined as 50 years or older. Data was analyzed using fisher exact testing.

Results: 29.4% (n=5) of patients were male and 70.6% (n=12) were female with a median age of 58 years. 76.0% (n=13) were Hispanic, including all males and 8 females. 7 patients (41.2%) had amyopathic DM, 4 (23.5%) had DM, and 6 (35.3%) had ILD without inflammatory myositis. 76.5% (n=13) of patients had ILD, including all of the males and 8 females. 23.5% (n=4) of patients were deceased, all of whom were males with ILD. Of 12 patients with advanced age, 25% (n=3) were deceased and 83.3% (n=10) had ILD. 9 patients had available LDH levels. Of these, five patients had elevated LDH and 4 were deceased. 8 patients had available ferritin levels, all of which were elevated. Of those patients, 88.5% (n=7; 3 males and 4 females) had ILD, and 37.5 % (n=3) were deceased. Lymphopenia was found in 35.3% (n=6; 4 males and 2 females). Mean ALC was 564 cells/microliter. Of these patients, 83.0% (n=5; 4 males and 1 female) had ILD and 66.7% (n=4) were deceased. A Fisher-exact-test showed significant associations between deceased and lymphopenia (p=0.006), males and lymphopenia (p=0.028), and males and deceased (p=0.002). There was no significant association of advanced age, elevated LDH level, and ILD with increased mortality. Elevated ferritin was not included in this analysis as all those tested had elevated levels.

Table 1: Comparison between males and females based on various classification groups.

Groups	Male	Female
Hispanic (%)	100.0	67.0
Median Age (years-old)	60.4	55.5
Average LDH (U/L)	255.0	301.0
Average Ferritin (ng/mL)	454.5	403.4
ILD (%)	100.0	69.0
Lymphopenia (%)	80.0	16.6
Average ALC (cells/μL) of Lymphopenic Patients	565.0	580.0
Mortality (%)	80.0	0.0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our cohort suggests a possible increased risk of mortality in anti-MDA5 antibody positive ILD patients who are male and have lymphopenia. We looked at a largely Hispanic population, which is underrepresented in anti-MDA5 antibody literature. Due to the limited sample size, larger cohorts should be examined to see if this association remains.

Disclosure: S. Maldonado Chaar: None; **K. Corbitt**: None.

Abstract Number: 2075

Ferritin trends differentiate anti-MDA5 Dermatomyositis from anti-Jo1 Antisynthetase Syndrome

Silvia Grazzini[1], Edoardo Conticini[1], Marco Fornaro[2], Chiara Rizzo[3], Lidia La Barbera[3], Maria Rosa Pellico[4], Stefano Stano[5], Florenzo Iannone[6], Giuliana Guggino[3], Nicoletta Del Papa[4], Luca Cantarini[7] and Bruno Frediani[7], [1]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Italy, Siena, Italy, [2]Unit of Rheumatology, Department of Precision and Regenerative Medicine, Area Jonica (DiMePRe-J), University of Bari, Italy., Bari, Italy, [3]Rheumatology Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties (ProMISE) University of Palermo, Palermo, Italy, [4]ASST Pini-CTO, Clinical Rheumatology Unit, Milano, Italy, [5]6. Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari, Bari, Italy, [6]Rheumatology DiMePReJ, University of Bari, School of Medicine, Bari, Italy, Bari, Italy, [7]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University Hospital of Siena, Siena, Italy, Siena, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Serum ferritin (FERR) is a recognized marker of immune activation and a key laboratory feature of anti-MDA5 Dermatomyositis (DM). It has been increasingly studied as a potential biomarker of disease activity, particularly due to its association with complications like rapidly progressive interstitial lung disease (RP-ILD), treatment response and prognosis. Its role in Antisynthetase Syndrome (ASS) remains less clear. This study aimed to assess the longitudinal variation of FERR and its correlation with disease activity in anti-MDA5 DM and, secondarily, to explore whether similar patterns were observed in matched anti-Jo1 ASS patients.

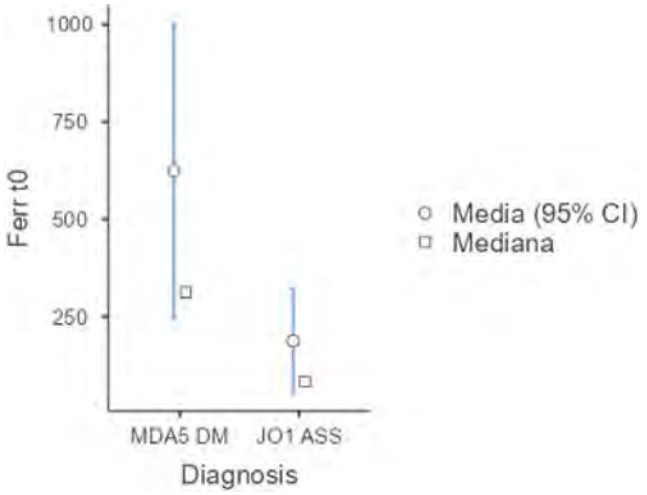


Image 1: serum ferritin levels at baseline.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

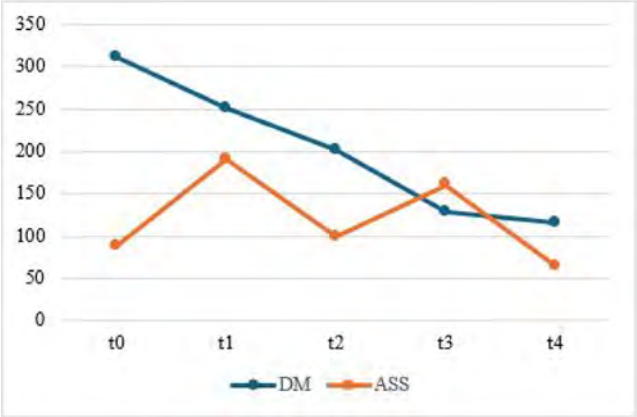


Image 2: serum ferritin levels during follow-up.

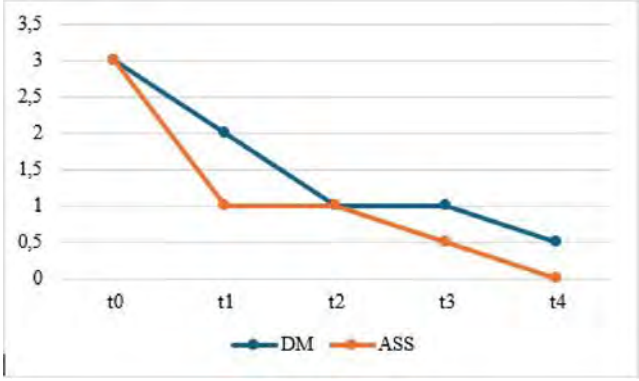


Image 3: PhGA trend during follow-up.

Methods: We retrospectively included adult patients with active anti-MDA5 DM or anti-Jo1 ASS (according to 2017 ACR/EULAR and Connor's criteria, respectively), all with ILD, evaluated across four Italian Myositis Centers. Inclusion criteria required demographic, clinical and serological data at baseline and at least two follow-up timepoints (3, 6, 12, and 18 months - t1, t2, t3 and t4, respectively). Disease activity was assessed by Physician Global Activity (PhGA). FERR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and creatinkinase (CK) were collected at each timepoint. Patients were treated according to local clinical practice, without a standardized therapeutic protocol.

Results: A total of 23 patients were included (11 DM, 12 ASS). Despite ASS patients exhibiting more extensive organ involvement - with 66% of them presenting ≥ 4 affected domains, compared to 36% in the DM group - baseline FERR was significantly higher in DM patients (median 312 vs 82 ng/mL, $p = 0.007$, **image 1**), while CK was increased in ASS (median 336 vs 101 U/L, $p = 0.05$). During follow-up, DM patients showed a progressive and significant reduction in FERR levels (**image 2**), with differences reaching statistical significance at 12 months (*t3 - t0*, $p = 0.025$) and 18 months (*t4 - t0*, $p = 0.017$). PhGA also significantly improved in DM group (*t2 - t0*, $p = 0.019$; *t3 - t0*, $p = 0.013$; *t4 - t0*, $p = 0.002$), closely mirroring the ferritin decline. In contrast, no significant changes in FERR were seen in ASS cohort, despite a parallel clinical improvement (*t4 - t0*, $p = 0.005$, **image 3**). CRP levels did not vary significantly in either group during follow-up and ESR showed fluctuating values without consistent trends.

Conclusion: To the best of our knowledge, this is the first study comparing longitudinal FERR trends in anti-MDA5 DM and anti-Jo1 ASS with lung involvement. In the DM cohort, FERR significantly declined over time along with disease activity, thus supporting its role as a biomarker in this subtype of myositis. The absence of a similar trend in ASS suggests differing inflammatory pathways and reinforces the need for disease-specific biomarkers. These findings may be especially relevant in the management of DM patients with lung involvement, where early and reliable indicators of response are urgently needed.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Despite limitations (small sample size, short follow-up, treatment heterogeneity), we believe that these findings offer preliminary evidence for the utility of FERR in monitoring anti-MDA5 DM: further prospective studies are needed to validate our results in larger and more diverse cohorts.

Disclosure: S. Grazzini: None; **E. Conticini**: GlaxoSmithKlein(GSK), 2, 6; **M. Fornaro**: None; **C. Rizzo**: None; **L. La Barbera**: None; **M. Pellico**: None; **S. Stano**: None; **F. Iannone**: None; **G. Guggino**: None; **N. Del Papa**: None; **L. Cantarini**: None; **B. Frediani**: None.

Abstract Number: 2076

Nutritional Discourse in Online Myositis Communities: A Reddit Analysis of Patient-led Discussions

Latika Gupta[1], **Taanya Talreja**[2] and Peter Kerkhof[3], [1]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom, [2]KEM Hospital, Mumbai, Maharashtra, India, [3]Department of Communication Science, Vrije Universiteit Amsterdam, Amsterdam, Netherlands

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The intersection of nutrition and autoimmune myopathies represents a significant yet understudied domain in rheumatological care. We conducted a meticulous analysis of online myositis communities to characterise the prevalence, content and temporal patterns of diet-related discussions amongst patients, providing insight into self-reported nutritional priorities that may inform clinical practice.

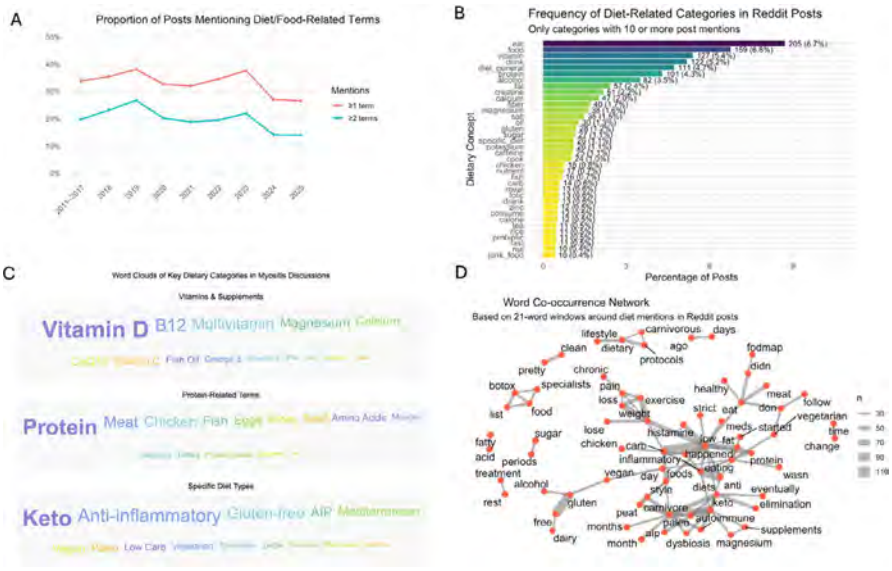
Methods: Using a bespoke Python script, we extracted all submissions (excluding comments) from the AcademicTorrents Reddit data dumps (2005–feb. 2025, ∼24 billion items), and added all posts from three myositis-focused subreddits, which in total yielded 17,902 posts. After rigorous filtering for relevance—retaining only posts explicitly mentioning myositis or related terminologies (e.g., necrotizing or inflammatory myopathy) with sufficient content—2,356 posts from 1,704 unique authors were analyzed (Figure 1A). An exhaustive lexicon of 190 precisely defined nutritional and dietary terms was systematically applied, with results subsequently classified into 77 discrete categories.

Results: Nutritional content featured prominently in myositis-related discourse, appearing in 31.5% of all posts and contributed by 36.1% of unique authors (Figure 1B). As demonstrated in Figure 1C, when categorized beyond general terminology (e.g., "eat", "food"), the most salient specific domains emerged as:

1. Vitamins and supplements, with particular emphasis on vitamin D
2. Protein consumption and its purported relationship to muscle health
3. Structured dietary approaches

Notably, within structured dietary approaches, ketogenic protocols garnered significant attention, followed by anti-inflammatory and autoimmune-specific regimens. The sophistication of these discussions reflects considerable patient engagement with nutritional literature, often citing both scientific studies and anecdotal experiences.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



We analyzed posts mentioning diet-related terms by extracting 21-word windows (±10 words) around each mention. After cleaning and filtering, we constructed a word co-occurrence network to visualize which concepts most frequently appear in close proximity to dietary references in patient-generated discussions (Fig. 1D). This word co-occurrence network, derived from Reddit posts mentioning "diet," reveals clusters of frequently associated terms, highlighting popular dietary approaches like keto and paleo, as well as the strong connection between diet and discussions around health, symptoms, and personal experiences. The thickness of the connecting lines indicates the frequency of these word pairings within a 21-word window

Conclusion: This comprehensive analysis reveals that nutritional considerations constitute a substantial component of patient-led myositis discussions, with particular emphasis on targeted supplementation and specialised diets. These findings highlight a critical opportunity for rheumatologists to address nutrition more systematically in clinical encounters and research agendas, potentially enhancing therapeutic approaches to this complex spectrum of disorders.

Disclosure: L. Gupta: None; **T. Talreja**: None; **P. Kerkhof**: None.

Abstract Number: 2077

Statin-Associated Immune-Mediated Necrotizing Myopathy in Native Americans

Tam Dinh[1], Evelyn Inga[1], Janelle Francisco[1], Yvonne Waters[1], Krystle Tapia[2], Maheswari Muruganandam[3], N. Suzanne Emil[1], Frank O'Sullivan[1] and Wilmer Sibbitt[3], [1]University of New Mexico, Albuquerque, [2]University of New Mexico Hospital, Albuquerque, NM, [3]University of New Mexico, Albuquerque, NM

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Immune-mediated necrotizing myopathy (IMNM) is an aggressive subtype of idiopathic inflammatory myopathy (IIM) associated anti-3-hydroxy-3-methylglutaryl coenzyme A reductase (anti-HMGCR) antibodies. Recently there have been reports of increased statin-associated IMNM in certain Native American groups. To address this, this research compared the proportion, characteristics, and clinical outcomes of Native American and non-Native American adults diagnosed with IIM and IMNM from the same Southwest region.

Methods: This is a retrospective single institution study approved by the Institutional Review Board. Myositis diagnosis was established based on the 2017 European Alliance of Associations for Rheumatology/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies, and statin-associated IMNM diagnosis required the presence of anti-HMGCR antibodies. We identified 147 patients with IIM, with 32 patients who self-identified as Native American and 115 patients who self-identified as non-Native American. The proportion of IIM and IMNM in each group, the relevant clinical and laboratory parameters, and the outcomes were compared.

Results: Table 1 shows the baseline characteristics for the two groups. Compared to non-Native Americans, Native Americans with IIM had higher incidence of hyperlipidemia (HLD) (75% compared to 49.6%; p=0.015), statin exposure at diagnosis (71.9% compared to 40.0%; p=0.002), pre-existing diabetes mellitus (DM) (62.5% compared to 34.8%; p=0.044), and esophageal dysmotility (93.8% compared to 77.4%; p=0.042).

Table 1. Inflammatory Myositis in Native Americans and Non-Native Americans

	Native Americans	Non-Native Americans*		
Number	32	115	Confidence Interval** or Odds Ratio ***	P value
Age (years)	58.3±15.5	61.5±15.2	CI: -9.2 <-3.2<5.8	0.30
Women	71.9 % (23/32)	68.7% (79/115)	OR: 1.16 CI: (0.49, 2.77)	0.83
Men	28.1 % *(9/32)*	31.3% (36/115)	OR: 0.86 CI: (0.36, 2.04)	0.83
Diabetes Mellitus	62.5% (20/32)	34.8% (40/115)	OR: 2.41 CI: (1.08, 5.4)	0.044
Hyperlipidemia	75.0% (24/32)	49.6% (57/115)	OR: 3.05 CI: (1.27, 7.36)	0.015
Malignancy	6.3% (2/32)	17.4% (20/115)	OR: 0.3 CI: (0.07, 1.34)	0.16
Age at myositis diagnosis	54.1±15.8	55.2±16.8	CI: -5.7<-1.1< 3.5	0.74
Disease Duration (Months)	57.8±49.6	77.2±67.8	CI: -44.8<-19.4<6.0	0.11
Statin Exposure at Diagnosis	71.9% (23/32)	40.0% (46/115)	OR: 3.83 CI: (1.63, 9.02)	0.002
Creatine Kinase at Presentation (IU)	6532±6641	5785±12118	CI: -3667<747<5161	0.74
Abnormal MRI of muscle	92.9% (13/14)	84.0% (42/50)	OR: 2.48 CI: (0.28, 21.7)	0.67
Abnormal Muscle Biopsy	95.2% (20/21)	100% (66/66)	OR: Not applicable.	0.24
Proximal Muscle Weakness	93.8% (30/32)	92.2% (106/115)	OR:1.27 CI: (0.26, 6.21)	1.00
Distal Muscle Weakness	21.9% (7/32)	21.7% (25/115)	OR:1.01 CI: (0.39, 2.6)	1.00
Inflammatory Arthritis	9.4% (3/32)	37.4% (43/115)	OR: 0.11 CI: (0.03, 0.49)	0.002
Distal Scleroderma	9.4% (3/32)	4.3% (5/115)	OR: 2.28 CI: (0.51, 10.1)	0.37
Proximal Scleroderma	6.3% (2/32)	6.1% (7/115)	OR: 1.02 CI: (0.20, 5.21)	1.00
Telangiectasia	12.5% (4/32)	13.0% (15/115)	OR: 0.95 CI: (0.29, 3.10)	1.00
GERD/Esophageal dysmotility	93.8% (30/32)	77.4% (89/115)	OR: 4.38 CI: (0.98, 19.57)	0.042
Raynaud's Phenomenon	28.1% (9/32)	24.3% (28/115)	OR: 1.23 CI: (0.51, 2.93)	0.65
Heliotrope Rash	15.6% (5/32)	27.0% (31/115)	OR: 0.5 CI: (0.18, 1.42)	0.25
Shawl Sign	12.5% (4/32)	20.0% (24/115)	OR: 0.54 CI: (0.17, 1.69)	0.44
Groton's Sign	12.5% (4/32)	20.9% (13/115)	OR: 1.12 CI: (0.34, 3.71)	0.76
Groton's Papules	9.4% (3/32)	11.3% (13/115)	OR: 0.81 CI: (0.22, 3.04)	1.00
Photosensitivity Dermatitis	18.8% (6/32)	26.1% (30/115)	OR: 0.65 CI: (0.25, 1.74)	0.49
Dilated Capillary Loops	15.6% (5/22)	18.3% (21/115)	OR: 0.83 CI: (0.29, 2.40)	1.00
Hyperpigmentation	25.0% (8/32)	23.5% (27/115)	OR: 1.09 CI: (0.44, 2.70)	0.82
Subcutaneous calcifications	9.4% (3/32)	2.6% (3/115)	OR: 3.86 CI: (0.14, 20.14)	0.12

* Non-Native Americans consisted of 100 Caucasians, 9 African Americans, and 5 Asian Americans.
**95% Confidence Interval (CI) of difference of means (Wald) for measurement data.
***Odds Ratio (OR) with 95% Confidence Interval (CI: (lower, upper)).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical Outcomes of Statin-Associated Immune-Mediated Necrotizing Myopathy in Native Americans and Non-Native Americans

	Native Americans	Non-Native Americans		
Number	15	19	Confidence Interval* or Odds Ratio **	P value
Disease Duration (Months)	32.9±27.9	48.7±29.8	CI: -36.2<-15.8< 4.6	0.12
Length of Time to Normalize Creatine Kinase (Months)	26.5±26.7	23.4±26.7	CI: -15.7<3.1< 21.9	0.74
Use of High Dose Corticosteroids for Induction	93.3% (14/15)	100% (19/19)	OR: not applicable	0.44
Rituximab	20.0% (3/15)	34.3% (5/19)	OR: 0.70 CI: (0.14, 3.56)	1.00
Intravenous immunoglobulin	66.7% (10/15)	42.9% (14/19)	OR: 0.71 CI: (0.71, 3.14)	0.72
Methotrexate	46.7% (7/15)	54.3% (9/19)	OR: 0.97 CI: (0.25, 3.77)	1.00
Mycophenolate	26.7% (4/15)	25.7% (4/19)	OR: 1.36 CI: (0.28, 6.68)	1.00
Azathioprine or Mercaptopurine	33.3% (5/15)	37.1% (4/19)	OR: 1.88 CI: (0.40, 8.74)	0.46
Ongoing therapy necessary for myositis syndrome	73.3% (11/15)	68.4% (13/19)	OR: 1.27 CI: (0.28, 5.68)	1.00
Creatine Kinase Most Recent Visit	1222±2149	740±1094	CI: -673 <482< 1637	0.40
Pulmonary Artery Hypertension	13.3% (2/15)	14.3% (3/19)	OR: 0.97 CI: (0.14, 6.67)	1.00
Pulmonary Artery Pressure (PAP) mm Hg****	23.5±9.0	20.6±14.6	CI: -5.9<2.9< 11.7	0.51
Cancer Diagnosis	6.7% (1/15)	31.4% (4/19)	OR: 0.27 CI: (0.03, 2.7)	0.35
Interstitial Lung Disease	0% (0/15)	5.3% (1/19)	OR: not applicable	1.00
Work Disability	46.7% (7/15)	57.9% (11/19)	OR: 0.64 CI: (0.16, 2.49)	0.73
All Cause Death over Observational interval	33.3% (5/15)	31.6% (6/19)	HR: 1.08*** CI: (0.26, 4.6)	1.00

*95% Confidence Interval (CI) of difference of means (Wald) for measurement data.
**Odds Ratio (OR) with 95% Confidence Interval (CI: (lower, upper)).
***Hazard Ratio (HR) with 95% Confidence Interval (CI: (lower, upper)).
**** Pulmonary Artery Pressure (PAP) estimated with right ventricular systolic pressure (RVSP)

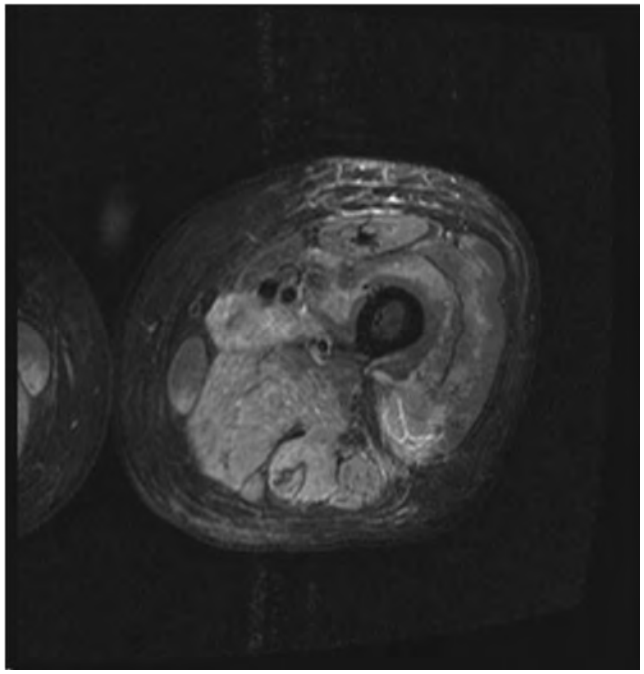


Figure 1. Muscle Edema by Magnetic Resonance Imaging in a Native American Patient Diagnosed with Immune-Mediated Necrotizing Myopathy

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Additionally, Native Americans were found to have significantly higher frequency of positive anti-HMGCR antibody, with 46.9% compared to 16.5% in non-Native Americans (p=0.0007). Native Americans also had higher frequency of positive anti-RNP antibody, with 15.6% compared to 2.6% in non-Native Americans (p=0.013). There was no significant difference in the clinical outcomes and treatment received between the two groups (Table 2). When statin-associated IMNM was specifically compared between the two groups, there were no significant differences in IMNM clinical features or outcomes. This has not been reported before.

Conclusion: Statin-associated IMNM is increased in Native Americans compared to non-Native Americans in the American Southwest. There may be underlying genetic or environmental components to explain the findings above, including certain HLA types, an increased prevalence of diabetes mellitus, hyperlipidemia, and statin exposure. However, the manifestations and outcomes of statin-associated IMNM in Native Americans and non-Native Americans appear to be similar. Given that the outcome of statin-associated IMNM depends on early initiation of appropriate therapy and that Native Americans historically have experienced healthcare disparities, it is particularly important that statin-associated IMNM in this population is recognized and treated early.

Disclosure: T. Dinh: None; **E. Inga**: None; **J. Francisco**: None; **Y. Waters**: None; **K. Tapia**: None; **M. Muruganandam**: None; **N. Emil**: None; **F. O'Sullivan**: None; **W. Sibbitt**: None.

Abstract Number: 2078

Neutrophil Extracellular Traps from Patients with Idiopathic Inflammatory Myopathies Induce Interferogenic Responses in Macrophages and Myeloid Dendritic Cells

Yatzil Reyna Juarez[1], Jennifer Tiaré Balderas Miranda[2], Beatriz Alcalá Carmona[3], María José Ostos Prado[4], karina santana[5], Diana Gómez-Martín[6] and Jiram Torres Ruiz[7], [1]Instituto Politècnico Nacional, Tultitán de Mariano Escobedo, Mexico State, Mexico, [2]Universidad Nacional Autónoma de México, Coyoacán, Federal District, Mexico, [3]INCMNSZ, Cdmx, Distrito Federal, Mexico, [4]Instituto Nacional De Ciencias Médicas Y Nutrición Salvador Zubirán, Mexico City, Distrito Federal, Mexico, [5]INCMNSZ, Ciudad de México, Federal District, Mexico, [6]INCMNSZ, Mexico city, Federal District, Mexico, [7]INCMNSZ, Mexico, Federal District, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2052–2078) Muscle Biology, Myositis & Myopathies – Basic & Clinical Science Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Dermatomyositis (DM) and anti-synthetase syndrome (AS) are idiopathic inflammatory myopathies (IIM) with perifascicular pathology involving vasculopathy, macrophages, dendritic cells and an overexpression of interferon-stimulated genes. Increased production and deficient elimination of neutrophil extracellular traps (NETs) are characteristic of the IIM, but their role as inducers of proinflammatory responses in the perifascicular pathology has not been addressed. The aim of this study was to assess the potential contribution of NETs to the perifascicular pathology in IIM.

Methods: We included 5 healthy donors (HD), 13 patients with DM and 12 with AS according to the ACR/EULAR 2017 and Connors' criteria, either with moderate to severe disease activity or complete clinical response. We assessed the localization of macrophages and NETs in the muscle biopsies by confocal microscopy. From peripheral blood, we isolated normal density neutrophils to obtain spontaneous NETs and CD14+ monocytes for *in vitro* differentiation into macrophages and mDC for 7 days. Differentiated macrophages and myeloid dendritic derived cells from patients (PDM and PDmDC) and HD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

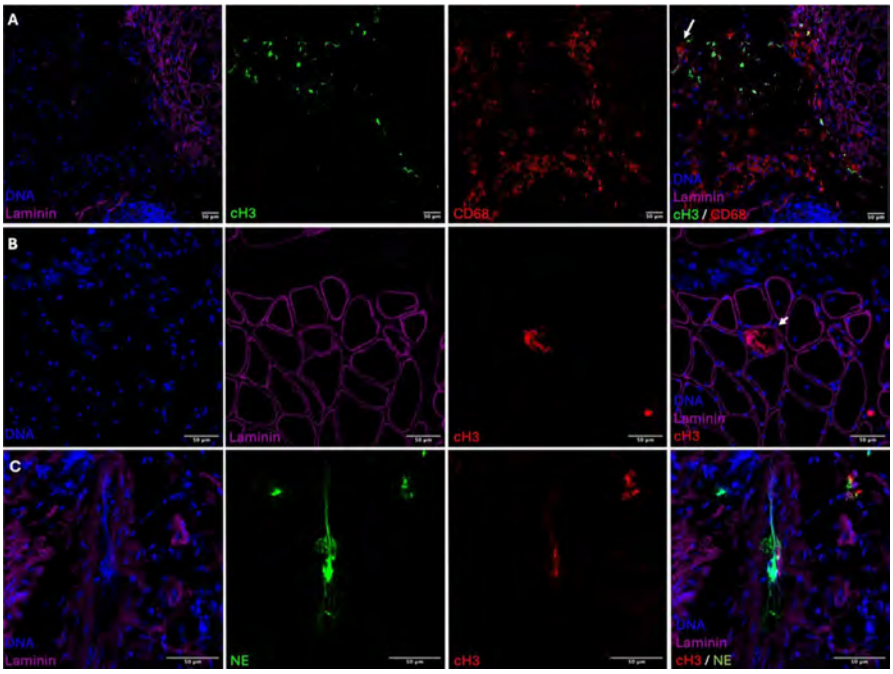


Figure 1. Localization of NETs in key areas of perifascicular pathology. Macrophages interact with NETs in the perifascicular area (A). NETs are internalized by muscle cells (B) and neutrophils produce NETs in the intravascular space (C).

(HDM and HDmDC) were then stimulated for 6 hours with 50 μg of spontaneous NETs from patients and HD. Interferon signature was assessed by RT-qPCR differential gene expression of ISG15, IFI44, IFI44L, IFIT1, IFI27, CXCL9, RSAD2 (ΔΔCt equation) and IFN score was obtained by compound Z score.

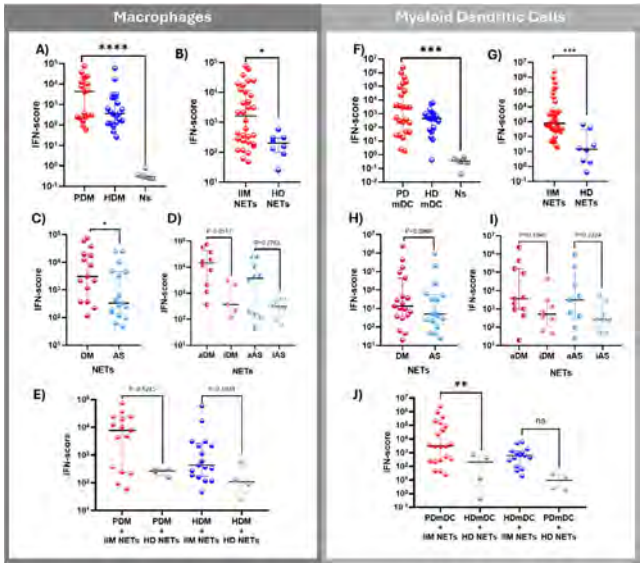


Figure 2. In vitro evaluation of interferon score induction in macrophages and myeloid dendritic cells stimulated with NETs. Each figure represents an individual value. Bars represent the median and lines the interquartile range. Each figure represents an individual value. Bars represent the median and lines the interquartile range. (A) IFN-score in patients-derived macrophages (PDM) and healthy donor-derived macrophages (HDM), with or without NET stimulation (Ns). (B) IFN-score in HDM stimulated with NETs derived from IIM patients or healthy donors. (C) IFN-score in HDM stimulated with NETs from patients with dermatomyositis (DM) or antisynthetase syndrome (AS). (D) IFN-score in HDM stimulated with NETs from patients with active (aDM, aAS) or inactive (iDM, iAS) disease. (E) IFN-score in macrophages according to both cell origin (HDM vs PDM) and NET origin (HD vs IIM). (F) IFN-score in myeloid dendritic cells (mDCs) from patients (PDmDC) and healthy donors (HDmDC), with or without NET stimulation. (G) IFN-score in HDmDC and PDmDC stimulated with NETs from IIM patients or healthy donors. (H) IFN-score in mDCs stimulated with NETs from patients with DM or AS. (I) IFN-score in mDCs stimulated with NETs from patients with active (aDM, aAS) or inactive (iDM, iAS) disease. (J) IFN-score in mDCs based on both cell origin (HDmDC vs PDmDC) and NET origin (HD vs IIM). Mann-Whitney U test and Kruskal-Wallis test with Dunn post-hoc test; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: As shown in Figure 1, NETs are localized in key areas of perifascicular pathology, interacting with macrophages (A), inside muscle cells (B) and in the blood vessels (C). Stimulation with NETs significantly increased IFN-scores in patient and HD-derived macrophages and mDC compared to non-stimulated (Ns) cells (Figure 2 A and F). NETs isolated from IIM patients induced significantly stronger IFN responses than NETs from HD in both macrophages and mDCs (*Figure 2B, 2G*). Stratification by disease subtype revealed that NETs from DM patients elicited higher IFN-scores than those from AS patients in macrophages ($p = 0.0354$, *Figure 2C*), though this difference was not observed in mDCs (*Figure 2H*). No significant differences were detected based on disease activity (active vs inactive disease) in either cell type (*Figure 2D, 2I*). When analyzing combinations of cell type and NET origin, NETs from IIM patients consistently induced higher IFN responses across all cell types. In mDCs, IIM-derived NETs triggered significantly higher IFN-scores than HD-derived NETs in PDmDCs ($p < 0.01$, *Figure 2J*), while the difference in macrophages did not reach statistical significance (*Figure 2E*).

Conclusion: NETs from IIM patients trigger strong type I IFN responses in macrophages and mDC, particularly in cells derived from patients. This suggests that both, the composition of IIM NETs and the heightened response of *in vivo* primed myeloid cells contribute to the sustained IFN activity characteristic of IIM, pointing to a possible pathogenic loop of NETs driving chronic inflammation.

Disclosure: Y. Reyna Juarez: None; **J. Balderas Miranda**: None; **B. Alcalá Carmona**: None; **M. Ostos Prado**: None; **k. santana**: None; **D. Gómez-Martín**: None; **J. Torres Ruiz**: None.

Abstract Number: 2079

Association Between Symptomatic Knee Osteoarthritis and Health-related Quality of Life in Individuals with Type 2 Diabetes: A Cross-sectional Study

Abdalmohsen Almodahka[1], Alanna Weisman[2], Baiju Shah[3], Tristan Watson[4], Ian stanaitis[5], Amish Parikh[6], Robert Goldberg[6], Lorraine Lipscombe[7], Gillian Hawker[1] and Lauren King[1], [1]University of Toronto, Toronto, ON, Canada, [2]University Health Network Toronto General Hospital Site/Sinai Health System, Toronto, ON, Canada, [3]Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [4]Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada, [5]Research and Innovation Institute, Women's College Hospital, Toronto, ON, Canada, Toronto, ON, Canada, [6]Division of Endocrinology, Department of Medicine, Trillium Health Partners, Mississauga, ON, Canada, Toronto, ON, Canada, [7]Department of Medicine, University of Toronto, Research and Innovation Institute, Women's College Hospital, Toronto, ON, Canada, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Knee osteoarthritis (OA) and type 2 diabetes (T2D) commonly coexist, but their combined impact on health-related quality of life (HRQoL) remains understudied. Our objective was to assess the relationship between symptomatic knee OA (yes/no) and HRQoL in persons with type 2 diabetes and, if a relationship was found, to determine if it is due to depressed mood, sleep disturbance, fatigue, and/or walking limitation, which we hypothesized could be explanatory factors.

Methods: We conducted a secondary analysis of a cross-sectional study of individuals with T2D recruited from endocrinology clinics at three academic hospitals in Canada. Participants completed standardized online questionnaires that assessed sociodemographic factors, comorbidities to calculate the Functional Comorbidity Index (FCI), depressed mood (PROMIS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

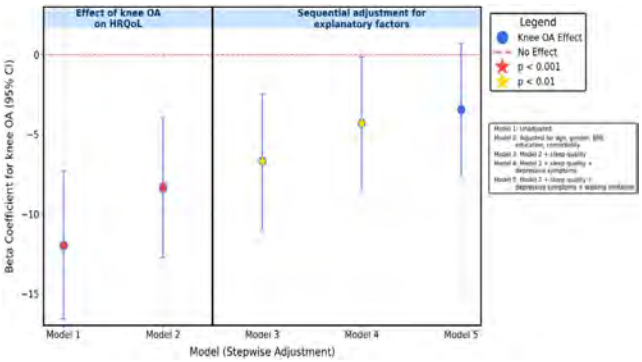


Figure 1: Linear regression modeling demonstrating the association between knee osteoarthritis and health-related quality of life before and after adjusting for potential confounders and sequential adjustment for potential explanatory factors.

Depression 8b), sleep disturbance (PROMIS Sleep Disturbance 4a), fatigue (PROMIS Fatigue 4a), walking limitation (Health Assessment Questionnaire walking difficulty item), HRQoL (EQ-VAS, 0–100), and joint symptoms. Symptomatic knee OA was defined using NICE criteria (age ≥45 years, activity-related knee pain, morning stiffness ≤30 minutes; no inflammatory arthritis). Linear regression modelled associations between knee OA and HRQoL, adjusting for age, gender, BMI, education, and comorbidities. The explanatory effects of sleep disturbance, depressed mood, and mobility limitation were assessed via sequential adjustment.

Results: Our study included 341 participants. Mean age was 66.4 (SD 9.7) years, 51.9% were women, 80.1% had post-secondary education, mean BMI was 29.1 (SD 6.7) kg/m^2, and 99 (29.0%) fulfilled NICE criteria for symptomatic knee OA (Table 1). Median HRQoL (EQ-VAS) was 68/100 (IQR 50, 80), with lower scores reported by individuals with knee OA

Table 1. Characteristics of participants by symptomatic knee osteoarthritis status (N = 341)

Table 1. Characteristics of participants by symptomatic knee osteoarthritis status (N = 341)

Characteristic	Overall	With OA (N =99)	Without OA (N=242)	p-value
Demographics				
Age, years, mean (SD)	66.4 (9.7)	65.9 (9.6)	66.6 (9.8)	0.61
Gender: Woman - n (%)	177 (51.9%)	56 (56.6%)	115 (47.5%)	0.09
Post-secondary education – n (%)	273 (80.1%)	77 (77.8%)	196 (81.0%)	0.90
Race and Ethnicity				
Asian[1]	69	19	50	
Black	14	7	7	
Indigenous	10	4	6	
Jewish	32	7	25	0.17
Multiracial	32	9	23	
Other[2]	18	9	9	
White	164	43	121	
Clinical Characteristics				
Diabetes management				
Diet control/diabetes diet	174 (51%)	52 (52.5%)	122 (50.4%)	0.81
Physical activity/exercise	149 (43.7%)	45 (45.5%)	104 (43%)	0.77
Oral antihyperglycemic agents	292 (85.6%)	89 (89.9%)	203 (83.9%)	0.21
Insulin injections	162 (47.5%)	54 (54.5%)	108 (44.6%)	0.12
GLP-1 receptor agonists	102 (29.9%)	37 (37.4%)	65 (26.9%)	0.07
Diabetes complications[3](yes), n (%)	109 (31.9%)	36 (36.4%)	73 (30.2%)	0.32
BMI (kg/m^2) Mean (SD)	29.1 (6.7)	31.9 (7.2)	27.9 (6.1)	<0.0001
FCI Median (IQR)	3.0 (2, 4)	3.0 (2, 5)	2.0 (1, 4)	0.0065
Potential Explanatory Factors				
Sleep T score - Mean (SD)[4]	51.1 (8.9)	53.9 (8.5)	49.9 (8.7)	0.0001
Fatigue T score - Mean (SD)[4]	51.7 (10.7)	57.1 (9.9)	49.5 (10.2)	<0.0001
Depression T score - Mean (SD)[4]	49.9 (10.4)	54.9 (10.4)	47.9 (9.8)	<0.0001
Walking Limitation (yes), n (%)[5]	124 (36.4%)	54 (54.5%)	70 (28.9%)	<0.0001
Quality of Life Measures				
EQ-VAS Score (0-100): Median (IQR)	68 (50, 80)	54 (40, 70)	70 (50, 80)	<0.0001

[1] "Asian" includes East Asian, South Asian, Southeast Asian, Central Asian, and West Asian populations
[2] "Other" includes Middle Eastern, Latin American, individuals who preferred not to answer, or those whose background was not listed
[3] Diabetes complications refer to the presence of microvascular complications, including neuropathy, nephropathy, or retinopathy (i.e., impact on nerves, kidneys, or eyes), self-reported by participant.
[4] Sleep, Fatigue, and Depression T scores were measured using the Patient-Reported Outcomes Measurement Information System (PROMIS).
[5] Dichotomized as "Yes" if participants reported walking with some, much, or complete difficulty; "No" if without any difficulty (HAQ walking item)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(median 54 vs. 70). Compared to those without OA, participants with knee OA had worse sleep, fatigue, depressive symptoms, and higher rates of walking limitation ($p < 0.0001$ for all). After adjustment for age, gender, BMI, education, and comorbidities, the presence of symptomatic knee OA remained associated with lower HRQoL (β = −8.33, 95% CI: −12.72 to −3.94). Model performance improved with sequential adjustment, with adjusted R^2 increasing from 0.068 in the unadjusted model to 0.381 in the final model. The association was fully attenuated in the final model including sleep, mood, and walking limitation (β = −3.46, 95% CI: −7.63 to 0.71) (Figure 1).

Conclusion: Symptomatic knee OA is strongly associated with impaired HRQoL in T2D, explained by sleep disturbance, low mood, and mobility limitation. Integrated care addressing OA may improve quality of life in this population.

Disclosure: A. Almodahka: None; **A. Weisman**: None; **B. Shah**: None; **T. Watson**: None; **I. stanaitis**: None; **A. Parikh**: None; **R. Goldberg**: None; **L. Lipscombe**: None; **G. Hawker**: None; **L. King**: None.

Abstract Number: 2080

Foot laterality does not modify outcome of knee and/or hip osteoarthritis

Simon Fondin[1], Armand Eyraud[1], Estelle Nkonda[1], Anne-Christine Rat[2], Bruno Fautrel[3], SELLAM JEREMIE[4], Christian Roux[5], Jacques Pouchot[6], Joel Coste[7], Francis Guillemin[8] and **Alain SARAUX**[9], [1]Centre Hospitalier Regional Universitaire (CHU) de Brest, Brest, France, [2]Caen University hospital, UMR 1075 Caen normandy university, Caen, France, [3]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [4]Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, CRSA, F-75012 Paris, France, /Rheumatology Department, AP-HP Saint-Antoine Hospital, 184, rue du Faubourg Saint-Antoine, 75012, Paris, France., Paris, France, [5]CHU Nice, Nice, France, [6]AP-HP, Rueil Malmaison, France, [7]APHP, Paris, France, [8]CHU Nancy, Nancy, France, [9]CHU Brest, Brest, France

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hip and knee osteoarthritis (OA) are among the leading causes of global disability. Global OA is more prevalent on the right side. This discordance in symmetry suggests an importance of biomechanical factors, including dominant side, in the pathogenesis of OA. The objective of this study is to investigate the relationship between the foot dominant side and the most symptomatic side and location in knee or hip OA, as well as its evolution over a 10-year follow-up.

Methods: The KHOALA (Knee and Hip Osteoarthritis Long-term Assessment) cohort is a representative, population-based multicenter study that included 878 patients with symptomatic knee and/or hip OA, aged between 40 and 75 years, and established between 2007 and 2009. They were asked at year 6 whether they were right-handed, left-handed, left-handed contrarian, or ambidextrous, as well as which foot they used to kick a ball. Khi^2 or Fisher tests were used for binary variables, while Student's t-test was used for continuous variables.

Results: From 538 patients evaluated for laterality, 47 (8.7%) were left footers. Among the 47 left footers, only 14 were left handers (20 are right handers, 3 ambidextrous, and 10 frustrated left-handers). Proportion of right and left knee OA, among patients with unilateral OA, were 58.6% (212/364) and 41.8% (152/364), respectively. Proportion of right and left hip OA were 51.6% (78/151) vs 48,3% (73/151), respectively. Left footers were slightly younger (59.0 SD 8.1 vs 61.6 SD 8.0 years; p=0.04) and more frequently men (52.2% vs 30.2%; p=0.004) than right footers. At 0, 5 and 10 years, pain did not differ between left footers and right footers. In contrast, WOMAC was lower in left footers than in right footers at year 0 (24.3 SD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

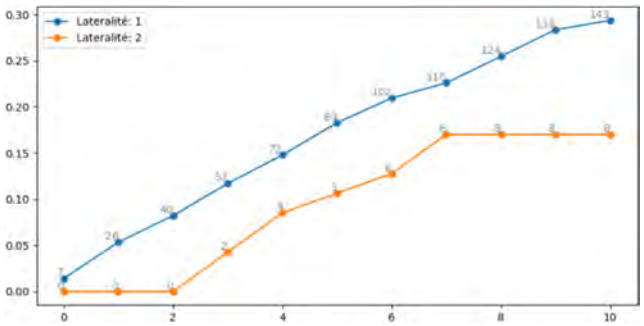


Fig 1

16.6 vs 32.8 SD 19.7; p=0.002), year 5 ((26.0 SD 17.1 vs 32.3 SD 17.7; p=0.02), and year 10 (26.0 SD 14.5 vs 31.6 SD 18.9; p=0.05). WOMAC function was also lower in left footers than in right footers at year 0 (23.6 SD 18.0 vs 32.3 SD 21.0; p=0.004), year 5 (25.0 SD 17.4 vs 31.8 SD 18.4; p=0.02), and year 10 (25.4 SD 15.7 vs 31.4 SD 19.9; p=0.05). There was not any difference for radiological stage (Kellgren Lawrence). After 10 years right footers did not received significantly more hip or knee replacement of the more painful joint than left footers (29.9%, 143/478, versus 18.2%, 8/44, respectively; p=0.13) (Fig 1).

Conclusion: Womac function is lower in left than in right footers suffering from symptomatic knee and/or hip OA, but we did not observe any difference between right and left footers for pain, radiograph and evolution.

Disclosure: S. Fondin: None; **A. Eyraud**: None; **E. Nkonda**: None; **A. Rat**: AbbVie/Abbott, 6, Eli Lilly, 6, Galapagos, 6, Merck/MSD, 6; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **S. JEREMIE**: None; **C. Roux**: None; **J. Pouchot**: None; **J. Coste**: None; **F. Guillemin**: None; **A. SARAUX**: Novartis, 6.

Abstract Number: 2081

Radiologic surveillance in the Phase II RCT of LEVI-04, a novel neurotrophin-3 inhibitor, in people with knee osteoarthritis: exclusions at screening

Ali Guermazi[1], Philip Conaghan[2], C Michael Perkins[3], Claire Herholdt[4], Iwona Bombelka[5] and Simon Westbrook[6], [1]Boston University, West Roxbury, MA, [2]University of Leeds, Leeds, United Kingdom, [3]Levicept, Sandwich, United Kingdom, [4]Levicept Ltd, Ashtead, United Kingdom, [5]Levicept, Sandwich, Kent, United Kingdom, [6]Levicept Ltd, Sandwich, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: LEVI-04 is a first-in-class fusion protein (p75NTR-Fc) that supplements the endogenous p75NTR binding protein, providing analgesia via inhibition of NT-3 activity. Like p75NTR, LEVI-04 binds all the neurotrophins (NTs) with differing affinities, with highest to NT-3 and lowest affinity and reversibly to NGF, distinguishing the LEVI-04 mechanism of action from that of anti-NGF antibodies. As serious joint adverse events were seen in the anti-NGF trials, rigorous

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	X-Ray			MRI
	Knees	Hips	Shoulders	Knees
Number of Participants with Imaging Performed, n	1253	1253	1253	766
Number of Participants Excluded, n (%)	514[1] (41.0)	30 (2.4)	4 (0.3)	234 (30.5)
Reasons for exclusion[2], n (%)				
Posterior Meniscal Root Tear	0	N/A	N/A	168 (22.9)
KL<2 in the target knee	108 (8.6)	N/A	N/A	N/A
Excessive Malalignment	43 (3.4)	N/A	N/A	0
Atrophic OA	42 (3.3)	7 (0.6)	0	0
Subchondral Insufficiency Fracture	19 (1.5)	0	2 (0.3)	42 (5.4)
Congenital Hip Dysplasia with Degenerative Joint Disease	N/A	12 (1.6)	N/A	N/A
Articular Bone Fragmentation	6 (0.5)	2 (0.3)	0	3 (0.4)
Inflammatory Joint Disease	0	0	0	10 (1.3)
Primary/Metastatic Tumor[3]	1 (0.1)	0	0	7 (0.9)
Severe Pseudogout	7 (0.6)	1 (0.1)	0	0
Extensive Subchondral Cysts	6 (0.5)	4 (.)	0	3 (0.4)
Stress Fracture/Reaction	0	0	0	6 (0.8)
Osteochondritis Dissecans	1 (0.1)	0	0	3 (0.4)
Osteonecrosis	0	4 (0.3)	0	4 (0.5)
Recent Fracture	0	1 (0.1)	1 (0.1)	5 (0.7)
Paget's Disease	0	1 (0.1)	0	0
Significant Articular Bone Loss	1 (0.1)	0	0	0
Synovial chondromatosis	1 (0.1)	0	0	4 (0.5
Severe bone marrow reconversion	0	0	0	2 (0.3)
Enchondroma (large)	1 (0.1)	0	0	1 (0.1)
Hereditary Multiple Osteochondromatosis (HMO)[4]	2 (0.3)[4]	1 (0.1)[4]	1 (0.1)[4]	0
Heterotopic Ossification	1 (0.1)	0	0	0
Lipoma (large)	0	0	0	1 (0.1)
Medial Meniscal Cyst (large, complex)	0	0	0	1 (0.1)
Chronic Osteomyelitis	0	0	0	1 (0.1)

[1]Includes 207 (left knee) and 188 (right knee) exclusions for KL<2; for inclusion only one knee was required to meet KL ≥ 2, therefore the final number excluded due to KL <2 was 108.

[2]Some patients presented more than one finding, potentially in more than one joint in the same patient, so the number of exclusions exceeds the number of people excluded.

[3]Findings suggestive of the following tumors were detected on X-ray: large benign bone tumor of the femur (unicameral bone cyst) with risk of pathological fracture (1); and on MRI: tenosynovial giant cell tumor of the Hoffa-fat pad (4), tenosynovial giant cell tumor of the patellar tendon (1), tenosynovial giant cell tumor around the knee (1) and large benign enchondroma of the femur (with possibility of low grade chondrosarcoma)

[4]HMO was reported for knees (bilateral), hip, and shoulder X-rays for one patient.

Radiologic Exclusions

surveillance of joint safety was performed in this study. In order to properly categorise the risk of adverse joint events with LEVI-04, participants with potentially confounding findings at screening were excluded. LEVI-04 was well tolerated, with no increased incidence of joint pathologies compared to placebo.[1]

Methods: This was a phase II multicentre (Europe and Hong Kong) RCT in adults with knee OA. Participants were randomized to 4-weekly IV placebo or 0.3, 1, or 2 mg/kg LEVI-04 through week 16, with the final visit at week 20 and a telephone safety follow-up at week 30. Participants who met initial clinical inclusion criteria underwent X-rays of bilateral shoulders, hips and knees, and then MRI of both knees (in some cases, MRI was performed in parallel with X-rays). All images were read centrally and assessed for eligibility. At week 20, all X-rays were repeated, and MRI of the target knee was performed.

Results: 1598 people with painful knees were screened and 518 participants enrolled. 1080 people (86%) did not proceed past screening. 345 people exited the study before X-rays were performed (151 due to not meeting initial minimum pain in at least one knee, others due to other entry criteria, or sponsor, investigator or participant decision), such that a total of 1253 participants had X-rays of the large joints (Table 1). 514 (41%) people had knee exclusion criteria on X-ray, however this included 207 (left) and 188 (right) knees of KL grade< 2. Only one knee was required to have KL grade >2, resulting in 108 (8.6%) people failing on KL grade. Excessive malalignment and atrophic OA were the next highest criteria, with 43 (3.4%) and 42 (3.3%) failures respectively. 766 people proceeded to MRI of both knees. 234 (30.5%) of these failed, 168 (22.9%) due to meniscal root tear, and 42 (5.4%) due to subchondral insufficiency fracture. There were 7 (0.9%) cases of findings suggestive of primary or metastatic tumor detected on MRI and 1 (0.1%) on knee X-ray. 30 (2.4%) people were excluded on hip and 4 (0.3%) on shoulder X-rays. 5 hip and 24 knee joints had arthroplasty, but these were not exclusionary. Several people exhibited more than one pathology, so reasons for exclusion slightly exceed the total number of people excluded.

Conclusion: A significant proportion of people with OA show radiologic findings at screening. Excluding these patients is important to distinguish existing pathologies from treatment-emergent events in early trials. Rigorous radiologic surveillance supported determination of LEVI-04 joint safety; LEVI-04 was not associated with an increase in adverse joint events compared to placebo in this study[1]. Phase 3 trials are in planning.

1. Conaghan P, et al. Arthritis Rheumatol. 2024;76 (suppl 9).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Guermazi: 4Moving, 2, BICL, LLC, 8, Coval, 2, Formation Bio, 2, ICM, 2, Levicept, 2, Medipost, 2, Novartis, 2, Pacira, 2, Paradigm, 2, Peptinov, 3, Scarcell, 2, TissueGene, 2; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6; **C. Perkins**: Levicept Ltd, 2; **C. Herholdt**: Levicept Ltd, 3; **I. Bombelka**: Levicept Ltd, 3; **S. Westbrook**: Levicept Ltd, 3.

Abstract Number: 2082

Pharmacokinetic Profile of MM-II Following a Single Intra-Articular Injection in Patients with Knee Osteoarthritis in a Phase 2b Randomized, Controlled, Dose-Ranging Trial

Thomas Schnitzer[1], Xavier Chevalier[2], Helene Rovsing[3], Edith Lau[4], Sidsel Boll[5], **Ballari Brahmachari**[6], Richard Chou[7], Tarini Joshi[8], Roni Wechsler[9], Sveta Weiner[10], Mudgal Kothekar[11], Asger Bihlet[12] and Philip Conaghan[13], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Henri Mondor Hospital, University Paris XII UPEC, Créteil, France, [3]Sanos Clinic, Gandrup, Denmark, [4]Hong Kong Center for Clinical Research, Hong Kong, Hong Kong, [5]Sanos Clinic, Vejle, Denmark, [6]Sun Pharmaceuticals Industries Ltd., mumbai, Maharashtra, India, [7]Sun Pharmaceutical Industries, Inc., Princeton, NJ, [8]Sun Pharmaceutical Industries Limited, Mumbai, India, [9]Moebius Medical, Tel Aviv, Israel, [10]Sun Pharma Advanced Research Company Limited, Princeton, NJ, [11]Sun Pharma Advanced Research Company Limited, Andheri (E), Princeton, NJ, [12]NBCD A/S, Herlev, Denmark, [13]University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: MM-II is a first-in-class investigational treatment for knee OA pain that consists of a one-time IA injection of empty liposomes comprised of phospholipids dipalmitoylphosphatidylcholine (DPPC) and 1,2-dimyristoylphosphatidylcholine (DMPC). DPPC is a major surface-activated phospholipid that is a part of the cartilage boundary lubrication system. In a phase 2b, dose-finding clinical trial, a single injection of 3 mL MM-II provided sustained reduction in knee pain (measured by weekly average of daily knee pain score as well as WOMAC pain score) compared to placebo, starting from 6 weeks after injection and sustained through 26 weeks. MM-II was safe and well tolerated, with no serious treatment-emergent adverse events, and safety profiles were consistent between placebo and MM-II. Here, we report the pharmacokinetic (PK) profiles of DMPC and DPPC from the trial following a single IA injection of MM-II compared to placebo.

Methods: In a phase 2b, randomized, double-blind, dose-ranging, placebo-controlled trial (NCT04506463), 397 participants with chronic knee OA were randomized 3:3:3:1:3:1 to receive 1, 3, or 6 mL MM-II or 1, 3, or 6 mL placebo through a single IA injection. All participants met the ACR Clinical and Radiological Criteria for chronic knee OA. Blood samples for PK measurements were taken from participants at a subset of study centers, at the following time points: pre-injection (at baseline), and post-injection at 4 hours, 2 days (48 hours), and 7 days (168 hours). Plasma DPPC and DMPC concentrations (ng/mL) were quantified at each time point and for each study arm using liquid chromatography tandem mass spectrometry. Concentrations below the lower limit of quantification were analyzed as 0 before the first quantifiable concentration and as missing after the first quantifiable concentration. Analyses were based on the modified PK analysis set, which included participants who received the single dose of IA injection, had at least 1 quantifiable post-dose concentration, and did not have major protocol deviations. PK parameters were summarized using descriptive statistics based on baseline-adjusted values.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

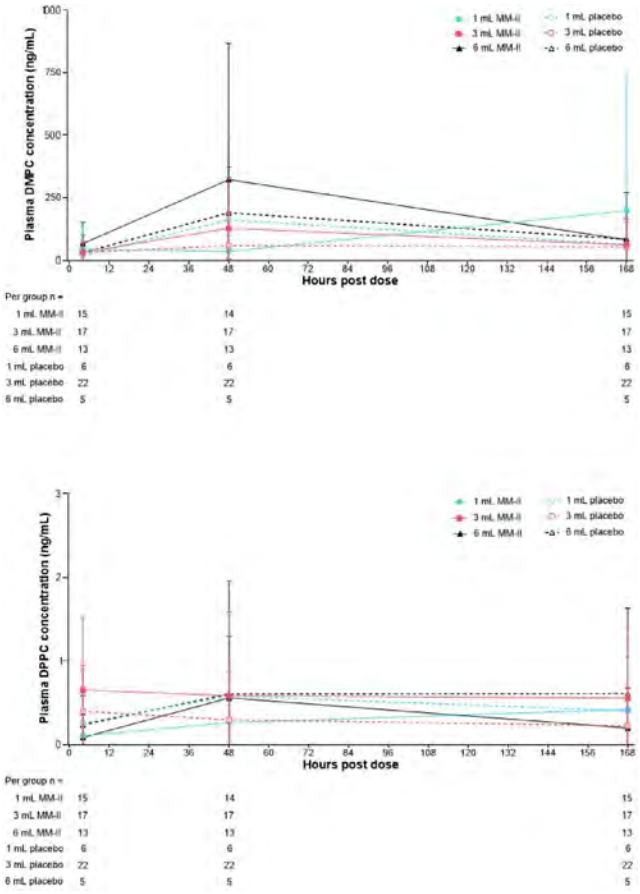


Figure 1. Mean ± SD baseline-adjusted DMPC and DPPC concentrations up to 168 h after intra-articular injection of MM-II or placebo. DMPC, 1,2-dimyristoyl-phosphatidylcholine; DPPC, dipalmitoylphosphatidylcholine; SD, standard deviation.

Results: The modified PK analysis set included 78 participants. Quantifiable levels of both DMPC and DPPC were found in pre-dose samples from MM-II and I placebo controls. There were no considerable changes in plasma DMPC and DPPC concentrations from pre-dose to post-dose time points (Figure 1). Furthermore, the concentrations of DMPC and DPPC appeared to be comparable between MM-II and corresponding placebo groups at all time points. These data suggest there was no increase in measurable DMPC or DPPC levels after administration of MM-II within the time points analyzed.

Conclusion: Based on these results, treatment of OA knee pain with a single IA injection of MM-II did not appear to increase circulating DMPC and DPPC levels compared with placebo within the time points analyzed. Further studies with additional sampling are necessary to enhance interpretation due to limited sampling time points and inherent variability in PK parameters.

Disclosure: T. Schnitzer: AstraZeneca, 1, 2, Eli Lilly, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Horizon, 1, 2, IBSA Group, 1, 2, Merck, 1, 2, Moebius Medical, 1, 2, Orion, 1, 2, Pfizer, 1, 2, Regeneron Pharmaceuticals, 1, 2, Xalud, 1, 2; **X. Chevalier**: IBSA Group, 2, 6, KiOmed, 2, 6; **H. Rovsing**: None; **E. Lau**: None; **S. Boll**: None; **B. Brahmachari**: Sun Pharmaceutical Industries Limited, 3, 11; **R. Chou**: Sun Pharmaceutical Industries, Inc., 3; **T. Joshi**: Sun Pharmaceutical Industries Limited, 3, 11; **R. Wechsler**: Moebius Medical, 3, 11; **S. Weiner**: Sun Pharma Advanced Research Company Limited, 3, 11; **M. Kothekar**: Sun Pharma Advanced Research Company Limited, 3, 11; **A. Bihlet**: NBCD A/S, 3, 11; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2083

Evaluation of a Parent-Trial as a Run-In Period: Efficacy and Safety of Repeat Injections of Lorecivivint over Three Years

Christopher Swearingen[1] and Yusuf Yazici[2], [1]Biosplice Therapeutics, Inc, San Diego, CA, [2]NYU Grossman School of Medicine, La Jolla, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Lorecivivint (LOR) is an intra-articular CLK/DYRK inhibitor in clinical development for the treatment of knee OA. A Phase 3 Trial, OA-11 (NCT03928184), assessed clinical and radiographic outcomes over one year following a single LOR injection in advanced knee OA versus placebo (PBO). Patients successfully completing OA-11 were invited to enroll into OA-07 (NCT04520607), a multi-year treatment trial providing annual study treatment injections. The purpose of this analysis was to evaluate OA-11 for any possible differences that could be associated with choosing to enroll into OA-07 or not and thereby impacted the interpretability of the OA-07 results.

Methods: Demographic, outcome and safety data from OA-11 was abstracted by enrollment status into OA-07. Equivalence testing was conducted by enrollment status into OA-07 using two one-sided t-tests. Permutation tests via Monte Carlo simulation (1000 replicated datasets) were also conducted to further assess any predictability in OA-07 enrollment status. Baseline-adjusted ANCOVA was also conducted as a part of each study's analysis plan.

Results: 501 patients enrolled into OA-11; 276 (55.1%) enrolled into OA-07 (N PBO = 138, N LOR = 138). Overall, the adverse event profile was similar between those subjects that enrolled into OA-07 and those that did not. Age, Body Mass Index, baseline WOMAC Pain and Function, as well as medial joint space width (JSW) were equivalent between those that enrolled into OA-07 and those that did not. Percentages of female, white race, Hispanic/Latino ethnicity, KL Grade 2 and unilateral symptomatic OA were similar between studies but could not be determined as equivalent. WOMAC Pain, WOMAC Function and medial JSW, however, at the end of OA-11 were also equivalent between those that enrolled into OA-07 and those that did not. Permutation tests also indicated that the population enrolled into OA-07 appeared to be a random sample, as all results were stable and not predictive of enrollment status.

Statistically significant improvements were observed for LOR vs PBO in WOMAC Pain [0-100] in OA-07 six months after injection (Visit 2E Δ=-4.52, 95% CI [-8.92, -0.13], P=0.044), as well as at twelve months (Visit 3E Δ=-5.19, 95% CI [-9.86, -0.53], P=0.029) (Figure 1). WOMAC Function [0-100] was numerically improved in OA-07 at six months but was

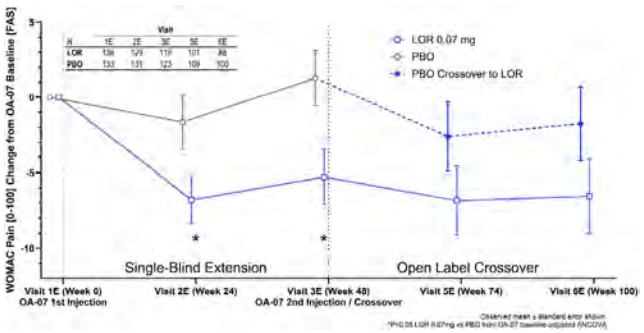


Figure 1. Change from OA-07 Baseline in WOMAC Pain

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

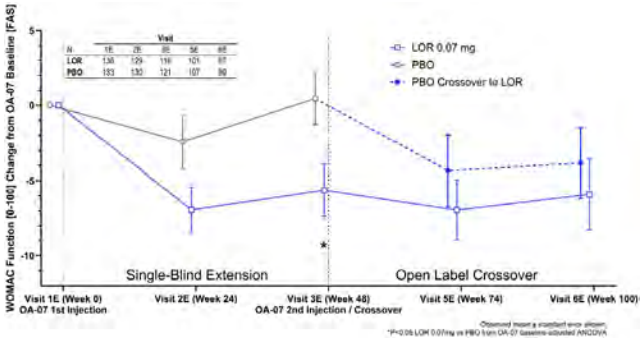


Figure 2. Change from OA-07 Baseline in WOMAC Function

significantly improved at twelve months (Visit 3E Δ=-4.86, 95% CI [-9.36, -0.35], P=0.035) (Figure 2). In Year 2 (crossover portion) of OA-07, all PBO patients receiving LOR showed mean improvements in WOMAC Pain and Function from Visit 3E observations.

Conclusion: Examining demographics, outcomes and safety data from the OA-11 trial did not elicit any prediction to patients that enrolled into OA-07 but supports OA-07 as a random sample of the OA-11 population. The impact of COVID on the conduct and results of OA-11 may have relegated the Phase 3 trial into a large run-in, possibly allowing patients to normalize over the course of a year prior to the start of OA-07. In OA-07, improvements in pain and function in LOR compared to PBO were seen at six and twelve months. LOR continues to show promise as a safe, disease-modifying knee OA treatment.

Disclosure: C. Swearingen: Biosplice Therapeutics, Inc, 3, 10, 11; **Y. Yazici**: Biosplice Therapeutics, Inc., 3, 10, 11.

Abstract Number: 2084

Predictors of Change in Physical Activity Level Among Veterans with Knee Osteoarthritis in a Behaviorally Designed Incentive Program

Criswell Lavery[1], Ori Needleman[1], Bryant England[2], Katherine Wysham[3], Mercedes Quinones[4], Marianna Olave[5], Sarah Wetzel[6], Hannah Brubeck[7], Rachel Gillcrist[8], Natalie Keller[9], Kimberly Hayes[10], Bibiana Ateh[11], Bridget Kramer[2], Rui Xiao[1], Kaitian Jin[1], Alexis Ogdie[12], Daniel K. White[13], Tuhina Neogi[14], Carla Scanzello[1] and Joshua Baker[1], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [4]Washington DC VA Medical Center, Bethesda, MD, [5]Brown University, Philadelphia, PA, [6]Drexel University, Pittsburgh, PA, [7]VA Puget Sound Health Care System, Seattle, WA, [8]Dartmouth College, Lebanon, NH, [9]University of Oklahoma, Philadelphia, PA, [10]Teachers College, Columbia University, Philadelphia, PA, [11]Washington VA Medical Center, Washington, District of Columbia, [12]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [13]University of Delaware, Newark, DE, [14]Boston University School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Physical activity may help reduce symptoms in adults with knee osteoarthritis (KOA), yet few meet the recommended levels. This analysis identified participant characteristics associated with improvement in physical activity over 28 weeks in a clinical trial setting aimed at testing an incentive program utilizing elements of gamification and social

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Factors associated with change in average step counts in univariate models. **Also tested but not significant: smoking status, heart disease, degenerative disc disease, heart failure, depression, employment status.

	Association with Change in Average Daily Steps	
	Beta (95% CI)	p-value
Age (per 1 year)	-25 (-54, 3)	0.08
Female (v. male)	-844 (-1388, -301)	0.002
BMI (1 kg/m^2)	-49 (-82, -16)	0.004
Self-efficacy tertile (v. 1)		
2	709 (158, 1259)	0.012
3	1145 (483, 1806)	0.001
Site (v. Omaha)		
Philadelphia	597 (-67, 1261)	0.078
Seattle	1212 (413, 2010)	0.003
Washington, DC	499 (-211, 1209)	0.168
KL grade (v. 1)		
2	-217 (-1046, 611)	0.607
3	-314 (-1086, 457)	0.425
4	-592 (-1411, 228)	0.157
ADI Quartiles (v. 1)		
2	12 (-741, 765)	0.975
3	-2 (-831, 828)	0.997
4	-714 (-1338, -89)	0.025
Fibromyalgia	1207 (-176, 2589)	0.087
Kidney disease	-911 (-1463, -360)	0.001
Sleep apnea	-469 (-976, 39)	0.07
Anxiety	442 (-186, 1070)	0.17
Pain interference score	-48 (-79, -17)	0.002
Pain behavior score	-64 (-108, -19)	0.005
Pain intensity score	-56 (-87, -25)	<0.001
KOOS score	19 (4, 34)	0.014
Sleep Quality (PSQI)	-95 (-163, -27)	0.006
Unsafe neighborhood	-520 (-1018, -22)	0.041
Fatigue Index (MFI)	39 (4, 74)	0.03
Barriers to exercise		
Time	362 (-385, 1110)	0.34
Pain	-452 (-1011, 107)	0.11
Motivation	-140 (-735, 454)	0.64
No interest	-301 (-1235, 633)	0.53
Other	906 (31, 1780)	0.042
KL= Kelgren Lawrence; ADI= Area Deprivation Index; KOOS= Knee Osteoarthritis Outcome Score (0-100, higher is better); PSQI=Pittsburgh Sleep Quality Index (higher is worse sleep); MFI= Multi-inventory Fatigue Index		

incentivization. We hypothesized that greater self-efficacy (confidence in their ability to exercise) would be a significant predictor of improvements in average daily step counts.

Table 2: Factors associated with changes in average step counts in a multivariable model.

	Multivariable	
	Beta (95% CI)	p-value
Age (year)	-49 (-76, -22)	<0.001
Female (v. male)	-854 (-1339, -369)	0.001
BMI (1 kg/m2)	-43 (-75, -12)	0.007
Fibromyalgia	1906 (725, 3086)	0.002
Self-efficacy tertile (v. 1)		
2	554 (46, 1061)	0.032
3	1058 (425, 1691)	0.001
Site (v. Omaha)		
Philadelphia	732 (125, 1340)	0.018
Seattle	1033 (314, 1752)	0.005
Washington, DC	557 (-160, 1275)	0.128
Note: Variables associated with a p<0.1 from univariate model were tested in the multivariable model, and we performed backwards selection to identify independent predictors with p<0.05.		

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

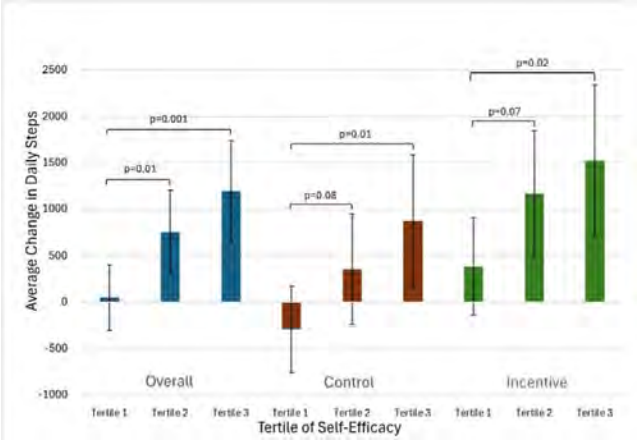


Figure 1. Average change in daily steps (with 95% CI) overall and by incentive group among Veterans with knee osteoarthritis, predicted from univariate linear regression models.

Methods: This was a multi-center randomized controlled trial with a factorial design. The study included 221 participants aged 40-85 years from 4 Veterans Affairs centers with a Kellgren-Lawrence (KL) knee radiograph grade ≥1 and clinical indication for a corticosteroid joint injection. Participants were randomized into either the incentive program or control and then further randomized to receive corticosteroid or lidocaine-only injections. A web-based platform collected daily step counts (from a Fitbit activity monitor) and patient-reported outcomes. Daily step counts were averaged over 2-week periods throughout the 28-week trial. Self-efficacy was measured at enrolment using the Exercise Self-Efficacy Scale. Linear regression incorporating generalized estimating equations was used to evaluate the association of participant characteristics with the change in average daily step counts. Variables associated with the outcome ($p< 0.1$) in univariate analyses were tested in multivariable models and removed in a backwards selection process to arrive at a final model.

Results: A total of 221 participants were randomized. Mean participant age was 64 years-old and 87% male. Unadjusted associations between participant characteristics and change in average daily steps are shown in **Table 1**. Individuals with greater self-efficacy for exercise demonstrated significantly greater increases in the average daily step count (**Figure 1**). This effect was greatest for participants in the highest tertile, whose daily step counts increased about 1145 steps more than those in the lowest tertile (**Figure 1**). This pattern was observed in both incentive and control arms and was an independent predictor in the multivariable model (**Table 2)**. Patient characteristics associated with less improvement in average daily step count included higher pain scores, worse sleep quality, greater fatigue, kidney disease, and higher BMI. Participants that lived in areas in the highest quartile of Area Deprivation Index (ADI) also failed to improve.

Conclusion: We identified predictors of improvement in physical activity level among patients with KOA in the context of a clinical trial. Higher self-efficacy for exercise was a strong predictor of greater improvement in physical activity levels throughout follow-up. Less improvement was observed among those with greater pain, comorbidity, BMI, fatigue, and among those living in unsafe areas or areas with high ADI. These observations highlight the need to address low self-efficacy and other barriers in order successfully promote exercise in this population.

Disclosure: C. Lavery: None; **O. Needleman**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **K. Wysham**: None; **M. Quinones**: None; **M. Olave**: None; **S. Wetzel**: None; **H. Brubeck**: None; **R. Gillcrist**: None; **N. Keller**: None; **K. Hayes**: None; **B. Ateh**: None; **B. Kramer**: None; **R. Xiao**: None; **K. Jin**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **D. White**: None; **T. Neogi**: None; **C. Scanzello**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10; **J. Baker**: Amgen, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2085

Estimating the Association between Effusion-synovitis and Knee Pain in a Subset of Participants with Radiographic Knee Osteoarthritis: Data from the Osteoarthritis Initiative (OAI)

Dagoberto Robles[1], Greg Gilles[2], Nathaniel H. Christiansen[3], Luke Grawer[4], Karim Jayyusi[4], Ali Shaikh[4], Rongrong Tang[5], Mihra S. Taljanovic[4], Jeffrey Duryea[6], Edward J. Bedrick[5] and C. Kent Kwoh[7], [1]University of Arizona, Tucson, AZ, [2]University of Arizona Arthritis Center, The University of Arizona College of Medicine, Tucson, AZ, [3]University of Arizona, Stockton, NJ, [4]University of Arizona, Tucson, [5]The University of Arizona Arthritis Center, University of Arizona, Tucson, [6]Brigham and Women's Hospital, Boston, MA, [7]The University of Arizona Arthritis Center, University of Arizona, Tucson, AZ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Even though knee pain is ubiquitous in knee osteoarthritis (KOA) patients, currently there are limited treatment options which are only minimally or moderately efficacious for relieving pain and may lead to undesired side effects. Effusion-synovitis (ES) is present during all stages of OA and has been reported to be associated with increased knee pain. Though the validated WOMAC-Pain subscale was the primary assessment tool in most of these studies, it was used as a composite measure (i.e., only the total score was reported) so the associations between ES and pain during specific types of activities are unknown. Therefore, the main objective of this study is to evaluate the longitudinal associations between MRI-detected quantitative ES (qES) and self-reported total and activity-specific knee pain.

Methods: This study included a random longitudinal subsample of Osteoarthritis Initiative (OAI) participants with diagnosed radiographic KOA (Kellgren-Lawrence [KL] grade 2,3) who had both X-ray and MRI assessments of both knees at baseline (n = 534). Our primary outcome was self-reported knee pain in the past 7 days, reported at baseline, 12-, and 24-month visits for each knee. Knee pain was measured using the WOMAC-Pain and Knee injury and Osteoarthritis Outcome Score (KOOS) Pain subscales. The questions on both subscales were scored from 0-4, which correspond to: None (0), Mild (1), Moderate (2), Severe (3), and Extreme (4). Our primary exposure was whole knee joint qES, assessed on non-contrast

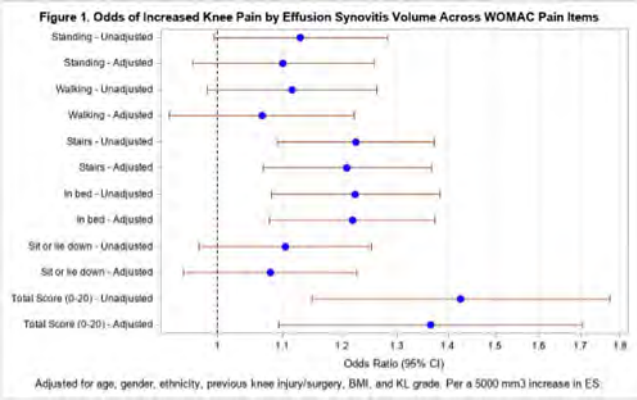
Table 1 - Baseline characteristics of the OAI sub sample of participants with radiographic KOA at baseline by Kellgren-Lawrence (KL) grade

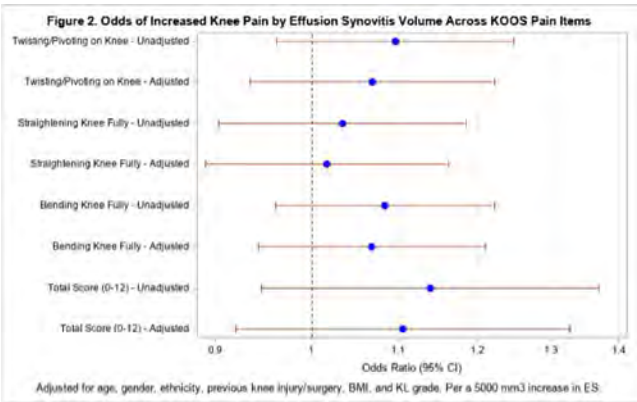
Characteristics, n (%)	KL=2 (N=333)	KL=3 (N=201)	Total (N=534)
Age, mean (SD), years	60.6 (8.9)	62.8 (8.7)	61.4 (8.9)
Female Gender	217 (65.2)	102 (50.8)	319 (59.7)
Ethnicity			
White or Caucasian	263 (79.0)	167 (83.1)	430 (80.5)
Black or African American	63 (18.9)	25 (12.4)	88 (16.5)
Other Non-White	7 (2.1)	9 (4.5)	16 (3.0)
Previous Knee Injury	89 (27.4)	82 (41.0)	171 (32.6)
Previous Knee Surgery	50 (15.1)	73 (36.5)	123 (23.1)
BMI (kg/m2) mean (SD)	28.9 (4.7)	29.9 (4.6)	29.2 (4.7)
Quantitative ES (mm3) median (25th and 75th percentile)	4847.1 (3148, 7597)	6763.4 (4249, 12088)	5437.5 (3410, 8983)

Acronyms: OAI Osteoarthritis Initiative, OA Osteoarthritis, ES effusion-synovitis, SD standard deviation, BMI body mass index

* Radiographic Kellgren-Lawrence score of 2 or 3

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





enhanced 3T MRI at baseline, 12-, and 24-month visits. Total qES volume (mm^3) was measured using our semi-automated multi-planar MRI quantification approach. We applied generalized estimating equations to evaluate the association between qES and the individual items of both subscales. These models were fitted using a multinomial distribution with a cumulative logit link function and unadjusted and adjusted odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were reported. We adjusted for age, gender, ethnicity, previous knee injury/surgery, BMI, and KL grade. The ORs and adjusted ORs and their associated 95% CIs were reported per a 5000 mm^3 increase in qES.

Results: Whole-knee ES was significantly associated with the total WOMAC-Pain subscale score in the unadjusted and adjusted models. As shown in Figure 1, participants with greater qES had higher odds of experiencing worse knee pain (OR: 1.43 [1.15,1.77], adjusted OR: 1.37 [1.09, 1.70]). Regarding pain with specific activities, qES was significantly associated with knee pain at night while in bed (OR: 1.22 [1.08, 1.38], adjusted OR: 1.22 [1.08, 1.37]) and when going up or down the stairs (OR: 1.22 [1.08, 1.38], adjusted OR: 1.21 [1.07, 1.37]), as also shown in Figure 1. There was no significant association between pain with the three KOOS-specific activities and qES (Figure 2).

Conclusion: For KOA patients, longitudinal whole-knee qES was significantly associated with total WOMAC-Pain and particularly with knee pain during bedtime and climbing stairs. Our whole knee qES measure may be valuable for patient screening/phenotyping and outcome assessment in KOA trials.

Disclosure: D. Robles: None; **G. Gilles**: None; **N. Christiansen**: None; **L. Grawer**: None; **K. Jayyusi**: None; **A. Shaikh**: None; **R. Tang**: None; **M. Taljanovic**: None; **J. Duryea**: None; **E. Bedrick**: None; **C. Kwoh**: Apos Health, 1, 2, Express Scripts, 1, 2, Kolon Tissue Gene, 2, Mobieus Sun, 1, 2, TLC, 1, 2, Xalud, 1, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2086

WOMAC Physical Function and 3D MRI Bone Shape: Advancing a "Virtual" Total Knee Replacement Endpoint for Knee Osteoarthritis Clinical Trials

Dawn McGuire[1], Alan Brett[2], Neil Segal[3], Meghan Miller[4], David Rosen[1] and Yoshi Kumagai[5], [1]OrthoTrophix, Inc, Foster City, CA, [2]Imorphics, Manchester M20 2HJ, England, United Kingdom, [3]KUMC, Kansa City, KS, [4]OrthoTrophics, Foster City, CA, [5]OrthoTrophix, Foster City, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: TPX-100, a peptide derived from matrix extracellular phosphoglycoprotein (MEPE), is in development as a potential disease-modifying osteoarthritis drug (DMOAD) for mild to severe knee osteoarthritis (KOA). While total knee replacement (TKR) remains the FDA's "gold standard" outcome measure for this regulatory pathway, it presents practical and ethical limitations as a trial endpoint. Surrogate markers predictive of TKR would enable more efficient clinical trials. Data from the Multicenter Osteoarthritis Study demonstrate that poor WOMAC Physical Function scores (40–68) are associated with a >15-fold increased risk of TKR, with a clear dose-response gradient across impairment levels. Longitudinal analyses from the Osteoarthritis Initiative (OAI) have shown that MRI-derived femoral bone shape predicts TKR risk over 48 months. Study TPX-100-5 was designed to evaluate these measures and their interrelationships in order to explore the idea of a surrogate marker for TKR.

Methods: Participants in TPX-100-5 met ACR diagnostic criteria for bilateral KOA based on history, examination and imaging. All had previously completed a randomized, double-blind, placebo-controlled Phase 2 study (TPX-100-1), and received four weekly injections of TPX-100 (200 mg) in one knee and saline placebo in the contralateral knee in a triple-blinded fashion. Subjects' MRIs were analyzed at a single center per published protocols, blind to treatment assignment and clinical data. Femoral bone shape, defined by "B-score", differentiates pathologic bone shapes associated with OA onset, progression and joint failure from bone shapes of normal, non-OA knees. B-score is based on a vector derived from modelling of 3-D femoral bone shape from >9,000 knee MRIs in the OAI database. Per the statistical analysis plan, finalized prior to study start, subjects with knees whose B-scores were ≥1.5 (n=70), equivalent to KL ≥2 on x ray, made up the study cohort.

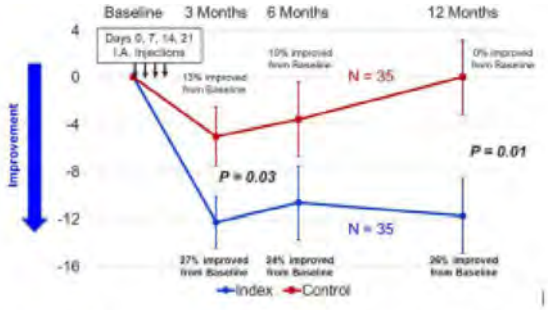


Figure 2. TPX-100 showed statistically significant reduction in WOMAC Function as compared to control in the knees with baseline B score ≥ 1.5.
Mean baseline scores were 44.8 and 37.1 of 100, respectively (p = 0.14). Error bars indicate standard errors of the mean. Statistical analyses were by Student's t-test (unpaired and unequal variance).

Comparative WOMAC Function Scores, IA TPX-100 treatment versus Placebo Controls

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

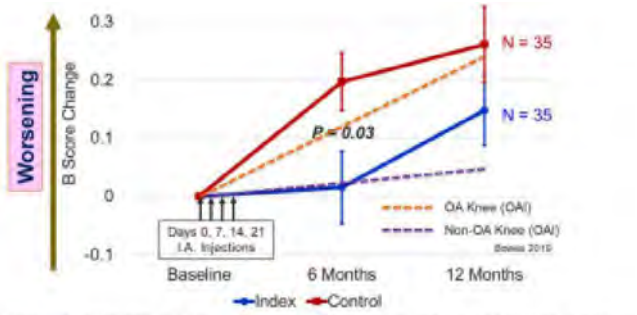


Figure 2. TPX-100 significantly reduced pathological femoral bone shape (B score) change as compared to control in the knees with baseline B score ≥ 1.5. Mean baseline B scores of Index and Control knees were 3.08 and 3.02, respectively. Error bars indicate standard errors of the mean. Statistical analyses were by Student's t-test (unpaired and unequal variance).

Bone-shape ("B") Scores, IA TPX-100 versus Placebo Controls: Comparison to Historical Controls from the Osteoarthritis Initiative

Results: Demographics of the study cohort were similar to those of the total study population from TPX-100-1. Knees that received TPX-100versus placebo were well matched in terms of baseline WOMAC function, B-scores and all other clinical measures. TPX-100 treatment was associated with WOMAC scores that demonstrated statistically significant and clinically meaningful improvements compared with controls at 6 and 12 months, and pathological B-score changes that were significantly reduced versus controls. Notably, at 6 months, the trajectory of B-score change in TPX-100-treated knees almost perfectly mirrored that of "non-OA" knees from the OAI, while placebo-treated knees followed a trajectory nearly identical to that of OAI disease progressors. (Figures 1, 2).

Conclusion: The demonstration of concordant drug-associated improvements in WOMAC function and MRI-based bone-shape scores suggest that these measures-- independently associated with knee joint failure and TKR—may be useful when appropriately combined in order to advance a viable surrogate marker for DMOAD development. Furthermore, the observed structural and functional benefits demonstrated with TPX-100 treatment, while requiring confirmatory trials, support the potential of TPX-100 as a candidate DMOAD.

Disclosure: D. McGuire: OrthoTrophix, Inc, 3, 4, 10; **A. Brett**: Imorphics, Inc, 3; **N. Segal**: None; **M. Miller**: OrthoTrophix, Inc, 3; **D. Rosen**: OrthoTrophix, Inc, 2, 4, 10; **Y. Kumagai**: OrthoTrophix, Inc, 3, 4, 10.

Abstract Number: 2087

Does Carbamazepine Impact Risk of Developing Osteoarthritis? Results of a Real-World Data Analysis

Erfan Afshar[1] and Andrew Long[2], [1]VCUSOM, Richmond, VA, [2]Virginia Commonwealth University Health System, Midlothian, VA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Carbamazepine has shown chondroprotective effects in OA animal models by modulating Nav1.7 channels. This study aimed to examine the association between Carbamazepine use and the risk of developing Osteoarthritis (OA). We hypothesized that Carbamazepine users would have a lower incidence of OA compared to matched controls.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

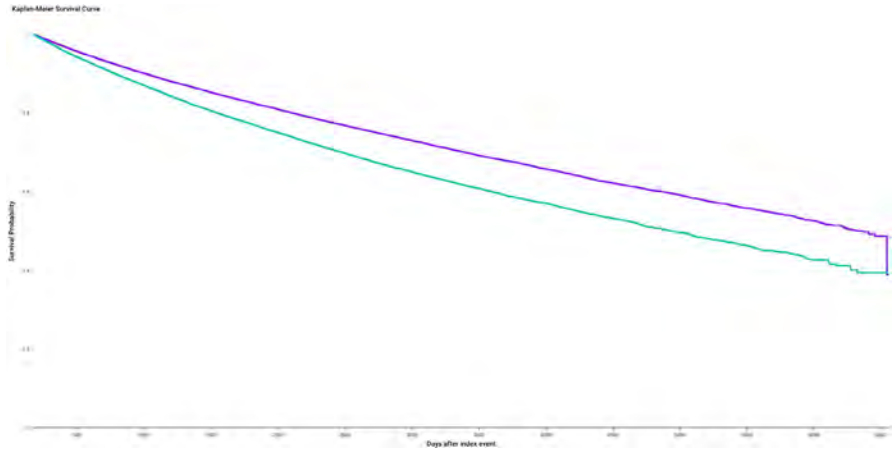


Figure 1. Kaplan-Meier curve comparing OA-free survival between Carbamazepine users and matched controls over time.

Methods: The data for this retrospective cohort study were gathered from the aggregated electronic health records research network, TriNetX. Cohorts included patients aged 40 years or older with a history of using Carbamazepine and the control group consisted of patients with no history of exposure to Carbamazepine. Cohorts were matched through propensity score matching (PSM) for confounding variables known to influence OA risk, including age, sex, race, obesity, metabolic conditions, joint disorders, prior injury and use of cardiovascular or anti-inflammatory medications. Outcomes were assessed through risk ratio (RR), of the development of osteoarthritis at least 180 days after receiving carbamazepine.

Results: Among 385,903 patients in the initial Carbamazepine cohort, 174,970 patients remained post-PSM for the OA analysis (mean [SD] age, 67.8 [13.3] years; 77.1% female) and 174,970 in the matched control cohort (mean [SD] age, 68.3 [10.6] years; 76.5% female). In the osteoarthritis analysis, 37,746 patients were excluded in the Carbamazepine group and 42,867 patients were excluded from the control group for having the outcome prior to the study window. Osteoarthritis occurred in 20, 254 (14.8%) of the Carbamazepine group compared to 24,533 patients (18.6%) in the control group, yielding a risk ratio (RR) of 0.795 (95% CI, 0.781–0.808; $p < 0.0001$), indicating a statistically significant reduced risk of OA for Carbamazepine users.

Conclusion: This data highlights the potential for Carbamazepine to reduce the risk of developing OA. Using Carbamazepine to target chondrocytes appears to offer a promising treatment strategy in OA, and it calls for future clinical studies. This study highlights a potential role for carbamazepine as a preventative agent for OA and underscores the need for prospective clinical trials to validate this real-world observation.

Disclosure: E. Afshar: Geron Corporation, 12, Kyverna Therapeutics, 12, Maia Biotechnology, 12,; **A. Long**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2088

Aging Unevenly: National Trends and Inequities in Osteoarthritis Mortality, 1999–2020

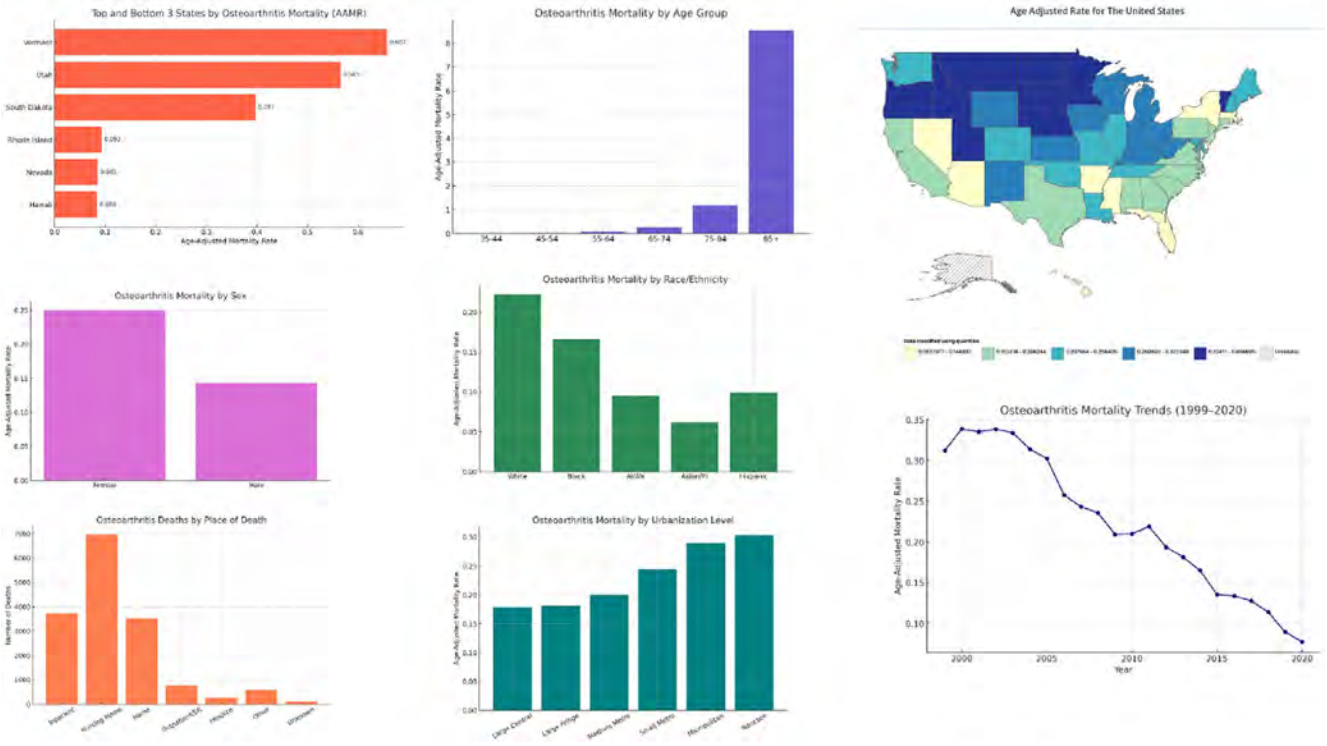
Ghassan Makhoul[1], Aziz-ur-Rahman Khalid[2], Hasan Munshi[1], Islam Rajab[1], MD Walid Akram Hussain[1], Reshma John[1], Elvira Assaf[1], Amer Al Badawy[1], Barbare Khatiashvili[1], Rouba Isshak[1], Nargis Mateen[3] and Robert Lahita[4], [1]St. Josephs University Medical Center, Paterson, [2]St. Joseph's University Medical Center, wayne, [3]St. Josephs University Medical Center, Paterson, NJ, [4]St. Josephs University Medical Center, Wayne, NJ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is a leading cause of disability and pain in older adults. While not traditionally viewed as fatal, OA contributes significantly to morbidity and, in some cases, mortality. This study evaluates national mortality trends and demographic disparities associated with OA (ICD-10 M15–M19) from 1999 to 2020 using U.S. death certificate data.

Methods: Mortality data were extracted from the CDC WONDER Multiple Cause of Death database. Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated using census-adjusted standard populations. Deaths were stratified by year, state, sex, 10-year age group, race/ethnicity, Hispanic origin, place of death, and urban-rural classification based on the 2013 NCHS scheme.



Graphs showing state, demographic, gender, race, age group, year, place of death, mortality from Osteoarthritis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: From 1999 to 2020, there were 15,948 deaths attributed to osteoarthritis (OA) in the United States. The age-adjusted mortality rate (AAMR) declined by 75% over the study period, dropping from 0.31 per 100,000 in 1999 to 0.08 in 2020. Despite this progress, notable disparities remain. Females experienced nearly twice the mortality burden of males, with an AAMR of 0.25 compared to 0.14. Mortality rose steeply with advancing age, reaching 8.5 per 100,000 among adults aged 85 and older. Racial and ethnic differences showed the highest AAMRs among White (0.22) and Black (0.17) individuals, while Hispanic and Asian/Pacific Islander groups had lower rates at 0.10 and 0.06, respectively. AAMRs increased with rurality, ranging from 0.18 in large metropolitan areas to 0.30 in noncore rural regions. State-level variation was substantial, with AAMRs ranging from 0.08 in Hawaii to 0.66 in Vermont, highlighting a greater burden in rural and mountain states. Regarding place of death, 43.6% of OA-related deaths occurred in nursing homes or long-term care facilities, 23.4% in inpatient medical settings, and 22.2% in the decedent's home.

Conclusion: Osteoarthritis mortality in the U.S. has declined significantly over the past two decades, likely reflecting improved awareness and comorbidity management. However, consistent disparities by age, sex, race, geography, and care setting underscore the unequal burden of this chronic disease. These findings highlight the need for targeted health policy and equitable access to supportive care, particularly in aging and rural populations.

Disclosure: G. Makhoul: None; **A. Khalid**: None; **H. Munshi**: None; **I. Rajab**: None; **M. Hussain**: None; **R. John**: None; **E. Assaf**: None; **A. Al Badawy**: None; **B. Khatiashvili**: None; **R. Isshak**: None; **N. Mateen**: None; **R. Lahita**: None.

Abstract Number: 2089

Traction Therapy May Improve Hand Function in Those with Distal Interphalangeal Osteoarthritis

Grace Lo[1], Lauren Drillock[2], Kimberly Staines[3], Michael Strayhorn[4], Katherine Tse[5], Gerald Virtanen[6], Laura Welsh[2], Monica Seu[2], Eugene Gersh[2], Ida Kristin Haugen[7], Andrew Grainger[8] and Jonathan Samuels[9], [1]Baylor College of Medicine / MEDVAMC, Houston, TX, [2]NYU Langone Health, New York City, NY, [3]MEDVAMC, Saltburn By The Sea, United Kingdom, [4]Baylor College of Medicine, Houston, TX, [5]NYU Langone Health, Brooklyn, NY, [6]MEDVAMC, Houston, TX, [7]Diakonhjemmet Hospital, Oslo, Norway, [8]University of Cambridge, Cambridge, United Kingdom, [9]NYU Langone, Rye Brook, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hand osteoarthritis (OA) is the most common form of arthritis affecting the hand, but therapeutic options for OA at the distal interphalangeal (DIP) joint have limited efficacy. While the primary outcome of a randomized controlled clinical trial evaluating traction of the DIPs was null, we explored whether secondary outcome measures indicated a benefit of the treatment.

Methods: In this pilot multi-center, double-blind, controlled trial, of DIP hand OA in at least 3 joints, patients were randomized to a traction device (fig 1) along with standard of care vs standard of care. Patients were evaluated at baseline and at weeks 4, 12, and 24 for multiple measures of pain as well as functional assessments using questionnaires (the Disabilities of Arm Shoulder and Hand (DASH), the Michigan Hand Questionnaires, the Functional Index for Hand Osteoarthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of all participants and stratified by treatment allocation group.

	All participants (n = 33)	Traction +Standard of Care (n = 16)	Standard of Care (n = 17)
Age (mean (SD))	65.8 (6.7)	65.2 (6.5)	66.5 (7.1)
BMI (mean (SD))	32.1 (7.3)	31.5 (6.6)	32.6 (8.0)
Sex (n, column%)			
Female	16 (49%)	6 (38%)	10 (59%)
Male	17 (51%)	10 (62%)	7 (41%)
Race (n, column%)			
White	19 (58%)	10 (62%)	9 (53%)
Black	12 (36%)	5 (31%)	7 (41%)
Other	2 (6%)	1 (6%)	1 (6%)
Location (n, column%)			
Houston	23 (70%)	11 (69%)	12 (71%)
New York	10 (30%)	5 (31%)	5 (29%)
Handedness (n, column%)			
Right	28 (85%)	14 (88%)	14 (82%)
Left	5 (15%)	2 (12%)	3 (18%)
Study hand (n, column%)			
Right	14 (42%)	8 (50%)	6 (35%)
Left	19 (58%)	8 (50%)	11 (65%)
Study Joint (n, column%)			
2nd DIP	11 (33%)	5 (31%)	6 (35%)
3rd DIP	10 (30%)	6 (38%)	4 (24%)
4th DIP	5 (15%)	0 (0%)	5 (29%)
5th DIP	7 (21%)	5 (31%)	2 (12%)
Sum of KL scores of DIPs 2-5 in the study hand (mean (SD))	2.7 (2.6)	2.4 (2.4)	2.9 (2.8)
CESD (depression scale)	20.5 (8.7)	22.9 (8.6)	18.3 (8.5)
Number of weeks the participant indicated he/she wore assigned orthosis (mean (SD))	15.2 (8.9)	15.9 (9.3)	14.4 (8.7)
% family history of hand OA	14 (42%)	7 (44%)	7 (41%)

(FIHOA)) and clinical tests including the Functional Dexterity test, grip strength test, pinch strength test, and tenderness on joint palpation. All participants randomized into the study were included. We used a last observation carried forward strategy to address missing data.

Results: 33 participants were enrolled and randomized to either the experimental or control arm. Of the secondary outcome measures that we evaluated, two were statistically significant in when looking at the 24 week timepoints, these included the DASH and the Michigan Hand Outcome ADLs of both hands. The DASH scores were significantly better in the traction arm compared to the control by nearly 11 points (-10.9 (95% CI -21.8 – -0.2)), and the Michigan Hand Outcome ADLs of both hand scores were also better by 12.0 points (12.0 (1.1 - 22.8)). The 4 other functional hand outcomes, FIHOA, grip strength, AUSCAN function, and the Michigan Hand Outcome overall hand scores, did not meet statistical significance but all showed more improvement in the traction arm compared to the control arm. None of the pain outcome measures showed a signal for being more beneficial in either arm.

Conclusion: In our pilot RCT of finger traction for DIP hand OA, based on our secondary outcomes, there is a signal that function may be improved in the treatment arm. Our findings suggest that functional assessments might be a better outcome measure to evaluate treatment benefit for hand OA interventions compared to pain assessments. A larger clinical trial, perhaps with a focus on function instead of pain as an outcome, is warranted.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Outcome Measures by treatment allocation.

	Traction + Standard of Care					Standard of Care					
	0W	4W	12W	24W	Difference (24W-0W) (95% CI)	0W	4W	12W	24W	Difference (24W-0W) (95% CI)	Difference of (24W – 0W) between the 2 arms (95%CI)
Primary outcome											
Study hand VAS	59.4	51.7	45.3	43.8	-15.7 (-30.0 - -1.4)	69.3	59.6	59.6	53.2	-16.1 (-31.3 - -0.8)	0.4 (-19.8 – 20.5)
Secondary outcomes											
Most Symptomatic DIP VAS (high values are worse outcomes)	61.3	46.9	42.2	46.4	-14.9 (-32.8 – 3.1)	67.8	45.0	48.5	44.1	-23.6 (-40.3 - -6.9)	8.8 (-14.7 – 32.3)
DASH (high values are worse outcomes)	80.1	74.3	75.2	70.2	-9.9 (-17.9 – -2.0)	79.1	79.2	79.9	80.0	0.9 (-6.9 – 8.7)	-10.9 (-21.8 – -0.2)
FIHOA (high values are worse outcomes)	12.0	10.9	10.4	9.4	-2.6 (-5.1 – -0.2)	10.4	10.2	11.5	11.1	0.6 (-2.9 – 4.2)	-3.3 (-7.4 – 0.9)
Functional Dexterity Test (seconds) (high values are worse outcomes)	45.8	40.8	40.0	39.3	-6.4 (-11.0 – -1.9)	46.3	46.1	41.8	42.5	-3.8 (-11.8 – 4.3)	-2.7 (-11.9 – 6.6)
Grip Strength (pounds) (high values are better outcomes)	56.2	61.3	62.6	61.5	5.3 (1.5 –9.1)	41.5	41.1	40.6	44.6	3.1 (-0.5 – 6.7)	2.19 (-2.9 – 7.2)
Pinch Strength (pounds) (high values are better outcomes)	13.2	14.0	14.0	13.4	0.2 (-0.8 – 1.3)	11.0	11.0	10.3	11.4	0.4 (-1.3 – 2.0)	-0.1 (-2.0 – 1.8)
AUSCAN (high values are worse outcomes)											
AUSCAN PAIN	10.6	10.4	10.0	9.4	-1.25 (-2.1 – -0.4)	10.4	10.1	9.9	9.5	-0.9 (-3.1 – 1.3)	-0.4 (-2.7 – 1.9)
AUSCAN STIFFNESS	2.4	2.4	2.2	2.0	-0.4 (-1.0 – 0.1)	2.4	2.3	2.4	2.1	-0.3 (-0.7 – 0.1)	-0.1 (-0.7 – 0.5)
AUSCAN FUNCTION	20.6	17.8	16.9	15.3	-5.3 (-9.0 – -1.5)	20.1	19.2	20.9	19.6	-0.5 (-5.6 – 4.5)	-4.7 (-10.8 – 1.4)
Michigan Hand Outcome (s) (high values are better outcomes)											
Overall Hand Function	43.4	51.3	55.0	54.7	11.3 (1.8 – 20.7)	54.1	55.3	51.5	54.4	0.3 (-7.3 – 7.9)	11.0 (-0.6 – 22.5)
ADLs in one hand	54.4	60.9	65.0	63.4	9.1 (-3.5 – 21.6)	54.7	52.6	54.4	50.0	-4.7 (-18.7 – 9.3)	13.7 (-4.4 – 31.9)
ADLs in both hands	60.3	64.5	69.6	70.8	10.5 (1.9 – 19.0)	62.2	62.8	61.3	60.7	-1.5 (-8.9 – 5.9)	12.0 (1.1 - 22.8)
Pain	70.0	68.8	72.5	74.1	4.1 (-9.1 – 17.2)	71.8	72.4	76.5	72.4	0.6 (-6.0 – 7.2)	3.5 (-10.4 – 17.3)
Aesthetics	56.3	66.0	60.9	63.3	7.0 (-2.6 – 16.7)	58.8	59.2	57.0	60.3	1.5 (-3.9 – 6.9)	5.6 (-4.9 – 16.0)
Satisfied	29.4	35.9	36.7	40.6	11.2 (-0.8 – 23.2)	36.8	36.5	34.3	38.7	2.0 (-8.3 – 12.2)	9.2 (-5.8 – 24.3)
Work	47.5	52.8	52.2	59.4	11.9 (2.8 – 20.9)	52.1	54.4	47.6	54.4	2.4 (-7.6 – 12.2)	9.5 (-3.4 – 22.5)
Tenderness of study joint (high values are worse outcomes)	2.4	1.4	2.1	1.9	-0.4 (-1.1 – 0.2)	2.6	2.6	2.2	2.4	-0.2 (-0.7 – 0.4)	-0.3 (-1.1 – 0.6))

Outcomes highlighted in orange were statistically significantly different. Outcomes highlighted in light blue did not meet statistical significance but favored traction therapy.

Disclosure: G. Lo: None; **L. Drillock**: None; **K. Staines**: None; **M. Strayhorn**: None; **K. Tse**: None; **G. Virtanen**: None; **L. Welsh**: None; **M. Seu**: None; **E. Gersh**: None; **I. Haugen**: None; **A. Grainger**: None; **J. Samuels**: None.

Abstract Number: 2090

Don't Throw Out X-Rays! Radiographic Osteoarthritis Severity is Prognostic for Onset of Frequent Knee Pain

Grace Lo[1], Julieann Patarini[2], Timothy McAlington[3], Charles Eaton[4] and Jeffrey Driban[5], [1]Baylor College of Medicine / MEDVAMC, Houston, TX, [2]UMass Chan Medical School, Worcester, MA, [3]UMass Chan School of Medicine, Arlington, MA, [4]Brown University, Pawtucket, RI, [5]University of Massachusetts Chan Medical School, Marlborough, NH

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is the most common form of arthritis, a condition associated with substantial disability. Radiographic severity of OA is associated with the presence or absence of frequent knee pain cross-sectionally. Our purpose was to test the prognostic potential of radiographs among knees without frequent pain by evaluating whether radiographic disease severity predicts frequent knee pain over time.

Methods: This is a knee-based longitudinal study of participants of the Osteoarthritis Initiative (OAI). We only included knees that were free of frequent pain at the baseline visit. Posterior-Anterior semi-flexed knee radiographs were obtained at the baseline visit and scored for Kellgren-Lawrence (KL) grade (0-4). At the baseline and annual visits, participants reported whether they had knee-specific frequent pain using the question, of whether the participant has had had (right/left) knee pain, aching or stiffness on more than half the days of a month in the last 12 months?

We performed knee-based logistic regression analyses, using generalized estimating equations to account for correlation between knees within a person, where the independent variable was baseline KL grade and the outcome of interest was frequent knee pain at the 12-month visit. Analyses were repeated with outcome at the 48-month visit.

Results: 6159 knees from 3714 participants were included in this study, 58% were female, mean age was 61.5 (9.2) years, mean body mass index was 28.3 (4.7) m^2/kg.

Conclusion: Radiographic disease severity, based on KL grades, is a prognostic biomarker for frequent knee pain among those without existing symptoms in as short as one year of follow-up. Radiographs could be a screening tool to identify those at high risk of developing frequent knee pain. This may be a useful strategy for testing potential therapies aimed at the preventing the onset of frequent knee pain.

Table. KL Grade at Baseline Visit Associated with Frequent Knee Pain at 12- and 48- month follow up.

KL Grade at the Baseline Visit	Frequent Knee Pain at 12 months (n = 3488 participants, 5800 knees)	Odds Ratio for Frequent knee pain at 12 months	Frequent Knee Pain at 48 months (n = 3324 participants, 5541 knees)	Odds Ratio for Frequent knee pain at 48 months
0 (n = 2529)	12%	referent	15%	referent
1 (n = 1109)	16%	1.3 (1.0 – 1.6)	18%	1.2 (1.0 – 1.5)
2 (n = 1431)	19%	1.6 (1.3 – 2.0)	25%	1.9 (1.6 – 2.3)
3 (n = 623)	25%	2.3 (1.8 – 2.9)	32%	2.7 (2.1 – 3.3)
4 (n = 96)	37%	4.2 (2.7 – 6.5)	50%	5.6 (3.6 – 8.6)
Missing	N = 476		N = 732	

Disclosure: G. Lo: None; **J. Patarini**: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **C. Eaton**: None; **J. Driban**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2091

Multiplanar MRI Quantification of Effusion-Synovitis: Reliability and Potential Investigative Utility for Inflammation-Mediated Knee Conditions

Greg Gilles[1], Dagoberto Robles[2], Luke Grawer[3], Nathaniel H. Christiansen[4], Karim Jayyusi[3], Ali Shaikh[3], Rongrong Tang[5], Mihra S. Taljanovic[3], Jeffrey Duryea[6], Edward J. Bedrick[5] and C. Kent Kwoh[7], [1]University of Arizona Arthritis Center, The University of Arizona College of Medicine, Tucson, AZ, [2]University of Arizona, Tucson, AZ, [3]University of Arizona, Tucson, [4]University of Arizona, Stockton, NJ, [5]The University of Arizona Arthritis Center, University of Arizona, Tucson, [6]Brigham and Women's Hospital, Boston, MA, [7]The University of Arizona Arthritis Center, University of Arizona, Tucson, AZ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Effusion-synovitis (ES) is often seen in knee osteoarthritis (KOA), and MRI-detected ES may serve as a potential imaging biomarker of disease activity, progression, and treatment response. However, reproducible and scalable fully quantitative methods to assess ES remain limited. We developed a multiplanar, semi-automated system for trained non-expert readers to segment ES using two non-contrast enhanced (NCE) 3 T MRI sequences simultaneously and assessed its reliability and validity as an efficient method of quantifying ES in KOA patients.

Methods: OAI participants with radiographic KOA (Kellgren-Lawrence grades 2-3) at baseline were randomly selected (n=80 knees; 1 knee per participant). Following a validated single-slice ES method, a three-monitor setup was employed featuring custom post-processing algorithms to standardize homologous ES on axial DESS and sagittal TSE NCE-MRI images (Figure 1). Variable grayscale thresholding, 3D visualization/localization, and rapid refinement was facilitated by a multi-button mouse (Figure 2). Measurement was performed on both views in parallel with real-time quantification to achieve sub-millimeter volume differences across planes or simultaneously via cross-plane projective segmentation. Fifty knees were segmented in parallel by an MSK radiologist. One non-expert reader was trained using the first 20 scans and then made repeated measurements on the following 30 knees ("validity set"). Three non-experts repeated the parallel approach on 30 different knees ("reliability set"). We evaluated agreement using mean absolute difference (MAD), and intra- and inter-reader reliability using intraclass correlation coefficients (ICC) from a linear mixed model with random effects for knee, reader, and interaction between knee and reader.

Results: Scan reading times averaged < 5 minutes for simultaneous ES segmentation. ES volumes averaged between 7683 mm^3 and 8911 mm^3 across comparison groups. In the validity set, the multiplanar (axial, sagittal) inter-reader ICCs were 0.995, 0.996 (MADs: 424 mm^3, 470 mm^3) and intra-reader ICCs were 0.991, 0.993 (470 mm^3, 493 mm^3) (Figure 3).

Figure 1: Triple-monitor, multi-view effusion-synovitis (ES) quantification system showing the tile view of the axial DESS images with segmentations and cross-plane sagittal projections and scan localization on the left monitor, the tile view of the sagittal TSE images with sagittal segmentations and active slice identification on the right monitor, and semi-automated ES software with real-time ES quantification, localization and projection on the center monitor.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Diagram of mouse displaying software functions programmed as buttons and button combinations that can be performed rapidly to generate precise effusion-synovitis shadings.

Validity Set	Parallel Segmentation		Cross-Planar Projective Segmentation	
	Axial (95% CI)	Sagittal (95% CI)	Axial-Sagittal Overlap (95% CI)	Sagittal (95% CI)
Non-expert intra-reader ICC	0.991 (0.983, 0.997)	0.993 (0.989, 0.996)	0.993 (0.983, 0.998)	0.993 (0.988, 0.997)
Non-expert intra-reader MAD (mm³)	470 (291, 720)	493 (316, 746)	427 (269, 646)	503 (324, 733)
Expert vs. Non-expert inter-reader ICC	0.995 (0.979, 0.996)	0.996 (0.971, 0.997)	0.995 (0.975, 0.996)	0.996 (0.967, 0.997)
Expert vs. Non-expert inter-reader MAD (mm³)	424 (297, 592)	479 (336, 619)	452 (339, 592)	514 (388, 652)
Reliability Set				
Non-expert intra-reader ICC	0.989 (0.968, 0.996)	0.991 (0.969, 0.995)		
Non-expert intra-reader MAD (mm³)	567.9 (457.5, 682.1)	604.2 (469.3, 772.8)		
Non-expert inter-reader ICC	0.977 (0.966, 0.986)	0.984 (0.978, 0.989)		
Non-expert inter-reader MAD (mm³)	915.6 (762.6, 1082.2)	963.9 (805.5, 1128.7)		

Acronyms: KL Kellgren-Lawrence, MSK musculoskeletal, CI Confidence Interval, ICC Intraclass Correlation Coefficient, MAD Mean Absolute Difference, 2D two-dimensional, IW intermediate-weighted, FS fat-suppressed, TSE turbo spin-echo, 3D three-dimensional, MPR multiplanar reformation, DESS dual-echo steady-state, WE water excitation

Figure 3. Reader performance in our study. The "validity set" composed of 29 KL grade 2 and 3 (19 and 10, respectively) knees segmented in parallel by an expert MSK radiologist on sagittal 2D IW FS TSE and axial 3D MPR DESS WE images. One non-expert reader made repeated measurements on the set using parallel and cross-planar projective segmentation to assess non-expert intra-reader and inter-reader reliability and validity using both approaches. Three additional non-experts repeated parallel measurements of 29 different KL 2 and 3 knees (16 and 13, respectively, "reliability set") to assess non-expert inter- and intra-reader reliability.

When measuring both views simultaneously via projection, the multiplanar inter-reader ICCs were 0.995, 0.996 (452 mm3, 514 mm3) and intra-reader ICCs were 0.993, 0.993 (427 mm3, 503 mm3). In the reliability set, the multiplanar inter-reader ICCs were 0.977, 0.984 (916 mm3, 964 mm3) and intra-reader ICCs were 0.989, 0.991 (568 mm3, 604 mm3).

Conclusion: By employing a system with custom artifact correction, tissue standardization and hardware and software tools, non-expert readers were able to be trained to segment ES. They demonstrated high reliability and concurrent validity with excellent agreement with an expert MSK radiologist's measurements for both multi-view ES measurement methods. Our method allows for expedited simultaneous segmentation to produce rapid, detailed assessment of ES large knee MRI datasets, and facilitate the development of objective, critical measures of joint inflammation.

Disclosure: G. Gilles: None; **D. Robles**: None; **L. Grawer**: None; **N. Christiansen**: None; **K. Jayyusi**: None; **A. Shaikh**: None; **R. Tang**: None; **M. Taljanovic**: None; **J. Duryea**: None; **E. Bedrick**: None; **C. Kwoh**: Apos Health, 1, 2, Express Scripts, 1, 2, Kolon Tissue Gene, 2, Mobieus Sun, 1, 2, TLC, 1, 2, Xalud, 1, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2092

Associations Among Biomarkers, Cytokines, and Ultrasound Features of Knee Osteoarthritis: A Cross-sectional Analysis in the Johnston County Health Study

Jasmine Kimber[1], Carolina Alvarez[2], Virginia Kraus[3], Janet Huebner[3], Liubov Arbeeva[4], Todd Schwartz[5], Yvonne Golightly[6], Richard Loeser[7] and Amanda Nelson[1], [1]University of North Carolina at Chapel HIll, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]Duke University, Durham, NC, [4]University of North Carolina, Chapel Hill, Carrboro, NC, [5]University of North Carolina-Chapel Hill, Chapel Hill, NC, [6]University of Nebraska Medical Center, Omaha, NE, [7]University of North Carolina, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is a leading cause of disability worldwide, characterized by progressive joint degeneration, chronic pain and functional impairment (PMID: 24024017). While imaging modalities such as radiographs are standard for OA diagnosis, emerging research suggests that ultrasound (US) imaging, potentially in combination with other disease markers such as soluble biomarkers and cytokines, may offer a more dynamic assessment of joint health (PMID: 39201072). This study aims to explore these associations utilizing data from the Johnston County Health Study (JoCoHS), a population-based cohort initiated in 2019 in North Carolina.

Methods: Participants (N=91) in JoCoHS who underwent bilateral knee US and serum and plasma biomarker assessment by ELISA as part of a substudy (**Table 1**) were included. US images were acquired by a trained sonographer and scored by two expert readers using standardized criteria for distinct structural and inflammatory joint pathologies including synovitis, osteophytes, meniscal and cartilage damage (**Table 2**, described in PMID 39989271). Separate linear regression models of associations between each log-transformed biomarker with each US feature were used to produce adjusted mean differences (betas) and 95% confidence intervals (CI), adjusted for age, sex, race/ethnicity, body mass index (BMI), education (as a proxy for socioeconomic status), Charlson Comorbidity index (CCI), and symptoms in other sites (i.e., hip, wrist, or hand).

Results: Among 91 participants (mean age 55 [range 35-70] years, 39% male, 35% Black, 12% Hispanic, mean BMI 34 kg/m^2) with US and biomarker data, joint pathology and GS synovitis were common, with 92% of participants having at least one knee with cartilage damage on US. On average, elevated cartilage oligomeric matrix protein levels (COMP) were modestly but significantly associated with the presence of mild medial osteophytes (**Table 2**). Hyaluronic acid (HA) levels were significantly higher in participants with severe effusion/synovitis, severe GS synovitis, and medial meniscal extrusion. Increased interleukin-6 (IL-6) levels were observed in association with both PD synovitis and lateral cartilage damage. Both HA and IL-6 were higher in those with severe medial cartilage damage, but this was not statistically significant. Additionally, tumor necrosis factor-alpha (TNF-a) levels were on average slightly higher in individuals with severe GS synovitis, lateral osteophytes and medial meniscal extrusion (**Table 2**).

Table 1. Descriptive statistics of the OA biomarkers and inflammatory cytokines in a subsample of the JoCoHS (n=91).

Serum Biomarker	*Vendor*	*Mean*	*±SD*	*Range*	*LLOD*	*Intra-assay CV (%)*	*Inter-assay CV (%)*
COMP ng/ml	Biovendor	682	274	282-2002	0.4	1.2	6.7
HA ng/ml	Corgenix	39.4	36.2	10-172	20	6.7	4.2
IL-6 pg/ml	MSD VPLEX	1.13	0.74	0.32-3.54	0.06	4.4	7.6
TNF-a pg/ml	MSD VPLEX	2.42	0.61	0.89-4.23	0.04	7.5	3.4

Abbreviations: SD: standard deviation; LLOD: Lower limit of detection; COMP: Cartilage Oligomeric Matrix Protein; HA: Hyaluronic Acid; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-alpha. COMP is a marker for cartilage turnover; HA is a marker for synovitis; IL-6 and TNF-α are pro-inflammatory cytokines.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adjusted* mean differences (95% CI) for log-transformed OA biomarkers and inflammatory cytokines by US features.

	Biomarker Outcomes			
Ultrasound features	**ln (COMP)**	**ln (HA)**	**ln (IL-6)**	**ln (TNF-a)**
	Beta (95% CI)			
GS effusion/synovitis				
1 (vs 0)	0.04 (-0.11, 0.18)	-0.01 (-0.30, 0.29)	-0.05 (-0.34, 0.24)	0.03 (-0.08, 0.13)
2 (vs 0)	-0.11 (-0.26, 0.05)	-0.08 (-0.39, 0.23)	-0.21 (-0.51, 0.10)	0.03 (-0.08, 0.14)
3 (vs 0)	0.12 (-0.13, 0.38)	**0.74 (0.23, 1.25)**	0.28 (-0.22, 0.78)	0.11 (-0.08, 0.30)
GS synovitis				
1 (vs 0)	0.03 (-0.11, 0.17)	-0.04 (-0.32, 0.25)	-0.00 (-0.28, 0.28)	0.05 (-0.06, 0.15)
2 (vs 0)	-0.09 (-0.24, 0.06)	-0.09 (-0.40, 0.21)	-0.25 (-0.54, 0.05)	-0.01 (-0.12, 0.10)
3 (vs 0)	0.16 (-0.11, 0.43)	**0.84 (0.30, 1.38)**	0.35 (-0.18, 0.88)	**0.21 (0.01, 0.41)**
GS effusion (vs absent)	0.03 (-0.11, 0.16)	0.18 (-0.11, 0.47)	0.00 (-0.27, 0.28)	0.01 (-0.10, 0.11)
PD for synovitis				
1 (vs 0)	0.14 (-0.00, 0.28)	0.10 (-0.20, 0.40)	**0.36 (0.09, 0.64)**	-0.05 (-0.15, 0.06)
2 (vs 0)	0.19 (-0.11, 0.50)	-0.24 (-0.88, 0.41)	0.34 (-0.25, 0.93)	-0.00 (-0.23, 0.23)
Osteophytes, medial				
1 (vs 0)	**0.21 (0.08, 0.35)**	0.23 (-0.07, 0.53)	0.12 (-0.16, 0.40)	-0.00 (-0.11, 0.11)
2 (vs 0)	0.05 (-0.11, 0.21)	-0.04 (-0.37, 0.30)	0.07 (-0.24, 0.39)	0.11 (-0.01, 0.23)
3 (vs 0)	0.14 (-0.08, 0.35)	0.29 (-0.18, 0.76)	0.40 (-0.04, 0.84)	-0.02 (-0.18, 0.15)
Osteophytes, lateral				
1 (vs 0)	0.05 (-0.10, 0.19)	0.25 (-0.05, 0.56)	-0.15 (-0.44, 0.14)	-0.02 (-0.13, 0.09)
2 (vs 0)	-0.01 (-0.20, 0.17)	0.18 (-0.19, 0.55)	0.18 (-0.17, 0.54)	**0.20 (0.07, 0.33)**
3 (vs 0)	0.18 (-0.21, 0.57)	0.59 (-0.20, 1.39)	-0.06 (-0.82, 0.70)	-0.09 (-0.37, 0.18)
Meniscal extrusion, medial (vs absent)	-0.03 (-0.19, 0.14)	**0.41 (0.06, 0.75)**	-0.23 (-0.56, 0.10)	**0.15 (0.03, 0.27)**
Meniscal extrusion, lateral (vs absent)	0.08 (-0.09, 0.24)	0.16 (-0.18, 0.49)	0.11 (-0.21, 0.43)	0.10 (-0.01, 0.22)
Cartilage damage, medial				
1 (vs 0)	0.05 (-0.12, 0.21)	0.02 (-0.33, 0.36)	0.09 (-0.23, 0.40)	0.07 (-0.05, 0.19)
2 (vs 0)	0.01 (-0.14, 0.17)	-0.06 (-0.39, 0.27)	0.30 (-0.01, 0.60)	-0.04 (-0.15, 0.08)
3 (vs 0)	0.10 (-0.30, 0.50)	0.47 (-0.36, 1.30)	0.55 (-0.22, 1.32)	0.17 (-0.12, 0.47)
Cartilage damage, lateral				
1 (vs 0)	0.00 (-0.15, 0.15)	-0.00 (-0.33, 0.32)	0.13 (-0.17, 0.43)	-0.07 (-0.18, 0.05)
2 (vs 0)	0.14 (-0.02, 0.30)	-0.03 (-0.36, 0.31)	**0.37 (0.06, 0.67)**	-0.00 (-0.12, 0.12)
3 (vs 0)	0.01 (-0.32, 0.33)	0.10 (-0.59, 0.79)	0.39 (-0.24, 1.02)	-0.04 (-0.28, 0.21)
Popliteal cyst				
1 (vs 0)	**0.15 (0.01, 0.31)**	0.18 (-0.13, 0.50)	-0.07 (-0.37, 0.23)	0.03 (-0.08, 0.14)
2 (vs 0)	-0.13 (-0.36, 0.11)	0.19 (-0.31, 0.69)	0.04 (-0.44, 0.51)	-0.02 (-0.19, 0.15)
Calcium crystal deposition (vs absent)	-0.03 (-0.19, 0.12)	0.29 (-0.03, 0.61)	-0.05 (-0.36, 0.25)	0.06 (-0.08, 0.17)

Abbreviations: CI, Confidence Interval; GS, Gray Scale; PD, Power Doppler. Linear regression modeling natural log of each inflammatory biomarker outcome and its association with each US feature, separately. Each model adjusts for age, sex, race/ethnicity, BMI, education, CCI, hip, wrist, and hand PAS. Shown **BOLD** when significant at 0.05 level.

Conclusion: Our findings demonstrate that specific US features of joint pathology relevant to OA are associated with distinct biomarkers in a diverse population, particularly HA and GS synovitis, which had the strongest associations. These results support the role of structural changes and inflammation in the pathogenesis of OA and highlight the utility of US imaging (which allows visualization of soft tissues in a more accessible manner than does MRI) and biomarker data for characterizing disease variation and tailored avenues of assessment, monitoring and treatment.

Disclosure: J. Kimber: None; **C. Alvarez**: None; **V. Kraus**: 4-P Pharma, 1, Genascence, 1, Pacira, 1, Paradigm Biopharma, 1; **J. Huebner**: None; **L. Arbeeva**: None; **T. Schwartz**: None; **Y. Golightly**: None; **R. Loeser**: None; **A. Nelson**: Novo Nordisk, 1.

Abstract Number: 2093

Association of Acetaminophen Use with Clinical Outcomes in Older Adults with Osteoarthritis: A Global Propensity-matched Retrospective Cohort Analysis

Justin Riley Lam[1], Laith Alomari[2], Emmanuel Otabor[2], Michael Hamilton[2], Bal Subedi[3], Maxim Barnett[2], Fabian Rodriguez Quinonez[4] and Irene Tan[5], [1]Albert Einstein Medical Center, Philadelphia, PA, [2]Jefferson Einstein Hospital Philadelphia, Philadelphia, PA, [3]Jefferson Einstein Montogmery Hospital, Philadelphia, [4]Einstein Medical Center Philadelphia, Philadelphia, PA, [5]Einstein Healthcare Network Philadelphia - Jefferson Health, Bala Cynwyd, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Acetaminophen is widely recommended for osteoarthritis (OA) pain management due to its perceived safety profile. However, its long-term effects on clinical outcomes among older adults remain poorly defined. This study aimed to assess the association between acetaminophen use and mortality, cardiovascular, gastrointestinal, and laboratory outcomes in a large OA population.

Methods: We conducted a retrospective cohort study using the TriNetX Global Collaborative Network. Adults aged ≥65 years with osteoarthritis were identified between January 1, 2004, and December 31, 2024. Cohort 1 (n=1,090,625) included patients who initiated acetaminophen within one year of OA diagnosis; Cohort 2 (n=2,174,179) included patients with OA who did not receive acetaminophen. After 1:1 propensity score matching for demographics, comorbidities, and medications, 483,647 patients per cohort were analyzed. Outcomes over three years included death, peptic ulcer disease (PUD), lower gastrointestinal bleeding (LGIB), myocardial infarction (MI), stroke, and laboratory measures of creatinine and hemoglobin. Comparative analyses included measures of association and Kaplan-Meier survival.

Results: Post-matching, baseline characteristics were balanced. Acetaminophen use was associated with increased risks of death (HR 1.46, 95% CI 1.43–1.48, p< 0.001), PUD (HR 3.11, 95% CI 2.91–3.32, p< 0.001), LGIB (HR 1.98, 95% CI 1.91–2.05, p< 0.001), MI (HR 2.12, 95% CI 2.05–2.19, p< 0.001), and stroke (HR 1.70, 95% CI 1.65–1.75, p< 0.001). Survival probability at three years was lower in acetaminophen users compared to non-users (89.7% vs 92.7%). Laboratory analysis revealed higher mean creatinine (1.07 vs 1.00 mg/dL, p< 0.001) and lower mean hemoglobin (12.39 vs 13.29 g/dL, p< 0.001) among acetaminophen users.

Conclusion: In a large cohort of older adults with OA, acetaminophen use was associated with significantly increased risks of mortality, gastrointestinal bleeding, cardiovascular events, and laboratory abnormalities compared to non-use. These findings challenge the notion of acetaminophen as a universally benign analgesic in older patients with OA and highlight the need for more cautious prescribing practices and patient monitoring.

Disclosure: J. Lam: None; **L. Alomari**: None; **E. Otabor**: None; **M. Hamilton**: None; **B. Subedi**: None; **M. Barnett**: None; **F. Rodriguez Quinonez**: None; **I. Tan**: Navidea Radiopharmaceuticals, 12, Principal Investigator in a clinical trial, Novartis, 12, Principal Investigator in a clinical trial.

Abstract Number: 2094

Evaluating the Accuracy of Knee Acoustic Emissions Classification of Varus Thrust

Kari Falaas[1], Ahmet Emirdagi[2], Christopher Nichols[2] and David Ewart[3], [1]University of Minnesota, Minneapolis, [2]Georgia Institute of Technology, Atlanta, [3]Minneapolis Veterans Affairs Medical Center, Minneapolis

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) of the knee is a leading cause of disability, healthcare expenditures, and is associated with diminished quality of life and increased mortality. Varus thrust is a pathologic gait pattern that is more prevalent in individuals with obesity and associated with incident and progressive knee osteoarthritis. Knee acoustic emissions (KAE) is a practical, point-of-care assessment of knee health that can inform several pathological states, including early and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

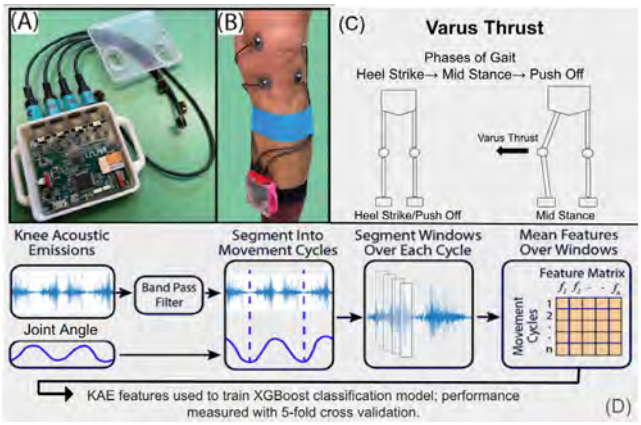


Figure 1. Workflow for measurement and extraction of KAE. A. Contact microphones and associated hardware for KAE measurement. B. Microphones and hardware mounted on participant's knee. C. Assessment for varus thrust at mid-stance phase of gait during ambulation. D. Extraction of KAE features by biomechanically-defined gait cycle into feature matrix for training classification model. KAE: knee acoustic emissions.

established knee OA. Whether KAE is sensitive to knee OA risk or prognostic factors, such as varus thrust, is unknown. This study aims to evaluate the accuracy of a KAE-based model for classification of knees with varus thrust.

Methods: We recruited 20 adult participants with obesity with or without frequent and persistent knee pain from the Minneapolis Veterans Affairs Medical Center (MVAMC), whose institutional review board approved the study. During motion analysis, KAE was measured from bilateral knees using four contact microphones placed medially and laterally on the superior and inferior aspect of the patella. The presence of varus thrust was assessed by two independent reviewers using videos

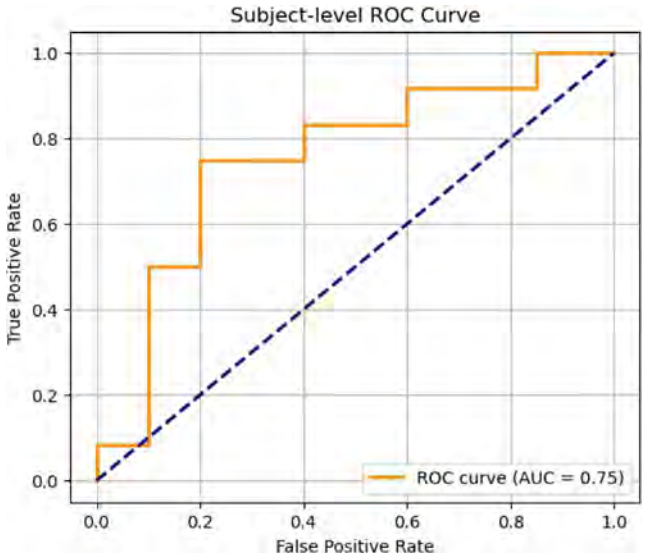


Figure 2. Receiver Operating Characteristic Curve of KAE Classification Model for Varus Thrust. Model performance area under the curve was 0.75. ROC: Receiver operating characteristic; AUC: area under the curve.

Table 1. KAE Model Results

Sensitivity	70%
Specificity	76%
Accuracy	82%

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of ambulation. Participants ambulated at self-selected slow, medium, and fast speeds. KAE from each condition were isolated from one another to specific phases of gait using 30 ms windows with 20 ms overlap. 73 spectral, temporal, and amplitude-based features were extracted per window to train an XGBoost classifier for varus thrust detection. Knees with a percentage of positively classified windows above an empirically derived optimal threshold were classified as thrust-positive. Performance was assessed via 5-fold cross validation to obtain average values for accuracy, sensitivity, and specificity.

Results: Twenty participants (13 males) were recruited, with a mean age of 54.5 years and average body mass index (BMI) of 39.2. Eleven participants reported frequent and persistent knee pain. Twenty-three knees were graded Kellgren–Lawrence ≥2. Aggregate Knee Injury and Osteoarthritis Outcome Score (KOOS) subscale scores were: Activities of Daily Living – 80, Sports– 62, and Quality of Life – 58. Twenty-five percent of knees had varus thrust. The KAE model had a sensitivity, specificity, and accuracy of 70%, 76%, and 82%, respectively.

Conclusion: Models trained with KAE can accurately classify knees with varus thrust. KAE likely contain information about the larger biomechanical status of the knee and future studies should assess whether acoustics can predict other pathologic biomechanics of the knee.

Disclosure: K. Falaas: None; **A. Emirdagi**: None; **C. Nichols**: None; **D. Ewart**: None.

Abstract Number: 2095

Trends in Mortality and Disability-Adjusted Life Years (DALYs) from Osteoarthritis in the United States Compared to Global Estimates: A GBD-Based Analysis (1990–2021)

Khadija Mohib[1], Rameez Qasim[2], ZAUHA FAWAD MEMON[3], Muhammad Asjad Saleem[4], Matia Fawad Memon[5] and Zaiya Waseem[6], [1]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, [2]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [3]Peoples University of Medical and Health Sciences for Women, Tando Allahyar, Sindh, Pakistan, [4]Indus Hospital Karachi, Karachi, [5]Peoples University of Medical and Health Sciences for Women, Tando Allahyar, Pakistan, [6]AtlantiCare Regional Medical Center, New Jersey

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) represents a growing public health concern, particularly among the aging population, contributing significantly to both mortality and Disability-Adjusted Life Years (DALYs). This study evaluates trends in OA-related DALY and mortality from 1990 to 2021, utilizing data from the Global Burden of Disease (GBD) database, with a comparative focus on the United States and global trends.

Methods: Data from the 2021 Global Burden of Disease (GBD) database were analyzed to evaluate osteoarthritis-related mortality and Disability-Adjusted Life Years (DALYs) among individuals aged 65 years and older in the United States and globally. DALY and mortality rates were reported per 100,000 population. Long-term trends from 1990 to 2021 were assessed using Annual Average Percentage Change (AAPC), with statistical significance determined by 95% confidence intervals (CIs) and p-values. Annual Percentage Change (APC) was also calculated for specific time intervals to identify periods of significant deviation from the overall trend.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: DALYs attributed to osteoarthritis showed a consistent upward trend globally, with a D-AAPC of 0.30% (95% CI: 0.28–0.31, $p < 0.000001$), observed similarly in both females (0.30%) and males (0.31%). Notably, a significant spike in DALY-APC (0.85%) was recorded between 2006 and 2009.

In the United States, 44,590 OA-related deaths were reported between 1990 and 2021. The AAPC for mortality increased by 0.76% (95% CI: 0.11–0.41, $p = 0.0215$), aligning with the global trajectory. However, mortality trends showed fluctuations over time, with the lowest APC of -2.90% (95% CI: -3.93 to -1.18, $p = 0.000035$) between 2011 and 2018 and the highest APC of 13.03% (95% CI: 4.33–20.08, $p = 0.0068$).

In the U.S., the D-AAPC over the last three decades increased by 1.68% (95% CI: 0.04–0.29, $p = 0.0707$), with a gender-specific increase of 0.12% for men and 0.24% for women. Several intervals showed declining mortality rates, notably between 1993–1996, 1996–1999, and 1999–2005 with D-APCs of -0.11%, -2.19%, and -1.08% respectively.

Conclusion: This study demonstrates a rising burden of osteoarthritis, reflected in both DALY and mortality trends, in the United States and globally over the past three decades. While some fluctuations exist, the overall trajectory suggests worsening impact, especially among older adults. These findings underscore the urgent need for targeted prevention strategies, improved access to musculoskeletal care, and investment in early intervention programs to reduce long-term disability and mortality. Further research is warranted to identify modifiable risk factors and health system inefficiencies contributing to these escalating trends.

Disclosure: K. Mohib: None; **R. Qasim**: None; **Z. MEMON**: None; **M. Saleem**: None; **M. Memon**: None; **Z. Waseem**: None.

Abstract Number: 2096

Gamification and Social Incentivization to Promote Physical Activity in Adults with Knee Osteoarthritis: Results from a Multi-site Randomized Trial

Kimberly Hayes[1], Bryant England[2], Katherine Wysham[3], Mercedes Quinones[4], Marianna Olave[5], Sarah Wetzel[6], Hannah Brubeck[7], Rachel Gillcrist[8], Criswell Lavery[9], Natalie Keller[10], Bibiana Ateh[11], Bridget Kramer[2], Rui Xiao[9], Kaitian Jin[9], Alexis Ogdie[12], Daniel K. White[13], Tuhina Neogi[14], Carla Scanzello[9] and Joshua Baker[9], [1]Teachers College, Columbia University, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [4]Washington DC VA Medical Center, Bethesda, MD, [5]Brown University, Philadelphia, PA, [6]Drexel University, Pittsburgh, PA, [7]VA Puget Sound Health Care System, Seattle, WA, [8]Dartmouth College, Lebanon, NH, [9]University of Pennsylvania, Philadelphia, PA, [10]University of Oklahoma, Philadelphia, PA, [11]Washington VA Medical Center, Washington, District of Columbia, [12]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [13]University of Delaware, Newark, DE, [14]Boston University School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Promotion of physical activity is important in the management of knee osteoarthritis (KOA), though effective strategies for behavioral change to promote exercise are lacking. The aim of the study was to determine if an incentive program based on principles from behavioral economics including gamification and social incentivization could promote physical activity and reduce self-reported pain and disability in adults with KOA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

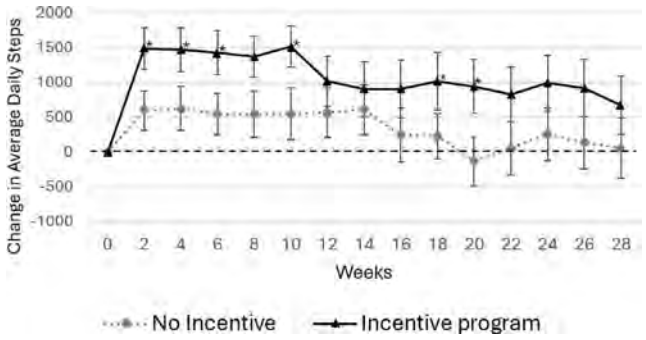


Figure 1: Change in average weekly step count changes in incentive (black triangles) and control groups (grey circles). Brackets indicate 95% confidence interval.

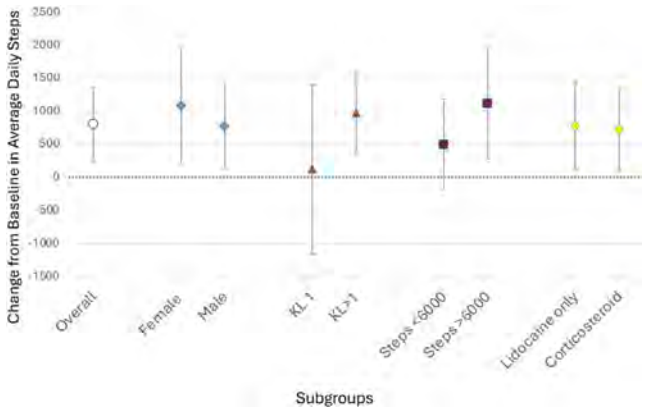


Figure 2: Effect of the intervention (difference between incentive and control by subgroup). Brackets indicate 95% confidence interval.

Methods: This was a factorially-designed multi-site randomized controlled clinical trial. Participants were randomized to receive an incentive program to promote greater physical activity or an attention control. Participants received a Fitbit monitor and completed patient-reported outcomes through a web-based platform. Participants who were randomized into the incentive program received points for achieving step goals and advanced in a game on a weekly basis based on their success. The control arm received a Fitbit and answered surveys but did not receive an incentive. Participants were also randomized to receive blinded corticosteroid injections v. lidocaine only in a factorial design. The analysis used mixed-effects models to evaluate the time-averaged effect of the intervention over a 28-week study follow-up on both average daily step counts (averaged over 2 weeks) as well as secondary patient-reported outcomes, including the Knee Osteoarthritis

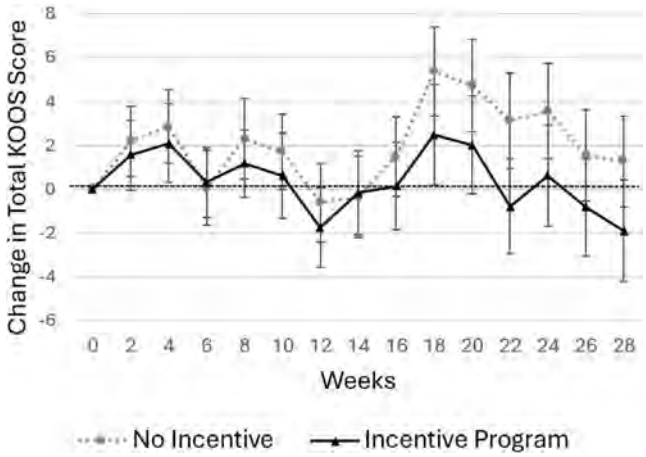


Figure 3: Change in the total KOOS score over 28 weeks among the incentive (black triangles) and control (grey circles) groups. Brackets indicate 95% confidence intervals.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Outcome Score (KOOS). Secondary outcomes also included the Patient-Reported Outcomes Measurement Information System (PROMIS) pain assessments.

Results: Of 231 that were enrolled, 221 were randomized with an average age of 64 years and 84% male. Those that were randomized to the incentive (N=110) walked an average of 830 (95% CI: 254, 1405) more steps/day than the control arm (N=111) (p=0.005). The increase in steps/day compared to the control arm was similar across the 28-week study (Figure 1), though step counts generally declined with time in both groups. There were no significant differences in the effect of the intervention on the change in step counts by gender, Kelgren-Lawrence grade, baseline step count, or receipt of corticosteroid (v. lidocaine only) (Figure 2). While the incentive program resulted in an improvement in average daily step counts, there was no difference in the change in KOOS scores over the study period in the incentive group compared to the control group [β: -1.59 (95% CI: -4.51, 1.33) p=0.29] (Figure 3). The incentive group also did not report significant differences in change in pain intensity, pain behavior, or pain interference.

Conclusion: An incentive program designed with elements of gamification and social incentivization resulted in a significant increase in average daily steps compared to a control arm in participants with KOA. This difference equates to about a 10–15-minute walk or ½ mile a day and is considered meaningful. While there was improvement in activity, this study does not support prior evidence suggesting that an increase in walking will result in an improvement in symptoms. However, longer duration of sustained increased activity may be needed for symptomatic benefits. Notably the greater activity in the incentive arm did not result in worsening of symptoms.

Disclosure: K. Hayes: None; **B. England**: Boehringer-Ingelheim, 2, 5; **K. Wysham**: None; **M. Quinones**: None; **M. Olave**: None; **S. Wetzel**: None; **H. Brubeck**: None; **R. Gillcrist**: None; **C. Lavery**: None; **N. Keller**: None; **B. Ateh**: None; **B. Kramer**: None; **R. Xiao**: None; **K. Jin**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **D. White**: None; **T. Neogi**: None; **C. Scanzello**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10; **J. Baker**: Amgen, 5.

Abstract Number: 2097

Trajectories of psychological symptoms during an 18-month Diet + Exercise intervention in overweight or obese adults with osteoarthritis

Lily Alomari[1], Daniel Beavers[2], Kate Queen[3], Shannon Mihalko[4], Gary Miller[4], Elena Losina[5], Paul DeVita[6], david Hunter[7], Jovita Newman[4], Sara Quandt[8], Mary Lyles[8], Sandra Soto[3], Joanne Jordan[9], Leigh Callahan[3], Stephen Messier[10] and Becki Cleveland[11], [1]Kansas City University, Raleigh, [2]Wake forest university, Winston Salem, [3]UNC, Chapel Hill, [4]WFU, Winston Salem, [5]BWH, Boston, MA, [6]East Carolina University, Greenville, [7]Sydney Musculoskeletal Health, University of Sydney, St Leonards, New South Wales, Australia, [8]WFU, Winston-Salem, [9]University of North Carolina at Chapel Hill, Chapel Hill, NC, [10]WFU, Winston-Salem, NC, [11]University of North Carolina, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

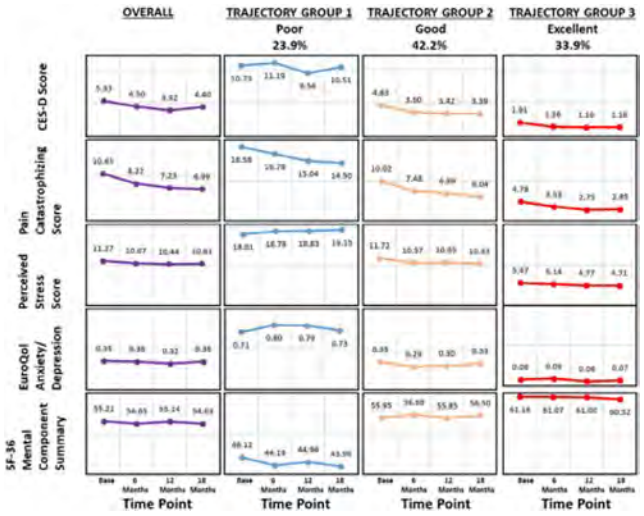
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Psychological symptoms (PsySx) have been associated with osteoarthritis (OA), and exercise may improve PsySx. We aimed to identify unique trajectories of PsySx over the course of 18-months,and examine whether randomization to Diet and Exercise (D+E) vs. attention control (AC) was associated with trajectory class.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Methods: We used data from WE-CAN, a randomized trial of overweight/obese individuals aged 50+ years diagnosed with OA. Outcomes were assessed at baseline and at 6, 12, and 18 months. PsySx assessmentincluded Center for Epidemiological Studies-Depression Scale, Pain Catastrophizing Scale, SF-36 MentalComponent Summary, Perceived Stress Scale, and EuroQol Quality of Life Anxiety/Depression. Group-basedmulti-trajectory model analysis (GBMTM) was used to identify subgroups of individuals with similar change patterns across the 5 PsySx measures. Multinomial logistic regression was used to evaluate the association between randomization group and trajectory class. We further explored associations when stratified by social determinants of health (education, occupation, income, area deprivation).

Results: Among 616 participants, GBMTM identified 3 trajectory classes for PsySx: "poor" [GRP 1;REFERENT], "good" [GRP 2], and "excellent" [GRP 3]. Compared with AC, participants in the D+E groupwere more likely to belong to GRP 2 (adjusted odds ratio [OR] 1.57, 95% confidence interval [CI] 1.02-2.43).This association was stronger among individuals with an income less than $50K per year (OR 1.80, 95% CI1.00-3.24) and living in a low deprivation area (OR 1.75, 95% CI 1.00-3.06).

Conclusion: Our results suggest that OA patients with moderate PsySx may experience improved symptomswith a D+E program. However, those who had severe PsySx at baseline (GRP1) may not experienceimprovements with D+E, possibly due to more serious underlying problems that would require treatments beyond D+E. Further, D+E may not have an effect in those mild PsySx, possibly due to little room for improvement.

Disclosure: L. Alomari: None; **D. Beavers**: None; **K. Queen**: None; **S. Mihalko**: None; **G. Miller**: None; **E. Losina**: None; **P. DeVita**: None; **d. Hunter**: None; **J. Newman**: None; **S. Quandt**: None; **M. Lyles**: None; **S. Soto**: None; **J. Jordan**: None; **L. Callahan**: None; **S. Messier**: None; **B. Cleveland**: None.

Abstract Number: 2098

Responder Phenotype Analysis for Intra-Articular Injections: Secondary Analysis from a Large Multi-Site Crossover Clinical Trial

Natalie Keller[1], Bryant England[2], Katherine Wysham[3], Mercedes Quinones[4], Marianna Olave[5], Sarah Wetzel[6], Hannah Brubeck[7], Rachel Gillcrist[6], Criswell Lavery[8], Bibiana Ateh[9], Bridget Kramer[2], Kimberly Hayes[6], Rui Xiao[8], Kaitian Jin[8], Alexis Ogdie[8], Daniel K. White[10], Tuhina Neogi[11], Carla Scanzello[12] and Joshua Baker[8], [1]University of Oklahoma, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]VA PUGET SOUND/UNIVERSITY OF

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

WASHINGTON, Seattle, WA, [4]Howard University Hospital and Washington DC Veterans Affairs Medical Center, Washington, District of Columbia, [5]Brown University, Philadelphia, PA, [6]Corporal Michael J. Crescenz VA Medical Center, Philadelphia, [7]VA Puget Sound Health Care System, Seattle, WA, [8]University of Pennsylvania, Philadelphia, PA, [9]Washington VA Medical Center, Washington, District of Columbia, [10]University of Delaware, Newark, DE, [11]Boston University School of Medicine, Boston, MA, [12]University of Pennsylvania, Philadelphia

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Intra-articular (IA) corticosteroid injections are commonly utilized for pain management in knee osteoarthritis (KOA). However, clinical characteristics associated with a greater benefit from corticosteroid above placebo are not well defined. We aimed to identify participant characteristics associated with superior response to corticosteroid plus lidocaine compared to lidocaine-only, leveraging data from a large multi-site crossover trial.

Methods: In this factorially-designed, double-blinded, randomized trial also evaluating an exercise incentive program, participants were randomized to IA corticosteroid injections with lidocaine or a lidocaine-only placebo, followed by crossover to the other injection at 16 weeks. Participants were age 40-80 years with KOA recruited from 4 VA Medical Centers, had a clinical indication for joint injection, and a Kellgren-Lawrence (K-L) radiographic grade of $\geq$1. The primary outcome was the change in the total Knee Osteoarthritis Outcome Score (KOOS) measured over multiple time points (bi-weekly) for

Table 1. Unadjusted associations between baseline characteristics and greater corticosteroid-attributable benefit from injections in the crossover trial analysis.

	Corticosteroid-Attributable Benefit Univariable Associations	
Participant Characteristics	**B (95% CI)**	**p-value**
Age (per 1 year)	-0.088 (-0.36, 0.18)	0.52
Female (v. Male)	-5.15 (-9.94, -0.37)	0.04
BMI (per 1 kg/m2)	0.07 (-0.26, 0.41)	0.66
Waist Circumference (per 1 cm)	**0.14 (0.00, 0.28)**	**0.06**
Working (v. unemployed)	2.03 (-2.28, 6.33)	0.36
Average Daily Steps (per 1 step)	0.00 (0.00, 0.00)	0.95
Fluid Aspirated from Knee	0.41 (-4.60, 5.42)	0.87
Previously Received Injection(s)	-0.03 (-5.21, 5.14)	0.99
Alcohol Use	-3.44 (-7.57, 0.69)	0.10
Opioid Medication Use	-0.56 (-5.09, 3.98)	0.81
KL Grade		
2 (v. 1)	**6.78 (-0.15, 13.71)**	**0.06**
3 (v. 1)	2.77 (-4.19, 9.72)	0.44
4 (v. 1)	3.29 (-3.06, 9.65)	0.31
Knee PPT*	**0.66 (0.06, 1.26)**	**0.03**
Wrist PPT	0.79 (-0.12, 1.69)	0.09
Smoking (v. Current)		
Former Smoker	4.17 (-2.08, 10.42)	0.19
Never Smoker	**6.81 (1.17, 12.46)**	**0.02**
Area Deprivation Index Quartile		
2 (v. 1)	-2.03 (-7.17, 3.11)	0.44
3 (v. 1)	-0.55 (-7.93, 6.82)	0.88
4 (v. 1)	-3.59 (-9.20, 2.02)	0.21
Comorbidities		
Fibromyalgia	**-6.41 (-12.55, -0.27)**	**0.04**
Anxiety	2.56 (-1.95, 7.06)	0.27
Depression	1.90 (-2.47, 6.28)	0.39
Apnea	-2.36 (-6.68, 1.96)	0.29
Degenerative Disc Disease	-3.82 (-8.34, 0.69)	0.10
Diabetes	1.66 (-3.39, 6.72)	0.52
Neuropathy	-0.97 (-7.19, 5.26)	0.76
Patient Reported Outcomes		
PSQI**	0.06 (-0.51, 0.62)	0.84
Pain Catastrophization Scale***	0.02 (-0.20, 0.24)	0.85
Total KOOS Score†	-0.02 (-0.15, 0.11)	0.72
Believes Injection Will Work	1.42 (-2.82, 5.65)	0.51
PROMIS Pain Intensity	0.03 (-0.25, 0.32)	0.81

Abbreviations: BMI=Body Mass Index; PPT= Pain Pressure Threshold; PSQI=Pittsburgh Sleep Quality Index; KOOS=Knee Injury and Osteoarthritis Outcome; PROMIS=Patient Reported Outcome Measurement Information System

* Higher PPT indicates decreased sensitivity to pain
** Higher PSQI indicates worse sleep quality
*** Higher Pain Catastrophization Scale score indicates higher levels of catastrophic thoughts
† Higher KOOS score indicates fewer knee symptoms

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

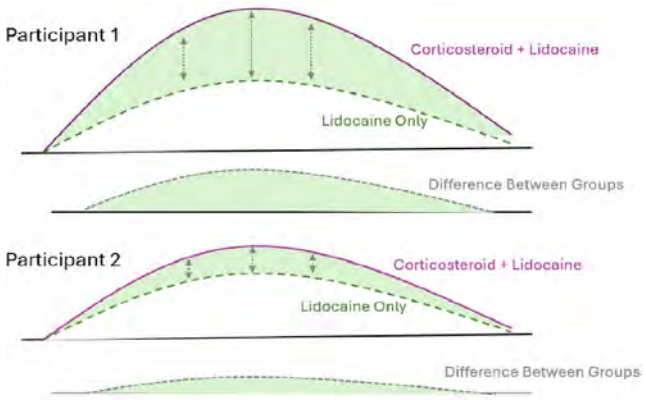


Figure 1. Visualization of "Corticosteroid-Attributable Benefit" (CAB) as Difference in Change in Total KOOS Score at Each Weekly Interval. The CAB was calculated as the average difference in change in total KOOS score at each weekly interval.

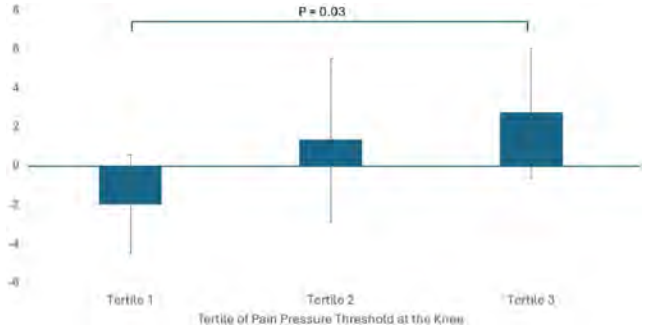


Figure 2. Corticosteroid-Attributable Benefit (CAB) for Each Tertile of Knee Pain Pressure Threshold (PPT). The lowest tertile of PPT demonstrated significantly lower CAB than the highest tertile (p=0.03).

12 weeks after each injection (~1 month washout). The minimal clinically important difference (MCID) was defined as a change of $\geq$10. Participants that received both injections were included in the crossover trial analysis. For each participant, we determined the difference in the change in total KOOS score at each bi-weekly interval to determine the 'corticosteroid-attributable benefit (CAB)' (**Figure 1**). Linear regression incorporating generalized estimating equations identified participant characteristics associated with higher CAB 2-12 weeks after injection.

Results: Among 196 participants, several clinically relevant participant characteristics were associated with CAB (**Table 1**). For example, fibromyalgia (N=11) was associated with lower CAB [B: -6.41 (95% CI: -12.55, -0.27), p=0.04] (**Table 1**). Participants in the lowest tertile of pain pressure threshold (PPT) (N=63), suggesting greater pain sensitization, also had lower CAB (p=0.03) (**Table 1**); the lowest PPT tertile demonstrated smaller CAB compared to the highest (**Figure 2**). Never smokers (N=103) (compared to current smokers) had higher CAB (p=0.02), and CAB was numerically greater among those with higher waist circumference per 1 cm (p=0.06) and among those with a KL grade of 2 (v. 1) (N=42) (p=0.06), though these were not statistically significant (**Figure 2**). When excluding patients with fibromyalgia, KL-scores < 2, and current smokers, there was a significantly greater likelihood of achieving MCID when receiving corticosteroid compared to placebo [OR 2.02 (95% CI: 1.20, 3.40) p=0.008; NNT=10], while no benefit was observed in the overall sample [OR 1.36 (0.93, 1.98) p=0.11; NNT= 23].

Conclusion: In this analysis from a large crossover trial, KOA participants with fibromyalgia and greater pain sensitization experienced significantly less added benefit from IA corticosteroid compared to lidocaine only. These findings suggest reduced benefits of corticosteroids among those with evidence of pain sensitization and may help clinicians select patients most likely to benefit from IA corticosteroids for KOA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Keller: None; **B. England**: Boehringer-Ingelheim, 2, 5; **K. Wysham**: None; **M. Quinones**: None; **M. Olave**: None; **S. Wetzel**: None; **H. Brubeck**: None; **R. Gillcrist**: None; **C. Lavery**: None; **B. Ateh**: None; **B. Kramer**: None; **K. Hayes**: None; **R. Xiao**: None; **K. Jin**: None; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **D. White**: None; **T. Neogi**: None; **C. Scanzello**: None; **J. Baker**: None.

Abstract Number: 2099

Incidence and Prevalence of Osteoarthritis in the United States Compared to Global Trends: Insights from the Global Burden of Disease Study (1990–2021)

Khadija Mohib[1], Rameez Qasim[2], **Nicolas Barnechea Alvarado**[1], ZAUHA FAWAD MEMON[3] and Muhammad Asjad Saleem[4], [1]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV, [2]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [3]Peoples University of Medical and Health Sciences for Women, Tando Allahyar, Sindh, Pakistan, [4]Indus Hospital Karachi, Karachi

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is the most prevalent musculoskeletal condition, predominantly affecting individuals over the age of 55. According to the World Health Organization (WHO), OA has a global prevalence of 7.6%, with women comprising approximately 60% of cases. This study evaluates the global and U.S. trends in osteoarthritis incidence and prevalence from 1990 to 2021 using data from the Global Burden of Disease (GBD) study, highlighting the evolving burden on aging populations.

Methods: Data from the 2021 GBD database were analyzed to assess age-standardized incidence and prevalence rates of OA per 1,000,000 individuals aged 55 years and older. Trends from 1990 to 2021 were examined using the Annual Average Percentage Change (AAPC), with 95% confidence intervals (CIs) and p-values reported to determine statistical significance. Annual Percent Change (APC) was calculated across selected time intervals to capture fluctuations in trend patterns.

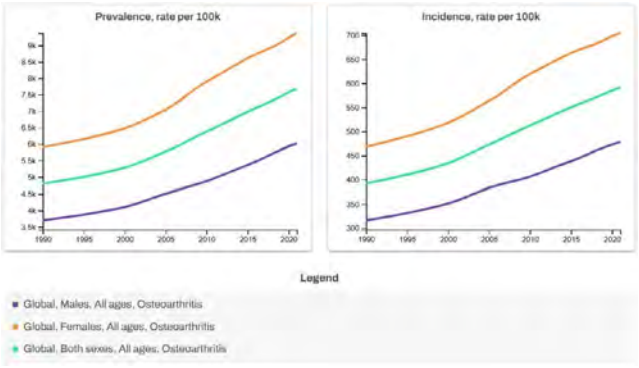
Results: Incidence:

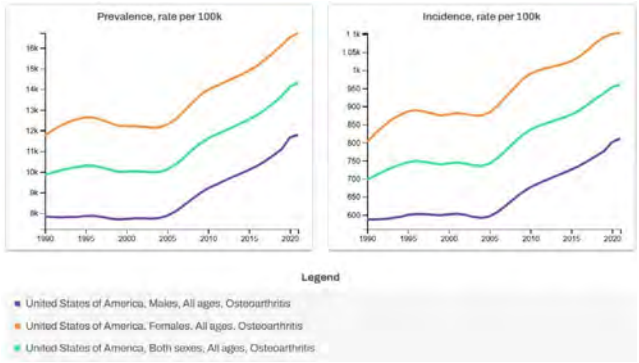
Globally, the incidence of OA increased significantly over the 31-year period, with an overall I-AAPC of 0.28% (95% CI: 0.26–0.30, $p < 0.000001$). Incidence rose by 0.286% in females and 0.28% in males, indicating similar upward trends across sexes. The global I-APC remained relatively stable, with no major deviations.

In the United States, the I-AAPC was slightly lower at 0.20% (95% CI: 0.12–0.29, $p < 0.000001$). Males showed a lower rate of increase (0.16%) compared to females (0.28%), aligning closely with global female trends. However, APC varied significantly across intervals:

- **1990–1995:** Increase of 0.78% per year (95% CI: 0.49–0.94, $p = 0.000002$)
- **1995–2005:** Decline of -1.24% (95% CI: -1.32 to -1.15, $p < 0.000001$)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License





- **2005–2009:** Sharp increase of 1.84% (95% CI: 1.38–2.29, $p < 0.000001$)

Prevalence: The global prevalence of OA also rose steadily, with a P-AAPC of 0.277% (95% CI: 0.26–0.27, $p < 0.000001$). Prevalence increased similarly among both males (0.28%) and females (0.29%). The most significant rise occurred between 2006–2009 with a P-APC of 0.69% (95% CI: 0.58–0.80, $p < 0.000001$), while the smallest change occurred between 2015–2018 (0.05%; 95% CI: -0.05 to 0.15, $p = 0.315$).

In the United States, the P-AAPC was 0.1737% (95% CI: 0.0912–0.2563, $p = 0.000037$). Males showed a lower rate (0.14%) compared to females (0.24%). While overall prevalence increased, notable declines occurred:

- **1995–1999:** -1.46% (95% CI: -1.83 to -1.09, $p < 0.000001$)
- **1999–2005:** -0.89%
- The most significant rise occurred from 2005–2009, with a P-APC of 1.99%.

Conclusion: Between 1990 and 2021, both incidence and prevalence of osteoarthritis have increased among individuals aged 55 and older, in both the United States and globally. Despite some temporal fluctuations, the overall trend is upward, especially among women. These findings emphasize the growing burden of OA on aging populations and highlight the need for public health strategies focused on prevention, early diagnosis, and long-term management of osteoarthritis to reduce disability and healthcare costs associated with this chronic condition.

Disclosure: K. Mohib: None; **R. Qasim**: None; **N. Barnechea Alvarado**: None; **Z. MEMON**: None; **M. Saleem**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2100

Trabecular Bone Texture is Associated with Structural and Pain Progression in Later Stages of Knee Osteoarthritis: Longitudinal Data from the FNIH OAI Cohort

Pawel Podsiadlo[1], C. Kent Kwoh[2], Marcin Wolski[1], Justin Crawmer[3], Rongrong Tang[4], Shen Liu[5], Xiaoxiao Sun[2], Tuhina Neogi[6], Amanda Nelson[7], Jean Liew[8] and Jeffrey Duryea[9], [1]Curtin University, Bentley, Western Australia, Australia, [2]The University of Arizona Arthritis Center, University of Arizona, Tucson, AZ, [3]Mass General Brigham, Boston, [4]The University of Arizona Arthritis Center, University of Arizona, Tucson, [5]University of Arizona, Tucson, AZ, [6]Boston University School of Medicine, Boston, MA, [7]University of North Carolina at Chapel Hill, Chapel Hill, NC, [8]Boston University, Boston, MA, [9]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Trabecular bone has been increasingly recognized as being important in the pathogenesis of OA. Although an earlier study has shown that medial trabecular bone texture (TBT) predicted OA progression, the predictive validity of medial and lateral TBT regions as structural biomarkers for radiographic and pain progression at different stages of radiographic knee OA is not clear. Therefore, we investigated the predictive validity of longitudinal compartmental changes in TBT at different KL stages, as these have important implications for prognosis and treatment.

Methods: We used data from the FNIH OAI sub-study of 600 participants selected based on their 48-month progression status: Group 1: radiographic and pain, Group 2: radiographic-only, Group 3: pain-only, Group 4: non-progressors. Regions of interest (ROIs) were defined with anatomical landmarks based on an automated delineation of the tibial plateau as shown in Figure 1. The inter-edge tibial plateau distance (D) was used to consistently define ROI size and placement in each compartment. For each knee image, an augmented variance orientation method was applied to the ROIs. For each region, the mean (FD_{MEAN}), vertical (FD_V) and horizontal (FD_H) fractal dimensions were calculated. The FD_{MEAN} was the average of FDs in all directions. Minor axis FD (FD_{Sta}) was also calculated, quantifying texture roughness in the direction of the roughest part of trabecular bone, which contains the shortest bone length components. Higher values of FDs indicate rougher texture, i.e., more complex and irregular bone architecture. TBT assessments were performed at the baseline and

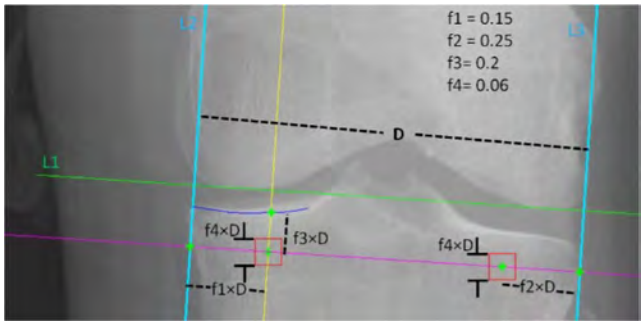


Figure 1. Coordinate system for ROI (red square) positioning The system is flexible in that f1, f2, f3 and f4 are arbitrary distances that can be adjusted automatically once D, L1, L2 and L3 are placed. L1 (green line) = line parallel to the inferior edge of the femoral condyles L2 (left blue line) = line parallel to the medial edge of the tibial plateau L2 (right blue line) = line parallel to the lateral edge of the tibial plateau D (black dotted line) = distance between L2 and L3 and used as a constant to place the region of interest (ROI) f1 = proportion used to place the medial tibial ROI from the medial edge of the tibial plateau f2 = proportion used to place the lateral tibial ROI from the lateral edge of the tibial plateau f3 = proportion used to place the ROI inferior to the rim of the tibial plateau f4 = proportion used to determine the size of the ROI red square = region of interest (ROI) defined as squares with side length of f4×D

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics

Characteristic	Group 1* (n = 194)	Group 2† (n = 103)	Group 3 ‡ (n =103)	Group 4** (n = 200)
Age, mean ± SD years	62.0 ± 8.8	63.1 ± 8.3	59.2 ± 8.7	61.5 ± 9.1
Sex, no. (%) female	110 (56.7)	46 (44.7)	67 (65.0)	130 (65.0)
BMI, mean ± SD kg/m^2	30.7 ± 4.8	30.7 ± 4.7	31.1 ± 5.0	30.5 ± 4.8
Race, no. (%) white	155 (79.9)	91 (88.3)	74 (71.8)	155 (77.5)
WOMAC pain, mean ± SD	2.0 ± 2.6	3.3 ± 4.0	1.9 ± 2.7	2.6 ± 3.2
Baseline KLG, no. (%)				
1	24 (12.4)	14 (13.6)	13 (12.6)	24 (12.0)
2	84 (43.3)	47 (45.6)	61 (59.2)	114 (57.0)
3	86 (44.3)	42 (40.8)	29 (28.2)	62 (31.0)

* radiographic and pain progressors † radiographic-only progressors ‡ pain-only progressors **non-progressors

Table 2. Summary of the results obtained for group comparisons stratified by KLG and compartment

FD	KLG	Group Comparisons	OR_{adj} (95% CI)
FD_{Sta} L	2	1 vs. 4	0.77 (0.63 – 0.93)
FD_{Sta} M		(Radiographic and pain progression vs. non-progressors)	1.32 (1.06 – 1.64)
FD_{Sta} L	2	1 vs. 2, 3, 4	0.81 (0.69 – 0.95)
FD_{Sta} M		(Radiographic and pain progression vs. all other comparators)	1.20 (1.01 – 1.44)
FD_{Sta} L	2	1, 2, 3 vs. 4	0.84 (0.72 -0.98)
FD_{Sta} M		(All progressors vs. non-progressors)	1.16 (0.99 – 1.4)
FD_{mean} L	2	1, 3 vs. 2, 4	1.18 (1.01 – 1.38)
FD_{mean} M		(Any pain progression vs. no pain progression)	0.9 (0.77 – 1.05)
FD_{Sta} L			0.81 (0.69 – 0.94)
FD_{Sta} M			1.16 (0.99 – 1.36)
FD_{V} L	3	2 vs. 3	1.34 (1.06 – 1.70)
FD_{V} M		(Radiographic only progression vs. pain only progression)	1 (0.76 – 1.32)
FD_{H} L			1.27 (1.04 – 1.54)
FD_{H} M			0.87 (0.7 – 1.08)

L = lateral; M = medial; FDSta = roughest fractal dimension; FD mean = the average of the fractal dimensions in all directions : FDV = vertical fractal dimension; FDH = horizontal fractal dimension. Higher fractal dimension indicates rougher bone texture (i.e. more complex and irregular bone architecture). ORadj = odds ratio adjusted for baseline age, sex, race, BMI, WOMAC pain, pixel spacing and ROI size; 95% CI = 95% confidence interval. ORs are based on every 0.01 increase in the fractal dimension.

24-month time points. Multiple logistic regression models were used to examine the associations between pain and/or radiographic progression and baseline to 24-month changes in FDs stratified by Kellgren-Lawrence grade (KLG) 2 and 3 and by compartment. The models were adjusted for baseline age, sex, race, BMI, WOMAC pain, pixel spacing and ROI size.

Results: The demographic characteristics and the significant results are summarized in Tables 1 and 2, with the roughest FDs identified as the strongest predictors of combined pain and radiographic progressor status. The associations were most evident between radiographic and pain progressors (Group 1) vs. non-progressors (Group 4) and vs. all other comparators (Groups 2, 3 and 4) for both the medial and lateral compartments at KLG2. The mean and roughest FDs were identified as the predictors of pain progressor status (1, 3 vs. 2, 4) and the roughest FD was identified as the predictor of any OA progressor status (1, 2, 3 vs. 4) for the lateral compartment at KLG2. The vertical and horizontal FDs were identified as predictors that differentiate structural progression without pain from pain progression without structural change (2 vs. 3) for the lateral compartment at KLG3.

Conclusion: The risk of radiographic OA and pain progression increases with increasing medial trabecular bone texture roughness in knee joints; the risk of radiographic OA and pain progression with lateral roughness is variable. Our results suggest that fractal bone texture analysis may serve as a potential biomarker for risk prediction for structural and symptomatic knee OA progression.

Disclosure: P. Podsiadlo: None; **C. Kwoh**: Apos Health, 1, 2, Express Scripts, 1, 2, Kolon Tissue Gene, 2, Mobieus Sun, 1, 2, TLC, 1, 2, Xalud, 1, 2; **M. Wolski**: None; **J. Crawmer**: None; **R. Tang**: None; **S. Liu**: None; **X. Sun**: None; **T. Neogi**: None; **A. Nelson**: Novo Nordisk, 1; **J. Liew**: None; **J. Duryea**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2101

LEVI-04, a Novel Neurotrophin-3 Inhibitor, Demonstrates Clinically Meaningful Improvements in Pain and Physical Function across a Range of OA Outcomes, Including the Staircase-Evoked Pain Procedure (StEPP)

Philip Conaghan[1], nathaniel katz[2], Asger Bihlet[3], Laus W Wullum[4], Kerry af Forselles[5], C Michael Perkins[5], Bernadette Hughes[6], Claire Herholdt[7] and Iwona Bombelka[8], [1]University of Leeds, Leeds, United Kingdom, [2]Rin Sof Innovation, Ltd, Boston, MA, [3]NBCD A/S, Herlev, Denmark, [4]Omicron A/S, Copenhagen, Denmark, [5]Levicept, Sandwich, United Kingdom, [6]Levicept, Ashtead, United Kingdom, [7]Levicept Ltd, Ashtead, United Kingdom, [8]Levicept, Sandwich, Kent, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2079–2105) Osteoarthritis – Clinical Poster II

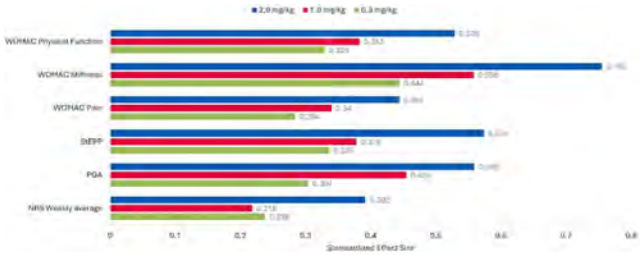
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: When evaluating new osteoarthritis (OA) therapies, we need to understand their clinical meaningfulness. LEVI-04, a first-in-class p75 neurotrophin receptor-Fc fusion protein that primarily inhibits neurotrophin-3, demonstrated statistically significant benefits on pain and function in a phase II RCT in people with moderate-to-severe knee OA. Pain and physical function are usually assessed by patient-reported measures with varying recall periods and no allowance for variable activity levels. This trial also included the Staircase-Evoked Pain Procedure (StEPP) as a standardized measure of evoked pain on movement. The purpose of this study was to explore the clinical meaningfulness of improvements in pain and physical function with LEVI-04 and determine the proportion of participants achieving the minimum clinically important difference (MCID) in the StEPP for LEVI-04 compared to placebo.

Methods: These analyses were based on data from a multicentre, randomized controlled trial[1]. Adults with painful (≥4/10 WOMAC and ≥4/10 average weekly NRS pain), and radiographic (KL≥2) knee OA were included. Participants received IV placebo or LEVI-04 (0.3, 1.0 or 2 mg/kg) at baseline and every 4 weeks (wks) to wk16. The primary endpoint was change in WOMAC pain to wk17, with changes in WOMAC function, StEPP (where participants walk up and down a single, standardised stair 24 times, rating their pain intensity at the end), patient global assessment (PGA), WOMAC stiffness and average weekly NRS pain were also assessed. Clinical meaningfulness was examined using effect size, calculated using Cohen's d. The proportion of LEVI-04-treated participants achieving a MCID of 2 points in the StEPP (on a 0–10 NRS for pain severity after performing the task) was calculated.

Results: The primary results from this trial are presented elsewhere[1]. 518 participants were randomized to 0.3, 1.0, and 2.0 mg/kg LEVI-04 or placebo. LEVI-04 significantly improved the primary endpoint, WOMAC pain at wk17 for all doses vs placebo. Calculated effect sizes were greater with LEVI-04 vs placebo and increased with dose (Figure 1). Similarly, a greater



Standardized Effects (Cohen's d) by Outcome and Treatment Arm at Week 17

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	0.3 mg/kg N = 111	1.0 mg/kg N = 110	2.0 mg/kg N = 113	Placebo N = 110
Achieved StEPP MCID, n (%)	71 (64%)	83 (75%)	86 (76%)	61 (55%)
Chi-square test vs placebo	0.29	0.046	0.0019	

StEPP, staircase-evoked pain procedure; MCID, minimum clinically important difference

Proportion of Participants who Achieve Minimum Clinically Important Difference in StEPP Assessment

proportion of participants achieved the MCID for the StEPP with higher doses of LEVI-04, and statistical significance from placebo was seen in LEVI-04 1.0 and 2.0 mg/kg groups (Table 1).

Conclusion: Effect sizes at or above those reported for NSAIDs[2] were observed with LEVI-04, especially with higher doses. LEVI-04 1.0 and 2.0 mg/kg resulted in significantly more patients achieving StEPP MCID, and at levels comparable or better than naproxen[3].Phase 3 trials are in planning.

References: 1.Conaghan P, et al. Arthritis Rheumatol. 2024;76 (suppl 9), 2. Dworkin RH, et al. J Pain. 2008;9(2):105-21, 3.Mayorga AJ, Scand J Pain, 2017: 134–143.

Disclosure: P. Conaghan: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6; **n. katz**: Levicept Ltd, 2; **A. Bihlet**: NBCD A/S, 3, 11; **L. Wullum**: None; **K. af Forselles**: Levicept Ltd, 2; **C. Perkins**: Levicept Ltd, 2; **B. Hughes**: Levicept Ltd, 2; **C. Herholdt**: Levicept Ltd, 3; **I. Bombelka**: Levicept Ltd, 3.

Abstract Number: 2102

Construct Validity of the Six-Minute Walk Test in Knee Osteoarthritis

Sivakami Mylvaganam[1], Ian stanaitis[2], Gillian Hawker[3] and Lauren King[3], [1]Department of Medicine, University of Toronto, Toronto, Canada, [2]Research and Innovation Institute, Women's College Hospital, Toronto, ON, Canada, Toronto, ON, Canada, [3]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Knee osteoarthritis (OA) significantly affects physical function, making function a core outcome in OA research. The Osteoarthritis Research Society International recommends the six-minute walk test (6MWT) as a performance-based measure of physical function in knee OA. Originally developed for cardiopulmonary conditions, the 6MWT is now used in OA populations, though its validity in this context remains unclear. Limited and conflicting evidence regarding its correlation with other function measures in OA raises questions about its utility and interpretation. This study aimed to evaluate the construct validity of the 6MWT in individuals with symptomatic knee OA and identify patient factors influencing six-minute walk distance (6MWD).

Methods: In this cross-sectional study within the BEST-Knee cohort, participants with knee OA completed standardized questionnaires and the 6MWT one month before total knee arthroplasty. Construct validity was assessed per COSMIN guidelines. Convergent validity was tested through hypothesized moderate-to-strong Spearman correlations ($r > 0.4$) between 6MWD and patient-reported physical function (KOOS-PS), pain (WOMAC pain subscale), and perceived walking

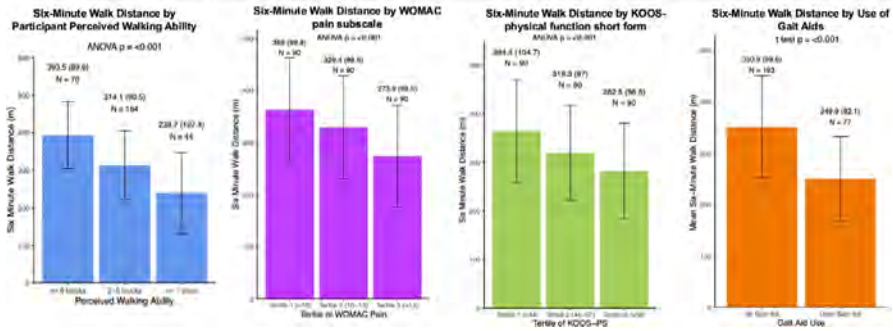
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Participant characteristics

Characteristic	
Demographics	
Mean age (years) (SD)	67.10 (8.52) / 278
Female – no. (%)	182 (65.47) / 278
Post-secondary education – no. (%)	155 (56.57) / 274
Knee OA characteristics	
Mean WOMAC pain (0-100) (SD)	57.22 (16.53) / 278
Mean KOOS physical function short form (0-100) (SD)	52.92 (16.25) / 278
Perceived walking ability	
≥ 6 blocks	72 (26%) / 276
2-5 blocks	160 (58%) / 276
≤ 1 block	44 (15%) / 276
Comorbidities	
Body mass index (kg/m^2) (SD)	32.19 (6.08) / 278
Number of troublesome lower extremity joints – no. (%)	
1	79 (29%) / 276
2	88 (32%) / 276
≥ 3	109 (39) / 276
Presence of lower back pain – no. (%)	148 (54%) / 272
Number of non-musculoskeletal comorbidities – no. (%)	
0	94 (33.81%) / 278
1	101 (36.33%) / 278
2	58 (20.86%) / 278
≥ 3	25 (8.99%) / 278
Mean PHQ-8 depressive symptoms (0-24) (SD)	6.76 (5.72)

WOMAC Western Ontario and McMaster Universities Osteoarthritis Index, KOOS Knee injury and osteoarthritis outcome score, PHQ-8 Patient health questionnaire - 8.

Figure 1: Associations Between Mean Six-Minute Walk Distance and Patient-Reported Measures of Knee OA Severity



Bars represent mean six-minute walk distance (6MWD) for each category. Error bars indicate standard deviations. Mean (standard deviation) and sample size (N) indicated for each bar.

ability (in blocks). Discriminant validity was tested examining correlation between 6MWD and the Lubben Social Network Scale, a measure unrelated to physical function. Known-groups validity compared 6MWD in participants who used gait aids versus not. A multivariable linear regression model assessed the association between demographic (age, sex), OA-related

Table 2: Multivariable linear regression analysis assessing the association between patient factors with the six-minute walk distance in individuals with knee osteoarthritis.

	Dependent variable: Six-minute Walk Distance		
Independent variables	**Beta-Estimate**	**95% Confidence Interval**	
Age, per year	-4.167	-5.467	-2.866
Female sex	45.018	22.802	67.234
Attainment of post-secondary education	21.215	0.336	42.094
WOMAC pain subscale (0-100), per unit	-1.147	-1.954	-0.341
KOOS-PS (0-100), per unit	-0.850	-1.688	-0.012
Number troublesome joints	2.009	-5.542	9.559
Presence of back pain	-5.693	-27.437	16.052
Obesity	-46.531	-68.525	-24.537
Number non-musculoskeletal comorbidities	-10.232	-19.851	-0.614
PHQ8 (depressive symptoms), per unit	-1.640	-4.233	0.954
Gignac Arthritis Coping Efficacy, per unit	5.135	1.605	8.666

Positive beta-estimates indicate greater walking distance associated with higher values or presence of the respective independent variable; negative estimates indicate reduced distance. Confidence intervals that do not include zero suggest statistically significant associations. KOOS-PS = Knee Injury and Osteoarthritis Outcome Score–Physical Function Shortform; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; PHQ8 = Patient Health Questionnaire–8. Obesity was defined as a BMI ≥30 kg/m2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(WOMAC pain, KOOS-PS), biomedical (symptomatic joints, comorbidities, obesity, back pain), and psychosocial (PHQ-8, coping, social network, education) factors with 6MWD.

Results: Among 278 participants (mean age 67 years, 65% female; Table 1), greater perceived walking difficulty, higher WOMAC pain, worse KOOS-PS, and gait aid use were associated with lower 6MWD (Figure 1). Correlations were moderate with perceived walking ability (ρ = -0.451, $p < 0.001$) and fair with WOMAC pain (ρ = -0.323, $p < 0.001$) and KOOS-PS (ρ = -0.328, $p < 0.001$). No correlation was seen with the Lubben scale (ρ = 0.067, $p = 0.281$) as hypothesized. In multivariable analysis, WOMAC pain, KOOS-PS, age, sex, obesity, comorbidities, education level, and arthritis coping were associated with 6MWD (Table 2).

Conclusion: While 6MWD declines with increasing OA symptom severity, its correlations with patient-reported function are only fair-to-moderate so we cannot confirm construct validity. Performance on the 6MWT is influenced by multiple biomedical and psychosocial factors which should be accounted for in knee OA research.

Disclosure: S. Mylvaganam: None; **I. stanaitis**: None; **G. Hawker**: None; **L. King**: None.

Abstract Number: 2103

PCRX-201 High-Capacity Adenovirus Serotype 5 Gene Therapy Demonstrates Sustained Clinical Efficacy and Safety in Patients With Knee Osteoarthritis

Stanley Cohen[1], Philip Conaghan[2], Marc C. Hochberg[3], Alan Kivitz[4], MiJeong Kim[5], Nino Joy[6], Shoshanna Jiang[6], Mary DiGiorgi[7], Jonathan Slonin[6] and Derek Slonin[6], [1]Metroplex Clinical Research Center, dallas, TX, [2]University of Leeds, Leeds, United Kingdom, [3]Marc C. Hochberg University of Maryland School of Medicine, Baltimore, MD, [4]Altoona Center for Clinical Research, Duncansville, PA, [5]Pacira BioSciences, Inc., Brisbane, [6]Pacira BioSciences, Inc., Brisbane, CA, [7]Pacira BioSciences, Inc, Brisbane, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Knee OA is a common disease affecting ~15 million people in the United States. There is an urgent unmet need for additional OA treatments as current treatments provide only short-term pain relief often associated with unwanted side effects and contraindications. Gene therapy using viral vectors has emerged as a novel therapeutic modality with the potential to treat many diseases. PCRX-201 (enekinragene inzadenovec) is a novel high-capacity adenovirus serotype 5 (Ad5) vector carrying a transgene encoding for the inflammation-inducible expression of IL-1 receptor antagonist (IL-1Ra) that is under investigation to treat knee OA via IA injection. This open-label phase 1 trial (NCT04119687) investigated the safety and efficacy of PCRX-201, for which long-term follow-up is ongoing.

Methods: Patients aged 30-80 years (N=72) with painful OA of the index knee and Kellgren/Lawrence (K/L) grade 2, 3, or 4 were eligible. The first group (n=36) received IA injection of PCRX-201 in the target knee at 1 of 3 doses (low: 1.4E10 genome copies [GC]; middle: 1.4E11 GC; high: 1.4E12 GC); the second group (n=36) was pretreated with IA methylprednisolone 40 mg immediately before PCRX-201 administration at the same doses. WOMAC pain (WOMAC-A) and stiffness (WOMAC-B) subscale scores and Knee Injury and Osteoarthritis Outcome Score Activities of Daily Living (KOOS ADL) were measured up to 156 weeks. Anti-Ad5 neutralizing antibody (NAb) titers in serum were measured at baseline before PCRX-201 administration and up to 52 weeks.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1. Summary of Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events, TEAEs ≥Grade 3, and TEAEs Occurring in ≥10% of Participants in Either Pretreatment Cohort

	Low Not Pretreated (N=12)	Middle Not Pretreated (N=16)	High Not Pretreated (N=8)	Low Pretreated (N=13)	Middle Pretreated (N=15)	High Pretreated (N=8)
≥1 TEAEs	11 (91.7)	16 (100)	8 (100)	12 (92.3)	14 (93.3)	8 (100)
≥1 SAEs	3 (25)	1 (6.2)	1 (12.5)	1 (7.7)	2 (13.3)	2 (25)
≥1 TEAEs ≥grade 3	3 (25)	3 (18.8)	3 (37.5)	2 (15.4)	4 (26.7)	2 (25)
≥1 TEAEs occurring in ≥10% of participants in either pretreatment cohort						
Arthralgia	6 (50)	4 (25)	1 (12.5)	5 (38.5)	5 (33.3)	6 (75)
Back pain	0 (0)	0 (0)	2 (25)	2 (15.4)	1 (6.7)	1 (12.5)
Fall	1 (8.3)	0 (0)	1 (12.5)	2 (15.4)	2 (13.3)	0 (0)
Headache	2 (16.7)	1 (6.2)	2 (25)	1 (7.7)	2 (13.3)	1 (12.5)
Hypertension	2 (16.7)	2 (12.5)	0 (0)	1 (7.7)	0 (0)	0 (0)
Joint effusion	6 (50)	10 (62.5)	8 (100)	5 (38.5)	5 (33.3)	5 (62.5)
Joint swelling	7 (58.3)	1 (6.2)	1 (12.5)	0 (0)	2 (13.3)	0 (0)
Musculoskeletal pain	0 (0)	0 (0)	0 (0)	2 (15.4)	0 (0)	2 (25)
Osteoarthritis	0 (0)	0 (0)	0 (0)	1 (7.7)	2 (13.3)	3 (37.5)
Synovial cyst	3 (25)	1 (6.2)	1 (12.5)	0 (0)	0 (0)	0 (0)

Data are the n (%), where n is the number of participants in each category. Participants who reported >1 TEAE are counted only once per category. N is the number of participants in each steroid-pretreatment status and dose cohort and is used as the denominator for percents.

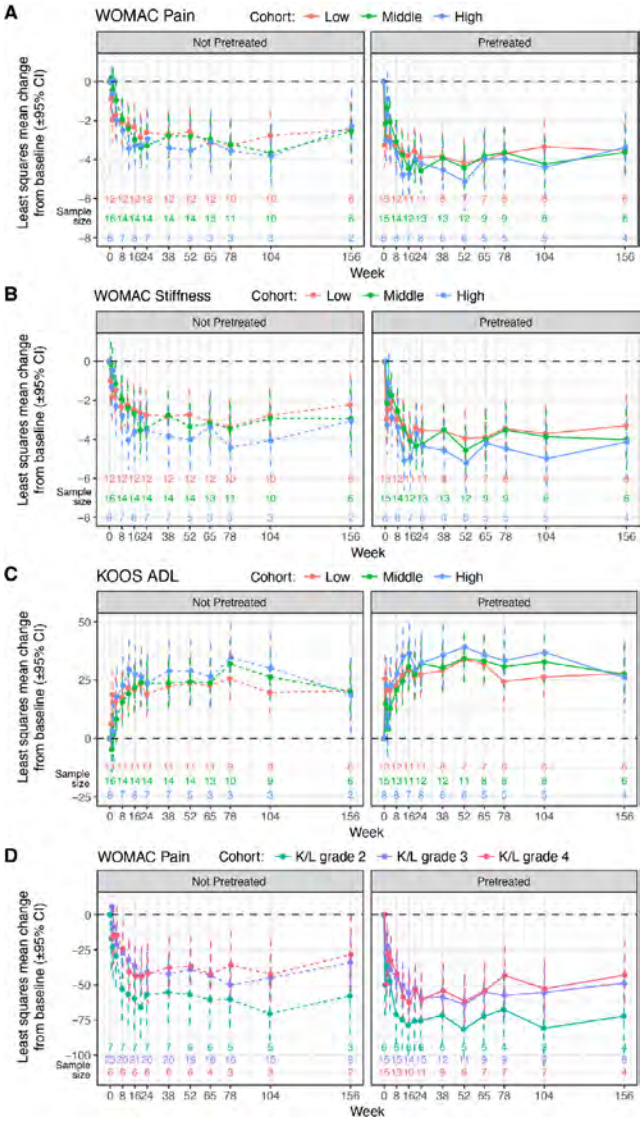


Figure 1. (A) WOMAC pain scores over time by dose for each cohort. (B) WOMAC stiffness scores over time by dose for each cohort. (C) KOOS ADL scores over time by dose for each cohort. (D) WOMAC pain scores by K/L grade for each cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

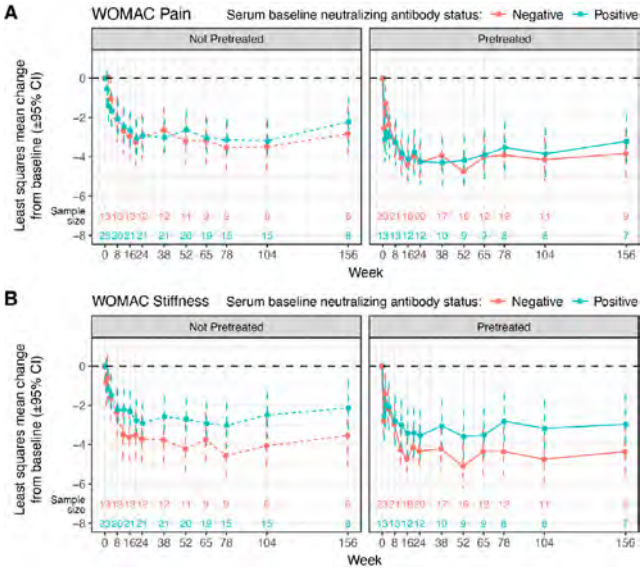


Figure 2. WOMAC pain scores (A) and WOMAC stiffness scores (B) by serum baseline neutralizing antibody status for each cohort.

Results: Pain and function improvements were observed at all doses and across both the not pretreated and corticosteroid pretreated groups up to 156 weeks after PCRX-201 IA administration (Figure 1). The pretreated group showed greater improvements for WOMAC-A (range of least squares mean [LSM] improvement from baseline across dose levels, 3.37-3.62 [of 10] points; Figure 1A), WOMAC-B (3.31-4.13 [of 10] points; Figure 1B), and KOOS ADL (Figure 1C) than the not pretreated group. Patients in the pretreated group with K/L grades of 2, 3, and 4 showed LSM reductions from baseline in WOMAC-A, with greater numerical reductions observed in those with K/L grade 2 than those with K/L grades 3 or 4 (Figure 1D). Importantly, preexisting serum NAbs did not affect PCRX-201 efficacy as determined by WOMAC-A pain (Figure 2A) and WOMAC-B stiffness (Figure 2B). The most commonly reported treatment-related adverse event (AE), index joint effusion, occurred less frequently for participants in the pretreated (15/36; 42%) than the not pretreated group (24/36; 67%) (Table 1).

Conclusion: A single IA injection of PCRX-201 with corticosteroid pretreatment in patients with knee OA had an acceptable safety profile and sustained clinical efficacy for up to 156 weeks. Preexisting NAbs did not affect PCRX-201 efficacy or safety at all 3 doses, and corticosteroid pretreatment demonstrated greater improvement in the clinical scores than no pretreatment. These results support the ongoing phase 2 study strategy of PCRX-201 with a 10-fold lower dose (1.4E11 GC) and steroid pretreatment.

Disclosure: S. Cohen: Abbvie, 2, Lifordi, 2, 11, Lilly, 2, Pacira, 2, Pfizer, 2, Spyre, 2, UCB, 2; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6; **M. Hochberg**: Pacira, 2, Regenosine, 11, Therologix LLC, 11; **A. Kivitz**: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2; **M. Kim**: Pacira, 3, 11; **N. Joy**: Pacira, 3, 11; **S. Jiang**: Pacira, 3, 11; **M. DiGiorgi**: Pacira, 3, 11; **J. Slonin**: Pacira, 3, 11; **D. Slonin**: Pacira, 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2104

Pain 0-10 visual analog scale (VAS) and RAPID3 (routine assessment of patient index data) in OA and RA are similar in 2024 to 1979 and 1989

Theodore Pincus[1], Tengfei Li[2] and Juan Schmukler[1], [1]Rush University Medical Center, Chicago, IL, [2]Rush, chicago, IL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: A 1979 report by Huskisson, who developed the 0-10 pain visual analog scale (VAS) , entitled "Another look at osteoarthritis" indicated mean pain VAS scores of 5.3 in osteoarthritis RA (OA) and 5.25 in rheumatoid arthritis (RA) (Table). The earliest RAPID3 (routine assessment of patient index data) scores compiled in OA were 11.0 in 2009 and 11.7-13.6 in RA in 1989-2009. We analyzed subsequent databases from routine care which included pain and RAPID3 scores in patients with OA or RA, some of which also included 28 swollen joint counts (SJC) in patients with RA, presented to support credibility of the RA findings with recognized considerable improvement in inflammatory activity in RA, for comparisons of pain scores over time.

Methods: Available reports from routine care databases which included a 0-10 pain VAS in patients with RA or OA from 1979-2024, RAPID3 from 1989-2024, and 28 SJC in RA from 1985-2024 were compiled. Some reports presented mean and others median data; differences between median and mean values were less than 10% in reports which included both. Many reports were from a single investigator, and all but one of the databases were from the United States.

Results: Mean pain 0-10 VAS score reported in OA was 5.3 in 1979 and medians and means ranged from 3.9 to 7.0 through 2024, including 7.0 in 2024. Mean pain VAS in RA was 5.25 in 1979 and medians and means ranged from 2.5 to 5.5 through 2024, including 5.5 in 2024. Initial mean RAPID3 scores were 12.7 in OA and 13.6 in RA in 1989 (retrospectively computed according to group data); medians and means and ranged from 10.3 to 16.8 in OA and 6.2 to 13.3 in RA through 2024, including 14.0 in OA and 13.3 in RA in 2024. By contrast, mean SJC in RA was 12/28 in 1989 and ranged from 1.4 to 6.2 through 2024, including 1.4 in 2024 (data included to support credibility of non-SJC data).

Year	Pain VAS (0-10)		RAPID3 (0-30)		Swollen 28 Jt ct
	OA	RA	OA	RA	RA
1979	5.3	5.25	NA	NA	NA
1985	NA	5.2	NA	NA	12
1989	6.0	5.2	12.7	13.6	NA
1999	4.3	3.7	NA	10.5	NA
2000	NA	5.0	NA	NA	5
2009	4.0	3.6	11.0	11.7	2
2013	3.9	3.9	10.3	9.2	NA
2017a	7.0	4.3	16.8	9.7	NA
2017b	7.0	5.0	15.5	11.8	NA
2017c	5.0	4.7	11.7	11.0	NA
2017d	5.0	2.5	12.2	6.2	NA
2019	6.1	4.9	14.3	11.9	NA
2021	NA	NA	NA	8.2	2.7
2021	NA	NA	NA	7.6	6.2
2023	NA	4.6	NA	11.6	1.7
2024	7.0	5.5	14.0	13.3	1.4

Mean or median pain 0–10 visual analog scale (VAS) and 0-30 RAPID3 (routine assessment of patient index data) in routine care patients with osteoarthritis (OA) or rheumatoid arthritis (RA), and 28 swollen joint counts in RA from 1979 to 2024; initial and most recent values in each column are highlighted

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Mean or median pain scores were similar in reports of OA and RA databases over 45 years from 1979 to 2024. Furthermore, RAPID3 in OA and RA were similar over 35 years from 1989 through 2024, whereas mean SJC in RA declined from 12 to 1.4 over this period. These findings document the effectiveness of modern anti-inflammatory therapy for RA, but suggest that the perception of status and illness experience for most OA and RA patients have improved minimally over decades. Important limitations of this review include comparisons of mean or median scores, although results were within 10% in databases which included both mean and median, and that all databases were from the USA other than one from Australia. These results are presented in part to encourage reporting of pain scores in OA and RA to recognize and account for possible differences from data presented in this abstract, toward better care and outcomes for OA and RA patients.

Disclosure: T. Pincus: Medical history services, LLC, 8, 9, 10; **T. Li**: None; **J. Schmukler**: None.

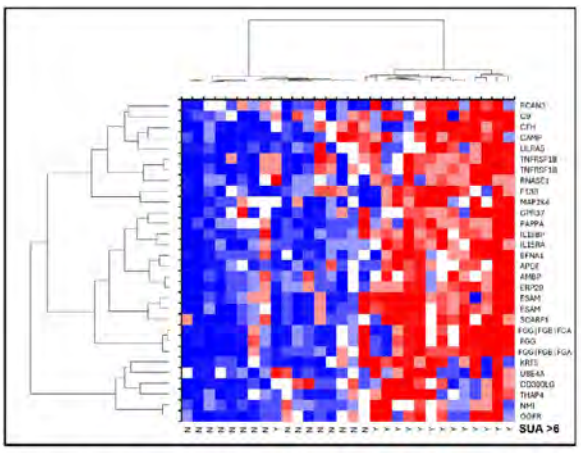
Abstract Number: 2105

Stratification for elevated urate identifies a pro-inflammatory synovial fluid proteome in knee osteoarthritis: a pilot study

Tuhina Neogi[1], Sayali Dhamne[2], Robert Terkeltaub[3], Virginia Kraus[4], Simon Dillon[5] and Towia Libermann[5], [1]Boston University School of Medicine, Boston, MA, [2]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, [3]Retired, San Diego, CA, [4]Duke University, Durham, NC, [5]Beth Israel Deaconess Medical Center, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2079–2105) Osteoarthritis – Clinical Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The causes of inflammation, pain fluctuations, and disease progression in osteoarthritis (OA) are not well understood. Soluble urate is a "danger signal", and synovial fluid urate and IL-18, which along with IL-1β is a product of NLRP3 inflammasome activation, are associated with OA severity on imaging (PMID: 21245324) . In a pilot study, we evaluated differences in proteomic profiles of OA synovial fluid stratified by serum urate among people with OA but without gout to examine potential distinct OA phenotypes. We further explored whether the profiles differed by obesity or age as potential confounders in the association between urate and OA.



*note: some proteins appear twice because >1 aptamer in SomaScan detected the particular protein

Figure 1: Hierarchical Clustering of the Top 30 proteins* that had an absolute fold-change of ≥1.3 and p<0.05 in differentiating the elevated urate group (>6mg/dL) from lower urate group

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

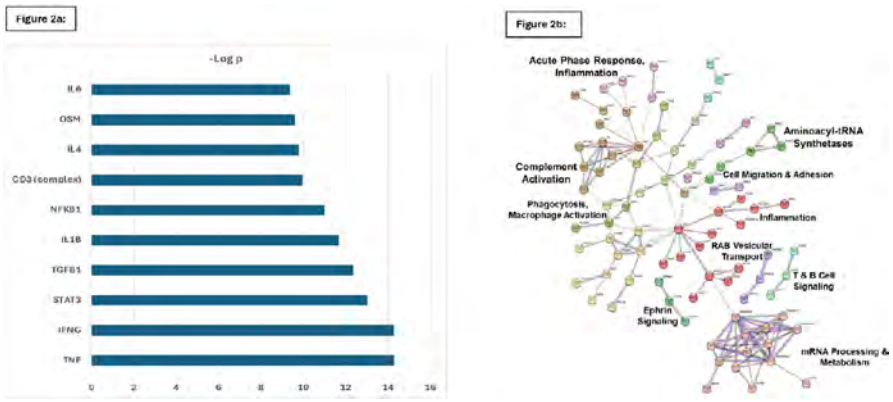


Figure 2a: Upstream Regulators identified with Ingenuity Pathways Analysis (IPA) from among the top 30 proteins that had an absolute fold-change of ≥1.3 and p<0.05 in differentiating the elevated urate group (>6mg/dL) from lower urate group based upon gene expression data. Proteins are listed in ascending order of statistical significance Figure 2b: Clusters of Protein-Protein Interaction Networks identified with STRING Analysis from among the top 30 proteins that had an absolute fold-change of ≥1.3 and p<0.05 in differentiating the elevated urate group (>6mg/dL) from lower urate group based upon protein expression data.

Methods: We obtained synovial fluid from individuals with knee OA but without a diagnosis of gout (and on no urate-lowering therapy) who had knee aspirations performed as part of standard clinical care (no crystals detected), and who consented to having their synovial fluid used for this pilot research study. The synovial fluid was immediately stored at 4°C, processed within 4 hours of collection, and then stored at -80°C. The samples were prepared with hyaluronidase and analyzed using the 11k SomaScan v5.0 proteomics assay that measures 10,778 proteins. Differentially expressed proteins were identified by t-tests and further evaluated using XLSTAT statistical software. Systems biology analysis used Ingenuity Pathway analysis (IPA) and STRING to define enriched pathophysiological pathways.

Results: We enrolled 30 participants (mean age 67 ± 11.6, 77% female, mean BMI 32.3 ± 6.9), of whom 47% (n=14) had serum urate >6 mg/dL (Elevated Urate Group (EUG). SomaScan analysis identified 186 proteins associated with the EUG that had an absolute fold change of at least 1.3 and p< 0.05. The top 30 proteins accurately discriminated between EUG and lower urate (Fig.1). IPA (Fig.2a) revealed enrichment of inflammatory response, particularly enhanced activity of the myeloid lineage and phagocytosis as key pathophysiological pathways in the EUG. Upstream regulator analysis confirmed that the predicted regulators with highest statistical significance involved enhanced activity of pro-inflammatory cytokines such as IL-1β and TNF and their downstream signaling mediators such as STAT3 and NFKB1. STRING analysis (Fig.2b) defined clusters of interacting proteins linked to inflammation, acute phase response, complement activation, and mRNA processing as key pathways. BMI-and age-associated protein signatures showed only limited overlap with the hyperuricemia-associated protein signature (Fig.3).

Figure 3: Venn Diagram comparing differentially expressed proteins identified with p<0.05 in the EUG vs. lower urate group, with differentially expressed proteins based upon obesity (BMI>30 vs. not) or Age (>65 vs. younger), demonstrating minimal overlap.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The synovial fluid proteome associated with higher urate in patients with OA included differential upregulation of pathways related to inflammation, phagocytosis, and the complement cascade compared with those whose serum urate was lower than 6.0 mg/dL. Furthermore, the protein signature associated with the EUG had minimal overlap with synovial fluid protein signatures associated with obesity or older age. Elevated urate, a biomarker of OA disease severity, may therefore contribute to an inflammatory profile in OA synovial fluid.

Disclosure: T. Neogi: None; **S. Dhamne**: None; **R. Terkeltaub**: Atom Bioscience, 2, BPG Bio, 2, Crystalys, 2, Novartis, 2, Shanton, 2; **V. Kraus**: 4-P Pharma, 1, Genascence, 1, Pacira, 1, Paradigm Biopharma, 1; **S. Dillon**: None; **T. Libermann**: None.

Abstract Number: 2106

Prevalence and Characteristics of Morphometric Vertebral Fractures in the Spanish Population: Data from the OsteoSER Study

Carmen Gomez Vaquero[1], Montserrat Roig Kim[2], Jordi Fiter Areste[3], Marta Domínguez-Álvaro[4], Luis María Jiménez Liñán[5], Miguel Bernad[6], Antonio Álvarez-Cienfuegos[7], Blanca Correa[8], Antonio Pascual-Vergara[9], Alejandra Montero Costa[10], Cristina Momblan Trejo[11], Manuel Jiménez Rodríguez[12], María Anadón González[13], Sara Josefina Barcat Zarate[14], Sara Alvar Pariente[15], Cristina Ruiz Pavón[16], Pedro J. Lacalle Chanivet[17], Balbina Marín de Prada[18], Soledad García Frías[19], Francisco Javier Maestro Saavedra[20], Marta Poch i Mora[21], José Luis Gea González[22], Carlota Quiroga Fernández[23], Eduardo Acevedo Martel[24] and Enrique González-Dávila[25], [1]Hospital Universitari de Bellvitge, 08907 L'Hospitalet, Spain, [2]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [3]Hospital Universitari Son Espases, Palma de Mallorca, Spain, [4]Sociedad Española de Reumatología, Madrid, Spain, [5]Hospital Don Benito-Villanueva, Don Benito, Spain, [6]Hospital Universitario La Paz, Madrid, Spain, [7]Hospital Vega Baja, Orihuela, Spain, [8]Clínica Sanz y Correa, A Coruña, Spain, [9]Centro de Salud Ronda-Norte y Ronda-Sur, Ronda, Spain, [10]Centro de Salud Fuencarral, Madrid, Spain, [11]Centro de Atención Primaria Viladecans Montbaig, Sant Climent de Llobregat, Spain, [12]Centro de Salud Don Benito Oeste, Don Benito, Spain, [13]Consultorio de Pedrezuela, Pedrezuela, Spain, [14]Centro de Salud Orihuela 1-El Rabaloche, Orihuela, Spain, [15]Centro de Salud Malpica, Malpica, Spain, [16]Centro de Salud Ronda-Norte, Ronda, Spain, [17]Centro de Salud de Santa Amalia, Santa Amalia, Spain, [18]Centro de Atención Primaria Ramona Via i Pros, El Prat de Llobregat, Spain, [19]Centro de Salud de Cortes de la Frontera, Cortes de la Frontera, Spain, [20]Centro de Salud Elviña Mesoiro, A Coruña, Spain, [21]Centro de Atención Primaria CAP 17 de Setembre, El Prat de Llobregat, Spain, [22]Centro de Salud de Benejúzar, Benezujar, Spain, [23]Centro de Salud Os Mallos, A Coruña, Spain, [24]Centro de Salud Ronda-Sur Santa Bárbara, Ronda, Spain, [25]Departamento de Matemáticas. Universidad de La Laguna, Tenerife, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Most vertebral fractures (VFs) are asymptomatic. Vertebral Fracture Assessment (VFA) using DXA is a low-radiation method to detect morphometric vertebral fractures (MVFs). This study aimed to estimate MVF prevalence in Spanish adults aged ≥40 years and characterize affected individuals.

Methods: This population-based, cross-sectional study included individuals aged 40-80 years from 15 primary care centers across six Spanish provinces. VFA was performed with a mobile DXA unit (Hologic® Horizon W). Two rheumatologists independently evaluated vertebrae T10-L4 using Genant's method (grade 1: 20-25% height loss; grade 2: 26-40%; grade 3: >40%), resolving discrepancies by consensus. Bone mineral density (BMD), clinical data, and fracture risk factors were recorded. After VFs were identified, primary care centers reviewed spine imaging and clinical records, and interviewed patients to classify fractures as fragility, traumatic, or morphometric.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Sample characteristics according to the presence of MVFs on VFA and the underlying cause of the fracture.

	Morphometric vertebral fractures (MVFs)					No MVFs n: 911	p-value FVs vs no FVs	All n: 1082
	Fragility n: 52	Traumatic n: 19	Morfometric n: 100	p value causes of VF	All VFs n: 171			
Sex, n(%)				0.003			0.003	
Men	24 (46.2)	17 (89.5)	64 (62.0)		104 (60.8)	440 (48.3)		544 (50.3)
Women	28 (53.8)	2 (10.5)	37 (37.0)		67 (39.2)	471 (51.7)		538 (49.7)
Age (years)	68.3 ± 9.2	62.9 ± 10.4	62.0 ± 11.3	0.003	64.0 ± 10.9	59.7 ± 10.7	<0.001	60.4 ± 10.8
Age, n (%)				0.153			<0.001	
40-49	4 (7.7)	3 (15.8)	21 (21.0)		28 (16.4)	202 (22.2)		230 (21.3)
50-59	4 (7.7)	2 (10.5)	15 (15.0)		21 (12.3)	244 (26.8)		265 (24.5)
60-69	19 (36.5)	9 (47.4)	32 (32.0)		60 (35.1)	261 (28.6)		321 (29.7)
70-80	25 (48.1)	5 (26.3)	32 (32.0)		62 (36.3)	204 (22.4)		266 (24.6)
BMI (kg/m^2)	27.5 ± 4.3	25.8 ± 2.7	28.0 ± 3.8	0.070	27.6 ± 3.9	27.4 ± 4.5	0.603	27.5 ± 4.4
BMI, n (%)				0.086			0.764	
Underweight (<18.5 kg/m^2)	1 (1.9)				1 (0.6)	9 (1.0)		10 (0.9)
Normal range (18.5-25 kg/m^2)	15 (28.8)	7 (36.8)	25 (24.0)		47 (27.5)	277 (30.4)		324 (29.9)
Overweight (25-30 kg/m^2)	20 (38.5)	12 (63.2)	43 (43.0)		75 (43.9)	396 (43.5)		471 (43.5)
Obese (>30 kg/m^2)	16 (30.8)	-	32 (32.0)		48 (28.1)	229 (25.1)		277 (25.6)
Health status, n (%)				0.001			0.440	
Very good	5 (9.6)	7 (36.8)	12 (12.0)		24 (14.0)	172 (18.9)		196 (18.1)
Good	33 (63.5)	7 (36.8)	61 (61.0)		101 (59.1)	479 (52.6)		580 (53.6)
Normal	13 (25.0)	3 (15.8)	24 (24.0)		40 (23.4)	214 (23.5)		254 (23.5)
Poor	1 (1.9)	-	3 (3.0)		4 (2.3)	33 (3.6)		37 (3.4)
Very poor		2 (10.5)			2 (1.2)	13 (1.4)		15 (1.4)
Limitations to activity, n (%)				0.405			0.724	
No limitations	33 (63.5)	9 (47.4)	62 (62.0)		104 (60.8)	580 (69.7)		684 (63.3)
Limited, but not seriously	18 (34.6)	8 (42.1)	35 (35.0)		61 (35.7)	296 (22.5)		357 (33.0)
Seriously limited	1 (1.9)	2 (10.5)	3 (3.0)		6 (3.5)	34 (3.7)		40 (3.7)
Chronic conditions associated with secondary osteoporosis, n (%)	15 (28.8)	7 (36.8)	35 (35.0)	0.704	57 (33.3)	279 (30.7)	0.529	336 (31.1)
Asthma/COPD	4 (7.7)	3 (15.8)	11 (11.0)	0.599	18 (10.5)	51 (5.6)	0.025	69 (6.4)
Depression	6 (11.5)	1 (5.3)	6 (6.0)	0.406	13 (7.6)	57 (6.3)	0.499	70 (6.5)
Type II diabetes	5 (9.6)	3 (15.8)	12 (12.0)	0.765	20 (11.7)	93 (10.2)	0.586	113 (10.5)
Hypothyroidism	5 (9.6)	1 (5.3)	6 (6.0)	0.675	12 (7.0)	74 (8.1)	0.758	86 (8.0)
Other	1 (1.9)	4 (21.1)	8 (8.0)	0.026	13 (7.6)	69 (7.6)	1.000	82 (7.6)
Treatments with harmful effects on bone, n (%)	24 (46.2)	10 (52.6)	43 (43.0)	0.727	77 (45.0)	327 (35.9)	0.025	404 (37.4)
Oral anticoagulants	3 (5.8)	1 (5.3)	9 (9.0)	0.714	13 (7.6)	25 (2.7)	0.005	38 (3.5)
Betablockers	5 (9.6)	4 (21.1)	10 (10.0)	0.342	19 (11.1)	67 (7.4)	0.121	86 (7.9)
Selective serotonin reuptake inhibitors	6 (11.5)	1 (5.3)	11 (11.0)	0.726	18 (10.5)	92 (10.1)	0.890	110 (10.2)
Thiazides	6 (11.5)	2 (10.5)	7 (7.0)	0.618	15 (8.8)	66 (7.2)	0.526	81 (7.5)
Proton pump inhibiters	14 (26.9)	7 (36.8)	31 (31.0)	0.709	52 (30.4)	193 (21.2)	0.010	245 (22.6)
Other	9 (17.3)	4 (21.1)	11 (11.0)	0.368	24 (14.0)	102 (11.2)	0.299	126 (11.6)

Results: Among 1082 participants (50.3% male; mean age 60.4 years), MVFs were found in 171 (16%), totaling 244 fractures.

MVFs were more frequent in men and associated with older age, prior fragility fractures, and osteoporosis. Proximal femur BMD was significantly lower in those with MVFs.

Fracture severity was grade 1 in 63%, grade 2 in 31%, and grade 3 in 6%, with higher grades linked to older age and lower BMD. Most MVFs were wedge-shaped (type A, 80%), followed by biconcave (type M, 18%) and crush (type P, 2%). Type A was more frequent in men and younger individuals; types M/P were linked to osteoporosis and lumbar location. Most MVFs occurred at the thoracolumbar region (D12-L2).

After review, 52 participants (4.8%) were classified as having clinical fragility VFs (CFVFs); 30 were undiagnosed, although 14 had prior radiographic evidence; 19 were traumatic and 100 morphometric VFs.

CFVFs were mostly grade 2, type A, and thoracolumbar; traumatic VFs were mainly grade 1 and type A; morphometric VFs were predominantly grade 1, type A, with a dorsal-thoracolumbar distribution. Grade 3 and type P were rare but more common in CFVFs.

CFVFs were more frequent in women and occurred at older age. They were associated with more prior non-vertebral fragility fractures, without significantly lower BMD or increased osteoporosis prevalence compared to other VF types.

Conclusion: In Spanish adults ≥40 years, MVFs were identified in nearly one-sixth of participants, more common in men and older individuals, and associated with lower BMD and prior fragility fractures. CFVFs represented an underdiagnosed subset, more prevalent among older women and associated with prior fragility fractures. Fracture characteristics differed by etiology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Variables related to bone metabolism according to the presence of vertebral fracture on VFA and the underlying cause of the fracture.

	Morphometric vertebral fractures (MVFs)							
	Fragility n: 52	Traumatic n: 19	Morfometric n: 100	p-value causes of VF	All VFs n: 171	No MVFs n: 911	p-value FVs vs no FVs	All n: 1082
Risk factors for fracture, n (%)								
Previous non-vertebral fracture	33 (63.5)	1 (5.3)	6 (6.0)	**<0.001**	40 (23.4)	46 (5.0)	<0.001	86 (7.9)
Parent fractured hip	8 (15.4)	4 (21.1)	9 (9.0)	0.244	21 (12.3)	73 (8.0)	0.076	94 (8.7)
Glucocorticoids	1 (1.9)	-	1 (1.0)	0.777	2 (1.2)	29 (3.2)	0.210	31 (2.9)
Current smoking	10 (19.2)	3 (15.8)	16 (16.0)	0.872	29 (17.0)	146 (16.0)	0.735	175 (16.2)
Alcohol 3 or more units/day	7 (13.5)	2 (10.5)	5 (5.0)	0.181	14 (8.2)	59 (6.5)	0.407	73 (6.7)
Bone mineral density (BMD)								
Lumbar spine BMD (g/cm^2)	0.948 ± 0.179	0.976 ± 0.129	0.964 ± 0.175	0.792	0.961 ± 0.171	0.971 ± 0.158	0.444	0.969 ± 0.160
T-score*	-0.61 ± 0.21	-0.30 ± 0.24	-0.50 ± 0.15	0.722	-0.51 ± 0.11	-0.41 ± 0.04	0.345	-0.42 ± 0.04
Femoral neck BMD (g/cm^2)	0.701 ± 0.117	0.738 ± 0.090	0.743 ± 0.133	0.133	0.730 ± 0.125	0.764 ± 0.127	0.001	0.759 ± 0.127
T-score*	-1.38 ± 0.13	-1.28 ± 0.13	-1.18 ± 0.10	0.458	-1.25 ± 0.07	-0.88 ± 0.03	<0.001	-0.93 ± 0.03
Total hip BMD (g/cm^2)	0.841 ± 0.127	0.874 ± 0.121	0.888 ± 0.149	0.141	0.872 ± 0.141	0.911 ± 0.137	<0.001	0.905 ± 0.138
T-score*	-1.19 ± 0.15	-1.10 ± 0.19	-0.94 ± 0.12	0.420	-1.03 ± 0.09	-0.58 ± 0.04	<0.001	-0.65 ± 0.04
WHO diagnostic categories, n (%)				0.160			0.005	
Normal/BMD not below expected for age (Z-score > -2)	13 (25.0)	6 (31.6)	45 (45.0)		64 (37.4)	442 (48.5)		506 (46.8)
Osteopenia	30 (57.7)	11 (57.9)	44 (44.0)		85 (49.7)	406 (44.6)		491 (45.4)
Osteoporosis	9 (17.3)	2 (10.5)	11 (11.0)		22 (12.9)	60 (6.6)		82 (7.6)
BMD below expected for age (Z-score ≤ -2)						3 (0.3)		3 (0.3)
Current or previous treatment of osteoporosis, n (%)	10 (19.2)	-	-	**<0.001**	10 (5.8)	22 (2.4)	0.024	32 (3.0)
Alendronate/Risedronate	6 (11.5)			**<0.001**	6 (3.5)	16 (1.8)	0.141	22 (2.0)
Denosumab	4 (7.7)	-	-	**0.009**	4 (2.3)	3 (0.3)	0.014	7 (0.6)
Other	1 (1.9)	-	-	0.316	1 (0.6)	3 (0.3)	0.498	4 (0.4)
Calcium and/or vitamin D supplementation, n (%)	25 (48.1)		10 (10.0)	**<0.001**	35 (20.5)	128 (14.1)	0.036	163 (15.1)

WHO: World Health Organization. *Data are presented as mean ± standard error.

Disclosure: C. Gomez Vaquero: None; **M. Roig Kim**: None; **J. Fiter Areste**: None; **M. Domínguez-Álvaro**: None; **L. Jiménez Liñán**: None; **M. Bernad**: None; **A. Álvarez-Cienfuegos**: None; **B. Correa**: None; **A. Pascual-Vergara**: None; **A. Montero Costa**: None; **C. Momblan Trejo**: None; **M. Jiménez Rodríguez**: None; **M. Anadón González**: None; **S. Barcat Zarate**: None; **S. Alvar Pariente**: None; **C. Ruiz Pavón**: None; **P. Lacalle Chanivet**: None; **B. Marín de Prada**: None; **S. García Frías**: None; **F. Maestro Saavedra**: None; **M. Poch i Mora**: None; **J. Gea González**: None; **C. Quiroga Fernández**: None; **E. Acevedo Martel**: None; **E. González-Dávila**: None.

Abstract Number: 2107

Experience of a Fragility Fracture Coordination Unit Integrated Across Two Hospitals: An Innovative Multidisciplinary Model for Optimizing the Management of Geriatric and Non-Geriatric Patients Beyond Surgery After an Osteoporotic Bone Fragility Fracture

César Antonio Egües Dubuc[1], Esther Laso Lucas[2], Nerea Alcorta Lorenzo[3], Carlos Maria Lizasoain Alustiza[4], Leire Unanue Pumar[4], Gabriela Jimenez Clemente[2], Claudia Murillo Erazo[2], Vicente Lavilla Garcia[2], Ander Alberdi Arbelaiz[4], Elena Zubillaga Azpiroz[4], Imanol Gabarain Morcillo[4], Jorge Jesus Cancio Fanlo[5], Maria Ariztia Sarratea[2], Iñaki Maria Arruabarrena Echeverria[4], Gaspar de La Herran Nuñez[4], Antonio Martin Garcia[4] and LUIS LOPEZ DOMINGUEZ[6], [1]Donostia University Hospital, San Sebastián, Pais Vasco, Spain, [2]Matia Hospital, San Sebastian, Pais Vasco, Spain, [3]University Hospital Donostia, san sebastian, Spain, [4]Donostia University Hospital, San Sebastian, Pais Vasco, Spain, [5]Donostia University Hospital, San Sebastian, [6]Hospital Universitario Donostia, San Sebastian, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Fracture Coordination Units typically function within a single hospital using a multidisciplinary approach. Our unit, established in February 2024, pioneers a model coordinating care between two hospitals: University Hospital of Donostia (UHD) and Matía Hospital (MH). It integrates Rheumatology (REU), Internal Medicine (I.M.), and

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of Clinical Characteristics, Fractures, and Lifestyle Factors in REU and OG Groups

Variable		REU	OG	P-value
Female		150 (78.1%)	191 (76.7%)	0.724
Age (years)		80 (45-99)	87 (64-102)	<0.0001
Fracture	Hip	158 (82.3%)	240 (96.4%)	<0.0001
	Humerus	19 (9.9%)	-	
	Radius	3 (1.6%)	-	
	Vertebra	2 (1.0%)	-	
	Multiple	4 (2.1%)	5 (2.0%)	
	Others	6 (3.1%)	2 (0.8%)	
	Missing	-	2 (0.8%)	
Previous fracture	Yes	97 (50.5%)	79 (31.7%)	0.023
	No	95 (49.5%)	121 (48.6%)	
	Missing	-	49 (19.7%)	
Number of previous fractures	1	50 (51.54%)	54 (68.35%)	0.015
	2	16 (16.5%)	10 (12.66%)	
	3	14 (14.43%)	4 (5.06%)	
	4 to 6	15 (15.46%)	1 (1.3%)	
	>6	3 (3.1%)	1 (1.3%)	
Maternal or paternal hip fracture	Yes	25 (13.0%)	3 (1.2%)	<0.0001
	No	125 (65.1%)	103 (41.36%)	
	Missing	42 (21.9%)	70 (28.1%)	
Early menopause	Yes	12 (6.25%)	13 (5.22%)	0.012
	No	114 (59.38%)	76 (30.5%)	
	Missing	66 (24.4%)	160 (64.3%)	
Alcohol intake	Yes	26 (13.5%)	14 (5.6%)	0.041
	No	141 (73.4%)	167 (67.07%)	
	Previous	3 (1.6%)	1 (0.4%)	
	Missing	22 (11.5%)	67 (26.9%)	
Current smoker	Yes	70 (36.46%)	14 (5.6%)	<0.0001
	No	101 (52.6%)	168 (67.47%)	
	Missing	21 (10.9%)	67 (26.9%)	
Dairy intake	Yes	116 (60.4%)	150 (60.2%)	0.018
	No	49 (25.5%)	32 (12.85%)	
	Missing	27 (14.1%)	66 (26.5%)	
Osteopenizante treatment	Yes	15 (7.8%)	36 (14.5%)	0.004
	No	162 (84.4%)	142 (57.03%)	
	Missing	15 (7.8%)	70 (28.1%)	
Corticosteroids intake	Yes	7 (3.6%)	13 (5.2%)	0.520
	No	157 (81.8%)	170 (68.27%)	
	Previous	5 (2.6%)	5 (2.008%)	
	Missing	23 (12%)	61 (24.5%)	

Traumatology at UHD, alongside Orthogeriatrics (OG) at MH, ensuring a patient-centered approach. Patients at UHD are assessed by I.M.; those with a geriatric profile transfer to MH for OG management, while others receive osteoporotic treatment from REU at UHD. After over a year of operation, evaluating clinical differences and therapeutic approaches between REU and OG group to understanding the impact of multidisciplinary coordination on patient care and osteoporosis treatment.

Methods: This study analyzes the clinical differences and management of patients treated by REU and OG between February 1, 2024, and April 15, 2025, using a cross-sectional descriptive design. Clinical, analytical, and treatment variables were collected, with statistical analyses performed in SPSS. Categorical variables were expressed as frequencies and percentages, continuous variables were presented as medians with confidence intervals. Chi-square and Mann-Whitney U tests assessed associations. Missing data were handled through regression-based imputation to ensure result integrity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Comparison of Biochemical Parameters in RHE and OG Groups

Variable	UHD	MH	P-value
Ca (mg/dL)	n = 186	n = 243	<0.0001
	9.3 (7.5-11.10)	8.9 (7.70-10.5)	
P (mg/dL)	n = 170	n = 137	0.113
	3.2 (1.10-5.30)	2.9 (1.60-86)	
TP (g/dL)	n = 183	n = 232	0.009
	6 (4.3-28)	6.2 (3.2-8.2)	
TSH (mU/L)	n = 165	n = 220	0.312
	1.74 (0.07-43)	1.68 (0.34-15.80)	
PTH (pg/mL)	n = 181	n = 191	0.126
	47.5 (4-404)	50 (8-202)	
Vit-D (ng/mL)	n = 182	n = 226	0.468
	13 (1-83)	12 (3-82)	

Ca: Calcio, P: Phosphorus; TP: Total proteins; TSH: Thyroid Stimulating Hormone; PTH: Parathyroid Hormone; Vit-D: Vitamin D

Table 3: Comparison of Previous Treatment, Discharge Care, and Follow-Up in RHE and OG Groups

Variable		UHD	OG	P-value
Previous treatment	Yes	30 (15.6%)	28 (11.2%)	0.188
	No	162 (84.4%)	219 (87.95%)	
	Missing	-	2 (0.8)	
Good adherence of previous treatment	Yes	17 (56.67%)	23 (82.14%)	0.035
	No	11 (36.66%)	4 (14.3%)	
	Missing	2 (6.66%)	1 (3.6%)	
Discharge treatment	No	40 (20.8%)	63 (25.3%)	<0.0001
	ZOL	69 (35.9%)	37 (14.86%)	
	Dmab	51 (26.6%)	28 (11.2%)	
	TPTD	6 (3.125%)	4 (1.6%)	
	ROMO	3 (1.6%)	-	
	ALN	19 (9.9%)	62 (24.9%)	
	ABL	4 (2.1%)	-	
	Missing	-	55 (22.1%)	
Ca+vit-D post discharge	Yes	181 (94.3%)	153 (61.4%)	<0.0001
	No	10 (5.2%)	34 (13.7%)	
	Missing	1 (0.5%)	62 (24.9%)	
Why did patients not receive treatment?	PD of BMD	26 (65%)	3 (4.7%)	<0.0001
	Limited life expectancy	5 (12.5%)	26 (41.27%)	
	Patient decision	5 (12.5%)	9 (14.29%)	
	Died	1 (2.5%)	-	
	Others	3 (7.5%)	22 (34.9%)	
	Missing	-	3 (4.7%)	
Discharge destination	Rheumatology	152 (79.2%)	36 (14.5%)	<0.0001
	Primary care	37 (19.3%)	148 (59.4%)	
	Died	1 (0.5%)	-	
	Others	2 (1.04%)	-	
	Missing	1 (0.5%)	65 (26.1%)	

ZOL: Zoledronate; Dmab: Denosumab; TPTD: Teriparatide; ROMO: Romosozumab, ALN: Alendronate; ABL: Abaloparatide; PD: Pending

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Significant differences were observed between the RHE (n=192) and OG (n=249) groups. OG were older (87 vs. 80 years; p< 0.0001), and hip fractures were more prevalent (96.4% vs. 82.3%; p< 0.0001). Risk factors were more common in RHE, including early menopause (p=0.012), family history of hip fracture (p< 0.0001), smoking (p< 0.0001), and alcohol consumption (p=0.041). Previous fractures were more frequent in RHE (50.5% vs. 31.7%; p=0.023), with greater variability in fracture count (Table 1).

Biochemically, RHE showed higher serum calcium levels (9.3 mg/dL vs. 8.9 mg/dL; p< 0.0001), while OG had slightly higher total protein levels (6.2 g/dL vs. 6 g/dL; p=0.009) (Table 2).

Discharge treatment, RHE patients received higher rates of calcium and vitamin D supplementation (94.3% vs. 61.4%; p< 0.0001) and osteoporosis therapy (79.2%; p< 0.0001). Zoledronate and denosumab were more commonly prescribed in RHE, while alendronate was the predominant treatment in OG. Reasons for lack of treatment differed between groups: in RHE, the primary reason was pending bone mineral density (BMD) evaluation before initiating therapy (65% vs. 4.7%; p< 0.0001). In OG, limited life expectancy was the most cited reason (41.27%) (Table 3).

Conclusion: These findings highlight distinct management approaches: REU follows a structured osteoporosis treatment strategy, while OG prioritizes patient stability. Higher fracture prevalence in REU correlates with greater risk factors, and rheumatologists tend to be more precise in fracture identification than geriatricians. A multidisciplinary approach is essential for optimizing osteoporosis care and tailoring treatments effectively.

Disclosure: C. Egües Dubuc: None; **E. Laso Lucas**: None; **N. Alcorta Lorenzo**: None; **C. Lizasoain Alustiza**: None; **L. Unanue Pumar**: None; **G. Jimenez Clemente**: None; **C. Murillo Erazo**: None; **V. Lavilla Garcia**: None; **A. Alberdi Arbelaiz**: None; **E. Zubillaga Azpiroz**: None; **I. Gabarain Morcillo**: None; **J. Cancio Fanlo**: None; **M. Ariztia Sarratea**: None; **I. Arruabarrena Echeverria**: None; **G. de La Herran Nuñez**: None; **A. Martin Garcia**: None; **L. LOPEZ DOMINGUEZ**: None.

Abstract Number: 2108

Multidisciplinary Fragility Fracture Management Across Two Coordinated Hospitals: Evaluating Risk Factors, Treatment Approaches, and Long-Term Patient Outcomes in Those With and Without Prior Fractures

César Antonio Egües Dubuc[1], Nerea Alcorta Lorenzo[2], Esther Laso Lucas[3], Carlos Maria Lizasoain Alustiza[4], Claudia Murillo Erazo[3], Gabriela Jimenez Clemente[3], Gaspar de La Herran Nuñez[4], Vicente Lavilla Garcia[3], Imanol Gabarain Morcillo[4], Leire Unanue Pumar[4], Irene Corcuera Elosegui[4], Antonio Martin Garcia[4], Jorge Jesus Cancio Fanlo[5], Maria Ariztia Sarratea[3], Ander Alberdi Arbelaiz[4], Iñaki Maria Arruabarrena Echeverria[3], Elena Zubillaga Azpiroz[4] and LUIS LOPEZ DOMINGUEZ[6], [1]Donostia University Hospital, San Sebastián, Pais Vasco, Spain, [2]University Hospital Donostia, san sebastian, Spain, [3]Matia Hospital, San Sebastian, Pais Vasco, Spain, [4]Donostia University Hospital, San Sebastian, Pais Vasco, Spain, [5]Donostia University Hospital, San Sebastian, [6]Hospital Universitario Donostia, San Sebastian, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Our Fracture Coordination Unit operates across two hospitals: University Hospital of Donostia (UHD) and Matía Hospital (MH). Patients with a geriatric profile are transferred to MH for Orthogeriatric care, while others

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Comparison of Clinical Characteristics, Previous Treatment, and Discharge Care Between Patients With and Without Prior Fragility Fractures

Variable		With pFF	Without pFF	P-value
Gender	Female	155 (88.07%)	150 (68.8%)	<0.0001
Age	Median (range)	85.50 (39-98)	83 (45-103)	0.055
FF	Hip	162 (92.05%)	189 (86.70%)	0.108
	Humerus	3 (1.70%)	16 (7.3%)	
	Radius	2 (1.14%)	1 (0.5%)	
	Vertebra	0 (0.00%)	2 (0.92%)	
	Multiple	4 (2.27%)	5 (2.29%)	
	Others	4 (2.27%)	4 (1.83%)	
	Missing	1 (0.6%)	1 (0.5%)	
Early menopause	Yes	17 (9.7%)	8 (3.7%)	<0.0001
	No	103 (58.5%)	81 (37.2%)	
	Missing	56 (31.8%)	129 (59.4%)	
Maternal or paternal hip fracture	Yes	11 (6.25%)	17 (7.80%)	0.006
	No	112 (63.6%)	111 (50.9%)	
	Missing	53 (30.1%)	90 (41.3%)	
Alcohol intake	Yes	19 (10.8%)	21 (9.6%)	0.953
	No	137 (77.84%)	165 (75.69%)	
	Previous	2 (1.1%)	2 (0.9%)	
	Missing	18 (10.2%)	30 (13.8%)	
Smoking status	Yes	41 (23.3%)	42 (19.3%)	0.437
	No	117 (66.5%)	147 (67.4%)	
	Missing	18 (10.2%)	29 (13.3%)	
Dairy intake	Yes	121 (68.8%)	141 (64.7%)	0.629
	No	35 (19.89%)	44 (20.18%)	
	Missing	20 (11.4%)	32 (14.7%)	
Hormone replacement therapy	Yes	6 (3.4%)	19 (8.7%)	<0.0001
	No	129 (73.3%)	116 (53.2%)	
	Missing	39 (22.2%)	85 (39%)	
Corticosteroids intake	Yes	7 (4.0%)	13 (6.0%)	0.066
	No	151 (85.8%)	171 (78.4%)	
	Previous	1 (0.6%)	8 (3.7%)	
	Missing	17 (9.7%)	26 (11.9%)	
Osteopenizante treatment	Yes	24 (13.64%)	25 (11.47%)	0.553
	No	133 (75.6%)	167 (76.6%)	
	Missing	19 (10.8%)	28 (12%)	
Previous treatment	Yes	50 (28.4%)	7 (3.2%)	<0.0001
1st previous treatment period (years)	Median (SE)	5 (0.5)	4.5 (2.245)	0.768
2nd previous treatment period (years)	Median (range)	4 (0.5-12)	2 (2-2)	0.800
1st previous treatment		n = 50	n = 7	0.749
	ZOL	3 (6%)	1 (14.28%)	
	Dmab	8 (16%)	-	
	TPTD	3 (6%)	-	
	ROMO	1 (2%)	-	
	ALN	30 (60%)	5 (71.42%)	
	RSN	3 (6%)	-	
	IBN	2 (4%)	1 (14.28%)	
	RNL	1 (2%)	-	
2nd prior treatment	Dmab	7 (14%)	1 (14.28%)	0.919
	TPTD	1 (2%)	-	
	ALN	3 (6%)	-	
	IBN	2 (4%)	-	
	RNL	1 (2%)	-	
	Missing	36 (72%)	6 (85.7%)	
Ca. and vitD supplements at discharge	Yes	152 (86.4%)	177(81.2%)	0.040
	No	12 (6.82%)	29 (13.30%)	

receive Rheumatology management at UHD. This study analyzes fragility fracture (FF) risk factors and compares clinical differences between patients with and without previous fractures (pFF) admitted from February 2024 to April 2025.

Methods: A cross-sectional descriptive study was conducted. Clinical, analytical, and treatment variables were collected and processed using the SPSS statistical software. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as medians with confidence intervals. Associations were evaluated using Chi-square and Mann-Whitney U tests, while ANOVA, logistic regression, and multinomial regression were applied to identify factors related to FF.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Location and Age Distribution of Previous Fragility Fractures

Location of pFF	1st FF	2nd FF	3rd FF	4th FF	5th FF
Hip	35 (19.9%)	7 (3.98%)	3 (1.70%)	1 (0.57%)	
Humerus	12 (6.82%)	6 (3.41%)	4 (2.27%)	1 (0.57%)	
Radius	35 (19.9%)	4 (2.27%)	5 (2.84%)	2 (1.14%)	
Pelvis	9 (5.11%)	7 (3.98%)	1 (0.57%)	2 (1.14%)	2 (1.14%)
Vertebra	45 (25.6%)	26 (14.77%)	14 (7.95%)	10 (5.68%)	6 (3.41%)
Multiple	31 (17.61%)	11 (6.3%)	9 (5.11%)	1 (0.57%)	1 (0.57%)
Missing	9 (5.1%)	115 (65.3%)	140 (79.5%)	159 (90.3%)	167 (94.9%)
Age at pFF	75 (57-80)	75 (59-80)	75 (59-83)	75 (63-85)	77 (63-86)

Results: A total of 176 patients with pFF and 218 without were analyzed. Women were more prevalent in pFF group (88.1% vs. 68.8%, $p < 0.0001$). Hip fractures were the most common in both groups ($p = 0.108$). Early menopause was more frequent in pFF (9.7% vs. 3.7%, $p < 0.0001$), as were familial hip fractures ($p = 0.006$). Prior osteoporosis treatment was more common in pFF group (28.4% vs. 3.2%, $p < 0.0001$) (Table 1).

Most patients had one pFF (59.1%), while 14.8% had two, 10.2% had three, and 9.09% had between four and six (Table 2).

Biochemical analysis showed no significant differences in calcium or phosphorus levels. Total protein levels were lower in pFF ($p = 0.028$), PTH was significantly reduced (44.5 pg/mL vs. 50 pg/mL, $p = 0.029$), while vitamin D was lower in both group (14 ng/mL vs. 11.5 ng/mL, $p = 0.012$).

Upon discharge, Ca + VitD supplementation was more frequent in pFF group (86.4% vs. 81.2%, $p = 0.040$). Differences in prescribed treatments were significant ($p < 0.0001$), with a higher prescription rate of ZLN and Dmab in pFF group.

Age was the key factor in FF, with medians of 85 years for hip fractures, 72.5 for humerus, and 65 for others ($p < 0.0001$). PTH was highest in multiple fractures ($p = 0.013$), while TSH showed a marked increase in vertebral FF ($p < 0.0001$). Dairy intake, alcohol consumption, and smoking had no significant impact ($p > 0.05$). Regression analysis confirmed that hip fracture risk increases by 15.6% per year ($p = 0.015$, OR = 1.156) (table 3).

Table 3: Distribution of Demographic, Clinical, Biochemical, and Treatment-Related Characteristics in Patients Hospitalized for Different Types of Fractures

Variable		Type of fracture						p-value
		Hip (n=398)	Humerus (n=19)	Radius (n=3)	Vertebra (n=2)	Multiple (n=9)	Others (n=8)	
Gender female		308.0 (77.4%)	15.0 (78.9%)	3.0 (100.0%)	2.0 (100.0%)	8.0 (88.9%)	4.0 (50.0%)	0.364
Age		85 (56-102)	72.5 (55-85)	74 (66-80)	79 (78-80)	81 (72-95)	65 (45-89)	<0.0001
Ca (mg/dL)		9.1 (7.30-11.10)	9.4 (8.5-10.2)	9.2 (8.8-9.60)	8.55 (8.40-8.70)	8.8 (8.5-10)	8.7 (7.80-9.30)	0.262
P (mg/dL)		3 (1.10-86)	3.25 (2.20-4.10)	3.5 (2.9-3.9)	4.1 (4.10-4.10)	2.5 (2.2-4.5)	3 (1.70-3.50)	1.000
TP (g/dL)		6.2 (3.2-28)	6.25 (5.3-7.5)	6.1 (5.8-7)	4.75 (4.3-5.2)	5.6 (7.3-2.4)	5.35 (4.8-7.2)	0.647
PTH (pg/mL)		48 (4-284)	45.5 (29-88)	39 (35-39)	35 (21-49)	54 (22-86)	75.5 (31-404)	0.013
TSH (mU/L)		1.67 (0.07-43)	1.89 (0.42-8.34)	1.13 (0.71-12)	22.56 (5.53-39.60)	1.05 (0.38-3.72)	2.6 (0.41-5.80)	<0.0001
Vit-D (ng/mL)		13 (1-83)	15.5 (7-72)	13 (11-22)	19.5 (12-27)	6 (4-16)	3 (1-12)	0.827
Dairy intake	Yes	237.0 (59.5%)	15.0 (78.9%)	1.0 (33.3%)	1.0 (50.0%)	4.0 (44.4%)	6.0 (75.0%)	0.725
	No	73.0 (18.3%)	1.0 (5.3%)	2.0 (66.7%)	1.0 (50.0%)	2.0 (22.2%)	2.0 (25.0%)	
Smoker	Yes	71.0 (17.8%)	7.0 (36.8%)	0.0 (0.0%)	1.0 (50.0%)	2.0 (22.2%)	3.0 (37.5%)	0.320
	No	244.0 (61.3%)	10.0 (52.6%)	3.0 (100.0%)	1.0 (50.0%)	4.0 (44.4%)	5.0 (62.5%)	
Alcohol	Yes	36.0 (9.0%)	1.0 (5.3%)	0.0 (0.0%)	0.0 (0.0%)	1.0 (11.1%)	2.0 (25.0%)	0.975
	No	274.0 (68.8%)	16.0 (84.2%)	3.0 (100.0%)	2.0 (100.0%)	5.0 (55.6%)	6.0 (75.0%)	
	Previous	4.0 (1.0%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	
Maternal or paternal fracture	Yes	22.0 (5.5%)	5.0 (26.3%)	0.0 (0.0%)	0.0 (0.0%)	1.0 (11.1%)	0.0 (0.0%)	0.57
	No	204.0 (51.3%)	11.0 (57.9%)	3.0 (100.0%)	2.0 (100.0%)	3.0 (33.3%)	5.0 (62.5%)	
Early menopause	Yes	24.0 (6.0%)	0.0 (0.0%)	1.0 (33.3%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	0.398
	No	164.0 (41.2%)	14.0 (73.7%)	2.0 (66.7%)	2.0 (100.0%)	5.0 (55.6%)	4.0 (50.0%)	
Previous fracture	Yes	162.0 (40.7%)	3.0 (15.8%)	2.0 (66.7%)	0.0 (0.0%)	4.0 (44.4%)	4.0 (50.0%)	0.108
	No	189.0 (47.5%)	16.0 (84.2%)	1.0 (33.3%)	2.0 (100.0%)	5.0 (55.6%)	4.0 (50.0%)	
THS	Yes	23.0 (5.8%)	1.0 (5.3%)	1.0 (33.3%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	0.733
	No	222.0 (55.8%)	14.0 (73.7%)	2.0 (66.7%)	2.0 (100.0%)	5.0 (55.6%)	5.0 (62.5%)	
Corticosteroids intake	Yes	17.0 (4.3%)	1.0 (5.3%)	0.0 (0.0%)	2.0 (100.0%)	0.0 (0.0%)	1.0 (12.5%)	0.740
	No	292.0 (73.4%)	16.0 (84.2%)	3.0 (100.0%)	0.0 (0.0%)	6.0 (66.7%)	7.0 (87.5%)	

Ca: Calcio, P: Phosphorus; TP: Total proteins; TSH: Thyroid Stimulating Hormone; PTH: Parathyroid Hormone; Vit-D: Vitamin D

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The results reveal significant differences between the groups. Women, with early menopause or a family history of hip FF, face a higher risk. Both groups had insufficient VitD, emphasizing the need for better detection and treatment. Prior osteoporosis treatment was more frequent in pFF group, where fracture recurrence underscores the importance of adherence and treatment optimization.

In the pFF group, the first FF occurred at a median age of 75 years. As fracture count increased, tracking patient history became more challenging.

The multinomial logistic regression model confirms age as the primary determinant of fracture risk.

These findings highlight the need for prevention and clinical monitoring, as patients with a pFF are at greater risk of future fractures.

Disclosure: C. Egües Dubuc: None; **N. Alcorta Lorenzo**: None; **E. Laso Lucas**: None; **C. Lizasoain Alustiza**: None; **C. Murillo Erazo**: None; **G. Jimenez Clemente**: None; **G. de La Herran Nuñez**: None; **V. Lavilla Garcia**: None; **I. Gabarain Morcillo**: None; **L. Unanue Pumar**: None; **I. Corcuera Elosegui**: None; **A. Martin Garcia**: None; **J. Cancio Fanlo**: None; **M. Ariztia Sarratea**: None; **A. Alberdi Arbelaiz**: None; **I. Arruabarrena Echeverria**: None; **E. Zubillaga Azpiroz**: None; **L. LOPEZ DOMINGUEZ**: None.

Abstract Number: 2109

Comparative Effects of IL-6 inhibition, Methotrexate, and Glucocorticoid Monotherapy on Bone Mineral Density, 3D-DXA femoral structure and Bone Turnover Markers in GCA and PMR

Edgar Wiebe[1], Lien Meerkatt[2], Andriko Palmowski[3], Zhivana Boyadzhieva[4], Kerstin Rubarth[5], Sandra Hermann[1], Burkhard Muche[3], Gerhard Krönke[6] and FRANK BUTTGEREIT[7], [1]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Berlin, Germany, [5]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Berlin, Germany, [6]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Berlin, Germany, [7]Charité University Medicine Berlin, Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Individuals with giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are at increased risk for osteoporosis and fragility fractures due to long-term glucocorticoid (GC) use and underlying Interleukin-6 (IL-6)–driven inflammation. IL-6 inhibition is an effective treatment that also reduces GC exposure. In rheumatoid arthritis, IL-6 receptor blockade with tocilizumab reduces bone resorption markers and increases femoral neck bone mineral density (BMD). However, longitudinal data on the effects of IL-6 blockade on bone health in large-vessel vasculitis are lacking, and no study has yet compared its impact to methotrexate (MTX) or GC monotherapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient characteristics at baseline. Comparison of confounder variables between treatment groups. MTX: methotrexate; GC: glucocorticoids; BMI (body mass index); CRP: C-reactive protein; ESR: erythrocyte sedimentation rate

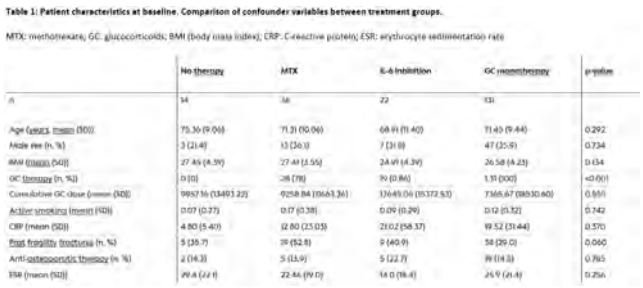


Table 1: Patient characteristics at baseline. Comparison of confounder variables between treatment groups.

MTX: methotrexate; GC: glucocorticoids; BMI (body mass index); CRP: C-reactive protein; ESR: erythrocyte sedimentation rate

	No therapy	MTX	IL-6 inhibition	GC monotherapy	p-value
n	14	36	22	131	
Age (years, mean (SD))	75.36 (9.06)	71.31 (10.06)	68.91 (11.40)	71.45 (9.44)	0.292
Male sex (n, %)	3 (21.4)	13 (36.1)	7 (31.8)	47 (35.9)	0.734
BMI (mean (SD))	27.46 (4.39)	27.47 (3.55)	24.49 (4.39)	26.58 (4.23)	0.034
GC therapy (n, %)	0 (0)	28 (78)	19 (0.86)	131 (100)	<0.001
Cumulative GC dose (mean (SD))	9857.16 (13493.22)	9258.84 (10663.36)	13649.04 (15372.53)	7366.67 (8830.60)	0.651
Active smoking (mean (SD))	0.07 (0.27)	0.17 (0.38)	0.09 (0.29)	0.12 (0.32)	0.742
CRP (mean (SD))	4.80 (5.40)	12.80 (25.03)	21.02 (58.37)	19.52 (31.44)	0.570
Prior fragility fractures (n, %)	5 (35.7)	19 (52.8)	9 (40.9)	58 (29.0)	0.060
Anti-osteoporotic therapy (n, %)	2 (14.3)	5 (13.9)	5 (22.7)	19 (14.5)	0.765
ESR (mean (SD))	29.6 (22.1)	22.44 (19.0)	14.0 (16.4)	25.9 (21.4)	0.256

This study aimed to compared the effects of IL-6 inhibition, MTX and GC monotherapy on bone health in patients with GCA and PMR.

Methods: This longitudinal analysis uses data from the prospective Rh-GIOP study at Charité–Universitätsmedizin Berlin (2015–2024). Patients with GCA or PMR undergoing osteoporosis checkup were included up to the second follow-up visit. Bone health was assessed using dual-energy X-ray absorptiometry (DXA), trabecular bone score (TBS), 3D structural femur parameters (3D-Shaper v2.12), and bone turnover markers (bone-specific alkaline phosphatase, osteocalcin and desoxypyridinoline [DPD]).

Linear mixed-effects models were used to assess associations between treatment (IL-6 inhibitors, MTX, GC monotherapy) and bone outcomes, adjusting for age, sex, BMI, GC dose, erythrocyte sedimentation rate (ESR), prior fragility fractures, and anti-osteoporotic therapy. Estimated marginal means compared adjusted group differences.

Results: A total of 203 patients (81 with GCA; mean age 72 years; 66% female, all postmenopausal) were included. At baseline visit for osteoporosis check-up 22 received IL-6 inhibitors (21 tocilizumab, 1 Sarilumab), 36 MTX, and 131 GC monotherapy; 14 received no immunosuppressive treatment. Seventy-five patients had at least one follow-up visit (mean follow-up: 2.6 ± 1.3 years), and 27 had a second (4.6 ± 1.3 years). Osteoporosis by DXA and fragility fracture prevalence at baseline were 20% and 36%, respectively. Baseline characteristics were balanced across treatment groups.

Table 2: Estimated marginal means (EMM) for the comparison between GC monotherapy and IL-6 inhibition vBMD: volumetric bone mineral density

Table 2: Estimated marginal means (EMM) for the comparison between GC monotherapy and IL-6 inhibition

vBMD: volumetric bone mineral density

	estimate	standard error	p-value
Direct DEXA parameters			
Lumbar Spine T-Score	-0.244	0.49	0.618
Total Hip T-Score	-0.168	0.327	0.607
Trabecular Bone Score (TBS)	0.021	0.151	0.892
3D-DXAparameters			
Integral vBMD	**-13.919**	**4.926**	**0.006**
Trabecular vBMD	-7.715	5.119	0.138
Cortical vBMD	**-20.38**	**9.417**	**0.036**
Cortical thickness	0.003	0.16	0.987
Cortical surface BMD	-4.847	3.017	0.112
Bone turnover parameters			
Bone-specific alkaline phosphatase	-1.579	1.242	0.204
osteocalcin	-0.492	1.282	0.701
Desoxypridinoline	-0.591	0.965	0.54

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Male sex and higher BMI were positively associated with lumbar spine T-scores (estimate: +1.427, SE: 0.235, p < .005; and +2.754, SE: 0.028, p = .007), femoral T-Scores and bone structure. Higher age correlated with increased DPD levels (+0.071, SE: 0.036, p = .048).

No significant overall effect was observed for IL-6 inhibitors, MTX, or GC treatment. However, compared to IL-6 inhibitors, GC monotherapy was associated with lower cortical volumetric BMD (–20.38, SE: 9.41, p = .036) and integral vBMD (–13.9, SE: 4.96, p = .006). No significant differences were found between IL-6 inhibitors and MTX, nor between MTX and GC monotherapy.

Conclusion: In patients with GCA and PMR, sex and BMI were key predictors of BMD and femoral bone structure. Treatment with IL-6 inhibitors was associated with more favorable cortical and trabecular bone parameters than GC monotherapy. This suggests that GC-sparing IL-6 blockade may help preserve bone microarchitecture in patients with inflammatory vasculitis.

Disclosure: E. Wiebe: Sobi, 6; **L. Meerkatt**: None; **A. Palmowski**: Novartis, 1; **Z. Boyadzhieva**: None; **K. Rubarth**: None; **S. Hermann**: None; **B. Muche**: AbbVie/Abbott, 6, Amgen, 6, Celltrion, 6, Theramex, 6, UCB, 6; **G. Krönke**: None; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

Abstract Number: 2110

Effect of Proton-Pump-Inhibitors on Bone Mineral Density and Microarchitecture in Patients with Inflammatory Rheumatic and Musculoskeletal Diseases

Edgar Wiebe[1], Kerstin Rubarth[2], Zhivana Boyadzhieva[3], Sandra Hermann[1], Burkhard Muche[4], Gerhard Krönke[5], Andriko Palmowski[4] and FRANK BUTTGEREIT[6], [1]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [5]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Berlin, Germany, [6]Charité University Medicine Berlin, Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with inflammatory rheumatic and musculoskeletal diseases (iRMDs) are at increased risk of osteoporosis and fragility fractures due to systemic inflammation and glucocorticoid (GC) use. Proton pump inhibitors (PPIs), frequently prescribed in this population, have also been linked to fracture risk, although findings remain inconsistent. Our previous cross-sectional analysis suggested a negative impact of PPIs on bone mineral density (BMD) but not on microarchitecture in iRMDs.

This study aimed to assess the longitudinal effects of PPI use on BMD and bone microarchitecture.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: The prospective Rh-GIOP cohort includes patients with iRMDs fulfilling German guidelines for osteoporosis check-up. Participants underwent dual-energy X-ray absorptiometry (DXA) and evaluation of microstructure by trabecular bone score (TBS) and 3D-DXA. This analysis included all patients with IRMDs who had data available up to the second follow-up visit (2015–2024). Follow-up timing was determined by clinical routine. Patients with manifest hyperparathyroidism and hyperthyroidism were excluded.

Daily intake of PPI was ascertained via chart review and self-report. As-needed PPI use was combined with regular use to form the composite variable "any PPI use". Primary outcomes were T-scores at the lumbar spine, total hip, TBS and 3D-DXA parameters of the femur. Linear mixed-effects models assessed the effect of any PPI use as well as daily PPI use on the primary outcomes and were weighted by propensity scores accounted for potential confounders such as age, sex, BMI, GC dose, C-reactive protein, disability and comorbidity. Missing data was handled by multiple imputation (predicitive mean matching).

Results: At baseline, 1,909 patients (74% women; mean age 63 ± 13 years) were included; 45% reported daily and 51% any PPI use. 713 had at least one follow-up (mean 2.7 ± 1.3 years), and 267 had a second (mean 4.6 ± 1.4 years).

Any PPI use was associated with lower T-Scores at the lumbar spine (estimate: –0.115; standard error (SE): 0.052; P = .029). In contrast, total hip T-Score was not significantly affected by any PPI use (–0.027; SE: 0.024; P = 0.258) or daily use (–0.038; SE: 0.026; P = 0.37). TBS was related to a negative impact by any PPI use (–0.017; SE: 0.006; P = .004), and daily use (–0.021; SE: 0.006; P = .001). Femoral cortical thickness was also negatively affected by both any PPI use (–0.012; SE: 0.006; P = .050) and daily PPI use (–0.015; SE: 0.006; P = .017).

Adjusted interaction analysis showed that PPI-related reduction in TBS also occurred in low-dose GC users (0-7.5 mg/day), suggesting a synergistic impact. For cortical thickness, PPI effects were particularly relevant in the absence of GC use.

Daily PPI use was further linked to lower calcium levels (–0.010; SE: 0.004; P = .016) and higher parathyroid hormone levels (2.275; SE: 0.964; P = .019).

Conclusion: Our results indicate that PPIs may also impair bone microarchitecture in patients with iRMDs. This effect appears to be most prominent in individuals without GC use or on low-dose GCs, potentially linked to reduced calcium absorption. This underscores the need for cautious PPI use, especially in patients already at high risk for osteoporosis.

Disclosure: E. Wiebe: Sobi, 6; **K. Rubarth**: None; **Z. Boyadzhieva**: None; **S. Hermann**: None; **B. Muche**: AbbVie/Abbott, 6, Amgen, 6, Celltrion, 6, Theramex, 6, UCB, 6; **G. Krönke**: None; **A. Palmowski**: Novartis, 1; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2111

Cost-effectiveness Analysis of Biosimilar Denosumab for the Treatment of Women with Post-menopausal Osteoporosis in the United States: A Risk Based Analysis

Edward Li[1], Rebecca McTavish[2], Fatemeh Mirzayeh fashami[2], Sarah Kane[2] and Marion Schauf[3], [1]Sandoz Inc., West Princeton, NJ, [2]EVERSANA, Burlington, ON, Canada, [3]Sandoz International GmbH, Holzkirchen, Bayern, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Post-menopausal osteoporosis (PMO) significantly increases the risk of fractures in women, necessitating effective treatment strategies. The introduction of biosimilar denosumab offers the opportunity to re-evaluate the value of common treatments for PMO. This study evaluates the cost-effectiveness of biosimilar denosumab versus bisphosphonates and no intervention across groups of women with PMO who have different underlying risks of fracture.

Methods: A previously developed Markov model was used. Subjects were stratified to 4 risk categories (i.e., from risk 1 [lowest risk] to risk 4 [highest risk]) based on occurrence of a prior vertebral fracture (yes/no) and T-score (-2.5 or ≤ -2.5; **Table 1**). Model inputs, including baseline fracture risks, drug efficacy, administration costs, and utility values were estimated from publicly available data and literature. Biosimilar drug acquisition costs were assumed, based on trends of previously available biosimilars. The incremental costs, incremental quality-adjusted life-years (QALYs), and incremental cost-utility ratio (ICUR) were calculated from a US payer perspective.

Table 1: Stratification of Women with Post-Menopausal Osteoporosis and the Related Relative Risks of Fracture Used in the Model

Risk Category	Prior VF	T-score	Age Group	Relative Risk of Fracture			
				HF	VF	WF	OF
Risk 1	No	-2.5	65 – 69	1.82	1.21	1.06	1.06
			70 – 74	1.42	1.04	0.94	0.94
			75 – 79	1.11	0.89	0.82	0.82
			80 – 84	0.86	0.76	0.73	0.73
			85 +	0.66	0.65	0.64	0.64
Risk 2	No	≤ -2.5	65 – 69	3.51	2.34	2.05	2.05
			70 – 74	2.95	2.16	1.96	1.96
			75 – 79	2.43	1.97	1.81	1.81
			80 – 84	2.09	1.85	1.77	1.77
			85 +	1.8	1.58	1.56	1.56
Risk 3	Yes	-2.5	65 – 69	3.90	4.29	1.59	1.59
			70 – 74	3.04	3.69	1.41	1.41
			75 – 79	2.36	3.16	1.23	1.23
			80 – 84	1.84	2.70	1.10	1.10
			85 +	1.41	2.31	0.96	0.96
Risk 4	Yes	≤ -2.5	65 – 69	7.51	8.31	3.08	3.08
			70 – 74	6.31	7.67	2.94	2.94
			75 – 79	5.20	7.00	2.72	2.72
			80 – 84	4.47	6.57	2.66	2.66
			85 +	3.42	5.61	2.34	2.34

Abbreviations: HF = hip fracture; OF = other fractures; VF = vertebral fracture; WF = wrist fracture.

Table 2: Deterministic Results for Women with Post-Menopausal Osteoporosis Across Different Fracture Risk Categories

Risk Category	Outcome	Biosimilar Denosumab vs. Alendronate	Biosimilar Denosumab vs. Risedronate	Biosimilar Denosumab vs. Ibandronate	Biosimilar Denosumab vs. Zoledronic acid	Biosimilar Denosumab vs. No intervention
Risk 1	Incremental QALYs	0.021	0.021	0.021	0.015	0.026
	Incremental costs	$5,748	$5,444	$5,647	$5,561	$5,597
	ICUR ($ per QALYs)	$272,031	$257,435	$273,624	$364,346	$213,660
Risk 2	Incremental QALYs	0.042	0.042	0.041	0.030	0.052
	Incremental costs	$4,445	$4,123	$4,318	$4,430	$4,036
	ICUR ($ per QALYs)	$105,129	$97,572	$104,149	$149,478	$77,088
Risk 3	Incremental QALYs	0.051	0.051	0.050	0.034	0.063
	Incremental costs	$4,294	$3,967	$4,208	$4,419	$3,854
	ICUR ($ per QALYs)	$83,755	$77,550	$83,660	$130,787	$60,976
Risk 4	Incremental QALYs	0.091	0.090	0.090	0.059	0.112
	Incremental costs	$1,160	$792	$1,070	$1,838	$107
	ICUR ($ per QALYs)	$12,799	$8,760	$11,925	$31,337	$954

Abbreviations: ICUR = incremental cost-utility ratio; QALYs = quality-adjusted life-years.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The use of biosimilar denosumab in women with PMO across risk categories 1, 2, 3, and 4 resulted in ICURs of $272,031, $105,129, $83,755, and $12,799, respectively, compared to alendronate. When compared to no intervention, biosimilar denosumab yielded ICURs of $213,660, $77,098, $60,976, and $954 for risk categories 1, 2, 3, and 4, respectively. This trend was consistent across all other comparators, demonstrating that as fracture risk increases, the ICURs for biosimilar denosumab compared to bisphosphonates and no intervention decrease (**Table 2**). Further decreases in biosimilar denosumab price led to improved cost-effectiveness and in some cases, domination.

Conclusion: Relative to common willingness-to-pay thresholds of $100,000 and $150,000, biosimilar denosumab is cost-effective for patients in risk categories 2, 3 and 4 when compared to bisphosphonates and no intervention in the treatment of PMO.

Disclosure: E. Li: Sandoz Inc, 3; **R. McTavish**: EVERSANA, 3; **F. Mirzayeh fashami**: EVERSANA, 3; **S. Kane**: EVERSANA, 3; **M. Schauf**: Sandoz International, 3.

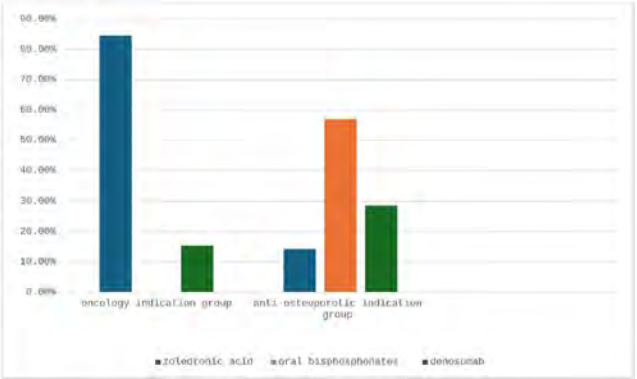
Abstract Number: 2112

Which drugs are associated with the development of osteonecrosis of the jaw? clinical and epidemiological analysis of a cohort of patients diagnosed with osteonecrosis of the jaw.

Esther Monleon Acosta[1], Alicia Pérez González[2], José Andrés Rodríguez Fernández[2], Pedro José Manuel Hernández[2], María del Rosario Oliva Ruiz[2], José María Andreu Ubero[2], Paloma Valentina Castillo Dayer[2], Gloria Albaladejo Paredes[3], Carlos Fernández Díaz[4], Angela Egea Fuentes[2], Montserrat Fernández Salamanca[2] and Vicente Cogolludo Campillo[5], [1]Hospital Santa Lucia, Cartagena, Spain, [2]Hospital General Universitario Santa Lucia, Cartagena, Spain, [3]Hospital General Universitario Santa Lucia, CARTAGENA, Spain, [4]H.U. Santa Lucia, Murcia, Spain, [5]Hospital General Universitario Santa Lucia, Santa Lucia, Cartage, Spain

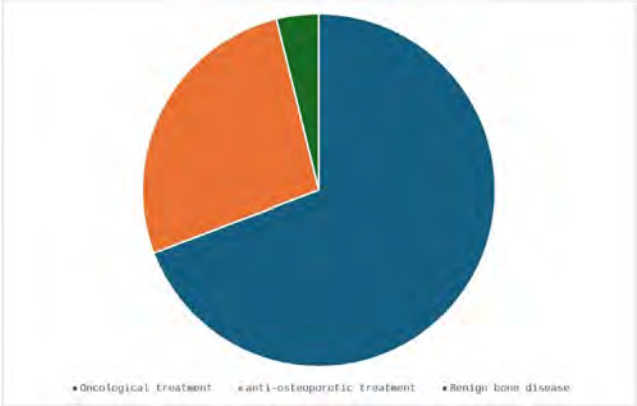
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteonecrosis of the jaw (ONJ) is defined as avascular necrosis of bone located in the maxillofacial region with the presence of exposed bone or bone accessible through an extra or intraoral fistula that does not heal within 8 weeks and excludes osteoradionecrosis secondary to radiotherapy. ONJ can be secondary to drugs and it is referred to



1. Distribution of cases of MRONJ according to antiresorptive drug and clinical indication.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



2. Distribution of patients (with MRONJ) treated with bisphosphonates according to clinical indication.

Medication-related osteonecrosis of the jaw (MRONJ). To define a MRONJ is required a current or previous treatment with antiresorptive therapy alone or in combination with immune modulators or antiangiogenic medications.

With this study we want to analyse which drugs are associated with the development of MRONJ as well as to describe the clinical and epidemiological characteristics of patients diagnosed with MRONJ.

Methods: A descriptive, observational and retrospective study was carried out at the Santa Lucia hospital in Cartagena. Individuals with MRONJ was collected from 2015 to 2024 at the Santa Lucia Hospital, in Cartagena. Clinical-epidemiological variables were collected and a statistical analysis was carried out using SPSSv21.

Results: 24 individuals with a diagnosis of MRONJ was collected. Fifty-six per cent of the blind were women and the remainder (44 per cent) were men. The average age was 69 +- 13.2 years. Of these patients 56% were hypertensive, 20% diabetic, 32% had dyslipidaemia and 12% had stage 3-4 chronic kidney disease. 78.1% of the individuals had an underlying oncological disease and 4.9% had a rheumatological disease. Of all people, 22% had previously had an invasive dental procedure.

At the time of MRONJ diagnosis, 100% of the individuals were being treated with antiresorptive drugs: 85.2% were treated with bisphosphonates and 14.8% with denosumab. The average treatment time with these drugs was 4.15 +- 3.7 years.

Of those on bisphosphonate therapy, 66.6% were on intravenous bisphosphonates (zoledronic acid) and the remainder on oral therapy (11,1% risendronate, 11,1% Alendronate and 11,1% other). These treatments were indicated as oncological treatment in 69.23% of cases, while only 26.9% were used as anti-osteoporotic treatment. In 3.87% of cases they were indicated as a treatment for benign bone disease.

In the oncology indication group, 84.6% of the MRONJ cases were due to the use of zoledronate, while in the anti-osteoporotic indication group only 14.2% of the MRONJ cases were caused by zoledronate. These differences were statistically significant ($p< 0.001$). Therefore, the development of ONMR in patients treated with zoledronate was more frequent when it was used as an oncology treatment.

In the anti-osteoporotic indication group the 57,8% of the patients with MRONJ were on oral bisphosphonate therapy and 28,57% with denosumab.

Conclusion: The drug most associated with the development of MRONJ in our sample of patients was zoledronic acid, being the development of this entity much more frequent when it is administered as an oncological treatment. Therefore, it could be hypothesised that the risk of MRONJ does not depend so much on the drug as on the indication and administration schedule, but more studies are needed to clarify the association between MRONJ and the different drugs.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Monleon Acosta: None; **A. Pérez González**: None; **J. Rodríguez Fernández**: None; **P. Manuel Hernández**: None; **M. Oliva Ruiz**: None; **J. Andreu Ubero**: None; **P. Castillo Dayer**: None; **G. Albaladejo Paredes**: None; **C. Fernández Díaz**: None; **A. Egea Fuentes**: None; **M. Fernández Salamanca**: None; **V. Cogolludo Campillo**: None.

Abstract Number: 2113

Mortality rate in patients with hip fracture: is it recommendable to establish fracture units?

Esther Monleon Acosta[1], Alicia Pérez González[2], José Andrés Rodríguez Fernández[2], Pedro José Manuel Hernández[2], María del Rosario Oliva Ruiz[2], José María Andreu Ubero[2], Paloma Valentina Castillo Dayer[2], Gloria Albaladejo Paredes[3], Carlos Fernández Díaz[4], Angela Egea Fuentes[2], Montserrat Fernández Salamanca[2] and Vicente Cogolludo Campillo[5], [1]Hospital Santa Lucia, Cartagena, Spain, [2]Hospital General Universitario Santa Lucia, Cartagena, Spain, [3]Hospital General Universitario Santa Lucia, CARTAGENA, Spain, [4]H.U. Santa Lucia, Murcia, Spain, [5]Hospital General Universitario Santa Lucia, Santa Lucia, Cartage, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hip fracture is the second most common osteoporotic fracture and the one with the highest socio-economic cost. It is associated with high morbidity and mortality rates, reaching a mortality rate of 30% in the first year. It should be noted that the presence of a fracture with an osteoporotic profile is one of the most important risk factors for the appearance of new fractures. Despite this, less than 25% initiate treatment for osteoporosis (OP). These data reflect the importance of applying both primary and secondary prevention measures, as well as the creation of fracture units (FU).

With this study we want to evaluate the need to establish a fracture unit as well as a system of referral to rheumatology after the existence of a fragility fracture. And secondly, to analyse the clinical-epidemiological characteristics of a cohort of patients with a history of osteoporotic hip fracture.

Methods: A descriptive, observational and retrospective study was conducted at the Santa Lucia hospital in Cartagena. Individuals with osteoporotic hip fracture were included from January 2017 to January 2023. A total of 28 clinical-epidemiological variables were collected and a statistical analysis was carried out using SPSSv21.

Results: 615 patients were collected, 72.8% of whom were women and 27.2% men. The mean age was 81 ±10.5 years. 72.5% were hypertensive, 41.5% were dyslipidaemic and 68.8% diabetic. 17.8% were diagnosed with chronic kidney disease , with Stage 3 being the most frequent.

Table 1. Summary of the percentage of individuals with osteoporotic treatment and supplements before and after suffering an osteoporotic hip fracture (OP: osteoporosis, Ca/VitD; calcium/vitamin D).

	YES	NO
Previous OP treatment	2,7%	97,4%
Previous Ca/VitD supplementation	11,9%	88,1%
Later OP treatment	11,8%	88,2%
Later Ca/VitD supplementation	38,3%	61,7%

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Summary of epidemiological, clinical and therapeutic characteristics of patients who suffered an osteoporotic femoral neck fracture.

CLINICAL-EPIDEMIOLOGICAL CHARACTERISTICS	% OF PATIENTS IN WHOM THEY ARE PRESENT
Women	72,8%
Men	27,2%
Hypertension	72,5%
Dyslipidaemia	41,5%
Diabetes	68,8%
Chronic kidney disease	17,8%
Rheumatological pathology	2,76%
Oncological pathology	13,17%
Haematological pathology	3,08%
Respiratory pathology	8,78%
Previous osteoporotic fracture	22,1%
Surgical treatment	95,9%
Exitus during admission	6,8%
Mortality at 5 years	43,8%%
Subsequent osteoporotic fracture	24,3%
Follow-up in rheumatology	7,95%
Follow-up in Rehabilitation	23,21%
Follow-up in geriatrics	19,48%

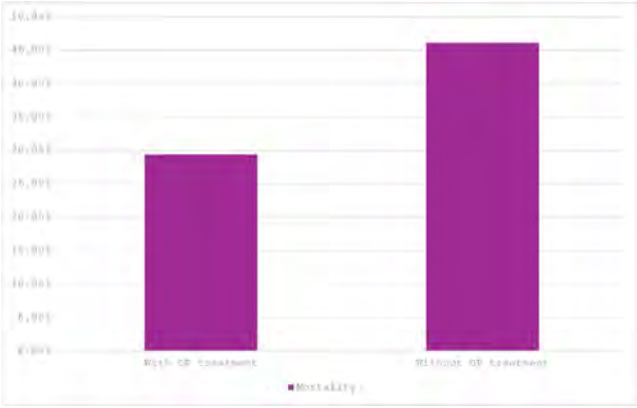
2.27% of the individuals who suffered a hip fracture had previously been prescribed osteoporotic treatment, despite the fact that 22.1% of them had a history of previous osteoporotic. 11.9% were taking calcium and vitamin D supplements and none underwent a densitometric study.

After the hip fracture, 38.3% started calcium and vitamin D supplements and 11.8% osteoporotic treatment. 24.3% of the individuals suffered a new osteoporotic fracture, the most frequent location being at the vertebral level followed by the hip. Of the patients who suffered new fractures, 76.69% were not receiving osteoporotic treatment.

Mortality during hospital admission was 6.8%, at one year it was 23.6%, at 3 years 39.7% and at 5 years 43.8% of the individuals. When we analysed mortality according to the establishment of osteoporotic treatment after hip fracture, we found a mortality rate of 28.3% in those in whom osteoporotic treatment was established, rising to 45.8% when it was not, these differences being statistically significant (p=0.21). It should be noted that only 3.1% of the individuals had been referred to rheumatology.

Conclusion: Osteoporotic treatment had been prescribed in only 2.27% of the cases, despite the fact that 22.1% of the individuals had already suffered a previous fragility fracture. After the hip fracture, osteoporotic treatment was initiated in 11.8% of the individuals, finding in these individuals a lower mortality at 5 years compared to those in whom it was not

Table 3. Percentage of mortality at 5 years according to having received osteporotic treatment after hip fracture (OP: osteoporosis).



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

initiated. Bearing these data in mind, it would be advisable to set up a fracture unit for the assessment of osteoporotic treatment by a doctor with expertise in bone metabolism, as well as the establishment of a referral system after suffering a fracture of this type.

Disclosure: E. Monleon Acosta: None; **A. Pérez González**: None; **J. Rodríguez Fernández**: None; **P. Manuel Hernández**: None; **M. Oliva Ruiz**: None; **J. Andreu Ubero**: None; **P. Castillo Dayer**: None; **G. Albaladejo Paredes**: None; **C. Fernández Díaz**: None; **A. Egea Fuentes**: None; **M. Fernández Salamanca**: None; **V. Cogolludo Campillo**: None.

Abstract Number: 2114

Development of a Fracture Prediction Model for Patients Aging with HIV

Evelyn Hsieh[1], Terrence E. Murphy[2], Baylah Tessier-Sherman[3], Linda Leo-Summers[3], Farah Kidwai-Khan[4], Samah Fodeh[5], Rixin Wang[6], Barbara Gulanski[3], Michael T. Yin[7], Melissa Skanderson[8], Cynthia Brandt[9], Amy C. Justice[4] and Julie Womack[10], [1]Section of Rheumatology, Allergy and Immunology, Yale School of Medicine / VA Connecticut Healthcare System, New Haven, CT, [2]Department of Public Health Sciences, Pennsylvania State University College of Medicine, Hershey, PA, [3]Department of Internal Medicine, Yale School of Medicine, New Haven, CT, [4]Department of Internal Medicine, Yale School of Medicine / VA Connecticut Healthcare System, New Haven, CT, [5]Department of Emergency Medicine, Yale School of Medicine, New Haven, CT, [6]Department of Biomedical Informatics & Data Science, Yale School of Medicine, New Haven, CT, [7]Columbia University Irving Medical Center, New York, NY, [8]VA Connecticut Healthcare System, West Haven, CT, [9]Department of Biomedical Informatics & Data Science, Yale School of Medicine / VA Connecticut Healthcare System, New Haven, CT, [10]Yale School of Nursing / VA Connecticut Healthcare System, Orange, CT

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Fragility fractures are a critical outcome for people ageing with HIV (PAH). Studies demonstrate higher prevalence, incidence, and earlier onset than for the general population. Current fragility fracture prediction models for the general population underestimate risk in PAH. To address this gap, we developed one- and three-year predictive models for risk of fragility fracture that better capture risk among PAH.

Methods: We used data from the Veterans Aging Cohort Study (VACS), a national electronic health records-based cohort that includes all individuals diagnosed with HIV receiving care within the Veterans Health Administration. We included all PAH (≥50 years of age) and followed them from 01/01/2009 through 12/31/2019. Observations consisted of one-year person-intervals and three-year person-intervals. Fragility fracture outcomes (at the spine, hip/femur, wrist/forearm, and shoulder/upper arm) were identified using validated ICD9 and ICD10 codes. From an initial pool of 27 candidate predictors (including HIV-specific variables) selected from the literature, clinical experience, and prior research, multivariable logistic regression chose 15 predictors that were subsequently reduced to a set of 10 based on statistical criteria and feedback from HIV providers. This feedback motivated two versions of each model that permit optional inclusion of race.

Results: The cohort included 32,842 individuals contributing a total of 223,607 person-years of data. **Table 1** shows the distribution of the 15 short-listed candidate predictors in the first year of follow-up. Over the follow up period, there were 2,355 incident fractures. The ten final predictors, with odds ratios from the one year model, included: age OR = 1.02 (95% CI 1.01 – 1.02), albumin OR = 0.7 (0.64 – 0.76), alcohol use ≥3 drinks per day OR = 1.19 (1.11 – 1.27), BMI OR = 0.96 (0.95 – 0.97), chronic medication count OR = 1.05 (1.05 – 1.06), COPD OR = 1.36 (1.23 – 1.50), fall in previous year OR =

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Distribution of the 15 short-listed candidate predictors in the first year of follow-up within the study cohort.

Predictors	Full Sample N=32842	With Fracture N=292	Without Fracture N=32550	Missing Observations (%)
Age, mean±SD[a]	57.7±7.0	58.8± 7.4	57.7±7.0	0
Female sex, n(%)[c]	960(2.9)	6(2.1)	954(2.9)	0
BMI (kg/m2), mean±SD[a]	26.3±5.4	25.3± 5.1	27.0±5.4	2617(8.0)
Nonwhite race, n(%)[a]	18161(55.3)	128(43.8)	18033(55.4)	23(<1.0)
Alcohol use, ≥3 drinks per day, n(%)[b]	2384(10.1)	32(13.1)	2352(10.1)	9219(28.1)
Fall in prior 12 months, n(%)[a]	822(2.5)	29(9.9)	793(2.4)	0
Fracture in prior 12 months, n(%)[a]	258(0.8)	44(15.1)	214(0.66)	0
Albumin g/dL, mean± SD [a]	4.0±0.5	3.9± 0.5	4.0± 0.5	3690(11.2)
Liver disease, n(%)[a]	8727(26.6)	133(45.6)	8594(26.4)	0
Diagnosis of COPD, n(%)[a]	4868(14.8)	91(31.2)	4777(14.7)	0
Diagnosis of CVD, n(%)[a]	2349(7.2)	43(14.7)	2306(7.1)	0
Diagnosis of OA, n(%)[a]	6472(19.7)	78(26.7)	6394(19.6)	0
Chronic med count, median[IQR][a]	9[6,13]	11[7,17]	9[6,13]	3944(12.0)
Anti-depressants, n(%)[a]	11405(34.7)	161(55.1)	11244(34.5)	0
Opioid prescription order, n(%)[a]	10535(32.1)	213(73.0)	10322(31.7)	0

Abbreviations: g = gram, dL = deciliter, BMI = body mass index, kg = kilogram, m = meter, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular disease, OA = osteoarthritis

[a] p<0.01; [b] p=0.12; [c] p=0.49

P-values derived from t-test for age, albumin, BMI, and chronic medication count, Fisher's exact test for female sex, chi-square test for all others

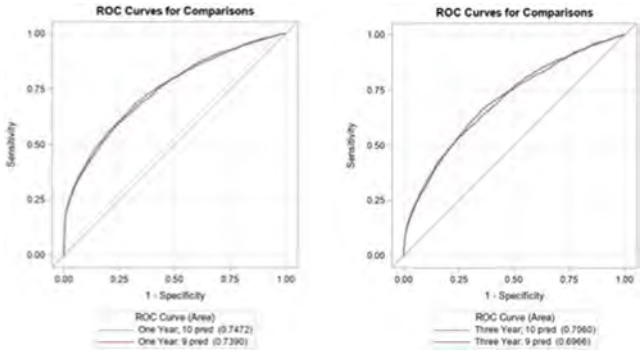


Figure 2. Receiver Operating Characteristic (ROC) Curves of Models for Risk of Fragility Fracture in One- (left) and Three-Year (right) Periods.

1.57 (1.35 – 1.82), female sex OR = 1.66 (1.33 – 2.08), fracture in previous year OR = 15.46 (13.45 – 17.77), and nonwhite race OR = 0.62 (0.57 – 0.68). The one-year and three-year models with race exhibited good discrimination, with areas under the curve (AUC) of 74.7% and 70.6%, respectively. For the models without race, the AUCs were 73.9% and 69.7% for the one- and three-year models. **Figure 1** presents the ROC curves for all four models; all four exhibited excellent calibration.

Conclusion: Based upon rigorous statistical analysis and provider input, we present a new risk prediction model for fragility fracture that is statistically robust and uniquely optimized for the care of PAH. Future studies will externally validate this model using datasets from outside the VA.

Disclosure: E. Hsieh: None; **T. Murphy**: None; **B. Tessier-Sherman**: None; **L. Leo-Summers**: None; **F. Kidwai-Khan**: None; **S. Fodeh**: None; **R. Wang**: None; **B. Gulanski**: None; **M. Yin**: None; **M. Skanderson**: None; **C. Brandt**: None; **A. Justice**: None; **J. Womack**: None.

Abstract Number: 2115

METHOFRACT, a methotrexate osteopathy multicentric binational cohort study.

François ROBIN[1], Roba Ghossan[2], Nadia Mehsen-Cetre[3], Louise Triquet[1], Guillaume LARID[4], Guillaume Coiffier[5], Marine Mina[6], Marie-Eva Pickering[7], Claire Barthe[8], Julien Paccou[9], Julien Herman[10], Emmanuel Massy[11], Isabelle Roitg[12], Martine Branquet[13], Julien Lasnier Siron[3], Manon Guillouard[14], Camille Desmonet Trousset[15], Aurore Aubrun[16], Bertrand Godfrin[17], Jean-Philippe Hauzeur[18], Emmanuel Chatelus[19], Eugénie Koumakis[2], Jean-Louis Legrand[20], Thierry

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Schaeverbeke[3], Alexia Leloix[1], Maeva Masson[21], Julia Nicolau[15], Charles Ghiringhelli[22], Marijke Decrock[12], Durel Cécile-Audrey[23], Béatrice Bouvard[24], Bernard Cortet[9], Charlotte Casadepax-Soulet[25], Olivier Malaise[6], Rose Marie Javier[26], Karine Briot[2] and Pascal Guggenbuhl[1], [1]Rennes University Hospital, Rennes, France, [2]APHP, Paris, France, [3]Bordeaux University Hospital, Bordeaux, France, [4]Poitiers University Hospital - Poitiers University - LITEC Laboratory UR 15560, Poitiers, France, [5]Dinan Hospital, Dinan, France, [6]Liege University Hospital, Liège, Belgium, [7]Clermon-Ferrand University Hospital, Clermont-Ferrand, France, [8]Clinique Tivoli Ducos, Bordeaux, France, [9]Lille University Hospital, Lille, France, [10]La Roche Sur Yon Hospital, La Roche-sur-Yon, France, [11]Lyon University Hospital, Lyon, France, [12]Perpignan Hospital, Perpignan, France, [13]Ploemeur Rheumatology Liberal Structure, Ploemeur, France, [14]Aurillac Hospital, Aurillac, France, [15]Dieppe Hospital, Dieppe, France, [16]Nice Rheumatology Liberal Stucture, Nice, France, [17]St Gaudens Rheumatology Liberal Structure, St Gaudens, France, [18]Liege University Hospital, Liege, Belgium, [19]Department of Rheumatology, University Hospital Strasbourg, France, Strasbourg, France, [20]Arras Hospital, Arras, France, [21]Toulouse University Hospital, Toulouse, France, [22]Pauillac Rheumatology Liberal Structure, Pauillac, France, [23]Saint Joseph Saint Luc Hospital, Lyon, France, [24]Angers University Hospital, Angers, France, [25]West Reunion Hospital, Saint Paul, France, [26]Strasbourg University Hospital, Strasbourg, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

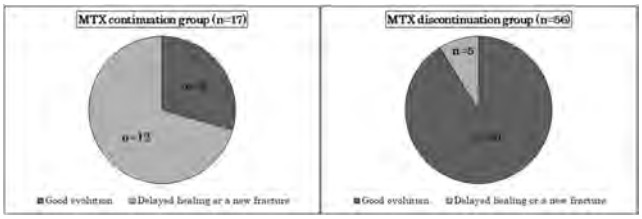
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Methotrexate-induced osteopathy is a rare condition. The clinical presentation is often typical, associating lower limb involvement with metaphyseal bone fractures/cracks, mainly of the tibia or foot bones. The main aim of this study was to identify the affected population and to better describe patients and fracture characteristics and possible risk factors leading to poor clinical evolution.

Methods: We conducted a multicenter retrospective study including all patients identified by a GRIO (osteoporosis research and information group, group of osteoporosis and bone disease specialists) member as a MTX-induced osteopathy. Were included all patients with suggestive clinical and/or imaging presentation, confirmed by a bone expert. Patients not already included and identified by national pharmacovigilance as being suggestive of methotrexate-induced osteopathy were also included, after analysis of the medical file by the principal investigator. The data collected included imaging features (characteristic, location and evolution of the bone lesions), clinical (search for classic causes and risk factors for bone fragility, treatment methods after diagnosis), results of bone mineral density (BMD) at diagnosis and during follow-up if available, biochemical (mainly phosphocalcic metabolism, kidney function).

Results: Between 2012 and 2024, we included a total of 92 patients, identified as affected by MTX-induced osteopathy. Population affected was mainly post-menopausal women (86/92, 93%) with seropositive RA (68/92, 74%), with previous history of major fracture in 22% of patients, and BMD osteoporosis at diagnosis in 56% of patients. The underlying rheumatism was classically considered as inactive or with low disease activity (93%). Prednisone was used in only 34 patients (37%) at diagnosis, with a mean dose of 8 mg (± 7) per day. Site of fracture was mainly on tibial metaphyseal region (88%) or foot bones (49%), with frequent multiple sites at diagnosis (76%) and with frequently repeated fractures in the patient's recent history (63%). Diagnosis was mainly done using MRI of painful site (84%), but bone scintigraphy was also used (41 patients, 45%) for general skeletal mapping. Management was the discontinuation of methotrexate (79%) with the addition of a



Comparison of evolution according MTX management. n=number

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Good evolution of fracture (n=57)	Delay of fracture healing or refracture (n=16)	p
General characteristics			
Age, mean ± SD	67 ± 10	65 ± 10	NS
BMI kg/m² mean ± SD	25 ± 4	24 ± 4	NS
T-Score Lumbar site mean ± SD	-1.7 ± 1.1	-1.5 ± 1.1	NS
T-Score Total Hip mean ± SD	-2.1 ± 0.9	-2.1 ± 0.8	NS
T-Score Femoral Neck mean ± SD	-2.3 ± 0.9	-2.3 ± 0.9	NS
Densitometric osteoporosis, n (%)	28 (49%)	9 (56%)	NS
Major Fracture medical history, n (%)	11 (19%)	4 (25%)	NS
Anti-osteoporotic treatment history, n (%)	26 (46%)	6 (38%)	NS
MTX treatment			
Duration at diagnosis in months, mean ± SD	120 ± 77	141 ± 81	NS
Dose at diagnosis (mg), mean ± SD	19,0 ± 6	17,5 ± 6	NS
Cumulate dose (g) at diagnosis, mean ± SD	8,6 ± 9,8	8,6 ± 5,7	NS
Oral way, n (%)	16 (28%)	3 (19%)	NS
Sub-cutaneous way, n (%)	41 (72%)	13 (81%)	NS
Corticosteroid treatment			
Corticosteroid use, n (%)	25 (44%)	3 (19%)	NS
Corticosteroid dose (mg), mean ± SD	1,6 ± 4,0	2,9 ± 4,5	NS
MTX-Induced osteopathy management			
MTX discontinuation, n (%)	52 (91%)	4 (25%)	p<0.001
Anti-osteoporotic treatment, n (%)	28 (49%)	12 (75%)	NS
Anti-resorptive treatment alone, n (%)	24 (42%)	8 (50%)	NS
Teriparatide alone, n (%)	3 (5%)	1 (6%)	NS
Sequential or concomitant combo therapy, n (%)	1 (2%)	3 (19%)	p<0.001

Comparison between good and poor evolution of fracture. N= number, SD = standard deviation.

complementary treatment in 51 patients (55%). In global population, evolution of fracture (decrease pain and fracture healing) was good in 77% of cases. The critical information was that evolution was good in 91% in case of MTX discontinuation against only 29% in case of MTX continuation (p< 0.001). If we compared patients with good evolution of fracture (n=57) and without good evolution (n=16), only main significant difference between group was MTX continuation (p< 0,001).

Conclusion: Methotrexate-induced osteopathy remains a rare condition but has to be known and searched, especially in cases of pain in the lower limbs of postmenopausal women, not explained by inflammatory activity of the underlying rheumatism. MRI of painful sites or bone scintigraphy appear to be the best choice for diagnosis. In the majority of cases, stopping methotrexate leads to rapid improvement of symptoms and above all avoids the risk of further fractures.

Disclosure: F. ROBIN: AbbVie/Abbott, 6, 12, invitations to conferences, Novartis, 12, invitations to conferences; **R. Ghossan**: None; **N. Mehsen-Cetre**: None; **L. Triquet**: None; **G. LARID**: AbbVie/Abbott, 6, Amgen, 12, Support for attending meetings, Eli Lilly, 12, Support for attending meetings; **G. Coiffier**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **M. Mina**: None; **M. Pickering**: None; **C. Barthe**: None; **J. Paccou**: None; **J. Herman**: None; **E. Massy**: AbbVie/Abbott, 2, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, Novartis, 2, 5, Pfizer, 2, Roche, 2, UCB, 2; **I. Roitg**: None; **M. Branquet**: None; **J. Lasnier Siron**: None; **M. Guillouard**: None; **C. Desmonet Trousset**: None; **A. Aubrun**: None; **B. Godfrin**: None; **J. Hauzeur**: None; **E. Chatelus**: None; **E. Koumakis**: None; **J. Legrand**: None; **T. Schaeverbeke**: None; **A. Leloix**: None; **M. Masson**: AbbVie/Abbott, 6, Amgen, 5, Eli Lilly, 2, Novartis, 5; **J. Nicolau**: None; **C. Ghiringhelli**: None; **M. Decrock**: None; **D. Cécile-Audrey**: None; **B. Bouvard**: None; **B. Cortet**: Alexion, 6, Amgen, 6, Besins, 6, Kyowa-Kirin, 6, Theramex, 6, UCB, 4, Viatris, 6; **C. Casadepax-Soulet**: None; **O. Malaise**: AbbVie/Abbott, 5, 6, 12, Support for attending meeting, Amgen, 6, Eli Lilly, 6, Pfizer, 6, UCB, 6; **R. Javier**: None; **K. Briot**: None; **P. Guggenbuhl**: Amgen, 6, Eli Lilly, 5, kyowa Kirin Pharma, 5.

Abstract Number: 2116

Romosozumab in Multiple Myeloma Patients at High Risk of Fracture

Giovanni Adami[1], Mariana Diz Lopes[2], Martina Tinelli[2], Angela Bonalumi[2], Ombretta Viapiana[2] and Maurizio Rossini[2], [1]University of Verona, Italy, Verona, Italy, [2]University of Verona, Verona, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 – Baseline Characteristics of the 8 patients with SMM (IgG subtype) that received romosozumab for 12 months

	Age	Sex	BMI (kg/m²)	Disease duration (years)	Smoking Status	Previous fracture	Lumbar Spine BMD (g/cm²) T-Score	Femoral Neck BMD (g/cm²) T-Score	Total Hip BMD (g/cm²) T-Score	M-protein (g/L)	Serum FLC ratio (K/λ)	Fractures during FU	Disease progression during FU	After ROMO
1	59	F	19.5	5	No	Yes (peripheric + vertebral)	0.858 -1.8	0.888 -2.6	0.782 -1.9	19.5 (λ)	0.5	No	No	ZOL
2	77	F	26.3	<1	No	Yes (vertebral)	0.810 -3	0.752 -1.9	0.833 -1.4	19 (λ)	0.1	No	No	DMAB
3	77	F	22.2	26	No	No	0.763 -3.8	0.695 -2.4	0.811 -1.6	19 (K)	34.9	No	No	DMAB
4	78	F	22.3	10	No	No	0.900 -3.2	0.826 -1.3	0.801 -1.5	14 (K)	101.9	No	No	DMAB
5	62	F	19.7	<1	No	No	0.650 -5	0.690 -2.4	0.736 -2.2	31 (K)	59.7	No	No	DMAB
6	51	F	21.6	16	Yes, actual	Yes (vertebral)	0.916 -2.2	0.798 -1.5	0.820 -1.5	28 (λ)	0.8	No	No	DMAB
7	71	F	30.9	1	Yes, actual	Yes (vertebral)	0.834 -2.9	0.851 -2	0.886 -1.1	26 (K)	13.8	No	No	DMAB
8	84	F	20.7	2	Yes, former	Yes (vertebral)	0.709 -3.8	0.740 -2	0.872 -1.1	37 (λ)	0.1	No	No	DMAB

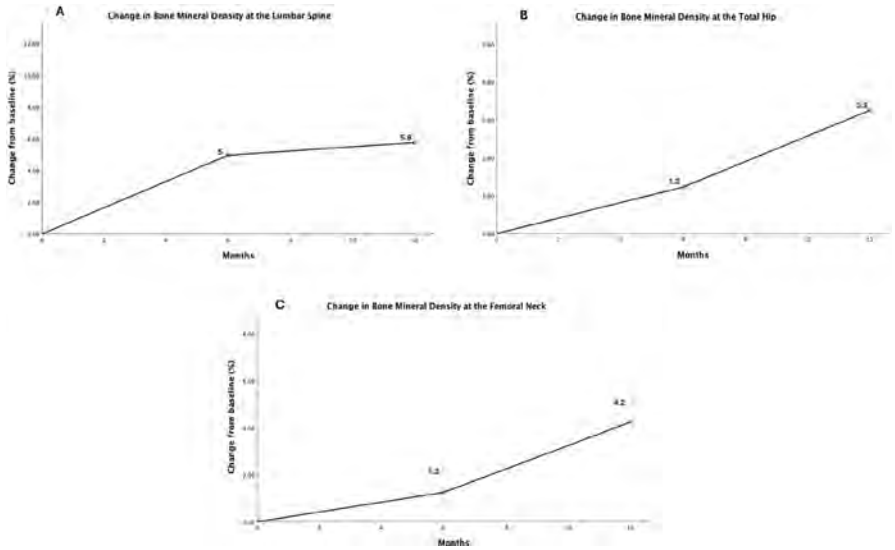
Footnote: BMI – body mass index; MM – multiple myeloma; BMD – bone mineral density; FLC – free light chains; FU – follow-up; ROMO – romosozumab; ZOL – zoledronic acid; DMAB – denosumab

Baseline characteristics of the study population

Background/Purpose: Bone damage is a key feature of multiple myeloma (MM). Romosozumab (ROMO), a sclerostin inhibitor, has dual anabolic and antiresorptive properties and may offer benefit in this group with high fracture risk.

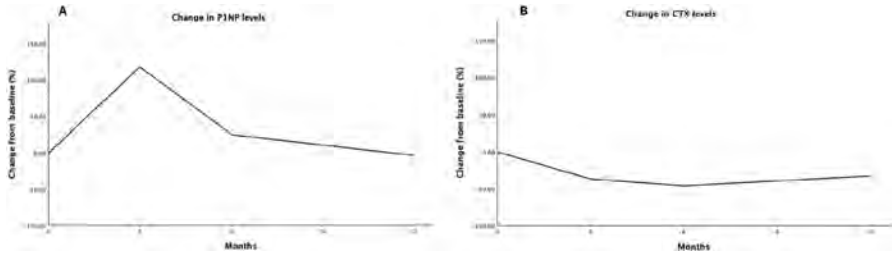
Methods: We did a 12-month prospective observational study in patients with multiple myeloma (MM) and osteoporosis treated with ROMO. Inclusion criteria were: (1) diagnosis of MM according to the International Myeloma Working Group (IMWG) definition, (2) absence of CRAB disease, (3) treatment with ROMO deemed necessary by the treating physician. The primary outcome was bone mineral density (BMD) change at 12 months, other outcomes were bone turnover markers (BTMs) change, high-resolution peripheral computed tomography (HR-pQCT) parameters and MM related parameters (M-protein, immunoglobulins free light chains, β2-microglobulin). We used mixed model for repeated measures analyses with random intercepts by participant with time as independent variables with an unstructured correlation matrix.

Results: Eight female patients with MM (mean age 67.4±9.9 years) completed 12 months of ROMO (**table 1**). A significant BMD increase was observed at all evaluated sites over the study period (**figure 1**). Lumbar spine BMD increased by 5.8% (7.7) at 12 months (p=0.048). Femoral neck increased by 4.2% (3.9) (p=0.020) and total hip by 3.3% (2.4) (p=0.002). Bone-alkaline phosphatase (B-ALP) showed a significant decrease by month 12 (13.5 (9.3-17) to 9 (6.12) ng/mL, p=0.022). P1NP rose sharply by month 3, from 60 (49.5-70.3) to 98 (77-115.5) ng/mL (mean change of 117.8%), but then declined, approaching baseline by month 12 (p=0.006). Conversely, CTX showed a tendency for reduction at all time points (p=0.060), with a maximal decrease at the end of the 12 months (-53.6%, **figure 2**). No significant changes occurred in immunoglobulins, M-protein, or light chains. β2-microglobulin showed a downward trend (from 2.35 to 2.1mg/L at month 12, p=0.042), though overall changes were not significant (p=0.092). HR-pQCT parameters remained stable throughout



Percentage Change from Baseline in Bone Mineral Density at the lumbar spine (A), total hip (B) and femoral neck (C)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Percentage Change from Baseline in P1NP levels (A) and CTX levels (B)

the study, revealing no changes in volumetric BMD, microarchitecure or biomechanical properties of the bone assessed with this method.

Conclusion: In this exploratory study of patients with MM and osteoporosis, ROMO significantly improved BMD and modulated BTMs, without any evidence of disease progression over the 12-month period. These findings support ROMO as a potential bone-targeted therapy in patients with osteoporosis and plasma cell disorders.

Disclosure: G. Adami: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Eli Lilly, 2, 6, UCB, 2, 6; **M. Diz Lopes**: None; **M. Tinelli**: None; **A. Bonalumi**: None; **O. Viapiana**: None; **M. Rossini**: None.

Abstract Number: 2117

Denosumab Discontinuation and Switching in Glucocorticoid-Induced Osteoporosis: A Multi-site Randomized Clinical Trial

Giovanni Adami[1], Kenneth Saag[2], Gary Cutter[3], Rahima Begum[3], Elizabeth Dye[4], Phillip Foster[5], Camilla Benini[6], Carmela Dartizio[6], Davide Gatti[6] and Maria I. (\"Maio\") Danila[7], [1]University of Verona, Italy, Verona, Italy, [2]The University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama at Birmingham, Birmingham, [4]UAB, Birmingham, AL, [5]University of Alabama at Birmingham, Birmingham, AL, [6]University of Verona, Verona, Italy, [7]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Prompt anti-resorptive treatment with bisphosphonates after denosumab discontinuation is generally recommended. Glucocorticoid users may not require longer term denosumab and are at greater fracture risk, yet the timing and route of bisphosphonate (BP) administration after denosumab (DMAB) discontinuation in glucocorticoid users has not been studied. A strategy of delayed administration of a pulse (IV) BP could be of greater benefit than other strategies.

Objective: To test different exit strategies in patients on chronic glucocorticoids who discontinued denosumab

Methods: We conducted an open-label, randomized, parallel group, multicenter, clinical trial in which participants with ≥2 doses of DMAB 60 mg were assigned 1:1:1 to weekly oral alendronate for 6 months (70 mg; started 6 months after last DMAB dose, ALN group) OR 1 dose of IV zoledronic acid (5 mg; 6 months after last DMAB dose, EARLY ZA) OR 1 dose of IV zoledronic acid (5 mg; 9 months after last DMAB dose, LATE ZA). Participants were recruited at 2 sites. Inclusion criteria: post-menopausal women and men ≥50 years; on prednisone ≥7.5 mg /day; baseline BMD T-score of ≤ -1.0 at the

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of participants by randomization assignment

Characteristics	Alendronate (70 mg, 6 months after the last denosumab dose) n=15	Early ZA (5 mg, 6 months after the last denosumab dose) n=14	Late ZA (5 mg, 9 months after last denosumab dose) n=16
Age in yrs., Mean (SD)	65.4 (10.56)	66.8 (11.81)	58.3 (14.91)*
Sex, Female, N (%)"	11 (73.33)	9 (64.29)	11 (73.33)
Enrollment site, N (%)			
Birmingham (AL, USA)	7 (46.67)	6 (42.86)	7 (43.75)
Verona (Italy)	8 (53.33)	8 (57.14)	9 (56.25)
Race, N (%)			
African American/Black	1 (6.67)	1 (7.14)	5 (31.25)
Asian	1 (6.67)	0 (0.00)	1 (6.25)
White	12 (80.00)	13 (92.86)	10 (62.50)
Other	1 (6.67)	0 (0.00)	0 (0.00)
Ethnicity, N (%)			
Hispanic/Latino	1 (6.67)	1 (7.14)	0 (0.00)
Not Hispanic/Latino	14 (93.33)	13 (92.86)	16 (100.00)
Rheumatic Disease, N (%)	15 (100)	14(100)	16 (100)
BMD lumbar-spine T-score at Randomization, Mean (SD)	-1.33 (1.51)	-1.17 (0.98)	-0.83 (0.94)
BMD Total Hip T-score at Randomization, Mean (SD)[a]	-1.59 (0.91)	-1.19 (1.12)	-0.57 (0.85)
BMD femoral neck T-score at Randomization, Mean (SD)[b]	-2.06 (0.67)	-1.71 (1.00)	-1.02 (1.03)
CTX at baseline (ng/mL), Mean (SD)[c]	0.07 (0.06)	0.05 (0.05)	0.11 (0.16)
P1NP at baseline (ng/mL), Mean (SD)[f]	31.04 (20.66)	23.24 (11.64)	45.35 (55.92)

** missing for 1 individual, [a]missing for 2 individuals, [b]missing for 2 individuals, [c]missing for 8 individuals. [f]missing for 9 individuals

lumbar spine, total hip, or femoral neck. Exclusion criteria: no past BPs, > 24 months (> 4 injections) of prior DMAB treatment. Primary outcome was difference in CTX between randomization (baseline) and 6 months post randomization (+6M) between groups. Secondary outcomes were markers changes at follow-up times and bone mineral density (BMD) changes. We used repeated measures models with random intercepts by participant, time, and time x treatment as independent variables with an unstructured correlation matrix.

Results: A total of 45 patients were randomized (N=15 to ALN, N=14 to EARLY ZA, N=16 to LATE ZA). Baseline characteristics are reported in **Table 1**. Median glucocorticoid dose at baseline (DMAB discontinuation) was 5.0 mg/day (IQR 5.0-10.0). Groups were well balanced except for BMD at femoral neck and total hip. **Figure 1** shows the bone turnover markers (**Figure 1**) data by group at baseline, +3M and +6M. **Figure 2** shows the BMD data for groups at +6M. At 6 months, we found a non-significant trend for change in CTX in the LATE ZA compared to ALN (p=0.07), but there was no difference in CTX between the LATE ZA and EARLY ZA groups (p=0.12). However, at 3 month there was a significant difference in change in CTX between LATE ZA vs ALN (p=0.0182) but not between LATE ZA and EARLY ZA (p=0.757). For lumbar spine BMD, at 6 months, we observed a non-significant trend between LATE ZA and EARLY ZA (p=0.059), but there was no statistically significant difference in the BMD between LATE ZA and ALN (p=0.28). At 12 months, there was a statistically significant difference in BMD between LATE ZA and ALN (p=0.04), but not between LATE ZA and EARLY ZA (p=0.11).

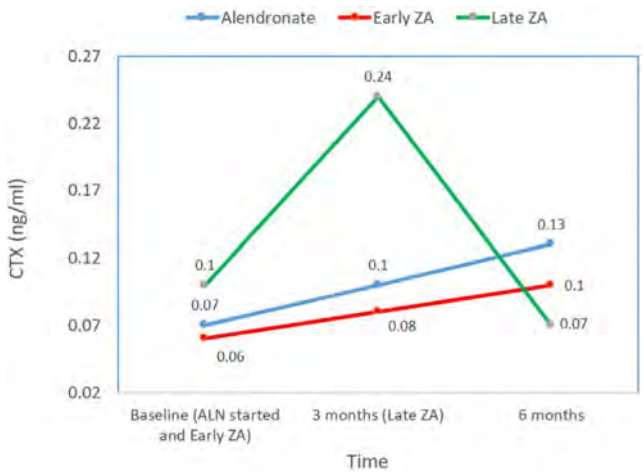


Figure 1. CTX changes over the study periodchanges over the study period

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Bone mineral density (BMD) in gm/cm2 at lumbar spine at baseline, 3-, 6- and 12 months

Conclusion: Among those receiving delayed ZA, an escape in bone turnover at 3 months could create a window for fractures. However, it could be offset by greater BMD gain at 6 months, which, however, was not sustained at12 months, albeit not significantly greater than the other two groups. Larger studies are needed to assess relative safety and benefit of different post-DMAB strategies among this higher risk population.

Disclosure: G. Adami: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Eli Lilly, 2, 6, UCB, 2, 6; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2; **G. Cutter**: Consulting or Advisory BoardsAlexion, Antisense Therapeutics/Percheron, Avotres, Biogen, Clene Nanomedicine, Clinical Trial Solutions LLC, Endra Lif, 1, 2, Data and Safety Monitoring BoardsApplied Therapeutics, AI therapeutics, AMO Pharma, Argenx, Astra-Zeneca, Avexis Pharmaceuticals, Bristol Meyers Squ, 2, Pythagoras, Inc., 4, 8; **R. Begum**: None; **E. Dye**: None; **P. Foster**: None; **C. Benini**: None; **C. Dartizio**: None; **D. Gatti**: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5.

Abstract Number: 2118

Risks of Fracture in Current and Previous Anticonvulsant Users, An Observational Study

Grace Hyeyeon Lee[1], Hamzah Amin[2] and marwan Bukhari[1], [1]University Hospitals of Morecambe bay NHS foundation trust, Lancaster, United Kingdom, [2]Lancaster University, Lancaster, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anticonvulsants are commonly used to manage neurological and psychiatric disorders such as epilepsy, migraines and bipolar disorder. These medications are often prescribed long-term, and in some cases, lifelong. Prolonged anticonvulsant use has been associated with an increased risk of fractures in adults and lower bone mineral density in children, likely due to their effect on bone metabolism. This study aimed to investigate the association between fracture risk and anticonvulsant use in each group of patients who are currently taking anticonvulsants with those who have previously used them.

Methods: This retrospective study was conducted at a district general hospital in the northwest of England, from July 2004 to February 2024. There were 1,368 patients, with 332 patients who were previous anticonvulsant users and 1,036 patients who were current anticonvulsant users. In both groups, the predictors of fracture risk were examined, including age, gender,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

height, weight, body mass index (BMI), percentage total body fat, current smoker, current alcohol drinker, current steroid use, previous fractures and bone mineral density (BMD) values at the L1-L4 vertebrae, right and left femur neck, and right and left femur total. These factors were compared between the two groups of current and previous anticonvulsant users using independent t-tests for continuous factors and chi-square tests for categorical factors. A logistic regression model was used to assess the relationship between anticonvulsant use (current and previous users) and fracture risk (history of fracture), taking into account the predictors of fracture.

Results: The mean age was 65, and 87% were female in both groups. Initially the predictors of fracture were compared between current and previous anticonvulsant users; right and left femur neck and total BMD were found to be significantly lower in current anticonvulsant users ($P< 0.05$). In the first logistic regression analysis, the fracture risk was assessed in previous and current anticonvulsant users, taking into account the predictors of fracture. Current anticonvulsant users were associated with increased odds of fracture (OR = 1.48, 95% CI: 1.06–2.07, p = 0.020). Another independent factor, percentage total body fat, was also found to be significantly associated with fracture (p = 0.007). Second logistic regression analysis examined the interaction between anticonvulsant use and percentage body fat, which was not found to be significant (p = 0.288). This suggests that percentage body fat did not significantly change the association between anticonvulsant use and fracture risk.

Conclusion: In conclusion, the results show current anticonvulsant use is associated with an increased fracture risk, compared to previous users. In addition, the current anticonvulsant users were found to have lower femur neck and femur total BMD, which is likely to have an increased risk for major fractures. Percentage total body fat was an independent factor which was found to be a significant predictor of fracture risk.

Disclosure: G. Lee: None; **H. Amin**: None; **m. Bukhari**: None.

Abstract Number: 2119

Fracture rates in 6475 individuals with osteogenesis imperfecta stratified by age, sex and clinical severity

Winnie Liu[1], **Jeffrey Curtis**[2], Lars Folkestad[3], Emily Holladay[4], Jingyi zhang[2], Shanette Daigle[5], Ye Liu[2], Fenglong Xie[6] and Eric Orwoll[1], [1]Oregon Health and Science University, Portland, OR, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Southern Denmark, Odense, Denmark, Odense, Denmark, [4]Foundation for Advancing Science Technology Education and Research, Hoover, AL, [5]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [6]The University of Alabama at Birmingham, Birmingham, AL

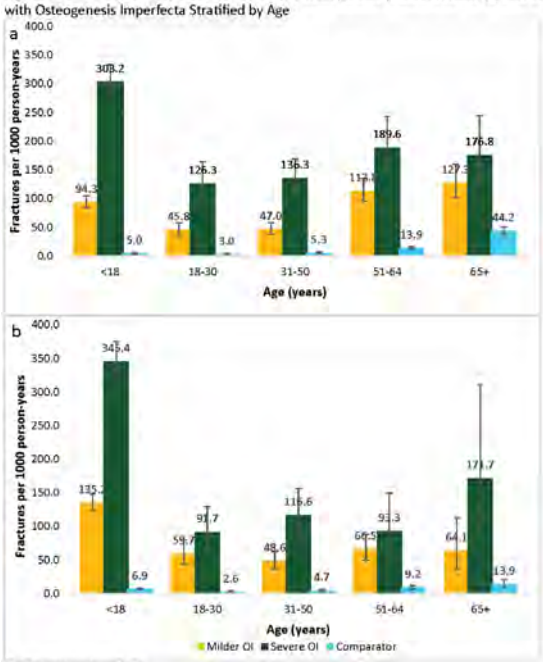
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteogenesis imperfecta (OI) is a rare genetic disorder characterized by bone fragility caused by mutations related to type 1 collagen biosynthesis. Fractures are a cardinal manifestation of OI, but fracture incidence across the lifespan is poorly understood. We used a large US-based cohort to describe fracture rates in individuals living with OI, stratified by clinical severity.

Methods: Individuals with OI were identified by ICD-9 (756.5) and/or ICD-10 (O78.0) diagnosis codes among ~30 million people included in MarketScan claims data (2006-2022) and a 5% random sample of US Medicare Fee-for-Service

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Follow-Up Fracture Incidence Rates per 1000 patient-years in Female (a) and Male (b) Patients with Osteogenesis Imperfecta Stratified by Age



OI: Osteogenesis Imperfecta.
Note: Vertical error bars depict the 95% confidence intervals (CIs).

data (2006-2021). Severe OI was defined by long-term wheelchair use, identified using durable medical equipment (DME) claims. Incident fractures were identified using an adaptation of a previously validated algorithm with high specificity.

Results: We included 6,475 individuals with OI. Median age was 21.0 years (IQR: 8.0, 43.0) and severe OI was present in 20%. A reference cohort (N=32,375) was matched 5:1 within each data source to those with OI by age, sex, race, index calendar year, and baseline length of continuous coverage. Median follow-up time was 2.1 years (IQR: 0.9, 4.5) in OI and 2.0 years (IQR: 0.8, 4.3) in the comparator group. In OI, the overall fracture rate was 129.6 (95% CI: 124.7, 134.6) per 1000 person-years (py) vs 8.0 (95% CI: 7.4, 8.6) in the reference cohort (incidence rate ratio (IRR): 16.2, 95% CI: 15.0, 17.2). Across all ages, the fracture rates were higher in severe vs milder OI (IRR: 238.6, 95% CI: 226.1, 251.7) vs 87.8 (95% CI: 83.2, 92.8) per 1000py (Figure 1). In both sexes, fracture rates were highest in childhood and lowest in early adulthood. In women with milder OI, fracture rates were highest at age 51 years and older, which coincides with the typical age range of menopause. In women with severe OI, the rates of fracture also increased in those aged 51 years and older. In men with milder OI fracture rates were stable with increased age, but were higher in older men with severe OI.

Conclusion: We report fracture rates stratified by sex, age and clinical severity in one of the largest datasets ever assembled of US individuals living with osteogenesis imperfecta. These data provide unique and necessary information for the clinical care of individuals living with OI and for the design of trials for new therapeutics.

Disclosure: W. Liu: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **L. Folkestad**: None; **E. Holladay**: None; **J. zhang**: None; **S. Daigle**: None; **Y. Liu**: Amgen, 5; **F. Xie**: None; **E. Orwoll**: amgen, 2, Angitia, 2, AstraZeneca, 2, bayer, 2, Biocon, 2, radius, 2, Ultragenyx, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2120

Analyzing Gender and Racial Disparities in Paget's Disease of Bone: A Large-scale Observational Study

Kinga Grzybowski[1], Ahmer Khan[2] and Arthur Lau[3], [1]Jefferson Einstein Montgomery Hospital, Maspeth, NY, [2]Jefferson Einstein Philadelphia Hospital, Philadelphia, [3]Jefferson Einstein Hospital, Maple Glen, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Osteitis deformans, commonly referred to as Paget's Disease of the Bone (PDB), affects adults over the age of 55, mainly of European descent and is characterized by accelerated turnover of bone with abnormalities to remodeling and overgrowth involving multiple regions of the body. Studies have shown a slight male predominance, although others have found equal distributions between genders. Most PDB cases are asymptomatic, however some may develop complications such as arthritis, fractures and diffuse pain. An observational, retrospective cohort study using the TriNetX database was conducted which uses electronic health records from over 140 global collaborative networks to explore both racial and gender differences between patients with PDB.

Methods: Patients 18 years and older were included using ICD-10 code M88 for the diagnosis of PDB. Two cohorts were studied: males and females above the age of 18. The index event was defined as the first appearance of the diagnosis of PDB. Propensity matching included age, race/ethnicity, hypertension, obesity, diabetes, tobacco use, acute myocardial infarction, cerebral infarction, hyperlipidemia and medications commonly used in the treatment of PDB. Outcomes evaluated included mortality, chronic pain syndrome, heart failure, hearing loss, osteosarcoma, osteoporosis, fractures, chronic kidney disease, anxiety, depression and OA. Those who experienced any of the above outcomes prior to the index event were excluded from the study and a risk/risk ratio calculation was measured.

Results: The dataset included 10,972 females and 11,904 males. After propensity matching a total of 4,862 people were excluded, which left 9,007 in each group. The average age after matching was 70.7 in the female group, and 71 in the male group respectively. Most patients were not Hispanic or Latino and were mostly White or of unknown ethnicity. Analysis of the outcomes showed a statistically significant difference in chronic pain (RR 1.18, 95% CI 1.09-1.278, P< 0.0001), osteoporosis (RR 2.44, 95% CI 2.188-2.721, P< 0.0001), anxiety (RR 1.62, 95% CI 1.464-1.794, P< 0.0001), depression (RR 1.49, 95% CI 1.336-1.671, P< 0.0001) and OA (RR 1.295, 95% CI 1.202-1.395, P< 0.0001) in females. Additionally, heart failure

Table 1: Baseline Characteristics of Both Cohorts Before (Left) and After (Right) Propensity Matching

Characteristics	Males	Females	p-value	Males	Females	p-value
Demographics	Before Matching			After Matching		
Age at Index; mean ± SD	71.5 ± 13.8	70.4 ± 14.7	<0.0001	70.9 ± 14.3	70.7 ± 14.5	0.4366
Ethnicity						
Not Hispanic/Latino	60.1%	61.3%	0.0427	60.5%	60.8%	0.6473
Hispanic/Latino	3.3%	4.2%	0.0006	3.8%	3.7%	0.9062
Unknown Ethnicity	36.7%	34.4%	0.0006	35.8%	35.4%	0.6744
Race						
White	57.5%	57.6%	0.3135	57.7%	57.5%	0.8094
Unknown Race	17.0%	16.5%	0.0013	17.0%	16.9%	0.7506
Black/African American	20.5%	20.6%	0.9556	20.2%	20.4%	0.6700
Asian	2.3%	2.3%	0.8021	2.2%	2.3%	0.6526

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Differences in the Outcomes of Both Cohorts

Outcomes		Males (9,007)	Females (9,007)	RR (95% CI), P-value
Mortality	*n* after matching	365	317	RR 0.87 (95% CI 0.751-1.009)
	Patients with outcome (%)	4.1%	3.6%	P 0.0649
Chronic Pain	*n* after matching	974	1,126	RR 1.18 (95% CI 1.09-1.278)
	Patients with outcome (%)	12.6%	14.8%	P<0.0001
Heart Failure	*n* after matching	759	662	RR 0.864 (95% CI 0.782-0.954)
	Patients with outcome (%)	9.6%	8.3%	P 0.0038
Hearing Loss	*n* after matching	419	440	RR 1.042 (95% CI 0.915-1.187)
	Patients with outcome (%)	5.0%	5.2%	P 0.5359
Osteosarcoma	*n* after matching	28	26	RR 0.927 (95% CI 0.544-1.58)
	Patients with outcome (%)	0.31%	0.29%	P 0.7808
Osteoporosis	*n* after matching	440	931	RR 2.44 (95% CI 2.188-2.721)
	Patients with outcome (%)	5.2%	12.7%	P<0.0001
Fractures	*n* after matching	137	150	RR 1.102 (95% CI 0.876-1.386)
	Patients with outcome (%)	1.6%	1.7%	P 0.4086
CKD	*n* after matching	776	737	RR 0.9 (95% CI 0.818-0.991)
	Patients with outcome (%)	10.5%	9.4%	P 0.0315
Anxiety	*n* after matching	569	846	RR 1.62 (95% CI 1.464-1.794)
	Patients with outcome (%)	7.0%	11.4%	P<0.0001
Depression	*n* after matching	489	680	RR 1.49 (95% CI 1.336-1.671)
	Patients with outcome (%)	6.0%	8.9%	P<0.0001
Osteoarthritis	*n* after matching	1,049	1,230	RR 1.295 (95% CI 1.202-1.395)
	Patients with outcome (%)	16.0%	20.7%	P<0.0001

(RR 0.864, 95% CI 0.782-0.954, P 0.0038) and chronic kidney disease (RR 0.9, 95% CI 0.818-0.991, P 0.0315) were found to be statistically significant in males. There was no difference in the incidence of mortality, hearing loss, osteosarcoma or fractures between the two cohorts.

Conclusion: The findings demonstrated females with PDB are at a higher risk for chronic pain, osteoporosis, anxiety, depression and OA, whereas men are at higher risk for heart failure and chronic kidney disease. Most participants in this study were non-Hispanic and White, consistent with previous demographic data. However, there was also significant representation from Black/African American and Asian patients. This study signifies that racial and gender differences exist in patients with PDB and more research needs to be conducted to further explain these findings and to potentially identify any confounding or causative variables which may have influenced the observed findings.

Disclosure: K. Grzybowski: None; **A. Khan**: None; **A. Lau**: None.

Abstract Number: 2121

Prevention of Bone Mass Loss Associated With Aromatase Inhibitors in Breast Cancer. A Study in Real-World Clinical Practice.

Lucía Paz Liñeira[1], Beatriz Villapún Burgoa[1], Isabel Castrejón Fernández[2], José María álvaro-Gracia álvaro[3], Teresa González Hernández[1], Sara López Tarruella[1] and Yolanda Jerez gilarranz[1], [1]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [2]Department of Rheumatology. Hospital General Universitario Gregorio Marañon. IiSGM. Universidad Complutense Madrid, Madrid, Spain, [3]Department of Rheumatology, Hospital General Universitario

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain. Department of Medicine, Complutense University, Madrid, Spain., Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Treatment with aromatase inhibitors (AIs) in patients with breast cancer is associated with accelerated bone mineral density (BMD) loss, leading to an increased risk of fracture, even in patients with BMD levels in the osteopenic range. In this context, treatment algorithms with higher BMD thresholds (T-score ≤ -2.0) than general population recommendations have been proposed. However, the implementation of these recommendations in clinical practice has been poorly evaluated.

Methods: Prospective observational study. Postmenopausal women with breast cancer receiving AIs who initiated antiresorptive therapy between October 2021 and April 2025 were included. Demographic, laboratory, and bone densitometry data (baseline and at 18 months) were collected from electronic medical records. Two groups were established based on

Age (mean ± SD)	66.2 ± 9.7
BMI (mean ± SD)	26.3 ± 7.0
Age at cancer diagnosis (mean ± SD)	60.8 ± 11.1
Smoker, n (%)	25 (22.3)
Previous fractures, n (%)	9 (8.0)
Parental hip fracture, n (%)	17 (15.1)
Type of AI Letrozole (%)	93 (83.0)
Antiresorptive treatment	
Alendronate n (%)	88 (78.5)
Risedronate n (%)	2 (1.7)
Zoledronic acid n (%)	14 (12.5)
Denosumab n (%)	8 (7.1)
Time in AI before antiresorptive therapy	
≤ 6 months n (%)	43 (38.3)
> 6 months n (%)	69 (61.6)
BMD T-score	
≤-2,0 and > -2,5 n (%)	17 (15.1)
≤ -2.5 n (%)	95 (84.8)
Median baseline T-score lumbar spine (p50, p25-p75)	-2.6 (-3, -2.2)
Median baseline T-score femoral neck (p50, p25-p75)	-2.05 (-2.7, -1.5)
Median T-score at 18 months lumbar spine (p50, p25-p75)	-2.2 (-2.7, -1.85)
Median T-score at 18 months femoral neck (p50, p25-p75)	-1.8 (-2.4, -1.2)
Percentage BMD gain at 18 months lumbar spine (p50, p25-p75)	3.95 (1.83, 8.54)
≤ 6 months	3.78 (1.67, 8.21)
> 6 months	4.49 (1.87, 8.79)
≤-2,0 and > -2,5	5.85 (2.79, 8.91)
≤ -2.5	3.95(1.54, 8.54)
Percentage BMD gain at 18 months femoral neck (p50, p25-p75)	3.21 (-1.01, 8.23)
≤ 6 months	3.77 (-0.5, 7.73)
> 6 months	2.88 (-1.1, 8.64)
≤-2,0 and > -2,5	5.67 (0, 16.5)
≤ -2.5	3.11 (-1.13, 7.77)
Fractures during treatment, n (site)	1 (hip)

Patients characteristics.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

T-score at initiation of antiresorptive therapy: T-score ≤ -2.0 and > -2.5, and T-score ≤ -2.5. Comparisons between groups were performed using the Mann-Whitney test (for two variables) or the Kruskal-Wallis test (for three or more variables).

Results: A total of 220 women met inclusion criteria by April 2025; 129 completed the 18-month follow-up, with 17 excluded due to discontinuation of antiresorptive therapy before 18 months. Mean age was 66.2 ± 9.7 years; 88 (78.5%) were treated with alendronate. 38.3% had been on AIs for less than 6 months before initiating antiresorptive therapy. 84.8% started therapy with a T-score ≤ -2.5 and 15.1% with a T-score ≤ -2.0 and > -2.5. At 18 months, the median percentage increase in BMD at the lumbar spine (LS) was 3.9% (1.8; 8.5), and at the femoral neck (FN) 3.2% (-1.0; 8.2). BMD gain was higher in the group initiating antiresorptive treatment at T-score ≤ -2.0 and > -2.5 compared to the ≤ -2.5 group, both at LS and FN (5.85% vs. 3.95%, p=0.31 at LS; and 5.67% vs. 3.11%, p=0.12 at FN). No statistically significant differences in BMD gain were found based on AI exposure duration (< or > 6 months) prior to antiresorptive therapy. Similarly, no significant differences were observed based on osteoporosis risk factors or the type of antiresorptive agent used.

Conclusion: Our findings suggest a greater increase in BMD among patients who begin antiresorptive therapy at a T-score of ≤ -2.0 compared to those who start at the general population threshold of ≤ -2.5. Initiating antiresorptive therapy in AI-treated patients is recommended regardless of the duration of AI use, as it does not appear to significantly affect BMD gain.

Disclosure: L. Paz Liñeira: None; **B. Villapún Burgoa**: None; **I. Castrejón Fernández**: None; **J. álvaro-Gracia álvaro**: None; **T. González Hernández**: None; **S. López Tarruella**: None; **Y. Jerez gilarranz**: None.

Abstract Number: 2122

Safety and Efficacy of Romosozumab in the Treatment of Patients with High-Risk Fracture Osteoporosis in Clinical Practice: Experience from a Tertiary University Hospital in Spain

Maryia Nikitsina[1], Cristina Valero[2], Miren Uriarte Ecenarro[3], Ana M Ortiz[3], María Ahijón Lana[3], Irene Llorente[3], Marina Dueñas-Ochoa[4], Juan C Saez[5], EVA GLORIA TOMERO MURIEL[6], Esther Vicente-Rabaneda[6], Isidoro Gonzalez-Alvaro[7], Rosario Garcia Vicuña[6] and Santos Castañeda[8], [1]University Hospital La Princesa, Madrid, Madrid, Madrid, Spain, [2]Hospital de la Princesa, Madrid, Spain, [3]Hospital Universitario La Princesa, Madrid, Spain, [4]Hospital La Princesa, Madrid, Spain, [5]Hospital Universitario La Princesa, Madrid, Madrid, Spain, [6]Hospital Universitario de la Princesa, Madrid, Spain, [7]Department of Rheumatology, Hospital Universitario La Princesa, IIS, Madrid Spain, Madrid, Spain, [8]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Romosozumab (RSZ) is a dual osteoanabolic agent that stimulates bone formation and reduces bone resorption, emerging as a promising option for treating osteoporosis (OP) in patients at very high fracture risk.

This study aims to analyze the safety and efficacy of RSZ treatment in patients with severe OP under real-world clinical conditions.

Methods: This is a single-center, ambispective, and observational study. Patients who initiated RSZ treatment between December 2022 and August 2024 were included, with prospective follow-up until March 2025. Data were collected from

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the population treated with romosozumab.

Characteristics	N = 68 patients (67 women)	
Age at initiation, mean ± SD	71.3 ± 7.5	
Patients with CVRF, n (%):	45 (66.1)	
1 CVRF / ≥2 CVRF, n (%)	25 (36.7) / 20 (29.4)	
Osteoporosis risk factors:		
Smoker, n (%)	15 (22.0)	
Early menopause (n = 67 women), n (%)	15 (22.1)	
Family history of hip fracture, n (%)	8 (11.7)	
Hyperparathyroidism, n (%)	4 (5.8)	
Hypothyroidism, n (%)	16 (23.5)	
Chronic lung disease*, n (%)	7 (10.3)	
Rheumatic or autoimmune diseases, n (%)	10 (14.7)	
Treatment with OP-inducing drugs, n (%)	30 (44.1)	
Previous history of fractures:		
Vertebral fractures, n (%)	53 (77.0)	
Hip fractures, n (%)	6 (9.1)	
Other osteoporotic fractures**, n (%)	15 (22.0)	
Prior osteoporosis treatments:	54 (79.4)	
Antiresorptives, n (%)	51 (75.0)	
Bisphosphonates (oral or IV), n (%)	48 (70.6)	
Denosumab, n (%)	22 (32.3)	
Teriparatide, n (%)	21 (30.9)	
Romosozumab treatment		
Completed (12 doses), n (%)	38 (55.9)	
Active (<12 doses), n (%)	24 (35.3)	
Discontinuation, n (%)	9 (8.8)	
Number of total AEs, n (%)	12 (17.6) in 11 patients (16.1)	
Type of AEs	2 CV events, 5 skin reactions, 3 myalgia, 1 headache	
Discontinuation due to AEs, n (%)	6 (8.8)	
Dual x-ray densitometry and bone markers	**Baseline**	**12 months**
Femoral Neck T-score, mean ± SD (n=34)	-2.70 ± 0.9	-2.72 ± 0.8
Lumbar Spine T-score, mean ± SD (n=25)	-3.48 ± 1.17	-2.66 ± 1.06
TBS, mean ± SD (n=19)	1.180 ± 0.106	1.208 ± 0.099
Calcium (mg/dL), mean ± SD (n=35)	9.32±0.54	9.21±0.36
Alkaline Phosphatase, mean ± SD (U/L) (n=33)	89±27	83±30
PTH (pg/mL), mean ± SD (n=18)	81.5±28	82±29
Osteocalcin (ng/mL), mean ± SD (n=8)	19.9±7	29.2±11
CTX (ng/mL), mean ± SD (n=8)	0.397±0.26	0.148±0.03

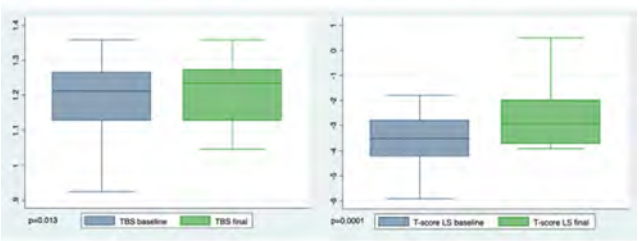
*Chronic lung disease refers to patients with COPD, chronic bronchiectasis, and asthma.
**Including radius and humerus.
Abbreviations: AEs: adverse events; BMD: bone mineral density; CTX: C-terminal telopeptide of type 1 collagen; CV: cardiovascular; COPD: chronic obstructive pulmonary disease; CVRF: cardiovascular risk factors; OP: osteoporosis; PTH: parathyroid hormone; SD: standard deviation; TBS: trabecular bone score.

electronic medical records, including demographic information, OP-related data, laboratory results (bone remodeling markers [BRM]), bone mineral density (BMD) of the lumbar spine (LS) and femoral neck (FN) measured by dual x-ray densitometry (DXA) (Hologic Horizon®), and Trabecular Bone Score (TBS) at LS (Medimaps®). Data related to RSZ use, such as adverse events (AEs) and clinical fractures, were also registered. Changes in BRM and BMD from baseline to the end of follow-up were analyzed, and a bivariate analysis was conducted to assess factors associated with higher BMD gain in LS.

Results: Sixty-eight patients (Table 1) were included, with a marked prevalence of vertebral fractures (VF) (77.9%). Cardiovascular risk factors (CVRF) were present in 66.1% of the cohort. Prior to RSZ therapy, 75% of patients had received antiresorptive therapy, and 31% had received teriparatide.

At the time of analysis, 38 patients (56%) had completed 12 doses of RSZ, while 21 patients (30%) were still receiving treatment. RSZ was discontinued in 9 patients (13.2%), 6 of them due to AEs. Two elderly patients with >1 CVRF experienced ischemic strokes, occurring one month and seven months after completing RSZ, respectively.

Figure 1. Evolution of LS bone dual x-ray densitometry under romosozumab therapy.



Abbreviations: LS: lumbar spine; TBS: trabecular bone score.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In patients who completed RSZ and had BMD data (34 for FN and 25 for LS), BMD was stable in FN without significant T-score changes (p=0.808). However, the LS T-score showed a significant increase (-3.48 at baseline vs. -2.66 at the end; p=0.0001) (Figure 1). Additionally, LS BMD gain was >5% in 84% (21/25) of patients and >10% in 40% (10/25) of them. Factors associated with LS-BMD improvement included no prior anti-OP treatment with bisphosphonates (p=0.02) and fewer previous anti-OP therapies (p=0.20), but no correlation was found with age, OP risk factors, or the number/type of previous fractures. TBS also showed significant improvement (1.180 at baseline vs. 1.208 at 12-month follow-up; p=0.01). Only one osteoporotic fracture (Colles' fracture) was reported in a patient eight months after completing RSZ.

Regarding BRM, significantly lower carboxy-terminal telopeptide of type 1 collagen (CTX-I) levels (p=0.01) and a trend toward lower alkaline phosphatase (p=0.09) were observed post-RSZ, with no differences in osteocalcin (p=0.83), calcium (p=0.19), or PTH (p=0.80).

Conclusion: In our experience, RSZ treatment for severe OP demonstrated acceptable tolerance, with significant densitometric gain in LS and stabilization in FN. Long-term real-world studies are needed to assess RSZ effectiveness in reducing fractures and its long-term cardiovascular safety profile.

Disclosure: M. Nikitsina: None; **C. Valero**: None; **M. Uriarte Ecenarro**: None; **A. Ortiz**: None; **M. Ahijón Lana**: None; **I. Llorente**: None; **M. Dueñas-Ochoa**: None; **J. Saez**: None; **E. TOMERO MURIEL**: None; **E. Vicente-Rabaneda**: None; **I. Gonzalez-Alvaro**: None; **R. Garcia Vicuña**: None; **S. Castañeda**: None.

Abstract Number: 2123

Sclerostin in Aging Bone and Muscle: A Comparative Study of Osteoporosis, Sarcopenia, and Osteosarcopenia

Mohamed Tharwat Hegazy[1], Fatma Fayed[1], Shirihan Mahgoub[1], Yasmin El Ebrashy[2] and Maha Hossam Al-Din Ibrahim[1], [1]Faculty of Medicine, Cairo University, Cairo, Egypt, [2]National institute of Diabetes and Endocrinology, Cairo, Egypt

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2106–2123) Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoporosis, sarcopenia, and frailty are the 3 determinants of aging. A novel syndrome of combined osteosarcopenia has negative health outcomes among geriatric populations. In the last decades, studies have been conducted to assess sclerostin role in the bone and muscle cross-talk. Sclerostin is a protein produced by osteocytes, but recently it has been proposed to be secreted from myocytes as well. This study aimed to assess the level of serum sclerostin in osteoporosis, sarcopenia, and osteosarcopenia to address its possible dual role on bone and muscle units.

Methods: This cross-sectional study included 66 females aged ≥ 60 years old equally divided into 3 groups: "osteoporosis", "sarcopenia" and "osteosarcopenia" as follows: (a) females with osteoporosis were assessed by dual-energy X-ray absorptiometry (DXA) scan at the hip, lumbar spine, or distal 1/3 of the radius with a T-score ≤ -2.5 standard deviation (SD). (b) Females with sarcopenia were diagnosed according to the 2018 revised criteria of the European Working Group on Sarcopenia in Older People (EWGSOP). (c) Females with osteoporosis or osteopenia (T-score -1 to < -2.5) **and** sarcopenia were in osteosarcopenia group. Fracture risk assessment score (FRAX) was done using an online FRAX calculator

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

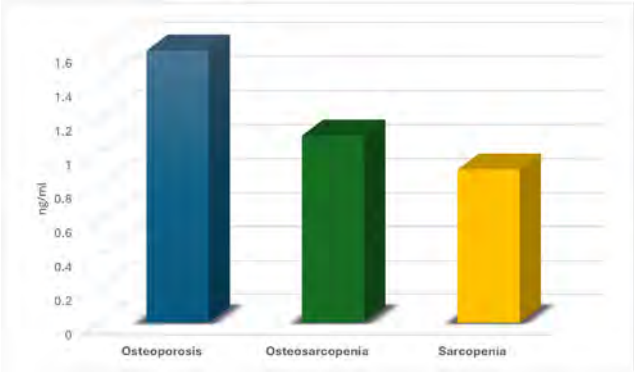


Figure 1: Mean sclerostin (ng/ml) in the 3 study groups

according to our geographic region. Anthropometric measurements and comprehensive geriatric assessment, including frailty, nutritional, functional assessment, and serum sclerostin level, were done for all subjects.

Results: We determined the optimum cut-off value of sclerostin in differentiating between each 2 groups. Results were adjusted for age and BMI. Serum sclerostin showed the highest level in the osteoporosis group with a cutoff level ≥ 1.29 ng/ml (sensitivity 66.7%, specificity 68.2%). The lowest level was among the sarcopenia group with a cutoff level < 0.7 ng/ml (sensitivity 75%, specificity of 59.1%). In osteosarcopenia, we found that sclerostin level was ≥ 0.7 ng/ml and < 1.29 ng/ml (sensitivity of 66.7%, specificity of 68.2%). Osteosarcopenia group had the least serum albumin, body mass index (BMI), muscle mass, bone mineral density (BMD), and android/gynecoid (A/G) ratio. They had the most advanced age, the highest fracture risk (FRAX) score of major osteoporotic and hip fractures. They had the worst nutritional state and the most functional impairment.

Conclusion: Sclerostin could have an anabolic effect on muscles and a catabolic effect on bone. Advanced age, low serum albumin, low body weight, and poor nutritional state are highest in osteosarcopenia. Osteosarcopenia patients are at higher risk for developing future fractures.

Table 1: Summary of the group that had the highest and the lowest statistically significant mean values for each variable.

Variable	Highest Significant mean	Lowest significant mean	P- value
Age	Osteosarcopenia	Sarcopenia	0.003
Weight	Sarcopenia	Osteosarcopenia	< 0.001
BMI	Sarcopenia	Osteosarcopenia	< 0.001
WC	Osteoporosis	Osteosarcopenia	< 0.001
HC	Sarcopenia	Osteosarcopenia	< 0.001
Hand grip	Osteoporosis	Osteosarcopenia	0.018
SMI (BIA)	Osteoporosis	Osteosarcopenia	< 0.000
A/G ratio	Osteoporosis	Osteosarcopenia	0.001
ASM/height^2	Osteoporosis	Osteosarcopenia	< 0.001
BMD (T-score at AP, forearm, spine)	Sarcopenia	Osteosarcopenia	< 0.001
FRAX of MOF	Osteosarcopenia	Sarcopenia	0.001
FRAX of hip fracture	Osteosarcopenia	Sarcopenia	< 0.001
Serum albumin	Osteoporosis	Osteosarcopenia	0.001
Serum sclerostin	Osteoporosis	Sarcopenia	0.026
MNA score	Osteoporosis	Osteosarcopenia	0.001
Functional assessment score	Osteoporosis	Osteosarcopenia	0.048

Abbreviations: BMI: body mass index, WC: waist circumference, HC: hip circumference, SMI: skeletal muscle index, A/G ratio: android/gynecoid ratio, ASM: appendicular skeletal mass, BMD: bone mineral density, AP: anteroposterior, FRAX: fracture risk assessment tool, MOF: major osteoporotic fracture, MNA: mini- nutritional assessment.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Hegazy: None; **F. Fayed**: None; **S. Mahgoub**: None; **Y. El Ebrashy**: None; **M. Hossam Al-Din Ibrahim**: None.

Abstract Number: 2124

Reliability and Validation of the Physician's Global Assessment of Lung Disease (PGALD) in Systemic Juvenile Idiopathic Arthritis -Associated Lung Disease (SJIA-LD)

Eileen Rife[1], Guihua Zhai[2], Mekibib Altaye[3], Jennifer Andringa[4], Hermine Brunner[5], Scott Canna[6], Lauren Henderson[7], Yukiko Kimura[8], Scott Lieberman[9], Mona Riskalla[10], Tiphanie Vogel[11], Holly Wobma[12] and Grant Schulert[5], [1]University of Alabama at Birmingham, birmingham, AL, [2]UAB, Birmingham, [3]Cincinnati Children's Hospital, Cincinnati, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, [5]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [6]Children's Hospital of Philadelphia, Philadelphia, PA, [7]Boston Children's Hospital, Watertown, MA, [8]Hackensack Meridian School of Medicine, New York, NY, [9]University of Iowa, Iowa City, IA, [10]University of Minnesota Masonic Children's Hospital, Minneapolis, MN, [11]Baylor College of Medicine, Houston, TX, [12]Boston Children's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The physician global assessment of lung disease (PGALD) is a recently proposed disease activity measure for patients with systemic juvenile idiopathic arthritis-associated lung disease (SJIA-LD) – a significant cause of morbidity and mortality in SJIA. This study evaluates the reliability and construct validity of the PGALD.

Methods: 20 SJIA-LD clinical vignettes were created, informed by historical patient encounters as templates. Vignettes included brief patient medical histories, physical examination findings, a list of prescribed medications, laboratory results, diagnostic imaging, pulmonary function test results, and biopsy results – when available. Fifty-seven pediatric rheumatologists and pulmonologists with experience caring for children with SJIA-LD were invited to rate vignettes utilizing the PGALD, a 10-point Likert scale (0 = inactive SJIA-LD; 10 = highly active SJIA-LD). Raters who completed the initial round of 20 vignettes were asked three days later to rate a subset of 8 repeat vignettes. Inter- and intra-rater reliability were assessed using intraclass correlation coefficients (ICC). Based on the 95% confidence interval of ICC estimates, values less than 0.5

Table 1: Demographics, specialty, and practice experience of physician raters

	No.	(%)
Total Respondents	38	100
Sex		
Female	28	74
Practice Setting		
Academic	38	100
Practice Location		
United States	38	100
Specialty		
Pediatric Rheumatology	36	95
Medicine /Pediatric Rheumatology	1	2.5
Pediatric Pulmonology	1	2.5
Years in Practice		
< 5 years	4	10
5 - 10 years	6	16
> 10 years	28	74
SJIA-LD Patients Managed		
1 - 2 patients	14	37
3+ patients	24	63

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Variable Present N (%)	Mean PGALD Scores Variable Present	Mean PGALD Scores Variable Not Present	P value
Total Vignettes	20 (100)			-
Clinical Variables (Y/N)				
Crackles on exam	6 (30)	5.7	3.0	0.001
Clubbing on exam	11 (55)	4.5	2.9	0.061
Oxygen Requirement	2 (10)	6.3	3.5	0.048
Hypoxemia (Sp02<90%)	5 (25)	5.6	3.2	0.015
MAS present in vignette	8 (40)	4.0	3.6	0.637
MAS at diagnosis	13 (65)	4.2	3.0	0.176
Laboratory Elevation (Y/N)				
Ferritin > 75 ng/mL	11 (55)	4.7	2.9	0.041
IL-18 >475 pg/mL	16 (80)	4.3	2.1	0.003
CRP >0.5 mg/dL	8 (40)	5.2	2.9	0.006
Diagnostic Imaging Features (Y/N)				
Ground Glass Opacities	9 (45)	5.1	2.8	0.004
Reticulation or Honeycombing	8 (40)	5.0	3.0	0.019
Pleural or Septal Thickening	10 (50)	5.0	2.6	0.002
Pulmonary Nodules	2 (10)	4.1	1.5	0.079
Bronchial thickening	3 (15)	5.5	3.5	0.109
Number of Medications Prescribed				
1	2 (10)	0.5		-
2	3 (15)	2.6		0.207
3	8 (40)	4.0		0.010
4	6 (30)	4.7		0.004
5	1 (5)	7.1		0.003
	Variable Present	**Median (IQR)**	**R value**	**P value**
Laboratory Values				
Ferritin (ng/mL)	11	300 (43, 877)	0.070	0.78
IL-18 (pg/mL)	16	10794 (1310, 38560)	0.001	0.99
CRP (mg/dL)	8	0.48 (0.1, 1.1)	0.390	0.09
sIL-2r (U/mL)	7	900 (286, 1500)	0.053	0.86
CXCL9 (pg/L)	8	242 (107, 859)	-0.181	0.46
Pulmonary Function Test Values				
FVC (<80%)	6	85 (70, 102)	-0.71	0.01
TLC (<80%)	5	77 (64, 94)	-0.92	0.01
DLCO (<80%)	6	71 (61, 89	-0.97	0.0002

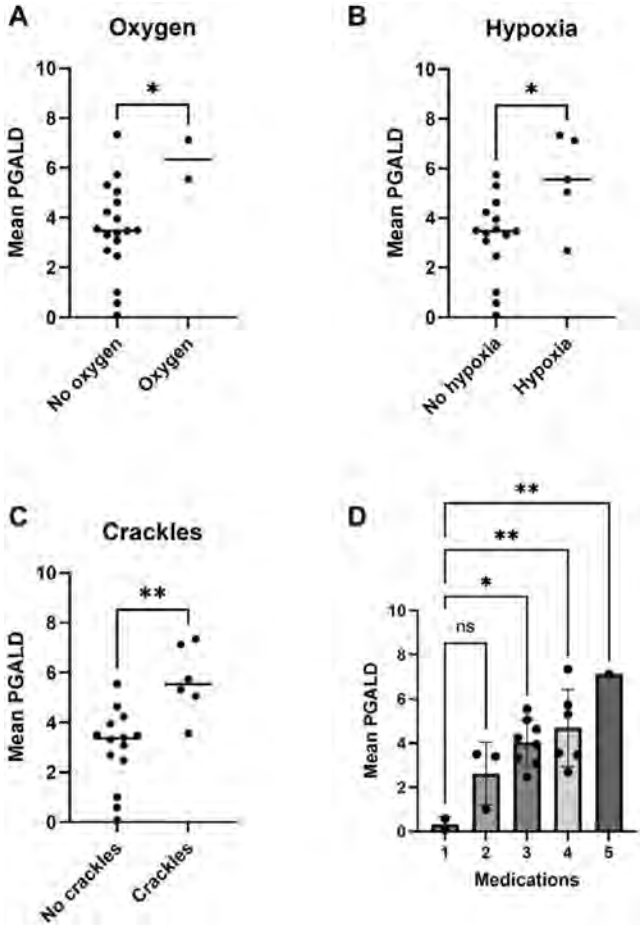
Sp02 – Peripheral saturation of oxygen; MAS – macrophage activation syndrome; IL-18 - Interleukin 18; CRP – C-reactive protein; CXCL9 chemokine c-x-c-motif; FVC - forced vital capacity; TLC – Total Lung capacity; DLCO – lung diffusion capacity. Unpaired t test performed for Clinical Variables, Laboratory Elevation and Diagnostic Imaging Features; Pearson Correlation Coefficient performed for Laboratory Values and Pulmonary function Test Values; ANOVA performed for Number of Medications Prescribed.

indicated poor reliability, between 0.5-0.75 moderate-, between 0.76-0.9 good-, and >0.9 excellent reliability. SJIA-LD features influencing PGALD ratings were assessed in univariate analysis.

Results: The ICC for all raters was 0.678 (0.543, 0.819), indicating moderate to good inter-rater reliability. The intra-rater ICC was 0.863 (0.823, 0.893) indicating good intra-rater reliability. Factors associated with higher mean PGALD scores included the presence of crackles on auscultation (5.7 vs. 2.9; p=0.001), hypoxemia on pulse oximeter (5.6 vs. 3.2; p=0.01), current oxygen requirement (6.3 vs. 3.5; p=0.04), suggestive diagnostic imaging features (p≤0.01), and three or more prescribed medications for SJIA-LD (p≤0.01). Pulmonary function measures demonstrated significant negative correlations with mean PGALD scores, including forced vital capacity (r=–0.71; p=0.01), total lung capacity (r=–0.92; p=0.01), and diffusion capacity (r=–0.97; p=0.0002). Only the CRP was weak-to-moderately correlated with PGALD scores (r=0.39; p=0.09), while other laboratory values including ferritin, IL-18, CXCL9, and sIL2R were not significantly correlated.

Conclusion: The PGALD is a novel measure of SJIA-associated LD activity. Its initial validation suggests acceptable construct validity and reliability. Additional studies are needed to assess its responsiveness to change over time.

23652205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Association between clinical features and mean PGALD scores. A: Mean PGALD scores in patients with vs. without supplemental oxygen. B: Mean PGALD scores in patients with vs. without hypoxia. C: Mean PGALD scores in patients with vs. without crackles on exam. D: Mean PGALD scores by number of medications (1-5) used to treat SJIA-LD. *p=<0.05, **p=<0.01

Disclosure: E. Rife: None; **G. Zhai**: None; **M. Altaye**: None; **J. Andringa**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **L. Henderson**: Bristol-Myers Squibb(BMS), 5, Pfizer, 2, Sobi, 2; **Y. Kimura**: None; **S. Lieberman**: None; **M. Riskalla**: SOBI, 2; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6; **H. Wobma**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2.

Abstract Number: 2125

Development and Validation of Minimal Clinically Important Difference for Children with Chronic Nonbacterial Osteomyelitis Using a Consensus and Data-Driven Approach

Farzana Nuruzzaman[1], Natalie Rosenwasser[2], Xing Wang[3], Ava Klein[3], Ian Muse[4], Erin Balay-Dustrude[5], Megan Nguyen[6], Emily Deng[3], Jonathan Akikusa[7], Matthew Basiaga[8], Lindsey Bergstrom[9], Fatma Dedeoglu[10], Bin Huang[11], Jenna King[12], Sivia Lapidus[13], Tzielan Lee[14], Cassandra Levesque[15], Aleksander Lenert[16], Lillian Lim[17], Kimberly Martin[18], Elizabeth Murray[19], Melissa Oliver[20], Karen Onel[21], Seza zen[22], Lauren Potts[23], Sara M. Stern[24], Robin Villaverda[25], Eveline Wu[26], Ronald laxer[27], Polly Ferguson[28], Daniel Lovell[29] and Yongdong (Dan) Zhao[30], on behalf of CHOIR network and CARRA CNO workgroup, [1]Stony Brook Children's Hospital, Stony Brook, NY, [2]Seattle Children's Hospital, seattle, WA, [3]Seattle Children's Hospital, Seattle, [4]University of Washington, Department of Pediatrics, Seattle Children's Hospital,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

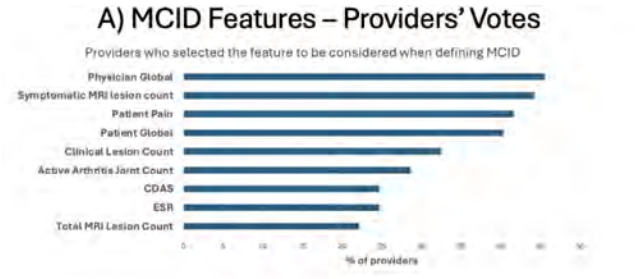
Seattle, [5]University of Washington, Seattle, WA, [6]Seattle Children's Research Institute, Seattle, [7]The Royal Children's Hospital, Parkville, Victoria, Australia, [8]Mayo Clinic, Rochester, MN, [9]Patient/parent research partner, Harpswell, ME, [10]Boston Children's Hospital, Boston, MA, [11]Cincinnati Children's Hospital, Cinciannati, OH, [12]Patient/parent Research Partner, Planation, FL, [13]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Montclair, NJ, [14]Stanford University School of Medicine, Palo Alto, CA, [15]Patient/parent research partners, DC district, DC, [16]Iowa Carver College of Medicine, Iowa City, IA, [17]University of Alberta, Edmonton, AB, Canada, [18]Patient/parent research partners, Houston, TX, [19]Patient/parent research partners, Lynnwood, WA, [20]Indiana University, Indianapolis, IN, [21]HSS, New York, NY, [22]Hacettepe University Medical Faculty, Ankara, Turkey, [23]Patient/parent research partners, Santa Cruiz, CA, [24]University of Utah, Salt Lake City, UT, [25]Patient/parent research partners, Thorton, CO, [26]UNC Chapel Hill, Chapel Hill, NC, [27]The Hospital for Sick Children, Toronto, ON, Canada, [28]University of Iowa Carver College of Medicine, Iowa City, IA, [29]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [30]Seattle Children's Research Institute, Redmond, WA

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is an inflammatory bone disease that can result in bone deformity, persistent pain and pathological fractures which is frequently treated empirically. Clinical trials to compare and evaluate medication efficacy necessitates quantifying a minimal clinically important difference (MCID). We aimed to develop and validate this metric in CNO.

Methods: A Delphi survey on priorities for defining MCID was sent to providers via the Childhood Arthritis and Rheumatology Research Alliance (CARRA's) CNO Workgroup (180 members). Using the survey's results, 664 cases were identified from over 3000 real world patient visits from our multisite prospective registry (CHronic nonbacterial Osteomyelitis International Registry, CHOIR) to define MCID. The interval between visits was between 3 and 12 months. At least 1 or more values at the follow up visits had improved while no more than 1 value worsened. An expert panel of 13 international pediatric rheumatologists and 7 patient/caregivers reviewed the cases individually to determine if they showed MCID. Cases which did not



B) Thresholds of MCID Features – Providers

Feature	Absolute change Median [IQR] (N)	% change Median [IQR] (N)
Patient pain score improved by greater than or equal to...	2 [2, 3] (31)	30 [20, 50] (32)
Patient global assessment improved by greater than or equal to...	2 [2, 3] 30)	30 [21, 50] (34)
Total clinical lesion count improved by greater than or equal to...	1.5 [1, 2] (22)	30 [25, 50] (26)
Physician global assessment improved by greater than or equal to...	2 [2, 2.5] (31)	30 [20, 50] (35)
Symptomatic MRI lesion count improved by greater than or equal to...	1 [1, 2] (28)	28 [20,50] (34)
Total MRI lesion count improved by greater than or equal to...	2 [2, 3] (13)	30 [25,50] (20)
Inflammatory markers, ESR, improved by greater than...(mm/hr)	10 [6, 14] (14)	40 [30,50] (21)
CDAS (clinical disease activity score)	3 [3, 5] (15)	30 [25, 50] (21)

Figure 1: Provider Priorities in Defining Minimal Clinically Important Difference in CNO Delphi Survey Results: Frequencies and Thresholds

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of Cohorts Used to Develop Definitions of Minimal Clinically Important Difference in CNO

n= 664	MCID Cohort (baseline visit)*	MCID Cohort (followup visit)	p-values^
Age: median [IQR]	12 [9,14]		
Sex: n (%)	Female: 391 (60) Male: 257 (40)		
Extracted Parameters			
Pain Level (0-10): median [IQR]	5 [3, 6]	2 [0, 4]	<0.0001
Patient global assessment (PAGA) (0-10): median [IQR]	5 [3, 6]	2 [0, 4]	<0.0001
Physician global assessment (PHGA) (0-10): median [IQR]	2 [1, 4]	1 [0, 2]	<0.0001
CNO clinical lesion count: median [IQR]	1 [0, 2]	0 [0, 1]	<0.0001
Total MRI lesion count: median [IQR]	3 [2, 5]	2 [1, 3]	<0.0001
Active spinal lesion on MRI: n (%)	No: 510 (77) Yes: 154 (23)	No: 588 (89) Yes: 76 (11)	<0.0001
Active sacroiliitis on MRI: n (%)	No: 544 (82) Yes: 120 (18)	No: 610 (92) Yes: 54 (8)	<0.0001
New spinal lesion on MRI: n (%)	N/A	No: 647 (97) Yes: 17 (3)	N/A
New non-spinal lesion on MRI: n (%)	N/A	No: 366 (55) Yes: 298 (45)	N/A
Erythrocyte Sedimentation Rate (ESR): n (%)	Abnormal: 205 (31) Normal: 459 (69)	Abnormal: 73 (11) Normal: 591 (89)	<0.0001
C-Reactive Protein (CRP): n (%)	Abnormal: 75 (11) Normal: 589 (89)	Abnormal: 30 (5) Normal: 634 (96)	<0.0001
CNO Disease Activity Score (CDAS)*: median [IQR]	10 [7, 14]	4 [1, 8]	<0.0001

*Inclusion criteria for baseline visit were: MRI lesion count and the sum of patient pain and PHGA as well as the sum of PAGA and PHGA are >0
^p-values calculated using Wilcoxon signed rank test for continuous variables and McNemar's test for categorical variables
*CDAS: Sum of patient pain score (0-10), PAGA (0-10), and total number of active CNO clinical lesions defined as focal tenderness, and/or swelling, and/or warmth

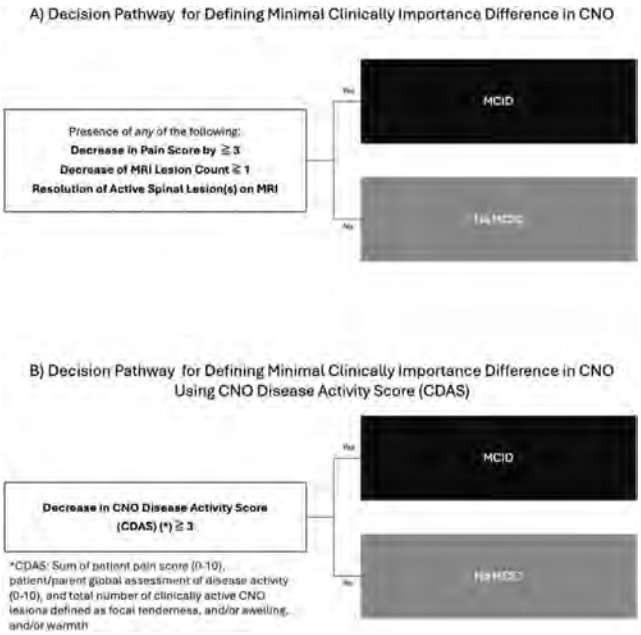


Figure 2: Decision Pathways for Defining Minimal Clinically Important Difference in CNO

reach consensus (80% agreement) were evaluated by >5 reviewers at an in-person consensus meeting. Reviewers were asked to vote whether a case demonstrated MCID. A decision tree was used to determine the cutoff point that best differentiated patients with and without MCID, and the model was validated using 10-fold cross-validation to ensure generalizability.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 80 providers (44% response rate) from 5 continents completed the survey. The frequency of items selected were listed and the absolute and relative change were reported (Figure 1). Cohort characteristics and parameters extracted from paired baseline and follow up visits are in Table 1. 638 (96%) of 664 paired visits reached consensus. 423 were classified as MCID, 215 as no MCID and 26 were inconclusive. A generalized linear model analysis showed that the change of pain level (p=0.03), baseline MRI lesion count (p=0.02), change of MRI lesion count (p< 0.001) and change of active spinal lesion on MRI (p< 0.02) were associated with the classification of MCID. The median [IQR] change of clinical disease activity score (CDAS) was -7 [-11,-4] in cases with MCID, compared to -2 [-5, 0] in those without MCID (p< 0.001). Decision trees based on all parameters or CDAS alone with accuracy of 0.73 and 0.71, respectively are in Figure 2.

Conclusion: A Delphi survey identified important variables to include when defining MCID per providers. We developed definitions for MCID, and specified measurement characteristics. A 30% improvement in these variables with improvement of CDAS by 3 were considered meaningful by providers and consensus data.

Disclosure: F. Nuruzzaman: None; **N. Rosenwasser**: None; **X. Wang**: None; **A. Klein**: None; **I. Muse**: None; **E. Balay-Dustrude**: None; **M. Nguyen**: None; **E. Deng**: None; **J. Akikusa**: None; **M. Basiaga**: None; **L. Bergstrom**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **B. Huang**: None; **J. King**: None; **S. Lapidus**: None; **T. Lee**: None; **C. Levesque**: None; **A. Lenert**: None; **L. Lim**: None; **K. Martin**: None; **E. Murray**: None; **M. Oliver**: None; **K. Onel**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **L. Potts**: None; **S. Stern**: None; **R. Villaverda**: None; **E. Wu**: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **R. Iaxer**: Akros pharma, 2, Eli Lilly Canada, 2, Novartis, 2, Sanofi, 2; **P. Ferguson**: None; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **Y. Zhao**: american board of pediatrics, 4, Bristol-Myers Squibb(BMS), 5, UpToDate, 9.

Abstract Number: 2126

Preliminary Results of a Large, Global Registry Characterizing Childhood-Onset Takayasu Arteritis

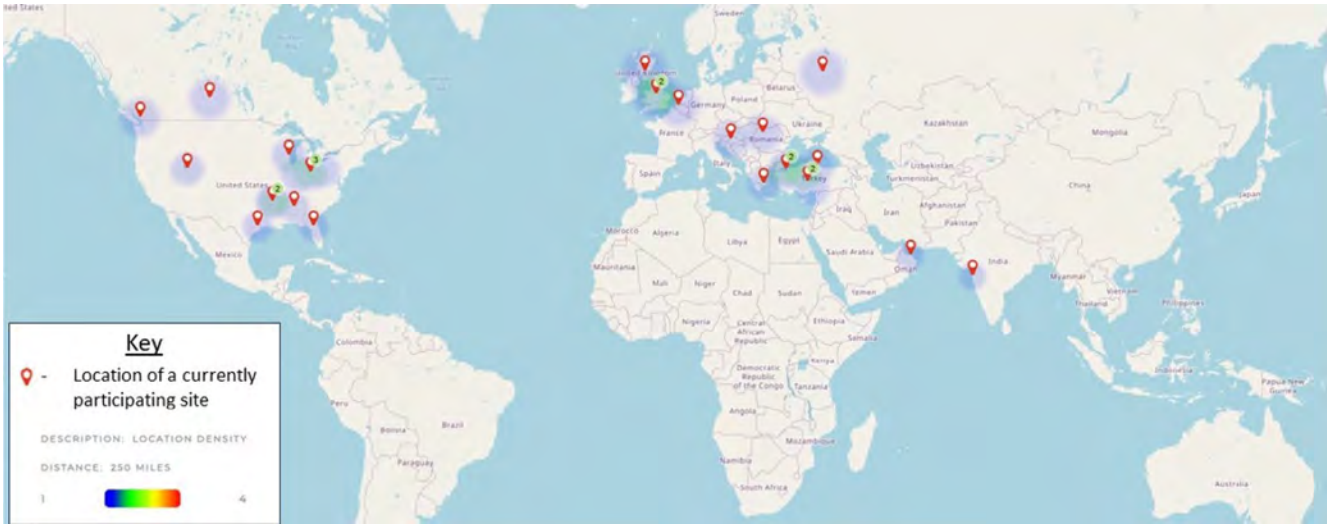
Muserref Kasap Cuceoglu[1], **James Bistolarides**[2], Mario Sestan[3], Samuel Gagne[4], Nick McPhate[5], Kimberly Morishita[6], Vidya Sivaraman[7], Linda Wagner-Weiner[8], Seza zen[9], Marija Jelusic[10], David Cabral[11] and International childhood-onset Takayasu Arteritis (IcTAK) Workgroup, [1]Hacettepe University, Ankara, Turkey, [2]Medical College of Wisconsin, Wauwatosa, WI, [3]University of Zagreb School of Medicine, Zagreb, Croatia, [4]University of Pittsburgh, Pittsburgh, PA, [5]BC Children's Hospital, Vancouver, Canada, [6]University of British Columbia, Vancouver, BC, Canada, [7]Nationwide Children's Hospital/ The Ohio State University, Columbus, OH, [8]University of Chicago, Chicago, IL, [9]Hacettepe University Medical Faculty, Ankara, Turkey, [10]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Zagreb, Croatia, [11]BC Children's Hospital and University of British Columbia, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The rarity of childhood-onset Takayasu arteritis (c-TAK) has resulted in small cohorts for study that has limited the potential for evaluating its course and outcomes. The objective of this study is to engage Pediatric Rheumatologists internationally to contribute patient data to a research network targeted to characterizing c-TAK and improving

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Location of clinical sites that have patients included in the current abstract submission

disease outcomes. This will be achieved through the following: *Aim 1*: Create an international c-TAK registry, *Aim 2*: Evaluate the performance of existing disease activity measures, and *Aim 3:* Create and validate a preliminary disease activity score specifically for c-TAK.

Methods: Member sites of Childhood Arthritis Rheumatology Research Alliance (CARRA) and Pediatric Rheumatology European Society (PReS) are invited to enroll patients in this c-TAK registry. The registry is to capture children with a physician diagnosis of c-TAK aged ≤ 18 years at disease onset. Data entry is hosted on Research Electronic Data Capture (REDCap) platform. Registry data includes demographic characteristics, clinical symptoms, organ involvement, laboratory features, vascular imaging, treatment, physician global assessment (PGA) of disease activity, and the features needed to calculate the Pediatric Vasculitis Activity Score (PVAS), Indian Takayasu Activity Score (ITAS2010 and ITAS-A), and 2018 European League Against Rheumatism (EULAR) criteria for active large vessel vasculitis. The assessment of damage using the pediatric vasculitis damage index (PVDI) is collected at follow-up. Data is collected retrospectively from patient medical records at diagnosis, 12-months, and at the final visit on file beyond 15 months (if applicable).

Results: As of abstract submission, the registry has collected data on 72 patients from 12 countries and 31 unique clinical sites. Additional enrollment has begun at 40 other sites, including from 13 additional counties. To date the cohort comprises 80% females. The average age at diagnosis is 12.14 +/- 4.81 years; the average time to diagnosis after first symptoms is 7.53 +/- 13.07 months; 66% received intravenous pulse glucocorticoids (GC) at time of diagnosis, while 85% were started on oral GC. Primary treatments (n=63) prescribed at time of diagnosis include methotrexate (62%), anti-TNF biologic (27%) cyclophosphamide (24%), ongoing intermittent pulse IV GC (11%), and tocilizumab (11%). Secondary treatments included antihypertensives (54%) and anti-coagulants (48%).

Conclusion: Creation of an international c-TAK registry is feasible owing to global collaborations between member sites of CARRA and PReS, and the capabilities for electronic communications and data transmission. Registry data will improve knowledge of presenting symptoms and treatment of c-TAK and increase understanding of the value of current disease activity measures. The successful realization of further project aims is expected.

Disclosure: M. Kasap Cuceoglu: None; **J. Bistolarides**: None; **M. Sestan**: None; **S. Gagne**: None; **N. McPhate**: None; **K. Morishita**: None; **V. Sivaraman**: None; **L. Wagner-Weiner**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **M. Jelusic**: None; **D. Cabral**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2127

Chronic Non-Bacterial Osteomyelitis of the Petrous Bone: A Case Series

Jeanine McColl[1], Ingrid Goh[2], Helen Branson[3], Karen Peralta[4], Dorsa Aeenfar[4], Sharon Cushing[3], Rayfel Schneider[3] and Ronald laxer[5], [1]University of Calgary, Calgary, Canada, [2]University of Toronto The Hospital for Sick Children, Toronto, ON, Canada, [3]University of Toronto The Hospital for Sick Children, Toronto, Canada, [4]University of Toronto, The Hospital for Sick Children, Toronto, [5]The Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic Nonbacterial Osteomyelitis (CNO) is an autoinflammatory disorder of bone usually beginning in children between the ages of 7-12. It typically affects metaphyses of the long bones, vertebral bodies, and the clavicle. Although, any bone can be affected, involvement of the skull is extremely uncommon. The objectives of our study are to 1) illustrate presenting features associated with CNO of the temporal bone, its treatment, & response to therapy. 2) Increase awareness that CNO can involve the temporal bone to facilitate earlier diagnosis and treatment.

Methods: Patients diagnosed with CNO between June 2002-May 2022 at The Hospital for Sick Children were identified by searching Bialogics,™ the Electronic Medical Records Epic, and Chart Maxx. Charts were searched for the term "skull" to identify cases. To obtain records prior to 2018 (prior to the Epic electronic medical record) we ran a word search of pertinent synonyms to identify cases of CNO involving the temporal bone in the ISYS word text search program. Research Ethics Board approval was obtained for this study.

Results: Three cases of CNO affecting the petrous temporal bone were identified. All had been previously diagnosed with CNO. Age of onset of CNO was 2.3 to 9 years of age; all were female (Table 1). Time from CNO diagnosis to onset of petrous bone lesions ranged from 6-17 months. Two patients developed a Bell's Palsy and hearing loss. All patients were treated with a non-steroidal anti-inflammatory drug (NSAID) and the one patient with hearing loss also received anti-TNF therapy (adalimumab) and responded well with resolution of hearing loss. The other patient received NSAID therapy and has persistent bilateral hearing loss, in the context of recurrent otitis media.

Conclusion: The skull is rarely involved in CNO, with ∼1% of patients presenting with lesions in the frontal bone. Temporal bone involvement has rarely been reported with only two cases to our knowledge . It is unknown why CNO rarely affects the skull. One presumption is that CNO tends to affect the metaphyses and epiphyses of the long bones which the skull does not have, although, the pelvis also does not have a metaphysis and is a common site for CNO lesions. Another thought is the increased metabolic activity and blood supply at the epiphysis with chondrocyte maturation could result in increased propensity of immune dysregulation and inflammatory lesions. With less osteo metabolic activity the risk of dysregulation may be less. Interestingly all three cases developed skull involvement while on treatment for CNO.

There is no standardized treatment for CNO. Consensus guidelines provide options including non-steroidal anti-inflammatories (first line), glucocorticoids, disease modifying drugs (methotrexate, sulfasalazine), Tumor Necrosis Factor (TNF) inhibitors with or without methotrexate, and bisphosphates (pamidronate or zolendronic acid). In case one anti-TNF therapy was used due to the severity of hearing loss. CNO is challenging to diagnose, with 7% of patients being diagnosed five years after symptom onset.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

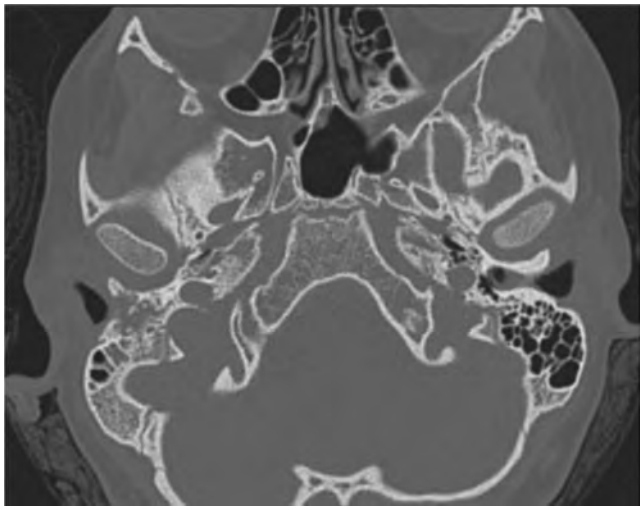


Figure 1: Case 1 Right Temporal Bone Erosion

Table 1: Results

Demographic	Case 1	Case 2	Case 3
Age at onset Skull lesions (years)	10	8	2
Sex (M/F)	F	F	F
7th Cranial Nerve involvement	Yes	No	Yes
Conductive Hearing Loss	Yes	No	Yes
Previous CNO Treatment	Pamidronate & NSAIDs	NSAIDs, Zoledronate & Prednisone	NSAIDs
Bone Biopsy Findings	Bone & granulation tissue with chronic inflammation	Trabecular bone with acute and chronic inflammation suggestive of osteomyelitis	Lymphocytic infiltrate with histiocytic cells and abundant eosinophilic neutrophils
Bone Cultures	Negative	Gram + bacilli (normal flora)	Negative
Treated with anti TNF (adalimumab)	Yes	Yes	No
Hearing loss resolution post anti TNF therapy	Yes	N/A	No

It is important to consider CNO on the differential in patients who present with cranial nerve abnormalities, hearing loss, and those with presumed infectious osteomyelitis.

Disclosure: J. McColl: None; **I. Goh**: None; **H. Branson**: None; **K. Peralta**: None; **D. Aeenfar**: None; **S. Cushing**: Akouos (Eli Lilly), 2, Cochlear Corporation, 1, 2, 5, 6, Decibel (Regeneron), 2, Nova Publishing, 9, Plural publishing, 9, Sensorion, 1; **R. Schneider**: None; **R. Iaxer**: Akros pharma, 2, Eli Lilly Canada, 2, Novartis, 2, Sanofi, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2128

Prevalence of Risks and Complications in a Longitudinal International Cohort of Children with Chronic Nonbacterial Osteomyelitis (CNO)

Jessica Kent[1], Eveline Wu[2], Melissa Oliver[3], Sivia Lapidus[4], Ummusen Akca[5], Adriel Liau[6], Pratyush Kore[7], Ian Muse[8], Ava Klein[6], Emily Deng[6], Iris Hamilton[6], Haodong Chen[7], Megan Nguyen[7], Tianai Li[9], Avril Wilson[7], Jasmine Morden[7], Shima Yasin[10], Aleksander Lenert[11], Sara M. Stern[12], Antonella Insalaco[13], Manuela Pardeo[14], Gabriele Simonini[15], Edoardo Marrani[16], Xing Wang[6], Bin Huang[17], Leonard Kovallick[18], Natalie Rosenwasser[19], Erin Balay-Dustrude[20], Doaa Mosa[21], Katerina Bouchalova[22], Andrea Cabova[23], Jenna Thomason[20], Lori Tucker[24], Hermann Girschick[25], Ronald laxer[26], Marinka Twilt[27], Georgina Tiller[28], Jonathan Akikusa[29], Christian Hedrich[30], Karen Onel[31], Fatma Dedeoglu[32], Seza Kzen[33], Polly Ferguson[34] and Yongdong (Dan) Zhao[35], [1]Medical College of Wisconsin, Wauwatosa, WI, [2]UNC Chapel Hill, Chapel Hill, NC, [3]Indiana University, Indianapolis, IN, [4]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Montclair, NJ, [5]Hacettepe University, Ankara, Turkey, [6]Seattle Children's Hospital, Seattle, [7]Seattle Children's Research Institute, Seattle, [8]University of Washington, Department of Pediatrics, Seattle Children's Hospital, Seattle, [9]Seattle Children's Research institute, Seattle, [10]Univeristy of Iowa, Iowa City, [11]University of Iowa, Iowa City, IA, [12]University of Utah, Salt Lake City, UT, [13]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Italy, [14]IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, [15]Rheumatology Unit, ERN-ReCONNET center, Meyer Children's Hospital IRCCS, Firenze, Firenze, Italy, [16]University of Florence, Firenze, Italy, [17]Cincinnati Children's Hospital, Cinciannati, OH, [18]The University of North Carolina at Chapel Hil, Chapel Hill, [19]Seattle Children's Hospital, seattle, WA, [20]University of Washington, Seattle, WA, [21]Mansoura University Hospitals, Mansoura City, Egypt, [22]Palacký University Olomouc, Olomouc, Czech Republic, [23]Faculty of Medicine and Dentistry Palacky University Olomouc, Olomouc, Czech Republic, [24]BC Children's Hospital, Vancouver, BC, Canada, [25]Vivantes Clinic Friedrichshain, Wuerzburg, Germany, [26]The Hospital for Sick Children, Toronto, ON, Canada, [27]Alberta Children's Hospital, Alberta, Canada, [28]Royal Children's Hospital, Melborne, Australia, [29]The Royal Children's Hospital, Parkville, Victoria, Australia, [30]University of Liverpool, Liverpool, United Kingdom, [31]HSS, New York, NY, [32]Boston Children's Hospital, Boston, MA, [33]Hacettepe University Medical Faculty, Ankara, Turkey, [34]University of Iowa Carver College of Medicine, Iowa City, IA, [35]Seattle Children's Research Institute, Redmond, WA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is associated with various comorbidities and long-term complications. The CHronic nonbacterial Osteomyelitis International Registry (CHOIR) is a multi-national database that allows researchers to determine the prevalence of long-term risks, growth outcomes, and medication use and related adverse effects over time in children with CNO.

Methods: Children with CNO enrolled in CHOIR across 17 global sites between August 1, 2018 to December 31, 2024. Demographic and disease-related data were collected at baseline and follow-up visits. Data were summarized via descriptive statistics.

Results: A total of 585 children with CNO were included with a median age of 9.5 years at disease onset (**Table 1**). Of these, 171 had follow-up for greater than 5 years. Whole body (WB) MRIs were done in 469 patients at least once, and 233 at diagnosis. Rate of active spinal lesions confirmed by MRI decreased from 12% at diagnosis to 2% at 5 years. At baseline, height, weight, and body mass index (BMI) were within normal ranges and persisted over 5 years (**Table 2**).

Of 459 patients with a total of 1,649 patient-years of follow-up and complete data on comorbidities and adverse events, the mean follow-up was 3.6 years since diagnosis. Prior to diagnosis of CNO, the most common comorbidities were inflammatory bowel disease (IBD) (32), inflammatory arthritis (27), and psoriasis (26). After diagnosis, new autoimmune conditions that

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic and clinical data of patients at baseline and 5-year follow-up

Demographics	At Diagnosis (n=585)	5 Year Follow-Up (n=171)
Female, n (%)	332 (57)	93 (55)
Race (White)	471 (81)	133 (78)
Age at Onset	9.5 [7.3, 12.0]	8.8 [6.5, 10.0]
Age at Diagnosis	11.0 [8.1, 13.0]	9.4 [7.1, 12.0]
Time Between Onset and Diagnosis (months)	5.6 [2.3, 15.0]	5.5 [2.1, 14.8]
Bone Biopsy Obtained	244 (42)	101 (60)
Active Spinal Lesion on MRI	68 (12)	3 (2)

Table 2: Distribution of height, weight, and BMI z-scores at diagnosis and 5-year follow-up

	At Diagnosis	5 Year Follow-Up
Height (n)	352	91
Median, [IQR]	0.16 [-0.59, 0.84]	0.36 [-0.37, 0.95]
Above 2, (%)	20 (6)	9 (10)
Below -2, (%)	11 (3)	0 (0)
Weight (n)	352	92
Median, [IQR]	0.26 [-0.63, 1.00]	0.40 [-0.42, 1.30]
Above 2, (%)	23 (7)	9 (10)
Below -2, (%)	12 (3)	1 (1)
BMI (n)	353	91
Median, [IQR]	0.27 [-0.62, 1.00]	0.36 [-0.42, 1.30]
Above 2, (%)	17 (5)	9 (10)
Below -2, (%)	16 (5)	5 (5)

Chi square analysis showed no significant difference in frequency of z score >2 or <-2 between baseline and follow-up

developed were psoriasis (37), arthritis (18), IBD (5), and less commonly (< 5) pustulosis, hidradenitis, celiac disease, and type 1 diabetes (**Table 3**). Amplified pain syndrome occurred in 13 patients at baseline and 15 more during follow-up. Vertebral compression fractures occurred in 25 patients initially and 6 more during follow-up. Seven had vertebral plana prior to diagnosis of CNO. Additionally, 12 patients prior to and 17 more after diagnosis experienced fractures at non-lesion sites related to trauma. Of these, 81% of vertebral and 41% of non-vertebral fractures occurred before diagnosis. The most

Table 3: Pattern of medication usage and number of events of interests

	Prior to Diagnosis of CNO (n=585)	During Follow-up Among Sites with Full Data (n=459)
Medications: n (%)		Ever
NSAIDs	197 (34)	205 (45)
Steroids	10 (2)	52 (11)
Bisphosphonates	7 (1)	169 (37)
JAK Inhibitor	1 (0)	16 (3)
Non TNFi Biologic[a]	3 (0)	27 (6)
TNFi	32 (5)	217 (47)
DMARDs	62 (11)	229 (50)
Patient Years on Medication		
NSAIDs	1870	594
Steroids	7	39
Bisphosphonates	1	104
JAK Inhibitor	0	18
Non TNFi Biologic[a]	2	43
TNFi	52	469
DMARDs	44	610
Number of Events		New
Inflammatory Arthritis	27	18
Sacroiliitis	13	0
Inflammatory Bowel Disease	32	5
Psoriasis	26	37
Pustulosis	0	3
Hidradenitis	2	2
Celiac disease	6	2
Hashimoto Thyroiditis	6	0
Type 1 Diabetes	4	1
Acne Vulgaris	0	3
Infection Requiring IV Antibiotics	0	5[b]
Fracture (not vertebrae)[c]	12	17
All Spine Fractures	25	6
Height Loss	21	6
Vertebrae Plana	7	0
Amplified Pain Syndrome (fibromyalgia)	13	15

[a]Includes Abatacept, Canakinumab, Tocilizumab, Ustekinumab
[b]4 of the 5 patients were simultaneously treated with TNFi for CNO
[c]Most common were hand (8), tibia (5), femur (4), clavicle (3), arm (2)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

common vertebral and non-vertebral fracture sites were the thoracic spine (81%) and hand (26%) (Table 3). During follow-up, 333 patients received second-line treatments with one or more conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), tumor necrosis factor inhibitors (TNFi), bisphosphonates, or JAK inhibitors. Twenty-four (65%) of 37 patients who developed psoriasis after diagnosis were exposed to csDMARDs and/or TNFi at a mean of 2 years post-diagnosis. Additionally, four of five patients requiring intravenous antibiotics for infection were treated with TNFi within 60 days.

Conclusion: We were able to leverage CHOIR to estimate the frequency of various comorbidities, long-term risks, and growth impacts on children with CNO. Over 5-years of follow-up, the number of active spinal lesions on MRI decreased and fewer compression fractures occurred after diagnosis compared to before diagnosis. Growth metrics remained within normal range at the population level. The most common medical events after diagnosis of CNO were psoriasis and inflammatory arthritis.

Disclosure: J. Kent: None; **E. Wu**: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **M. Oliver**: None; **S. Lapidus**: None; **U. Akca**: None; **A. Liau**: None; **P. Kore**: None; **I. Muse**: None; **A. Klein**: None; **E. Deng**: None; **I. Hamilton**: None; **H. Chen**: None; **M. Nguyen**: None; **T. Li**: None; **A. Wilson**: None; **J. Morden**: None; **S. Yasin**: None; **A. Lenert**: None; **S. Stern**: None; **A. Insalaco**: None; **M. Pardeo**: Novartis, 2; **G. Simonini**: None; **E. Marrani**: None; **X. Wang**: None; **B. Huang**: None; **L. Kovallick**: None; **N. Rosenwasser**: None; **E. Balay-Dustrude**: None; **D. Mosa**: None; **K. Bouchalova**: None; **A. Cabova**: None; **J. Thomason**: None; **L. Tucker**: None; **H. Girschick**: None; **R. Iaxer**: Akros pharma, 2, Eli Lilly Canada, 2, Novartis, 2, Sanofi, 2; **M. Twilt**: None; **G. Tiller**: None; **J. Akikusa**: None; **C. Hedrich**: None; **K. Onel**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **P. Ferguson**: None; **Y. Zhao**: american board of pediatrics, 4, Bristol-Myers Squibb(BMS), 5, UpToDate, 9.

Abstract Number: 2129

Distinct endotypes of SURF associated with clinical phenotypes, inflammatory cytokines, and treatment responses

Marci Macaraeg[1], Nadine Saad[2], Tiphanie Vogel[3], Fatma Dedeoglu[4], Kyle McBrearty[4], Qin Sun[5], Chunyan Liu[5] and Grant Schulert[5], [1]University of Arizona College of Medicine, Tucson, AZ, [2]University of Michigan, Ann Arbor, MI, [3]Baylor College of Medicine, Houston, TX, [4]Boston Children's Hospital, Boston, MA, [5]Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Syndrome of Undifferentiated Recurrent Fevers (SURF) refers to patients with recurrent fevers who do not meet clinical or classification criteria for Periodic Fevers, Aphthous stomatitis, Pharyngitis, and Adenitis (PFAPA) syndrome or Hereditary Recurrent Fever syndromes (HRFs). Most studies on patients with SURF reveal heterogeneous presentations and responses to treatment. The aims of this study were to define endotype groups within SURF, and their treatment responses.

Methods: SURF was defined as at least 3 stereotypical recurrent fever episodes not fitting clinical criteria for PFAPA or HRFs. Patient data were collected from Cincinnati Children's Hospital Medical Center (CCHMC), University of Michigan (UofM), Texas Children's Hospital (TCH), and Boston Children's Hospital (BCH). Cytokine analysis was performed on

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Demographics	n=110
Ethnicity	*n (%)*
White/Caucasian	90 (81.2)
Black/African American	7 (6.4)
Asian	2 (1.8)
Hispanic	1 (0.9)
Native American	4 (3.6)
Hawaiian/Pacific Islander	0
Middle Eastern/North African	1 (0.9)
Other	2 (1.8)
Declined to answer	2 (1.8)
Mixed	2 (1.8)
Not reported	6 (5.5)
Gender	
Female	60 (54.5)
Male	50 (45.5)
Family History	
Recurrent Fevers	5 (4.5)
Autoinflammatory Disease	4 (3.6)
Inflammatory Bowel Disease	3 (2.7)
Autoimmune Disease	15 (13.6)

Patient Demographics

available samples. Patients were clustered using age and clinical characteristics by Partitioning Around Medoids (PAM), Hierarchical, and K-prototype clustering methods. Characteristics associated with treatment responses were analyzed using univariable and multivariable regression.

Results: A total of 110 patients were included (CCHMC=65, UofM=15, BCH=15, TCH=15). PAM clustering showed three main groups: group 1 (n=57) largely resembled PFAPA but with frequent abdominal pain and myalgia; group 2 (n=30) had rash and arthralgias; and group 3 (n=23) was fever predominant. Cytokine analysis of these clusters showed elevated levels of IFN- β in group 3, a group that was also more likely to have complete response to on demand steroids. Regression analyses supported that patients without musculoskeletal complaints tended to have a complete response to on demand steroids, patients without GI complaints tended to have complete response to colchicine, patients with anorexia tended to have a complete response to tonsillectomy/adenoidectomy, and that patients with headache and arthralgias tended to receive anti-IL1 treatment and have a complete response. Genetic analysis showed high enrichment for genes associated with innate immunity in Groups 1 and 2 (enrichment score 5.75 and 4.72, respectively).

Conclusion: We found three distinct groups of SURF patients: 1. PFAPA-like, 2. rash and arthralgias, and 3. fever predominant. This third group was immunologically distinct and most likely to respond to on-demand steroids. Groups 1 and 2 tended to have high enrichment scores for genes important in innate immunity. Larger prospective studies are needed to better define the groups that exist within SURF.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variable	Cluster 1 (n=57) n (%)	Cluster 2 (n=30) n (%)	Cluster 3 (n=23) n (%)	P-value
Age	3.8 (3.6)	2.3 (2.8)	2.0 (2.5)	**0.025**
Fatigue	29 (50.9)	14 (46.7)	14 (60.9)	0.577
Malaise	9 (15.8)	1 (3.3)	3 (13.0)	0.222
Headache	24 (42.1)	6 (20.0)	4 (17.4)	**0.036**
Enlarged lymph nodes	28 (49.1)	5 (16.7)	1 (4.3)	**<0.001**
Painful lymph nodes	3 (5.3)	0 (0.0)	1 (4.3)	0.537
Oral ulcers	35 (61.4)	5 (16.7)	0 (0.0)	**<0.001**
Pharyngitis	33 (57.9)	29 (96.7)	23 (100.0)	**<0.001**
Maculopapular rash	4 (7.0)	0 (0.0)	3 (13.0)	0.107
Unspecified rash	16 (28.1)	21 (70.0)	0 (0.0)	**<0.001**
Genital sores	2 (3.5)	0 (0.0)	0 (0.0)	0.715
Conjunctivitis	2 (3.5)	1 (3.3)	0 (0.0)	1.000
Photosensitivity	2 (3.5)	0 (0.0)	1 (4.3)	0.596
Periorbital edema	3 (5.3)	0 (0.0)	0 (0.0)	0.426
Other ocular	2 (3.5)	1 (3.3)	0 (0.0)	1.000
Mild Abdominal Pain	42 (73.7)	3 (10.0)	5 (21.7)	**<0.001**
Severe Abdominal Pain	3 (5.3)	0 (0.0)	0 (0.0)	0.426
Nausea	6 (10.5)	1 (3.3)	1 (4.3)	0.551
Emesis	11 (19.3)	3 (10.0)	4 (17.4)	0.585
Diarrhea	8 (14.0)	2 (6.7)	0 (0.0)	0.139
Anorexia	7 (12.3)	2 (6.7)	3 (13.0)	0.777
Arthralgia	31 (54.4)	24 (80.0)	0 (0.0)	**<0.001**
Myalgia	17 (29.8)	4 (13.3)	0 (0.0)	**0.003**
Arthritis	7 (12.3)	6 (20.0)	1 (4.3)	0.219

PAM Cluster Analysis of age and clinical characteristics

Treatments	Cluster 1 (n=57)	Cluster 2 (n=30)	Cluster 3 (n=33)	P-value
Trialed on NSAIDs	11 (20.0)	9 (30.0)	9 (40.9)	0.168
Complete response to NSAIDs	0 (0.0)	2 (22.2)	3 (37.5)	0.119
Trialed on On-demand steroids	37 (66.1)	12 (40.0)	12 (54.5)	0.065
Complete response to ODS	16 (47.1)	4 (33.3)	10 (83.3)	**0.033**
Received a T&A	14 (25.0)	4 (13.3)	7 (30.4)	0.282
Complete response to T&A	4 (30.8)	1 (33.3)	2 (33.3)	1.000
Complete response to colchicine	7 (22.6)	6 (31.6)	5 (55.6)	0.180
Trial of treatment with anti-IL1	27 (47.4)	8 (26.7)	11 (47.8)	0.143
Complete response to anti-IL1	13 (48.1)	4 (50.0)	7 (63.6)	0.681
Complete response to anakinra	5 (62.5)	1 (50.0)	0 (0.0)	0.697
Complete response to canakinumab	4 (50.0)	3 (50.0)	2 (100.0)	0.621

Treatment responses per cluster

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Macaraeg: None; **N. Saad**: None; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6; **F. Dedeoglu**: Sobi, 6, UptoDate, 9; **K. McBrearty**: None; **Q. Sun**: None; **C. Liu**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2.

Abstract Number: 2130

Systemic juvenile idiopathic arthritis- Fifteen-year experience from a tertiary centre at Bristol, United Kingdom

Ashwini Batchu Prithvi, Chaitra Govardhan, Bushra Aladaileh and Athimalaipet V Ramanan, Bristol Royal Hospital for Children, Bristol, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is a chronic disease that results in significant morbidity and mortality in children1. Improved understanding of the pathophysiology of sJIA has led to recent therapeutic advances including a growing evidence base for the earlier use of IL-1 or IL-6 blockade2. We aim to describe our experience of sJIA over a period of 15 years which includes clinical presentation, therapeutic interventions and the heterogeneity around the use of biologics spanning over this period, and the clinical outcomes at different time points over the course of the disease.

Methods: Children with a diagnosis of sJIA treated at Bristol Royal Hospital for children from 2010 to 2025 were included. Electronic medical records were reviewed retrospectively. Details regarding patient demographics, clinical features, laboratory parameters, treatment and outcomes were recorded. Patients were categorized as monocyclic, polycyclic and persistent depending on the disease course. Data was analyzed using descriptive statistics.

Results: A total of 80 children diagnosed with sJIA-29 (36.25%) monocyclic, 12(15%) polycyclic, 39(48.75%) were persistent. The mean age of diagnosis 7.6 (0.8-16) years. 43(53.75%) were females. Apart from fever (in 100%), other common presentations included rash 67(83.8%), arthritis 54(67.5%), splenomegaly 23(28.8%). Median(IQR) laboratory investigations at diagnosis included haemoglobin 98gm/L(85-112), white cell count $18*10^9$(10-26), platelets 411 $*10^9$(288-549), C-reactive protein 121mg/L(63-195), ESR 75mm/hr(25-136),D-dimer 3089ng/mL(1359-6106), LDH 501U/L(345-902), fibrinogen 5.2ng/mL(3.4-6.4), ferritin 1443mcg/L(459-4415), triglycerides 1.5mmol/L(1-2.3), ALT 26 U/L(12-65). Treatment received primarily was variable over the 15 year span and included combination of corticosteroids, disease modifying anti-rheumatic drug, IL-1 and IL-6 blockade. IL-1/IL-6 blocker therapy initiated in 15(18.8%) within 3 months of diagnosis and 39(48.7%) by the end of 1 year. Maximum disease inactivity off treatment was achieved in the monocyclic group(80.8%). Disease activity controlled on treatment was achieved in 62.5% in polycyclic and 56.4% in persistent group. At the end of 5 years, 5/8 in polycyclic and 6/30 in persistent achieved clinical remission off treatment.

Conclusion: sJIA is a disease with the variable course that determines the outcome. Based on our study, it has been observed that children in persistent category required combination of therapies to keep the disease under control.

1 Singh-Grewal D, Schneider R, Bayer N, Feldman BM. Predictors of disease course and remission in systemic juvenile idiopathic arthritis: significance of early clinical and laboratory features. Arthritis Rheum. 2006 May;54(5):1595–601.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table-1 Baseline demographic, clinical and laboratory characteristics at diagnosis

Table-1 Baseline demographic, clinical and laboratory characteristics at diagnosis

Clinical Information	Children with SJIA			
Category of sJIA n(%)	Monocyclic (n=29)	Polycyclic (n=12)	Persistent (n=39)	Over all (n=80)
Demographics				
Age at diagnosis, years (range)	8.97 (1.6-15)	6.75 (4.2-9.75)	7.0 (0.8 – 16)	7.6 (0.8 – 16)
Gender (M: n(%), F: n(%))	M:16 (55.2) F:13 (44.8)	M:8 (66.7) F:4 (33.3)	M: 13 (33.3) F: 26 (66.7)	M:37 (46.25) F: 43 (53.75)
Clinical manifestations				
Fever, n(%)	29(100)	12 (100)	39 (100)	80 (100)
Rash, n(%)	27(93.1)	8 (66.7)	32 (82.1)	67
Lymphadenopathy, n(%)	4(13.8)	2 (16.6)	10 (25.6)	16
Hepatomegaly, n(%)	6(20.7)	3 (25)	10 (25.6)	19
Splenomegaly, n(%)	8(27.6)	4 (33.3)	11 (28.2)	23
Serositis, n(%)	6(20.7)	1 (8.3)	2 (5.1)	9
Pleuritis (n)	2	0	1	3
Pericarditis (n)	3	1	1	5
Pleuritis+Pericarditis (n)	1	0	0	1
Arthralgia, n(%)	24 (82.8)	8 (66.7)	26 (66.7)	58
Arthritis, n(%)	14 (46.3)	8 (66.7)	32 (82.1)	54
Monoarthritis (n)	3	1	8	12
Oligoarthritis (n)	7	2	11	20
Polyarthritis (n)	3	5	13	21
MAS at diagnosis, n(%)	7 (24.1)	3 (25)	4 (10.3)	14
Bone marrow study n(%)	19 (65.5)		23 (59)	
Laboratory investigations				
Haemoglobin (IQR) gm/L	104 (85-115)	91 (73-115)	97 (86-106)	98 (85-112)
White cell count (IQR) * 10^9	17.9 (9.0 – 27.8)	14.5 (9.8-30.2)	17.2 (9.7-24.2)	18 (10-26)
Platelets (IQR) * 10^9	410 (272 - 511)	479 (262-743)	413 (280-590)	411 (288-549)
CRP (IQR) mg/L	134 (42-209)	90 (70-196)	121 (76-202)	121 (63-195)
ESR (IQR) mm/hour	71 (20 – 138)	47 (15-148)	82 (48-129)	75 (25-136)
Ferritin (IQR) mcg/L	1267 (525-2748)	2027 (998-6342)	2035 (389-5602)	1443 (459-4415)
D-dimer (IQR) ng/mL	3191 (1245-9492)	4972 (1909-9395)	2822 (1368-6495)	3089 (1359-6106)
LDH (IQR) U/L	513 (362-719)	1216 (740-1719)	450 (306-794)	501 (345-902)
Fibrinogen (IQR) ng/mL	5 (3 – 6.2)	3.9 (2.9-156.4)	5.4 (4.5-6.6)	5.2 (3.4-6.4)
Triglycerides (IQR) mmol/L	2 (0.9-2.2)	1.3 (0.3-4.9)	1.4 (1.0-2.2)	1.5 (1-2.3)
ALT (IQR) U/L	28 (18-65)	37.5 (10.3-63.6)	18 (10-64)	26 (12-65)

Table 2: Treatment received during the disease course

Table 2: Treatment received during the disease course

Treatment received within 3 months of diagnosis				
Oral/IV Glucocorticoids n(%)	25 (86.2)	8(66.6)	28(71.7)	61
Glucocorticoids+ DMARDs/IL-1/IL-6 blocker n(%)	2(6.8)	3(25)	10(25.6)	15
Glucorticoids+ Intravenous immunoglobulins n(%)	2(6.8)	1(8.4)	1(2.5)	4
Treatment received between 6 to 12 months of diagnosis				
Oral/IV Glucocorticoids n(%)	1(3.4)	1(8.3)	0	2
Methotrexate n(%)	1(3.4)	2(16.6)	9(23.0)	12
Glucocorticoids+ DMARD/IL-1/IL-6 blocker	2(6.8)	3(25.0)	14(35.8)	19
IL-1 blockade (anakinra), n(%)	1(3.4)	1(8.3)	5(12.8)	7
IL-6 blockade (Tocilizumab), n(%)	6(20.6)	2(16.6)	2(5.1)	10
Glucocorticoids+Mtx+Cyclosporine	0	1(8.3)	0	1
Glucorticoids+Etanercept+Mtx	0	0	2(5.1)	2
Anakinra+Mtx	0	0	2(5.1)	2
Other immune modulation				
Cyclosporine alone n(%)	0	2(16.6)	3(7.6)	5
Canakinumab n(%)	0	0	1(2.5)	1
Baricitinib n(%)	0	0	1(2.5)	1
No Treatment n(%)	19(65.5)	0	0	19
Treatment after 1 year				
Time since diagnosis, years (range)	4.9 (1 – 13)	9.2 (2 - 18)	7.3 (1-18)	
Oral/IV Glucocorticoids n(%)	0	0	0	0
Methotrexate n(%)	0	1(8.3)	9(23.0)	10
Glucocorticoids+Methotrexate	0	0	2(5.1)	2
IL-1 blockade (anakinra), n(%)	0	2(16.6)	3(7.6)	5
IL-6 blockade (Tocilizumab), n(%)	0	3(25.0)	6(15.4)	9
Tocilizumab+Methotrexate	0	0	7(17.9)	7
Other immune modulation				
Etanercept	0	1(8.3)	1(2.5)	2
Cyclosporine	0	1(8.3)	1(2.5)	2
Cyclosporine+Infliximab+Canakinumab	0	1(8.3)	0	1
Etanercept+Adalimumab	0	1(8.3)	0	1
Tocilizumab+Etanercept+Methotrexate	0	0	1(2.5)	1
Tocilizumab+Canakinumab+Cyclopsorine+Mtx	0	0	1(2.5)	1
Tocilizumab+Anakinra+Methotrexate	0	0	1(2.5)	1
Methotrexate+Adalimumab	0	0	1(2.5)	1
Steroids+Adalimumab	0	0	1(2.5)	1
Steroids+Baricitinib	0	0	1(2.5)	1
Etoposide	0	0	1(2.5)	1
No treatment n(%)	0	2(16.6)	0	2
No information	0	0	4(10.2)	4

2 Foley CM, McKenna D, Gallagher K, McLellan K, Alkhdher H, Lacassagne S, et al. Systemic juvenile idiopathic arthritis: The Great Ormond Street Hospital experience (2005-2021). Front Pediatr. 2023;11:1218312.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disease outcome following treatment

Disclosure: A. Batchu Prithvi: None; **C. Govardhan**: None; **B. Aladaileh**: None; **A. V Ramanan**: None.

Abstract Number: 2131

Transition from Juvenile Dermatomyositis to Spondyloarthritis: A Novel Overlapping Inflammatory Phenotype

Austen Grooms[1], Ioannis Karageorgiou[2], Kerry Mychaliska[2] and James Birmingham[3], [1]William Beaumont University Hospital, Auburn Hills, MI, [2]William Beaumont University Hospital, Royal Oak, MI, [3]River City Rheumatology, Grand Rapids, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile Dermatomyositis (JDM) is a rare inflammatory disease primarily affecting muscle, skin, and vasculature. Characterized by muscle weakness, distinctive skin lesions, and autoantibodies, it is thought to be driven predominantly by adaptive immunity. Conversely, Spondyloarthritis (SpA) represents a group of inflammatory disorders involving the axial skeleton and peripheral joints that are driven by both innate and adaptive immune mechanisms. Here we describe features in patients initially diagnosed with JDM who later developed SpA. The transition from JDM to SpA has not previously been reported.

Methods: This IRB (2024-180) exempt retrospective study collected demographic information, clinical symptoms, laboratory findings, imaging, treatments, and outcomes from a convenience sample of patients with JDM who subsequently developed SpA. Inclusion criteria were patients meeting diagnostic criteria for JDM before age 18 who later developed SpA using the Assessment of Spondyloarthritis International Society (ASAS) classification criteria and Classification Criteria for Psoriatic Arthritis (CASPAR). Exclusion criteria were patients who developed SpA before JDM or did not meet ASAS or CASPAR criteria. Descriptive statistics were used to examine data from patients with JDM to explore potential predictors associated with the subsequent development of SpA.

Results: A total of 7 patients met inclusion criteria; 57 % (4/7) were female, 86 % (6/7) were Caucasian. The mean age at diagnosis of JDM was 7.4 years (SD = 3.6) and the mean interval from JDM onset to SpA diagnosis was 11.7 years (SD = 6.9). In all patients with JDM diagnosis, neopterin was elevated in 100 % (4 /4) of patients tested and 100% (7/7) had myositis on Magnetic Resonance Imaging. Of these patients, 71 % (5/7) had additional complications prior to SpA onset (table 3).

Of those diagnosed with SpA, 100% (7/7) met ASAS criteria for peripheral SpA and 29 % (2/7) met CASPAR criteria. Lastly, 83 % (5/6) responded to standard treatment protocols for SpA, 1 was treated with rituximab and azathioprine for calcinosis, and 1 was lost to follow up. HLA-B27 was positive for 14 % (1/7) of patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1Patient Demographics

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Sex/Ethnicity	M/Caucasian	M/Caucasian	F/Caucasian	F/Caucasian	F/Caucasian	F/Caucasian	M/Hispanic
Current age (years)	26	38	20	26	9	21	34
Age of onset of JDM	10	8	5	13	2	6	8
Age of onset of SpA	16	22	18	20	7	20	33
Duration of Follow up (years from JDM to SpA)	16 (6)	17 (*)	15 (13)	13 (7)	7 (5)	14 (14)	2 (*)
Family History of autoimmune disease	none	none	none	Hashimoto's Thyroiditis / RA / Crohn's Disease	Raynaud's Syndrome / Sarcoidosis / RA	Grave's Disease	none

* Lost to follow up until onset of SpA symptoms. JDM: Juvenile Dermatomyositis. SpA: Spondylarthritis. RA: Rheumatoid Arthritis.

Table 2 Onset of Juvenile Dermatomyositis Features & Initial Treatment of Patients Prior to Onset of Spondyloarthritis

Disease Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Site of Muscle Weakness	Shoulders / Hips	Hips / Shoulders	Cervical /Shoulders / Hips	Cervical / Shoulders / Hips / Ankles	Shoulders / Hips	Shoulders / Hips	Hips
Cutaneous Findings	Gottron Sign	Gottron Sign / Raynaud's Syndrome / Telangiectasia	Gottron Sign	Heliotrope rash / Shawl Sign / Gottron Sign / Raynaud's Syndrome	Heliotrope Rash / Shawl Sign	Gottron sign / Heliotrope rash /Oral Ulcers	Gottron Sign
Other Systemic Symptoms	Abdominal Pain / Fever	Photosensitivity	Abdominal Pain / Fever	Abdominal Pain	Abdominal pain	Fever / Polycythemia	none
Muscle Biopsy Positive for JDM	Yes	NA	Yes	Yes	Yes	Insufficient sample	NA
MRI Consistent for JDM / Myositis	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Laboratory Findings at Disease Onset							
Aldolase (0-14.4 U/L)	12.2	NA	10.3	341	7.9	20.0	NA
Neopterin (2.0-10.0 nmol/L)	33.7	NA	25	50	NA	26.6	NA
ESR (0-15 mm/hr)	6	NA	17	17	2	19	NA
CRP (0.0-9.9 mg/L)	0.3	NA	0.2	0.9	0.3	1	NA
AST (10-40 U/L)	61	NA	40	363	38	346	NA
ALT (10-40 U/L)	56	NA	86	264	10	156	NA
Elevated CK (age dependent, units in U/L)	No (62)	NA	Yes (324)	Yes (17194)	No (172)	No (73)	NA
Elevated LDH (age dependent, units in U/L)	Yes (303)	NA	Yes (405)	Yes (1130)	No (185)	Yes (436)	NA
Autoantibodies	ANA, Antiscl-1, RF, SCL-70 (-)		ANA (+)	ANA, Antiscl-1, Centromere, Chromatin (+)	ANA (+)	ANA (-)	ANA (-), NXP2 (+)
Treatment Prescribed for JDM							
At diagnosis	HCQ/MTX/PDN (CR)	HCQ/MTX/PDN (*)	HCQ/MTX/PDN (CR)	HCQ/MTX/PDN (PR)	HCQ/MTX/PDN (CR)	HCQ/MTX/PDN (PR)	HCQ/MTX/PDN (*)
Subsequent treatments	HCQ/Meloxicam (CR)	Started on AZA 2008 (PR)	HCQ/Meloxicam (CR)	RTX for ILD (CR)	HCQ/MTX/Meloxicam (CR)	IVIG (CR); HCQ/MTX/Meloxicam (CR), HCQ/Meloxicam (CR)	*

* Lost to Follow-up; AZA: Azathioprine; CR: Complete Response; HCQ: Hydroxychloroquine; ILD: Interstitial Lung Disease; JDM: Juvenile Dermatomyositis; MTX: Methotrexate; NA: Not Available; PR: Partial Response; PDN: Prednisone; RTX: Rituximab; Unk: Unknown

CK Range: Case 1 (80-625 U/L); Case 2 (20-175 U/L); Case 4 (26-175 U/L); Case 5 (29-175 U/L); LDH Range: Case 1 (129-300 U/L); Case 2 (186-269 U/L); Case 4 (125-390 U/L); Case 5 (139-409 U/L); Case 6 (156-340 U/L)

Table 3 Onset of Spondyloarthritis Features & Subsequent Treatment

Disease Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Additional Complications Prior to Spa	none	Calcinosis / Squamous Cell Carcinoma	Hashimoto's Thyroiditis	ILD	none	Septic Shock / Adrenal Insufficiency	Esophagitis
Medications During Onset of Spa	HCQ / Meloxicam	AZA alone	HCQ / Meloxicam / Synthroid	HCQ / MTX / PDN / Hizentra	HCQ / MTX / Meloxicam	HCQ / Meloxicam	HCQ / MTX / PDN
Arthralgia (tender joint count)	Yes (10)	Yes (6)	Yes (8)	Yes (4)	Yes (4)	Yes (6)	Yes (4)
Arthritis (swollen joint count)	Yes (6)	Yes (6)	Yes (10)	Yes (6)	Yes (4)	Yes (12)	Yes (2)
Enthesitis (enthesitis count)	Yes (5)	Yes (2)	Yes (6)	Yes (4)	Yes (4)	Yes (11)	Yes (4)
Inflammatory Back Pain	Yes	No	Yes	Yes	No	Yes	Yes
Current Skin Psoriasis	No	No	No	Yes	Yes	No	No
Sacroiliitis on Imaging	Yes	NA	NA	Yes	NA	No	NA
Meets ASAS Axial Criteria	Yes	No	No	Yes	No	No	No
Meets ASAS Peripheral Criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Meets CASPAR PsA Criteria	No	No	No	Yes	Yes	No	No
Laboratory Findings at Disease Onset							
Aldolase (0-14.4 U/L)	8	NA	2	5.1	5	4.4	15.8
ESR (0-15 mm/hr)	2	NA	7	7	1	NA	8
CRP (0.0-9.9 mg/L)	NA	NA	<3.0	1.4	<0.3	<0.3	4.5
AST (10-40 U/L)	14	NA	17	21	34	25	64
ALT (10-40 U/L)	22	NA	14	16	20	23	40
Elevated CK (age dependent, units in U/L)	Yes (347)	NA	No (90)	No (68)	No (156)	No (97)	Yes (573)
Elevated LDH (age dependent, units in U/L)	No (176)	NA	No (121)	Yes (245)	Yes (286)	NA	Yes (334)
HLA-B27	Negative	Positive	Negative	NA	Negative	Negative	NA
Treatment Prescribed for SpA							
At diagnosis	ETN/HCQ/ Meloxicam (PR)	RTX (calcinosis)/AZA (CR)	ETN / Synthroid / Meloxicam (CR)	GOL/HCQ/Hizentra/ Meloxicam/MTX (PR)	HCQ / MTX / Meloxicam / TOF (CR)	HCQ/MTX/ Meloxicam (*)	ETN/ HCQ/ PDN/MTX (CR)
Subsequent treatments	ADA/HCQ/ Meloxicam (CR)	-	-	ABA/HCQ/Hizentra/ Meloxicam/MTX/UPA (PR)	-	-	-

* Lost to follow up; ABA: Abatacept; ADA: Adalimumab; AZA: Azathioprine; CR: Complete Response; Etanercept: ETN; GOL: Golimumab; HCQ: Hydroxychloroquine; ILD: Interstitial Lung Disease; JDM: Juvenile Dermatomyositis; MTX: Methotrexate; NA: Not Available; PR: Partial Response; PDN: Prednisone; PsA: Psoriatic Arthritis; RTX: Rituximab; SpA: Spondylarthritis; TOF: Tofacitinib; UPA: Upadacitinib

CK Range: Case 1 (80-225 U/L); Case 2 (20-175 U/L); Case 4 (26-175 U/L); Case 5 (26-180 U/L); Case 6 (29-143 U/L); Case 7 (80-225 U/L); LDH Range: Case 1 (186-228 U/L); Case 3 (188-210 U/L); Case 4 (160-229 U/L); Case 5 (140-280 U/L); Case 7 (180-280 U/L)

Conclusion: This preliminary small study identified a cohort of patients diagnosed with JDM, an adaptive immune disease, who later were diagnosed with SpA, an innate driven illness. The clinical and serologic data examined offer some data points that may support the novel idea that there are predictors of disease overlap. However, future research is required to better understand this possible evolution from an adaptive to an innate immune disease state and inform predictive models.

Disclosure: A. Grooms: None; **I. Karageorgiou**: None; **K. Mychaliska**: None; **J. Birmingham**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2132

The Bridge to Adult Care from Childhood for Young Adults with Rheumatic Disease (BACC YARD) Program, a Pediatric-To-Adult Rheumatology Transition Program, Reduces Median Time between Final Pediatric, First Adult, and Second Adult Visits

Ayah Eltoum[1], Eileen Rife[2], Livie Timmerman[3], Emily Smitherman[4], Melissa Mannion[4] and John Bridges[5], [1]University of Alabama at Birmingham, Hoover, AL, [2]University of Alabama Birmingham, Vestavia Hills, AL, [3]University of Alabama at Birmingham, Gardendale, AL, [4]University of Alabama at Birmingham, Birmingham, AL, [5]University of Alabama at Birmingham/Children's of Alabama, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The transition from pediatric to adult-oriented rheumatology care is a critical period for young adults with childhood-onset rheumatic diseases. The Bridge to Adult Care from Childhood for Young Adults with Rheumatic Disease (BACC YARD) Program offers a dual provider pre-transfer visit to facilitate successful transition. This study evaluates whether the dual provider pre-transfer visit improves intervals for subsequent adult rheumatology visits, compared to historical controls without a formal pre-transfer visit.

Methods: We conducted a retrospective cohort study of 189 young adults with childhood-onset rheumatic disease who transferred from Children's of Alabama to the University of Alabama, Birmingham adult rheumatology clinic. The intervention group (n=144) enrolled in the BACC YARD Program between July 2020-April 2024 and completed a dual provider pre-transfer visit. The historical control group (n=45) transferred between March 2018-February 2020 without a structured pre-transfer visit. The primary exposure was participation in the BACC YARD program and the primary outcome was the number of days from the last pediatric visit to the first adult visit. Secondary outcomes included the interval (in days) between first and second adult visits, and adherence to provider-recommended follow-up intervals. Wilcoxon rank-sum and Kruskal-Wallis tests were used to compare median intervals between groups. Logistic regression models were used to estimate associations between successful adherence to provider-recommended intervals, adjusted for age, sex, race, ethnicity, and diagnosis in the BACC YARD group.

Table 1: Patient Characteristics, BACC YARD and Historical Control Cohorts

	Overall	BACC YARD Cohort	Historical Control Cohort
Total (n)	189	144	45
Age in years, median (range)	20 (17-27)	20 (17-27)	19 (17-22)
Sex, Female n (%)	148 (78)	108 (75)	40 (88.9)
Race n (%)			
White	126 (66.7)	99 (68.8)	27 (60.0)
Black	62 (32.8)	44 (30.6)	18 (40.0)
Asian	1 (0.5)	1 (0.7)	0 (0)
Ethnicity n (%)			
Hispanic	14 (7.4)	10 (6.9)	4 (8.9)
Rheumatic Disease of Childhood n (%)			
JIA	105 (55.6)	82 (56.9)	23 (51.1)
SLE and related CTDs	56 (29.6)	39 (27.1)	17 (37.8)
Other*	28 (14.8)	23 (16.0)	5 (11.1)

*Other included vasculitis, uveitis, inflammatory myopathy, relapsing polychondritis, morphea, and autoinflammatory syndromes

BACC YARD: Bridge to Adult Care from Childhood for Young Adults with Rheumatic Disease; CTD: connective tissue disease; JIA: juvenile idiopathic arthritis; SLE: systemic lupus erythematosus

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Characteristics, BACC YARD and Historical Control Cohorts

Table 2: Days from last pediatric visit to first adult visit, BACC YARD Cohort vs Historical Control Cohort

	BACC YARD from Children's of Alabama Transferred to UAB (7/2020-4/2024, N=144)		Historical Control Cohort from Children's of Alabama Transferred to UAB (3/2018-2/2020, N=45)		p value[1]
Diagnosis	**n**	**Median (range)**	**n**	**Median (range)**	
JIA	82	148 (9-553)	23	316 (17-1810)	0.0145
SLE	39	120 (20-391)	17	169 (8-1308)	0.2187
Other*	27	172 (97-358)	5	1281 (76-1888)	0.0412
Total	**144**	143 (9-553)	**45**	261 (8-1888)	0.0049

[1]p <0.05 indicates significance. Wilcoxon rank-sum test was used to compare medians.
*Other included vasculitis, uveitis, inflammatory myopathy, relapsing polychondritis, morphea, and autoinflammatory syndrome
BACC YARD: Bridge to Adult Care from Childhood for Young Adults with Rheumatic Disease; JIA: juvenile idiopathic arthritis; SLE: systemic lupus erythematosus

Table 3: Days from first to second adult visit, BACC YARD Cohort (7/2020-4/2024, N=144)

		Requested^ follow-up interval	Actual follow-up interval	p value[1]
Diagnosis	**n**	**Median (range)**	**Median (range)**	0.4220
JIA	82	123 (31-488)	153 (28-360)	
SLE	39	92 (59-365)	128 (63-488)	
Other*	27	122 (31-366)	152 (22-605)	
Total	**144**	122 (31-488)	148 (22-605)	

^Requested timing for adult rheumatology visits was determined by joint decision between the adult/pediatric rheumatologist and the childhood pediatric rheumatologist
[1]p <0.05 indicates significance. Kruskal-Wallis test was used to compare medians.
*Other included vasculitis, uveitis, inflammatory myopathy, relapsing polychondritis, morphea, and autoinflammatory syndrome
BACC YARD: Bridge to Adult Care from Childhood for Young Adults with Rheumatic Disease; JIA: juvenile idiopathic arthritis; SLE: systemic lupus erythematosus

Results: The median age was 20 years in both cohorts. Females comprised 75% of the BACC YARD group and 89% of the control group. Juvenile idiopathic arthritis (JIA) was the most common diagnosis (56%, n=105) in both cohorts, followed by systemic lupus erythematosus (SLE) (30%, n=56). The BACC YARD group demonstrated significantly shorter median time from the last pediatric to the first adult visit compared to controls (143 vs. 261 days, p=0.0049), particularly among patients with JIA (148 vs. 316 days, p=0.0145). No significant difference was observed for patients with SLE. Among the BACC YARD group, the median interval between the first and second adult visits was 148 days (range: 22 to 605), with no significant differences across diagnosis groups. 71% (n=102) had their first adult visit within 30 days of their recommended follow-up date with no factors significantly associated with first visit adherence. 58% (n=83) had a second visit within 30 days of their recommended follow-up date. Hispanic patients were 80% less likely to adhere to the second visit compared to non-Hispanic patients (OR= 0.2, 95% CI: 0.05-0.90, p=0.035).

Conclusion: Participation in the BACC YARD program was associated with a shorter time interval to initial adult rheumatology clinic visit, particularly for patients with JIA. While most patients in the program continued to adhere to recommended timing for follow-up, disparities were observed by ethnicity in second visit adherence. These findings support embedding pre-transfer coordination into transition models to improve continuity for adolescents with rheumatic disease.

Disclosure: A. Eltoum: None; **E. Rife**: None; **L. Timmerman**: None; **E. Smitherman**: None; **M. Mannion**: None; **J. Bridges**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2133

Examination of HLA-DRB1*15-linked Candidate Antigens in Still's Disease with and without Lung Disease and Features of Drug Hypersensitivity

Dale Kobrin[1], Garrett Brown[2], Mariana Correia Marques[1], Carol Lake[3], Michelle Millwood[4], Lisa Workman[5], Monica Lawrence[5], Zuoming Deng[6], Sanchita Das[2] and Michael Ombrello[7], [1]Translational Genetics and Genomics Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [2]Department of Laboratory Medicine, National Institutes of Health, Bethesda, MD, [3]NIH, GAITHERSBURG, MD, [4]National Institutes of Health (NIH), Bethesda, MD, [5]Division of Asthma, Allergy, and Immunology, University of Virginia School of Medicine, Charlottesville, VA, [6]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [7]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), North Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Lung disease in systemic juvenile idiopathic arthritis and adult-onset Still's disease (Still's-LD) is a severe manifestation that strongly associates with features of drug hypersensitivity reactions (fDHR), including eosinophilia, non-Still's rashes, and elevated liver function tests. In patients with Still's disease, both LD and fDHR are strongly associated with HLA-DRB1*15 alleles; however, the pathogenesis of these phenomena remain unknown. This study investigates whether Still's-LD and fDHR are associated with pathogenic antigens through hypersensitivity reactions to *Aspergillus*

Table 1: Clinical characteristics and results of testing for Aspergillus fumigatus antibodies and viral nucleic acids Continuous variables are presented as mean ± standard deviation (range), categorical variables are presented as N (% of non-missing values). LD: lung disease, fDHR: features of drug hypersensitivity reactions, PAH: pulmonary arterial hypertension, TTE: transthoracic echocardiography, RHC: right heart catheterization, LFT: liver function test, EBV: Epstein-Barr virus, CMV: cytomegalovirus, HHV-6: human herpesvirus 6. Anti-Aspergillus fumigatus IgE via ImmunoCap Allergen m3 assay. EBV, CMV, and HHV-6 nucleic acids by PCR and/or VIRTUS.

	Hypersensitivity (N=8)	Lung disease (N=11)	Neither (N=36)	P value (LD + fDHR vs neither)
Age at diagnosis, mean ± SD (range), years	7.7 ± 9.9 (1.1 - 30.6)	16.4 ± 13.6 (1 - 34.9)	22.2 ± 16.6 (3 - 66.9)	
Disease duration, mean ± SD (range), months	66.3 ± 38.6 (18 - 125)	39.5 ± 26 (10 - 87)	75.1 ± 122.5 (3 - 635)	
Female	5 (63%)	8 (73%)	27 (75%)	
Still's like	0 (0%)	0 (0%)	6 (17%)	
Exposed to anakinra, canakinumab, tocilizumab	8 (100%)	11 (100%)	27 (75%)	
DRB1*15:XX	6 (75%)	8 (73%)	7 (19%)	
Lung Disease Details				
Parenchymal disease		9 (82%)		
PAH (N=8)		5 (63%)		
Features of Drug Hypersensitivity				
Eosinophilia	3 (38%)	5 (45%)		
Elevated LFTs	2 (25%)	6 (55%)		
Drug reactions	3 (38%)	5 (45%)		
Atypical rashes	7 (88%)	10 (91%)		
Number of features, mean ± SD (range)	1.6 ± 0.7 (1 - 3)	2.4 ± 0.9 (1 - 4)		
Aspergillus Testing	**N=4**	**N=6**	**N=23**	
Aspergillus fumigatus	0 (0%)	0 (0%)	0 (0%)	1
Viral Testing	**N=8**	**N=11**	**N=31**	
EBV	0 (0%)	0 (0%)	2 (9%)	0.52
CMV	0 (0%)	0 (0%)	0 (0%)	1
HHV-6	0 (0%)	0 (0%)	0 (0%)	1
Viral testing within 1 year	3 (38%)	8 (73%)		

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

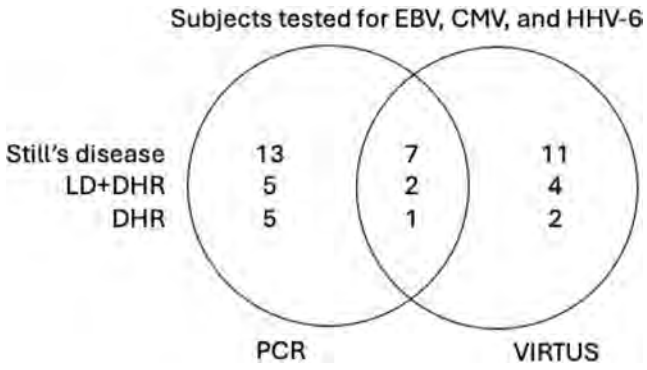


Figure 1: Subjects tested for EBV, CMV, and HHV-6 by PCR and VIRTUS

fumigatus, for which HLA-DRB1*15 is a known risk allele, or drug reaction with eosinophilia and systemic symptoms (DRESS), which is frequently associated with human herpesvirus reactivation.

Methods: Pediatric and adult subjects were drawn from the NIH Still's disease cohort, subjects with Still's-LD and/or fDHR were identified by chart review. Serum samples were analyzed for anti-*Aspergillus fumigatus* IgE via ImmunoCap assay. Subjects were screened for EBV, CMV, and HHV-6 by PCR assay for viral nucleic acids and/or Viral Transcript Usage Sensor (VIRTUS) analysis of whole blood RNAseq data for viral transcripts. The prevalence of anti-*Aspergillus fumigatus* IgE antibodies and viral nucleic acids were compared between groups using two-tailed Fisher's exact tests with a significance level set at 0.05.

Results: Fifty-five subjects were included in the study, 11 had LD and fDHR and 8 had fDHR alone. Thirty-three subjects were tested for anti-*Aspergillus* antibodies and all were negative. Fifty subjects were tested for EBV, CMV, and HHV-6, 23 by PCR only, 17 by VIRTUS only, and 10 by both PCR and VIRTUS. All subjects were negative for CMV and HHV-6 by PCR and VIRTUS. Two subjects without LD or fDHR had detectable EBV nucleic acids by PCR and no subjects with LD or fDHR had detectable EBV by PCR or VIRTUS, a difference which was not statistically significant ($p = 0.52$). Of those tested for viral nucleic acids, 11/19 (58%) had testing performed within 1 year of active LD or fDHR.

Conclusion: The absence of anti-*Aspergillus* IgE antibodies and detectable herpesvirus nucleic acids in subjects with Still's-LD and fDHR does not support a mechanistic association with hypersensitivity to *Aspergillus fumigatus* or with human herpesvirus reactivation. Additional work is needed to improve the mechanistic understanding of Still's-LD and fDHR.

Disclosure: D. Kobrin: None; **G. Brown**: None; **M. Correia Marques**: None; **C. Lake**: None; **M. Millwood**: None; **L. Workman**: None; **M. Lawrence**: Pharming, 2, Takeda, 5; **Z. Deng**: None; **S. Das**: None; **M. Ombrello**: None.

Abstract Number: 2134

Krebs von den Lungen-6 (KL-6) as a Potential Diagnostic Biomarker of Lung Disease in Pediatric Systemic Juvenile Idiopathic Arthritis: Preliminary Findings from a Multisite US Cohort

Eileen Rife[1], Lexi Auld[2], Guihua Zhai[3], Esraa Eloseily[4], Grant Schulert[5] and Yukiko Kimura[6] For the CARRA Registry Investigators, [1]University of Alabama at Birmingham, birmingham, AL, [2]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [3]UAB, Birmingham, [4]UT Southwestern Children's Medical Center, Dallas, TX, [5]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [6]Hackensack Meridian School of Medicine, New York, NY

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

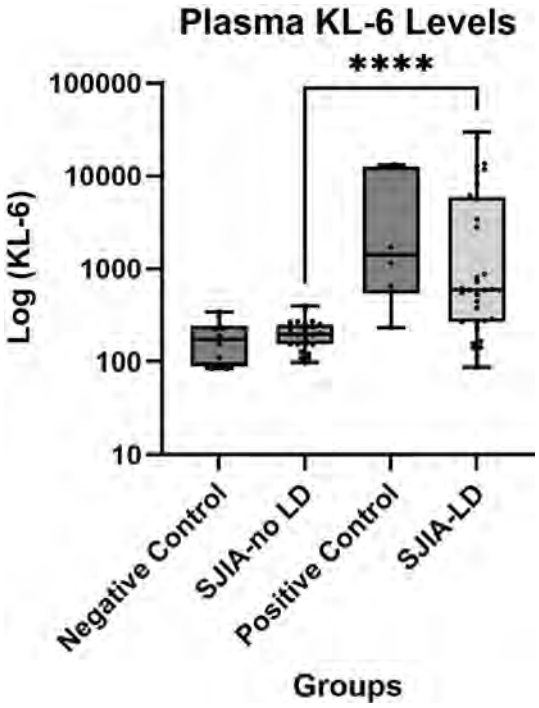
SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Children with Systemic Juvenile Idiopathic Arthritis (SJIA) who develop lung disease (LD) are at significantly increased risk of serious complications and even death. Early detection and intervention are critical for improving outcomes and stabilizing disease progression. However, diagnosing LD in children presents many unique challenges. No single pulmonary measurement can be easily applied for diagnosis and conventional methods are not always safe or feasible in young children. Krebs von den Lungen 6 (KL-6) is a promising diagnostic and prognostic blood-based biomarker of LD in adult studies, however its utility in pediatric LD is unclear. This study evaluates KL-6 as a diagnostic biomarker for LD in pediatric patients with SJIA.

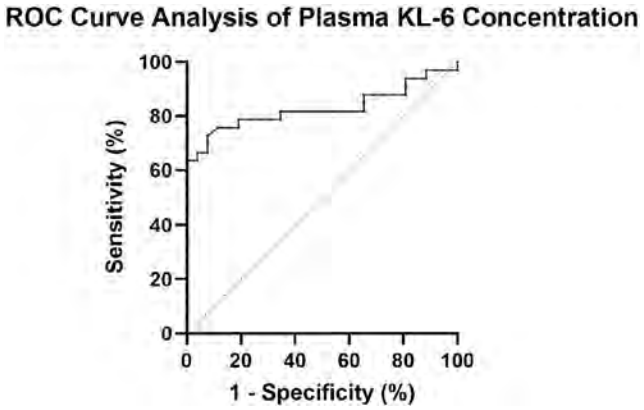
Methods: Thirty-three patients enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry (from 18 US clinical sites) SJIA-LD cohort were included. As comparators, we included 26 patients with SJIA and no LD (SJIA-no LD) from the CARRA First-Line Options for SJIA Treatment (FROST) study, 6 children with primary protein alveolar proteinosis (PAP) as positive controls and 10 healthy children as negative controls. The primary outcome was plasma KL-6 concentration in each group as quantitated by ELISA. Secondary outcomes included clinical characteristics associated with elevated KL-6 levels.

Results: Median plasma KL-6 level in SJIA-LD was 593 U/mL (interquartile range [IQR]:268-5,896), compared to 194 U/mL (IQR:152-253) in the SJIA-no LD group (p< 0.0001) and 172 U/ml (IQR:89-245) in healthy controls (p=0.0003). No significant difference was observed between SJIA-LD and PAP patients (593 vs. 1430, p=0.258). At a cut-off of 260 U/mL by receiver operating curve (ROC), plasma KL-6 yielded a sensitivity of 79% and specificity of 81% for SJIA with LD (area under



Box and Whisker plot of Plasma KL-6 Concentrations within each group - median, interquartile range (IQR), and outliers displayed. Median plasma KL-6 concentration in SJIA-LD was 593 U/mL (IQR:268-5,896); 194 U/mL (IQR:152-253) in the SJIA-no LD group (p<0.0001) and 172 U/ml (IQR:89-245) in healthy controls (p=0.0003). **** = p<0.0001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



ROC analysis of the plasma KL-6 concentration in systemic juvenile idiopathic arthritis-associated lung disease (SJIA-LD) with SJIA-no LD as the control. At a cut-off of 260 U/mL, plasma KL-6 yielded a sensitivity of 79% and specificity of 81% for SJIA-LD (area under the curve = 0.83, p<0.0001). A cut-off of 421 U/mL yielded a sensitivity of 63% with specificity reaching 100%.

the curve = 0.83, p< 0.0001). At a cut-off of 421 U/mL, sensitivity was 63% with specificity reaching 100%. Clinical features in SJIA-LD associated with higher mean KL-6 levels included tachypnea on examination (7,627 vs. 1,719, p=0.03), hypoxemia on pulse oximeter (9,769 vs. 3,096, p=0.049), abnormal chest-Xray findings (3,177 vs. 198, p=0.04), and steroid requirement at any point (6,156 vs. 449, p=0.01). The Physician Global Assessment of Lung Disease (PGALD) was strongly correlated with mean KL-6 (r=0.75, p< 0.0001). KL-6 levels were not significantly associated with the presence of macrophage activation syndrome (p=0.66) or markers of systemic inflammation: C-reactive protein, ferritin, interleukin (IL)-18, CXCL9, or sIL2r. We were unable to evaluate the relationship between computed chest tomography (CT) abnormalities and KL-6 levels as there was an insufficient number of CT scans performed within a month of the blood sample.

Conclusion: KL-6 is a useful diagnostic biomarker of LD in pediatric SJIA; a cut-off level of 421 U/mL yielded a specificity of 100% in our cohort. Future efforts should focus on the utility of KL-6 for monitoring disease progression, evaluating treatment response, and for predicting long-term disease trajectories.

Disclosure: E. Rife: None; **L. Auld**: None; **G. Zhai**: None; **E. Eloseily**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **Y. Kimura**: None.

Abstract Number: 2135

Medication Use and Disease Activity in Systemic Juvenile Idiopathic Arthritis in the Childhood Arthritis and Rheumatology Research Alliance Registry

Christina Gulla[1], Mary Beth Son[2], Tara Lozy[3], Yukiko Kimura[4], **Ginger Janow**[5] and the CARRA Registry Investigators, [1]Hackensack University Medical Center, Hackensack, NJ, [2]Boston Children's Hospital, Boston, MA, [3]Joseph M. Sanzari Children's Hospital, Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Nutley, [4]Hackensack Meridian School of Medicine, New York, NY, [5]Joseph M. Sanzari Children's Hospital at Hackensack Meridian Health, Hackensack, NJ

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic characteristics

Characteristics	Entire cohort of SJIA patients in Registry	sJIA patients enrolled ≥ 60 days	Eligible sJIA patients enrolled < 60 days		
	n=920	n=737	n=183	Effect Size	P value
Female, n (%)*	486 (52.8)	390 (52.9)	96 (52.5)	0.00	0.93
Age at diagnosis (Year), median (IQR)**	6 (3 - 10)	5 (3 - 9)	7 (4 - 11)	0.12	<.001
Disease duration (Month), median (IQR)**	12 (2 - 39)	19 (6 - 51)	1 (1 - 2)		
Race, n (%)*					
Asian	46 (5.1)	33 (5.0)	13 (7.3)	0.05	0.13
Black	89 (9.8)	73 (11.1)	16 (9.0)	0.01	0.68
White	597 (65.8)	482 (73.4)	115 (64.6)	0.01	0.70
Other	85 (9.4)	69 (10.5)	16 (9.0)	0.01	0.85
Hispanic Ethnicity, n (%)*	90 (9.9)	72 (9.8)	18 (10.1)	0.00	0.92
Median time from symptom onset to diagnosis (Month), median (IQR)**	1 (1 - 2)	1 (1 - 3)	1 (0 - 2)	0.05	0.14

* Effect size calculated using Phi (interpretation: Small = 0.1, Medium = 0.3, Large = 0.5)

** Effect size calculated using Cohen's d (interpretation: Small = 0.2, Medium = 0.5, Large = 0.8)

Background/Purpose: Historically, treatment for systemic juvenile idiopathic arthritis (sJIA) included high dose glucocorticoids (GC) and conventional systemic (cs) disease modifying anti-rheumatic drugs (DMARDs) with significant side effects and poor outcomes. While studies of sJIA patients treated with biologic (b) DMARDs (i.e. IL-1 inhibitors (IL-1i) and IL-6 inhibitors (IL-6i) demonstrated decreased GC use and improved outcomes, less is known regarding longer term outcomes. Using data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, we aimed (1) to describe longitudinal trends in medication use over the first 24 months of disease and (2) assess the impact of increased early biologic use on GC use & disease activity (DA) in this observational registry.

Methods: Patients with sJIA enrolled in the CARRA Registry between 2015-2024 were stratified based on disease duration at enrollment. Those enrolled within 60 days of diagnosis and had clinical data at enrollment visit (EV), 6 mo and 12 mo were included in medication and DA analysis. DA assessments included fever, use of systemic GC, and clinical juvenile arthritis disease activity score based on 10 joints (cJADAS10). Chi-Square and Mann–Whitney tests were used to compare the

Figure 1: Medication use over time

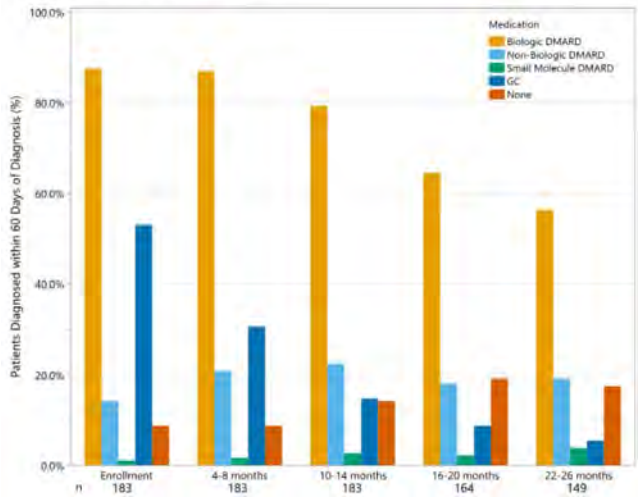


Figure 1: Medication use over time

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

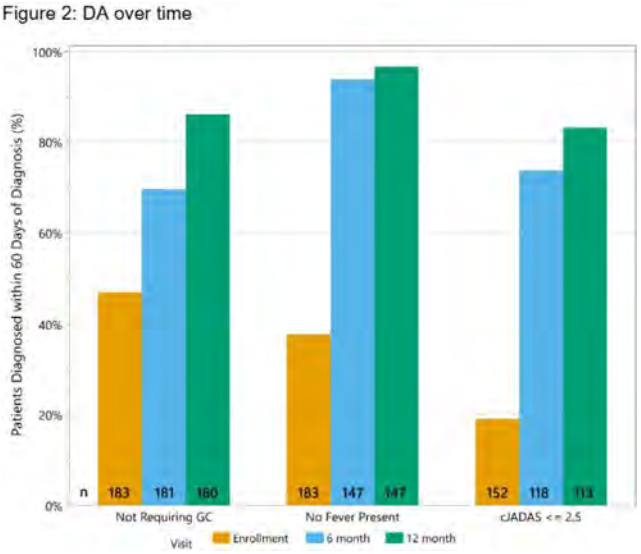


Figure 2: DA over time

study cohort with all SJIA patients enrolled in the registry. Summary statistics were used to describe medication usage and DA at 6 mo intervals.

Results: Of 920 patients with sJIA, 183 patients (19.9%) met recent diagnosis criteria. Median time from symptom onset to diagnosis was 1 mo (IQR 1-2mo) (Table 1). 87.4% were started on a bDMARD within 60 days of diagnosis (37.7% anakinra and 16.9% canakinumab), and 79.2% were on a bDMARD at some point during their 2 year course (Fig 1). 56.6% of patients who started anakinra switched to canakinumab and 6.5% started on canakinumab switched to anakinra. Of the 12 patients whose first bDMARD was an IL6i, 16.7% switched to an IL1i. bDMARD use decreased over time 79.2% at 12 mo and 18.3% at 24 mo). 14.2% were off all medications by 12 mo and 17.5% by 24 mo (Fig 1). GC use decreased over time, with 64.5% at EV, 30.6% at 6 mo and 13.6% at 12 mo. 14.8% had inactive disease per cJADAS10 (< 2.5) at EV, with 83.2% achieving inactive disease by 12 mo (Fig 2).

Conclusion: Overall, baseline features of recently diagnosed sJIA patients were not significantly different from other sJIA patients in the Registry. Despite the high incidence of bDMARD use within the first 60 days of diagnosis, nearly half of all patients were exposed to GC early in disease course. The proportion of patients achieving inactive cJADAS10 with or without fever reached 64% and 59.6% respectively by 12mo. At 2 years of follow-up, 17.5% of patients were off all medication.

Disclosure: C. Gulla: None; **M. Son**: None; **T. Lozy**: Eli Lilly & Company, 11; **Y. Kimura**: None; **G. Janow**: None.

Abstract Number: 2136

Confirming The Validity Of The New EULAR/ACR Classification Criteria For Pediatric Chronic Nonbacterial Osteomyelitis

Greta Mastrangelo[1], Edan Itzkovitz[2], Katherine Sawicka[3], Ingrid Goh[4], Ari Bitnun[5], Sevan Hopyan[5], Paul Nathan[2], Ronald laxer[1] and Brian Feldman[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]The Hospital for Sick Children, Toronto, [3]The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada, [4]University of Toronto The Hospital for Sick Children, Toronto, ON, Canada, [5]The Hospital for Sick Children, Toronto, Canada

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is a noninfectious autoinflammatory bone disease which remains a diagnosis of exclusion, as existing diagnostic criteria are not widely accepted. Recently, the European Alliance of Associations for Rheumatology (EULAR) and the American College of Rheumatology (ACR) developed new classification criteria for CNO, demonstrating 82% sensitivity and 98% specificity in an initial study.

We aimed to investigate sensitivity and specificity of the new EULAR/ACR classification criteria for pediatric CNO, in a distinct real-world clinical setting and compare it to the sensitivity and specificity of the existing Jansson and Bristol diagnostic criteria.

Methods: This was a single-center cross-sectional study including children ≤18 years, diagnosed with CNO, acute infectious osteomyelitis (AOM) and bone malignancy from June 1, 2018 to May 31, 2024. Patients with other mimicking conditions, immunodeficiency, sickle cell disease, or those previously included in the original development cohort were excluded. Patients were divided into two groups: a CNO group and a non-CNO group (AOM and bone malignancy), from the latter a representative, random, sample was selected (www.random.org). Demographic, clinical, laboratory, imaging and pathology data were collected at disease onset. EULAR/ACR criteria were retrospectively applied to the entire cohort, independently from the initial diagnosis. Patients with an aggregate score ≥ 55 points were classified as having CNO. A sensitivity analysis was also conducted where patients with criteria with missing data were excluded. Classification results using the new criteria were compared with the final clinical diagnosis based on physician assessment (criterion standard). The same analysis was applied to Jansson and Bristol criteria. From contingency tables, sensitivity and specificity were calculated.

Results: Of the 164 children included, 82 had CNO, 41 were randomly selected from 274 cases of AOM, and 41 from 849 cases of bone malignancy. The median age was 10 years (IQR 3–16), with 62% girls and 37% boys, 66% had a bone biopsy. Overall, 40% scored ≥ 55 and 60% did not, with 3 false positive and 19 false negative (Table 1). The EULAR/ACR criteria demonstrated 77% sensitivity and 96% specificity, with a positive predictive value (PPV) of 95% and negative predictive value (NPV) of 80%. In our sensitivity analysis excluding patients with incomplete data, results remained consistent (sensitivity 79%, specificity 96%, PPV 95%, NPV 81%). In comparison, the Jansson criteria showed 78% sensitivity, 67%

Table 1. Contingency Table of EULAR/ACR Criteria Performance in Classifying Pediatric CNO

Category	EULAR/ACR CNO Positive (≥ 55)	EULAR/ACR CNO Negative (<55)
CNO	63	19
Non-CNO	3	79

Table 2. Comparison of Diagnostic Performance Across CNO Classification Criteria

Criteria	Sensitivity	Specificity	PPV	NPV
EULAR/ACR	77%	96%	95%	80%
EULAR/ACR (sensitivity analysis)	79%	96%	95%	81%
Jansson	78%	67%	70%	75%
Bristol	89%	70%	86%	74%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

specificity, PPV of 70%, and NPV of 75%. The Bristol criteria yielded 89% sensitivity, 70% specificity, PPV of 86%, and NPV of 74% (Table 2).

Conclusion: Based on its favorable sensitivity and specificity, especially in comparison to existing criteria, the new EULAR/ACR criteria appeared to be more effective in distinguishing CNO from AOM and bone malignancy at disease onset. These results were consistent with findings from the original validation cohort.

Disclosure: G. Mastrangelo: None; **E. Itzkovitz**: None; **K. Sawicka**: None; **I. Goh**: None; **A. Bitnun**: None; **S. Hopyan**: None; **P. Nathan**: None; **R. Iaxer**: Akros pharma, 2, Eli Lilly Canada, 2, Novartis, 2, Sanofi, 2; **B. Feldman**: Cabelleta, 1, Pfizer, 12, DSMB.

Abstract Number: 2137

Therapeutic Strategies in Newly Diagnosed Still's Disease: Real-Life Clinicians' Choices from the METAPHOR Project Worldwide Survey

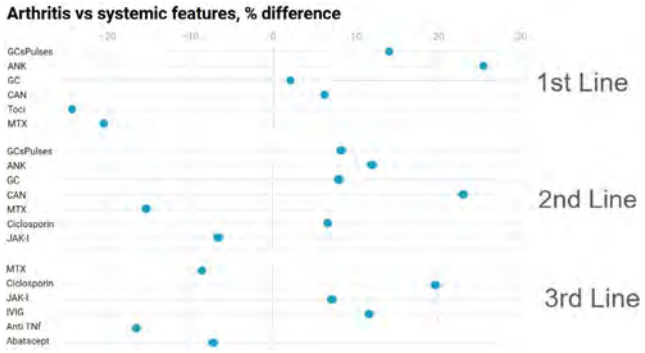
Francesco Baldo[1], **Greta Rogani**[2], Claudia Bracaglia[3], Dirk Foell[4], Marco Gattorno[5], Jordi anton[6], Paul Brogan[7], Scott Canna[8], randy Cron[9], Alexiei GROM[10], Merav Heshin Bekenstein[11], Raju Khubchandani[12], Seza zen[13], Pierre Quartier[14], Angelo Ravelli[15], Grant Schulert[16], Mao Mizuta[17], Joost Swart[18], Rashmi Sinha[19], AnnaCarin Horne[20], Fabrizio De Benedetti[21], Christiaan Scott[22], Marija Jelusic[23], Masaki Shimizu[24], Bruno Fautrel[25], Nicolino Ruperto[26], Sebastiaan Vastert[2], Francesca Minoia[27] PReS MAS/sJIA Working Party, [1]ASST-Pini-CTO, Milano, Milan, Italy, [2]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [3]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Rome, Italy, [4]Universisty Hospital of Muenster, Muenster, [5]IRCCS G. Gaslini, Genova, Genoa, Italy, [6]Hospital Sant Joan de Du. Universitat de Barcelona, Barcelona, Spain, [7]UCL Institute of Child Health and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [8]Children's Hospital of Philadelphia, Philadelphia, PA, [9]University of Alabama at Birmingham, Birmingham, AL, [10]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [11]Tel Aviv Medical Center Israel, Binyamina, Tel Aviv, Israel, [12]Jaslok Hospital and Research Center, Mumbai, India, [13]Hacettepe University Medical Faculty, Ankara, Turkey, [14]Hôpital Necker-Enfants Malades, Paris, France, [15]IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genoa, Genoa, Italy, [16]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [17]Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan, Kobe, Japan, [18]Wilhelmina Children's Hospital / UMC Utrecht, Utrecht, Utrecht, Netherlands, [19]Systemic JIA Foundation, Cincinnati, OH, [20]Karolinska University Hospital, Sollentuna, Sweden, [21]Bambino Gesu Children's Hospital, Rome, Rome, Italy, [22]Childrens Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada, [23]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Zagreb, Croatia, [24]Tokyo Medical and Dental University, Bunkyo-ku, Kanazawa, Japan, [25]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [26]Universit Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy, [27]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Milan, Italy

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite continuous advances in care and the recent publication of updated international recommendations, relevant discrepancies in the management of Still's disease (SD) may still exist, due to different clinical presentation and practice setting. The aim of the study is to assess current intial treatment strategies in SD worldwide, and to identify factors influencing clinical decision-making.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize treatment in SD and macrophage activation syndrome, a global survey on SD treatment was developed and distributed (Dec 3, 2024–Feb 14, 2025). Topics were selected by 22 experts. The survey included demographic data, clinical practice insights, a patient-led section on unmet needs. International physicians part of the PReS/PRINTO network and adult rheumatologists involved in SD care were invited to complete the anonymous online survey (Dec 3, 2024–Feb 14, 2025).

Results: A total of 206 clinicians, mainly pediatric rheumatologists (91%), from 56 countries completed the survey. In newly diagnosed SD patients without MAS, 34% of respondents would initiate anti-IL1/IL6 biologic without glucocorticoids (GCs); the rest would use GCs alone (24%) or in combination with biologics (42%). Factors favoring GCs use included severe pericarditis (64%), severe arthritis (55%), and refractory disease risk factors (16%), as hyperferritinemia, lung involvement, early onset and Trisomy 21.Anakinra was the most frequently used biologic in 1st line (59%), followed by Tocilizumab (25%). Only 1.5% reported unavailability of any anti-IL1/IL-6 therapy. Factors driving anakinra's choice were safety (72%), cost (41%), and predominant systemic phenotype (73%), while Tocilizumab was chosen for compliance (56%) and arthritis-dominant profile (80%). Difficult access to medication influenced decisions for Rilonacept (67%), Canakinumab (27%), Anakinra (17%); Tocilizumab was rarely unavailable (1.5%).In systemic-predominant SD, clinicians used NSAIDs (50%), GCs (46%), GCs pulses (42%),

and Anakinra (45%) as first-line options. Second-line strategies included Tocilizumab (39%), GCs (31%), Anakinra (29%), GCs pulses (22%), and MTX (21%), while Tocilizumab (37%), JAK inhibitors (29%), and cyclosporin (24%) were the most selected options as third-line therapies. In SD patients with a prominent articular involvement at onset, half of the respondents would not change their therapeutic approach. Physician who modified thor strategy would use as a first line f therapies GCs (47%), oral steroids (44%), Tocilizumab (39%), MTX (34%), and intra-articular steroids (31%). Second-line choices were mostly Tocilizumab and MTX (~40%). Differences in management by clinical phenotype are detailed in Figure 1.

Conclusion: Still's disease still represents a therapeutic challenge, mainly due to its heterogeneity in clinical expression. Our data reveals significant differences in treatment approaches, driven by clinical phenotype and drug availability. Future research is essential to optimize clustering of patients to foster tailored target treatments, while ensuring equitable access to effective therapies worldwide.

Disclosure: F. Baldo: None; **G. Rogani**: None; **C. Bracaglia**: None; **D. Foell**: None; **M. Gattorno**: Fresenius Kabi SwissBioSim GmbH, 6, Novartis, 1, 2, 5, 6, SOBI, 2, 6; **J. anton**: Sobi, 1, 5, 6; **P. Brogan**: Sobi, 6; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **r. Cron**: AbbVie/Abbott, 1, American Board of Pediatrics, 12, Board Question Writer, AS2 Biotherapeutics, 2, Career-Physician, 1, Neurogene, 2, Pfizer, 1, Sobia, 1, Springer, 9, VIDA Ventures, 2; **A. GROM**: National Institutes of Health, 5, Novartis, 2, 5, sJIA Foundation, 5, Sobi, 2, 5, Up-To-Date, 9; **M. Heshin Bekenstein**: None; **R. Khubchandani**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **P. Quartier**: AbbVie, 2, 6, Chugai-Roche, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 1, 2, Sobi, 2, 6; **A. Ravelli**: AbbVie, 2, 5, 6, Alexion, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, SOBI, 2, 5, 6; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **M. Mizuta**: None; **J. Swart**: None; **R. Sinha**: None; **A. Horne**: None; **F. De Benedetti**: AbbVie, 2, 5, Apollo, 2, 5, Elixiron, 2, 5, Kiniksa, 2, 5, Novartis, 2, 5, Sanofi, 2, 5, Sobi, 2, 5; **C. Scott**: None; **M. Jelusic**: None; **M. Shimizu**: None; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **F. Minoia**: None.

Abstract Number: 2138

Factors driving therapeutic decision-making in Still's Disease: When to Start and When to Stop? Data from the METAPHOR Project Worldwide Survey

Francesco Baldo[1], **Greta Rogani**[2], Claudia Bracaglia[3], Dirk Foell[4], Marco Gattorno[5], Marija Jelusic[6], Jordi Anton[7], Paul Brogan[8], Scott Canna[9], Randy Cron[10], Fabrizio De Benedetti[11], Alexei Grom[12], Merav Heshin Bekenstein[13], AnnaCarin Horne[14], Raju Khubchandani[15], Mao Mizuta[16], Seza Kzen[17], Pierre Quartier Dit Maire[18], Angelo Ravelli[19], Masaki Shimizu[20], Grant Schulert[12], Christiaan Scott[21], Rashmi Sinha[22], Nicolino Ruperto[23], Joost Swart[24], Bruno Fautrel[25], Sebastiaan Vastert[2] and Francesca Minoia[26], [1]ASST-Pini-CTO, Milano, Milan, Italy, [2]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [3]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Rome, Italy, [4]University Hospital Muenster, Muenster, Germany, [5]IRCCS G. Gaslini, Genova, Genoa, Italy, [6]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Zagreb, Croatia, [7]Hospital Sant Joan de Déu. Universitat de Barcelona, Esplugues de Llobregat (Barcelona), Spain, [8]UCL Institute of Child Health and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [9]Children's Hospital of Philadelphia, Philadelphia, PA, [10]University of Alabama at Birmingham, Birmingham, AL, [11]Bambino Gesu Children's Hospital, Rome, Rome, Italy, [12]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [13]Tel Aviv Medical Center Israel, Binyamina, Tel Aviv, Israel, [14]Karolinska University Hospital, Sollentuna, Sweden, [15]SRCC Childrens Hospital Mumbai, Mumbai, India, [16]Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan, Kobe, Japan, [17]Hacettepe University Medical Faculty, Ankara, Turkey, [18]Necker hospital, Paris Cedex 15, France, [19]IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genoa, Genoa, Italy, [20]Tokyo Medical and Dental University, Bunkyo-ku, Kanazawa, Japan, [21]Childrens Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada, [22]Systemic JIA Foundation, Cincinnati, OH, [23]Universitä Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy, [24]Wilhelmina Children's Hospital / UMC Utrecht, Utrecht, Utrecht, Netherlands, [25]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [26]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Milan, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Despite continuous improvement in care and the recent update of international recommendations, relevant discrepancies in the diagnostic and treatment approach to Still's disease (SD) may still exist, in particular in the timing and factors influencing treatment start and withdraw. The study was aimed to explore current global treatment strategies for SD, focusing on parameters driving the decision-making process at treatment start and at withdrawal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize treatment in SD and macrophage activation syndrome, a global survey on SD treatment was developed based. Topics were selected by 22 experts, including 1 patient representative and 1 adult rheumatologist. The survey included demographic data, clinical practice insights, a patient-led section on unmet needs. International physicians part of the PReS/PRINTO network and adult rheumatologists involved in SD care were invited to complete the anonymous online survey (Dec 3, 2024–Feb 14, 2025).

Results: A total of 206 responses, mainly from pediatric rheumatologists (91%) from 56 countries were collected. Infectious tests performed at SD onset included TB, EBV, and blood cultures (80%), parvovirus, HBV, HCV, and SARS-CoV-2 (50%). Most physicians performed peripheral blood smears (85%), while 54% bone marrow aspiration, 38% immunophenotyping and 17% bone marrow biopsy. Imaging was commonly performed, with chest X-ray, abdominal ultrasound, and echocardiography as the most frequent investigations (∼80%). Among biomarkers, ferritin was almost always tested, while IL-18 (25%), S100 proteins (19%), and HLA-DRB1*15 (17%) were less frequently assessed. Before starting glucocorticoids (GCs) 68% of clinicians deemed certain investigations mandatory: bone marrow aspiration (74%), blood coltures and TB screening (50%), chest-abdomen CT scan and bone marrow biopsy (∼20%).

Beginning of steroid tapering was guided mostly by clinical and laboratory parameters: acute phase reactants (95%) and ferritin (87%) reduction, fever resolution (82%, ≥1 week: 37%; ≥72h: 29%; ≥2 weeks: 16%), arthritis improvement (75%), steroid side effects (42%); 29% and 25% requires normalization of acute phase reactants and ferritin, respectively, to start GCs tapering. More than half of physicians took patient/parent-reported outcomes (51% global VAS, 35% pain VAS) in consideration.

Steroid discontinuation required at least 4-6 weeks of inactive disease for 40% of participants, and ≥3 months for 34%. Biologics withdrawal was considered after at least 6 months (35%), 1 year (35%) and 3 months (36%) of inactive disease. Factors driving biologics withdrawal were similar to ones influencing steroid tapering.

Conclusion: A considerable heterogeneity in clinical practice still exist, in particular in

timing and factors guiding treatment tapering and withdrawal. Fostering harmonization of management of SD is essential to ensure consistent and optimal care for patients across different clinical settings

Disclosure: F. Baldo: None; **G. Rogani**: None; **C. Bracaglia**: None; **D. Foell**: None; **M. Gattorno**: Fresenius Kabi SwissBioSim GmbH, 6, Novartis, 1, 2, 5, 6, SOBI, 2, 6; **M. Jelusic**: None; **J. Anton**: None; **P. Brogan**: Sobi, 6; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **R. Cron**: AbbVie/Abbott, 12, MAS Adjudication committee, American Board of Pediatrics, 12, Question writer for pediatric rheumatology boards, AS2 Biotherapeutics, 2, 12, Data Safety monitoring board, CareerPhysician, 1, 2, Neurogene, 2, Pfizer, 12, MAS Adjudication committee, Sobi, 1, 2, 5, Springer, 9, VIDA Ventures, 2; **F. De Benedetti**: AbbVie, 2, 5, Apollo, 2, 5, Elixiron, 2, 5, Kiniksa, 2, 5, Novartis, 2, 5, Sanofi, 2, 5, Sobi, 2, 5; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9; **M. Heshin Bekenstein**: None; **A. Horne**: None; **R. Khubchandani**: None; **M. Mizuta**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **P. Quartier Dit Maire**: AbbVie/Abbott, 2, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai-Roche, 6, Lilly, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, SOBI, 2, 5; **A. Ravelli**: AbbVie, 2, 5, 6, Alexion, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, SOBI, 2, 5, 6; **M. Shimizu**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **C. Scott**: None; **R. Sinha**: None; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6; **J. Swart**: None; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **F. Minoia**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2139

Real-Life Treatment Strategies for Refractory Still's Disease: Results from a Worldwide Survey, the METAPHOR Project

Greta Rogani[1], Francesco Baldo[2], Claudia Bracaglia[3], Dirk Foell[4], Marco Gattorno[5], Marija Jelusic[6], Jordi Anton[7], Paul Brogan[8], Scott Canna[9], Randy Cron[10], Fabrizio De Benedetti[11], Alexei Grom[12], Merav Heshin Bekenstein[13], AnnaCarin Horne[14], Raju Khubchandani[15], Mao Mizuta[16], Seza zen[17], Pierre Quartier Dit Maire[18], Angelo Ravelli[19], Masaki Shimizu[20], Grant Schulert[12], Christiaan Scott[21], Rashmi Sinha[22], Nicolino Ruperto[23], Joost Swart[24], Bruno Fautrel[25], Sebastiaan Vastert[1], Francesca Minoia[26] and PReS MAS/sJIA Working Party, [1]University Medical Center Utrecht, Utrecht, Utrecht, Netherlands, [2]ASST-Pini-CTO, Milano, Milan, Italy, [3]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Rome, Italy, [4]University Hospital Muenster, Muenster, Germany, [5]IRCCS G. Gaslini, Genova, Genoa, Italy, [6]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Zagreb, Croatia, [7]Hospital Sant Joan de Du. Universitat de Barcelona, Esplugues de Llobregat (Barcelona), Spain, [8]UCL Institute of Child Health and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom, [9]Children's Hospital of Philadelphia, Philadelphia, PA, [10]University of Alabama at Birmingham, Birmingham, AL, [11]Bambino Gesu Children's Hospital, Rome, Rome, Italy, [12]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [13]Tel Aviv Medical Center Israel, Binyamina, Tel Aviv, Israel, [14]Karolinska University Hospital, Sollentuna, Sweden, [15]SRCC Childrens Hospital Mumbai, Mumbai, India, [16]Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan, Kobe, Japan, [17]Hacettepe University Medical Faculty, Ankara, Turkey, [18]Necker hospital, Paris Cedex 15, France, [19]IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genoa, Genoa, Italy, [20]Tokyo Medical and Dental University, Bunkyo-ku, Kanazawa, Japan, [21]Childrens Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada, [22]Systemic JIA Foundation, Cincinnati, OH, [23]Universit Milano Bicocca and Fondazione IRCSS S. Gerardo dei Tintori, Monza, Monza and Brianza, Italy, [24]Wilhelmina Children's Hospital / UMC Utrecht, Utrecht, Utrecht, Netherlands, [25]Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136-5, PARIS, France, Paris, France, [26]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Milan, Italy

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The outcome of Still's disease (SD) has significantly improved due to new therapeutic options [37923864], early biologic initiation [24623686] and treat-to-target strategies [39317417]. Nonetheless, a substantial proportion of patients still experiences a refractory course, severely impacting their quality of life. Treatment strategies in these

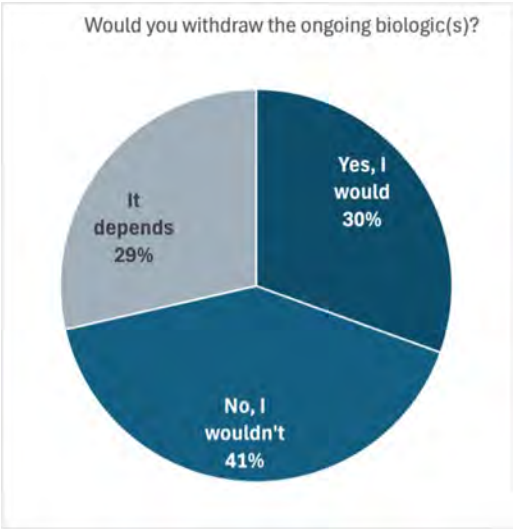


Figure 1 – Answer to the question "In a patient with Still disease and first detection of lung involvement while on therapy with IL-1 or IL-6 inhibitors, would you withdraw the ongoing biological treatment?"

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

cases are not standardized and are affected by medication availability and clinician experience. This real-life study aims to describe current treatment practices and major unmet needs, fostering a uniform approach to refractory SD.

Methods: As part of the METAPHOR project, a PReS/PRINTO initiative to optimize therapy in SD and Macrophage Activation Syndrome (MAS), a global survey on refractory SD treatment was developed, with the following proposed subtypes: 1) persistent arthritis, 2) recurrent/refractory MAS and 3) SD-associated lung disease (SD-LD). Topics were selected by 22 expert pediatric rheumatologists, including 1 patient representative and 1 adult rheumatologist. The survey covered demographic data, clinical practice insights and a patient-focused section on unmet needs. International physicians part of the PReS/PRINTO network together with adult rheumatologists involved in SD care were invited to complete the web-survey between 3/12/24 and 14/2/25.

Results: A total of 206 physicians completed the survey, predominantly pediatric rheumatologists (91%), from 56 countries. Methotrexate was the most common 1st-line choice for SD-refractory arthritis, followed by anti-TNF agents and intra-articular steroids. JAK inhibitors (JAK-i) were considered mainly as 2nd- or 3rd-line option. If systemic symptoms co-occurred, 62% of respondents would modify their strategy, favoring methylprednisolone (MPN) pulses, JAK-i and ciclosporin. In SD patients with recurrent/refractory MAS, ciclosporin, anakinra, and MPN pulses were the most frequently selected medications. Treatment decisions were mainly guided by clinical severity, inflammatory markers, history of ICU admission and concomitant complications. Biomarkers played a minor role, partly due to limited access, reported by 22% of clinicians. For SD-LD, 41% would continue ongoing biologics, 30% withdraw and 29% decide case by case (figure 1).

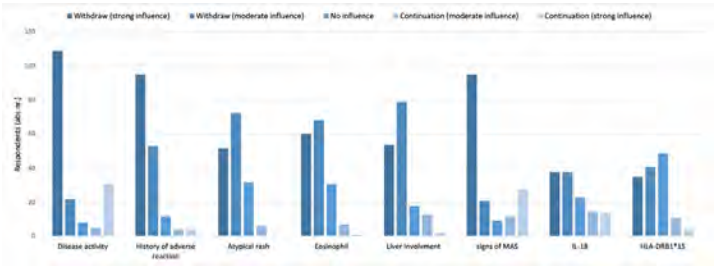


Figure 2 - Answer to the question: "In a patient with Still disease and first detection of lung involvement while on therapy with IL-1 or IL-6 inhibitors, which parameters influence your decision regarding withdrawal/continuation of IL-1 or IL-6 blockade"

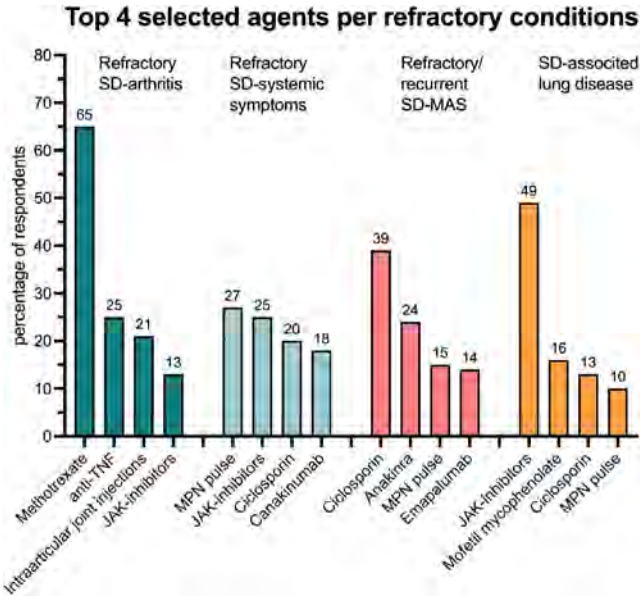


Figure 3 - Top 4 most commonly used first line agents for each subtype of refractory SD

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Factors influencing withdrawal included persistent disease activity, history of adverse reactions and impending MAS. HLA genotyping was rarely considered relevant (figure 2). The most used 1st-line agents for SD-LD included JAK-i, mycophenolate mofetil, and ciclosporin and only 8% would add Pneumocystis Jiroveci prophylaxis. Most respondents (82%) would consider Hematopoietic Stem-Cell Transplantation (HSCT) in difficult-to-treat SD patients, particularly for refractory MAS or SD-LD. Differences in management by clinical phenotype are detailed in figure 3.

Conclusion: Management for refractory SD is widely heterogeneous and varies by phenotype. JAK-i are the most commonly used agents alongside standard therapies and HSCT is increasingly considered a potential option, especially for refractory MAS and SD-LD. A consensus effort is essential to refine the definition and identify optimal treatment strategies for refractory cases.

Disclosure: G. Rogani: None; **F. Baldo**: None; **C. Bracaglia**: None; **D. Foell**: None; **M. Gattorno**: Fresenius Kabi SwissBioSim GmbH, 6, Novartis, 1, 2, 5, 6, SOBI, 2, 6; **M. Jelusic**: None; **J. Anton**: None; **P. Brogan**: Sobi, 6; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6; **R. Cron**: AbbVie/Abbott, 12, MAS Adjudication committee, American Board of Pediatrics, 12, Question writer for pediatric rheumatology boards, AS2 Biotherapeutics, 2, 12, Data Safety monitoring board, CareerPhysician, 1, 2, Neurogene, 2, Pfizer, 12, MAS Adjudication committee, Sobi, 1, 2, 5, Springer, 9, VIDA Ventures, 2; **F. De Benedetti**: AbbVie, 2, 5, Apollo, 2, 5, Elixiron, 2, 5, Kiniksa, 2, 5, Novartis, 2, 5, Sanofi, 2, 5, Sobi, 2, 5; **A. Grom**: Novartis, 2, 5, Sobi, 2, 5, UpToDate, 9; **M. Heshin Bekenstein**: None; **A. Horne**: None; **R. Khubchandani**: None; **M. Mizuta**: None; **S. Kzen**: Novartis, 6, Pfizer, 6, Sobi, 6; **P. Quartier Dit Maire**: AbbVie/Abbott, 2, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Chugai-Roche, 6, Lilly, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, SOBI, 2, 5; **A. Ravelli**: AbbVie, 2, 5, 6, Alexion, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Galapagos, 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, SOBI, 2, 5, 6; **M. Shimizu**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **C. Scott**: None; **R. Sinha**: None; **N. Ruperto**: Abbvie, 2, 6, AClaris, 2, 6, AlfaSigma, 2, 6, Amgen, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol Myers and Squibb, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genentech, 2, 6, Guidepoint, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Takeda, 2, 6; **J. Swart**: None; **B. Fautrel**: AbbVie, 2, 5, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Chugai, 2, Eli Lilly & Co., 2, 5, Fresenius Kabi, 2, Galapagos, 2, Janssen, 2, Medac, 2, MSD, 2, 5, Nordic Pharma, 2, Novartis, 2, OW KIN, 2, Pfizer, 2, 5, Roche, 2, Sandoz, 2, Sanofi-Genzyme, 2, SOBI, 2, UCB, 2, Viatris, 2; **S. Vastert**: Novartis, 2, 6, Sobi, 2, 5, 6; **F. Minoia**: None.

Abstract Number: 2140

Identification of immune phenotypes in systemic juvenile idiopathic arthritis associated lung disease (SJIA-LD) using high parameter flow cytometry

Haeja Kessler[1], Noel Gibson[1], Alyssa Sproles[2], Celine Lages[1], Paul Dascani[3], Sherry Thornton[4] and Grant Schulert[4] For the CARRA Registry Investigators, [1]Cincinnati Children's Hospital Medical Center, Cincinnati, [2]Cincinnati Children's Hospital, Cincinnati, OH, [3]Cytek Biosciences, Pittsburgh, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (sJIA) is a unique subtype of juvenile idiopathic arthritis with life threatening complications including macrophage activation syndrome and chronic lung disease. Chronic lung disease

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Specificity	Fluorochrome	Purpose
Viability	Zombie NIR	Viability
CD45RA	cFluor V450	T Cells, NK Cells
CD56	BV750	NK Cells
PD-1	BV785	T Cell Inhibitory Receptor
IFN-gamma	Vio515	Cytokine
CXCR3	BUV737	Chemokine receptor; dendritic cell, T cell, B cell activation
HLA-DR	cFluor B690	Monocyte, B Cells
CD38	BV711	Monocyte, Dendritic Cell, T Cell, B cell activation
Granzyme B	AlexaFluor 647	NK Cells
CD4	cFluor YG584	CD4 T Cells, NKT-like cells
CCR7	BV421	M1/M2 Marker, T Cell subsetting
CD8	PE-Fire 700	CD8 T Cells, NK Cells, NKT-like Cells
CD127	APC R700	Cytokine Receptor; T Cell differentiation
CD3	BV570	Pan T Cell, NKT-like Cells
CD19	cFluor R685	B Cells
CCR6	BUV661	Immature Dendritic Cells and Memory T Cells
CD27	cFluor R840	T Cell and B Cell Differentiation
CD25	BV480	T Regulatory
CCR4	BV605	TH2 Chemokine Receptor
CD152	PE-Cy5	Activated T Cells
CD16	cFluor BYG610	Monocyte subsetting, NK Cells
CD119	BV650	IFN-gamma alpha receptor
CD11c	cFluor BYG781	Myeloid, Dendritic cells
CD14	cFluor B548	Monocyte Subsetting
CD11b	BUV805	Myeloid
CXCL9	APC	IFN-induced chemokine
CD163	PE	Monocyte/Macrophage
CD45	cFluor R780	Leukocytes

Table 1: High Parameter Flow Cytometry Panel

encompasses interstitial lung disease, pulmonary fibrosis, pulmonary arterial hypertension, and pulmonary alveolar proteinosis, and associated with poor prognosis. The immunopathogenesis of sJIA lung disease (sJIA-LD) is poorly understood but has been associated with unique lymphocyte activation signatures. Our objective was to define myeloid and lymphoid subsets from sJIA-LD patients using high-parameter flow cytometry, and to correlate differences with disease activity.

Methods: Peripheral blood mononuclear cells (PBMC) were obtained from the CARRA Registry sJIA-LD cohort, after informed consent and approval from the CARRA Biorepository. Controls were healthy control children enrolled at CCHMC after informed consent. Full spectrum flow cytometry using the Auora platform was utilized, and cell populations were identified using manual gating. Previously reported from our lab, a high parameter flow cytometry panel (28-parameters) was created to investigate myeloid and lymphoid cell subsets (Table 1). Graph Pad PRISM was used to visualize and analyze the data. Statistical analysis utilized unpaired two-tailed t-test or Mann-Whitney for data that was not normally distributed. Relationships between physician global assessment of lung disease (PGALD) and cell populations used simple linear regression.

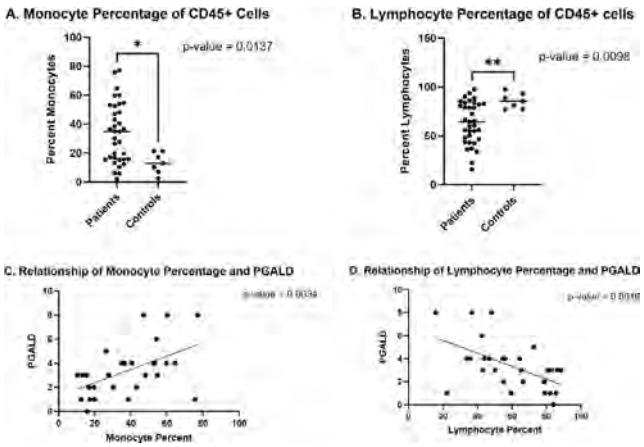


Figure 1: A. Percent monocytes of CD45+ cells B. Percent lymphocytes of CD45+ cells C. Relationship between PGALD and monocyte percentage D. Relationship between PGALD and lymphocyte percentage

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

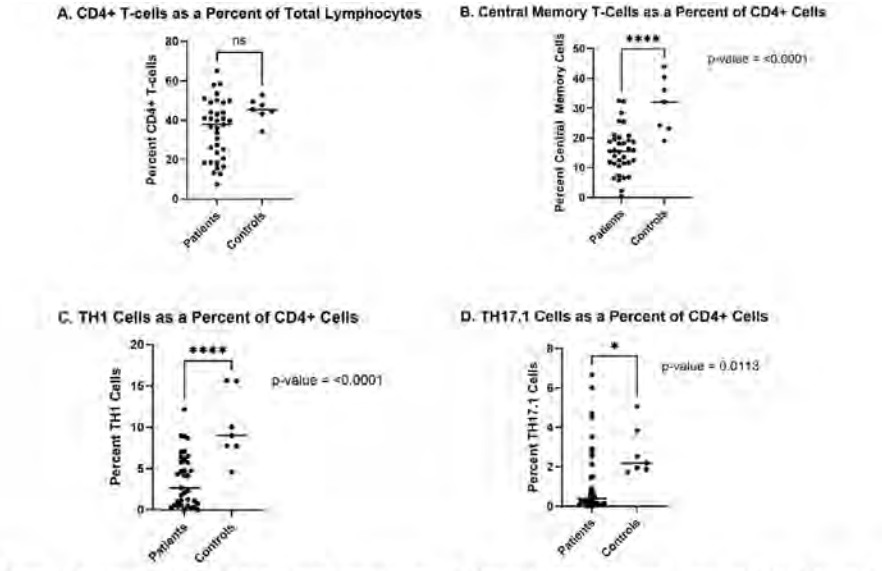


Figure 2: A. Percent CD4+ T-cells of total lymphocytes B. Percent central memory T-cells of CD4+ T-cells C. Percent TH1 cells of CD4+ T-cells D. Percent TH17.1 cells of CD4+ cells. Mann-Whitney analysis was used given data was not normally distributed

Results: We examined samples from 35 sJIA-LD patients and 7 controls. There was no significant difference between the number of live singlet cells and percentage of CD45+ cells in patients compared to controls. Overall, sJIA-LD patients had a significant increase in circulating monocyte percentage compared to controls, but no difference in relative abundance of monocyte subpopulations. There was a significant positive correlation between monocyte percentage and PGALD score, where a higher monocyte percentage correlates with higher PGALD score (R^2=0.2761, p< 0.0034). We also found a significant decrease in lymphocyte percentage, with lower percentages similarly correlating with a higher PGALD score (Fig. 1). The sJIA-LD patients had similar percentages of CD4+ cells compared to controls. Further subdivision of CD4+ T-cells revealed a significantly lower percentages of central memory T-cells, Th1 cells, and Th17.1 cells in patients compared to controls (Fig. 2). We did not find any significant differences between CD8+ cells and their subsets.

Conclusion: Our results demonstrate an increase in peripheral monocytes in SJIA-LD patients, the degree of expansion positively correlated with higher disease activity. We also find differences in circulating lymphocyte profile in sJIA-LD patient versus controls. The consequences of this decrease in Th1, Th17.1, and central memory T-cells is unknown. Our future work involves comparison with SJIA patients without lung disease, as well as unsupervised analysis and evaluation of activation markers – all in hopes to better understand disease pathogenesis and predictors of disease severity in sJIA-LD.

Disclosure: H. Kessler: None; **N. Gibson**: None; **A. Sproles**: None; **C. Lages**: None; **P. Dascani**: None; **S. Thornton**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2.

Abstract Number: 2141

Treatment of Refractory Still's/Systemic Juvenile Idiopathic Arthritis Lung Disease with the bi-specific IL-1Beta/IL-18 neutralizing antibody MAS825

Hallie Carol[1], Monica Manglani[2], Abass Noor[2], Edward Behrens[3], Jon Burnham[4], Jessica Lee[2], Jordan Moreno[2], Alexandra Chop[5], Kader Cetin Gedik[6], Catherine Poholek[7], Ginger Janow[8], Lindsay Waqar-Cowles[1] and Scott Canna[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, [3]CHOP, West Chester, PA, [4]Children's Hospital of Philadelphia, Bryn Mawr, PA, [5]UPMC, Pittsburgh, PA, [6]UPMC Children's Hospital of Pittsburgh/University of Pittsburgh, Pittsburgh, PA, [7]University of Pittsburgh, Pittsburgh, PA, [8]Joseph M. Sanzari Children's Hospital at Hackensack Meridian Health, Hackensack, NJ

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite major advances in the understanding, diagnosis, and treatment of Still's disease (including Systemic Juvenile Idiopathic Arthritis, sJIA), many patients experience a refractory course. Among potential organ-involvements, sJIA-associated lung disease (sJIA-LD) has arisen as a major comorbidity, prompting some patients to seek stem cell transplantation. Herein, we report the safety and efficacy of an investigational bi-specific IL-1b/IL-18 neutralizing antibody (aIL-1b/18, MAS825) in 7 refractory sJIA patients.

Methods: All patients received bimonthly MAS825 infusions via single-patient extended-use protocols at The Children's Hospital of Philadelphia (CHOP), University of Pittsburgh, or Hackensack University Medical Center. Parents/guardians provided informed consent for a registry study approved by The CHOP Institutional Review Board. Clinical, laboratory, radiologic, and pathologic information were extracted from electronic medical records.

Results: Disease onset was observed between 1.25 and 11 years of age. All patients met provisional classification criteria for refractory sJIA prior to MAS825 treatment. Other baseline characteristics included a systemic course with at least one Macrophage Activation Syndrome (MAS) episode (7/7), persistent itchy rash (6/7), sJIA-LD (6/7), and peak total IL-18 levels from 77,000 to >650,000 pg/mL. All patients had received high-dose glucocorticoids, IL-1 blockade, and at least one JAK inhibitor prior to MAS825 (Table 1).

Six of 7 patients remained on MAS825 at the time of data acquisition, with a duration of 0.9 to 3.6 years exposure. One patient stopped MAS825 after 4 months for lack of efficacy. Of the 6 patients remaining on MAS825, all made substantial systemic glucocorticoid dose reductions, and 5 weaned off entirely (Figure 1). All showed a substantial reduction or discontinuation of other Still's therapy. Five of 6 patients' Still's biomarkers improved and had clinically significant functional improvement (physician global and/or pulmonary function test). Chest CT's were stable or improved in 5/6 (Figure 2).

No infusion reactions were reported. One patient developed pseudomonal line infection. Another was found to have *S. Aureus* vertebral osteomyelitis 5 months after MAS825 initiation. Symptoms and inflammatory markers initially improved with antibiotics and holding MAS825, but MAS soon flared. Re-initiation of MAS825 with antibiotics led to clinical improvement, but the infection has required long-term antibiotic treatment.

Table 1: Patient demographics and medications relative to MAS825 initiation

	Sex	Age at dx	MAS	Arthritis	Rash	Clubbing	HLA-DRB1* 15:XX	Lung Dis.	Max IL-18	Pre-tx IL-18	Dx to MAS825	Treatment Pre-MAS825#	Co-treatment#
1	M	2y	2	Poly	Yes	Yes	n/a	Yes	142,856	25,197	10.3	anakinra, azathioprine, canakinumab, cyclosporine, cyclophosphamide, MTX, HCQ, tacrolimus, tofacitinib	
2	F	4y	4	Poly	Yes	No	No	Yes	99,168	1,003	7.2	anakinra, canakinumab, dupilumab, emapalumab, IVIG, MTX, ruxolitinib, tacrolimus, tocilizumab, tofacitinib	Dupilumab
3	F	11y	6	Poly	Yes	No	Yes	No	145,182	5,8181	3.5	anakinra, canakinumab, cyclophosphamide, emapalumab, ruxolitinib, tacrolimus, tofacitinib	
4	F	1.25 y	1	Oligo	Yes	Yes	No	Yes	200,733	26,641^	2.2	anakinra, canakinumab, ruxolitinib	Ruxolitinib (off @ ~ +365)
5	F	1.3y	3	No	No	No*	No	Yes	216,559	79,900	1	anakinra, canakinumab, emapalumab, ruxolitinib	
6	F	7y	4	No	Yes	No	Yes	Yes	414,926	42,566	2.5	anakinra, canakinumab, emapalumab, ruxolitinib	Ruxolitinib
7	M	2.5y	1	No	Yes	No	Yes	Yes	229,172	8,091	0.83	anakinra, baricitinib, canakinumab, cyclosporine, emapelumab, PLEX, ruxolitinib	IVIG (replacement)

*Pt. 5 developed clubbing during her course, after stopping MAS825. ^Drawn ~180 days prior to MAS825 initiation. #=No including GC's and anti-microbial prophylaxis
Dx=diagnosis; Tx=treatment; GC=glucocorticoids, AMP=anti-microbial prophylaxis; Hx=history

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

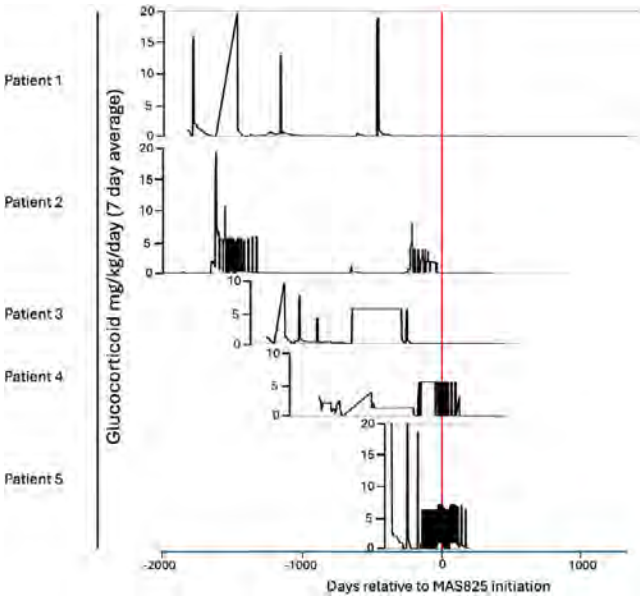


Figure 1: Steroid exposure (rolling 7-day average) relative to MAS825 initiation for patients 1-5.

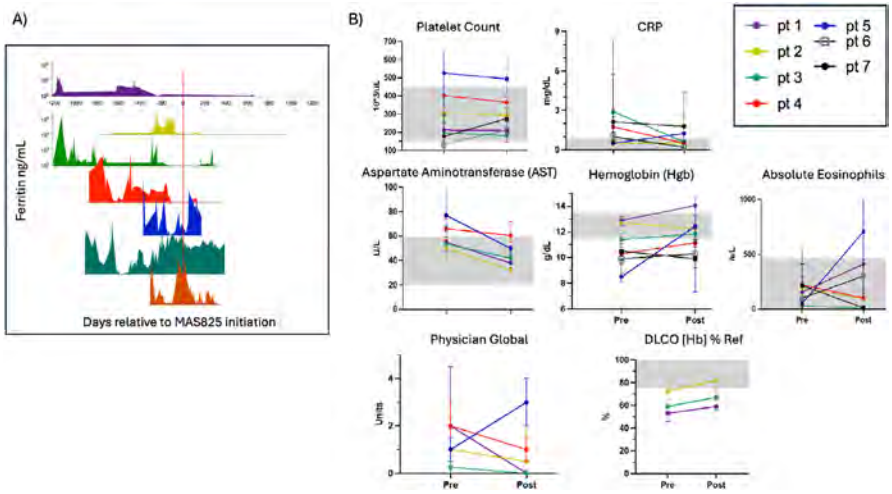


Figure 2: A) ferritin values relative to MAS825 initiation. B) Pre- and Post- MAS825 disease activity markers, physician global assessment, and DLCO [Hb] % Ref of patient's pulmonary function tests. (Median, interquartile-range).

Conclusion: In this highly refractory cohort, MAS825 was overall well-tolerated, and 5/7 patients showed clinical improvement and significant reduction in glucocorticoid and other Still's therapies. These data strongly support prospective trials, with careful monitoring particularly for invasive bacterial infection, in this immunosuppressed population with life-threatening sJIA disease.

Acknowledgment: All patients were provided MAS825 via Managed Access Program. Novartis has conducted a scientific accuracy and intellectual property review of this abstract, but has not otherwise instigated or influenced the content of this publication.

Disclosure: H. Carol: None; **M. Manglani**: None; **A. Noor**: None; **E. Behrens**: Ab2Bio, 5, Sobi, 2, 5, UpToDate, 9; **J. Burnham**: Cabaletta Bio, 5; **J. Lee**: None; **J. Moreno**: None; **A. Chop**: None; **K. Cetin Gedik**: None; **C. Poholek**: None; **G. Janow**: None; **L. Waqar-Cowles**: None; **S. Canna**: AB2Bio, 2, Bristol-Myers Squibb(BMS), 2, Novartis, 2, Simcha Therapeutics, 12, In-kind provision of a reagent, Sobi, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2142

Multidisciplinary Rheumatology Transition Clinic for Young Adults Shows Improved Experience, Utilization, and Health Maintenance: A Mixed-Methods Evaluation

Hannah Concannon[1], Jasmine Oesch[2], Sara Mazzarelli[2], Anne Fields[2], Keisha-Gaye O'Garo[2] and Rebecca Sadun[3], [1]Duke University School of Medicine, Chapel Hill, NC, [2]Duke University School of Medicine, Durham, NC, [3]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The transition from pediatric to adult care can pose a challenge for patients with SLE and other rheumatic diseases. These patients often face preventable disease flares, unintended pregnancies, depression, anxiety, and other complications. The Young Adult Rheumatology Clinic (YARC) was established in 2020. Based on the medical home model, the YARC provides integrated primary care and social work to young adults with pediatric-onset rheumatic diseases. This study investigated the impact of the multidisciplinary, transition-focused YARC for the care of recently transferred patients.

Methods: We generated descriptive statistics for YARC patients and control patients who transferred without enrolling in the YARC. Over the three years following transfer, we tracked immunizations, contraception, and unintended pregnancy among YARC and control patients. We also looked for changes in inpatient admissions, ED visits, and rheumatology show/cancellation rates, comparing patients in their third year after transfer to themselves before transfer. To identify the YARC's strengths and areas for improvement, we administered a post-clinic survey and conducted interviews.

Results: YARC (n=22) and control (n=13) patients who transitioned to adult care between July 2017 and October 2023 were included. Age, race, and ethnicity were similar between groups. Most (59%) YARC patients had SLE, as did all control patients (Table 1).

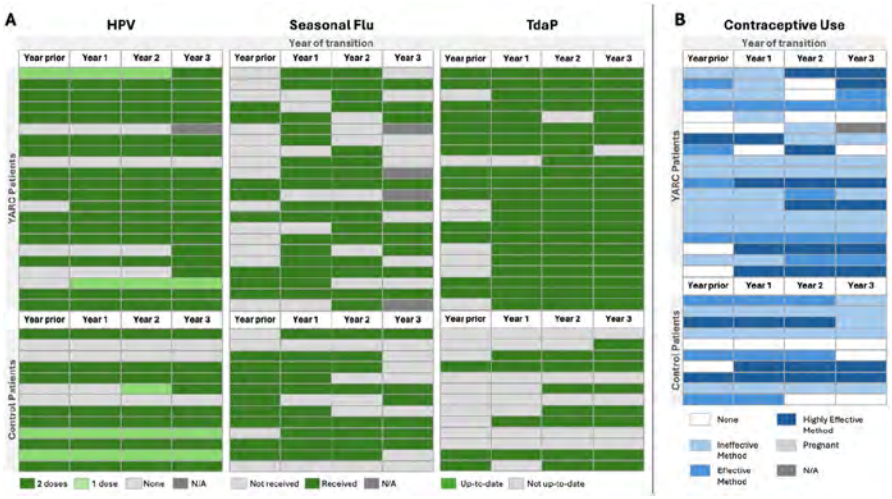


Figure 1. Vaccination status (A) and contraception use (B) among YARC patients and control young adult SLE patients Contraception use is shown only for female patients. "N/A" indicates lack of data for year 3 due to later transfer of care in some YARC patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Subject demographics and characteristics at time of transition from pediatrics to adult care Values presented as n (%) unless otherwise indicated. *Other diagnoses include UCTD (n=1), and Behcet's disease (n=1); **positive screen defined as a score of 3 or higher on PHQ-2/GAD-2 or 10 or higher on PHQ-9/GAD-7 on earliest available post-transition questionnaire.

	YARC, all	YARC, SLE	Control, SLE
N	22	13	13
Age at transition, years, median (IQR)	21 (20.8-22.3)	21 (20.5-23)	22 (21-23)
Race			
Black	12 (55%)	11 (85%)	8 (62%)
White	9 (41%)	1 (8%)	4 (31%)
Other	1 (5%)	1 (8%)	1 (8%)
Hispanic	1 (5%)	1 (8%)	2 (15%)
Female	19 (86%)	11 (85%)	10 (77%)
Primary Rheumatologic Diagnosis			
SLE	13 (59%)	13 (100%)	13 (100%)
Juvenile Idiopathic Arthritis	7 (32%)	0 (0%)	0 (0%)
Other*	2 (9%)	0 (0%)	0 (0%)
Co-diagnosis of fibromyalgia	3 (14%)	2 (16%)	1 (8%)
Positive depression screen**	9 (41%)	7 (54%)	2 (15%)
Positive anxiety screen**	6 (27%)	3 (23%)	4 (of 7 screened)
SLEDAI at transition, median (IQR)	--	3 (1-6)	4 (4-10)

Table 2. Rheumatology visit attendance and high-cost healthcare utilization among YARC patients before and after transfer of care

	Year Relative to Date of Pediatric-to-Adult Transfer						
	Before Transfer	After Transfer	*Two Years Prior*	*One Year Prior*	*Year One After Transfer*	*Year Two After Transfer*	*Year Three After Transfer*
Rheumatology Clinic No-Shows (% of scheduled visits)	12.9%	9.5%	10.2%	15.4%	11.3%	9.6%	5.8%
Rheumatology Clinic Cancellations (% of scheduled visits)	26.2%	19.0%	24.5%	27.9%	14.2%	20.5%	26.9%
Rheumatology Clinic Attended Visits (% of scheduled visits)	60.9%	71.4%	65.3%	56.7%	74.5%	69.9%	67.3%
ED Visits (per patient per year)	0.8	0.8	1.0	0.7	1.3	0.7	0.6
Hospital Admissions (per patient per year)	0.4	0.2	0.1	0.7	0.3	0.1	0.3

YARC patients attended 61% of scheduled visits prior to transition and 71% after transition. No-show rate decreased from 13% to 10% and cancellation rate fell from 26% to 19%. ED visits were similar before and after transition, but hospitalizations decreased from 0.4 to 0.2 per patient per year (Table 2).

Use of highly effective contraception (implant or intrauterine device) among YARC patients increased from 5% to 33% but was unchanged in the control group (20%) (Figure 1). There were two unintended pregnancies after transition to the YARC and four unintended pregnancies in the control group.

More YARC patients were up to date on TDaP (96% vs. 62%, p=0.02) and had received at least two doses of HPV vaccine (91% vs. 62%, p=0.08). Flu vaccine uptake was similar between YARC and controls (Figure 1).

In surveys and interviews, patients said the most useful aspect of the clinic was having a "one stop shop." Many also said that they appreciated a non-judgmental attitude and respect from YARC providers. However, multiple patients thought the facility was outdated; other pain points were travel times to and wait times at the clinic.

Conclusion: We saw promising signs that multidisciplinary, coordinated management of the pediatric-to-adult transition can improve clinical and economic outcomes for young adults with rheumatic disease, though conclusions are limited by sample size and availability of control data. YARC patients had improved pregnancy prevention and immunization rates compared to SLE patients who did not attend a transition clinic. Overall utilization also improved among YARC patients, despite literature suggesting that hospitalizations typically increase following transfer. Thus, the YARC model may reduce unnecessary healthcare utilization while maintaining rheumatology continuity.

Disclosure: H. Concannon: None; **J. Oesch**: None; **S. Mazzarelli**: None; **A. Fields**: None; **K. O'Garo**: None; **R. Sadun**: The Expert Institute, 12,.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2143

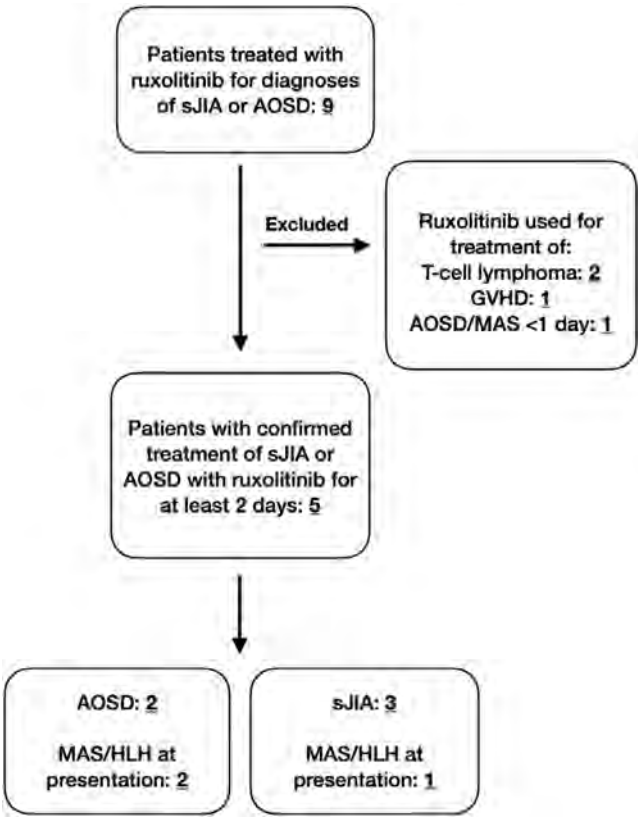
Ruxolitinib for Refractory sJIA/AOSD: A Single Center Case Series

Jacqueline Madison[1], Andrew Grim[2] and **Janna Shim**[3], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan Medicine, Ann Arbor, MI, [3]Midwestern University Chicago College of Osteopathic Medicine, Downers Grove

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult-onset Still's disease (AOSD) are rare, chronic, autoinflammatory diseases distinct from other forms of chronic inflammatory arthritis. Potential life-threatening complications include macrophage activation syndrome (MAS)/secondary hemophagocytic lymphohistiocytosis (HLH) and interstitial lung disease (ILD). Despite advances in targeted therapies, there remain patients with refractory disease. JAK inhibitors offer a promising new treatment option, with case reports and series suggesting efficacy and safety in treating refractory sJIA and AOSD, but the amount of information on ruxolitinib is limited. We present a case series of three patients with sJIA and two with AOSD who were treated with ruxolitinib at a single center.

Methods: We queried the electronic medical record (EMR) of a large tertiary health system for patients who received ruxolitinib within the past ten years for diagnosed sJIA or AOSD. Nine patients were identified, five older than 16 and four younger



Patients included in the series were those treated with Ruxolitinib for at least one day for diagnoses of sJIA or AOSD, with or without MAS/HLH. sJIA, systemic juvenile idiopathic arthritis; AOSD, Adult Onset Still's Disease; MAS, Macrophage Activation Syndrome; HLH, Hemophagocytic Lymphohistiocytosis; GVHD, Graft-Versus-Host Disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Diagnosis	AOSD	sJIA	AOSD	sJIA	sJIA
Age at start of Ruxolitinib	18 yo.	7 yo.	33 yo.	7 yo.	16 yo.
Complications of Disease	MAS	MAS, ILD	MAS	None	Pericarditis, Pleural Effusion
Medications prior to Ruxolitinib	Systemic corticosteroids, Anakinra, Tofacitinib, Canakinumab, MAS/IOS	Systemic corticosteroids, Methotrexate, Anakinra, Tocilizumab, Cyclosporine, Canakinumab	Systemic corticosteroids, Anakinra	Systemic corticosteroids, NSAIDs, Tocilizumab, Anakinra, Abatacept, Methotrexate, Canakinumab, Tofacitinib, Leflunomide	Systemic corticosteroids, NSAIDs, Anakinra, Canakinumab, Methotrexate, Tocilizumab, Cyclosporine, Tacrolimus, Hydroxychloroquine, Abatacept, Infliximab, Adalimumab, Etanercept, Golimumab, Azathioprine, Ruxolitinib, Tofacitinib
Reason for starting Ruxolitinib	Persistent disease activity, elevated inflammatory markers, multiple admissions for MAS	Persistently elevated inflammatory marker elevation, and recurrent MAS	MAS not responding to systemic steroids and anakinra	Continued arthritis, elevated IL-1β	Continued systemic symptoms with daily rash, fever, ankle arthritis
Efficacy: Clinical Improvement	Unclear, self-discontinued, reported minimal improvement	Able to wean off supplemental O2, weaned off anakinra and cyclosporine. Weaning canakinumab	Reached clinical remission without recurrence	Improvement and near resolution of systemic symptoms, more active. Arthritis/arthralgia with muted clinical improvement	Clinically inactive on medications
Efficacy: Lab improvement	Unclear due to poor adherence and self-discontinuation	Normalization of ESR and CRP in 7 and 2 months respectively. Normalization of ferritin in 6 months.	Normalization of ferritin in 55 days, normalization of sIL-2r in 13 days (in conjunction with steroids)	Normalization of sIL-2r and IL-1β	Labs prior to starting were in normal range
Safety/Adverse Events	Possible GI bleed	None	None	None	None
Duration on Ruxolitinib	7 months	35 months	91 months	12 months	9 months
Medication Regimen at time of writing	Tofacitinib, Cyclosporine, Systemic corticosteroids	Ruxolitnib, Canakinumab	Ruxolitinib	Ruxolitinib, Canakinumab, Leflunomide	Ruxolitinib, Azathioprine, Cyclosporine, Hydroxychloroquine

Clinical characteristics of patients included in series. sJIA, systemic Juvenile Idiopathic Arthritis, AOSD, Adult Onset Still's Disease; MAS, Macrophage Activation Syndrome; ILD, Interstitial Lung Disease; ESR, Erythrocyte Sedimentation Rate, CRP, C-reactive protein

at the time of diagnosis (Figure 1). Then via record review, we confirmed that ruxolitinib was specifically used for treating sJIA or AOSD, excluding three adults who were treated for T cell lymphoma (2) and graft vs host disease (1). One patient was excluded for receiving one dose of ruxolitinib hours before dying from systemic organ failure. For the remaining five patients (3 sJIA, 2 AOSD), we collected data on demographics, previous medications used, laboratory abnormalities, disease complications and clinical outcomes.

Results: All five patients were treated with other medications prior to starting ruxolitnib including systemic steroids (5), conventional DMARDs (4), biologics (5), and other JAK inhibitors (3). Three of five patients had adverse effects to other medications prior to starting ruxolitinib.

Disease complications prior to the use of ruxolitinib included: MAS/HLH (3), ILD confirmed by CT (1), pericarditis and pleural effusion (1), and opportunistic infection (1). All patients had refractory disease prior to starting ruxolitinib. The mean length of treatment with ruxolitinib was 30.8 months (median 12 months, range 7-91 months).

Since starting ruxolitinib, 4 of 5 demonstrated clinical response to therapy according to clinical documentation and remained on ruxolitinib with good disease control and no adverse effects at the time of last follow-up. One is on monotherapy and three on combination therapy. One patient discontinued ruxolitinib in the context of severe MAS with concern that ruxolitinib could have contributed to a GI bleed, though there were other risk factors. Inflammatory markers, cytokines, and chemokines improved in some patients, though lab acquisition was inconsistent between patients (Table 1).

Conclusion: Ruxolitinib represents an alternative treatment employed for refractory sJIA or AOSD that in our case series led to a favorable outcome regarding safety and efficacy. Our ability to evaluate response was limited by the data available in an EMR chart review. This series highlights the need for more rigorous study of ruxolitinib as a possibly safe and effective treatment strategy for treatment-refractory sJIA and AOSD.

Disclosure: J. Madison: None; **A. Grim**: None; **J. Shim**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2144

The Association Between Age at Diagnosis and Health-Related Quality of Life in ANCA-Associated Vasculitis

Jessica Bloom[1], Kaci Pickett-Nairne[2], Lori Silveira[1], Cristina Burroughs[3], Katrina Bargender[4], Amy Bolton[4], Christine Yeung[4], Jennifer Gordon[5], Peter Merkel[6] and Karen James[7], [1]University of Colorado, Aurora, CO, [2]University of Colorado, Denver, [3]University of South Florida, Tampa, FL, [4]Vasculitis Patient-Powered Research Network, Philadelphia, PA, [5]Vasculitis Foundation, Kansas City, MO, [6]University of Pennsylvania, Philadelphia, PA, [7]University of Utah, Salt Lake City, UT

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA-associated vasculitis (AAV) is a chronic autoimmune condition that significantly impacts patients' quality of life. It is unknown whether this impact varies based on age at diagnosis, from childhood through older adulthood. This study examined the relationship between age at diagnosis of AAV and health-related quality of life (HRQoL).

Methods: The data source was the Vasculitis Patient-Powered Research Network, an online, longitudinal, prospective cohort of adults with AAV (granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis) enrolled from 2014-2024. Cohorts were stratified by age (years) at diagnosis: children (< 18), young adults (18–40), middle-aged adults (41–65), and older adults (> 65). Descriptive statistics were summarized. Differences were tested via Student's t-tests or Kruskal-Wallis tests for continuous variables and Pearson's chi squared tests or Fisher's exact tests for categorical variables. Multivariable linear regressions assessed associations between age at diagnosis and Patient-Reported Outcomes Measurement Information System (PROMIS) results at last follow-up visit. Models were adjusted for gender and age at HRQoL assessment.

Table 1. Characteristics of patients with ANCA-associated vasculitis based on age at diagnosis.

	Age at Diagnosis				
	Child *<18 years old*	Young Adult *18-40 years old*	Middle-Aged *>40-65 years old*	Older Adult *>65 years old*	All
	N = 110	N = 507	N = 1172	N = 220	N = 2009
Characteristic	*Mean (standard deviation) or n (percentage)*				***p*-value***
Age at diagnosis (years)	13.3 (3.7)	30.7 (6.6)	53.5 (6.8)	69.9 (3.7)	47.4 (15.9)	< 0.001
Sex (male)	21 (19.1%)	125 (24.7%)	368 (31.4%)	83 (37.7%)	597 (29.7%)	0.008
Disease category						< 0.001
GPA	78 (70.9%)	375 (74.0%)	761 (64.9%)	137 (62.3%)	1351 (67.2%)	
MPA	21 (19.1%)	49 (9.7%)	177 (15.1%)	54 (24.5%)	301 (15.0%)	
EGPA	11 (10.0%)	83 (16.4%)	234 (20.0%)	29 (13.2%)	357 (17.8%)	
Time since diagnosis at quality of life assessment (years)	12.6 (13.3)	11.3 (10.5)	8.1 (6.5)	5.1 (4.7)	8.8 (8.3)	< 0.001

GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; EGPA, eosinophilic granulomatosis with polyangiitis.
Unknown or missing responses for each score were not included.
*Statistical significance was set at 0.05.

Table 2. Differences in PROMIS scores among Patients with ANCA-associated vasculitis based on age at diagnosis.

		Differences[1] by Age at Diagnosis*		
PROMIS Measure	**N**	**Child vs Young Adult**	**Child vs Middle Age**	**Child vs Older Age**
Lower score indicates better health-related quality of life				
Fatigue	1983	-4.38 (-6.82, -1.94)	-7.47 (-10.32, -4.63)	-8.39 (-11.97, -4.81)
Sleep Disturbance	1363	-4.39 (-6.69, -2.09)	-7.14 (-9.83, -4.45)	-6.16 (-9.64, -2.69)
Depression	1985	-4.24 (-6.36, -2.13)	-7.06 (-9.51, -4.6)	-8.11 (-11.2, -5.02)
Anxiety	1982	3.25 (1.4, 5.1)	5.88 (3.73, 8.04)	7.77 (5.06, 10.48)
Pain Interference	1984	-3.21 (-5.51, -0.92)	-5.52 (-8.19, -2.85)	-5.00 (-8.37, -1.63)
Higher score indicates better health-related quality of life				
Social Satisfaction	1363	3.87 (1.11, 6.63)	10.03 (6.78, 13.27)	11.23 (7.03, 15.44)
Physical Functioning	1991	0.72 (-1.36, 2.79)	3.07 (0.66, 5.49)	4.1 (1.07, 7.14)

PROMIS, Patient-Reported Outcomes Measurement Information System
*Child: < 18 years, Young Adult: 18-40 years old, Middle-Aged: >40-65 years old, Older Adult: >65 years old
Unknown or missing responses for each score were not included. *Statistical significance was set at 0.05.
[1]Differences in scores between age at diagnosis groups were assessed via multivariable linear regression adjusting for gender and age at time of quality-of-life assessment. If the confidence interval includes zero, the difference is not significant. A positive estimated difference in scores represents a higher score for those diagnosed in childhood compared to the reference group, while a negative difference represents a lower score for those diagnosed in childhood compared to the reference group.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

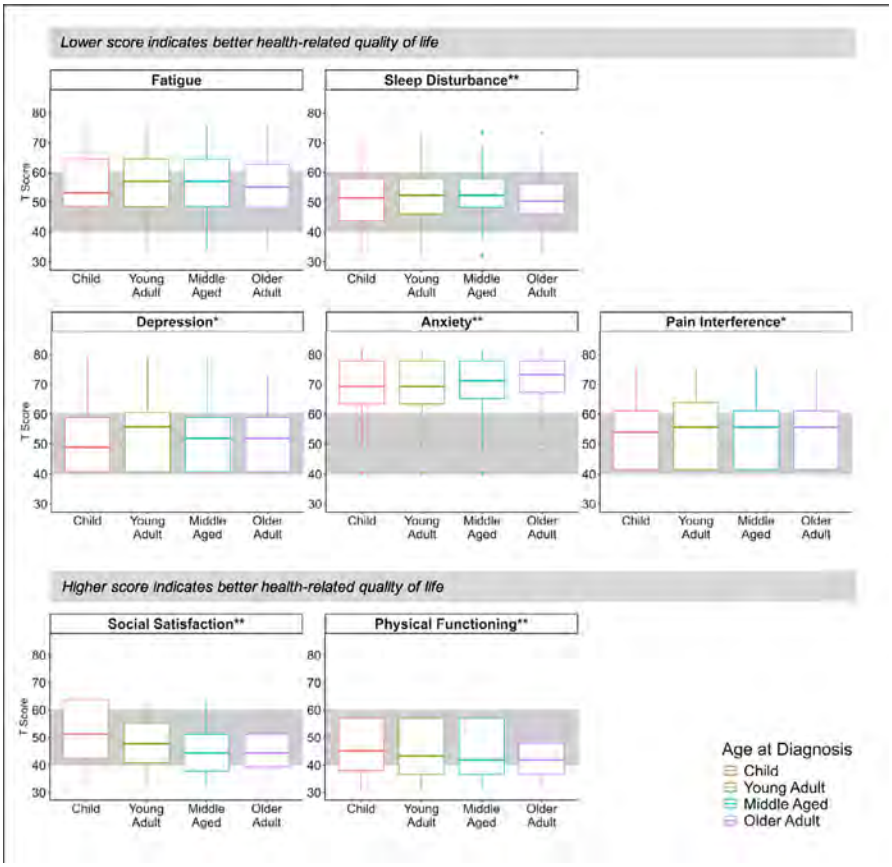


Figure 1. Patient-Reported Outcomes Measurement Information System T-Scores Based on Age at Diagnosis with ANCA-associated vasculitis. Boxplot of the distribution of Patient-Reported Outcomes Measurement Information System T-Scores stratified by age at diagnosis with ANCA-associated vasculitis. The boxes represent the 25th to 75th percentile T scores, with the middle line within each box representing the median T score. The solid lines extending out signify the range with dots representing possible outliers. The dashed gray line represents the mean score of the referent general pediatric population (50), with one standard deviation above and below represented in gray. Better health-related quality of life is represented by a lower score in the top five measures and a higher score in the bottom two measures. Statistical significance indicates that the median T score for at least one age at diagnosis group is different from another age at diagnosis group within that measure. *statistical significance at $p < 0.05$; **statistical significance at $p < 0.01$.

Results: Analysis included 2009 patients with AAV. The majority had GPA and there was a female predominance that decreased with age at diagnosis. Those diagnosed at younger ages had longer follow-up at time of last PROMIS measure (Table 1). All cohorts had impaired HRQoL in every domain (Figure 1). When adjusted for gender and age at HRQoL assessment, those diagnosed with AAV in childhood had worse HRQoL related to anxiety than those diagnosed as young, middle-aged, or older adults. Additionally, those diagnosed in childhood had better HRQoL related to fatigue, sleep disturbance, depression, pain interference, satisfaction with participation in social roles, and physical functioning (Table 2).

Conclusion: Patients with AAV have impaired HRQoL, especially related to anxiety. Additionally, age at diagnosis with AAV is associated with differences in HRQoL. Compared to patients diagnosed with AAV at older ages, those diagnosed at younger ages have worse HRQoL related to anxiety and better HRQoL related to fatigue, sleep disturbance, depression, pain interference, satisfaction with participation in social roles, and physical functioning. Understanding the mechanisms by which age at diagnosis impacts HRQoL will be useful for developing targeted clinical interventions in AAV.

Disclosure: J. Bloom: None; **K. Pickett-Nairne**: None; **L. Silveira**: None; **C. Burroughs**: None; **K. Bargender**: None; **A. Bolton**: None; **C. Yeung**: None; **J. Gordon**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **K. James**: Sobi, 1.

Abstract Number: 2145

EOS® Imaging System Is a Novel, Rapid, Safe, and Effective Technique To Detect And Assess Calcinosis In JDM

Jessica Perfetto[1], Ciara Maguire[2], Carli Needle[3], Shailee Lala[4], Vikash Oza[2] and Philip Kahn[5], [1]Pediatric Rheumatology, Hassenfeld Children's Hospital at NYU Langone, New York, [2]Pediatric Dermatology, Ronald O Perelman Department of Dermatology, NYU Grossman School of Medicine, New York, [3]NYU Grossman School of Medicine, New York, [4]Department of Radiology, NYU Grossman School of Medicine, New York, [5]Pediatric Rheumatology, Hassenfeld Children's Hospital at NYU Langone, New York

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Calcinosis, reported in up to 47% of children with juvenile dermatomyositis (JDM), can cause significant morbidity, including ulceration, infection, and contractures. Given associations of diagnostic delay and duration of active disease with risk of developing calcinosis, early identification and treatment are critical. However, there is no standardized approach to assess or quantify calcinosis. Various imaging modalities, including conventional radiographs (X-rays), computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US), are used to assess calcinosis. However, they have not been directly compared, and they have limitations including 2-dimensional (2D) nature (X-rays), radiation (CT), cost and potential need for sedation (MRI), limited ability to detect deep lesions (US). The EOS® imaging system involves whole body evaluation via 2D X-rays in ~20 seconds with much lower doses of radiation than conventional X-rays. It is used for disorders of the spine, legs, and hips; however, its use in assessing calcinosis has not been assessed. Our objectives were to compare the ability of EOS® versus conventional X-rays in detecting calcinosis in children with JDM.

Methods: Children diagnosed with JDM before age 19 with calcinosis (confirmed with conventional X-rays and/or physical exam) at Hassenfeld Children's Hospital at NYU Langone with at least one EOS® scan for calcinosis were included. Sociodemographics, clinical information (including detailed information on calcinosis), imaging modalities, and treatment were collected retrospectively via manual chart review. X-ray and EOS® images were independently assessed by two radiologists blinded to patient information; evaluation of calcinosis by each modality was recorded and compared. Descriptive statistics were used to summarize each variable. Bivariate analysis was performed using t-test or Chi-squared test, or their nonparametric equivalents (Mann Whitney or Fisher's exact tests).

Results: Seven children with calcinosis and JDM had at least one EOS® scan for calcinosis; 57% of children had an EOS® within one year of JDM diagnosis. All patients were receiving systemic therapy. Three patients (43%) had clinically active skin and/or muscle disease at the time of EOS®. In most children, calcinosis was initially detected by physical exam; however, in 57%, additional calcinosis was detected by EOS® that was missed on physical exam. There were no significant differences in detection of any given calcinosis lesion by EOS® compared to X-rays; however, EOS® detected additional calcinosis lesions compared to X-rays.

Conclusion: This is the first study to explore the use of EOS® in detecting calcinosis in JDM and to compare EOS® to conventional X-rays. Our single-center retrospective study suggests that EOS® may be comparable to X-rays in detecting a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

given calcinosis lesion with the advantage of detecting additional lesions given whole-body imaging with much less radiation than conventional X-rays or ultra-low dose whole body CT. Future prospective multi-center studies with a larger sample size comparing other imaging modalities will be critical to further understand the role of EOS® in detecting and monitoring calcinosis.

Disclosure: J. Perfetto: None; **C. Maguire**: None; **C. Needle**: None; **S. Lala**: None; **V. Oza**: None; **P. Kahn**: None.

Abstract Number: 2146

Impact of a Clinical Pathway on Medication Use and Outcomes in Kawasaki Disease

Jonathan Yu[1], Matthew Elias[1], Deborah Whitney[1], Sanjeev Swami[1], Kaylie Shojaie[1], Caroline Burlingame[1], Isabel Armendi[1], Malki Peskin[2], Melissa Lerman[1], Jerri Miller[1], Jane Lavelle[1], Brandon Ku[1] and Jon Burnham[3], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Bala Cynwyd, PA, [3]Children's Hospital of Philadelphia, Bryn Mawr, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Kawasaki disease (KD) is an acute, systemic vasculitis which can lead to coronary artery (CA) aneurysms in young children. In 2018, we developed a clinical pathway to standardize KD care and improve outcomes. In this retrospective quality improvement (QI) study, we aimed to assess patients admitted with KD and determine the impact of the pathway on medication use and outcomes to inform QI initiatives.

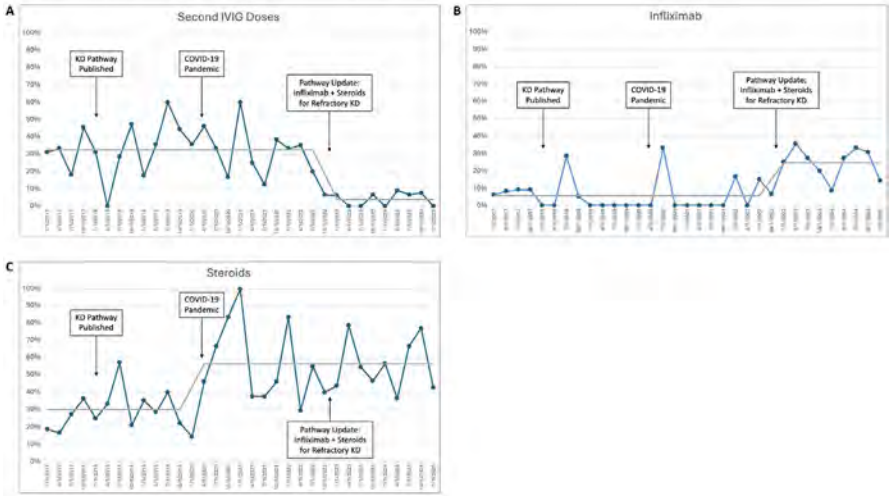
Table 1. Cohort characteristics among index admissions for Kawasaki disease (January 1, 2017 to March 31, 2025)

Demographics	Total (n=413)	Normal initial echo (n=328)	Abnormal initial echo (n=85)	p
Age at admission, years, mean (SD)	3.7 (2.8)	3.9 (2.9)	3.0 (2.6)	<0.05
Sex, n (%)				
Male	241 (58)	187 (57)	54 (64)	0.28
Race, n (%)				
Asian	45 (11)	37 (11)	8 (9)	<0.05
Hispanic or Latino	54 (13)	40 (12)	14 (16)	
Non-Hispanic Black	137 (33)	114 (35)	23 (27)	
Non-Hispanic White	130 (31)	105 (32)	25 (29)	
Other	47 (11)	32 (10)	15 (18)	
Process measures				
ED order set usage, n (%)	160 (39)	130 (40)	30 (35)	0.46
Inpatient order set usage, n (%)	319 (77)	255 (78)	64 (75)	0.63
Number of echos done, mean (SD)	3.2 (1.9)	3.0 (1.3)	4.3 (3.1)	<0.001
Treatment				
Multiple IVIG administrations, n (%)	89 (22)	76 (23)	13 (15)	0.12
Infliximab administration, n (%)	45 (11)	29 (9)	16 (19)	<0.01
Steroid administration, n (%)	177 (43)	114 (35)	63 (74)	<0.001
Echo findings and outcomes				
Normal initial echo, n (%)	328 (79)	-	-	-
Normal final echo, n (%)	354 (86)	296 (90)	58 (68)	<0.001
Highest severity of CA abnormality, n (%)				
No involvement	304 (74)	296 (90)	8 (9)	<0.001
Dilation only	30 (7)	11 (3)	19 (22)	
Small aneurysm	62 (15)	15 (5)	47 (55)	
Medium aneurysm	11 (3)	3 (1)	8 (9)	
Large/giant aneurysm	6 (1)	3 (1)	3 (4)	
Developed CA aneurysm, n (%)	79 (19)	21 (6)	58 (68)	<0.001
Length of stay, days, mean (SD)	4.5 (2.2)	4.5 (1.9)	4.8 (2.9)	0.25

Echo = echocardiogram; CA = coronary aneurysm. Z-score classification of CA abnormalities is defined as: no involvement: <2; dilation only: ≥2 and <2.5; small: ≥2.5 and <5; medium: ≥5 and <10; large: ≥10. p values were calculated using Chi-square tests for categorical measures and two-tailed t tests for continuous measures.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Medication Administration in All KD Admissions (2017-2025)



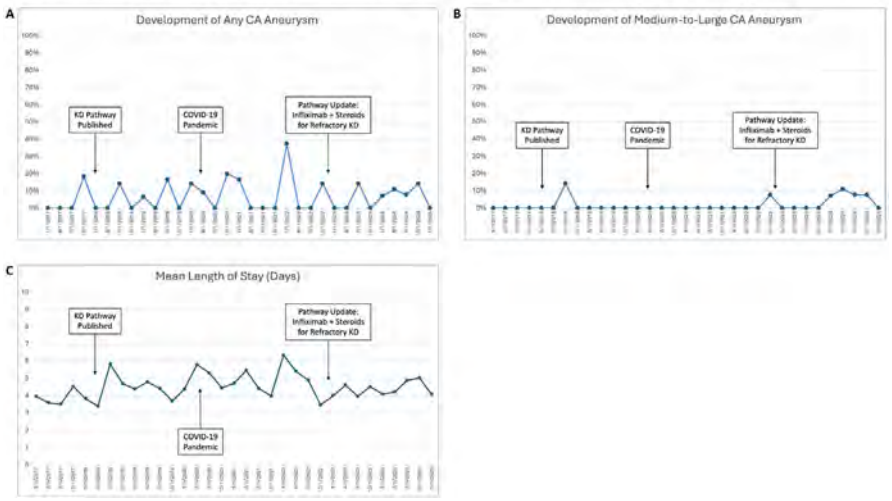
Methods: We examined index admissions for KD with IVIG administration from January 2017 to March 2025. All echocardiogram (echo) data ≤60 days after the admission date were included. The right coronary and left anterior descending arteries were assessed. CA changes were classified based on 2024 American Heart Association guidelines. A normal initial echo was defined as CA Z-scores between -2 and 2 on the first echo within 3 days of admission.

The KD pathway was published in January 2018 and updated in November 2022. The original pathway standardized steroid use for patients less than 6 months of age and those with CA aneurysms (Z-score ≥2.5). The updated pathway recommended infliximab and steroids for all IVIG-resistant patients. Electronic health record (EHR) order sets were created to implement the pathway's diagnostic and treatment recommendations. All EHR and echo data are updated daily and displayed in a data visualization tool.

Standard run chart rules were used to analyze process and outcome measures over time. p values were calculated using the Chi-square and t-tests for categorical and continuous measures, respectively, and the F-test to compare variances.

Results: Demographic, echo, and treatment data are shown in Table 1 (n=413). The mean age at admission was 3.7 ± 2.8 years, and 58% of patients were male. The emergency department and inpatient KD pathway order sets were used in 39% and 77% of cases, respectively. Abnormal initial echos were observed in 85 patients (21%), who were younger (3.0

Figure 2. Outcomes in KD Patients with Normal Initial Echocardiograms (2017-2025)



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

vs 3.9 years, $p< 0.05$), had more echos (4.3 vs 3.0, $p< 0.001$), and were more likely to develop aneurysms (68% vs 6%, $p< 0.001$) and receive steroids (74% vs 35%, $p< 0.001$) and infliximab (19% vs 9%, $p< 0.01$).

After the 2022 pathway update, second IVIG doses decreased from 33% to 4%, while infliximab administration increased from 6% to 25% (Figure 1). Steroid use increased after the onset of the COVID-19 pandemic in 2020 and remained higher after the pathway update. Among patients with normal initial echos, there was no change in the rate of CA aneurysm development or length of stay (LOS) (Figure 2). However, there was a decrease in LOS variance (0.16 vs 0.64, $p< 0.05$). In 2024, we identified 4 patients with normal initial echos who developed medium or large CA aneurysms.

Conclusion: After KD pathway implementation, we observed an increase in steroid and infliximab use and a decrease in second doses of IVIG. Though LOS remained stable, its variation decreased after updated pathway recommendations on management of IVIG-resistant KD, which may represent improved standardization of care. Though CA aneurysm development has not changed overall, we are currently using our real-time data visualization tools to investigate recent cases of medium and large aneurysms to further optimize KD care.

Disclosure: J. Yu: None; **M. Elias**: None; **D. Whitney**: None; **S. Swami**: None; **K. Shojaie**: None; **C. Burlingame**: None; **I. Armendi**: None; **M. Peskin**: None; **M. Lerman**: None; **J. Miller**: None; **J. Lavelle**: None; **B. Ku**: None; **J. Burnham**: None.

Abstract Number: 2147

Elevated fMET and GDF-15 Circulating Levels in Pediatric CNO Patients with Psoriasis Define a Distinct Mitochondrial-Inflammatory Signature

Arpit Rathee[1], Noor Kaur[1], **Jorge A. Gonzalez-Chapa**[2], Ryan D. Stultz[1], Emily Deng[3], Ian Muse[4], Yongdong Zhao[3] and Christian Lood[2], [1]University of Washington, Division of Rheumatology, Seattle, WA, [2]University of Washington, Division of Rheumatology, Seattle, [3]University of Washington, Department of Pediatrics, Seattle Children's Hospital, Seattle, WA, [4]University of Washington, Department of Pediatrics, Seattle Children's Hospital, Seattle

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is a pediatric autoinflammatory bone disorder marked by sterile skeletal inflammation. A subset of CNO patients presents with comorbid psoriasis, suggesting the existence of overlapping inflammatory circuits beyond the musculoskeletal system. Mitochondria-derived formyl peptides (fMET) and the stress-responsive cytokine GDF-15 are emerging as biomarkers of cellular damage and mitochondrial dysfunction, yet their role in CNO, particularly in psoriasis-associated cases, remains poorly defined.

Methods: We analyzed plasma samples from 120 pediatric participants: 30 healthy controls, 30 with inactive CNO, 30 with active CNO, and 30 juvenile idiopathic arthritis (JIA) patients serving as disease controls. Twenty-two participants had comorbid psoriasis (9 CNO-inactive, 11 CNO-active, 2 JIA). Levels of GDF-15 and fMET were analyzed using ELISA. Statistical analysis was conducted in R using ANOVA, Dunn's multiple comparisons, and unpaired t-tests.

Results: The CNO cohort included 54.2% female participants, with a mean age of 12.56 years. Active and inactive subgroups showed consistent distributions in age and sex. fMET concentrations were significantly elevated in CNO-active

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients compared to healthy controls ($p < 0.05$). GDF-15 levels were significantly higher in participants with comorbid psoriasis compared to those without ($p = 0.0312$). Notably, within the psoriasis subgroup, patients with active CNO exhibited the highest GDF-15 levels compared to those with inactive disease ($p = 0.0044$), suggesting enhanced mitochondrial stress when both skeletal and cutaneous inflammation are present.

Conclusion: These findings uncover a distinct immunometabolic profile in pediatric CNO patients with psoriasis, characterized by elevated fMET and GDF-15. This mitochondrial-inflammatory axis may represent a novel endotype within CNO, providing mechanistic insights into extra-skeletal involvement and offering potential avenues for biomarker-guided stratification and targeted therapy.

Disclosure: A. Rathee: None; **N. Kaur**: None; **J. Gonzalez-Chapa**: None; **R. Stultz**: None; **E. Deng**: None; **I. Muse**: None; **Y. Zhao**: None; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11.

Abstract Number: 2148

Initial MRI Findings as Predictors of Disease Phenotype in Juvenile Dermatomyositis: A Comparative Study of Myositis Specific Antibodies NXP2-Positive and Myositis Specific Antibody-Negative Patients in a Large Tertiary Hospital

Juan Torres Sanchez[1], Pritish Bawa[2], Andrea Ramirez[1], MaiLan Nguyen[3], Amit Thakral[4], Xiaofan Huang[1], J Herman Kan[2] and Marietta De Guzman[1], [1]Baylor College of Medicine, Houston, TX, [2]Texas Childrens Hospital, Houston, TX, [3]Baylor College of Medicine, Austin, TX, [4]Texas Children's Hospital, Houston, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy of childhood, characterized by proximal muscle weakness and distinctive cutaneous findings. Magnetic resonance imaging (MRI) has emerged as a valuable, noninvasive diagnostic tool, reducing the reliance on interventional procedures such as muscle biopsy. Myositis-specific antibodies (MSAs) have become important in characterizing disease phenotypes, predicting prognosis, and guiding management strategies. Among these, NXP2 antibodies are associated with a more severe disease course, including higher disease burden, chronicity, and an increased risk of calcinosis. However, although MSA testing may not be as costly as MRI, limited access and specialized processing makes testing potentially challenging, whereas MRI is more routinely accessible in clinical settings. This study aims to evaluate whether pretreatment MRI findings can serve as early predictors of disease phenotype by correlating imaging patterns with MSA status, specifically comparing NXP2-positive and MSA-negative JDM patients.

Methods: With IRB approval, we conducted a retrospective review of NXP2-positive and MSA-negative JDM at Texas Children's Hospital over the past 10 years. Included patients had at least 1 year of data and initial MRI without prior systemic treatment. All patients met 2017 EULAR/ACR criteria for probable or definite idiopathic inflammatory myopathies. MRI scans of the pelvis and thighs were assessed by a musculoskeletal radiologist blinded to MSA status and clinical outcomes. MRI findings were evaluated using the Ladd et al. scoring tool, focusing on muscle and fascial signal abnormalities and reticulated

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Demographics and Clinical Characteristics

Patient Demographics				
	N	MSA negative N=15	NXP2 positive N=18	p-value
Age in years	33			0.62
Mean (SD)		6.83 (3.80)	8.00 (5.10)	
Median (Q1, Q3)		6.00(3.00, 10.00)	7.00(4.00, 13.00)	
Min, Max		1.40, 13.00	2.00, 16.00	
Sex at birth, n / N (%)	33			0.49
Male		9 / 15 (60%)	8 / 18 (44%)	
Female		6 / 15 (40%)	10 / 18 (56%)	
Race, n / N (%)	32			0.83
White		11 / 15 (73%)	13 / 17 (76%)	
Black or African American		4 / 15 (27%)	3 / 17 (18%)	
Asian		0 / 15 (0%)	1 / 17 (5.9%)	
Ethnicity, n / N (%)	33			0.48
Hispanic		5 / 15 (33%)	9 / 18 (50%)	
Not Hispanic or Not Latino		10 / 15 (67%)	9 / 18 (50%)	
Time to Diagnosis (months)	32			0.83
Mean (SD)		4.21 (3.09)	5.33 (4.39)	
Median (Q1, Q3)		3.00(2.00, 6.00)	3.50(2.00, 9.00)	
Min, Max		2.00, 13.00	1.00, 13.00	
Constitutional symptoms n / N (%)	33			
None		3 / 15 (20%)	3 / 18 (17%)	>0.99
Fatigue		12 / 15 (80%)	15 / 18 (83%)	>0.99
Fever		4 / 15 (27%)	3 / 18 (17%)	0.67
Weight loss		1 / 15 (6.7%)	6 / 18 (33%)	0.1
Lymphadenopathy		0 / 15 (0%)	2 / 18 (11%)	0.49
Mucocutaneous findings, n / N (%)	33			
None		0 / 15 (0%)	3 / 18 (17%)	0.23
Gottron's Papules		14 / 15 (93%)	9 / 18 (50%)	**0.009**
Shawl Sign		1 / 15 (6.7%)	2 / 18 (11%)	>0.99
Heliotrope Rash		12 / 15 (80%)	7 / 18 (39%)	**0.033**
Malar Rash		10 / 15 (67%)	8 / 18 (44%)	0.3
Periungual nailfold capillary changes		13 / 15 (87%)	11 / 18 (61%)	0.13
Cutaneous ulceration		2 / 15 (13%)	2 / 18 (11%)	>0.99
Calcinosis		0 / 15 (0%)	3 / 18 (17%)	0.23
Lipodystrophy		0 / 15 (0%)	1 / 18 (5%)	>0.99
Cardiopulmonary findings, n / N (%)	33			
None		9 / 15 (60%)	13 / 18 (72%)	0.49
Interstitial Lung Disease		1 / 15 (6.7%)	0 / 18 (0%)	0.45
Hoarseness		3 / 15 (20%)	2 / 18 (11%)	0.64
Musculoskeletal findings, n/N (%)	33			
None		3 / 15 (20%)	0 / 18 (0%)	0.083
Upper Extremity Weakness		11 / 15 (73%)	17 / 18 (94%)	0.15
Lower Extremity Weakness		11 / 15 (73%)	17 / 18 (94%)	0.15
Truncal Weakness		8 / 15 (53%)	13 / 18 (72%)	0.3
Neck Weakness		5 / 15 (33%)	10 / 18 (56%)	0.3
Mild Arthritis		6 / 15 (40%)	4 / 18 (22%)	0.45
Moderate Arthritis		1 / 15 (6.7%)	3 / 18 (17%)	0.61
Severe Arthritis		0 / 15 (0%)	1 / 18 (5.6%)	>0.99
Joint Contractures		1 / 15 (6.7%)	1 / 18 (5.6%)	>0.99

subcutaneous fat changes. Associations between MRI findings and clinical outcomes, including the Disease Activity Score (DAS)—a validated tool—were analyzed.

Results: Thirty-three patients with JDM met inclusion criteria: 18 NXP2-positive and 15 MSA-negative. Initial MRI scores did not identify significant differences between the two groups. However, when analyzed irrespective of MSA status, pretreatment MRI of the anterior thigh ($p < 0.001$), adductors ($p = 0.006$), pelvis ($p = 0.006$) and fat signal abnormalities ($p=0.047$) were associated with higher disease activity scores. At six months, NXP2-positive patients continued to exhibit upper, truncal, and neck muscle weakness, though not statistically significant. At two years, they showed persistently elevated muscle enzymes (AST/ALT and aldolase) and a higher prevalence of calcinosis (28% vs. 5.6%). MSA-negative patients had more mucocutaneous features, including Gottron's papules (93% vs 50%) and heliotrope rash (80% vs 39%).

Conclusion: Pretreatment MRI findings did not differentiate NXP2-positive from MSA-negative JDM. However, abnormalities in subcutaneous fat and specific muscle groups were linked to higher disease activity regardless of antibody status. Limitations include retrospective design, small sample size, and single-center cohort, which may limit the generalizability and statistical power of subgroup comparisons. Larger, multicenter studies are needed to confirm whether initial MRI can serve as a prognostic tool in JDM.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: MRI Signal Abnormalities by Myositis Specific Antibody

MRI Signal Abnormality by Myositis Specific Antibody			
MRI Signal Intensity Abnormality	MSA Negative N=15	NXP-2 Positive N=18	p value
Fat, n / N (%)			0.31
Negative	3 (20%)	1 (5.6%)	
Positive	12 (88%)	17 (94.4%)	
Fascia, n / N (%)			0.37
Negative	4 (27%)	2 (11.1%)	
Positive	11 (73%)	16 (88.9%)	
General severity, n / N (%)			0.18
Normal	0 (0%)	1 (5.6%)	
Mild	3 (20%)	0 (0%)	
Moderate	11 (73%)	15 (83.3%)	
Severe	1 (6.7%)	2 (11.1%)	
Anterior thigh, n / N (%)			0.93
Grade 0	0 (0%)	1 (5.6%)	
Grade 1	0 (0%)	0 (0%)	
Grade 2	3 (20%)	1 (5.6%)	
Grade 3	2 (13%)	4 (22%)	
Grade 4	10 (67%)	12 (66.8%)	
Adductors, n / N (%)			0.051
Grade 0	0 (0%)	1 (5.6%)	
Grade 1	3 (21.4%)	0 (0%)	
Grade 2	0 (0%)	0 (0%)	
Grade 3	2 (14.3%)	0 (0%)	
Grade 4	9 (64.3%)	17 (94.4%)	
Posterior thigh, n / N (%)			0.21
Grade 0	0 (0%)	1 (5.6%)	
Grade 1	3 (20%)	0 (0%)	
Grade 2	2 (13.3%)	1 (5.6%)	
Grade 3	2 (13.3%)	3 (16.6%)	
Grade 4	8 (53.4%)	13 (72.2%)	
Pelvic muscles, n / N (%)			0.21
Grade 0	0 (0%)	1 (5.6%)	
Grade 1	4 (28.6%)	0 (0%)	
Grade 2	0 (0%)	0 (0%)	
Grade 3	1 (7.1%)	2 (11%)	
Grade 4	9 (64.3%)	15 (83.3%)	
Wilcoxon rank sum test; Fisher's exact test			

Table 3 Univariable Regression MRI findings on the Disease Activity Score at Diagnosis

Univariable regression of Disease Activity Score (DAS) at Diagnosis				
	N	Beta	95% CI	p-value
Fat	32			
Negative		—	—	
Positive		4.4	0.07, 8.7	**0.047**
Fascia	32			
Negative		—	—	
Positive		3.5	-0.19, 7.2	0.062
Anterior Thigh	32	2.5	1.2, 3.9	**<0.001**
Adductors	31	1.8	0.56, 3.1	**0.006**
Posterior Thigh	32	1.1	-0.19, 2.4	0.092
Pelvis	31	1.7	0.54, 2.9	**0.006**
DAS: Assessment of global disease activity in juvenile dermatomyositis				

Disclosure: J. Torres Sanchez: None; **P. Bawa**: None; **A. Ramirez**: None; **M. Nguyen**: None; **A. Thakral**: None; **X. Huang**: None; **J. Kan**: None; **M. De Guzman**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2149

Rheumatology Transitions of Care: Patient Stability and Follow-Up at a Single Center

Julia Witowska[1], Marianne Kerski[1], Uzochi Nwoko[2], Lakshmi Meyyappan[2], Catherine McDermott[2] and Jacqueline Madison[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The transition period for adolescents transferring from pediatric to adult care is a recognized period of vulnerability. In rheumatology, the majority of adolescents reach adulthood with ongoing disease activity, and patterns of healthcare utilization during this time remain poorly understood. The aim of this study was to evaluate how rheumatology patients interact with the healthcare system during the period of transfer from pediatric to adult care and assess how systemic factors may affect transfer outcomes.

Methods: A retrospective chart review was conducted of patients aged 18-27 who transferred from pediatric to adult rheumatology between 2020 and 2023 at a single tertiary care center without a formal transition program. Data collected included sociodemographic characteristics, healthcare utilization during the transition period, and logistical aspects of the transfer process. Descriptive statistics were used to analyze the data.

Results: A total of 230 young adults with rheumatic disease transferred from pediatric to adult rheumatology in our study period. The cohort included 118 (51.3%) patients with JIA, 39 (17%) with SLE, 33 (14.3%) with connective tissue disease (excluding SLE), 20 (8.6%) with vasculitis, 9 (3.9%) with autoinflammatory disease inclusive of systemic JIA, and 11 (4.7%) with other diagnoses (sarcoidosis, antiphospholipid syndrome, chronic recurrent multifocal osteomyelitis, idiopathic uveitis). An average of 276 days (median 170 days) elapsed between the final visit with pediatrics and the first adult visit; this is more than twice the average duration between visits before (every 114 days) or after (every 122 days) transfer. Almost half (47.8%) of patients had more than six months and 20% had over a year elapse prior to establishing with adult rheumatology. During this period of transfer, 28 (12.1%) presented to the emergency department and 27 (11.7%) were prescribed a burst of corticosteroids. Eight (3.5%) patients did not have a second adult rheumatology visit.

Conclusion: The results of our review demonstrate a need for greater patient support in their transfer between seeing pediatric and adult rheumatologists. When connected with a physician, patients saw their rheumatologist about every 3-4 months, but during the transfer period, the average patient went longer than twice this duration without seeing a rheumatologist. Though the ramifications of this delay are not yet clear, the rates of emergency department utilization and steroid prescriptions during transition suggest that ensuring a more expedited and supported transfer process may be important for maintaining disease control and improving patient satisfaction. This study lays the groundwork for the development of a formalized transition program and provides a baseline for evaluating its impact, reinforcing the need for more structured support during the vulnerable period of transferring from pediatric to adult rheumatologic care.

Disclosure: J. Witowska: None; **M. Kerski**: None; **U. Nwoko**: None; **L. Meyyappan**: None; **C. McDermott**: None; **J. Madison**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2150

Rheum to Grow:An Approach Towards Human Centered Design through a Qualitative Analysis on the Transition from Pediatric to Adult Rheumatology

Lillian Chang[1], Rhea Sharma[2], Elyse Guziewicz[1], Jordan Jackson[3], Katrina Romagnoli[1], Gemme Campbell[1], Saritha Korukonda[1], Priyanka Pawar[1], Jonida Cote[4], Thomas Davis[1], Emily Brunner[1] and Geisinger Medical Center Rheumatology Department, [1]Geisinger, Danville, PA, [2]Geisinger Medical Center Internal Medicine Residency, Danville, PA, [3]Geisinger Medical Center Medicine-Pediatrics Residency, Danville, PA, [4]Geisinger Health System, Wilkes-Barre, PA

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Up to half of patients who transition to adult care are lost to follow up within 2 years of transfer from pediatric to adult rheumatology (Hart, *Clin. Pediatr*. 2019; 58 (11-12): 1277-1283). Complicating matters is the lack of training for pediatric and adult specialists in transition, with nearly 50% of adult rheumatologists reporting no transitional care training (Zizman, *Arth. Care Res*. 2020; 72:432–40) .

The goal of this exploratory pilot study is to assess patient independence, transition readiness, understanding of disease and attitudes towards existing transition documents through qualitative interviews. Through input from providers, patients and their parents, we intend to apply human-centered-design to create a single page transfer summary and tools for transition to be incorporated into clinical practice.

Table 1. *Participant Demographics*

N= 21		
Patient Demographics	n= 8	
Gender		
	Female	6 (75%)
	Male	2 (25%)
Age		
	11-14	2 (25%)
	15-17	1 (12.5%)
	18-21	2 (25%)
	22-25	3 (37.5%)
Parent Demographics	n= 7	
Mother		7 (100%)
Age		
	30-39	2 (28.6%)
	40-49	4 (57.1%)
	50-59	1 (14.3%)
Provider Demographics	n= 6	
Years in Practice		
	0-5	4 (66.7%)
	6-10	0 (0%)
	11-15	1 (16.7%)
	16 - 20	1 (16.7%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Examples of Abstractions

Theme	Description	Quote
Medical Independence	Transportation to appointments is a barrier to medical independence.	"Mom and dad drive to appointments."
	Shyness with communication and lack of self-advocacy is a barrier to medical independence.	"Hate talking to people and hate talking to doctors"
	Barriers to medical independence include unwillingness to take on more responsibility despite having capability	"She's just rather be dependent on us until she can't anymore .. She just loves being catered to. She calls herself a "Passenger Princess" she doesn't need to get a license because she wants to be driven everywhere. There's no reason to why she doesn't want to do it, she can eat on her own she can do laundry, she can sew she can cook. She just doesn't want to. . . . . .She can read it all and gets alerts on my chart, she feels its one less responsibility so she doesn't want to do it. She's 18 but the less responsibility the less she has to worry about. She needs to have less stress in her life. At least the less stress she has the better her health is. .. She knows that if she doesn't have someone there, like taking medication, She will do it herself, like she will know to remember to take an medication. Put it in her reims or set alarms, she knows how to do it herself."
Impression of Pediatric Clinic	Pediatric clinics are associated with a warm peaceful environment with attention to detail and care for the patient	"[Pediatric clinic] is a very nice place and very happy and very caring about your well being. Every time I was hospitalized someone came to check up on me every appointment the staff was very kind to me, environment is very friendly and peaceful." "They're very attentive to every little thing that you know that a child is going through, no matter what the smallest thing it is. It can be the smallest detail and they take it to consideration. They're very good at making a child understand things. Serenity opens up in ways that she didn't before. Peaceful and Friendly. Make her feel comfortable in all her appointments I have no complaints Pediatrics is amazing."
Impression of Adult Clinic	Adult clinics are associated with long wait times, less attention to detail, lack of insurance coverage.	"[What comes to mind when I think of the adult clinic is] scary. Adult health care has a really bad name on it. You hear that doctors don't care, you hear [people] complain about the health care system." "You can clearly see the difference, and from the staff to the doctors to everything. As an adult things are overlooked, adults they push things back wait 3-4 months, will wait again. . . For children they're determined to find the answers. . . the health insurance will cover anything any treatment up until 21. Past 21 then what? Are they going to decide what is beneficial or not or what I have to pay for? That basically just sums it up. . . As she is getting older, the only time its serious is when health insurance is going to pay for."
Transition readiness barriers	Barriers to transition to adult clinic include lack of emotional/mental readiness, reluctance to more responsibility	"Like no one wants to actually transfer. So unless they dislike the provider or dislike the clinic or the staff, they're not really ready to transfer. None of them want to mentally transfer....we just tell them, like, hey, it's kind of like part of life. It's part of growing up." -Provider "Just that I'm getting up there in age, eventually will want to be take responsibility. Everyone feels not ready, [don't] want to take on responsibility if you don't have to"
Transition readiness tactics	Informal transition tactics include mentally preparing patients for subsequent transition	"We mentally prepare them by just saying that you're going to be sitting with like 60 and 70 year olds instead of other like cute kids. " "Well, we again we try to have them act more like adults and the, you know, we prepare them like a few that have gone over to the adult world. We sort of prepare them .... I mean these adult providers staff are not going to baby you like we were . . [we] try to have them act more like adults we prepare them. .
	Facilitators of transition readiness include attending appointments solo and allowing patients to speak independently	"It would be great to teach the kids to be independent in their teens. ... I wouldn't mind dropping them off and sitting in the car. Maybe things would be missed but it would make the patient speak more. . . . it would end up being a win-win situation. --you got to make these kids talk"
SLE document for providers	SLE document is useful for physicians to understand patient disease	"Seems it like would be helpful for doctors." "I think this would certainly make it a little easier to hold together a summary of your of the patient" "I loved it, I thought it was pretty comprehensive, with all the checkboxes."
SLE document for patients	SLE document may be too technical for patients to understand	"I . . kids will be confused. . . .the medical terms a child won't understand"
Transition document attitudes	Documents with additional personal details are useful to build rapport	"One key fact that you can give the adult rheumatologist to help build rapport "loves dog"; has "six cats", something they can build on to build rapport; something the pediatric rheumatologists has done when they're at the sickest. The adult rheumatologist is trying to build rapport in 30 minutes." "Like the demographics, and the personal details that might help the doctor connect with you" "This letter is [not] just about the medical part, its more about the personality part. This is more about her as a person as who she is. So it allows the doctor to understand her in both ways personally and medically"

Methods: Semi-structured interviews were conducted on rheumatologists, pre and post-transfer young adult patients (aged 14-26 with an established pediatric rheumatic disease diagnosis, with at least two visits with a pediatric or adult rheumatology provider within the last 24 months) and their parents/guardians (Table 1). Open-ended and Likert scale questions were asked regarding topics ranging from independence, transfer readiness, understanding of disease and opinions towards existing medical summaries on Systemic Lupus Erythematosus (SLE), and Juvenile Idiopathic Arthritis (JIA). Themes were analyzed using the Rapid Data Analysis and Reporting (RADaR) approach by 2 independent reviewers (Table 2). Descriptive analysis of exploratory pilot data was done with top-box scoring and median.

Results: Barriers to medical independence included lack of self-transportation, socio-economic factors, inability to self-administer medications, schedule appointments, self-advocate and an unwillingness to take on increased responsibility despite having capability to do so.

There was a discrepancy between providers rating of patients' general independence as compared to medical independence (Table 3).

Pediatric clinics were associated with attentiveness, friendly staff, peaceful environment and caring doctors. Adult clinics were associated with fear, lack of insurance coverage, less attention to detail and long wait times.

Transfer readiness was facilitated by mentally preparing patients for adult clinic expectations, patients' ability to self-advocate, attend appointments alone, rapport with adult physician and adult physician's knowledge of patient.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Views on Independence: adls vs medical

3a. Independance, as ascertained by providers:

	What percentage of pediatric patients > 18 years of age are independent with their care (ADLS) prior to transferring to the adult clinic?	[illegible]
Provider 2001	35	50
Provider 2002	90	70
Provider 2003	NA	NA
Provider 2004	100	NA
Provider 2005	98	65
Provider 2006	90	20
Provider 2008	95	10
Median:	96.50	50
Top box scoring: Percentage Rating 80/100 or above	85.71	0

3b. Independence, as ascertained by parents:

	How independent do you feel your child is (adls)?	Overall how independent is your child with medical care?
1003G Guardian	10	10
1010G Guardian	8	5
1011G Guardian	10	7
1013G Guardian	10	9
1025G Guardian	5	7
1026G Guardian	9	7
1031G Guardian	10	5
Median:	10.00	7.00
Top box scoring: Percentage Rating 8/10 or above	85.71	28.57

3c. Independence as ascertains by patients:

	How independent do you feel overall (adls)?	Overall, how independent are you with your medical care?
1003 Patient	5	10
1010 Patient	0	2
1011 Patient	10	10
1012 Patient	7	10
1013 Patient	8	5
1025 Patient	8	5
1026 Patient	9	9
1028 Patient	7	7
1031 Patient	10	10
Median:	8.00	9.00
Top box scoring: Percentage Rating 8/10 or above	66.67	55.56

SLE document was useful for physicians' understanding of patient disease, yet cumbersome for physicians to fill out and difficult for patients to understand. Documents with additional personal patients' details were deemed useful to build rapport.

Limitations include patient population in rural healthcare system as well as small sample size though further interviews are currently in progress.

Conclusion: Through semi-structured interviews we identified key barriers in transition readiness, independence and gained insight on existing transition documents. We intend to apply principles of human centered design to create an improved transition document and transition process.

Disclosure: L. Chang: None; **R. Sharma**: None; **E. Guziewicz**: None; **J. Jackson**: None; **K. Romagnoli**: None; **G. Campbell**: None; **S. Korukonda**: None; **P. Pawar**: None; **J. Cote**: None; **T. Davis**: None; **E. Brunner**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2151

Real-World Experience with IL-1 Blockade in Children with Undifferentiated Systemic Autoinflammatory Diseases (uSAIDs)

Maryam Ashoor[1], Kosar Asna Ashari[2], Kyle McBrearty[2], Joyce Chang[3], Jonathan Hausmann[4] and Fatma Dedeoglu[2], [1]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Brookline, MA, [2]Boston Children's Hospital, Boston, MA, [3]Boston Children's Hospital, Boston, [4]Boston Children's Hospital, bosto, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Autoinflammatory Diseases (SAIDs) are a group of rare disorders caused by dysregulation of the innate immune system. Over 50 genes have been identified as causative for SAIDs. However, 40-60% of patients presenting with features consistent with SAIDs remain without a definitive diagnosis and are often categorized as undifferentiated SAIDs (uSAIDs).

Treatment can be challenging due to heterogeneous presentations and uncertain disease mechanisms. This study aimed to evaluate the clinical and laboratory response to IL-1 blockade in pediatric patients with uSAIDs.

Methods: We conducted a retrospective chart review of patients diagnosed with uSAIDs and treated with IL-1 inhibitors (anakinra, canakinumab, or rilonacept) at a single tertiary pediatric center between January 2010 and December 2023. Inclusion required a clinical diagnosis of uSAID, treatment with IL-1 blockade, and documented follow-up within one year of initiation of treatment. Data collected included demographics, clinical phenotype, flare frequency and severity, laboratory markers (CRP, CBC), treatment characteristics, and adverse events. Response to treatment was assessed through laboratory values, clinical presentation, the need for rescue medications, and the overall physician assessment of improvement.

Results: Thirty-three patients (51.5% female) with uSIADs who contributed to fifty-five IL-1 blockade treatment instances were identified. The mean age at symptom onset was 4.3 years (range 0–20), and the mean age at diagnosis was 7.8 years (range 0.6–21). All patients underwent genetic testing not revealing a known monogenic systemic autoinflammatory disease. Common clinical features included recurrent fevers (87.9%), arthralgia (57.6%), abdominal pain (51.5%), and urticarial rash (42.4%). Most patients (75.8%) had trialed colchicine before starting IL-1 blockade. Treatments included Anakinra (49%), canakinumab (45.5%), or Rilonacept (5.5%). Rescue medications were used in 49.1% of instances with corticosteroids being the most common in 55.6%, NSAIDs in 37.0% and Anakinra in 7.4%. Flares occurred a mean of 4.11 per month (range 0.5–30) at baseline which reduced to a mean of 0.8 (range 0-3) per month on first follow up after initiating treatment. Physician-assessed clinical improvement was noted in 92.7% of treatment instances. CRP levels decreased from a mean of 3.38 ± 7.06 mg/dL pre-treatment to 0.45 ± 1.49 mg/dL post-treatment (normal < 0.5 mg/dL). Treatment was generally well-tolerated; adverse events occurred in 11% of instances, most commonly injection site reactions and elevated liver enzymes. At last follow-up, 97% remained on IL-1 therapy, most commonly canakinumab.

Conclusion: Our study demonstrates that IL-1 blockade therapy can yield favorable outcomes in patients with uSAIDs, as reflected by improvements in flare frequency and decreased reliance on rescue medications clinically and improved inflammatory markers. These findings underscore the potential of IL-1 blockade as an effective therapeutic strategy for this challenging patient population. Nevertheless, additional research is essential to validate these results and establish standardized treatment protocols for uSAIDs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Ashoor: None; **K. Asna Ashari**: None; **K. McBrearty**: None; **J. Chang**: Century Therapeutics, 2; **J. Hausmann**: None; **F. Dedeoglu**: Sobi, 6, UptoDate, 9.

Abstract Number: 2152

Blau Syndrome: features beyond the classic triad and proposal for clinical criteria

Narendra Bagri[1], Nawazish Shaikh[2], Manisha jana[3], Sushain kalsotra[4], Krithika Rajkumar[2], Madhumita Roy Chowdhury[2], Neerja Gupta[2], Danveer Bhadu[5], Vishal Gupta[2] and Rohan Chawla[2], [1]All India Institute of Medical Sciences(AIIMS), New Delhi, Delhi, India, [2]All India Institute of Medical Sciences, Delhi, Delhi, India, [3]ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Delhi, [4]All India Institute of Medical Sciences, Delhi, India, [5]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: This study describes the characteristic clinical and radiological findings and outcomes of patients with Blau syndrome from a single tertiary care hospital.

Methods: A retrospective chart review of patients with Blau syndrome with NOD2 mutation was conducted to describe key clinical and imaging findings.

Children diagnosed with Blau syndrome and followed in the Pediatrics Rheumatology clinic, Department of Pediatrics, XXX, from January 2022 to July 2024, were enrolled for this retrospective chart review.

The inclusion criteria included children with clinical features consistent with Blau syndrome (boggy synovial swelling and dermatitis ± ocular features such as uveitis) and pathogenic or likely pathogenic variants in the NOD 2 gene. The molecular analysis was done on the peripheral blood sample drawn after obtaining written consent. Mutational hotspot, exon 4 of the *NOD2* gene, was amplified using previously reported primers and Bi-directional Sanger sequencing was carried out. The variants were classified according to the American College of Medical Genetics and Genomics guidelines. The variant calling was performed using the Franklin platform (https://franklin.genoox.com, accessed 8 May 2024).

Results: The diagnosis of Blau syndrome in all nine patients (8 children and one adult) was confirmed genetically. The mean (range) age of children at diagnosis was 60 months (24-108 months). The mean (SD) age of symptom onset was 13 (7.7) months, with an age range of 3 to 24 months. The classic triad of uveitis, arthritis and dermatitis was present in 75% of children. The other manifestations include fever (n=4), cervical lymphadenopathy (n=1), hepatosplenomegaly (n=3) and dysmorphism (n=2). The ultrasound of joints showed synovial proliferation, giving a rounded or globular contour similar to the "sac of marbles". The most common debilitating morbidity noted was visual impairment. We propose a clinical criterion to facilitate early diagnosis of Blau syndrome in resource-limited settings. Table 1 summarises the key clinical features of our study subjects.The skin lesions include dull-red micropapular eruption on face and extremities and icthyosiform scaling on bilateral legs (Fig 1E,F,I & J).On US imaging, the wrist was the most affected joint (7/8), followed by the knee (6/8). Synovial thickening with a characteristic echogenic appearance was a universal observation in all subjects (Figure 2). A distinct nodular/ finger-like projection of synovium was noted in all cases.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

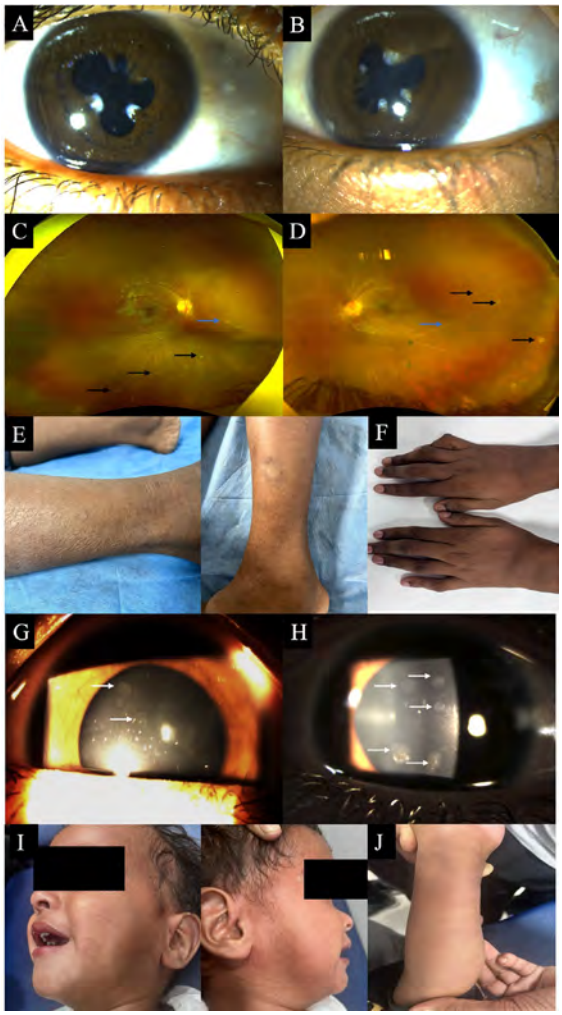
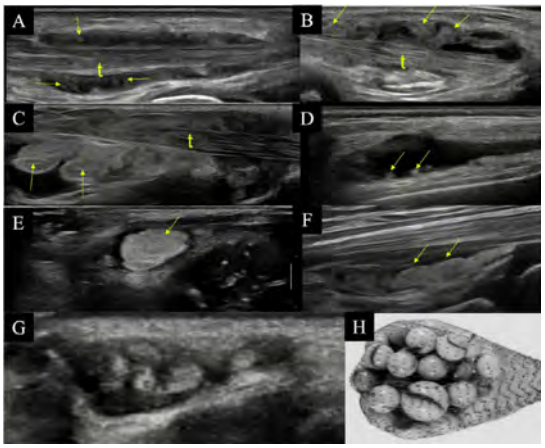


Figure 1: Representative Features of Blau Syndrome in Case 4 – Ocular features: Posterior synechiae and festooning of pupil (A&B;) Focal patches of chorioretinal atrophy in the mid-periphery, periphery (black arrow, C & D) and peripheral vasculitis (blue arrow, C & D). Dermatological features: Scaly ichthyotic patches on bilateral legs and hands(E&F). Features seen in Case 7: Superficial nummular corneal opacities (white arrow, G & H) with no other ocular features. Dermatological features: Flat-topped erythematous micropapules on face and extremities (I & J)



Ultrasonographic features of Blau syndrome. A-C. Tenosynovitis in 3 different patients (A-Case 4; B-Case 7;C-Case 8). There is minimal fluid in the tendon (t) sheath, along with significant filiform echogenic synovial thickening (arrows). D-G. Intra-articular synovitis in 4 patients (D-Case 1;E-Case 2;F-Case 4; G-Case 5).Knee joint US showing finger-like echogenic projection in the suprapatellar bursa (arrows), along with some joint effusion (D). The synovial proliferation was bright echogenic and nodular (E) in some cases and undulated globular in others (F). The nodular lobulated appearance of intra-articluar synovial proliferation (G), akin to 'sac of marbles'; as seen in H

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 : Key clinical features in Blau Syndrome in our cohort

S. No	Age (in)	Gender (M/F)	Age at onset (in)	Clinical Features	Genetic Variant NOD 2, Exon 4	Treatment	Status at Last Follow-up (Duration in months)
1	48	M	7	Arthritis, dermatitis, camptodactyly	c.1013D>A (p.Arg338Gln)	Methotrexate, Adalimumab (Off Adalimumab for 3months), Topical therapy for uveitis *	Remission (24)
2#	44	M	3	Fever, arthritis, camptodactyly, dermatitis, uveitis, Hepatosplenomegaly Mild proteinuria (Up:Uc:0.1) Early nephrocalcinosis on USG	c.1013D>A (p.Cys466Tyr)	Methotrexate, Adalimumab Topical therapy for uveitis *	Remission(3) Unexplained death at home (after this follow-up)
3	51	F	6	Fever, arthritis, dermatitis, uveitis, hepatosplenomegaly	c.920G>A (p.Arg307Gln)	Adalimumab,Methotrexate	Remission(13)
4	96	F	24	Fever, arthritis, dermatitis, uveitis	c.1006G>C (p.Gly336Gln)	Methotrexate Topical therapy for uveitis *	Remission(15)
5	10 8	M	24	Fever, arthritis, dermatitis, uveitis, hepatosplenomegaly, coarse facial features	c.1013D>A (p.Arg338Gln)	Methotrexate, Adalimumab Topical therapy for uveitis *	Remission(54)
6	53	M	24	Arthritis, dermatitis, uveitis	c.919C>T (p.Arg307Trp)	Adalimumab, Methotrexate Topical therapy for uveitis *	Remission(12)
7	24	M	6	Arthritis, camptodactyly, dermatitis	c.919C>T (p.Arg307Trp)	Methotrexate	Remission(10)
8	16 8	F	10 yrs JIA	Fever, arthritis, uveitis, hepatosplenomegaly	c.1013D>A (p.Arg338Gln)	Methotrexate, Adalimumab	Remission(6)
9	36 0	F	5 yrs	Uveitis, arthritis, camptodactyly	c.919C>T (p.Arg307Trp)	Methotrexate Topical therapy for uveitis *	Active anterior uveitis (1 week)

Topical therapy for uveitis: Topical Prednisolone 1% with topical cycloplegic
Unexplained death at home (telephonically conveyed); * Incidentally diagnosed

Table 2 : Key Ocular features in Blau Syndrome in our cohort

Sr. No	At enrolment						At last follow-up						
	Vision and IOP		Type of Uveitis		Ocular findings		Vision and IOP		Uveitis		Duration of Follow-up (months)	Complications	Therapy (Topical and Oral)
	R	L	R	L	R	L	R	L	R	L			
1	20/20,16	20/20,14	No Uveitis	No Uveitis	-	-	20/20,16	20/20,14	No	No	24	None	None
2	20/200,12	20/200,14	Anterior Uveitis	Anterior Uveitis	Posterior synechiae with festooned pupil with PSC and optic nerve edema	Posterior synechiae with festooned pupil, PSC, optic nerve edema	20/200,14	20/200,14	No activity	No Activity	15	PSC	Topical Prednisolone (Single drop) Oral MTX Injection Ada 40mg SC
3	PL+,8	No PL,8	Panuveitis	Panuveitis	360 degree posterior synechiae with total cataract with RD	360 degree posterior synechiae with total cataract with RD	PL+,12	No PL,6	No activity	No activity	13	Both eye Cataract with RD	Topical prednisolone (Single drop) Oral Corticosteroids (<0.2mg/kg)
4	20/30,14	20/200,16	Panuveitis	Panuveitis	Posterior synechiae, festooned pupil, focal cataractous changes, mid-peripheral focal healed choroiditis patches	Posterior synechiae, festooned pupil, focal cataractous changes, mid-peripheral focal healed choroiditis patches with peripheral healed vasculitis	20/40,16	20/60,16	No Activity	No Activity	15	Both eye focal cataractous changes	Topical Prednisolone (single drop) Oral Corticosteroids (<0.2mg/kg) MTX Injection Ada 40mg SC
5	20/200,10	20/200,10	Panuveitis	Panuveitis	Superficial nummular corneal opacity, posterior synechiae, festooned pupil, mid-peripheral healed choroiditis patches	Superficial nummular corneal opacity, posterior synechiae, festooned pupil, mid-peripheral healed Choroiditis patches	20/200,12	20/200,12	No Activity	No Activity	54	Both eye: Focal cataractous changes	Topical prednisolone (single drop) Oral corticosteroids (<0.2mg/kg) MTX Injection Ada 40mg SC
6	20/40,18	20/32,18	Anterior Uveitis	Anterior Uveitis	Superficial nummular corneal opacity, no synechiae	Superficial nummular corneal opacity, no synechiae	20/20,14	20/20,14	No Activity	No Activity	12	None	Topical prednisolone (single drop) Oral MTX Injection Ada 40mg SC
7	20/20,16	20/20,16	No uveitis	No Uveitis	Superficial nummular corneal opacity	Superficial nummular corneal opacity	20/20,14	20/20,14	No	No	10	None	Oral MTX Injection Ada 40mg SC
8	20/32,10	20/20,10	Panuveitis	Panuveitis	Superficial nummular corneal opacity, no posterior synechiae, mid-peripheral healed focal choroiditis patches	Superficial nummular corneal opacity, no posterior synechiae, mid-peripheral healed focal choroiditis patches.	20/20,12	20/20,12	No Activity	No Activity	6	None	Topical prednisolone (single drop) Oral corticosteroids (<0.2mg/kg) MTX Injection Ada 40mg SC
9	20/200,14	20/200,10	Panuveitis	Panuveitis	Superficial nummular corneal opacity, posterior synechiae, mid-peripheral healed focal choroiditis patches with optic nerve edema	Superficial nummular corneal opacity,360-degree posterior synechiae, mid-peripheral healed focal choroiditis patches with optic nerve edema	20/200,14	20/200,10	Active	Active	1 week	L: PSC	Topical Prednisolone (6times/day) Oral Corticosteroids (1mg/kg)

R: Right, L: left, PL: perception of light, PSC: posterior subcapsular cataract, MTX: Methotrexate, Ada:Adalimumab, RD: Retinal Detachment

Key clinical features in Blau Syndrome in our cohort

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Based on our findings and existing literature, we propose clinical criteria to facilitate early diagnosis of Blau syndrome in such settings.

Arthritis with boggy synovial swelling ***plus two of the following***
· Skin lesions: flat-topped red-skin coloured micropapules
· Uveitis: Anterior uveitis with superficial nummular corneal opacity or Panuveitis with focal chorioretinal atrophy patches in mid-periphery/periphery or granulomatous uveitis
· Fever

And either of two**:**
· Biopsy (Synovial/ Skin) suggestive of granulomatous inflammation
· USG joints: exuberant nodular echogenic synovial proliferation out of proportion to joint effusion

Disclosure: N. Bagri: None; **N. Shaikh**: None; **M. jana**: None; **S. kalsotra**: None; **K. Rajkumar**: None; **M. Chowdhury**: None; **N. Gupta**: None; **D. Bhadu**: None; **V. Gupta**: None; **R. Chawla**: None.

Abstract Number: 2153

Giant Coronaries in Children with Kawasaki Disease: A Single Centre Experience

Pavneet Kaur[1], Mayank Goyal[2], Shivaprasad P Mohankumar[2], Lamk Kidyani[2], Sanjeev Kumar[2], Saurabh Gupta[3], Sivasubramanian Ramakrishnan[2] and Narendra Bagri[4], [1]All India Institute of Medical Sciences, New Delhi, India, [2]AIIMS, New Delhi, India, New Delhi, Delhi, India, [3]All India Institute of Medical Sciences, New Delhi, Delhi, [4]ALL INDIA INSTITUTE OF MEDICAL SCIENCES, New Delhi, Delhi, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Coronary artery abnormalities (CAA) are a dreaded yet potentially preventable stigmata of Kawasaki disease (KD). Giant CAA are rare but at higher risk of complications and adverse outcomes. We aimed to evaluate the medium-term outcomes of children with KD with giant coronary aneurysms (Z score >10).

Methods: KD cases registered in our tertiary care centre were retrospectively reviewed, and data of children with giant CAA was analysed.

Results: Of the 34 KD cases in our register (2018-2024), we encountered 5 children (14.7%) with giant coronaries. All children presented as incomplete KD, with delayed immunomodulation and IVIg resistance. One patient had extensive systemic vascular involvement beyond the coronaries. The high proportion of children with giant coronaries as opposed to the reported literature might be due to a referral bias. The diagnosis of KD and initiation of immunomodulation took a median (IQR) of 12 (10-14) days. All received IVIg and oral steroids, with IV methylprednisolone pulse in two. All but one received primary intensification with Infliximab. CAAs persisted in all, noted during the 22 patient-years of follow-up. There was one mortality owing to a cardiovascular event. Our experience, although limited, was concordant with published literature suggesting that male sex, aneurysms at onset, delayed IVIG therapy and IVIg resistance are heralds of giant CAAs in KD. Similarly, systemic vascular involvement was associated with a poor outcome.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

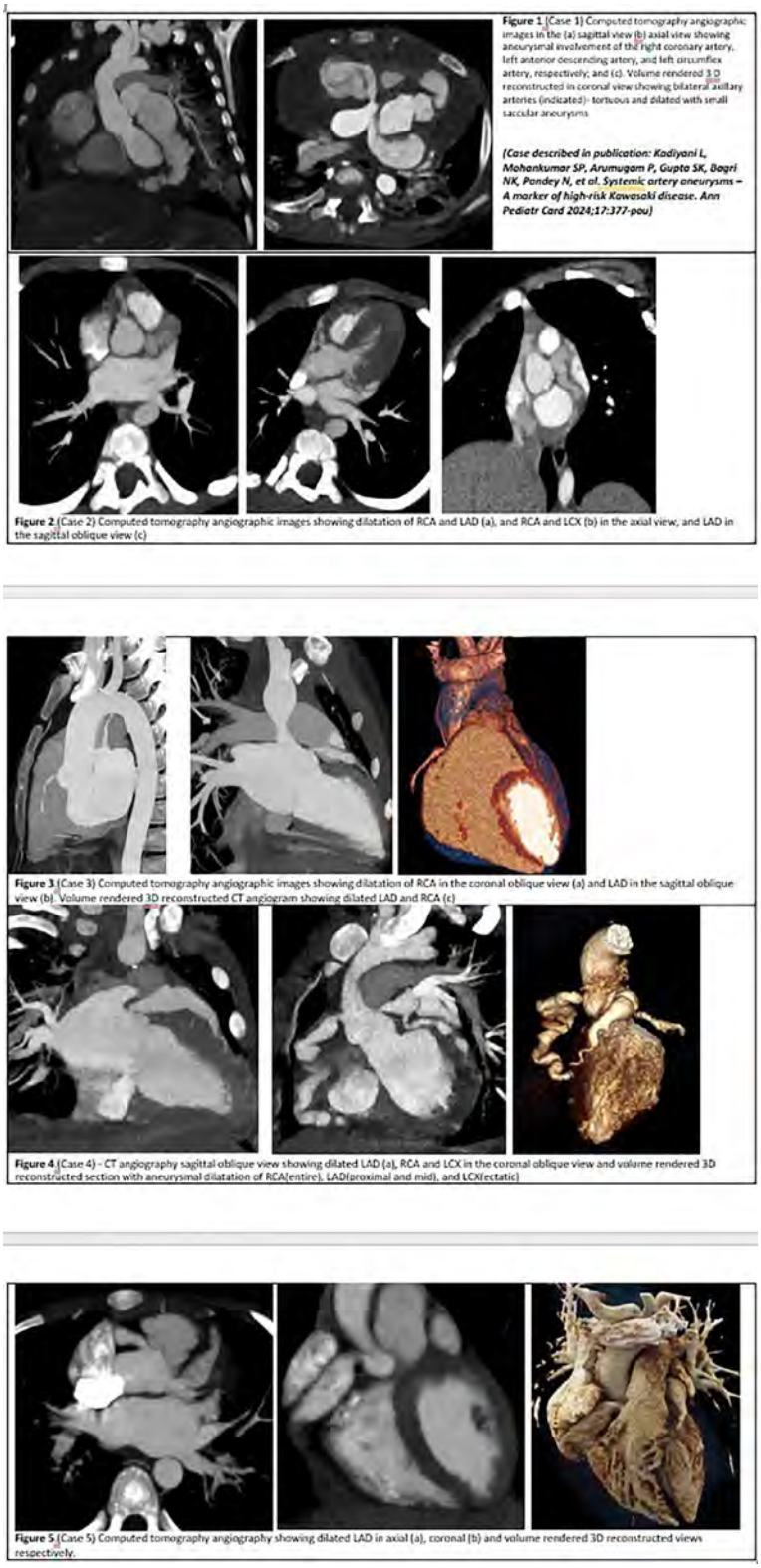


Figure 1 (Case 1) Computed tomography angiographic images in the (a) sagittal view (b) axial view showing aneurysmal involvement of the right coronary artery, left anterior descending artery, and left circumflex artery, respectively; and (c). Volume rendered 3 D reconstructed in coronal view showing bilateral axillary arteries (indicated)- tortuous and dilated with small saccular aneurysms

(Case described in publication: Kadiyani L, Mohankumar SP, Arumugam P, Gupta SK, Bagri NK, Pandey N, et al. Systemic artery aneurysms – A marker of high-risk Kawasaki disease. Ann Pediatr Card 2024;17:377-pou)

Figure 2 (Case 2) Computed tomography angiographic images showing dilatation of RCA and LAD (a), and RCA and LCX (b) in the axial view, and LAD in the sagittal oblique view (c)

Figure 3 (Case 3) Computed tomography angiographic images showing dilatation of RCA in the coronal oblique view (a) and LAD in the sagittal oblique view (b). Volume rendered 3D reconstructed CT angiogram showing dilated LAD and RCA (c)

Figure 4 (Case 4) - CT angiography sagittal oblique view showing dilated LAD (a), RCA and LCX in the coronal oblique view and volume rendered 3D reconstructed section with aneurysmal dilatation of RCA(entire), LAD(proximal and mid), and LCX(ectatic)

Figure 5 (Case 5) Computed tomography angiography showing dilated LAD in axial (a), coronal (b) and volume rendered 3D reconstructed views respectively.

CT images of children with Kawasaki disease with giant coronaries

Conclusion: Incomplete KD may have a high propensity to develop giant coronaries, possibly refractory to immunomodulation. As is evident in our series, delayed diagnosis and immunomodulation (12 (10-14) days) are important factors determining CAA prognosis. Although rare, giant and systemic arterial aneurysms in KD are life-threatening and difficult to manage. They may progress despite appropriate immunomodulation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

S.No.	Age*	Sex	Presentation	Pre-immunomodulation Parameters	Immuno-modulations	Post-immunomodulation	Antithrombotic prophylaxis	Latest coronary imaging	Follow-up (Outcome)
1.R	5	F	Fever Diaphoresis Pulsatile axillary swelling	Echocardiography: Dilated coronaries with aneurysmal LAD, dilated descending thoracic aorta, subclavian and axillary axis, dilated common femoral artery	On day 10 of illness	Echocardiography: Dilated coronaries with aneurysmal LAD Common Femoral 11mm x 6 mm Axillary 12mm x 20mm	Enoxaparin Aspirin	Dilated coronaries with aneurysmal LAD on echocardiography	2 months (Mortality)
				TLC- 16,200/mm³ Neutrophilia 70% Platelet- 3,20,000/mm³ ESR-32mm/hr CRP- 125 mg/dL Urinalysis- Sterile pyuria (leukocytes 20-30/hpf). s.Sodium- 135 mEq/L SGPT-49 U/L Hemoglobin- 8.5 g/dL s.Albumin- 3.6 g/dL Kobayashi score 2	IVIg IVMP pulse Oral steroids Infliximab Cyclosporine	CRP- 4.1 mg/dL			
2.S	24	M	Fever Edema and desquamation Conjunctivitis	Echocardiography: giant CAA LMCA 6.6 mm(11.6 SDS) LAD-8 mm LCX 7.3mm RCA 5.5 mm no thrombosis evident	On day 12 of illness	Echocardiography for coronary sizes: giant CAA LMCA 6.6(10.2) LAD-8 mm (9) LCX 7.3mm (7.9) RCA 5.5mm (8.5) CT Angiography- no thrombosis	Aspirin Enoxaparin Atorvastatin (Enoxaparin switched to Warfarin)	Persistent GCAA on CT LMCA bifurcation and LAD aneurysm 21x11mm Proximal LCX fusiform aneurysm-10 mm x 6 mm	6 years
				TLC- 16,200/mm³ Neutrophilia 70% Platelet- 10,00,000/mm³ ESR-100 mm/hr CRP- 150 mg/L Urinalysis- normal SGPT-12 U/L s.Sodium-134 mEq/L Hemoglobin- 8.6 g/dL s.Albumin 3.5 g/dL Kobayashi score 1	IVIg Infliximab	ESR-22 mm/hr CRP- 5.9 mg/dL			
3.J	60	M	Fever Edema and desquamation Strawberry tongue	Echocardiography: giant CAA LMCA 3 mm(1) LAD- 6.5mm (15.1) LCX-4mm (-) RCA- 5.1mm (8.8)	On day 8 of illness	Echocardiography for coronary sizes: giant CAA LMCA 6.6(9.7) LAD-8 mm (20.2) LCX 7.3mm ( ) RCA 5.5 (9.6) CT Angiography- no thrombosis	Aspirin Heparin Warfarin Atorvastatin	Persistent GCAA on CT LMCA- 3mm(1) LAD-6mm (13.4) LCX-4mm(-) RCA-5.2mm (8.8) (3 years after onset)	3 years
				TLC- 17,000/mm³ Neutrophilia 76% Platelet- 4,52,000/mm³ ESR 60 mm/hr CRP- 245 mg/L Urinalysis- normal SGPT- 37 (U/L s.Sodium- 136 mEq/L Hemoglobin- 10.6 g/dL s.Albumin- 2.7 g/dL Kobayashi score 2	IVIg Infliximab Oral steroids	ESR 68 mm/hr CRP 18 mg/dL			
4.H	6	M	Fever Conjunctivitis Rash	Echocardiography for coronary sizes: giant CAA (no sizes provided)	On day 10 of illness	Echocardiography: LAD- Dilated RCA- Dilated (no progression)	Aspirin Clopidogrel Warfarin	Persistent GCAA on CT LMCA-4mm (8) Aneurysmal LAD-5mm(6.7) LCX – 2 mm RCA-3mm (9) No thrombosis	6 years
				TLC- 16,140/mm³ Neutrophilia 83% Platelet- 774,000/mm³ *post IVIg dose* ESR 80 mm/hr CRP- 18.9 mg/L SGPT- 9 Hemoglobin- 10.9 g/dL Urinalysis, s.Sodium and Albumin- data unavailable Kobayashi score 2	IVIg Oral Steroids (treated outside, presented 1 month after illness onset)	ESR- 7 mm/hr CRP- 0.37 mg/dL			
5.A	9y	M	Fever Conjunctivitis Desquamation Strawberry tongue	Echocardiography: (only 2 scores available) LMCA-9.4 LAD- 14 LCX-not available RCA-9.4	On day 14 of illness	Echocardiography: LMCA-5.4mm (6) LAD-9mm (9.7) LCX-4mm (4.1) RCA-8.7mm (10)	Beta blocker Warfarin Enoxaparin Atorvastatin	Persistent GCAA on CT LMCA-2.5mm (0.1) LAD-15 mm (13.7) LCX-4.8 mm (5.1) RCA-2.5mm (1)	7 years
				TLC- 17,000/mm³ Neutrophilia 76% Platelet- 8300/mm³ ESR-67 mm/hr CRP- 225 mg/L Urinalysis- normal SGPT- 17 U/L Hemoglobin- 4.4 g/dL s.Sodium- 143 mEq/L s.Albumin- 3.6 g/dL Kobayashi score 1	IVIg IVMP pulse Oral steroids Repeat IVig Infliximab	ESR 70 mm/hr CRP 4.4 mg/dL		(6 years after onset)	

*Age represented in months, Kobayashi formula used for calculating coronary Z scores, sizes expressed as mm (Z score)
RCA: Right coronary artery, LAD: Left anterior descending artery, LCX: Left circumflex artery
IVIg: Intravenous immunoglobulin (2g/kg), IVMP 30 mg/kg/dose for 3 days followed by oral steroids, infliximab: 10mg/kg/dose, oral steroids: 2mg/kg/ dose, tapered over 2-3 weeks
M: male, F: female; ESR- erythrocyte sedimentation rate, CRP- C reactive protein

Series of children with Kawasaki disease with giant coronaries

Disclosure: P. Kaur: None; **M. Goyal**: None; **S. P Mohankumar**: None; **L. Kidyani**: None; **S. Kumar**: None; **S. Gupta**: None; **S. Ramakrishnan**: None; **N. Bagri**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2154

Whole-Body MRI Findings in a Cohort of Children with Chronic Nonbacterial Osteomyelitis

Mara Rodriguez[1], Maurice Davenport Munoz[2], Kiery Braithwaite[3], Lori Ponder[4], Kelly Rouster-Stevens[5], Solveig Argeseanu Cunningham[6] and **Sampath Prahalad**[7], [1]Emory University School of Medicine / Children's Healthcare of Atlanta, Atlanta, GA, [2]Emory University School of Medicine, Pediatrics, Atlanta, [3]Children's Healthcare of Atlanta, Atlanta, GA, [4]Emory University, Atlanta, GA, [5]Emory University/Children's Healthcare of Atlanta, Peachtree Corners, GA, [6]Emory Rollins School of Public Health Department of Global Health, Atlanta, GA, [7]Emory + Children's Pediatric Institute, Atlanta, GA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is an autoinflammatory bone disorder characterized by multifocal, sterile bone inflammation in childhood. Whole-body magnetic resonance imaging (WB-MRI) allows for a comprehensive assessment of skeletal involvement in CNO, which can enhance our understanding of the disorder and its implication for child wellbeing. Our objective was to provide a novel perspective of CNO, leveraging WB-MRI methods linked with clinical records to identify the demographic, clinical, and imaging characteristics of the children receiving care at a tertiary pediatric center.

Methods: We conducted a retrospective review of the pediatric patients diagnosed with CNO over a 10-year period (n=76). To be included children had to have a diagnosis of CNO confirmed by a pediatric rheumatologist, be less than 18 years old at time of diagnosis, and had a WB-MRI within 12 months of symptom onset. Demographic data, clinical features, extraosseous involvement, diagnostic and treatment modalities, and lesion distribution were ascertained by review of the electronic medical record. Lesion counts and locations were extracted from MRI reports and were validated by a musculoskeletal radiologist.

Table 1: Characteristics of the CNO Cohort	Frequency (%) *n = 76*
Race	
White	52 (68%)
Black or African American	19 (25%)
Asian	4 (5%)
American Indian/Alaskan Native	1 (1%)
Gender: Female	42 (55%)
Modalities of Diagnosis	
Whole Body MRI	76 (100%)
XRAY	66 (87%)
Bone Biopsy	31 (41%)
Bone Scan	2 (3%)
Age	
Age of onset of symptoms; years, Median (IQR)	10.2 (7.7 – 12.8)
Age of diagnosis in years; years, Median (IQR)	10.7 (8.2 – 13.4)
Time to WB-MRI; months, Median (IQR)	2.2 (0.5 – 5.7)
No. of lesions per patient; Median (Range)	4 (1 - 23)
Extra Osseous Features	
Arthritis	6 (8%)
Psoriasis	6 (8%)
IBD	3 (4%)
HLA B27 Positive (Total tested n=50)	8 (16%)
Medications	
Non-steroidal anti-inflammatory drugs (NSAIDS)	71 (93%)
Tumor Necrosis Factor-Inhibitors (TNF-I)	29 (38%)
Disease-modifying antirheumatic drugs (DMARDS)	21 (28%)
Pamidronate / Bisphosphonates	2 (3%)

Characteristics of the CNO cohort

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

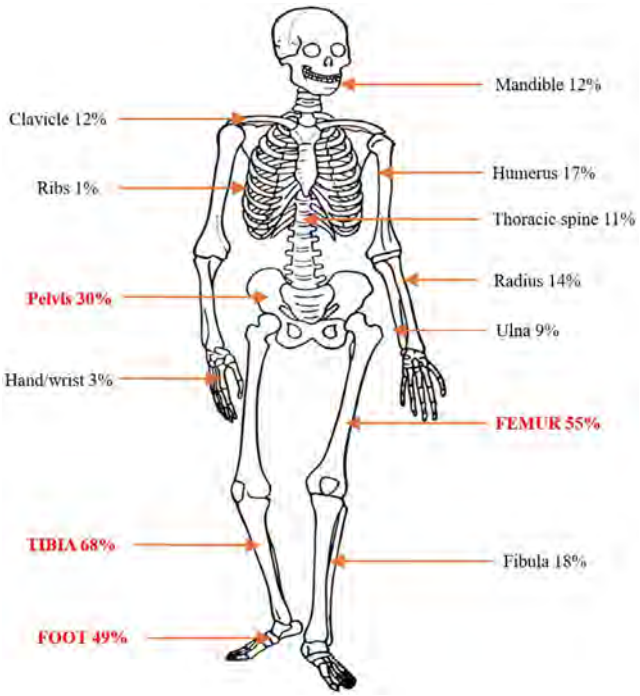
Table 2: Characteristics of skeletal lesions in patients with CNO

Bone involved	Patients affected (%) *n = 76*	Total lesions at site *n = 410*
Mandible	9 (12%)	9
Clavicle	9 (12%)	9
Ribs	1 (1%)	3
Thoracic Spine	8 (11%)	14
Pelvis	23 (30%)	43
Humerus	13 (17%)	21
Ulna	7 (9%)	9
Radius	11 (14%)	15
Hand/Wrist	2 (3%)	5
Femur	42 (55%)	81
Tibia	52 (68%)	109
Fibula	14 (18%)	20
Foot	37 (49%)	72

Characteristics of skeletal lesions in patients with CNO

Results: Among the 76 patients (55% female), the median age at symptom onset was 10.2 years (Inter quartile range 7.7–12.8), and the median age at diagnosis was 10.7 years (IQR 8.2-13.1). WB-MRI was performed within a median 2.2 months after onset (IQR 0.5-5.7 months) and identified 410 lesions across the cohort. Asymptomatic lesions were common, highlighting the diagnostic value of WB-MRI. The median number of lesions per patient was 4 (range 1-23). The tibia (68%), the femur (55%) and the foot (49%) were the most frequently involved sites. Thoracic vertebral lesions were seen in 8 children. The mandible was involved in 9 children; interestingly 5 patients (56%) had extra-mandibular lesions. Extraosseous features including arthritis, psoriasis, and inflammatory bowel disease were seen only in a small subset of patients. HLA-B27 was positive in 16% of those tested. NSAIDs were the most used medication (93%), followed by TNF inhibitors (38%) and DMARDs (27%). At the last visit 19% were described by their pediatric rheumatologist as being in remission.

Conclusion: This is one of the largest single center cohorts of CNO with WB-MRI evaluation. Among children with CNO attending a tertiary care clinic, WB-MRI revealed a high burden of multifocal disease, often with clinically asymptomatic lesions. Confirming other published reports, CNO was more common in girls and onset age was around 10. Tibia, femur and the bones of the feet were frequently affected comparable to several multicenter CNO cohorts. Mandibular lesions were



Distribution of lesions in patients with CNO

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

more frequent than in other reported cohorts. The diversity of lesion sites underscores the importance of WB-MRI in comprehensive evaluation. These findings support routine WB-MRI in the diagnostic work-up and monitoring of pediatric CNO.

Disclosure: M. Rodriguez: None; **M. Davenport Munoz**: None; **K. Braithwaite**: None; **L. Ponder**: None; **K. Rouster-Stevens**: Accordant, 2; **S. Argeseanu Cunningham**: None; **S. Prahalad**: None.

Abstract Number: 2155

A Novel TNFAIP3 Mutation Associated with Large Vessel Vasculitis: Expanding the Phenotypic Spectrum of A20 Haploinsufficiency

Sirada Panupattanapong[1], roshini Abraham[2], Urekha Karri[3], Harry Lesmana[1] and Daniella Schwartz[4], [1]Cleveland Clinic Foundation, Cleveland, OH, [2]Nationwide Children's Hospital, Columbus, OH, [3]School of public health, Pittsburgh, PA, [4]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Loss-of-function pathogenic variants in *TNFAIP3* lead to haploinsufficiency of A20 (HA20), a complex immune dysregulation disorder that can mimic Behcet's disease, IBD, periodic fever syndrome, and varied other rheumatic diseases. This study, we describe a novel *TNFAIP3* variant in an adolescent diagnosed with large vessel vasculitis.

Methods: A targeted genetic panel on the proband and parental single-gene testing were conducted by Invitae. Variant effect on canonical function was evaluated by NF-kB luciferase reporter (Cignal) in A20-deficient HEK293T cells transfected with empty vector, WT, and mutant *TNFAIP3*, and then stimulated with TNF-a. A20 protein expression was measured in primary cells using Western blot. NFkB and inflammasome activity in patient's cells were evaluated after stimulating PBMCs (monocytes) with LPS or LPS+ATP for 2h or 24h. Then cytokine production (IL-18, IL-1b, TNF-a and IL-6 in pg/mL) was measured at each time-point, using clinical ELISA testing, and compared to data from 73 pediatric and adult healthy controls.

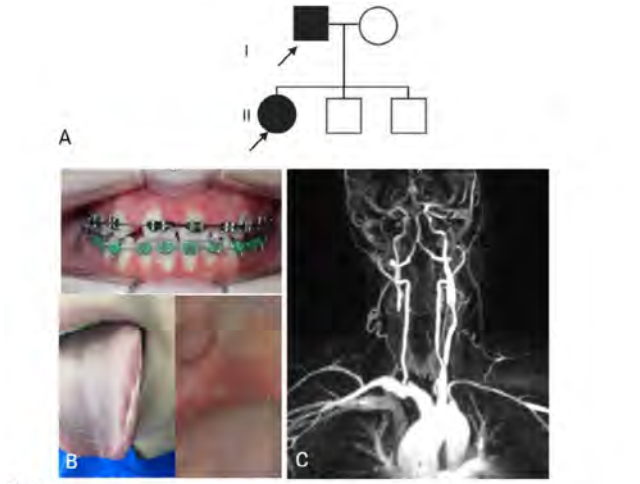


Figure 1
A. Pedigree of patient/family shows segregation of genotype and phenotype
B. Photo of the patient showing gum swelling (with histopathology revealing granulomatous inflammation), along with tongue and oral ulcers
C. MRA brain and carotid arteries revealed abnormalities in aorta, carotid arteries, subclavian arteries and other branches, consistent with large vessel vasculitis

Figure 1 Clinical presentation of the proband and the family pedigree

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Proinflammatory cytokine production from stimulated PBMC of the patient compared to healthy controls

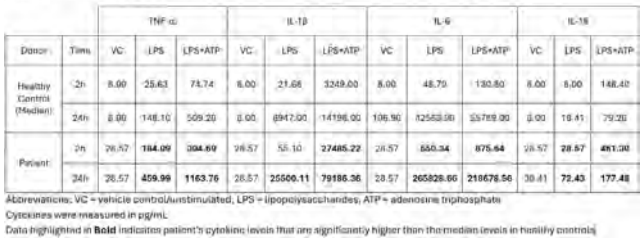


Table 1 Proinflammatory cytokine productions from stimulated PBMC of patients compared to healthy controls

		TNF-α			IL-1β			IL-6			IL-18		
Donor	Time	VC	LPS	LPS+ATP	VC	LPS	LPS+ATP	VC	LPS	LPS+ATP	VC	LPS	LPS+ATP
Healthy Control (Median)	2h	8.00	25.63	73.74	8.00	21.68	3249.00	8.00	48.70	130.80	8.00	8.00	148.40
	24h	8.00	148.10	509.20	8.00	6947.00	14196.00	106.90	12563.00	35789.00	8.00	16.41	79.20
Patient	2h	28.57	**184.09**	**304.69**	28.57	55.10	**27485.22**	28.57	**550.34**	**875.64**	28.57	**28.57**	**461.00**
	24h	28.57	**459.99**	**1163.76**	28.57	**25500.11**	**79186.36**	28.57	**265828.66**	**218676.56**	30.41	**72.43**	**177.48**

Abbreviations: VC = vehicle control/unstimulated, LPS = lipopolysaccharides, ATP = adenosine triphosphate
Cytokines were measured in pg/mL
Data highlighted in **Bold** indicates patient's cytokine levels that are significantly higher than the median levels in healthy controls

Results: The proband presented at age 16-year with chronic anemia, progressive oral ulcers, corneal ulcers, erythema nodosum, granulomatous gingivitis, and ultimately large vessel vasculitis involving thoracic/abdominal aorta and branches (Figure 1). She had history of hyperinflammatory skin reactions to injections/bug bites since age 2, and an episode of severe aseptic meningitis at age 5. Clinical genetic testing revealed a paternally-inherited heterozygous missense variant in *TNFAIP3*, c.1504C >T (p. Arg502Trp, NM_006290.3). The patient's father reported a history of childhood onset oral ulcers, a self-resolving PFAPA-like syndrome, adult-onset psoriasiform rash, IBD, and arthritis (Figure 1).

This variant has CADD score of 26.2 and REVEL score of 0.356. It is listed in ClinVar as a VUS and has an ACMG score of 5 (VUS), PM1, PM2 and PP3. *In vitro*, the variant was weakly hypomorphic (p = 0.04); basal A20 expression was normal in PBMC from patient and her father. Proband's cells stimulated with LPS +/- ATP displayed enhanced production of TNF-a, IL-6 and IL-18 at 2 hours and 24 hours. For IL-1b, there was an increase observed at 24h after LPS stimulation and at 2h and 24h with LPS+ATP (Table 1). Consistent with this result, S100A8/9 were elevated in proband and her father. The proband's cells also exhibited enhanced expression of Siglec-1, indicating Type 1 interferon activation. Expression of interferon-stimulated genes (ISG) was elevated in the proband and her father relative to healthy volunteers. Together, these data suggest acute and chronic activation of canonical NFkB, inflammasome, and Type 1 interferon signaling align with prior immunologic findings in *TNFAIP3* loss-of-function variants.

Conclusion: The clinical phenotype, pedigree, and functional immune evaluation of the patient and her father provide evidence supporting a pathogenic role for the *TNFAIP3* variant. Further, we extend the HA20 clinical phenotype to include large-vessel vasculitis. This case also underscores the essential role of comprehensive functional evaluation in interpreting novel VUS which is crucial for advancing our understanding of their impact on key biological pathways.

Disclosure: S. Panupattanapong: None; **r. Abraham**: Amgen, 5; **U. Karri**: None; **H. Lesmana**: Pharming, 2; **D. Schwartz**: Eli Lilly, 5, Jeffrey Modell Foundation, 5, National Institutes of Health, 5, Samuel and Emma Winters Foundation, 5, Sobi, 1, 5.

Abstract Number: 2156

Bridging the Gap: Juvenile Spondyloarthritis (JSpA) vs. Chronic Non-bacterial Osteomyelitis (CNO)

Sophia Elfrink[1], Timothy Brandon[1], Jahan Jazayeri[1] and Pamela Weiss[2], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical information about study cohort (n=137). ^HLA-B27 status unavailable on 4 JSpA patients, 43 CNO patients, and 5 JSpA/CNO patients.

	JSpA (n=53)	CNO (n=64)	JSpA/ CNO (n=20)	p-value
Age at index (median, IQR)	13.1 (9.3-15.7)	10.6 (7.5-12.9)	14.9 (11.6-15.8)	<0.001
Sex				0.254
Female	29 (54.7%)	41 (64.1%)	15 (75.0%)	
Male	24 (45.3%)	23 (35.9%)	5 (25.0%)	
Race				0.797
Asian	2 (3.8%)	2 (3.1%)	0 (0.0%)	
Black	5 (9.4%)	4 (6.3%)	0 (0.0%)	
White	35 (66.0%)	48 (75.0%)	17 (85.0%)	
Other	9 (17.0%)	8 (12.5%)	3 (15.0%)	
Unknown	2 (3.8%)	2 (3.1%)	0 (0.0%)	
Ethnicity				0.273
Hispanic	3 (6.0%)	3 (4.8%)	3 (15.0%)	
Non-Hispanic	47 (94.0%)	60 (95.2%)	17 (85.0%)	
Closest family member with autoimmune disease				0.176
1st degree	22 (41.5%)	19 (29.7%)	10 (50.0%)	
2nd degree	18 (34.0%)	18 (28.1%)	6 (30.0%)	
Human Leukocyte Antigen B27 (HLA-B27)^	14 (28.6%)	3 (14.3%)	5 (33.3%)	0.352
Psoriasis	11 (20.8%)	2 (3.1%)	11 (55.0%)	<0.001
Inflammatory Bowel Disease (IBD)	6 (11.3%)	1 (1.6%)	2 (10.0%)	0.084
Enthesitis	28 (52.8%)	7 (10.9%)	11 (55.0%)	<0.001
Peripheral arthritis	33 (62.3%)	5 (7.8%)	12 (60.0%)	<0.001
Sacroiliitis	16 (30.2%)	4 (6.3%)	3 (15.0%)	0.003
Classification criteria				
ILAR ERA	26 (49.1%)	0 (0.0%)	6 (30.0%)	<0.001
ILAR PsA	12 (22.6%)	0 (0.0%)	10 (50.0%)	<0.001
ESSG	35 (66.0%)	0 (0.0%)	14 (70.0%)	<0.001
Bristol	0 (0.0%)	55 (85.9%)	7 (35.0%)	<0.001
Jansson	0 (0.0%)	40 (62.5%)	14 (70.0%)	<0.001

Background/Purpose: The relationship between juvenile spondyloarthritis (JSpA) and chronic nonbacterial osteomyelitis (CNO) remains poorly defined. This study aimed to assess the proportion of pediatric patients who meet classification criteria for both JSpA and CNO, characterize the clinical and radiologic overlap between the two conditions, and compare initial treatment approaches within the first 6 months following diagnosis.

Methods: This was a retrospective cohort study conducted on children (≤18 years) diagnosed with JSpA and CNO between 2016 and 2024 at a tertiary care children's hospital. Subjects were identified by electronic health record coding and included if they had: at least 2 rheumatology visits, no prior biologic therapy, and met at least one set of classification criteria: ILAR PsA/ERA or European Spondyloarthropathy Study Group (ESSG) (for JSpA), or Bristol or Jansson (for CNO). Overlap was defined as present if at least one set of JSpA and CNO criteria were met. The index visit was defined as the first clinical encounter with a JSpA or CNO diagnostic code. Data from the 6 months following the index visit - including demographics, clinical symptoms, family history, lab values, and imaging - were abstracted into a REDCap database. Descriptive statistics were calculated using medians and interquartile ranges (IQR) and proportions. Between-group comparisons were conducted using Mann-Whitney U and Chi-square tests, as appropriate.

Figure 1. Sites of active disease were identified through clinical examination and/or imaging. Statistically significant values ($p < 0.05$) are highlighted in blue and red.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

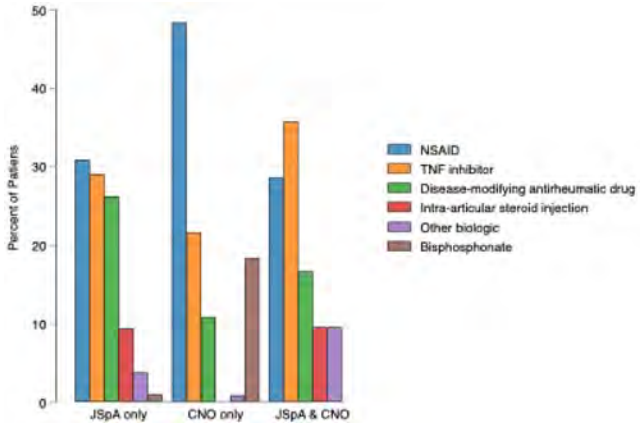


Figure 2. Treatments prescribed in the first six months after the index visit.

Results: A total of 137 subjects met inclusion criteria. Of these, 20 (14.6%) met criteria for both JSpA and CNO. This overlap group was significantly older ($p< 0.001$) and predominantly female (75.0%) (Table 1). Psoriasis was observed significantly more frequently in the overlap group compared to JSpA or CNO alone (55%, 20.8%, 3.1%, respectively; $p< 0.001$). In contrast, peripheral arthritis and enthesitis were significantly less common in the CNO cohort (both $p< 0.001$). Whole-body/pelvic MRI were obtained in 13.2%/50.9% of JSpA, 89.1%/25.0% of CNO, and 30.0%/30.0% of overlap patients, respectively. Figure 1 shows the distribution of the most frequently involved sites of disease activity across the 3 groups. Pelvic osteitis and/or sacroiliitis affected approximately one-third of cases across all groups, with sacroiliitis significantly more common in JSpA ($p=0.003$). NSAIDs and TNF inhibitors were the most frequently prescribed therapies in all 3 groups (Figure 2). DMARDs were used more often in the JSpA and overlap groups, while bisphosphonates were more commonly prescribed for CNO. The most commonly met criteria in each diagnosis was ESSG criteria (66.0%) for JSpA patients, Bristol criteria (85.9%) for CNO patients, and ESSG (70.0%) and Jansson (70.0%) for overlap patients.

Conclusion: A subset of pediatric patients fulfilled classification criteria for both JSpA and CNO, with overlapping clinical and radiologic features. The co-occurrence of these conditions may represent a distinct phenotype, characterized by older age, female predominance, and a higher prevalence of psoriasis. Differences in imaging use and treatment strategies highlight the importance of recognizing this overlap for appropriate diagnostic clarity, evaluation and therapeutic decision-making.

Disclosure: S. Elfrink: None; **T. Brandon**: None; **J. Jazayeri**: None; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

Abstract Number: 2157

Optimizing the Diagnosis and Treatment of Kawasaki Disease-Associated Macrophage Activation Syndrome: A Clinical Cohort and Literature Analysis

Xi Yang[1], Yuanhao Zhao[2], Zhihan Tang[2], Haixia Liu[2] and Xuemei Tang[2], [1]Department of Rheumatology & Immunology, Children's Hospital of Chongqing Medical University, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, National Clinical Research Center for Child Health and Disorders (Chongqing), Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Infection and Immunity, Chongqing, China., Chongqing, China (People's Republic), [2]Department of Rheumatology and Immunology, Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing Key Laboratory of Child Rare Diseases in Infection and Immunity, Chongqing, China, Chongqing, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Through a single-center retrospective cohort study and systematic literature review, we aimed to evaluate the applicability of current diagnostic criteria (HLH-2004/2009 and 2016 sJIA-MAS) for Kawasaki disease-associated macrophage activation syndrome (KD-MAS) and assess the clinical value of immunomodulatory treatment strategies.

Methods: A dual-cohort design was employed: (1) Retrospective analysis of pediatric patients treated at our institution from 2015 to 2025 who met the 2024 AHA Kawasaki disease diagnostic criteria and at least one MAS diagnostic criterion (HLH-2004/2009 or 2016 sJIA-MAS); (2) Systematic literature search for KD-MAS case reports. Data on demographic characteristics, clinical manifestations, biomarker dynamics, treatment responses, and outcomes were collected. Treatment efficacy was stratified and compared based on glucocorticoid dosage (Mann-Whitney U test).

Results: Analysis of 44 KD-MAS cases (22 from our center and 22 from literature) revealed an incidence rate of 0.6% (22/3,786) at our institution, with a male-to-female ratio of 2.1:1 and median age of 4.2 years. Diagnostically, 72.7% (32/44) met all diagnostic criteria, 93.2% (41/44) fulfilled the 2016 sJIA-MAS criteria, and 72.7% (32/44) met the HLH-2004/2009 criteria. All patients received IVIG, with 90% requiring additional immunomodulatory therapy. Among 13 patients treated with methylprednisolone alone at our center, no significant difference in CRP improvement was observed between high-dose (≥10 mg/kg/day, n=7) and low-dose (< 10 mg/kg/day, n=6) groups (P=0.23). The overall cure rate was 95% (39/41, excluding 3 lost-to-follow-up cases), with two fatal cases at our institution associated with treatment delay.

Conclusion: This study is the first to demonstrate the superior sensitivity of the 2016 sJIA-MAS criteria for KD-MAS diagnosis. Initial low-dose glucocorticoids (< 10 mg/kg/day) are effective for mild KD-MAS, but treatment escalation is warranted if no clinical improvement is observed. Treatment delay was identified as an independent risk factor for poor prognosis.

Table 1. Clinical manifestations in KD-MAS patients: comparison of our center with literature cases

	Our center	literature-reported cases	Total
fever	(22/22, 100%)	(22/22, 100%)	(44/44, 100%)
splenomegaly	(11/22, 50.0%)	(20/20, 100%) 2 cases with missing data	(31/42, 73.8%)
anemia	(21/22, 95.5%)	(21/22, 95.5%)	(42/44, 95.9%)
thrombocytopenia	(18/22, 81.8%)	(21/22, 95.5%)	(39/44, 88.6%)
neutropenia	(7/22, 31.8%)	(17/22, 77.2%),	(24/44, 54.5%)
hepatic nipairment	(17/22, 77.2%)	(21/22, 95.4%)	(38/44, 86.3%)
hypertriglyceridemia	(17/20, 85.0%) 2 cases with missing data	(22/22, 100%)	(39/42, 92.8%)
hyperferritinemia	(18/22, 81.8%)	(22/22, 100%)	(40/44, 90.9%)
hypofibrinogenemia	(17/22, 77.3%)	(12/19, 63.2%) 3 cases with missing data	(29/41, 70.7%)
hemophagocytosis	(16/19, 84.2%) 3 cases with missing data	(14/21, 66.7%) 1 case with missing data	(30/40, 75%)
low NK-cell-activity	(3/5, 60%) 17 cases with missing data	(2/2, 100%) 20 cases with missing data	(5/7, 71.4%)
high-soluble interleukin-2-receptor levels	(4/5, 80%) 17 cases with missing data	(1/1, 100%) 21 cases with missing data	(5/6, 83.3%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Distribution of Outcomes of KD-MAS by Treatment Scheme

	Number of cases	Favorable	Death / Abandoned
Only IVIG	4	4 (100 %)	0 (0 %)
IVIG + Steroid (low dose)	7	7 (100 %)	0 (0 %)
IVIG + Steroid (high dose)	14	13 (92.9 %)	1 (7.1 %)
IVIG+Steroid+cyclosporine	7	5 (71.4 %)	2 (28.6 %)
IVIG + Steroid + Biologic / PE / HLH-based	12	10 (83.3 %)	2 (16.7 %)
Total	44	39 (88.6 %)	5 (11.4 %)

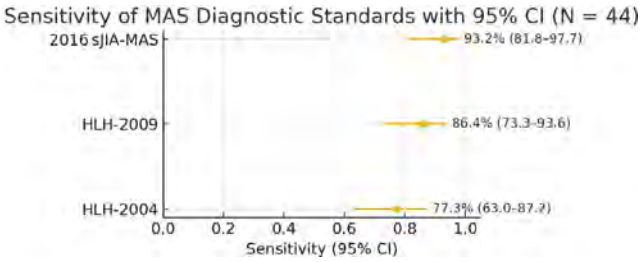


Figure 1. Sensitivity of MAS diagnostic standards with corresponding 95% confidence intervals (CI)

Disclosure: X. Yang: None; **Y. Zhao**: None; **Z. Tang**: None; **H. Liu**: None; **X. Tang**: None.

Abstract Number: 2158

Evaluating Nailfold Capillary Changes as Indicators of Disease Activity in Juvenile Dermatomyositis

Zilan Zheng[1], Laila Metni[2], Susan Kim[3] and Jessica Neely[4], [1]University of California, San Francisco, San Francisco, CA, [2]University of California, Berkeley, Berkeley, CA, [3]UCSF Benioff Children's Hospital, San Francisco, CA, [4]UCSF, San Francisco, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2124–2158) Pediatric Rheumatology – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile dermatomyositis (JDM) is a rare pediatric autoimmune myopathy characterized by skin and muscle inflammation, resulting in microvascular changes that can be visualized in the nailfold capillaries. Nailfold video capillaroscopy (NVC) at 200x magnification is a promising non-invasive measure to study disease activity. Here, we studied the association of nailfold capillary measurements with disease activity and compared rheumatologists' examination (RE) at 10x magnification to NVC.

Methods: Patients diagnosed with JDM at a single tertiary care pediatric rheumatology center had nailfold capillaries imaged during clinic visits following published protocols. Clinical data (e.g., skin assessments and visual analog scale (VAS) scores) and notes on capillary appearances were extracted from medical records. Two cohorts were defined based on disease activity status at time of imaging: active JDM (physician VAS score $\geq$ 0.5) and inactive JDM (physician VAS score < 0.5).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics & Disease Activity of Patients with Juvenile Dermatomyositis (JDM) with Nailfold Capillary imaging

Sex Assigned at Birth	Active JDM n=14[a]	Inactive JDM n=15[a]	Total JDM n=29[a]
Female	10 (71.4%)	6 (40.0%)	16 (55.2%)
Male	4 (28.6%)	9 (60.0%)	13 (44.8%)
Race & Ethnicity			
Asian	1 (7.1%)	0 (0.0%)	1 (3.0%)
Black	2 (14.2%)	1 (6.7%)	3 (10.3%)
Latino or Hispanic	5 (35.7%)	3 (20.0%)	8 (27.6%)
Middle East or North Africa	0 (0.0%)	1 (6.7%)	1 (3.4%)
White	4 (28.6%)	5 (33.3%)	9 (31.0%)
2 or more	2 (14.3%)	5 (33.3%)	7 (24.1%)
	N=14[b]	N=15[b]	N=29[b]
Age at Visit (years)	5.68 ± 10.93	6.01 ± 12.6	11.79 ± 5.81
Age at Diagnosis (years)	7.29 ± 5.37	6.6 ± 4.97	6.93 ± 5.08
Months from Symptom Onset to Diagnosis	9.71 ± 15.06	5.87 ± 9.49	7.72 ± 12.42
	N=14[c]	N=15[c]	N=29[c]
Myositis Specific Antibodies (MSA)			
Anti-Tif1γ (formerly p155)	4 / 14 (28.6%)	5 / 15 (33.3%)	9 / 29 (31.0%)
Anti-NXP2 (formerly MJ)	3 / 13 (23.1%)	3 / 15 (20.0%)	6 / 28 (21.4%)
Anti-MDA5	0 / 13 (0.0%)	1 / 14 (7.1%)	1 / 27 (3.7%)
Anti-Mi2	2 / 13 (15.4%)	3 / 14 (21.4%)	5 / 27 (18.5%)
MSA Negative	5 / 12 (41.7%)	5 / 14 (35.7%)	10 / 26 (38.5%)
Myositis Associated Antibodies (MAA)			
ANA	6 / 14 (42.9%)	5 / 12 (41.7%)	11 / 26 (42.3%)
Anti-Ro (SSA)	1 / 11 (9.1%)	3 / 13 (23.1%)	4 / 24 (16.7%)
Anti-PM-Scl	1 / 11 (9.1%)	0 / 15 (0.0%)	1 / 26 (3.8%)
MSA & MAA Negative	2 / 8 (25.0%)	3 / 10 (30.0%)	5 / 18 (27.8%)
Clinical Test			**P-Value[e]**
Muscle Weakness	6 / 12 (50.0%)	0 / 14 (0.0%)	*<0.01*
	N = 14[d]	N=15[d]	
CDASI Activity	5.0 [2.0, 7.0] / 1	0.0 [0.0, 0.5] / 3	*<0.01*
CDASI Damage	1 [0, 5.0] / 1	0.0 [0.0, 0.0] / 3	*0.04*
VAS Physician Global	2.0 [0.63, 4.38] / 0	0.0 [0.0, 0.0] / 0	*<0.01*
VAS Skin	2.5 [1.0, 5.0] / 0	0.0 [0.0, 0.0] / 0	*<0.01*
VAS Extramuscular	0.0 [0.0, 2.25] / 0	0.0 [0.0, 0.0] / 1	*<0.01*
VAS Muscle	0.25 [0.0, 2.38] / 0	0.0 [0.0, 0.0] / 1	*0.01*
VAS Patient	1.0 [0.4, 4.5] / 5	0.0 [0.0, 0.85] / 1	0.05
MMT8	79 [76, 80] / 5	79.5 [78.3, 80.0] / 5	0.28
Skin Assessments	N=14[a]	N=15[a]	P-Value[f]
Periungual capillary loop changes	7 (50.0%)	1 (6.7%)	*0.01*
Malar or facial erythema	8 (57.1%)	2 (13.3%)	*0.02*
Active calcinosis	4 (28.6%)	0 (0.0%)	*0.04*
"V" sign	3 (21.4%)	0 (0.0%)	0.10
Shawl sign	3 (21.4%)	1 (6.7%)	0.33
Gottron's papules or rash	4 (28.6%)	2 (13.3%)	0.39
Heliotrope rash	3 (21.4%)	2 (13.3%)	0.65

[a]n (%)
[b]Mean (SD)
[c]n positive / n total (%)
[d]Median [IQR] / n unknown
[e]Wilcoxon Rank Sum P-Value
[f]Fisher Test P-Value

Anti-Io1, SRP, HMGCR, La (SSB), and Ku are excluded because no patients were positive for these antibodies. Extensive cutaneous erythema, cutaneous ulceration, mucus membrane lesions, mechanics hand, subcutaneous oedema, and panniculitis are excluded because no patients had these symptoms. VAS scores for pulmonary and cardiovascular systems were 0 for all patients.

Significant results are italicized.

Automated analysis of the NVC images were completed by Capillary.io, measuring capillary limb widths and apical diameters, followed by manual review for accuracy, apex widths, and internal diameters (Table 2, Fig 1). Each capillary characteristic was averaged per patient before analysis. Fisher and Wilcoxon rank sum tests were applied for categorical and continuous variables respectively. Data was stratified by RE at 10x: normal, mild-minimal, and abnormal. One-way ANOVA on ranks was applied, to assess for differences across the groups (P-value < 0.01). NVC measurements were compared to a published study of healthy pediatric capillaries.

Results: 29 JDM patients (mean age 11.79 ± 5.81) had 169 images analyzed, divided into 2 groups of 14 active and 15 inactive patients. Analysis of clinical variables between the two cohorts revealed active JDM exhibited more active skin disease and presence of periungual capillary loop change, active calcinosis, malar erythema, and chronic muscle weakness (Table 1). Active JDM was associated with decreased capillary density and enlarged arterial limb widths, apex widths, and internal diameters on NVC (Table 2, Fig 1). There was no significant difference in abnormal morphology between the two groups, but inactive JDM had significantly more normal capillaries per millimeter (Table 2). Between 80% to 100% of inactive

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Analysis of capillaries

Capillary Characteristic	Active JDM n=14[a]	Inactive JDM n=15[a]	Normal ranges[`] (Mean ± SD)	P-Value[c]
Density	6.1 [5.0, 7.3] 6 (43.9%)	7 [6.7, 8.1] 13 (86.7%)	8.1 ± 1.7[`]	*0.02*
Arterial Limb Width	15.2 [12.3, 19.9] 8 (57.1%)	12.2 [11.7, 13.0] 15 (100.0%)	11.9 ± 4[`]	*0.03*
Venous Limb Width	19.3 [16.4, 24.9] 7 (50.0%)	15.4 [14.6, 17.0] 15 (100.0%)	15.1 ± 4.6[`]	0.23
Apical Diameter	20.6 [19.1, 26.6] 8 (57.1%)	18.4 [16.4, 20.2] 12 (80.0%)	16.3 ± 5.5[`]	0.06
Apex Width	43.4 [32.4, 57.7] 4 (28.6%)	34.4 [32.6, 35.9] 11 (73.3%)	41.5 ± 9.0[`]	*0.03*
Internal Diameter	14.0 [12.3, 22.0]	10.6 [9.5, 11.5]	---	*<0.01*
Morphology & Features	**N=14[b]**	**N=15[b]**	**P-Value[c]**	**P-Value[d]**
Normal	1 [0.25, 2.13]; 12	2.10 [1.15, 2.80]; 15	*P=0.03*	P=0.22
Giant Capillaries	0.05 [0, 0.425]; 7	0 [0, 0]; 2	P=0.05	P=0.05
Tortuous	1.75 [1.23, 3.48]; 13	3.1 [2.25, 3.65]; 15	P=0.09	P=0.48
Hemorrhages	0.0 [0, 0.2]; 6	0 [0, 0.15]; 5	P=0.47	P=0.71
Abnormal	0.65 [0.23, 1.15]; 12	0.4 [0.25, 0.95]; 14	P=0.53	P=0.60
Avascular areas	1.0 [0.25, 3.0]; 10	2 [0.5, 3.5]; 11	P=0.64	P=1.00
Enlarged	3.1 [2.15, 3.73]; 14	3.2 [2.0, 4.1]; 15	P=1.00	P=1.00
Rheumatologists' Examination	**Normal n=17[e]**	**Mild-Minimal n=8[e]**	**Abnormal n=4[e]**	**P-Value[e]**
Density	7.2 [6.7, 8.0] 15 (88.2%)	6.4 [5.7, 7.3] 4 (50.0%)	4.8 [4.2, 5.5] 0 (0.0%)	*<0.01*
Arterial Limb Width	12.2 [11.4, 12.8] 17 (100.0%)	14.7 [13.2, 15.8] 6 (75.0%)	30.95 [25.8, 35.6] 0 (0.0%)	*<0.01*
Venous Limb Width	15.3 [13.9, 16.8] 17 (100.0%)	17.9 [17.0, 21.2] 5 (62.5%)	45.8 [35.8, 137.5] 0 (0.0%)	*<0.01*
Apical Diameter	18.1 [15.7, 19.4] 14 (82.4%)	19.8 [19.2, 22.2] 6 (75.0%)	44.2 [35.8, 51.4] 0 (0.0%)	*<0.01*
Apex Width	33.7 [32.2, 35.7] 11 (64.7%)	38.4 [35.6, 48.2] 5 (62.5%)	88.8 [77.3, 97.9] 0 (0.0%)	*<0.01*

[a]Median [IQR]; n in range (n%)
[b]# capillary/mm Median [IQR]; n present
[c]Wilcoxon Rank Sum P-Value
[d]Fisher Test P-Value
[e]One-Way ANOVA on Ranks P-Value
[`]Dundar HA, Adrovic A, Demir S, et al. Description of the characteristics of the nailfold capillary structure in healthy children: a multi-centric study. Rheumatology (Oxford). 2024;63(SI2):SI152-SI159. doi:10.1093/rheumatology/kead296

Significant results are italicized.

JDM had NVC measurements within normal ranges, compared to about half of those with active JDM. Analysis of RE revealed patients described as "normal" on 10x met 4-5 of the normal 200x ranges, while "abnormal" met none.

Conclusion: Abnormal capillaries observed at 10x and 200x magnification were associated with active skin disease and muscle weakness in JDM, suggesting that nailfold capillaries, specifically arterial limb and apex widths, may serve as a clinical biomarker of disease activity. In addition, NVC showed abnormal measures could be detected and quantified in patients described clinically as "abnormal" or "mild-minimal" changes. Determining the clinical utility added by NVC will be an important area of future study along with identifying features that can help predict future flares, remission, and guide medications tapering.

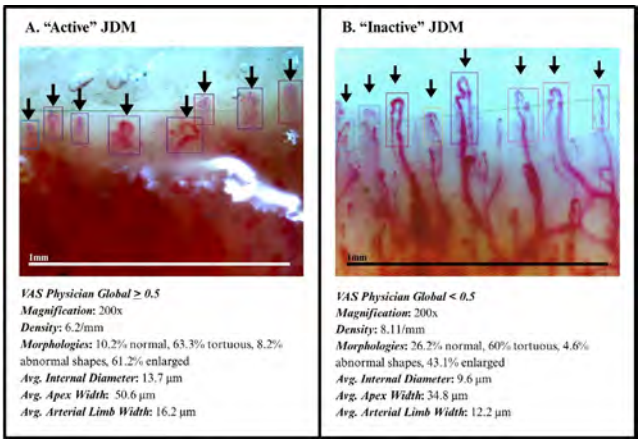


Figure 1. "Active" versus "Inactive" JDM Capillaries

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Z. Zheng: None; **L. Metni**: None; **S. Kim**: Cabaletta, 1; **J. Neely**: None.

Abstract Number: 2159

Teaching Musculoskeletal Ultrasound Improves Knowledge and Confidence in the Knee Exam: A Pilot Session with Internal Medicine Trainees

Ann Cameron Barr[1], David Leverenz[1], Lisa Criscione-Schreiber[2] and Philip Chu[3], [1]Duke University, Durham, NC, [2]Duke University School of Medicine, Durham, NC, [3]Duke University Hospital, Raleigh, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Poor confidence in musculoskeletal (MSK) care among practicing internists and internal medicine (IM) trainees is well described in the literature. A needs assessment of IM residents at our institution showed similar results with little training and low confidence in MSK physical examination (ACR 2024, abstract #1291). We implemented and evaluated a pilot MSK ultrasound (US) session on the knee for IM interns with the goals of improving knowledge of MSK anatomy, improving MSK physical examination, and optimizing arthrocentesis skills.

Methods: The pilot MSKUS session occurred in the fall of 2024 at a single academic residency program. The session included 30 minutes of didactic teaching on anatomy and an overview of 5 standard US views of the knee with both normal findings and common pathology. Following the didactic session, the interns split into small groups for 90 minutes of hands-on US practice, supervised by a rheumatologist. We surveyed participating interns on prior instruction in MSK exam and US, pre-post confidence in physical examination of the knee on a 1-6 scale (1 = not at all confident, 6 = extremely confident), and pre-post confidence in performing arthrocentesis of the knee on the same 1-6 scale. Survey questions were adapted from a survey on resident MSK exam confidence with evidence for validity (ACR 2014, abstract #1983). Finally, we administered an eight question pre- and post-session test to assess their knowledge of physical exam, anatomy, and US pathology of the knee. We analyzed data in aggregate using paired two sample T-tests.

Table 1: Interns were asked to quantify their experiences learning musculoskeletal physical exam and ultrasound by answering the following questions: "How much training have you had in physical examination of the following joints?", "How much ultrasound training have you received in your medical training?", and "Did your previous ultrasound training include any training in musculoskeletal ultrasound?"

	None	Some (2-3 sessions)	A lot (> 2-3 sessions)	Extensive	Total
Physical exam experience					
Knee	6 (17%)	25 (69%)	5 (14%)	0 (0%)	36
Hand/wrist	12 (33%)	22 (61%)	2 (6%)	0 (0%)	36
Foot/ankle	16 (44%)	19 (53%)	1 (3%)	0 (0%)	36
Ultrasound experience	8 (22%)	14 (39%)	11 (31%)	3 (8%)	36
Musculoskeletal ultrasound experience	32 (89%)	4 (11%)*	N/A	N/A	36

* Prior training in musculoskeletal ultrasound was assessed on yes/no basis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

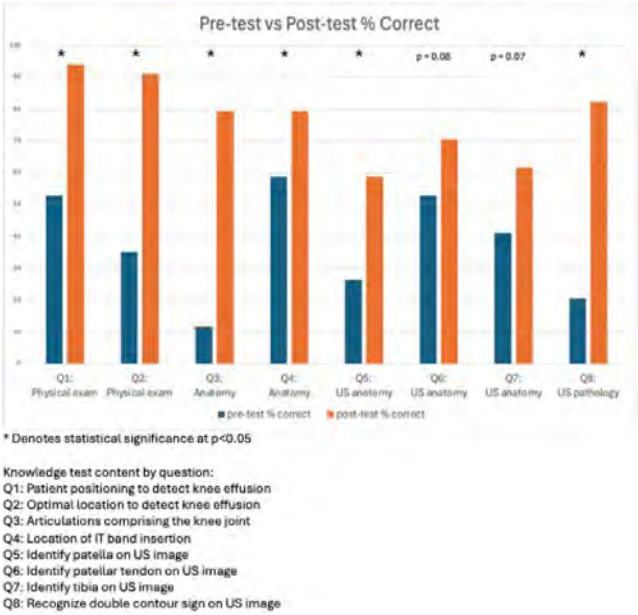


Figure 1: Intern knowledge about physical exam, anatomy, and musculoskeletal ultrasound pathology of the knee pre- and post-musculoskeletal ultrasound (MSKUS) session.

Results: Thirty-six of 39 (92%) interns responded to the pre-session survey, and 34 of 39 (87%) interns responded to both pre- and post-session surveys. Most reported having 3 or fewer sessions in physical examination of the knee (n=31, 86%), hand/wrist (n=24, 94%), and foot/ankle (n=35, 97%) during their medical training (Table 1). Although 78% of interns reported prior POCUS training, only 11% reported prior training in MSKUS. Pre-session intern confidence in examination and arthrocentesis of the knee was very low, with fewer than 25% rating >3/6 for any domain. Confidence in all domains was significantly improved post-session (Figure 1). MSK knowledge of the knee was significantly improved post-session for 6 of 8 questions, including those focused on physical exam (2 of 2), MSKUS pathology (1 of 1), anatomy (3 of 5). For the remaining 2 questions focused on anatomy, there was a trend toward improvement (Figure 2).

Conclusion: IM residents receive little training in MSK physical exam or MSKUS, and their confidence in performing MSK examination and procedures is low. Our prior needs assessment data suggests that this improves minimally over three years of IM residency. Intern participation in a targeted MSKUS training session was associated with improved confidence in MSK skills and improved MSK knowledge of the knee. Next steps include implementation of a longitudinal curriculum incorporating additional joint regions and the opportunity for time-distributed practice of MSKUS.

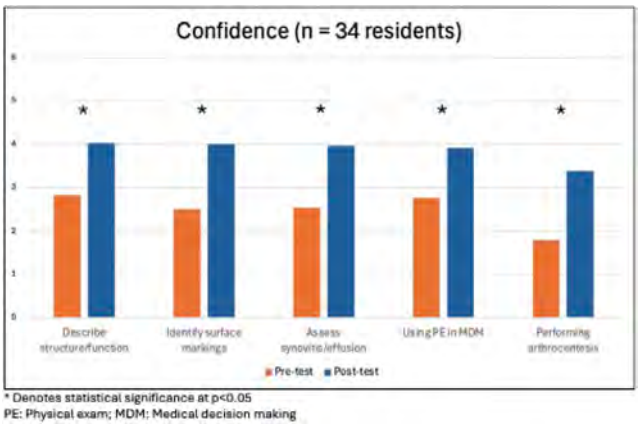


Figure 2: Resident confidence in performing musculoskeletal physical exam and arthrocentesis of the knee pre- and post-musculoskeletal ultrasound (MSKUS) session.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Barr: None; **D. Leverenz**: Pfizer, 5, Sanofi, 2, UCB, 2; **L. Criscione-Schreiber**: UCB, 5; **P. Chu**: None.

Abstract Number: 2160

RadRheum: Improving Resident and Medical Student Musculoskeletal Radiology Interpretation Skills Utilizing an Interactive Module

Elizabeth Konon[1], Laura Nichols[2] and Meredith Morcos[2], [1]University of Colorado Internal Medicine Residency Program, Denver, CO, [2]University of Colorado, Aurora, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Plain radiographs remain a cornerstone for diagnosis in rheumatology. Despite the importance of radiograph interpretation in rheumatology, there is little formalized instruction documented in the literature. The purpose of this curricular quality project was to develop and assess a virtual, instructional module for teaching internal medicine residents and medical students both general and rheumatology-specific radiology skills.

Methods: An interactive virtual module including musculoskeletal (MSK) radiographs was created and administered voluntarily to internal medicine residents and medical students at a single academic site. Participants were asked to complete a pre- and post-test to evaluate their knowledge and confidence in interpreting radiographs prior to and after participation in the module. Participants were also asked about their prior instructional experiences with MSK radiology. High-yield and commonly seen topics in the field of rheumatology including rheumatoid arthritis, psoriatic arthritis, gout, spondyloarthritis, and osteoarthritis were chosen based on relevance in terms of representation in the American College of Physicians Medical Knowledge Self-Assessment Program (MKSAP) and rheumatology attending decision. Fellows (n=4) and attendings (n=5) also completed the pre/post-test to evaluate whether this information is used in practice and learned over time.

Results: Forty-three trainees completed the pre-test. Thirty-three trainees completed the post-test. The average scores on the pre-test compared to the post-test improved from 4.5/10 to 6.5/10. Fellows and attendings scored 7.8/10 and 9.8/10, respectively. Student and resident scores on multiple topics, including identifying osteoarthritis, psoriatic arthritis, and rheumatoid arthritis on hand radiographs, improved after participation in the program (Table 1). Formal didactics reported in MSK radiology were low, particularly during residency (Figure 1). In the post-test survey, 52% of participants selected "somewhat agree" and 33% selected "strongly agree" when asked whether the module increased their ability to interpret MSK

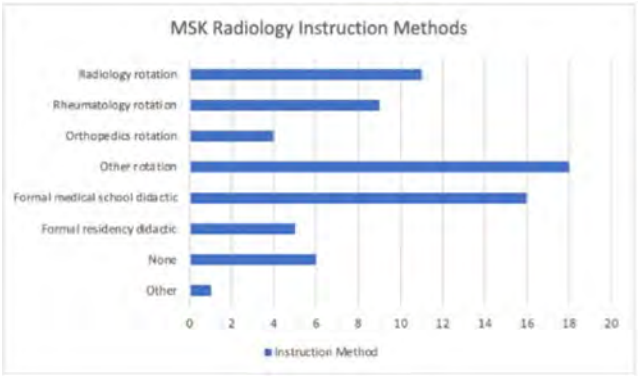
Topic Assessed	Pre-Test Correct N (%) Total N=43	Post-Test Correct N (%) Total N=33
Identify osteoarthritis on hand x-ray	20 (47%)	26 (79%)
Diagnose osteoarthritis on hand x-ray	31 (72%)	30 (91%)
Identify changes of erosive osteoarthritis on x-ray	4 (10%)	7 (21%)
Diagnose psoriatic arthritis on hand x-ray*	10 (24%)	10 (30%)
	12 (29%)	19 (58%)
Identify chondrocalcinosis on knee x-ray and associate with disease	23 (55%)	32 (97%)
Identify changes of rheumatoid arthritis on hand x-ray	4 (10%)	14 (42%)
Diagnose spondyloarthritis on sacroiliac joint x-ray*	36 (86%)	29 (88%)
	18 (44%)	16 (48%)
Identify erosions typical of gout on x-ray	17 (43%)	31 (94%)

Pre and post test scores for topics assessed in interactive module. *Two separate questions were asked on diagnosis of psoriatic arthritis and spondyloarthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Pre-Test N (%) Total N=39	Post-Test N (%) Total N=33
Very confident	0 (0%)	0 (0%)
Somewhat Confident	3 (8%)	11 (33%)
Neutral	3 (8%)	6 (18%)
Somewhat unconfident	17 (44%)	11 (33%)
Very unconfident	16 (41%)	5 (15%)

Self-reported confidence level in diagnosing musculoskeletal conditions using radiographs



Musculoskeletal radiograph instruction methods reported by trainees

radiographs. Furthermore, confidence levels also increased (Table 2). One study limitation is that 10 participants did not complete the post-test.

Conclusion: Participating in this interactive module improved trainee scores and self-reported confidence in interpreting radiographs and diagnosing MSK conditions such as osteoarthritis, rheumatoid arthritis, psoriatic arthritis, and spondyloarthritis. Though scores improved after participation in the module, many remained low. Next steps include reviewing content to improve identification of erosive OA, RA, and PsA changes and disseminating to other institutions to assess reproducibility. A structured curriculum surrounding the use of radiography in rheumatology is a useful tool for medical students and residents.

Disclosure: E. Konon: None; **L. Nichols**: None; **M. Morcos**: None.

Abstract Number: 2161

Perceptions of the Importance of Pediatric Rheumatology Education in Pediatric Residency: A Needs Assessment

Katherine Nowicki[1], Lori Silveira[2], Megan Curran[1] and Laura Lockwood[1], [1]University of Colorado | Children's Hospital Colorado, Aurora, CO, [2]University of Colorado, Aurora, CO

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The shortage of pediatric rheumatologists and resulting limited patient access necessitates that pediatricians receive adequate training in core pediatric rheumatology (PR) topics to address patient concerns. University of Colorado pediatric residency (UCPR) trainees receive training from pediatric rheumatologists, but resident and alumni

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Resident & Alumni Demographics

	Resident, N (%)	Alumni N (%)
Survey Response Rate	56/117 (47.9)	102/283 (36.0)
Current year of post-graduate training		
2014		11 (10.8)
2015		9 (8.8)
2016		6 (5.9)
2017		5 (4.9)
2018		13 (12.7)
2019		8 (7.8)
2020		17 (16.7)
2021		15 (14.7)
2022		4 (3.9)
2023		10 (9.8)
2024	3 (5.4)	4 (3.9)
2025	15 (26.8)	
2026	18 (32.1)	
2027	20 (35.7)	
Residency Program		
Pediatrics	42 (75.0)	90 (88.2)
Medicine-Pediatrics	7 (12.5)	6 (5.9)
Pediatrics-Child Neurology	4 (7.1)	5 (4.9)
Pediatrics-Medical Genetics	2 (3.6)	1 (1.0)
Pediatrics-Physical Medicine and Rehabilitation	1 (1.8)	0 (0.0)
Post-residency graduation plans		
Fellowship	27 (48.2)	
Primary care	11 (19.6)	
Hospital medicine	9 (16.1)	
Chief year	4 (7.1)	
Undecided	4 (7.1)	
Other	1 (1.8)	
Current Practice		
General pediatrics		52 (51.0)
Subspecialty		49 (48.0)
Internal medicine primary care		1 (1.0)
Time spent on a pediatric rheumatology elective		
Less exposure (0 to less than 2 weeks)	44 (78.6)	84 (82.4)
More exposure (2 or more weeks)	10 (17.9)	13 (12.7)
Missing response	2 (3.6)	5 (4.9)

Table 2. Key Resident Survey Responses

	Overall	Low exposure	High exposure	p-value
At this time, how important do you think learning pediatric rheumatology topics is to your education as a general pediatrician?				
Somewhat important	14 (25.9)	13 (29.5)	1 (10.0)	0.263
Very important	40 (74.1)	31 (70.5)	9 (90.0)	
At this time, how confident are you that you have the pediatric rheumatology knowledge you will need after graduation?				
Not at all confident	25(46.3)	21 (47.7)	2 (20.0) *	<0.001
Somewhat confident	27 50.0)	23 (52.3)	4 (40.0) **	
Very Confident	4 (7.4)	0 (0.0)	4 (40.0)	
At this time, how confident are you that you have the musculoskeletal exam skills you will need after graduation?				
Not at all confident	17(31.5)	15 (34.1)	2 (20.0)	0.061
Somewhat confident	32(59.3)	27 (61.4)	5 (50.0)	
Very Confident	5(9.2)	2 (4.5)	3 (30.0)	
How important do you think knowledge of pediatric rheumatology topics will be in your clinical practice after graduation?				
Not at all confident	1(1.9)	1 (2.3)	0 (0.0)	1.000
Somewhat confident	23(42.6)	19 (43.2)	4 (40.0)	
Very Confident	30(55.5)	24 (54.5)	6 (60.0)	
Regardless of how much time you have or have not already spent on a rheumatology rotation in residency, do you intend to rotate with pediatric rheumatology for 2 or more (additional) weeks by the time of graduation?				
Yes	17(31.5)	14 (31.8)	3 (30.0)	0.106
No	25(46.3)	18 (40.9)	7 (70.0)	
Unsure	12(22.2)	12 (27.3)	0 (0.0)	

* comparison not at all confident to very confident between groups p <0.05
** comparison somewhat confident to very confident between groups p < 0.05

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Key Alumni Survey Responses

	Overall (n=102)	Less exposure (n=84)	More exposure (n=13)	p-value
Thinking back to your time as a pediatric resident, how important did you think learning pediatric rheumatology topics were to your education as a general pediatrician at that time?				
Not at all important	1 (1.0)	0 (0.0)	0 (0.0)	0.355
Somewhat important	54 (54.0)	49 (58.8)	5 (41.7)	
Very important	45 (45.0)	35 (41.7)	7 (58.3)	
Thinking back to your time as a pediatric resident, how confident were you at the time of graduation that you had the pediatric rheumatology knowledge you needed for your next phase of clinical practice?				
Not at all confident	13 (13.0)	12 (14.3)	0 (0.0)	0.378
Somewhat confident	75 (75.0)	63 (75.0)	10 (83.3)	
Very Confident	12 (12.0)	9 (10.7)	2 (16.7)	
In your current clinical practice, how important is knowledge of pediatric rheumatology topics?				
Not at all important	9 (5.0)	4 (4.8)	0 (0.0)	0.053
Somewhat important	52 (52.0)	48 (57.1)	3 (25.0)	
Very important	43 (43.0)	32 (38.1)	9 (75.0)	
In your current clinical practice, how confident are you that you have the pediatric rheumatology knowledge you need?				
Not at all confident	16 (16.0)	15 (17.9)	1 (8.3)	0.033
Somewhat confident	73 (73.0)	63 (75.0)	7 (58.3)[λ]	
Very Confident	11 (11.0)	6 (7.1)	4 (33.3)	
In your current clinical practice, how confident are you that you have the musculoskeletal exam skills you need?				
Not at all confident	28 (28.0)	24 (28.6)	3 (25.0)	0.421
Somewhat confident	52 (52.0)	45 (53.6)	5 (41.7)	
Very Confident	20 (20.0)	15 (17.9)	4 (33.3)	
In your current clinical practice, how confident are you that you consider rheumatologic diagnoses when they should be considered?				
Not at all confident	1(10.0)	1 (1.2)	0 (0.0)	0.008
Somewhat confident	69(69.0)	63 (75.0)	4 (33.3)	
Very confident	30(30.0)	20 (23.8)	8 (66.7)[λ]	
In your current clinical practice, how confident do you feel in your ability to start a workup before consulting rheumatology, when a rheumatologic diagnosis is on your differential?				
Not at all confident	22(22.0)	21 (25.0)	1 (8.3)	0.055
Somewhat confident	61(61.0)	52 (61.9)	6 (50.0)	
Very confident	17(17.0)	11 (13.1)	5 (41.7)	
If you did not complete a pediatric rheumatology elective (2 or more weeks of total time in residency dedicated to pediatric rheumatology) during residency, do you now wish you did?				
Yes	46(46.0)	46(58.2)	NA	NA
No	34(34.0)	33(41.8)	NA	NA

*the proportions between not at all confident to very confident between the groups are different,
**the proportions between not at all important to very important between the groups are different,
ζ) Somewhat confident to very confident p<0.05,
α not at all confident to very confident p < 0.05,
β Somewhat confident to very confident p<0.05,
λ Somewhat confident to very confident p<0.05

opinions on its importance and effectiveness are unknown. This study aimed to describe the perceived importance of PR education and current programs' effectiveness in preparing UCPR graduates for their next phase of practice via needs assessment surveys sent to residents and residency alumni.

Methods: Anonymous surveys were sent to (1) current trainees and (2) alumni (graduated 2014 - 2023) in spring 2024. Results were analyzed using descriptive statistics. To explore possible effects from exposure to the PR elective, respondents were split into groups based on total PR elective time: less exposure (0 to < 2 weeks) versus more exposure (≥ 2 weeks). Differences between groups were analyzed using ANOVA.

Results: The survey response rate was 47.9% (56/117) and 36.0% (102/283) for residents and alumni, respectively. Most residents (78.6 %) and alumni (82.4%) completed < 2 weeks of a PR elective. Overall, 41.1% of residents felt not at all confident they have the PR knowledge needed after graduation while only 15.7% of alumni felt not at all confident that they have the PR knowledge needed in their current clinical practice. Both residents and alumni in the more exposure groups reported greater confidence that they have the PR knowledge they (will) need compared to peers in the less exposure groups (p = < 0.001 and p= 0.033). 30.4% of residents and 27.4% of alumni were not at all confident they have the MSK exam skills

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

needed after graduation or in their current clinical practice and confidence did not differ between exposure groups. Alumni in the more exposure group were more confident that they consider rheumatologic diagnoses when they should be on the differential (66.7% vs. 23.8%, p=0.008).

Conclusion: Although patient access to PR specialists is limited, most UCPR pediatric residents do not complete a 2 or more-week PR elective. This may disadvantage graduates and patients, as alumni who had less exposure to PR training reported less confidence in their PR knowledge. Results also suggest that current PR education opportunities do not significantly improve MSK examination skill confidence. Results highlight the importance of resident PR education and illuminate curricular improvement opportunities, specifically with respect to the MSK exam. Planned next steps include curricular revision focusing on MSK exam training and development of novel learning tracks for future generalists and subspecialists.

Disclosure: K. Nowicki: None; **L. Silveira**: None; **M. Curran**: Guidepoint, 2, NYU Langone Rheumatology department, 6, Rheumatology, research foundation, 6, Wolters Kluwer, 9; **L. Lockwood**: None.

Abstract Number: 2162

An Updated Needs Assessment for the Virtual Rheumatology Program for Fellows in Training (V-FIT)

Laura Arneson[1], M. Dave Dimachkie[2], Juliet Aizer[3], Janet Mitchell[4], David Leverenz[5], Anisha Dua[6], Lisa Zickuhr[7] and The American College of Rheumatology Committee on Training, [1]Northwestern University, Chicago, IL, [2]Washington University in Saint Louis, St. Louis, MO, [3]Hospital for Special Surgery, New York, NY, [4]ACR, Winston-Salem, NC, [5]Duke University, Durham, NC, [6]Northwestern University Feinberg School of Medicine, Chicago, IL, [7]Washington University/B-JH/SLCH Consortium, St. Louis, MO

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The American College of Rheumatology (ACR) created the Virtual Rheumatology Program for Fellows in Training (V-FIT) in 2020 to provide rheumatology fellowship training programs with virtual curricular resources during the COVID pandemic. V-FIT includes two lecture series: the Virtual Practicum for Adult Rheumatology Fellows (ViP) on foundational topics, and the Virtual Rheumatology Teaching Lessons (ViTLS) on advanced topics. Sessions were delivered via Zoom from 2020-2025, and made available in a video archive. The educational landscape has shifted post-pandemic, prompting this study to re-assess fellowship curricular needs and how V-FIT can evolve to meet them.

Methods: We conducted an online survey of program directors (PDs) and virtual focus groups of PDs and fellows in training (FITs). Invitations were shared with all PDs and FITs via ACR email listservs between August-November 2024. Participants provided electronic consent for surveys and verbal consent for focus groups. Survey results were analyzed with descriptive statistics. Focus group leaders took notes summarizing discussion content. Focus group recordings were transcribed with Trint software. The notes and transcriptions were reviewed to identify themes and representative quotes. The study protocol was approved by the Washington University in St. Louis IRB.

Results: Survey responses were received by 17 of 123 PDs, with a median of 4 fellows per program (range 2-9); 10 PDs completed all questions. Of the responding PDs, 7/17 (41%) indicated they did not have sufficient resources to create a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Themes, application to future ViP and ViTLs programming, and representative quotes from fellow-in-training and program director focus groups. ViP = Virtual Practicum for Adult Rheumatology Fellows, ViTLs = Virtual Rheumatology Teaching Lessons, PD = program director, FIT = fellow in training.

Theme	Summary of Theme	Quotes
Content	A large amount of foundational content exists; future direction should expand advanced topics in rheumatology that feature rare diseases and expert opinion, landmark trials, and musculoskeletal radiology.	"We don't have a radiologist right now who has time to go over cases on a regular basis." (PD) "You can... partner topics when you make your curriculum. So the first year is going to watch the basic RA stuff. And then the challenging RA cases, that's what gets directed to the second year." (PD) "Having a time to like sit down with an expert on something and pick their brain is really interesting to me because there's only so much we see in fellowship in the two years that we're here and depending where you are geographically, you may see more conditions more than others and there's just certain things you don't see all that often." (FIT)
Session Duration	FITs and PDs preferred short lectures lasting 20-30 minutes, and FITs suggested podcasts.	"It's just hard to focus on a YouTube lecture for over 20 minutes." (PD) "I do like comprehensive lectures, but at the same time, the shorter the better." (FIT)
Active Learning Methods	All participants emphasized the value of engagement in the learning process through tools such as flipped classrooms, case discussions, access to expert clinicians' clinical reasoning, and board review questions.	"There just aren't enough board review questions. It's a big problem. It's one of the things that used to be [in] ACR CARE questions, and *that* was... not enough. And now that that's been...disbanded, we're just ... having to make it up ourselves, which is... a lot of work." (PD) "If you had...a 20-minute talk and then 20 minutes of ...practicum stuff, I think it'd be really cool." (PD) "Having that feedback from an attending and going through [cases] is good... being able to ask questions and see things in real time." (FIT)
Virtual Learning Environment	Virtual learning is advantageous only when it supports active learning while preserving psychological safety. Examples include anonymous participation (e.g., polling) and eliminating fellow requirements for pre-work or presentations.	"[For] new fellows, having this expectation you may have to participate in the discussion. I think people are going to be very shy about that, especially when they're just entering fellowship." (FIT) "For residency, we used to do like anonymous clicker [questions]... And then when everybody had submitted, it would show like the percentage of people who answered each option. And so then that kind of would spawn a discussion." (FIT)
Program Administration	Scheduling is an obstacle, though programs are most able to commit their fellows to virtual learning over the noon hour. FITs and PDs have trouble navigating the American College of Rheumatology website	"I think that noontime is probably the best time for most programs because most people have breaks for lunch, and people can lunch and learn." (PD) "The ACR website...it's not that easy to find stuff." (PD) "You have to like log on to the ACR website and it's just like a lot of clicking and getting into stuff and it's not the most convenient." (FIT)

comprehensive curriculum (Figure 1); limitations in faculty expertise and faculty time to lead sessions were the top obstacles identified. ViP sessions were required by 6/13 (46%) PDs, and 5/10 (50%) PDs incorporated 16 or more ViP sessions per year in their curriculum. Several approaches and barriers to ViP utilization were identified (Figure 1). Two FIT focus groups were conducted with 6 total participants, and three PD focus groups were conducted with 8 total participants. Themes and representative quotes are presented in Table 1. Participants expressed interest in lectures ≤30 minutes, with active learning methods that preserve psychological safety, such as anonymous polls and review questions. In both survey and focus group responses, board review content and opportunities to learn from content experts were highly valued, while scheduling conflicts and difficulty navigating the ACR website were obstacles to V-FIT use (Figure 2, Table 1).

Conclusion: PDs of large and small rheumatology fellowship programs expressed a need for curricular resources. Both PDs and FITs would value virtual programming that is ≤30 minutes, promotes active learning while maintaining psychological safety, provides access to content experts, and addresses board exam preparation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

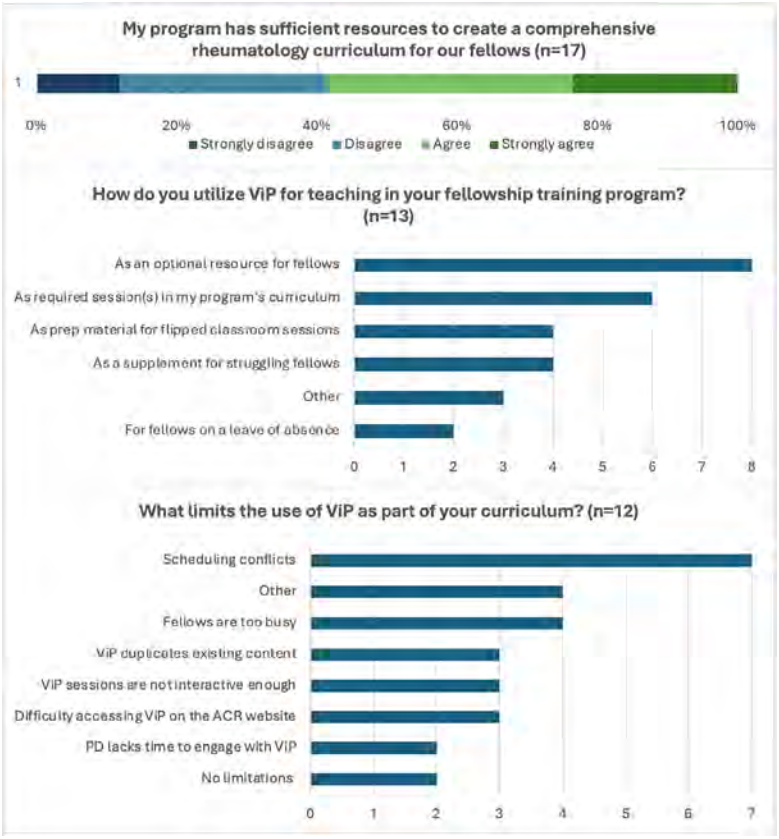


Figure 1. Rheumatology fellowship program director survey responses: factors influencing curriculum development and use of the Virtual Practicum for Adult Rheumatology (ViP). PD = program director, ACR = American College of Rheumatology.

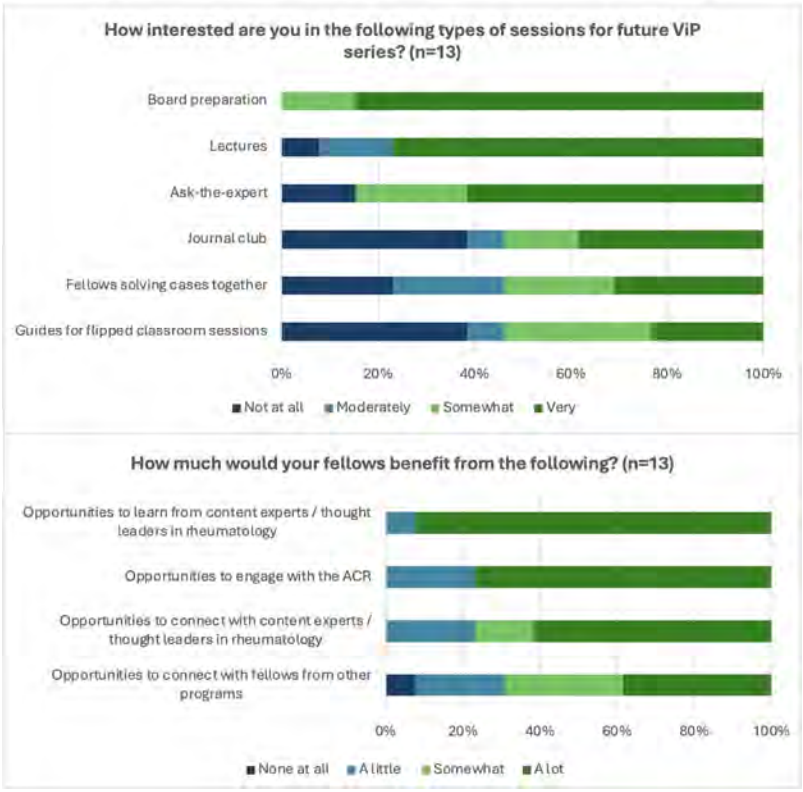


Figure 2. Rheumatology fellowship program director survey responses: future directions for the Virtual Practicum for Adult Rheumatology (ViP). PD = program director, ACR = American College of Rheumatology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Arneson: Novartis, 12,; **M. Dimachkie**: None; **J. Aizer**: None; **J. Mitchell**: None; **D. Leverenz**: Pfizer, 5, Sanofi, 2, UCB, 2; **A. Dua**: AbbVie/Abbott, 2, Amgen, 2, 5, 12, Clinical Trials, AstraZeneca, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, 12, Clinical Trials, Rheumatology Research Foundation, 4, 5, 12, Clinical Trials, Sanofi, 2, Vasculitis Foundation, 4; **L. Zickuhr**: Janssen, 5.

Abstract Number: 2163

Enhancing Post-Conference Engagement Through Expert Q&A: A Pilot Collaboration Between ACR Convergence & theMednet.org

Nina Couette[1], Herveen Singh[2], Melissa Briones[3], Nadine Housri[4] and Rebecca Manno[5], [1]The Ohio State University, Columbus, OH, [2]theMednet.org, New York, NY, [3]Loyola University, Maywood, IL, [4]theMednet.org, New York, [5]University of The Virgin Islands / The Arthritis and Rheumatology Center of the Caribbean, St. Thomas

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: ACR Convergence is a key platform for sharing cutting-edge research and clinical insights in rheumatology. To extend the educational value of select sessions beyond the meeting itself, a pilot collaboration between ACR and theMednet.org was developed. The initiative, titled "Continue the Conversation," aimed to foster enduring post-conference engagement. This was accomplished by posing timely clinical questions from ACR Convergence sessions to theMednet experts and distributing their answers, sometimes paired with interactive polls, via email to the broader rheumatology community.

Summary of engagement per question

	QUESTION	VIEWS	UNIQUE VIEWERS	INSTITUTIONS	UNIQUE VOTERS
1	How do you screen rheumatoid arthritis patients for lung disease (modality, frequency, patient selection)?	975	305	272	-
2	What is the most impactful career advice you have received from a colleague or mentor?	793	262	233	-
3	How long do you continue rituximab in patients with ANCA associated vasculitis who have achieved remission? **Poll Question:** *How long do you continue rituximab in patients with ANCA associated vasculitis who have achieved remission?*	679	252	222	98
4	What is the role of the rheumatologist in recommending and providing GLP-1 medications to their patients given the benefits across many disease domains including osteoarthritis? **Poll Question:** *How do you plan to utilize GLP-1 analogs in patients with knee OA and obesity in your rheumatology practice?*	660	247	216	104
5	How do you determine which patients with ANCA associated vasculitis may be good candidates for reduced dose glucocorticoid tapering?	619	223	200	-
6	What strategies or initiatives do you think could be most effective in addressing the rheumatology workforce shortage?	604	189	165	-
7	Do you pursue coronary artery calcium scoring in patients with metabolic risk factors and autoimmune disease in order to guide decisions regarding GLP-1 medications? **Poll Question:** *Do you pursue coronary artery calcium scoring in patients with metabolic risk factors and autoimmune disease in order to guide decisions regarding GLP-1 medications?*	250	104	96	57
8	Do you continue biologics in sJIA patients who develop lung disease on anti IL-1 or anti IL-6 therapies? **Poll Question:** *Do you continue biologics in sJIA patients who develop lung disease on anti IL-1 or anti IL-6 therapies?*	157	59	53	12
9	What is your approach to screening patients with sJIA for associated lung disease?	108	53	50	-
	TOTAL	4,845	675	560	201

Image 1: Summary of Engagement Per Question

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

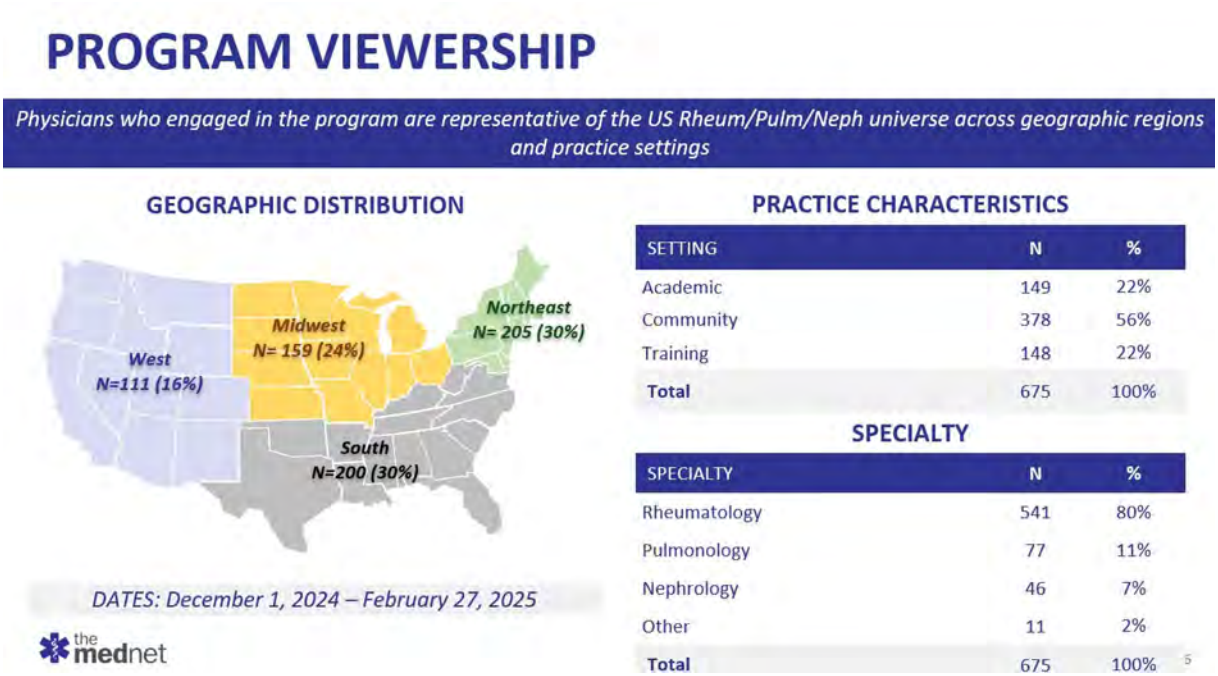


Image 2: Program Viewership

Methods: Clinically relevant questions were curated by theMednet editorial team based on pre-selected presentations from ACR Convergence 2024. These questions were sent to experts (including session presenters) for commentary. Polls were created for some questions to encourage participation, and a custom ACR-specific program tag was added to promote visibility and searchability. Each question included contextual information and direct reference to the corresponding ACR session. The Q&A was disseminated via email newsletters over a 6-8 week period, and a comprehensive summary was shared with physicians at the end of the program. Engagement metrics were tracked across multiple domains. CME credit claims were also reviewed.

Results: A total of nine questions and four polls were created based on the ACR Convergence presentations. During the program, 675 physicians engaged with Q&A content. The content reached a broad audience, with 4,845 total views across the nine questions with an average of 2.7 views per physician per question. Individual Q&A posts received an average of 538 views, and engagement with associated polls came from 201 unique voters with participation spanning 560 institutions (Image 1). Viewers spent an average of 12 minutes on the site viewing program content. Engagement was broad-based with poll participants and viewers representing diverse geographic regions and practice settings across rheumatology, pulmonology, and nephrology (Image 2). A total of 345 CME credits were claimed for 169 unique physicians. Of those claims, in regard to*impact* on clinical practice, 37% of respondents stated they gained a deeper understanding of a topic, 37% learned something new, 10% stated they understand how to apply what they know to clinical practice, 8% stated there was no impact, and 8% responded "other" (Image 3).

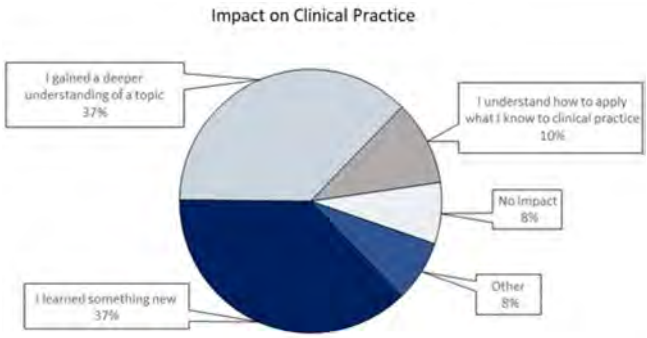


Image 3: Impact on Clinical Practice

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The "Continue the Conversation" initiative effectively extended the impact of ACR Convergence 2024 by fostering sustained engagement with key clinical topics through expert-led Q&A on theMednet.org. High levels of participation, CME activity, and reported practice relevance demonstrate that digital platforms can play a critical role in translating conference content into lasting educational value. These findings support continued innovation in post-conference learning and highlight opportunities to further integrate digital engagement into future ACR educational strategies.

Disclosure: N. Couette: None; **H. Singh**: theMednet, 3; **M. Briones**: theMednet.org, 3, 8; **N. Housri**: Mednet, 8, 12, I do not believe this fits the definition of an ineligible company but I do want to disclose that I am the co-founder and Chief Medical Officer; **R. Manno**: None.

Abstract Number: 2164

East Meets West: A Novel Tofu-Pasta-Cardstock Phantom Model for Teaching Ultrasound-Guided Procedures

Philip Chu[1], Erin Chew[2], Lily Kao[3], Karina Torralba[4], Fawad Aslam[5] and Janeth Yinh[6], [1]Duke University Hospital, Raleigh, NC, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Evergreen Medical Group, San Jose, CA, [4]Loma Linda University School of Medicine, Redlands, CA, [5]Mayo Clinic, Arizona, Scottsdale, AZ, [6]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Certain ultrasound (US)-guided procedures may be integral to the diagnosis and management of arthritis. US-guided carpal tunnel (CT), flexor tendon sheath (FTS), and hip injections are more accurate than landmark-guided injections, but they can be more challenging to perform. Soft tissue phantom models simulating anatomic areas give trainees the opportunity to practice. However, cadaver-based models, commercial phantoms, and homemade models require special handling. Affordable, accessible, and soft tissue consistency type phantom models are needed. The tofu phantom model has been used to simulate scenarios of basic categories of US-guided procedures. In this study we use a Tofu-Pasta-Cardstock (TPC) phantom model to simulate challenging scenarios of avoiding neurovascular structures (CT), navigating a superficial narrow target (FTS), and navigating a deep angle (hip).

The purpose of this study is to assess improvements to learner confidence in performing CT, FTS and hip US-guided injections after receiving instruction using a practical TPC phantom anatomic simulation model.

Methods: Dried pasta, such as rigatoni, bucatini, and fettuccine (simulating transverse carpal ligament, arteries, and bony contour, respectively), and cardstock (simulating the hip joint) were used for anatomic representation (Figure 1). Locations of insertion within the tofu were approximated to simulate the location and scale of real-world anatomy. Tofu blocks were submerged under water to improve echogenicity of the tofu and to avoid the problem of phantom needle tracks encountered in existing models (Figure 2).

Prior to the hands-on training workshop, participants in a beginner/intermediate US course underwent a 20-minute lecture regarding US-guided procedure techniques pertinent to each region. With a learner-to-instructor ratio of 5:1, each participant rotated for 15 minutes through the 3 tofu models, guiding the needle to the target site with sonographic guidance. Immediate feedback related to handling of the syringe, proper ergonomics, US image optimization, and needle approach

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

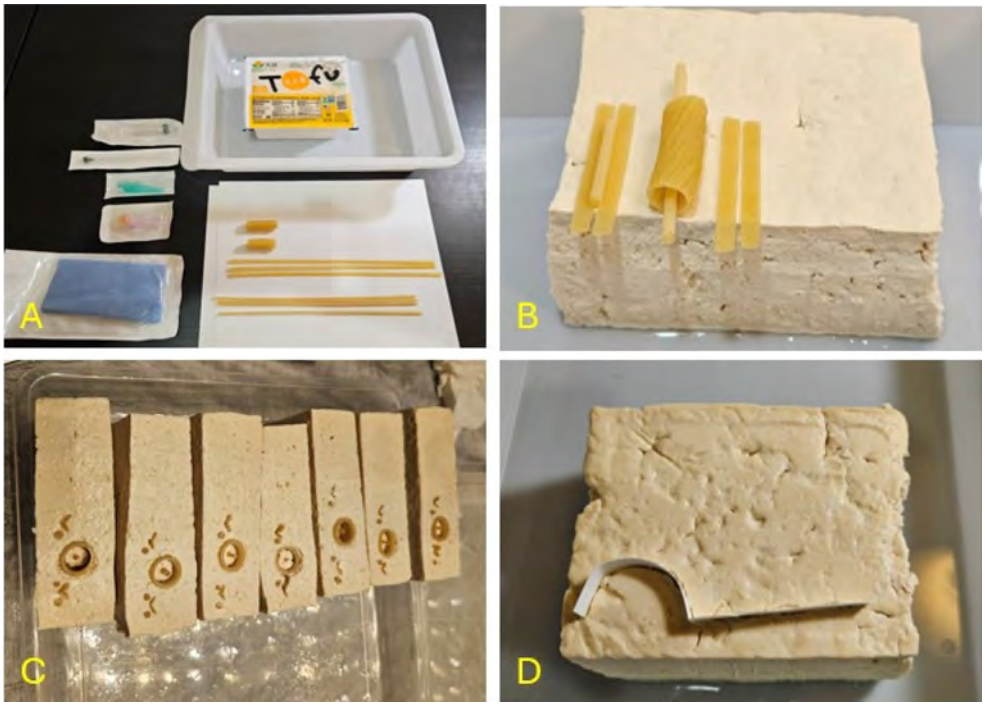


Figure 1. A) Materials needed for set up. B) Dried pasta approximated and arranged prior to insertion into the tofu. C) Multiple tofu pasta cardstock models can be produced relatively quickly. D) Cardstock inserted into tofu to simulate the hip joint.

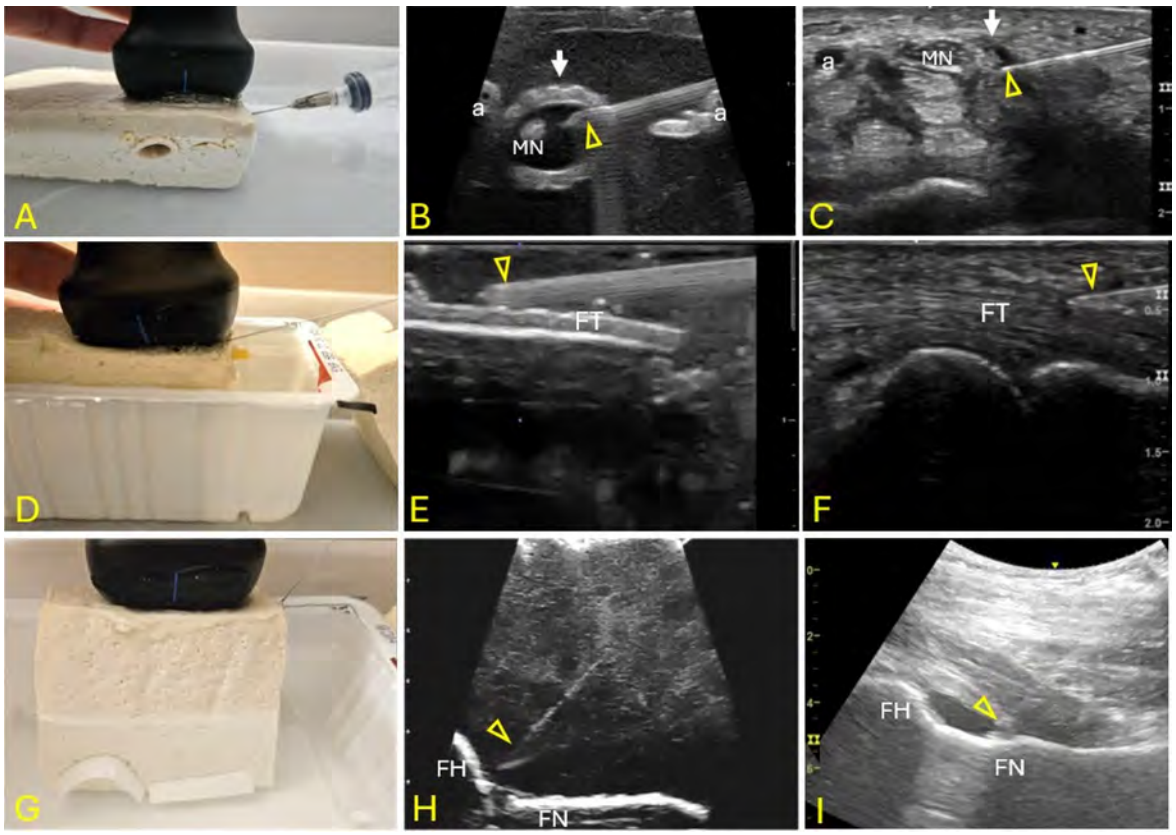


Figure 2. A) TPC model, B) corresponding US image, and C) patient example of carpal tunnel injection. D) TPC model, E) corresponding US image, and F) patient example of flexor tendon sheath injection. G) TPC model, H) corresponding US image, and I) patient example of hip injection. White solid arrow = transverse carpal ligament/rigatoni, yellow arrowhead = needle, a = artery/bucatini, FH = femoral head/cardstock, FN = femoral neck/cardstock, FT = flexor tendon/bucatini, MN = median nerve/spaghetti.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

to the targeted injection site were provided by the instructor. Post workshop, participants were invited to complete a survey accessed via Redcap QR code.

Results: Out of 35 participants, 68.6% responded. 70.8% had less than 1 year of US-guided injection experience. Pre and post workshop confidence of participants increased 75%, 87.5%, and 79% in their US-guided CT, FTS, and hip injection skills, respectively. 58.3% of participants felt that the models were easy to use and that they were likely to recreate this model for personal practice. The TPC models remained intact for the full 90 minutes with at least 5 learners and 1 instructor using each model with multiple needle passes.

Conclusion: The novel combination of tofu, dried pasta, and cardstock is effective in improving learner confidence in their US-guided CT, hip and FTS injection skills and demonstrates many advantages compared to existing phantom models. This accessible and affordable model can simulate challenging injections commonly encountered in rheumatology by demonstrating structures to avoid, depth adjustments and more precise placement of the needle tip.

Disclosure: P. Chu: None; **E. Chew**: None; **L. Kao**: None; **K. Torralba**: Amgen, 3; **F. Aslam**: None; **J. Yinh**: Janssen, 2, Springer, 9.

Abstract Number: 2165

Targeted Needs Assessment of Provider Medical Knowledge of Juvenile Scleroderma, a Mixed Methods Study

Rachel Guess[1], Megan Curran[2], Lisa Zickuhr[3], Rachel Moquin[1] and Childhood Arthritis and Rheumatology Research Alliance (CARRA) Scleroderma Workgroup, [1]Washington University School of Medicine, St. Louis, MO, [2]University of Colorado | Children's Hospital Colorado, Aurora, CO, [3]Washington University/B-JH/SLCH Consortium, St. Louis, MO

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Juvenile scleroderma (JS) is an autoimmune disease that can cause skin sclerosis leading to deformity, disability, and early mortality especially with delayed diagnosis. A general needs assessment performed by the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Scleroderma Workgroup identified gaps in provider medical knowledge as the main barrier to diagnosis and treatment of the child, from the caregiver perspective. The aim of this study is to characterize the knowledge gap, barriers to referral and preferred educational methods to inform the production of provider-facing educational materials. The researchers hypothesize that pediatric primary care providers harbor low awareness and disease misconceptions regarding JS.

Methods: A targeted needs assessment was built to survey providers in pediatrics, family medicine, and dermatology. After 8 rounds of expert review, pilot testing with 7 physicians, and approval by the Washington University Institutional Review Board, the consent and survey were distributed through email invitation to provider groups and on social media. Providers were recruited and consented via email to participate in 15-minute-long interviews to better understand providers' knowledge and preferences for education on JS. Interviews were recorded, transcribed, and inductively analyzed by 3 team members to reduce bias.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

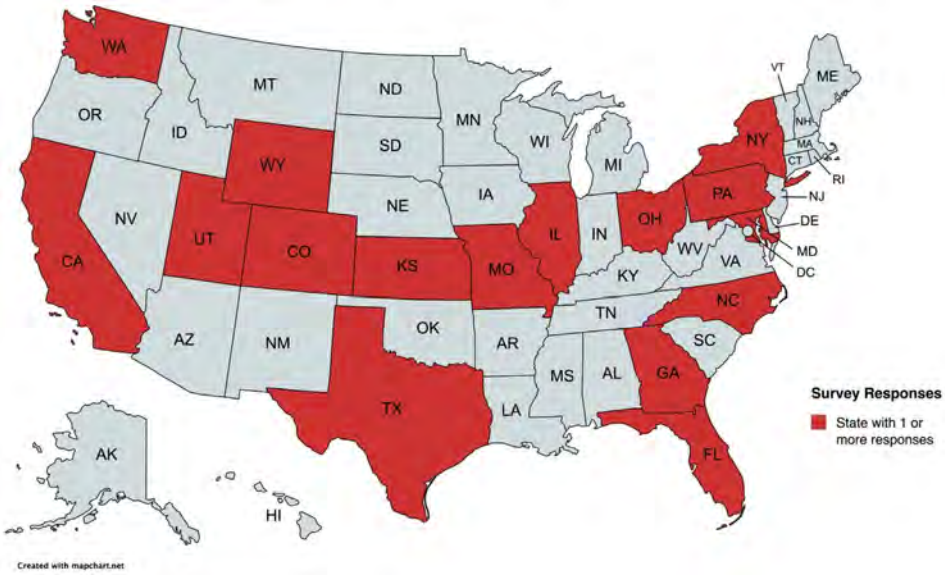


Figure 1: Map representing state origin of survey responses.

Figure 2: Table depicting aggregate responses to questions related to juvenile localized scleroderma knowledge.

Localized juvenile scleroderma (jLS) Knowledge Check Statement	Didn't Know (%)	Somewhat or Strongly Agree (%)	Somewhat or Strongly Disagree (%)
jLS is a cosmetic disease.	12	1	87
jLS is a serious disease.	13	76	11
jLS will burn out on its own without treatment.	32	6	62
jLS requires systemic immunosuppressive therapy to treat.	32	60	8
Systemic immunosuppressive therapy is more dangerous to the child than jLS.	31	2	66
Some jLS patients do not need to see pediatric rheumatology.	31	18	51

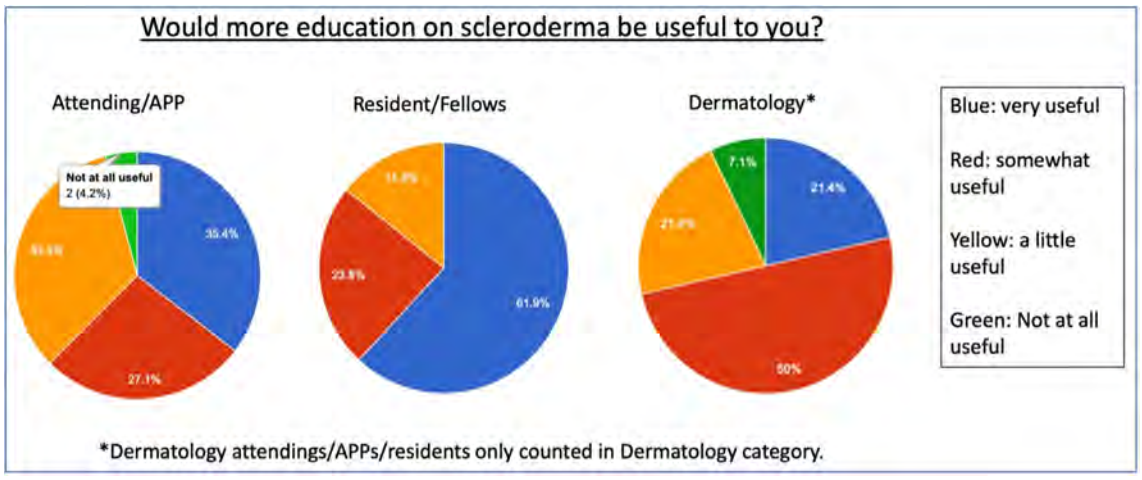


Figure 3: Diagram of preferences on additional education on juvenile scleroderma.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: 88 of 1092 invited providers (8%) from all 5 geographic regions of the United States (Figure 1) responded to the survey, with 58 physicians out of training, 25 physicians-in-training, and 5 advanced practice providers. The responses came from 63 providers in pediatrics, 10 in family medicine, and 14 in dermatology. 24% of respondents didn't know or thought that juvenile localized scleroderma (jLS) was not a serious disease (Figure 2). 38% didn't know or thought jLS would burn out without needing treatment. 49% either didn't know or thought some jLS patients do not need to see pediatric rheumatology. 5/12 participants that treat jLS incorrectly chose the most common subtype of jLS. 38% of providers felt that rheumatology wait list was a barrier to referral. 70% felt that additional education in scleroderma would be very or somewhat useful (Figure 3). 65% preferred an interactive online module for education and 70% preferred it be less than 15 minutes in duration. The qualitative analysis identified time and low prioritization on rare conditions as barriers to education on scleroderma, recommended education be focused on presenting features, and conference presentations as preferred delivery.

Conclusion: This study demonstrates knowledge gaps regarding JS among pediatric primary care providers. Opportunities for education include the presentation and seriousness of the disease in children, and differences from adult disease. Limitations of this study include limited responses and response bias. Next steps include making educational resources such as a brief interactive module to address the gap and reduce barriers to referral. This has the potential to increase early diagnosis, which would improve outcomes of children with JS.

Disclosure: R. Guess: None; **M. Curran**: Guidepoint, 2, NYU Langone Rheumatology department, 6, Rheumatology, research foundation, 6, Wolters Kluwer, 9; **L. Zickuhr**: Janssen, 5; **R. Moquin**: None.

Abstract Number: 2166

Clinical Disease Activity Index (CDAI) for Rheumatoid Arthritis: A Clinical Educational Workshop

Ahmed Rubia[1], Nancy Olsen[2], Saurav Suman[3], Sharon Banks[4], Shirley Albano Aluquin[1], Kristie Pepper[5] and Rayford June[6], [1]Penn State Milton S. Hershey Medical Cen, Hershey, PA, [2]Penn State University/Milton S Hershey, Hershey, PA, [3]Penn State Milton S. Hershey Medical Cen, Harrisburg, PA, [4]Penn State Milton S. Hershey Medical Center, Hershey, PA, [5]Penn State Milton S. Hershey Medical Cen, Lebanon, PA, [6]Penn State College of Medicine/Lebanon VA Medical Center, Hummelstown, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The Clinical Disease Activity Index (CDAI) is one of six assessment measures for rheumatoid arthritis (RA) recommended for management of RA in clinical practice. RA assessment measures were developed and validated for clinical research but since adoption of treat-to-target (TTT) principles as the standard of care for RA, there is a need for professional education to implement these measures in the clinic. As the CDAI does not require laboratory data, this RA composite outcome measure is preferred for the point-of-care management of RA. Standardization of joint examination technique has been shown to decrease interobserver variability in performing the CDAI. The purpose of this study was to create a medical educational workshop curriculum for learners and providers to improve knowledge and familiarity with the CDAI in RA management.

Methods: An educational workshop for the CDAI was developed and this curriculum proposal was presented at our institutional Rheumatology grand rounds for process improvement. Based on the feedback from this presentation, a 6-minute video demonstrating a 28 joint count exam was then developed (Image 1). 8 months later, Rheumatology providers and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

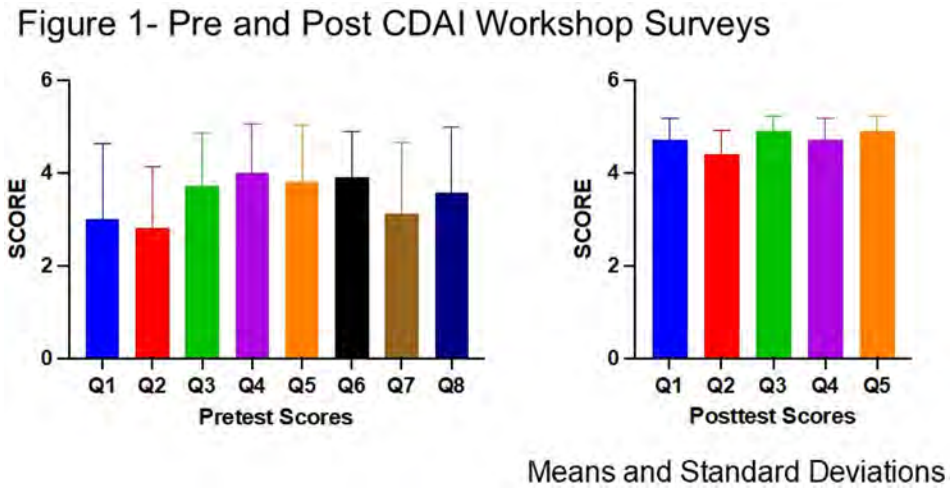


Figure 1

learners, including rheumatology fellows, were invited to a CDAI education workshop. The workshop included learning objectives, an 8-question pre-and 5 question post-workshop questionnaire, didactic presentation, a joint examination video followed by a series of three RA case discussions. Time was built in for group discussion on CDAI score on the RA cases. The workshop ended with a post-workshop questionnaire. Data were analyzed using descriptive statistics and t-tests to compare groups. A P value of < 0.05 was considered significant.

Results: The workshop was facilitated by a second-year rheumatology fellow and a rheumatology attending physician. There were 10 participants including rheumatology fellows, advanced practice providers, and attending physicians. All participants completed the pre and post-knowledge questionnaire (Table 1). The mean participant response for confidence in performing CDAI prior to the curriculum was a mean of 3 (SD 1.63), based on a 5-point Likert scale. After the curriculum, the likelihood of performing CDAI in clinic was a mean of 4.7 (SD 0.48). Prior to the workshop, confidence in performing

Table 1

Table 1: CDAI Workshop Knowledge Surveys

Pre-workshop Questionnaire			
Question		Mean	Standard Deviation
1	Overall, I can perform CDAI accurately	3	1.63
2	I can perform and assess tender and swollen joints of the shoulders	2.8	1.32
3	I can perform and assess tender and swollen joints of the elbows	3.7	1.16
4	I can perform and assess tender and swollen joints of the wrists	4	1.05
5	I can perform and assess tender and swollen joints of the small joints of hands	3.8	1.23
6	I can perform and assess tender and swollen joints of the knees	3.9	0.99
7	Overall, I can perform provider global activity	3.11	1.54
8	Overall, I can perform patient global activity	3.56	1.42
Post-workshop Questionnaire			
1	After the teaching intervention, I am more likely to perform CDAI score	4.7	0.48
2	After the teaching intervention, I am confident that I can perform a 28 joint count exam appropriately	4.4	0.52
3	After the teaching intervention, my understanding of provider global assessment of disease activity has improved	4.9	0.32
4	After the teaching intervention, my understanding of patient global assesment of disease activity has improved	4.7	0.48
5	Overall, this course has been resourceful for my knowledge	4.9	0.32

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Image 1

the provider global was 3.1 (SD 1.54) and improved to 4.9 (SD 0.32). Similarly, confidence in assessing patient global activity, increased from 3.6 (SD 1.42) to 4.9 (SD 0.31) after the workshop. Overall, the participants responded that the course was helpful in increasing awareness and confidence in performing the CDAI. Pre and post means improved significantly after the workshop (p=0.0001) suggesting generalized knowledge improvement from the training workshop.

Conclusion: A clinical educational workshop on CDAI for Rheumatology providers improved self-reported knowledge of the CDAI for rheumatology training. Further investigation is needed to know if the education workshop translates into higher and proper utilization of CDAI in clinical care.

Disclosure: A. Rubia: None; **N. Olsen**: Atare Bio, 5, GlaxoSmithKlein(GSK), 1, UCB, 5, Zenas, 5; **S. Suman**: None; **S. Banks**: None; **S. Albano Aluquin**: None; **K. Pepper**: None; **R. June**: None.

Abstract Number: 2167

Rheum4Games: A Game-Based Rheumatology Board Review for Internal Medicine Residents

Sonam Kiwalkar[1], Megan Schermerhorn[2], Sarah Donohue[3] and Christine Sharkey[4], [1]The Vancouver Clinic, Portland, OR, [2]Providence Portland Medical Center, Portland, OR, [3]University of Wisconsin, Madison, WI, [4]UNIVERSITY of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology is often viewed as a niche and intellectually demanding subspecialty in internal medicine (IM). Consequently, there is a trend toward lower In-Training Examination (ITE) scores in this area, which are predictive of American Board of Internal Medicine (ABIM) exam performance. Structured electives improve outcomes but are not mandatory, leading to variable rheumatology exposure. Traditional lectures dominate teaching, however, with a new generation of learners, gamification, described as the of applying game elements in education, has shown promise in enhancing engagement, motivation, and knowledge retention. To date, its application in rheumatology board preparation remains underexplored. We developed Rheum4Games (R4G), a Snakes-and-Ladders-style game to reinforce high-yield rheumatology concepts. We hypothesized that this format would enhance resident engagement, confidence, and ITE performance.

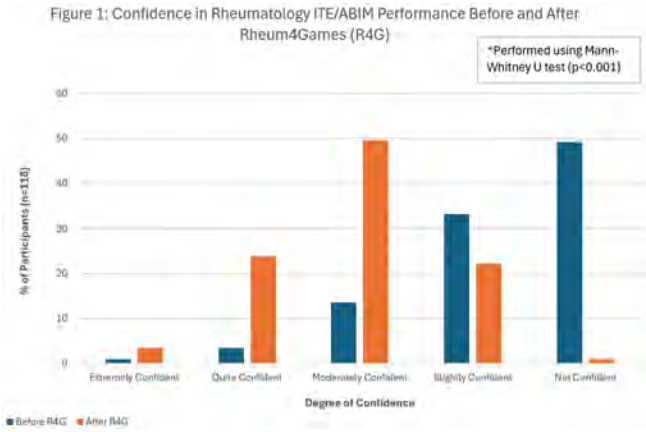
Methods: This pre-post intervention study examined the impact of a gamified rheumatology board review on resident satisfaction and ITE scores. Five IM residency programs (4 community, 1 university) incorporated R4G into their didactic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

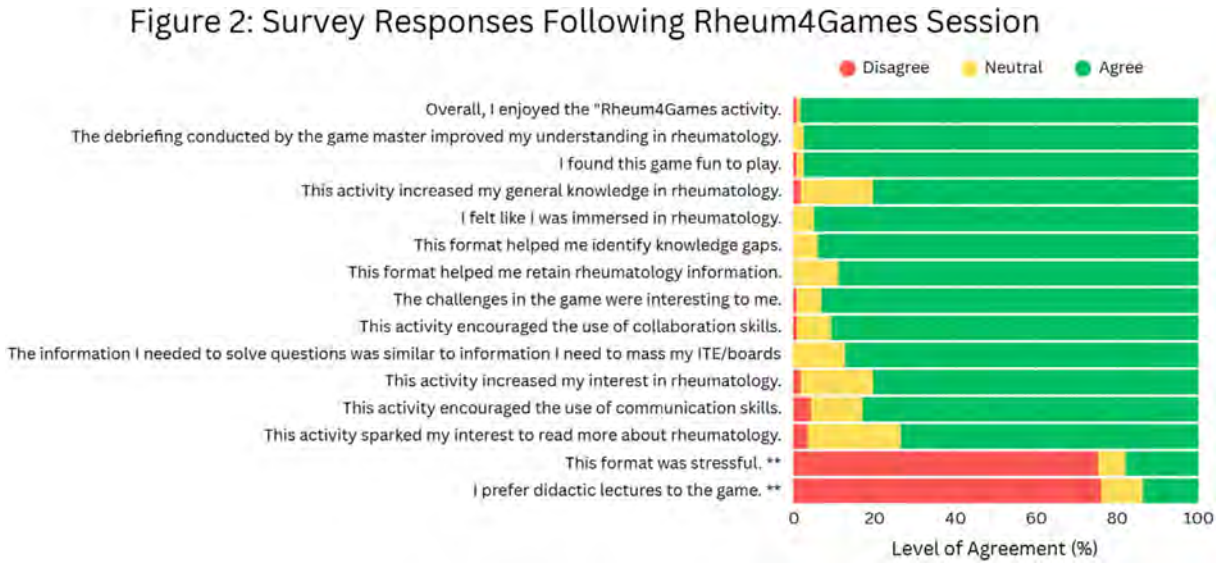
Table 1: Comparison of Median Rheumatology Score Improvements Between R4G Participants and Non-Participants

Group	n	Median Rheumatology Percent Change (2024-2023)	Q1-Q3	p-value*
Attended R4G	68	9	4-21	0.63
Did not attend R4G	38	9	5-18	

*Performed using Mann-Whitney U test.



curricula. A total of 12 sessions were conducted with 121 participants. A total of 45 questions with short explanations were developed using ABIM blueprint, reviewed by experts (5 rheumatologists, 2 internists), and piloted prior to implementation. Sessions included a pre-survey, R4G session, and post-survey. ITE scores and confidence levels were compared pre- and post-intervention utilizing Mann-Whitney U tests, while descriptive statistics were used for survey results.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 121 residents participated, with high pre- and post-session survey completion rates (97.5% and 96.7%, respectively). Among the 106 residents with matched ITE data (defined as those with available scores for both the 2023 and 2024 ITE exams), there was no significant difference in the median score change between R4G participants and non-participants (Table 1). However, a subgroup analysis revealed that R4G participants from community-based programs demonstrated significantly greater score improvement compared to those from university settings. In addition, self-reported confidence in the rheumatology section of the ITE/ABIM improved significantly post-session ($p < 0.0001$; Figure 1). Residents rated the session highly for enjoyment, engagement, and educational value (Figure 2), and open-ended responses highlighted the activity's interactivity, effectiveness, and novelty.

Conclusion: R4G effectively enhanced resident engagement, confidence, and satisfaction, as evidenced by high survey ratings and significant self-reported gains in preparedness for the ITE/ABIM rheumatology content. While overall ITE score improvements were not statistically significant, the greater gains observed in community programs suggest that R4G may be beneficial in settings with less structured rheumatology exposure. Further studies should explore the long-term retention effects of game-based learning as well as potential strategies to optimize its effectiveness in diverse training environments.

Disclosure: S. Kiwalkar: None; **M. Schermerhorn**: None; **S. Donohue**: None; **C. Sharkey**: None.

Abstract Number: 2168

Training Objective Structured Clinical Examinations in a Clinical Immunology department: Expectations and Perceptions of Medical students at Graduating Level

Aïcha Kante[1], Damien Sène[2], Venceslas Bourdin[3], Dikélélé Elessa[3], William Bigot[3], Valentine Pagis[3], Frédéric Truffinet[3], Stéphane Mouly[3] and Cloé Comarmond[1], [1]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, INSERM U942, Paris, France, [2]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, Paris, Ile-de-France, France, [3]Department of Internal Medicine, Lariboisière University Hospital, Université Paris Cité, Assistance Publique Hôpitaux de Paris, Paris, France

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Objective Structured Clinical Examinations (OSCEs) are based on various starting clinical scenarios conducted in a simulated environment that allow for the standardized assessment of medical students' competencies, recently introduced in France. Our aim was to evaluate expectations and perceptions of medical students at graduating level regarding this new method of clinical education.

Methods: Medical students participated in a weekly training OSCE station during their Clinical Immunology rotation. A questionnaire assessing expectations and perceptions regarding this new teaching method during clinical placements was distributed to medical students who completed a rotation in the Department of Clinical Immunology between January 2024 and January 2025. The questionnaire consisted of 10 questions estimated on a Likert scale or open-ended written response. Responses were analyzed using the Chi-squared test for qualitative variables and the Wilcoxon test for ordinal variables.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Over their 10-week clinical immunology rotation, 10 training OSCE stations were offered to medical students, covering various initial clinical scenarios relevant to clinical immunology: single and multiple lymphadenopathy, erythema nodosum, dyspnea, hyperthermia, headaches, weight loss, joint pain, visual disturbances, discoloration of the extremities, purpura, corticosteroid prescription, writing a prescription, elevated CRP, leukocyte abnormalities, and calcium metabolism disorders. In total, 63 consecutive medical students completed the questionnaire. The clinical scenarios addressed in the OSCE stations were rated as highly relevant to their curriculum, receiving a Likert score ≥ 4/5 from 59 students (93%), including 45 (71%) who gave a score of 5/5 and 14 (22%) a score of 4/5. The scenarios were considered better suited for reinforcing theoretical rather than practical training, with 45 students (71%) rating them 5/5 for theoretical consolidation, *versus* 35 (56%) for practical consolidation. Medical students at graduating level expressed a greater demand for more training OSCEs, with a median of one session per week ($p = 0.002$). The training OSCEs in clinical immunology were rated as highly useful for future clinical practice by 44 students (70%) with a score of 5/5 and by 13 students (21%) with a score of 4/5 on the Likert scale, with no significant difference between academic years ($p=0.7$). Among open-ended responses, 13 sixth-year students (54%) mentioned stress as the main difficulty encountered with this type of teaching, compared to 9 fifth-year students (23%) ($p = 0.012$). Difficulties related to time constraints ($p > 0.9$), organization ($p > 0.9$), and knowledge application ($p > 0.7$) were similar between the different academic years.

Conclusion: Over 90% of medical students acknowledged the high usefulness of training OSCEs during clinical immunology rotations for their future clinical practice. Training OSCEs were associated with increased performance anxiety especially when students are at graduating level.

Disclosure: A. Kante: None; **D. Sène**: None; **V. Bourdin**: None; **D. Elessa**: None; **W. Bigot**: None; **V. Pagis**: None; **F. Truffinet**: None; **S. Mouly**: None; **C. Comarmond**: Roche, 5.

Abstract Number: 2169

Bridging the Gap: A National Needs Assessment of Rheumatology Fellowship Training in Adolescent and Young Adult Care

Amanda Moyer[1], Megha Tandel[1], Michelle Benjamin[1], Rufei Lu[2], Julia F Simard[3] and Rebecca Sadun[4], [1]Stanford University, Palo Alto, CA, [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Stanford Medicine, Stanford, CA, [4]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Adolescents and young adults (AYAs) with rheumatic diseases require specialized care, particularly when transitioning from pediatric to adult healthcare. However, most residents and fellows receive little to no formal education in AYA care. One study found that over half of internal medicine trainees reported no instruction in AYA transition care, resulting in low confidence and potentially suboptimal patient outcomes. Targeted, high-quality transition education has been shown to improve trainee performance, but data on rheumatology fellowship training remain limited.

Methods: A national survey of pediatric, adult, and med-peds (MP) rheumatology fellows and program directors (PDs) was conducted from 2/2024–7/2024 to assess AYA training, priorities, exposure, beliefs, confidence, and practices. Survey items used Likert scales. Quality of AYA education and clinical tools was assessed using weighted scoring systems (high-quality education: exposure to ≥4 education techniques; high-quality transition tools: use of ≥3 transition tools). Fellows were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1.

Table 1: Participant Characteristics

	Rheumatology Fellows				Rheumatology Fellowship Program Directors			
	Overall N=173 n (%)	Pediatric n=45 n (%)	MP n=11 n (%)	Adult n=117 n (%)	Overall N=75 n (%)	Pediatric n=20 n (%)	MP n=11 n (%)	Adult n=44 n (%)
Year in Fellowship Training								
1	71 (41.04)	7 (15.56)	3 (27.27)	61 (52.14)	—	—	—	—
2	75 (43.35)	20 (44.44)	2 (18.18)	53 (45.30)	—	—	—	—
3	24 (13.87)	18 (40.00)	4 (36.36)	2 (1.71)	—	—	—	—
4	3 (1.73)	0 (0)	2 (18.18)	1 (0.85)	—	—	—	—
Residency training								
Pediatrics	44 (25.42)	44 (97.78)	0 (0)	0 (0)	—	—	—	—
Internal Medicine	116 (67.05)	0 (0)	0 (0)	116 (99.15)	—	—	—	—
Med-Peds	13 (7.15)	1 (2.22)	11 (100)	1 (0.85)	—	—	—	—
Years as a rheum attending								
< 5	—	—	—	—	6 (8.00)	2 (10.00)	2 (18.18)	2 (4.55)
5 - <10	—	—	—	—	20 (26.67)	3 (15.00)	3 (27.27)	14 (31.82)
10 - <15	—	—	—	—	16 (21.33)	6 (30.00)	4 (36.36)	6 (13.64)
15 - < 20	—	—	—	—	14 (18.67)	8 (40.00)	1 (9.09)	5 (11.36)
> 20	—	—	—	—	19 (25.33)	1 (5.00)	1 (9.09)	17 (38.64)
Affiliation								
Adult/Peds provider but no fellowship	61 (35.26)	4 (8.89)	—	57 (48.72)	22 (29.33)	2 (10.00)	1 (9.09)	19 (43.18)
Adult/Peds Fellowship program present	72 (41.62)	39 (86.67)	—	33 (28.21)	42 (56.00)	17 (85.00)	9 (81.82)	16 (36.36)
No affiliated Adult/Peds rheumatologist	28 (16.18)	4.44 (2)	—	26 (22.22)	10 (13.33)	1 (5.00)	0 (0)	9 (20.45)
Unknown/No response	12 (6.94)	0 (0)	—	1 (0.85)	1 (1.33)	0 (0)	1 (9.09)	0 (0)
Percent of patients seen 16 – 26 yoa, median (IQR)	20 (10, 35)	40 (33, 60)	35 (15, 65)	15 (8, 21)	20 (10, 50)	50 (34, 60)	50 (16, 65)	13 (10, 21)

considered prepared if ≥66% of skill items were endorsed as "prepared" or "completely prepared." Frequent AYA best practice use was defined as performing ≥4/7 care tasks ≥60% of the time. Data was analyzed descriptively and with non-parametric approaches.

Results: Surveys were distributed to 167 programs (130 adult, 37 pediatric/MP). Of those, 75 PDs and 173 fellows responded (47% and 29% response rates, respectively). Among respondents, 22% of adult fellows and 20% of adult PDs lacked an affiliated pediatric rheumatologist. Adult PDs estimated only 13% of their patients were aged 16–26 years, compared to 50% for pediatric/MP PDs; fellows reported similar trends (Table 1).

Table 2.

Table 2: Fellow Reported Preparedness

	Pediatric** (n=45)	MP** (n=11)	Adult** (n=117)	p-value
Prepared*	56%	100%	38%	
Prepare the AYA patient for differences between pediatric and adult rheum care	4 (3, 4)	5 (4, 5)	3 (2, 3)	**<0.0001**
Prepare the AYA patient's family for differences between pediatric and adult rheum care	4 (3, 4)	5 (4, 5)	3 (2, 3)	**<0.0001**
Ensure successful transition and transfer from pediatric to adult rheum care	3 (3, 4)	4 (3, 4)	3 (2, 4)	**0.0304**
Assess a patient's readiness for self-management of his/her health	3 (3, 4)	4 (3, 4)	3 (2, 4)	**0.0279**
Establish rapport with an AYA patient	5 (4, 5)	5 (4, 5)	4 (3, 4)	**<0.0001**
Establish rapport with an AYA patient's family or support system	4 (4, 5)	4 (4, 5)	4 (3, 4)	**<0.0001**
Ask parents or other individuals to leave the room to talk to an AYA patient alone	4 (4, 5)	5 (4, 5)	3 (2, 4)	**<0.0001**
Take a complete social history	4 (4, 5)	5 (4, 5)	4 (3, 5)	**0.0029**
Set appropriate self-management goals	4 (3, 4)	5 (4, 5)	3 (3, 4)	**0.0017**
Educate AYA patients of childbearing age	4 (3, 5)	5 (4, 5)	4 (4, 5)	0.0871
Discuss safe contraception	4 (3, 4)	4 (4, 5)	4 (4, 4)	**0.0268**
Discuss pregnancy plans	3 (2, 4)	4 (4, 5)	4 (4, 4)	**<0.0001**
Counsel on vaccines	4 (4, 5)	4 (3, 5)	4 (3, 5)	0.8355
Recognize complications related to treatment of childhood onset disease	4 (3, 4)	4 (4, 5)	4 (3, 4)	**0.0324**
Manage complications of childhood-onset disease	3 (3, 4)	4 (3, 4)	4 (3, 4)	**0.0948**

AYA, adolescent and young adult; Rheum, rheumatology; MP, Med-Peds
*Fellows were considered overall prepared if they answered 10/15 of preparedness questions as "prepared" or "completely prepared".
** Displayed as median (IQR)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

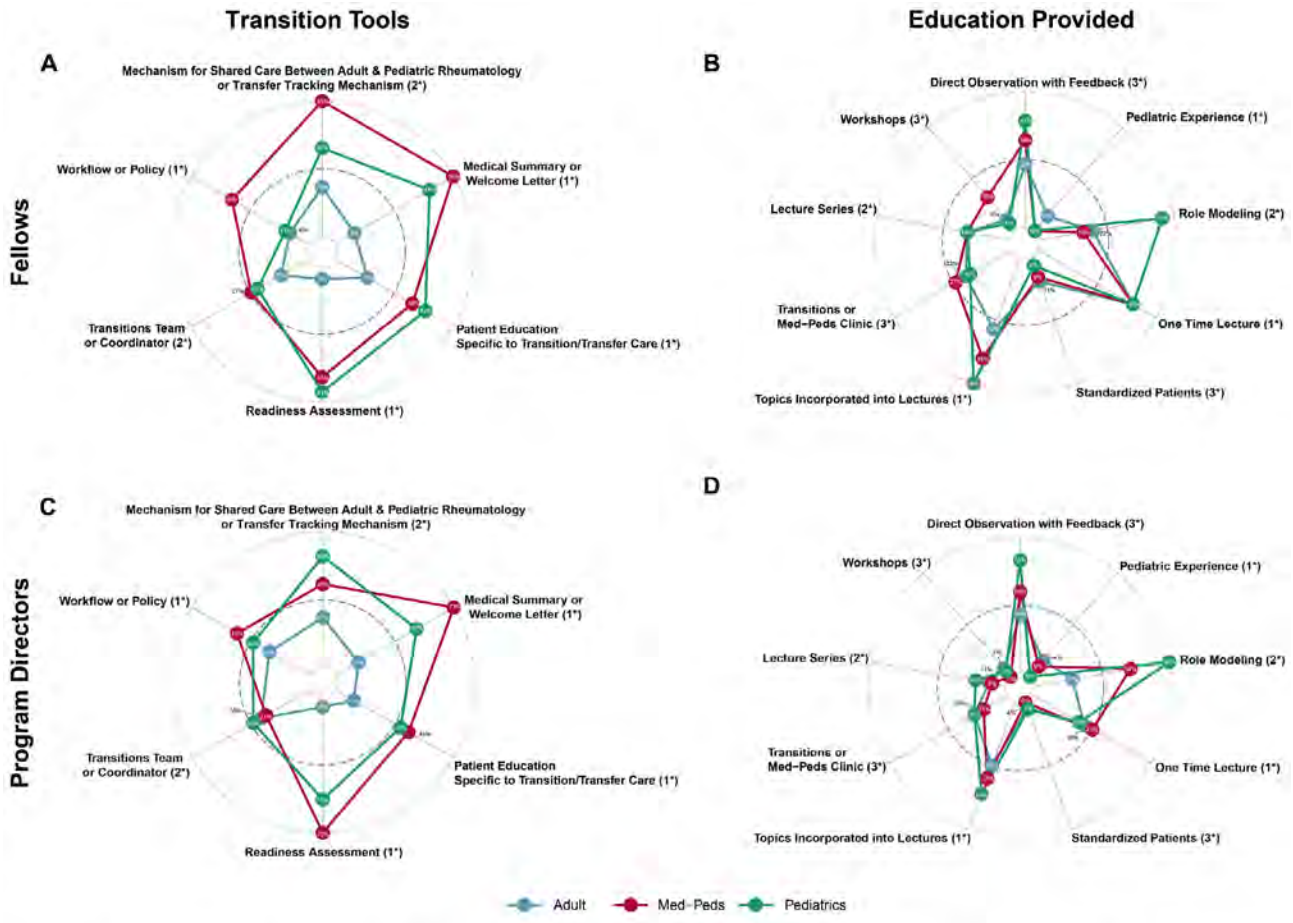


Figure 1: Reported Available AYA-Specific Clinical Tools and Education Provided. * Weight assigned to each clinical tool available and education modality provided as reported by rheumatology fellowship program directors (PDs) and fellows. High-quality education: weighted score ≥4. High-quality transitions tools: weighted score ≥3. *Not shown: Some PDs and fellows reported no access, or were unsure the availability, to listed clinical tools (40% and 9%, respectively) or educational modalities (3% and 6%, respectively).*

Figure 1.

All respondents rated AYA topics (transition, reproductive health, bone health, cardiovascular disease risk, vaccination) as important for training. Only 38% of adult fellows felt prepared to optimally care for AYA patients vs. 64% of pediatric/MP fellows. Preparedness was highest among MPs (Table 2). Fellows caring for more AYA patients reported greater preparedness.

Pediatric/MP fellows reported more diverse and higher quality AYA education than adult fellows (61% vs. 39%). Exposure to high-quality education was associated with more frequent AYA best practice use in pediatric/MP fellows, compared to those who received lower quality education (68% vs. 32%), but less so with self-reported preparedness.

Pediatric/MP fellows reported more access to high-quality transition tools (Figure 1) than adult fellows (50% vs. 17%). Additionally, pediatric/MP fellows with access to these tools used clinical best practices more frequently than those without (55% vs. 45%).

Conclusion: Despite broad recognition of the importance of AYA care, rheumatology fellowship training in these skills remains insufficient, especially in adult programs. Direct exposure to AYA patients, access to high-quality education and clinical tools, and MP training were all associated with increased preparedness and best practice adherence. A standardized, structured framework for AYA-focused training is needed to prepare rheumatology trainees to best care for this vulnerable patient population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Moyer: None; **M. Tandel**: None; **M. Benjamin**: None; **R. Lu**: None; **J. Simard**: None; **R. Sadun**: The Expert Institute, 12,.

Abstract Number: 2170

I Know It When I See It! Improving Visual Diagnosis Education in Rheumatology Fellowship Training

Amarjyot Randhawa[1], Laura Nichols[2], Jason Kolfenbach[3], Meredith Morcos[2] and Steven Taylor[3], [1]University of Colorado Anschutz Medical Campus, Denver, CO, [2]University of Colorado, Aurora, CO, [3]University of Colorado, Denver, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Visual diagnosis, based on both physical exam and imaging studies, is of great importance in clinical practice and for board exam purposes in rheumatology. The rarity of many rheumatologic diseases limits fellow exposure to the full range of physical and radiologic disease manifestations during training. There is a continued need to develop high-quality learning materials within rheumatology training programs. We report on a quality improvement education project which aims to develop and continually improve a question-based visual diagnosis curriculum.

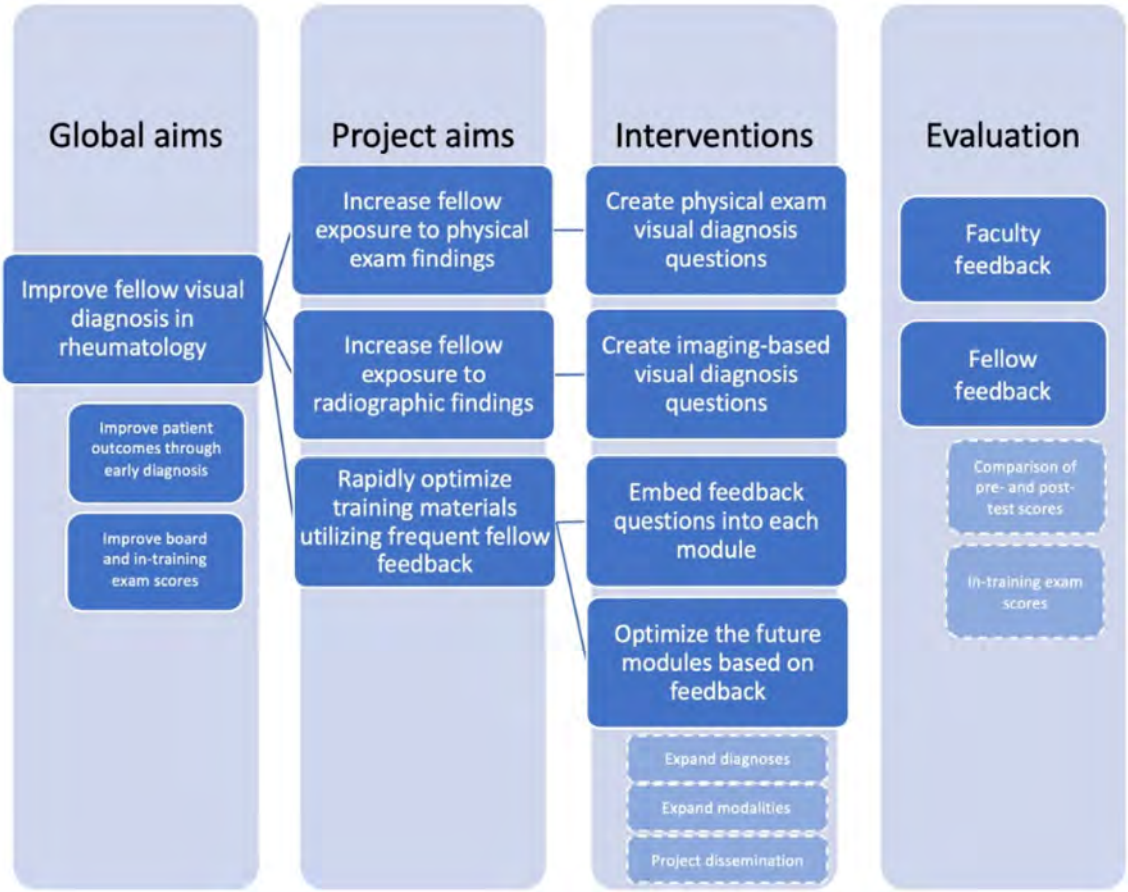


Figure 1: Project aims, interventions and evaluation. Future directions noted in lighter, dashed boxes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

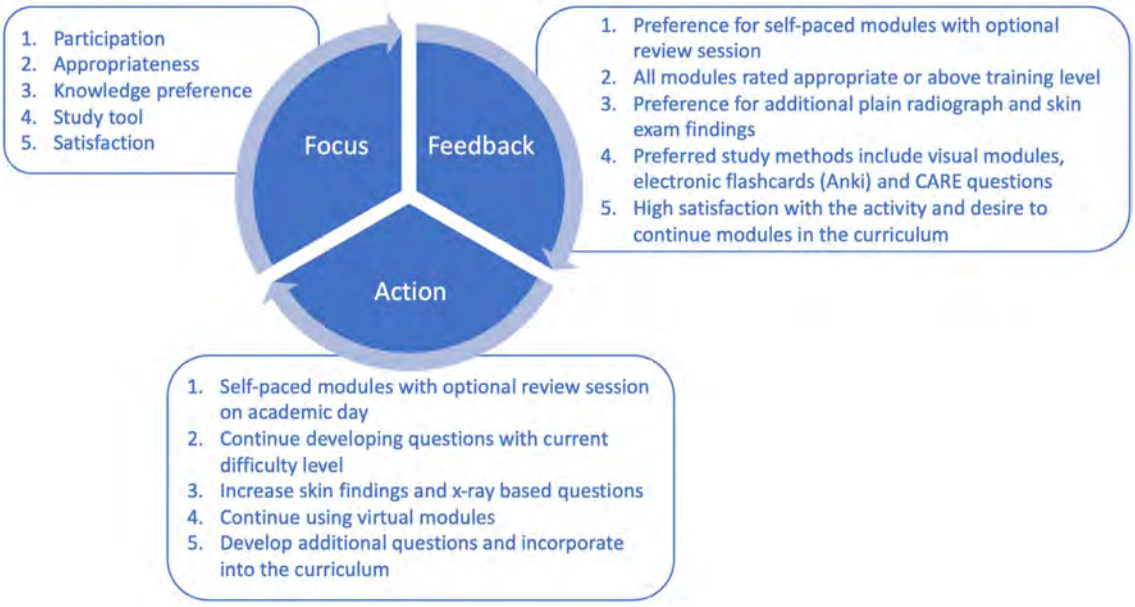


Figure 2: Process of module modification using a focus, feedback and action cycle.

Methods: Visual diagnosis questions were created using the American College of Rheumatology Image Library as well as clinical cases at a single academic center. Topics were chosen based on relevance with a focus on rheumatoid arthritis, dermatomyositis, systemic lupus erythematosus, crystalline arthropathy and spondylarthritis. Questions were created by two fellows and reviewed by faculty for content accuracy. Visual diagnostic modalities included physical exam findings, plain radiographs, and advanced imaging such as MRI and CT. Five separate modules consisting of seven questions each were delivered to six fellows between March 21, 2025 and May 5, 2025 via Qualtrics. Survey questions were embedded into each module and feedback incorporated into the next PDSA cycle.

Results: Five to six fellows completed each module. Project aims, interventions, and evaluation are outlined in Figure 1. Continuous improvement of the modules based on focused areas of feedback took place throughout the project period as noted in Figure 2. Fellows demonstrated a measurable increase in confidence from pre-module to post-module assessments (Figure 3). Prior to module dissemination, fellows rated level of satisfaction with visual diagnosis curriculum as "somewhat

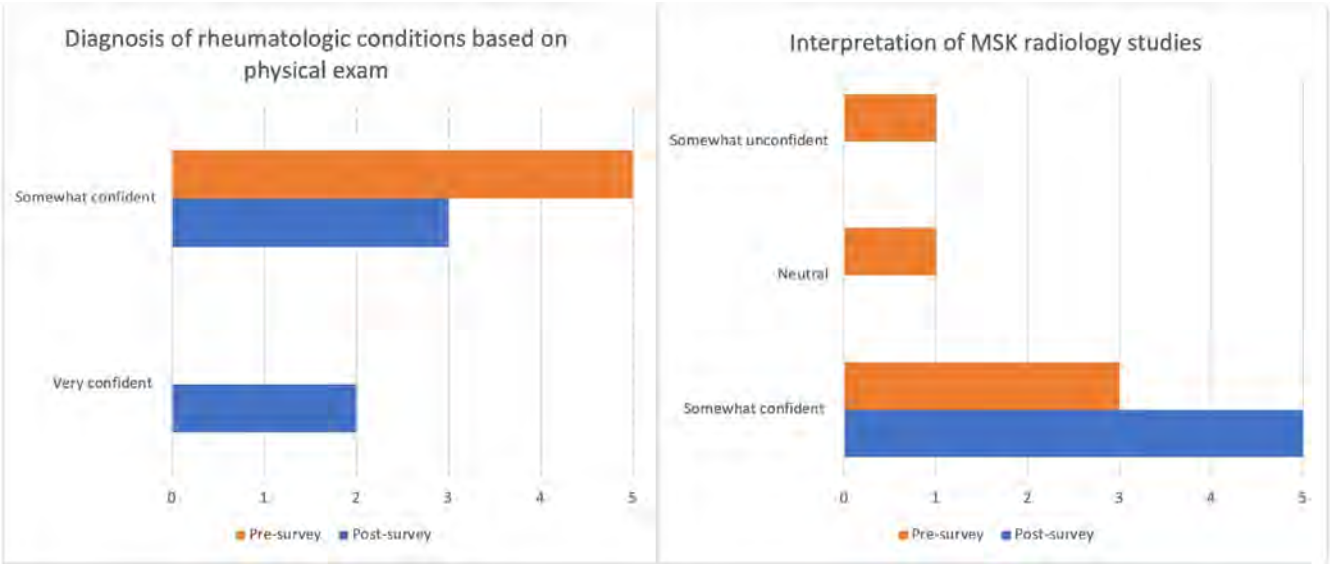


Figure 3: Self-reported confidence levels before and after the module, measured through surveys using a 5-point Likert scale.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

satisfied" (n=3) or "neutral" (n=2). Conversely, all respondents (n=5) were "very satisfied" with the module questions for their training and preferred to continue this as a part of the fellowship curriculum.

Conclusion: There were high levels of engagement in this visual diagnosis curriculum utilizing fellow-generated, faculty-reviewed questions. Integration of feedback with curricular material for rapid changes into the curriculum may serve as a model for future educational quality improvement. Next steps include expanding topics to include additional imaging modalities such as ultrasound and diagnoses such as vasculitis, increasing the number of questions for expansion as a broader curriculum within the fellowship and eventually creating modules that can be disseminated to other institutions.

Disclosure: A. Randhawa: None; **L. Nichols**: None; **J. Kolfenbach**: None; **M. Morcos**: None; **S. Taylor**: None.

Abstract Number: 2171

Knowledge of Fertility and Infertility Treatments Among Physicians Treating Women with Rheumatic Diseases: FIT-KS Survey

Andres M. Ortiz-Rios[1], Mara Alejandra Ponce-Santillan[1], Braulio R. Avalos-Garcia[1], Eva Abigaid Galindo-Calvillo[1], Carolina Treviño-Sanchez[1], Samantha Lynn Salinas-Rodriguez[1], Arantza Michelle Núñez-Elizondo[2], Erendira Berenice Noyola-Sauceda[1], Guadalupe Valentina Vazquez-Guerra[1], Jesus Alberto Cardenas-de la Garza[3], Lorena Perez-Barbosa[1], Dionicio A. Galarza-Delgado[4] and Cassandra Michele Skinner-Taylor[1], [1]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Universidad Autónoma de Nuevo León, Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, Nuevo León, México., Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatic diseases frequently affect individuals of reproductive age, and up to 40–70% may experience fertility issues related to disease activity, medications, delayed childbearing, and sexual dysfunction. Fertility knowledge among physicians is often limited, emphasizing the need for education in reproductive health when managing autoimmune conditions. This study aimed to assess fertility and infertility treatment knowledge among physicians treating women with rheumatic diseases in Mexico using the validated Fertility and Infertility Treatment Knowledge Score (FIT-KS).

Methods: A cross-sectional survey was conducted among residents and specialists in Internal Medicine, Rheumatology, Dermatology, Nephrology, Gynecology, Obstetrics, Maternal-Fetal Medicine, and Reproductive Biology. After accepting the informed consent, the physicians completed an online survey including sociodemographic items and the 29-item FIT-KS, which evaluates knowledge of natural fertility (21 items) and infertility treatments (8 items). Scores ranged from 0 to 29, with higher scores reflecting greater knowledge. Descriptive statistics, t-tests, and ANOVA were used for analysis. A p-value < 0.05 was considered significant.

Results: Ninety physicians participated (mean age 39.8 ± 13.3 years; 64.4% female). The most common specialties were rheumatology (47.8%), internal medicine (24.4%), and obstetrics/gynecology (18.9%). Most correctly identified the fertile

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Sociodemographic characteristics and mean FIT-KS score and average

	N = 90	Mean FIT-KS score and average (maxscore 29 and 100%)	p-value
Age, n (%)			
<35	44 (48.9)	19.11 ± 2.79 (65.90%)	**p = 0.008**
>35	46 (51.1)	17.48 ± 2.89 (60%)	
Sex, n (%)			
Female	58 (64.4)	18.88 ± 2.70 (65.10%)	**p = 0.012**
Male	32 (35.6)	17.19 ± 3.09 (59.26%)	
Marital Status, n (%)			
Single	48 (53.3)	18.85 ± 2.79 (65.01%)	p = 0.150
Married	30 (33.3)	17.93 ± 3.33 (61.83%)	
Divorced	5 (5.6)	16.40 ± 2.07 (56.55%)	
Common-Law	7 (7.8)	17.14 ± 1.86 (59.11%)	
Level of training, n (%)			
Specialty resident	31 (34.4)	18.94 ± 2.67 (65.29%)	p = 0.318
Subspecialty resident	6 (6.7)	19 ± 2.44 (65.51%)	
Specialist	11 (12.2)	17.36 ± 2.87 (59.87%)	
Subspecialist	42 (46.7)	17.93 ± 3.18 (61.82%)	
Specialty area, n (%)			
Internal medicine	26 (28.9)	17.69 ± 2.81 (61%)	p = 0.053
Rheumatology	43 (47.8)	17.98 ± 3.13 (61.98%)	
Obstetrics and gynecology	21 (23.3)	19.62 ± 2.37 (67.65%)	

age range (91.1%), optimal timing for intercourse (94.4%), egg release per cycle (87.7%), and infertility risks related to smoking (95.6%), obesity (98.9%), and STIs (96.7%). However, fewer were aware of the sharp fertility decline at 35–39 years (52.2%) or monthly conception chances at age 30 or 40 (35.6%). Misunderstandings included miscarriage rates (28.9% correct) and effects of moderate alcohol (33.3%) and caffeine intake (77.8%). While knowledge of in vitro fertilization (IVF) (92.2%) and intrauterine insemination (IUI) (93.3%) was generally accurate, fewer participants knew IVF success rates by age, cost (21.1%), or live birth rates from frozen eggs (15.6%). The study revealed a trend toward higher knowledge in OBGYNs compared to rheumatologists (p = .064) and internists (p = .917), though differences were not statistically significant.

Conclusion: Physicians treating women with rheumatic diseases demonstrated notable gaps in fertility knowledge critical to patient counseling, especially among non-OBGYN specialties. These findings support the need for targeted reproductive health education in rheumatology and internal medicine training programs to enhance fertility-related care in this vulnerable population.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Fertility and Infertility Treatment Knowledge Score (FIT-KS) correct answers.

Question	Answer	Correct
1. At what age are women most fertile?	20-29	82 (91.1)
2. Over which age range does a woman's ability to get pregnant decline most precipitously?	35-39	47 (52.2)
3.- Over the course of 1 month, what is the percent chance that a 30-year-old woman who is trying to get pregnant will get pregnant?	20%	32 (35.6)
4.- Over the course of 1 month, what is the percent chance that a 40-year-old woman who is trying to get pregnant will get pregnant?	≤5%	32 (35.6)
5.- On average, for a woman in her peak reproductive years, what is the percent chance that a pregnancy (recognized or unrecognized) will end in a miscarriage?	16-25%	26 (28.9)
6. A woman and a man can both contribute to a couple's infertility	True	88 (97.8)
7. A man's age is a factor that affects a couple's fertility.	True	62 (68.9)
8.- Having less than 9 periods in a year can be normal for some women and doesn't require any further evaluation:	False	62 (68.9)
9.- What is the average survival time of normal sperm in the female reproductive tract?	3-5 days	39 (43.3)
10.- When is the optimal time to have sexual intercourse in order to get pregnant?	About halfway through the cycle	85 (94.4)
11. Where does fertilization most commonly occur?	In the Fallopian tubes	78 (86.7)
12.- How many eggs are typically released per cycle?	1	79 (87.7)
The following are likely to decrease a woman's chance of fertility:		
13. Smoking	True	86 (95.6)
14.- Occasional caffeine intake	False	70 (77.8)
15.- Moderate alcohol consumption	False	30 (33.3)
16.- Safe pregnancy termination	False	49 (54.4)
17. Obesity	True	89 (98.9)
18. Gonorrhea/Chlamydia infection	True	87 (96.7)
19. Prior use of contraceptive pills	False	42 (46.7)
20.- Being underweight due to frequent exercise or limited caloric intake	True	78 (86.7)
21. Using certain types of sexual lubricants	True	39 (43.3)

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The remainder of questions relate to infertility treatment:		
22.- In vitro fertilization (IVF) refers to a treatment in which:	A man's sperm and a woman's egg are combined inside a laboratory and the resulting embryo is transferred into the uterus	83 (92.2)
The following 3 questions refer to the most recent national statistics published by the Centers for Disease Control & Prevention and the Society for Assisted Reproductive Technology:		
23.- For a woman under 35 years old, undergoing IVF with her own eggs, what is the pregnancy rate per cycle?	41-60%	23 (25.6)
24.- For a woman over 44 years old, undergoing IVF with her own eggs, what is the pregnancy rate per cycle?	≤5%	35 (38.9)
25.- In women who are undergoing IVF, what is the percent of pregnancies that result in twins?	21-35%	39 (43.3)
26. What is the average cost of an IVF cycle in the USA?	$12,000	19 (21.1)
27.- Intrauterine insemination (IUI) refers to a treatment in which:	A thin catheter is used to deposit a man's sperm past the cervix directly into the uterus	84 (93.3)
28.- Egg cryopreservation (freezing) refers to an infertility treatment in which:	Eggs are frozen following ovarian stimulation and egg retrieval	66 (73.3)
29. When using frozen eggs from women less than 37 years old, what is the live birth rate per thawed egg?	≤10%	4 (15.6)

Disclosure: A. Ortiz-Rios: None; **M. Ponce-Santillan**: None; **B. Avalos-Garcia**: None; **E. Galindo-Calvillo**: None; **C. Treviño-Sanchez**: None; **S. Salinas-Rodriguez**: None; **A. Núñez-Elizondo**: None; **E. Noyola-Sauceda**: None; **G. Vazquez-Guerra**: None; **J. Cardenas-de la Garza**: None; **L. Perez-Barbosa**: None; **D. Galarza-Delgado**: None; **C. Skinner-Taylor**: None.

Abstract Number: 2172

Automating the Curation and Summarization of Rheumatology Fellowship Applications using Generative AI Agents and Transformer Models

Andrew Trotter[1], Angelo Gaffo[2], Amanda Alexander[3], John Osborne[1] and Jeffrey Curtis[4], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [3]University of Alabama at Birmingham, Homewood, AL, [4]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The rheumatology medical fellowship application review process requires significant time from program directors and faculty who manually analyze dozens of multi-part applications each year. A typical year may yield ∼200 applicants and require 50+ hours for fellowship program director(s) to pre-screen them and decide which should be offered interviews. Each application typically includes a 40-page PDF document and a structured Excel export from (ERAS) with > 2,500 columns of data per applicant. The possibility that artificial intelligence (AI) and large language models (LLMs) might concisely summarize fellow applications, protect applicant privacy, and highlight criteria to make subsequent interview decisions remains unexplored.

Methods: We developed an AI pipeline to help automate the fellowship screening process. It uses GPT-4o combined with GPU-accelerated optical character recognition (OCRs) to reduce manual review time. For each applicant, the two de-identified text files were concatenated and fed into an AI agent that uses GPT-4o to generate 1-2 page summaries aligned to specific feature domains (e.g., Clinical Potential, Awards, USMLE scores, Research Output) developed as part of the project and curated by subject matter experts (e.g. program directors and clinical faculty) in Table 1.

The output of the pipeline was a concise narrative summary that reduced each ∼40 page application to 1-2 pages. A GPT 4o-mini HIPAA-complaint Azure instance was then used to analyze a 169-document corpus of previously reviewed fellowship applications. Reduction in the amount of time for the narrative pre-review was the primary endpoint for evaluation. As a secondary metric, each applicant was scored on a scale of 1-100, where a score of at last 70 would receive an interview to align with institutional reviewing capacity. The scores were then compared to the manually annotated corpus, relating the scores to applicants who received interviews and those who did not receive interviews, versus what the model predicted.

Results: Across the 2017-2024 application cycles, and after implementation of the AI pipeline, the amount of manual effort to pre-screen fellow applicants for a single annual cycle (n = 180 fellow applicants) was decreased from approximately 50 hours to approximately 2 hours total The analysis finished in 2 minutes and 26 seconds using the Azure OpenAI API and is scalable to larger datasets. Overall accuracy compared to who was offered interviews was 0.69 with recall of 0.59 (Figure 1), with the confusion matrix shown in Figure 2.

Conclusion: Results indicate that this novel pipeline can assist with rheumatology fellowship screening and save dramatic amounts of human reviewer time. Ongoing refinement is underway to improve model performance compared to the both the interview outcome and subsequent program director and faculty reviews, and to make this tool more widely available.

Table 1: Themes Developed by Subject Matter Experts for AI-based Curation of Rheumatology Program Fellow Application Content

- Demographics & Geography
- International considerations
- Standardized Scores (e.g. USMLE, COMLEX)
- Achievements/Awards
- Professional Experience
- Research Interest
- Publications
- Training performance (from LLM)
  - Medical school performance
  - Residency performance
  - Letters of recommendation
- Overall summary (from LLM)

AI = artificial intelligence; LLM = large language model
USMLE = U.S. Medical Licensing Exam; COMLEX = Comprehensive Osteopathic Medical Licensing Examination of the United States

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

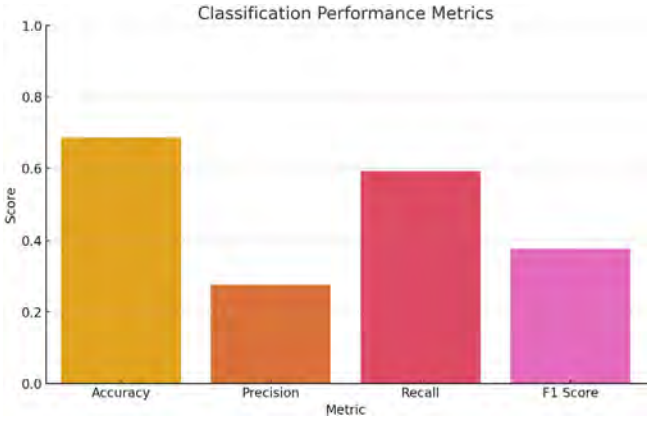
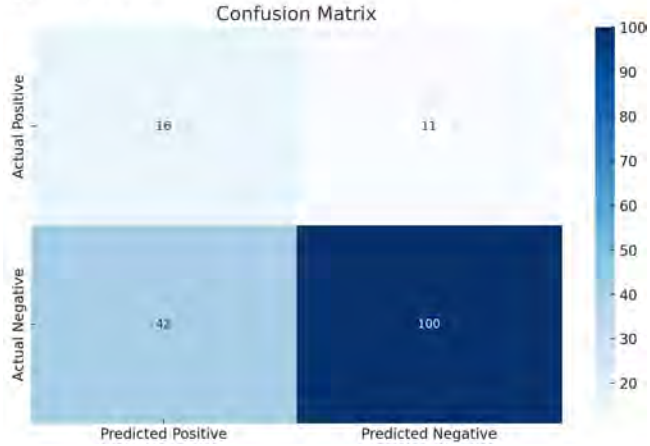


Figure 2: Confusion Matrix Describing Performance of AI Pipeline for rheumatology fellow applicants offered interviews, Actual vs. Predicted



Disclosure: A. Trotter: None; **A. Gaffo**: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **A. Alexander**: None; **J. Osborne**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 2173

Developing Musculoskeletal Ultrasound Clinical Electives: Bridging the Basic Sciences and Clinical Application in Undergraduate Medical Education

Brittany Lively[1], Cody Quirk[1], Katherine Brakora[1] and **Beth Scholz**[2], [1]Texas A&M University College of Medicine, Bryan, TX, [2]Baylor Scott and White Health, Temple, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Musculoskeletal ultrasound (MSKUS) conveys diagnostic and therapeutic value in rheumatology, sports medicine, and other specialties. However, formal MSKUS training is rarely integrated into undergraduate medical education (UME) curricula in the United States, with scant literature in this setting. Our institution incorporates MSKUS into its pre-clinical curriculum to facilitate integration of gross anatomy and MSK physical exam skills. To address the gap between our pre-clinical MSKUS learning experience and the clinical curriculum, we developed two structured electives offering exposure to clinical applications of MSKUS.

These electives vertically and horizontally integrate clinical skills and reasoning with the basic sciences, including gross anatomy and MSK radiology. This improves UME learners' understanding of anatomy, develops their US diagnostic and procedural skills, and provides more in-depth exposure to rheumatology and other specialties.

Methods: The shoulder, wrist, knee, and ankle were selected as body sites based on course developer consensus as the highest yield across a variety of specialties. Content was divided into two 2-week electives with upper extremity covered in the fall semester and lower extremity in the spring semester. Each week focuses on one joint. Content is delivered by self-study materials, hands-on practice scanning, guided MSK radiology imaging interpretation, and observation of clinical applications. UME learners study pre-recorded didactic materials covering standard US views of the joint, common pathologic findings, and a demonstration scan. One rheumatologist and one MSK radiologist serve as content experts demonstrating and supervising hands-on practice scanning on peers and volunteers. UME learners then practice MSK image interpretation (radiograph, MSKUS, CT, MRI) with the MSK radiologist and rotate through sports medicine clinics to practice integrating physical exam, MKSUS findings and clinical decision-making. Lastly, cadaver-based arthrocentesis training teaches additional procedural skills. Competency is assessed via a checklist evaluating image acquisition and identification of key anatomical structures.

Results: 100% of UME learners who enrolled in our MSKUS elective successfully completed the MSKUS skills checklist for each body site.

Conclusion: Based on our results of all UME learners demonstrating proficiency in fundamental MSKUS image acquisition skills, our elective presents a replicable framework for further integration of MSKUS education within medical curricula and reinforces both vertical and horizontal integration, allowing a bridge between the basic sciences and clinical practice. In addition to enhancing learners' anatomical and US knowledge, this elective also gives UME learners earlier exposure to procedural aspects in the field of rheumatology in hopes of increasing interest in rheumatology careers, while equipping them with invaluable clinical and diagnostic skills.

Disclosure: B. Lively: None; **C. Quirk**: None; **K. Brakora**: None; **B. Scholz**: None.

Abstract Number: 2174

Using Natural Language Processing to Identify Character Strengths in Rheumatology Fellowship Candidate Applications: A Feasibility Study

Amir Abidov, Manish Suneja and **Bharat Kumar**, UNVERSITY OF IOWA HOSPITALS AND CLINICS, Iowa City, IA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Holistic review is an approach to candidate selection that emphasizes alignment of candidate attributes to a program's mission. Identifying character strengths in personal statements and letters of recommendation within fellowship applications is a vital but time-consuming and subjective task. The increasing volume and competitiveness of rheumatology fellowship applications raises the stakes even further. We describe a natural language processing (NLP) approach to identify VIA (Values in Action) Character Strengths in fellowship application personal statements and letters of recommendation, providing a data-driven method to support holistic applicant review based on the principles of positive psychology.

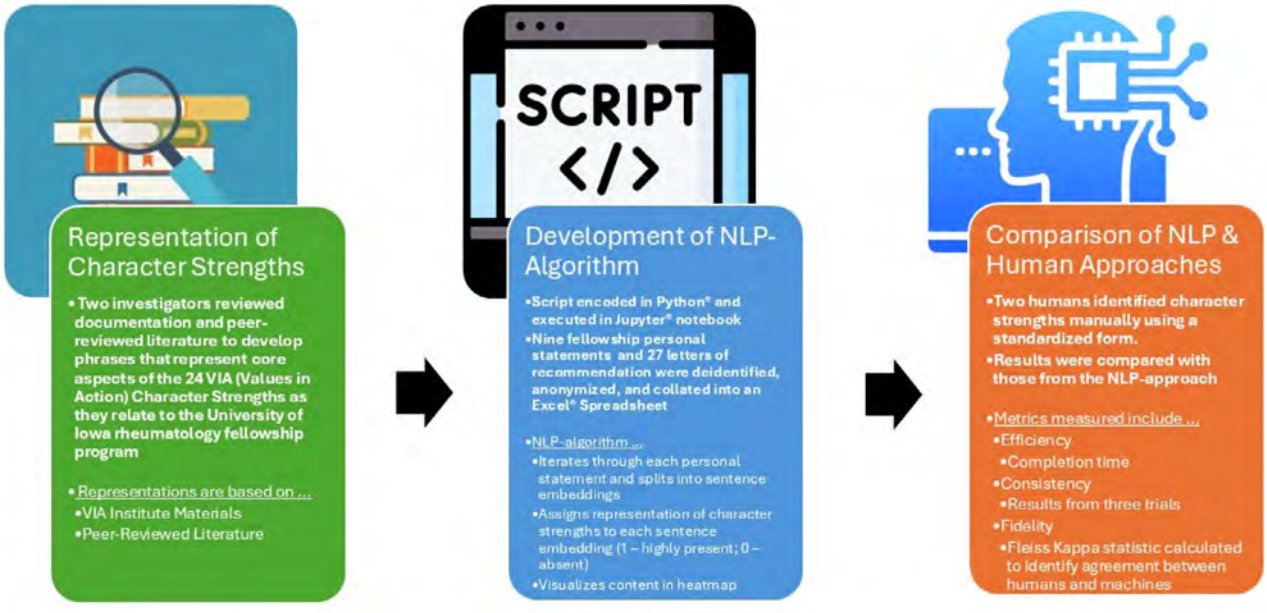
Methods: This feasibility study was conducted in three steps: (1) representation of character strengths, (2) computer assignment of character strengths, and (3) comparison to human-based approaches.

First, two physicians first represented the 24 VIA character strengths using documentation from the VIA Institute and peer-reviewed literature. For each character strength, five phrases were developed that aligned with the University of Iowa rheumatology fellowship program's mission statement.

Secondly, an algorithm using NLP was devised using the python computer language that employed sentence-BERT (SBERT) embeddings. The algorithm analyzes semantic similarity of sentences within the personal statements and letters of recommendation to each of 24 VIA Character Strengths. For each candidate, a score between 0 and 1 was assigned for the presence of each strength. This was then represented as a heat map for easy visualization of each candidate's character strengths.

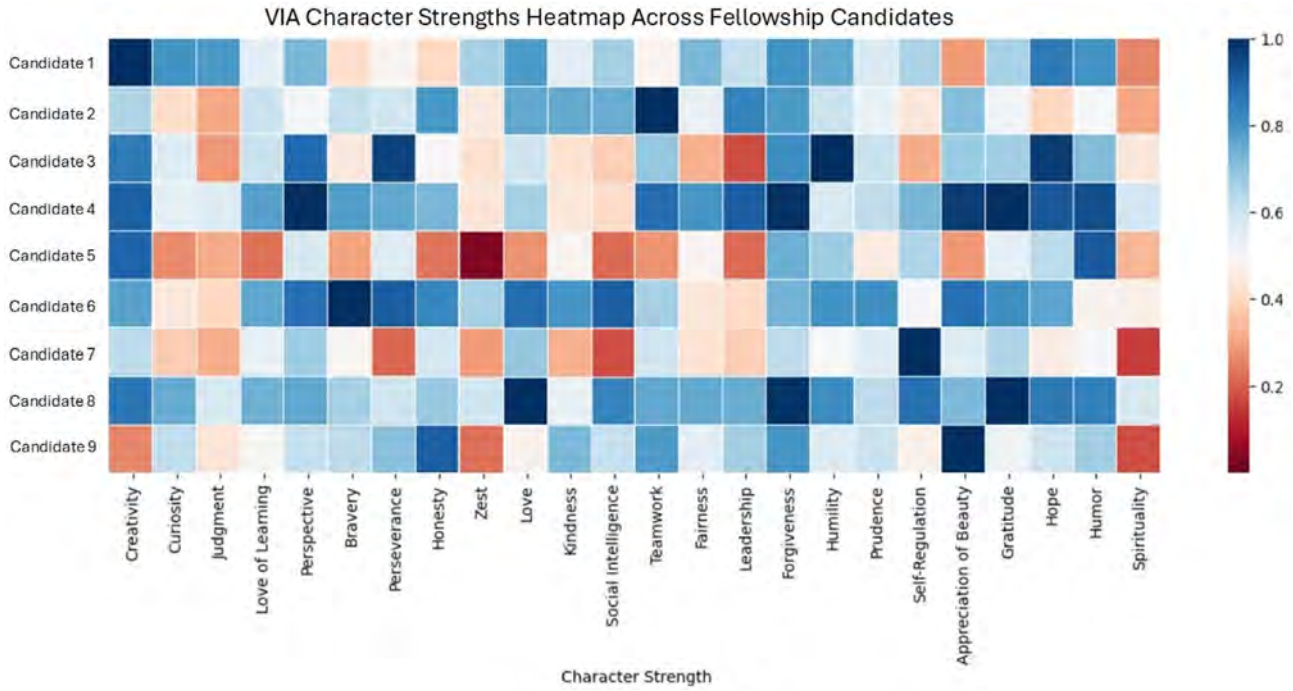
Lastly, this was repeated three times to ensure consistency of computer-generated results. Two physicians independently reviewed the personal statements and letters of recommendation for character strengths. Results of the human- and computer-based approaches were then compared for consistency and for time to complete the task.

Results: The algorithm successfully identified character strengths across 9 personal statements and 27 letters of recommendation from a sample of 9 prior applications, demonstrating individual differences in the representation of character strengths within candidate applications.



This feasibility study consisted of three steps: (1) Representation and calibration of character strengths with the program mission statement, (2) Development of the NLP-algorithm, and (3) Comparison of NLP & human approaches

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



This heatmap illustrates the distribution of character strengths among the documents for each of the fellowship candidates. Such a heatmap can be used to rapidly appreciate representations of character strengths within candidate applications.

There was high concordance between character strengths assigned by human reviewers and those identified by the algorithm (kappa=0.89). The strengths with highest concordance between the algorithm and human reviewers were *teamwork* and *leadership*, while the lowest were *spirituality* and *forgiveness*.

Output and performance of the model was consistent and reduced the time to identify strengths from 240 minutes to 35 seconds.

Conclusion: This study presents a novel NLP-based algorithm for analyzing personal statements, offering a scalable and customizable approach for rheumatology program directors and other leaders to rapidly evaluate character strengths. By integrating machine learning into holistic review based on a positive psychology framework, this method provides structured insights into applicants' personal attributes, complementing holistic selection processes in a rapid and reproducible manner.

Disclosure: A. Abidov: None; **M. Suneja**: None; **B. Kumar**: None.

Abstract Number: 2175

Skin Manifestations of Rheumatic Diseases: Educating Providers to Improve Diagnostic Skills

Brittany Ashe[1], Ellen Koch[2], Tiffany Yang[1] and Kathryn Torok[2], [1]UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Among pediatric patients with scleroderma, there is a significant delay between onset of symptoms and diagnosis ranging from 1.2-1.6 years for Localized Scleroderma (LS) to 1.9-2.8 years for Systemic Sclerosis (SSc). Stubbs et al explored caregivers' perceptions of navigating their child's diagnosis with LS and SSc: their work identified that the number one barrier parents identified was lack of provider knowledge(1). Our aim is to create an intervention for front-line providers to improve the recognition of rashes associated with rheumatologic disease with the ultimate goal to improve referral patterns and decrease time to diagnosis.

Methods: Using Kern's Model of curriculum development, we created a needs assessment to evaluate competency among a range of pediatric providers by querying their skills, knowledge, and attitudes surrounding rash identification. We also obtained qualitative data which was coded and used to generate themes to inform the quantitative results.

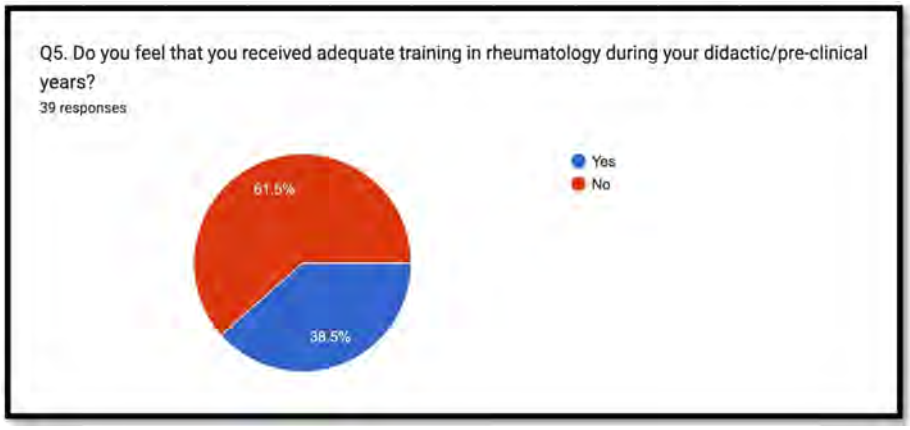
Results: We received 39 responses (53% resident, 28% attending, 18% APP). Approximately a third were currently practicing or planning to become primary care providers, another third planned to go into subspecialties other than rheumatology, and the remaining third were planning to continue or pursue hospitalist or ED positions. The majority of respondents (61.5%) did not feel they received adequate training in rheumatology during their pre-clinical years. On recall, most reported 5-10 hours of pre-clinical education spent on rheumatology.

Regarding skill identifying rashes, the majority of respondents (64%) rated themselves as only slightly knowledgeable, 25.6% as moderate and 10% having no knowledge/skill identifying rheumatic skin disease. Reassuringly, 100% of participants responded that identification of rashes was somewhat important or very important.

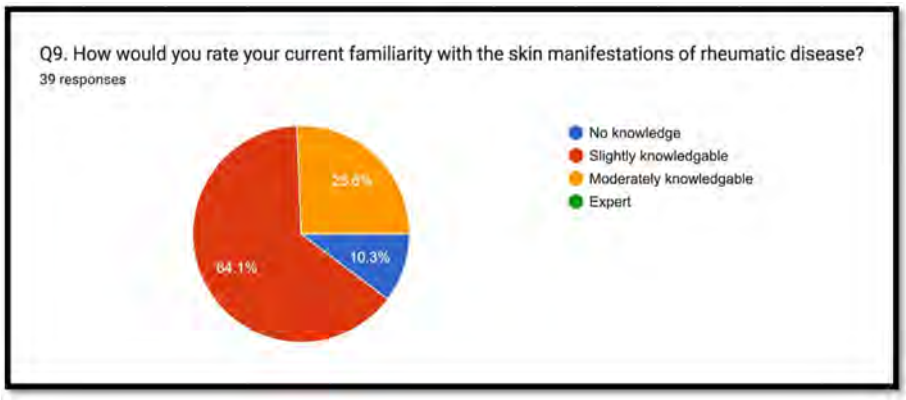
Additionally, we queried respondents for qualitative responses. Themes that emerged included that rheumatology was frequently taught as an "afterthought", with inadequate content, and without pediatric-specific examples. Many also identified that their skills identifying rashes were poor because they had little experience.

Conclusion: A needs assessment of front-line pediatricians revealed that there is a lack of knowledge and skill surrounding rheumatic diseases and the common rashes that can provide clues to their diagnosis. More education is needed to ensure that providers are familiar with these rare diagnoses to facilitate early and appropriate rheumatology referral to prevent accumulation of damage with delayed diagnosis. Our group is creating a 45min didactic intervention dedicated to recognizing skin manifestations of key pediatric rheumatic conditions to further address these needs. We will assess efficacy via pre- and post-testing as well as qualitative responses.

(1) Stubbs LA, Ferry AM, Guffey D, et al. Barriers to care in juvenile localized and systemic scleroderma: an exploratory survey study of caregivers' perspectives. Pediatr Rheumatol Online J 2023;21(1):39. DOI: 10.1186/s12969-023-00819-6.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: B. Ashe: None; **E. Koch**: None; **T. Yang**: None; **K. Torok**: None.

Abstract Number: 2176

Addressing Hesitancy in JAK Inhibitor Use: Outcomes from Continuing Medical Education Reveal Confidence-knowledge Gaps Among Community Rheumatologists

Carole Drexel[1], Eve Wilson[2], Vibeke Strand[3] and Jon Giles[4], [1]Medlive, Pasadena, MD, [2]Medlive, Needham, MA, [3]Stanford University School of Medicine, Palo Alto CA, Portola Valley, CA, [4]Cedars Sinai Medical Center, Los Angeles, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite supportive real-world evidence, the use of Janus kinase inhibitors (JAKi) for rheumatoid arthritis (RA) remains limited in community settings. Concerns stemming from the ORAL Surveillance Trial and related regulatory restrictions have contributed to clinician hesitation. To better understand persistent barriers to the use of JAK inhibitors in clinical practice, we analyzed outcomes data from a continuing medical education (CME) program focused on JAKi use in RA.

Methods: A 60-minute expert panel discussion was launched online in December 2024 and remains available on-demand for one year. The activity is targeted to rheumatologists and primary care providers (PCPs) with experience managing RA. Targeted outreach included short video segments delivered via social media to NPI-verified rheumatologists. Change in knowledge, confidence (via Likert scale), and remaining educational needs post activity were assessed. Paired responses were analyzed using chi-square tests (pre vs post; $P < 0.05$).

Results: As of May 2025, 926 HCPs had participated (41% rheumatologists; 28% PCPs), with most reporting care of ≥10 RA patients per month. The activity significantly improved awareness of the JAK1 selectivity of upadacitinib (28% pre vs 50% post). However, knowledge of the relationship between venous thromboembolism and associated risk factors with tofacitinib and efficacy of baricitinib in clinical trials remained unchanged (pre 46% vs post 47% and pre 43% vs post 47%). Key educational needs identified post-activity included: selecting appropriate JAKi candidates (37%), managing side effects and risks (37%), and differentiating among JAK inhibitors by safety and efficacy (33%). Confidence in prescribing JAKi increased from 2.0 to 3.7 (5-point scale).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Knowledge surrounding the efficacy and safety risks JAKi remained largely unchanged following the activity, and participants continued to identify unmet educational needs in selecting appropriate candidates, managing risks, and differentiating among JAKi. These persistent gaps suggest that key aspects of JAKi use remain poorly understood. Notably, this limited knowledge stood in contrast to a substantial increase in self-reported prescribing confidence, indicating a potential overestimation of preparedness that underscores the need for deeper, more targeted educational interventions.

[Support from an independent medical education grant from AbbVie was provided for the CME activity, not for the work associated with the abstract.]

Disclosure: C. Drexel: None; **E. Wilson**: None; **V. Strand**: AbbVie/Abbott, 2, Alumis, 2, Amgen, 2, Arthrosi, 2, Artiva, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer-Ingelheim, 2, catalys, 2, contura, 2, Cullinan, 2, Fate Therapeutics, 2, Fortress Biotech, 2, genasence, 2, GlaxoSmithKlein(GSK), 2, Inmedix, 2, Lipum, 2, Longitude Capiral, 2, MED institute, 2, Novartis, 2, RAPT, 2, Royalty Pharma, 2, Sanofi, 2, scipher medcine corp, 2, SetPoint Medical, 2, Sobi, 2, Spherix, 2, Synact, 2, Takeda, 2, Topography, 2, Zoe, 2; **J. Giles**: AbbVie/Abbott, 2, Eli Lilly, 2, Genentech, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Sana, 2.

Abstract Number: 2177

A Rheumatologic Ultrasound (RhUS) Educational Framework: Expert Consensus on Rhus Skills for Adult Rheumatology Fellows in the United States

Christine Parsons[1], irene Ma[2], Amy Cannella[3], Eugene Kissin[4], Paul DeMarco[5], Midori Nishio[6], Edward Oberle[7], Catherine Bakewell[8], Ralf Thiele[9], Anthony M. Reginato[10], Norman Madsen[11], Jonathan Samuels[12], Patricia Vega-Fernandez[13], Clara Lin[14], Marcy Bolster[15] and Minna Kohler[16], [1]Massachusetts General Hospital, Boston, MA, [2]University of Calgary, Calgary, Canada, [3]University of Nebraska Medical Center, Omaha, NE, [4]Boston University, Newton, MA, [5]Mobile Medical Care, Olney, MD, [6]John Muir Specialty Medical Group, Lafayette, CA, [7]Nationwide Children's Hospital, Columbus, OH, [8]Intermountain Healthcare, Salt Lake City, UT, [9]University of Rochester, PITTSFORD, NY, [10]Brown University, Providence, RI, [11]URMC, Rochester, NY, [12]NYU Langone, Rye Brook, NY, [13]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [14]Children's Hospital Colorado, Aurora, CO, [15]Massachusetts General Hospital, Concord, MA, [16]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2159–2194) Professional Education Poster

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Over the past decade, point-of care ultrasound (POCUS) has expanded rapidly within fellowship training programs. There is strong interest in rheumatology ultrasound (RhUS) education among U.S. rheumatology fellowship training programs, however there is inconsistency in curricular offerings and not all programs are able to offer a formal RhUS curriculum. The 2019 American College of Rheumatology (ACR) RhUS Mini-Curriculum offers an optional, comprehensive model curriculum for educators[1]. However, learners vary in their interest and available time for RhUS practice. Educators face the challenge of tailoring their teaching to a broad array of learners, from those seeking only basic knowledge to those pursuing advanced mastery. This project aimed to gain expert consensus on an updated set of RhUS skills and stratify them by level to provide a structured educational framework for trainees with a range of learning goals.

Methods: An application to update the 2019 RhUS Mini-Curriculum was approved by the ACR Curriculum Subcommittee. The project was approved by the Massachusetts General Hospital Institutional Review Board. RhUS experts were invited to participate in three virtual focus group meetings. Experts had extensive RhUS teaching experience and were RhMSUS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Summary of RhUS skills designated as All Fellows – Fundamental. Strong agreement was defined as agreement of 70% or greater. Moderate agreement was defined as agreement of 51-69%. Dark Blue: Strong Agreement. Light Blue: Moderate agreement.

All Fellows - Fundamental	Agreement (%)
Reasonable Use of RhUS	
Recognize indications for and limitations of musculoskeletal ultrasound	100
Recognize the association between musculoskeletal ultrasound findings and rheumatic disease states	100
Recognize the role of vascular ultrasound in diagnosis of Giant Cell Arteritis	80
Image Interpretaton	
Recognize the following anatomic structures on an ultrasound image: joint, tendon, ligament, bursa, bone, vessel, nerve, fat	90
Recognize effusion	80
Recognize Baker's Cyst	80
Recognize double contour sign	80
Recognize bursitis	70
Recognize grade 3 synovial thickening	70
Recognize positive Doppler signal	60
Recognize erosion	60
Procedural Skills	
Identify appropriate target	80
Mark area for arthrocentesis when indirect visualization is used	70

certified. All were Ultrasound School of North American Rheumatologists (USSONAR) faculty with more than 5 years of RhUS teaching experience, the majority (80%) of whom had more than 10 years of experience. The experts reviewed RhUS skills adapted from the 2019 ACR RhUS Mini-Curriculum as well as additional skills recommended by the expert panel. The modified Nominal Group Technique (NGT) was used to reach consensus on which RhUS skills to include and how to classify them by level. Participants were identified through non-probability sampling. Strong agreement was defined a priori as agreement of 70% or greater. Moderate agreement was defined a priori as agreement of 51-69%.

Results: The NGT comprised 10 experts who voted on a total of 83 RhUS skills. Thirteen RhUS skills were designated as "All Fellows–Fundamental" (11 with strong agreement, 2 with moderate agreement) (Table 1). Thirty-four skills were designated as "Ultrasonographer Fellow-Advanced" (21 with strong agreement, 13 with moderate agreement) (Table 2). Seventeen skills were designated as "Ultrasonographer-Aspirational" (13 with strong agreement, 4 with moderate agreement) (Table 3). Moderate agreement supported removal of one skill. Consensus on level was not reached for 19 skills. Additionally, there was strong consensus (90% agreement) around adding ultrasound images alongside joint scanning protocols to enhance the 2019 ACR RhUS Mini-Curriculum.

Conclusion: This study establishes expert consensus on a tiered set of RhUS skills, enhancing the 2019 ACR RhUS Mini-Curriculum by adding a practical framework to tailor rheumatology ultrasound education to varying learner needs and performance goals, enabling more scalable training in rheumatology ultrasound.

References:

1. Cannella, Amy C, et al. 2019 Rheumatologic Ultrasound (RhUS) Curriculum Supplement to the American College of Rheumatology 2015 Core Curriculum Outline, American College of Rheumatology, 2019.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Summary of RhUS skills designated as Ultrasonographer Fellow – Advanced. Strong agreement was defined as agreement of 70% or greater. Moderate agreement was defined as agreement of 51-69%. Tier 1 and Tier 2 views reference previously published consensus of North American rheumatologists (Bethina NK, et al 2022; Yinh J et al, 2021). Dark Blue: Strong Agreement. Light Blue: Moderate Agreement.

Ultrasonographer Fellow - Advanced	Agreement (%)
Image Interpretaton	
Understand basic ultrasound physics	60
Recognize grade 1 synovial thickening	60
Recognize grade 2 synovial thickening	90
Grade Doppler signal	60
Recognize tenosynovitis	60
Recognize tendinopathy	70
Recognize tendon tear	60
Recognize paratenonitis	80
Recognize joint subluxation	70
Recognize loose body	80
Recognize prosthetic joint	70
Recognize foreign body	90
Recognize calcium pyrophosphate deposits based on shape, echogenicity, localization, and dynamic assessment	70
Recognize hyperechoic aggregates (HAGs) and micro crystalline deposition	90
Recognize the ultrasound appearance of tophi	60
Recognize linear calcification in tendon	90
Recognize erosive osteoarthritis	70
Recognize rheumatoid nodule	70
Recognize meniscal degeneration	70
Recognize dynamic view of trigger finger	70
Recognize PIP/DIP enthesitis	60
Recognize anechoic/hypoechoic foci in salivary gland	80
Image Acquisition	
Maneuver probe to optimize image (i.e. translation, rotation, angulation, pressure, compression, heel-toe, rocking)	70
Understand how machine settings can be adjusted to optimize an image (i.e depth, frequency, focal zones, gain, pulse repetition frequency)	70
Adjust machine setting to optimize Doppler sensitivity and specificity	80
Demonstrate pathology in orthogonal planes	60
Perform a directed set of ultrasound views specific to a consult question	80
Obtain Tier 1 Views	60
Obtain Tier 2 Views	90
Obtain medial subtalar view	60
Obtain lateral subtalar view	60
Obtain midfoot transverse view	60
Procedural Skills	
Ultrasound-guided aspiration and injection of medium joints	60
Ultrasound-guided aspiration and injection of small joints	70

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Summary of RhUS skills designated as Ultrasonographer Fellow – Aspirational. Strong agreement was defined as agreement of 70% or greater. Moderate agreement was defined as agreement of 51-69%. Tier 3 views reference previously published consensus of North American rheumatologists (Bethina NK, et al 2022; Yinh J et al, 2021). Dark Blue: Strong Agreement. Light Blue: Moderate Agreement.

Ultrasonographer Fellow - Aspirational	Agreement (%)
Image Interpretaton	
Recognize fracture	60
Grade tendon tear	90
Recognize periostitis	70
Recognize nerve subluxation	80
Recognize tendon subluxation	80
Recognize Morton's neuroma	60
Recognize labral tear	80
Recognize snapping iliopsoas	90
Recognize muscle damage	60
Image Acquisition	
Use ultrasound to assess a patient with systemic sclerosis (i.e. measure thickness, echogenicity, and elastography of skin)	100
Incorporate lung ultrasound into RhUS assessment when indicated	90
Obtain Tier 3 Views	90
Obtain anterolateral longitudinal view of ATFL ligament	60
Obtain anterior transverse view of the hip proximal to iliopsoas tendon	70
Obtain posterior fibular-calcaneal view	70
Procedural Skills	
Perform needle tenotomy	80
Perform synovial biopsy	100

Disclosure: C. Parsons: None; **i. Ma**: Elsevier, 6; **A. Cannella**: None; **E. Kissin**: None; **P. DeMarco**: None; **M. Nishio**: None; **E. Oberle**: Pfizer, 1; **C. Bakewell**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 2, 6, UCB, 2, 6; **R. Thiele**: Clario, 2, GCUS, 9, Janssen, 5, Perceptive, 2; **A. Reginato**: None; **N. Madsen**: None; **J. Samuels**: None; **P. Vega-Fernandez**: None; **C. Lin**: None; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9.

Abstract Number: 2178

Online Education Significantly Improved Rheumatologists' Knowledge of the Diagnosis and Management of Sjögren's Disease

Elaine Bell[1], michele Bombardieri[2] and Alessia Piazza[3], [1]MEDSCAPE GLOBAL, LONDON, United Kingdom, [2]Experimental Medicine and Rheumatology, William Harvey Research Institute, Queen Mary University of London, UK, London, United Kingdom, [3]Medscape, london, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease is a chronic autoimmune disease affecting multiple organ systems beyond the eyes and mouth. Diagnosis is challenging and therapy is often initiated late. The need for a patient-centered individualized management approach is often underappreciated.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Our goal was to assess whether online accredited education could improve rheumatologists' understanding of the heterogeneous clinical presentation of Sjögren's disease, the diagnostic approach and the role of B cells in the pathogenesis of Sjögren's disease, and enhance their confidence in implementing a tailored, patient-centric management approach.

Methods: This online educational activity titled 'Challenges and Opportunities in the Management of Sjögren's Disease' was a 30-minute roundtable discussion with 3 panelists and a patient, accompanied by slides and video. Responses to 3 multiple-choice knowledge questions and 1 self-efficacy, 5-point Likert scale confidence question were analyzed. Educational effect was assessed using a repeated-pair design, pre-/post-assessment. A paired samples t-test was conducted for significance testing on overall average number of correct responses and for confidence rating. A series of McNemar's tests were conducted at the question level (5% significance level, $P < .05$). Cohen's d with correction for paired samples estimated the effect size of the education on number of correct responses (< .20 modest, .20-.49 small, .59-.79 moderate, ≥.80 large). The activity was launched on 13 August 2024 with data collection through 3 October 2024.

Results: Of 1205 rheumatologists who viewed the education within this time period, 80 completed all pre- and post-assessment questions. The average percentage of correct responses across all questions increased from 76% at baseline to 88% post-activity ($P < .001$), and there was a moderate educational impact (Cohen's d=0.59). The proportion of rheumatologists answering all 3 questions correctly rose from 49% at baseline to 71% post-activity.

Rheumatologists significantly improved their knowledge of the diagnostic approach for Sjögren's disease (68% correct responses at baseline rising to 85% post-activity; $P < .001$) and the presence of germinal centers in the salivary glands as an indicator of the role of B cells in the pathogenesis of Sjögren's disease (66% pre- vs 81% post-activity; $P < .001$). Knowledge of the heterogeneous clinical presentation of Sjögren's disease was high at baseline and did not change post education (95% pre- vs 96% post-activity; $P = .317$).

After completing the activity, 33% of rheumatologists reported improved confidence in implementing a tailored, patient-centric management approach in Sjögren's disease.

Conclusion: This online activity significantly improved rheumatologists' knowledge of the diagnostic approach for Sjögren's disease and the role of B cells in the pathogenesis of disease. Given the evolving treatment landscape, rheumatologists would benefit from additional education to build their confidence in managing this challenging condition & improve their knowledge of emerging B-cell targeted therapies.

Disclosure: E. Bell: None; **m. Bombardieri**: Amgen, 5, 12, Personal fees, GlaxoSmithKlein(GSK), 5, 12, Personal fees, Janssen, 5, 12, Personal fees, Ono Pharmaceuticals Co. Ltd, 1, 2, UCB, 12, Personal fees; **A. Piazza**: None.

Abstract Number: 2179

Educational online webinars of European Reference Network (ERN) on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ReCONNET) for patients, caregivers and healthcare professionals: six years' experience

Emanuele Gotelli[1], Rosanna Campitiello[1], Eric HACHULLA[2], Vanessa Smith[3], João Eurico Fonseca[4], Tadej Avcin[5], Gabriele Simonini[6], Silvia Aguilera[7], Lisa Matthews[8], Charissa Frank[9], Wiebke Lautré[10], Monica Testoni[11], Diana Marinello[11], Rosaria Talarico[12], Marta Mosca[13] and Maurizio Cutolo[14], [1]University of Genoa, Genoa, Liguria, Italy, [2]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-Immunes et Auto-Inflammatoires Rares du Nord, Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille, France, Lille, France,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[3]Ghent University Hospital, Gent, Belgium, [4]Faculdade Medicina, Universidade de Lisboa, ULS Santa Maria, Centro Académico Medicina de Lisboa, Lisboa, Lisboa, Portugal, [5]University Children's Hospital, University Medical Center Ljubljana, Ljubljana, Slovenia, [6]Rheumatology Unit, ERN-ReCONNET center, Meyer Children's Hospital IRCCS, Firenze, Firenze, Italy, [7]Spanish Antiphospholipid Association, Alicante, Spain, [8]Relapsing Polychondritis Awareness and Support, London, United Kingdom, [9]Flemish Association for Hereditary Connective Tissue Disorders, Koersel, Belgium, [10]CHU Bordeaux Pellegrin, Centre de Références Maladies Auto-Immunes Systémiques Rares, Bordeaux, France, [11]ERN ReCONNET, Pisa, Italy, [12]Azienda Ospedaliero Universitaria Pisana, Pisa, Pisa, Italy, [13]University of Pisa, Pisa, Pisa, Italy, [14]University of Genova, Genova, Italy

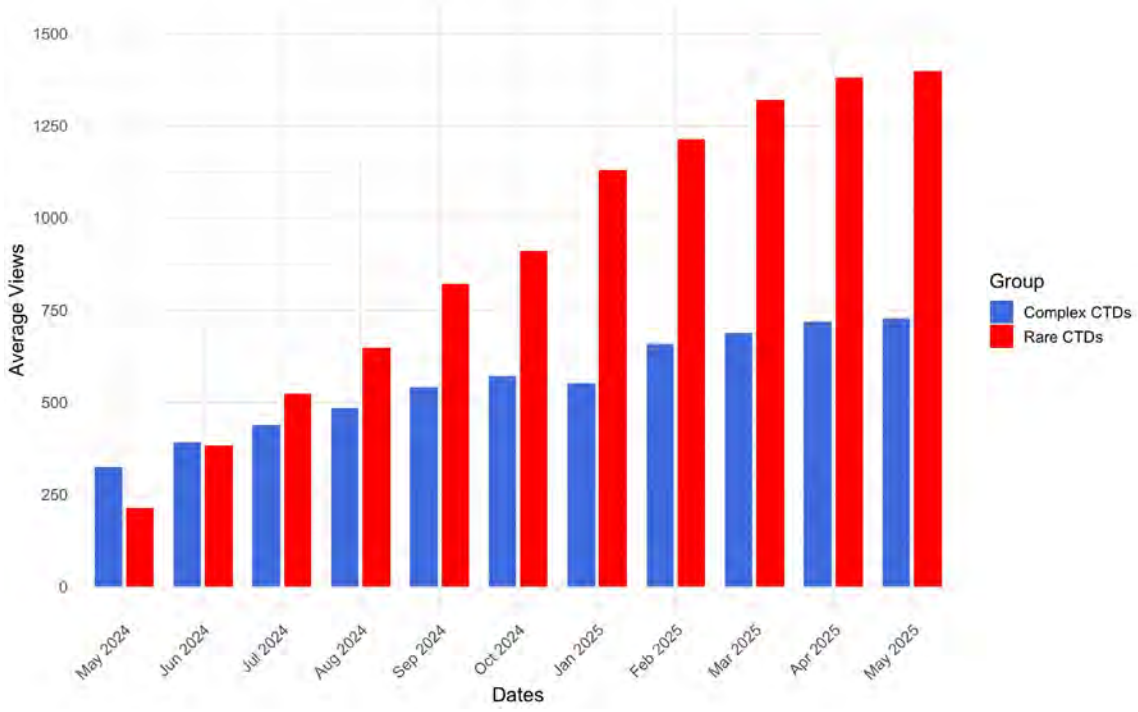
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The European Reference Network on Connective Tissue and Musculoskeletal Diseases (ERN ReCONNET), founded in 2017 by the European Union (EU) Commission, aimed to improve the management of rare connective tissue diseases (CTDs) across the EU. ReCONNET includes rare (Ehlers-Danlos Syndromes, IgG4-Related Diseases, Mixed Connective Tissue Disease, Relapsing Polychondritis) and complex with low prevalence (Antiphospholipid Syndrome, Idiopathic Inflammatory Myopathies, Sjögren's Syndrome, Systemic Lupus Erythematosus, Systemic Sclerosis, and Undifferentiated Connective Tissue Disease) CTDs. Since 2019, ReCONNET Educational Committee organized free online webinars accessible live on Zoom platform and recorded on ReCONNET YouTube (YT) page.

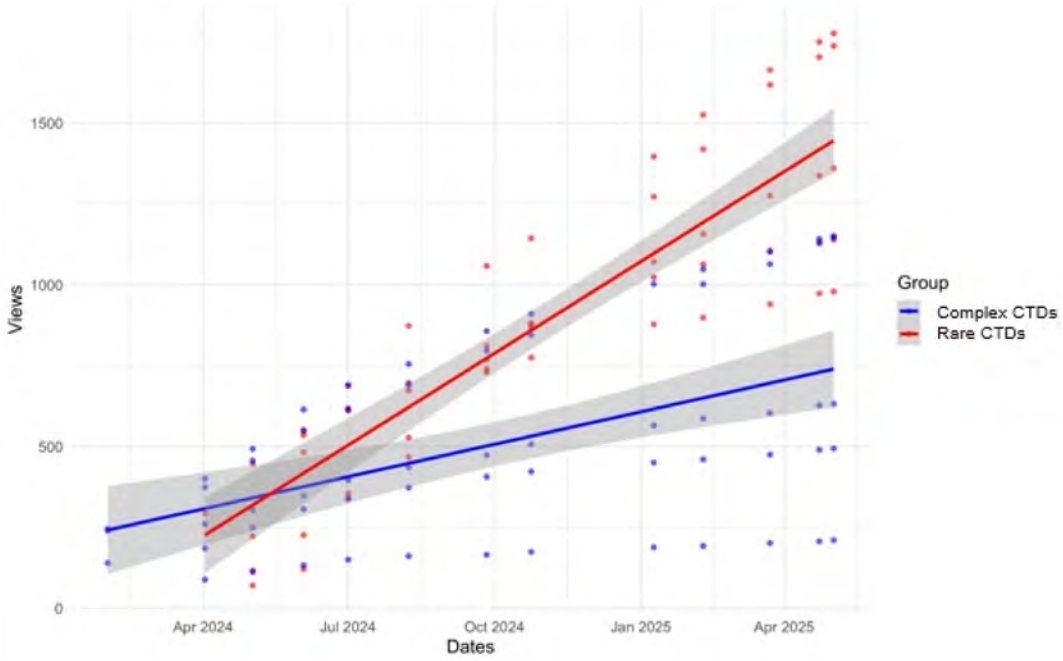
So, the aim of the current study was to assess the interest and size of webinar viewers (wv) and views from ReCONNET patients/caregivers, HCPs, or both, for the different CTDs.

Methods: Live view data (available from October 2023) were obtained from Zoom, while YT views (available from 2019) were collected as of 2nd May 2025.



One-year average views (2024-2025) on YouTube recordings in rare (red bar) and complex low-prevalence (blue bar) connective tissue diseases from ERN ReCONNET achieving the ERN target for an increased education on rare connective tissue diseases (CTDs).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Linear regression analysis shows the increase overtime of YouTube views in rare and complex low-prevalence connective tissue diseases (CTDs) (one-year views). The initial number of views did not differ significantly between disease groups (β=84.54, p=0.487), while the rare CTDs group exhibited a significantly steeper increase of views over time compared to the complex CTDs group (β=1.85, p<0.001). β in regression shows how much the dependent variable (YouTube views) changes when the independent variable (time) increases by one unit. Figure created with R software.

Results: From 2019 up to 2nd May 2025, ERN ReCONNET organized 73 webinars, totaling 147,030 YT views. Webinars on rare CTDs (n=20) collected 70,307 YT views (average 3,515±4,271 per webinar), and webinars on complex CTDs (n=53) totalized 76,723 YT views (average of 1,447±1,838 per webinar), the former with a significantly higher number of YT views per webinar (p< 0.01).

By considering Zoom data available from October 2023, live webinars targeted at patients/caregivers got a total number of 158 wv (6 webinars, average 26±18 per webinar); those for HCPs got a total of 265 wv (11 webinars, average 24±9 per webinar) and finally those for both classes got a total of 132 wv (6 webinars, average 22±15 per webinar) without statistically significant differences interclasses.

The YT recording of the above webinars for patients/caregivers averaged 541±507 views (total of 3,244), those for HCPs averaged 902±816 views (total of 9,925), and those for both classes averaged 581±598 views (total of 3,486), again without statistically significant differences interclasses.

Finally, when the number of live wv and YT views was counted for the webinar on rare and complex CTDs, then rare CTDs got a total of 172 wv (5 webinars, average 34±17 per webinar) together with 6,993 YT views (average 1,399±345 per webinar). The webinars on complex CTDs collected 383 live wv (18 webinars, average 21±10 per webinar) and 9,662 YT views (average 537±642 per webinar) (Figure 1). The difference between rare and complex CTDs was statistically significant for YT views (p< 0.01), but not for wv.

Linear regression analysis of YT views showed that the rare CTDs group exhibited a significantly steeper increase of views over time compared to the complex CTDs group (β=1.85, p< 0.001) (Figure 2).

Conclusion: ERN ReCONNET's online webinars achieved a considerable number of views on YT, with significantly higher interest shown for webinars on rare CTDs compared to complex low-prevalence CTDs. Main users of this earlier six years'

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

educational experience on webinars from ReCONNET were found to be HCPs, and further efforts are ongoing to attract more patients and caregivers.

Disclosure: E. Gotelli: None; **R. Campitiello**: None; **E. HACHULLA**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **J. Fonseca**: None; **T. Avcin**: Novartis, 6, Octapharma, 1, 6, Pfizer, 6, Takeda, 6; **G. Simonini**: None; **S. Aguilera**: None; **L. Matthews**: None; **C. Frank**: None; **W. Lautré**: None; **M. Testoni**: None; **D. Marinello**: None; **R. Talarico**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **M. Cutolo**: None.

Abstract Number: 2180

Helping Hands: Curriculum using Simulators to Teach the Hand Exam and Assessment of Small Joint Swelling in Inflammatory Arthritis

Ibtissam Gad[1], Christopher Podgorski[2], Kylie Springer[3], amita Bishnoi[4] and Lisa Zickuhr[5], [1]University of Michigan, Ann Arbor, MI, [2]Park Nicollet, Lake Elmo, MN, [3]Henry Ford Health, Detroit, [4]Henry Ford Health System, Troy, MI, [5]Washington University/B-JH/SLCH Consortium, St. Louis, MO

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The hand examination is crucial for internal medicine (IM) residents to learn, as it is important for the diagnosis and treatment of patients with inflammatory arthritides. However, there is mounting evidence that trainee confidence in the musculoskeletal examination is low. Moreover, there are limited curricula available to teach the hand physical examination, none of which leverage simulation as an educational strategy. We describe a feasible and effective simulation-based curriculum, utilizing a hand model, to teach IM residents the hand examination and assessment of small joint swelling, as seen in inflammatory arthritis.

	Pre (N=36)	Post (N=36)	P-value
Assessing Small Joint Swelling, n (%)			**<0.01**
Very Unconfident	5 (13.9%)	0 (0.0%)	
Unconfident	23 (63.9%)	2 (5.6%)	
Confident	7 (19.4%)	20 (55.6%)	
Very Confident	1 (2.8%)	14 (38.9%)	
Performing a Hand Examination, n (%)			**<0.01**
Very Unconfident	5 (13.9%)	0 (0.0%)	
Unconfident	23 (63.9%)	1 (2.8%)	
Confident	6 (16.7%)	21 (58.3%)	
Very Confident	2 (5.6%)	14 (38.9%)	

The distribution of responses for self-perceived confidence on a 4-point Likert scale before and after our educational initiative. Trainees rated confidence in two specific skills: performing a hand examination and assessing small joint swelling as seen in inflammatory arthritis. Improved confidence was reported after completion of the curriculum, which included a video, live demonstration, hand-on practice, and a 3-station assessment ($p<0.01$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We designed a physical examination curriculum for IM residents rotating through their rheumatology elective. Residents watched a short video, viewed a real-life demonstration, and then participated in hands-on practice with the hand model. Residents then participated in a three-station objective structured clinical exam (OSCE) with clinical vignettes and hand models to assess knowledge. IM residents examined the hand models at each OSCE station and identified sites of perceived palpable small joint swelling on an accompanying worksheet. Afterwards, residents completed a pre-post survey evaluating perceived confidence in performing a hand examination and assessing small joint swelling.

Results: During the duration of the study, 36 IM residents participated in the workshop and completed the survey. There was a statistically significant improvement in resident self-reported confidence in performing a hand examination and assessing small joint swelling ($p< 0.01$). All IM residents (100%) reported that they would use the skills learned in this curriculum in their clinical practice.

Conclusion: After participating in our simulation-based curriculum, IM residents reported improved confidence in performing a hand examination and assessing small joint swelling as seen in inflammatory arthritis. This workshop is feasible and may be an effective method to teach trainees these important skills. This workshop shows potential for teaching other groups of learners including medical students, early rheumatology fellows, and advanced practice providers. Future studies should compare our simulation-based curriculum with conventional methods in the teaching of the hand musculoskeletal examination.

Disclosure: I. Gad: None; **C. Podgorski**: None; **K. Springer**: None; **a. Bishnoi**: None; **L. Zickuhr**: Janssen, 5.

Abstract Number: 2181

A Pilot High-fidelity Simulation for Pediatric Rheumatology Learners

John Bridges[1], Livie Timmerman[2] and Nicholas Rockwell[3], [1]University of Alabama at Birmingham/Children's of Alabama, Birmingham, AL, [2]University of Alabama at Birmingham, Gardendale, AL, [3]University of Alabama at Birmingham, Birmingham

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The ACGME's core competencies for pediatric residency training include medical knowledge, patient care, and interpersonal communication skills. At our institution, residents only spend two weeks or fewer rotating through pediatric rheumatology. A needs assessment among pediatric rheumatology attendings identified key rare disease states that are unlikely to be clinically encountered by learners during this short time. High-fidelity simulation is an effective tool in pediatric medical education[1]. We designed a simulation module to expose pediatric learners to two such rheumatologic diseases with clinically distinct, recognizable disease presentation patterns. Learning objectives included: 1) Recognize juvenile dermatomyositis (JDM); 2) Recognize macrophage activation syndrome (MAS); 3) Successfully consult a subspecialist. This intervention was developed to increase learner exposure to rare rheumatologic diseases during limited time on the pediatric rheumatology rotation.

Methods: We collaborated with our institution's pediatric simulation center to create these educational modules focused on pediatric rheumatology. After several months of development, we piloted the modules with final- year medical students and pediatric residents during their clinical rotations.. Local IRB approval was obtained. Participants completed the simulation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1: Pre- and Post-Simulation Multiple Choice Scores by Topic

Topic	Pre-Simulation Scores, N=25 *Mean (SD)*	Post-Simulation Scores, N=16 *Mean (SD)*	*p*-value
Juvenile Dermatomyositis	65.3 (29.1)	84.4 (23.9)	<0.05
Macrophage Activation Syndrome	50 (50.8)	68.8 (47.9)	0.12
One sided t-test, assuming equal variance			

Table 2

Table 2: Pre- and Post-Simulation Confidence Ratings by Topic

Confidence Categories	Pre-Simulation, N=25 *Mean (SD)*	Post-Simulation, N=16 *Mean (SD)*	*p*-value
Diagnostic suspicion of JDM	2.78 (1.07)	3.8 (0.74)	<0.005
Diagnostic suspicion of MAS	2.88 (1.28)	3.9 (0.83)	<0.005
Subspecialist Consultation	3.45 (0.87)	4.3 (0.48)	<0.005
All (100%) post-simulation survey respondents found the simulation module to be a helpful learning activity for the rotation			

module as a group and underwent botha pre- and post-simulation questionnaire assessing knowledge pertaining to subject material covered in the module. A post-simulation debriefing simulation in accordance with the standard simulation teaching modality. Descriptive statistics and one-sided t-tests assuming equal variance were used for data analysis.

Results: A multiple choice questionnaire was distributed as a pre- and post-module assessment of learner knowledge regarding MAS and JDM. Learner confidence in diagnostic recognition and in subspecialist consultation was measured using a 5 point Likert scale. Mean percent correct responses increased from 65.3 (SD 29.1) to 84.4 (SD 23.9) for JDM and from 50 (SD 50.8) to 68.8 (SD 47.9) for MAS, respectively. Confidence in diagnostic suspicion of JDM increased from mean of 2.78 to 3.8 and for MAS increased from 2.88 to 3.9. Confidence in subspecialist consultation increased from 3.45 to 4.3. 100% of learners surveyed reported that the simulation module was a helpful learning activity for the rotation.

Conclusion: This pilot module of high-fidelity simulation for pediatric learners demonstrates knowledge acquisition and increased learner confidence in important core competencies. The long-term goal of this work is to design additional sessions into a modular curriculum for utilization by any training program with access to a simulation center. High-fidelity simulation in pediatric rheumatology is a promising educational method that has the potential to increase access to pediatric learning during medical school and residency training, which could lead to significant improvements in disease recognition and prompt referral in the setting of pediatric rheumatology workforce challenges and large numbers of unnecessary referrals[2,3].

Disclosure: J. Bridges: None; **L. Timmerman**: None; **N. Rockwell**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2182

Rheum for Improvement: A Needs Assessment Survey for an Internal Medicine Resident Curriculum

Kailey Singh[1], Lara El Khoury[2], Karen Friedman[3] and Julie Schwartzman-Morris[4], [1]Northwell Health-NS/LIJ, Queens, NY, [2]Zucker School of Medicine at Hofstra/Northwell Health, Great Neck, NY, [3]Zucker School of Medicine at Hofstra/Northwell Health, Manhasset, NY, [4]Northwell Health Physician Partners, roslyn heights, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology is a core Internal Medicine (IM) residency requirement, yet IM residents report low confidence in their knowledge and skills. This project aimed to identify areas of weakness in resident rheumatology education with a needs assessment to develop a targeted curriculum to improve resident confidence and competency.

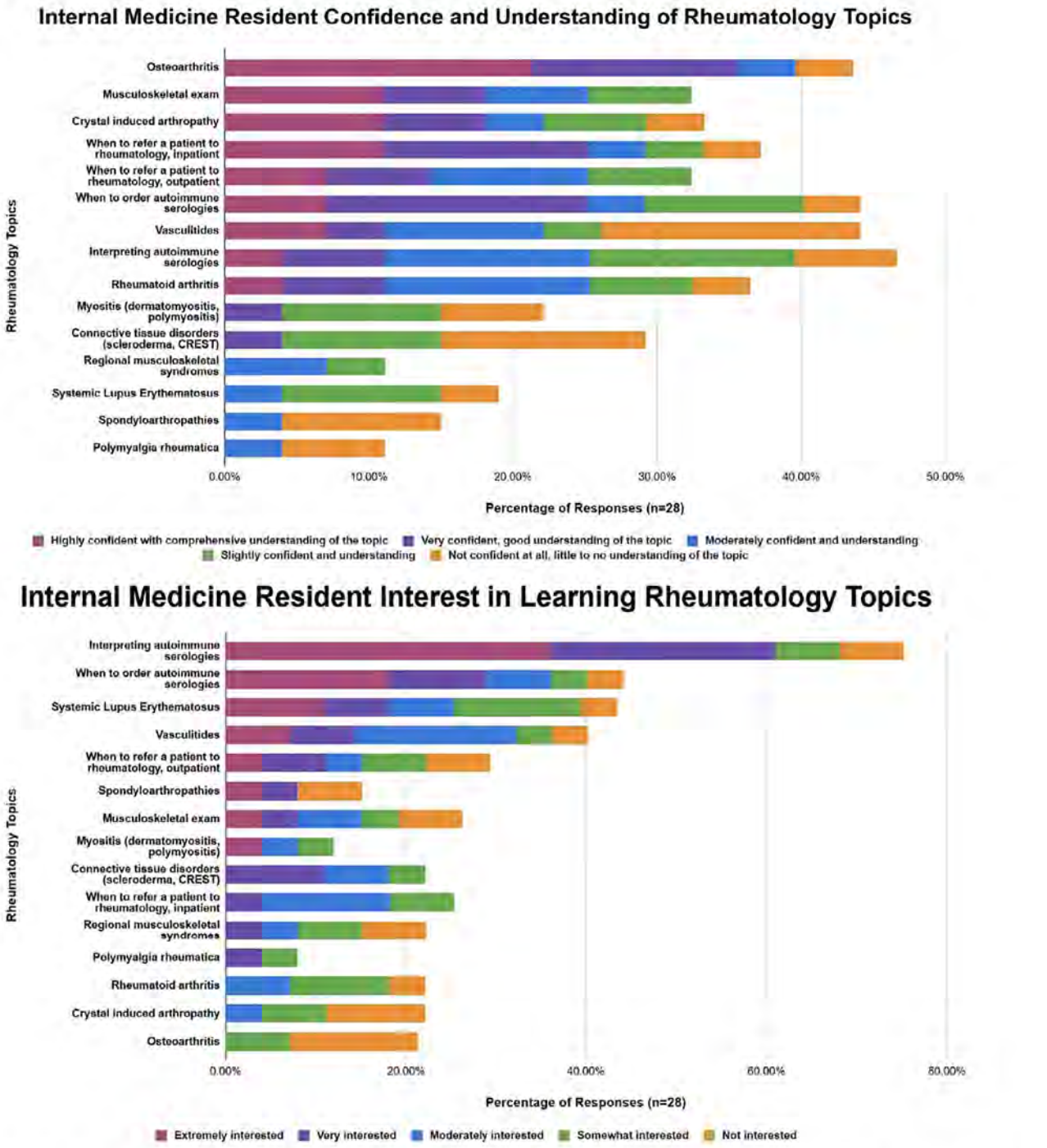
Methods: We surveyed IM residents and rheumatology faculty at a single academic center and analyzed resident in-training exam (ITE) rheumatology scores from 2021-2024. Residents completed a 10-item questionnaire that assessed resident confidence and interest in five American Board of Internal Medicine-based rheumatology topics from a list of topics. Faculty completed a 7-item questionnaire, ranking five topics from a list based on their perceived resident understanding and importance to resident education. Correlation between resident confidence and faculty perceived proficiency was analyzed with a Pearson correlation coefficient. Both surveys included open-ended questions on preferred teaching methods.

Results: 28 IM residents completed the survey, including 12 PGY-1s, 9 PGY-2s and 7 PGY-3s. Most residents had no exposure (n=6, 21.4%) or limited exposure (n=15, 53.6%) to rheumatology in residency, and few (17.9%, n=5) had pursued a rheumatology elective. Three rheumatology fellows and seven attendings completed the survey, with most attendings having over 5 years of experience (n=5, 71.4%). Median ITE rheumatology percentile scores from 2021-2024 were lower at our institution (61st) compared to nationally (65th), with deficits in scleroderma, systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Our residents scored higher in osteoarthritis (OA) and gout. Residents reported high confidence in OA (n=10, 36%), consulting rheumatology inpatient (n=7, 25%) and when to order autoimmune serologies (n=7, 25%), but lower confidence in connective tissue disorders (n=7, 25%), vasculitis (n=6, 21.4%) and interpreting autoimmune serologies (n=6, 21.4%). High interest was expressed in learning how to interpret serologies (n=17, 61%) and when to order them (n=8, 29%). Interest was lower in topics they reported higher confidence in, including OA (n=6, 21.4%) and crystal arthropathy (n=5, 18%) (Figure 1). Faculty identified ordering serologies (n=5, 50%) and interpreting them (n=4, 40%) as key areas for improvement. Ordering serologies (n=7, 70%) and crystal induced arthropathy (n=4, 40%) were perceived as most important to resident education compared to unrated topics including OA and myositis (Figure 2). No significant correlation was found between resident confidence and faculty perceived proficiency (r= -0.38, p=0.153) (Figure 3). Both residents and faculty favored workshops and clinical experience as preferred teaching methods (n=20, 71%), (n=7, 70%).

Conclusion: This needs assessment identified areas of improvement in rheumatology including interpreting autoimmune serologies, connective tissue disorders and vasculitis based on objective ITE data and subjective assessments from residents and faculty. These findings highlight the need for a tailored curriculum and will be used to develop and implement a curriculum in the upcoming academic year.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

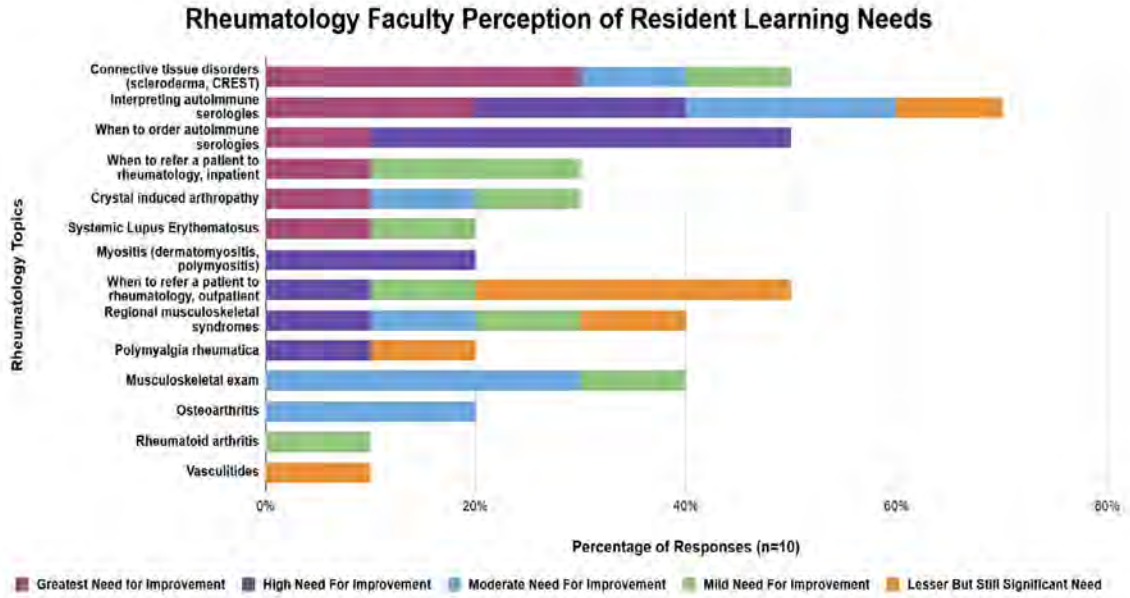
Figure 1: Internal Medicine Resident Confidence, Understanding and Interest in Rheumatology Topics

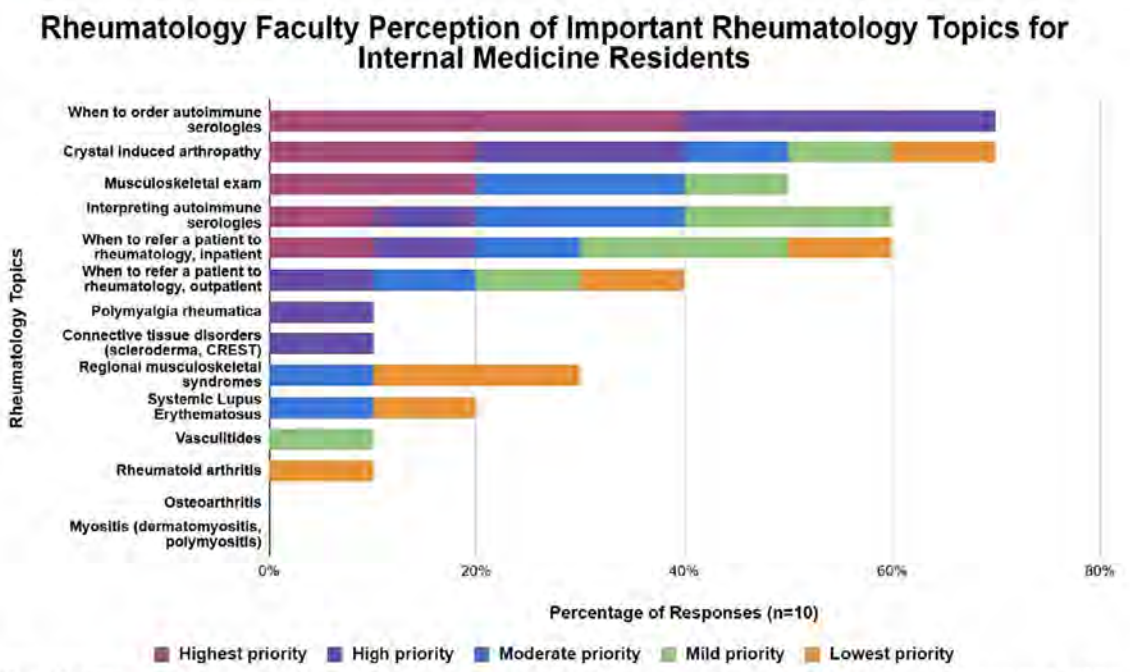


1a: Self-perceived Internal Medicine resident confidence and understanding of rheumatology topics, **1b:** Internal Medicine resident interest in learning rheumatology topics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

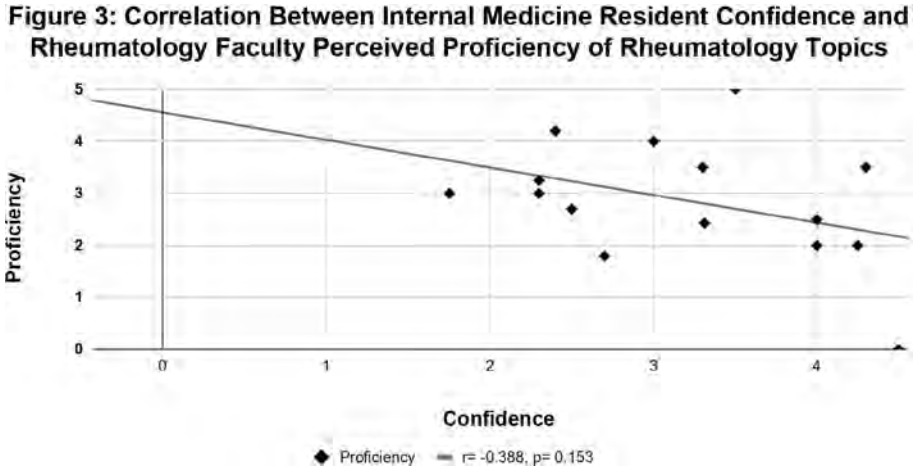
Figure 2: Rheumatology Faculty Perception of Resident Learning Needs and Perceived Importance of Rheumatology Topics for Internal Medicine Training





2a: Rheumatology faculty perception of proficiency of Internal Medicine residents, **2b:** Rheumatology faculty perception of important topics for Internal Medicine residency training

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disclosure: K. Singh: None; **L. El Khoury**: None; **K. Friedman**: None; **J. Schwartzman-Morris**: None.

Abstract Number: 2183

Bridging the Musculoskeletal Ultrasound Training Gap: Analysis of Confidence, Competency, and Clinical Readiness

Kamini Shah[1], Jonathan Samuels[2], Jennifer Medlin[3], Philip Chu[4], Midori Nishio[5], Norman Madsen[6], Michelene Hearth-Holmes[3], Shivani Shah[7], Catherine Bakewell[8], Anthony M. Reginato[9] and Minna Kohler[10], [1]Northwell Health, New York, NY, [2]NYU Langone, Rye Brook, NY, [3]University of Nebraska Medical Center, Omaha, NE, [4]Duke University Hospital, Raleigh, NC, [5]John Muir Specialty Medical Group, Lafayette, CA, [6]URMC, Rochester, NY, [7]University of Chicago, New York, NY, [8]Intermountain Healthcare, Salt Lake City, UT, [9]Brown University, Providence, RI, [10]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose:

While point-of care ultrasound (POCUS) training is increasingly introduced during rheumatology fellowship, limited exposure may not provide the depth or continuity needed to build clinical readiness. Structured, mentored experiential learning, grounded in hands-on skill building and real-time feedback, may help bridge this gap by fostering both technical proficiency and learner confidence.

Methods: Survey data were collected from participants in the 2024 and 2025 Ultrasound School of North American Rheumatologists (USSONAR) Fundamentals Musculoskeletal Ultrasound (MSKUS) workshops, part of a national hands-on training program in rheumatology-focused ultrasound. Participants included fellows and post-fellowship clinicians in academic and private practice settings. Demographic characteristics were comparable across cohorts, supporting the validity of pooled confidence analysis. Retrospective pre-post surveys (administered post-course) assessed perceived knowledge, confidence in scanning and interpretation, and clinical application. Due to a split survey format in 2024, knowledge and application responses could not be individually paired, limiting analysis to confidence data only. 2025 survey data included all survey domains. Confidence scores from both years were pooled for aggregate analysis. Knowledge and clinical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE.1 Demographic Characteristics of Workshop Participants in 2024 and 2025				
	2024		2025	
Gender	**n**	**Percent**	**n**	**Percent**
Female	24	49.0%	33	47.8%
Male	24	49.0%	36	52.2%
Prefer not to say	1	2.0%	0	0.0%
Age (years)				
<30	1	2.0%	0	0.0%
30-39	43	87.8%	62	89.9%
Greater than 40	5	10.2%	7	10.1%
Training Level				
Fellow	40	81.6%	57	82.6%
Post Fellow	9	18.4%	12	17.4%
Practice Setting				
Academic	42	85.7%	64	92.8%
Private practice	3	6.1%	3	4.3%
Not Specified	4	8.2%	2	2.9%
Profession				
Physicians, Allopathic Medicine	39	79.6%	59	85.5%
Physicians, Osteopathic Medicine	7	14.3%	7	10.1%
Student- Health	0	0.0%	1	1.4%
Not Specified	2	4.1%	2	2.9%
Nurse Practitioner	1	2.0%	0	0.0%

TABLE.1 Demographic Characteristics of Workshop Participants in 2024 and 2025

application scores were converted to a 0-10 scale to align with the confidence variable. Responses were analyzed using paired t-tests and Spearman correlations.

Results: Among the 2025 cohort (n = 69), perceived knowledge increased by a mean of 2.25 points (SD = 1.7, $p < 0.0001$), with a post-course mean of 8.33 (SD = 1.4). Post-course confidence in scanning and interpretation, available from both 2024 and 2025 cohorts, averaged 7.34 across the combined group (SD= 1.38, n = 116), suggesting moderate-to-high technical assurance. Correlation analyses, conducted using 2025 data, showed post-course knowledge was positively

Figure 1: Relationship between perceived knowledge and confidence in scanning (2025 cohort, n = 69)

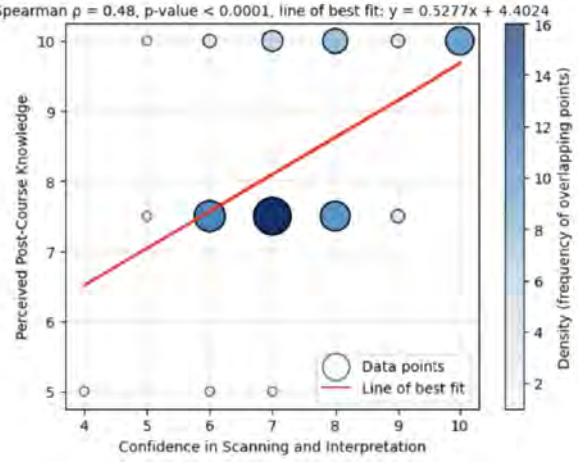


Figure 1: Relationship between perceived knowledge and confidence in scanning

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

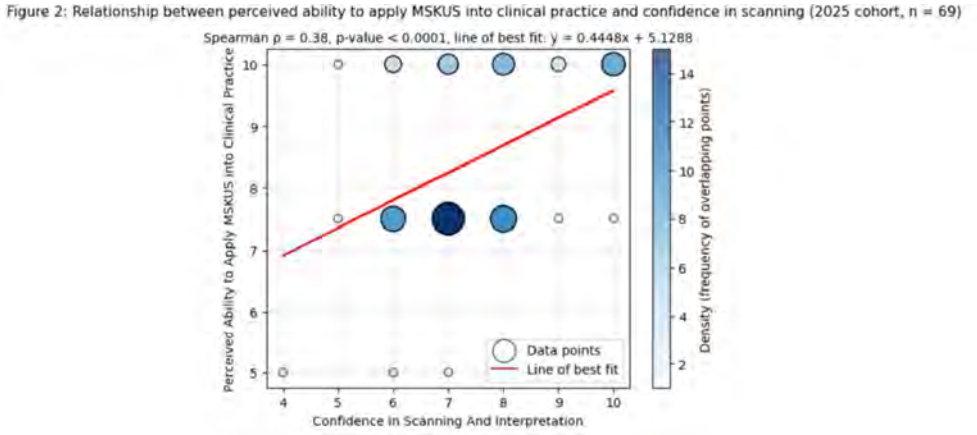


Figure2: Relationship between perceived ability to apply MSKUS into clinical practice and confidence in scanning

associated with confidence in MSKUS scanning and interpretation (Spearman's ρ= 0.48, p < 0.0001). Confidence in scanning also correlated with perceived ability to apply ultrasound skills in clinical practice (ρ = 0.38, p < 0.0001). A one-point increase in confidence was associated with a 0.5-point increase in perceived knowledge. There was no significant difference in post-course confidence scores between fellows and post-fellowship clinicians (p= 0.30), suggesting a reproducible and equitable impact across training levels.

Conclusion: These findings suggest that structured, mentored hands-on training increases learner confidence and technical proficiency, and supports clinical utilization of POCUS in clinical practice. The results support a confidence-driven development model in which experiential learning contributes to clinical readiness. Consistent confidence scores across cohorts support the reproducibility of this model and highlight reliable learning patterns. As POCUS becomes more integrated into rheumatology practice, these findings underscore the need to expand structured training and promote curriculum alignment with competency benchmarks, as reflected in the RhMSUS certification pathway.

Disclosure: K. Shah: None; **J. Samuels**: None; **J. Medlin**: None; **P. Chu**: None; **M. Nishio**: None; **N. Madsen**: None; **M. Hearth-Holmes**: None; **S. Shah**: None; **C. Bakewell**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, Pfizer, 2, 6, UCB, 2, 6; **A. Reginato**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9.

Abstract Number: 2184

Diagnosing the Deficit: Addressing Gaps in Rheumatology Training for Internal Medicine Residents

Kristen Young[1], Samantha Kohn[2] and Brenda Shinar[3], [1]Mayo Clinic, Phoenix, AZ, [2]University Nebraska Medical Center, Omaha, [3]University of Arizona College of Medicine Pheonix, Phoenix

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatologic diseases are common and complex, requiring internal medicine physicians to develop skills in musculoskeletal examination, diagnosis, and management. Despite this, exposure during residency is often limited, leading to low confidence and variable competence. We conducted a needs assessment among residents to

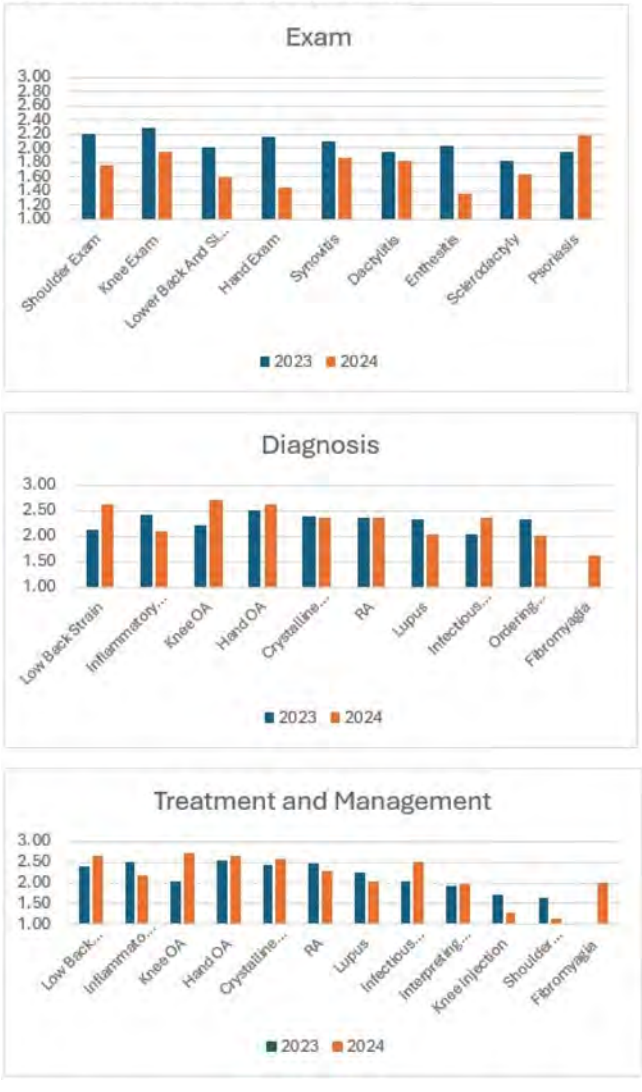
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

evaluate prior exposure, perceived confidence in core domains, and learning sources. This informed a targeted rheumatology curriculum implemented over one academic year, with evaluation of its impact on resident confidence.

Methods: In May 2023, an anonymous 31-item Likert scale (1-3) survey was administered to internal medicine residents at a large academic center to assess confidence across three domains: physical exam, diagnosis, and treatment. Based on survey data and in-training exam performance, targeted educational interventions were developed. These included a joint injection workshop with Sports Medicine and Rheumatology faculty, low back pain and SI exam sessions, and enhanced didactic content with small-group learning and structured feedback. Included in the survey were questions about preferred learning modalities and where they felt that they gained rheumatology knowledge during residency. The same survey was repeated in May 2024, with additional questions on preferred learning methods and perceived sources of rheumatology learning.

Results: Of 77 eligible residents, 36 (47%) responded in 2023 and 22 (29%) in 2024. In 2024, 32% had completed a rheumatology rotation during residency, compared to 19% in 2023. Confidence in musculoskeletal exams remained low, with declines in hand (–0.71), SI/lower back (–0.44), and enthesitis (–0.68) exams. Modest gains were seen in psoriasis exam (+0.24). In diagnosis, confidence improved in low back strain (+0.50) and knee OA (+0.51), but decreased for lupus

Figure 1. Confidence ratings by residents.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(–0.27) and inflammatory back pain (–0.34). Treatment confidence improved for knee OA (+0.67), and infectious arthritis (+0.47), while decreasing for knee (–0.44) and shoulder injections (–0.48). Residents reported highest confidence in diagnosing/treating knee OA, hand OA, and low back strain; lowest in performing joint injections and specialized physical exams.

Residents preferred case-based instruction, followed by patient narratives, lectures, and question banks. Least preferred were journal articles, flashcards, and podcasts. University inpatient wards were the most cited learning setting (86%), followed by Academic Half Day (AHD) lectures (57%), rheumatology rotations (33%), and ambulatory clinics (29%) for gaining new rheumatology knowledge. When asked which most contributed to their knowledge, the top responses were rheumatology rotation (29%) and AHD/simulations (24%).

Conclusion: Targeted didactics improved confidence in diagnosis and management of common rheumatologic conditions, but gaps persist in musculoskeletal and procedural skills. Residents value case-based and narrative instruction, with inpatient and elective experiences being key learning sources. A multifaceted curriculum integrating clinical exposure, hands-on practice, and engaging didactics is essential for building rheumatology competence.

Disclosure: K. Young: None; **S. Kohn**: None; **B. Shinar**: None.

Abstract Number: 2185

The Evolving Digital Landscape of Social Media among Rheumatology Professionals: A Global Analysis by the EULAR SoMeR Study Group

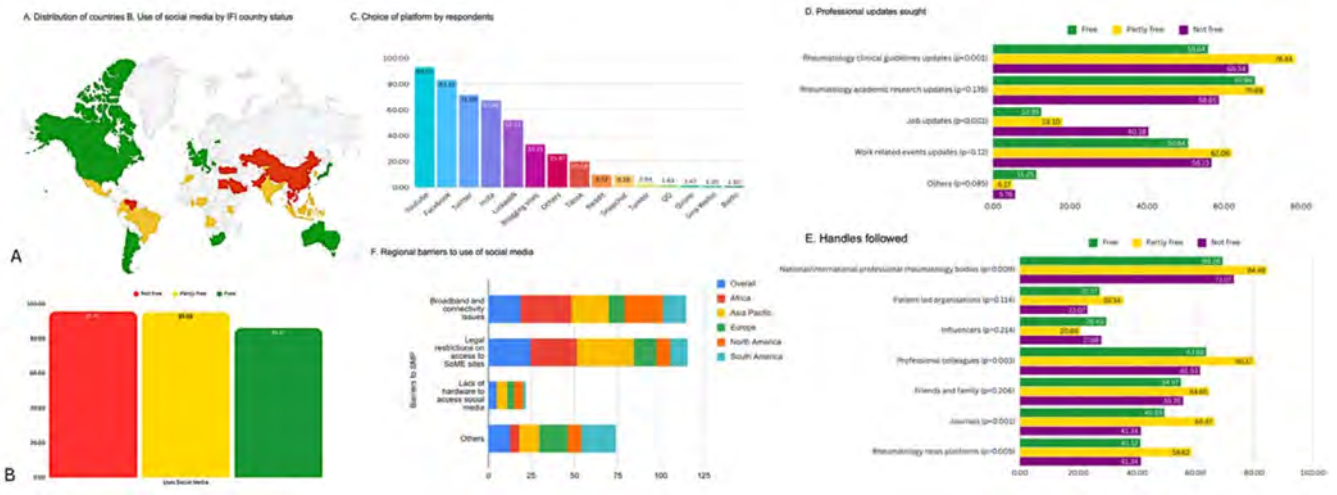
Latika Gupta[1], Manali Sarkar[2], Jeffrey Sparks[3], Loreto Carmona[4], Vikas Agarwal[5], Carlo Vinicio Caballero Uribe[6], Dzifa Dey[7], Chris Edwards[8], Francis BERENBAUM[9] and Elena Nikiphorou[10], [1]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham; Royal Wolverhampton NHS Trust; Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester; Francis Crick Institute, London, Birmingham, UK, United Kingdom, [2]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, Maharashtra, India., Mumbai, Maharashtra, India, [3]Brigham and Women's Hospital, Boston, MA, [4]Instituto de Salud Musculoesquelletica (InMusc), Madrid, Spain, [5]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [6]Department of Medicine, Hospital Universidad del Norte, Barranquilla, Atlantico, Colombi, Barranquilla, Colombia, [7]Rheumatology Unit Department of Medicine and Therapeutics, Korle bu Teaching Hospital, University of Ghana Medical School, Accra, Ghana, [8]University Hospital Southampton, Southampton, United Kingdom, [9]Sorbonne University/Inserm/AP-HP/4Moving Biotech, Paris, France, [10]King's College London, London, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Social media (SoMe) has become an indispensable tool in healthcare, providing platforms for information sharing, networking, and education. However, its use presents challenges including misinformation, professional boundaries, and platform-specific limitations. Building upon the EULAR EMEUNET survey, we aimed to characterize SoMe utilization within rheumatology globally, identifying variations in usage patterns and integration into practice.

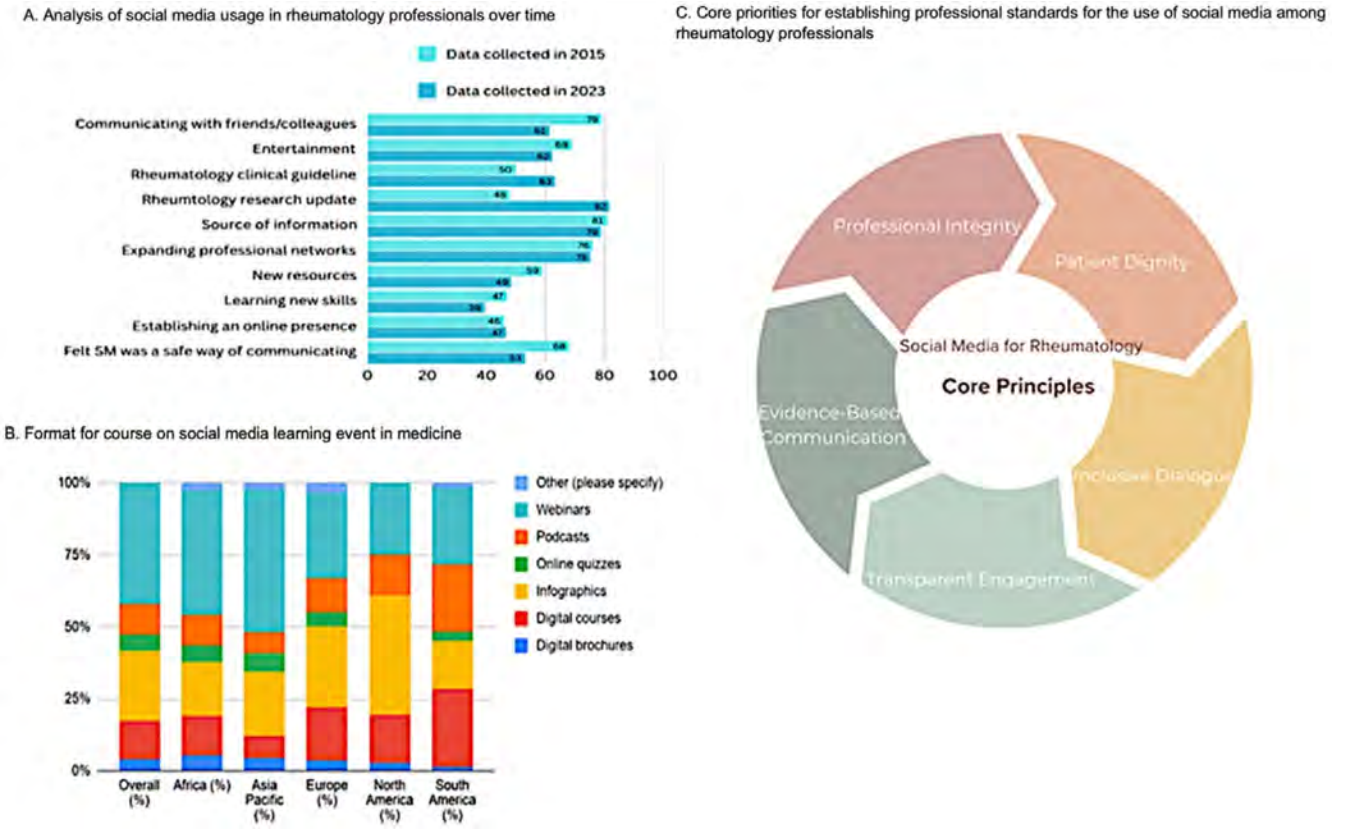
Methods: The EULAR study group on social media (SoMeR) convened in July 2023 with global, multiprofessional representation, identifying key priorities: advocacy, understanding SM use, and developing a position statement on appropriate use. A 30-item survey was designed with group inputs following adoption from the previous EMEUNET survey, validated by professionals and public, translated into 6 languages, and distributed via mailing lists and social media channels of EMEUNET,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



PANLAR Joven, and APLAR Young Rheumatology. Analysis employed Human Development Index (HDI) and Internet Freedom Index (IFI) to assess digital divides.

Results: 840 respondents among whom 597 used social media (M:F ratio 1:1.12), with characteristics in Table 1. Primary reasons for non-use included privacy concerns (15.40%), time constraints (12.80%), perceived unsuitability (12.10%), and misinformation risks (9.40%). SoMe adoption varied by region and in purpose: Europe (97.3%) vs Asia-Pacific (88.6%) (Fig 1A,B, D and E). Twitter/X was predominant in Europe/North America (66.1%/75.0%) while YouTube was preferred in Asia-Pacific/South America (79.9%/73.3%) (Fig 1D). Lower HDI regions reported more connectivity issues (28.1% vs



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Respondent characteristics	N =597 mean (SD) or n (%)
Age	40.35 (10.07)
Gender F: M	1:1.12
Region (%)	
Asia Pacific	342 (57.28)
Europe	112 (18.76)
South America	65 (10.88)
Africa	39 (6.53)
North America	39 (6.53)
HDI, n (%)	
Very High	391 (65.60)
High	114 (19.12)
Medium	46 (7.71)
Low	45 (7.55)
Professional title, n (%)*	
Student	37 (6.79)
Practicing physician rheumatologist	387 (64.82)
Non-clinical academic/researcher	32 (5.36)
Clinical academic/researcher	210 (35.17)

16.7%), while higher HDI cited legal restrictions (24.4%) (Fig 1C and F). IFI analysis showed countries with restricted internet freedom paradoxically reported higher positive impact from SoMe (4.04/5 vs 3.86/5, p=0.008). Female professionals showed higher SoMe adoption (94.4% vs 88.8%, p=0.016). Longitudinal analysis (2015-2023) revealed trends toward professional applications and away from networking functions (Fig 2A). Respondents increasingly reported feeling overwhelmed by SoMe content (56.9%), particularly in South America and Africa (73.3%/70.3%, p=0.007). Following these results, the SoMeR Study Group developed a consensus "Digital Equity Declaration for Rheumatology" (Fig 2C) focusing on professional integrity, evidence-based communication, cohesive platforms, patient dignity, and inclusive engagement. Interest in SoMe training was high (83.3%), with webinars preferred (41.1%) (Fig 2B).

Conclusion: This global survey demonstrates SoMe's integral role in rheumatology with significant regional variations. The disparities call for targeted interventions addressing connectivity in lower-resource settings and legal concerns in higher-resource regions. Through strategic engagement with social media while upholding professionalism and scientific integrity, we can transform rheumatology's digital presence from isolated efforts to a cohesive global community. Future projects include revision of the EMEUNET X course and focused group interviews to enhance digital engagement in rheumatology.

Disclosure: L. Gupta: None; **M. Sarkar**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **L. Carmona**: None; **V. Agarwal**: None; **C. Uribe**: None; **D. Dey**: None; **C. Edwards**: AbbVie/Abbott, 6, alphasigma, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen, 6, pfizer, 6, Roche, 1, 6, sanofi, 6, ucb, 6; **F. BERENBAUM**: 4Moving Biotech, 2, 8, 10; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2186

Developing Rheumatology Specific Anki Electronic Flashcards for Teaching Preclinical Students United States Medical Licensing Examination Board Relevant Topics

Madison Bellamy[1], Grant Stalker[2], Laura Nichols[3], Jennifer Strouse[2], Miriah Gillispie-Taylor[4], Beth Scholz[5] and Sonam Kiwalkar[6], [1]University of Iowa, Coralville, IA, [2]University of Iowa, Iowa City, [3]University of Colorado, Aurora, CO, [4]Baylor College of Medicine/Texas Children's Hospital, Houston, TX, [5]Baylor Scott and White Health, Temple, TX, [6]The Vancouver Clinic, Portland, OR

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Electronic flashcards (EF) have become a widely used study tool by medical students. One of the most well-known is the spaced repetition program Anki. There are many widely available online decks with thousands of cards that have been crowd sourced. Of the decks available, there is a lack of vetting by experts in the field of rheumatology to confirm the accuracy of the information. The aim of this project is to develop a free and accurate resource to aid medical students in learning relevant teaching points related to adult and pediatric rheumatology.

Methods: A collaborative group of four rheumatologists, one rheumatology fellow, one internal medicine resident, and one medical student was assembled. The decision was made to target United States Medical Licensing Examination (USMLE) Step content with the intention of developing an EF deck for undergraduate medical education. Using a backward design approach questions were developed based on USMLE content outlines. Learning objectives and subsequent testing points were created. These were reviewed by the rheumatologist and rheumatology fellow co-authors for accuracy.

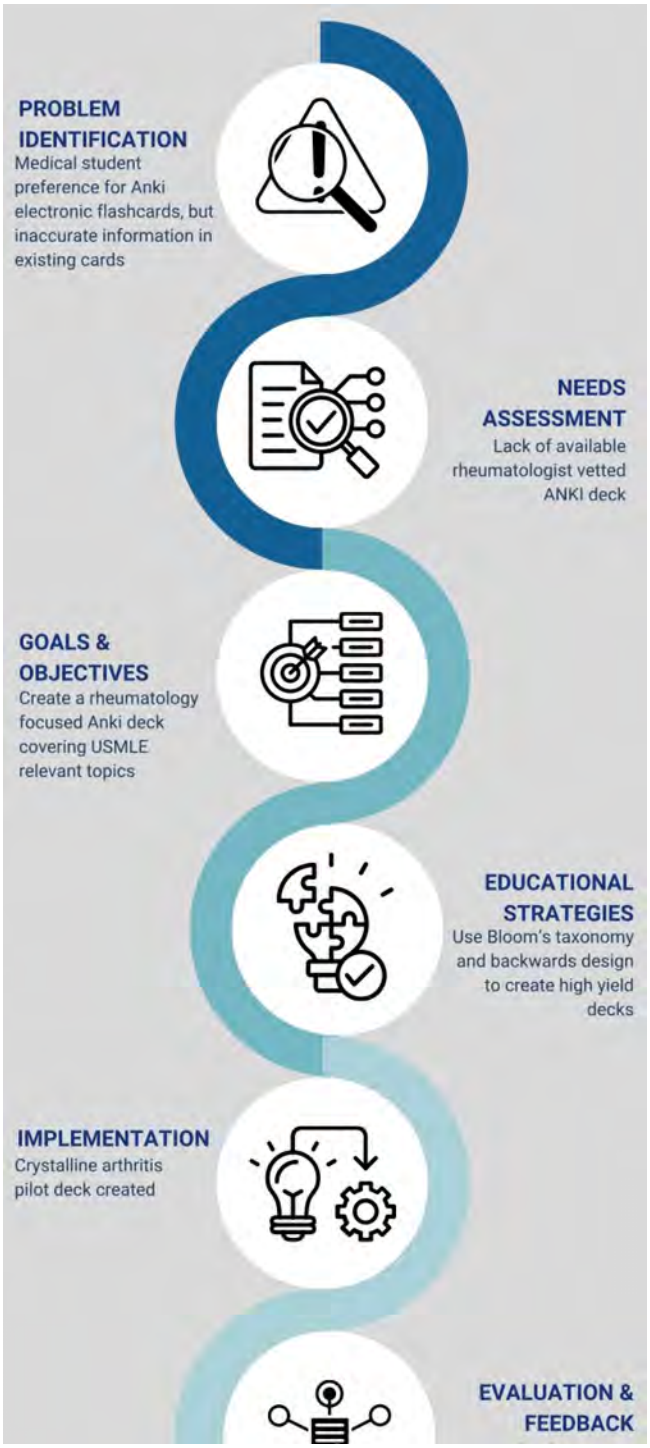
A pilot deck of Anki flashcards was created for crystalline arthritis. These were again reviewed. The approved deck is being distributed to medical students to provide quantitative and qualitative feedback.

Results: We identified 12 USMLE organ systems with rheumatology related content, 29 categories within these, 15 subcategories, and subsequent listed conditions were then identified. From these listed conditions, 15 topic condition groups were developed. Through the selection process, crystalline arthritis was selected for a pilot deck. Fifteen learning objectives pertaining to crystalline arthritis were created using Bloom's taxonomy followed by 50 testing points. After review and feedback by co-authors 55 questions were developed from the testing points. Ranking of the fifteen highest yield questions by team members narrowed this to the 15 most relevant questions. During the development of Anki cards to best fit this format 28 cards were created.

Conclusion: Using backward design to work from content outline topics to objectives to testing points was helpful in guiding the development of a comprehensive yet succinct deck of Anki EFs. Having diverse levels of training in the collaborative group was helpful given the student's and resident's experience using Anki cards. Students provided faculty development sessions regarding effective use of Anki EFs. Creation of a deck of EFs by experts in rheumatology was feasible.

These cards are being piloted with medical students to obtain both qualitative and quantitative student feedback. Based on feedback from this pilot the goal is to have multi-center implementation of a standardized and broadly applicable deck.

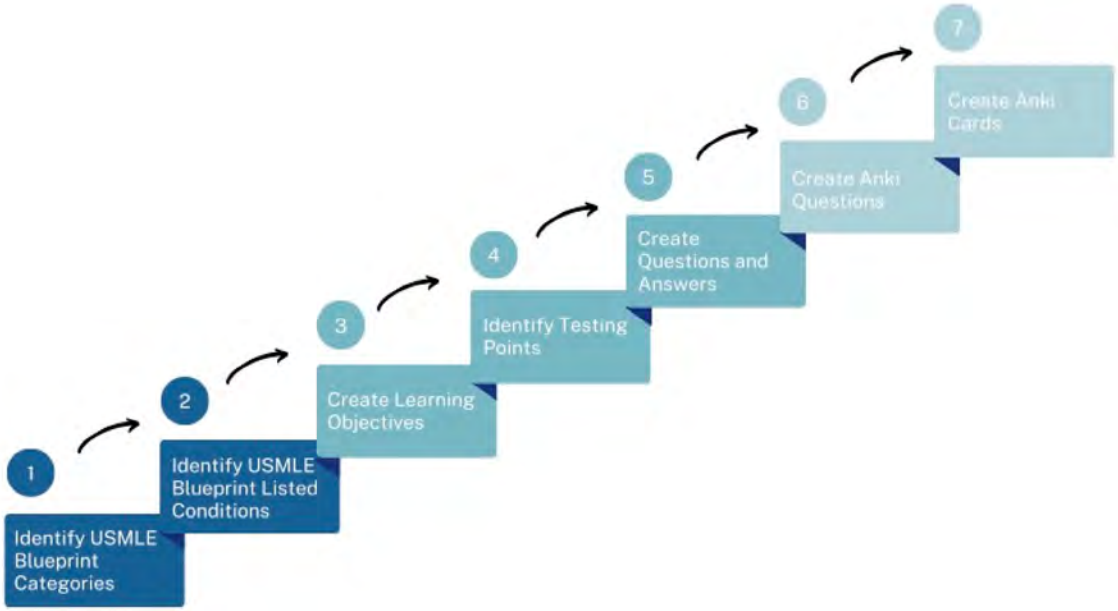
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



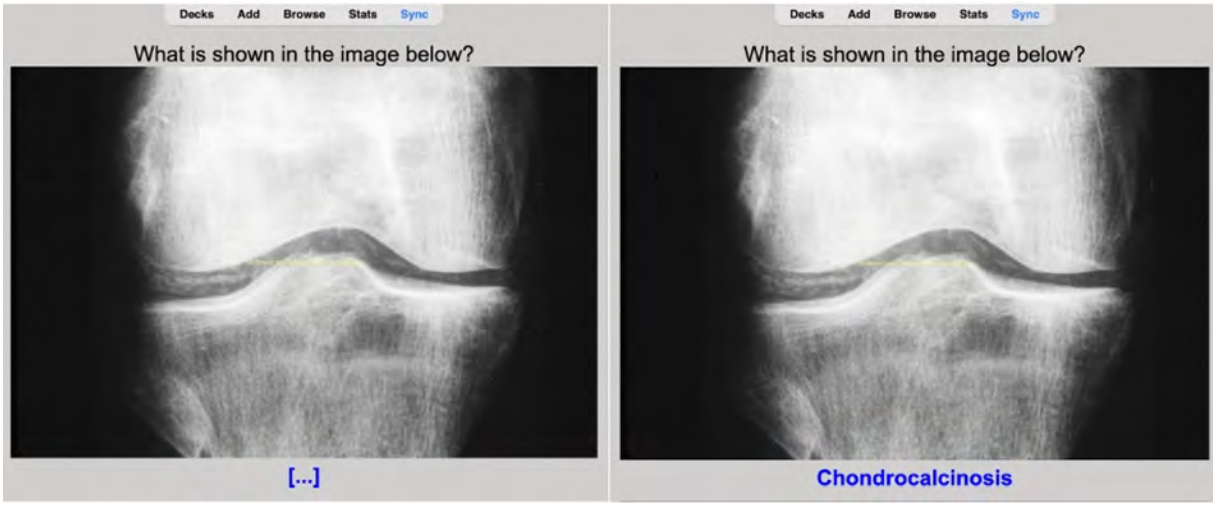
Use of Kern's Six Step Approach in the Development of Anki Electronic Flashcards for Teaching Preclinical Students Board Relevant Topics

Additional future directions include developing a broader range of rheumatology relevant EF decks such as one focused towards internal medicine residents and rheumatology fellows.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Backward Design Process of Content Development



Example Anki Card

Disclosure: M. Bellamy: None; **G. Stalker**: None; **L. Nichols**: None; **J. Strouse**: None; **M. Gillispie-Taylor**: None; **B. Scholz**: None; **S. Kiwalkar**: None.

Abstract Number: 2187

Transforming MSUS Access in Mexico: A Comparative Study of National Trends and a Hybrid Training Cohort

Mario R. Garcia-Pompermayer[1], SARAH G. AYTON[2], Karina Silva Luna[3], Ricardo Ramirez-Morales[4] and Mario Garza Elizondo[5], [1]Hospital San Jose Tecnologico de Monterrey, Monterrey, Mexico, [2]Columbia University, New York, NY, [3]Centro Médico Zambrano Hellion, Monterrey, Mexico, [4]Private Rheumatology Practice, Monterrey, Mexico, Monterrey, Nuevo Leon, Mexico, [5]Hospital Zambrano-Hellion TecSalud, Monterrey, Mexico

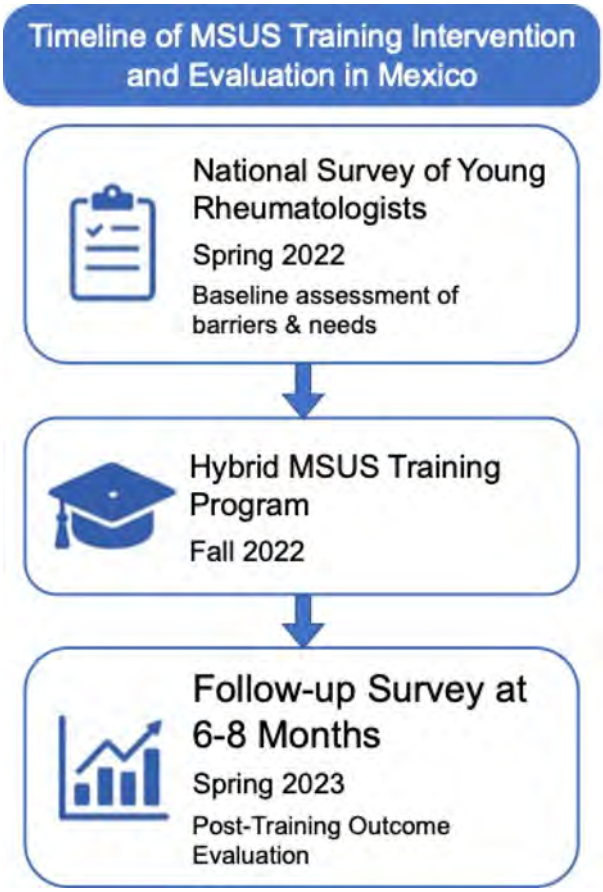
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal ultrasound (MSUS) is a valuable diagnostic tool in rheumatology, yet access to formal MSUS training in Latin America remains limited. In a 2022 national survey, early-career Mexican rheumatologists reported high interest in MSUS but faced substantial barriers. To address this gap, we implemented and evaluated a hybrid MSUS training course. This study compares national survey data with outcomes from course participants to assess the impact of targeted hybrid training on clinical use, training exposure, and institutional integration of MSUS.

Methods: We conducted a cross-sectional analysis of two cohorts. The 2022 cohort (N=96) consisted of early-career rheumatologists across Mexico who responded to a national survey on MSUS access, training, and clinical use. The 2023 cohort (N=21) included participants who completed a structured hybrid MSUS training program (online modules + in-person workshop) and completed a follow-up survey three months post-course. Surveys assessed prior training, current MSUS use, educational preferences, institutional context, and barriers. Descriptive statistics and chi-square or Fisher's exact tests were used to compare groups.



Timeline of a hybrid MSUS training intervention and evaluation in Mexico. Figure 1. Timeline of a hybrid MSUS training intervention and evaluation in Mexico. A three-phase study was conducted to assess access to musculoskeletal ultrasound (MSUS) training and the impact of a hybrid education intervention among early-career rheumatologists in Mexico. In Phase 1 (Spring 2022), a national needs assessment survey (N = 96) identified barriers to MSUS training and utilization. In Phase 2 (Fall 2022), a structured hybrid MSUS course combining online modules and in-person workshops was delivered. In Phase 3 (Spring 2023), a follow-up survey of course participants (N = 21) evaluated changes in MSUS practice, training exposure, and institutional support. The intervention was associated with higher MSUS usage and training engagement relative to national trends.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparative characteristics of MSUS knowledge, clinical practices, and perceived barriers among early-career rheumatologists.

Characteristic	Overall (N = 117)	Cohort		P-value
		Young Rheumatologists, 2022 (N = 96)	Course Participants, 2023 (N = 21)	
Demographic Characteristics				
Age (years)				0.3
Mean (SD)	35.63 (3.66)	35.38 (3.36)	36.75 (4.71)	
Median (25%-75%)	35.18 (32.91-38.00)	35.08 (32.79-37.73)	35.66 (32.93-41.19)	
Gender				0.6
Female	62 (52.99%)	52 (54.17%)	10 (47.62%)	
Male	55 (47.01%)	44 (45.83%)	11 (52.38%)	
Knowledge				
Knowledge of MSUS Programs Available in Mexico				
In-Person Classes	74 (63.25%)	70 (72.92%)	4 (19.05%)	
Online Classes	41 (35.04%)	38 (39.58%)	3 (14.29%)	0.028
Workshops	57 (48.72%)	53 (55.21%)	4 (19.05%)	0.003
Specialty	1 (0.85%)	1 (1.04%)	0 (0.00%)	>0.9
Unknown	30 (25.64%)	19 (19.79%)	11 (52.38%)	0.002
MSUS Knowledge: Prior MSUS Training				
Any Prior MSUS Training	71 (60.68%)	55 (57.29%)	16 (76.19%)	0.11
Practices				
MSUS Use in Practice				
Used or Referenced in Clinical Practice	92 (78.63%)	74 (77.08%)	18 (85.71%)	0.6
Performs MSUS in Clinical Practice	30 (25.64%)	20 (20.83%)	10 (47.62%)	0.011
Application of MSUS Use in Practice				
Diagnosis	62 (52.99%)	52 (54.17%)	10 (47.62%)	0.6
Pathology (Tendon/Muscular/Ligament)	55 (47.01%)	46 (47.92%)	9 (42.86%)	0.7
Synovitis/Inflammatory joint disease	60 (51.28%)	50 (52.08%)	10 (47.62%)	0.7
Sjogren's syndrome	9 (7.69%)	8 (8.33%)	1 (4.76%)	>0.9
Vasculitis	6 (5.13%)	6 (6.25%)	0 (0.00%)	0.6
Guided Infiltration/Aspiration Procedures	35 (29.91%)	32 (33.33%)	3 (14.29%)	0.084
Experience Using MSUS (years)				0.078
< 1 year	22 (43.14%)	14 (34.15%)	8 (80.00%)	
1-5 years	24 (47.06%)	22 (53.66%)	2 (20.00%)	
5-10 years	4 (7.84%)	4 (9.76%)	0 (0.00%)	
>10 years	1 (1.96%)	1 (2.44%)	0 (0.00%)	
Utilization (per week)				0.3
Almost never	15 (25.86%)	14 (29.79%)	1 (9.09%)	
1-2 days/week	20 (34.48%)	15 (31.91%)	5 (45.45%)	
3-5 days/week	14 (24.14%)	12 (25.53%)	2 (18.18%)	
Everyday	9 (15.52%)	6 (12.77%)	3 (27.27%)	
Years MSUS Used in Rheumatology Department				0.026
< 1 year	16 (23.19%)	10 (18.18%)	6 (42.86%)	
1-2 years	11 (15.94%)	7 (12.73%)	4 (28.57%)	
3-4 years	9 (13.04%)	8 (14.55%)	1 (7.14%)	
>4 years	16 (23.19%)	13 (23.64%)	3 (21.43%)	
Unknown	17 (24.64%)	17 (30.91%)	0 (0.00%)	
Attitudes				
Believe MSUS is or should become a standard tool in Rheumatology	113 (97.41%)	93 (97.89%)	20 (95.24%)	0.5
Believe MSUS is a standard tool in Rheumatology	98 (85.22%)	79 (83.16%)	19 (95.00%)	0.3
Believe MSUS should become a standard tool in Rheumatology	109 (93.16%)	89 (92.71%)	20 (95.24%)	>0.9

Results: Participants in the hybrid training intervention demonstrated significantly higher MSUS utilization (47.6% vs. 20.8%, p=0.011) and more frequently had ≤1 year of MSUS experience (80% vs. 34.2%). Prior MSUS training was also more common (76.2% vs. 57.3%), while awareness of workshops (19.1% vs. 55.2%, p=0.003) and online courses (14.3% vs. 39.6%,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

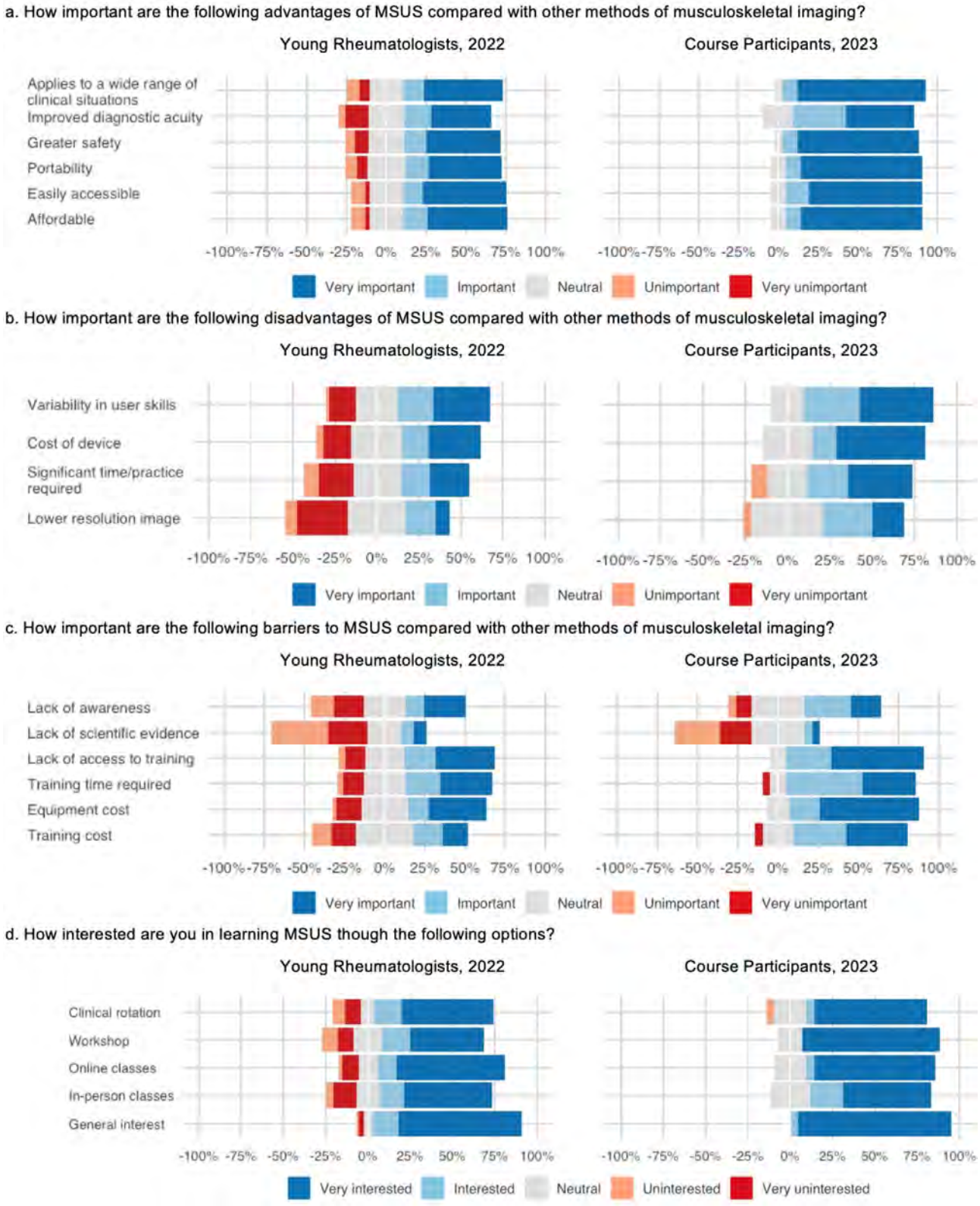


Figure 2. Comparative perceptions of musculoskeletal ultrasound among early-career rheumatologists following a national survey and a hybrid training intervention. Perceptions of MSUS access, training, and clinical use were assessed in two cohorts of early-career rheumatologists in Mexico. The figure illustrates differences in reported advantages, disadvantages, barriers, and preferences for future education modalities. Between-group comparisons highlight the potential impact of targeted hybrid training on early adoption and institutional integration of MSUS.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

p=0.028) was lower. Hybrid participants showed greater preference for online training formats (p=0.014), and more frequently cited training cost (p=0.018) and equipment access (p=0.064) as barriers. Institutional MSUS use and departmental experience were also significantly more prevalent in the course cohort (p=0.026).

Conclusion: A hybrid MSUS training intervention for early-career rheumatologists in Mexico led to increased MSUS utilization, institutional integration, and training exposure compared to national trends. These findings highlight the potential of scalable hybrid education models to address training gaps and promote equitable MSUS adoption in underserved settings. This underscores the need for broader implementation strategies and institutional investment to build rheumatologic imaging capacity across Latin America.

Disclosure: M. Garcia-Pompermayer: None; **S. AYTON**: None; **K. Silva Luna**: None; **R. Ramirez-Morales**: None; **M. Garza Elizondo**: None.

Abstract Number: 2188

Enhancing Pediatric Rheumatology Education Through Case-Based Learning: Impact on Knowledge, Confidence, and Elective Interest

Nayimisha Balmuri, Hopkins, Baltimore

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Pediatric rheumatic diseases are rare and frequently under-recognized by trainees, leading to delayed diagnosis and referral. To address this gap, we developed a case-based curriculum to enhance resident knowledge, confidence, and interest in pediatric rheumatology. The objective of this study was to evaluate the impact of a four-

Figure 1. Pre- and Post-session knowledge scores by session topic.
Mean knowledge scores (out of 5) improved for all topics. Paired t-tests showed statistically significant improvements for JDM (p = 0.0097) and SLE (p = 0.0021), a strong trend for JIA (p = 0.055), and no significant change for Systemic Vasculitis (p = 0.31).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

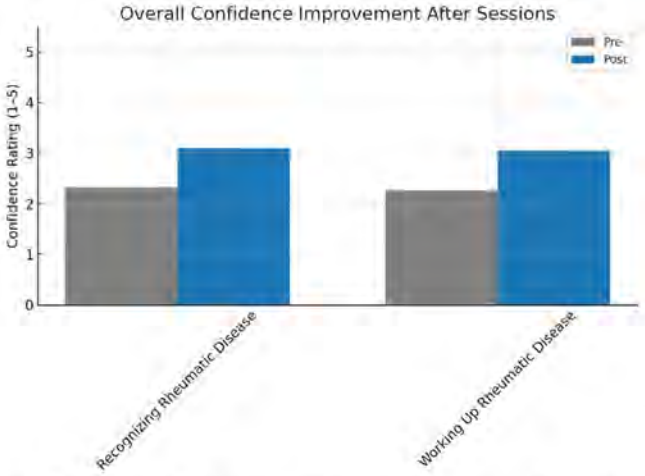


Figure 2. Overall confidence improvements across all sessions.
Across all sessions, confidence in recognizing rheumatic disease improved from a mean of 2.37 to 3.13, and confidence in working up disease improved from 2.36 to 3.10. Both differences were statistically significant ($p < 0.001$, Wilcoxon signed-rank tests).

session case-based curriculum on resident knowledge, confidence in recognizing patients with rheumatic disease and initiating workup for pediatric rheumatology patients, and creating subspecialty interest in pediatric rheumatology.

Methods: Four interactive, case-based group learning sessions were delivered on systemic vasculitis, juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), and juvenile dermatomyositis (JDM). Participants completed identical pre- and post-session knowledge assessments (5-item quizzes) and a post-session survey assessing retrospective pre- and post-confidence in recognizing and working up pediatric rheumatic diseases (5-point Likert scale). The survey evaluated session usefulness, prior pediatric rheumatology elective experience, and elective interest. Paired t-tests and Wilcoxon signed-rank tests were used for pre/post comparisons; ANOVA and Kruskal-Wallis tests were used for PGY-level comparisons.

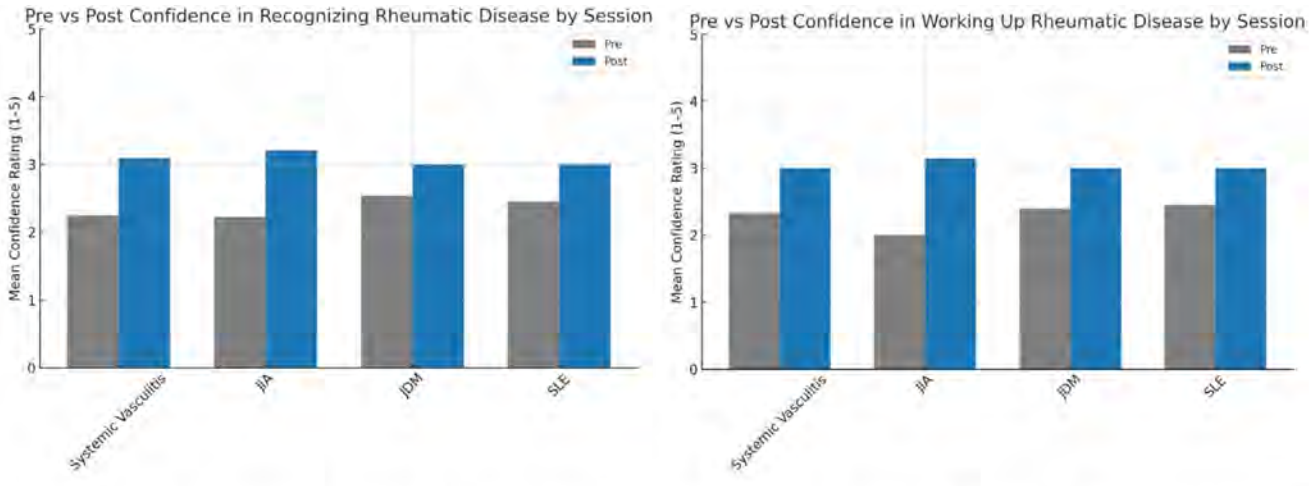


Figure 3. Pre - and Post-session confidence in recognizing rheumatic disease and working up rheumatic disease by session topic. Mean confidence ratings (1–5 scale) improved across all topics. Wilcoxon signed-rank tests showed statistically significant increases for all sessions. All changes were statistically significant ($p < 0.05$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Forty-six evaluations were collected. Knowledge scores significantly improved for JDM (p= 0.0097) and SLE (

p= 0.0021); JIA showed a positive trend (p= 0.055), while vasculitis did not reach significance (p= 0.31). Confidence significantly improved in all sessions for both recognizing and working up rheumatic disease ($p < 0.05$ for all). PGY2 residents had the highest post-session knowledge scores (p= 0.034); PGY3s had the lowest baseline confidence in recognizing disease (p= 0.040), though post-session confidence was similar across PGY levels. All participants reported that the sessions were helpful for general pediatrics. While only 8–33% had previously completed a pediatric rheumatology elective, 67–78% reported increased interest in pursuing one after the session.

Conclusion: A brief, structured case-based curriculum significantly improved resident knowledge and confidence in evaluating pediatric rheumatic disease and enhanced interest in subspecialty electives. These findings support broader integration of targeted rheumatology education into pediatric residency training.

Disclosure: N. Balmuri: None.

Abstract Number: 2189

Physician Practices and Perspectives in the Diagnosis and Management of Fibromyalgia: A US Chart Review Study

Daniel Clauw[1], **Parul Houston**[2], Zhao Yang[2], Todd Grinnell[2] and Lesley Arnold[3], [1]Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI, [2]Axsome Therapeutics, Inc, New York, NY, [3]University of Cincinnati College of Medicine, Cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia (FM) is a chronic, widespread pain disorder driven by dysregulated central pain processing, which impairs daily function and quality of life. Current understanding of clinicians' knowledge, practices, and perceptions towards FM in the real world is critical to identifying gaps in FM management and informing future treatment strategies. A national chart review was conducted among US-based healthcare providers (HCPs) caring for patients with FM to characterize their views and understanding of FM, diagnostic and treatment practices, and satisfaction with current therapies.

Methods: An online chart review was conducted from December 2023 to January 2024 among 199 US HCPs with FM expertise, including primary care physicians (PCPs), rheumatologists, pain specialists, and aligned nurse practitioners and physician assistants. Eligible HCPs had been practicing ≥2 years, treated ≥20 adult patients with FM over the past 3 months, and were aware of duloxetine, milnacipran, or pregabalin. Each HCP contributed data from 2 patient charts.

Results: A total of 398 patient charts were reviewed by 199 HCPs, including 99 rheumatologists, 50 pain specialists, and 50 PCPs. Respondents were highly experienced, managing an average of 91 patients with FM each over the past 3 months. Among all respondents, 70% of treating rheumatologists had also diagnosed the patients themselves (vs 58% of PCPs and 38% of pain specialists). Across specialties, multiple diagnostic tools were used: tender point exams (79%), diagnosis by exclusion (69%), and American College of Rheumatology or ACTTION-APS Pain Taxonomy criteria (68%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The average age of patients with audited charts was 48 years, with most respondents agreeing that the age of their newly diagnosed patients had decreased in recent years. Across specialties, pain (81%), followed by fatigue (57%) and muscle tenderness (51%) were key drivers of treatment decisions. There was no clearly defined standard of care among pharmacotherapies. Across all respondents' treated patients, duloxetine, gabapentin, and pregabalin were evenly used across lines of therapy; use of opioids (including tramadol) was more common in the third line and beyond (33% of ≥third line patients). Most respondents (88%) were comfortable prescribing multiple pharmacotherapies for FM, despite 76% expressing concern about drug-drug interactions. Respondents reported that 39-51% of patients were dissatisfied or coping but interested in switching treatments. Most (59%) viewed FM patients as time-consuming to manage, and 32% believed most of their patients were unlikely to improve despite treatment. A large majority (85%) believed FM is stigmatized by the HCP community.

Conclusion: This recent patient chart review among US-based HCPs who are highly experienced in managing patients with FM shows continuing variability in diagnostic and treatment practices, limited satisfaction with current therapies, and concern that patients are unlikely to improve despite treatment even though progress has been made in disease area knowledge and earlier identification. Greater knowledge of FM, its diagnosis and management, and new treatment options will help further support patient care and improve outcomes.

Disclosure: D. Clauw: Tonix, 2, 5; **P. Houston**: Axsome Therapeutics, Inc., 3; **Z. Yang**: Axsome Therapeutics, Inc., 3; **T. Grinnell**: Axsome Therapeutics, Inc., 3; **L. Arnold**: Axsome Therapeutics, 2, Ono Pharmaceutical Co., 2, Scilex, 2.

Abstract Number: 2190

Successful Implementation of an Innovative Rheumatology Curriculum for Internal Medicine Residents: Fellow-Initiated Rheumatology EDUcation Project (FIRED UP)

Raeann Bowman[1], Edward Huddleston[2], Bailey Lipham[3] and Amanda Alexander[4], [1]University of Alabama Birmingham / UT Southwestern, Gardendale, AL, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama Medical School, Vestavia Hills, AL, [4]University of Alabama at Birmingham, Homewood, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology is an important field with topics encountered commonly on board exams and clinically, yet it remains an area of low confidence for trainees. This innovative project seeks to increase resident competency and confidence in rheumatology topics. As a part of this unique project, fellows also expand and gain confidence in their teaching skills.

Methods: Internal medicine residents rotating on the rheumatology consult service at University of Alabama Birmingham (UAB) were asked to answer a pre-rotation quiz and survey to gauge initial rheumatology knowledge and confidence. Rheumatology fellows voluntarily signed up to develop and deliver weekly didactics to the residents on common or high-yield rheumatology topics of their choice.

The primary outcome was residents' gain in rheumatology knowledge as measured by changes in objective quiz assessment and subjective self-assessment obtained at baseline compared with assessments obtained after rotation completion. The pre- and post-tests contained similar, but not identical, questions randomized from a set in order to best gauge learners'

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Resident assessments show increased rheumatology knowledge by objective measures and self-assessed measures. Objective assessment was based on percent correct of 10 randomized unique multiple choice quiz questions both before and after rotation. Self-assessments were rated on a 1 to 10 scale, with 10 being the highest.

	Before Intervention	After Intervention	Difference
Objective Assessment			
Average % correct (range)	*n=12*	*n=8*	
Knowledge Assessment	62.5% (30-90%)	83.8% (70-100%)	+21.3%
Self Assessment			
Score on 10-point scale (range)	*n=13*	n=7	
Interest in Rheumatology	6.15 (2-10)	5.14 (1-10)	-1.01
Importance of Rheumatology	7.38 (4-10)	7.86 (5-10)	+0.48
General Rheumatology Knowledge	4.83 (2-7)	5.86 (3-8)	+1.03
Ability to Recognize Rheumatic Disease	5.62 (2-8)	6.86 (3-10)	+1.24
Confidence in diagnosis of:			
Gout	6.85 (4-9)	7.57 (4-10)	+0.72
Rheumatoid Arthritis	5.77 (3-9)	6.71 (4-10)	+0.94
Lupus	5.38 (3-9)	6.43 (3-10)	+1.05
Systemic Sclerosis	4.15 (1-6)	5.86 (2-8)	+1.71
Confidence in treatment of:			
Gout	6.92 (5-9)	7.57 (5-9)	+0.65
Osteoarthritis	7.62 (5-10)	8.29 (5-10)	+0.67
Scleroderma Renal Crisis	3.31 (1-8)	6.29 (2-9)	+2.98

increase in knowledge rather than recalling the correct answers. We also evaluated changes in learner confidence in diagnosing common rheumatic diseases (gout, rheumatoid arthritis, lupus, scleroderma), and confidence in treating common or important diseases encountered in rheumatology (gout, osteoarthritis, scleroderma renal crisis). First year fellows completed surveys before and after participation in the project regarding career plans and confidence in teaching skills.

Table 2: Fellows gained confidence in overall teaching skills and ability to plan and deliver a teaching session after implementation of the program. Self-assessments were rated on a 1 to 10 scale, with 10 being the highest. Post-fellowship plans were determined by a multiple-choice question, absolute difference is reported.

Self-Assessment	**Before Intervention**	**After Intervention**	**Difference**
Score on 10-point scale (range)	*n=3*	*n=3*	
Interest in Medical Education	8 (7-10)	8 (7-9)	0
Confidence in:			
Overall Teaching Skills	6 (6-6)	7.33 (7-8)	+1.33
Planning a Session	6.33 (6-7)	8.66 (7-10)	+2.33
Delivering a Session	6 (6-6)	8 (7-10)	+2
Post-fellowship plans			
Multiple choice n(%)			
Private practice	0	0	
Academics - research	0	0	
Academics - clinical educator	0	2 (67%)	+2 clinical
Academics - undecided focus	1 (33.3%)	0	educators
Undecided	2 (67.%)	1 (33.3%)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

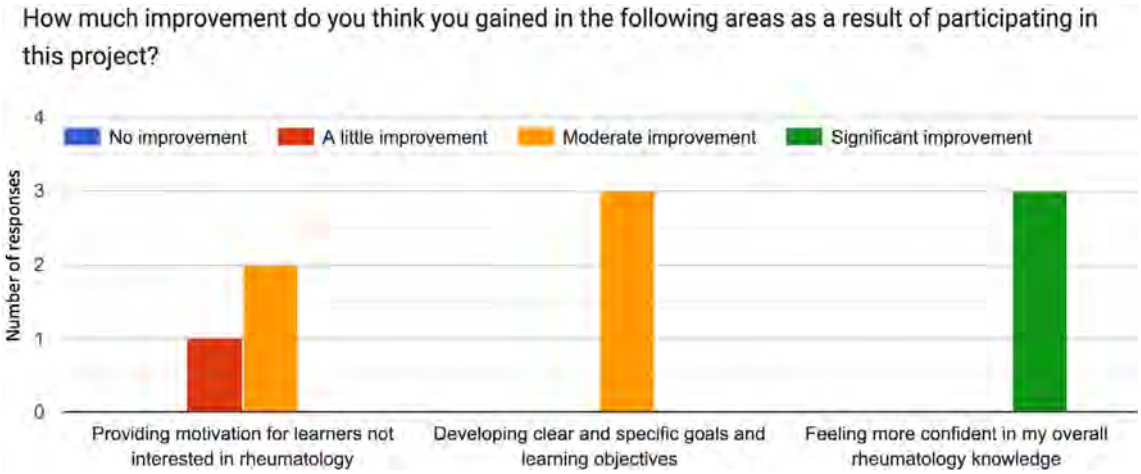


Figure 1: All fellows reported some level of improvement in key teaching skills. All fellows reported significant improvement in their personal overall rheumatology knowledge.

Results: A total of 15 internal medicine residents voluntarily completed at least one portion of the evaluations (n=12 pre-rotation quiz, n=8 post-rotation quiz; n=13 pre-rotation survey, n=7 post-rotation survey). Average pre-rotation quiz scores were 62.5% correct compared with 83.8% correct post-rotation (Table 1). The lowest area of confidence for learners was perception of the ability to treat scleroderma renal crisis (3.31 out of 10 confidence). The area of highest confidence for learners was perception of the ability to treat osteoarthritis (7.62 out of 10 confidence). Post-rotation, there was observed increase in self-assessed confidence in all surveyed areas, with the largest increase in treatment of scleroderma renal crisis (from 3.31 out of 10 confidence to 6.29 out of 10 confidence). Fellows reported increased confidence in overall teaching skills as well as ability to plan and deliver a successful teaching session (Table 2). All fellows reported significant improvement in their overall rheumatology knowledge as a result of participating in the project (Figure 1).

Conclusion: This project highlights the importance of dedicated rheumatology education within internal medicine and provides a unique way to directly engage rheumatology fellows in the education of medicine residents with mutually beneficial effects.

Disclosure: R. Bowman: None; **E. Huddleston**: None; **B. Lipham**: None; **A. Alexander**: None.

Abstract Number: 2191

Development, Validation and Performance of a Questionnaire for Assessing the Knowledge Base of Primary Care Physicians About Management of Rheumatoid Arthritis and Impact of an Information Course

Ranjan Gupta, Rudra Prosad Goswami and Anju Mohan, All India Institute of Medical Sciences, New Delhi, Delhi, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table – 1 Question-wise assessment of responses before and after the information course and the statistical significance of the change

S. No.	Question	Pre-Test Performance (n=293)			Post-Test Performance (n=76)			Statistical Significance (p<0.05)*
		Correct (%)	Incorrect (%)	I don't know (%)	Correct (%)	Incorrect (%)	I don't know (%)	Y/N
1.	Etiology of disease	73.7	19.1	7.2	82.4	16.2	1.4	N
2.	Hereditary nature	53.2	38.6	8.2	84.0	13.3	2.7	Y
3.	Causative Habits for RA	60.4	14.3	25.3	68.4	11.6	20.0	N
4.	Damage as a cause of joint pain in RA	60.1	36.2	3.8	76.3	23.7	0.0	N
5.	Dietary restrictions in RA	54.3	29.4	16.4	80.3	11.7	8.0	Y
6.	Extra-articular organ involvement	3.4	94.5	2.0	94.7	2.6	2.7	Y
7.	Complications of long-standing disease	44.0	50.2	5.8	76.3	21.0	2.7	Y
8.	Possibility of cure	60.8	36.8	2.4	82.9	15.8	1.3	Y
9.	Acceptable levels of SGOT and SGPT	35.2	49.8	15	72.4	20.9	6.7	Y
10.	Methotrexate Missed dose	79.9	13.2	6.8	84.2	11.8	4.0	N
11.	Drugs in leucopenia	43.3	46.8	9.9	77.6	17.1	5.3	Y
12.	Drugs in transaminitis	36.5	47.8	15.7	72.4	22.3	5.3	Y
13.	Drugs in thrombocytopenia	39.6	44.7	15.7	76.3	19.7	4.0	Y
14.	Leucocytosis management	49.5	38.6	11.9	69.7	26.6	6.7	Y
15.	Pancytopenia management	60.8	27.9	11.3	81.6	13.1	5.3	Y
16.	Transaminitis management	58.4	29.3	12.3	80.3	14.4	5.3	Y
17.	Repeat Rf and Anti-CCP	76.8	15.4	7.8	81.6	13.1	5.3	N
18.	Repeat ESR and CRP	85.7	9.5	4.8	90.8	7.9	1.3	N
19.	Drugs in raised ESR	40.6	49.2	10.2	73.7	21.0	5.3	Y
20.	Safe drugs in pregnancy	52.6	34.1	13.3	84.2	11.8	4	Y
21.	Duration of treatment in RA	74.7	16.4	8.9	89.5	7.8	2.7	Y
22.	Use of alternative medicine	64.8	22.6	12.6	82.9	11.8	5.3	Y
23.	Biologics	69.3	20.8	9.9	86.8	7.9	5.3	Y
24.	Onset of DMARDs action	53.9	33.8	12.3	80.3	11.7	8.0	Y
25.	Role of exercise in RA	45.1	28.9	26.0	44.7	38.0	17.3	N
26.	Role of exercise in RA	73.4	14.3	12.3	68.4	22.3	9.3	N
27.	Exercise from swollen/painful joints	58.4	30.3	11.3	44.7	48.7	6.7	N
28.	Prevention of joint damage	33.1	48.8	18.1	65.8	27.5	6.7	Y
29.	Energy conservation in RA	35.8	40.7	23.5	70.7	18.6	10.7	Y

Background/Purpose: Long-term outcomes in rheumatic diseases are impacted by their timely diagnosis, institution of correct treatment, management of complications and rigorous joint preservation strategies. The first point of contact in countries like India is the primary care physicians (PCP) who is either a general physician or an orthopaedician. Therefore, we designed this study to assess their knowledge base about various aspects of RA management and to show if this knowledge base could be improved by giving a short information course.

The aim of the study is to develop, validate and assess the performance of a self-prepared questionnaire for assessing PCP's knowledge about managing various aspects of RA and to use this tool to assess the impact of an information course in improving the above-mentioned elements among them.

Methods: A self-prepared questionnaire (in English) containing 29 multiple choice or true-false type questions with single correct answer assessing PCP's knowledge about RA in 3 domains (a. etiology, disease process, signs & symptoms b. drug therapy & monitoring c. joint protection, exercise, coping) was prepared. All questions had an item-level content validity index (I-CVI) of at least 0.9. The scale-level content validity index based on the universal agreement method (S-CVI/UA) was 0.8 for the whole questionnaire as assessed by 6 experts. All questions had an option of 'I don't know' which would prevent them from guessing the answer from the available options. Each question was given a score of 1 if answered correctly. The questionnaire was applied 2 times: at baseline and immediately after an information course to see the immediate impact. Information on the PCP's experience with treating RA and their specialty was also collected. Frequency data were compared using McNemar test for paired nominal data & kappa statistics for ordinal data. Student's paired t-test was used for comparison of mean scores to see the impact.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: At baseline, the questionnaire was applied to 293 PCPs (General Physicians: Orthopedicians = 81.2:18.8) and the mean(±SD) score was modest (16.68±6.027). Among these, 76 PCPs recorded a response after the information course. The option 'I don't know' was exercised 998 times (11.74%) before the information course which reduced to 127 (5.76%) times after the course.

After the information course, 26 out of 29 questions recorded a higher absolute number of correct responses than before the course. This increase in 20 out of 29 questions achieved statistical significance (Table–1). The mean(±SD) score for the questionnaire improved from 16.68(±6.027) to 22.2(±7.17) ($p< 0.001$) (Table-1).

The scores before the information course were significantly different among general physicians and orthopedics. However, after the information course, no difference was noted among their scores, which suggests that the information course was equally effective for PCPs from both specialties.

Conclusion: Indian PCPs have a modest knowledge base about various aspects of RA management which can be improved significantly by short information course. The information course is equally effective irrespective of their specialization background.

Disclosure: R. Gupta: None; **R. Goswami**: None; **A. Mohan**: None.

Abstract Number: 2192

Survey of Healthcare Providers' Knowledge and Attitudes Toward the Management of Uncontrolled Gout

Shilpa Sharan[1], Clare Sonntag[2], Beth Miller[1], Kaitlyn Mayer[1] and Nissreen Elfadawy[3], [1]The HWP Group, Upper Saddle River, NJ, [2]The HWP Group, Upper Saddle River, [3]University Hospitals, Geauga Medical Center, Chardon, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Although uncontrolled gout (UG) is an inflammatory arthritis triggered by crystallization of monosodium urate within joints following hyperuricemia, increasing evidence supports its classification as a systemic disorder with significant renal implications.[1] Despite this evolving paradigm, UG management remains fragmented across the specialties of rheumatology and nephrology. We deployed a survey intended to evaluate rheumatologists' and nephrologists' understanding of UG, elucidate their attitudes toward evolving UG management paradigms, and identify barriers to nephrology-led care across specialties.

Methods: A 10-question online survey was distributed to practicing rheumatologists and nephrologists. The survey assessed respondents' clinical demographics, UG classification preferences, UG management strategies, perceptions of nephrologists' role in UG care, and resources needed to support nephrologists' involvement. Descriptive statistics were used to summarize results.

Results: In total, 48 nephrologists and 13 rheumatologists completed the survey. The majority of respondents currently work in an academic setting (82%) and have been practicing for over 10 years (52%; **Fig. 1**). Although both specialties

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

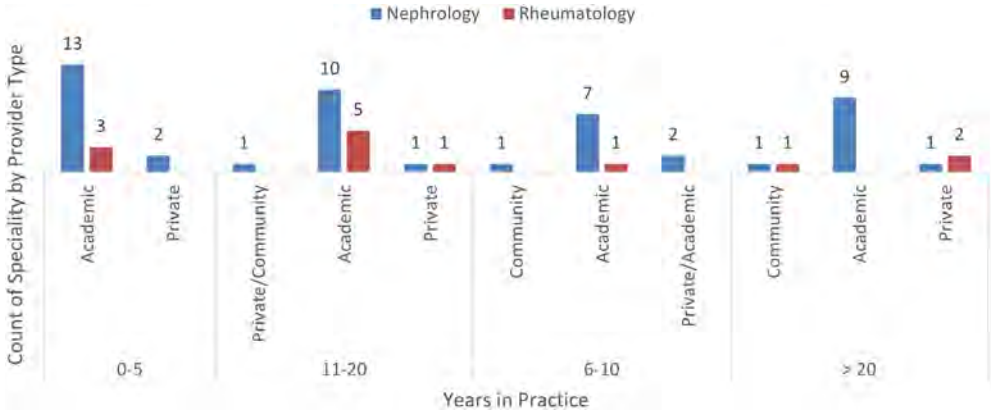


Figure 1. Respondents' clinical practice demographics.

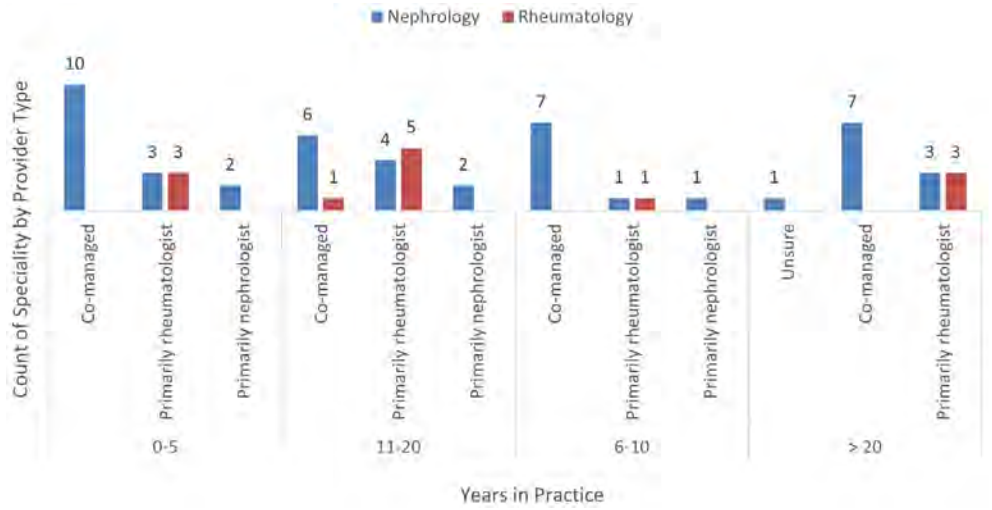


Figure 2. Respondents' preferred uncontrolled gout management approach.

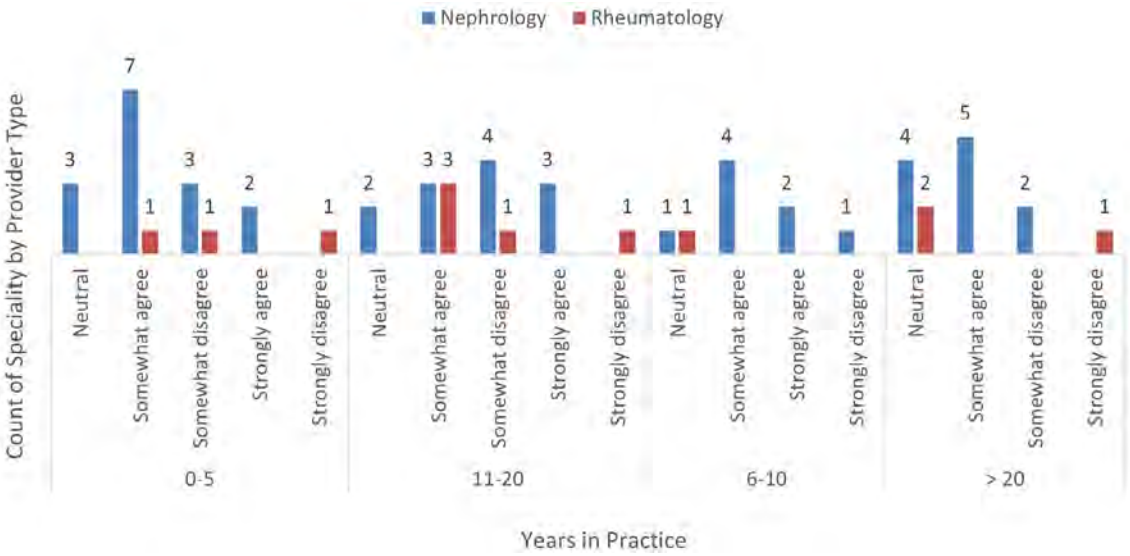


Figure 3. Respondents' expectations of nephrologist-led uncontrolled gout care over the next 5 years.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

largely agreed on the systemic nature of UG, respondents diverged sharply on preferred strategies for disease management. Rheumatologists overwhelmingly supported rheumatology-led care (92%). In contrast, 23% of nephrologists favored rheumatology-led care, 63% preferred co-management with a rheumatologist, and 10% believed that nephrologists should primarily manage UG (**Fig. 2**). Support of co-management across specialties was highest among early-career nephrologists (57% in 0-10 years) but declined with seniority (23% in >20 years). Similarly, 50% of early-career nephrologists (0-10 years) vs 20% of nephrologists practicing for over 10 years believe nephrologists will increasingly manage UG over the next 5 years. Only 31% of rheumatologists anticipated growing nephrology involvement in care over the next 5 years (**Fig. 3**).

Barriers to nephrology-led care were consistent across groups: unclear treatment guidelines, limited renal-safe therapies, and insufficient education/training. Academic nephrologists prioritized guidelines and renal-safe options, whereas those in private/community settings cited medication access as a barrier. Both groups emphasized the need for stronger collaboration to bridge specialty silos.

Conclusion: This survey reveals a shared recognition of the systemic complexity of UG, but specialists are not precisely aligned in how they envision its care. Although this expectation is not supported by rheumatologists, nephrologists—especially those early in their careers and in academic settings—anticipate playing a larger role in UG care. Across both groups, the lack of clear nephrologist-focused treatment guidelines, renal-safe treatment options, and formal collaboration pathways remain formidable obstacles. Empowering nephrologists through education, collaborative frameworks, and tailored treatment guidance may accelerate adoption of this evolving paradigm.

Reference: 1. Khanna P, et al. *J Clin Med*. 2020;9(10):3204.

Disclosure: S. Sharan: None; **C. Sonntag**: None; **B. Miller**: None; **K. Mayer**: None; **N. Elfadawy**: Amegn, 2, Astrazenca, 2, Otsuka, 2, Sobi, 2.

Abstract Number: 2193

Inpatient Rheumatology Consultations at a Tertiary Academic Medical Center: A Retrospective Cohort Study

Shivang Chaudhary[1], Ruizhi Huang[2], Roxann Kirkwood[2], Laura Upton[1], Paula Buchanan[2] and Adam Kilian[1], [1]Saint Louis University, St. Louis, MO, [2]Advanced Health Data (AHEAD) Institute, St. Louis, MO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatology consultations are essential for managing complex inpatient cases, yet patterns and outcomes remain understudied. Prior work has shown that consult data can inform fellowship curricula. This study characterizes the timing, indications, and diagnoses of inpatient rheumatology consults at a large academic hospital, with the goal of informing future educational initiatives and improving inpatient rheumatology care and training.

Methods: We performed a retrospective cohort study of inpatient rheumatology consults at a tertiary academic medical center from July 2021 to July 2024. Adult patients (≥18 years) admitted to non-rheumatology services and received an inpatient rheumatology consult were included. We analyzed timing, diagnostic categories, and impact using descriptive

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

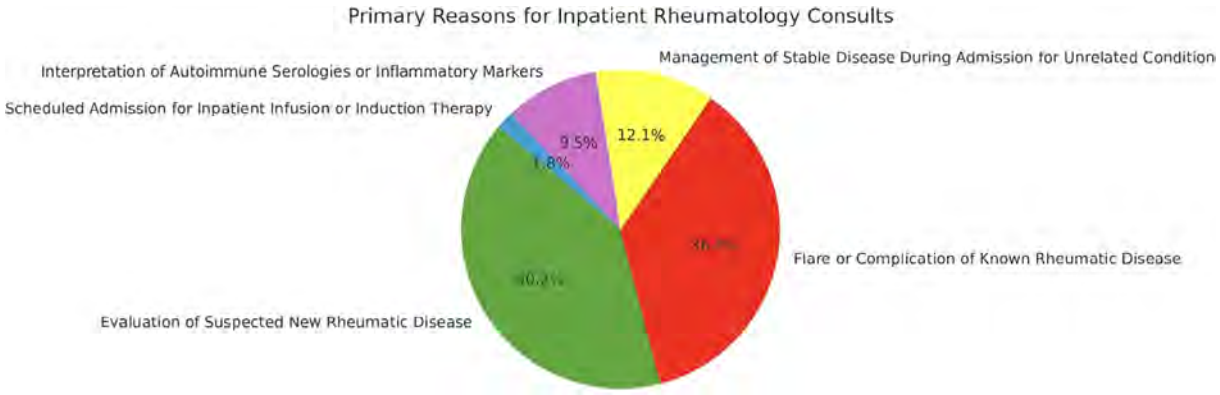


Figure 1: Distribution of the primary reasons for inpatient rheumatology consults

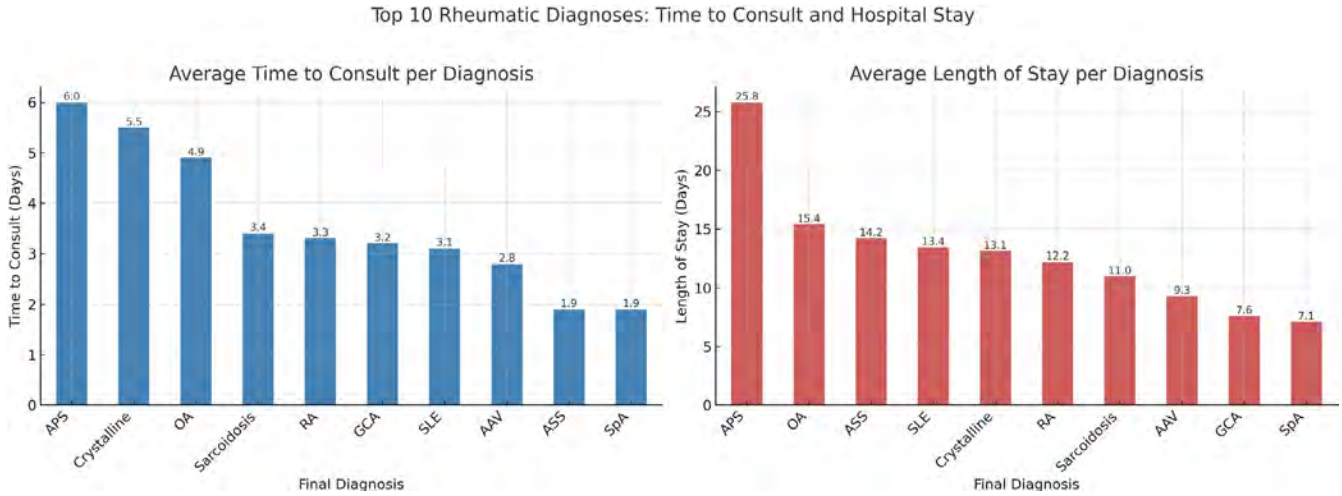


Figure 2: Average time to rheumatology consultation and hospital length of stay for the ten most common rheumatic diagnoses among inpatient consults.

statistics. Mann–Whitney U tests compared hospital stay duration and time to consult between patients with and without prior outpatient rheumatology follow-up. Significance was set at $p < 0.05$. All analyses were performed using RStudio (version 2023).

Results: Among 503 consults reviewed, the median time to consult was 1 day (mean 3.0), and average length of stay was 12.5 days. Most consults occurred on day 4 or later. The most common consult indications were suspected new rheumatic disease (40%) and flares of known disease (36%) (Figure 1). New rheumatic diagnoses were made in 21% of cases, most often crystalline arthritis (18), SLE (11), and necrotizing myopathy (8). Suspected new disease consults frequently resulted in non-rheumatic diagnoses (50%), while SLE (22%) and crystalline arthritis (10%) were the most common diagnoses among flares.

The most common rheumatic diagnoses were SLE (75), crystalline arthritis (36), RA (36), ANCA-associated vasculitis (15), spondylarthritis (14), OA (10), sarcoidosis (10), antisynthetase syndrome (9), GCA (9), and APS (8). Among these, APS had the longest average hospital stay (25.8 days) and longest mean time to consult (6.0 days). Crystalline arthritis and

Table 1: Impact of prior outpatient rheumatology follow up on inpatient consult timing and hospital stay

Variables	*Overall*	Yes	No	p
	N = 222	N = 92	N = 130	
Time to Consult, IQR	*2(1, 4)*	2(1, 3)	3(2, 5)	0.001
Length of Stay, IQR	*9(6, 16)*	9(6, 15)	9(5.25, 16)	0.873
Notes: Mann-Whitney U test				

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

sarcoidosis also had delayed consultations (5.5 and 3.4 days, respectively), while antisynthetase syndrome and SLE were linked to longer stays (14.2 and 13.4 days, respectively) (Figure 2).

Among patients with these diagnoses, those with outpatient rheumatology follow-up within 12 months were evaluated more promptly, with a median time to consultation of 2.0 days (IQR 1.0–3.0) versus 3.0 days (IQR 2.0–5.0) for those without ($p = 0.001$). Median length of stay was similar between groups (9.0 days; $p = 0.873$) (Table 1).

Conclusion: Inpatient rheumatology consults are often delayed and frequently involve diagnostic uncertainty, particularly for suspected new disease. Among the most common rheumatic diagnoses, conditions like APS, crystalline arthritis, and SLE were associated with longer consult times and extended stays, highlighting opportunities for earlier recognition. Patients with recent outpatient rheumatology follow-up were seen significantly earlier, underscoring the value of continuity. We hope to use these findings to identify data-driven educational targets for hospital providers and improve inpatient rheumatology care.

Disclosure: S. Chaudhary: None; **R. Huang**: None; **R. Kirkwood**: None; **L. Upton**: None; **P. Buchanan**: None; **A. Kilian**: Amgen, 2, 6, AstraZeneca, 2, 6.

Abstract Number: 2194

Utilizing Case-Based Learning to Teach the Teacher and Improve Health Insurance Literacy

Tyler Reese, Vanderbilt University Medical Center, Madison, TN

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2159–2194) Professional Education Poster
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: It is expected that pediatric rheumatology providers prepare adolescent and young adult (AYA) patients to successfully navigate the transition from a pediatric to an adult model of care. Health insurance literacy, and how to acquire health insurance, is one often neglected topic in this preparation. The loss of health insurance can be a highly disruptive event when transitioning to adult care and preparation in the pediatric clinic could reduce the incidence and duration of such an event. The Health Insurance Marketplace is a new way for many individuals to acquire health insurance at a significant discount; however, many pediatric providers have themselves never needed to navigate the health insurance marketplace and as a result may be unprepared to counsel patients on this topic.

Methods: This educational intervention utilized a case-based learning (CBL) technique to navigate the Healthcare.gov and consider health plans for an AYA in need of health insurance amongst pediatric rheumatology providers. It was hypothesized the pediatric rheumatology providers will have high health insurance literacy (as measured by the validated Health Insurance Literacy Measure (HILM)) but low familiarity with the health insurance marketplace (as measured by a novel Affordable Care Act (ACA) instrument) that will be improved following the CBL activity. Self-reported abilities were analyzed before and after as well. Two-tailed t-tests were used. Feasibility data were gathered for using the CBL tool in clinic with AYA patients.

Results: A total of 11 pediatric rheumatology providers, representing all providers in the division, participated in the intervention. 2 participants had incomplete data that was excluded. The minority of participants had ever needed to acquire individual health insurance (33.3%) or to navigate Healthcare.gov (33.3%). Time (100%) and knowledge (88.9%) were the most

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

HILM = Health Insurance Literacy Measure. 21 items with 4 item choices converting numerically to 1-4 with higher numbers indicated greater health insurance literacy. Possible scores range from 21 to 84. ACA = Affordable Card Act. 7 items (see Table 4 for individual items) with 1 correct and 3 incorrect answer choices. Possible scores range from 0 to 7 with higher numbers indicating a greater percentage of correct answers. Abilities were self-reported on 5 items (see Table 5 for individual items) on a score range from 0 to 100 using a sliding scale where 0 = strongly disagree, 50 = neutral, and 100 = strongly agree. Possible scores range from 0 to 500 with higher numbers indicating greater self-reported abilities.

Table 1 – Pre- and Post-Intervention Results

Participant	HILM Pre	HILM Post	ACA Pre	ACA Post	Abilities Pre	Abilities Post
2	70	77	4	7	239	423
3	64	64	3	6	315	358
5	68	68	5	6	335	466
6	56	71	4	7	268	497
7	75	76	2	5	200	385
8	42	71	4	6	244	444
9	64	75	4	6	220	381
10	77	64	5	7	309	436
11	54	73	3	6	189	425
Mean	63.33	73.22	3.78	6.22	257.67	423.89
Standard Deviation	11.10	5.74	0.97	0.67	52.45	43.82
p-value (t-test)		0.016		7.91E-06		3.24E-05

Table 2 - Feedback and Feasibility

(100 point sliding scale (0=strongly disagree, 50=neutral, and 100 = strongly agree))	Mean	SD
This learning activity could help patients learn more about health insurance	94.22	6.59
This learning activity could help providers learn more about health insurance.	96.11	5.44
I could complete this activity in clinic with patients.	58.00	23.99

frequent barriers to having health insurance discussions with patients. The pre-intervention and post-intervention results are displayed in Table 1 with significant improvements in the HILM, ACA instrument, and self-reported abilities. Quantitative feedback shown in Table 2 indicated that participants strongly agreed that the learning activity could help both patients and providers learn more about health insurance (mean 94.22 ± 6.59 and mean 96.11 ± 5.44 respectively on 100-point sliding scale). The result was more neutral if providers felt that they could complete this same learning activity in clinic with their patients (mean 58.00 ± 23.99). Time was noted as the greatest barrier by all participants in a free text response.

Conclusion: This study piloted the use of a CBL activity focused on navigating Healthcare.gov with pediatric rheumatology providers. It was hypothesized that most pediatric rheumatology providers would have a high health insurance literacy measured by the HILM but would have improvements in knowledge specific to the Affordable Care Act and Healthcare.gov. Contrary to the hypothesis, there were statistically significant improvements in both the HILM and ACA measures suggesting that providers may benefit more from this activity than anticipated.

Disclosure: T. Reese: None.

Abstract Number: 2195

Enhancing MTX and LEF Safety for Immunosuppressed Women of Childbearing Age with Rheumatic Diseases

Angela Bobak[1], Rhea Sharma[2], Jordan Jackson[3], Maritza Nary[2], Andrea Berger[4], Lifang Zhang[4] and Jonida Cote[5], [1]Geisinger Medical Center Rheumatology Fellowship, Danville, PA, [2]Geisinger Medical Center Internal Medicine Residency, Danville, PA, [3]Geisinger Medical Center Medicine-Pediatrics Residency, Danville, PA, [4]Geisinger Health System, Danville, PA, [5]Geisinger Health System, Wilkes-Barre, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The rates of contraceptive counseling and treatment in immunosuppressed women of childbearing age remain low in the United States, despite ACR's Reproductive Health Guidelines on recommended contraception and pregnancy planning. This study evaluated contraceptive counseling, treatment rates, and the role of a rheumatology-pharmacy collaborative effort in a rheumatology clinic.

Methods: This cross-sectional study of reproductive-aged women on MTX or LEF, examined the rates of contraception counseling and use. Patients were screened from the rheumatology clinic schedule from 11/1/2024-1/31/2025 for female gender at birth, age 14-45, rheumatic diagnosis, and prescribed MTX or LEF. They completed a survey assessing demographics, contraceptive counseling, and treatment. Review of the electronic health record (EHR) provided information on health insurance, education level, established gynecological care, and enrollment in rheumatology-pharmacy co-managed care. We compared the counseling and contraceptive treatment rates for all patients, co-managed patients, and usual care for patients with rheumatologist alone. Comparison of co-managed care vs rheumatologist care alone for counseling and treatment were made with Fisher's exact test.

Results: One hundred three patients were identified by EHR. Sixty-eight patients completed the survey, of which 22 were excluded due to hysterectomy or tubal ligation. The study population consisted of the remaining 46 patients, requiring contraceptive counseling. Of these patients,16 were excluded post-counseling due to reporting partner vasectomy or abstinence, leaving 30 patients with indication for contraception (Figure 1). The patient characteristics were average age of 36.1 years, 85% white, 41% receiving gynecologic care, 63% with commercial insurance, 70% with college or higher education, and 39% enrolled in rheumatology-pharmacy co-management vs 61% rheumatology care alone (Figure 2). Contraceptive counseling was documented in 40/46 (87%) of patients (Figure 3). Rheumatology-pharmacy co-management counseling was documented in 18/18 (100%) vs rheumatology alone 22/28 (79%) (p=0.0678) (Figure 3). Of the 30 patients indicated for contraception, 24/30 (80%) were using contraception (Figure 3). Contraceptive use was reported in 10/11 (91%) of co-managed patients vs 14/19 (74%) of rheumatologist managed alone (p=0.3717) (Figure 3). Comparing to national data, our rates were superior for both contraceptive counseling (87% vs 35-56%) (Thiel de Bocanegra, Health Serv Res Manag Epidemiol.2018;5) and contraceptive treatment (80% vs 45-52%) (Ingram, JCR.2019; 27(3), 97-101).

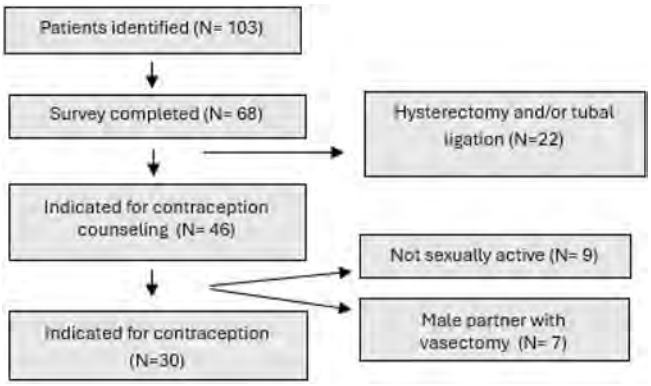


Figure 1. Patient stratification for contraception counseling and contraception use analysis. The initial patient screening revealed 103 qualifying patients. Only 68 surveys were completed. Patients who underwent a hysterectomy and/or tubal ligation were excluded from contraception counseling analysis, resulting in 46 patients indicated for counseling. Patients who endorsed they were not sexually active or had a male partner with a vasectomy were excluded from contraception use analysis, resulting in 30 patients indicated for contraception.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Patient characteristics. * The group categorized as "Other" included reported ethnicites of Asian, Black/African American, Multi-ethnic, and Arabic. The remaining patient characteristics, including patient age, receiving gynecologic care, primary insurance type, presence of higher education, and enrollment in the pharmacy co-management program, were obtained via EHR review of the 46 patients indicated for contraceptive counseling.

Patient characteristics	N (%)
Reported race/ethnicity	
Caucasian/White	39/46 (84.8%)
Hispanic, Latino, Spanish	2/46 (4.3%)
Other*	5/46 (10.9%)
Patient age range	
30-39	21/46 (45.7%)
<30	11/46 (23.9%)
>= 40	14/46 (30.4%)
Receiving regular gynecologic care	
Yes	19/46 (41.3%)
No	27/46 (58.7%)
Primary insurance	
Commercial	29/46 (63.0%)
Medicaid	14/46 (30.4%)
Medicare	1/46 (2.2%)
Unknown	2/46 (4.3%)
Presence of higher education	
Grade 12 or less	13/46 (28.3%)
Higher education	32/46 (69.6%)
Unknown	1/46 (2.2%)
Enrolled in pharmacy co-management program	
Enrolled	18/46 (39.1%)
Not enrolled	28/46 (60.9%)

Table 3. Contraception counseling and treatment rates with usual care of rheumatologist alone versus rheumatology-pharmacy co-managed care. We compared the counseling and contraceptive treatment rates for all patients, co-managed patients, and usual care patients with rheumatologist alone. Comparison of co-managed care vs rheumatologist care for counseling and treatment were made with Fisher's exact test. *The lower section of the table is limited to the subset of patients indicated for contraception.

	Total patients	Pharmacy co-management	No pharmacy co-management	p-Value
Indicated for counseling	46	18/46 (39%)	28/46 (61%)	
Documented contraception counseling	40/46 (87%)	18/18 (100%)	22/28 (79%)	p=0.0678
No documented contraception counseling	6/46 (13%)	0/18 (0%)	6/28 (21%)	
Indicated for contraceptive treatment	30*	11/30 (37%)	19/30 (63%)	
Reported contraceptive use	24/30 (80%)	10/11 (91%)	14/19 (74%)	p=0.3717
No reported contraceptive use	6/30 (20%)	1/11 (9%)	5/19 (26%)	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our overall contraceptive counseling and treatment were superior to the national average. All patients who enrolled in the rheumatology-pharmacy co-management received counseling and 91% received treatment. This trend suggests that our co-management has contributed to our higher rates of both contraceptive counseling and treatment; however the analysis is underpowered due to the small co-managed population. This study indicates that we have made meaningful progress toward enhancing the safety of care provided to women with rheumatic diseases.

Disclosure: A. Bobak: None; **R. Sharma**: None; **J. Jackson**: None; **M. Nary**: None; **A. Berger**: None; **L. Zhang**: None; **J. Cote**: None.

Abstract Number: 2196

Recognition and Treatment of Idiopathic Granulomatous Mastitis: A Case Series

Jenny Solomon[1], Julie Piccione[1], Julie Nusbaum[2], Steven Carsons[3] and Gregg Blumberg[1], [1]NYU Langone Long Island, Mineola, [2]NYU Langone Health, New York, NY, [3]NYU Long Island School of Medicine, Mineola, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic Granulomatous Mastitis (IGM) is a rare benign inflammatory condition of the breast usually affecting women of childbearing age with a history of breastfeeding. It is characterized clinically by breast pain, erythema, mass(es), and recurrent or non-healing wounds, and is diagnosed histologically by the presence of non-necrotizing granulomatous lesions. It is theorized that when ductal epithelium is damaged, like in milk stasis, luminal secretions leak into surrounding lobular connective tissue and trigger the recruitment of macrophages and lymphocytes, causing local inflammation. It can be difficult to distinguish IGM from infectious mastitis or inflammatory breast cancer, often delaying diagnosis. The treatment of IGM largely consists of surgical intervention, local steroids, systemic steroids, and/or disease modifying anti-rheumatic drugs (DMARDs) without a universally accepted treatment algorithm.

Methods: Here, we present 8 patients evaluated in the NYU-Langone Long Island rheumatology academic office in 2025 diagnosed with IGM via histology and explore the patients' demographics, management, and outcomes after referral to rheumatology via chart review. We obtained IRB approval, s25-00399. We reviewed imaging of the affected areas, histopathology, and microbiology data.

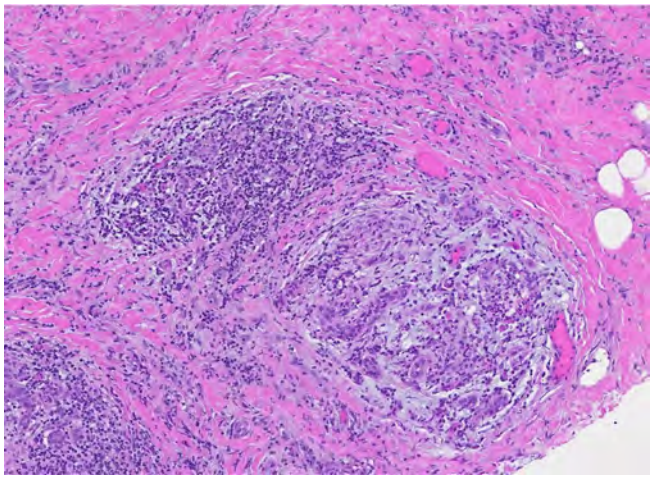
Results: 8 cases were included, all of which were biological females. 3 patients (37.5%) identified as Hispanic, 3 (37.5%) identified as Asian (including East and Southeast Asian), and 2 (25%) identified as European/Caucasian. 50% used oral contraception. Radiographic information from patients' ultrasounds and/or mammograms was especially notable for 62.5% of cases containing tubular components, which is a more unique finding to IGM. 100% of patients underwent biopsy and histopathologic features included granulomatous inflammation (100%), fibrosis (25%), mastitis (25%), and necrosis (12.5%). All 8 patients in the series had healing of wounds, resolving of pain, and diminishing mass sizes. 7 patients (87.5%) were treated with prednisone with symptom improvement, with the addition of methotrexate in the 4 refractory cases (50%). 4 patients (50%) underwent multiple procedures including incision and drainage.

Conclusion: Greater understanding and recognition of IGM may expedite diagnosis and reduce morbidity. When histopathologic diagnosis of IGM is made, rheumatology referral should be made promptly. Our patients had a gap of approximately

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographics	
Sex	
Female	8
Male	0
Median Age of Diagnosis (Years)	35.5
Ethnicity	
Hispanic	3
Bengali	2
Asian	1
European	1
Caucasian	1
Median Number of Pregnancies	1.5
Median Number of Deliveries	1.5
Oral Contraception Use	
Yes	4
No	4
Ultrasound Findings	
Ill-defined mass/hyperechoic/hypoechoic area	7
Lymphadenopathy	2
Dilated/ Debris-filled ducts	3
Diffuse edema	1
Inflammation	1
Tubular Component	5
Biopsy Results	
Granulomatous inflammation	8
Fibrosis	2
Mastitis	2
Necrosis	1
Mean Time to Rheumatology Evaluation (Weeks)	10
Number of Surgical Procedures (including biopsy and incision/drainage)	
1	4
2	2
3 or more	2
Treatment	
Colchicine	1
Prednisone	7
Methotrexate	3
Patients with Flare Requiring Escalation of Therapy	4

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Lobulocentric mastitis with acute and chronic inflammation evidenced by neutrophils and lymphocytes including few giant cells and focal ill-defined granuloma formation.

10 weeks from diagnosis of IGM to first rheumatology visit, with no further surgical procedures after rheumatology medical management. Patients often underwent multiple procedures including incision and drainage prior to diagnosis, which in conjunction with the inflammatory state of the breast, led to high risk of poor wound healing. This suggests earlier rheumatological evaluation may lead to swift treatment with glucocorticoids and DMARDs, resolution of symptoms, and prevention of deformity from repetitive surgical procedures. Our case series adds data to the knowledge base about IGM and may contribute to the development of treatment guidelines for the future.

Disclosure: J. Solomon: None; **J. Piccione**: None; **J. Nusbaum**: None; **S. Carsons**: None; **G. Blumberg**: None.

Abstract Number: 2197

Mechanisms of Fetal Growth Restriction in Rheumatologic Autoimmune Diseases: Insights into Placental Pathology and Immune Dysregulation

Larabe Farrukh[1], Ananya Venkatesh[2], Mana Parast[2] and Chelsey Smith[3], [1]University of California San Diego, San Diego, CA, [2]University of California San Diego, San Diego, [3]University of California San Diego, LA JOLLA, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Fetal growth restriction (FGR) significantly contributes to adverse pregnancy outcomes (APOs) in women with rheumatologic diseases. Understanding the immunopathologic mechanisms underlying FGR is critical for risk stratification and management. The objective of this study is to systematically review the immunologic/vascular mechanisms underlying FGR in systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS), rheumatoid arthritis (RA), systemic sclerosis (SSc), ANCA-associated vasculitis (AAV), and seronegative spondyloarthropathies (SpA), and to characterize mechanistic pathways linking autoimmunity to FGR.

Methods: We conducted a systematic search of PubMed and Google Scholar for studies published between 1995 and 2024 that evaluated placental pathology, immune dysregulation, and pregnancy outcomes in women with rheumatologic diseases. Eligible studies included prospective cohorts, retrospective analyses, and placental histopathology investigations. Findings were synthesized narratively due to the heterogeneity of mechanisms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In SLE and APS, abnormal complement activation, impaired angiogenic signaling, and trophoblast dysfunction contribute to placental insufficiency and FGR. Elevated levels of complement activation products (Bb, sC5b-9) throughout gestation were associated with APOs. In APS, anti-phospholipid antibodies induce trophoblast apoptosis, impair spiral artery remodeling, promote thrombosis, and placental infarction. In RA, cytokine dysregulation, including elevated IL-6 and TNF-α levels and decreased IL-10, were linked to decidual vasculopathy and reduced pro-angiogenic signaling, contributing to low birth weight and preterm birth. In AAV, injury to the syncytiotrophoblasts and endothelial cells of the spiral veins can lead to chorangiosis and focal placental infarction associated with FGR and pre-eclampsia. In SSc, extensive decidual vasculopathy, stromal fibrosis, and hypoperfusion of chorionic villi led to high rates of FGR, preterm birth, and stillbirth. In SpA, elevated rates of preterm birth and cesarean delivery were observed, with limited but suggestive evidence of inflammatory placental lesions. Across diseases, impaired trophoblast function, vascular remodeling, and angiogenic imbalance emerged as overlapping mechanisms of placental insufficiency.

Conclusion: Autoimmune rheumatic diseases contribute to fetal growth restriction through diverse pathways involving immune-mediated placental injury and vascular dysfunction. Early identification of at-risk pregnancies and targeted therapeutic interventions addressing these mechanisms may improve neonatal outcomes. Further research is warranted to delineate disease-specific versus shared pathways to guide precision management strategies.

Disclosure: L. Farrukh: None; **A. Venkatesh**: None; **M. Parast**: None; **C. Smith**: AstraZeneca, 1.

Abstract Number: 2198

Sociocultural Influences on Pregnancy Planning for Individuals Diagnosed with SLE in an Urban Hispanic Population: A Qualitative Study with Considerations for a Holistic Approach

Andrew Ramirez[1], Alexa Montes de Oca[1], Martha Delgado[1], Mellissa withers[1] and **Leanna Wise**[2], [1]University of Southern California, Los Angeles, [2]LAGMC/Keck Medicine of USC, Los Angeles

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: As systemic lupus erythematosus (SLE) often affects women of child-bearing age, understanding how this population makes reproductive health decisions is critical for well-rounded healthcare. Individuals often need more than just SLE medical optimization to feel comfortable with attempting pregnancy; many extrinsic, non-medical factors play a role. In this qualitative thematic analysis study, we explored the perspectives of female participants of Hispanic ethnicity diagnosed with SLE to understand sociocultural non-clinical factors that influence pregnancy planning and contraception use.

Methods: We conducted a qualitative study using semi-structured interviews with 30 Hispanic women diagnosed with SLE, recruited from Los Angeles General Medical Center and LupusLA. Eligible participants were aged 18–45, of Hispanic ethnicity, sexually active with a male partner or considering pregnancy within three years, and fluent in English or Spanish. Interviews were conducted virtually in the participant's preferred language, recorded, and transcribed; Spanish interviews were translated into English. Interviews were conducted from June 2024 – March 2025. Sociocultural influences were collected via interview questions asking what non-clinical factors play a role in participants' decision-making to attempt pregnancy and/or use contraception, with a focus on participants' significant others, family, and sociocultural background. Data

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Participant demographics and clinical characteristics

Characteristics	English Interview Participants (n = 17)	Spanish Interview Participants (n = 13)
Age at time of interview (years)	32.47 ± 7.22	36.08 ± 7.71
Average length of time since SLE diagnosis at time of interview (years)	12.64 ± 6.60	12.46 ± 6.82
U.S. born	9 (52.94)	1 (7.69)
LAGMC recruitment	10 (58.82)	13 (100)
Any college education	12 (70.59)	3 (23.08)
Ever pregnant	9 (52.94)	11 (85.62)
Unplanned pregnancy after SLE diagnosis*	4 (23.53)	7 (53.85)
Desire for future pregnancy	11 (64.71)	8 (61.54)
Ever diagnosis of lupus nephritis	5 (29.41)	9 (69.23)

Data presented as mean ± SD or number of patients (%).

*Unplanned pregnancy defined as a pregnancy conceived when the individual was not actively intending/expecting to become pregnant with intercourse

Table 2. Themes, subthemes, and representative quotes from grounded theory analysis on sociocultural influences for pregnancy planning

Theme	Representative quotes
1. Financial, and to some, career stability, are extremely crucial when planning to conceive	"I wouldn't consider having a kid until I'm closer to 30 with a stable partner in a stable home with a stable income and little more used to and acclimated to my profession and everything". (25yo; English-speaking, 1 child; SLE for 13 years) "A human being comes into the world, and if you make that decision, it should be so that this human being can have a full life. And now, in these times, we think a lot about the economic aspect, about whether they'll have the opportunities they deserve." (34yo; Spanish-speaking; 2 children; SLE for 18 years)
2. Family support – significant other and primarily female family members have varying input	"Basically, [my partner] always told me, 'Whatever you decide, it's your body.] He saw how bad things were for me. I was in a life-threatening situation—essentially, one foot on the other side. He had to decide between me or the baby, and he chose me. But thank God, my son is fine […] it was scary for him too. I think that's why we decided not to have more children. We talked about it a lot beforehand and just decided no." (43yo; Spanish-speaking; 2 children; SLE for 18 years) "I've mentioned to my mom and my sister that we were discussing maybe having another child [...] my mom doesn't think it's a good idea. She's really, 'no, no, no, no, no. You're doing well like it is, and, you know, we're thankful everything went well with [your son]. And then I think you should just stop right there'. My sister, same thing" (44yo; English-speaking; 1 child; SLE for 25 years)
3. Background religious/cultural views have some influence on reproductive health *This participant noted the following regarding reproductive health in contemplation of her first and only pregnancy after SLE diagnosis.* *This participant was asked about how she would approach an unintended pregnancy regardless of disease control.* *A Spanish-speaking patient noted that reproductive health topics may be communicated less well because of cultural stigma (similar concerns were also voiced by English-speaking participants).*	"At the end of the day, you're not in control of it. The only person who's in control of it is God. And you know, if you're going to decide to let it go and just let him be the one to kind of take the wheel, then you got to do it, like 100%. It was those conversations where it's like you can't just keep going into the what ifs, because you're not in control anymore, you know. So I think that was helpful for me, where it was like, okay, God, let's do this together and figure this out. You're here by my side, just like the whole time I was pregnant, going to church every Sunday and seeing it through and taking it day by day [...] If you keep thinking you're going to be able to control everything, you're going to make yourself sick" (38yo; English-speaking; 1 child; SLE for 15 years) "Oh, look, I'm going to keep [him, past unplanned male pregnancy] because it's a miracle. I said, I didn't think I was going to get pregnant anymore. So yeah, it was more like that's my third child. That's how it happened. Oh, well, he's already here, you know? God sent him for a reason. I'm, you know, like, I'm going to keep this baby" (41yo; English-speaking; 3 children; SLE for 21 years) "It's very important that we know about [reproductive health and lupus] because there are a lot of fears, a lot of dread. I think there are women who decide, 'Oh, I'd rather not get pregnant because I don't want to know what could happen to me.' They don't even ask the questions they need to ask because they're afraid, or because the information isn't out there, or because it's not communicated well. And in our culture, I feel like it's still a taboo subject to talk about these things." (34yo; Spanish-speaking; 2 children; SLE for 18 years)
4. Online resources provide a diversity of information; some helpful/encouraging and some overwhelming *These quotes were in response to participants being asked about any other sources of reproductive health information that influence the way they view pregnancy.*	"Honestly, now that I'm thinking about it, it really was that support group that I was like ok, I think I can do this [attempt conception] [...] You're giving me that emotional and mental strength to be able to be like, I'm not alone, I can do this. Yes, it might not be a pretty picture. But they would talk about their kids and how much joy, and I was like, yes. Like I want this, and I want to try" (38yo; English-speaking; 1 child; SLE for 15 years) "I've actually kind of strayed away from the support groups because it's a lot of bad news. And sometimes it's hard to willingly sign up to listen to bad news." (28yo; English-speaking; no children; SLE for 10 years) "And the internet, really—all the tools and information you could possibly need, the internet is a very good source. Like Google or ChatGPT, things like that. They're good tools for accessing any kind of information you might want." (26yo; Spanish-speaking, no children; SLE for 11 years)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

collection continued until thematic saturation was reached, and transcripts were analyzed using a grounded theory approach to identify sociocultural themes related to reproductive health decision-making. Coding was conducted by a multilingual, multidisciplinary team.

Results: A total of 17 English-speaking participants and 13 Spanish-speaking participants were interviewed (Table 1). Four sociocultural themes (Table 2) arose in both language groups which strongly influence patients' views on pregnancy: 1) financial/career security; 2) support of their family (significant others and extended family support); 3) underlying cultural or religious beliefs (largely being against termination for unexpected pregnancy unless absolutely necessary, as well as divine control of the reproductive journey; 4) virtual media (a spectrum of both positive/negative influence). These themes emerged consistently among both English- and Spanish-speaking participants.

Conclusion: For women diagnosed with SLE, addressing reproductive health decision-making requires the clinician to approach the patient from a holistic perspective that considers the complex social and cultural factors influencing pregnancy decisions. While many patients with SLE should be timing pregnancy to be medically safe, our patient-reported qualitative data also demonstrates that pregnancy planning (or avoiding) is heavily influenced by non-medical extrinsic factors. Clinicians who acknowledge and address these factors may be better equipped to support patients in navigating pregnancy planning safely and confidently, promoting shared decision-making that aligns with patients' lived experiences and values.

Disclosure: A. Ramirez: None; **A. Montes de Oca**: None; **M. Delgado**: None; **M. withers**: None; **L. Wise**: AstraZeneca, 1, 6, 7, Aurinia Pharma, 5, 6, GlaxoSmithKlein(GSK), 6.

Abstract Number: 2199

Disparities in Reproductive Health Counseling Among Hispanic Women with Autoimmune Rheumatic Diseases: Insights from a Patient-Reported Survey in an Urban Safety-Net Setting

Eaman Alhassan[1], Laura Kobashigawa[2], Vanessa Ramos[2], Jack Rodman[2] and **Leanna Wise**[3], [1]University of Pittsburgh Medical Center, Pittsburgh, PA, [2]University of Southern California, Los Angeles, [3]LAGMC/Keck Medicine of USC, Los Angeles

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Reproductive-age Hispanic women with rheumatoid arthritis, juvenile idiopathic arthritis (combined, inflammatory arthritis; IA), and systemic lupus erythematosus (SLE) often bear a higher disease burden and experience worse outcomes compared to other populations. In addition, careful attention must be given to appropriate medication use and contraception use during childbearing years. While the 2020 ACR Reproductive Health Guideline provides recommendations for contraception counseling, little is known about how these are experienced by patients in under-resourced settings. We examined patient-reported experiences with reproductive health counseling and contraceptive practices in an urban safety-net clinic.

Methods: An anonymous survey was administered to 304 women (aged 18–50) with SLE or IA at Los Angeles General Medical Center, a public hospital serving a predominantly Hispanic, state-insured population in urban east Los Angeles. The survey was based on topics from the 2020 ACR Guideline for the Management of Reproductive Health in Rheumatic

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Significant demographic associations between survey language groups

	Total Population (n = 304)	Arthritis (n = 151)	Lupus (n = 153)	p-value
Age	39.31 (8.87)	41.87 (7.23)	36.75 (9.62)	<0.01*
Ethnicity				<0.01*
Hispanic	274 (91.03%)	147 (98.00%)	127 (84.11%)	
Non-Hispanic	25 (8.31%)	3 (2.00%)	22 (14.57%)	
Prefer not to state	2 (0.66%)	0 (0.00%)	2 (1.32%)	
Survey Language				
English	112 (37.10%)	26 (17.22%)	86 (56.95%)	<0.01*
Spanish	190 (62.91%)	125 (82.78%)	65 (43.05%)	
Education level				<0.01*
Less than high school	102 (34.11%)	75 (50.00%)	27 (18.12%)	
High school diploma or equivalent	129 (43.14%)	53 (35.33%)	76 (51.01%)	
Technical/vocational training	38 (12.71%)	13 (8.67%)	25 (16.78%)	
Bachelor's degree	29 (9.70%)	9 (6.00%)	20 (13.42%)	
Master's degree or above	1 (0.33%)	0 (0.00%)	1 (0.67%)	
Marital Status				0.02*
Never married	106 (35.57%)	39 (26.35%)	67 (44.67%)	
Married, or in a domestic partnership	125 (41.95%)	72 (48.65%)	53 (35.33%)	
Widowed	4 (1.34%)	2 (1.35%)	2 (1.33%)	
Divorced or separated	45 (15.10%)	26 (17.57%)	19 (12.67%)	
Prefer not to state	18 (6.04%)	9 (6.08%)	9 (6.00%)	
Nativity				
Born in the United States	74 (24.67%)	23 (15.33%)	51 (34.00%)	<0.01*
Born outside of the United States	226 (75.33%)	127 (84.67%)	99 (66.00%)	

Numbers represent frequency (column percent) for categorical variables and mean (standard deviation) for continuous variables.
*Significant at $p \leq 0.05$

and Musculoskeletal Diseases, and was administered in English or Spanish. Multivariable logistic regression was used to assess factors associated with receiving contraception counseling and patients' perceptions of their physicians' reproductive health knowledge.

Results: Most respondents (91%) identified as Hispanic, and 63% completed the survey in Spanish (Table 1). Only 51% reported receiving contraception counseling in the past year. English-speaking participants had significantly *higher* odds of receiving such counseling compared to Spanish speakers (OR 3.93; 95% CI 1.82-8.51; p< 0.01) (Table 2). Spanish-speaking individuals were *less likely* to perceive their physician as knowledgeable about reproductive health (OR 0.46; 95% CI 0.22-0.95; p=0.04) (Table 3). Furthermore, each additional year in age was associated with a 4% *lower* odds of reporting contraception counseling in the past year (OR: 0.96; 95% CI 0.92-0.99; p=0.02), as well as a 5% *lower* odds of confidence in their rheumatologist's knowledge to address reproductive health and rheumatic disease (OR 0.95; 95% CI 0.91-0.99; p< 0.01) (Table 2, Table 3). Among sexually active patients on teratogenic medications who were not trying to conceive, those who received contraception counseling had increased odds of using long-acting reversible contraception (OR 5.69; 95% CI 1.38-23.48; p=0.02). Notably, 27% of these patients reported no contraceptive use.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariable analysis of factors influencing patient-reported contraception counseling

Variable	Adjusted Odds Ratio** (95% CI)	P value
Disease type: Arthritis vs. Lupus (ref)	0.92 (0.53, 1.61)	0.77
Age	0.96 (0.92, 0.99)	0.02*
Survey Language: English vs Spanish (ref)	3.93 (1.82, 8.51)	<0.01*
Marital Status (married ref)		
Never Married	1.23 (0.64, 2.39)	0.41
Widowed	0.78 (0.09, 7.05)	0.83
Divorced or separated	0.91 (0.43, 1.94)	0.94
Prefer not to state	0.83 (0.28, 2.45)	0.80
Place of birth: United States (US) vs. Not in the United States (US) (ref)	0.59 (0.26, 1.35)	0.21

*Indicates significant p value
**Each factor is adjusted for all covariates in the model

Table 3. Multivariable analysis of influences on patient-reported perception of physician knowledge on reproductive health and rheumatic disease

	Adjusted Odds Ratio** (95% CI)	P value
Disease type: Lupus vs. Arthritis (ref)	2.35 (1.30, 4.24)	<0.01*
Age	0.95 (0.91, 0.99)	<0.01*
Survey Language: Spanish vs. English (ref)	0.46 (0.22, 0.95)	0.04*

*Indicates significant p value
**Each factor is adjusted for all covariates in the model

Conclusion: Spanish-speaking and older patients with SLE or IA were significantly less likely to receive reproductive health counseling or feel confident in their rheumatologist's ability to address the intersection of reproductive health and rheumatic disease. However, counseling was strongly associated with the use of highly effective contraception for patients on teratogenic medications. These findings underscore the importance of integrating proactive and culturally informed reproductive health counseling into the rheumatology clinic to improve patient safety and equity.

Disclosure: E. Alhassan: None; **L. Kobashigawa**: None; **V. Ramos**: None; **J. Rodman**: None; **L. Wise**: AstraZeneca, 1, 6, 7, Aurinia Pharma, 5, 6, GlaxoSmithKlein(GSK), 6.

Abstract Number: 2200

Obstetric and Neonatal Complications in Women living with Axial Spondyloarthritis: a population-based, matched cohort study

Sinead Maguire[1], John Snelgrove[2], Priscila Pequeno[3], Michael Paterson[4], Fangyun Wu[4], Laura Passalent[5], Anthony Perruccio[6], Dharini Mahendira[7], Elie Karam[8], Robert Inman[9] and Nigil Haroon[10], [1]Our Lady's Hospital Navan, Dublin, Dublin, Ireland, [2]Mount Sinai Hospital, Toronto, Canada, [3]Institute for Clinical Evaluative Sciences (ICES), Toronto, Canada, [4]Institute of Clinical & Evaluative Sciences, Toronto, Canada, [5]Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada, [6]Schroeder Arthritis Institute and Krembil Research Institute, University Health Network, Toronto, Canada, [7]St Michael's Hospital, Toronto, Canada, [8]Canadian Spondylitis Association, Toronto, Canada, [9]University Health Network, Toronto, ON, Canada, [10]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Women with axial spondyloarthritis (axSpA) are frequently diagnosed during their childbearing years. While studies have reported on pregnancy complications in this population, deriving generalizable prevalence estimates has been hampered by smaller study cohorts. Where reported, there is a concerning trend toward increased pregnancy complications in axSpA compared to the general population. Severe maternal morbidity (SMM) is a serious adverse physical or psychological event related to pregnancy which negatively impacts maternal health. Clinically recognized in the general population, SMM has not been studied in women with rheumatic diseases, including axSpA.

The aim of this study was to determine if there is a higher prevalence of pregnancy and neonatal complications, including SMM, in women with axSpA compared to women in the general population.

Methods: This was a population-based cohort study of administrative healthcare data from Ontario, Canada. Primary data source was the Mombaby Database, allowing near-complete capture of all hospital-based livebirths and stillbirths. The study included all women aged 10 to 55 years with a livebirth recorded between April 1st, 2002 and March 31st, 2020. Diagnosis of axSpA was based on the presence of an axSpA diagnosis code on at least two healthcare claims within a two-year period with at least one made by a Rheumatologist. Pregnancies in axSpA women were matched in a 1:5 ratio with pregnancies of women without axSpA (controls) according to maternal age, year of first pregnancy, and geographic location. Prevalence of pregnancy and neonatal outcomes were compared between axSpA women and controls. Multivariable logistic regression was used to identify factors associated with SMM in axSpA pregnancies.

Table 1: Pregnancy characteristics & maternal outcomes among women with axSpA and matched controls

	Controls	AxSpA Pregnancies	*p value*
n	26,350	5,176	
Maternal age at delivery (years) *Mean (SD)*	31.24 ± 5.09	31.20 ± 5.12	0.60
Gestation age at delivery (weeks) *Mean (SD)*	38.77 ± 2.02	38.61 ± 2.00	<0.01
Gestational diabetes	1,745 (6.6%)	386 (7.5%)	0.03
Preterm Prelabour rupture of membranes (PPROM)	2,829 (10.7%)	566 (10.9%)	0.67
Caesarean section	7,840 (29.8%)	1,529 (29.5%)	*0.76*
Fetal growth restriction (FGR)	657 (2.5%)	143 (2.8%)	0.26
Pre-eclampsia	430 (1.6%)	80 (1.5%)	0.65
Eclampsia	23 (0.1%)	6 (0.1%)	0.53
Gestational hypertension	1,243 (4.7%)	226 (4.4%)	0.27
Antepartum haemorrhage	170 (0.6%)	48 (0.9%)	0.03
Postpartum haemorrhage	101 (0.4%)	29 (0.6%)	0.07
Maternal ICU admission	82 (0.3%)	20 (0.4%)	0.38
Puerperal infection	75 (0.3%)	19 (0.4%)	0.32
Maternal death	6 (0.0%)	<=5*	0.51
Severe Maternal Morbidity	970 (3.7%)	227 (4.4%)	0.02

**Suppressed to protect patient privacy*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Neonatal Outcomes in axSpA and non-axSpA (control) pregnancies

	Control Pregnancies	AxSpA Pregnancies	p value
n	26,350	5,176	
Birthweight (grams)			
Mean (SD)	3,365.64 ± 593.21	3,352.98 ± 596.63	0.16
Median (IQR)	3,391 (3,055-3,730)	3,385 (3,040-3,735)	0.24
Preterm Birth	2,129 (8.1%)	503 (9.7%)	<0.01
Spontaneous	849 (3.2%)	189 (3.7%)	0.11
Physician Induced	1,230 (4.7%)	301 (5.8%)	<0.01
Very PTB (<32 weeks)	387 (1.5%)	81 (1.6%)	0.60
Low Birth Weight	276 (1.0%)	53 (1.0%)	0.88
NICU admission	3,435 (13.0%)	711 (13.7%)	0.17
Congenital abnormality	1,112 (4.2%)	231 (4.5%)	0.43
Neonatal death	77 (0.3%)	10 (0.2%)	0.21
Severe Neonatal Morbidity	1,591 (6.0%)	337 (6.5%)	0.19
Sepsis	191 (0.7%)	37 (0.7%)	0.94
Respiratory Distress	365 (1.4%)	70 (1.4%)	0.85
Need for resuscitation	50 (0.2%)	12 (0.2%)	0.53
Need for ventilatory support	1,061 (4.0%)	219 (4.2%)	0.50

Results: In total, 3,010 women with axSpA were matched with 15,050 non-axSpA controls, each contributing 5,176 and 26,350 study pregnancies, respectively. Most of axSpA and control women were nulliparous (70.9% vs 72.7%, p=0.72), and median age was 31 years. For pregnancy complications, gestational diabetes (7.5% vs 6.6%, p=0.03), antepartum haemorrhage (0.9% vs 0.6%, p=0.03), and SMM (4.4% vs 3.7%, p=0.02) were significantly more prevalent in axSpA pregnancies (Table 1). For neonatal complications, preterm birth was more prevalent in axSpA pregnancies (9.7% vs 8.1%, p< 0.01) (Table 2). In multivariable analyses, factors associated with SMM in axSpA women were maternal age (aOR 1.03, 95% CI 1.00-1.06), comorbidity burden (defined by the Elixhauser Comorbidity Index; aOR 1.27, 95% CI 1.16-1.38), and gestational age at delivery (aOR 0.76, 95% CI 0.73-0.78) (Table 3).

Table 3: Factors associated with Severe Maternal Morbidity (SMM) in AxSpA Pregnancies

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p value	aOR (95% CI)	p value
Maternal age at delivery	1.03 (1.00, 1.06)	0.046	1.03 (1.002, 1.06)	0.04
Parity	0.95 (0.83, 1.09)	0.44	0.88 (0.76, 1.02)	0.10
Gestational age at delivery	0.76 (0.73, 0.80)	<0.01	0.76 (0.73, 0.78)	<0.01
Elixhauser Comorbidity Index*	1.30 (1.21, 1.41)	<0.01	1.27 (1.16, 1.38)	<0.01
Income Quintile 2**	0.64 (0.42, 0.99)	0.04	0.63 (0.40, 0.98)	0.04
Income Quintile 3	0.79 (0.53, 1.18)	0.25	0.81 (0.53, 1.22)	0.31
Income Quintile 4	0.88 (0.60, 1.29)	0.51	0.77 (0.51, 1.17)	0.22
Income Quintile 5	0.40 (0.24, 0.66)	<0.01	0.37 (0.22, 0.62)	<0.01
Diabetes	0.97 (0.23, 4.02)	0.97	0.60 (0.14, 2.63)	0.50
Hypertension	0.98 (0.31, 3.13)	0.97	0.61 (0.17, 2.26)	0.47
Cardiovascular disease	1.41 (0.34, 5.93)	0.64	1.40 (0.27, 7.25)	0.69
Inflammatory bowel disease	1.63 (1.03, 2.57)	0.04	1.34 (0.83, 2.17)	0.24
Rural residence	1.03 (0.67, 1.59)	0.88	1.21 (0.77, 1.90)	0.41

*Per 1 point increase, **Compared to income quintile 1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this large, population-based cohort study, women with axSpA were more likely to experience SMM, preterm birth, gestational diabetes and antepartum haemorrhage compared to controls. Furthermore, experiencing SMM was associated with increasing maternal age, lower gestational age and increasing comorbidity burden. These results are concerning and call for further studies to identify and develop strategies to limit SMM in women with axSpA. To the best of our knowledge, this is the largest population-based study of pregnancy in axSpA women and the first study of SMM in axSpA.

Disclosure: S. Maguire: None; **J. Snelgrove**: None; **P. Pequeno**: None; **M. Paterson**: None; **F. Wu**: None; **L. Passalent**: AbbVie/Abbott, 6, Novartis, 6, UCB, 2, 5; **A. Perruccio**: None; **D. Mahendira**: None; **E. Karam**: None; **R. Inman**: AbbVie/Abbott, 2, Janssen, 2, Novartis, 2, 5, UCB, 2, 5; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2.

Abstract Number: 2201

Adherence to Reproductive Health Guidelines in Lupus Care: Insights from Patient and Physician Surveys

Akhil Sood[1], Leanna Wise[2], Sadaf Sediqi[1], Alyssa Howren[1], Amanda Moyer[1], Ellie Diamond[1], Yashaar Chaichian[3] and Julia F Simard[4], [1]Stanford University, Palo Alto, CA, [2]LAGMC/Keck Medicine of USC, Los Angeles, [3]Stanford University, Stanford, CA, [4]Stanford Medicine, Stanford, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The American College of Rheumatology has established guidelines for managing reproductive health in patients with rheumatic diseases. We assessed contraception use and counseling of patients with systemic lupus erythematosus (SLE) through two parallel surveys of patients and physicians in alignment with these guidelines.

Methods: Females with SLE (ages 18-50 years) who received care from a rheumatologist at an academic medical center were invited to complete a survey assessing contraception use, including effective or highly effective contraception (EHEC), and whether they received contraception counseling from their rheumatologist. Contraception counseling was defined as: a) discussion of contraception in the past year, or b) explanation of contraception given their SLE by a rheumatologist. The survey also asked about sources of reproductive health information and perceived barriers to reproductive health counseling with their rheumatologist. The physician survey invited rheumatologists and obstetricians/gynecologists (OBGYN) to complete a survey about confidence in contraception counseling rated on a Likert-scale (1= Least Confident, 5= Extremely Confident). Rheumatologists were specifically asked about timing of contraception counseling after initiating a teratogenic medication. Descriptive statistics were summarized as frequency (n, %) or median [interquartile range]. Chi-square, Fisher's exact, and Student's t tests were used for bivariate comparisons.

Results: Among 102 females with SLE who completed the survey, the majority identified as White (37, 36%) or Asian/Pacific Islander (33, 32%), and had a bachelor's degree or higher (71, 69%). Most (67, 66%) reported being sexually active and avoiding pregnancy or neutral towards pregnancy. Only 33% of all participants reported receiving contraception counseling within the past year. Fewer participants reported using EHEC (34, 33%) compared to less effective methods (47, 46%). Use of EHEC significantly differed by race ($p< 0.05$), with higher use among Whites (20, 54%) and lower among Asians/Pacific Islanders (7, 21%). Contraception counseling significantly differed by age, employment status, marital status, and teratogenic medication use, but these factors were not associated with the use of EHEC. Despite identifying rheumatologists as

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient Demographics and Characteristics, presented as n(%)	
Variable	Responses (n=102)
Age (years)	
Mean (SD)	35.0 (8.2)
Range	19-50
Education Level	
Less than High School	0 (0)
High school diploma or equivalent	16 (15.7)
Technical/vocational training	14 (13.7)
Bachelor's degree	42 (41.2)
Master's degree or above	29 (28.4)
Race	
American Indian/Alaskan Native	2 (2.0)
Asian/Pacific Islander	33 (32.4)
Black/African American	6 (5.9)
Mixed Race	10 (9.8)
White	37 (36.3)
Prefer not to state	2 (2.0)
Other	9 (8.9)
Ethnicity	
Hispanic	25 (24.5)
Non-Hispanic	70 (68.6)
Prefer not to State	3 (2.9)
Marital Status	
Never Married	38 (37.3)
Married/in a domestic partnership	57 (55.9)
Widowed	1 (1.0)
Divorced or separated	6 (5.9)
Employment Status	
Employed, Full Time	55 (53.9)
Employed, Part Time	13 (12.7)
Unemployed	21 (20.6)
Other	3 (2.9)
Disabled	8 (7.8)
Student	2 (2.0)
Nativity (place of birth)	
In the USA	83 (81.4)
Outside of the USA	19 (18.6)
Language	
English	99 (97.1)
Spanish	3 (2.9)

the primary source of information on SLE and reproductive health (64, 63%), many patients viewed being directed to their OBGYN as a barrier to engaging in these discussions with their rheumatologist (31, 30%).

Among 200 physician respondents (rheumatologists: 116, (58%), OBGYN: 84, (42%)), rheumatologists reported higher confidence in contraception counseling (Median 4 [IQR 3–4]) compared to OBGYNs (Median 3 [3–4]). While most rheumatologists (88, 76%) reported contraception counseling at the initiation of teratogenic medications, fewer (40, 35%) reported also counseling at follow-up visits.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Physician Demographics and Characteristics, presented as n(%)		
	Rheumatology 116 (58)	Obstetrics/Gynecology 84 (42)
Female	54 (46.6)	63 (75)
Race		
Asian	27 (23.3)	14 (16.7)
Black/African American	2 (1.7)	7 (8.3)
Middle Eastern/North African	5 (4.3)	2 (2.4)
Mixed Race	5 (4.3)	3 (3.6)
White	68 (58.6)	56 (66.7)
Prefer not to state	9 (7.8)	2 (2.4)
Ethnicity		
Hispanic	6 (5.2)	6 (7.1)
Prefer not to state	7 (6)	2 (2.4)
Practice Setting		
Academic	60 (51.7)	33 (39.3)
Health System (Non-Academic)	22 (19)	30 (35.7)
Private Practice	32 (27.6)	19 (22.6)
Other	2 (1.7)	2 (2.4)
Location		
Urban	71 (61.2)	46 (54.8)
Suburban	38 (32.8)	33 (39.3)
Rural	7 (6)	5 (6)
Number of Lupus Patients seen in a Month		
None	3 (2.6)	3 (3.6)
Less than 1 patient per month	0 (0)	31 (36.9)
1-2 Patients per month	8 (6.9)	28 (33.3)
3 to 4	16 (13.8)	17 (20.2)
5 or more	89 (76.7)	5(6)

Conclusion: The study highlights gaps in contraception use and counseling among females with SLE. Future studies should include focus groups to identify patient, physician, and systems-level barriers to improve reproductive health delivery in SLE.

Disclosure: A. Sood: None; **L. Wise**: AstraZeneca, 1, 6, 7, Aurinia Pharma, 5, 6, GlaxoSmithKlein(GSK), 6; **S. Sediqi**: None; **A. Howren**: None; **A. Moyer**: None; **E. Diamond**: None; **Y. Chaichian**: Lupus Therapeutics, Lupus Research Alliance, 5; **J. Simard**: None.

Abstract Number: 2202

Epidemiologic Evaluation of Postpartum Mental Health for Women Living with Systemic Lupus Erythematosus: A Population-Based Cohort Study Among Medicaid Enrollees

Alyssa Howren[1], Amadeia Rector[2], Sadaf Sediqi[3] and Julia F Simard[4], [1]Stanford University, Menlo Park, CA, [2]Stanford University, San Francisco, CA, [3]Stanford University, Palo Alto, CA, [4]Stanford Medicine, Stanford, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Demographics and clinical characteristics of singleton live birth pregnancies among females with systemic lupus erythematosus.

	All pregnancies (N= 7870)
Maternal age, median (IQR), years	29 (8)
Gestational age, mean (SD), weeks	37.4 (2.5)
Parity, No. (%)	
Nulliparous	3727 (47)
Multiparous	4143 (53)
Race and Ethnicity, No. (%)	
White	2549 (32)
Black	2238 (28)
Asian	173 (2)
American-Indian/Alaskan Native	121 (2)
Hawaiian/ Pacific Islander	37 (0.5)
Multiracial	31 (0.4)
Hispanic, any race	1321 (17)
Unknown	1400 (18)
Income relative to federal poverty level (FPL), No. (%)	
Below FPL (≤100% FPL)	3354 (43)
Low income (101 to 133% FPL)	390 (5)
Low-moderate income (134 to 150% FPL)	71 (1)
Moderate income (151 to 200% FPL)	105 (1)
Middle income (201 to 250 FPL)	25 (0.3)
High income (≥251 FPL)	18 (0.1)
Null/missing	3907 (50)

Abbreviations: IQR – interquartile range, SD – standard deviation

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune rheumatic disease, predominately affecting women during their reproductive years. Despite widespread evidence that individuals with SLE have a significantly increased risk for depression and anxiety, insight into postpartum depression (PPD) and postpartum anxiety (PPA) is limited. This highlights a significant quality-of-care issue given these conditions are associated with several negative maternal and fetal health outcomes and is a leading cause of maternal death. To address this, we examined national claims data to estimate PPD/PPA prevalence among publicly-insured women with SLE.

Methods: We identified all singleton live births among females aged 15-44 years in Medicaid TAF (T-MSIS Analytic File) between 01/01/2014 and 12/31/2019 applying validated algorithms to inpatient and outpatient files for diagnostic and procedure claims related to end of pregnancy. SLE was defined prior to delivery using the following algorithm: ≥2 SLE coded outpatient visits or ≥1 inpatient visit (ICD9: 710.0; ICD10: M32.1, M32.8, M32.9). PPD, PPA, and post-traumatic stress

Table 2 Prevalence of postpartum depression, postpartum anxiety, and post-traumatic stress disorder among systemic lupus erythematosus pregnancies in the 60-day and 365-day postpartum Medicaid coverage periods, stratified by parity. Presented as No.(%)

	60-day coverage postpartum			365-day coverage postpartum		
	All (N= 7870)	Nullipara (N= 3727)	Multipara (N= 4143)	All (N= 5180)	Nullipara (N= 2515)	Multipara (N= 2665)
Prevalence of PPD	449 (6)	159 (4)	290 (7)	834 (16)	362 (14)	472 (18)
Prevalence of PPA	290 (4)	111 (3)	179 (4)	722 (14)	305 (12)	417 (16)
Prevalence of PTSD	115 (2)	38 (1)	77 (2)	219 (4)	88 (4)	131 (5)

Abbreviations: PPA – postpartum anxiety, PPD – postpartum depression, PTSD – post-traumatic stress disorder

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disorder (PTSD) were conservatively defined as ≥2 outpatient claims or ≥1 inpatient claim coded as depression, anxiety, and PTSD, respectively. All outcomes were assessed within the 60-day postpartum coverage period and up to 365-days postpartum (for those with ongoing coverage). To examine heterogeneity we stratified by parity, and race and ethnicity.

Results: We identified 7870 singleton live births among 6914 women with a diagnosis of SLE. The median maternal age was 29 years (IQR, 8 years), with the majority of participants identifying as White (32%), Black (28%), and Hispanic (17%). (**-Table 1**). The prevalence of PPD for SLE pregnancies was estimated at 6% within the 60-day postpartum coverage period and 16% among those with up to 365 days of continuous coverage. We observed heterogeneity by parity, with a slightly higher prevalence of PPD observed among multipara SLE pregnancies (**Table 2**). Stratification by race and ethnicity showed the highest prevalence of PPD among White SLE pregnancies (7%, 178/2549), followed by Black (5%, 111/2238) and Hispanic individuals (5%, 68/1321) during the 60-day postpartum period. The prevalence of PPA was 4% within 60-days postpartum, increasing to 14% among those with 365-days of coverage. PTSD was less prevalent, affecting 2-4% of SLE pregnancies in the postpartum period.

Conclusion: Findings highlight that PPD and PPA are important comorbidities to consider in SLE patients and underscores the need for appropriate screening and management strategies. Future analyses will include comparisons with the general obstetric population to enhance the interpretation of these results.

Disclosure: A. Howren: None; **A. Rector**: None; **S. Sediqi**: None; **J. Simard**: None.

Abstract Number: 2203

Maternal and Fetal Outcomes Associated with IL-17 Inhibitor Exposure During Pregnancy in Patients with Seronegative Arthritis: A Case Series of Nine

Arshdeep Waring[1], Sofia Rieger-Torres[2], Jeremiah Tan[3], Viktoria Pavlova[4] and Neda Amiri[5], [1]University of British Columbia, Abbotsford, BC, Canada, [2]University of British Columbia, Vancouver, BC, Canada, [3]Arthritis Research Canada, Vancouver, BC, Canada, [4]McMaster University, Ancaster, ON, Canada, [5]University of British Columbia, North Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin-17 (IL-17) inhibitors, such as ixekizumab and secukinumab, are increasingly used in the treatment of seronegative inflammatory arthritis, including psoriatic arthritis and axial spondyloarthritis. However, data on their safety and outcomes during pregnancy remain limited. Given the expanding use of IL-17 inhibitors in individuals of reproductive age, further characterization of maternal and fetal outcomes is needed to inform clinical decision-making.

Methods: Nine pregnant individuals with seronegative inflammatory arthritis who were treated with IL-17 inhibitors were identified through the Pregnancy and Rheumatic Diseases Clinics at two Canadian centers. Clinical data were prospectively extracted by a trained research assistant using REDCap, electronic medical records, and relevant consult notes. Outcomes of interest included maternal disease activity during pregnancy, pregnancy complications, neonatal outcomes, and the presence of congenital anomalies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics including: maternal age at conception, diagnosis, gravidity, current biologic therapy, gestational age (GA) at delivery, mode of delivery, fetal birth weight, congenital malformations.

Patient	Maternal Age at Conception	Diagnosis	Gravidity	Current Biologic Therapy	GA at delivery	Mode of delivery	Fetal birth weight (g)	Congenital Malformations
P1	31	PsA	G1	Ixekizumab	36+2	Emergency C-Section	3004	None
P2	33	PsA	G2	Ixekizumab	41+3	Emergency C-Section	3390	None
P3	31	PsA	G4	Secukinumab	40+0	Emergency C-section	3645	None
P4	41	SpA	G1	Secukinumab	40+3	SVD	3550	None
P5	32	SpA	G1	Secukinumab	Pregnant	Pregnant	N/A	N/A
P6	34	PsA	G2	Ixekizumab	39+0	Vacuum assisted vaginal delivery	3592	None
P7	30	PsA	G2	Secukinumab	39+1	Emergency C-section	4000	None
P8	34	PsA	G6	Secukinumab	38+1	SVD	3590	None
P9	37	SpA	G1	Secukinumab	38+1	Elective C-Section	2720	None

PsA=psoriatic arthritis; SpA=Spondyloarthropathy; SVD=spontaneous vaginal delivery

Results: These patients were managed throughout all trimesters of pregnancy, and followed for six weeks postpartum. The mean maternal age at conception was 34 years. Patient characteristics are summarized in Table 1. No birth defects were observed in any of the infants. One infant was noted to have jaundice (not requiring phototherapy). Another infant required a brief admission to neonatal intensive care unit for hypoglycemia and transaminitis (P7).

Conclusion: In this prospective case series, IL-17 inhibitor exposure during pregnancy was not associated with an increased risk of congenital anomalies or adverse neonatal outcomes. These findings suggest that IL-17 inhibitors may be a safe treatment option for select patients with seronegative inflammatory arthritis during pregnancy. Larger, multicenter studies are needed to confirm these observations and better inform clinical guidance.

Disclosure: A. Waring: None; **S. Rieger-Torres**: None; **J. Tan**: None; **V. Pavlova**: None; **N. Amiri**: None.

Abstract Number: 2204

A Novel Framework for Teratogenicity Counseling for Adolescents and Young Adults (AYAs) with Rheumatic Disease on Teratogenic Medications

Brittany Huynh[1], Elizabeth Pfeiffer[2] and Stacey Tarvin[3], [1]Indiana University School of Medicine, Fishers, IN, [2]Rhode Island College, Providence, RI, [3]Riley Hospital for Children at Indiana University, Indianapolis, IN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Participant characteristics, N=21

Variable	Avg (Range)
Age (years)	16.3 (14-21)
Time since diagnosis	4.4 (0.25-18)
Duration of teratogen use	2.4 (1 mo-9 yrs)
Race/Ethnicity	**n (%)**
White	8 (38)
Black	7 (33)
Latinx	4 (19)
Asian	1 (5)
Mixed Race	1 (5)
Rheumatic diagnosis	
Juvenile idiopathic arthritis	9 (43)
Systemic lupus erythematosus	7 (33)
Discoid lupus	1 (5)
Juvenile dermatomyositis	1 (5)
Linear scleroderma	1 (5)
Mixed connective tissue disease	1 (5)
TINU	1 (5)
Current Teratogen Use	
Methotrexate	15 (71)
Mycophenolate	6 (29)
Cyclophosphamide	2 (10)
ACE inhibitor	2 (10)
Warfarin	1 (5)
LGB+	5 (24)
Sexually experienced	7 (33)
Currently sexually active	4 (19)
Ever sex without hormonal contraception or LARC[a]	2 (10)
Current contraceptive use	8 (38)
LARC[a]	2 (10)
Depo medroxyprogesterone acetate	1 (5)
Pill/patch/ring	4 (20)
Condoms only	1 (5)

[a]Long-acting reversible contraception, including the implant, copper intrauterine devices (IUDs), and hormonal IUDs

Participant Characteristics

Background/Purpose: Prior studies demonstrate low levels of knowledge and reported counseling regarding teratogenicity among AYAs with rheumatic disease. The aim of this study was to explore the teratogenicity counseling experiences of AYAs on teratogenic medications treated in pediatric rheumatology clinics and explore on how to best address their needs in teratogenicity counseling.

Methods: AYAs age 14-21 years, assigned female at birth, with a rheumatic disease, and taking teratogenic medications were recruited from pediatric rheumatology clinics in Indiana to participate in semi structured interviews in 2024 assessing teratogenicity knowledge, counseling experiences, and recommendations to improve counseling in the clinical setting. Interviews were recorded and transcribed by a professional transcription service. Data were analyzed in Dedoose by two of the authors (BH, EP) who engaged in inductive initial coding to identify themes from the data, resolving differences through discussions until theoretical saturation was reached. After identifying key themes and creating a codebook ,categories were developed through exploration of how key concepts fit together. Analysis proceeded using constant comparison analysis, the standard analysis technique utilized in grounded theory as described by Charmaz (2008). Hypothesized relationships among categories were explored through reexamination of the data using an iterative approach. We then reanalyzed the transcripts to perform a priori coding to develop and confirm our theoretical framework.

Results: 21 AYAs with a variety of rheumatic diseases participated in interviews. Participants were on average 16.3 years of age. 29% knew the reproductive effects of their medication, 24% had limited knowledge, and 43% no knowledge. 43% reported counseling on teratogenicity by their rheumatologist.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SPIKE STAR Teratogenicity Counseling Framework

The key theme that emerged is teratogenicity counseling is seen as receiving bad news due to AYAs' interpretation of this information to mean it will be challenging to plan a future pregnancy. This was rooted in weighing the challenges of navigating a disease they perceive will be poorly controlled without use of their current teratogenic medication. Notably, most participants frame teratogenicity information in terms of their future family planning with few recognizing the risk of unintended pregnancy.

This finding drew us to the SPIKES (Setting, Perception, Invitation, Knowledge, Empathy, Strategy) framework for breaking bad news, which further mapped onto central themes from AYA recommendations on teratogenicity counseling. We used this model and adapted it for AYAs receiving news on teratogenicity based on subsequent themes that emerged to produce the SPIKES-STAR framework for teratogenicity counseling. This model includes the following additions: Stigma reduction, Tailoring, Agency, and Revisiting counseling.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: We present a novel framework for teratogenicity counseling of AYAs on teratogenic medications treated in pediatric rheumatology clinics. Next steps include development of a model for implementation in clinical practice, evaluation of model, and application to the broader population of AYAs with chronic disease on teratogenic medication.

Disclosure: B. Huynh: None; **E. Pfeiffer**: None; **S. Tarvin**: AbbVie/Abbott, 5, American Academy of Pediatrics, 12, Editor, Amgen, 5, Childhood Arthritis Rheumatology Research Alliance, 5, Roche, 5, UCB, 5.

Abstract Number: 2205

Effectiveness of Reproductive Health Counseling for Rheumatology Patients

Caroline Maretz[1], Daniele Marcy[2], Kristin Sturm[3], JoAnn Zell[3] and Kristen Demoruelle[4], [1]University of Colorado Anschutz Medical Campus, Denver, CO, [2]University of Colorado, Northglenn, CO, [3]University of Colorado Anschutz Medical Campus, Aurora, CO, [4]University of Colorado Anschutz Medical Campus, Golden, CO

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic autoimmune diseases are often treated with medications that have known teratogenic effects or unknown safety profiles in pregnancy. As these diseases frequently affect women of childbearing potential, it is important for rheumatologists to provide reproductive health counseling to patients. While studies have shown variable rates of reproductive health counseling by rheumatology providers, less is known about the effectiveness of that counseling. In this study, we used patient-reported questionnaires to evaluate the effectiveness of prior reproductive health counseling of rheumatology patients.

Methods: Female patients followed at an academic rheumatology outpatient practice were invited to complete on-line questionnaires if they were of childbearing potential (i.e., 18-50 years without surgical sterilization, hysterectomy, or menopause), had an established autoimmune condition, and had no plans for pregnancy in the next year. To assess prior reproductive health counseling, patients were asked if they had ever received contraception counseling or been counseled about the pregnancy risks of their medications by their rheumatologist. Counseling effectiveness was assessed by asking "Do you think you are safe to become pregnant now?" and "If you decided to become pregnant in the future, would you talk to your

Table 1. Reproductive health questionnaire results stratified by patient-reported history of prior reproductive health counseling by a rheumatologist

	Prior counseling (N=71)	No prior counseling (N=30)	p-value
Women who answered 'Unsure' when asked "Do you think you are safe to become pregnant now?"			
• All women	6 (8.5%)	11 (36.7%)	<0.01
• Women currently taking teratogenic medications*	0/27 (0%)	2/5 (40.0%)	0.02
Women who answered 'Yes' when asked "If you decided to become pregnant in the future, would you talk to your rheumatologist about those plans?"			
• All women	70 (98.6%)	25 (83.3%)	<0.01
• Women currently taking teratogenic medications*	27/27 (100.0%)	4/5 (80.0%)	0.16

*Teratogenic medications could include methotrexate, leflunomide, cyclophosphamide, mycophenolate mofetil or warfarin

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

rheumatologist about those plans?" Demographics, medication use, and contraception use were also collected by questionnaire. Results were compared between women who did vs. did not report prior reproductive health counseling.

Results: One hundred and one patients completed the questionnaire. Seventy-one (70.3%) reported having ever received reproductive health counseling by their rheumatologist. Reproductive health counseling rates were higher in women < 40 years of age ($p< 0.01$) and in women currently or previously taking teratogenic medications ($p=0.01$). We found that women who had received reproductive health counseling were less likely to be 'unsure' whether they were safe to become pregnant compared to women who did not report prior reproductive health counseling (8.5% vs. 36.7%, $p< 0.01$). This difference was also present in the subset of 32 women currently taking teratogenic medications (0% vs. 40%, $p=0.02$) (Table 1). Women who had previously received reproductive health counseling from their rheumatologist were also more likely to report that they would talk to their rheumatologist if they decided to become pregnant in the future (98.6% vs. 83.3%, $p< 0.01$) (Table 1).

Conclusion: This study demonstrates the significant impact that reproductive health counseling by rheumatologists can have on patient outcomes. Patients who received prior counseling reported greater confidence regarding the safety of a potential pregnancy, which may contribute to improved pregnancy outcomes. Additionally, our findings emphasize the importance of counseling all patients about reproductive health, regardless of their current pregnancy intentions, as those not actively planning pregnancy were still more likely to engage in discussions about future pregnancy plans with their rheumatologist, which can also support better outcomes.

Disclosure: C. Maretz: None; **D. Marcy**: None; **K. Sturm**: None; **J. Zell**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5.

Abstract Number: 2206

Adolescents with Systemic Lupus Erythematosus at Highest Risk of Adverse Pregnancy Outcomes

Catherine Deffendall[1], Sarah Green[2], Ashley Suh[2], Bryan Han[2] and April Barnado[2], [1]Vanderbilt University, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Few studies exist that examine pregnancy outcomes in adolescents with SLE. To our knowledge, there have been no studies comparing SLE adolescent pregnancies to both adolescent control and adult SLE pregnancies. Using a de-identified electronic health record (EHR), we compared rates of pregnancy outcomes in adolescents ≤ 21 years with and without SLE to older individuals with SLE.

Methods: We identified SLE pregnancies in a de-identified EHR with >3.8 million individuals using a validated algorithm of ≥ 4 SLE ICD billing codes and ≥ 1 pregnancy or delivery codes. On chart review, we confirmed SLE diagnosis by a rheumatologist and excluded deliveries occurring before SLE diagnosis. Pregnancies at a maternal age ≤ 21 years were counted as adolescent pregnancies and pregnancies at a maternal age ≥ 22 years were considered adult pregnancies. We identified control individuals as those without ICD codes for autoimmune diseases and ≥ 1 pregnancy or delivery codes. Maternal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

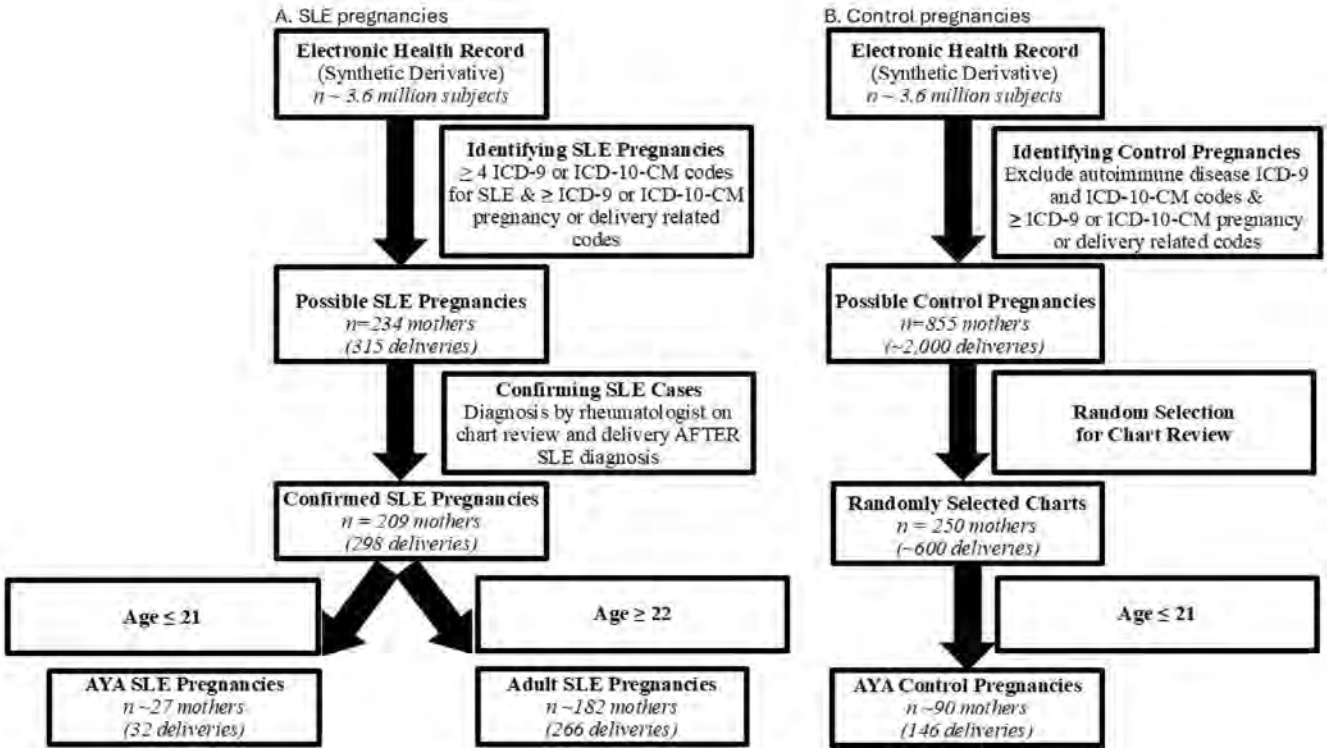


Figure 1. Flowchart of study individuals. (A) SLE pregnancies were selected from the de-identified electronic health record (EHR) using four or more SLE ICD-9 or ICD-10-CM codes while also requiring one or more ICD-9 or ICD-10-CM pregnancy or delivery-related codes. We then performed chart review to confirm SLE diagnosis by a rheumatologist and ensure pregnancy occurred after SLE diagnosis. After applying age criteria, we identified adolescent SLE pregnancies and adult SLE pregnancies. (B) Control pregnancies were selected from the same de-identified EHR as the SLE pregnancies. Controls were required to have the same pregnancy and delivery-related codes used for SLE deliveries and to not have ICD-9 or ICD-10-CM codes for autoimmune diseases. We then performed chart review on a random set of 250 controls to ensure no autoimmune diseases. After applying age criteria, we identified adolescents without SLE.

outcomes included gestational diabetes, preeclampsia, postpartum hemorrhage, peripartum infection. Fetal outcomes were pregnancy loss, which included elective termination, spontaneous abortion, and stillbirth. Other fetal outcomes were premature birth, defined as delivery < 37 weeks, and small for gestational age, defined as birth weight < 10th percentile for gestational age. Covariates were assessed on chart review. Using Chi-square and Kruskal-Wallis tests, we compared demographics and pregnancy outcomes. Since individuals could contribute multiple pregnancies and parity can impact outcomes, we performed mixed effects models to estimate the association of pregnancy loss, preterm birth, and preeclampsia with age at delivery, race, and SLE case status.

Results: We identified 32 pregnancies to 27 individuals with SLE ≤ 21 years, 146 pregnancies to 90 adolescent control individuals without SLE, and 266 pregnancies to 182 individuals with SLE aged ≥ 22 years (Table 1). Adults with SLE were more likely to be White than adolescents with or without SLE ($p < 0.001$), and SLE pregnancies were more likely to be complicated by hypertension compared to controls ($p < 0.001$). Compared to adolescent control pregnancies, adolescent SLE pregnancies were more likely to experience preeclampsia ($p < 0.001$), postpartum hemorrhage ($p = 0.001$), and preterm delivery ($p = 0.001$). Among SLE pregnancies, SLE adolescents were more likely to have antiphospholipid antibody syndrome ($p = 0.01$) and nephritis ($p = 0.001$) compared to SLE adults. Adolescents with SLE were more likely to have pregnancy loss than adults with SLE ($p = 0.02$). In mixed effects models, SLE cases were more likely to experience preterm delivery (OR = 9.11, 95% CI 4.10-20.22) and preeclampsia (OR = 5.55, 95% CI 2.38 – 12.92) after adjusting age at delivery and race.

Conclusion: Adolescent SLE pregnancies were more likely to have preterm birth, preeclampsia, and post-partum hemorrhage than control adolescents and more likely than adults with SLE to have pregnancy loss. Adolescents with SLE represent a high-risk pregnancy group that needs close monitoring.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and baseline risk factors for adverse pregnancy outcomes among adolescents without SLE, adolescents with SLE, and adults with SLE.

Characteristics	Adolescent Control pregnancies % (n) (n = 146)	Adolescent SLE pregnancies % (n) (n = 32)	Adult SLE pregnancies % (n) (n = 266)	*p*
Mean maternal age at delivery, years, ± standard deviation	**19 ± 2**	**20 ± 1**	**30 ± 5**	**<0.001**
EHR duration*	5 ± 4.9	4 ± 3.0	6.3 ± 6	0.17
Race %**				
White	44% (61/138)	50% (16/32)	68% (180/265)	<0.001
African American	54% (74/138)	47% (15/32)	27% (71/26)	
Asian/Pacific Islander	1% (2/138)	0% (0/35)	3% (7/265)	
Multiple and Other	0% (0/138)	3% (1/35)	3% (7/265)	
Native American	1% (1/138)	0% (0/35)	0% (0/265)	
Ethnicity**				
Not Hispanic	90% (130/144)	93% (28/30)	94% (228/243)	0.43
Risk Factors				
Hypertension	**10% (11/112)**	**59% (13/22)**	**32% (73/226)**	**< 0.001**
Type I Diabetes	1% (2/143)	0% (0/26)	2% (5/222)	0.65
Type II Diabetes	**0% (0/141)**	**0% (0/26)**	**4% (9/226)**	**0.03**
Smoking	17% (17/102)	16% (4/25)	11% (27/245)	0.32
Multiple gestation	5% (6/124)	0% (0/32)	10% (27/280)	0.07
Prenatal Care	98% (97/99)	90% (18/20)	97% (213/220)	0.18
SLE duration**	---	**4 ± 2**	**8 ± 6**	**<0.001**
Antiphospholipid antibody syndrome	---	**43% (12/28)**	**21% (52/246)**	**0.01**
Nephritis	---	**66% (19/29)**	**34% (84/249)**	**0.001**

*EHR duration defined as time in years from first ICD code for any condition to date of delivery.
**SLE duration defined as time in years from first SLE billing code in the EHR or date documented by a rheumatology note, whichever came first, to delivery date.

Table 2. Comparing pregnancy outcomes among adolescent controls, adolescent SLE, and adult SLE individuals.

Adolescent control vs. Adolescent SLE pregnancies			
Outcomes	**Adolescent Control (n = 146)**	**Adolescent SLE (n = 32)**	***p* value**
Pregnancy Loss	26% (33/129)	38% (11/29)	0.18
Preterm birth	**18% (17/96)**	**56% (10/18)**	**0.001**
Small for gestational age	15% (7/48)	20% (3/15)	0.62
Gestational Diabetes	1% (2/143)	7% (2/28)	0.07
Preeclampsia	**6% (9/145)**	**33% (8/24)**	**<0.001**
Postpartum hemorrhage	**3% (2/74)**	**24% (5/21)**	**0.001**
Peripartum infection	5% (4/78)	17% (4/23)	0.06
Adult SLE vs. Adolescent SLE pregnancies			
Outcomes	**Adult SLE (n = 266)**	**Adolescent SLE (n = 32)**	***p* value**
Pregnancy loss	**21% (56/266)**	**38% (11/29)**	**0.02**
Preterm birth	45% (91/203)	56% (10/18)	0.38
Small for gestational age	31% (46/147)	20% (3/15)	0.36
Gestational Diabetes	7% (16/233)	7% (2/28)	0.96
Preeclampsia	18% (38/212)	33% (8/24)	0.07
Postpartum hemorrhage	13% (21/161)	24% (5/21)	0.19
Peripartum infection	16% (27/168)	17% (4/23)	0.87

Disclosure: C. Deffendall: None; **S. Green**: None; **A. Suh**: None; **B. Han**: None; **A. Barnado**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2207

Menopause Experiences of Veterans from Minoritized Populations with Rheumatoid Arthritis

Catherine Sims[1], Yujung Choi[2], Abigail Shapiro[3], Jennifer Gierisch[1], Elizabeth Strawbridge[2], Teresa Howard[2], Ankoor Shah[1] and Karen Goldstein[1], [1]VA Durham Healthcare System, Duke University, Durham, [2]VA Durham Healthcare System, Durham, [3]VA Durham Healthcare System, Cleveland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: There is a significant gap in understanding the reproductive health experiences of women Veterans with rheumatoid arthritis (RA). This study explores their experiences with menopause within the VA healthcare system, including perceptions of rheumatologists' roles in symptom management and care coordination between rheumatology and other providers.

Methods: Semi-structured interviews with 9 VA healthcare providers (5 rheumatologists, 4 primary care providers) and 7 Veterans with RA explored reproductive healthcare experiences and needs within the VA. All Veterans self-identified as Black and had been evaluated by a rheumatologist for RA. Veterans were identified via the Corporate Data Warehouse. Of the 128 Veterans contacted, 31 consented. Interview guides were developed using the Chronic Care and Cumulative Complexity Models to explore contraception, pregnancy, and menopause. Interviews were audio-recorded and transcribed using Microsoft Teams. Data were analyzed using Hamilton's rapid qualitative method. Two analysts summarized individual and cross-participant levels, with input from a third analyst. Overall themes were identified through structured matrix analysis.

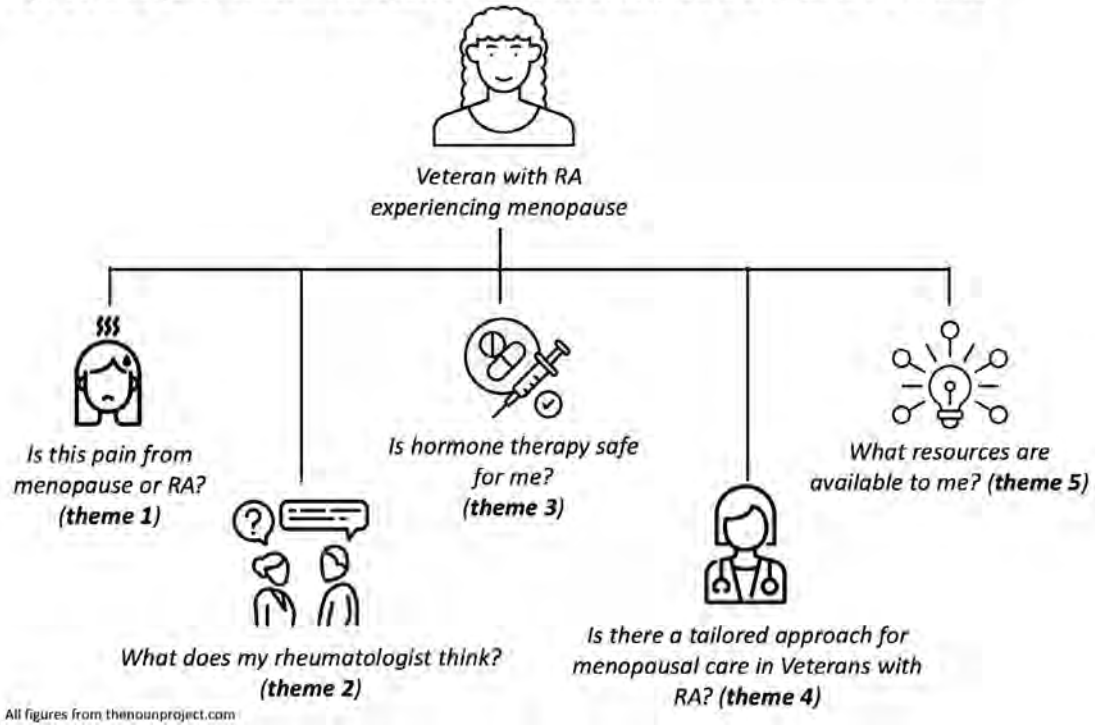
Results: We interviewed 7 Veterans about experiences with menopause symptoms and therapies, median age 61 years (**-Table 1**). Veterans reported joint pain and swelling that disrupted daily activities related to their RA. Veterans described difficulty with differentiating menopause symptoms from RA and relied on rheumatologists for guidance. They valued discussions with their rheumatologists about menopause and hormone therapy (HT) and its impacts on RA. Veterans drew on clinical advice and personal considerations when making decisions about menopause therapy. Some utilized supportive care, supplements, or HT to address menopausal symptoms. Some Veterans decided against HT due to medication burden or history of thrombosis. VA rheumatologists and PCPs expressed lower confidence in managing menopause compared to other reproductive health concerns and reported a generalized approach, as opposed to a disease-tailored approach, to

Table 1. Patient Characteristics

Demographic (n=7)	
Age	Median: 61 years (range 28-66)
Race	Black: 7 (100%)
Ethnicity	Not Hispanic: 7 (100%)
Age at RA diagnosis	Median: 30 years (range 21-52)
Age at menopause (n=3)	Median: 52 years (range 35-58)
Years receiving VA healthcare	Median: 16 years (range 5-34)
Current rheumatology care	Within VA: 5 (71%) Outside VA: 2 (29%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Emergent Themes in Menopause Experiences of Veterans with Rheumatoid Arthritis



menopause in Veterans with RA. Both Veterans and providers noted a lack of patient and provider resources for women with autoimmune disease undergoing menopause. Veterans believed that better access to reliable, personalized resources would have enhanced their menopause experience (**Figure 1**).

Conclusion: These findings highlight the challenges faced by Veterans with RA in managing menopause symptoms, particularly in distinguishing between RA-related and menopause-related symptoms. Veterans valued the involvement of their rheumatologists and want more guidance on menopause and HT, especially in relation to its impact on RA. Both Veterans and VA providers identified a gap in tailored resources and personalized approaches for women with RA undergoing menopause.

Disclosure: C. Sims: None; **Y. Choi**: None; **A. Shapiro**: Amgen, 12, Patient Advisory Board member- unrelated to this work; **J. Gierisch**: None; **E. Strawbridge**: None; **T. Howard**: None; **A. Shah**: None; **K. Goldstein**: None.

Abstract Number: 2208

Contraception and Pregnancy Experiences of Veterans from Minoritized Populations with Rheumatoid Arthritis

Catherine Sims[1], Yujung Choi[2], Abigail Shapiro[3], Elizabeth Strawbridge[2], Jennifer Gierisch[1], Teresa Howard[2], Ankoor Shah[1] and Karen Goldstein[1], [1]VA Durham Healthcare System, Duke University, Durham, [2]VA Durham Healthcare System, Durham, [3]VA Durham Healthcare System, Cleveland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

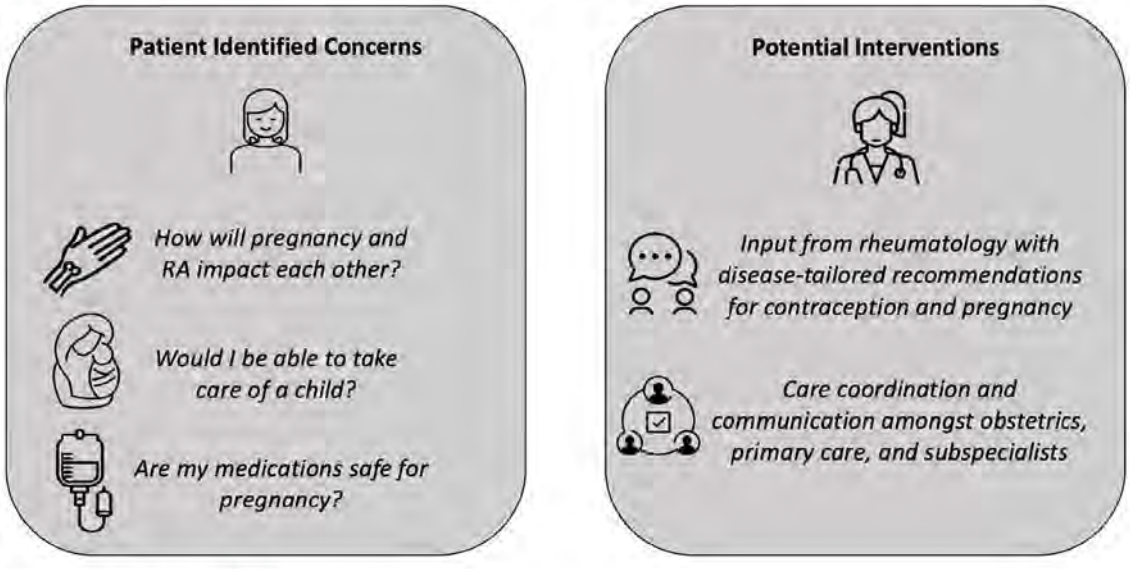
Table 1. Patient Characteristics

Demographic (n=13)	
Age	20-30 years: 5 (38%) 31-50 years: 1 (8%) 51-60 years: 3 (23%) > 61 years: 4 (31%)
Race	Black: 13 (100%)
Ethnicity	Hispanic: 2 (15%) Non-Hispanic: 10 (77%) Not reported: 1 (8%)
Veterans interviewed about contraception (n=9)	
Forms of contraception used throughout lifetime	Median number of contraception forms per Veteran: 2 (range 0-3) *Oral contraceptives: 5* *Barrier methods: 4* *Subdermal implant: 3* *Intrauterine device: 2* *Withdrawal method: 2* *Medroxyprogesterone acetate: 1* *Estrogen patches: 1*
Veterans interviewed about pregnancy planning (n=8)	
Prior pregnancies	Yes: 7 No: 1
Number of pregnancies (n=7)	Median: 1.5 (range 0-5) *Currently pregnancy (n=1)* *Live birth (n=8)* *Spontaneous abortion (n=5)* *Therapeutic abortion (n=2)*
Breastfeeding with prior live births (n=5)	Yes: 5 (100%)

Background/Purpose: More than 8,500 women Veterans carry a diagnosis of rheumatoid arthritis (RA), however, there are limited data on the reproductive health and experiences of this population. We engaged these Veterans and Veterans Affairs (VA) providers to examine the impact of RA on reproductive healthcare and identify gaps in services provided by the VA.

Methods: We conducted semi-structured interviews with 9 VA healthcare providers (5 rheumatologists, 4 primary care providers (PCPs)) and 13 Veterans with RA between February-October 2024. Veterans were identified through the Corporate Data Warehouse; 31 of 128 contacted via mail consented to participate. All patients self-identified as Black and/or Hispanic and were seen by a rheumatologist in the VA Healthcare System. Interview guides, informed by the Chronic Care Model and

Figure 1. Veteran Identified Areas for Improvement of Reproductive Healthcare



All figures from TheNounProject.com

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

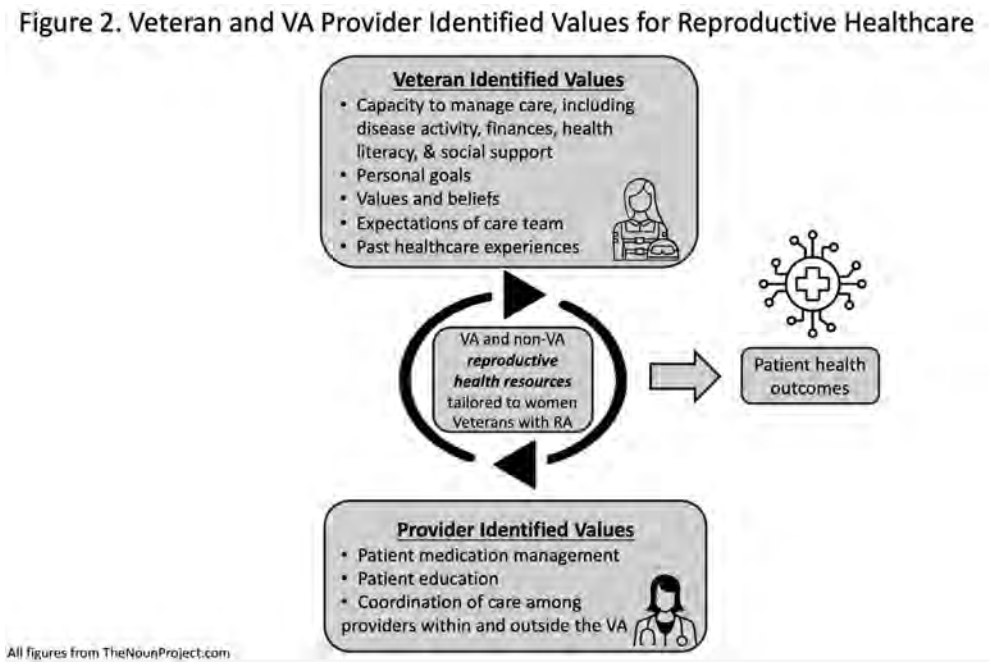


Figure 2. Veteran and VA Provider Identified Values for Reproductive Healthcare

the Cumulative Complexity Model, explored how rheumatic disease affects reproductive healthcare and gaps in VA services. Interviews lasted 45–60 minutes, focused on 2 of 3 reproductive milestones (contraception, pregnancy, menopause), and were audio-recorded and transcribed via Microsoft Teams. Data were analyzed using Hamilton's rapid qualitative method, with summaries by participant and question. Summaries were organized in a matrix to facilitate memo writing and thematic analysis.

Results: We interviewed 13 Veterans, ages 25-66 years, about contraception (n=9) and/or pregnancy/breastfeeding (n=8) depending on their reproductive history and experiences (**Table 1**) and 9 VA healthcare providers. Analysis identified 7 key takeaways. (1) Veterans considered reproductive health relevant to managing their RA including disease activity, physical capabilities, immunosuppression, and family planning goals. (**Figure 1**). (2) Navigating tradeoffs between chronic condition management and family planning felt overwhelming and emotionally burdensome. (3) Women Veterans reported taking between 0-3 types of contraceptives throughout their lifetime. Most had not discussed contraception with a VA rheumatologist, assuming obstetrics (OB) providers or PCPs would address this. When discussed, rheumatologists focused on teratogenic medications and pregnancy safety. (4) Veterans valued input from PCPs and rheumatologists when making reproductive decisions. (5) Rheumatology support during pregnancy varied; some saw only OBs and PCPs while others maintained rheumatology care. When providers communicated, Veterans reported improved care, less adverse impacts, and more shared decision-making among providers and with patients. (6) Breastfeeding decisions were influenced by provider input, immunosuppression safety, and personal preferences. (7) Veterans identified gaps in postpartum rheumatology care such as disease-specific resources, care coordination, and difficulty reengaging with VA after delivery (**Figure 2**).

Conclusion: Veterans with RA highly value their rheumatologists' advice on reproductive health and emphasized the importance of provider communication when making decisions about contraception, pregnancy, and breastfeeding. Care coordination was seen as especially critical during pregnancy.

Disclosure: C. Sims: None; **Y. Choi**: None; **A. Shapiro**: Amgen, 12, Patient Advisory Board member- unrelated to this work; **E. Strawbridge**: None; **J. Gierisch**: None; **T. Howard**: None; **A. Shah**: None; **K. Goldstein**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2209

Pregnancy outcomes in Systemic Lupus Erythematosus: Insights from a multicenter Spanish Study on the impact of antiphospholipid antibodies and APS

cristiana Sieiro[1], Jose Ordas Martínez[2], Ana Merino[3], Helena Amar Muñoz[4], Stefanie Burger[5], Ignacio Braña Abascal[5], Carmen Jose Mendéz[6], Raquel Dos Santos Sobrín[7], Jose Luis Puga Guzman[7], Ricardo Blanco[8] and Víctor Taboada Martínez[3], [1]Univrsity of Manchester, Manchester, United Kingdom, [2]Complejo Asistencial Universitario de León, León, Spain, [3]Hospital Universitario Marqués de Valdecilla, Santader, Spain,, Santander, Spain, [4]Hospital General Universitario Gregorio Marañón, Rheumatology, Madrid, Spain, Madrid, Spain, [5]Hospital Universitario Central de Asturias, Rheumatology, Oviedo, Spain, Oviedo, Spain, [6]Complexo Hospitalario Universitario A Coruña, Rheumatology, A Coruña, Spain, Coruña, Spain, [7]Hospital Universitario de Santiago de Compostela, Rheumatology, Santiago de Compostela,, Santiago de Compostela, Spain, [8]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Pregnancy in patients with systemic lupus erythematosus (SLE) is associated with significant maternal and obstetric risks, particularly in the context of antiphospholipid syndrome (APS). While these risks are well-documented, the impact of isolated antiphospholipid antibodies (aPL) without overt APS remains unclear. Bridging this knowledge gap is critical to tailoring management strategies for this subgroup of patients, who may face unique clinical challenges. This study aimed to compare clinical characteristics, maternal comorbidities, obstetric complications, and pregnancy outcomes among three groups of SLE patients: those without aPL, those with isolated aPL, and those with secondary APS, using data from a multicenter Spanish registry of pregnancies.

Methods: A multicenter retrospective cohort study included pregnancies in women fulfilling the 2012 SLICC or 2019 ACR/EULAR classification criteria for SLE. Patients were classified into three subgroups: SLE without aPL, SLE with isolated aPL, and SLE with secondary APS. Data were collected at preconception visits, during each trimester, and post-delivery.

	SLE without APL	SLE with APL	SLE-APS	P value
Age (years), m ± SD	32.5±3.8	33.2±3.4	34.2±5.2	0.83
Time to diagnosis, mean (IQR)	30 (14.2-57.3)	28.4 (9.7-54.3)	32 (15.2-57.2)	0.65
Follow-up (months), m±SD	120 (81.4-206.8)	98 (34.2-201)	194 (78-234)	**0.04**
Obesity (n, %)	5 (12%)	2 (6%)	5 (20%)	0.14
Smoking (n, %)	15 (35%)	12 (39%)	9 (45%)	0.35
Hypertension (n, %)	5 (12%)	3 (9.7%)	5 (11%)	0.57
Diabetes (n, %)	3 (7%)	3 (10%)	2 (10%)	0.45
Dyslipidemia (n, %)	4 (13%)	4 (13%)	3 (10%)	0.67
Hereditary thrombophilia (n, %)	5 (12%)	5 (16%)	6 (30%)	0.42
Thyroid disease (n, %)	7 (16%)	1 (3%)	3 (15%)	0.52
Obstetric comorbidity (n, %)	10 (23%)	10 (32%)	6 (20%)	0.49

Table 1: Demographic characteristics, cardiovascular risk factors and main comorbidities in the different groups

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	SLE without APL	SLE with APL	SLE-APS	P value
Damage by SLICC (n, %)	14 (13%)	12 (18%)	6 (20%)	0.24
SLEDAI before pregnancy (mean±SD)	2.1+3.37	2.5+3.60	2.6+3.44	0.61
Adverse pregnancy outcomes (n, %)	21 (20%)	3 (5%)	**18 (60%)**	**<0.0001**
Live births (n, %)	82 (77%)	47 (72%)	21 (70%)	0.34
Preterm delivery <37 weeks (n, %)	15 (14%)	4 (6%)	8 (27%)	**0.04**
Fetal death <10 weeks (n, %)	10 (9%)	3 (5%)	9 (30%)	**0.02**
Fetal death >10 weeks (n, %)	5 (5%)	2 (3%)	3 (10%)	0.45
Preeclampsia/Eclampsia (n, %)	3 (3%)	1 (2%)	2 (7%)	0.38
Abruption placentae (n, %)	-	1 (2%)	-	0.78
IVF Failures (more than 2) (n, %)	3 (3%)	9 (14%)	1 (30%)	0.06
Intrauterine growth restriction (n, %)	3 (3%)	1 (2%)	2 (7%)	0.08
Ectopic pregnancies (n, %)	5 (5%)	1 (2%)	0	0.15

Table 2: Maternal and Pregnancy Outcomes in SLE Patients Stratified by aPL and APS Status

Key variables included clinical and immunological profiles, maternal comorbidities, obstetric history, pregnancy complications, and delivery outcomes. Comparative analyses were performed to evaluate maternal and fetal outcomes across the subgroups

Results: A total of 201 pregnancies were analyzed across three groups: SLE without aPL (n=43), SLE with isolated aPL (n=31), and SLE-APS (n=20). While the groups were similar in demographic characteristics and comorbidities, there were striking differences in pregnancy outcomes. The SLE-APS group, experienced the highest rates of adverse pregnancy outcomes. In fact, 60% of pregnancies in this group faced complications, a stark contrast to only 20% in the SLE without aPL group and 5% in the SLE with isolated aPL group ($p< 0.0001$).

The SLE-APS group also had significantly higher rates of preterm delivery (27%) and fetal death before 10 weeks (30%) compared to SLE without aPL (14% and 9%, respectively) and SLE with isolated aPL (6% and 5%, respectively, $p=0.04$ and $p=0.02$). The risk of fetal death before 10 weeks was particularly concerning in the SLE-APS group, with nearly one-third of pregnancies affected.

Interestingly, despite the increased risk of complications, live birth rates remained relatively similar across all groups, with 70–77% of pregnancies resulting in live births ($p=0.34$). However, the SLE-APS group showed a notable trend towards higher IVF failure rates (30% compared to 3% in the SLE without aPL group), which may suggest a more complex reproductive challenge for women with APS ($p=0.06$).

Conclusion: This multicenter study highlights the increased risk of adverse pregnancy outcomes in women with SLE-APS, particularly fetal death before 10 weeks and preterm delivery. Although women with isolated aPL also face higher pregnancy risks compared to those without aPL, their outcomes are less severe than those with APS.

Disclosure: c. Sieiro: None; **J. Ordas Martínez**: None; **A. Merino**: None; **H. Amar Muñoz**: None; **S. Burger**: None; **I. Braña Abascal**: None; **C. Jose Mendéz**: None; **R. Dos Santos Sobrín**: None; **J. Puga Guzman**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6; **V. Taboada Martínez**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2210

Changes in Treatment Pathways Over Time in Pregnancies with Active Lupus Nephritis

Dahima Cintron[1], Amanda Eudy[2], Michelle Petri[3], Rebecca Fischer-Betz[4], Abeer Mockbel[5], Cecilia Nalli[6], Laura Andreoli[7], Angela Tincani[8], Yair Molad[9], Dafna D. Gladman[10], Murray Urowitz[11], Stephen Balevic[12] and Megan Clowse[13], [1]Duke Health, Durham, NC, [2]Duke University, Raleigh, NC, [3]Johns Hopkins University School of Medicine, Timonium, MD, [4]Heinrich Heine University of Düsseldorf, Düsseldorf, Germany, [5]Cairo University/Kasr- AlAiny Medical School, Cairo, Egypt, [6]ASST SPEDALI CIVILI DI BRESCIA, Brescia, Italy, [7]University of Brescia, Brescia, Brescia, Italy, [8]ASST Spedali Civili-University of Brescia, Gussago, Brescia, Italy, [9]Rabin Medical Center, Beilinson Hospital, and Tel Aviv University, Petah-Tikva, Israel, [10]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [11]University of Toronto, Toronto, ON, Canada, [12]Duke University, Durham, NC, [13]Duke University, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

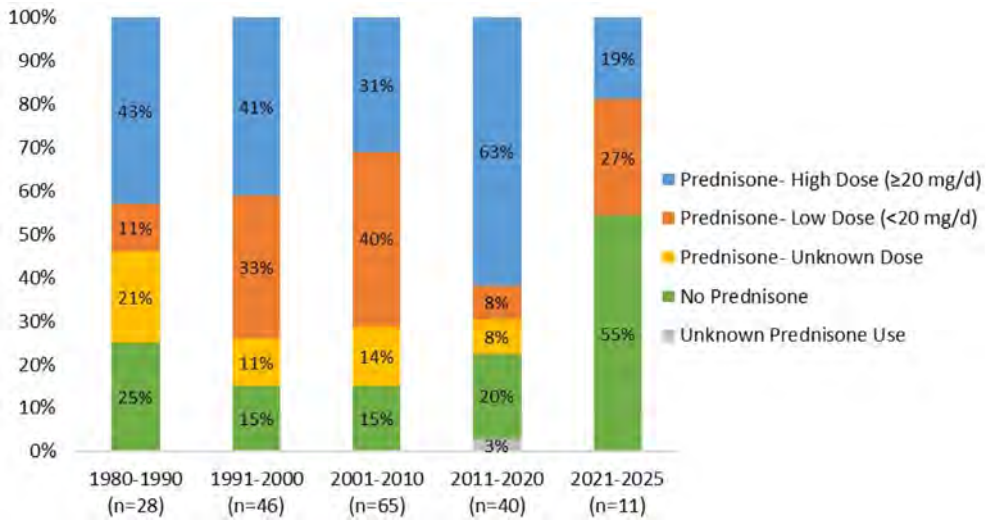
Background/Purpose: Women with SLE experience higher rates of adverse pregnancy outcomes. Among those with active SLE during pregnancy, lupus nephritis (LN) is associated with particularly poor pregnancy outcomes. Despite the significant impact of LN on pregnancy and offspring, treatment modalities have remained largely unchanged over the past decades. This study aims to utilize data from six international prospective pregnancy registries to describe changes in treatment patterns **for active LN during pregnancy** over several decades.

Methods: We identified prospective cohorts of pregnancies among women with SLE. We included data from six international prospective registries from the US (North Carolina, Maryland), Italy, Germany, Canada and Israel. Data from each cohort were collected and extracted individually into a harmonized dataset. Active LN was defined as proteinuria scored on the SLEDAI during pregnancy or urine protein–creatinine ratio >500 during any trimester. Pregnancies spanned over

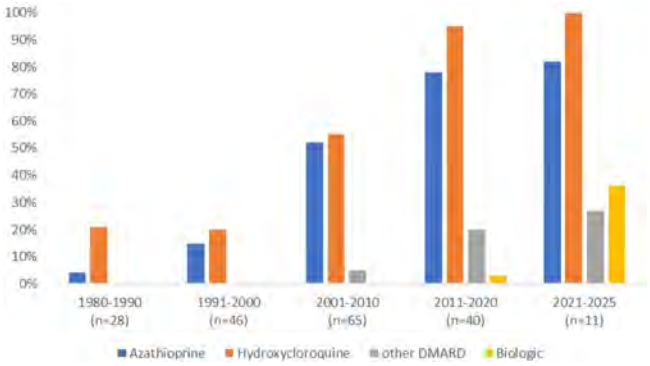
	1987-1990 n=28	1991-2000 n=46	2001-2010 n=65	2011-2020 n=40	2021-2025 n=11
Maternal Age, years Mean (range)	27.9 (20.0-34.6)	27.9 (19.0-41.6)	29.7 (19.8-40.4)	30.1 (21.0-43.9)	28.7 (24.2-32.6)
Maternal Race					
Asian	1 (4%)	3 (7%)	3 (5%)	0 (0%)	2 (18%)
Black	6 (21%)	20 (43%)	24 (37%)	21 (53%)	5 (45%)
White	21 (75%)	14 (30%)	12 (18%)	9 (23%)	2 (18%)
Other	0 (0%)	2 (4%)	3 (5%)	5 (13%)	1 (9%)
Unknown/Not Collected	0 (0%)	7 (15%)	23 (35%)	5 (13%)	1 (9%)
Center					
Canada	12 (43%)	5 (11%)	9 (14%)	3 (8%)	0 (0%)
Germany	0 (0%)	5 (11%)	22 (34%)	5 (13%)	0 (0%)
Italy	0 (0%)	0 (0%)	3 (5%)	1 (3%)	0 (0%)
Israel	0 (0%)	2 (4%)	1 (2%)	0 (0%)	0 (0%)
Maryland	16 (57%)	34 (74%)	23 (35%)	15 (38%)	2 (18%)
North Carolina	0 (0%)	0 (0%)	8 (11%)	16 (40%)	9 (82%)
Pregnancy Outcomes					
Preeclampsia	5 (28%)	9 (23%)	13 (24%)	11 (38%)	4 (44%)
Miscarriage	8 (29%)	3 (7%)	4 (7%)	2 (5%)	0 (0%)
Stillbirth	2 (7%)	2 (4%)	3 (5%)	2 (5%)	0 (0%)

Maternal characteristics and pregnancy outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Pattern of prednisone dosing across time for pregnancies with active LN.



Use of DMARDs and biologics across time for all pregnancies with active LN.

three decades (thirty-seven years) and were divided within five time periods. Only pregnancies with active LN, medication data, and known delivery dates were included, allowing for comparison of medication trends over time. Differences in pregnancy outcomes and medication use across time periods were measured using simple statistics.

Results: We included 190 pregnancies with active LN during pregnancy. Overall, the average maternal age was 28 years, ranging from 19 to 44 years, and maternal age was unchanged over time (Table 1). Included pregnancies were multiracial, with most identifying as Black (40%). When evaluating pregnancy outcomes, among those with delivery after 20 weeks gestation, 29% developed preeclampsia, ranging from 23% to 44% over time periods. Rates of miscarriage and stillbirth stayed similar across time periods.

While overall exposure to prednisone remained relatively stable over time, the percent of active LN pregnancies treated with high-dose prednisone (≥20 mg/day) was variable across time (Figure 1). An increasing trend for both hydroxychloroquine and azathioprine was observed, with hydroxychloroquine increasing from 21% to 100% and azathioprine increasing from 4% to 82% over time. This trend remained similar in analyses stratified by racial groups. Use of other pregnancy compatible DMARDs and/or biologics, including tacrolimus and cyclosporine, are more recent (Figure 2).

Conclusion: Our descriptive study indicates that treatment patterns for active LN during pregnancy across the past three decades have predominately included prednisone, azathioprine and hydroxychloroquine. Despite these treatments, outcomes remain poor, with nearly one-third of pregnancies among women with active LN complicated by preeclampsia. Future research will focus on investigating specific medication dosages and evaluating the treatment effects of azathioprine

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

on adverse pregnancy outcomes, aiming to identify the most effective treatment regimen for women with active LN during pregnancy.

Disclosure: D. Cintron: None; **A. Eudy**: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **R. Fischer-Betz**: None; **A. Mockbel**: None; **C. Nalli**: None; **L. Andreoli**: Pfizer, 2, UCB, 2; **A. Tincani**: Galapagos, 1, UCB, 1; **Y. Molad**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **M. Urowitz**: AstraZeneca, 6, GSK, 2, Merck/MSD, 2; **S. Balevic**: Purdue Pharma, 5, ReveraGen, 2, UCB, 2; **M. Clowse**: None.

Abstract Number: 2211

Maternal Adverse Pregnancy Outcomes and Risk Factors in Patients with Systemic Lupus Erythematosus in the United States

Grace Haeun Lee[1], Jacquelyn Nestor[2], Baijun Zhou[3] and April Jorge[2], [1]Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital, Boston

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Despite significant advances in SLE management, women with systemic lupus erythematosus (SLE) are at risk of adverse pregnancy outcomes (APOs). We sought to determine the risk and risk factors for maternal APOs among females with SLE in the US.

Methods: Using a large, multicenter, electronic health record (EHR) database (TriNetX), we performed a retrospective cohort study of reproductive-age females (age 15-44 years) with SLE. SLE was defined by ≥2 ICD codes >30 days and < 2 years apart. We identified pregnancies occurring before and after SLE diagnosis using ICD and CPT codes. We assessed APOs identified by ICD codes, including pre-eclampsia, preterm delivery, peripartum infection, venous thromboembolism, cardiomyopathy, maternal death, and a composite outcome including any of these events. We also assessed postpartum hospitalizations for SLE. We assessed potential risk factors, including demographics, geographic region, SLE severity index, SLE manifestations of lupus nephritis (LN) and antiphospholipid antibody syndrome (APS), and medication use in the six months prior to pregnancy onset, including hydroxychloroquine, oral glucocorticoids, belimumab, and known teratogenic immunosuppressant medications (i.e., methotrexate, mycophenolate, or leflunomide). We used multivariate logistic regression analysis to compare the odds of APOs according to potential risk factors.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of Females of Reproductive Age with SLE

Characteristics	All SLE females of childbearing age (n= 41,558)
Age, years, mean (SD)	32.6 (8.7)
Female, n (%)	41,558 (100)
Race/Ethnicity, n (%)	
White	17,085 (41.1)
Black	13,190 (31.7)
Asian	1,248 (3.0)
Hispanic	5,100 (12.3)
Other	4,935 (11.9)
Geographic Region, n (%)	
East	7,226 (17.4)
Midwest	6,809 (16.4)
South	21,982 (52.9)
West	4,585 (11.0)
Unknown	956 (2.3)
Charlson Comorbidity Index, mean (SD)	1.22 (0.94)
Chronic Kidney Disease stage ≥3	3,216 (7.7)
Early Lupus Nephritis, n (%)	4,571 (11.0)
SLE Severity Index, n (%)	
Mild	26,366 (63.4)
Moderate	10,540 (25.4)
Severe	4,652 (11.2)
Medication Use, n (%)	
Glucocorticoids	16,154 (38.9)
Hydroxychloroquine	15,957 (38.4)
Methotrexate	2,010 (4.8)
Mycophenolate	3,803 (9.2)
Leflunomide	274 (0.7)
Azathioprine	1,942 (4.7)
Cyclophosphamide	479 (1.2)
Rituximab	364 (0.9)
Belimumab	474 (1.1)
Other immunosuppressant	903 (2.2)
Healthcare Utilization	
Outpatient encounters, median (IQR)	2 (6)
ER/Inpatient visits, n (%)	15,302 (36.8)

Assessed in 12-months prior to date of meeting SLE definition unless otherwise specified. Early LN is defined as diagnosis within 6 months after SLE onset. SLE Severity Index is adapted from Garrison algorithm for administrative data. Other immunosuppressant use includes sulfasalazine, cyclosporine, tacrolimus, abatacept, tocilizumab, TNF inhibitors, IL17 inhibitors, IL12/23 inhibitors, and JAK inhibitors

Results: From January 2000 to August 2021, we identified 41,558 females of childbearing age with SLE and 9,180 with ≥1 pregnancy before or after the first SLE code (Table 1). There were 12,598 total SLE pregnancies, with 7,539 occurring before and 5,059 occurring after SLE diagnosis. Among pregnancies that occurred after diagnosis, 15.7% were exposed to teratogens within 6 months prior to pregnancy. The incidence of composite APOs among total SLE pregnancies was 22.8% (Table 2). Pre-eclampsia (11.4%), hospitalization for SLE (8.5%), and thromboembolism (8.0%) were the most common adverse maternal outcomes. Black and Hispanic patients were at increased risk for composite APOs and SLE hospitalizations (aORs for composite APOs: 1.34 [95% CI 1.17-1.53] and 1.20 [1.03-1.41]) for Black and Hispanic patients compared to White patients, respectively, and aORs for SLE hospitalizations: 1.42 [1.19-1.69] and 1.32 [1.07-1.62] for

Table 2. Maternal Adverse Pregnancy Outcomes in Patients with Systemic Lupus Erythematosus

Outcomes	Total SLE pregnancies N (%)	SLE Pregnancies Before SLE Diagnosis N (%)	SLE Pregnancies After SLE Diagnosis N (%)
Pre-Eclampsia/ Eclampsia	1240 (11.4)	767 (11.2)	473 (11.5)
Pre-term Delivery	718 (5.7)	461 (6.0)	257 (5.1)
Peripartum Infection	156 (1.2)	97 (1.3)	59 (1.2)
Thromboembolism	1007 (8.0)	489 (6.5)	518 (10.2)
Cardiomyopathy	88 (0.7)	59 (0.8)	29 (0.6)
Maternal Death	72 (0.6)	28 (0.4)	44 (0.9)
Composite APO Outcome	2,767 (22.8)	1,578 (20.9)	1,189 (23.5)
Hospitalization for SLE	1,076 (8.5)	541 (7.2)	535 (10.6)

Denominator is 12,598 total pregnancies for all outcomes other than pre-eclampsia/eclampsia outcome, which was assessed among pregnancies that were at least 26 weeks long, excluding spontaneous/elective abortions (n = 10,840).
APO, adverse pregnancy outcomes. Composite APO Outcome includes pre-eclampsia/eclampsia, pre-term delivery, peripartum infection, thromboembolism, cardiomyopathy, and maternal death.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Risk Factors for Composite Adverse Pregnancy Outcomes

	N (%)	Events (%)	Unadjusted OR	Adjusted OR*
Age at Pregnancy Onset				
<35 years	8,498 (78.4)	1,926 (22.7)	ref	ref
≥35 years	2,342 (21.6)	567 (24.2)	1.09 (0.97-1.23)	1.06 (0.94-1.20)
Race/Ethnicity				
White, non-Hispanic	4,485 (41.4)	901 (20.1)	ref	ref
Black	3,462 (31.9)	934 (27.0)	1.47 (1.30-1.67)	1.34 (1.17-1.53)
Hispanic	1,717 (15.8)	429 (25.0)	1.32 (1.14-1.55)	1.20 (1.03-1.41)
Asian	227 (2.1)	44 (19.4)	0.96 (0.67-1.37)	0.92 (0.64-1.32)
Other	949 (8.8)	185 (19.5)	0.96 (0.79-1.17)	0.94 (0.77-1.14)
Geographic Region				
East	2,132 (19.7)	443 (20.8)	ref	ref
South	5,414 (49.9)	1,267 (23.4)	1.16 (1.02-1.33)	1.05 (0.92-1.21)
Midwest	2,204 (20.3)	522 (23.7)	1.18 (0.99-1.42)	1.12 (0.93-1.35)
West	1,090 (10.1)	261 (23.9)	1.20 (0.99-1.45)	1.09 (0.90-1.32)
SLE severity				
Mild	8,263 (76.2)	1,623 (19.6)	ref	ref
Moderate	1,748 (16.1)	449 (25.7)	1.41 (1.22-1.64)	1.14 (0.97-1.35)
Severe	829 (7.6)	421 (50.8)	4.22 (3.60-4.95)	3.35 (2.80-4.01)
SLE Manifestations				
No Antiphospholipid Syndrome	9,006 (83.1)	1,793 (19.9)	ref	ref
Antiphospholipid syndrome	1,834 (16.9)	700 (38.2)	2.48 (2.19-2.81)	2.07 (1.81-2.36)
No Lupus nephritis	9,669 (89.2)	2,024 (20.9)	ref	ref
Lupus nephritis	1,171 (10.8)	469 (40.1)	2.52 (2.19-2.90)	1.75 (1.48-2.07)
Medication Use				
Hydroxychloroquine	2,021 (18.6)	552 (27.3)	1.33 (1.18-1.51)	0.96 (0.84-1.11)
Glucocorticoids	1,985 (18.3)	576 (29.0)	1.48 (1.31-1.67)	1.05 (0.93-1.20)
Teratogenic immunosuppressant†	534 (4.9)	210 (39.3)	2.28 (1.85-2.81)	1.26 (0.98-1.63)
Belimumab	81 (0.7)	31 (38.3)	2.09 (1.30-3.35)	1.38 (0.86-2.21)

Denominator includes pregnancies of duration ≥ 26 weeks, excluding spontaneous/elective abortions (total n = 10,840). *Adjusted for age, race and ethnicity, geographic region, SLE severity, lupus nephritis. † Includes methotrexate, mycophenolate, and leflunomide. Variables were assessed in the 12 months prior to pregnancy onset, other than medication use which was assessed in the 6 months prior to pregnancy onset.

Black and Hispanic patients compared to White patients, respectively). Patients with severe disease were at 3 times higher odds of APOs (Table 3) and a higher risk of SLE hospitalization (aOR 1.73, CI 95% 1.37-2.20). APS and LN also increased the risk of APOs and hospitalizations. When adjusted for SLE severity, medication use was not associated with the risk of composite APOs.

Conclusion: In this large EHR-based cohort of SLE pregnancies, we identified a high burden of composite and specific APOs. Patient factors associated with higher risks of APOs included Black race, Hispanic ethnicity, higher SLE severity, and disease manifestations of LN and APS. These findings highlight the importance of pregnancy counseling for reproductive-age females with SLE and efforts to improve maternal pregnancy care and outcomes.

Disclosure: G. Lee: Bristol-Myers Squibb(BMS), 12, Travel to Investigator Meeting; **J. Nestor**: None; **B. Zhou**: None; **A. Jorge**: Bristol-Myers Squibb(BMS), 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2212

Impact of the 2020 ACR Reproductive Health Guidelines on Treatment Strategies and Pregnancy Outcomes in Women with Systemic Lupus Erythematosus: A Single-Center Retrospective Study

Hiromi Shimada[1], Rina Mino[2], Taichi Miyagi[3], Koichi Sugihara[2], Yusuke Ushio[3], Mao Mizusaki[2], Kanako Chujo[3], Naoto Manabe[3], Mayuko Wada[2], Shusaku Nakashima[2] and Hiroaki Dobashi[2], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Kita-gun, Kagawa, Japan, [2]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa, Japan, [3]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Women with systemic lupus erythematosus (SLE) are at increased risks for adverse pregnancy outcomes (APOs) including preterm birth, low birth weight and preeclampsia (1,2). We previously reported that these APOs are related to uncontrolled high disease activity and specific treatments, particularly the dose of glucocorticoid (3,4). In 2020, the American College of Rheumatology (ACR) published guideline for the management of reproductive health, emphasizing the importance of preconception care and transitioning to pregnancy-compatible medication (5). This study aimed to assess whether treatment strategies and pregnancy outcomes in women with SLE changed after the publication of the 2020 ACR guideline at a single center.

Methods: We analyzed the data from SLE patients who had been treated at our institution during planning for pregnancy and subsequently gave birth from rheumatic disease pregnancy registry. Patients were divided into two groups: those who conceived before 2020 and those who conceived after 2020. We retrospectively compared patients' characteristics, disease activity, treatments, and pregnancy outcomes between the two groups.

Results: A total of 73 pregnancies in 55 patients were included: 54 pregnancies occurred before 2020 and 19 after 2020. Table 1 showed patients' characteristics and disease activity. There were no significant differences in age at conception or disease duration between two groups. However, the rate of preconception care implementation was significant higher after 2020 (P=0.031). No significant differences were observed in any disease activity parameters between two groups. Regarding treatment before and during pregnancy, the proportion of glucocorticoid (GC) use was significantly higher after 2020 (P=0.008 and 0.016, respectively, Figure a), although the mean GC dose was lower compared to the group before 2020 (P=0.067 and 0.022, respectively, Figure b). The use of immunosuppressants and hydroxychloroquine was significantly more common after 2020 (P< 0.001, Figure c,d). While no significant differences in pregnancy outcomes were found (Table 2), the incidence of SLE flares and preterm premature rupture of membrane tended to be lower in the cases after 2020 (P=0.126, 0.182, respectively), whereas the rate of hypertensive disorder of pregnancy tended to be higher (P=0.078).

Conclusion: Following the publication of the 2020 ACR guideline, preconception care became more widely implemented Additionally, the use of immunosuppressants and hydroxychloroquine during pregnancy increased, while lower doses of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patients' characteristics and disease activity parameters between before and after 2020

	Before 2020 (n=54)	After 2020 (n=19)	P value
Mean age at conception (years old)#	31.9 ± 4.4	31.9 ± 5.0	0.910
Mean disease duration (years)#	10.3 ± 5.3	13.2 ± 5.5	0.052
Preconception care (n (%))##	26 (48.2)	15 (79.0)	0.031*
SLEDAI#			
first trimester	2 [0, 2]	2 [0, 2]	0.959
third trimester	0 [0, 2]	0 [0, 2]	0.767
LLDAS achievement (n(%))##			
first trimester	34 (62.9)	14 (77.9)	0.387
third trimester	28 (58.4)	12 (80.0)	0.219
LLDAS achievement without glucocorticoid dose (n(%))##			
first trimester	41 (75.9)	16 (88.9)	0.327
third trimester	41 (85.4)	13 (86.7)	1.000
C3#			
first trimester	92.3 ± 21.2	86.6 ± 21.9	0.538
third trimester	103.1 ± 22.3	100.3 ± 25.7	0.657
C4#			
first trimester	18.3 ± 7.0	18.8 ± 6.1	0.719
third trimester	18.2 ± 7.5	17.4 ± 6.0	0.779
CH50#			
first trimester	41.9 ± 9.8	39.7 ± 10.6	0.403
third trimester	43.4 ± 9.4	43.1 ± 13.3	0.898
Titer of anti-dsDNA antibody#			
first trimester	0 [0, 14.3]	0 [0, 5.6]	0.311
third trimester	0 [0, 8.2]	0 [0, 3.1]	0.458

(Values are presented as the mean ± standard deviation or median [interquartile ranges] or number (percentile). #Wilcoxon rank sum test, ##Fisher's exact test.*P<0.05. LLDAS: low lupus disease activity status; SLEDAI: systemic lupus disease activity index.)

GC were used. These findings suggest that the 2020 ACR guidelines have significantly influenced treatment strategies for women with SLE who desire pregnancy.

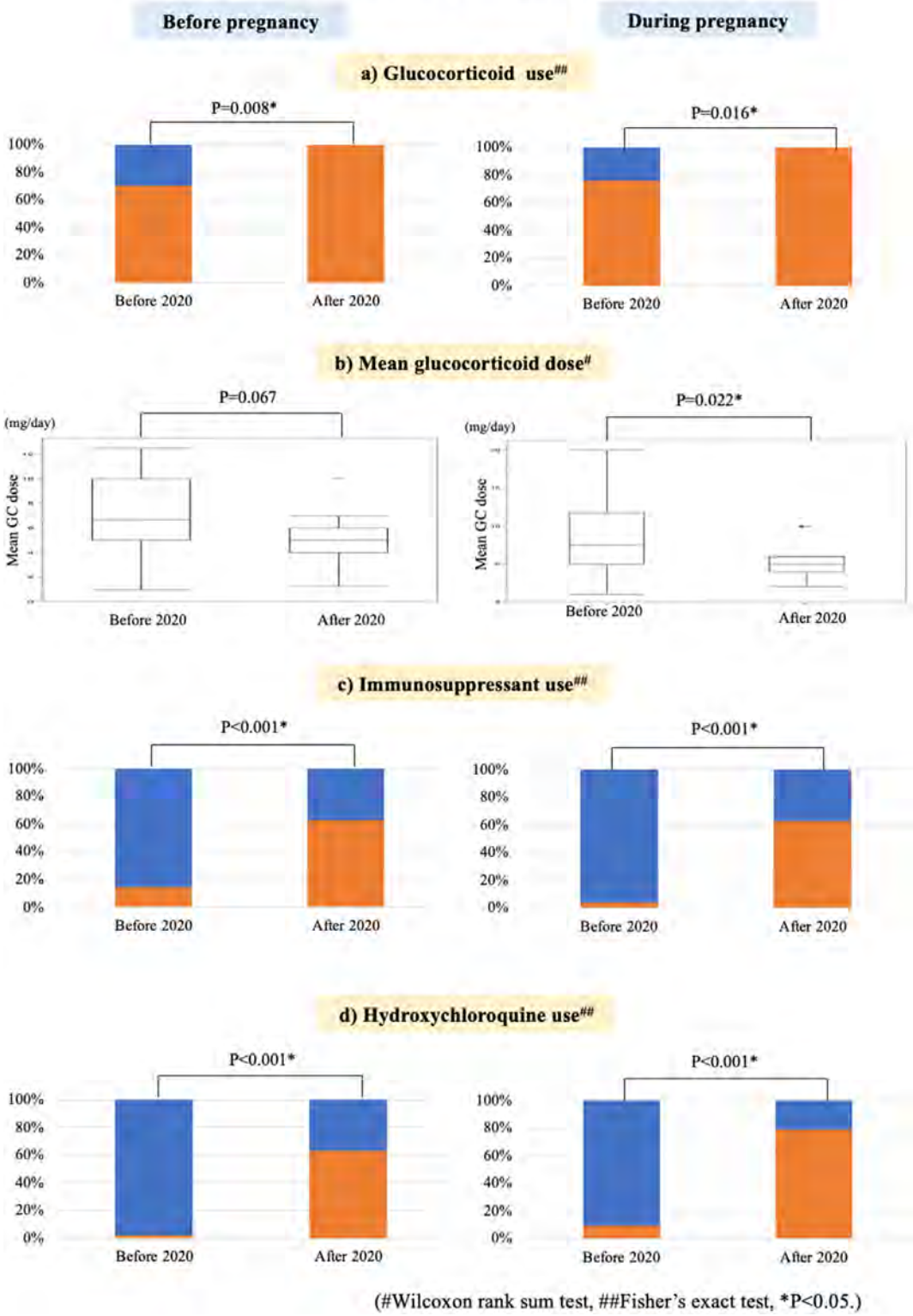
Reference:

1. Clowse ME, Jamison M, Myers E, James AH. Am J Obstet Gynecol. 2008;199:127.e1-6.
2. Bundhun PK, Soogund MZ, Huang F. J Autoimmun. 2017;79:17-27.
3. Shimada H, Wakiya R, Kanenishi K, et al. Arthritis Res Ther. 2022;24:10.
4. Shimada H, Wakiya R, Kameda T, et al. Lupus. 2023;32(7):833-841.
5. Sammaritano LR, Bermas BL, Chakravarty EE, et al. Arthritis Care Res. 2020;72:461-88.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure. Treatment before and during pregnancy



(#Wilcoxon rank sum test, ##Fisher's exact test, *P<0.05.)

Table 2. Pregnancy outcomes between before 2020 and after 2020

	Before 2020 (n=54)	After 2020 (n=19)	P value
Live birth (n (%))##	47 (87.0)	17 (89.5)	1.000
Mean gestational age at delivery (weeks)*	37.7 ± 2.7	37.8 ± 1.7	0.722
Mean gestational age of preterm birth	33.9 ± 3.2	35.0	1.000
Mean birth weight of newborns (gram)*	2716.9 ± 643.4	2555.9 ± 406.7	0.215
Mean birth weight of LBW newborn	2013.3 ± 510.4	2102.2 ± 262.9	0.876
Overall APOs (n (%))##	24 (44.4)	11 (57.9)	0.424
Maternal APOs (n (%))##	17 (31.5)	5 (26.3)	0.777
SLE flare (n (%))##	17 (31.5)	2 (10.5)	0.126
Hypertensive disorder of pregnancy (n (%))##	3 (6.5)	4 (23.5)	0.078
Neonatal APOs (n (%))##	28 (51.9)	9 (47.4)	0.794
Spontaneous abortion (n (%))##	5 (9.3)	2 (10.5)	1.000
Stillbirth (n (%))##	2 (3.7)	0 (0)	1.000
Preterm birth (n (%))##	11 (23.4)	3 (17.7)	0.745
Low birth weight (n (%))##	15 (31.9)	6 (35.3)	1.000
Small for gestational age (n (%))##	6 (12.8)	4 (23.5)	0.435
preterm premature rupture of membrane (n (%))##	6 (12.8)	0 (0)	0.182
Low Apgar score at 1 and 5 minutes (n (%))##	7 (14.9)/2 (4.3)	2 (11.8)/1 (5.9)	1.000/1.000
NICU administration (n (%))##	13 (27.7)	6 (35.3)	0.552

(Values are presented as the mean ± standard deviation or or number (percentile). #Wilcoxon rank sum test, ##Fisher's exact test.*P<0.05. APO: adverse pregnancy outcome, NICU: neonatal intensive care unit.)

Disclosure: H. Shimada: None; **R. Mino**: None; **T. Miyagi**: None; **K. Sugihara**: None; **Y. Ushio**: None; **M. Mizusaki**: None; **K. Chujo**: None; **N. Manabe**: None; **M. Wada**: None; **S. Nakashima**: None; **H. Dobashi**: None.

Abstract Number: 2213

Awareness Regarding Contraceptive Measures, Drug Usage And Factors Affecting Pregnancy Among Patients With Autoimmune Rheumatic Diseases

Juhi Dixit, Shri Balaji Institute of Medical Sciences, Mowa Raipur, Raipur, Chhattisgarh, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: This study aims to find out knowledge, attitude, practices and beliefs of patients with autoimmune rheumatic diseases regarding family planning, contraception, drug use and various factors which can affect pregnancy.

Methods: It was a cross-sectional observational study conducted in a tertiary care center of North India. A validated questionnaire-based survey was filled by 255 married females in the reproductive age group attending rheumatology OPD

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

over a period of one year. Postmenopausal women, widowed/divorced/separated couple and those not giving consent were excluded from the study.

Simple descriptive analysis of data was performed using absolute numbers and percentages for categorical variables and mean ± standard deviation for continuous variables.

Results: Section 1: Contraceptive awareness and usage

Most of the patients (245/255, 96%) were aware regarding family planning and contraception with most information sourced from mass media or the internet (136/255, 53.3%) followed by friends or relatives (87/255, 34%). Only 61/255 (24%) learned about contraception from physicians, suggesting a potential gap in physician-patient discussions on family planning. 198/255 (77.64%) patients reported that they were never told anything about the contraceptives during OPD visits. Barrier method (condoms) was most widely known (204/255, 80%) and most preferred (160/212, 75.47%). The most common reasons for not using contraception included lack of knowledge (32/96, 33.3%) and safety concerns (22/96, 22.91%).

Section 2: Awareness regarding rheumatological drugs and their impact on fertility and breastfeeding

Over half of patients (142/255, 55.68%) were unaware of the medications they were prescribed for their rheumatological condition and majority of them (220/255, 86.27%) were unaware of the availability of safe drugs for use during pregnancy. Nearly two third of the patients (165/255, 64.7%) believed that taking medications during pregnancy could adversely affect fetal growth. More than half of them (151/255, 59.21%) thought breastfeeding could lead to disease transmission.

Section 3: Awareness of the impact of rheumatic diseases on pregnancy and vice versa

Table 1: Baseline Characteristics

Baseline characteristics	
Age (years, mean±SD)	34.17 ±5.76
Education (Percentage, (n))	
Illiterate	5.8 (15)
School education (primary/middle/high school)	30.98 (79)
Graduate	32.15 (82)
Post-graduate	23.92 (61)
PhD	3.92 (10)
Others (Diploma courses)	6.27 (16)
Occupation (Percentage, (n))	
Employed	16.07 (41)
Home-maker	83.92 (214)
Duration of Illness (Years, mean ± SD)	4.5±4.62
Autoimmune rheumatic disease (percentage, (n))	
Rheumatoid arthritis	50.98 (130)
Spondyloarthritis	7.05 (18)
Systemic Lupus Erythmatosus	13.72 (35)
Sjogren Syndrome	4.70 (12)
Systemic Sclerosis	7.45(19)
Idiopathic Inflammatory myositis	2.35(6)
Others	13.72(35)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

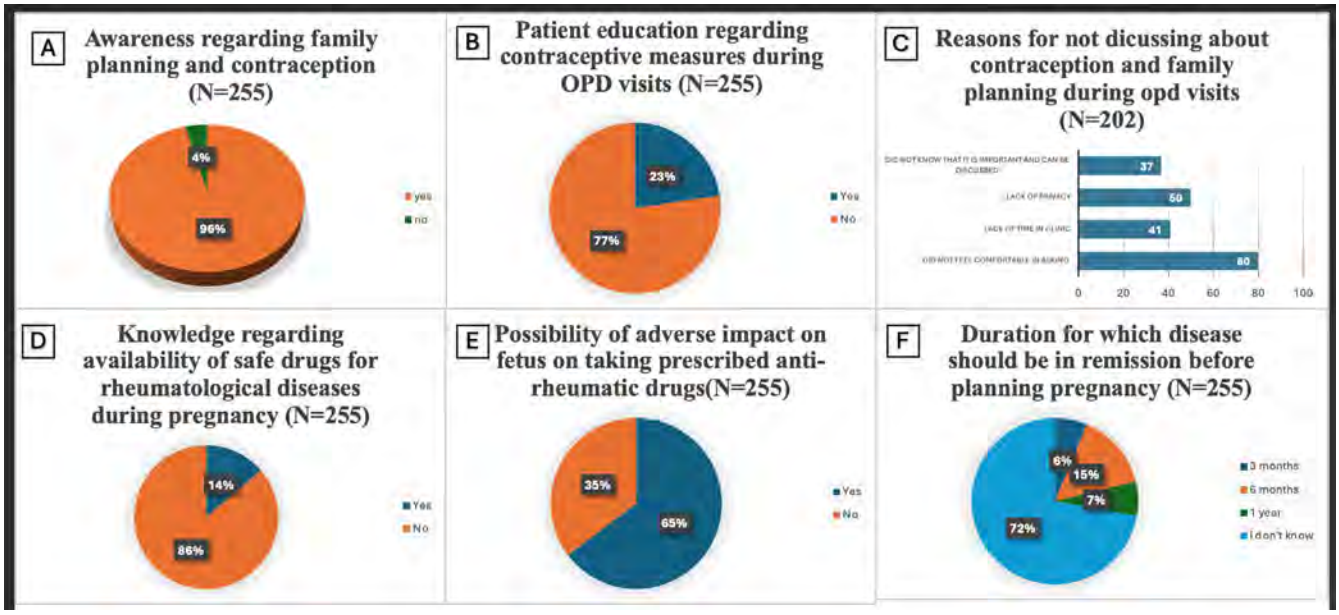


Figure 1 A : Pie chart showing awareness regarding family planning and contraception in patients attending rheumatology OPD, 1B : Pie chart showing physician initiated discussions for patient education regarding contraceptive measures in OPD, 1C: Bar graph showing reasons stated by patients for not initiating discussions regarding family planning and contraception by themselves during OPD visits, 1D : Pie chart showing knowledge among patients regarding the availability of safe drugs for rheumatologic diseases during pregnancy, 1E: Pie chart showing patients' belief regarding possibility of adverse impact on fetus on taking prescribed anti-rheumatic drugs, 1F: Pie chart depicting awareness among patients regarding the duration of remission of rheumatologic disease prior to planning pregnancy

More than two third of the patients (176/255, 69.01%) were unaware of how disease activity could affect pregnancy. Similarly, 174/255 (68.23%) were unaware of how pregnancy could affect disease activity. A significant number (184/255, 72.15%) were unaware of the duration of disease remission needed before conceiving, and only 38/255 (14.9%) were aware of the recommended six months of remission.

Conclusion: Study highlights the need for improved physician-patient communication which could significantly enhance the reproductive health and outcomes for patients with rheumatological conditions

Disclosure: J. Dixit: None.

Abstract Number: 2214

Hydroxychloroquine and Pregnancy Outcomes in Lupus: Results from a population-based cohort study

Sadaf Sediqi[1], leo lu[2], J. Antonio Aviña-Zubieta[3] and **Julia F Simard**[4], [1]Stanford University, Palo Alto, CA, [2]Arthritis Research Canada, Vancouver, BC, Canada, [3]University of British Columbia/Arthritis Research Canada, Vancouver, BC, Canada, [4]Stanford Medicine, Stanford, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) can pose an increased risk of adverse pregnancy outcomes such as preeclampsia and preterm delivery. Hydroxychloroquine (HCQ), commonly used to manage SLE, especially during pregnancy, has shown conflicting associations with pregnancy outcomes, highlighting an important knowledge gap. In this study, we explored the association between HCQ use and the risk of preeclampsia/eclampsia and preterm delivery, while accounting for important maternal covariates in a cohort of SLE pregnant patients.

Methods: We studied SLE singleton pregnancies among publicly insured patients in the British Columbia Perinatal Data Registry (BCPDR). We studied pregnancies where SLE was recorded before pregnancy and defined HCQ treatment during pregnancy multiple ways, including at least two fills or minimum of 60 days' supply during the first 20 weeks of pregnancy. For binary outcomes modified Poisson models estimated risk ratios (RRs) and 95% confidence intervals (CIs) using propensity scores to address confounders. For preterm delivery, we also conducted a time-to-event analysis using a Cox proportional hazards model. Multiple sensitivity analyses explored definitions of SLE, HCQ exposure, and outcomes and stratified analyses examined effect modification.

Results: We studied 847 pregnancies to 597 women with SLE during pregnancy. Most pregnancies were among non-smokers at the start of pregnancy (93.9%). The mean age was 33 years old (SD=4.6 years). Use of HCQ, defined as ≥2 fills

Table 1. Association between hydroxychloroquine use in the first 20 weeks of pregnancy and adverse pregnancy outcomes in patients with SLE (RR: Risk Ratio; 95% CI: 95% confidence intervals; HR: Hazard Ratio)

All Pregnancies			
	Preeclampsia/Eclampsia		
Exposure	N cases/at risk	RR (95% CI)*	
2+ fill or over 60 days	20/303 vs. 20/490	0.92 (0.47, 1.80)	
1+ fill or any day	23/357 vs. 20/490	0.93 (0.49, 1.76)	
	Preterm Delivery (34 Weeks Cut-off)		
Exposure	N cases/person-weeks	HR (95% CI)*	RR (95% CI)*
2+ fill or over 60 days	18/4951 vs. 20/8144	1.06 (0.54, 2.10)	1.05 (0.53, 2.09)
1+ fill or any day	23/5812 vs. 20/8144	1.31 (0.68, 2.54)	1.29 (0.68, 2.44)
	Preterm Delivery (37 Weeks Cut-off)		
Exposure	N cases/person-weeks	HR (95% CI)*	RR (95% CI)*
2+ fill or over 60 days	74/4951 vs. 72/8144	1.40 (0.98, 2.00)	1.40 (0.99, 1.98)
1+ fill or any day	83/5812 vs. 72/8144	1.36 (0.97, 1.93)	1.35 (0.96, 1.89)
Parity: Nulliparous			
	Preeclampsia/Eclampsia		
Exposure	N cases/person-weeks	HR (95% CI)*	
2+ fill or over 60 days	16/148 vs. 14/194	0.92 (0.41, 2.03)	
1+ fill or any day	17/171 vs. 14/194	0.88 (0.42, 1.87)	
	Preterm Delivery (< 34 weeks)		
Exposure	N cases/person-weeks	HR (95% CI)*	RR (95% CI)*
2+ fill or over 60 days	11/2419 vs. 9/3219	1.14 (0.45, 2.93)	1.15 (0.45, 2.94)
1+ fill or any day	14/2783 vs. 9/3219	1.42 (0.56, 3.60)	1.42 (0.59, 3.41)
	Preterm Delivery (< 37 weeks)		
Exposure	N cases/person-weeks	HR (95% CI)*	RR (95% CI)*
2+ fill or over 60 days	39/2419 vs. 26/3219	1.70 (0.97, 2.97)	1.69 (1.00, 2.85)
1+ fill or any day	44/2783 vs. 26/3219	1.73 (1.01, 2.98)	1.70 (1.02, 2.81)

*Propensity score adjusted

Primary analysis results

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

or ≥60 days' supply compared to no fills, had an adjusted RR of 0.92 (95% CI: 0.47, 1.80) for preeclampsia/eclampsia overall. Results were similar when expanding the exposure window to include three months preconception. In sensitivity analyses, the RR for the early-onset phenotype was smaller (0.72 CI: 0.27, 1.92) although based on smaller numbers. For preterm delivery, we found generally no association across different definitions and approaches. For example, ≥2 fills had an adjusted hazard ratio (HR) of 1.06 (95% CI: 0.54, 2.10). The stratified analyses results showed no appreciable differences.

Conclusion: HCQ use during early pregnancy was not significantly associated with the risk of preeclampsia or preterm delivery. Like past work, the RR was below the null for preeclampsia, but not statistically significant. Residual confounding and misclassification cannot be excluded, and further larger studies with detailed clinical data may shed light on these findings as the potential impact of HCQ on pregnancy outcomes is needed.

Disclosure: S. Sediqi: None; **I. Iu**: None; **J. Aviña-Zubieta**: None; **J. Simard**: None.

Abstract Number: 2215

Placenta Abnormalities in Systemic Lupus Erythematosus: Novel Marker of Adverse Pregnancy Outcomes

Kaitlin Nuechterlein[1], Karl Grenier[1], Luisa Ciofani[2], Kalliopi Panaritis[2], Sasha Bernatsky[2] and Evelyne Vinet[2], [1]McGill University, Montreal, QC, Canada, [2]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Placenta-mediated adverse pregnancy outcomes (APO) are a huge concern in SLE. Recent efforts to understand APO include the establishment of the 2016 Amsterdam classification criteria, developed to standardize placental pathology evaluation. No study to date evaluated the Amsterdam criteria in SLE. Using the prospective "Lupus prEGnAnCY (LEGACY)" biobank, we assessed the relationship between placental abnormalities, lupus anticoagulant (LAC), and APO, applying the Amsterdam criteria.

Methods: LEGACY is a prospective cohort enrolling SLE pregnancies (before the 17th gestational week). Relevant information is collected at each trimester and/or end-of-pregnancy visits. We evaluated pregnancies delivered beyond 17 weeks at the Montreal site. Placenta pathology was defined as abnormal if fulfilling at least one of the 4 main Amsterdam classification subtypes: 1) maternal vascular malperfusion, 2) fetal vascular malperfusion, 3) acute chorioamnionitis, and/or 4) villitis of unknown etiology. Pregnancies with and without abnormal pathology were further characterized based on presence of LAC and APO (i.e. stillbirth, placental insufficiency, gestational hypertension, preeclampsia, small-for-gestational age neonate < 5%).

Results: Of 44 LEGACY pregnancies delivered (beyond 17 weeks), 30 (68%) had placenta pathology available. Among these 30, 13 (43%) had abnormal pathology. Of those with abnormal pathology, 6/1 (46%) had maternal vascular malperfusion, 5/13 (38%) acute chorioamnionitis, 4/13 (31%) villitis of unknown etiology, and 1/13 (8%) fetal vascular malperfusion. Mean gestational age at delivery was substantially lower in pregnancies with abnormal pathology [mean 33.7 weeks, standard deviation (SD) 6.8] versus those with normal pathology (mean 37.8 weeks, SD 1.7), with a difference in mean gestational age of -4.1 weeks (95% CI -0.6, -7.6). LAC was more frequent in pregnancies with abnormal pathology (4/13; 31%) as opposed to pregnancies with normal pathology (2/17; 12%). APO occurred in 8/13 (62%) pregnancies with abnormal pathology (including 3 with early preterm preeclampsia < 34 weeks) as opposed to 7/17 (41%) pregnancies with normal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pathology (none with early preterm preeclampsia). Maternal vascular malperfusion was strongly associated with APO (odds ratio 8.1; 95% CI 0.8, 83.7), although the CI included the null.

Conclusion: In this cross-sectional analysis, SLE pregnancies with abnormal placental pathology, particularly maternal vascular malperfusion, experienced shorter gestation and more severe placenta-mediated APO, including early preterm preeclampsia. Future studies will aim to expand the sample, and investigate if placental abnormalities in one pregnancy helps predict APO in subsequent pregnancies.

References: Khong T. Arch Pathol Lab Med 2016; 140(7): 698-713.

Disclosure: K. Nuechterlein: None; **K. Grenier**: None; **L. Ciofani**: None; **K. Panaritis**: None; **S. Bernatsky**: None; **E. Vinet**: None.

Abstract Number: 2216

Expanding Reproductive Health Assessments in Rheumatic Diseases: A Comparative Analysis of Demographic and Disease-Specific Factors

Krista Topalsky[1], Chelsea Guan[2], Lindsay Frumker[3], Dana Nachawati[2], Areeb Tiwana[4], Meghan Gump[2], Omer Pamuk[5] and Marina Magrey[6], [1]University Hospitals, Shaker Heights, OH, [2]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [3]University hospitals Cleveland medical center, Highland Heights, OH, [4]Canton Medical Education Foundation, Canton, OH, [5]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [6]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Building on our 2024 ACR study (Topalsky et al.) that described broad knowledge gaps and interest in reproductive health education among women with rheumatic diseases, we designed a follow-up study to assess whether these needs vary across clinical and demographic subgroups. This study aimed to explore whether disease type, time since diagnosis, or age significantly influence sexual and reproductive health (SRH) concerns amongst our patients.

Methods: In this follow-up study, a revised survey was sent to our female patients aged 18-45 years with autoimmune rheumatic diseases seen in the Rheumatology Department at our institution. We developed a mixed-format questionnaire expanding on the 2024 survey to further assess demographic, clinical, and attitudinal data.

Subjects were identified using Slicer Dicer, a data exploration tool in the EPIC EMR that allows for customized searches on large patient populations. Surveys were sent and patient responses collected through REDCap, a secure web application for building and managing online surveys and databases. We conducted chi-square analyses comparing outcomes across subgroups (disease type, time since diagnosis, age group) to identify any differential needs. The study received IRB approval at our institution.

Results: 200 patients received an online survey, of which 61 replied, yielding a 30.5% response rate. Respondents were predominantly middle-aged white patients with a range of rheumatologic diagnoses, most of whom felt their disease was stable (Figure 1). About half reported ever receiving pregnancy-related information and understanding of pregnancy risks

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

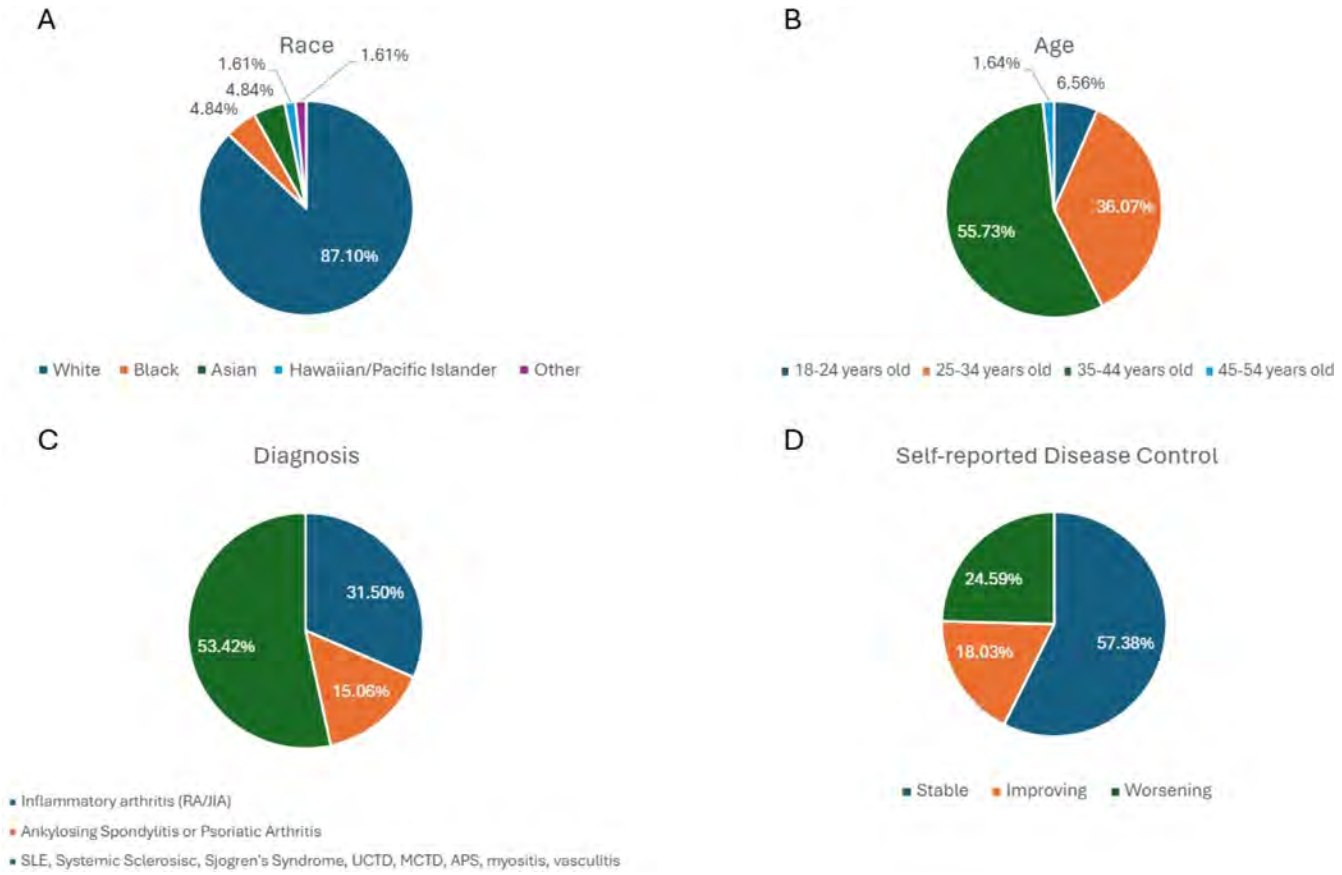


Figure 1. Demographic and Clinical Characteristics of Respondents

varied, with a large portion feeling only somewhat or not informed (Figure 2). Interest in targeted reproductive-health education was high across all subgroups, particularly around fertility and conception as well as managing parenthood with a chronic illness (Figure 3).

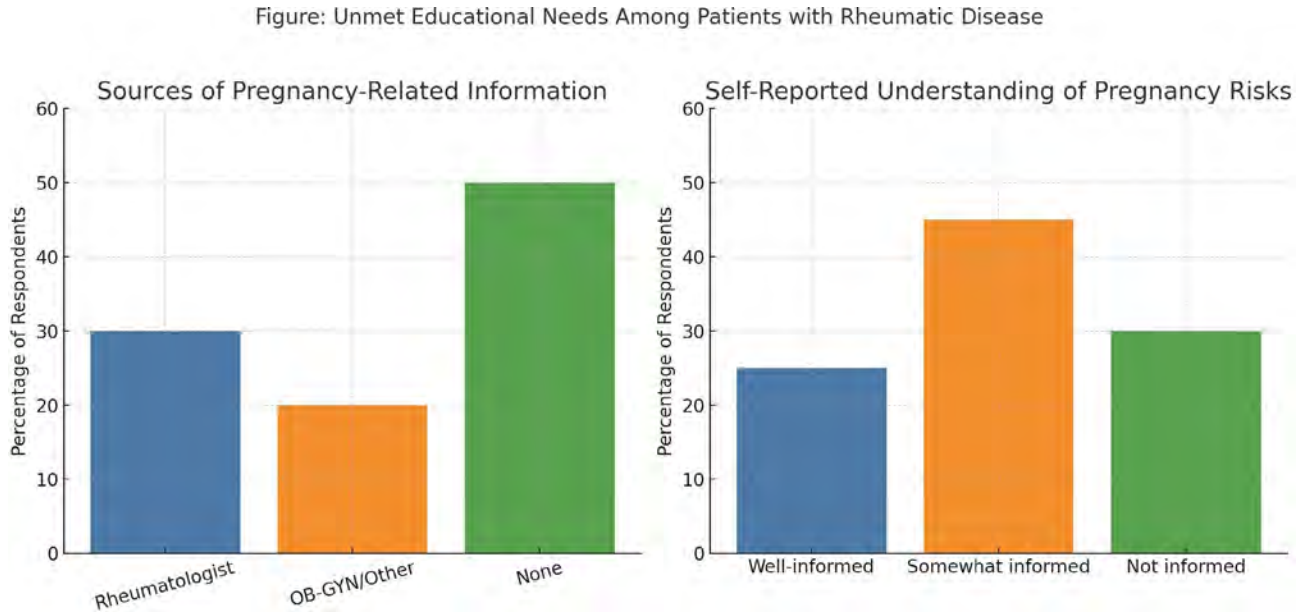


Figure 2. Unmet Educational Needs: Information Sources and Risk Understanding

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

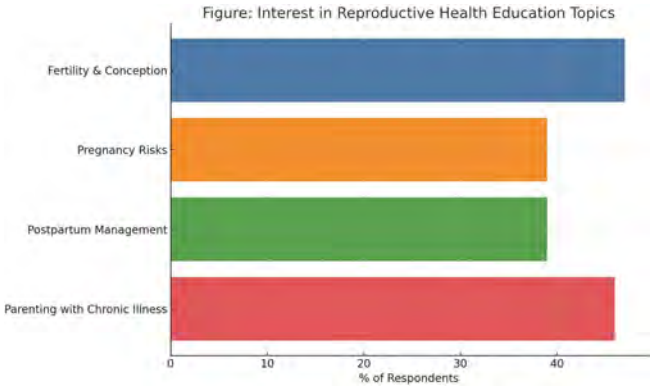


Figure 3. Interest in Reproductive Health Education Topics

Subgroup analyses revealed no significant differences by disease type, diagnosis duration, or age in disease control, contraception use, pregnancy concerns, information receipt, risk understanding, or interest in educational sessions (all $p > 0.05$), suggesting that reproductive-health needs are uniformly shared across all patient subgroups.

Conclusion: While our 2024 abstract described widespread informational gaps and a strong preference for online education, this follow-up with novel subgroup analysis reveals that these gaps and needs are uniformly experienced across all patient groups. This supports the development of universally accessible reproductive health education for rheumatology patients. These insights go beyond earlier descriptive findings and directly inform the design of inclusive educational interventions.

Disclosure: K. Topalsky: None; **C. Guan**: None; **L. Frumker**: None; **D. Nachawati**: None; **A. Tiwana**: None; **M. Gump**: None; **O. Pamuk**: None; **M. Magrey**: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5.

Abstract Number: 2217

Improving Patient Counseling on Medication Safety During Reproductive Years

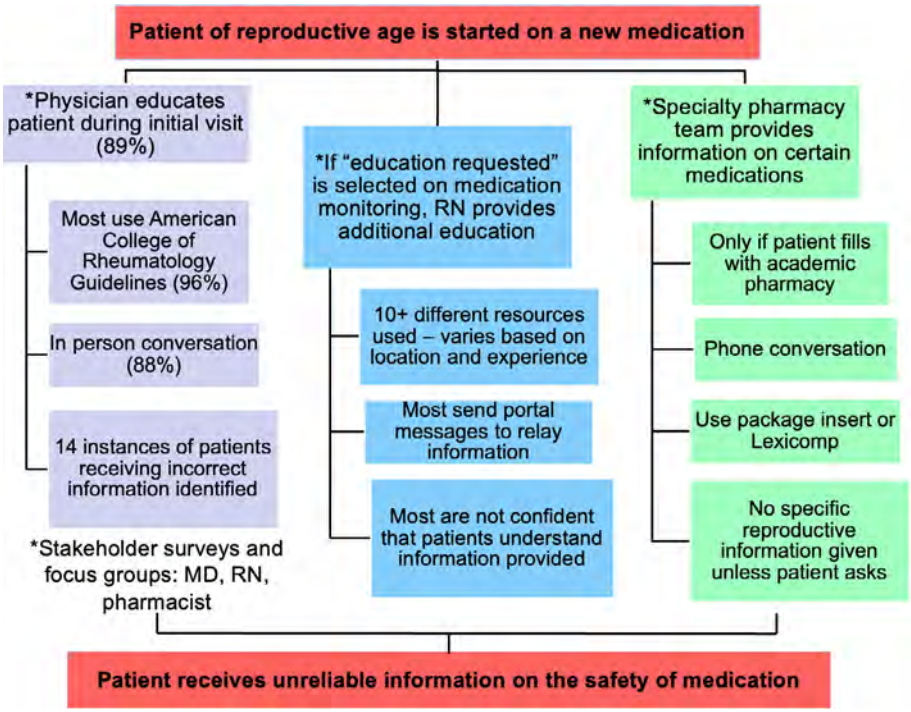
Lauren He[1], Anne Carlton[2], Rocio Bautista-Sanchez[1], Yasmin Khader[3] and Puja Khanna[4], [1]University of Michigan, Ann Arbor, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan/VA Ann Arbor, Ann Arbor, [4]Division of Rheumatology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatic diseases require dedicated counseling on reproductive planning from their rheumatologist.[1] Information shared on safety of medications during pregnancy and lactation can be disparate depending on clinical setting, educational sources, method of communication, and type of provider. This wide variability can lead to patients receiving inconsistent information and miscommunications contributing to psychosocial distress, provider mistrust, and medication non-adherence, ultimately resulting in poor outcomes.[2] The objective of this study was to evaluate current practices of patient counseling on medication safety during reproductive years at a large academic institution.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Root Cause Analysis: Stakeholder focus groups and surveys

Methods: Electronic medical records of patients ages 18-45 years who were prescribed methotrexate, azathioprine, leflunomide, mycophenolate, tacrolimus, or adalimumab from July 2023 - December 2024 were analyzed to quantify demographics, prescription patterns, and documented medication counseling processes. Stakeholder focus groups including physicians, registered nurses (RNs), and pharmacists were conducted to understand workflows in use to counsel patients, with a specific focus on pregnancy and lactation. A provider survey was created to appraise common educational resources in use and quantify incidence rates of inaccurate information being given to patients.

Results: There were 2448 patients of reproductive age during the study period: 58.6% (n=1436) of this population had been historically prescribed a teratogenic medication, and 616 were currently on an active prescription of methotrexate (n=296), mycophenolate (n=246), or leflunomide (n=74). Forty percent of clinicians reported at least one instance of a patient receiving incorrect information regarding medication safety. Resources used were evidence-based, however geared toward specific audiences and provider categories, leading to significant discrepancy in reliable translation of this information at the patient's level. Nurses and pharmacists had predetermined workflows, therefore counseled patients differently compared

Resource/References	Care Team Member Utilization		
	Physicians	RNs	Pharmacists
ACR website	x		x
Cleveland Clinic/Mayo Clinic websites		x	
Clinical reference in Epic warehouse (MiChart)	x	x	
Google/Artificial Intelligence summaries		x	
LactMed	x		
Lexicomp	x		x
MotherToBaby website	x	x	
OTIS Registry	x		
Package insert/manufactures websites	x		x
Rheuminfo.com		x	
Shared Smart Phrases/Dot Phrases		x	
Uminfo.com	x	x	
UpToDate	x		

Resources used by various care team members

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

to clinicians (Figure 1). There were at least 13 resources with contrasting levels of accuracy used to educate patients on this topic (Table 1).

Conclusion: There are fundamental variances in patient-oriented educational protocols and practice patterns among practitioners including clinicians, nurses and pharmacists at a large academic practice despite existing guidelines. Standardization of accurate evidence-based resources is key to help eliminate discrepancies when providing reliable and quality education on medication related safety to patients.

Disclosure: L. He: None; **A. Carlton**: None; **R. Bautista-Sanchez**: None; **Y. Khader**: None; **P. Khanna**: Arthrosi, 5, Olatec, 5, Selecta Biosciences, 5, Sobi, 2.

Abstract Number: 2218

Pregnancy Outcomes and Placental Findings in Women with IgA Vasculitis: A Case-Control Study

Edgar Iván Mendoza Ríos, **María Del Carmen Zamora Medina**, Mario Isaac Lumbreras Márquez, Diana Yazmin Copado mendoza, Oralia Alejandra Orozco Guillén, Maria José rodríguez Sibaja, Martha Leticia Palafox Vargas and Sandra Acevedo gallegos, Instituto Nacional de Perinatología, Mexico City, Distrito Federal, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IgA vasculitis (IgA-V) is a systemic vasculitis involving small vessels, most frequently affecting children. There is few information about pregnancy outcomes in women with history of IgA-V and no data regarding placental findings in these pregnancies.

The aim of this study is to compare vasculitic, maternal and fetal outcomes, and placental findings in pregnant patients with IgA-V and healthy patients.

Methods: We conducted a retrospective case-control study in a single third level center in Mexico City. We included pregnant women and prior IgA-V diagnosis (cases), with placental histopathology available. Control group included healthy

Table 1. Characteristics of the study population.

	IgA Vasculitis cases	Controls	Standardized difference
Feature	N = 20	N = 60	
Age, years, mean, SD	25.10 ± 4.90	20.72 ± 5.21	0.86
BMI, kg/m^2, mean, SD	25.49 ± 5.87	25.80 ± 6.90	0.04
Tobacco exposure, n (%)	0 (0.0)	1 (1.7)	0.18
Twin pregnancy, n (%)	0 (0.0)	1 (1.7)	0.18
Gravidity, median, IQR	1 [1, 2]	1 [1, 1]	0.08
Fetal death history, n (%)	0 (0.0)	0 (0.0)	—
Type 1 diabetes, n (%)	0 (0.0)	0 (0.0)	—
Type 2 diabetes, n (%)	0 (0.0)	1 (1.7)	0.18
Chronic hypertension, n (%)	1 (5.0)	0 (0.0)	0.31
Hypothyroidism, n (%)	0 (0.0)	2 (3.3)	0.26
Hyperthyroidism, n (%)	0 (0.0)	1 (1.7)	0.18

SD = Standard deviation; BMI = Body mass index; IQR = Interquartile range.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Vasculitis features	N (%)
Age at diagnosis, median, IQR	12.0 [7.5, 15.5]
Constitutional symptoms, n (%)	6 (31.6)
Cutaneous activity, n (%)	20 (100.0)
Arthritis, n (%)	3 (15.0)
Arthralgia, n (%)	5 (26.3)
Myalgia, n (%)	4 (20.0)
Abdominal pain, n (%)	3 (15.8)
Diarrhea, n (%)	0 (0.0)
Ileum, n (%)	0 (0.0)
Gastrointestinal hemorrhage, n (%)	1 (5.0)
Intestinal perforation, n (%)	0 (0.0)
Renal activity, n (%)	3 (15.8)
Baseline corticosteroid use, n (%)	11 (55.0)
Baseline corticosteroid bolus treatment, n (%)	3 (15.0)
Baseline azathioprine, n (%)	3 (15.0)
Mycophenolate use, n (%)	0 (0.0)
Flares during gestation, n (%)	2 (10.0)
Renal	0 (0.0)
Cutaneous	2 (100.0)
Joints	0 (0.0)
Gastrointestinal	0 (0.0)
Constitutional	0 (0.0)
Other	0 (0.0)
Hospital admission due to flare, n (%)	1 (50.0)

pregnant patients matched by age, number of pregnancies, number of fetuses, BMI and smoking status. Placental findings were categorized per the 2016 Amsterdam Working Group: 1) Maternal vascular malperfusion (MVM), 2) fetal vascular malperfusion (FVM), 3) inflammation/infection, and 4) villitis of unknown etiology.

Results: We analyzed 20 pregnancies in patients with history of IgA vasculitis and 60 matched controls. The median age at IgA-V diagnosis was 12.0 [IQR 7.5, 15.5] years and mean age at gestation was 25.10 ± 4.90 years. During pregnancy two patients (10%) flared, presenting cutaneous manifestations. No differences were observed in hypertensive disorders of pregnancy (5% vs 6.7%; p=0.99), gestational diabetes (0% vs 3.3%; p=0.99), preterm delivery (mean gestational age at birth 38.83 ± 0.99 vs 38.49 ± 2.16; p=0.50), fetal growth restriction (15% vs 5%; p=0.16), stillbirth (0% vs 1.7%; p=0.99),

Table 2. Fetal, neonatal, obstetric, and placental outcomes.

Outcome	IgA Vasculitis cases N = 20	Controls N = 60	*P*-value
EFW in last ultrasound, grams, mean, SD	2652.90 ± 585.82	2492.30 ± 670.88	0.340
EFW percentile in last ultrasound, mean, SD	44.90 ± 26.83	37.82 ± 21.52	0.240
Fetal growth restriction, n (%)	3 (15.0)	3 (5.0)	0.161
Fetal death, n (%)	0 (0.0)	1 (1.7)	0.999
Hypertensive disorders of pregnancy, n (%)	1 (5.0)	4 (6.7)	0.999
Gestational diabetes, n (%)	0 (0.0)	2 (3.3)	0.999
Maternal death, n (%)	0 (0.0)	0 (0.0)	–
Gestational age at delivery, weeks, mean, SD	38.83 ± 0.99	38.49 ± 2.16	0.500
Delivery mode, n (%)			0.539
Spontaneous vaginal delivery	11 (55.0)	28 (46.7)	
Assisted vaginal delivery	2 (10.0)	3 (5.0)	
Elective cesarean delivery	6 (30.0)	20 (33.3)	
Emergency cesarean delivery	1 (5.0)	9 (15.0)	
Miscarriage	0 (0.0)	0 (0.0)	
Birthweight, grams, mean, SD	3013.85 ± 358.91	3031.67 ± 535.12	0.890
Five-minute Apgar, median, IQR	9 [9, 9]	9 [9, 9]	0.220
NICU admission, n (%)	1 (5.0)	4 (6.8)	0.999
Perinatal death, n (%)	1 (5.0)	1 (1.7)	0.440
Placental weight, grams, mean, SD	443.62 ± 85.61	465.24 ± 93.06	0.450
Placental weight <10th percentile, n (%)	3 (23.1)	11 (21.6)	0.999
Maternal vascular malperfusion, n (%)	9 (45.0)	22 (36.7)	0.599
Fetal vascular malperfusion, n (%)	8 (40.0)	14 (23.3)	0.161

SD = Standard deviation; IQR = Interquartile range; EFW = Estimated fetal weight; NICU = Neonatal intensive care unit admission.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

NICU admission (5% vs 6.8%; p=0.99) and perinatal death (5% vs 1.7%; p=0.44). Placental weight averaged 443.62 ± 85.61 grams in IgA-V group, similar to control group (p=0.45). Maternal vascular malperfusión (45% vs 36.7%; p=0.599) and fetal vascular malperfusion (40% vs 23%; p=0.16) were the main placental findings in both groups.

Conclusion: Women with a history of IgA-V have favourable maternal and fetal outcomes, similar to the healthy population matched by age. Placental findings, such as MVM and FVM, were not more frequent in patients with IgA-V.

Disclosure: E. Mendoza Ríos: None; **M. Zamora Medina**: None; **M. Lumbreras Márquez**: None; **D. Copado mendoza**: None; **O. Orozco Guillén**: None; **M. rodríguez Sibaja**: None; **M. Palafox Vargas**: None; **S. Acevedo gallegos**: None.

Abstract Number: 2219

Transcriptomic and Immune Landscape of Recurrent Pregnancy Loss and Unexplained Infertility in Systemic Lupus Erythematosus

Rodolfo Martinez-Canales[1], Braulio R. Avalos-Garcia[2], Andres M. Ortiz-Rios[2], Eva Abigaid Galindo-Calvillo[2], Lorena Perez-Barbosa[2], Dionicio A. Galarza-Delgado[3], Cassandra Michele Skinner-Taylor[2], Mario Cesar Salinas-Carmona[1] and **Noe Macias-Segura**[1], [1]Immunology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

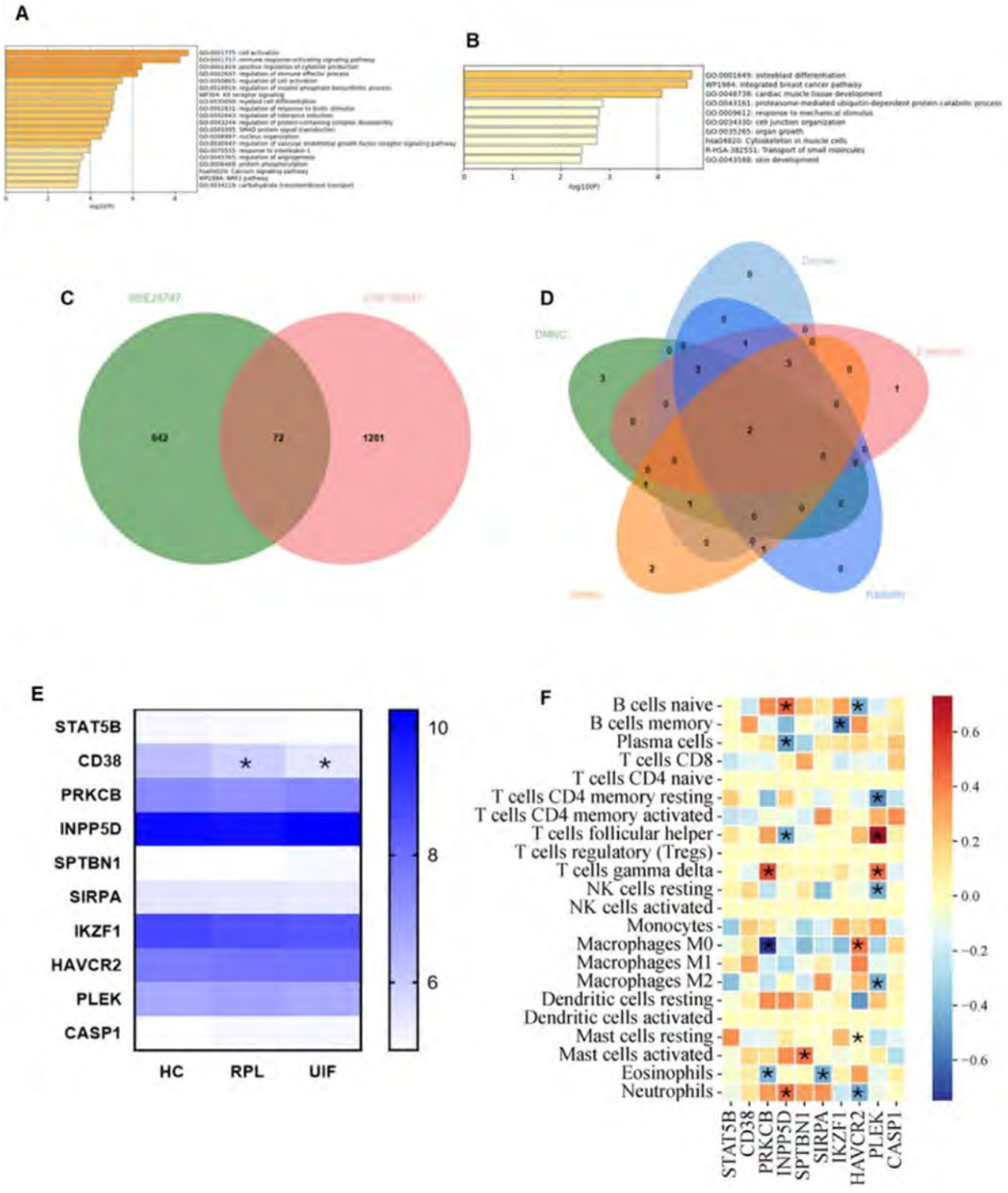
Background/Purpose: Recurrent pregnancy loss (RPL) and unexplained infertility (UIF) are significant reproductive health challenges in patients with systemic lupus erythematosus (SLE). SLE causes systemic inflammation and multi-organ involvement, potentially affecting reproductive outcomes. This study uses transcriptomic data to analyze the pathogenesis of RPL and UIF in patients with SLE.

Methods: Datasets GSE185047, GSE26787, and GSE165004 were downloaded from the Gene Expression Omnibus. Table 1 summarizes dataset characteristics. Dysregulated genes (DEGs) were identified using GEO2R with thresholds: false discovery rate < 0.05, log2 fold change > 1 for upregulated genes, and < -1 for downregulated genes. Enrichment analysis was performed using Metascape to retrieve enriched terms. Shared upregulated DEGs were visualized with a Venn diagram.

A gene activation network of overlapping upregulated DEGs was constructed using Cytoscape. The top ten hub genes (HGs) were identified using five algorithms: DMNC, Degree, Eccentricity, Stress, and Radiality. Validation was conducted in GSE165004. Immune profiling analyzed 22 immune cell types using CIBERSORT. A two-way ANOVA with the two-stage step-up method compared immune cell abundances across groups. Spearman correlation tests analyzed relationships between gene expression and immune cell proliferation, using mean fluorescence intensity values and immune cell percentages as variables.

Results: We identified 74 upregulated and 75 downregulated DEGs. Upregulated DEGs were enriched in pathways related to cytokine production, myeloid differentiation, and immune response signaling (Figure 1A). Downregulated DEGs were enriched in osteoblast differentiation, breast cancer, and cardiac muscle development (Figure 1B). 72 upregulated genes

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



overlapped across datasets, and ten HGs were consistently identified by at least three algorithms: STAT5B, CD38, PRKCB, INPP5D, SPTBN1, SIRPA, IKZF1, HAVCR2, PLEK, and CASP (Figure 1D)

Immune profiling revealed decreased CD38 expression in RPL and UIF groups compared to healthy controls (Figure 1E). Correlations were observed between gene expression and immune cell proportions: PRKCB with eosinophils, macrophages M0, and T cells gamma delta; INPP5D with naïve B cells, plasma cells, follicular helper T cells, and neutrophils; SPTBN1 with activated mast cells; SIRPA with eosinophils; IKZF1 with memory B cells; HAVCR2 with naïve B cells,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

macrophages M0, resting mast cells, and neutrophils; and PLEK with CD4+ memory T cells, follicular helper T cells, T cells gamma delta, resting NK cells, and macrophages M2 (Figure 1F).

Conclusion: This study analyzed the pathogenesis of RPL and UIF in SLE patients using transcriptomic data. Ten candidate hub genes were identified that may predict reproductive risks in SLE patients. Decreased CD38 expression was observed in RPL and UIF groups. Correlations between hub genes and infiltrated immune cell proportions highlight their role in disease mechanisms. These findings provide a molecular framework for understanding pregnancy loss and infertility in SLE, warranting validation in longitudinal cohort studies.

Disclosure: R. Martinez-Canales: None; **B. Avalos-Garcia**: None; **A. Ortiz-Rios**: None; **E. Galindo-Calvillo**: None; **L. Perez-Barbosa**: None; **D. Galarza-Delgado**: None; **C. Skinner-Taylor**: None; **M. Salinas-Carmona**: None; **N. Macias-Segura**: None.

Abstract Number: 2220

Human Milk Fatty Acid Profiles Among Breastfeeding Mothers With and Without Systemic Autoimmune Rheumatic Diseases

Rashmi Dhital[1], Kerri Bertrand[2], Dilli Poudel[3], Christina Chambers[4] and Monica Guma[2], [1]Vanderbilt University Medical Center, Brentwood, TN, [2]University of California San Diego, San Diego, CA, [3]Vanderbilt University Medical Center, Nashville, TN, [4]University of California, San Diego, La Jolla, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic autoimmune rheumatic diseases (SARDs) such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are characterized by chronic systemic inflammation and often require immunomodulatory therapies, both of which may affect lipid metabolism and influence breast milk composition, However, data on milk lipidomics in SARDs are scarce. We aimed to characterize and compare fatty acid (FA) profiles in breast milk of mothers with and without SARDs.

Methods: We analyzed archived milk samples from 29 breastfeeding women with SARDs (15 RA, 11 SLE, 3 both) and 15 healthy controls in the UCSD Human Milk Biorepository (HMB). FA (pmol/ml of milk) was assessed using liquid chromatography-mass spectrometry, and median FA levels compared between groups using the Wilcoxon rank-sum test. To estimate the association between FAs and SARDs, FAs were log-transformed to approximate normality and multivariable linear regression was performed. Model[a] adjusted for maternal and child age, maternal body mass index, parity, gestational age at delivery, infant sex, frequency of feeds, time of milk collection, and hours since last feed. Model[b] incorporated variables in Model[a] plus the milk storage length, and Model[c] also accounted for SARD therapies. In subgroup analyses, median FA levels were evaluated by SARD type (RA and SLE) and sample storage length.

Results: Baseline characteristics were comparable, except for earlier gestational age at delivery (38.40 vs. 39.72 weeks) and markedly longer storage duration (40.42 months vs 3.24 months) among SARDs versus controls. Conventional DMARDs (55.17%) and biologic DMARDs (41.38%) were exclusive to SARDs, and corticosteroid use (34.48% vs 6.67%, p=0.07) was more common. Milk macronutrient content did not differ by SARD status. Individual FAs, specifically, medium and long-chain saturated FAs [*lauric acid* (12:0) and *myristic acid* (14:0), *palmitic acid* (16:0)], and long-chain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of fatty acids in archived milk samples from 44 women with and without systemic autoimmune rheumatic diseases (SARDs)*

Common name (notation)	Controls (Median (IQR); n=15	SARDs (Median (IQR); n=29	Direction	P-value (Wilcoxon rank-sum test)
Lauric acid (12:0)	1,059,555 (919,174–1,285,811)	1,683,464 (1,231,623–1,983,149)	**Higher in SARD**	**0.002**
Myristic acid (14:0)	928,499 (821,597–1,291,536)	1,525,263 (876,807–1,905,784)	**Higher in SARD**	**0.019**
Pentadecylic acid (15:0)	48,613 (31,573–63,743)	64,315 (29,919–94,983)	Higher in SARD	0.238
Palmitic acid (16:0)	1,881,974 (1566216–2160036)	2,334,708 (1,763,990–2,786,549)	Higher in SARD	**0.039**
cis-9 Palmitoleic acid (16:1)	383,823 (266,737–629,569)	445,479 (255,710–744,560)	Higher in SARD	0.540
Margaric acid (17:0)	24,496 (20,905–33,215)	31,846 (21,444–41,161)	Higher in SARD	0.280
Margaroleic acid (17:1)	23,783 (17,145–40,950)	34,862 (19,869–52,402)	Higher in SARD	0.302
Stearic acid (18:0)	506,802 (443,258–655,859)	597,666 (419,388–755,890)	Higher in SARD	0.540
Oleic acid (18:1)	2,587,443 (2,299,441–3,144,863)	3,488,529 (2,980,145–4,566,587)	**Higher in SARD**	**0.006**
Linoleic acid (18:2)	2,171,870 (1,736,661–2,544,474)	2,821,638 (1,878,426–3,545,425)	Higher in SARD	0.063
Alpha-linolenic acid (18:3 N3)	257,205 (185,409–303,024)	311,614 (166,836–430,059)	Higher in SARD	0.248
Gamma-linolenic acid (18:3 N6)	15,153 (9,873–27,649)	26,468 (12,348–32,210)	Higher in SARD	0.132
Stearidonic acid (18:4)	4,691 (2,494–5,759)	5,705 (2,808–7,581)	Higher in SARD	0.219
Arachidic acid (20:0)	4,411 (3,632–5,070)	5,505 (3,294–7,883)	Higher in SARD	0.351
cis-Gondoic acid (20:1)	12,217 (8,989–15,139)	14,700 (10,177–24,740)	Higher in SARD	0.092
Eicosadienoic acid (20:2)	13,501 (10,849–19,863)	16,146 (12,050–29,018)	Higher in SARD	0.103
Dihomo-alpha-linolenic acid (20:3 N3)	2,819 (2,202–3,733)	3,294 (2,548–6,644)	Higher in SARD	0.153
Bis-homo-gamma-linolenic acid (20:3 N6)	29,590 (25,462–45,416)	43,767 (26,718–65,345)	Higher in SARD	0.120
Mead acid (20:3 N9)	2,205 (1,550–4,233)	2,425 (1,221–6,007)	Higher in SARD	0.864
Arachidonic acid (20:4)	50,756 (37,826–85,257)	64,609 (46,986–82,862)	Higher in SARD	0.404
Eicosapentaenoic acid (20:5)	14,422 (11,025–18,829)	16,543 (9,921–34,963)	Higher in SARD	0.433
Behenic acid* (22:0)	1,348 (798–1,445)	1,004 (686–2,071)	Lower in SARD	0.831
cis-Erucic acid (22:1)	1,559 (1,358–2,218)	2,455 (1,457–3,697)	Higher in SARD	0.059
Docosadienoic acid (22:2)	1,095 (926–1,860)	1,382 (953–2,360)	Higher in SARD	0.351
Docosatrienoic acid (22:3)	93 (83–154)	128 (77–212)	Higher in SARD	0.520
Adrenic acid (repeat) (22:4)	12,919 (10,189–20,109)	16,028 (10,762–21,517)	Higher in SARD	0.291
Docosapentaenoic acid (22:5 N3)	23,080 (18,724–32,567)	35,164 (24,187–54,562)	Higher in SARD	0.079
Docosapentaenoic acid 22:5 N6	10,695 (8,817–14,308)	11,313 (5,475–15,452)	Higher in SARD	0.769
Docosahexanoic acid (22:6)	56,050 (42,578–118,873)	64,792 (41,384–102,530)	Higher in SARD	0.732
Tricosylic acid* (23:0)	93 (83–154)	128 (77–212)	Higher in SARD	0.520
Lignoceric acid (24:0)	1,138 (982–1,169)	958 (813–1,410)	Lower in SARD	0.607
Nervonic acid (24:1)	233 (157–313)	282 (179–589)	Higher in SARD	0.168
Cerotic acid (26:0)	2,301 (1790–2813)	1,476 (1,244–1,757)	**Lower in SARD**	**0.0001**
Total fatty acids	10,591,091 (8,394,532–12,384,802)	13,600,972 (9,884,785–18,077,326)	Higher in SARD	0.017

Bold when p<0.05
For **each fatty acid**, the tests were run **only on the subset** of patients who have a non-missing value for that fatty acid

monounsaturated FA *oleic acid* (18:1) were significantly higher in SARDs. Very-long-chain saturated FA - cerotic acid (26:0) was lower (**Table 1**). Compared to controls, those with SLE, but not RA, had significantly higher levels of lauric, myristic, oleic, and linoleic acids. Most FAs showed peak levels at ~ 12-24 months storage duration. In multivariable regression analysis, SARD remained associated with higher levels of many of the FAs studied. Furthermore, the magnitude of associations generally increased with sequential model adjustments (**Figure 1**).

Conclusion: Breast milk in SARDs, particularly SLE, showed higher levels of several medium and long-chain FAs compared to controls. The associations persisted and generally became stronger after sequential adjustments for maternal and infant characteristics, milk storage length, and SARD therapies, providing some indication that inflammatory diseases and therapies may affect the milk FA environment. However, given the marked difference in storage length in our sample and the observed impact of prolonged storage on milk FAs, future studies should match controls on storage length to reduce bias and improve data interpretability.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

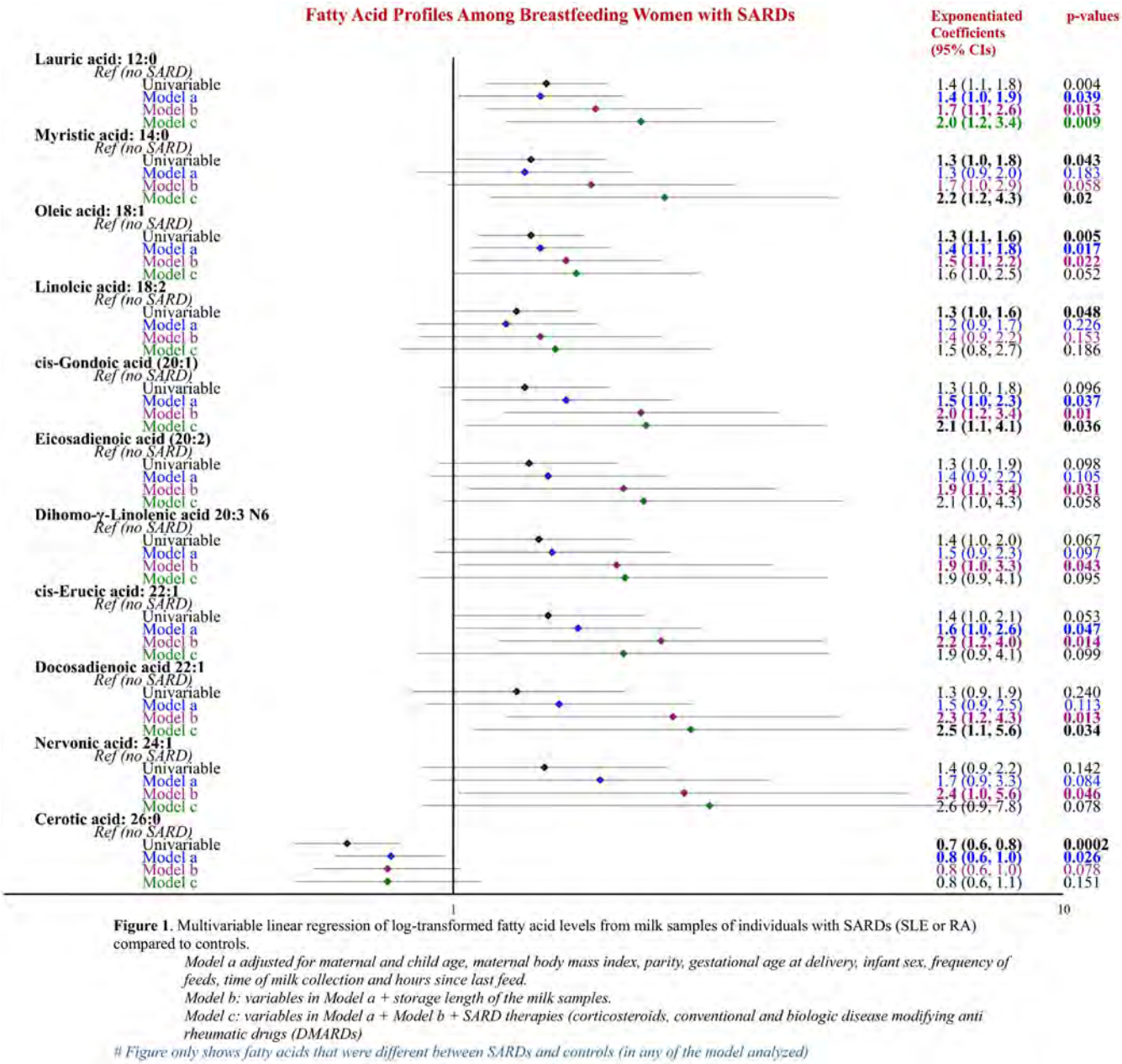


Figure 1. Multivariable linear regression of log-transformed fatty acid levels from milk samples of individuals with SARDs (SLE or RA) compared to controls.

Model a adjusted for maternal and child age, maternal body mass index, parity, gestational age at delivery, infant sex, frequency of feeds, time of milk collection and hours since last feed.

Model b: variables in Model a + storage length of the milk samples.

Model c: variables in Model a + Model b + SARD therapies (corticosteroids, conventional and biologic disease modifying anti rheumatic drugs (DMARDs)

 # Figure only shows fatty acids that were different between SARDs and controls (in any of the model analyzed)

Figure 1. Impact of systemic autoimmune rheumatic diseases (SARDs) on human milk fatty acid composition: results from multivariable regression models

Disclosure: R. Dhital: None; **K. Bertrand**: None; **D. Poudel**: None; **C. Chambers**: Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Genzyme Sanofi-Aventis, 5, Gerber Foundation, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Hoffman La-Roche-Genentech, 5, Janssen, 5, Leo Pharma, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Sanofi, 5, Sun Pharma Global FZE, 5, Takeda Pharmaceutical Company Limited, 5, UCB Pharma, 5; **M. Guma**: AbbVie, 5, Sonoma, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2221

Racial Differences in Cardiovascular Events and Adverse Pregnancy Outcomes Among Pregnant Individuals With Systemic Lupus Erythematosus

Rashmi Dhital[1], Rebecca Baer[2] and Christina Chambers[3], [1]Vanderbilt University Medical Center, Brentwood, TN, [2]University of California San Diego, San Diego, CA, [3]University of California, San Diego, La Jolla, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Baseline sociodemographic characteristics and clinical comorbidities compared between racial groups in pregnant individuals with SLE, 2005 – 2020

Table 1. Baseline sociodemographic characteristics and clinical comorbidities compared between racial groups in pregnant individuals with SLE, 2005 – 2020

	Asian	Hispanic	Non-Hispanic Black	Non-Hispanic White	Others **	p-value
	n (%)	n (%)	n (%)	n (%)	n (%)	
Sample	**1,095 (13.0)**	**3,600 (42.7)**	**782 (9.3)**	**2,334 (27.7)**	**611 (7.3)**	
Maternal age (years)						**< 0.0001**
< 18	a	28 (0.8)	a	a	a	
18 – 34	696 (63.6)	2,842 (78.9)	592 (75.7)	1,600 (68.6)	436 (71.4)	
35 - 44	395 (36.1)	724 (20.1)	180 (23.0)	715 (30.6)	173 (28.3)	
≥ 45	a	a	a	a	a	
Expected payer						**< 0.0001**
Private	862 (78.7)	1,571 (43.6)	321 (41.1)	1,651 (70.7)	351 (57.5)	
Public	169 (15.4)	1,849 (51.4)	408 (52.2)	557 (23.9)	234 (38.3)	
Self-pay	18 (1.6)	26 (0.7)	a	a	a	
Other	46 (4.2)	154 (4.3)	49 (6.3)	119 (5.1)	22 (3.6)	
Maternal education						**< 0.0001**
≤12	126 (11.5)	1,774 (49.3)	285 (36.5)	520 (22.3)	115 (18.8)	
>12	942 (86.0)	1,754 (48.7)	483 (61.8)	1,778 (76.2)	280 (45.8)	
Missing	27 (2.5)	72 (2.0)	14 (1.8)	36 (1.5)	216 (35.4)	
Pre-pregnancy BMI						**< 0.0001**
<18.5	94 (8.6)	99 (2.8)	31 (4.0)	97 (4.2)	23 (3.8)	
18.5 to < 25	640 (58.5)	1,210 (33.6)	242 (31.0)	1,049 (44.9)	251 (41.1)	
25 to < 30	167 (15.3)	931 (25.9)	170 (21.7)	427 (18.3)	146 (23.9)	
≥ 30	80 (7.3)	913 (25.4)	234 (29.9)	409 (17.5)	136 (22.3)	
Missing^	114 (10.4)	447 (12.4)	105 (13.4)	352 (15.1)	55 (9.0)	
Hypertension						**< 0.0001**
None	815 (74.4)	2,625 (72.9)	498 (63.7)	1,800 (80.6)	433 (70.9)	
Preexisting	94 (8.6)	298 (8.3)	115 (14.7)	146 (6.3)	52 (8.5)	
Gestational	38 (3.5)	150 (4.2)	44 (5.6)	117 (5.0)	29 (4.8)	
Preeclampsia	148 (13.5)	527 (14.6)	125 (16.0)	191 (8.2)	97 (15.9)	
Diabetes mellitus						**0.0003**
None	960 (87.7)	3,166 (87.9)	685 (87.6)	2,105 (90.2)	546 (89.4)	
Preexisting	16 (1.5)	84 (2.3)	33 (4.2)	45 (1.9)	11 (1.8)	
Gestational	119 (10.9)	350 (9.7)	64 (8.2)	184 (7.9)	54 (8.8)	
Hyperlipidemia	13 (1.2)	53 (1.5)	11 (1.4)	18 (0.8)	a	0.1378
Smoking during pregnancy	11 (1.0)	113 (3.1)	62 (7.9)	181 (7.8)	54 (8.8)	**< 0.0001**
Alcohol use during pregnancy	a	19 (0.5)	a	23 (1.0)	a	**0.0040**
Drug use during pregnancy	a	124 (3.4)	67 (8.6)	123 (5.3)	37 (6.1)	**< 0.0001**
Depression	40 (3.7)	215 (6.0)	71 (9.1)	215 (9.2)	56 (9.2)	**< 0.0001**
SLE disease characteristics						
SLE with LN	190 (17.4)	441 (12.3)	98 (12.5)	105 (4.5)	69 (11.3)	**< 0.0001**
SLE with APS	65 (5.9)	228 (6.3)	50 (6.4)	121 (5.2)	49 (8.0)	0.0965

Bold when p < 0.05

Other race includes American Indian/Alaska Native, Native Hawaiian/Pacific Islander, other race, two or more races, not stated/unknowna

[a]not displayed when n < 11

^BMI is not available for 2005 and 2006 births

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Cardiovascular events (CVEs) and adverse pregnancy outcomes (APOs) compared between racial groups in pregnant individuals with SLE, 2005 – 2020

Table 2. Cardiovascular events (CVEs) and adverse pregnancy outcomes (APOs) compared between racial groups in pregnant individuals with SLE, 2005 – 2020					
	Asian	**Hispanic**	**Non-Hispanic Black**	**Non-Hispanic White**	**Others****
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
	RR (95% CI)	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**
	aRR (95% CI)	**aRR (95% CI)**	**aRR (95% CI)**	**aRR (95% CI)**	**aRR (95% CI)**
Sample	**1,095**	**3,600**	**782**	**2,334**	**611**
Any CVE	18 (1.6)	72 (2.0)	31 (4.0)	43 (1.8)	12 (2.0)
	0.9 (0.5, 1.5)	1.1 (0.7, 1.6)	**2.2 (1.4, 3.4)**		1.1 (0.6, 2.0)
	0.8 (0.4, 1.4)	0.8 (0.5, 1.2)	1.6 (1.0, 2.6)		0.8 (0.4, 1.6)
VTE CVE (DVT and PE)	[a]	32 (0.9)	13 (1.7)	19 (0.8)	[a]
	[b]	1.1 (0.6, 1.9)	**2.1 (1.0, 4.2)**		1.8 (0.8, 4.0)
	[b]	0.8 (0.4, 1.5)	1.7 (0.8, 3.6)		1.4 (0.6, 3.3)
Non-VTE CVE	14 (1.3)	41 (1.1)	20 (2.6)	26 (1.1)	[a]
	1.1 (0.6, 2.2)	1.0 (0.6, 1.7)	**2.3 (1.3, 4.1)**		[b]
	0.9 (0.5, 1.9)	0.7 (0.4, 1.2)	1.6 (0.8, 3.0)		[b]
	[b]	[b]	[b]	[b]	[b]
Any maternal APO	148 (13.5)	598 (16.6)	192 (24.6)	317 (13.6)	95 (15.6)
	1.0 (0.9, 1.2)	**1.2 (1.1, 1.4)**	**1.8 (1.5, 2.2)**		1.1 (0.9, 1.4)
	1.0 (0.8, 1.2)	1.0 (0.9, 1.2)	**1.3 (1.1, 1.6)**		0.9 (0.7, 1.1)
Non-cardiac SMM	39 (3.6)	119 (3.3)	43 (5.5)	58 (2.5)	16 (2.6)
	1.3 (1.0, 2.2)	1.3 (1.0, 1.8)	**2.2 (1.5, 3.3)**		1.1 (0.6, 1.8)
	1.0 (0.6, 1.5)	0.8 (0.6, 1.2)	1.3 (0.8, 2.0)		0.6 (0.4, 1.2)
Maternal ICU use at delivery	[a]	18 (0.5)	[a]	[a]	[a]
	2.7 (0.7, 9.9)	2.9 (1.0, 8.6)	**3.7 (1.0, 13.9)**		**6.7 (2.0, 22.8)**
	1.8 (0.4, 7.4)	1.7 (0.5, 5.3)	1.9 (0.4, 8.0)		3.2 (0.8, 12.4)
Maternal readmission in first year	124 (11.3)	537 (14.9)	171 (21.9)	290 (12.4)	83 (13.6)
	0.9 (0.7, 1.1)	**1.2 (1.0, 1.4)**	**1.8 (1.5, 2.1)**		1.0 (0.9, 1.4)
	0.9 (0.8, 1.2)	1.0 (0.9, 1.2)	**1.3 (1.1, 1.6)**		0.9 (0.7, 1.1)
Maternal death in first year	[a]	[a]	[a]	[a]	[a]
	[b]	0.9 (0.3, 2.9)	**4.8 (1.6, 14.6)**		[b]
	[b]	0.7 (0.2, 2.6)	2.7 (0.8, 9.1)		[b]
Any infant APO	541 (49.4)	1,645 (45.7)	419 (54.6)	807 (34.6)	261 (42.7)
	1.4 (1.3, 81.6)	**1.3 (1.2, 1.4)**	**1.5 (1.4, 1.7)**		**1.2 (1.1, 1.4)**
	1.3 (1.2, 1.5)	**1.2 (1.1, 1.3)**	**1.4 (1.2, 1.6)**		1.2 (1.0, 1.3)
Gestation <37 weeks	251 (22.9)	844 (23.4)	230 (29.4)	355 (15.2)	120 (19.6)
	1.5 (1.3, 1.8)	**1.5 (1.4, 1.7)**	**1.9 (1.6, 2.3)**		**1.3 (1.0, 1.6)**
	1.2 (1.0, 1.5)	**1.2 (1.1, 1.4)**	**1.5 (1.3, 1.8)**		1.0 (0.8, 1.3)
Early (<32 WGA)	57 (5.2)	191 (5.3)	64 (8.2)	49 (2.1)	29 (4.8)
	2.6 (1.8, 3.8)	**2.7 (2.0, 3.7)**	**4.3 (3.0, 6.2)**		**2.3 (1.5, 3.7)**
	1.7 (1.1, 2.5)	**1.5 (1.1, 2.1)**	**2.3 (1.5, 3.4)**		1.1 (0.7, 1.8)
Moderate (32 - <34 WGA)	29 (2.7)	122 (3.4)	22 (2.8)	31 (1.3)	15 (2.5)
	2.2 (1.3, 3.6)	**2.7 (1.9, 4.1)**	**2.5 (1.4, 4.3)**		**1.9 (1.0, 3.6)**
	1.4 (0.8, 2.5)	**1.8 (1.2, 2.8)**	1.7 (0.9, 3.0)		1.4 (0.7, 2.8)
Late (34- <37 WGA)	165 (15.1)	531 (14.8)	144 (18.4)	275 (11.8)	76 (12.4)
	1.3 (1.1, 1.6)	**1.3 (1.1, 1.5)**	**1.7 (1.4, 2.1)**		1.1 (0.9, 1.4)
	1.2 (1.0, 1.4)	1.1 (1.0, 1.3)	**1.4 (1.2, 1.8)**		1.0 (0.7, 1.3)
SGA	272 (24.8)	647 (18.0)	166 (21.2)	289 (12.4)	97 (15.9)
	2.0 (1.7, 2.4)	**1.5 (1.3, 1.7)**	**1.7 (1.4, 2.1)**		**1.3 (1.0, 1.6)**
	1.8 (1.5, 2.1)	**1.4 (1.2, 1.6)**	**1.6 (1.3, 1.9)**		1.2 (1.0, 1.6)
Neonatal ICU at birth	159 (14.5)	455 (15.7)	153 (19.6)	246 (10.5)	102 (16.7)
	1.4 (1.1, 1.7)	**1.5 (1.3, 1.7)**	**1.9 (1.5, 2.3)**		**1.6 (1.3, 2.0)**
	1.2 (0.9, 1.4)	**1.2 (1.0, 1.4)**	**1.4 (1.1, 1.7)**		1.3 (1.0, 1.6)
Infant readmission in the first year	114 (10.4)	477 (13.3)	101 (12.9)	241 (10.3)	71 (11.6)
	1.0 (0.8, 1.3)	**1.3 (1.1, 1.5)**	1.3 (1.0, 1.6)		1.1 (0.9, 1.5)
	1.0 (0.8, 1.3)	1.2 (1.0, 1.4)	1.1 (0.8, 1.4)		1.0 (0.8, 1.4)
Infant death in the first year	[a]	31 (0.9)	14 (1.8)	13 (0.6)	12 (2.0)
	1.5 (0.6, 3.5)	1.5 (0.8, 3.0)	**3.2 (1.5, 6.8)**		**3.5 (1.6, 7.7)**
	1.8 (0.7, 4.4)	1.1 (0.5, 2.2)	2.2 (1.0, 5.1)		**2.7 (1.2, 6.4)**

Bold when p < 0.05

[a]not displayed when n < 11; [b]not calculated when n < 5

Comparison group (reference): Non-Hispanic White individuals with SLE

aRR adjusted for race/ethnicity propensity score created from age, primary payer, maternal education, pre-pregnancy BMI, clinical comorbidities (preexisting and gestational DM and HTN, pregnancy-induced HTN, hyperlipidemia, depression, alcohol, tobacco, and drug use during pregnancy), presence of LN, presence of APS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Risk of an APO among individuals with SLE with a CVE versus SLE without a CVE, stratified by race/ethnicity

Table 3. Risk of an APO among individuals with SLE with a CVE versus SLE without a CVE, stratified by race/ethnicity				
	Asian	Hispanic	Non-Hispanic Black	Non-Hispanic White
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)	aRR (95% CI)
Any maternal APO	**3.9 (2.0, 7.6)**	**2.7 (1.9, 3.8)**	**2.2 (1.3, 3.7)**	**1.9 (1.0, 3.5)**
	3.1 (1.5, 6.1)	**2.5 (1.8, 3.6)**	**1.9 (1.1, 3.2)**	**1.9 (1.0, 3.4)**
Non-cardiac SMM	**8.8 (3.4, 22.5)**	**5.0 (2.7, 9.3)**	[a]	[a]
	5.4 (2.0, 14.0)	**4.1 (2.2, 7.7)**	[a]	[a]
Acute renal failure	**29.3 (10.9, 85.6)**	**5.2 (1.9, 14.5)**	[a]	[a]
	13.7 (4.4, 42.3)	**3.4 (1.2, 9.7)**	[a]	[a]
Blood transfusion	[a]	**6.2 (2.8, 13.5)**	[a]	[a]
	[a]	**5.2 (2.3, 11.5)**	[a]	[a]
Maternal readmission in first year	**3.0 (1.3, 6.9)**	**2.2 (1.4, 3.3)**	1.7 (0.9, 3.1)	1.7 (0.9, 3.3)
	2.4 (1.1, 5.6)	**2.1 (1.4, 3.2)**	1.4 (0.8, 2.6)	1.6 (0.8, 3.2)
Any infant APO	1.6 (0.9, 2.7)	**1.6 (1.2, 2.2)**	**1.6 (1.1, 2.4)**	**1.7 (1.1, 2.5)**
	1.4 (0.8, 2.3)	**1.5 (1.1, 1.9)**	**1.5 (1.0, 2.2)**	**1.7 (1.2, 2.6)**
Gestation <37 weeks	**3.3 (1.9, 5.7)**	**2.0 (1.4, 2.8)**	**2.2 (1.4, 3.5)**	1.5 (0.8, 2.9)
	2.5 (1.4, 4.4)	**1.8 (1.2, 2.5)**	**1.9 (1.2, 3.1)**	1.6 (0.9, 3.0)
SGA	[a]	**1.6 (1.0, 2.4)**	1.2 (0.6, 2.5)	1.5 (0.8, 3.1)
	[a]	1.5 (0.9, 2.3)	1.1 (0.6, 2.3)	1.5 (0.8, 3.1)
Neonatal ICU at birth	**2.3 (1.0, 5.3)**	**2.2 (1.4, 3.3)**	**2.2 (1.3, 4.0)**	**3.0 (1.7, 5.2)**
	1.8 (0.8, 4.0)	**1.9 (1.3, 2.9)**	1.6 (0.9, 2.9)	**3.0 (1.7, 5.3)**
Infant readmission in first year	[a]	0.9 (0.5, 1.8)	**2.7 (1.4, 5.1)**	1.8 (0.9, 3.7)
	[a]	0.9 (0.5, 1.7)	**2.5 (1.3, 4.8)**	1.8 (0.9, 3.7)

[a]Not calculated when n < 5
aRR adjusted for race/ethnicity propensity score created from age, primary payer, maternal education, pre-pregnancy BMI, clinical comorbidities (preexisting and gestational DM and HTN, pregnancy-induced HTN, hyperlipidemia, depression, alcohol, tobacco, and drug use during pregnancy), presence of LN, presence of APS

Background/Purpose: Pregnant individuals with systemic lupus erythematosus (SLE) face an increased risk of cardiovascular events (CVEs) as well as adverse pregnancy outcomes (APOs). While racial differences in various SLE outcomes are known, the relationship between race/ethnicity, maternal CVEs, and APOs remains poorly understood.

Methods: Utilizing a California population-based birth cohort from 2005-2020, we identified pregnant individuals with SLE via International Classification of Diseases codes on maternal discharge records. The primary exposure was self-reported race/ethnicity, categorized as Asian, Hispanic, non-Hispanic Black, non-Hispanic White, and Other. Outcomes of interest included the occurrence of CVEs and APOs across racial groups. We also assessed APOs by race, separately for SLE pregnancies with and without CVEs. To assess how CVEs affect APO risk within each race, we estimated adjusted relative risks (aRRs) for APOs in SLE by CVE status for each race category. aRRs were adjusted using a propensity score created for race/ethnicity, incorporating age, payer, maternal education, clinical, and SLE-related variables.

Results: Among 8,422 live-born singletons from women with SLE, majority were from Hispanic (42.7%), followed by non-Hispanic White (27.7%) individuals. Private insurance was more common among Asian (78.7%) and non-Hispanic White (68.6%) women, while Hispanic and non-Hispanic Black patients more often had public insurance (51.4% and 52.2%, respectively). Non-Hispanic Black women had the highest prevalence of hypertensive disorders (**Table 1**). Compared to other racial groups, non-Hispanic Black women had the highest prevalence of CVEs during pregnancy (4.0% vs 1.6-2.0%), maternal APOs (24.6% vs 13.5-15.6%) and infant APOs (54.6% vs 34.6%-49.4%), including the highest infant death rate (1.8%) (**Table 2**).

Stratified analysis by race/ethnicity and CVE status showed the highest occurrences of maternal and infant APOs in non-Hispanic Black women, regardless of CVE status (23.4% and 42.1% without CVEs; 51.6% and 83.9%, with CVEs, respectively). In non-Hispanic White women, maternal and infant APOs occurred in 13.4% and 27.7% without CVEs, and 25.6% and 58.1% of those with CVEs, respectively. (**Table not shown**).

In the subanalysis, CVEs in SLE were associated with higher risks of most APOs across all groups. The aRR for maternal APOs was 3.1-fold in Asian patients, 2.5-fold in Hispanic patients, and 1.9-fold in both non-Hispanic Black and White

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients. For infant APO, aRRs ranged from 1.4- 1.7-fold in SLE pregnancies with CVEs compared to those without, across all groups (**Table 3**).

Conclusion: CVEs in SLE were linked to higher APO risks. The relative impact of CVEs on maternal APOs was higher for Asian (aRR 3.1) and Hispanic (aRR 2.5) women than the 1.9-fold higher risk of maternal APO observed in non-Hispanic Black and White women with CVEs as compared to those without CVEs. However, non-Hispanic Black women consistently experienced the highest absolute burden of CVEs and maternal and infant APOs, including infant deaths. These findings underscore the importance of integrating cardiovascular disease risk and social determinants of health into the clinical care of pregnant patients with SLE.

Disclosure: R. Dhital: None; **R. Baer**: None; **C. Chambers**: Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Genzyme Sanofi-Aventis, 5, Gerber Foundation, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, Hoffman La-Roche-Genentech, 5, Janssen, 5, Leo Pharma, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Sanofi, 5, Sun Pharma Global FZE, 5, Takeda Pharmaceutical Company Limited, 5, UCB Pharma, 5.

Abstract Number: 2222

Neonatal Myocardial Strain in Offspring born to Mothers with Systemic Lupus Erythematosus: Pilot Data from the LEGACY Cohort

Reem Farhat[1], Lawrence Rudski[2], Natalie Dayan[3], Catherine Henin[4], Daniela Villegas Martinez[4], Sariya Sahussarungsi[1], Pasinee Kanaprach[1], Sasha Bernatsky[5], Gabriel Altit[4] and Evelyne Vinet[5], [1]McGill University, Faculty of Medicine and Health Sciences, Montreal, QC, Canada, [2]Jewish General Hospital, Montreal, QC, Canada, [3]McGill University Health Centre, Montreal, QC, Canada, [4]Montreal Children's Hospital, Montreal, QC, Canada, [5]Research Institute of the McGill University Health Centre, Montreal, QC, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) increases the risk of placenta-mediated adverse pregnancy outcomes (APO) and may impact offspring cardiovascular health. Transplacental maternal anti-Ro antibodies can affect fetal cardiac function, while hydroxychloroquine (HCQ), though protective against APO, has been linked to cardiotoxicity in adults at high cumulative doses. Speckle tracking echocardiography (STE), a sensitive tool for detecting early cardiac dysfunction, remains underused in neonates. We used STE to assess the influence of maternal anti-Ro antibodies, gestational cumulative HCQ exposure, and APO on neonatal myocardial strain.

Methods: Participants were recruited from the Montreal site of the Lupus prEGnAnCY (LEGACY) cohort, a multicenter prospective cohort enrolling SLE pregnancies at < 17 gestational weeks. APO was evaluated at each trimester and postpartum, and included: 1) gestational hypertension, preeclampsia and/or eclampsia, 2) placental insufficiency, 3) placental abruption, and/or 4) small for gestational age (SGA < 5^{th} percentile). Neonatal cardiac function was assessed ≤4 weeks postpartum using STE, with global longitudinal strain (GLS) reported via apical endocardial GLS or apical four-chamber peak longitudinal strain. GLS is expressed as a negative percentage, with more negative values indicating better myocardial contractile function. We summarized maternal and neonatal characteristics using descriptive statistics and evaluated GLS with univariable and multivariable regression analyses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Maternal and pregnancy characteristics. * LLDAS: Lupus Low Disease Activity State defined as 1) SLEDAI-2K score ≤ 4, with no activity in major organ systems (renal, CNS, cardiopulmonary), and no hemolytic anemia or gastrointestinal activity, 2) no new features of lupus disease activity compared to the previous assessment, 3) Physician Global Assessment (PGA) ≤ 1, 4) prednisone (or equivalent) dose ≤ 7.5 mg/day, and 5) the patient is on standard immunosuppressive drugs and/or biologics, including antimalarials, at well-tolerated, maintenance doses. ¶ Fetal death <20 gestational weeks ǂ Placenta-mediated adverse pregnancy outcome: defined as a composite measure including: 1) gestational hypertension, preeclampsia and/or eclampsia, 2) placental insufficiency (i.e. Doppler flow suggestive of fetal hypoxemia, oligohydramnios, and/or relevant pathology), 3) placental abruption, and/or 4) SGA (<5th percentile). ‡ SGA: small for gestational age < 5th percentile § PPROM: Preterm premature rupture of membranes

Maternal Characteristics	**Total, *n=26***
Age (years), *mean ± SD*	35.9 ± 4.7
Ethnic group, *n (%)*	
Caucasian	6 (23)
Native north American	1 (4)
Hispanic	1 (4)
Black	3 (12)
Asian	6 (23)
Mixed	2 (8)
Other	7 (26)
Education, *n (%)*	
High school	2 (8)
Undergraduate/college	11 (42)
Postgraduate	13 (50)
BMI (kg/m^2), *mean ± SD*	27 ± 9.6
Categories, *n (%)*	
Healthy weight (18.5-24.9)	13 (50)
Overweight (25-29.9)	5 (19)
Obese (≥ 30)	8 (31)
Co-morbidities, *n (%)*	
Current or past lupus nephritis	7 (27)
Chronic hypertension	1 (4)
Diabetes (type 1 or type 2)	1 (4)
Cardiovascular disease	0 (0)
History of antiphospholipid syndrome	1 (4)
SLE disease duration (years), *mean ± SD*	9.9 ± 7.4
Medications used during pregnancy, *n (%)*	
Steroids	7 (27)
Acetylsalicylic acid (ASA)	26 (100)
Hydroxychloroquine	24 (92)
Azathioprine	10 (39)
Tacrolimus	5 (19)
Rituximab	1 (4)
Belimumab	3 (12)
Prophylactic anticoagulation	3 (12)
Positive autoantibodies, *n (%)*	
Anti-Ro	14 (54)
Anticardiolipin IgG	0 (0)
Anticardiolipin IgM	0 (0)
Antibeta2glycoprotein IgG	1 (4)
Lupus Anticoagulant	0 (0)
Positive anti-Ro levels (RU/mL), *mean ± SD*	156.5 ± 34.4
LLDAS*, *n (%)*	
Baseline visit	22 (85)
Maintained throughout pregnancy	15 (65)
Pregnancy outcome, *n (%)*	
Live birth	23 (89)
Fetal death[¶]	3 (11)
Placenta-mediated APO[ǂ], *n (%)*	
Gestational hypertension	4 (15)
Preeclampsia	6 (23)
Eclampsia	0 (0)
Placental insufficiency	2 (8)
Placental abruption	2 (8)
SGA < 5th percentile[‡]	3 (12)
Other pregnancy complications*, *n (%)*	
Premature onset of labor	2 (8)
PPROM[§]	1 (4)
Preterm birth	2 (8)
Placenta previa	0 (0)
Gestational diabetes	0 (0)
Neonatal death	0 (0)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Neonatal characteristics (n=16) *HCQ: hydroxychloroquine

Newborn Characteristics	Total n=16	Exposed to Anti-Ro n=8	Unexposed to Anti-Ro n=8
Sex, *n (%)*			
Male	10 (63)	4 (50)	6 (75)
Female	6 (38)	4 (50)	2 (25)
Gestational age at delivery (weeks), *mean ± SD*	37.9 ± 2.1	38.5 ± 1.0	37.2 ± 2.8
Neonatal age at time of STE (days), *mean (SD)*	11.8 ± 26.2	17.6 ± 36.7	5.9 ± 6.7
Birth weight (kg), *mean ± SD*	3.2 ± 0.6	3.3 ± 0.5	3.2 ± 0.8
HCQ* exposure, n (%)	16 (100)	8 (100)	8 (100)
Cumulative gestational HCQ exposure (mg x days/kg), *mean ± SD*	1103.2 ± 294.6	1236.1 ± 205.9	970.4 ± 321.3
Placenta-mediated APO, *n (%)*			
Gestational hypertension	3 (19)	2 (25)	1 (13)
Preeclampsia	5 (31)	2 (25)	3 (38)
Eclampsia	0 (0)	0 (0)	0 (0)
Placental insufficiency	2 (13)	1 (13)	1 (13)
Placental abruption	1 (6)	1 (13)	0 (0)
SGA (<5th percentile)	2 (13)	2 (25)	0 (0)
Other complications, *n (%)*			
Preterm birth	1 (6)	0 (0)	1 (13)
Neonatal ICU admission	1 (6)	0 (0)	1 (13)
Congenital malformation	1 (6)	1 (13)	0 (0)
Cutaneous neonatal lupus	0 (0)	0 (0)	0 (0)
Cardiac neonatal lupus	0 (0)	0 (0)	0 (0)

Results: This study included 26 pregnant women with SLE (each with a singleton pregnancy), of mean maternal age 35.9 ± 4.7 years and disease duration 9.9 ± 7.4 years. Most were in Lupus Low Disease Activity State (LLDAS) at baseline (85%), and 65% (15/26) maintained LLDAS throughout pregnancy. Live birth occurred in 89% (23/26) and fetal death in 11% (3/26). APO occurred in 42% (11/26), including gestational hypertension (15%), preeclampsia (23%), placental insufficiency (8%), placental abruption (8%), and SGA < 5th percentile (12%). Among 23 live births, 3 missed the STE assessment and 4 had suboptimal images preventing GLS estimation. Thus, GLS was assessed in 16 neonates of mean age 11.8 ± 26.2 days at STE. HCQ was used by all mothers (16/16), with mean cumulative gestational exposure of 1103.2 ± 294.6 mg x days/kg. Mean GLS was -26.3 ± 4.2%, with term neonates at -26.2 ± 4.3%. Lower mean GLS was observed in neonates born to mothers with APO (-25.2 ± 4.3%), anti-Ro antibodies (-24.8 ± 4.5%), and cumulative HCQ exposure in highest quartile (-24.6 ± 5.2%) versus their respective counterparts (-27.2 ± 4.1%, -27.9 ± 3.4%, and -28.2 ± 3.1%). GLS was not significantly associated with cumulative HCQ exposure, APO, or anti-Ro positivity in multivariable models adjusting for neonatal age and birth weight.

Conclusion: We observed lower GLS in neonates born to SLE mothers with anti-Ro antibodies and those with APO. Though not statistically significant, potentially due to small sample size, the trends may reflect subclinical cardiac alterations. These findings support the need for larger studies to clarify the impact of maternal antibodies, APO, and HCQ on fetal cardiac health.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Neonatal global longitudinal strain (GLS) according to maternal and neonatal characteristics

	Neonatal GLS (%), *mean ± SD*
Overall, *n=16*	-26.3 ± 4.2
Term births >37 weeks of gestation, *n=15*	-26.2 ± 4.3
Maternal age	
< 35 years, *n=9*	-25.4 ± 4.7
≥ 35 years, *n=7*	-27.6 ± 3.5
Maternal BMI	
< 30 kg/m^2, *n=10*	-25.8 ± 4.5
≥ 30 kg/m^2, *n=6*	- 27.2 ± 3.7
SLE Disease duration	
≤ 5 years, *n=5*	-26.2 ± 3.6
>5 years, *n=11*	- 26.4 ± 4.6
≤ 10 years, *n=10*	-27.2 ± 4.1
>10 years, *n=6*	- 24.8 ± 4.1
LLDAS throughout pregnancy	
In LLDAS, *n= 9*	- 27.1 ± 4.1
Not in LLDAS, *n=7*	-25.3 ± 4.2
Birth weight	
<2.5 kg, *n=3*	-25.6 ± 4.1
≥ 2.5 kg, *n=13*	-26.5 ± 4.3
Anti-Ro	
Positive, *n=8*	-24.8 ± 4.5
Negative, *n=8*	-27.9 ± 3.4
Placenta-mediated APO	
Yes, *n=9*	-25.2 ± 4.3
No, *n=7*	-27.2 ± 4.1
Cumulative gestational HCQ exposure	
Highest quartile (1261.9 mg x days/kg), *n=4*	-24.6 ± 5.2
Lowest quartile (998.2 mg x days/kg), *n=4*	-28.2 ± 3.1

Disclosure: R. Farhat: None; **L. Rudski**: None; **N. Dayan**: None; **C. Henin**: None; **D. Villegas Martinez**: None; **S. Sahussarungsi**: None; **P. Kanaprach**: None; **S. Bernatsky**: None; **G. Altit**: None; **E. Vinet**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2223

Improving collaboration between rheumatology and OBGYN in the reproductive health care of patients with rheumatic disease

Sara Heard[1], Isha Vasudeva[2], Juvena Hitt[2] and Jeanne Gosselin[3], [1]University of Vermont Medical Center, Burlington, VT, [2]University of Vermont Medical Center, Burlington, [3]University of Vermont Medical Center, Waterbury, VT

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Contraception management, preconception planning, and prenatal, antenatal, and postnatal care vary significantly in clinical practice for patients with rheumatic disease. Rheumatologists recognize the need for efficient referral systems to facilitate collaboration with reproductive health providers; however, they may not have professional relationships with obstetrician-gynecologist (OBGYN) colleagues and an established referral pathway. We conducted a needs assessment at our institution, including surveys of OBGYN residents and OBGYN generalists, to better understand their access to resources and referral patterns to maternal-fetal medicine (MFM) and rheumatology. This quality improvement project aims to improve collaboration between women's health providers and rheumatologists to improve the reproductive health care of patients with rheumatic disease within our health system.

Methods: Online REDCap surveys were administered to OBGYN residents (N=16, 9 pre-intervention, 7 post-intervention) and OBGYN generalists (N=8). OBGYN residents and generalists were asked about resources and access to specialist (MFM and rheumatology) assistance when managing patients with rheumatic disease, when they refer patients to MFM and rheumatology, and preference for electronic versus in-person rheumatology consults. Our primary intervention was a lecture on reproductive health in rheumatic disease for OBGYN residents. Resident survey results were collected pre- and post-intervention and analyzed using Stata 18 software.

Results: Post-intervention data showed an increase in the percentage of OBGYN residents who feel they have the knowledge, skillset, and resources to manage patients with rheumatic disease during pregnancy, from 0% to 57%. The percentage of residents who knew when to refer patients with rheumatic disease to MFM and/or rheumatology increased from 0% to 100%, and those who felt they could identify teratogenic medications in patients with rheumatic disease increased from 33% to 86% post-intervention. Preconception, OBGYN generalists report referring patients with rheumatic disease to rheumatology only (50%), or to both rheumatology and MFM (33%), and less often to MFM only (17%). When referring patients to rheumatology, 50% of generalists choose in-person consults and 50% choose both in-person and electronic consults.

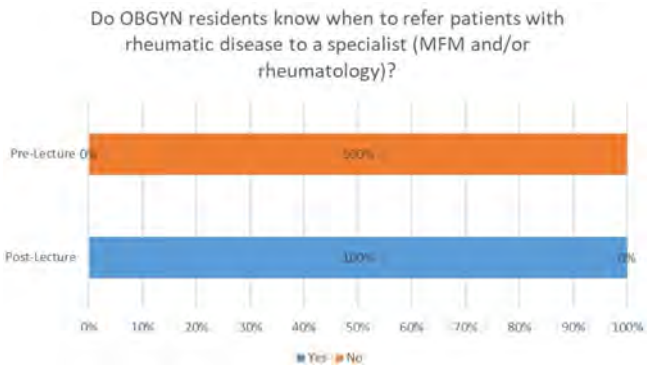


Figure 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

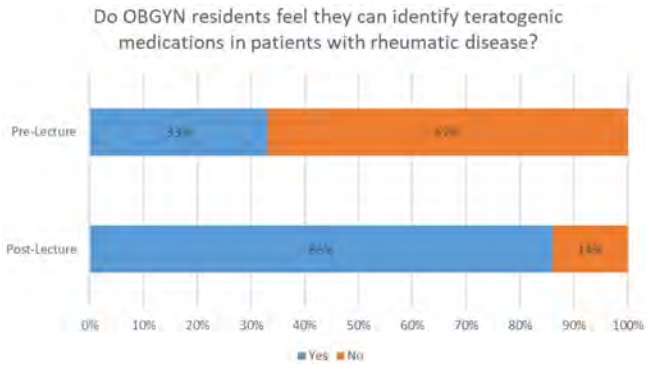


Figure 2

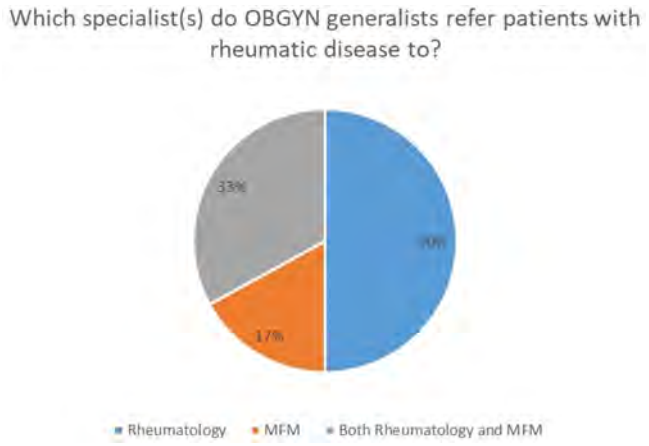


Figure 3

Conclusion: We implemented an effective educational intervention that improved OBGYN resident knowledge regarding when to refer patients to rheumatology, with post-intervention data showing a 100% increase from baseline. The intervention also increased the percentage of residents who felt they could identify teratogenic medications. The OBGYN generalist survey served as a needs assessment and showed that generalists typically refer patients to rheumatology, or both rheumatology and MFM, preconception. Next steps in this quality improvement project include examination of bidirectional referral pathways, indications for referral to rheumatology and OBGYN, and access to each specialty for urgent and non-urgent indications, including contraception and high-risk pregnancy management, to streamline referral processes and improve collaboration.

Disclosure: S. Heard: None; **I. Vasudeva**: None; **J. Hitt**: None; **J. Gosselin**: None.

Abstract Number: 2224

Failure of Steroid and Antimalarial Therapy to Normalize Placental Interferon and Angiogenic Gene Expression in SLE

Seemal Faisal[1], Alexandra Anderson[2], Luke Sharrock[3], James Tran[4] and Milena Vukelic[5], [1]Louisiana State University Health Science Center New Orleans, New Orleans, [2]Louisiana State University Health Science Center New Orleans, Phoenix, AZ, [3]Louisiana State University Health Science Center, New Orleans, LA, [4]Louisiana State University Health Science Center, New Orleans, [5]Rheumatology Fellowship Program Director Louisiana State University, New Orleans, LA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with an increased risk of placental insufficiency and adverse pregnancy outcomes, even when the disease is clinically quiescent. This suggests the existence of underlying molecular pathologies not reflected by standard clinical disease activity measures or serological markers. This study aimed to determine whether steroid and hydroxychloroquine (HCQ) exposure during pregnancy has the potential to restore placental transcriptomic abnormalities compared to healthy controls.

Methods: We analyzed publicly available RNA-seq data from the NCBI GEO dataset (GSE177029), which included placental samples obtained from 8 SLE patients matched to healthy donors (HD) following delivery. Differential gene expression analysis was performed using the DESeq2 R package. Benjamin & Hochberg correction (false discovery rate) was applied, with significance set at $p < 0.05$. Out of 19,151 genes, the analysis identified 1,051 differentially expressed genes between the SLE and HD groups.The interferon signature was calculated using a standard set of genes (IFI27, IFI44L, ISG15, RSAD2, IFIT1, MX1, OAS1). For other statistical comparisons between groups, a t-test was used.

Results: Characteristics of the SLE patients are shown in Table 1. On average, disease duration was 57 months prior to delivery (IQR: 10–157). The median SLEDAI score was 3. All SLE patients were on daily prednisone (< 15 mg) and HCQ (200–400 mg). Aspirin was used by 3 patients. There were no differences in maternal age, gestational age, or BMI between the SLE and HD groups (30 ± 2 years; 28 ± 1 weeks; 27 ± 2; $p > 0.05$). There was no history of preeclampsia in either group. Newborn weight was significantly lower in the SLE group (2,950 ± 491 g vs. 3,378 ± 261 g; $p < 0.05$). Despite low SLEDAI scores and steroid or HCQ use, placentas obtained from SLE patients showed almost a threefold increase in the type I interferon gene signature (IFN score 1.566, $\log_2$ fold change; *padj* = 0.0034), indicating unresolved immunological activation. Additionally, genes encoding epithelial cytoskeletal proteins, such as keratin 14 and keratin 24, were significantly upregulated—by more than 5- and 7-fold, respectively—in SLE placentas compared to HD, suggesting impaired maturation and dedifferentiation in response to inflammation. Importantly, angiopoietin-2 (ANG-2), a critical regulator of angiogenesis, was significantly downregulated in SLE placentas ($\log_2$ fold change = –1.59; *padj* = 0.0296), corresponding to a 67% reduction in expression compared to healthy controls. This suggests persistent defects in placental vascular remodeling and endothelial homeostasis. In SLE patients with SLEDAI scores of 4–6, there was a 19% reduction in ANG-2 expression compared to those with SLEDAI scores of 0–4.

Conclusion: Low disease activity and the use of steroids or HCQ were insufficient to normalize placental gene expression in SLE pregnancies. Persistent interferon signaling, angiogenic dysregulation, and impaired cytoskeletal remodeling highlight a disconnect between clinical disease control and molecular placental health, underscoring the need for biomarkers and interventions targeting subclinical placental inflammation.

Table 1. Clinical and serological characteristics

Patient #	Disease duration (month)	SLEDAI score	Gestation age (weeks)	Fetal weight (gram)	ANA	dsDNA	SSA	ApL	Proteinuria	Hypocomplementemia
SLE-1	10	5	38.43	3300	+	+	-	-	NO	YES
SLE-2	45	3	38.43	2900	+	-	-	+	NO	YES
SLE-3	10	4	39.71	2400	+	-	-	-	YES	NO
SLE-4	11	2	38.57	3300	+	-	-	+	NO	YES
SLE-5	70	0	39.57	3850	+	-	-	-	NO	NO
SLE-7	95	6	37.00	2600	+	+	-	-	YES	NO
SLE-8	107	0	37.29	3150	+	-	-	-	NO	NO
SLE-9	167	4	34.86	2150	+	-	-	+	YES	NO

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Faisal: None; **A. Anderson**: None; **L. Sharrock**: None; **J. Tran**: None; **M. Vukelic**: None.

Abstract Number: 2225

The Impact of Pregnancy Planning on the Prevalence of Adverse Pregnancy Outcomes in Women with Systemic Lupus Erythematosus: A Retrospective Study from Three Japanese Tertiary Referral Centers

Takehiro Nakai[1], Nanase Honda[2], YORIKAZU HASHIMOTO[3], Eri Soga[4], Sho Fukui[5], Ayako Kitada[6], Kensuke Nakanishi[7], Naoto Yokogawa[8] and Masato Okada[9], [1]Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, [2]Tokyo Metropolitan Matsuzawa hospital, Setagaya-ku, Tokyo, Japan, [3]Nanbu Medical Center & Children's Medical Center, Naha, Japan, [4]Tokyo Metropolitan Tama Medical Center, Tama, Tokyo, Japan, [5]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [6]St Luke's International hospital, nagareyama-shi, chiba- ken, Japan, [7]Okinawa Prefectural Nanbu Medical Center & Children's Medical Center, Haebaru, Okinawa, Japan, [8]Tokyo Metropolitan Tama Medical Center, Taito City, Tokyo, Tokyo, Japan, [9]St. Luke's International Hospital, Tokyo, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with a higher risk of adverse pregnancy outcomes (APOs) compared to the general population. Although several APO risk factors have been identified in SLE pregnancies, standardized criteria for pregnancy planning remain undefined. The 2024 EULAR guidelines recommend tapering glucocorticoids to a prednisolone-equivalent dose of ≤5 mg/day prior to conception; however, the optimal threshold for pregnancy planning remains unclear. This study aimed to address these gaps.

Methods: This retrospective cohort study included patients with SLE who received care and delivered at three tertiary referral centers in Japan. Logistic regression and receiver operating characteristic (ROC) curve analyses were used to identify preconception factors associated with APOs. Odds ratios (ORs) were calculated based on pregnancy planning status.

Results: We analyzed 130 pregnancies in 123 women. Based on exploratory analysis, planned pregnancy was defined by the absence of teratogenic medications, clinical disease inactivity for ≥6 months before conception, prednisolone dosage ≤5 mg/day, and absence of proteinuria (≤0.5 g/day). According to this definition, 44.6% (58/130) was classified to planned pregnancy. This model was associated with significantly lower APO rates. Compared to unplanned pregnancies, planned pregnancies had reduced overall APOs (OR 0.29, 95% CI 0.13–0.61, p = 0.0012), maternal APOs (OR 0.50, 95% CI 0.22–1.13, p = 0.097), neonatal APO (OR 0.33, 95% CI 0.16–0.68, p = 0.0026), and low birth weight (OR 0.46, 95% CI 0.21–1.01, p = 0.053).

Multivariate analysis adjusted for hydroxychloroquine use, aspirin use, and renal involvement confirmed a lower risk of APOs: overall APO (aOR 0.30, 95% CI 0.13–0.70, p = 0.0055), maternal APO (aOR 0.50, 95% CI 0.19–1.27, p = 0.15), and neonatal APO (aOR 0.39, 95% CI 0.17–0.86, p = 0.019). Additionally, analysis using multiple models demonstrated that a prednisolone dosage ≤5 mg/day at conception was not significantly associated with an increased risk of APOs or SLE flares during pregnancy, even when compared with higher dosage thresholds.

Conclusion: Planned pregnancy is significantly associated with improved outcomes in SLE. These findings support the 2024 EULAR recommendation and highlight the importance of structured preconception planning

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

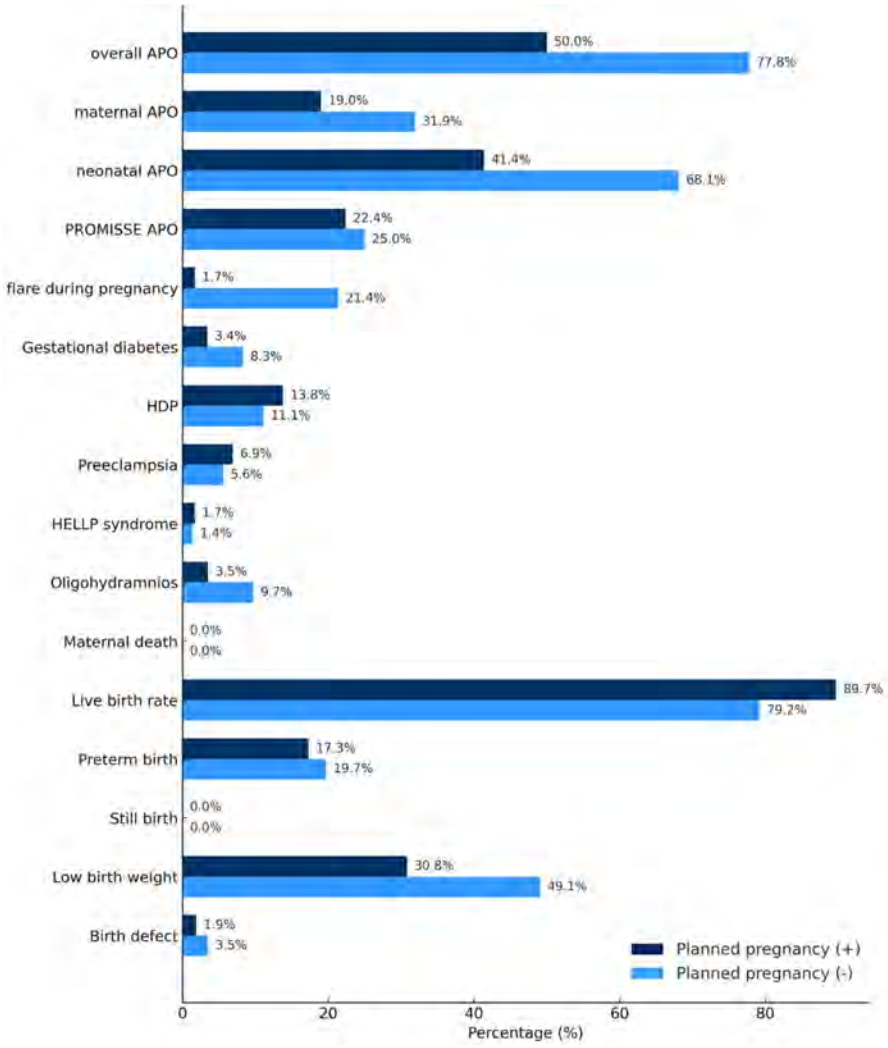


Figure 1. prevalence of each adverse pregnancy outcome according to pregnancy planning

Table 1. Baseline characteristics

Factor	Planned pregnancy (-)	Planned pregnancy (+)	p value
n	72	58	
Age at conception (yo)	32.00 [28.00, 35.00]	33.00 [29.00, 35.00]	0.433
BMI	20.75 [19.13, 22.84]	19.92 [18.18, 21.53]	0.069
Infertility treatment (%)	16 (22.2)	17 (29.3)	0.419
Skin and mucocutaneous (%)	50 (69.4)	38 (65.5)	0.707
Joint and muscular (%)	52 (72.2)	47 (81.0)	0.302
Renal manifestation (%)	36 (50.0)	14 (24.1)	0.004
Lupus nephritis class III/IV (%)	17 (23.6)	4 (6.9)	0.015
Serositis (%)	8 (11.1)	14 (24.1)	0.061
Neurological manifestation (%)	1 (1.4)	8 (13.8)	0.011
Hematological manifestation (%)	55 (76.4)	48 (82.8)	0.395
Anti-dsDNA antibody (%)			
Anti-RNP antibody (%)	22 (47.8)	17 (32.1)	0.149
Anti-Sm antibody (%)	13 (21.0)	22 (37.9)	0.047
Anti-Ro/SSA antibody (%)	43 (60.6)	42 (72.4)	0.193
LAC (%)	11 (15.5)	8 (14.0)	1
Anti-CL antibody (%)	13 (18.8)	15 (26.8)	0.389
Anti-CLβ2 antibody (%)	10 (14.1)	6 (10.5)	0.601
Low C3 (%)	52 (75.4)	38 (65.5)	0.245
Low C4 (%)	63 (91.3)	45 (77.6)	0.045
GC dosage at conception (mg/d)	10.00 [8.00, 12.50]	4.00 [0.00, 5.00]	<0.001
HCQ at conception (%)	19 (26.4)	35 (60.3)	<0.001
Aspirin at conception (%)	21 (29.2)	28 (48.3)	0.03
Teratogen use at conception (%)	69 (95.8)	58 (100.0)	0.253

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adverese pregnancy outcome ratio according to pregnancy planning

n	Univariate analysis			Multivariate analysis		
Factor	OR	95% CI	p value	aOR	95% CI	p value
overall APO (%)	0.29	0.13-0.61	0.0012	0.30	0.13-0.70	0.0055
maternal APO (%)	0.50	0.22-1.13	0.097	0.50	0.19-1.27	0.15
neonatal APO (%)	0.33	0.16-0.68	0.0026	0.39	0.17-0.86	0.019
PROMISSE APO (%)	0.87	0.38-1.96	0.731			
flare during pregnancy (%)	0.64	0.008-0.50	0.0090	0.052	0.006-0.45	0.0074
Gestational diabetes (%)	0.39	0.076-2.02	0.26			
HDP (%)	1.28	0.49-3.65	0.64			
Preeclampsia (%)	1.26	0.30-5.27	0.75			
HELLP syndrome (%)	1.25	0.08-20.40	0.88			
Oligohydramnios (%)	0.34	0.067-1.69	0.18			
Maternal death (%)						
Live birth rate (%)	2.26	0.82-6.32	0.11			
Preterm birth (%)	0.86	0.33-2.22	0.75			
Still birth (%)						
Low birth weight (%)	0.46	0.21-1.01	0.053	0.456	0.179-1.16	0.099
Birth defect (%)	0.54	0.048-6.13	0.62			

Disclosure: T. Nakai: None; **N. Honda**: None; **Y. HASHIMOTO**: None; **E. Soga**: None; **S. Fukui**: None; **A. Kitada**: None; **K. Nakanishi**: None; **N. Yokogawa**: Asahi-Kasei Pharma, 6, Bristol-Myers Squibb(BMS), 6, Chugai Pharmaceutical, 6, GlaxoSmithKline K.K., 6, Mitsubishi Tanabe Pharma, 6, Ono pharmaceutical, 6; **M. Okada**: Abbott, 6, Eli Lilly, 6, Mitsubishi Tanabe Pharma, 6, Pfizer, 6, Santen Pharmaceutical, 6.

Abstract Number: 2226

Factors Associated with Contraceptive Counseling by Rheumatologists for Reproductive-Aged Female Patients Prescribed Teratogenic Medications

Yongjay Kim[1], Kelsey Gripp[2], Deanna Jannat-Khah[3], Emily Wu[4], Mehret Birru Talabi[5], Nancy Pan[3], Lisa Sammaritano[3] and Caroline Siegel[3], [1]Hospital for Special Surgery, Englewood Cliffs, NJ, [2]Hospital for Special Surgery, New York, [3]Hospital For Special Surgery, New York, NY, [4]Hospital for Special Surgery, Union City, NJ, [5]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2195–2226) Reproductive Issues in Rheumatic Disorders Posters

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Guidelines advise rheumatologists to provide contraceptive counseling for all patients with pregnancy potential prescribed teratogenic medications, however, adherence is inconsistent. We assessed the frequency of, and factors associated with, rheumatologists' documented contraceptive counseling for this group to elucidate opportunities for intervention.

Methods: This single-center retrospective chart review included premenopausal females aged 18-45 seen by a rheumatologist ≥2 times, December 2022-December 2024, with a prescribed teratogenic medication at the most recent visit. We compared patient demographic and clinical variables and rheumatology provider characteristics between patients with and without documented contraceptive counseling. We performed logistic regression to predict receipt of contraceptive counseling, adjusting for age, race, insurance, preferred language, diagnosis, teratogenic medication, and provider gender and experience level.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics of Female Rheumatology Patients Aged 18-45 Prescribed Teratogenic Medications, Stratified by Contraceptive Counseling Documentation

Variable	Overall (N=338) N (%)	Contraceptive Counseling (N=107) N (%)	No Contraceptive Counseling (N=231) N (%)	p-value
Demographics				
Age, years – mean (SD)	34.5 (7.3)	32.7 (7.0)	35.3 (7.3)	*<0.01*
Race	**N=321**	**N=102**	**N=219**	*0.01*
• White	163 (50.8)	39 (38.2)	124 (56.6)	
• Black	47 (14.6)	22 (21.6)	25 (11.4)	
• Asian	42 (13.1)	15 (14.7)	27 (12.3)	
• Other	69 (21.5)	26 (25.5)	43 (19.6)	
• *Unknown*[1]	*17*	*5*	*12*	
Ethnicity	**N=326**	**N=103**	**N=223**	0.27
• Hispanic/Latino	79 (24.2)	29 (28.2)	50 (22.4)	
• Not Hispanic/Latino	247 (75.8)	74 (71.8)	173 (77.6)	
• *Unknown*[1]	*12*	*4*	*8*	
Employment Status	**N=335**		**N=228**	0.68
• Employed	230 (68.7)	70 (65.4)	160 (70.2)	
• Student	31 (9.3)	10 (9.3)	21 (9.2)	
• Disabled	14 (4.2)	4 (3.7)	10 (4.4)	
• Not Employed	60 (17.9)	23 (21.5)	37 (16.2)	
• *Unknown*[1]	*3*	*0*	*3*	
Insurance				*<0.01*
• Medicare/Medicaid	63 (18.6)	31 (29.0)	32 (13.9)	
• Commercial	275 (81.4)	76 (71.0)	199 (86.1)	
Preferred Language				*0.02*
• English	324 (95.9)	98 (91.6)	226 (97.8)	
• Other	14 (4.1)	9 (8.4)	5 (2.2)	
Smoking History				0.35
• Never smoked	300 (88.8)	98 (91.6)	202 (87.4)	
• Ever smoked	38 (11.2)	9 (8.4)	29 (12.6)	
Body Mass Index				1.00
• Underweight (<18.5)	14 (4.1)	4 (3.7)	10 (4.3)	
• Normal (18.5 - 24.9)	146 (43.2)	46 (43.0)	100 (43.3)	
• Overweight/Obese (≥25)	178 (52.7)	57 (53.3)	121 (52.4)	
Clinical Information				
Diagnostic				*<0.01*
• SLE/APS	91 (26.9)	42 (39.3)	49 (21.2)	
• Other	247 (73.1)	65 (60.7)	182 (78.8)	
Teratogenic Medication[2]	**N=325**	**N=104**	**N=221**	0.19
• Leflunomide	23 (7.1)	3 (2.9)	20 (9.0)	
• Methotrexate	166 (51.1)	56 (53.8)	110 (49.8)	
• Mycophenolate	123 (37.8)	42 (40.4)	81 (36.7)	
• Warfarin	13 (4.0)	3 (2.9)	10 (4.5)	
• *>1 of above*[1]	*13*	*3*	*10*	
Contraception[3]	**N=228**	**N=89**	**N=139**	0.14
• None/Least Effective	121 (53.1)	53 (59.6)	68 (48.9)	
• Moderately/Highly Effective/Permanent	107 (46.9)	36 (40.4)	71 (51.1)	
• *Other/Missing*[1]	*110*	*18*	*92*	
Rheumatology Provider Characteristics				
Provider Gender				0.48
• Female	266 (78.7)	87 (81.3)	179 (77.5)	
• Male	72 (21.3)	20 (18.7)	52 (22.5)	
Provider Experience				*<0.01*
• Fellow	46 (13.6)	27 (25.2)	19 (8.2)	
• Attending <10 years	108 (32.0)	45 (42.1)	63 (27.3)	
• Attending >10 years	184 (54.4)	35 (32.7)	149 (64.5)	

Comparisons done using t-tests for continuous and Fisher's Exact tests for categorical variables (no contraceptive counseling vs. contraceptive counseling columns); a p-value <0.05 was considered statistically significant.
1. Excluded from analysis.
2. No patients were prescribed cyclophosphamide, lenalidomide, or thalidomide.
3. Least effective (N=50): condom; Moderately effective (N=40): combined estrogen-progestin pill, vaginal ring, progestin-only pill; Highly effective (N=51): intrauterine device, subdermal progestin implant, injection, abstinence; Permanent (N=6): tubal ligation, partner vasectomy

Results: Of 338 rheumatology female patients aged 18-45 prescribed a teratogen, 107 (31.7%) received contraceptive counseling at their most recent visit. Patients who received vs did not receive counseling were more frequently non-White race (21.6% vs 11.4% Black; 14.7% vs 12.3% Asian; 25.5% vs 19.6% Other; p=0.01), publicly insured (29.0% vs 13.9%, p< 0.01),

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Logistic Regression Model Evaluating the Association Between Patient and Provider Characteristics and Contraceptive Counseling for Female Rheumatology Patients Aged 18-45 Prescribed Teratogenic Medications

Variable	Odds Ratio	95% Confidence Interval	p-value
Demographics			
Age	0.95	0.92 – 0.99	*0.01*
Race			
• *White*	*Referent*		
• Black	2.50	1.09 – 5.73	*0.03*
• Asian	1.58	0.69 – 3.67	0.28
• Other	1.28	0.62 – 2.61	0.51
Insurance			
• Private insurance	*Referent*		
• Medicare/Medicaid	0.89	0.35 – 2.24	0.81
Preferred Language			
• *Other*	*Referent*		
• English	0.51	0.13 – 2.01	0.33
Rheumatic Disease			
• *Other*	*Referent*		
• SLE and/or APS	3.65	1.66 – 8.04	*<0.01*
Teratogenic Medication			
• *Methotrexate*	*Referent*		
• Leflunomide	0.28	0.07 – 1.07	0.06
• Mycophenolate	0.48	0.23 – 1.03	0.06
• Warfarin	0.19	0.04 – 1.01	0.05
Provider Gender			
• *Female*	*Referent*		
• Male	0.72	0.35 – 1.49	0.38
Provider Experience			
• *Attending >10 years*	*Referent*		
• Attending <10 years	3.13	1.70 – 5.77	*<0.01*
• Fellow	5.31	1.82 – 15.47	*<0.01*

A p-value of <0.05 was considered statistically significant

non-English-speaking (8.4% vs 2.2%, p=0.02), had SLE and/or APS (39.3% vs 21.2%, p< 0.01), and were seen by a rheumatology fellow (25.2% vs 8.2%) or by an attending with < 10 years of experience (42.1% vs 27.3%) (p< 0.01). Overall, 231 (68.3%) patients reported no/least effective contraception (n=121) or had no contraception documentation (n=110) [**Table 1**].

In multivariable analysis, the odds of receiving contraceptive counseling decreased 5% with each increasing year of age (OR 0.95, 95% CI [0.92-0.99], p=0.01). Counseling was more likely for patients with Black vs White race (OR 2.5, 95% CI [1.09-5.73], p=0.03), SLE and/or APS vs other diagnoses (OR 3.65, 95% CI [1.66-8.04], p< 0.01), and—as compared to those seen by an attending with >10 years' experience—for patients seen by a rheumatology fellow (OR 5.31, 95% CI [1.82-15.47], p< 0.01) or by an attending with < 10 years' experience (OR 3.13, 95% CI [1.7-5.77], p< 0.01). Compared to methotrexate use, use of another teratogen was associated with decreased odds of counseling that was not statistically significant (for leflunomide: OR 0.28, 95% CI [0.07-1.07], p=0.06; for mycophenolate: OR 0.48, 95% CI [0.23-1.03], p=0.06; for warfarin: OR 0.19, 95% CI [0.04 – 1.01], p=0.05) [**Table 2**].

Conclusion: In this study, most reproductive-aged female patients prescribed a teratogenic medication did not have documentation of effective contraception, and less than one-third received contraceptive counseling at their most recent rheumatology visit. Patients with Black race, SLE and/or APS, and those seen by rheumatology providers closer to training were more likely to receive contraceptive counseling. Although documentation may not fully reflect practice, our findings suggest a need for quality improvement interventions to increase contraceptive counseling and consistent documentation for all high-risk rheumatology patients.

Disclosure: Y. Kim: None; **K. Gripp**: None; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **E. Wu**: None; **M. Birru Talabi**: None; **N. Pan**: None; **L. Sammaritano**: None; **C. Siegel**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2227

The Paraoxonase-1 Q192R Polymorphism is Associated with Increased Risk of Incident Clinical Rheumatoid Arthritis in an Anti-Citrullinated Protein Antibody-Positive Population

Amir Razmjou[1], Rong Guo[2], David Elashoff[2], Kevin Deane[3], Jill Norris[4], Marie Feser[5], Lauren Vanderlinden[6], Jennifer Wang[7], Ani Shahbazian[7] and Christina Charles-Schoeman[8], [1]UCLA / Veterans Affairs, Los Angeles, CA, [2]UCLA, Division of General Internal Medicine and Health Services Research, Los Angeles, [3]University of Colorado Denver Anschutz Medical Campus, Aurora, CO, [4]Colorado School of Public Health, Denver, CO, [5]University of Colorado Anschutz Medical Campus, Aurora, CO, [6]University of Colorado Anschutz Medical Campus, Monument, CO, [7]UCLA, Los Angeles, [8]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

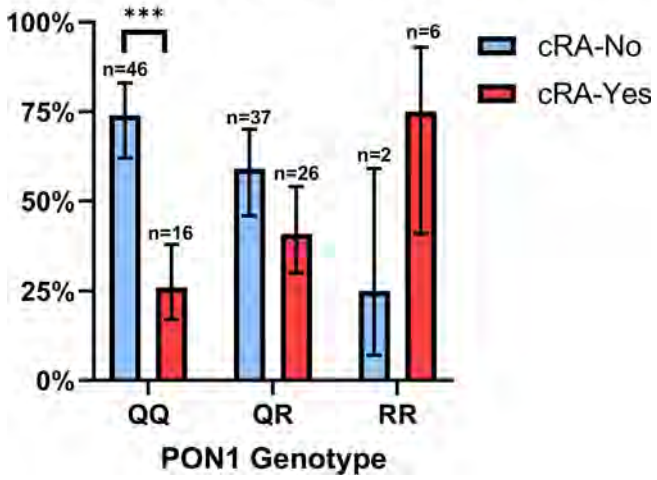
Table 1. Baseline demographics for ACPA+ at-risk individuals by clinical rheumatoid arthritis development.

	Clinical RA (n=49, 37%)	No Clinical RA (n=84, 63%)
Patient Characteristics		
Age (yrs)	55.4 (11.1)	58.1 (13.9)
Female	38 (77.6)	54 (64.3)
White	38 (77.6)	68 (81.0)
BMI (kg/m^2)	28.7 (5.3)	27.4 (4.5)
First-Degree Relative RA	13 (26.5)	11 (12.9)
Ever Smoker (yes)	20 (40.8)	32 (38.1)
Current Smoker (yes)	4 (10.5)	5 (6.0)
Omega Supplements	16 (34.0)	22 (27.2)
Cholesterol Meds Ever	12 (34.3)	14 (24.1)
Classifiable RA	40 (81.6)	-
Enrollment to Clinical RA (days)	570.2 (520.3)	-
Enrollment to Classifiable RA (days)	597.8 (590.6)	-
Enrollment to Last Follow-up (days)	-	1313.3 (1018.4)
RA Immunologic Parameters		
RF IgA+	12 (24.5)	10 (11.9)
RF IgM+	18 (36.7)	22 (26.2)
Shared Epitope+	**32 (65.3)***	33 (39.3)
C-Reactive Protein High	16 (37.2)	26 (32.9)
PON1 Activity (Baseline)		
Paraoxonase (U/mL)	**783.0 (508.0)***	547.8 (358.8)
Lactonase (U/mL)	32.6 (10.1)	32.9 (12.9)
Arylesterase (U/mL)	265.2 (71.0)	264.7 (65.6)
PON1 Q192R Polymorphism		
QQ	**16 (33.3)***	46 (54.1)
QR	26 (54.2)	37 (43.5)
RR	6 (12.5)	2 (2.4)

Values are mean (SD) or N (%) *p<0.05 PON values are baseline values at first sample, divided by 10. Significance testing done by Student's T-test for continuous variables, and Chi-Square test for categorical variables. RA: rheumatoid arthritis, BMI: body mass index, RF: rheumatoid factor, IgA: immunoglobulin A, IgM: immunoglobulin M, PON1: paraoxonase-1, QQ/QR/RR: PON1 Q192 R genotype polymorphisms (rs662).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Percent of Patients With/Without Clinical RA Per PON1 Genotype



Legend: ***p<0.001. Brackets are 95% CI. Percents and numbers represent participants with, and without clinical RA within each of the 3 PON1 genotypes. RA: rheumatoid arthritis, cRA: clinical RA, PON1: paraoxonase-1, QQ/QR/RR: PON1 Q192 R genotype polymorphisms (rs662).

Table 2. Univariate and multivariate Cox proportional hazards models for time to clinical RA development.

PON1 Genotype without PON1 Activity			
Predictor	**Univariate HR (95% CI)**	**Multivariate[%] HR (95% CI)**	**Multivariate[#] HR (95% CI)**
PON1 Genotype			
# of R Alleles	**1.96 (1.21, 3.16)***	**1.70 (1.06, 2.73)***	-
QR vs QQ	1.67 (0.88, 3.16)	-	1.63 (0.86, 3.11)
RR vs QQ	**4.37 (1.67, 11.41)***	-	**2.98 (1.07, 8.29)***
Shared Epitope +	1.81 (0.99, 3.3)	1.54 (0.82, 2.88)	1.53 (0.82, 2.88)
RF-IgA +	**1.90 (1.03, 3.53)***	1.30 (0.64, 2.66)	1.28 (0.61, 2.68)
RF-IgM +	**2.35 (1.32, 4.18)***	1.82 (0.94, 3.52)	1.82 (0.94, 3.53)

PON1 Genotype with PON1 Activity				
Predictor	**Univariate HR (95% CI)**	**Multivariable HR^ (95% CI) ΔPON**	**Multivariable HR^ (95% CI) ΔLAC**	**Multivariable HR^ (95% CI) ΔARYL**
PON1 Genotype (# of R Alleles)	**1.96 (1.21, 3.16)***	**1.67 (1.03, 2.73)***	**1.70 (1.04, 2.76)***	**1.64 (1.01, 2.67)***
ΔPON	0.99 (0.97, 1.01)	1.00 (0.99, 1.02)	-	-
ΔLAC	**0.69 (0.49, 0.98)***	-	0.70 (0.49, 1.00)	-
ΔARYL	0.95 (0.88, 1.02)	-	-	0.98 (0.91, 1.06)

*p<0.05 %Multivariate model includes PON1 Q192R genotype (# of R alleles), shared epitope positivity and RF isotypes (IgA/IgM), and. # of R Alleles: QQ=0, QR=1, RR=2. #Multivariate models include PON1 Q192R genotype (categorical variable QR or RR vs QQ), shared epitope positivity and RF isotypes (IgA/IgM),. ^Multivariate models include PON1 Q192R genotype (# of R alleles), respective change of PON1 activity since last visit (PON, LAC, or ARYL), RF isotypes (IgA/IgM), shared epitope positivity, and age, gender, and BMI (age/gender/BMI included due to known relevance in PON1 activity). %#Models were chosen by step-wise regression of different predictors (including age, BMI, gender which were not significant). Shared epitope was included in the model due to its known biologic importance. RA: rheumatoid arthritis, PON1: paraoxonase-1, QQ/QR/RR: PON1 Q192 R genotype polymorphisms (rs662), RF: rheumatoid factor, IgA: immunoglobulin A, IgM: immunoglobulin M, PON: paraoxonase activity, LAC: lactonase activity, ARYL: arylesterase activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid arthritis (RA) has a pre-clinical state. In particular, elevation of antibodies to citrullinated proteins (ACPA) is a strong risk factor for future clinically-apparent inflammatory arthritis that can be termed 'clinical RA', however not all ACPA+ individuals who are 'at-risk' develop clinical RA. Furthermore, we have limited understanding into which factors drive the transition from preclinical to clinical RA. Paraoxonase-1 (PON1) is an HDL-associated enzyme which metabolizes pro-inflammatory oxidized lipids. We have previously shown that increasing PON1 activity over time is associated with decreased risk of incident clinical RA in ACPA+ at-risk individuals (ARI) (Razmjou, et al. ACR Abstract #464, 2024). The PON1 Q192R polymorphism (rs662) has been shown to affect PON1 enzyme activities. This study aimed to investigate if the PON1 Q192R polymorphism associates with incident clinical RA in an ACPA+ ARI population.

Methods: ACPA+ (determined by the anti-CCP3 assay) ARI who did not have clinical RA at baseline were evaluated; 49 (37%) of whom developed clinical RA during longitudinal follow-up. PON1 Q192R polymorphism ('Q192R') were tested as previously described (Charles-Schoeman, et al. *J Rheumatol*, 2023). PON1 activity was measured as previously described (Charles-Schoeman, et al. *Sci Rep*, 2020) by its paraoxonase, lactonase, and arylesterase enzymatic functions. Cox-proportional hazards models were used to evaluate the effect of Q192R on time to clinical RA, with multivariate models including variables with p-values < 0.05 in univariate models. Q192R was analyzed as an ordinal variable (0, 1, or 2 R alleles), and a categorical variable (QR or RR v QQ, ref QQ).

Results: The baseline characteristics of ACPA+ ARI are in Table 1. A greater proportion of ARI with QR, and RR genotypes developed clinical RA (Figure 1). In univariate Cox-proportional hazards models with Q192R, the # of R alleles and RR vs QQ were significantly associated with increased risk of developing clinical RA over time. Significance was maintained in multivariable models after including shared epitope (SE) positivity, and RF IgA/IgM positivity (Table 2). Multivariable models including change in PON1 enzyme activity, SE, RF IgA/IgM, age, sex and BMI also showed that increased # of R alleles were associated with an elevated risk of clinical RA ($p < 0.05$) (Table 2).

Conclusion: In a population of ACPA+ ARI, the PON1 Q192R genotype was significantly associated with increased risk of developing clinical RA, even after controlling for the presence of SE and RF positivity as well as PON1 activity. PON1 activity by lactonase function was inversely associated with the development of clinical RA. Future studies include validating these findings in additional cohorts and incorporating these findings into predictive models for future clinical RA, as well as evaluating the mechanisms of the effect of the PON1 Q192R polymorphism on clinical RA development.

Disclosure: A. Razmjou: None; **R. Guo**: None; **D. Elashoff**: None; **K. Deane**: Inova Diagnostics, 1; **J. Norris**: None; **M. Feser**: None; **L. Vanderlinden**: None; **J. Wang**: None; **A. Shahbazian**: None; **C. Charles-Schoeman**: AbbVie/Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Immunovant, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2, Sana Biotechnology, 2.

Abstract Number: 2228

COVID-19 Outcomes in Rheumatoid Arthritis Patients Prescribed Biologic vs. Conventional DMARDs: A Propensity-Matched Analysis

Chase Verdugo[1], Yazin Hindosh[1], Akram Hindosh[1], Jonathan Sayegh[1], Bassam Mitri[1], Johnny Youssef[1], Tyler On[1], Faissal Stipho[2] and Issa Batarseh[2], [1]University of Arizona College of Medicine Tucson, Tucson, AZ, [2]Department of Internal Medicine, Banner University Medical Center / University of Arizona, Tucson, Arizona, Tucson, AZ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid Arthritis (RA) is an autoimmune disease characterized by immune system dysregulation, and it is commonly treated with either conventional or biologic Disease-Modifying Antirheumatic Drugs (DMARDs). Because RA and its therapies suppress the immune system, patients are more susceptible to infections, including COVID-19. However, it remains unclear whether conventional DMARDs or biologic DMARDs confer some benefit with respect to COVID-19 outcomes. This study aims to compare COVID-19 outcomes in RA patients treated with biologic versus conventional DMARDs. We hypothesize that the broader, less targeted immunosuppressive effects of conventional DMARDs may play a more protective role for patients who develop COVID-19 infections.

Methods: The TriNetX Database was queried to identify patients ≥ 18 years old with RA and a COVID-19 diagnosis. These individuals were then divided into two subgroups: those prescribed biological DMARDs (adalimumab, etanercept, infliximab, rituximab, and tocilizumab, n=4,166) and those who were prescribed conventional DMARDs (methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, and azathioprine, n=35,792) within 1 year of the COVID-19 diagnosis. These groups were 1:1 propensity score matched (n=4,163) for demographics and relevant comorbidities. Primary outcomes included 30-day, 90-day, and 1-year medical complications following a COVID-19 diagnosis, and these were compared using risk ratios (RR) with statistical significance set to $p< 0.05$.

Results: RA patients prescribed biological DMARDs before COVID-19 diagnosis had a significantly higher 30-day risk of ventilator use (RR=2.295, $p< 0.001$), mortality (RR=1.907, $p< 0.001$), and pulmonary fibrosis (RR=2.389, p=0.001), an increased 90-day risk of ventilator use (RR=2.092, $p< 0.001$), mortality (RR=1.819, $p< 0.001$), and pulmonary fibrosis (RR=2.528, $p< 0.001$), and an increased 1-year risk of ventilator use (RR=2.076, $p< 0.001$), mortality (RR=1.726, $p< 0.001$), and pulmonary fibrosis (RR=2.137, $p< 0.001$).

Conclusion: Our study suggests that patients with RA taking biological DMARDs have worse COVID-19 outcomes than those taking conventional DMARDs. Patients receiving conventional DMARDs required less ventilatory support during COVID-19 infection, indicating a milder disease course. This may be attributed to the less specific immunosuppressive mechanism of conventional DMARDs when compared to the more targeted mechanism of biological DMARDs, which potentially could lead to a weaker immune response against COVID-19.

Disclosure: C. Verdugo: None; **Y. Hindosh**: None; **A. Hindosh**: None; **J. Sayegh**: None; **B. Mitri**: None; **J. Youssef**: None; **T. On**: None; **F. Stipho**: None; **I. Batarseh**: None.

Abstract Number: 2229

National Multicenter study of Baricitinib in Rheumatoid Arthritis - Interstitial Lung Disease: effectiveness and progressive lung disease

Ana Serrano-Combarro[1], Belén Atienza-mateo[2], Jess Loarce[3], César Antonio Egües Dubuc[4], Marta Pastor Mena[5], Rafael B. Melero-González[6], Sara Maria Rojas Herrera[7], Carmen Carrasco-Cubero[8], Carolina Perez Garcia[9], Juan María Blanco-Madrigal[10], Nuria Vegas Revenga[11], Deseada Palma-Sanchez[12], Andrea García-Valle[13], Virginia Ruiz-Esquide[14], Jose Ramón Lamua-Riazuelo[15], Santos Castañeda[16], Ricardo Blanco[17], and Spanish Collaborative Group of JAKi in Interstitial Lung Disease Associated with Rheumatoid Arthritis [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, PALMA DE MALLORCA/BALEARES, Spain, [3]Ramn y Cajal University Hospital, Madrid, Spain, [4]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [5]Hospital de Jerez de la Frontera, Jerez de la Frontera, Spain, [6]COMPLEXO HOSPITALARIO UNIVERSITARIO DE OURENSE, O Carballino, Spain, [7]Hospital de Mérida, Rheumatology, Badajoz, Badajoz, Spain, [8]Complejo Hospitalario Universitario de Badajoz, Badajoz, Spain, [9]Hospital del Mar, Barcelona, Spain, [10]Rheumatology. Hospital Universitario Araba., Vitoria, Pais Vasco, Spain, [11]Galdakao- Usansolo University Hospital, Galdakao, Spain, [12]Rheumatology. Hospital Rafael Méndez, Lorca, Murcia, Spain, [13]Rheumatology. Hospital General Río Carrión, Palencia, Castilla y Leon, Spain, [14]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [15]Hospital Universitario del Henares,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Madrid, Spain, [16]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [17]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: **Tuesday, October 28, 2025**
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) in Rheumatoid Arthritis (RA) determines a worse prognosis with an increased mortality. Abatacept and rituximab may be the preferred therapies. JAK inhibitors (JAKi) have demonstrated effectiveness in observational studies of RA-ILD, especially with tofacitinib or baricitinib (BARI). While both articular and pulmonary domains may respond to JAKi, some patients experience ILD progression. Identifying this subgroup of patients is essential for early detection and appropriate management. In a large series of RA-ILD patients treated with BARI, we aimed to **a)** study the effectiveness, and **b)** characterize the subgroup with progressive ILD.

Methods: From a large observational multicenter study of 72 RA-ILD patients treated with BARI, we selected those with available pulmonary function tests (PFTs) follow-up data. Progressive ILD was defined as an absolute decline of forced vital capacity (FVC) of ≥10% within 1 year of follow-up since BARI initiation **(Figure)**. We compared patients with and without progressive ILD. *Results are expressed as percentage, mean±SD or median [IQR], as appropriate*.

Table. Baseline characteristics of RA-ILD patients treated with BARI.

Baseline characteristics	Overall (n=72)	Progressive ILD (n=11)	Non-progressive ILD (n=31)	Progressive vs non-progressive ILD p
Age, years mean±SD	68 ± 10	66 ± 10	69 ± 10	0.44
Women, n (%)	52 (73)	4 (36)	25 (81)	**0.016**
Smoker ever, n (%)	42 (58)	9 (82)	19 (61)	0.12
Time since ILD diagnosis, months, median [IQR]	25 [13-63]	22 [15-60]	24 [8-57]	0.50
RF // ACPA, n (%)	68 (94) // 68 (94)	11(100) // 11(100)	30 (97) // 31 (100)	0.35 // 0.52
FVC (% of the predicted), mean±SD	86 ± 28	105 ± 20	83 ± 19	0.35
DLCO (% of the predicted), mean±SD	69 ± 20	80 ± 19	65 ± 17	0.38
UIP-like fibrotic pattern on HRCT, n (%)	33 (49)	7 (64)	15 (48)	0.18
NSIP-like fibrotic pattern on HRCT, n (%)	22 (32)	4 (36)	11 (35)	0.18
DAS28-ESR, mean±SD	4±1	4±1	4±	0.40
Previous immunosuppressive therapy, n (%)	72 (100)	11 (100)	31 (100)	
Methotrexate	62 (86)	9 (82)	28 (90)	0.67
Leflunomide	51 (70)	8 (73)	21 (68)	0.88
Abatacept	45 (62)	6 (55)	23 (74)	0.25
Rituximab	17 (24)	3 (27)	8 (26)	0.86
Anti-TNF drugs	39 (54)	4 (36)	17 (55)	0.43
Concomitant immunosuppressive therapy, n (%)	29 (40)	4 (36)	13 (42)	0.95
Prednisone at baseline, mg/day, median [IQR]	5 [2.5-10]	2.5 [0-5]	5 [5-10]	0.18
Concomitant antifibrotic therapy, n (%)	8 (11)	4 (36)	3 (10)	**0.034**

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; DMARD, disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; JAKi, JAK inhibitor; RA, rheumatoid arthritis; RF, rheumatoid factor; UIP, usual interstitial pneumonia; ADA, Adalimumab; ETN, Etanercept.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

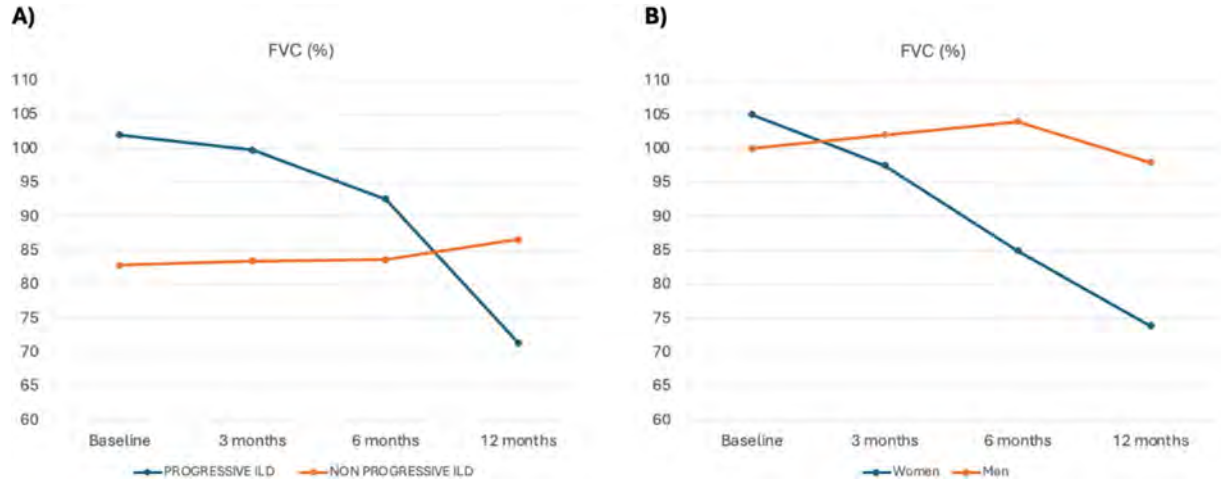


Figure. FVC evolution in A) both groups (progressive and non-progressive ILD) and B) by sex. Progressive ILD was defined as an absolute decline of forced vital capacity (FVC) of ≥10% within 1 year of follow-up since BARI initiation).

Results: A total of 42 patients with available data on FVC evolution were included. Progressive and non-progressive ILD was observed in 11 (26%) and 31 (74%) patients, respectively. The baseline general features are summarized in **Table**. Both groups were similar in age, smoking, positivity of rheumatoid factor or anti-citrullinated protein autoantibodies, ILD duration up to BARI initiation, prednisone dose, baseline PFTs or radiological pattern. Progressive ILD was more frequent in women and as expected required more combined treatment with antifibrotics. FVC evolution in both groups (progressive and non-progressive ILD) and by sex is displayed in **figure**.

Conclusion: BARI may be useful in RA-ILD. However, progression may be present in around a quarter of patients, especially in women. Effectiveness should be closely monitored with PFTs to early detect progressive ILD.

Disclosure: A. Serrano-Combarro: None; **B. Atienza-mateo**: None; **J. Loarce**: None; **C. Egües Dubuc**: None; **M. Pastor Mena**: None; **R. Melero-González**: None; **S. Rojas Herrera**: None; **C. Carrasco-Cubero**: None; **C. Perez Garcia**: None; **J. Blanco-Madrigal**: None; **N. Vegas Revenga**: None; **D. Palma-Sanchez**: None; **A. García-Valle**: None; **V. Ruiz-Esquide**: None; **J. Lamua-Riazuelo**: None; **S. Castañeda**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2230

Racial and Ethnic Disparities in Rheumatoid Arthritis-Associated Interstitial Lung Disease and Their Impact on Antifibrotic Therapy

Andrea Galecio Chao, Baylor College of Medicine, Houston, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is a significant cause of morbidity and mortality among patients with rheumatoid arthritis (RA), often leading to progressive pulmonary function decline. Although antifibrotic therapies, such as pirfenidone and nintedanib, are being used in managing RA-ILD, disparities in their use and clinical outcomes persist across different racial and ethnic groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This retrospective study analyzed data from the BCM ILD Registry with 215 CTD-ILD patients in total. FVC and DLCO values were compared across racial/ethnic groups (White, African American, Hispanic/Latino, others). ANOVA and Ridge regression are used to examine pulmonary function differences and predictors of antifibrotic use.

Results: Within RA-ILD group, the cohort was racially and ethnically diverse: 45.2% Hispanic, 16.1% White, 12.9% Black, and 22.6% Multiracial. The mean FVC and mean DLCO were lowest in Hispanic and Black patients, respectively. Mean FVC for Hispanic patients was 50.5%, and mean DLCO for Black patients was 45.2%, while White patients had the highest mean FVC of 61.25% and mean DLCO of 50.59%. 67% of African American and Hispanic/Latino patients did not receive pirfenidone or nintedanib despite severe impairment. ANOVA showed significant differences in FVC and DLCO, with White patients showing better pulmonary function. Ridge regression analysis identified race/ethnicity as a significant predictor of antifibrotic therapy use, with minority patients less likely to receive treatment even after adjusting for disease severity.

Conclusion: Racial and ethnic disparities in **RA-ILD** care contribute to unequal access to treatment, resulting in poorer pulmonary outcomes for **minority patients**. These disparities are likely influenced by **socioeconomic**, and **healthcare access** factors, including lack of insurance, limited access to healthcare providers, and underrepresentation in clinical trials. To address these gaps, actions are needed such as expanding healthcare coverage, enhancing clinical trial representation, and providing cultural competence training to healthcare providers.

Disclosure: A. Galecio Chao: None.

Abstract Number: 2231

Inverse Correlation Between Neutrophil Activation and Rheumatoid Factor Concentrations in Rheumatoid Arthritis (RA)

Anne-Christine Bay-Jensen[1], Dovile Sinkeviciute[2], Christian Thudium[2], shu Sun[1], Mathilde Christensen[1], Morten Karsdal[1], marta Alexdottir[1] and Joachim mortensen[1], [1]Nordic Bioscience A/S, Herlev, Denmark, [2]Nordic Bioscience, Herlev, Denmark

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Neutrophils are crucial in fibro-inflammatory diseases like Crohn's disease (CD) and rheumatoid arthritis (RA), but their biomarkers are better established in CD than in RA. Neutrophils are present in the inflamed synovium of the joints, however data on neutrophil count and assessment of blood levels of calprotectin – an alarmin released from neutrophils and monocytes – have pointed in different directions, which may be attributed to patient heterogeneity and/or treatment effect. The novel biomarker CPa9-HNE is a fragment of calprotectin generated by human neutrophil elastase during neutrophil activation and offers potential insight into neutrophil activity in RA. This study aims to explore the association between neutrophil activity, as measured by CPa9-HNE, and disease activity in patients with moderate to severe RA.

Methods: Serum samples from 76 predominantly white (90%), female (76%), seropositive RA patients and active disease (DAS25-CRP >3.4) aged 22-85 years were retrieved from several different biorepositories (Discovery Lifesciences, BioIVT LLC, Protogenex Inc.). None of the patients were biological naïve. CPa9-HNE was measured in the serum sample using the NordicCPA9™ manual ELISA. The markers of fibrogenesis and fibrolysis, PRO-C3 and C3M, were measured to study the link between fibro-inflammation and neutrophil activity. Data from a published Crohn's disease study (n=65), including

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

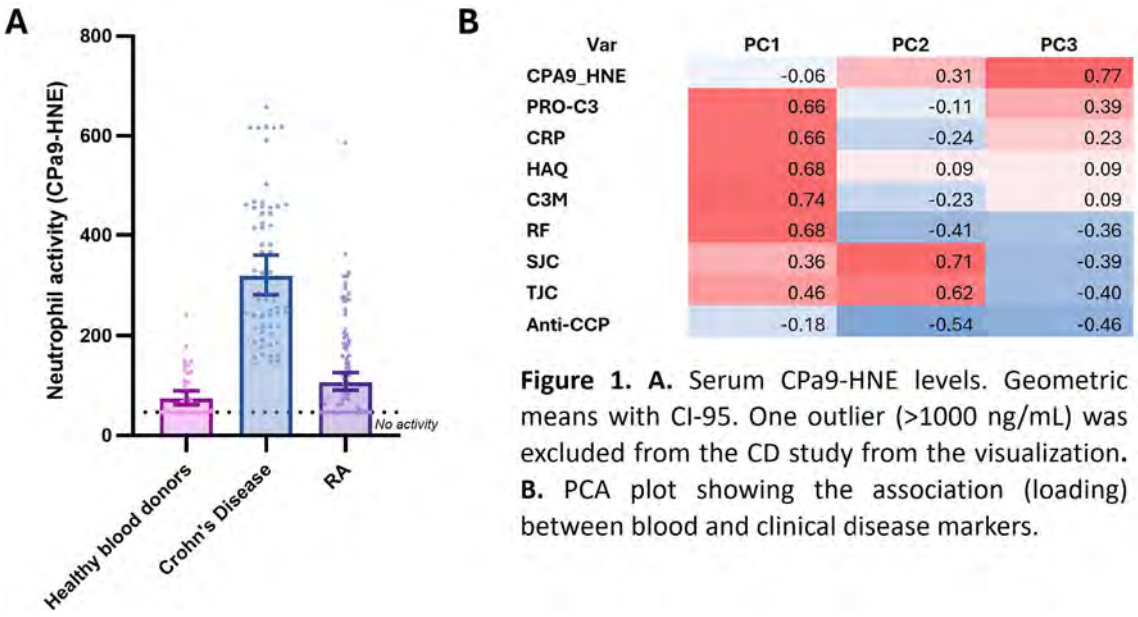


Figure 1. A. Serum CPa9-HNE levels. Geometric means with CI-95. One outlier (>1000 ng/mL) was excluded from the CD study from the visualization. **B.** PCA plot showing the association (loading) between blood and clinical disease markers.

healthy blood donors (n=32), was used to compare levels of CPa9-HNE between CD and RA (Mortensen et al. 2022). Undetectable samples were given the value of the assay detection limit (47 ng/ml).

Results: Of the RA patients, 23 out of 76 had undetectable levels of CPa9-HNE, compared to 14 out of 32 healthy donors and none in the of the CD group. The geometric mean [95%-CI] levels were significantly lower in RA patients (107.2 [90.9-126]) than in CD (319 [281-361]), but higher than healthy controls 74.5 [61.7-90.0] (Figure 1A). CPa9-HNE was inversely correlated with rheumatoid factor (rho =-0.62) and to a lesser degree with anti-CCP levels (rho = -0.40). CPa9-HNE showed no correlation (rho >0.4) or association with age, BMI, gender, disease duration, DAS28, CRP, or swollen or tender joint count (SJC/TJC). Nor the fibro-inflammatory markers PRO-C3 and C3M. PCA analysis revealed three clusters explaining 64% of the variation in the dataset: PC1, fibro-inflammatory driven by C3M, RF, HAQ, CRP and PRO-C3, BUT not CPa9-HNE; PC2, symptomatic driven by SJC and TJC; PC3, neutrophilic driven by CPa9-HNE (Figure 1B).

Conclusion: The observation of high RF and low neutrophil activity in RA patients may be due to the heterogeneity of RA, differing immune pathways, treatment effects and disease stage. Thus CPa9-HNE is a relevant biomarker for the neutrophilic RA endotype, as precision medicine tool for RA.

Disclosure: A. Bay-Jensen: Nordic Bioscience A/S, 3, 11; **D. Sinkeviciute**: Nordic Bioscience, 3, 11; **C. Thudium**: Nordic Bioscience A/S, 3, 11; **s. Sun**: Nordic Bioscience, 3, 11; **M. Christensen**: Nordic Bioscience, 3; **M. Karsdal**: Nordic Bioscience, 3, 8, 11; **m. Alexdottir**: Nordic Bioscience, 3; **J. mortensen**: no, 3, 11.

Abstract Number: 2232

Risk factors for hospitalizations in a large, contemporary rheumatoid arthritis patient cohort

Argyro Lazarini[1], Konstantinos Thomas[2], EVRIPIDIS KALTSONOUDIS[3], Paraskevi V Voulgari[4], Alexandros Drosos[5], Argyro Repa[6], Ainour Molla ismail Sali[6], Prodromos Sidiropoulos[6], Kalliopi Fragkiadaki[1], Maria Tektonidou[7], Petros Sfikakis[8], Panagiota Tsatsani[9], Sousana Gazi[9], Evangelia Argyriou[10], Kyriaki Boki[10], Pelagia Katsimpri[1], Dimitrios Boumpas[1], Gerasimos Evangelatos[11], Alexios Iliopoulos[12], Konstantina Karagianni[13], Lazaros Sakkas[13], Konstantinos Melissaropoulos[14], Panagiotis Georgiou[14], Eleftheria Grika[1], PANAYIOTIS VLACHOYIANNOPOULOS[1], Theodoros Dimitroulas[15], Alexandros Garyfallos[16], Konstantinos Georganas[17], Periklis Vounotrypidis[18], Konstantinos Ntellis[19],

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Georgios Kitas[20] and Dimitrios Vassilopoulos[21], [1]Joint Rheumatology Program, University of Athens Medical School, Athens, Greece, [2]Joint Rheumatology Program, University of Athens Medical School, Athens, Greece, [3]Rheumatology Clinic, University of Ioannina, IOANNINA, Ioannina, Greece, [4]Department of Rheumatology, School of Health Sciences, Faculty of Medicine, University of Ioannina, Ioannina, Ioannina, Greece, [5]Rheumatology Clinic, University of Ioannina, Ioannina, Greece, [6]Department of Rheumatology, Clinical Immunology and Allergy, University Hospital of Heraklion, Heraklion, Greece, [7]National and Kapodistrian University of Athens, Athens, Greece, [8]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [9]Rheumatology Unit, KAT Hospital, Athens, Greece, [10]Rheumatology Unit, Sismanoglio Hospital, Athens, Greece, [11]Third Department of Medicine, National and Kapodistrian University of Athens, School of Medicine, Sotiria Hospital, Athens, Attiki, Greece, [12]417 Army Share Fund Hospital (NIMTS), Department of Rheumatology, Athens, Greece, ZOGRAFOU, Greece, [13]Department of Rheumatology, University of Thessaly, Larissa, Greece, [14]Rheumatology Unit, Agios Andreas Hospital, Patras, Greece, [15]Hippokration University Hospital, Medical School, Aristotle University of Thessaloniki, Fourth Department of Internal Medicine, Thessaloniki, Greece, Thessaloniki, Greece, [16]4th Department of Medicine, Aristotle University, Thessaloniki, Greece, [17]Private office, Athens, [18]Private office, Thessaloniki, Greece, [19]Private office, Kalamata, Greece, [20]Hygeia Hospital, Athens, Greece, [21]Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine, General Hospital of Athens "Hippokration", Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine and Laboratory, Athens, Greece, Athens, Greece

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: There are limited data regarding the recent trends and risk factors for hospitalization in patients with rheumatoid arthritis (RA). Our aim was to estimate the rate, causes and predictors for hospitalizations in a real world, contemporary RA patient cohort.

Methods: Data from a multi-center, longitudinal cohort of RA patients regarding patient and disease characteristics were collected at baseline, 1 and 3 years later. The number and causes for hospitalizations by ICD-10 categories were recorded and the incidence rate was calculated. Risk factors for hospitalizations were evaluated with multivariable poisson regression analysis.

Results: 1195 RA patients were included; 78% were females with a mean age of 62 and a median disease duration of 7 years, repsectively. At baseline, 83% were on conventional synthetic DMARDs, 46% on biologic DMARDs and 39% on prednisolone (median dose: 5 mg/day). Baseline DAS28-ESR was 3.1 (median) and HAQ-DI 0.25 (median), respectively. During follow-up (3585 patient-years), 262 hospitalizations were recorded in 204 patients (17.1%) with an estimated incidence rate of 7.3/100 patient-years. The most frequent causes of hospitalization were infections (2/100 patient-years, primary of the respiratory tract), cardiovascular diseases (0.84/100 patient-years, mainly acute myocardial infarction and stroke), arthroplasties (0.78/100 patient-years) and gastrointestinal diseases (0.72/100 patient-years). By multivariable analysis, seropositivity was associated with a lower incidence (IRR=0.66, 95% CI: 0.47–0.94) while a higher disease activity status (DAS-28-ESR: 3.2-5.1 - Medium Disease Activity: IRR=1.88, 95% CI: 1.27–2.79 or High Disease Activity: IRR=2.74, 95% CI: 1.61–4.56 *vs*. DAS-28-ESR< 3.2: Low disease activity or remission), a higher baseline HAQ (IRR=1.64, 95% CI: 1.06–2.48), male sex (IRR=1.88, 95% CI: 1.22-2.84) and diabetes (IRR=1.99, 95% CI: 1.32–2.94, p = 0.003) were associated with a higher risk of hospitalizations, respectively.

Conclusion: In this large, longitudinal, prospective, real-life cohort of RA patients, the incidence of hospitalizations was 7.3/100 patient-years, with infections being the most common cause. Higher disease activity, impaired functional status, male sex and diabetes were independently associated with hospitalizations. These findings underscore the critical importance of tight disease control and close monitoring for infectious complications in RA patients.

Disclosure: A. Lazarini: None; **K. Thomas**: None; **E. KALTSONOUDIS**: None; **P. Voulgari**: None; **A. Drosos**: None; **A. Repa**: None; **A. Molla ismail Sali**: None; **P. Sidiropoulos**: None; **K. Fragkiadaki**: None; **M. Tektonidou**: None; **P. Sfikakis**: None; **P. Tsatsani**: None; **S. Gazi**: None; **E. Argyriou**: None; **K. Boki**: None; **P. Katsimpri**: None;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

D. Boumpas: None; **G. Evangelatos**: None; **A. Iliopoulos**: None; **K. Karagianni**: None; **L. Sakkas**: Bristol-Myers Squibb(BMS), 5; **K. Melissaropoulos**: None; **P. Georgiou**: None; **E. Grika**: None; **P. VLACHOYIANNOPOULOS**: None; **T. Dimitroulas**: None; **A. Garyfallos**: None; **K. Georganas**: None; **P. Vounotrypidis**: None; **K. Ntellis**: None; **G. Kitas**: None; **D. Vassilopoulos**: None.

Abstract Number: 2233

Spatial Multi-omics Demonstrates Shared Immune States Across Autoimmune Diseases and Target Tissues in the Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM)

Caleb Marlin[1], Roopa Madhu[2], Erin Theisen[3], Liz Bradshaw[4], Ce Gao[5], Thomas Eisenhaure[6], Nicolas Sugiarto[7], Accelerating Medicines Partnertship: Autoimmune and Immune Mediated Diseases[8], Jill Buyon[9], Michelle Petri[10], Brad Rovin[11], Victoria Werth[12], Ellen M. Gravallese[13], Jennifer Anolik[14], Larry Moreland[15], Laura Donlin[16], Christopher Ritchlin[17], Jose Scher[18], Johann Gudjonsson[19], Wilson Liao[20], Alexis Ogdie[21], Caroline Shiboski[22], A. Darise Farris[1], Alan Baer[23], Blake M. Warner[24], Jose Clemente[25], Adriana Heguy[26], Michael Brenner[27], Nir Hacohen[28], Joel Guthridge[1], Judith James[1], Soumya Raychaudhuri[29], Lam Tsoi[19], Xiang Zhou[30], Joshua Welch[30], Rachael Clark[3], ilya Korsunsky[29], Christopher Lessard[1] and Kevin Wei[31], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Brigham and Women's Hospital, Brookline, MA, [3]Brigham and Women's Hospital, Boston, [4]Oklahoma Medical Research Foundation, Oklahoma City, [5]Division of Rheumatology, Inflammation and Immunity, DOM, BWH; Harvard Medical School, Boston, MA, [6]Broad Institute, Cambridge, MA, [7]Broad Institute, Boston, [8]Multiple Institutions, Oklahoma City, [9]NYU Grossman School of Medicine, New York, NY, [10]Johns Hopkins University School of Medicine, Timonium, MD, [11]The Ohio State University, Columbus, OH, [12]University of Pennsylvania, Wynnewood, PA, [13]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA, [14]University of Rochester Medical Center, Rochester, NY, [15]University of Colorado, Denver, CO, [16]Hospital for Special Surgery, New York, NY, [17]University of Rochester Medical Center, Canandaigua, NY, [18]New York University School of Medicine, New York, NY, [19]University of Michigan, Ann Arbor, MI, [20]UCSF, San Francisco, CA, [21]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [22]University of California San Francisco, San Francisco, CA, [23]Johns Hopkins University School of Medicine, Baltimore, MD, [24]National Institutes of Health, Bethesda, MD, [25]Icahn School of Medicine at Mount Sinai, New York, NY, [26]NYU Grossman School of Medicine, New York, [27]Brigham and Women's Hospital, Harvard Medical School, Newton, MA, [28]Broad Institute of MIT Harvard, Cambridge, MA, [29]Brigham and Women's Hospital, Boston, MA, [30]University of Michigan, Ann Arbor, [31]Brigham and Women's Hospital at Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune diseases affect more than 23.5 million Americans involving nearly every organ system of the human body. To identify shared, unique, and novel pathways underlying the pathogenesis of common autoimmune diseases, The Accelerating Medicines Partnership: Autoimmune and Immune-Mediated Diseases Network (AMP AIM) was launched to investigate Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Psoriatic Disease (PsD), and Sjogren's Disease (SD) using single-cell and spatial technologies.

Methods: The Disease Teams, Technology Cores, System Biology Groups, Tissue Research Center, and Research Management Units collaborated on pilot projects to evaluate spatial and single-cell technologies for their feasibility, sensitivity, and scalability. These assessments aimed to inform the selection of omics approaches that would provide the greatest utility and reproducibility across the network's diverse research settings.

Results: Following two years of focused investigation, the AMP AIM network developed a standard operating procedure which enables a multi-institutional, spatial multi-omics workflow of deep phenotyping of study participants. This protocol

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

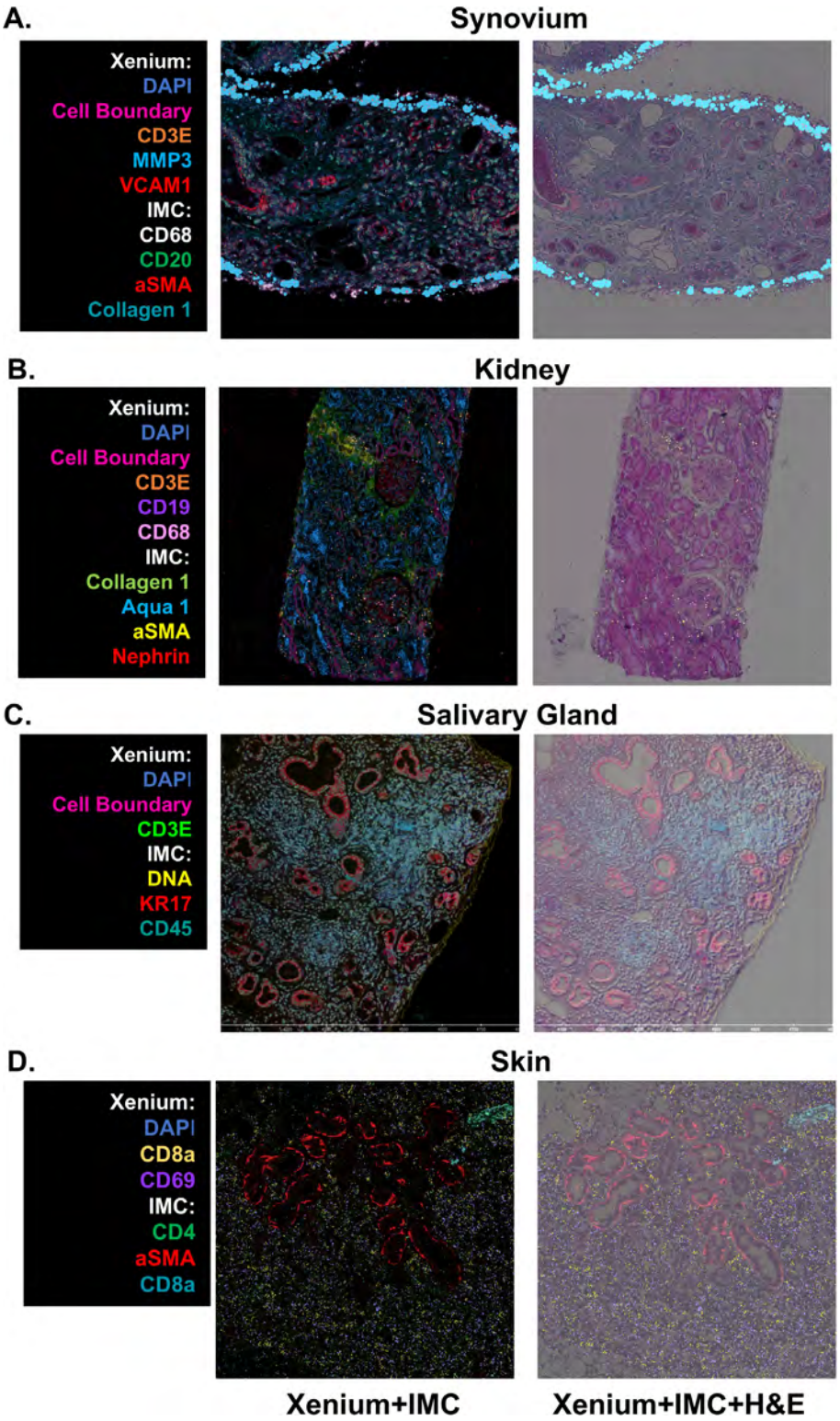


Figure 1: Spatial Characterization of Target Tissues. Representative images from all four target tissues (Synovium, Kidney, Salivary Gland, and Skin) processed and imaged on the Xenium spatial transcriptomics (10X Genomics), stained and whole slide imaged for H&E, and then stained and imaged for ~40 surface proteins via Imaging Mass Cytometry (Standard Biotools), all on the same tissue section and slide. Similar cell types (IMC) or transcripts (Xenium) are highlighted in the example projections to demonstrate agreement across technologies.

leverages centrally collected, FFPE-preserved target tissues (e.g., synovium, skin, salivary gland, and kidney) and integrates spatial transcriptomics (ST) using Xenium (10x Genomics), histological evaluation via H&E staining, and protein-level spatial profiling with Imaging Mass Cytometry (IMC) on the Hyperion platform (Standard BioTools), all on the same slide.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

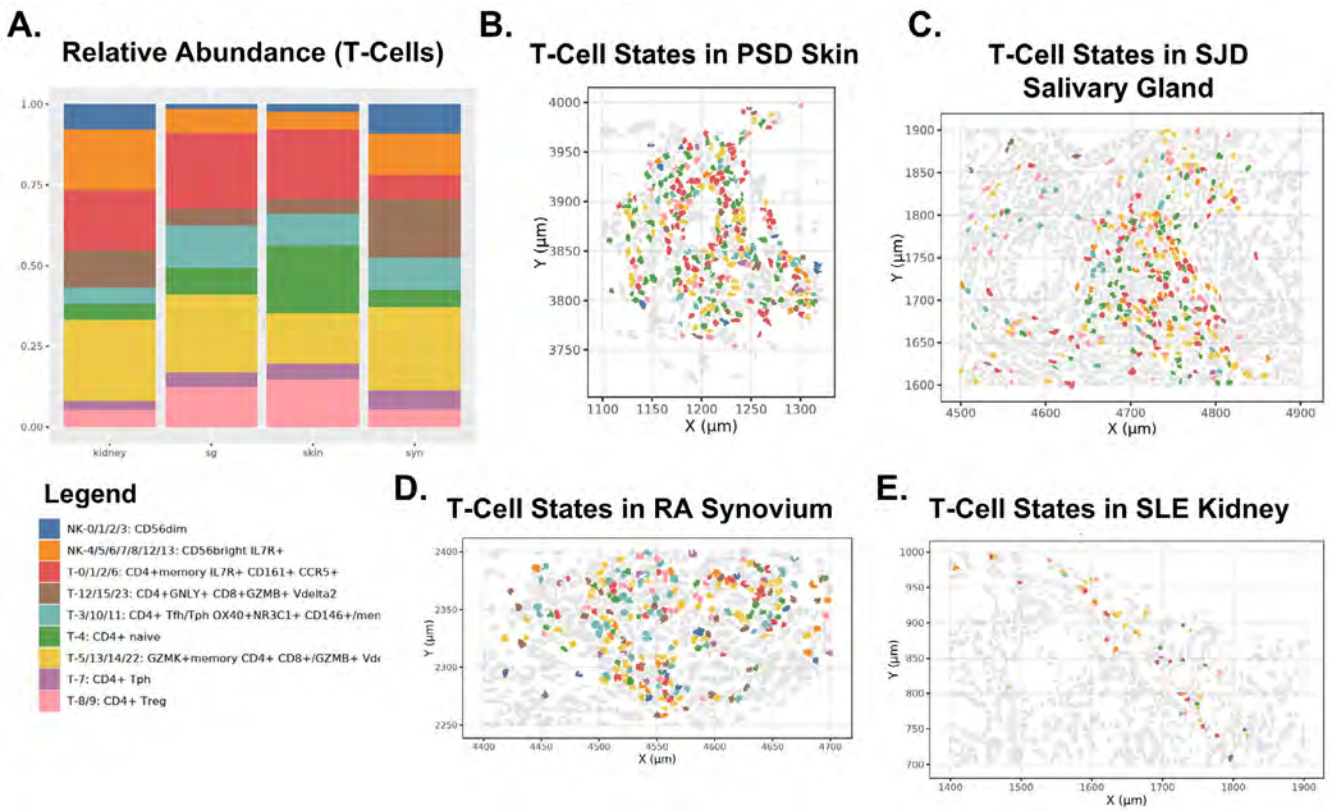


Figure 2: Assessment of Spatial Transcriptomics Technologies demonstrates shared T-cell states across tissues. (A) Median abundance of T-cell states, shown as the proportion relative to the number of T-cells within each tissue. (B-E) Spatial localization of T-cell states within selected regions of interest. in: (B) skin, (C) salivary gland, (D) synovium, and (E) kidney tissues. T-cells are colored by their state, and non-T-cells are colored in grey.

1. Successful implementation of combined spatial transcriptomics and proteomics. With the network selecting Xenium as the preferred ST platform and post-run H&E stain, we developed a workflow which integrates Xenium and IMC from the same tissue section. This results in a unified dataset comprising ~5,000 spatially resolved transcripts, 40 protein markers, and histological context, enabling single-cell level correlation of gene and protein expression within intact tissue architecture (**Fig 1**).

2. Defining shared immune cell states in target tissues across RA, SLE, PSD, and SD. To identify shared immune cell states across autoimmune diseases and target tissues, we implemented a computational pipeline for robust cell type and state annotation in spatial transcriptomic datasets. To evaluate the generalizability of this pipeline, we used a unified scRNA-seq reference to annotate T and NK cell states across spatially profiled tissues. This approach identified 9 distinct T cell states (**Fig 2A**), each exhibiting comparable transcriptional signatures across RA, SLE, PSD, and SD.

Conclusion: This integrated spatial multi-omics platform is being applied across disease-specific (e.g., RA, SLE, PSD, and SD) and cross-disease studies to uncover shared and distinct cellular programs in autoimmune pathogenesis. Through robust, high-resolution, single cell analyses within the tissue context, our approach lays the foundation for discovering common and unique mechanisms and advancing targeted therapeutics across autoimmune diseases.

Disclosure: C. Marlin: None; **R. Madhu**: None; **E. Theisen**: None; **L. Bradshaw**: None; **C. Gao**: None; **T. Eisenhaure**: None; **N. Sugiarto**: None; **A. Autoimmune and Immune Mediated Diseases**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **V. Werth**: AbbVie/Abbott, 2, Amgen, 2, 5, Anaptysbio, 2, Argenx, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta Bio, 2, Calyx, 2, CSL Behring, 5, Cugene, 2, Eli Lilly, 2, EMD Serona, 2, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 5, Immunovant, 2, Janssen, 2, Kwoya Kirin, 2, Merck/MSD, 2, Novartis, 2, Nuvig, 2, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, Rome Pharmaceuticals, 5, Sanofi, 2, Takeda, 2, UCB, 2, 2, Ventus, 2, Viela, 5; **E. Gravallese**: Beam Therapeutics, 11, CRISPR Therapeutics, 11, Editas Medicine, 11, Elsevier, 9, Ginkgo Bioworks, 11, Intellia Therapeutics, 11, New England Journal of Medicine, 1, UpToDate, 9; **J. Anolik**: None; **L. Moreland**: None; **L. Donlin**: Bristol-Myers Squibb (BMS), 2, Karius, Inc., 5, Stryker, 2; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **J. Gudjonsson**: None; **W. Liao**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **C. Shiboski**: None; **A. Farris**: Johnson & Johnson Innovative Medicine, 5; **A. Baer**: Bristol-Myers Squibb(BMS), 2; **B. Warner**: Mitobridge, subsidiary of Astellas Bio, 5, Pfizer, Inc., 5; **J. Clemente**: None; **A. Heguy**: None; **M. Brenner**: AbbVie/Abbott, 2, Johnson & Johnson, 5, Mestag Therapeutics, 2, 8, Moderna, 2, Ono Pharma, 5, Simcere, 2; **N. Hacohen**: Calico Biosciences, 5, Cytoreason, 1, 11, Danger Bio, 1, 11, Moderna, 5, Repertoire Immune Medicines, 1, 11, Takeda, 5; **J. Guthridge**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **S. Raychaudhuri**: Bonito, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Mestag, 1, 8, Nimbus, 2, Pfizer, 1, Sonoma, 1, 8, Visterra, 6; **L. Tsoi**: Galderma, 5, Janssen, 5; **X. Zhou**: None; **J. Welch**: None; **R. Clark**: None; **i. Korsunsky**: Mestag therapeutics, 2; **C. Lessard**: Janssen Global Services, 2, Johnson & Johnson Innovative Medicine, 2, 5; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2.

Abstract Number: 2234

Early Sustained Remission Resulted in Superior Long-term Patient-Reported Outcomes in Rheumatoid Arthritis

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: This study compared the impact of achieving early sustained remission (sREM) versus early sustained low disease activity (sLDA) on patient-reported outcomes (PROs) after 5 years in early rheumatoid arthritis (RA) patients, according to DAS28-CRP, SDAI, and Boolean 2.0 remission criteria. It also assessed PRO differences among patients achieving sREM across these criteria.

Methods: Data were analyzed from 336 early RA patients (symptom onset < 2 years) in the Clinical Rheumatology Systematic Treat-to-Target in Asia Leadership (CRYSTAL) study who completed 5-year follow-up. Patients were classified into sREM, sLDA, or active disease (AD) groups based on DAS28-CRP and SDAI criteria, and sREM or AD for Boolean 2.0, at

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics and Patient-Reported Outcomes by DAS28-CRP Disease Activity Status in Early Rheumatoid Arthritis

Characteristic	sREM (n=99)	sLDA (n=83)	AD (n=154)	P-value
Demographic Characteristics				
Gender (female), n (%)	77 (77.8%)	64 (77.1%)	110 (71.4%)	0.444
Age (years), mean ± SD	50.15 ± 13.85	53.65 ± 11.79	54.47 ± 11.38	0.073
Disease Characteristics				
Disease duration (days), median (IQR)	32.0 (15.0–76.0)	32.0 (13.0–69.0)	32.0 (16.0–63.0)	0.874
Positive RF, n (%)	73 (73.7%)	65 (78.3%)	131 (85.1%)	0.084
Positive ACPA, n (%)	80 (80.8%)	65 (78.3%)	129 (83.8%)	0.707
Disease Activity				
DAS28-CRP Score, mean (SD)	4.03 ± 1.29	4.45 ± 1.18	4.67 ± 1.11	**<0.001**
SDAI score, mean (SD)	19.87 ± 12.18	23.98 ± 13.01	25.94 ± 12.41	**<0.001**
Tender joint count 28, median (IQR)	5.0 (2.0–10.0)	6.0 (3.0–9.0)	7.0 (4.0–12.0)	**0.003**
Swollen joint count 28, median (IQR)	3.0 (1.0–5.0)	4.0 (2.0–6.0)	3.0 (2.0–6.0)	0.065
ESR (mm/hour), median (IQR)	22.0 (16.0–35.0)	30.0 (18.0–55.0)	35.0 (21.0–60.0)	**0.008**
CRP (mg/L), median (IQR)	5.0 (2.2–12.4)	9.0 (4.0–22.8)	11.3 (4.3–34.7)	**<0.001**
Patient global assessment (VAS), median (IQR)	50.0 (30.0–70.0)	50.0 (40.0–70.0)	51.0 (39.0–70.0)	0.275
Physician global assessment (VAS), median (IQR)	40.0 (20.0–61.0)	50.0 (35.0–71.0)	50.0 (35.0–70.0)	**0.009**
Patient Reported Outcomes				
Pain (VAS), mean ± SD	42.40 ± 24.96	47.29 ± 21.81	50.31 ± 22.48	**0.034**
Fatigue (FACIT-Fatigue), mean ± SD	15.53 ± 9.62	16.23 ± 9.37	20.52 ± 10.34	**<0.001**
Functional ability (HAQ-DI), mean ± SD	0.74 ± 0.62	0.79 ± 0.55	0.97 ± 0.66	**0.005**
Work ability (WAI), mean ± SD	4.10 ± 2.40	5.80 ± 7.60	5.30 ± 2.60	**0.001**
Anxiety (HADS-A), mean ± SD	5.28 ± 3.54	5.64 ± 3.48	6.46 ± 3.91	0.066
Depression (HADS-D), mean ± SD	5.34 ± 3.72	5.66 ± 3.46	6.81 ± 4.03	**0.014**
Physical function (SF-36 PCS), mean ± SD	31.43 ± 13.74	27.53 ± 10.32	24.38 ± 11.85	**<0.001**
Mental Function (SF-36 MCS), mean ± SD	44.81 ± 10.19	43.20 ± 10.64	42.10 ± 11.30	0.073

P-values derived from ANOVA, Kruskal-Wallis, or chi-square tests as appropriate

Abbreviations:

- sREM: Sustained Remission
- sLDA: Sustained Low Disease Activity
- AD: Active Disease
- SD: Standard Deviation
- IQR: Interquartile Range
- RF: Rheumatoid Factor
- ACPA: Anti-Citrullinated Protein Antibody
- DAS28-CRP: Disease Activity Score 28-joint count with C-Reactive Protein
- SDAI: Simplified Disease Activity Index
- ESR: Erythrocyte Sedimentation Rate
- CRP: C-Reactive Protein
- VAS: Visual Analog Scale
- FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue
- HAQ-DI: Health Assessment Questionnaire-Disability Index
- WAI: Work Ability Index
- HADS-A: Hospital Anxiety and Depression Scale-Anxiety
- HADS-D: Hospital Anxiety and Depression Scale-Depression
- SF-36 PCS: Short Form-36 Physical Component Summary
- SF-36 MCS: Short Form-36 Mental Component Summary

Baseline Characteristics and Patient-Reported Outcomes by DAS28-CRP Disease Activity Status in Early Rheumatoid Arthritis

6, 9, and 12 months. PROs, including fatigue (FACIT-Fatigue), functional disability (HAQ-DI), joint pain (VAS), anxiety and depression (HADS), work ability (WAI), and health-related quality of life (SF-36 physical [PCS] and mental [MCS] components), were evaluated over 5 years. Generalized estimating equations (GEE) models, adjusted for age, gender, and baseline disease activity, compared PROs between sREM and sLDA groups for DAS28-CRP and SDAI, and among sREM groups across DAS28-CRP, SDAI, and Boolean 2.0 criteria.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Longitudinal Effects of Sustained Remission vs. Low Disease Activity on Patient-Reported Outcomes Over 5 Years by DAS28-CRP and SDAI Criteria

Patient-Reported Outcome	DAS28-CRP sREM vs. sLDA β (95% CI)	P-value[1]	SDAI sREM vs. sLDA β (95% CI)	P-value[1]
Pain (VAS)	-8.48 (-11.44, -5.52)	**<0.001**	-9.59 (-13.52, -5.66)	**<0.001**
Fatigue (FACIT-Fatigue)	-2.02 (-3.88, -0.15)	**0.034**	-2.18 (-4.17, -0.18)	**0.032**
Functional Ability (HAQ-DI)	-0.08 (-0.16, 0.00)	0.060	-0.04 (-0.16, 0.08)	0.517
Work Ability (WAI)	-0.89 (-1.38, -0.40)	**<0.001**	-0.66 (-1.22, -0.09)	**0.022**
Anxiety (HADS-A)	-0.44 (-1.28, 0.40)	0.306	-0.55 (-1.62, 0.51)	0.307
Depression (HADS-D)	-0.56 (-1.35, 0.22)	0.160	-0.32 (-1.25, 0.61)	0.501
Physical Function (SF-36 PCS)	5.12 (2.74, 7.51)	**<0.001**	3.78 (0.61, 6.95)	**0.019**
Mental Function (SF-36 MCS)	1.85 (-0.42, 4.13)	0.110	1.37 (-1.10, 3.83)	0.276

[1]P-value for the difference between sustained remission (sREM) and sustained low disease activity (sLDA) under the respective remission criteria (DAS28-CRP or SDAI), with sLDA as the reference group.

Abbreviations:

- β: Beta coefficient
- CI: Confidence Interval
- sREM: Sustained Remission
- sLDA: Sustained Low Disease Activity
- DAS28-CRP: Disease Activity Score 28-joint count with C-Reactive Protein
- SDAI: Simplified Disease Activity Index
- VAS: Visual Analog Scale
- FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue
- HAQ-DI: Health Assessment Questionnaire-Disability Index
- WAI: Work Ability Index
- HADS-A: Hospital Anxiety and Depression Scale-Anxiety
- HADS-D: Hospital Anxiety and Depression Scale-Depression
- SF-36 PCS: Short Form-36 Physical Component Summary
- SF-36 MCS: Short Form-36 Mental Component Summary

Longitudinal Effects of Sustained Remission vs. Low Disease Activity on Patient-Reported Outcomes Over 5 Years by DAS28-CRP and SDAI Criteria

Results: Of 336 patients, 99 (29%) achieved DAS28-CRP sREM, 38 (11%) SDAI sREM, and 36 (11%) Boolean 2.0 sREM, with 27 (8%) achieving sREM across all three criteria. Compared to DAS28-CRP sLDA, the DAS28-CRP sREM group had significantly better PROs in pain (β = -8.48, $p < 0.001$), fatigue (β = -2.02, $p = 0.034$), work ability (β = -0.89, $p < 0.001$), and SF-36 PCS (β = 5.12, $p < 0.001$) at year 5. Similarly, the SDAI sREM group outperformed SDAI sLDA in pain (β = -9.59, $p < 0.001$), fatigue (β = -2.18, $p = 0.032$), work ability (β = -0.66, $p = 0.022$), and SF-36 PCS (β = 3.78, $p = 0.019$). No significant differences were observed in functional disability, anxiety, depression, or SF-36 MCS for either comparison.

All patients achieving SDAI or Boolean 2.0 sREM also achieved DAS28-CRP sREM. Compared to DAS28-CRP sREM (n = 99), SDAI sREM (n = 38) was associated with significantly lower pain (β = -6.84, $p = 0.002$) but no other PRO differences. Compared to DAS28-CRP sREM, Boolean 2.0 sREM group (n = 36) had better PROs in pain (β = -10.43, $p < 0.001$), fatigue (β = -2.91, $p = 0.016$), work ability (β = -0.75, $p = 0.017$), SF-36 PCS (β = 3.90, $p = 0.022$), and SF-36 MCS (β = 3.51, $p = 0.018$) after 5 years, but not in functional disability, anxiety, or depression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Longitudinal Effects of SDAI and Boolean 2.0 Sustained Remission vs. DAS28-CRP Sustained Remission on Patient-Reported Outcomes Over 5 Years

Patient-Reported Outcome	SDAI sREM vs. DAS28-CRP sREM β (95% CI)	P-value[1]	Boolean 2.0 sREM vs. DAS28-CRP sREM β (95% CI)	P-value[1]
Pain (VAS)	-6.84 (-11.09, -2.59)	**0.002**	-10.43 (-14.17, -6.70)	**<0.001**
Fatigue (FACIT-Fatigue)	-1.83 (-4.16, 0.50)	0.123	-2.91 (-5.29, -0.54)	**0.016**
Functional Ability (HAQ-DI)	0.01 (-0.11, 0.13)	0.857	-0.08 (-0.20, 0.03)	0.161
Work Ability (WAI)	-0.26 (-0.87, 0.36)	0.418	-0.75 (-1.36, -0.13)	**0.017**
Anxiety (HADS-A)	-0.44 (-1.67, 0.79)	0.486	-0.65 (-1.87, 0.57)	0.295
Depression (HADS-D)	0.06 (-1.03, 1.15)	0.913	-0.10 (-2.04, 0.04)	0.059
Physical Function (SF-36 PCS)	1.70 (-1.71, 5.10)	0.329	3.90 (0.55, 7.25)	**0.022**
Mental Function (SF-36 MCS)	0.97 (-1.93, 3.87)	0.512	3.51 (0.59, 6.43)	**0.018**

[1]P-value for the difference between SDAI sustained remission (sREM) or Boolean 2.0 sREM and DAS28-CRP sREM, with DAS28-CRP sREM as the reference group.

Abbreviations:

- β: Beta coefficient
- CI: Confidence Interval
- sREM: Sustained Remission
- DAS28-CRP: Disease Activity Score 28-joint count with C-Reactive Protein
- SDAI: Simplified Disease Activity Index
- VAS: Visual Analog Scale
- FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue
- HAQ-DI: Health Assessment Questionnaire-Disability Index
- WAI: Work Ability Index
- HADS-A: Hospital Anxiety and Depression Scale-Anxiety
- HADS-D: Hospital Anxiety and Depression Scale-Depression
- SF-36 PCS: Short Form-36 Physical Component Summary
- SF-36 MCS: Short Form-36 Mental Component Summary

Longitudinal Effects of SDAI and Boolean 2.0 Sustained Remission vs. DAS28-CRP Sustained Remission on Patient-Reported Outcomes Over 5 Years

Conclusion: Early sustained remission, as defined by DAS28-CRP and SDAI criteria, is associated with significantly better pain, fatigue, work ability, and physical health-related quality of life compared to sustained low disease activity in early RA patients over 5 years. DAS28-CRP sREM is less stringent, as all patients achieving SDAI or Boolean 2.0 sREM also met DAS28-CRP criteria. However, SDAI sREM is associated with lower pain, and Boolean 2.0 sREM offers broader PRO benefits compared to DAS28-CRP sREM. These findings highlight the importance of early tight disease control using stricter criteria like SDAI or Boolean 2.0 to maximize long-term patient outcomes in early RA.

Disclosure: C. Tam: None; **H. So**: None; **L. Tam**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2235

Proportion of Early Rheumatoid Arthritis Patients with Improved, Stable, or Worsened Lung Function Over 1-Year: Results from a Multicenter, Prospective Cohort Study

Erica Mulcaire-Jones[1], Suiyuan Huang[1], Xiaosong Wang[2], Misti Paudel[3], Ying Qi[4], Grace Qian[5], Liya Sisay Getachew[6], Emily Kowalski[6], Kevin Mueller[5], Alene Saavedra[5], Lauren O'Keeffe[5], Natalie Davis[7], Alison Puri[8], Kathleen Vanni[5], Caleb Bolden[9], Tina Mahajan[10], Marzieh Jamali[1], Pierre Antoine Juge[11], Tracy J. Doyle[12], Marcy Bolster[13], Kevin Deane[14], Raul San Jose Estepar[5], George Washko[5], Gregory McDermott[7], Bryant England[10], Jeffrey Sparks[6] and Dinesh Khanna[1], [1]University of Michigan, Ann Arbor, MI, [2]Brigham and Women's Hospital, Natick, MA, [3]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [4]Brigham and Women's Hospital, Boston, [5]Brigham and Women's Hospital, Boston, [6]Brigham and Women's Hospital, Boston, MA, [7]Brigham and Women's Hospital, Brookline, MA, [8]Boston University, Brookline, MA, [9]Massachusetts General Hospital, Boston, [10]University of Nebraska Medical Center, Omaha, NE, [11]Hopital Bichat, APHP, Paris, France, [12]Brigham and Women's Hospital, West Roxbury, MA, [13]Massachusetts General Hospital, Concord, MA, [14]University of Colorado Denver Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Several lung diseases are associated with rheumatoid arthritis (RA), including interstitial lung disease (ILD) and emphysema. In RA-ILD baseline lung function and decline in lung function may act as predictors of survival. We aimed to explore change in lung function over 1 year in cohort of participants with early RA.

Methods: SAIL-RA (Study of Inflammatory Arthritis and ILD in Early RA) is a prospective, longitudinal, multicenter study of patients with RA within 2 years of RA diagnosis. Participants were enrolled from 2017 to 2025 at 5 U.S sites. We analyzed participants who completed baseline and 1 year assessments; including baseline high-resolution CT chest (HRCT) as well as pulmonary function tests (PFT) and disease activity assessment (DAS28-ESR) at both visits. We assessed changes in lung function by evaluating mean change in % predicted forced vital capacity (FVC) and diffusion capacity of carbon monoxide (DLCO) from baseline to 1 year using student's T-test. We categorized participants into 3 groups based on change in PFTs (improved, stable, worsened). 'Improved' and 'worsened' FVC were defined as an increase or decrease of >5% predicted from baseline to 1 year. 'Improved' and 'worsened' DLCO were defined as an increase or decrease of >10% predicted from baseline to 1 year. We compared change in lung function based on baseline disease activity and presence/absence of ILD using Chi-square and Fisher's exact tests. We compared distribution of participants with worsened, stable or improved lung function based on presence/absence of lung disease and continuation/discontinuation of methotrexate (MTX) in baseline MTX users by ANOVA. Low and moderate/high disease activity were defined as DAS28-ESR of $\leq$3.2 and $\geq$3.3. ILD was defined by radiologists' interpretation of HRCT. Obstructive lung disease was defined as emphysema on HRCT or $FEV_1/FVC < 0.7$.

Results: 121 participants completed baseline and 1 year assessments with PFTs (**Table 1**). In the whole cohort approximately half of participants had worsened or improved FVC and/or DLCO at 1 year (**Fig 1**). The percentage of participants with worsened, stable, or improved FVC was 27.3%, 46,3%, and 26.4%. For DLCO 12.6%, 65%, and 22.3% had worsened, stable, or improved values. In participants with ILD versus no ILD at baseline there was a trend toward worsened FVC % predicted at 1 year in participants with ILD (p=0.089), although mean absolute change in FVC did not differ (2.26% vs 0.16%, p=0.44). There was no difference in the change FVC or DLCO % predicted from baseline to 1 year based on presence or absence of lung disease nor MTX continuation at 1 year (**Fig 2**). In participants with low versus moderate/high

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1 Baseline characteristics of SAIL-RA cohort who completed baseline and 1 year follow-up (n=122)

Variables	Value
Demographics	
Age at RA diagnosis (mean, SD)	55.4 (13.6)
Age at HRCT (mean, SD)	56.2 (13.5)
Sex, n (%)	
Female	89 (73.0%)
Male	33 (27.0%)
Race, n (%)	
Asian	4 (3.3%)
Black	7 (5.7%)
White	105 (86.1%)
Other	6 (4.9%)
Ethnicity, n (%)	
Hispanic or Latino	9 (7.4%)
Not Hispanic or Latino	110 (90.2%)
Unknown/Not reported/Prefer not to answer	3 (2.5%)
Smoking status, n (%)	
Current	9 (7.4%)
Past	40 (32.8%)
Never	73 (59.8%)
Pack-year history of smokers (n=49), median (Q1, Q3)	14.0 (2.5, 30.0)
BMI, mean (SD)	29.3 (6.6)
RA Characteristics	
RA diagnosis duration (median, [Q1, Q3])	0.8 (0.4, 1.6)
RA symptom duration (median, [Q1, Q3])	1.6 (0.9, 2.4)
PtGA (mean, SD)	29.5 (26.4)
TJC28 (mean, SD; median, [Q1, Q3])	3 (4.4); 1 (0, 5)
SJC28 (mean, SD; median, [Q1, Q3])	2.5 (3.9); 1 (0, 3)
DAS28-ESR (n=114), (mean, SD)	3.2 (1.5)
Disease activity (n, %)	
Remission	47 (38.5%)
Low	20 (16.4%)
Moderate	41 (33.6%)
High	14 (11.5%)
Seropositivity (n, %)	
anti-CCP positivity	94/122 (77.0%)
RF positivity	84/121 (69.4%)
anti-CCP or RF positivity	103/122 (84.4%)
Baseline Medication Use	
Methotrexate (n, %)	89 (73.0%)
TNFi (n, %)	19 (15.6%)
Glucocorticoids (n, %)	36 (29.5%)
Lung Disease Characteristics	
ILD (n, %)	14 (11.5%)
Obstructive lung disease (n, %)	26 (21.3%)
Any lung disease (n, %)	35 (28.7%)
FEV_1 % predicted (mean, SD) (n=121)	93.3 (20.1)
FVC % predicted (mean, SD) (n=121)	96.0 (15.1)
FEV_1/FVC ratio (mean, SD) (n=121)	0.77 (0.09)
DLCO % predicted (mean, SD) (n=114)	86.5 (17.6)

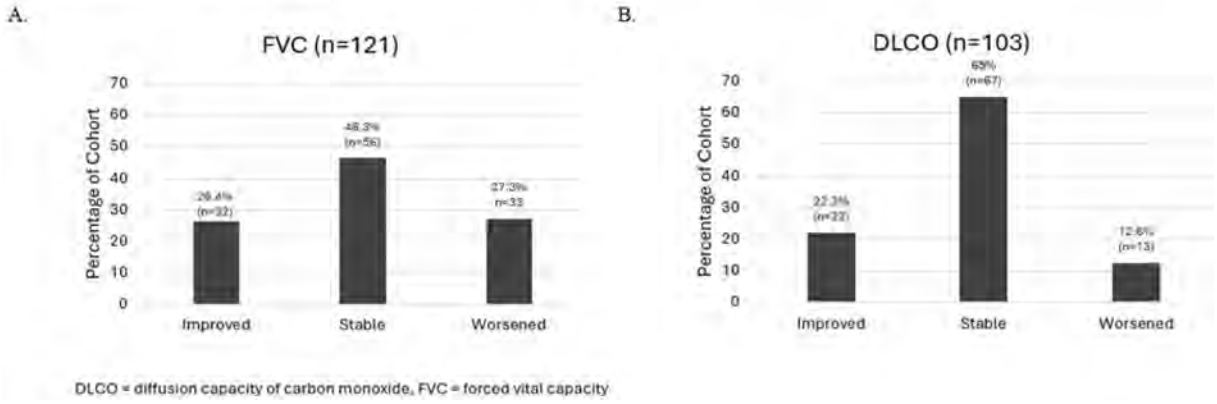
Anti-CCP = anti-cyclic citrullinated peptide antibody; DAS28-ESR = disease activity score of 28 joints with erythrocyte sedimentation rate, DLCO = diffusion capacity of the lung for carbon monoxide, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, HRCT = High resolution CT Chest, ILD = interstitial lung disease, PtGA = patient global assessment, RA = rheumatoid arthritis, RF = rheumatoid factor, SJC = swollen joint count, TJC = tender joint count, TNFi = tumor necrosis factor inhibitor

disease activity at baseline there was no difference in distribution of improved, stable or worsened FVC or DLCO at 1 year (p=0.54, p=0.21).

Conclusion: In this prospective cohort of participants with early RA mean change in the FVC and DLCO at a population level was small, although there was significant individual variability over 1 year. While about 20% had worsened FVC or DLCO,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

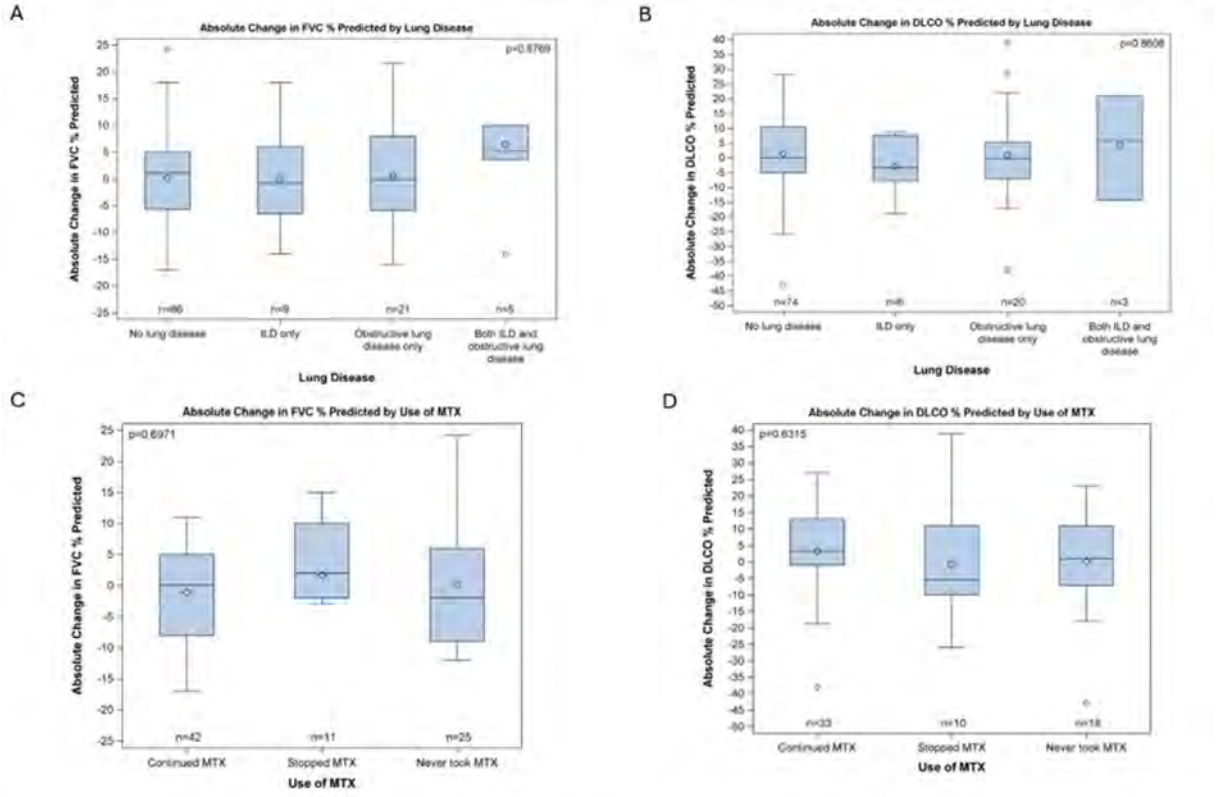
Figure 1 Absolute Change in Lung Function Parameters in Whole Cohort at 1-Year Compared to Baseline Classified by Change Category



DLCO = diffusion capacity of carbon monoxide, FVC = forced vital capacity

Figure 1

Figure 2 Comparison of Change in Lung Function Parameters by Lung Disease Characteristics and Methotrexate Use Persistence at 1 Year



DLCO = diffusion capacity of carbon monoxide, FVC = forced vital capacity, ILD = interstitial lung disease, MTX = methotrexate

Figure 2

most were stable or improved. There was a trend towards a higher proportion of participants with ILD to have worsened FVC compared to those without ILD. MTX use over 1 year was not associated with changes in FVC or DLCO.

Disclosure: E. Mulcaire-Jones: Caribou Pharmaceuticals, 2; **S. Huang**: None; **X. Wang**: None; **M. Paudel**: None; **Y. Qi**: None; **G. Qian**: None; **L. Getachew**: None; **E. Kowalski**: None; **K. Mueller**: None; **A. Saavedra**: None; **L. O'Keeffe**: None; **N. Davis**: None; **A. Puri**: None; **K. Vanni**: None; **C. Bolden**: None; **T. Mahajan**: None; **M. Jamali**:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

None; **P. Juge**: None; **T. Doyle**: Bayer, 5, Sanofi, 3; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **K. Deane**: Inova Diagnostics, 1; **R. Estepar**: Boehringer-Ingelheim, 5, Gossamer Bio, 5, Lung Biotechnology, 7, Quantitative Imaging Solutions, 12,; **G. Washko**: Apogee, 2, AstraZeneca, 2, Boehringer-Ingelheim, 5, Intellia Therapeutics, 2, Pieris Therapeutics, 2, Quantitative Imaging Solutions, 12,, Regeneron, 2, Sanofi, 2, Verona, 1, 2; **G. McDermott**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2.

Abstract Number: 2236

Treatment-induced autoantibodies in Rheumatoid Arthritis patients receiving anti-TNF inhibitors or JAK inhibitors

EVRIPIDIS KALTSONOUDIS[1], Nikolaos Kougkas[2], Panagiota Karagianni[3], Tereza Memi[4], Nikolaos Koletsos[5] and Eleftherios Pelechas[6], [1]Rheumatology Clinic, University of Ioannina, IOANNINA, Ioannina, Greece, [2]4th Department of Internal Medicine, Aristotle University, Thessaloniki, Thessaloniki, Greece, [3]BioAcuHealth.gr, Ioannina, Ioannina, Greece, [4]University Hospital of Ioannina, Ioannina, Ioannina, Greece, [5]School of Health Sciences, Faculty of Medicine, University of Ioannina, Department of Rheumatology, Ioannina, Greece, Ioannina, Ioannina, Greece, [6]Hatzikosta General Hospital of Ioannina, Ioannina, Ioannina, Greece

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) can coexist with other autoimmune disorders such as Sjögren's syndrome and systemic lupus erythematosus (SLE). In these cases, the terms secondary Sjögren's syndrome or Sjögren's syndrome overlap and lupus-like syndrome or Rupus are applied. All available biological treatments aim to suppress the autoimmune responses locally as well as systematically. On the other hand, they may interfere with the immune system by inducing autoantibodies such as the ANAs by the use of the anti-TNF inhibitors. To compare the risk of autoantibody-induction in RA patients under treatment with anti-TNFs and JAK inhibitors, as well as to evaluate their importance at a clinical level.

Methods: 83 patients with a new diagnosis of RA and were about to be treated with a biological agent were divided in 2 groups and were followed for 2 years. Patients' age was 40-50 years. 42 patients with seropositive RA and without the presence of other autoantibodies (Group 1) and 42 with/without RA seropositivity but with ANA/ENA positivity (Group 2). 21 of both groups received an anti-TNF inhibitor and 21 received a JAK inhibitor.

Table 1

Table 1

	TNF inhibitor	JAK inhibitor
ANA	7	0
ENA	2	0
SSA/Ro (52)	1	0
SSA/Ro και SSB/La	1	0
dsDNA	0	0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In group 1, no patient under treatment with JAK inhibitors showed any new autoantibodies. In contrast to those receiving anti-TNF, 7 showed ANA+ in a titer >1/80 and 2 of them ENA+ (1 with Ro52 and the other Ro52 and La). In group 2, the autoantibodies remained unchanged in all patients under JAK inhibitors and none of them manifested symptoms of the overlap syndrome. In contrast, in the anti-TNF treated patients, 8 experienced symptoms of secondary Sjögren's syndrome (6 only sicca syndrome and 2 lung disease) and one patient manifested a lupus-like syndrome (rash, weakness and serositis).

Conclusion: This is the first study to show the different effects on autoantibodies in a series of patients with RA and other connective tissue disease under biological and targeted-synthetic therapy. The effect of non-anti-TNF bDMARDs on autoantibodies (ANA, ENA) is clearly smaller, which reflects possibly the different mechanism of action leading to a less possible autoimmune derangement. Further studies are needed to confirm these findings.

Disclosure: E. KALTSONOUDIS: None; **N. Kougkas**: None; **P. Karagianni**: None; **T. Memi**: None; **N. Koletsos**: None; **E. Pelechas**: None.

Abstract Number: 2237

Safety of DMARD therapy in veterans with rheumatoid arthritis following melanoma diagnosis: a survival analysis

Gabriella Girolami[1], Shamey Kassim[2], Alexander Peterson[3], Aaron Baraff[3], Alexandra Schmidt[3], Shailender Bhatia[4], Natalie Miller[4], Jennifer Barton[5], Jeffrey Curtis[6], Christopher Li[4] and Namrata Singh[7], [1]University of Washington, Seattle, [2]University of Washington, Seattle, WA, [3]VA Puget Sound Health Care System, Seattle, WA, [4]Fred Hutch Cancer Center, Seattle, [5]VA Portland Health Care System/OHSU, Portland, OR, [6]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [7]University of Washington, Bellevue, WA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: While disease-modifying anti-rheumatic drugs (DMARDs) are critical in managing rheumatoid arthritis (RA), their immunosuppressive effects raise concerns about cancer-related outcomes. In patients with RA who develop melanoma, evidence is limited on how post-diagnosis use of conventional synthetic (csDMARDs), biologic (bDMARDs), or targeted synthetic (tsDMARDs) DMARDs impacts mortality. This study aimed to evaluate the association between DMARD use after melanoma diagnosis and 3-year all-cause mortality in patients with RA.

Methods: This retrospective cohort study utilized data from the national Veterans Affairs (VA) Corporate Data Warehouse (CDW), spanning 2002 to 2024. Included patients had ≥2 RA International Classification of Diseases (ICD) codes within a period of 7-365 days. Patients with melanoma and their stage at diagnosis were identified through the VA Oncology Raw Domain. The main exposure was type of DMARD use, categorized as none, csDMARDs, or b/tsDMARDs (with or without csDMARDs). The primary outcome was all-cause mortality three years after melanoma diagnosis. Demographic and clinical variables–including age, sex, marital status, race, ethnicity, region, rurality, tobacco use, comorbidities, cancer stage (American Joint Committee on Cancer, AJCC)–were included. Kaplan-Meier survival analysis and multivariable Cox proportional hazards models were used to assess the association between DMARD exposure and mortality, adjusting for relevant confounders.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of Patients with Incident Melanoma by DMARD Use

Category	No DMARDs (N=211)	csDMARDs (N=267)	b/ts/Combo (N=166)	Total (N=644)
Cancer Stage				
0	103 (48.8%)	120 (44.9%)	76 (45.8%)	299 (46.4%)
I	82 (38.9%)	99 (37.1%)	65 (39.2%)	246 (38.2%)
II	13 (6.2%)	23 (8.6%)	15 (9.0%)	51 (7.9%)
III	<10 (4.3%)	17 (6.4%)	<10	31 (4.8%)
IV	<10	<10	<10	17 (2.6%)
Age (years)				
<60	27 (12.8%)	16 (6.0%)	17 (10.2%)	60 (9.3%)
60-69	54 (25.6%)	87 (32.6%)	62 (37.3%)	203 (31.5%)
70-79	85 (40.3%)	98 (36.7%)	68 (41.0%)	251 (39.0%)
80+	45 (21.3%)	66 (24.7%)	19 (11.4%)	130 (20.2%)
Male	203 (96.2%)	257 (96.3%)	155 (93.4%)	615 (95.5%)
Area of residence				
Urban	125 (59.2%)	147 (55.1%)	97 (58.4%)	369 (57.3%)
Rural	85 (40.3%)	120 (44.9%)	69 (41.6%)	274 (42.5%)
Cohort Entry Date				
2002-2009	29 (13.7%)	58 (21.7%)	17 (10.2%)	104 (16.1%)
2010-2015	60 (28.4%)	75 (28.1%)	46 (27.7%)	181 (28.1%)
2016-2021	96 (45.5%)	111 (41.6%)	76 (45.8%)	283 (43.9%)
2022-2024	26 (12.3%)	23 (8.6%)	27 (16.3%)	76 (11.8%)

cs: conventional synthetic; DMARDs: disease modifying anti-rheumatic drugs

Results: We identified 644 patients with RA and incident melanoma. The cohort had a mean age of 71 years, with 39% aged 70-79 years. It was predominantly male (95.5%), with most residing in urban areas (57.3%). Cancer stage distribution was 46.4% Stage 0, 38.2% Stage I, 7.9% Stage II, 4.8% Stage III, and 2.6% Stage IV. Most patients entered the cohort between 2016-2021 (43.9%) (**Table 1**).

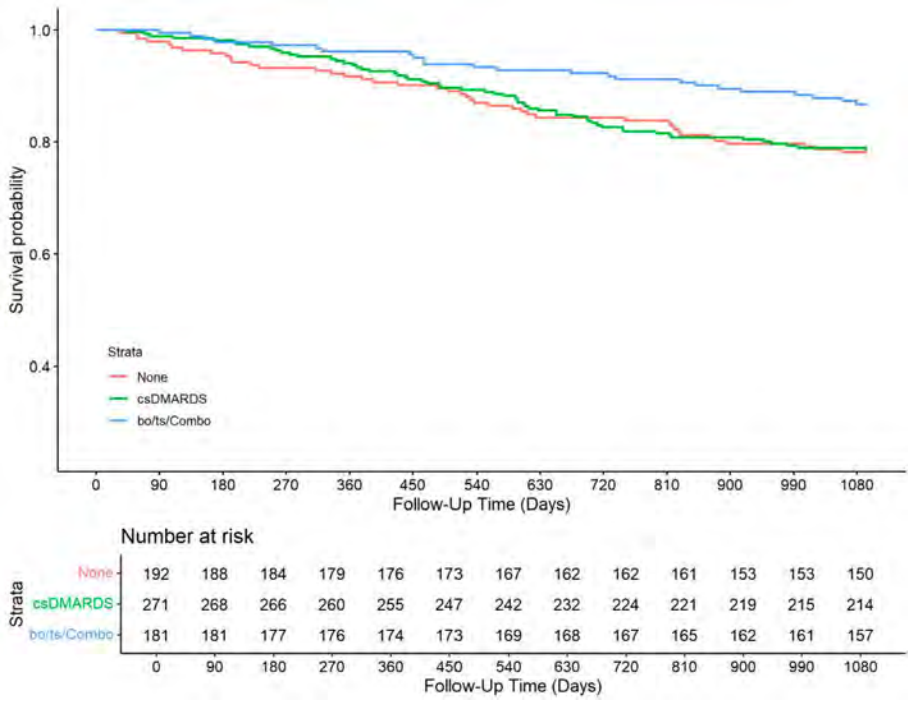


Figure 1. Kaplan-Meier Survival Curves by DMARD Use Within 12 Months of Melanoma Diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

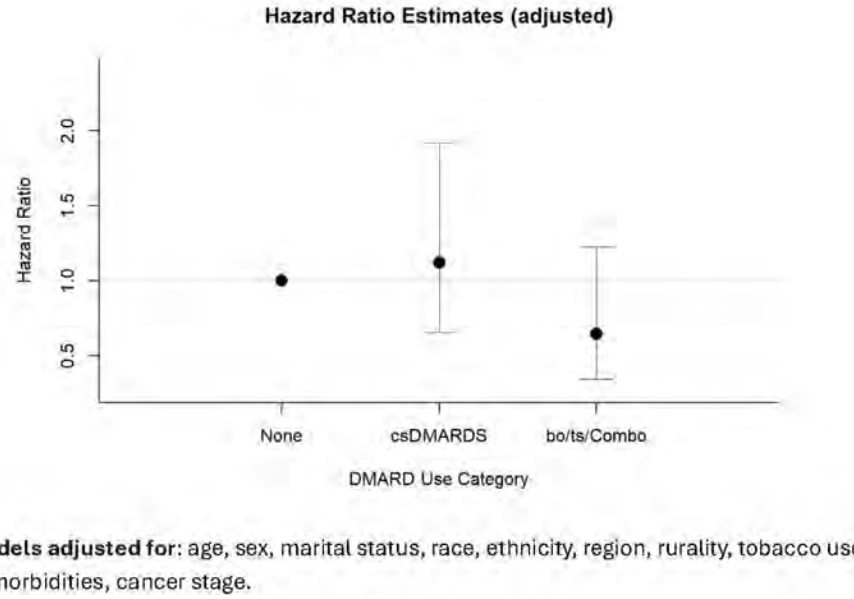


Figure 2. Hazard Ratio estimates (adjusted) for the association between DMARD use and three-year mortality after melanoma diagnosis in RA.

Twelve-month post-melanoma DMARD exposure was categorized as no use (n=211, 32.8%), csDMARD use only (n=267, 41.4%), or b/tsDMARD/combination use (b/ts/Combo, n=166, 25.8%). Kaplan-Meier survival curves suggested lower three-year all-cause mortality among patients treated with b/ts/Combo compared to those receiving csDMARDs or no DMARD (**Figure 1**). Adjusted models showed hazard ratio (HR) of 1.12 (95% CI: 0.65–1.92) for csDMARDs relative to those on no DMARDs, and 0.65 (95% CI: 0.34–1.23) for b/ts/combination DMARDs (**Figure 2**).

Conclusion: In this retrospective cohort study of veterans with RA who developed melanoma, cs/b/tsDMARD use after melanoma diagnosis was not associated with increased three-year all-cause mortality. However, the study is limited by the lack of melanoma-specific mortality data and the relatively short follow-up period. These findings may help guide clinical decision-making regarding DMARD use in RA patients with a history of melanoma, particularly when balancing treatment efficacy with cancer risk.

Disclosure: G. Girolami: None; **S. Kassim**: None; **A. Peterson**: None; **A. Baraff**: None; **A. Schmidt**: None; **S. Bhatia**: None; **N. Miller**: None; **J. Barton**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **C. Li**: None; **N. Singh**: None.

Abstract Number: 2238

Impact of Type 2 Diabetes on Cardiovascular and Renal Outcomes in Rheumatoid Arthritis: Insights from a Large-Scale Multi-Center Analysis

Godbless Ajenaghughrure[1], Sila Mateo Faxas[2], **Gurjot Singh**[3], Nirys Mateo Faxas[4], Kim Nguyen[3], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Trihealth Good Samaritan Hospital, Cincinnati, OH, [2]Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid arthritis (RA) is associated with increased cardiovascular risk, but the additional impact of type 2 diabetes mellitus (T2DM) on the cardiorenal outcomes in this population remains insufficiently characterized. This study aimed to quantify the additional risk conferred by T2DM in RA patients for developing specific cardiovascular and renal complications.

Methods: We performed a retrospective cohort study using the TriNetX global federated health research network, comprising electronic health records from 100 healthcare organizations. We identified adult patients (18-99 years) with RA (ICD-10 M06.9), stratified by T2DM status (ICD-10 E11). After propensity score matching for demographic and clinical factors, 129,630 patients were included in each cohort. Patients were followed for up to 5 years to evaluate cardiorenal outcomes.

Results: RA patients with T2DM had significantly higher risk of acute kidney failure (HR 2.57, 95% CI 2.49-2.66, p< 0.001) compared to those without diabetes. The T2DM cohort also showed increased risk of heart failure (HR 1.93, 95% CI 1.86-1.96, p< 0.001), cerebral infarction (HR 1.67, 95% CI 1.60-1.75, p< 0.001), and pulmonary hypertension (HR 1.93, 95% CI 1.84-2.03, p< 0.001). Additionally, patients with both conditions demonstrated higher incidence of acute pulmonary edema (HR 1.93, 95% CI 1.84-2.03, p< 0.001) and sepsis (HR 2.57, 95% CI 2.49-2.66, p< 0.001). Mortality was significantly elevated in the comorbid group (HR 1.73, 95% CI 1.69-1.78, p< 0.001).

Conclusion: The coexistence of T2DM in RA patients substantially increases the risk of adverse cardiorenal outcomes and mortality. These findings emphasize the importance of early screening and aggressive management of cardiovascular and renal risk factors in RA patients with comorbid T2DM. Collaborative care models involving rheumatologists, endocrinologists, and cardiologists may be essential for optimal management of this high-risk population.

Disclosure: G. Ajenaghughrure: None; **S. Mateo Faxas**: None; **G. Singh**: None; **N. Mateo Faxas**: None; **K. Nguyen**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 2239

Increased Cardiovascular Morbidity in Patients with Rheumatoid Arthritis and Type 2 Diabetes: A Large-Scale Electronic Health Record Analysis

Godbless Ajenaghughrure[1], Sila Mateo Faxas[2], **Gurjot Singh**[3], Nirys Mateo Faxas[4], Kim Nguyen[3], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Trihealth Good Samaritan Hospital, Cincinnati, OH, [2]Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is associated with increased cardiovascular risk, but the additional impact of comorbid type 2 diabetes mellitus (T2DM) on cardiovascular outcomes in this population remains incompletely characterized. This study evaluated the cardiovascular burden in patients with both RA and T2DM compared to patients with RA alone.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Using the TriNetX global federated health research network, we conducted a retrospective cohort study of 187,967 patients with RA from 100 healthcare organizations. Patients aged 18-99 years with RA (ICD-10 M06.9) were stratified by T2DM status (ICD-10 E11). After propensity score matching for cardiovascular risk factors and comorbidities, we analyzed 129,630 patients in each cohort. Cardiovascular outcomes were assessed over a 5-year follow-up period.

Results: Patients with comorbid RA and T2DM demonstrated significantly higher risk of mortality (HR 1.73, 95% CI 1.69-1.78, p< 0.001), cardiac arrest (HR 2.85, 95% CI 2.61-3.10, p< 0.001), and heart failure (HR 1.93, 95% CI 1.86-1.96, p< 0.001) compared to patients with RA alone. Additionally, the comorbid group showed increased risk of atrial fibrillation (HR 1.97, 95% CI 1.92-2.02, p< 0.001), ventricular arrhythmias (HR 2.18, 95% CI 2.05-2.32, p< 0.001), cerebral infarction (HR 1.67, 95% CI 1.60-1.75, p< 0.001), and acute kidney failure (HR 2.57, 95% CI 2.49-2.66, p< 0.001). Patients with both conditions also required more cardiac device implantations (HR 2.65, 95% CI 2.50-2.80, p< 0.001).

Conclusion: Coexisting T2DM in patients with RA substantially increases the risk of major adverse cardiovascular events and mortality. These findings highlight the need for aggressive cardiovascular risk assessment and management strategies in this high-risk population. Interdisciplinary care involving rheumatologists and endocrinologists may be crucial for optimal management of this patient group.

Disclosure: G. Ajenaghughrure: None; **S. Mateo Faxas**: None; **G. Singh**: None; **N. Mateo Faxas**: None; **K. Nguyen**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 2240

Diabetes Significantly Amplifies Risk of Cardiac Arrhythmias in Rheumatoid Arthritis Patients: Results from a Multi-Center Electronic Health Record Study

Godbless Ajenaghughrure[1], Sila Mateo Faxas[2], **Gurjot Singh**[3], Nirys Mateo Faxas[4], Kim Nguyen[3], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Trihealth Good Samaritan Hospital, Cincinnati, OH, [2]Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Both rheumatoid arthritis (RA) and type 2 diabetes mellitus (T2DM) are independently associated with increased cardiovascular risk. However, the impact of T2DM on cardiac arrhythmia development specifically in patients with RA remains poorly understood.

Methods: We conducted a retrospective cohort study using the TriNetX global federated health research network, analyzing electronic health records from 100 healthcare organizations. We identified patients aged 18-99 years with RA (ICD-10 M06.9) with and without T2DM (ICD-10 E11). After propensity score matching for demographic factors and relevant comorbidities, we compared 129,630 patients in each cohort. Patients were followed for up to 5 years to assess arrhythmia-related outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Patients with both RA and T2DM demonstrated significantly increased risk of atrial fibrillation (HR 1.93, 95% CI 1.88-1.98, p< 0.001) compared to patients with RA alone. Similarly, the risk for ventricular arrhythmias was substantially higher, with a hazard ratio of 2.18 (95% CI 2.05-2.32, p< 0.001) for ventricular tachycardia and 2.72 (95% CI 2.46-3.01, p< 0.001) for ventricular fibrillation. The comorbid group also demonstrated a 2.11-fold increased risk (95% CI 1.94-2.29, p< 0.001) for sick sinus syndrome and required significantly more pacemaker implantations (HR 2.65, 95% CI 2.50-2.80, p< 0.001).

Conclusion: The presence of T2DM in patients with RA is associated with a substantial increase in risk for multiple cardiac arrhythmias. Our findings suggest that patients with both RA and T2DM should undergo more intensive cardiac monitoring and may benefit from early interventions to prevent arrhythmia development. These results highlight the importance of integrated care across specialties for patients with these comorbid conditions.

Disclosure: G. Ajenaghughrure: None; **S. Mateo Faxas**: None; **G. Singh**: None; **N. Mateo Faxas**: None; **K. Nguyen**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 2241

RADAR: A Deep Learning Pipeline for Automated Scoring of Joint Damage in Rheumatoid Arthritis Radiographs

Hugo PENSEC[1], Alain SARAUX[2], florent garrigues[3], yoann le duault[1], sandrine jousse[4], baptiste quere[4], nathan foulquier[5], Valerie Devauchelle[6] and ikram brahim[7], [1]CHRU Brest, Brest, France, [2]CHU Brest, Brest, France, [3]CHU de BREST, Brest, Bretagne, France, [4]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [5]LBAI, UMR1227, Univ Brest, Inserm, Brest, France, Brest, France, [6]UBO, Brest, France, [7]CHRU, LBAI, UMR1227, Univ Brest, Inserm, LaTIM, UMR 1101, Brest, France, Brest, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is a persistent inflammatory disorder inducing joint space narrowing and erosion at both hands and feet. Reading of X-ray images remains extremely time-consuming and subject to interobserver variability.

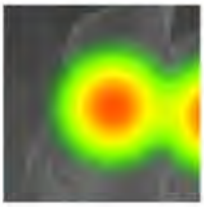
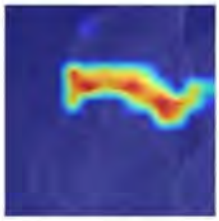
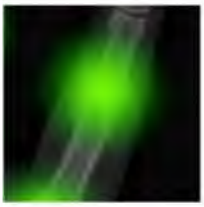
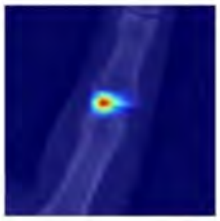
Methods: Data were obtained from a subset of a large prospective multicentric cohort of RA patients (BCD study). All hand and foot radiographs were scored using the modified van der Heijde score by four trained readers. We developed a deep learning pipeline called RADAR to detect joints and classify radiographs from hands and feet: we employed a YOLO-based object detection for the joints used as input for a classification model. We trained two models: a binary classifier to

Table 1: RADAR classification results for binary and multiclass tasks.

		AUC (Binary)	Accuray (Binary)	Accuray (Multiclass)
Erosion	Hand	0.9988	0.9893	0.9728
	Feet	0.9640	0.9255	0.8669
Joint space narrowing	Hand	0.9994	0.9888	0.9863
	Feet	0.9789	0.9477	0.9233

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1 : Example of heat maps showing the ability to detect joints – a) reading by a rheumatologist evaluated by eye-tracking b) reading by RADAR

	A (Eye tracking)	B (RADAR)
joint space narrowing		
Erosion		

distinguish erosion and joint space narrowing (present or absence), and a multi-class classifier for joint space narrowing [Mild (scores 1–2) and Moderate (3–4)] and an additional severe category (score 5+) for erosion. The models were implemented in PyTorch. The dataset of 140 patients was split into training, validation, and test sets. We also used the Pytorch Gradcam library to develop explainability heatmaps. Reader reliability was evaluated using both kappa statistics and the intraclass coefficient.

Results: Reliabilities between the four human experts evaluated on 30 radiographs were good (0.7-0.9). A total of 7560 joints were analysed using RADAR . Figure 1 shows examples of joint detection by both readers and RADAR. Table 1 shows that results were excellent for both binary classification and score. This was true in the absence of lesions as well as for elevated scores.

Conclusion: Our results demonstrate the pipeline's ability to identify the presence and absence of joint damage with high accuracy, giving the opportunity to avoid a large number of human readings in a cohort of patients. The global score is also reliable.

Disclosure: H. PENSEC: None; **A. SARAUX**: Novartis, 6; **f. garrigues**: None; **y. le duault**: None; **s. jousse**: None; **b. quere**: AbbVie, 2, 6, Alfasigma, 6, Eli Lilly, 6; **n. foulquier**: None; **V. Devauchelle**: None; **i. brahim**: None.

Abstract Number: 2242

Analysis of Bronchoalveolar Fluid Cytokine Profile as a Way to Understand the Lung Disease Associated with Systemic Juvenile Idiopathic Arthritis

Ivanna Romankevych[1], Donna Do[1], Alyssa Sproles[2], Lexi Auld[1], Taskin Sabit[1], Richard Chhaing[1], Joy Baker[1], John Brewington[3], Christopher Towe[4], Alexiei GROM[5] and Grant Schulert[6], [1]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [2]Cincinnati Children's Hospital, Cincinnati, OH, [3]Cincinnati Children's Hospital Medical Center, Division of Pulmonary Medicine; University of Cincinnati, Cincinnati, OH, [4]Cincinnati Children's Hospital

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medical Center, Division of Pulmonary medicine; University of Cincinnati, Cincinnati, OH, [5]Cincinnati Children's Hospital Medical Center, Division of Rheumatology, Cincinnati, OH, [6]Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The lung disease associated with systemic JIA (SJIA-LD) remains poorly understood. Measurement of cytokine levels in bronchoalveolar lavage fluid (BALF) may offer insights into disease pathogenesis, activity, and progression. However, there is currently limited data on the bronchoalveolar inflammatory environment in children with SJIA-LD. The purpose of the study was to measure levels of proinflammatory cytokines and chemokines in BALF from patients with SJIA-LD.

Methods: Children with SJIA-LD were included in the study at the time of diagnostic bronchoscopy as part of routine clinical care. As controls we included patients undergoing routine bronchoscopy for tracheostomy surveillance or other known inflammatory diseases, including SJIA without LD, autoimmune alveolar proteinosis, IBD with lung disease, and lymphoma. Children from the control group were divided into inflammatory (IC, n=9) and non-inflammatory (NIC, n=7) controls based on underlying disease. Interleukin-6, 8 and 18, S100A8/9, S100A12, CD25, CCL25, CCL17, CCL11, MMP7 and CXCL-9 were measured by ELISA or Multiplex.

Table 1 Levels of cytokines in BAL in children in the SJIA-LD and controls

Marker	sJIA-LD (n=14)	All control (n=16)	Inflammatory control (IC) (n=9)	Non-inflammatory control (NIC) (n=7)
	M±SE			
Il-6, pg/mL	10.6±3.2	17.25±8.8	12.32±8.4	**27.6±20.1^**
IL-8, pg/mL	319±96.1	518.8±305	203.785±85	**1056.7±769.2^**
IL-18, pg/mL	**1012.2±289.6***	106.5±36.7	154±59	37.1±15.1
S100A8/9, ng/mL	7009±3349.9	14400.9±5718.	8361.9±4224.6	1825.1±595.7
S100A12, mcg/mL	13854.1±11785.6	405093.2±764236.2	314540±200669	14950.3±6070.1
CD-25, pg/mL	**35.7±5.5***	35.77±5.76	25.3±8.1	2.5±2.5
CCL-11, pg/mL	**20.48±2.22***	8.71±4.1	10.7±5.6	7.7±7.7
CCL-17, pg/mL	32.92±17.5	11.1±5.85	20.7±9.7	Undetectable
CCL-25, pg/mL	undetectable	0.89±3.5	undetectable	0.98±3.5
MMP-7, pg/mL	**17952.8±2869.2****	16238.5±8695.1	22267.4±15226.8	10675.6±8485.4
CXCL-9, pg/mL	122.8±36.35	**227.4±101.1^**	**243.7±157.3^**	**246.4±159.7^**

IL-6 – interleukin 6, IL-8 – interleukin 8, IL-18 – interleukin 18, CCL-11 (Eotaxin-1) – C-C motif chemokine ligand 11, CCL17 (TARC) – C-C motif chemokine ligand 17, CCL25 – C-C motif chemokine ligand 25, MMP-7 – matrix metalloproteinase 7, CXCL9 – C-X-C motif chemokine ligand 9 *- group with a significantly higher level of marker compared to control overall and/or control subgroups ($p<0.05$) ** - significantly higher level compared to non-inflammatory control group ($p<0.0001$) ^ - significantly higher level compared to the main group ($p<0.05$)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2 Levels of cytokines and chemokines in BALF in a patient during SJIA flare-up, worsening of respiratory status, before and after therapeutic whole lung lavage

Marker	Baseline	Visit 4	Visit 5	Visit 6
	Levels in BALF			
IL-18, pg/mL	1406	1205	477.5	178.8
S100A8/9, ng/mL	>8000	10500	10500	11641
S100A12, mcg/mL	3799	375212	414876	601.4
IL-6, pg/mL	6.77	105.4	21.3	25.8
IL-8, pg/mL	280.05	4041.7	3746.1	4310.7
CD-25, pg/mL	44.355	206.7	107.64	57.5
CCL-11, pg/mL	29.37	59.7	28.3	28.3
CCL-17, pg/mL	48.1	114.5	48.1	129.5
CCL-25, pg/mL	undetectable	undetectable	undetectable	undetectable
MMP-7, pg/mL	34786.63	87903.8	61873.4	61644.5
CXCL-9, pg/mL	131.325	494.5	200.5	100.3
	Level in plasma			
IL-18, pg/mL	35217*	7017	7870	5835
S100A8/9, ng/mL	13025*	3077	6489	1345
S100A12, mcg/mL	262*	232	472	54
CXCL-9, ng/mL	<31, neg*	<31, neg	<31, neg	<40, neg
CRP, mg/dL	<0.4, neg*	<0.4, neg	<0.4, neg	<0.4, neg
Clinical status Girl with SJIA. Recurrent MAS. PAP/ILD	Uncontrolled disease with worsening of hypoxia and findings on high-resolution chest CT; *-measured 10 days after bronchoscopy	Therapeutic WWL of one lung due to worsening of the respiratory status	Therapeutic WWL of another lung done 7 days after the first lavage.	Worsening of respiratory status

Results: BALF samples were obtained from 14 patients with SJIA-LD (mean age 7.4±1.98 years and disease duration 4.4 ±0.9 years) and 16 patients without SJIA-LD (mean age 8.6±0.24 years). Seven (50%) SJIA-LD patients required O2 support intermittently or continuously and one patient required BiPAP. Serial samples were obtained for two patients before and after whole lung lavage and BMT, respectively.

BALF levels of IL-18, CD-25, CCL-11 and MMP-7 were significantly elevated in patients with SJIA-LD compared to controls, while CXCL-9 was significantly higher in controls and IL-6 and IL-8 were significantly higher in the NIC group (Table 1). Levels of CD-25, CXCL-9, CCL-11 and CCL-17 were undetectable in most patients from both groups, but detection of CD25 ($\chi 2=2.16$, p= 0.0027) occurred more often in SJIA-LD.

Linear regression analysis didn't show the relationship between BALF IL-18 level and disease duration (p=0.15), oxygen requirement (p=0.11), dose of Anakinra (p=0.4) or plasma levels of ferritin (p=0.9), CXCL-9 (p=0.6) and IL-18 (p=0.9). However, there was a direct relation with daily prednisone dose (p=0.03, CI 13.93 to 230.1) and number of immunosuppressive medications (p=0.0015, CI 288.6 to 935.9).

Of the 3 SJIA-LD patients who underwent BMT, we observed a higher BALF/plasma IL-18 ratio compared to other patients, although this was not significant (176±99 vs 34±16.5 (p=0.1)).

For two SJIA-LD patients with serial samples, the changes of cytokine profile for one during disease flare-up and after therapeutic WLL are shown in Table 2, and before and after bone marrow transplant are in Table 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 Levels of cytokines and chemokines in BALF and plasma in a patient before and after bone marrow transplant

Marker	Pre-BMT	Post-BMT
IL-18, pg/mL	1182	532.99
S100A8/9, ng/mL	10500	3028.5
S100A12, mcg/mL	672000	49339.5
IL-6, pg/mL	0.29	8.51
IL-8, pg/mL	83.95	105.675
CD-25, pg/mL	30.25	26.695
CCL-11, pg/mL	undetectable	undetectable
CCL-17, pg/mL	undetectable	undetectable
CCL-25, pg/mL	undetectable	undetectable
MMP-7, pg/mL	17589.36	19808.8

Conclusion: Patients with SJIA-LD showed a distinct BALF cytokine profile, with elevated IL-18, MMP-7, and CCL-11 but lower levels of other cytokines. These profiles also vary with flares and management, including WLL and BMT. Further prospective work is needed to determine the relationship with disease course and treatments.

Disclosure: I. Romankevych: None; **D. Do**: None; **A. Sproles**: None; **L. Auld**: None; **T. Sabit**: None; **R. Chhaing**: None; **J. Baker**: None; **J. Brewington**: None; **C. Towe**: Boehringer-Ingelheim, 1, Sanofi, 1; **A. GROM**: National Institutes of Health, 5, Novartis, 2, 5, sJIA Foundation, 5, Sobi, 2, 5, Up-To-Date, 9; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2.

Abstract Number: 2243

Differences In GDF-15 Levels In Rheumatoid Arthritis Patients With Remission Or Mild Disease Activity Are Associated With Fewer Depressive Symptoms: Clinical Data And Bioinformatic Analysis

Jessica Roldan Ortega[1], Mario Peña[2], Evelyn Aranda Cano[3], Luz Viruel[4], Itzel Palafox Sosa[5], David Vera Bustamante[6], Fausto Sanchez-Muñoz[2], Yaneli Juarez-Vicuña[7] and Laura Aline Martinez-Martinez[8], [1]INSTITUTO NACIONAL DE CARDIOLOGIA, Ciudad de México, Federal District, Mexico, [2]Instituto Nacional de Cardiologia Ignacio Chavez, Mexico city, Mexico, [3]Departament of rheumatology Instituto Nacional de Cardiología Ignacio Chávez, Ciudad de Mexico, Federal District, Mexico, [4]Universidad Autónoma del Estado de Hidalgo, Tula de Allende, Hidalgo, Mexico, [5]Escuela Superior de Medicina-Instituto Politècnico Nacional, ciudad de mexico, Federal District, Mexico, [6]Benemérita Universidad Autónoma de Puebla, Heroica Puebla de Zaragoza, Puebla, Mexico, [7]Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico, Mexico City, Mexico, [8]Rheumatology Department at National Institute of Cardiology Ignacio Chávez, Mexico City, Federal District, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Depression is a common comorbidity in rheumatoid arthritis patients and has a significant effect on the disease course. [Brock J, et al. *Nat Rev Rheumatol*. 2023;19(12):790-804]. Growth differentiation factor 15 (GDF-15), a member of the TGFβ family, has been associated not only with endothelial dysfunction but also with several mental diseases, such as depression and psychosis [Kumar P, et al. *Sci Rep*. 2017;7(1):7906]. This study aimed to determine the differences in GDF-15 levels between RA patients with and without depressive symptoms and to explore the correlation between GDF-15 levels and depression symptoms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

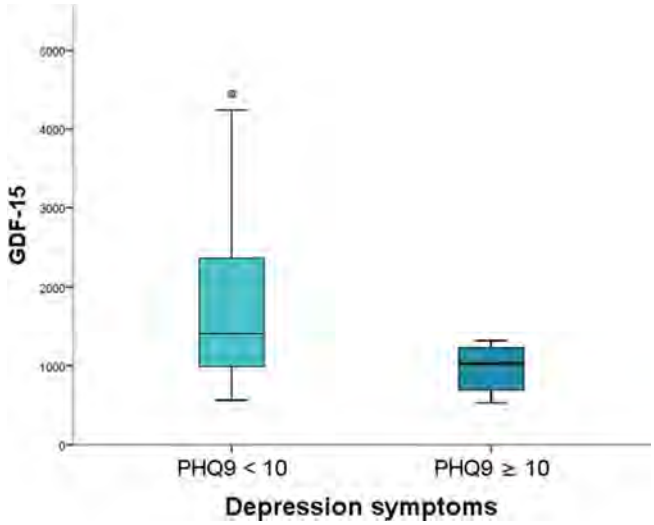


Figure 1. GDF-15 levels between RA patients with and without depressive symptoms

Methods: Patients fulfilling the 2010 ACR/EULAR classification criteria for seropositivity RA were included in this cross-sectional observational study. Patients with moderate or severe disease activity according to DAS28 and fibromyalgia were excluded. The PHQ-9 was used for the evaluation of depressive symptoms, and a score of 10 was considered the cutoff point. GDF15 was measured in the serum by ELISA and is expressed in picograms/milliliters. Exploratory bioinformatics analysis was conducted via the miRNet 2.0 platform (https://www.mirnet.ca/) in order to explore shared microRNA regulators potentially linking these conditions in patients with RA. This analysis was performed by selecting "Diseases" as the input category to include rheumatoid arthritis and depression and "Genes" to include GDF-15. The data are presented as percentages, means ± standard deviations or medians, and interquartile ranges (IQRs) according to their distributions. The Mann–Whitney U test was used for comparison. The correlation between the GDF-15 score and PHQ-9 score was evaluated via Spearman's method. A value of $p \leq 0.05$ was considered statistically significant.

Results: Fifty-six patients were invited; however, 2 were excluded because they were negative for RF and ACPA, 10 because they had moderate or severe RA disease activity, and 5 because they had fibromyalgia. A total of 39 patients were analyzed. Thirty-six (92%) were female. The mean age was 58 ± 11 years. Thirty-four patients were in remission, and only 5 had mild disease activity according to the DAS28. The most common comorbidities were hypertension (41%), diabetes (26%) and Sjögren´s syndrome (15%). In the group of patients with fewer depressive symptoms (PHQ-9 < 10, n=30), the mean GDF-15 score was 1410 (993–2359), whereas it was 1027 (697–1236) in the group with severe depressive

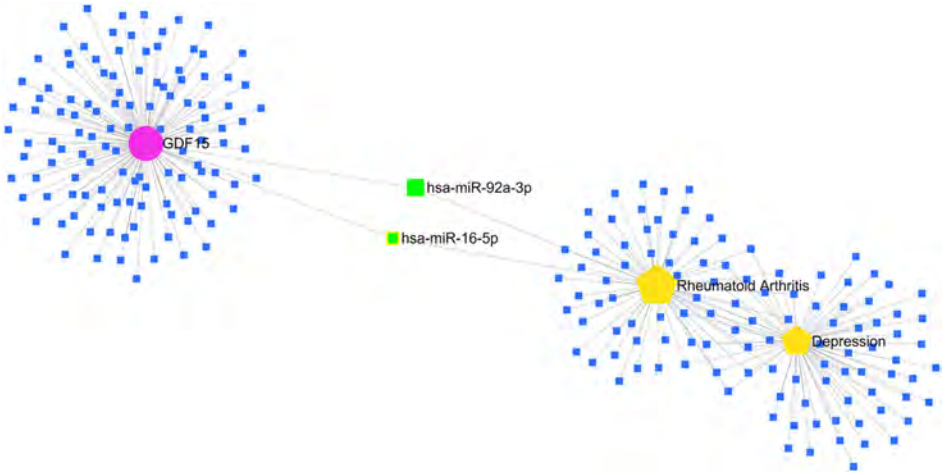


Figure 2. Interaction network: bioinformatic analysis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

symptoms (PHQ-9 ≥10, n=9), figure 1 (p=0.007). A negative correlation between PHQ-9 and GDF-15 levels was found (Rho= -0.377, p=0.018). According to bioinformatics (figure 2), the analysis identified two microRNAs, hsa-miR-16-5p and hsa-miR-92a, as shared elements associated with RA, GDF-15, and depression.

Conclusion: The levels of GDF-15 are inversely correlated with the severity of depression, and similar results in other mental diseases (psychosis) have been reported. A possible molecular connection may exist between RA and depressive symptoms, primarily through GDF15-related mechanisms and independent of active inflammatory status. However, further studies are needed.

Disclosure: J. Roldan Ortega: None; **M. Peña**: None; **E. Aranda Cano**: None; **L. Viruel**: None; **I. Palafox Sosa**: None; **D. Vera Bustamante**: None; **F. Sanchez-Muñoz**: None; **Y. Juarez-Vicuña**: None; **L. Martinez-Martinez**: None.

Abstract Number: 2244

Bone Mineral Density Trajectories and Fracture Risk in Rheumatoid Arthritis: A 7-Year Longitudinal Analysis Using Group-Based Trajectory Modeling

Kei Hirose[1], Keigo Hayashi[2], Natsuki Kubota[2], Yuya Terajima[2], Kazuya Matsumoto[2], Takato Nakadoi[2], Shoichi Nawachi[2], Yoshia Miyawaki[3], Eri Katsuyama[4], Takayuki Katsuyama[2], Haruki Watanabe[2], Mariko Narazaki[2], Yoshinori Matsumoto[2] and Jun Wada[2], [1]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama city, Japan, [2]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, [3]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Okayama, Japan, [4]Faculty of Health Science, Okayama University Medical School, Graduate School of Health Sciences, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

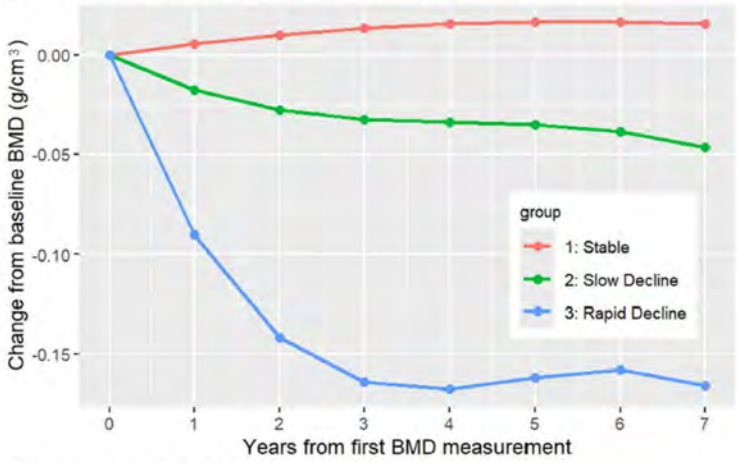
Background/Purpose: Rheumatoid arthritis (RA) is a well-established risk factor for fractures, due to both systemic inflammation and treatment-related effects on bone metabolism. This study aimed to identify clinical factors contributing to BMD decline and fracture under current RA and osteoporosis treatment strategies.

Methods: We conducted a retrospective cohort study at a university hospital in Japan, including RA patients with at least two dual-energy X-ray absorptiometry (DXA) scans of the femoral neck between 2010 and 2024. Group-based trajectory modeling (GBTM) was used to classify patients according to longitudinal BMD changes over 7 years since the initial measurement. Baseline characteristics and treatment exposures during follow-up were compared across the identified trajectory groups. Factors associated with BMD trajectory were explored using multinomial logistic regression. Incident fractures during the observation period were also assessed for each group.

Results: We analyzed 1,681 BMD measurements from 435 RA patients (mean age: 62 years; 78% female; 81% seropositive). GBTM identified three distinct BMD trajectory groups: Stable (n=211), Slow Decline (n=149), and Rapid Decline (n=75) (Figure 1). The Stable group had the lowest baseline BMD (mean: 0.59 g/cm^3), while the Rapid Decline group had the highest (mean: 0.76 g/cm^3). Use of denosumab and vitamin D supplements was significantly higher in the Stable group, whereas

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Trajectories of change from baseline BMD at the femoral neck among patients with RA patients (n=435)



BMD: bone mineral density; RA: rheumatoid arthritis.

glucocorticoid use was more prevalent in the Rapid Decline group (Table 1). Multivariable analysis revealed that older age, female sex, and higher baseline BMD were independently associated with the Rapid Decline trajectory (ORs: age 1.05 [95%CI 1.02 to 1.09], female 2.79 [95%CI 1.10 to 7.05], BMD 3.92 [2.76 to 5.58]). Additionally, the use of osteoporosis medications was negatively associated with decline trajectories (Table 2). The incidence of new fractures per 100 person-years was 1.49 in the Stable group, 2.79 in the Slow Decline group, and 2.06 in the Rapid Decline group, with no statistically significant difference (p=0.20).

Conclusion: This 7-year longitudinal analysis identified three distinct BMD trajectories in RA patients. Notably, those in the Rapid Decline group had relatively high baseline BMD but did not exhibit lower fracture rates. The higher prevalence of glucocorticoid use and lower use of osteoporosis treatment in the decline groups suggest that suboptimal osteoporosis

Table 1. Patient characteristics of RA patients stratified by trajectory of femoral BMD.

Variables	Stable (n=211)	Slow Decline (n=149)	Rapid Decline (n=75)	p-value
Characteristics				
Age, years, mean (SD)	62 (12)	60 (13)	63 (11)	0.32
Female, n (%)	171 (81.0%)	114 (76.5%)	56 (74.7%)	0.41
RA duration, years, median (IQR)	5 (0.8 to 12)	3 (0.3 to 10)	3 (0.2 to 10)	0.18
Seropositivity, n (%)	172 (81.5%)	120 (80.5%)	59 (78.7%)	0.86
Current smoking, n (%)	16 (7.6%)	12 (8.1%)	1 (1.3%)	0.12
Alcohol drinking (daily), n (%)	19 (9.0%)	8 (5.4%)	4 (5.3%)	0.34
BMI, kg/m², mean (SD)	21.8 (3.8)	22.6 (4.3)	22.4 (3.0)	0.11
BMD at baseline, g/cm², mean (SD)	0.59 (0.12)	0.65 (0.12)	0.76 (0.15)	<0.01
Osteoporosis medications*				
BPs, n (%)	87 (41.2%)	35 (23.5%)	31 (45.3%)	<0.01
Denosumab, n (%)	42 (19.9%)	13 (8.7%)	2 (2.7%)	<0.01
Vitamin D supplements, n (%)	67 (31.8%)	28 (18.8%)	14 (18.7%)	<0.01
Other bone medications, n (%)	1 (0.5%)	3 (2.0%)	2 (2.7%)	0.27
RA medications*				
Methotrexate, n (%)	69 (32.7%)	100 (67.1%)	55 (73.3%)	0.39
Other csDMARDs, n (%)	69 (32.7%)	58 (38.9%)	33 (44.0%)	0.18
bDMARDs, n (%)	62 (29.4%)	42 (28.2%)	20 (26.7%)	0.90
tsDMARDs, n (%)	7 (3.3%)	8 (5.4%)	0 (0.0%)	0.03
Glucocorticoids, n (%)	74 (35.1%)	51 (34.2%)	38 (50.7%)	0.03
PSL dose, mg/day, median (IQR)	0.31 (0.0 to 2.8)	0.50 (0.0 to 2.5)	1.3 (0.0 to 3.0)	0.15

*Use of each medication was defined as prescription for more than half of the observation period.
BMD: mineral bone density; BMI: body mass index; BPs: bisphosphonates; bDMARDs: biologic disease-modifying antirheumatic drugs; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; IQR: interquartile range; PSL: prednisolone; RA: rheumatoid arthritis; SD: standard deviation; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table2. Association of femoral BMD trajectory group and characteristics in RA patients: multivariable multinomial logistic regression

	Odds Ratios for slow decline trajectory (ref. stable trajectory)		Odds Ratios for rapid decline trajectory (ref. stable trajectory)	
Variables	**OR (95%CI)**	**p-value**	**OR (95%CI)**	**p-value**
Female	1.09 (0.58 to 2.06)	0.78	2.79 (1.10 to 7.05)	0.03
Age	1.02 (1.00 to 1.03)	0.13	1.05 (1.02 to 1.09)	<0.01
RA duration	0.99 (0.96 to 1.02)	0.46	1.01 (0.97 to 1.06)	0.53
BMI	1.00 (0.94 to 1.06)	0.95	0.90 (0.82 to 0.99)	0.03
Seropositive	0.96 (0.53 to 1.74)	0.89	1.01 (0.41 to 2.44)	0.99
Smoking history	0.71 (0.29 to 1.77)	0.47	0.04 (0.00 to 0.51)	0.01
Drinking history	0.42 (0.16 to 1.09)	0.07	1.10 (0.27 to 4.47)	0.90
Methotrexate	0.85 (0.49 to 1.50)	0.58	1.57 (0.69 to 3.60)	0.28
Other csDMARDs	1.43 (0.84 to 2.44)	0.19	1.99 (0.94 to 4.24)	0.07
bDMARDs	1.21 (0.71 to 2.06)	0.48	0.86 (0.41 to 1.85)	0.72
tsDMARDs	2.56 (0.79 to 8.30)	0.11	NA: 0 case	–
GCs	0.77 (0.36 to 1.63)	0.49	1.55 (0.58 to 4.15)	0.38
PSL dose (mg/day)	1.10 (0.93 to 1.29)	0.26	1.00 (0.80 to 1.23)	0.97
Denosumab	0.32 (0.15 to 0.69)	<0.01	0.17 (0.03 to 0.91)	0.04
BPs	0.31 (0.17 to 0.54)	<0.01	0.85 (0.40 to 1.79)	0.66
Vitamin D analogues	0.60 (0.34 to 1.07)	0.09	0.93 (0.40 to 2.15)	0.86
Other bone meds	4.68 (0.39 to 55.4)	0.22	5.75 (0.38 to 86.0)	0.21
BMD at baseline (by 0.10g/cm^2)	1.38 (1.07 to 1.76)	<0.01	3.92 (2.76 to 5.58)	<0.01

*Use of each medication was defined as prescription for more than half of the observation period.
BMD: bone mineral density; BMI: body mass index; BPs: bisphosphonates; bDMARDs: biologic disease-modifying antirheumatic drugs; CI: confidence interval; csDMARDs: conventional synthetic disease-modifying antirheumatic Drugs; GCs: glucocorticoids; OR: Odds Ratio; PSL: prednisolone; RA: rheumatoid arthritis; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs.

management may contribute to accelerated BMD loss and fracture risk, even in patients with initially preserved bone density. These findings highlight the need for proactive osteoporosis prevention strategies throughout the course of RA.

Disclosure: K. Hirose: None; **K. Hayashi**: None; **N. Kubota**: None; **Y. Terajima**: None; **K. Matsumoto**: None; **T. Nakadoi**: None; **S. Nawachi**: None; **Y. Miyawaki**: None; **E. Katsuyama**: None; **T. Katsuyama**: None; **H. Watanabe**: None; **M. Narazaki**: None; **Y. Matsumoto**: AbbVie/Abbott, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **J. Wada**: None.

Abstract Number: 2245

Add-on of Coronary Artery Calcium Score Significantly Improves the Risk Prediction of Cardiovascular Diseases in Patients with Rheumatoid Arthritis: From a Real-world Cohort Study

Yao-Wei Zou, Ying Yang, Zhi-Ming Ouyang, Ran Shi, Tao Wu, Kui-Min Yang, Jian-Da Ma and **Lie Dai**, Department of Rheumatology and Immunology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular diseases (CVD) are the first cause of death in patients with rheumatoid arthritis (RA). The guidelines recommend risk prediction in all RA patients. However, there is currently no precise prediction model for RA patients. Coronary artery calcium (CAC) score by coronary angiography or chest computed tomography (CT) can improve CVD risk prediction in the general population, but no report in RA patients. We aimed to investigate whether adding CAC score to risk algorithms could improve CVD risk prediction in RA patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 The CVD Risk Prediction Models in RA patients

Table 1 The CVD Risk Prediction Models in RA patients

Variables	Clinical model			CAC model		
	HR (95% CI)	Beta Coefficient	*P* value	HR (95% CI)	Beta Coefficient	*P* value
Age, years	1.085 (1.058,1.113)	0.082	<0.001	1.061 (1.031,1.091)	0.059	<0.001
Male	2.492 (1.568,3.959)	0.913	<0.001	2.592 (1.626,4.129)	0.952	<0.001
BMI, kg/m^2	1.072 (1.002,1.146)	0.069	0.043	1.079 (1.006,1.158)	0.076	0.033
Hypertension	2.938 (1.798,4.799)	1.078	<0.001	2.626 (1.591,4.336)	0.966	<0.001
CRP, mg/L	1.005 (1.000,1.009)	0.004	0.034	1.005 (1.001,1.009)	0.005	0.017
CDAI	1.017 (1.004,1.029)	0.016	0.009	1.016 (1.003,1.028)	0.015	0.016
Glucocorticoid	2.094 (1.333,3.291)	0.739	0.001	2.122 (1.348,3.340)	0.752	0.001
Ln (CAC score+1)	-	-	-	1.521 (1.210,1.912)	0.419	<0.001

The *P* values are based on a standard Cox proportional hazards model. To estimate the CVD risk for a particular person, multiply the values of the risk factors by the corresponding beta coefficient and sum these quantities up to yield a value (call it A). Then calculate: B = exp (A). Finally, the CVD risk is given by 1 - S (10) [B].

Abbreviations: CVD, cardiovascular disease; RA, rheumatoid arthritis; BMI, body mass index; CRP, C-reactive protein; CDAI, clinical disease activity index; CAC, coronary artery calcium.

Methods: RA patients from January 1, 2010 to September 30, 2024 were included retrospectively from a RA cohort at the Department of Rheumatology and Immunology, Sun Yat-sen Memorial Hospital, Guangdong, China (SYSEC-2009-06). The inclusion criteria included free of CVD at baseline, and having intact clinical data. CAC scores based on chest CT at baseline were calculated by the Agatston method. The endpoint was CVD, which included coronary heart disease, stroke, heart failure, peripheral arterial disease, and CVD death.

LASSO-Cox regression were performed to construct prediction model for CVD. The list of candidate covariates included traditional CVD risk factors (age, sex, BMI, history of hypertension and diabetes, TC, HDL-C, LDL-C), RA-related factors (disease duration, RF, ACPA, ESR, CRP, CDAI, HAQ-DI, and the use of glucocorticoid, csDMARDs, and biologic agents), and CAC score. Harrell's C-statistic and NRI were used to compare the performance between models with and without CAC, as well as existing RA specific model (ESR-RA).

Results: A total of 822 RA patients were enrolled in this study, with mean age at baseline 54.5 ± 12.0 years, 79.8% females, and median RA disease duration 6.3 years. During a mean follow-up time of 3.9 years, 81 (9.8%) incident CVD events occurred. The LASSO-Cox regression was performed to identify risk factors associated with CVD, and the final clinical model consisted of age, male, BMI, history of hypertension, CRP, CDAI, the use of glucocorticoid, and CAC score (**Table 1**). **Table 2** illustrates the internal discrimination properties of CAC model, with a C-index of 0.888 (95% CI 0.844-0.933), indicating excellent discrimination between events and non-events. The C-index of CAC model was significantly higher than that of the clinical model (0.859) and the ESR-RA model (0.847, both $P < 0.05$). While, no significant difference was found

Table 2 The ability of CAC score to predict CVD risk in RA patients

Table 2 The ability of CAC score to predict CVD risk in RA patients

	C-index (95% CI)	Change in C-index (95% CI)		NRI (95% CI)	
ESR-RA model	0.847(0.800,0.893)	Ref	-	Ref	-
Clinical model	0.859(0.810,0.908)	0.012(0.010,0.015)	Ref	0.147(-0.091,0.369)	Ref
CAC model	0.888(0.844,0.933)	0.041(0.040,0.044)*	0.029(0.025,0.034)*	0.477(0.248,0.655)*	0.316(0.159,0.628)*

Abbreviations: CVD, cardiovascular disease; RA, rheumatoid arthritis; CAC, coronary artery calcium; NRI, net reclassification improvement. * $P < 0.05$.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

between the clinical and ESR-RA models, supporting the significant improvement achieved by incorporating CAC. When comparing the CAC model against clinical model, the NRI showed that the accuracy of the model was improved 31.6% (95% CI 15.9-0.62.8) after adding CAC scores to the clinical model, while no significant improvement was observed when comparing the clinical model with the ESR-RA model (**Table 2**).

Conclusion: Add-on of CAC score significantly improves the prediction of CVD risk in RA patients. Further validation in large-sample, multi-center prospective cohorts are needed in future.

Disclosure: Y. Zou: None; **Y. Yang**: None; **Z. Ouyang**: None; **R. Shi**: None; **T. Wu**: None; **K. Yang**: None; **J. Ma**: None; **L. Dai**: None.

Abstract Number: 2246

Different Populations, Different SDAI Cut-Off? A Proposal for a New Remission Threshold in Brazilian RA Patients from a National Multicenter Study

Lucas Pires[1], Alisson Pugliesi[1], Cleandro Pires[2], Ana Carolina Hidaka[3], Vitor Cruz[4], Manoel Barros Bertolo[1], Ana Paula Reis[5], Rina Dalva Neubarth Giorgi[6], Leticia Pereira[7], Sebastião Cezar Radominski[8], Ivanio Alves Pereira[9], Maria Fernanda Brandão de Resende Guimarães[10], Paulo Louzada Junior[11], Maria de Fátima Lobato da Cunha Sauma[12], Karina Bonfiglioli[13], Claiton Viegas Brenol[14], Licia Maria Henrique da Mota[2] and Geraldo da Rocha Castelar Pinheiro[7], [1]Unicamp, Campinas, Brazil, [2]UNB, Brasilia, Distrito Federal, Brazil, [3]UNB, Brasilia, Brazil, [4]UFG, Goias, Brazil, [5]UniCEUB, Brasilia, Brazil, [6]IAMSPE, São Paulo, Brazil, [7]UERJ, Rio de Janeiro, Brazil, [8]UFPR, Curitiba, Brazil, [9]UFSC, Florianopolis, Brazil, [10]UFMG, Belo Horizonte, Brazil, [11]USP-RP, Ribeirão Preto, Brazil, [12]UFPA, Belem, Brazil, [13]USP-SP, São Paulo, Brazil, [14]UFRGS, Porto Alegre, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Remission criteria in Rheumatoid Arthritis (RA) have continuously evolved to balance the risks of both overtreatment and undertreatment. The most recent update includes the revised ACR/EULAR Boolean Criteria 2.0 (BC 2.0).

While most RA activity indices include patient-reported outcomes such as pain and global assessment, these measures are inherently subjective and can be influenced by cultural, socioeconomic, and ethnic factors. This study aimed to evaluate the agreement between commonly used RA activity indices (DAS28-CRP, DAS28-ESR, CDAI, SDAI) and the BC 2.0, as well as determine the most accurate cut-off values for remission in Brazilian patients, using data from a large, multicenter real-world cohort.

Methods: This cross-sectional analysis used baseline data from a national multicenter observational study conducted across 11 public hospitals in Brazil. All participants met the 2010 ACR/EULAR Classification Criteria for Rheumatoid Arthritis.

Sociodemographic and clinical variables were analyzed using descriptive statistics. Agreement between remission definitions was assessed using the Kappa coefficient, and ROC curves were constructed to determine the most sensitive and specific cut-off points for each index, using BC 2.0 as a reference.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

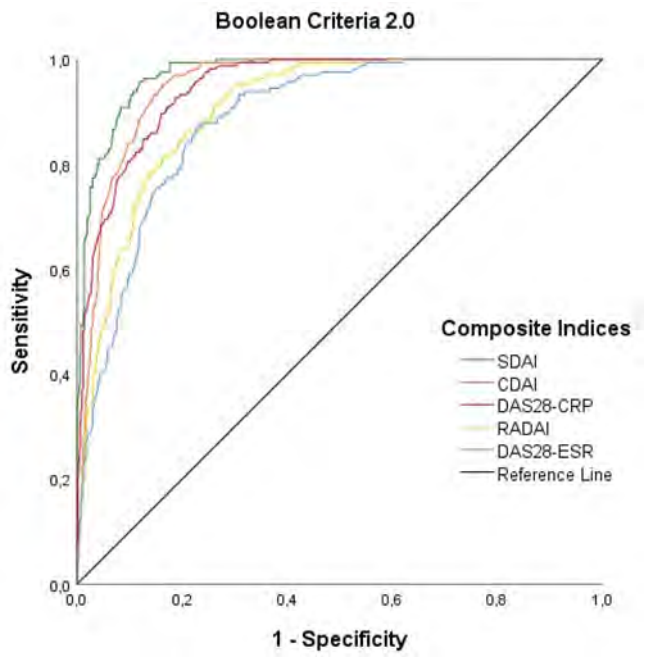


Figure 1: ROC curve illustrating the sensitivity and 1-specificity of the different metrics in relation to BC 2.0.

Metric	Cut-off	Sensitivity (%)	Specificity (%)
DAS28-CRP	≤2.6*	97.6	75.0
	≤2.3	86.0	85.9
DAS28-ESR	≤2.6*	75.6	84.8
	≤2.8	81.7	79.9
CDAI	≤2.8*	77.4	93.2
	≤3.9	88.4	88.3
SDAI	≤3.3*	81.1	95.9
	≤4.3	90.9	91.7

*Current reference threshold

Figure 2: Sensitivity and Specificity of of Proposed Cut-off Points for Remission.

Results: A total of 840 RA patients were included (89.8% female; mean age 57 years, SD ±11; median disease duration: 12.2 years, IQR 6.8–19.3). Rheumatoid factor was positive in 78.1%, and methotrexate was used by 68.1%, corticosteroids by 44.5%, and biologic DMARDs by 37.7%. Remission rates varied widely across indices: DAS28-CRP (39.2%), DAS28-ESR (27.0%), CDAI (20.6%), SDAI (19.2%), BC 2.0 (19.5%), and Boolean 1.0 (15.1%).

SDAI showed the highest agreement with BC 2.0 (Kappa: 0.775), followed by CDAI (K: 0.692), while DAS28-CRP and ESR demonstrated moderate agreement (K: 0.525 and 0.527, respectively).

In ROC analysis (figure 1), SDAI had the highest accuracy (AUC = 0.973; 95% CI 0.964-0.983), outperforming the other indices: DAS28 CRP (AUC = 0.947; 95% CI 0.933-0.962), DAS28 ESR (AUC = 0.888; 95% CI 0.864-0.912) and CDAI (AUC = 0.951; 95% CI 0.937-0.964). The optimal SDAI threshold was ≤4.3, superior to the conventional ≤3.3 cut-off (figure 2).

Conclusion: Conventional SDAI remission thresholds may underestimate disease control in Brazilian RA patients. A revised cut-off of SDAI ≤4.3 demonstrated greater accuracy and better alignment with BC 2.0, suggesting they are more appropriate remission cut-off for clinical use and research in Brazilian RA patients. These results have potential implications for both clinical care and international RA research, particularly for underrepresented populations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Pires: None; **A. Pugliesi**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Johnson, 6, Pfizer, 6, UCB, 6; **C. Pires**: None; **A. Hidaka**: None; **V. Cruz**: None; **M. Barros Bertolo**: AbbVie/Abbott, 6, Pfizer, 6; **A. Reis**: None; **R. Neubarth Giorgi**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **L. Pereira**: None; **S. Radominski**: AbbVie/Abbott, 6, Amgen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Pfizer, 6, Roche, 6; **I. Alves Pereira**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, Pfizer, 6, Roche, 6, UCB, 6; **M. Brandão de Resende Guimarães**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **P. Louzada Junior**: None; **M. Lobato da Cunha Sauma**: None; **K. Bonfiglioli**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Janssen, 6, Novartis, 6, Roche, 6; **C. Viegas Brenol**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Janssen, 6, Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6; **L. Henrique da Mota**: None; **G. da Rocha Castelar Pinheiro**: None.

Abstract Number: 2247

A Pilot Study to Identify Novel Autoantibody Biomarkers in Rheumatoid Arthritis (RA) Patients Using Immunome Protein Array

Margaret Ma[1], Peter Cheung[1], ee tzun koh[2], janique peyper[3], bermet abylova[3] and Khai Pang Leong[2], [1]National University Hospital, Singapore, Singapore, [2]Tan Tock Seng Hospital, Singapore, Singapore, [3]Standard BioTools, Singapore, Singapore

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: RA is a heterogenous condition with variable outcomes. The identification of novel autoantibodies and autoantibody signatures could help us identify potential diagnostic and prognostic biomarkers which could guide treatment decisions. We carried out this pilot study using a high-throughput protein microarray platform to identify autoantibodies against native autoantigens in RA patients.

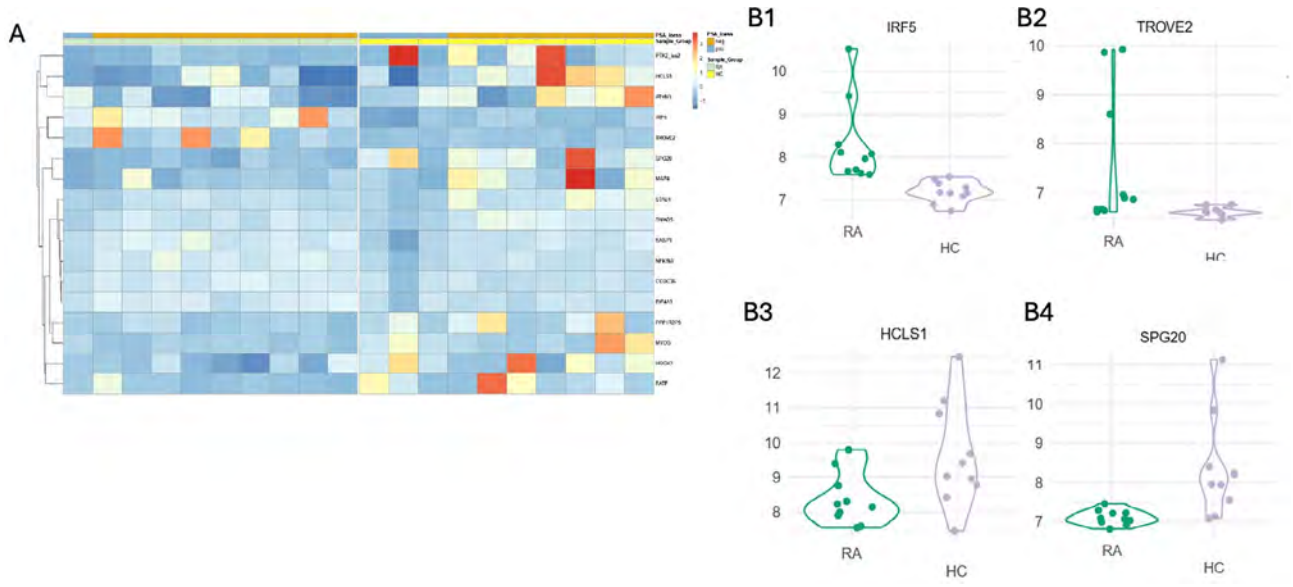


Figure: A = annotated heatmap of the signals for antigens surpassing significance threshold during linear modeling analysis, with both row and column clustering. B1-4 = violin plots of the autoantibodies of the most significance.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Sera from 10 RA and 10 gender-, age-, and ethnicity-matched healthy controls (HC) were screened for seroreactivity (IgG) to more than 1,600 disease-associated protein antigens in their native conformation. R package limma was used to perform a linear modeling analysis between comparison classes across all signals representing cognate antibody-antigen interactions. This analysis employs a moderated t-statistical method which calculates, for each antigen, the difference between two specified classes, and determines the significance of these differences by measure of fold changes and p-values .The significance threshold for identifying differential Abs (DAbs) was set at $p < 0.05$ and $|\text{fold-change}| > 1.1$. ROC analysis was performed between comparison classes across all antigens surpassing significance threshold during the above-described linear modeling analysis.

Results: 17 antibodies were identified to be differentially expressed (Figure A heatmap). Of note, higher levels of anti-TROVE2 IgG (fold change of 1.97, p value = 4.09e-02, ROC AUC = 0.89) and anti-IRF5 IgG (fold change of 2.06, p value = 3.2e-03, ROC AUC = 1) were observed solely among RA patients, whereas higher levels of anti-HCLS1 IgG (fold change of 1.54, p value = 6.16e-03, ROC AUC 0.79) and anti-SPG20 IgG (fold change of 1.26, p value = 4.63e-03, ROC AUC 0.91) were nearly unique to HC (Figure B1-4).

Conclusion: A high-throughput protein microarray platform allows detection and quantification of autoantibodies which maybe of potential pathophysiological and prognostic significance in RA patients. TROVE2 is a well-known classical rheumatological autoantigen and has been shown to be a biomarker for predicting ADAb

development and therapeutic response in adalimumab-treated patients. IRF5 is involved in signal transduction eliciting type I IFN expression. Additionally, upregulation of antibodies targeting HCLS1 (involved in leukopoiesis and leukocyte clonal deletion) and SPG20 (involved in lipid degradation and mitochondrial function) in HC suggests possible protection against RA by pathways incorporating those proteins, or indeed by the antibodies that target them. Our preliminary findings suggest a complex relationship between autoantibody signatures and RA.

Disclosure: M. Ma: None; **P. Cheung**: None; **e. koh**: None; **j. peyper**: Standard BioTools, 2; **b. abylova**: Standard BioTools, 3; **K. Leong**: None.

Abstract Number: 2248

Elevated Anti-PAD Autoantibodies in a Singaporean Chinese Rheumatoid Arthritis (RA) Cohort with Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibodies (ACPA) Positivity: A Case-control Exploratory Study

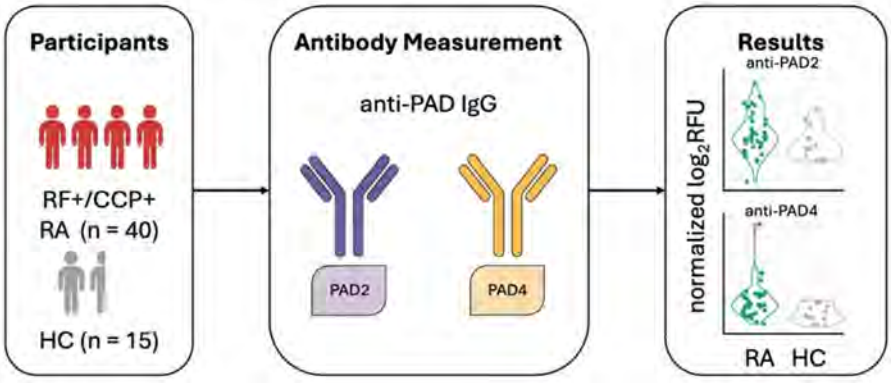
Margaret Ma[1], Khai Pang Leong[2], ee tzun koh[2], Preeti Dhanasekaran[3], janique peyper[4], bermet abylova[4], Anselm Mak[3] and Peter Cheung[1], [1]National University Hospital, Singapore, Singapore, [2]Tan Tock Seng Hospital, Singapore, Singapore, [3]National University of Singapore, Singapore, Singapore, [4]Standard BioTools, Singapore, Singapore

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoantibody-based biomarkers including ACPA and RF are of established clinical use in rheumatoid arthritis (RA) and are ingrained in international classification criteria. However, other antibodies are also likely to be of relevance. The presence of autoantibodies in Chinese RA populations has not been well studied. The aim of this study was to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Elevated anti-PAD antibodies in a Chinese seropositive rheumatoid arthritis cohort: a case-control exploratory study



determine an autoantibody signature in a homogenous population of ACPA/RF-positive Chinese RA patients by using a broad explorative screen of IgG antibodies to autoantigen specificities.

Methods: We selected 40 RA patients and 10 matched healthy controls. Plasma samples were screened only for IgG seroreactivity, against a panel of >1,800 protein autoantigens using the KREX technology-based i-Ome Discovery array. Differential analysis was performed using R package limma. The significance threshold for identifying differential Abs (DAbs) was set at $p < 0.05$ and $|\text{fold-change}| > 1.1$. ROC analysis was carried out for each DEAb, yielding discriminative performance metrics e.g., sensitivity, specificity, area under the curve (AUC), and accuracy.

Results: Anti-PAD2 and anti-PAD4 autoantibodies exhibited significantly higher signals in the RA class. Class-wise, anti-PAD4 exhibited a fold-change of 1.54 (p = 5.46e-3), while anti-PAD2 exhibited a fold-change of 1.22 (p = 3.9e-2). Because only a proportion of individuals within a target class typically exhibits the signal of interest, class-wise autoantibody fold-changes are often diluted, and are therefore still meaningful at a threshold of 1.20. Both autoantibodies exhibited good sensitivity in discriminating RA from HC (0.90 and 0.74, respectively), although specificities were moderate (0.60 and 0.67, respectively). The ROC AUC were 0.79 for anti-PAD4 and 0.69 for anti-PAD2.

Conclusion: PAD2 and PAD4 have been reported as the most strongly implicated PAD enzymes in RA pathogenesis on the basis of genetic, histological and animal studies (1). In addition, anti-PAD4 antibodies are associated with severe joint damage, and anti-PAD2 antibodies are associated lung involvement but less severe joint disease (1). Elevated anti-PAD2 and anti-PAD4 autoantibody prevalence in our Singaporean Chinese RA patients are consistent with Western cohort findings (1,2), as well as a China cohort (3). This supports the diagnostic relevance of these autoantibodies beyond Western populations and highlight the potential role of PAD 2/4 autoantibodies to enhance early RA diagnosis and prognosis in a Singaporean Chinese population.

< !(1) Curran, A.M., Naik, P., Giles, J.T. *et al*. PAD enzymes in rheumatoid arthritis: pathogenic effectors and autoimmune targets. *Nat Rev Rheumatol* **16**, 301–315 (2020)

< ((2) Martinez-Prat L et al. Autoantibodies to protein-arginine deiminase (PAD) 4 in rheumatoid arthritis: immunological and clinical significance, and potential for precision medicine. Expert Rev Clin Immunol. 2019 Oct;15(10):1073-1087

(C(2) Clinical relevance of autoantibodies targeting peptidylarginine deiminases 2 and 4 in rheumatoid arthritis Minghua ZHAN; Huizhang BAO; Jiali CHEN; Changsheng XIA; Chunhong FAN; Yudong LIU. Chinese Journal of Laboratory Medicine ; (12): 1035-1042, 2021

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Ma: None; **K. Leong**: None; **e. koh**: None; **P. Dhanasekaran**: None; **j. peyper**: Standard BioTools, 2; **b. abylova**: Standard BioTools, 3; **A. Mak**: Sengenics, 5; **P. Cheung**: None.

Abstract Number: 2249

Evaluation of a Screening Tool for Identifying Risk of Subclinical Interstitial Lung Disease in Rheumatoid Arthritis Patients Treated with Targeted Therapies

Marina Pavía-Pascual[1], Marina Sánchez-Lucas[2], Camille Bourgeois[3], Maria Teresa Schiaffino Garcia-Villanova[4], Julia Martínez Barrio[5], Juan Molina-Collada[6], Esther Chamorro De Vega[7], José María álvaro-Gracia álvaro[8] and Isabel Castrejón Fernández[9], [1]Department of Rheumatology, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Madrid, Spain, [2]Department of Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Madrid, Spain, [3]Hospital general universitario Gregorio Marañon, Madrid, Madrid, Spain, [4]Department of Immunology, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Madrid, Spain, [5]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [6]Department of Rheumatology, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Spain, [7]Pharmacy department, Hospital General Universitario Gregorio Marañón.Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Madrid, Spain, [8]Department of Rheumatology, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain. Department of Medicine, Complutense University, Madrid, Spain., Madrid, Madrid, Spain, [9]MD, PhD, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is the second leading cause of mortality in rheumatoid arthritis (RA) but often goes underdiagnosed due to its variable clinical presentation, ranging from subclinical involvement to progressive fibrosis. Despite its impact on prognosis, data to guide evidence-based screening and treatment remain limited. Recently, The American College of Rheumatology (ACR) and the American College of Chest Physicians (CHEST) issued conditional recommendations for RA-ILD management, reflecting low-certainty evidence. The real-world application of these therapies is not well understood. This study aims to evaluate a risk factor–based screening tool for RA-ILD and compare treatment patterns between RA patients with and without ILD in a real world-setting.

Methods: We conducted a cohort study at a single academic centre including patients with RA receiving targeted therapies. Risk factors for ILD development and treatment patterns were compared between RA patients with and without ILD using chi-square and Student's *t*-tests. A risk score incorporating age, sex, smoking status, RA duration, rheumatoid factor, and anti-cyclic citrullinated peptide antibodies was calculated. Receiver operating characteristic (ROC) curve analysis was used to determine optimal cut-off points for identifying patients at risk for subclinical ILD.

Results: Among 688 RA patients treated with targeted therapies, 31 (4.5%) had ILD. RA-ILD patients were older at disease onset (mean 54.9 vs. 45.2 years, $p< 0.05$) and more frequently smokers (48.4% vs. 14%, $p< 0.05$). Treatment patterns differed: RA-ILD patients more often received abatacept (32%), tocilizumab (22%), and JAK inhibitors (19%) versus patients with RA without ILD. Guideline-recommended first-line therapies for RA-ILD were infrequently used in our cohort. Three different cut-off points for the risk score were evaluated: 5 (Sens 86.7%, Spec 48.7% LR+1.7), corresponding to 228 patients (36.5%) in our cohort; 6 (Sens 76.7%, Spec 63.5% LH+ 2.1), corresponding to 59 patients (9.5%), and 7 (Sens 36.7%, Spec 90.5% LH+ 3.9), corresponding to 14 patients (2.2%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Characteristics of patients with RA with and without ILD

	Overall RA N= 688	RA-no ILD N= 657	RA-ILD N = 31	p
Sex (female)	567 (82.4)	547 (83.3)	20 (64.5)	0.007
Age, mean (SD)	62.3 (13.9)	62.0 (14.1)	68.7 (9.0)	0.004
Age at RA onset, mean (SD)	45.6 (14.8)	45.2 (14.7)	54.9 (12.2)	<0.001
RA duration, median (IQR) years	15 (9-23)	15 (9-23)	11 (8-19)	0.05
ACPA positive high titer	354 (54)	334 (53.4)	20 (66.7)	0.68
RF positive	489 (73.2)	462 (72.4)	27 (90)	0.034
Ever smoker	107 (15.5)	92 (14.0)	15 (48.4)	<0.001
Treatment, n (%)				
Methotrexate	254 (37)	247 (37)	7 (22)	<0.001
TNFi	379 (55)	375 (57)	4 (13)	<0.001
JAKi	104 (15)	98 (15)	6 (19)	
Tocilizumab	99 (14)	92 (14)	7 (23)	
Abatacept	56 (8)	46 (7)	10 (32)	
Rituximab	50 (7)	46 (7)	4 (13)	
Number of previous biologics	1 (1-3)	1 (1-3)	2 (1-3)	0.52
Risk score value (median (IQR)	5 (3-6)	5 (3-6)	6 (6-7)	<0.001
*Except where indicated otherwise, values are the number (%)				

Conclusion: The prevalence of ILD in this cohort of RA patients receiving targeted therapies was 4.5%. The risk score stratified 36% of patients as low risk, 9.5% as moderate risk, and 2.2% as high risk for subclinical RA-ILD. Risk-based screening tools may facilitate earlier detection and intervention, potentially improving clinical outcomes. Real-world treatment patterns varied from current ACR/CHEST guideline recommendations, underscoring the need for further research to individualized treatment decisions based on patient characteristics and ILD severity.

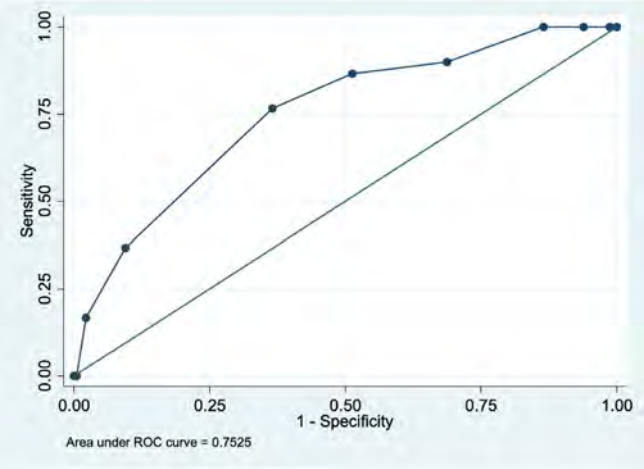


Figure. Performance of the proposed risk score for detection of RA-ILD. Result is shown as area under the receiver operating characterize curves (AUC) with 95% confidence interval (Stata roctab). AUC: 0.75 95%CI (0.67-0.84)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Pavía-Pascual: None; **M. Sánchez-Lucas**: None; **C. Bourgeois**: None; **M. Schiaffino Garcia-Villanova**: None; **J. Martínez Barrio**: None; **J. Molina-Collada**: None; **E. Chamorro De Vega**: None; **J. álvaro-Gracia álvaro**: None; **I. Castrejón Fernández**: None.

Abstract Number: 2250

Clinical and Serological Predictors of Interstitial Lung Disease in Rheumatoid Arthritis: Are Anti-Citrullinated Protein Antibodies Truly Relevant?

Martí Aguilar-Coll[1], Javier Narváez[2], Montserrat Roig Kim[1], Laia De Daniel Bisbe[1], Pol Maymó-Paituvi[1], Judith Palacios-Olid[1] and Joan Miquel Nolla[1], [1]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [2]Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Evidence on which risk factors predict the development of interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA) is scarce and of low scientific quality. This study examines whether several clinical and serological variables are associated with an increased risk of developing this complication.

Methods: A prospective study was performed in a cohort of patients with early RA (1987 ARA or 2010 ACR/EULAR criteria and symptom duration ≤12 months) diagnosed between 2003 and 2023. All patients underwent ILD screening at diagnosis, which included targeted anamnesis for respiratory symptoms, chest auscultation for fine "velcro-like" crackles, chest X-ray

Table 1. Comparison of cumulative incidence curves of each variable using Log-Rank test

	Log-Rank p-value
Male sex	0.001
Age (≥60 years)	0.024
Smoking	
Ever vs never smoker	0.164
1-20 vs 0 pack-years	0.249
>20 vs 0 pack-years	0.137
>20 vs 1-20 pack-years	0.923
Rheumatoid factor (RF)	
(+) vs (-)	0.728
(+) ≤3 times the ULN vs (-)	0.232
(+) >3 times the ULN vs (-)	0.511
(+) >3 times the ULN vs (+) ≤3 times the ULN	0.108
Anti-citrullinated protein antibodies (ACPA)	
(+) vs (-)	0.493
(+) ≤3 times the ULN vs (-)	0.352
(+) >3 times the ULN vs (-)	0.408
(+) >3 times the ULN vs (+) ≤3 times the ULN	0.265

Abbreviations: (+) = positive; (-) = negative; ULN = upper limit of normal

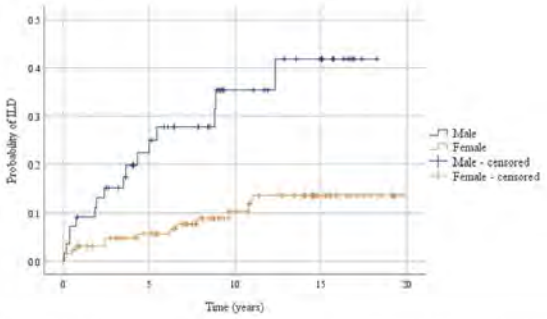
Table 2. Cox regression model including all five variables

	HR	95% CI	p-value
Male sex	3.62	1.44-9.15	0.006
Age (10-year increase)	1.45	1.03-2.04	0.034
Smoking	0.92	0.56-1.49	0.722
Rheumatoid factor (RF)	1.34	0.68-2.63	0.392
Anti-citrullinated protein antibodies (ACPA)	0.95	0.52-1.74	0.875

Abbreviations: HR = hazard ratio; 95% CI = 95% confidence interval

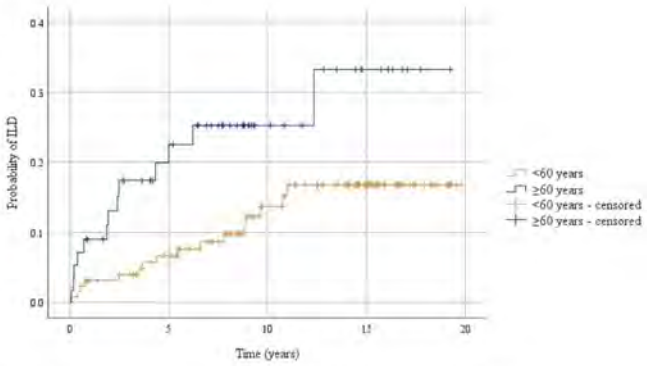
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Cumulative incidence curve of ILD according to sex



The time of RA diagnosis was used as a starting point, with censoring at death or last follow-up appointment.

Figure 2. Cumulative incidence curve of ILD according to age at RA diagnosis



The time of RA diagnosis was used as a starting point, with censoring at death or last follow-up appointment.

(CXR) and pulmonary function tests (PFTs) with spirometry and DLCO. A thoracic high-resolution computed tomography (HRCT) was performed in case of symptoms, crackles or alterations in CXR or PFTs. In patients without initial abnormalities, screening was repeated between the second and fifth year of follow-up. Sex, age at RA onset, smoking history and cumulative dose, rheumatoid factor (RF), and anti-citrullinated protein antibodies (ACPA) variables were collected. Cumulative incidence curves (i.e. 1 minus Kaplan-Meier-estimated probability), Log-Rank test and a Cox regression model were applied to determine whether or not these variables are associated with an increased risk of ILD.

Results: One hundred and eighty-eight RA patients without known ILD were included in the study. After a median follow-up time of 10.2 years (IQR 7.0 to 15.0), 30 new cases of ILD (16.0%) were diagnosed. The risk of developing lung involvement was higher among males and in patients aged ≥60 years (unadjusted Log-Rank p-value of 0.001 and 0.024, respectively) [table 1]. Cumulative incidence curves for these two variables are displayed in figures 1 and 2, respectively. In contrast, smoking, RF and ACPA showed no statistical differences, neither when tobacco dose or antibody titre were considered (p >0.05 in all scenarios). The results of a Cox regression model including all five variables is shown in table 2. Male sex showed a hazard ratio (HR) of 3.62 (95% CI 1.44 to 9.15) for the development of ILD compared to females (p=0.006). A 10-year increase in the age at the time of RA diagnosis entailed a risk 45% higher (95% CI 1.03 to 2.04) for the development of this complication (p=0.034). Smoking, RF and ACPA also failed to show significant results in the multivariate analysis (p >0.05 in all three cases).

Conclusion: In accordance with published evidence, both male sex and older age at diagnosis are associated with a greater risk of developing ILD. However, the increased risk attributed to tobacco exposure and the presence of RF and/or ACPA, especially at high titres, has not been demonstrated in this prospective study.

Disclosure: M. Aguilar-Coll: None; **J. Narváez**: None; **M. Roig Kim**: None; **L. De Daniel Bisbe**: None; **P. Maymó-Paituvi**: None; **J. Palacios-Olid**: None; **J. Nolla**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2251

Dual Diagnoses, Diminished Survival: Association between rheumatoid arthritis and survival among older adults with lung cancer

Michelle Nguyen[1], Aaron Baraff[2], Alexandra Schmidt[2], Alexander Peterson[2], Aliyah Pabani[3], Nicholas Smith[1], Shelly Gray[1], Jose Garcia[4], Noel Weiss[1] and Namrata Singh[5], [1]University of Washington, Seattle, WA, [2]VA Puget Sound Health Care System, Seattle, WA, [3]Johns Hopkins, Washington, DC, **[4]VA Puget Sound Health Care System**, VA GRECC, and University of Washington, Seattle, WA, [5]University of Washington, Bellevue, WA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased risk of malignancies, particularly lung cancer, relative to the general population[1]. However, the association between RA and overall survival in those who develop lung cancer has not been well characterized. The objective of this study was to evaluate the relationship between RA and overall survival among older adults diagnosed with lung cancer.

Methods: Data spanning 2005-2023 was obtained from the Veteran's Health Administration's (VHA) electronic medical records, commonly referred to as the Corporate Data Warehouse (CDW). Patients with lung cancer were identified from the Oncology Raw domain, which contains records of patients diagnosed with cancer and associated information, such

Table 1: Baseline Characteristics of Patients with RA and Lung Cancer

Table 1: Baseline Characteristics of Patients with RA and Lung Cancer

	Non-RA patients (n = 125,427)	RA Patients (n = 2864)	Total (n = 128,291)
Age			
50-64	36,252 (28.9%)	639 (22.3%)	36,891 (28.8%)
65+	89,175 (71.1%)	2,225 (77.7%)	91,400 (71.2%)
Sex			
Male	122,274 (97.5%)	2,719 (94.9%)	124,993 (97.4%)
Female	3,153 (2.5%)	145 (5.1%)	3,298 (2.6%)
Race*			
White	94,500 (75.3%)	2,268 (79.2%)	96,768 (75.4%)
Black	19,452 (15.5%)	354 (12.4%)	19,806 (15.4%
Other	2,420 (1.9%)	49 (1.7%)	2,469 (1.9%)
Ethnicity**			
Non-Hispanic	114,971 (91.7%)	2,666 (93.1%)	117,637 (91.7%)
Hispanic	2,890 (2.3%)	57 (2.0%)	2,947 (2.3%)
Tobacco Use***			
Never	11,918 (9.5%)	290 (10.1%)	12,208 (9.5%)
Former	30,457 (24.3%)	850 (29.7%)	31,307 (24.4%)
Current	65,377 (52.1%)	1,312 (45.8%)	66,689 (52.0%)
Cohort Entry			
2005-2010	40,624 (32.4%)	811 (28.3%)	41,435 (32.3%)
2011-2016	42,235 (33.7%)	951 (33.2%)	43,186 (33.7%)
2017-2023	42,568 (33.9%)	1,102 (38.5%)	43,670 (34.0%)
Lung Cancer Stage			
Stage 0	322 (0.3%)	10 (0.3%)	332 (0.3%)
Stage I	37,142 (29.6%)	942 (32.9%)	38,084 (29.7%)
Stage II	11,052 (8.8%)	265 (9.3%)	11,317 (8.8%)
Stage III	28,381 (22.6%)	615 (21.5%)	28,996 (22.6%)
Stage IV	48,530 (38.7%)	1,032 (36.0%)	49,562 (38.6%)

*Race data is missing: 9,055 (7.2%) in non-RA patients, 193 (6.7%) in RA patients and 9,248 (7.2%) in total patients.
**Ethnicity data is missing: 7,566 (6.0%) in non-RA patients, 141 (4.9%) in RA patients and 7,707 (6.0%) in total patients.
***Tobacco use data is missing: 17,675 (14.1%) in non-RA patients, 412 (14.4%) in RA patients and 18,087 (14.1%) in total patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Age-Adjusted Mortality Rates and Multivariable Adjusted Hazard Ratio

Table 2: Age-Adjusted Mortality Rates and Multivariable Adjusted Hazard Ratio

	Deaths	Person-Years (in 1,000)	Mortality Rate (95% CI)	Adjusted Hazard Ratio*
Non-RA Patients	103,840	280.37	370.38 (368.13, 372.64)	Referent
RA Patients	2,375	5.89	402.97 (386.70, 419.73)	1.09 (1.05,1.14)
Total Patients	106,215	286.25	371.05 (368.82, 373.29)	

*Models adjusted for age, sex, race, ethnicity, tobacco use, cohort entry, hypertension, coronary artery disease, stroke, asthma, bronchitis/emphysema, renal disease, diabetes, liver disease, depression, heart failure, hepatitis B, hepatitis C, other hepatitis, HIV, tuberculosis, prior cancer, and lung cancer staging.

as cancer stage and treatments. The cohort included patients aged 50 years or older at the time of lung cancer diagnosis. Pre-existing rheumatoid arthritis (RA) was identified based on the presence of ≥ 2 ICD-9 or ICD-10 codes for RA, 1 to 365 days apart, prior to the lung cancer diagnosis.

The association between RA and all-cause mortality was evaluated using Cox proportional hazards regression models, adjusting for demographic characteristics, smoking status, comorbid conditions, prior history of malignancy, and cancer stage at diagnosis.

Results: Among 128,291 patients with lung cancer, 2,864 (2.2%) had pre-existing RA. The cohort was predominantly male (97.4%), White (75.4%) and current smokers (52%) (Table 1). During follow-up, mortality rates were 370.4 and 403.0 per 1,000 person-years in the non-RA and RA groups, respectively. After adjusting for demographics, smoking status, comorbidities, prior malignancy, and lung cancer stage, RA was associated with increased all-cause mortality (adjusted hazard ratio 1.09; 95% CI: 1.05-1.14) (Table 2).

Conclusion: In this study using national VA data, pre-existing RA was associated with a modest but statistically significant increase in all-cause mortality. After adjusting for key clinical and demographic factors, patients with RA had a 9% higher risk of death compared to those without RA. These findings suggest that RA may independently contribute to poorer survival in patients with lung cancer, highlighting the need for integrative care strategies that address both oncologic and rheumatologic complexities in this high-risk population.

Disclosure: M. Nguyen: None; **A. Baraff**: None; **A. Schmidt**: None; **A. Peterson**: None; **A. Pabani**: None; **N. Smith**: None; **S. Gray**: None; **J. Garcia**: Aveo Oncology, 2, Catalym, 2, Pfizer, 5; **N. Weiss**: None; **N. Singh**: None.

Abstract Number: 2252

Association Between Frailty and Survival Among Older Adults with Rheumatoid Arthritis and Lung Cancer

Michelle Nguyen[1], Aaron Baraff[2], Alexander Peterson[2], Alexandra Schmidt[2], Katherine Wysham[3], Aliyah Pabani[4], Carolyn Presley[5], Nicholas Smith[1], Shelly Gray[1], Jose Garcia[6], Ariela Orkaby[7] and Namrata Singh[1], [1]University of Washington, Seattle, WA, [2]VA Puget Sound Health Care System, Seattle, WA, [3]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [4]Johns Hopkins, Washington, DC, [5]Ohio State University Medical Center, Columbus, [6]VA Puget Sound Health Care System, VA GRECC, and University of Washington, Seattle, WA, [7]VA Boston Healthcare System & Division of Aging, Brigham and Women's Hospital, Harvard Medical School & VA Geriatrics Research Education and Clinical Center, Boston, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Individuals with rheumatoid arthritis (RA) have a higher prevalence of frailty, even at younger ages, compared to the general population[1]. Among persons with lung cancer, frailty is associated with decreased survival[2]. However, this association has not yet been assessed among patients with lung cancer and pre-existing RA. The objective of this study was to better characterize the contribution of frailty to survival differences among older adults with RA and lung cancer.

Methods: Using nationwide electronic medical records data from the Veterans Health Administration, we included patients aged ≥ 50 years with a lung cancer diagnosis. RA was defined by ≥ 2 RA ICD-9/10 codes 1–365 days apart prior to cancer diagnosis. The validated Veterans Affairs Frailty Index (VA-FI) was used to characterize patient's frailty status. VA-FI is a validated electronic frailty index developed to measure frailty using administrative claims and electronic health records data in Veterans. Patients were characterized as robust, pre-frail, or frail. Cox proportional hazards regression models were used to assess the association between frailty status and survival, adjusting for demographics, smoking history, rheumatic disease comorbidity index (RDCI), prior cancer history, and tumor stage.

Table 1: Baseline Characteristics of Patients with RA and Frailty Veterans Affairs Frailty Index

	Robust (n = 999)	Pre-Frail (n = 735)	Frail (n =1,130)	Total (n = 2,864)
Age				
50-64	306 (30.6%)	178 (24.2%)	155 (13.7%)	639 (22.3%)
65+	693 (69.4%)	557 (75.8%)	975 (86.3%)	2,225 (77.7%)
Sex				
Male	955 (95.6%)	698 (95.0%)	1,066 (94.3%)	2,719 (94.9%)
Female	44 (4.4%)	37 (5.0%)	64 (5.7%)	145 (5.1%)
Race*				
White	773 (77.4%)	577 (78.5%)	918 (81.2%)	2,268 (79.2%)
Black	115 (11.5%)	100 (13.6%)	139 (12.3%)	354 (12.4%)
Other	< 10	20 (2.7%)	21 (1.9%)	49 (1.7%)
Ethnicity**				
Non-Hispanic	909 (91.0%)	694 (94.4%)	1,063 (94.1%)	2,666 (93.1%)
Hispanic	18 (1.8%)	15 (2.0%)	24 (2.1%)	57 (2.0%)
Cohort Entry				
2005-2010	487 (48.7%)	201 (27.3%)	123 (10.9%)	811 (28.3%)
2011-2016	467 (46.7%)	233 (31.7%)	251 (22.2%)	951 (33.2%)
2017-2023	45 (4.5%)	301 (41.0%)	756 (66.9%)	1,102 (38.5%)

*Race data is missing: 103 (10.3%) in robust patients, 38 (5.2%) in pre-fail patients, 52 (4.6%) in frail patients, and 193 (6.7%) in total patients.

**Ethnicity data is missing: 72 (7.2%) in robust patients, 26 (3.5%) in pre-fail patients, 43 (3.8%) in frail patients, and 141 (4.9%) in total patients.

Table 2: Age-Adjusted Mortality Rates and Multivariable Adjusted Hazard Ratio

	Deaths	Person-Years (in 1,000)	Mortality Rate (95% CI)	Adjusted Hazard Ratio*
Robust	930	2.40	403.29 (377.27, 430.59)	
Pre-Frail	605	1.56	398.85 (367.33, 432.33)	1.11 (1.00,1.24)
Frail	840	1.93	410.77 (382.24, 440.80)	1.27 (1.12,1.43)
Total	2375	5.89	403.40 (387.33, 419.95)	

*Models adjusted for age, sex, race, ethnicity, tobacco use, cohort entry, rheumatic disease comorbidity index (RDCI), RF positive, CCP positive.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We identified 2,864 patients with pre-existing RA and lung cancer; 77.7% were > 65 years, 94.9% were male, 79.2% were White, 93.1% non-Hispanic. Based on the VA-FI, 34% were categorized as robust, 26% pre-frail, and 39% frail (Table 1).

Age-adjusted mortality rates per 1,000 person-years were 403.3 for robust, 398.9 for pre-frail, and 410.8 for frail patients. In multivariable analysis, compared with robust persons, pre-fail persons had a mild increased risk of mortality (aHR 1.11; 95% CI: 1.00-1.24), while frail patients had a statistically significant higher risk (aHR 1.27; 95% CI: 1.12-1.43) (Table 2).

Conclusion: Among Veterans with RA and lung cancer, frailty was common and associated with worse survival. These findings highlight the prognostic importance of frailty and suggest it may be routinely assessed to guide risk stratification and clinical decision-making in this population.

Disclosure: M. Nguyen: None; **A. Baraff**: None; **A. Peterson**: None; **A. Schmidt**: None; **K. Wysham**: None; **A. Pabani**: None; **C. Presley**: None; **N. Smith**: None; **S. Gray**: None; **J. Garcia**: Aveo Oncology, 2, Catalym, 2, Pfizer, 5; **A. Orkaby**: None; **N. Singh**: None.

Abstract Number: 2253

Wrist-worn Wearable Device Data Can Be a New Digital Biomarker For Disease Activity In Rheumatoid Arthritis: a Multicenter Single-arm Prospective Study

Misako Higashida-Konishi[1], Keisuke Izumi[2], Shuntaro Saito Saito[3], Hiroki Tabata[4], Satoshi Hama[4], Tatsuhiro Oshige[4], Yutaka Okano[4], Hisaji Oshima[4], Katsuya Suzuki[4], Jiro Sakamoto[5], Toshikazu Fukami[5], Kazumichi Minato[5], Nobuhiko Kajio[6], Yasushi Kondo[3], Hiroaki Taguchi[6] and Yuko Kaneko[3], [1]NHO Tokyo Medical Center, Tokyo Meguroku, Japan, [2]Division of Rheumatology, Department of Medicine, NHO Tokyo Medical Center/Keio University School of Medicine/TechDoctor, Inc., Tokyo, Japan, [3]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [4]Division of Rheumatology, Department of Medicine, NHO Tokyo Medical Center, Tokyo, Japan, [5]TechDoctor, Inc., Tokyo, Japan, [6]Department of Rheumatology, Kawasaki Municipal Hospital, Kanagawa, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Previous studies have estimated physical and mental states using wearable device data such as from smartwatches [1–3]. This study aimed to identify digital biomarkers for RA to support telemedicine and clinical care.

Methods: Patients with RA who consented to participate in the study at the 3 sites wore a wristwatch-type wearable device for 3 months, and their RA-related patient-reported outcomes were prospectively recorded daily on a smartphone application which the authors had developed [1]. Attending physicians examined the participants every month for 3 months and the clinical data were also collected. From the wearable device, data on number of steps, metabolic equivalents (METs), heart rate-related data, and sleep- related data were obtained. Relationship between wearable device data and clinical disease activity index (CDAI) were evaluated, as well as the relationship between inflammation blood biomarkers (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)) and CDAI as controls. Correlation was analyzed univariately. Machine learning (ML) techniques, which included Lasso regression, Ridge regression, Random Forest, and XGBoost, were employed to model disease activity indices such as CDAI and simplified disease activity index (SDAI), using daily data from the wearable

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

device. We also implemented a ML classifier to detect elevated CRP (>0.14 mg/dL), and validated its performance with ROC analysis.

Results: A total of 129 patients successfully completed the 3-month observation period. At the start of the study, the mean age of patients was 55±13 years with a mean disease duration of 8.5±10.3 years. The mean CDAI and CRP levels were 13.5 ±10.7 and 0.39±0.71 mg/dL, respectively. Statistical analysis revealed that an increased number of daily steps was associated with lower disease activity (CDAI) (r = -0.28; 95% CI [-0.46, -0.047]; P = 0.018). In contrast, elevated heart rate during sleep (r = 0.23; 95% CI [0.03, 0.41]; P = 0.025), increased sympathetic activity (r = 0.33; 95% CI [0.09, 0.53]; P = 0.009), and a trend toward higher overall heart rate (r = 0.32; 95% CI [0.12, 0.50]; P = 0.002) were correlated with higher CDAI scores. Additionally, inflammation markers including CRP and ESR showed moderate correlations with CDAI (CRP: r = 0.33, 95% CI [0.24 to 0.42] P < 0.001) (ESR: r = 0.32, 95% CI [0.23 to 0.41]; P < 0.001). ML approaches demonstrated predictive ability, achieving an AUC of 0.90 for CDAI remission and a median absolute error (MAE) of 5.04 in predicting CDAI values. Similarly, performance for SDAI was strong, with an AUC of 0.82 and MAE of 5.12.

Conclusion: Metrics from wearable devices, including step counts and heart rate, were significantly associated with RA disease activity, supporting their potential as digital biomarkers. These correlations were comparable to those of traditional markers like CRP and ESR. Moreover, ML models using wearable data accurately predicted disease activity and inflammation, demonstrating their utility in practice and telemedicine.

References:

[1] Izumi K *et al*. *Ann Rheum Dis* 2021;80:1099-1100.
[2] Izumi K *et al*. *Front Psychiatry* 2021;12:611243.
[3] Izumi K *et al*. *Ann Rheum Dis* 2024;83:1587-1588.

Acknowledgement: M HK and KI are contributed equally.

Disclosure: M. Higashida-Konishi: Chugai, 6; **K. Izumi**: Abbvie, 6, Asahi Kasei, 6, Chugai, 6, Eisai, 6, Gilead Sciences, 6, TechDoctor, Inc, 4, Teijin Pharma, 6; **S. Saito**: None; **H. Tabata**: None; **S. Hama**: None; **T. Oshige**: None; **Y. Okano**: None; **H. Oshima**: None; **K. Suzuki**: AbbVie, 6, Asahi Kasei, 5, 6, Boehringer-Ingelheim, 6, Chugai, 6, Eisai, 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKline, 6, Mitsubishi Tanabe, 6, Pfizer, 6, Sanofi, 6, Taisho, 6, UCB, 6, Viatris, 6; **J. Sakamoto**: None; **T. Fukami**: None; **K. Minato**: None; **N. Kajio**: None; **Y. Kondo**: None; **H. Taguchi**: None; **Y. Kaneko**: AbbVie/ Abbott, 6, Asahi Kasei, 5, 6, Chugai, 5, 6.

Abstract Number: 2254

Association of Disease Activity with Insomnia, Depression, and Fatigue in Patients with Rheumatoid Arthritis: A Multicenter Prospective Observational Study

Misako Higashida-Konishi[1], Keisuke Izumi[2], Shuntaro Saito Saito[3], Hiroki Tabata[4], Satoshi Hama[4], Tatsuhiro Oshige[4], Yutaka Okano[4], Hisaji Oshima[4], Katsuya Suzuki[4], Jiro Sakamoto[5], Toshikazu Fukami[5], Kazumichi Minato[5], Nobuhiko Kajio[6], Yasushi Kondo[3], Hiroaki Taguchi[6] and Yuko Kaneko[3], [1]NHO Tokyo Medical Center, Tokyo Meguroku, Japan, [2]Division of Rheumatology, Department of Medicine, NHO Tokyo Medical Center/Keio University School of Medicine/ TechDoctor, Inc., Tokyo, Japan, [3]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [4]Division of Rheumatology, Department of Medicine, NHO Tokyo Medical Center, Tokyo, Japan, [5]TechDoctor, Inc., Tokyo, Japan, [6]Department of Rheumatology, Kawasaki Municipal Hospital, Kanagawa, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) often experience not only joint-related symptoms but also systemic issues such as insomnia, depression, and fatigue [1–3]. These symptoms may persist despite therapeutic advances and significantly impair quality of life [1]. This study aimed to clarify the prevalence of insomnia, depression, and fatigue in RA and examine their relationship with disease activity.

Methods: This prospective study enrolled RA patients who could respond to a structured questionnaire. Insomnia was assessed using the Athens Insomnia Scale (AIS), depressive symptoms were evaluated via the Patient Health Questionnaire-9 (PHQ-9), and fatigue was measured using both the Brief Fatigue Inventory (BFI) and the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Disease activity of RA was measured by the Disease Activity Score in 28 joints with CRP (DAS28-CRP), Clinical Disease Activity Index (CDAI), and Simplified Disease Activity Index (SDAI). Functional status of RA was determined through the Health Assessment Questionnaire-Disability Index (HAQ-DI). All patients met the 2010 American College of Rheumatology/ European League Against Rheumatism classification criteria [4] for RA.

Results: A total of 107 RA patients (90 female, 17 male) participated, with a mean age of 55 years and a mean disease duration of 82 months. The median DAS28-CRP was 2.9, CDAI was 10.2, SDAI was 10.2, and HAQ-DI was 0.5. Insomnia was reported in 85% of participants, and the AIS score was significantly associated with DAS28-CRP ($r=0.22$, $p=0.03$), CDAI ($r=0.23$, $p=0.03$), SDAI ($r=0.22$, $p=0.03$), and HAQ-DI ($r=0.22$, $p=0.03$). Depression was reported in 13% of participants, and the PHQ-9 score was significant associations with DAS28-CRP ($r=0.34$, $p< 0.01$), CDAI, ($r=0.34$, $p< 0.01$) and SDAI ($r=0.34$, $p< 0.01$). Severe fatigue was also reported in 85% of participants, with BFI scores significantly correlated with DAS28-CRP ($r=0.43$, $p< 0.01$), CDAI ($r=0.35$, $p< 0.01$), SDAI ($r=0.37$, $p< 0.01$), and HAQ-DI ($r=0.31$, $p< 0.01$). FACIT-F scores showed inverse correlations with DAS28-CRP ($r=0.47$, $p< 0.01$), CDAI ($r=0.42$, $p< 0.01$), SDAI ($r=0.43$, $p< 0.01$), and HAQ-DI ($r=0.25$, $p=0.01$). In addition, the components of disease activity assessment, especially the patient global visual analogue scale, were correlated with AIS ($r=0.32$, $p< 0.01$), PHQ-9 ($r=0.40$, $p< 0.01$), FACIT-F ($r=0.45$, $p< 0.01$), and BFI ($r=0.42$, $p< 0.01$).

Conclusion: Insomnia and fatigue were highly prevalent among RA patients, affecting over 80% of patients, while depression was identified in 13%. All symptoms showed associations with disease activity and functional impairment. These findings suggest that optimal RA management should also address psychological and fatigue-related symptoms.

References:

[1] Latocha KM *et al. Rheumatology (Oxford)*. 2023;62:1097-1107.
[2] Kwiatkowska B *et al. Psychol Health Med*. 2019;24:333-343.
[3] Pope JE. *RMD Open*. 2020;6:e001084.
[4] Aletaha D *et al. Arthritis Rheum*. 2010;62:2569-81.

Acknowledgement: M HK and KI are contributed equally.

Disclosure: M. Higashida-Konishi: Chugai, 6; **K. Izumi**: Abbvie, 6, Asahi Kasei, 6, Chugai, 6, Eisai, 6, Gilead Sciences, 6, TechDoctor, Inc, 4, Teijin Pharma, 6; **S. Saito**: None; **H. Tabata**: None; **S. Hama**: None; **T. Oshige**: None; **Y. Okano**: None; **H. Oshima**: None; **K. Suzuki**: AbbVie, 6, Asahi Kasei, 5, 6, Boehringer-Ingelheim, 6, Chugai, 6, Eisai, 6, Eli Lilly,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Gilead, 6, GlaxoSmithKline, 6, Mitsubishi Tanabe, 6, Pfizer, 6, Sanofi, 6, Taisho, 6, UCB, 6, Viatris, 6; **J. Sakamoto**: None; **T. Fukami**: None; **K. Minato**: None; **N. Kajio**: None; **Y. Kondo**: None; **H. Taguchi**: None; **Y. Kaneko**: AbbVie/Abbott, 6, Asahi Kasei, 5, 6, Chugai, 5, 6.

Abstract Number: 2255

Diagnostic Accuracy of Anti-Carbamylated Protein Antibodies in Rheumatoid Arthritis: A Systematic Review and Meta-analysis

Pannathorn Nakaphan[1], Patavee Pajareya[2], Priabprat Jansem[3], Somkiat Phutinart[2], Nattanicha Chaisrimaneepan[4] and Noppachai Siranart[2], [1]Department of Internal Medicine, Weiss Memorial Hospital, Chicago, IL, [2]Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [3]Department of Psychiatry, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand, [4]Department of Medicine, Texas Tech University Health Sciences Center, Lubbock, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-carbamylated protein antibodies (anti-CarP Ab) are emerging serologic markers in rheumatoid arthritis (RA). Anti-CarP Ab has a controversial diagnostic utility in RA but may be particularly useful in patients who are negative for traditional markers such as rheumatoid factor and anti-citrullinated protein antibodies (ACPA). This study aimed to evaluate the diagnostic accuracy of anti-CarP Ab in RA patients with both ACPA-negative (ACPA-) and ACPA-positive (ACPA+) subgroups.

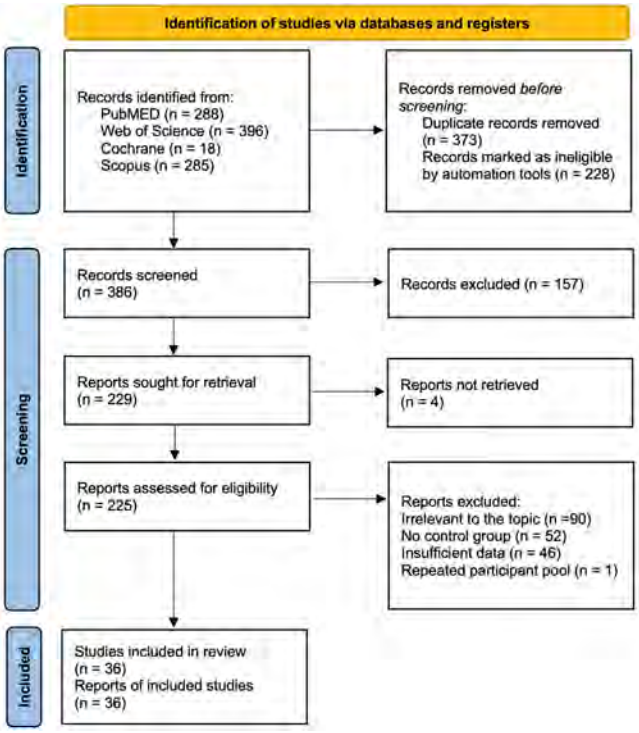


Figure 1. PRISMA Flow Diagram of Studies Included In the Meta-analysis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Diagnostic Accuracy of Anti-carbamylated Protien Antibodies in Rheumatoid Arthritis Patients

A) All

	Overall		ACPA-		ACPA+	
Outcome	Outcomes	I^2	Outcomes	I^2	Outcomes	I^2
Sensitivity	44% (39-49%)	91.5%	24% (18-31%)	87.2%	49% (41-57%)	94.0%
Specificity	96% (94-97%)	65.5%	95% (93-97%)	70.3%	95% (93-97%)	72.0%
PLR	9.27 (7.17-11.36)	99.3%	6.01 (3.96-8.060)	97.3%	14.09 (8.58-19.60)	99.8%
NLR	0.62 (0.55-0.68)	0.0%	0.85 (0.75-0.94)	0.0%	0.51 (0.42-0.61)	0.0%
DOR	14.72 (10.75-20.15)	62.1%	5.29 (3.64-7.67)	41.3%	18.38 (10.36-32.61)	82.0%
SROC (AUC)	0.825		0.755		0.855	

B) FCS Subgroup

	Overall		ACPA-		ACPA+	
Outcome	Outcomes	I^2	Outcomes	I^2	Outcomes	I^2
Sensitivity	41% (38-45%)	82.3%	17% (14-22%)	75.1%	52% (46-59%)	87.1%
Specificity	96% (95-98%)	59.6%	97% (96-98%)	0.0%	97% (96-98%)	0.0%
PLR	13.31 (8.34-18.28)	99.5%	7.47 (3.92-11.02)	97.9%	20.90 (13.21-28.60)	99.6%
NLR	0.62 (0.53-0.70)	0.0%	0.87 (0.76-0.98)	0.0%	0.49 (0.38-0.60)	0.0%
DOR	16.94 (12.04-23.85)	38.1%	5.57 (3.90-7.96)	0.0%	34.69 (21.26-56.60)	44.5%
SROC (AUC)	0.749		0.955		0.964	

C) IgG Subgroup

	Overall		ACPA-		ACPA+	
Outcome	Outcomes	I^2	Outcomes	I^2	Outcomes	I^2
Sensitivity	43% (38-48%)	92.8%	21% (16-27%)	83.7%	54% (47-61%)	91.8%
Specificity	96% (94-98%)	60.7%	96% (93-97%)	67.9%	96% (93-97%)	67.9%
PLR	9.66 (6.47-12.85)	99.3%	6.73 (3.64-9.83)	97.9%	17.29 (10.10-24.48)	99.7%
NLR	0.61 (0.53-0.70)	0.0%	0.85 (0.74-0.97)	0.0%	0.49 (0.38-0.60)	0.0%
DOR	15.20 (9.95-23.23)	59.6%	5.38 (3.35-8.63)	43.4%	25.33 (14.08-45.58)	71.8%
SROC (AUC)	0.791		0.669		0.847	

Diagnostic Accuracy of Anti-carbamylated Protien Antibodies in Rheumatoid Arthritis Patients
ACPA, anti-citrullinated protein antibodies; FCS, fetal calf serum; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; SROC, summary receiver operating characteristic curve; AUC, area under the curve

Methods: We systematically searched MEDLINE, Scopus, Web of Science and the Cochrane Library through April 2025. Studies reporting sensitivity and specificity of anti-CarP Ab testing in established RA patients were included. The primary outcome was diagnostic accuracy compared to healthy controls. Secondary outcomes included subgroup analyses of ACPA- and ACPA+ patients.

Results: Thirty-six studies comprising 7431 RA patients and 3347 healthy controls were included. Most used in-house ELISA platforms; fetal calf serum (FCS) was the most common antigen, and IgG was the predominant isotype for detection. Primary outcomes: Anti-CarP Ab showed high accuracy as a diagnostic tool in detecting RA with pooled sensitivity and specificity of 44% (95% CI: 39-49%, I^2 = 91.5%) and 96% (95% CI: 94-97%, I^2 = 65.5%), respectively. The positive likelihood ratio was 9.27 (95% CI: 7.17–11.36, I^2 = 99.3%), negative likelihood ratio was 0.62 (95% CI: 0.55–0.68, I^2 = 0.0%), and diagnostic odds ratio (DOR) was 14.72 (95% CI: 10.75–20.15, I^2 = 62.1%). The area under the curve (AUC) of the summary receiver operating characteristic curve (SROC) was 0.825. Subgroup analysis among studies using FCS (n = 16) showed pooled sensitivity of 41% (95% CI: 38-45%, I^2 = 82.3%) and specificity of 96% (95% CI: 95-98%, I^2 = 59.6%). In studies detecting IgG only (n =19), sensitivity was 43% (95% CI: 38-48%, I^2 = 92.8%) and specificity was 96% (95% CI: 94-98%, I^2 = 60.7%). Secondary outcomes: **ACPA- group:** pooled sensitivity and specificity were 24% (95% CI: 18-31%, I^2 = 87.2%) and 95% (95% CI: 93-97%, I^2 = 70.3%). DOR was 5.29 (95% CI: 3.64-7.67, I^2 = 41.3%) and AUC of SROC was 0.755 **ACPA+ group:** pooled sensitivity and specificity were 49% (95% CI: 41-57%, I^2 94.0%) and 95% (95% CI: 93-97%, I^2 = 72.0%). DOR was 18.38 (95% CI: 10.36-32.61, I^2 = 82.0%) and AUC of SROC was 0.855.

Conclusion: Anti-CarP Ab demonstrates high specificity but low sensitivity for RA diagnosis. Anti-CarP Ab is recommended as a complementary diagnostic tool, particularly in patients who are negative for ACPA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

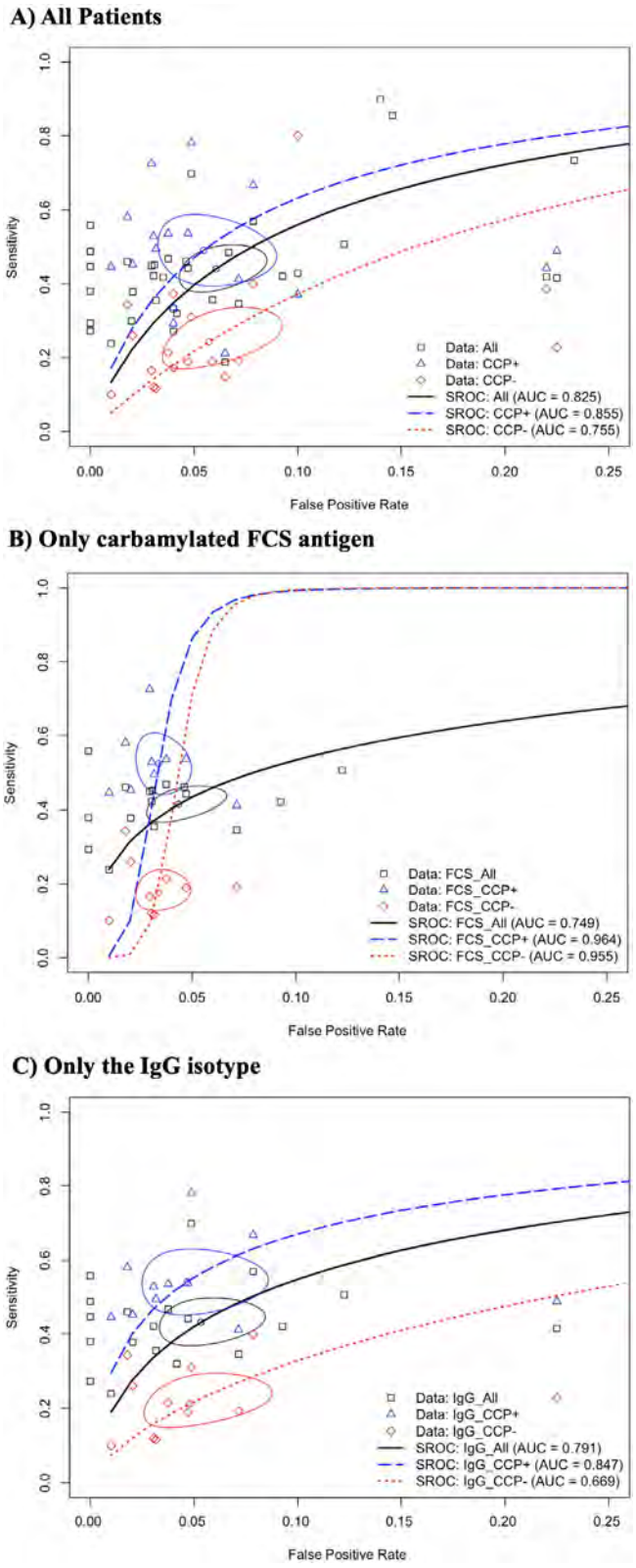


Figure 3. Summary Receiver Operating Characteristic Curve of Anti-carbamylated Protien Antibodies

Disclosure: P. Nakaphan: None; **P. Pajareya**: None; **P. Jansem**: None; **S. Phutinart**: None; **N. Chaisrimaneepan**: None; **N. Siranart**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2256

Improved Outcomes of Acute Myocardial Infarction Among Patients with Rheumatoid Arthritis: A Propensity Matched National Study

Qurat Ul Ain[1] and MIrza faris Ali Baig[2], [1]Medstar Georgetown University Hospital, Arlington, VA, [2]Medstar Health, Arlington, VA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The increased risk of cardiovascular morbidity and mortality with rheumatoid arthritis has been increasingly acknowledged over the past decades. Cardiovascular disease risk management for patients with rheumatoid arthritis is essential. This retrospective population-based study investigated in-hospital outcomes among adult patients admitted with acute myocardial infarction (AMI), with a specific focus on the impact of rheumatoid arthritis (RA) on these outcomes.

Methods: Data was derived from the National Inpatient Sample (NIS) database, between January 1, 2018 and December 31, 2021,

encompassing a large and diverse cohort of hospitalized individuals. The primary outcome analyzed was in-hospital mortality, with secondary outcomes being the utilization of diagnostic angiography, rates of percutaneous coronary intervention (PCI), and the incidence of complications such as acute kidney injury (AKI), cardiogenic shock, cardiac arrest, ventricular tachycardia (VT), ventricular fibrillation (VF), as well as requirements for mechanical ventilation, tracheal intubation, and mechanical circulatory support (MCS). Additional parameters examined were length of stay (LOS) and total hospitalization charges.

The study population comprised of 2,275,150 patients, predominantly Caucasian (71%), followed by African American patients (11%), with females representing 36.4% of the cohort. The mean age across the population was 66.5 years (±2.8 years). Among these patients, 39,270 (1.7%) had a documented history of rheumatoid arthritis. Owing to the significant difference in sample size between patients with AMI in the presence and absence of RA, a propensity score matching

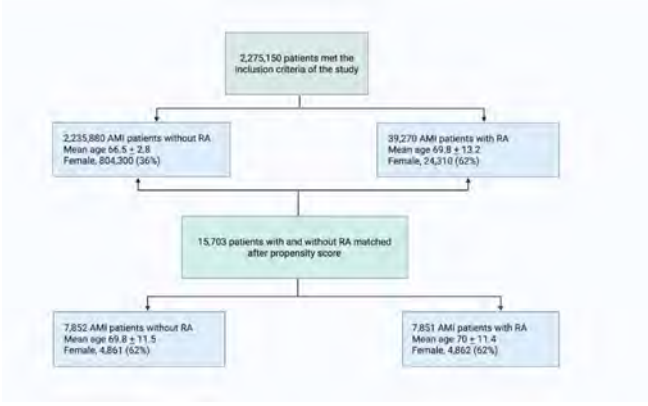


Figure 1.0 Schema representing study population pre and post propensity score matching.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Demographics	AMI without RA	AMI with RA	p-value
Women, no. (%)	4,861 (62%)	4,862 (62%)	0.88
Age, mean (SD)	69.8 (11.5)	70 (11.4)	0.14
Race/Ethnicity:			
- Caucasian	6,078 (79.3%)	5,951 (77.6%)	<0.001
- African American	697 (9%)	808 (10.5%)	<0.001
- Hispanic	460 (6%)	565 (7.4%)	<0.001
Charlson Comorbidity Index:			
- 1	9 (0.1%)	0 (0%)	<0.001
- 2	28 (0.3%)	366 (4.6%)	<0.001
- 3	20 (0.2%)	436 (5.5%)	<0.001
- >4	7,796 (99.2%)	7,051 (89.8%)	<0.001
Diabetes mellitus, no. (%)	1,909 (24.3%)	1,912 (24.3%)	0.59
Hypertension, no. (%)	1,431 (80%)	1,418 (79.4%)	0.58
Hyperlipidemia, no. (%)	4,990 (63.5%)	4,976 (63.4%)	0.18
Obesity, no. (%)	1,631 (20.7%)	1,555 (20%)	0.13
COPD, no. (%)	1,956 (25%)	1,980 (25.2%)	0.65
Chronic kidney disease, no. (%)	1,395 (17.7%)	1,439 (18.3%)	0.36
Chronic liver disease (CLD), no. (%	52 (0.6%)	76 (1%)	0.03
Atrial fibrillation, no. (%)	1,429 (18.2%)	1,603 (20.4%)	<0.001
Coronary artery disease (CAD), n	6,147 (78.2%)	6,122 (78%)	0.26

Figure-2 Post propensity pateint characteristics

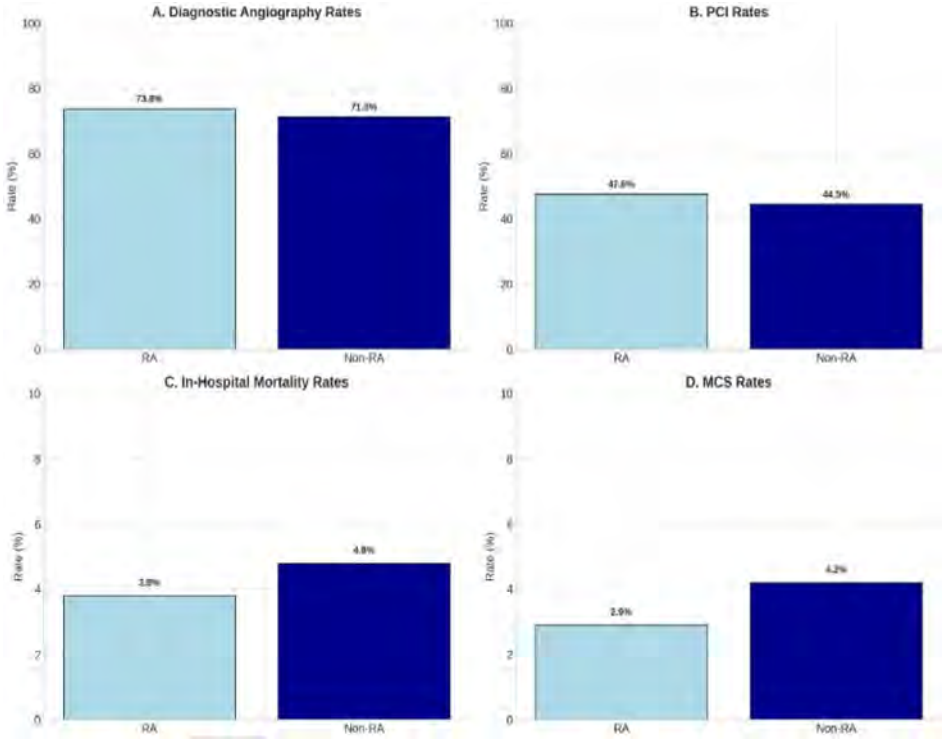


Figure-3 Outlines lower rate of Acute myocardial infarction (AMI) moratality, lower utilization of mechanical circulatory support, higher rates of diagnostic angiography and PCI in RA group.

(PSM) algorithm was employed to generate comparable groups. Post-matching, 15,703 patients from each cohort were selected, ensuring a similar distribution of age, sex, race, and Charlson Comorbidity Index score.

Results: Comparative analysis of the matched cohorts revealed notable differences in outcomes. Patients with RA experienced a lower rate of in-hospital mortality (3.8% vs. 4.8%, $P < 0.001$) compared to those without RA. Additionally, the utilization of mechanical circulatory support was lower in the RA group (2.9% vs. 4.2%). In contrast, the RA cohort demonstrated higher rates of diagnostic angiography (74% vs. 71%, $P < 0.001$) and PCI (48% vs. 44%), suggesting a more aggressive diagnostic and interventional approach.

Conclusion: The study highlights that despite previous associations of rheumatoid arthritis with increased mortality largely due to cardiovascular complications, advancements in disease management and therapeutic interventions may have contributed to improved in-hospital outcomes in this subgroup. The observed higher utilization of diagnostic and interventional

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

procedures in the RA group may reflect heightened clinical vigilance and a lower threshold for invasive testing in this high-risk population. Overall, these findings underscore the importance of continued physicain and pateint education, along with implementation of preventive strategies, to optimize outcomes in patients with Rheumatoid arthritis.

Disclosure: Q. Ul Ain: None; **M. Baig**: None.

Abstract Number: 2257

Impact of Family History of RA in Patients Evaluated for Arthralgia: A Comprehensive Analysis of the Reuma-check Cohort

Rodrigo García Salinas[1], Juan Arguello[2], Santiago Ruta[3], Ronald Perez[2] and Sebastian Magri[4], [1]Hospital Italiano La Plata, La Plata, Argentina, [2]Hospital Italiano de La Plata, La Plata, Argentina, [3]Hospital San Martin de La Plata, La Plata, Argentina, [4]Hospital Italiano La Plata, Melchor Romero, Argentina

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

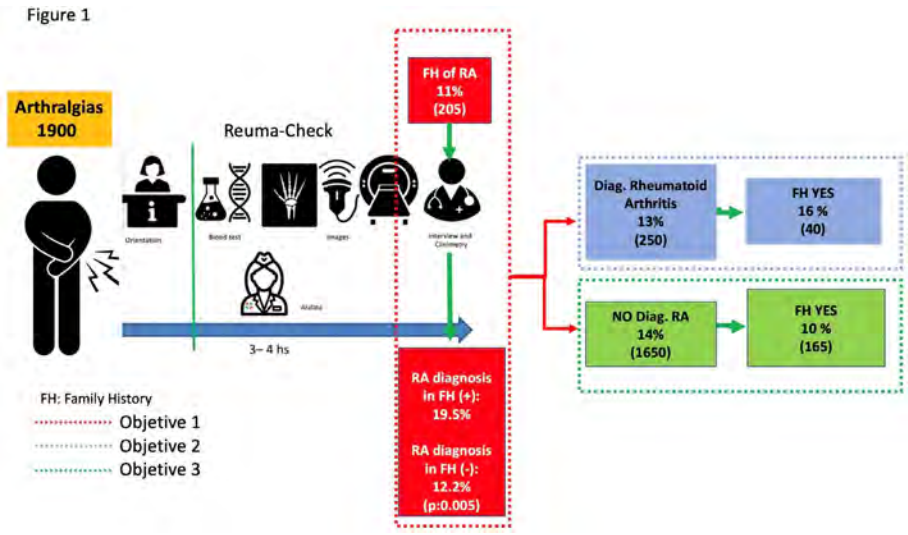
Background/Purpose: First-degree family history of rheumatoid arthritis (RA) is a relevant factor in genetic predisposition and early diagnosis of the disease. Objectives: 1)Estimate the frequency of family history (FH) in consecutive patients with arthralgia and its association with the final diagnosis of RA. 2) Analyze the differences between patients diagnosed with RA, according to the presence or absence of FH. 3) Compare the characteristics of patients with arthralgia without a diagnosis of RA, differentiating those with and without FH.

Methods: This was an observational study where patients with arthralgia were admitted to the Reuma-check program. At baseline, laboratory tests (ESR, CRP, RF, and ACPA), ultrasonography (US), and X-ray were performed. Sociodemographic,

Table 1:

RA Diagnosis (n=250)	FH Yes (n=40)	FH No (n=210)	p-value	OR (95% CI)
Comorbidities (any) %	75	55	0.02	2.4 (1.1-5.2)
Sex Female(%)	90	72	0.01	3.5 (1.2–10)
Symptoms >1 year, %	49	30	0.02	2.2 (1.1-4)
MCP Joint Symptoms, %	87.5	61	0.002	4.5 (1.69–12.22)
Morning Stiffness > 60 Min (%)	62	32	<0.001	3.5 (1.7–7)
Difficulty to Make Fist (%)	47	28	0.006	2.3 (1–4.71)
Positive MCP Squeeze Test (%)	65	38	0.001	2.6 (1.3–5.3)
X-ray Narrowing %	16	39	0.007	0.3 (0.1-0.7)
VAS (mean ± SD)	62 ± 17	54 ± 19	0.02	-
DAS28 (mean ± SD)	4.7 ± 1.47	4.1 ± 1.38	0.006	-
Non-RA Patients (n=1651)	**FH Yes (n=165)**	**FH No (n=1486)**	**-**	**OR (95% CI)**
Sex Female(%)	89	78	0.01	2.3 (1.3–3.8)
Hypertension (%)	17.6	25.4	0.03	0.63 (0.41–0.95)
Morning Symptom Severity (%)	60	52	0.04	1.4(1.01–1.9)
MCP Joint Symptoms (%)	60	47	0.001	1.7 (1.2–2.3)
Difficulty to Make Fist (%)	28	18	0.001	1.8 (1.2–2.6)
Morning Stiffness > 60 Min (%)	25	15	0.001	1.9 (1.2–2.7)
Positive MCP Squeeze Test (%)	42	21	<0.001	2.67 (1.9–3.7)
Age (years, mean ± SD)	47.8 ± 13.4	52.5 ± 14.4	<0.001	-
ANA+, %	26	19	0.04	1.5 (1.1-2.3)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



clinical, and clinimetry data (28-joint count – HAQ), including first-degree family history of RA, were also collected. Each evaluator was blinded to the results of the other studies (fig1). Once the circuit was completed, the diagnosis of RA was established. Descriptive statistics and logistic regression were performed.

Results: A total of 1900 patients with arthralgia were evaluated: 77% were women, with a mean age of 52 years (SD 14). 10.8% (n=205; 95% CI: 9.5%-12.3%) had FH. Patients with FH showed a higher prevalence of RA (19.5% vs. 12.2%; OR: 1.75; 95% CI: 1.2-2.55; p=0.005).

Patients diagnosed with RA (n=250) and FH (16%, n=40) presented distinct characteristics compared to those without FH, showing a more severe RA, Significant differences in univariate analysis between patients diagnosed with RA with and without FH are shown in Table 1. Significant variables in the univariate analysis were included in the multivariate logistic regression model. The results showed that involvement of metacarpophalangeal (MCP) joints presented an independent association in patients with RA and FH (OR = 4.24, 95% CI: 1.35–13.31, p = 0.013).

In patients with arthralgia without a diagnosis of RA (n=1651), those with FH (10%, n=165) showed more severe features in the univariate analysis (Table 1). Logistic regression showed an independent association with positive MCP squeeze (OR: 2.26; 95% CI: 1.57-3.27; p< 0.001), female sex (OR: 1.92; 95% CI: 1.14-3.21; p=0.013) and Youngest age at consultation (OR: 0.8 CI: 0.78-0.9; p=0.001).

Conclusion: The frequency of FH is 11% in patients with arthralgia and is associated with a higher risk of RA diagnosis. Patients with RA and FH present distinct severity characteristics. In patients with arthralgia without a diagnosis of RA, the presence of FH is associated with more severe clinical features of arthralgia.

Disclosure: R. García Salinas: AbbVie/Abbott, 2, 5, 6, Adium, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Raffo, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **J. Arguello**: None; **S. Ruta**: None; **R. Perez**: None; **S. Magri**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2258

Clinical Associations of Pulmonary Hypertension in RA Patients with and Without Interstitial Lung Disease

Sanjita Gowda[1], Yuri Matusov[2], Amara Seng[1], Nunzio Bottini[3] and Jon Giles[4], [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]Cedars-Sinai Medical Center, Los Angeles, [3]Cedars Sinai Medical Center, Beverly Hills, CA, [4]Cedars Sinai Medical Center, Los Angeles, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Pulmonary diseases are contributors to the morbidity and mortality of RA. Despite the recent surge in studies of RA-associated interstitial lung disease (RA-ILD), there have been few studies of pulmonary hypertension (PH) in and out of the context of symptomatic RA-ILD. We explored clinical associations and mortality of PH in RA.

Methods: Data were extracted from the electronic medical record of a large, urban, referral medical system between 1/1/2012 and 10/25/24. RA, ILD, and PH were defined based on ICD-10 codes at two distinct time points. We compared clinical characteristics within the RA cases according to the presence/absence of ILD and/or PH. These were further compared with non-RA controls with ILD and/or PH. Generalized linear models were used to adjust for relevant confounders.

Results: A total of 10,824 RA patients were identified. ILD was diagnosed in 526 (5%), among whom 171 (33%) were also diagnosed with PH. PH without ILD was diagnosed in 595 (6%). Among 6,954 non-RA controls with ILD, only 1,649 (24%) also had PH (OR 1.55; p< 0.001 compared with RA). This difference was maintained after adjustment for demographics and smoking (OR=1.41; p=0.001). Within the RA group, those with RA+ILD were less likely to be female than those with RA only (72% vs 78%, respectively, p=0.007), while those with RA+PH and RA+ILD+PH did not differ significantly on sex compared with those with RA only. Black race was more frequent in those with RA+PH and RA+ILD+PH compared with those with RA only (23% and 25% vs. 12%, respectively; p< 0.0001 for both comparisons). Ever smoking was more common for all subtypes of RA lung involvement compared with those with RA only, but current smoking did not differ substantially. Current alcohol use was lower among those with all subtypes of RA lung disease compared with those with RA only. Median CRP was highest in those with RA+ILD and RA+ILD+PH (4.2 and 4.0 mg/L, respectively), and was higher than in those with RA only and RA+PH. Age at death was the lowest for those with RA+ILD+PH (Fig. 1), with a trend to lower age at death for those

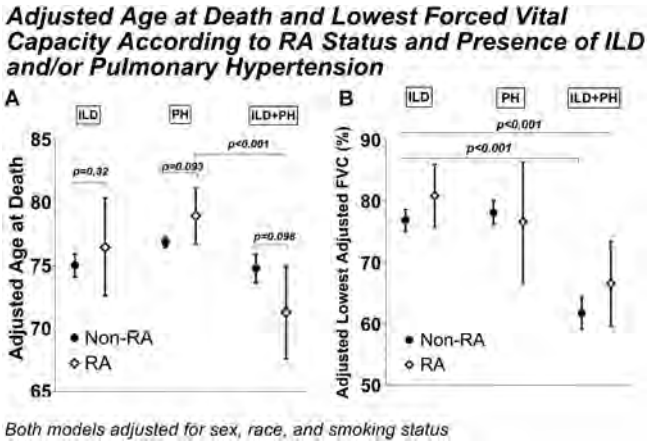


Figure 1: Adjusted Age at Death and Lowest Forced Vital Capacity According to RA Status and Presence of ILD and/or Pulmonary Hypertension

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

with RA+ILD+PH compared with those without RA with ILD+PH. Compared with those with ILD, those with ILD+PH, regardless of RA status, had lower adjusted FVC % predicted (Fig. 1).

Conclusion: The combination of ILD and PH may be more prevalent among RA patients compared with those with ILD who do not have RA and is associated with higher morbidity and mortality. Improved screening and management of PH in RA-ILD may reduce this burden.

Disclosure: S. Gowda: None; **Y. Matusov**: Aerovate, 5, Jupiter Endovascular, 2, Mallinckrodt, 5, Penumbra, 5, Tenax, 5; **A. Seng**: None; **N. Bottini**: Merck/MSD, 2; **J. Giles**: AbbVie/Abbott, 2, Eli Lilly, 2, Genentech, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Sana, 2.

Abstract Number: 2259

Lung Transplant Outcomes in Patients with Rheumatoid Arthritis Associated Interstitial Lung Disease Compared to Idiopathic Pulmonary Fibrosis: A Multicentric Retrospective Analysis and Meta-analysis

Saud AlHajeri[1], Matthew Major[2], Darya S. Jalaledin[3], Beatrice Daviault[4], Arusa Shah[5], Alec Yu[6], Sabrina Hoa[7], Robert Levy[8], Jennifer Wilson[1], Charles Poirier[4], James Choi[6], John Yee[6], Océane Landon-Cardinal[9], Kun Huang[10] and Hyein Kim[11], [1]UBC, Vancouver, BC, Canada, [2]University of British Columbia, Vancouver, Canada, [3]Universitä de Montréal, Saint-Lambert, QC, Canada, [4]University of Montreal, Montreal, QC, Canada, [5]University of Montreal, Montreal, BC, Canada, [6]University of British Columbia, Vancouver, BC, Canada, [7]University of Montreal, Brossard, QC, Canada, [8]University of British Columbia, Deerfield, IL, [9]Centre hospitalier de l'Universitä de Montréal, Montréal, QC, Canada, [10]University of British Columbia, Vancouver, Surrey, BC, Canada, [11]The University of British Columbia, Vancouver, BC, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a frequent complication of rheumatoid arthritis (RA), ranging from subclinical ILD to advanced fibrosis, and is associated with significant morbidity and mortality. Despite advancing immunosuppressive and antifibrotic therapies, many progress to end-stage respiratory failure and may require lung transplantation. The aim of this study was to compare clinical characteristics and lung transplant outcomes in patients with RA to idiopathic pulmonary fibrosis (IPF). In addition, a meta-analysis was performed to evaluate RA-ILD lung transplant outcomes in the literature.

Methods: We retrospectively analyzed clinical data collected in patients with ILD diagnosed with RA and IPF who underwent bilateral lung transplant between January 1, 2014 and April 30, 2024 at the Vancouver General Hospital, and between January 1, 2012 and December 31, 2024 at the Centre hospitalier de l'Université de Montréal. All RA patients satisfied their respective ACR classification criteria. Continuous variables were analyzed using the Mann-Whitney U test, categorical variables with Fisher's Exact test, and survival using Kaplan-Meier analysis.

For meta-analysis, we searched MEDLINE, Embase and the Cochrane Database of Systematic Reviews from database inception to April 6, 2025. Participants were individuals with RA-ILD who underwent lung transplants. The outcomes studied were overall survival and morbidity following transplant. Bibliographies of selected articles were hand-searched for additional

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

references. Data were extracted using a standardized extraction form. Study quality was assessed using the Newcastle-Ottawa Scale. Pooled post-transplant survival was combined for RA-ILD and IPF individually using a random effects model.

Results: In the retrospective analysis, we identified 27 RA and 64 IPF patients. RA patients were younger than IPF patients at ILD diagnosis (median age 57 vs 60.5, p=0.0028), more likely to be on pre-transplant immunosuppression (92.6% vs 6.2%, p< 0.001), and less likely to receive antifibrotics (22.2% vs 64.1%, p< 0.001). No difference was seen in one-year or cumulative survival. Post-transplant lung function, acute rejection, infection-related hospitalization, malignancy, and chronic lung allograft dysfunction (CLAD) were similar. IPF patients had more UIP patterns on explant pathology, whereas RA patients had more NSIP or mixed NSIP/UIP patterns.

Table 1. Patient baseline characteristics, pre-transplant variables and post-transplant outcomes.

Variables	RA (n=27)	IPF (n=64)	P value
Demographics			
Age at RA diagnosis, median [IQR]	52.5 [40.3-59.3]	NA	
Age at ILD Diagnosis, median [IQR]	57 [47.8-60.5]	60.5 [58 - 64]	**0.0028**
Age at lung transplant, mean [IQR]	62.2 [54.5-67.7]	65 [62 – 68]	0.054
Female, n (%)	11 (37)	11 (17)	0.056
White, n (%)	25 (93)	51 (80)	0.14
Smoker, n (%)	20 (74)	47 (73)	0.81
BMI, median [IQR]	28 [25-29.5]	27.6 [24 – 29.2]	0.49
Charleson Comorbidity index, median [IQR]	3 [2-4]	3 [2 - 4]	0.55
Variables at transplant			
FVC (% of predicted), median [IQR]	50 [44.5 – 66.8]	51 [39 – 64]	0.48
DLCO (%of predicted), median [IQR]	31 [25.2 – 43.2]	31 [24 – 38]	0.84
PASP (mmHg), median [IQR]	37 [33 – 43]	35 [31 – 42]	0.33
RA diagnosis to transplant (years), median [IQR]	6.1 [4.2-12.4]	NA	
ILD diagnosis to transplant (years), median [IQR]	3.9 [2.4 – 8.5]	3.9 [2.3 – 5.8]	0.63
Prior use of immunosuppressants, n (%)	25 (92.6)	4 (6.2)	**< 0.001**
Prior use of antifibrotic, n (%)	6 (22.2)	41 (64.1)	**< 0.001**
ICU admission prior to transplant, n (%)	3 (11.1)	9 (14.1)	0.75
CMV mismatch Donor (+) / Recipient (-), n (%)	6 (22.2)	9 (14.1)	0.38
Emergent transplant, n (%)	9 (33.3)	15 (23.4)	0.32
Dominant explant pathology			
UIP, n (%)	14 (51.8)	62 (96.9)	**< 0.001**
NSIP, n (%)	5 (18.5)	0 (0)	**0.003**
OP, n (%)	0 (0)	0 (0)	NA
Mixed NSIP/UIP, n (%)	6 (22.2)	0 (0)	**< 0.001**
Mixed NSIP/OP, n (%)	2 (7.4)	0 (0)	1
Unclassifiable, n (%)	0 (0)	2 (3.1)	1
1 Year outcomes			
Alive, n (%)	25 (92.6)	59 (92)	1
Post-transplant ICU days, median [IQR]	5 [3 - 8]	4 [3 – 9]	0.45
Post-transplant hospitalization days, median [IQR]	25 [18- 38]	22 [17 – 31]	0.63
FVC (% of predicted), median [IQR]	78 [68 – 98]	84 [67 – 99]	0.71
DLCO (%of predicted), median [IQR]	57 [44 – 66]	61 [45 – 75]	0.59
Acute Rejection, n (%)	12 (44)	31 (48)	0.66
Pneumonia requiring hospitalization, n (%)	7 (26)	20 (31)	0.63
Non-pulmonary infection requiring hospitalization, n (%)	5 (18)	14 (22)	0.79
Fungal infection requiring therapy, n (%)	5 (18)	22 (34)	0.21
CMV viremia requiring therapy, n (%)	6 (22)	15 (23)	0.79
Long-term outcomes			
Follow-up duration (years), median [IQR]	3.9 [1.8 – 5.1]	3.6 [2.1 – 6.2]	0.55
Alive at last follow-up, n (%)	19 (70)	42 (66)	0.98
CLAD, rate per 100 person years	4.81	6.57	0.54
CLAD, Rate Ratio [95% CI]	0.73 [0.27, 1.97]	reference	
Post-transplant malignancy, rate per 100 person years	1.92	4.38	0.28
Post-transplant malignancy, Rate Ratio [95% CI]	0.44 [0.1, 1.96]	reference	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan Meier survival curve

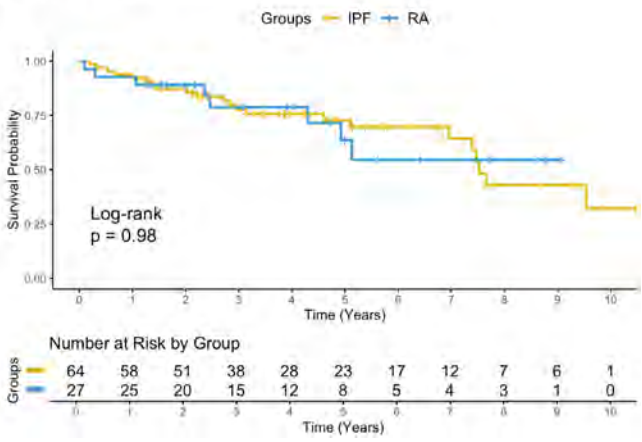
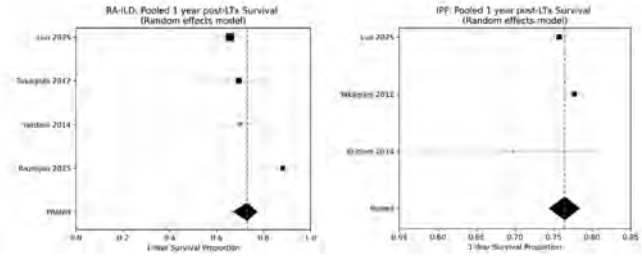


Figure 2: Meta-analysis forest plot of one-year post-transplant survival rate of RA-ILD patients and IPF patients.



For our meta-analysis, four studies met inclusion criteria. At one year post-transplant, the pooled survival rate of RA-ILD patients was 72.1% (60.5-82.3% 95% CI, I^2=45.8%), whereas in IPF patients, the pooled survival was 76.5% (74.6-78.2% 95% CI, I^2=61.8%).

Conclusion: Post-transplant survival, lung function, and complication rates were comparable between RA and IPF patients at one year and at last follow-up, with the median follow up duration being 3.9 years and 3.6 years respectively. Our meta-analysis demonstrated improved short-term survival following lung transplantation compared to previously reported studies.

Disclosure: S. AlHajeri: None; **M. Major**: None; **D. S. Jalaledin**: None; **B. Daviault**: None; **A. Shah**: None; **A. Yu**: None; **S. Hoa**: None; **R. Levy**: None; **J. Wilson**: None; **C. Poirier**: None; **J. Choi**: None; **J. Yee**: None; **O. Landon-Cardinal**: None; **K. Huang**: AbbVie/Abbott, 6, Fresenius Kabi, 6, Novartis, 6, Pfizer, 5; **H. Kim**: Abbvie, 6, Boehringer Ingelheim, 6, Fresenius Kabi, 6, Johnson and Johnson, 6, Mallinckrodt, 6, Norvatis, 6, Pfizer, 6.

Abstract Number: 2260

Generative AI model identifies patients with Rheumatoid Arthritis (RA) months prior the diagnosis date: results from a large real-world RA cohort

Shant Ayanian[1], Siavash Rezaei[2], Daniel Darveaux[3], Marc Blasi[3] and Elena myasoedova[1], [1]Mayo Clinic, Rochester, MN, [2]Cerebras, Santa Clara, CA, [3]Mayo Clinic, Rochester

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Clinical notes typically contain a valuable trove of information which is rarely used in predictive modeling given the complexity of working with unstructured data. As artificial intelligence (AI) advances and multimodal models become necessary to discern complex clinical relationships, the data encoded in clinical notes become extremely important to use. We aimed to apply a generative AI model, i.e. Jina-embeddings –V3 (Jina) model to medical records of patients with rheumatoid arthritis (RA) and show its ability to extract relevant phenotypic features of RA, testing the hypothesis that the model will be able to predict RA diagnosis before the clinical diagnosis.

Methods: The study included 4100 patients with RA diagnosis between 2000 and 2024 mean age was 61.1 (13.4) , 2870 (70%) females, 2450 (59.7%) RF and/or CCP antibody positive). RA was defined as 2 ICD 9/10 codes at least 30 days apart, and each case was confirmed by manual record review, as well as around 80000 persons without RA with notes from the same time period. The notes were arranged in chronological order. Jina was chosen as the embedding model to fine tune given its excellent performance as compared to its relatively small size of 570 million parameters. The model was hosted on a Google cloud container which also hosted a separate storage bucket for all clinical notes extracted for the manually curated dataset of patients with and without RA. The Jina model was fine-tuned on 70% of these notes while the rest of the notes were saved for testing and validation. The fine tuning was performed on the equivalent of 8 H100 GPU (graphic processing units) over the course of 12 hours.

Results: The total number of notes used during the fine-tuning process was 7.8 million. This included 1.2 million notes from patients with RA and 6.6 million notes from persons without RA. These notes included all physician provider notes from any specialty, as well as allied health notes such as nursing notes and clinical communications, as summarized in Table 1. After the model was trained, it was tested on 3.2 million notes (2.6 million non RA and 650K RA patients). Mean duration of available follow up prior to RA diagnsis was: 8.7 yrs (SD 11 yrs). The model was able to discern between patients with RA and without RA with an average precision of 0.8 up to 12 months in advance of their RA diagnosis date.

Conclusion: We showed the ability of the generative AI model (i.e., the fine-tuned Jina embedding model) to predict RA onset months prior to the clinical diagnosis, based on clinical notes. Such predictions can be used to alert a non-rheumatological provider about a concern for RA in advance, enabling earlier referral to a rheumatologist. The work is ongoing on benchmarking this model against a manually curated set of phenotypic characteristics specifically as it relates to the model's ability to encode clinically relevant information which can be used in different clinical predictive models.

Note type	Training (%)	Testing(%)
Progress	50.25	21.54
H&P (including consult)	4.48	1.92
Assessment and plan (short consult)	1.59	0.68
General (including nursing and clinical communication)	13.68	5.86

Disclosure: S. Ayanian: None; **S. Rezaei**: None; **D. Darveaux**: None; **M. Blasi**: None; **E. myasoedova**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2261

Palindromic Rheumatism and Predictors of Progression to Rheumatoid Arthritis: Experience from a Tertiary Care Center in Northern India

Sryla Punjadath[1], Venkatesh Srinivasa Pai[1], Prativa Priyadarshani Sethi[1], ritu sangwan[2], Abhishek Rai[3] and Ravi Kant[1], [1]All India Institute of Medical Sciences, Rishikesh, Rishikesh, Uttarakhand, India, [2]AIIMS ,Rishikesh, Rishikesh, Uttarakhand, India, [3]AIIMS ,RISHIKESH, Bhilai, Chhattisgarh, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Palindromic Rheumatism (PR) is recognized as a clinical syndrome of intermittent episodes of pain, swelling, and erythema in and around joints, which are severe and unpredictable. It has been historically associated with Rheumatoid Arthritis (RA), with many considering PR as a pre-RA stage. We conducted the first-ever study on PR in Northern India to identify the risk factors for progression to RA.

Methods: Electronic medical record data were collected from the Rheumatology clinic at our tertiary care hospital. Thirty patients were identified as having PR. Patients having a history or examination findings consistent with synovial swelling that returned to normal in between episodes without any alternative diagnosis, as determined by a rheumatologist, were included

Table 1: The characteristics of selected demographic, clinical, laboratory, and treatment in patients remaining as PR and progressing to RA. Data expressed as frequency (percentage) for categorical variables and mean (SD) for continuous variables {*t-test or chi2 test as applicable, ** Logistic regression; applied to RF, CRP and number of joints involved and adjusted for duration of follow up, # Age at onset of disease, ESR, CRP, RF, ANA and Anti-CCP expressed as positive or negative as per laboratory cut-off values (ESR- 0-30mm and corrected for age; CRP: 0-1mg/L; RF: >20 IU/L, positive or negative by latex agglutination in 12 patients; ACCP: >10 IU/L), ANA: 5 available values, RF: 28 available values, Anti-CCP: 29 available values}[Abbreviations: ANA: Anti-nuclear antibodies, RF: Rheumatoid Factor, Anti-CCP: Anti- Citrullinated peptide, ESR: Erythrocyte Sedimentation Rate, CRP: C- reactive protein]

	Remained as PR n=16	Progressed to RA N=14	Univariate p value*	Multivariate OR (95% CI)**
Age, years#	37.37 (11.49)	40.64(11.11)	0.44	
Sex, female	13 (81.25)	11 (78.57)	0.85	
Follow up, months	50.25 (53.88)	91.71(41.73)	0.03	
Number of attacks per year	11.38 (7.16)	15.78 (16.72)	0.40	
Duration of attack, days	3.285714 (1.49)	3.142857 (.69)	0.81	
Extra-articular manifestations	1 (sicca symptoms)	3 (ILD)	-	
Joint involvement				
Total Number	7.19 (5.50)	16.36 (7.23)	0.0005	1.34 (1.10- 1.75)]
DIP	1 (6.25)	0 (0)	-	
PIP	8 (50)	12 (85.71)	-	
MCP	11 (68.75)	13 (92.86)	-	
Wrist	13 (81.25)	12 (85.71)	-	
Elbow	3 (18.75)	5 (35.71)	-	
Shoulder	7 (43.75)	7 (50.00)	-	
Knee	8 (50)	7 (50)	-	
Ankle	4 (25.00)	4 (28.57)	-	
Laboratory investigations				
ESR	4 (25.00)	8 (57.14)	0.07	
CRP	4 (25.00)	10 (71.43)	0.01	10.68(0.68 - 167.10)
RF positivity	8/16 (50)	11/ 12 (91.67)	0.02	28.18 (0.89- 888.10)
Anti-CCP positivity	11/15 (73.33)	13/14 (92.86)	0.16	
ANA positivity	1/4 (25)	0/1 (0)	0.58	
Treatment				
Methotrexate	9 (56.25)	14 (100)	-	
Sulfasalazine	2 (12.5)	2 (14.29)	-	
HCQ	2 (12.5)	6 (42.86)	-	
Leflunomide	0 (0)	5 (35.71)	-	
Rituximab	0 (0)	0 (0)	-	
Anti-TNF	0 (0)	0 (0)	-	
Tofacitinib	0 (0)	4 (28.57)	-	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

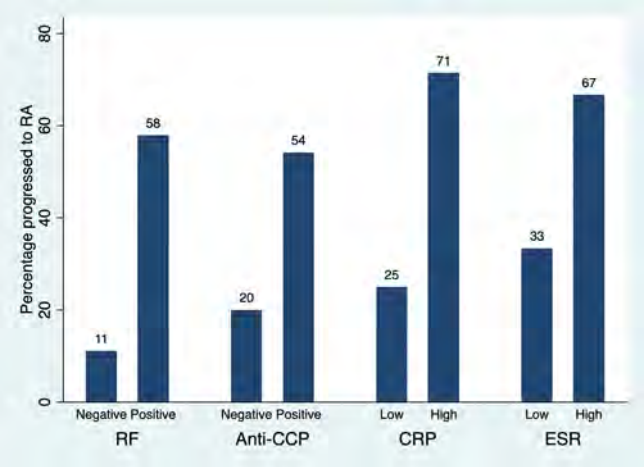


Figure 1: Laboratory characteristics of patients progressing to RA [Abbreviations: RF: Rheumatoid Factor, Anti-CCP: Anti-Citrullinated peptide, ESR: Erythrocyte Sedimentation Rate, CRP: C-reactive protein]

in the study. History, examination findings, and all available laboratory data were collected. Comparisons were made between the group that remained stable as PR and the group that progressed to RA according to the ACR/EULAR 2010 criteria. Comparisons were made using a t-test or chi-squared test, as per data type. Multivariate logistic regression was performed on the significant risk factors. Data were analyzed using STATA version 14 (StataCorp, College Station, TX, USA).

Results: Out of 30 patients, 16 (53.3%) remained as PR and 14 (46.7%) progressed to RA. One patient progressed to primary Sjögren's syndrome, with the arthritis remaining palindromic. The average duration of classification as RA from a diagnosis of PR was 48.50 months (SD-33.92). Age of onset, gender, duration of an arthritis flare, and time interval between the attacks were not different in the two groups. The total number of joints involved ever was higher in the group that progressed to RA (p-value: 0.0005; T-test). The results are tabulated in Table 1. Wrist and metacarpophalangeal joints were most frequently involved. ESR, CRP, RF, and ACCP values were recorded as elevated or normal as per laboratory cutoff values. CRP and RF positivity were significantly higher in the RA progression group, as depicted in Figure 1. The multivariate adjusted Odds Ratio for the number of joints involved was significant for the progression to RA [OR: 1.34 (1.10- 1.75)]. CRP and RF positivity were not statistically significant predictors for progression to RA in multivariate analysis. Additionally, two patients with erosions and deformity developed them after progression to RA. The acute arthritis responded to steroids in 24(80%) and to NSAIDS in 13(43%). As expected, only the patients progressing to RA required treatment with the tsDMARDs (4 out of 14).

Conclusion: In this cohort of patients with PR, approximately half progressed to RA. Raised CRP, RF positivity, and a higher number of joints involved may increase the risk of progression to RA. Being a retrospective study of a small sample size, we acknowledge its low power to capture differences in the other domains. It could also represent a difference in the progression of PR in the Indian Subcontinent as compared to studies published from elsewhere. Our study contributes to the management and follow-up of these patients and also lays the groundwork for future studies in PR.

Disclosure: S. Punjadath: None; **V. Pai**: None; **P. Sethi**: None; **r. sangwan**: None; **A. Rai**: None; **R. Kant**: None.

Abstract Number: 2262

Assessment of Small Airway Disease in Rheumatoid Arthritis

Stéphane HILLIQUIN[1], Huy-Thong HUA[2], Hà Pham-Ngoc[2], Frédérique Aubourg[2], Nhât-Nam Lê-Dông[2], Sven Günther[3], Nicolas ROCHE[4], Jérôme AVOUAC[5], Yannick Allanore[6] and Anh-Tuan Dinh-Xuan[2], [1]Département de Rhumatologie, Hôpital Cochin, Assistance publique des Hôpitaux de Paris, Université Paris-Cité, Paris, France, PARIS, France, [2]Unité

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

exploration fonctionnelle respiratoire, Pneumology department, Cochin Hospital, APHP, PARIS, France, [3]Unité exploration fonctionnelle respiratoire, Georges-Pompidou Hospital, APHP, PARIS, France, [4]Pneumology department, Cochin Hospital, APHP, PARIS, France, [5]Rheumatology department, Cochin hospital, Paris, France, [6]Universitä Paris Cité, Paris, France

SESSION INFORMATION

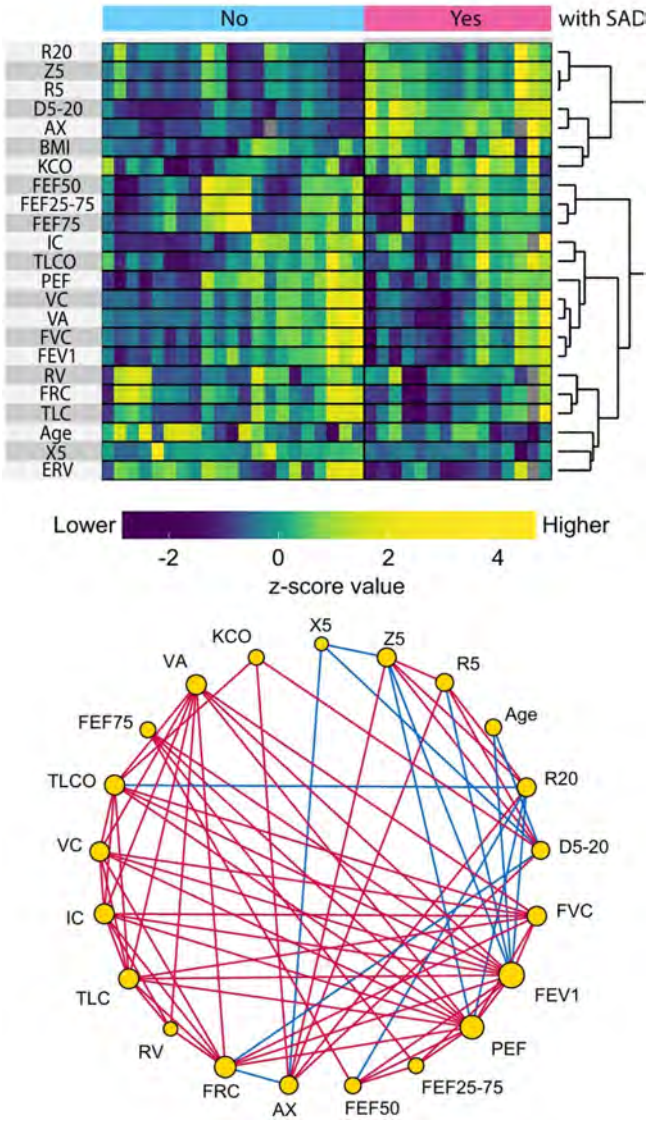
Session Date: Tuesday, October 28, 2025

Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The risk of interstitial lung disease is well established in Rheumatoid Arthritis (RA). Less is known about the airway involvement which has been estimated to occur in 39% to 60%, varying according to populations and investigative tools [1]. Small airways are defined as non-cartilaginous airways with an internal diameter less than 2 mm, and are characterized by lesions affecting the smallest bronchi and bronchioles [2]. Pulmonary function tests (PFT) are



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

commonly used to measure small airway disease (SAD) but impulse oscillometry (IOS) appears as an innovative technique to more accurately determine SAD. IOS is a very sensitive measure of airway resistance particularly developed in asthma. This latter tool has never been used so far in RA patients.

We sought to explore the distribution of key PFT and IOS features and the structure of their interrelationship in a cohort of RA patients

Methods: Included patients were followed for RA, with the exclusion of those with documented ILD. They were offered screening for RA airway using chest computed tomography (CT), PFT, and iOS. SAD involvement on CT was assessed by expert radiologists. Mosaic perfusion and expiratory air trapping were considered indicative of SAD.

Key parameters from forced spirometry, body plethysmography, diffusing lung capacity for carbon monoxide, and IOS were obtained RA patients without known ILD. Hierarchical clustering and correlation network analysis were performed. Distal airway involvement is assessed using iOS with the R5-R20 parameter, where a value > 0.07 kPa/L/s indicates small airway disease [3].

Results: The study population included 36 patients with RA (78% of female, mean age of 61.5 ± 10.5 y-o). A history of smoking was reported in 64% of patients. Seropositivity for rheumatoid factor and/or anti-citrullinated protein antibodies (ACPA) was observed in 97% of cases. At the time of inclusion, 44% of patients were receiving biologic DMARDs, mainly TNF inhibitors (9/36 patients). Respiratory symptoms (cough and/or dyspnea) or abnormal lung auscultation were present in 14% of patients. CT scans revealed SAD in 4 patients and ILD was observed in 5 out of 36 patients, predominantly with a pattern consistent with NSIP (3/5).

Visually the data structure (Figure) showed that each PFT modality independently contributed to identify respiratory physiological status in RA. Although most PFT outcomes stayed within normal limits, the overall distribution clearly differentiated patients with SAD (n=15, 42%) from those without (n=21). The correlation network (Figure) revealed a robust interrelationship pattern among 20 PFT parameters, identifying 74 statistically significant correlations, predominantly positive (60 links), with 50 exhibiting strong correlations (r > 0.5).

Conclusion: Lung involvement appears as one of the key extra-articular damages occurring in RA. Beyond the risk of ILD, combined PFT and IOS can be efficient and complementary for detection of SAD in RA patients. This is offering a valuable strategy for identifying accurately subclinical respiratory involvement. Further studies are needed to clarify the prevalence, the prognosis and the management of SAD in RA.

Disclosure: S. HILLIQUIN: None; **H. HUA**: None; **H. Pham-Ngoc**: None; **F. Aubourg**: None; **N. Lê-Dông**: None; **S. Günther**: None; **N. ROCHE**: None; **J. AVOUAC**: None; **Y. Allanore**: None; **A. Dinh-Xuan**: None.

Abstract Number: 2263

Comparison of a Patient-Reported Disease Activity Measure with Physician-Based Indices in Rheumatoid Arthritis Patients in Nigeria

Uchechukwu Tralagba[1], Courage Uhunmwangho[2], Olufemi Adelowo[3], Henry Nwankwo[4], Dasetima Altraide[1], Ejiehi Aigbokhan[5], Ako Itam[6], Omokhowa Asekhame[4] and Hakeem Olaosebikan[3], [1]University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers, Nigeria, [2]Jos University Teaching Hospital, Jos, Plateau, Nigeria, [3]Lagos state university teaching hospital, Ikeja, Lagos, Nigeria, [4]Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra, Nigeria, [5]University of Benin Teaching Hospital, Benin, Edo, Nigeria, [6]University of Calabar Teaching Hospital, Calabar, Cross River, Nigeria

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammation of synovial joints with extra articular manifestations. Disease activity indices in Rheumatoid arthritis are composite tools to assess disease activity and ascertain if treatment targets are met. Patient reported outcomes are increasingly recognized in medicine and have been incorporated in RA treatment guidelines. Routine Assessment of Patient Index3 (RAPID3) is a validated patient reported outcome measure calculated in less than 10 seconds, with no need for acute phase reactants. Previous studies comparing RAPID3 with the traditional physician measured disease activity indices have all been outside sub-Saharan Africa. We compared RAPID3 with physician measured indices in RA patients attending the Lagos State University Teaching Hospital (LASUTH) Rheumatology clinic.

Methods: A comparative study of 72 Rheumatoid Arthritis patients who presented to the outpatient Rheumatology clinic. Consenting patients who fulfilled the 2010 ACR/EULAR classification criteria for Rheumatoid Arthritis were recruited consecutively. Each participant was required to fill out the Multidimensional Health Assessment Questionnaire (MDHAQ), from which the RAPID3 score was calculated. For the physician-measured disease activity, the DAS 28 ESR, DAS 28 CRP, Simplified Disease Activity Index, and Clinical Disease Activity Index were calculated by the investigator following clinical and laboratory evaluations, then disease activity determined. Historical data about the disease and patient demographics were recorded in a proforma. Data was analyzed with SPSS version 25, using Spearman's correlations and kappa statistics. A p-value of < 0.05 was considered significant for statistical tests.

Results: The mean age of the study participants was 48.40 ± 14.46 years, with a median of 50 years and a range of 18-79 years. There was a female-to-male ratio of 17:1. There was fair to moderate agreement between RAPID3 and the physician-driven indices in classifying participants into four disease activity categories (k=0.27- 0.52; p< 0.001). This increased to substantial agreement when disease activity was dichotomized into active versus inactive (k=0.63-0.71; p=0.0001). Overall, 83.3%–92.1% of patients who met moderate/high activity criteria according to the physician-measured indices met similar RAPID3 criteria, and 70.6%–100% who met remission/low disease activity criteria according to the physician-measured indices also met similar RAPID3 criteria. Patient-reported disease activity correlated significantly with the physician-measured indices. ($r > 0.79$, $p < 0.001$).

Table 1 Comparison of RAPID3 with the physician driven indices in four disease activity categories among the study population

Variables (N = 72)	RAPID-3 High severity n (%)	Moderate Severity n (%)	Low Severity n (%)	Remission n (%)	Total n (%)
CDAI					
High	9 (64.3)	4 (28.6)	1 (7.1)	0 (0.0)	14 (100.0)
Moderate	12 (50.0)	10 (41.7)	1 (4.2)	1 (4.2)	24 (100.0)
Low	1 (4.5)	9 (40.9)	8 (36.4)	4 (18.2)	22 (100.0)
Remission	0 (0.0)	0 (0.0)	2 (16.7)	10 (83.3)	12 (100.0)
	*Kappa value =0.351; p-value = 0.0001**				
SDAI					
High	9 (64.3)	4 (28.6)	1 (7.1)	0 (0.0)	14 (100.0)
Moderate	12 (46.2)	11 (42.3)	2 (7.7)	1 (3.8)	26 (100.0)
Low	1 (4.5)	8 (36.4)	6 (27.3)	7 (31.8)	22 (100.0)
Remission	0 (0.0)	0 (0.0)	3 (30.0)	7 (70.0)	10 (100.0)
	*Kappa value =0. 273; p-value = 0.001**				
DAS28ESR					
High	17 (65.4)	7 (26.9)	1 (3.8)	1 (3.8)	26 (100.0)
Moderate	5 (17.9)	16 (57.1)	6 (21.4)	1 (3.6)	28 (100.0)
Low	0 (0.0)	0 (0.0)	4 (57.1)	3 (42.9)	7 (100.0)
Remission	0 (0.0)	0 (0.0)	1 (9.1)	10 (90.9)	11 (100.0)
	*Kappa value =0.516; p-value = 0.0001**				
DAS28 CRP					
High	10 (66.7)	3 (20.0)	1 (6.7)	1 (6.7)	15 (100.0)
Moderate	12 (44.4)	13 (48.1)	2 (7.4)	0 (0.0)	27 (100.0)
Low	0 (0.0)	6 (50.0)	4 (33.3)	2 (16.7)	12 (100.0)
Remission	0 (0.0)	1 (5.6)	5 (27.8)	12 (66.7)	18 (100.0)
	*Kappa value =0.378; p-value = 0.0001**				

*Statistically significant

Comparison of RAPID3 with the physician driven indices in four disease activity categories among the study population

Variable (N = 72)	RAPID3 Active disease n (%)	Inactive disease n (%)	Total n (%)
CDAI			
Active disease	35 (92.1)	3 (7.9)	38 (100.0)
Inactive disease	10 (29.4)	24 (70.6)	34 (100.0)
	*Kappa value =0.634; p-value = 0.0001**		
SDAI			
Active disease	36 (90.0)	4 (10.0)	40 (100.0)
Inactive disease	9 (28.1)	23 (71.9)	32 (100.0)
	*Kappa value =0.629; p-value = 0.0001**		
DAS28ESR			
Active disease	45 (83.3)	9 (16.7)	54 (100.0)
Inactive disease	0 (0.0)	18 (100.0)	18 (100.0)
	*Kappa value =0.714; p-value = 0.0001**		
DAS28 CRP			
Active disease	38 (90.5)	4 (9.5)	42 (100.0)
Inactive disease	7 (23.3)	23 (76.7)	30 (100.0)
	*Kappa value =0.651; p-value = 0.0001**		

*Statistically significant

Comparison of RAPID3 with Physician measured indices in classifying as active versus inactive disease in the study population

Conclusion: RAPID3, although not a perfect substitute for the traditional indices, provides an alternative for Rheumatoid arthritis disease activity assessment, with potential usefulness in busy clinic settings and areas with paucity of Rheumatologists like Nigeria. It has shown significant correlation and substantial agreement with the traditional indices in classifying as active versus inactive disease.

Disclosure: U. Tralagba: None; **C. Uhunmwangho**: None; **O. Adelowo**: None; **H. Nwankwo**: None; **D. Altraide**: None; **E. Aigbokhan**: None; **A. Itam**: None; **O. Asekhame**: None; **H. Olaosebikan**: None.

Abstract Number: 2264

Male Sex and Obesity Are Risk Factors for Sarcopenia in RA: Korea National Health and Nutrition Survey 2008–2011

Yoon-Jeong Oh[1], Jin-Wuk Hur[2] and Chang-Nam Son[3], [1]Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Republic of Korea, [2]Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Republic of Korea, [3]UIJEONGBU EULJI MEDICAL CENTER, EULJI UNIVERSITY, UIJEONGBU, Republic of Korea

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2227–2264) Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sarcopenia is a medical condition characterized by the progressive loss of skeletal muscle mass, strength, and function. It is primarily associated with aging, but is also influenced by chronic diseases, malnutrition, and physical inactivity. In the absence of timely and adequate management, sarcopenia can impair the ability to perform activities of daily living, contributes to mobility limitations, and leads to a reduced quality of life. Sarcopenia is a prevalent but often underrecognized comorbidity in patients with rheumatoid arthritis (RA). In this study, we aim to investigate the risk factors associated with sarcopenia in patients with RA.

Methods: We analyzed data from the 2008–2011 Korea National Health and Nutrition Examination Survey (KNHANES) to investigate factors associated with sarcopenia in RA patients. Sarcopenia was defined based on appendicular skeletal muscle mass (ASM) adjusted for body weight using the formula ASM/weight * 100, with cutoffs of < 29.0% for men and < 22.9% for women. Obesity was defined as a body mass index (BMI) ≥ 25 kg/m^2, according to the Asia-Pacific criteria. Multivariate logistic regression was used to identify independent predictors of sarcopenia, incorporating sample weights and complex survey design.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Baseline characteristics of study subjects

Variables	Non-sarcopenia (N=194)	Sarcopenia (N=44)	*p* value
Age, years	56.03 (53.44–58.62)	52.20 (45.43–58.98)	0.279
Male, %	15.3 (9.7–23.2)	55.0 (37.0–71.8)	<0.001
BMI, kg/m^2	23.30 (22.80–23.80)	26.06 (24.93–27.18)	<0.001
Waist circumference (cm)	79.02 (77.51–80.53)	86.88 (84.22–89.55)	<0.001
Smoking, %	60.6 (43.5–75.5)	66.2 (45.8–82.0)	0.662
Alcohol, %	39.0 (30.7–48.0)	51.9 (33.7–69.6)	0.212
Obesity, %	25.9 (19.6–33.3)	54.1 (35.9–71.2)	0.003
Meets WHO Physical activity guideline	88.1 (81.3–92.7)	73.5 (51.5–87.8)	0.070
EQ-5D index	0.86 (0.82–0.90)	0.81 (0.69–0.93)	0.448
Intake energy, g/day	1665.75 (1524.50–1807.01)	1642.43 (1408.65–1876.21)	0.868
Protein, g/kg/day	57.73 (51.38–64.09)	58.47 (45.67–71.27)	0.920
Fasting glucose	96.32 (91.47–101.16)	106.18 (86.76–125.60)	0.337
Total cholesterol	189.04 (183.51–194.57)	189.50 (173.39–205.61)	0.958
25 (OH) Vitamin D	18.51 (16.83–20.19)	17.32 (15.08–19.56)	0.401
Comorbidities, %			
Hypertension	28.0 (21.5–35.7)	24.3 (12.1–42.7)	0.679
Hyperlipidemia	95.6 (94.5–96.4)	96.3 (74.4–99.6)	0.845
Osteoarthritis	98.3 (88.0–99.8)	85.7 (40.3–98.2)	0.073
Osteoporosis	36.6 (28.8–45.1)	21.9 (10.4–40.5)	0.114
MDD	50.9 (37.0–64.7)	64.5 (35.6–85.6)	0.314

Values are presented as mean (95% confidence interval) for continuous variables and percentage for categorical variables. *P*-values are from complex-samples general linear model (CSGLM) adjusted for sample weights, strata, and clusters.

Values are presented as mean (95% confidence interval) for continuous variables and percentage for categorical variables. P-values are from complex-samples general linear model (CSGLM) adjusted for sample weights, strata, and clusters.

Table 2 Logistic regression analysis of factors associated with sarcopenia in RA patients

Variables	Univariate		Multivariate	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Male	6.785 (2.762–16.667)	<0.001	4.166 (1.475–11.765)	0.007
Age	0.984 (0.957–1.012)	0.256	0.995 (0.961–1.030)	0.781
Obesity	3.373 (1.511–7.527)	0.003	3.059 (1.159–8.071)	0.024
Meets WHO physical activity guideline	0.373 (0.125–1.117)	0.078	0.385 (0.141–1.056)	0.064
Daily protein intake	1.001 (0.987–1.014)	0.919	0.996 (0.981–1.011)	0.597

Values are presented as odds ratio (OR) with 95% confidence interval (CI) for univariate and multivariate logistic regression models. Multivariate analysis includes adjustments for age, sex, obesity, physical activity, and daily protein intake, along with sample weights, strata, and clusters based on the complex survey design.

Values are presented as odds ratio (OR) with 95% confidence interval (CI) for univariate and multivariate logistic regression models. Multivariate analysis includes adjustments for age, sex, obesity, physical activity, and daily protein intake, along with sample weights, strata, and clusters based on the complex survey design.

Results: Among 238 RA patients included in the analysis, 44 (18.5%) had sarcopenia. The sarcopenia group had a significantly higher proportion of males (55.0% *vs*. 15.3%, $p < 0.001$), higher BMI (26.06 *vs*. 23.30 kg/m^2, $p < 0.001$), and greater waist circumference (86.88 *vs*. 79.02 cm, $p < 0.001$) compared to the non-sarcopenia group. In multivariate logistic regression adjusted for age, sex, obesity, physical activity, and daily protein intake, male sex (OR 4.17, 95% CI 1.48–11.77, $p = 0.007$) and obesity (OR 3.06, 95% CI 1.16–8.07, $p = 0.024$) were independently associated with sarcopenia. Adherence to the World Health Organization (WHO) physical activity guidelines was associated with a trend toward a protective effect, although the association did not reach statistical significance (OR 0.39, 95% CI 0.14–1.06, $p = 0.064$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Male sex and obesity are significant factors associated with sarcopenia in Korean patients with RA. These findings underscore the critical role of male sex and obesity in the development of sarcopenia in RA patients. Future studies should explore the mechanisms underlying these associations and investigate the effectiveness of targeted interventions to mitigate sarcopenia in this population.

Disclosure: Y. Oh: None; **J. Hur**: None; **C. Son**: None.

Abstract Number: 2265

Progressive Interstitial Lung Disease associated to Rheumatoid Arthritis despite Abatacept therapy. Data from a large national multicenter cohort of 526 patients

Ana Serrano-Combarro[1], Belén Atienza-mateo[2], Adrian Martin-Gutierrez[3], Marta López-Maraver[4], Libe Ibarrola[5], Ivette Casafont-Solé[6], Jess Loarce[7], Juan María Blanco-Madrigal[8], Santos Castañeda[9], Rafaela Ortega-Castro[10], Natalia Mena Vzquez[11], Nuria Vegas Revenga[12], Lucia C. Domínguez-Casas[13], Cilia Peralta-Ginés[14], Carlos Fernández Díaz[15], Javier Loricera[16], Ricardo Blanco[17] and Spanish Collaborative Group of Interstitial Lung Disease Associated with Rheumatoid Arthritis, [1]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL, Inmunopathology group, Santander, Santander, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, PALMA DE MALLORCA/BALEARES, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Pilagos, Spain, [4]Hospital Universitario Araba, Vitoria, Spain, [5]Galdakao-Usansolo University Hospital, GALDAKAO, Spain, [6]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [7]Ramn y Cajal University Hospital, Madrid, Spain, [8]Rheumatology. Hospital Universitario Araba., Vitoria, Pais Vasco, Spain, [9]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [11]Hospital Regional Universitario de Malaga, Malaga, Spain, Mlaga, Spain, [12]Galdakao- Usansolo University Hospital, Galdakao, Spain, [13]Hospital Universitario San Agustin, Aviles, Spain, Aviles, [14]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [15]H.U. Santa Lucia, Murcia, Spain, [16]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [17]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Interstitial lung disease (ILD) is a severe extra-articular manifestation of rheumatoid arthritis (RA). Abatacept (ABA) has demonstrated effectiveness in the treatment of RA-ILD, regardless radiological pattern. Although global results are satisfactory, there are patients who present progression of ILD. The early identification of this group of patients is crucial for a prompt and adequate treatment. In a wide series of RA-ILD treated with ABA, our aim was to characterize the subgroup of patients with progressive RA-ILD.

Methods: From a large observational multicenter study of 526 RA-ILD patients treated with ABA, we selected those with available pulmonary function tests (PFTs) at baseline and in follow-up. Progressive ILD was defined as an absolute decline of forced vital capacity (FVC) of ≥10% within 2 years of follow-up since ABA initiation. Results are expressed as percentage, mean±SD or median [IQR] as appropriate. A comparative study and multivariable analysis of patients with progressive ILD and the remaining patients was performed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of main baseline (abatacept initiation) features of RA-ILD patients treated with ABA divided into progressive ILD and non-progressive groups.

	Progressive ILD (n=80)	Non-Progressive ILD (n=253)	p
Age, years, mean±SD	66±10	65±10	0.46
Sex, man/women, n/n	50 (63)	141 (54)	0.16
Smoker ever, n (%)	39 (49)	151 (57)	0.17
Time since AR diagnosis to ILD diagnosis, months, median [IQR]	36 [1-131]	48 [8-139]	0.82
ILD duration up to ABA initiation, months, median [IQR]	10 [2-30]	11 (3-36)	0.38
RF // ACPA, n (%)	70 (88); 70 (88)	234 (89); 224 (85)	0.71; 0.7
Active arthritis, n (%)	44 (77)	133 (180)	0.62
FVC // DLCO (% of the predicted), mean±SD	66±20; 62±19	84±21; 65±21	0.60; 0.16
Dyspnea Score (mMRC), median [IQR]	1 [1-2]	1 [0-2]	**0.01**
UIP pattern, n (%)	43 (51)	132 (51)	0.66
NSIP pattern, n (%)	20 (25)	78 (30)	
Previous immunosuppressive therapy, n (%)			
MTX / SSZ / LFN	50 (63); 11 (14); 31 (39)	186 (76); 34 (13); 123 (47)	**0.02**; 0.85; 0.21
Anti-TNF drugs // RTX // TCZ	17 (80); 8 (10); 4 (5)	77 (29); 38 (14); 34 (13)	0.16; 0.3; **0.048**
JAK inhibitors	1 (1)	12 (5)	0.16
ABA monotherapy/combined with cDMARD, n (%)	31 (39)	127 (49	0.29
Route of ABA administration, iv/sc, n/n	12 (15); 66 (85)	48 (20); 193 (80)	0.37
Concomitant antifibrotics, n (%)	8 (13)	22 (10)	0.64
Prednisone at baseline, mg/day, median [IQR]	7.5 [5-10]	5 [5-10]	0.69

ACPA, anti-citrullinated protein antibodies; DLCO, diffusing capacity of the lung for carbon monoxide; cDMARD, conventional disease-modifying antirheumatic drug; FVC, forced vital capacity; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; IQR, interquartile range; iv, intravenous; mMRC, modified Medical Research Council scale; MTX, methotrexate; NSIP, non-specific interstitial pneumonia; RA, rheumatoid arthritis; RF, rheumatoid factor; RTX, rituximab; sc, subcutaneous; SD, standard deviation; TCZ, tocilizumab; TNF, tumor necrosis factor; UIP, usual interstitial pneumonia.

Results: We finally included a total of 343 patients with available data on FVC of which 80 (23.3%) presented progressive ILD and 263 (76.7%) had a favorable lung function course (**Figure**). The differential baseline general characteristics between both groups are displayed in **Table 1**. We found no statistically differences in age, sex, smoking, ILD duration up to ABA initiation, positivity of rheumatoid factor or anti-citrullinated protein autoantibodies, combined treatment, prednisone dose, baseline PFTs or radiological pattern. Patients with progressive-ILD had a statistically higher dyspnea score and a lower proportion of patients had received previously methotrexate (63% vs 76%, p=0.02) and tocilizumab (5% vs 13%, p=0.048). Multivariable analysis (**Table 2**) showed that previous treatment with methotrexate or golimumab or joint activity (measured by DAS28ESR) multiplies by 0.453, 10.009 or 1.284, respectively, the probability of progressive ILD.

Conclusion: Almost a quarter of patients with ABA therapy presented progressive ILD. The main general features at ABA initiation are very similar in progressive and non-progressive ILD groups. Previous treatment with methotrexate seems to be a protective factor for ILD progression. Although ABA has consistently demonstrated effectiveness in the treatment of RA-ILD, its response, including joint inflammation, should be closely monitored.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariable analysis through logistic regression of associative factors of ILD progression at 24 months.

	Univariable		Multivariable	
	OR (IC 95%)	P	OR (IC 95%)	p
Age, years, mean±SD	1.019 (0.993-1.046)	0.162	1.025 (0.988-1.064)	0.191
Sex, men/women, n/n	0.693 (0.415-1.159)	0.162	0.812 (0.385-1.714)	0.585
Smoker ever, n (%)	0.706 (0.427-1.165)	0.173	0.882 (0.416-1.870)	0.743
Time since AR diagnosis to ILD diagnosis, months, median [IQR]	0.999 (0.997-1.002)	0.684		
ILD duration up to ABA initiation, months, median [IQR]	0.998 (0.990-1.005)	0.522		
RF, n (%)	0.868 (0.403-1.868)	0.716		
ACPA, n (%)	1.156 (0.547-2.444)	0.704		
DAS28, median [IQR]	1.239 (1.028-1.493)	0.024	1.284 (1.040-1.586)	**0.020**
Active arthritis, n (%)	1.196 (0.593-2.414)	0.617		
FVC % of the predicted), mean±SD	1.004 (0.992-1.016)	0.481		
DLCO % of the predicted), mean±SD	0.991 (0.977-1.005)	0.213		
Dyspnea Score (mMRC), median [IQR]	1.248 (0.979-1.592)	0.073	1.181 (0.864-1.614)	0.296
HRCT pattern UIP pattern, n (%)	0.976 (0.709-1.345)	0.884		
Previous immunosuppressive therapy, n (%)				
Methotrexate	0.539 (0.316-0.918)	0.023	0.453 (0.225-0.912)	**0.027**
Leflunomide	0.720 (0.432-1.200)	0.206		
Sulfasalazine	1.074 (0.517-2.231)	0.849		
JAK inhibitors	0.257 (0.033-2.012)	0.196	0.447 (0.040-5.051)	0.515
Adalimumab	0.491 (0.211-1.138)	0.097	1.006 (0.357-2.834)	0.991
Golimumab	3.377 (0.668-17.069)	0.141	10.009 (1.321-75.843)	**0.026**
Tocilizumab	0.354 (0.122-1.031)	0.057	0.510 (0.124-2.095)	0.350
Rituximab	0.658 (0.293-1.475)	0.309		
ABA monotherapy/combined with cDMARD, n (%)	1.060 (0.957-1.175)	0.264		
Route of ABA administration, iv/sc, n (%)	1.368 (0.685-2.731)	0.375		
Concomitant antifibrotics, n (%)	1.205 (0.736-1.975)	0.459		
Prednisone at baseline, mg/day, median [IQR]	1.004 (0.978-1.031)	0.755		

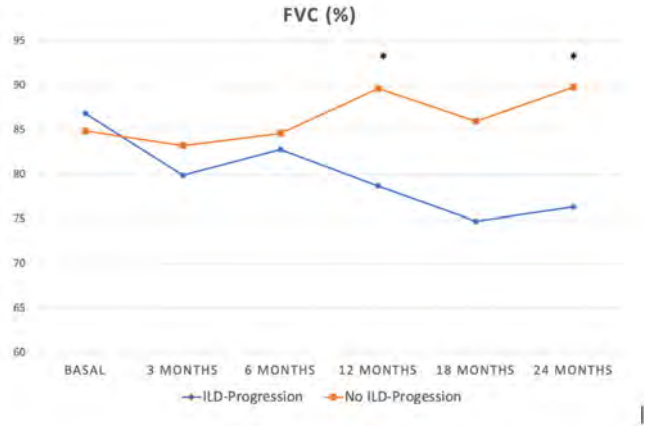


Figure. Evolution of FVC in patients included in "ILD progression" group vs in those included in "non ILD progression" (progression of ILD was defined as an absolute decline of forced vital capacity (FVC) of ≥10% within 2 years of follow-up since ABA initiation). * p <0.05.

Disclosure: A. Serrano-Combarro: None; **B. Atienza-mateo**: None; **A. Martin-Gutierrez**: None; **M. López-Maraver**: None; **L. Ibarrola**: None; **I. Casafont-Solé**: None; **J. Loarce**: None; **J. Blanco-Madrigal**: None; **S. Castañeda**: None; **R. Ortega-Castro**: None; **N. Mena Vázquez**: None; **N. Vegas Revenga**: None; **L. Domínguez-Casas**: None;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

C. Peralta-Ginés: None; **C. Fernández Díaz**: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2266

Impact of Rheumatoid Arthritis Therapeutic Classes on Risk of All-Cause Mortality and All-Cause Cancer: A Population-Based Cohort Study

Mohammad Movahedi[1], Angela Cesta[1], Sibel Aydin[2], Pooneh Akhavan[3], Tetyana Kendzerska[4], Claire Bombardier[1] and **Bindee Kuriya**[5] on behalf of OBRI investigators, [1]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, [2]Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [3]self-employed, Toronto, ON, Canada, [4]Ottawa Hospital Research Institute, Mississuaga, ON, Canada, [5]University of Toronto - Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Observational studies on RA therapeutic classes have shown conflicting results on their impact on mortality and cancer. When analyzing long-term outcomes, it is essential to account for changes in patient treatment over time. We assessed the association between RA therapeutic classes and risk of all-cause mortality and cancer in a large, population-based RA cohort.

Methods: Patients with RA were identified from the Ontario Rheumatoid Arthritis Database (ORAD), a population-based registry derived using a validated algorithm and maintained at ICES. We included individuals aged >67 years diagnosed between January 1, 2008, and December 30, 2013, and followed them through to December 30, 2023, with a minimum of 6 months follow-up. The outcomes of interest were all-cause mortality and health care utilization due to all-cause cancer requiring hospital admission, emergency department (ED) visits, or physician encounters. RA therapeutic class was treated as a time-varying exposure and categorized into 4 mutually exclusive groups: (1) No csDMARDs or AT use, (2) oral glucocorticoid (GC) use, (3) csDMARDs use only (reference), or (4) AT use (with or without csDMARDs). Given that CVD is the leading cause of death in RA and shares risk factors with cancer, the cohort was stratified by CVD risk at RA diagnosis. High-risk patients had established CVD, diabetes, or hypertension. Associations between treatment class and outcomes were evaluated using the Andersen-Gill Cox model, adjusted for baseline covariates and csDMARD use.

Results: A total of 10,020 RA patients (mean age 75.5 years; 67.3% female) were included in the study. Of these, 80% were classified as high CVD risk and 20% as low CVD risk. Over a median follow-up period of 9.4 years, there were 5,004 deaths and 1,762 cancer events in the high-risk group, compared to 845 deaths and 436 cancer events in the low-risk group. In the high-risk group, no csDMARD/AT use (HR: 2.37) and oral GC use (HR: 2.32) were significantly associated with increased all-cause mortality, while AT use was associated with a lower mortality hazard (Table). Similar findings were seen in the low-risk cohort. Lack of csDMARD/AT use was associated with a higher likelihood of cancer-related hospitalizations or visits in both high and low CVD risk groups (Table).

Conclusion: In this population-based cohort of older RA patients, treatment choice was significantly associated with mortality hazard. Advanced therapies were protective, while GC use and lack of RA treatment were associated with higher mortality. RA treatment had no significant impact on cancer hazard.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Adjusted hazard ratios (HR) and 95% confidence intervals for all-cause mortality or all-cause cancer by RA therapeutic class and baseline cardiovascular (CVD) risk.

	High Risk CVD cohort	Low Risk CVD cohort
	N=8,016 (person-years 69,638)	N=2,004 (person-years 20,353)
All-cause mortality		
csDMARD (reference)		
No csDMARD/AT use	2.37 (2.18, 2.58)	2.43 (2.02, 2.94)
Oral GC use	2.32 (2.07, 2.60)	2.73 (2.12, 3.50)
AT use	0.06 (0.02, 0.20)	0.15 (0.04, 0.62)
All-cause cancer		
csDMARD (reference)		
No csDMARD/AT use	38.8 (26.3, 57.2)	39.9 (20.2, 78.8)
Oral GC use	1.75 (0.95, 3.20)	1.79 (0.60, 5.39)
AT use	N/A	1.39 (0.17, 11.3)

csDMARD, conventional synthetic disease modifying antirheumatic drug use; AT, advanced therapy; GC, glucocorticoid; n/a, not applicable.

Disclosure: M. Movahedi: None; **A. Cesta**: None; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **P. Akhavan**: AbbVie/Abbott, 1, Fresenius-Kabi, 1, Janssen, 1, Sandoz, 6; **T. Kendzerska**: None; **C. Bombardier**: None; **B. Kuriya**: AbbVie/Abbott, 1, Pfizer, 1, UCB, 1.

Abstract Number: 2267

Impact of Baseline Cardiovascular Risk Factors Comorbidities on an Adalimumab Biosimilar Efficacy, Quality of Life and Safety In Patients with Patients with Moderately to Severely Active Rheumatoid Arthritis: Results from the AURIEL-RA study

Chris Edwards[1], Janet Pope[2], Joelle Monnet[3] and Maria Romanova Michailidi[4], [1]University Hospital Southampton, Southampton, United Kingdom, [2]University of Western Ontario, London, ON, Canada, [3]Fresenius Kabi SwissBioSim, Eysins, Switzerland, [4]University of Geneva, Eysins, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: RA has been associated with an increase risk of cardiovascular morbidity and mortality[1]. The present analysis was performed to assess the efficacy (on ACR response and DAS28), safety (adverse events) and quality of life (QoL) (HAQ-DI) of an adalimumab biosimilars (FK-Ada) in patients with baseline cardiovascular (CV) diseases risk factors. Biosimilars offer similar efficacy and safety compared to their originators, thereby improving patient access to affordable treatments. K-ada was approved for the treatment of inflammatory diseases including Rheumatoid Arthritis. FK-ada development included 1,234 subjects treated up to 52 weeks (420 patients-year). Since first FK-ada approval in 2019 in EU and in 2022 in US, no unexpected safety signals have been reported. AURIEL-RA study evaluated the safety, immunogenicity and efficacy of FK-ada in patients with moderately to severely active rheumatoid arthritis (RA) compared to reference adalimumab up to 52 weeks[2].

Methods: Patients with moderately to severely active RA receiving treatment with methotrexate were randomised 1:1 to FK-ada or reference adalimumab in the double-blind, multicentre, phase III AURIEL-RA study (NCT03052322). Safety, efficacy and immunogenicity endpoints were assessed at scheduled visits up to week 52, safety being the study primary objective. Following baseline CV risk factors were assessed: Age ≥ 65 y, BMI ≥ 30kg/m2, Smoking status, and diagnostic of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hypertension, cardiac disorders or Diabetes). Patients were categorized as "No", "One" or " >1" reported CV risk(s) at baseline and efficacy, safety and QoL were summarized for these subgroups.

Results: 288 patients with RA were randomised (FK-ada, n = 143; reference, n = 145). The 3 baseline CV diseases risk factors subgroups were similarly represented in the two treatment groups, each subgroup representing about 1/3 of each treatment arm. Patient baseline characteristics including CV diseases risk factors were comparable between treatment arms (Table 1). After one year, DAS28-ESR decreased in all subgroups in the two F-ada and reference treatment arms. However more subjects with no baseline CV risk were in DAS28-ESR remission status compared to subjects with CV risks. QoL improved in all patients. (Table 2). Subjects with several baseline CV risk factors experienced more adverse events compared to subjects without risks factors. (Table 3).

Conclusion: FK-ada and reference adalimumab were effective across subjects with and without CV risk factors. The safety profile of subjects with and without CV risks factors at baseline was as expected for these categories of patients.

1. Singh S, et al., Arthritis Care Res (Hoboken). 2020 Apr;72(4):561-576.

2. Edwards CJ, et al., Clin Rheumatol. 2019 Dec;38(12):3381-3390.

Table 1 - Demographics and baseline per subgroup of cardiovascular risks factors – ITT Analysis Set

	FK-ada			Reference adalimumab		
	0 risk	1 risk	>1 risk	0 risk	1 risk	>1 risk
Demographics & baseline	n=44	n=48	n=51	n=51	n=47	n=47
Sex, male (%)	9 (20.5%)	14 (29.2)	12 (23.5)	8 (15.7%)	8 (17.0)	10 (21.3)
Age, mean (SD)	46.66 (11.6)	51.84 (9.5)	61.97 (9.3)	48.16 (9.2)	54.11 (10.9)	60.34 (9.6)
<5y since first diagnosis of RA	22 (50.0)	22 (45.8)	24 (47.1)	26 (51.0	16 (34.0)	23 (48.9)

Table 2 - Efficacy and Quality of life at Week 52 per subgroup of cardiovascular risks factors – ITT Analysis Set

	FK-ada			Reference adalimumab		
	0 risk	1 risk	>1 risk	0 risk	1 risk	>1 risk
ACR Response rate at Week 52	n=37	n=41	n=43	n=42	n=39	n=37
ACR20 responder	31 (83.8)	33 (80.5)	35 (81.4)	38 (90.5)	32 (82.1)	32 (86.5)
ACR50 responder	26 (70.3)	24 (58.5)	28 (65.1)	32 (76.2)	25 (64.1)	21 (56.8)
ACR70 responder	12 (32.4)	19 (46.3)	17 (39.5)	19 (45.2)	17 (43.6)	14 (37.8)
DAS28-ESR response at Week 52	n=37	n=41	n=43	n=42	n=39	n=37
Remission	17 (45.9)	17 (41.5)	15 (34.9)	19 (45.2)	14 (35.9)	10 (27.0)
Low	4 (10.8)	6 (14.6)	10 (23.3)	4 (9.5)	9 (23.1)	11 (29.7)
Moderate	14 (37.8)	18 (43.9)	18 (41.9)	19 (45.2)	14 (35.9)	14 (37.8)
Severe	2 (5.4)	0	0	0	2 (5.1)	2 (5.4)
Change from baseline in HAQ-Di score at Week 52	n=37	n=41	n=43	n=42	n=39	n=37
Mean (SD)	-0.60 (0.71)	-0.75 (0.68)	-0.68 (0.65)	-0.65 (0.76)	-0.58 (0.63)	-0.71 (0.52)

Table 3 - Adverse Events per subgroup of cardiovascular risks factors – Safety Analysis Set

	FK-ada			Reference adalimumab		
	0 risk	1 risk	>1 risk	0 risk	1 risk	>1 risk
	n=44	n=48	n=51	n=51	n=47	n=47
Subjects n (%) with						
At least one AE	21 (47.7)	32 (66.7)	30 (58.8)	32 (62.7)	30 (63.8)	31 (66.0)
At least one related AE	7 (15.9)	15 (31.3)	9 (17.6)	25 (49.0)	17 (36.2)	16 (34.0)
At least one related grade ≥3 AE	0 (0.0)	1 (2.1)	1 (2.0)	1 (2.0)	0	2 (4.3)
Most Common Preferred Terms						
Injection site erythema	2 (4.5)	2 (4.2)	0	5 (9.8)	3 (6.4)	4 (8.5)
Nasopharyngitis	2 (4.5)	1 (2.1)	3 (5.9)	5 (9.8)	6 (12.8)	2 (4.3)
Injection site pruritus	0	0	1 (2.0)	6 (11.8)	1 (2.1)	1 (2.1)
Injection site pain	0	2 (4.2)	0	5 (9.8)	5 (10.6)	0
Upper respiratory tract infection	2 (4.5)	3 (6.3)	0	2 (3.9)	2 (4.3)	3 (6.4)
Bronchitis	0	0 (0.0)	3 (5.9)	3 (5.9)	1 (2.1)	3 (6.4)
Erythema	0	1 (2.1)	1 (2.0)	4 (7.8)	1 (2.1)	3 (6.4)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Edwards: AbbVie/Abbott, 6, alphasigma, 6, AstraZeneca, 1, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen, 6, pfizer, 6, Roche, 1, 6, sanofi, 6, ucb, 6; **J. Pope**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Frese, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Mallinckrodt Pharmaceuticals, 2, 5, Merck/MSD, 2, Mitsubishi Tanabe Pharma, 2, Novartis, 2, Roche, 2, Sandoz, 2, Sanofi, 2, Teva, 2, UCB, 2, Viatris, 2; **J. Monnet**: Fresenius Kabi SwissBio-Sim GmbH, 3; **M. Romanova Michailidi**: Fresenius Kabi SwissBioSim GmbH, 3.

Abstract Number: 2268

Differential Impact of Certolizumab Pegol, Etanercept, and Adalimumab on Rheumatoid Factor Reduction and Seroconversion in Rheumatoid Arthritis: A Propensity Score–Matched Study

Clementina López Medina[1], Rafaela Ortega-Castro[2], Francisco Jose Cepas[3], Montserrat Robustillo-Villarino[4], Andres Zuniga-Vera[4], Ana Martinez-Feito[5], Ester Costa-Moya[6], Delia Taverner-Torrent[6], Luis Sainz Comas[7], Cesar Diaz-Torne[7], Virginia Ruiz-Esquide[8], Cynthia Rojas[9], Lourdes Martin-de la Sierra Lopez[10], Laura Jimenez-Rodriguez[10], David Velasco-Sanchez[10], Regina Faré Garcia[11], Antonio Juan-Mas[12], Marina soledad Moreno Garcia[13], Ana Valeria Acosta Alfaro[14], Santiago Muñoz[15], Maria Martín López[16], Raquel Zas[17], FRANCISCO JAVIER GODOY NAVARRETE[18], Isabel Anon Onate[19], Fernando Ortiz-Márquez[20], Natalia Mena Vázquez[21], Paula Estrada-Alarcón[22], Jerusalén Calvo[23], Alejandro Escudero Contreras[23] and Chamaida Plasencia-Rodríguez[24], [1]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [3]University of Cordoba, Cordoba, Spain, [4]Department of Rheumatology, Hospital Universitario de la Plana, Vila-real, Castellón, Spain, Vila-real, Castellón, Spain, [5]Hospital Universitario La Paz, Madrid, Madrid, Spain, [6]Hospital Sant Joan Reus, Reus, Spain, [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, [8]Hospital Clínic de Barcelona, Barcelona, Catalonia, Spain, [9]Hospital Clinic, Barcelona, Spain, [10]Hospital General Universitario de Ciudad Real, Ciudad Real, Spain, [11]Hospital Son Llàtzer, Palma, Spain, [12]Son Llazter University Hospital, Madrid, Spain, [13]Hospital Universitario Miguel Servet, Zaragoza, Spain, [14]Hospital Universitario Infanta Sofia; Universidad Europea de Madrid; FIIB HUIS-HUHEN, Madrid, Spain, [15]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Spain, [16]Hospital 12 de Octubre, Madrid, Spain, [17]Hospital Universitario Doce de Octubre, Madrid, Spain, [18]Jaen University Hospital, Spain, Jaen, Spain, [19]Hospital Universitario de Jaén, Jaén, Spain, [20]Department of Rheumatology, Hospital Regional Universitario de Málaga, Málaga, Spain, Malaga, Spain, [21]Hospital Regional Universitario de Malaga, Malaga, Spain, Málaga, Spain, [22]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [23]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [24]Hospital Universitario La Paz, MADRID, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid factor (RF) is an antibody that contributes to the development of rheumatoid arthritis (RA) and is associated with greater disease severity. Seroconversion of RF after biological DMARD (bDMARD) treatment has been reported as infrequent. However, little is known about changes in serological status and their association with disease activity across different TNF inhibitors (TNFi).

The objectives of this study were: a) To compare the change in RF levels and the rate of seroconversion over 6 months of treatment with certolizumab pegol (CZP), etanercept (ETN), and adalimumab (ADA); and b) To evaluate the association between the reduction in RF levels and the change in disease activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Longitudinal, retrospective, multicentre study including RA patients treated with CZP, ETN, or ADA between 2010 and 2024. RF levels and DAS28-ESR scores before TNFi initiation and after 6 months were collected. Two propensity score (PS) matching approaches (CZP vs. ETN and CZP vs. ADA) were used to balance the groups based on baseline imbalances. Paired t-tests evaluated changes in RF levels within treatments groups, and Pearson correlations assessed association between RF and DAS28 changes after confirming data normality. The proportions of seropositive patients who converted to seronegative and those achieving >50% reduction in RF after 6 months were compared using chi-square tests.

Results: A total of 1,185 RA patients treated with TNFi (246 CZP, 343 ETN, and 513 ADA) were included. After PS matching, 203 CZP vs. 203 ETN and 224 CZP vs. 224 ADA were analyzed, achieving balance in age, sex, disease duration, concomitant MTX use, and TNFi treatment line.

ETN showed no significant difference in mean RF change after 6 months, whereas CZP showed a significant reduction (Figure 1A-B). Among seropositive, CZP-treated patients more often achieved >50% RF reduction than those on ETN (21.7% vs. 8.6%, p=0.010) (Figure 2A), and showed a numerically higher rate of seroconversion (9.4% vs. 5.2%). After 6 months, a direct association between RF and DAS28 reductions was observed in CZP-treated patients, whereas an inverse association was found in ETN-treated patients (Figure 3A–B), suggesting RF reduction was linked with an increase DAS28 in the ETN group.

In the ADA vs. CZP comparison (Figure 1C–D), CZP showed a significant reduction in RF levels, while ADA did not. Among seropositive patients, more CZP-treated patients achieved >50% RF reduction than those on ADA (24.4% vs. 11.1%, p=0.028), and showed a numerically higher seroconversion rate (9.4% vs. 5.9%) (Figure 2B). After 6 months, RF and DAS28 changes were not associated in ADA-treated patients, while a significant association was seen in CZP group (Figure 3C–D).

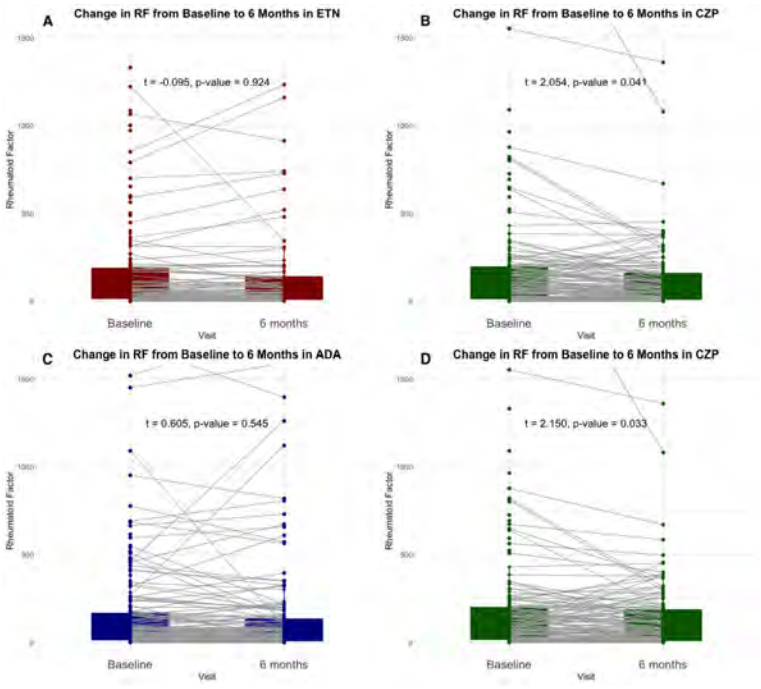


Figure 1. Paired t-Test Analysis of Rheumatoid Factor Changes at 6 Months in Propensity Score-Matched Comparisons Between ETN vs. CZP (A,B) and ADA vs. CZP (C,D).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

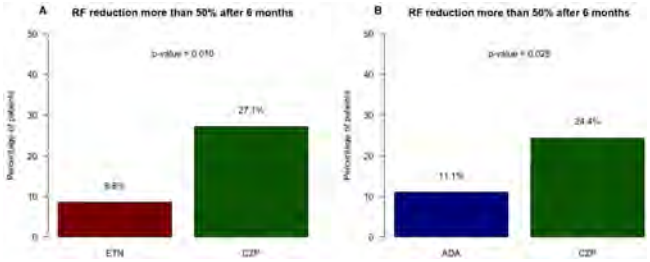


Figure 2. Proportion of Patients Achieving >50% Reduction in Rheumatoid Factor at 6 Months in Propensity Score–Matched Comparisons: ETN vs. CZP (A) and ADA vs. CZP (B)

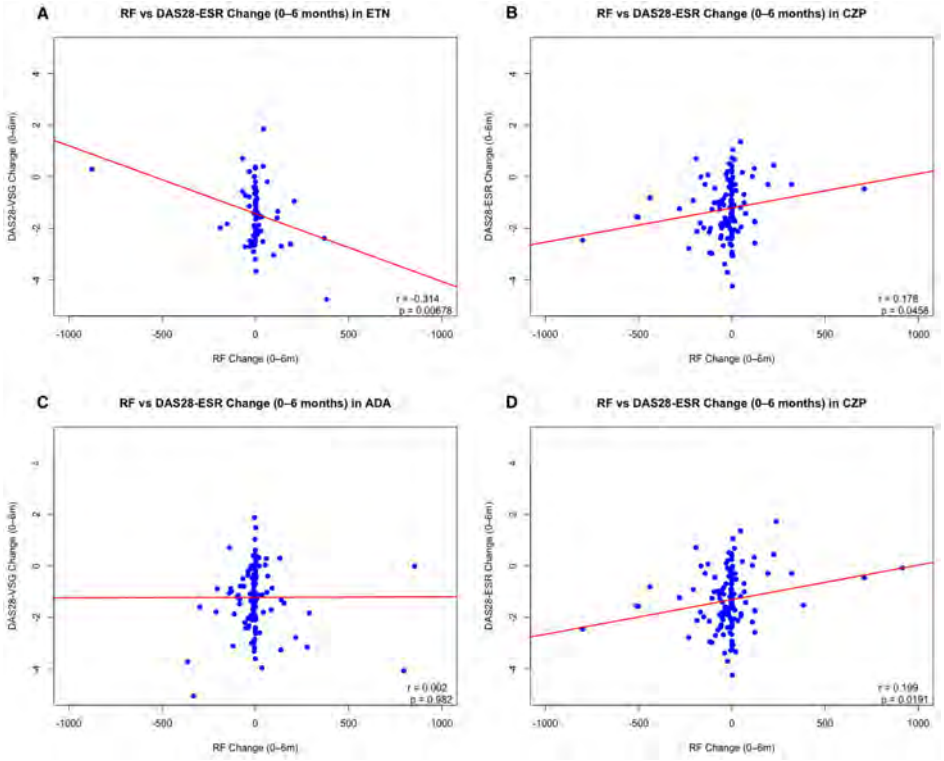


Figure 3. Correlation Analysis of Rheumatoid Factor Changes and DAS28-ESR changes at 6 Months in Propensity Score-Matched Comparisons Between ETN vs. CZP (A,B) and ADA vs. CZP (C,D).

Conclusion: CZP treatment was associated with a significant reduction in absolute RF levels and in the proportion of patients achieving >50% RF reduction compared to both ETN and ADA after 6 months. In CZP-treated patients, RF reduction was positively associated with improved in disease activity, suggesting a potential biomarker role for RF in CZP therapy follow-up. These findings suggest that RF reduction and seroconversion may vary across TNFi, with CZP showing a more favorable serological and clinical profile.

Disclosure: C. López Medina: None; **R. Ortega-Castro**: None; **F. Cepas**: None; **M. Robustillo-Villarino**: None; **A. Zuniga-Vera**: None; **A. Martinez-Feito**: None; **E. Costa-Moya**: None; **D. Taverner-Torrent**: None; **L. Sainz Comas**: None; **C. Diaz-Torne**: None; **V. Ruiz-Esquide**: None; **C. Rojas**: None; **L. Martin-de la Sierra Lopez**: None; **L. Jimenez-Rodriguez**: None; **D. Velasco-Sanchez**: None; **R. Faré Garcia**: None; **A. Juan-Mas**: None; **M. Moreno Garcia**: None; **A. Acosta Alfaro**: None; **S. Muñoz**: Janssen, 1, 2, 5, 6, 7; **M. Martín López**: None; **R. Zas**: None; **F. GODOY NAVARRETE**: None; **I. Anon Onate**: None; **F. Ortiz-Márquez**: None; **N. Mena Vázquez**: None;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

P. Estrada-Alarcón: None; **J. Calvo**: None; **A. Escudero Contreras**: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6.

Abstract Number: 2269

Key factors in optimizing the dose of Baricitinib in rheumatoid arthritis: a study based on routine clinical practice and its therapeutic implications

Daniel Campos-Martin[1], Nerea Alcorta-Lorenzo[2], César Antonio Egües Dubuc[2], Luis Maria Lopez-Dominguez[3], Lucia Otero[4], Fernando Sánchez-Alonso[5] and Joaquin Maria Belzunegui-Otano[6], [1]Rheumatology Department, Donostia University Hospital, San Sebastian-Donostia, Pais Vasco, Spain, [2]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [3]Rheumatology Department, Donostia University Hospital., San Sebastián, Pais Vasco, Spain, [4]Spanish Society of Rheumatology, Madrid, Spain, [5]Sociedad Española de Reumatología, Madrid, Spain, [6]Rheumatology Department, Donostia University Hospital., San Sebastian-Donostia, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Baricitinib, a selective JAK1/JAK2 inhibitor, has demonstrated efficacy in rheumatoid arthritis (RA). In patients with stable disease control for at least six months, reducing the dose by half (dosage optimization, OP) may improve safety and cost-effectiveness. Since the literature on this approach is limited, it is crucial to analyze the factors that influence the time required to implement this optimization.

Methods: A single-center retrospective study was conducted at the Donostia University Hospital, Spain, in patients with rheumatoid arthritis (RA) treated with Baricitinib between October 2017 and December 2023. Demographic and clinical-analytical variables were analyzed to identify factors associated with dose optimization. Using logistic regression and survival analysis with Cox regression, the probability and time to dose reduction were evaluated. Furthermore, safety and tolerance were compared between patients with optimized dose (OP) and full dose (DP), providing information on the clinical benefits of therapeutic optimization.

Results: 149 patients were found, mostly women (79.9%), with a mean age of 63.3 years, 38 were optimized (OP), while 111 continued with full dose (DP). The duration of treatment was significantly longer in the OP group, with a mean of 4.6 years compared to 2.6 years in the DP group (p = 0.0001) (Table 1).

In the univariate and multivariate analysis using logistic regression, no variable showed a statistically significant influence on the probability of dose optimization. However, in Cox regression analysis, the presence of anti-CCP antibodies was associated with a higher likelihood of optimization (HR = 2.12; 95% CI: 1.08 - 4.15; p = 0.028) (Table 2).

No significant difference in safety was observed between the two groups, indicating comparable outcomes (Table 3).

Conclusion: Baricitinib dose optimization appears to be influenced by the presence of anti-CCP antibodies, while factors such as previous treatments, number of drugs used, monotherapy and markers of poor prognosis did not show a significant association. Furthermore, patients on optimized doses demonstrated better tolerance to the treatment without an increase in adverse effects supporting its safety and clinical benefit in the management of rheumatoid arthritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics, comorbidities, treatment history, and clinical outcomes of patients receiving Baricitinib therapy, categorized by treatment optimization status (Not optimized vs. Optimized).

Table 1	Not optimized (n=111)	Optimized (n=38)	Total (n=149)	p-value
	n (%)	n (%)	n (%)	
Sex				0,527
Women	90 (81.1)	29 (76.3)	119 (79.9)	
Man	21 (18.9)	9 (23.7)	30 (20.1)	
Extra-articular manifestation				0,836
No	68 (61.3)	24 (63.2)	92 (61.7)	
Yes	43 (38.7)	14 (36.8)	57 (38.3)	
Sjogren				0,544
No	95 (85.6)	34 (89.5)	129 (86.6)	
Yes	16 (14.4)	4 (10.5)	20 (13.4)	
EPID				0,393
No	93 (83.8)	34 (89.5)	127 (85.2)	
Yes	18 (16.2)	4 (10.5)	22 (14.8)	
Nodules				0,18
No	104 (93.7)	33 (86.8)	137 (92.0)	
Yes	7 (6.3)	5 (13.2)	12 (8.1)	
Osteoporosis				0,764
No	85 (76.6)	30 (79.0)	115 (77.2)	
Yes	26 (23.4)	8 (21.1)	34 (22.8)	
STC				0,269
No	102 (91.9)	33 (86.8)	135 (90.6)	
Yes	8 (7.2)	5 (13.2)	13 (8.7)	
Unknown	1 (0.9)	0 (0.0)	1 (0.7)	
Vasculitis				0,428
No	109 (98.2)	37 (97.4)	146 (98.0)	
Yes	1 (0.9)	1 (2.6)	2 (1.3)	
Unknown	1 (0.9)	0 (0.0)	1 (0.7)	
FR				0,505
No	71 (64.0)	22 (57.9)	93 (62.4)	
Yes	40 (36.0)	16 (42.1)	56 (37.6)	
CCP				0,131
No	79 (71.2)	22 (57.9)	101 (67.8)	
Yes	32 (28.8)	16 (42.1)	48 (32.2)	
Erosions				0,284
No	62 (55.9)	25 (65.8)	87 (58.4)	
Yes	49 (44.1)	13 (34.2)	62 (41.6)	
FRCV				-
Yes	110 (99.1)	37 (97.4)	147 (98.7)	
Unknown	1 (0.9)	1 (2.6)	2 (1.3)	
Tobacco				0,255
No	87 (78.4)	33 (86.8)	120 (80.5)	
Yes	24 (21.6)	5 (13.2)	29 (19.5)	
HTA				0,989
No	79 (71.2)	27 (71.1)	106 (71.1)	
Yes	32 (28.8)	11 (29.0)	43 (28.9)	
HDL				0,405
No	2 (1.8)	0 (0.0)	2 (1.3)	
Yes	109 (98.2)	38 (100.0)	147 (98.7)	
Diabetes				0,075
No	100 (90.1)	30 (79.0)	130 (87.3)	
Yes	11 (9.9)	8 (21.1)	19 (12.8)	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariate Cox regression analysis of factors associated with treatment outcomes in patients receiving Baricitinib, including demographic variables, disease duration, serological markers, smoking status, and prior targeted therapies. Anti-CCP antibody (CCP). Disease-modifying anti-rheumatic drugs (DMARDs)

Table 2		
Multivariate Cox		
	HR (95% CI)	P>z
Sex (ref woman)	1.41 (0.60 - 3.33)	0,427
Age at start	0.99 (0.97 - 1.02)	0,62
Duration of illness (years)	1.03 (0.99 - 1.06)	0,173
CCP	2.12 (1.08 - 4.15)	0,028
Tobacco (non-smoking ref)	0.56 (0.20 - 1.52)	0,254
Monotherapy	0.78 (0.38 - 1.63)	0,514
Prior targeted FAME (ref no prior FAME)		
Previous bDMARD	0.53 (0.23 - 1.22)	0,137
previous bDMARD/sd	3.16 (0.27 - 36.78)	0,358

Table 3. Cardiovascular disease (CVD), CVD type, herpes zoster (VHZ), and thrombosis events in patients treated with Baricitinib, comparing optimized and not optimized treatment groups.

Table 3	Not optimized (n=138)	Optimized (n=45)	Total (n=183)	p-value
CVD				0,768
No	106 (95.5)	37 (97.4)	143 (96.0)	
Yes	4 (3.6)	1 (2.6)	5 (3.4)	
Unknown	1 (0.9)	0 (0.0)	1 (0.7)	
CVD Type				0,223
IAM	2 (1.8)	0 (0.0)	2 (1.3)	
Stroke	1 (0.9)	0 (0.0)	1 (0.7)	
Thrombosis	1 (0.9)	2 (5.3)	3 (2.0)	
VHZ				0,554
No	101 (91.0)	36 (94.7)	137 (92.0)	
Yes	9 (8.1)	2 (5.3)	11 (7.4)	
Unknown	1 (0.9)	0 (0.0)	1 (0.7)	
Thrombosis				0,098
No	110 (99.1)	36 (94.7)	146 (98.0)	
Yes	1 (0.9)	2 (5.3)	3 (2.0)	

Disclosure: D. Campos-Martin: None; **N. Alcorta-Lorenzo**: None; **C. Egües Dubuc**: None; **L. Lopez-Dominguez**: None; **L. Otero**: None; **F. Sánchez-Alonso**: None; **J. Belzunegui-Otano**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2270

ACKR1 and Leukopenia in Patients with Rheumatoid Arthritis Treated with Disease Modifying Antirheumatic Drugs

Daniela Chavez de Paz Solis[1], Puran Nepa[2], Laura Daniel[3], Yan Guo[4], Jonathan Mosley[5], Michael Stein[6] and Cecilia Chung[4], [1]University of Maine, Caribou, ME, [2]University of Miami, Research Service, Miami VA Healthcare System, Miami, FL, [3]University of Miami, Nashville, TN, [4]University of Miami, Miami, [5]UT Southwestern Medical Center, Dallas, [6]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, sulfasalazine, and leflunomide are commonly prescribed for RA treatment but carry the risk of leukopenia. The ACKR1 promoter genotype (rs2814778-CC) has been associated with leukopenia and is predominantly present among individuals of African ancestry. This study aimed to examine whether leukopenia is more frequent among patients with RA who carried the rs2814778-CC genotype compared to patients without the rs2814778-CC genotype when using these DMARDs.

Methods: Retrospective cohort study using the All of Us research program data. We collected genetic and EHR data, including reported race, as well as laboratory data including white blood cell (WBC) and platelet counts after starting sulfasalazine, leflunomide, or methotrexate. Leukopenia was defined as a WBC count <3,000 cells/mm^3, and thrombocytopenia as a platelet count <100,000 cells/mm^3. We utilized short-read whole- genome sequencing (srWGS) data from the All of Us Curated Data Release (v7), with direct genotyping of the ACKR1 SNP rs2814778 (C/T). We compared patients of EHR reported Black race with the CC genotype to those with TT/TC genotypes, as well as to patients of EHR reported White race, because of the known association of the CC genotype with lower WBC counts among patients of Black race.

Results: Among RA patients, 463 individuals who were prescribed sulfasalazine, leflunomide, or methotrexate and had recorded WBC counts after diagnosis were included in the study. The median age at RA diagnosis was 66 years [IQR: 58.0,73.0], and more than 80% of patients were female. Notably, the rs2814778-CC genotype was absent in the patients of EHR reported White race but found in 68% of the patients of EHR reported Black race. The overall leukopenia rate was 36.0% in patients of Black race and 30.9% in patients of White race (p= 0.39). patients of Black race with the CC genotype had the highest leukopenia risk (45.6%), followed by patients of White race with the TT/TC genotypes (30.9%), while patients of Black race with the TT/TC genotypes had the lowest risk (15.6%) (P = 0.01), indicating a significant correlation between genotype and leukopenia risk. The rates of thrombocytopenia were statistically similar across all groups (P = 1.00).

Table 1. Characteristics of RA Patients with Usage of Sulfasalazine, Leflunomide, and Methotrexate

Variable	Overall (n=463)	CC	TT/TC	P
Age, median [Q1, Q3]	66.0 [58.0,73.0]	66.0 [57.0,70.2]	66.0 [58.0,74.0]	0.386
Leukopenia (WBC <3,000 cells/mm³), n (%)	148 (32.0)	31 (45.6)	117 (29.6)	0.014
Leukopenia (WBC < 4,000 cells/mm³), n (%)	259 (55.9)	46 (67.6)	213 (53.9)	0.048
Thrombocytopenia (platelet count < 100,000 cells/mm³), n (%)	29 (6.9)	<20	<20	1.000

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our findings emphasize that individuals of black race with the CC genotype had the highest rates of leukopenia; highlighting the potential impact of the ACKR1 rs2814778-CC genotype on the risk of leukopenia in patients with RA treated with sulfasalazine, leflunomide, or methotrexate.

Disclosure: D. Chavez de Paz Solis: None; **P. Nepa**: None; **L. Daniel**: None; **Y. Guo**: None; **J. Mosley**: None; **M. Stein**: None; **C. Chung**: None.

Abstract Number: 2271

Assessing the Real-world Impact of Earlier Initiation of Adalimumab vs. Conventional Synthetic Dmards on Healthcare Resource Utilization in Patients with Rheumatoid Arthritis in Europe

Daniel Aletaha[1], **Dr. Carmen Bremer**[2], Jack Milligan[3], Zichun Cao[4], Rachael Meadows[3] and Xenofon Baraliakos[5], [1]Medical University Vienna, Wien, Austria, [2]Sandoz International GmbH, Holzkirchen, Germany, [3]Adelphi Real World, Macclesfield, United Kingdom, [4]Sandoz Incorporated, Princeton, [5]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Early use of targeted therapy (TT), such as anti-tumor necrosis factor (anti-TNF) biologics, show improved outcomes for RA[1], but costs often limit access. Biosimilars, such as Sandoz adalimumab (SZ-ADL), are generally less expensive than their reference medicines and offer comparable efficacy[2]. Early initiation of anti-TNF biosimilar therapy could yield higher cost efficiency than conventional synthetic DMARDs (csDMARDs).

This study compared healthcare resource utilization (HCRU) and costs of RA patients (pts) receiving SZ-ADL as first line TT (1L) with csDMARD pts never prescribed a TT (TT-naïve).

Methods: Data were drawn from the Adelphi RA Disease Specific Programme (DSP™), a cross-sectional survey of rheumatologists and their next consulting pts with RA in a real-world clinical setting in France, Italy, Germany, Spain and the United Kingdom between July 2023 and August 2024. Rheumatologists, referring to pt medical records, provided information on demographics, disease and treatment history, HCRU and clinical outcomes.

HCRU was assessed in SZ-ADL pts (1L) using inverse probability weighted regression adjustment (IPWRA) with csDMARD (TT-naïve) pts as a comparison group. Both groups had been receiving their therapy for ≥3 months. Pts were weighted for age, DAS-28 at treatment initiation, sex, Charlson Comorbidity Index, autoimmune comorbidities, total duration of prior csDMARDs and time from diagnosis to treatment initiation. Weighted regression adjusted for these variables and for treatment duration. Costs were sourced per country from diagnostic-related groups, national tariffs and government reports. Pre-weighting was performed to account for population and cost differences between countries. Results are reported as weighted means along with p-values.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Mean Number of Tests, Consultations and Hospitalizations Since Initiating Current Treatment

Figure 2. Mean Per-Patient Cost of Tests, Consultations and Hospitalizations Since Initiating Current Treatment

Results: A total of 329 pts were included in the analysis, 172 in the SZ-ADL and 157 in the csDMARD group. SZ-ADL pts had significantly fewer tests to monitor their RA during their treatment (8.59 vs 11.53, p< 0.0001) and fewer hospitalizations (0.19 vs 0.36, p=0.001) than csDMARD patients, but more consultations (4.00 vs 3.44, p< 0.0001) (Figure 1).

This translated to significantly lower per-pt cost of tests to monitor RA (€4.99 vs €9.85, p< 0.0001), consultations (€226.65 vs €324.59, p< 0.0001) and hospitalizations (€265.04 vs €323.26, p=0.0032) for SZ-ADL pts (Figure 2).

Conclusion: Earlier initiation of SZ-ADL may provide cost savings to healthcare systems in Europe by reducing costs of testing, consultations and hospitalizations compared to pts remaining on csDMARDs. Residual confounding variables within the groups may be a potential limitation of the analysis.

References:

[1]Combe, B., Landewe, R., Daien, C.I., Hua, C., Aletaha, D., Álvaro-Gracia, J.M., Bakkers, M., Brodin, N., Burmester, G.R., Codreanu, C. and Conway, R., 2017. 2016 update of the EULAR recommendations for the management of early arthritis. *Annals of the rheumatic diseases*, *76*(6), pp.948-959.

[2]Baumgart, D.C., Misery, L., Naeyaert, S. and Taylor, P.C., 2019. Biological therapies in immune-mediated inflammatory diseases: can biosimilars reduce access inequities?. *Frontiers in pharmacology*, *10*, p.279.

Disclosure: D. Aletaha: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, Sandoz, 6, Sanofi, 6; **D. Bremer**: Sandoz, 12, Employee and shareholder; **J. Milligan**: Adelphi Real World, 3; **Z. Cao**: Sandoz, 12, Employee and shareholder; **R. Meadows**: Adelphi Real World, 3; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor.

Abstract Number: 2272

Combination Therapy with TNF Inhibitors and JAK Inhibitors in Multi-Drug-Resistant Rheumatoid Arthritis: A Case Series from the RA UCLouvain Brussels Cohort

Francesco NATALUCCI[1], Cécile VAN MULLEM[1], Aleksandra AVRAMOVSKA[1], Tatiana SOKOLOVA[2] and Patrick Durez[1], [1]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium, [2]Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Brussels Hoofdstedelijk Gewest, Belgium

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disease with persistent synovial inflammation.

Several bDMARDs and tsDMARDs target different key players in the immune-regulatory pathways, including cytokines, JAK, T cells, and B cells. These molecules enable the achievement of remission or LDA in the majority of patients. However, about 20% to 40% of patients fail to achieve remission, and a smaller percentage, recognized as (multi-drug resistance) MDR-RA, fail several bDMARDs and tsDMARDS. In this subset of severe and multi-resistant patients, the combination of a TNFi and a JAKi might be a promising approach, despite not risk-free.

Methods: We performed a descriptive study of patients from the RA UCLouvain Brussels Cohort, who received a combination of TNFi and JAKi. Disease activity trajectory and tolerability, as well as different therapeutic agents received over time, were recorded.

Results: We report five patients (3F, 2M). They received a combination therapy after a median time of 184 months (IQR 116) from diagnosis. The demographic and clinical features for each patient are reported in Table 1. Figure 1 shows disease activity at the moment of each b/tsDMARDs discontinuation (A), reason for discontinuation (B), and the sequence of the b/tsDMARDs (C) for each patient. All of these pts were refractory to 7 bDMARDs and to 2 JAKi. Of note, all the patients received csDMARDs alongside b/tsDMARDs. Variable-dose glucocorticoids have been part of the therapeutic strategy in combination with standard therapy. None of the patients suffered from major adverse events due to b/tsDMARDs as severe infection. All the patients were treated with a TNFi (infliximab or etanercept) associated with a JAKi (Upatacitinib or Filgotinib). Three patients had a minimum follow-up time of 3 months after the combination and then a second evaluation. Pt 1 achieved a persistent remission state up to 3 years of follow-up. We observed a significant decrease in disease activity in two patients, reaching disease remission. None of the patients developed major side effects, including severe infection or hospitalisation, in the observation period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

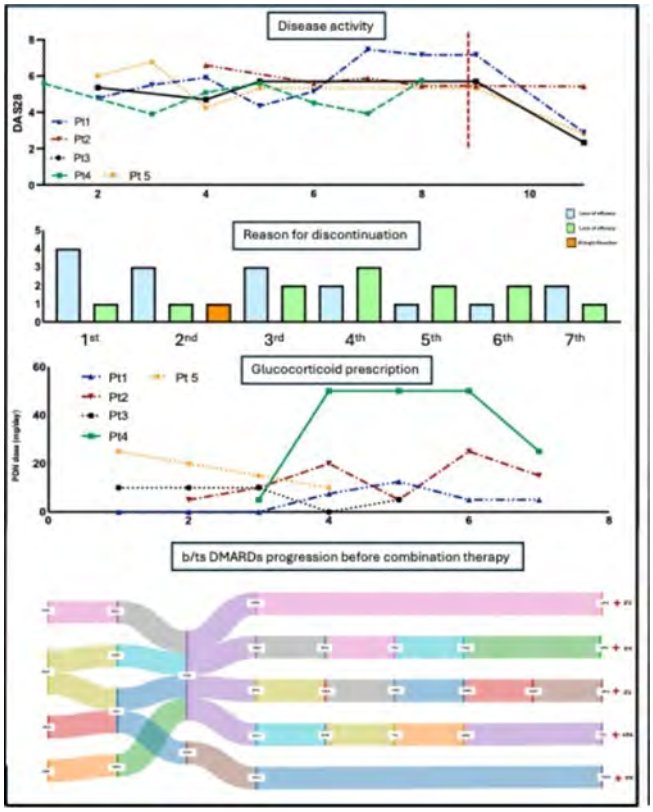


Figure 1 A-D A. Disease activity for each patient according DAS28 disease activity score before starting combination therapy (left) and after initiation of combination therapy (right). B. Reason for discontinuation for each b/tsDMARDs. From the 5th b/tsDMARDs on, only 3 patients are considered. C. b/tsDMARDs prescription progression for each patient. D. Glucocorticoid dosage at each b/tsDMARD change

Table 1. Demographic and disease feature for each patient

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5
Sex	Female	Male	Female	Female	Male
ACPA	No	No	Yes	Yes	No
FR	No	1	Yes	Yes	No
Erosive	Yes	Yes	Yes	Yes	Si
Age at combination (years)	36 years	35 years	43 years	56 years	35 years
Extra articular manifestation	No	No	No	No	No
Time to combination	204 Months	164 Months	156 Months	348 Months	216 Months
csDMARDs	Ye	Ye	Ye	Yes	Yes
Follow-up after combination	36 months	4 months	3 months	–	12 months
Infection after combination therapy	No	No	No	No	No

Conclusion: Our preliminary results indicate that a combination therapy of a TNFi and a JAKi provided good clinical results without safety concerns. In severe and multi-resistant patients, when all classical approach fails to reach a good disease control, the combination therapy could be an option. As infection is the major risk for those patients, a b/tsDMARDs combination should be restricted to young patients with a low infection risk and after adequate vaccinations.

Disclosure: F. NATALUCCI: None; **C. VAN MULLEM**: None; **A. AVRAMOVSKA**: None; **T. SOKOLOVA**: None; **P. Durez**: AbbVie/Abbott, 6, Galapagos, 6, Lilly, 6, Nordimed, 6, Thermofischer, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2273

Impact of Upadacitinib on Glucocorticoid Reduction in Patients with Moderate-to-Severe RA Who Achieved and Maintained Clinical Remission in the 2-Year UPHOLD Study

FRANK BUTTGEREIT[1], Andrew Ostor[2], Philip Conaghan[3], Ana Romero[4], Ivan Lagunes[5], Andrew Garrison[6], Tianming Gao[7] and Suzan Attar[8], [1]Charité University Medicine Berlin, Berlin, Berlin, Germany, [2]Australian National University, Canberra, Australia, [3]University of Leeds, Leeds, United Kingdom, [4]AbbVie, Barcelona, Spain, [5]Abbvie Inc, North Chicago, IL, [6]AbbVie, USA, North Chicago, IL, [7]AbbVie, North Chicago, IL, [8]King Abdulaziz University, Saudi Arabia, Jeddah, Saudi Arabia

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

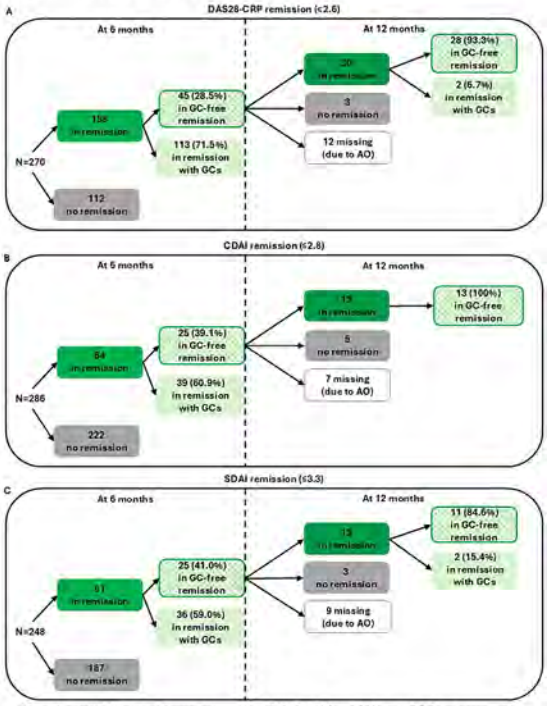
Background/Purpose: Glucocorticoids (GCs) are fast-acting drugs used to support csDMARD therapy for RA, but should be used sparingly and for short periods.[1] Upadacitinib, an oral Janus kinase inhibitor, is approved for the treatment of adults with moderate-to-severe RA.[2] This post hoc analysis assessed the real-world impact of upadacitinib on GC discontinuation, and the effect of GC discontinuation on efficacy and safety, in patients with RA taking GCs at study onset, who achieved and maintained remission through 2 years in the UPHOLD study.

Methods: UPHOLD (NCT04497597), a 2-year, non-interventional, multi-country, observational, cohort study, assessed the real-world effectiveness and safety of upadacitinib (15 mg QD) in upadacitinib-naïve adults with moderate-to-severe RA. This post hoc analysis assessed the impact of upadacitinib in achieving and maintaining GC-free clinical remission (defined as 28-joint DAS with CRP [DAS28-CRP] < 2.6, Clinical Disease Activity Index [CDAI] ≤2.8, and Simplified Disease Activity Index [SDAI] ≤3.3) at 6, 12, and 24 months (mo) among patients taking GCs at baseline. Safety was assessed by DAS28-CRP remission status subgroup (yes/no) and reported as exposure-adjusted events/100 patient-years. Data are presented as observed.

Results: At baseline, 455 patients had concomitant GC use; mean (standard deviation [SD]) GC dose: 8.1 (7.6) mg/day; patient number (%) by GC dose (mg/day): 65 (14.3), < 5; 207 (45.5), 5; 120 (26.4), >5–10; and 63 (13.8), >10; mean (SD) disease duration: 9.8 (8.8) years; and mean (SD) disease activity scores: DAS28-CRP, 4.76 (1.2); CDAI, 27.9 (12.4); SDAI, 30.2 (13.7). At 6 mo, DAS28-CRP remission was achieved by 58.5% (n/N: 158/270), CDAI remission by 22.4% (64/286), and SDAI remission by 24.6% (61/248) of patients. Of patients achieving DAS28-CRP, CDAI, and SDAI remission at 6 mo, 28.5% (45/158), 39.1% (25/64), and 41.0% (25/61), respectively, were GC-free. Of patients with GC-free remission at 6 mo, who maintained remission and had data available at 12 mo (DAS28-CRP, 90.9% [30/33]; CDAI, 72.2% [13/18]; SDAI, 81.3% [13/16]), most were GC-free (DAS28-CRP, 93.3% [28/30]; CDAI, 100.0% [13/13]; SDAI, 84.6% [11/13]) (**-Figure 1**). At 12 mo, 64.6% (144/223) patients had DAS28-CRP, 27.3% (65/238) had CDAI, and 28.8% (62/215) had SDAI remission, and almost half were GC-free (DAS28-CRP, 41.0% [59/144]; CDAI, 49.2% [32/65]; SDAI, 48.4% [30/62]). Of patients with GC-free remission at 12 mo, who maintained remission and had data available at 24 mo (DAS28-CRP, 80.4% [37/46]; CDAI, 83.3% [20/24]; SDAI, 77.3% [17/22]), 100% were GC-free (DAS28-CRP, 37/37; CDAI, 20/20; SDAI, 17/17) (**Figure 2**). Treatment-emergent adverse events were similar regardless of DAS28-CRP remission status at 6, 12, and 24 mo, and consistent with previously published UPHOLD dat

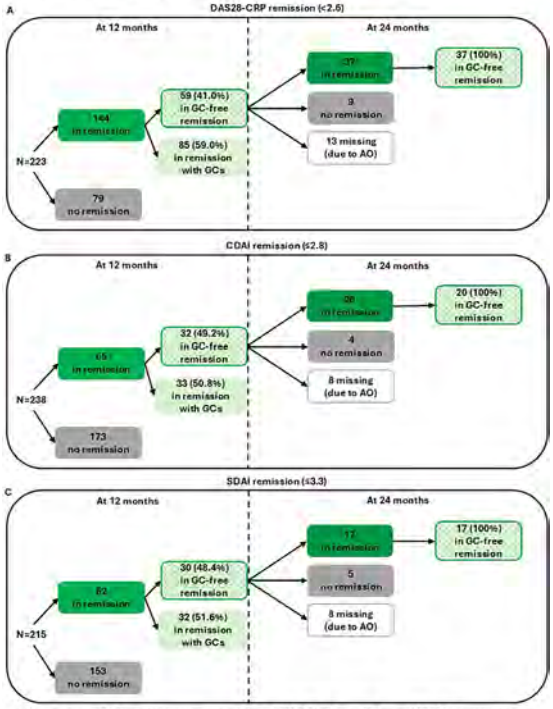
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Effect of upadacitinib on GC reduction in patients with RA who achieved (6 months) and maintained (12 months) clinical remission per (A) DAS28-CRP (<2.6), (B) CDAI (≤2.8), or (C) SDAI (≤3.3) among patients taking GCs at baseline.



AO, as observed; CDAI, clinical disease activity index; DAS28-CRP, 28-joint DAS using CRP; GC, glucocorticoid; SDAI, simplified disease activity index

Figure 2. Effect of upadacitinib on GC reduction in patients with RA who achieved (12 months) and maintained (24 months) clinical remission per (A) DAS28-CRP (<2.6), (B) CDAI (≤2.8), or (C) SDAI (≤3.3) among patients taking GCs at baseline.



AO, as observed; CDAI, clinical disease activity index; DAS28-CRP, 28-joint DAS using CRP; GC, glucocorticoid; SDAI, simplified disease activity index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Upadacitinib reduced GC use in patients with moderate-to-severe RA and enabled persistent GC-free clinical remission through 2 years in a real-world setting.

References

1. Buttgereit F. *Nat Rev Rheumatol*. 2020;16:239–46.
2. Rinvoq prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211675s015lbl.pdf. Accessed April 2025.

Disclosure: F. BUTTGEREIT: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6; **A. Ostor**: AbbVie Inc., 1, 2, 12, Clinical Trials, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Eli Lilly, 1, 2, 12, Clinical Trials, GlaxoSmithKlein, 1, 2, 12, Clinical Trials, Janssen, 1, 2, 12, Clinical Trials, Merck, 2, 5, Novartis, 1, 2, 12, Clinical Trials, Pfizer, 1, 2, 12, Clinical Trials, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6; **A. Romero**: AbbVie/Abbott, 3; **I. Lagunes**: AbbVie, 3, 11; **A. Garrison**: AbbVie/Abbott, 3; **T. Gao**: AbbVie, 3, 11; **S. Attar**: AbbVie/Abbott, 1, 5, 6, Amgen, 1, 5, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 5, 6, Gilead, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Hikma, 1, 5, 6, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Organon, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, Sandoz, 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6.

Abstract Number: 2274

Importance Of Fc Region On Therapeutic Survival In Rheumatoid Arthritis Patients With Anti-TNF Therapy

ELENA GRAU GARCIA[1], **Iago Alcantara Alvarez**[2], Jose Ivorra Cortes[3], Pablo Muñoz Martinez[4], Laura Mas Sanchez[5], Alba Maria Torrat Noves[6], Daniel Ramos Castro[7], Belen Villanueva Manes[8], Miguel Simeo Vinaixa[4], Andres Perez Hurtado[9] and José Andrés Román Ivorra[10], [1]HUP La Fe, Valencia, Comunidad Valenciana, Spain, [2]Hospital Universitari i Politènic La Fe, Valencia, Spain, [3]Hospital Universitario La Fe, Valencia, Comunidad Valenciana, Spain, [4]Rheumatology Department. HUP La Fe, Valencia, Spain, [5]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [6]Hospital Universitari i Politècnic La Fe de Valencia, Valencia, Spain, [7]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [8]Hospital La Fe, Valencia, Spain, [9]Hospital Universitario y Politècnico La Fe, Valencia, Comunidad Valenciana, Spain, [10]Hospital Universitari i Politècnic La Fe, Valencia, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: In patients affected by rheumatoid arthritis (RA), it has been studied a relation between high rheumatoid factor (RF) and a favorable response to anti-TNF therapy, regarding the presence of Fc region in the drug (1,2). Nonetheless, there is limited evidence about the therapeutic survival in function of the kind of anti-TNF and the levels of RF in these patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The goal of this investigation is to analyze the survival and persistence of anti TNF drugs, depending on whether they have Fc region and the levels of RF in RA.

Methods: Observation cross-sectional study of anti-TNF treatments administered in RA patients between 2001 and 2022. We collected levels of RF and anti-citrullinated peptide antibodies (ACPAs) at start of medication, clinical activity, duration of treatment and withdrawal cause from the clinical record.

Results: We have included 377 anti-TNF treatments corresponding to 310 RA patients (79% female), with a mean age at diagnosis of 45 (13) years.

Of 377 treatments, 87% were drugs with Fc region in their structure, 75% associated DMARD (mainly methotrexate) and 67% have not received prior biologic therapy. Mean time of evolution of RA until the start of anti-TNF was 110 (103) months and the mean duration of treatment was 75 (71) months, finalizing treatment 64,2%. When initiating therapy, 64% were RF positive (RF) and 72%, ACPA positive (table 1).

We have classified patients according to the positivity of RF and the presence of Fc region in the therapy. We have observed a tendency towards discontinuing treatment in patients with high RF titers (P=0,06), which are treated mainly with an anti-TNF with Fc fraction (P=0,06).

Finally, we have conducted a Kapplan-Meier analysis to evaluate the drug survival considering the presence of Fc region in the medication, with no observed differences between groups. We came up with the same result when comparing treatment regarding RF positivity at beginning of therapy. We classified patients combining the presence of Fc and RF positivity, discovering a greater therapeutic survival in treatments with Fc region and RF negativity (P=0,018). Furthermore, in treatments without Fc region, we report a tendency towards greater therapeutic survival in RF negative cases in comparison with RF positives (P=0,07) (view Image 1).

Table 1

Variable	No Fc fraction N=49	Fc fraction N=328	P-valor
	Mean (SD) / n(%)	Mean (SD) / n(%)	
Age at diagnose (years)	43,49 (13,91)	45,66 (12,31)	0,26
Age at start of treatment (years)	53,22 (12,73)	54,57 (11,88)	0,464
Female	41 (83,67%)	262 (79,88%)	0,666
RA time of evolution until start of drug (months)	118,37 (113,15)	108,36 (102,03)	0,528
Duration of treatment (months)	**38,8 (46,7)**	**80,17 (72,53)**	**<0,001**
RF	207,57 (267,11)	163,27 (265,97)	0,287
ACPA	185,8 (199,66)	181,22 (178,51)	0,896
RCP	**8,48 (11,44)**	**18,61 (24,31)**	**0,006**
ESR	**30,08 (18,49)**	**38,94 (25,89)**	**0,022**
DAS28-ESR	4,93 (1,12)	5,2 (1,29)	0,181
Drug withdrawal	26 (53,06%)	214 (65,24%)	
inefficacy	5 (19,23%)	26 (12,15%)	0,793
loss of efficacy	8 (30,77%)	96 (44,86%)	0,086
adverse reaction	12 (46,15%)	64 (29,91%)	0,536
other	1 (3,85%)	28 (13,08%)	0,212
Prior biologic therapy	**28 (57,14%)**	**97 (29,57%)**	**<0,001**
Associated DMARD	38 (77,55%)	245 (74,7%)	0,799

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

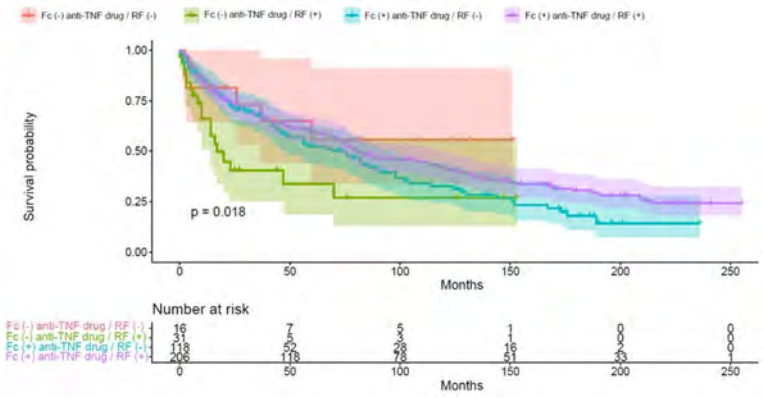


Image 1

Conclusion: We report on a higher percentage of drug withdrawal in patients with RA and anti-TNF treatment with Fc region in their structure, as well as in those cases with higher titers of RF. In addition, we observed a greater therapeutic survival in treatments with low titers of RF and anti-TNF drug without Fc region than in other groups.

Disclosure: E. GRAU GARCIA: None; **I. Alcantara Alvarez**: None; **J. Ivorra Cortes**: None; **P. Muñoz Martinez**: None; **L. Mas Sanchez**: None; **A. Torrat Noves**: None; **D. Ramos Castro**: None; **B. Villanueva Manes**: None; **M. Simeo Vinaixa**: None; **A. Perez Hurtado**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6.

Abstract Number: 2275

Agreement Between Two Rheumatoid Arthritis Response Measures Across Bts DMARD Treatment Classes in a Large, Prospective Observational Study Supporting the Development and Clinical Validation of a Novel Blood based Precision Medicine Test

Peter Taylor[1], **Jason Carlson**[2], Shirley Vu[2], Signe Fransen[3], Diana Abdueva[4] and Jeffrey Curtis[5], [1]University of Oxford, Oxford, United Kingdom, [2]Aqtual Inc, Hayward, CA, [3]Aqtual, sf, CA, [4]Aqtual, Hayward, CA, [5]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Contemporary pharmacological management of rheumatoid arthritis (RA) is set within a treat-to-target framework. This requires quantitative, longitudinal assessments of disease activity with a view to treatment adjustment where necessary. There are many composite scores of RA disease activity and methods to assess response, including improvement in CDAI based on its minimum clinically important difference (MCID) and EULAR response criteria based on the DAS28-CRP. These response measures were employed in the PRIMA-102 (NCT05936970) study supporting development of a novel blood-based assay to predict response to biologic and targeted synthetic DMARDs. The objective of the study is to investigate the agreement between the CDAI MCID and EULAR response criteria and identify correlates of discordance.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: An interim analysis was performed on 636 participants treated with ≥ 1 prior cs/b/tsDMARD who initiated a new b/tsDMARD, TNFi (n=187), JAKi (n=178), Anti T-Cell (n=171), Anti IL-6R (n=77), Anti B-Cell (n=23), contributing data to a prospective, multi-center, observational cohort requiring baseline (BL) blood collection and clinical outcome measures at BL and week 12. Agreement between the two clinical response measures was computed using kappa (k) coefficients and correlates of discordance were assessed using analysis of variance (continuous variables) or chi-square variance (categorical variables) and Hedges' g values were computed to estimate the magnitude of the difference between the groups, with positive values indicating a higher mean in the MCID-only subgroup and negative values corresponding to a higher mean in the EULAR-only subgroup.

Results: 410 participants (64%) had a CDAI MCID response, and 431 participants (68%) had moderate or good DAS28-CRP EULAR response (Table 1). 34 participants (5.3%) were responders per CDAI MCID only, and 55 participants (8.6%) were responders per EULAR response criteria only. Agreement between the two measures was substantial and did not differ by MOA (overall κ=0.69, 95% CI [0.63-0.75], TNFi κ=0.68, JAKi κ=0.67, Anti T-Cell κ=0.69, Anti IL-6R κ=0.72, Anti B-Cell κ=0.68). Baseline characteristics and RA disease activity measures associated with discordance included serostatus, line of therapy, joint counts, and patient/provider global assessment; changes from baseline that were associated with discordance with large relative effect sizes included swollen joint count, provider global assessment, patient VAS, and CRP (Table 2).

Table 1: Agreement Between Response Measures for Each Drug Class

Category	n	No Response on Either Measure	Response on MCID Only	Response on EULAR Only	Responses on Both Measures	Percent Agreement	Percent Discordance	Kappa*	95% CI
All b/ts DMARD Classes	636	171 (26.9%)	34 (5.3%)	55 (8.6%)	376 (59.1%)	86	14	0.69	0.63 - 0.75
TNFi	187	54 (28.9%)	15 (8%)	13 (7%)	105 (56.1%)	85	15	0.68	0.57 - 0.79
JAKi	178	37 (20.8%)	10 (5.6%)	13 (7.3%)	118 (66.3%)	87.1	12.9	0.67	0.55 - 0.79
Anti T-Cell	171	47 (27.5%)	9 (5.3%)	15 (8.8%)	100 (58.5%)	86	14	0.69	0.57 - 0.81
Anti IL-6R	77	28 (36.4%)	0 (0%)	11 (14.3%)	38 (49.4%)	85.7	14.3	0.72	0.56 - 0.88
Anti B-Cell	23	5 (21.7%)	0 (0%)	3 (13%)	15 (65.2%)	87	13	0.68	0.35 - 1.01

* Concordance was measured using kappa coefficients. Conventional interpretation of the kappa coefficient is: < 0 poor agreement; 0 – 0.20 slight agreement; 0.21 – 0.40 fair agreement; 0.41 – 0.60 moderate agreement; 0.61 – 0.80 substantial agreement; and 0.81 – 1.00 near perfect agreement

Table 2: Correlates of Discordance Between MCID CDAI and EULAR DAS CRP Response Labels in the PRIMA-102 Study Population

	Neither Response	MCID CDAI Only	EULAR DAS CRP Only	Both Responses	P	Hedges' g
n = 636 Patients	171	34	55	376		
% Women	86 (2.7)	73.5 (7.6)	85.5 (4.8)	83 (1.9)	0.330	-0.301
% Seropositive	48 (3.8)	38.2 (8.3)	49.1 (6.7)	59 (2.5)	0.016	-0.215
Age, years	58.3 (13.2)	58.8 (13.8)	57 (13.8)	58.5 (13.5)	0.887	0.126
RA Duration, years	8.8 (9.4)	6.2 (8.5)	9.4 (10.2)	9 (9.6)	0.400	-0.335
% with 0-2 Prior b/ts DMARDs	69.6 (3.5)	79.4 (6.9)	70.9 (6.1)	80.6 (2)	0.027	0.191
Measures at study entry						
Tender joint count (0-28)	12.5 (6.7)	17.7 (7.9)	9.8 (4.6)	12.1 (6.8)	< 0.001	1.294
Swollen joint count (0-28)	8.7 (4.5)	14.2 (6.6)	6.5 (2.7)	9.3 (5.1)	< 0.001	1.655
Patient global score (1-10)	6.7 (2.2)	7.8 (1.7)	6.2 (2.3)	6.4 (2.3)	0.003	0.755
Provider global score (0-10)	6.3 (2.1)	7.8 (1.6)	5.7 (1.7)	6.4 (1.9)	< 0.001	1.224
Patient VAS (0-100)	65.5 (23.5)	66.3 (27.3)	69.6 (24)	65.6 (23.6)	0.692	-0.131
CRP, mg/L	8 (14.7)	8.1 (16.1)	13 (17.7)	10.3 (21.3)	0.307	-0.283
Absolute changes during the study						
Tender joint count	-1.3 (4.9)	5.6 (4.6)	3.2 (2.5)	8.7 (5.5)	< 0.001	0.665
Swollen joint count	0.3 (4.2)	7.5 (5.5)	2 (3.4)	7.4 (4.9)	< 0.001	1.261
Patient global score	0 (2.4)	1.9 (2.9)	0.8 (2.7)	2.8 (2.6)	< 0.001	0.397
Provider global score	0.3 (2.3)	3.1 (2.3)	0.9 (1.5)	3.7 (2.3)	< 0.001	1.187
Patient VAS	-4.5 (26.7)	-0.9 (26.3)	23.6 (26.6)	29.9 (29.1)	< 0.001	-0.918
CRP, mg/L	0.9 (13.3)	-10.8 (27.6)	7.3 (15.1)	5.4 (18.9)	< 0.001	-0.863

Values are mean (standard error). Continuous variables (e.g., joint counts) were compared between response groups using one-way analysis of variance. For categorical variables (e.g., serostatus), associations with the response groups were assessed using the chi-square test. Hedges' g was also computed for each of the variables.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: There was generally good agreement between CDAI MCID and EULAR Response criteria, suggesting that either method could support development of a precision medicine test to predict treatment response. However, the higher percentage of positive responses unique to the DAS28-CRP EULAR criteria suggests that EULAR response based on DAS28-CRP may introduce bias when assigning response status for drug classes (e.g., IL-6R) that directly modulate CRP levels.

Disclosure: P. Taylor: AbbVie, 2, Acelyrin, Inc., 2, Alfasigma S.p.A., 2, 5, Biogen, 2, Eli Lilly & Co., 2, Fresenius Kabi, 2, Gilead, 2, Immunovant, 2, Moonlake, 2, Nordic Pharma, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB, 2; **J. Carlson**: Aqtual Inc., 3; **S. Vu**: Aqtual Inc., 3; **S. Fransen**: Aqtual Inc., 3; **D. Abdueva**: Aqtual Inc., 3, 4, 8, 10; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5.

Abstract Number: 2276

Long-Term Cardiovascular Risk Following Tnfi vs Triple Therapy: A Post-hoc Analysis Integrating Randomized Clinical Trial and Electronic Health Record Data

Jennifer Hanberg[1], David Cheng[2], Xuan Wang[3], Rahul Sangar[4], Yuk-Lam Ho[4], Lauren Costa[4], Rachael Matty[4], Candace Feldman[1], Tate Johnson[5], Joshua Baker[6], Bryant England[5], J. Michael Gaziano[1], Kelly Cho[7], James O'Dell[5], Grant Cannon[8], Paul Monach[4], Ted Mikuls[5], Tianxi Cai[7] and Katherine Liao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, MA, [3]University of Utah, Salt Lake City, UT, [4]VA Boston Healthcare System, Boston, MA, [5]University of Nebraska Medical Center, Omaha, NE, [6]University of Pennsylvania, Philadelphia, PA, [7]Harvard Medical School, Boston, MA, [8]University of Utah and Salt Lake City VA, Salt Lake City, UT

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) are often avoided when treating rheumatoid arthritis (RA) patients with decompensated heart failure (HF), based on increased rates of HF exacerbation in a trial of advanced HF patients without RA. In RA, recent data suggest that reducing inflammation, including with TNFi, is beneficial for HF risk reduction. We sought to leverage a unique cohort with data from an RA randomized clinical trial (TNFi vs triple therapy), linked to longitudinal electronic health records (EHR), enabling comparison of major adverse cardiovascular events (MACE) and HF events after trial completion.

Methods: We studied subjects from the Therapies for Active Rheumatoid Arthritis after Methotrexate (MTX) Failure (RACAT) trial, where 16 of the 36 sites were Veteran Affairs (VA) hospitals; participants were randomized to etanercept (ETA) plus MTX or triple therapy (hydroxychloroquine, sulfasalazine, MTX) for 48 weeks. Exclusion criteria included subjects with New York Heart Association class III or IV HF. Participants in the trial were linked to longitudinal VA EHR data, allowing assessment of outcomes after trial completion (4/2011). Participants were followed in the VA EHR from randomization (index date), for up to 5 years after trial completion. HF events and MACE related to atherosclerotic cardiovascular disease were defined by previously published ICD and CPT codes. As cross-over was allowed in RACAT at 24 weeks, the primary exposure was defined based on intention-to-treat (ITT) and as-treated (within the trial). We used unadjusted Cox regression to evaluate the association between the primary exposure (randomization to ETA+MTX versus triple therapy (referent)) and MACE, HF or death.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of the Therapies for Active Rheumatoid Arthritis after Methotrexate Failure (RACAT) trial participants in the VA with EHR follow-up based on intention-to-treat, at randomization.

Characteristic	Etanercept + methotrexate (49%)	Triple therapy (51%)
Age, mean (SD)	60 (11)	63 (10)
Male	85%	92%
White self-reported race	83%	87%
RA duration, mean years (SD)	5.8 (8.6)	6.8 (11)
DAS28, mean (SD)	5.9 (0.8)	5.9 (0.9)
History of MACE	3%	3%
History of HF	7%	3%
Statin use	51%	54%
TNFi use, post-study (intention-to-treat population)*	79%	43%
TNFi use, post-study (as-treated population)**	83%	35%

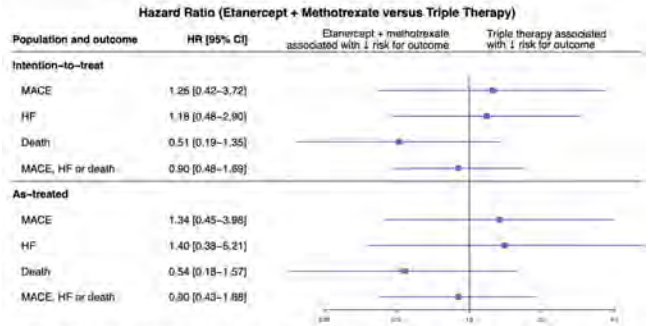
RA: rheumatoid arthritis; MACE: major adverse cardiac events; HF: heart failure; DAS28: disease activity score in 28 joints. Subjects were considered as having either continued or initiated a TNFi post-study if ≥2 TNFi prescriptions were present in the 5 years after the trial. *Intention-to-treat population defined by randomization to etanercept + methotrexate versus triple therapy. **As-treated population defined by continuation of assigned treatment, rather than crossover, at 24 weeks.

Table 2. Incident MACE and HF events 5 years after trial completion in the intention-to-treat and as-treated populations.

Characteristic	Etanercept + methotrexate	Triple therapy
Intention-to-treat population*		
MACE	9%	8%
HF	13%	11%
Death from any cause	8%	15%
MACE, HF or Death	24%	27%
As-treated population**		
MACE	14%	10%
HF	10%	7%
Death from any cause	10%	17%
MACE, HF or Death	25%	28%

MACE: major adverse cardiac events; HF: heart failure. *Intention-to-treat population defined by randomization to etanercept + methotrexate versus triple therapy. **As-treated population defined by continuation of assigned treatment, rather than crossover, at 24 weeks.

Figure 1. Hazard ratios for major adverse cardiac events and heart failure in patients randomized to etanercept plus methotrexate versus triple therapy in the intention-to-treat and as-treated populations.



MACE: major adverse cardiac events. HF: heart failure. HR: hazard ratio. 95% CI: 95 percent confidence interval.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 353 participants in RACAT, 66% were rheumatoid factor positive, and 44%* were followed at VA. Of these participants, 49% were randomized to ETA+MTX and 51% to triple therapy (**Table 1**). The mean age at randomization was 62 years, 89% were male, and 85% were self-reported White. Prior diagnoses of HF or MACE were present in 5% and 3% of the population, respectively, before randomization. After the 48-week trial period, TNFi use was more frequent in the group randomized to ETA+MTX (79%) compared to the triple therapy (43%).

For ITT, incident MACE occurred in 8% of participants within 5 years of trial completion (**Table 2**), and the risk for incident MACE was comparable between the treatment groups (HR 1.25, 95% CI 0.42-3.72; **Figure 1**). Incident HF events occurred in 12% of participants within 5 years, and the risk for HF was comparable between the two treatment groups (HR 1.18, 95% CI 0.48-2.90). MACE, HF or death occurred in 25% of participants, and the risk was comparable between groups (HR 0.90, 95% CI 0.48-1.69). Similar effect estimates were observed in the as-treated analysis.

* VA data privacy regulations require reporting as percentages due to some groups with n < 11

Conclusion: In this post-hoc analysis of a randomized controlled trial using EHR data to extend long term follow-up to 5 years after trial completion, we observed a similar incidence of MACE and HF irrespective of randomization to ETA+MTX or triple therapy.

Disclosure: J. Hanberg: None; **D. Cheng**: AstraZeneca, 5; **X. Wang**: None; **R. Sangar**: None; **Y. Ho**: None; **L. Costa**: None; **R. Matty**: None; **C. Feldman**: American College of Rheumatology, 2, Arthritis Foundation, 5, 12, Task Force Member, Bain Capital, 2, Bristol-Myers Squibb Foundation, 5, Harvard Pilgrim, 2, Lupus Foundation of America, 1, 12, Associate Editor, Medical-Scientific Advisory Board Member, OM1, Inc., 2; **T. Johnson**: None; **J. Baker**: Amgen, 5; **B. England**: Boehringer-Ingelheim, 2, 5; **J. Gaziano**: None; **K. Cho**: None; **J. O'Dell**: None; **G. Cannon**: None; **P. Monach**: Boehringer-Ingelheim, 2; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **T. Cai**: None; **K. Liao**: Merck/MSD, 2, UCB, 2.

Abstract Number: 2277

Immunophenotyping of peripheral blood mononuclear cells reveals potential cellular biomarkers of disease in rheumatoid arthritis

John Bui[1], Jason Dubovsky[2], Jennifer Abrams[3], Sara Charmsaz[4], Michelle Blake[1], Joshua Beilke[4], Anne-Renee van der Vuurst de Vries[1], Joseph Arron[5], Jonathan Graf[6] and Jeffrey Bluestone[7], [1]Sonoma Biotherapeutics, Seattle, WA, [2]Sonoma Biotherapeutics, South San Francisco, [3]Sonomabio, San Francisco, CA, [4]Sonoma Biotherapeutics, Seattle, [5]Sonoma Biotherapeutics, San Francisco, CA, [6]UCSF, San Francisco, CA, [7]Sonoma Biotherapeutics, South San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Emerging cell-based therapies for rheumatoid arthritis (RA) target the underlying immunologic activity of disease. Objective biomarkers to-date are downstream sequelae of RA immunologic drivers. In this study, we sought to identify direct cellular biomarkers in RA by comprehensively profiling immune subsets from whole blood.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Here, three flow cytometry panels measuring 18 markers were used to identify T cell subsets. PBMC were profiled from 30 RA subjects with varying disease severity measured by DAS28-CRP, DAS28-ESR and CDAI in addition to 23 age-, gender-, and race-matched healthy donor control subjects (HD). A two-tiered approach was applied for data analysis: Tier 1) Identify cell subsets significantly different between RA and HD and Tier 2) Correlate cell subsets identified in Tier 1 with RA clinical disease severity.

Results: The analysis revealed a significant difference ($p \leq 0.001$) between RA (12%) and HD (39%) in the frequency of an effector regulatory T cells (Treg) phenotype defined by $CD4^{+}FOXP3^{+}CD25^{hi}CD45RA^{-}$. Furthermore, the frequency of these cells was inversely correlated with disease severity measured by DAS28-CRP ($r = -0.525$, $p = 0.039$). Activation and proliferation markers on the Tregs in the RA subjects were similarly inversely correlated with DAS28-CRP (r= -0.53 HLA-DR, r= -0.49 CTLA-4, r= -0.52 Ki67). In contrast, the T effector cell subset phenotype data reveal significantly higher frequency ($p=0.001$) of CD4+CD45RA-CCR7+ central memory $CD4^{+}$ T cells (Tcm) in RA (31%) compared to HD (20%). Moreover, the frequency of $CD4^{+}$ Tcm was positively correlated with DAS28-ESR ($r = 0.615$, $p = 0.037$).

Conclusion: We show that, compared to healthy subjects, RA patients have significantly reduced proportion of Tregs with an effector phenotype and a higher proportion of CD4 Tcm. These phenotypic frequencies correlate with disease severity, highlighting a relationship of these immune subsets to the pathogenesis of RA. Additional characterization of these subsets will be pursued to determine their potential utility as pharmacodynamic biomarkers.

Disclosure: J. Bui: Sonoma Biotherapeutics, 3; **J. Dubovsky**: Sonoma Biotherapeutics, 3; **J. Abrams**: None; **S. Charmsaz**: None; **M. Blake**: Sonoma Biotherapeutics, 3, 11; **J. Beilke**: Sonoma Biotherapeutics, 3; **A. van der Vuurst de Vries**: None; **J. Arron**: Sonoma Biotherapeutics, 12,, 3, 4; **J. Graf**: None; **J. Bluestone**: Gilead, 4.

Abstract Number: 2278

Neuroimmune modulation for the Treatment of Rheumatoid Arthritis: Results at 12 months from a Randomized, Sham-Controlled, Double-Blind Study

John Tesser[1], Angela Crowley[2], Jane Box[3], Joshua June[4], Pendleton Wickersham[5], Guillermo Valenzuela[6], Norman Gaylis[7], Gordon Lam[8], Leroy Pacheco[9], David Ridley[10], Gineth Pinto-Patarroyo[11], Stuart Novack[12], Melvin Churchill[13], Minna Kohler[14], Eric Lee[15], Jose A Pando[16], Glenn R. Parris[17], Jeff Peterson[18], Tina Shah[19], Atul Singhal[20], Victoria Vuong[21], Jeffrey Curtis[22] and David Chernoff[23], [1]Arizona Arthritis & Rheumatology Associates, Phoenix, AZ, [2]Illinois Bone and Joint Institute - Hinsdale Orthopaedics, Hinsdale, IL, [3]DJL Clinical Research, PLLC, Charlotte, NC, [4]Great Lakes Center of Rheumatology, Lansing, MI, [5]Arthritis Associates PA, San Antonio, TX, [6]Integral Rheumatology & Immunology Specialists, Plantation, FL, [7]Arthritis & Rheumatic Disease Specialties, Aventura, FL, [8]Arthritis and Osteoporosis Consultants of the Carolinas, Cornelius, NC, [9]Albuquerque Ctr for Rheumatology, Albuquerque, NM, [10]Saint Paul Rheumatology, Eagan, MN, [11]Annapolis Rheumatology, Herndon, VA, [12]Nuvance Health network, NORWALK, CT, [13]Arthritis Center of Nebraska, Lincoln, NE, [14]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [15]Inland Rheumatology and Osteoporosis Medical Group, Upland, CA, [16]Delaware Arthritis, Lewes, DE, [17]PARRIS & ASSOCIATES, Lilburn, GA, [18]Western Washington Arthritis Clinic, Seattle, WA, [19]Kansas City Physician Partners, Kansas City, MO, [20]SouthWest Arthritis Research Group, Mesquite, TX, [21]Long Island Regional Arthritis & Osteoporosis Care, Hicksville, NY, [22]University of Alabama at Birmingham, Birmingham, AL, [23]SetPoint Medical, Sausalito, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Neuroimmune modulation by electrical stimulation of the left cervical vagus nerve represents a novel treatment option for rheumatoid arthritis (RA). We present 12-month efficacy and safety outcomes for an implantable vagus nerve stimulation device to treat biologic-experienced patients with RA (the RESET-RA study, ClinicalTrials.gov, NCT04539964).

Methods: In this multicenter, randomized, double-blind, sham-controlled, pivotal trial, patients with prior inadequate response or intolerance to at least one biologic or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) were randomly assigned to stimulation (treatment) or sham. The primary endpoint of ACR20 response was assessed 3 months after randomization. After 3 months, sham crossed over to treatment, and all patients received stimulation during open-label follow-up, with results reported through 12 months. Secondary endpoints included safety measures, disease activity scores, and use of RA drugs in combination with stimulation.

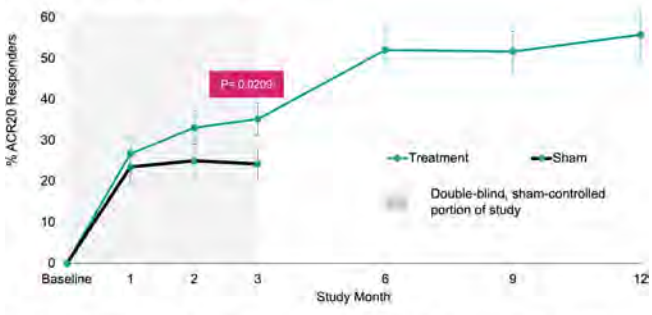
Results: 242 participants across 41 US study sites were consented and underwent device implantation followed by 1:1 randomization to treatment or sham. Baseline characteristics were well-balanced with mean age of 56 years, 86% female, RA duration 12.4 years, 15 tender joints, and 10 swollen joints (28 joint count). Overall, 39% of patients had been treated with exactly 1 prior b/tsDMARD, 22% with exactly 2, and 39% with 3 or more. 43% of all patients were exposed to b/tsDMARDs with differing mechanisms of action.

At 3 months, a significantly greater percentage of patients in the treatment group were ACR20 responders (treatment 35.2% [43/122] vs. sham 24.2% [29/120], p=0.0209). Response rates continued to improve for treatment group: 52.1% at 6 months, 51.7% at 9 months, and 55.8% at 12 months (**Figure 1**). Disease activity scores showed a similar trend with 49.3% attaining DAS28-CRP low disease activity or remission, 47.4% attaining CDAI low disease activity or remission and 77.3% attaining EULAR good/moderate response at 12 months (**Figure 2**).

Augmentation of stimulation therapy with a b/tsDMARD was allowed without restriction following the 3-month, controlled portion of participation. By 12 months, only 24.8% of patients added a b/tsDMARD to stimulation therapy and 97.5% of all patients remained persistent with stimulation therapy.

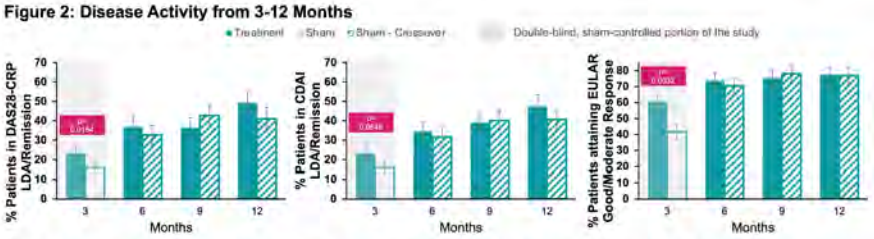
The implant procedure was well-tolerated, with a serious adverse rate of 1.7%, all occurring during the perioperative period. The most common, related adverse event was transient vocal cord paresis presenting as hoarseness following the implant procedure. Stimulation was well-tolerated, with few non-serious events, such as pain or sleep disturbance. These were typically managed by adjusting the stimulation dose. No deaths or unanticipated adverse device effects occurred (**Table 1**).

Figure 1: ACR20 Response Rates



ACR20 response rates at 3 months, 6 months, 9 months, and 12 months. Patients imputed as non-responders if missing or rescued with high-dose steroid or b/tsDMARDs up to 3 months. 6, 9, and 12-month results exclude patients that augmented stimulation with a high-dose steroid or b/tsDMARD.

Figure 2: Disease Activity from 3-12 Months



Percentage of patients in low disease activity or remission (DAS-28-CRP </+ 3.2 [left], CDAI </= 10 [center]), and EULAR good to moderate response (right) at 3, 6, 9, and 12 months. Patients imputed as non-responders if missing or rescued with high-dose steroids or b/tsDMARDs up to 3 months. 6, 9, and 12 Month results exclude patients that augmented stimulation therapy with high-dose steroid or b/tsDMARD.

Table 1: Summary of Safety by Adverse Event Reporting

	Sham-Control, Blinded Period through Month 3		Open-Label through Month 12		
	Treatment N=122	Sham N=120	Treatment N=121	Sham-Crossover N=120	All N=241
Number of pts (%) with Adverse Event	81 (66.4%)	86 (71.7%)	84 (69.4%)	88 (73.3%)	172 (71.4%)
Procedure or Device Related[1]	16 (13.1%)	22 (18.3%)	1 (0.8%)	2 (1.7%)	3 (1.2%)
Stimulation Related[2]	10 (8.2%)	0	4 (3.3%)	5 (4.2%)	9 (3.7%)
Serious Adverse Events	4 (3.3%)	5 (4.2%)	7 (5.8%)	14 (11.7%)	21 (8.7%)
Related, Serious Adverse Event[3]	3 (2.5%)	1 (0.8%)	0	0	0
Unrelated, Serious Adverse Event	2 (1.6%)	4 (3.3%)	7 (5.8%)	14 (11.7%)	21 (8.7%)
Serious Infection (unrelated)	0	1 (0.8%)	0	5 (4.2%)	5 (2.1%)
AE leading to study discontinuation	0	0	0	1 (0.8%)	1 (0.4%)
Death	0	0	0	0	0

[1] AEs with frequency ≥3% included mild/moderate vocal cord paresis or dysphonia, resolved or stable with no significant sequelae

[2] AEs with frequency ≥3% included mild/moderate pain, managed with adjustment to stimulation level

[3] SAEs included incision site swelling where participant was hospitalized for evaluation, but no infection was identified (resolved); vocal cord paresis with dysphagia that led to hospitalization (resolved); dysphonia at worse severity deemed by investigator significant enough to impair daily activities (resolved, mild sequelae), and pharyngeal injury repaired intraoperatively, no hospitalization required (resolved).

Conclusion: RESET-RA met its primary efficacy and safety endpoints, demonstrating that vagus nerve-mediated neuroimmune modulation by electrical stimulation using an implantable device is well-tolerated with durable efficacy through 12-months among adults with active RA disease and inadequate response or intolerance to at least one b/tsDMARD.

Disclosure: J. Tesser: AbbVie/Abbott, 2, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, 6, Celgene, 5, Eli Lilly, 2, 5, 6, Genentech, 5, Gilead, 5, GlaxoSmithKlein(GSK), 2, 5, 6, IGM Biosciences, 5, Janssen, 2, 5, 6, Merck/MSD, 5, Novartis, 2, 5, Pfizer, 5, 6, Roche, 5, SetPoint Medical, 2, UCB, 2, 5, 6; **A. Crowley**: None; **J. Box**: Setpoint, 5; **J. June**: Janssen, 2, SetPoint Medical, 2, 5; **P. Wickersham**: AbbVie/Abbott, 1, 5, 6, 7, Amgen, 6, AstraZeneca, 1, 2, 6, 7, Eli Lilly, 5, 6, Janssen, 1, 6, Novartis, 6, UCB, 1; **G. Valenzuela**: AbbVie, 1, 2, 2, 6, 6, Alexion, 1, 2, Amgen, 1, 2, 6, Artiva Biotherapeutics, 2, 5, AstraZeneca, 6, Boehringer-Ingelheim, 1, 2, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 1, 2, 6, Centocor, 6, Eli Lilly, 1, 2, 6, Esaote, 1, Exagen, 1, 2, Genentech, 1, 2, 6, Gilead, 1, 2, Global Healthy Living Foundation, 1, 2, Horizon, 1, 2, 6, Image Analysis Group, 1, Janssen, 1, 2, 6, Mallinckrodt, 5, 6, Merck, 1, 2, Novartis, 1, 2, 6, Pfizer, 1, 2, 6, Pharmacia, 1, 2, 6, Radius, 6, Regeneron, 1, 2, 6, Sandoz, 1, 2, Sanofi, 1, 2, 6, Takeda, 6, Theramex, 6, UCB, 1, 2, 6, Vividion therapeutics, 1, 2; **N. Gaylis**: AB solutions, 4, AbbVie/Abbott, 5, Acelyrn, 5, Alumis, 5, Amgen, 5, aqtual, 5, Artiva, 5, Biogen, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, galapagos, 5, Genentech, 5, Gilead, 5, GlaxoSmithKlein(GSK), 5, 5, Horizon, 5, IGM Biosciences, 5, Inmedix, 1, Moonlake, 5, Novartis, 5, Sanofi, 5, SetPoint Medical, 5, Takeda, 5, UCB, 5; **G. Lam**: AbbVie/Abbott, 1, 2, 6, Amgen, 1, 6, AstraZeneca, 1, 6, Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 1, 6, Janssen, 1, 6, Pfizer, 2, 6, Setpoint, 1, 2, UCB, 1, 6; **L. Pacheco**: AbbVie, 5, Amgen, 5, Eli Lilly, 5, Horizon, 5, Janssen, 5, SetPoint Medical, 5, UCB, 5;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

D. Ridley: Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Johnson and Johnson, 5, UCB, 5; **G. Pinto-Patarroyo**: None; **S. Novack**: None; **M. Churchill**: None; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **E. Lee**: None; **J. Pando**: None; **G. Parris**: None; **J. Peterson**: Amgen, 1, 2, 5, 6, 10, Arthrosi, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 1, 2, 5, 6, Johnson and Johnson, 6, Novartis, 2, SOBI, 2, UCB, 1, 6; **T. Shah**: AbbVie/Abbott, 2, 5, 11, Amgen, 5, Johnson and Johnson, 5, 6, 11, Merch, 5, Novartis, 5, Tukeda, 5, UCB, 5; **A. Singhal**: AbbVie/Abbott, 5, 6, Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, Fujifilm, 5, Gilead, 5, Janssen, 5, Mallinckrodt, 5, MedImmune, 5, Nichi-Iko, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Roche, 5, Sanofi, 5, UCB, 5; **V. Vuong**: AstraZeneca, 5, scipher medcine corp, 5, SetPoint Medical, 5; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **D. Chernoff**: SetPoint Medical, 12,, 3, 8, 10, 11.

Abstract Number: 2279

Long-Term Prevention of RA in high-risk individuals after a 6-Month Placebo-Controlled Intervention with Abatacept -The ARIAA Trial

Koray Tascilar[1], Mikkel Ostergaard[2], Verena Schoenau[3], Uta Kiltz[4], Xenofon Baraliakos[4], David Kofler[5], Martin Feuchtenberger[6], Ulrike Steffen[7], Mario Zaiss[8], Michael Zaenker[9], Reinhard Voll[10], Cornelia. Glaser[11], Holger Bang[12], Eugen feist[13], Gerd Burmester[14], Kirsten Karberg[15], Joachim Strunk[16], Juan Cañete[17], Esperanza Naredo[18], Mária Filková[19], Ladislav Šenolt[19], Georg Schett[20] and Juergen Rech[7], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [2]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, and Copenhagen Center for Arthritis Research, Center for Rheumatology, Rigshospitalet, Glostrup, Denmark, [3]- Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany., Erlangen, Germany, [4]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [5]University of Cologne, Cologne, Germany, [6]MED | BAYERN OST GmbH, Fachbereich Rheumatologie, Burghausen, Germany, Burghausen, Bayern, Germany, [7]Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany, Erlangen, Bayern, Germany, [8]1Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany, Erlangen, Bayern, Germany, [9]Immanuel Klinikum Bernau , Herzzentrum Brandenburg, Abteilung Innere Medizin, Bernau, Germany, Berlin, Germany, [10]University Medical Center Freiburg, Freiburg, Germany, [11]Department of Rheumatology and Clinical Immunology, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, Freiburg, Baden-Wurttemberg, Germany, [12]Orgentec, Mainz, Germany, [13]Helios Department of Rheumatology, Vogelsang-Gommern, Germany, [14]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin, Berlin, Germany, [15]Praxis für Rheumatologie und Innere Medizin, Rheumatologie, Berlin, Germany, Berlin, Germany, [16]Krankenhaus Porz am Rhein GmbH, Rheumaklinik, Köln (Porz), Germany, Köln-Porz, Germany, [17]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [18]Department of Rheumatology and Joint and Bone Research Unit. Fundación Jiménez Díaz University Hospital and Health Research Institute FJD-UAM, Madrid, Spain, MADRID, Spain, [19]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [20]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: A 6-month intervention with abatacept in the ARIAA trial (EUDRA-CT 2014–000555–93) significantly retarded the development of RA compared to placebo in ACPA-positive individuals with joint pain and subclinical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

inflammation on hand MRI. This inhibitory effect peaked at the end of the 6-month treatment period and was still discernible after 1-year of follow-up without any intervention. The durability of the inhibitory effect on development of RA is not known.

Objectives: To assess the durability of the inhibitory effect of abatacept to develop RA observed in the ARIAA trial.

Methods: The ARIAA trial recruited individuals with positive ACPA antibodies, joint pain and findings of synovitis, tenosynovitis or bone marrow edema on the MRI of the dominant hand. Subjectswere randomized to receive a 6-month course of abatacept 125 mg sc weekly or placebo and followed without any treatment for additional 12 months. Individuals who did not develop RA during the study period of December 2014 and June 2021 were contacted up to November 2024 to ascertain their latest status for RA diagnosis based on the discretion of their primary physician. We used survival analysis methods and calculated restricted mean survival time difference, net average RA-free time gained due to treatment over time to evaluate the durability of treatment effect and compared the characteristics of participants who developed RA during study to those who developed RA later and who never developed RA

Results: 98 individuals with a positive ACPA were randomized to abatacept (49) or placebo (49). At the end of treatment (6 months) and observation (18 months) periods, RA developed in 4 (8%) and 17 (35%) participants in the abatacept group as opposed to 17 (35%) and 28 (57%) participants in the placebo group resulting in 15.3 weeks (95%CI, 4.3 to 26.3) of RA-free time gain on average in the abatacept group compared to placebo by the end of the study. After the closure of the study, 17 participants in the abatacept group and 8 participants in the placebo group developed RA during a median follow-up duration of 5.3 years after randomization (IQR, 1.9 to 7.2 years) which cumulated to 34/49 (69%) in the abatacept group and 36/49 (73%) in the placebo group. During this period the RA-free survival gain in the Abatacept group persisted for up to 5 years (figure 1A) increasing to ∼40 weeks (figure-1B). The first derivative (Figure-1C) of the RMST difference curve

Table-1 Characteristics of the study population by RA status at long-term follow-up.

Characteristic	Overall N = 98[1]	No RA N = 28[1]	RA after study N = 25[1]	RA during study N = 45[1]	p-value[2]
Age	49 (42, 59)	49 (46, 62)	52 (41, 59)	49 (42, 56)	0.5
Female gender	70 (71%)	22 (79%)	15 (60%)	33 (73%)	0.3
Abatacept use	49 (50%)	15 (54%)	17 (68%)	17 (38%)	0.048
RF	33 (20, 112)	20 (13, 23)	55 (22, 111)	62 (25, 281)	<0.001
ACPA above median	49 (50%)	13 (46%)	12 (48%)	24 (53%)	0.8
Never smoker	40 (41%)	14 (52%)	12 (48%)	14 (31%)	0.2
MRI synovitis score	6.0 (4.0, 9.0)	5.0 (4.0, 9.0)	9.0 (5.0, 11.0)	6.0 (3.0, 8.0)	0.084
MRI tenosynovitis score	4.0 (2.0, 7.0)	4.0 (2.0, 5.0)	4.0 (3.0, 8.0)	4.5 (2.0, 7.5)	0.4
MRI osteitis score	1.00 (0.00, 2.00)	0.00 (0.00, 1.00)	0.00 (0.00, 2.00)	1.00 (0.00, 3.00)	0.13
ESR	13 (8, 20)	9 (5, 14)	13 (8, 24)	16 (9, 26)	0.024
Painful joints	3.0 (0.0, 6.0)	0.5 (0.0, 2.5)	3.0 (0.0, 6.0)	4.0 (2.0, 8.0)	0.001
DAS-28 ESR	2.92 (2.28, 3.97)	2.30 (1.49, 2.79)	3.19 (2.29, 4.06)	3.39 (2.88, 4.41)	<0.001
Pain VAS, mm	45 (13, 69)	15 (3, 46)	45 (22, 65)	55 (21, 77)	0.001
Patient global VAS	44 (10, 72)	13 (3, 35)	51 (21, 70)	56 (20, 79)	<0.001
Physician global VAS	18 (4, 36)	5 (1, 18)	18 (10, 40)	30 (12, 44)	<0.001
RAID	3.87 (1.87, 5.68)	2.02 (0.58, 3.95)	4.90 (2.48, 6.09)	5.15 (2.61, 6.53)	<0.001
SF-36 PCS	41 (31, 47)	46 (39, 50)	41 (31, 50)	35 (29, 43)	0.005

RF rheumatoid factor, ACPA anti-citrullinated protein antibodies, MRI magnetic resonance imaging, ESR erythrocyte sedimentation rate, CRP c-reactive protein, VAS visual analog scale, RAID, rheumatoid arthritis impact of disease questionnaire, SF-36 short form 36 items, PCS physical component summary 1 Median (Q1, Q3); n (%) 2 Kruskal-Wallis rank sum test; Pearson's Chi-squared test

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

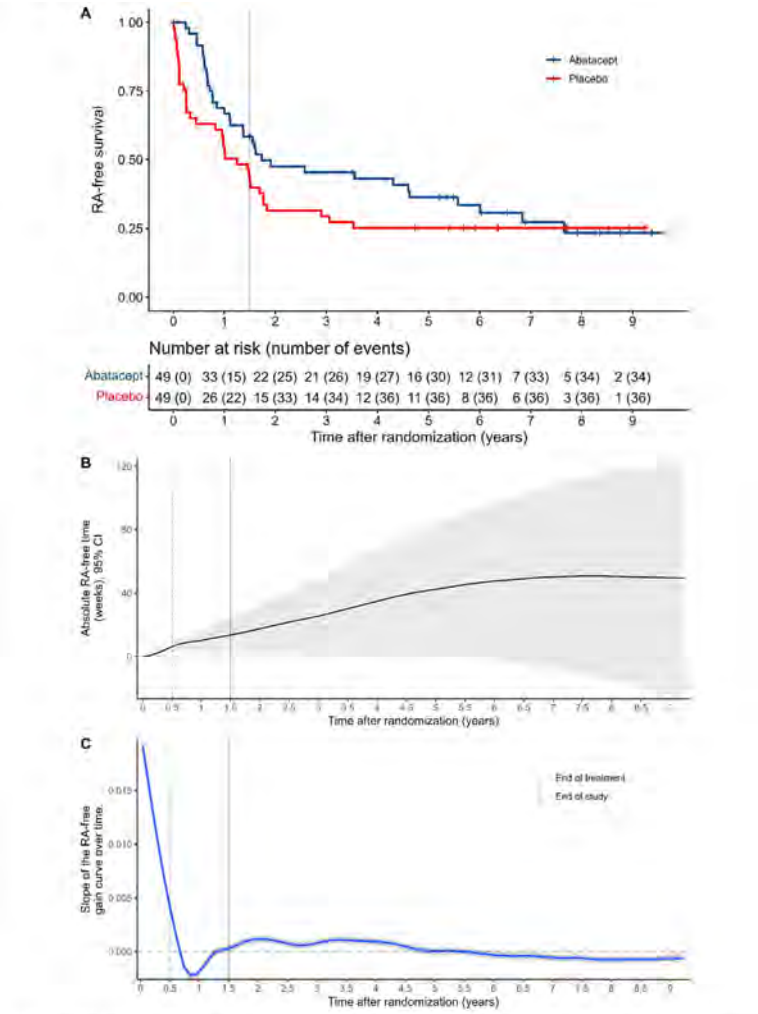


Figure-1 A) Kaplan-Meier Curve showing RA-free survival during and after ARIAA. B) Restricted-mean-survival difference between Abatacept and Placebo arms showing average RA-free time gained over follow-up. C) Slope of the restricted mean survival time ratio over time. Positive values indicate diverging survival curves i.e., accelerated gain of RA-free time in the treatment arm, negative values indicate convergence of survival curves. Dashed vertical lines indicate the end of study treatment and solid vertical lines indicate end of study. Error bands indicate 95% CI

indicates that the inhibitory effect (a positive slope for RA-free time gain) of abatacept during the treatment-period is offset initially during the first year after treatment cessation but then persisted for up-to five years after randomization and waned afterwards resulting in an ultimate catch-up of the placebo arm. A descriptive comparison of participants who never developed RA indicate that these had a lower ESR, lower RF levels, lower pain scores and better functional status at baseline (Table-1).

Conclusion: Abatacept showed a delayed inhibitory effect against the development of RA lasting for up-to 5 years after the initial 6-month intervention. Systemic inflammation, autoimmunity, pain, and function could help improve risk stratification while selecting individuals at risk of RA for a preventive intervention

Disclosure: K. Tascilar: None; **M. Ostergaard**: AbbVie, 2, 5, 6, Amgen, 5, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, MEDAC, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Sandoz, 6, UCB, 2, 5, 6; **V. Schoenau**: AbbVie/Abbott, 1, 6, Chugai, 5, 6, Novartis, 1, 6, Roche, 5; **U. Kiltz**: AbbVie, 2, 5, Amgen, 2, 5,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Biocad, 2, 5, Biogen, 2, 5, BMS, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Fresenius, 2, 5, Gilead, 2, 5, Grünenthal, 2, 5, GSK, 2, 5, Hexal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, onkowissen.de, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Viatris, 2, 5; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **D. Kofler**: AbbVie, 1, UCB, 1; **M. Feuchtenberger**: None; **U. Steffen**: None; **M. Zaiss**: None; **M. Zaenker**: None; **R. Voll**: None; **C. Glaser**: None; **H. Bang**: Orgentec, 3; **E. feist**: AB2Bio, 6, AbbVie/Abbott, 6, Alfasigma, 6, AstraZeneca, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Eli Lilly, 6, Galapagos, 6, Hexal, 6, Janssen, 6, Medac, 6, Novartis, 6, Pfizer, 6, Roche/Chugai, 6, R-Pharm, JSC, 6, Sandoz, 6, Sanofi, 6, Sobi, 6, UCB, 6; **G. Burmester**: Celltrion, 6, Chugai, 6, Fresenius, 6, Gedeon Richter, 6, Sanofi, 6; **K. Karberg**: None; **J. Strunk**: None; **J. Cañete**: None; **E. Naredo**: None; **M. Filková**: None; **L. Šenolt**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **J. Rech**: Novartis, Sobi, 1, 2, 5, 6.

Abstract Number: 2280

Changes of B Cell Subsets During Treatment with Abatacept in Patients with Rheumatoid Arthritis

Athanasios Mavropoulos[1], Christos Liaskos[2], Ioannis Alexiou[3], Christina Katsiari[4], Dimitrios Bogdanos[5] and **Lazaros Sakkas**[6], [1]University of Thessaly, Volos, Greece, [2]University of Thessaly, Faculty of Medicine, Larisa, Greece, [3]University General Hospital of larissa, Larissa, Greece, [4]University General Hospital of Larisa, University of Thessaly Faculty of Medicine, Larisa, Greece, [5]Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece, [6]Department of Rheumatology, University of Thessaly, Larissa, Greece

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Abatacept, an efficacious therapy for rheumatoid arthritis (RA), inhibits the interaction between CD28 on T cells and CD80/CD86 on antigen-presenting cells (APCs). The aim of our study was to examine the effect of abatacept on B cell subtypes in patients with RA.

Methods: Twenty-five patients with RA, not responding to conventional DMARDs, received Abatacept and included in the study. DAS28 (ESR), DAS28(CRP) and SDAI were measured at baseline and at 6 months post-treatment. Serum sample and peripheral blood mononuclear cells were collected at baseline and at 6 months post-treatment.

ACPA were tested using commercial ELISA and LINEBLOT (for CCP3, citrullinated vimentin, citrullinated a-enolase peptide). Five subsets of B cells including regulatory B cells (Bregs) were analyzed at baseline and 6-months post-Abatacept treatment by flow cytometry using a FACS Calibur cytometer (Becton Dickinson): B cells, naive B cells, PDL-1^{+}B cells, PDL-1^{+}CD27^{+}B cells, PDL-1^{+}CD27^{-}B cells, PDL-1^{hi}Bregs (CD19+ PD-L1++).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: At baseline ACPA positivity was found in 52% of patients. All patients who were positive for ACPA at baseline remained positive at 6 months post-treatment without significant changes of their titers. In addition, none of ACPA-negative patients become positive at 6-months post-treatment.

Response to therapy was found in 84.6% ACPA(+) patients and in 58.3% of ACPA(-) (p=0.0034). DAS28(ESR), DAS28 (CRP) and SDAI scores at baseline were (mean±SD, 5.64±1.36, 5.19±1.40, and 34.13±18.23, respectively and significantly decreased at 6-months post-treatment (3.03±1.14, 2.9±1.02 and 9.06±7.82, respectively).

At baseline, levels of B cell subtypes were higher in ACPA(+) compared to ACPA(-) patients (naïve Bregs, 44.89±11.48 vs 35.66±14.6, p=0.095; PDL1^{+}B cells, 24.19±9.13 vs 17.7±5.73, p=0.044; PDL-1^{+} of CD27^{+}B cells, 29.37±8.41 vs 18.45 ±7.13, p=0.002; PDL-1^{hi}Bregs, 7.64±2.29 vs 5.84±2.00, p=0.048).

At 6 months post-treatment, ACPA(+) patients compared to ACPA(-) patients exhibited higher percentage increase in PDL-1^{+} of CD27^{-}B cells (39.3±28.04 vs 14.45±18.87, p=0.016) and in PDL-1^{hi}Bregs cells (38.02±23.2 vs 12.9±15.38, p=0.004).

High levels of B cell subtypes at baseline were associated with SDAI remission at 6 months post-Abatacept treatment. At baseline, responders compared to non-responders had higher levels of naïve B cells (45.01±10.37 vs 28.64±14.56, p=0.025), PDL-1^{+}B cells (24.07±7.61 vs 13.4±3.3, p< 0.001), PDL-1+ of CD27+ B cells (27.51±8.51 vs 15.44±5.58, p=0.001), and PDL-1^{hi}Bregs (7.69±1.94 vs 4.40±1.25, p< 0.001).

At 6-months post-treatment PDL-1+ of CD27-Bcells increased in responders vs non-responders (36.26±26.13% vs 4.52 ±9.39, p< 0.001). Finally, DAS28(ESR) score during treatment was negatively correlated with change of levels of PDL-1^{+}CD27^{-}B cells (p=0.029, r=-0.437).

Conclusion: In patients with RA treated with Abatacept, remission was higher in ACPA(+) than ACPA(-) patients. High levels of B cell subtypes at baseline were associated with SDAI remission at 6 months. DAS28(ESR) score during treatment was negatively correlated with PDL-1^{+}CD27^{-}B cells.

Disclosure: A. Mavropoulos: None; **C. Liaskos**: None; **I. Alexiou**: None; **C. Katsiari**: AbbVie/Abbott, 12, travel support, AstraZeneca, 6, 12, travel support, Boehringer-Ingelheim, 6, 12, travel support, GlaxoSmithKlein(GSK), 6, 12, travel support, Novartis, 12, travel support, UCB, 1, 6, 12, travel support, advisory Boad, Vianex Hellas, 12, travel support, Viatris, 12, travel support; **D. Bogdanos**: AbbVie/Abbott, 12, travel support, Amgen, 6, Boehringer-Ingelheim, 5, 12, travel support, educational grant, GlaxoSmithKlein(GSK), 6, IFT Hellas, 12, travel support, Novartis, 6, Vianex Hellas, 12, travel support; **L. Sakkas**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 2281

Effectiveness of Upadacitinib in Patients with Rheumatoid Arthritis in Canadian Real-World Practice: Final Results from the CLOSE-UP Post-Marketing Observational Study

Louis Bessette[1], Andrew Chow[2], Raman Rai[3], Hugues Allard-Chamard[4], Pauline Boulos[5], Guylaine Roy[6] and Dalinda Liazoghli[6], [1]Centre de l'Ostéoporose et de Rhumatologie de Québec, Quebec, QC, Canada, [2]Credit Valley Rheumatology, Mississauga, McMaster University, Hamilton, University of Toronto, Toronto, ON, Canada, [3]Drs. Rai & Sekhon Medicine Professional Corporation, Brampton, ON, Canada, [4]Université de Sherbrooke, Sherbrooke, Canada, [5]McMaster University, Hamilton, ON, Canada, [6]AbbVie Corporation, Saint-Laurent, QC, Canada

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Upadacitinib (UPA) is an oral, selective Janus kinase (JAK)-inhibitor proven effective and well-tolerated in patients with rheumatoid arthritis (RA) in 6 randomized clinical trials. The objective of the CLOSE-UP study was to evaluate the real-world effectiveness and safety of UPA among Canadian patients with prior exposure to conventional synthetic (cs)DMARD, biologic (b)DMARD, and targeted-synthetic (ts)DMARD experienced patients in real-world settings.

Methods: CLOSE-UP was a prospective, multicenter, observational post-marketing study in adults with moderate-to-severe RA who were treated with UPA 15 mg once daily, with the decision to initiate UPA therapy made prior to study participation. Patients were followed for 24 months after UPA initiation with data collected at routine clinic visits. The primary endpoint was the proportion of patients achieving a Disease Activity Score 28 Joint Count – C-reactive protein (DAS28-CRP) < 2.6 at 6 months. Secondary endpoints included pain score using a visual analog scale, fatigue (FACIT-F), physical function as measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI) and other assessments of disease activity including Clinical Disease Activity Index (CDAI) score. Per protocol, eligible subjects were grouped by

Table 1. Demographics and Baseline Characteristics (Safety Population)

	Bio-naïve[a] N = 194	Bio-experienced[b] N = 170	tsDMARD-IR[c] N = 44	All patients[d] N = 412
Gender, female, n (%)	149 (76.8)	137 (80.6)	33 (75.0)	323 (78.4)
Age, years, mean (SD)	59.7 (11.6)	61.1 (11.6)	58.9 (13.7)	60.2 (11.8)
Disease duration, years, mean (SD)	7.88 (8.94)	11.83 (9.69)	10.83 (7.79)	9.86 (9.28)
CRP (mg/dL), mean (SD)	1.54 (2.58) [188]	1.62 (4.44) [167]	0.86 (1.01) [43]	1.49 (3.38) [402]
RF+ or ACPA+, n (%)	122(75.8) [161]	99 (76.2) [130]	25 (83.3) [30]	247 (76.2) [324]
TJC68, mean (SD)	15.0 (10.7) [192]	13.7 (9.5) [167]	12.5 (8.9) [44]	14.2 (10.1) [407]
SJC66, mean (SD)	11.2 (6.7) [192]	10.1 (5.5) [167]	9.1 (5.0) [44]	10.6 (6.2) [407]
PtGA, mean (SD)	58.3 (23.9) [190]	61.3 (23.1) [169]	55.3 (24.2) [44]	59.3 (23.6) [407]
PGA, mean (SD)	60.5 (20.8) [192]	58.6 (19.7) [170]	51.0 (21.0) [44]	58.6 (20.5) [410]
DAS28-CRP, mean (SD)	4.44 (0.98) [186]	4.32 (0.95) [165]	4.12 (0.98) [43]	4.35 (0.98) [398]
< 2.6, n (%)	9 (4.8)	6 (3.6)	3 (7.0)	19 (4.8)
≥ 2.6 but ≤ 3.2, n (%)	11 (5.9)	16 (9.7)	4 (9.3)	31 7.8)
> 3.2 but ≤ 5.1, n (%)	123 (66.1)	107 (64.8)	30 (69.8)	261 (65.6)
> 5.1, n (%)	43 (23.1)	36 (21.8)	6 (14.0)	87 (21.9)
CDAI, mean (SD)	30.44 (12.00)[187]	28.36 (10.88) [167]	25.81 (10.72)	29.08 (11.56) [402]
≤ 2.8 (remission), n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
> 2.8 but ≤ 10 (low), n (%)	6 (3.2)	4 (2.4)	2 (4.5)	12 (3.0)
> 10 but ≤ 22 (moderate), n (%)	39 (20.9)	51 (30.5)	13 (29.5)	105 (26.1)
> 22 (high), n (%)	142 (75.9)	112 (67.1)	29 (65.9)	285 (70.9)
Pain score, mean (SD)	59.3 (22.6) [192]	63.3 (21.4) [168]	56.7 (24.2) [44]	60.7 (22.4) [408]
Fatigue FACIT-F, mean (SD)	28.45 (11.31)[191]	25.01 (12.05) [167]	29.97 (12.89) [43]	27.20 (11.87) [405]
HAQ-DI, mean (SD)	1.32 (0.62) [189]	1.45 (0.68) [170]	1.31 (0.72) [44]	1.37 (0.66) [407]
Prior use of bDMARD, n (%)	0 (0.0)	170 (100.0)	14 (31.8)	188 (45.6)
Use of any csDMARD at baseline, n (%)	189 (97.1)	108 (63.5)	29 (65.9)	307 (74.5)
Use of MTX at baseline, n (%)	116 (59.8)	68 (40.0)	18 (40.9)	203 (49.3)
Dose (mg/week), mean (SD)	20.24 (4.91) [114]	19.26 (5.50) [68]	22.65 (12.91) [17]	20.11 (6.17) [200]
Baseline use of corticosteroid, n (%)	31 (16.0)	30 (17.6)	4 (9.1)	66 (16.0)
Dose (mg/day), mean (SD)	13.43 (11.73) [22]	11.79 (7.02) [17]	7.50 (3.54) [2]	12.29 (9.66) [42]
Prior herpes zoster vaccination, n (%)	94 (48.5)	86 (50.9)	27 (61.4)	209 (51.4)
Former or current smoker, n (%)	91 (46.9)	70 (41.2)	22 (50.0)	184 (44.7)
Presence of CV risk factors, n (%)[e]	146 (75.3)	133 (78.2)	33 (75.0)	314 (76.2)

Abbreviations: ACPA+, anti-citrullinated protein antibodies positive; b, biologic; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; CV, cardiovascular; DAS28, Disease Activity Score – 28 Joint Count; DMARD, disease-modifying antirheumatic drugs; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate response; MTX, methotrexate; N, sample size; n, number of patients in a category; PtGA, Patient's Global Assessment; PGA, Physician's Global Assessment; RF+, rheumatoid factor positive; SJC66, swollen 66 joint count; TJC68, tender 68 joint count; ts, targeted synthetic. N are presented in square brackets [N] when different than in the header. a - Have not been previously exposed to any bDMARD or tsDMARD. b - Have not been previously exposed to tsDMARD and have been previously exposed to ≤ 2 bDMARDs. c - Have been previously treated with 1 tsDMARD and ≤ 1 bDMARD prior to treatment with that tsDMARD. d - Including 4 patients enrolled although it was discovered later they did not meet the eligibility criteria for the prespecified groups. e - CV risk factors included past or current smoking, hyperlipidemia; body mass index ≥ 30, hypertension, diabetes, atherosclerosis, ischemic heart disease, and others.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1a. Proportion of Patients Achieving DAS28-CRP <2.6 (Solid Bars) or ≤3.2 (Shaded Bars) by Patient Group and Study Visit (Efficacy Population)

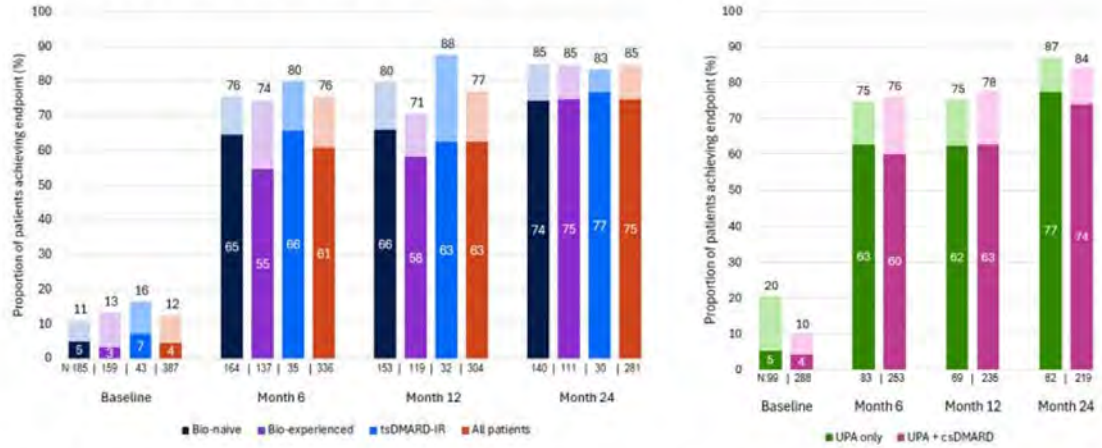
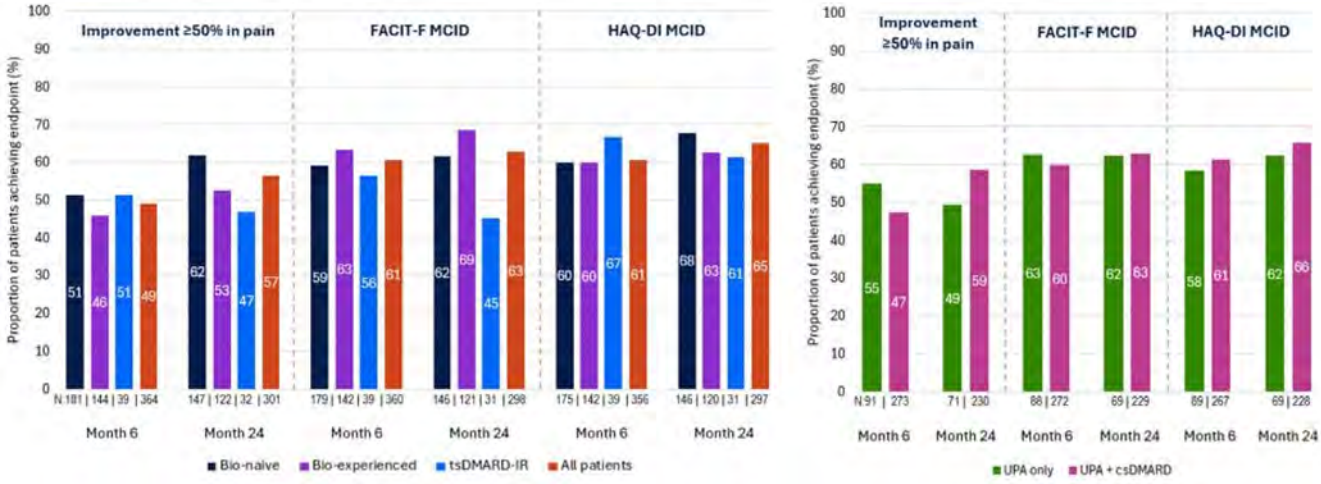


Figure 1b. Proportion of Patients Achieving ≥50% Improvement in Pain, MCID in FACIT-F, and MCID in HAQ-DI[a] (Efficacy Population)



Abbreviations: CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; cs, conventional synthetic; DAS28, Disease Activity Score – 28 Joint Count; DMARD, disease-modifying antirheumatic drugs; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate response; MCID, minimal clinically important difference; N, sample size; ts, targeted synthetic; UPA, upadacitinib. Bio-naïve patients have not been previously exposed to any bDMARD or tsDMARD. Bio-experienced patients have not been previously exposed to tsDMARD and have been previously exposed to ≤ 2 bDMARDs. tsDMARD-IR patients have been previously treated with 1 tsDMARD and ≤ 1 bDMARD prior to treatment with that tsDMARD. a - MCID for FACIT-F was defined as a change from baseline ≥ 3.56; MCID for HAQ-DI was defined as a change from baseline ≥ 0.22.

prior/most recent exposure to no b/tsDMARDs (bio-naïve); ≤2 bDMARDs but no tsDMARD (bio-experienced), and a maximum of 1bDMARD followed by a tsDMARD (tsDMARD-inadequate response [IR]). Data are presented as observed and summarized descriptively.

Results: Analysis included 412 patients, with 47.1% identified as bio-naïve, 41.3% as bio-experienced, and 10.7% as tsDMARD-IR (Table 1). At baseline, most patients (84.5%) exhibited a DAS28-CRP > 3.2. After 6 months of UPA treatment initiation, 60.7% of patients achieved a DAS28-CRP < 2.6 (primary endpoint) and 75.6% achieved a DAS28-CRP ≤ 3.2, (Figure 1a) with a response rate maintained for up to 24 months. Similar trends were observed using CDAI definitions for clinical remission and LDA. The type of prior/most recent DMARD exposure did not impact response rates. Additionally, the proportion of patients achieving a DAS28-CRP < 2.6 at the 6-month visit were similar between those on UPA monotherapy (62.7%) and those on UPA in combination with a csDMARD (60.1%). Improvements in pain score, fatigue, and physical

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Safety Summary

Patients, rate/100 PYs [n]	**N = 412** **682.6 PY**
Any TEAE	37.2 [254]
Any treatment-emergent SAE	5.1 [35]
Serious infections	2.2 [15]
Death [a]	0.6 [4]
Any TEAEs leading to UPA discontinuation	8.6 [59]
TEAEs of special interest	
Any infections	16.6 [113]
Herpes zoster	2.3 [16]
Malignancy excluding NMSC	0.4 [3]
NMSC	0.9 [6]
Gastrointestinal perforation	0.3 [2]
VTE	0.3 [2]
MACE	0.7 [5]

Abbreviations: MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PY, patient-years; SAE, serious adverse events; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolic events. a - 1 patient had cardiac arrest (not related); 1 patient had acute myocardial infarction, COVID-19, acute kidney injury, and respiratory failure (all not related, main cause of death was identified as complications related to dialysis); 2 patients had pneumonia (1 possibly related, 1 not related)

function were observed throughout the study (Figure 1b). At 6 months, 86.5% of patients persisted in their treatment on UPA and 67.5% persisted up to Month 24. The safety profile of UPA was consistent with that seen in Phase 3 trials with no new safety signals (Table 2).

Conclusion: Consistent with clinical trial findings, this real-world Canadian study demonstrated a reduction in disease activity and improvements in patient-reported outcomes, supporting a favorable benefit-risk profile for patients treated with UPA. Notably, response rates were consistent irrespective of prior bDMARDs/tsDMARDs use or concomitant csDMARD.

Disclosure: L. Bessette: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, AstraZeneca, 5, Bristol-Myers Squibb(BMS), 2, 5, 6, Fresenius Kabi, 2, 6, JAMP Pharma, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Organon, 2, 6, Pfizer, 2, 5, 6, Sandoz, 2, 6, Sanofi, 2, 5, 6, TEVA, 2, 6, UCB, 2, 5, 6; **A. Chow**: AbbVie, 12,, 1, 2, 6, Celltrions, 2, 5, Organon, 2, Pfizer, 2, 5, UCB, 2; **R. Rai**: AbbVie, 2, 7, UCB, 2; **H. Allard-Chamard**: AbbVie, 1, 6, Amgen, 1, 6, AstraZeneca, 1, 5, 6, Bristol-Myers Squibb(BMS), 6, Celltrion, 1, 5, 6, GlaxoSmithKlein(GSK), 1, Janssen, 1, 5, 6, Kabi, 1, 5, 6, Novartis, 1, 6, Otsuka, 1, 6, Pfizer, 1, 5, 6, Sandoz, 1, 6, Sobi, 1, 5, 6; **P. Boulos**: AbbVie, 1, 5, 6, JAMP, 1, 5, 6, Janssen, 1, 5, 6, Lilly, 5, 6, Novartis, 1, 5, 6, UCB, 1, 6; **G. Roy**: AbbVie, 3; **D. Liazoghli**: AbbVie, 3.

Abstract Number: 2282

Effect of Online Continuing Education on Advancing Care for Rheumatoid Arthritis: A Real-World Outcome Analysis

Nimish Mehta[1], Katie Lucero[2], Freddy Green[3] and Karen Badal[4], [1]Medscape, Three Bridges, NJ, [2]Medscape, Newark, [3]Medscape, London, United Kingdom, [4]Medscape, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: In recent years, an increasing number of cytokines and their function in the pathophysiology of immunologic conditions have been identified, leading to the development of new targeted therapies such as the Janus kinase (JAK) inhibitors that may provide better patient-centric treatment options. The objective of this study was to determine if an online, continuing education curriculum could advance the care of patients with rheumatoid arthritis in real world clinical practice with appropriate use of JAK inhibitors after inadequate response or intolerance to anti-TNF inhibitors.

Methods: The educational program consisted of 4 CME activities in various formats including panel discussions, clinician-patient video-vignettes with expert faculty commentary, and virtual patient simulation case-studies that allow learners to order lab tests, assess disease, and prescribe treatments in a manner matching the scope and depth of actual practice. This real-world outcome study (RWO) was designed to assess the impact of the CME activities on the appropriate use of JAK inhibitors in patients who have failed an anti-TNF therapy by rheumatologists, physician assistants, and nurse practitioners. A retrospective matched case-control study was conducted using medical and pharmacy claims aggregated with patients and the coding clinicians between December 2023 through November 2024. Learners and non-learners were matched based upon specialty, geographic location, number of patients with RA, number of treated with biologics, and number of patients treated with JAK inhibitors. Independent t-tests were used to assess significance between the number of patients receiving JAK inhibitors by clinicians in the CME group and those in the control group. Data were pulled for 3 months pre and 3 months-post first CME activity participation date ("index date").

Results: The sample includes 654 CME learners who participated in at least 1 of the 4 CME activities between March 2024 and August 2024, and 654 matched comparison non-participants. All data are time aligned 3 months pre-/post-index date. After participating in case-based education, rheumatologists demonstrated 20% increase in evidence-based selection of individualized pharmacologic therapy for patients with RA who have failed a TNF inhibitor. Learners who participated in 1 or more activity were more likely to switch patients to JAK inhibitors following an anti-TNF therapy . Patients of CME learners were 26% more likely to be treated with JAK inhibitors versus the control group (P< .05).

Conclusion: The results of this RWO study confirms that participation in 1 or more CME activities within a curriculum is associated with improving the adoption of the latest evidence-based recommendations for use of novel therapies such as JAK inhibitors by rheumatologists, NPs, and PAs, aiming to improve the management and outcomes of patients with rheumatoid arthritis.

Disclosure: N. Mehta: None; **K. Lucero**: None; **F. Green**: None; **K. Badal**: None.

Abstract Number: 2283

Arrhythmia Risk in Diabetic Rheumatoid Arthritis Patients: Comparative Analysis of IL-6 Inhibitors versus TNF-α Inhibitors

Sila Mateo Faxas[1], Godbless Ajenaghughrure[2], Gurjot Singh[3], Kim Nguyen[3], Nirys Mateo Faxas[4], Nicole Tejeda[5] and Kimberly Ramirez Bonetti[6], [1]Good Samaritan Hospital, Cincinnati, OH, [2]Trihealth Good Samaritan Hospital, Cincinnati, OH, [3]Trihealth Good Samaritan Hospital, Cincinnati, [4]Independent Author, Santo Domingo, Dominican Republic, [5]Independent Author, Cincinnati, [6]Independent Author, cincinnati, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Background: Both rheumatoid arthritis (RA) and type 2 diabetes mellitus (T2DM) are independently associated with increased cardiovascular risk, including cardiac arrhythmias. The impact of different biologic therapies on arrhythmia risk in patients with both conditions remains unclear. This study evaluates arrhythmia outcomes in RA patients with T2DM treated with IL-6 inhibitors (IL-6i) versus TNF-α inhibitors (TNFi).

Methods: Methods: We conducted a retrospective cohort study using TriNetX, a global federated health research network. Adult patients with RA and T2DM receiving either IL-6i (sarilumab/tocilizumab) without TNFi or TNFi without IL-6i were identified. After propensity score matching (n=1,579 per cohort), we compared the incidence of various arrhythmias including atrial fibrillation, ventricular tachycardia, ventricular fibrillation, supraventricular tachycardia, and sick sinus syndrome over a 5-year follow-up period.

Results: Results: IL-6i treatment was associated with significantly higher risk of ventricular tachycardia compared to TNFi (HR=1.419, 95% CI: 1.006-2.002, p=0.045). Though not statistically significant, there were trends toward increased risk with IL-6i for atrial fibrillation (HR=1.104, 95% CI: 0.894-1.365, p=0.357), supraventricular tachycardia (HR=1.138, 95% CI: 0.767-1.688, p=0.521), and ventricular fibrillation (HR=1.628, 95% CI: 0.964-2.747, p=0.066). Notably, the need for pacemaker implantation was higher in the IL-6i group (HR=1.394, 95% CI: 1.006-1.933, p=0.045). The 5-year arrhythmia-free survival rate was lower in IL-6i-treated patients compared to TNFi-treated patients (p< 0.05).

Conclusion: Conclusions: In RA patients with comorbid T2DM, treatment with IL-6i was associated with higher risk of cardiac arrhythmias, particularly ventricular tachycardia, compared to TNFi therapy. These findings suggest that TNFi may offer a more favorable cardiac safety profile in this high-risk population. Clinicians should consider arrhythmia risk when selecting biologic therapy for patients with both RA and T2DM, and closer cardiac monitoring may be warranted for those receiving IL-6i.

Disclosure: S. Mateo Faxas: None; **G. Ajenaghughrure**: None; **G. Singh**: None; **K. Nguyen**: None; **N. Mateo Faxas**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None.

Abstract Number: 2284

Cardiovascular Outcomes in Diabetic Rheumatoid Arthritis Patients: TNF-α Inhibitors versus IL-6 Inhibitors

Sila Mateo Faxas[1], Godbless Ajenaghughrure[1], Gurjot Singh[2], Kim Nguyen[2], Nirys Mateo Faxas[3], Nicole Tejeda[4], Kimberly Ramirez Bonetti[5] and Erick Perez Mejias[4], [1]Trihealth Good Samaritan Hospital, Cincinnati, OH, [2]Trihealth Good Samaritan Hospital, Cincinnati, [3]Independent Author, Santo Domingo, Dominican Republic, [4]Independent Author, Cincinnati, [5]Independent Author, cincinnati, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) and type 2 diabetes mellitus (T2DM) face increased cardiovascular risk. Different biologic disease-modifying antirheumatic drugs (bDMARDs) may have varying effects on cardiovascular outcomes in this high-risk population. This study compared cardiovascular outcomes between RA patients with T2DM treated with IL-6 inhibitors (IL-6i) versus TNF-α inhibitors (TNFi).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Using the TriNetX global federated health research network, we conducted a retrospective cohort study of adult patients with RA and T2DM. Patients were divided into two cohorts: those receiving IL-6i (sarilumab or tocilizumab) without TNFi (n=1,579) and those receiving TNFi without IL-6i (n=1,579), matched using propensity score on 20+ potential confounders. Outcomes included mortality, major adverse cardiovascular events (MACE), arrhythmias, heart failure, and other cardiovascular conditions over a 5-year follow-up period.

Results: IL-6i-treated patients demonstrated significantly higher risk for mortality (HR=1.626, 95% CI: 1.308-2.021, p< 0.001), acute kidney failure (HR=1.772, 95% CI: 1.420-2.212, p< 0.001), and heart failure (HR=1.399, 95% CI: 1.193-1.640, p< 0.001) compared to TNFi-treated patients. Additionally, IL-6i recipients had higher risk for ventricular arrhythmias (HR=1.459, 95% CI: 1.006-2.175, p=0.045), pulmonary embolism (HR=2.092, 95% CI: 1.420-3.081, p< 0.001), and infections/inflammatory reactions related to cardiac devices (HR=3.485, 95% CI: 1.122-10.821, p=0.021). However, TNFi-treated patients had significantly higher frequency of diabetes-related follow-up visits (17.46 vs 14.69 visits, p=0.004).

Conclusion: In this propensity-matched analysis of RA patients with T2DM, treatment with IL-6i was associated with significantly higher risk of mortality and multiple cardiovascular adverse events compared to TNFi treatment. While both drug classes effectively manage RA symptoms, our findings suggest TNFi may be preferable for this specific patient population from a cardiovascular safety perspective. These results highlight the importance of considering cardiovascular risk profiles when selecting biologic therapy for RA patients with comorbid T2DM.

Disclosure: S. Mateo Faxas: None; **G. Ajenaghughrure**: None; **G. Singh**: None; **K. Nguyen**: None; **N. Mateo Faxas**: None; **N. Tejeda**: None; **K. Ramirez Bonetti**: None; **E. Perez Mejias**: None.

Abstract Number: 2285

Synovium-on-a-chip – Development of a Humanized Rheumatoid Arthritis Model that Mimics Disease and Patient Biological Heterogeneity

Theresa Wampler Muskardin[1], Ruiqi Chen[2], Yeji Lee[3], Azka Ali[3], Andrra Nimoni[3], Christele Felix[3], Hattie Heiland[3], Romy Kallas[3], Daniel Ramirez[4], David Mayman[3], Timothy Niewold[5] and Weiqiang Chen[6], [1]Hospital for Special Surgery and Weill Cornell Medicine, New York, NY, [2]New York University - Tandon School of Engineering, New York, NY, [3]Hospital for Special Surgery, New York, NY, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [5]Hospital for Special Surgery, New York, New York, [6]New York University, Tandon School of Engineering, New York, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: In rheumatoid arthritis (RA), reasons for treatment resistance and alternate strategies that would be more effective in treatment-resistant patients remain unknown. Accurate methodology to study mechanisms of treatment resistance and screen novel therapies in individual patients remains a critical unmet need.

Methods: We engineered a microfluidic synovium-on-a-chip device incorporating a central synovial fluid region, a pericentral lining region, and an outer sublining zone (Fig. 1). The chip was seeded with fibroblast-like synoviocytes (FLS) from patient synovial tissue and matched immune cells (T cell, B cell, monocyte, and monocyte-derived macrophage), embedded with HUVECs in a 3D fibrin hydrogel to reconstruct spatially organized niches. Migratory dynamics of the immune cells were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

monitored in real time using time-lapse fluorescence microscopy. Upon niche maturation on day 8, devices were processed for further analysis of inflammatory states and cell subset-specific marker expression. Morphological analysis was performed at multiple time points, and supernatants were collected daily for cytokine profiling. We stratified RA synovial chips into high-, mixed-, and low-inflammatory groups based on histological synovitis scores derived from H&E stains from the same patient tissues.

Results: RA FLS exhibited hyperplastic morphology and spatial heterogeneity similar to in vivo tissues, including $PRG4^{+}$ lining FLS, $CD90^{+}$ sublining FLS, and immune cell infiltration (Fig. 2). Notably, progressive ECM degradation was significantly greater in RA chips compared to osteoarthritis (OA) chips.

Compared to the OA niche, **i**mmune cells in RA-derived chips exhibited more directed and enhanced immune cell migration toward the sublining region. Concurrently, immune cells within the RA synovial niche underwent pro-inflammatory differentiation, including Th17 cells, plasma cells, $CD16^{++}$ monocytes, and M1-like macrophages. RA synovial chips exhibited increased in IL-6 secretion following immune cell addition on Day 7. Cytokine secretion profiling revealed upregulation of pro-inflammatory cytokines, chemokines, and matrix-degrading enzymes in RA chips compared to OA controls.

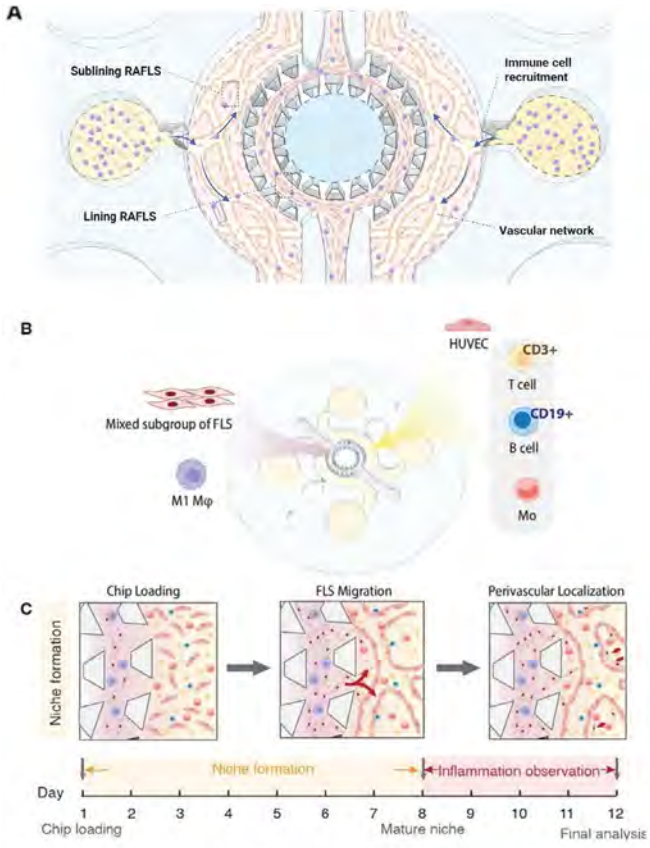


Figure 1. (A) Microfluidic chip layout consisting of four spatially organized zones: a central synovial fluid region, a pericentral lining region, an outer sublining region, and side immune recruitment ports. Regions are partitioned by trapezoidal micropillars that permit cell migration and interaction. (B) Patient-derived RA-FLS and M1 macrophages were encapsulated in fibrin hydrogel and loaded into the lining region, while HUVECs, $CD3^{+}$ T cells, $CD19^{+}$ B cells, and monocytes were introduced into the sublining region to reconstruct a 3D inflamed synovial niche. (C) Experimental timeline showing an 8-day niche formation phase followed by an inflammation observation window from Day 8 to 12, during which tissue morphology and inflammatory responses were analyzed.

Figure 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

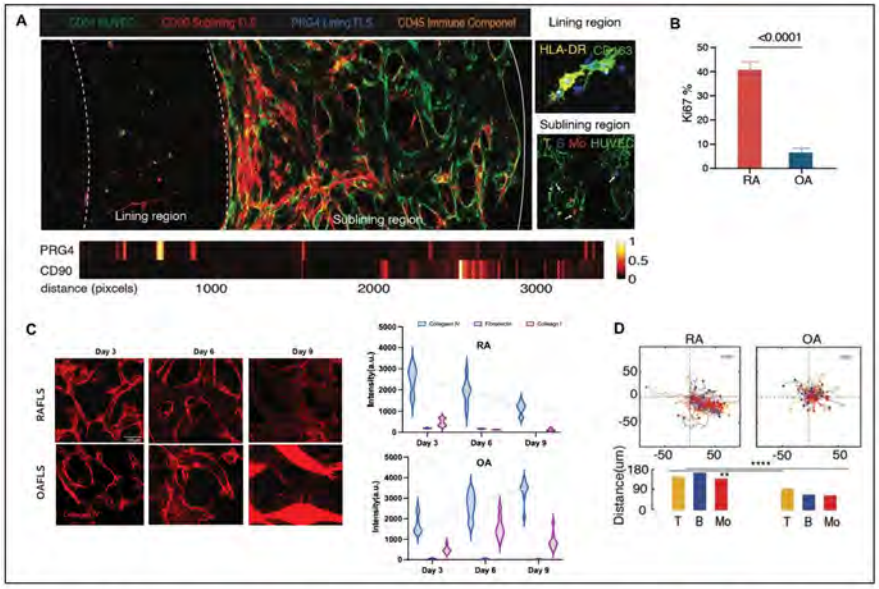


Figure 2. (A) FLS exhibited spatial heterogeneity similar to *in vivo* tissues, including PRG4^{+} lining FLS, CD90^{+} sublining FLS, and immune cell infiltration. (B) RA FLS demonstrated hyperplastic morphology, with increased Ki67 expression compared to OA FLS on the microfluidic organ-on-a-chip platform. (C) ECM degradation was progressive and greater in RA chips compared to OA chips. (D) Compared to the OA niche, immune cells in RA-derived chips exhibited more directed and enhanced immune cell migration toward the sublining region.

Figure 2

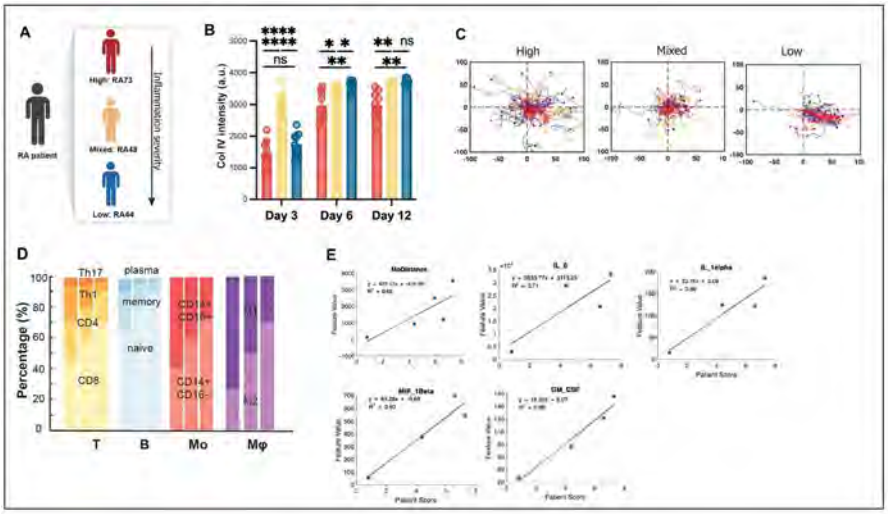


Figure 3. Patient-specific inflammatory variation characterized using synovium-on-a-chip models. (A) Schematic of RA patient stratification into high (RA73), mixed (RA48), and low (RA44) inflammation groups. (B) Quantification of collagen IV intensity over time across RA patients with distinct inflammatory profiles (two-way RM ANOVA, time: ****p < 0.0001; group: ****p < 0.0001; interaction: ****p < 0.0001; n = 9). (C) The migration trajectory of high, mixed, and low inflammation groups. Individual T cells

Figure 3

Across RA patient groups, the high-inflammatory group had the most collagen IV loss, enhanced migration of immune cells , and a higher proportion of Th17/Th1 T cells, plasma B cells, CD16^{++} monocytes, and M1-like macrophages, in contrast to the mixed and low-inflammatory chips (Fig. 3). High inflammation chips had higher levels of pro-inflammatory cytokines and chemokines (IL-6, IL-1α, TNF-α,MCP-3, MIP-1β, IL-2, IL-7, IL-15) compared to the low-inflammation chip.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our synovium-on-a-chip recapitulates the human stromal and immune cellular organization of the vascularized synovium niche. We establish an immunologically active synovial niche in our RA chip model, capable of capturing key cellular interactions and molecular outputs observed in RA patient tissues and characteristics that differ amongst RA endotypes.

Disclosure: T. Wampler Muskardin: None; **R. Chen**: None; **Y. Lee**: None; **A. Ali**: None; **A. Nimoni**: None; **C. Felix**: ACR, 6, Lupus Research Alliance, 1, 6, 7; **H. Heiland**: None; **R. Kallas**: None; **D. Ramirez**: None; **D. Mayman**: None; **T. Niewold**: AstraZeneca, 2, Pioneering Medicines, 2, Progentec, 2, 4, Zenas, 5; **W. Chen**: None.

Abstract Number: 2286

Association of Semaglutide Prescription with Improved Joint Outcomes in Rheumatoid Arthritis Patients

Faissal Stipho[1], **Yazin Hindosh**[2], Jonathan Sayegh[2], Akram Hindosh[2], Bassam Mitri[2] and Issa Batarseh[1], [1]Department of Internal Medicine, Banner University Medical Center / University of Arizona, Tucson, Arizona, Tucson, AZ, [2]University of Arizona College of Medicine Tucson, Tucson, AZ

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatoid Arthritis (RA) is an autoimmune disorder that results in immune dysfunction and swelling of major joints, leading to discomfort, pain, stiffness, and loss of function1. Semaglutide is a GLP-1 agonist increasing in popularity for its metabolic benefits and ability to reduce inflammation and swelling2. However, the potential benefit of semaglutide use for RA flare-ups has not yet been investigated.. The objective of this study was to quantify this relationship by assessing the risk of RA flare-ups in patients prescribed semaglutide.

Methods: The TriNetX Database was queried to identify patients ≥ 18 years old with RA. These individuals were then divided into two subgroups: those prescribed semaglutide (n=12,139) and those who were not (n=292,558). These groups were 1:1 propensity score matched (n=12,125) for age, sex, ethnicity, BMI, diabetes mellitus, nicotine dependence, and mood disorders. Primary outcomes included 30-day, 90-day, and 1-year risk of synovitis, stiffness of joints, swelling of joints, and pain in joints within one year of semaglutide prescription. Risk Ratios (RR) were calculated between each cohort, and statistical significance was set to $p< 0.05$.

Results: RA Patients prescribed semaglutide had a significantly lower 30-day risk of stiffness of joints (RR=0.635, p=0.023), pain in joints (RR=0.605, p< 0.001), and swelling of joints (RR=0.588, p< 0.001),a significantly lower 90-day risk of synovitis (RR=0.729, p=0.001), stiffness of joints (RR=0.716, p=0.019), pain in joints (RR=0.728, p< 0.001), and swelling of joints (RR=0.704, p< 0.001), and a significantly lower 1-year risk of synovitis (RR=0.806, p< 0.001), stiffness of joints (RR=0.800, p=0.019), pain in joint (RR=0.884, p=0.004), and swelling of joints (RR=0.769, p< 0.001).

Conclusion: RA patients with a semaglutide prescription had lower risks of RA flare-ups such as synovitis, stiffness, swelling, and pain of joints compared to those without. This may be attributed to semaglutide's mechanism of action, which has been shown to modulate the immune system and reduce inflammatory cytokine levels. Future studies should be conducted to further investigate the efficacy of semaglutide as a potential agent against RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: F. Stipho: None; **Y. Hindosh**: None; **J. Sayegh**: None; **A. Hindosh**: None; **B. Mitri**: None; **I. Batarseh**: None.

Abstract Number: 2287

Interpretable Ensemble Machine Learning Explaining Nonadherence and the Risk of Nonpersistence of Targeted Disease-Modifying Antirheumatic Agents in Older Adults with Rheumatoid Arthritis

yinan huang[1] and Sandeep Agarwal[2], [1]Department of Pharmacy Administration, University of Mississippi, Oxford, MS, US, MS, [2]Baylor College of Medicine, Houston

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interpretable machine learning (ML) method can identify factors associated with biological or targeted synthetic disease modifying antirheumatic drugs (b/tsDMARDs) nonadherence and nonpersistence for rheumatoid arthritis (RA) based on big data. This study is to develop and validate several interpretable ML models in evaluating the nonadherence and the risk of nonpersistence of b/tsDMARDs among older adults with RA.

Methods: This retrospective, new-user study used 5% national Medicare administrative claims data between 2012-2020, and included older (≥65) patients initiating b/tsDMARDs (the index date) between 2013-2019 and having a diagnosis of RA identified using the International Classification of Diseases, Ninth and Tenth revision codes. Nonadherence outcome was defined as medication possession ratio (MPR) < 80%, evaluated during the 12-month follow-up. Nonpersistence, defined as time from the index date until treatment gap ≥ 60 days observed during the follow-up, or censored for loss to follow-up. Patient-level data was split into 75% for model training and 25% for evaluation, with patients' demographics and clinical characteristics measured in the baseline period. ML classification models (random forest [RF], eXtreme Gradient Boosting [XGBoost] and prediction rule ensembles [PRE]) evaluated the binary nonadherence outcomes and the ML survival model (random survival forest [RSF] and regularized Cox regression [RegCox]) assessed time on nonpersistence. Using the testing cohort, C-index and integrated Brier Score were reported for the ML survival model and AUROC was reported for ML classification models. Top influential predictive features for nonadherence and the risk of nonpersistence were identified according to variable importance (VIMP) procedure from both types of ML algorithms, respectively.

Results: We identified 3,927 eligible patients with RA (mean age 73 ±6; female 75%). Approximately 18.5% of RA patients had the risk of nonpersistence after initiating their index b/tsDMARDs (mean time to nonpersistence 1,110 ±670 days). RSF (C-index 0.6629, iBS 0.1629) and Reg-Cox model (C-index 0.6810) found index year, age, Elixhauser score, frailty score, inpatient visit, outpatient visits, the type of b/tsDMARDs, and CIRAS as top 8 influential predictors for nonpersistence. 53.65% of RA patients were adherent (MPR 0.72 [0.31]; 0.01-1) in the 12-month follow-up. Compared to ML-based classification models (PRE 0.5407 [0.509-0.5722]; RF 0.6029 [0.5715-0.6336]; XGBoost 0.6018 [0.5704-0.6326]) had comparable performance in predicting nonadherence. Frailty score, CIRAS, age, index_year and Elixhauser comorbidity index were ranked commonly as the top influential features for nonadherence.

Conclusion: We effectively developed ML-based survival and classification models to explain the nonadherence and the risk of nonpersistence of b/tsDMARDs, respectively for older adults with RA. There is potential to leverage ML models for understanding patients' behavior of utilizing b/tsDMARDs treatment with a goal to improve RA care.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: y. huang: None; **S. Agarwal**: None.

Abstract Number: 2288

Efficacy of Ivarmacitinib in Patients with Moderate-to-severe Rheumatoid Arthritis Stratified by Baseline Characteristics: A Post-hoc Study of a Phase III Clinical Trial

Yuan Xue, Bo Wei, Xiaojing Huang and Rui Ding, Zhongshan Hospital Xiamen University, Xiamen, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Ivarmacitinib (SHR0302), a selective Janus kinase 1 inhibitor, has demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA). This post-hoc study aimed to evaluate the efficacy of Ivarmacitinib stratified by baseline patient characteristics.

Methods: This post-hoc analysis was based on data from a phase III clinical trial (NCT04333771, Liu J, Jiang Y, Zhang S, et al. Ivarmacitinib, a selective Janus kinase 1 inhibitor, in patients with moderate-to-severe active rheumatoid arthritis and inadequate response to conventional synthetic DMARDs: results from a phase III randomised clinical trial. Ann Rheum Dis. Published online November 27, 2024. doi:10.1136/ard-2024-226385). Patients were randomized to receive Ivarmacitinib 4 mg (n=189), Ivarmacitinib 8 mg (n=189) or placebo (n=188) for the initial 24-week treatment period. After week 24, patients on placebo switched to Ivarmacitinib 4mg, while the other groups continued their initial regimen until 52 weeks. Efficacy outcomes were analyzed by subgroups based on demographic factors, disease characteristics, and treatment history.

Table 1. Comparison of ACR20 response at W24 and W52 based on subgroups. *, P <0.05 between placebo vs. Ivarmacitinib 8 mg; **, P <0.01 between placebo vs. Ivarmacitinib 8 mg; ***, P <0.001 between placebo vs. Ivarmacitinib 8 mg. #, P <0.05 between placebo vs. Ivarmacitinib 4 mg; ##, P <0.01 between placebo vs. Ivarmacitinib 4 mg; ###, P <0.001 between placebo vs. Ivarmacitinib 4 mg. ACR20, American College of Rheumatology criteria improvement of 20%; W24, 24 weeks; W52, 52 weeks; RA, rheumatoid arthritis; ACR, American College of Rheumatology; CRP, C reactive protein; DAS28, 28-joint Disease Activity Score; DMARDs, disease-modifying antirheumatic drugs.

Items	ACR20 response at W24, No. (%)			ACR20 response at W52, No. (%)		
	Placebo	Ivarmacitinib 4 mg	Ivarmacitinib 8 mg	Placebo	Ivarmacitinib 4 mg	Ivarmacitinib 8 mg
Age						
<45 years	17 (37.8)	31 (63.3)#	46 (78.0)***	25 (58.1)	31 (66.0)	43 (82.7)
≥45 years	59 (41.3)	102 (72.9)###	96 (73.8)***	90 (72.0)	101 (75.9)	101 (84.9)
Sex						
Male	13 (48.1)	15 (88.2)**	20 (64.5)	16 (66.7)	15 (93.8)	22 (81.5)
Female	63 (39.1)	118 (68.6)###	122 (77.2)***	99 (68.8)	117 (71.3)	122 (84.7)
Time since RA diagnose						
<3 years	12 (35.3)	24 (68.6)##	33 (82.5)***	20 (69.0)	26 (76.5)	32 (86.5)
≥3 years	64 (41.6)	108 (70.6)###	109 (73.2)***	95 (68.3)	105 (72.4)	112 (83.6)
ACR functional class						
I	11 (52.4)	19 (70.4)	17 (73.9)	12 (66.7)	20 (80.0)	20 (90.9)
II	43 (36.4)	75 (71.4)###	83 (71.6)***	71 (66.4)	70 (70.0)	85 (81.7)
III	22 (44.9)	39 (68.4)#	42 (84.0)***	32 (74.4)	42 (76.4)	39 (86.7)
CRP						
<10 mg/L	43 (42.2)	61 (68.5)###	65 (79.3)***	62 (70.5)	67 (78.8)	64 (84.2)
≥10 mg/L	33 (38.4)	72 (72.0)###	77 (72.0)***	53 (66.3)	65 (68.4)	80 (84.2)
DAS28-CRP						
<4.9	29 (44.6)	49 (67.1)##	53 (76.8)***	38 (69.1)	53 (76.8)	53 (85.5)
≥4.9	47 (38.2)	84 (72.4)###	89 (74.2)***	77 (68.1)	79 (71.2)	91 (83.5)
Previous biologic DMARDs received						
Without	57 (41.3)	102 (74.5)###	111 (76.0)***	83 (68.6)	98 (75.4)	112 (85.5)
With	19 (38.0)	31 (59.6)#	31 (72.1)**	32 (68.1)	34 (68.0)	32 (80.0)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: At week 24, both Ivarmacitinib 4 mg and 8 mg demonstrated significantly higher American College of Rheumatology (ACR) criteria improvement of 20% (ACR20) response rate compared to placebo across all subgroups, including age, sex (except for males who received Ivarmacitinib 8 mg), disease duration, ACR functional class (grades II and III), C-reactive protein (CRP), 28-joint Disease Activity Score-CRP (DAS28-CRP), and prior exposure to biologic disease-modifying antirheumatic drugs (DMARDs). By week 52, both Ivarmacitinib 4 mg (e.g., 93.8% in males) and 8 mg (e.g., 90.9% in patients with ACR functional class of I and 86.5% in patients with RA duration < 3 years) achieved high ACR20 response rates across all subgroups. Patients who switched from placebo at week 24 also achieved substantial benefits in week 52 ACR20 response across subgroups (Table 1). Regarding safety, the incidences of adverse events were generally comparable between Ivarmacitinib 4 or 8 mg versus placebo across all subgroups.

Conclusion: Ivarmacitinib provides consistent efficacy across various subgroups in patient with moderate-to-severe RA.

Disclosure: Y. Xue: None; **B. Wei**: None; **X. Huang**: None; **R. Ding**: None.

Abstract Number: 2289

Effects of Transcutaneous Auricular Vagus Nerve Stimulation on Disease Activity in Patients with Rheumatoid Arthritis: A Pilot Study

Yuichiro Fujieda[1], Kaoru Murakami[2], Hiroki Tanaka[2], Yuichi Kojima[2], Yuki Kudo[1], Kohei Karino[1], Hiroyuki Nakamura[1], Ryo Hisada[1], Michihito Kono[1], Masaaki Murakami[2] and Tatsuya Atsumi[1], [1]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [2]Institute for Genetic Medicine, Graduate School of Medicine, Hokkaido University, Sapporo, Japan

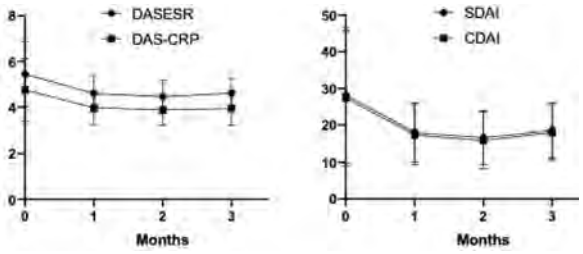
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2265–2289) Rheumatoid Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Vagus nerve stimulation (VNS) has emerged as a potential therapeutic strategy for inflammatory diseases by modulating inflammatory reflex pathways. Transcutaneous auricular vagus nerve stimulation (taVNS) is a non-invasive approach that may offer symptomatic relief for rheumatoid arthritis (RA). This study aims to investigate the effects of taVNS on disease activity, pain, and inflammation in RA patients.

Methods: This exploratory, open-label clinical study enrolled patients diagnosed with RA who required treatment modification. Participants received daily taVNS treatments (25Hz, 1-10mA, 1 hour/day) for 12 weeks. Clinical assessments, including swollen and tender joint counts, Visual Analogue Scale (VAS), Clinical Disease Activity Index (CDAI), and Simplified Disease Activity Index (SDAI), Disease Activity Score 28-erythrocyte sedimentation rate (DAS28-ESR), and DAS28-C-reactive protein (DAS28-CRP), were conducted at baseline, weeks 4, 8, and 12. Laboratory analyses included inflammatory markers and immune cell profiling. Additionally, an exploratory proteomic analysis was performed using SomaScan® Assay to comprehensively measure plasma proteins in both RA patients and Collagen Antibody-Induced Arthritis (CAIA) model mice before and after VNS treatment. Proteins commonly elevated in both species following taVNS were identified.

Results: Seven RA patients (mean age: 61.9 years; 100% female) were included in this analysis. Baseline disease activity scores were as follows: CDAI median [IQR] 24 [12:49.5], SDAI 25.1 [12.4:49.8], DAS28-ESR 4.66 [3.92:5.16], DAS28-CRP 3.94 [3.16:4.62], tender joint count 5 [4:21], swollen joint count 5 [2:14], VAS 24 [12:49.5]. After 12 weeks of taVNS, disease activity scores showed a decreasing trend; however, the differences did not reach statistical significance.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disease activity in rheumatoid arthritis during 12 weeks of transcutaneous auricular vagus-nerve stimulation. Mean (±SD) CDAI, SDAI, DAS28-ESR, and DAS28-CRP for seven patients are plotted at baseline and at weeks 4, 8, and 12; none of the observed declines reached significance (repeated-measures ANOVA, $p > 0.05$).

Proteomic analysis by using SomaScan® Assay revealed that Protein X was significantly upregulated in both RA patients and CAIA mice following taVNS. Notably, plasma levels of Protein X increased significantly in CAIA mice treated with taVNS (1007.0 ± 49.4) compared to untreated CAIA mice (886.5 ± 13.5, p=0.02). In contrast, no significant changes were observed in inflammatory proteins related to RA pathogenesis (TNF-α, IL-1β, IL-6, IL-17A, GM-CSF) or pain-associated neuropeptides (Substance P, CGRP, β-Endorphin, Enkephalin, Neuropeptide Y).

Conclusion: Protein X is a protein that modulates inflammatory pathways, particularly via STAT1 signaling. Preliminary findings suggest a potential association between taVNS and disease activity in RA, possibly involving Protein X and STAT1 signaling.

Disclosure: Y. Fujieda: None; **K. Murakami**: None; **H. Tanaka**: None; **Y. Kojima**: None; **Y. Kudo**: None; **K. Karino**: None; **H. Nakamura**: None; **R. Hisada**: None; **M. Kono**: None; **M. Murakami**: None; **T. Atsumi**: None.

Abstract Number: 2290

Patterns and Predictors of Clinical Improvement in Patients with Sjögren's Disease: A Longitudinal Analysis of ESSDAI and ESSPRI Improvements

Alejandro Gómez Gómez[1], Sergio H. Martínez Mateu[2], Jose Luis Tandaipan[3], Monica Fernandez Castro[4], Guillermo gonzalez[5], Sheila Melchor-Díaz[6], Miren Uriarte Ecenarro[7], Raúl Menor Almagro[8], Paloma Vela Casasempere[9], Beatriz Paredes-Romero[10], Judit Font-Urgelles[11], Paula Estrada-Alarcón[12], Sara Manrique-Arija[13], Mª Angeles Blazquez Cañamero[14], Clara Moriano[15], Juan José Alegre-Sancho[16], Marina Rodríguez López[17], Marta López[18], Gema Bonilla[19], Rafaela Ortega-Castro[20], Sara Maria Rojas Herrera[21], Ignacio Braña[22], Lilian López-Núñez[23], Javier Narváez[24], Jose Rosas Gómez de Salazar[25], Ruben D. López-Sánchez[26], Carles Galisteo Veiga[27], Javier Martínez-Ferrin[28], Jose Javier Pérez Venegas[29], Guadalupe Manzano-Canabal[30], Cilia Peralta-Ginés[31], Lara Sánchez Bilbao[32], José Andrés Román Ivorra[33], Rafael Cáliz-Cáliz[34], Belén Serrano-Benavente[35], Sabela Fernández-Aguado[36], Natalia Boix- Martí[37], Eric Kirkegaard-Biosca[38], Iago Alvarez Saez[39], Ares Selles-Rius[40], Maribel Pérez[41], Juan Cañete[42], Sara Marsal[1] and Jose Luis Andreu[43], [1]Vall d'Hebron Hospital Research Institute, Rheumatology Research Group, Barcelona, Spain, [2]IMIDomics, Barcelona, Spain, [3]Rheumatology. Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Spain, [4]PUERTA DE HIERRO HOSPITAL, Madrid, Spain, [5]Hospital Universitario de A Coruña, A Coruña, Spain, [6]Hospital Universitario 12 de Octubre, Rheumatology, Madrid, Madrid, [7]Hospital Universitario La Princesa, Madrid, Spain, [8]Department of Rheumatology, Hospital de Jerez, Spain, Puerto De Santa María, Spain, [9]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [10]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, San Sebastian de los Reyes, Spain, [11]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [12]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [13]Hospital Regional Universitario Málaga, Malaga, Spain, [14]Hospital Ramon y Cajal, Madrid, Spain, [15]Hospital León, LEON, Castilla y Leon, Spain, [16]Hospital Universitario Doctor Peset, Valencia, Spain, [17]Complejo Hospitalario Universitario de Santiago,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rheumatology, Santiago de Compostela., Santiago de Compostela, Spain, [18]Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain, [19]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [20]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [21]Hospital de Mérida, Rheumatology, Badajoz, Badajoz, Spain, [22]Hospital Universitario Central de Asturias, Oviedo, Spain, [23]Hospital Son Llatzer, Rheumatology, Palma de Mallorca, Palma de Mallorca, Spain, [24]Hospital Universitario de Bellvitge, Barcelona, Spain, [25]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [26]Hospital Universitario de Gran Canaria Dr. Negrín, Gran Canaria, Spain, [27]Hospital Parc Taulí, Rheumatology, Sabadell, Sabadell, Spain, [28]Hospital Universitario Virgen de la Arrixaca, Rheumatology, Murcia, Murcia, Spain, [29]Virgen Macarena University Hospital, Sevilla, Spain, Sevilla, Spain, [30]Hospital Virgen de la Concha (Zamora), Zamora, Spain, [31]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [32]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [33]Hospital Universitari i Politècnic La Fe, Valencia, Spain, [34]Hospital Universitario Virgen de las Nieves, Rheumatology, Granada, Granada, Spain, [35]Hospital Gregorio Marañon, Madrid, Spain, [36]Hospital Universitario de Pontevedra, Pontevedra, Spain, [37]Hospital Univetsitari Vall d'Hebron, Rheumatology Department, Barcelona, Spain, [38]Hospital Univetsitari Vall d'Hebron, Ophthalmology Department, Barcelona, Spain, [39]Hospital Univetsitari Vall d'Hebron, Maxilofacial Surgery Department, Barcelona, Spain, [40]Rheumatology Research Group, Vall d'Hebron University Hospital, Barcelona, Spain, [41]IMIDomics, Barcelona, Barcelona, Spain, [42]Rheumatology Department, Hospital Clínic and IDIBAPS, Barcelona, Spain, Barcelona, Spain, [43]Hospital Universitario Puerta de Hierro, Majadahonda, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Assessing clinical improvements in Sjögren's Disease (SjD) is challenging. Our objective was to describe patterns of improvement in SjD using ESSDAI and ESSPRI indices and identify factors associated with these improvements.

Methods: Patients from the prospective SSAD cohort, which collects biological and clinical data from SjD cases, were included. ESSDAI improvement (ESSDAI-I) was defined by improvement in ≥1 ESSDAI domain (transition from high (H) or moderate (M) to low (L) or no activity (NA) in most domains; from M to L or NA in the glandular domain; and from H to M or NA in the CNS domain) without worsening in any other. ESSPRI improvement (ESSPRI-I) was defined as a reduction ≥2 points or ≥30% from baseline.

Patients were classified as improvers if improvement between two visits (3 months apart) was maintained at a subsequent visit 3 months later; the visit preceding improvement was considered baseline. Non-improvers (NI) were defined as patients with baseline ESSDAI or ESSPRI >0 but without observed improvement.

Among ESSDAI-I patients, clinical (ClinESSDAI) and isolated biological improvements were analyzed separately. As not all patients received therapeutic interventions at baseline, analyses were conducted for the entire cohort and separately for a subgroup initiating rituximab (RTX) at baseline.

Logistic regression models assessed the association of clinical variables with improvement status, adjusting for sex, age, disease duration, and baseline ESSDAI and ESSPRI scores. Fisher's exact test and Kruskal–Wallis tests were used for categorical and continuous variables, respectively. Unadjusted p-values < 0.05 were considered statistically significant. Analyses were performed using R v4.4.

Results: A total of 363 patients susceptible to improvement were analyzed. Improvement was observed in 30 patients (8.3%): 15 (4.1%) showed ESSDAI-I, 14 (3.86%) ESSPRI-I, and 1 patient (0.27%) showed simultaneous improvement in ESSDAI and ESSPRI. Four of the 16 ESSDAI-I cases improved only in the biological domain.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Table 1: Demographic and disease characteristics of the cohort

Variable	NI N = 333	ESSDAI improvements		ESSPRI-I N = 14	p-value[1]
		ClinESSDAI-I N = 12	OnlyBiological-I N = 4		
Sex, n (%)					0.58
Female	314 (94%)	11 (92%)	4 (100%)	13 (93%)	
Male	19 (5.7%)	1 (8.3%)	0 (0%)	1 (7.1%)	
Age, Median (Q1, Q3)	59 (50, 67)	56 (50, 62)	52 (49, 57)	63 (54, 68)	0.44
Evolution Years, Median (Q1, Q3)	7 (3, 13)	7 (6, 14)	6 (5, 11)	14 (5, 20)	0.19
PreviousGCs, n (%)	67 (21%)	1 (8.3%)	1 (25%)	5 (36%)	0.33
PreviousDMARDs, n (%)	90 (27%)	6 (50%)	1 (25%)	6 (43%)	0.19
PreviousSITs*, n (%)					0.034
0	311 (95%)	11 (92%)	3 (75%)	12 (86%)	
1	16 (4.9%)	1 (8.3%)	0 (0%)	2 (14%)	
2	1 (0.3%)	0 (0%)	1 (25%)	0 (0%)	
ACR_FocusPositive, n (%)	167 (50%)	5 (42%)	3 (75%)	7 (50%)	0.80
ACR_TotalScore, Median (Q1, Q3)	5.00 (4.00, 7.00)	5.00 (4.00, 7.00)	7.50 (5.50, 8.00)	5.50 (4.00, 7.00)	0.23
ESSDAI_Baseline, Median (Q1, Q3)	2.0 (0.0, 4.0)	9.0 (6.0, 14.5)	5.0 (3.0, 13.5)	1.0 (0.0, 3.0)	<0.001
ESSPRI_Baseline, Median (Q1, Q3)	6.33 (4.00, 8.00)	6.33 (4.50, 8.00)	8.17 (4.83, 9.17)	4.17 (2.67, 6.67)	0.13

[1]Fisher's exact test; Kruskal-Wallis rank sum test

* rituximab n=36. belimumab n=7. adalimumab n=2.

GCS: glucocorticoids; DMARDs: Disease Modifying Antirheumatic Drugs, SIT: Selective immunosuppressive treatment.

Table 2

Table 2: Characteristics of improvements

Variables, n (%)	NI N = 333	ESSPRI-I N = 14	ESSDAI-I	
			ClinESSDAI-I N = 12	Only Biological-I N = 4
Constitutional_Baseline	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Constitutional_Improvement	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Constitutional_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lymphadenopathy_Baseline	3 (0.9%)	0 (0%)	0 (0%)	0 (0%)
Lymphadenopathy_Improvement	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lymphadenopathy_Worsening	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Glandular_Baseline	5 (1.5%)	0 (0%)	4 (33%)	0 (0%)
Glandular_Improvement	0 (0%)	0 (0%)	4 (33%)	0 (0%)
Glandular_Worsening	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Articular_Baseline	13 (3.9%)	0 (0%)	7 (58%)	0 (0%)
Articular_Improvement	1 (0.3%)	0 (0%)	7 (58%)	0 (0%)
Articular_Worsening	2 (1.1%)	0 (0%)	0 (0%)	0 (0%)
Cutaneous_Baseline	5 (1.5%)	0 (0%)	2 (17%)	0 (0%)
Cutaneous_Improvement	1 (0.3%)	0 (0%)	2 (17%)	0 (0%)
Cutaneous_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pulmonary_Baseline	15 (4.5%)	1 (7.1%)	0 (0%)	0 (0%)
Pulmonary_Improvement	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pulmonary_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Renal_Baseline	3 (0.9%)	0 (0%)	1 (8.3%)	0 (0%)
Renal_Improvement	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Renal_Worsening	0 (0%)	1 (7.1%)	0 (0%)	0 (0%)
Muscular_Baseline	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Muscular_Improvement	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Muscular_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
PNS_Baseline	4 (1.2%)	1 (7.1%)	0 (0%)	0 (0%)
PNS_Improvement	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
PNS_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CNS_Baseline	0 (0%)	0 (0%)	0 (0%)	1 (25%)
CNS_Improvement	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CNS_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hematological_Baseline	6 (1.8%)	0 (0%)	1 (8.3%)	0 (0%)
Hematological_Improvement	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Hematological_Worsening	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Biological_Baseline	32 (9.6%)	2 (14%)	7 (58%)	4 (100%)
Biological_Improvement	6 (1.9%)	2 (14%)	5 (42%)	4 (100%)
Biological_Worsening	5 (2.8%)	0 (0%)	1 (8.3%)	0 (0%)
Dryness_Baseline, Median (Q1, Q3)	7.00 (5.00, 9.00)	5.50 (4.00, 7.00)	8.00 (7.00, 9.00)	6.50 (4.00, 8.50)
Dryness_Improvement	31 (18%)	8 (57%)	3 (25%)	0 (0%)
Dryness_Worsening	60 (34%)	3 (21%)	1 (8.3%)	2 (50%)
Fatigue_Baseline, Median (Q1, Q3)	6.0 (3.0, 8.0)	4.0 (0.0, 7.0)	5.0 (3.5, 8.5)	9.5 (6.0, 10.0)
Fatigue_Improvement	38 (22%)	9 (64%)	3 (25%)	1 (25%)
Fatigue_Worsening	60 (34%)	0 (0%)	5 (42%)	1 (25%)
Pain_Baseline, Median (Q1, Q3)	7.0 (3.0, 8.0)	3.0 (2.0, 8.0)	5.5 (4.0, 9.0)	8.5 (4.0, 9.5)
Pain_Improvement	32 (18%)	10 (71%)	5 (42%)	2 (50%)
Pain_Worsening	62 (36%)	2 (14%)	3 (25%)	0 (0%)

PNS: peripheral nervous system; CNS: central nervous system

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3

Table 3: Factors associated to improvement (with significant p-value)

Variable	OR (95% CI)	p-value	FDR
Improvers (ESSDAI or ESSPRI) *vs.* NI			
Biological_Baseline	2,03 (1,23-3,51)	0,01	0,19
Rituximab_Baseline	3,67 (1,44-10,20)	0,01	0,19
SerologyHypergammaglobulinemia_Improvement	4,72 (1,10-20,29)	0,04	0,45
SchirmerTest_Improvement	0,18 (0,04-0,91)	0,04	0,45
SerologyHighBeta2Microglobulin_Baseline	0,27 (0,07-1,13)	0,04	0,45
ESSDAI-I *vs.* NI			
Articular_Baseline	2,29 (1,52-3,44)	0,0001	0,004
SerologyLowC3_Baseline	0,02 (0,00-0,81)	0,005	0,10
Rituximab_Baseline	6,60 (1,76-24,80)	0,01	0,10
Biological_Baseline	2,83 (1,32-7,51)	0,01	0,14
Glandular_Baseline	1,72 (1,06-2,80)	0,02	0,24
Methotrexate_Baseline	4,85 (1,16-20,26)	0,03	0,28
SerologyCryoglobulinemia_Baseline	0,03 (0,00-1,21)	0,05	0,40
ESSPRI-I *vs.* NI			
Articular_Baseline	0,24 (0,07-0,91)	0,04	0,96
ESSDAI-I *vs.* ESSPRI-I			
Articular_Baseline	0,25 (0,08-0,78)	0,02	0,61
RTX-I *vs.* RTX-NI			
Biological_Baseline	4,30 (1,29-14,36)	0,02	0,53
SerologyAntiRoSSA52kd_Baseline	9,74 (1,05-90,27)	0,05	0,53

Overall improvement (ESSDAI or ESSPRI) was positively associated with higher baseline biological domain scores, initiation of RTX at baseline, and improvements in hypergammaglobulinemia and Schirmer's test, but negatively with elevated β2-microglobulin (B2M).

ESSDAI-I patients showed higher baseline scores in articular, biological, and glandular domains and more frequent RTX or MTX initiation than NI patients. Negative associations were noted with low C3 levels and cryoglobulinemia.

ESSPRI-I was positively associated with RTX initiation, higher peripheral nervous system domain and lower articular domain scores. ESSDAI-I patients had significantly higher baseline articular domain scores compared to ESSPRI-I patients.

In patients initiating RTX therapy, higher baseline biological scores predicted improvement, and Ro52 positivity trended toward significance.

Conclusion: ESSDAI and ESSPRI improvements rarely coincided in our cohort. Higher baseline biological and articular domain scores predicted ESSDAI improvement. Initiation of RTX strongly correlated with improvement, whereas elevated B2M, low C3 levels, and cryoglobulinemia negatively predicted improvement.

Disclosure: A. Gómez Gómez: None; **S. Martínez Mateu**: None; **J. Tandaipan**: None; **M. Fernandez Castro**: None; **G. gonzalez**: None; **S. Melchor-Díaz**: None; **M. Uriarte Ecenarro**: None; **R. Menor Almagro**: None; **P. Vela Casasempere**: None; **B. Paredes-Romero**: None; **J. Font-Urgelles**: None; **P. Estrada-Alarcón**: None; **S. Manrique-Arija**: None; **M. Blazquez Cañamero**: Astrazeneca, 12, conference registrations, Gsk, 6, Novartis, 12, conference registrations, Rubio, 12, conference registrations; **C. Moriano**: None; **J. Alegre-Sancho**: None; **M. Rodríguez López**: None; **M. López**: None; **G. Bonilla**: None; **R. Ortega-Castro**: None; **S. Rojas Herrera**: None; **I. Braña**: None; **L. López-Núñez**: None; **J. Narváez**: None; **J. Rosas Gómez de Salazar**: None; **R. López-Sánchez**: None; **C. Galisteo Veiga**: None; **J. Martínez-Ferrin**: None; **J. Pérez Venegas**: AstraZeneca, 6, Janssen, 4, 6, UCB, 6; **G. Manzano-Canabal**: None; **C. Peralta-Ginés**: None; **L. Sánchez Bilbao**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6; **R. Cáliz-Cáliz**: None; **B. Serrano-Benavente**: None;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

S. Fernández-Aguado: None; **N. Boix- Martí**: None; **E. Kirkegaard-Biosca**: None; **I. Alvarez Saez**: None; **A. Selles-Rius**: None; **M. Pérez**: None; **J. Cañete**: None; **S. Marsal**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 1, 5, IMIDomics, 4, 8, Janssen, 5, Merck/MSD, 5, Novartis, 5, Roche, 5, UCB, 5; **J. Andreu**: None.

Abstract Number: 2291

Correlation and Concordance Between the Oxford Grading Scale, Ocular Staining Score, and van BijsterveldScore in the diagnosis of Sjögren's Disease

Alejandro Gómez Gómez[1], Eric Kirkegaard-Biosca[2], Sergio H. Martínez Mateu[3], Iago Alvarez Saez[4], Natalia Boix- Martí[5], Antonio Julià[1], Jose Luis Andreu[6] and Sara Marsal[1], [1]Vall d'Hebron Hospital Research Institute, Rheumatology Research Group, Barcelona, Spain, [2]Hospital Univetsitari Vall d'Hebron, Ophthalmology Department, Barcelona, Spain, [3]IMIDomics, Barcelona, Spain, [4]Hospital Univetsitari Vall d'Hebron, Maxilofacial Surgery Department, Barcelona, Spain, [5]Hospital Univetsitari Vall d'Hebron, Rheumatology Department, Barcelona, Spain, [6]Hospital Universitario Puerta de Hierro, Majadahonda, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

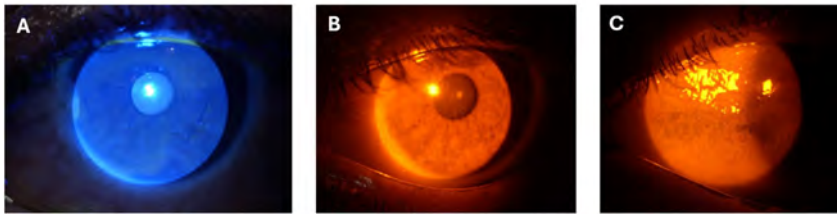
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's Disease (SjD) is a systemic autoimmune disorder marked by mucosal dryness and ocular surface damage. For diagnosis, the ACR-EULAR 2016 criteria require the Ocular Staining Score (OSS) or the van Bijsterveld score (vBs), both rarely used in routine care. The Oxford Grading Scale (OGS), a simpler and widely applied tool, may offer a more accessible alternative. The objective of this study is to assess the correlation and diagnostic agreement of OGS with OSS and vBs in patients fulfilling the ACR-EULAR 2016 criteria for SjD, aiming to support its use as a practical screening method.

Methods: We conducted a cross-sectional study of 20 patients from the SSAD project at a single center (June–December 2024), all meeting ACR-EULAR 2016 criteria for SjD. Each underwent ocular surface staining assessments using the OSS, vBs, and OGS on the same day, following standardized protocols (Figures A-C).

OSS evaluates corneal and conjunctival staining (0–12) with fluorescein and lissamine green; vBs scores three conjunctival zones (0–9) using the same dyes; OGS assesses corneal epithelial damage (0–5) via fluorescein staining. Positive thresholds were OSS ≥5 or vBs ≥4 per ACR-EULAR criteria. OGS thresholds were explored to determine optimal concordance with OSS and vBs.



Figures A–C: Simultaneous ocular surface staining in a patient with Sjögren's disease (SjD). A: Fluorescein staining of the ocular surface. B–C: Lissamine green staining of the cornea (B) and conjunctiva (C).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

We analyzed correlations using Spearman's rho for continuous scores and assessed agreement through percentage concordance and Cohen's kappa for binary classifications. OGS positivity was determined across various thresholds, selecting the one maximizing Cohen's kappa for further analysis. OSS and vBs served as reference standards to calculate OGS's positive and negative predictive values at different thresholds.

Results: A total of **20 patients** (mean age 57 years, 16 women [80%]) who met the classification criteria for SjD, regardless of their OSS or vBS results, were included.

- A **Near-perfect agreement** between standard scoring systems (OSS and vBs) was observed (rho = 0.94, $p < 0.001$ for both eyes).
- A **Moderate-to-good agreement** was observed for positive/negative classification based on ACR-EULAR thresholds (OSS ≥5, vBS ≥4), with 85% concordance (kappa = 0.67). Discrepancies were partially atributable to the treshold differences; for instance, some cases had a vBS of 4 (classified as positive) but an OSS of 3 or 4 (negative).
- **OGS** showed **Moderate correlations** with both OSS and vBs, ranging from rho=0.44 to rho=0.6, slightly higher for OSS than for vBS.
- An **OGS threshold of ≥1** in at least one eye yielded the **highest agreement** with OSS and vBS (kappa: 0.5 for OSS, 0.6 for vBS), with **excellent negative predictive values** (NPV: 1.0 for OSS, 0.9 for vBS) but modest positive predictive values (PPV: 0.5 for OSS, 0.7 for vBS).
- The **PPV-maximizing cutoffs** were OGS ≥3 for OSS (PPV = 1) and OGS ≥2 for vBS (PPV = 0.70). These are conservative thresholds with only 1 and 3 positive cases, respectively.
- Notably, all patients with a positive vBS were also OSS-positive, suggesting OSS may be the more conservative assessment.

Conclusion: OGS moderately correlates with OSS and vBs and shows excellent rule-out capability when the score is 0. Given its simplicity and high NPV, OGS could serve as a practical screening tool for ocular damage in SjD, especially in settings lacking access to OSS or vBs.

Disclosure: A. Gómez Gómez: None; **E. Kirkegaard-Biosca**: None; **S. Martínez Mateu**: None; **I. Alvarez Saez**: None; **N. Boix- Martí**: None; **A. Julià**: None; **J. Andreu**: None; **S. Marsal**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 1, 5, IMIDomics, 4, 8, Janssen, 5, Merck/MSD, 5, Novartis, 5, Roche, 5, UCB, 5.

Abstract Number: 2292

Safety and Humoral Response to Recombinant Herpes Zoster Vaccine in immunosuppressed Sjögren's Disease Patients: Results From a Double-Blinded Placebo-Controlled Study

Sandra G Pasoto[1], Talita Ribeiro[2], Nadia Emi Aikawa[3], **Ana C Medeiros-Ribeiro**[1], Bruno Borges[2], Andre Franco[4], Henrique Silva[2], Eloisa Bonfa[5] and Clovis Artur Silva[6], [1]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [2]Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, São Paulo, Brazil, [3]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Sao Paulo, Brazil, [5]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [6]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Immunosuppressed Sjögren's disease (SjD) patients are at increased risk of herpes zoster (HZ). Despite this vulnerability, data on safety and immunogenicity of the recombinant HZ vaccine (RZV, Shingrix®) in these patients remain limited. Concerns about disease flares following vaccine, as highlighted in studies of COVID-19 vaccination, further underscore the need for target evaluation. **Purpose:** To evaluate the safety and immunogenicity of RZV in immunosuppressed SjD.

Methods: In this randomized, double-blind, placebo-controlled trial, 67 adults immunosuppressed SjD patients (excluding rituximab) were enrolled, alongside 201 non-immunosuppressed control individuals (CG). SjD patients were randomized to receive vaccine (P1) or placebo (P2) at day 0 (D0) and D42, with placebo recipients vaccinated after unblinding (D84 and D126). CG were immunized at D0 and D42. Disease activity [ESSDAI (European League Against Rheumatism-EULAR Sjögren's Syndrome Disease Activity Index)] and adverse events (AEs) were monitored at all visits. Humoral immunogenicity was assessed by serum anti-gE antibody concentrations using a GSK ELISA. The humoral response to VZR was defined as anti-gE concentration ≥4-fold the pre-vaccination concentration. Geometric Mean Titer (GMT) and Factor Increase (FI-GMT) were calculated.

Results: Vaccine (P1) and placebo (P2) groups were comparable in terms of age (p=0.5), sex (p=1.0), prednisone use (p=0.3) and dosage (0.6), as well as treatment with hydroxychloroquine (p=0.7), methotrexate (p=0.5), leflunomide (p=0.4), azathioprine (p=0.5), and mycophenolate mofetil (p=0.8). Baseline disease activity, assessed by ESSDAI, was similar between P1 and P2 [2.0 (0.0-2.0) vs. 1.0 (0.0-2.5), p=0.7], and most patients presented low disease activity (ESSDAI< 5) in both groups (87.1% vs. 88.9%, p=1.0), respectively. No significant changes in ESSDAI were observed six weeks after the 1st (p=0.5) or 2nd (p=0.2) RZV dose. Flare rates, defined as increase ≥3 points in ESSDAI and/or increased glucocorticoid/immunosuppressant therapy, were also comparable between groups throughout the study (p >0.05). Regarding AEs, after the 1st RZV dose, local reactions were less frequent among SjD than in CG (70.1% vs. 84.6%, p=0.009), as were systemic reactions (50.7% vs. 62.2%, p=0.1). After the 2nd RZV dose, the rates were comparable between groups (p >0.05). No serious AEs were observed. Analysis of immunogenicity comparing SjD and age [55.0 (48.3-63.8) vs. 55.0 (52.0-64.0) years, p=0.1] and sex (female: 95.5% vs. 90.5%, p=0.3, respectively) balanced CG revealed a reduced humoral response in SjD patients (90.6% vs. 99.5%, p=0.0009). Furthermore, GMT and FI-GMT were significantly lower in SjD patients compared to controls (Table).

Table. Humoral response rates 6 weeks after the 2nd RZV dose and anti-gE IgG titers before (D0) and after two doses in patients with SjD and CG
CG – control group, SjD – Sjögren's disease. RZV – recombinant herpes zoster vaccine, GMT – geometric mean titers (mIU/mL). Frequencies of humoral response are presented as number (%) and they were compared using two-sided chi-square test between SjD and CG at 6 weeks after the 2nd RZV dose. Anti-gE IgG titers and factor increase (FI) in GMT are expressed as geometric means with 95% confidence interval (95%CI). Data regarding anti-gE titers were analyzed using ANOVA with repeated measures and 2 factors [2 groups (SjD vs. CG), at 2 time points (D0 and 6 weeks after the 2nd RZV dose)], followed by Bonferroni's multiple comparisons at neperian logarithm (ln)-transformed data. GMT and FI-GMT were compared using Mann-Whitney test for intergroup comparisons in ln-transformed data at pre-specified time points (D0 and 6 weeks after de 2nd dose). All analyses were two-sided. P1 – SjD patients who received the RZV on the day of randomization (D0) and after 6 weeks (D42). P2 – SjD patients who initially received placebo and were vaccinated 12 weeks after randomization, on D84 and after 6 weeks (D126).

	Humoral response 6 weeks after 2nd dose	GMT			FI-GMT
		D0	6 weeks after 2nd dose	p (D0 vs. 6 weeks after 2nd dose)	D0 to 6 weeks after 2nd dose
SjD (P1 +P2), n=64	58 (90.6)	0.30 (0.21-0.43)	7.11 (5.27-9.61)	<0.001	23.94 (16.0-35.8)
CG, n=201	200 (99.5)	0.18 (0.15-0.21)	12.58 (11.43-13.85)	<0.001	70.43 (58.60-84.35)
p (SjD vs. CG)	<0.001	0.019	<0.001		<0.001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: RZV demonstrated an excellent safety profile in immunosuppressed SjD patients, without triggering significant disease flares. Although the vaccine induced a high rate of humoral response, the magnitude of the response was significantly lower compared to healthy controls, which may have implications for long-term protection. (ClinicalTrials NCT05879419).

Disclosure: S. Pasoto: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **T. Ribeiro**: None; **N. Aikawa**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **B. Borges**: None; **A. Franco**: None; **H. Silva**: None; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

Abstract Number: 2293

CLN-978, a CD19 x CD3-Directed T Cell Engager, Leads to Rapid and Deep B Cell Depletion In Vitro and In Vivo, Supporting Clinical Development Across Multiple Autoimmune Diseases

Ella Ioffe, Karsten Sauer, Todd Shearer, Jennifer Michaelson, Jeffrey Jones, Yue Zhang, Stephen Wax and **Antoine Sreih**, Cullinan Therapeutics Inc, Cambridge, MA

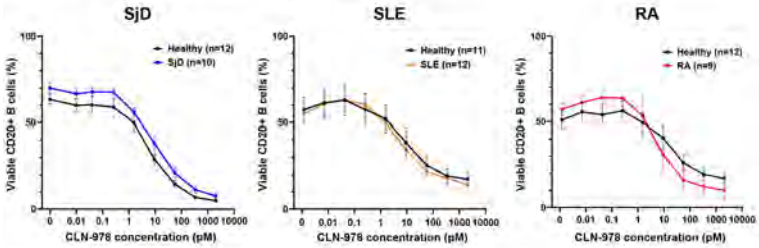
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Treatments depleting CD19-expressing B cells have shown benefit in a range of autoimmune diseases. T cell engagers (TCE) offer off-the-shelf convenience, the predictable pharmacokinetic/pharmacodynamic properties of monoclonal antibodies, and the potential to achieve deep target cell depletion as seen with chimeric antigen receptor (CAR) T cell therapy. CLN-978 is a T cell engager comprised of tandemly arranged CD19- and CD3-specific single-chain fragment variable domains and a single-domain albumin binder for serum half-life extension. CLN-978 has high affinity for CD19 and moderate affinity for CD3 (Meetze K, et al. J Immunother Cancer 2023;11:e007398) and is administered via subcutaneous (SC) injection. In a phase 1, first-in-human study (NCT05879744), patients with B cell non-Hodgkin lymphoma (B-NHL) were treated with the starting dose of 30 micrograms (mcg) SC weekly of CLN-978, which demonstrated a favorable safety profile and a complete metabolic response in 1 of 3 treated patients. We report preclinical and translational studies in autoimmune diseases.

Methods: Peripheral blood mononuclear cells (PBMC) derived from healthy donors and patients with Sjögren's disease (SjD), SLE, or RA, were cultured in the presence of CLN-978 for 48 hours. In a mouse model of SLE, NOD scid gamma (NCG) mice engrafted with PBMC from a patient with SLE were treated with CLN-978 weekly for 3 weeks. Cynomolgus monkeys were administered single and up to 4 weekly SC doses of CLN-978 at dose levels ranging from 2 to

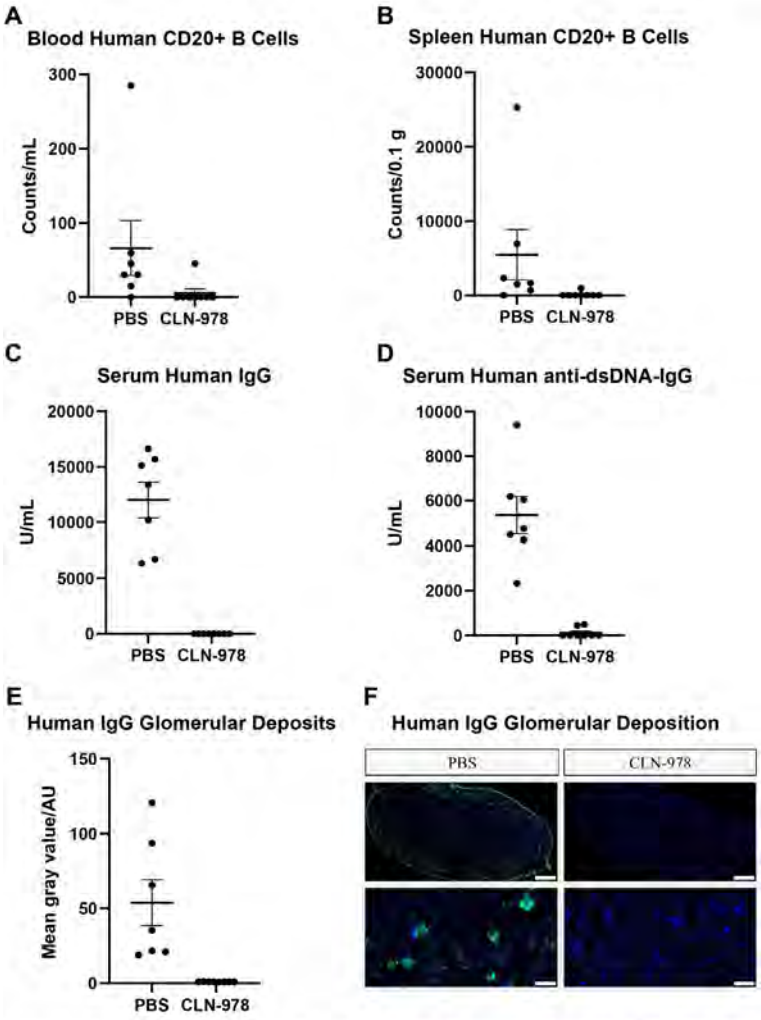
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: CLN-978 induces similar B cell killing in PBMCs across patients with autoimmune diseases and healthy donors



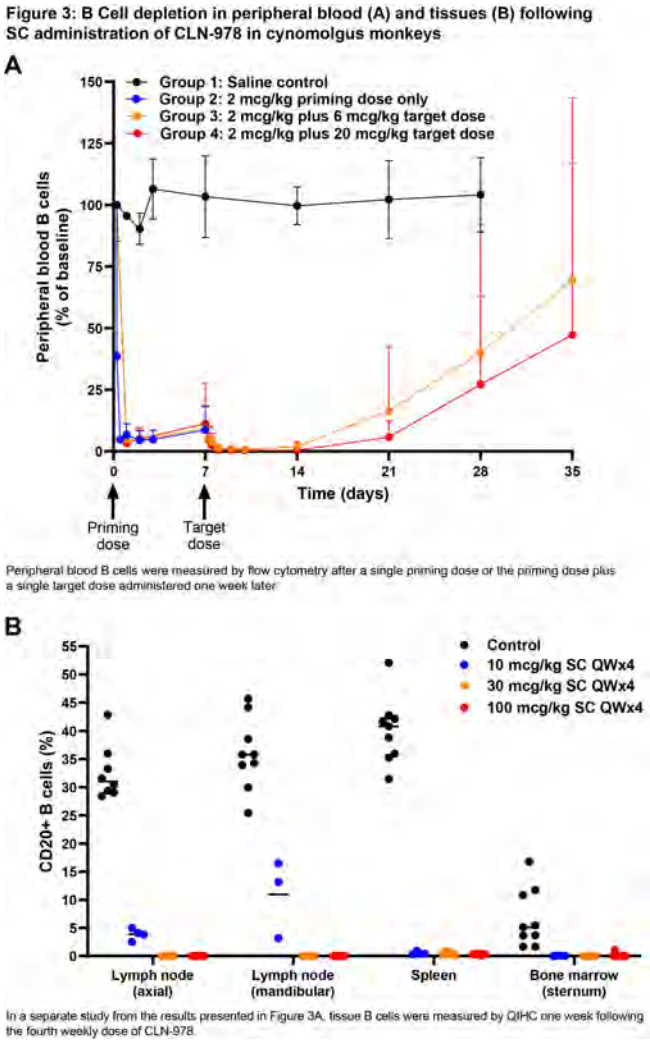
PBMC from healthy volunteers or patients with SjD, SLE, or RA were cultured in the presence of CLN-978 for 48 hours. B cells were analyzed by flow cytometry and normalized to PBMC-only control. Error bars denote standard error of the mean.

Figure 2: CLN-978 treatment depletes human B cells, reduces anti-dsDNA antibodies, and abrogates human IgG deposition in the kidneys of NCG mice engrafted with PBMC from SLE patients



NCG mice harboring PBMC from a patient with SLE were injected SC with phosphate-buffered saline (PBS) or CLN-978 (30 mcg/kg) on days 7, 14, and 21 before analysis on day 28. (A-E) Levels of human CD20+ B cells in blood (A) and spleen (B), human IgG (C) and anti-dsDNA IgG (D) in serum, and human IgG deposits in kidney glomeruli (E). Dots denote values for individual mice, and horizontal lines the means (n=7 or n=8, respectively, for PBS or CLN-978 treatment). Error bars denote standard error of the mean. (F) Representative immunofluorescence microscopic images of human IgG deposits (green) and cell nuclei (blue) in kidneys. Scale bars, 1 mm (top) or 0.1 mm (bottom).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



100 mcg/kg. Peripheral blood and tissues (lymph nodes, spleen, and bone marrow) were assessed for B cell depletion by flow cytometry and quantitative immunohistochemistry (QIHC), respectively.

Results: In vitro, CLN-978 induced similar B cell killing (Figure 1) and T cell activation in PBMCs from healthy donors and in patients with SjD, SLE, or RA. In mice engrafted with human SLE PBMC, CLN-978 treatment depleted human B cell populations in blood and spleen, reduced human IgG and anti-dsDNA IgG blood levels, and abrogated human IgG deposition in kidney glomeruli compared with controls (Figure 2).

In cynomolgus monkeys, a dose-related B cell depletion was observed in peripheral blood following administration of a single priming dose +/- a single target dose of CLN-978 (Figure 3A). Dose-related B cell depletion was also observed in lymphoid tissues, spleen, and bone marrow following administration of 4 weekly SC doses (Figure 3B). CLN-978 was well tolerated in monkeys following multiple weekly SC doses up to 100 mcg/kg.

Conclusion: CLN-978 is a highly potent, SC-administered, CD19-directed TCE. Preclinical in vitro and in vivo data including deep B cell depletion in both peripheral blood and tissue, along with existing clinical data in B-NHL patients, support broad development across autoimmune diseases. Phase 1b studies of CLN-978 are currently being conducted in patients with CLN-978 in SjD, SLE, and RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: E. Ioffe: Cullinan Therapeutics, 3, 11; **K. Sauer**: Cullinan Therapeutics, 12,, 3, 11; **T. Shearer**: Cullinan Therapeutics, 3, 11; **J. Michaelson**: Cullinan Therapeutics, 3, 11; **J. Jones**: Cullinan Therapeutics, 3, 11; **Y. Zhang**: Cullinan Therapeutics, 3, 11; **S. Wax**: Cullinan Therapeutics, 3, 11; **A. Sreih**: AstraZeneca, 11, Bristol-Myers Squibb(BMS), 11, Cullinan Therapeutics, 3, 11.

Abstract Number: 2294

Comparative Analysis of Patients Included in Trials Utilizing Biologic Drugs in the Treatment of Primary Sjögren's Syndrome

Carlota Navarro Joven[1], Silvia Piunno[2], Maryia Nikitsina[3], CARMEN SAN JOSE MENDEZ[4] and David A. Isenberg[5], [1]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, [2]Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy, [3]University Hospital La Princesa, Madrid, Madrid, Madrid, Spain, [4]Complejo Hospitalario Universitario de A Coruña (CHUAC), A Coruña, Spain, [5]University College London, London, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's syndrome is a heterogeneous autoimmune disease with no approved disease-modifying treatments. The aim of this systematic review was to evaluate primary Sjögren's syndrome (pSS) patient characteristics included in clinical trials (CTs).

Methods: This systematic review was undertaken according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. The search was performed using PubMed, EMBASE, OVID, and ClinicalTrials.gov for phase II and III clinical trials of biologic drugs in pSS including ≥30 adult patients and published between 2010 and 2024. Baseline characteristics of participants and trial-related information were collected. Descriptive statistics were used for analysis.

Results: A total of 16 publications were eligible to be included in this review, with 87.5% being published after 2017. The CTs were predominantly randomized controlled trials with a placebo arm (93.8%) and phase II trials (62.5%). The mean follow-up period was 32 weeks. The majority of the CTs (56.3%) were fully sponsored by industry sources. A summary of the main characteristics of CTs selected is shown in **Table 1**.

Inclusion criteria often focused on high disease activity, as measured by the ESSDAI score, with 62.5% requiring an ESSDAI score ≥5. Salivary flow measures were also common, used in 43.8% of the CTs. The primary outcomes were diverse, but 56.3% of the CTs focused on reducing ESSDAI scores.

The CTs included in the analysis reported a total of 1607 patients, predominantly female (94%), with a mean age of 51.0 (4.04) years. The mean time from diagnosis was 6.47 (2.48) years. Racial diversity was underreported, with only 37.5% of CTs providing data on race. Among those, 77.8% of participants were White, 11.9% were Asian, and 5.2% were Black.

Disease characteristics included high anti-SSA/Ro antibody positivity (92.9%), while other immunological and serological features are shown in **Table 2**. Mean ESSDAI score was 9.6 (2.8) and mean ESSPRI score was 6.3 (0.88). Other measurements of subjective symptoms notably a numerical rating scale (NRS) were also assed, including an NRS for dryness, fatigue and pain mean values of 7.2/10, 6.7/10 and 5.7/10, respectively. Patient-reported measures of disease burden are shown in Table 3.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Selected trials for biologics in pSS RCT: randomized clinical trial

Authors	Year of publication	Study design	Drug evaluated	Patient population
Meijer JM et al.	2010	RCT, phase II	Rituximab	30
Devauchelle-Pensec V et al.	2014	RCT, phase II/III	Rituximab	120
Mariette X et al.	2015	Open-label trial, phase II	Belimumab	30
Bowman SJ et al.	2017	RCT, phase III	Rituximab	133
St Clair EW et al.	2018	RCT, phase II	Baminercept	52
van Nimwegen JF et al.	2020	RCT, phase III	Abatacept	80
Shao Q et al.	2021	RCT, phase II/III	Iguratimod	66
Baer AN et al.	2021	RCT, phase III	Abatacept	187
Felten R et al.	2021	RCT, phase II/III	Tocilizumab	110
Mariette X et al.	2022	RCT, phase II	Belimumab, rituximab	86
He J et al.	2022	RCT, phase II	Recombinant human IL-2Ala125	60
Bowman SJ et al.	2022	RCT, phase II	Ianalumab	190
Bentley D et al.	2023	RCT, phase II	RO5459072	75
Dong X et al.	2024	RCT, phase II	Telitacicept	42
Dörner T et al.	2024	RCT, phase II	Remibrutinib	73
Fisher BA et al.	2024	RCT, phase II	Iscalimab	273

Table 2 : Serological features of patients included in the CTs Data are mean (SD), median (min, max), or percentages. ANA=antinuclear antibodies; anti-La/SSB= antibodies against Sjögren's Syndrome B; RF=Rheumatoid Factor; IgG=Immunoglobulin G

Serological feature	Statistical measures	Trials reporting
ANA positivitiy	83.1	4/16
Anti-La/SSB positivity	61.2	9/16
RF positivitiy	58.7	6/16
RF (U/mL)	116.3 (60.1)	3/16
C3 (g/L)	113.7 (20.9)	3/16
C3 (g/L)	105.0 (97.0, 130.0)	3/16
C4 (g/L)	21.6 (4.4)	6/16
C4 (g/L)	20.0 (20.0, 25.0)	2/16
IgG (g/L)	18.4 (4.4)	11/16
IgG (g/L)	20.7 (17.4, 22.9)	2/16
Hypergammaglobulinemia	63.1	3/16
Cryoglobulinemia	10,3	1/16
β2-microglobulin (nmol/L)	245.7 (41.5)	1/16

Table 3: Patient-reported measures of disease burden Data are mean (SD), median (min, max), or percentages. SF-36: Short Form-36; PCS: Physical Component Summary of SF-36; MCS: Mental Component Summary of SF-36; MFI-20: Multidimensional Fatigue Inventory-20.

Scale assesed	Statistical measures	Trials reporting
SF-36 total	52.4 (11.5)	2/16
PCS	37.8 (1.7)	5/16
PCS	50.4 (50.3, 50.4)	1/16
MCS	40.8 (3.5)	4/16
MCS	47.0 (44, 50.1)	2/16
MFI-20 score	56.4 (4.949)	1/16
MFI-20 score	51.3 (51.0, 51.5)	1/16

Concomitant treatments were common, with 87.5% of the CTs allowing simultaneous therapies. Despite most of the CTs being multicentric (75%), global representation was limited: only five CTs recruited patients in more than two continents and no CTs recruited in Africa.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This review highlights key challenges in pSS CTs: notably limited patient diversity, high subjective symptom burden, and heterogeneous outcomes measures. While the use of ESSDAI/ESSPRI is rising and reporting of race and ethnicity is improving, standardization remains incomplete. Earlier intervention and broader recruitment are needed to advance pSS therapies.

Disclosure: C. Navarro Joven: None; **S. Piunno**: None; **M. Nikitsina**: None; **C. SAN JOSE MENDEZ**: None; **D. A. Isenberg**: None.

Abstract Number: 2295

Autoantibody Profiles and Their Association with Organ Involvement in Primary Sjögren's Syndrome: Insights from ESSDAI

Deepak Rath[1], Sholen Acharya[2] and Dr Alakendu Ghosh[3], [1]John H Stroger Hospital Jr of Cook County, Chicago, Illinois, USA, 60612, Chicago, IL, [2]Department of Reproductive Medicine and Surgery, Government Medical College Thiruvananthapuram, Kerala, India, 695004, Chicago, IL, [3]Self employed, Kolkata, West Bengal, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: To evaluate the clinical manifestations, systemic disease activity, and serological profile of patients of Primary Sjögren's syndrome, and to assess associations between specific autoantibodies and ESSDAI domain involvement, with the aim of identifying patterns that could guide diagnosis, disease monitoring, and management.

Methods: This prospective observational study was conducted in the Department of Rheumatology at XYZ Hospital from July 2017 to January 2019, following institutional ethical approval. Patients diagnosed with primary Sjögren's syndrome based on ACR classification criteria[1] were included. Exclusion criteria encompassed coexisting infections, malignancies, radiation history, or other autoimmune conditions. Informed consent was obtained from all participants.

Each patient underwent a detailed clinical evaluation, laboratory testing (including ANA, RF, ACPA, and a panel of autoantibodies), and additional assessments like Schirmer's test, imaging, and minor salivary gland biopsy. Systemic disease activity was assessed using ESSDAI and patient-reported symptoms via ESSPRI. Data analysis was performed using Jamovi software.[2] Categorical data were presented as frequencies; continuous data as mean ± SD. Associations were tested using chi-square and t-tests.

Results: Out of 144 screened individuals, 105 were included in the final analysis. The mean age was 38.5±11.1 years; 95.2% were female. Sicca symptoms (ocular and oral dryness), dental caries (61.9%), fatigue (30.5%), and glandular swelling were common. Mild to moderate breathlessness was reported by 19%. (Table 1A)

Laboratory findings (Table 1B) showed elevated ESR (mean 48.3 mm/hr), mild anemia (mean hemoglobin 10.8 g/dL), and low vitamin D levels (mean 20.7 ng/dL). IgG was elevated in many patients (mean 1853.7 mg/dL), with RF positivity in 45 (42.9%) and anti-CCP positivity in 35 (49.3%). ANA patterns were predominantly coarse speckled (48 patients).

ESSDAI analysis revealed minimal disease activity in most domains (Figure 1), except articular (43.8% had moderate to high activity), biological (50.5% had low/moderate activity), and lymphadenopathy domains.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A. Clinical Symptoms				
Symptomatology		N	Present	Percentage
Fever		105	19	18.1
Weight Loss		105	3	2.9
Fatigue		105	32	30.5
Foreign Body sensation in the Eye		105	46	43.8
Loss of lacrimation		105	25	23.8
Difficulty in swallowing dry foods		105	39	37.1
Caries Tooth		105	65	61.9
Atypical Caries		105	27	25.7
Swelling of the parotid gland		105	21	20
Swelling of sublingual gland		105	21	20
mMRC Grade of Breathlessness	No Breathlessness		85	81
	Grade 1		3	2.9
	Grade 2		10	9.5
	Grade 3		6	5.7
	Grade 4		1	1
mMRC: modified Medical Research Council				

B. Laboratory Parameters						
	N	Mean	Median	SD	Minimum	Maximum
ESR (mm/1st hour)	65	48.369	42	30.391	5	150
Haemoglobin (g/dl)	105	10.845	11.1	1.677	5.1	14.2
25-OH-Vit D (ng/dl)	81	20.685	19	12.13	5.97	87.4
hsCRP (mg/dl)	94	1.233	0.3	2.527	0.3	17
RF (IU/ml)	103	101.7	0	308.5	0	2180
Anti-CCP (RU/ml)	71	59.4	0	97.7	0	419
Anti-Ro (RU/ml)	73	123.3	129	53.1	0	217
Anti-La (RU/ml)	71	33.1	12	53.5	0	246
C3 (mg/dl)	101	116.7	116	31	15	189
C4 (mg/dl)	99	24.1	23.4	10.2	1.4	62.2
dsDNA (IU/ml)	73	42.9	22	87.6	0	646
IgG (mg/dl)	102	1853.7	1815	560.6	810	4000
IgM (mg/dl)	102	133	118	88.4	26.3	691
IgA (mg/dl)	102	275.7	252.5	120.1	22	761

Clinical Symptoms and Laboratory Parameters of the study population

Table 2 Chi-square test values of the various auto-antibodies and ESSDAI domains

		CONSTITUTIONAL	LYMPHNODE	GLANDULAR	ARTICULAR	CUTANEOUS	PULMONARY	RENAL	MUSCULAR	PNS	CNS	HEMATOLOGIC	BIOLOGIC
RNPSM	Sig.	0.238	1	0.214	0.898	0.542	0.207	0.084	0.53	0.837	0.44	0.635	0.128
SM	Sig.	0.706	0.477	0.637	0.138	0.67	0.096	.000, *	0.841	0.693	0.805	0.44	0.626
SSA	Sig.	0.904	1	.032, *	0.898	0.719	0.207	0.368	0.53	0.218	0.44	0.333	0.526
RO52	Sig.	0.992	0.603	0.598	0.684	0.424	0.12	0.588	0.556	0.248	0.469	0.133	.020, *
SSB	Sig.	.093	.267	.202	.603	.315	.836	0.242	0.813	.115	0.79	.853	.329
SCL70	Sig.	0.596	0.517	0.91	0.573	0.761	0.49	0.511	0.647	0.072	0.573	0.416	.017, *
PMSCL100	Sig.	0.706	0.477	0.637	0.496	0.67	0.545	0.773	0.841	.010, *	0.805	0.44	.038, *
PCNA	Sig.	0.706	0.155	.033, *	0.496	0.67	0.545	0.773	0.841	0.693	0.805	0.191	0.626
DSDNA	Sig.	0.443	0.149	0.338	0.778	0.387	0.282	0.558	0.683	0.484	0.616	0.11	0.323
NUCLEOSOMECDE	Sig.	0.26	0.603	0.669	0.239	0.823	.001, *	0.054	0.556	0.942	0.469	0.46	0.153
HISTONE	Sig.	0.443	0.149	0.715	0.415	.049, *	.026, *	0.182	0.683	0.484	0.616	0.587	0.323
RIBOP	Sig.	0.264	0.214	0.409	.009, *	0.456	0.112	0.089	0.725	0.491	0.665	0.177	0.394
AMA	Sig.	0.103	0.614	.002, *	0.334	0.545	0.451	0.682	.001, *	0.124	0.725	0.704	0.489

Chi-square test values of the various auto-antibodies and ESSDAI domains. Chi-square test p-values showing associations between various auto-antibodies and ESSDAI domains in patients with Sjögren's Syndrome. This table presents the statistical significance (p-values) of associations between the presence of different autoantibodies and disease activity across 12 ESSDAI domains. Significant associations ($p < 0.05$) are highlighted in green and marked with an asterisk (*). Notable associations include SSA with the Glandular domain ($p = .032$), PCNA with the Glandular domain ($p = .033$), and AMA with the Renal ($p = .002$) and Muscular ($p = .001$) domains. These findings may indicate domain-specific immunological patterns in Sjögren's Syndrome.

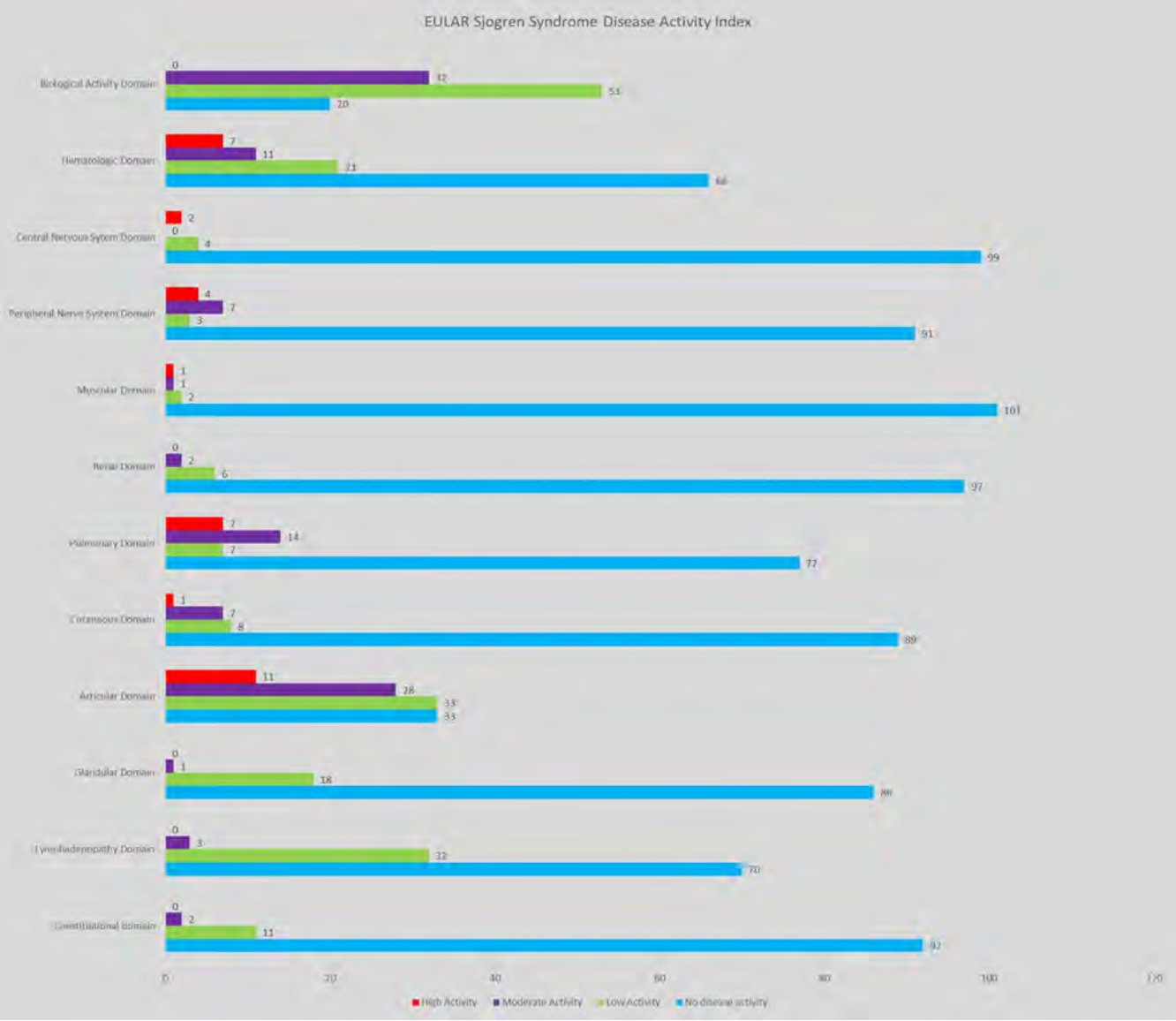


Figure 1: Distribution of disease activity across domains of the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). The bar chart illustrates the frequency of disease activity levels—high (red), moderate (purple), low (green), and no activity (blue)—across 12 clinical domains of ESSDAI in a cohort of patients. The Central Nervous System, Muscular, and Renal domains show the highest number of cases with no disease activity, whereas domains such as the Articular and Biological Activity domains demonstrate a wider distribution across all activity levels. The data highlights the heterogeneity of systemic involvement in Sjögren's Syndrome.

Significant associations were observed between autoantibodies and ESSDAI domains (Table 2): anti-SSA with glandular (p=0.032), anti-Ro52 and anti-SCL70 with biological (p=0.020, p=0.017), anti-nucleosome with pulmonary (p=0.001), anti-histone with pulmonary and cutaneous (p=0.026, p=0.049), and anti-AMA with glandular and muscular (p=0.002, p=0.001) domains.

Conclusion: This study demonstrates the systemic heterogeneity of Sjögren's syndrome, with prominent articular and biological domain involvement. Significant associations between autoantibody profiles and specific organ/system involvement can help to identify distinguishing disease subgroups.

Disclosure: D. Rath: None; **S. Acharya**: None; **D. Ghosh**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2296

Evaluation of the Dual Mode of Action of Ianalumab (VAY736) in the Circulation and Salivary Gland Tissue of Patients With Sjögren's Disease: Results From a Phase 2 Mechanistic Study

Divi Cornec[1], Rainer Hillenbrand[2], Patrice Hemon[3], Diego Saldana Miranda[2], Marion Le Rochais[4], Aida Santos Da Costa[2], Marie Frutoso[3], Cristian Iperi[5], Ulrike Sommer[2], Arnaud Uguen[4], Christophe Jamin[4], Patricia Baley[6], Caroline Denis[6], Dewi Guellec[4], Alice Tison[4], Daniel Strasser[2], sandrine jousse[4], Shuqi Chen[7], Noemi Giglioli[2], CAROLE SIPS[2], Alain SARAUX[8], Richard Siegel[9], Wolfgang Hueber[10], Sophie Hillion[4], Valerie Devauchelle[11] and Claire Bonal[2], [1]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, Bretagne, France, [2]Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland, [3]LBAI, UMR1227, University of Brest, Brest, France, Brest, France, [4]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [5]LBAI, UMR1227, University of Brest, Brest, France, Basel, France, [6]CHU Brest, Brest, France, Brest, France, [7]China Novartis Institutes for BioMedical Research, Shanghai, China, Shangai, China (People's Republic), [8]CHU Brest, Brest, France, [9]Novartis Biomedical Research, Basel, Switzerland, [10]Novartis Pharmaceuticals, Basel, Switzerland, [11]UBO, Brest, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Ianalumab, a glycoengineered, fully human, IgG1 mAb directed against B cell-activating factor (BAFF)-receptor (BAFF-R), targets B cells and their functions via a dual mechanism of action: depletion of B cells through enhanced antibody-dependent cellular cytotoxicity, and blockade of BAFF:BAFF-R–mediated signals. The purpose of this study is to better understand the dual mechanism of action of ianalumab in the blood and labial salivary gland (SG) tissue of patients with Sjögren's disease (SjD).

Methods: This is an open-label, single-center, non-randomized, phase 2 mechanistic study (NCT05124925) with a 5-week screening period, a 6-month treatment period, and a follow up period of up to 2 years after the last dose. Eligible participants included those who fulfilled the 2016 ACR/EULAR classification criteria for SjD with anti-Ro/SSA autoantibodies, EULAR Sjögren's Syndrome Patient Reported Index score of ≥5, labial SG focus score (FS) of ≥0.3/4mm^2, and B/B+T cell ratio of ≥0.2 at screening. This interim analysis reports the results of patients who completed the 24-week treatment period (ianalumab 300 mg monthly subcutaneous injection). The primary outcome was change in B/B+T cell ratio from baseline (BL) to week (W) 25. Other outcomes included mass cytometry and single-cell RNA sequencing of circulating immune cells, biomarkers of B cell activation, and labial SG histologic parameters, as well as clinical evaluations, safety, and tolerability.

Results: In the safety analysis set (N=21), ianalumab was well-tolerated with no drug-related serious adverse events (AEs) and one AE leading to discontinuation. Overall, 17 participants completed 24-week open-label treatment, underwent paired screening and W25 labial SG biopsy, and were analyzed. Clinical outcomes and biomarkers of B cell hyperactivity improved numerically. Total CD19+ B cell counts in blood decreased by 99% vs BL. B cells were almost completely depleted in most subsets, notably in naïve B cells, but to a lower extent in double negative effector memory cells (89.5%) and plasmablasts (69.5%; **Figure 1a**). Median depletion was significantly correlated with median BAFF-R expression in these subsets at BL (p=0.008; **Figure 1b**). Gene expression analysis revealed downregulation of B cell signaling, proliferation, and chemotaxis, and upregulation of oxidative phosphorylation and mitochondrial/cellular stress in the remaining naive B cells present at W25. IFN pathway genes were downregulated in plasmablasts at W25. While the FS was slightly reduced, based on regression analyses, the B/B+T cell ratio was statistically significantly reduced by 41% (80% CI: 22, 55) and the B cell density was reduced by 84% (80% CI: 68, 91) at W25 vs BL (**Figure 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

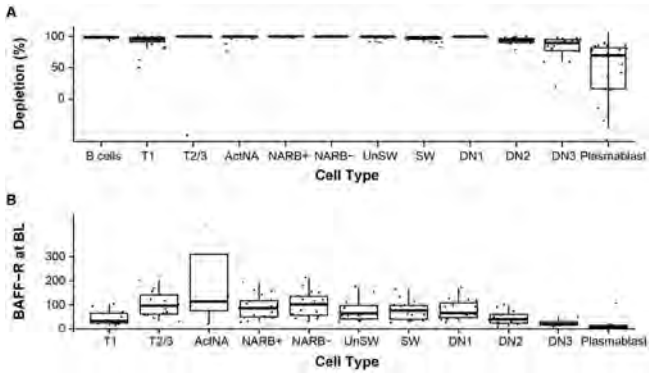


Figure 1. Extent of depletion of circulating B cells and B cell subsets at W25 (A) in relation to BAFF-R expression at BL (B). ActNA, activated naïve cells; BAFF-R, B cell-activating factor-receptor; BL, baseline; CD, cluster of differentiation; DN1–3, double negative effector memory cells; NARB; naïve cells (CD45RB); SW, switched memory cells; T1–3, transitional cells; UnSW, unswitched memory cells.

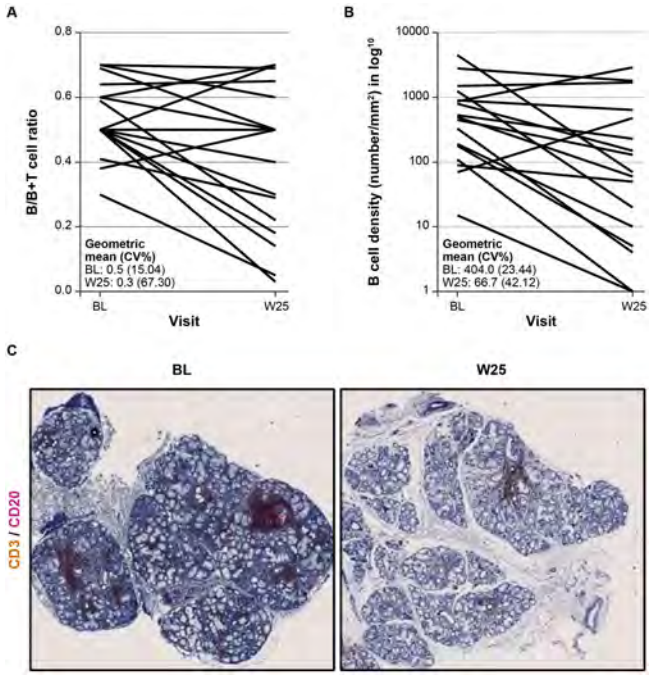


Figure 2. Labial SG B/B+T cell ratio (A), B cell density in log scale of base 10 (B), and a representative example of immunohistochemistry staining for CD3/CD20 (C) at BL and W25. BL, baseline; CD, cluster of differentiation; CV, coefficient of variation; SG, salivary gland; w, week.

Conclusion: Ianalumab 300 mg monthly treatment almost completely depleted B cells in the circulation, and to a large extent in labial SG tissue, in line with improvement in clinical and serological parameters at W25 vs BL. These observations suggest direct and relevant effects of ianalumab 300 mg monthly on the target tissue in patients with SjD. Additionally, ianalumab 300 mg monthly modified the phenotype of the remaining B cells in circulation, shedding new light on the dual mechanism of action of ianalumab.

Disclosure: D. Cornec: None; **R. Hillenbrand**: Novartis, 3, 11; **P. Hemon**: None; **D. Saldana Miranda**: Novartis, 3, 11; **M. Le Rochais**: None; **A. Santos Da Costa**: Novartis, 3, 11; **M. Frutoso**: None; **C. Iperi**: None; **U. Sommer**: Novartis, 3, 11; **A. Uguen**: None; **C. Jamin**: None; **P. Baley**: None; **C. Denis**: None; **D. Guellec**: None; **A. Tison**: Celltrion Healthcare France, 12, Support for attending a congress, Galapagos, 2; **D. Strasser**: Novartis, 3, 11; **s. jousse**: None; **S. Chen**: Novartis, 3; **N. Giglioli**: Novartis, 3, 11; **C. SIPS**: Novartis, 3, 11; **A. SARAUX**: Novartis, 6; **R. Siegel**: Novartis, 3, 11; **W. Hueber**: Novartis, 3, 11; **S. Hillion**: None; **V. Devauchelle**: None; **C. Bonal**: Novartis, 3, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2297

Clinically Relevant Anti-Vaccine and Virus Antibodies in Patients with Sjogren's Disease Treated with Nipocalimab: Post-Hoc Analysis of the DAHLIAS Study

Faye Yu[1], Eugene Myshkin[1], Jonathan J. Hubbard[2], Kim Campbell[2], Matthew Loza[3], Dessislava Dimitrova[2], Carolyn Cuff[1] and Sheng Gao[3], [1]Johnson & Johnson, Cambridge, MA, USA, Cambridge, MA, [2]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [3]Johnson & Johnson, Spring House, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Nipocalimab is a fully human, high affinity, aglycosylated, effectorless IgG1 monoclonal antibody designed to selectively block neonatal fragment crystallizable receptor (FcRn), thereby lowering serum IgG levels. Results from a randomized, open-label vaccine study in healthy volunteers suggest that nipocalimab does not impact the development of IgG responses to T-cell–dependent/–independent vaccines.[1] In the DAHLIAS study (NCT04968912), participants with moderate to severe Sjögren's Disease received nipocalimab 5 mg/kg, 15 mg/kg, or placebo intravenously every 2 weeks for 22 weeks; 15 mg/kg nipocalimab treatment led to significant improvement over placebo in ClinESSDAI (Clinical European League Against Rheumatism Sjögren's Syndrome Disease Activity Index) at 24 weeks and was well-tolerated.[2] Here, we assessed the impact of nipocalimab on pre-existing clinically relevant anti-vaccine antibodies against tetanus toxoid (TT), varicella zoster virus (VZV), and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) spike protein and on the humoral response to SARS-CoV-2 vaccination or infection in DAHLIAS participants.

Methods: Serum IgG antibody levels against TT and VZV were measured at baseline and post-treatment samples in a subset of participants. In participants with documented SARS-CoV-2 vaccination or infection during the study, antibodies against different epitopes of SARS-CoV-2 were measured. Participants with available samples were included in the analysis.

Results: Nipocalimab reduced pre-existing anti-TT and anti-VZV antibodies to a similar extent as total IgG (observed median pre-dose/minimal reduction: ~61%), consistent with its mechanism of action. Anti-TT and anti-VZV antibody levels returned to baseline by Week 30, 8 weeks post-last dose. All participants receiving SARS-CoV-2 vaccination in the 15 mg/kg nipocalimab group (n=2) elicited a humoral response as indicated by increases in anti-spike antibodies, while all participants with SARS-CoV-2 acute infection in the 15 mg/kg nipocalimab group (n=3, 2 mild and 1 moderate, all recovered) had increased levels of anti-spike and anti-nucleocapsid antibodies.

Conclusion: In nipocalimab-treated participants, preexisting anti-TT and anti-VZV antibodies followed a similar pattern as total IgG, consistent with its mechanism of action. Additionally, nipocalimab did not prevent humoral responses to SARS-CoV-2 infection or vaccination in participants with Sjögren's Disease in the DAHLIAS study. These observations suggest that patients treated with nipocalimab can follow recommended vaccination schedules concomitant with nipocalimab treatment as appropriate.

1. Cossu M, et al. *Hum Vaccin Immunother*. 2025;21(1):2491269.
2. Gottenburg J, et al. *Arthritis Rheumatol*. 2024;76(suppl 9).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: F. Yu: Johnson & Johnson, 3, 11; **E. Myshkin**: Johnson & Johnson, 3, 11; **J. Hubbard**: Johnson & Johnson, 3, 11; **K. Campbell**: Johnson & Johnson, 3, 11; **M. Loza**: Johnson & Johnson, 3, 11; **D. Dimitrova**: Johnson & Johnson, 3, 11; **C. Cuff**: Johnson & Johnson, 3, 11; **S. Gao**: Johnson & Johnson, 3, 11.

Abstract Number: 2298

When Imaging and Biopsy Disagree: Diagnostic Value of Doppler Ultrasound and Histologic Features beyond the Focus Score

kyung-Ann Lee[1], Yeonhee Kim[1], Se Hee Kim[2] and Hyun-Sook Kim[3], [1]Soonchunhyang University Hospital Seoul: Soonchunhyang University Hospital, Seoul, Republic of Korea, [2]Kyung Hee University College of Medicine, Seoul, Republic of Korea, [3]Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Salivary gland ultrasound (SGUS) and minor salivary gland biopsy (MSGB) are widely used in the diagnosis of primary Sjögren's syndrome (pSS). However, discordance between these modalities is frequently encountered, raising questions about their respective diagnostic value and the optimal strategy for resolving inconsistencies. This study aimed to investigate the prevalence and diagnostic relevance of discordance between SGUS and MSGB in pSS, and to evaluate whether Doppler ultrasound and histologic markers beyond the focus score provide additional diagnostic value in discordant cases.

Methods: Methods

We retrospectively analyzed 128 patients (91 pSS, 37 non-pSS) who underwent both SGUS and MSGB within 12 months. SGUS was scored using the OMERACT system; grayscale ≥2 in at least one gland was defined as positive. Color Doppler signals were graded 0–3, and both total scores and a binary threshold (≥2 in any gland) were assessed. Patients were categorized into four groups: SGUS+/MSGB+ (Group 1), SGUS+/MSGB– (Group 2), SGUS–/MSGB+ (Group 3), and SGUS–/MSGB– (Group 4). MSGB was evaluated for focus score and additional histologic features (atrophy, fibrosis, ductal dilatation, lymphoepithelial lesions and germinal centers). The final diagnosis of pSS was determined by expert clinical judgment

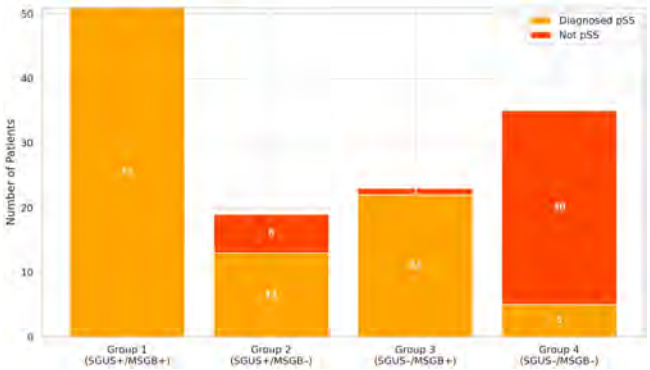


Figure 1. Diagnostic Distribution Across SGUS/MSGB Discordant Groups Bar graph showing the number of patients diagnosed with primary Sjögren's syndrome (pSS) versus not diagnosed, across discordant SGUS/MSGB groups. Group 2: SGUS positive / MSGB negative Group 3: SGUS negative / MSGB positive Group 3 exhibited a significantly higher pSS diagnosis rate (95.7%) compared to Group 2 (68.4%), with an odds ratio (OR) of 10.18 (95% CI: 1.03–100.0, p = 0.047).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

based on comprehensive evaluation, and served as the diagnostic gold standard for this study. Agreement between SGUS and MSGB was assessed using Cohen's kappa. Logistic regression and ROC analysis were performed to evaluate the diagnostic value of Doppler in SGUS-negative patients and of extended histologic markers in MSGB-negative patients.

Results: Among the 128 patients, Group 1 included 51, Group 2 had 19 (13 pSS), Group 3 had 23 (22 pSS), and Group 4 had 35 (5 pSS). The overall discordance rate was 32.8%, and agreement between SGUS and MSGB was fair (κ = 0.334, $p < 0.001$). Among discordant cases, Group 3 (SGUS–/MSGB+) had a significantly higher pSS diagnosis rate than Group 2 (SGUS+/MSGB–) (95.7% vs. 68.4%, OR = 10.15, p = 0.034) (Figure 1), despite no significant differences in age, sex, USFR, or serologic status. In SGUS-negative patients (OMERACT grade 0–1), color Doppler signal showed a trend toward increased odds of pSS diagnosis (aOR = 1.57, p = 0.090), though its discriminatory power was limited (AUC ≈ 0.55). In the MSGB-negative subgroup (n=57), SGUS positivity (aOR = 1.51, p = 0.027) and fibrosis (aOR = 1.18, p = 0.040) were independently associated with pSS diagnosis and had the highest diagnostic performance (AUC = 0.666 and 0.621), whereas color Doppler signal and other extended histologic features showed limited diagnostic utility.

Conclusion: Diagnostic discordance between SGUS and MSGB is common in suspected pSS, with histologic positivity more strongly associated with diagnosis than SGUS findings alone. While OMERACT-based color Doppler ultrasound offered limited additional value in grayscale-negative patients, grayscale SGUS positivity and histologic fibrosis may help support the diagnosis in biopsy-negative cases. No significant clinical differences were found between discordant subgroups.

Disclosure: k. Lee: None; **Y. Kim**: None; **S. Kim**: None; **H. Kim**: None.

Abstract Number: 2299

Real-world clinical effectiveness of rituximab rescue therapy in patients with progressive interstitial lung disease associated with primary sjögren's syndrome

Paula Estrada-Alarcón[1], Delia Reina[2], JUAN JOSE ALEGRE SANCHO[3], Montserrat Roig Kim[4], martí Aguilar-Coll[5], Laia De Daniel Bisbe[4], Aina Fabregat[5], Monica Cubells[5] and Javier Narváez[6], [1]Hospital de San Juan Despí Moisès Broggi, Barcelona, Spain, [2]Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain, [3]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain, [4]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [5]Hospital Universitari de Bellvitge, Barcelona, Spain, [6]Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: To evaluate the real-world, long-term effectiveness of rituximab (RTX) as rescue therapy in patients with primary Sjögren's syndrome-associated interstitial lung disease (pSS-ILD).

Methods: Multicentre observational retrospective longitudinal study of a cohort of pSS-ILD patients who initiated RTX due to progressive or refractory ILD despite treatment with glucocorticoids and conventional immunosuppressants.

Results: To date, 16 patients have been treated with RTX. The main demographic, clinical, functional, serological, and therapeutic characteristics of the entire cohort are summarised in Table 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sex (%, women)	93.75
Age at ILD, diagnosis, mean (SD)	62.69 (10.78)
ILD first; SS after, n (%)	11 (68,75)
Total follow-up; months, median [Q1-Q3]	55.5 [30.3-69.2]
Months between ILD and SjD, median [Q1-Q3]	56.5 [32.8-91.5]
Immunological characteristics:	
ANA positive, n(%)	13 (81.25)
anti-Ro 52, n(%)	8 (50)
anti-Ro 60, n(%)	8 (50)
Rheumathoid factor, n(%)	10 (62.5)
anti-La, n(%)	6 (37.5)
Hypergammaglobulinemia, n(%)	5 (31.25)
Sjögren's disease characteristics	
Raynaud's phenomenon, n (%)	4 (25)
Parotidomegalia, n(%)	2 (12.5)
Arthritis, n (%)	5 (31.25)
Renal disease, n (%)	1 (6.25)
Liver involvement, n (%)	2 (12.5)
ESSDAI, mean (SD)	13.31 (3.88)
ILD basal characteristics:	
Nonspecific interstitial pneumonia (NSIP), n (%)	14 (88)
Combined pulmonary fibrosis and emphysema, n (%)	1 (6)
Lymphoid intersticial pneumonia (LIP), n (%)	1 (6)
Small airway involvement	3 (18.75)
Basal FVC, %; (n = 15); mean (SD)	81.6 (29.29)
Basal DLCO, %; (n=14); mean (SD)	53.07 (15.45)
6 min walking distance, mts (n= 15); mean (SD)	259,73 (134,73)
Oxygen requirement (n = 13)	5 (38.46)
ILD treatment	
GC initial dose, mg; mean (SD)	26.9 (11.8)
Mycophenolate, n (%)	14 (87.5)
Rituximab, cycles; median [Q1-Q3]	2 [1-4]
antifibrotic,n (%)	4 (25)
Lung transplant, n (%)	2 (12.5)
ILD follow-up characteristics:	
Follow-up FVC, %; mean (SD)	82.91 (25.55)
Follow-up DLCO, %; mean (SD)	46.66 (14.10)
6 min walking distance, mts; mean (SD)	328.82 (136.65)
Progresive lung fibrosis criteria	8 (50)
CT follow-up	
Improvement	2 (16.66)
Stable	3 (25)
Worsening	7 (58.88)

The most frequent ILD pattern on high resolution CT-scan was Nonspecific interstitial pneumonia (NSIP) (88%), while lymphoid interstitial pneumonia (LIP) and combined pulmonary fibrosis and emphysema were each observed in one patient (6%). The median follow-up from ILD diagnosis to the last visit was 55.2 months (IQR: 30.3–69.2).

RTX was administered in combination with mycophenolate mofetil (31%), azathioprine (19%), or tacrolimus (13%), while one patient (6%) received RTX as monotherapy. Four patients (25%) were treated concurrently with antifibrotic agents (nintedanib, n=3; pirfenidone, n=1).

At last follow-up, 7 patients (44%) remained on RTX. Treatment was discontinued in 9 patients (56%) due to lack of efficacy (n=3; 19%), death (n=3; 19%), lung transplantation (n=2; 13%), or adverse events (n=1; 6%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Among patients who continued RTX, mean declines in %FVC and %DLCO from ILD diagnosis to RTX initiation were –11.7% and –11.4%, respectively, followed by mean improvements of +7.8% (FVC) and +6.3% (DLCO) from RTX initiation to the last available follow-up. However, these improvements did not reach statistical significance (p=0.31 for FVC; p=0.34 for DLCO). Adverse events were reported in 5 patients (31%), mostly consisting of non-severe infections.

Conclusion: RTX achieved stabilisation or improvement in only 44% of patients, indicating limited overall effectiveness and underscoring the need for more effective therapeutic strategies in progressive pSS-ILD.

Disclosure: P. Estrada-Alarcón: None; **D. Reina**: None; **J. ALEGRE SANCHO**: None; **M. Roig Kim**: None; **m. Aguilar-Coll**: None; **L. De Daniel Bisbe**: None; **A. Fabregat**: None; **M. Cubells**: None; **J. Narváez**: None.

Abstract Number: 2300

Evaluation of the Ianalumab Treatment Effects on Major Salivary Glands of Patients With Sjögren's Disease by Multimodal Ultrasound: Results From a Phase 2 Mechanistic Study

sandrine jousse[1], Valerie Devauchelle[2], baptiste quere[1], Divi Cornec[3], Caroline Denis[4], Thierry MARHADOUR[1], Alice Tison[1], Patricia Baley[4], Alain SARAUX[5], Noemi Giglioli[6], CAROLE SIPS[6], Shuqi Chen[7], Rainer Hillenbrand[6], Richard Siegel[8], Wolfgang Hueber[9], Claire Bonal[6] and Didier Laurent[6], [1]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, France, [2]UBO, Brest, France, [3]LBAI, UMR1227, University of Brest, CHU Brest, Brest, France, Brest, Bretagne, France, [4]CHU Brest, Brest, France, Brest, France, [5]CHU Brest, Brest, France, [6]Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland, [7]China Novartis Institutes for BioMedical Research, Shanghai, China, Shangai, China (People's Republic), [8]Novartis Biomedical Research, Basel, Switzerland, [9]Novartis Pharmaceuticals, Basel, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Ianalumab, a glycoengineered, fully human IgG1 mAb directed against B cell-activating factor (BAFF)-receptor (BAFF-R), targets B cells and their functions through dual mechanism of action: depletion of B cells through enhanced antibody-dependent cellular cytotoxicity and blockade of BAFF:BAFF-R–mediated signals. Here we present a

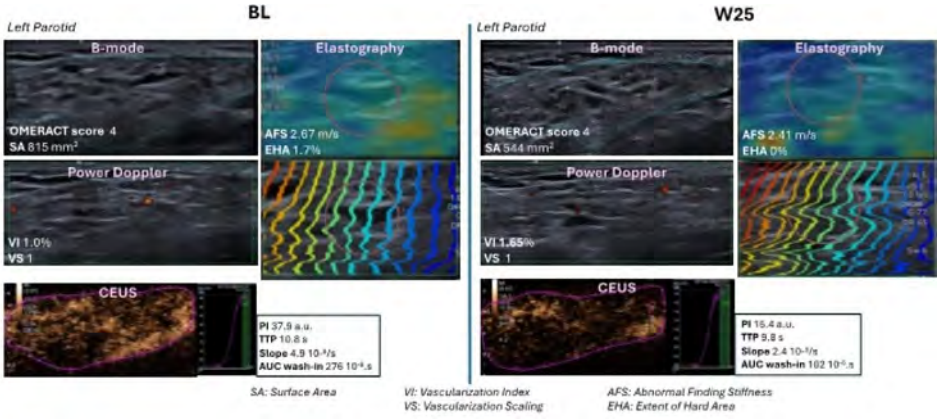


Figure 1. Multimodal SGUS from a single patient at BL and W25

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Mean (SD) SGUS parameters at BL and W25

Parameters		Baseline	W25
B-mode	OMERACT Score (0-4) PGs	2.53 (1.053)	2.12 (1.153)
	OMERACT Score (0-4) SMGs	2.24 (1.120)	2.00 (1.275)
	Surface Area (mm2) PGs	632 (143)	587 (166)
	Surface Area (mm2) SMGs	226 (75)	199 (65)
Doppler	Vascularization Index (%) PGs	2.86 (3.808)	1.34 (1.132)
	Vascularization Index (%) SMGs	5.44 (4.834)	4.13 (2.821)
	Vascularization Scaling (0-3) PGs	1.03 (0.672)	0.76 (0.752)
	Vascularization Scaling (0-3) SMGs	0.74 (1.017)	0.50 (0.771)
Stiffness	Stiffness Of Abnormal Finding (m/sec) PGs	2.55 (0.405)	2.45 (0.264)
	Stiffness Of Abnormal Finding (m/sec) SMGs	2.06 (0.358)	2.09 (0.424)
	Relative Hard Area (%) PGs	5.37 (8.740)	3.04 (4.569)
	Relative Hard Area (%) SMGs	0.99 (3.008)	1.08 (2.385)

PGs: Parotid glands; SMGs: Submandibular glands

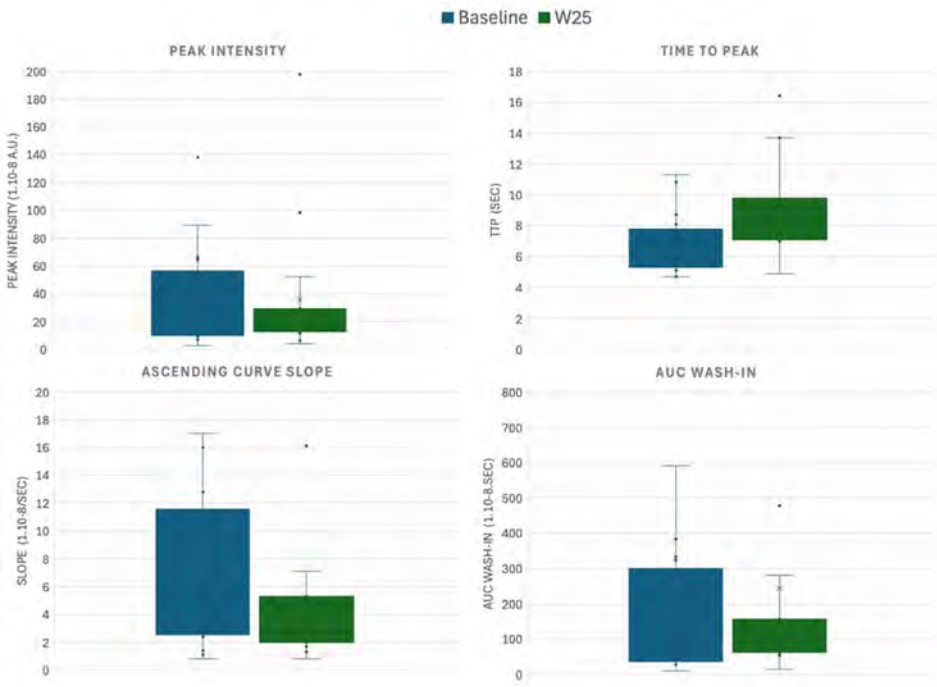


Figure 2. Left parotid CEUS parameters at BL and W25

multi-modal ultrasound (US) assessment of major salivary glands (SG) to better understand the mode of action of ianalumab on parotid (PGs) and submandibular glands (SMGs) in patients with Sjögren's disease (SjD).

Methods: This is an open-label, single-center, non-randomized, phase 2 mechanistic study (NCT05124925) with a 5-week screening period, a 6-month treatment period, and a follow up period of up to 2 years after the last dose. Eligible participants included those who fulfilled the 2016 ACR/EULAR classification criteria for SjD with anti-Ro/SSA autoantibodies, EULAR Sjögren's Syndrome Patient Reported Index score of ≥5, labial SG focus score (FS) of ≥0.3/4mm2, and B/B+T cell ratio of ≥0.2 at screening. This interim analysis reports the results of patients who completed the 24-week treatment period (ianalumab 300 mg monthly subcutaneous injection). As secondary outcome of the study, multimodal US assessment of major SGs was evaluated at W25 compared with BL. PGs and SMGs were assessed individually and analyzed by pairs for the following SGUS parameters: 1) B-mode (size and OMERACT score[1]), 2) Power Doppler (macrovascularization scaling and index), 3) contrast-enhanced US (CEUS) (microvascularization parameters derived from microbubbles injection for PGs only) and 4) sonoelastography (stiffness).

Results: In the safety analysis set (N=21), ianalumab was well-tolerated with no drug-related serious adverse events (AEs) and one AE leading to discontinuation. SGUS assessment and contrast agent administration were well tolerated. Overall, 17 participants completed the 24-week open-label treatment, underwent paired screening and W25 labial SG biopsy, and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

were analyzed. **Figure 1** displays multimodal SGUS acquisitions from a single patient pre and post treatment. Overall, BL SGUS features indicated moderate glandular involvement, with mean OMERACT scores of 2.53 and 2.24, and Doppler Vascularization Scaling of 1.03 and 0.74, in PGs and SMGs, respectively (**Table 1**). At W25, B-mode, Doppler and CEUS vascularization and elastography stiffness parameters numerically decreased, and to a larger extent in the PGs compared with SMGs (**Table 1**). Notably, the mean OMERACT score reduced by -0.41 and -0.24, and the mean Doppler Scaling reduced by -0.26 and -0.24, in PGs and SMGs, respectively. The reduction in tissue perfusion was further supported by CEUS measurements derived from the time intensity curve observed in response to the microbubble injection, as shown for the left PGs in **Figure 2**.

Conclusion: Patients treated with ianalumab 300 mg monthly showed improvement in PGs structure and vascularization at W25 vs BL using multimodal ultrasound assessment. Innovative measures with CEUS display a good sensitivity to change after treatment and should be considered in future clinical trials.

Reference

1. Jousse-Joulin et al. Ann Rheum Dis. 2019;78:967-973

Disclosure: s. jousse: None; **V. Devauchelle**: None; **b. quere**: AbbVie, 2, 6, Alfasigma, 6, Eli Lilly, 6; **D. Cornec**: None; **C. Denis**: None; **T. MARHADOUR**: None; **A. Tison**: Celltrion Healthcare France, 12, Support for attending a congress, Galapagos, 2; **P. Baley**: None; **A. SARAUX**: Novartis, 6; **N. Giglioli**: Novartis, 3, 11; **C. SIPS**: Novartis, 3, 11; **S. Chen**: Novartis, 3; **R. Hillenbrand**: Novartis, 3, 11; **R. Siegel**: Novartis, 3, 11; **W. Hueber**: Novartis, 3, 11; **C. Bonal**: Novartis, 3, 11; **D. Laurent**: Novartis, 3, 11.

Abstract Number: 2301

Use of lived experiences in childhood Sjogren Disease to develop outcome measures for an N-of-1 treatment trial

Sara M. Stern[1], Angela Merritt[2], Ludovic Trinquart[3], Emma Barnboym[4], Michelle LeeBravatti[3], Suzy Richins[5], Tressie L. Rollins[5], Hanna M. Salzman[5], Marisha Palm[3], Cortney M. Wieber[6], Hermine Brunner[7] and Nora G. Singer[8], [1]University of Utah, Salt Lake City, UT, [2]Cincinnati Childrens Hospital Medical Center, Cincinnati, OH, [3]Tufts University School of Medicine, Boston, MA, [4]The MetroHealth System at Case Western Reserve University School of Medcine, Cleveland, OH, [5]Pediatric Rheumatology, University of Utah, Salt Lake City, UT, [6]Institute for Clinical Research and Health Policy Studies (ICRHPS) and CTSI, Tufts School of Medicine, Boston, MA, [7]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]The MetroHealth System at Case Western Reserve University School of Medicine, Cleveland, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Childhood Sjogren Disease (cSjD) is a rare disease that presents with a wide variety of symptoms. Compared to adult SjD, cSjD more frequently manifests with parotitis and glandular swelling. Despite causing marked morbidity and mortality, no treatments are currently approved for cSjD. In this work, we develop a personalized N-of-1 design to compare cSjD therapies. Our innovative design generates patient-level randomized evidence to inform individualized treatment decision and allows for evaluation of comparative effectiveness between drugs when aggregating data across participants. Moreover, to capture the full spectrum of the treatment effects on the multiple cSjD manifestations, we incorporate patient-prioritized outcomes in the design. The purpose of this abstract is to perform item development and reduction as

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the next step to development of patient-focused outcome measures. Here, we present the tools we developed to elicit from patients how they rank outcome measures by importance.

Methods: To design surveys for patients, caregivers, and providers about cSjD symptoms, we systematically reviewed the literature to delineate common signs and symptoms of cSjD and to ensure we were not missing any major symptoms (item generation). We then compared this list to the ESSDAI, a validated outcome measure for adult SjD, which includes signs and a wide variety of symptoms, but does not emphasize those glandular features that are more prominent in cSjD. The resulting cSjD symptom survey was reviewed by research professionals and a patient/parent dyad engaged as research partners.

Results: The survey uses the Q-methodology that asks participants to sort 10 symptom domains in relation to each other according to a predetermined distribution. Participants can adjust their ranking until they are satisfied with the ordering of symptoms by importance. The Q-sort will be distributed to an online cSjD group that is validated by the parent of a cSjD patient and contains > 250 parents of children with cSjD and will also be disseminated via the Childhood Arthritis and Rheumatology Research Alliance (CARRA) which champions collaborative research to prevent, treat, and cure pediatric rheumatic disease. After two survey rounds, responses will be adjudicated at an in-person meeting to reach consensus on endpoint prioritization. Administration of the surveys and consensus meetings will be compliant with the Declaration of Helsinki.

Conclusion: An N-of-1 trial of two therapeutic agents will use these prioritized outcome measures to determine the efficacy of both agents with each patient serving as their own control. Data will be aggregated to determine if one or both agents meet the primary outcome, using either each personalized prioritized endpoint or the consensus-derived hierarchical endpoint. The trial will serve as a platform to evaluate additional agents in cSjD and other rare childhood rheumatic diseases.

Disclosure: S. Stern: None; **A. Merritt**: None; **L. Trinquart**: None; **E. Barnboym**: None; **M. LeeBravatti**: None; **S. Richins**: None; **T. Rollins**: None; **H. Salzman**: None; **M. Palm**: None; **C. Wieber**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **N. Singer**: None.

Abstract Number: 2302

Clustering by ESSPRI and PROMIS domain measures defines distinct subtypes and facilitates longitudinal assessment of patients with Sjogren's disease

Thomas Grader-Beck[1], Jennifer Reed[2], Priya Patel[3], Ji Soo Kim[4] and Alan Baer[5], [1]Johns Hopkins, Reisterstown, MD, [2]Johns Hopkins, Freeland, MD, [3]Johns Hopkins, Annville, PA, [4]Johns Hopkins, Baltimore, MD, [5]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics in clusters of patients with Sjogren's disease. 1 Adjusted n to account for missing data. 2 Ever present. Abbreviations: LSHF (low symptoms/high function), HSBF (high symptoms/balanced function), MSBF (moderate symptoms, balanced function), HSPF (high symptoms/poor function

Variable	Overall	Cluster 1	Cluster 2	Cluster 3	Cluster 4	P-Value
Name		LSHF	HSBF	MSBF	HSPF	
n	467	77	130	116	144	
Age at baseline, mean (SD)	55.7 (13.9)	56.4 (14.2)	56.0 (14.5)	54.9 (14.3)	55.7 (13.1)	0.549
Sex, n (%)						0.137
Female	429 (91.9)	66 (85.7)	123 (94.6)	106 (91.4)	134 (93.1)	
Male	38 (8.1)	11 (14.3)	7 (5.4)	10 (8.6)	10 (6.9)	
Race, n (%)						0.433
White	358 (76.7)	53 (68.8)	105 (80.8)	91 (78.4)	109 (75.7)	
Black	64 (13.7)	14 (18.2)	19 (14.6)	13 (11.2)	18 (12.5)	
Asian	25 (5.4)	5 (6.5)	4 (3.1)	7 (6.0)	9 (6.2)	
Other	20 (4.3)	5 (6.5)	2 (1.5)	5 (4.3)	8 (5.6)	
Positive Lip Biopsy[2], n (%)	73/119[1] (61.3)	12 (63.2)	23 (65.7)	19 (61.3)	19 (55.9)	0.865
Positive Anti-Ro/SSA[2], n (%)	438/461[1] (95.0)	74 (97.4)	118 (93.7)	111 (95.7)	135 (94.4)	0.698
Abnormal Schirmer[2], n (%)	353/444[1] (79.5)	64 (84.2)	102 (85.7)	92 (80.7)	95 (70.4)	0.012
Abnormal OSS[2], n (%)	151/232[1] (65.1)	30 (71.4)	38 (62.3)	30 (54.5)	53 (71.6)	0.169
Abnormal UWSF[2], n (%)	234/361[1] (64.8)	29 (49.2)	75 (71.4)	52 (59.1)	78 (71.6)	0.008
Positive RF[2], n (%)	358/397[1] (90.2)	63 (92.6)	99 (90.0)	90 (88.2)	106 (90.6)	0.818
Hypergammaglobulinemia[2] n (%)	175/452[1] (38.7)	34 (44.7)	51 (40.8)	50 (45.0)	40 (28.6)	0.025
C4 hypocomplementemia[2], n (%)	67/434[1] (15.4)	12 (16.9)	20 (16.5)	16 (14.5)	19 (14.4)	0.939
DMARD exposure[2], n (%)	322 (69.0)	49 (63.6)	93 (71.5)	85 (73.3)	95 (66.0)	0.387

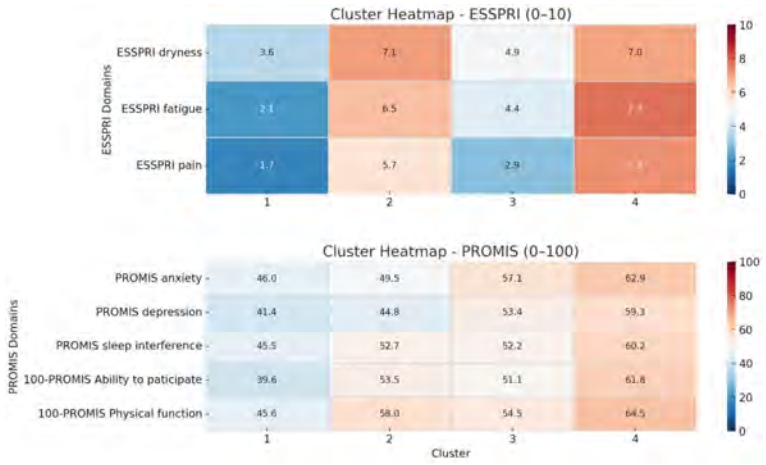


Figure 1:Heatmap of clusters 1-4. Average values of each PRO measure are shown. PROMIS Ability to Participate and Physical Function values are subtracted from 100 to reflect reverse significance.

Background/Purpose: Patient-reported outcomes (PROs) measure a patient's health-related quality of life. The role of ESSPRI and PROMIS measures in identifying subsets of patients with Sjogren's disease is not established and longitudinal stability of these measures has not been assessed. This study uses PRO-based clustering to define distinct patient populations and measure cluster attribution in individual patients over time.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

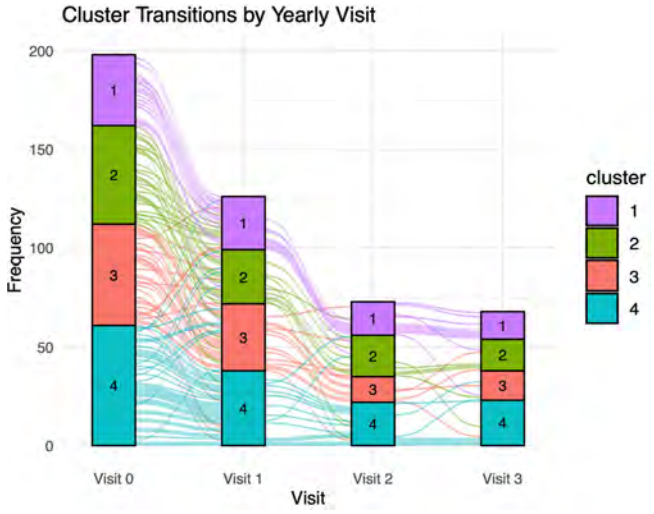


Figure 2: Alluvial plot demonstrating cluster attribution of individual patients over time.

Methods: Data from 467 patients meeting ACR2016 criteria for Sjogren's disease with at least 1 complete set of PRO data (ESSPRI Dryness/Fatigue and Pain and PROMIS Physical function/Ability to participate/Sleep Interference/Anxiety and Depression) were extracted from the Epic Electronic Health Record system. Baseline Clustering was completed using k-means clustering algorithm. For longitudinal analysis, an alluvial plot of 198 patients with at least two visits with complete PRO data was created to visualize transitions of patients between clusters. Statistical analysis between clusters was done using ANOVA, Chi-squared, and Fisher's exact tests.

Results: K-means algorithm identified 4 clusters of patients at baseline: cluster 1 (77/467; 16.5%), Low symptoms/high function (LSHF), cluster 2 (130/467; 27.8%), High symptoms/balanced function (HSBF), cluster 3 (116/467; 24.8%), Moderate symptoms/balanced function (MSBF), and cluster 4 (144/467; 30.8%), High symptoms/poor function (HSPF) (Figure 1). Demographic variables, including age, sex, and race, anti-SSA/Ro positivity, disease phenotypic markers and DMARD exposure did not differ between clusters (Table 1). Abnormal salivary flow was least frequent in the LSHF cluster (29/77; *p=0.008* by Chi-squared test). Abnormal Schirmer's and hypergammaglobulinemia were least frequent in the HSPF cluster (95/144;70.4% *p=0.012* and 40/144; 28.6% *p=0.025* by Chi-squared test, respectively). Longitudinal analysis of cluster stability in 198 patients over 2 to 4 visits demonstrated that most patients (54.0%) remained in the same cluster over time (Figure 2). Transitions between extreme clusters (LSHF and HSBF) were significantly less frequent than other transitions (3/35 vs 93/96; $p< 1X10^{22}$, Fisher's exact test).

Conclusion: ESSPRI and PROMIS measures define distinct clusters in patients with Sjogren's disease. Cluster attribution of individual patients remains relatively stable over time and changes between extreme clusters is rare. Prospective studies are needed to further define the relationship between cluster stability, disease flares and response to therapy.

Disclosure: T. Grader-Beck: Argenx, 5, 12, Consulting fees, Bristol-Myers Squibb(BMS), 5, 12, Consulting fees, Novartis, 5, 12, Consulting fees; **J. Reed**: None; **P. Patel**: None; **J. Kim**: None; **A. Baer**: Bristol-Myers Squibb(BMS), 2.

Abstract Number: 2303

Metabolic impact of low dose IL-2 therapy for primary Sjögren's Disease in a double-blind, randomized clinical trial

Ruiling Feng, Bo Huang and **Yuebo Jin**, Peking University People's Hospital, Beijing, China (People's Republic)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

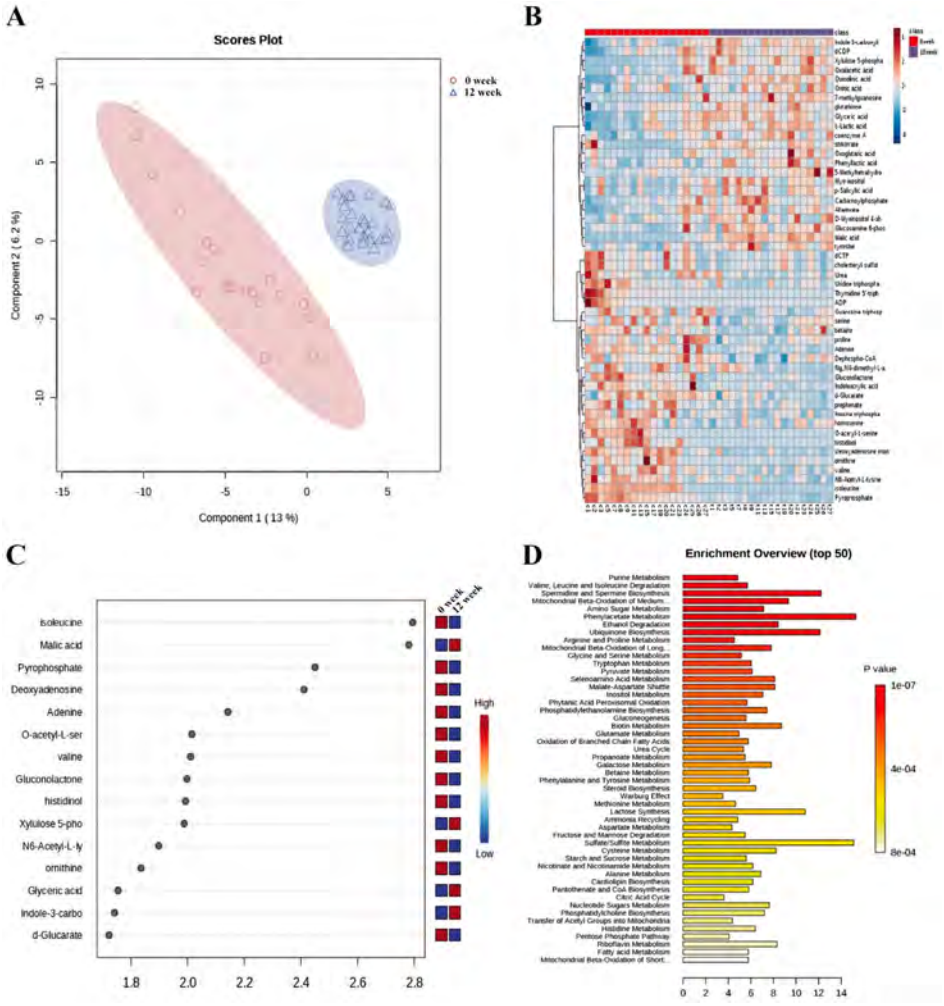
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Low-dose interleukin 2 (Ld-IL2) is increasingly being explored as an immune-modulating treatment for autoimmune diseases which mainly affect T cell subsets. This study investigates the metabolic effects of Ld-IL2 therapy in patients with primary Sjögren's disease (pSjD).

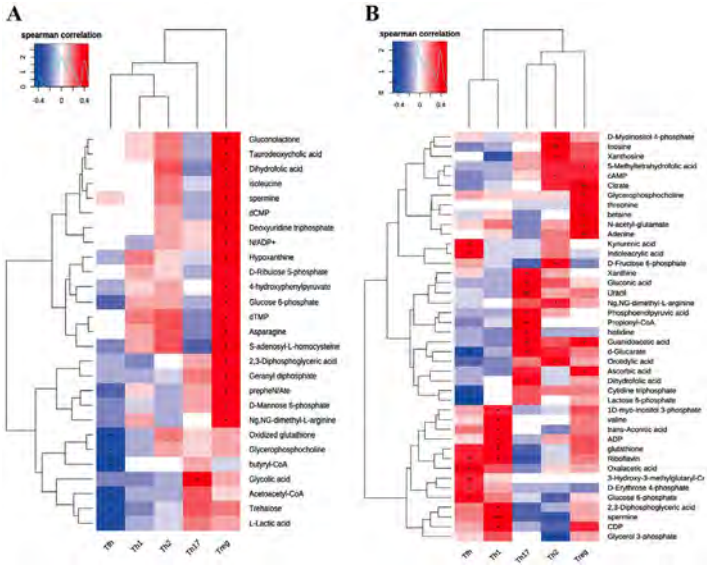
Methods: A total of 60 patients were recruited to conduct a double-blind, randomized clinical trial. Of these patients, 50% (30/60) received Ld-IL2 therapy along with standard treatment for 12 weeks, followed by 12 weeks of follow-up. The effectiveness was evaluated by Sjögren's Tool for Assessing Response (STAR). An untargeted analysis was performed to profile hydrophilic metabolites.

Results: Metabolic profiling revealed significant alterations post-treatment, notably in metabolites like acetyl-CoA, ascorbic acid, and glutathione, which are beneficial in managing autoimmune diseases. In addition, the levels of metabolite accumulation were correlated with variations in immune cell subsets ($p < 0.05$), particularly Tregs. Moreover, patients exhibiting a

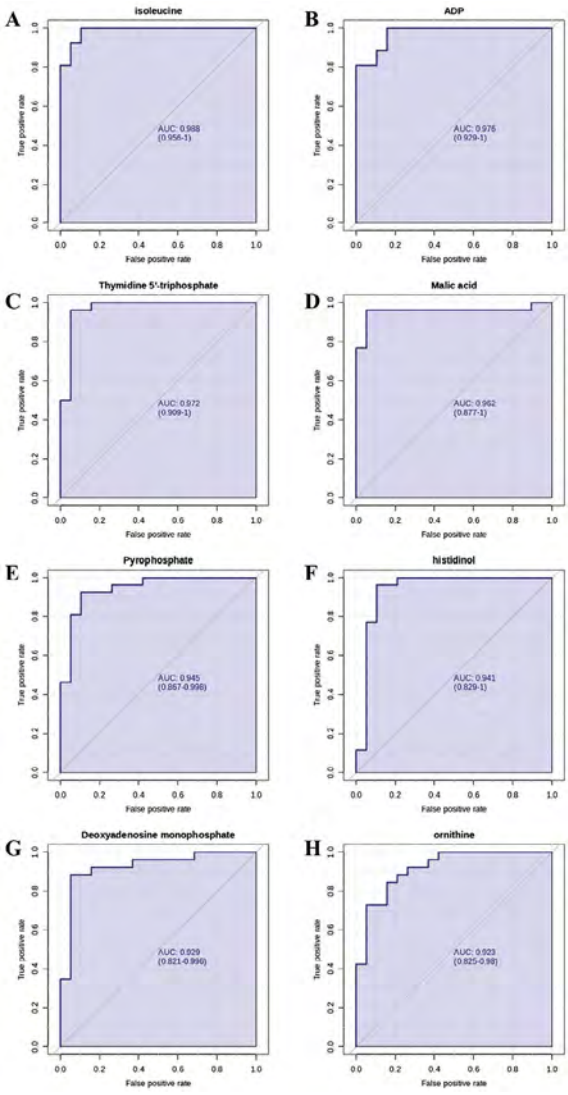


Impact of Ld-IL2 on serum metabolites from pSjD patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Association between metabolites and CD4+T cells.



Metabolites Biomarker Identification for Ld-IL2 Treatment Response.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

specific metabolic profile, including lower serum levels of isoleucine, ADP, Thymidine 5'-triphosphate, and other metabolites, had a high response rate (91.7%-98.6%), as indicated by the receiver operating characteristic (ROC) curve.

Conclusion: These findings suggest that Ld-IL2 therapy influences metabolic pathways in pSjD, offering insights into the systemic effects of Ld-IL2 therapy beyond immune modulation.

Disclosure: R. Feng: None; **B. Huang**: None; **Y. Jin**: None.

Abstract Number: 2304

Updates in the local treatments in Primary Sjögren's Syndrome "Efficacy and Safety"

Marta Ramírez[1], Maryia Nikitsina[2], Rym Abadi[3] and David A. Isenberg[4], [1]Univeristy Hospital Principe de Asturias, MADRID, Madrid, Spain, [2]University Hospital La Princesa, Madrid, Madrid, Madrid, Spain, [3]University College London, London, UK, London, England, United Kingdom, [4]University College London, London, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2290–2304) Sjögren's Disease – Basic & Clinical Science Poster III: Treatment and Trial Outcome Measures
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease characterised by lymphocytic infiltration of exocrine glands, leading to sicca symptoms that severely impact quality of life. While systemic immunomodulatory therapies continue to evolve, local treatments remain the mainstay for symptom relief. This systematic literature review evaluated the efficacy and safety of currently available and emerging local interventions for dryness in ocular, oral, and other mucosal domains in pSS.

Methods: A systematic search was conducted across PubMed, Ovid Medline, and the Cochrane Library from 2010 to 2024. Eligible studies included randomised clinical trials, systematic reviews, and meta-analyses assessing local therapies for dryness symptoms in adult patients diagnosed with pSS according to 2016 ACR/EULAR criteria. Studies were screened based on pre-defined inclusion criteria, with a minimum sample size of 10 participants. Outcomes included both subjective symptom scores and objective measures of glandular function.

Results: Assessing a total of 44 trials of xeropthalmia it was evident that sodium hyaluronate with trehalose, lipid-based drops showed superior efficacy over standard artificial tears. Topical cyclosporine A, tacrolimus, and low-potency corticosteroids were effective in moderate to severe cases, while biologic tear substitutes (e.g., autologous for ocular dryness serum, PRP) demonstrated potential in refractory disease. Novel agents such as lifitegrast, diquafosol, and lacritin reported favourable results with minimal adverse effects. In the management of xerostomia, pilocarpine and cevimeline improved salivary output (pilocarpine concentrations significantly increased whole salivary flow compared to placebo ($p < 0.01$)) and symptom perception (but were limited by systemic adverse effects. Non-pharmacologic approaches—including xylitol-based lozenges, malic acid tablets, mentholated gum, and intraoral electrostimulation devices—proved beneficial in selected patients with residual gland function. Saliva substitutes, while safe, provided only short-lived relief and were often limited by palatability or low adherence. For dryness in other mucosal domains (nasal, vaginal, pharyngeal), evidence remains sparse and largely empirical.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Local therapies remain a cornerstone in the management of sicca symptoms in pSS, particularly given the limited access to systemic immunomodulatory drugs. While several interventions demonstrated promising efficacy and safety profiles, most evidence was derived from small, heterogeneous studies. Further research is needed to establish standardised outcome measures, clarify long-term benefits, and guide personalised therapeutic strategies.

Disclosure: M. Ramírez: None; **M. Nikitsina**: None; **R. Abadi**: None; **D. A. Isenberg**: None.

Abstract Number: 2305

Predictors of Hospitalization and Emergency Department Visits Among Patients with Psoriatic Disease: Insights from the Forward Psoriasis Registry

Alexis Ogdie[1], Ellen Romich[2], Brian Coburn[3], Rebecca Schumacher[4] and Kaleb Michaud[5], [1]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [2]University of Pennsylvania, Media, PA, [3]Hospital of the University of Pennsylvania, Philadelphia, PA, [4]FORWARD, The National Databank for Rheumatic Diseases, Wichita, KS, [5]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Baseline Characteristics

Table 1. Baseline characteristics (N=1,354 patients)

Demographics	Age	51 (SD 15.8)
	Female	890 (66%)
	Northeast	124 (9%)
	Midwest	216 (16%)
	South	755 (56%)
	West	252 (19%)
	Puerto Rico	2 (0%)
Body surface area by PREPI*	Minimal (<1%)	312 (23%)
	Mild (1-2%)	546 (40%)
	Moderate (3-10%)	400 (30%)
	Severe (>10%)	85 (6%)
Comorbidities	PsA	407 (30%)
	Obesity	445 (33%)
	Hypertension	470 (35%)
	Depression	479 (35%)
	Anxiety	578 (43%)
	Obstructive Sleep Apnea	209 (15%)
	Asthma	211 (16%)
	Cancer	147 (11%)
	ADHD	148 (11%)
Psoriasis type	Guttate	330 (24%)
	Inverse	238 (18%)
	Pustular	84 (6%)
Current therapies	TNFi	105 (8%)
	IL17i	108 (8%)
	IL23i	221 (16%)
	JAKi	17 (1%)
	NSAID	303 (22%)
	Opioid	34 (3%)
	Glucocorticoid	66 (5%)
	Antidepressant	376 (28%)
	Statin	257 (19%)
Patient reported outcomes	PROMIS Mental Health T score (0-100)	48.3 (SD 9.4)
	PROMIS Physical Health T score (0-100)	47.9 (SD 8.4)
	PROMIS Sleep Disturbance T score (0-100)	50 (SD 8.3)
	Patient Pain (0-10)	2.7 (SD 2.7)
	Psoriasis Symptoms and Signs Diary (PSSD, 0-100)	27.7 (SD 26)

***Abbreviations**: PREPI = Patient Report of Extent of Psoriasis Involvement; PROMIS = Patient Reported Outcome Measure Information System*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Univariable and multivariable models

Table 2. Univariable and multivariable models for ED visits and Hospitalization				
	Emergency Room Visit (N=135)		Hospitalization (N=59)	
	Univariable	Multivariable	Univariable	Multivariable
Age	0.99 (0.98 - 0.99)	0.99 (0.98 - 0.99)	0.99 (0.98 - 0.99)	0.99 (0.98 - 0.99)
Sex	1.03 (0.92 - 1.15)	1.14 (1.01 - 1.29)	1.07 (0.96 - 1.20)	1.21 (1.07 - 1.36)
BMI	0.99 (0.98 – 1.00)		0.99 (0.98 – 1.00)	
Obese (binary)	0.90 (0.8 – 1.00)		0.86 (0.77 - 0.96)	
Psoriatic arthritis	1.00 (0.89 - 1.13)		1.02 (0.91 - 1.15)	
Body surface area				
Minimal (<1%)	REF		REF	
Mild (1-2%)	1.16 (1.01 - 1.34)	1.07 (0.92 - 1.24)	1.17 (1.02 - 1.35)	1.06 (0.91 - 1.23)
Moderate (3-10%)	1.26 (1.08 - 1.46)	1.12 (0.94 - 1.33)	1.22 (1.06 - 1.42)	1.05 (0.88 - 1.24)
Severe (>10%)	1.19 (0.93 - 1.51)	1.01 (0.77 - 1.31)	1.18 (0.93 - 1.5)	0.97 (0.74 - 1.27)
Current therapy				
JAKi	2.05 (1.3 - 3.22)		2.16 (1.37 - 3.41)	
IL23i	0.91 (0.79 - 1.05)		0.95 (0.82 - 1.10)	
IL17i	1.08 (0.89 - 1.31)		1.05 (0.87 - 1.28)	
TNFi	1.41 (1.16 - 1.72)		1.45 (1.19 - 1.76)	
Apremilast	0.84 (0.68 - 1.04)		0.83 (0.67 - 1.03)	
Opioid	1.22 (0.86 - 1.73)		1.22 (0.86 - 1.74)	
Glucocorticoid	1.30 (1.01 - 1.68)		1.34 (1.04 - 1.73)	
NSAID	1.05 (0.9 - 1.22)		1.03 (0.88 - 1.2)	
Topical	1.03 (0.92 - 1.14)		1.00 (0.89 - 1.11)	
Biologic/tsDMARD experienced	1.16 (1.02 - 1.32)		1.19 (1.05 - 1.35)	
Patient reported outcomes				
PROMIS Sleep Disturbance	1.01 (1.01 - 1.02)		1.01 (1.01 - 1.02)	
PROMIS10 Mental Health Score	0.99 (0.98 - 0.99)		0.99 (0.98 - 0.99)	
PROMIS10 Physical Health	0.99 (0.98 - 0.99)		0.99 (0.98 - 0.99)	
Patient Pain	1.04 (1.02 - 1.06)		1.05 (1.03 - 1.07)	
PEST	0.99 (0.96 - 1.03)		1.00 (0.96 - 1.03)	
DLQI	1.04 (1.02 - 1.05)		1.04 (1.02 - 1.05)	
PSSD	1.01 (1.00 - 1.01)	1.01 (1.00 - 1.01)	1.01 (1.00 - 1.01)	1.01 (1.00 - 1.01)
Treatment satisfaction	1.07 (1.02 - 1.12)		1.06 (1.02 - 1.11)	
Health Satisfaction	1.08 (1.03 - 1.14)		1.08 (1.03 - 1.13)	
Comorbidities				
Depression	1.18 (1.05 - 1.32)	1.13 (1.00 - 1.28)	1.17 (1.05 - 1.31)	1.14 (1.01 - 1.28)
Anxiety	1.17 (1.05 - 1.3)		1.14 (1.02 - 1.27)	
ADHD	1.25 (1.05 - 1.48)		1.27 (1.07 - 1.51)	
Hypertension	0.86 (0.77 - 0.96)		0.85 (0.76 - 0.95)	

Background/Purpose: Patients with psoriasis and psoriatic arthritis (PsA) are at increased risk for metabolic comorbidities and poorer long-term outcomes compared to the general population. Identifying patients at risk for adverse outcomes can facilitate targeted interventions to improve quality of life.This study aimed to evaluate the risk of hospitalization and emergency department (ED) visits among adults with psoriatic disease and identify predictors of these outcomes.

Methods: We utilized data from the Forward Psoriasis Registry, a cohort recruited from U.S. dermatology practices, two academic institutions, and the Forward registry website. Participants enrolled between August 2023 and March 2025 completed baseline and monthly surveys, with longer assessments every six months. Surveys included comorbidity data, psoriasis severity (measured by the Patient Report of Extent of Psoriasis Involvement [PREPI]), patient-reported outcomes (Psoriasis Symptoms and Signs Diary [PSSD]), medication changes, and adverse events, including hospitalization and ED visits. Participants with psoriasis (with or without PsA) who completed enrollment and had at least one follow-up visit were included. We report baseline demographics, disease characteristics, treatments, and comorbidities. Cox proportional hazards models were used to identify predictors of hospitalization and ED visits, with a multivariable model developed using purposeful selection modeling.

Results: ong 2,606 enrollees, 1,354 had at least one follow-up visit, with a mean follow-up time of 213 days (SD 145). The cohort had a mean age of 51 years (SD 16), 66% were female, and 56% were from the southern United States. Most had mild to moderate psoriasis (23% with < 1% BSA, 40% with 1-2% BSA, 30% with 3-10% BSA, and 6% with >10% BSA). A total of 135 participants experienced an ED visit (incidence 0.18 per person-year), and 59 were hospitalized (incidence 0.08 per person-year). Predictors of ED visits and hospitalization were similar. Lower psoriasis severity (< 1% BSA) was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

associated with the lowest risk for both outcomes. Higher PSSD scores, depression, and female sex were significantly associated with increased risk. Although a diagnosis of ADHD was initially significant, it was removed from the final model due to lack of consistency.

Conclusion: In this cohort with psoriatic disease, predictors of hospitalization and ED visits included higher PSSD scores, depression, and female sex. The PSSD, a patient-reported outcome, demonstrated predictive value beyond the psoriasis severity measured by body surface area, underscoring the importance of patient-reported outcomes in assessing disease impact.

Disclosure: A. Ogdie: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **E. Romich**: Lungpacer Medical, Inc., 11, Teva Pharmaceuticals, 12, Spouse employment; **B. Coburn**: None; **R. Schumacher**: None; **K. Michaud**: None.

Abstract Number: 2306

Prevalence and Clinical Significance of the Gastrointestinal Fat Halo Sign in Patients with Psoriatic Arthritis: A Cross-Sectional Study

Amir Haddad[1], Kathrien Mousa[1], Kateryna Milman[1], Najwan Nassrallah[1], Devy Zisman[2] and Sharbell Hashoul[3], [1]Carmel Medical Centre, Haifa, Israel, [2]Carmel Medical Center, Haifa, Israel, [3]The Faculty of Humanities and Social Sciences. Uno Academic College, Haifa, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

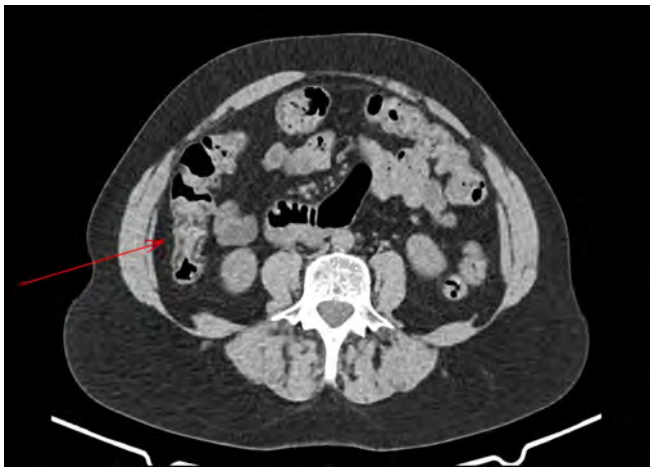
Background/Purpose: The existence of a gut-joint axis is widely described in spondyloarthritis, linking intestinal dysbiosis, subclinical gut inflammation, and arthritis. The fat halo sign is believed to arise from chronic inflammation, leading to transmural edema and infiltration of the bowel wall by inflammatory cells and fat. This radiologic finding has a high prevalence in patients with inflammatory bowel disease(IBD). This study aims to define the prevalence of the fat halo sign in a well-defined cohort of patients with psoriatic arthritis (PsA) and assess its potential clinical significance.

Methods: This is a cross-sectional study involving PsA patients followed prospectively from a collaborative site of an international cohort. All patients fulfilled the CASPAR criteria. Patients who have undergone routine abdominal CT scan for various clinical indications constituted the study population. Two radiologists have independently recorded the presence of the fat halo sign in the stomach, terminal ileum, and the ascending/transverse/descending colon and rectum. Demographics and disease characteristics of patients with positive fat halo were compared to patients without fat halo using descriptive statistics as appropriate.

Results: Of the 328 patients followed, 101 completed an abdominal CT scan. The mean age was 63.7±15 of whom 49 (48.5%) were males with a disease duration of 8.4±8.7 years, 19% on non-steroidal anti-inflammatory drugs, 55% were on disease-modifying anti-rheumatic drugs and 57% were on biologics. 3.9% had a history of IBD, and 4.2% had a history of uveitis. 38/101 (37.6%) patients had a positive halo sign in at least one section (as illustrated in Figures 1 and 2). The presence of halo sign was more common in males (65.8 vs. 31.8%, p=0.007) and more likely in patients with nail lesions (31.6 vs 15.9%, p=0.06). Other patient's demographic and disease characteristics, disease activity parameters and treatment regimen were not statistically different.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Contrast-enhanced coronal CT image shows fatty infiltration within the bowel wall of the descending colon at the level of the left colic flexure.



Non-contrast axial CT image shows fatty infiltration within the bowel wall of the ascending colon at the level of the right colic flexure

Conclusion: Fat halo is common in patients with psoriatic arthritis and was observed in 38% of patients, of whom only a minority had IBD. It was more frequent in males, however, not associated with any of other patient's demographics, disease characteristics, disease activity parameters or treatment regimen.

Disclosure: A. Haddad: AbbVie/Abbott, 6, AstraZeneca, 6, Janssen, 6, Novartis, 6; **K. Mousa**: None; **K. Milman**: None; **N. Nassrallah**: None; **D. Zisman**: AbbVie/Abbott, 1, 6, AstraZeneca, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 1, Neopharm, 1, 6, Novartis, 6, Pfizer, 1, 5; **S. Hashoul**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2307

Peripheral Manifestations In Axial And Peripheral Spondyloarthritis: A Systematic Literature Review On Their Assessment In Clinical Trials

AUGUSTA ORTOLAN[1], Casper Webers[2], Elena Nikiphorou[3], Alexandre Sepriano[4], Louise Falzon[5], Clementina López Medina[6], Dafne capelusnik[7], Désirée Van Der Heijde[8], Anna Molto[9] and Sofia Ramiro[10], [1]Policlinico Universitario Agostino Gemelli IRCSS, Rome, Italy, [2]Maastricht University Medical Centre, Maastricht, Netherlands, [3]King's College London, London, United Kingdom, [4]Department of Rheumatology, Leiden University Medical Centre, Portela Loures, Portugal, [5]Sheffield Centre for Health and Related Research, University of Sheffield, Sheffield, United Kingdom, [6]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [7]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [8]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [9]Assistance Publique Hôpitauxde Paris, Paris, France, [10]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Peripheral manifestations (peripheral arthritis, enthesitis, dactylitis) of axial spondyloarthritis (axSpA) and peripheral spondyloarthritis (pSpA) represent a significant burden for patients, but are understudied. Our aim was to evaluate the frequency of 1) assessment and reporting of peripheral manifestations in clinical trials of axSpA and pSpA (psoriatic arthritis excluded) 2) use of specific instruments for each peripheral manifestation.

Methods: A systematic literature review (SLR) was carried out, starting from available SLRs conducted for the 2016/2022 updates of the ASAS-EULAR axSpA management recommendations (≤2021).[1-3] The search was updated to March 2024 (PROSPERO CRD42024532666). The research question followed the PICOT framework: Population: adult patients with axSpA or pSpA; Intervention: biological and targeted synthetic DMARDs; Comparator: active comparator, placebo; Outcomes: Frequency of assessment of each peripheral manifestation, and of use of various specific instruments (e.g swollen joint count [SJC] for arthritis); Type of studies: randomised controlled trials (RCTs), controlled clinical trials. Study protocols, if available, or trial descriptions from ClinicalTrials.gov were checked for information on peripheral manifestations assessment. Risk of bias (RoB) was assessed by the Cochrane tool. For synthesis, descriptive statistics were used.

Results: In total, 100 trials were included for axSpA and 4 for pSpA (55 and 2 at low RoB, respectively). In axSpA, n=54 trials assessed peripheral arthritis, n=64 enthesitis and n=10 dactylitis. Not all of the studies actually reported these results, and only few addressed the subpopulation with the peripheral manifestation at baseline (**Fig 1**). The most frequently used instruments for peripheral arthritis (out of n=54) were SJC based on 44 (50%), 66 (11%) and 64 (9%) joints, and tender joint counts (TJC) based on 44 (24%), 46 (15%) and 68 (11%) joints. No studies assessed composite scores involving joint counts (e.g. DAS). For enthesitis (n=64 trials), the majority of studies used the MASES (87%), followed by the SPARCC enthesitis index (11%), question 4 of the BASDAI (8%) and the LEI (3%). The main instrument used for dactylitis was digit count (4/10, 10%); in 3/10 trials dactylitis was collected as adverse event. There was a tendency towards a higher frequency of reporting, and reporting in subpopulations with peripheral manifestations, in RCTs at lower RoB (**Fig 2**). In pSpA, all 4 trials assessed (and reported on) peripheral arthritis; 2 also assessed enthesitis and dactylitis.

Conclusion: In axSpA, peripheral manifestations were assessed as outcome in less than 2/3 of trials. The most frequently used instruments were SJC and TJC for peripheral arthritis, MASES for enthesitis and digit count for dactylitis. Outcomes were typically not reported in the subpopulation with known peripheral arthritis/enthesitis/dactylitis at baseline.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

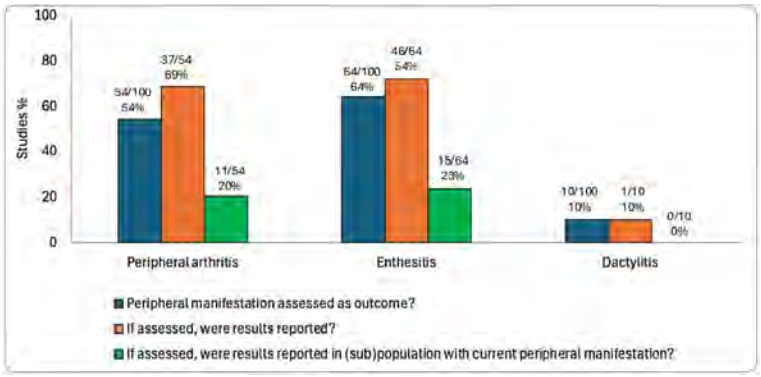


Fig 1. Frequency of assesment and reporting, including reporting in subpopulations, of each peripheral manifestations

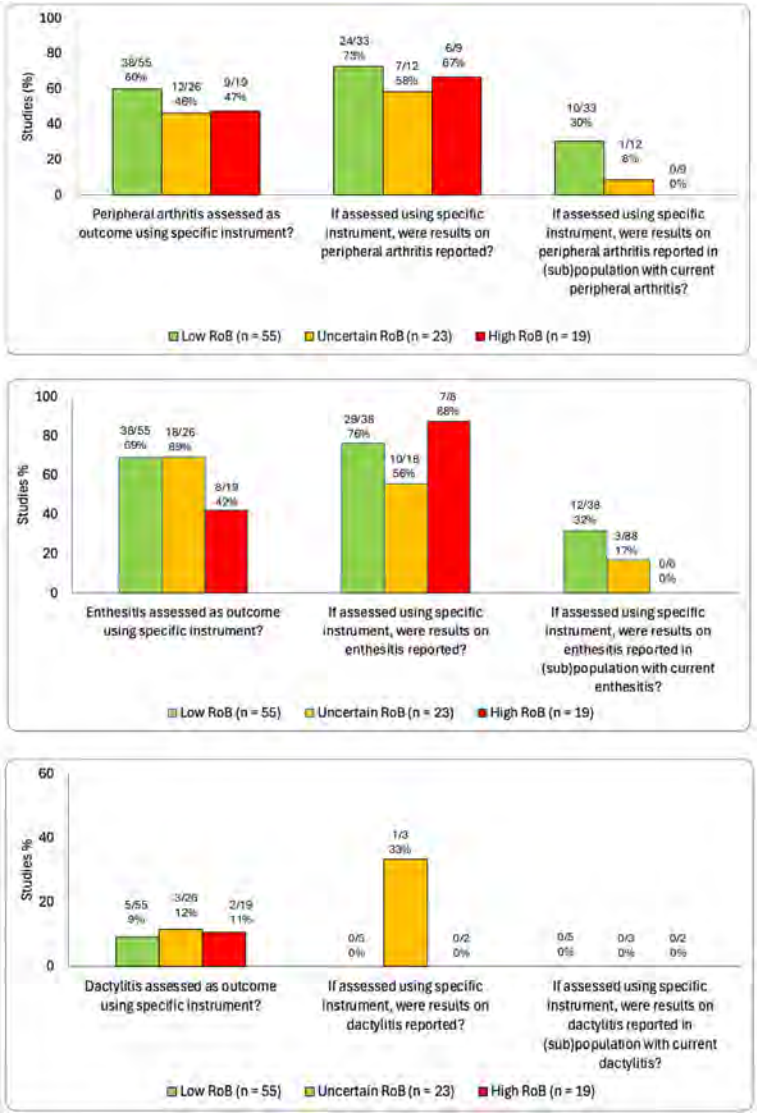


Fig 2. Frequency of assesment and reporting, including reporting in subpopulations, according to Risk of Bias

Disclosure: A. ORTOLAN: AbbVie/Abbott, 6, AstraZeneca, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Novartis, 6; **C. Webers**: Novartis, 6; **E. Nikiphorou**: AbbVie/Abbott, 1, 2, 6, Alfasigma, 1, 6, Eli Lilly, 1, 2, 5, 6, Fresenius, 1, 6, Galapagos, 1, 6, Gilead, 1, 6, Novartis, 1, 2, 6, Pfizer, 1, 2, 5, 6, UCB, 1, 2, 6; **A. Sepriano**: AbbVie/Abbott, 2, 6, Eli Lilly,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 6, UCB, 2, 6; **L. Falzon**: None; **C. López Medina**: None; **D. capelusnik**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2308

Physical Function Mediates Most—but Not All—of the Effect of Disease Activity on Health-Related Quality of Life in Axial Spondyloarthritis: A 10-Year Longitudinal Analysis

AUGUSTA ORTOLAN[1], Désirée Van Der Heijde[2], Laure Gossec[3] and Sofia Ramiro[4], [1]Policlinico Universitario Agostino Gemelli IRCSS, Rome, Italy, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [3]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [4]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Health-related quality of life (HRQoL) is an overarching outcome in axial spondyloarthritis (axSpA), and is considered influenced by disease activity and physical function. However, this relationship has never been demonstrated in a longitudinal framework. The impact of disease activity on HRQoL may be either direct, or occur indirectly by

Table 1. Mediation analysis considering a direct and indirect (mediated by function, BASFI) effect of disease activity (ASDAS) on HRQoL, according to the main mediation hypothesis (ASDAS and BASFI influence HRQoL one year later)

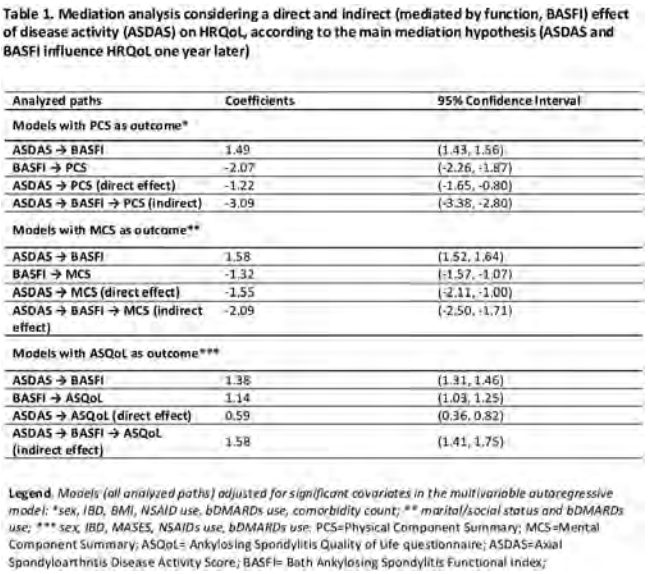


Table 1. Mediation analysis considering a direct and indirect (mediated by function, BASFI) effect of disease activity (ASDAS) on HRQoL, according to the main mediation hypothesis (ASDAS and BASFI influence HRQoL one year later)

Analyzed paths	Coefficients	95% Confidence Interval
Models with PCS as outcome*		
ASDAS → BASFI	1.49	(1.43, 1.56)
BASFI → PCS	-2.07	(-2.26, -1.87)
ASDAS → PCS (direct effect)	-1.22	(-1.65, -0.80)
ASDAS → BASFI → PCS (indirect)	-3.09	(-3.38, -2.80)
Models with MCS as outcome**		
ASDAS → BASFI	1.58	(1.52, 1.64)
BASFI → MCS	-1.32	(-1.57, -1.07)
ASDAS → MCS (direct effect)	-1.55	(-2.11, -1.00)
ASDAS → BASFI → MCS (indirect effect)	-2.09	(-2.50, -1.71)
Models with ASQoL as outcome***		
ASDAS → BASFI	1.38	(1.31, 1.46)
BASFI → ASQoL	1.14	(1.03, 1.25)
ASDAS → ASQoL (direct effect)	0.59	(0.36, 0.82)
ASDAS → BASFI → ASQoL (indirect effect)	1.58	(1.41, 1.75)

Legend. *Models (all analyzed paths) adjusted for significant covariates in the multivariable autoregressive model: *sex, IBD, BMI, NSAID use, bDMARDs use, comorbidity count; ** marital/social status and bDMARDs use; *** sex, IBD, MASES, NSAIDs use, bDMARDs use.* PCS=Physical Component Summary; MCS=Mental Component Summary; ASQoL= Ankylosing Spondylitis Quality of Life questionnaire; ASDAS=Axial Spondyloarthritis Disease Activity Score; BASFI= Bath Ankylosing Spondylitis Functional Index;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

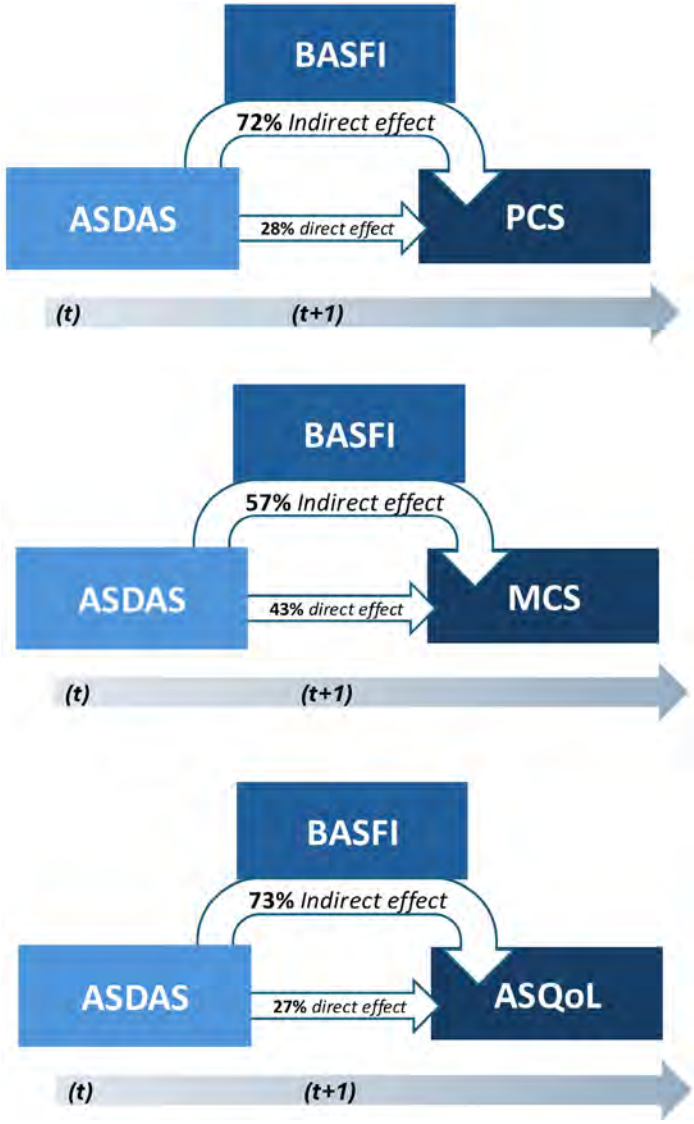


Figure 1. Mediation structure, with estimation of direct and indirect effects Legend. t = time point; t+1 = time point plus 1 year

worsening physical function. The aim of this study was to investigate whether the effect of disease activity on HRQoL is primarily direct or mediated by physical function over time in early axSpA.

Methods: AxSpA patients from the DESIR cohort were analysed over 10 years of follow-up. Disease activity (assessed by the Ankylosing Spondylitis Disease Activity Score, ASDAS), physical function (Bath Ankylosing Spondylitis Functional Index, BASFI), and HRQoL outcomes (Physical Component Summary [PCS] and Mental Component Summary [MCS] of the SF-36, with higher values representing better HRQoL, and Ankylosing Spondylitis Quality of Life [ASQoL], with higher values corresponding to worse HRQoL) were assessed. Structural equation modeling (SEM) was performed to assess mediation, including direct and indirect (i.e. mediated) effects of disease activity on HRQoL. The hypothesis regarding mediation was that ASDAS and BASFI (assessed at the same time point) impact HRQoL at a subsequent time point (ie one year later). All models were adjusted for significant covariates (eg sex, marital/social status, BMI, NSAID use, bDMARDs use, enthesitis, IBD, comorbidity count) .Results are presented as beta coefficient (95% confidence intervals).

Results: A total of 663 patients were analysed, 46% males, mean age 33.5 (8.6) years. At 10 years, both ASDAS and BASFI were on the low range (ASDAS 2.0 [1.0] BASFI 2.3 [2.2]), and QoL scores were moderate at the group level (PCS 42.9 [10.4], MCS 45.0 [10.5], ASQoL 6.5 [5.5]). BASFI significantly mediated the association between ASDAS and HRQoL (**Table 1**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

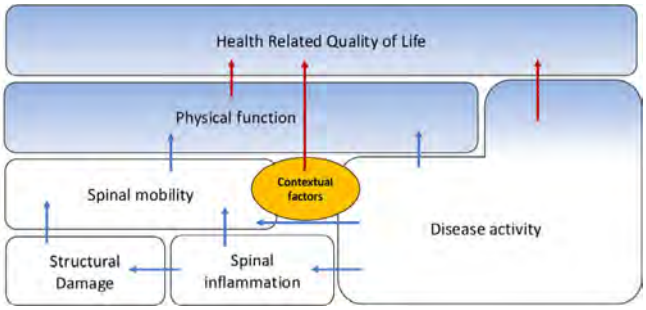


Figure 2. Longitudinal framework with Health Related Quality of Life as the overarching outcome Legend. The shadowed blocks represent the main variables of interest for this analysis. Red arrows represent the longitudinal relationships clarified by this current analysis. Blue arrows represent (longitudinal) associations previously described in the literature.

The indirect effects through BASFI were consistently larger than the direct effects. For PCS, the indirect effect was -3.09 (-3.38,-2.80) and the direct effect was -1.22 (-1.65,-0.80). For MCS, the indirect effect was -2.09 (-2.50,-1.71) versus a direct effect of -1.55 (-2.11,-1.00). For ASQoL, the indirect effect was 1.58 (1.41,1.75) and the direct effect was 0.59 (0.36, 0.82). Despite the majority of the effect of ASDAS on HRQoL being mediated, about a quarter of the effect was direct (**Figure 1**). These findings confirm HRQoL as a higher-order outcome, supported by its longitudinal association with both ASDAS and BASFI. We then propose a model of disease outcomes in axSpA, with proven longitudinal relationships (**Figure 2**).

Conclusion: In early axSpA, disease activity impacts HRQoL mainly through its negative influence on physical function; however a direct, independent effect also exists. These findings reinforce the hierarchical model of disease outcomes and emphasize the central role of targeting disease activity to optimize HRQoL, through its direct and indirect effects.

Disclosure: A. ORTOLAN: AbbVie/Abbott, 6, AstraZeneca, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Janssen, 6, Novartis, 6; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2309

Lifestyle behaviours and disease activity in patients with psoriatic arthritis: the Dutch south west psoriatic arthritis study

Batoul Hojeij[1], Ilja Tchetverikov[2], Marijn Vis[1], Marc R Kok[3], Yvonne Goekoop-Ruiterman[4], Jessica Bijsterbosch[5], Paul Baudoin[6], Reinhard Bos[7], Jos H van der Kaap[8], Petra Kok[9], Lindy-Anne Korswagen[10] and Jolanda J Luime[1], [1]Erasmus MC, Rotterdam, Netherlands, [2]Albert Schweitzer Hospital, Dordrecht, Netherlands, [3]Maasstad Hospital, Rotterdam, Netherlands, [4]Haga Hospital, the Hague, Netherlands, [5]Amphia Hospital, Breda, Netherlands, [6]Reumazorg Zuid West Nederland, Roosendaal, Netherlands, [7]Medisch Centrum Leeuwarden, Leeuwarden, Netherlands, [8]Admiraal De Ruyter Hospital, Goes, Netherlands, [9]Reinier de Graaf Hospital, Delft, Netherlands, [10]Franciscus Gasthuis and Vlietland, Rotterdam, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Multivariable associations between baseline lifestyle risk score and one year PsA disease activity

	β, 95%CI	P-value
PASDAS	**0.15 (0.08, 0.23)**	**<0.0001**
DAPSA	**1.18 (0.65, 1.71)**	**<0.0001**
	OR, 95%CI	P-value
PASDAS-LDA	**0.59 (0.45, 0.77)**	**<0.0001**
DAPSA-LDA	**0.74 (0.59, 0.92)**	**0.009**
PASDAS remission	0.77 (0.55, 1.07)	0.123
DAPSA remission	0.76 (0.58, 1.01)	0.059
MDA	**0.72 (0.57, 0.90)**	**0.004**

Number of patients with at least one disease activity measurement during follow-up: PASDAS, n=642; DAPSA, n=773; MDA, n=837. Abbreviations: DAPSA, Disease Activity index for Psoriatic Arthritis; LDA, low disease activity; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score.
Model adjusted for baseline disease activity, study visit, age, sex, geographic origin, education, and medication.
Covariates are imputed using mice predictive mean matching and classification and regression trees (pmm and CART; M=20)

Background/Purpose: Comprehensive assessment of multiple lifestyle behaviours and disease activity outcomes in psoriatic arthritis (PsA) is scarce. We aim to investigate lifestyle behaviours in patients with PsA and their association with disease activity measurements.

Methods: This multicenter cohort included 938 patients newly diagnosed with PsA from the DEPAR study, between 2013 and 2023. Lifestyle behaviours were assessed at baseline and included: body mass index (BMI), waist circumference, smoking, alcohol consumption and physical activity. A comprehensive lifestyle risk score was calculated (range 0 to 5) using these five lifestyle behaviours (BMI outside normal range, abdominal obesity, current smoking, no alcohol consumption, physical inactivity), with higher scores indicating more risk behaviours. No specific treatment protocols were applied. Disease activity was assessed every three months over the course of one year and included: Psoriatic Arthritis Disease Activity Score (PASDAS), disease activity in psoriatic arthritis (DAPSA), PASDAS and DAPSA low disease activity (LDA) and remission, and minimal disease activity (MDA). The associations between the lifestyle risk score and disease activity were analyzed using mixed models adjusted for baseline disease activity, study visit, age, sex, geographic origin, education and medication. Multiple imputations to handle missing data for all covariates were performed in R (version 4.4.2) using mice predictive mean matching and classification and regression trees (pmm and CART; M=20).

Results: The rate of overweight/obesity was 72%, abdominal obesity was 39% in men and 64% in women, current smoking was 22% (of them 41% classified as moderate-to-heavy smoking (>10 cigarettes per day)), and alcohol consumption was 82% (of them 22% classified as heavy consumption) with 3% of patients physically inactive. Using multivariable analyses, a higher lifestyle risk score was associated with higher PASDAS (βadj 0.15; 95%CI 0.08, 0.23), and lower odds for achieving PASDAS-LDA (ORadj 0.59; 95%CI 0.45, 0.77), and MDA (OR adj 0.72; 95%CI 0.57, 0.90) at one year of follow-up. Similar associations were observed for DAPSA and DAPSA-LDA. Analysis of individual lifestyle behaviours showed that obesity, abdominal obesity and moderate-to-heavy current smoking, were also significantly associated with higher PASDAS and DAPSA, and lower odds for achieving PASDAS-LDA and MDA.

Conclusion: Lifestyle behaviours seem to influence one year disease activity in PsA. Adiposity and smoking were associated with higher disease activity. Patients newly diagnosed with PsA also showed unhealthy lifestyle behaviours.

Disclosure: B. Hojeij: None; **I. Tchetverikov**: None; **M. Vis**: None; **M. Kok**: None; **Y. Goekoop-Ruiterman**: None; **J. Bijsterbosch**: None; **P. Baudoin**: None; **R. Bos**: None; **J. van der Kaap**: None; **P. Kok**: None; **L. Korswagen**: None; **J. Luime**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2310

Neuropeptide influence in nociception and inflammation through immune system modulation in SPA patients

ELENA GRAU GARCIA[1], SAMUEL LEAL[2], Jose Ivorra Cortes[3], Pablo Muñoz-Martínez[4], Laura Mas Sanchez[5], Daniel Ramos Castro[6], Alba Maria Torrat Noves[7], Iago Alcantara Alvarez[8], Belen Villanueva Manes[9], Miguel Simeo Vinaixa[8], Andres Perez Hurtado[10] and José Andrés Román Ivorra[11], [1]HUP La Fe, Valencia, Comunidad Valenciana, Spain, [2]Rheumatology Department. HUP La Fe, Valencia, Comunidad Valenciana, Spain, [3]Hospital Universitario La Fe, Valencia, Comunidad Valenciana, Spain, [4]Hospital Universitario y Politécnico La Fe, Sagunto, Spain, [5]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [6]Hospital Universitari i Politecnic La Fe, Valencia, Spain, [7]Hospital Universitari i Politècnic La Fe de Valencia, Valencia, Spain, [8]Rheumatology Department. HUP La Fe, Valencia, Spain, [9]Hospital La Fe, Valencia, Spain, [10]Hospital Universitario y Politècnico La Fe, Valencia, Comunidad Valenciana, Spain, [11]Hospital Universitari i Politècnic La Fe, Valencia, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: NGFβ and CGRP are neuropeptides with a significant role in peripheral inflammation, pain modulation and immune responses. Neuropeptides regulatory mechanisms in spondyloarthritis (SpA) remain poorly characterized, however, they may influence inflammatory processes indirectly through immune system modulation. Notably, their interaction with cytokines may contribute to chronic inflammation and heightened pain sensitivity observed in SpA.

Aim: to evaluate the association of NGFβ and CGRP serum levels with nociception, immune system modulation and clinical Spa activity.

Methods: A longitudinal, observational prospective study with evaluations at baseline and 2 months follow-up in SpA patients initiating biological therapy (BT) was performed. In SpA patients complete laboratory test, BASFI, BASDAI, HAQ and VAS pain scale and ASDAS score in each visit was carried out. We analyzed by colorimetric methods cytokine (TNFa,

Variable	Healthy controls N=67	SpA patients V0 N=69	SpA patients V1 N=69	P-Value SpA vs HC	P-Value V0 vs V1
	Mean (SD) / n(%)	Mean (SD) / n(%)	Mean (SD) / n(%)		
CGRP	84.22 (74.52)	279.64 (633.57)	289.18 (634.37)	<0.001	
NGFb	118.22 (282.04)	232.48 (590.14)	278.32 (639.23)	<0.001	
IFNg	184.29 (161.64)	101.06 (83.19)	104.64 (86.56)	<0.001	
IL2	10.34 (8.36)	6.28 (3.81)	6.16 (3.71)	<0.001	
IL10	43.21 (67.42)	25.25 (55.98)	21.95 (37.83)	0.03	
IL17a	48.86 (48.71)	29.08 (24.36)	33.46 (21.7)	0.001	
IL23	1039.66 (1011.58)	480.91 (394.79)	469.38 (341.28)	<0.001	
TNFa	18.67 (10.48)	16.27 (20.94)	10.96 (7.99)	0.001	
CRP		9.48 (13.02)	4.09 (8.63)		<0.001
ESR		22.09 (20.33)	12.74 (13.95)		<0.001
VAS pain		5.49 (2.6)	4.19 (3.16)		0.009
HAQ		0.9 (0.64)	0.76 (0.68)		0.241
BASDAI		5.91 (2.3)	4.7 (2.81)		0.006
BASFI		4.41 (2.67)	3.95 (3.04)		0.352
ASDAS-CRP		3.16 (0.96)	2.38 (1.19)		<0.001
ASDAS-ESR		3.25 (0.93)	2.51 (1.16)		<0.001

Table. Clinical activity and molecule levels throughout the follow-up

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

IFNg, IL2, IL10, IL17a and IL23) and neuropeptide (CGRP and NGFb) serum levels in SpA patients and in healthy controls (HC).

Results: 69 SpA patients (65.2% male) were recruited with a mean age of 48 (12) years and a mean time of disease evolution of 7 (8) years. 67 HC with a mean age of 45 (13) years (43.2% male) were also recruited. At baseline the 39.1% of patients showed elevation of CRP and the 21.7% ESR. The 86.9% displayed high/very high clinical activity by ASDAS score. The 66.7% were under anti-TNF therapy and 33.3% under anti-IL17 treatment, the 31.9% with previous BT administered, 21.7% treated with DMARDs and 4.4% with corticoids.

There are significant differences in the analyzed molecules levels between patients and HC (table). Age and sex do not appear to influence molecule levels.

CGRP and NGFb showed no correlation and no differences during the follow-up. No association between neuropeptide levels and clinical activity was found, but a tendency where incremented CGRP was associated to low HAQ (P=0.06) and incremented NGFb was associated to low pain perception (P=0.06) was observed.

Analyzing the neuropeptides influence on cytokines, high CGRP and NGFb levels were related to high IL10 levels (P=0.047 and P=0.005) and low IL2 levels (P=0.003 and P=0.025). Moreover high CGRP was associated to low IFNg (P=0.002).

Differences in cytokine levels during the follow-up were only seen for IL17a (P=0.003) and TNFa (P< 0.001), as well as a decrease of CRP and ESR levels (P< 0.001), VAS pain (P=0.009), BASDAI (P=0.006) and ASDAS score (P< 0.001). Clinical activity was associated to IFNg (P=0.038) and IL17a (P=0.005) levels, and elevated ESR with high IL2 (P=0.019).

Related to BT, patients treated with anti-TNF showed low TNF levels (P=0.006) and those treated with anti-IL17 showed low IL17a levels (P=0.008).

Conclusion: Our findings indicate that neuropeptide levels were higher in SpA patients than in HC. A tendency of a decrease in pain and disability perception with high neuropeptide levels was observed, probably due to neuropeptides have been depleted from the presynaptic terminal and secreted into the bloodstream. Although no association between neuropeptides and clinical disease activity was observed, indirect influence on clinical activity is highlighted with the downregulation of IL2 and IFNg.

Disclosure: E. GRAU GARCIA: None; **S. LEAL**: None; **J. Ivorra Cortes**: None; **P. Muñoz-Martínez**: None; **L. Mas Sanchez**: None; **D. Ramos Castro**: None; **A. Torrat Noves**: None; **I. Alcantara Alvarez**: None; **B. Villanueva Manes**: None; **M. Simeo Vinaixa**: None; **A. Perez Hurtado**: None; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6.

Abstract Number: 2311

Obstructive Sleep Apnea Syndrome in Patients with Psoriatic Arthritis and Its Relationship with Disease Activity and Comorbidities

Esther Toledano[1], Carolina Cristina Chacón[2], Cristina Hidalgo Calleja[2], Belén Miguel[2], Laura Blanco[2], Ana Turrión[3], Olga Compán[4], Manuel Martín[3], Susana Gómez[2] and Carlos Montilla[2], [1]Rheumatology Service, San Carlos Clinical Hospital, Madrid, Spain, [2]Rheumatology Service, University Hospital of Salamanca, Salamanca, Castilla y Leon, Spain, [3]Rheumatology Service, University Hospital of Salamanca, Salamanca, Spain, [4]Rheumatology Service, University Hospital of Salamanca, Carbajosa de la Sagrada, 37191, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Obstructive sleep apnea syndrome (OSAS) is a chronic respiratory disorder characterized by intermittent upper airway collapse during sleep. This mechanism can trigger systemic inflammation and metabolic dysregulation. Psoriatic arthritis (PsA) is associated with metabolic syndrome and emotional disorders, both of which are classic comorbidities of OSAS. Given the established relationship between PsA and metabolic syndrome, an association between PsA and OSAS would be expected; however, no studies to date have explored this potential relationship.

Therefore, the aim of this study was to evaluate the presence of OSAS and its association with clinical, inflammatory, and functional features, as well as sleep quality in a cohort of PsA patients.

Methods: A cross-sectional observational study was conducted with 247 PsA patients, classified according to the presence (n=22) or absence (n=225) of OSAS. Demographic, clinical, functional, disease activity, functional impairment, disease impact, sleep quality, and comorbidity variables were collected. Logistic regression analysis was performed to identify factors associated with OSAS.

Variable	Total (n=247)	OSAS (n=22)	No OSAS (n=225)	p-value
Age* (years)	55 (14)	58 (18)	54 (12.0)	0.02
Disease duration (years)	8 (9)	10.5 (8)	8.0 (9)	0.1
Smoking status, n (%)				
Current smoker	72 (29)	4 (18)	68 (30)	0.4
Former smoker	102 (41)	11 (50)	91 (41)	
Never smoker	73 (30)	7 (32)	66 (29)	
Smoking, pack-years	13 (25.2)	28.5 (50.1)	12,8 (25,2)	0.1
csDMARDs, n (%)	146 (59)	16 (72)	130 (58)	0.1
Methotrexate	107 (73)	12 (76)	95 (73)	
Sulfasalazine	30 (21)	2 (12)	28 (22)	
Leflunomide	9 (6)	2 (12)	7 (5)	
tsDMARDs o bDMARDs, n (%)	64 (26)	6 (27)	58 (26)	0.8
TNFi	44 (69)	5 (83)	39 (67)	
IL-17i	7 (11)	0 (0)	7 (12)	
Ustekinumab	3 (4)	1 (17)	2 (3)	
Guselkumab	2 (3)	0 (0)	2 (3)	
JAKi	3 (5)	0 (0)	3 (6)	
Apremilast	5 (8)	0 (0)	5 (9)	
Filure to tsDMARDs/bDMARDs,n (%)	25 (39)	3 (50)	22 (38)	0.6
Clinical presentation, n (%)				0.2
Peripheral	206 (82)	21 (92)	185 (72)	
Mixed	34 (15)	1 (8)	33 (22)	
Axial	7 (3)	0 (0)	7 (6)	
Cervical involvement (%)	8 (3.2)	1 (4.5)	7 (3.1)	0.5
Dactylitis (%)	40 (18)	5 (12)	35 (22)	0.07
mMASES	0.5 (1.2)	0.7 (3)	0 (2)	0.3
PASI	0.4 (2.6)	1 (3)	0.2 (2.6)	0,5
FACIT-F	38 (18)	30,5 (22)	39 (17)	0.04
CRP (mg/dL)	0,2 (0.4)	0.2 (0,7)	0,2 (0.4)	0.1
Pain (VAS)	4 (4)	4.5 (4)	4 (4)	0.2
Global activity (VAS)	4 (4)	4 (4.2)	4 (4)	0.7
TJC	1 (2)	1 (1.0)	1 (2)	0.02
SJC	1 (2.1)	2 (2.0)	1 (2)	0.8
cDAPSA	11 (8.7)	13.2 (9.2)	10.6 (9.3)	0.09
ASDAS-CRP	2 (0.8)	2.4 (1.6)	2 (1.8)	0.6
HAQ-DI	0.5 (1)	1.1 (0.9)	0.3 (0.8)	0.002
BASFI	2.6 (4.5)	5.2 (6.2)	2.5 (4.3)	0.1
PsAID-12	3.1 (3.7)	3.8 (4.8)	2.8 (3.6)	0.04
BMI (kg/m²)	26 (5.8)	29.7 (8.1)	25.4 (5.6)	0.02
IL-6 (ng/mL)	2 (3.6)	3 (4.8)	2 (3.2)	0.1
TNF	7.7 (5)	8.8 (4.7)	7.5 (5.2)	0.3
HADS-A	5 (6)	7 (6.5)	5 (6)	0.02
HADS-D	3.5 (6)	7 (6.0)	3 (6)	0.005
ISI	8.1 ± 4.7	9,3 ± 4.9	7 ± 4.3	0.001

Abbreviations: ASDAS-PCR: *Ankylosing Spondylitis Disease Activity Score*-CRP; BASFI: *Bath Ankylosing Spondylitis Functional Index*; bDMARD: Biologic Disease-Modifying Antirheumatic Drug; BMI: Body Mass Index; cDAPSA: *Clinical Disease Activity Index for Psoriatic Arthritis*; CRP: C-reactive protein; PsA: psoriatic arthritis; PSAID: *Psoriatic Arthritis Impact of Disease*; csDMARD: Conventional Synthetic Disease-Modifying Antirheumatic Drug; FACIT: *Functional Assessment of Chronic Illness Therapy*; HADS-A: *Hospital Anxiety and Depression Scale – Anxiety subscale*; HADS-D: *Hospital Anxiety and Depression Scale – Depression subscale*; HAQ-DI: *Health Assessment Questionnaire Disability Index*; IL-6: Interleukin 6; ISI: *Insomnia Severity Index*; m: Mean; mMASES: Modified Maastricht *Ankylosing Spondylitis Enthesitis Score*; n: Number; PASI: *Psoriasis Area Severity Index*; SD: Standard Deviation; SJC: Swollen Joint Count; TJC: Tender Joint Count; TNFi: Tumor Necrosis Factor Inhibitor; tsDMARD: Targeted Synthetic Disease-Modifying Antirheumatic Drug; VAS: Visual Analogue Scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Patients with OSAS had a higher mean age (58 vs. 54 years; p=0.02) and higher body mass index (BMI) (29.7 vs. 25.4 kg/m^2; p=0.02). Regarding inflammatory parameters, they exhibited greater disease activity (DAPSA 13.2 vs. 10.6; p=0.09) and a higher number of enthesitis sites according to mMASES (0.7 vs. 0.0; p=0.3), although not reaching statistical significance. Functionally, OSAS patients showed significantly greater impairment according to the HAQ-DI (1.1 vs. 0.3; p=0.002) and greater disease impact (PsAID-12: 3.8 vs. 2.8; p=0.04). They also presented higher levels of fatigue (FACIT-F: 30.5 vs. 38; p=0.04), anxiety (HADS-A: 7 vs. 5; p=0.02), depression (HADS-D: 7 vs. 3.5; p=0.005), and worse sleep quality (ISI 9.3 vs. 7.0; p=0.001). In logistic regression analysis, BMI was the only variable significantly associated with OSAS (OR: 1.1; 95% CI: 1.01–1.2; p=0.04).

Conclusion: OSAS was associated with obesity, greater functional impairment, higher levels of fatigue, anxiety, depression, and poorer sleep quality in PsA patients. These findings highlight the importance of early detection strategies for comorbidities and a multidisciplinary approach in the assessment of PsA patients, including evaluation for OSAS.

Disclosure: E. Toledano: None; **C. Chacón**: None; **C. Hidalgo Calleja**: None; **B. Miguel**: None; **L. Blanco**: None; **A. Turrión**: None; **O. Compán**: None; **M. Martín**: None; **S. Gómez**: None; **C. Montilla**: None.

Abstract Number: 2312

Sociodemographic Characteristics and Healthcare Utilization in Patients with IBD-Associated Arthritis vs. IBD Alone: A Nationwide Inpatient Analysis

Faria Sami[1], Maria I. (\"Maio\") Danila[2], Liron Caplan[3] and Rouhin Sen[4], [1]The University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, [3]Medicine Service, Rocky Mountain Regional VAMC, Aurora, CO, [4]University of Alabama at Birmingham, Department of Medicine, Division of Clinical Immunology & Rheumatology, Birmingham

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Inflammatory bowel disease (IBD)-associated arthritis (IBD-A) can affect 24-44% of IBD patients and may represent an enhanced inflammatory state. IBD-A patients often experience a more severe disease course, increased hospitalizations, a higher need for surgical or biologic therapies, and worse outcomes compared to IBD alone. Prior studies have examined the reasons for hospitalizations for IBD, but the inpatient burden of IBD-A remains underexplored. Understanding differences in sociodemographic characteristics and healthcare utilization in patients with IBD-A vs IBD alone may help inform resource management and policy

Methods: We used the National Inpatient Sample (NIS) database to identify adult hospitalizations with a primary or secondary diagnosis of IBD from 2016 to 2020. Admissions with concurrent diagnosis of IBD-A were identified using ICD-10 codes. We compared demographics, insurance type, median household income, geographic location, length of stay (LOS), total hospital charges, and in-hospital mortality between patients with IBD-A and IBD alone. Survey-weighted analyses were used to generate national estimates. A p-value < 0.05 was considered statistically significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Weighted Descriptive Characteristics of IBD-associated Arthritis (IBD-A) Hospitalizations from the 2016-2020 National Inpatient Sample (n=1880)

Hospitalization Characteristics	IBD alone (n=1595045)	IBD- A (n=1880)	P-value
Age, median (IQR) in years	55 (38-70)	42 (31-57)	<0.001
Age Groups			
Age 18-40 years	438, 265 (27.5%)	820 (43.6%)	<0.001
Age 40-60 years	476,140 30.0%	660 35.1%	0.028
Age 60-80 years	526, 930 33.0%	360 19.1%	<0.001
Age > 80 years	153, 710, 9.6%	40, 2.0%	<0.001
Female, n (%)	896,560 (56.2%)	1205 (64.1%)	0.002
Race/Ethnicity			
White	1219810, 76.5%	1380, 73.4%	0.178
African American	174335 10.9%	220 11.7%	0.633
Hispanic	94815, 5.9%	125, 6.6%	0.572
Asian or Pacific Islander	18610, 1.2%	15, 0.8%	0.504
Native American	5875, 0.4%	NR	0.942
Other Race	35310, 2.2%	55, 0.3%	0.351
Length of Stay, mean (SD)	4 (2-6)	4 (2-7)	0.751
Total Charges, mean (SD)	$58,227 (98703.71)	$57291.52 (79253.71)	0.829
[1]Median Household Income			
Income Q1	385005 24.1%	305, 16.2%	<0.001
Income Q2	404334 25.3%	435, 23.1%	0.330
Income Q3	405480, 25.4%	510, 27.1%	0.457
Income Q4	376630 23.6%	595, 31.6%	0.337
In-hospital Mortality, n (%)	26130 (1.6%)	20 (1.1%)	—
Insurance status			
Medicare	681710, 42.7%	475 25.3%	<0.001
Medicaid	234785, 14.7%	400, 21.3%	<0.001
Private insurance	573070, 35.9%	905, 48.1%	<0.001
Self-pay	55955, 3.5%	70, 3.7%	0.820
Hospital Region in USA			
Northeast	342550, 21.5%	535, 28.5%	0.002
Midwest	393675, 24.7%	525, 30.0%	0.166
South	585545, 36.7%	420, 22.3%	<0.001
West	273275, 17.1%	400, 21.7%	0.046
Charlson Comorbidity Index, median (IQR)	1 (0-2)	0 (0-1)	<0.001

[1]*Income Q1–Q4 = Income quartiles based on median household income by patient ZIP code: Q1 = lowest quartile (<$55,999 Q2 = $56,000–$70,999, Q3 = $71,000–$93,999, Q4 = highest quartile (≥$94,000).*

Results: A total of 1880 adult IBD-A hospitalization events were included. The top reasons for hospitalizations for IBD-A patients were: Ulcerative colitis (12.2%), followed by sepsis (10.6%), and then Crohn's disease with and without complications (6.0%). Compared with IBD patients without arthritis, patients with IBD-A were more likely to be younger (median age 42 vs 55 years, p value < 0.001) and females (64.1% versus 56.2%, p value 0.002), more frequently had private insurance (48.1% vs 35.9%, p value < 0.001) or Medicaid (21.3% vs 14.7%, p value < 0.001), and less commonly were from lowest quartile of household income [$1 - 55,999] (16.2 % vs 24.1%, p value < 0.001). Geographically, compared to IBD-only patients, IBD-A admissions were more common in the Northeast (28.5% vs 21.5%, p value 0.002) and West (21.7% vs 17.1%, p value 0.046) and less frequent in the South (22.3% vs 36.7%, p value < 0.001). Compared to IBD admissions, IBD-associated arthritis admissions had a similar length of stay, total hospital charges, and in-hospital mortality (1.1% vs 1.6%) as shown in Table 1.

Conclusion: Hospitalizations with IBD-A were more prevalent in younger people and females. There were no differences in race/ethnicity, length of stay, or total hospital charges between the two groups of patients. Future studies should investigate the causes of admissions in patients who are younger and female, and explore if they are sub-optimally treated for their IBD or arthritis, leading to more hospitalizations.

Disclosure: F. Sami: None; **M. Danila**: Boehringer-Ingelheim, 2, Pfizer, 5; **L. Caplan**: None; **R. Sen**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2313

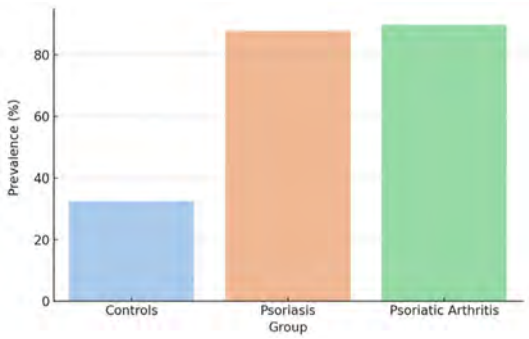
From Plaque to Plaque: Bridging Oral and Systemic Inflammation in Psoriasis and PsA

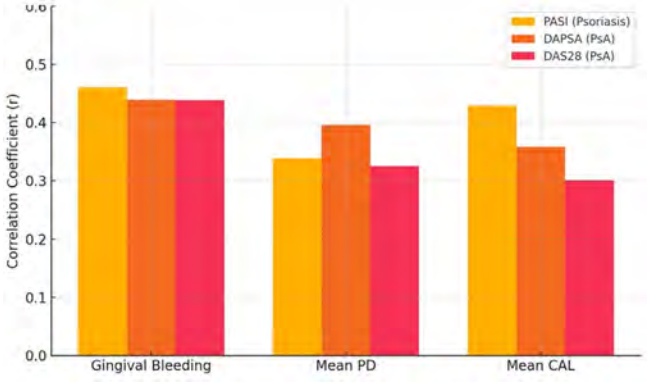
guru Vijay Chagalakondu, Vijaya prasanna Parimi and Pradeep S Anand, ESIC Medical College and Super Specilaity Hospital, hyderabad, Telangana, India

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriasis and psoriatic arthritis (PsA) are two chronic inflammatory conditions which have similar immunopathological mechanisms which also cause periodontal disease. The association between these conditions is often underrecognized. This study aims to assess the prevalence and severity of periodontitis in psoriasis and psoriatic arthritis, evaluate its correlation with disease activity indices and identify the potential of oral health as a surrogate marker of systemic inflammation.

Methods: In this prospective triple-arm, case-control study, 120 participants were recruited into the study and were equally divided into three groups- healthy subjects as controls, patients with psoriasis and patients with PsA. A detailed periodontal examination was conducted which included measurement of Oral hygiene Index (OHI), gingival bleeding, probing depth (PD), clinical attachment loss (CAL) and missing teeth. Disease activity was measured using Psoriasis Area and Severity Index (PASI) for psoriasis, DAS28 and DAPSA for psoriatic arthritis. Statistical analysis was done using Kruskal Wallis and Spearman's correlation coefficients and p value < 0.05 was considered as significant.





23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Periodontitis was found to be more prevalent in PsA (89.7%) and psoriasis (87.8%) groups compared to healthy controls (32.5%) (p< 0.001). PsA group demonstrated severe periodontal disease activity with higher OHI, bleeding scores, PD and CAL (p < 0.05 for all). The correlation between indices of psoriasis and PsA with periodontal disease was positive.

- **PASI** correlated with bleeding (r=0.460), PD (r=0.338), and CAL (r=0.429), all p< 0.001.
- **DAPSA** correlated with bleeding (r=0.439, p< 0.001), PD (r=0.396, p=0.013), and CAL (r=0.358, p=0.025).

DAS28 correlated with bleeding (r=0.438, p< 0.001), PD (r=0.325, p=0.043), and CRP (r=0.328, p=0.041) (Figure 2).

Conclusion: This study highlights the striking significant association between periodontal disease and disease activity of psoriasis. The study also highlights the fact that higher disease activity of periodontitis was observed in PsA group. Given the ease of periodontal assessment, it may serve as a non-invasive reflective biomarker of systemic inflammation in patients with PsA and psoriasis. The study also emphasizes the need for early periodontal screening in patients with psoriasis for timely identification and integrated approach of disease management (oral-systemic axis).

Disclosure: g. Chagalakondu: None; **V. Parimi**: None; **P. Anand**: None.

Abstract Number: 2314

Radiographic and Ultrasonographic Assessments of Sesamoid Index in Patients with Psoriatic Arthritis

Hung Vo[1], Eugene Kissin[2] and Pablo Weilg[3], [1]Boston Medical Center, Peabody, MA, [2]Boston University, Newton, MA, [3]Kymera Independent Physicians, Roswell, NM

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The sesamoid index (SI), a radiographic measure of medial thumb sesamoid area, was originally described as a diagnostic tool in acromegaly[1] and later proposed as a tool to differentiate psoriatic arthritis (PsA) from other arthritides[2]. We investigated the relationship between SI and disease type, sex, age, and disease duration using both radiographic and ultrasonographic measurements, and examined longitudinal changes.

Methods: We enrolled PsA (n=41), RA (n=41), and OA (n=40) patients in a cross-sectional study. SI was measured on hand X-rays (length × width) and by ultrasound in medial and lateral planes using a 20 MHz probe. For the longitudinal analysis, 17 patients with ≥2 serial X-rays were included: RA (n=9), PsA (n=5), and OA (n=3). Group differences in SI were analyzed using Kruskal-Wallis with Dunn's test; sex differences by t-tests; and medial vs. lateral ultrasound SI by Wilcoxon signed-rank test. Spearman correlation assessed associations with age, BMI, and disease duration. Linear regression evaluated independent predictors, and mixed-effects modeling assessed longitudinal change.

Results: Radiographic SI was significantly higher in males across all groups (PsA: 31.8 vs. 18.2 mm^2, p=0.007; RA: 34.8 vs. 22.8, p=0.0016; OA: 28.7 vs. 22.8, p=0.011). SI correlated strongly with medial ultrasound SI ($\rho = 0.64$, $p < 0.001$) and moderately with lateral SI ($\rho = 0.45$, $p < 0.001$) (Figure 1). Lateral SI was larger than medial SI across all groups ($p < 0.01$). In a linear model ($R^2 = 0.27$), female sex predicted lower SI ($\beta = -11.4$ mm^2, $p < 0.001$), followed by age ($\beta = +0.16$ mm^2/year, $p = 0.046$) and disease duration ($\beta = +0.38$ mm^2/year, $p = 0.022$). In an interaction model ($R^2 = 0.29$),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Demographic characteristics of the enrolled patients

	RA N = 41[1]	PsA N = 41[1]	OA N = 40[1]
Age (years)	56.2 ± 13.0	49.4 ± 14.9	66.7 ± 10.0
Sex			
Male	14 / 41 (34%)	24 / 41 (59%)	10 / 40 (25%)
Female	27 / 41 (66%)	17 / 41 (41%)	30 / 40 (75%)
Weight (kg)	77.5 ± 18.8	85.3 ± 19.2	72.4 ± 15.1
Height (m)	1.6 ± 0.1	1.7 ± 0.1	1.6 ± 0.1
BMI (kg/m²)	28.7 ± 5.6	29.7 ± 4.8	27.9 ± 5.7
Rheumatoid Factor	32 / 41 (78%)	0 / 40 (0%)	0 / 39 (0%)
Anti-CCP	32 / 41 (78%)	1 / 40 (2.5%)	0 / 39 (0%)
1st MCP Erosion	8 (23%)	4 (11%)	1 (3.1%)
1st MCP Erosion Size (mm)	0.10 ± 0.44	0.03 ± 0.13	0.03 ± 0.19
Any Biologic / Targeted Therapy	28 / 41 (68%)	37 / 41 (90%)	0 / 39 (0%)
NSAID Use	1 / 41 (2.4%)	10 / 41 (24%)	17 / 40 (43%)
Steroid Use	9 / 41 (22%)	0 / 41 (0%)	2 / 40 (5.0%)
Disease Duration (years)	4.8 ± 7.1	3.8 ± 6.2	2.3 ± 4.1

[1]Mean ± SD; n / N (%)

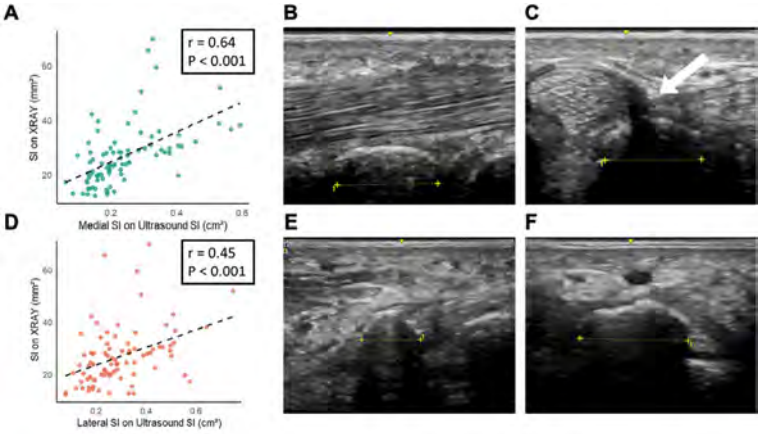


Figure 1. Correlation between Sesamoid Index (SI) measured by Radiographic XRAY and Ultrasound (US). Radiographic SI was calculated as maximum length x width on X-ray. Medial and lateral SI on US was derived from the longitudinal (B, E) and transverse (C, F) measurements respectively. Careful adjustment of the ultrasound probe is necessary to avoid edge shadowing artifacts on the transverse view of the medial sesamoid (white arrow in C). The Spearman correlation between radiographic SI and ultrasonographic medial SI was better than the correlation for lateral SI.

PsA showed a greater rate of SI increase per disease year vs. RA (β = +0.77 mm^2/year, p = 0.042), with no effect in OA. BMI had no impact. Group diagnosis was not independently significant at baseline. A linear mixed-effects model of 47 radiographs from 17 patients showed distinct SI trajectories. PsA patients exhibited progressive SI growth from 18.2 mm^2 (95% CI: 5.6–30.8) at timepoint 1 to 33.2 mm^2 (95% CI: 19.5–46.9) at timepoint 4, while SI remained stable in RA (32.7–36.2 mm^2) and OA (31.1–34.1 mm^2) in Figure 2. This supports greater periosteal remodeling in PsA.

Conclusion: SI is higher in males and increases with age and disease duration. PsA demonstrates the most robust longitudinal SI growth, supporting its potential as a structural marker of disease progression. Ultrasound, particularly medial SI, correlates well with radiography and may serve as a non-radiographic alternative for tracking periosteal changes. Future studies with larger longitudinal cohorts are warranted to validate these findings.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

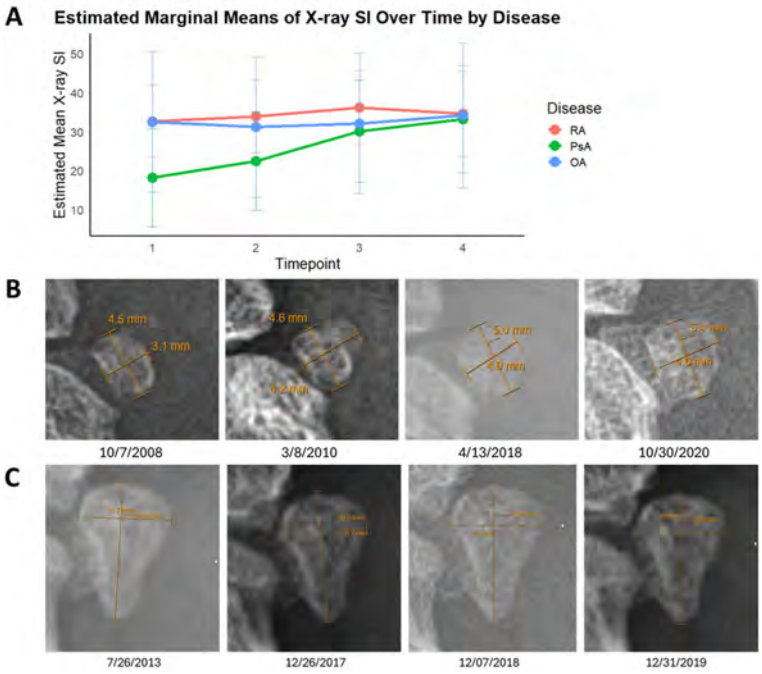


Figure 2. (A) Estimated marginal means of X-ray sesamoid index (SI) over time by disease group. PsA patients showed a progressive increase in SI from timepoint 1 to 4, while RA and OA patients exhibited minimal change. Error bars represent 95% confidence intervals. (B) Representative radiographs from a PsA patient showing progressive enlargement of the medial sesamoid bone over time. (C) Serial radiographs from a RA patient showing stable SI measurements across timepoints, with minimal change in sesamoid size.

Disclosure: H. Vo: None; **E. Kissin**: None; **P. Weilg**: None.

Abstract Number: 2315

Alterations in the Gut Microbiome in Ankylosing Spondylitis and Their Correlation with Disease Activity

Hyemin Jeong[1], Eun-Jung Park[2] and Chan Hong Jeon[1], [1]Soonchunhyang University Bucheon Hospital, Bucheon, Republic of Korea, [2]National Medical Center, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The microbiome significantly influences immune dysfunction and gut dysbiosis in patients with ankylosing spondylitis (AS). This study seeks to define the distinct microbial characteristics of AS and biomarkers associated with disease activity.

Methods: Forty-four patients with AS and 50 healthy controls (HC) were recruited. 16S rRNA gene sequencing was performed to assess the microbiota in stool samples. The Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP) was calculated for all AS patients; scores ≥ 2.1 indicated high disease activity, and < 2.1 indicated low disease activity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The mean age of the AS group was 42.5 years, with 39 males (88.6%). Although the alpha diversity did not differ significantly between the AS and HC groups, marked differences were observed in beta diversity. The relative abundance of Proteobacteria, particularly Gammaproteobacteria, and Enterobacterales, including *Escherichia* spp., was significantly increased in the AS group. In contrast, the abundance of beneficial taxa, including Firmicutes, Clostridia, Clostridiales, Lachnospiraceae, Ruminococcaceae, and *Faecalibacterium*, was higher in the HC group. Among patients with AS, alpha diversity decreased in the high disease activity group compared to the low disease activity group, while beta diversity did not differ significantly. Moreover, *Coprobacter* spp. abundance positively correlated with the Bath Ankylosing Spondylitis Disease Activity Index ($p = 0.032$) and the ASDAS-CRP ($p = 0.023$).

Conclusion: Patients with AS exhibit distinct gut microbiota profiles, with increased Proteobacteria and decreased beneficial taxa such as Firmicutes. Higher disease activity is associated with reduced alpha diversity, while *Coprobacter* spp. abundance correlates with disease activity, suggesting its potential as a biomarker.

Disclosure: H. Jeong: None; **E. Park**: None; **C. Jeon**: None.

Abstract Number: 2316

Sexual Dysfunction in Women with Axial Spondyloarthritis: A Meta-Analysis of FSFI Total and Domain Scores

Gabriela Moreira[1], Hemerli De Cinque Almeida Esteves[2], Nicole Felix[3] and **Jose Fernando Verztman**[1], [1]Hospital Federal dos Servidores do Estado do Rio de Janeiro, Rio de Janeiro, Rio de Janeiro, Brazil, [2]No current affiliation, Columbus, OH, [3]Federal University of Campina Grande, Fortaleza, Ceara, Brazil

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Beyond musculoskeletal manifestations, there is growing recognition of the systemic and psychosocial burden of axial spondyloarthritis (axSpA). Sexual health is an often-overlooked aspect of quality of life in affected women. However, the impact of axSpA on sexual dysfunction (SD) in women remains unknown.

Methods: We systematically searched PubMed, Embase, and Cochrane library for observational studies comparing women with axSpA fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria versus age-matched healthy controls. Our outcomes of interest were total FSFI and individual domain scores (desire, arousal, lubrication, orgasm, satisfaction, and pain). Mean differences (MD) and 95% confidence intervals (CI) were calculated using a random-effects model in R version 4.5.0.

Results: We included four cross-sectional studies comparing women with axSpA to age-matched healthy controls. A total of 174 women with axSpA were included (114 with radiographic axSpA and 60 with non-radiographic axSpA). The mean age was 38.3 years. The FSFI total score was significantly lower in women with axSpA compared to healthy controls (MD -4.69 points; 95% CI -8.83 to -0.54). Significant impairments were also observed in the following FSFI domains: desire (MD -0.81; 95% CI -1.53 to -0.09), arousal (MD -1.07; 95% CI -1.64 to -0.50), lubrication (MD -0.87; 95% CI -1.57 to -0.16) and pain scores (MD -0.59; 95% CI -1.13 to -0.05). However, there were no significant differences in terms of orgasm (MD -0.79; 95% CI -1.83 to 0.26) or satisfaction (MD -0.63; 95% CI -1.75 to 0.49).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

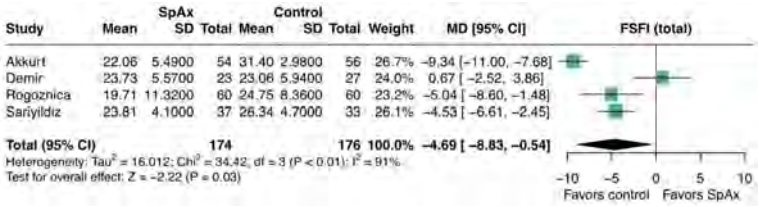


Figure 1. Forest plot showing lower total FSFI scores in women with axial spondyloarthritis compared to healthy controls.

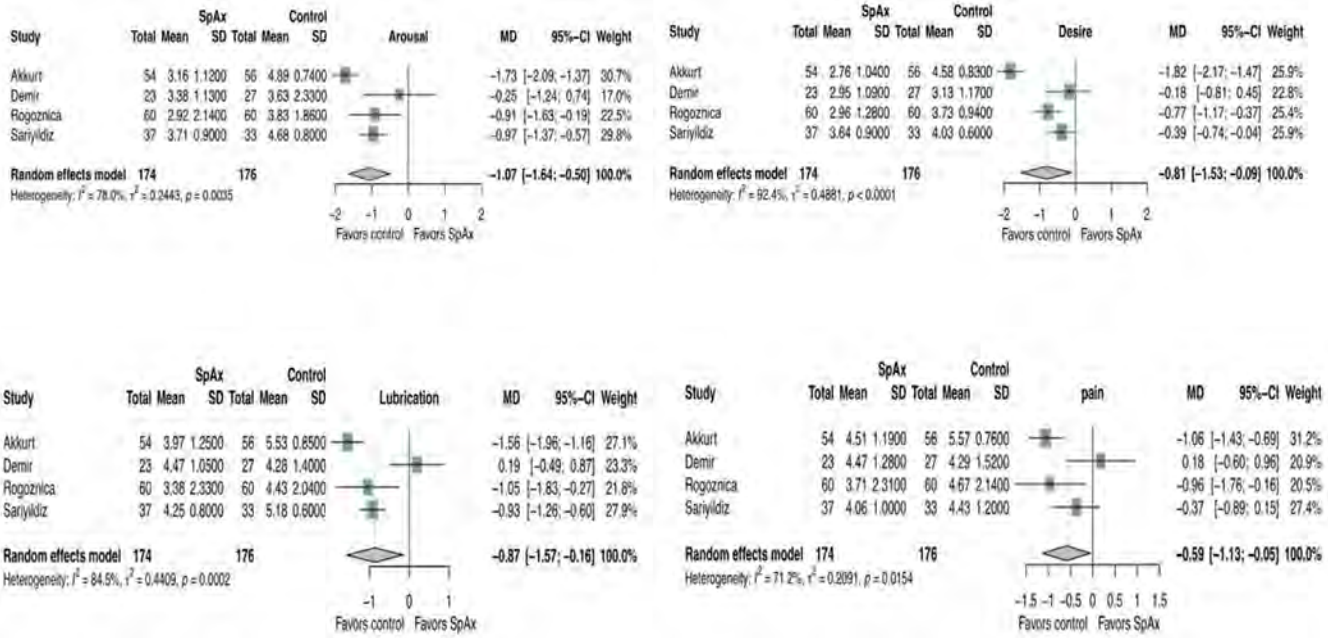


Figure 2. Forest plots showing lower FSFI scores in desire, arousal, lubrication, and pain domains among women with axSpA vs. controls. All differences were statistically significant.

Conclusion: In this meta-analysis, women with axSpA had signs of sexual dysfunction and worse sexual health as compared with age-matched healthy controls, highlighting the importance of incorporating sexual health evaluation into routine axSpA care, regardless of radiographic status.

Disclosure: G. Moreira: Janssen, 6, Novartis, 6; **H. De Cinque Almeida Esteves**: None; **N. Felix**: None; **J. Verztman**: Janssen, 6, UCB, 6.

Abstract Number: 2317

Cardiovascular Risk and Psoriatic Arthritis Features: Dactylitis may Predict Cardiovascular Events

Roel Sanchez Baez[1], **Katherine Benson**[1], Arthur Kavanaugh[2] and Monica Guma[1], [1]University of California, San Diego, La Jolla, CA, [2]Division of Rheumatology, Autoimmunity and Inflammation, UC San Diego School of Medicine, La Jolla, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with PsA have an elevated risk of cardiovascular (**CV**) disease. We assessed whether specific PsA features may predict CV events among PsA patients.

Methods: Data are presented from patients seen at the University of California, San Diego's Healthcare system. Data were collected from 1/1/2012 through 4/5/2025 from all patients with a PsA ICD-10 code, and were procured through data extraction concierge services. All charts were then reviewed and 766 met inclusion criteria: at least one office visit, PsA diagnosis and features confirmed by a rheumatologist.

Participant characteristics were assessed at office visits. Patients were tracked from time of PsA diagnosis until occurrence of a CV event, or their last office visit before the end of the follow-up period. We define a CV event as a new occurrence of one of the following ICD-10 codes: coronary artery disease, peripheral vascular disease, heart failure and transient ischemic attack or stroke. We considered the following PsA features: dactylitis, enthesitis, nail pitting and severe psoriasis (PsO; defined as body surface area ≥%4). Presence/absence of each predictor was ascertained and was assessed as a binary predictor of CV events. Peripheral arthritis was not included as it was inconsistently noted in the charts reviewed.

Unadjusted Kaplan-Meier curves were estimated for each primary predictor. Cox regression models estimated CV risk (Hazard Ratios: HR) and are presented as unadjusted, adjusted for gender, age and smoking status (Model 1), and adjusted for gender, age, smoking status, BMI and race (Model 2).

Results: Mean tracked follow-up time was 4.35 years (SD 3.60) and the median was 3.53. Participant characteristics are shown in **Table 1**. 56 CV events were reported. **Table 2** shows estimated HRs (95% CI) for each predictor and model. Among the variables examined, the presence of dactylitis emerged as a significant predictor of CV events in the adjusted model 2 (HR 1.83; 95% CI [1.04, 3.23]; p=0.036) and neared significance in the adjusted model 1 (HR 1.75; 95% CI [1.00, 3.07]; p=0.05). Kaplan Meier survival curves are presented in **Figure 1**.

Table 1. Participant characteristics (N=766*)

Characteristic	Mean (SD)
Age	57.5 (15.0)
BMI	29.1 (6.3)
PsA duration (yrs)	4.35 (3.60)
	N (%)
Sex	
Male	337 (44.0)
Female	429 (56.0)
Smoking status	
Never	480 (63.3)
Former	224 (29.2)
Current	54 (7.12)
BMI category	
Underweight (<18.5)	12 (1.59)
Normal weight (18.5-25)	189 (25.0)
Overweight (25-30)	268 (35.5)
Obese (≥30)	297 (38.8)
CV event	56 (7.31)
Diabetes	89 (11.6)
Enthesitis	318 (41.5)
Dactylitis	308 (40.2)
Nail involvement	352 (46.0)
Severe psoriasis	300 (39.3)

*Values were not procured for every characteristic in all participants. Smoking status was available for 758 participants, BMI was available for 755, and severe psoriasis status was available for 764.

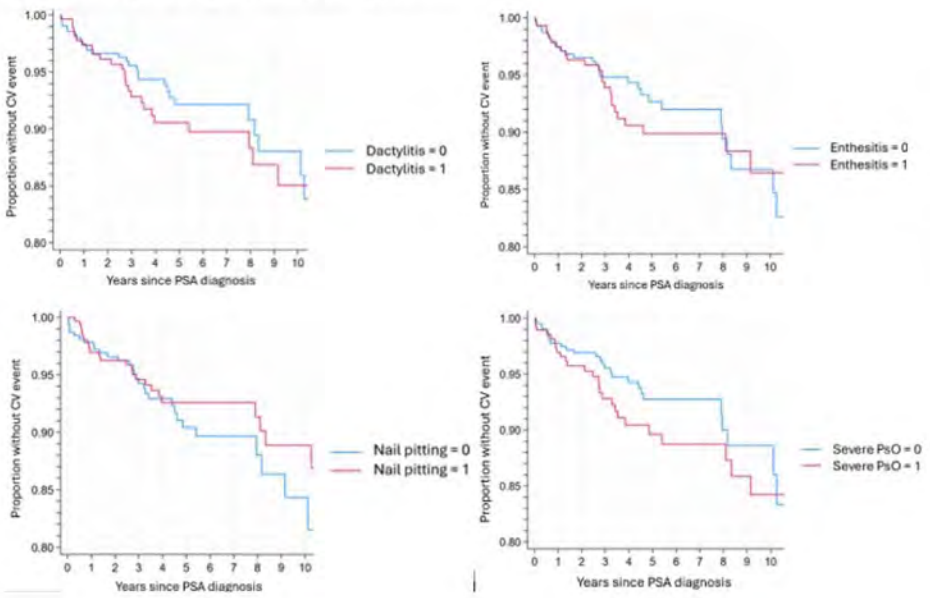
Table 2. Prediction of CV events by PsA features

Predictor	Unadjusted HR (SE) [95% CI] p	Adjusted model 1* HR (SE) [95% CI] p	Adjusted model 2 † HR (SE) [95% CI] p
Dactylitis	1.20 (0.33) [0.70, 2.06] 0.50	**1.75 (0.50) [1.00, 3.07] 0.05**	**1.83 (0.53) [1.04, 3.23] 0.036‡**
Enthesitis	1.11 (0.31) [0.65, 1.91] 0.70	1.19 (0.33) [0.69, 2.05] 0.52	1.13 (0.32) [0.66, 1.96] 0.65
Nail pitting	0.79 (0.22) [0.46, 1.36] 0.38	1.12 (0.32) [0.64, 1.96] 0.69	1.10 (0.31) [0.63, 1.93] 0.73
Severe PsO	1.35 (0.37) [0.79, 2.32] 0.27	1.47 (0.41) [0.85, 2.53] 0.17	1.41 (0.40) [0.81, 2.46] 0.22

*Adjusted for gender, age and smoking status
† Adjusted for gender, age, smoking status, BMI, and race
‡In models adjusting for each covariate independently, only the model adjusted for age is significant: HR (SE) [95% CI] p= 1.77 (0.51) [1.01, 3.10] 0.046 for dactylitis; 1.07 (0.01) [1.05, 1.10] <0.001 for age. Those with dactylitis are significantly younger than those without (mean difference=3.77 yrs, p=0.0008, Wilcoxon rank sum test).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan Meier survival analysis.



0 = No; 1 = Yes

Conclusion: Dactylitis was a significant predictor of CV events in the adjusted model 2. We suggest that confounding by age may have masked this association in the unadjusted model. Individuals with dactylitis were significantly younger than those without, and older age was associated with increased CV risk.

No significant association was observed between CV events and the other PsA features. Some limitations may have affected the strength of our conclusions. We did not have available complete information on PsA treatments, obviating the ability to adjust for this potential confounder. Nor were we able to definitively ascertain prior history of CV events, preventing exclusion of such higher risk patients. Our median tracked follow-up period was shorter than the 7.3 years found in a meta-analysis of 112 cohort studies examining CV outcomes (Magnussen C, et. al. N Engl J Med 2023). Future studies incorporating adjustment for treatment status, more stringent exclusion criteria and a longer follow-up period may help to adjudicate the discrepancy between our findings and literature reporting a link between PsA features and CV risk.

Disclosure: R. Sanchez Baez: None; **K. Benson**: None; **A. Kavanaugh**: Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MoonLake, 2, 5, Novartis, 2, Pfizer, 2, 5, Takeda, 2, 5, UCB, 2, 5; **M. Guma**: Abbvie, 5, Sonoma, 5.

Abstract Number: 2318

Practice Patterns and Barriers in the Referral, Management and Monitoring of Axial Spondyloarthritis: Insights from an Online Survey of Rheumatologists

Khalid Alnaqbi[1], Mohammed Alaswad[2], Tariq Al Araimi[3], Amr Mahmoud[4], Samar Al emadi[5], Hanan Al Rayyes[6], Khuloud Mohammed[7] and Xenofon Barliakos[8], [1]Sheikh Tahnoon Medical city, Al Ain, United Arab Emirates, [2]Faculty of Human Medicine, University of Hama, Hama, Syria, [3]Royal Hospital, Muscat, Oman, [4]Department of Pharmacology, Pharmacy Program, Oman College of Health Sciences, Muscat, Oman, [5]Hamad medical corporation, Doha, Qatar, [6]Department of Medicine, Prince Sultan Military Medical City, Riyad, Saudi Arabia, [7]Farwaniya Hospital, Kuwait, Kuwait, [8]Ruhr-University Bochum, Rheumazentrum Ruhrgebiet, Herne, Germany

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: There is a dearth of literature exploring challenges faced by rheumatologists in the referral, diagnosis, management, and monitoring of patients with suspected axial spondyloarthritis (axSpA) worldwide. Our study aims to understand such challenges faced by rheumatologists in the Gulf countries.

Methods: A cross-sectional online survey was conducted among practicing rheumatologists in six countries using 35-close ended questions. Items underwent refinement using a sensibility assessment framework and were pilot-tested among 12 rheumatologists, and followed international survey reporting guidelines. The survey assessed demographic characteristics, referral patterns, diagnostic features, monitoring practices, and management challenges related to axSpA. Descriptive statistics were applied and normalized average scores were computed for ranking questions and converted into percentages. Data collection occurred between April and May 2021.

Results: A total of 188 responses were received and analyzed (response rate 50.6% during COVID pandemic). Most respondents were consultants (68.1%), practiced in tertiary governmental hospitals (52.7%) and located in urban settings (95.1%) (Table 1).

Table 1: Participants' demographics

	N = 188[/]		N = 188[/]
Professional role in rheumatology		**Years practice**	
Rheumatology fellow/trainee	17 (9.0%)	Missing	4
Practicing internist working in rheumatology setting	13 (6.9%)	0–5	56 (30.4%)
Practicing specialist rheumatologist	30 (16.0%)	6–10	32 (17.4%)
Practicing consultant rheumatologist	128 (68.1%)	11–15	36 (19.6%)
		16–20	24 (13.0%)
		>20	36 (19.6%)
Gender		**Sector of practice**	
Missing	4	Missing	4
Male	111 (60.3%)	Private practice	40 (21.7%)
Female	73 (39.7%)	Secondary government hospital or clinic	47 (25.5%)
		Tertiary government hospital	97 (52.7%)
Country of practice		**Geographic area of practice**	
Missing	4	Missing	4
Saudi Arabia	64 (34.8%)	Urban	175 (95.1%)
United Arab Emirates	40 (21.7%)	Rural	9 (4.9%)
Kuwait	33 (17.9%)	**Certified/trained nurse in rheumatology**	
Qatar	23 (12.5%)	Missing	4
Oman	18 (9.8%)	No	162 (88.0%)
Bahrain	6 (3.3%)	Yes	22 (12.0%)

[/]n (%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

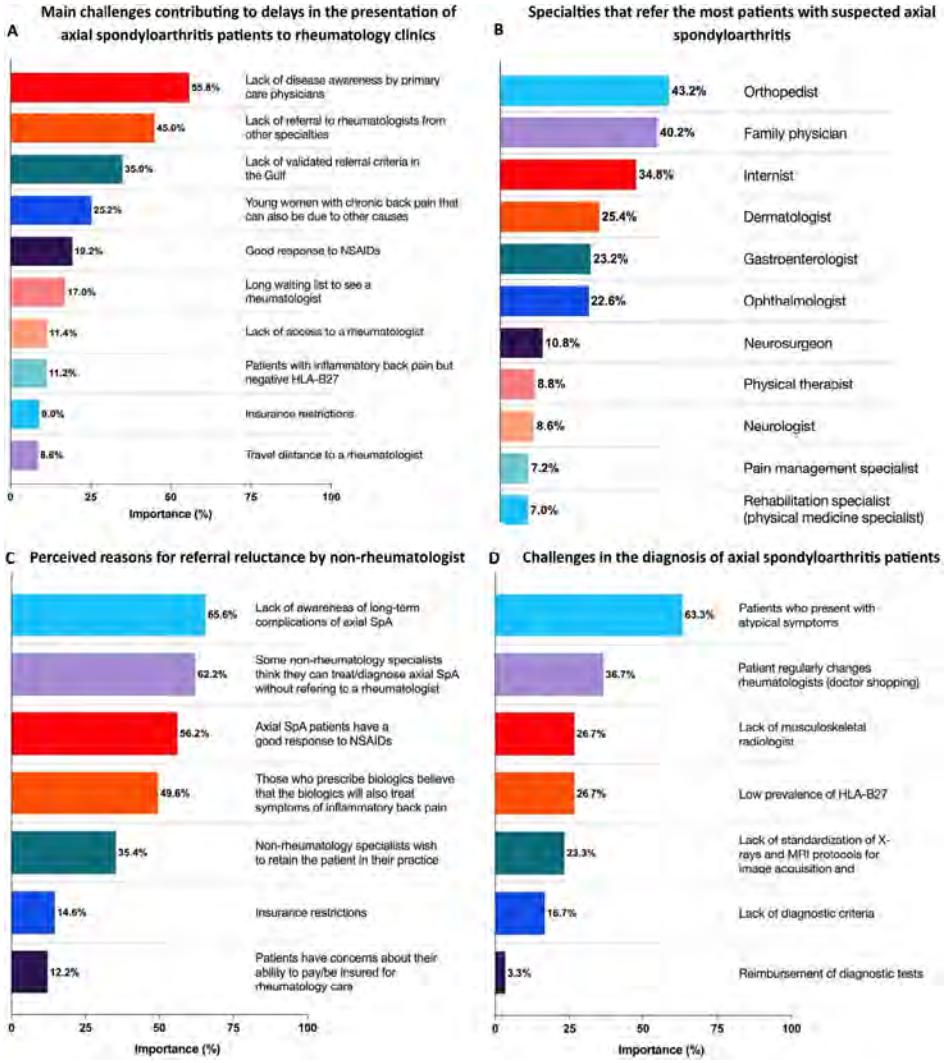


Figure 1. Perceived challenges and referral patterns in axial spondyloarthritis care: (A) Delays in referral to rheumatology, (B) Specialties most frequently referring patients, (C) Reasons for referral reluctance from non-rheumatologists, and (D) Diagnostic challenges.

A majority (88.6%) reported delayed presentation of axSpA patients, primarily due to low disease awareness among primary care physicians (55.8%) and absence of validated referral criteria (35.0%), Figure 1. Orthopedists, family physicians, and internists were among the top referring specialties. Nearly half of respondents believed that non-rheumatology specialists are reluctant to refer their axSpA patients to a rheumatologist.

Diagnostic challenges were reported by 65.5% of respondents, especially in patients with atypical symptoms or limited access to HLA-B27 testing and advanced imaging. Only 28.8% experienced difficulty ordering or interpreting HLA-B27, primarily due to test unavailability (66.7%), or perceived low prevalence of HLA-B27 in their patient population (31%).

The majority (76.6%) had access to a musculoskeletal radiologist to read X-rays and MRIs. Trust in radiology reports of sacroiliac X-rays and MRI for assessing suspected axSpA was generally moderate to high.

Figure 2 illustrates the preferred frequency of monitoring various axSpA disease metrics across different time intervals, including those rarely or never used.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

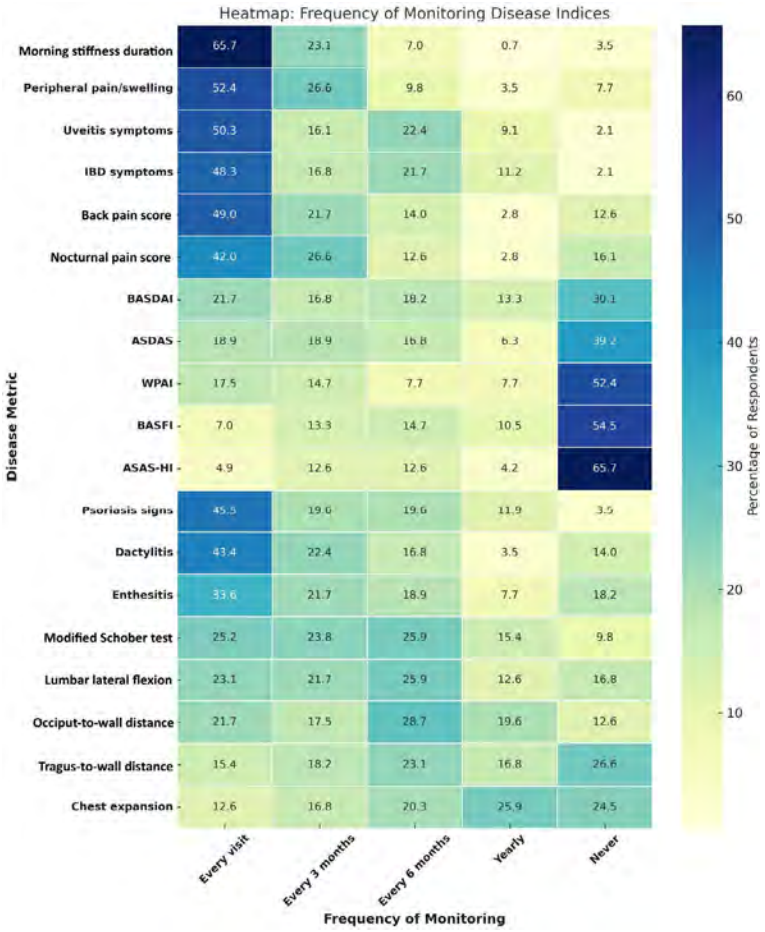


Figure 2: Frequency of monitoring disease metrics perceived by rheumatologists

About 47% and 31.5% of respondents reported difficulties in tracking patient-reported outcomes and physical exam findings, respectively—mainly due to busy schedule and lack of a nurse to support.

In terms of management, patient non-adherence due to fear of drug side effects (44.1%) or symptom improvement (43.1%) were leading obstacles. Only 12% had access to a rheumatology-trained nurse. Physiotherapy was considered to be usually useful by 45.2% of rheumatologists.

Conclusion: This is the first comprehensive study from the Middle East and North Africa region to explore clinical practices and challenges in the referral, diagnosis, management, and monitoring of axSpA among rheumatologists. Delays in diagnosis and referral suggest the need for educational initiatives targeting non-rheumatologists, and improved multidisciplinary support.

Disclosure: K. Alnaqbi: None; **M. Alaswad**: None; **T. Al Araimi**: None; **A. Mahmoud**: None; **S. Al emadi**: None; **H. Al Rayyes**: None; **K. Mohammed**: None; **X. Barliakos**: Abbvie, 1, 2, 5, Advanz, 1, 2, Alexion, 1, 2, Alfasigma, 1, 2, Amgen, 1, 2, Astra Zeneca, 1, 2, Bristol-Myers Squibb(BMS), 1, 2, Celltrion, 1, 2, 5, Cesas, 1, 2, Clarivate, 1, 2, Eli-Lilly, 1, 2, Galapagos, 1, 2, Janssen, 5, Johnson and Johnspn, 1, 2, Moonlake, 1, 2, 5, Novartis, 1, 2, 5, Peervoice, 1, 2, Pfizer, 1, 2, Roche, 1, 2, Sandoz, 1, 2, Springer, 1, 2, Stada, 1, 2, Takeda, 1, 2, UCB Pharma, 1, 2, Zuellig, 1, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2319

Reducing selection bias while maintaining precision through an integrated analysis: 2-year longitudinal analysis of imaging outcomes in the SPondyloArthritis Caught Early cohort

Liese de Bruin[1], Floris A. van Gaalen[1], Manouk de Hooge[2], Miranda van Lunteren[1], Mary Lucy Marques[3], Monique Reijnierse[4], Roberta Ramonda[5], Inger Jorid Berg[6], Carl Turesson[7], Robert Landewé[8], Désirée Van Der Heijde[1] and Sofia Ramiro[9], [1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [2]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [3]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [4]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [5]Rheumatology Unit-DIMED-University of Padova ITALY, Padova, Padua, Italy, [6]6Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Nepal, [7]Lund University, Malmö, Sweden, [8]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [9]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Imaging outcomes in ongoing cohort studies are typically evaluated across multiple reading rounds by several readers. Often, only scores from the most recent reading round are used, disregarding valuable data from previous rounds and potentially introducing selection bias by excluding participants lost to follow-up. Using an integrated analysis is an alternative incorporating scores from multiple readers and rounds. This method provides a more truthful reflection, but may introduce additional variability, potentially reducing the estimates' precision. Therefore, we assessed if an integrated analysis, using available imaging data over time from different reading rounds, affects the precision of change estimates in early axSpA, using a completers analysis as reference.

Methods: Patients with chronic back pain (≥3 months; ≤2 years; onset < 45 years) from the SPondyloArthritis Caught Early cohort with a rheumatologist's diagnosis of axSpA after two years of follow-up were included. MRIs and radiographs of the sacroiliac joints (SIJ) and spine obtained at baseline, 3 months, 1 and 2 years of follow-up were scored for inflammatory and structural lesions by ≥2 readers in two reading rounds: in round A, baseline, 3 months and 1 year were scored; in round B, baseline, 3 months, 1 and 2 years were scored. Change of each imaging outcome over time was analyzed with multilevel generalized estimating equations (considering the reader level), with time as explanatory variable. Two approaches were used: i) 'integrated analysis' (patients with ≥1 score from ≥1 reader from ≥1 reading round); ii) 'completers-only analysis' (patients with ≥1 score from ≥1 reader from round B at 2-year follow-up). The second and commonly used approach was considered the reference. We tested different time transformations to investigate which yielded the lowest quasi-likelihood under the independence model criterion, and the best model fit. In cases of comparable fit, the model with the simplest time format was chosen.

Results: In total, we analyzed 332 patients with axSpA (mean age 30 (SD 8) years; 53% males) of which 279 (84%) patients were included in the completers-only analysis. Binary and continuous variables for inflammatory lesions decreased over time in the MRI of the SIJ and spine, while structural lesions increased (Tables 1 and 2). Due to the best or very comparable fit, models with a linear time representation were used for all outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Change per year in the percentage of positive cases for binary imaging outcomes over 2 years of follow-up, according to the integrated analysis and completers-only analysis methods, in early axSpA patients

Imaging outcomes	Integrated analysis % change per year (95% CI) (*n* = 315-326)	Completers-only analysis % change per year (95% CI) (*n* = 273-279)
SACROILIAC JOINTS		
Inflammatory lesions (MRI-SIJ)		
Sacroiliitis (ASAS criteria)	-5.57 (-8.31; -2.83)	-5.78 (-8.57; -2.99)
Structural lesions (radiograph-SIJ)		
Sacroiliitis (mNY criteria)	0.90 (0.06; 1.74)	0.84 (0.05; 1.63)
SPINE		
Inflammatory lesions (MRI-spine)		
MRI-spine positive (ASAS criteria)	-1.55 (-3.13; 0.02)	-1.29 (-2.85; 0.27)
Structural lesions (radiograph-spine)		
≥1 syndesmophyte	1.28 (0.05; 2.52)	1.34 (0.07; 2.60)

The 'integrated analysis' included patients with ≥1 score from ≥1 reader from ≥1 reading round, and the 'completers-only analysis' included patients with ≥1 score from ≥1 reader from round B at 2-year follow-up. ASAS, Assessment of Spondyloarthritis International Society; axSpA: axial spondyloarthritis; BME, bone marrow edema; CI, confidence interval; mNY, sacroiliitis according to the modified New York criteria; MRI, magnetic resonance imaging; No, number; SIJ, sacroiliac joints.

Table 2. Change per year in continuous imaging outcomes over 2 years of follow-up, according to the two different analytical methods, in early axSpA patients

Imaging outcomes	Integrated analysis Unit change per year (95% CI) (*n* = 309-325)	Completers analysis Unit change per year (95% CI) (*n* = 273-278)
SACROILIAC JOINTS		
Inflammatory lesions (MRI-SIJ)		
SPARCC SIJ score (0-72)	-1.54 (-2.05; -1.02)	-1.68 (-2.19; -1.16)
Structural lesions (MRI-SIJ)		
No. of fat lesions and/or erosions (0-80)	0.52 (0.32; 0.72)	0.58 (0.38; 0.77)
No. of erosions (0-40)	0.18 (0.09; 0.27)	0.22 (0.12; 0.31)
No. of fat lesions (0-40)	0.34 (0.18; 0.50)	0.36 (0.20; 0.52)
No. of (partial) ankylosis (0-24)	0.04 (0.01; 0.07)	0.04 (0.01; 0.07)
Total structural lesions (0-144)	0.55 (0.35; 0.75)	0.61 (0.41; 0.82)
Total structural lesions without sclerosis (0-104)	0.56 (0.36; 0.76)	0.62 (0.42; 0.82)
Structural lesions (radiograph-SIJ)		
mNY continuous grade (0-8)	0.06 (0.02; 0.09)	0.06 (0.03; 0.10)
SPINE		
Inflammatory lesions (MRI-spine)		
SPARCC spine score (0-414)	-0.56 (-0.90; -0.22)	-0.45 (-0.76; -0.15)
Structural lesions (MRI-spine)		
No. of erosions (0-92)	0.01 (-0.02; 0.03)	0.02 (-0.01; 0.04)
No. of fat lesions (0-92)	0.28 (0.13; 0.44)	0.35 (0.19; 0.50)
No. of bone spurs (0-92)	0.02 (-0.02; 0.06)	0.04 (-0.00; 0.08)
No. of ankylosis (0-46)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)
Total structural lesions (0-322)	0.37 (0.18; 0.55)	0.41 (0.23; 0.59)
No. of fat and/or erosions and/or bone spurs (0-276)	0.32 (0.15; 0.50)	0.41 (0.23; 0.59)
Structural lesions (radiograph-spine)		
mSASSS (0-72)	0.08 (0.01; 0.15)	0.08 (0.01; 0.16)

The 'integrated analysis' included patients with ≥1 score from ≥1 reader from ≥1 reading round, and the 'completers-only analysis' included patients with ≥1 score from ≥1 reader from round B at 2-year follow-up. The total of structural lesions in the MRI of the sacroiliac joints is a sum of erosions, fat lesions, (partial) ankylosis, and sclerosis. The total of structural lesions in the MRI of the spine is a sum of erosions, fat lesions, bone spurs and ankylosis. AxSpA: axial spondyloarthritis; CI, confidence interval; mNY continuous grade, sacroiliitis grade score conform the modified New York criteria; MRI, magnetic resonance imaging; mSASSS, modified stoke ankylosing spondylitis spinal score; No., number; SIJ, sacroiliac joints; SPARCC SIJ score, SpondyloArthritis Research Consortium of Canada score for inflammatory lesions.

Comparing both analyses, the integrated analysis included more patients but with similar levels of precision of the change estimates as the completers-only analysis for both the binary and continuous variables. Particularly for binary outcomes, a similar change was found by the integrated analysis with more precision compared to the completers-only analysis, e.g. sacroiliitis according to the ASAS criteria [estimated yearly % change (95% CI): -5.57 (-8.31; -2.83) vs -5.78 (-8.57; -2.99)].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this longitudinal study, the integrated analysis was shown to allow for the inclusion of all available data, thereby reducing selection bias in determining the population for analysis, while maintaining precision of change estimates in patients with early axSpA.

Disclosure: L. de Bruin: None; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **M. de Hooge**: UCB pharma, 2; **M. van Lunteren**: None; **M. Marques**: Novartis, 2, 6; **M. Reijnierse**: None; **R. Ramonda**: None; **I. Berg**: None; **C. Turesson**: AbbVie/Abbott, 1, 6, Nordic Drugs, 2, 6, Novartis, 1, 6; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2320

Sleep Disturbance in Psoriatic Arthritis: Prevalence by Minimal Disease Activity Status and Associated Clinical Factors

Lourdes Perez Chada[1], Vivi Feather[2], Grace Carter[2], Helen Early[3], Emily Tsai[2], Jing Cui[4], Avery LaChance[5], Rochelle Castillo[6], Neda shahriari[2], Alexis Ogdie[7], Monika Haack[2], Elizabeth Klerman[2], Michael Weinblatt[8], Nancy Shadick[9], Joseph Merola[10] and Chinmayi Naik[3], [1]Harvard Medical School, Wayland, MA, [2]Mass General Brigham, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham Women's Hospital, Boston, MA, [5]Brigham and Women's Hospital, Jamaica Plain, MA, [6]Brigham and Women's Hospital, Brookline, MA, [7]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [8]Brigham and Women's Hospital/ Harvard Medical School, Waban, MA, [9]Brigham & Women's Hospital, Boston, MA, [10]UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Sleep disturbance is a common and burdensome symptom in psoriatic arthritis (PsA), but its clinical determinants remain poorly understood. Using data from the Cohort for Psoriasis and Psoriatic Arthritis (COPPAR), we aimed to (1) compare the prevalence of sleep disturbance between patients who met Minimal Disease Activity (MDA) criteria and those who did not, and (2) identify clinical and patient-reported factors associated with sleep disturbance.

Methods: This cross-sectional study included patients with PsA enrolled in COPPAR. The primary outcome was the sleep item from the PsAID-9 questionnaire (0–10 scale). We compared the prevalence of clinically meaningful sleep disturbance (defined as PsAID sleep score > 4) between patients in MDA and those not in MDA using chi-square tests. We evaluated predictors using a general linear model (GLM) for the continuous PsAID sleep score. The initial models included age, sex, pain, itch, PHQ-8, FACIT fatigue, PROMIS anxiety, skin and joint global assessments, DLQI, MDHAQ, enthesitis score, tender/swollen joint counts, and topical treatment use. Sleep disorder diagnosis was added in sensitivity analysis.

Results: Among 204 patients with PsA, 112 (54.9%) were female, and 191 (93.6%) identified as White. MDA was achieved by 101 participants (49.5%). A diagnosis of sleep disorder was reported in 36 participants (17.6%). Most (n = 173, 84.8%) were on biologic, targeted synthetic, or conventional systemic therapy, and 111 (55%) used topical agents.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Associations Between PsAID-9 Sleep Score and Clinical, Demographic, and Patient-Reported Factors: Results From Primary Analysis Using General Linear Model

Predictor	Estimate (B)	95% CI	Standard Error	p-value
Pain Global (NRS)	0.47	0.34 to 0.60	0.07	<0.0001
Itch Assessment (NRS)	0.25	0.12 to 0.39	0.07	0.0003
Topical Treatment Use (Yes vs No)	–0.60	–1.17 to –0.03	0.29	0.0386
FACIT Fatigue Score	–0.09	–0.12 to –0.05	0.02	<0.0001
PHQ-8 Score	0.08	–0.03 to 0.20	0.06	0.1441
Age*	0.00	–0.02 to 0.02	0.01	0.9573
Sex (Female vs Male)*	–0.02	–0.59 to 0.55	0.29	0.9494

NRS, Numerical Rating Scale

All estimates are from a fully adjusted model.
Beta coefficients represent the mean change in PsAID-9 sleep score per unit increase in the predictor (or the difference in means for binary predictors).

*Age and sex were retained in all models regardless of statistical significance

NRS, Numerical Rating Scale All estimates are from a fully adjusted model. Beta coefficients represent the mean change in PsAID-9 sleep score per unit increase in the predictor (or the difference in means for binary predictors). *Age and sex were retained in all models regardless of statistical significance

Table 2. Associations Between PsAID-9 Sleep Score and Clinical, Demographic, and Patient-Reported Factors: Results From A Sensitivity Analysis Including Sleep Disorder Diagnosis Using General Linear Model

Predictor	Estimate (B)	95% CI	Standard Error	p-value
Pain Global (NRS)	0.46	0.34 to 0.58	0.06	<0.0001
Itch Assessment (NRS)	0.24	0.10 to 0.38	0.07	0.0007
Topical Treatment Use (Yes vs No)	–0.64	–1.20 to –0.09	0.28	0.024
FACIT Fatigue Score	–0.05	–0.10 to –0.01	0.02	0.0287
PHQ-8 Score	0.11	0.00 to 0.22	0.05	0.0498
Sleep Disorder Diagnosis	0.90	0.20 to 1.61	0.36	0.013
Age*	0.00	–0.03 to 0.03	0.01	0.825
Sex (Female vs Male)*	0.05	–0.53 to 0.63	0.29	0.8689

NRS, Numerical Rating Scale

All estimates are from a fully adjusted sensitivity model including sleep disorder diagnosis.
Beta coefficients represent the mean change in PsAID-9 sleep score per unit increase in the predictor (or the difference in means for binary predictors).

*Age and sex were retained in all models regardless of statistical significance

NRS, Numerical Rating Scale All estimates are from a fully adjusted sensitivity model including sleep disorder diagnosis. Beta coefficients represent the mean change in PsAID-9 sleep score per unit increase in the predictor (or the difference in means for binary predictors). *Age and sex were retained in all models regardless of statistical significance

Among those in MDA, 9 (8.9%) reported a PsAID-9 sleep score > 4, compared to 37 (35.9%) among those not in MDA. PsAID-9 sleep scores were significantly associated with MDA status ($\chi^2 = 20.53$, $p < 0.0001$).

In the primary GLM ($R^2 = 0.52$), pain severity ($\beta = 0.47$, $p < 0.0001$) was the strongest independent predictor of worse sleep. Greater itch ($\beta = 0.25$, $p = 0.0003$) and fatigue (lower FACIT; $\beta = –0.09$, $p < 0.0001$) were also significantly associated with worse sleep. Current topical agent use was associated with better sleep ($\beta = –0.60$, $p = 0.039$). PHQ-8 score was not retained in the final model.

In the sensitivity model ($R^2 = 0.55$), sleep disorder diagnosis was independently associated with worse sleep ($\beta = 0.90$, $p = 0.013$). Pain ($\beta = 0.46$, $p < 0.0001$), itch ($\beta = 0.24$, $p = 0.0007$), fatigue ($\beta = –0.05$, $p = 0.0287$), and PHQ-8 score ($\beta = 0.11$, $p = 0.0498$) were also independently associated with worse sleep. Topical treatment use remained protective ($\beta = –0.64$, $p = 0.024$).

Conclusion: Patients in MDA were significantly less likely to report clinically meaningful sleep disturbance. In multivariable models, worse sleep was consistently associated with higher pain, greater itch, and more fatigue. Longitudinal studies are needed to better understand temporal relationships and inform targeted sleep interventions in PsA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Perez Chada: Bristol-Myers Squibb(BMS), 2, 6, Takeda, 2; **V. Feather**: None; **G. Carter**: None; **H. Early**: None; **E. Tsai**: None; **J. Cui**: None; **A. LaChance**: Guidepoint, 2, 6, Janssen, 2, 6, MedaCorp, 2, 6, Merck/MSD, 5, Pfizer, 5, TD Cowen, 2, 6; **R. Castillo**: Chronicle Medical Software, Inc., 2; **N. shahriari**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **M. Haack**: None; **E. Klerman**: Buck Institute on Aging, 2, Chronsulting, 12, Partner is founder and CSO, Lorentz Center, 12, Travel support, Sleep Research Society, 6, 12, Travel support, Society for Research in Biological Rhythms, 12, Travel support; **M. Weinblatt**: aclaris, 2, amgen, 2, anaptysbio, 2, Artiva Bio, 2, Biohaven, 2, Bristol-Myers Squibb(BMS), 2, 5, Canfite, 11, Curie Bio, 2, Deep Cure, 2, Eli Lilly, 2, Gilead, 2, Ignite, 2, Inmedix, 11, Janssen, 5, Janux Therapeutics, 2, Johnson and Johnson, 2, Lifordi, 2, Marvel Bio, 2, Matchpoint, 2, Merck/MSD, 2, Neutrolis, 2, Novartis, 2, Sana, 2, Santa Ana, 2, Sci Rhom, 2, scipher medcine corp, 11, SetPoint Medical, 2, Surf Therapeutics, 2, Thymmune, 2, Xencorp, 2, ZuraBio, 2; **N. Shadick**: Bristol-Myers Squibb(BMS), 5, Janssen, 5; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **C. Naik**: None.

Abstract Number: 2321

Uncovering Clinical Phenotypes of Sexual Dysfunction in Spondyloarthritis: A Multidimensional Analysis

Martín Valdez-López[1], Ana Barrera-Vargas[1], Javier Merayo-Chalico[2], Irazú Contreras-Yañez[3], Carlos Abdiel Abitia Borboa[4], Iris Paola García-Herrera[1], Raúl Pérez-Gamboa[1] and Guillermo Arturo Guaracha-Basáñez[1], [1]Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Tlalpan, Distrito Federal, Mexico, [2]Reumátika, Centro de Vanguardia en Reumatologáa, Ciudad de México, Federal District, Mexico, [3]Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Tlalpan, Mexico, [4]Universidad Autónoma de Sinaloa Facultad de Medicina Culiacan, Culiacan, Sinaloa, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Spondyloarthritis (SpA) impacts patient's life, including functionality, QoL, emotional state, and sexual function. The current study was conducted to determine the frequency of sexual function abnormalities and the risk factors associated with this complication.

Methods: We conducted a study at a tertiary care center in Mexico City from Oct 2024 to Apr 2025. We included patients diagnosed with SpA and used self-administered questionnaires to assess different PROs (disease activity, QoL, physical function, anxiety, and depression). Sexual function was evaluated using CSFQ-14. Additionally, patients were asked which specific manifestation of their disease harmed their sexual function from multiple different options, or to write it if not present. We also asked whether patients had discussed sexual health with their rheumatologist.

Results: Seventy-eight patients were included; 63% were men, with a median age of 48 years (IQR 34-57). Most patients had axial disease (n=44, 56.4%), and 55.7% (n=43) had a positive HLA-B27. Sexual dysfunction was reported by 60.3% (n=47). Table 1 summarizes the characteristics of patients with and without sexual dysfunction. Patients with sexual dysfunction had a higher prevalence of radiographic disease, more comorbidities, and higher depression scores. In the logistic regression, hypertension (OR 12.5, 95%CI 1.3-122.1) and depression score (OR 1.2, 95%CI 1.0-1.4) were associated with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient characteristics according to the presence or absence of sexual dysfunction

	Total sample n=78	Sexual dysfunction n=47 (60.3%)	No Sexual dysfunction n=31 (39.7 %)	p
Demographic characteristics				
Male sex- n, (%)	49 (63)	32 (68.1)	17 (54.8)	0.24
Age, years, median (IQR)	48 (34-57)	43 (34-56)	51 (3-58)	0.19
Reported having a partner- n, (%)	52 (67)	29 (61.7)	23 (74.2)	0.25
Schooling, years, median (IQR)	15 (10.8-16)	15 (12-17)	13(10-16)	0.07
Weight- kg, median (IQR)	73.5 (62-82)	78 (67-85.5)	67 (58-74.5)	**0.01**
Reported any physical activity- n, (%)	45 (57.7)	30 (63.8%)	15 (48.4%)	0.17
Spondyloarthritis specific characteristics				
Years since diagnosis, median (IQR)	10.5 (3-22.5)	14 (3-25)	9 (2-14)	0.14
Axial involvement- n, (%)	44 (56.4)	27 (57.4)	17 (54.8)	0.82
Radiographic SpA- n, (%)	23 (29.5)	10 (21.3)	13 (41.9)	**0.05**
Non-radiographic SpA- n, (%)	15 (19.2)	14 (29.8)	1 (3.2)	**0.001**
Positive HLAB-27 - n, (%)	43 (55.1)	27 (57.4)	12 (38.7)	0.56
Treatment with cDMARD- n, (%)	37 (47.4)	20 (42.6)	17 (54.8)	0.29
Treatment with bDMARD- n, (%)	34 (43.6)	21 (44.7)	13 (41.9)	0.81
Comorbidities				
Lung disease- n, (%)	3 (3.8)	0 (0.0)	3 (9.7)	**0.03**
Peripheral artery disease- n, (%)	5 (6.4)	1 (2.1)	4 (12.9)	**0.05**
High blood pressure- n, (%)	8(10.2)	2 (4.3)	6 (19.4)	**0.03**
Obesity - n, (%)	15 (19.2)	12 (25.5)	3 (9.7)	0.08
Smoking- n, (%)	10 (12.8)	8 (17.0)	2 (6.5)	0.17
Patient reported outcomes				
HADS depression score, median (IQR)	4 (1-7)	3 (1-7)	6 (2-9)	**0.05**
ASQoL score, median (IQR)	5.5 (2-9)	6 (1-9)	5 (2-9)	0.92
BASFI score , median (IQR)	1.8 (0.5-3.9)	1.4(0.4-3.9)	2.3(0.5-4.1)	0.65
BASDAI score, median (IQR)	3(1.4-5.2)	2.9(1-5.8)	3.8(1.5-4.9)	0.79
ASAS-HI score, median (IQR)	4.2(2-9.3)	4(1.9-10)	6(2-9)	0.58
ASDAS CRP, median (IQR)	1.8(1.2-2.7)	1.8(1.2-2.9)	1.7(1.2-2.5)	0.46
Modified Schober- cm median (IQR)	5.5(5-6.5)	5(5-6.5)	6(5-6)	0.70
HAQ score, median (IQR)	0.1(0-0.6)	0.1(0-0.5)	0.3(0-0.9)	0.23

Abbreviations: IQR: Interquartile range, ASAS-HI: Assessment of Spondyloarthritis International Society Health Index, ASDAS: Axial Spondyloarthritis Disease Activity Score, ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index HADS: Hospital Anxiety and Depression Scale, SpA: spondyloarthritis

sexual dysfunction; conversely, lower weight (OR 0.93, 95%CI 0.8-0.9) and non-radiographic axial disease (OR 0.06, 95%CI 0.007-0.53) were associated with a protective effect.

Three distinct patient clusters were identified using principal component analysis (PCA) of four standardized clinical variables (CSFQ-14, HAQ, BASDAI, ASQoL): cluster 1 (preserved sexual function, low disease activity, and better QoL), cluster 2 (moderate impairment across domains), cluster 3 (marked sexual dysfunction, high functional limitation, and poor QoL). PCA1 reflected the overall clinical burden (HAQ, BASDAI, ASQoL), while PCA2 distinguished the sexual function. This confirms that sexual health forms a distinct axis, partially independent from physical and inflammatory burden. (Figure 1A).

Most patients (n=47, 60.3%) considered that at least one disease manifestation harmed their sexual function (Figure 2). A high proportion of patients (n=53, 67.9%) reported they never talked about sexual function with their rheumatologist, but most (n=71, 91%) considered it was important for their rheumatologist to discuss these issues.

Conclusion: Sexual dysfunction is a frequent and often under-recognized complication in these patients. Radiographic disease, hypertension, and depression were independent risk factors, whereas non-radiographic SpA was associated with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

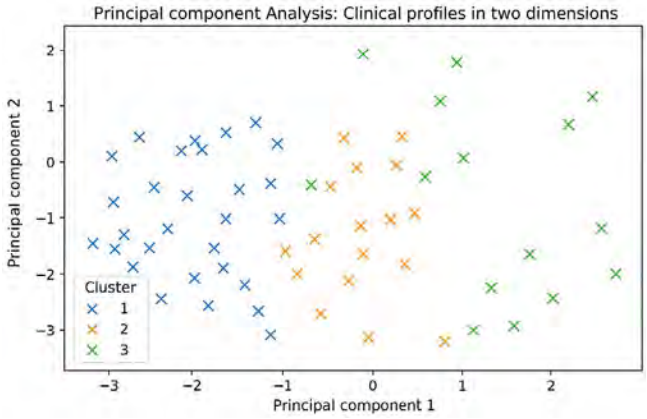


Figure 1. Principal component analysis identified two axes. Component 1 (52.7%) captured overall clinical burden (HAQ, BASDAI, ASQoL). Component 2 (25.7%) was defined by CSFQ-14, representing a distinct dimension of sexual dysfunction. Three clinical clusters emerged across these axes, including one with high disease burden and severe sexual dysfunction..

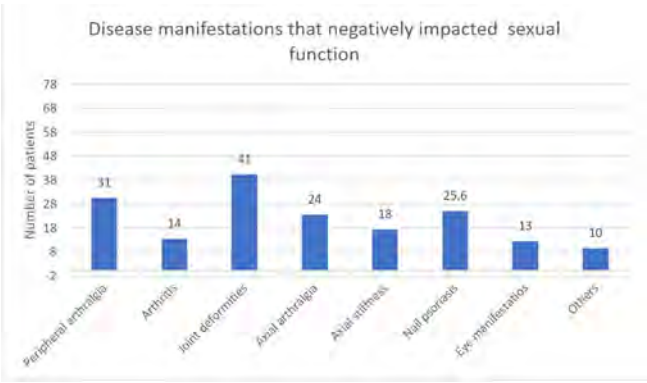


Figure 2. Most frequently reported disease manifestations that patients identified to have a negative impact on their sexual function

preserved sexual function. Cluster analysis revealed three distinct clinical profiles, highlighting a subgroup with substantial clinical impairment and another with preserved sexual function despite active disease, suggesting resilience mechanisms. These findings underscore the need for personalized strategies and for proactively addressing sexual health.t

Disclosure: M. Valdez-López: None; **A. Barrera-Vargas**: None; **J. Merayo-Chalico**: AbbVie/Abbott, 6, Janssen, 6, Pfizer, 6; **I. Contreras-Yañez**: None; **C. Abitia Borboa**: None; **I. García-Herrera**: None; **R. Pérez-Gamboa**: None; **G. Guaracha-Basáñez**: None.

Abstract Number: 2322

Gender-related Differences in Peripheral and Axial Spondyloarthritis

Mehmet Tuncay Duruöz[1], Halise Hande Gezer[1], İlknur Aktaş[2], Servet Akar[3], Nilay Şahin[4], Özgür Akgül[5], Sami Hizmetli[6], Meltem Alkan Melikoğlu[7], Umut Kalyoncu[8], Erhan Çapkın[9], fatma Gülçin Ural[10], Figen Yılmaz[11], Sebnem ATAMAN[12] and İlhan Sezer[13], [1]Marmara University Medical School PMR Department, Rheumatology Division, Istanbul, Turkey, [2]Istanbul Fatih Sultan Mehmet Training and Research Hospital, PMR, Turkey, Istanbul, Turkey, [3]Department of Medicine, Izmir Katip çelebi University School of Medicine, Izmir, Turkey, [4]Balikesir University School of Medicine, PMR, Turkey, Balıkesir, Turkey, [5]Manisa Celal Bayar University School of Medicine, Rheumatology, Turkey, Manisa, Turkey, [6]Sivas Cumhuriyet University School of Medine, Rheumatology, Turkey, Sivas, Turkey, [7]Erzurum Atatürk University School of Medicine, Rheumatology, Turkey, Erzurum, Turkey, [8]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [9]Karadeniz Teknik University School of Medicine, PMR, Turkey, Trabzon, Turkey, [10]Ankara Yildirim Beyazit University School of Medicine, PMR, Turkey, Ankara, Turkey, [11]Istanbul Sisli Etfal Training and Research Hospital, PMR, Turkey, Istanbul, Turkey, [12]Ankara University School of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medicine, Rheumatology, Turkey, Ankara, Turkey, [13]Akdeniz University School of Medicine, Rheumatology, Turkey, Antalya, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: This study sought to compare clinical characteristics between female and male patients with spondyloarthritis (SpA) in a Turkish population.

Methods: This study included 489 peripheral and axial SpA patients recruited from different regions of Türkiye in the ASAS-PerSpA study. Demographic and clinical characteristics such as axial involvement, peripheral arthritis, enthesitis, dactylitis, uveitis, psoriasis, and intestinal involvement, and clinometric information including BASDAI, ASDAS, tender joint count, swollen joint count, enthesitis count and FiRST fibromyalgia score were evaluated according to gender.

Results: Of the patients included in the study, 256 were male and 233 were female. The mean age was 40.24 (SD:11.27) years for males and 43.61 (SD:11.01) years for females (p=0.002). Body mass index was 26.23 (SD:3.97) kg/m^2 for males and 27.01 (SD:5.58) kg/m^2 for females (p=0.006). In axial SpA (n=391), 230 were male and 161 were female (p< 0.001), whereas in peripheral SpA (n=96), 43 were male and 53 were female (p=0.09), and in psoriatic arthritis (n=80), 19 were male and 61 were female (p< 0.001).

Back pain with age at onset < 45 years, sacroiliitis on pelvis x-ray, and HLAB27 positivity were more common in males than females (p< 0.05). While axial involvement of SpA was more common in males, past or present arthritis compatible with SpA, peripheral articular disease, spondyloarthritis-related enthesitis, psoriasis, and dactylitis were more common in females (p< 0.05). There were no significant differences between the genders in the uveitis and inflammatory bowel disease. Regarding

Table. Comparison of Clinical Characteristics According to Gender

	Sex mean (SD) or n (%)		Total	p
	Male	Female		
Age	40,24 ± 11,27	43,61 ± 11,01	41,84 ± 11,26	**0,002**
BMI	26,23 ± 3,97	27,88 ± 6,84	27,01 ± 5,58	**0,006**
Axial spondyloarthritis, Yes	230 (89,8)	161 (69,1)	391 (80)	**<0,001**
Peripheral spondyloarthritis, Yes	43 (16,8)	53 (22,7)	96 (19,6)	0,098
Psoriatic arthritis, Yes	19 (7,4)	61 (26,2)	80 (16,4)	**<0,001**
Disease Characteristics				
Back pain with age at onset <45 years, Yes	235 (91,8)	200 (85,8)	435 (89)	**0,036**
Sacroiliitis on pelvic X-rays, Yes	172 (67,2)	126 (54,1)	298 (60,9)	**0,012**
Sacroiliitis on MRI, Yes	190 (74,2)	164 (70,4)	354 (72,4)	0,293
HLA - B 27 positivity, Yes	104 (40,6)	67 (28,8)	171 (35)	**0,002**
Axial involvement of SpA? Yes	234 (91,4)	186 (79,8)	420 (85,9)	**<0,001**
Acute anterior uveitis, Yes	41 (16)	23 (9,9)	64 (13,1)	0,063
Crohn's disease or ulcerative colitis, Yes	13 (5,1)	7 (3)	20 (4,1)	0,364
Urethritis or cervicitis or diarrhea within 1 month before the onset of arthritis/enthesitis/dactylitis, Yes	2 (0,8)	4 (1,7)	6 (1,2)	0,629
Psoriasis, Yes	22 (8,6)	63 (27)	85 (17,4)	**<0,001**
Peripheral musculoskeletal manifestations				
Past or present arthritis compatible with SpA, Yes	94 (36,7)	114 (48,9)	208 (42,5)	**0,003**
Root joint disease (e.g., hip, shoulder), Yes	64 (25)	50 (21,5)	114 (23,3)	0,355
Peripheral articular disease (excluding the root joints), Yes	76 (29,7)	114 (48,9)	190 (38,9)	**<0,001**
Spondyloarthritis-related enthesitis, Yes	100 (39,1)	127 (54,5)	227 (46,4)	**0,001**
Dactylitis, Yes	13 (5,1)	24 (10,3)	37 (7,6)	**0,044**
Clinometric information				
Fibromyalgia Doctor Opinion, Yes	20 (7,8)	65 (27,9)	85 (17,4)	**<0,001**
First Total Score	1,78 ± 1,92	3,1 ± 2,23	2,4 ± 2,17	**<0,001**
Swollen Joint Count	1,05 ± 7,28	0,96 ± 5,3	1,01 ± 6,41	**0,002**
Tender Joint Count	1,36 ± 6,57	4,3 ± 8,36	2,76 ± 7,61	**<0,001**
Dactylitis Count	0,27 ± 1,67	0,3 ± 1,16	0,28 ± 1,45	**0,020**
Enthesitis Count	1,85 ± 4,45	6,58 ± 10,15	4,1 ± 8,06	**<0,001**
CRP mg/dL	10,53 ± 28,01	10,63 ± 24,31	10,57 ± 26,29	0,279
BASDAI	2,98 ± 2,1	4,47 ± 2,47	3,69 ± 2,4	**<0,001**
ASDAS	2,26 ± 1,01	2,77 ± 1,11	2,5 ± 1,09	**<0,001**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disease activity tender joint count, dactylitis, enthesitis, BASDAI and ASDAS scores of females were significantly higher than males ($p< 0.05$). FiRST fibromyalgia score were higher in females ($p< 0.001$) (Table).

Conclusion: There are some clinical differences according to gender in SpA. In our population, males had higher axial involvement and radiographic sacroiliitis, while females had more peripheral involvement, including arthritis, enthesitis, and dactylitis, as well as a higher prevalence of fibromyalgia and disease activity.

Disclosure: M. Duruöz: None; **H. Gezer**: None; **İ. Aktaş**: None; **S. Akar**: None; **N. Şahin**: None; **Ö. Akgül**: None; **S. Hizmetli**: None; **M. Alkan Melikoğlu**: None; **U. Kalyoncu**: None; **E. Çapkın**: None; **f. Ural**: None; **F. Yılmaz**: None; **S. ATAMAN**: None; **İ. Sezer**: None.

Abstract Number: 2323

Short-term predictive factors for the development of psoriatic arthritis in patients with psoriasis: findings from a joint consultation between Rheumatology and Dermatology

Mitndbaim Parra[1], Marta Flores[2], María Ángeles Puche-Larrubia[3], Alejandro Escudero Contreras[4], María Dolores López-Montilla[5] and Clementina López Medina[6], [1]1. Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., Cordoba, Spain, [2]1. Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., Spain, Spain, [3]Reina Sofia University Hospital, Granada, Spain, [4]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [5]Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., CORDOBA, Spain, [6]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Univariate and multivariate analysis of predictors for Psoriatic Arthritis development after 12 months of follow-up.

	Final diagnosis of PsA N = 41	No final diagnosis of PsA N = 68	p-value	OR (95%CI) Multivariate	p-value
Age, mean (SD)	51.4 (11)	50.4 (12.8)	0.673	-	-
Gender					
- Female	14/59 (23.7%)	45/59 (76.3%)		Reference	
- Male	27/50 (54.0%)	23/50 (46.0%)	0.001	3.6 (1.3 – 9.5)	0.011
Cause of referral					
- Arthralgias	21/72 (29.2%)	51/2 (70.8%)		Reference	Reference
- Arthritis	11/18 (61.1%)	7/18 (38.9%)	0.027	0.5 (0.1 – 1.9)	0.321
- Other	9/19 (47.4%)	10/19 (52.6%)		0.2 (0.1 – 0.7)	0.014
Type of Psoriasis					
- Other Psoriasis	6/42 (14.3%)	36/42 (85.7%)		Reference	
- Plaques	33/61 (54.1%)	28/61 (45.9%)	<0.001	6.0 (2.0 – 7.2)	<0.001
Family history of Psoriasis					
- No Psoriasis	29/69 (42.0%)	40/69 (58.0%)		-	-
- Yes	12/40 (30.0%)	28/40 (70.0%)	0.245		
Nail involvement					
- No	13/49 (26.5%)	36/49 (73.5%)		-	n.s.
- Yes	28/60 (46.7%)	32/60 (53.3%)	0.021		
CRP, mean (SD)	12.0 (15.4)	5.3 (2.4)	0.019	-	n.s.
Biological Treatment					
- No				-	n.s.
- Yes	26/82 (31.7%)	56/82 (68.3%)			
	15/27 (55.6%)	12/27 (44.4%)	0.021		

n.s.: not significant; OR: Odds Ratio

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Psoriatic Arthritis (PsA) is a chronic rheumatic disease that develops in up to one-third of patients with psoriasis. Identifying predictive factors for PsA in patients with psoriasis referred to rheumatology clinics can facilitate early detection and improve disease outcomes.

Objectives: To identify predictive factors for the development of psoriatic arthritis (PsA) after 12 months of follow-up in patients with a diagnosis of psoriasis referred to a rheumatology clinic.

Methods: An observational, analytical, retrospective study was conducted on 109 patients with psoriasis referred to rheumatology from the dermatology department. Demographic, clinical and analytical data were collected at the first visit to the rheumatology clinic and after 12 months of follow-up. Patients were classified as having PsA yes/no at the 12-month visit based on the rheumatologist's opinion. Baseline characteristics potentially predictive of a PsA diagnosis were analysed using chi-squared and Student's t-tests. Finally, multivariate logistic regression was performed to evaluate the predictive factors independently associated with the development of PsA.

Results: Among the 109 patients evaluated, 54.1% were female and the mean age was 50.8 (12.1) years. A total of 52.9% had plaque psoriasis, and 55.6% had nail involvement. The most frequent reasons for referral were arthralgias (66.1%) and arthritis (16.5%). Additionally, 25% of the referred patients were already receiving biologic treatment prescribed by the dermatologist. A total of 41 patients (37.6%) were diagnosed with PsA after 12 months of follow-up.

Univariate analysis (table 1) showed that factors significantly associated with the development of PsA were: male gender (54.0% vs. 23.7%), arthritis as the reason for referral (61.0% vs. 29.2%), plaque psoriasis (54.1% vs. 14.3%), nail involvement (46.7% vs. 26.5%), elevated CRP (mean 12.0 vs. 5.3 mg/L) and being on biologic treatment (55.6% vs. 31.7%).

Finally, multivariate logistic regression (Table 1) demonstrated that male gender (OR 3.6, 95% CI 1.3 - 9.5) and plaque psoriasis (OR 6.0, 95% CI 2.0 - 7.2) were the most important predictors for the development of PsA. Conversely, patients referred for symptoms other than arthralgias or arthritis had a lower risk of developing PsA (OR 0.2, 95%CI 0.1 - 0.7).

Conclusion: This study in routine clinical practice suggests that male gender, the presence of plaque psoriasis and referral for arthritis or arthralgia are independently associated with the development of PsA. Further long-term prospective studies are required to confirm these findings.

Disclosure: M. Parra: None; **M. Flores**: None; **M. Puche-Larrubia**: None; **A. Escudero Contreras**: None; **M. López-Montilla**: None; **C. López Medina**: None.

Abstract Number: 2324

Early Prediction of Complex Forms of Spondyloarthritis Using Artificial Intelligence: A Modeling Study Based on Routine Clinical Data

mohammed khalil jnyah, imane el mezouar, Nessrine Akasbi, Khaoula tahir and Taoufik Harzy, UNIVERSITY HOSPITAL CENTER HASSAN II OF FEZ. FACULTY OF MEDICINE, DENTISTRY AND PHARMACY SIDI MOHAMED BEN ABDELLAH OF FEZ, FEZ, Morocco

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Spondyloarthritis (SpA) is a chronic inflammatory disease with heterogeneous clinical manifestations. While some patients exhibit mild forms, others progress to complex forms characterized by persistent inflammation, organ involvement (pulmonary, cardiovascular), or severe structural damage. Early identification of high-risk profiles is crucial for tailoring therapeutic strategies. Artificial intelligence (AI) represents a promising tool to predict disease progression based on simple, readily available clinical data.

The objective was to evaluate the performance of a machine learning model (Random Forest) in predicting complex clinical forms of SpA using routine clinical variables that are independent of the criteria defining complexity.

Methods: The study included 319 patients with SpA. A complex form was defined by the presence of at least two of the following criteria:

- Elevated CRP (>10 mg/L)
- Uveitis
- Pulmonary involvement
- Cardiovascular complications
- Hip involvement (coxitis)

The model was trained using five clinical variables unrelated to the definition of complexity:

- Age
- Sex
- CRP
- Erythrocyte sedimentation rate (ESR)
- Glomerular filtration rate (GFR)

The dataset was split into a training set (80%) and a test set (20%). The performance of the Random Forest model was assessed using accuracy, AUC-ROC, sensitivity, precision, and confusion matrix.

Results: The Random Forest model, based on five simple clinical variables (age, sex, CRP, ESR, GFR), achieved an overall accuracy of 78% on the test set. Its discriminative capacity, as measured by the area under the ROC curve (AUC), was high at 0.88, indicating strong ability to distinguish between simple and complex forms of SpA. The model correctly identified 71% of patients with a complex form (sensitivity), while maintaining a specificity of 81% for simple forms. The precision for complex cases was 65%, suggesting useful performance for identifying high-risk patients. It also demonstrated a high negative predictive value, indicating good reliability in ruling out severe forms.

Among the variables used, CRP was the most predictive factor, followed by ESR and GFR. Age and sex provided complementary contributions to model stability but were not major determinants.

Conclusion: This study shows that an artificial intelligence model based on simple and accessible clinical data can reliably anticipate complex forms of spondyloarthritis. AI does not replace the clinician but serves as a strategic partner in personalizing care and improving patient outcomes in rheumatology.

Disclosure: m. jnyah: None; **i. el mezouar**: None; **N. Akasbi**: None; **K. tahir**: None; **T. Harzy**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2325

Association of galectin-3 and Myocardial Dysfunction in Patients with Psoriatic Arthritis

Natalia Guajardo-Jauregui[1], Iris J. Colunga-Pedraza[2], Dionicio A. Galarza-Delgado[2], Jose R Azpiri-Lopez[3], Jesus Alberto Cardenas-de la Garza[4], Diana E. Flores-Alvarado[5] and Rosa Arvizu-Rivera[6], [1]Hospital Universitario "Dr. Jose Eleuterio Gonzalez", Monterrey, Mexico, [2]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [3]Cardiology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [4]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [5]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [6]Hospital Universitario \"Dr. José Eleuterio Gonzalez\", Escobedo, Nuevo León, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is an immune-mediated condition associated with an increased risk of cardiovascular (CV) events due to disease-specific characteristics. Galectin-3 (Gal-3) is a beta-galactoside-binding protein involved in cellular adhesion, proliferation, differentiation, and apoptosis. It is expressed by endothelial cells and fibroblasts, contributing to the secretion of multiple pro-inflammatory cytokines. This protein promotes angiogenesis and fibrosis in various tissues and is considered a biomarker for heart failure, coronary disease, and CV mortality. However, there is limited information regarding Gal-3 as a CV risk biomarker in patients with PsA. This study aimed to associate Gal-3 levels with echocardiographic parameters and disease characteristics in PsA patients.

Methods: This was a cross-sectional study including 78 patients diagnosed with PsA, according to the 2006 CASPAR classification criteria, aged >18 years. Patients with a history of major CV events were excluded. All study participants underwent transthoracic echocardiography performed by two certified cardiologists blinded to clinical information. Blood samples were collected to analyze Gal-3 levels using the ELISA method (Abcam, Cambridge, UK). Disease activity was assessed using the Disease Activity Index for Psoriatic Arthritis (DAPSA), the Psoriasis Area Severity Index (PASI), and the Nail Psoriasis Severity Index (NAPSI). Correlations between Gal-3 levels and other variables were analyzed using Spearman's correlation coefficient (rs). A p-value < 0.05 was considered significant.

Results: The mean age of PsA patients was 52.12 ± 11.91 years, and the median Gal-3 level was 11.5 (5.9–18.1) ng/mL. Clinical and demographic characteristics are shown in Table 1. A moderate positive correlation was observed between Gal-3 and global longitudinal strain (GLS) (rs = 0.305, p = 0.021), a low negative correlation between Gal-3 and left ventricular ejection fraction (LVEF) (rs = -0.255, p = 0.024), a moderate positive correlation between Gal-3 and PASI (rs = 0.331, p = 0.003), a low positive correlation between Gal-3 and DAPSA (rs = 0.237, p = 0.037), and a moderate positive correlation between Gal-3 and C-reactive protein (CRP) (rs = 0.332, p = 0.003) (Figure 1). No significant correlations were found with other variables. A multivariate analysis adjusted for age, body mass index, glycated hemoglobin, systolic blood pressure, and non-HDL cholesterol showed that Gal-3 levels were independently associated with worse GLS (β = 0.358, p = 0.013).

Conclusion: Elevated Gal-3 levels were independently associated with impaired GLS, a parameter reflecting early and subclinical left ventricular dysfunction. Normal GLS values range from -18% to -22%, with more positive values indicating worse myocardial strain. Additionally, higher Gal-3 concentrations were associated with lower LVEF, indicative of left ventricular

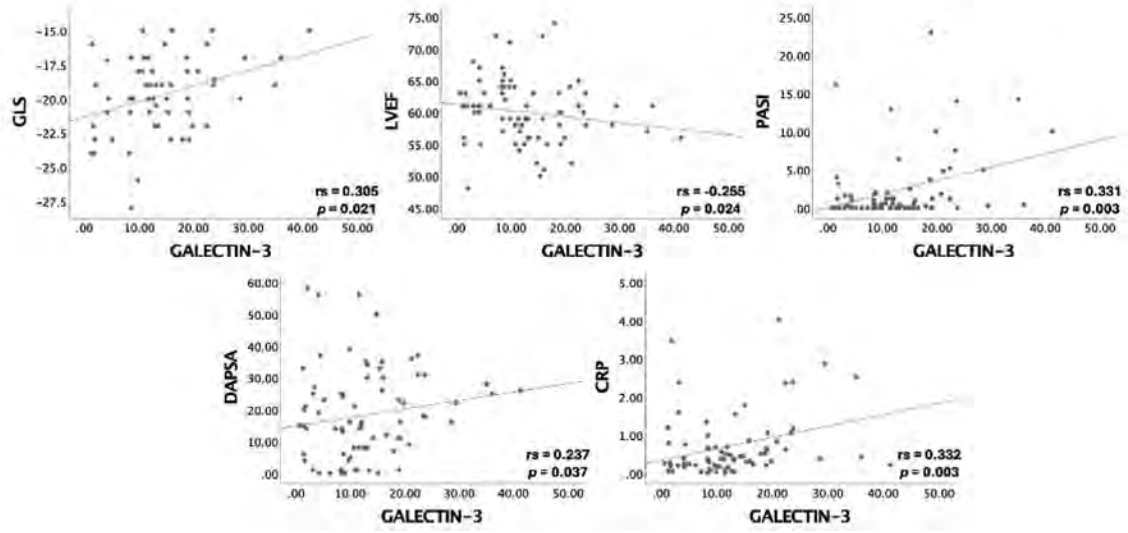
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of psoriatic arthritis patients.

Characteristics	PsA patients (n=78)
Age, years, mean ± SD	52.12 ± 11.91
Women, n (%)	49 (62.8)
T2DM, n (%)	13 (16.7)
Hypertension, n (%)	18 (23.1)
Dyslipidemia, n (%)	38 (48.7)
Obesity, n (%)	29 (37.2)
Galectin-3, ng/ml, median (IQR)	11.5 (5.9-18.1)
Disease duration, years, median (IQR)	4.0 (1.0-10.2)
DAPSA, median (IQR)	16.0 (6.7-27.2)
PASI, median (IQR)	0.4 (0.0-1.8)
NAPSI, median (IQR)	0.0 (0.0-4.0)
CRP, median (IQR)	0.38 (0.19-0.80)
LV mass index, g/m^2, median (IQR)	76.9 (60.8-121.8)
LVEF, %, median (IQR)	60.0 (56.0-63.0)
GLS, %, mean ± SD	-19.72 ± 2.84
TAPSE, mm, median (IQR)	22.0 (20.0-25.0)
PASP, mmHg, median (IQR)	21.3 (12.7-28.0)

PsA, psoriatic arthritis; T2DM, type 2 diabetes mellitus; DAPSA, Disease Activity Index for Psoriatic Arthritis; PASI, Psoriasis Area Severity Index; NAPSI, Nail Psoriasis Severity Index; CRP, C-reactive protein; LV, left ventricle; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; TAPSE, tricuspid annular plane systolic excursion; PASP, pulmonary artery systolic pressure.

Figure 1. Correlations between galectin-3 and disease characteristics in psoriatic arthritis patients.



systolic dysfunction, as well as higher PASI and DAPSA scores, which measure skin and joint disease activity, respectively, and elevated CRP levels, an acute-phase reactant. Gal-3 levels may be a useful biomarker for myocardial dysfunction and disease activity in patients with PsA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Guajardo-Jauregui: None; **I. Colunga-Pedraza**: None; **D. Galarza-Delgado**: None; **J. Azpiri-Lopez**: None; **J. Cardenas-de la Garza**: None; **D. Flores-Alvarado**: None; **R. Arvizu-Rivera**: None.

Abstract Number: 2326

Impact of Regular Exercise, Mobility Impairment, and Obesity on Quality of Life in Patients with Axial Spondyloarthritis: A Cross-Sectional Analysis from the Brazilian Registry of Spondyloarthritis

Rafael Bassara Macedo[1], Maria Eduarda Veiga[2], Gustavo Resende[3], Marcelo Pinheiro[4], Claudia Marques[5], Adriana Marinho[6], Andressa Soares[7], Cleandro Pires[8], Débora Rodrigues[9], Eduarda Souza[10], Glaucio Castro[11], Guilherme Bulbol[12], Jamile Carneiro[13], José Mauro Fernandes[14], Manuella Ochtrop[15], Maria Bernadete Gavi[16], Michel Yazbek[17], Nara Cavalcanti[18], Natalia Machado[19], Olivio Malheiro[20], Rejane Vieira[21], Ricardo Lage[20], Rita Menin[22], Rywka Golebiovski[23], Sandra Ribeiro[12], Thauana Oliveira[23], Valquiria Diniz[16], Percival Sampaio-Barros[24] and Carla Saad[2], [1]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [3]Hospital das Clinicas UFMG, Belo Horizonte, Brazil, [4]UNIFESP/ EPM, São Paulo, São Paulo, Brazil, [5]Hospital das Clinicas - Universidade Federal de Pernambuco - UFPE, Recife, Pernambuco, Brazil, [6]Fundação Hospital do Acre - AC, Rio Branco, Brazil, [7]Hospital Universitário da Universidade Federal de Santa Catarina (UFSC) - SC, Florianópolis, Brazil, [8]UNB, Brasilia, Distrito Federal, Brazil, [9]Fundação Hospital do Acre - AC, Rio Branco, Acre, Brazil, [10]Faculdade de Medicina da Universidade Federal do Amazonas (UFAM) - AM, Manaus, Brazil, [11]Hospital Governador Celso Ramos (HCR) - SC, Florianópolis, Santa Catarina, Brazil, [12]Faculdade de Medicina da Universidade Federal do Amazonas (UFAM) - AM, Manaus, Amazonas, Brazil, [13]Hospital de Base do Distrito Federal (HBDF) - DF, Brasilia, Distrito Federal, Brazil, [14]Universidade Federal do Maranhão (UFMA) - MA, São Luiz, Maranhao, Brazil, [15]Hospital Universitário Pedro Ernesto / UERJ - RJ, Rio de Janeiro, Rio de Janeiro, Brazil, [16]Universidade Federal do Espírito Santo (UFES) - ES, Vitória, Espirito Santo, Brazil, [17]Universidade Estadual de Campinas (UNICAMP) - SP, Campinhas, Sao Paulo, Brazil, [18]Hospital das Clínicas da Universidade Federal de Pernambuco (UFPE) - PE, Recife, Pernambuco, Brazil, [19]Universidade Fedral do Paraná (UFPR) - PR, Curitiba, Parana, Brazil, [20]Hospital das Clínicas da Universidade Federal de Minas Gerais (UFMG) - MG, Belo Horizonte, Minas Gerais, Brazil, [21]Universidade Estadual do Ceará (UECE) - CE, Fortaleza, Ceara, Brazil, [22]Faculdade de Medicina de São José do Rio Preto (FAMERP) - SP, São José do Rio Preto, Sao Paulo, Brazil, [23]Escola Paulista de Medicina (EPM) - Universidade Federal de São Paulo (UNIFESP) - SP, São Paulo, Sao Paulo, Brazil, [24]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial Spondyloarthritis (axSpA) is a chronic inflammatory disease that impairs quality of life. While pharmacological treatment is central to axSpA management, non-pharmacological strategies are increasingly recognized for their benefits on disease outcomes. This study evaluates the impact of physical activity, obesity, and mobility impairment on the quality of life in patients with axSpA.

Methods: This was a cross-sectional data analysis from the Brazilian Spondyloarthritis Registry, including 19 centers nationwide. All patients included were diagnosed with axSpA by a rheumatologist and met the ASAS classification criteria for axSpA. Physical activity was measured using the International Physical Activity Questionnaire (IPAQ), obesity was defined by body mass index (BMI), mobility impairment was evaluated using the Bath Ankylosing Spondylitis Metrology Index (BASMI), and quality of life was measured by the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

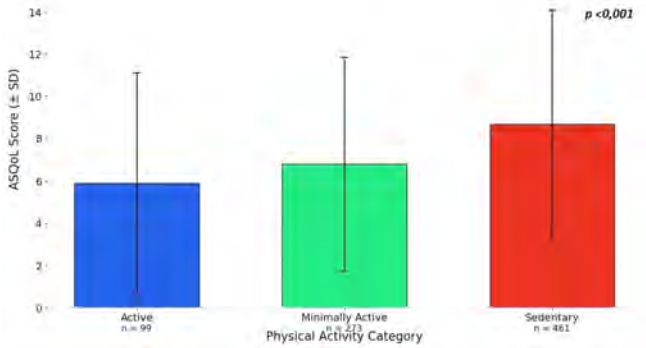


Figure 1. Comparison of Ankylosing Spondylitis Quality of Life (ASQol) values among Physical Activity levels - International Physical Activity Questionnaire (IPAQ) in axSpA paients.

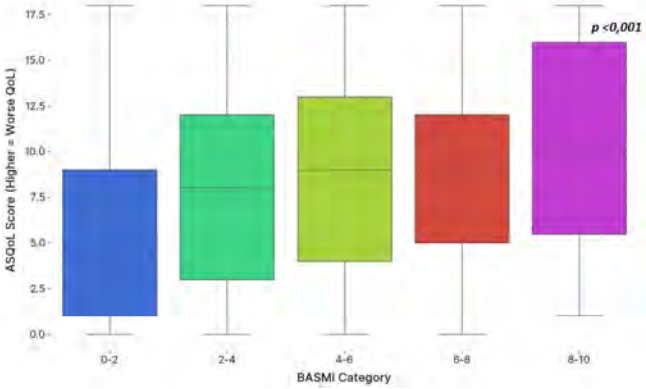


Figure 2. Comparison of Ankylosing Spondylitis Quality of Life (ASQol) values between Bath Ankylosing Spondylitis Metrology Index (BASMI) category in axSpA patients.

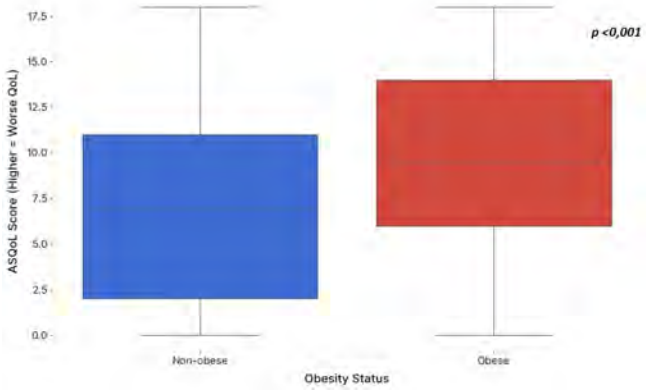


Figure 3. Comparison of Ankylosing Spondylitis Quality of Life (ASQol) values between Obesity status in axSpA patients. Obesity=Body Mass Index(BMI) ≥30.

Results: A total of 965 patients with axSpA were included (70.7% male; mean age 47.8 ± 12.9 years). HLA-B27 was positive in 631 patients (65.4%), negative in 204 (21.1%), and unknown or untested in 130 (13.5%). Subsequent analysis focused on 833 patients with complete data on physical activity (11.9% active; 32.8% minimally active; 55.3% sedentary). ASQoL values progressively worsened with lower physical activity levels: active, minimally active, and sedentary (5.9 ± 5.2 vs. 6.8 ± 5.0 vs. 8.7 ± 5.4, $p < 0.001$) (Figure 1). Pairwise comparisons showed differences between active vs. sedentary ($p < 0.001$) and minimally active vs. sedentary ($p < 0.001$), but no significant difference between active and minimally active

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

groups (p = 0.092). A positive correlation between BASMI and ASQoL was observed (Spearman r = 0.236, p < 0.001) (Figure 2), and patients classified as obese (BMI ≥30) exhibited significantly higher ASQoL compared to non-obese patients (9.3 ± 5.16 vs. 7.5 ± 5.07; p < 0.001) (Figure 3). Interestingly, no difference was observed between physical activity levels (active, minimally active, and sedentary) and BASMI (3.90 ± 2.09 vs. 3.94 ± 2.00 vs. 4.25 ± 2.11, p = 0.097) and frequency of obesity (28.4% vs. 22.9% vs. 23.8%, p = 0.523). Additionally, when comparing obese and non-obese axSpA patients, BASMI values were similar (4.25 ± 1.89 vs. 4.08 ± 2.13, p = 0.211).

Conclusion: Regular exercise was associated with a better quality of life, while obesity and mobility limitations independently had a negative impact. Remarkably, these variables did not influence each other, suggesting that additional factors may influence physical function, mobility, and body composition. These findings highlight the importance of incorporating non-pharmacological interventions, such as promoting physical activity, preventing disability, and managing weight, into the comprehensive care of axSpA patients to improve their quality of life.

Disclosure: R. Bassara Macedo: None; **M. Veiga**: None; **G. Resende**: None; **M. Pinheiro**: AbbVie/Abbott, 2, Johnson & Johnson, 2, UCB, 2; **C. Marques**: None; **A. Marinho**: None; **A. Soares**: None; **C. Pires**: None; **D. Rodrigues**: None; **E. Souza**: None; **G. Castro**: None; **G. Bulbol**: None; **J. Carneiro**: None; **J. Fernandes**: None; **M. Ochtrop**: None; **M. Gavi**: None; **M. Yazbek**: None; **N. Cavalcanti**: None; **N. Machado**: None; **O. Malheiro**: None; **R. Vieira**: None; **R. Lage**: None; **R. Menin**: None; **R. Golebiovski**: None; **S. Ribeiro**: None; **T. Oliveira**: None; **V. Diniz**: None; **P. Sampaio-Barros**: None; **C. Saad**: None.

Abstract Number: 2327

Persistent Pain in PsA: A Distinct Phenotype of Depression, Fatigue, And Catastrophizing

Rebecca Haberman[1], Kyra Chen[2], Adamary Felipe[3], Stephanie Eichman[3], Uma Scher[4] and Jose Scher[5], [1]NYU Langone Health, New York, NY, [2]NYU Grossman School of Medicine and NYU Langone Health Psoriatic Arthritis Center, New York, [3]NYU Grossman School of Medicine, New York, [4]NYU School of Medicine, Scarsdale, NY, [5]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Targeted synthetic and biologic DMARDs have transformed psoriatic arthritis (PsA) treatment. Still, a substantial subset of patients reports persistent joint pain despite well-controlled inflammation. We previously demonstrated that such patients fare worse across multiple PSAID domains. In this study, we aimed to more precisely characterize the psychological and functional profile of this potentially distinct phenotype.

Methods: PsA patients meeting CASPAR criteria were prospectively enrolled at the NYU Psoriatic Arthritis Center. Participants underwent a standardized clinical evaluation and completed multiple surveys, including Pain Catastrophizing Scale (PCS), Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F), Hospital Anxiety and Depression Scale (HADS- A/D), Patient Health Questionnaire-9 (PHQ-9), RAPID3, PROMIS29, and EQ-5D. Patients were categorized into three groups: active (≥1 SJC, ≥0 TJC), persistent pain (0 SJC, ≥1 TJC), or remission (0 SJC, 0 TJC).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics

	Total (n=91)	Remission (n=40)	Persistent Pain (n=24)	Active (n=27)	p-value
Demographics-- n(%)					
Age	48.0 (36.0, 58.0)	41.5 (35.3, 58.3)	50.0 (40.5, 58.0)	51.0 (34.0, 58.0)	0.611
Female	51 (56.0)	17 (42.5)	19 (79.2)	15 (55.6)	0.017
Race					0.436
White	78 (85.7)	34 (85.0)	20 (83.3)	24 (88.9)	
Black	0 (0)	0 (0)	0 (0)	0 (0)	
Asian	5 (5.5)	3 (7.5)	1 (4.2)	1 (3.7)	
Other	8 (8.8)	3 (7.5)	3 (12.5)	2 (7.4)	
Comorbidities-- n(%)					
Hypertension	24 (26.4)	12 (30.0)	6 (25.0)	6 (22.2)	0.766
Hyperlipidemia	24 (26.4)	10 (25.0)	6 (25.0)	8 (29.6)	0.901
IBD	5 (5.5)	2 (5.0)	1 (4.2)	2 (7.4)	0.629
Diabetes	12 (13.2)	3 (7.5)	8 (33.3)	1 (3.7)	0.003
Anxiety	21 (23.1)	6 (15.0)	9 (37.5)	6 (22.2)	0.117
Depression	16 (17.6)	5 (12.5)	6 (25.0)	5 (18.5)	0.440
Osteoarthritis	9 (9.9)	4 (10.0)	3 (12.5)	2 (7.4)	0.829
Fibromyalgia	15 (16.5)	2 (5.0)	9 (37.5)	4 (14.8)	0.005
Disease Phenotype-- n(%)					
Dactylitis	26 (28.6)	10 (25.0)	7 (29.2)	9 (33.3)	0.758
Axial Disease	39 (42.9)	21 (52.5)	9 (37.5)	9 (33.3)	0.247
Enthesitis	33 (36.3)	12 (30.0)	11 (45.8)	10 (37.0)	0.483
Nails	42 (46.2)	14 (35.0)	12 (50.0)	16 (59.3)	0.135
Erosions	25 (27.5)	10 (25.0)	7 (29.2)	8 (29.6)	0.896
Physical Exam-- median (IQR)					
TJC	1 (0, 4)	--	3 (1.3, 5)	4 (1, 6)	--
SJC	0 (0,1)	--	--	2 (1, 5)	--
Enthesitis	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,1)	0.230
Dactylitis	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0.004^
BSA	0.13 (0, 1)	0.4 (0, 1)	0 (0,0.5)	0.3 (0,1)	0.320
BMI	28.1 (24.5, 33.2)	26.1 (22.8, 30.9)	30.9 (26.5, 35.5)	29.3 (25.0, 32.5)	0.027*
Current Medication Use -- n(%)					
cDMARD	26 (28.6)	13 (32.5)	8 (33.3)	5 (18.5)	0.386
b/tsDMARD	82 (90.1)	35 (87.5)	24 (100.0)	23 (85.2)	0.159

IBD denotes inflammatory bowel disease, TJC tender joint count, SJC swollen joint count, BSA percent body surface area affected by psoriasis, BMI body mass index, cDMARD conventional disease modifying antirheumatic drug, b/ts biologic/targeted synthetic.
^ Dactylitis is significant between remission-active and remission-persistent pain.
* BMI significant between remission-perisstent pain.

Summary data was presented as numbers/percentages or medians/interquartile regions (IQR). Group comparisons were performed using Chi-squared tests and Kruskal-Wallis tests with post-Hoc Dunn's test for pair-wise comparisons with Bonferroni correction.

Results: 91 patients were assessed; 24 (26.4%) had persistent joint pain, 40 (43.9%) were in remission, and 27 (29.7%) had active inflammation (**Table 1**). Patients with persistent pain were more likely to be female (p=0.02), meet criteria for fibromyalgia (p=0.005), and have diabetes (p=0.003). Compared to those in remission, patients with persistent pain had a higher body mass index (30.9 (IQR 26.5, 35.5) vs 26.1 (22.8, 30.9), p=0.022) and worse psychologic profiles (**Figure 2**). They demonstrated higher levels of catastrophizing (PCS 11 (5.0, 15.8) vs 1.5 (0, 10.0), p= 0.004), depressive symptoms (PHQ-9 6.0 (48.6, 62.1) vs 2.5 (0.3, 4), p=0.001; HADS-D (5.0 (3.0, 8.5) vs 2.0 (0, 5.0), p=0.011) and fatigue (FACIT 33.0 (20.8, 42.8) vs 44.0 (40.0, 47.5), p< 0.001). There was no difference in anxiety level (HADS-A 6.5 (4.0, 11.8) vs 5.0 (2.0, 6.0), p=0.256). They reported decreased physical function (41.6 (37.0, 45.0) vs 47.6 (42.1, 56.9), p< 0.001), decreased ability to participate in social activities (48.2 (39.0, 51.8) vs 57.6 (48.2, 64.2), p= 0.004), more pain interference, (56.7 (52.2, 62.1) vs 51.7 (41.6, 55.7), p=0.008) and worse overall QoL (EQ5D 0.63 (0.4, 0.8) vs 0.8 (0.7, 0.9), p< 0.001). Patients with persistent pain had profiles similar to those with active inflammatory disease (and in many domains were numerically worse, **Table 2**).

Conclusion: Persistent joint pain in PsA, even without objective inflammation, is linked to a reproducible cluster of psychosocial distress and functional impairment. These patients may not fit the traditional treat-to-target approaches that focus on inflammation mitigation alone. Our findings underscore an unmet therapeutic need: integrative interventions targeting

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

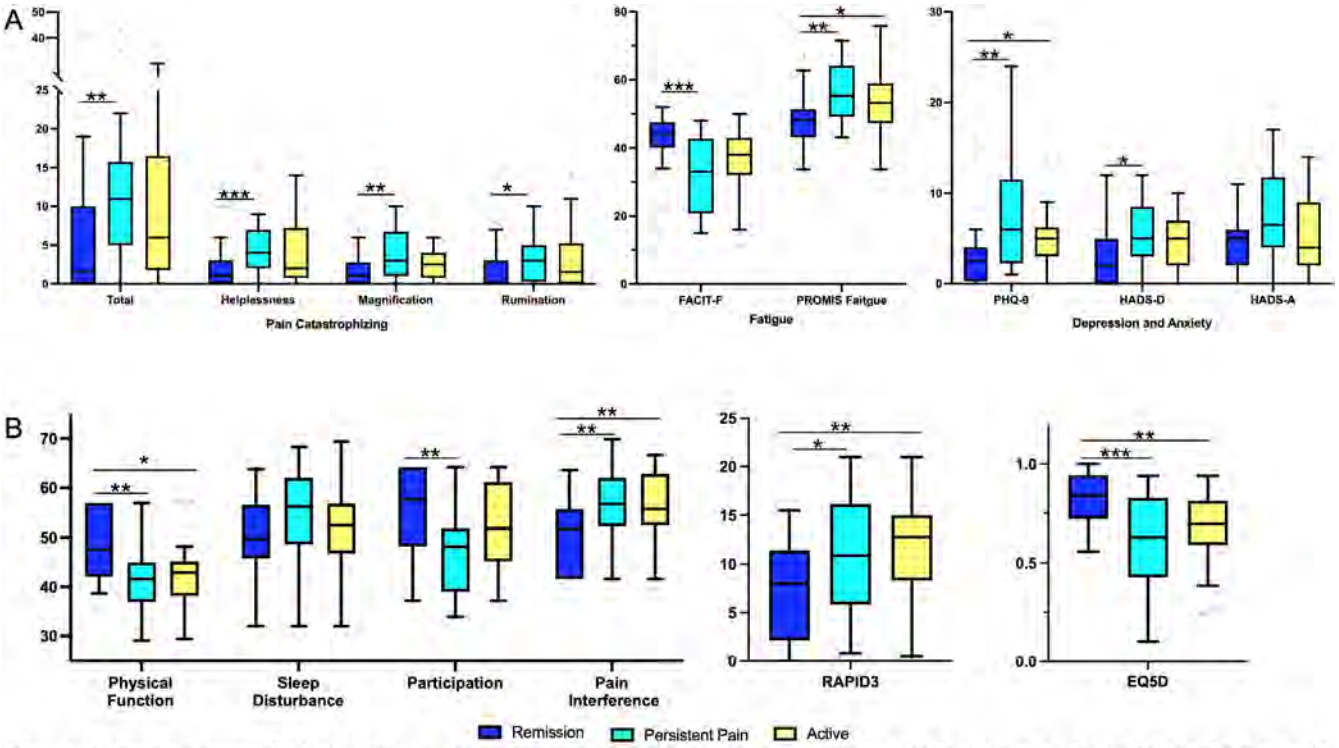


Figure 1. Comparison of physiologic indices (A) and patient reported outcomes (B) between patients in remission, with persistent joint pain, and active inflammatory disease. Medians and interquartile regions plotted with outliers in gray. Pain catastrophizing scale 0-52 possible range with higher numbers reflecting increased levels of catastrophizing. FACIT-F denotes Functional Assessment of Chronic Illness Therapy-Fatigue Scale and ranges 0-52 with lower scores indicating more fatigue. PROMIS Fatigue is reported as t-scores with higher scores indicating more fatigue. PHQ-9 denotes Patient Health Questionnaire-9 and ranges 0-27 with higher scores indicating more depressive symptoms. HADS-D and HADS-A denote Hospital Anxiety and Depression Scale-Depression and Anxiety, each ranging 0-21 with higher numbers indicating higher levels of depression and anxiety. Physical function, sleep disturbance, participation, and pain interference are all derived from PROMIS measures and are reported as t-scores with higher score indicating higher levels of that category (i.e., higher physical function scores reflect better physical function, lower participation score reflects decreased ability to participate). RAPID 3 is a composite index of physical function, pain, and patient global scores, ranging 0-30 with higher numbers indicating worse disease state. EQ5D measures quality of life (QoL), ranging 0-1 with one indicating the best overall health QOL status. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 2. Comparison of physiologic indices and patient reported outcomes between patients with persistent joint pain and those with active inflammation

	Persistent Pain (n=24)	Active (n=27)	p-value
Psychologic Indices- median (IQR)			
PCS total	11 (5, 15.8)	6 (1.8, 16.5)	>0.999
PCS helplessness	4 (2,7)	2 (0.8, 7.3)	>0.999
PCS magnification	3 (1,6.8)	2.5 (0.8, 4)	0.692
PCS rumination	3 (0.3, 5)	1.5 (0, 5.3)	>0.999
FACIT-F	33 (20.8, 42.8)	38 (32, 43)	>0.999
PROMIS Fatigue	55.2 (49.2, 64.2)	53.2 (47.3, 59.0)	0.984
PHQ-9	6 (2.3, 11.5)	5 (3, 6.3)	0.883
HADS-D	5 (3, 8.5)	5 (2, 7)	>0.999
HADS-A	6.5 (4, 11.8)	4 (2, 9)	0.257
Patient Outcomes- median (IQR)			
Physical function	41.6 (37.0, 45.0)	42.9 (38.2, 45.2)	>0.999
Sleep disturbance	56.2 (48.6, 62.1)	52.4 (46.8, 56.8)	>0.999
Social participation	48.2 (39, 51.8)	51.8 (45.2, 61.2)	0.221
Pain inteference	56.7 (52.2, 62.1)	55.7 (52.4, 62.9)	>0.999
RAPID3	10.9 (5.8, 16.2)	12.8 (8.3, 15.0)	>0.999
EQ5D	0.63 (0.4, 0.8)	0.7 (0.6, 0.8)	>0.999

IQR denotes interquartile region, PCS denotes pain catatrophizing scale, FACIT-F denotes Functional Assessment of Chronic Illness Therapy-Fatigue Scale, PHQ-9 denotes patient Patient Health Questionnaire, HADS denotes Hospital Anxiety and Depression Scale.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

depression, fatigue, and catastrophizing—such as cognitive behavioral therapy or pharmacologic treatment of mood disorders— which may be critical to achieving remission and improving quality of life in PsA.

Disclosure: R. Haberman: Johnson and Johnson, 1, 5, Novartis, 1; **K. Chen**: None; **A. Felipe**: None; **S. Eichman**: None; **U. Scher**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2.

Abstract Number: 2328

Increased Risk of Stroke In Patients With Psoriasis: A Systematic Review And Meta-Analysis

Rubab Rizwan, Sehneet Grewal, Sri Varsha Banda and Mohammad Hazique, Nuvance Health, poughkeepsie, NY

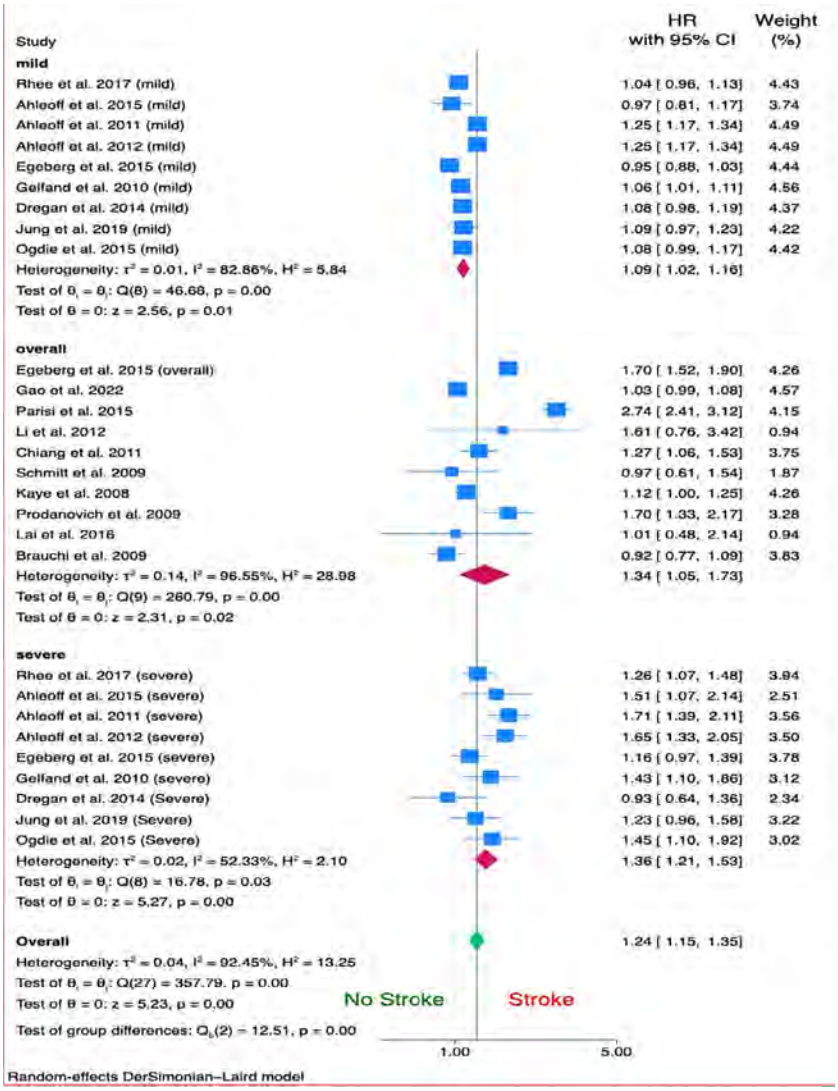
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Psoriasis, affecting 2–3% of the global population, is a chronic inflammatory disease with systemic effects beyond the skin. Its immune-mediated inflammation contributes to cardiovascular comorbidities including hypertension, diabetes, and atherosclerosis. Th1/Th17-driven pathways accelerate vascular risk, linking psoriasis to stroke. However, data on stroke risk remain limited due to small cohorts and insufficient confounder adjustment.

Methods: This meta-analysis evaluated the association between psoriasis and stroke by systematically reviewing observational studies published through December 2024. Study selection followed PRISMA guidelines, extracting data on patient characteristics and adjusted risk estimates.

Results: This meta-analysis of 18 studies encompassing 705,602 psoriasis patients and over 17.9 million controls demonstrated a significant association between psoriasis and stroke, with a pooled hazard ratio (HR) of 1.24 (95% CI: 1.15–1.35). Stratified analyses showed elevated stroke risk across all severities: mild (HR: 1.09; 95% CI: 1.02–1.16), overall (HR: 1.34; 95% CI: 1.05–1.73), and severe psoriasis (HR: 1.36; 95% CI: 1.21–1.53). Region-specific estimates indicated consistent associations in Asia (HR: 1.08), Europe (HR: 1.26), and North America (HR: 1.49), though with some heterogeneity. Age subgroup analysis also confirmed increased stroke risk in both older (≥45 years, HR: 1.27) and younger (< 45 years, HR: 1.18) patients. No significant publication bias or small-study effects were detected by funnel plot analysis and statistical testing.

Conclusion: This analysis confirms that psoriasis is associated with an increased risk of stroke, particularly in patients with severe disease. The association remains consistent across age groups and geographic regions. These findings highglight the need for routine cardiovascular risk assessment in psoriasis care. Future research should explore targeted anti-inflammatory therapies and lifestyle interventions to mitigate stroke risk in this population.

Disclosure: R. Rizwan: None; **S. Grewal**: None; **S. Banda**: None; **M. Hazique**: None.

Abstract Number: 2329

Increased Risk of Atrial Fibrillation In Patients With Psoriasis: A Systematic Review And Meta-Analysis

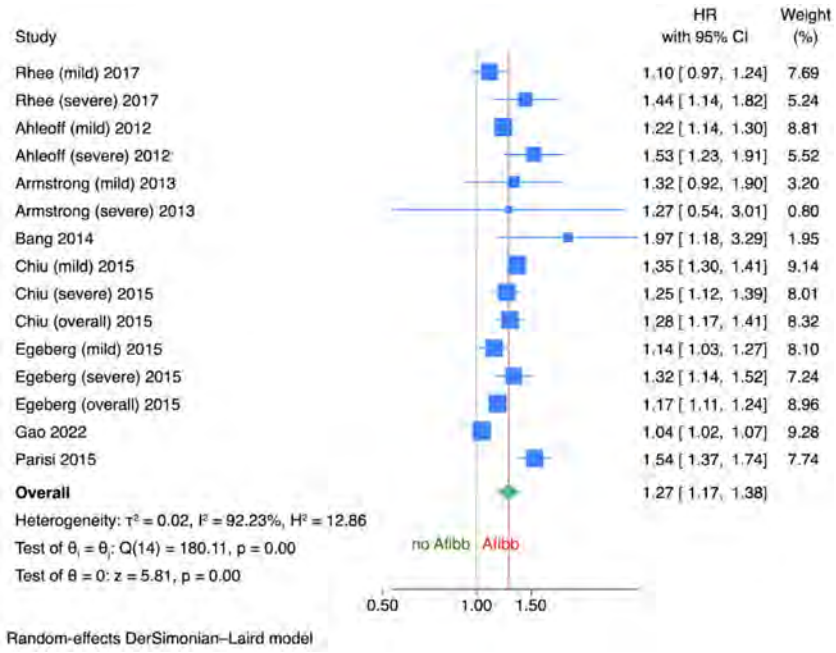
Sehneet Grewal, Rubab Rizwan, Sri Varsha Banda and Mohammad Hazique, Nuvance Health, Poughkeepsie, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

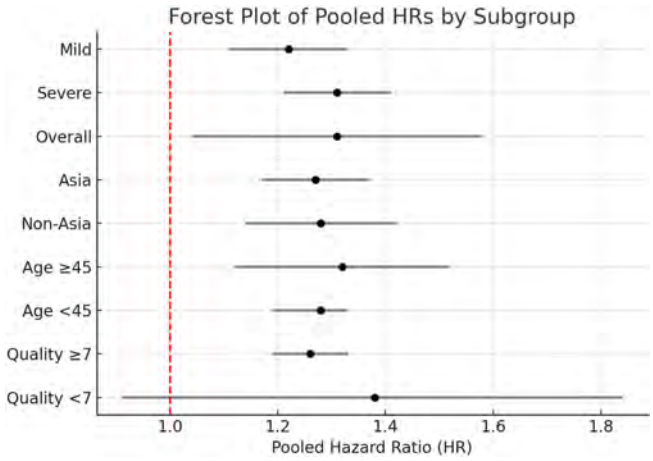
Background/Purpose: Psoriasis, a chronic inflammatory skin condition, is increasingly linked to systemic cardiovascular risks. Atrial fibrillation (AF), the most common cardiac arrhythmia, is associated with elevated risks of stroke, heart failure, and mortality. This study evaluates the association between psoriasis and AF.

Methods: This meta-analysis evaluated the association between Psoriasis and Atrial Fibrillation by systematically reviewing observational studies published through December 2024. Study selection followed PRISMA guidelines, extracting data on patient characteristics and adjusted risk estimates.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot Showing the Association Between Risk of Atrial Fibrillation in Psoriasis



Results: Eight studies comprising 11,579,730 participants (277,597 with psoriasis and 11,302,133 controls) were included. Psoriasis was associated with a significantly higher risk of AF (HR: 1.27; 95% CI: 1.17–1.38). Subgroup analyses revealed that severe psoriasis was associated with a higher risk of AF (HR: 1.32; $p < 0.05$) as compared to mild psoriasis (HR: 1.22; $p < 0.05$), but the difference was not statistically significant ($p = 0.41$). Age-stratified analysis showed an elevated risk in individuals aged ≥45 years (HR: 1.40; $p < 0.05$) compared to those < 45 years (HR: 1.21; $p < 0.05$). Regional analysis demonstrated comparable risks in Asia (HR: 1.27; $p < 0.05$) and non-Asia (HR: 1.28; $p < 0.05$), with no significant subgroup differences ($p = 0.93$). Publication bias was not evident based on visual inspection of the funnel plot and Egger's regression test ($p = 0.24$).

Conclusion: This analysis of observational studies shows an association between psoriasis and increased risk of AF risk. Subgroup analysis shows that risk of AF is higher in severe psoriasis and older patients. Future large studies are needed to clarify underlying mechanisms, and assess the potential role of AF screening in improving outcomes for this high-risk population.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Grewal: None; **R. Rizwan**: None; **S. Banda**: None; **M. Hazique**: None.

Abstract Number: 2330

Correlation of Comorbidities with Psoriatic Arthritis Duration in Elderly Veterans - A Retrospective Cohort Study

Siba Raychaudhuri[1], Smriti K Raychaudhuri[2], Jessica A. Walsh[3], Gail Kerr[4], Maureen Dubreuil[5], Bernard Ng[6], Elizabeth Chang[7], Andreas Reimold[8] and Liron Caplan[9], [1]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [2]Sacramento VA Medical Center, Davis, CA, [3]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [4]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [5]Boston University School of Medicine, Milton, MA, [6]Veteran Affairs, Seattle, WA, [7]PVAHCS, Phoenix, AZ, [8]Dallas VA Medical Center, Dallas, TX, [9]Rocky Mountain Regional VAMC, Aurora, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriasis and psoriatic arthritis (PsA) are associated with several comorbid conditions including metabolic disease, chronic kidney disease as well as mental health disorders. However, limited studies have been conducted on the impact of duration of PsA on comorbidities, and long-term change in practice to manage these comorbidities and improve patient care.

The objective of this study is to determine the prevalence of comorbidities in patients with PsA in a cohort of elderly veterans and determine the correlation of prevalence of comorbidities with the duration of PsA.

Methods: Our cohort included PsA patients from PULSAR (Program to Understand Long-term Outcomes in Spondylarthritis) registry and VA Sacramento Medical Center. The duration of PsA disease was identified by age of onset of PsA noted in the databases and categorized as < 5 years, 6-10 years, 11-15 years, 16-20 years and >20 years. Various comorbidities were identified via ICD-10 codes (hypertension, hyperlipidemia, diabetes mellitus, gout and mental health disorders) and studied in these patients and classified according to the duration of PsA (Table 1).

Table 1: The prevalence of comorbidities in patients with psoriatic arthritis in elderly veterans: Data on the grouping of patients based on disease duration and prevalence of comorbidities.

Duration of PsA (years)	Median age at PsA diagnosis(year)	Number of patients (n=220)	Hyperlipidemia	Hypertension	Gout	Diabetes	Mental Health
0-5	57	73	63.0%	54.8%	9.6%	31.5%	41.1%
6-10	49	35	42.9%	37.1%	2.9%	22.9%	45.7%
11-15	43	40	52.5%	65.0%	5.0%	35.0%	40.0%
16-20	38	20	40.0%	55.0%	10.0%	35.0%	35.0%
>20	30	52	57.7%	73.8%	9.6%	26.9%	34.6%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

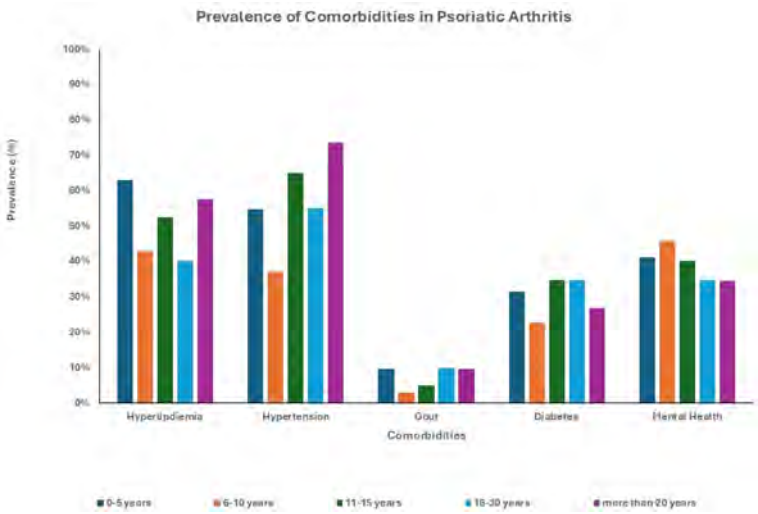


Figure 1: Bar diagram representative of correlation of prevalence of several comorbidities and disease duration.

Results: There were 220 patients available for study. PsA disease duration was as follows: < -5 years (73, 33.2%), 5-10 years (35,15.9%), 11-15 years (40,18.18%), 16-20 years (20, 9%) and more than 20 years (52, 23.6%). The prevalence of comorbidities in each of these groups was then calculated as listed in (Table 1). On subsequent comparison amongst the groups, as noted in Figure 1, the prevalence of hypertension increased with longer disease duration. A similar trend was not noted for the rest of the comorbidities. However, comorbidities that contribute to CVD risk were prevalent in one third to almost half of the PsA cohort, regardless of disease duration (Figure 1).

Conclusion: In this study, the prevalence of hypertension increased with PsA duration. Prevalence of the other comorbidities did not correlate with disease duration. Given the increased cardiovascular disease risks in PsA patients, our findings emphasize the need for hypertension control in PsA patients of longer disease duration. In addition, our findings demonstrate that PsA patients are at increased risk for several comorbidities, especially metabolic syndrome and mental health disorders irrespective of the duration of disease. So, preventive measures should be taken early in the disease course to screen and comprehensively manage these comorbidities and underlying psychosocial issues.

Disclosure: S. Raychaudhuri: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **S. Raychaudhuri**: None; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **M. Dubreuil**: None; **B. Ng**: None; **E. Chang**: None; **A. Reimold**: None; **L. Caplan**: None.

Abstract Number: 2331

Coping with Rheumatic Stressors in Axial Spondyloarthritis: Association with Patient Characteristics and Disease Phenotypes and Changes Over Time

Marc van Essen[1], Dafne capelusnik[2], Désirée Van Der Heijde[3], Robert Landewé[4], Wim van Lankveld[5], Astrid Van Tubergen[6], **Sofia Ramiro**[7] and Annelies Boonen[8], [1]Maastricht University, Zeist, Netherlands, [2]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [3]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [4]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [5]HAN University of Applied Sciences, Arnhem, Netherlands, [6]Maastricht university, Maastricht, Netherlands, [7]Leiden University Medical Center, Bunde, Netherlands, [8]Maastricht University Medical Centre+ & Maastricht University, Maastricht, Limburg, Netherlands

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: To identify patient characteristics and disease phenotypes associated with coping strategies in axial spondyloarthritis (axSpA), and assess whether coping strategies change over time.

Methods: Data from the Outcome in AS International Study (OASIS) were used. Coping was assessed using Coping with rheumatic stressors (CORS) at 4 and 6 years of follow-up. The CORS assesses coping with three stressors – pain, limitations, and dependence –, based on 61 items across eight strategies (score 1–4 for each strategy). Factors associated with each strategy were analysed with Generalized Estimation Equations (GEE). Age, sex and education were the main independent variables of interest. Variables with $p < 0.20$ in univariable analyses were added to age, sex and education using manual forward selection and comprised of other patient characteristics (e.g., BMI, comorbidities) and disease phenotypes (e.g., peripheral and extra-musculoskeletal manifestations). Interactions and confounders were tested and evaluated. Additional models were built where axSpA health scores (e.g., ASDAS, BASFI) were added. In separate GEE analyses, changes in coping strategies over time were assessed, with time as the independent variable.

Results: In total 116 patients [72% male, mean age 48 years (SD 12)] had CORS data at ≥1 timepoint. Patients made most use of *comforting cognitions* (mean: 3.0; (SD: 0.5)) to cope with pain, of *pacing* (2.4; (0.5)) to cope with limitations and of *showing considerations* (2.8; (0.5)) to cope with dependence (Tables 1–3). Several differences in preference for coping

TABLE 1: Mean coping strategy scores and multivariable associations between patient characteristics/disease phenotypes and strategies to cope with pain. Included additional model with health scores for comforting cognitions (2nd column)

	Pain: Comforting cognitions, range 1-4 **Mean (SD): 3.0 (0.5)** (n=110)	Pain: Comforting cognitions **Additional model with health scores** (n=99)	Pain: Decreasing activities, range 1-4 **Mean (SD): 2.4 (0.5)** (n=112)	Pain: Diverting attention, range 1-4 **Mean (SD): 2.4 (0.5)** (n=114)
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI
Age, years	0.01 (0.00 to 0.02)	0.01 (0.00 to 0.01)	0.00 (-0.01 to 0.01)	0.00 (0.00 to 0.01)
Sex (male vs female)	-0.08 (-0.24 to 0.09)	0.02 (-0.15 to 0.18)	0.17 (-0.03 to 0.36)	**0.21 (0.04 to 0.38)**
Lower education vs higher education	**-0.22 (-0.41 to -0.03)**	-0.15 (-0.37 to 0.07)	0.19 (-0.08 to 0.46)	0.12 (-0.11 to 0.34)
BMI, kg/m2	**0.01 (0.00 to 0.03)** [a]	**0.02 (0.00 to 0.03)** [a]	[b]	[b]
RDCI, 0-9	[b]	[b]	0.03 (-0.07 to 0.15) [a]	**-0.13 (-0.23 to -0.03)** [a]
Currently working (yes vs no)	-0.07 (-0.25 to 0.12) a	-0.05 (-0.24 to 0.15) a	0.17 (-0.05 to 0.38) [a]	[b]
Presence of psoriasis (ever)	[b]	[b]	**0.36 (0.02 to 0.71)** [a]	[b]
Mander Enthesitis Index, 0-90	[b]	[b]	0.00 (0.00 to 0.01) [a]	[b]
BASFI, 0-10	n.a. [c]	-0.02 (-0.06 to 0.02) [a]	n.a. [c]	n.a. [c]
SF36 MCS, 0-100	n.a. [c]	**0.01 (0.00 to 0.02)** [a]	n.a. [c]	n.a. [c]
ASDAS-CRP	n.a. [c]	0.01 (-0.08 to 0.09) [a]	n.a. [c]	n.a. [c]

[a] Confounded the relationship between one of the three main variables of interest (age, sex, education level) and the outcome in this model.

[b] In univariable analysis not significant for this strategy.

[c] Not part of this analysis.

Bold indicates significance ($p<0.05$). Disease duration, presence of IBD, presence of peripheral arthritis, presence of uveitis, HLA-B27 status, BASMI and BASDAI Q1 were also analysed but not included in the table as they were not significant in univariable analyses in any of the models ($p>0.20$). BMI: Body Mass Index. RDCI: Rheumatic Disease Comorbidity Index. BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BASDAI Q1: Bath Ankylosing Spondylitis Disease Activity Index (Question 1); SF36 MCS: Short Form (36) Mental Component Summary score; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score (C-reactive protein).

TABLE 2: Mean coping strategy scores and multivariable associations between patient characteristics/disease phenotypes and strategies to cope with limitations

	Limitations: Optimism, range 1-4 **Mean (SD): 3.1 (0.5)** (n=110)	Limitations: Pacing, range 1-4 **Mean (SD): 2.7 (0.6)** (n=114)	Limitations: Creative solution seeking, range 1-4 **Mean (SD): 2.6 (0.6)** (n=114)
	β (95% CI)	β (95% CI)	β (95% CI)
Age, years	**0.02 (0.01 to 0.03)**	**0.01 (0.01 to 0.02)**	0.01 (0.00 to 0.01)
Sex (male vs female)	-0.08 (-0.27 to 0.10)	0.14 (-0.07 to 0.35)	0.13 (-0.07 to 0.33)
Lower education vs higher education	**-0.36 (-0.58 to -0.13)**	0.11 (-0.19 to 0.40)	-0.03 (-0.32 to 0.26)
Disease duration, years	0.00 (-0.01 to 0.01) [a]	[b]	[b]
RDCI, 0-9	**-0.11 (-0.20 to -0.02)**	0.05 (-0.07 to 0.16) [a]	
Currently working (yes vs no)	[b]	0.15 (-0.10 to 0.41) [a]	0.15 (-0.09 to 0.39) [a]

[a] Confounded the relationship between one of the three main variables of interest (age, sex, education level) and the outcome in this model.
[b] In univariable analysis not significant for this strategy.
Bold indicates significance (p<0.05). Presence of IBD, presence of peripheral arthritis, presence of uveitis, presence of psoriasis, Mander Enthesitis index, HLA-B27 status and BMI were also analysed but not included in the table as they were not significant in univariable analyses in any of the models (p>0.20). RDCI: Rheumatic Disease Comorbidity Index.

TABLE 3: Mean coping strategy scores and multivariable associations between patient characteristics/disease phenotypes and strategies to cope with dependence

	Dependence: Accepting dependence, range 1-4 **Mean (SD): 2.3 (0.7)** (n=112)	Dependence: showing consideration, range 1-4 **Mean (SD): 2.8 (0.4)** (n=113)
	β (95% CI)	β (95% CI)
Age, years	0.01 (0.00 to 0.02)	0.00 (0.00 to 0.01)
Sex (male vs female)	0.03 (-0.19 to 0.25)	0.14 (-0.02 to 0.30)
Lower education vs higher education	0.13 (-0.21 to 0.46)	-0.09 (-0.32 to 0.14)
RDCI, 0-9	0.01 (-0.18 to 0.20) [a]	**-0.10 (-0.19 to 0.00)** [a]
Currently working (yes vs no)	0.12 (-0.16 to 0.39) [a]	[b]
Presence of peripheral arthritis (ever)	[b]	0.13 (0.00 to 0.27) [a]
Presence of psoriasis (ever)	**0.28 (0.07 to 0.49)** [a]	0.20 (-0.04 to 0.44) [a]
Mander Enthesitis Index, 0-90	**0.01 (0.00 to 0.01)** [a]	0.00 (0.00 to 0.01) [a]

[a] Confounded the relationship between one of the three main variables of interest (age, sex, education level) and the outcome in this model.
[b] In univariable analysis not significant for this strategy.
Bold indicates significance (p<0.05). Disease duration, presence of IBD, presence of uveitis, HLA-B27 status and BMI were also analysed but not included in the table as they were not significant in univariable analyses (p>0.20). RDCI: Rheumatic Disease Comorbidity Index.

strategy were seen between patients but without clear patterns. Using the strategies that were most used per stressor as an example, it can be seen that using *comforting cognitions* to cope with pain was associated with lower (vs higher) education (β: -0.22; (95%CI: -0.41 to -0.03)) and with a higher BMI (0.01; (0.00 to 0.03) (Table 1). *Pacing*, to cope with limitations, was used more by older individuals (0.01; (0.01 to 0.02)) (Table 2). *Showing considerations*, to cope with dependence, was used less by those with more comorbidities (-0.10; (-0.19 to 0.00)) (Table 3). When adding axSpA health scores as additional variables to the initial models, coefficients remained largely unchanged across all strategies. As an example, the effect of adding health scores to the *comforting cognitions* model is shown in table 1 (2nd column). ASDAS, BASFI and MCS (SF-36) had no independent effect, were not effect modifiers and only had some confounding effect on the main relationships of interest. Finally, for the analyses of change over time, 102 patients had full CORS data on both timepoints. Analyses showed that coping strategies did not change over time (range β_{time}: -0.04 to 0.07/year).

Conclusion: Coping strategies in axSpA appear more strongly influenced by patient characteristics, to a lesser extent disease phenotypes but not by axSpA related health scores. Furthermore, no change over time was found supporting that coping is a trait and more dependent on the person than the disease.

Disclosure: M. van Essen: None; **D. capelusnik**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **W. van Lankveld**: None; **A. Van Tubergen**: Janssen, 2, Novartis, 2, 5, 6, UCB, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **A. Boonen**: AbbVie/Abbott, 5, Alfasigma, 2, Celgene, 5, Eli Lilly, 2, Novartis, 2, Sandoz, 2, UCB, 2.

Abstract Number: 2332

Development and validation of a Disease Activity index for PSoriatic Arthritis based on 44 joints: DAPSA44

Dafne capelusnik[1], Clementina López Medina[2], Désirée Van Der Heijde[3], Daniel Aletaha[4], Josef Smolen[5], Anna Molto[6] and **Sofia Ramiro**[7], [1]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [2]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain, [3]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [4]Medical University Vienna, Wien, Austria, [5]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria, Vienna, Austria, [6]Assistance Publique Hôpitauxde Paris, Paris, France, [7]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Recent studies have highlighted the potential of composite scores such as the DAPSA for assessing peripheral arthritis in axSpA and pSpA. However, the swollen (SJC66) and tender (TJC68) joint counts required for the DAPSA calculation are often unavailable in axSpA randomized controlled trials.

This study aimed to develop and evaluate the construct validity of a modified-DAPSA score using the 44-joint count in patients with SpA (axSpA, pSpA, and PsA).

Methods: In this ancillary analysis of the ASAS-PerSpA study, patients with axSpA, pSpA, or PsA were included and allocated at random by diagnosis and country into two a derivation (33%) and a validation cohort (66%). The derivation cohort was used to calculate conversion factors for SJC66/TJC68 to SJC44/TJC44, to allow the calculation of DAPSA44, using mixed-effects linear regression models. The validation cohort assessed the new score's construct validity through: i) agreement between original-DAPSA and DAPSA44, evaluated as a continuous score with the Intraclass Correlation Coefficient (ICC) and categorically with disease activity states with weighted kappa coefficients, along with Bland-Altman plots; ii) original-DAPSA and DAPSA44 correlations with external constructs, with a predefined 0.3-wide acceptable range of difference between the scores; iii) the discrimination between known groups, calculated using standardized mean differences (SMDs) after stratifying patients into active/inactive based on a combination of PGA (≥5/< 5) and SJC (≥1/0 or ≥2/< 2, median SJC). An SMD with higher absolute value indicates better discriminatory ability, and an SMD above 0.8 is considered as 'good'.

Results: A total of 4121 patients with complete data on disease activity measures were analyzed, including 2679 (65%) with axSpA, 428 (10%) with pSpA, and 1014 (25%) with PsA. A history of peripheral arthritis was reported in 2291 (56%) patients, predominantly with oligoarticular (43%) or polyarticular involvement (45%). The prevalence of peripheral arthritis varied across disease phenotypes: 36% in axSpA, 95% in pSpA and 91% in PsA. Conversion factors from the derivation cohort (n=1364) from TJC68 and SJC66 to TJC/SJC44 were 1.3 and 1.3, respectively. The mean DAPSA44 scores were similar

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Agreement between original-DAPSA and DAPSA44

	DAPSA44				
DAPSA	Remission 1.98 (1.21)	Low disease activity 8.52 (2.85)	Moderate disease activity 19.45 (3.83)	High disease activity 41.58 (14.37)	Total
Remission 1.97 (1.20)	**588 (99%)/(97%)**	6 (1%)/(0.5%)	0 (0%)/(0%)	0 (0%)/(0%)	594
Low disease activity 8.56 (2.85)	20 (1.5%)/(3.3%)	**1252 (97%)/(97%)**	24 (1.8%)/(3.7%)	0 (0%)/(0%)	1296
Moderate disease activity 19.42 (3.71)	0 (0%)/(0%)	32 (4.8%)/(2.5%)	**604 (90%)/(93%)**	30 (4.5%)/(3.4%)	666
High disease activity 40.73 (14.83)	0 (0%)/(0%)	0 (0%)/(0%)	22 (10.9%)/(3.4%)	**179 (89%)/(86%)**	201
Total	608	1290	650	209	

Agreement 98.6%
Kappa: 0.95
n (%) within DAPSA disease activity states/(%) within DAPSA44 disease activity states
Below each disease activity state, mean (SD)

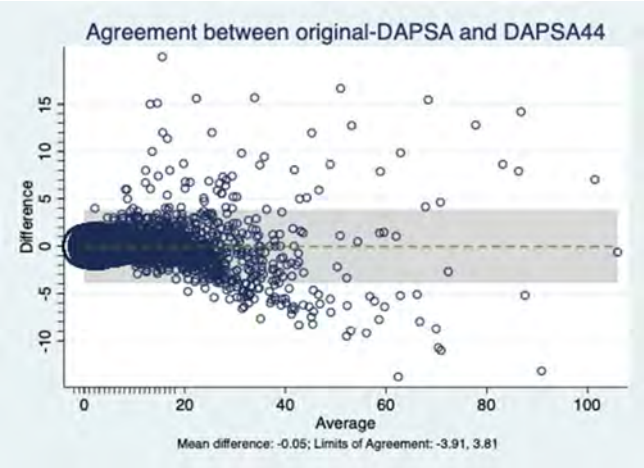


Figure 1. Bland–Altman plot. Agreement between original-DAPSA and DAPSA44.

between cohorts: 12.6 (SD 12.3) in the derivation and 12.2 (SD 12.4) in the validation cohort (p=0.33). The validation cohort (n=2757) analyses showed near-perfect agreement between DAPSA-original and DAPSA44, with a ICC 0.98, 95% CI 0.98–0.99 and kappa=0.95. The Bland–Altman plot demonstrated a mean difference of 0.25 points with a 95% limit of agreement between 0.25 and –0.02. (Figure 1)

In correlation analyses, Spearman coefficients between DAPSA44 and external constructs fell within the predefined 0.3-wide range of corresponding DAPSA-original coefficients, with some coefficients even showing identical values. For discrimination between active and inactive disease, DAPSA44 demonstrated excellent discriminatory ability (SDM >0.8) across all scenarios.

Conclusion: These findings support the use of DAPSA44 as a comparable tool to DAPSA-original for assessing disease activity due to peripheral arthritis, in situations where only a reduced joint count is available.

Disclosure: D. capelusnik: None; **C. López Medina**: None; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **D. Aletaha**: AbbVie/Abbott, 2, 6, Eli Lilly, 2, 5, Galapagos, 2, Gilead, 6, Janssen, 6, Johnson & Johnson, 2, 6, Merck/MSD, 6, Novartis, 6, Pfizer,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, Sandoz, 6, Sanofi, 6; **J. Smolen**: AbbVie/Abbott, 5, 6, Ananda, 6, AstraZeneca, 5, 6, Astro, 6, Bristol-Myers Squibb(BMS), 6, Celgene, 6, Celltrion, 6, Chugai-Roche, 6, Galapagos, 5, 6, Immunovant, 6, Janssen, 6, Lilly, 5, 6, Pfizer, 6, R-Pharma, 6, Samsung, 6, Sandoz, 6, Sanofi, 6; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2333

Validation of a Corrected Axial Spondyoarthritis Metrology Index in 9 Randomized Clinical Trials

Dafne capelusnik[1], Philip Gardiner[2], Annelies Boonen[3], Elena Nikiphorou[4] and **Sofia Ramiro**[5], [1]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [2]Altnagelvin Hospital, Londonderry, United Kingdom, [3]Maastricht University Medical Centre+ & Maastricht University, Maastricht, Limburg, Netherlands, [4]King's College London, London, United Kingdom, [5]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The MOBILITY study showed that BASMI often misclassifies spinal mobility, especially in older and taller individuals. To address this, the Corrected AxSpA Metrology Index (CASMI) was developed by adjusting BASMI for age, height, and sex to remove the variability introduced by these factors. This study evaluates CASMI's psychometric properties and compares them with BASMI in RCTs of axSpA patients treated with b/tsDMARDs.

Methods: RCTs in axSpA patients with complete BASMI component data (lateral spinal flexion, tragus-to-wall distance, intermalleolar distance, cervical rotation, and lumbar flexion) at baseline and the timing of the primary endpoint were included. Data were accessed and analyzed via the data-sharing platform Vivli. Age, sex, and height were used to adjust individual spinal mobility measures. BASMI- and CASMI-linear were calculated, and the following psychometric properties were analyzed: Construct validity: Known-group discrimination (Standardized Mean Difference -SMD) at baseline to distinguish between low and high functional impairment (BASFI< 3 vs >6); Longitudinal construct validity: Standardized Response Mean (SRM), Guyatt's responsiveness index (GRI), and effect size (ES); Trial discrimination: SMD. For all these psychometric properties, performance was classified as follows: low performance:< 0.5; adequate performance: ≥0.5 and < 0.8; good performance: ≥0.8. Lastly, a sensitivity analysis was conducted in patients with early disease (≤2 years of symptom duration).

Results: Nine RCTs, all having reached the primary endpoint, with complete BASMI component data and available age, sex, and height information were included. Six involved radiographic axSpA, three non-radiographic axSpA. Only 5 studies included patients with early disease and in varying proportions: 3–48%.

In seven of nine trials, CASMI had a lower mean value than BASMI (Table). For construct validity, most trials showed good discriminatory capacity, except COAST-W (TNFi-insuficient response population) and SELECT-AXIS. EMBARK was the only trial where CASMI showed a good discrimination between know-groups, while for BASMI it was only adequate. Regarding longitudinal construct validity, results were inconclusive, showing high variability across measures, but without important differences between BASMI and CASMI. All trials in bDMARD-naïve r-axSpA patients showed significant BASMI/CASMI improvements with active treatment, but trial discrimination was generally low for both, except for CASMI in ASSERT

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Summary of the psychometric properties assessment for BASMI and CASMI across RCTs.

Trial (active treatment vs PBO)	Population	BASMI improvement reported	Baseline mean values		Mean change from baseline in each arm						Construct validity		Longitudinal construct validity						Clinical trial discrimination	
					BASMI (0-10)			CASMI (0-10)			SMD*		GRI		SRM		ES		SMD	
			BASMI (0-10)	CASMI (0-10)	Active treatment	PBO	p-value	Active treatment	PBO	p-value	BASMI (0-10)	CASMI (0-10)	BASMI (0-10)	CASMI (0-10)	BASMI (0-10)	CASMI (0-10)	BASMI (0-10)	CASMI (0-10)	BASMI (0-10)	CASMI (0-10)
ASSERT (IFX vs PBO)	r-axSpA TNFi naive	Yes	2.7 (1.2)	2.1 (1.2)	**-0.62 (0.98)**	**-0.19 (0.57)**	**<0.001**	**-0.71 (1.09)**	**-0.17 (0.61)**	**<0.001**	-1.00	-0.92	-1.08	-1.16	-0.63	-0.66	-0.38	-0.36	-0.48	-0.55
COAST-V (IXE vs PBO)	r-axSpA TNFi naive	NR	4.2 (1.5)	3.8 (1.8)	**-0.47 (0.81)**	**-0.18 (0.71)**	**0.004**	**-0.55 (0.96)**	**-0.21 (0.86)**	**0.003**	-1.08	-0.92	-0.66	-0.65	-0.58	-0.58	-0.31	-0.31	-0.37	-0.37
COAST-W (IXE vs PBO)	r-axSpA TNFi IR	NR	4.5 (1.7)	4.5 (1.9)	-0.29 (0.89)	-0.09 (0.92)	0.076	-0.36 (1.04)	-0.12 (1.15)	0.082	-0.49	-0.63	-0.32	-0.31	-0.33	-0.35	-0.19	-0.19	-0.23	-0.23
GO-RAISE (GOL vs PBO)	r-axSpA TNFi naive	No*	4.1 (1.7)	3.7 (2.0)	**-0.38 (0.78)**	**-0.17 (0.72)**	**0.031**	**-0.45 (0.90)**	**-0.15 (0.74)**	**0.004**	-1.00	-0.93	-0.60	-0.61	-0.49	-0.50	-0.22	-0.22	-0.33	-0.33
SELECT-AXIS1 (UPA vs PBO)	r-axSpA TNFi naive	Yes	3.6 (1.5)	3.2 (1.7)	**-0.41 (0.76)**	**-0.17 (0.63)**	**0.029**	**-0.46 (0.87)**	**-0.14 (0.62)**	**0.005**	-0.30	-0.44	-0.61	-0.72	-0.53	-0.52	-0.26	-0.27	-0.31	-0.41
TOFACITINIB (TOF vs PBO)	r-axSpA TNFi naive	Yes	4.4 (1.8)	4.3 (2.1)	**-0.64 (0.72)**	**-0.13 (0.55)**	**<0.001**	**-0.75 (0.84)**	**-0.14 (0.61)**	**<0.001**	-1.25	-1.28	-1.16	-1.23	-0.89	-0.90	-0.37	-0.36	-0.80	-0.84
ABILITY-1 (ADA vs PBO)	nr-axSpA TNFi naive	No	4.5 (1.7)	4.5 (2.0)	-0.11 (0.67)	-0.11 (0.66)	0.984	-0.11 (0.8)	-0.10 (0.79)	0.896	-1.08	-0.91	-0.16	-0.13	-0.16	-0.13	-0.09	-0.08	0.003	-0.01
COAST-X (IXE vs PBO)	nr-axSpA TNFi naive	NR	3.2 (1.2)	2.4 (1.3)	-0.39 (0.84)	-0.23 (0.82)	0.110	-0.43 (0.98)	-0.26 (0.88)	0.153	-1.03	-0.88	-0.48	-0.48	-0.46	-0.43	-0.32	-0.33	-0.19	-0.17
EMBARK (ETN vs PBO)	nr-axSpA TNFi naive	No	2.1 (1.0)	1.6 (1.1)	-0.42 (1.03)	-0.19 (0.70)	0.077	**-0.45 (0.12)**	**-0.18 (0.07)**	**0.049**	-0.77	-0.83	-0.61	-0.64	-0.41	-0.41	-0.40	-0.40	-0.27	-0.30

*Discrimination ability to discriminate between know-groups (BASFI<3 and BASFI >6)
Construct validity: SMD < 0.5 Low (red); >=0.5 & <0.8 Moderate (amber); >=0.8 Good (green)
Longitudinal construct validity: Guyatt's ES, SRM, ES < 0.5 Low (red); >=0.5 & <0.8 Adequate (amber); >=0.8 Good (green)
Clinical trial discrimination: SMD < 0.5 Low (red); >=0.5 & <0.8 Adequate (amber); >=0.8 Good (green)
NR, not reported; SMD, Standardized Mean Difference; ES, Effect Size; GRI, Guyatt's responsiveness index; SRM, Standardized Response Mean.

(adequate) and TOFACITINIB (good). In all nr-axSpA studies, trial discrimination was low for both BASMI and CASMI. In analyses restricted to early disease patients, trial discrimination improved numerically but remained low (except for TOFACITINIB, where it remained good), with the exception of SELECT-AXIS, where discrimination became good for BASMI and adequate for CASMI.

Conclusion: While CASMI has been developed to be a more truthful measure than BASMI, both CASMI and BASMI have largely comparable measurement properties. This means that the current adjustments are still insufficient to detect change over time in spinal mobility.

Disclosure: D. capelusnik: None; **P. Gardiner**: AbbVie/Abbott, 1, Galapagos, 1, Gilead, 1, Pfizer, 1, UCB, 1; **A. Boonen**: AbbVie/Abbott, 5, Alfasigma, 2, Celgene, 5, Eli Lilly, 2, Novartis, 2, Sandoz, 2, UCB, 2; **E. Nikiphorou**: AbbVie/Abbott, 1, Alfasigma, 1, Eli Lilly, 1, 5, Fresenius, 1, Galapagos, 1, Gilead, 1, Novartis, 1, Pfizer, 1, 5, UCB, 1; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2334

Development and validation analysis of a Corrected Axial Spondyloarthritis Metrology Index

Dafne capelusnik[1], Philip Gardiner[2], Elena Nikiphorou[3], Désirée Van Der Heijde[4], Robert Landewé[5], Astrid Van Tubergen[6], Annelies Boonen[7] and **Sofia Ramiro**[8], [1]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [2]Altnagelvin Hospital, Londonderry, United Kingdom, [3]King's College London, London, United Kingdom, [4]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [5]Department of Rheumatology, Amsterdam University Medical Center, Amsterdam, Netherlands; and Zuyderland Medical Center, Heerlen, Netherlands, [6]Maastricht university, Maastricht, Netherlands, [7]Maastricht University Medical Centre+ & Maastricht University, Maastricht, Limburg, Netherlands, [8]Leiden University Medical Center, Bunde, Netherlands

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The MOBILITY study, a study on spinal mobility measures in healthy individuals, showed that the Bath Ankylosing Spondylitis Metrology Index (BASMI) often overestimates spinal mobility as these measures also depend on height, sex and age, with a significant impact on older and taller individuals. To better address this, we developed a Corrected AxSpA Metrology Index (CASMI) and compared its construct validity with that of BASMI in patients with established axSpA.

Methods: Data from the MOBILITY study on spinal mobility in healthy individuals were used to develop a corrected version of the BASMI (CASMI). Age-, sex-, and height-specific normal limits were derived for each component (lateral spinal flexion -LSF-, tragus-to-wall -TTW-, intermalleolar distance -IMD-, Schobert's test, cervical rotation -CR-) from regression models or trigonometric calculations. Components were anchored using the 50th percentile of healthy individuals (MOBILITY study, score = 0) and the 95th percentile of axSpA patients (cohort study of axSpA used, score = 10). TTW was corrected using fixed thresholds. Construct validity of several CASMI versions were compared to BASMI in an axSpA population included in the OASIS cohort. Construct validity was assessed by comparing means, minimum and maximum values, floor and ceiling effects of BASMI and CASMI, and correlations with age, height and disease outcomes (BASFI, BASDAI, ASDAS, mSASSS and number of syndesmophytes). It was hypothesized that CASMI would reduce correlations with age and height while maintaining correlations with disease measures. Differences between BASMI and CASMI in the score distributions were visualized with density plots. Known group discrimination, as part of construct validity, was tested by comparing standardized mean differences (SMD) between known groups, stratified by: i) BASFI (≤3 vs ≥6), ii) mSASSS (≥1 vs >10), and iii) syndesmophyte count (≤1 vs 5). Higher absolute SMD values indicate better discrimination, with >0.8 considered as 'good'.

Results: Table 1 presents the formulae for the five components of BASMI, as well the formulae for the CASMI components. In the OASIS cohort, mean values for some corrected components were lower, whereas minimum values remained unchanged, and were slightly lower for CASMI. Floor effects increased in individual items (e.g., TTW: 0.5% to 52%) but

Table 1. Equations for the conversion of the assessments (A) into scores (S) for the five components of the BASMI and CASMI, including applied adjustments§

Instruments		S=0 (Normal Limit)# if:	S between 0-10:	S=10 (Severe limit)# if:	Age	Sex	Height
Lateral spinal flexion (cm)	BASMI	A≥21.1	S = (21.1-A)/2.1	A≤0.1			
	CASMI	≥22.1-adjustments	S = (Normal limit-A)/(Normal limit – Severe limit)/10)	≤2.25-adjustments	✓		✓
Tragus-to-wall distance (cm)	BASMI	A≤8	S = (A-8)/3	A≥38			
	CASMIa	A≤11	S = (A-11)/1.5	A≥26			
	CASMIb	A≤11.5	S = (A-11.5)/1.45	A≥26			
	CASMIc	A≤12	S = (A-12)/1.4	A≥26			
	CASMId	A≤12.5	S = (A-12.5)/1.35	A≥26			
Lumbar flexion (cm)	BASMI	A≥7.4	S = (7.4-A)/0.7	A≤0.4			
	CASMI	≥5.2-adjustments	S = (Normal limit-A)/(Normal limit – Severe limit)/10)	≤0.2-adjustments	✓		
Intermalleolar distance (cm)	BASMI	A≥124.5	S = (124.5-A)/10	A≤24.5			
	CASMI	≥119-adjustments	S = (Normal limit-A)/(Normal limit – Severe limit)/10)	≤29.5-adjustments	✓	✓	✓
Cervical rotation angle (°)	BASMI	A≥89.3	S = (89.3-A)/8.5	A≤4.3			
	CASMI	≥81±1.92*-adjustments	S = (Normal limit-A)/(Normal limit – Severe limit)/10)	≤11.5±0.27**-adjustments	✓	✓	

§ BASMI formulae are the ones from BASMI linear and the CASMI ones the same, with adjustments of the normal and severe limits
#Normal and severe limits for CASMI components were calculated based on appropriate adjustments for each individual's age, sex, or height
For CASMI components, age and sex correction factors were derived from the regression coefficients obtained in the MOBILITY study, whereas for height, both regression-based coefficients and those calculated using trigonometric formulae were applied. Adjustments reflected a specific formula for each normal/severe limit, for each spinal mobility measure.
* If male sex "+1.92", if female sex "-1.92"
** If male sex "+0.27", if female sex "-0.27"
A, assessment (of the individual spinal mobility measure); S, score

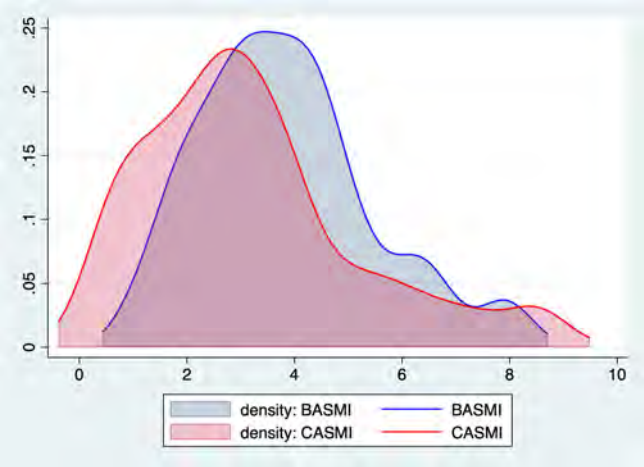


Figure 1. Density plots for BASMI and CASMI. CASMI represented here is CASMI_Ma which formula was adjusted using age, sex and hight correction factors derived from the regression coefficients obtained in the MOBILITY study.

Table 2. Descriptive data and construct of the BASMI/CASMI and their components in OASIS (n=204-216)

Instruments	Scale characteristics					Correlations							
	Mean (sd) score value (0-10)	Min score value (0-10)	Floor effect n (%)	Max score value (0-10)	Ceiling effect n (%)	Age (Rho)	Height (Rho)	Disease duration (Rho)	BASFI (Rho)	BASDAI (Rho)	ASDAS (Rho)	mSASSS (Rho)	Syndesmophytes (Rho)
Lateral spinal flexion score	**5.5 (2.6)**	**0**	**6 (3)**	**9.68**	**0 (0)**	**0.372**	**-0.307**	**0.264**	**0.484**	**0.158**	**0.184**	**0.440**	**0.338**
Lateral spinal flexion_T score	5.8 (2.9)	0	9 (4)	10	5 (2)	0.216	-0.185	0.194	0.451	0.131	0.188	0.376	0.283
Lateral spinal flexion_M score	5.5 (3.1)	0	14 (7)	10	6 (3)	0.230	-0.251	0.198	0.457	0.148	0.199	0.376	0.280
Tragus to wall score	**2.1 (1.6)**	**0**	**1 (0.5)**	**8.8**	**0 (0)**	**0.361**	**-0.067**	**0.340**	**0.339**	**-0.007**	**0.135**	**0.543**	**0.446**
Tragus to wall_Ma score	2.2 (2.8)	0	55 (26)	10	7 (3)	0.376	-0.082	0.346	0.358	0.001	0.138	0.549	0.446
Tragus to wall_Mb score	2.0 (2.8)	0	84 (39)	10	7 (3)	0.364	-0.090	0.338	0.352	-0.005	0.135	0.559	0.453
Tragus to wall_Mc score	1.9 (2.8)	0	99 (46)	10	7 (3)	0.341	-0.096	0.340	0.366	-0.013	0.137	0.554	0.446
Tragus to wall_Md score	1.8 (2.8)	0	113 (52)	10	7 (3)	0.344	-0.118	0.360	0.369	-0.016	0.118	0.562	0.473
Intramalleolar distance	**2.1 (1.9)**	**0**	**41 (19)**	**8.65**	**0 (0)**	**0.403**	**-0.537**	**0.243**	**0.459**	**0.222**	**0.203**	**0.342**	**0.230**
Intramalleolar distance_T score	1.2 (1.7)	0	88 (42)	8.38	0 (0)	0.154	-0.231	0.061	0.396	0.223	0.200	0.194	0.151
Intramalleolar distance_M score	1.6 (1.8)	0	56 (27)	8.58	0 (0)	0.189	-0.319	0.150	0.418	0.210	0.216	0.270	0.250
Cervical rotation score	**3.0 (2.6)**	**0**	**27 (12)**	**10**	**2 (1)**	**0.373**	**-0.357**	**0.314**	**0.492**	**0.211**	**0.296**	**0.425**	**0.394**
Cervical rotation_M score	2.1 (2.8)	0	83 (38)	10	5 (2)	0.147	-0.229	0.220	0.425	0.156	0.301	0.337	0.336
Schobert's test	**6.5 (2.0)**	**0**	**0 (0)**	**10**	**10 (5)**	**0.183**	**-0.164**	**0.231**	**0.425**	**0.116**	**0.199**	**0.435**	**0.342**
Schobert's_M test	4.5 (2.9)	0	9 (4.2)	10	3 (1)	0.137	-0.120	0.156	0.381	0.124	0.192	0.392	0.304
BASMI	**3.8 (1.6)**	**0.9**	**0 (0)**	**8.4**	**0 (0)**	**0.450**	**-0.356**	**0.258**	**0.594**	**0.212**	**0.273**	**0.584**	**0.473**
CASMI_Ta	3.2 (2.0)	0.1	0 (0)	9.0	0 (0)	0.294	-0.204	0.227	0.549	0.180	0.272	0.542	0.431
CASMI_Tb	3.1 (2.0)	0.1	0 (0)	9.0	0 (0)	0.288	-0.205	0.224	0.547	0.180	0.272	0.539	0.436
CASMI_Tc	3.1 (2.0)	0.1	0 (0)	9.0	0 (0)	0.285	-0.204	0.224	0.546	0.180	0.271	0.536	0.433
CASMI_Td	3.1 (2.0)	0.1	0 (0)	9.0	0 (0)	0.283	-0.209	0.222	0.548	0.185	0.273	0.533	0.433
CASMI-Ma	3.2 (2.0)	0.1	0 (0)	9.1	0 (0)	0.279	-0.282	0.314	0.585	0.169	0.298	0.552	0.450
CASMI-Mb	3.1 (2.0)	0.1	0 (0)	9.1	0 (0)	0.277	-0.284	0.314	0.580	0.171	0.300	0.552	0.448
CASMI-Mc	3.1 (2.0)	0.1	0 (0)	9.1	0 (0)	0.274	-0.284	0.314	0.587	0.172	0.299	0.547	0.446
CASMI-Md	3.1 (2.0)	0.1	0 (0)	9.1	0 (0)	0.271	-0.288	0.314	0.586	0.174	0.299	0.543	0.445

Missing data for LSF=11; IMD=2; LF=1; BASMI/CASMI=11

*The normal limit (anchor zero) for the BASMI components was defined based on their established minimal values, while for the CASMI components, it was set using the 50th percentile of BASMI values from the MOBILITY study (healthy individuals). The severe limit (anchor 10) for the BASMI components was defined based on their established maximum values, while for the CASMI components, it was set using the worse values from a longstanding established r-axSpA cohort.

In bolded BASMI/BASMI components values.

T: trigonometric-based adjustment formula; M: MOBILITY coefficient-based adjustment formula (except by TTW_M, where the normal limit was based on the mean value from the MOBILITY study.

a-d version correspond to the Tragus to wall version used.

Cells are colored green when the CASMI component reduces unwanted correlation of the CASMI (components) is reduced by more than 10% (>0.100) the correlation with age or height (i.e., improves), and red when it increases the correlation (by at least 10% i.e., worsens) in relation, when compared to BASMI (components).

remained 0% in the composite scores. Maximum values and ceiling effects increased in individual components but not in CASMI. As intended, correlation with age and height decreased in CASMI and several components, but no major changes in correlations with disease outcomes, confirming the hypotheses made (Table 2). The density plots showed that CASMI systematically yields lower scores and has a higher floor effect, suggesting better calibration and better sensitivity to capture subtle impairments in spinal mobility. Discrimination between known groups was good across all score versions and external constructs (SMD >0.80).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: An age-, sex- and height-corrected mobility score, the CASMI, has been developed as a more personalised and truthful measure of mobility in axSpA, compared to BASMI.

Disclosure: D. capelusnik: None; **P. Gardiner**: AbbVie/Abbott, 1, Galapagos, 1, Gilead, 1, Pfizer, 1, UCB, 1; **E. Nikiphorou**: AbbVie/Abbott, 1, Alfasigma, 1, Eli Lilly, 1, 5, Fresenius, 1, Galapagos, 1, Gilead, 1, Novartis, 1, Pfizer, 1, 5, UCB, 1; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **R. Landewé**: AbbVie/Abbott, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, Joint Imaging BV, 12, Director, Novartis, 2, Pfizer, 2, Rheumatology Consultancy BV, 12, Director, UCB, 2; **A. Van Tubergen**: Janssen, 2, Novartis, 2, 5, 6, UCB, 5; **A. Boonen**: AbbVie/Abbott, 5, Alfasigma, 2, Celgene, 5, Eli Lilly, 2, Novartis, 2, Sandoz, 2, UCB, 2; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2335

The 14-3-3 eta AAb biomarker improves discriminative performance of CRP and HLA-B27 to differentiate people with radiographic axSpA from those with mechanical back pain

Walter P. Maksymowych[1], Raj Sengupta[2], Anthony Marotta[3], Stephanie Wichuk[4], Charlotte Cavill[5], Stephen Bleakley[3] and Norma Biln[6], [1]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [2]Royal National Hospital for Rheumatic Diseases, Bath, England, United Kingdom, [3]Augurex Life Sciences Corp, Vancouver, BC, Canada, [4]University of Alberta, Edmonton, AB, Canada, [5]Royal United Hospitals Bath NHS Foundation Trust, Bath, England, United Kingdom, [6]Augurex Life Sciences, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Reducing diagnostic delay for people presenting with back pain who have axial spondyloarthritis (axSpA) has become a clinical imperative since effective treatments can limit progression of this debilitative disease. The absence of a simple blood test that is accessible by referring primary care physicians contributes to this delay. We presented data from the Bath Spondyloarthritis Biobank demonstrating that 14-3-3η AAbs distinguish referred patients with axSpA from those with mechanical backpain (MBP), with an 88% PPV. This challenge also exists at the community rheumatologist level, where experienced interpretation of radiographs and MRI scans may be limited. This study evaluates the performance of the 14-3-3η AAbs in combination with existing clinical parameters in an established Edmonton radiographic (r-axSpA) patient cohort.

Methods: Serum samples from 159 patients with a rheumatologist confirmed diagnosis and classified as r-axSpA (AS-modified New York criteria) were tested on the anti-14-3-3η multiplex assay. The control group comprised the 51 MBP patients previously tested from the Bath cohort. The serum differential expression of 14-3-3η AAbs, CRP and HLA-B27 between patients with r-axSpA and MBP was evaluated by ROC AUC. Regression models combining the 14-3-3η AAb Score derived from the Bath study were tested in two predictive models: one with CRP and HLA-B27 markers only and the other adding Age and Sex variables. Corresponding specificity (SP), sensitivity (SN), predictive values (PPV, NPV),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

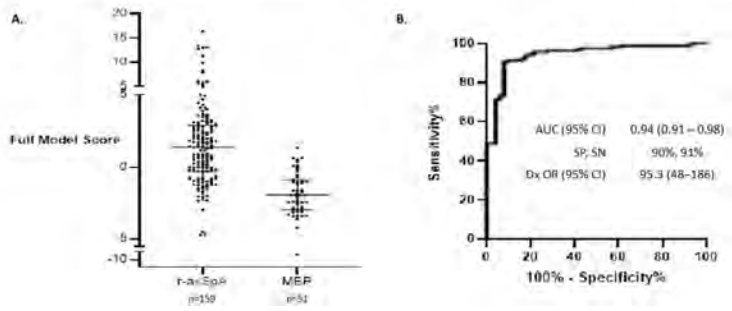
Table 1. Patient characteristics

	Edmonton r-axSpA	Bath MBP
Sample Size (n)	159	51
Age Median (IQR)	42 (33-51)	30 (22-36)
Age Mean (SD)	42 (12)	30 (9)
Sex Male n(%)	109 (68.6%)	30 (58.8%)
Sex Female n(%)	50 (31.4%)	21 (41.2%)
CRP Median (IQR)	7.2 (1.9-15.6)	1 (0-2)
CRP Mean (SD)	12.6 (17.8)	1.7 (2.4)
HLA-B27 Pos n(%)	135 (84.9%)	7 (14.3%)
HLA-B27 Neg n(%)	24 (15.1 %)	42 (85.7%)
Disease Duration Med (IQR)	17 (10-25)	
Disease Duration Mean (SD)	18.1 (10.6)	

Table 2. Marker and model performance

Models	14-3-3η AAbs	CRP	HLA-B27	14-3-3η AAb Score + (CRP, HLA-B27)	14-3-3η AAb Score + (Age, Sex, CRP, HLA-B27)
AUC (95% CI)	0.70 (0.62-0.78)	0.81 (0.75 – 0.87)	0.84 (0.77 – 0.91)	0.93 (0.90-0.97)	0.94 (0.91 – 0.98)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
SP, SN	90%, 40%	90%, 55%	85%, 82%	90%, 81%	90%, 91%
PPV	93%	95%	94%	96%	97%
NPV	33%	39%	60%	61%	77%
LR+	4.1	5.6	4.8	8.2	9.3
LR-	0.67	0.50	0.21	0.21	0.10
Dx OR (95% CI)	6.2 (2.8 - 13.5)	11.1 (5.6–22.5)	24.1 (12.3–45.1)	39.6 (20.5–76.3)	95.3 (48–186)
AIC	221	183	158	115	109

Figure 1. A. Score distribution for model that includes all markers with age and sex, and B. ROC AUC



likelihood (LR) and diagnostic odds ratios (DxOR) are provided. The Akaike Information Criterion (AIC) statistical measure was reported to compare the relative quality of predictive models.

Results: Mean age of patients with r-axSpA was 42 (69% male) and for MBP, 30 years (59% male), (Table 1). Differential expression of each of the biomarkers delivered significant ROC AUCs; 0.70 for 14-3-3η AAbs, 0.81 for CRP and 0.84 for HLA-B27. The latter two delivered respectively higher DxOR (6.2, 11.1, 24.1) as expected, considering that they were used in patient diagnosis. The model that included the 14-3-3η AAb score with CRP and HLA-B27 added had better discrimination of patients with axSpA versus MBP with an AUC of 0.93 and DxOR of 39.6 that further improved to an AUC of 0.94 and DxOR of 95.3 when age and sex variables were added (Figure 1). As shown in Table 2, the AIC of the predictive models supported the full model as the best fit.

Conclusion: This study demonstrates that the 14-3-3η AAb score when added to currently used CRP and HLA-B27 markers, improves the differentiation of people with MBP from established r-axSpA. While the pretest probability of CRP and HLA-B27 performance is higher in this cross-sectional study than would be expected in an early referral cohort,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

including 14-3-3η AAb score may reduce diagnostic delay and potentially enable more confident and prompt initiation of therapy to improve outcomes.

Disclosure: W. Maksymowych: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **R. Sengupta**: AbbVie, 6, Eli Lilly and Company, 6, Novartis, 5, 6, Pfizer, 6, UCB Pharma, 5, 6; **A. Marotta**: Augurex Life Sciences Corp., 12,, 2; **S. Wichuk**: None; **C. Cavill**: None; **S. Bleakley**: Augurex Life Sciences Corp., 3, 11; **N. Biln**: Augurex Life Sciences Corp., 3, 4, 8, 11.

Abstract Number: 2336

Early Axial Spondyloarthritis in Latin America: Prevalence and Regional Differences from the "ESPALDA" Multinational Registry

Wilson bautista molano[1], Guillermo Guaracha[2], Fernando Sommerfleck[3], Rodrigo García Salinas[4], Julio Cesar Casasola Vargas[5], John Londono[6], Daniel Fernandez[7], Diego Vila[8], Lorena Brance[9], Jossiel Then[10], francisco Zeballos[11], Lysseth Macias[12], Marilu mestanza[13], Daisy Sanchez[14], IYN chinchay[15], Patricia Melgarejo[16], Angel Castillo[17], Gimena Gomez[18], Leandro ferreryra[19], Dora candia[20], Gustavo medina[21], Maria Erguez[22], Einer Sanchez[4] and Daniel Palleiro[23], [1]University Hospital Fundacion Santa Fe de Bogota, Bogota, Colombia, [2]Instituto Nacional de Ciencias Médicas y Nutrición 'Salvador Zubirán', Ciudad de México, Mexico, Mexico, [3]Sanatorio Julio Mendez, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [4]Hospital Italiano La Plata, La Plata, Argentina, [5]CAVJ7111038Q9, MEXICO CITY, Mexico, [6]Hospital Militar Central , Universidad de La Sabana, Colombia, Bogota, Colombia, [7]Facultad de Medicina, Pontificia Universidad Javeriana, Bogotá, Colombia; Departamento de Medicina Interna, Unidad de Reumatología, Hospital Universitario San Ignacio, Bogotá, Colombia, BOGOTA, Colombia, [8]Hospital Virgen del Carmen, Buenos Aires, Argentina, Buenos Aires, Argentina, [9]School of Medicine, Rosario National University, Argentina, Rosario, Argentina, [10]HOMS, Santiago, Dominican Republic, [11]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Peru, [12]Consultorio sse, Hospital Metropolitano, Ecuador, Quito, Ecuador, [13]Hospital Metropolitano, Ecuador, Quito, Ecuador, [14]Sociedad Ecuatoriana de Reumatologáa, GUAYAS - GUAYAQUIL, Ecuador, [15]Hospital Guillermo Kaelin de La Fuente, Perú, Lima, Peru, [16]Instituto de Previsión Social, Villarrica, Paraguay, [17]Centro Médico de las Americas, Merida, Mexico, [18]Sanatorio Guemes, Buenos Aires, Argentina, [19]HIBA, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [20]Hospital Regional Primero de Octubre ISSTE, Fuerzas Armadas, México, Durango, Mexico, [21]Clinical Hospital Buenos Aires University, Quilmes, Argentina, [22]SAR, Guayaquil, Ecuador, [23]INRU, Montevideo, Uruguay

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

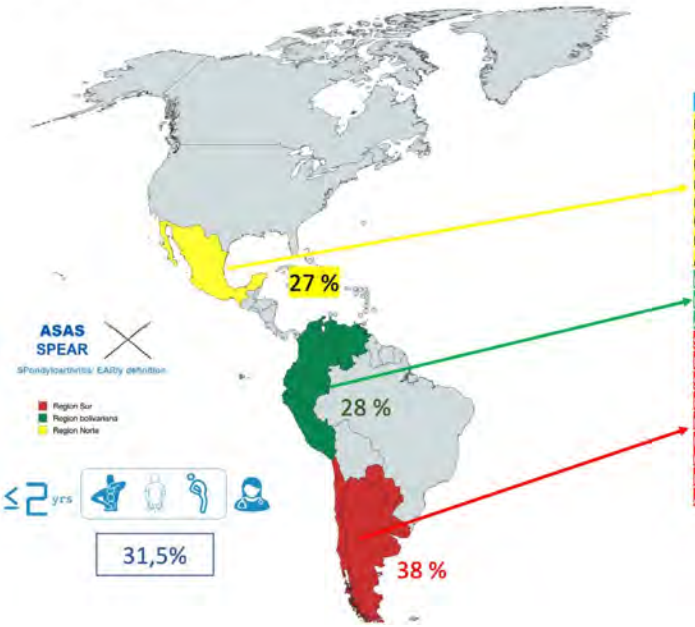
Session Time: 10:30AM–12:30PM

Background/Purpose: The ESPALDA registry, developed by PANLAR, collects data from Latin America to better understand the clinical and epidemiological characteristics of patients with axial spondyloarthritis (axSpA). This analysis focuses on early axSpA, defined by ASAS criteria as a duration from the onset of back pain to diagnosis of less than two years, across the entire cohort and by region.

Methods: Patients aged ≥18 years meeting the ASAS 2009 criteria for axSpA were included. Data were collected from medical centers in nine LATAM countries. Baseline data included demographics, disease duration, clinical manifestations, comorbidities, disease activity (ASDAS, BASDAI), functionality (BASFI), laboratory tests (ESR, CRP, HLA-B27), and imaging (X-ray, MRI). Regions were categorized as South (Argentina, Chile, Uruguay, Paraguay), Andean (Colombia, Peru, Venezuela, Ecuador), and North (Mexico). Descriptive statistics and comparative analyses were performed using Chi-square tests and parametric or non-parametric methods as appropriate. Multivariable analysis was performed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: ESPALDA - Regions



axSpA Characteristic	EarlySpA Yes (1)	EarlySpA No (0)	p-value	OR (95% CI)
Enthesitis (yes/no)	32	10	0.01	4.30 (1.59-11.64)
Elevated CRP %	62	22	<0.001	5.56 (2.34-13.26)
Pain (0-10)	13.2 (19.3)	10.0 (18.1)	<0.001	NA
Night pain (0-10)	6.7 (2.6)	4.1 (2.6)	0.04	NA
Morning stiffness duration (minutes)	29.9 (32.8)	15.2 (20.8)	0.03	NA
BASDAI	6.1 (1.6)	3.1 (2.1)	0.04	NA
ASDAS	3.8 (0.7)	2.2 (1.1)	0.02	NA
Enthesitis (yes/no) %	59	24	0.0001	4.73 (1.83-12.23)
Pain (0-10)	9.7 (14.8)	6.0 (14.4)	0.00	NA
ASDAS	3.8 (0.6)	1.9 (0.9)	<0.001	NA
Smoking %	42	22	0.01	2.46 (1.30-4.64)
Elevated CRP %	51	32	0.01	2.25 (1.24-4.11)
Sacroiliac maneuver %	69	42	0.00	3.14 (1.58-6.26)
Pain (0-10)	10.9 (16.1)	5.3 (2.6)	<0.001	NA
Night pain (0-10)	7.2 (8.3)	4.7 (2.2)	0.00	NA
Morning stiffness duration (minutes)	46.4 (31.4)	28.1 (24.0)	0.01	NA
BASDAI	5.7 (1.3)	3.2 (1.8)	<0.001	NA
ASDAS	3.9 (0.6)	2.4 (1.1)	<0.001	NA

axSpA Characteristic (419)	Early SpA Yes (130)	Early SpA No (289)	p-value	OR (95% CI)
Sex male	52.21%	61.92%	0.075	0.67 (0.44-1.02)
Smoking	34.59%	27.47%	0.175	1.40 (0.89-2.18)
Inflammatory back pain	84.09%	81.82%	0.670	1.17 (0.67-2.05)
Uveitis	16.79%	21.79%	0.287	0.72 (0.43-1.23)
IBD	6.62%	4.63%	0.536	1.46 (0.61-3.51)
Psoriasis	18.25%	14.23%	0.358	1.34 (0.78-2.33)
NSAID response	72.26%	68.33%	0.479	1.21 (0.77-1.90)
Arthritis (yes)	19.71%	21.00%	0.860	0.92 (0.55-1.54)
Enthesitis (yes)	42.34%	21.00%	**<0.001**	2.76 (1.77-4.31)
Elevated CRP	53.79%	27.71%	**<0.001**	3.04 (1.95-4.72)
HLA-B27 +	62.50%	66.67%	0.462	0.83 (0.54-1.29)
Family history of SpA	32.85%	29.20%	0.515	1.19 (0.76-1.84)
Sacroiliac (ruposak)	69.35%	41.38%	**0.001**	3.21 (1.61-6.38)
Anterior chest pain	28.57%	15.25%	0.132	2.22 (0.89-5.56)
BASDAI >4	92.65%	35.51%	**<0.001**	32 (11-45)
ASDAS IDA (Inactivity)	0.00%	14.23%	**<0.001**	-
ASDAS LDA (Low Disease Activity)	0.00%	25.27%	**<0.001**	-
ASDAS MDA (Moderate Disease Activity)	35.77%	44.84%	0.097	0.68 (0.45-1.04)
ASDAS HDA (High Disease Activity)	64.23%	4.27%	**<0.001**	40.26 (20.49-79.12)
SI Joint X-Ray	56.82%	72.43%	**0.002**	0.50 (0.32-0.77)
MRI Edema	36.36%	40.70%	0.489	0.83 (0.53-1.30)
Chronic changes MRI (yes/no)	46.09%	51.46%	0.371	0.81 (0.53-1.23)
>4 SpA features	48.87%	49.08%	0.9	0.99 (0.65-1.50)
Years of education	13.00 (3.50)	13.00 (5.00)	0.631	
Age at back pain onset	34.00 (22.00)	33.00 (22.00)	0.925	
Pain (0-10)	7.00 (2.00)	5.00 (5.00)	**<0.001**	
Night pain (0-10)	7.00 (3.00)	5.00 (3.50)	**<0.001**	
Morning stiffness duration (minutes)	30.00 (45.00)	15.00 (30.00)	**<0.001**	
MASES (Enthesitis Score)	3.00 (4.00)	2.00 (3.00)	0.034	
BASFI (Functional Index)	5.60 (3.20)	3.50 (3.65)	**<0.001**	
BASDAI (Activity Index)	5.80 (2.30)	3.20 (2.60)	**<0.001**	
ASDAS (Activity Index)	3.70 (0.80)	2.20 (1.20)	**<0.001**	
CRP (C-reactive protein)	1.00 (4.62)	1.00 (3.55)	0.986	
ESR (Erythrocyte Sedimentation Rate)	11.00 (16.00)	12.00 (17.25)	0.457	
Number of SpA features	3.00 (2.00)	3.00 (2.00)	0.669	

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In 419 patients, the prevalence of early axSpA was 31.49% (95% CI: 27.31% - 36.01%). Regional differences in prevalence were observed: South (38.19%), Andean (28.42%), and North (27.42%) (p=0.07). Differential characteristics of the entire cohort are detailed in Table 1. Multivariable analysis identified key factors positively associated with early axSpA: ASDAS high disease activity (HDA, OR = 17.808, 95% CI: 2.446 - 129.645, p=0.004) and BASDAI ≥4 (OR = 44.378, 95% CI: 4.943 - 398.394, p=0.001). Regional analyses highlighted distinct characteristics among early axSpA patients: South: Smoking (OR = 2.46, 95% CI: 1.30-4.64, p=0.01), positive sacroiliac maneuver (OR = 3.14, 95% CI: 1.58-6.26, p< 0.001), elevated CRP (OR = 2.25, 95% CI: 1.24-4.11, p=0.01), BASDAI (p< 0.001), and prolonged morning stiffness (p=0.01) were significantly associated. Andean: Enthesitis (OR = 4.73, 95% CI: 1.83-12.23, p< 0.001) was a key feature, while elevated CRP showed marginal significance (OR = 2.79, 95% CI: 1.02-7.62, p=0.08). North: Enthesitis (OR = 4.30, 95% CI: 1.59-11.64, p=0.01), elevated CRP (OR = 5.56, 95% CI: 2.34-13.26, p< 0.001), BASDAI (p=0.04), and prolonged morning stiffness (p=0.03) were highly distinctive, all variables in fig 1.

Conclusion: The ESPALDA registry highlights significant regional variations in early axSpA characteristics across LATAM.

Disclosure: W. bautista molano: None; **G. Guaracha**: None; **F. Sommerfleck**: None; **R. García Salinas**: AbbVie/ Abbott, 2, 5, 6, Adium, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Raffo, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **J. Casasola Vargas**: None; **J. Londono**: None; **D. Fernandez**: None; **D. Vila**: None; **L. Brance**: None; **J. Then**: None; **f. Zeballos**: None; **L. Macias**: None; **M. mestanza**: None; **D. Sanchez**: None; **I. chinchay**: None; **P. Melgarejo**: None; **A. Castillo**: None; **G. Gomez**: None; **L. ferreryra**: None; **D. candia**: None; **G. medina**: None; **M. Erguez**: None; **E. Sanchez**: None; **D. Palleiro**: None.

Abstract Number: 2337

A Mediation Analysis of Tofacitinib's Effects on SF-36: The Roles of Fatigue, Pain, Stiffness, and Mobility in Ankylosing Spondylitis

Xenofon Baraliakos[1], Andrew G. Bushmakin[2], Joseph C. Cappelleri[2], Eleni Nikitopoulou[3], You-Li Ling[4], Mostafa Zayed[5] and Jonathan Dominick Cicci[6], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany, [2]Pfizer Inc., Groton, CT, [3]Pfizer Hellas, Athens, Greece, [4]Pfizer Inc, New York, NY, USA, New York, NY, [5]Pfizer Gulf FZ LLC, Dubai, United Arab Emirates, [6]Pfizer Inc., New York, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2305–2337) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Mediation modeling is used to determine mechanisms underlying the relationship between independent and dependent variables via other explanatory variables ("mediators"). Fatigue, pain, and morning stiffness are common ankylosing spondylitis (AS) symptoms that can contribute to decreased functional capacity and health-related quality of life (HRQoL) in AS patients. This study aimed to assess how tofacitinib affects HRQoL improvement directly and indirectly (via symptom improvement) in patients with AS.

Methods: Mediation modeling was used to analyze pooled data from phase 2 (NCT01786668) and phase 3 (NCT03502616) studies of tofacitinib. The initial mediation model is depicted by **Figures 1A** and **1B**; superimposition of both figures represents the full mediation model. The independent variable was treatment (tofacitinib 5 mg BID vs placebo) and the dependent variables were the SF-36 domains. Mediators included in the model were CRP, stiffness (represented

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Initial mediation model: Path diagrams representing (A) the effect of treatment on SF-36 domains, and (B) hypothesized interrelationships between mediators

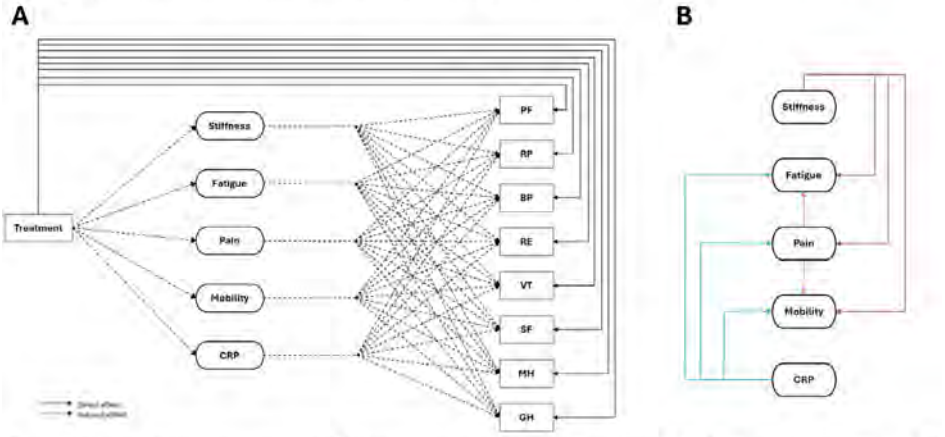
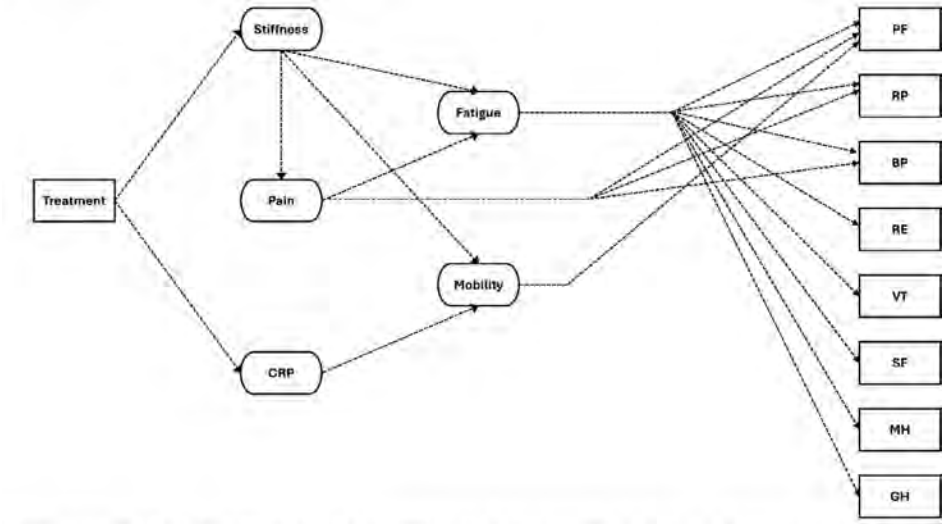


Figure A shows only the overall relationships between treatment and SF-36 domains including direct paths and indirect paths via mediators. Figure B shows relationships between mediators. SF-36, 36-item Short Form Survey; PF, Physical Functioning; RP, Role Physical; BP, Bodily Pain; RE, Role Emotional; VT, Vitality; SF, Social Functioning; MH, Mental Health; GH, General Health

Figure 2. Final respecified mediation model



PF, Physical Functioning; RP, Role Physical; BP, Bodily Pain; RE, Role Emotional; VT, Vitality; SF, Social Functioning; MH, Mental Health; GH, General Health

by the mean of BASDAI questions 5 and 6), mobility (measured by BASMI), fatigue (measured by FACIT-Fatigue total score), and pain (latent factor measured by two numerical rating scales [0-10] for nocturnal pain and total back pain). All available data from week 12 (phase 2 trial) and week 16 (phase 3 trial) were used. Based on the initial model results, the final model was respecified to include only paths that were statistically significant ($p < 0.05$) and/or meaningful (standardized path coefficient >0.1). The relative contribution of each path from treatment to SF-36 domain was reported in terms of percentages of the total effect of tofacitinib on an SF-36 domain.

Results: Data from 360 patients were included. The initial model demonstrated that tofacitinib treatment affects SF-36 mainly indirectly. In the final model (**Figure 2**), improvements in HRQoL were collectively mediated through five indirect pathways: (1) treatment→stiffness→pain→SF-36 domain, (2) treatment→stiffness→fatigue→SF-36 domain, (3) treatment→stiffness→pain→fatigue→SF-36 domain, (4) treatment→stiffness→mobility→SF-36 domain, and (5) treatment→CRP→mobility→SF-36 domain. For the Physical Functioning and Bodily Pain domains, paths via changes in stiffness and pain had the largest effect, mediating 35.3% ($p < .0001$) and 64.5% ($p < .0001$) of the tofacitinib treatment

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Contributions of final model pathways to the indirect effects of tofacitinib on SF-36 domains

Path	Mediated effect of treatment on SF-36 domain, %[a]							
	PF	RP	BP	RE	VT	SF	MH	GH
Treatment→Stiffness→Fatigue→SF-36 domain	23.6	37.6	18.3	51.5	51.5	51.5	51.5	51.5
Treatment→Stiffness→Pain→SF-36 domain	35.3	27.0	64.5					
Treatment→Stiffness→Pain→Fatigue→SF-36 domain	22.2	35.4	17.2	48.5	48.5	48.5	48.5	48.5
Treatment→Stiffness→Mobility→SF-36 domain	10.9							
Treatment→CRP→Mobility→SF-36 domain	8.0							

[a] All mediated effects are significant ($p<0.05$).

SF-36, 36-item Short Form Survey; PF, Physical Functioning; RP, Role Physical; BP, Bodily Pain; RE, Role Emotional; VT, Vitality; SF, Social Functioning; MH, Mental Health; GH, General Health

effect (**Table**). For remaining domains, paths via changes in stiffness and fatigue had the largest effect, mediating 37.6% (p=.0002) of the tofacitinib effect on the Role Physical domain and 51.5% (p< .0001) for the other domains. The effect of treatment mediated via changes in stiffness and mobility (10.9%, p< .0001) and via CRP and mobility (8.0%, p=.003) was present only for the Physical Functioning domain.

Conclusion: In patients with AS, the effect of tofacitinib treatment on HRQoL as measured by SF-36 domains was fully mediated via changes in fatigue, pain, stiffness, CRP, and mobility. Tofacitinib reduces the signs and symptoms of AS, which improves HRQoL. By closely assessing the signs and symptoms of AS, physicians can better improve patients' HRQoL and hence patient care and treatment. The results also suggest that HRQoL measurements may play an important role in assessing the signs and symptoms of AS.

Disclosure: X. Baraliakos: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor; **A. Bushmakin**: Pfizer, 3, 11; **J. Cappelleri**: Pfizer, 3, 11; **E. Nikitopoulou**: Pfizer, 3, 11; **Y. Ling**: Pfizer, 3, 11; **M. Zayed**: Pfizer, 3, 11; **J. Cicci**: Pfizer, 3, 11.

Abstract Number: 2338

Real-World Outcomes of Combined Tofacitinib and TNF Inhibitor Therapy in Refractory Inflammatory Arthritis: A Tertiary Care Experience from India

Aashish Agrawal and Balakrishnan Canchi, Hinduja Hospital, Mumbai, Maharashtra, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The use of combination biologic and targeted synthetic DMARDs remains controversial due to safety concerns, yet may offer benefit in refractory inflammatory arthritis. This study examines the outcomes of patients treated with a combination of tofacitinib and TNF inhibitors.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient	Age	Sex	Diagnosis	Comorbidities	Disease Duration (yrs)	Failed csDMARDs	Failed biologic /tsDMARD	Combination Used	Follow-up (months)	Remission	Discontinued	TB/Infection requiring admission
1	27	Female	PsA	Hypothyroid	2	MTX, SFZ, LEF	ADA	TOFA + ADA	12	Yes	No	No
2	55	Female	SpA	Hypertension	8	MTX, SFZ	ETN	TOFA + ETN	12	Yes	No	No
3	43	Female	PsA	None	4	MTX, SFZ, LEF	ADA	TOFA + ADA	8	Yes	No	No
4	51	Male	SpA	None	8	MTX, SFZ, LEF	ADA	TOFA + ADA	6	Yes	No	No
5	14	Female	JIA	None	2	MTX, SFZ	TOFA	TOFA + ETN	6	Yes	No	No
6	62	Male	SpA	None	6	MTX, SFZ, LEF	ADA	TOFA + ADA	2	Partial	No	No
7	51	Female	RA	DM, HTN, Hypothyroid	3	MTX, SFZ	ETN	TOFA + ETN	31	Yes	No	No
8	54	Female	RA	DM	17	MTX, SFZ	TOFA	TOFA + ADA	7	Yes	No	No
9	44	Male	SpA	None	32	MTX, SFZ	ADA, IFX	TOFA + ADA	30	Yes	No	No
10	15	Male	SpA-axial	None	1	NA	TOFA	TOFA + ADA	17	Yes	No	No

Patient Characteristics and Outcomes

csDMARD: conventional synthetic DMARD; tsDMARD: targeted synthetic DMARD; TB: Tuberculosis PsA: Psoriatic arthritis; SpA: Spondyloarthritis; JIA: Juvenile Idiopathic Arthritis; RA: Rheumatoid arthritis; DM: Diabetes Mellitus type 2; MTX: Methotrexate; SFZ: Sulfasalazine; LEF: Leflunomide; ADA: Adalimumab; ETN: Etanercept; TOFA: Tofacitinib

Methods: We retrospectively analyzed patients with inflammatory arthritis treated with both tofacitinib and TNF inhibitors at our tertiary care centre. Demographic details, comorbidities, diagnosis, prior DMARD exposure, treatment duration, clinical response, adverse events, and remission status were recorded.

Results: A total of 10 patients were included: Spondyloarthritis (n=7), Rheumatoid arthritis (n=2), and Juvenile Idiopathic Arthritis (n=1). Except for one axial SpA patient, all had failed ≥2 conventional DMARDs and either tofacitinib or a TNF inhibitor previously.

The total follow-up duration was 131 patient-months. At last follow-up, 9 patients were in complete remission and 1 in partial remission. No patient discontinued therapy due to adverse effects. No serious infections, tuberculosis, or hospitalizations were reported. Only limited use of additional DMARDs was required. No patient was on steroids at last follow up.

Conclusion: In this real-world Indian cohort, combination therapy with tofacitinib and TNF inhibitors was effective in selected patients with refractory inflammatory arthritis, with a favorable safety profile. Larger, prospective studies are warranted to confirm these findings and guide clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Agrawal: None; **B. Canchi**: None.

Abstract Number: 2339

Joint Groups Involved in Early Oligoarticular Psoriatic Arthritis and the Impact of Apremilast Treatment: Data From FOREMOST

Alen Zabotti[1], Joseph F Merola[2], Ulrich Mrowietz[3], Philip J. Mease[4], Laure Gossec[5], mitsumasa kishimoto[6], Michele Brunori[7], Lichen Teng[8], Dafna D. Gladman[9] and Laura Coates[10], [1]Division of Rheumatology, Department of Medicine (DMED), Academic Hospital "Santa Maria della Misericordia", ASUFC, University of Udine, Udine, Italy, Udine, Italy, [2]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [3]Department of Dermatology, University Medical Center Schleswig-Holstein, Kiel, Germany, [4]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [5]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France, [6]Kyorin University School of Medicine, Tokyo, Japan, [7]Amgen Inc, Zurich, Switzerland, [8]Amgen Inc., Thousand Oaks, [9]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [10]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Data on disease progression and joint involvement patterns in early oligoarticular (oligo) PsA are sparse. In the FOREMOST study (NCT03747939), apremilast (APR) decreased the number of involved joints vs placebo (PBO) at Week (Wk) 16.[1] We assess patterns of involved joints at baseline and effect of APR on joint groups through Wk 48.

Methods: FOREMOST enrolled 308 patients (pts) with early oligo PsA (>1–≤4 swollen, >1–≤4 tender joints; 66–68 joints assessed). Pts were randomized 2:1 to APR (n=203) or PBO (n=105) for 24 wks (early escape at Wk 16), after which all pts received APR through Wk 48. Overall, 291 pts received ≥1 dose of APR (as randomized, n=203; switched from PBO, n=88). Concomitant NSAIDs and/or synthetic DMARDs were permitted at a stable dose for ≥2 wks or ≥3 months before baseline, respectively, and maintained through Wk 24. For each joint group (**Table 1**), percentage of pts (pt incidence) with ≥1 of the following was calculated at baseline, Wks 16 and 48: swollen and tender, swollen and/or tender, swollen only, and tender only. Baseline and Wk 16 data were analyzed for all randomized pts with the last observation carried forward for missing data; Wk 48 data were analyzed as observed for pts who received ≥1 dose of APR.

Results: Pts had low baseline joint involvement: mean swollen and tender joint count, 2.6 and 3.2, respectively;[1] baseline pt incidence of "swollen and tender" and "swollen and/or tender" joints was similar and higher than "swollen only" and "tender only" (**Fig 1A**). Based on "swollen and tender" joints, the most commonly involved joint groups at baseline included large and small joints: finger PIP (39.0% pts with ≥1 involved joint) and MCP (33.1%), followed by knee (19.8%), and ankle and tarsus/midfoot (18.8%) (**Fig 1A**). Baseline patterns of swollen and tender joints were similar for APR and PBO (**Fig 1B**).

Greater improvements in swollen and tender finger PIP, MCP, knee and ankle/tarsus/midfoot joints were observed from baseline to Wk 16 for APR vs PBO: finger PIP, –23.6% vs –9.5% pt incidence; MCP, –21.7% vs –13.3%; knee –16.3% vs +2.9%; and ankle/tarsus/midfoot, –12.3% vs –8.6% (**Fig. 1B, C**). Across joint groups, risk of ≥1 swollen and tender joint at Wk 16 was lower for APR vs PBO (**Fig. 1D**), with significant differences observed for the most commonly involved joints: odds ratio (APR vs PBO) (95% CI) for finger PIP, 0.55 (0.31, 0.98); MCP, 0.51 (0.27, 0.97); knee, 0.33 (0.16, 0.71); ankle/tarsus/midfoot, 0.41 (0.17, 0.94) (**Fig. 1D**). Improvements in joint involvement observed with APR at Wk 16 were maintained in pts continuing or switching to APR through Wk 48.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Joint groups analyzed

Joint group	Number of joints
Temporomandibular and shoulder	8
Elbow	2
Wrist	2
MCP	10
Finger PIP	10
Finger DIP	8
Knee	2
Ankle and tarsus/midfoot	4
MTP	10
Toe PIP	10

DIP, distal interphalangeal; MCP, metacarpophalangeal; PIP, proximal interphalangeal; MTP, metatarsal phalangeal.

Figure 1. Joint involvement in the FOREMOST study of early oligoarticular PsA

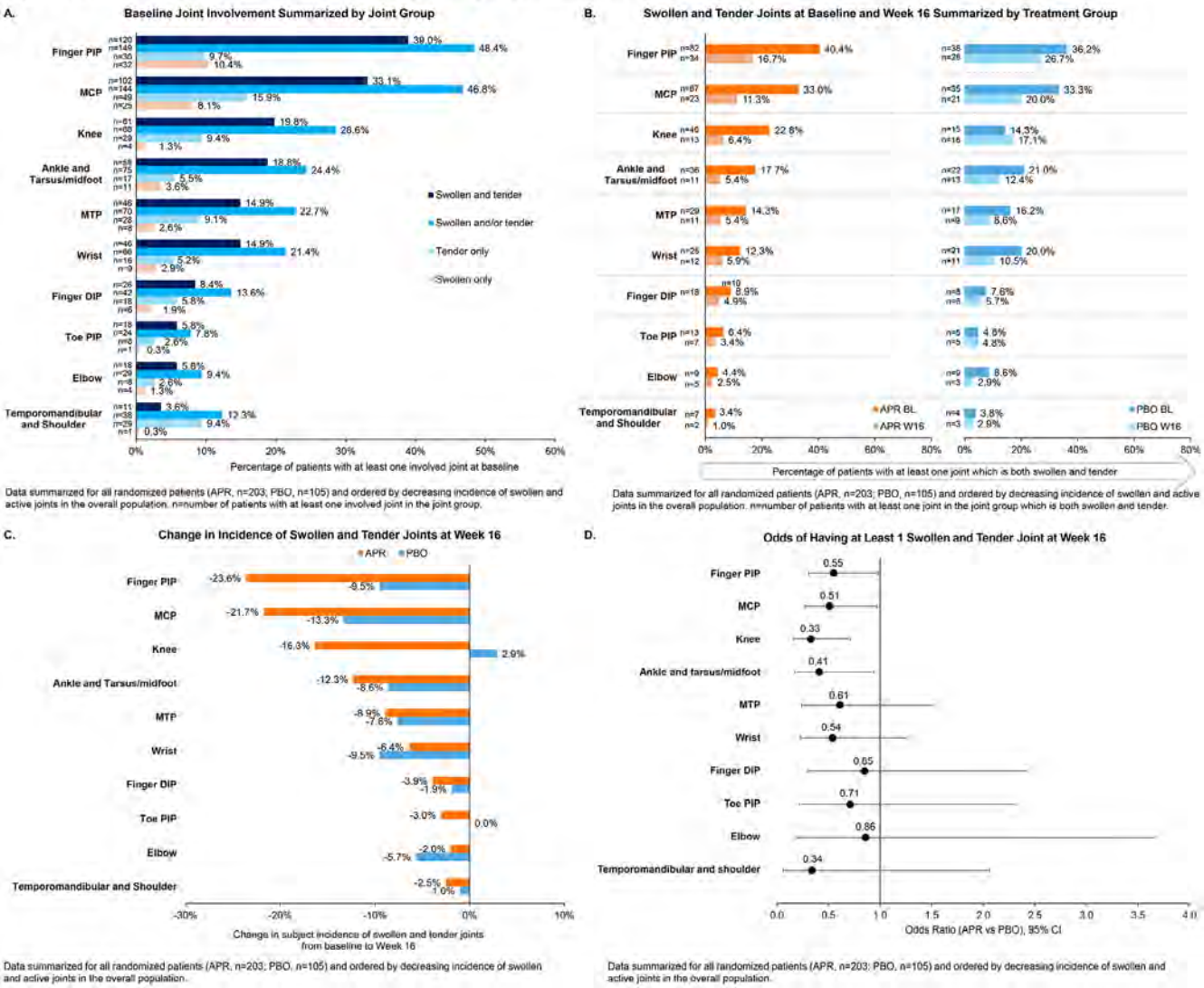


Figure 1. Joint involvement in the FOREMOST study of early oligoarticular PsA

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Our data indicate a mix of large and small joints involved in early oligo PsA, with hand and finger most common. We observed similar joint patterns as reported at PsA onset in real-world cohorts,[2,3] underscoring the value of FOREMOST in understanding early oligo PsA. Compared with PBO, APR significantly reduced joint involvement across large and small joints. Our findings can help orient physicians treating early oligo PsA.

References:

1 Gossec. *Ann Rheum Dis*. 2024;83(11):1480-1488
2 Zabotti. *RMD Open*. 2024;10(2):e004314
3 Gladman. *J Rheumatol*. 2021;48(12):1824-1829

Disclosure: A. Zabotti: AbbVie/Abbott, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, UCB, 2, 5; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **U. Mrowietz**: AbbVie, 1, 5, 6, Aditxt, 1, Almirall, 1, Amgen, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Immunic Therapeutics, 1, Janssen-Cilag, 1, LEO Pharma, 1, Merck/MSD, 1, Novartis, 1, Phi-Stone, 1, selectION, 1, Sharp & Dohme, 1, 5, 6, UCB, 1, UNION therapeutics, 1, 5, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **M. Brunori**: Amgen, 3; **L. Teng**: Amgen Inc., 3, 11; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2340

Lighten the Load: Artificial Intelligence Reveals Body Mass Index Outranks Treatment in One-Year Psoriatic Arthritis Outcomes—Findings from the SPEED Trial

Alexander Garaiman[1], Sophia Massa[1], Elnaz Saeedi[2], Nicola Gullick[3], William Tillett[4], Raphaël Hurtubise[1], jean-guillaume letarouilly[5] and Laura Coates[6], [1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK., Oxford, United Kingdom, [2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK., Oxford, [3]Rheumatology Department, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, Coventry, United Kingdom, [4]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, United Kingdom, [5]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK, Oxford, United Kingdom, [6]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Personalizing care in early psoriatic arthritis (PsA) is challenging. We set out to identify predictors of one-year response on the PASDAS using AI-based methods to guide treatment decisions and improve outcomes.

Methods: We analyzed the SPEED trial, a multicenter, open-label study of patients with early PsA and poor prognostic factors. Participants were randomized to standard step-up csDMARD therapy, combination csDMARD therapy, or early TNF inhibitor induction. Recursive partitioning (RPART) modeling identified predictors of PASDAS response at 48 weeks based on baseline variables, including BMI, treatment arm, baseline PASDAS, disease phenotype, disease duration, sex, age, education level, smoking status, and alcohol use. This approach mirrors clinical reasoning by breaking complex data into clear, logical steps, generating a decision tree based on real-world patient characteristics. The resulting tree begins with the most influential predictor and branches by relevant cutoffs. An importance plot showed each variable's contribution to the outcome, and decision rules derived from the tree offer actionable insights to guide personalized treatment.

Results: Among 192 patients (median age 49 [IQR: 34–58]; median BMI 28.96 kg/m^2 [IQR: 26.06–33.63]), baseline PASDAS was 5.60 (IQR: 4.94–6.34), improving to 3.84 (IQR: 2.38–4.99) at week 48, with 37.1% achieving "good" PASDAS (< 3.2). Most (82.8%) had polyarticular involvement; 53.5% were non-smokers, and 64.7% reported alcohol use.

BMI was deemed the most influential baseline predictor of lower PASDAS at 48 weeks (fig. 1); treatment ranked sixth.

Table 1. Recursive partitioning-derived prediction rules for PASDAS at week 48

Predicted PASDAS	Baseline PASDAS	BMI (kg/m²)	Age (years)	Phenotype	Disease Duration	Treatment
2.6	≥ 5.4	< 27	–	–	–	Early TNFi
3.2	–	27–29	< 74	Polyarticular	< 12 months	–
3.2	–	≥ 27	< 74	Oligoarticular	–	–
3.4	< 5.4	25–27	–	–	–	–
4.0	≥ 5.4	< 27	–	–	–	Standard/ csDMARD combination
4.3	–	≥ 29	< 74	Polyarticular	< 12 months	–
4.6	–	≥ 27	< 51	Polyarticular	≥ 12 months	–
6.0	–	≥ 27	51–74	Polyarticular	≥ 12 months	–

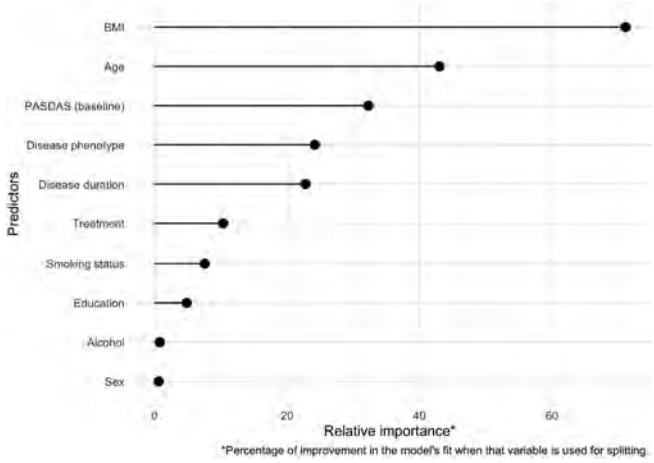


Figure 1. Variable Importance Plot from Recursive Partitioning Model Identifying Key Predictors of ASDAS at One Year

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

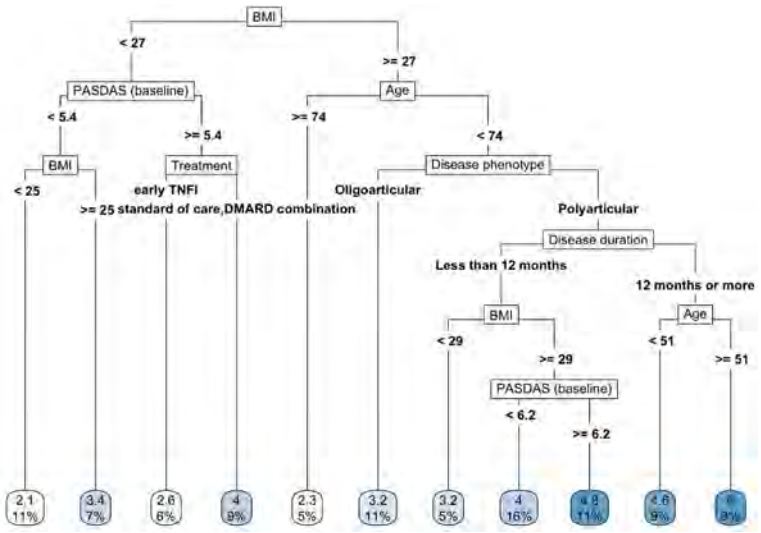


Figure 2. Decision Tree Plot Depicting Prediction Rules for One-Year PASDAS Based on BMI and Other Baseline Characteristics. Each node represents a decision point based on key patient characteristics (e.g., BMI, baseline PASDAS). The final leaves show the predicted PASDAS score at 48 weeks, with the numbers representing the mean PASDAS value and the percentage indicating the proportion of patients in that group. To interpret the tree, follow the path from the root to the leaves, where each branch splits based on the patient's characteristics, leading to a predicted treatment outcome.

The RPART-derived prediction rules reveal important trends in treatment response (tbl. 1, fig. 2): (1) patients with BMI < 25 kg/m^2 and lower baseline disease activity (PASDAS < 5.4) experienced the most favorable outcomes (predicted PASDAS = 2.1) at week 48—regardless of treatment type; (2) among patients with higher baseline disease activity (PASDAS ≥ 5.4) and BMI < 27 kg/m^2, early TNF inhibitor therapy was associated with better outcomes (PASDAS = 2.6) compared to standard or combination csDMARD therapy (PASDAS = 4.0), highlighting the potential benefit of early biologic intervention; (3) poorer outcomes were observed in patients with higher BMI (≥ 27 kg/m^2), longer disease duration (≥ 12 months), and polyarticular disease, particularly among those aged 51–74, with predicted PASDAS scores reaching as high as 6.0. Findings highlight the cumulative negative effect of obesity, chronicity, and disease severity.

Conclusion: BMI was the most influential predictor of achieving a lower PASDAS at one year, even more so than treatment exposure. As a modifiable factor, maintaining a BMI below 27 kg/m^2—ideally under 25 kg/m^2— can significantly improve patient outcomes. High baseline disease activity, obesity, and chronicity predicted poorer responses, and in these groups, treatment with early TNF inhibitors was superior to csDMARDs reinforcing the need for aggressive therapy in such patients. The predictive rules derived from this analysis offer clinicians valuable insights to support personalized care and encourage patients to prioritize weight management as a key component of their PsA treatment strategy.

Disclosure: A. Garaiman: None; **S. Massa**: None; **E. Saeedi**: None; **N. Gullick**: AbbVie, 2, 5, 6, Alfasigma, 2, AstraZeneca, 5, Eli Lilly, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Takeda, 2, UCB, 2, 5, 6; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ono Pharma, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6; **R. Hurtubise**: Biojamp, 6, Celltrion, 6, UCB, 6; **j. letarouilly**: Abbvie, 6, Celltrion, 6, Janssen, 6, MSD, 6, Pfizer, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2341

Bimekizumab Treatment Resulted in Long-Term Sustained Reductions in Disease Impact Assessed by the Psoriatic Arthritis Impact of Disease (PsAID)-12 Questionnaire in Patients with Active Psoriatic Arthritis: Up to 3-Year Results from Two Phase 3 Studies

Ana-Maria Orbai[1], Dafna D. Gladman[2], Laura Coates[3], Maarten de Wit[4], Barbara Ink[5], Rajan Bajracharya[5], Patrick Healy[6], Jérémy Lambert[7] and Laure Gossec[8], [1]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [2]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [3]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [4]Patient Research Partner, Stichting Tools, Amsterdam, Netherlands, [5]UCB, Slough, England, United Kingdom, [6]UCB, Morrisville, NC, [7]UCB, Colombes, France, [8]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. The PsA Impact of Disease-12 (PsAID-12) questionnaire is a disease-specific patient (pt)-reported outcome measure that assesses impact of PsA on 12 physical, social, and psychological domains.[1,2] We report long-term efficacy of BKZ treatment using the PsAID-12 questionnaire to 3 years (yrs) in pts with active PsA.

Methods: BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve) and BE COMPLETE (NCT03896581; TNF inhibitor inadequate response/intolerance [TNFi-IR]) assessed subcutaneous (sc) BKZ 160 mg every 4 weeks (wks; Q4W) in pts with PsA; both were placebo (PBO)-controlled to Wk 16. At Wk 16, PBO pts switched to BKZ (PBO/BKZ). BE OPTIMAL included a reference arm (sc adalimumab 40 mg Q2W; data not shown). BE OPTIMAL Wk 52 and BE COMPLETE Wk 16 completers could enter BE VITAL (open-label extension; NCT04009499).

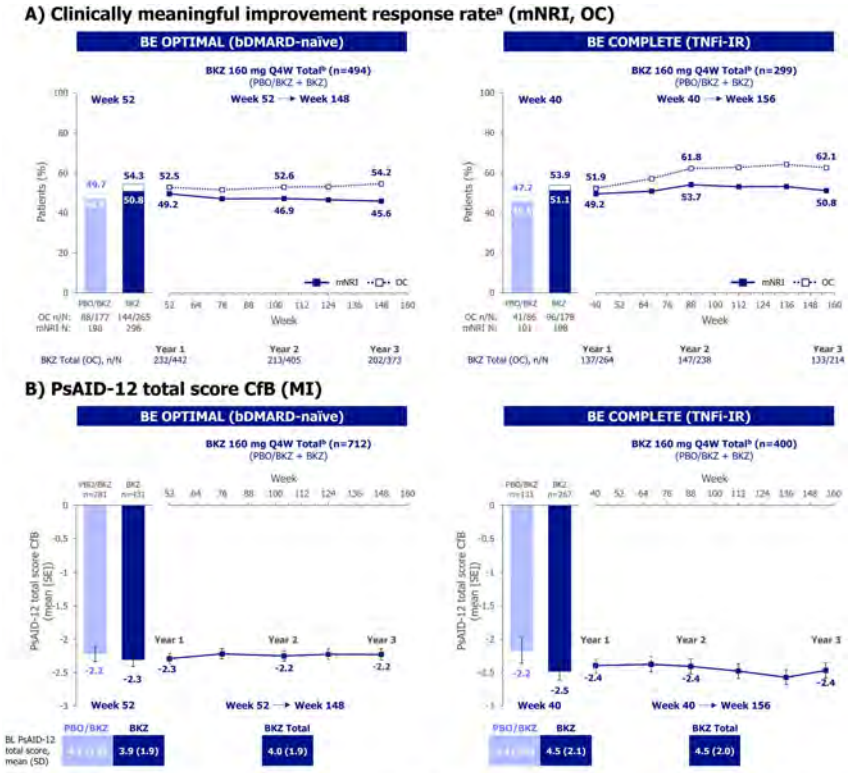
PsAID-12 total and single-item domain scores range from 0–10; higher scores indicate worse status.[2] Change from baseline (BL; CfB), clinically meaningful improvement response rates (≥3-point decrease from BL when respective BL PsAID-12 score ≥3) and symptom or impact severity based on PsAID-12 total score were assessed.[1]

PsAID-12 questionnaire was administered to Wk 148/156 (BE OPTIMAL/BE COMPLETE). Data reported for the BKZ Total group (PBO/BKZ and BKZ-randomized pts) as observed case, modified non-responder imputation (mNRI; binary) or multiple imputation (MI; continuous). mNRI considered all visits following discontinuation due to adverse events or lack of efficacy as non-response; all other missing data imputed with MI and the response derived from the imputed values.

Results: Overall, 555/712 (77.9%) bDMARD-naïve and 299/400 (74.8%) TNFi-IR BKZ Total group pts completed Wk 148/156.

Achievement of clinically meaningful improvement responses in PsAID-12 total score observed at Wk 52 (49.2%) and Wk 40 (49.2%) in bDMARD-naïve and TNFi-IR pts were sustained to Wk 148 (45.6%) and Wk 156 (50.8%; **Figure 1A**). Clinically meaningful improvement responses were achieved by 47.5–70.7% of pts across all single-item domains at Wk 148/156.

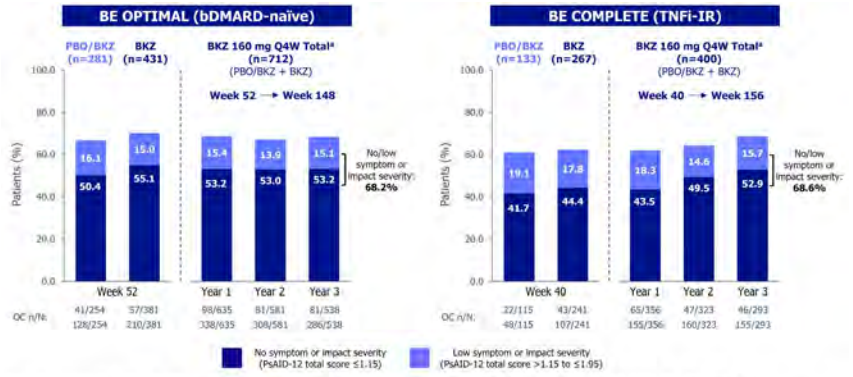
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Randomized set. Data reported from Year 1 (Week 52 in BE OPTIMAL and Week 40 in BE COMPLETE) to Year 2 (Week 104 in BE OPTIMAL and Week 88 in BE COMPLETE) and Year 3 (Week 148 in BE OPTIMAL and Week 156 in BE COMPLETE). [a] Clinically meaningful improvement response: ≥3-point decrease from baseline when respective PsAID-12 score is ≥3 at baseline; [b] BKZ Total group includes BKZ-randomized patients and PBO patients that switched to BKZ at Week 16. PsAID 12 scores range from 0–10; higher scores indicate worse status.[1]

bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; MI: multiple imputation; mNRI: modified non-responder imputation; OC: observed case; PBO: placebo; PsAID-12: Psoriatic Arthritis Impact of Disease-12; Q4W: every 4 weeks; SD: standard deviation; SE: standard error; TNFi-IR: prior inadequate response or intolerance to tumor necrosis factor inhibitors.

Figure 1. (A) Clinically meaningful improvement response rate and (B) PsAID-12 total score CfB to Year 3 (MI, mNRI, OC)

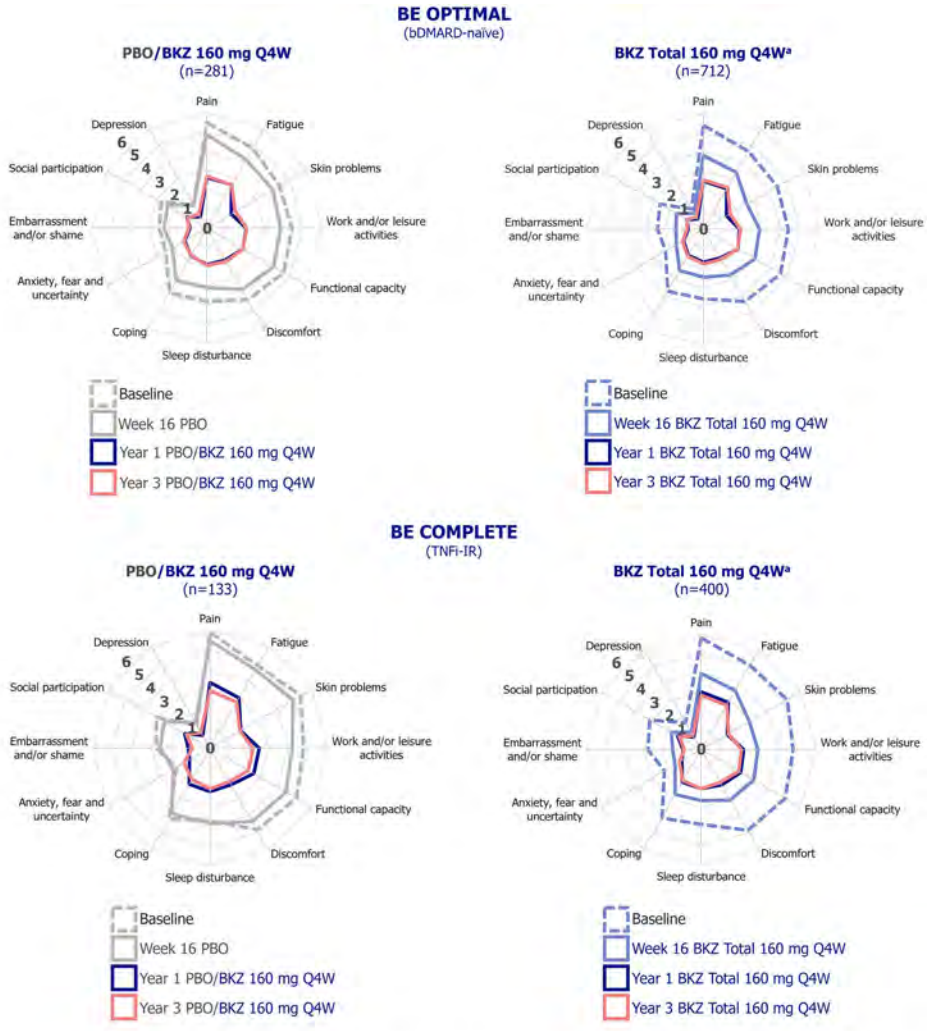


Randomized set. Data reported from Year 1 (Week 52 in BE OPTIMAL and Week 40 in BE COMPLETE) to Year 2 (Week 104 in BE OPTIMAL and Week 88 in BE COMPLETE) and Year 3 (Week 148 in BE OPTIMAL and Week 156 in BE COMPLETE). No or low symptom or impact severity defined by a PsAID-12 total score of score ≤1.95.

bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; OC: observed case; PBO: placebo; PsAID-12: Psoriatic Arthritis Impact of Disease-12; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumor necrosis factor inhibitors.

Figure 2. No or low symptom or impact severity by visit for PsAID-12 total score to Year 3 (OC)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Randomized set. Data reported from Week 16 to Year 1 (Week 52 in BE OPTIMAL and Week 40 in BE COMPLETE) and Year 3 (Week 148 in BE OPTIMAL and Week 156 in BE COMPLETE). [a] BKZ Total group includes BKZ-randomized patients and PBO patients that switched to BKZ at Week 16. PsAID-12 scores range from 0–10; higher scores indicate worse status.[1]

bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; MI: multiple imputation; PBO: placebo; PsAID-12: Psoriatic Arthritis Impact of Disease-12; Q4W: every 4 weeks; TNFi-IR: prior inadequate response or intolerance to tumor necrosis factor inhibitors.

Figure 3. PsAID-12 single-item domain mean scores at baseline, Week 16, Year 1, and Year 3 (MI)

Similarly, proportions of pts achieving no/low symptom or impact severity for PsAID-12 total score (score ≤1.95) at Wk 52/40 were sustained to Wk 148/156 in 68.2% bDMARD-naïve and 68.6% TNFi-IR pts (**Figure 2**).

Improvements from BL in PsAID-12 total score were sustained from 1 yr to 3 yrs of BKZ treatment: mean CfB (standard error) –2.3 (0.1) at Wk 52 and –2.2 (0.1) at Wk 148 in bDMARD-naïve pts; –2.4 (0.1) at Wk 40 and –2.4 (0.1) at Wk 156 in TNFi-IR pts (**Figure 1B**). Improvements from BL across all PsAID-12 single item domain mean scores observed at Wk 52/40 were sustained or further improved to Wk 148/156 in the BKZ Total group (**Figure 3**).

Conclusion: BKZ treatment resulted in clinically meaningful improvements in PsAID-12 scores across physical, social and psychological domains in pts with active PsA, indicating reduced disease impact. Improvements were sustained to 3 yrs and consistent responses were seen in pts who were bDMARD-naive or had TNFi-IR.

References: 1. Gossec L. RMD Open 2024;10:e003548; **2**. Gossec L. Ann Rheum Dis 2014;73:1012–9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Orbai: AbbVie, 5, Amgen, 5, BMS, 2, Janssen, 2, 5, Sanofi, 2, UCB, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. de Wit**: Celgene, 2, Eli Lilly, 2, Janssen-Cilag, 2, Pfizer, 2, UCB, 2; **B. Ink**: AbbVie, 11, GSK, 11, UCB, 3, 11; **R. Bajracharya**: UCB, 3, 11; **P. Healy**: UCB, 3, 11; **J. Lambert**: UCB, 3, 11; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5.

Abstract Number: 2342

Real-World Effectiveness and Satisfaction in Biologic-Naïve Patients With Psoriatic Arthritis and Limited Joint Involvement Treated With Risankizumab in the United States and Europe

Andrew Ostor[1], Jessica A. Walsh[2], Christopher Saffore[3], Xiaolan Ye[4], Manish Patel[5], Ana Biljan[6], Jamie Vora[7], Isabel Truman[8], Molly Edwards[8], Gary Milligan[8] and William Tillett[9], [1]Australian National University, Canberra, Australia, [2]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [3]AbbVie Inc., waukegan, IL, [4]AbbVie Inc., Mettawa, IL, [5]AbbVie Inc., North Chicago, IL, [6]AbbVie Inc., Buffalo Grove, IL, [7]AbbVie Inc., Palatine, IL, [8]Adelphi Real World, Bollington, United Kingdom, [9]Department of Life Sciences, Centre for Therapeutic Innovation, University of Bath, Bath, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

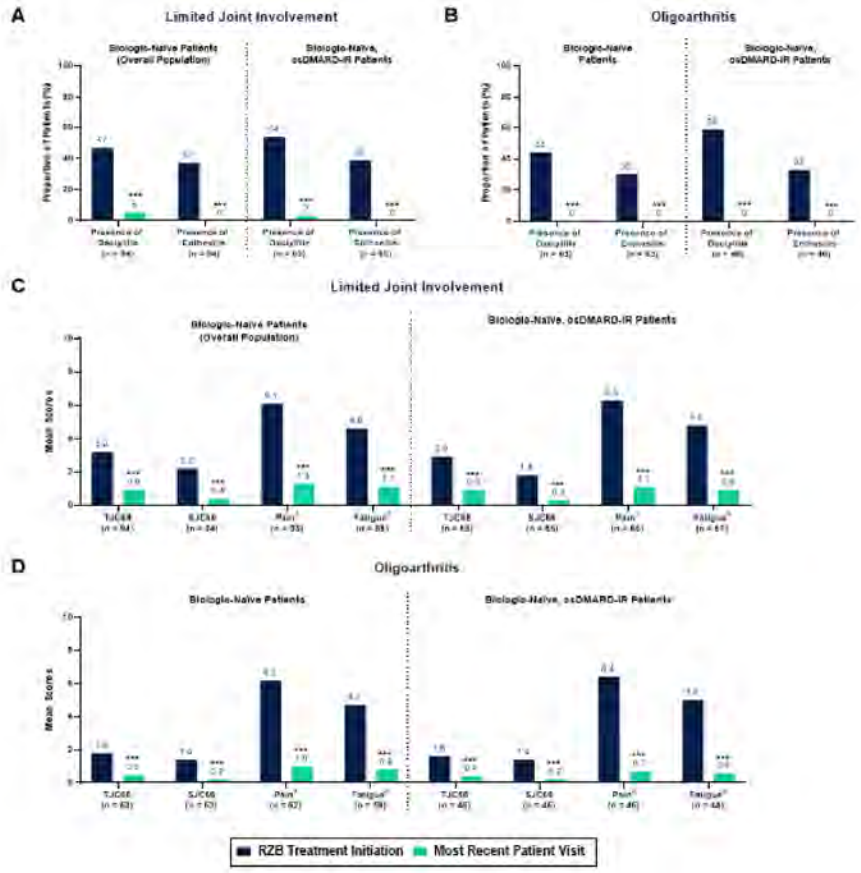
Background/Purpose: This study evaluated real-world effectiveness and patient- and physician-satisfaction with risankizumab (RZB) for biologic-naïve PsA patients with limited joint involvement or oligoarthritis.

Methods: Data were drawn from the Adelphi Spondyloarthritis VI Disease Specific Programme™ collected from June 2023 to June 2024 focusing on biologic-naïve patients with PsA who received RZB 150 mg and had limited joint involvement (≥ 1 to ≤ 8 TJC or SJC ≥ 1 to ≤ 8 ; 1–16 total active joints) or oligoarthritis (≥ 1 to ≤ 4 TJC or ≥ 1 to ≤ 4 SJC; 1–8 total active joints) at treatment initiation. Patients were located in the US and Europe (France, Germany, Italy, Spain, and the UK). Data were collected from cross-sectional questionnaires completed by physicians (treatment effectiveness and satisfaction) and their consulting patients (satisfaction) during recent visits. Outcomes were evaluated in the overall population of patients naïve to biologics with limited joint involvement and 3 subgroups: (1) patients naïve to biologics with limited joint involvement and an inadequate response to ≥ 1 conventional synthetic DMARD (csDMARD-IR), (2) patients with oligoarthritis naïve to biologics, and (3) patients with oligoarthritis naïve to biologics and csDMARD-IR.

Results: In the overall population, there were 94 biologic-naïve patients were included (23% [n = 22] from the US, 77% [n = 72] from Europe); mean age 43.3 years old, 40% female, 16.1% BSA affected by PsO at treatment initiation. Mean RZB treatment duration was 9.3 months in the overall population; mean TJC and SJC at treatment initiation was 3.2 and 2.2, respectively. Baseline characteristics were similar across the subgroups. Improvements in the presence of dactylitis and enthesitis and mean changes in TJC68, SJC66, pain, and fatigue were reported from treatment initiation to most recent visit for all groups ($P \leq .001$ for all) (**Figure 1**). High rates of complete resolution of dactylitis (89%) and enthesitis (100%), TJC68 ≤ 1 (69%), SJC66 ≤ 1 (79%), and clinically meaningful improvements in pain (94%) and fatigue (76%) were observed with RZB

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Proportion of Patients With Presence of Dactylitis or Enthesitis and Mean Scores in TJC68, SJC66, Pain, and Fatigue in PsA Patients Treated with RZB



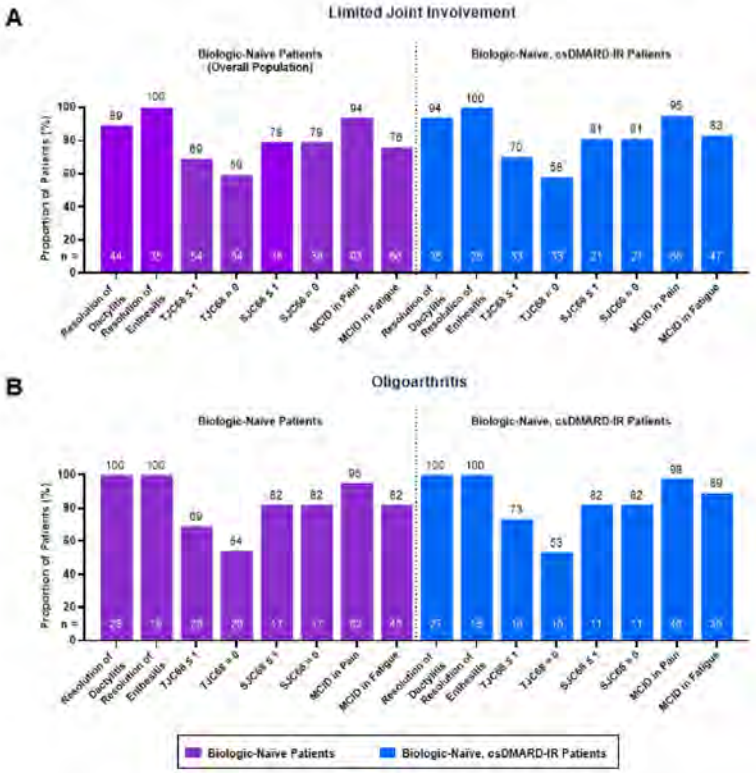
csDMARD, conventional synthetic DMARD; IR, inadequate response; RZB, risankizumab.
Proportion of patients with presence of dactylitis or enthesitis in patients with limited joint involvement (A) or oligoarthritis (B). Mean scores in TJC68, SJC66, pain, and fatigue at the time of treatment initiation with RZB and at the most recent visit for patients with limited joint involvement (C) and those with oligoarthritis (D).
***P < .001. Probability was evaluated from the initiation of RZB treatment to most recent visit via McNemar test (proportion of patients) or t test (mean scores).
[a]Assessed using a numeric rating scale (range 0 to 10), where higher scores indicate worse pain or fatigue outcomes.

in the overall population (**Figure 2A**). Effectiveness results were consistent in the csDMARD-IR subgroup (n = 65) with limited joint involvement (**Figures 1-2**). Patients with oligoarthritis who presented with dactylitis or enthesitis at treatment initiation, including 100% of both the biologic-naïve (n = 63) and csDMARDs-IR (n = 46) subgroups, demonstrated complete resolution of dactylitis and enthesitis. Clinically meaningful improvements were also seen in TJC68 ≤ 1 (69% and 73%), SJC66 ≤ 1 (82% for both), pain (95% and 98%), and fatigue (82% and 89%) in the biologic-naïve and csDMARD-IR oligoarthritis subgroups, respectively (**Figure 2B**). In the overall population, high patient (100%, n = 18) and physician (98%, n = 94) satisfaction rates were reported for the ability of RZB to control the disease.

Conclusion: In biologic-naïve patients with PsA and limited joint involvement or oligoarthritis, RZB treatment demonstrated effectiveness and high levels of satisfaction among patients and physicians in real-world clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Proportion of PsA Patients Achieving Clinically Meaningful Improvements in Dactylitis, Enthesitis, TJC68, SJC66, Pain, and Fatigue With RZB Treatment At Most Recent Visit



csDMARD, conventional synthetic DMARD; IR, inadequate response; MCID, minimal clinically important difference; NRS, numeric rating scale; RZB, risankizumab.
Sample sizes (n) are shown within each column.
(A, B) Clinically meaningful improvements defined as resolution of dactylitis (in patients with dactylitis at initiation), resolution of enthesitis (in patients with enthesitis at initiation), TJC68 = 0 or TJC68 ≤ 1 (in patients with TJC68 > 1 at initiation), SJC66 = 0 or SJC66 ≤ 1 (in patients with SJC66 > 1 at initiation), ≥ 1.0-unit decrease on 0 to 10 NRS for pain (in patients with a pain score ≥ 1 at initiation, and ≥ 3.0-unit decrease on 0 to 10 NRS for fatigue (in patients with a fatigue score ≥ 3 at initiation.

Disclosure: A. Ostor: AbbVie Inc., 1, 2, 12, Clinical Trials, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Eli Lilly, 1, 2, 12, Clinical Trials, GlaxoSmithKlein, 1, 2, 12, Clinical Trials, Janssen, 1, 2, 12, Clinical Trials, Merck, 2, 5, Novartis, 1, 2, 12, Clinical Trials, Pfizer, 1, 2, 12, Clinical Trials, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **C. Saffore**: AbbVie, 3, 11; **X. Ye**: AbbVie, 3, 11; **M. Patel**: AbbVie, 3, 11; **A. Biljan**: AbbVie, 3, 11; **J. Vora**: AbbVie, 3, 11; **I. Truman**: AbbVie, 2, Adelphi Real World, 3; **M. Edwards**: AbbVie, 2, Adelphi Real World, 3; **G. Milligan**: AbbVie, 2, Adelphi Real World, 3; **W. Tillett**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Ono Pharma, 2, 5, 6, Pfizer, 2, 5, 6, Takeda, 2, 5, 6, UCB, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2343

Risk of Arrhythmias Following IL-17 Inhibitor Use; A Pharmacosurvellience Study of FDA Adverse Event Reporting System (FAERS)

Asim Khanfar[1], Omar Hamdan[2], Anil Regmi[3], Mayra Goreja[4] and Anthony Ocon[5], [1]Rochester General Hospital, Rochester, NY, [2]University of Jordan, Az-Zarqa, Jordan, [3]Parkview Health, Fort Wayne, IN, [4]Rochester General Hospital, Rochester, [5]Rochester Regional Health, Fairport, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Interleukin-17 (IL-17) inhibitors, such as secukinumab and ixekizumab, are used for their anti-inflammatory effects in conditions like psoriasis and ankylosing spondylitis. IL-17 signaling has been implicated in cardiovascular disease pathogenesis, including atrial fibrillation and other arrhythmias. This study evaluates the incidence and characteristics of arrhythmias associated with IL-17 inhibitors using the FDA Adverse Event Reporting System (FAERS).

Methods: The FAERS database was searched for cardiac arrhythmias (Tachycardia, bradycardia, atrial fibrillation, QRS complex abnormalities, QT interval abnormalities, bundle branch block (BBB), atrioventricular blocks (AV blocks), and supraventricular tachycardia (SVT)) associated with the use of IL-17 inhibitors (secukinumab, ixekizumab, bimekizumab). Disproportionality analysis was done and data were reported as frequencies and as reporting odds ratios (ROR) with a 95% confidence interval (95% CI). RORs were only reported for adverse reactions with frequencies of 3 or more.

Results: We analyzed 30,179,725 adverse event reports from the FAERS database. A total of 181,052 reports were associated with the use of the three anti-IL-17 drugs; 60.9% of them were females, and 33.2% were in the age group between 18-64 years. Cardiac arrhythmias were reported in 0.54% of cases. Most of the cases were associated with secukinumab use (88.9%), followed by ixekizumab (9.5%). Among bimekizumab users, atrial fibrillation was the most common arrhythmia and accounted for 57.1% of all arrhythmias included in our analysis (Figure 1). However, when tested using ROR, the reporting odds of atrial fibrillation weren't higher in bimekizumab users compared to other drugs users. On the other hand, the most reported arrhythmias among secukinumab were tachycardia (45.6%) and bradycardia (41.9%) (Figure 2). When compared to other anti IL-17 medications, secukinumab was significantly associated with

Figure 1. Frequency of arrhythmias

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

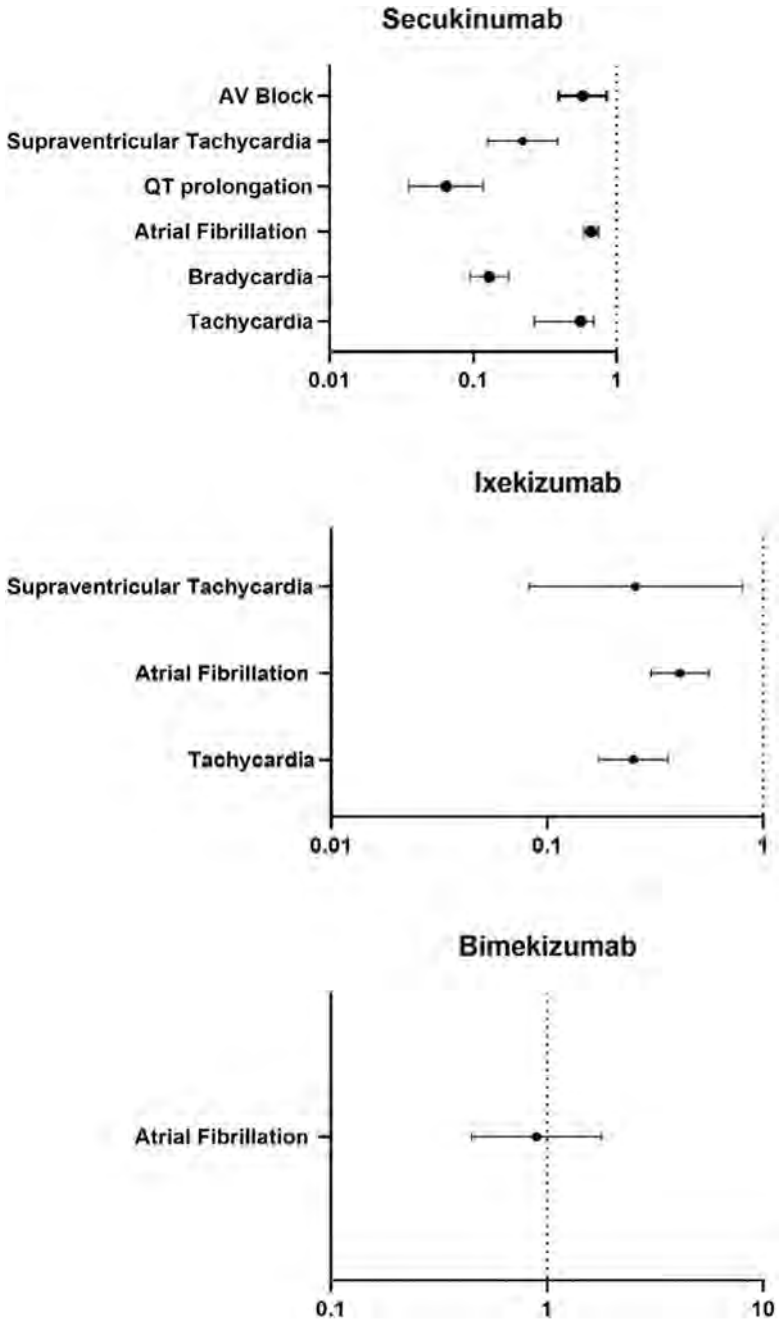


Figure 2. Reported Odds Ratio (ROR) of Anti-IL 17 drugs

higher odds of multiple arrhythmias, including tachycardia (ROR=12.27; 95% CI: 8.623-17.47), bradycardia (ROR=12.27; 95% CI: 4.469 – 34.91), atrial fibrillation (ROR=7.101; 95% CI: 5.317 – 9.484), Supraventricular Tachycardia (ROR=3.747; 95% CI: 1.208 – 11.62) and AV block (ROR=8.118; 95% CI: 2.833 – 23.26) (Table 1).

Conclusion: This study suggests that IL-17 inhibitors, particularly secukinumab, may be associated with increased reporting of cardiac arrhythmias, including tachycardia, bradycardia, atrial fibrillation, supraventricular tachycardia, and atrioventricular block. These findings support the need for further investigation into the cardiovascular safety of IL-17 inhibitors to guide clinical decision-making.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. ROR of anti-IL 17 drugs

Adverse reaction	Odds Ratio	95% Confidence Interval
Bimekizumab		
Tachycardia	0.3514	0.08749 – 1.411
Bradycardia	1.497	0.2061 – 10.88
Atrial Fibrillation	1.460	0.7239 – 2.946
QT prolongation	0	Not Available
QRS abnormalities	0	Not Available
Supraventricular Tachycardia	4.293	0.5669 – 32.51
Bundle Branch Block	0	Not Available
AV Block	4.601	1.096 – 19.33
Secukinumab		
Tachycardia	12.27	8.623 – 17.47
Bradycardia	12.49	4.469 – 34.91
Atrial Fibrillation	7.101	5.317 – 9.484
QT prolongation	Not Available	Not Available
QRS abnormalities	Not Available	Not Available
Supraventricular Tachycardia	3.747	1.208 – 11.62
Bundle Branch Block	2.498	0.2265 – 27.55
AV Block	8.118	2.833 – 23.26
Ixekizumab		
Tachycardia	0.4927	0.3371 – 0.7200
Bradycardia	0.2745	0.06645 – 1.134
Atrial Fibrillation	0.7382	0.5332 – 1.022
QT prolongation	0	Not Available
QRS abnormalities	0	Not Available
Supraventricular Tachycardia	1.331	0.3792 – 4.670
Bundle Branch Block	2.883	0.2614 – 31.80
AV Block	0.4118	0.09810 – 1.729

Disclosure: A. Khanfar: None; **O. Hamdan**: None; **A. Regmi**: None; **M. Goreja**: None; **A. Ocon**: Amgen, 2, 6.

Abstract Number: 2344

Impact of Bimekizumab Use in Spondyloarthritis and Psoriatic Arthritis: Persistence Study in Routine Clinical Practice in Spain (BIMPACT study)

Cristina Valero[1], Chamaida Plasencia-Rodríguez[2], Maria Beatriz Paredes Romero[3], Silvia Montes[4], Josefina Marin[5], Aranzazu Rubio[6], Cristina Macea-Villa[7], Laura Gonzalez Hombrado[8], Maria Luisa Gonzalez Gomez[9], Maria Carmen Ortega de la O[10], Mercedes Morcillo Valle[11], Rosario Garcia Vicuña[12], EVA GLORIA TOMERO MURIEL[12], Diana Peiteado[2] and BEATRIZ JOVEN[13], [1]Hospital de la Princesa, Madrid, Spain, [2]Hospital Universitario La Paz, MADRID, Spain, [3]Infanta Sofia University Hospital, Madrid, Spain, [4]Hospital de Talavera, Talavera, Castilla-La Mancha, Spain, [5]Hospital Universitario Rey Juan Carlos, Madrid, Spain, [6]Hospital Universitario Infanta Cristina, Madrid, Spain, [7]Hospital Universitario Ramon y Cajal, Madrid, Spain, [8]Hospital Universitario del Tajo, Aranjuez (MADRID), Madrid, Spain, [9]Hospital Universitario El Escorial, Majadahonda, Spain, [10]Hospital Universitario Getafe, Madrid, Madrid, Spain, [11]Hospital El Escorial, San Lorenzo de El Es, Spain, [12]Hospital Universitario de la Princesa, Madrid, Spain, [13]H. Universitario 12 Octubre, Madrid, Spain

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal antibody that simultaneously blocks IL-17A, IL-17F, and their heterodimer, key cytokines involved in the pathogenesis of spondyloarthritis (SpA) and psoriatic arthritis (PsA). Unlike other therapies targeting IL-17A alone, BKZ has demonstrated rapid and sustained efficacy in both joint and skin manifestations

Table 1. Demographic, clinical and treatment-related characteristics at baseline

Table 1. Demographic, clinical and treatment-related characteristics at baseline

Variable	Values		
Type of MSK disease	**Total =124 pts**	**PsA= 71 pts**	**SpA=51 pts**
Age (years), mean± SD	53.6±11.3		
Female sex, n (%)	74 (59.6)	44 (61.9)	29 (56.8)
BMI, mean ± SD	28.6±5.6	28.6±5.8	28.4±5.4
Smoker	30 (24.4)	17 (23.9)	12 (23.5)
Former smoker	37 (30)	19 (26.7)	18 (35.2)
Comorbidities			
HTN	42 (33.8)	25 (35.2)	15 (29.4)
T2DM,	19 (15.3),	15 (18.3)	6 (11.7)
DL	46 (37.1)	27 (38)	17 (33)
Cardiovascular events, n (%)	6 (4.8)	2 (2.8)	4 (7.8)
Fibromyalgia, n (%)	13 (10.4)	6 (8.4)	7 (13.7)
Depression n (%)	22 (17.7)	10 (14)	12 (23.5)
Anxiety, n (%)	22 (17.7)	7 (9.8)	15 (29.4)
Active neoplasm, n (%)	3 (2.4)	0 (0)	3 (5.8)
Cured neoplasm, n (%)	9 (7.2)	5 (7)	3 (5.8)
Duration of disease (years), median (IQR)	11.1±9.3		
Predominant MSK involvement			
Axial, n (%)	29 (23.4)	8 (11.2)	21 (41.1)
Peripheral, n (%)	40 (32.2)	35 (49.3)	3 (5.8)
Mixed (Peripheral and axial), n (%)	55 (44.3)	28 (39.4)	27 (52.9)
Other MSK domain, n (%)			
Enthesitis, n (%)	64 (52.9)	31 (43.6)	32 (62.7)
Dactylitis, n (%)	27 (22.3)	24 (33.8)	3 (5.8)
Extra-MSK involvement			
Uveitis, n (%)	2 (1.6)	0 (0)	2 (3.9)
Psoriasis, n (%)	57 (48.3),	51 (71.8)	5 (9.8)
Nail psoriasis, n (%)	32 (26.6)	29 (40.8)	1 (1.9)
Inflammatory bowel disease, n (%)	0 (0)	0 (0)	0 (0)
HLA-B27 positive, n (%)	36 (31.8)	13 (18.3)	23 (45)
Previous treatments, n (%)			
Type of csDMARDs			
Methotrexate, n (%)	83 (70.3)	57 (80.2)	24 (47)
Leflunomide, n (%)	30 (26)	23 (32.3)	5 (9.8)
Sulfasalazine, n (%)	48 (42.4)	21 (29.5)	27 (52.9)
Other, n (%)	15 (13.6)	11 (15.5)	4 (7.8)
Type of t/bDMARDs			
TNFi, n (%)	106 (85.4)	58 (81.6)	46 (90.2)
IL17i, n (%)	61 (49.2)	33 (46.4)	27 (52.9)
IL23i or IL12-23i, n (%)	35 (28.2)	29 (40.8)	5 (9.8)
JAKi, n (%)	26 (21)	12 (16.9)	14 (27.4)
Apremilast, n (%)	18 (14.5)	15 (21.1)	3 (5.8)
Number of previous b/tsDMARDs, n (%)			
0, n (%)	10 (8.2)	7 (9.8)	3 (5.8)
1, n (%)	32 (26.4)	34 (47.8)	12 (23.5)
2, n (%)	29 (24)	14 (19.7)	12 (23.5)
≥3, n (%)	50 (40)	10 (14)	22 (43.1)

Abreviations: BMI: body mass index. *b/tsDMARDs*: biologic/ targeted Disease-Modifying Anti-Rheumatic Drugs; CRFs: Cardiovascular risk factors. *csDMARDs:* conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; DL: dyslipidemia. HTN: hypertension;

MSK: musculoskeletal; PsA: psoriatic arthritis; pts: patients; SD: standart deviation; SpA: spondyloarthritis; T2DM: type 2 diabetes mellitus.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Bimekizumab treatment characteristics and disease activity data

Table 2. Bimekizumab treatment characteristics and disease activity data.

Variables	N=124 patients	
Reason for BKZ prescription		
MSK, n (%)	89 (73.5)	
Cutaneous, n (%)	5 (4.1)	
Mixed, n (%)	27 (22.1)	
Starting BKZ dose		
160mg and 80mg/4 weeks	115 (92.7)	
320mg and 160mg/4 weeks	9 (7.3)	
Concomitant csDMARD treatment	59 (47.5)	
Methotrexate, n (%)	31 (25)	
Leflunomide, n (%)	15 (12)	
Sulfasalazine, n (%)	12 (9.6)	
Active MSK domain at baseline	124 (100)	
Axial, n (%)	31 (25.6)	
Peripheral, n (%)	46 (38)	
Mixed (Peripheral and axial), n (%)	44 (36.3)	
Active cutaneous domain at baseline, n (%)	40 (34.7)	
Active nail domain at baseline,n (%)	18 (17.1)	
C-reactive protein levels (mg/dl) ± SD		
Baseline / 6 months	3,6±7,2 / 2,6±7,28	
Disease activity indices	Baseline	6 months
BASDAI, mean ± SD	6.8±1.5	4.7±1.9
ASDAS-CRP ± SD	3.6±0.7	2.5±0.9
Axial VAS ± SD	7.1±2.2	4.7±2.5
Peripheral VAS ± SD	6.3±2.2	4.8±2.5
DAPSA, n (%)	22.5±11	15±11
66 swollen joint count, *mean (SD)*	3.1±4.3	1.2±2.6
66 tender joint count, *mean (SD)*	5±5.8	2.3±5.1
PASI	4.7±5.8	0.6±1.7
BSA	4.6±8.5	0.7±2

Abreviations: BSA: body surface area; BKZ: bimekizumab; *csDMARDs:* conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; MSK: musculoskeletal; SD: standart deviation; VAS: visual analog scale

Figure 1. Changes in disease activity indices in patients under bimekizumab at 6-months of follow-up; A) DAPSA B) ASDAS-CRP; C) BASDAI.

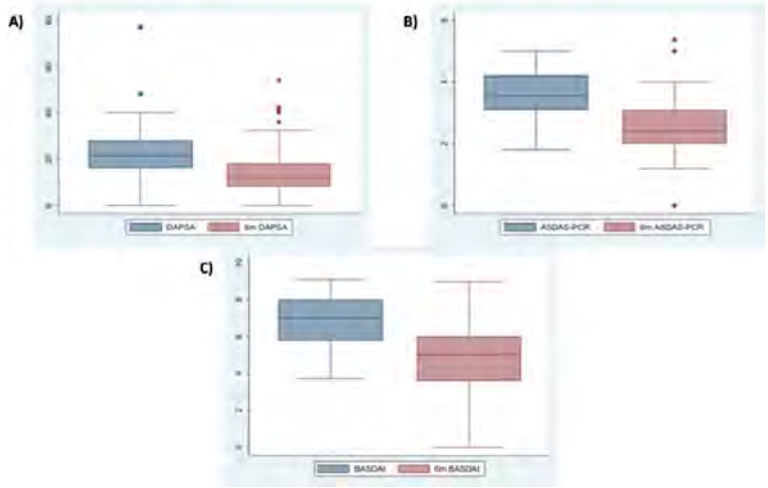


Figure 1. Changes in disease activity indices in patients under bimekizumab at 6-months of follow-up; A) DAPSA B) ASDAS-CRP; C) BASDAI.

in clinical trials. Benefits have been observed in both biologic-naïve patients and those previously exposed to treatment, with a favorable safety profile. This study aims to broaden real-world experience with BKZ by evaluating its persistence, effectiveness, and patterns of use in routine clinical practice.

Methods: This is an observational, ambispective and multicenter study conducted in Spain. The study included patients >18 years diagnosed with SpA (according to ASAS classification criteria and/or the modified New York criteria) or PsA (according to CASPAR classification criteria) who initiated treatment with BKZ between January 1, 2024, and December 31, 2024. Demographic and clinical characteristics, as well as treatment patterns and response to BKZ were described

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

using data from the electronic database. Changes in musculoskeletal (MSK) disease activity indices at 6 months and psoriasis (PsO) from baseline (start of BKZ treatment) were assessed.

Results: A total of 124 patients receiving BKZ were identified (41.1% SpA, 57.2% PsA), mainly women in both groups, with a median age of 53.6 ± 11 years and a long disease duration averaging 11.1 ± 9.3 years. Eleven patients presented active or previous neoplasms (8.8%). The most frequent MSK domain was mixed (peripheral and axial) in 44.3% of patients, and enthesitis was present in 52.9%, slightly more common in SpA. Patients had previously received a mean of 2.6 ± 2 b/tsDMARDs, mainly TNF inhibitors (85.4%) and IL-17 inhibitors (49.2%), with similar patterns in SpA and PsA.

Most patients initiated BKZ as third-line therapy or beyond (67.7%), with concomitant DMARD use in nearly half of cases. The main reason for prescription was MSK involvement, though one-third also had active PsO (Table 2). At the 6-month follow-up (n=88/124 patients; 33 SpA, 55 PsA), an overall retention rate of 86.3% (n=76/88) for BKZ was observed, being greater in SpA (90.9%; n=30/33) compared to PsA (83.6%; n=46/55). BKZ was discontinued in 10 patients (3 SpA/ 8 PsA): 7 due to loss of effectiveness and 3 due to adverse events.

Among the patients with effectiveness data available for MSK disease at 6 months (Table 2), 42% (45% PsA, 30,3% SpA) achieved low disease activity and 9% (3% SpA, 12,7% PsA) achieved remission. A significant improvement in MSK outcomes was observed across all axial and peripheral measures (axial and peripheral VAS, BASDAI, ASDAS-CRP, DAPSA, 68/66 joint counts all $p< 0.01$). In patients with PsO and data available, a significant ($p< 0.01$) reduction in PASI (n=20) and BSA (n=28) was observed at 6 months.

Conclusion: BKZ was mainly used in patients with long-standing, refractory SpA/PsA, with prior IL-17 inhibitor use in half of the cases. Despite this, the 6-month retention rate was high (86.3%), with favorable efficacy across all domains.

Disclosure: C. Valero: None; **C. Plasencia-Rodríguez**: AbbVie/Abbott, 5, 6, Eli Lilly, 6, Novartis, 6, Pfizer, 5, 6, UCB, 6; **M. Paredes Romero**: None; **S. Montes**: None; **J. Marin**: None; **A. Rubio**: None; **C. Macea-Villa**: None; **L. Gonzalez Hombrado**: None; **M. Gonzalez Gomez**: None; **M. Ortega de la O**: None; **M. Morcillo Valle**: None; **R. Garcia Vicuña**: None; **E. TOMERO MURIEL**: None; **D. Peiteado**: None; **B. JOVEN**: Johsson & Johsson, 2, 5, 6.

Abstract Number: 2345

Biological Sex-Related Differences in Radiographic Progression and Relationship with Early Clinical Response: Post Hoc Analysis of a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study in Biologic-Naive Participants with Active Psoriatic Arthritis Treated with Guselkumab

Dafna D. Gladman[1], Lihi Eder[2], Carlo Selmi[3], Philip J. Mease[4], Alexis Ogdie[5], Karissa Lozenski[6], Mohamed Sharaf[7], Emmanouil Rampakakis[8], Laura Pina Vegas[9] and Laura Coates[10], [1]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Humanitas University, Milan, Italy, [4]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [5]University of Pennsylvania, Philadelphia, PA, [6]Johnson & Johnson, Horsham, PA, [7]Janssen - Johnson & Johnson, Dubai, United Arab Emirates, [8]JSS Medical Research, Montréal, QC, Canada, [9]Epidemiology in Dermatology and Evaluation of Therapeutics (EpiDermE), University Paris-Est Créteil Val de Marne, Créteil, France; Rheumatology, Hospital Henri Mondor, AP-HP, Créteil, France, Creteil, France, [10]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Previous research has shown that women with psoriatic arthritis (PsA) often have lower rates of clinical response to medication but less severe radiographic joint damage. Despite this, few randomized controlled trials (RCTs) in PsA report sex-disaggregated results. Here, we assessed sex-disaggregated radiographic progression (RP) in DISCOVER-2 (NCT03158285), a Phase 3 study of biologic-naïve PsA pts treated with GUS, considering sex differences in structural damage and whether this is associated with early improvements in joint disease activity (DA).

Methods: Biologic-naïve pts with active PsA were randomized (1:1:1) to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo with crossover to GUS 100 mg Q4W at W24. Early (W8) response in joint DA, (based on clinical DA Index for PsA [cDAPSA LDA; ≤13]), was assessed among pts with cDAPSA >13 at BL, without adjustment for sex-specific differences at BL. Multivariate repeated measures mixed models assessed associations between sex and changes in total PsA-modified van der Heijde-Sharp [vdH-S] score through W100 (**Fig 1**), association between early response in joint DA and RP when stratified by sex (**Fig 2**); time-averaged and visit-specific LSM changes.

Results: Of 739 PsA pts enrolled, 47.5% were female. At BL, female vs male pts were more likely to be older (29.3% vs 21.9% ≥55 years of age; p=0.0204) and have dactylitis (60.6% vs 50.3%; p=0.0049), and on average had higher BMI (29.5 vs 28.4 kg/m^2; p=0.0144), lower CRP levels (1.6 vs 2.3; p< 0.0001), less extensive/severe psoriasis (Psoriasis Area and Severity Index [PASI] score: 7.5 vs 12.1; p< 0.0001), more functional disability (Health Assessment Questionnaire-Disability Index [HAQ-DI] score: 1.4 vs 1.2; p< 0.0001), and worse fatigue (Functional Assessment of Chronic Illness Therapy [FACIT]-Fatigue score: 28.5 vs 30.9; p=0.0007). BL cDAPSA (46.1 vs 46.4) and PsA-modified vdH-S (26.2 vs 25.5) scores were similar (p >0.05) between sexes.

In unadjusted analyses of GUS-treated pts, male sex was associated with greater progression of structural damage through W100 (ΔLSM=1.02; p=0.0260). After adjusting for known risk factors of RP, BL characteristics with sex-specific differences in the pooled cohort, and disease duration and non-biologic DMARD use at BL, the difference between sexes in RP decreased but remained significant (ΔLSM=0.90; p=0.0406); LSM changes from BL in PsA-modified vdH-S scores in males vs females were 1.36 vs 0.69 (p=0.0502) at W52 and 2.22 vs 1.10 (p=0.0475) at W100 (**Fig 1**). Early (W8) cDAPSA LDA was achieved by 18.9% of men vs 15.3% of women. In men, this was associated with significantly less RP through W100 (time-averaged change in PsA-modifed vdH-S scores from BL to W100 in cDAPSA LDA responders vs nonresponders: 0.39 vs 2.24; p=0.0288); in females only, numerical differences were observed (-0.15 vs 0.91; p=0.1732; **Fig 2**).

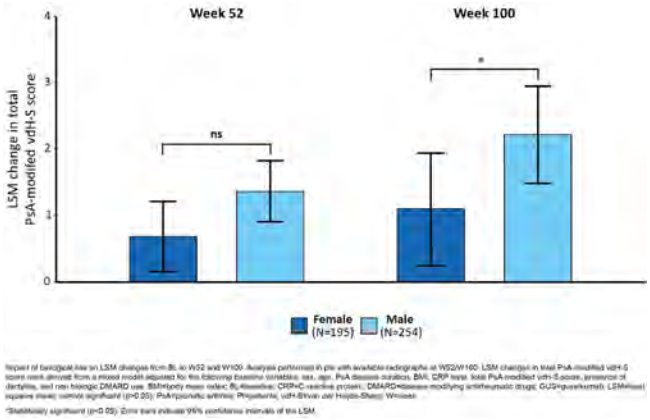


Figure 1. Change in Total PsA-modified vdH-S Score from BL Through W100 in Male and Female PsA Pts Treated with GUS

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

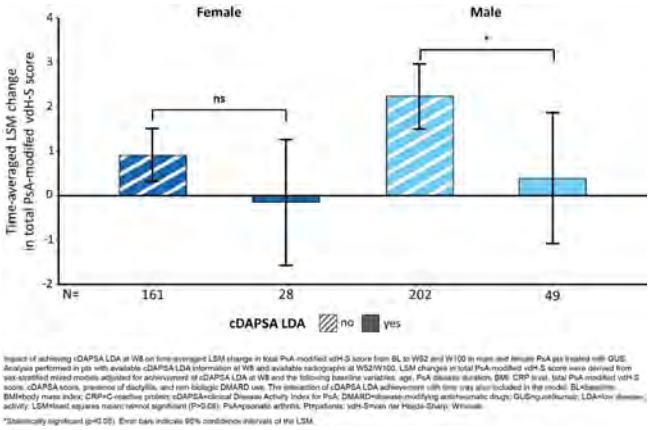


Figure 2. Multivariate Association of cDAPSA LDA Achievement at W8 with Time-Averaged Change in Total PsA-modified vdH-S Score from BL Through W100 in Male and Female PsA Pts Treated with GUS

Conclusion: These results confirm the independent association of male sex with more rapid RP. The previously reported relationship between early improvement in joint DA and diminished RP (Mease PJ, et al. Clin Rheumatol 2024) was found to be stronger in males than females, which may be due to the lower rate of RP in females.

Disclosure: D. Gladman: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **C. Selmi**: AbbVie, 2, 5, 6, Alfa-Wassermann, 2, 6, Amgen, 2, 5, 6, Biogen, 2, 6, Eli Lilly, 2, 6, EUSA, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 5, SOBI, 2, 6; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **K. Lozenski**: BMS, 11, Johnson & Johnson, 3, 11; **M. Sharaf**: Johnson & Johnson, 3, 11; **E. Rampakakis**: Johnson & Johnson, 2, JSS Medical Research, 3; **L. Vegas**: Novartis, 12, Support for attending meeting; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2346

Back in Action: Six Months of Biological Therapy Improve Sexual Function in Men with Ankylosing Spondylitis

Daniel Zavada[1], Barbora Vala[2], Adela Navratilova[2], Veronika Losterova[2], Lenka Moravcova[2], Jiri Vencovsky[3], Ladislav Šenolt[4], Karel Pavelka[5] and Michal Tomcik[5], [1]Institute of Rheumatology, Prague; Charles University, Third Faculty of Medicine, Hlavní mesto Praha, Czech Republic, [2]Institute of Rheumatology, Praha, Czech Republic, [3]Institute of Rheumatology, Praha 8, Czech Republic, [4]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [5]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing spondylitis (AS) significantly impacts quality of life across multiple domains. To date, no studies have evaluated the impact of initial biological therapy on sexual function, despite its critical role in overall quality of life.

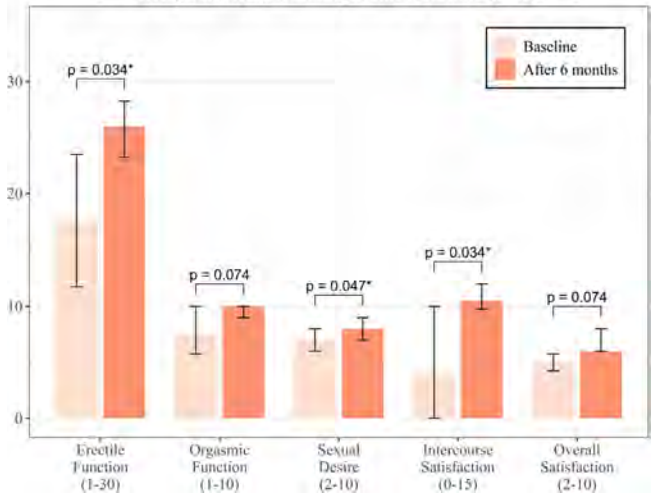
We aimed to evaluate the impact of initial biologic/targeted synthetic disease modifying anti-rheumatic drug (b/tsDMARD) therapy on sexual function in men with AS.

Methods: Men with AS initiating b/tsDMARD therapy within the Czech ATTRA registry completed the International Index of Erectile Function (IIEF; higher score represents better function) at baseline (M0) and after six months (M6). Routine clinical and laboratory data was collected, with patient-reported outcomes regarding function and quality of life (Health Assessment Questionnaire (HAQ), 36-Item Short Form Health Survey (SF-36), EuroQoL 5-Dimension Questionnaire (EuroQoL) and Multidimensional Health Assessment Questionnaire (MDHAQ)). Comparisons were performed using the Wilcoxon test, with p-values adjusted for multiple comparisons using the Benjamini-Hochberg method. Variable selection for baseline predictors and factors associated with improvement in IIEF domains was performed using Elastic Net regression.

Results: 52 sexually active men completed the study (mean±SD age: 40±9 years; 92.3% HLA-B27 positive). 96.2% received anti-TNF agents, 3.8% an IL-17 inhibitor (Table 1). At M6, we observed significant reductions in inflammatory markers (ESR, CRP) and disease activity (ASDAS), as well as improvements in function and quality of life (HAQ, MDHAQ, EuroQoL, SF-36) ($p< 0.05$ for all). Due to the potential ceiling effect in IIEF scores, we stratified participants by baseline presence of erectile dysfunction (ED) (IIEF Erectile Function < 26, n=12). The patients with ED experienced a significant median (IQR) increase in erectile function from 17.5 (11.5-23.5) to 26.0 (23.3-28.3) ($p=0.033$). There were also significant improvements in the domains of sexual desire ($p=0.046$) and intercourse satisfaction ($p=0.033$) (Figure 1). In contrast, patients without ED at baseline (n=40) maintained consistently high scores.

On the level of bivariate analysis, improvements in sexual function were linked with reduced disease activity, and improvements in physical and mental health. LASSO regression identified baseline IIEF domain scores as the strongest predictors of sexual function outcomes. Weaker predictions were observed for functional status (thoracic expansion, occiput-to-wall

Figure 1. International Index of Erectile Function
Group: Erectile dysfunction present at baseline (n = 12)



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics

Characteristic (score range: worst-best)	Overall n = 52	ED n = 12	no ED n = 40
Age [years]	40.7 (32.5, 46.3)	42.2 (34.1, 50.5)	39.1 (32.0, 46.0)
Biological Therapy - Agent			
Adalimumab	31 (60%)	6 (50%)	25 (63%)
Etanercept	12 (23%)	3 (25%)	9 (23%)
Golimumab	2 (3.8%)	1 (8.3%)	1 (2.5%)
Infliximab	5 (9.6%)	2 (17%)	3 (7.5%)
Secukinumab	2 (3.8%)	0 (0%)	2 (5.0%)
Biological Therapy - MoA			
anti-IL-17	2 (3.8%)	0 (0%)	2 (5.0%)
anti-TNF	50 (96%)	12 (100%)	38 (95%)
CRP [mg/L]	12.6 (7.0, 26.2)	11.8 (5.3, 22.8)	13.6 (7.3, 26.2)
ESR [mm/hour]	13.0 (5.0, 24.0)	7.5 (3.5, 17.0)	14.0 (6.0, 28.0)
ASDAS	3.50 (2.93, 4.21)	3.04 (2.40, 3.98)	3.65 (3.09, 4.21)
HAQ (3-0)	0.75 (0.38, 1.13)	0.81 (0.31, 1.38)	0.75 (0.44, 1.06)
MDHAQ - RAPID3 (30-0)	14.8 (11.0, 18.2)	11.8 (9.5, 17.6)	15.8 (12.4, 18.3)
EuroQol (0-1)	0.21 (0.16, 0.73)	0.64 (0.13, 0.74)	0.20 (0.16, 0.73)
SF-36: Mental Component Score (5.5–63.6)	45.9 (34.9, 52.5)	37.7 (28.8, 45.9)	48.3 (40.0, 52.9)
SF-36: Physical Component Score (16.6–57.9)	31.8 (24.1, 41.1)	36.5 (25.5, 45.0)	31.1 (23.9, 38.6)

Table 1 shows the baseline characteristics overall and divided into subgroups based on the baseline presence of erectile dysfunction (defined as IIEF Erectile Function <26). Data are shown as median (IQR) or n (%). Acronyms: ASDAS, Ankylosing Spondylitis Disease Activity Score; CRP, C-reactive protein; ED, Erectile Dysfunction; ESR, Erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; IIEF, International Index of Erectile Function; MDHAQ – RAPID3, Multidimensional Health Assessment Questionnaire; SF-36, Short Form Health Survey Questionnaire.

Table 2. Predictors of Sexual Function Improvement

IIEF Domain (follow-up – baseline)	Coefficients
IIEF Erectile Function	IIEF Erectile Function (-3.56), IIEF Orgasmic Function (-2.15), Thoracic Expansion (0.32), EuroQoL (0.29), Chin to chest distance (-0.21), Morning Stiffness (-0.13), Disease Activity (-0.09), Cardiovascular Disease (-0.02)
IIEF Orgasmic Function	IIEF Orgasmic Function (-2.23), Occiput-to-wall Distance (-0.14), Schober Test (0.09), COX-2 Inhibitor Use (-0.07), SF-36 Mental Component Score (0.05)
IIEF Sexual Desire	IIEF Sexual Desire (-0.52), Antidepressant Use (0.27), ASDAS (-0.19), NSAIDs Use (0.17), Alcohol Consumption (-0.15), IIEF Orgasmic Function (-0.12), COX-2 Inhibitor Use (-0.09), Chin to Chest Distance (-0.02), Occiput-to-wall Distance (-0.02), SF-36 Mental Component Score (-0.02)
IIEF Intercourse Satisfaction	IIEF Intercourse Satisfaction (-1.88), IIEF Orgasmic Function (-0.49), ESR (-0.1), Thoracic Expansion (0.05), SF-36 Physical Component Score (0.04)
IIEF Overall Satisfaction	IIEF Orgasmic Function (-0.61), IIEF Overall Satisfaction (-0.39), Metabolic Disease (-0.12)

Table 2 shows the baseline predictors associated with improvements in IIEF domains. These variables were selected using the LASSO regression method – we are reporting the standardized coefficients to better report the effect of the variables. Acronyms: ASDAS, Ankylosing Spondylitis Disease Activity Score; COX-2, Cyclooxygenase-2; ESR, Erythrocyte Sedimentation Rate; EuroQoL, European Quality of Life; IIEF, International Index of Erectile Function; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs; SF-36, 36-Item Short Form Health Survey.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

distance, Schober test), quality of life (EuroQoL, SF-36 mental component score), comorbidities (cardiovascular disease, metabolic disease), medication use (antidepressants, NSAIDs, COX-2 inhibitors), and disease activity measures (ASDAS, CRP, ESR) (Table 2).

Conclusion: Initial biological therapy significantly improved sexual function in men with AS, with the most striking benefits observed in those with baseline erectile dysfunction. Improvements were linked to better quality of life and reduced disease activity. These findings highlight the broader benefits of b/tsDMARD therapy beyond disease control.

Supported by MHCR 023728

Disclosure: D. Zavada: None; **B. Vala**: None; **A. Navratilova**: None; **V. Losterova**: None; **L. Moravcova**: None; **J. Vencovsky**: None; **L. Šenolt**: None; **K. Pavelka**: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **M. Tomcik**: None.

Abstract Number: 2347

Bimekizumab Treatment Resulted in Patients with Axial Spondyloarthritis Maintaining Their Clinical Responses Over 3 Years: Results from Two Phase 3 Studies and Their Open-Label Extension

Fabian Proft[1], Désirée Van Der Heijde[2], Sergio Schwartzman[3], Vanessa Taieb[4], Sarah Kavanagh[5], Gaëlle Varkas[6], Victoria Navarro-Compan[7] and Xenofon Baraliakos[8], [1]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [3]Weill Cornell Medical Center, New York Presbyterian Hospital, and Hospital for Special Surgery, New York, NY, [4]UCB, Colombes, France, [5]UCB, Morrisville, NC, [6]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [7]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [8]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

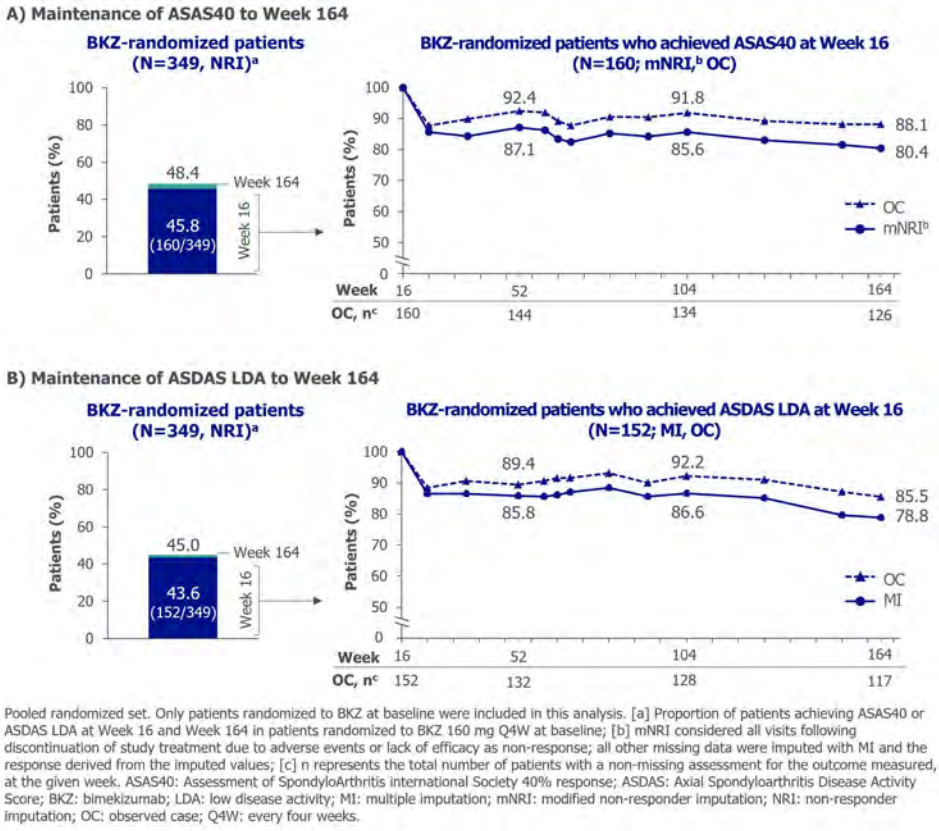
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease which requires optimal management.[1] In clinical trials, Assessment of SpondyloArthritis international Society ≥40% improvement (ASAS40) is a stringent outcome used to assess efficacy, while in clinical practice, focus is on axSpA Disease Activity Score (ASDAS) low disease activity (LDA; < 2.1). Maintenance of response, an internationally recommended axSpA treatment target,[1] can be measured by these outcomes.

Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. In patients (pts) across the full disease spectrum of axSpA (i.e., non-radiographic [nr-] and radiographic [r-]axSpA), BKZ has demonstrated sustained clinical efficacy to 2 years in the phase 3 studies BE MOBILE 1 and 2, and their combined open-label extension (OLE).[2] This analysis assessed the maintenance of response to BKZ over 3 years in pts who achieved responses at Week (Wk) 16 in these studies, including in pts who never lost their response at any subsequent visit.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Pooled randomized set. Only patients randomized to BKZ at baseline were included in this analysis. [a] Proportion of patients achieving ASAS40 or ASDAS LDA at Week 16 and Week 164 in patients randomized to BKZ 160 mg Q4W at baseline; [b] mNRI considered all visits following discontinuation of study treatment due to adverse events or lack of efficacy as non-response; all other missing data were imputed with MI and the response derived from the imputed values; [c] n represents the total number of patients with a non-missing assessment for the outcome measured, at the given week. ASAS40: Assessment of SpondyloArthritis international Society 40% response; ASDAS: Axial Spondyloarthritis Disease Activity Score; BKZ: bimekizumab; LDA: low disease activity; MI: multiple imputation; mNRI: modified non-responder imputation; NRI: non-responder imputation; OC: observed case; Q4W: every four weeks.

Figure 1. Maintenance of (A) ASAS40 and (B) ASDAS LDA to Week 164 among BKZ-randomized patients who achieved each respective outcome at Week 16

Methods: BE MOBILE 1 (NCT03928704; nr-axSpA) and 2 (NCT03928743; r-axSpA) both comprised a 16-wk double-blind, placebo-controlled period followed by a 36-wk maintenance period.[3] From Wk 16, all pts received subcutaneous BKZ 160 mg every 4 wks. At Wk 52, eligible pts could enroll in the OLE (BE MOVING; NCT04436640).

The proportion of pts achieving ASAS40 or ASDAS LDA at Wk 164 was assessed among BKZ-randomized pts that achieved each respective outcome at Wk 16. The proportion of pts who achieved ASDAS LDA at Wk 16 and never lost their response at every subsequent visit from Wk 16 to Wk 164 is also reported, including those who achieved ASDAS major improvement (ASDAS-MI; ≥2.0-unit change from baseline [CfB]) and ASDAS clinically important improvement (ASDAS-CII; ≥1.1-unit CfB).

Presented data, pooled across studies, use non-responder imputation (NRI), modified non-responder imputation (mNRI) or multiple imputation (MI; ASDAS only). Observed case (OC) data are also reported.

Results: A total of 128 pts and 221 pts were randomized to BKZ across BE MOBILE 1 and 2, respectively (N=349). A high proportion of pts who achieved a response at Wk 16 maintained their response at Wk 164 (**Figure 1**).

Of the 160 pts (45.8%; NRI) who achieved ASAS40 at Wk 16, 80.4% still achieved ASAS40 at Wk 164 (mNRI). Of the 152 pts (43.6%; NRI) who achieved ASDAS LDA at Wk 16; 78.8% still achieved ASDAS LDA at Wk 164 (MI; **Figure 1**).

From Wk 16 through to Wk 164, 50% of pts never lost their ASDAS LDA status at any assessed visit (MI), with a further 22.4% only losing their ASDAS LDA status at one visit, and 6.1% at two visits, respectively (MI). The majority of pts who never lost their ASDAS LDA status from Wk 16 and entered the OLE achieved ASDAS-MI or ASDAS-CII at Wk 52, 104 and 164 (94.5%, 94.5%, and 90.9%, respectively; **Figure 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

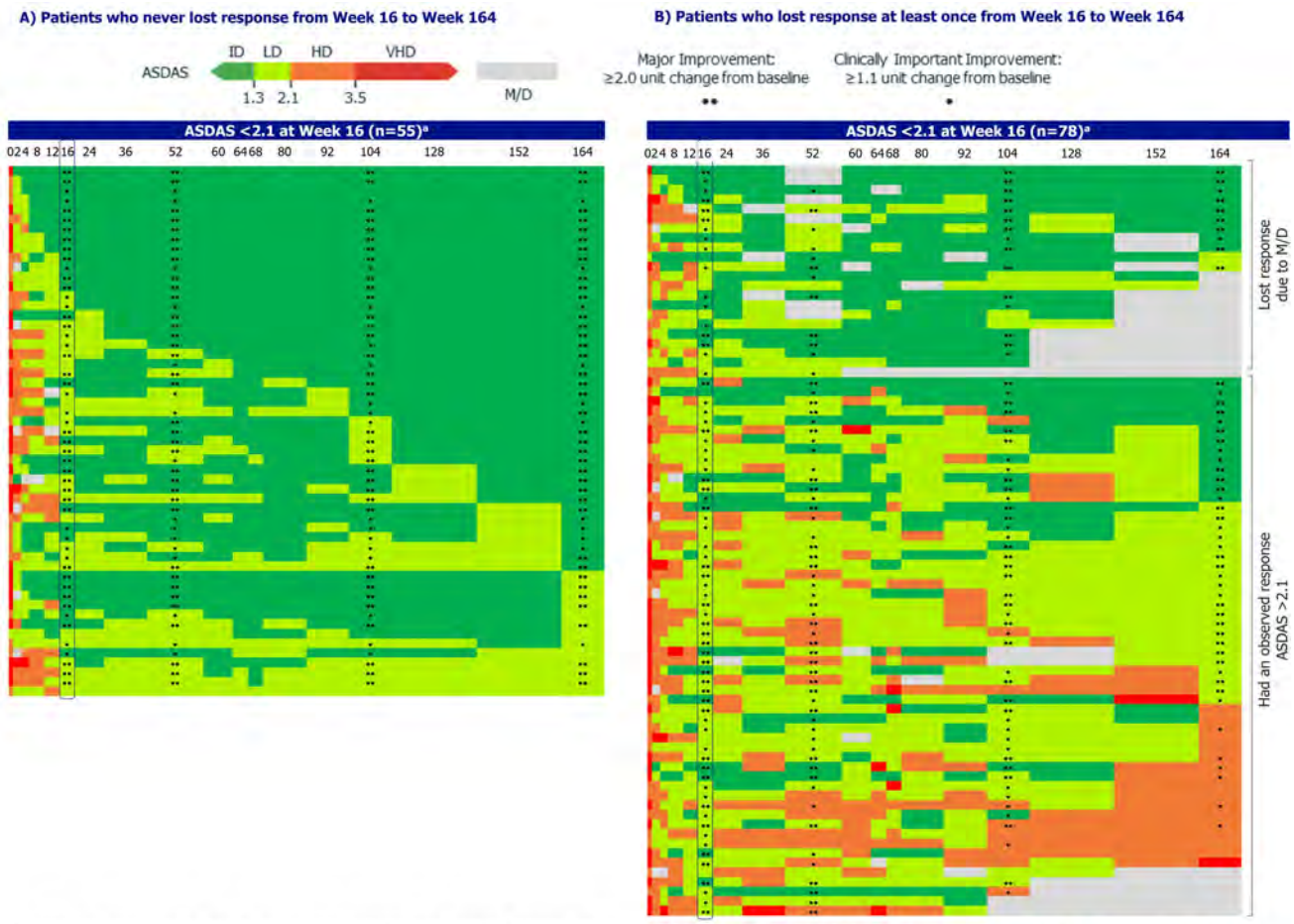


Figure 2. BKZ-randomized patients who achieved ASDAS LDA (<2.1) at Week 16 and (A) never lost their ASDAS LDA status to Week 164 or (B) lost their ASDAS LDA status at least once to Week 164 (OC)

Conclusion: A high proportion of BKZ-randomized pts who achieved stringent clinical responses at Wk 16 maintained these to Wk 164 across the full disease spectrum of axSpA. Half of pts achieving ASDAS LDA at Wk 16 never lost their response up to Wk 164.

References: 1. Ramiro S. Ann Rheum Dis 2023;82:19–34; 2. Baraliakos X. Rheumatology 2025;keaf009; 3. Baraliakos X. Ann Rheum Dis 2024;83:199–213.

Disclosure: F. Proft: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Hexal, 2, 6, Janssen, 2, 6, Medscape, 2, 6, MoonLake Pharma, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 5, 6; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **S. Schwartzman**: AbbVie, 2, 6, Eli Lilly and Company, 2, 5, 6, Janssen, 2, 6, National Psoriasis Foundation, 12, Medical Board member, Pfizer, 6, Teijin, 2, UCB, 2, 6, UpToDate, 2; **V. Taieb**: UCB, 3, 12, Shareholder; **S. Kavanagh**: Aclipse Therapeutics, 2, Aliada Therapeutics, 2, Allay Therapeutics, 2, Autobahn Therapeutics, 2, Cognition Therapeutics, 2, Colorado Prevention Center, 2, Karuna Therapeutics, 2, Kisbee

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Therapeutics, 2, LB Pharmaceuticals, 2, Nesos, 2, Novartis, 2, Onward Medical, 2, PharPoint Research, 2, Summit Analytical, 2, Therini Bio, 2, Tonix Pharmaceuticals, 2, Tornado Therapeutics, 2, UCB, 2, 3, Whitsell Innovations, 2, Worldwide Clinical Trials, 2, Zosano Pharma, 2; **G. Varkas**: AbbVie, 2, 5, 6, Amgen, 2, 6, Celltrion, 2, 5, 6, EG, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, MSD, 5, Novartis, 2, 6, Pfizer, 2, 5, 6, Takeda, 5, UCB, 2, 6; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor.

Abstract Number: 2348

Efficacy and safety of dual biological therapy in the treatment of rheumatic diseases: experience from a single highly specialized center

Francesco Fulvio Bizzarri[1], Luis Alberto Menchén Viso[2], Esther Chamorro De Vega[3], Ofelia Baniandrés Rodríguez[4] and Juan Carlos Nieto[2], [1]Hospital Universitario Clinico San Cecilio, Granada, Spain, [2]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [3]Pharmacy department, Hospital General Universitario Gregorio Marañón.Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain, Madrid, Madrid, Spain, [4]Hospital General Universitario Gregorio Marañon, Madrid, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Immune-mediated rheumatic diseases (IMRDs) are chronic inflammatory disorders driven by multiple overlapping immunological pathways. Although biologic DMARD monotherapy has substantially improved outcomes, a subset of patients remains refractory due to compensatory "immune escape" mechanisms and incomplete pathway inhibition. Off-label combination therapy targeting two distinct immune axes has been proposed to overcome these challenges, yet real-world data on its efficacy and safety are sparse and not reflected in current guidelines.

Methods: We conducted a retrospective, cross-sectional study at a tertiary reference center (CEIMI, Hospital General Universitario Gregorio Marañón, Madrid) including twenty adult patients (13 women; mean age 48.5 years) diagnosed with rheumatoid arthritis (n = 5), psoriatic arthritis (n = 5), psoriasis (n = 1), spondyloarthritis (n = 3), inflammatory bowel disease (n = 2), systemic lupus erythematosus (n = 2), or juvenile idiopathic arthritis (n = 2). All had failed a median of four prior st/bDMARDs (6.6 in RA) and initiated off-label dual therapy with agents targeting distinct immune pathways. Clinical, laboratory, efficacy (remission or low disease activity [LDA] by standardized indices), and safety data were extracted at baseline and at 1, 3, 6, 12, and up to 36 months post-CBT. Descriptive statistics summarized outcomes.

Results: At CBT initiation, 65 % of patients had high disease activity and were on glucocorticoids. Sixteen regimens were used; the most common paired a CD20 inhibitor with a JAK inhibitor (25 %), and rituximab featured in nine. Mean exposure was 27 months (range 2–68), and 80 % remained on CBT. By month 1, 65 % achieved remission or low disease activity

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16	Patient 17	Patient 18	Patient 19	Patient 20
Age; Sex	62; F	69; F	58; F	51; F	58; F	74; M	66; F	57; F	58; F	51; F	56; M	50; M	54; M	69; F	57; F	50; M	57; F	59; M	58; F	58; F
Disease (duration)	RA (17 years)	RA (7 years)	RA (29 years)	RA (10 years)	RA (22 years)	Rituximab-refractory polyarticular RA (12 years)	RF-positive polyarticular RA (7 years)	PsA (10 years)	PsA (14 years)	PsA (6 years)	PsA (23 years)	PsA (24 years)	Pso (41 years)	SpA (21 years)	SpA + IBD (45 years)	SpA + IBD (13 years)	IBD + PsO (19 years)	IBD (3 years)	SLE (4 years)	SLE (3 years)
Previous bDMARDs / stDMARDs	6 (IFX, ADA, ETN, TCZ, ABA, GOL)	5 (ETZ, IFX, TCZ, ADA, TOF, ABA, GOL, RTX, UPA)	9 (ETN, ETN, CTZ, TCZ, ABA, ABR, SCK, TOF, BAR)	3 (ETN, ADA, TOF, TCZ, ABA, CTZ, SCK)	2 (ETN, ADA)	4 (ETN, ADA, TCZ, ANK)	3 (ETN, TCZ, ADA)	3 (ADA, ETN, SCK)	4 (ADA, ETN, SCK, GUS)	4 (; SCK; ADA, USK, IFX)	2 (ETN; ADA)	5 (ADA, ETN, TCZ, ABA, IFX, USK, SCK, GUS, UPA	1 (ADA, BRO)	1 (SCK)	3 (ADA, IFX, CTZ, VED, ETN)	5 (IFX; ADA, UPA, CTZ, FIM)	1 (ADA)	2 (ADA, ETN)	0	0
CBT (exposure)	RTX + TOF (68 months)	RTX + CTZ (10 months)	RTX + UPA (13 months)	RTX + ADA (68 months)	RTX + TOF (24 months)	ETN + TOF (8 months)	RTX + TOF (24 months)	IXK + APR (50 months)	SCK + APR (24 months)	ANK + GUS (29 months)	ADA + UPA (3 months)	ETN + IXE (12 months)	ABA + APR (18 months)	RTX + UPA (18 months)	USK + UPA (11 months)	GUS + QZL (2 months)	ADA + APR (27 months)	CTZ + USK (12 months)	BEL + RTX (23 months)	BEL + RTX (6 months)
Indication for starting CBT	MSK disease	MSK disease	MSK disease	MSK disease	MSK disease	MSK disease	MSK disease	Cutaneous disease	Cutaneous disease	Cutaneous disease	MSK disease	MSK disease	Cutaneous disease	MSK disease	MSK disease	MSK disease	IBD activity + Cutaneous disease	IBD activity	SLE activity	SLE activity
Disease activity — Basal	DAS28-CRP: 5,97	DAS28-CRP: 7,72	DAS28-CRP: 5,10	DAS28-CRP: 5,81	DAS28-CRP: 4,66	DAS28-CRP: 6,84	DAS28-CRP: 6,23	DAPSA: 32,7 ;	DAPSA: 4,8 ; PASI: 0,4	DAPSA: 7 ; PASI: 10,8	DAPSA:43,1	DAPSA: 20,5	PASI: 19,2	ASDAS: 4,91	ASDAS: 2,91	ASDAS: 5,29 ; HBI: 5	HBI: 7 ; PASI: 19,2	HBI: 9	SLEDAI-2K: 12	SLEDAI-2K: 14
Disease activity — 1 month	/	DAS28-CRP: 3,1	DAS28-CRP: 3,9	DAS28-CRP: 3,01	DAS28-CRP: 2,24	DAS28-CRP: 6,03	DAS28-CRP: 3,85	DAPSA: 3,4 ;	DAPSA: 4,4 ; PASI: 1,8	PASI: 1,8	/	/	PASI: 8,2	ASDAS: 2,31	ASDAS: 1,89	ASDAS: 1 ; HBI: 2	HBI: 2 ; PASI: 3	/	SLEDAI-2K: 2	SLEDAI-2K: 0
Disease activity — 3 month	DAS28-CRP: 3,24	DAS28-CRP: 3,93	/	DAS28-CRP: 2,65	DAS28-CRP: 2,94	DAS28-CRP: 4,83	DAS28-CRP: 3,2	DAPSA: 3,2 ; PASI: 1,2	DAPSA: 4,4 ; PASI: 1,8	PASI: 7,4	DAPSA: 10	DAPSA: 13,5	PASI: 0	ASDAS: 1,59	/	/	HBI: 0 ; PASI: 3,3	/	SLEDAI-2K: 4	SLEDAI-2K: 3
Disease activity — 6 month	DAS28-CRP: 3,15	DAS28-CRP: 2,68	/	DAS28-CRP: 2,81	DAS28-CRP: 2,94	/	/	DAPSA: 0,4 ; PASI: 0,1	DAPSA: 4,4 ; PASI: 0	PASI: 1,3	/	/	PASI: 0	/	ASDAS: 2,2	/	HBI: 0 , PASI: 2	/	SLEDAI-2K: 2	/
Disease activity — Last evaluation	DAS28-CRP: 3,82 (85 months)	DAS28-CRP: 2,08 (6 months)	DAS28-CRP: 3,36 (15 months)	DAS28-CRP: 2,03 (78 months)	DAS28-CRP: 2,47 (24 months)	DAS28-CRP: 4,89 (4 months)	DAS28-CRP: 4,06 (18 months)	DAPSA: 0,4 ; PASI: 0 (18 months)	PASI: 1,2 (14 months)	PASI: 1,2 (14 months)	DAPSA: 10 (3 months)	DAPSA: 10 (12 months)	PASI: 0 (18 months)	ASDAS: 1,2 (12 months)	ASDAS: 1,27 (18 months)	ASDAS: 1 , HBI: 1 (1 month)	HBI: 0 , PASI 1 (24 months)	HBI: 6 (12 months)	SLEDAI-2K: 4 (24 months)	SLEDAI-2K: 4 (6 months)
Glucocorticoids — Previous CBT	Prednisone 5 mg/day	Methylprednisolone 1 mg/kg IV	Methylprednisolone 0,2 mg/kg IV	Prednisone 6 mg/day	Prednisone 5 mg/day	Prednisone 2,5 mg/day	Prednisone 5 mg/day	0	0	0	Prednisone 5 mg/day	0	0	Prednisone 5 mg/day	Methylprednisolone 1 mg/kg IV	0	0	0	Prednisone 5 mg/day	Prednisone 7,5 mg/day
Glucocorticoids — 3 months	0	0	0	0	0	0	0	0	0	0	0	0	0	Prednisone 2,5 mg/day	0	/	0	/	Prednisone 10 mg/day	Prednisone 5 mg/day
CRP — Basal	1,03 mg/dL	1,4 mg/dL	3,31 mg/dL	1,6 mg/dL	0,4 mg/dL	12,2 mg/dL	4,2 mg/dL	0,7 mg/dL	1,08 mg/dL	1,8 mg/dL	7,5 mg/dL	0,51 mg/dL	/	12,8 mg/dL	0,4 mg/dL	9,93 mg/dL	/	0,98 mg/dL	/	0,3 mg/dL
CRP — 3 months	0,4 mg/dL	0,4 mg/dL	0,4 mg/dL	0,4 mg/dL	0,4 mg/dL	4,5 mg/dL	1,5mg/dL	0,5 mg/dL	0,9 mg/dL	1,1 mg/dL	1,5 mg/dL	0,11 mg/dL	/	0,5 mg/dL	0,4 mg/dL	/	/	/	/	0,3 mg/dL
Adverse events (type)	No	No	No	Yes (promoted lymph)	Yes	No	No	No	No (planned)	Yes (planned)	No	Yes (pancytopenia, administrative treatment)	No	No	No	No	No	No	No	Yes (progressive neutropenia)
Permanent Withdrawal (reason)	No	No	No	No	No	No	Yes (pre-treatment)	No	No	Yes (negative surgical procedure)	No	No	No	No	No	No	Yes (sustained control of the symptoms at month 6)	No	No	Yes (administrative)

ABA (Abatacept), ADA (Adalimumab), ANK (Anakinra), APR (Apremilast), ASDAS (Axial Spondyloarthritis Disease Activity Score), BAR (Baricitinib), BEL (Belimumab), BRO (Brodalumab), CRP (C-reactive protein), CTZ (Certolizumab), DAPSA (Disease Activity in PSoriatic Arthritis), DAS28-CRP (Disease Activity Score 28), ETN (Etanercept), F (Female), GOL (Golimumab), GUS (Guselkumab), HBI (Harvey-Bradshaw Index), IBD (Inflammatory bowel disease), IFX (Infliximab), IXE (Ixekizumab), JIA (Juveniile idiopathic arthritis), M (Male), MSK (Musculoskeletal), PASI (Psoriasis Area Severity Index), RA (Rheumatoid arthritis), RF (Rheumatoid factor), RIS (Risankizumab), RTX (Rituximab), SCK (Secukinumab), SLE (Systemic erythematosus lupus), SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index 2000), SpA (Spondyloarthritis), TCZ (Tocilizumab), TOF (Tofacitinib), UPA (Upadacitinib), USK (Ustekinumab), VED (Vedolizumab).

Main clinical and serological features and outcomes of patients under CBT

(LDA), rising to 87 % at month 3. At 6 months (n=12), 100 % were in remission/LDA and 78 % had reduced or stopped glucocorticoids. Sustained rates were 71 % at 12 and 91 % at 18 months.

All five RA patients reached remission/LDA by month 3, with one flare at 24 months. Both RF-positive JIA cases improved by month 1; one achieved LDA at month 3 and both discontinued steroids. PsA patients showed durable PASI and DAPSA score improvements. Two of three SpA patients remained in remission; one experienced worsened gastrointestinal symptoms. Both IBD patients improved clinically; one ceased CBT upon stable remission. In SLE patients, SLEDAI-2K scores dropped by 9–10 points at month 1. Four regimens (20 %) were discontinued—one for progressive neutropenia (resolved after stopping rituximab + belimumab), one for surgery, one at patient request, and one due to sustained remission.

Conclusion: In this real-world cohort of refractory IMRD patients, dual biologic/synthetic targeted therapy produced rapid, sustained remission or LDA across diverse diagnoses, enabled glucocorticoid tapering, and demonstrated a manageable safety profile. These findings warrant prospective studies to define the role of multidimensional pathway blockade in difficult-to-treat rheumatic disease.

Disclosure: F. Bizzarri: None; **L. Menchén Viso**: None; **E. Chamorro De Vega**: None; **O. Baniandrés Rodríguez**: None; **J. Nieto**: None.

Abstract Number: 2349

Classification of "Difficult-to-Manage Axial Spondyloarthritis": A Real-World Cohort Study Evaluating the ASAS 2024 Criteria Over Time

Gözde Sevgi Kart bayram[1], Muhammed Çağrı Akdemir[2], Mustafa Ekici[3], Gizem Ayan[4], Büşra Fırlatan Yazgan[1], Erdinç Ünaldı[3], Buğu Bulat[1], Ali Aytuğ Kuştaş[3], Ali Akdoğan[5], Omer Karadağ[5], Şule Apraş Bilgen[1], Ali İhsan Ertenli[1], Sedat Kiraz[3], Umut Kalyoncu[1] and Levent Kılıç[1], [1]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Turkey, [2]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey, Ankara, Turkey, [3]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara, Ankara, Turkey, [4]Ankara Research and Training Hospital, Ankara, Turkey, [5]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey, Ankara

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The concept of difficult-to-manage axial spondyloarthritis (D2M-axSpA)[1], may vary over time. Transitions between D2M and non-D2M classifications throughout the disease course remain unclear. This study evaluates the consistency of the D2M-axSpA classification over time and identifies differences of non-D2M and persistent and episodic D2M-axSpA cases at the b/tsDMARD initiation.

Methods: This is a cross-sectional assessment patients with axSpA who were on b/tsDMARD for at least one year and visited our rheumatology clinic between April-December 2023. Patients were assessed at two timepoints for fullfillment of D2M-axSpA: first visit at the study inclusion period and second visit between 6-12 months after the first visit. Using these two-timepoint data patients were categorized into three groups as follows:'persistent D2M' (D2M-axSpA' patients at both assessments), 'persistent non-D2M'(non-D2M-axSpA' patients at both assessments), 'episodic D2M-axSpA' (D2M-axSpA in only one of the assessments). Demographic, clinical and disease activity indices as well as comorbidities of the patients at the initiation of b/ts DMARD were evaluated and compared between groups. The factors associated with D2M-axSpA status on univariate analysis with significance at the 0.20 level were entered into a multivariable model. Backward elimination method was used at a significance of 0.05 level.

Table 1. Comparison of demographic, clinical and therapeutic characteristics of patients with Persistent D2M, Persistent Non-D2M and Episodic D2M receiving at least one b/tsDMARD

	Persistent D2M (n:62)	Episodic D2M (n:81)	Persistent non-D2M (n:635)	p values
Current Age,mean(SD)	48.04(9.5)	44.58(10.9)	45.45(11.6)	0.109
Female,n(%)	42(67.7%)	48(59.2%)	271(42.6%)	**<0.01**
Current disease duration,mean(SD) (years)	10.66(7.48)	10.61(7)	12.53(7.98)	0.055
Time from b/ts DMARD start to assessment visit(years)	7.79(4.13)	7.66(4.66)	7.77(4.67)	0.8
Time from diagnosis to first b/tsDMARD start(years)	3.33(5.38)	3.57(4.15)	4.85(6.05)	0.021
Age of diagnose,years,mean	37.86(9.87)	34.49(10.82)	34.14(10.28)	0.18
Ever smoked,n(%)	41(66.1%)	39(48.1%)	400(62.9%)	0.03
BMI	29.26(6.16)	28.28(5.62)	27.67(5.48)	0.127
Positive HLA-B27	13(20.9%)	24(29.6%)	225(35.4%)	0.07
Arthritis,n(%)	3(4.8%)	1(1.2%)	16(2.5%)	0.46
Number of comorbidities,median (IQR 25-75)	1(0-2)	0(0-1)	0(0-1)	**<0.001**
Comorbidities,n(%)				
Hypertension	26(41.9%)	22(27.1%)	139(21.8%)	**0.002**
Coronary Artery Disease	3(4.8%)	3(3.7%)	20(3.14%)	0.751
Diabetes mellitus	13(20.9%)	7(8.64%)	60(9.44%)	**0.015**
COPD/Asthma	15(24.19%)	7(8.64%)	43(6.77%)	**<0.001**
FMF	2(3.2%)	4(4.93%)	63(9.92%)	0.09
Malignancy	1(1.61%)	1(1.23%)	10(1.57%)	0.85
Extra-articular Manifestations,n(%)				
Psoriasis	10(16.12%)	20(24.69%)	62(9.76%)	**<0.001**
IBD	2(3.22%)	5(6.17%)	21(3.3%)	0.425
Uveitis	10(16.12%)	11(13.5%)	90(14.17%)	0.901
Disease activity at start of b/tsDMARD				
BASDAI mean(SD)	6.74(1.54)	6.46(1.74)	5.65(2.02)	**<0.001**
BASFI mean(SD)	5.61(2)	5.9(1.96)	4.5(2.4)	**<0.001**
HAQ mean(SD)	1.01(0.44)	1.02(0.42)	0.71(0.48)	0.002
VAS Global	73.24(14.53)	71.86(17.05)	62.97(21.16)	0.001
Crp mg/dl	1.78(2.94)	2.99(5.58)	2.41(3.24)	0.78

D2M: Difficult to Manage;SD:Standard deviation,BMI:Body Mass Index;COPD: Chronic obstructive pulmonary disease;FMF: Familial Mediterranean Fever;IBD: Inflammatory bowel disease; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index;BASFI: Bath Ankylosing Spondylitis Functional Index;HAQ: Health Assessment Questionnaire;VAS: Visual Analog Scale; Crp: C-reactive protein

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Multivariate logistic regression analysis of factors associated with the development of D2T (episodic or persistent) in patients classified as non-D2T

	Univariable analysis		Multivariable analysis	
Predictors	Odds ratio (95% CI)	p	Odds ratio (95%)	p
Female gender	2.28(1.56-3.31)	**<0.001**		
Current disease duration	0.96(0.94-0.99)	**0.011**		
Age of diagnosis	1.01(0.99-1.03)	0.063		
Time from diagnosis to first b/tsDMARD start(years)	0.95(0.91-0.99)	**0.013**		
BMI at b/ts DMARD initiation	1.03(1.00-1.06)	0.046		
Positive HLA-B27	1.59(1.00-2.54)	0.048		
Smoking status (ever)	0.74(0.51-1.08)	**0.124**		
Number of comorbidities	1.50(1.22-1.85)	**<0.001**		
Hypertension	0.55(0.37-0.82)	0.003		
Diabetes mellitus	0.64(0.37-1.10)	0.109		
COPD/Asthma	2.80(1.61-4.89)	<0.001		
Psoriasis	0.40(0.24-0.64)	**<0.001**		
BASDAI,b/tsDMARD initiation	1.28(1.13-1.47)	**<0.001**	1.48(1.15-1.91)	0.002
BASFI, b/tsDMARD initiation	1.28(1.13-1.47)	**<0.001**		
HAQ, b/tsDMARD initiation	3.40(1.5-7.35)	**0.002**		
VAS Global, b/tsDMARD initiation	1.28(1.13-1.47)	**<0.001**		
Crp, b/tsDMARD initiation	1.00(0.95-1.06)	0.82		

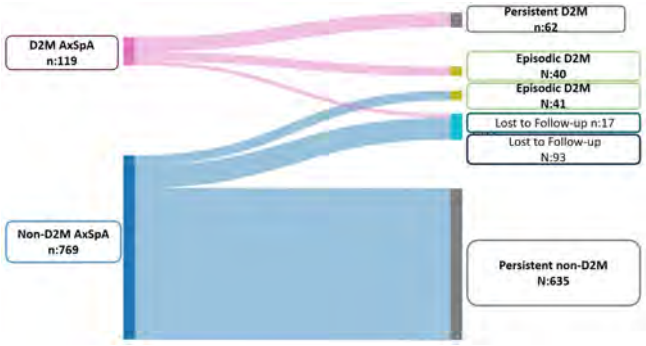


Figure 1. Temporal changes in D2M AxSpA and Non-D2M AxSpA patients

Results: Overall 888 patients were included in this assessment . From the initial D2M-axSpA patients(n=119), 52.1% were persistent-axSpA, 33.6% were episodic D2M-axSpA. 14.2% (17/119) did not attend follow-up visits. Of the initial non-D2M-axSpA (n=769), 82.5% were persistent non-D2M-axSpA, 5.33%were episodic D2M-axSpA, and 12.09% did not participate in follow-up visits (Figure 1). Persistent D2M-axSpA patients were more often female and had higher rates of hypertension, COPD/asthma, and diabetes mellitus. BASDAI and VAS global scores were significantly higher in the persistent D2M-group at b/tsDMARD initiation (Table 1). In the multivariable logistic regression analysis, a higher BASDAI score at the initiation of b/tsDMARD therapy was identified as a significant factor associated with the development of D2M-axSpA (either episodic or persistent) among patients initially classified as non-D2M (OR: 1.48 [1.15–1.91], p = 0.002) (Table 2).

Conclusion: Our study revealed that 33.6% of patients initially diagnosed with D2M-axSpA eventually transitioned to a non-D2M state and overall 10% of the population has transitioned from one category to another. Persistent D2M-axSpA patients were more often female and had a higher prevalence of comorbidities. Physicians should be aware that D2M-axSpA criteria fullfilments may change over time, with factors that potentially affecting subjective measures like BASDAI, HAQ, and VAS global scores.

References:

1. Poddubnyy D, B.X., et al ., Arthritis Rheumatol, 2024. **76**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Kart bayram: None; **M. Akdemir**: None; **M. Ekici**: None; **G. Ayan**: None; **B. Fırlatan Yazgan**: None; **E. Ünaldı**: None; **B. Bulat**: None; **A. Kuştaş**: None; **A. Akdoğan**: None; **O. Karadağ**: None; **Ş. Apraş Bilgen**: None; **A. Ertenli**: None; **S. Kiraz**: None; **U. Kalyoncu**: None; **L. Kılıç**: None.

Abstract Number: 2350

Multicenter study on the use of Upadacitinib: sex specific results in Spondyloarthritis

Guillermo Gonzalez Mozo de Rosales[1], Luis Maria Lopez-Dominguez[2], Nerea Alcorta-Lorenzo[3], oihane ibarguengoitia Barrena[4], David Montero[5], Ana Ruibal Escribano[6], estibaliz barastay Alberdi[7], Jesus Alejandro Valero Jaimes[8], Libe Ibarrola[9], Paula Garcia Escudero[10], Marta Lopez I Gomez[11], Eva Galindez Aguirregoicoa[12] and Maria Luz Garcia Vivar[13], [1]Basurto University Hospital, Bilbao, Spain, [2]Rheumatology Department, Donostia University Hospital., San Sebastián, Pais Vasco, Spain, [3]Rheumatology Department, Donostia University Hospital., San Sebastian, Spain, [4]Galdakao-Usansolo University Hospital, GALDAKAO, Spain, [5]Galdakao-Usansolo University Hospital, Bilbao, Spain, [6]Urduliz Hospital, Urduliz, Pais Vasco, Spain, [7]Urduliz Hospital, Urduliz, Spain, [8]Hospital Bidasoa, Iran, Spain, [9]Galdakao-Usansolo University Hospital, Galdakao, [10]H.U.Araba, Vitoria, [11]Araba University Hospital, Vitoria, Pais Vasco, Spain, [12]Basurto University Hospital, Bilbao, Pais Vasco, Spain, [13]Basurto Hospital, Bilbao, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Upadacitinib (UPA) is a Janus Kinase inhibitor (JAKi) selective for JAK1, approved for the treatment of both Psoriatic Arthritis (PsA) and Axial Spondyloarthritis (axSpA). In May 2022, the Basque Health Service prioritized UPA use over other JAK inhibitors following the failure of Adalimumab biosimilars.

The aim of this study is to describe the demographic and clinical characteristics of patients with axSpA and PsA treated with UPA and to explore sex-related differences.

Methods: 7 hospitals in our region (1.5 million inhabitants) participated in a multicenter, observational and ambispective study that included patients with UPA prescription from June 2021 to May 2024, with follow-up until Dec 2024.

Among the 415 patients enrolled, 87 were diagnosed with AxSpA and 78 with PsA. Data were collected on comorbidities, disease duration and pattern, extra-articular manifestations (EAMs) and disease activity (measured by BASDAI and ASDAS for AxSpA, and DAPSA for PsA)

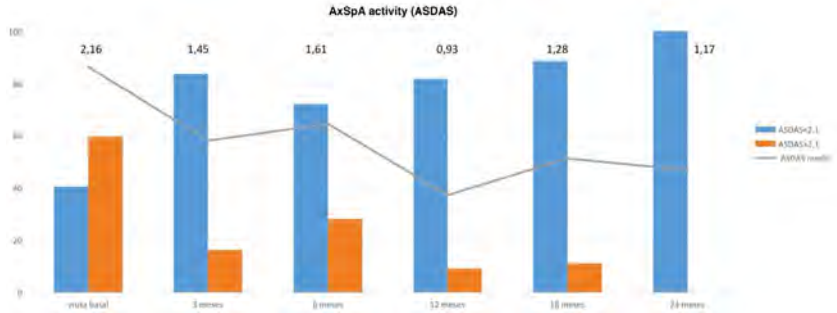


FIgure 1. AxSpA Activity (ASDAS).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

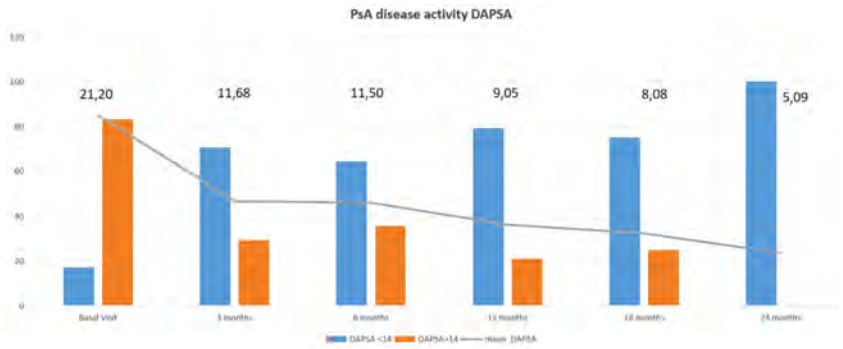


Figure 2. ApS activity (DAPSA)

Results: Axial Spondyloarthritis (AxSpA) Subgroup (n=87):

49.1% were women, with a mean age of 52.2 years (SD 11.6) and a mean disease duration of 102.2 months (SD 92.7), longer in men (123.7 vs. 76.3 months). HLA-B27 was positive in 55%, 65.1% had radiographic disease, and 19.3% had ankylosis (more frequent in men). Peripheral manifestations were observed in 51.2% (arthritis), 23.5% (enthesitis). EAMs included inflammatory bowel disease (16.5%), uveitis (9.6%), and psoriasis (9.9%). UPA median persistence was 13.1 months (SE 2.73), with no significant difference by sex or prior biologic exposure. The disease activity was shown in Figure 1.

Psoriatic Arthritis (PsA) Subgroup (n=78):

54.5% were women, with a mean age of 53.5 years (SD 10.2) and a disease duration of 116.5 months (SD 93.9). Age at diagnosis was later in women (46.6 vs. 40.3 years). The majority had peripheral (61.5%) or mixed (35.9%) patterns, with axial-only forms being rare (2 men). Women more frequently presented with peripheral PsA (76%), while men showed more mixed forms (51.4%). Cutaneous psoriasis was present in 80.8%, mostly plaque-type (65%), with no sex-based differences.

The disease activity was shown in Figure 2. UPA median persistence was 19 months (95% CI 11.6), slightly longer in women (16.4 months in men), though not statistically significant.

Sex-related differences in clinical presentation were observed in both diseases: men had longer disease duration and more axial involvement, while women had more peripheral manifestations and delayed diagnosis. Despite these differences, there were no significant sex-based differences in treatment history, response to UPA, or persistence in either AxSpA or PsA. A non-significant trend toward better persistence in women with PsA was noted.

Conclusion: UPA appears effective in the treatment of both AxSpA and PsA, even among patients with refractory and long-standing disease. While sex-based differences in clinical patterns were observed, outcomes and persistence were similar between men and women. These findings support the role of UPA across the Spondyloarthritis spectrum. Further studies with larger sample sizes are warranted to confirm potential sex-related differences in treatment outcomes.

Disclosure: G. Gonzalez Mozo de Rosales: None; **L. Lopez-Dominguez**: None; **N. Alcorta-Lorenzo**: None; **o. ibarguengoitia Barrena**: None; **D. Montero**: None; **A. Ruibal Escribano**: None; **e. barastay Alberdi**: None; **J. Valero Jaimes**: None; **L. Ibarrola**: None; **P. Garcia Escudero**: None; **M. Lopez I Gomez**: None; **E. Galindez Aguirregoicoa**: None; **M. Garcia Vivar**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2351

Modulation of Tyrosine Kinase 2- and Disease-Related Biomarkers by Zasocitinib (TAK-279), an Oral, Allosteric, Highly Selective and Potent Tyrosine Kinase 2 Inhibitor, Is Associated With Clinical Response in Patients with Active Psoriatic Arthritis

Amit Choudhury[1], Jie Cheng[2], Feng Hong[1], Sachin Kumar[1], Jay Tang[1], Paresh Thakker[1], Banishree Saha[1], Vinayagam Arunachalam[3], Ting Hong[3], Elena Tomaselli Muensterman[1], Haakan Wennbo[3] and **Iain McInnes**[4], [1]Takeda Development Center Americas, Inc.,, Cambridge, MA, [2]Takeda Development Center Americas, Inc., Cambridge, MA, [3]Takeda Development Center Americas, Inc, Cambridge, MA, [4]University of Glasgow, Glasgow, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

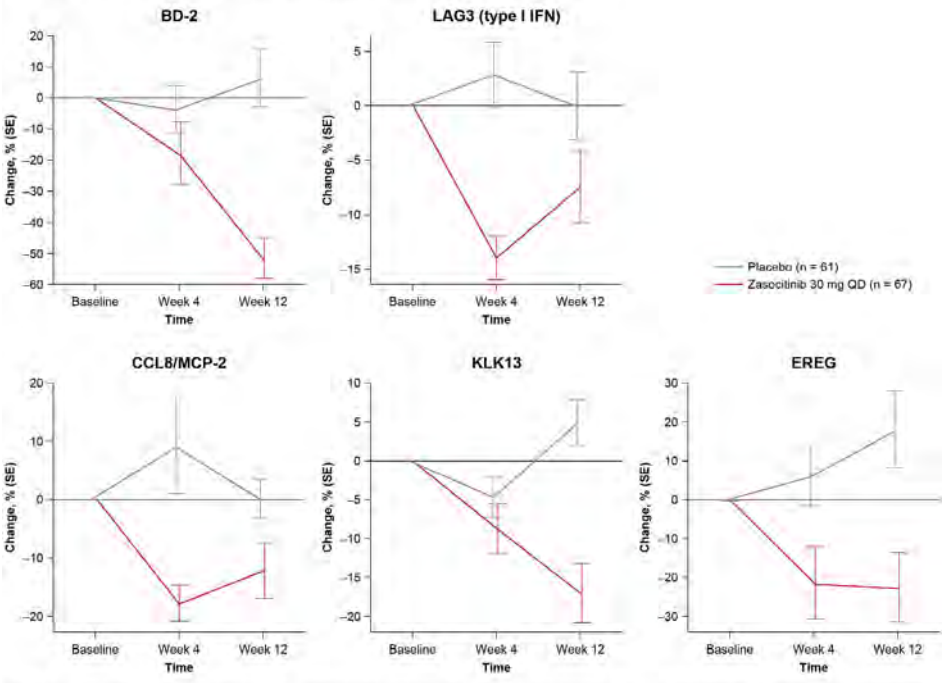
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: There is a significant unmet need for clinically informative biomarkers of disease activity and therapeutic response in immune-mediated inflammatory diseases (IMIDs). Tyrosine kinase 2 (TYK2) is a crucial mediator of pro-inflammatory pathways fundamental to the pathophysiology of some IMIDs, including psoriasis and psoriatic arthritis (PsA).

Zasocitinib (TAK-279) is an investigational, oral, allosteric, highly selective, and potent TYK2 inhibitor for IMIDs. This *post hoc* analysis of a phase 2b trial of patients with active PsA evaluated the effect of zasocitinib 30 mg once daily (QD) on TYK2

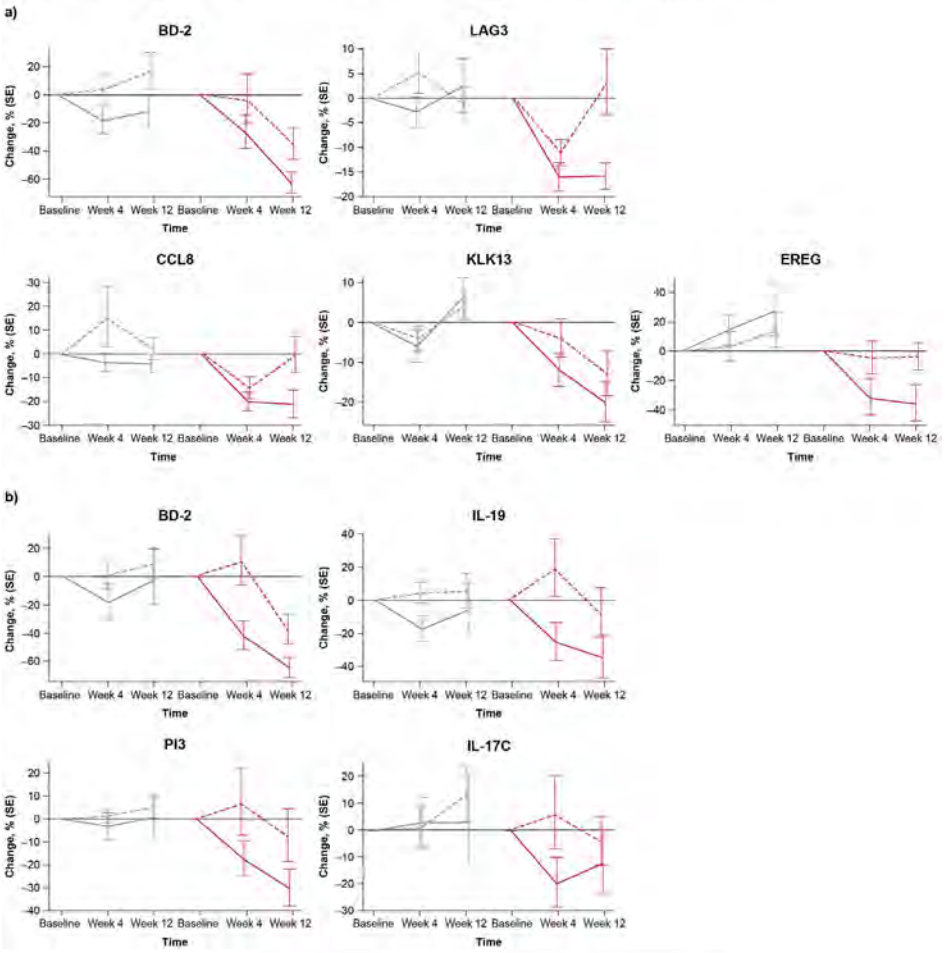
Figure 1. Modulation of TYK2 pathway- and PsA activity-related biomarkers in plasma.



Percent change from baseline in the levels of TYK2 pathway- and PsA activity-related proteins at Week 4 and Week 12 in patients given placebo and zasocitinib 30 mg QD. Relative abundance of biomarkers in serum was quantified using the Olink Explore HT platform, based on the binding of oligonucleotide-labeled antibodies pairs to the target protein. These unique hybridization sequences are then amplified and sequenced on Illumina platforms. The raw count was processed and normalized across blocks using reference samples based on normalization. The biomarker quantification, reported on a relative and logarithmic 2 scale as NPX values, were used for downstream expression modulation comparison across different dosing arms.
BD-2, β-defensin-2; CCL8, CC-chemokine ligand 8; EREG, epiregulin; IFN, interferon; KLK13, kallikrein-related peptidase 13; LAG3, lymphocyte activation gene-3; MCP-2, monocyte chemotactic protein 2; NPX, Normalized Protein eXpression; PsA, psoriatic arthritis; QD, once daily; SE, standard error; TYK2, tyrosine kinase.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Modulation of a) TYK2- and b) PsA disease-specific biomarkers, in ACR20 responders and non-responders with PsA.



Percent change from baseline in the levels of TYK2 pathway- and PsA activity-related proteins at Week 4 and Week 12 in patients given placebo and zasocitinib 30 mg QD. Biomarker levels, reported on a relative and logarithmic 2 scale as NPX values, in each treatment group were quantified at different time points and were compared between treatment groups. To calculate change from baseline, the NPX for biomarkers of interest at baseline were subtracted from the NPX at each time point (baseline, Week 4, and Week 12) for each patient. The longitudinal change from baseline for each biomarker was modeled using a mixed-effect model, with baseline value, treatment, time, and treatment–time interaction as fixed effects, and the patient as the random effect. The least-squares mean and standard error were back transformed to percent change and plotted for each biomarker at each time point. ACR20/PASI 75 responders were defined as patients who achieved ACR20/PASI 75 response at Week 12.

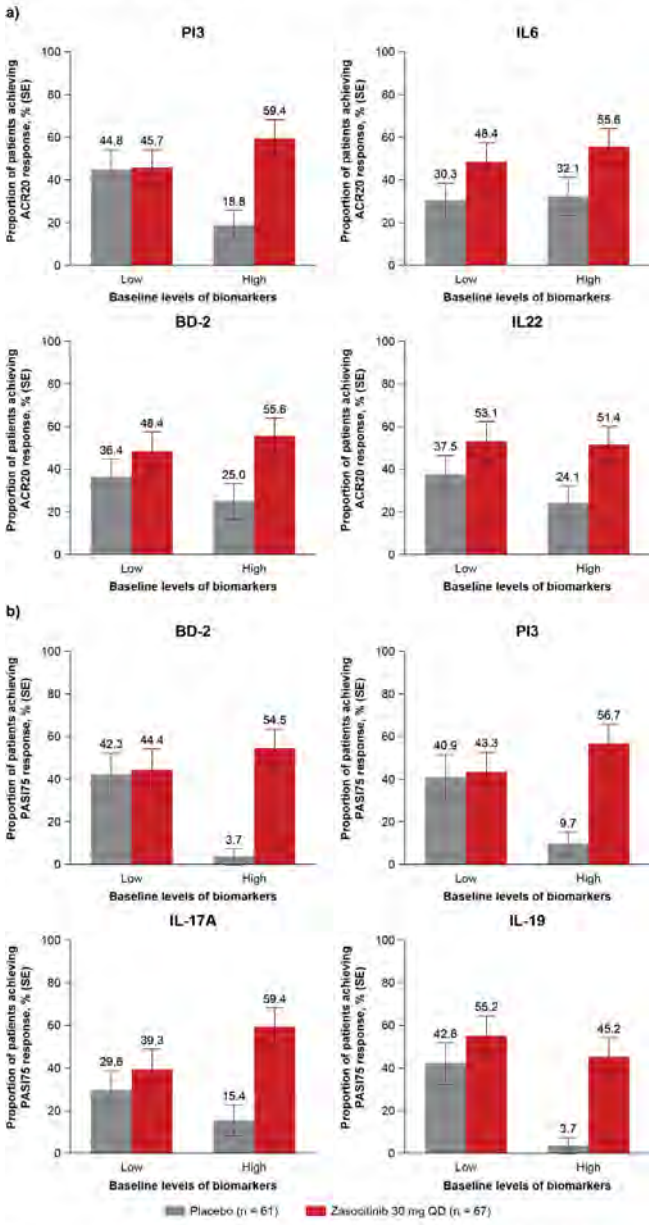
ACR20, American College of Rheumatology 20; BD-2, β-defensin-2; CCL8, CC-chemokine ligand 8; EREG, epiregulin; IL, interleukin; KLK13, kallikrein-related peptidase 13; LAG3, lymphocyte activation gene-3; NPX, Normalized Protein eXpression; PASI, Psoriasis Area and Severity Index; PI3, peptidase inhibitor 3; QD, once daily; TYK2, tyrosine kinase.

pathway- and PsA activity-related biomarkers, and reported the association between baseline levels of biomarkers and American College of Rheumatology (ACR20) and Psoriasis Area and Severity Index (PASI 75) response.

Methods: In a phase 2b multicenter, double-blind, placebo-controlled, dose-ranging study, 290 patients with active PsA were randomized 1:1:1:1 to receive oral zasocitinib (5, 15, or 30 mg) or placebo QD for 12 weeks (NCT05153148). Blood samples were collected from patients in each group at baseline, Week 4, and Week 12 (pre-dose, if applicable). Concentrations of plasma biomarkers associated with the TYK2 pathway (β-defensin-2 [BD-2] and lymphocyte activation gene-3 [LAG3]) and with PsA (CC-chemokine ligand 8 [CCL8], kallikrein-related peptidase 13 [KLK13], epiregulin [EREG], interleukin [IL]-19, peptidase inhibitor 3 [PI3], IL-17C, IL-6, IL-22, and IL-17A) were measured using the Olink Explore HT. Biomarker levels in each treatment group were quantified at each timepoint; results for zasocitinib 30 mg are described.

Results: Zasocitinib 30 mg induced modulation of TYK2 pathway-related biomarkers (BD-2 and LAG3) and PsA activity related biomarkers (CCL8, KLK13, and EREG) as early as Week 4 and through Week 12 ($p < 0.01$; **Figure 1**); modulation of these biomarkers was numerically greater in ACR20 responders versus non-responders ($p < 0.01$; **Figure 2a**), and modulation of BD-2, IL-19, PI3, and IL-17C was numerically greater in PASI 75 responders versus non-responders ($p < 0.01$; **Figure 2b**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



For each biomarker, the median cutoff was used to group patients into "biomarker low" and "biomarker high" groups. For each group and each treatment, the mean and standard error of the biomarker were calculated.
ACR20, American College of Rheumatology 20; BD-2, β-defensin-2; IL, interleukin; PASI, Psoriasis Area and Severity Index; PI3, peptidase inhibitor 3; QD, once daily; SE, standard error.

In patients with elevated baseline plasma levels of PI3, IL-6, BD-2, and IL-22, zasocitinib 30 mg treatment resulted in greater ACR20 response rates versus those receiving placebo ($p < 0.01$; **Figure 3a**). In patients with elevated baseline serum levels of BD-2, PI3, IL-17A, and IL-19, zasocitinib 30 mg treatment demonstrated greater PASI 75 response rates versus those receiving placebo ($p < 0.01$; **Figure 3b**).

Conclusion: In this phase 2b trial, zasocitinib 30 mg QD treatment led to modulation of key TYK2 pathway- and PsA activity-related biomarkers that mediate pathophysiology in patients with active PsA, particularly in ACR20 clinical responders. Baseline levels of key biomarkers may predict joint and skin responses to zasocitinib.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Choudhury: Takeda Development Center Americas, Inc., 3, 11; **J. Cheng**: Takeda Development Center Americas, Inc., 3, 11; **F. Hong**: Takeda Development Center Americas, Inc., 3, 11; **S. Kumar**: Takeda Development Center Americas, Inc., 3, 11; **J. Tang**: Takeda Development Center Americas, Inc., 3, 11; **P. Thakker**: Takeda Development Center Americas, Inc., 3, 11; **B. Saha**: Takeda Development Center Americas, Inc., 3, 11; **V. Arunachalam**: Takeda Development Center Americas, Inc., 3, 11; **T. Hong**: Takeda Development Center Americas, Inc., 3, 11; **E. Muensterman**: Takeda Development Center Americas, Inc., 3, 11; **H. Wennbo**: Takeda Development Center Americas, Inc., 3, 11; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2352

Long-Term Uveitis Rates with Bimekizumab Treatment Across Pooled Phase 2b and Phase 3 Studies in Patients with Axial Spondyloarthritis or Psoriatic Arthritis: 3-Year Update

Martin Rudwaleit[1], **Irene E. van der Horst-Bruinsma**[2], Floris A. van Gaalen[3], Nigil Haroon[4], Lianne S. Gensler[5], Myriam Manente[6], Chetan Prajapati[7], Katy White[7], Atul Deodhar[8] and Matthew A. Brown[9], [1]Bielefeld University, Medical School and University Medical Centre OWL, Klinikum Bielefeld, Department of Rheumatology, Bielefeld, Germany, [2]Department of Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands, [3]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [4]Department of Medicine/Rheumatology, University Health Network, Schroeder Arthritis Institute, University of Toronto, Toronto, ON, Canada, [5]Department of Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, [6]UCB, Braine-L'Alleud, Belgium, [7]UCB, Slough, United Kingdom, [8]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [9]Genomics England, London, United Kingdom

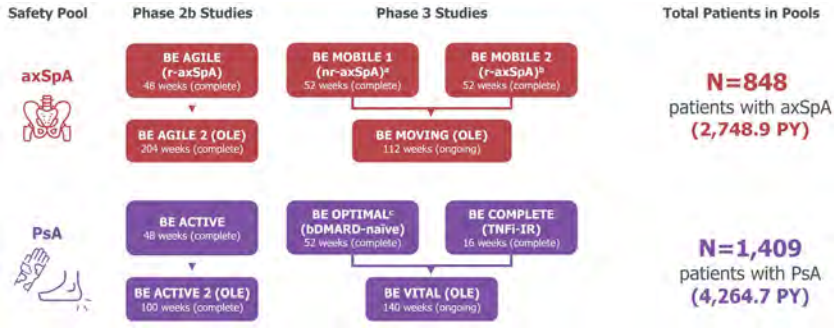
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

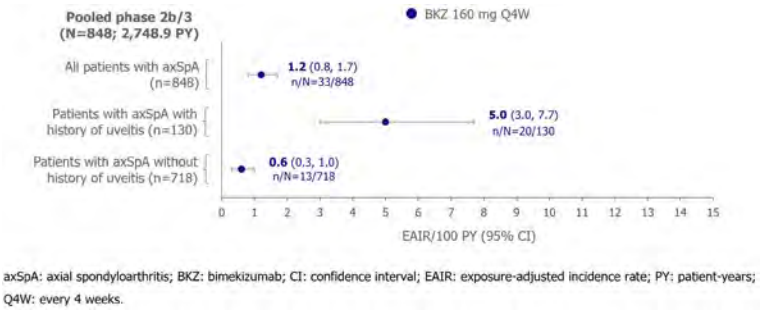


Data from the September 2024 (axSpA) and August 2024 (PsA) data-cuts shown; including all patients who received ≥1 dose of BKZ 160 mg Q4W in the phase 2b/3 studies. Duration of overall treatment period shown; BKZ treatment duration by data-cut varied between patients, depending on study duration and initial randomization in the feeder studies. [a] Patients with nr-axSpA met Assessment of SpondyloArthritis international Society (ASAS) classification criteria. Patients with radiographic sacroiliitis were excluded; [b] Patients with r-axSpA met modified New York criteria and fulfilled ASAS classification criteria; [c] BE OPTIMAL also included an adalimumab treatment arm. Data from patients treated with adalimumab were not included in the PsA safety pool prior to switching to BKZ, but were included following the switch. ASAS: Assessment of SpondyloArthritis international Society; axSpA: axial spondyloarthritis; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; nr-axSpA: non-radiographic axSpA; OLE: open-label extension; PsA: psoriatic arthritis; PY: patient-year; Q4W: every 4 weeks; r-axSpA: radiographic axSpA; TNFi-IR: tumor necrosis factor inhibitor inadequate response.

BE AGILE: NCT02963506; BE AGILE 2: NCT03355573; BE MOBILE 1: NCT03928704; BE MOBILE 2: NCT03928743; BE MOVING: NCT04436640; BE ACTIVE: NCT02969525; BE ACTIVE 2: NCT03347110; BE OPTIMAL: NCT03895203; BE COMPLETE: NCT03896581; BE VITAL: NCT04009499.

Figure 1. Two safety pools (axSpA, PsA) of patients treated with BKZ 160 mg Q4W across six phase 2b/3 studies and their open-label extensions

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



axSpA: axial spondyloarthritis; BKZ: bimekizumab; CI: confidence interval; EAIR: exposure-adjusted incidence rate; PY: patient-years; Q4W: every 4 weeks.

Figure 2. Incidence of uveitis in patients with axSpA stratified by history of uveitis

Background/Purpose: Uveitis is a common extra-musculoskeletal manifestation in patients (pts) with spondyloarthritis (SpA); incidence varies with SpA type and disease duration.[1–3] IL-17 has been implicated in uveitis pathogenesis.[4] However, previous data demonstrating IL-17A inhibition efficacy in managing uveitis are limited and conflicting.[5–7]

The exposure-adjusted incidence rate (EAIR) per 100 pt-years (PY) of uveitis was lower in pts with non-radiographic and radiographic axial SpA (axSpA) randomized to bimekizumab (BKZ; 1.8/100 PY), which selectively inhibits IL-17F in addition to IL-17A, vs placebo (15.4/100 PY) after 16 weeks in phase (Ph)3 studies.[8] Previously reported long-term data over ~2 years (data cut-off: Jul 2023) showed that uveitis rates remained low in BKZ-treated pts with axSpA (1.3/100 PY) and psoriatic arthritis (PsA; 0.1/100 PY).[9]

We report updated uveitis incidence in BKZ-treated pts with axSpA or PsA in Ph2b/3 studies with an additional year of treatment duration in the Ph3 studies (data cut-off in axSpA: Sep 2024; PsA: Aug 2024).

Methods: Data are reported for two pools, each comprising one Ph2b and two Ph3 studies and their open-label extensions, in pts with axSpA and PsA, respectively (**Figure 1**).

Uveitis events were identified using the preferred terms "autoimmune uveitis", "iridocyclitis", "iritis", and "uveitis", classified using the MedDRA v19.0; "acute anterior uveitis" was not a specific preferred term available in MedDRA v19.0.

Uveitis rates and EAIR/100 PY for pts who received ≥1 BKZ 160 mg every four weeks (Q4W) dose are reported.

Results: Pts with axSpA (N=848) and PsA (N=1,409) had a mean (SD) age of 40.3 (11.9) and 49.3 (12.4) years, respectively. Mean (SD) time since diagnosis was 6.1 (7.8) years in pts with axSpA and 7.0 (8.0) in pts with PsA. Of pts with axSpA, 130 (15.3%) had a history of uveitis (PsA: 21 [1.5%]). Most pts with axSpA were HLA-B27 positive (717/848 [84.6%]).

In pts with axSpA across the pooled Ph2b/3 data, BKZ exposure was 2,748.9 PY. In total, uveitis occurred in 33/848 (3.9%; EAIR [95% CI]: 1.2/100 PY [0.8, 1.7]) pts overall and in 20/130 (15.4%; 5.0/100 PY [3.0, 7.7]) pts with history of uveitis. In pts without a history of uveitis, 13/718 (1.8%; 0.6/100 PY [0.3, 1.0]) pts had uveitis events (**Figure 2**). Most events were mild/moderate, one was severe; two (0.2%) patients discontinued treatment due to uveitis.

Incidence of uveitis in pts with PsA was low across the pooled Ph2b/3 data (total BKZ exposure: 4,264.7 PY); uveitis occurred in 4/1,409 (0.3%; 0.1/100 PY [0.0, 0.2]) pts overall; two had a history of uveitis. No uveitis events led to treatment discontinuation.

Conclusion: With an additional year of BKZ treatment from previously reported data, the incidence of uveitis in pts with SpA receiving BKZ long-term, over 3 years, remained low.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References: 1. Robinson PC. Arthritis Rheumatol 2015;67:140–51; **2**. López-Medina C. RMD Open 2019;5:e001108; **3**. De Vicente Delmás A. RMD Open 2023;9:e002781; **4**. Hysa El. Eur. J. Clin. Invest 2021;51:e13572; **5**. Dick AD. J. Ophthalmol 2013;120:777–87; **6**. Kwon OC. Rheumatol 2025;64:588–96; **7**. Letko E. J. Ophthalmol 2015;122:939–48; **8**. Brown MA. Ann Rheum Dis 2024;1722–30; **9**. van der Horst-Bruinsma IE. Arthritis Rheumatol 2024;76(suppl 9). Abstract 2351.

Disclosure: M. Rudwaleit: AbbVie, 2, Boehringer Ingelheim, 2, Janssen, 2, 6, Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2; **I. van der Horst-Bruinsma**: AbbVie, 2, 5, 12, Fees received for lectures, BMS, 12, Fees received for lectures, Eli Lilly, 2, MSD, 2, 5, 12, Fees received for lectures, Novartis, 2, Pfizer, 5, 12, Fees received for lectures, UCB, 2, 5; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **N. Haroon**: AbbVie, 2, Eli Lilly, 2, Janssen, 2, UCB, 2; **L. Gensler**: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **M. Manente**: UCB, 3, 11; **C. Prajapati**: UCB, 7, Veramed, 3; **K. White**: UCB, 3, 11; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **M. Brown**: Clementia, 2, Grey Wolf Therapeutics, 2, Incyte, 2, Ipsen, 2, Novartis, 6, Pfizer, 2, 6, Regeneron, 2, UCB, 5, Xinthera, 2.

Abstract Number: 2353

Efficacy of Vunakizumab in Reducing Pain in Ankylosing Spondylitis: A Post-Hoc Analysis of a Phase 2/3 Clinical Trial

Jian Xu, Yifan Yang, Shuang Liu, Ru Bai, Shu Li, Guofang Zhang, Xiangyu Wang, Xinyu Xu, Mai Zheng and Daying Feng, The First Affiliated Hospital of Kunming Medical University, Kunming, China (People's Republic)

SESSION INFORMATION

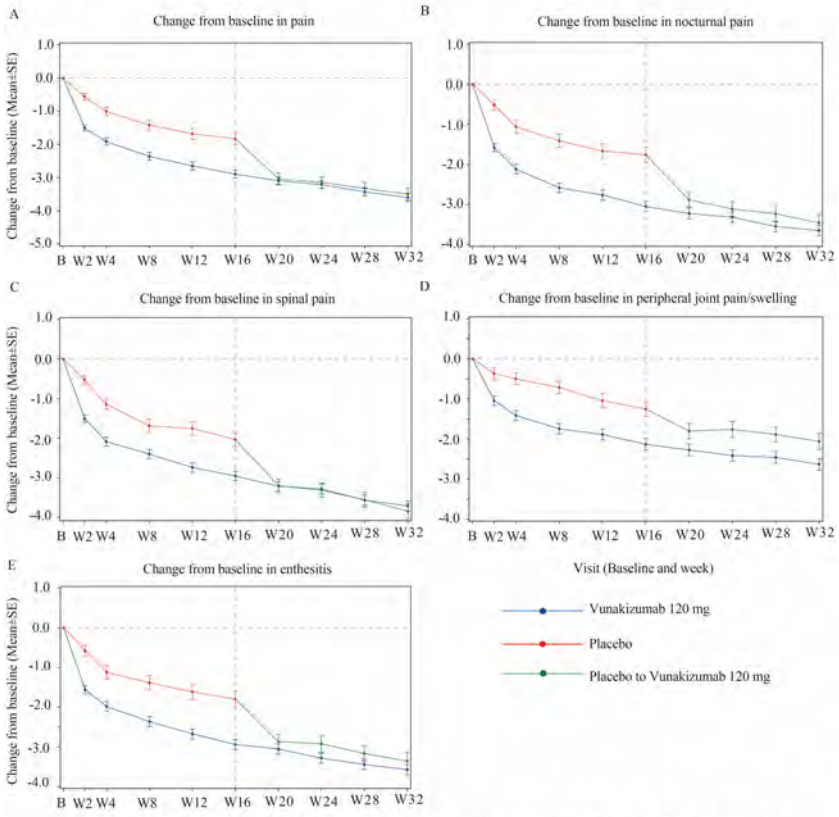
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease that primarily affects the spine and sacroiliac joints, resulting in significant pain, stiffness, and functional impairment. The interleukin-17 (IL-17) signaling pathway plays a central role in the pathogenesis of AS. Vunakizumab, a humanized monoclonal antibody targeting IL-17A, has demonstrated clinical efficacy in a randomized, double-blind, phase 2/3 trial. Since pain is the most common and serious symptom experienced by patients with AS, it is very important to develop and use effective treatment strategies to manage it. This post-hoc analysis aimed to evaluate the efficacy of vunakizumab in reducing pain outcomes in patients with active AS.

Methods: Eligible participants were adults with active AS, diagnosed according to the modified New York criteria (1984 revision), who had an inadequate response to, intolerance of, or contraindications to non-steroidal anti-inflammatory drugs (NSAIDs). All patients included in this study fulfilled the American College of Rheumatology (ACR) classification criteria. In phase 2, patients were randomized in a 2:2:1 ratio to receive either 120 mg or 240 mg of vunakizumab, or placebo. At week 16, patients initially receiving placebo were re-randomized 1:1 to one of the treatment groups. In phase 3, patients were randomized in a 2:1 ratio to receive 120 mg of vunakizumab or placebo. Study drug was administered at weeks 0, 2, 4, 8, and 12, followed by dosing every four weeks through week 32. Pain outcomes included total back pain, nocturnal back pain, and questions 2–4 from the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): spinal pain (pain in the back, neck, or hip), peripheral joint pain/swelling, and enthesitis (pain in areas tender to touch).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Pain Scores in the Placebo and Vunakizumab Groups from Baseline to Week 32.



(A) Total back pain; (B) Nocturnal back pain; (C) Spinal pain; (D) Peripheral joint pain/swelling; (E) Enthesitis.

Table 1. Comparison of Pain Scores Between Placebo and Vunakizumab Groups from Baseline to Week 16.

	Placebo Baseline (N=146)			Vunakizumab (N=294)				
	Baseline	Week 16	Change in Week 16 Relative to Baseline	Baseline	Week 16	Change in Week 16 Relative to Baseline	Nominal P value for Baseline vs Week 16[a]	Nominal P value for the Overall Period from 0 to 16 Weeks[b]
Total back pain VAS score, mean (standard deviation [SD])	6.20 (1.26)	4.39 (2.07)	-1.83 (2.06)	6.16 (1.24)	3.27 (1.95)	-2.89 (2.11)	<0.0001	<0.0001
Nocturnal pain VAS score, mean (SD)	5.77 (1.66)	4.04 (2.18)	-1.76 (2.20)	5.78 (1.61)	2.72 (1.94)	-3.06 (2.20)	<0.0001	<0.0001
Spinal pain, mean (SD)	6.51 (1.31)	4.48 (2.29)	-2.03 (2.09)	6.41 (1.24)	3.48 (2.00)	-2.95 (2.03)	<0.0001	<0.0001
Peripheral joint pain/swelling, mean (SD)	3.96 (2.44)	2.72 (2.26)	-1.25 (2.17)	4.22 (2.50)	2.12 (2.00)	-2.13 (2.38)	0.0001	<0.0001
Enthesitis, mean (SD)	5.77 (1.46)	3.95 (2.10)	-1.80 (2.32)	5.80 (1.43)	2.87 (1.95)	-2.94 (2.08)	<0.0001	<0.0001

[a]Change from baseline to week 16 between groups was compared using an independent-samples t-test (one-sided).

[b]P values for the overall period from 0 to 16 weeks were calculated using a mixed-effects model for repeated measures.

Results: This post-hoc analysis demonstrated significant reductions in all five pain outcome scores for patients receiving vunakizumab 120 mg compared to placebo over the 16-week period (all nominal $p < 0.0001$ by repeated measures mixed-effects model; Figure 1). Specifically, at week 16, the vunakizumab group showed a mean reduction in total back pain of -2.89 versus -1.83 in the placebo group (nominal $p < 0.0001$). Similar significant improvements were observed in nocturnal back pain (-3.06 vs. -1.76, nominal $p < 0.0001$), spinal pain (-2.95 vs. -2.03, nominal $p < 0.0001$), peripheral joint pain/swelling (-2.13 vs. -1.25, nominal $p = 0.0001$), and enthesitis (-2.94 vs. -1.80, nominal $p < 0.0001$) (Table 1).

From weeks 16 to 32, patients initially assigned to placebo who switched to vunakizumab 120 mg at week 16 experienced accelerated reductions in all five pain outcomes after the switch, although the magnitude of improvement remained slightly less than that observed in patients who received continuous vunakizumab throughout the study.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Vunakizumab provided statistically significant and clinically meaningful reductions in pain outcomes in patients with active AS. Importantly, patients who switched from placebo to vunakizumab at week 16 experienced rapid pain improvement, supporting vunakizumab as an effective treatment strategy for managing pain in AS.

Disclosure: J. Xu: None; **Y. Yang**: None; **S. Liu**: None; **R. Bai**: None; **S. Li**: None; **G. Zhang**: None; **X. Wang**: None; **X. Xu**: None; **M. Zheng**: None; **D. Feng**: None.

Abstract Number: 2354

ChatGPT or SPSS? A comparison between AI-based and Traditional Statistical Analysis of Longitudinal Inflammatory Marker Data in Spondyloarthritis

José Miguel Seque-Sabater[1], Pablo Beltrán Martin-Lorente[2], Sonia Pastor Navarro[3], Maria del Carmen Lopez Gonzalez[4], Maria Sanchez-Wonenburger[5], DESAMPARADOS CASADO POVEDA[3] and Anna Martínez Cristóbal[6], [1]La Ribera University Hospital, Rheumatology Department, Gandía, Spain, [2]Universidad Católica de Valencia "San Vicente Mártir", Valencia, Comunidad Valenciana, Spain, [3]La Ribera University Hospital, Rheumatology Department, Valencia, Comunidad Valenciana, Spain, [4]La Ribera University Hospital, Rheumatology Department, Cullera, Comunidad Valenciana, Spain, [5]Hospital Universitario de La Ribera, Valencia, Comunidad Valenciana, Spain, [6]La Ribera University Hospital, Rheumatology Department, Alzira, Comunidad Valenciana, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: While traditional analysis relies on statistical software such as SPSS, emerging tools like ChatGPT introduce the possibility of performing statistical tests, interpreting results, and generating figures via natural language prompts.

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are accessible inflammatory markers increasingly used in the monitoring of chronic diseases like Spondyloarthritis.

This study aims to compare traditional statistical analysis using SPSS (V.20.0) with AI-based analysis using ChatGPT (Model 4o) in longitudinal NLR and PLR data, evaluating their consistency, usability, and impact on research efficiency.

Methods: We performed a retrospective observational study of 85 Spondyloarthritis patients treated with Secukinumab from 2016 to 2023. NLR and PLR were recorded at baseline and every six months for four years. The Friedman test was applied to assess variation over time using both SPSS v25 and ChatGPT's 4o built-in Python environment (Advanced Data Analysis). Results, narrative outputs, and figures were compared

Results: Patients showed a mean age of 53.6 years; 66% had axial Spondyloarthritis and 34% Psoriatic Arthritis, with balanced sex distribution. Common comorbidities included smoking (41.2%), Hypertension (27.1%), Diabetes (21.2%), and Dyslipidaemia (28.2%).

Both platforms detected a decreasing trend in NLR and PLR over time. Neither test showed statistically significant differences across timepoints (NLR $p = 0.41$, PLR $p = 0.62$ in both SPSS and ChatGPT). Outputs were numerically identical, with ChatGPT also providing clinical context and suggestions for graphical representation. While SPSS required software setup and manual processing, ChatGPT offered a simplified, efficient alternative with real-time interpretation.

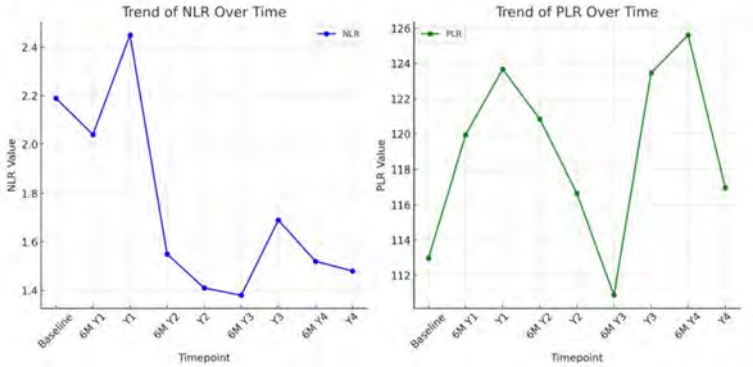
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Differences between ChatGPT and SPSS.

Table 1. Differences between SPPS and ChatGPT

Feature	SPSS	ChatGPT
Requires installation	Yes	No
Interface type	Graphical interface	Conversational interface
Type of analysis	Parametric and non-parametric tests	Prompt-guided and contextual analysis
Exact reproducibility	High	Variable (depends on prompt)
Assistance with interpretation	Limited	High (clinically contextualized)
Learning curve	Moderate	Low

Figures 1 and 2: Trend of NLR and PLR over time (created with ChatGPT)



Figures 1 and 2. Trend of NLR and PLR over time.

Table 2. Study of the variation in NLR and PLR Ratios and their related variables (with ChatGPT and SPSS).

Mean (±SD)	Basal	6M	Year 1	6M	Year 2	6M	Year 3	6M	Year 4	p*	p+
C Reactive Protein (mg/L)	7,50 (±8,68)	6,64 (±7,40)	7,53 (±8,42)	9,37 (±13,41)	8,41 (±8,43)	7,5 (±7,96)	20,25 (±51,16)	12,09 (±16,8)	7,82 (±7,40)	0,35	0,35
Erythrocyte Sedimentation Rate (ESR)	17,83 (±15,35)	16,47 (±11,35)	17,24 (±13,82)	17,92 (±13,91)	17,93 (±14,17)	17,85 (±13,81)	22,02 (±16,7)	21,66 (±15,43)	17,9 (±13,95)	0,52	0,52
Neutrophils (x10e9)	4,50 (±2,14)	4,32 (±1,76)	4,30 (±1,99)	4,31 (±1,65)	4,1 (±1,72)	4,08 (±1,42)	4,62(±2, 39)	4,27 (±2,24)	4,37(±1,67)	0,67	0,79
Lymphocytes (x10e9)	2,54 (±0,84)	2,29 (±0,81)	2,22 (±0,81)	2,37 (±0,87)	2,35 (±0,81)	2,39 (±0,81)	2,41 (±0,99)	2,44 (±0,92)	2,57 (±1,06)	0,87	0,89
Platelets (x10e9)	260,48 (±69,76)	251,51 (±65,4)	245,66(±6 9,55)	260,80 (65,78)	252,40(± 63,63)	240,63 (±66,64)	263,02 (±52,70)	275,62 (±77,30)	266,05 (±74,98)	0,58	0,55
Ratio NLR	2,19 (±3,23)	2,04 (±0,92)	2,45 (±2,37)	1,55 (±1,07)	1,41 (±1,06)	1,38 (±0,95)	1,69 (±1,41)	1,52 (±1,24)	1,48 (±0,81)	0,41	0,41
Ratio PLR	112,98 (±45,78)	119,95 (±50,46)	123,68 (±65,07)	120,85 (±50,77)	116,66 (±43,8)	110, 87 (±48,67)	123,47 (±54,85)	125,62 (±55,21)	116,97 (±47,47)	0,62	0,62

*Statistical significance according to Friedman's test with ChatGPT 4o (Python module) *Statistical significance according to Friedman's test with SPSS*

Conclusion: ChatGPT with integrated statistical capabilities provides a reliable, efficient alternative for exploratory data analysis in clinical research. Its results matched those from SPSS while offering added value in interpretability and ease of use. Although not a replacement for regulated statistical tools in all contexts, its potential to accelerate early-stage research and support non-specialists is notable.

Disclosure: J. Seque-Sabater: None; **P. Beltrán Martin-Lorente**: None; **S. Pastor Navarro**: None; **M. Lopez Gonzalez**: None; **M. Sanchez-Wonenburger**: None; **D. CASADO POVEDA**: None; **A. Martínez Cristóbal**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2355

Ixekizumab Provided Rapid Improvement in Key Patient Subgroups with Psoriatic Arthritis: Findings from a Prospective Observational Study in the United States of Patients Initiating Ixekizumab or Interleukin-23 Inhibitors

KURT OELKE[1], Sarah Ross[2], Emily Edson-Heredia[3], Jennifer Pustizzi[4], Ali Sheikhi Mehrabadi[5], Natalia Bello[5], Frederick Murphy[6], Shikha Singla[7], Siba Raychaudhuri[8], Philip J Mease[9] and Arthur Kavanaugh[10], [1]rheumatic disease center, Glendale, WI, [2]Lilly, Indianapolis, IN, [3]eli lilly, indianapolis, [4]Eli Lilly, Hammonton, NJ, [5]Eli Lilly, Indianapolis, IN, [6]Altoona Arthritis & Osteoporosis Center, Duncansville, PA, [7]Medical College of Wisconsin, Milwaukee, WI, [8]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [9]University of Washington, Seattle, WA, [10]University of California, San Diego, School of Medicine, San Diego, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Ixekizumab (IXE) is an FDA-approved monoclonal antibody that targets interleukin-17A.

Methods: Psoriatic Arthritis Real-World Study in the US (PARTUS) was a prospective, multicenter, non-interventional cohort study in patients with active Psoriatic Arthritis (PsA) beginning treatment with either IXE or an interleukin-23 inhibitor (IL-23i). The study assessed the effectiveness of Ixekizumab or Interleukin-23 in disease domains and subgroups. Clinical Disease Activity Index for PsA (cDAPSA) endpoints for key subgroups and outcomes in PsA disease domains were assessed at baseline (BL), week (W) 4, and W12. Change from baseline (CFB) in cDAPSA was assessed in the following subgroups: prior biologic failure (failure due to lack of efficacy and/or intolerance), duration of disease, sex, body mass index (BMI) (normal: BMI < 25 kg/m^2, patients with overweight BMI 25 to < 30 kg/m^2, patients with obesity: BMI ≥30 kg/m^2), patients with baseline presence of enthesitis, dactylitis, nail psoriasis, or Body Surface Area (BSA) of psoriasis skin involvement (BSA < 3%, BSA ≥ 3%) (Figure (Fig.) 1). To assess PsA domains, CFB in tender/swollen joint count (TJC)/ (SJC), Leeds enthesitis index, dactylitis count and nail psoriasis Visual Analogue Scale (VAS) score and proportion of patients achieving BSA < 3 were evaluated (Table 2). Descriptive statistics are presented for both IXE and IL-23i arms.

Results: BL characteristics of 121 patients from the IXE cohort and 116 patients from the IL-23i cohort (risankizumab) (n=67) and guselkumab (n=49)) are presented in Table 1.

The mean (SD) CFB in the cDAPSA score at W4 was -13.8 (15.9) and -9.3 (15.4), and at W12 was -17.3 (19.6) and -14.0 (19.3) in the IXE and IL-23i cohort respectively. At W4, 10.6% in the IXE cohort and 3.0% in the IL-23i cohort achieved remission of disease activity. These proportions increased for both cohorts by W12 (Table 2).

Improvements in disease activity, as measured by the mean (SD) CFB in cDAPSA are reported for the following subgroups in the IXE cohort: ≤2 Years duration of disease since diagnosis (W4:-12.1 (15.0), W12: -16.3 (16.4)), >2 Years duration of disease since diagnosis (W4:-14.4 (16.3), W12 -17.7 (20.8)), male patients (W4:-16.0 (16.2), W12:-19.1 (20.1)), female patients (W4:-11.8 (15.6), W12 -15.7 (19.2)), patients with prior failure to any biologic (W4:-16.8 (16.8), W12: -21.5 (19.9)), patients with no prior failure to any biologic (W4:-12.4 (15.4), W12:-15.4 (19.4)). The mean (SD) CFB in cDAPSA in the above subgroups in the IL-23i cohort is in Fig. 1.

The mean (SD) CFB in cDAPSA by PsA domains is in Fig. 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics at Baseline in patients with active PsA treated with IXE or IL-23i (GUS and RZB) Note: Data are mean (SD) unless otherwise stated. Abbreviations: BSA= body surface area; cDAPSA= clinical Disease Activity Index for Psoriatic arthritis; GUS=-guselkumab; IL-23i=interleukin-23p19 inhibitor; IXE=ixekizumab; LEI=Leeds enthesitis index; N=number of patients in each cohort; n=number of patients in the specified category; PsO=psoriasis; RZB=risankizumab; SD=standard deviation; VAS=visual analogue scale

Parameter	IXE (N=121)	IL-23i (N=116)
Age, years	54.4 (13.3)	53.0 (14.1)
Female, n (%)	63 (52.1)	75 (64.7)
BMI, kg/m^2	33.1 (6.8)	31.4 (7.3)
Years since PsA diagnosis	7.5 (8.8)	9.0 (10.5)
Tender joint count	16.1(13.1)	16.4 (15.4)
Swollen joint count	7.7(7.5)	7.1 (7.0)
Clinical version of the disease activity index (cDAPSA)	35.5(19.8)	34.6(21.4)
Presence of enthesitis (LEI>0), n (%)	72 (59.5)	84 (72.4)
Leeds enthesitis index (Among patients with LEI >0)	2.5(1.5)	3.0(1.6)
Presence of dactylitis (dactylitis count >0), n (%)	45 (37.2)	35 (30.2)
Nail PsO VAS	18.2 (20.4)	21.1(25.3)
Presence of PsO affecting BSA, %	7.1(13.4)	11.9(17.7)

Table 2. Efficacy results in patients with active PsA treated with IXE or IL-23i (GUS and RZB) Note: Data are mean (SD) unless otherwise stated. Abbreviations: BL=Baseline; BMI=Body mass index; BSA= body surface area; cDAPSA= clinical Disease Activity Index for Psoriatic arthritis; GUS=guselkumab; IL-23i=interleukin-23p19 inhibitor; IXE=ixekizumab; N=number of patients in each cohort; n=number of patients in the specified category; PsO=psoriasis; RZB=risankizumab; SD=standard deviation; VAS=visual analogue scale

Clinical outcomes	IXE (N=121)	IL-23i (N=116)
Disease activity by mean (SD) CFB in cDAPSA		
Week 4	-13.8 (15.9)	-9.3 (15.4)
Week 12	-17.3 (19.6)	-14.0 (19.3)
Remission of disease activity (cDAPSA ≤4), n (%)		
Week 4	11 (10.6)	3 (3.0)
Week 12	18 (18.8)	10 (10.8)
Low disease activity (cDAPSA ≤13, cDAPSA score >13 at BL), n (%)		
Week 4	29 (29.9)	16 (17.8)
Week 12	38 (43.7)	36 (43.4)
mean (SD) CFB in tender joint count (TJC)		
Week 4	-5.9 (10.6)	-4.8(11.7)
Week 12	-7.7 (12.2)	-7.1 (14.4)
mean (SD) CFB in swollen joint count (SJC)		
Week 4	-4.6 (6.8)	-2.6 (4.6)
Week 12	-5.7 (7.8)	-4.1 (5.2)
mean (SD) CFB in Leeds Enthesitis Index (LEI) (LEI > 0 at BL)		
Week 4	-1.0 (1.4)	-1.2 (1.6)
Week 12	-1.4 (1.7)	-1.8 (2.0)
mean (SD) CFB in dactylitis count (DC) (DC > 0 at BL)		
Week 4	-1.4 (2.2)	-1.0 (2.2)
Week 12	-1.4 (2.3)	-1.8 (2.3)
mean (SD) CFB in nail PsO VAS (nail PsO VAS score ≥ 1 at BL)		
Week 4	-8.0 (16.7)	-11.2 (15.4)
Week 12	-13.4 (16.6)	-10.8 (22.6)
Proportion of patients who achieved BSA <3% (BSA > 3 at BL), n (%)		
Week 4	24 (47.1)	17 (27.4)
Week 12	29 (67.4)	31 (57.4)

Conclusion: The results from the PARTUS study showed that patients with active PsA treated with IXE achieved rapid and meaningful improvements at W4 in disease activity across different subgroups of patients including BMI, sex, disease duration, prior biologic experience and PsA domains in real-world settings reaching the target of disease activity control as recommended in treatment guidelines. Further improvements were observed at W12. Trends in improvement were also

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

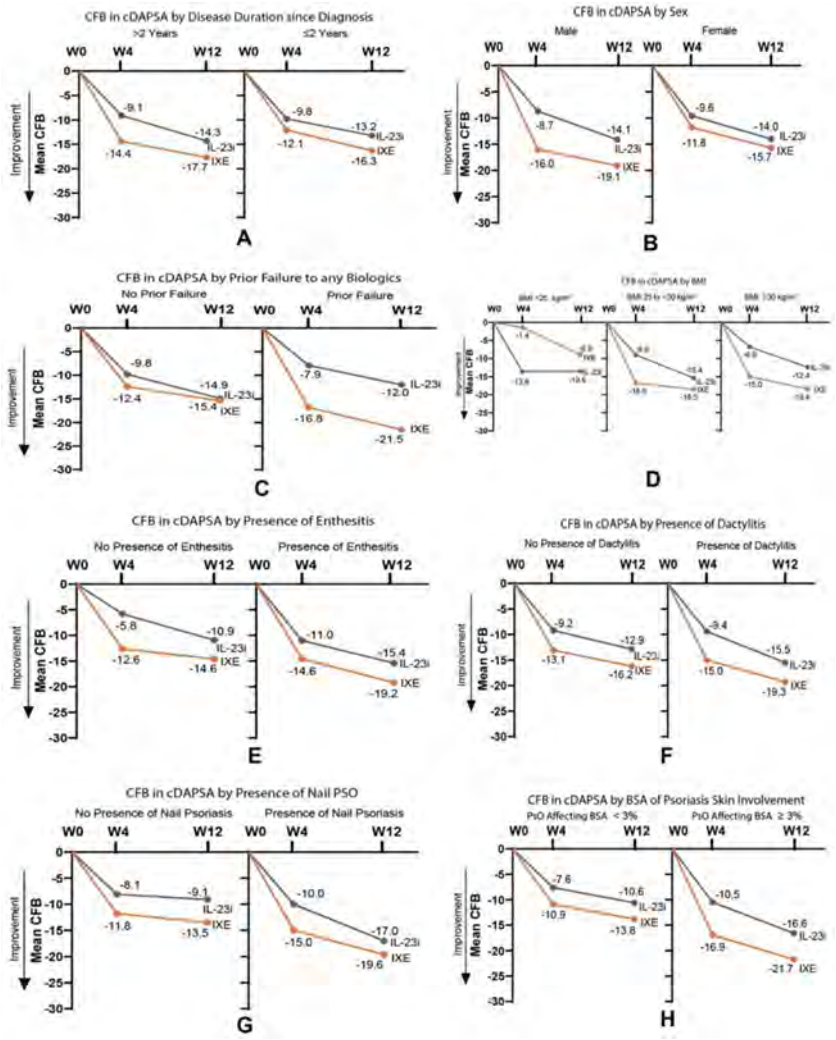


Figure 1. Clinical outcomes at W4 and W12 in patients with PsA treated with IXE or IL-23i (GUS and RZB): A. Change from baseline in cDAPSA by disease duration since diagnosis; B. Change from baseline by sex; C. Change from baseline by prior failure to any biologic; D. Change from baseline by BMI (Section 1: number of patients treated with IXE and BMI<25: 11, number of patients treated with IL-23i and BMI<25: 19); E. Change from baseline by presence of enthesitis; F. Change from baseline by presence of dactylitis; G. Change from baseline by presence of nail psoriasis: H. Change from baseline by presence of PsO affecting BSA Note: The study was not powered for comparative analysis, therefore only descriptive results are presented. Abbreviations: BMI=Body mass index; cDAPSA=clinical Disease Activity Index for PsA; CFB=change from baseline; GUS=-guselkumab; IL-23i=interleukin 23p19 inhibitor; IXE=ixekizumab; PsA=psoriatic arthritis: PsO=psoriasis.

observed in the patients treated with IL-23i, although to a less numerical extent. These data may guide rheumatologists treatment decisions for their diverse patient populations.

Disclosure: K. OELKE: AbbVie, 6, Amgen, 6, AstraZeneca, 6, Johnsson & Johnsson, 6, UCB, 6; **S. Ross**: Eli Lilly, 3, 11; **E. Edson-Heredia**: Eli Lilly, 3, 3, 11; **J. Pustizzi**: Eli Lilly, 3, 11; **A. Mehrabadi**: Eli Lilly, 3, 11; **N. Bello**: Eli Lilly, 3, 11, Eli Lilly and Company, 3; **F. Murphy**: None; **S. Singla**: AbbVie/Abbott, 2, Eli Lilly, 5, Janssen, 2, 6, Prometheus Biosciences, 5, UCB, 2; **S. Raychaudhuri**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **P. Mease**: AbbVie, 2, 5, Acelyrin, 2, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Century, 2, Cullinan Biotech, 3, Eli Lilly, 2, 5, 6, Genascence, 1, Inmagene, 2, Johnsson & Johnsson, 2, 5, 6, Moonlake, 2, 5, Novartis, 2, 5, Pfizer, 2, Takeda, 2, 5, UCB, 2, 5, 6; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2356

Clinical Efficacy in Male and Female Patients With Active Psoriatic Arthritis Treated With Deucravacitinib: A Pooled Analysis of Pivotal Phase 3 Studies

Lihi Eder[1], Philip J. Mease[2], Joseph F Merola[3], Alexis Ogdie[4], Atul Deodhar[5], Laura Coates[6], Stefan Varga[7], Navya Kalapala[7], Ying-Ming Jou[8], Eleni Vritzali[9] and Laure Gossec[10], [1]University of Toronto, Toronto, ON, Canada, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [4]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [5]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [6]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [7]Bristol Myers Squibb, Princeton, NJ, [8]Bristol Myers Squibb, Princeton, [9]Bristol Myers Squibb, Boudry, Switzerland, [10]Sorbonne Universite and Pitie-Salpetriere Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

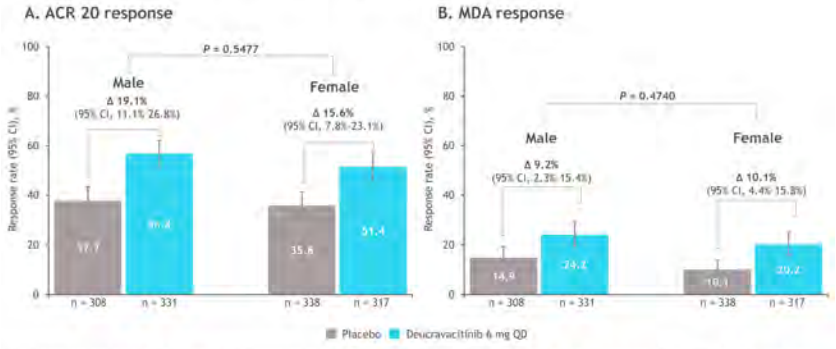
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: PsA affects male and female patients equally; however, variations in clinical manifestations and treatment responses between sexes have been reported. Deucravacitinib is an oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor under investigation for the treatment of PsA. This post hoc pooled analysis of 2 pivotal randomized, placebo (PBO)-controlled, phase 3 studies (POETYK PsA-1 [NCT04908202] and POETYK PsA-2 [NCT04908189]) evaluated the clinical efficacy of deucravacitinib vs PBO and patient-reported outcomes (PROs) by sex at W16 in patients with active PsA.

Methods: Patients in POETYK PsA-1 and PsA-2 were randomized to PBO or deucravacitinib 6 mg once daily (in PsA-2, a group included only as a safety reference arm received apremilast) through W16. The primary endpoint was ACR 20 at W16. Secondary endpoints included assessments of PsA disease activity, joints, skin, and quality of life vs PBO at W16. Binary data were analyzed using a logistic regression model that included treatment, sex, and treatment-sex interaction. Continuous data were analyzed using an ANCOVA model that included treatment, sex, baseline value, and treatment-sex

Figure 1. ACR 20 (A) and MDA (B) responses at W16 by sex



All randomized patients in PsA-1 and PsA-2 were included. Nonresponder imputation was used for the occurrence of the ICE of study treatment discontinuation prior to W16. After ICEs were handled, nonresponder imputation was used for missing data. The 95% CI was calculated using the Clopper-Pearson exact method. The *P* value corresponds to the treatment-sex interaction in the logistic regression model, including treatment, sex, and treatment-sex interaction.

ACR 20, American College of Rheumatology 20% improvement in response; ICE, intercurrent event; MDA, minimal disease activity; QD, once daily; W, week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Select clinical efficacy endpoints at W16 by sex

Endpoint at week 16	Male			Female			*P* value
	Placebo (n = 308)	Deucravacitinib 6 mg QD (n = 331)	% Δ (95% CI)	Placebo (n = 338)	Deucravacitinib 6 mg QD (n = 317)	% Δ (95% CI)	
Binary data, % (95% CI)							
PASI 75[a]	9.4 (5.6-14.7)	44.0 (36.5-51.7)	34.6 (25.5-43.1)	12.9 (7.9-19.7)	49.6 (41.1-58.2)	36.7 (26.0-46.6)	0.7628
DAPSA disease remission or LDA	28.2 (23.3-33.6)	39.6 (34.3-45.1)	11.3 (3.5-18.6)	21.3 (17.1-26.1)	37.9 (32.5-43.4)	16.6 (9.1-23.5)	0.2165
DAS28-CRP disease remission or LDA	28.9 (23.9-34.3)	42.9 (37.5-48.4)	14.0 (6.1-21.3)	21.0 (16.8-25.7)	39.1 (33.7-44.7)	18.1 (10.8-25.1)	0.2714
Enthesitis (SPARCC) resolution[b]	39.8 (32.8-47.1)	49.7 (42.4-57.1)	9.9 (-0.2-19.9)	32.9 (26.6-39.6)	44.6 (37.7-51.7)	11.7 (1.6-21.0)	0.7458
Dactylitis resolution[c]	38.8 (29.4-48.9)	53.2 (44.1-62.1)	14.3 (1.0-27.1)	50.6 (39.5-61.6)	64.3 (53.1-74.4)	13.7 (-1.4-28.4)	0.9669
Continuous data, mean CfB (95% CI)			Adj mean diff (SE) (95% CI)			Adj mean diff (SE) (95% CI)	
DAPSA	-13.1 (-14.8 to -11.4)	-18.7 (-20.3 to -17.0)	-5.59 (1.21) (-7.96 to -3.22)	-12.5 (-14.3 to -10.8)	-19.6 (-21.4 to -17.8)	-7.10 (1.27) (-9.60 to -4.60)	0.3708

All randomized patients in PsA-1 and PsA-2 were included. Study treatment discontinuation prior to W16 was considered an ICE. For binary variables, nonresponder imputation was used for handling ICEs. For continuous variables, the CfB value was set to 0 to imply no improvement or worsening relative to baseline. After ICEs were handled, nonresponder imputation was used for missing binary data, and a control-based pattern multiple imputation was used for missing continuous data. The logistic regression mode (for binary variables) included treatment, sex, and treatment-sex interaction. The ANCOVA model (for continuous variables) included baseline value, treatment, sex, and treatment-sex interaction. The *P* value corresponds to the treatment-sex interaction. PASI 75 was defined as a ≥ 75% improvement in PASI score vs baseline. DAPSA disease remission and LDA were defined as a score ≤ 4 and a score > 4 and ≤ 14, respectively. DAS28-CRP disease remission and LDA were defined as a score < 2.6 and score ≥ 2.6 and ≤ 3.2, respectively. Enthesitis (SPARCC) resolution was defined as a SPARCC score of 0 in patients with a SPARCC score ≥ 1 at baseline. Dactylitis resolution was defined as a tender dactylitis count of 0 in patients with a tender dactylitis count ≥ 1 at baseline.

[a]Assessed in patients with a BSA ≥ 3% and an sPGA score ≥ 2 at baseline (male patients: PBO, n = 180 and deucravacitinib, n = 175; female patients: PBO, n = 139 and deucravacitinib, n = 141). [b]Assessed in patients with a SPARCC score ≥ 1 at baseline (male patients: PBO, n = 191 and deucravacitinib, n = 189; female patients: PBO, n = 216 and deucravacitinib, n = 204). [c]Assessed in patients with a tender dactylitis count ≥ 1 at baseline (male patients: PBO, n = 103 and deucravacitinib, n = 126; female patients: PBO, n = 85 and deucravacitinib, n = 84).

adj, adjusted; ANCOVA, analysis of covariance; BSA, body surface area; CfB, change from baseline; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28-CRP, Disease Activity Score 28 with C-reactive protein; diff, difference; ICE, intercurrent event; LDA, low disease activity; PASI, Psoriatic Area and Severity Index; PASI 75, ≥ 75% improvement in the Psoriasis Area and Severity Index; PBO, placebo; QD, once daily; SPARCC, Spondyloarthritis Research Consortium of Canada; sPGA, static Physician Global Assessment; W, week.

Table 2. Select PROs at W16 by sex

Endpoint at week 16	Male			Female			*P* value
	Placebo (n = 308)	Deucravacitinib 6 mg QD (n = 331)	% Δ (95% CI)	Placebo (n = 338)	Deucravacitinib 6 mg QD (n = 317)	% Δ (95% CI)	
Binary data, % (95% CI)							
HAQ-DI clinically meaningful improvement, % (95% CI)[a]	43.8 (37.7-50.0)	54.1 (48.1-60.0)	10.3 (1.2-18.7)	38.4 (33.0-44.0)	46.5 (40.8-52.3)	8.1 (0.2-15.9)	0.7296
Continuous data, mean CfB (95% CI)			Adj mean diff (SE) (95% CI)			Adj mean diff (SE) (95% CI)	
HAQ-DI	-0.2 (-0.3 to -0.2)	-0.4 (-0.4 to -0.3)	-0.14 (0.04) (-0.21 to -0.07)	-0.2 (-0.3 to -0.2)	-0.4 (-0.4 to -0.3)	-0.14 (0.04) (-0.21 to -0.06)	0.8529
SF-36 PCS	4.1 (3.3, 4.8)	6.1 (5.4, 6.9)	2.04 (0.53) (1.01, 3.08)	4.1 (3.3, 4.8)	6.4 (5.6, 7.2)	2.35 (0.56) (1.25, 3.46)	0.8075
SF-36 MCS	-0.3 (-1.2-0.6)	1.0 (0.1-1.8)	1.26 (0.63) (0.03-2.49)	0.4 (-0.5-1.2)	2.3 (1.4-3.2)	1.93 (0.64) (0.68-3.19)	0.4094
FACIT-Fatigue	1.9 (1.1-2.7)	3.2 (2.4-4.0)	1.30 (0.58) (0.10-2.40)	2.1 (1.2-3.1)	4.4 (3.4-5.3)	2.20 (0.67) (0.90-3.50)	0.3087

All randomized patients in PsA-1 and PsA-2 were included. Study treatment discontinuation prior to W16 was considered an ICE. For binary variables, nonresponder imputation was used for handling ICEs. For continuous variables, the CfB value was set to 0 to imply no improvement or worsening relative to baseline. After ICEs were handled, nonresponder imputation was used for missing binary data, and a control-based pattern multiple imputation was used for missing continuous data. The logistic regression mode (for binary variables) included treatment, sex, and treatment-sex interaction. The ANCOVA model (for continuous variables) included baseline value, treatment, sex, and treatment-sex interaction. The *P* value corresponds to the treatment-sex interaction.

[a]Assessed in patients with an HAQ-DI score ≥ 0.35 at baseline. Clinically meaningful improvement in HAQ-DI was defined as ≥ 0.35 improvement from baseline HAQ-DI score.

adj, adjusted; ANCOVA, analysis of covariance; CfB, change from baseline; diff, difference; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy - Fatigue; HAQ-DI, Health Assessment Questionnaire Disability Index; ICE, intercurrent event; MCS, mental component summary; PCS, physical component summary; PRO, patient-reported outcome; QD, once daily; SF-36, 36-Item Short Form Questionnaire; W, week.

interaction. *P* values were provided for the treatment-sex interaction. A *P* value > 0.05 indicated that the treatment effect between deucravacitinib and PBO was similar for male and female patients.

Results: Across POETYK PsA-1 and PsA-2, 646 patients were randomized to PBO (male, n = 308; female, n = 338), and 648 were randomized to deucravacitinib (male, n = 331; female, n = 317). At W16, ACR 20 was achieved in more patients treated with deucravacitinib vs PBO, with no difference between male and female patients (male, 56.8% vs 37.7%; female, 51.4% vs 35.8%; *P* = 0.5477) (**Figure 1A**). Similar trends in both male and female patients were observed for ACR 50 and ACR 70 responses. MDA was also achieved in more patients treated with deucravacitinib vs PBO at W16 (male, 24.2% vs 14.9%; female, 20.2% vs 10.1%; *P* = 0.4740) (**Figure 1B**). Response rates in patients treated with deucravacitinib were higher at W16 vs PBO for secondary endpoints of PASI 75, DAPSA and DAS28-CRP disease remission or low disease activity, enthesitis (SPARCC) resolution, and dactylitis resolution as well as a greater change from baseline (CfB) in DAPSA score in both male and female patients (**Table 1**). For PROs, more patients treated with deucravacitinib vs PBO achieved a clinically meaningful improvement in HAQ-DI score and showed greater CfB in HAQ-DI, SF-36 PCS and MCS, and FACIT-Fatigue scores at W16 in both male and female patients (**Table 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Efficacy at W16 was similar for male and female patients who received deucravacitinib, and patients treated with deucravacitinib had superior efficacy vs PBO across multiple endpoints, including overall disease activity measures, musculoskeletal and dermatologic manifestations, and quality of life. Results of this post hoc pooled analysis were consistent with that of the overall POETYK PsA-2 population W16 results at a study level and those observed in the phase 2 study of deucravacitinib in active PsA in the overall population and by sex.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **S. Varga**: Bristol Myers Squibb, 3, 11; **N. Kalapala**: Bristol Myers Squibb, 3, 11; **Y. Jou**: Bristol Myers Squibb, 3, 11; **E. Vritzali**: Bristol Myers Squibb, 3, 11; **L. Gossec**: AbbVie, 2, 5, Amgen, 2, Biogen, 5, BMS, 2, Celltrion, 2, Eli Lilly, 2, 5, Janssen, 2, MSD, 2, Novartis, 2, 5, Pfizer, 2, UCB, 2, 5.

Abstract Number: 2357

Impact of Sonelokimab, a Novel IL-17A- and IL-17F-Inhibiting Nanobody, in Active Psoriatic Arthritis: Key Subgroup Analyses in the Randomized, Double-Blind, Placebo-Controlled Phase 2 ARGO Trial

Lihi Eder[1], Iain McInnes[2], Christopher Ritchlin[3], Alexis Ogdie[4], Arthur Kavanaugh[5], Laura Coates[6], Georg Schett[7], Alan Kivitz[8], Nuala Brennan[9], Alex Godwood[9], Matthew R. Thomas[9], Eva Cullen[9], Kristian Reich[10], Joseph F Merola[11] and Philip J. Mease[12], [1]University of Toronto, Toronto, ON, Canada, [2]University of Glasgow, Glasgow, United Kingdom, [3]University of Rochester Medical Center, Canandaigua, NY, [4]University of Pennsylvania, Philadelphia, PA, [5]University of California, San Diego, School of Medicine, San Diego, CA, [6]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [7]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [8]Altoona Center for Clinical Research, Duncansville, PA, [9]MoonLake Immunotherapeutics AG, Zug, Switzerland, [10]MoonLake Immunotherapeutics AG and Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, Zug, Switzerland, [11]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [12]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: PsA is a chronic inflammatory disease affecting heterogeneous tissues, with unmet need for therapies with robust efficacy across disease domains. Sonelokimab (SLK) is a novel Nanobody that binds to both IL-17A and IL-17F with similarly high affinity. The Phase 2 ARGO trial in active PsA met the primary endpoint of ACR50 at Week (W) 12 for

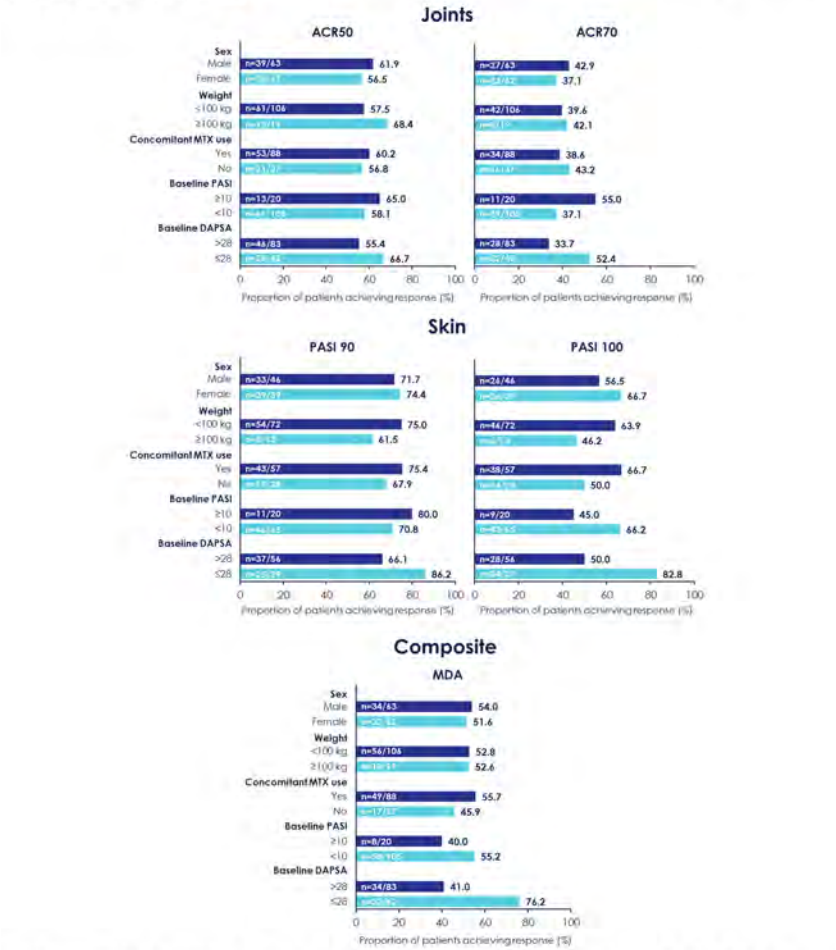
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Baseline characteristics in the SLK treatment arms of the ARGO trial

	SLK 60mg NI (n=41)	SLK 60mg WI (n=41)	SLK 120mg WI (n=43)
Sex, n (%)			
Male	20 (48.8)	21 (51.2)	22 (51.2)
Female	21 (51.2)	20 (48.8)	21 (48.8)
Weight [kg], n (%)			
<100 kg	35 (85.4)	36 (87.8)	35 (81.4)
≥100 kg	6 (14.6)	5 (12.2)	8 (18.6)
Concomitant MTX use, n (%)			
Yes	33 (80.5)	24 (58.5)	31 (72.1)
No	8 (19.5)	17 (41.5)	12 (27.9)
Baseline PASI, n (%)			
≥10	7 (17.1)	6 (14.6)	7 (16.3)
<10	34 (82.9)	35 (85.4)	36 (83.7)
Baseline DAPSA, n (%)			
>28	29 (70.7)	28 (68.3)	26 (60.5)
≤28	12 (29.3)	13 (31.7)	17 (39.5)

Where values do not add up to 100%, this is due to rounding.
DAPSA, Disease Activity in Psoriatic Arthritis; MTX, methotrexate; NI, no induction; PASI, Psoriasis Area and Severity Index; SLK, sonelokimab; WI, with induction.

Figure. Key outcomes at Week 24 with pooled sonelokimab doses according to clinical characteristics at baseline*



*Non-responder imputation, except for patients who switched treatment due to lack of joint response or who completed the study at Week 12 where the last observation during Part A was carried forward.
ACR, American College of Rheumatology; DAPSA, Disease Activity in Psoriatic Arthritis; MDA, minimal disease activity; MTX, methotrexate; PASI, Psoriasis Area Severity Index.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SLK 60mg with induction (WI) and SLK 120mg WI, with robust responses observed for high-hurdle endpoints including ACR70, PASI 100, and minimal disease activity (MDA) through W24 (McInnes *et al*, EULAR 2024). Patient characteristics, including sex, weight, concomitant methotrexate (MTX) use, and baseline disease activity levels may influence responses to bDMARDs (Eder *et al*, *Lancet Rheumatol*. 2023). Hence, we analyzed efficacy outcomes in ARGO according to key patient baseline characteristics.

Methods: ARGO (NCT05640245) was a global, randomized, prospective, double-blind Phase 2 trial of SLK in patients with active PsA that comprised a 12-week PBO-controlled phase followed by a further 12-week active-treatment phase. Three SLK doses were assessed: 60mg no induction (NI), SLK 60mg WI, or SLK 120mg WI (induction doses at W0, 2, 4, and 6). We report efficacy outcomes at W24 for patients assigned to the SLK arms throughout the study. *Post hoc* analyses were conducted to assess efficacy outcomes according to key baseline characteristics. For these analyses, data were pooled from all three SLK dose arms to maximize patient numbers.

Results: 207 patients were randomized; 49% female, 17% with weight ≥100 kg, 71% with concomitant MTX use, 17% with PASI ≥10, and 68% with DAPSA score >28 (**Table**). By W24, 58.1–61.0% of patients randomized to the SLK arms achieved the primary endpoint of ACR50, with robust achievement irrespective of sex, weight, concomitant MTX use, baseline PASI (≥10 vs. < 10), or DAPSA (>28 vs. ≤28) score (**Figure**). The higher threshold of ACR70 was achieved by 39.0–41.9% of patients randomized to the SLK arms, with robust ACR70 responses observed across key patient subgroups, including female patients, patients with weight ≥100 kg, no concomitant MTX use, baseline PASI ≥10, and baseline DAPSA score >28 (**Figure**). Overall, 68.8–80.8% of patients randomized to the SLK arms achieved PASI 90 at W24, and 59.4–63.0% of patients achieved PASI 100. High levels of PASI response were observed across different subgroups, including patients with moderate-to-severe psoriasis at baseline. Overall, 46.3–61.0% of patients randomized to the SLK arms achieved MDA, with robust achievement across key subgroups, as well as in ≥40% of patients with PASI ≥10 or DAPSA score >28 at baseline (**Figure**). Sonelokimab was well tolerated, with a safety profile consistent with IL-17 inhibition.

Conclusion: Robust efficacy with SLK was observed irrespective of key baseline clinical characteristics in ARGO, including for populations in which disparate outcomes of treatment have been reported, such as female patients. Ongoing Phase 3 studies (IZAR-1: NCT06641076; IZAR-2: NCT06641089) will further evaluate SLK 60mg and 120mg in active PsA.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **A. Kivitz**: AbbVie/Abbott, 2, 6, Amgen, 6, 11, Coval, 2, EcoR1, 2, Eli Lilly, 6, Fresenius Kabi, 1, 2, Genzyme, 12, Scientific expert fees, Gilead, 2, 11, GlaxoSmithKlein(GSK), 2, 6, 11, Grünenthal, 2, Halia, 2, Horizon, 1, 2, Innovaderm, 2, Janssen, 1, 2, Novartis, 1, 11, Pacira, 2, Pfizer, 6, 11, Prime, 6, Princeton Biopartners, 1, Prometheus, 2, Sanofi-Regeneron, 6, Santa Ana Bio Inc, 2, Selecta, 2, SynAct, 2, Takeda, 2, UCB, 1, 2, 6, XBiotech, 2; **N. Brennan**: MoonLake Immunotherapeutics AG, 3, 11; **A. Godwood**: MoonLake Immunotherapeutics,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3, 11; **M. Thomas**: MoonLake Immunotherapeutics AG, 3, 11; **E. Cullen**: MoonLake Immunotherapeutics AG, 3, 11; **K. Reich**: AbbVie, 1, 6, 12, Participated in clinical trials, Almirall, 1, 6, 12, Participated in clinical trials, Amgen, 1, 6, 12, Participated in clinical trials, Boehringer Ingelheim, 1, 6, 12, Participated in clinical trials, Bristol-Myers Squibb(BMS), 1, 6, 12, Participated in clinical trials, Eli Lilly, 1, 6, 12, Participated in clinical trials, Galderma, 1, 6, 12, Participated in clinical trials, Janssen-Cilag, 1, 6, 12, Participated in clinical trials, Kyowa Kirin, 1, 6, 12, Participated in clinical trials, LEO Pharma, 1, 6, 12, Participated in clinical trials, Medac, 1, 6, 12, participated in clinical trials, MoonLake Immunotherapeutics AG, 3, 11, Novartis, 1, 6, 12, participated in clinical trials, Ocean Pharma, 1, 6, 12, participated in clinical trials, Pfizer, 1, 6, 12, participated in clinical trials, Sanofi, 1, 6, 12, participated in clinical trials, UCB, 1, 6, 12, participated in clinical trials; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6.

Abstract Number: 2358

Bimekizumab Demonstrated Early and Sustained Efficacy Regardless of Baseline Characteristics in Patients with Active Psoriatic Arthritis: Pooled Post Hoc Results up to 1-Year from Two Phase 3 Studies

Lihi Eder[1], Philip J. Mease[2], Iain McInnes[3], M. Elaine Husni[4], Mitsumasa Kishimoto[5], Barbara Ink[6], Rajan Bajracharya[6], Jason Coarse[7] and Fabian Proft[8], [1]University of Toronto, Toronto, ON, Canada, [2]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [3]University of Glasgow, Glasgow, United Kingdom, [4]Department of Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH, [5]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, [6]UCB, Slough, England, United Kingdom, [7]UCB, Morrisville, NC, [8]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated clinical efficacy and safety to 3 years (yrs) in patients (pts) with PsA.[1,2] Given PsA is a chronic inflammatory condition with a heterogenous clinical presentation,[3] it is critical to understand how varying baseline (BL) demographics, disease characteristics, and comorbidities influence treatment efficacy. Here, we assess the impact of BL characteristics on the efficacy of BKZ in pts with PsA at Week (Wk) 16 vs placebo (PBO), and longer-term to 1 yr.

Methods: Pooled post hoc analysis of data from BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve) and BE COMPLETE (NCT03896581; TNF inhibitor inadequate response/intolerance [TNFi-IR]). Both studies assessed subcutaneous BKZ 160 mg every 4 wks in pts with PsA and were PBO-controlled to Wk 16, then PBO pts switched to BKZ (PBO/BKZ). BE COMPLETE Wk 16 completers could enter BE VITAL (NCT04009499; open-label extension), in which all pts received BKZ.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Baseline demographics and disease characteristics in patients

Mean (SD) unless otherwise specified	Pooled BE OPTIMAL and BE COMPLETE[a] (bDMARD-naive and TNFi-IR) PBO n=414	BKZ 160 mg Q4W n=698
Age, years	49.5 (12.2)	49.1 (12.5)
<45, n (%)	153 (37.0)	251 (36.0)
≥45, n (%)	261 (63.0)	447 (64.0)
Sex, n (%)		
Male	187 (45.2)	331 (47.4)
Female	227 (54.8)	367 (52.6)
BMI, kg/m^2	29.4 (5.9)	29.6 (6.7)
<25, n (%)	102 (24.6)	172 (24.6)
25–<30, n (%)	138 (33.3)	232 (33.2)
≥30, n (%)	174 (42.0)	294 (42.1)
Weight, kg	84.5 (18.5)	85.8 (20.2)
<100, n (%)	330 (79.7)	556 (79.7)
≥100, n (%)	84 (20.3)	142 (20.3)
Time since PsA diagnosis, [b] years	6.8 (7.3)	7.4 (8.6)
<2, n (%)	123 (29.7)	198 (28.4)
≥2, n (%)	288 (69.6)	491 (70.3)
Prior TNFi exposure, n (%)		
Inadequate response to 1 TNFi	103 (24.9)	203 (29.1)
Inadequate response to 2 TNFi	15 (3.6)	30 (4.3)
Intolerance to TNFi	15 (3.6)	34 (4.9)
hs-CRP mg/L, median (Q1, Q3)	4.6 (1.7, 11.8)	4.1 (1.5, 12.3)
<6, n (%)	234 (56.5)	422 (60.5)
≥6, n (%)	180 (43.5)	276 (39.5)
SJC (of 66 joints)	9.7 (7.6)	9.2 (6.7)
TJC (of 68 joints)	17.8 (13.1)	17.4 (12.5)

Randomized set from BE OPTIMAL and BE COMPLETE (including data from BE VITAL). [a] Data were pooled for all PBO/BKZ and BKZ-randomized patients who were bDMARD-naive or TNFi-IR; [b] PBO n=411; BKZ n=689.

bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BMI: body mass index; hs-CRP: high sensitivity C-reactive protein; PBO: placebo; PsA: psoriatic arthritis; Q4W: every 4 weeks; SD: standard deviation; SJC: swollen joint count; TJC: tender joint count; TNFi: tumor necrosis factor inhibitors; TNFi-IR: prior inadequate response or intolerance to TNFi.

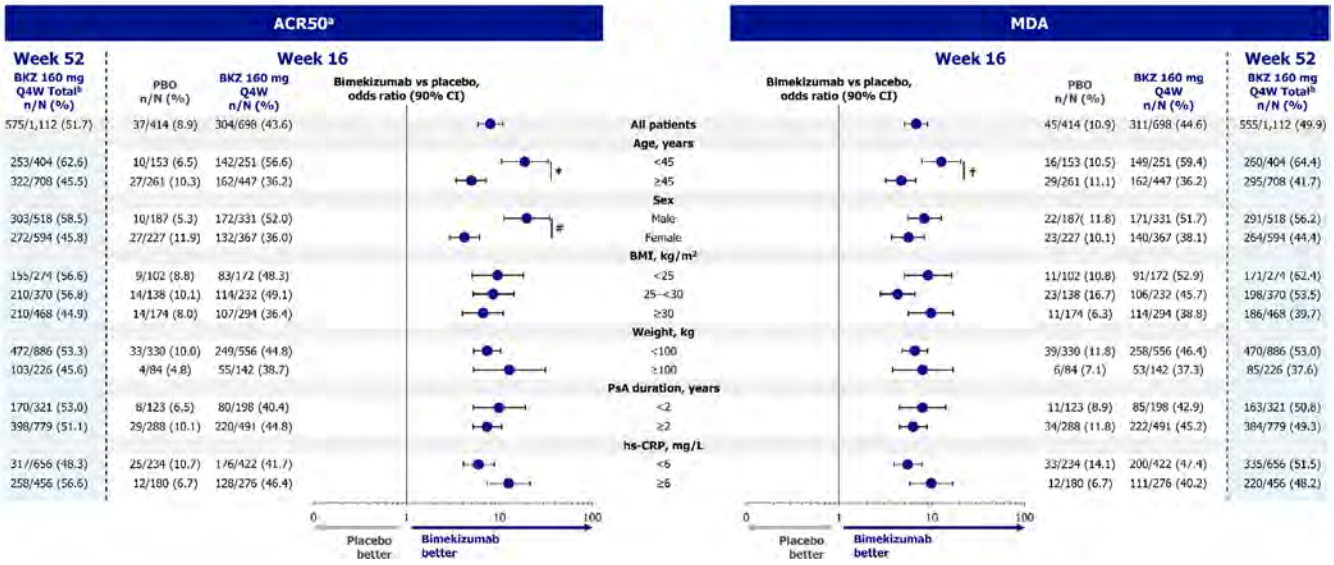
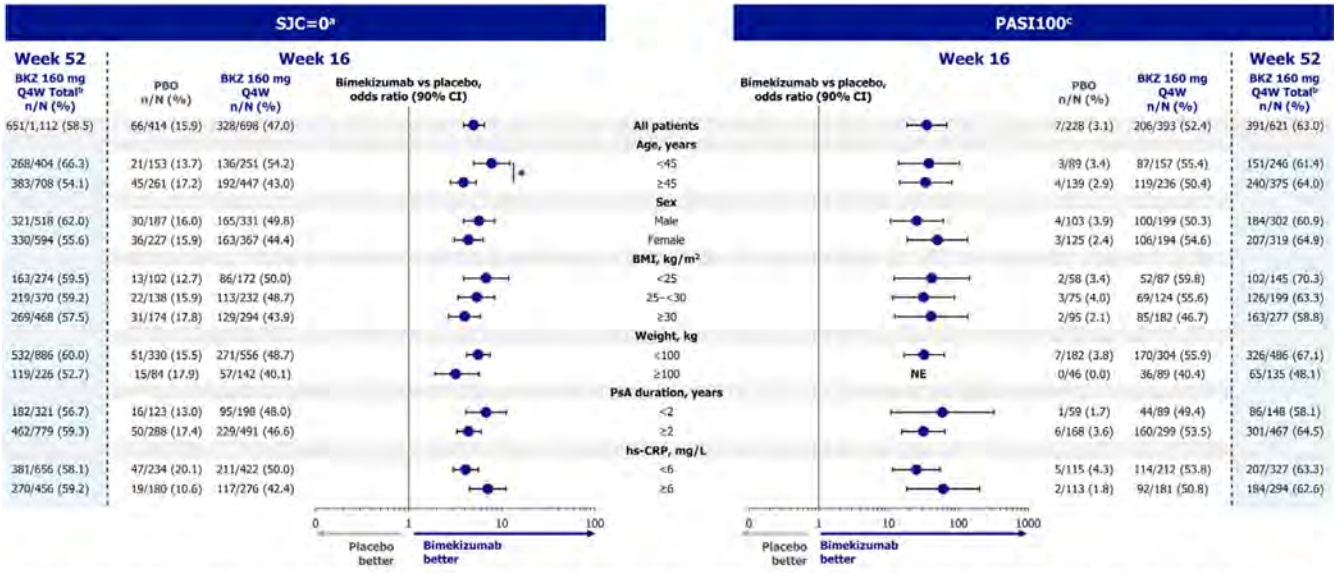


Figure 1. ACR50 and MDA response rates at Week 16 and Week 52 by baseline demographics and disease characteristics (NRI)

Efficacy outcomes are reported by BL pt characteristic subgroups. Efficacy outcomes included ≥50% improvement from BL in ACR response criteria (ACR50), the composite outcome minimal disease activity (MDA), complete resolution of swollen joint count (SJC=0), and 100% improvement from BL in Psoriasis Area and Severity Index (PASI100; in pts with BL psoriasis ≥3% body surface area). Data are reported by randomization group at Wk 16; for the BKZ Total group (PBO/BKZ and BKZ-randomized) at Wk 52. The association of BKZ-treated vs PBO pts achieving Wk 16 response overall and for each subgroup was estimated via odds ratios using logistic regression with factors for treatment, study, region, subgroup, and treatment by subgroup interaction (subgroup and interaction excluded in the overall). All p values are nominal and generated for the treatment by subgroup interaction term; missing data imputed using non-responder imputation.

Results: Of the 1,112 pts randomized to PBO (n=414) or BKZ (n=698), 1,073 (96.5%) completed Wk 16 and 1,002 (90.1%) completed Wk 52. Overall BL demographics and disease characteristics were generally similar across the treatment groups (**Table**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Randomized set from BE OPTIMAL and BE COMPLETE (including data from BE VITAL). At Week 16, data were pooled for all PBO-randomized patients or all BKZ-randomized patients who were bDMARD-naive or TNFi-IR. At Week 52, data were pooled for patients in the BKZ Total group who were bDMARD-naive or TNFi-IR. *Indicates significance of treatment by subgroup interaction, p=0.035. P values are generated for the treatment by subgroup interaction term from the logistic regression model. A significant p value for the interaction term suggests that the effect of treatment on the outcome differs across the subgroups. [a] SJC=0 is assessed in 66 joints; [b] BKZ Total group includes BKZ-randomized patients and PBO patients that switched to BKZ at Week 16; [c] In patients with psoriasis affecting ≥3% BSA at baseline; PBO n=228, BKZ n=393, BKZ Total n=621.

bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BSA: body surface area; BMI: body mass index; CI: confidence interval; hs-CRP: high sensitivity C-reactive protein; NE: not evaluable; NRI: non-responder imputation; OR: odds ratio; PASI100: 100% improvement from baseline in Psoriasis Area and Severity Index; PBO: placebo; PsA: psoriatic arthritis; Q4W: every four weeks; SJC: swollen joint count; TNFi-IR: prior inadequate response or intolerance to tumor necrosis factor inhibitors.

Figure 2. SJC=0 and PASI100 response rates at Week 16 and Week 52 by baseline demographics and disease characteristics (NRI)

Achievement of ACR50, MDA, SJC=0, and PASI100 responses were greater with BKZ vs PBO within all pt subgroups at Wk 16, with consistent efficacy responses with BKZ treatment for most pt subgroups. Younger pts (< 45 yrs) treated with BKZ were significantly more likely than older pts (≥45 yrs) to achieve ACR50 (p=0.001), MDA (p=0.006), and SJC=0 (p=0.035) at WK 16. Males were significantly more likely than females to attain ACR50 (p< 0.001). Improved efficacy responses with BKZ treatment were sustained or increased from Wk 16 to Wk 52 across all subgroups (**Figure 1–2**).

Conclusion: BKZ demonstrated durable and greater improvements in clinical joint, skin, and composite outcomes measures vs PBO at Wk 16, which were sustained to 1 yr, regardless of pt demographics and clinical presentation at BL.

References: 1. Gossec L. Ann Rheum Dis 2025:*In press*; **2**. McInnes IB. Ann Rheum Dis 2025:*In press*; **3**. McInnes IB. RMD Open 2024;10:e004494.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **I. McInnes**: AbbVie, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Cabaletta, 2, 6, Causeway Therapeutics, 2, 6, Celgene, 2, 5, Eli Lilly and Company, 2, 6, Evelo, 2, Gilead, 5, 6, Janssen, 2, 5, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 5, 6, Pfizer, 5, 6, Sanofi/Regeneron, 5, 6, UCB, 2, 5, 6; **M. Husni**: AbbVie, 1, 2, Amgen, 1, 2, BMS, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **M. Kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Ayumi Pharma, 2, 6, BMS, 2, 6, Chugai, 2, 6, Daiichi Sankyo, 6, Eisai, 6, Gilead, 2, 6, Janssen, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Takeda, 2, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **B. Ink**: AbbVie, 11, GSK, 11, UCB, 3, 11; **R. Bajracharya**: UCB, 3, 11; **J. Coarse**: UCB, 3, 11; **F. Proft**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celgene, 2, 6, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Hexal, 2, 6, Janssen, 2, 6, Medscape, 2, 6, MoonLake Pharma, 2, 6, MSD, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 6, UCB, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2359

Combination Of TNF Inhibitors And NSAIDs Versus TNF Inhibitors Alone On The Progression Of Structural Damage In The Spine And Hip: a Retrospective Study In 262 Patients With Radiographic Axial Spondyloarthritis

MARIA KONSTA[1], Michael Nurmohamed[2], Alexios Iliopoulos[3], Petros Sfikakis[4], Ingrid Visman[5], Grigorios Sakellariou[6] and Irene E. van der Horst-Bruinsma[7], [1]Sismanoglion Hospital, Athens, Greece, Marousi, Attiki, Greece, [2]Amsterdam Rheumatology and Immunology Center, Reade; Department of Rheumatology and Amsterdam Rheumatology Center, Amsterdam University Medical Centers, Amsterdam, Netherlands, [3]417 Army Share Fund Hospital (NIMTS), Department of Rheumatology, Athens, Greece, ZOGRAFOU, Greece, [4]NKUA - SCHOOL OF MEDICINE, Athens, Greece, [5]Reade Amsterdam, Amsterdam, Noord-Holland, Netherlands, [6]424 General Military Hospital, Thessaloniki, Greece, [7]Department of Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The inhibitory effect of TNF inhibitor (TNFi) treatment on spinal radiographic progression in patients with radiographic Axial Spondyloarthritis (r-axSpA), remains controversial. However, current evidence suggests that TNFi treatment seems to stabilize the structural damage of hip arthritis in these patients[1]. The aim of this studyis to investigate whether the addition of an NSAIDS to TNFi therapy in patients with r-axSpA, might have a better inhibitory effect on radiographic progression in the spine and hip, compared to TNFi therapy alone.

Methods: 262 patients with r-axSpA [189 men; age: 44±12years, disease duration: 7.3 years (IQR:2;15)] were included. Radiographs of spine and pelvis, obtained at baseline (i.e., before TNFi initiation), compared retrospectively to those obtained after 2.5±0.7 and 7±2.3 years of TNFi combined, or not with NSAIDs. Spinal X-rays were scored by mSASSS. Both hips were scored by BASRI-hip score and mean joint space width (MJSW)[1]. The spinal radiographic progression was assessed as the formation of new syndesmophytes (at corners with at least 1 at baseline) or ΔmSASSS-score/year ≥1 unit/year. Hip involvement was assessed radiographically as mean baseline BASRI-hip score ≥2. The significance of changes was tested by mixed linear models for longitudinal data.

Results: Combination therapy with TNFi and NSAIDs received 100/262 (38%) patients. Indeed, more females (52/73, 71%) than males (110/189, 58%), (p=0.052) were under concomitant NSAIDs. New syndesmophytes occurred in 58% of patients in TNFi monotherapy vs. 36% of those in concomitant NSAIDs (p=0.001). Moreover, the

ΔmSASSS-score/year was significantly higher in patients receiving only TNFi [0.7 (IQR:0.1;1.50], compared to those under combination therapy [0.1 (IQR:0;0.7], (p=0.0009).The mSASSS increased significantly both after 2.5±0.7 and 7±2.3 years of TNFi treatment. Nevertheless, the concomitant NSAIDs intake correlated negatively with the mSASSS (table 1). In patients with hip involvement at baseline, BASRI-hip score and MJSW did not change significantly during follow up (table 2). In those without baseline hip involvement, the BASRI-hip score remained unchanged after 2.5±0.7 years, but increased significantly compared to the baseline score after 7±2.3 years. The latter increase could be attributed to aging (b=0.007, CI:0.0006;0.01). In contrast, the MJSW did not change significantly during follow up (table 3). The NSAIDs co-administration had no effect on the evolution of both MJSW and BASRI-hip scores, irrespective of the baseline structural damage level (table 2 and 3).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Parameter	Coefficient (b)	95% CI	P value
year 2.5±0.7 vs baseline	2.3	1.67; 2.9	**<0.00001**
year 7±2.3 vs baseline	4	3.3; 4.6	**<0.00001**
Concomitant NSAIDs intake	-4	-7.9; -0.3	**0.035**
Baseline presence of syndesmophytes	24.4	20.5; 28.3	**<0.00001**
Age	0.36	0.2; 0.5	**<0.00001**
Sex (male)	2.9	-1.1;6.9	NS
Baseline CRP >5 mg/L	3.6	-0.1;7.4	NS

Longitudinal linear mixed-¬effect model to evaluate the time course of mSASSS

Hip involvement, n=95						
	BASRI-hip score			Mean Joint Space width		
Parameter	Coefficient (b)	95% CI	P-value	Coefficient (b)	95% CI	P-value
year 2.5±0.7 vs. baseline	0.01	-0.05; 0.07	NS	-0.04	-0.1; 0.05	NS
year 7±2.3 vs baseline	0.05	-0.01; 0.1	NS	-0.009	-0.09; 0.08	NS
Concomitant NSAIDs intake	-0.07	-0.3; 0.1	NS	0.08	-0.2; 0.4	NS
Age	0.005	-0.003; 0.01	NS	-0.001	-0.01; 0.009	NS
Sex (male)	0.1	-0.1; 0 .36	NS	0.14	-0.2; 0.4	NS

Longitudinal linear mixed-¬effect model to evaluate the time course of BASRI-hip score and Mean Joint Space width in patients with baseline hip involvement

Conclusion: Concomitant NSAIDs intake seems to have an inhibitory effect only on spinal radiographic progression but not

Without hip involvement, n=167						
	BASRI-hip score			Mean Joint Space width		
Parameter	Coefficient (b)	95% CI	P-value	Coefficient (b)	95% CI	P-value
year 2.5±0.7 vs. baseline	0.02	-0.03;0.065	NS	-0.04	-0.09; 0.01	NS
year 7±2.3 vs baseline	0.08	0.03; 0.1	**0.002**	-0.05	-0.1; 0.001	NS
Concomitant NSAIDs intake	0.045	-0.1;0.2	NS	-0.08	-0.3; 0.1	NS
Age	0.007	0.0006;0.01	**0.03**	0.008	0.00009;0.02	**0.048**
Sex (male)	0.3	0.1; 0.4	**0.001**	0.08	-0.1; 0.3	NS

Longitudinal linear mixed-¬effect model to evaluate the time course of BASRI-hip score and Mean Joint Space width in patients without baseline hip involvement

on hip structural damage, compared to TNFi monotherapy in patients with r-axSpA. These different therapeutic outcomes could be attributed to the spinal osteoproliferative and peripheral osteodestructive changes, that occur in parallel in r-axSpA.

References

1) Konsta M, Nurmohamed MT, Iliopoulos A et al. Prevalence and Radiographic Progression of Hip Involvement in Patients With Ankylosing Spondylitis Treated With Tumor Necrosis Factor Inhibitors. J Rheumatol. 2023;50:342-350

Disclosure: M. KONSTA: None; **M. Nurmohamed**: None; **A. Iliopoulos**: None; **P. Sfikakis**: None; **I. Visman**: None; **G. Sakellariou**: None; **I. van der Horst-Bruinsma**: AbbVie, 2, 5, 12, Fees received for lectures, BMS, 12, Fees received for lectures, Eli Lilly, 2, MSD, 2, 5, 12, Fees received for lectures, Novartis, 2, Pfizer, 5, 12, Fees received for lectures, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2360

Treatment adherence in ankylosing spondylitis: A comparison of TNFi, IL-17i, and JAKi using real-world data

Marina Magrey[1] and Jennifer Murphy[2], [1]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH, [2]University Hospitals, Cleveland Medical Center, cleveland, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Treatment adherence is essential for achieving sustained disease control and improving outcomes in patients with ankylosing spondylitis (AS). This study aimed to evaluate real-world drug survival and treatment adherence among patients with AS treated with tumor necrosis factor inhibitors (TNFi), interleukin-17 inhibitors (IL-17i), or Janus kinase inhibitors (JAKi).

Methods: We conducted a retrospective cohort study using a de-identified, federated electronic health record database (TriNetX Research Network, Cambridge, MA; Date of access: May 28, 2024), which includes data from 89 healthcare organizations and over 125 million patients.

Table 1. Baseline characteristics between therapeutic class cohorts, before and after propensity score matching for demographics and comorbidities. Separate propensity score models were conducted to compare TNFi vs. IL-17i and TNFi vs. JAKi.

	Before Matching			After Matching			
	Ref. Group	Comparison 1	Comparison 2	Comparison 1		Comparison 2	
	TNFi N = 12,180[1]	IL-17i N = 1,211[1]	JAKi N = 327[1]	TNFi N = 1,120[1]	IL-17i N = 1,120[1]	TNFi N = 326[1]	JAKi N = 326[1]
Age at index	44.2 ± 14.5	46.6 ± 13.5*	52.9 ± 13.9*	46.4 ± 13.8	46.6 ± 13.5	53.7 ± 14.1	52.8 ± 13.9
Sex							
Male	6,177 (50.7)	491 (43.8)*	77 (23.5)*	477 (42.6)	491 (43.8)	77 (23.6)	77 (23.6)
Female	5,507 (45.2)	576 (51.4)*	235 (71.9)*	601 (53.7)	575 (51.3)	232 (71.2)	234 (71.8)
Race							
Black or African American	757 (6.2)	47 (4.2)*	25 (7.6)	43 (3.8)	47 (4.2)	31 (9.5)	25 (7.7)
White	8,446 (69.3)	756 (67.4)	244 (74.6)*	777 (69.4)	756 (67.5)	241 (73.9)	243 (74.5)
Other Race	1,109 (9.1)	138 (12.3)*	25 (7.6)	134 (12.0)	137 (12.2)	20 (6.1)	25 (7.7)
Unknown race	1,868 (15.3)	180 (16.1)	33 (10.1)*	166 (14.8)	180 (16.1)	34 (10.4)	33 (10.1)
Ethnicity							
Hispanic or Latino	685 (5.6)	57 (5.1)	30 (9.2)*	62 (5.5)	56 (5.0)	16 (4.9)	30 (9.2)*
Non-Hispanic	8,953 (73.5)	778 (69.4)*	238 (72.6)	812 (72.5)	778 (69.5)	245 (75.2)	237 (72.7)
Unknown ethnicity	2,542 (20.9)	286 (25.5)*	59 (18.0)	246 (22.0)	286 (25.5)	65 (19.9)	59 (18.1)
CRP (mg/L)	14.6 ± 27.8	13.8 ± 25.1	16.2 ± 30.2	14.2 ± 25.0	13.8 ± 25.1	15.3 ± 22.3	16.2 ± 30.2
Comorbidities							
Diabetes	917 (7.5)	106 (9.5)*	42 (12.9)*	100 (8.9)	105 (9.4)	41 (12.6)	41 (12.6)
Smoking	750 (6.2)	59 (5.3)*	30 (9.2)*	51 (4.6)	59 (5.3)	24 (7.4)	29 (8.9)
Obesity	1,089 (8.9)	140 (12.5)*	59 (18.0)*	141 (12.6)	139 (12.4)	51 (15.6)	58 (17.8)
CKD	368 (3.0)	33 (2.9)	22 (6.7)*	44 (3.9)	33 (2.9)	14 (4.3)	22 (6.7)
Depression	1,479 (12.1)	160 (14.3)*	73 (22.3)*	160 (14.3)	159 (14.2)	67 (20.6)	72 (22.1)
Crohn's Disease	582 (4.8)	11 (1.0)*	20 (6.1)	12 (1.1)	11 (1.0)	20 (6.1)	19 (5.8)
Ulcerative colitis	396 (3.3)	10 (0.9)*	20 (6.1)*	10 (0.9)	10 (0.9)	16 (4.9)	19 (5.8)
Psoriasis	767 (6.3)	143 (12.8)*	43 (13.1)*	138 (12.3)	142 (12.7)	30 (9.2)	42 (12.9)
Outcome Non-Adherence	267 (2.2)	80 (7.1)*	30 (9.2)*	29 (2.6)	79 (7.1)*	10 (3.1)	30 (9.2)*

[1]Mean ± SD; n (%)
*P < 0.05 based on Welch Two Sample t-test or Pearson's Chi-squared test between TNFi vs IL-17i and TNFi vs. JAKi

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Odds ratios (95% Confidence interval) and Hazard Ratios (95% Confidence interval) of medication non-adherence as a function of initial therapeutic class, before and after propensity score matching for demographics and clinical characteristics.

	Before Matching			After Matching		
	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
TNFi vs.	—	—		—	—	
IL-17i	3.43	2.64, 4.42	**<0.001**	2.85	1.87, 4.47	**<0.001**
JAKi	4.51	2.98, 6.58	**<0.001**	3.20	1.59, 7.00	**0.002**
	Hazard Ratio	**95% CI**	**p-value**	**Hazard Ratio**	**95% CI**	**p-value**
TNFi vs.	—	—		—	—	
IL-17i	3.34	2.60, 4.29	**<0.001**	2.76	1.80, 4.22	**<0.001**
JAKi	4.42	3.03, 6.45	**<0.001**	3.15	1.54, 6.44	**0.002**

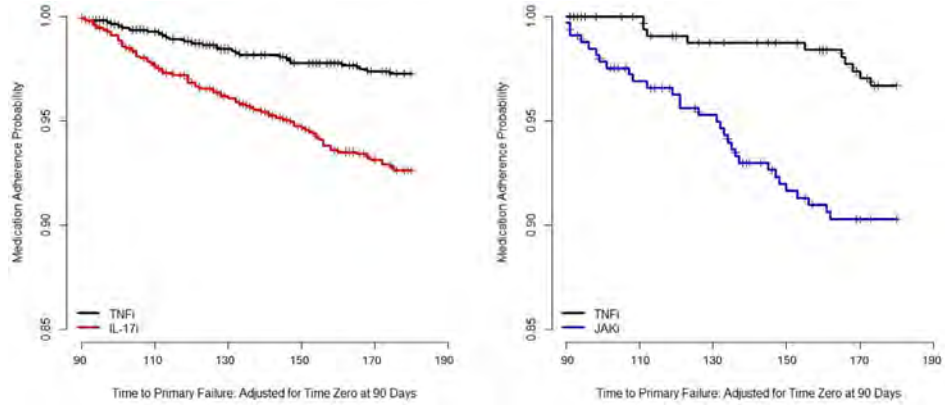


Figure 1. Kaplan-Meier survival curve for medication adherence probability 90-180 days following initial prescription date by TNFi vs. IL-17i (left panel) and TNFi vs. JAKi (right panel), after propensity score matching for demographics and comorbidities.

We included adult patients (≥18 years old) with a diagnosis of AS; ICD-10: M45.9) between 2004 and 2024 who were initially treated with a tumor necrosis factor inhibitor (TNFi), interleukin-17 inhibitor (IL-17i), or Janus kinase inhibitor (JAKi) for at least 90 days following their AS diagnosis. Patients receiving combination therapy (i.e., multiple medication classes initiated on the same day) or who did not meet the 90-day treatment duration threshold were excluded. The primary outcome was medication non-adherence, defined as a switch to a different medication class within 180 days of the initial prescription date.

To address baseline differences across treatment groups, we performed 1:1 greedy nearest-neighbor propensity score matching with a caliper = 0.1, conducted separately for the TNFi vs. IL-17i and TNFi vs. JAKi comparisons. Matching covariates included age at index, race, ethnicity, and additional comorbidities (see Table 1). Logistic regression models were used to assess the association between therapeutic class and non-adherence, with results presented as odds ratios (ORs) and 95% confidence intervals (CIs). Time to treatment withdrawal (TPTW) was evaluated using Cox proportional hazards regression, with results presented as hazard ratios (HR) and 95% confidence intervals. The results were visualized using Kaplan-Meier Curves. Results are reported both before and after propensity score matching.

Results: The study included patients with AS, 12,180 were initiated on TNFi, 1,211 on IL-17i, and 327 on JAKi. After propensity matching for age, sex, race, ethnicity and co-morbidities, the groups were well balanced (Table 1). Non-adherence risk was seen in 2.6% on TNFi compared to 7.1% on IL-17i and 3.1% on TNFi compared to 9.2% on JAKi. Non-adherence odds were significantly higher in patients initially prescribed IL-17i before and after matching (OR= 2.85, 95% CI:1.87, 4.4.47) than in patients started on TNFi. Similarly, the odds of non-adherence were higher in patients with JAKi before and after matching (OR=3.20, 95% CI: 1.59, 7.00) than in patients on anti-TNF (Table 2). Kaplan-Meier analysis (Figure 1) demonstrated higher treatment adherence and drug survival among TNFi users, compared to both IL-17i and JAKi (Figure 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this large real-world cohort of AS patients, initial treatment with TNFi was associated with significantly better adherence and drug survival compared to IL-17i and JAKi therapies. These findings may inform therapeutic decision-making and highlight the importance of initial treatment choice in AS management.

Disclosure: M. Magrey: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **J. Murphy**: None.

Abstract Number: 2361

Secondary Outcomes from a Series of N-of-1 NSAID Trials in Axial Spondyloarthritis: Functional, Quality-of-Life, and Safety Results from a Bayesian Analysis

Mark Hwang[1], Seokhun Kim[2], Shervin Assassi[3], Joyce Samuel[1], Charles Green[1], Jon Tyson[2] and John Reveille[4], [1]UTHealth Houston, Houston, TX, [2]UTHealth Houston, Houston, [3]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [4]Department of Medicine, University of Texas Medical Center, Houston, TX

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: We previously reported primary outcomes from a Bayesian series of N-of-1 trials comparing celecoxib, meloxicam, and naproxen in axial spondyloarthritis (axSpA), demonstrating improved ASDAS disease activity with individualized NSAID selection. Here, we present secondary outcomes evaluating function, quality of life, and safety, hypothesizing that the preferred NSAID would also yield superior patient-reported and disease-specific outcomes compared to eliminated NSAIDs.

Methods: This single-center, double-blind, randomized N-of-1 trial enrolled adults with active axSpA (ASDAS ≥2.1). Participants completed two treatment cycles in random sequence, receiving each of three NSAIDs for four weeks. Of 42 enrolled, 30 completed the full trial series and were included in the secondary analysis. Prespecified secondary outcomes included BASDAI, BASFI, BASMI, CRP, Maastricht enthesitis score (MASES), VAS Pain, VAS Global, Standard Gamble (SG), and PROPr utility scores. Bayesian multilevel models estimated both average NSAID-specific effects and within-patient

Table 1. Secondary Outcomes from the series of N-of-1 trials (n=30)

	Chosen Drug*	Eliminated Drug*	Chosen vs Eliminated*
BASDAI	1.74 (1.18 to 2.3), PPBB>0.99	0.35 (-0.25 to 0.96), PPB =0.87	1.39 (0.99 to 1.78), PPB>0.99
BASFI	0.82 (0.4 to 1.25), PPB >0.99	-0.04 (-0.54 to 0.46), PPB= 0.44	0.86 (0.44 to 1.28), PPB>0.99
BASMI	0.17 (-0.03 to 0.38), PPB=0.95	-0.09 (-0.33 to 0.14), PPB=0.21	0.27 (0.09 to 0.45), PPB>0.99
CRP	1.65 (-0.52 to 3.73), PPB =0.93	1.24 (-1.02 to 3.42), PPB=0.86	0.41 (-0.65 to 1.46), PPB=0.77
VAS GLOBAL	15.74 (8.57 to 22.66), PPB>0.99	14.58 (7.35 to 21.60), PPB>0.99	1.13 (-0.82 to 3.06), PPB=0.87
VAS PAIN	12.51 (5.78 to 19.05), PPB>0.99	11.28 (4.47 to 17.91), PPB>0.99	1.24 (-0.69 to 3.19), PPB=0.89
MASES	-0.04 (-0.89 to 0.79), PPBB=0.06	-0.69 (-1.59 to 0.20), PPBB=0.46	0.65 (0.05 to 1.24), PPBB=0.98
Standard Gamble†	-0.06 (-0.2 to 0.04), PPB=0.08	-0.03 (-0.16 to 0.1), PPB=0.32	-0.06 (-0.14 to 0.03), PPB=0.10
Propr†	-0.13 (-0.18 to -0.08), PPB>0.99	-0.08 (-0.13 to -0.03), PPB>0.99	-0.05 (-0.09 to 0.0), PPB=0.98

*Average reduction, range, posterior probability of reduction=0
†Given increased scores represent improved health states in these scores, negative values represent improvement unlike the other listed PROs

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adverse events from the series of N-of-1 trials (n=30)*

Medications	Celecoxib		Meloxicam		Naproxen	
Frequency Threshold for Reporting Other Adverse Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	2/30 (6.67%)		5/30 (16.66%)		5/30 (16.67%)	
Eye disorders						
Uveitis†1	0/30 (0.00%)	0	0/30 (0.00%)	0	1/30 (3.33%)	1
Gastrointestinal disorders						
Diarrhea†1	1/30 (3.33%)	1	1/30 ‡ (3.33%)	1	1/30 (3.33%)	1
Gastritis†1	0/30 (0.00%)	0	1/30 (3.33%)	1	2/30 (6.67%)	2
Hemorrhoids†1	0/30 (0.00%)	0	1/30 (3.33%)	1	0/30 (0.00%)	0
Stomach Pain†1	0/30 (0.00%)	0	1/30 (3.33%)	1	0/30 (0.00%)	0
Musculoskeletal and connective tissue disorders						
Bone pain†1	0/30 (0.00%)	0	1/30 (3.33%)	1	0/30 (0.00%)	0
Skin and subcutaneous tissue disorders						
Rash maculo-papular†1	1/30 (3.33%)	1	0/30 (0.00%)	0	0/30 (0.00%)	0
Urticaria†1	0/30 (0.00%)	0	0/30 (0.00%)	0	1/30 (3.33%)	11

* Term from vocabulary, CTCAE version 5.0.

† Indicates events were collected by systematic assessment.

‡Serious adverse event

Table 3. Secondary Outcomes comparing medications from the series of N -of-1 trials (n=30)

	Celecoxib vs. Meloxicam*	Celecoxib vs. Naproxen*	Meloxicam vs. Naproxen*
BASDAI	-0.12 (-0.54 to 0.31), PPB=0.29	-0.1 (-0.5 to 0.32), PPB=0.32	0.02 (-0.39 to 0.44), PPB=0.54
BASFI	0.02 (-0.35 to 0.39), PPB=0.55	0.18 (-0.18 to 0.53), PPB=0.84	0.15 (-0.21 to 0.52), PPB=0.80
BASMI	0.12 (-0.06 to 0.3), PPB=0.9	0.04 (-0.14 to 0.22) PPB=0.67	-0.08 (-0.26 to 0.11), PPB=0.19
CRP	-0.13 (-1.26 to1.03), PPB=0.42	0.24 (-0.8 to 1.28), PPB=0.67	0.37 (-0.69 to 1.4), PPB=0.75
VAS Global	-0.04 (-2.62 to 2.54), PPB=0.48	-0.1 (-1.97 to 1.75), PPB=0.45	-0.06 (-1.92 to 1.8), PPB=0.47
VAS Pain	0.03 (-2.51 to 2.59), PPB=0.50	-0.03 (-1.87 to 1.83), PPB=0.48	-0.06 (-1.91 to 1.78), PPB=0.47
MASES	0.22 (-0.42 to 0.87), PPB=0.76	0.48 (-0.13 to 1.09), PPB=0.94	0.26 (-0.36 to 0.89), PPB=0.80
Standard Gamble†	-0.03 (-0.1 to 0.05), PPB=0.25	-0.02 (-0.1 to 0.06), PPB=0.31	0.01 (-0.07 to 0.09), PPB=0.57
PRoPr†	0.02 (-0.02 to 0.05), PPB=0.80	0.02 (-0.02 to 0.05), PPB=0.81	0.0 (-0.04 to 0.04), PPB=0.51

*Average reduction, range, posterior probability of reduction=0
†Given increased scores represent improved health states in these scores, negative values represent improvement unlike the other listed PROs

comparisons between preferred and eliminated NSAIDs. Posterior probabilities of benefit (PPB) were calculated to assess clinical meaningfulness.

Results: The preferred NSAID was associated with substantial improvements across multiple domains. Mean differences (preferred minus eliminated) included: BASDAI 1.39 (95% credible interval [CrI]: 0.99–1.78; PPB >0.99), BASFI 0.86 (95% CrI: 0.44–1.28; PPB >0.99), BASMI 0.27 (95% CrI: 0.09–0.45; PPB >0.99), and MASES 0.65 (95% CrI: 0.05–1.24; PPB = 0.98). Smaller differences were observed for VAS Pain (1.24; CrI: –0.69 to 3.19; PPB = 0.89) and VAS Global (1.13; CrI: –0.82 to 3.06; PPB = 0.87). Utility improved with PROPr (–0.05; CrI: –0.09 to 0.00; PPB = 0.98), though SG showed non-significant trends. Adverse events were infrequent and mild across all NSAIDs, with only one serious adverse event (diarrhea) reported (Table 2). Average differences between NSAIDs across all patients were smaller and less consistent (Table 3).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Bayesian N-of-1 trials not only individualized NSAID selection in axSpA but also identified clinically meaningful improvements in function, pain, and quality of life with preferred medications. These findings support the broader utility of this personalized approach beyond disease activity metrics, offering a feasible strategy to optimize treatment in axSpA.

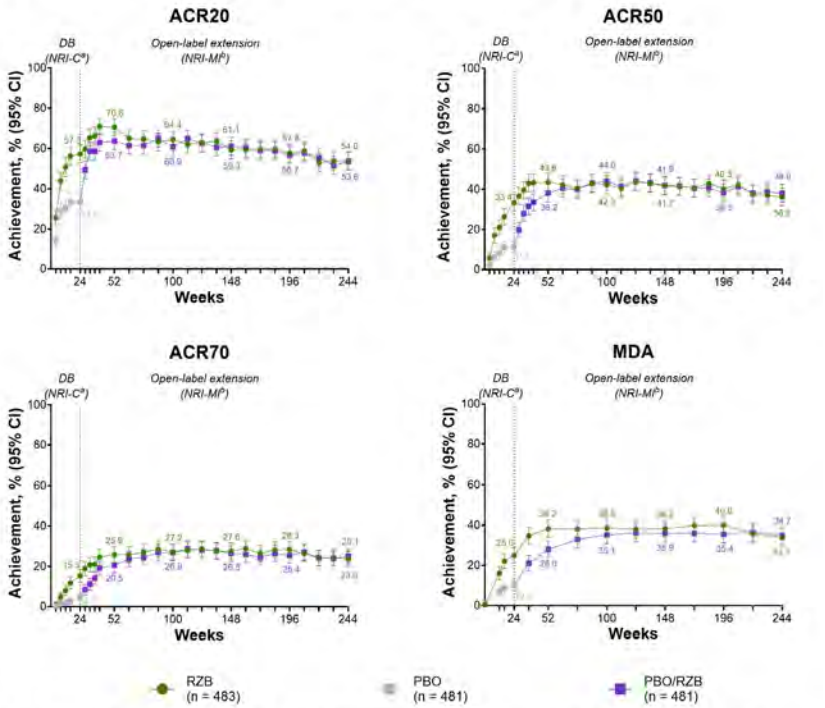
Disclosure: M. Hwang: None; **S. Kim**: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **J. Samuel**: None; **C. Green**: None; **J. Tyson**: None; **J. Reveille**: Surf Therapeutics, 5.

Abstract Number: 2362

Long-Term Efficacy and Safety of Risankizumab for csDMARD-IR Patients With Active Psoriatic Arthritis: 244-Week Results From the KEEPsAKE 1 Trial

Mauro Keiserman[1], Kim Papp[2], Douglas White[3], Angela Crowley[4], Joseph F Merola[5], Hayley Barnard[6], Ana Biljan[7], Thomas Iyile[8], Lingfeng luo[6], Douglas Ashley[6], Arathi Setty[8], Hayato Yamazaki[6] and Frank Behrens[9], [1]Rheumatology Section, Pontifical Catholic University, School of Medicine, Porto Alegre, Brazil, [2]Probity Medical Research and Alliance Clinical Trials, Waterloo, and Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada, [3]Rheumatology Department, Waikato Hospital, Hamilton, New Zealand, [4]Willow Rheumatology and Wellness,

Figure 1. Achievement of ACR Responses and MDA at Week 244



ACR, American College of Rheumatology score; ACR20/50/70, ≥ 20%/≥ 50%/≥ 70% improvement in American College of Rheumatology score; DB, double-blind period; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; MI, multiple imputation; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PBO, placebo; RZB, risankizumab; VAS, visual analog scale.

[a]The NRI-C analysis handled missing data using NRI except for data missing due to COVID-19, which were imputed by MI.

[b]The NRI-MI analysis handled missing data using NRI except for data missing due to COVID-19 or geopolitical conflict, which were imputed by MI.

MDA is defined as achieving 5 of the 7 following criteria: tender joint count ≤ 1; swollen join count ≤ 1; PASI ≤ 1 or psoriasis affecting ≤ 3% of body surface area; patient's assessment of pain (VAS) ≤ 15; patient's global assessment of disease activity (VAS) ≤ 20; HAQ-DI ≤ 0.5; tender entheseal points ≤ 1.

Figure 1. Achievement of ACR Responses and MDA at Week 244

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Willowbrook, IL, [5]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [6]AbbVie Inc., North Chicago, IL, [7]AbbVie Inc., Buffalo Grove, IL, [8]AbbVie Inc, North Chicago, IL, [9]Goethe-University & Fraunhofer ITMP, Frankfurt, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Risankizumab (RZB), an anti-interleukin 23p19 monoclonal antibody, is approved for the treatment of adults with active PsA. We report the efficacy and safety of RZB in patients with active PsA through week 244 of the KEEPsAKE 1 trial.

Methods: The ongoing, global, phase 3 KEEPsAKE 1 trial evaluates RZB for patients with moderately to severely active PsA (NCT03675308). Eligible patients were aged ≥ 18 years, naïve to biologic therapy, and demonstrated an inadequate response, intolerance, or contraindication to ≥ 1 conventional synthetic DMARD (csDMARD-IR). After a 24-week double-

Table 1. Efficacy Outcomes at Week 244

Table 1. Efficacy Outcomes at Week 244

Outcomes	RZB 150 mg	PBO to RZB 150 mg
ACR20,[a] n/N (%)	261/483 (54.0)	258/481 (53.6)
ACR50,[a] n/N (%)	175/483 (36.2)	183/481 (38.0)
ACR70,[a] n/N (%)	114/483 (23.6)	121/481 (25.1)
MDA,[a] n/N (%)	163/483 (33.7)	167/481 (34.7)
PASI 90,[a,b] n/N (%)	176/273 (64.5)	163/272 (59.9)
mNAPSI change from baseline,[c,g] LS mean (95% CI)	−14.7 (−15.4, −14.0) N = 306	−14.7 (−15.4, −14.0) N = 334
PGA-F change from baseline,[c,d] LS mean (95% CI)	−1.6 (−1.7, −1.5) N = 306	−1.5 (−1.6, −1.4) N = 334
Resolution of enthesitis,[a,e] n/N (%)	178/297 (59.9)	176/290 (60.7)
Resolution of dactylitis,[a,f] n/N (%)	109/148 (73.6)	107/147 (72.8)
PsA-mTSS change from baseline,[c] LS mean (95% CI)	0.9 (0.2, 1.7) N = 337	2.1 (1.3, 2.8) N = 342
No radiographic progression,[a,h] n/N (%)	298/337 (88.4)	276/342 (80.7)
Modified BASDAI change from baseline,[i,j] LS mean (95% CI)	−2.2 (−2.7, −1.7) N = 91	−2.4 (−2.9, −1.9) N = 93
HAQ-DI change from baseline,[c] LS mean (95% CI)	−0.38 (−0.42, −0.33) N = 479	−0.34 (−0.39, −0.29) N = 476
SF-36 PCS change from baseline,[c] LS mean (95% CI)	7.7 (6.7, 8.7) N = 476	7.9 (6.9, 8.9) N = 473
FACIT-Fatigue change from baseline,[c] LS mean (95% CI)	7.2 (6.3, 8.1) N = 476	6.0 (5.1, 6.9) N = 473

ACR, American College of Rheumatology score; ACR20/50/70, ≥ 20%/≥ 50%/≥ 70% improvement in American College of Rheumatology score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; LS, least squares; MDA, minimal disease activity; mNAPSI, modified Nail Psoriasis Severity Index; PASI 90, ≥ 90% improvement from baseline in Psoriasis Area and Severity Index; PBO, placebo; PGA-F, Physician's Global Assessment of Fingernail Psoriasis; PsA-mTSS, Psoriatic Arthritis modified Total Sharp Score; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.

[a]Results are based on as observed data with missing data imputed as nonresponse except for those missing due to COVID-19 or geopolitical conflict, which were imputed by multiple imputation (NRI-MI).

[b]Reported for patients psoriasis affecting ≥ 3% of body surface area at baseline.

[c]Results are based on mixed effect model repeated measurement; data as observed are included in the model.

[d]Reported for patients with nail psoriasis at baseline.

[e]Defined as LEI = 0; reported for patients with LEI > 0 at baseline.

[f]Defined as LDI = 0; reported for patients with LDI > 0 at baseline.

[g]Defined as PsA-mTSS change from baseline ≤ 0.

[h]Results are based on as observed data.

[i]Reported for patients with axial spondylitis at baseline.

[j]Modified BASDAI consists of BASDAI without the question related to peripheral joint pain/swelling.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Safety Overview

Table 2. Safety Overview

Parameter, E (E/100 PY)	Double-Blind Period[a] RZB 150 mg N = 483 PY = 224.1	Double-Blind Period[a] PBO N = 481 PY = 223.5	Long-Term Extension Period Any RZB 150 mg N = 946 PY = 3820.6
TEAE	398 (177.6)	387 (173.2)	4546 (119.0)
Serious TEAE	15 (6.7)	22 (9.8)	289 (7.6)
TEAE leading to study drug discontinuation	6 (2.7)	4 (1.8)	69 (1.8)
COVID-19–related TEAE	1 (0.4)	2 (0.9)	260 (6.8)
Adjudicated MACE	0	0	13 (0.3)
Cardiovascular death	0	0	3 (< 0.1)
Nonfatal MI	0	0	6 (0.2)
Nonfatal stroke	0	0	4 (0.1)
Serious infection	6 (2.7)	8 (3.6)	57 (1.5)
Opportunistic infections (excluding tuberculosis and herpes zoster)	0	0	1 (< 0.1)
Active tuberculosis	0	0	0
Herpes zoster	2 (0.9)	1 (0.4)	11 (0.3)
Malignant tumors	0	2 (0.9)	26 (0.7)
NMSC	0	0	5 (0.1)
Excluding NMSC	0	2 (0.9)	21 (0.5)
Serious hypersensitivity	0	0	2 (< 0.1)
Adjudicated anaphylactic reaction	0	0	0
All deaths	1 (0.4)	0	12 (0.3)[c]

MACE, major adverse cardiovascular event; MI, myocardial infarction; NMSC, nonmelanoma skin cancer; PBO, placebo; PY, patient-years; RZB, risankizumab; TEAE, treatment-emergent adverse events.

Any RZB 150 mg includes all patients who received RZB 150 mg during the study, regardless of whether they started on RZB at randomization or switched from PBO to RZB.

Treatment-emergent is defined as onset on or after the first dose and up to 140 days after the last dose of RZB.

[a]Data have been previously reported in Kristensen, et. al. *Ann Rheum Dis*. 2022;81(2):225–31.

[c]There were 11 treatment-emergent deaths: 2 related to COVID-19; 1 due to complications of acute leukemia; 1 due to dyspnea; 1 due to multiorgan failure as a complication from anastomosis surgery; 1 patient was hospitalized for pneumonia, developed urosepsis and died from related complications; 1 patient was hospitalized for anxiety and depression, developed septicemia, and died from unknown causes a week later; 4 due to of unknown causes; and 1 patient died due to cardiorespiratory arrest on day 363 (166 days after the last dose; nontreatment emergent).

blind treatment period where patients were randomized to subcutaneous (SC) RZB 150 mg or PBO patients receive open-label SC RZB 150 mg every 12 weeks in an extension period. Efficacy outcomes at week 244 and treatment-emergent adverse events (TEAEs) through data cutoff for all randomized patients who received ≥ 1 dose of study drug are reported.

Results: Of 964 randomized patients, 939 (97.4%) entered the extension period and 714 were actively enrolled at the data cutoff date. At week 244, 36.2% of patients receiving continuous RZB 150 mg (RZB) and 38.0% of patients who switched from PBO to RZB 150 mg (PBO/RZB) achieved ACR50 (**Figure 1**). Rates of achieving minimal disease activity were 33.7% with RZB and 34.7% with PBO/RZB. In patients with psoriasis affecting ≥ 3% of their body surface area at baseline, a ≥ 90% improvement from baseline in the Psoriasis Area and Severity Index was achieved by 64.5% of patients with RZB and 59.9% of patients with PBO/RZB (**Table 1**). In patients with nail psoriasis at baseline, the modified Nail Psoriasis Severity Index and the Physician's Global Assessment of Fingernail Psoriasis scores least squares (LS) mean improvements from baseline were 14.7 points and 1.6 points with RZB and 14.7 points and 1.5 points with PBO/RZB, respectively. In patients with enthesitis at baseline, resolution was achieved by 59.9% with RZB and 60.7% with PBO/RZB. For patients with dactylitis at baseline, 73.6% in the RZB group and 72.8% in the PBO/RZB group achieved resolution. The LS mean change from baseline in Psoriatic Arthritis modified Total Sharp Score (PSA-mTSS) was 0.9 with RZB and 2.1 with PBO/RZB; 88.4% of patients receiving RZB and 80.7% of patients receiving PBO/RZB showed no radiographic progression (PSA-mTSS change from baseline ≤ 0). In patients with axial spondylitis at baseline, the LS mean change from baseline in the modified Bath Ankylosing Spondylitis Disease Activity Index was –2.2 with RZB and –2.4 with PBO/RZB. Patient-reported measures of quality

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of life and fatigue maintained improvements from baseline. Rates of TEAEs (119.0 events/100 person-years [E/100PY]), serious TEAEs (7.6 E/100PY), and TEAEs leading to discontinuation of study drug (1.8 E/100PY) remained stable and were comparable to rates in the double-blind period (**Table 2**).

Conclusion: The 244-week results of the ongoing KEEPsAKE 1 trial demonstrate the durable efficacy of RZB 150 mg in treating clinical manifestations of PsA, sustaining bone structure, and improving quality of life for patients with PsA who are csDMARD-IR. RZB continues to be well tolerated, with no new safety signals identified.

Disclosure: M. Keiserman: AbbVie, 5, Biogen, 5, Bristol Myers Squibb, 5, GlaxoSmithKline, 5, Horizon Therapeutics Ireland DAC, 5, Janssen, 5, Lilly, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche, 5; **K. Papp**: AbbVie, 1, 2, 4, 5, 6, 12, Investigator, Acelyrin, 1, 2, 4, 5, 6, 12, Investigator, Akros, 1, 2, 4, 5, 6, 12, Investigator, Alumis, 1, 2, 4, 5, 6, 12, Investigator, Amgen, 1, 2, 4, 5, 6, 12, Investigator, Arcutis, 1, 2, 4, 5, 6, 12, Investigator, Bausch Health/Valeant, 1, 2, 4, 5, 6, 12, Investigator, Boehringer-Ingelheim, 1, 2, 4, 5, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 4, 5, 12, Investigator, Can-Fite Biopharma, 1, 2, 4, 5, 12, Investigator, Celltrion, 1, 2, 4, 5, 12, Investigator, Concert Pharmaceuticals, 1, 2, 4, 5, 12, Investigator, Dermavant, 1, 2, 4, 5, 6, 12, Investigator, Dermira, 1, 2, 4, 5, 6, 12, Investigator, Dice Pharmaceuticals, 1, 2, 4, 5, 6, 12, Investigator, Dice Therapeutics, 1, 2, 4, 5, 6, 12, Investigator, Eli Lilly and Company, 1, 2, 4, 5, 6, 12, Investigator, Evelo Biosciences, 1, 2, 4, 5, 6, 12, Investigator, Forbion, 1, 2, 4, 5, 6, 12, Investigator, Galderma, 1, 2, 4, 5, 6, 12, Investigator, Horizon Therapeutics, 1, 2, 4, 5, 6, 12, Investigator, Incyte, 1, 2, 4, 5, 12, Investigator, Janssen, 1, 2, 4, 5, 6, 12, Investigator, Kymab, 1, 2, 4, 5, 6, 12, Investigator, Kyowa Hakko Kirin, 1, 2, 4, 5, 6, 12, Investigator, LEO Pharma, 1, 2, 4, 5, 6, 12, Investigator, Meiji Seika Pharma, 1, 2, 4, 5, 6, 12, Investigator, Mitsubishi Pharma, 1, 2, 4, 5, 6, 12, Investigator, Nimbus Therapeutics, 1, 2, 4, 5, 6, 12, Investigator, Novartis, 1, 2, 4, 5, 6, 12, Investigator, Pfizer, 1, 2, 4, 5, 6, 12, Investigator, Reistone, 1, 2, 4, 5, 6, 12, Investigator, Sandoz, 1, 2, 4, 5, 6, 12, Investigator, Sanofi-Aventis/Genzyme, 1, 2, 4, 5, 6, 12, Investigator, Sun Pharma, 1, 2, 4, 5, 6, 12, Investigator, Takeda, 1, 2, 4, 5, 6, 12, Investigator, Tarsus Pharmaceuticals, 1, 2, 4, 5, 6, 12, Investigator, UCB, 1, 2, 4, 5, 6, 12, Investigator, Zai Lab, 1, 2, 4, 5, 6, 12, Investigator; **D. White**: AbbVie, 1, 2, 6; **A. Crowley**: AbbVie/Abbott, 2, 5, 6, Amgen, 2, 5, 6, Aqtual, 2, 5, 6, AstraZeneca, 6, Eli Lilly, 5, Exagen, 2, 5, 6, GSK, 2, 5, 6, Horizon, 2, 5, 6, Janssen, 2, 5, 6, Kyowa Kirin, 2, 5, 6, Novartis, 2, 5, Scipher Medicine, 2, 5, 6, SetPoint Medical, 2, 5, 6, Sun Pharma, 2, 5, 6, UCB, 2, 6; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **H. Barnard**: AbbVie, 3, 11; **A. Biljan**: AbbVie, 3, 11; **T. Iyile**: AbbVie, 3, 11; **L. luo**: AbbVie, 3, 11; **D. Ashley**: AbbVie, 3, 11; **A. Setty**: AbbVie, 3, 11; **H. Yamazaki**: AbbVie, 3, 11; **F. Behrens**: AbbVie, 2, 6, BMS, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Genzyme, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 5, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 6, UCB, 2, 6.

Abstract Number: 2363

Impact of Biologic Therapies on Cardiovascular and Venous Thromboembolic Events in Psoriatic Arthritis: Real-World Evidence

Milad Heydari-Kamjani[1], Jennifer Murphy[2] and Marina Magrey[3], [1]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [2]University Hospitals, Cleveland Medical Center, cleveland, OH, [3]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Patients with psoriatic arthritis (PsA) are at increased risk for major adverse cardiovascular events (MACE) and venous thromboembolism (VTE), yet the comparative safety of biologic therapies remains poorly defined. This study aimed to compare the risk of MACE and VTE among users of IL-17, IL-12/23, and IL-23 inhibitors, with anti-TNF agents serving as the reference group.

Methods: We conducted a retrospective cohort study using the TriNetX Research Network, a de-identified, federated electronic health record database (accessed May 28, 2024). Adults (≥18 years) diagnosed with PsA (ICD-10: L40.5) between 2004 and 2024 on at least one biologic agent including anti-TNF, anti-IL-17, IL-23 or IL-12/23 were included. Eligible patients had at least one year of follow-up. Exclusion criteria included: use of multiple biologic agents from different drug classes, known hypercoagulable state, pregnancy and malignancy (prostate, lung, colon, bladder, kidney, lymphoma, leukemia, endometrial, ovarian, stomach, and pancreatic). Primary outcomes were new onset myocardial infarction (MI), stroke (ischemic and hemorrhagic), deep vein thrombosis (DVT), and pulmonary embolism (PE). Patients with prior history of these outcomes were excluded from analyses.

To address baseline differences across treatment groups, we conducted weighted logistic regression using inverse probability of treatment weighting (IPTW) based on the average treatment effect (ATE) and a threshold of < 0.1. Propensity scores were estimated using covariates listed in Table 1. These weights were then applied in logistic regression models to assess

Table 1. Baseline characteristics across biologic therapy classes, with standardized mean differences (SMD) shown before and after inverse probability of treatment weighting (IPTW) adjusted by the average treatment effect (ATE).

Baseline Characteristics	Overall N = 28,973[1]	Anti-TNF N = 21,589[1]	IL 12/23 N = 1,405[1]	IL-17 N = 4,697[1]	IL-23 N = 1,282[1]	Unadjusted Max SMD[3]	Adjusted Max SMD[3]
Age at index	52.2 ± 14.0	51.8 ± 14.1	53.3 ± 14.2	52.9 ± 13.3	54.2 ± 14.2	0.173*	0.012
Sex							
Female	16,259 (56.1)	11,883 (55.0)	838 (59.6)	2,800 (59.6)	738 (57.6)	0.05*	0.003
Male	12,714 (43.9)	9,706 (45.0)	567 (40.4)	1,897 (40.4)	544 (42.4)	0.05*	0.003
Race							
Black or African American	1,029 (3.6)	737 (3.4)	67 (4.8)	164 (3.5)	61 (4.8)	0.01*	0.002
Other	2,336 (8.1)	1,632 (7.6)	124 (8.8)	469 (10.0)	111 (8.7)	0.02*	0.002
Unknown	2,541 (8.8)	1,838 (8.5)	116 (8.3)	492 (10.5)	95 (7.4)	0.03*	0.003
White	23,067 (79.6)	17,382 (80.5)	1,098 (78.1)	3,572 (76.0)	1,015 (79.2)	0.05*	0.007
BMI (within 365 days of index)	30.8 ± 6.8	30.8 ± 6.7	30.8 ± 6.8	31.4 ± 7.0	31.0 ± 6.7	0.09*	0.03
Comorbidities							
Anticoagulant Medication	4,013 (13.9)	2,739 (12.7)	235 (16.7)	763 (16.2)	276 (21.5)	0.09*	0.005
Diabetes mellitus	3,535 (12.2)	2,394 (11.1)	193 (13.7)	730 (15.5)	218 (17.0)	0.06*	0.005
Hyperlipidemia	8,228 (28.4)	5,884 (27.3)	432 (30.7)	1,409 (30.0)	503 (39.2)	0.12*	0.005
Hypertension	9,009 (31.1)	6,504 (30.1)	471 (33.5)	1,529 (32.6)	505 (39.4)	0.09*	0.006
Obesity	5,728 (19.8)	3,978 (18.4)	310 (22.1)	1,045 (22.2)	395 (30.8)	0.12*	0.007
Smoking	2,809 (9.7)	2,002 (9.3)	138 (9.8)	483 (10.3)	186 (14.5)	0.05*	0.001

[1] Mean ± SD; n (%)
[2] A "*" indicates a P-value <0.05; ANOVA, Pearson's Chi-squared test, or Fisher's exact test
[3] Standardized mean difference (SMD) before and after adjustment by IPTW using ATE, with threshold of <0.1 considered to be balanced

Table 2. Incidence (n (%)) and odds ratios (OR; 95% confidence interval) between biologic classes, before and after adjustment for covariates by IPTW. Reference category is denoted by "—."

			Unweighted		Weighted	
Primary outcome	Incidence (%)	Sample	OR (95% CI)	P-value	OR (95% CI)	P-value
Stroke						
Anti TNF vs.	416 (2.0)	21,273	—	—	—	—
IL 12/23	42 (3.1)	1,376	1.58 (1.13, 2.15)	**0.005**	1.41 (1.00, 1.95)	**0.04**
IL 17	56 (1.2)	4,613	0.62 (0.46, 0.81)	**<0.001**	0.56 (0.41, 0.74)	**<0.001**
IL 23	11 (0.9)	1,253	0.44 (0.23, 0.77)	**0.008**	0.35 (0.17, 0.64)	**0.002**
Pulmonary Embolism						
Anti TNF vs.	236 (1.1)	21,407	—	—	—	—
IL 12/23	12 (0.9)	1,386	0.78 (0.41, 1.34)	0.4	0.72 (0.38, 1.25)	0.3
IL 17	25 (0.5)	4,647	0.49 (0.31, 0.72)	**<0.001**	0.45 (0.28, 0.67)	**<0.001**
IL 23	2 (0.2)	1,262	0.14 (0.02, 0.44)	**0.006**	0.12 (0.02, 0.40)	**0.005**
DVT						
Anti TNF vs.	343 (1.6)	21,343	—	—	—	—
IL 12/23	17 (1.2)	1,391	0.76 (0.45, 1.20)	0.3	0.66 (0.38, 1.07)	0.12
IL 17	48 (1.0)	4,643	0.64 (0.47, 0.86)	**0.004**	**0.58 (0.42, 0.79)**	**<0.001**
IL 23	11 (0.9)	1,263	0.54 (0.28, 0.93)	**0.04**	**0.49 (0.24, 0.88)**	**0.02**
Myocardial Infarction						
Anti TNF vs.	442 (2.1)	21,297	—	—	—	—
IL 12/23	36 (2.6)	1,374	1.27 (0.88, 1.76)	0.2	1.15 (0.79, 1.62)	0.4
IL 17	55 (1.2)	4,603	0.57 (0.43, 0.75)	**<0.001**	0.50 (0.36, 0.66)	**<0.001**
IL 23	9 (0.7)	1,243	0.34 (0.16, 0.63)	**0.002**	0.29 (0.13, 0.54)	**<0.001**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the association between biologic therapy and the primary outcomes. Results are presented as odds ratios with 95% confidence intervals, and findings from both unweighted and weighted models are reported.

Results: A total of 28,973 patients with PsA treated with biologic agents were included in the study. The majority received anti-TNF therapy, followed by IL-17 inhibitors, IL-12/23 inhibitors, and IL-23 inhibitors (Table 1). Prior to weighting, comorbid conditions varied across groups; however, after IPTW baseline characteristics were well balanced. The mean age was 52.2 years, 56% were female, and common comorbidities included hypertension (31.1%), hyperlipidemia (28.4%), obesity (19.8%), and diabetes (12.2%) (Table 1).

In PsA cohort, IL-17 inhibitor use was associated with significantly reduced odds of DVT (OR 0.58, $p < 0.001$), PE (OR 0.45, $p < 0.001$), MI (OR 0.50, $p < 0.001$), and stroke (OR 0.56, $p < 0.001$). Similarly, IL-23 inhibitor use was associated with lower odds of DVT (OR 0.49, $p = 0.02$), PE (OR 0.12, $p = 0.005$), MI (OR 0.29, $p < 0.001$), and stroke (OR 0.35, $p = 0.002$) compared to anti-TNF agents. In contrast, IL-12/23 inhibitor use was associated with increased odds of stroke (OR 1.41, $p = 0.04$), with no significant differences observed for DVT, PE, or MI (Table 2).

Conclusion: In PsA, IL-17 and IL-23 inhibitors were consistently associated with significantly lower odds of stroke, MI, DVT, and PE compared to anti-TNF agents. In contrast, IL-12/23 inhibitor use was linked to increased odds of stroke and showed no significant protective effect across other outcomes.

Disclosure: M. Heydari-Kamjani: None; **J. Murphy**: None; **M. Magrey**: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5.

Abstract Number: 2364

Real-World Characteristics and Treatment Patterns of Difficult-to-Treat Psoriatic Arthritis

Milad Heydari-Kamjani[1], Jennifer Murphy[2] and Marina Magrey[3], [1]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [2]University Hospitals, Cleveland Medical Center, cleveland, OH, [3]Case Western Reserve University School of Medicine/University Hospitals Cleveland, Richfield, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease with variable clinical presentation and treatment response. A subset of PsA patients are difficult to treat (D2T). This study compared baseline characteristics, extra-articular manifestations (EAMs), and comorbid conditions between D2T and non-difficult-to-treat (ND2T) PsA patients.

Methods: We performed a retrospective study using a de-identified federated database with 89 contributing healthcare organizations, including over 125 million patients (TriNetX Research Network, Cambridge, MA; date of data access: Feb 28, 2025). Patients with PsA (ICD-10: L40.59), ≥18 years, and at least one follow-up were included. We identified 7,403 adults with PsA treated with conventional DMARDs (Sulfasalazine, Methotrexate, Leflunomide) and recorded post-treatment CRP levels. There is no consensus for definition of D2T PsA, but we proposed the following: prior cDMARD use, ≥2 biologic/targeted synthetic DMARDs from two different classes and elevated CRP (≥8 mg/L). Demographics, comorbidities, and

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics between difficult to treat and not difficult to treat psoriatic arthritis, before and after propensity score matching for demographics (age, sex, race, and ethnicity).

	Before matching			After matching		
	Not difficult to treat N = 6,154[1]	Difficult to treat N = 1,249[1]	p-value[2]	Not difficult to treat N = 1,248[1]	Difficult to treat N = 1,248[1]	p-value[2]
Age at index	52.3 ± 13.5	47.6 ± 12.8	<0.001	47.6 ± 12.7	47.6 ± 12.8	0.931
Sex			**<0.001**			
Female	3,736 (60.7%)	852 (68.2%)		857 (68.7%)	851 (68.2%)	0.796
Race						
White	4,774 (77.6%)	1,006 (80.5%)	**0.021**	1,032 (82.7%)	1,006 (80.6%)	0.179
Black or African American	263 (4.3%)	50 (4.0%)	0.665	50 (4.0%)	50 (4.0%)	>0.999
American Indian or Alaska Native	33 (0.5%)	7 (0.6%)	0.915	3 (0.2%)	7 (0.6%)	0.205
Asian	141 (2.3%)	46 (3.7%)	**0.004**	35 (2.8%)	45 (3.6%)	0.256
Ethnicity						
Not Hispanic or Latino	4,503 (73.2%)	981 (78.5%)	**<0.001**	984 (78.8%)	980 (78.5%)	0.845
Unknown	1,166 (18.9%)	164 (13.1%)	**<0.001**	169 (13.5%)	164 (13.1%)	0.769
BMI	31.1 ± 6.7	33.1 ± 7.2	**<0.001**	31.7 ± 7.0	33.1 ± 7.2	**0.001**
Obesity (BMI > 30)	1,607 (26.1%)	354 (28.3%)	0.104	356 (28.5%)	354 (28.4%)	0.929
C-reactive protein (baseline)	14.0 ± 28.1	17.8 ± 27.5	**0.021**	14.6 ± 29.0	17.8 ± 27.5	0.148
C-reactive protein (post-cDMARDS)	28.0 ± 62.8	50.4 ± 63.4	**<0.001**	28.4 ± 59.9	50.4 ± 63.4	**<0.001**
HLA-B27 Positive	67 (1.1%)	27 (2.2%)	**0.002**	10 (0.8%)	27 (2.2%)	**0.005**
Conventional- DMARDS						
Methotrexate	4,900 (79.6%)	1,051 (84.1%)	**<0.001**	1,032 (82.7%)	1,050 (84.1%)	0.333
Sulfasalazine	1,786 (29.0%)	410 (32.8%)	**0.007**	371 (29.7%)	410 (32.9%)	0.092
Leflunomide	1,241 (20.2%)	456 (36.5%)	**<0.001**	218 (17.5%)	456 (36.5%)	**<0.001**
Comorbidities						
Hypertension	1,106 (18.0%)	188 (15.1%)	**0.013**	181 (14.5%)	188 (15.1%)	0.693
Dyslipidemia	685 (11.1%)	126 (10.1%)	0.282	103 (8.3%)	126 (10.1%)	0.111
Diabetes	1,068 (17.4%)	208 (16.7%)	0.55	197 (15.8%)	208 (16.7%)	0.55
Smoking	245 (4.0%)	60 (4.8%)	0.182	53 (4.2%)	60 (4.8%)	0.5
Chronic kidney disease	258 (4.2%)	27 (2.2%)	**<0.001**	39 (3.1%)	27 (2.2%)	0.134
Anxiety	912 (14.8%)	224 (17.9%)	**0.005**	217 (17.4%)	224 (17.9%)	0.713
Depression	665 (10.8%)	159 (12.7%)	**0.049**	147 (11.8%)	159 (12.7%)	0.464
Crohn's Disease	107 (1.7%)	40 (3.2%)	**<0.001**	24 (1.9%)	40 (3.2%)	**0.043**
Ulcerative colitis	84 (1.4%)	22 (1.8%)	0.282	13 (1.0%)	22 (1.8%)	0.126
Iridocyclitis	89 (1.4%)	19 (1.5%)	0.84	19 (1.5%)	19 (1.5%)	>0.999
Other Psoriasis	3,753 (61.0%)	824 (66.0%)	**<0.001**	768 (61.5%)	824 (66.0%)	**0.02**

[1]Mean ± SD; n (%)
[2] Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test

Table 2: Use of biologic and targeted synthetic DMARDs between not difficult to treat and difficult to treat psoriatic arthritis, before and after propensity score matching for demographics (age, sex, race, and ethnicity).

	Before matching			After matching		
	Not difficult to treat N = 6,154[1]	Difficult to treat N = 1,249[1]	p-value[2]	Not difficult to treat N = 1,248[1]	Difficult to treat N = 1,248[1]	p-value[2]
Anti-TNF	2,961 (48.1%)	1,103 (88.3%)	<0.001	648 (51.9%)	1,102 (88.3%)	<0.001
Adalimumab	1,788 (29.1%)	689 (55.2%)	<0.001	409 (32.8%)	689 (55.2%)	<0.001
Certolizumab	233 (3.8%)	173 (13.9%)	<0.001	55 (4.4%)	172 (13.8%)	<0.001
Etanercept	1,277 (20.8%)	542 (43.4%)	<0.001	285 (22.8%)	542 (43.4%)	<0.001
Golimumab	275 (4.5%)	184 (14.7%)	<0.001	63 (5.0%)	184 (14.7%)	<0.001
Infliximab	653 (10.6%)	364 (29.1%)	<0.001	121 (9.7%)	364 (29.2%)	<0.001
CTLA-4	126 (2.0%)	195 (15.6%)	<0.001	24 (1.9%)	195 (15.6%)	<0.001
Abatacept	126 (2.0%)	195 (15.6%)	<0.001	24 (1.9%)	195 (15.6%)	<0.001
Anti-IL17	910 (14.8%)	1,077 (86.3%)	<0.001	197 (15.7%)	1,077 (86.3%)	<0.001
Ixekizumab	301 (4.9%)	358 (28.7%)	<0.001	73 (5.8%)	358 (28.7%)	<0.001
Secukinumab	609 (9.9%)	719 (57.6%)	<0.001	124 (9.9%)	719 (57.6%)	<0.001
Anti-IL-23	294 (4.8%)	375 (28.0%)	<0.001	73 (5.8%)	375(30.1%)	<0.001
Guselkumab	161 (2.6%)	225 (18.0%)	<0.001	45 (3.61%)	225 (18.0%)	<0.001
Risankizumab	133 (2.2%)	150 (12.0%)	<0.001	28 (2.2%)	150 (12.0%)	<0.0001
Anti-IL12/23	345 (5.6%)	454 (36.3%)	<0.001	82 (6.6%)	453 (36.3%)	<0.001
Ustekinumab	345 (5.6%)	454 (36.3%)	<0.001	82 (6.6%)	453 (36.3%)	<0.001
JAK-inhibitor	321 (5.2%)	394 (31.6%)	<0.001	73 (5.9%)	394 (31.6%)	<0.001
Tofacitinib	228 (3.7%)	283 (22.7%)	<0.001	51 (4.1%)	283 (22.7%)	<0.001
Upadacitinib	93 (1.5%)	111 (8.9%)	<0.001	22 (1.8%)	111 (8.9%)	<0.001
TYK2	3 (0.0%)	10 (0.8%)	<0.001	2 (0.2%)	10 (0.8%)	0.021
Deucravacitinib	3 (0.0%)	10 (0.8%)	<0.001	2 (0.2%)	10 (0.8%)	0.021

EAMs were collected. We performed 1:1 propensity score matching for age, sex, race, and ethnicity. Continuous and categorical variables were analyzed using t-tests and chi-squared tests ($\alpha = 0.05$).

Results: The study included 7,403 patients (6,154 ND2T, 1,249 D2T). After propensity score matching, both groups had 1,248 patients. The D2T cohort had a higher BMI (33.1 vs. 31.7, $p < 0.001$) (Table 1). Comorbidities, including Crohn's disease (3.2% vs. 1.9%, $p = 0.045$) and other psoriasis types (66% vs. 61.5%, $p = 0.02$), were more prevalent in the D2T group.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Number of drug classes and total biologic and targeted synthetic used between difficult to treat and not difficult to treat psoriatic arthritis, before and after propensity score matching for demographics (age, sex, race, and ethnicity).

	Before matching		After matching	
	Not difficult to treat N = 6,154[1]	Difficult to treat N = 1,249[1]	Not difficult to treat N = 1,248[1]	Difficult to treat N = 1,248[1]
Number of b/tsDMARDs drug classes				
0	2,481 (40.3%)	0 (0.0%)	450 (36.1%)	0 (0.0%)
1	2,953 (48.0%)	0 (0.0%)	635 (50.9%)	0 (0.0%)
2	492 (8.0%)	764 (61.2%)	112 (9.0%)	763 (61.1%)
3	178 (2.9%)	389 (31.1%)	34 (2.7%)	389 (31.2%)
≥4	50 (0.8%)	96 (7.7%)	17 (1.4%)	96 (7.7%)
Total b/ts DMARDs used after c-DMARD				
0	2,481 (40.3%)	0 (0.0%)	450 (36.1%)	0 (0.0%)
1	2,188 (35.6%)	0 (0.0%)	454 (36.4%)	0 (0.0%)
2	884 (14.4%)	370 (29.6%)	214 (17.1%)	369 (29.6%)
3	343 (5.6%)	350 (28.0%)	73 (5.8%)	350 (28.0%)
≥4	258 (4.2%)	529 (42.4%)	57 (4.6%)	529 (42.4%)

[1]n (%)

D2T patients also had elevated CRP levels (50.4 vs. 28.4 mg/L, $p < 0.001$) and higher HLA-B27 positivity (2.2% vs. 0.8%, $p = 0.005$). Additionally, the D2T group demonstrated significantly greater use of biologic and targeted synthetic DMARDs across all major therapeutic classes (Table 2). TNF inhibitors were used in 88.3% of D2T patients vs. 51.9% of ND2T ($p < 0.001$), with adalimumab most frequently prescribed (55.2% vs. 32.8%, $p < 0.001$). Abatacept was also more common in D2T (15.6% vs. 1.9%, $p < 0.001$). IL-17 inhibitors were more frequent in D2T (86.3% vs. 15.7%, $p < 0.001$), primarily secukinumab (57.6% vs. 9.9%, $p < 0.001$). IL-23 use was higher in D2T (30.1% vs. 5.8%, $p < 0.001$), with guselkumab most used (18.0% vs. 3.6%, $p < 0.001$). IL-12/23 inhibition with ustekinumab was also more common (36.3% vs. 6.6%, $p < 0.001$). JAK inhibitor use was greater in D2T (31.6% vs. 5.9%, $p < 0.001$), mainly tofacitinib (22.7% vs. 4.1%, $p < 0.001$). Though rare overall, TYK2 inhibition with deucravacitinib was more common in D2T (0.8% vs. 0.2%, $p = 0.021$). Nearly half of the D2T group (42.4%) received four or more individual b/tsDMARDs after cDMARDs (Table 3).

Conclusion: Our study showed that in a matched cohort, D2T PsA patients had higher BMI, greater prevalence of Crohn's disease, additional psoriasis types, higher CRP levels, and more HLA-B27 positivity. They also had significantly higher use of biologics and targeted synthetic DMARDs across all major classes.

Disclosure: M. Heydari-Kamjani: None; **J. Murphy**: None; **M. Magrey**: AbbVie, 2, 5, Amgen, 5, BMS, 2, 5, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5.

Abstract Number: 2365

Sustained Efficacy up to 3 Years with Bimekizumab Treatment Across GRAPPA Core Domains in Patients with Psoriatic Arthritis: Long-Term Results from Two Phase 3 Trials

Joseph F Merola[1], Laura Coates[2], Atul Deodhar[3], Alice B. Gottlieb[4], Enrique R. Soriano[5], Barbara Ink[6], Rajan Bajracharya[6], Jason Coarse[7] and **Philip J. Mease**[8], [1]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [3]Division of Arthritis and Rheumatic Diseases, Oregon Health & Science University, Portland, OR, [4]Department of Dermatology, UT Southwestern Medical Center, Dallas, TX, [5]Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires and University Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [6]UCB, Slough, England, United Kingdom, [7]UCB, Morrisville, NC, [8]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Efficacy outcomes at baseline, Year 1, and Year 3 from BE OPTIMAL, BE COMPLETE, and both BE MOBILE 1 and BE MOBILE 2 by GRAPPA domain (mNRI, NRI, MI, OC)

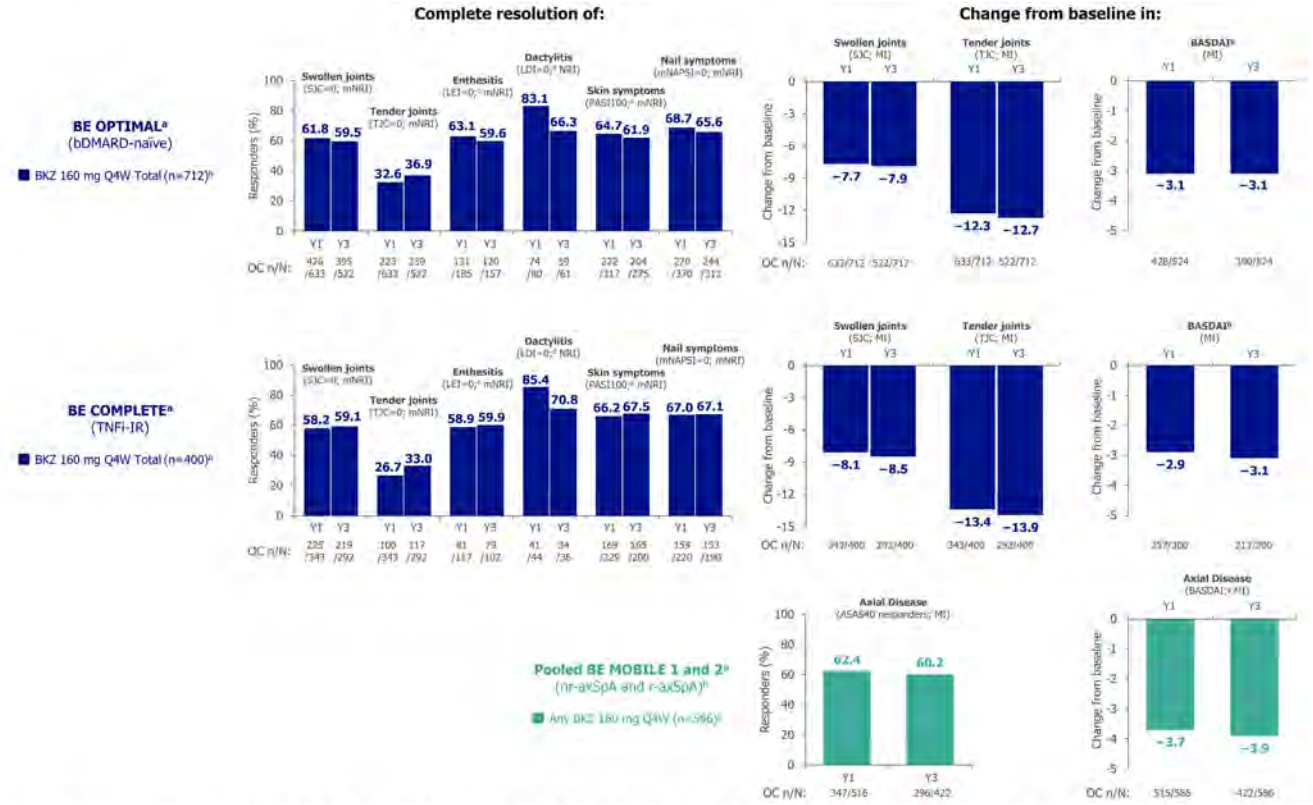
	BE OPTIMAL[a] (bDMARD-naïve)		BE COMPLETE[a] (TNFi-IR)	
	BKZ 160 mg Q4W Total[b] n=712		BKZ 160 mg Q4W Total[b] n=400	
	Year 1	Year 3	Year 1	Year 3
Peripheral arthritis				
SJC score (of 66 joints), BL, mean (SE)	9.2 (0.3)		9.9 (0.4)	
SJC CfB (MI), mean (SE)	−7.7 (0.2)	−7.9 (0.2)	−8.1 (0.4)	−8.5 (0.4)
SJC=0 (mNRI), % (95% CI)	61.8 (58.2–65.5)	59.5 (55.7–63.3)	58.2 (53.2–63.1)	59.1 (54.0–64.2)
TJC score (of 68 joints), BL, mean (SE)	16.9 (0.5)		18.7 (0.7)	
TJC CfB (MI), mean (SE)	−12.3 (0.4)	−12.7 (0.4)	−13.4 (0.6)	−13.9 (0.7)
TJC=0 (mNRI), % (95% CI)	32.6 (29.1–36.2)	36.9 (33.2–40.6)	26.7 (22.2–31.1)	33.0 (28.2–37.8)
Enthesitis				
LEI score,[c] BL, mean (SE)	2.6 (0.1)		2.7 (0.1)	
LEI CfB (MI),[c] mean (SE)	−1.8 (0.1)	−2.0 (0.1)	−1.9 (0.1)	−1.9 (0.2)
Complete resolution of enthesitis, LEI=0 (mNRI),[c] % (95% CI)	63.1 (56.5–69.7)	59.6 (52.7–66.5)	58.9 (50.6–67.2)	59.9 (51.4–68.4)
Dactylitis				
LDI score,[d,e] BL, mean (SD)	47.0 (49.6)		70.9 (117.0)	
LDI CfB (OC),[d,e] mean (SD)	−45.5 (50.9)	−46.1 (53.3)	−57.2 (76.7)	−56.7 (93.6)
Complete resolution of dactylitis, LDI=0 (NRI),[d] % (95% CI)	83.1 (75.4–90.9)	66.3 (56.5–76.1)	85.4 (75.4–95.4)	70.8 (58.0–83.7)
Skin psoriasis				
PASI score,[f] BL, mean (SE)	8.1 (0.3)		9.6 (0.5)	
PASI CfB (MI),[f] mean (SE)	−7.7 (0.3)	−7.7 (0.3)	−9.0 (0.5)	−9.0 (0.5)
Complete skin clearance, PASI100 (mNRI),[f] % (95% CI)	64.7 (59.6–69.8)	61.9 (56.6–67.3)	66.2 (60.3–72.1)	67.5 (61.6–73.4)
Nail psoriasis				
mNAPSI score,[g] BL, mean (SE)	4.1 (0.1)		4.4 (0.2)	
mNAPSI CfB (MI),[g] mean (SE)	−3.5 (0.1)	−3.5 (0.1)	−3.6 (0.2)	−3.7 (0.2)
Complete resolution of nail psoriasis, mNAPSI=0 (mNRI),[g] % (95% CI)	68.7 (64.1–73.3)	65.6 (60.5–70.6)	67.0 (61.0–73.0)	67.1 (60.9–73.4)
Axial disease				
BASDAI score,[h] BL, mean (SE)	6.2 (0.1)		6.3 (0.1)	
BASDAI CfB (MI),[h] mean (SE)	−3.1 (0.1)	−3.1 (0.1)	−2.9 (0.1)	−3.1 (0.2)

	Pooled BE MOBILE 1 and 2[a,i] (nr-axSpA and r-axSpA)	
	Any BKZ 160 mg Q4W[b] n=586	
	Year 1	Year 3
ASAS40 responder rate (MI), % (95% CI)	62.4 (58.4, 66.4)	60.2 (56.0, 64.5)
BASDAI score,[h] BL, mean (SE)	6.6 (0.1)	
BASDAI CfB (MI),[h] mean (SE)	−3.7 (0.1)	−3.9 (0.1)

Randomized set from BE OPTIMAL (including data from BE VITAL), BE COMPLETE (including data from BE VITAL), and BE MOBILE 1 and BE MOBILE 2 (including data from BE MOVING). Data reported at Year 1 (Week 52) and Year 3 (Week 160 in BE OPTIMAL, Week 156 in BE COMPLETE, and Week 164 in BE MOBILE 1 and BE MOBILE 2). mNRI considered all visits following discontinuation due to adverse event or lack of efficacy as non-response; all other missing data were imputed with MI and the response derived from the imputed values. [a] Patient populations are referred to by the name of their starting study; [b] Includes patients who switched from placebo to BKZ at Week 16; [c] In patients with enthesitis at baseline (LEI >0; BE OPTIMAL: n=213; BE COMPLETE: n=142); [d] In patients with dactylitis at baseline (LDI >0; BE OPTIMAL: n=89; BE COMPLETE: n=48); missing data imputed using NRI as MI was not estimable as it would not converge; [e] OC data reported, as the MI was not estimable as it would not converge; [f] In patients with ≥3% body surface area affected by psoriasis at baseline (BE OPTIMAL: n=357; BE COMPLETE: n=264); [g] In patients with nail psoriasis at baseline (mNAPSI >0; BE OPTIMAL: n=400; BE COMPLETE: n=242); [h] In patients with BASDAI ≥4 (BE OPTIMAL: n=524; BE COMPLETE: n=300; all patients in BE MOBILE 1 and 2); [i] Data were pooled for all randomized patients with nr-axSpA and r-axSpA in BE MOBILE 1 and 2.

BL: baseline; CfB: change from baseline; CI: confidence interval; PASI: Psoriasis Area and Severity Index; SD: standard deviation; SE:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Randomized set from BE OPTIMAL (including data from BE VITAL), BE COMPLETE (including data from BE VITAL), and BE MOBILE 1 and BE MOBILE 2 (including data from BE MOVING). Data reported at Year 1 (Week 52) and Year 3 (Week 160 in BE OPTIMAL, Week 156 in BE COMPLETE, and Week 164 in BE MOBILE 1 and BE MOBILE 2). mNRI considered visits following discontinuation due to adverse event or lack of efficacy as non-response; all other missing data were imputed with MI and the response derived from the imputed values. [a] Patient populations are referred to by the name of their starting study; [b] Includes patients originally randomized to PBO up to Week 16; [c] In patients with enthesitis at baseline (LEI >0; BE OPTIMAL: n=213; BE COMPLETE: n=142); [d] In patients with dactylitis at baseline (LDI >0; BE OPTIMAL: n=89; BE COMPLETE: n=48); missing data imputed using NRI as MI was not estimable as it would not converge; [e] In patients with ≥3% body surface area affected by psoriasis at baseline (BE OPTIMAL: n=357; BE COMPLETE: n=264); [f] In patients with nail psoriasis at baseline (mNAPSI >0; BE OPTIMAL: n=400; BE COMPLETE: n=242); [g] In patients with baseline BASDAI ≥4 (BE OPTIMAL: n=524; BE COMPLETE: n=300; all patients in BE MOBILE 1 and 2); [h] Data were pooled for all randomized patients with nr-axSpA and r-axSpA in BE MOBILE 1 and 2.

ASAS40: Assessment in SpondyloArthritis international Society 40% improvement; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; bDMARD: biologic DMARD; BKZ: bimekizumab; GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MI: multiple imputation; mNAPSI: modified nail psoriasis severity index; mNRI: modified NRI; nr-axSpA: non-radiographic axSpA; NRI: non-responder imputation; OC: observed case; PASI100: 100% improvement from baseline in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every four weeks; r-axSpA: radiographic axSpA; SJC: swollen joint count; TJC: tender joint count; TNFi-IR: inadequate response or intolerance to tumor necrosis factor inhibitors; Y1: Year 1; Y3: Year 3.

Figure. GRAPPA individual domain response and change from baseline at Year 1 and Year 3 from BE OPTIMAL, BE COMPLETE, and pooled BE MOBILE 1 and BE MOBILE 2 (MI, mNRI, NRI, OC)

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated sustained efficacy to 3 years (yrs) in phase 3 clinical trials of patients (pts) with PsA, psoriasis, or axial spondyloarthritis (axSpA).[1–4] The Group for Research and Assessment of Psoriasis and PsA (GRAPPA)-based treatment recommendations focus on six core domains and the PsA-related conditions uveitis and IBD.[5] Here, long-term BKZ efficacy is shown across GRAPPA domains up to 3 yrs, corresponding to an additional 1 yr of BKZ treatment, from phase 3 trials in PsA and axSpA.

Methods: Included pts were randomized to subcutaneous BKZ 160 mg or placebo (PBO) every 4 weeks (wks; Q4W) in BE OPTIMAL (NCT03895203; biologic DMARD [bDMARD]-naïve pts with PsA), BE COMPLETE (NCT03896581; pts with PsA with inadequate response or intolerance to TNF inhibitors [TNFi-IR]), BE MOBILE 1 (NCT03928704; non-radiographic axSpA) and BE MOBILE 2 (NCT03928743; radiographic axSpA, i.e., AS). From Wk 16, all PBO-randomized pts received BKZ 160 mg Q4W. Wk 52/16 BE OPTIMAL/BE COMPLETE completers were eligible for BE VITAL open-label extension (OLE; NCT04009499); BE MOBILE 1 and 2 Wk 52 completers could enter BE MOVING (OLE; NCT04436640).

Outcomes reported by GRAPPA domain (**Table**) to Yr 3 (Wk 160/156 BE OPTIMAL/BE COMPLETE) in PsA; uveitis and IBD reported to Wk 156 (BE OPTIMAL/BE COMPLETE). We report axial domain outcomes in axSpA to assess BKZ efficacy in axial disease, in accordance with GRAPPA recommendations,[5] to Wk 164 (BE MOBILE 1/2). Missing data imputed using modified non-responder and multiple imputation (mNRI; MI) for binary and continuous outcomes, and reported using observed case (OC).

22265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Wk 160/156/164 completion was similar across all trials (BE OPTIMAL: 546/712 [76.7%], BE COMPLETE: 299/400 [74.8%], BE MOBILE 1: 175/254 [68.9%], BE MOBILE 2: 247/332 [74.4%]). Baseline demographics and disease characteristics were previously reported.[6–8]

For the majority of GRAPPA domains, 1-yr improvements were sustained to 3 yrs across all studies. Individual domain responses were consistent between bDMARD-naïve and TNFi-IR pts (**Figure**). Improvements in axial outcomes were sustained to 3 yrs in BE MOBILE 1 and 2 (**Table, Figure**). Exposure-adjusted incidence rates per 100 pt-yrs for uveitis and definite or probable adjudicated IBD to Wk 156 were 0.2 (95% confidence interval 0.1, 0.6) and 0.3 (0.1, 0.7) in BE OPTIMAL and 0 and 0.1 (0.0, 0.6) in BE COMPLETE, respectively.

Conclusion: BKZ treatment resulted in sustained and consistent improvements across GRAPPA domains from 1 to 3 yrs in both bDMARD-naïve and TNFi-IR pts with PsA, with low rates of IBD and uveitis reported. Results from studies in pts across the full disease spectrum of axSpA further support BKZ efficacy in the axial domain and suggest BKZ efficacy for axial disease in PsA.[8]

References: 1. Gossec L. Ann Rheum Dis 2025:*In press*; **2**. McInnes IB. Ann Rheum Dis 2025:*In press*; **3**. Warren RB. Br J Dermatol 2025;00:1–12; **4**. Baraliakos X. Ann Rheum Dis 2025:*In press*; **5**. Coates LC. Nat Rev Rheumatol 2022;18:465–79; **6**. Ritchlin CT. Ann Rheum Dis 2023;82:1404–14; **7**. Coates LC. RMD Open 2024;10:e003855; **8**. van der Heijde D. Ann Rheum Dis 2023;82:515–26.

Disclosure: J. Merola: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **A. Deodhar**: BMS, 2, 5, Eli Lilly and Company, 2, 5, 6, J&J, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **A. Gottlieb**: Amgen, 2, 4, 6, Avalo Therapeutics, 5, BMS, 5, Eli Lilly and Company, 2, 4, 6, Highlights Therapeutics, 2, 4, 6, Janssen, 2, 4, 5, 6, MoonLake Immunotherapeutics, 5, Novartis, 2, 4, 6, Sanofi, 2, 4, 6, Sun Pharma, 2, 4, 6, Takeda, 2, 4, 6, Teva, 2, 4, 6, UCB, 2, 4, 5, 6; **E. Soriano**: AbbVie, 5, 6, BMS, 5, 6, Eli Lilly, 5, 6, GSK, 5, 6, J&J, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, Raffo, 5, 6, UCB, 5, 6; **B. Ink**: AbbVie, 11, GSK, 11, UCB, 3, 11; **R. Bajracharya**: UCB, 3, 11; **J. Coarse**: UCB, 3, 11; **P. Mease**: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6.

Abstract Number: 2366

Association Between Skin and Joint Symptom Control and Patient-reported Pain and Health Status Among Patients with Psoriatic Arthritis in the Corevitas Psoriatic Arthritis/spondyloarthritis Registry Initiating Biologic or Targeted Synthetic Disease-modifying Antirheumatic Drugs

Philip J. Mease[1], Nicole Middaugh[2], Yolanda Muñoz Maldonado[2], Chao Song[3], Skyler Peterson[4], Robert Low[3] and Alexis Ogdie[5], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]CorEvitas, LLC, Waltham, MA, [3]UCB, Smyrna, GA, [4]CorEvitas, LLC, Waltham, [5]University of Pennsylvania, Philadelphia, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory condition primarily affecting the joints and skin.[1] More severe symptoms are associated with lower health-related quality of life, and many patients (pts) on recommended treatments (txs) achieve suboptimal responses.[2,3] This study evaluated association between degree of joint and/or skin symptom resolution and improvements in patient-reported outcomes (PROs) among pts with PsA who initiated biologic or targeted synthetic (b/ts) DMARDs in the CorEvitas PsA/Spondyloarthritis Registry, a prospective, non-interventional United States research registry.

Methods: Eligible pts had a PsA diagnosis and initiated a b/tsDMARD on or after registry entry (first therapy in Registry) between April 2017–March 2025. Included pts had either body surface area (BSA) affected by psoriasis ≥3% or swollen joint count in 66 joints (SJC) ≥1 at initiation and were tx-persistent at follow-up 6 months (range: 5–9 months) post-initiation. Changes from initiation to follow-up in EuroQoL Visual Analog Scale (EQ-VAS) and pain VAS scores were each fit to linear regression models using BSA and SJC at follow-up as continuous exposure variables with their interaction, and using a categorical variable combining BSA and SJC with 6 levels: BSA=0% and SJC=0; BSA=0% and SJC ≥1; BSA >0% to < 3% and SJC=0; BSA >0% to < 3% and SJC ≥1; BSA ≥3% and SJC=0; BSA ≥3% and SJC ≥1. Results were summarized with counts, means, and standard deviation (SD) for continuous variables, and counts and percentages for categorical variables.

Table 1. Baseline demographic, lifestyle, and disease characteristics among patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry initiating a b/tsDMARD therapy[a]

Characteristic	Total Patients Included (N=994)
Demographic Characteristics	
Age (years), mean (SD) [N]	54.1 (12.8) [994]
Sex (female), n/N (%)	581/991 (58.6)
Race (white), n/N (%)	877/977 (89.8)
Ethnicity (non-Hispanic or Latino), n/N (%)	811/893 (90.8)
Lifestyle Characteristics	
BMI, n/N (%)[b]	
Underweight/Normal (<25 kg/m²)	133/991 (13.4)
Overweight (≥25–<30 kg/m²)	261/991 (26.3)
Obese (≥30 kg/m²)	597/991 (60.2)
Private Insurance Only, n/N (%)	718/993 (72.3)
Full-Time Work Status, n/N (%)	547/992 (55.1)
Current Smoker, n/N (%)	125/987 (12.7)
Disease Characteristics	
Duration of PsA (years), mean (SD) [N]	6.2 (7.8) [990]
Age at PsA Onset (years), mean (SD) [N]	44.1 (14.2) [983]
Family History of PsA, n/N (%)	27/994 (2.7)
Treatment Characteristics	
Current PsA Therapy by MOA, n/N (%)	
TNFi[c]	419/994 (42.2)
IL-17i[d]	312/994 (31.4)
IL-23i[e]	118/994 (11.9)
JAKi[f]	76/994 (7.6)
IL-12/23i[g]	44/994 (4.4)
CD80/86i[h]	25/994 (2.5)
Comorbidities, n/N (%)	
Depression	199/994 (20.0)
Diabetes	167/994 (16.8)
Anxiety	122/994 (12.3)
Malignancies	106/993 (10.7)
Cardiovascular Disease	102/994 (10.3)
Osteoporosis	27/994 (2.7)
IBD	21/994 (2.1)
Uveitis	10/994 (1.0)

[a] Approved bDMARDs: abatacept, adalimumab, bimekizumab, certolizumab pegol, etanercept, golimumab, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, and ustekinumab; approved tsDMARDs: tofacitinib and upadacitinib; **[b]** CDC BMI categories for adults 20 year of age and older; **[c]** Adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab and its biosimilars; **[d]** Bimekizumab, ixekizumab, and secukinumab; **[e]** Guselkumab and risankizumab; **[f]** Tofacitinib and upadacitinib; **[g]** Ustekinumab; **[h]** Abatacept. b/tsDMARD: biologic or targeted synthetic disease-modifying antirheumatic drug; BMI: body mass index; CD: cluster of differentiation; CDC: Centers for Disease Control and Prevention; i: inhibitor; IBD: inflammatory bowel disease; IL: interleukin; JAK: Janus kinase; MOA: mechanism of action; PsA: psoriatic arthritis; SD: standard deviation; TNF: tumor necrosis factor.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Disease Activity and PRO Measures at Baseline and Follow-Up[a] among Patients with PsA in the CorEvitas PsA/Spondyloarthritis Registry

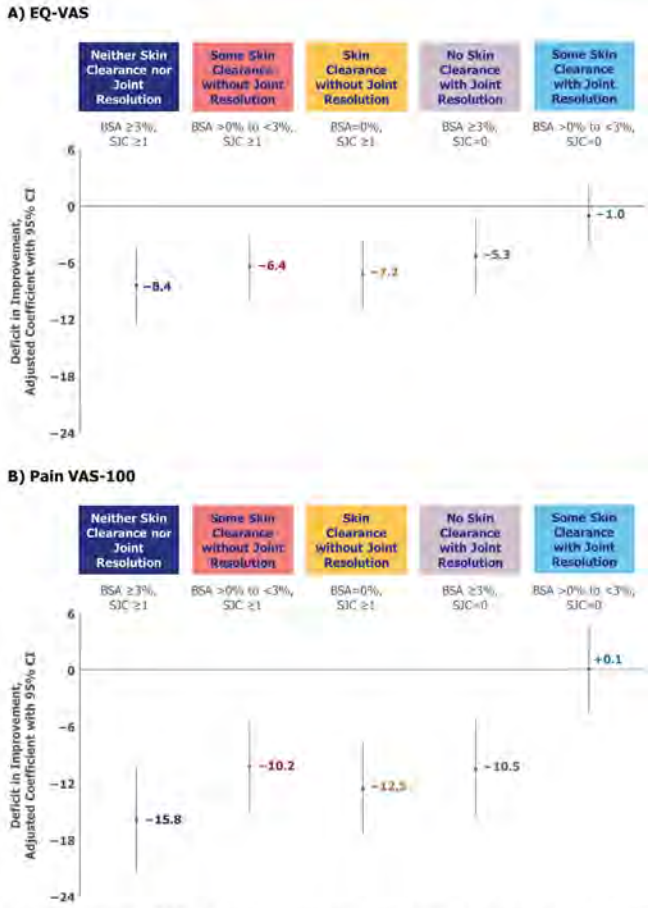
Characteristic	Baseline Visit at Biologic Initiation (N=994)	Follow-Up Visit 6 Months Post-Initiation (N=994)
Disease Activity Measures		
PGA of Arthritis (VAS-100), mean (SD) [N]	37.5 (24.0) [991]	18.7 (20.3) [974]
PGA of Arthritis and Psoriasis (VAS-100), mean (SD) [N]	42.9 (24.5) [993]	21.1 (21.6) [973]
BSA (% Involvement), mean (SD) [N]	7.7 (13.4) [980]	2.4 (5.2) [950]
BSA Category, n/N (%)		
Mild Disease (≥0–<3%)	464/980 (47.3)	721/950 (75.9)
Moderate Disease (≥3–<10%)	277/980 (28.3)	163/950 (17.2)
Severe Disease (10–100%)	239/980 (24.4)	66/950 (6.9)
Nail Psoriasis (VAS-100), mean (SD) [N]	10.8 (20.9) [978]	5.8 (14.4) [952]
TJC68, mean (SD) [N]	8.3 (10.4) [992]	4.6 (8.4) [946]
SJC66, mean (SD) [N]	4.3 (6.0) [992]	1.9 (3.7) [946]
cDAPSA (Score: 0–154), mean (SD) [N]	22.7 (16.7) [977]	14.2 (13.8) [929]
cDAPSA Category, n/N (%)		
Remission (≥0–≤4)	58/977 (5.9)	229/929 (24.7)
Low (>4–≤13)	218/977 (22.3)	297/929 (32.0)
Moderate (>13–≤27)	437/977 (44.7)	289/929 (31.1)
High (≥27–≤154)	264/977 (27.0)	114/929 (12.3)
IGA of Psoriasis, n/N (%)		
Clear (Score: 0)	219/984 (22.3)	412/963 (42.8)
Almost Clear (Score: 1)	147/984 (14.9)	252/963 (26.2)
Mild Disease (Score: 2)	275/984 (27.9)	183/963 (19.0)
Moderate Disease (Score: 3)	263/984 (26.7)	102/963 (10.6)
Severe Disease (Score: 4)	80/984 (8.1)	14/963 (1.5)
mPASDAS (Score: 0–10), mean (SD) [N]	4.8 (1.3) [699]	3.5 (1.6) [565]
Dactylitis Count (Score: 0–20), mean (SD) [N]	0.5 (1.5) [994]	0.2 (0.9) [994]
SPARCC Enthesitis Index (Score: 0–16), mean (SD) [N]	1.1 (2.4) [994]	0.6 (1.7) [994]
LEI (Score: 0–6), mean (SD) [N]	0.5 (1.1) [911]	0.3 (0.9) [892]
MDA, n (%) [N]	124 (12.5) [992]	371 (38.1) [974]
VLDA, n (%) [N]	15 (1.5) [993]	138 (14.0) [986]
mACR50 at Index Visit, n (%) [N]	–	96 (9.9) [969]
PRO Measures, mean (SD) [n]		
PtGA of Arthritis (VAS-100)	46.1 (26.5) [983]	36.0 (28.0) [978]
PtGA of Arthritis and Psoriasis (VAS-100)	46.7 (26.8) [984]	35.8 (28.0) [975]
HAQ-DI (Score: 0–3)	0.9 (0.7) [990]	0.7 (0.7) [983]
Pain (VAS-100)	53.5 (27.5) [987]	40.6 (28.5) [986]
Fatigue (VAS-100)	51.5 (28.3) [990]	42.6 (29.2) [986]
Spine Pain (VAS-100)	34.9 (31.2) [986]	28.9 (29.6) [982]
Morning Stiffness (VAS-100)	55.8 (28.8) [990]	41.9 (30.4) [984]
EQ-VAS (Score: 0–100)	62.0 (20.9) [990]	67.0 (20.7) [987]
EQ-5D-5L (Score: 0–1)	0.6 (0.3) [988]	0.7 (0.3) [982]
BASDAI (VAS-10)	5.1 (2.4) [982]	4.0 (2.5) [976]
WPAI: Currently Employed, n/N (%)	594/989 (60.1)	583/986 (59.1)
WPAI (Score: 0–100%)		
Absenteeism	9.7 (22.8) [551]	5.2 (16.5) [525]
Presenteeism	30.7 (27.8) [587]	23.0 (24.6) [569]
Work Impairment	35.8 (30.5) [548]	26.4 (26.8) [472]
Activity Impairment	43.0 (29.6) [979]	32.3 (28.8) [971]

[a] Follow-up was 6 months (range: 5–9 months) post-initiation. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BSA: body surface area; cDAPSA: Clinical Disease Activity Index for PsA; EQ-5D-5L: EuroQoL 5-Dimension 5-Level; EQ-VAS: EuroQoL VAS; HAQ-DI: Health Assessment Questionnaire Disability Index; IGA: Investigator Global Assessment; LEI: Leeds Enthesitis Index; mACR50: 50% Improvement in modified American College of Rheumatology response; MDA: minimal disease activity; mPASDAS: modified Psoriatic Disease Activity Score; PGA: Physician Global Assessment; PRO: patient-reported outcome; PsA: psoriatic arthritis; PtGA: Patient Global Assessment; SD: standard deviation; SJC66: swollen joint count in 66 joints; SPARCC: Spondyloarthritis Research Consortium of Canada; TJC68: tender joint count in 68 joints; VAS: Visual Analog Scale; VLDA: very low disease activity; WPAI: Work Productivity and Activity Impairment.

Results: Among 994 enrolled pts, mean age was 54.1 years; 581 (58.6%) were female, and 877 (89.8%) were white (-**Table 1**). At tx initiation, mean (SD) BSA was 7.7% (13.4%) and mean (SD) SJC was 4.3 (6.0). At follow-up, BSA and SJC decreased to 2.4% (5.2%) and 1.9 (3.7), respectively. Mean EQ-VAS increased 5.0 points and pain decreased 12.9 points from initiation (**Table 2**). Compared with pts achieving optimal response at follow-up (235 [25.2%]; BSA=0% and SJC=0), pts who did not achieve optimal response had improvements in EQ-VAS with deficits ranging from −1.0 (BSA >0% to < 3% and SJC=0) to −8.4 (BSA ≥3% and SJC ≥1) and improvements in pain VAS with deficits ranging from −10.2 (BSA >0% to < 3% and SJC ≥1) to −15.8 (BSA ≥3% and SJC ≥1). Pts with BSA >0% to < 3% and SJC=0 at follow-up had minimal deficit in pain VAS improvement (**Figure 1**). Using continuous BSA and SJC, pts who had joint resolution without skin clearance, or had skin clearance without joint resolution, had deficits in EQ-VAS and pain VAS improvement compared with pts who achieved both at follow-up.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Deficits in (A) EQ-VAS and (B) Pain VAS-100 improvement compared with patients who achieved optimal response[a] stratified by combined BSA and SJC categorical exposure variable



Negative values indicate a deficit in improvement compared with patients who achieved optimal response. P values for all categorical exposure variable coefficients in the linear regression models were <0.001 with the exceptions of change in EQ-VAS in BSA >0% to <3% and SJC=0 (p=0.562), change in EQ-VAS in BSA ≥3% and SJC=0 (p=0.010), and change in pain VAS in BSA >0% to <3% and SJC=0 (p=0.963). Values were adjusted for covariates. Covariates included in the model for change in EQ-VAS were age, BSA and SJC at biologic initiation and at follow-up 6 months post-initiation, fatigue, stiffness severity, EQ-VAS, PtGA of Arthritis and Psoriasis, and current use of opioids. Covariates included in the model for change in pain VAS-100 were PGA of Arthritis and Psoriasis, BSA and SJC at biologic initiation and at follow-up 6 months post-initiation, pain, fatigue, spine pain, WPAI, current employed status, prior use of b/tsDMARDs, current use of NSAIDs, and current use of opioids. **[a]** Optimal response was defined as BSA=0 and SJC=0. BSA: body surface area; b/tsDMARD: biologic or targeted synthetic disease-modifying antirheumatic drug; CI: confidence interval; EQ-VAS: EuroQoL VAS; NSAID: nonsteroidal anti-inflammatory drug; PGA: Physician Global Assessment; PtGA: Patient Global Assessment; SJC: swollen joint count in 66 joints; VAS: Visual Analog Scale; WPAI: Work Productivity and Activity Impairment.

Conclusion: In this real-world cohort, optimal achievement of both joint resolution and skin clearance remained low 6 months after b/tsDMARD initiation and was associated with greater improvements in PROs compared with achieving only joint resolution, only skin clearance, or neither. These results highlight the importance of complete skin and joint symptom control for pts with PsA compared with focusing on either aspect alone.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **N. Middaugh**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **Y. Muñoz Maldonado**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple pharmaceutical companies. This study was a collaborative effort with UCB.; **C. Song**: UCB, 3, 11; **S. Peterson**: CorEvitas, LLC, 3, 12, CorEvitas is supported through contracted subscriptions with multiple

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pharmaceutical companies. This study was a collaborative effort with UCB.; **R. Low**: UCB, 3, 11; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5.

Abstract Number: 2367

Real-World Effectiveness of Risankizumab on Axial Symptoms in Biologic-Naïve Patients With Psoriatic Arthritis in the United States and Europe

Philip J. Mease[1], Andrew Ostor[2], Christopher Saffore[3], Xiaolan Ye[4], Manish Patel[5], Ana Biljan[6], Ralph Lippe[5], Molly Edwards[7], Iwan Armstrong[7] and Xenofon Baraliakos[8], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Australian National University, Canberra, Australia, [3]AbbVie Inc., waukegan, IL, [4]AbbVie Inc., Mettawa, IL, [5]AbbVie Inc., North Chicago, IL, [6]AbbVie Inc., Buffalo Grove, IL, [7]Adelphi Real World, Bollington, United Kingdom, [8]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Axial involvement is a clinically relevant manifestation of psoriatic arthritis (PsA) that can influence management strategies. Evidence on the real-world effectiveness of advanced therapies, in particular, interleukin-23's (IL-23), on axial symptoms in PsA is scarce. This study aimed to evaluate the real-world effectiveness of risankizumab (RZB) on axial symptoms in routine clinical practice among biologic-naïve (bDMARD) patients with PsA across the United States (US) and Europe.

Methods: In this retrospective analysis (June 2023 to June 2024) using data from the Adelphi Spondyloarthritis VI Disease Specific Programme™, biologic-naïve patients with PsA receiving RZB 150 mg were included from the US and Europe (France, Germany, Italy, Spain, and the United Kingdom). The analysis was based on cross-sectional questionnaires completed by physicians and their consulting patients during their most recent visits. Effectiveness assessments of axial symptoms at treatment initiation and the most recent patient visit included change in the proportion of patients with physician-reported inflammatory back pain (IBP) or spinal pain, morning stiffness, pain on movement, pain at rest, nocturnal pain, persistent lower back pain, pain associated with morning stiffness, sleep disturbance, and sacroiliitis (either by X-ray or MRI). These outcome assessments were compared using McNemar tests ($P < .05$). Outcomes were evaluated in bDMARD-naïve ± conventional synthetic (cs)DMARD patients with PsA (overall patient population) and in bDMARD-naïve patients with an inadequate response (IR) to ≥ 1 csDMARD (csDMARD-IR/bDMARD-naïve).

Results: A total of 162 patients who initiated treatment with RZB were included in the analysis, with 62 (38%) from the US and 100 (62%) from Europe (**Table 1**). Patients were on average 44.8 years old at the time of data collection, 42% were female, 73% managed by rheumatologists, and body surface area (BSA) affected by psoriasis was 13.7% at treatment initiation. The mean duration of RZB treatment was 9.8 months, and the mean TJC68 and SJC66 at treatment initiation were 5.5 and 3.4, respectively. The csDMARD-IR/bDMARD-naïve subgroup comprised 96 patients with a mean age of 43.8, BSA of 16.4%, and mean TJC68 and SJC66 at treatment initiation of 5.1 and 2.5, respectively. The prevalence of IBP at treatment initiation was 28% in the overall group and 34% in the csDMARD-IR/bDMARD-naïve subgroup. Overall, the presence of all axial symptoms significantly decreased from treatment initiation to the most recent visit (all comparisons, $P < .001$) (**-Figure 1**). Significant improvements in axial symptoms were observed in the overall population and the csDMARD-IR/bDMARD-naïve subgroup (**Figure 1**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient Demographics and Clinical Characteristics

	bDMARD-naive (overall population)	csDMARD-IR/bDMARD-naive
Patient age	n=162	n=96
Mean (SD)	44.8 (10.2)	43.8 (8.8)
Patient Sex	n=162	n=96
Male	94 (58%)	56 (58%)
Female	68 (42%)	40 (42%)
Country	n=162	n=96
5EU	100 (62%)	83 (86%)
US	62 (38%)	13 (14%)
Ethnicity	n=157	n=91
White	133 (85%)	80 (88%)
Black	14 (9%)	6 (7%)
Other	11 (7%)	6 (7%)
Managing physician	n=162	n=96
Rheumatologist	118 (73%)	73 (76%)
Dermatologist	44 (27%)	23 (24%)
Months since risankizumab initiation	n=162	n=96
Mean (SD)	9.8 (5.4)	9.8 (5.4)
Years since diagnosis	n=158	n=95
Mean (SD)	3.5 (3.6)	4.9 (3.9)
Years since symptom onset	n=133	n=81
Mean (SD)	3.7 (3.4)	4.8 (3.8)
BSA at initiation	n=119	n=60
Mean (SD)	13.7 (10.0)	16.4 (9.3)
TJC at initiation	n=162	n=96
Mean (SD)	5.5 (7.4)	5.1 (7.2)
SJC at initiation	n=162	n=96
Mean (SD)	3.4 (5.6)	2.5 (5.2)
Concurrent medication use	n=162	n=96
csDMARDs	25 (15%)	25 (26%)
NSAIDs	11 (7%)	10 (10%)

Figure 1. Proportion of Patients with Presence of Axial Symptoms at Treatment Initiation and Most Recent Patient Visit

Note: Mean time between treatment initiation and most recent patient visit was 9.8 months for bDMARD-naïve patients and csDMARD-IR/bDMARD-naïve patients.

Conclusion: In real-world clinical settings, biologic-naïve patients with PsA who initiated RZB treatment demonstrated significant improvements in axial symptoms, highlighting effectiveness of RZB in managing a key manifestation of PsA.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **A. Ostor**: AbbVie Inc., 1, 2, 12, Clinical Trials, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Eli Lilly, 1, 2, 12, Clinical Trials, GlaxoSmithKlein, 1, 2, 12, Clinical Trials, Janssen, 1, 2, 12, Clinical Trials, Merck, 2, 5, Novartis, 1, 2, 12, Clinical Trials, Pfizer, 1, 2, 12, Clinical Trials, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **C. Saffore**: AbbVie, 3, 11; **X. Ye**: AbbVie, 3, 11; **M. Patel**: AbbVie, 3, 11; **A. Biljan**: AbbVie, 3, 11; **R. Lippe**: AbbVie, 3, 11; **M. Edwards**: AbbVie, 2, Adelphi Real World, 3; **I. Armstrong**: Adelphi Real World, 3, 12, Adelphi Real

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

World acted as a consultant to AbbVie for this analysis; **X. Baraliakos**: AbbVie, 2, 5, 6, 12, Paid Instructor, Advanz, 2, 6, 12, Paid instructor, Alexion, 2, 6, 12, Paid instructor, Alphasigma, 2, 6, 12, Paid instructor, Amgen, 2, 6, 12, Paid instructor, BMS, 2, 6, 12, Paid instructor, Celgene, 6, Celltrion, 2, 5, 6, 12, Paid instructor, Cesas, 2, 6, 12, Paid instructor, Chugai, 2, 6, Clarivate, 6, 12, Paid instructor, Galapagos, 2, 6, 12, Paid instructor, J&J, 2, 6, 12, Paid instructor, Janssen, 5, Lilly, 2, 6, 12, Paid instructor, Merck, 6, MoonLake, 2, 5, 6, 12, Paid instructor, MSD, 2, Novartis, 2, 5, 6, 12, Paid instructor, Peervoice, 2, 6, 12, Paid instructor, Pfizer, 2, 6, 12, Paid instructor, Roche, 2, 6, 12, Paid instructor, Sandoz, 2, 6, 12, Paid instructor, Springer, 2, 6, 12, Paid instructor, Stada, 2, 6, 12, Paid instructor, Takeda, 2, 6, 12, Paid instructor, UCB, 2, 6, 12, Paid instructor, Zuellig, 2, 6, 12, Paid instructor.

Abstract Number: 2368

Inhibition of Structural Damage Progression with Guselkumab, a Selective IL-23i, in Participants with Active PsA: Results Through Week 24 of the Phase 3b, Randomized, Double-Blind, Placebo-Controlled APEX Study

Philip J. Mease[1], Christopher Ritchlin[2], Laura Coates[3], Alexa P. Kollmeier[4], Bei Zhou[5], Yusang Jiang[5], Karen Bensley[5], Koeun Im[6], Rattandeep Batra[7], Soumya Chakravarty[8], Proton Rahman[9] and Désirée Van Der Heijde[10], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]University of Rochester Medical Center, Canandaigua, NY, [3]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom, [4]Johnson & Johnson, San Diego, CA, USA, San Diego, CA, [5]Johnson & Johnson, Spring House, PA, USA, Spring House, PA, [6]Johnson & Johnson, Cambridge, MA, USA, Cambridge, MA, [7]Johnson & Johnson, Toronto, ON, Canada, Toronto, ON, Canada, [8]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [9]Division of Rheumatology, Craig L. Dobbin Genetics Research Centre, Discipline of Medicine, Memorial University of Newfoundland, St. John's, Canada, [10]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

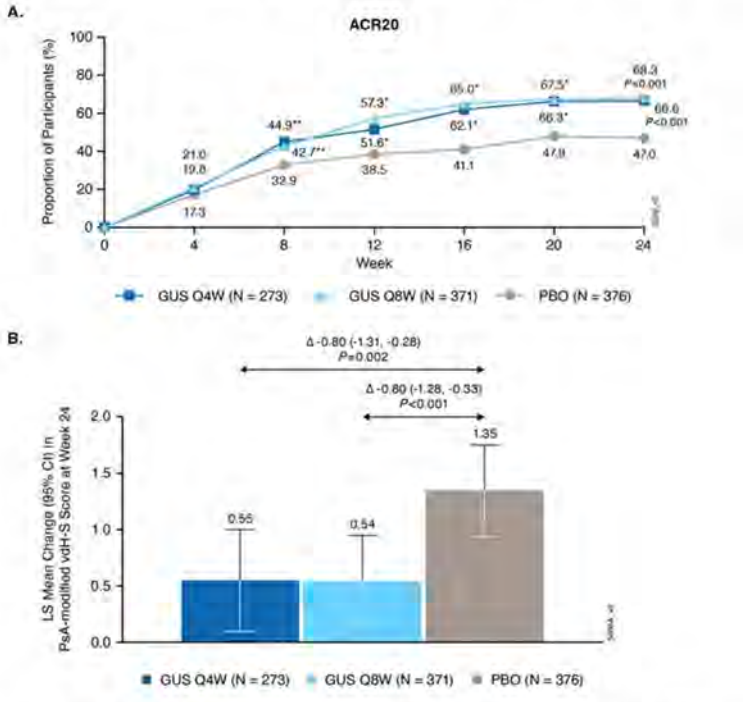
Session Time: 10:30AM–12:30PM

Background/Purpose: Patients with active psoriatic arthritis (PsA) are at risk of irreversible joint damage that may significantly impact quality of life. Guselkumab (GUS), a fully human monoclonal antibody that selectively targets IL-23p19 subunit and shows enhanced potency for inhibiting IL-23 signaling, has demonstrated efficacy and a favorable safety profile in patients with active PsA. The study reported findings through Week (W)24 of the ongoing phase 3b, randomized, double-blind, placebo (PBO)-controlled APEX study (NCT04882098), aimed at further evaluating GUS effects on clinical and radiographic outcomes in participants (pts) with active PsA.

Methods: APEX enrolled biologic-naïve adults with active PsA (≥3 tender and ≥3 swollen joints; C-reactive protein ≥0.3 mg/dL) and ≥2 joints with erosions on radiographs of hands and feet, despite previous non-biologic DMARDs, apremilast, or NSAIDs. Pts were randomized 5:7:7 to subcutaneous GUS 100mg Q4W; GUS 100mg at W0, W4, then Q8W; or PBO Q4W. The primary and major secondary endpoints were: 1) proportion of pts achieving ≥20% improvement in ACR response criteria (ACR20); 2) mean change from baseline (BL) in PsA-modified van der Heijde-Sharp (vdH-S) score (average of 2 readers blinded to chronological order), respectively, at W24 (both multiplicity-controlled for each GUS regimen vs PBO). Efficacy analyses include all randomized pts except those from Ukrainian sites unable to support key study operations (modified full analysis set [mFAS], N=1020); safety analyses include all pts who received ≥1 dose of study treatment through W24 (N=1054).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fig 1. Proportions of pts (mFAS) achieving ACR20 over time through W24 (A) and LS mean change from baseline to W24 in PsA-modified vdH-S score (Reading Session 1; B)



* nominal $P \leq 0.001$; ** nominal $P < 0.01$. P-values at W24 are multiplicity controlled using a fixed sequence testing procedure. For ACR20, p-values for W4-W20 are not multiplicity controlled, are considered nominal, and may not be used to claim statistical significance. For ACR20, p-values are based on CMH test. Participants were considered nonresponders if they discontinued study treatment for any reason other than ND/MD, initiation or increase in dose of csDMARD or oral corticosteroid, or initiation of protocol-prohibited PsA therapies. Missing data due to ND/MD, as well as data impacted by ND/MD, were imputed using multiple imputation. Other missing data were imputed using NRI. PsA-modified vdH-S score was an average of scores from two readers who were blinded to treatment and radiographic sequence. For PsA-modified vdH-S score at W24, statistics are based on ANCOVA. For PsA-modified vdH-S score at W24, missing data and data impacted by ND/MD were imputed using multiple imputation.

ACR20, ≥20% improvement in American College of Rheumatology response criteria; ANCOVA, Analysis of Covariance; CMH, Cochran Mantel Haenszel; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; GUS, guselkumab; LS, least squares; ND/MD, natural disaster/major disruption; NRI, nonresponder imputation; PBO, placebo; PsA, psoriatic arthritis; Q8W, every 8 weeks; Q4W, every 4 weeks; vdH-S, van der Heijde-Sharp; W, week.

Results: In mFAS (Q4W: 273, Q8W: 371, PBO: 376 pts), BL characteristics were generally balanced across treatment groups. The mean age was 53 yrs; 55% of pts were male. At BL, mean duration of PsA (7.3 yrs), PsA-modified vdH-S total (27.0) and erosion (13.5) scores, and tender (20.7) and swollen (11.9) joint counts indicated established and highly active joint disease. The primary and major secondary endpoints were met. Significantly greater proportions of GUS Q4W (67%) and Q8W (68%) vs PBO (47%) pts achieved ACR20 response at W24 ($P < 0.001$; **Fig 1A**). Pts receiving GUS Q4W and Q8W exhibited significantly less radiographic progression vs PBO at W24 (least squares mean changes in PsA-modified vdH-S score of 0.55 and 0.54 vs 1.35; $P=0.002$ and < 0.001, respectively; **Fig 1B**). Similar response patterns were seen for changes in joint space narrowing and erosion scores, proportions of pts with no radiographic progression, and additional clinical efficacy outcomes at W24 (**Table 1**).

Through W24, AEs occurred in 38%, 42%, and 37% of pts (most commonly respiratory infections, headache, diarrhea, and psoriatic arthropathy), and serious AEs occurred in 2%, 3%, and 3% of pts, in GUS Q4W, GUS Q8W, and PBO groups, respectively. No new safety signals were identified.

Conclusion: APEX is the first study to show significant inhibition of structural progression with both Q4W and Q8W of GUS, a dual-acting selective IL-23i. The GUS safety profile in these biologic-naïve pts with active PsA is consistent with that previously established for GUS across a broad range of pts with PsA, psoriasis, and/or inflammatory bowel disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Summary of other structural damage and clinical efficacy endpoints at W24 (mFAS)

	GUS Q4W (N=273)	GUS Q8W (N=371)	PBO (N=376)
Structural damage (Reading Session 1)			
Erosion score[a]	0.35 (0.07, 0.63)	0.32 (0.07, 0.57)	0.87 (0.61, 1.12)
P-value[a]	*0.002*	*<0.001*	
JSN score[a]	0.22 (0, 0.43)	0.24 (0.05, 0.43)	0.50 (0.31, 0.69)
P-value[a]	*0.025*	*0.027*	
No radiographic progression[b]	67%	63%	53%
P-value[c]	*<0.001*	*0.007*	
Clinical efficacy			
ACR50 response	41%	42%	20%
P-value[c]	*<0.001*	*<0.001*	
ACR70 response	22%	22%	11%
P-value[c]	*<0.001*	*<0.001*	
HAQ-DI[d,e]	-0.41 (-0.47, -0.35)	-0.42 (-0.47, -0.36)	-0.26 (-0.32, -0.21)
P-value[e]	*<0.001*	*<0.001*	
IGA 0/1 response[f,g]	73%	68%	31%
P-value[f]	*<0.001*	*<0.001*	
PASI 90 response[f,g]	69%	60%	22%
P-value[f]	*<0.001*	*<0.001*	

Data shown are LS Mean change from baseline or estimated response rates at Week 24. P-values comparing GUS Q4W and Q8W vs PBO are not multiplicity controlled. [a] Based on ANCOVA on MI data. [b] Defined as change in PsA-modified vdH-S score ≤0. [c] Based on CMH on MI data. [d]Among 271, 365, and 372 pts in the GUS Q4W, GUS Q8W, and PBO groups, respectively. [e] Based on MMRM. [f] Based on GLMM. [g]Among 159, 231, and 223 pts with ≥3% BSA and an IGA ≥2 at BL in the GUS Q4W, GUS Q8W, and PBO groups, respectively.

ACR50, ≥50% improvement in American College of Rheumatology response criteria; ACR70, ≥70% improvement in American College of Rheumatology response criteria; ANCOVA, Analysis of Covariance; BL, baseline; CI, confidence interval; CMH, Cochran Mantel Haenszel; GLMM, Generalized Linear Mixed Models; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire – Disability Index; IGA, Investigator's Global Assessment; JSN, joint space narrowing; LS, least squares; MI, multiple imputation; PASI 90, ≥90% improvement in Psoriasis Area and Severity Index; PBO, placebo; MMRM, mixed model repeated measures; PsA, psoriatic arthritis; Q8W, every 8 weeks; Q4W, every 4 weeks; vdH-S, van der Heijde-Sharp; W, week.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **C. Ritchlin**: AbbVie, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, Janssen, 2, 5, MoonLake Pharma, 2, Novartis, 2, 5, Solara, 2, UCB, 2; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **A. Kollmeier**: Johnson & Johnson, 3, 11; **B. Zhou**: Johnson & Johnson, 3, 11; **Y. Jiang**: Johnson & Johnson, 3, 11; **K. Bensley**: Johnson & Johnson, 3, 11; **K. Im**: Johnson & Johnson, 3, 11; **R. Batra**: Johnson & Johnson, 3, 11; **S. Chakravarty**: Johnson & Johnson, 3, 11; **P. Rahman**: Abbott, 2, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, UCB, 2; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2.

Abstract Number: 2369

Real-World On-Label Treatment Persistence Through 24 Months in Biologic-Naïve and Biologic-Experienced Patients with Psoriatic Arthritis: Comparison of Guselkumab versus Subcutaneous Interleukin-17A Inhibitors

Philip J. Mease[1], Jessica A. Walsh[2], Timothy P. Fitzgerald[3], Soumya Chakravarty[4], Elizabeth Adamson[5], Bruno Emond[6], Carmine Rossi[7], Samuel Schwartzbein[7], Kana Yokoji[7], Yuxi Wang[7], Patrick Lefebvre[7], Dominic Pilon[7], Shikha Singla[8] and Joseph F Merola[9], [1]Department of Rheumatology, Providence-Swedish Medical Center and University of Washington, Seattle, WA, [2]Division of Rheumatology, Salt Lake City Veterans Affairs Health and University of Utah Health, Salt Lake City, UT, [3]Johnson & Johnson, Horsham, PA, USA, PA, [4]Johnson & Johnson, Horsham, PA, USA; Drexel University College of Medicine, Philadelphia, PA, USA, Villanova, PA, [5]Johnson & Johnson, Horsham, PA, USA, Horsham, PA, [6]Analysis Group,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Inc., Montreal, QC, Canada, QC, [7]Analysis Group, Inc., Montreal, QC, Canada, QC, Canada, [8]Medical College of Wisconsin, Milwaukee, WI, [9]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Prior research reported that patients (pts) with psoriatic arthritis (PsA) treated with guselkumab (GUS) were 1.5x more likely to remain persistent with on-label treatment (tx) at 24 months (mo) vs those treated with subcutaneous (SC) interleukin-17A inhibitors (IL-17Ai; secukinumab or ixekizumab; Mease et al., CCR West 2024). However, there is a need for long-term real-world evidence comparing on-label tx persistence among biologic-naïve and biologic-experienced pts with active PsA initiating GUS vs SC IL-17Ai.

Methods: Adults with active PsA and ≥1 claim for GUS or SC IL-17Ai were selected from the IQVIA PharMetrics® Plus database (1/1/2011–6/30/2023; first claim = index date) to compare tx persistence among biologic-naïve and biologic-experienced pts. Pts were classified as biologic-experienced if they had ≥1 claim for PsA-indicated biologic DMARD (bDMARD) during the period of continuous insurance eligibility prior to the index date, and biologic-naïve otherwise. Pts had ≥12 mo of continuous insurance eligibility and no claims for confounding diseases/study medications prior to index date. On-label persistence was defined as no tx discontinuation and no dose modification per FDA-approved label. Baseline characteristics (12 mo prior to index date) between GUS and SC IL-17Ai cohorts were balanced separately for biologic-naïve and biologic-experienced pts using propensity score overlap weighting. For both populations, on-label persistence through 24 mo was compared between tx cohorts using weighted Kaplan-Meier (KM) curves and weighted Cox proportional hazards model.

Results: Among biologic-naïve pts, 362 GUS pts (mean age: 49.5 years [y]; 59.9% female [F]) and 845 SC IL-17Ai pts (mean age: 50.1y; 55.9% F) were included. Among biologic-experienced pts, 487 GUS pts (mean age: 49.9y; 59.5% F) and 1,756 SC IL-17Ai pts (mean age: 49.5 y; 60.7% F) were included. Weighted baseline characteristics were well-balanced between both tx cohorts among biologic-naïve and biologic-experienced pts. Among biologic-naïve pts, median time-to-discontinuation was 22.4 (GUS) vs 14.9 mo (SC IL-17Ai). For biologic-experienced pts, median time-to-discontinuation was 18.1 (GUS) vs 11.6 mo (SC IL-17Ai). Weighted KM on-label persistence rates among biologic-naïve pts at 6, 12, 18, 24 mo: 85.7%, 72.6%, 62.6%, 47.5% (GUS) vs 70.6%, 55.2%, 45.2%, 40.3% (SC IL-17Ai); for biologic-experienced pts, weighted KM on-label persistence rates: 76.7%, 54.4%, 51.0%, 43.3% (GUS) vs 67.1%, 48.6%, 39.3%, 32.0% (SC IL-17Ai) (all log-rank p≤0.01). Pts initiating GUS were significantly more likely to be persistent at 24 mo among both biologic-naïve (HR: 1.70, 95% CI: 1.32–2.20; p< 0.001) and biologic-experienced populations (HR: 1.33, 95% CI: 1.11–1.59; p=0.002).

Conclusion: This real-world study assessing long-term tx persistence among pts with active PsA in the US showed that GUS was associated with significantly greater rates of on-label tx persistence through 24 mo among both biologic-naïve and biologic-experienced pts, compared to pts using SC IL-17Ai. Sustained long-term on-label use may enhance disease management, leading to better functional status and quality of life.

Disclosure: P. Mease: AbbVie, 2, 5, 6, Acelyrin, 2, 5, Amgen, 2, 5, 6, BMS, 2, 5, Century, 2, Cullinan, 2, Eli Lilly and Company, 2, 5, 6, Inmagene, 2, J&J Innovative Medicine, 2, 5, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sana, 5, Spyre, 5, Takeda, 2, UCB, 2, 5, 6; **J. Walsh**: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Spyre, 2, 5, UCB, 2, 5; **T. Fitzgerald**: Johnson & Johnson, 3, 11;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

S. Chakravarty: Johnson & Johnson, 3, 11; **E. Adamson**: Johnson & Johnson, 3, 11; **B. Emond**: Analysis Group, Inc., 3, 11; **C. Rossi**: Analysis Group, Inc., 3, 11; **S. Schwartzbein**: Analysis Group, Inc.,, 3, 11; **K. Yokoji**: Analysis Group, Inc., 3, 11; **Y. Wang**: Analysis Group, Inc., 3, 11; **P. Lefebvre**: Analysis Group, Inc., 3, 11; **D. Pilon**: Analysis Group, Inc., 3, 11; **S. Singla**: AbbVie/Abbott, 2, Eli Lilly, 5, Janssen, 2, 6, Prometheus Biosciences, 5, UCB, 2; **J. Merola**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5.

Abstract Number: 2370

Comparative Efficacy and Safety of IL-17 Inhibitors Versus Adalimumab in Biologic-Naive Psoriatic Arthritis Patients: A Meta-Analysis of Randomized Controlled Trials

Punith Chirumamilla[1], Ravi Medarametla[2], Anjani Mahesh Kumar Cherukuri[3], Sri Laxmi Priya Sunkara[4], Pranathi Bandarupalli[5], Rithish Nimmagadda[6], Greeshma Erasani[7], Pavana Sakhamuri[8] and Stephen Lindsey[9], [1]Baptist Memorial Hospital North Mississippi, Oxford, MS, [2]Mamata Medical College, Guntur, Andhra Pradesh, India, [3]Guntur Medical College, Guntur, Andhra Pradesh, India, [4]White river medical center, batesville, AR, [5]Mercy St Vincent Medical Center, Toledo, OH, [6]One Brooklyn Health, New York, NY, [7]University of Missouri-Kansas city school of medicine, KCMO, MO, [8]LSUHSC, Lafayette, LA, [9]LSU Health Sciences Center-New Orleans, Baton Rouge, LA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic immune-mediated disease which involves joints, skin, and nails, leading to deformities, decreased function, lower quality of life, and in many cases higher mortality. While traditional synthetic DMARDs and TNF inhibitors(TNFi), such as adalimumab, are effective existing treatments, they both have their shortcomings. Despite this, most patients with PsA do not achieve complete disease remission with synthetic DMARDs, and TNFi may be ineffective for skin, and lose efficacy over time, or be limited for long-term use due to safety concerns. IL-17 inhibitors target a separate inflammatory pathway and have demonstrated greater skin clearance and comparable joint improvement compared with TNFi in clinical trials at 52 weeks. This meta-analysis compares IL-17i versus adalimumab in biologic-naive PsA populations to evaluate safety and efficacy of using IL-17i in PsA patients.

Methods: We systematically searched PubMed, Embase, Cochrane for English-language studies involving comparison of treatment effects between IL-17i and Adalimumab, and reported at least one relevant outcome. Three studies met inclusion criteria. Data were pooled using the inverse variance weighting method with a random-effects model in R Studio. Confidence intervals and heterogeneity were assessed, and forest plots were generated to visualise the pooled effect estimates.

Results: Three studies(Randomized controlled trials) involving 1990 patients were included. Analysis of IL-17i versus Adalimumab revealed comparable ACR50 responses (RR=1.06, 95% CI: 0.97–1.16, p=0.22) but significantly higher PASI75 achievement with IL-17i (RR=1.21, 95% CI: 1.11–1.31, p< 0.0001). The primary composite outcome (ACR50+PASI100) strongly favored IL-17i (RR=1.49, 95% CI: 1.26–1.78, p< 0.01). Serious adverse events were slightly less in IL-17i group but that change is not significant (RR=0.72, 95% CI: 0.35–1.50, p=0.38), and also IL-17i demonstrated significantly lower discontinuation rates due to adverse events (RR=0.56, 95% CI: 0.38–0.82, p< 0.01).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1a: ACR50

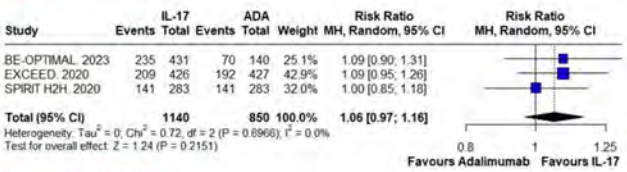


Figure 1b: PASI75

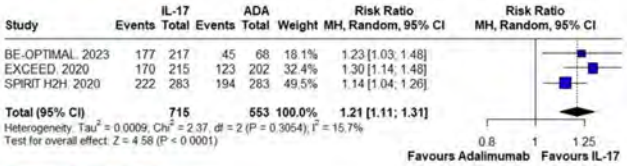


Figure 1c: PASI100

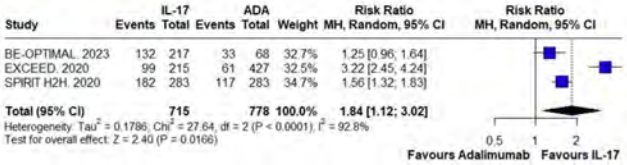


Figure 2a: ACR50 + PASI100

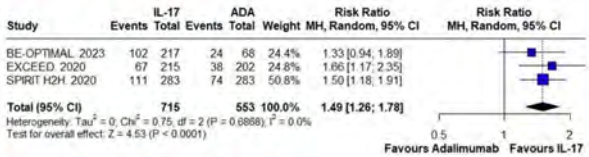


Figure 2b: Serious Adverse Events

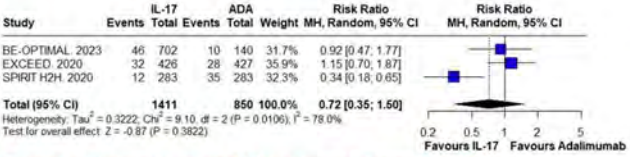
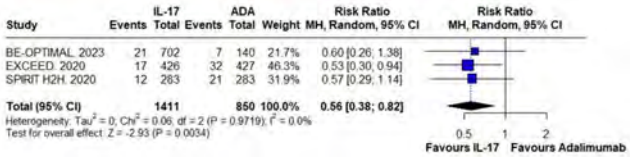


Figure 2c: Discontinuation of Drug due to Adverse Events



Conclusion: In biologically naive PsA patients, IL-17i showed comparable joint response, but has higher skin clearance compared to Adalimumab. IL-17i also has fewer discontinuations due to drug adverse events and overall it showed to be a great treatment option. Future Research should direct towards long-term outcomes and combination therapies to improve treatment algorithms.

Disclosure: P. Chirumamilla: None; **R. Medarametla**: None; **A. Cherukuri**: None; **S. Sunkara**: None; **P. Bandarupalli**: None; **R. Nimmagadda**: None; **G. Erasani**: None; **P. Sakhamuri**: None; **S. Lindsey**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2371

A Predictive Model Combining Clinical and Laboratory Parameters to Predict Anti-tnf Response in Patients with Psoriatic Arthritis

Raquel Granados[1], Jesús Eduardo Martín Salazar[2], María Ángeles Puche-Larrubia[3], Pedro Ortiz Buitrago[4], María Dolores López-Montilla[5], Jerusalén Calvo[6], Rafaela Ortega-Castro[7], Montserrat Romero-Gómez[8], Alejandro Escudero-Contreras[9], Nuria Barbarroja[10] and Clementina López Medina[11], [1]Hospital Universitario Reina Sofia, Cordoba, Andalucia, Spain, [2]Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba/ Reina Sofia University Hospital, Rheumatology service/Department of Medical and Surgical Sciences, Cordoba, Spain, Cordoba, Andalucia, Spain, [3]Reina Sofia University Hospital, Granada, Spain, [4]Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), Cordoba, Andalucia, Spain, [5]Rheumatology Department, Reina Sofía University Hospital, Cordoba/IMIBIC/University of Cordoba., CORDOBA, Spain, [6]IMIBIC / Reina Sofia Hospital / University of Cordoba, Córdoba, Spain, [7]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [8]Reina Sofia University Hospital, Cordoba, Andalucia, Spain, [9]Reina Sofia University Hospital/Maimonides Institute of Biomedical Research of Córdoba (IMIBIC)/University of Cordoba, Cordoba, Andalucia, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S. l, Cordoba, Spain, Cordoba, Spain, [11]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease requiring individualized treatment strategies. Early identification of patients likely to respond to therapy is essential to optimize outcomes and avoid unnecessary treatment exposure. Hematologic and inflammatory biomarkers, readily available in clinical practice, may offer predictive value in guiding treatment decisions. In this study, we aimed to identify a combination of clinical data and routinely available laboratory markers capable of reliably predicting which patients with PsA will respond to TNF inhibitors (TNFi).

Methods: This was a prospective analysis including 68 patients diagnosed PsA who fulfilled the CASPAR criteria. A multivariable logistic regression model was initially constructed using routinely measured inflammatory and hematologic parameters, with Disease Activity index for Psoriatic Arhritis (DAPSA) response as the dependent variable, defined as an improvement of >50% in the DAPSA score. To optimize model simplicity and performance, stepwise variable selection was applied in both forward and backward directions, based on the Akaike Information Criterion (AIC). This method iteratively adds or removes predictors to identify the model with the best balance between goodness-of-fit and parsimony. Model performance was evaluated using classification accuracy and the area under the ROC curve (AUC).

Table 1. Multivariate Analysis of Independent Factors Associated with Achieving >50% improvement in DAPSA after 6 months.

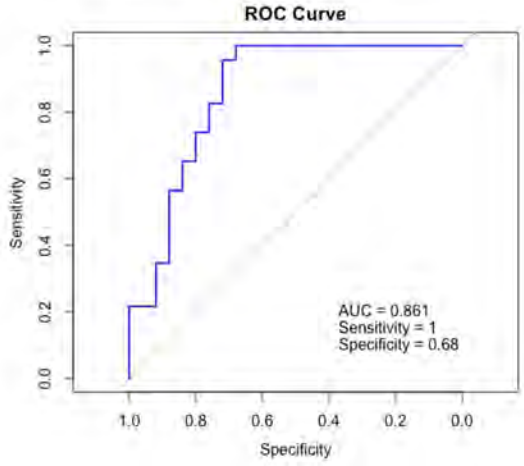
Table 1. Multivariate Analysis of Independent Factors Associated with Achieving >50% improvement in DAPSA after 6 months.

	OR (95%CI)	p-value
NLR	1.56 (0.87 – 3.23)	0.192
LMR	0.69 (0.40 – 1.06)	0.121
Complement C3 (mg/dL)	1.04 (1.01 – 1.08)	0.023
ESR (mm/H)	0.93 (0.87 – 0.98)	0.016
Baseline DAPSA	1.08 (0.98 – 1.21)	0.135

Hosmer and Lemeshow goodness of fit (GOF) test: X-squared = 8.2451, df = 8, p-value = 0.4099
DAPSA: Disease Activity index for Psoriatic Arhritis; ESR: erythrocyte sedimentation rate; LMR: lymphocyte-to-monocyte ratio; NLR: neutrophil-to-lymphocyte ratio;

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Receiver Operating Characteristic (ROC) Curve for the Prediction of TNFi response in PsA.



Results: A total of 68 patients were included, 55.8% of whom were male, with a mean age of 50 years (SD 16.7) and a mean disease duration of 7.2 years. A total of 31 patients (45.6%) responded to TNFi. The multivariable analysis (Table 1) identified five independent factors associated with achieving >50% improvement in DAPSA after 6 months: neutrophil-to-lymphocyte ratio (NLR) (OR 1.56), lymphocyte-to-monocyte ratio (LMR) (OR 0.69), complement C3 (OR 1.04), erythrocyte sedimentation rate (ESR) (OR 0.93), and baseline DAPSA score (OR 1.08). The final model demonstrated excellent discrimination, with an AUC of 0.861 (95% CI: 0.752–0.970) (Figure 1). It correctly classified 100% of the responders (sensitivity = 1.00) and 68% of the non-responders (specificity = 0.68).

Conclusion: A combination of routinely available hematologic and inflammatory markers can effectively predict clinical response to TNFi in patients with PsA, but further validation of this model is needed in independent cohorts. This predictive model may support more personalized and efficient treatment decisions in routine clinical practice.

Disclosure: R. Granados: None; **J. Martín Salazar**: None; **M. Puche-Larrubia**: None; **P. Ortiz Buitrago**: None; **M. López-Montilla**: None; **J. Calvo**: None; **R. Ortega-Castro**: None; **M. Romero-Gómez**: None; **A. Escudero-Contreras**: None; **N. Barbarroja**: None; **C. López Medina**: None.

Abstract Number: 2372

Treatment Outcome and Persistence of IL-23 Inhibitors in Real World Cohort of PsA Patients- A Retrospective Study

Dana Rosenberg[1], Dafne capelusnik[2], Shai Shtrozberg[3], Ori Elkayam[4] and **Reut Tzemach**[5], [1]Sourasky medical center Tel aviv ISRAEL, TEL AVIV, Israel, [2]Tel Aviv Sourasky Medical Center, Ramat Gan, Israel, [3]Sourasky medical center Tel aviv ISRAEL, TEL AVIV, [4]Tel Aviv medical center, Tel Aviv, Israel, [5]Sourasky medical center Tel aviv ISRAEL, Tel Aviv-Yafo, Israel

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: In recent years, IL-23 inhibitors (IL23i)-have emerged as promising therapeutic options for psoriatic arthritis patients (PsA). Clinical trials have demonstrated their efficacy in both treatment-naïve patients and those with an inadequate response to TNF inhibitors [1-2] . However, real-world data on their effectiveness and long-term drug survival remain limited. This study aimed to evaluate the effectiveness, drug survival and reasons for therapy discontinuation of two IL-23i - Guselkumab and Risankizumab- in a cohort of PsA patients, reflecting real-world clinical practice.

Methods: We conducted a retrospective study of PsA patients, diagnosed according to the CASPAR criteria, who initiated treatment with Guselkumab or Risankizumab between 2019 and July 2024.

Data was extracted from medical records and included demographic and clinical parameters, along with disease activity scores - DAPSA and PASI- assessed at four time points during follow up: baseline (treatment initiation), 6 months, 12 months and the last follow up visit. IL-23i effectiveness was evaluated by means of DAPSA score with DAPSA≤14 indicating good clinical response. Reasons for treatment discontinuation were documented, and drug survival was analyzed using Kaplan-Meier plots.

Results: A total of 61 PsA patients were included (Table 1).

At baseline, the majority (57%) had moderate to high disease activity (DAPSA >14), while 18% were in remission (DAPSA ≤4) but had active skin involvement (mean PASI 6.75).

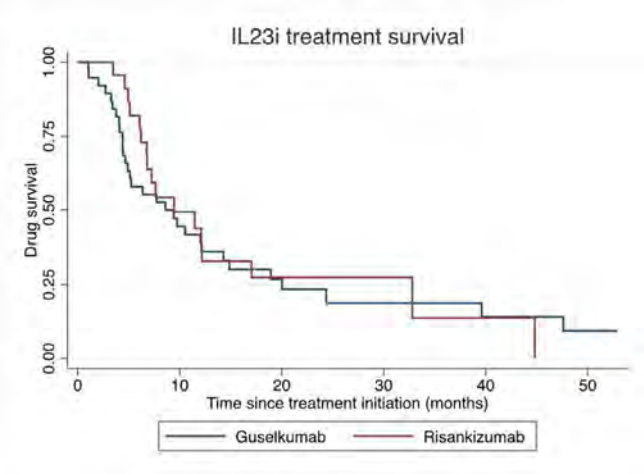
For most patients (80%), IL-23 inhibitors were the fourth or later b/tsDMARDs used, indicating a difficult-to-treat population.

By 6 months, 43% of patients achieved a DAPSA score ≤14, of whom 52% had a baseline DAPSA ≤14. This proportion declined to 30% by 12 months. Treatment discontinuation occurred in 30% of patients at 6 months and in 54% at 12 months. The primary reasons for discontinuation were persistent joint disease (65% at 6 months and 42% at 12 months) and combined joint and skin non-response (18% at 6 months, 24% at 12 months). Only 9% of patients discontinued therapy due to isolated skin disease activity.

Table 1. Clinical characteristics of PsA patients at baseline

	Total population (n=61)
Age, years, mean (±sd)	55 (13)
Female sex (%)	31 (51)
IL23 drug	
Guselkumab (%)	38 (62)
Risankizumab (%)	23 (38)
Concomitant DMARDs (%)	19 (32)
MTX	7 (58)
LFN	2 (17)
Apremilast	1 (8)
Prednisone	2 (17)
Last treatment before IL23i	
TNFi (%)	19 (32)
IL17i (%)	24 (40)
JAKi (%)	8 (13)
IL23i (%)	8 (13)
IL12/23i (%)	1 (2)
Number of b/tsDMARDs before IL23i, mean (±sd)/median (range)	4.4 (2.0) / 4 (3-5)
Baseline DAPSA (n=57), mean (±sd)	20.5 (15.4)
DAPSA categories	
Remission (%)	10 (18)
Low disease activity (%)	12 (21)
Moderate disease activity (%)	21 (37)
High disease activity	14 (25)
Calculated CRP (n=58), mean (±sd)	0.50 (0.97)
Reported CRP (n=23), mean (±sd)	1.14 (1.21)
TJC68 (n=57), mean (±sd))/median (range)	5.3 (5.7) / 2 (0-6)
SJC66 (n=57), mean (±sd)median (range)	3.8 (4.9) / 4 (0-8)
PGA (n=57), mean (±sd)	5.5 (3.3)
PASI (n=47), mean (±sd)	6.4 (5.4)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



IL23i treatment survival

Overall, 78% of patients discontinued treatment, with a median duration of 9.4 months (range: 4.9–24.4 months).

No significant differences were observed between Guselkumab and Risankizumab treatment groups.

Conclusion: In this real-world cohort of biologic-experienced, difficult-to-treat PsA patients, IL-23 inhibitors demonstrated modest effectiveness and low treatment persistence. The high discontinuation rate—primarily due to insufficient joint disease control—underscores the need for alternative therapeutic strategies in this challenging patient population.

Bibliography:

1. Deodhar, Atul et al. *Lancet*. 2020.
2. Östör, Andrew et al. *Annals of the rheumatic diseases*. 2022.

Disclosure: D. Rosenberg: None; **D. capelusnik**: None; **S. Shtrozberg**: None; **O. Elkayam**: AbbVie/Abbott, 6, Janssen, 6; **R. Tzemach**: None.

Abstract Number: 2373

Effectiveness and Tolerability of Guselkumab or TNF inhibitors as Second-Line Treatment After Receiving a TNF inhibitor as First-Line Therapy to Treat Active Psoriatic Arthritis: 52-Week Interim Data from the Manhattan Study

Rocio Gonzalez Molina[1], BEATRIZ JOVEN[2], Marta Llanes[3], Vanesa Hernandez[4], Manuel Jose Moreno[5], Elena Blanco[6], Carolina Marin[7], Lourdes Mateo[8], Meritxell Salles Lizarzaburu[9], Martina Steiner[10], Laura Nuño[11], Antonio Fernández-Nebro[12], raúl Veroz González[13], ana Urruticoechea-Arana[14], Evelin Cervantes[15], emilio Giner[16], Lola Fernandez de la fuente Burson[17], Alba Erra[18], Oscar Camacho[19], Elisabet Garcia[20], Angeles Hernandez[21], Janire Malave[22], Laia Orpinell[23], Inmaculada Ros Vilamajo[24], Sonia Castro[25], Patricia Lopez Viejo[26], Luis Sarabia[27], Rosa María García Portales[28], Jorge Cabezon[29], Puerto Moreno Gil[30], Francisco Maceiras[31], Daniel Pielfort[32], Sabela Diaz-Castroverde[33], Manuel Cuervasmons[33], Jose Pinto-Tasende[34], Santiago Muñoz[35] and Julio Ramirez[36], [1]Hospital Reina Sofia, Murcia, Spain, [2]H. Universitario 12 Octubre, Madrid, Spain, [3]H Juan Ramón Jimenez, Huelva, Spain, [4]Hospital Universitario Canarias, Tenerife, Spain, [5]Hospital Universitario Virgen de la Arrixaca, El Palmar Murcia, Spain, [6]Hospital Virgen del Rocio, Sevilla, Spain, [7]Hospital Infanta Leonor, Madrid, Madrid, Spain, [8]Hospital Trías i Pujol, Barcelona, Catalonia, Spain, [9]Rheumatology Department, Althaia Xarxa Assistencial Universitària Manresa Manresa (Spain)., Manresa, Spain, [10]Hospital Universitario Infanta Sofía;Universidad Europea de Madrid. Faculty of Medicine, Health and Sports.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Department of Medicine; FIIB HUIS-HUHEN, Madrid, Madrid, Spain, [11]Hospital Universitario Puerta de Hierro, Madrid, Spain, [12]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [13]Rheumatology. Hospital de Mérida. Mérida, Spain., Mérida, Spain, [14]Rheumatology Division. Hospital Universitario Son Espases, Palma de Mallorca, Spain, [15]Hospital Provincial de Pontevedra, Pontevedra, Spain, [16]Hospital Royo Vilanova, Zaragoza, Spain, [17]Hospital Quironsalud Infanta Luisa, Sevilla, Spain, [18]Hospital Vall d´Hebron, Barcelona, Spain, [19]Hospital de Sant Joan Despí Moisès Broggi, Barcelona, Spain, [20]Hospital Mollet, Barcelona, Spain, [21]Hospital Naval, A Coruña, Spain, [22]Hospital Virgen del Puerto, Caceres, Spain, [23]Hospital Universitari Sagrat Cor, Barcelona, Spain, [24]Hospital Son Llàtzer, Palma de Mallorca, Spain, [25]ALTHAIA Hospital Sant Joan de Deu, Barcelona, Spain, [26]Hospital Universitario Getafe, Getafe, Spain, [27]Complejo Hospitalario de Jaén, Jaén, Spain, [28]HOSP. UNIVERSITARIO VIRGEN DE LA VICTORIA, Malaga, Spain, [29]HOSP. PUNTA DE EUROPA, Algeciras, Spain, [30]HOSPITAL SAN PEDRO DE ALCANTARA, Caceres, Spain, [31]HOSPITAL DO MEIXOEIRO, Vigo, Spain, [32]Hospital General Universitario de Toledo, Toledo, Spain, [33]Johnson and Johnson, Madrid, Spain, [34]Complexo Hospitalario Universitario de A Coruña, A Coruña, Spain, [35]Hospital Universitario Infanta Sofía; Universidad Europea de Madrid. Faculty of Medicine, Health and Sports. Department of Medicine; FIIB HUIS-HUHEN, Madrid, Spain, [36]Clinic Barcelona Hospital Universitari, Barcelona, Catalonia, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease affecting joints, entheses, skin, nails, and spine. While treatment options have expanded, TNF inhibitors (TNFis) remain the most common first-line biologic in Spain due to favorable efficacy, safety, and reimbursement. However, evidence on biologic therapeutic sequencing remains limited, particularly regarding effectiveness and drug persistence.

The Manhattan study (CNTO1959PSA4009) assessed persistence, effectiveness, and tolerability of guselkumab (GUS), an anti-IL-23 inhibitor, compared to a second TNFi in adults with PsA who had failed to a prior first-line TNFi therapy.

Table 1. Demographic characteristics.

	Second-line GUS	Second-line TNFi
Sex, n (%)		
Male	39 (39.8%)	36 (46.8%)
Female	59 (60.2%)	41 (53.2%)
Age at PsA diagnosis (years), mean (SD)	44.8 (11.7)	44.2 (11.9)
BMI (kg/m²), mean (SD)	28.1 (6.3)	26.6 (5.5)
Comorbidities[1]	62 (63.3%)	52 (67.5%)
Arterial hypertension	19 (30.6%)	21 (40.4%)
Diabetes	13 (21.0%)	6 (11.5%)
Anxiety/drepression	12 (19.4%)	6 (11.5%)
Heart disease	7 (11.3%)	6 (11.5%)
PsA characteristics, n (%)		
Polyarticular PsA	58 (59.2%)	49 (63.6%)
Oligoarticular PsA*	34 (35.1%)	21 (27.3%)
Axial affectation*	22 (22.7%)	19 (24.7%)
Active psoriasis	66 (67.3%)	34 (44.2%)
Nail psoriasis*	33 (34.0%)	26 (33.8%)
Dactylitis*	15 (15.5%)	14 (18.2%)
Enthesitis*	21 (21.6%)	28 (36.4%)
Distal interphalangeal arthritis*	11 (11.3%)	15 (19.5%)
Mutilating arthritism*	4 (4.1%)	3 (3.9%)
TJC**, mean (SD)	6.1 (7.0)	5.2 (5.4)
SJC**, mean (SD)	3.3 (4.5)	2.7 (3.8)
DAPSA*, mean (SD)**	22.9 (13.4)	21.4 (11.5)
BSA**, mean (SD)**	4.3 (6.8)	2.3 (5.0)
Most common first-line TNFi, n (%)	Adalimumab, 71 (72.4%)	Adalimumab, 50 (64.9%)
Most common second-line TNFi, n (%)	NA	Etanercept, 31 (40.3%)
Concomitant conventional DMARDs, n (%)	42 (42.9%)	34 (44.2%)

[1]Based on n=114 patients (65.1%) with any comorbidity; * Of a total of 97 patients in the GUS group and 77 in the TNFi group; ** Of a total of 74 patients in the GUS group and 65 patients in the TNFi group; *** Of a total of 64 patients in the GUS group and 51 patients in the TNFi group; **** Of a total of 60 patients in the GUS group and 40 patients in the TNFi group.
NA: non applicable; DMARDs: disease-modifying antirheumatic drugs

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

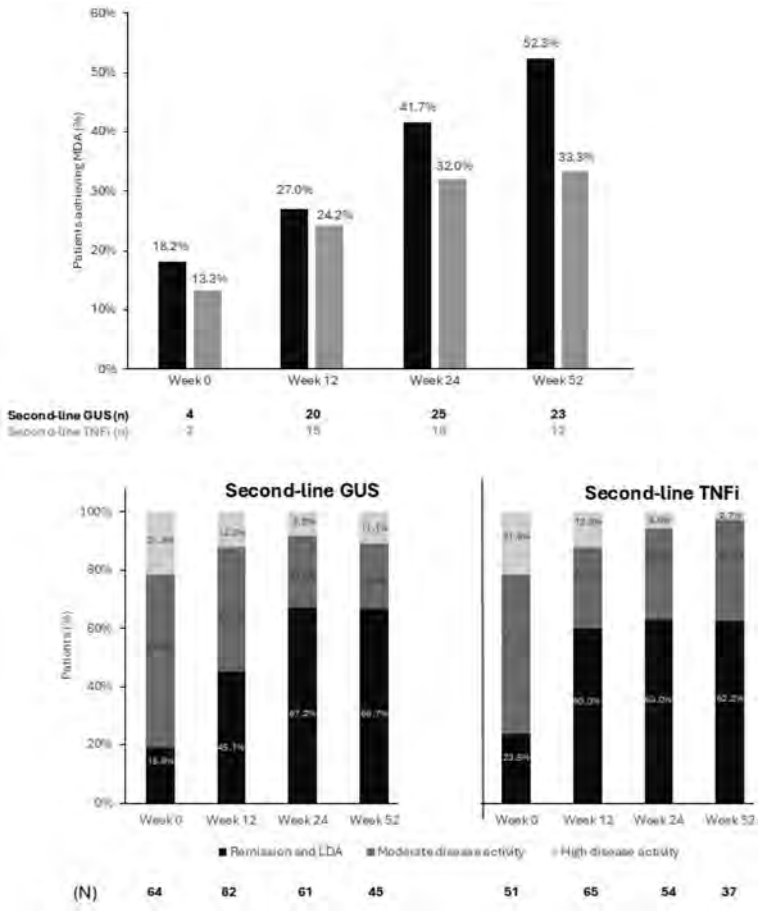


Figure 1. a) Percentage of patients achieving minimal disease activity (MDA) in second-line treatment (GUS or TNFi at week 0, week 12, 24 and 52). MDA was achieved if 5 of 7 criteria were met: TJC ≤1; SJC ≤1; BSA ≤ 3%; patient's assessment of pain by visual analogue scale (VAS) ≤15 mm; patient's global assessment of disease activity by VAS ≤20 mm; Health Assessment Questionnaire ≤0.5; and tender entheseal points ≤ 1 (assessed by the Leeds Enthesitis Index). b) percentage of patients achieving remission and low disease activity, moderate or high disease activity.

Methods: Manhattan is an ongoing ambispective, observational study across 37 Spanish centers. It includes PsA patients who switched to GUS or a second-line TNFi following first-line TNFi use. Among 193 recruited, 175 (98 on GUS and 77 on TNFi) patients were evaluated in this interim analysis regarding effectiveness and tolerability. Baseline data, and prior/ concomitant treatments were recorded. Endpoints included rates of disease activity (minimal (MDA), DAPSA low (LDA)/ remission), presence of dactylitis, nail psoriasis, enthesitis measurement (by the Leeds Enthesitis Index [LEI]), functioning and disability using the Health Assessment Questionnaire (HAQ), mean changes in psoriatic body surface area (BSA), and tender (TJC), and swollen joint count (SJC). Adverse events (AE) and drug-related events were recorded. Effectiveness and tolerability interim results up to week (W) 52 are presented.

Results: Baseline characteristics were similar across groups (Table 1).

MDA achievements increased to 52.3% (GUS) and 33.3% (TNFi) at W52 (Fig. 1A). DAPSA Remission/LDA rates rose from 18.8% at baseline to 66.7% at W52 (GUS), and from 23.5% to 62.2% (TNFi), respectively (Fig. 1B). TJC improved in both groups, showing mean absolute changes from baseline of –2.4 (W12) and -3.1 (W52) for GUS, and of –1.5 (W12) to –3.5 (W52) for TNFi. Similarly, SJC decreased over time: mean absolute changes of –1.9 and –2.1 (GUS), and of –1.2 and –2.4 (TNFi), at W12 and W52, respectively. Dactylitis prevalence decreased in both groups (Fig. 2A) and it disappeared in 46.2% (6/13) patients W12, 80.0% (8/10) W24, and 71.4% (5/7) W52 (GUS), and in 88.9% (8/9) W12, 75.0% (6/8) W24,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

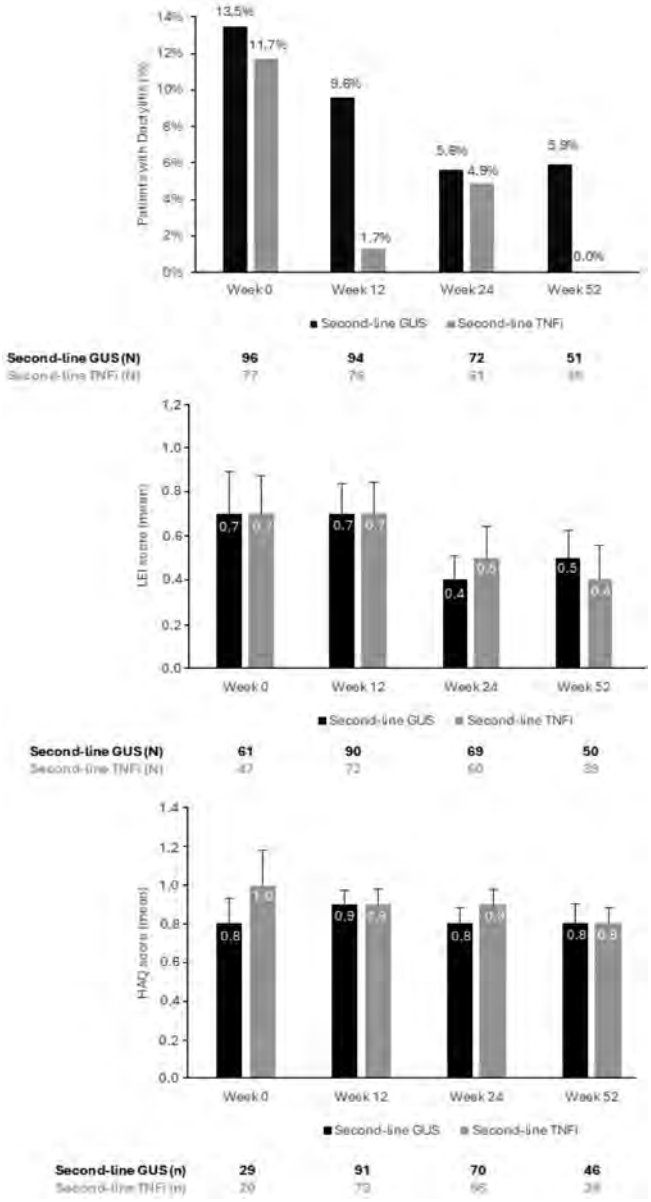


Figure 2. a) Percentage of patients with dactylitis, b) representation of the mean LEI score, c) representation of HAQ score in second-line treatment (GUS or TNFi at week 0, week 12, 24 and 52).

and 100.0% (5/5) at W52 (TNFi). LEI scores marginally improved with both treatments, whereas HAQ remained stable with GUS and slightly improved with TNFi (from 1.0 to 0.8 [W52]) (Fig. 2B and C).

Nail psoriasis mean absolute changed from baseline: –1.8 (W12), –3.2 (W24), and –10.5 (W52) in TNFi group, versus –0.9, –1.8, and –1.3, respectively, in the GUS group. BSA improvement favored GUS, showing mean absolute changes of –2.6 (W12), –3.2 (W24), and –3.9 (W52), versus –0.8, –1.1, and –1.7, respectively in the TNFi group.

Reported AEs in 35 patients: 19 (19.4%) GUS and 16 (20.8%) TNFi. Of total AEs, 4 (14.8%) and 7 (31.8%) were considered drug-related, respectively.

Conclusion: Guselkumab and second-line TNFis showed effectiveness through 52 weeks in diverse domains. GUS provided earlier MDA response and greater improvement in both skin outcomes and LDA/remission, supporting its use as a durable second-line option

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Gonzalez Molina: None; **B. JOVEN**: Johsson & Johsson, 2, 5, 6; **M. Llanes**: None; **V. Hernandez**: None; **M. Moreno**: None; **E. Blanco**: None; **C. Marin**: None; **L. Mateo**: None; **M. Salles Lizarzaburu**: None; **M. Steiner**: None; **L. Nuño**: None; **A. Fernández-Nebro**: Argenx, 5, AstraZeneca, 2, 5, 6, Chemo, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Gebro Pharma, 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 5, Merck Serono, 5, MSD, 5, Novartis, 2, 5, 6, Takeda, 5, UCB, 5; **r. Veroz González**: None; **a. Urruticoechea-Arana**: None; **E. Cervantes**: None; **e. Giner**: None; **L. Fernandez de la fuente Burson**: None; **A. Erra**: None; **O. Camacho**: None; **E. Garcia**: None; **A. Hernandez**: Janssen, 2; **J. Malave**: None; **L. Orpinell**: None; **I. Ros Vilamajo**: None; **S. Castro**: None; **P. Lopez Viejo**: None; **L. Sarabia**: None; **R. García Portales**: None; **J. Cabezon**: None; **P. Moreno Gil**: None; **F. Maceiras**: None; **D. Pielfort**: None; **S. Diaz-Castroverde**: Janssen, 3; **M. Cuervas-mons**: Janssen, 3; **J. Pinto-Tasende**: None; **S. Muñoz**: Janssen, 1, 2, 5, 6, 7; **J. Ramirez**: Janssen, 2.

Abstract Number: 2374

Bimekizumab Efficacy And Safety Through 5 Years In Patients With Moderate To Severe Plaque Psoriasis In The US And Canada

Andrew Blauvelt[1], **Saakshi Khattri**[2], Phoebe Rich[3], Ronald Vender[4], Kenneth B. Gordon[5], Balint Szilagyi[6], Heather Herr[7], Bertram Knapp[6], Delphine Deherder[8], Sarah Kavanagh[9] and Kim Papp[10], [1]Blauvelt Consulting, LLC, Portland, OR, [2]The Mount Sinai Hospital, New York, NY, [3]Oregon Dermatology and Research Center, Portland, OR, [4]Dermatrials Research Inc., Hamilton, ON, Canada, [5]Department of Dermatology, Medical College of Wisconsin, Milwaukee, WI, [6]UCB, Monheim am Rhein, Germany, [7]UCB, Smyrna, GA, [8]UCB, Braine-l'Alleud, Belgium, [9]UCB, Morrisville, NC, [10]Probity Medical Research and Alliance Clinical Trials, Waterloo, and Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Given the chronic nature of psoriasis, and the loss of response observed with biologic therapies over time, it is crucial to establish the long-term efficacy and safety of biologic therapies for psoriasis. Here, we evaluate the efficacy and safety of bimekizumab (BKZ) treatment through 5 years in patients with moderate to severe plaque psoriasis from the US and Canada.

Methods: A US/Canadian patient subgroup completing the BE VIVID (NCT03370133)/BE SURE (NCT03412747)/BE READY (NCT03410992) phase 3 trials and their open-label extension (OLE), BE BRIGHT (NCT03598790; 4 years' total treatment) could enter a second 48-week extension (OLE2), in which they received BKZ 320 mg every 4 weeks (Q4W) or Q8W depending on Investigator's Global Assessment (IGA) response at entry.[1–4] Included patients received BKZ continuously from feeder study baseline to OLE2 entry; patients receiving BKZ Q4W to Week 16 then Q8W thereafter (BKZ Q4W/Q8W; approved dosing regimen) were also analyzed.[5]

Five-year efficacy data are reported (244 weeks' total treatment). Patients discontinuing treatment due to lack of efficacy/treatment-related adverse events were considered non-responders; multiple imputation was used for other missing data (modified non-responder imputation). Treatment-emergent adverse events (TEAEs) are reported through 5 years (Weeks 0–244) using exposure-adjusted incidence rates/100 patient-years [PY]).

Results: In total, 153 US/Canadian patients were analyzed; 52 received BKZ Q4W/Q8W.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

At Year 1 (Week 52) and Year 5 (Week 244), 75.2% and 67.7% patients treated with BKZ achieved 100% improvement from baseline in Psoriasis Area and Severity Index (PASI 100), respectively (BKZ Q4W/Q8W: 78.8% and 76.9%). At Year 1 and Year 5, 92.8% and 84.9% achieved PASI 90 (BKZ Q4W/Q8W: 96.2% and 88.5%).

Over 5 years, serious TEAEs (3.6/100 PY) and discontinuations due to TEAEs (0.3/100 PY) were low; zero deaths occurred. Most common TEAEs were nasopharyngitis (9.7/100 PY), oral candidiasis (7.6/100 PY), and corona virus infection (6.1/100 PY). The vast majority (99.3%) of oral candidiasis events were mild/moderate; none led to discontinuation. Safety results were generally similar in BKZ Q4W/Q8W patients.

Conclusion: BKZ demonstrated high rates of clinical response, which were durable over 5 years, in patients from the US and Canada with moderate to severe plaque psoriasis. BKZ was well-tolerated in this patient subgroup, with no unexpected safety findings.

References: 1. Reich K. Lancet 2021;397:487–98; **2**. Warren RB. N Engl J Med 2021;385:130–41; **3**. Gordon KB. Lancet 2021;397:475–86; **4**. Strober B. Br J Dermatol 2023;188:749–59; **5**. Bimekizumab Summary of Product Characteristics. 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761151s000lbl.pdf [Accessed April 2025].

Previously presented at AAD 2025.

Disclosure: A. Blauvelt: AbbVie, 1, Acelyrin, 12, Clinical study investigator, Almirall, 1, 12, Clinical study investigator, Alumis, 1, 12, Clinical study investigator, Amgen, 1, 12, Clinical study investigator, Anaptysbio, 1, Apogee, 1, Arcutis, 1, 12, Clinical study investigator, Boehringer Ingelheim, 1, 12, Clinical study investigator, Bristol Myers Squibb, 1, Celltrion, 1, Corvus, 1, Dermavant, 1, 12, Clinical study investigator, Eli Lilly and Company, 1, 6, 12, Clinical study investigator, Galderma, 1, 12, Clinical study investigator, GlaxoSmithKline, 1, Immunovant, 1, Incyte, 1, 12, Clinical study investigator, IQVIA, 1, Janssen, 1, 12, Clinical study investigator, Leo, 1, 12, Clinical study investigator, Lipidio, 1, 11, Merck, 1, 12, Clinical study investigator, Novartis, 1, 12, Clinical study investigator, Oruka, 1, 11, Paragon, 1, Pfizer, 1, 12, Clinical study investigator, Regeneron, 1, 12, Clinical study investigator, Sanofi, 1, 12, Clinical study investigator, Spherix Global Insights, 1, Sun Pharma, 1, 12, Clinical study investigator, Syncona, 1, Takeda, 1, 12, Clinical study investigator, UCB, 1, 6, Union, 1; **S. Khattri**: AbbVie, 1, 2, 5, 6, Acelyrin, 5, Bristol Myers Squibb, 5, Eli Lilly and Company, 1, 2, 6, Incyte, 5, Janssen, 1, 2, 6, LEO Pharma, 1, 2, 6, Regeneron, 1, 2, 6, UCB, 1, 2, 6; **P. Rich**: AbbVie, 12, Principal Investigator/clinical trials, Amgen, 12, Principal Investigator/clinical trials, Arcutis, 12, Principal Investigator/clinical trials, Bristol Myers Squibb, 2, 12, Principal Investigator/clinical trials, Dermavant, 12, Principal Investigator/clinical trials, Eli Lilly and Company, 12, Principal Investigator/clinical trials, Janssen, 12, Principal Investigator/clinical trials, Sun Pharma, 12, Principal Investigator/clinical trials, UCB, 12, Principal Investigator/clinical trials; **R. Vender**: AbbVie, 2, 5, 6, Actelion, 2, 6, Amgen, 2, 5, 6, Bausch Health, 2, 6, Celgene, 2, 6, Centocor, 5, Cipher, 2, 6, Dermavant, 5, Dermira, 5, Eli Lilly and Company, 2, 5, 6, Galderma, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 6, LEO Pharma, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Palladin, 2, Pfizer, 2, 5, 6, Regeneron, 5, Takeda, 5, UCB, 2, 5, 6; **K. Gordon**: AbbVie, 2, 5, Almirall, 2, Amgen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Dermira, 2, Eli Lilly and Company, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, Sun Pharma, 2, UCB, 2, 5; **B. Szilagyi**: UCB, 3, 12, Shareholder; **H. Herr**: UCB, 3, 12, Shareholder; **B. Knapp**: UCB, 3, 12, Shareholder; **D. Deherder**: UCB, 3, 12, Shareholder; **S. Kavanagh**: Aclipse Therapeutics, 2, Aliada Therapeutics, 2, Allay Therapeutics, 2, Autobahn Therapeutics, 2, Cognition Therapeutics, 2, Colorado Prevention Center, 2, Karuna Therapeutics, 2, Kisbee Therapeutics, 2, LB Pharmaceuticals, 2, Nesos, 2, Novartis, 2, Onward Medical, 2, PharPoint Research, 2, Summit Analytical, 2, Therini Bio, 2, Tonix Pharmaceuticals, 2, Tornado Therapeutics, 2, UCB, 2, 3, Whitsell Innovations, 2, Worldwide Clinical Trials, 2, Zosano Pharma, 2; **K. Papp**: AbbVie, 1, 2, 4, 5, 6, 12, Investigator, Acelyrin, 1, 2, 4, 5, 6, 12, Investigator, Akros, 1, 2, 4, 5, 6, 12, Investigator, Alumis, 1, 2, 4, 5, 6, 12, Investigator, Amgen, 1, 2, 4, 5, 6, 12, Investigator, Arcutis, 1, 2, 4, 5, 6, 12,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Investigator, Bausch Health/Valeant, 1, 2, 4, 5, 6, 12, Investigator, Boehringer-Ingelheim, 1, 2, 4, 5, 12, Investigator, Bristol-Myers Squibb(BMS), 1, 2, 4, 5, 12, Investigator, Can-Fite Biopharma, 1, 2, 4, 5, 12, Investigator, Celltrion, 1, 2, 4, 5, 12, Investigator, Concert Pharmaceuticals, 1, 2, 4, 5, 12, Investigator, Dermavant, 1, 2, 4, 5, 6, 12, Investigator, Dermira, 1, 2, 4, 5, 6, 12, Investigator, Dice Pharmaceuticals, 1, 2, 4, 5, 6, 12, Investigator, Dice Therapeutics, 1, 2, 4, 5, 6, 12, Investigator, Eli Lilly and Company, 1, 2, 4, 5, 6, 12, Investigator, Evelo Biosciences, 1, 2, 4, 5, 6, 12, Investigator, Forbion, 1, 2, 4, 5, 6, 12, Investigator, Galderma, 1, 2, 4, 5, 6, 12, Investigator, Horizon Therapeutics, 1, 2, 4, 5, 6, 12, Investigator, Incyte, 1, 2, 4, 5, 12, Investigator, Janssen, 1, 2, 4, 5, 6, 12, Investigator, Kymab, 1, 2, 4, 5, 6, 12, Investigator, Kyowa Hakko Kirin, 1, 2, 4, 5, 6, 12, Investigator, LEO Pharma, 1, 2, 4, 5, 6, 12, Investigator, Meiji Seika Pharma, 1, 2, 4, 5, 6, 12, Investigator, Mitsubishi Pharma, 1, 2, 4, 5, 6, 12, Investigator, Nimbus Therapeutics, 1, 2, 4, 5, 6, 12, Investigator, Novartis, 1, 2, 4, 5, 6, 12, Investigator, Pfizer, 1, 2, 4, 5, 6, 12, Investigator, Reistone, 1, 2, 4, 5, 6, 12, Investigator, Sandoz, 1, 2, 4, 5, 6, 12, Investigator, Sanofi-Aventis/Genzyme, 1, 2, 4, 5, 6, 12, Investigator, Sun Pharma, 1, 2, 4, 5, 6, 12, Investigator, Takeda, 1, 2, 4, 5, 6, 12, Investigator, Tarsus Pharmaceuticals, 1, 2, 4, 5, 6, 12, Investigator, UCB, 1, 2, 4, 5, 6, 12, Investigator, Zai Lab, 1, 2, 4, 5, 6, 12, Investigator.

Abstract Number: 2375

Ixekizumab Provided Rapid Improvements in Quality of Life and Disease Activity in Patients with Psoriatic Arthritis: Findings from a Real-World Study in the United States of Patients Initiating Ixekizumab or Interleukin-23 Inhibitors

KURT OELKE[1], Emily Edson-Heredia[2], Sarah Ross[3], Jennifer Marie Pustizzi[4], Ali Sheikhi Mehrabadi[4], Natalia Bello[4], Frederick Murphy[5], **Shikha Singla**[6], Siba Raychaudhuri[7], Philip J Mease[8] and Arthur Kavanaugh[9], [1]rheumatic disease center, Glendale, WI, [2]eli lilly, indianapolis, [3]Lilly, Indianapolis, IN, [4]Eli Lilly, Indianapolis, IN, [5]Altoona Arthritis & Osteoporosis Center, Duncansville, PA, [6]Medical College of Wisconsin, Milwaukee, WI, [7]UC Davis, School of Medicine/ VA Medical Center, Sacramento, Davis, CA, [8]University of Washington, Seattle, WA, [9]University of California, San Diego, School of Medicine, San Diego, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Ixekizumab (IXE) is a selective interleukin-17A antagonist that has proven effective in Phase 3 and 4 clinical trials for patients with psoriatic arthritis (PsA).

Methods: Psoriatic Arthritis Real-World Study in the US (PARTUS) was a prospective, multicenter, non-interventional study conducted in patients with PsA who were starting treatment with IXE or an interleukin-23p19 inhibitor (IL-23i). We present improvements in patient-reported outcomes (PROs) from the study.

The following outcomes were assessed at Week (W) 4 and W12: proportion of patients achieving Psoriatic Arthritis Impact of Disease (PsAID)-12 remission, change from baseline (CFB) in the patient spinal pain score measured by question 2 (Q2) (spinal pain item) of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (in patients with axial involvement), and CFB in Patient Global Assessment of Disease Activity (PtGA) Visual Analog Scale (VAS) score. Minimal Clinically Important Differences were evaluated: proportion of patients achieving a ≥ 10 score decrease in patient pain VAS score, a ≥ 10 score decrease in PtGA VAS score, and a ≥4 score increase in Functional Assessment of Chronic Illness Therapy (FACIT)- Fatigue score. Abbreviated Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9) scores were also assessed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and Clinical Characteristics at Baseline in patients with active PsA treated with IXE or IL-23i (GUS and RZB) Notes: Data are mean (SD) unless otherwise stated. Abbreviations: BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BMI=body mass index; FACIT = Functional Assessment of Chronic Illness Therapy; GUS= guselkumab; IL-23i=interleukin-23p19 inhibitor; IXE=ixekizumab; N=number of patients in each cohort; n=number of patients in the specified category; PsA=psoriatic arthritis; PsAID-12=Psoriatic Arthritis Impact of Disease; RZB=risankizumab; SD=standard deviation; TSQM-9, abbreviated Treatment Satisfaction Questionnaire for Medication-9.

	IXE (N=121)	IL-23i (N=116)
Age, years	54.4 (13.3)	53.0 (14.1)
Female, n (%)	63 (52.1)	75 (64.7)
BMI, kg/m^2	33.1 (6.8)	31.4 (7.3)
Years since PsA diagnosis	7.5 (8.8)	9.0 (10.5)
PsAID Score	5.9 (2.1)	5.6 (2.0)
Q2 (patient spinal pain score) of BASDAI (in patients with axial involvement)	5.8 (2.7)	6.0 (2.8)
Patient's assessment of pain	52.9 (23.9)	50.9 (24.9)
Patient's assessment of disease activity	60.4 (21.7)	57.2 (24.5)
FACIT-Fatigue score	25.1 (11.1)	25.1 (10.3)

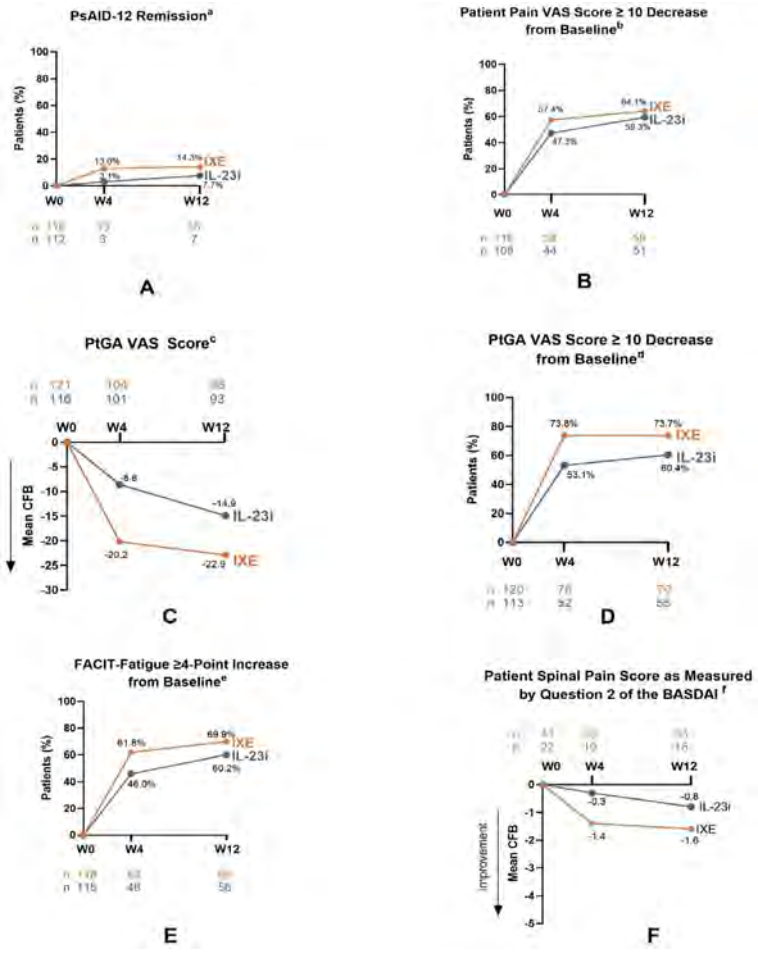


Figure 1. Patient-reported outcomes at W4 and W12 in patients with PsA treated with IXE or IL-23i (GUS and RZB): A. Proportion of patients achieving PsAID-12 Remission; B. Proportion of patients achieving a ≥ 10 score decrease in patient pain VAS score; C. Change from baseline in PtGA VAS score; D. Proportion of Patients achieving a ≥ 10 score decrease in PtGA VAS score; E. Proportion of patients achieving ≥ 4 score increase from baseline in the FACIT-Fatigue score; F. Change from baseline in patient spinal pain score as measured by question 2 of the BASDAI. Note: The study was not designed for comparative analysis, so only descriptive results are provided. a In patients with PSAID-12 score > 1.4 at Baseline. b In patients with patient pain VAS score ≥ 10 at baseline c In patients with baseline score >0 d In patients with PtGA VAS Score ≥ 10 at baseline e In patients with FACIT-Fatigue score ≤ 48 at baseline f In patients with axial involvement at baseline Abbreviations: BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BL=Baseline; CFB=Change from baseline; GUS=guselkumab; IL-23i=interleukin-23p19 inhibitor; IXE=ixekizumab; n=number of patients in the specified category; PsAID-12=Psoriatic Arthritis Impact of Disease; PtGA=Patient Global Assessment of Disease Activity; RZB=risankizumab; VAS = Visual Analog Scale.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. TSQM-9 scores from patients with active PsA treated with IXE or IL-23i (GUS and RZB) Note: Data are mean (SD) unless otherwise stated. Abbreviations: GUS=guselkumab; IL-23i=interleukin-23p19 inhibitor; IXE=ixekizumab; N=number of patients in each cohort; PsA=psoriatic arthritis; RZB=risankizumab; SD=standard deviation; TSQM-9, abbreviated Treatment Satisfaction Questionnaire for Medication-9.

TSQM-9 scores	IXE (N=121)	IL-23i (N=116)
Effectiveness		
Week 4	62.4 (23.2)	57.6 (18.6)
Week 12	63.7 (24.1)	56.2 (23.7)
Convenience		
Week 4	82.3 (16.0)	79.3 (15.7)
Week 12	81.3 (16.6)	79.3 (15.8)
Global Satisfaction		
Week 4	65.0 (27.2)	61.7 (19.6)
Week 12	63.9 (27.2)	60.1 (25.7)

Descriptive statistics for IXE and IL-23i groups are presented.

Results: BL characteristics of 121 patients from the IXE cohort and 116 patients from the IL-23i cohort (risankizumab (n=67) and guselkumab (n=49)) are in Table 1.

At W4, 57.4% in the IXE cohort and 47.3% in the IL-23i cohort reported a ≥ 10 point decrease in patient pain VAS score. Both cohorts had additional progress by W12 (Figure (Fig.) 1B). The mean (SD) CFB in PtGA VAS score at W4 was -20.2 (24.5) and -8.6 (27.2), and at W12 was -22.9 (27.4) and -14.9 (27.6) in the IXE and IL-23i cohorts respectively (Fig. 1C). At W4, 73.8% and 53.1%, and at W12, 73.7% and 60.4% reported a ≥ 10 point decrease in PtGA VAS score in the IXE and IL-23i cohorts, respectively (Fig. 1D). At W4, 61.8% in the IXE cohort and 46.0% in the IL-23i cohort, and at W12, 69.9% in the IXE cohort and 60.2% in the IL-23i cohort reported ≥ 4point improvements in fatigue (Fig. 1E). The mean (SD) CFB in spinal pain score by Q2 of BASDAI was -1.4 (1.9) and -0.3 (2.9) at W4 and -1.6 (1.7) and -0.8 (2.5) at W12 for IXE and IL-23i cohorts (Fig. 1F). The proportions of patients achieving PsAID-12 remission at W4 were 13.0% and 3.1% in the IXE and IL-23i cohorts, respectively, with further improvements reported by W12 in both cohorts of patients (Fig. 1A).

The TSQM-9 convenience domain scores were higher than the other domains of effectiveness and global satisfaction (Table 2).

Conclusion: The findings from the PARTUS study demonstrate that IXE rapidly improves quality of life and disease severity as early as week 4 in real-world settings for patients with PsA, with further improvements through week 12. Meaningful improvements were observed in PsAID-12, BASDAI, patient pain VAS, PtGA VAS score, as well as in FACIT-Fatigue scores. Convenience was the highest scoring treatment satisfaction domain. The rapid week 4 improvements in IXE treated patients were also observed in IL-23i treated patients, although to a less numerical extent.

Disclosure: K. OELKE: AbbVie, 6, Amgen, 6, AstraZeneca, 6, Johnsson & Johnsson, 6, UCB, 6; **E. Edson-Heredia**: Eli Lilly, 3, 3, 11; **S. Ross**: Eli Lilly, 3, 11; **J. Pustizzi**: Eli Lilly, 3, 11; **A. Mehrabadi**: Eli Lilly, 3, 11; **N. Bello**: Eli Lilly, 3, 11, Eli Lilly and Company, 3; **F. Murphy**: None; **S. Singla**: AbbVie/Abbott, 2, Eli Lilly, 5, Janssen, 2, 6, Prometheus Biosciences, 5, UCB, 2; **S. Raychaudhuri**: AbbVie, 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharma, 5; **P. Mease**: AbbVie, 2, 5, Acelyrin, 2, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Century, 2, Cullinan Biotech, 3, Eli Lilly, 2, 5, 6, Genascence, 1, Inmagene, 2, Johnsson & Johnsson, 2, 5, 6, Moonlake, 2, 5, Novartis, 2, 5, Pfizer, 2, Takeda, 2, 5, UCB, 2, 5, 6; **A. Kavanaugh**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, 5, GRAPPA, 12, Co-President, Janssen, 2, 5, MoonLake Immunotherapeutics, 2, Pfizer, 2, 5, Takeda, 2, UCB, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2376

Efficacy And Safety of Vunakizumab in Patients with Active Ankylosing Spondylitis Stratified by Disease Course: A Post-hoc Analysis of a Randomized, Double-Blind, Phase 2/3 Trial

XiaoFei Shi, Liqing Zhou and He Zhang, The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2338–2376) Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Vunakizumab, also known as SHR-1314, is a novel a recombinant humanized monoclonal antibody against interleukin-17A. A randomised, double-blind, phase 2/3 trial (NCT04840485) demonstrated a significant benefit of vunakizumab over placebo in active ankylosing spondylitis (AS) at week 16, with sustained improvements through 32 weeks. However, it remains unknown whether the effect of vunakizumab on AS varies according to disease course (DC). Here, we conducted a post-hoc analysis of this randomized, double-blind, phase 2/3 trial to assess the efficacy and safety of vunakizumab in patients with active AS stratified by DC (< 5 versus ≥ 5 years).

Methods: In the phase 2/3 trial, adult patients with active AS who had either an inadequate response, intolerance, or contraindication to non-steroidal anti-inflammatory drugs were enrolled. All patients in this study fulfilled the 1984 modified New York criteria for AS and also met the American College of Rheumatology classification criteria. Data for this analysis were obtained from those eligible patients who were randomly assigned to receive either vunakizumab 120 mg or placebo at weeks 0, 2, 4, 8 and 12; from week 16, all patients transitioned to treatment with vunakizumab 120 mg until week 32. The primary endpoint was the proportion of patients who met the Assessment of Spondyloarthritis International Society 20 (ASAS20) response criteria at week 16. Key secondary endpoints included ASAS40, ASAS5/6 and safety.

Table 1. ASAS response stratified by disease course

	Disease course of ≥ 5 years			Disease course of < 5 years		
	Placebo (n = 58)	Vunakizumab (n = 116)	OR (95% CI)[1]/Difference (95% CI)[2]	Placebo (n = 88)	Vunakizumab (n = 178)	OR (95% CI)[1]/Difference (95% CI)[2]
At week 2						
ASAS20	5 (8.62)	31 (26.72)	3.84 (1.40, 10.51)	12 (13.64)	69 (38.76)	3.99 (2.02, 7.88)
ASAS40	1 (1.72)	12 (10.34)	6.75 (0.85, 53.44)	2 (2.27)	27 (15.17)	7.57 (1.75, 32.72)
ASAS5/6	2 (3.45)	29 (25.00)	9.24 (2.12, 40.29)	6 (6.82)	45 (25.28)	4.72 (1.92, 11.57)
At week 16						
ASAS20	25 (43.10)	72 (62.07)	2.15 (1.13, 4.09)[a]	37 (42.05)	121 (67.98)	2.98 (1.75, 5.07)[c]
ASAS40	12 (20.69)	52 (44.83)	3.18 (1.52, 6.68)[b]	23 (26.14)	84 (47.19)	2.52 (1.44, 4.42)[d]
ASAS5/6	9 (15.52)	60 (51.72)	5.82 (2.61, 13.01)[c]	24 (27.27)	103 (57.87)	3.78 (2.16, 6.62)[c]
At week 24*						
ASAS20	32 (66.67)	83 (71.55)	4.83 (-9.81, 20.84)	46 (64.79)	132 (74.16)	9.37 (-2.92, 22.52)
ASAS40	22 (45.83)	59 (50.86)	4.16 (-9.83, 18.00)	32 (45.07)	90 (50.56)	4.48 (-6.79, 15.62)
ASAS5/6	23 (47.92)	65 (56.03)	6.76 (-7.20, 20.77)	37 (52.11)	113 (63.48)	9.68 (-1.77, 21.42)
At week 32*						
ASAS20	30 (62.50)	79 (68.10)	5.20 (-9.15, 20.59)	47 (66.20)	139 (78.09)	12.83 (-0.09, 26.59)
ASAS40	25 (52.08)	65 (56.03)	3.30 (-10.60, 17.45)	39 (54.93)	111 (62.36)	6.32 (-5.05, 18.08)
ASAS5/6	20 (41.67)	65 (56.03)	11.91 (-2.07, 25.67)	43 (60.56)	120 (67.42)	6.18 (-5.44, 18.45)

Data are n (%), OR (95% CI), difference (95% CI) or P value. *At weeks 24 and 32, patients in the placebo group were those who switched from placebo to vunakizumab 120 mg at week 16 (n = 48 for disease course of ≥ 5 years; n = 71 for disease course of < 5 years). [1]At weeks 2 and 16, data are presented as OR (95% CI). [2]At weeks 24 and 32, data are presented as difference (95% CI) in response rates between the two groups. [a]P = 0.0196; [b]P = 0.0022; [c]P < 0.0001; [d]P = 0.0012. ASAS, Assessment of Spondyloarthritis International Society; CI, confidence interval; OR, odds ratio.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 440 patients were included in this analysis, of which 174 had a DC of ≥ 5 years (vunakizumab 120 mg, n = 116; placebo, n = 58) and 266 had a DC of < 5 years (vunakizumab 120 mg, n = 178; placebo, n = 88). At week 16, the ASAS20 response rates were 62.07% for vunakizumab versus 43.10% for placebo (OR 2.15, 95% CI 1.13 to 4.09, P = 0.0196) in patients with a DC of ≥ 5 years; and in patients with a DC of < 5 years, the corresponding rates were 67.98% versus 42.05% (OR 2.98, 95% CI 1.75 to 5.07, P < 0.0001). Moreover, patients switching from placebo to vunakizumab at week 16 showed improved ASAS20 at week 32 (62.50% for DC of ≥ 5 years; 66.20% for DC of < 5 years), which was comparable to those who continued on vunakizumab (68.10% and 78.09%, respectively). Similar improvements were also observed for ASAS40 and ASAS5/6 (Table 1). In terms of safety, during the 16-week period, 110 (94.83%) of 116 patients with a DC of ≥ 5 years in the vunakizumab group and 54 (93.10%) of 58 such patients in the placebo group had at least one treatment-emergent adverse event (TEAE); while among patients with a DC of < 5 years, TEAEs occurred in 164 (92.13%) of 178 patients and 82 (93.18%) of 88 patients, respectively. The overwhelming majority of TEAEs were mild to moderate, with the most common being upper respiratory infection (DC of ≥ 5 years: 31 [26.72%] for vunakizumab versus 20 [34.48%] for placebo; DC of < 5 years: 42 [23.60%] versus 20 [22.73%]). No treatment-related deaths were reported.

Conclusion: Vunakizumab 120 mg showed improved efficacy with a manageable safety profile in patients with active AS, irrespective of DC.

Disclosure: X. Shi: None; **L. Zhou**: None; **H. Zhang**: None.

Abstract Number: 2377

Statin Use for Primary Prevention of Atherosclerotic Cardiovascular Disease Among Patients with Systemic Lupus Erythematosus

Aakash V. Patel[1], Lingxiao Zhang[2], Emily S. Lau[3], Hyon K. Choi[4] and April Jorge[5], [1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Massachusetts General Hospital, Harvard Medical School, Boston, [4]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [5]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular disease (CVD) is the most common cause of mortality among patients with systemic lupus erythematosus (SLE). Statin medications play a crucial role for the primary prevention of atherosclerotic cardiovascular disease (ASCVD), but data characterizing statin usage among patients with SLE are scarce. We sought to identify patterns of statin use for primary prevention of ASCVD in patients with SLE.

Methods: We identified an SLE cohort from TriNetX, an electronic health record (EHR) database with patients from academic, community, and private medical centers across the United States. We included patients with SLE (≥2 ICD codes ≥30 days and ≤2 years apart) between January 2000 and August 2021. We utilized the 2018 American Heart Association Guideline on the Management of Blood Cholesterol and the Pooled Cohort Equation (PCE) to identify SLE patients with an indication for treatment with a moderate or high intensity statin for primary prevention of ASCVD (indications include a 10-year risk of ASCVD ≥7.5%, diabetes, or LDL ≥190 mg/dL. We also performed a variation of ASCVD risk estimation by

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

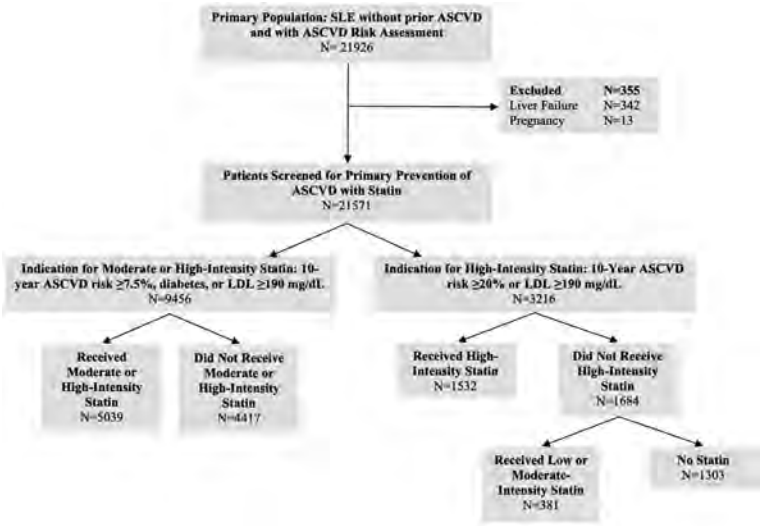


Figure 1: Assessment of Statin Use in Patients with Systemic Lupus Erythematosus for the Primary Prevention of Atherosclerotic Cardiovascular Disease (ASCVD) According to the 2018 American Heart Association Guideline on the Management of Blood Cholesterol

Table 1: Factors Associated with Moderate or High-Intensity Statin Use Among Patients with Systemic Lupus Erythematosus with an Indication for Primary Prevention of Atherosclerotic Cardiovascular Disease

Characteristic	N	Moderate or High-Intensity Statin Use, N (%)	No Moderate or High-Intensity Statin Use, N (%)	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)*
Age					
≥60, ref	5081	2553 (50.2)	2528 (49.8)	1.00 (ref)	1.00 (ref)
<60	4375	2486 (56.8)	1889 (43.2)	1.30 (1.20-1.41)	2.09 (1.90-2.30)
Sex					
Male, ref	1559	862 (55.3)	697 (44.7)	1.00 (ref)	1.00 (ref)
Female	7897	4177 (52.9)	3720 (47.1)	0.91 (0.81-1.01)	1.07 (0.96-1.20)
Race/Ethnicity					
White, ref	4471	2227 (49.8)	2244 (50.2)	1.00 (ref)	1.00 (ref)
Black	2124	1246 (58.7)	878 (41.3)	1.32 (1.20-1.46)	1.40 (1.27-1.54)
Asian	97	56 (57.7)	41 (42.3)	1.20 (0.80-1.80)	1.19 (0.79-1.79)
Hispanic	460	238 (51.7)	222 (48.3)	0.94 (0.78-1.13)	1.03 (0.85-1.24)
Geographic Location					
South, ref	4220	2155 (51.1)	2065 (48.9)	1.00 (ref)	1.00 (ref)
Midwest	2349	1327 (56.5)	1022 (43.5)	1.19 (1.08-1.30)	1.19 (1.08-1.31)
Northeast	2134	1145 (53.7)	989 (46.3)	1.02 (0.93-1.12)	0.99 (0.90-1.09)
West	681	392 (57.6)	289 (42.4)	1.20 (1.03-1.41)	1.27 (1.08-1.49)
Comorbidities					
Diabetes					
No, ref	4831	2272 (47.0)	2559 (53.0)	1.00 (ref)	1.00 (ref)
Yes	4625	2767 (59.8)	1858 (40.2)	1.68 (1.55-1.82)	1.91 (1.76-2.08)
Hypertension					
No, ref	4062	2045 (50.3)	2017 (49.7)	1.00 (ref)	1.00 (ref)
Yes	5395	2994 (55.5)	2400 (44.5)	1.23 (1.13-1.34)	1.16 (1.07-1.26)
Hyperlipidemia					
No, ref	5682	2653 (46.7)	3029 (53.3)	1.00 (ref)	1.00 (ref)
Yes	3774	2386 (63.2)	1388 (36.8)	1.96 (1.80-2.14)	1.91 (1.75-2.08)
Tobacco Use					
No, ref	8366	4460 (53.3)	3906 (46.7)	1.00 (ref)	1.00 (ref)
Yes	1090	579 (53.1)	511 (46.9)	0.99 (0.87-1.13)	0.98 (0.86-1.11)
Obesity					
No, ref	8293	4426 (53.4)	3867 (46.6)	1.00 (ref)	1.00 (ref)
Yes	1163	613 (52.7)	550 (47.3)	0.97 (0.86-1.10)	1.06 (0.93-1.20)
CKD ≥ 4					
No, ref	9253	4928 (53.3)	4325 (46.7)	1.00 (ref)	1.00 (ref)
Yes	203	111 (54.7)	92 (45.3)	1.06 (0.80-1.40)	1.13 (0.86-1.50)
Lupus Nephritis					
No, ref	8446	4526 (53.6)	3920 (46.4)	1.09 (ref)	1.00 (ref)
Yes	1010	513 (50.8)	497 (49.2)	0.89 (0.78-1.02)	0.95 (0.84-1.09)
Anti-Phospholipid Antibody Syndrome					
No, ref	9215	4912 (53.3)	4303 (46.7)	1.00 (ref)	1.00 (ref)
Yes	241	127 (52.7)	114 (47.3)	0.98 (0.76-1.26)	1.04 (0.80-1.34)
Medication Use					
Hydroxychloroquine†					
No, ref	6441	3636 (56.5)	2805 (43.5)	1.00 (ref)	1.00 (ref)
Yes	3015	1403 (46.5)	1612 (53.5)	0.67 (0.62-0.73)	0.72 (0.66-0.78)
Glucocorticoids					
No, ref	6470	3507 (54.2)	2963 (45.8)	1.00 (ref)	1.00 (ref)
Yes	2986	1532 (51.3)	1454 (48.7)	0.89 (0.82-0.97)	0.94 (0.86-1.02)
Healthcare Utilization					
Total number of Outpatient Encounters					
0-1 Encounters, ref	3164	1892 (59.8)	1272 (40.2)	1.00 (ref)	1.00 (ref)
≥2 Encounters	6292	3147 (50.0)	3145 (50.0)	0.67 (0.62-0.73)	0.67 (0.61-0.73)
Hospitalized/ER Visit					
No, ref	6149	3315 (53.9)	2834 (46.1)	1.00 (ref)	1.00 (ref)
Yes	3307	1724 (52.1)	1583 (47.9)	0.93 (0.86-1.01)	0.96 (0.88-1.05)

*Adjusted for 10-year risk of atherosclerotic cardiovascular disease, assessed per the Pooled Cohort Equation.
†Hydroxychloroquine use assessed any time ever prior to the first atherosclerotic cardiovascular disease risk assessment date

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

doubling the risk calculated by the PCE (modified PCE) to account for increased risk conferred by SLE. We assessed statin use patterns among eligible patients and examined factors associated with underutilization using multivariable logistic regression, adjusting for 10-year ASCVD risk.

Results: There were 21,926 SLE patients between ages 40-75 without prior ASCVD who underwent at least one ASCVD risk assessment with cholesterol and blood pressure monitoring **(Figure 1)**. After excluding 355 patients with contraindications to statin therapy (i.e., pregnancy and liver failure), 9,456 patients (43.8%) had an indication for a moderate or high-intensity statin. Of these, 5,039 (53.3%) received a statin. Among the 3216 patients with a PCE risk score ≥20% or LDL ≥190 mg/dL, 1303 (40.5%) never received a statin. Employing the modified PCE, an additional 2827 patients (13.1%) were eligible for a moderate or high-intensity statin, of whom 871 (30.8%) received a statin in primary prevention. Among those with an indication, Black individuals (adjusted OR [aOR] 1.40 [95% CI 1.27-1.54]) and patients below the age of 60 (aOR 2.09 [95% CI 1.90-2.30]) were more likely to receive a moderate or high-intensity statin, as were those with comorbidities such as diabetes (aOR 1.91 [95% CI 1.76-2.08]), hypertension (aOR 1.16 [95% CI 1.07-1.26]) and hyperlipidemia (aOR 1.91 [95% CI 1.75-2.08], **Table 1)**. There was no difference in statin use in the subset of patients with lupus nephritis (aOR 0.95 [95% CI 0.84-1.09]).

Conclusion: In this large EHR-based cohort of patients with SLE, 44% met criteria for a moderate or high-intensity statin for primary prevention of ASCVD, but only around half of eligible patients received a statin. These findings highlight the significant underutilization of statin therapy among patients with SLE, a population of individuals with enhanced risk for CVD.

Disclosure: A. Patel: None; **L. Zhang**: None; **E. Lau**: Amissa Health, 1, Roche, 6, Systole Health, Inc, 1; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **A. Jorge**: Bristol-Myers Squibb(BMS), 5.

Abstract Number: 2378

Factors Associated With Fatigue In Systemic Lupus Erythematosus: Data From The Almenara Lupus Cohort

Alvaro Oyarce-Calderon[1], Rocío Gamboa-Cárdenas[2], Victor Pimentel-Quiroz[3], Samira Garcia-Hirsh[4], Zoila Rodríguez-Bellido[5], Cesar Pastor-Asurza[6], Risto Perich-Campos[7], Graciela Alarcón[8] and Manuel Ugarte-Gil[9], [1]Hospital Nacional Guillermo Almenara Irigoyen, San Miguel, Lima, Peru, [2]Universidad Científica del Sur, Lima, Peru, [3]Universidad Científica del Sur, San Isidro, Peru, [4]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Peru, [5]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, Lima, Peru, [6]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Pakistan, [7]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [8]The University of Alabama at Birmingham, Oakland, CA, [9]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by a wide spectrum of clinical manifestations, fatigue being one of them; it is quite frequent and it is found in up to 90% patients. Thus, understanding its determinants is important; this has not been well studied in Latin-American patients. The aim of this study is to determine the factors associated with fatigue in SLE patients from a Latin American cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Factors associated with fatigue as assessed by the FACIT questionnaire.

	Univariable		Multivariable	
	B (SE)	*p* value	B (SE)	*p* value
Male gender	2.69 (2.00)	0.179		
Age at diagnosis	-0.14 (0.04)	<0.001		
Ethnic group				
Mestizo	Ref.		Ref.	
Black	9.67 (2.18)	<0.001	1.70 (0.60)	0.004
White	-6.23 (2.65)	0.019	-1.34 (1.38)	0.331
Socioeconomic status				
High	Ref.			
Medium	-1.82 (0.94)	0.052		
Low	-4.21 (1.30)	0.001		
Educational level, years	0.34 (0.14)	0.017		
Civil status, with couple	-0.52 (1.01)	0.605		
Disease duration	0.04 (0.06)	0.576		
SLEDAI-2K	0.07 (0.10)	0.456		
SDI	-0.43 (0.28)	0.130		
CCI	-1.38 (0.36)	<0.001		
Sicca	-3.51 (0.92)	<0.001	-1.77 (0.41)	<0.001
Fibromyalgia	-5.94 (1.22)	<0.001	-1.37 (0.67)	0.039
Prednisone daily dose	-0.09 (0.06)	0.162		
Antimalarials				
Never	Ref.			
Past	-3.37 (1.96)	0.087		
Current	-4.01 (1.52)	0.008		
Immunosuppressive drugs				
Never	Ref.			
Past	3.19 (1.52)	0.035		
Current	2.86 (1.17)	0.015		
PCS	0.32 (0.01)	<0.001	0.14 (0.02)	<0.001
MCS	0.32 (0.01)	<0.001		
Previous FACIT	0.64 (0.03)	<0.001	0.42 (0.04)	<0.001

* SE=standard error. Ref: Reference. SDI: SLICC/ACR Damage Index. CCI: Charlson's comorbidity index. MCS and PCS: mental and physical component summary measures of the SF-36, respectively.

Methods: Patients from a single-center prevalent Peruvian SLE cohort [the Almenara Lupus cohort] were included. Fatigue was assessed with the FACIT-Fatigue Scale, which has been validated in SLE and is frequently used. This 13-item questionnaire is based on the patients' experience over the previous 7 days; higher scores indicate less fatigue. Potentially associated factors were sex, age at diagnosis, ethnicity, educational level, relationship status (single or couple), socioeconomic status (SES), disease duration, disease activity (ascertained with the SLEDAI-2K), damage accrual (ascertained with the SLICC/ACR damage index), comorbidities (ascertained with the Charlson's comorbidity index), sicca symptoms, fibromyalgia, glucocorticoid dose, antimalarial and immunosuppressive drugs use, as well as the mental and physical component summary measurements of the SF-36 (PCS and MCS).

To determine the predictors of fatigue during the follow-up, generalized estimating equations (GEE) were used. Potential predictors were sex, age at diagnosis, ethnicity, educational level, relationship status, SES, disease duration, disease activity, damage, comorbidities, sicca symptoms, fibromyalgia, glucocorticoid dose, antimalarial and immunosuppressive drugs use, PCS and MCS. The multivariable models were done using a backward selection procedure with an alpha to stay in the model of 0.05.

Results: Four-hundred and one patients with 2228 visits were included and evaluated; 31 (7.7%) of the patients were male, 393 (98.0%) were Mestizo and their mean age at diagnosis was 35.1 (13.3) years. The mean FACIT score was 33.0 (10.8). In the multivariable analysis, the Afro-Latin American ethnicity, the PCS and the previous FACIT were associated with lower levels of fatigue, whereas having sicca symptoms and fibromyalgia were associated with higher levels of fatigue (Table 1).

Conclusion: In our SLE patients, the Afro-Latin American ethnic group, a higher PCS and the previous FACIT were associated with less fatigue; sicca symptoms and fibromyalgia were associated with more. Further studies are needed to evaluate these findings in other populations and seek better strategies to improve fatigue in SLE patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Oyarce-Calderon: None; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **S. Garcia-Hirsh**: Adium, 3; **Z. Rodríguez-Bellido**: None; **C. Pastor-Asurza**: None; **R. Perich-Campos**: None; **G. Alarcón**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6.

Abstract Number: 2379

Predicting Type 1 and Type 2 SLE Activity Using the LupusPRO

Amanda Eudy[1], Megan Clowse[2], Meenakshi Jolly[3], Dana Burshell[4], David Pisetsky[5], Connor Drake[4], Tamara Somers[6], Ralph Snyderman[7], Kai Sun[8], Rebecca Sadun[8], Lisa Criscione-Schreiber[4], Mithu Maheswaranathan[4], Nathaniel Harris[5], Jayanth Doss[9] and Jennifer Rogers[4], [1]Duke University, Raleigh, NC, [2]Duke University, Chapel Hill, NC, [3]Rush University, Chicago, [4]Duke University School of Medicine, Durham, [5]Duke University Medical Center, Durham, NC, [6]Duke University School of Medicine, Durham, NC, [7]Duke Center for Personalized Health Care, Durham, NC, [8]Duke University, Durham, NC, [9]Division of Rheumatology and Immunology, Duke University Department of Medicine, Durham, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The Type 1 & 2 SLE Model separates lupus disease activity into two groups: Type 1 (e.g. arthritis, rash, nephritis) and Type 2 SLE (e.g. widespread pain, fatigue, brain fog). A patient-reported outcome measure that accurately assesses Type 1 & 2 SLE activity would facilitate the monitoring of disease activity outside clinical settings. This study evaluates the utility of the LupusPRO in predicting Type 1 and Type 2 SLE activity.

Table 1. Cohort characteristics and LupusPRO domains across Type 1 & 2 SLE activity groups.

	Minimal n=105	Type 1 n=33	Type 2 n=85	Mixed n=72	p-value
Demographics					
Age, *mean (SD)*	45.0 (13.4)	34.4 (10.9)	48.0 (12.7)	42.4 (13.0)	<0.0001
Female, *n (%)*	93 (89%)	29 (88%)	82 (96%)	70 (97%)	0.04
Black, *n (%)*	58 (55%)	23 (70%)	43 (51%)	51 (71%)	0.03
Hispanic, *n (%)*	4 (4%)	4 (12%)	2 (2%)	6 (8%)	0.09
Clinical Characteristics					
Active LN, *n (%)*	0 (0%)	14 (42%)	0 (0%)	24 (33%)	<0.0001
SLEDAI, *mean (SD)*	1.2 (1.5)	6.2 (4.4)	0.8 (1.3)	6.0 (4.3)	<0.0001
Type 1 PGA, *mean (SD)*	0.1 (0.2)	1.1 (0.7)	0.2 (0.2)	1.3 (0.6)	<0.0001
Type 2 PGA, *mean (SD)*	0.2 (0.2)	0.2 (0.3)	1.0 (0.5)	1.2 (0.8)	<0.0001
PSD, *mean (SD)*	3.3 (2.2)	3.2 (2.2)	12.9 (5.6)	13.8 (5.7)	<0.0001
LupusPRO Domains					
HRQoL, Median (IQR)					
Lupus Symptoms	92 (75-100)	83 (67-100)	75 (67-92)	58 (42-83)	<0.0001
Cognition	88 (75-100)	88 (63-100)	50 (38-75)	50 (25-75)	<0.0001
Lupus Medications	100 (88-100)	88 (75-100)	100 (75-100)	75 (50-100)	<0.0001
Procreation	100 (100-100)	100 (75-100)	100 (100-100)	100 (94-100)	0.0003
Physical Health	100 (90-100)	100 (80-100)	80 (60-90)	68 (50-88)	<0.0001
Sleep	75 (58-92)	75 (50-83)	42 (25-58)	42 (25-50)	<0.0001
Fatigue	88 (69-100)	75 (50-94)	50 (25-75)	50 (25-56)	<0.0001
Pain	94 (75-100)	75 (50-100)	50 (31-75)	47 (25-63)	<0.0001
Emotional Health	83 (67-92)	67 (58-79)	63 (38-79)	42 (21-63)	<0.0001
Body Image	95 (75-100)	85 (70-100)	75 (55-95)	60 (43-83)	<0.0001
Non-HRQoL, Median (IQR)					
Desires-Goals	94 (75-100)	75 (63-94)	63 (50-88)	63 (44-75)	<0.0001
Social support	100 (63-100)	100 (75-100)	75 (50-100)	75 (50-100)	0.004
Coping	83 (67-100)	83 (75-100)	75 (50-92)	75 (58-92)	0.03
Satisfaction with care	100 (91-100)	100 (88-100)	100 (75-100)	97 (81-100)	0.09

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

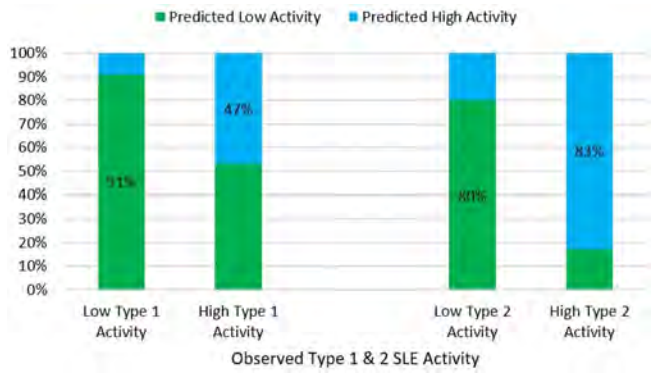


Figure 1. Observed Versus Predicted Type 1 & 2 SLE Activity.

Methods: Individuals meeting criteria for SLE were enrolled in a lupus registry. At routine visits, rheumatologists completed the SLEDAI and physician's global assessments (PGA) for Type 1 and Type 2 SLE activity. Patients completed the Polysymptomatic Distress Score (PSD) and LupusPRO, which consists of 10 health-related quality of life (HRQoL) and 4 non-HRQoL domains scored from 0 (worst) to 100 (best).

High Type 1 SLE activity was defined as SLEDAI ≥6, clinical SLEDAI ≥4, Type 1 PGA ≥1, or active nephritis. High Type 2 SLE activity was defined as PSD ≥8 or Type 2 PGA ≥1. Patients were categorized into 4 groups:

- Minimal SLE (low Type 1 and Type 2)
- Type 1 SLE (high Type 1 only)
- Type 2 SLE (high Type 2 only)
- Mixed SLE (high Type 1 and Type 2)

Median LupusPRO domain scores were compared across groups by the Kruskal–Wallis test. Logistic regression models, using all LupusPRO domains as predictors, estimated predicted probabilities for high Type 1 and high Type 2 SLE separately. We compared models' predicted probabilities with study definitions, calculated the proportion of correctly predicted outcomes, and calculated the Huberty's I index (>0.35 indicating predictive ability over chance)

Results: The LupusPRO was completed by 295 patients (mean age 44 years, 93% female, 59% Black). Among them, 36% had Minimal SLE activity, 11% Type 1 SLE activity, 29% Type 2 SLE activity, and 24% Mixed SLE activity. Differences in LupusPRO domain scores were observed across groups, with the Mixed SLE group having the lowest scores (Table 1). While scores were similar between the Type 2 SLE and Mixed SLE groups, lupus symptoms, lupus medications, emotional health and body image scores were significantly lower in the Mixed SLE group.

LupusPRO domains accurately predicted Type 2 SLE activity in 82% of patients (Huberty's I index = 0.64; Fig 1). Cognition, sleep and pain were key predictors of high Type 2 SLE activity. For Type 1 SLE activity, LupusPRO domains accurately predicted outcomes in 75% of patients (Huberty's I index = 0.46), with higher accuracy for low Type 1 activity (91%) than high Type 1 activity (47%). Among patients with high Type 1 SLE activity classified as low Type 1 activity, nearly half had active nephritis. Lupus symptoms, procreation and emotional health were significant predictors of high Type 1 SLE activity.

Conclusion: The LupusPRO effectively captures unique aspects of HRQoL and non-HRQoL that patients with SLE experience, particularly patients with active Type 2 SLE. While it was less able to predict active Type 1 SLE, due to small sample size or active lupus nephritis presenting asymptomatically, the LupusPRO offers valuable insights into patient experiences. Utilizing the LupusPRO can enhance the care provided to SLE patients, addressing their specific concerns and better targeting treatment strategies.

Disclosure: A. Eudy: Aurinia, 2, GlaxoSmithKlein(GSK), 5, Immunovant, 5; **M. Clowse**: None; **M. Jolly**: LRA, 1, Rush University, 9, 10; **D. Burshell**: Immunovant, 5; **D. Pisetsky**: Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 2, Immunovant, 2, 5; **C. Drake**: ZealCare, 12,, 10; **T. Somers**: None; **R. Snyderman**: DNAnexus, 4, Heartland Whole

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Health Institute, 4, iRhythm Technologies, 4, OrthoTheapeutics, Inc., 1, ZealCare, 4; **K. Sun**: Aurinia, 2; **R. Sadun**: The Expert Institute, 12,; **L. Criscione-Schreiber**: UCB, 5; **M. Maheswaranathan**: AstraZeneca, 2, UCB, 2; **N. Harris**: None; **J. Doss**: None; **J. Rogers**: AstraZeneca, 1, 1, Aurinia, 2, 5, Exagen, 5, Immunovant, 2, 5.

Abstract Number: 2380

Factors Influencing Time to Diagnosis in Systemic Lupus Erythematosus: A Real-World Retrospective Analysis

Amiah Griffin, Pat Phisitkul, Sarah Green, Ashley Suh, Bryan Han, Jiaming Li, Catherine Mao and April Barnado, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Individuals with Systemic lupus erythematosus (SLE) face diagnostic delays that can lead to increased disease activity and organ damage. Using a large electronic health record (EHR)-based incident SLE cohort, we examined if demographic, clinical, and provider factors impact time to SLE diagnosis.

Methods: We identified potential SLE individuals using ≥ 4 instances of SLE ICD-10-CM codes (M32.1, M32.8, M32.9) from a de-identified EHR database. Chart review confirmed diagnosis by a specialist (rheumatologist, nephrologist, or dermatologist) and incident case status as newly diagnosed SLE at our institution. We examined age, sex, race, ethnicity, and insurance type closest to SLE diagnosis as well as time to SLE diagnosis, first outpatient provider seen at our institution, and first SLE-related billing code prior to SLE diagnosis. Time to SLE diagnosis was defined as time from first code for any condition to SLE diagnosis by a specialist. First outpatient provider was categorized as primary care, rheumatology, surgical specialties, or internal medicine subspecialties. SLE-related billing codes capture signs or symptoms from the SLE classification criteria but do not mention SLE in the code name and were grouped into positive ANA or other autoantibody, hematologic, neurologic, serositis, renal, skin, and joints. We calculated mean time from first SLE-related code to SLE diagnosis. We used descriptive statistics for cohort characteristics and Mann-Whitney U and Kruskal-Wallis tests for comparisons.

Table 1. Characteristics of Incident SLE individuals.

Characteristics	n = 976 % (n)
Sex	**(n = 976)**
Male	14% (132)
Female	86% (844)
Race	**(n = 949)**
White	70% (668)
Black	26% (246)
Other	4% (35)
Ethnicity	**(n = 834)**
Hispanic	8% (69)
Not Hispanic	92% (765)
Insurance	**(n = 975)**
Commercial	64% (623)
Medicaid	16% (150)
Medicare	11% (110)
Military	5% (49)
Uninsured (Private Pay)	4% (43)
Mean age at SLE diagnosis ± standard deviation	37 ± 18
EHR Duration* (years)	12 ±8
Time to SLE Diagnosis**(years)	5 ±6

*EHR (electronic health record) duration was defined as the time from the first ICD code to the last ICD code for any condition.
**Time to SLE diagnosis was time from first ICD code for any condition to a clinical SLE diagnosis by a specialist.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Time to Diagnosis by Demographic and Clinical Characteristics.

Characteristics	Mean ± SD (years)	*p* value
Sex		
Female	5 ± 6	p = 0.60
Male	5 ± 6	
Race		
White	5 ± 6	p = 0.19
Black	5 ± 6	
Other	3 ± 6	
Ethnicity		
Hispanic	5 ± 6	p = 0.51
Not Hispanic	5 ± 6	
Insurance		
Commercial	4 ± 6	**p < 0.001**
Medicaid	5 ± 6	
Medicare	7 ± 7	
Military	2 ± 4	
Uninsured	6 ± 7	
Provider Specialty*		
Primary Care	6 ± 6	**p < 0.001**
Rheumatology	3 ± 5	
Surgical Specialties**	8 ± 6	
Internal Medicine Subspecialties***	6 ± 6	

*Provider specialty refers to the first outpatient encounter upon entry into the health system
Surgical Specialties: OBGYN, dentistry/oral surgery, neurosurgery, ophthalmology, orthopedics, otolaryngology, plastic surgery, sports medicine, general surgery, surgical oncology, urology *
***Internal Medicine Subspecialties: hematology, nephrology, neurology, allergy, autonomics, cardiology, endocrinology, gastroenterology, hepatology, infectious disease, oncology, pain management, pulmonary, psychiatry

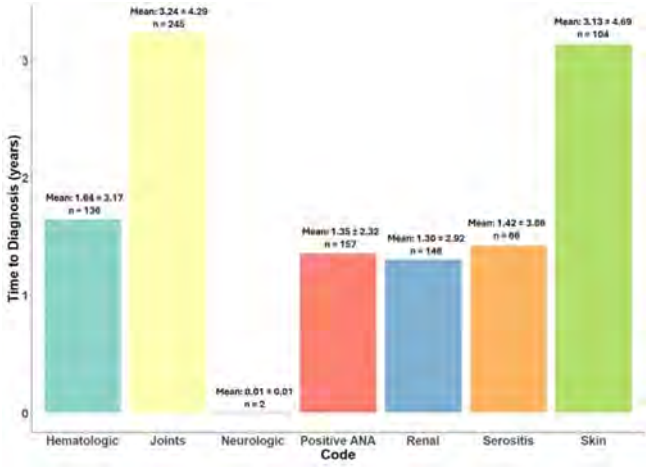


Figure 1. Time to SLE Diagnosis from first SLE-related billing code. We examined the first SLE-related billing code for individuals prior to SLE diagnosis. Mean time ± standard deviation from first SLE-related billing code to time of SLE diagnosis is labeled for the billing code categories. Billing codes were categorized into positive ANA/other autoantibody, hematologic manifestations (hemolytic anemia, anemia of chronic disease, pancytopenia, thrombocytopenia, leukopenia), neurologic (non-infectious encephalitis), serositis (pericarditis, pleurisy, pleural effusion), renal (nephritis, renal failure, proteinuria), skin (disorders or skin, alopecia, and dermatitis due to solar radiation), and joints (symptoms and disorders of joints and pain in joint).

Results: We identified 976 incident SLE individuals, predominantly female and White, with a mean time to SLE diagnosis of 5 ± 6 years (Table 1). Time to SLE diagnosis did not differ significantly by sex, race, or ethnicity (Table 2). Insurance status was significantly associated with time to diagnosis ($p < 0.001$). Individuals with military insurance had the shortest time to diagnosis (2 ± 4 years), and individuals with Medicare had the longest time (7 ± 7 years) (Table 2). Provider specialty at first outpatient visit was also significantly associated with time to SLE diagnosis ($p < 0.001$). Individuals seen first by rheumatologists had the shortest time to diagnosis (3 ± 5 years), while those seen by surgical specialties had the longest time (8 ± 6 years). The first SLE-related code was associated with time to SLE diagnosis ($p = 0.004$). Individuals with codes for encephalitis, renal disease (nephritis, renal failure, or proteinuria), positive ANA/other autoantibody, and serositis all had shorter times to diagnosis than individuals with first codes for hematologic abnormalities, skin findings, and joint pain (Figure 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In a large, real-world cohort at an academic medical center, time to SLE diagnosis was long with a mean time of 5 years. Time to SLE diagnosis varied by insurance, specialty of first provider seen, and clinical presentation. Ongoing studies are examining the trajectory of how SLE individuals interact with the healthcare system prior to SLE diagnosis. Our findings demonstrate that access to specialty care and insurance type can significantly shape the SLE diagnostic timeline and highlight areas to focus future interventions.

Disclosure: A. Griffin: None; **P. Phisitkul**: None; **S. Green**: None; **A. Suh**: None; **B. Han**: None; **J. Li**: None; **C. Mao**: None; **A. Barnado**: None.

Abstract Number: 2381

Renal Tubular Complement C9 Deposition is Linked to Tubulointerstitial Fibrosis and Progression to Chronic Kidney Disease in Lupus Nephritis

Angela Lu[1], Daming Shao[2], Ying Jin[1], Luis Chiriboga[3], Ming Wu[4], James Pullman[5], Anna Broder[6] and Shudan Wang[5], [1]Albert Einstein College of Medicine, Bronx, NY, [2]University of Chicago, Chicago, IL, [3]NYU Langone Medical Center, New York City, [4]Northwell Health, New Hyde Park, [5]Montefiore Medical Center, Bronx, NY, [6]Hackensack University Medical Center, Hackensack, NJ

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

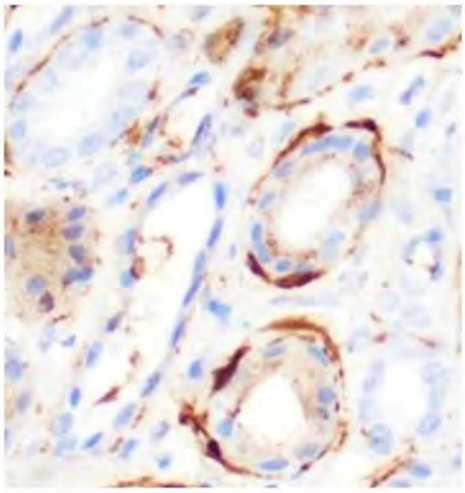
Background/Purpose: The complement system is known to play a central role in the pathogenesis of lupus nephritis (LN), one of the most severe manifestations of SLE. Emerging data suggest complement activation, particularly via membrane attack complex (MAC), mediates tubulointerstitial injury in LN. Studies have shown that tubulointerstitial damage leads to CKD progression in LN. Therefore, it is important to understand the mechanisms driving tubulointerstitial injury in LN to identify potential therapeutic targets. The objective of this study is to investigate C9 deposition, a part of the MAC, as a potential marker of tubulointerstitial injury and its association with chronic kidney disease (CKD) progression.

Methods: This retrospective cohort study included 30 LN patients who underwent kidney biopsies between February 2017 to November 2019 at an urban tertiary center. C9 deposition in proximal renal tubules was assessed via chromogenic immunohistochemistry on paraffin-embedded LN biopsy specimens stained with murine anti-human C9 antibody. C9 staining intensity was graded on a semi quantitative scale of 0 to 3 and categorized as present (1-3) vs absent (0). The percentage of staining in the tubules was also recorded. CKD progression was defined as $\geq$30% decline in estimated glomerular filtration rate (eGFR) within 5 years post biopsy, and those with stable or missing eGFR values were defined as non-progressors. Interstitial fibrosis/tubular atrophy (IFTA) was defined as $\geq$10% affected interstitium. Non-responders were defined as < 50% improvement in UPCR from baseline with no improvement in eGFR. CKD progression rates, treatment response, and IFTA were compared between C9 Positive (C9+) and C9 Negative (C9-).

Results: Among 30 LN patients, mean (SD) age was 34 (10.3) years, 23 (77%) were women, and 17 (57%) had proliferative LN (Class III, IV, III+V, and IV+V). Eighteen (60%) had tubular C9 deposition and 10 (33%) progressed to CKD. An example of an LN patient with tubular C9 stain is shown in Figure 1. Tubular C9 deposition was associated with IFTA: 71% in the C9+ group vs. 25% in the C9- group (p=0.016). LN patients with IFTA had greater C9 stain intensity (mean (SD) 1.0(0.6) vs 0.39 (0.56)) and percentage of tubules with C9 stain (14.67% (13.95) vs 5.36% (8.43)) as compared to LN without IFTA. Compared with C9- group, C9+ group had a lower median (IQR) urine-to-protein ratio (1.5 (0.9, 3.1) vs. 3.5 (2.2, 4.8) g/g,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Complement C9 Deposition in an LN patient



Legend: An example of a patient with Class IV+V LN who had 2+ tubular C9 deposition and 30 to 40% IFTA.

Table 1: Comparison of Demographics, Labs, and IFTA between LN Patients with and without Tubular C9 Staining

	Overall Sample, N = 30	Tubular C9 Positive, N = 18	Tubular C9 Negative, N = 12	p-value
Age, years, mean (SD)	34 (10.3)	37 (11.8)	30 (5.6)	0.11
Female sex, n (%)	23 (77%)	14 (78%)	9 (75%)	>0.99
Black, n (%)	14 (47%)	9 (50%)	5 (42%)	0.93
Hispanic, n (%)	12 (40%)	6 (33%)	6 (50%)	0.46
Prednisone, n (%)	26 (87%)	14 (78%)	12 (100%)	0.13
Immunotherapy*^, n (%)	11 (37%)	7 (39%)	4 (33%)	>0.99
eGFR, mL/min/1.73 m2	75.57 [47.75, 104.25]	78.50 [35-120] [48.00, 106.75]	71.17 [53.75, 89.25]	0.35
Creatinine, mg/dL	0.90 [0.72, 1.43]	0.85 [0.72, 1.43]	1.0 [0.78, 1.40]	0.66
UPCR at biopsy (g/g)	2.32 [1.19, 4.15]	1.50 [0.90, 3.11]	3.45 [2.21, 4.82]	0.043*
UPCR at 6 mo (g/g)	0.75 [1.25, 4.26]	0.84 [0.90, 3.11]	0.70 [2.74, 5.12]	0.84
Serum C3 <70 mg/dL, n (%)	18 (60%)	8 (44%)	10 (83%)	0.058
Serum C4 <14 mg/dL, n (%)	19 (63%)	10 (56%)	9 (75%)	0.44
dsDNA ≤75 IU/mL, n (%)	10 (33%)	5 (28%)	5 (42%)	0.46
Non-responder at 6 mo, n (%)	12 out of 29 (41%)	9 out of 18 (50%)	3 out of 11 (27%)	0.27
Proliferative LN Class, n (%)	17 (57%)	10 (56%)	7 (58%)	0.82
Tubular Fibrosis (IFTA) <10%, n (%)	14 out of 29** (48%)	5 out of 17 (31%)	9 out of 12 (75%)	0.016*
Tubular Fibrosis (IFTA) ≥ 10%, n (%)	15 out of 29** (52%)	12 out of 17 (71%)	3 out of 12 (25%)	
Tubular inflammation none, n (%)	25 out of 29** (86%)	16 out of 17 (94%)	9 out of 12 (75%)	0.28
Tubular inflammation present, n (%)	4 out of 29** (14%)	1 out of 17 (6%)	3 out of 12 (25%)	

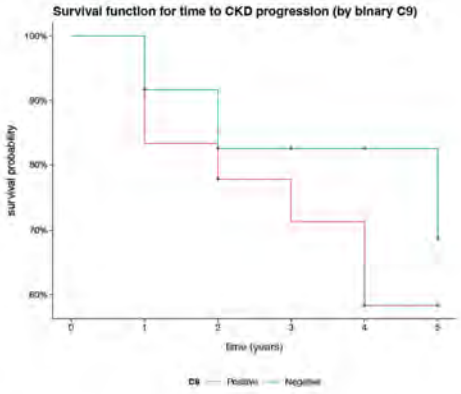
Legend: Tubular C9+ represents a stain intensity of 1-3, while Tubular C9- represents a stain intensity of 0. All continuous variables presented as median (IQR) unless otherwise specified. N (%) indicates "patient count (proportion of total N)".
*Significant p-value defined as $p < 0.05$. The Wilcoxon rank sum test and Fisher's exact test were used to assess continuous and categorical variables respectively.
**Missing tubular data for 1 patient, therefore N = 29
*^Mycophenolate mofetil, cyclophosphamide, tacrolimus, azathioprine, rituximab, voclopsorin, or belimumab

p=0.04) [Table 1]. Kaplan-Meier curves showed longer times to CKD progression in C9- group, with separation of the curves occurring after 2 years [Figure 2]. There was no difference in eGFR, serum creatinine, and treatment response at 6 months between the two groups.

Conclusion: This study demonstrates an association between C9 deposition in kidney tubules of LN patients with tubulointerstitial fibrosis. Patients with higher tubular C9 intensity trended towards shorter renal survival although not statistically significant, likely due to limited sample size. These findings highlight tubular MAC deposition as a potential marker for IFTA and CKD progression, underscoring the complement pathway as a potential therapeutic target for tubulointerstitial disease in LN.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Analysis of CKD progression over 5 years between LN patients with and without C9 Deposition in Kidney Tubules



Legend: Kaplan-Meier curves indicate that patients with negative tubular C9 staining have a longer survival time compared to those with positive C9 staining.

Disclosure: A. Lu: None; **D. Shao**: None; **Y. Jin**: None; **L. Chiriboga**: None; **M. Wu**: None; **J. Pullman**: None; **A. Broder**: None; **S. Wang**: None.

Abstract Number: 2382

Autoimmune Hemolytic Anemia in SLE: A Real-World National Cohort Study

Bana Shawareb[1], Muhannad Haddadin[1], lindsay Frumker[2], Keri Ann Pfeil[3], Meghan Gump[3], **Ansaam Daoud**[4] and Omer Pamuk[5], [1]Cleveland Clinic Akron General, Akron, OH, [2]Case Western Reserve University, Cleveland, [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [4]Case Western Reserve University/ University Hospitals, Cleveland, OH, [5]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune hemolytic anemia (AIHA) is a rare but serious hematologic manifestation of SLE. The prognostic implications of AIHA, particularly long-term mortality and organ involvement, remain poorly understood in real-world populations.

Methods: We conducted a multi-center, retrospective cohort analysis using the TriNetX research platform. Two cohorts were defined based on ICD-10 codes: SLE patients with AIHA and SLE without AIHA, selected via 1:1 propensity score matching across 59 variables, including demographics, comorbidities, and medication exposures. Outcomes were assessed using Kaplan-Meier survival methodology and risk remodeling. The primary outcome was all-cause mortality.

Results: Among 146,197 patients with SLE, 1,424 (0.97%) had AIHA. Before matching, the SLE+AIHA group was younger (mean age 39.5 ± 19.2 vs. 46.7 ± 17.3, p< 0.001), with higher proportions of males, non-White race, and Hispanic ethnicity. (Table 1) They also had a higher prevalence of antiphospholipid syndrome (9.7% vs. 3.7%, p< 0.001), end-stage renal disease (ESRD) (5.9% vs. 3.5%, p< 0.001), neutropenia, lymphocytopenia, and other cytopenias. (Table 1) Glucocorticoids,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Key Demographics and Diagnoses in SLE Patients With vs Without AIHA before and after propensity matching

A. Demographics

Variable	Before Matching - AIHA	Before Matching - Non-AIHA	Before Matching - p-value	After Matching - AIHA	After Matching - Non-AIHA	After Matching - p-value
Age at Index (Mean ± SD)	39.5 ± 19.2	46.7 ± 17.3	<0.001	39.6 ± 19.2	38.7 ± 18.4	0.263
Female (%)	82.7	86.7	<0.001	82.6	84.3	0.277
Male (%)	14.6	10.4	<0.001	14.7	13.7	0.487
Black or African American (%)	25.1	24.4	0.547	25.1	24.5	0.708
White (%)	37.1	48.9	<0.001	37.0	35.4	0.401
American Indian or Alaska Native (%)	0.9	0.4	0.011	0.9	0.8	0.827
Asian (%)	17.8	7.3	<0.001	17.9	20.1	0.164
Native Hawaiian or Pacific Islander (%)	1.4	0.8	0.012	1.4	0.8	0.176
Hispanic or Latino (%)	15.0	9.3	<0.001	14.8	16.2	0.372
Not Hispanic or Latino (%)	66.4	66.4	0.999	66.5	66.3	0.343

B. Diagnosis

Variable	Before Matching - AIHA	Before Matching - Non-AIHA	Before Matching - p-value	After Matching - AIHA	After Matching - Non-AIHA	After Matching - p-value
Glomerular disease in SLE	144 (11.7%)	8,057 (5.9%)	<0.001	143 (11.7%)	123 (10.0%)	0.194
End stage renal disease	72 (5.9%)	4,784 (3.5%)	<0.001	72 (5.9%)	63 (5.1%)	0.426
Dependence on renal dialysis	37 (3.0%)	2,458 (1.8%)	0.002	37 (3.0%)	24 (2.0%)	0.092
Antiphospholipid syndrome	119 (9.7%)	5,076 (3.7%)	<0.001	117 (9.5%)	119 (9.7%)	0.891
Other venous embolism/thrombosis	114 (9.3%)	5,500 (4.0%)	<0.001	112 (9.1%)	95 (7.7%)	0.217
Immune thrombocytopenic purpura	94 (7.6%)	1,878 (1.4%)	<0.001	91 (7.4%)	91 (7.4%)	1

Table 2. Key medication use and lab characteristics in SLE Patients With vs Without AIHA before and after propensity matching

C. Medication Use

Medication	Before Matching - AIHA	Before Matching - Non-AIHA	Before Matching - p-value	After Matching - AIHA	After Matching - Non-AIHA	After Matching - p-value
Hydroxychloroquine	629 (51.1%)	57,678 (42.4%)	<0.001	628 (51.3%)	633 (51.6%)	0.840
Glucocorticoids	886 (72.0%)	73,152 (53.7%)	<0.001	882 (71.9%)	879 (71.7%)	0.893
Azathioprine	125 (10.2%)	6,635 (4.9%)	<0.001	124 (10.1%)	130 (10.6%)	0.691
Mycophenolate mofetil	210 (17.1%)	11,052 (8.1%)	<0.001	206 (16.8%)	201 (16.4%)	0.786
Mycophenolic acid	43 (3.5%)	2,918 (2.1%)	0.001	42 (3.4%)	42 (3.4%)	1
Mycophenolate (unspecified)	10 (0.8%)	347 (0.3%)	<0.001	10 (0.8%)	10 (0.8%)	1
Cyclophosphamide	91 (7.4%)	1,994 (1.5%)	<0.001	89 (7.3%)	80 (6.5%)	0.473
Methotrexate	52 (4.2%)	8,803 (6.5%)	0.001	52 (4.2%)	46 (3.8%)	0.536
Belimumab	10 (0.8%)	2,085 (1.5%)	0.041	10 (0.8%)	10 (0.8%)	1
Rituximab	114 (9.3%)	1,785 (1.3%)	<0.001	110 (9.0%)	85 (6.9%)	0.062
Anifrolumab	0 (0%)	92 (0.1%)	0.362	0 (0%)	10 (0.8%)	0.002
Dapsone	39 (3.2%)	1,024 (0.8%)	<0.001	38 (3.1%)	39 (3.2%)	0.908
Danazol	14 (1.1%)	70 (0.1%)	<0.001	14 (1.1%)	10 (0.8%)	0.412

D. Laboratory Characteristics

Lab	Before Matching - AIHA	Before Matching - Non-AIHA	Before Matching - p-value	After Matching - AIHA	After Matching - Non-AIHA	After Matching - p-value
Neutropenia	76 (6.2%)	2,347 (1.7%)	<0.001	74 (6.0%)	74 (6.0%)	1
Low C3 (<80 mg/dL)	420 (34.1%)	11,463 (8.4%)	<0.001	418 (34.1%)	260 (21.2%)	<0.001
Low C4 (<10 mg/dL)	294 (23.9%)	7,039 (5.2%)	<0.001	294 (24.0%)	174 (14.2%)	<0.001
dsDNA Ab (U/mL)	130.6 ± 503.1 (n=178)	81.3 ± 645.3 (n=14,585)	0.310	131.3 ± 504.5 (n=177)	213.7 ± 1248.0 (n=164)	0.419
Smith+RNP Ab (U)	1.0 ± 1.1 (n=10)	1.8 ± 2.2 (n=145)	0.218	1.0 ± 1.1 (n=10)	0.2 ± 0 (n=10)	0.042
Sjogren's A Ab (U/mL)	54.9 ± 134.4 (n=100)	29.6 ± 108.6 (n=7,172)	0.021	54.9 ± 134.4 (n=100)	42.8 ± 136.8 (n=87)	0.543
Sjogren's B Ab (U/mL)	31.0 ± 102.1 (n=101)	14.6 ± 64.9 (n=7,552)	0.013	31.0 ± 102.1 (n=101)	18.0 ± 66.1 (n=85)	0.315

MMF, CYC, and rituximab were more frequent in the AIHA group (p< 0.001 for all). (Table 2) Following matching (n=1,226 per group), cohorts were balanced across covariates.

Low complement levels remained significantly more frequent in the AIHA group, including low C3 (< 80 mg/dL: 34.1% vs. 21.2%) and C4 (< 10 mg/dL: 24.0% vs. 14.2%) (p< 0.001 for both) (Table 2). Rituximab use remained elevated in AIHA group after matching (9.0% vs. 6.9%, P=0.062). (Table 2) Although glomerular disease appeared more prevalent in the AIHA

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

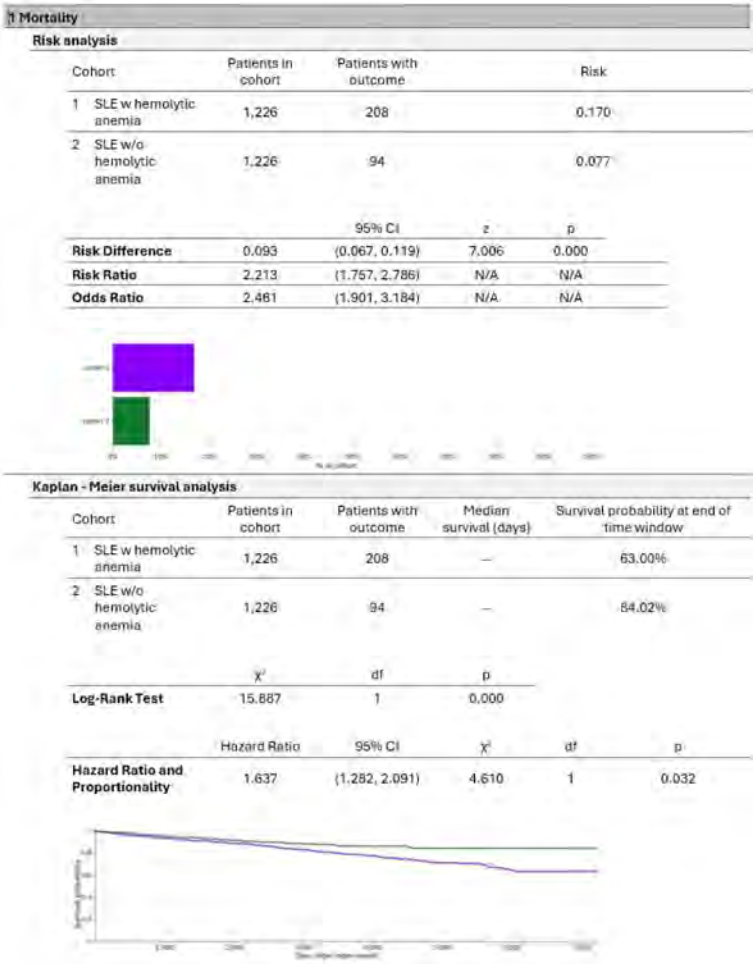


Figure 1. Mortality and Kaplan-Meier survival analysis in SLE Patients With vs Without AIHA before and after propensity matching

group before matching, this was attenuated after adjustment. Nephritis, ESRD, and dialysis did not differ significantly after matching.

Patients with SLE+AIHA exhibited significantly worse outcomes compared to matched controls. (Figure 1) Mortality was higher in the AIHA group (17.0% vs 7.7%), yielding a 9.3% absolute risk difference (95% CI: 6.7–11.9, $p < 0.001$), which is clinically meaningful. The risk ratio was 2.21 (95% CI: 1.76–2.79), and the odds ratio was 2.46 (95% CI: 1.90–3.18), indicating more than a twofold increased risk. Kaplan-Meier survival analysis at follow-up was 63% in the AIHA group vs. 84% in controls. Log-rank testing confirmed a significant difference ($\chi^2 = 15.89$, $p < 0.001$); hazard ratio was 1.64 (95% CI: 1.28–2.09, $p = 0.032$), reflecting a 64% higher mortality hazard in the AIHA group after accounting for survival duration.

Conclusion: In this national real-world cohort, AIHA was associated with significantly higher mortality risk and reduced long-term survival among SLE patients. These findings highlight AIHA as a prognostic marker of disease severity, supporting the need for early recognition and monitoring. Its association with low complement levels may further signal more aggressive disease phenotypes.

Disclosure: B. Shawareb: None; **M. Haddadin**: None; **I. Frumker**: None; **K. Pfeil**: None; **M. Gump**: None; **A. Daoud**: None; **O. Pamuk**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2383

The Age-Adjusted Charlson Comorbidity Index (CCI) Predicts All-Cause Mortality in Systemic Lupus Erythematosus (SLE) Patients: Data from the Almenara Lupus Cohort

Benny Rashuamán-Conche[1], Rocío Gamboa-Cárdenas[2], Victor Pimentel-Quiroz[3], Cristina Reategui-Sokolova[4], Claudia Elera-Fitzcarrald[4], Cesar Pastor-Asurza[5], Zoila Rodriguez-Bellido[6], Risto Perich-Campos[7], Graciela Alarcón[8] and Manuel Ugarte-Gil[9], [1]Hospital Guillermo Almenara Irigoyen, Lima, Lima, Peru, [2]Universidad Científica del Sur, Lima, Peru, [3]Universidad Científica del Sur, San Isidro, Peru, [4]Hospital Guillermo Almenara Irigoyen, Lima, Peru, [5]Hospital Nacional Guillermo Almenara Irigoyen, Lima, Pakistan, [6]Universidad Nacional Mayor de San Marcos, Lima, Peru, [7]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [8]The University of Alabama at Birmingham, Oakland, CA, [9]Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistémicas, Universidad Científica del Sur, Lima, Peru; Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru, Lima, Peru

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The CCI has been associated with adverse health-related outcomes in SLE-patients worldwide. Its modified version, the age-adjusted CCI (ACCI) has been associated with organ damage and mortality in Korean and Taiwanese SLE-patients cohorts. However, there are no studies addressing the impact of ACCI in mortality in Latin-American SLE cohorts. The aim of this study was to evaluate the ACCI as a predictor of mortality in Latin-American patients with SLE.

Table 1. Impact of the ACCI on mortality in SLE patients. *Adjusted for age at diagnosis, gender, ethnic group, socioeconomic status, years of education, tobacco use, disease duration, SLEDAI-2K, SLICC/ACR damage index, prednisone daily dose, antimalarial and immunosuppressive drugs use and the number of prescribed drugs. ACCI: Age-adjusted Charlson Comorbidity Index; HR: Hazard Ratio

	Unadjusted HR (95% CI)	*p* value	Adjusted* HR (95% CI)	*p* value
Main model				
ACCI score per 1.0 increase	1.442 (1.291-1.611)	<0.001	1.322 (1.083-1.615)	0.006
Alternative model				
ACCI score				
0	Ref.		Ref.	
1	1.907 (0.775-4.694)	0.16	1.965 (0.728-5.305)	0.183
2	3.447 (1.473-8.063)	0.004	2.640 (0.929-5.305)	0.068
3	4.144 (1.543-11.127)	0.005	2.838 (0.821-9.816)	0.099
4	6.502 (2.420-17.470)	<0.001	4.295 (1.030-17.913)	0.045
≥5	9.424 (3.904-22.747)	<0.001	5.246 (1.180-23.325)	0.029

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A secondary analysis was performed on the data from the Almenara Lupus Cohort. The follow-up period assessed was from January 2012 to March 2025. To enter this cohort, patients had to meet the ACR 1997 or the SLICC 2012 criteria set and to be older than 18 years of age at the baseline visit. Patients who had been diagnosed with other autoimmune disease, except Sjögren's or the antiphospholipid syndromes were excluded. Mortality was determined as the vital status according to the official information from the Peruvian Department of Health. ACCI scores were used to measure comorbidity status, excluding the point for connective tissue disease. It was calculated at baseline as a continuous variable. Unadjusted and adjusted Cox regression models were performed to assess the impact of ACCI on mortality. The model was adjusted for age at diagnosis, gender, ethnic group, socioeconomic status, years of education, tobacco use, disease duration, the SLEDAI-2K, the SLICC/ACR damage index, the prednisone daily dose, antimalarial and immunosuppressive drugs use and the number of prescribed drugs. In an alternative model, the ACCI was categorized as 0,1,2,3,4 and ≥ 5.

Results: Five-hundred and nine patients were included, 470 (92.3%) were women, their mean (SD) age at diagnosis was 35.0 (14.0) years, their disease duration at baseline was 6.7 (6.1) years, their mean (SD) ACCI was 1.4 (1.7) and their mean follow-up time was 8.5 (4.1) years. Fifty-seven (11.2%) patients died during the follow-up. A higher ACCI predicted mortality in both, the unadjusted [HR=1.442, (95% CI: 1.291-1.611; p≤0.001)] and adjusted analyses [HR=1.322, (95% CI: 1.083-1.615); p=0.006]. Main and alternative models are depicted in **Table 1**.

Conclusion: Higher ACCI scores predicted mortality after adjusting for potential confounders in a Latin-American SLE cohort. The active evaluation of comorbidities and their proper management will result in SLE patients having a better survival.

Disclosure: B. Rashuamán-Conche: None; **R. Gamboa-Cárdenas**: None; **V. Pimentel-Quiroz**: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **C. Reategui-Sokolova**: None; **C. Elera-Fitzcarrald**: None; **C. Pastor-Asurza**: None; **Z. Rodriguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcón**: None; **M. Ugarte-Gil**: AstraZeneca, 2, 6, Ferrer, 2, 6, GSK, 2, 6, Johnson & Johnson, 5, Novartis, 2, 6, Tecnofarma, 2, 6.

Abstract Number: 2384

Patient-Reported Quality of Life in SLE: Association with Biomarker-Derived Disease Activity Index (L-DAI) and hSLEDAI in a Prospective Cohort

Bernard Rubin[1], Rou Sore[1], Melissa Munroe[1], Daniele DeFreese[1], Adrian Holloway[1], Mohan Purushothaman[1], Yangfen Li[2], Hu Zeng[2], Uma Thanarajasingam[2], Judith James[3] and Eldon Jupe[1], [1]Progentec Diagnostics, Inc., Oklahoma City, OK, [2]Mayo Clinic, Rochester, MN, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systematic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by unpredictable disease activity. The Lupus Disease Activity Index (L-DAI) is a blood-based assessment informed by 10 immune biomarkers that objectively measures current disease activity, while the hybrid SLEDAI (hSLEDAI) is a clinician assessed measure of disease activity. This study evaluated the association between both L-DAI and hSLEDAI and patient reported quality of life (HRQol) in a small real-world community-based, prospectively followed SLE cohort.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective analysis from a small cohort of adults with classified SLE longitudinally and serially followed at the Mayo clinic from 2018 to 2021. L-DAI, hSLEDAI were collected quarterly for 12 months but clinicians were blinded to the L-DAI score throughout the study period. HRQol was assessed using the LupusPRO score (0-100 scale) at each visit. Linear regression was used to evaluate the association between HRQol and both L-DAI and hSLEDAI scores.

Results: Among 30 patients contributing to 145 visits, 27 (90%) were female and 3 (10.00%) were male. HRQol ranged from 28 to 100 (mean= 70.79 ± 16.34). In multivariable linear regression, both an increase in hSLEDAI (β = -0.89, p= 0.006) and an increase in L-DAI (β = -0.25, p= 0.020) were independently associated with a lower HRQol.

Conclusion: Our study demonstrated that both L-DAI and hSLEDAI were significantly associated with patient reported HRQol. In fact, an incremental increase in both L-DAI and hSLEDAI correlated with a decrease in patient reported quality of life. These findings highlight the utility of L-DAI and hSLEDAI in assessing disease activity and patient-reported quality of life measures. However, larger, more diverse patient cohorts are needed to validate these findings.

Disclosure: B. Rubin: Progentec Diagnostics, Inc., 3, 4; **R. Sore**: Progentec Diagnostics, Inc., 3; **M. Munroe**: Progentec Diagnostics, Inc., 3; **D. DeFreese**: Progentec Diagnostics, Inc., 3; **A. Holloway**: Progentec Diagnostics, Inc., 3; **M. Purushothaman**: Progentec Diagnostics, Inc., 3, 4, 10; **Y. Li**: None; **H. Zeng**: None; **U. Thanarajasingam**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **E. Jupe**: Progentec Diagnostics, Inc., 3, 4, 10.

Abstract Number: 2385

The Presence of Avascular Necrosis in Patients with Systemic Lupus Erythematosus Undergoing Total Knee Arthroplasty is Not Associated with Worse Outcomes

Billy Kim[1], Ahmed Deeb[1], Douglas Mintz[1], Susan Goodman[2], Jose Rodriguez[2], Mark Figgie[2] and Jason Blevins[3], [1]Hospital for Special Surgery, New York, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [3]Hospital for Special Surgery, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

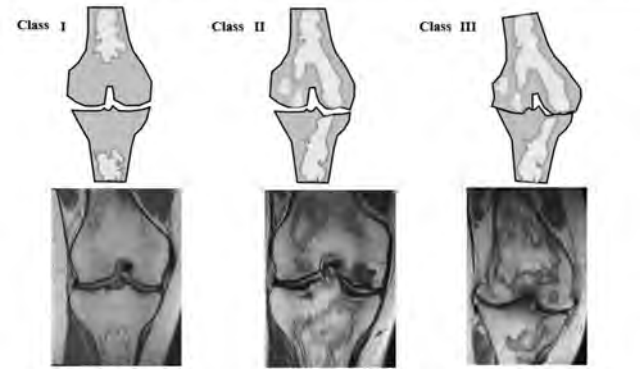
Background/Purpose: Systemic lupus erythematosus (SLE) patients seeking total knee arthroplasty (TKA) may present with secondary avascular necrosis (AVN) of the knee due to high-dose glucocorticoid use. Whether presence of AVN negatively impacts TKA outcomes in this high-risk population has not previously been studied.

Methods: A retrospective analysis of 184 knees (150 patients) with SLE undergoing TKA between 2015 and 2023 at a large academic institution was conducted. The cohort was stratified by the presence of AVN on preoperative X-ray and/or magnetic resonance imaging (MRI) when available. Imaging diagnosis was validated by an experienced musculoskeletal radiologist. Patient characteristics, clinical outcomes, and patient-reported outcome measures (PROMs) were compared between groups using univariable and multivariable analyses. Mean follow-up was 4.1 years (range: 0.1-8.5).

Results: AVN was present in 13% (n=23/184) of SLE knees. Patients with AVN were younger (P< 0.01) and had lower BMI than patients without AVN (P=0.05). Multivariable analyses demonstrated that younger age was associated with increased

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Class	Metadiaphyseal involvement	Articular Involvement (subchondral collapse, cartilage defect)	Deformity/Significant Bone Loss
I	+	-	-
II	+	+	-
III	+	+	+



MRI patterns of osteonecrosis inSLE patients with AVN

risk of 90-day readmission (P=0.03) and revision (P< 0.01). There were no significant differences in complication rates or postoperative PROMs between SLE patients with and without AVN (P >0.05). Based on osteonecrosis patterns on MRI, knee AVN was categorized into three sequential classes: I) primarily metadiaphyseal; II) metadiaphyseal with articular extension; III) progression with severe deformity or bone loss.

Conclusion: TKA outcomes in SLE patients with AVN are comparable to those without. Primary cemented implants provide durable results. In advanced stages of knee osteonecrosis, however, judicious preoperative evaluation is warranted, as significant bone deformities and defects may necessitate augments, cones, and/or stems.

Disclosure: B. Kim: None; **A. Deeb**: None; **D. Mintz**: American College of Radiology, 4, New York State Radiological Society, 4, Society of Skeletal Radiology, 4; **S. Goodman**: Johnson and Johnson, 2, Novartis, 5, Pfizer, 2; **J. Rodriguez**: ASS ASC Development Network, LLC, 8, BICMD, 2, 8, Exactech, Inc., 2, 9, HS2, LLC, 8, Joint Effort Administrative Services Organization, 8, Restor3d, 2, 9, Smith & Nephew, 2, 9, Wishbone, 8; **M. Figgie**: Bone Solutions, Inc, 2, Diffusion Rx, Inc., 1, 8, Enovis, 2, 9, HS2, LLC, 8, Icarus Medical, 8, Joint Effort Administrative Services Organization, 8, Mekanika, Inc., 8, Sylke, Inc., 1, 8, Wishbone Medical, 1, 2, 8, 9; **J. Blevins**: Globus Medical, 2, LimaCorporate, 2, Smith & Nephew, 2.

Abstract Number: 2386

anti-trim72 Auto-antibodies in Systemic Lupus Erythematosus Patients and a Lupus Mouse Model with Myocarditis Compromise Membrane Repair in Mouse & Human Cardiomyocytes

Braden Zeno[1], Shane Bruckner[2], kassidy Banford[3], Hannah Bulgart[4], Stacy Ardoin[5], noah weisleder[4] and Wael Jarjour[6], [1]Ohio State University, upper arlington, OH, [2]OSU, Columbus, OH, [3]Loyola University Chicago, Columbus, OH, [4]University of Kentucky, Lexington, KY, [5]Nationwide Children's Hospital, Columbus, OH, [6]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

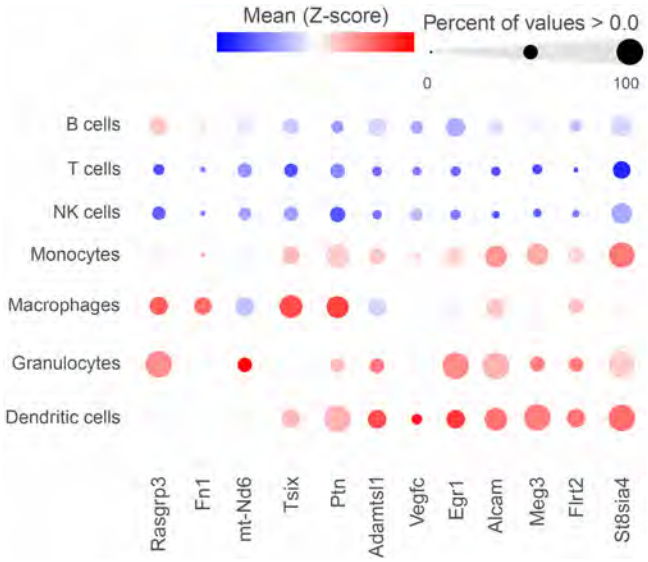
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that causes inflammation in many of the body's tissues, including the heart. Recent studies attribute almost 50% of mortality in lupus patients to cardiovascular (CV) disease after the first 10 years. Myocardial inflammation is present in up to 40% of lupus patients. Understanding the pathogenic mechanisms that drive CV disease in SLE is essential for its management and for developing new therapeutic approaches. Given the importance of the membrane barrier function in preventing exposure of intracellular antigens to the extracellular space where they could act as autoantigens, compromised membrane repair may be a contributory mechanism to SLE pathogenesis.

We identified TRIM72, which is essential for membrane repair, as an autoantigen in myositis patients. Our current studies indicate this may be the case in lupus as well. Given the potential contribution of membrane repair in development of lupus myocarditis and the role of TRIM72 in membrane repair, we hypothesized that defective membrane repair leads to aberrant extracellular exposure of membrane repair proteins, such as TRIM72, and autoantibody generation which creates a positive feedback loop causing further exposure of intracellular antigens contributing to lupus myocarditis pathogenesis.

Methods: A custom TRIM72 antibody ELISA was used to quantify serum levels of TRIM72 antibodies in serum. Multiphoton confocal laser microscopy was used to measure the dynamics of membrane repair *in vitro*. snRNAseq of NZM2410 mouse hearts was performed on young and old mice. Partek™ Flow™ software was used to analyze the transcriptomic expression data.

Results: We demonstrate that anti-TRIM72 auto-antibodies were elevated in both SLE patient serum diagnosed with myocarditis and serum of NZM2410 mice with myocarditis. Murine cardiomyocyte membrane repair is significantly reduced by exposure to myocarditis positive SLE patient serum with high levels of TRIM72 antibodies but not to healthy control serum. Removal of TRIM72 antibodies from serum reduces this effect on membrane repair. Preliminary data demonstrate similar trends of lupus sera containing anti-TRIM72 antibodies on human cardiomyocytes. snRNAseq revealed that cardiomyocytes are reduced and fibroblasts increase as NZM2410 mice age. Specific CV disease pathways are enriched in cells of aged hearts of NZM2410 mice as compared to young mice. Genes linked to lupus disease pathology are differentially expressed in immune cells. Subcluster analysis of specific cell populations, e.g. cardiomyocytes, fibroblasts, etc. revealed several cell types and gene expression profiles associated with development of SLE myocarditis.



Transcriptomic analysis of cardiac tissue reveals multiple differentially expressed genes linked to lupus. A partial list of statistically significant differentially expressed genes in immune cells is shown.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The plasma membrane repair protein TRIM72 is an autoantigen in SLE associated myocarditis and potentially contributes to disease pathogenesis. We demonstrate the presence of TRIM72 antibodies in SLE patients that can compromise membrane repair in cardiomyocytes in vitro. Ongoing studies will examine if these defects lead to membrane repair protein exposure to the extracellular space causing the production of autoantibodies which contribute to a vicious cycle that exacerbates SLE pathology.

Disclosure: B. Zeno: None; **S. Bruckner**: None; **k. Banford**: None; **H. Bulgart**: None; **S. Ardoin**: None; **n. weisleder**: None; **W. Jarjour**: None.

Abstract Number: 2387

Lupus Damage Index Revision – Item Generation and Reduction Phases

Burak Kundakci[1], Megan Barber[2], Ann Clarke[2], Sindhu Johnson[3], Ian Bruce[4] on behalf of the revised SLE organ damage index (SDI) collaborators, [1]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom, [2]Division of Rheumatology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [3]Division of Rheumatology, Department of Medicine, Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western and Mount Sinai Hospitals; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada, [4]Centre for Public Health, Faculty of Medicine, Health and Life Sciences, Queen's University Belfast, Belfast, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The current Systemic Lupus Erythematosus Damage Index (SDI) is a robust instrument, but is limited by missing items, restricted applicability in pediatric patients, and outdated item definitions. A data-driven and expert/patient consensus-based project to develop a revised Systemic Lupus International Collaborating Clinics (SLICC)/ American College of Rheumatology (ACR), Damage Index (SDI) is underway supported by SLICC, ACR and the Lupus Foundation of America. Our objective was to report the item generation and item reduction phase results for developing a revised SDI.

Methods: Item generation included a literature review by Literature Review Groups and a Delphi exercise of international SLE experts and patients. Item reduction involved Delphi rounds where items with a median appropriateness score of $\leq$ 4 out of 9 were excluded. A 14-member Item Reduction Committee assessed the remaining items and removed those that did not reflect the damage construct, were excessively rare, or were not feasible to assess. The Clinical Domain Groups then refined the remaining items, and their definitions.

Results: The Delphi panel included 146 individuals from 35 countries. Item generation identified 226 initial candidate items. The Delphi exercise, review by the Item Reduction Committee and Clinical Domain Groups resulted in removal of 36, 126 and 25 items, respectively. This resulted in 39 items across 13 clinical domains. Eleven items from the original SDI, including chronic peritonitis, cranial neuropathy, mesenteric insufficiency, muscle atrophy or weakness, osteomyelitis, pancreatic insufficiency requiring enzyme replacement or with pseudocyst, pleural fibrosis, proteinuria, shrinking lung, skin ulceration (excluding thrombosis), and stricture or upper gastrointestinal tract surgery were removed. Several new items were proposed, such as growth failure/reduced final height and adrenal insufficiency. Sub-categorizing items based on severity or grade is proposed for 17 (43.6%) proposed items. Additionally, the Clinical Domain Groups developed definitions for each of the items, based on their clinical expertise, current evidence-based practice or specialty guidelines.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This data-driven and expert/patient consensus-based process has proposed 39 candidate items, some with sub-items, and with definitions for a revised SDI. Weighting of items and sub-items is now underway to increase the sensitivity and responsiveness of any new index.

Disclosure: B. Kundakci: None; **M. Barber**: AstraZeneca, 1, GlaxoSmithKlein(GSK), 1; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, Novartis, 2, Roche, 2; **S. Johnson**: None; **I. Bruce**: AstraZeneca, 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Merck/MSD, 2, Novartis, 5, Otsuka, 5, UCB, 2.

Abstract Number: 2388

Correlation between Activity Index, Organ Damage Index, and HAQ in Systemic Lupus Erythematosus: a single-center study

Carmen Lasa Teja[1], Carmen Bejerano-Herreria[2], Laura Muñoz-Llopis[2], Pilar Ortiz-Lavin[2], Carolina Aguirre-Portilla[2], Virginia Portilla González[3] and Ricardo Blanco[4], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [2]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, [4]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) presents a highly heterogeneous clinical course and prognosis. In line with EULAR recommendations and treat-to-target (T2T) strategies, comprehensive assessment of disease activity, organ damage, and patient-reported outcomes (PROs) is essential to optimizing long-term patient care.

This study aimed to analyze the correlation between disease activity, organ damage, and PROs in a well-characterized cohort of SLE patients, providing insights into clinical management and functional outcomes.

Methods: We conducted an observational, cross-sectional study including the first 208 consecutive SLE patients assessed under a prospective Treat-to-Target (T2T) strategy from March 31, 2023, at a university hospital in Northern Spain.

Disease activity was measured using the SLE Disease Activity Index 2000 (SLEDAI-2K) and SLE-Disease Activity Score (SLE-DAS). Remission was defined according to DORIS criteria (clinical SLEDAI-2K = 0, Physician Global Assessment (PGA) = 0). Lupus Low-Disease Activity State (LLDAS) was defined as SLEDAI-2K ≤4, no disease activity in major organ systems, no new disease activity compared to previous evaluations, PGA ≤1, and prednisone ≤7.5 mg/day.

Organ damage was assessed using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI, SDI). Patient-reported outcomes (PROs) included the Health Assessment Questionnaire (HAQ) and Lupus Impact Tracker (LIT).

Data are presented as percentages, mean±SD, or median [IQR], as appropriate. Correlations between HAQ, SDI, and remission criteria (DORIS and LLDAS) were analyzed to explore their interrelationship in clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. General features of patients and clinical outcome of 208 patients with Systemic Lupus Erythematosus (SLE).

DEMOGRAPHIC DATA		ORGAN DAMAGE	
Female, n (%)	180 (86.5)	**SDI**, median [IQR]	0 [0-1]
Age, years, mean±SD	46.9±14.3	**SDI = 0**, n (%)	117 (56.3)
Caucasian, n (%)	185 (88.9)	**SDI > 0**, n (%)	91 (43.7)
SLE follow-up, months, median [IQR]	145 [53-362]	Ocular	40 (19.2)
		Neuropsychiatric	30 (14.4)
MAIN ORGAN INVOLVEMENT, n (%)		Musculoskeletal	20 (9.7)
LN	60 (28.8)	Gastrointestinal	13 (6.3)
CNS	14 (6.7)	Malignancy	11 (5.4)
Hemolityc anemia	13 (6.3)	**TREATMENT (CURRENT/EVER)** n (%)	
		Prednisone	88(42.3)/175(84.3)
ACTIVITY INDEX		Antimalarial agents	164(78.8)/70(33.6)
SLEDAI-2K, median [IQR]	0 [0-2]	Belimumab	55(26.4)/21(10.1)
SLE-DAS, median [IQR]	0.4 [0.4-2.6]	Mycophenolate Mofetil	36(17.3)/23(11.1)
Remission DORIS, n (%)	116 (55.7)	Rituximab	6(2.9)/47(22.6)
LLDAS, n (%)	58 (27.9)	Cyclophosphamide	0/53(25.5)
		Anifrolumab	3(1.4)/0
FUNCTIONAL SCORE		Azathioprine	31(14.9)/51(24.5)
HAQ, median [IQR]	0.5 [0-1.1]	Methotrexate	12(5.7)/51(24.5)
LIT, median [IQR]	40 [15-55]	Tacrolimus	6(3.8)/0

Abbreviations
Lupus Nephritis **(LN)**, Central Nervous System **(CNS)**, Health Assessment Questionnaire **(HAQ)**, Lupus Impact Tracker **(LIT)**, Lupus Low Disease Activity State **(LLDAS)**, SLICC/ACR Damage Index **(SDI)**, Systemic Lupus Erythematosus Disease Activity Score **(SLE-DAS)**, Systemic Lupus Erythematosus Disease Activity Index 2000 **(SLEDAI-2K)**.

Table 2. A comparative table between remission according to DORIS, Lupus Low Disease Activity (LLDAS) and organ damage involvement and HAQ.

Total SLE patients, n= 208				
	Total	DORIS Remission N= 116	LLDAS N= 58	Non Remission / non LLDAS N= 34
SDI, score				
SDI=0, n (%)	117	61 (52.6)	37 (63.8)	19(55.9)
SDI=1, n (%)	38	21 (18.10)	10 (17.2)	7 (20.6)
SDI>2, n (%)	53	34 (29.3)	11 (19)	8 (23.5)
HAQ				
HAQ= 0-1, n (%)	151	100(86.2)	35(60.3)	16(47.1)
HAQ= 1-2, n (%)	50	13 (11.2)	21(36.2)	15(44.1)
HAQ >2, n (%)	9	3(2.6)	2 (3.5)	3 (6.8)

Results: We analyzed 208 SLE patients (86.5% women, mean age 46.9 ± 14.3 years). After a median follow-up of 145 [53–361] months, lupus nephritis was present in 60 (28.8%), corticosteroids were used by 88 (42.3%), and antimalarials by 164 (78.8%). At evaluation, 116 (55.7%) met DORIS remission criteria, while 58 (27.9%) were in LLDAS. Organ damage (SDI) was observed in 38 (18.2%) with SDI ≥1 and in 53 (25.4%) with SDI ≥2. Notably, 55.9% of non-remission patients had SDI = 0, indicating variability in disease progression. Among patients in remission, 86.2% had a HAQ score between 0 and 1, versus 47.1% of non-remission patients.

Conclusion: While 55.7% achieved DORIS-defined remission, nearly half had organ damage (SDI ≥1), highlighting a weak correlation between disease activity indices and organ damage. Concurrent assessment of both measures is essential. The stronger correlation between HAQ and SDI suggests PROs may better reflect disease burden than activity indices alone.

Disclosure: C. Lasa Teja: None; **C. Bejerano-Herreria**: None; **L. Muñoz-Llopis**: None; **P. Ortiz-Lavin**: None; **C. Aguirre-Portilla**: None; **V. Portilla González**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2389

A Comparison of Patients with Older Onset vs. Younger Onset SLE: A Retrospective Cohort Study

Chelsea Guan[1], Milad Heydari-Kamjani[2], Keri Ann Pfeil[1], Elleson Harper[1], Lindsay Frumker[3], Meghan Gump[1] and Omer Pamuk[2], [1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, [2]University Hospitals Cleveland Medical Center/ Case Western Reserve University, Cleveland, OH, [3]University hospitals Cleveland medical center, Highland Heights, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: SLE is a systemic autoimmune disease that can present at different ages and with various multiorgan complications. In this study, we aimed to analyze the differences in characteristics in patients with older onset SLE (age of diagnosis >50) and younger onset SLE (age of diagnosis <49).

Methods: A retrospective cohort study was performed using TriNetX, a global federated health research network that provides access to electronic medical records across large health care organizations (HCOs). Data was used from 99 different

Table 1. Baseline Characteristics of Older Onset SLE Patients vs. Younger Onset SLE Patients

Variable	Before Matching			After Matching		
	SLE-Older (n = 62,242)	SLE-Younger (85,011)	P-Value	SLE-Older (n = 45,733)	SLE-Younger (45,733)	P-Value
Demographics						
Age at Index (Mean ± SD)	62.1 ± 8.3	34.0 ± 10.4	**<0.001**	61.3 ± 8.0	35.7 ± 10.0	**<0.001**
Female	52,781 (84.8%)	75,403 (88.7%)	**<0.001**	39,647 (86.7%)	39,681 (86.8%)	0.740
Male	7,170 (11.5%)	7,906 (9.3%)	**<0.001**	4,715 (10.3%)	4,600 (10.1%)	0.209
Black or African American	13,782 (22.1%)	22,998 (27.1%)	**<0.001**	10,884 (23.8%)	11,025 (24.1%)	0.275
White	34,666 (55.7%)	37,036 (43.6%)	**<0.001**	23,817 (52.1%)	23,840 (52.1%)	0.879
Asian	3,396 (5.5%)	7,306 (8.6%)	**<0.001**	2,920 (6.4%)	2,636 (5.8%)	**<0.001**
SLE related comorbidities						
Glomerular disease	2,258 (3.6%)	6,890 (8.1%)	**<0.001**	2,038 (4.5%)	2,041 (4.5%)	0.962
End-stage renal disease	2,156 (3.5%)	3,162 (3.7%)	**0.009**	1,653 (3.6%)	1,711 (3.7)	0.308
Dependence on renal dialysis	1,204 (1.9%)	1,767 (2.1%)	0.092	892 (2.0%)	919 (2.0%)	0.522
Kidney transplant	735 (1.2%)	972 (1.1%)	0.051	580 (1.3%)	537 (1.2%)	0.195
APS	2,106 (3.4%)	3,556 (4.2%)	**<0.001**	1,657 (3.6%)	1,666 (3.6%)	0.874
Venous thromboembolism	3,007 (4.8%)	3,172 (3.7%)	**<0.001**	1,891 (4.1%)	1,860 (4.1%)	0.605
Arterial thromboembolism	525 (0.8%)	404 (0.5%)	**<0.001**	295 (0.6%)	288 (0.6%)	0.771
Discoid lupus	5,798 (9.3%)	6,920 (8.1%)	**<0.001**	3,889 (8.5%)	3,875 (8.5%)	0.868
scLE	638 (1.0%)	428 (0.5%)	**<0.001**	317 (0.7%)	315 (0.7%)	0.936
Epilepsy and recurrent seizures	1,961 (3.2%)	3,077 (3.6%)	**<0.001**	1,512 (3.3%)	1,477 (3.2%)	0.515
Mononeuropathies of upper limb	3,181 (5.1%)	2,324 (2.7%)	**<0.001**	1,790 (3.9%)	1,786 (3.9%)	0.946
Hemolytic anemias	1,113 (1.8%)	2,661 (3.1%)	**<0.001**	920 (2.0%)	851 (1.9%)	0.098
Lymphocytopenia	375 (0.6%)	804 (0.9%)	**<0.001**	296 (0.6%)	269 (0.6%)	0.255
Nicotine dependence	6,803 (10.9%)	7,511 (8.8%)	**<0.001**	4,609 (10.1%)	4,603 (10.1%)	0.947
Alcohol related disorders	1,311 (2.1%)	1,360 (1.6%)	**<0.001**	859 (1.9%)	864 (1.9%)	0.903
Type 2 diabetes mellitus	9,276 (14.9%)	3,922 (4.6%)	**<0.001**	3,694 (8.1%)	3,547 (7.8%)	0.072
Essential hypertension	30,662 (49.3%)	17,626 (20.7%)	**<0.001**	15,328 (33.5%)	15,299 (33.5%)	0.839
Overweight and obesity	9,191 (14.8%)	9,503 (11.2%)	**<0.001**	5,789 (12.7%)	5,860 (12.8%)	0.481
Inflammatory polyarthropathies	15,783 (25.4%)	12,916 (15.2%)	**<0.001**	9,310 (20.4%)	9,179 (20.1%)	0.281
Pleurisy	555 (0.9%)	964 (1.1%)	**<0.001**	426 (0.9%)	412 (0.9%)	0.627
Acute pericarditis	378 (0.6%)	785 (0.9%)	**<0.001**	301 (0.7%)	281 (0.6%)	0.406
Sjogren's syndrome	7,300 (11.7%)	6,020 (7.1%)	**<0.001**	4,595 (10.0%)	4,614 (10.1%)	0.835
Thrombocytopenia	3,195 (5.1%)	4,018 (4.7%)	**<0.001**	2,046 (4.5%)	1,919 (4.2%)	**0.039**
Neutropenia	791 (1.3%)	1,090 (1.3%)	0.848	554 (1.2%)	520 (1.1%)	0.297

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Serological Profiles and Medications Used in Older Onset SLE patients vs. Younger Onset SLE Patients

Variable	Before Matching			After Matching		
	SLE-Older (n = 62,242)	SLE-Younger (85,011)	P-Value	SLE-Older (n = 45,733)	SLE-Younger (45,733)	P-Value
Antibody profile						
dsDNA-Ab (+/-)	5,495 (8.8%)	9,356 (11.2%)	**<0.001**	4,109 (9.0%)	4,612 (10.1%)	**<0.001**
Ro/SSA-Ab (+/-)	2,679 (4.3%)	4,766 (5.6%)	**<0.001**	2,019 (4.4%)	2,262 (4.9%)	0.998
La/SSB-Ab (+/-)	2,735 (4.4%)	4,726 (5.6%)	0.310	2,026 (4.4%)	2,412 (5.3%)	0.170
RNP-Ab (+/-)	2,106 (3.4%)	3,755 (4.4%)	**0.002**	1,589 (3.5%)	1,815 (4.0%)	**<0.001**
Anti-Smith-Ab	44 (0.1%)	107 (0.1%)	**0.001**	30 (0.1%)	48 (0.1%)	0.351
Anti-Chromatin Ab	444 (0.7%)	623 (0.7%)	0.743	338 (0.7%)	326 (0.7%)	0.640
Ribosomal P Ab	330 (0.5%)	568 (0.7%)	**0.001**	257 (0.6%)	291 (0.6%)	0.145
Complement C3 (low)	2,636 (4.2%)	9,539 (11.2%)	**<0.001**	2,119 (4.6%)	3,805 (8.3%)	**<0.001**
Complement C4 (low)	1,542 (2.5%)	6,145 (7.2%)	**<0.001**	1,234 (2.7%)	2,403 (5.3%)	**<0.001**
Medications						
Hydroxychloroquine	23,954 (38.5%)	37,698 (44.3%)	**<0.001**	18,325 (40.1%)	18,214 (39.8%)	0.454
Glucocorticoids	34,758 (55.8%)	46,022 (54.1%)	**<0.001**	24,506 (53.6%)	24,412 (53.4%)	0.533
Azathioprine	2,595 (4.2%)	4,538 (5.3%)	**<0.001**	2,012 (4.4%)	1,897 (4.1%)	0.060
Mycophenolate mofetil	3,620 (5.8%)	8,588 (10.1%)	**<0.001**	3,049 (6.7%)	3,056 (6.7%)	0.926
Mycophenolic acid	998 (1.6%)	2,226 (2.6%)	**<0.001**	828 (1.8%)	849 (1.9%)	0.605
Cyclophosphamide	468 (0.8%)	1,538 (1.8%)	**<0.001**	422 (0.9%)	396 (0.9%)	0.361
Belimumab	693 (1.1%)	1,492 (1.8%)	**<0.001**	598 (1.3%)	594 (1.3%)	0.907
Rituximab	695 (1.1%)	1,189 (1.4%)	**<0.001**	508 (1.1%)	462 (1.0%)	0.138

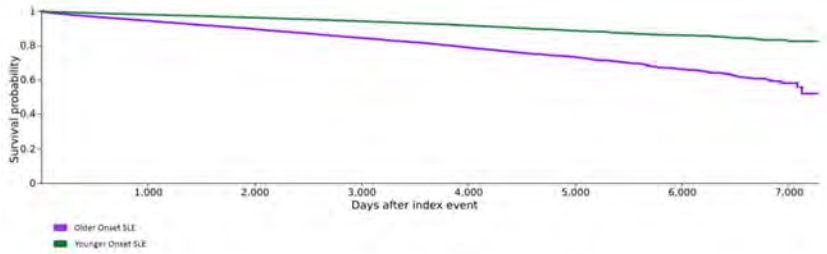


Figure 1. Kaplan-Meier Survival Analysis of Mortality in Older Onset SLE Patients vs. Younger Onset SLE Patients

HCOs. Adult patients (>18 years of age) were divided into two cohorts, older and younger onset SLE, based on age of SLE diagnosis (ICD-10: M32.9). 1:1 propensity score matching was performed using 58 different baseline patient characteristics, including demographics, comorbidities, medication usage, and serological profiles (Table 1 and Table 2). Kaplan-Meier survival analysis was performed to examine differences in mortality between both cohorts.

Results: 62,242 patients were included in the older onset SLE cohort and 85,011 patients were included in the younger onset SLE cohort before propensity score matching. After propensity score matching, 45,733 patients were included in the older onset SLE and younger onset SLE cohorts respectively.

Univariate analysis before matching showed several significant differences in characteristics between both cohorts (Table 1 and Table 2). After propensity score matching, the frequency of thrombocytopenia was higher in the younger onset SLE group compared to the older onset SLE cohort ($p < 0.001$), otherwise the frequency of SLE related comorbidities was not significantly different (Table 1). Patients in the younger onset SLE cohort had a higher frequency of positive anti-dsDNA ($p < 0.001$), positive anti-RNP ($p < 0.001$), and low complement C3 and C4 ($p < 0.001$) (Table 2). There were no statistically significant differences in the frequencies of medications used (Table 2).

Risk analysis showed that 4,658 (10.2%) of older onset SLE patients died and 1,896 (4.1%) of younger onset SLE patients died during the study period (7,000 days) (RR = 2.457, 95% CI 2.333, 2.587, p = < 0.001).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Survival analysis revealed that the older onset SLE group had a markedly lower survival probability at the end of the observation period (51.79%) compared to those diagnosed before age 49 (82.38%). The difference in survival between groups was statistically significant (log-rank test $\chi^2 = 1515.153$, $p < 0.001$). Cox proportional hazards modeling showed that older onset SLE was associated with a significantly increased risk of mortality (hazard ratio: 2.77; 95% CI: 2.63–2.92). The assumption of proportional hazards was met ($\chi^2 = 1.466$, $p = 0.226$), supporting the validity of the model (Figure 1).

Conclusion: This retrospective cohort study suggests that younger onset SLE patients are more likely to develop thrombocytopenia, otherwise have no significant difference in the examined comorbidities. Patients with younger onset SLE are also more likely to have positive anti-dsDNA, positive anti-RNP, and hypocomplementemia. Medications used between younger and onset SLE patients are not significantly different. Patients with older onset SLE have a significantly increased risk of mortality.

Disclosure: C. Guan: None; **M. Heydari-Kamjani**: None; **K. Pfeil**: None; **E. Harper**: None; **L. Frumker**: None; **M. Gump**: None; **O. Pamuk**: None.

Abstract Number: 2390

SLE Genetic Risk Loci in the Context of Environmental Exposure: A Gene-Based Classification and Clinical Insight

Nina Oparina[1], Holme Vestin[1], Sarah Reid[1], Ahmne Sayadi[1], Maija-Leena Eloranta[1], Martina Frodlund[2], Karoline Lerang[3], Andreas Jönsen[4], Øyvind Molberg[3], Solbritt Rantapää-Dahlqvist[5], Anna Rudin[6], Chrisopher Sjöwall[7], Anders Bengtsson[4], Lars Rönnblom[1] and **Dag Leonard**[1], [1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [2]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Linkoping, Sweden, [3]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [4]Department of Clinical Sciences, Lund University, Lund, Sweden, [5]Department of Public Health and Clinical Medicine/Rheumatology, Umeå University, Umeå, Sweden, [6]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy of University of Gothenburg, Gothenburg, Sweden, [7]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Growing evidence supports the role of chemical exposures as contributors to the development of Systemic lupus erythematosus (SLE)[1]. Several of the gene variants associated with SLE appear to be responsive to various environmental substances. We aimed to classify SLE-associated loci based on gene-chemical connection and to reveal potential exposure-based differences. We performed functional enrichment analysis, constructed polygenic risk scores (PRSs) and analyzed clinical phenotype associations.

Methods: A total of 155 genome-wide association study (GWAS) significant (p=5e-8) SLE single nucleotide variants (SNVs) were selected (based on European ancestry). Comparative Toxicogenomics Database (CTD[2]) was scanned for chemical exposure connection with these genes. A gene-chemical interaction analysis was performed. The top 1/3 of the genes with the highest number of gene–chemical connections were selected and denoted as total (TOT). Separately, we analyzed the number of interactions for endocrine-disrupting chemicals (EDCs)[3].

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Scandinavian patients with SLE (n=1419), fulfilling ≥4 ACR-97 criteria, were genotyped by Illumina Global Screening Array. Clinical data was collected from charts. SLE environmental exposure weighted polygenic risk scores (PRSs) were developed including the TOT and EDC risk loci. Regression analysis compared the top quartile to the remaining individuals adjusting for sex and age. Functional enrichment was carried out using KEGG, TRRUS[4] and Reactome databases.

Results: In total, 19 of top genes identified in the CTD database were included exclusively in the TOT-PRS (including *IL7R* and *STAT4*), and 17 were specific to the EDC-PRS (including *ATXN2 and TYK2*). The highest number of interactions was observed for *IL10* (n=3169).

Pathway analysis showed enrichment of Toll-like receptor signaling in both groups (p=1.0e-4), while B-cell receptor signaling (p=1.6e-3) was enriched in TOT-PRS only.

Both scores were associated with higher risk of malar rash (OR 1.6, p=4.4e-8, TOT-PRS; OR 1.6, p=6.9e-8, EDC-PRS), nephritis (OR 1.7, p=8.1e-14, TOT-PRS; OR 1.6, p=9.2e-14, EDC-PRS) and serositis (OR 1.5, p=7.8e-7, TOT-PRS; OR 1.5, p=5.1e-7, EDC-PRS). No association was observed for discoid rash or arthritis (both p >0.05). Further, the PRSs showed association with thrombocytopenia (OR 1.1, p=0.02, TOT-PRS; OR 1.5, p=5.5e-3, EDC-PRS) and leukopenia/lymphopenia (OR 1.3, p=2.4e-4, TOT-PRS; OR 1.7, p=2.8e-5, EDC-PRS).

Conclusion: We demonstrated that classification of SLE loci based on gene-chemical connections can identify potential connections between selected risk genes and chemical compounds. A strong association between specific risk genes and a large number of chemical compounds suggests that these genes may be important targets when investigating the role of environmental exposures to risk for disease. Leveraging public functional gene-based information can also help to reveal exposome-associated mechanisms behind SLE clinical heterogeneity.

References:

1. Kosarek et al. 2024, doi:10.1007/s40572-024-00444-9.
2. Davis et al. 2024, doi:10.1093/nar/gkae883.
3. Liu et al. 2022, doi:10.1016/j.ecoenv.2022.113382.
4. Han et al. 2017, doi:10.1093/nar/gkx1013.

Disclosure: N. Oparina: None; **H. Vestin**: None; **S. Reid**: None; **A. Sayadi**: None; **M. Eloranta**: None; **M. Frodlund**: None; **K. Lerang**: None; **A. Jönsen**: None; **Ø. Molberg**: None; **S. Rantapää-Dahlqvist**: None; **A. Rudin**: None; **C. Sjöwall**: Bristol-Myers Squibb(BMS), 3; **A. Bengtsson**: None; **L. Rönnblom**: AstraZeneca, 6, Biogen, 2; **D. Leonard**: None.

Abstract Number: 2391

Antinuclear Antibody Positivity in Patients with Psoriasis and Psoriatic Arthritis and the Risk of Developing Clinical Symptoms of SLE Following TNF Inhibitor Therapy

Damira Sereda[1], Leilani Leechalad[1] and Andras Perl[2], [1]SUNY Upstate Medical University, Syracuse, NY, [2]SUNY, Syracuse, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: It has been reported that the presence of positive ANA in patients treated with TNF inhibitors (TNFi) could be associated with the development of new clinical symptoms of SLE. The aim of this study is to review the prevalence of positive ANA titers by immunofluorescence assay (IF-ANA) in patients with psoriasis (PSO) and PsA, as well as the associated risk of developing clinical symptoms of SLE after treatment with TNFi.

Methods: The study utilized the electronic medical record system to generate a list of patients who were diagnosed with PSO or PsA between 2014 and 2024. From this list, patients with a positive IF-ANA titer (>1:80) who were treated with TNFi were selected. A detailed chart review was then performed to identify those who developed drug-induced SLE-like symptoms following TNFi therapy.

Descriptive statistics were used to analyze demographic data (Table 1), and the Chi-square and Fisher's exact tests were employed to assess relationships between groups and binary outcomes.

Results: Over the ten-year period, 9,273 individuals were diagnosed with PSO or PsA. Among them, 1,171 patients were tested for IF-ANA, of whom 518 tested positive and 653 tested negative. Among the IF-ANA positive patients, 187 were treated with TNFi (Table 2). Some of these patients received more than one TNFi agent during the course of treatment. Notably, 20 patients developed IF-ANA positivity only after initiating TNFi therapy.

Based on clinical visit notes, 42 patients were suspected of developing drug-induced lupus. Among them, 7 reported worsening joint pain and fatigue, 17 developed worsening or new skin rashes, 3 patients had a significant increase in IF-ANA titers (>6,000), 2 patients developed new anti-dsDNA antibodies, and 1 patient developed anti-histone antibodies. Additional findings included transaminitis in 3 patients, a demyelinating disorder in 1 patient, and paresthesia in 4 patients. Four patients developed other symptoms, including one case each of pericarditis, allergic reaction, diverticular rupture, and pancytopenia (Table 3). Furthermore, 69 IF-ANA–positive patients did not respond to TNFi treatment.

Conclusion: The association between TNFi use and SLE-like symptoms remains a clinical concern. TNFi can elevate ANA titers in ANA-positive patients and may induce new ANA positivity in ANA- negative individuals (2). TNFi have been linked to drug-induced lupus, presenting with arthralgias, rashes, and serositis (1). Diagnosis typically requires symptom onset after TNFi initiation, one positive autoantibody (e.g., ANA or anti-dsDNA), and one non-serologic criterion such as rash (4).

Table 1. Demographics.

Demographics	N (%)
Female N (%)	148(74%)
Male N (%)	53 (26%)
Age	56 (mean)
BMI	32.5 (mean)

Table 2. Percentage of patients treated with different TNFi agents.

Medication	N of patients (%)
Total N	187 (100)
Adalimumab	145 (72)
Etanercept	55 (27)
Golimumab	22 (11)
Infliximab	44 (22)
Certolizumab	15 (7)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Chi-square statistics.

Patients with positive IF-ANA before and after TNFi		SLE-like symptoms		Positive IF-ANA		Worsening of joint pain		Worsening or new rash		Significant increase in IF-ANA titer		New positive anti-dsDNA antibody		New positive anti-histone antibody		Transaminitis		Demyelinating disorder		Paresthesia		Other symptoms	
		No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
TNFi	Before	187	0	20	167	187	0	187	0	187	0	187	0	187	0	187	0	187	0	187	0	187	0
	After	145	42	0	187	180	7	170	17	184	3	185	2	186	1	184	3	186	1	183	4	183	4
Chi-square p-value		<0.0001		0.1239		0.0076		<0.0001		0.082		0.1562		0.3167		0.082		0.3167		0.0461		0.0461	
Fisher's exact test p-value		<0.0001		0.2286		0.0148		<0.0001		0.248		0.4987		1		0.248		1		0.123		0.123	

In our review, 20 of 187 patients developed new ANA positivity. Although ANA and anti-dsDNA positivity were low, SLE-like symptoms were statistically significant, with joint pain and rash being the most common. The 72% of affected patients were on adalimumab. Prior studies suggest higher lupus risk with adalimumab and infliximab, though all TNFi can induce ANA (1). Some patients may tolerate a different TNFi without recurrence (5). Proposed mechanisms include reduced CD44 expression, infection-induced autoantibodies, and a cytokine shift toward Th2 responses (3), possibly explaining variable risk across TNFi agents.

Disclosure: D. Sereda: None; **L. Leechalad**: None; **A. Perl**: None.

Abstract Number: 2392

Does Obesity Influence Disease Activity and Biomarkers in Systemic Lupus Erythematosus Patients?: A Retrospective Study

Daniyal Nadeem[1], Anusheh Ali[2], Shravya Balmuri[2], Megan Mattison[3], Upasana Agrawal[4], Alexandra Zamora-Smith[5], Karan Sachdeva[6], Teresa leeth[1], Robert Quinet[7], William Davis[8], Jerald Zakem[9], Chandana Keshavamurthy[10], Xin Zhang[11], Sarwat Umer[12] and Samina Hayat[13], [1]Louisiana State University Health Science, Shreveport, LA, [2]Louisiana State University, Shreveport, LA, [3]Louisiana State University- Shreveport, Shreveport, LA, [4]Louisiana State University Health Sciences, Shreveport, Shreveport, LA, [5]LSU Health Science Center in Shreveport, Shreveport, LA, [6]Louisiana state university health shreveport, shreveport, [7]Department of Rheumatology, Ochsner Health, New Orleans, LA, [8]Ochsner Health System, New Orleans, LA, [9]Ochsner Health Systems, Metairie, LA, [10]banner university medical center, phoenix, AZ, [11]Ochsner Medical Center, New Orleans, LA, [12]LSUHSC Shreveport, Shreveport, LA, [13]Louisiana state university Shreveport, Shreveport, LA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Obesity, a prevalent condition, is known to exacerbate inflammation and could potentially influence the progression and severity of autoimmune diseases like Systemic lupus erythematosus (SLE). Despite this, limited research has explored the impact of obesity on disease activity and biomarkers in SLE patients. This retrospective study aims to investigate how obesity affects disease activity, as measured by the SLEDAI, and various biomarkers, and renal function, in SLE patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Using data from Slicer Dicer (via EPIC) and Redcap, we analyzed 150 SLE patients at LSU Health Shreveport in 2021, divided into 78 obese (BMI ≥ 30 kg/m^2) and 72 non-obese (BMI < 30 kg/m^2) patients. We examined SLEDAI, WBC count with lymphocytes, anti-dsDNA, ANA levels, C3 and C4 levels, ESR, CRP, creatinine, lupus nephritis presence, LDL to HDL ratio, total HDL, and triglycerides. Results are presented as mean±SD. Statistical analyses were made using the unpaired Student's t-test, with $p< 0.05$ considered significant.

Table 1

Table1:

Variable		BMI≥30 (78) Obese	BMI <30 (72) Non-Obese	P-value
Age (SD)		45.0(10.4)	42.9(15.6)	0.37
Race	Caucasian	9 (11.5%)	11 (15.3 %)	0.68
	African American	66 (84.6%)	57 (79.2 %)	
	Hispanic	3 (3.8%)	4 (5.6%)	
Gender	Male	6 (7.7 %)	8 (11.1%)	0.47
	Female	72 (92.3%)	64 (88.9%)	
DsDNA (n-146)	Positive	30	31	0.58
	Negative	45	40	
ANA (n-82)	Positive	37	36	0.66
	Negative	6	3	
SLEDAI score	mean	10.4 (7.8)	8.6 (6.7)	0.15
	≥6 (n, %)	(46, 63.9%)	(52, 66.7%)	0.72
WBC		5.9 (2.8)	5.6(2.7)	0.54
Lymph		1.5 (0.7)	1.4 (0.66)	0.28
Mean BMI		38.0 (7.7)	23.7 (3.4)	<0.001
C3 (n-145)	mean	116 (32.6)	97.6 (31.9)	<0.001
	median	120.0	98.0	
C4 (n-144)	mean	28.4 (26.3)	23.0 (11.9)	0.08
	median	25.0	20.0	
CRP (n-115)	mean	1.6 (4.1)	0.64 (0.69)	0.08
	median	0.70	0.29	
ESR (n-105)		41.1 (27.4)	37.1 (33.5)	0.50
LDL: HDL (n-80)		2.05 (1.0)	1.76 (1.05)	0.20
Total HDL (n-80)		3.5 (1.34)	3.5 (1.70)	0.80
TG (n-81)		128.3 (162)	154 (172.9)	0.48
Lupus nephritis(n-148)		27 (34.6 %)	29 (40.3%)	0.23
Creatinine (n-140)	mean	1.46 (2.3)	1.47 (1.7)	0.97
	median	0.80	0.92	

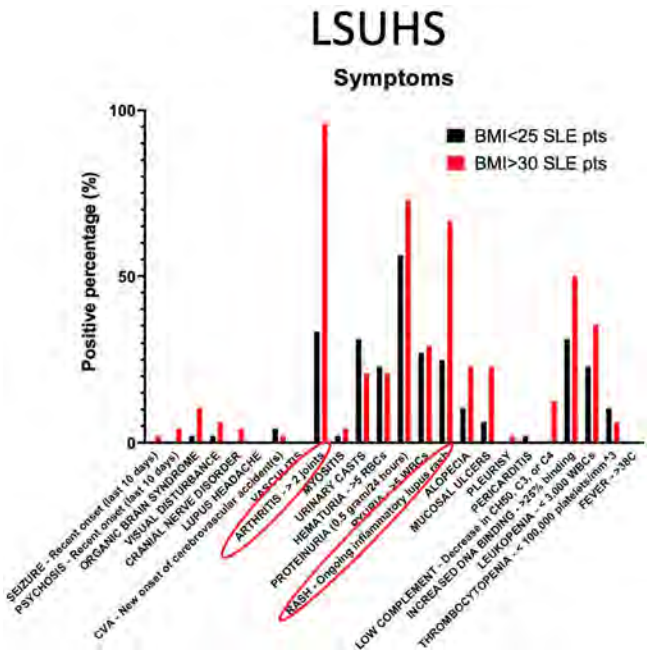


figure1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: This study enrolled 150 lupus patients: 136 females (90.7%), 14 males (9.3%); 123 African Americans (82.0%), 20 Caucasians (13.3%), 7 Hispanics (4.7%). Although anti-dsDNA and ANA interpretations were similar between obese and non-obese groups, obese patients demonstrated worse outcome with a higher trend of SLEDAI score compared to the non-obese group (10.8±7.8 vs 8.6±6.7). In addition, obese lupus patients showed significantly higher frequencies of more than two joints arthritis (95.83% vs 33.33%) and lupus rush (66.67% vs 25%) than the non-obese group. The increasing trend of CRP(70 mg/L+4.1 vs 29mg/L+0.69) and ESR level (41.1±27.4 mm/hr vs 37.1±33.5mm/hr) was found in the obese lupus patients compared to nonobese lupus patients, but didn't reach statistical significance. No difference was observed in triglyceride level, LDL: HDL ratio, WBC counts, creatinine level, and lupus nephritis between the obese group and the non-obese group. Surprisingly, we found that the obese group had significantly higher C3 levels (116±32.6 mg/dL) compared to the non-obese group (96.7±31.9 mg/dL) ($p < 0.001$). The C4 level was also higher in the obese group (28.4 ±26.3 mg/dL) than in the non-obese group (23.0±11.9 mg/dL).

Conclusion: Our results indicate that obesity in lupus patients is associated with elevated C3 levels, higher mean SLEDAI scores, and inflammation-related parameters, suggesting a potential link between obesity and worse outcomes in SLE. Other clinical and laboratory parameters (such as autoantibody, lupus nephritis) did not show significant differences, implying that obesity may not affect humoral immunity in SLE. Further research at the cellular and molecular levels on obese lupus patients will help us understand the impact of obesity on lupus progression and management.

Disclosures: No Disclosures

Disclosure: D. Nadeem: None; **A. Ali**: None; **S. Balmuri**: None; **M. Mattison**: None; **U. Agrawal**: None; **A. Zamora-Smith**: None; **K. Sachdeva**: None; **T. Ieeth**: None; **R. Quinet**: None; **W. Davis**: None; **J. Zakem**: None; **C. Keshavamurthy**: None; **X. Zhang**: None; **S. Umer**: None; **S. Hayat**: None.

Abstract Number: 2393

Improving Clinical Outcomes In SLE Arthritis Trials: Post-Hoc Analysis Of A Prospective Intervention Study

Samuel Wood[1], Khaled Mahmoud[2], Md Yuzaiful Md Yusof[2], Philip Conaghan[2], Elizabeth Hensor[2] and **Ed Vital**[3], [1]University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [2]University of Leeds, Leeds, United Kingdom, [3]University of Leeds, Leeds, England, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Musculoskeletal (MSK) manifestations of SLE are the most frequently assessed domain in clinical trials. Optimal MSK assessment is contested; candidates include the binary or ordinal SLEDAI and BILAG, tender joint count (TJC), swollen joint count (SJC) and "active" joint counts, (either tender or swollen, or both).Ultrasound studies in SLE have identified imaging-only synovitis, such that the BILAG A/B criterion has a sensitivity of just 56% for US synovitis.

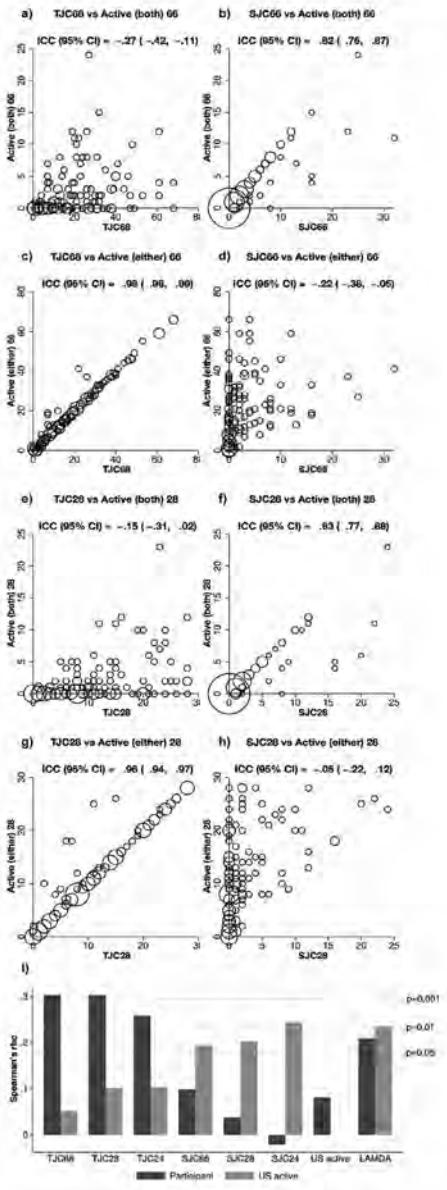
Our aim was to assess sensitivity and specificity of a set of candidate joint counts against US synovitis, as well as patient and US defined response to therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Sensitivity and specificity of clinical assessment in the detection of ultrasound-detected synovitis.

	All participants				No fibromyalgia			
	Tender		Swollen		Tender		Swollen	
	No	Yes	No	Yes	No	Yes	No	Yes
GS<2 & PD0	1318	854	1986	187	1006	638	1534	110
GS≥2 | PD≥1	109	112	129	92	89	85	104	70
Sensitivity	50.7 (39.0, 62.3)		41.6 (30.0, 53.3)		48.9 (35.6, 62.1)		40.2 (26.3, 54.2)	
Specificity	60.7 (55.0, 66.4)		91.4 (88.1, 94.7)		61.2 (54.7, 67.7)		93.3 (90.3, 96.3)	
PPV	11.6 (7.7, 15.5)		33.0 (23.1, 42.9)		11.8 (7.0, 16.6)		38.9 (26.3, 51.5)	
NPV	92.4 (89.0, 95.7)		93.9 (91.5, 96.3)		91.9 (87.7, 96.1)		93.7 (90.7, 96.6)	
% pos agree	18.9		36.8		19.0		39.6	
% neg agree	73.2		92.6		73.5		93.5	

Figure 1 | a-h: Weighted scatter plots of joint counts versus active definitions at baseline. Intraclass correlation coefficients (ICCs) displayed; i: Associations between changes in joint assessments and participant- or US-defined response at 6 weeks



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Components of the LAMDA
Swollen joint count (66/68)
Physician musculoskeletal disease activity VAS (scored 0-100)
Patient reported musculoskeletal pain VAS (scored 0-100)
Erythrocyte Sedimentation Rate (ESR)

Components of the composite lupus arthritis and MSK disease activity (LAMDA) score.

Methods: We performed a post-hoc analysis of a multi-centre study [USEFUL; PMID: 33792659]. Patients with inflammatory arthralgia were assessed clinically and using US at 0, 2 and 6 weeks following single-dose intra-muscular glucocorticoid therapy.

Candidate joint sets were defined as: 68 TJC and SJC, 28 TJC and SJC, or 24 TJC and SJC (MCPs, PIPs, elbows, wrists). Joint counts were compared with weighted scatter plots and intraclass correlation coefficients (ICCs).

Participant-reported change was measured using a Likert scale (-7 to 7). For US response, changes in number of 'active' joints (grey scale ≥2 and/or power Doppler ≥1) were calculated. Spearman rank correlation measured associations between changes in the candidate joint counts, participant-reported changes and changes in the number of US active joints. Associations are also reported for the composite lupus arthritis and MSK disease activity score (LAMDA) (Table 2).

Results: Of 133 patients, 95% female and 62% European ancestry, 63% had ≥1 SJC at baseline. TJC and SJC had poor sensitivity (50.7% and 41.6% respectively), and TJC had lower specificity than SJC (60.7% and 91.4% respectively)(Table 1). Active "either" and active "both" almost exactly matched TJC and SJC respectively (Figure 1a-h).

In joint-by-joint analysis the most commonly swollen joints were MCPs 2-5.Tenderness was most common in MCP 2 and 3, wrist, shoulder and knee. Reduced joint counts were more strongly correlated with US-defined response than full joint counts (Figure 1i) but not with participant-defined response. Changes in TJCs correlated with participant-defined response and changes in SJCs with US-defined response but not vice-versa. LAMDA was modestly correlated with both response definitions.

Conclusion: (1) TJC and SJC have limited sensitivity for imaging-detected synovitis, but SJC has high specificity. (2) Active 'either' and 'both' joint counts almost exactly match TJC and SJC respectively and are therefore redundant. (3) Diagnostic accuracy of clinical assessment varies by joint area; shoulders and knees likely contribute little to assessment of joint inflammation and often have non-inflammatory pathology. (4) SJC is the most responsive measure of objective synovitis; SJC24 is the most responsive set for US response, but is not correlated with participant-defined response.

Given the relative insensitivity of SJC, and importance of patient defined response, the composite measure, LAMDA may be optimal in RCTs. Future work will evaluate these variables in randomised trials and define inclusion and response thresholds.

Disclosure: S. Wood: None; **K. Mahmoud**: None; **M. Md Yusof**: GlaxoSmithKlein(GSK), 1, Novartis, 1, 6, UCB, 2, 6; **P. Conaghan**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Eli Lilly, 2, 6, Eupraxia, 2, 6, Formation Bio, 2, 6, Galapagos, 2, Genascence, 2, 6, Grunenthal, 2, 6, Janssen, 2, Kolon TissueGene, 2, 6, Levicept, 2, 6, Medipost, 2, Moebius Medical, 2, 6, Novartis, 2, 6, Orion, 2, 6, Pacira, 2, 6, Sandoz, 2, 6, Stryker, 2, 6, Takeda, 2, 6; **E. Hensor**: None; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2394

Impact of Immunosuppressive Regimens on Major Cardiac Events in Patients with Systemic Lupus Erythematosus (SLE): A Survival Analysis

Emily Cosentino[1], Melissa Akselrad[2], Niurka Liranzo Tejera[2], Christine Lenchur[2], Takemichi Matsui[2], Adal Abonamah[2], Priscilla Abate Namnum[1], Olga Marushchak[2], Martin John[3], Sophia Lutgen[4], Celestine He[5], Boluwatito Oladeinde[6], Harleen Sidhu[7] and Chrisanna Dobrowolski[5], [1]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York, [2]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York, NY, [3]Icahn School of Medicine at Mount Sinai, New York, [4]Mount Sinai Morningside/West Hospitals, Icahn School of Medicine at Mount Sinai, New York City, NY, [5]Icahn School of Medicine at Mount Sinai, New York, NY, [6]Icahn School of Medicine, New York, NY, [7]Icahn School of Medicine at Mount Sinai/NYC H+H- Elmhurst, Queens, NY, Rego Park, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular events are a significant source of morbidity and mortality in SLE patients, occurring more frequently than in the general population owing to immune dysregulation and chronic inflammation. While certain medications such as glucocorticoids may inherently increase cardiovascular risk, we hypothesize that non-glucocorticoid medications could potentially be associated with reduced cardiovascular risk.

Table 1. Patient Demographics

Variable	No MACE (N=319, 81%)	MACE (N=74, 19%)	P-Value
Age in years, Mdn (IQR)	49 (39, 61)	61.5 (50, 70)	<0.01
Sex			0.16
Male, n (%)	23 (7)	9 (12)	
Female, n (%)	296 (93)	65 (87)	
Ethnicity			0.12
White, n (%)	66 (21)	11 (15)	
Black, n (%)	88 (28)	27 (37)	
Hispanic, n (%)	109 (34)	30 (41)	
Asian, n (%)	22 (7)	1 (1)	
Age at SLE diagnosis in years, Mdn (IQR)	37 (30, 48)	44 (33, 55)	0.04
Renal disease, n (%)	63 (20)	25 (34)	0.01
HTN, n (%)	127 (40)	53 (72)	<0.01
HLD, n (%)	72 (23)	40 (54)	<0.01
Diabetes, n (%)	30 (9)	17 (23)	0.01
Smoking history, n (%)	72 (23)	33 (45)	<0.01
Hydroxychloroquine, n (%)	293 (92)	60 (81)	0.01
Glucocorticoids, n (%)	146 (46)	52 (70)	<0.01
Azathioprine, n (%)	63 (20)	15 (20)	0.92
Cyclophosphamide, n (%)	15 (5)	9 (12)	0.02
Methotrexate, n (%)	78 (25)	16 (22)	0.61
Mycophenolate, n (%)	99 (31)	47 (50)	<0.01
Tacrolimus, n (%)	29 (10)	10 (14)	0.25
Anifrolumab, n (%)	8 (3)	0 (0)	0.17
Belimumab, n (%)	19 (6)	7 (10)	0.28
Rituximab, n (%)	8 (3)	3 (4)	0.47
No Medications, n (%)	35 (11)	10 (14)	0.54

Demographic information of study participants. Data are expressed as the median and interquartile range (Mdn [IQR]) or number and percent [n (%)]. All participants meet ACR-EULAR 2019 Classification Criteria as determined by a Rheumatologist. MACE: Major Adverse Cardiac Event (non-fatal myocardial infarction (MI), non-fatal stroke, unstable angina, hospitalization for heart failure, and/or all-cause death) HTN: Hypertension HLD: Hyperlipidemia SLE: Systemic Lupus Erythematosus

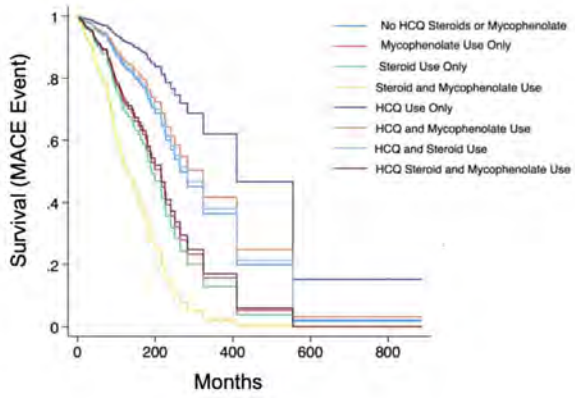
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Hazard Ratios of Cox Regression Models

Variable	Hazard Ratio	Standard Error	Z	P-Value	95% CI
Hydroxychloroquine	0.5	0.2	-2.3	0.02	0.25, 0.87
Glucocorticoids	2.0	0.5	2.7	0.01	1.20, 3.40
Mycophenolate	1.8	0.4	2.5	0.01	1.10, 2.90
HCQ, Glucocorticoids, and Mycophenolate	1.8	0.3	2.4	0.02	1.10, 3.00
HCQ and Mycophenolate	1.2	0.3	0.7	0.50	0.70, 1.90
HCQ and Glucocorticoids	1.4	0.2	2.1	0.04	1.18, 2.20
Glucocorticoids and Mycophenolate	2.1	0.2	3.1	0.02	1.30, 3.40
Age	0.9	0.1	-2.8	0.01	0.90, 0.98
Age of SLE diagnosis	1.1	0.1	3.8	<0.01	1.00, 1.10
HLD	2.1	0.5	2.9	<0.01	1.30, 3.40
Smoking	2.1	0.5	2.9	<0.01	1.30, 3.40

Cox regression with Breslow method for ties with reported hazard ratios and 95% Confidence Intervals of multiple medications and risk factors. HLD: Hyperlipidemia CI: Confidence Interval HCQ: hydroxychloroquine

Figure 1. Cox Proportional Hazard Regression



Cox Proportional hazards regression model comparing combinations of hydroxychloroquine, corticosteroids, and mycophenolate versus survival-time for MACE. MACE: Major Adverse Cardiac Event (non-fatal myocardial infarction (MI), non-fatal stroke, unstable angina, hospitalization for heart failure, and/or all-cause death) HCQ: hydroxychloroquine

Methods: This is a retrospective cohort study utilizing data from a diverse, single health system in a major urban center in North America. We completed a survival analysis examining risk of major adverse cardiac events (MACE) defined by a 5-point MACE scale, with respect to immunosuppressant use. Survival time was measured from SLE diagnosis to event or last follow-up. Kaplan-Meier, log-rank test, and Cox proportional hazards models were used to compare survival curves. Model fit and assumptions were evaluated using Schoenfeld residuals and likelihood ratio tests. A final multivariable Cox regression analysis was developed using a backward regression approach including 7 final variables. Immunosuppressant medications were tested in individual models and statistically significant regimens were included in the final analyses.

Results: 393 patients were included. Demographics are listed in Table 1. Nineteen percent of participants experienced ≥1 MACE. These included stroke (42%), myocardial infarction (26%), heart failure hospitalization (21%), unstable angina requiring cardiac revascularization (11%), cardiovascular death (0%). Kaplan-Meier curves demonstrated a lower time to event in patients taking corticosteroids and mycophenolate (MMF), while patients taking hydroxychloroquine (HCQ) had a higher survival probability (Table 2, Figure 1). Log-rank test demonstrated statistical significance (p=0.03, 0.03, 0.03, respectively). Corticosteroid and MMF use were independently associated with increased risk of MACE (HR 2.02, 95% CI 1.21–3.37, p<0.01, and HR 1.82, 95% CI 1.14–2.92, p=0.01). Use of HCQ was associated with a reduced risk of MACE (HR 0.47, 95% CI 0.25–0.88, p=0.02) (Table 2, Figure 1). Other disease modifying anti-rheumatic drugs and biologic medications tested did not reach statistically significant conclusions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Given the increased risk of cardiovascular events in SLE patients, identifying modifiable risk factors is crucial for pinpointing high-risk patients. While we expected non-corticosteroid immunosuppressants to be associated with reduced MACE, the opposite was true, except for HCQ. A major limitation of this study is unaccounted-for confounding variables including indication bias (i.e. patients with more severe SLE may receive stronger immunosuppression). Additionally, statistical power was limited for several classes of medications due to smaller numbers of patients using these treatments. As longitudinal databases expand, and biologics become more widely available, future studies should focus on evaluating the effects of specific biologic and DMARD therapies. Ultimately, developing models to assess cardiovascular risk in SLE patients will enhance outcomes and personalized care in the future.

Disclosure: E. Cosentino: None; **M. Akselrad**: None; **N. Liranzo Tejera**: None; **C. Lenchur**: None; **T. Matsui**: None; **A. Abonamah**: None; **P. Abate Namnum**: None; **O. Marushchak**: None; **M. John**: None; **S. Lutgen**: None; **C. He**: None; **B. Oladeinde**: None; **H. Sidhu**: None; **C. Dobrowolski**: Novartis, 1.

Abstract Number: 2395

Analysis of Histopathological Changes in the Placenta of Patients with Systemic Lupus Erythematosus

Bartira Melo[1], Elizabeth Avvad[2], Marcela lacerda[2], Nilson jesus[2], **Evandro Klumb**[2] and Guilherme Ramires de Jesus[3], [1]UERJ- Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, [2]UERJ - Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, [3]Universidade do Estado do Rio de Janeiro, Rio De Janeiro, Rio de Janeiro, Brazil

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is more frequent in women of reproductive age and pregnancy in these patients is considered as high risk. The inflammatory environment, with exacerbated activation of the complement system, formation, and tissue deposition of immune complexes promote placental histopathological changes that predispose to pregnancy complications. The objective of this study was to describe histopathological findings in the placentas of pregnant women with SLE and correlate them with adverse outcomes.

Methods: Patients with SLE (ACR criteria 1997) and singleton pregnancies, who received prenatal care at a tertiary hospital and delivered at the same institution, were included. They were divided in four groups: Group 1 – Preeclampsia (PE)/intrauterine growth restriction (IUGR); Group 2 – Active SLE (SLEPDAI $\geq$ 4); Group 3 – Systemic infection during pregnancy; Group 4 – patients without PE/IUGR, active SLE or infection. Histopathological analysis of the placentas was performed according to Amsterdan Placental Workshop Group Consensus Statement.

Results: Ninety-seven patients were included and histopathological study of the placenta was performed in all cases by blinded pathologists for pregnancy outcome. Adverse outcomes were observed in 49 (50.5%) pregnancies. PE/IUGR was the most frequent, being found in 28 (28.8%) patients. Disease activity during pregnancy was diagnosed in 23 (23.7%) cases and an episode of systemic infection was identified in 13 (13.4%) pregnant women. Fifteen women were analyzed in more than one group due to multiple events (e.g., PE/CIUR and SLE activity). Considering all patients, maternal vascular hypoperfusion abnormalities (MVHA) were the most frequent histopathological findings: 19 (19.6%) had moderate to severe major MVHA; 59 (60.8%) had mild major MVHA; and 83 (85.6%) presented minor MVHA. Patients in Group 2 (PE/IUGR) had more frequently moderate to severe major MVHA compared to the other groups (32.1% x 14.5%, p=0.047), while patients in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Group 4 (no studied outcomes) had significantly less acute fetal vascular hypoperfusion abnormalities (FVHA) (14.3% x 33.3%, p=0.027). In both Groups 2 (active SLE) and 3 (systemic infection), the most common finding was minor MVHA (82.6% and 84.6%, respectively), but there was no statistical difference compared to the other groups. Significant risk predictors for the outcome PE/IUGR were absence of acute (FVHA) (p=0.025), presence of hematogenous infection (p=0.005), presence of small for gestational age (SGA) newborn (p< 0.0001), need for neonatal intensive care unit (p=0.002), lower gestational age at delivery (p=0.0003) and lower birth weight (p< 0.0001). No variable was a significant predictor for the outcome disease activity and systemic infection. Based on multivariate analysis, it was observed that SGA newborn (p< 0.0001) and hematogenous infection (p=0.015) were significant independent variables to predict the PE/IUGR outcome.

Conclusion: This study demonstrates that MVHA are commonly found in placentas of patients with SLE. Moderate to severe MVHA are more frequent in patients who develop PE/IUGR, which may be linked to the pathophysiology of these obstetric adverse outcomes.

Disclosure: B. Melo: None; **E. Avvad**: None; **M. Iacerda**: None; **N. jesus**: None; **E. Klumb**: None; **G. Ramires de Jesus**: None.

Abstract Number: 2396

A Machine Learning Algorithm Based on a 15-autoantibody Profile by a Novel Fully Automated Multiplexed Microarray Immunoassay for the Diagnosis of Autoimmune Connective Tissue Diseases

Gerber Gomez[1], Yipeng Cheng[2], Kristiana Nita[2], Michael Hausmann[3], Christian Fischer[1] and Yasemin Ataman-Önal[3], [1]Scientific & Medical Affairs, AliveDx Suisse SA, Eysins, Switzerland, [2]AliveDx, Edinburgh, United Kingdom, [3]AliveDx Suisse SA, Eysins, Switzerland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Detection of relevant autoantibodies is key in the identification of autoimmune connective tissue diseases (CTD). The evaluation of multiple autoantibodies for extended serological profiling may improve the diagnosis of these conditions. We evaluated the diagnostic utility, in patients with CTD and disease controls, of machine learning classifiers based on the 15-autoantibody profile performed by a novel, single-use, multiplexed microarray immunoassay, used with its fully automated high-throughput proprietary system for simultaneous the detection of IgG autoantibodies directed to dsDNA, SS-A 60, TRIM21 (SS-A 52), SS-B, Sm, Sm/RNP, U1RNP, Jo-1, Scl-70, Centromere B, Chromatin, Ribosomal P, DFS70, RNAP III and CCP2.

Methods: De-identified sera from 475 patients diagnosed with autoimmune CTD in accordance with current guidelines [127 patients with systemic lupus erythematosus (SLE), 74 with systemic sclerosis, 76 with Sjögren's syndrome (SjS), 71 with idiopathic inflammatory myopathies, 54 with mixed CTD, 73 with rheumatoid arthritis] and 652 patients with other disorders, who served as disease controls were analyzed using the investigational MosaiQ AiPlex® CTDplus (AliveDx, Switzerland) assay. Classification models were developed using all 15 autoantibodies or a selected subset, employing the RandomForest algorithm (XGBoost and Logistic L1 L2 were also used). Diagnostic performance was evaluated by receiver operating characteristic (ROC) curve analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

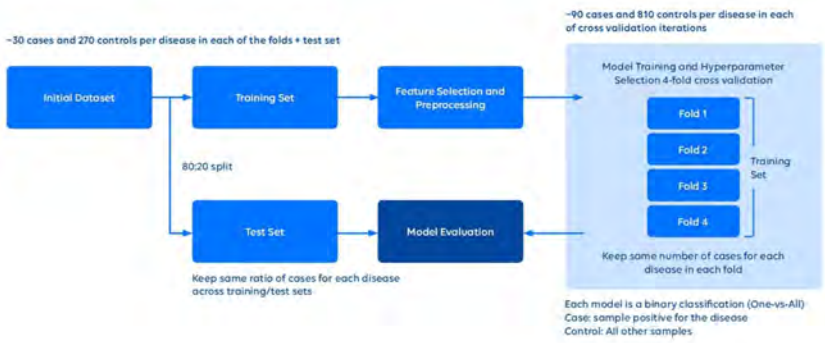


Figure 1. Model Pipeline

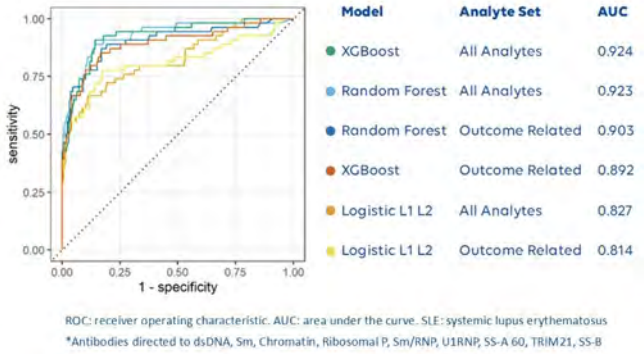


Figure 2. ROC Curves and AUCs - SLE: All 15 analytes vs. 9 Outcome-related analytes*

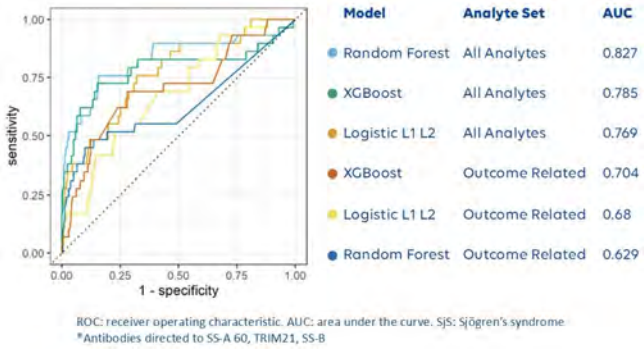


Figure 3. ROC Curves and AUCs - SjS: All 15 analytes vs. 3 Outcome-related analytes*

Results: A RandomForest classifier incorporating all 15 autoantibodies demonstrated robust performance in predicting SLE, achieving an area under the curve (AUC) of 0.92. In comparison, the individual SLE-specific markers dsDNA and Sm yielded lower AUCs of 0.68 and 0.60, respectively. For SjS, the 15-plex RandomForest classifier achieved an AUC of 0.83, outperforming a 3-plex RandomForest classifier based on SS-A 60, TRIM21, and SS-B autoantibodies, which had an AUC of 0.62. The individual AUCs for these markers were 0.63, 0.59, and 0.58, respectively. Similarly, for other CTDs, 15-plex classifiers consistently outperformed the individual disease-specific markers.

Conclusion: Multiplex autoantibody testing combined with machine learning algorithms has the potential to improve the diagnosis of autoimmune CTD.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: G. Gomez: AliveDx, 3; **Y. Cheng**: AliveDx, 3; **K. Nita**: AliveDx, 3; **M. Hausmann**: AliveDx, 3; **C. Fischer**: AliveDx, 3; **Y. Ataman-Önal**: AliveDx, 3.

Abstract Number: 2397

Analytical Performance of a Fully Automated Multiplexed Microarray Immunoassay for the Simultaneous Detection of Fifteen Autoantibodies Associated with Connective Tissue Diseases in a Reference Laboratory in Southern France

Guillaume Nardella[1], **Gerber Gomez**[2], Christian Fischer[2] and Claire Monat[1], [1]Inovie Labosud Provence, Specialized Autoimmunity Analyses, Marseille, France, [2]Scientific & Medical Affairs, AliveDx Suisse SA, Eysins, Switzerland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoantibodies are key diagnostic markers in autoimmune connective tissue diseases (CTD). Conventional testing often requires multiple single-measurand assays, which can be labor-intensive and time-consuming. We evaluated the analytical performance of a multiplex microarray immunoassay (MosaiQ AiPlex® CTDplus; AliveDx, Switzerland) for the simultaneous detection of 15 autoantibodies associated with CTD, used with its fully automated proprietary platform, compared to routine methods in a reference laboratory.

Methods: A cohort of analytically characterized sera (572 reactive and 2,686 non-reactive) were included in the study. Reference methods included a multiplex bead-based immunoassay for most measurands, indirect immunofluorescence assay (IFA) for DFS70, and a chemiluminescence assay for CCP. Samples were tested with the investigational microarray immunoassay that detects IgG autoantibodies to dsDNA, SS-A 60, TRIM21 (SS-A 52), SS-B, Sm, Sm/RNP, U1RNP, Jo-1, Scl-70, CENP B, Chromatin, Ribosomal P, DFS70, RNAP III, and CCP. Performance was assessed using positive (PPA), negative (NPA) and overall percent agreement (OPA). Additionally, Cohen's kappa coefficient was calculated.

Results: The microarray immunoassay demonstrated substantial agreement with the reference methods (overall Cohen's kappa: 0.72), with total PPA of 86.6% (95% CI: 83.4, 89.3), total NPA of 92.3% (95% CI: 91.2, 93.3) and total OPA of 91.3%. Individual measurands showed PPA ranging from 59.1% (Sm) to 100% (TRIM21, Jo-1), and NPA ranging from 72.6% (Chromatin) to 100% (Sm, Jo-1, CCP). Notably, high kappa values for almost perfect agreement were observed for SS-A 60 (0.92), TRIM21 (0.85) Sm/RNP (0.97), and CENP B (0.87). Cohen's kappa values for substantial agreement were observed for dsDNA (0.72), SS-B (0.75) and Sm (0.73); whereas U1RNP (0.49), Scl-70 (0.41) and Ribosomal P (0.43) showed moderated agreement. Finally, kappa values for fair agreement were found for Chromatin (0.33) and CCP (0.34). No samples were available for RNAP III and thus, no comparison was made. Due to limited sample availability, results for Jo-1 (reactive, overall) and CCP (non-reactive, overall) should be interpreted with caution. Detailed results are shown in Table 1.

Conclusion: This fully automated multiplex microarray immunoassay demonstrated overall substantial agreement with established methods for the detection of CTD-associated autoantibodies, with particularly high concordance for key targets such as SS-A 60, Sm/RNP, and CENP B. Its ability to simultaneously detect multiple autoantibodies in a single, automated run may streamline the serologic evaluation and support more efficient clinical workflows in autoimmune diagnostics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Agreement of the Microarray Immunoassay with Comparators

Measurand	Reactive results (n)	PPA (%)	95% CI	Non-reactive results (n)	NPA (%)	95% CI	OPA (%)	Cohen's kappa
dsDNA	49	87.2%	74.3, 95.2	186	90.7%	85.5, 94.2	90.0%	0.72
SS-A 60	88	98.9%	93.8, 100	179	95.0%	90.7, 97.4	96.3%	0.92
TRIM21	70	100%	94.9, 100	197	91.3%	86.4, 94.5	93.6%	0.85
SS-B	43	81.1%	64.8, 92	224	95.8%	92.1, 97.8	93.6%	0.75
Sm	26	59.1%	36.4, 79.3	241	100%	98.5, 100	96.6%	0.73
Sm/RNP	48	97.9%	88.9, 99.9	219	99.5%	97.5, 100	99.2%	0.97
U1RNP	78	82.2%	71.5, 90.2	189	73.0%	65.7, 79	75.7%	0.49
Jo1*	2*	100%	15.8, 100	265	100%	98.6, 100	100%	1
Scl-70	20	82.4%	56.6, 96.2	247	84.9%	78.8, 89.4	84.7%	0.41
CENP B	26	88.0%	68.8, 97.5	241	98.8%	96.4, 99.7	97.7%	0.87
Chromatin	73	63.9%	50.6, 75.8	194	72.6%	65.1, 78.7	70.2%	0.33
Ribosomal P	11	81.8%	48.2, 97.7	256	92.5%	88.5, 95.1	92.0%	0.43
DFS70	19	88.9%	65.3, 98.6	47	95.7%	85.2, 99.2	93.8%	0.85
RNAP III	-	-	-	-	-	-	-	-
CCP*	19	82.4%	56.6, 96.2	1*	100%	2.5, 99	83.3%	0.34
TOTAL	572	86.6%	83.4, 89.3	2686	92.3%	91.2, 93.3	91.3%	0.72

Equivocal not included. *Low number of samples. CI: confidence interval; NA: Not applicable; NPA: negative percentage agreement; OPA: overall percent agreement PPA: positive percentage agreement.

Disclosure: G. Nardella: None; **G. Gomez**: AliveDx, 3; **C. Fischer**: AliveDx, 3; **C. Monat**: None.

Abstract Number: 2398

Analytical Performance of the hep-2 Substrate Diagnostic Kit for ANA as an Initial Step in the Evaluation of a Novel Fully Automated IFA Analyzer in a Laboratory in England

Jason Sillitoe[1], Ewa Fiorentino-Rozek[2], **Gerber Gomez**[3], Christian Fischer[3] and Caroline Wilson[1], [1]North East Innovation Lab, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, England, United Kingdom, [2]Clinical Affairs, AliveDx Suisse SA, Eysins, Vaud, Switzerland, [3]Scientific & Medical Affairs, AliveDx Suisse SA, Eysins, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Indirect immunofluorescence assay (IFA) on HEp-2 cells (HEp-2 IFA) remains a key tool in the diagnostic work-up of autoimmune connective tissue diseases (CTD). Traditionally performed manually, this method is labor-intensive, time-consuming, and subject to operator variability. While semi-automated and automated systems exist, there is still a need for fully automated platforms that integrate both slide processing and interpretation using computer-assisted image analysis. As a preliminary step in evaluating a novel fully automated IFA system (LumiQ®, AliveDx, Switzerland) in combination with the HEp-2 substrate Diagnostic Kit for ANA (investigational device), we assessed the analytical performance of the investigational device when used manually by a single operator, comparing results to historical IFA data from patients with suspected CTD.

Methods: Banked, de-identified human serum samples, previously manually characterized by the Mosaic Basic Profile (Euroimmun, Germany) (routine method) were included in the study. Samples were stored at -20°C for up to three months prior to being thawed for subsequent analysis with the investigational device. The study cohort consisted of 25 samples characterized as non-reactive and 60 samples characterized as reactive, with varying titers, covering a broad range of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patterns, as per the International Consensus on ANA Patterns (ICAP). Samples were tested with the investigational device at a 1:80 screening dilution. The testing protocols for both investigational device and routine method were manually conducted following the manufacturer's instructions for use (IFU), with all readings performed by a single operator using a manual fluorescent microscope to reduce inter-operator variability. Results were interpreted based on categorical classifications (reactive / non-reactive), pattern identification, and the grading of reactive samples from 1+ to 4+ at the screening dilution. Positive (PPA), negative (NPA) and overall percent agreement (OPA) were calculated for sample status (reactive or non-reactive). For reactive samples, percent agreement of each individual IFA pattern and overall pattern agreement were determined. From the 60 ANA reactive samples, 20 samples were selected to determine the end-point titer. Dilutions were prepared of these samples +/- one titer step around the pre-characterized end point titer (EPT).

Results: PPA was 100% (95% CI: 94.0, 100), with all 60 historically reactive samples yielding reactive results by the investigational device. NPA was 100% (86.3, 100), with all 25 historically non-reactive samples yielding non-reactive results by the investigational device. The overall agreement between methods was 100% (95% CI: 95.7, 100). The pattern agreement was 100% (95% CI: 86.3, 100). The end point titration of 20 positive samples showed EPT agreement of 100% (95% CI: 83.2, 100).

Conclusion: The manual preparation and readings using the investigational device showed high concordance with historical characterization. Future studies evaluating the fully automated capabilities of this solution will allow for an expanded assessment of the performance of the device and platform.

Disclosure: J. Sillitoe: None; **E. Fiorentino-Rozek**: AliveDx, 3; **G. Gomez**: AliveDx, 3; **C. Fischer**: AliveDx, 3; **C. Wilson**: None.

Abstract Number: 2399

Identification of an LN endotype linked to intestinal expansion of Pathogenic Strains of a Pathobiont Bacterium that induces Systemic Thrombo-inflammatory Pathways directly measurable in Urine

Gregg Silverman[1], Abhimanyu Amarnani[2], Zakia Azad[2] and Brad Rovin[3], [1]NYU Grossman School of Medicine, New York, NY, [2]New York University Grossman School of Medicine, New York, NY, [3]The Ohio State University, Columbus, OH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: During disease, ~50% of SLE patients develop lupus nephritis (LN), one of the most serious complication. Despite the best therapy, within 15 years, ~20% progress to renal failure (1). Diagnosis is based on urine protein-creatinine ratio and histology in renal biopsy; genetic factors are common, but penetrance is low, and the cause is unknown. A gut-kidney axis has been suggested. We therefore investigated pathogenetic urinary factors associated with host response to an implicated pathobiont in biopsy-proven patients.

Methods: Patients with SLE diagnosis met ACR criteria and had a SLE Disease activity scores. Urine protein-creatinine ratio was determined at the time of sample collection. As a marker of microbe-specific immune exposure, serum antibodies to cell wall lipoglycan (LG) in pathogenic strains of *Ruminococcus gnavus (RG)* were quantified by a

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

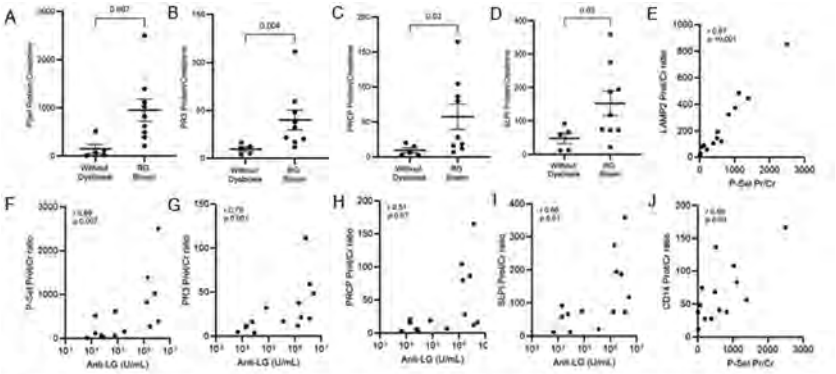


Figure 2. Urine from LN patients with RG gut blooms contains higher levels of A) platelet-associated P-selectin, B) neutrophil-associated proteinase 3 (PR3), C) endothelial cell-associated prolyl carboxypeptidase (PRCP), and D) phagocyte-associated secretory leukocyte protease inhibitor (SLP1). F-I) These urinary levels directly correlate with a patient's serum anti-RG lipoglycan (LG) levels. Within the urine, platelet-associated P-selectin levels also correlate with E) urinary mononuclear cell lysosomal-associated membrane protein 2 (LAMP-2) levels, and J) myeloid cell-associated CD14 levels.

standardized bead-based assay (2,3). Compared to active LN without dysbiosis, active LN with RG gut bloom and high anti-LG had elevated transcripts reflecting platelet (SPARC, SNCA, PROS1, PF4, PDGFA, MMRN1, EGF) and neutrophil activation (GATA1)(padj=2x10(-4))in whole blood(manuscript submitted). We therefore used the same proteomics assay as in AMP-sponsored high-dimensional discovery studies to detect self-proteins in urine to identify WHO class and activity of glomerular lesions by urine "liquid biopsy" (4). In contrast, we custom-designed multiplex arrays to detect 30 human proteins implicated in platelet-associated thrombo-inflammation and neutrophil extracellular TRAPs/NETosis, and in other immune pathways. By urine hybridization, antigens were detected, data normalized by creatinine levels.

Results: With this custom proteomics array, we tested urine of 14 LN at flare with coincident RG blooms and 6 LN patients at flare without bloom. For selected analytes (normalized to urine creatinine), significant increases were seen in urine of patients with gut dysbiosis (Figs. 1A-D). Analytes were proteins from platelets, neutrophils and endothelial cells. These data support the hypothesis that platelet & neutrophil-related pathways contribute to LN activity during RG blooms (Figs. 1A, B). Presence of these proteins in urine is positively associated with RG blooms, with significant correlations of platelet and neutrophil proteins with serum antibodies to RG lipoglycan (Figs. 1F, G). Findings were highly reproducible.

Hence, renal exposure to either the lipoglycan, or the induced antibodies to lipoglycan, may contribute to glomerular injury.

Conclusion: Our studies suggest that LN flares in patients with gut RG blooms are associated with peripheral platelet activation similar to that observed in patients with sepsis. In the affected LN patients, the level of urinary proteins from activated platelets, neutrophils, and endothelial cells documents underlying systemic immune activation, with release of proteases that likely injure the kidney. Taken together, these data indicate that intestinal expansions of the RG pathobiont can worsen LN flares through *thrombo-inflammation*. This previously unsuspected endotype of LN may be amenable to therapeutic interventions beyond the glucocorticoids and immunosuppressants commonly used to treat LN.

Disclosure: G. Silverman: None; **A. Amarnani**: None; **Z. Azad**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2400

Prevalence and Predictors of Types and Subtypes of Pulmonary Diseases in Systemic Lupus Erythematosus: A Population-Based Cross-Sectional Study Using High-Resolution Computed Tomography Scan and Pulmonary Function Testing

Henrik Zachar Langkilde[1], Jesper Davidsen[2], Stefan Harders[3], Stefan Luef[4], Susan Kay[5], Tine Lottenburger[6], Stavros Chrysidis[7], Karen Schreiber[8], Elisabet Svenungsson[9], Sille Fløjborg[10], Robin Christensen[11] and Anne Voss[12], [1]Research Unit of Rheumatology, Department of Clinical Research, University of Southern Denmark, Odense University Hospital, Denmark, Odense, Denmark, [2]South Danish Center for Interstitial Lung Diseases (SCILS) and Pulmo-Rheuma Frontline Center (PURE), Department of Respiratory Medicine, Odense University Hospital, Odense, Denmark, Odense, Syddanmark, Denmark, [3]Research Unit of Department of Radiology, University of Southern Denmark, Odense University Hospital, Denmark., Odense, Syddanmark, Denmark, [4]Odense Respiratory Research Unit (ODIN), Department of Clinical Research, University of Southern Denmark, Odense University Hospital, Odense, Denmark, Odense, Syddanmark, Denmark, [5]Research Unit of Rheumatology, Department of Clinical Research, University of Southern Denmark, Odense University Hospital, Denmark, Odense, Syddanmark, Denmark, [6]Department of Rheumatology, Vejle Hospital, Vejle, Denmark, Vejle, Syddanmark, Denmark, [7]Department of Rheumatology, Esbjerg Hospital, University Hospital of Southern Denmark, Esbjerg, Denmark, Esbjerg, Syddanmark, Denmark, [8]Danish Center for Expertise in Rheumatology (CeViG), Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark, Soenderborg, Syddanmark, Denmark, [9]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden, [10]Systemic Lupus Erythematosus Patient Research Partner, Department of Rheumatology, Odense University Hospital, Denmark, Odense, Syddanmark, Denmark, [11]Musculoskeletal Statistics Unit, The Parker Institute, Copenhagen, Hovedstaden, Denmark, [12]Research Unit of Rheumatology, Department of Clinical Research, University of Southern Denmark, Odense University Hospital, Denmark, Odense C, Syddanmark, Denmark

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that potentially affects any organ. Pulmonary diseases (PD) are common in SLE and cover several different subtypes including, interstitial lung diseases (ILD), shrinking lung syndrome (SLS), pleural and airway diseases. PD are associated with increased morbidity and mortality. The main purpose of this study is to determine the prevalence of PD and subtypes of PD in SLE and to identify predictors of PD.

Methods: In a cross-sectional study we identified all adult patients with SLE in Region Southern Denmark diagnosed and classified with SLE according to the 2019 EULAR/ACR classification criteria and invited eligible patients. Participants' damage accrual was scored according to SLICC/ACR damage index.

To diagnose PD, the participants underwent:

- High-resolution computed tomography scan of the thorax (HRCT)
- Pulmonary function tests (PFT) - body plethysmography, diffusion tests, and six-minute walk test (6MWT)

PFT measures included: Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, total lung capacity (TLC), diffusing capacity of the lung for carbon monoxide (DLCO). Participants were diagnosed with or without PD and classified according to subtype. We investigated associations between PD and subtypes of PD and risk factors with first univariate analyses, then significant associations were analyzed with multivariable regression analyses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Prevalence of pulmonary diseases and subtypes of pulmonary diseases among 185 patients with Systemic Lupus Erythematosus. PD – Pulmonary Diseases, ILD – Interstitial Lung Diseases, UIP – Usual Interstitial Pneumonia, NSIP – Non-Specific Interstitial Pneumonia, HP – Hypersensitivity Pneumonitis, LIP – Lymphoid Interstitial Pneumonia; OP – Organizing Pneumonia, SLS – Shrinking Lung Syndrome; COPD – Chronic Obstructive Pulmonary Diseases, % is the percentage of the total study population.

Types of PD	Selected subtypes of PD	Prevalence, no. (%)
PD		109 (59%)
ILD		22 (12%)
	UIP patterns	10 (5.4%)
	NSIP patterns	1 (0.54%)
	HP patterns	3 (1.6%)
	LIP	3 (1.6%)
	OP	1 (0.54%)
	Other	6 (3.2%)
SLS		1 (0.54%)
Pleural		35 (19%)
	Pleuritis	9 (4.9%)
	Pleuroparenchymal fibrosis	23 (12%)
	Other	3 (1.6%)
Airway		70 (38%)
	Asthma	1 (0.54%)
	Bronchiectasis	28 (15%)
	Bronchiolitis	3 (1.6%)
	COPD	8 (4.3%)
	Emphysema	20 (11%)
	Thickened airways	25 (14%)

Table 2. Prediction of any pulmonary disease and subtypes of pulmonary diseases in systemic lupus erythematosus by means of regression analyses. OR – Odds ratio, SDI - Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index, SDI, no PD - Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index without score from pulmonary diseases, APS – Anti-Phospholipid Syndrome, DLCO - Diffusing Capacity of the Lung for Carbon Monoxide, % - percentages of expected, low* - less than 80% of expected, TLC – Total Lung Capacity.

Predictor	Univariate analyses, OR (p-value)	Multivariate analyses, OR (p-value)
Any pulmonary diseases		
Age, years	1.05 (< 0.001)	1.08 (0.008)
SDI, Score 0-48	1.48 (< 0.001)	9.96 (< 0.001)
SDI, no PD, Score 0-43	1.31 (0.003)	0.0894 (< 0.001)
Interstitial lung diseases		
Age, years	1.06 (0.001)	1.07 (0.018)
SDI, Score 0-48	1.40 (0.001)	8.30 (0.001)
SDI no pd, Score 0-43	1.26 (0.015)	0.147 (0.002)
Pleural diseases		
SDI, Score 0-48	1.38 (< 0.001)	53.8 (< 0.001)
SDI no pd, Score 0-43	1.21 (0.020)	0.0179 (< 0.001)
APS	4.44 (< 0.001)	6.44 (0.041)
DLCO, %	0.975 (0.019)	1.12 (0.003)
DLCO low*	2.96 (0.017)	29.7 (0.003)
Airway diseases		
TLC low*	3.21 (0.010)	3.75 (0.036)

Results: We invited 318 patients with SLE and 185 (58%) participated. Participants were predominantly white (94%), female (87%), with a mean age of 52 years (standard deviance 14), a median disease duration of 15 years (interquartile range 5.7 to 24), and 54% had ever smoked. PD were diagnosed in 59% of the participants, of which 12% had ILD, 1% SLS, 19% pleural diseases, and 38% airway diseases (Table 1).

When predicting PD and subtypes of PD, ventilation parameters had low sensitivities ranging from 20% to 45%. DLCO was abnormal in 62% of all participants, including 46% of those without PD. Descriptions of HRCT scans were closely related to final diagnoses of PD, although some minor cystic changes and small nodules were insufficient to establish a diagnosis of PD. In univariate analyzes PD were significantly associated with decreased PFT measures such as decreased FEV_1, FVC, TLC, and DLCO, but not with measures from 6MWT. In univariable analyzes both ILD and pleural diseases were significantly associated with decreased FEV_1, FVC, TLC, and DLCO, while airway diseases associated with decreased FEV_1, FEV_1/FVC ratio, TLC, and DLCO. In multivariable logistic regression analyzes 12 variables had a significant association with PD or its subtypes (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In a large, population-based study of PD in well-characterized patients with SLE, we identified PD in 59% of the cases. The most common manifestations were airway and pleural diseases, with ILD occurring in 12% of the patients. PFT alone contributed only to a limited extent to identification of patients with PD which was also true in multivariable analyzes. As PD are frequent and often treatable, diligent diagnosis is important.

Disclosure: H. Langkilde: None; **J. Davidsen**: AstraZeneca, 1, 5, 6, Boehringer-Ingelheim, 1, 5, 6; **S. Harders**: None; **S. Luef**: None; **S. Kay**: None; **T. Lottenburger**: None; **S. Chrysidis**: None; **K. Schreiber**: None; **E. Svenungsson**: AstraZeneca, 11, Pfizer, 11; **S. Fløjborg**: None; **R. Christensen**: None; **A. Voss**: None.

Abstract Number: 2401

Associations Between Serum Levels of Soluble Urokinase Plasminogen Activator Receptor (suPAR) and Activity and Chronicity Features in Diagnostic and Per-protocol Repeat Kidney Biopsies in Patients with Lupus Nephritis

Sandra Jagerback[1], Frederic Houssiau[2], Dionysis Nikolopoulos[3], Lina Wirestram[4], Julius Lindblom[5], Farah Tamirou[6], Christopher Sjowall[7] and **Ioannis Parodis**[8], [1]Karolinska Institutet, Stockhom, Stockholms Lan, Sweden, [2]CUSL, BRUSSELS, Belgium, [3]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [4]Linköping University, Linköping, Sweden, [5]Karolinska Institutet, Stockholm, Sweden, [6]Cliniques universitaires Saint-Luc, Brussels, Belgium, [7]Linkoping University, Linkoping, Sweden, [8]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Serum levels of soluble urokinase plasminogen activator receptor (suPAR) have been associated with organ damage accumulation in patients with recent-onset systemic lupus erythematosus (SLE). In this study, we aimed to investigate serum suPAR levels in relation to lupus nephritis (LN), including activity and chronicity features in diagnostic and per-protocol repeat kidney biopsies.

Methods: Serum levels of suPAR from 23 well-characterised patients with LN (of whom 19 were incident cases) from the Cliniques Universitaires Saint-Luc, Brussels, Belgium (N=21) and the Karolinska University hospital, Stockholm, Sweden (N=2) were analysed using enzyme-linked immunosorbent assay (suPARnostic® AUTO Flex ELISA, ViroGates, Birkerød, Denmark) at the time of the diagnostic kidney biopsy and prior to commencement of immunosuppressant therapy for active LN, and twelve months after treatment initiation, at the time of a per-protocol repeat kidney biopsy. We also analysed levels of suPAR in serum samples from 15 healthy controls for the purpose of comparisons. The Spearman's rank correlation coefficient was used to compare levels of suPAR at baseline (BL) and month12 (M12) with serum levels of creatinine, estimated glomerular filtration rate (eGFR), urine protein-creatinine ratio (UPCR), Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) scores, extra-renal SLEDAI-2K scores (after exclusion of the renal descriptors), and renal histopathological features of activity or chronicity based on the National Institutes of Health (NIH) activity and chronicity index scores, at the same timepoints.

Results: At the time of active LN, patients had significantly higher suPAR levels compared to one year after treatment initiation (mean ± standard error: 5.37 ± 0.40 at BL versus 3.77 ± 0.20 at M12; 95% CI: 0.62–2.56; p=0.002), and compared with healthy controls (2.64 ± 0.25; BL vs HC: p< 0.001; M12 vs HC: p< 0.001; Figure 1). Furthermore, suPAR levels at BL

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

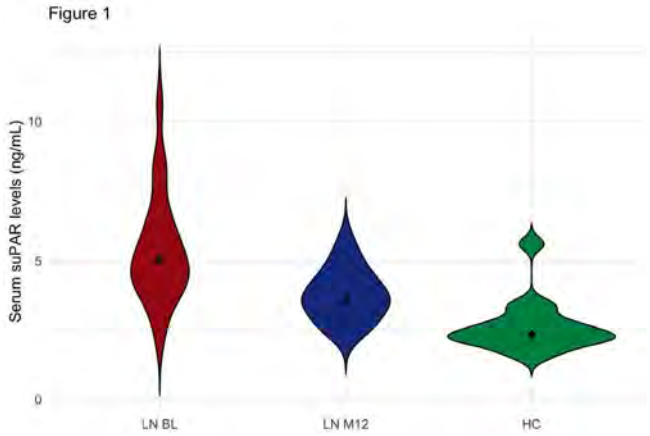


Figure 1.

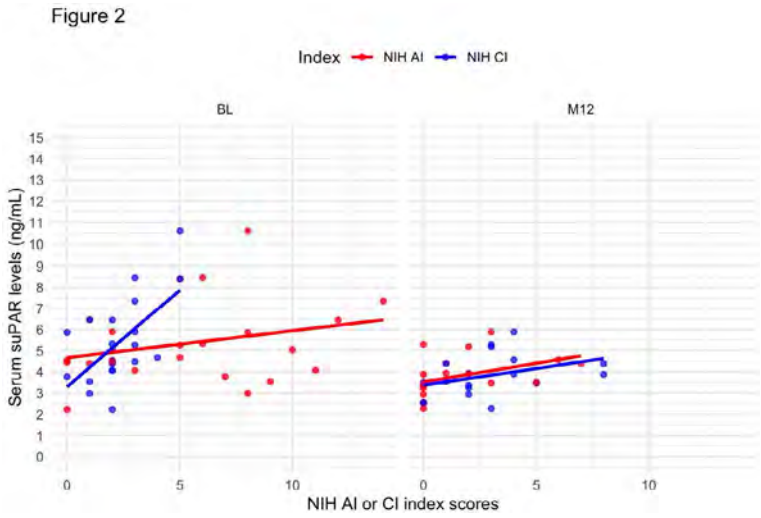


Figure 2

were not correlated with NIH activity index (AI) scores (rho=0.202; *p=0.368*), but a significant correlation could be seen at M12 (rho=0.595; *p*=0.007). In addition, suPAR levels were positively correlated with NIH chronicity index (CI) scores at BL (rho=0.541; *p*=0.008) and the same trend, although not significant, could be seen at M12 (rho=0.440; *p*=0.066; Figure 2). However, a moderate and statistically significant correlation was seen between baseline suPAR levels and NIH CI scores at M12 (rho=0.554; *p*=0.017).

Conclusion: In this cohort of LN with repeat kidney biopsies, serum suPAR levels were prominently elevated in patients with active LN compared with healthy individuals and compared to 12 months after initiation of treatment. Levels of suPAR were positively correlated with histopathological activity at month 12 from treatment initiation. An association with chronicity features was also seen at baseline, as well as a correlation between baseline suPAR levels and chronicity features at 12 months. These findings suggest that suPAR levels may prove useful as a biomarker for monitoring LN activity and an indicator of poor prognosis, warranting further investigation.

Disclosure: S. Jagerback: None; **F. Houssiau**: Roche-Genentech, 5; **D. Nikolopoulos**: None; **L. Wirestram**: None; **J. Lindblom**: None; **F. Tamirou**: None; **C. Sjowall**: Bristol-Myers Squibb(BMS), 3; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2402

High-Resolution Proteomic Profiling Validates BAFF Pathway Modulation and Reveals Novel Biomarker Signatures in Belimumab Treatment

Alexander Tsoi[1], Dionysis Nikolopoulos[2], Natalia Sherina[3] and **Ioannis Parodis**[1], [1]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [2]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [3]Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, and Karolinska University Hospital, Stockholm, Stockholm, Stockholms Lan, Sweden

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Belimumab, a BAFF inhibitor, is an effective treatment for systemic lupus erythematosus (SLE), but biomarkers predicting treatment response remain elusive. We aimed to identify protein signatures associated with clinical response to belimumab.

Methods: We conducted a prospective observational study of patients with SLE initiating belimumab treatment. Samples were available at baseline (prior to treatment initiation; T0; N=69), month 3 (T1; N=63), and month 6 (N=69). Complete clinical data were available for 64 patients, who were finally included for analysis. Using NUcleic acid Linked Immuno-Sandwich Assay (NULISA) technology (1), we simultaneously measured 250 protein markers at each timepoint in normalised protein quantification units (NPQ). Clinical response was defined as a ≥4-point reduction in SLEDAI-2K score at T2. Mixed-effects models were employed to identify proteins associated with response and temporal changes, with false discovery rate (FDR) correction.

Results: The main effects analysis demonstrated a strong modulation of BAFF pathway proteins at T2, with TNFRSF13C (BAFF-R) showing significant reduction from baseline to month 6 (NPQ: T0 13.059, T2 12.220; $p < 0.001$). Similar decreases were observed in TNFRSF9 (CD137; NPQ: T0 11.269, T2 10.704; $p < 0.001$) and TNFRSF13B (TACI; NPQ: T0 12.713, T2

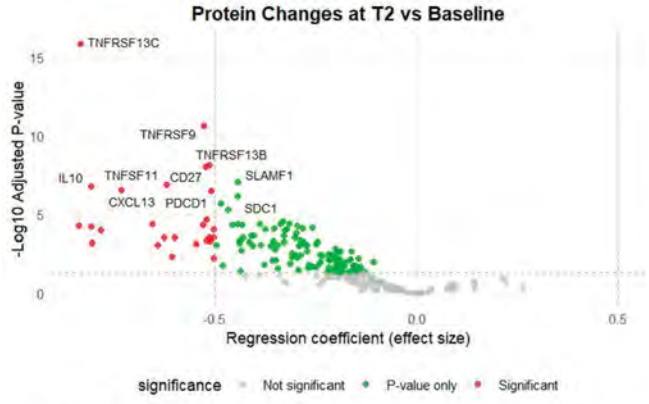


Figure 1. Protein changes following belimumab treatment.
Volcano plot showing protein expression changes at 6 months versus baseline. TNFRSF13C (BAFF-R), TNFRSF9 (CD137), and TNFRSF13B (TACI) show significant downregulation (p<0.001, FDR-adjusted) following treatment.

Figure 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

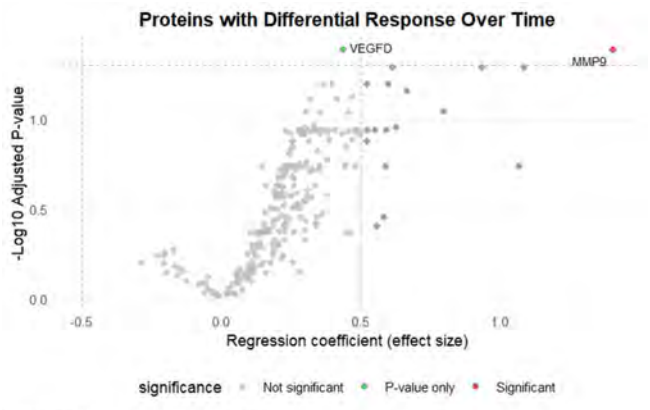


Figure 2

12.183; $p< 0.001$) with FDR-adjusted values (figure 1). Additionally, interaction analysis revealed distinct temporal patterns between responders and non-responders, with MMP9 and VEGFD showing significant treatment-response interactions at T2 (FDR-adjusted p=0.040 for both) (figure 2).

Conclusion: This high-resolution proteomic analysis provides molecular validation of belimumab mechanism of action through BAFF pathway modulation and identifies novel protein signatures associated with treatment response. The technical capabilities of NULISA enabled detection of both on-target drug effects as well as less well-described effects on other molecular targets, demonstrating its utility for biomarker discovery in SLE.

Disclosure: A. Tsoi: None; **D. Nikolopoulos**: None; **N. Sherina**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5.

Abstract Number: 2403

Differential Risk of Inpatient Admissions Among SLE Subgroups: A Population-Based Analysis

Jaime Flores-Gouyonnet[1], Erika Navarro-Mendoza[1], Mario Bautista-Vargas[1], Ali Ardekani[1], Maria Cuellar-Gutierrez[1], Gabriel Figueroa-Parra[2], Mariana Gonzalez-Treviño[3], Alain Sanchez-Rodriguez[4], Andrew C. Hanson[1], Cassondra Hulshizer[5], Cynthia Crowson[6] and Ali Duarte-Garcia[1], [1]Mayo Clinic, Rochester, MN, [2]Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico, [3]Vanderbilt University Medical Center, Nashville, TN, [4]ABC Medical Center, Ciudad de México, Federal District, Mexico, [5]Mayo Clinic, Rochester, [6]Mayo Clinic, Stewartvillle, MN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: SLE is clinically heterogeneous and associated with increased hospitalizations. However, it remains unclear which patient subgroups drive this excess in unplanned healthcare use. We aimed to determine 1) whether elevated hospitalization rates are concentrated among patients with LN or aPL, and 2) whether individuals with non-renal, aPL-negative SLE exhibit hospitalization risks comparable to the general population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Incident SLE cases (1995–2018) from a 27-county region in the US Midwest were matched 1:2 to non-SLE comparators on age, sex, race/ethnicity, and county. SLE onset was defined by fulfillment of the 2019 EULAR/ACR criteria with follow-up starting after discharge if diagnosed during hospitalization. Using a time-dependent variable (**Figure**), patients contributed person-time to the **SLE state** (non-renal, aPL-negative) until developing LN or aPL positivity. The **aPL state** began at detection of lupus anticoagulant or IgG anticardiolipin/β2-glycoprotein-1 (≥40 GPL). The **LN state** began at biopsy confirmation or proteinuria ≥500 mg/day. Patients meeting both LN and aPL criteria were analyzed in the LN state.

The primary outcome was inpatient stays ≥24 hours. Follow-up continued until December 2023, emigration, or death. Conditional frailty models—adjusted for sex, age, white race, and smoking—compared admission hazards across SLE states vs. comparators; secondary models examined time-varying hazards post-discharge (0–30 days, 31 days–1 year, >1 year).

Table 1. Demographics, Baseline Disease Characteristics, Clinical Outcomes and Unplanned Hospitalizations of an Incident (1995-2018) Cohort of Patients with Systemic Lupus Erythematosus (SLE) and Matched non-SLE Comparators from 27 counties in the Midwest Region of the United States.*

	Comparators (N=652)	SLE Cases (N=326)
Baseline Characteristics		
Age at Index, years (Median/IQR)	46 (33-61)	46 (33-61)
Sex		
Female	514 (78.8%)	257 (78.8%)
Charlson score		
Not calculated	36 (5.5%)	6 (1.8%)
0	389 (59.7%)	126 (38.7%)
1-2	170 (26.1%)	112 (34.4%)
3 or more	57 (8.7%)	82 (25.2%)
SLEDAI, n=322 †	N/A	6 (4, 8)
Organ Involvement, n=322		
No	0	13 (4.0%)
Yes	0	309 (96.0%)
SDI Score		
0	0	162 (49.7%)
1-2	0	113 (34.7%)
3-4	0	30 (9.2%)
5 or more	0	21 (6.4%)
Smoking Status		
Never	340 (52.1%)	145 (44.5%)
Quit/Former	164 (25.2%)	124 (38.0%)
Current	116 (17.8%)	56 (17.2%)
Unknown	32 (4.9%)	1 (0.3%)
Race/Ethnicity		
Black	28 (4.3%)	14 (4.3%)
Asian	50 (7.7%)	25 (7.7%)
American Indian	2 (0.3%)	1 (0.3%)
Other/Mixed	10 (1.5%)	5 (1.5%)
Non-Hispanic White	526 (80.7%)	263 (80.7%)
Hispanic	34 (5.2%)	17 (5.2%)
Unknown	2 (0.3%)	1 (0.3%)
BMI (kg/m²) (Median/IQR), n=872	27.8 (24.4-33.8)	26.3 (22.8-32.5)
Clinical Outcomes		
Years of Follow-Up		
Median (IQR)	9 (6-13)	9 (7-12)
Developed Conditions		
Lupus Nephritis	0	86
Antiphospholipid Antibody Positivity	0	69
Deaths	67	71
In-patient Admissions		
Inpatient admissions		
0	377	134
1	119	63
2-3	98	58
4-7	40	44
8 or more	18	27
Total	799	829
Per hospitalization Length of stay, days (Median/IQR)	3 (2-5)	3 (2-6)

*Unless otherwise indicated, values are the number (%) of patients. † Four patients did not have an SLEDAI calculated within 60 days following the index date. As a result, SLEDAI median and interquartile range (IQR) were calculated based on a total of 322 patients.

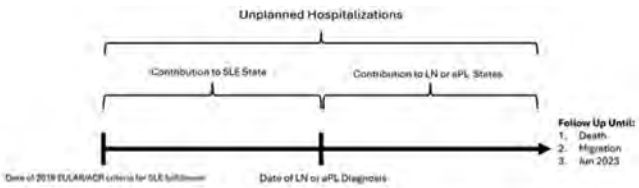


Figure. Timeline Representing the Contribution to Unplanned Hospitalizations Across Three Different Systemic Lupus Erythematosus (SLE) States: 1) Non-renal, antiphospholipid antibody-negative SLE (SLE State); 2)Lupus Nephritis (LN State); and 3) Antiphospholipid antibody-positive SLE (aPL State).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Inpatient Hospitalization Risk Estimates in Patients with Incident Diagnoses of Systemic Lupus Erythematosus (SLE), Positive Antiphospholipid Antibody Profile (aPL) and/or Lupus Nephritis (LN) in Relation to Matched non-SLE Comparators from 27 counties in the Midwest Region of the United States.*

Patient Group	First 30d Post-Diagnosis Period HR (95% CI)	Between 30d-1y Post-Diagnosis Period HR (95% CI)	After 1y Post-Diagnosis Period HR (95% CI)	Overall Adjusted HR (95% CI)
Non-SLE comparator	1 (reference)	1 (reference)	1 (reference)	1 (reference)
SLE State	1.82 (1.31-2.53)	1.54 (1.18-2.01)	1.43 (1.14-1.79)	1.51 (1.24-1.82)
aPL State	2.66 (1.61-4.37)	2.13 (1.38-3.28)	1.47 (0.96-2.26) †	1.85 (1.33-2.58)
LN State	3.78 (2.62-5.46)	2.72 (1.96-3.77)	2.19 (1.61-2.98)	2.59 (2.01-3.32)

*Results are adjusted for sex, age at baseline, white race, and ever smoking. 30d= 30 days, 1y= 1 year, HR= Hazard Ratio, 95% CI= 95% Confidence Intervals. †Result did not reach statistical significance.

Results: Among 326 SLE patients and 652 comparators (median age 46; 79% female; 81% non-Hispanic White), SLE patients had 829 admissions over 3,272 person-years, vs. 799 admissions over 6,654 person-years among comparators (**Table 1**). Of all the SLE patients, 86 transitioned to the LN state (25 were also aPL-positive) and 69 to the aPL state. In fully adjusted models, the SLE state was associated with a 51% higher hazard of hospitalization compared to controls (HR 1.51, 95% CI 1.24–1.82; $p < .001$). aPL state conferred an 85% increase (HR 1.85, 95% CI 1.33–2.58; $p < .001$), and LN state the greatest rise at 159% (HR 2.59, 95% CI 2.01–3.32; $p < .001$). Time-stratified analyses demonstrated peak risk in the first 30 days post-discharge—hazard ratios of 1.82 for SLE, 2.66 for aPL, and 3.78 for LN—with gradual attenuation thereafter (**Table 2**).

Conclusion: In this population-based cohort, patients with lupus nephritis demonstrated the greatest increase, those with antiphospholipid antibodies an intermediate rise, and non-renal, aPL-negative SLE the smallest—yet still substantial—elevation. These findings highlight the need for stratified risk assessment in SLE: while everyone with SLE is at increased risk of rehospitalization, the greatest attention—and potentially the most aggressive preventive strategies—should be directed toward those with LN and aPL.

Disclosure: J. Flores-Gouyonnet: None; **E. Navarro-Mendoza**: None; **M. Bautista-Vargas**: None; **A. Ardekani**: None; **M. Cuellar-Gutierrez**: None; **G. Figueroa-Parra**: None; **M. Gonzalez-Treviño**: None; **A. Sanchez-Rodriguez**: None; **A. Hanson**: None; **C. Hulshizer**: None; **C. Crowson**: None; **A. Duarte-Garcia**: None.

Abstract Number: 2404

Clinical features of Elderly-onset Systemic Lupus Erythematosus

Jessica Dai[1], Erin Carter[2], Mala Masson[3], Amit Saxena[4], H Michael Belmont[5], Peter Izmirly[6] and Jill Buyon[4], [1]New York University Grossman School of Medicine, Tenafly, NJ, [2]New York University Grossman School of Medicine, New York, NY, [3]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [4]NYU Grossman School of Medicine, New York, NY, [5]NYU School of Medicine, New York, NY, [6]New York University Grossman School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystemic chronic disease characterized by a wide range of clinical and serological manifestations. It most commonly affects young women, with incidence and disease activity typically declining with age. As a result, data regarding the diagnoses of SLE in individuals ≥60 years of age (elderly onset SLE) is scarce. To better characterize elderly-onset SLE, a multi-racial cohort of SLE patients was analyzed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This analysis leverages a cohort of 1141 SLE patients who met SLE criteria by at least one method: American College of Rheumatology (ACR), Systemic Lupus Erythematosus International Collaborating Clinics (SLICC), and/or 2019 ACR/European League Against Rheumatism (EULAR) classification criteria. Lupus manifestations at the time of diagnosis were compared between elderly-onset SLE patients and those diagnosed at < 60 years old. An analysis of SLE presentation and diagnosis was conducted for elderly-onset SLE patients, including whether SLE diagnoses occurred during hospitalization, following referral to a rheumatologist, or through ongoing rheumatology clinic follow-up.

Results: Of 1141 patients with SLE, 90% were female and 10% were male. The racial and ethnic composition was as follows: 30% Black, 26% Hispanic, 22% White, 16% Asian, and 5% of unknown race/ethnicity. Within this cohort, 43 individuals were diagnosed at age ≥60 years (3.8%), while 1,098 were diagnosed at age < 60 years (96.2%). Additionally, there was a trend toward men being more likely to be diagnosed at age ≥60 years compared to those under 60 (19% vs. 10%, p=0.06). Among the 43 elderly-onset SLE patients, 9 were diagnosed between the ages of 65-69 and 10 were diagnosed at age ≥ 70, with the oldest being 82 years old. In this group, 28% had lupus nephritis (LN), with 6 patients later confirmed by a kidney biopsy. Compared to the remainder of the cohort, elderly-onset SLE patients exhibited significantly lower frequencies of malar rash at presentation (12% vs. 41%, p=0.0001), arthritis (33% vs. 69%, p ≤0.0001), and lupus nephritis (28% vs. 50%, p=0.004. (Table 1.) A majority of patients were diagnosed with SLE during hospitalization (47%), with 80% presenting with lupus-related complaints, and 20% presenting for SLE-unrelated issues (Table 2). The remaining diagnoses were made following referrals from a primary care physician or general rheumatologist (44%), with 11% of these referrals seeking evaluation for conditions other than lupus (Table 3).

Conclusion: This analysis identifies a distinct clinical profile in elderly-onset systemic lupus erythematosus (SLE). Despite immunosenescence, nearly 30% developed lupus nephritis (LN), with almost half diagnosed during hospitalization following severe symptom onset. Only one of 12 LN cases was referred by a rheumatologist for proteinuria; in most, renal involvement

Table 1. Lupus clinical criteria profile for elderly-onset patients and patients diagnosed <60 years of age

Lupus Criteria	Dx=60 y/o n=43	Dx<60 y/o n=1098	P-values
Malar Rash	5 (12%)	448 (41%)	0.0001
Discoid	9 (21%)	207 (19%)	0.7330
Photosensitivity	9 (21%)	359 (33%)	0.1054
Alopecia	5 (12%)	234 (21%)	0.1258
Oral Ulcers	2 (5%)	237 (22%)	0.0074
Arthritis	14 (33%)	761 (69%)	=0.0001
Serositis	14 (33%)	302 (28%)	0.4676
Pleuritis	8 (19%)	183 (17%)	0.7384
Pericarditis	9 (21%)	188 (17%)	0.5169
Renal	12 (28%)	548 (50%)	0.0046
Proteinuria	12 (28%)	548 (50%)	0.0046
Cellular Casts	0 (0%)	0 (0%)	N/A
Neurological	4 (9%)	58 (5%)	0.2540
Seizures	1 (2%)	40 (4%)	0.6489
Psychosis	3 (7%)	18 (2%)	0.0106
Hematological	30 (70%)	688 (63%)	0.3438
Anemia	2 (5%)	82 (7%)	0.4878
Leukopenia	14 (33%)	404 (37%)	0.5717
Lymphocytopenia	23 (53%)	433 (39%)	0.0650
Thrombocytopenia	7 (16%)	162 (15%)	0.7824
Immunologic	39 (91%)	957 (87%)	0.4943
Anti-dsDNA	33 (77%)	835 (76%)	0.9163
Anti-smith	15 (35%)	405 (37%)	0.7895
Low complement	17 (40%)	373 (34%)	0.4505
Antiphospholipid antibodies	13 (30%)	310 (28%)	0.7753
Antinuclear antibodies	43 (100%)	1071 (98%)	0.2980

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Hospitalization chief complaints in elderly-onset lupus patients

Hospitalization Chief Complaints	n=20
Serositis/chest pain/SOB	6 (30%)
Neuropsychiatric	3 (15%)
Rash	2 (10%)
Arthritis	2 (10%)
Anemia	2 (10%)
Fall	1 (5%)
Nausea/vomiting	1 (5%)
Arthritis and serositis	1 (5%)
Low blood pressure	1 (5%)
Fatigue/fever	1 (5%)

Table 3. Reasons for rheumatology referrals in elderly-onset lupus patients

Referral Reasons	n=19
Arthritis	4 (21.1%)
Serologies	4 (21.1%)
Rash	4 (21.1%)
Antiphospholipid antibodies	1 (5.3%)
Antinuclear antibodies	1 (5.3%)
Nephritis	1 (5.3%)
Family history	1 (5.3%)
Non-lupus symptoms	1 (5.3%)
Arthritis and serositis	1 (5.3%)
Autoimmune hepatitis	1 (5.3%)

was recognized only after diagnosis of other SLE manifestations. These findings suggest new onset SLE and LN may be underrecognized in the elderly, leading to delayed diagnosis and increased disease severity.

Disclosure: J. Dai: None; **E. Carter**: None; **M. Masson**: None; **A. Saxena**: AbbVie/Abbott, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, 6, Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 5, Synthekine, 1, 2, UCB, 1, 6; **H. Belmont**: None; **P. Izmirly**: Hansoh Bio, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2.

Abstract Number: 2405

Machine Learning in SLE Diagnosis: Performance of the SLE Risk Probability Index Questionnaire in a Multicenter Cohort of Patients with Systemic Lupus Erythematosus

Joan Manuel Dapeña[1], Eliana Serrano[1], Juan Manuel Bande[2], María Alejandra Medina[2], Diana klajn[2], José Caracciolo[2], Cecilia Castro[3], Julieta Morbiducci[4], Aixa Lucia Merce[5], Rossella Tralice[6], Gabriela Vanesa Espasa[7], Yessika Jackeline Soria[7], Maria Lilia Leguizamón[8], Mariana Pera[7], Inés Verónica Bellomio[9], María Silvia Yacuzzi[10], Maximiliano Machado Escobar[11], Máximo Cosentino[12], Lucila Garcia[13], Mercedes Garcia[12], Carolina Aeschlimann[14], Graciela Noemi Gomez[15], Nicolas Perez[16] and Silvia Beatriz Papasidero[2], [1]Sanatorio Dr Julio Méndez, CABA, Ciudad Autonoma de Buenos Aires, Argentina, [2]Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, [3]Hospital Z.G.A Dr. Isidoro Iriarte de Quilmes, Quilmes, Buenos Aires, Argentina, [4]Hospital General de Agudos Bernardino Rivadavia, Capital Federal, Ciudad Autonoma de Buenos Aires, Argentina, [5]Hospital General de Agudos Bernardino Rivadavia, Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina, [6]Hospital General de Agudos Bernardino Rivadavia, Buenos Aires, Argentina, [7]Hospital Padilla de Tucumán, Tucumán, Argentina, [8]Hospital Padilla de Tucumán, San Miguel de Tucuman, Argentina, [9]Hospital Padilla, Tucumán, Argentina, San Miguel de Tucumán, Argentina, [10]Hospital Eva Perón de Tucumán, Tucuman, Argentina, [11]Hospital Eva Perón de Tucumán, Tucumán, Argentina, [12]Hospital Interzonal General de Agudos "General San Martín" de la plata, La Plata, Argentina, [13]Hospital San Martin de La Plata, La Plata, Argentina, La Plata, Argentina, [14]Hospital Provincial de Rosario, Rosario, Argentina, [15]Instituto de Investigaciones Médicas Dr. Alfredo Lanari, Don Torcuato, Argentina, [16]Instituto de Investigaciones Médicas Dr. Alfredo Lanari, Buenos Aires, Argentina

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The SLE Risk Probability Index (SLERPI), a clinical prediction model for systemic lupus erythematosus (SLE), was developed using machine-learning variable-selection techniques (Random Forest, LASSO). Its score reflects diagnostic certainty, ranging from unlikely to definite SLE. A dichotomous model that uses a cut-off > 7 points to distinguish SLE from non-SLE previously showed high specificity and sensitivity and excellent diagnostic performance in early SLE (disease onset < 5 years). This study aimed to (i) evaluate the dichotomous SLERPI's sensitivity, specificity, and likelihood ratios (LR) in a connective-tissue-disease cohort; (ii) correlate its score with SLE activity/damage indices; and (iii) assess its performance in early SLE, defined as disease duration < 5 years.

Table 1: Baseline Characteristics of Case and Control Groups (N=365)

Characteristic		Case Group (n=183)	Control Group (n=182)
Age in years, mean (SD)		38.9 (13.0)	53.6 (13.3)
Female, *n* (%)		169 (92.3)	154 (84.6)
Occupation, n (%)	Unemployed	52 (32.5)	45 (25.9)
	Employed	108 (67.5)	129 (74.1)
Ethnic group, n (%)	Mestizo	86 (50.3)	77 (47.2)
	Caucasian	52 (30.4)	59 (36.2)
	Other	33 (19.3)	27 (16.6)
Disease duration in months, median (IQR)		92 (37-150)	82.5 (38-151)
Less than 5 years from symptom onset, n (%)		61 (33.3)	64 (35.2)
General disease involvement, n (%)	Immunological	183 (100)	134 (73.6)
	Cutaneous	172 (94)	42 (23.1)
	Musculoskeletal	151 (82.5)	149 (81.9)
	Hematological	110 (60.1)	42 (23.1)
	Renal	103 (56.3)	4 (2.2)
	Constitutional	97 (53)	46 (25.3)
	Serosal	63 (34.4)	6 (3.3)
	Neurological	26 (14.2)	9 (4.9)
	Pulmonary	13 (7.1)	24 (13.2)
	Vascular	7 (3.8)	7 (3.8)
	Cardiac	5 (2.7)	2 (1.1)
	Gastrointestinal	2 (1.1)	2 (1.1)
SLEDAI, median (IQR)		2 (0-6)	-
SLICC-SDI score, median (IQR)		0 (0-1)	-
Current Treatment, n (%)	Glucocorticoids	71 (38.8)	61 (33.5)
	Hydroxychloroquine	158 (86.4)	35 (19.2)
	Mycophenolate mofetil	31 (17)	31 (16.9)
	Cyclophosphamide	8 (4.4%)	8 (4.4%)
	Methotrexate	13 (7.1)	96 (52.7)
	Leflunomide	1 (0.5)	16 (8.8)
	Sulfasalazine	-	2 (1.1)
	Azathioprine	-	11 (6)
	Cyclosporine	3 (1.7)	1 (0.5)
	tsDMARDs	-	4 (2.2)
	bDMARDs	8 (4.4)	21 (11.5)

Abbreviations: *SD = standard deviation; IQR = interquartile range; SLEDAI = Systemic Lupus Erythematosus Disease Activity Index; SLICC-SDI = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; tsDMARDs = targeted synthetic DMARDs; bDMARDs = biologic DMARDs;*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Performance of SLERPI Classification Criteria (N=365)

Classification Criteria	Sensitivity % (95 % CI)	Specificity % (95 % CI)	LR (+) (95 % CI)	LR (–) (95 % CI)
ACR 1997	93.4 % (88.8–96.6)	90.1 % (84.8–94.0)	9.45 (6.08–14.67)	0.07 (0.04–0.13)
SLICC 2012	98.4 % (95.3–99.7)	87.9 % (82.3–92.3)	8.14 (5.50–12.05)	0.02 (0.01–0.06)
ACR/EULAR 2019	99.5 % (97.0–100.0)	89.0 % (83.5–93.2)	9.05 (5.98–13.69)	0.01 (0.00–0.04)
SLERPI	98.4 % (95.3–99.7)	87.9 % (82.3–92.3)	8.14 (5.50–12.05)	0.02 (0.01–0.06)

Abbreviations: CI = confidence interval; LR (+) = positive likelihood ratio; LR (–) = negative likelihood ratio; SLERPI = SLE Risk Probability Index.

Methods: In this multicenter, cross-sectional study, we included consecutive adults (≥18 years) with SLE (cases) and other systemic autoimmune diseases (controls). Exclusion criteria were active infections, active onco-hematologic disease, drug-induced lupus, and SLE overlap syndromes. We recorded sociodemographics, disease characteristics, activity/damage indices (SLEDAI, SLICC-SDI), and treatments. Three blinded evaluators independently classified patients as SLE/No SLE; unanimous agreement served as the gold standard. Expert opinion was compared with ACR 1997, SLICC 2012, ACR/EULAR 2019, and SLERPI criteria. Analyses included descriptive statistics, sensitivity, specificity, LR ±, and Spearman correlations. All sites obtained institutional review-board approval and complied with the Declaration of Helsinki.

Results: From seven centers, 365 patients were enrolled (183 cases, 182 controls). **Table 1** for characteristics. SLERPI showed 98.3 % sensitivity (95 % CI 95.3–99.7), 88 % specificity (95 % CI 82.3–92.3), LR+ 8.1 (95 % CI 5.5–12.0) and LR- 0.02 (95 % CI 0.006–0.06). Comparative performance versus other criteria is presented in **Table 2**. SLERPI scores correlated with SLEDAI ($r = 0.24$; $p = 0.001$) and SLICC-SDI ($r = 0.23$; $p = 0.002$). SLERPI was higher in patients with damage (20 [IQR 16.5–22]) than in those without (17 [IQR 13.5–21]; $p = 0.02$). In the early-SLE subgroup ($n = 125$; duration < 5 years), sensitivity was 96.6 %, specificity 87.9 %, LR+ 8.0, and LR- 0.04. Frequently used treatments among SLE cases were hydroxychloroquine (86.4 %), glucocorticoids (38.8 %), and mycophenolate mofetil (17 %).

Conclusion: SLERPI demonstrated diagnostic accuracy in this multicenter cohort comparable to SLICC 2012 criteria. Although correlations with activity and damage indices were modest, the SLERPI score was significantly higher in patients with established damage. Diagnostic accuracy remained high in early SLE (disease duration < 5 years). SLERPI may serve as a rapid screening tool for SLE, particularly when serological testing is delayed.

Disclosure: J. Dapeña: None; **E. Serrano**: None; **J. Bande**: None; **M. Medina**: None; **D. klajn**: None; **J. Caracciolo**: None; **C. Castro**: None; **J. Morbiducci**: None; **A. Merce**: None; **R. Tralice**: None; **G. Espasa**: None; **Y. Soria**: None; **M. Leguizamón**: None; **M. Pera**: None; **I. Bellomio**: None; **M. Yacuzzi**: None; **M. Machado Escobar**: None; **M. Cosentino**: None; **L. Garcia**: None; **M. Garcia**: None; **C. Aeschlimann**: None; **G. Gomez**: None; **N. Perez**: None; **S. Papasidero**: None.

Abstract Number: 2406

Machine Learning-Based Artificial Intelligence in Systemic Lupus Erythematosus: A Systematic Review of Outcome Prediction and Patient Stratification

Jorge Juan Fragío Gil[1], Roxana González Mazario[2], Pablo Martínez Calabuig[3], Laura Salvador Maicas[4], Mireia Sanmartin Martínez[4], Iván Jesús Lorente Betanzos[4], Amalia Rueda Cid[4], Juan José Lerma Garrido[4], Isabel Martínez Cordellat[4] and Cristina Campos Fernández[5], [1]Hospital General Universitario, Valencia, Spain, [2]Hospital General de Valencia, Valencia, Spain, [3]Hospital General Universitario de Valencia, Spain/ Uversidad Catolica de Valencia San Vicente Martir, Valencia,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Spain, Ontinyent, Spain, [4]Hospital General Universitario de Valencia, Valencia, Comunidad Valenciana, Spain, [5]Hospital General de Valencia, Valencia

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systematic lupus erythematosus (SLE) is an autoimmune disease with prognostic challenges due to its cyclic diversity. Artificial intelligence and machine learning (ML) has emerged as a powerful tool for analyzing multifactorial SLE data. This systematic review aims to investigate the current use of ML in predicting clinical outcomes and stratifying SLE patients.

Methods: A comprehensive search of PubMed, Scopus, Web of Science, and the Cochrane Library was conducted for studies published up to May 2025 evaluating the use of machine learning for stratifying SLE patients and determining prognosis. Extracted data included study design, country, recruitment period, sample size, ML application and algorithms, study aims, inclusion criteria, and main results.

Results: Seventeen studies applying machine learning to 16,483 SLE patients were included, with 81% of participants being female. The majority of studies (58.8%) originated from the USA. Random Forest was the most frequently used algorithm (41.1%), followed by recurrent neural networks and support vector machines. Main applications included predicting disease activity/flares, lupus nephritis, hospitalization risk, and molecular subtypes. Model performance, assessed by area under the ROC curve in nine studies, ranged from 0.595 to 0.9375. Sensitivity and specificity, reported in three studies, ranged from 0.75 to 82.1 and 0.75 to 89.6, respectively.

Conclusion: Machine learning demonstrates strong performance in analyzing complex SLE datasets, enabling accurate prediction of prognosis, disease activity, hospitalization risk, and treatment response. These models consistently outperform traditional approaches, supporting more personalized care and clinical decision-making for SLE patients across diverse clinical scenarios.

Disclosure: J. Fragío Gil: Quibim, 1; **R. González Mazario**: None; **P. Martínez Calabuig**: None; **L. Salvador Maicas**: None; **M. Sanmartin Martínez**: None; **I. Lorente Betanzos**: None; **A. Rueda Cid**: None; **J. Lerma Garrido**: None; **I. Martínez Cordellat**: None; **C. Campos Fernández**: None.

Abstract Number: 2407

Mapping Neurological Involvement, Regional Disparities, and Moderators of the Central Nervous System in Adult-Onset Systemic Lupus Erythematosus: A Global Systematic Review and Meta-Analysis

Jorge Juan Fragío Gil[1], Roxana González Mazario[2], Pablo Martínez Calabuig[3], Laura Salvador Maicas[4], Mireia Sanmartin Martínez[4], Iván Jesús Lorente Betanzos[4], Amalia Rueda Cid[4], Isabel Martínez Cordellat[4], Juan José Lerma Garrido[4] and Cristina Campos Fernández[5], [1]Hospital General Universitario, Valencia, Spain, [2]Hospital General de Valencia, Valencia, Spain, [3]Hospital General Universitario de Valencia, Spain/ Uversidad Catolica de Valencia San Vicente Martir, Valencia, Spain, Ontinyent, Spain, [4]Hospital General Universitario de Valencia, Valencia, Comunidad Valenciana, Spain, [5]Hospital General de Valencia, Valencia

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: One common and clinically important form of systemic lupus erythematosus (SLE) is neuropsychiatric systemic lupus erythematosus (NPSLE). This systematic review and meta-analysis aimed to assess the prevalence, regional disparities, and moderators of seven neurological syndromes in adult-onset SLE, as defined by the criteria of the American College of Rheumatology 1999 (ACR1999).

Methods: PubMed, Scopus, Web of Science, and the Cochrane Library were searched for English-language studies (April 1999–April 2024) reporting on CNS neurological syndromes in adults (>18 years) using the 1999 ACR Case Definitions and including at least 30 patients. Pediatric studies, commentaries, case reports/series, and reviews were excluded. Methodological quality was assessed with the Newcastle-Ottawa Scale. Pooled prevalence with 95% confidence intervals (CIs) was calculated, heterogeneity was evaluated using the I-squared (I^2) test, and publication bias was assessed with Egger's test. Subgroup and meta-regression analyses for moderator and geographic effects were performed using R and a random-effects model.

Results: A total of 25 studies comprising 16,989 patients were included. The mean weighted age was 38.64 years, and 81.1% were female. The median Systemic Lupus International Collaborating Clinics/ACR-damage index (SDI) score at enrollment was 1.1 (range: 0.29–1.7). The most common syndromes were headache (25%, 95% CI [15, 36]), seizures (9%, 95% CI [5, 13]), and cerebrovascular disease (CVD) (9%, 95% CI [5, 13]). In contrast, syndromes such as aseptic meningitis, myelopathy, chorea, and demyelinating syndromes were rare (1%, 95% CI [0, 0.01]). Headache was most prevalent in African populations (55%), followed by Asians (22%), Europeans (19%), and Latin Americans (9%). Seizures were highest among Latin Americans (17%), followed by Asians (13%), Africans (8%), the USA (7%), and Europeans (3%). CVD was most frequent in Asians (13%), then Latin Americans (11%), Europeans (7%), and Africans (3%). Age at SLE diagnosis was not a significant moderator for headache (p=0.59) or CVD (p=0.81), though it showed a trend toward an inverse effect on seizures (p=0.09). Disease duration was not a significant moderator for seizures (p=0.12), but it trended inversely with headache (p=0.07) and CVD (p=0.08). Female gender did not significantly influence headache (p=0.5), seizures (p=0.4), or CVD (p=0.5). Renal involvement was also not a significant moderator for any of the three (headache p=0.76, seizures p=0.87, CVD p=0.81). Substantial heterogeneity and publication bias were present.

Conclusion: Neurological CNS symptoms, as defined per the ACR 1999 criteria, in adult-onset SLE vary significantly. Aseptic meningitis, myelopathy, and chorea were rare, while headaches, seizures, and cerebrovascular disease were most common. Common modifiers like age, sex, disease duration, and renal involvement showed some trends but did not consistently affect syndrome occurrence. Clear regional disparities were noted.

Disclosure: J. Fragío Gil: Quibim, 1; **R. González Mazario**: None; **P. Martínez Calabuig**: None; **L. Salvador Maicas**: None; **M. Sanmartin Martínez**: None; **I. Lorente Betanzos**: None; **A. Rueda Cid**: None; **I. Martínez Cordellat**: None; **J. Lerma Garrido**: None; **C. Campos Fernández**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2408

Direct Medical Cost Burden of Cutaneous Lupus Erythematosus (CLE): A Comparison with Psoriasis, Atopic Dermatitis, and a General Population

Joseph F Merola[1], Catherine Mak[2], Tiange Tang[2], Tricia Li[2], Margaret K Moseley[2], Janine Gaiha-Rohrbach[2] and Feng Zeng[2], [1]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [2]Biogen, Cambridge, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is an autoimmune disease primarily manifesting in skin that can significantly impact patients' quality of life. Current understanding of the direct healthcare cost of CLE is limited. This study was conducted to understand the direct costs of CLE compared with psoriasis, atopic dermatitis (AD), and a general patient population.

Table 1. Selected baseline characteristics of CLE, AD, psoriasis, and general patients

	CLE (N=3,714)	Psoriasis (N=90,133)	AD (N=83,589)	General patients (N=67,221)
Age at index year, mean (SD)	59.5 (15.4)	57.5 (16.8)	57.5 (19.6)	57.9 (19.1)
Age group, n (%)				
18–34	276 (7.4)	10,834 (12.0)	14,336 (17.2)	10,473 (15.6)
35–49	735 (19.8)	17,666 (19.6)	13,633 (16.3)	11,791 (17.5)
50–64	997 (26.8)	22,596 (25.1)	16,317 (19.5)	13,626 (20.3)
65–75	1,119 (30.1)	25,427 (28.2)	20,906 (25.0)	16,684 (24.8)
≥75	587 (15.8)	13,610 (15.1)	18,390 (22.0)	14,647 (21.8)
Sex, n (%)				
Female	2,915 (78.5)	49,429 (54.8)	53,489 (64.0)	35,614 (53.0)
Region, n (%)				
Northeast	923 (24.9)	21,794 (24.2)	12,923 (15.5)	15,904 (23.7)
Midwest	376 (10.1)	13,944 (15.5)	11,619 (13.9)	7,314 (10.9)
South	1,797 (48.4)	39,983 (44.4)	42,931 (51.4)	27,130 (40.4)
West	618 (16.7)	14,412 (16.0)	16,124 (19.3)	16,866 (25.1)
Race, n (%)				
Asian	85 (2.3)	2,010 (2.2)	2,917 (3.5)	2,037 (3.0)
Black	601 (16.2)	3,074 (3.4)	6,411 (7.7)	5,015 (7.5)
Did not report	1,370 (36.9)	36,928 (40.7)	31,856 (38.1)	28,602 (42.6)
White	1,658 (44.6)	48,383 (53.7)	42,405 (50.7)	31,567 (47.0)
CCI categories, n (%)				
Acute myocardial infarction	65 (1.8)	1,298 (1.4)	1,220 (1.5)	948 (1.4)
Congestive heart failure	135 (3.6)	3,128 (3.5)	3,653 (4.4)	2,702 (4.0)
Peripheral vascular disease	198 (5.3)	4,371 (4.9)	5,132 (6.1)	3,502 (5.2)
Cerebrovascular disease	165 (4.4)	3,037 (3.4)	3,736 (4.5)	2,232 (3.3)
Dementia	39 (1.1)	811 (0.9)	1,070 (1.3)	1,197 (1.8)
Chronic pulmonary disease	432 (11.6)	8,950 (9.9)	16,317 (19.5)	5,680 (8.5)
Rheumatic disease	291 (7.8)	2,253 (2.5)	2,223 (2.7)	995 (1.5)
Peptic ulcer disease	21 (0.6)	370 (0.4)	443 (0.5)	249 (0.4)
Mild liver disease	131 (3.5)	2,542 (2.8)	2,274 (2.7)	1,291 (1.9)
Diabetes without chronic complications	491 (13.2)	13,844 (15.4)	11,360 (13.6)	9,391 (14.0)
Renal disease	269 (7.2)	4,281 (4.8)	5,132 (6.1)	3,845 (5.7)
Hemiplegia	N<5	117 (0.1)	142 (0.2)	101 (0.2)
Cancer	122 (3.3)	3,092 (3.4)	3,603 (4.3)	2,111 (3.1)
Severe liver disease	10 (0.3)	189 (0.2)	125 (0.2)	94 (0.1)
Severe renal disease	25 (0.7)	297 (0.3)	401 (0.5)	309 (0.5)
Metastatic cancer	26 (0.7)	397 (0.4)	443 (0.5)	329 (0.5)
HIV infection	N<5	144 (0.2)	234 (0.3)	114 (0.2)
AIDS	98 (2.6)	2,217 (2.5)	2,483 (3.0)	941 (1.4)
CCI score (SD)	0.90 (1.67)	0.76 (1.60)	0.95 (1.74)	0.68 (1.50)
Depression comorbidity, n (%)	431 (11.6)	8,157 (9.1)	9,003 (10.8)	5,384 (8.0)
Anxiety comorbidity, n (%)	560 (15.1)	11,005 (12.2)	13,508 (16.2)	6,742 (10.0)

AD, atopic dermatitis; AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus; CCI, Charlson Comorbidity Index; SD, standard deviation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Annualized incremental costs incurred by patients with CLE compared with the psoriasis, AD, and general patient cohorts

Comparison:	CLE vs Psoriasis	
	No comorbidities controlled	Comorbidities controlled
	Total direct cost	Total direct cost
Estimate (SE)	944.77 (347.24)	-359.75 (329.31)
P-value	**	
Comparison:	**CLE vs AD**	
	No comorbidities controlled	**Comorbidities controlled**
	Total direct cost	Total direct cost
Estimate (SE)	5,060.13 (354.41)	5,635.62 (336.57)
P-value	***	***
Comparison:	**CLE vs General**	
	No comorbidities controlled	**Comorbidities controlled**
	Total direct cost	Total direct cost
Estimate (SE)	12,403.23 (384.13)	9,949.09 (364.13)
P-value	***	***

All costs are from 2023 and are in US dollars
*** P<0.001; ** P<0.01; * P<0.05; absent asterisk denotes P>0.05
AD, atopic dermatitis; CLE, cutaneous lupus erythematosus; SE, standard error

Methods: Data from January 1, 2016, to December 31, 2023, were extracted from the Optum® de-identified Clinformatics® Data Mart. Patients with CLE or psoriasis were identified by at least two relevant International Classification of Disease-9/10 (ICD-9/10) diagnosis codes, with at least one code from a dermatologist. Patients with AD had at least one relevant ICD-9/10 code and an additional claim of asthma or allergic rhinitis. The general patient cohort was a 1% random sample of those without a diagnosis of CLE, psoriasis, or AD. The index date was the first diagnosis date for each of the CLE, psoriasis, and AD cohorts. The index date for the general patient cohort was randomly assigned to simulate the index date distribution of the other cohorts. Eligible patients were at least 18 years old on the index date. Direct costs were calculated as the sum of post-index annualized all-cause utilizations, including outpatient, medications, and hospitalization. Linear regressions with propensity score weighting assessed the cost difference across cohorts. Patient demographics were balanced across different cohorts after propensity score weighting.

Results: The study identified 3,714 CLE, 90,133 psoriasis, 83,589 AD, and 67,221 general patients (**Table 1**). The CLE cohort had a higher mean age (59.5 years), and higher percentage of female (78.5%) and Black (16.2%) patients than other cohorts. In the CLE cohort, 60.0% had systemic lupus erythematosus (SLE); in the psoriasis cohort, 18.6% had psoriatic arthritis. The CLE group showed similar Charlson Comorbidity Index scores and depression and anxiety rates to the psoriasis and AD cohorts, but higher than the general population.

Regression models unadjusted for comorbidities showed that patients with CLE had significantly higher total direct healthcare costs than those with AD ($5,060, $P < 0.001$) and the general cohort ($12,403, $P < 0.001$) (**Table 2**). The CLE annualized total cost was slightly higher than psoriasis, reaching significance ($945, $P < 0.01$). After comorbidity adjustment, the CLE costs remained significantly higher than the general population and AD, while the total cost difference between CLE and psoriasis became non-significant (**Table 2**).

Conclusion: Adults with CLE, with or without SLE, had comparable comorbidity rates to AD and psoriasis, and higher than the general population. This CLE cohort had substantially higher excess total costs than AD and the general population, and similar total cost to the psoriasis cohort. The significant healthcare costs in this population underscore health policy and societal challenges, emphasizing the need for improved management and expedited research efforts to advance therapeutic options.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Merola: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **C. Mak**: Biogen, 3, 12, may hold Biogen stock; **T. Tang**: Biogen, 3, 12, may hold Biogen stock; **T. Li**: Biogen, 3, 12, may hold Biogen stock; **M. Moseley**: Biogen, 3, 12, may hold Biogen stock; **J. Gaiha-Rohrbach**: Biogen, 3, 12, shareholder, may hold Biogen stock; **F. Zeng**: Biogen, 3, 12, may hold Biogen stock.

Abstract Number: 2409

Cutaneous Lupus Activity Investigator's Global Assessment——Revised (CLA-IGA-R) Content Validity: Cutaneous Lupus Erythematosus (CLE) Patient Qualitative Study

Joseph F Merola[1], Weihong Yang[2], Qianyun Li[2], Helen Doll[3], Jason Randall[3], Catherine Barbey[4] and Feng Zeng[2], [1]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, TX, [2]Biogen, Cambridge, MA, [3]Clinical Outcomes Solutions, Folkestone, Kent, United Kingdom, [4]Biogen, Baar, Switzerland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The Cutaneous Lupus Activity Investigator's Global Assessment-Revised (CLA-IGA-R) is an emerging clinician-reported outcome measure for severity of Cutaneous Lupus Erythematosus (CLE) disease activity, developed with clinician input. It consists of three separate items ('Erythema', 'Other morphologic characteristics' [edema, scale, and secondary change], and 'Follicular activity').[1] Qualitative interviews with patients are an important step in assessing the content validity of a measure. The objectives of this concept elicitation study were to qualitatively explore the lived experience of the condition from the patient's perspective and to confirm whether all key signs experienced by patients with CLE are captured by the CLA-IGA-R.

Methods: In total, 15 US participants with a clinical diagnosis of CLE were invited to take part in a qualitative, semi-structured, face-to-face interview. The interview lasted approximately 60 minutes and focused on spontaneously reported signs, symptoms, and impacts of CLE. Key topics not spontaneously discussed were then probed by the interviewer. All interviews were audio recorded and transcribed verbatim; transcripts were then coded and subjected to thematic analysis by two independent researchers. Saturation analysis was performed by dividing the 15 participants into three equal sets.

Results: Participants had an average age of 43.8 (range 24–59) years. They included Black/African American (53.3%; n=8), White (26.6%; n=4), Asian/Asian American (6.6%; n=1), and multiracial (13.3%; n=2) individuals, and most were non-Hispanic (73.3%; n=11). Most were women (86.7%; n=13). Half of the participants had been diagnosed with CLE for at least 10 years, and most reported mild or moderate CLE symptom severity. Six participants had a diagnosis of subacute CLE (SCLE) and eight were diagnosed with chronic CLE (CCLE), including five with discoid lupus.

Red, pink, or purple skin (erythema) was discussed by all 15 participants; 13 reported this spontaneously (**Table 1**). Erythema was described as typically being the first sign of a lupus rash, which was then shortly followed by dry, ashy, or scaly skin (scale: n=13; mentioned spontaneously by 9 participants); this was sometimes followed by swelling, swollen, or bumpy skin (edema) (n=12). Open wounds (n=11) and skin crusting/scabbing (n=8) were associated with more severe rashes and typically occurred at the end of the rash. Little blisters were reported by less than half of participants (n=6). Participants also

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Frequency of reported skin-related lupus concepts during participant interview

Skin-related lupus signs of disease activity	Total (N=15)		
	Total	Spontaneously reported	Mentioned upon questioning
Skin-related lupus signs, n			
Red, pink, or purple skin (Erythema)	15	13	2
Dry, ashy, scaly skin (Scale)	13	9	4
Skin swelling, swollen or bumpy areas (Edema)	12	2	10
Open wounds (Erosion)	11	3	8
Crusting and scabbing after open wounds (Crusting)	8	1	7
Blistering (Vesicles)	6	2	4
Sores in mouth (Mucous membrane sores)	11	2	9
Signs of skin damage,* n			
Scarring	7	7	0
Symptoms,* n			
Hair loss	14	6	8
Skin pain	9	8	1
Itch	7	6	1

*The aim of the interview was to identify signs of CLE activity. Topics relating to signs of disease damage and symptoms were not probed during the interview. However, as these were spontaneously mentioned by participants, they have been included in the results

reported experiencing both current and previous hair loss on the scalp due to CLE (n=14). Saturation was supported as no skin-related lupus signs were introduced within the last group of interviews.

Conclusion: The findings from this qualitative analysis reveal the participants with CLE experienced a wide range of skin-related lupus signs. The key signs and symptoms experienced by participants (erythema, scale, edema, open wounds, crusting, and hair loss [hair loss is the downstream effect of follicular activity]) are captured in the CLA-IGA-R. These data support the content validity of the CLA-IGA-R, and thus its use as a measure of CLE disease activity.

1. Guo LN, et al. Lupus Sci Med 2021;8:e000529

Disclosure: J. Merola: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Biogen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, Dermavant, 2, 5, Eli Lilly and Company, 2, 5, Incyte, 2, Janssen, 2, 5, LEO Pharma, 2, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, Pfizer, 2, Sanofi-Regeneron, 2, 5, Sun Pharma, 5, UCB, 2, 5; **W. Yang**: Biogen, 3, 12, may hold Biogen stock; **Q. Li**: Biogen, 3, 12, may hold Biogen stock; **H. Doll**: Clinical Outcomes Solutions, 3; **J. Randall**: Clinical Outcomes Solutions, 3; **C. Barbey**: Biogen, 3, 12, may hold Biogen stock; **F. Zeng**: Biogen, 3, 12, may hold Biogen stock.

Abstract Number: 2410

Immune Cell/Pathway-Specific Polygenic Risk Scores Reveal Immune Pathway Associations in Childhood-Onset Lupus Nephritis

Liyoung Kim[1], Daniela Fernandez-Salinas[2], Gonzalo Villanueva Martin[3], Vitor Aguiar[3], Laura Lewandowski[4], Tiphanie Vogel[5], Carola Vinuesa[6], Linda Hiraki[7], Tracey Wright[8], Virginia Pascual[9], Joyce Chang[2], Maria Gutierrez-Arcelus[2] and Peter Nigrovic[1], [1]Boston Children's Hospital, Brookline, MA, [2]Boston Children's Hospital, Boston, MA, [3]Boston Children's Hospital, Boston, [4]NIAMS, NIH, Bethesda, MD, [5]Baylor College of Medicine, Houston, TX, [6]Francis Crick Institute, London, United Kingdom, [7]The Hospital for Sick Children, Toronto, ON, Canada, [8]UT Southwestern, Children's Medical Center, and Scottish Rite for Children, Dallas, TX, [9]Weill Cornell Medical College, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Polygenic risk scores (PRS) quantify an individual's genetic susceptibility to diseases by integrating genotype data across multiple loci. However, conventional PRS are limited in capturing the biological context of risk variants. Here, we applied a novel approach, cell-type PRS (csPRS) and pathway-specific PRS (psPRS), to assess genetic risk variants related to specific immune pathways associated with lupus nephritis (LN) phenotypes in childhood-onset SLE (cSLE).

Methods: The study cohort included 192 patients diagnosed with SLE before the age of 18, recruited from the University of Texas Southwestern Medical Center. Demographic and clinical phenotypes were collected during routine clinic visits. A total of 952 SLE risk variants were utilized based on an autoimmune multi-ancestry meta-GWAS. Using chromatin accessibility data, the variants were categorized by immune cell type - B cells, T cells, monocytes, and NK cells - and, using KEGG pathway annotation, the variants were grouped into four biological pathways - BCR, TLR, JAK-STAT, and MAPK. csPRS and psPRS were calculated using a high-performance PRS model (Pruning + Thresholding; p-value threshold: 5×10^{-4}; AUC > 0.7). To evaluate differences in csPRS and psPRS based on the presence of LN and classes (class I/II, proliferative [III, IV, III+V, IV+V], and membranous), ANOVA followed by post-hoc analysis were performed to assess group-wise differences. Overlap of SNP sets between pathways and immune cell types was visualized using R. Pearson correlation coefficients were calculated to assess the relationship between csPRS and psPRS.

Results: The majority of cSLE patients (63.5%) were classified genetically as admixed ancestry, followed by African ancestry (19.7%). There was no difference in overall PRS between patients with and without LN. Further analysis comparing csPRS and psPRS across LN classes showed that patients with proliferative LN had numerically higher T cell PRS than those with class I/II LN, while MAPK psPRS was significantly elevated in the proliferative group ($p = 0.016$). To assess the combined contribution of specific immune cell types and pathways, an integrated PRS was calculated. T cell + MAPK PRS revealed a significant difference between class I/II and proliferative LN ($p = 0.021$). To ensure the result was not driven by overlapping variants, the two SNPs shared between the T cell and MAPK sets were removed prior to computing the integrated score. Notably, there was no significant correlation between T cell and MAPK PRS.

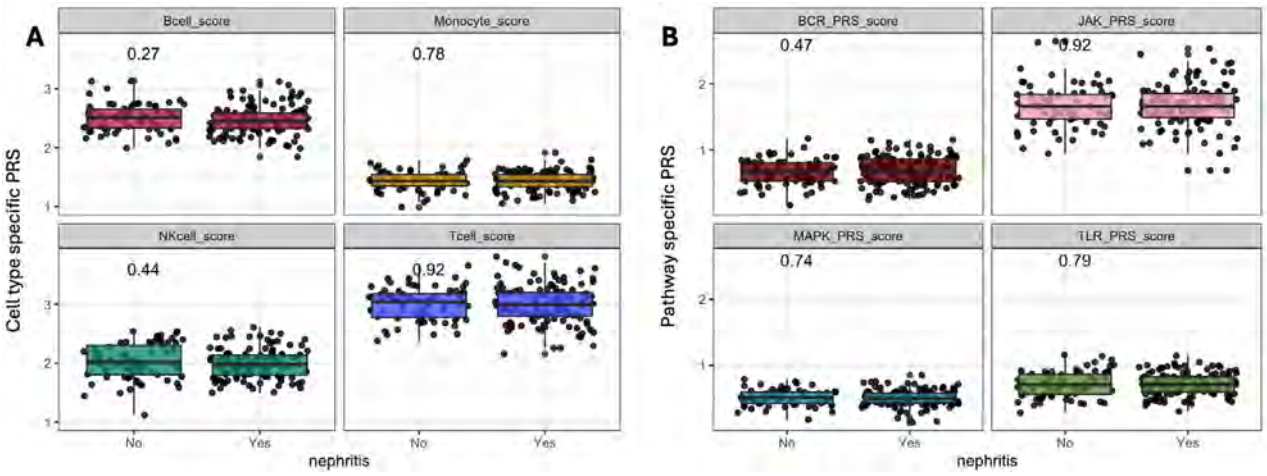
Conclusion: This study demonstrated the heterogeneity of genetic risk across immune pathways in cSLE. Applying csPRS and psPRS, we identified distinct immunogenetic signatures that may underlie differences between class I/II and proliferative LN, reflecting potential immunopathological distinctions between LN histologic subtypes. Expanding this approach in larger, ancestrally diverse cohorts will be essential to validate findings and improve patient stratification into biologically meaningful endotypes. Ultimately, this framework may inform the identification of key immune pathways driving disease phenotypes and support the development of targeted therapies in cSLE.

Table 1. Baseline Characteristics of cSLE Patients (n=192)

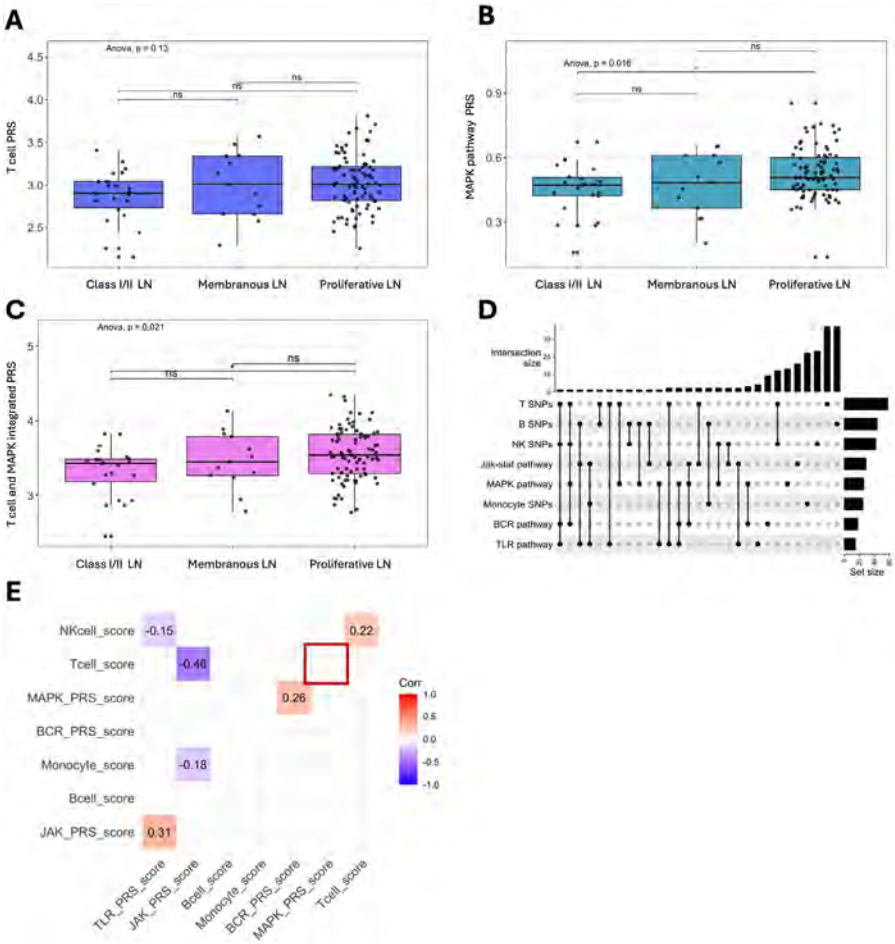
Sex: n (%)	
Female	163 (84.8)
Age at diagnosis (years): median (IQR)	
Total	12.2 (8.4-16.0)
Genetic ancestry: n (%)	
Admixed	122 (63.5)
African	38 (19.7)
East Asian	3 (1.5)
European	21 (10.9)
Native American	7 (3.6)
Southeast Asian	1 (0.5)
Lupus nephritis: n (%)	
No nephritis	70 (36.4)
Class I, II	22 (11.4)
Proliferative LN (Class III, IV, III+V, IV+V)	87 (45.3)
Membranous LN (Class V)	13 (6.8)

Ancestry was determined using ADMIXTURE analysis. Patients were assigned to a specific ancestry group if their first principal component (PC1) exceeded an 80% threshold; otherwise, they were classified as admixed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Comparison of csPRS and psPRS in cSLE patients with and without lupus nephritis, using t-test. (A) Immune csPRS (B cell, monocyte, NK cell, and T cell) in cSLE patients with lupus nephritis (n=122) versus those without lupus nephritis (n=70). (B) psPRS (BCR, JAK-STAT, MAPK, and TLR signaling pathways) in the same patient groups.



Comparison of csPRS and psPRS across lupus nephritis classes. Lupus nephritis classes were grouped as class I/II, proliferative lupus nephritis (classes III, IV, III+V, IV+V), and membranous lupus nephritis (class V) (A) T cell PRS was compared across lupus nephritis classes using ANOVA followed by post-hoc tests. (B–C) MAPK PRS and the integrated T cell + MAPK PRS were analyzed using the same approach as described for T cell PRS. (D) SNP set overlaps across pathways and immune cell types were visualized using an UpSet plot in R. "Set Size" indicates the number of SNPs in each category (e.g., T cell, B cell, MAPK, TLR), while "Intersection Size" shows the number of SNPs shared between sets. Intersections represent overlapping SNPs or pathways between sets, with each intersection corresponding to a shared subset. (E) Pearson correlation coefficients were calculated to the relationship between csPRS and psPRS. * indicates $p \leq 0.05$; ns indicates not statistically significant.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Kim: None; **D. Fernandez-Salinas**: None; **G. Villanueva Martin**: None; **V. Aguiar**: None; **L. Lewandowski**: None; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6; **C. Vinuesa**: Merck, 6; **L. Hiraki**: Janssen, 2, 5; **T. Wright**: None; **V. Pascual**: None; **J. Chang**: Century Therapeutics, 2; **M. Gutierrez-Arcelus**: None; **P. Nigrovic**: Alkermes, 2, Apollo, 2, Bristol-Myers Squibb(BMS), 5, Century, 2, Edelweiss Therapeutics, 11, Merck, 2, Monte Rosa, 2, Novartis, 2, Pfizer, 2, 5.

Abstract Number: 2411

The 2019 EULAR/ACR and 2012 SLICC Classification Criteria for SLE Should Be Applied with Caution as Diagnostic Criteria

Luca Mazzoleni[1], Francesca Crisafulli[2], Md Yuzaiful Md Yusof[3], Aamir Aslam[4], Andrew Barr[5], Lesley-Anne Bissell[6], Shouvik Dass[5], Jack E Arnold[7], Ed Vital[8], Franco Franceschini[9] and Porntip Intapiboon[10], [1]University of Brescia, Brescia, Italy, [2]ASST Spedali Civili and University of Brescia, Brescia, Italy, [3]University of Leeds, Leeds, United Kingdom, [4]Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [5]Leeds teaching hospitals- NHS trust, Leeds, United Kingdom, [6]Leeds Teaching Hospitals NHS Trust, Leeds, England, United Kingdom, [7]Leeds Institute of Rheumatic & Musculoskeletal Medicine, Leeds, United Kingdom, [8]University of Leeds, Leeds, England, United Kingdom, [9]University of Brescia, Brescia, Brescia, Italy, [10]Prince Of Songkla universitiy, Tambon Kohong, Thailand

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: To assess the 2012 SLICC and 2019 EULAR/ACR classification criteria performance as diagnostic criteria in two cohorts of ANA-positive patients clinically suspected of having CTDs.

Methods: An observational study of 286 ANA-positive, treatment-naïve patients with CTD-related symptoms (≤1 year) was conducted. The 2012 SLICC and 2019 EULAR/ACR criteria were assessed at enrollment (T0) and during a 3-year follow-up. T1 was defined as the visit when patients met classification criteria or their last follow-up. Anonymized charts from T0 and T1 were reviewed by four independent consultants to assess diagnoses and treatment decisions.

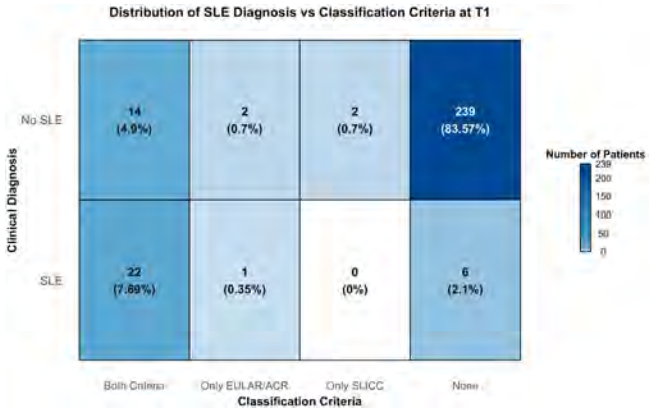
Results: At T1, consultants diagnosed SLE in 29 patients (10.14%). The 2012 SLICC criteria were met in 38 patients (13.29%) and the 2019 EULAR/ACR in 39 (13.64%). 6 patients (2.1%) were diagnosed with SLE despite not meeting either classification criteria, while 18 participants (6.29%) met at least one classification criterion but were not diagnosed with SLE by a consultant. Among these 18 patients, consultants recommended hydroxychloroquine monotherapy in 7 cases, immunosuppressive therapy alone in 6, a combination of the two in 1, and no treatment in 4.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy at T1 of the 2019 EULAR/ACR and 2012 SLICC SLE criteria are reported in table 1.

Table 1. *Comparison of Sensitivity, Specificity, Positive predictive value, Negative predictive value, Accuracy between 2012 SLICC and 2019 EULAR/ACR criteria*

	2012 SLICC	2019 EULAR/ACR
Sensitivity (95% CI)	75.86% (57.89–87.78)	79.31% (61.61–90.15)
Specificity (95% CI)	93.77% (90.13–96.13)	93.77% (90.13–96.13)
Positive predictive value (95% CI)	57.89% (42.19–72.15)	58.97% (43.42–72.92)
Negative predictive value (95% CI)	97.18% (94.29–98.6)	97.57% (94.8–98.88)
Accuracy (95% CI)	91.96% (88.22–94.58)	92.31% (88.63–94.87)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Conclusion: In a diagnostic setting, the criteria are less effective than in a classification context and should therefore be applied with caution. They are more useful for ruling out SLE rather than confirming it, given their moderate sensitivity and PPV, but high specificity and NPV.

Disclosure: L. Mazzoleni: None; **F. Crisafulli**: None; **M. Md Yusof**: GlaxoSmithKlein(GSK), 1, Novartis, 1, 6, UCB, 2, 6; **A. Aslam**: None; **A. Barr**: None; **L. Bissell**: None; **S. Dass**: None; **J. E Arnold**: None; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6; **F. Franceschini**: None; **P. Intapiboon**: None.

Abstract Number: 2412

Evolving Trends in Pulmonary Arterial Hypertension among Systemic Lupus Erythematosus Patients: A Nationwide Analysis

Maria Romero Noboa[1], Faria Sami[2], Almurtada Razok[3] and Shahzad Ahmed Sami[4], [1]University of Alabama at Birmingham, Birmingham, AL, [2]The University of Alabama at Birmingham, Birmingham, AL, [3]John H Stroger Jr Hospital of Cook County, Chicago, IL, [4]DCH Regional Medical Center, Birmingham

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a rare manifestation of Systemic Lupus Erythematosus (SLE) with increased morbidity and mortality. It has historically been underdiagnosed in SLE patients due to nonspecific symptoms and overlap with other conditions but has recently come into light as an important SLE associated complication due to increased awareness. This study aims to analyze yearly trends in PAH and its types in SLE population in the U.S. as well as in-hospital mortality.

Methods: We performed a retrospective review of annual trends in PAH among SLE patients using the National Inpatient Sample (NIS) from 2016 - 2020. Hospitalizations with SLE were identified using ICD-10 codes and cases with a concurrent PAH diagnosis were included. We examined the baseline demographic characteristics and inpatient mortality rate. Yearly trend in PAH among SLE patients was analyzed. Trends across various WHO groups of PAH in SLE patients were also

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

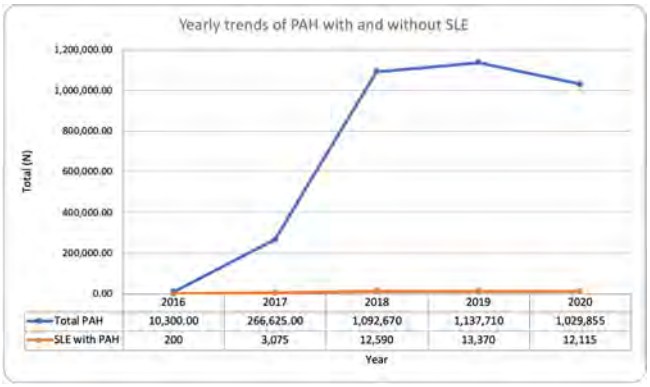


Figure 1: Yearly trends of PAH with and without SLE

Figure 2: Yearly trends of SLE with PAH by WHO GROUP

Figure 3: Yearly in-hospital mortality trend in SLE with PAH

compared. Statistical analysis was performed on STATA 7, with P-value less than 0.05 was considered statistically significant.

Results: A total of 41,445 hospitalizations with concurrent SLE and PAH were identified between 2016 and 2020. Most patients were females (89.4% in 2020) and by 2020, white race comprised 39.9%, African Americans 37.9%, Hispanic 13.2% and Asian 8.9%. Mean age increased from 54.5 years in 2016 to 57.4 years in 2020. Overall, yearly hospitalizations of SLE with PAH increased substantially from 200 in 2016 to over 12,000 by 2018 ($p < 0.001$). (Figure 1) This was also seen according to WHO groups of PAH, especially for Group 5 (Figure 2). There was a significant increase in comorbidity burden, with the proportion of patients with a CCI ≥4 increasing from 6.8% in 2016 to 77.2% in 2019. Comorbidities with notable uptrend included congestive heart failure (CHF) (47.5% to 63.1%, $p = 0.001$), hyperlipidemia (20.0% to 35.9%, $p = 0.005$),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and protein-energy malnutrition (PEM) (7.5% to 11.8%, p = 0.005). Despite rising complexity, in-hospital mortality was 5.0% in 2016 and continued like this to 2020 with 4.9% (p = 0.249). (Figure 3) Mean length of stay (7.3 days in 2016 vs 7.2 in 2020) and Total Hospital Charges ($86,676 in 2016 and $96,961 by 2020) remained stable. However, rates of adverse in-hospital events increased, including mechanical ventilation (MV) (2.5% to 8.1%, p =0.004), acute myocardial infarction (AMI) (5.0% to 7.5%, p = 0.001), acute respiratory failure (ARF) (12.5% to 16.6%, p = 0.001), and pulmonary embolism (PE) (0% to 2.1%, p =0.019). There was no change in the trend for sepsis, acute kidney injury (AKI), need for pressors, or cerebrovascular accident (CVA).

Conclusion: Hospitalizations of SLE patients with PAH increased significantly from 2016 to 2020, with an uptrend in comorbidities including CHF, hyperlipidemia and PEM. There was an increase in-hospital events including MV, AMI, ARF and PE. Despite this rise in complexity and events, mortality and healthcare utilization remained similar from 2016 to 2020. These findings highlight the evolving clinical profile of SLE patients with more frequent PAH diagnosis over time, and underscores the need for targeted interventions to improve outcomes in patients with SLE-related PAH.

Disclosure: M. Romero Noboa: None; **F. Sami**: None; **A. Razok**: None; **S. Sami**: None.

Abstract Number: 2413

Hydroxychloroquine and Adverse Cardiovascular Outcomes in Pregnant Patients with Systemic Lupus Erythematosus

Mariana Gonzalez-Treviño[1], Ashley L Ciosek[1], Genessis Maldonado[1], Catherine Deffendall[2], Tania Ruiz[1], Tracy Frech[1] and Rashmi Dhital[3], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University, Nashville, TN, [3]Vanderbilt University Medical Center, Brentwood, TN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is a medication used in SLE during pregnancy. An adverse effect of HCQ includes cardiotoxicity. Hormonal changes during pregnancy may trigger SLE cardiomyopathy. The objective of this study was to examine the association of HCQ use during pregnancy with new onset adverse cardiovascular (CV) outcomes during pregnancy and postpartum in subjects with SLE.

Methods: In this study, we used the Synthetic Derivative, a de-identified copy of the EHR containing billing codes and clinical data spanning 1989-2024. We identified pregnant subjects with SLE and CV outcomes using ICD-9/ICD-10 codes for 1) SLE, 2) labor/delivery, and 3) heart failure (HF)/peripartum cardiomyopathy or CPT codes for cardiac MRI. Charts were manually reviewed by a physician to ascertain SLE clinical diagnosis and pregnancy (inclusion criteria). Subjects without SLE, pregnancy prior to SLE, onset of HF prior to pregnancy, and pregnancies terminating < 20 weeks were excluded. Demographic and clinical characteristics, HCQ use during pregnancy, immunosuppressive therapy (IST), and maternal complications were abstracted. Medical records were reviewed from conception until six months after delivery to identify new onset adverse CV outcomes (HF, arrhythmias, valvular disease, pericarditis, Cor pulmonale) during pregnancy and postpartum. Comparisons were made using Mann-Whitney U test for continuous variables and Fisher's exact test or X^2-test for categorical variables, as appropriate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of individuals with systemic lupus erythematosus with or without use of hydroxychloroquine during pregnancy.

Table 1. Demographic and clinical characteristics of individuals with systemic lupus erythematosus with or without use of hydroxychloroquine during pregnancy.

Variable	Total (N= 33)	HCQ use during pregnancy (n= 17)	No HCQ use during pregnancy (n= 16)	*p*-value
Age at SLE diagnosis (years), median (IQR)	22 (15–26)	22 (15–26)	20 (15.5–31.7)	0.98
Age at delivery (years), median (IQR)	27 (24–31)	27 (25.5–31.5)	26.5 (22.2–32.5)	0.75
SLE duration at delivery (years), median (IQR)	4 (1–9)	4 (1–9)	3.5 (0–8.2)	0.53
Preterm birth, n (%)	20 (60.6%)	10 (58.8%)	10 (62.5%)	0.82
Comorbidities, n (%)				
Hypertension	11 (33.3%)	8 (47.1%)	3 (18.8%)	0.08
Diabetes mellitus	2 (6.1%)	0 (0%)	2 (12.5%)	0.22
Chronic kidney disease[a]	11 (33.3%)	7 (41.2%)	4 (25%)	0.32
Antiphospholipid syndrome	4 (12.1%)	2 (11.8%)	2 (12.5%)	1
Autoantibody profile, n (%)				
dsDNA	24/31 (77.4%)	12/16 (75%)	12/15 (80%)	1
Ro (SS-A)	7/27 (25.9%)	5/16 (31.3%)	2/11 (18.2%)	0.66
La (SS-B)	3/25 (12%)	1/14 (7.1%)	2/11 (18.2%)	0.56
RNP	8/20 (40%)	4/12 (33.3%)	4/8 (50%)	0.64
Sm	5/18 (27.7%)	3/11 (27.3%)	2/7 (28.6%)	1
Lupus anticoagulant	8/28 (28.6%)	5/16 (31.3%)	3/12 (25%)	1
Anticardiolipin IgG	3/22 (13.6%)	1/14 (7.1%)	2/8 (25%)	0.52
Anticardiolipin IgM	1/22 (4.5%)	1/14 (7.1%)	0/8 (0%)	1
Anti-β2 glycoprotein I IgG	2/20 (10%)	2/16 (12.5%)	0/4 (0%)	1
Anti-β2 glycoprotein I IgM	1/20 (5%)	1/16 (6.3%)	0/4 (0%)	1
HCQ use prior to pregnancy, n (%)	19 (57.6%)	13 (76.5%)	6 (37.5%)	**0.02**
HCQ dose at delivery (mg/day), median (IQR)	350 (200–400)	350 (200–400)	–	
IST use during pregnancy, n (%)	15 (45.5%)	11 (64.7%)	4 (25%)	**0.04**
Azathioprine	11/15 (73.3%)	8/11 (72.7%)	3/4 (75%)	
MMF	1/15 (6.7%)	1/11 (9.1%)	0/4 (0%)	
Cyclophosphamide	1/15 (6.7%)	1/11 (9.1%)	0/4 (0%)	
MTX	1/15 (6.7%)	0/11 (0%)	1/4 (25%)	
Other	1/15 (6.7%)	1/11 (9.1%)	0/4 (0%)	
Glucocorticoid use during pregnancy, n (%)	21 (63.6%)	14 (82.4%)	7 (43.8%)	0.09
Glucocorticoid dose at delivery (mg/day), median (IQR)[**]	15 (5–20)	10 (5–18.1)	20 (15–30)	**0.04**
Aspirin use during pregnancy, n (%)	20 (60.6%)	14 (82.4%)	6 (37.5%)	**0.01**
LMWH use during pregnancy, n (%)	6 (18.2%)	5 (29.4%)	1 (6.3%)	0.17

HCQ, hydroxychloroquine; IST, immunosuppressive therapy; LMWH, low molecular weight heparin; MMF, mofetil mycophenolate; MTX, methotrexate; SLE, systemic lupus erythematosus.
[a]Including but not limited to lupus nephritis.

Table 2. Cardiovascular and pregnancy outcomes of subjects with systemic lupus erythematosus with or without hydroxychloroquine use during pregnancy

Table 2. Cardiovascular and pregnancy outcomes of subjects with systemic lupus erythematosus with or without hydroxychloroquine use during pregnancy

Variable	Total (N= 33)	HCQ use during pregnancy (n= 17)	No HCQ use during pregnancy (n= 16)	*p*-value
Prior to pregnancy, n (%)				
Abnormal EKG[a]	6/13 (46.2%)	4/10 (40%)	2/3 (66.7%)	
Abnormal TTE[b]	2/7 (28.6%)	2/6 (33.3%)	0/1 (0%)	
Elevated troponin	2/7 (28.6%)	1/5 (20%)	1/2 (50%)	
Elevated BNP	0/3 (0%)	0/2 (0%)	0/1 (0%)	
During pregnancy, n (%)				
Abnormal EKG[a]	7/15 (46.7%)	5/10 (50%)	2/5 (40%)	
Abnormal TTE[b]	9/11 (81.8%)	6/7 (85.7%)	3/4 (75%)	
Elevated troponin	3/7 (42.9%)	2/6 (33.3%)	1/1 (100%)	
Elevated BNP	1/3 (33.3%)	1/3 (33.3%)	–	
Postpartum, n (%)				
Abnormal EKG[a]	6/13 (46.2%)	4/8 (50%)	2/5 (40%)	
Abnormal TTE[b]	4/8 (50%)	3/5 60%	1/3 (33.3%)	
Elevated troponin	5/10 (50%)	4/7 (57.1%)	1/3 (33.3%)	
Elevated BNP	3/5 (60%)	3/5 (60%)	0/0 (0%)	
Adverse CV outcomes, n (%)[c]	10 (30.3%)	5 (29.4%)	5 (31.3%)	1
Heart failure	6/10 (60%)	5/5 (100%)	1/5 (20%)	
Valvular disease	1/10 (10%)	–	1/5 (20%)	
Arrhythmia	1/10 (10%)	–	1/5 (20%)	
Cor pulmonale	2/10 (20%)	–	2/5 (40%)	
Maternal complications, n (%)[d]	22 (66.7%)	11 (64.7%)	11 (68.8%)	0.80
Gestational HTN	6/22 (27.2%)	3/11 (27.27%)	3/11 (27.3%)	
Gestational DM	2/22 (9.1%)	2/11 (18.18%)	0/11 (0%)	
Peripartum infection	2/22 (9.1%)	1/11 (9.09%)	1/11 (9.1%)	
Preeclampsia/eclampsia	12/22 (54.5%)	6/11 (54.54%)	6/11 (54.5%)	
Postpartum hemorrhage	3/22 (13.6%)	1/11 (9.09%)	2/11 (18.2%)	

BNP, brain natriuretic peptide; EKG, electrocardiogram; HCQ, hydroxychloroquine; TTE, transthoracic echocardiogram.
[a]EKG abnormalities included sinus tachycardia, sinus bradycardia, atrioventricular block, irregular rate, T wave abnormalities/inversions, RBBB, prolonged QTc, electrical alternance.
[b]TTE abnormalities included reduced ejection fraction, right/left ventricular hypertrophy, valvular abnormalities, wall motion abnormalities, diastolic dysfunction, pericardial effusion.
[c]New onset adverse CV outcomes in pregnancy and/or postpartum (up to 6 months from delivery).
[d]Some patients presented more than one maternal complication.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Demographics and clinical characteristics of pregnant individuals with systemic lupus erythematosus with or without adverse CV outcomes or maternal complications.

Table 3. Demographics and clinical characteristics of pregnant individuals with systemic lupus erythematosus with or without adverse CV outcomes or maternal complications.

Variable	Adverse CV outcome (n=10)[a]	No adverse CV outcome (n=23)	*p*-value	Maternal complications (n=22)[b]	No maternal complications (n=11)	*p*-value
Age at SLE diagnosis (years), median (IQR)	22 (17–33.2)	21 (15–26)	0.28	20 (15–23)	25.5 (20.2–29.7)	0.15
Age at delivery (years), median (IQR)	27.5 (21.2–32.7)	27 (25–32)	0.65	26.5 (22–30.2)	32 (28–33)	**0.008**
Time from SLE diagnosis to delivery (years), median (IQR)	2 (0–3.7)	5 (1–13)	**0.03**	4 (1–9)	3.5 (0–11.2)	0.74
Preterm birth, n (%)	8 (80%)	12 (52.2%)	0.24	17 (77.3%)	3 (27.3%)	**0.009**
Comorbidities, n (%)						
Hypertension	1 (10%)	10 (43.5%)	0.10	8 (36.4%)	3 (27.3%)	0.70
Diabetes mellitus	2 (20%)	0 (0%)	0.08	1 (4.5%)	1 (9.1%)	1
Chronic kidney disease	1 (10%)	10 (43.5%)	0.10	9 (40.9%)	2 (18.2%)	0.25
Antiphospholipid syndrome	0 (0%)	4 (17.4%)	0.28	3 (13.6%)	1 (9.1%)	1
Autoantibody profile, n (%)						
dsDNA	7/9 (77.8%)	17/22 (77.3%)	1	20/21 (95.2%)	4/10 (40%)	**0.002**
Ro (SS-A)	4/8 (50%)	3/19 (15.8%)	0.14	6/16 (37.5%)	1/11 (9.1%)	0.18
La (SS-B)	2/7 (28.6%)	1/18 (5.6%)	0.18	2/15 (13.3%)	1/10 (10%)	1
RNP	4/8 (50%)	4/12 (33.3%)	0.64	6/12 (50%)	2/8 (25%)	0.37
Sm	2/7 (28.6%)	8/11 (72.7%)	1	4/11 (36.4%)	1/7 (14.3%)	0.59
Lupus anticoagulant	2/9 (22.2%)	6/19 (31.6%)	1	6/20 (30%)	2/8 (25%)	1
Anticardiolipin IgG	0/6 (0%)	3/16 (18.8%)	0.53	2/14 (14.3%)	1/8 (12.5%)	1
Anticardiolipin IgM	0/6 (0%)	1/16 (6.3%)	1	0/14 (0%)	1/8 (12.5%)	0.36
Anti-β2 glycoprotein I IgG	0/4 (0%)	2/16 (12.6%)	1	1/13 (7.7%)	1/7 (14.3%)	1
Anti-β2 glycoprotein I IgM	0/4 (0%)	1/16 (6.3%)	1	1/13 (7.7%)	0/7 (0%)	1
HCQ use prior to pregnancy, n (%)	5 (50%)	14 (60.9%)	0.70	12 (54.5%)	7 (63.6%)	0.71
HCQ use during pregnancy, n (%)	5 (50%)	12 (52.2%)	1	11 (50%)	6 (54.5%)	1
HCQ dose at delivery (mg/day), median (IQR)	350 (225–400)	350 (200–400)	0.87	400 (200–400)	300 (225–375)	0.54
IST use during pregnancy, n (%)	7 (70%)	8 (34.8%)	0.13	14 (63.6%)	1 (9.1%)	**0.001**
Glucocorticoid use during pregnancy, n (%)	8 (80%)	13 (56.5%)	0.67	14 (63.6%)	4 (36.4%)	0.06
Glucocorticoid dose at delivery (mg/day), median (IQR)	20 (8.1–52.5)	10 (5–17.5)	0.05	17.5 (5–20)	7.5 (3.1–13.7)	0.08
Aspirin use during pregnancy, n (%)	7 (70%)	13 (56.5%)	0.70	13 (59.1%)	7 (63.6%)	1
LMWH use during pregnancy, n (%)	1 (10%)	5 (21.7%)	0.64	3 (13.6%)	3 (27.3%)	0.39

CV, cardiovascular; HCQ, hydroxychloroquine; IST, immunosuppressive therapy; LMWH, low molecular weight heparin; SLE systemic lupus erythematosus.
[a]Adverse CV outcomes during pregnancy and postpartum included HF (n=6), valvular disease (n=1), arrhythmia (n=1), Cor pulmonale (n=2)
[b]Maternal complications included preeclampsia (n=11), eclampsia (n=1), peripartum infections (n=2), postpartum hemorrhage (n=3), gestational HTN (n=6), and gestational DM (n=2). Some subjects presented more than one maternal complication.

Results: Of 131 identified cases, we included 33 pregnant subjects with SLE. Median (IQR) age at delivery was 27 (24–31) years. Seventeen (51%) of them were taking HCQ during pregnancy. Those on HCQ during pregnancy were more likely to have received IST (64% vs 25%, p=0.04) and aspirin (82% vs 37%, p=0.01) during pregnancy, and had lower median glucocorticoid (GC) dose at delivery (10 vs 20 mg/day, p=0.04). Demographic and clinical characteristics are shown in **Table 1**. Ten (30%) subjects developed new onset CV outcomes during pregnancy and/or the postpartum period, whereas 23 (70%) didn't have cardiac complications during the follow-up period. Half (n=5) of the subjects with adverse CV outcomes received HCQ during pregnancy (**Table 2**). All five adverse CV outcomes in the HCQ group were HF, one of whom had peripartum cardiomyopathy with recovery of myocardial function in the postpartum period without HCQ discontinuation. Twenty-two (66.7%) patients developed maternal complications, of whom 50% (n=11) were on HCQ during pregnancy. The use of HCQ was similar between individuals with or without adverse CV outcomes and maternal complications (**Table 3**). Those with adverse CV outcomes had shorter SLE duration (2 vs 5 years, p=0.03). Individuals with maternal complications were younger at delivery (26 vs 32 years, p=0.008), had higher rates of preterm birth (77% vs 27%, p=0.009), positivity of dsDNA antibody (95% vs 40%, p=0.002), and IST use (63% vs 9%, p=0.001).

Conclusion: In this study, there was no difference in adverse CV and maternal outcomes with or without the use of HCQ among pregnant individuals with SLE. Those with adverse outcomes had shorter SLE duration, were younger, and had more exposure to IST, suggesting higher SLE disease activity.

Disclosure: M. Gonzalez-Treviño: None; **A. Ciosek**: None; **G. Maldonado**: None; **C. Deffendall**: None; **T. Ruiz**: None; **T. Frech**: None; **R. Dhital**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2414

Autoantibody Clusters and SIGLEC1 are Predictive of Systemic Lupus Erythematosus Development

Alice Horisberger[1], Emily Oakes[2], Eilish Dillon[3], Ifeoluwakiisi Adejoorin[2], Julia Caldropoli[3], Kathryne Marks[2], Takanori Sasaki[3], Farbod Moghaddam[4], Paul Sciore[5], Marvin J. Fritzler[6], Deepak Rao[2], **May Choi**[7] and Karen H. Costenbader[8], [1]Lausanne University Hospital, University of Lausanne, Laussane, Switzerland, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, [4]University of Calgary, Calgary, Canada, [5]MitogenDx, Calgary, AB, Canada, [6]MitognDx, Calgary, AB, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

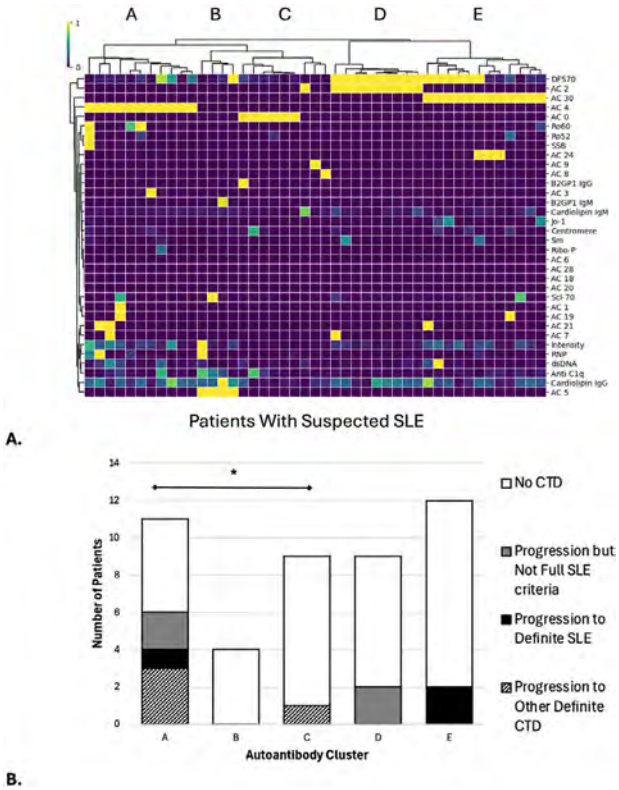


Figure 1. A) Five autoantibody clusters identified based on baseline samples of 45 samples of suspected SLE (left to right): Cluster A (n=11) AC-4 nuclear speckled pattern with the greatest autoantibody reactivity including anti-RNP, anti-dsDNA, and anti-Ro60/SSA, Cluster B (n=4) nuclear large speckled pattern, Cluster C (n=9) mostly no autoantibodies, Cluster D (n=9) monospecific anti-DFS70 antibody with dense fine speckled (AC2) pattern, and Cluster E (n=12) nuclear speckled with mitotic plate staining (AC-30). The ANA patterns were classified according to the most recently updated International Consensus on ANA Patterns recommendations and performed on Indirect immunofluorescence assay (IFA) using HEp-2 substrate (NovaLite,Werfen, San Diego, USA). In accord with the manufacturers' directions, a positive test was defined as a titer of >=1:80. IFA results (titres and patterns) were initially read by an automated digital IFA microscope (NovaView, Werfen) and then validated by technologists with >15 years of experience. SLE-related antibodies and anti-DFS70 antibodies were performed on the Aptiva® Connective Tissue Disease Essential kit, a fully automated multi-analyte system using particle-based multi-analyte technology (Werfen, San Diego, USA). IgG and IgM anti-cardiolipin and IgG and IgM anti–β2-glycoprotein-1 (β2GP1) and anti-C1q antibodies were performed using an ELISA (Werfen, San Diego, USA). B) Cluster A (AC-4 nuclear speckled pattern and high autoantibody reactivity) had the largest number of patients with disease progression +/- definite SLE or other CTD at follow-up. *denotes a significant difference in proportion of patients who had disease progression +/- definite SLE or other CTD at follow-up (Cluster A vs. C, diff. 43.43%, 95%CI 0.08%-0.79%).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Up to a third of those with suspected SLE progress to definite SLE; however, reliable predictive markers for disease progression remain unknown. Previously, we developed a Lupus Lymphocyte Activation Score (LLAS) based on key cell subsets (transitional B cells, age-associated B cells, plasmablasts, Tph cells, and Tfh cells) observed in those with or at risk of developing SLE (Horisberger, 2024). Here we examined the relationship between autoantibody profiles, including anti-dense fine speckled 70 (DFS70) antibodies, as well as sialic acid binding Ig like lectin 1 (SIGLEC1, a surrogate marker for type I interferon), LLAS, and SLE development among those with suspected disease.

Methods: Blood samples were collected from 45 patients with new onset (< 3 yrs) suspected SLE at Brigham and Women's Hospital Lupus Center. At baseline, subjects did not meet SLE classification criteria and received prednisone < 10mg/day and no immunosuppressants. Using baseline samples, SIGLEC1 was measured by flow cytometry on a subset of patients (n=20) and a comprehensive autoantibody profile on all patients: ANA by indirect immunofluorescence assay on HEp-2 cells and patterns classified according to the International Consensus on ANA Pattern anti-cell (AC) nomenclature, SLE-related autoantibodies, including anti-DFS70 by a fully automated multi-analyte system using particle-based multi-analyte technology, and anti-C1q and anti-phospholipid antibodies by ELISA. To examine patterns of autoantibodies, we used hierarchical clustering and investigated their relationships with disease progression, LLAS, and SIGLEC1 levels.

Results: Of 45 patients, 36 had multiple visits with a mean follow-up of 13.6 months. In follow-up, 3 patients were diagnosed with SLE and met 2012 SLICC or 2019 EULAR/ACR criteria; 4 were diagnosed with or suspected of new dermatomyositis or Sjögren's syndrome. We identified 5 clusters of suspected SLE patients based on autoantibody profiles (Fig. 1A, B). Cluster A (AC-4 nuclear speckled with multiple autoantibody reactivity including anti-RNP, -dsDNA, -anti-Ro60/SSA) was more likely progress or develop a CTD including SLE (OR 1.94, 95%CI 0.42-3.46) than others (Fig. 2A), particularly compared to Cluster C (no autoantibodies) (diff. 43.43%, 95%CI 0.08%-0.79%). Cluster A also had significantly

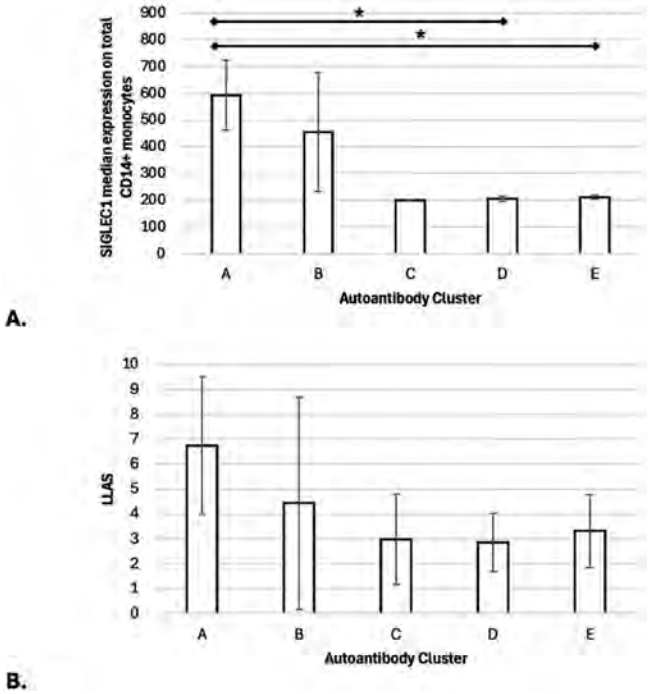


Figure 2. Autoantibody clusters of suspected SLE patients and their A) median SIGLEC1 expression on total CD14+ monocytes (n=20 patients selected sequentially based on enrolment date). *Cluster A (n=5) had higher median SIGLEC1 expression compared to Cluster D (n=5) and Cluster E (n=6). Of note, there are no error bars for cluster C (n=1) as there was only one patient with SIGLEC1 level. Cluster B had 3 patients with SIGLEC1 measurements. B) Lupus Lymphocyte Activation Score (LLAS) (n=45) was not statistically different among different autoantibody clusters.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

higher median SIGLEC1 expression on total CD14+ monocytes vs. Cluster D (monospecific antiDFS70 with AC2, diff. 388.00, 95%CI 86.78-689.22) and Cluster E (AC30, diff. 382.97, 95%CI 116.30-649.64). There was no difference in LLAS by autoantibody cluster (Fig. 2B).

Conclusion: Autoantibody profile characterized by nuclear speckled with multiple autoantibody reactivity, including anti-RNP, -dsDNA, and -Ro60/SSA, was predictive of CTD development. Although based on a smaller sample size, this cluster also had higher baseline SIGLEC1 vs. those with monospecific DFS70 antibodies or no autoantibodies. Further analysis will assess whether LLAS, SIGLEC1, and autoantibodies are complementary, and when combined, could enhance the prediction of SLE development.

Disclosure: A. Horisberger: None; **E. Oakes**: None; **E. Dillon**: None; **I. Adejoorin**: None; **J. Caldropoli**: None; **K. Marks**: None; **T. Sasaki**: None; **F. Moghaddam**: None; **P. Sciore**: None; **M. Fritzler**: Mitogen Diagnostics Corp., 8, 9, 12, Medical Director, Werfen, 1, 2, 6; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2; **M. Choi**: AstraZeneca, 2, 5, 6, Celltrion, 2, MitogenDx, 2, Organon, 6, Werfen, 2; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 2415

Evaluating the Readability and Comprehension of Patient Education Materials for Systemic Lupus Erythematosus (SLE) Available Online

Nagoor Shaik, Ugochukwu Nweke and **Meenakshi Jolly**, Rush University, Chicago

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic multisystemic autoimmune disease that had multidimensional adverse effects on patients lives, and preferentially inflicts young women, specially of color. Patient education materials (PEMs) help patients understand their condition and manage it better. However, these materials frequently exceed the reading ability of the general population, posing challenges for individuals with limited health literacy. The National Institutes of Health (NIH) and the American Medical Association (AMA) recommend that PEMs be written at or below a 6th-grade reading level.

We aimed to evaluate the readability and comprehension of SLE-related PEMs available online from both nonprofit and for-profit organizations.

Methods: We analyzed the SLE PEMs from four nonprofit organizations (American College of Rheumatology-ACR, Lupus Foundation of America-LFA, Lupus Research Alliance-LRA, and Lupus Society of Illinois-LSI) and three for-profit companies (Aurinia, AstraZeneca, and GlaxoSmithKline). Readability and comprehension scores were calculated using six standard tools, and group-level comparisons were performed using one-way ANOVA followed by Tukey's post-hoc analysis. A p-value of ≤0.05 was considered significant.

Results: The average Flesch–Kincaid Grade Level and Flesch Reading Ease scores across all patient education materials (PEMs) were 10.05 ± 0.7 and 52.68 ± 4.1, respectively. On average, materials from nonprofit organizations had a Flesch–Kincaid Grade Level of 10.3 ± 0.8 and a Reading Ease score of 51.1 ± 4.9, whereas for-profit organizations had a slightly lower Grade Level of 9.9 ± 0.4 and a higher Ease score of 54.3 ± 2.6. These differences were not statistically significant

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Readability and Comprehension of SLE Patient Education Materials

Readability Index	ACR (NPO)	LFA (NPO)	LRA (NPO)	LSI (NPO)	All NPO	Aurinia (FPO)	AstraZeneca (FPO)	GSK (FPO)	All FPO	p-value
Flesch–Kincaid Grade Level	10.6 ± 0.5	9.1 ± 0.4	10.5 ± 0.6	11.2 ± 0.4	10.3 ± 0.6	9.5 ± 0.4	9.9 ± 0.3	9.8 ± 0.2	9.9 ± 0.4	0.514
Flesch–Kincaid Ease Score	49.8 ± 2.2	58.3 ± 3.1	50.5 ± 2.6	45.6 ± 2.0	51.1 ± 4.9	55.7 ± 3.0	53.1 ± 2.4	54.2 ± 2.1	54.3 ± 2.6	0.198
Gunning Fog Index	12.0 ± 0.6	10.8 ± 0.5	11.7 ± 0.7	12.5 ± 0.5	11.7 ± 0.8	11.3 ± 0.7	12.2 ± 0.6	12.0 ± 0.5	11.8 ± 0.6	0.138
SMOG Index	10.8 ± 0.4	9.6 ± 0.3	10.5 ± 0.5	11.0 ± 0.4	10.5 ± 0.6	10.2 ± 0.5	10.7 ± 0.4	10.6 ± 0.3	10.5 ± 0.4	0.223
Coleman–Liau Index	12.5 ± 0.5	11.0 ± 0.6	12.1 ± 0.4	12.8 ± 0.7	12.1 ± 0.7	11.7 ± 0.6	12.0 ± 0.5	11.9 ± 0.4	11.9 ± 0.5	0.310
Automated Readability Index	10.2 ± 0.3	9.0 ± 0.4	9.8 ± 0.5	10.5 ± 0.6	9.9 ± 0.7	9.3 ± 0.5	9.8 ± 0.4	9.7 ± 0.3	9.6 ± 0.4	0.445

This table presents the mean readability scores (± SD) for materials from nonprofit and for-profit organizations, calculated using six standard readability indices. Reported p-values represent the results of one-way ANOVA tests comparing average scores across all NPO and FPO organizations for each index.

Abbreviations: FKGL - Flesch–Kincaid Grade Level, FRES – Flesch Reading Ease Score, GFI – Gunning Fog Index, SMOG – Simple Measure of Gobbledygook, CLI – Coleman-Liau Index, ARI – Automated Readability Index, NPO-Non Profit Organization, FPO-For profit Organization, SD – Standard Deviation

(p = 0.51 and 0.20respectively). However significant within-group differences were observed. Among nonprofit organizations, PEMs from the Lupus Foundation of America (LFA) had the best reading and comprehension metrics: (Flesch–Kincaid Grade Level of 9.1 ± 0.4 and a Reading Ease score of 58.3 ± 3.1), as compared to ACR (10.6 ± 0.5, 49.8 ± 2.2), LRA (10.5 ± 0.6, 50.5 ± 2.6), and LSI (11.2 ± 0.4, 45.6 ± 2.0) (p < 0.01). Among for-profit organizations, reading and comprehension levels for PEMs from Aurinia were significantly better in reading and comprehension (Flesch Kincaid Grade level 9.5 ± 0.4 and Reading Ease score of 55.7 ± 3.0), than AstraZeneca (9.9 ± 0.3, 53.1 ± 2.4) and GSK (9.8 ± 0.2, 54.2 ± 2.1) (both p < 0.001).

Conclusion: Most SLE patient education materials online (from both nonprofit and for-profit organizations) are written at or above 10th grade level. These findings highlight the urgent need to improve the reading and comprehension of patient education resources to better assist individuals in understanding and managing their health.

Disclosure: N. Shaik: None; **U. Nweke**: None; **M. Jolly**: LRA, 1, Rush University, 9, 10.

Abstract Number: 2416

Direct and Indirect Costs Associated with Damage Accrual: Results from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort

Megan Barber[1], John Hanly[2], Murray Urowitz[3], Ian Bruce[4], Yvan St-Pierre[5], Caroline Gordon[6], Sang-Cheol Bae[7], Juanita Romero-Diaz[8], Francisco Sanchez-Guerrero[9], Sasha Bernatsky[10], Daniel Wallace[11], David A. Isenberg[12], Anisur Rahman[12], Joan Merrill[13], Paul Fortin[14], Dafna D. Gladman[15], Michelle Petri[16], Ellen Ginzler[17], Mary Anne Dooley[18], Rosalind Ramsey-Goldman[19], Susan Manzi[20], Andreas Jönsen[21], Graciela Alarcón[22], Ronald van Vollenhoven[23], Cynthia Aranow[24], Meghan mackay[25], Guillermo Ruiz-Irastorza[26], S. Sam Lim[27], Murat Inan[28], Kenneth Kalunian[29], Soren Jacobsen[30], Christine Peschken[8], Diane Kamen[31], Anca Askanase[32] and Ann Clarke[1], [1]Division of Rheumatology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [2]Dalhousie University, Halifax, NS, Canada, Halifax, NS, Canada, [3]University of Toronto, Toronto, ON, Canada, [4]Centre for Public Health, Faculty of Medicine, Health and Life Sciences, Queen's University Belfast, Belfast, United Kingdom, [5]Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [6]Department of Inflammation and Ageing, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom, [7]Hanyang University Medical Center, Seoul, South Korea, [8]University of Manitoba, Winnipeg, MB, Canada, [9]University Health Network/Sinai Health system, Toronto, ON, Canada, [10]Research Institute of the McGill University Health Centre, Montreal, QC, Canada, [11]Cedars Sinai Medical Center, Studio City, CA, [12]University College London, London, United Kingdom, [13]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [14]Centre ARThrite - CHU de Québec - Universitä Laval, Quebec, QC, Canada, [15]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[16]Johns Hopkins University School of Medicine, Timonium, MD, [17]SUNY Downstate Health Sciences University, New York, NY, [18]UNC physician network, Chapel Hill, NC, [19]Northwestern University Feinberg School of Medicine, Chicago, IL, [20]Lupus Center of Excellence, Autoimmunity Institute, Allegheny Health Network, Pittsburgh, PA, [21]Department of Clinical Sciences, Lund University, Lund, Sweden, [22]The University of Alabama at Birmingham, Oakland, CA, [23]Department of Rheumatology, Amsterdam University Medical Centre, Amsterdam, Netherlands, [24]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [25]Feinstein Institutes for Medical Research, Manhasset, NY, [26]Biobizkaia Health Research Institute, Barakaldo, Spain, [27]Emory University School of Medicine, Atlanta, GA, [28]Istanbul University, Istanbul, Turkey, [29]UC San Diego, La Jolla, CA, [30]Rigshospitalet, Copenhagen, Denmark, [31]Medical University of South Carolina, Johns Island, SC, [32]Columbia University Medical Center, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: We reported partial direct healthcare costs associated with damage accrual in the SLICC Inception Cohort (Barber M. Arthritis Care Res 2020;72:1800). We have supplemented this data by querying a cohort subset on all healthcare use and lost time in paid/unpaid labour and now provide complete direct and indirect costs (DC, IDC) for the full cohort, stratified by damage.

Methods: Between 1999 and 2011, SLE patients from 31 centres in 10 countries were enrolled in the SLICC Inception Cohort within 15 months of diagnosis. Damage (SLICC/ACR Damage Index [SDI]) and limited healthcare use (hospitalizations, medications, and dialysis) were collected annually to July 2022. Starting in 2015, 18 sites collected supplemental economic data annually (physicians, non-physician healthcare professionals, emergency room, laboratory tests, radiological/other procedures, outpatient surgeries, help obtaining medical care, and lost time in paid/unpaid labour).

DC were calculated by multiplying each health resource by its corresponding 2024 Canadian unit cost. Total IDC included: 1) absenteeism (time lost from paid labour because of illness), 2) presenteeism (degree of patient self-reported productivity impairment in paid/unpaid labour, based on a visual analogue scale), and 3) opportunity costs (additional time patients would be working in paid/unpaid labour if not ill). Opportunity costs were calculated as the difference between time patients reported working versus that worked by an age, gender, and geographic-matched general population in paid/unpaid labour. IDC from paid/unpaid labour were valued using age-and-gender-specific wages from Statistics Canada. Multiple imputation was used to predict missing costs for patients in the full cohort who provided only limited economic data for all observations.

At each assessment, patients were assigned to one of six damage states (SDI = 0, 1, 2, 3, 4, >= 5) and annual costs, both unimputed and including imputations, were stratified by SDI. Means and 95% CIs were compared.

Table 1. Participant Characteristics

Characteristics	Full Cohort (n=1694)	Cohort Subset (n=766)
Baseline		
Female, %	88.8	89.7
White race and ethnicity, %	48.9	41.4
Age at diagnosis (years), mean	34.8	33.0
Disease duration (years), mean	0.5	0.4
Follow-up (years), mean (SD)	10.5 (5.3)	N/A
Introduction of Supplemental Economic Questionnaire		
Disease duration (years), mean, range	N/A	10.9 (3.9-10.5)
Duration of supplemental economic data (years), mean (SD)	N/A	3.5 (1.9)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Annual complete direct, indirect, and total costs (in 2024 Canadian dollars) for the cohort subset providing complete cost data, stratified by SDI (n = 2414 observations). Values are means.

SDI	0	1	2	3	4	≥5
Patients, n	369	187	142	82	47	48
Observations, n (%)	1098 (45.5)	502 (20.8)	351 (14.5)	213 (8.8)	126 (5.2)	124 (5.1)
Direct Costs	**5699**	**6018**	**6875**	**15071**	**13496**	**31159**
Hospital stays	882	1161	1311	1827	2346	4697
Medications	2148	1967	2611	2791	2786	2206
Physicians	966	1056	1016	1455	1680	1739
Tests/Procedures	644	841	974	914	807	1458
Dialysis	0	0	0	6625	3972	19452
Other*	1059	993	964	1458	1925	1606
Indirect Costs	**26553**	**40836**	**41485**	**47536**	**55885**	**54980**
Paid labour	**5901**	**10627**	**12740**	**18437**	**23133**	**22443**
Absenteeism	1312	1295	1287	1938	2063	1922
Presenteeism	6576	6951	7782	5195	5567	4886
Opportunity	-1988**	2381	3671	11304	15502	15635
Unpaid labour	**20652**	**30208**	**28745**	**29099**	**32752**	**32537**
Presenteeism	10868	11038	11372	12989	9932	11404
Opportunity	9784	19170	17373	16110	22820	21133
Total Costs	**32252**	**46854**	**48360**	**62606**	**69381**	**86138**

*Other includes non-physician healthcare professionals, emergency room visits, outpatient surgeries, and help obtaining medical care
**Opportunity costs for paid labour for patients with an SDI = 0 are negative because these patients reported working more than the matched general population.

Figure 1. Annual imputed complete direct, indirect, and total costs (in 2024 Canadian dollars) for the full cohort, stratified by SDI (n = 15,106 observations)

Results: 1694 patients (88.8% female, 48.9% White, mean age at diagnosis 34.6 years) were followed a mean of 10.5 years. Of these 1694 patients, 766 (89.7% female, 41.4% White, mean age at diagnosis 33.0 years) completed the supplemental economic questionnaire **(Table 1)**. Their mean disease duration at the time of this questionnaire was 10.9 years and this subset provided economic data a mean of 3.5 years.

Among the subset completing the supplemental questionnaire, on average, IDC, primarily from unpaid labour, accounted for 81.2% of total costs **(Table 2)**. For the full cohort, annual DC and IDC increased with increasing SDI (SDI = 0: total costs $35,417 [95%CI $32,563, $38,271]; SDI >= 5: total costs $95,149 [95%CI $86,178, $104,119]) **(Figure 1)**.

Conclusion: Patients with the highest versus the lowest SDI incurred complete DC that were 6.0-fold and IDC 2.1-fold higher. Even patients with no or minimal damage still experienced considerable IDC. IDC exceeded DC, on average, by

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

4.6-fold. Novel/emerging biologics, which potentially attenuate damage accrual, may be associated with substantial cost savings, particularly if IDC, which are a considerable portion of total costs, are incorporated in the economic analysis.

Disclosure: M. Barber: AstraZeneca, 1, GlaxoSmithKlein(GSK), 1; **J. Hanly**: None; **M. Urowitz**: AstraZeneca, 6, GSK, 2, Merck/MSD, 2; **I. Bruce**: AstraZeneca, 2, Eli Lilly, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Merck/MSD, 2, Novartis, 5, Otsuka, 5, UCB, 2; **Y. St-Pierre**: None; **C. Gordon**: Alumis, 2, Amgen, 2, AstraZeneca, 2, Sanofi, 2, UCB, 2; **S. Bae**: None; **J. Romero-Diaz**: None; **F. Sanchez-Guerrero**: None; **S. Bernatsky**: None; **D. Wallace**: PPD, 2; **D. A. Isenberg**: None; **A. Rahman**: None; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **P. Fortin**: AbbVie/Abbott, 1, AstraZeneca, 1, Moderna, 1, Roche, 1; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **E. Ginzler**: None; **M. Dooley**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **S. Manzi**: AstraZeneca, 2, CAQH, 1, Cartesian, 1, 2, Exagen Diagnostics, Inc, 2, 9, 10, GSK, 2, Lily, 2, Lupus Foundation of America, 4, UCB Advisory Board, 2; **A. Jönsen**: None; **G. Alarcón**: None; **R. van Vollenhoven**: AbbVie, 2, 6, Alfasigma, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 5, 6, Galapagos, 2, 5, 6, GSK, 2, 6, Janssen, 2, 6, MSD, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, 6, Roche, 5, Sanofi, 5, UCB, 2, 5, 6; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **M. mackay**: None; **G. Ruiz-Irastorza**: None; **S. Lim**: Accordant, 2, AstraZeneca, 2, Biogen, 5, BMS, 5, Genentech, 2, Gilead, 5, GSK, 2, Novartis, 5, UCB, 5; **M. Inan**: Amgen, 2, UCB, 2; **K. Kalunian**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Genentech, 1, GlaxoSmithKlein(GSK), 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, Roche, 1; **S. Jacobsen**: None; **C. Peschken**: None; **D. Kamen**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **A. Clarke**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 5, Novartis, 2, Roche, 2.

Abstract Number: 2417

Anti-dense Fine Speckled 70 Antibodies in Undefined Disease, Systemic Autoimmune Rheumatic Diseases and Controls

Rammohan Mylavarapu[1], **Meghna Gavali**[2], Bansi Kashyap Parijeya[3], Kaushik Puranam[4] and Liza rajasekhar[5], [1]NIZAMS INSTITUTE OF MEDICAL SCIENCES, Hyderabad, Telangana, India, [2]nizam's institute of medical sciences ,Hyderabad, Hyderabad, Telangana, India, [3]Synergy superspeciality hospital, Rajkot, Gujarat, India, [4]Nizams Institute Of Medical Sciences , Hyderabad, hyderabad, Telangana, India, [5]Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic autoimmune rheumatic diseases (SARD) are a heterogeneous group of disorders marked by the presence of antinuclear antibodies (ANA), commonly detected by HEp-2 cell-based indirect immunofluorescence (IIF). The dense fine speckled (DFS) antinuclear antibody (ANA) pattern, caused by anti-DFS70 antibodies, is often misunderstood due to reported low association with SARD and presence in healthy individuals. Some studies suggest presence of isolated anti-DFS70 antibodies exclude SARD. Given the limited data from the Indian subcontinent and the large volume of ANA IIF tested, this study aims to estimate the prevalence and clinical associations of anti-DFS70 antibodies in sera tested for ANA without well defined disease, in nonrheumatic disease controls and in SARD patients.

Methods: Sera from SARD patients, those without a well-defined disease, and from non-rheumatic disease controls displaying a DFS IIF pattern, were further investigated using an anti-DFS70 ELISA and Line Immunoassay (LIA). ANA IIF was performed utilising HEp-20-10 based IIF.

Results: The DFS IIF pattern was observed in 82 out of 32,285 (0.25%) sera from referrals for undefined disease, 2 out of 350 (0.57%) in SARD sera and 1 out of 250 (0.4%) non-rheumatic disease controls. ELISA anti-DFS70 was positive in 74 of 82 (90%) undefined disease sera, 54 of 350 (15.4%) SARD sera and in 1 of 1 (100%) non-rheumatic disease control sera. Anti DFS70 LIA was positive in 74 of 82 (90%) undefined disease sera, 20 of 350 SARD sera(5.7%) and in 1 of 1 (100%) non-rheumatic disease control sera. There was almost perfect agreement (kappa value = 0.861) between anti-DFS70 ELISA and LIA in the routine ANA referral group. In SARD,anti-DFS70 ELISA positivity was significantly associated with higher prevalence of SLE (87% vs. 67.6%; p = 0.0033) and lower prevalence of RA (1.9% vs. 15.2%; p = 0.0040). Mean DFS ELISA titres in SLE patients with LIA positivity (n=14) were higher (3.38±1.61) compared to those negative for anti-DFS70 antibodies in LIA (1.55±0.63).SLE patients with positive anti-dsdna were significantly more likely to be anti-DFS70 ELISA positive (p=0.0001).SLE patients who tested positive for anti-DFS70 by ELISA had significantly higher disease activity, with a median SLE Disease Activity Index (SLEDAI) score of 16 (range: 10–23), compared to 10 (range: 5–15) in ELISA-negative patients (p = 0.01)Renal involvement significantly correlated with anti-DFS70 positivity in SLE patients; p=0.014.

Table 1: Comparison of DFS IIF, Anti-DFS70 ELISA, LIA, and Monospecific Results Across Study Groups

Group	Total Patients	DFS IIF Positive (n, %)	ELISA Positive (n, %)	LIA Positive (n, %)	Monospecific Anti-DFS70 (n, %)
SARD Patients	350	2 (0.57%)	54 (15.4%)	20 (5.7%)	3 (15% of LIA^{+}) (All in UCTD)
Routine ANA Referrals	32,285	82 (0.25%)	74 (90.2% of DFS IIF^{+})	74 (90.2% of DFS IIF^{+})	55 (74.3% of LIA^{+})
Controls	250	1 (0.4%)	1 (100% of DFS IIF^{+})	1 (100% of DFS IIF^{+})	1 (100% of LIA^{+})

Table 2: Demographic and Clinical Characteristics – (SARD Group)

Parameter	***Value (n=350)***
Mean Age (years)	29.7 ± 11.8
Female Sex	313/350 (89.4%)
Diagnosis Distribution	
- Systemic Lupus Erythematosus (SLE)	247 (70.5%)
- Rheumatoid Arthritis (RA)	46 (13.1%)
- Undifferentiated CTD (UCTD)	35 (10%)
- Systemic Sclerosis (SSc)	15 (4.3%)
- Sjögren's Syndrome	3 (0.9%)
- Antiphospholipid Syndrome (APS)	1 (0.3%)
- Anti-Synthetase Syndrome (ASS)	1 (0.3%)
- Mixed CTD (MCTD)	1 (0.3%)
- Myositis	1 (0.3%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3: Distribution of anti-DFS70 positivity by ELISA and LIA in various SARD (n=54)

Diagnosis	Anti-DFS70 ELISA positive(n)	Anti-DFS70 LIA positive(n)	Monospecific anti-DFS 70 antibodies in LIA -n(%)
SLE	47	14	0
RA	1	1	0
UCTD	4	4	3 (75)
SSc	1	1	0
APS	1	0	0

Monospecific anti-DFS70 antibodies in LIA were observed only in UCTD (3/4;75%), and none of the other SARD patients

Conclusion: When the DFS-IIF pattern is seen in sera with monospecific anti-DFS antibodies (as tested in line immunoassay), SARD is less likely. Significant concordance between ELISA and Line immunoassay is noted for detecting anti-DFS70 antibodies. Anti-DFS70 antibodies, when present in SARD , coexist with other disease-associated antibodies and hence do not produce DFS IIF pattern. In SARD patients, anti-DFS70 ELISA positivity was significantly associated with SLE, higher disease activity (SLEDAI), anti-dsdna positivity, and renal involvement, while being inversely associated with RA.

Disclosure: R. Mylavarapu: None; **M. Gavali**: None; **B. Kashyap Parijeya**: None; **K. Puranam**: None; **L. rajasekhar**: None.

Abstract Number: 2418

ORF1p Expression Correlates with STING Activation and IFN Signatures in SLE Nonlesional Skin

Mehrnaz Gharaee-Kermani[1], Svenja Henning[2], John LaCava[3], Tomas Mustelin[4] and J. Michelle Kahlenberg[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Groningen, Groningen, Groningen, Netherlands, [3]Rockefeller University, New York City, NY, NJ, [4]University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Type I interferons (IFNs) are elevated in the skin and blood of patients with systemic (SLE) and cutaneous (CLE) lupus erythematosus. Upregulation of type I IFNs in non-lesional keratinocytes promotes myeloid activation and cell death in response to ultraviolet light, an important trigger for skin and systemic disease flares. The reasons for chronic type I IFN upregulation in non-lesional SLE remain under-explored but are important targets for disease flare prevention. Here, we examined upregulation of the protein ORF1p, which occurs with de-repression of LINE-1 elements, in conjunction with markers of STING activation and type I IFN signatures in non-lesional SLE skin biopsies.

Methods: Non-lesional skin biopsies were obtained from the upper thigh of 40 patients with SLE and were examined via bulk RNA sequencing and immunohistochemistry (IHC) for ORF1p and phosphorylated (activated) STING. IHC was scored for number of positively staining cells across the basal epidermis within10 field of view at 20x magnification. Expression of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ORF1p was correlated with clinical data of patients. Interferon scores using 138 epidermal specific genes regulated by type I IFN exposure was calculated as previously reported.

Results: Healthy control skin biopsies had very low levels of ORF1p expression with no subject having >1 positive cell per field at 20 X magnification (mean 0.395, SD 0.258). SLE patients, on the other hand, exhibited significantly higher expression of ORF1p (mean 16.018, SD18.510). There was a strong correlation between staining for ORF1p and phospho-STING in the basal epidermis (R^2=0.871, p< 0.0001). Type I IFN scores were significantly increased in SLE patients who had an average of $\geq$10 cells stained for ORF1p per field (mean of < 10 cells -12.070, SD 76.931; mean of $\geq$ 10 cells 151.080, SD 158.163; p=0.020). Evaluation of clinical data found a correlation between ORF1p epidermal staining and points on the EULAR/ACR classification criteria for SLE (R=0.55, p=0.002). No differences were noted in ORF1p positivity based on use of hydroxychloroquine, history of skin disease, or CLASI activity.

Conclusion: ORF1p staining is increased in non-lesional skin of SLE patients and correlates strongly with the activation of STING in the epidermis and the presence of an interferon signature in the skin. SLE patients with the most widespread disease exhibit the highest ORF1p expression. Further research is needed to determine if ORF1p upregulation (and the preceding de-repression of LINE1 elements) is a cause or consequence of type I IFN signaling in SLE skin. This understanding will lead to novel therapies to treat type I IFN-driven disease.

Disclosure: M. Gharaee-Kermani: None; **S. Henning**: None; **J. LaCava**: None; **T. Mustelin**: Bristol-Myers Squibb(BMS), 2; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5.

Abstract Number: 2419

Dried Blood Spots for Remote ANA and Autoantibody Screening

Miriam Li[1], Paul Sciore[2], Marvin J. Fritzler[3], Ashley Clarke[1], Wrechelle Ocampo[1], katherine Buhler[1], Jeremiah Seni[4], Lynden Crowshoe[1], Dianne Mosher[1] and May Choi[1], [1]University of Calgary, Calgary, AB, Canada, [2]MitogenDx, Calgary, AB, Canada, [3]MitognDx, Calgary, AB, Canada, [4]Catholic University of Health and Allied Sciences, Mwanza, Tanzania

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Antinuclear antibody (ANA) and SLE-related autoantibody testing are integral parts of SLE screening, diagnosis, and monitoring. However, these tests rely on access to phlebotomy for blood sample collection and a lab that can receive and perform these assays in a timely manner. This is a challenge for patients living in remote areas, including Indigenous populations and African countries, where SLE is likely underdiagnosed. Here, we investigated the performance of ANA and SLE-related autoantibody tests on dried blood spots (DBS) as a more resource-efficient and minimally invasive alternative for patients.

Methods: Patients with SLE meeting the 2012 SLICC or 2019 ACR/EULAR criteria or rheumatoid arthritis (RA) meeting the 2010 ACR/EULAR criteria as disease controls were enrolled from a single tertiary care centre. Serum was collected by both venipuncture and DBS at the same visit. DBS cards were subsequently stored under four conditions: 1) 25°C (room temperature) for one week, 2) 25°C for 4 weeks, 3) 4°C for one week, and 4) 4°C for 4 weeks. For each condition, ANA was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

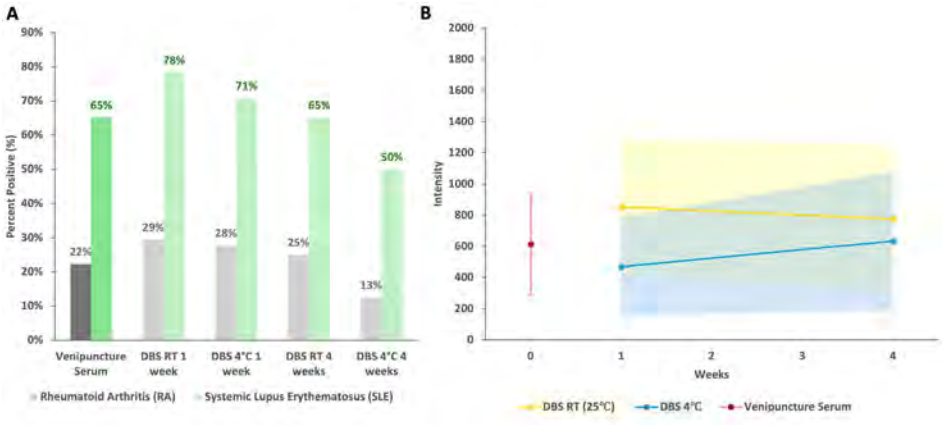


Figure 1. Venipuncture vs. DBS for A) ANA positivity (>=1:80) using indirect immunofluorescence on HEp2 substrate, stratified based on diagnosis (RA vs. SLE). There was no significant difference between venipuncture vs. DBS for all storage conditions; B) ANA titre over time (31 patients for 25°C, 30 patients for 4°C) represented by intensity level measured by an automated digital IFA microscope (NovaView, Werfen). Mean titres ± 95% confidence interval (CI) for 25°C were not significantly different after 1 week (853.68 ± 438.80) vs 4 weeks (776.00 ± 466.01) (McNemar paired chi-square test, p=0.554). Similarly, there were no significant differences for 4°C after 1 week (469.67 ± 315.6) vs. 4 weeks (634.27 ± 442.57) (p=0.321).

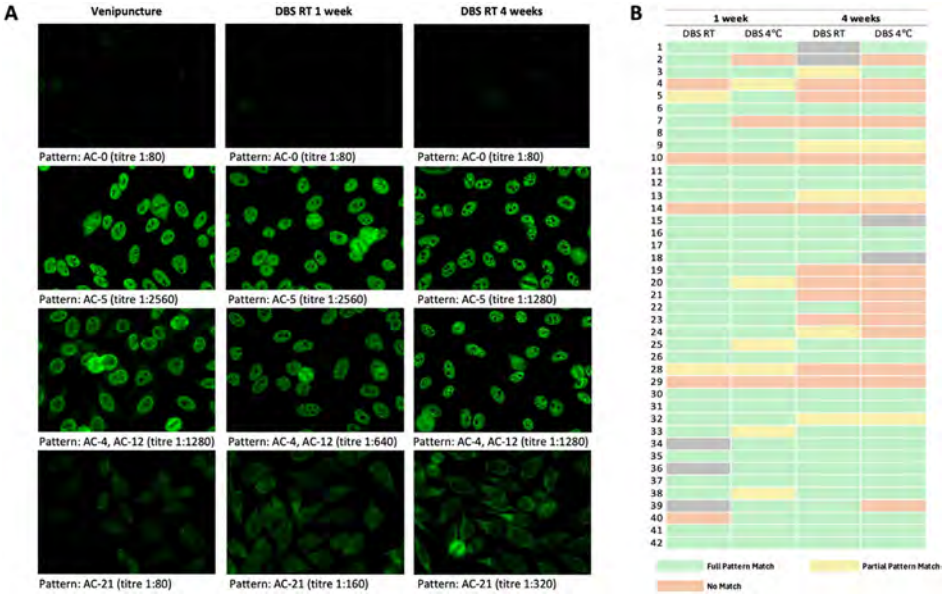


Figure 2. Venipuncture vs. DBS for A) ANA pattern, examples of ANA images shown and B) comparing pattern agreement under 4 different conditions. There was highest agreement at week 1, regardless of temperature condition. RT=room temperature. Full pattern match refers to identical pattern(s) between venipuncture and DBS. Partial pattern match refers to when there are multiple ANA patterns on venipuncture and at least one of those patterns matches a DBS pattern, but not all. No match refers to no patterns agree on venipuncture vs. DBS.

performed using an indirect immunofluorescence assay (IFA) on HEp-2 substrate (NovaLite,Werfen, CA). ANA patterns were classified according to the most recently updated International Consensus on ANA Patterns recommendations. Per manufacturers' directions, a positive test was defined as a titer of >=1:80. SLE-related antibodies (anti-U1-RNP, -histone, Jo-1, -ribosomal P, -Sm, -Sm-RNP, -Scl70, -PmScl, -centromere B, -PCNA, -Ro52/TRIM21, -Ro60/SSA, and -La/SSB) were performed on Connective-13 profile (addressable laser bead immunoassay by Theradiag, positive >80 AU/mL) and anti-dsDNA by ELISA (Werfen, CA, positive >300 IU/mL). We compared the ANA (titres and patterns) and autoantibody titres between venipuncture vs. DBS under the different storage conditions.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. SLE-related autoantibodies and correlation between venipuncture and DBS titres (1 week stored at room temperature shown only). All autoantibodies were analysed using Connective-13 profile (addressable laser bead immunoassay by Theradiag, positive >80 AU/mL) except for anti-dsDNA which was analyzed using ELISA (Werfen, CA, positive >300 IU/mL). Pearson correlation was used to evaluate the concordance of autoantibody titres.

	Correlation Coefficient (r)	p value
U1-RNP	0.964	<0.001
Histone	0.391	0.011
Jo-1	0.910	<0.001
Ribosome	0.869	<0.001
Sm	0.983	<0.001
Sm-RNP	0.998	<0.001
Scl-70	0.585	<0.001
PMScl	0.774	<0.001
CENP-B	0.911	<0.001
PCNA	0.869	<0.001
Ro-52	0.981	<0.001
SSA Ro60	0.985	<0.001
SSB	0.991	<0.001
ds-DNA	0.679	<0.001

Results: 42 patients were enrolled (24 SLE, 18 RA). There was no statistical difference in the frequency of ANA positivity between venipuncture vs. DBS under all four storage conditions for SLE and RA controls (Fig1A). The ANA titres as indicated by intensity level measured using the automated digital IFA microscope (NovaView, Werfen) did not change significantly from week 1 to 4 at 25°C and 4°C. Most ANA patterns were the same between venipuncture and DBS after 1 week at both 25°C (79.5%) and 4°C (71.4%) (Fig2). There were more discrepancies in ANA pattern between venipuncture and DBS after 4 weeks for both 25°C (57.5%) and 4°C (52.5%). The correlation between venipuncture vs. DBS SLE-related autoantibodies was moderate to strong for most, except for anti-dsDNA, anti-histone, and anti-Scl70 antibodies (Table 1). Specifically, the correlation for anti-dsDNA was r=0.68 ($p< 0.001$).

Conclusion: In the study, we demonstrated that DBS performance is comparable to venipuncture for ANA and SLE-related autoantibody testing. Antibody titre did not vary significantly over time or with temperature variation. This highlights the sustainability of DBS as a potential screening test in under-resourced populations.

Disclosure: M. Li: None; **P. Sciore**: None; **M. Fritzler**: Mitogen Diagnostics Corp., 8, 9, 12, Medical Director, Werfen, 1, 2, 6; **A. Clarke**: None; **W. Ocampo**: None; **k. Buhler**: None; **J. Seni**: None; **L. Crowshoe**: None; **D. Mosher**: None; **M. Choi**: AstraZeneca, 2, 5, 6, Celltrion, 2, MitogenDx, 2, Organon, 6, Werfen, 2.

Abstract Number: 2420

In-patient Outcomes of Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar Syndrome in SLE: US National Inpatient Database (2021-2022)

Nattanicha Chaisrimaneepan[1], Pitchaporn Yingchoncharoen[2] and Miriam Paz[2], [1]Department of Medicine, Texas Tech University Health Sciences Center, Lubbock, TX, [2]Texas Tech University Health Sciences Center, Lubbock

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of patients hospitalized with DKA and HHS with versus without SLE

Variables	DKA			HHS		
	With SLE (N=720)	Without SLE (N=314,715)	P-value	With SLE (N=170)	Without SLE (N=95120)	p-value
Female	605 (86.43%)	152231 (49.32%)	<0.01	140 (82.35%)	54365 (58.03%)	0.10
Age distribution (years)			0.19			0.39
<18	0 (0.0%)	2500(0.81%)		0(0.00%)	255 (0.27%)	
18-34	45(6.43%)	22575(7.31%)		10(5.888%)	2005(2.14%)	
35-49	215(30.71%)	60395(19.57%)		50(29.41%)	41880(44.70%)	
50-64	305(43.57%)	122795(39.79%)		90(52.94%)	21390(22.83%)	
65-79	130(18.57%)	83296(27.00%)		20(11.76%)	23360(24.93%)	
≥ 80	5(0.71%)	17075(5.53%)		0(0.00%)	4795(5.12%)	
Average age	52.93 +-1.02	57.20+-1.02	<0.01	53.29+-1.69	55.88+/-4.16	0.56
Racial distribution			0.57			0.08
Caucasian	340 (48.57%)	166585(53.97%)		50(29.41%)	68060 (72.65%)	
Black	200(28.57%)	85965(27.85%)		80(47.06%)	15405(16.44%)	
Hispanic	120 (17.14%)	41065 (13.31%)		25(14.71%)	7100(7.58%)	
Asian/Pacific Islandic	0 (0%)	52010(1.69%)		0(0.00%)	1329(1.42%)	
Native Americans	15 (2.14%)	30130 (0.98%)		5(2.94%)	470(0.50%)	
Others	25 (3.57%)	6800(2.20%)		10(5.88%)	1320(1.41%)	
Charlson comorbidity index score			NA			NA
0	0 (0.00%)	0 (0.00%)		0(0.00%)	0 (0.00%)	
1	0 (0.00%)	116450 (37.73%)		0(0.00%)	14450(15.42%)	
2	155(22.14%)	48950 (15.86%)		35(20.59%)	9630(10.28%)	
3	545 (77.96%)	143235 (46.41%)		135(79.41%)	69605(74.30%)	
Median Household income			0.15			0.15
$1-$43999	315 (45.32%)	161660 (52.21%)		70(42.42%)	19905 (21.21%)	
$44000-$55999	175 (25.18%)	64345 (20.78%)		30(18.18%)	23345(24.88%)	
$56000-$73999	100(14.39%)	54580 (17.63%)		40(24.24%)	10705(11.41%)	
$74000 or more	105(15.11%)	29030 (9.38%)		25(15.15%)	39885(42.50%)	
Insurance			0.12			
Medicare	310 (44.60%)	118811(38.37%)		80(48.49%)	56115(59.80%)	
Medicaid	220(31.65%)	66080(21.34%)		60(36.36%)	11300(12.04%)	
Private insurance	130(18.70%)	88565(28.60%)		15(9.09%)	9955(10.61%)	
Self-pay	25(3.60%)	28030(9.05%)		10(6.06%)	3430(3.66%)	
No charge	0 (0.00%)	1230(0.40%)		0(0.00%)	265(0.282%)	
others	10 (1.44%)	6900(2.23%)		0(0.00%)	12775 (13.61%)	
Hospital region			0.67			0.25
Northeast	85(12.23%)	30310(9.79%)		10(6.06%)	8320(8.87%)	
Midwest	125(17.99%)	70780(22.86%)		15(9.09%)	10295(10.97%)	
Southern	350(50.36%)	150716(48.68%)		90(54.55%)	63405(67.57%)	
Western	135(19.42%)	57810(18.67%)		50(30.30%)	11820(12.60%)	
Hospital location and teaching status			<0.01			0.73
Rural	80(11.51%)	96980(31.32%)		20(12.12%)	7625(8.13%)	
Urban, non-teaching	115(16.55%)	54945(17.75%)		40(24.24%)	16730(17.83%)	
Urban, teaching	500(71.94%)	157690 (50.93%)		105(63.64%)	69485(74.05%)	
Hospital bed size			0.26			<0.01
Small	140(20.14%)	77760(25.12%)		20(12.12%)	21580 (23.00%)	
Medium	225(32.37%)	76495(24.71%)		80(48.48%)	14050 (14.97%)	
large	330(47.48%)	155361(50.18%)		65(39.39%)	58210(62.03%)	
Co-morbidities						
Smoking	95(13.57%)	29150(9.44%)	0.12	10	7590	0.66
Alcohol use	40 (5.56%)	16370 (5.20%)	0.85	10(5.88%)	3675(3.86%)	0.62
Diabetes without complications	360(51.43%)	194135(62.90%)	0.049	90(52.94%)	36435(38.89%)	0.43
Diabetes with complication	440 (48.57%)	114500 (37.10%)	0.049	80(47.06%)	57250 (61.11%)	0.43
ESRD/renal transplant	245(17.94%)	55370 (35.00%)	<0.01	55(32.35%)	59590(63.61%)	0.09
Essential hypertension	245(35.00%)	121365(39.32%)	0.50	85(50.00%)	21700(23.16%)	0.04

Background/Purpose: Systemic lupus erythematosus (SLE is an autoimmune disease that attacks different organs. There have been reports of hyperglycemic hyperosmolar syndrome (HHS) from steroid use in SLE and insulin resistance in SLE, which results in DKA. However, the exact incidence and outcomes of DKA/HHS are unknown.

Methods: This population-based retrospective cohort study utilizes data from the National Inpatient Sample (NIS) database for the period 2021-2022. Patients hospitalized with DKA and HHS based on ICD-10 were identified. Patients were stratified into groups with and without SLE. The primary outcome is the incidence of patients with DKA/HHS and SLE. Secondary outcomes include mortality rate, length of stay (LOS), cost of hospitalization and risk of developing

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Primary and secondary in-hospital outcomes for DKA and HHS with SLE versus without SLE

	DKA			HHS		
Outcome	With SLE	Without SLE	p-value	With HHS	Without HHS	p-value
Inpatient mortality	60 (8.57%)	23300 (7.55%)	0.61	5 (2.94%)	2250 (2.40%)	0.86
LOS (days)	7.77+-0.78	6.45+-0.34	0.12	3.94+-0.48	3.97+-1.07	0.98
Cost ($)	114305.2+-18307.88	85236.48+-5856.333	0.13	42652.84 +-5327.639	45841.72 +-12887.63	0.82
Complications						
Sepsis/septic shock	150 (20.83%)	61405(19.51%)	0.80	15(8.82%)	6415(6.74%)	0.69
Acute myocardial infarction	55 (7.64%)	32360(10.28%)	0.54	0 (0.00%)	3045 (3.20%)	0.81
Acute renal failure	395(54.86%)	174900(55.57%)	0.91	70(41.18%)	65010(68.35%)	0.09
Acute hypoxic respiratory failure	160 (22.22%)	46890 (14.90%)	0.05	10(5.88%)	6385(6.71%)	0.87
Ischemic stroke	5 (0.69%)	6875 (2.18%)	0.22	0(0.00%)	1735(1.82%)	0.85
DVT	30 (4.17%)	7500 (2.38%)	0.17	5(2.94%)	1285(1.35%)	0.45
Pulmonary embolism	5 (0.69%)	4305(1.37%)	0.49	0	580	0.91
pancreatitis	35(4.86%)	12355(3.93%)	0.59	5(2.94%)	1310 (1.38%)	0.46
Congestive heart failure	140 (19.44%)	47650 (15.14%)	0.41	45	1135	0.07
Peripheral vascular disease	30(4.17%)	8400 (2.67%)	0.27	0	2405	0.83

Table 3: Outcomes of in-hospital DKA/HHS with versus without SLE

Outcome	DKA		HHS	
	aOR(CI)*	p-value	aOR(CI)*	p-value
Inpatient mortality	1.70 (0.86-3.36)	0.13	1.11(0.14-8.82)	0.92
Complications				
Sepsis/septic shock	1.34(0.81-2.22)	0.25	0.86(0.28-2.66)	0.80
Acute myocardial infarction	0.75(0.35-1.58)	0.44	1	-
Acute renal failure	1.10(0.70-1.72)	0.69	0.25(0.10-0.64)	<0.01
Acute hypoxic respiratory failure	1.67(1.01-2.76)	0.045	0.55(0.12-2.52)	0.44
Ischemic stroke	1	-	1	-
DVT	1.18(0.52-2.66)	0.69	1.68(0.21-13.32)	0.63
Pulmonary embolism	0.40(0.06-2.79)	0.35	1	-
pancreatitis	1.42(0.63-3.20)	0.40	1.85(0.22-15.49)	0.57
Congestive heart failure	1.04(0.61-1.78)	0.89	2.51(0.74-8.51)	0.14
Peripheral vascular disease	0.78(0.32-1.91)	0.59	1	-

sepsis/septic shock, acute kidney injury, myocardial infarction, acute hypoxic respiratory failure (AHRF), deep vein thrombosis, pulmonary embolism, congestive heart failure, and peripheral vascular disease. Confounders were adjusted using multivariable logistic analysis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The study included 315435 DKA patients, 95290 HHS patients, and 246427 SLE patients. The incidence of DKA and HHS in SLE is 0.3% and less than 0.01%, respectively. Table 1 summarizes the characteristics of the patients, Table 2 and Table 3 summarize primary and secondary outcomes of interest.

DKA patients with SLE were predominantly women (86.43% vs 49.32%, p< 0.01) with younger age (52.93=-1.02 vs 57.20 vs 1.02; p< 0.01) with no difference in racial distribution compared to non-SLE. They were more likely to have diabetes with complications (48.57% vs 37.10%. p=0.049) and long-term steroid use (8.57% vs 0.74%, p< 0.01), but less likely to have renal disease (17.4% vs 35.00%, p< 0.01%) as co-morbidities compared to those without SLE. No difference in the average LOS and the cost of hospitalization was observed. DKA patients with SLE had a significantly higher risk of developing AHRF (aOR=1.67, 95% CI 1.01-2.76, p=0.045). No significant increased risk of mortality (aOR=1.7, 95% CI 0.86-3.36, p=0.13) and risk of other in-hospital outcomes were detected.

HHS patients with SLE demonstrated no significant difference in gender, age, and racial distribution. They were more likely to have essential hypertension (50.0% vs 23.16%, p=0.04), insulin use (50.0% vs 21.41%, p=0.02), and long-term steroid use (5.88% vs 0.78%, p< 0.01) as co-morbidities compared to those without SLE. No difference in the average LOS and the cost of hospitalization was observed. HHS patients with SLE had a significantly lower risk of developing AKI (aOR=0.25, 95% CI 0.10-0.64, p< 0.01). No significantly increased risk of other in-hospital outcomes was detected.

Conclusion: DKA patients with SLE had a higher risk of developing AHRF, while HHS patients with SLE have a higher risk of AKI without significant difference in mortality, LOS and cost.

Disclosure: N. Chaisrimaneepan: None; **P. Yingchoncharoen**: None; **M. Paz**: None.

Abstract Number: 2421

Whole Blood Immune Phenotyping Reveals Cytometric Differences in B Cell Clusters Between Lupus Nephritis and Non-Lupus Nephritis SLE Patients with Minimal Proteinuria

Nicholas Bauer[1], Philip Carlucci[2], Rufei Lu[1], Carla Guthridge[1], Tayte Stephens[3], Benjamin Jones[4], Wade DeJager[5], Susan Macwana[1], Andrea Fava[6], Sanchit Sanyal[7], Erin Carter[8], Mala Masson[9], Jennifer Anolik[10], Jennifer Barnas[11], Peter Izmirly[12], H Michael Belmont[13], Kelly Ruggles[14], Study Team ALE06 Clinical[1], Brad Rovin[15], Jill Buyon[16], Michelle Petri[17], Judith James[1] and Joel Guthridge[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]New York University School of Medicine, New York, NY, [3]University of Oklahoma Health Science Center, Oklahoma City, OK, [4]Oklahoma State University, Oklahoma City, OK, [5]Oklahoma Medical Research Foundation, Oklahoma City, [6]Johns Hopkins University, Baltimore, MD, [7]Johns Hopkins University School of Medicine, Baltimore, MD, [8]New York University Grossman School of Medicine, New York, NY, [9]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [10]University of Rochester Medical Center, Rochester, NY, [11]University of Rochester, Rochester, NY, [12]New York University Grossman School of Medicine, New York, NY, [13]NYU School of Medicine, New York, NY, [14]NYU Grossman School of Medicine, Brooklyn, NY, [15]The Ohio State University, Columbus, OH, [16]NYU Grossman School of Medicine, New York, NY, [17]Johns Hopkins University School of Medicine, Timonium, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Clinical characteristics of patients with and without LN. Data are represented as median [IQR], or n (%). *4 non LN but unknown other histology, 2 arteriosclerosis, 1 diabetic nephropathy, 1 microangiopathy.

Baseline Characteristics	All Subjects (N=25)	LN (N=17)	No LN (N=8)
Age	45 [31-61]	41 [31-49]	60.5 [41-63]
Female	22 (88)	15 (88)	7 (88)
Hispanic	6 (24)	5 (29)	1 (13)
Race			
Black	13 (52)	9 (53)	4 (50)
White	7 (28)	4 (24)	3 (38)
Asian	1 (4)	1 (6)	0 (0)
Other	4 (16)	3 (18)	1 (13)
Biopsy Class			
Class I	2 (8)	2 (11)	NA
Class II	4 (16)	4 (24)	NA
Class III	5 (20)	5 (29)	NA
Class V	6 (24)	6 (35)	NA
No LN	8 (32)	0 (0)	8 (100)
Low C3	9 (36)	8 (47)	1 (13)
Low C4	11 (44)	9 (53)	2 (25)
Anti-dsDNA	19 (76)	14 (82)	5 (63)
UPCR	.38 [.310-.423)]	.394 [.318-.450)]	.328 [.286-.38]
Thrombocytopenia	2 (8)	2 (12)	0 (0)
Leukopenia	7 (28)	5 (29)	2 (25)
Total SLEDAI Score	4 [2-8]	5 [3.5-9]	3 [0-4.5]
Extrarenal Involvement	12 (48)	8 (47)	4 (50)

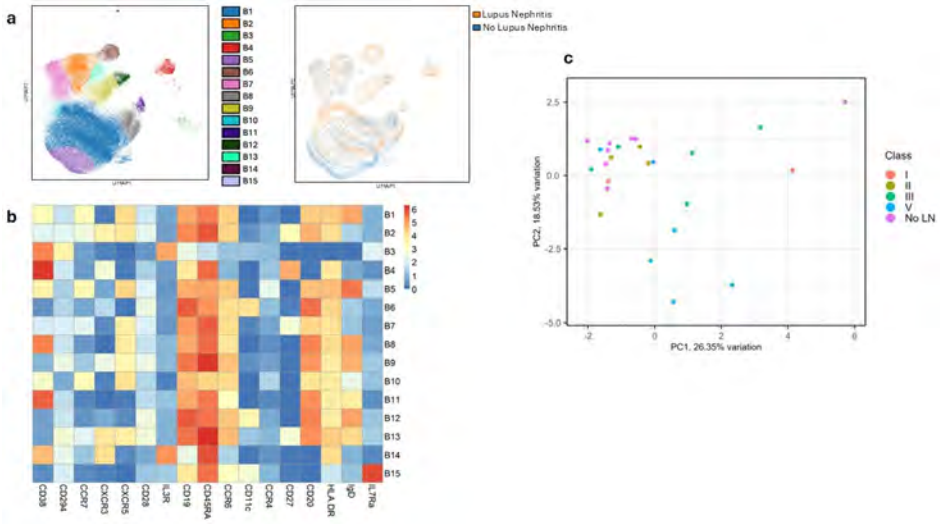


Figure 1. B cell clusters in LN and Non LN cases. (A): Uniform Manifold Approximation and Projection (UMAP) dimension reduction visualizing the different B cell clusters (top left) and the differences in their density (top right) (B): Marker expression in each of the B cell clusters (C): PCA based on B cell clusters colored by biopsy histology.

Background/Purpose: Autoreactive B cell populations play a key role in the pathogenesis of lupus nephritis (LN). Therefore, it is hypothesized that dysregulation in the B cell compartment may be an early indicator of kidney involvement in SLE. The AMP-AIM lupus nephritis study was initiated to identify molecular drivers of kidney disease in SLE patients with minimal proteinuria (considered "early" disease). Accordingly, this study leveraged CyTOF performed at the time of a kidney biopsy in AMP-AIM to characterize alterations within the B cell lineage between LN and non-LN cases and within LN disease classes.

Methods: Twenty-five patients fulfilling diagnostic criteria for SLE with a urine protein creatinine ratio between 0.25 – 0.49 without a history of LN but an additional risk factor for LN including active sediment and/or serologies were enrolled in AMP-AIM. Whole blood was collected at the time of their kidney biopsy and stained at the point of collection on the same day using the Maxpar Direct Immune Profiling Assay (MDIPA), a comprehensive panel of 30 markers to capture the broad immune phenotype of the samples. The samples were stabilized and shipped to a central location where data were captured

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

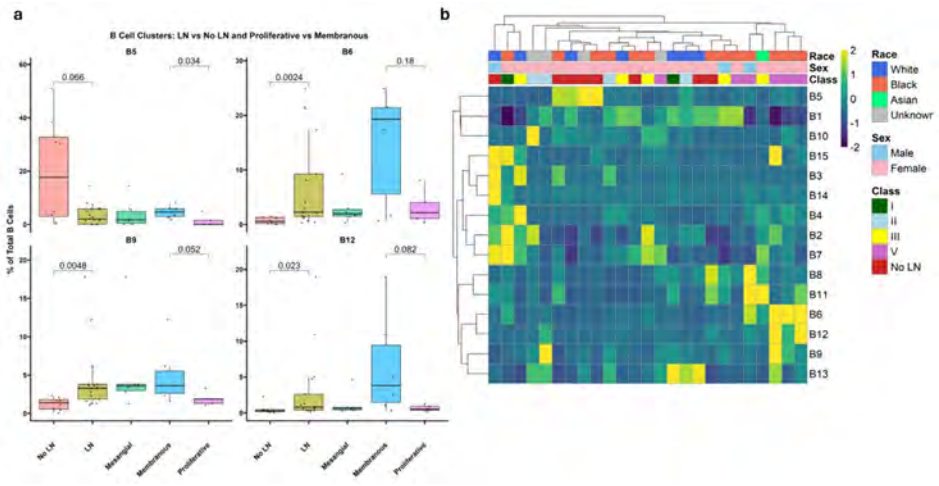


Figure 2. Four B cell clusters differentiate LN and non LN (A): Boxplots showing the four B cell clusters significantly different between Non LN and LN cases. LN is further divided into mesangial, membranous, and proliferative histology. P-values for Non LN vs LN and membranous vs proliferative are reported (B): Heatmap showing the expression of each cluster in all cases.

using the CyTOF XT platform. Low-quality events were excluded with FlowCut and cells were gated to include only the B cell lineage. Dimension reduction and clustering were performed using ClusterX. All pairwise comparisons were made with the Wilcoxon rank-sum test.

Results: Table 1 shows the clinical characteristics of the patients with and without LN at biopsy. ClusterX captured a total of 15 clusters within B cells (Figure 1A & 1B). Two clusters, both CD11c positive, were elevated in LN vs non-LN cases (Figure 2). One was IgD positive (B12) and the other was IgD negative (B6) (p=0.023 and p=0.0024 respectively). A naïve B cell cluster characterized as CXCR3 positive and CXCR5 positive (B9) was also expanded in LN compared to non-LN cases (p=0.0048). Surprisingly, elevated frequencies for all three clusters were seen in class V compared to class III (B6, p=0.18; B9, p=0.052; B12, p=0.082) (Figure 2). An additional CXCR5 and CCR7 positive naïve B cell cluster (B5) was also significantly elevated in class V compared to class III (p=0.034). These differences were also reflected in hierarchical clustering of the samples (Figure 2B).

Conclusion: Whole blood profiling at the point of collection, which likely reduced artifactual findings compared to prior studies which have relied on PBMCs, yielded several differences between LN and non-LN cases at the time of biopsy. These data suggest B cell dysregulation may be detected "early" in kidney involvement in SLE patients, especially with class V histology.

Whole blood profiling at the point of collection, which likely reduced artifactual findings compared to prior studies which have relied on PBMCs, yielded several differences between LN and non-LN cases at the time of biopsy. These data suggest B cell dysregulation may be detected "early" in kidney involvement in SLE patients, especially with class V histology.

Disclosure: N. Bauer: None; **P. Carlucci**: None; **R. Lu**: None; **C. Guthridge**: None; **T. Stephens**: None; **B. Jones**: None; **W. DeJager**: None; **S. Macwana**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **S. Sanyal**: None; **E. Carter**: None; **M. Masson**: None; **J. Anolik**: None; **J. Barnas**: None; **P. Izmirly**: Hansoh Bio, 2; **H. Belmont**: None; **K. Ruggles**: None; **S. ALE06 Clinical**: None; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **J. Guthridge**: None.

Abstract Number: 2422

Cluster Analysis of Autoantibodies in Patients with Systemic Lupus Erythematosus

Oihane Ibarguengoitia-Barrena[1], Leyre Riancho Zarrabeitia[2], Iñigo Rúa-Figueroa[3], Karen Roberts[4], Victor Martinez-Taboada[5], Raúl Menor Almagro[6], Belén Serrano-Benavente[7], Paula Rubio-Muñoz[8], María Galindo-Izquierdo[9], Antonio Fernández-Nebro[10], Maria Esther Ruiz Lucea[11], Jaime Calvo[12], Jose Francisco Garcia Llorente[13], EVA GLORIA TOMERO MURIEL[14], Maria Esther Uriarte[15], Mercedes Freire González[16], Angela Pecondón-Español[17], Javier García-Fernández[18], Lorena Expósito-Pérez[19], Monica Ibañez Barcelo[20], Elena Aurrecoechea[21], Carlos Montilla[22], Jose Rosas Gómez de Salazar[23], Maria Garcia-Villanueva[24], Rocío Caño[25], Francisco Javier Toyos[26], Francisco Javier Novoa[27], Clara Moriano[28], Gema Bonilla[29], Javier Narváez[30], Jose Luis Andreu[31], Marta Arévalo-Salaet[32], Loreto Horacda-Rubio[33], Tatiana Cobo-Ibáñez[34], Nuria Lozano Rivas[35], Cristina Bohorquez[36], Carlota Laura Iniguez Ubiaga[37], Eva salgado-Parez[38], Vicente Torrente Segarra[39], CARLOS TAREK SALMAN MONTE[40], JOSE ELOY OLLER RODRIGUEZ[41] and José María Pego-Reigosa[42], [1]Galdakao-Usansolo University Hospital, Bilbao, Spain, [2]Hospital Sierrallana, Santander, Spain, [3]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [4]Buenos Aires Instituto, West Reading, CA, [5]Facultad de Medicina. Universidad de Cantabria, Santander, Spain, [6]Department of Rheumatology, Hospital de Jerez, Spain, Puerto De Santa María, Spain, [7]Hospital Gregorio Marañon, Madrid, Spain, [8]Hospital Germans Trias i Pujol, Badalona, Spain, [9]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Madrid, Spain, [10]Hospital Regional Universitario de Malaga, Malaga, Spain, Malaga, Spain, [11]Basurto University Hospital, Bilbao, Spain, [12]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain, [13]Hospital de Gadakao Usansolo Osakidetza, Bilbao, Spain, [14]Hospital Universitario de la Princesa, Madrid, Spain, [15]Hospital Universitario Donostia, San Sebastian, Spain, [16]4 Hospital Universitario A Coruña, Rheumatology, A Coruña, La coruna, Spain, [17]Hospital Universitario Miguel Servet, Zaragoza, Spain, [18]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [19]University Clinical Hospital of Canarias, Tenerife, Spain, [20]Son Llàtzer University Hospital, Palma de Mallorca, Spain, [21]Hospital Sierrallana, CANTABRIA, Spain, [22]Rheumatology Service, University Hospital of Salamanca, Salamanca, Castilla y Leon, Spain, [23]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [24]Hospital Ramón y Cajal, Madrid, Spain, [25]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [26]Virgen Macarena University Hospital,, Sevilla, Spain, [27]Hospital Insular de Gran Canaria, Las palmas, [28]Hospital León, LEON, Castilla y Leon, Spain, [29]Hospital Universitario La Paz, Rheumatology, Madrid, Madrid, Spain, [30]Hospital Universitario de Bellvitge, Barcelona, Spain, [31]Hospital Universitario Puerta de Hierro, Majadahonda, Spain, [32]Consorci Corporació Sanitària Parc Taulí, Sabadell, Spain, [33]Hospital Complex of Navarra, Pamplona, Spain, [34]Infanta Sofia Hospital, Madrid, Spain, [35]Hospital Clínico Universitario Virgen de la Arrixaca,, Murcia, Spain, [36]La Paz University Hospital, Alcalá De Henares, Spain, [37]SERV. REUMATOLOGIA, Lugo, Spain, [38]Complejo Hospitalario de Orense, Santiago de Composte, Spain, [39]Hospital Comarcal del Alt Penedes, Madrid, Spain, [40]Hospital del Mar, Barcelona, Spain, [41]HOSPITAL UNIVERSITARI I POLITÈCNIC LA FE, VALENCIA, Spain, [42]Department of Rheumatology, University Hospital of Vigo, Vigo, Spain; IRIDIS Group (Investigation in Rheumatology and Immune-Diseases), Galicia Sur Health Research Institute, Vigo, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disorder characterized by multi-organ involvement and variable clinical manifestations. Recurrent clinical patterns suggest distinct phenotypes, where cluster analysis of autoantibodies could identify prognostic subtypes. The objective of this study is to define and describe serological clusters and their clinical-epidemiological characteristics, as well as their association with comorbidities, disease activity measures, severity, and damage.

Methods: Descriptive, observational, and multicenter study including SLE patients from the Spanish Registry RELESSER (includes a cross-sectional phase and a prospective phase with annual visits over four consecutive years). Gower distance was used for cluster analysis.

Results: A total of 1,740 patients from the cross-sectional phase and 718 from the prospective phase were included. Four serological clusters were identified. Cluster 1 ((negative for extractable nuclear antigen); 44.5% of the patients) was characterized by lower frequency of vasculitis (6.6%), leukopenia (49.1%) and lymphopenia (48.0%). Cluster 2 (positive antiphospholipid antibodies; 12.24%) was represented by higher frequency of high blood pressure (35.5%) as well as hemolytic anemia (13.5%), thrombocytopenia (39.9%), vasculitis (12.5%), visual disturbances (9.1%) and higher use of immunoglobulins (10.3%) and oral anticoagulants (39.0%). Cluster 3 (positive anti-Ro/anti-La; 26.7%) had the lowest frequency of lupus nephritis (24.9%). Patients from cluster 4 (positive anti-Sm/anti-RNP; 16.55%) were younger at disease onset (median age of 29.2 years) and had the highest frequency of lupus nephritis (38.5%), leukopenia (66.0%), lymphopenia (62.2%), hypocomplementemia (89.5%), myositis (5.6%) and cutaneous manifestations. Besides, they had a higher frequency of osteoporosis (11.0%) and severe infections (26.4%) and a higher use of glucocorticoids (93.5%), azathioprine (42.0%), cyclophosphamide (25.5%) and mycophenolate mofetil (24.0%).

Regarding disease activity assesed by SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), at visit 1 of the prospective phase, patients in cluster 4 had the highest scores: 2.5 ± 3.4. After 4 years of follow-up, no differences were observed between clusters.

Table 1. Epidemiological characteristics and comorbidities

	Cluster 1 (n=775)	Cluster 2 (n=213)	Cluster 3 (n=464)	Cluster 4 (n=288)	TOTAL (n=1740)	p
Age at diagnosis (median [Q1, Q3])	32.6 [24.2, 43.6]	32.8 [23.2, 41.3]	33.2 [25.3, 43.0]	29.2 [23.3, 38.0]	32.1 [24.1, 42.3]	0.001
Sex, n (%)						
Female	675 (87.3%)	185 (86.9%)	440 (94.8%)	263 (91.3%)	1563 (89.9%)	<0.001
Male	98 (12.7%)	28 (13.1%)	24 (5.2%)	25 (8.7%)	175 (10.1%)	
Ethnicity, n (%)						
African American	1 (0.1%)	0 (0%)	1 (0.2%)	1 (0.4%)	3 (0.2%)	0.227
Asian	3 (0.4%)	0 (0%)	2 (0.4%)	2 (0.7%)	7 (0.4%)	
Caucasian	703 (93.4%)	195 (94.2%)	430 (94.7%)	249 (88.3%)	1577 (93.0%)	
Latin American	41 (5.4%)	11 (5.3%)	18 (4.0%)	26 (9.2%)	96 (5.7%)	
Others	5 (0.7%)	1 (0.5%)	3 (0.7%)	4 (1.4%)	13 (0.8%)	
Tobacco, n (%)						
Previously	167 (23.5%)	48 (24.1%)	92 (21.5%)	52 (19.3%)	359 (22.3%)	0.358
Smoker	141 (19.9%)	37 (18.6%)	69 (16.1%)	47 (17.4%)	294 (18.3%)	
Never	402 (56.6%)	114 (57.3%)	267 (62.4%)	171 (63.3%)	954 (59.4%)	
Alcohol, n (%)						
Nowadays	6 (0.8%)	0 (0%)	3 (0.7%)	2 (0.7%)	11 (0.7%)	0.693
Previously	23 (3.2%)	8 (3.9%)	9 (2.0%)	6 (2.2%)	46 (2.8%)	
Never	700 (96.0%)	195 (96.1%)	428 (97.3%)	262 (97.0%)	1585 (96.5%)	
Diabetes Mellitus, n (%)	35 (4.6%)	13 (6.3%)	11 (2.4%)	12 (4.2%)	71 (4.2%)	0.103
High blood pressure, n (%)	230 (29.7%)	75 (35.5%)	102 (22.2%)	81 (28.4%)	488 (28.2%)	0.002
Dyslipidemia, n (%)	245 (32.7%)	75 (36.6%)	127 (28.3%)	82 (29.5%)	529 (31.5%)	0.138
Congestive heart failure, n (%)	27 (3.5%)	7 (3.3%)	9 (2.0%)	8 (2.8%)	51 (3.0%)	0.471
Tumor and lymphoma, n (%)	47 (6.1%)	13 (6.2%)	21 (4.5%)	16 (5.6%)	97 (5.6%)	0.675
Osteoporosis, n (%)	44 (5.8%)	16 (7.5%)	28 (6.1%)	31 (11.0%)	119 (7.0%)	0.025
Infections, n (%)	143 (19.6%)	49 (23.8%)	80 (18.1%)	72 (2.4%)	344 (20.8%)	0.032

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Clinical manifestations among the different clusters

	Cluster 1 (n 775)	Cluster 2 (n 213)	Cluster 3 (n 464)	Cluster 4 (n 288)	TOTAL (n 1740)	p
Fever, n (%)	18 (2.3%)	8 (3.8%)	14 (3.0%)	13 (4.5%)	53 (3.1%)	0.285
Weight loss, n (%)	65 (8.5%)	22 (10.4%)	27 (5.9%)	33 (11.5%)	147 (8.5%)	0.040
Lymphadenopathy, n (%)	63 (8.2%)	21 (9.9%)	40 (8.7%)	47 (16.4%)	171 (9.9%)	<0.001
Splenomegaly, n (%)	29 (3.8%)	14 (6.7%)	11 (2.4%)	13 (4.5%)	67 (3.9%)	0.063
Inflammatory skin rash, n (%)	447 (58.1%)	119 (56.7%)	306 (66.5%)	205 (71.2%)	1077 (62.4%)	<0.001
Oral or nasal sores, n (%)	291 (38.6%)	77 (36.5%)	199 (44.0%)	127 (45.2%)	694 (40.9%)	0.064
Alopecia, n (%)	245 (31.9%)	75 (35.4%)	167 (36.2%)	129 (45.6%)	616 (35.8%)	<0.001
Arthritis, n (%)	78 (10.2%)	24 (11.3%)	46 (10.0%)	39 (13.6%)	187 (10.9%)	0.4
Myositis, n (%)	22 (2.9%)	9 (4.3%)	8 (1.7%)	16 (5.6%)	55 (3.2%)	0.025
Alveolar hemorrhage, n (%)	5 (0.7%)	2 (1.0%)	0 (0%)	2 (0.7%)	9 (0.5%)	0.164
Pneumonitis, n (%)	26 (3.4%)	5 (2.4%)	15 (3.3%)	11 (3.8%)	57 (3.3%)	0.836
Myocarditis, n (%)	3 (0.4%)	2 (1.0%)	2 (0.4%)	2 (0.7%)	9 (0.5%)	0.599
Pericarditis, n (%)	12 (1.6%)	4 (1.9%)	7 (1.5%)	5 (1.7%)	28 (1.6%)	0.96
Vasculitis, n (%)	50 (6.6%)	26 (12.5%)	46 (10.1%)	33 (11.6%)	155 (9.1%)	0.009
Lupus nephritis, n (%)	228 (29.9%)	58 (27.4%)	113 (24.9%)	110 (38.5%)	509 (29.7%)	0.001
Seizures, n (%)	35 (4.6%)	17 (8.1%)	17 (3.7%)	15 (5.3%)	84 (4.9%)	0.096
Organic brain syndrome, n (%)	16 (2.1%)	5 (2.4%)	6 (1.3%)	10 (3.5%)	37 (2.1%)	0.246
Lupus headache, n (%)	41 (5.4%)	15 (7.1%)	20 (4.3%)	22 (7.7%)	98 (5.7%)	0.184
Transvers myelitis, n (%)	7 (0.9%)	3 (1.4%)	3 (0.7%)	2 (0.7%)	15 (0.9%)	0.767
Peripheral or cranial neuropathy, n (%)	22 (2.9%)	6 (2.9%)	16 (3.5%)	9 (3.2%)	53 (3.1%)	0.947
Visual disturbances, n (%)	35 (4.6%)	19 (9.1%)	9 (1.9%)	11 (3.9%)	74 (4.3%)	<0.001
Hemolytic anaemia, n (%)	60 (7.9%)	28 (13.5%)	23 (5.1%)	28 (9.9%)	139 (8.1%)	0.002
Leukopenia, n (%)	375 (49.1%)	112 (53.3%)	278 (61.5%)	188 (66.0%)	953 (55.7%)	<0.001
Lymphopenia, n (%)	365 (48.0%)	106 (51.2%)	250 (54.7%)	176 (62.2%)	897 (52.5%)	<0.001
Thrombocytopenia, n (%)	155 (20.7%)	81 (39.9%)	86 (19.3%)	65 (23.8%)	387 (23.2%)	<0.001
Hypocomplementemia, n (%)	555 (72.4%)	174 (82.1%)	348 (75.7%)	257 (89.5%)	1334 (77.3%)	<0.001
Anti-DNA, n (%)	564 (72.8%)	171 (80.3%)	310 (66.8%)	227 (78.8%)	564 (72.8%)	<0.001

Table 3, Treatments

	Cluster 1 (n=775)	Cluster 2 (n=213)	Cluster 3 (n=464)	Cluster 4 (n=288)	TOTAL (n=1740)	p
Glucocorticoids, n (%)	641 (86.4%)	176 (88.0%)	365 (84.7%)	259 (93.5%)	1441 (87.3%)	0.005
Methotrexate, n (%)	137 (18.6%)	37 (18.6%)	95 (22.1%)	56 (20.1%)	325 (19.8%)	0.516
Leflunomide, n (%)	31 (4.2%)	11 (5.5%)	20 (4.7%)	8 (2.9%)	70 (4.3%)	0.529
Anti-TNF, n (%)	12 (1.6%)	4 (2.0%)	9 (2.1%)	3 (1.1%)	28 (1.7%)	0.743
Abatacept, n (%)	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)	1
Azathioprine, n (%)	218 (29.5%)	68 (34.5%)	127 (29.7%)	116 (42.0%)	529 (32.3%)	<0.001
Cyclophosphamide, n (%)	159 (21.6%)	45 (22.6%)	73 (17.0%)	71 (25.5%)	348 (21.2%)	0.047
Mycophenolate Mofetil, n (%)	112 (15.3%)	31 (15.5%)	73 (17.1%)	66 (24.0%)	282 (17.2%)	0.011
Mycophenolic acid, n (%)	18 (2.5%)	3 (1.6%)	14 (3.3%)	10 (3.7%)	45 (2.8%)	0.463
Antimalarials, n (%)	612 (82.6%)	155 (77.1%)	379 (88.6%)	252 (90.3%)	1398 (84.8%)	<0.001
Immunoglobulins, n (%)	22 (3.0%)	20 (10.3%)	19 (4.5%)	12 (4.4%)	73 (4.5%)	<0.001
Rituximab, n (%)	54 (7.3%)	19 (9.5%)	41 (9.6%)	22 (8.0%)	136 (8.3%)	0.496
Acetylsalicylic acid, n (%)	217 (34.7%)	127 (69.8%)	133 (34.7%)	79 (32.4%)	556 (38.7%)	<0.001
Oral anticoagulants, n (%)	83 (12.0%)	78 (39.0%)	57 (13.4%)	40 (14.5%)	263 (16.1%)	<0.001

Concerning damage assessed by SLICC/ACR DI (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index), patients in cluster 2 exhibited the highest scores at visit 1: 1.9 ± 2.3. After 4 years of follow-up, a significant increase was observed across all clusters ($p < 0.001$), with differences between clusters persisting at the end ($p=0.049$).

Regarding severity (Katz index), patients in cluster 4 had the highest scores at visit 1: 5.2 ± 2.0. The differences persisted after follow-up ($p=0.005$).

As for mortality, 21 deaths were recorded: 5 in cluster 1 (1.7%), 6 in cluster 2 (5.5%), 6 in cluster 3 (2.9%) and 4 in cluster 4 (3.3%), with no significant differences between clusters ($p=0.427$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In our cohort, the serological profile constitutes a crucial factor for the clinical stratification of patients and predicting their prognosis.

Disclosure: O. Ibarguengoitia-Barrena: None; **L. Riancho Zarrabeitia**: None; **I. Rúa-Figueroa**: None; **K. Roberts**: None; **V. Martinez-Taboada**: None; **R. Menor Almagro**: None; **B. Serrano-Benavente**: None; **P. Rubio-Muñoz**: None; **M. Galindo-Izquierdo**: None; **A. Fernández-Nebro**: Argenx, 5, AstraZeneca, 2, 5, 6, Chemo, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Gebro Pharma, 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 5, Merck Serono, 5, MSD, 5, Novartis, 2, 5, 6, Takeda, 5, UCB, 5; **M. Ruiz Lucea**: None; **J. Calvo**: None; **J. Garcia Llorente**: None; **E. TOMERO MURIEL**: None; **M. Uriarte**: None; **M. Freire González**: None; **A. Pecondón-Español**: None; **J. García-Fernández**: None; **L. Expósito-Pérez**: None; **M. Ibañez Barcelo**: None; **E. Aurrecoechea**: None; **C. Montilla**: None; **J. Rosas Gómez de Salazar**: None; **M. Garcia-Villanueva**: None; **R. Caño**: None; **F. Toyos**: None; **F. Novoa**: None; **C. Moriano**: None; **G. Bonilla**: None; **J. Narváez**: None; **J. Andreu**: None; **M. Arévalo-Salaet**: None; **L. Horacda-Rubio**: None; **T. Cobo-Ibáñez**: None; **N. Lozano Rivas**: None; **C. Bohorquez**: None; **C. Iniguez Ubiaga**: None; **E. salgado-Parez**: None; **V. Torrente Segarra**: None; **C. SALMAN MONTE**: None; **J. OLLER RODRIGUEZ**: None; **J. Pego-Reigosa**: AstraZeneca, 1, 5, 6, GlaxoSmithKline (GSK), 1, 5, 6, Otsuka, 1, 6.

Abstract Number: 2423

Clinical and Sociodemographic Factors Associated with Diagnostic Delays in Pediatric Lupus Patients

Michaela Harter[1], **Rebecca Hetrick**[2], James Slaven[3] and Martha Rodriguez[4], [1]Indiana University School of Medicine, Indianapolis, IN, [2]Indiana University School of Medicine, Zionsville, IN, [3]Indiana University School of Medicine, Indianapolis, [4]Riley Hospital For Children At Indiana University, Carmel, IN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

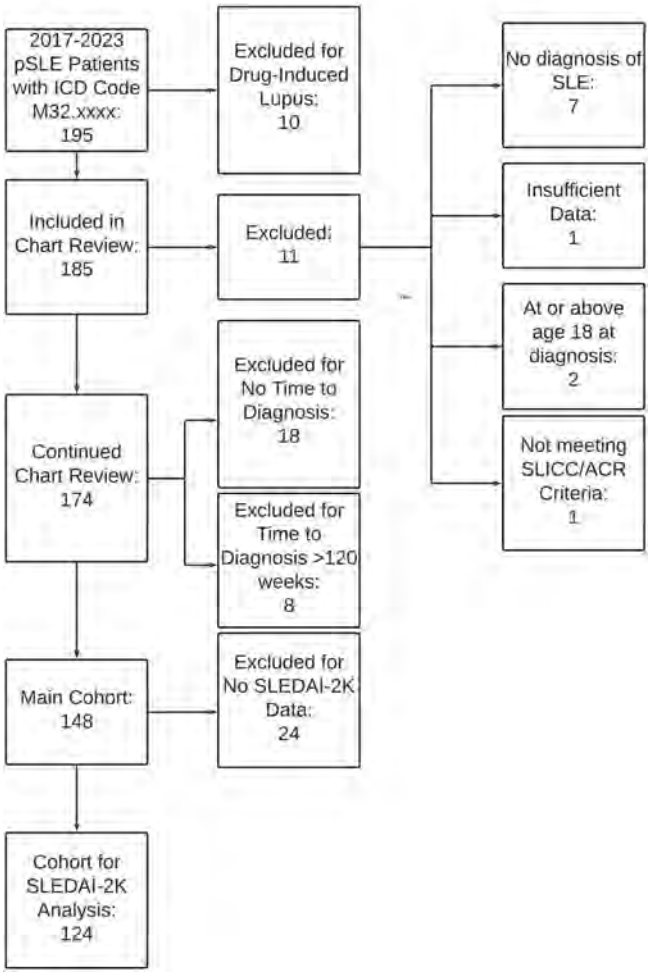
Background/Purpose: Early recognition and treatment of juvenile systemic lupus erythematosus (jSLE) improves outcomes and prevents disease-related mortality. This study examines the contributions of clinical factors (e.g. disease severity) and sociodemographic variables (e.g. neighborhood disadvantage, distance to care) to diagnostic delays.

Methods: This retrospective chart review included jSLE patients evaluated by the Division of Pediatric Rheumatology at Indiana University (IU) from Jan 2017 – Sept 2023. Participants were diagnosed before age 18 years and fulfilled the 1997 American College of Rheumatology (ACR) or Systemic Lupus Collaborating Clinics (SLICC) criteria for SLE (Figure 1). Time to diagnosis (TTD) was treated categorically: acute (< 4 weeks), subacute (5-12 weeks), and chronic (>12 weeks). Bivariate analyses were performed using Spearman correlation models and Wilcoxon-Kruskal-Wallis tests and multivariable analyses were performed using Generalized Linear Models, using SAS v9.4 (Figure 2).

Results: In bivariate analysis, the following clinical variables at diagnosis were associated with shorter TTD: neuropsychiatric symptoms (p=0.02), organ damage (p=0.04), pulse-dose corticosteroids (p=.01), and hospitalization (p=0.01). Higher disease activity at diagnosis, measured by SLEDAI-2K score, was associated with a trend towards shorter TTD when treated categorically, and this association reached significance when TTD was analyzed as a continuous variable (p= 0.04) (Figure 3). Renal disease was not associated with TTD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Exclusion Criteria



In bivariate analysis, private health insurance was associated with a longer TTD (p=0.04), while age, race, ethnicity, preferred language, urbanization level, distance to care, and ADI showed no association.

In multivariable analysis including all variables with p< 0.10 plus age and sex, only the presence of neuropsychiatric symptoms remained independently associated with a shorter TTD (p = 0.02).

Conclusion: Neuropsychiatric symptoms, organ damage, pulse steroid use, and hospitalization at diagnosis were associated with shorter diagnostic intervals, suggesting that more severe presentations may prompt faster evaluation. Private health insurance was associated with a longer time to diagnosis, potentially reflecting differences in healthcare access or referral patterns. Race, ethnicity, distance to care, and area-level deprivation index were not significantly associated with diagnostic delays. The lack of association may reflect the single-center design, which could limit variability in access to care and sociodemographic representation. While several clinical variables were associated with a shorter TTD in the bivariate analysis, only neuropsychiatric symptoms remained significant in the multivariate analysis. The diminished effects of the other clinical variables suggest either mediating or confounding effects which will be explored in further analysis. The study findings underscore the complex interplay between disease severity and healthcare system factors in influencing diagnostic timelines for pediatric lupus.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Bivariate and multivariable analysis of factors associated with Time to Diagnosis in juvenile Systemic Lupus Erythematosus (jSLE) (N=148)

	Acute (≤4 weeks) n=42	Subacute (5 – 12 weeks) n=47	Chronic (>12 weeks) n=59	Bivariate analysis p-value	Multivariable model p-value
Age at diagnosis, median (range)	14 (6 – 17)	13 (4 – 17)	14 (2 – 17)	.36	
Sex, n (%)					
Female	36 (28.4)	39 (30.7)	52 (40.9)	.69	
Male	6 (28.6)	8 (38.1)	7 (33.3)		
Race, n (%)					
American Indian/Alaskan Native	0 (0)	0 (0)	2 (100)	.80	
Asian	5 (41.7)	3 (25.0)	4 (33.3)		
Native Hawaiian or Other Pacific Islander	1 (100)	0 (0)	0 (0)		
Black	13 (28.9)	13 (28.9)	19 (42.2)		
White	20 (25.3)	30 (38.0)	29 (36.7)		
Multiracial	1 (33.3)	0 (0)	2 (66.7)		
Unknown	2 (33.3)	1 (16.7)	3 (50.0)		
Ethnicity, n (%)					
Hispanic	8 (27.6)	11 (37.9)	10 (34.5)	.77	
Non-Hispanic	34 (28.8)	36 (30.5)	48 (40.7)		
Insurance, n (%)					
Medicaid, CHIP, or Tricare	23 (35.9)	22 (33.3)	21 (31.8)	.04	.67
Private	19 (24.1)	24 (30.4)	36 (45.6)		
Uninsured	0 (0)	1 (33.3)	2 (66.7)		*excluded*[‡]
Primary Language, n (%)					
English	35 (26.9)	41 (31.5)	54 (41.5)	.21	
Other	7 (38.9)	6 (33.3)	5 (27.8)		
County Level Urbanization, n (%)					
Metropolitan (RUCC 1-3)	34 (27.0)	39 (31.0)	53 (42.1)	.20	
Non-Metropolitan (RUCC 4-9)	8 (36.4)	8 (36.4)	6 (27.3)		
Area Deprivation Index (tertials), n (%)					
0 – 2	15 (27.3)	18 (32.7)	22 (40.0)	.70	
3 – 6	14 (31.1)	10 (22.2)	21 (46.7)		
7 – 10	13 (27.1)	19 (39.6)	16 (33.3)		
Distance to Care (miles), median (range)	39.5 (2 – 642)	26 (2 – 177)	26 (2 – 192)	.96	
SLEDAI-2K score*, median (range)	18 (2 – 41)	16 (3- 57)	13 (3 – 36)	.10	
Presence of Neuropsychiatric Disease, n (%)					
Yes	9 (64.3)	2 (14.3)	3 (21.4)	.02	.02
No	29 (26.4)	37 (33.6)	44 (40.0)		
Presence of Renal Disease, n (%)					
Yes	22 (31.9)	24 (34.8)	23 (33.3)	.16	
No	20 (25.3)	23 (29.1)	36 (45.6)		
IV steroid pulse(s) within 3 months of diagnosis, n (%)					
Yes	26 (40.0)	18 (27.7)	21 (32.3)	.01	.40
No	16 (19.5)	29 (35.4)	37 (45.1)		
Hospitalized for lupus-related conditions within 3 months of diagnosis, n (%)					
Yes	32 (38.1)	27 (32.1)	25 (29.8)	<.01	
No	10 (15.9)	20 (31.8)	33 (52.4)		
Presence of damage, n (%)					
No (SLICC Damage Index =0)	22 (22.2)	34 (34.3)	43 (43.4)	.04	.93
Yes (SLICC Damage Index >0)	20 (40.8)	13 (26.5)	16 (32.7)		

*SLEDAI-2K N missing = 24; ‡excluded for small sample size

Abbreviations: CHIP = Children's Health Insurance Program; RUCC = United States Department of Agriculture Rural Urban Continuum Codes (2013); SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC = Systemic Lupus International Collaborating Clinics

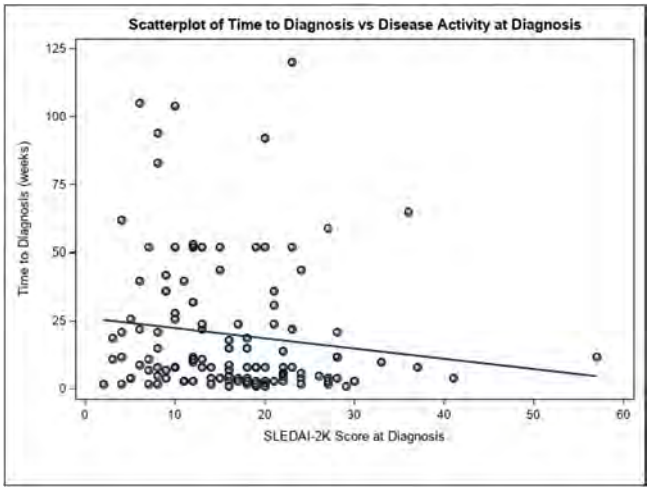


Figure 3. Scatterplot of Time to Diagnosis vs Disease Activity at Diagnosis

Disclosure: M. Harter: None; **R. Hetrick**: None; **J. Slaven**: None; **M. Rodriguez**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2425

Neutrophil Transcriptomics in SLE: Exploring Intrinsic, Ex Vivo Adaptation, and CAR-T Cell Therapy-Induced Changes

Ehsan Dehdashtian[1], Stefania Gallucci[2], Guangnan Hu[3], Dominic Borie[4] and **Roberto Caricchio**[5], [1]UMass Chan Medical School, Worcester, MA, [2]Temple University School of Medicine, Worcester, MA, [3]UMass Chan School of Medicine, Worcester, MA, [4]Kyverna Therapeutics, Emeryville, CA, [5]University of Massachusetts Chan Medical School, Worcester, MA

SESSION INFORMATION

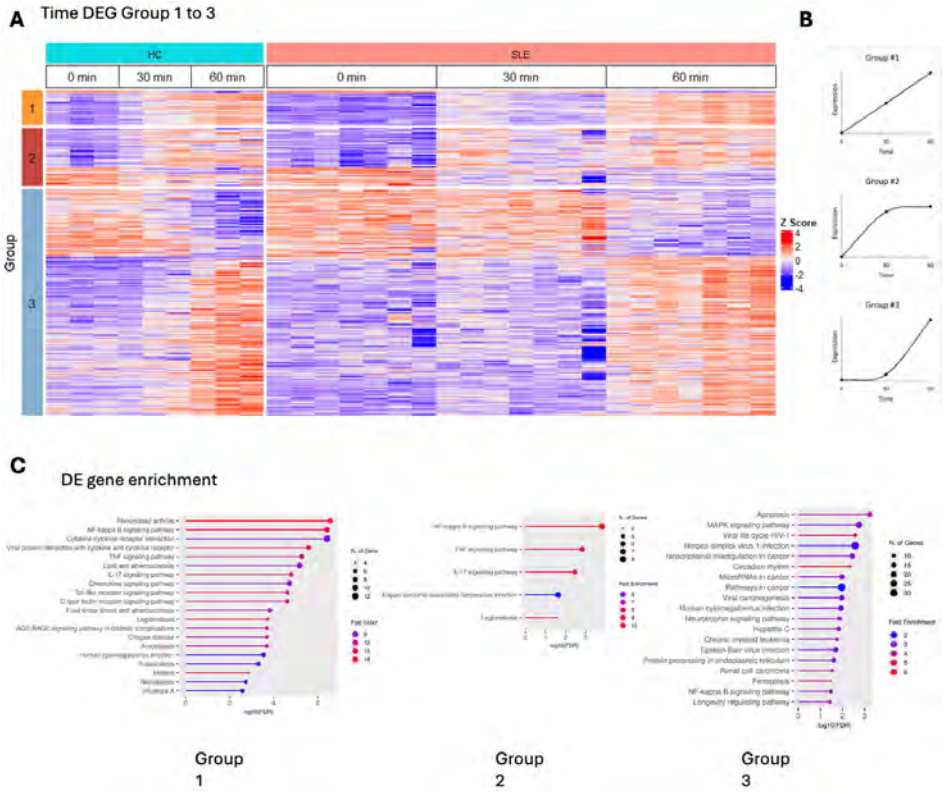
Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

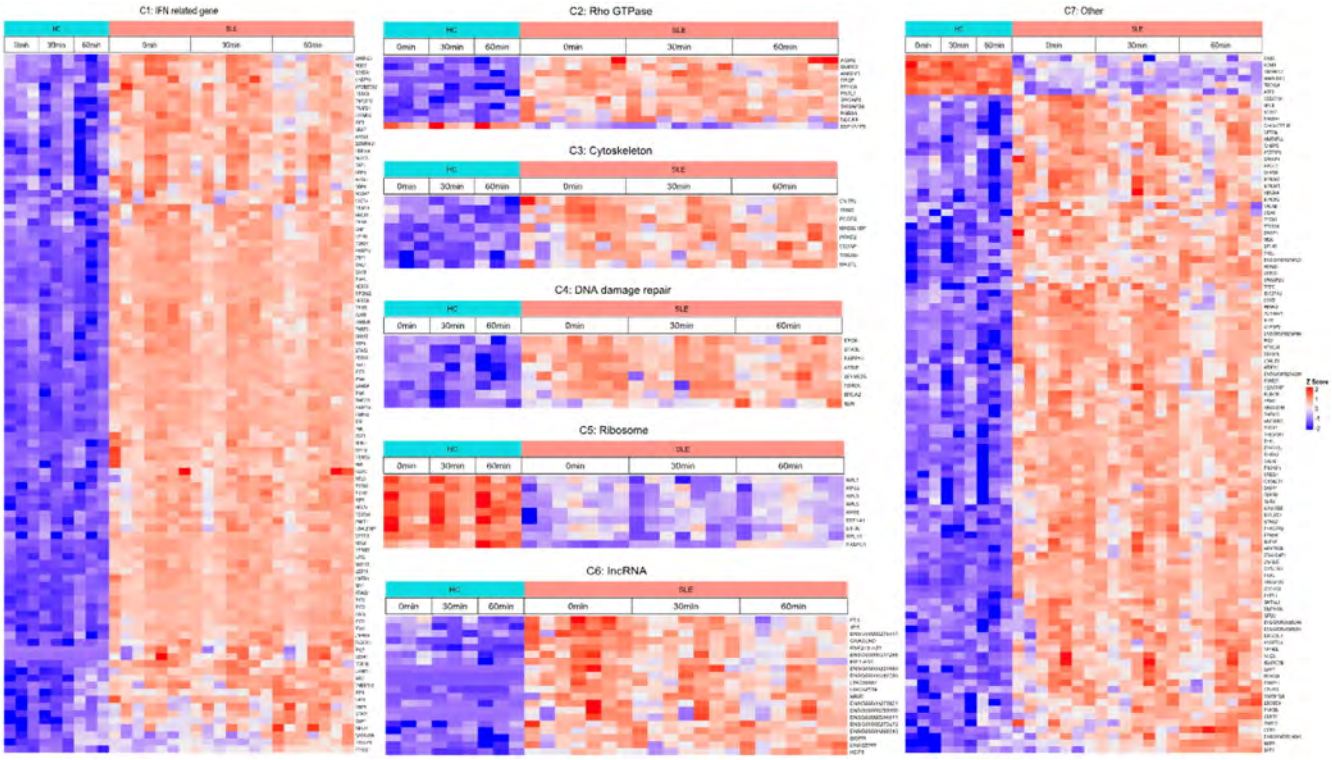
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by dysregulation of the adaptive and innate immune systems. Neutrophils, key players in innate immunity, significantly contribute to SLE pathogenesis. This study aimed to identify transcriptomic differences in neutrophils from SLE patients and healthy individuals, analyze ex vivo adaptation in gene expression dynamics, and evaluate the impact of chimeric antigen receptor (CAR)-T cell therapy on neutrophil transcriptomic profiles.

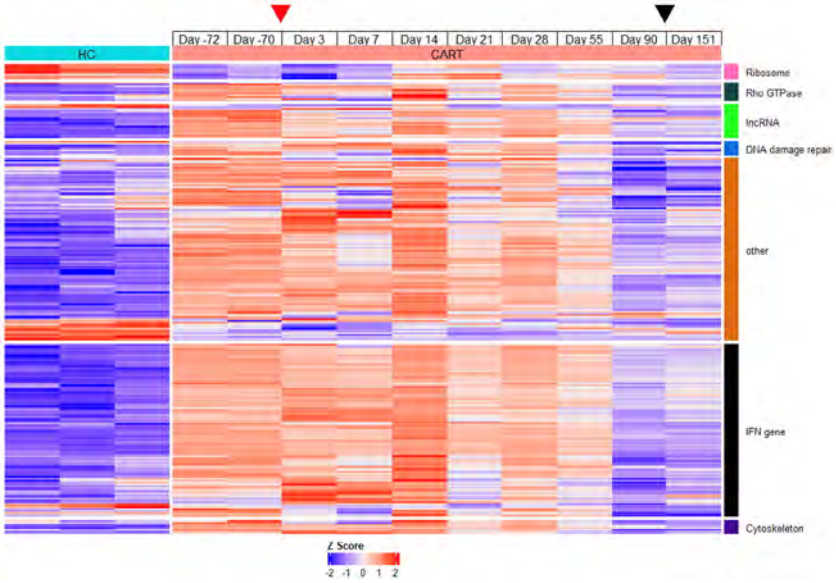


Heatmap of temporal transcriptomics in neutrophils and pathway enrichment analysis. (A) Heatmap displaying temporal transcriptomics of neutrophils categorized into three groups:(1) sustained changes from time 0 to 60 minutes, (2) changes from time 0 to 30 minutes followed by stabilization, and (3) changes only between 30 and 60 minutes. (B) Graphic Conceptualization of the 3 groups. (C) KEGG pathway enrichment analysis identifies key pathways impacted by time progression, including NF-κB activation, TNF signaling, and apoptosis, in neutrophils from both groups.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Clustered heatmap of intrinsic DEGs. Heatmap showing expression patterns of intrinsic DEGs categorized into seven clusters including interferon-related, Rho GTPase, cytoskeleton, DNA damage repair, ribosome, and long non-coding RNA (lncRNA). The "other" cluster includes genes with no clear pathway enrichment.



Longitudinal transcriptomic analysis post-CAR-T cell therapy. Heatmap visualizing intrinsic DEG expression in an SLE patient undergoing CAR T-cell therapy across baseline (two pre-treatment time points) and eight post-treatment time points. Samples from three healthy individuals serve as controls. Red arrowhead indicates day 0 (CAR T-cell infusion) and black arrowhead marks when the patient discontinued all immunosuppressive medications.

Methods: We utilized negative selection for neutrophil isolation from seven SLE patients and three healthy individuals. RNA sequencing was performed to assess transcriptomic differences between neutrophils from SLE and healthy individuals, ex vivo transcriptional dynamics over 60 minutes, and responses to lipopolysaccharide (LPS) stimulation. Additionally, longitudinal transcriptomic data from an SLE patient undergoing KYV-101 anti-CD19 CAR-T cell therapy were evaluated.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We identified 258 differentially expressed genes (DEGs) consistently distinguishing SLE neutrophils from healthy controls regardless of the ex vivo culture duration; these genes spanned multiple clusters, enriched in upregulation of interferon-related and DNA damage repair genes, and downregulation of ribosomal protein genes. Differential expression (DE) analysis for ex vivo adaptation revealed shared activation pathways, such as NF-κB and apoptosis, across time in neutrophils from both patients and healthy individuals. LPS stimulation highlighted overlapping inflammatory responses, demonstrating retained functional capacities in SLE neutrophils. Following CAR-T cell therapy of an SLE patient, the neutrophil transcriptomic profile realigned with healthy control characteristics, with most gene clusters approaching normalcy by three months post-treatment.

Conclusion: Neutrophils in SLE exhibit intrinsic, disease-specific transcriptomic alterations but also share certain ex vivo adaptation dynamics with healthy individuals across diverse biological pathways. Notably, anti-CD19 CAR-T cell therapy demonstrates a profound ability to reset neutrophil gene expression toward healthy patterns by three months post-treatment, despite targeting B cells rather than neutrophils directly. These findings provide insights into SLE pathogenesis and highlight potential therapeutic strategies targeting both adaptive and innate immunity.

Disclosure: E. Dehdashtian: None; **S. Gallucci**: None; **G. Hu**: None; **D. Borie**: Kyverna Therapeutics, 3, 8; **R. Caricchio**: Abbvie, 1, Cabaletta, 5, GlaxoSmithKlein(GSK), 1, Kyverna, 5, Novartis, 1.

Abstract Number: 2426

Physical Activity Patterns and Health-Related Quality of Life in Middle-Aged and Older Adults with Systemic Lupus Erythematosus

Sarah Lieber[1], Neha Nagpal[1], Julia Nguyen[2], Ashley Chung[2], Dongmei Sun[1], Iris Navarro-Millan[3], M. Carrington Reid[4] and Lisa Mandl[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, New York, [3]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY, [4]Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The benefits of physical activity are well established in older adults in the general population. Among older adults with rheumatic and musculoskeletal diseases, including systemic lupus erythematosus (SLE), physical activity has been associated with improved health-related quality of life [1]. However, the extent to which this relationship may be similar for sedentary behavior or impacted by SLE disease severity is not well understood. We sought to characterize the association of physical activity and sedentary behavior with patient-reported outcome measures and self-reported disability in middle-aged and older adults with SLE.

Methods: Adults ≥50 years with validated SLE were enrolled in a single-center cross-sectional study. Sociodemographic and disease features were self-reported. Patient-reported outcomes, disability status, and physical activity and sedentary behavior were ascertained using PROMIS-29, Valued Life Activities, and International Physical Activity Questionnaire surveys, respectively. Associations between physical activity and sedentary behavior and health-related quality of life domains were assessed using linear regression and adjusted for age, race, ethnicity, SLE duration, and SLE disease activity and organ damage.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of study participants with systemic lupus erythematosus (SLE)

Variable	N (%) or mean (SD)
Age (years) (N=80)	63.2 (8.5)
Gender (N=80)	
Female	76 (95.0)
Race (N=80)	
Asian	9 (11.3)
Black or African American	17 (21.3)
White	43 (53.8)
Other	11 (13.8)
Ethnicity (N=80)	
Hispanic or Latino	16 (20.0)
Not Hispanic or Latino	63 (78.8)
Declined to state	1 (1.3)
SLE duration (years) (N=79)	23.1 (14.5)
Hydroxychloroquine use (N=80)	62 (77.5)
Immunosuppressive medication[1] use (N=80)	34 (42.5)
SLE activity and organ damage	
Systemic Lupus Activity Questionnaire[2] score (N=72)	12.22 (7.2)
Brief Index of Lupus Damage[3] score (N=72)	2.64 (2.6)
Patient-reported outcome measures	
PROMIS-29[4] domain T-scores (N=80)	
Physical function	43.8 (10.3)
Anxiety	51.7 (10.7)
Depression	49.2 (10.1)
Fatigue	53.5 (11.5)
Sleep	53.9 (10.3)
Social roles	49.7 (10.8)
Pain	53.9 (11.7)
Disability	
Valued Life Activities[5] score (N=79)	0.8 (0.6)
Physical activity behaviors	
International Physical Activity Questionnaire[6]	
Physical activity (MET-minutes/week) (N=74)	3786 (3728)
Sedentary behavior (minutes/week) (N=71)	2213 (1136)

[1]Immunosuppressive medication: Methotrexate; Azathioprine; Mycophenolate mofetil; Mycophenolic acid; Belimumab; Cyclophosphamide; Rituximab; Tocilizumab; Cyclosporine; Tacrolimus
[2]Systemic Lupus Activity Questionnaire: Scores range from 0 to 47, with higher scores reflecting greater disease activity
[3]Brief Index of Lupus Damage: Scores range from 0 to 31, with higher scores reflecting greater disease damage
[4]PROMIS-29: Domain-specific scores are expressed in terms of T scores, where 50 represents the population mean
[5]Valued Life Activities: Scores range from 0-3, with higher scores reflecting greater disability
[6]International Physical Activity Questionnaire

Table 2. Unadjusted cross-sectional associations of physical activity and sedentary behavior with health-related outcomes in middle-aged and older adults with systemic lupus erythematosus

	Valued Life Activities	PROMIS-29 physical function	PROMIS-29 anxiety	PROMIS-29 depression	PROMIS-29 fatigue	PROMIS-29 sleep	PROMIS-29 social roles	PROMIS-29 pain
Parameter	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value
Physical activity	-2415.76 (-3646.52, -1185.01) **<0.01**	151.29 (83.43, 239.16) **<0.01**	-107.27 (-198.55, -16.00) **0.02**	-83.45 (-182.88, 15.98) 0.10	-195.12 (-270.46, -119.77) **<0.01**	-104.72 (-206.82, -2.61) **0.04**	222.49 (145.68, 299.31) **<0.01**	-117.15 (-197.62, -36.68) **<0.01**
Sedentary behavior	84.98 (-397.08, 527.05) 0.78	8.48 (-21.44, 38.39) 0.57	5.53 (-24.02, 35.08) 0.71	8.48 (-23.25, 40.21) 0.60	-0.55 (-27.87, 26.77) 0.97	-1.72 (-35.30, 31.86) 0.92	-15.20 (-44.07, 13.67) 0.30	-5.34 (-32.14, 21.46) 0.69

Table 3. Adjusted* cross-sectional associations of physical activity and sedentary behavior with health-related outcomes in middle-aged and older adults with systemic lupus erythematosus (SLE)

	Valued Life Activities	PROMIS-29 physical function	PROMIS-29 anxiety	PROMIS-29 depression	PROMIS-29 fatigue	PROMIS-29 sleep	PROMIS-29 social roles	PROMIS-29 pain
Parameter	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value	ß coefficient (95% CI) p-value
Physical activity	-1443.15 (-3574.61, 688.32) 0.18	47.21 (-99.09, 193.50) 0.52	-65.35 (-190.28, 59.58) 0.30	-37.24 (-179.95, 105.48) 0.60	-206.74 (-337.11, -76.36) **<0.01**	-17.93 (-147.71, 111.85) 0.78	253.42 (127.12, 379.72) **<0.01**	-1.17 (-141.78, 139.43) 0.99
Sedentary behavior	153.24 (-582.51, 888.98) 0.68	3.59 (-41.42, 48.59) 0.87	-6.97 (-43.78, 29.84) 0.71	9.92 (-32.01, 51.85) 0.64	1.86 (-39.72, 43.44) 0.93	-0.24 (-39.68, 39.20) 0.99	-34.85 (-75.97, 6.27) 0.09	-2.13 (-44.24, 39.97) 0.92

*Adjusted for age, race, ethnicity, SLE duration, disease activity, and organ damage

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Participants (N=80) were primarily female (95.0%) with mean age and SLE duration of 63.2 (standard deviation [SD] =8.5) and 23.1 (SD=14.5) years, respectively. Physical activity was associated with multiple health-related quality of life domains in unadjusted analyses, but after adjustment for covariates, only the association of physical activity with fatigue (ß coefficient -206.74, 95% confidence interval [CI] [-337.11, -76.36], $p < 0.01$) and social roles (ß coefficient 253.42, 95% CI [127.12, 379.72], $p < 0.01$) remained significant. Sedentary behavior was not significantly associated with any aspect of health-related quality of life pre- or post-covariate adjustment.

Conclusion: In this cross-sectional study of middle-aged and older adults with SLE, physical activity was associated with less fatigue and greater social engagement. Physical activity may have favorable effects on fatigue and social engagement in this growing population of patients.

Reference:
1. Kumthekar A et al. J Rheumatol 2023;50(6):835-41.

Disclosure: S. Lieber: None; **N. Nagpal**: None; **J. Nguyen**: None; **A. Chung**: None; **D. Sun**: None; **I. Navarro-Millan**: None; **M. Reid**: None; **L. Mandl**: ACP, 12, Associate Editor Annals of Internal Medicine, Wolters, 9.

Abstract Number: 2427

Kidney-Specific Four-Protein Index Outperforms Conventional Measures for Detecting Early Kidney Damage in Lupus Nephritis and Diabetic Kidney Disease

Sepehr Taghavi[1], Ines Silva[2], Jacob Vasquez[3], Vasileios Kyttaris[4], Tyler O'Malley[5] and Mike Nerenberg[6], [1]Exagen Inc, Escondido, CA, [2]Exagen, Carlsbad, CA, [3]Exagen, Inc., Vista, CA, [4]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, [5]Exagen, Vista, CA, [6]Exagen, DEL MAR, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Early detection of renal involvement in diabetic kidney disease (DKD) and lupus nephritis (LN) is critical but remains challenging. Conventional renal biomarkers (serum creatinine, eGFR, albuminuria) are often insensitive to subclinical damage and rise late in disease. We identified four kidney-specific plasma proteins (uromodulin [UMOD], myo-inositol oxygenase [MIOX], heparanase [HPSE], and AREL1) linked to distinct renal processes: tubular transport, metabolic stress, extracellular matrix remodeling, and immune signaling. We hypothesized that an index combining these mechanistically distinct markers could detect early renal pathology in DKD and LN, outperforming conventional measures.

Methods: Plasma UMOD, MIOX, HPSE, and AREL1 were measured by immunoassay in three patient cohorts: 1) biopsy-confirmed active LN (n=31), compared to SLE without active proteinuria (n=31) and matched apparently healthy volunteer controls (AHV, n=31), ; 2) early-stage type 1 DKD obtained from the NIH-sponsored PERL study (n=49, mean eGFR=66 mL/min/1.73m^2); and 3) late-stage type 2 DKD obtained from the FIND study (n=50, mean eGFR≈21 mL/min/1.73m^2). The latter two cohorts were compared to matched AHVs (total AHVs=99). Logistic regression models using these four biomarkers were trained to distinguish DKD and LN from matched AHVs, generating DKD and LN indices (predicted probabilities). ROC analyses compared biomarker indices against eGFR, including comparisons of early DKD stratified by iohexol-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

determined GFR (iGFR), cystatin C, and albuminuria. AHV versus LN were stratified by urinary protein-to-creatinine ratio (UPCR). Data from PERL and FIND were provided by NIDDK CR, a program of the National Institute of Diabetes and Digestive and Kidney Diseases.

Results: The LN Index strongly differentiated LN from AHVs (AUC=1.00) and from non-proteinuric SLE (AUC=0.99), significantly outperforming eGFR (AUC=0.27 for LN vs AHV, AUC=0.48 for LN vs non-proteinuric SLE). The DKD Index robustly discriminated both early DKD (PERL, AUC=0.92) and late DKD (FIND, AUC=0.97) from AHVs, surpassing eGFR performance (AUC=0.81 early DKD, AUC=0.94 late DKD). Subgroup analyses demonstrated superior sensitivity of biomarker

Table 1. Demographic and Clinical Characteristics of Study Cohorts

			DKD			SLE	
	Total (N=291)	AHV (DKD Matched) (N=99)	PERL (Early Disease) (N=49)	FIND (Late Disease) (N=50)	AHV (LN Matched) (N=31)	LN (N=31)	Non-active Proteinuria (N=31)
Sex - n(%)							
Female	173 (59.5%	47 (47.5%)	26 (53.1%)	21 (42.0%)	26 (83.9%)	26 (83.9%)	27 (87.1%)
Male	118 (40.5%	52 (52.5%)	23 (46.9%)	29 (58.0%)	5 (16.1%)	5 (16.1%)	4 (12.9%)
Race - n(%)							
Black	92 (31.6%)	33 (33.3%)	14 (28.6%)	19 (38.0%)	10 (32.3%)	10 (32.3%)	6 (19.4%)
White	137 (47.1%	47 (47.5%)	35 (71.4%)	12 (24.0%)	11 (35.5%)	11 (35.5%)	21 (67.7%)
Hispanic	42 (14.4%)	19 (19.2%)	0 (0.0%)	19 (38.0%)	0 (0.0%)	3 (9.7%)	1 (3.2%)
Asian	14 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (19.4%)	6 (19.4%)	2 (6.5%)
Other	6 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.9%)	1 (3.2%)	1 (3.2%)
Age							
Mean (SD)	50.0 (14.6)	56.6 (11.0)	55.0 (7.8)	58.1 (13.3)	34.7 (9.5)	35.0 (9.8)	38.0 (13.8)
Creatinie							
Mean (SD)	1.8 (2.3)	0.9 (0.2)	1.2 (0.2)	5.9 (3.2)	0.9 (0.2)	0.9 (0.5)	0.8 (0.2)
eGFR							
Mean (SD)	74.6 (35.3)	86.6 (22.7)	66.0 (16.0)	20.6 (29.0)	88.0 (16.6)	99.3 (30.5)	99.7 (21.7)

Table 1. Demographic and Clinical Characteristics of Study Cohorts
Demographic and clinical features of subjects included in the analysis. The cohorts consist of apparently healthy volunteers (AHV) matched to lupus nephritis (LN; biopsy-confirmed) and diabetic kidney disease (DKD), early-stage DKD from the PERL study (type 1 diabetes, mean eGFR 66 mL/min/1.73 m²), late-stage DKD from the FIND study (type 2 diabetes, mean eGFR 21 mL/min/1.73 m²), and patients with systemic lupus erythematosus (SLE) without active proteinuria. The distribution of sex, race, mean age, serum creatinine, and eGFR values are summarized for each group.

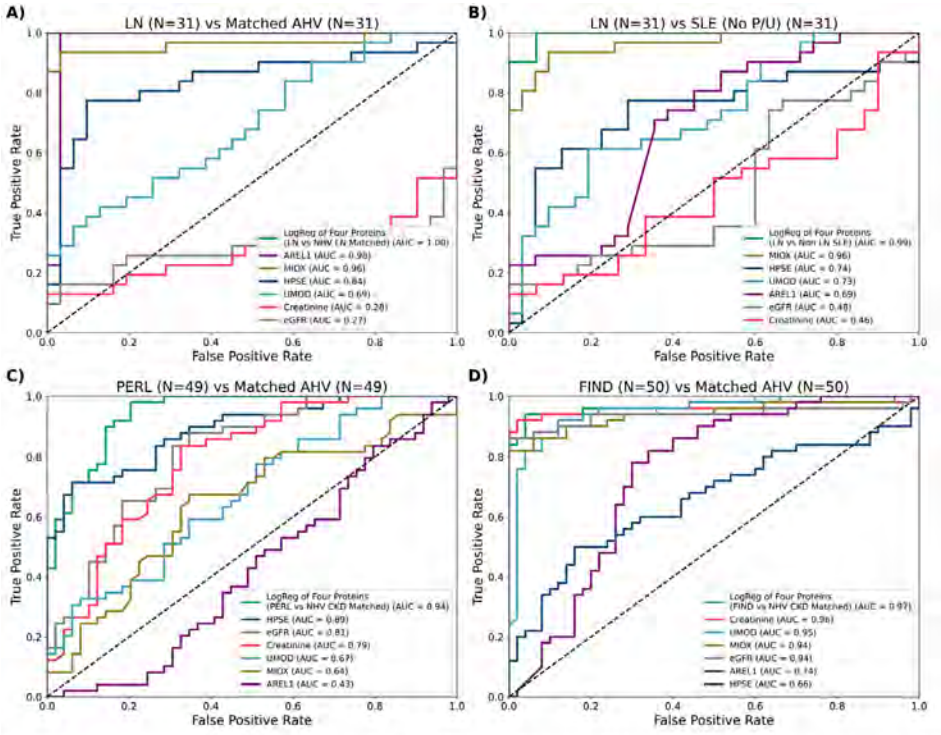


Figure 1. Receiver Operating Characteristic (ROC) Curve Analysis of Biomarker Performance. ROC curves evaluating the diagnostic accuracy of individual kidney-specific biomarkers (UMOD, MIOX, HPSE, AREL1), a combined logistic regression index (Four-Protein Index), and conventional measures (creatinine, eGFR) for distinguishing: (A) biopsy-confirmed lupus nephritis (LN) from matched apparently healthy volunteers (AHVs); (B) biopsy-confirmed LN from patients with systemic lupus erythematosus (SLE) without active proteinuria; (C) early-stage type 1 diabetic kidney disease (DKD; PERL cohort) from matched AHVs; and (D) late-stage type 2 DKD (FIND cohort) from matched AHVs. The Four-Protein Index consistently showed superior performance compared to eGFR and creatinine across all comparisons, demonstrating its robust utility for detecting kidney damage in both LN and DKD.

Figure 1. Receiver Operating Characteristic (ROC) curve analysis of biomarker performances

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

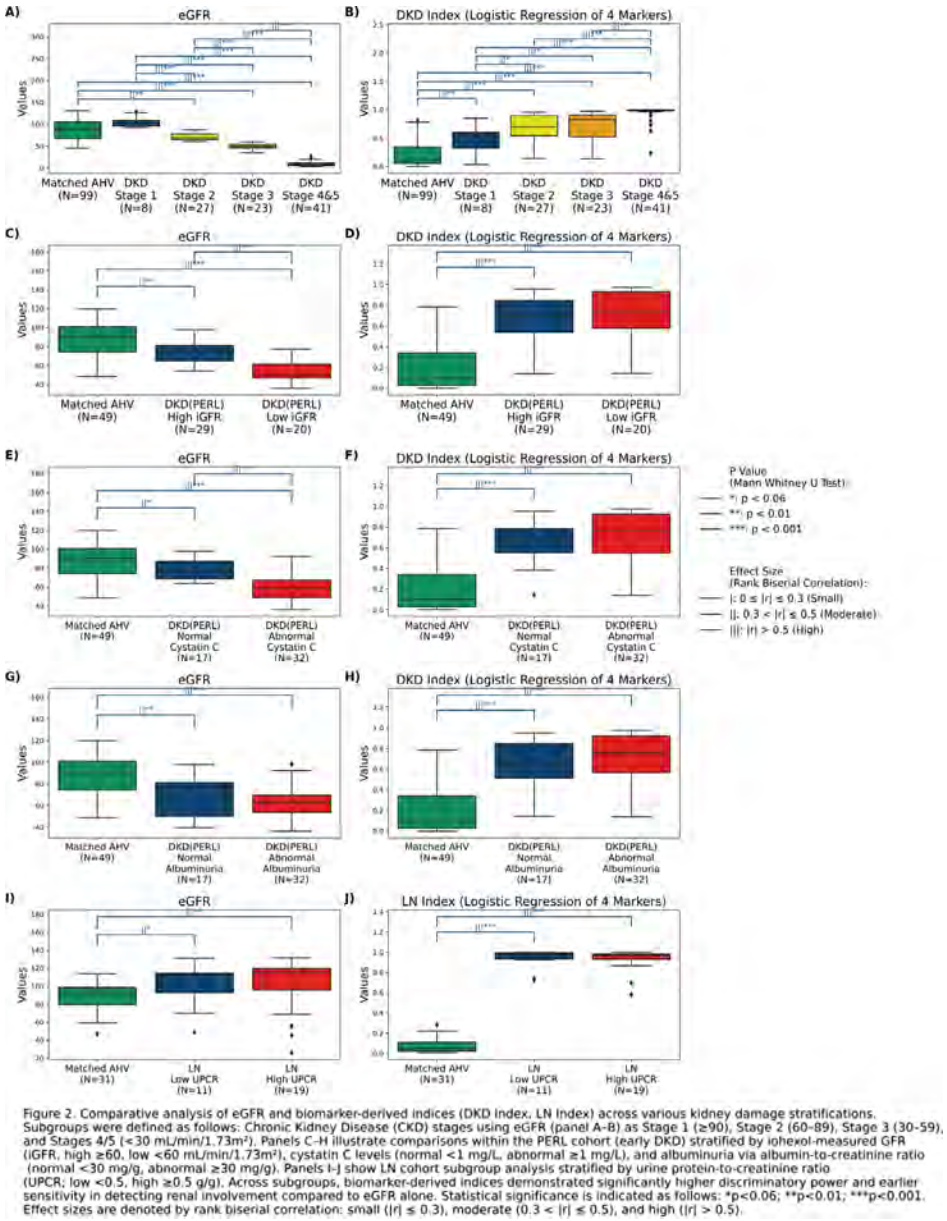


Figure 2. Comparative analysis of eGFR and biomarker-derived indices (DKD index, LN index) across various kidney damage stratifications. Subgroups were defined as follows: Chronic Kidney Disease (CKD) stages using eGFR (panel A–B) as Stage 1 (≥90), Stage 2 (60–89), Stage 3 (30–59), and Stages 4/5 (<30 mL/min/1.73m²). Panels C–H illustrate comparisons within the PERL cohort (early DKD) stratified by iohexol-measured GFR (iGFR, high ≥60, low <60 mL/min/1.73m²), cystatin C levels (normal <1 mg/L, abnormal ≥1 mg/L), and albuminuria via albumin-to-creatinine ratio (normal <30 mg/g, abnormal ≥30 mg/g). Panels I–J show LN cohort subgroup analysis stratified by urine protein-to-creatinine ratio (UPCR; low <0.5, high ≥0.5 g/g). Across subgroups, biomarker-derived indices demonstrated significantly higher discriminatory power and earlier sensitivity in detecting renal involvement compared to eGFR alone. Statistical significance is indicated as follows: *p<0.06; **p<0.01; ***p<0.001. Effect sizes are denoted by rank biserial correlation: small (|r| ≤ 0.3), moderate (0.3 < |r| ≤ 0.5), and high (|r| > 0.5).

indices compared to eGFR for detecting early kidney damage defined by iGFR, cystatin C, or albuminuria in DKD. The LN index also outperformed UPCR in LN, while eGFR values mostly remained in the normal range.

Conclusion: A plasma biomarker index combining UMOD, MIOX, HPSE, and AREL1 detects DKD and LN with high sensitivity and specificity, identifying organ damage earlier and more clearly than standard measures. These kidney-specific proteins capture distinct pathophysiologic axes of renal damage, supporting their use as early, disease-specific indicators of nephropathy in diabetes and lupus. Such a multi-marker approach could improve timely diagnosis and monitoring of renal involvement beyond conventional tests.

Disclosure: S. Taghavi: Exagen, 3; **I. Silva**: None; **J. Vasquez**: None; **V. Kyttaris**: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2; **T. O'Malley**: Exagen, 12,, 3, 11; **M. Nerenberg**: Exagen, 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2428

Differences in Dyspigmentation and Scarring Across Cutaneous Lupus Erythematosus Categories and Subtypes

Shae Chambers[1], Aretha On[2], Xiwei Yang[2], Lais Lopes Almeida Gomes[1], Touraj Khosravi-Hafshejani[3], Hammad Ali[3], Rui Feng[4] and Victoria Werth[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [3]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, U.S./Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, U.S., Philadelphia, PA, [4]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is a chronic autoimmune disease marked by skin lesions that can vary in appearance and severity. Subacute cutaneous erythematosus (SCLE), acute cutaneous erythematosus (ACLE), and chronic cutaneous erythematosus (CCLE) make up the CLE categories and CCLE may be further subtyped.

Table 1. Dyspigmentation & Scarring Scores Across CLE Categories & CCLE Subtypes

CLE Categories & CCLE Subtypes	*Median Dyspigmentation [Q1, Q3]*	*Dyspigmentation p-value*	*Median Scarring [Q1, Q3]*	*Scarring p-value*	*Dyspigmentation & Scarring Correlation r-value*	*Dyspigmentation & Scarring Correlation p-value*
ACLE (41)	3 [2,4]	0.0163	0 [0,0]	p<2.2e-16	0.123	.298
SCLE (130)	8 [2,12]		0 [0,0]		0.158	0.517
CCLE (329)	8 [4,12]		4 [1,7]		0.590	5.56e-34
DLE (293)	8 [4,14]	8.17e-4	5 [2,7]	4.14e-10	0.544	5.61e-24
LET (20)	1 [0,2.5]		0 [0,0.5]		0.132	0.0819
Panniculitis (12)	4 [2,4]		2 [2,6]		0.671	.017
Chilblain (4)	3 [2.5,3.5]		0 [0, 0.25]		-0.087	0.728

Key: CLE = cutaneous lupus erythematous, ACLE = acute cutaneous lupus erythematous, SCLE = subacute cutaneous lupus erythematous, CCLE = chronic cutaneous lupus erythematous, DLE = discoid lupus erythematous, LET = tumid lupus erythematous, Q1 = first quartile, Q3 = third quartile. Values for median dyspigmentation and median scarring correlate to Cutaneous Lupus Erythematous Disease Area and Severity Index damage score dyspigmentation and scarring aspects respectively. P-values in columns in columns three and five represent differences in dyspigmentation and scarring across CLE categories and CCLE subtypes using the Kruskal-Wallis test. R-values represent correlations between dyspigmentation and scarring across CLE categories and CCLE subtypes using the Spearman's rank-order correlation test.

Figure 1

Figure 1. Comparison of median dyspigmentation and scarring scores across Cutaneous Lupus Erythematosus Categories. Dunn-Bonferroni post-hoc test run to analyze pairwise comparisons following Kruskal-Wallis test. CLE = cutaneous lupus erythematosus, ACLE = acute cutaneous lupus erythematous, SCLE = subacute cutaneous lupus erythematous, CCLE = chronic cutaneous lupus erythematous.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

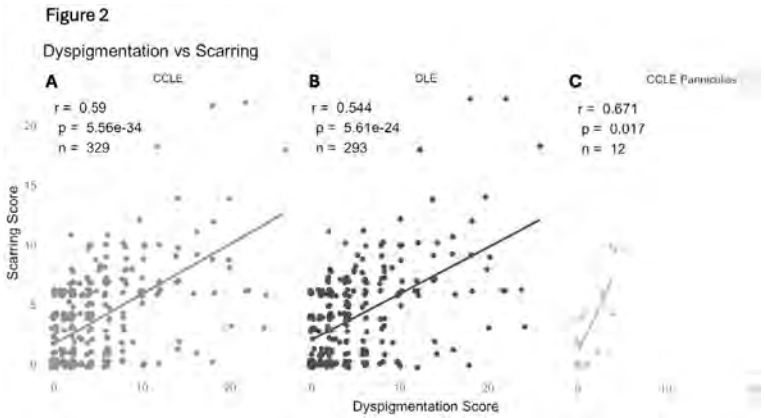


Figure 2. Correlation of scarring and dyspigmentation in Cutaneous Lupus Erythematosus Categories & Subtypes. Spearman's rank-order correlation between scarring and dyspigmentation scores for each patient visit where dyspigmentation was highest. (A) CCLE (B) DLE (C) Panniculitis. r = Spearman's rank correlation coefficient, CCLE = chronic cutaneous lupus erythematous, DLE = discoid lupus erythematous.

While dyspigmentation and scarring are recognized as complications of discoid lupus erythematosus (DLE), no studies have investigated scarring and dyspigmentation across all the CLE categories and subtypes.

Methods: To better characterize dyspigmentation and scarring in CLE, we conducted a cross-sectional review of our IRB-approved CLE database at the University of Pennsylvania. Patients were divided by category and CCLE subtype. Dyspigmentation and scarring were quantified using components of the CLE Disease Area and Severity Index damage (CLASI-D) score. Data on dyspigmentation and scarring were captured from the patient visit where dyspigmentation was highest. The Kruskal-Wallis test was used to compare dyspigmentation and scarring scores across CLE categories and CCLE subtypes. A Post-hoc Dunn analysis was used to check for pairwise comparisons between groups. The Spearman's rank-order correlation test was used to assess the correlations between dyspigmentation and scarring.

Results: A total of 500 patients were included in the study. Dyspigmentation and scarring significantly differed between CLE categories and CCLE subtypes ($p < .01$). Across categories, CCLE had the highest medians for dyspigmentation and scarring. Across CCLE subtypes, DLE had the highest medians for dyspigmentation and scarring. Dyspigmentation and scarring were significantly positively correlated in CCLE, DLE, and LE Panniculitis ($p < .01$).

Conclusion: Our findings show that scarring and dyspigmentation do not necessarily correlate in CLE except for CCLE as a whole and the CCLE subtypes of DLE and LE panniculitis. These CLE categories and CCLE subtypes are known to have higher rates of long-lasting disease damage. Dyspigmentation and scarring correlation differences highlight the importance of accurate assessment and documentation of both elements of damage. Our results reflect important differences in the CLE categories and CCLE subtypes which may be helpful for clinicians and patients as they navigate the course of the disease.

Disclosure: S. Chambers: None; **A. On**: None; **X. Yang**: None; **L. Lopes Almeida Gomes**: None; **T. Khosravi-Hafshejani**: Pfizer, 1; **H. Ali**: None; **R. Feng**: None; **V. Werth**: AbbVie/Abbott, 2, Alpine Immune Sciences, 2, Amgen, 2, 5, AnaptysBio, 2, argenx, 2, AstraZeneca, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Calyx, 2, Caribou, 2, CESAS Medical, 6, Corbus Pharmaceuticals, 5, Crisalis, 2, CSL Behring, 2, 5, Cugene, 2, Eli Lilly, 2, EMD Serono, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 2, 5, Immunovant, 2, Innovaderm, 2, Janssen, 2, Kyowa Kirin, 2, MAPI Trust, 9, Merck KGaA, Darmstadt, Germany, 2, N/A, 12, The University of Pennsylvania owns the copyright for the CLASI., Nektar, 2, Nuvig Pharmaceuticals, 2, Pfizer, 2, 5, Priovant, 5, Regeneron, 2, 5, Rome Therapeutics, 2, 5, Sanofi, 2, Takeda, 2, UCB, 2, Ventus, 2, 5, Viela Bio, 2, 5, Xencor, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2429

mHealth-enabled Peer Coaching for Fatigue in Systemic Lupus Erythematosus (SLE): Preliminary Results from the Restore Energy, Activity Can Help (REACH) Pilot Randomized Controlled Trial

Shanthini Kasturi[1], Erin Morrissey[1], Anna Deck[2], Nina Gulati[2], Zoe Gilbard[2], Kiran Singh[1], Monique Gore-Massy[3], Faye Chiu[4], Priscilla Calvache[5], Jillian Rose-Smith[5], Andre Ogura[6], Lucas Ogura Dantas[6], Wambui Machua[7], Julia Nguyen[8], Lisa Mandl[5], Hocine Tighiouart[1], Ludovic Trinquart[2], Iris Navarro-Millan[9] and Sara Folta[10], [1]Tufts Medical Center, Boston, MA, [2]Tufts University School of Medicine, Boston, MA, [3]N/A, West Orange, NJ, [4]N/A, New York, NY, [5]Hospital for Special Surgery, New York, NY, [6]Ambulomics, Arlington, MA, [7]Piedmont Healthcare, Atlanta, GA, [8]Hospital for Special Surgery, New York, [9]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY, [10]Tufts Friedman School of Nutrition, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Sociodemographic and clinical characteristics of participants

	REACH Peer Coaching Intervention (n=16)	REACH App Control (n=17)	All Participants (n=33)
Sociodemographics			
Age [mean (SD)]	41.1 (15.0)	43.6 (13.9)	42.4 (14.3)
Female	13 (81.3%)	15 (88.2%)	28 (84.9%)
Race			
Asian	2 (12.5%)	6 (35.3%)	8 (24.2%)
Black/African-American	5 (31.3%)	7 (41.2%)	12 (36.4%)
White	9 (56.3%)	3 (17.7%)	12 (36.4%)
Other	0 (0.0%)	1 (5.9%)	1 (3.0%)
Ethnicity			
Hispanic	3 (18.8%)	1 (5.9%)	4 (12.1%)
Insurance Type			
Medicaid	2 (12.5%)	3 (17.7%)	5 (15.2%)
Medicare	2 (12.5%)	3 (17.7%)	5 (15.2%)
Commercial/Private	11 (68.8%)	11 (64.7%)	22 (66.7%)
No Insurance	1 (6.3%)	0 (0.0%)	1 (3.0%)
Education			
High School	3 (18.8%)	2 (11.8%)	5 (15.2%)
Associates degree	4 (25.0%)	3 (17.7%)	7 (21.2%)
Bachelors degree	4 (25.0%)	6 (35.3%)	10 (30.3%)
Graduate degree	5 (31.3%)	6 (35.3%)	11 (33.3%)
Employment			
Part time	0 (0.0%)	2 (11.8%)	2 (6.1%)
Full time	11 (68.8%)	12 (70.6%)	23 (69.7%)
Looking	1 (6.3%)	0 (0.0%)	1 (3.0%)
Disabled	1 (6.3%)	1 (5.9%)	2 (6.1%)
Student	1 (6.3%)	1 (5.9%)	2 (6.1%)
Retired	2 (12.5%)	1 (5.9%)	3 (9.1%)
Smartphone Type			
Android	4 (25.0%)	5 (29.4%)	9 (27.3%)
iPhone	12 (75.0%)	12 (70.6%)	24 (72.7%)
Clinical information			
Lupus disease duration [median years (25th, 75th percentiles)]	8.0 (2.5, 14.1)	10.8 (5.8, 30.1)	9.7 (3.1, 23.8)
SLEDAI [median (25th, 75th percentiles)]	2.0 (0.0, 2.0)	0.5 (0.0, 2.0)	2.0 (0.0, 2.0)
SLICC/ACR Damage Index [median (25th, 75th percentiles)]	0.0 (0.0, 1.0)	0.5 (0.0, 2.0)	0.0 (0.0, 1.0)
Diagnosis of Fibromyalgia	2 (12.5%)	4 (23.5%)	6 (18.2%)
Diagnosis of Anxiety	5 (31.3%)	5 (29.4%)	10 (30.3%)
Diagnosis of Depression	6 (37.5%)	5 (29.4%)	11 (33.3%)
BMI [mean (SD)]	28.1 (7.3)	29.6 (4.7)	28.9 (6.1)
Baseline Fatigue Severity Scale Score [mean (SD)]	5.7 (0.9)	5.5 (0.7)	5.6 (0.8)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. REACH program adherence rates and acceptability ratings

Table 2. REACH program adherence rates and acceptability ratings (mean likelihood to recommend out of 10) with 95% confidence intervals*

	REACH Peer Coaching Intervention	REACH App Control	All Participants
Adherence	n=13	n=16	n=29
REACH Program Completion Rate	84.6% (55.6–96.4%)	93.8% (69.8–99.1%)	89.7% (73.6–96.4%)
Mean Educational Module Completion Rate	92.3% (77.2–100.0%)	81.9% (64.5–99.2%)	86.6% (74.9–98.2%)
Mean Weekly Physical Activity Log Completion Rate	64.2% (40.4–87.9%)	56.8% (39.4–74.2%)	60.1% (46.0–74.2%)
Mean Weekly Mood/Energy Check-In Completion Rate	96.8% (93.9–99.8%)	82.3% (67.9–96.7%)	88.8% (80.5–97.2%)
Mean Weekly Patient-Reported Outcome Survey Completion Rate	93.0% (87.1–98.8%)	85.9% (76.4–95.5%)	89.1% (83.2–95.0%)
Acceptability	n=12	n=15	n=27
Educational Modules	8.42 (7.57–9.27)	8.00 (6.74–9.26)	8.19 (7.41–8.97)
REACH App	7.50 (6.36–8.64)	6.93 (5.57–8.29)	7.19 (6.29–8.09)
REACH Peer Coaching	7.42 (5.89–8.95)	n/a	n/a
REACH Program	8.42 (7.64–9.20)	6.80 (5.65–7.95)	7.52 (6.74–8.30)

*Adherence rates are calculated for the 29 participants who had completed data collection at the time of submission. Acceptability rates are calculated for the 27 participants who submitted 12-week surveys.

Background/Purpose: Fatigue is a highly prevalent and debilitating symptom affecting up to 90% of individuals living with systemic lupus erythematosus (SLE). Despite its significant impact, fatigue remains difficult to treat due to its complex, multifactorial origin, including behavioral and psychosocial factors. While physical activity interventions have shown promise in reducing SLE-related fatigue, they often fail to address these multiple factors and have been limited by their in-person format. The aim of this study is to evaluate the feasibility and preliminary efficacy of the Restore Energy, Activity Can Help (REACH) mobile health (mHealth)-enabled peer coaching intervention for fatigue in SLE.

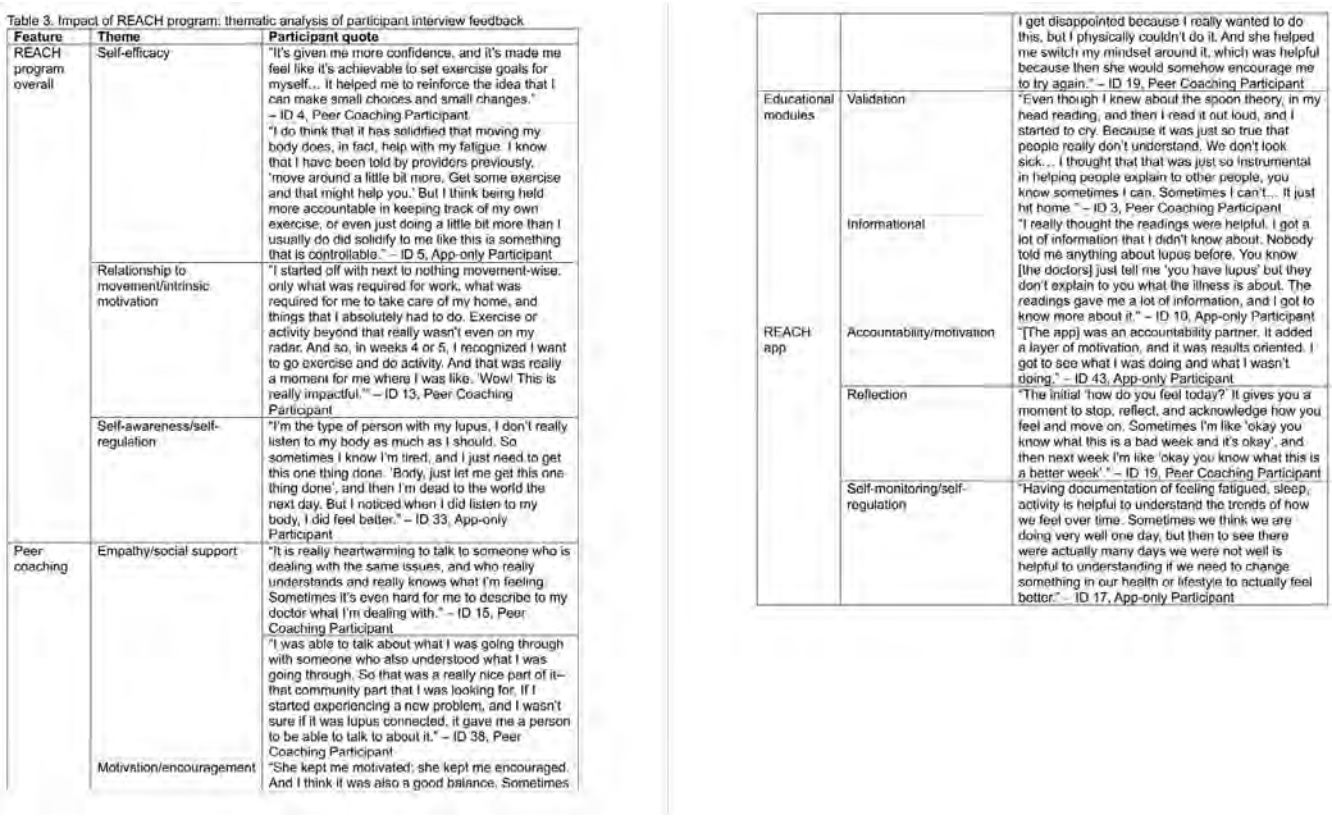
Methods: Individuals meeting 2019 ACR SLE classification criteria were enrolled in this open-label pilot randomized controlled trial. Participants were randomized to the REACH mHealth-enabled peer coaching intervention or the REACH mHealth application (app)-only control arm. Participants in the intervention arm were paired with trained coaches with lived SLE experience who supported participants through a 12-week structured program promoting physical activity facilitated by the REACH app. Program feasibility was assessed via enrollment and adherence rates, and acceptability was evaluated with participant net promoter scores. Preliminary efficacy of the intervention was examined by comparing Fatigue Severity Scale (FSS) scores between arms at 12 weeks using ANCOVA. All participants were interviewed for feedback at program completion.

Results: Thirty-three of 43 eligible individuals screened enrolled (76.7% enrollment rate), with a mean baseline FSS score of 5.6 (SD 0.8) (Table 1). In the 29 participants in whom data collection has been completed to date, 26 finished the program (completion rate 89.7%) (Table 2). Program adherence rates were high, especially in the peer coaching arm, in which mean completion rates of educational modules, weekly check-ins and patient-reported outcome surveys were over 90% (Table 2). At 12 weeks, mean FSS scores were 0.8 (95% CI 0.2 to 1.5) lower in the coaching arm than the app-only arm, and a clinically meaningful improvement of ^{3} 0.6 was achieved in 75% of participants in the coaching arm vs. 40% in the app arm. Likelihood to recommend the program and its individual components were higher in the coaching arm than the app-only arm (Table 2). Participants in both arms shared that the program was impactful, citing improvements in self-efficacy and increased self-awareness and self-regulation facilitated by the accountability and motivation provided by both the peer coach and the REACH app. (Table 3).

Conclusion: The REACH peer coaching intervention was feasible and demonstrated promising preliminary efficacy for reducing fatigue in SLE. Participants in the coaching arm showed greater improvement in fatigue, with a higher proportion achieving a clinically meaningful benefit than in the app-only arm. Participant engagement and satisfaction were high. These

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Impact of REACH program: thematic analysis of participant interview feedback



Feature	Theme	Participant quote
REACH program overall	Self-efficacy	"It's given me more confidence, and it's made me feel like it's achievable to set exercise goals for myself... It helped me to reinforce the idea that I can make small choices and small changes." – ID 4, Peer Coaching Participant
		"I do think that it has solidified that moving my body does, in fact, help with my fatigue. I know that I have been told by providers previously, 'move around a little bit more, Get some exercise and that might help you.' But I think being held more accountable in keeping track of my own exercise, or even just doing a little bit more than I usually do did solidify to me like this is something that is controllable." – ID 5, App-only Participant
	Relationship to movement/intrinsic motivation	"I started off with next to nothing movement-wise, only what was required for work, what was required for me to take care of my home, and things that I absolutely had to do. Exercise or activity beyond that really wasn't even on my radar. And so, in weeks 4 or 5, I recognized I want to go exercise and do activity. And that was really a moment for me where I was like, 'Wow! This is really impactful.'" – ID 13, Peer Coaching Participant
	Self-awareness/self-regulation	"I'm the type of person with my lupus, I don't really listen to my body as much as I should. So sometimes I know I'm tired, and I just need to get this one thing done. 'Body, just let me get this one thing done', and then I'm dead to the world the next day. But I noticed when I did listen to my body, I did feel better." – ID 33, App-only Participant
Peer coaching	Empathy/social support	"It is really heartwarming to talk to someone who is dealing with the same issues, and who really understands and really knows what I'm feeling. Sometimes it's even hard for me to describe to my doctor what I'm dealing with." – ID 15, Peer Coaching Participant
		"I was able to talk about what I was going through with someone who also understood what I was going through. So that was a really nice part of it– that community part that I was looking for. If I started experiencing a new problem, and I wasn't sure if it was lupus connected, it gave me a person to be able to talk to about it." – ID 38, Peer Coaching Participant
	Motivation/encouragement	"She kept me motivated; she kept me encouraged. And I think it was also a good balance. Sometimes I get disappointed because I really wanted to do this, but I physically couldn't do it. And she helped me switch my mindset around it, which was helpful because then she would somehow encourage me to try again." – ID 19, Peer Coaching Participant
Educational modules	Validation	"Even though I knew about the spoon theory, in my head reading, and then I read it out loud, and I started to cry. Because it was just so true that people really don't understand. We don't look sick... I thought that that was just so instrumental in helping people explain to other people, you know sometimes I can. Sometimes I can't... It just hit home." – ID 3, Peer Coaching Participant
	Informational	"I really thought the readings were helpful. I got a lot of information that I didn't know about. Nobody told me anything about lupus before. You know [the doctors] just tell me 'you have lupus' but they don't explain to you what the illness is about. The readings gave me a lot of information, and I got to know more about it." – ID 10, App-only Participant
REACH app	Accountability/motivation	"[The app] was an accountability partner. It added a layer of motivation, and it was results oriented. I got to see what I was doing and what I wasn't doing." – ID 43, App-only Participant
	Reflection	"The initial 'how do you feel today?' It gives you a moment to stop, reflect, and acknowledge how you feel and move on. Sometimes I'm like 'okay you know what this is a bad week and it's okay', and then next week I'm like 'okay you know what this is a better week'." – ID 19, Peer Coaching Participant
	Self-monitoring/self-regulation	"Having documentation of feeling fatigued, sleep, activity is helpful to understand the trends of how we feel over time. Sometimes we think we are doing very well one day, but then to see there were actually many days we were not well is helpful to understanding if we need to change something in our health or lifestyle to actually feel better." – ID 17, App-only Participant

findings support the potential of mHealth-enabled peer coaching to address behavioral and psychosocial drivers of fatigue in SLE and warrant further evaluation in larger trials.

Disclosure: S. Kasturi: GlaxoSmithKlein(GSK), 1; **E. Morrissey**: None; **A. Deck**: None; **N. Gulati**: None; **Z. Gilbard**: None; **K. Singh**: None; **M. Gore-Massy**: Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKlein(GSK), 1, Janssen, 1, 2, 6; **F. Chiu**: None; **P. Calvache**: None; **J. Rose-Smith**: None; **A. Ogura**: Ambulomics, 3; **L. Ogura Dantas**: Ambulomics, 3; **W. Machua**: Aurinia, 2, BMS Foundation, 5, Genentech, 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 1; **J. Nguyen**: None; **L. Mandl**: ACP, 12, Associate Editor Annals of Internal Medicine, Wolters, 9; **H. Tighiouart**: None; **L. Trinquart**: None; **I. Navarro-Millan**: None; **S. Folta**: None.

Abstract Number: 2430

Disease Activity Independently Correlates with Cognitive Impairment in Systemic Lupus Erythematosus

Steven Beiser[1], Asma Qureshi[1], Komel Safdar[2], Zachary Orban[1], Mary Carns[2], Vanessa Manada De Lobos[1], Cecilia Stumpf[3], Mohammad Daud Khan[1], Tyler Therron[4], Anh Chung[1], Katherine Puev[1], Neil Pillai[1], Kathleen Aren[5], John F Seagrist[2], Jing Song[6], Jason Ross[1], Harris R Perlman[2], Yvonne Lee[2], Deborah Rachelle Winter[7], Borna Bonakdarpour[1], Mariam Siddiqui[8], Laura Arneson[2], Rosalind Ramsey-Goldman[9], Lutfiyya muhammad[9], Mary Mahieu[9], Irene Blanco[10], Eric Larson[1], Elena Grebenciucova[1] and Carla Marie Cuda[2], [1]Northwestern University, Chicago, [2]Northwestern University, Chicago, IL, [3]Northwestern University, Elmhurst, IL, [4]Northwestern Feinberg School of Medicine, Chicago, IL, [5]Northwestern University Division of Rheumatology, Chicago, IL, [6]Northwestern University Feinberg School of Medicine, Worthington, MN, [7]Northwestern University, Skokie, IL, [8]Northwestern, Chicago, IL, [9]Northwestern University Feinberg School of Medicine, Chicago, IL, [10]Northwestern University, Oak Park, IL

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Mechanisms driving cognitive impairment (CI) in systemic lupus erythematosus (SLE) remain poorly understood; conflicting results exist regarding the relationship between CI and disease activity. NIH Toolbox for Assessment of Neurological and Behavioral Function (NIHT) is widely utilized to monitor CI in conditions like Alzheimer's disease and long COVID, yet few reports address its value in measuring CI in SLE. Further, the relationship between NIHT's subdomains and SLE disease activity has yet to be explored. We hypothesize that NIHT can effectively characterize CI in persons with and without active SLE and help clarify if disease activity contributes to poor cognitive performance. A secondary aim is to identify serum and cerebrospinal fluid (CSF) biomarkers mediating immune-related neuropathology.

Tables 1

Table 1. Demographic, Clinical, and Patient-Reported Characteristics of SLE Patient Cohort (n=22)

Characteristic	Value
Age, years	33.8 (11.8)
Female, %	100
Racial Category	
White, %	50.0
Black, %	32.0
Asian, %	9.0
Ethnic Category	
Hispanic or Latino, %	27.3
Not Hispanic or Latino, %	68.2
Body Mass Index, kg/m^2	29.6 (7.2)
Never Smoked, %	86.4
Highest Education Level	
High School Diploma/GED, %	18.2
College, %	63.6
Master's Degree, %	18.2
Married, %	50
Disease Duration, years	8.9 (6.0)
SLEDAI-2K Score (0-105)	4.6 (3.8)
Seizure, %	0
Psychosis, %	0
Organic Brain Syndrome, %	2.3
Visual Disturbance, %	0
Cranial Nerve Disorder, %	0
Lupus Headache, %	0
Cerebrovascular Accident, %	0
Vasculitis, %	0
Arthritis, %	34.1
Myositis, %	0
Urinary Casts, %	0
Hematuria, %	2.3
Proteinuria, %	9.1
Pyuria, %	2.3
Rash, %	25
Alopecia, %	11.4
Mucosal Ulcers, %	4.5
Pleurisy, %	2.3
Pericarditis, %	2.3
Low Complement, %	31.8
Increased DNA Binding, %	40.9
Fever, %	0
Thrombocytopenia, %	2.3
Leukopenia, %	9.1
PROMIS Fatigue (T-score)	58.2 (7.0)
PROMIS Sleep Disturbance (T-score)	50.1 (8.8)
Plaquenil/HCQ use, %	72.7
Azathioprine use, %	31.8
Steroid use, %	40.9
Methotrexate use, %	13.6
Cellcept/Myfortic use, %	31.8
Tacrolimus use, %	4.5
Belimumab use, %	18.1
Upacitinib use, %	9.1
NSAID use, %	18.1

Values are mean (standard deviation) or %.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2-4

Table 2. Association of Demographic, Clinical, Lab, and Cognitive Measures with Disease Activity

	SLEDAI-2K<6 (n=13)	SLEDAI-2K≥6 (n=9)	[p value]
Age	37.0 (12.1)	34.2 (10.8)	0.425
Racial Category			1.000
Ethnic Category			0.864
Body Mass Index, kg/m^2	29.4 (6.0)	28.9 (8.5)	0.515
Smoking Status			0.456
Education			0.868
Marital Status			0.199
Disease Duration	8.6 (5.8)	9.2 (6.8)	0.828
NIH Toolbox Scores			
Pattern Comparison Processing Speed	97.5 (12.4)	92.1 (16.5)	0.411
Flanker Inhibitory Control and Attention	98.0 (11.4)	94.2 (8.2)	0.416
Dimensional Cage Card Sort	**101.0 (16.9)**	**88.0 (4.4)**	*0.033*
List Sorting Working Memory	107.0 (17.1)	105.0 (17.4)	0.810
Picture Sequence Memory Form A	105.0 (11.4)	99.9 (12.9)	0.351
Fluid Composite Standard Score	103.0 (14.7)	92.1 (9.9)	0.070
Rey Auditory Verbal Learning Test	110.0 (28.5)	95.8 (14.8)	0.331
Rey Auditory Verbal Learning Test-Delay	**127.0 (19.7)**	**104.0 (11.2)**	*0.048*
Montreal Cognitive Assessment Score	15.2 (13.7)	12.6 (13.7)	0.482

Score is mean (standard deviation)

Table 3. Associations of SLEDAI-2K Subcomponents with Altered Cognitive Measures

SLEDAI-2K Subcomponent	Dimensional Cage Card Sort [p value]	Rey Auditory Verbal Learning Test-Delay [p value]
Arthritis	0.539	0.309
Rash	0.580	1.000
Alopecia	0.932	0.142
Low Complement	0.169	0.099
Increased DNA Binding	0.691	0.142

Table 4. Associations of Demographic, Patient-Reported, Clinical, and Lab Characteristics with Altered Cognitive Measures

	Dimensional Cage Card Sort (rho [p value])	Rey Auditory Verbal Learning Test-Delay (rho [p value])
Age	0.31 [0.141]	-0.04 [0.864]
Disease Duration	0.36 [0.083]	-0.04 [0.896]
SLEDAI	-0.31 [0.135]	**-0.61** [*0.014*]
PROMIS Fatigue (T-score)	-0.18 [0.520]	-0.17 [0.544]
PROMIS Sleep Disturbance (T-score)	0.01 [0.985]	-0.27 [0.335]
Lab		
Antiphospholipid Antibody	[0.541]	[0.415]
Complement C3	0.04 [0.869]	0.43 [0.107]
Complement C4	0.03 [0.887]	**0.62** [*0.013*]
White Blood Cells	-0.37 [0.07]	0.02 [0.924]
Neutrophils	0.07 [0.734]	-0.36 [0.183]
Lymphocytes	-0.08 [0.708]	0.28 [0.318]
Monocytes	0.29 [0.169]	-0.02 [0.939]

Methods: Cross-sectional data were analyzed from adult patients enrolled in our ongoing study of immune-mediated mechanisms of neuropsychiatric SLE. Eligible participants met 4 of 11 ACR 1997 or 3 of 11 ACR 1997 with SLICC 2012 criteria for SLE and did not have concurrent autoimmune or neurologic diseases, active or chronic infections, GFR< 60, liver enzymes >3× ULN, or sodium imbalance. Cognitive performance was assessed by the clinically validated Montreal Cognitive Assessment (MoCA), reported as total score, and a targeted NIHT battery, reported as age-adjusted standard scores. SLEDAI-2K≥6 defined moderate-high disease activity; SLEDAI-2K< 6 indicated low-moderately active or inactive disease. Note, only one participant scored for a neurological SLEDAI-2K descriptor. Descriptive statistics summarized demographic and clinical characteristics. Spearman correlations assessed relationships between continuous variables. Associations between continuous and categorical variables were assessed via Wilcoxon rank sum tests.

Results: Our sample included 22 female patients with SLE free of concurrent autoimmune or neurologic disease with mean (SD) age of 33.8 (11.8) years and disease duration of 8.9 (6.0) years (Table 1). Patients with moderate-high disease activity scored lower on the Dimensional Change Card Sort and Rey Auditory Verbal Learning Tests for executive function and delayed auditory-verbal memory, respectively, compared to those with inactive or low-moderate disease activity (Table 2,4). SLEDAI subcomponent scores did not associate with altered CI subdomains (Table 3). Yet, low circulating complement C4 correlated with worse delayed auditory-verbal memory. Findings were independent of demographic, patient-reported, clinical, and other lab characteristics (Table 2,4). MoCA did not differentiate groups, highlighting NIHT's superior sensitivity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The NIHT is a domain-specific, sensitive tool for detecting CI in SLE, outperforming the MoCA. Higher SLEDAI, but not subcomponent, scores correlate with executive function and memory impairments, supporting a role for generalized inflammation, and potentially C4, in SLE-related CI. Here, we advance the field by exploring the link between SLE disease activity and CI of domains essential for daily functioning and expanding immune profiling of serum and CSF to clarify the neuroimmune basis of these deficits.

Disclosure: S. Beiser: None; **A. Qureshi**: None; **K. Safdar**: None; **Z. Orban**: None; **M. Carns**: None; **V. Manada De Lobos**: None; **C. Stumpf**: None; **M. Khan**: None; **T. Therron**: None; **A. Chung**: None; **K. Puev**: None; **N. Pillai**: None; **K. Aren**: None; **J. Seagrist**: None; **J. Song**: None; **J. Ross**: None; **H. Perlman**: AbbVie/Abbott, 2; **Y. Lee**: CVS Health, 12,, GE Healthcare, 12,, Tonix, 1; **D. Winter**: None; **B. Bonakdarpour**: None; **M. Siddiqui**: None; **L. Arneson**: Novartis, 12,; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **L. muhammad**: None; **M. Mahieu**: None; **I. Blanco**: Cabaletta Bio, 5, Fate Therapeutics, 2, Novartis, 5, Zenas BioPharma, 2; **E. Larson**: None; **E. Grebenciucova**: Amgen, 6, AstraZeneca, 6, Genentech, 6, Tg therapeutics, 6; **C. Cuda**: None.

Abstract Number: 2431

Bone marrow- activity on 18F-FDG PET/CT as a Predictor of Hematologic Manifestations in Systemic Lupus Erythematosus

Sungwon Ko[1], Young-Eun Kim[1], Soyoon Yoon[2], Soo Min Ahn[1], Ji Seon Oh[1], Yong-Gil Kim[1], Chang-Keun Lee[3], Bin Yoo[1], Dong Yun Lee[4] and Seokchan Hong[1], [1]Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea, Seoul, Republic of Korea, [2]Department of Nuclear Medicine, University of Ulsan College of Medicine, Seoul, Republic of Korea, [3]Department of Rheumatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Seoul, Republic of Korea, [4]Department of Nuclear Medicine, University of Ulsan College of Medicine, Seoul, Seoul, Republic of Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is a noninvasive imaging modality widely used to assess inflammatory activity in various autoimmune and hematologic disorders. The bone marrow (BM), as the site of hematopoiesis, may play a key role in the pathogenesis of systemic lupus erythematosus (SLE). This study aimed to investigate whether BM metabolic activity on PET/CT is associated with hematologic manifestations and to assess its potential as a predictive biomarker in SLE.

Methods: We retrospectively analyzed patients with SLE who underwent ^{18}F-FDG PET/CT imaging at baseline and had available follow-up data for at least 6 months. Patients with malignancy were excluded. BM FDG uptake was quantified using standardized uptake values (SUV), and the BM-to-liver ratio (BLR) was calculated using both SUVmax and SUVmean. Hematologic manifestations were defined as leukopenia, anemia, and/or thrombocytopenia. Associations between BLR indices and hematologic involvement were assessed using Pearson correlation and multivariable logistic regression adjusted for age, sex, and comorbidities. Receiver operating characteristic (ROC) curve analysis was conducted to evaluate predictive performance.

Results: Among 76 patients with SLE (median age 48.0 years; 86.0% female), 21 (27.6%) exhibited baseline hematologic abnormalities. Median BM SUVmax and SUVmean were 2.40 (SD, 0.65) and 1.65 (SD, 0.50), respectively. Median BLRmax and BLRmean were 1.58 (SD, 0.52) and 1.10 (SD, 0.41), respectively. Both BLRmax and BLRmean were positively correlated with baseline hematologic involvement ($r = 0.282$, $p = 0.014$ and $r = 0.264$, $p = 0.021$, respectively). Elevated baseline

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	Total (n=76)	
Baseline characteristics		
Age (years, median [IQR])	48.0	30.0–60.3
Female, no. (%)	65	86.0
BMI (kg/m², median [IQR])	22.8	20.6–26.8
Comorbidities		
Hypertension	16	21.0
Diabetes	6	7.9
Chronic kidney disease	7	9.2
Laboratory data		
C3 (mg/dL, median [IQR])	69.4	45.4–110.1
C4 (mg/dL, median [IQR])	13.8	6.7–23.7
Anti-dsDNA (IU/mL, median [IQR])	7.5	3.9–21.1
ESR (mm/hr, median [IQR])	30	18–63
CRP (mg/dL, median [IQR])	0.6	0.1–3.3
SLEDAI	6	3–12
SLE involvement		
Constitutional	42	55.3
Renal	25	32.9
Hematological	21	27.6
Mucocutaneous	11	14.5
Musculoskeletal	10	13.2
Neurologic	9	11.8
Pulmonary	8	10.5
Cardiac	4	5.3
PET profile		
Liver SUVmean (mean, SD)	1.56	0.27
Bone marrow SUVmax (mean, SD)	2.40	0.65
Bone marrow SUVmean (mean, SD)	1.65	0.50
SLR max (mean, SD)	1.47	0.48
SLR mean (mean, SD)	1.12	0.38
BLR max (mean, SD)	1.58	0.52
BLR mean (mean, SD)	1.10	0.41

Baseline characteristics of patients with systemic lupus erythematosus who underwent 18F-FDG PET/CT.

BLR values were independently associated with the development of hematologic abnormalities at 6 months (adjusted ORs: 1.57 [95% CI: 1.15–2.13] for BLRmax and 1.42 [1.10–1.83] for BLRmean; both $p < 0.01$). ROC curve analysis yielded an AUC of 0.76 for BLRmax in predicting future cytopenia, with an optimal cut-off value of 1.8 (sensitivity 78%, specificity 72%).

Conclusion: Increased BM-metabolic activity relative to the liver on PET/CT is associated with both initial and subsequent hematologic manifestations in patients with SLE. BLR, particularly BLRmax, may serve as a noninvasive imaging biomarker for predicting hematologic involvement, underscoring a potential role of the BM in SLE pathophysiology.

Disclosure: S. Ko: None; **Y. Kim**: None; **S. Yoon**: None; **S. Ahn**: None; **J. Oh**: None; **Y. Kim**: None; **C. Lee**: Samsung Bioepis, 5; **B. Yoo**: None; **D. Lee**: None; **S. Hong**: None.

Abstract Number: 2432

Duffy Null Genotype and Autoantibodies Synergistically Contribute to Severe Leukopenia in Systemic Lupus Erythematosus

valerie Lewis[1], Faith Porter[2], Victoria Nwankwo[3], John Ice[4], Joshua Cavett[5] and R Hal Scofield[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Langston University, Langton, OK, [3]Emory University, Atlanta, GA, [4]OKC VA Healthcare System, Oklahoma City, OK, [5]Oklahoma Medicar Research Foundtion, Oklahoma City

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a common, complex inflammatory autoimmune disease in which dysregulation of both innate and adaptive immune responses has been implicated in disease pathogenesis. Leukopenia is a common hematologic manifestation in SLE, yet the mechanisms remain incompletely defined. Our published data show that anti-Ro autoantibodies can bind neutrophil surface proteins and potentially fix complement leading to leukopenic conditions. Additionally, the Duffy null genotype (ACKR1 rs2814778-CC), enriched in individuals of African and Arab ancestry, is associated with low neutrophil counts. Therefore, we investigated whether this Duffy null genotype, combined with autoantibody-mediated neutrophil targeting, contributes to more severe leukopenia and worse immunologic outcomes in SLE.

Methods: DNA from subjects who met the ACR classification criteria were obtained from the Oklahoma Medical Research Foundation (OMRF) Lupus Family Registry and Repository (LFRR). These subjects were genotyped for ACKR1 (rs2814778-CC) using biallelic discrimination assays. We analyzed the subjects corresponding clinical and serologic data and stratified them by autoantibody status and Duffy genotype (ACKR1 CC vs. CT/TT). Finally, we assessed white blood cell (WBC) counts across these groups. Statistical analysis was performed using the Kruskal-Wallis test to assess significant differences in WBC counts among stratified subgroups.

Results: WBC counts were lowest among SLE patients who were both anti-Ro or anti-dsDNA positive and Duffy antigen negative (*ACKR1*-CC genotype) compared to autoantibody negative/Duffy antigen positive (*ACKR1*-TT/CT genotype) SLE subjects. Additionally, subjects that were both anti-dsDNA positive and Duffy null had a significant decrease in WBC compared to subjects with anti-dsDNA antibodies and Duffy positive. These findings suggest an additive or synergistic effect of anti-dsDNA autoantibodies and Duffy null status on the severity of leukopenia.

Conclusion: Our previously published data support a model in which autoantibodies (anti-Ro60) directly contribute to leukopenia in SLE by binding neutrophil surface proteins and subsequently fixing complement. The current findings suggest this effect is amplified in subjects with the Duffy null genotype. These results highlight the importance of integrating ancestry-specific genetics (such as Duffy null genotype) and immunologic factors into our understanding of SLE pathogenesis and personalized care strategies.

Disclosure: v. Lewis: None; **F. Porter**: None; **V. Nwankwo**: None; **J. Ice**: None; **J. Cavett**: None; **R. Scofield**: IQVIA, 1, Jannsen Pharmaceuticals, 1.

Abstract Number: 2433

The Clinical Utility of a Multianalyte Lupus Risk Score Incorporating Cell-bound Complement Activation Products: A Systematic Evaluation

Vasileios Kyttaris[1], Sepehr Taghavi[2], Clayton Nagle[3], Christine Schleif[3], Brittany Partain[4] and Tyler O'Malley[5], [1]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, [2]Exagen Inc, Escondido, CA, [3]Exagen, Carlsbad, CA, [4]Exagen, Boston, MA, [5]Exagen, Vista, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Timely SLE diagnosis and treatment are critical to preventing irreversible organ damage and preserving quality of life. However, conventional biomarkers often underperform in patients presenting with non-specific signs and symptoms. We systematically evaluated a multianalyte assay panel (MAP) index incorporating cell-bound complement activation products (CB-CAPs) to address this diagnostic gap.

Methods: We analyzed biomarker data from multiple clinical studies (2011–2024), comprising 1,208 SLE patients meeting 1997 ACR criteria, 667 healthy controls, and 1,234 autoimmune rheumatic disease and chronic pain controls. CB-CAPs were measured by semi-quantitative flow cytometry and reported as net mean fluorescent intensity. Autoantibodies were measured by ELISA and complement C3 and C4 were measured by immunoturbidimetry. Diagnostic odds ratios (DOR), likelihood ratios (LR+/-), and sensitivities were calculated. Sensitivity comparisons between the MAP index, and conventional markers (anti-dsDNA, anti-Smith, and complement C3/C4) were performed within the SLE cohort using McNemar's test. Sensitivity odds ratios were calculated from discordant pairs, with p-values adjusted using the Benjamini-Hochberg method. Effect sizes were expressed as the difference in sensitivities with corresponding 95% confidence intervals.

Results: The SLE cohort was predominantly female (62%), mean age 43.5 (±14.1) years, and mostly White (40%) [Table 1]. The MAP index consistently outperformed conventional biomarkers across both healthy and disease control comparisons. Against healthy controls, MAP achieved the highest diagnostic odds (DOR = 101.6), compared to CB-CAPs alone (DOR = 55.1), anti-dsDNA/Smith antibodies (DOR = 36.2), and complement C3/C4 (DOR = 7.9) [Figure 1A]. Against autoimmune and chronic pain controls, MAP maintained superior performance (DOR = 22.3), exceeding that of anti-dsDNA/Smith (DOR = 20.3), CB-CAPs (DOR = 13.7), and complement (DOR = 9.1) [Figure 1B]. The MAP index yielded the highest positive likelihood ratio (LR+ = 32.7) and strongest rule-out utility (LR– = 0.3), outperforming all individual markers. Sensitivity comparisons within the SLE group revealed significantly higher odds of MAP positivity versus anti-dsDNA (OR = 24.8), anti-Smith (OR = 1382.0), and CB-CAP subsets (ORs = 17.3–19.0), all with adjusted p-values < 0.001 and moderate-to-large effect sizes (sensitivity differences = 0.31-0.57) [Figure 2A]. Integration of the MAP index identified 24% more SLE cases than conventional markers alone and reduced the proportion of patients testing negative for all biomarkers from 36% to 28% (Figure 2B-C). Overlap analysis confirmed MAP captured unique diagnostic information beyond traditional serologies and complement levels.

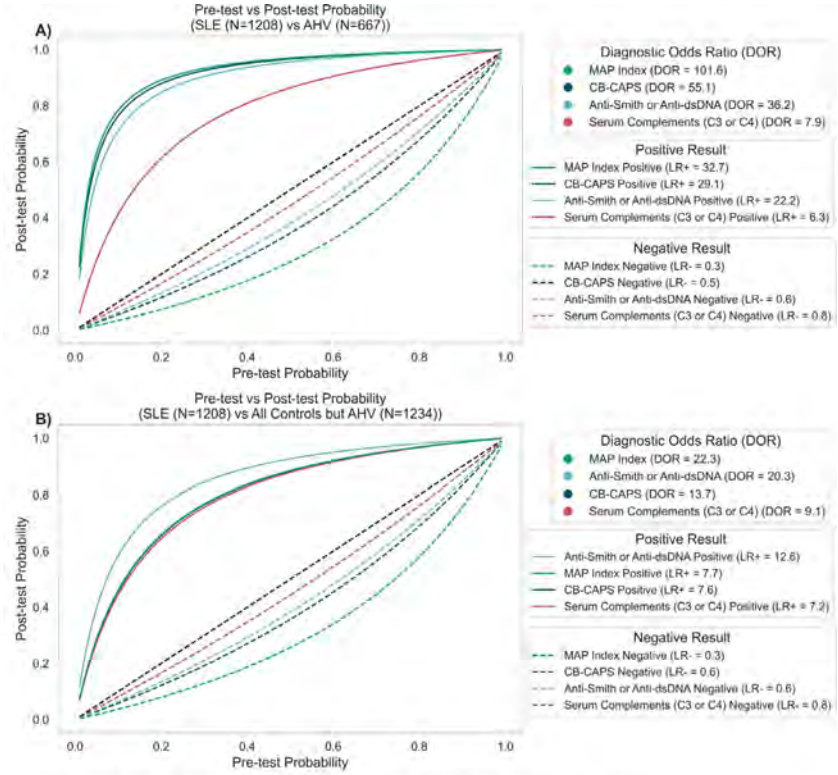
Conclusion: Systematic analysis demonstrates the MAP index integrating CB-CAPs improves lupus diagnostic precision. With unique utility for both rule-in and rule-out decisions, particularly in cases of intermediate lupus probability, the MAP index addresses critical diagnostic gaps. Robust performance across diverse patient populations further supports its clinical generalizability and practical value for enhancing lupus management.

Metric	Total (N=3109)	SLE (N=1208)	AHV (N=667)	RA (N=502)	Fibromyalgia (N=312)	Sjogren (N=156)	Chronic Localized Pain (N=54)	PsA (N=52)	Others* (N=158)
Ethnicity									
White	1767 (57%)	481 (40%)	377 (57%)	333 (67%)	265 (84%)	104 (66%)	46 (85%)	46 (88%)	115 (73%)
Hispanic	436 (14%)	155 (13%)	119 (18%)	96 (19%)	33 (11%)	12 (8%)	8 (15%)	2 (4%)	11 (7%)
Black	415 (13%)	243 (20%)	81 (12%)	44 (9%)	8 (3%)	21 (13%)	0 (0%)	1 (2%)	17 (11%)
Asian	147 (5%)	71 (6%)	51 (8%)	17 (3%)	5 (2%)	3 (2%)	0 (0%)	0 (0%)	0 (0%)
Other	67 (2%)	23 (2%)	23 (3%)	11 (2%)	0 (0%)	4 (3%)	0 (0%)	1 (2%)	5 (3%)
Not Disclosed	277 (9%)	235 (19%)	16 (2%)	1 (0%)	1 (0%)	12 (8%)	0 (0%)	2 (4%)	10 (6%)
Gender									
Female	1808 (58%)	754 (62%)	338 (51%)	363 (72%)	90 (29%)	106 (68%)	2 (4%)	27 (52%)	128 (81%)
Male	1189 (38%)	363 (30%)	329 (49%)	139 (28%)	222 (71%)	39 (25%)	52 (96%)	25 (48%)	20 (13%)
Not disclosed	112 (4%)	91 (8%)	0 (0%)	0 (0%)	0 (0%)	11 (7%)	0 (0%)	0 (0%)	10 (6%)
Age at Visit - Mean(SD)	47.73 (15.16)	43.53 (14.14)	41.87 (14.46)	58.73 (13.76)	53.79 (13.00)	54.16 (13.01)	50.59 (13.39)	53.08 (11.29)	53.49 (14.06)
ANA Positivity by ELISA	57%	88%	23%	43%	30%	81%	35%	25%	63%
ANA Positivity by Hep2	59%	87%	17%	56%	31%	78%	37%	40%	73%

Table 1: Demographic Table
*Others include: Myositis: (N=39), Autoimmune Hepatitis (N=37), Autoimmune Thyroiditis (N=35), Systemic Sclerosis (N=47)

Figure 1. Demographic characteristics

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Pre-test vs post-test probability curves demonstrate diagnostic performance of the Multianalyte Assay Panel (MAP) index, CB-CAPs, and conventional biomarkers (anti-dsDNA or anti-Smith antibodies, and serum complements C3 or C4) for distinguishing SLE patients (N=1208) from (A) healthy controls (AHV, N=667) and (B) autoimmune/chronic pain controls excluding AHV (N=1234). The MAP index showed the highest diagnostic odds ratio (DOR = 101.6 vs AHV; DOR = 22.3 vs other controls) and best rule-out utility (LR− = 0.3 in both comparisons). MAP also achieved the highest LR+ against AHV (32.7), while anti-dsDNA or anti-Smith antibodies had the highest LR+ (12.6) against other controls. CB-CAPs, presented as a separate biomarker category, consistently outperformed individual conventional markers but trailed the MAP index across all metrics.

Figure 1. Pre-test vs. post-test probability for SLE figures comparing MAP index to CB-CAPs and conventional markers

Sensitivity for SLE Comparison	Odds Ratio [95% CI]	Adjusted p-values (Benjamini-Hochberg)	Effect Size (Sensitivity Diff) [95% CI]
MAP Index vs anti-Smith Positive	1382.00 [86.35, 22118.03]	<0.001	0.57 [0.54, 0.60]
MAP Index vs anti-dsDNA Positive	24.76 [15.25, 40.22]	<0.001	0.33 [0.31, 0.36]
MAP Index vs BC4d Positive	19.00 [12.25, 29.47]	<0.001	0.31 [0.28, 0.34]
MAP Index vs EC4d Positive	17.33 [11.76, 25.55]	<0.001	0.37 [0.34, 0.39]
Either CB-CAPS Positive vs anti-Smith Positive	12.66 [9.10, 17.61]	<0.001	0.37 [0.34, 0.40]
MAP Index vs Either CB-CAPS Positive	6.77 [4.91, 9.32]	<0.001	0.21 [0.18, 0.23]
Either CB-CAPS Positive vs Either C3 or C4 Low	5.22 [4.06, 6.72]	<0.001	0.25 [0.22, 0.28]
Either CB-CAPS Positive vs anti-dsDNA Positive	2.16 [1.76, 2.66]	<0.001	0.13 [0.10, 0.16]

Figure 2. (A) The MAP Index shows significantly higher sensitivity for SLE compared to conventional markers, particularly anti-Smith (Δ = 0.57). All comparisons are statistically significant (adjusted p < 0.001).

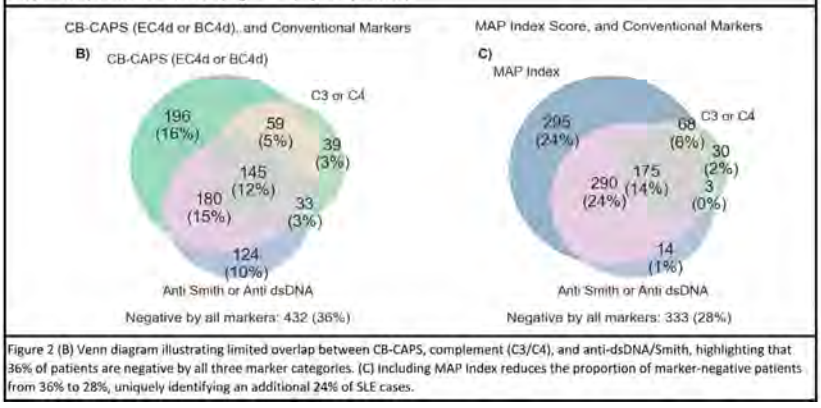


Figure 2 (B) Venn diagram illustrating limited overlap between CB-CAPS, complement (C3/C4), and anti-dsDNA/Smith, highlighting that 36% of patients are negative by all three marker categories. (C) Including MAP Index reduces the proportion of marker-negative patients from 36% to 28%, uniquely identifying an additional 24% of SLE cases.

Figure 2. Sensitivity for SLE comparison between MAP, CB-CAPs and conventional biomarkers

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: V. Kyttaris: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2; **S. Taghavi**: Exagen, 3; **C. Nagle**: Exagen, 3; **C. Schleif**: Exagen, 3; **B. Partain**: Exagen, 3; **T. O'Malley**: Exagen, 12,, 3, 11.

Abstract Number: 2434

Specificity of Cell-bound T Cell Biomarkers (TC4d, TIgG, TIgM) in Differentiating SLE from ANA-Associated Rheumatic Diseases

Vasileios Kyttaris[1], Sepehr Taghavi[2], Clayton Nagle[3], Christine Schleif[3], Brittany Partain[4] and Tyler O'Malley[5], [1]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, [2]Exagen Inc, Escondido, CA, [3]Exagen, Carlsbad, CA, [4]Exagen, Boston, MA, [5]Exagen, Vista, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: We previously validated T Cell-bound C4d (TC4d), T Cell-bound IgG (TIgG), and T Cell-bound IgM (TIgM) biomarkers, demonstrating high sensitivity and specificity for differentiating systemic lupus erythematosus (SLE) from apparently healthy volunteers (AHVs) and other autoimmune rheumatic diseases (ARDs). The current study aims to further evaluate the specificity of these biomarkers in distinguishing SLE from other suspected anti-nuclear antibody (ANA)-associated ARDs within a large cohort.

Methods: Three cohorts were analyzed: 71 clinically diagnosed SLE patients meeting the 2019 ACR/EULAR classification criteria; 162 AHVs; and 31,221 subjects from a de-identified population undergoing autoimmune testing (Jan–Apr 2025). Suspected ARDs were identified based on autoantibody levels exceeding ten times the diagnostic assay cutoffs (anti-CCP for RA; anti-Ro52, anti-Ro60, and anti-SSB/La for Sjögren's syndrome; anti-centromere protein B for limited scleroderma; anti-Scl-70 for diffuse scleroderma; and anti-Jo-1 for myositis) and negative for anti-dsDNA and anti-Smith antibodies. Semiquantitative flow cytometry was used to measure cell-bound TC4d, TIgG, and TIgM, reported as median fluorescence intensity (MFI). Autoantibody measurements utilized ELISA or enzyme linked fluorescent assay (ELFA) methods per kit recommendations (ThermoFisher, Phadia). Biomarker distributions, sensitivity, specificity, likelihood ratios (LRs), and diagnostic odds ratios (DORs) were assessed at thresholds achieving 95% specificity vs. AHVs, 95% specificity vs. ARDs, and 99% specificity vs. ARDs. Mann-Whitney U tests evaluated significant differences.

Results: SLE patients (N = 71) had a mean (SD) age of 42.6 (9.8) years, were predominantly female (83.1%), ANA IFA-positive (83.1%), and ANA ELISA-positive (97.2%). Suspected ARD groups included RA (N = 648), Sjögren's (N = 140), limited scleroderma (N = 366), diffuse scleroderma (N = 26), and myositis (N = 22) [Table 1]. At thresholds providing 95% specificity vs. AHVs, the T Cell biomarkers showed specificities of 87.5% (TC4d), 87.3% (TIgG), and 83.5% (TIgM) for differentiating SLE from ARDs (Table 2). Sensitivity for SLE at 95% specificity for SLE vs. ARD was 64.8% (TC4d), 54.9% (TIgG), and 36.6% (TIgM). At thresholds providing 99% specificity vs. ARDs, sensitivities ranged from 11% to 28%. The DORs at 95% specificity vs. AHVs were 24.1 (TC4d), 16.3 (TIgG), and 7.3 (TIgM). Median TC4d, TIgG, and TIgM levels were

Table 1. Demographic characteristics

	SLE	AHV	Suspected RA	Suspected Sjögren's	Suspected Limited Scleroderma	Suspected Diffuse Scleroderma	Suspected Myositis
N	71	174	648	140	366	26	22
Average Age (SD)	42.6 (9.8)	57.6 (15.9)	57.1 (14.3)	52.2 (16.5)	59.4 (14.7)	52.2 (19.3)	50.5 (10.4)
% Female	83.1	81.0	84.6	89.3	94.0	92.3	86.4
% ANA IFA+	83.1	Not Tested	53.2	100.0	99.7	96.2	68.2
% ANA ELISA+	97.2	Not Tested	54.8	100.0	99.7	96.2	100.0

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Performance characteristics

Biomarker	Specificity level	Sensitivity for SLE (%)	Specificity vs. ARD (%)	LR+	LR-	DOR
TC4d	95% vs. AHV	77.5% (66.0-86.5%)	87.5% (85.5-89.3%)	6.2	0.3	24.1
TC4d	95% vs. suspected ARDs	64.8% (52.5-75.8%)	94.9% (93.5-96.1%)	12.8	0.4	34.4
TC4d	99% vs. suspected ARDs	28.2% (18.1-40.1%)	98.9% (98.2-99.4%)	26.0	0.7	35.9
TIgG	95% vs. AHV	70.4% (58.4-80.7%)	87.3% (85.3-89.1%)	5.5	0.3	16.3
TIgG	95% vs. suspected ARDs	54.9% (42.7-66.8%)	94.8% (93.4-96.0%)	10.6	0.5	22.4
TIgG	99% vs. suspected ARDs	25.4% (15.8-37.1%)	98.9% (98.2-99.4%)	23.4	0.8	31.1
TIgM	95% vs. AHV	59.2% (46.8-70.7%)	83.5% (81.3-85.6%)	3.6	0.5	7.3
TIgM	95% vs. suspected ARDs	36.6% (25.5-48.9%)	94.9% (93.5-96.1%)	7.2	0.7	10.8
TIgM	99% vs. suspected ARDs	11.3% (5.0-21.0%)	98.9% (98.2-99.4%)	10.4	0.9	11.6

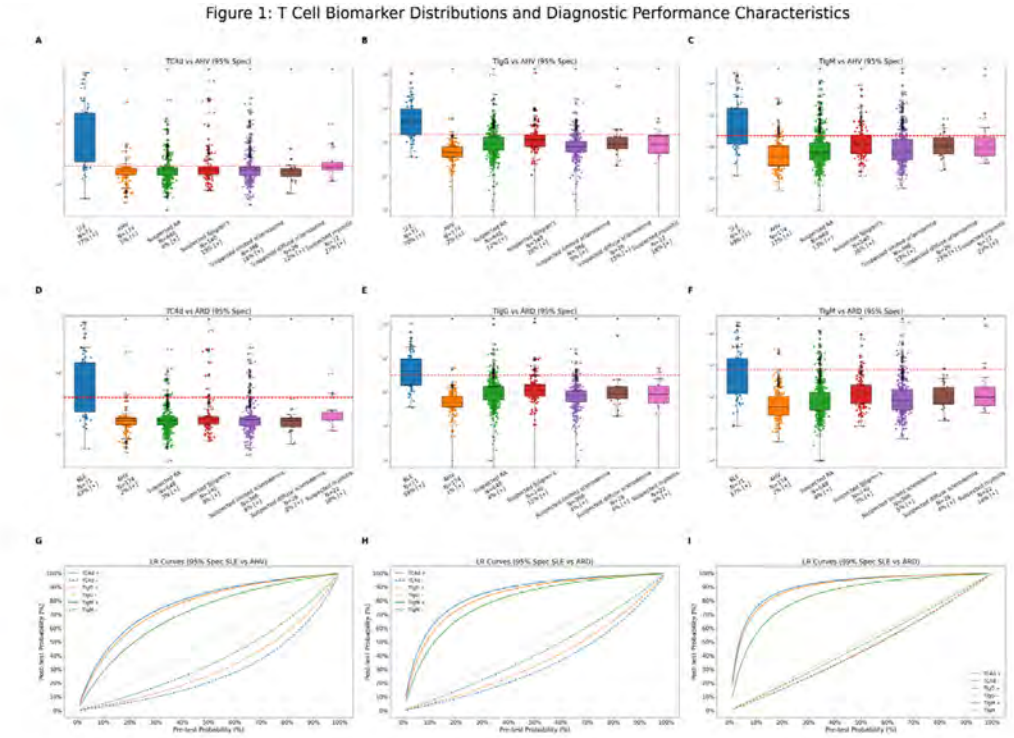


Figure 1. Biomarker distributions and diagnostic performances at varying levels of specificity for SLE

significantly higher in SLE patients compared to all other ANA-associated ARDs (Figure 1A-F, $p < 0.01$). At a moderate pre-test probability for SLE (30%), the post-test probabilities following a positive TC4d result were 72.7% (95% specificity vs. AHVs), 84.5% (95% specificity vs. ARDs), and 91.8% (99% specificity vs. ARDs) [Figure 1G-I]. Conversely, negative TC4d results reduced the post-test probability to 9.9%, 13.7%, and 23.7%, respectively.

Conclusion: Cell-bound TC4d, TIgG, and TIgM exhibit robust specificity for differentiating SLE from other ANA-associated ARDs. The availability of multiple threshold levels allows flexible clinical application, enhancing diagnostic decision-making through optimized rule-in or rule-out approaches.

Disclosure: V. Kyttaris: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2; **S. Taghavi**: Exagen, 3; **C. Nagle**: Exagen, 3; **C. Schleif**: Exagen, 3; **B. Partain**: Exagen, 3; **T. O'Malley**: Exagen, 12,, 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2436

Preload deficiency as a treatable cause of fatigue and exercise intolerance in SLE

Yoo Jin Kim[1], Phebe Ismail[1], Michelle Petri[2], Jennifer Lee[1], Luigi Adamo[3] and Andrea Fava[1], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Timonium, MD, [3]Johns Hopkins Unviersity, Baltimore, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2377–2436) Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Fatigue and exercise intolerance affect over 90% of patients with SLE, often persisting despite inactive disease and disrupting quality of life. Yet, the underlying mechanism remains poorly defined, and treatment options are limited. We report a detailed evaluation and therapeutic response in a series of ten women with SLE and disabling fatigue and exercise intolerance, identifying preload deficiency as a potential and treatable contributor.

Methods: A prospective cohort study of ten women with SLE who experienced exercise intolerance and fatigue was conducted as part of the Hopkins Lupus Cohort. All patients underwent extensive cardiopulmonary evaluation, including laboratory tests, transthoracic echocardiography (TTE), cardiac MRI, continuous cardiac monitoring, coronary CT, quantitative autonomic testing (QAT), and cardiac pulmonary exercise testing (CPET). A subset of these patients underwent right heart catheterization (RHC) with exertion.

Results: The median age was 41. All patients had no anemia, renal, or pulmonary dysfunction. TTE, cardiac MRI, continuous cardiac monitoring, and coronary CT were unremarkable, indicating no structural, coronary, or conduction abnormalities. QAT identified postural orthostatic tachycardia syndrome (POTS) in 2 patients. However, all demonstrated impaired aerobic capacity (peak VO_2 < 80% predicted) on CPET, with low anaerobic thresholds and elevated resting heart rates, indicating cardiovascular limitation to exercise. Jugular venous pressure (JVP) was < 5 cm H_2O in all cases, suggesting **preload deficiency**, a condition of inadequate augmentation of right-sided filling pressures during exertion. To confirm, five patients underwent RHC with exertion, all demonstrating preload deficiency defined as failure to increase right atrial pressure with exercise (ΔRAP< 5.5). Pro-BNP was undetectable in all, consistent with inadequate right atrial filling and suggesting its potential utility as a biomarker.

Patients were advised to increase fluid (128 oz/day) and sodium intake (>5g/day) and use compression garments. Ivabradine was introduced in a subset of patients with persistent symptoms, high resting heart rates, marked exertional tachycardia, or limited fluid/sodium tolerance. All patients reported significant symptomatic improvement. One patient, previously nearly bed-bound, returned to school and completed a doctoral degree.

Conclusion: Reduced peak VO_2 and anaerobic thresholds have been described in SLE. Our findings suggest that **preload deficiency**—a reversible cardiovascular abnormality—may underlie this impairment in selected patients, offering a previously unrecognized but treatable cause of exercise intolerance. Undetectable pro-BNP may serve as a biomarker of preload deficiency in this population, warranting further study. Recognition of this phenotype may enable effective, low-risk interventions and offer a mechanistic target for future studies aimed at defining the prevalence and pathophysiology of preload deficiency in SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and Clinical Characteristics

	All (N = 10)
Age, median (IQR)	41 (33-47)
Female sex, no. (%)	10 (100)
Race, no. (%)	
White	6 (60)
Black	2 (20)
Other	2 (20)
BMI (kg/m²), median (IQR)	26.1 (21.5-28.6)
Laboratory evaluation, median (IQR)	
Hemoglobin (g/dL)	13.3 (12.8-14.3)
Creatinine (mg/dL)	0.8 (0.7-0.8)
Complement 3	111.2 (100.2-133.4)
Complement 4	24.0 (16.4-34.7)
anti-dsDNA	0 (0-1:20)
pro-BNP (pg/mL)	<36 (<36-<36)
Clinical evaluation , median (IQR)	
Obstructive coronary artery disease, no. (%)	0 (0)
Transthoracic echocardiogram, median (IQR)	
LVEF (%)	55 (55-55)
GLS	-17 (-18,-16)
LVIDD (cm)	4.2 (4.0-4.7)
LA size (cm)	2.8 (2.5-3.3)
TAPSE	2.0 (1.9-2.1)
Cardiac MRI	
LVEF	59 (55-64)
RVEF	59 (53-59)
LGE	0 (0-0)
Mean septal T2	52 (50-53)
Pulmonary function testing (% predicted)	
FEV1	107 (99-119)
FVC	107 (97-115)
FEV1/FVC	98 (96-115)

Cardiopulmonary Exercise Testing, median (IQR)	
Resting	
Heart rate (beats/min)	94 (86-105)
Systolic blood pressure (mmHg)	115 (110-130)
Diastolic blood pressure (mmHg)	74 (67-81)
Oxygen saturation (%)	98 (98-98)
VO_2 (mL/kg/min)	0.35 (0.23-0.67)
Peak exercise	
Heart rate (beats/min)	152 (136-168)
Systolic blood pressure (mmHg)	165 (133-171)
Diastolic blood pressure (mmHg)	81 (75-88)
VE/VCO_2	32 (30-33)
VO_2 (mL/kg/min)	20.0 (18.4-22.2)
VO_2 (% Predicted)	67 (56-77)
RER	1.06 (1.05-1.13)
Anaerobic threshold	
Heart rate (beats/min)	120 (109-142)
Systolic blood pressure (mmHg)	132 (113-140)
Diastolic blood pressure (mmHg)	73 (68-78)
VO_2 (mL/kg/min)	11.5 (8.2-12.4)
RER	0.86 (0.81-0.88)
Right heart catheterization, median (IQR)	**(N=5)**
Mean pressures at rest (mmHg)	
Right atrium (RA)	3 (2-5)
Pulmonary artery	12 (11-14)
Pulmonary capillary wedge pressure	7 (5-8)
Mean pressures with exertion (mmHg)	
Right atrium	5 (1-7)
Pulmonary artery	19 (17-24)
Pulmonary capillary wedge pressure	9 (8-11)
Workload at peak exertion (watts)	85 (75-93)
Δ RA pressure (mmHg)	0 (-1-+2)

Disclosure: Y. Kim: None; **P. Ismail**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. Lee**: None; **L. Adamo**: kiniksa pharmaceuticals, 2, novo nordisk, 2; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2.

Abstract Number: 2437

Bupropion for Lupus-Induced Fatigue Treatment (B-LIFT): A Retrospective Analysis

Aaron Smith[1], Thuyvan Phan[2], Leah Luizza[3], Anthony Trujillo[3], Becki Cleveland[1], Shruti Saxena Beem[4], Tessa Englund[5], Claire Timon[4] and Saira Sheikh[5], [1]University of North Carolina, Chapel Hill, NC, [2]UNC Health, Chapel Hill, NC, [3]University of North Carolina, Chapel Hill, [4]University of North Carolina at Chapel Hill, Chapel Hill, [5]University of North Carolina at Chapel Hill, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, multi-system autoimmune disease with heterogenous presentation. Most patients with SLE report fatigue or brain fog, which often does not respond well to standard SLE therapies. As such, even patients with well-controlled SLE often continue to have debilitating fatigue. Bupropion is a combined dopamine/norepinephrine reuptake inhibitor used in the treatment of depression. Unlike most alternative antidepressants, bupropion has a stimulating effect, and has been shown to be effective for cancer-associated fatigue. Providers at the University of North Carolina (UNC) at Chapel-Hill Rheumatology and Nephrology clinics have been prescribing bupropion off-label for the treatment of lupus-associated fatigue for several years. The purpose of this study is to better understand patient acceptability, tolerability, and response to bupropion as a treatment for lupus-associated fatigue.

Methods: We identified patients with a lupus ICD-10 code (M32.X or L93.X), who received care at the UNC Rheumatology or Nephrology clinics and were prescribed bupropion 11/2019-10/2024. Data was manually reviewed and extracted from the electronic medical record (EMR) to confirm SLE diagnoses and to identify patients who started bupropion in this timeframe for fatigue, brain fog, poor concentration, low energy, or lack of motivation/apathy. Baseline demographic characteristics, SLE activity, mental health comorbidities, medications, and response to bupropion treatment were collected. Descriptive statistics, including means, standard deviations, and frequency distributions, were calculated.

Results: Data extraction has been completed for 34 EMRs. Mean follow-up was 2.5 yrs. The median age was 45, approximately 56% of patients identified as Black or African American, and 97% female. Over half (52%) of patients had SLEDAI-2K < 4 suggestive of low lupus disease activity. Depression (53%) and anxiety (29%) were frequent comorbidities. Thirty-two percent reported improvement in energy, fatigue, concentration, low motivation/apathy, or mood during the follow-up period. Forty-one percent currently have an active prescription for bupropion and remain on this medication. The most frequent reasons for bupropion cessation include side effects (24%), lack of efficacy (18%), and loss of initial efficacy (6%). The most frequently reported side effects included insomnia (26%), headache (12%), rash (6%), anxiety (6%), and tremor (6%).

Table 1: Baseline Characteristics

Table 1. Patient baseline characteristics (n=34)	
Age, Mean (SD)	45.2 (12.9)
Race, n (%)	
Asian	1 (2.9%)
Black or African American	19 (56%)
White	12 (34%)
Other	2 (5.9%)
Hispanic, n (%)	2 (5.9%)
Female, n (%)	33 (97%)
Comorbid psychiatric conditions	
Anxiety	10 (29%)
Depression	18 (53%)
Bipolar	1 (2.9%)
Schizophrenia	0 (0.00)
Schizoaffective disorder	0 (0.00)
Other	5 (15%)
SLEDAI-2K Score n (%)	
0	10 (30%)
2	7 (21%)
4	5 (15%)
6	4 (12%)
8	3 (9.1%)
10	1 (3.0%)
12	1 (3.0%)
14	2 (6.1%)

Mean (SD) or n (%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Outcomes

Table 2. Outcomes (n=34)	
Positive response to bupropion (improvement in energy, brain fog, fatigue, concentration, low motivation/apathy,or mood)	
Recorded at any follow-up visit	11 (32%)
Side effects from bupropion at any follow-up time point	
Anxiety	2 (5.9%)
Insomnia	9 (26%)
Headache	4 (12%)
Tremor	2 (5.9%)
Palpitations	1 (2.9%)
Seizures	1 (2.9%)
Rash	2 (5.9%)
Other	10 (29%)
Reasons for bupropion discontinuation	
No effect	6 (18%)
Side effects	8 (24%)
Lost efficacy	2 (5.9%)
Lost to follow-up	1 (2.9%)
Other	1 (2.9%)
Taking bupropion at final visit	14 (41%)

n (%)

Conclusion: Bupropion may be an efficacious treatment for SLE-associated fatigue and other cognitive symptoms with few side effects. Planned next steps include assessment of outcomes of interest in all eligible patients and utilization of efficient machine learning tools for validation, in order to reduce any errors and bias introduced by human data extraction.

Disclosure: A. Smith: None; **T. Phan**: None; **L. Luizza**: None; **A. Trujillo**: None; **B. Cleveland**: None; **S. Saxena Beem**: None; **T. Englund**: None; **C. Timon**: None; **S. Sheikh**: AstraZeneca, 1, Aurinia Pharmaceuticals, 5, Biogen, 1, Cabaletta Bio, 5, GlaxoSmithKlein(GSK), 1.

Abstract Number: 2438

SGLT2 Inhibitors in SLE: Impact on Pulmonary Hypertension, Mortality, and Renal Outcomes

Ahmad Alomari[1], Asim Khanfar[2], Miguel Rodriguez[3] and Diala Alawneh[4], [1]UCF- North Florida hospital, Gainesville, FL, [2]Rochester General Hospital, Rochester, NY, [3]SIMED Rheumatology, Gainesville, FL, [4]University of Florida, Gainesville, FL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose:

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease linked to significant morbidity, including pulmonary hypertension (PH). While SGLT2 inhibitors are known for cardiovascular and renal benefits, their impact on PH in SLE remains underexplored. This study assesses the association between SGLT2 inhibitor use and reduced risks of PH, mortality, and other cardiopulmonary outcomes in SLE patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

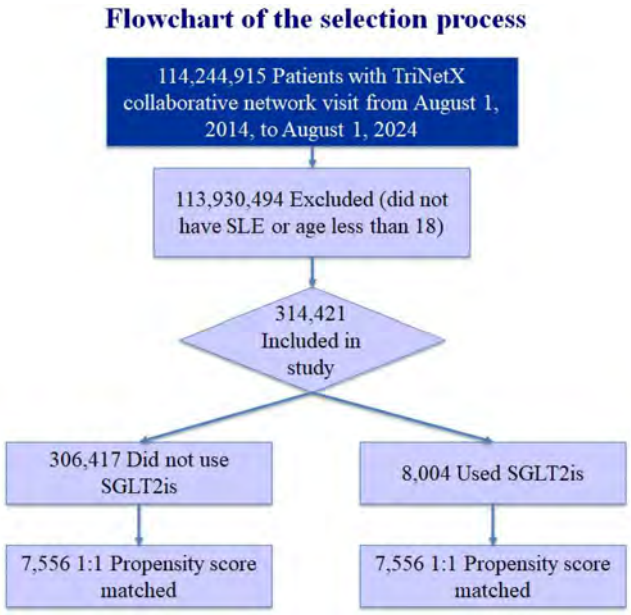
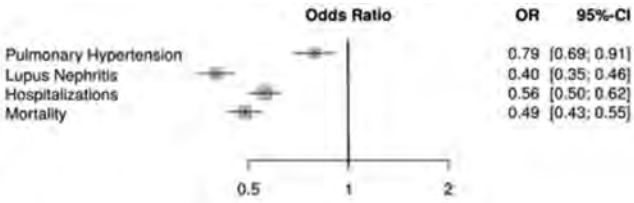


Table 1: Summary of primary and secondary outcomes with odds ratios and p-values.

Outcome	Number of Patients with Event (%)		Odds Ratio (95% CI)	P Value
	SLE with SGLT2i	SLE without SGLT2i		
Pulmonary Hypertension	368 (5.70%)	484 (7.10%)	0.79 (0.69–0.91)	0.001
Mortality	437 (5.80%)	843 (11.20%)	0.49 (0.43–0.55)	<0.001
Hospitalizations	753 (27.90%)	1,254 (40.80%)	0.56 (0.50–0.63)	<0.001
Lupus Nephritis	322 (4.90%)	863 (11.40%)	0.40 (0.35–0.46)	<0.001

Values are n (%) unless otherwise indicated.
SLE: Systemic Lupus Erythematosus.
SGLT2i: Sodium-glucose cotransporter 2 inhibitor



Forest plot summarizing odds ratios and 95% CIs for all primary and secondary outcomes.

Methods: This retrospective cohort study utilized the TriNetX Research Network to identify two cohorts of SLE patients—those prescribed SGLT2 inhibitors and non-users—between August 1, 2014, and August 1, 2024. SLE patients were identified using ICD-10 codes. Outcomes, including pulmonary hypertension (PH), mortality, hospitalizations, and lupus nephritis, were also defined using ICD-10 codes and additional codes available on the TriNetX platform. Data analysis was performed in January 2025.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Propensity score matching (PSM) in a 1:1 ratio was applied to achieve balanced baseline characteristics between the two cohorts, including demographics, steroid use, comorbidities, and SLE-specific laboratory markers. Following matching, outcomes were compared between the two groups over a follow-up period of five years. Statistical analysis was conducted using Cox proportional hazards models for time-to-event outcomes, Kaplan-Meier survival curves for visualizing survival differences, and log-rank tests to assess statistical significance between the matched cohorts.

Results: After propensity score matching, 7,556 patients were included in each cohort, ensuring balanced demographics (mean age: 61 years, 80% female, 46% White). SGLT2 inhibitor use was associated with a significantly lower incidence of pulmonary hypertension (PH) (5.7% vs. 7.1%; OR: 0.79, 95% CI: 0.69–0.91; $p < 0.001$).

All-cause mortality was reduced in the SGLT2i group (5.8% vs. 11.2%; OR: 0.49, 95% CI: 0.43–0.55; $p < 0.001$), and hospitalizations were less frequent among SGLT2i users (27.9% vs. 40.8%; OR: 0.56, 95% CI: 0.50–0.63; $p < 0.001$). Additionally, SGLT2i use was associated with a significantly lower incidence of lupus nephritis (4.9% vs. 11.4%; OR: 0.40, 95% CI: 0.35–0.46; $p < 0.001$).

Conclusion: SGLT2 inhibitors were significantly associated with reduced risk of PH, mortality, lupus nephritis, and other cardiopulmonary complications in SLE patients. These findings support the potential role of SGLT2 inhibitors as an adjunctive therapy in SLE management. Prospective studies are warranted to confirm these results.

Disclosure: A. Alomari: None; **A. Khanfar**: None; **M. Rodriguez**: None; **D. Alawneh**: None.

Abstract Number: 2439

Belimumab Versus Mycophenolate Mofetil in Lupus Nephritis: A Real-World Comparative Analysis

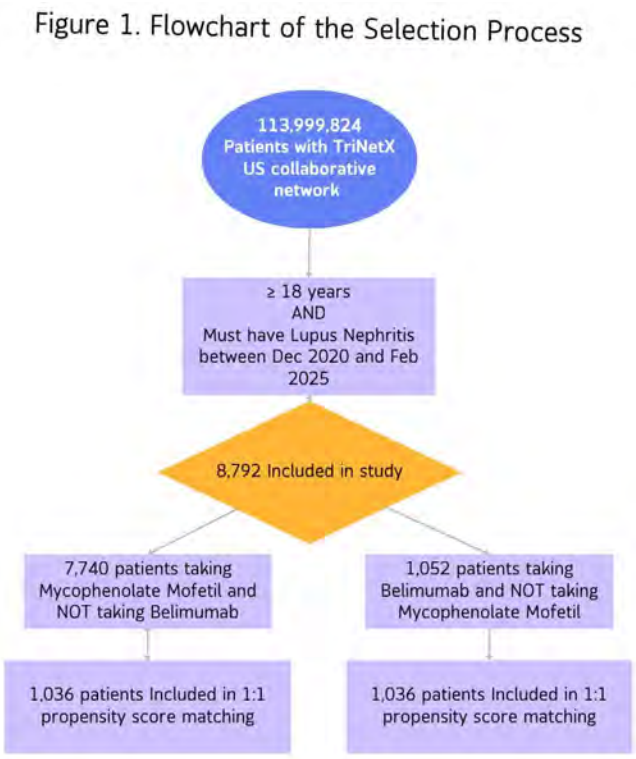
Ahmad Alomari[1], Nikita Shah[2], Miguel Rodriguez[3] and Diala Alawneh[4], [1]UCF- North Florida hospital, Gainesville, FL, [2]UCF/HCA Florida North Florida Hospital, Gainesville, FL, [3]SIMED Rheumatology, Gainesville, FL, [4]University of Florida, Gainesville, FL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE), often leading to chronic kidney disease (CKD) and end-stage renal disease (ESRD). Belimumab, a B-lymphocyte stimulator (BLyS) inhibitor, was FDA-approved for LN in 2020, offering a targeted approach to reduce B-cell activity. This study aims to compare renal outcomes in LN patients treated with Belimumab versus Mycophenolate Mofetil (MMF) using real-world data, providing insights into their relative effectiveness and safety.

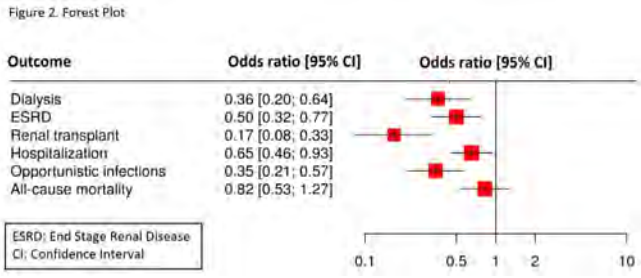
Methods: This multicenter retrospective cohort study utilized data from the TriNetX network, comprising electronic health records from 104 healthcare organizations. Adult patients (≥18 years) with lupus nephritis (LN) were identified using ICD-10 codes. Two cohorts were defined: patients receiving Belimumab (n=1,052) and those receiving mycophenolate mofetil (MMF) (n=7,740) between December 2020 and February 2025. To eliminate potential confounding, patients receiving concurrent use of both Belimumab and MMF were excluded from the analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Outcome	Number and percentage of events		Odds Ratio (95% CI)	P Value
	Belimumab (N, %)	MMF (N, %)		
Dialysis	17 (1.7%)	45 (4.7%)	0.36 (0.28–0.45)	<0.001
ESRD	33 (3.5%)	60 (6.8%)	0.50 (0.36–0.68)	0.001
Renal Transplant	10 (1.0%)	55 (5.6%)	0.17 (0.09–0.31)	<0.001
Hospitalization	71 (21.0%)	89 (29.0%)	0.65 (0.47–0.89)	0.02
Opportunistic Infections	22 (2.3%)	61 (6.3%)	0.35 (0.23–0.53)	<0.001
All-Cause Mortality	39 (3.8%)	47 (4.5%)	0.82 (0.61–1.10)	0.38

Comparative Outcomes in Belimumab vs. MMF for Lupus Nephritis



Propensity score matching (PSM) was applied to adjust for demographics, comorbidities, and laboratory values, achieving balanced baseline characteristics between the two groups. Outcomes were compared between the matched cohorts over a follow-up period of five years. The primary outcomes were end-stage renal disease (ESRD), dialysis, and renal transplant. Secondary outcomes included opportunistic infections, hospitalization, and all-cause mortality.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: After propensity score matching, 1,036 patients were included in each group. The Belimumab cohort had significantly lower odds of dialysis (OR 0.36, 95% CI 0.28–0.45, p < 0.001), ESRD (OR 0.50, 95% CI 0.36–0.68, p = 0.001), and renal transplant (OR 0.17, 95% CI 0.09–0.31, p < 0.001) compared to MMF. Additionally, Belimumab was associated with reduced hospitalization (OR 0.65, 95% CI 0.47–0.89, p = 0.02) and fewer opportunistic infections (OR 0.35, 95% CI 0.23–0.53, p < 0.001). No statistically significant difference was observed in all-cause mortality (OR 0.82, 95% CI 0.61–1.10, p = 0.38).

Conclusion: This real-world analysis suggests that Belimumab may provide superior renal outcomes compared to MMF in lupus nephritis, with reduced risks of dialysis, ESRD, and renal transplant. The findings support the potential of Belimumab as an alternative or adjunct to conventional therapy. Further prospective studies are necessary to confirm long-term efficacy and safety.

Disclosure: A. Alomari: None; **N. Shah**: None; **M. Rodriguez**: None; **D. Alawneh**: None.

Abstract Number: 2440

Effect of Cenerimod on Four Main Clinical Items of SLEDAI-2K Score in SLE Patients in a Phase 2b Study

Anca Askanase[1], **Bruno Flamion**[2], Ouali Berkani[2] and Cecile Dubois[2], [1]Columbia University Medical Center, New York, NY, [2]Viatris Innovation, Allschwil, Switzerland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Cenerimod is a selective $S1P_1$ receptor modulator that has the potential to reduce the abnormal immune response seen in Systemic lupus erythematosus (SLE) thereby leading to decreased disease activity and improved clinical outcomes for patients.

In a recent multicenter, randomized, double-blind, placebo-controlled phase 2b trial (CARE study, NCT03742037), the efficacy, safety, and tolerability of four doses of cenerimod (0.5 mg, 1 mg, 2 mg, and 4 mg) was compared to placebo in adults with moderate-to-severe SLE who were receiving standard of care background therapy. The primary endpoint was the change from baseline in mSLEDAI-2K scores from baseline to month 6. Cenerimod 4 mg is currently being investigated for the treatment of SLE in two 1-year treatment phase 3 trials (NCT05648500 and NCT05672576).

This post-hoc analysis of the CARE study was performed to compare the monthly changes (improvements) in four individual SLEDAI-2K items from baseline over 6 months between cenerimod 4 mg and placebo. These four main clinical items are: arthritis, rash, alopecia, and mucosal ulcers that are clinically significant manifestations of SLE. Arthritis affects around 82.6% of patients, rash is seen in approximately 69.2% of patients, alopecia affects about 58.2% of patients and mucosal ulcers occur in about 32.5% of patients.

Methods: The SLEDAI-2K values were measured on a monthly basis. Proportions of patients with each of the four selected SLEDAI-2K items improvements were calculated by treatment group and visit only for the cenerimod 4 mg and the placebo arm. Improvement was defined as a reduction vs baseline score.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SLEDAI-2K item	Group	Patients with involvement at baseline n (%)	Patients with improvement from baseline, n (%) Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
Arthritis	Cenerimod 4 mg	83 (97.6)	5 (6.0)	14 (16.9)	22 (26.5)	25 (30.1)	27 (32.5)	33 (39.8)
	Placebo	84 (97.7)	7 (8.3)	12 (14.3)	19 (22.6)	20 (23.8)	30 (35.7)	32 (38.1)
Rash	Cenerimod 4 mg	74 (87.1)	5 (6.8)	11 (14.9)	13 (17.6)	18 (24.3)	20 (27.0)	20 (27.0)
	Placebo	72 (83.7)	4 (5.6)	8 (11.1)	15 (20.8)	20 (27.8)	23 (31.9)	20 (27.8)
Alopecia	Cenerimod 4 mg	60 (70.6)	1 (1.7)	2 (3.3)	5 (8.3)	12 (20.0)	16 (26.7)	19 (31.7)
	Placebo	62 (72.1)	0	2 (3.2)	4 (6.5)	6 (9.7)	5 (8.1)	7 (11.3)
Mucosal Ulcers	Cenerimod 4 mg	39 (45.9)	8 (20.5)	15 (38.5)	18 (46.2)	25 (64.1)	29 (74.4)	27 (69.2)
	Placebo	44 (51.2)	8 (18.2)	6 (13.6)	17 (38.6)	20 (45.5)	21 (47.7)	20 (45.5)

≥5% greater improvement with Cenerimod vs placebo | ≥10% greater improvement with Cenerimod vs placebo | ≥5% greater improvement with placebo vs Cenerimod | ≥10% greater improvement with placebo vs Cenerimod

Proportions of patients with improvement in individual SLEDAI-2K items

Results: At baseline, involvement of individual SLEDAI-2K items was well balanced between cenerimod 4 mg and placebo arm. Numeric treatment differences ≥10% favoring cenerimod 4 mg were seen at months 4-6 for alopecia and months 2–6 (except month 3 which showed improvement of ≥5%) for mucosal ulcers. (Table 1).

Conclusion: This post-hoc analysis provided insights to the trends in improvements of four individual SLEDAI-2K clinical components when patients were treated with cenerimod 4 mg dose for 6 months. There was no obvious difference in arthritis or rash scores vs placebo. However, as compared to placebo, better early improvement was seen in alopecia (from month 4) and mucosal ulcers (from month 4) until month 6. The ongoing confirmatory Phase 3 program OPUS (NCT05648500 and NCT05672576) will further evaluate the safety and efficacy of 4 mg cenerimod in adults with SLE.

Disclosure: A. Askanase: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5; **B. Flamion**: Viatris Innovation, 3; **O. Berkani**: Viatris Innovation, 3; **C. Dubois**: Viatris Innovation, 3.

Abstract Number: 2441

Dapirolizumab Pegol Demonstrated Improvement in Quality of Life of Patients with Systemic Lupus Erythematosus: LupusQoL Results from a Phase 3 Trial

Zahi Touma[1], **Cynthia Aranow**[2], Ioannis Parodis[3], Rosalind Ramsey-Goldman[4], Matthias Schneider[5], Christine de La Loge[6], Teri Jimenez[7], Mina Nejati[8] and Laurent arnaud[9], [1]University of Toronto, Toronto, ON, Canada, [2]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [3]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden, [4]Northwestern University Feinberg School of Medicine, Chicago, IL, [5]Clinic of Rheumatology and Hiller Research Unit, Heinrich-Heine-University, Düsseldorf, Germany, [6]UCB, Brussels, Belgium, [7]UCB, Raleigh, NC, [8]Biogen, Cambridge, MA, [9]Service de rhumatologie, Hôpitaux Universitaires de Strasbourg, INSERM UMR-S 1109, Strasbourg, France, Strasbourg, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

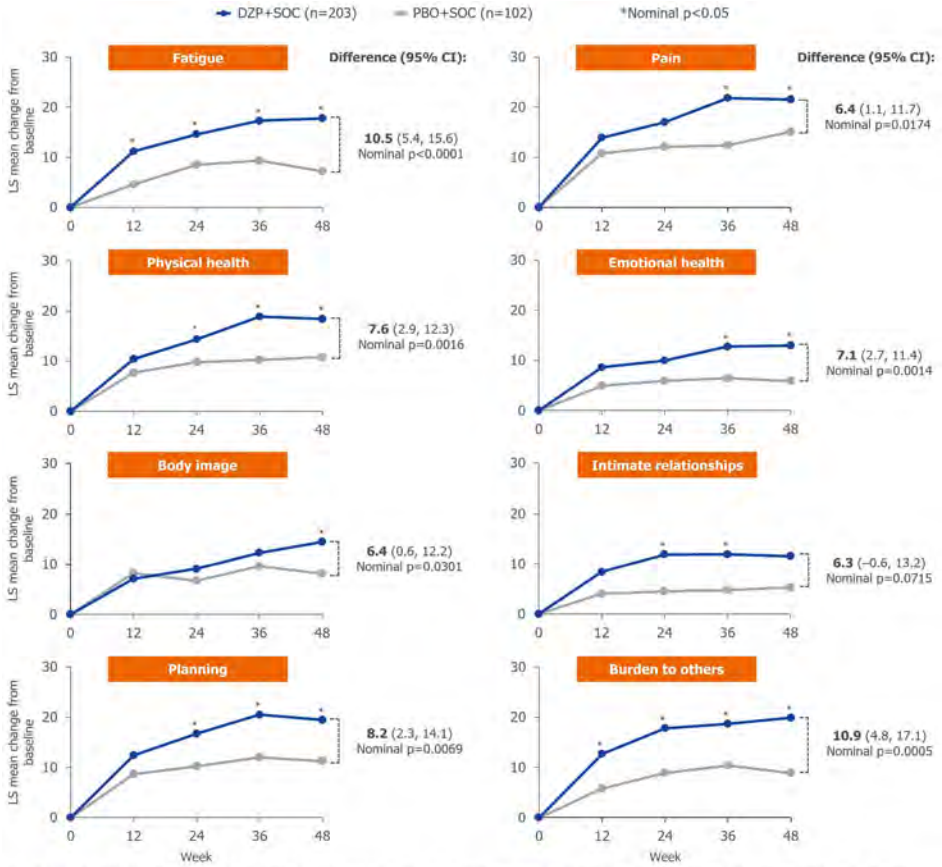
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Baseline LupusQoL domain scores

	DZP+SOC n=203	PBO+SOC n=102
LupusQoL domain scores, mean (SD)		
Fatigue	52.4 (25.6)	52.6 (24.5)
Pain	52.8 (26.1)	53.7 (25.9)
Physical health	54.2 (23.6)	55.8 (22.3)
Emotional health	66.1 (21.7)[a]	69.0 (19.9)
Body image	63.0 (24.0)[b]	64.3 (27.3)[c]
Intimate relationships	58.3 (32.4)[d]	60.0 (32.6)[e]
Planning	58.1 (29.5)	58.1 (29.3)
Burden to others	52.1 (28.3)	54.0 (27.7)

Full analysis set. [a] n=202; [b] n=184; [c] n=94; [d] n=174; [e] n=91.
DZP: dapirolizumab pegol; LupusQoL: Lupus Quality of Life; PBO: placebo; SD: standard deviation; SOC: standard of care.



Full analysis set; MMRM. All p-values are nominal and were not controlled for multiplicity. Higher LupusQoL scores correspond with better HRQoL. The LS mean, difference between DZP+SOC and PBO+SOC, 95% CIs, and p-values were computed using a MMRM.
CI: confidence interval; DZP: dapirolizumab pegol; HRQoL: health-related quality of life; LS: least square; LupusQoL: Lupus Quality of Life; MMRM: mixed model for repeated measurements; PBO: placebo; SOC: standard of care.

Figure. LS mean change from baseline in LupusQoL domain scores by visit

Background/Purpose: SLE imposes significant disease burden and diminishes health-related quality of life (HRQoL); improvement of HRQoL is therefore a key treatment goal in SLE.[1,2] Dapirolizumab pegol (DZP) is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[3,4] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain. In the phase 3 PHOENYCS GO trial (NCT04294667), the primary end-point was met; DZP plus standard of care (DZP+SOC) resulted in significantly higher rates of BILAG-based Composite

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lupus Assessment (BICLA) response vs placebo (PBO)+SOC at Week (Wk) 48.[5] We report the impact of DZP on HRQoL as measured by LupusQoL, completed by patients, in PHOENYCS GO.

Methods: PHOENYCS GO, a 48-wk, randomized, double-blind, PBO-controlled trial, included patients aged ≥16 years with moderate-to-severe, active SLE characterized by persistently active or frequently flaring/relapsing-remitting disease activity despite stable SOC medication (antimalarials, glucocorticoids and/or immunosuppressants). Patients were randomized 2:1 to intravenous DZP 24 mg/kg+SOC or PBO+SOC every 4 wks.

HRQoL outcomes were measured using LupusQoL, a patient-reported outcome based on responses on a 5-point Likert scale to 34 items across 8 domains.[1] Each domain score ranges from 0 to 100; higher scores indicate better HRQoL. The least square (LS) mean change from baseline in LupusQoL domain scores at Wk 12, 24, 36, and 48 are reported.

Results: In total, 97.6% (203/208) of patients receiving DZP+SOC and 95.3% (102/107) receiving PBO+SOC had LupusQoL responses available at any visit. Baseline LupusQoL scores were comparable between the treatment groups (**Table**).

Patients receiving DZP+SOC demonstrated consistently greater improvements from baseline over time in LupusQoL scores across all domains compared with PBO+SOC (**Figure**). Patients receiving DZP+SOC reported greater improvements in the 'Fatigue' and 'Burden to others' domains at all assessed visits compared with those receiving PBO+SOC, as of Wk 12 (all nominal $p < 0.05$). Additionally, greater improvements were reported for patients receiving DZP+SOC compared with PBO +SOC in the 'Physical health' and 'Planning' domains at Wks 24, 36, and 48, in the 'Pain' and 'Emotional health' domains at Wks 36 and 48, in the 'Intimate relationships' domain at Wks 24 and 36, and in the 'Body image' domain at Wk 48 (each nominal $p < 0.05$).

Conclusion: Improvements in HRQoL were greater in patients treated with DZP+SOC compared with PBO+SOC across all LupusQoL domains, starting at the earliest time point (Wk 12) for some domains. These data, along with the previously reported significant improvements in overall disease activity,[5] support the potential of DZP as a valuable treatment option in SLE to improve HRQoL.

References: 1. McElhone K. Arthritis Care Res 2007;57:972–9; **2**. Fanouriakis A. Ann Rheum Dis 2019;78:736–45; **3**. Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); **4**. Powlesland A. Annals Rheum Dis 2024;83 (suppl 1):261; **5**. Clowse M. Arthritis Rheumatol 2024;76 (suppl 9).

Disclosure: Z. Touma: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2; **M. Schneider**: AbbVie, 2, AstraZeneca, 2, 5, 6, BMS, 2, GSK, 2, 5, 6, Novartis, 2, Otsuka, 2, Roche, 2; **C. de La Loge**: UCB, 2; **T. Jimenez**: UCB, 3, 12, Shareholder; **M. Nejati**: Biogen, 3, 12, Shareholder; **L. arnaud**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 6, Boehringer-Ingelheim, 2, 6, Eli Lilly, 2, 6, Grifols, 2, 6, GSK, 2, 5, 6, Janssen, 2, 6, Kezar, 2, LFB, 2, 6, Medac, 2, 6, Merck, 2, Nordic Pharma, 2, Novartis, 2, 6, Pfizer, 2, 6, Roche-Chugaï, 2, 6, UCB, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2442

Reduction in Extrafollicular B Cell Responses in SLE Patients after CAR T Cell Therapy

Danae-Mona Nöthling[1], Kirill Anoshkin[1], Panagiotis Garantziotis[1], Laura Bucci[1], Tobias Rothe[2], Jule Taubmann[3], Futoshi Iwata[1], Melanie Hagen[1], Andreas Wirsching[1], Simon Völkl[4], Fabian Müller[5], Aline Bozec[1], Andreas Mackensen[6], Georg Schett[7] and Ricardo Grieshaber-Bouyer[8], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlagen, Germany, [3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [4]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [5]University Hospital of Erlangen, Erlangen, Germany, [6]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) and Uniklinikum Erlangen, Erlangen, Germany, [7]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [8]University Hospital Erlangen, Erlangen, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is characterized by aberrant B cell activation and autoantibody production. CD19-targeted chimeric antigen receptor (CAR) T-cell therapy induces a short, deep B cell depletion and showed promising clinical efficacy in patients with refractory SLE. However, it is poorly understood how the B cell system evolves after reconstitution and whether pathogenic immune phenotypes reemerge.

Methods: 18 patients with active, refractory SLE (15 with lupus nephritis) received autologous CD19-CAR T-cell therapy. Longitudinal, high dimensional phenotyping of blood B cells was performed using spectral flow cytometry. B cells were analyzed before therapy (N = 18), at first reappearance (N = 14) and at early (3-6 months, N = 10), late (12+ months, N = 10) and long-term (median 24 months) reconstitution. B cells from 10 healthy donors were included as control.

scRNA-Seq was performed at baseline and early reconstitution.

Results: Patients with active SLE showed aberrant B cell subsets and frequencies, including an increase in circulating plasmablasts and IgD– CD27– double negative (DN) memory B cells. CAR T cell therapy led to transient depletion of CD19+ B cells in all patients. After a median follow up of 17 (range: 3 – 36) months, B cells had reconstituted in 14/18 (78%) of patients. B cells recovered between 28 to 420 (mean: 169) days after CAR T, with a transient increase in immature B cells during reconstitution. At reconstitution and 6 months thereafter, the new B cell compartment consisted predominantly of CD20+ IgD+ CD27– naïve B cells. Accordingly, all other subsets, including switched and unswitched memory B cells and circulating plasmablasts were reduced. HLA-DR expression was decreased after reconstitution, indicating reduced stimulation. Surprisingly, IgD– CD27– double negative (DN) and Tbet+ age associated B cells (ABCs), reappeared one year after CAR-T cell therapy. However, fresh DN cells consisted almost exclusively of CXCR5+ CD11c– Tbet– DN1 cells, whereas disease associated CD11c+ CXCR5– Tbet+ DN2 cells stayed reduced, constituting less than 5% of peripheral CD19+ B cells. This was confirmed by identification of DN2 cells in scRNA-Seq showing reduced frequencies after therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Concordantly, new switched memory B cells, which slowly reappeared after a mean of 12 months after therapy, were mostly CXCR5+, while CXCR5– switched memory B cells were not accumulated. New plasmablasts were rarely detected (< 1% of CD19+ cells) and displayed substantially reduced activation ($CD95^{low}$ $HLA\text{-}DR^{low}$). Frequencies of atypical B cell subsets remained low and indistinguishable from healthy individuals even at late follow-up.

Conclusion: Deep B cell depletion, as mediated via CD19-CAR T cell therapy, profoundly remodels the B cell compartment. New B cells appear to predominantly repopulate from $CXCR5^{+}$ cells, suggesting less utilization of extrafollicular B cell maturation pathways. Accordingly, new B cells display overall reduced activation levels, while disease-associated DN2 cells, atypical B cell subsets and activated plasmablasts remained cleared long after reconstitution. These changes indicate a deep and durable reset of adaptive immunity even long after B cell reconstitution.

Disclosure: D. Nöthling: None; **K. Anoshkin**: None; **P. Garantziotis**: None; **L. Bucci**: None; **T. Rothe**: None; **J. Taubmann**: None; **F. Iwata**: None; **M. Hagen**: None; **A. Wirsching**: None; **S. Völkl**: None; **F. Müller**: AbbVie/Abbott, 6, ArgoBIO, 2, AstraZeneca, 2, 6, Beigene, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CRISPR Therapeutics, 2, EcoR1, 2, Incyte, 6, Janssen, 2, 6, Kite/Gilead, 2, 5, 6, Merck/MSD, 6, Miltenyi, 2, 6, Novartis, 2, 6, Pfizer, 6, Sobi, 2, 6, Takeda, 6; **A. Bozec**: None; **A. Mackensen**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6.

Abstract Number: 2444

Hydroxychloroquine-Induced Retinopathy in Systemic Lupus Erythematosus: Predictors of Progression Following Drug Discontinuation

Emily Gutowski[1], Jessica Dai[2], Erin Carter[3], Brooke Cohen[4], Jill Buyon[5], Chung-E Tseng[6], Mala Masson[7], Amit Saxena[5], H Michael Belmont[8], Joseph Colcombe[6], Yasha Modi[3], Carol Lee[6] and Peter Izmirly[9], [1]New York University Grossman School of Medicine, Brooklyn, NY, [2]New York University Grossman School of Medicine, Tenafly, NJ, [3]New York University Grossman School of Medicine, New York, NY, [4]Yale Physician Associate Program, New Haven, CT, [5]NYU Grossman School of Medicine, New York, NY, [6]New York University Grossman School of Medicine, New York, [7]NYU Langone Health, New York, [8]NYU School of Medicine, New York, NY, [9]New York University Grossman School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) is a cornerstone of systemic lupus erythematosus (SLE) management, but long-term use carries the risk of retinopathy. While prior studies have identified risk factors for HCQ-induced retinopathy and described varying degrees of progression even after drug discontinuation, existing literature is limited by small sample sizes. We aimed to characterize a cohort of SLE patients with confirmed HCQ retinopathy to identify factors associated with progression after discontinuation.

Methods: We queried an urban multi-ethnic lupus cohort (all ACR/SLICC or EULAR criteria longitudinally followed) for patients who had evidence of HCQ-induced retinopathy and identified 59 of 1,530 with documented retinopathy diagnoses. Of these, 28 had records available to confirm the onset of retinopathy and at least one ophthalmology follow-up to assess for progression. We conducted a chart review of these 28 patients and captured cumulative HCQ exposure, ophthalmologic screening adherence, and SLE activity preceding and following drug cessation. Ophthalmology notes were reviewed to assess for stability or progression of OCT imaging and/or Humphrey Visual Fields after discontinuation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic characteristics of cohort.

Sex		N (%)
	Female	26 (93%)
	Male	2 (7%)
Race		
	White	13 (46%)
	Asian	9 (32%)
	Black	5 (18%)
	Other	1 (4%)
Ethnicity		
	Non-Hispanic	9 (32%)
	Hispanic	19 (68%)

Factor	Progressed	Did not progress	P-value
Age (years)	Mean: 60.3 Median: 61	Mean: 49.7 Median: 50	**0.033**
Cumulative HCQ exposure (g)	Mean: 2033.7 Median: 1365.0	Mean: 1329.6 Median: 1204.5	0.704 (NS)
Duration of HCQ therapy (years)	Mean: 13.67 Median: 13	Mean: 13.87 Median: 16	0.949 (NS)
Ophthalmology visit interval	≤1 year: 87.5% >1 year: 12.5% Unknown: 0%	≤1 year: 53.3% >1 year: 13.3% Unknown: 33.3%	0.176 (NS)
SLEDAI-2K score	Mean: 2.3 Median: 3.0	Mean: 2.5 Median: 2.0	0.885 (NS)
SLICC Damage Index	Mean: 3.8 Median: 3.0	Mean: 3.8 Median: 3.0	0.501 (NS)

Results: Among 28 patients with confirmed HCQ retinopathy, 13 (46%) were White, 9 (32%) Asian, 5 (18%) Black, and 1 (4%) other; 9 patients (32%) identified as Hispanic; 26 (93%) were female. The average age at diagnosis was 53.3 years. The mean cumulative HCQ exposure across all patients with retinal toxicity was 1,827 g (SD 1,442 g) over a mean of 14.0 years (SD 8.1). Most patients (57%) were seeing ophthalmology at least yearly, while a smaller proportion (18%) had screening lapses preceding their diagnosis. At diagnosis of retinopathy, the mean SLEDAI-2K score was 2.3, and the average SLICC Damage Index was 3.13.

Retinal toxicity progressed in 35% of patients despite drug discontinuation. Patients who progressed were significantly older than those who did not (60.3 vs 49.7 years, p = 0.033). No statistically significant associations were found between retinopathy progression and race, ethnicity, cumulative HCQ exposure, duration of therapy, SLICC Damage Index, SLEDAI-2K or ophthalmology screening interval.

Conclusion: In this SLE-specific cohort with confirmed HCQ-induced retinopathy, retinal toxicity progressed in a third of patients despite HCQ discontinuation. There was a significant association between age and retinopathy progression despite equivalence of cumulative dosing and ophthalmologic screening intervals. These findings support the consideration of more frequent monitoring in older patients.

Disclosure: E. Gutowski: Run the List, 12, Creator of podcast (runs ads including those for medical tools, e.g., Open Evidence); **J. Dai**: None; **E. Carter**: None; **B. Cohen**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **C. Tseng**: None; **M. Masson**: None; **A. Saxena**: AbbVie/Abbott, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, 6, Bristol-Myers Squibb(BMS), 1, GlaxoSmithKlein(GSK), 5, Synthekine, 1, 2, UCB, 1, 6; **H. Belmont**: None; **J. Colcombe**: None; **Y. Modi**: 4DMT, 2, AbbVie/Abbott, 2, Alcon, 2, Eyepoint, 2, Genentech, 2, Neurotech, 2, Regeneron, 2, topcon, 2, Zeiss, 2; **C. Lee**: None; **P. Izmirly**: Hansoh Bio, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2445

Achievement of Treat to Target Measures with Upadacitinib in Patients with Systemic Lupus Erythematosus: Phase 2 Randomized Sleek Clinical Trial Results

Eric Morand[1], Joan Merrill[2], Martin Aringer[3], Zahi Touma[4], Richard Furie[5], Karim Masri[6], Christopher Saffore[7], Ling Cheng[8] and Ronald van Vollenhoven[9], [1]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [2]Oklahoma Medical Research Foundation, Oklahoma City 73104, OK, [3]University Medical Center, Dresden, Germany, [4]University of Toronto, Toronto, ON, Canada, [5]Division of Rheumatology, Northwell Health, Great Neck, NY, [6]AbbVie Inc., North Chicago, IL, [7]AbbVie Inc., waukegan, IL, [8]AbbVie, North, IL, [9]Department of Rheumatology, Amsterdam University Medical Centre, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

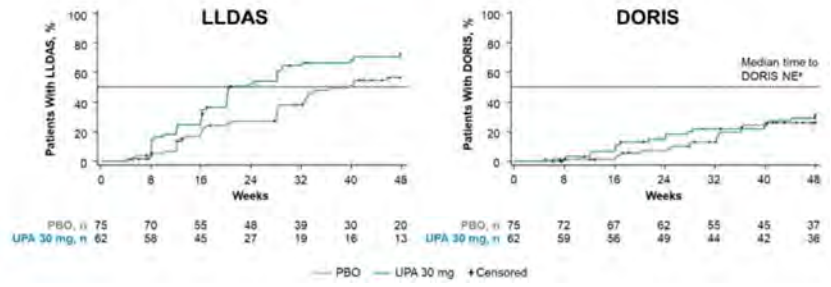
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Achievement of treat-to-target measures Lupus Low Disease Activity State (LLDAS) and Definition of Remission in SLE (DORIS) has been associated with improved outcomes and quality of life in patients with systemic lupus erythematosus (SLE).[1,2] Upadacitinib (UPA), an oral, selective JAK inhibitor, reduced SLE disease activity in the phase 2, randomized, double-blind SLEek study (NCT03978520) of adults with moderately to severely active SLE.[3] In this post hoc analysis of SLEek, we evaluate the achievement of LLDAS and DORIS with upadacitinib (UPA) monotherapy (30 mg) vs placebo (PBO).

Methods: LLDAS was defined as meeting a clinical SLE Disease Activity Index 2000 (SLEDAI-2K) score ≤ 4, absence of SLE disease activity in major organ systems, no new disease activity, by clinical criteria including SLE Disease Activity Index 2000 (SLEDAI-2K) score ≤ 4, no major organ activity, a Physician Global Assessment (PhGA) score ≤ 1, glucocorticoid (GC) dose ≤ 7.5 mg/day, and stable maintenance doses of standard immune-modulating drugs. In this analysis, DORIS was defined as meeting a clinical SLEDAI-2K score of 0, PhGA score < 0.5, GC ≤ 5 mg/day, and stable maintenance doses of standard immune-modulating drugs but with stricter criteria. Data were reported based on nonresponder imputation incorporating multiple imputation for missing data due to COVID-19. Between-group differences were adjusted using the Cochran-Mantel-Haenszel test and Cox proportional hazard model; adjustments were made for SLEDAI-2K score at screening (<

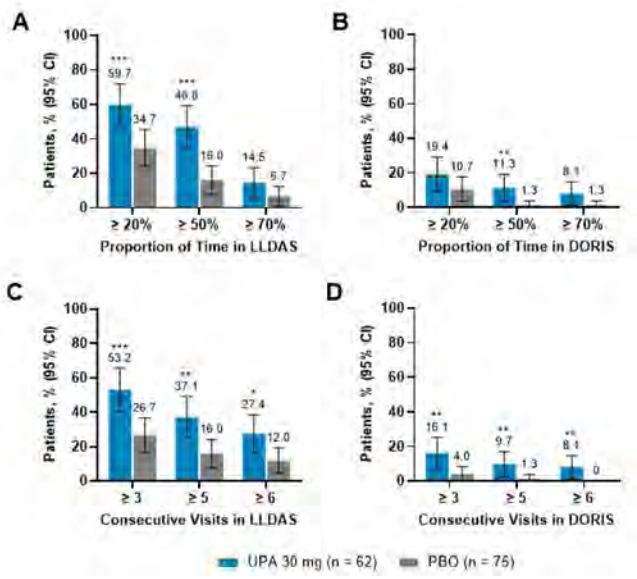
Figure 1. Time to First Reaching LLDAS or DORIS



DORIS, Definition of Remission in SLE; LLDAS, Lupus Low Disease Activity State; NE, not estimable; PBO, placebo; SLE, systemic lupus erythematosus; UPA, upadacitinib. Horizontal dashed lines are located at 50% on the y-axis. Vertical dashed lines represent the median time to first response for each treatment group. aThe median time to reach DORIS could not be estimated due to < 50% of participants reaching DORIS at any time point for either treatment group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Cumulative Time in (A) LLDAS and (B) DORIS and Sustained Consecutive Monthly Visits in (C) LLDAS and (D) DORIS



DORIS, Definition of Remission in SLE; LLDAS, Lupus Low Disease Activity State; PBO, placebo; SLE, systemic lupus erythematosus; UPA, upadacitinib. *P < .05; ** P < .01; *** P < .001 vs placebo.

10 or ≥ 10), baseline GC dose (< 10 mg or ≥ 10 mg), baseline immunosuppressant use (yes or no), and baseline IFN score (high, low, or not applicable). No multiplicity adjustments were applied; all P values are nominal.

Results: Data were included from 137 patients (UPA 30 mg, n = 62; PBO, n = 75; female: 96.4%, White: 56.2%). Rates of achievement of LLDAS and DORIS, respectively, with UPA vs PBO at week 48 were 50.0% vs 24.0% (P < 0.001) and 19.4% vs 9.3% (P = 0.063). Median time to first achievement of LLDAS was shorter with UPA vs PBO (20.4 vs 39.9 weeks; HR [95% CI]: 2.0 [1.2, 3.2]; P = 0.005); median time to DORIS could not be estimated due to < 50% of patients achieving DORIS at any time point (**Figure 1**). Cumulative % of time spent in LLDAS and DORIS was greater with UPA vs PBO; LLDAS: LS mean [95% CI]: 28.9% [19.8, 38.1] vs 12.5% [4.6, 20.5]; P = 0.001; DORIS: 9.1% [3.4, 14.7] vs 3.0% [–1.9, 8.0]; P = 0.051. Higher proportions of patients were in LLDAS or DORIS for various cumulative proportions of time with UPA vs PBO, and the proportions of patients who sustained LLDAS or DORIS for ≥ 3, ≥ 5, and ≥ 6 consecutive monthly visits were higher with UPA vs PBO (P < 0.05 for all; **Figure 2**).

Conclusion: Patients with SLE who received UPA achieved higher rates of LLDAS and DORIS, had a shorter time to first LLDAS, spent more cumulative time in LLDAS and DORIS, and experienced more consecutive visits in these states versus PBO. These data support the potential benefit of UPA in achieving stringent SLE treat-to-target measures.

Disclosure: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **J. Merrill**: AbbVie, 2, Alexion, 2, Almiral, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, Biogen, 2, BMS, 2, 5, Eli Lilly, 2, EMD Serono, 2, Equillium, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Kezar, 2, Merck, 2, Novartis, 2, Ono, 2, Remegen, 2, Sanofi, 2, Takeda, 2, Tenent, 2, UCB, 2, Veloxis, 2, Zenas, 2; **M. Aringer**: AbbVie/Abbott, 1, AstraZeneca, 1, Eli Lilly, 1, GlaxoSmithKlein(-GSK), 1, Novartis, 1; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **R. Furie**: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc.,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **K. Masri**: AbbVie, 3, 11; **C. Saffore**: AbbVie, 3, 11; **L. Cheng**: AbbVie/Abbott, 3, 11; **R. van Vollenhoven**: AbbVie, 2, 6, Alfasigma, 5, AstraZeneca, 2, 5, 6, Biogen, 2, 6, BMS, 2, 5, 6, Galapagos, 2, 5, 6, GSK, 2, 6, Janssen, 2, 6, MSD, 5, Novartis, 5, Pfizer, 2, 5, 6, RemeGen, 2, 6, Roche, 5, Sanofi, 5, UCB, 2, 5, 6.

Abstract Number: 2446

Use of Voclosporin in Pediatric Patients: A Summary of Available Data from Post-marketing Reports

Eugenia Chock[1], Ankana Daga[2], Tasim Begum[3], Kathryn Dao[3] and Michelle Dardeno[3], [1]Yale School of Medicine, New Haven, CT, [2]Boston Children's Hospital, Boston, MA, [3]Aurinia Pharmaceuticals Inc., Rockville, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Lupus nephritis (LN) is common in pediatric patients with systemic lupus erythematosus (SLE), with more than 50% developing renal manifestations, typically within the first 2 years. Treatment options for this patient population have been inadequately studied.[1]

Voclosporin is approved for use in adult patients with active LN. The Phase 3 AURORA studies showed that in patients ≥18 years, adding voclosporin to MMF and low-dose glucocorticoids yielded significant reductions in proteinuria with no unexpected safety signals associated with up to 3 years of treatment.[2,3]

The safety and efficacy of voclosporin in patients < 18 years old has not been established. A study in the pediatric population is ongoing (Voclosporin in Adolescents with Lupus Nephritis [VOCAL; NCT05288855]). There have been reports of off-label voclosporin use in patients < 18 years captured in Aurinia's global safety database as part of post-marketing spontaneous safety surveillance. Our objective was to summarize the post-marketing experience with voclosporin in the pediatric population.

Table 1. Summary of Serious Adverse Events

Serious reported adverse events*, n (%)	18/93 (19%)
Hospitalization	14
Reason unknown, after voclosporin initiation	2
Reason unknown, before voclosporin initiation	1
Reason unknown, unknown timing in relation to voclosporin	1
High creatinine and full blood count decreased	1
Asthma attack	1
High blood pressure	1
Sepsis	1
High potassium	1
Kidney problems	1
Lupus flare	1
Lupus flare, acute kidney injury, and COVID-19	1
Liquid retention	1
Urinary tract infection	1
Medically Significant	4
Renal failure	1
Stills disease	1
Seizure	1
Chronic kidney disease and hydrocephalus	1

*Events described as reported and entered in the Aurinia Global Safety Database.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Data included in this analysis were collected up until January 21, 2025, from the Aurinia Global Safety Database, which contains spontaneous, post-marketing reports of pediatric use. Post-marketing safety data are collected via a passive surveillance system with limitations, including possible underreporting, biased or incomplete reporting, and difficulties in attributing an adverse event (AE) to any specific drug. Use of voclosporin in patients < 18 years is considered an off-label use and is tracked in the safety database even in the absence of associated AEs. Data from the ongoing VOCAL study are not included in this analysis.

Results: As of January 21, 2025, 93 reports of pediatric use of voclosporin (in 70 unique patients) had been received, the majority from the US. Patients ranged in age from 7 to 17 years old and were mostly female. The most common indication for voclosporin was LN (83.8%). In most cases, the dose of voclosporin administered was the approved adult dose (23.7 mg twice daily; 57/93 reports). The duration of use of voclosporin was not consistently reported; where reported, the duration ranged from several weeks to 1 year, 9 months. In total, 44 of the 93 (47%) individual reports of pediatric use did not include any associated AEs following the initiation of voclosporin other than off-label use and other non-health-related events (ie. therapy interrupted, missed dose, insurance issue). Of the individual reports of pediatric use with associated AEs, 18 were considered to be serious (Table 1). There were no particular trends in the AEs reported. Data on kidney biopsies and concomitant medications were not consistently available.

Conclusion: Due to the limited number of reports and incomplete nature of spontaneous reporting, the emerging safety profile of voclosporin in pediatric patients requires further investigation, although no new safety signals were detected. Additional research is needed to better characterize the use of voclosporin in this population.

1. Wenderfer SE, et al. *Pediatr Clin North Am*. 2019;66(1):87-99.

2. Rovin BH, et al. *The Lancet*. 2021;397(10289):2070-2080.

3. Saxena A, et al. *Arthitis Rheum*. 2024;76(1)59-67.

Disclosure: E. Chock: None; **A. Daga**: None; **T. Begum**: Aurinia Pharmaceuticals Inc., 3, 11; **K. Dao**: Aurinia Pharmaceuticals Inc., 3, 11; **M. Dardeno**: Aurinia Pharmaceuticals Inc., 3, 11.

Abstract Number: 2447

Longitudinal Disease Activity Trajectories in Patients with Systemic Lupus Erythematosus Treated with Belimumab

Fumin Qi[1], Yin Zhao[2], Wei Bian[1], Jian Hao[1], Na zhang[1] and Wei Wei[1], [1]Tianjin Medical University General Hospital, Tianjin, China (People's Republic), [2]Affiliated Hospital of Yunnan University, Yunnan, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: To investigate the longitudinal disease activity trajectories in patients with systemic lupus erythematosus (SLE) treated with belimumab.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

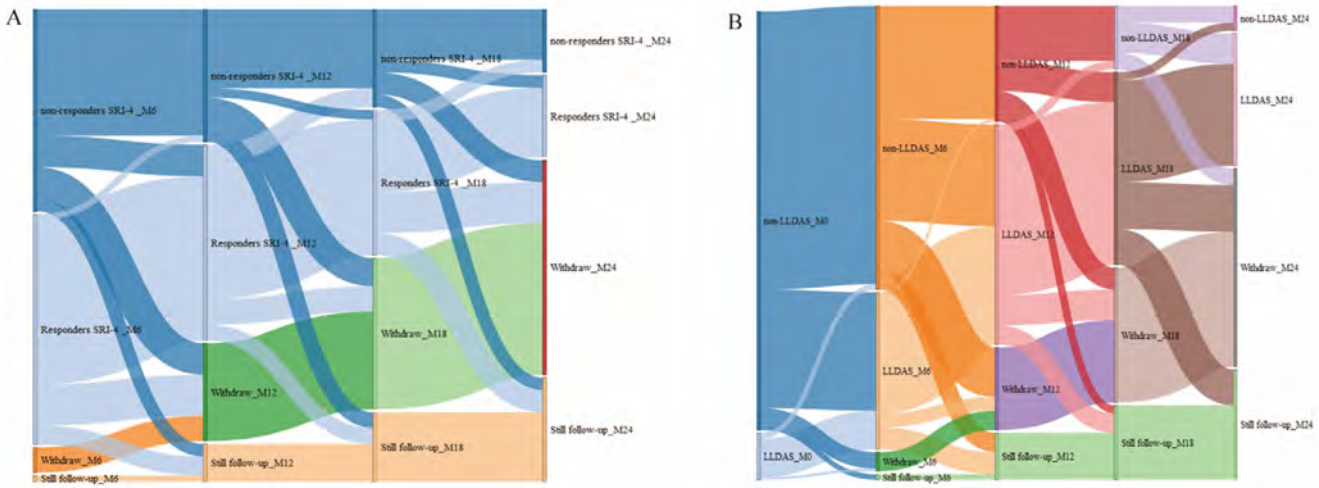


Figure 1. Changes in the number of SRI-4 and LLDAS responders at different time points during the follow-up period.

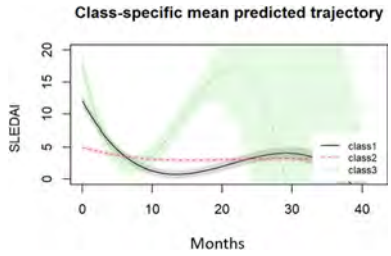


Figure 2. SLEDAI-2K score trajectories in patients with SLE with belimumab during follow-up.

Table 1. Exploring risk factors for different trajectory groups through a multinomial logistic regression.

	Slow improvement（vs Rapid Improvement）			Slow Improvement（vs Disease Fluctuation）			Rapid Improvement（vs Disease Fluctuation）		
	OR	95%CI	p value	OR	95%CI	p value	OR	95%CI	p value
Glucocorticosteroid	0.782	0.693-0.883	***0.000***	0.542	0.378-0.775	***0.001***	0.692	0.487-0.984	***0.040***
Kidney involvement	0.322	0.127-0.817	***0.017***	0.642	0.028-14.919	0.783	1.995	0.086-46.339	0.667
Joints involvement	0.283	0.108-0.740	***0.010***	0.110	0.009-1.407	0.090	0.390	0.030-5.001	0.469
Hematologic Involvement	0.402	0.155-1.040	0.060	3.643	0.264-50.217	0.334	9.070	0.680-121.063	0.095
Anti-SSA antibody positive	0.764	0.313-1.868	0.555	25.73 8	1.141-580.339	***0.041***	33.67 9	1.519-746.556	***0.026***
MMF	0.798	0.309-2.064	0.642	0.015	0.000-0.821	***0.040***	0.019	0.000-0.994	0.050
SLE disease course (ref.≥7 years)	0.282	0.108-0.735	***0.010***	0.136	0.011-1.730	0.124	0.481	0.037-6.249	0.576
Total B lymphocytes % (ref. ≥9%)	2.185	0.848-5.635	0.106	0.289	0.024-3.543	0.332	0.132	0.011-1.646	0.116

Methods: A prospective cohort of SLE treated with belimumab was established, with record assessments every 3 months after baseline and every 6 months after 12 months of belimumab infusion. Patients' baseline clinical data, SLE disease assessment data, and treatment regimens were collected, and latent class trajectory modeling was used to identify the trajectory of change in patients' SLE Disease Activity Index 2000 (SLEDAI-2K) scores during the follow-up period and multinomial logistic regression analyses were used to assess the baseline clinical characteristics associated with each group.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 169 patients with SLE with belimumab were enrolled in the study, including 155 females (91.7%). The median age of patients at baseline was 34 years, and the median duration of SLE was 7 years. The baseline SLEDAI score of the enrolled patients was 7.8±5.1. Three different SLEDAI-2K score change trajectories were identified through trajectory modeling: 24.3% in the rapid improvement group, 71.0% in the slow improvement group, and 4.7% in the disease fluctuation group. Of the three groups, patients in the disease fluctuating group were more likely to have renal involvement (*P*=0.012) and had the highest baseline urinary protein quantification (*P*=0.000), compared to the slow improvement group, and patients in the slow improvement group had the lowest baseline prednisone dose of the three groups (*P*=0.000). Using multinomial logistic regression analysis, it was found that SSA antibody positivity was more closely associated with patients in the slow improvement group (OR 25.738, *P*=0.041) or the rapid improvement group (OR 33.679, *P*=0.026) compared to patients in the fluctuating group.

Conclusion: SLEDAI-2K changes in SLE patients treated with belimumab can be divided into three different response trajectory groups: the rapid improvement group, the disease fluctuating group, and the slow improvement group. Early initiation of belimumab in patients with active SLE may enhance their therapeutic response and improve their prognosis. In patients with lupus nephritis, regular follow-up can help detect disease recurrence at an early stage and reduce the overall risk of disease damage.

Disclosure: F. Qi: None; **Y. Zhao**: None; **W. Bian**: None; **J. Hao**: None; **N. zhang**: None; **W. Wei**: None.

Abstract Number: 2448

Rituximab as the first line treatment in newly diagnosed systemic lupus erythematosus

Haiting Wang[1], Liling Zhao[2], Shuang Ye[3] and Shaoying Yang[2], [1]Renji Hospital, Rockville, MD, [2]Renji hospital, Shanghai, China (People's Republic), [3]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Rituximab (RTX) has been commonly used for the treatment of patients with severe or refractory systemic lupus erythematosus (SLE), yet real-world data concerning RTX as the first-line treatment in newly diagnosed moderate-to-severe SLE patients is lacking.

Methods: We conducted a retrospective cohort study using a newly diagnosed (< 3 months) hospitalized Systemic Lupus Inception Cohort (hSLIC) at our center between 1 April 2013 and 1 September 2022. All patients were followed up for at least 12 months or until death. The cohort included patients on RTX (n=104) as the first-line treatment and those on conventional immunosuppressants (IS) (n=154) as comparators. Propensity score-based inverse probability of treatment weighting (IPTW) was used to minimize possible confounding factors. Primary outcome analyses included attainment of modified lupus low disease activity state (mLLDAS) and remission, by 12 months. Secondary outcomes focused on mortality, major flare rates, and the incidence of adverse events of interest, i.e., major infections.

Results: After IPTW, 76.0%/50.5% of RTX-treated patients achieved mLLDAS/remission versus 45.8%/9.7% in the conventional IS group during 12 months follow-up, respectively (p=0.005 and p< 0.001). Sensitivity analyses with renal or neuropsychiatric lupus removal and timeline breakout (pre versus post November 2019) confirmed the robustness of RTX's

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

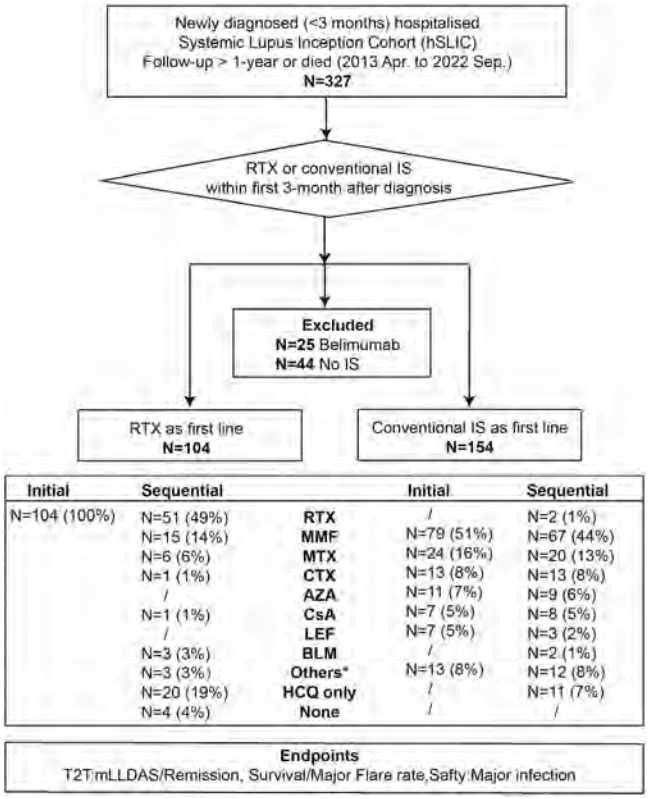


Figure 1. Flow chart of the study. Data are number (%) of patients. RTX: rituximab; IS: immunosuppressants; MMF: mycophenolate mofetil; MTX: methotrexate; CTX: cyclophosphamide; AZA: azathioprine; CsA: cyclosporine A; LEF: leflunomide; BLM: belimumab; Pred: prednisone; HCQ: hydroxychloroquine; T2T: treat-to-target; mLLDAS: modified lupus low disease activity state. *Other IS including tripterygium glycoside, tacrolimus, thalidomide and tofacitinib.

Table 1. Patient characteristics in the rituximab and conventional immunosuppressant groups before and after IPTW. Data are mean (SD) or number (%) of patients. IPTW: inverse probability of treatment weighting; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; BILAG: British Isles Lupus Assessment Group; IS: immunosuppressants; APL: antiphospholipid antibody; Prednisonemax(mg/day): The highest daily dose of intravenous methylprednisolone administered during the initial hospitalization period; Methylprednisolone pulse (%): Proportion of patients who received intravenous methylprednisolone pulse therapy, defined as ≥500 mg/day for 3 to 5 consecutive days, during the initial hospitalization period.

Variables	Before IPTW			After IPTW		
	Rituximab n=104	Conventional IS n=154	P value	Rituximab n=104	Conventional IS n=192	P value
Demographic characteristics						
Age (years)	32.4 (13.2)	37.25 (13.8)	**0.005**	30.21 (14.12)	33.13 (13.19)	0.424
Gender, n (%female)	102 (98.1)	132 (85.7)	**0.002**	80.9 (77.9)	176.8 (92.0)	0.219
Clinical manifestations						
SLEDAI-2K score	13.79 (7.72)	12.44 (5.68)	0.106	12.35 (6.31)	13.52 (6.31)	0.363
BILAG category						
General (%)	48 (46.2)	71 (46.1)	1	35.5 (34.2)	68.0 (35.4)	0.909
Mucocutaneous (%)	53 (51.0)	94 (61.0)	0.14	44.7 (43.1)	85.2 (44.4)	0.917
Neuropsychiatric (%)	27 (26.0)	6 (3.9)	**<0.001**	13.2 (12.7)	54.4 (28.3)	0.102
Musculoskeletal (%)	26 (25.0)	48 (31.2)	0.35	22.1 (21.3)	42.0 (21.9)	0.938
Cardiorespiratory (%)	64 (61.5)	96 (62.3)	1	71.0 (68.3)	117.9 (61.3)	0.537
Gastrointestinal (%)	9 (8.7)	8 (5.2)	0.399	7.0 (6.8)	18.6 (9.7)	0.608
Renal (%)	27 (26.0)	62 (40.3)	**0.025**	45.2 (43.5)	60.4 (31.5)	0.383
Haematological (%)	29 (27.9)	34 (22.1)	0.359	21.0 (20.2)	50.7 (26.4)	0.477
Serological markers						
Low Complement 3 (g/L)	88 (84.6)	130 (84.4)	1	91.6 (88.2)	170.0 (88.5)	0.943
Anti-dsDNA (%)	73 (70.2)	108 (70.1)	1	75.9 (73.0)	108.0 (56.2)	0.144
APL (%)	19 (18.3)	23 (14.9)	0.589	16.9 (16.3)	36.6 (19.1)	0.759
Treatment						
$Prednisone_{max}$ (mg/day)	189 (188)	120 (123)	**<0.001**	140(149)	173(170)	0.443
Methylprednisolone pulse (%)	17 (16.3)	11 (7.1)	0.033	10.9 (10.8)	36.6 (20.4)	0.284
Use of Hydroxychloroquine (%)	94 (90.4)	142 (92.2)	0.774	97.6 (93.9)	172.1 (89.6)	0.41

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

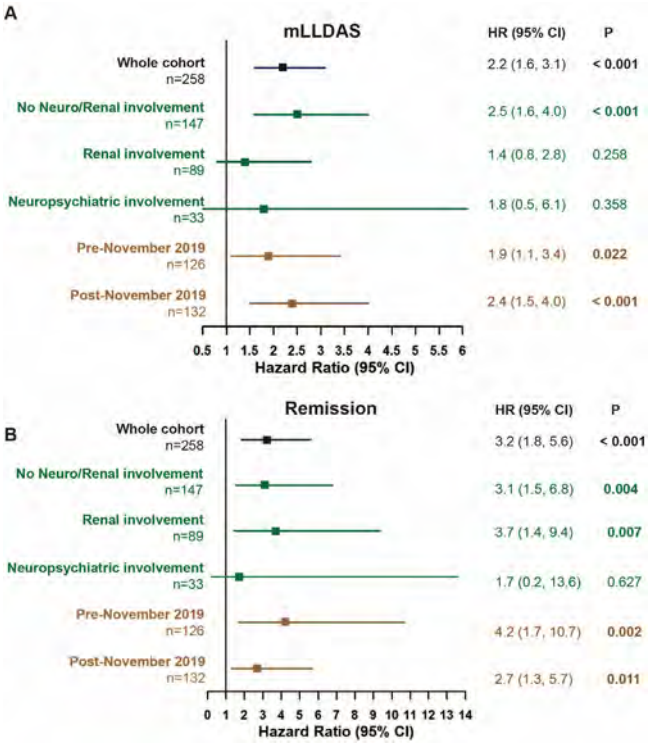


Figure 2. Treat-to-target outcomes. Attainment of mLLDAS (A) and remission (B) within 12 months in the whole cohort and sensitivity analyses (rituximab versus conventional immunosuppressants group). The model was adjusted for age, gender and maximum prednisone dosage. Pre-November 2019 (no COVID-19 exposure): Patients who completed their 12-month follow-up before November 2019. Post-November 2019 (COVID-19 exposure): Patients who completed their 12-month follow-up after November 2019. CI: Confidence interval; mLLDAS: modified lupus low disease activity state; SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000. Neuro: Neuropsychiatric; HR: Hazard ratio. At 12-month, follow-up data were missing for 12 out of 258 patients (4.6%) (3 in the RTX group and 9 in the conventional IS group). The last observation carries forward (LOCF) method was employed to address the missing data in the endpoint assessment by 12-month.

efficacy in achieving mLLDAS and remission outcomes. Additionally, the incidence of major infections was similar between the two groups (12.5% vs. 8.4%, p=0.288).

Conclusion: In patients with newly diagnosed moderate-to-severe SLE, upfront treatment with RTX was associated with improved clinical outcomes compared to conventional immunosuppressive therapy, in terms of achieving low disease activity or remission by 12 months.

Disclosure: H. Wang: None; **L. Zhao**: None; **S. Ye**: None; **S. Yang**: None.

Abstract Number: 2449

Patient Characteristics, Treatment and Prognosis in Patients with Neuromyelitis OpticaSpectrum Disorder Coexisting with Systemic Lupus Erythematosus or Sjögren's Syndrome: An Analysis Using Japanese Inpatient Database

Hiroshi Shiba[1], Mikio Nakajima[2], Kaito Nakamura[3], Yusuke Sasabuchi[4], Hiroyuki Ohbe[5], Yuya Kimura[6], Tadahiro Goto[7], Hiroki Matsui[8], Kiyohide Fushimi[9] and Hideo Yasunaga[5], [1]Suwa central hospital, Chino, Japan, [2]Emergency and Critical Care Center, Tokyo Metropolitan Hiroo Hospital, Hiroo, Tokyo, Japan, [3]Department of Rheumatology, Dokkyo Medical University, Shimotsuga, Tochigi, Japan, [4]Department of Real-world Evidence, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan, [5]Department of Clinical Epidemiology and Health Economics, School of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Public Health, The University of Tokyo, Bunkyo-ku, Tokyo, Japan, [6]Department of Health Services Research, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan, [7]Department of Health Data Science, Graduate School of Data Science, Yokohama City University, Yokohama, Kanagawa, Japan, [8]Department of Clinical Epidemiology and Health Economics, School of Public Health, Bunkyo-ku, Tokyo, Japan, [9]Department of Health Policy and Informatics, Institute of Science Tokyo, Bunkyo-ku, Tokyo, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Neuromyelitis optica spectrum disorder (NMOSD) can coexist with systemic lupus erythematosus (SLE) and Sjögren's syndrome (SS). Due to overlapping clinical presentations and the rarity of these conditions, specific treatment strategies for acute-phase NMOSD with SLE (NMOSD/SLE) and NMOSD with SS (NMOSD/SS) are lacking. This study aimed to investigate the clinical characteristics, treatment and prognosis of patients with NMOSD/SLE and NMOSD/SS.

	Total (n=8,029)	NMOSD alone (n=7,507)	NMOSD/SLE (n=217)	NMOSD/SS (n=305)	p-value
Patient characteristics					
Age, no (IQR*, 25-75)	55 (43-68)	55 (43-68)	51 (40-62)	55 (45-67)	0.011
Female, no (%)	6098 (75.9)	5627 (75.0)	198 (91.2)	273 (89.5)	<0.001
Charlson comorbidity index, no (%)					0.047
= 0	5,005 (62.3)	4,681 (62.4)	120 (55.3)	204 (66.9)	
= 1	1,969 (24.5)	1,825 (24.3)	69 (31.8)	75 (24.6)	
= 2	756 (9.4)	718 (9.6)	20 (9.2)	18 (5.9)	
≥ 3	299 (3.7)	283 (3.8)	8 (3.7)	8 (2.6)	
Admission status					
Disturbance of consciousness, no (%)					0.25
Mild (GCS** 14–15)	7,877 (98.1)	7,361 (98.1)	217 (100.0)	299 (98.0)	
Moderate (GCS 9–13)	131 (1.6)	125 (1.7)	0 (0.0)	6 (2.0)	
Severe (GCS 3–8)	21 (0.3)	21 (0.3)	0 (0.0)	0 (0.0)	
Activity of daily living, no (%)					0.014
BI*** 100	3,723 (46.4)	3,499 (46.6)	106 (48.8)	118 (38.7)	
BI 76-99	684 (8.5)	625 (8.3)	29 (13.4)	30 (9.8)	
BI 51-75	795 (9.9)	736 (9.8)	22 (10.1)	37 (12.1)	
BI 26-50	648 (8.1)	602 (8.0)	14 (6.5)	32 (10.5)	
BI 1-25	672 (8.4)	626 (8.3)	14 (6.5)	32 (10.5)	
BI 0	596 (7.4)	569 (7.6)	6 (2.8)	21 (6.9)	
Treatment					
Methylprednisolone pulse therapy, no (%)	6,385 (79.5)	5,969 (79.5)	172 (79.3)	244 (80.0)	0.97
Plasma exchange, no (%)	2,543 (31.7)	2,337 (31.1)	96 (44.2)	110 (36.1)	<0.001
Intravenous immunoglobulin, no (%)	696 (8.7)	636 (8.5)	28 (12.9)	32 (10.5)	0.038
Intravenous cyclophosphamide, no (%)	44 (0.5)	28 (0.4)	9 (4.1)	7 (2.3)	<0.001
Rituximab, no (%)	31 (0.4)	27 (0.4)	3 (1.4)	1 (0.3)	0.056
Azathioprine, no (%)	1,004 (12.5)	847 (11.3)	100 (46.1)	57 (18.7)	<0.001
Cyclosporin, no (%)	90 (1.1)	76 (1.0)	9 (4.1)	5 (1.6)	<0.001
Tacrolimus, no (%)	553 (6.9)	510 (6.8)	28 (12.9)	15 (4.9)	<0.001
Mycophenolate mofetil, no (%)	31 (0.4)	14 (0.2)	15 (6.9)	2 (0.7)	<0.001
Mizoribine, no (%)	28 (0.3)	24 (0.3)	4 (1.8)	0 (0.0)	<0.001
Hydroxychloroquine, no (%)	13 (0.2)	1 (0.0)	12 (5.5)	0 (0.0)	<0.001
Belimumab, no (%)	2 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	<0.001
Satralizumab, no (%)	41 (0.5)	37 (0.5)	1 (0.5)	3 (1.0)	0.5
Tocilizumab, no (%)	9 (0.1)	8 (0.1)	0 (0.0)	1 (0.3)	0.46
Eculizumab, no (%)	31 (0.4)	28 (0.4)	1 (0.5)	2 (0.7)	0.73
Inebilizumab, no (%)	8 (0.1)	8 (0.1)	0 (0.0)	0 (0.0)	0.76
Outcomes					
Disturbance of consciousness, no (%)					0.63
Mild (GCS 14–15)	7,716 (96.1)	7,208 (96.0)	214 (98.6)	294 (96.4)	
Moderate (GCS 9–13)	54 (0.7)	51 (0.7)	1 (0.5)	2 (0.7)	
Severe (GCS 3–8)	8 (0.1)	8 (0.1)	0 (0.0)	0 (0.0)	
Activity of daily living, no (%)					0.006
BI 100	4,614 (57.5)	4,329 (57.7)	132 (60.8)	153 (50.2)	
BI 76-99	694 (8.6)	633 (8.4)	23 (10.6)	38 (12.5)	
BI 51-75	617 (7.7)	573 (7.6)	14 (6.5)	30 (9.8)	
BI 26-50	433 (5.4)	394 (5.2)	16 (7.4)	23 (7.5)	
BI 1-25	556 (6.9)	524 (7.0)	9 (4.1)	23 (7.5)	
BI 0	349 (4.3)	336 (4.5)	1 (0.5)	12 (3.9)	
Length of hospital stay, no (IQR, 25-75)	29 (17-47)	29 (17-47)	30 (20-46)	33 (20-53)	0.001
Discharge to home, no (%)	2,071 (74.2)	5,566 (74.1)	181 (83.4)	211 (69.2)	0.001
Death, no (%)	107 (1.3)	104 (1.4)	1 (0.5)	2 (0.7)	0.29

*IQR = interquartile range, **GCS = glasgow coma scale, ***BI = barthel index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This retrospective descriptive study utilized the Diagnosis Procedure Combination (DPC) database, a nationwide inpatient database in Japan. We identified patients with NMOSD (ICD-10 codes, G360) between 2010 and 2023. Patients were categorized into three groups: NMOSD alone, NMOSD/SLE and NMOSD/SS. We extracted clinical data during hospitalization and compared patient characteristics, treatments and outcomes between these groups.

Results: A total of 8,029 patients were included: NMOSD alone (n=7,507), NMOSD/SLE (n=217), and NMOSD/SS (n=305). The median age was 55 years and 76% were female. NMOSD/SLE patients had a higher burden of comorbidities compared to those with NMOSD alone or NMOSD/SS. The treatment regimen included more frequent use of plasma exchange and cyclophosphamide, and a wider use of immunosuppressive agents in NMOSD/SLE patients. The percentage of plasma exchange were: NMOSD alone 31.1%, NMOSD/SLE 44.2%, NMOSD/SS 36.1% (p< 0.001). The percentage of intravenous cyclophosphamide administration were: NMOSD alone 0.4%, NMOSD/SLE 4.1%, NMOSD/SS 2.3% (p< 0.001). The percentage of rituximab administration were: NMOSD alone 0.4%, NMOSD/SLE 1.4%, NMOSD/SS 0.3% (p=0.056). The most common disease-modifying antirheumatic drug was azathioprine (NMOSD alone 11.3%, NMOSD/SLE 46.1%, NMOSD/SS 18.7%, p< 0.001), followed by tacrolimus, cyclosporine, and mycophenolate mofetil. Crude in-hospital mortality was 1.3%. There was no significant difference in in-hospital mortality across all groups; however, NMOSD/SLE patients had better activities of daily living scores and were more likely to be discharged to home. The proportion of patients with a Barthel index of 100 (total independent) in the three groups were: NMOSD alone 57.7%, NMOSD/SLE 60.8%, NMOSD/SS 50.2% (p=0.006). The percentage of discharge to home were: NMOSD alone 74.1%, NMOSD/SLE 83.4%, NMOSD/SS 69.2% (p=0.001).

Conclusion: Although NMOSD/SLE patients had a greater burden of comorbidities, they received a broader range of treatments during the acute phase and showed favorable outcomes in terms of functional status and discharge to home.

Disclosure: H. Shiba: None; **M. Nakajima**: None; **K. Nakamura**: None; **Y. Sasabuchi**: None; **H. Ohbe**: None; **Y. Kimura**: None; **T. Goto**: None; **H. Matsui**: None; **K. Fushimi**: None; **H. Yasunaga**: None.

Abstract Number: 2450

Spanish Real-World Ambispective Multicenter Registry of Anifrolumab in Systemic Lupus Erythematosus: Efficacy and Safety at 3- and 6-Month Follow-Up (ANIFRO-Reu Study)

Irene Carrión-Barberà[1], Tarek Salman Montes[2], Laura Triginer[3], Judit Font-Urgelles[4], Anne Riveros frutos[5], Sandra Garrote Corral[6], Maria Garcia-Villanueva[7], Carlos de Frías Polo[8], María Galindo-Izquierdo[9], Berta Magallares[10], Andrea Hernández-martín[11], Jorge Juan Fragío Gil[12], Sebastián Sandoval Moreno[13], Consuelo Ramos Giraldez[14], Josefina Cortés-Hernández[15], Elvira Díez García[16], Clara Moriano[17], Paloma Vela Casasempere[18], M.Pilar Bernabeu Gonzalvez[19], Irene Altabás-González[20], Samuel Hernández-Baldizón[21], Leyre Riancho[22], Inmaculada Ros Vilamajo[21], Carlos Marras Fernández-Cid[23], Maria Piqueras García[24], Angel Garcia-Aparicio[25], marta Garijo Bufort[26], José Gomez-Puerta[27], Beatriz Frade Sosa[28], Silvia García Cirera[29], Vicenç Torrente-Segarra[30], Luis Sala[31], Concepción Fito-Manteca[32], Natividad del Val del amo[33], Julia Martínez Barrio[34], Jose Rosas Gómez de Salazar[35], Sergi Heredia[36], ana Urruticoechea-Arana[37], Anahy Maria Brandy[38], Maria Esther Uriarte[39], José María Pego-Reigosa[40] and Iñigo Rúa-Figueroa[41], [1]Department of Rheumatology. Hospital del Mar, Barcelona, Spain, [2]Hospital del Mar/Parc de Salut Mar-IMIM, Barcelona, Spain, [3]Hospital del Mar, Barcelona, Spain, [4]Hospital Universitari Germans Trias i Pujol, Badalona, Spain, [5]Hospital Germans Trias i Pujol, Barcelona, Spain, [6]Hospital Ramón y Cajal, Madrid, [7]Hospital Ramón y Cajal, Madrid, Spain, [8]Hospital Universitario 12 de octubre, Madrid, Spain, [9]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain, Madrid, Madrid, Spain, [10]Hospital de Sant Pau, Bareclona, [11]Hospital Universitario de Gran Canaria Dr Negrín, Las palmas, Spain, [12]Hospital General Universitario, Valencia, Spain, [13]Hospital Universitario Vall d'Hebron, Barcelona, Spain, [14]Hospital Universitario Virgen de Valme, Servicio de Reumatología, Seville, Spain, [15]Hospital Universitari Vall d'Hebron-Universitat Autónoma de Barcelona, Barcelona, Spain, [16]Complejo Asistencial Universitario de León, León, Spain, [17]Hospital León, LEON, Castilla y Leon, Spain, [18]Hospital General Universitario Alicante, Alicante,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Comunidad Valenciana, Spain, [19]Rheumatology Department, Dr. Balmis General University Hospital, Alicante, Spain., Alicante, Spain, [20]Complejo Hospitalario de Vigo, Vigo, Spain, [21]Hospital Son Llàtzer, Palma de Mallorca, Spain, [22]Hospital de Sierrallana, Torrelavega, [23]Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain, [24]Servicio Murciano de Salud, Murcia, Spain, [25]Hospital Universitario de Toledo, Toledo, Spain, [26]Rheumatology Department, Hospital de Sagunto, Spain, Valencia, Spain, [27]Rheumatology Department, Hospital Clinic, Barcelona, Spain, Barcelona, Spain, [28]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [29]Consorci Coporació Sanitaria Parc Taulí, Sabadell, Spain, [30]Hospital Comarcal Alt Penedés Garraf, Vilafranca del Penedés, Spain, [31]Hospital Universitario de Torrejón, Madrid, Spain, [32]Rheumatology. Hospital Universitario de Navarra., Pamplona, Navarra, Spain, [33]Complejo Universitario de Navarra, Navarra, Spain, [34]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [35]Hospital Marina Baixa, PALMA DE MALLORCA, Spain, [36]Hospital Moisès Broggi, Barcelona, Spain, [37]Rheumatology Division. Hospital Universitario Son Espases, Palma de Mallorca, Spain, [38]Hospital Germans Trias i Pujol, Badalona, Spain, [39]Hospital Universitario Donostia, San Sebastian, Spain, [40]Department of Rheumatology, University Hospital of Vigo, Vigo, Spain; IRIDIS Group (Investigation in Rheumatology and Immune-Diseases), Galicia Sur Health Research Institute, Vigo, Spain, [41]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anifrolumab is a biologic recently approved for systemic lupus erythematosus (SLE), with efficacy shown in trials, but data from real-world practice remain limited. The aim of this registry is to evaluate the effectiveness and safety of anifrolumab at 3 and 6 months (m) in SLE patients under real-life routine care in Spanish rheumatology centers.

Methods: Multicenter, observational, ambispective study including SLE patients (2019 EULAR/ACR criteria) from 28 centers, treated with anifrolumab and followed at baseline, 3, and 6m. Clinical, lab, and treatment data were collected. Disease activity (SLEDAI-2k, SLE-DAS, PGA), damage (SLICC/ACR/DI), remission (DORIS-21), low disease activity (LLDAS), acute-

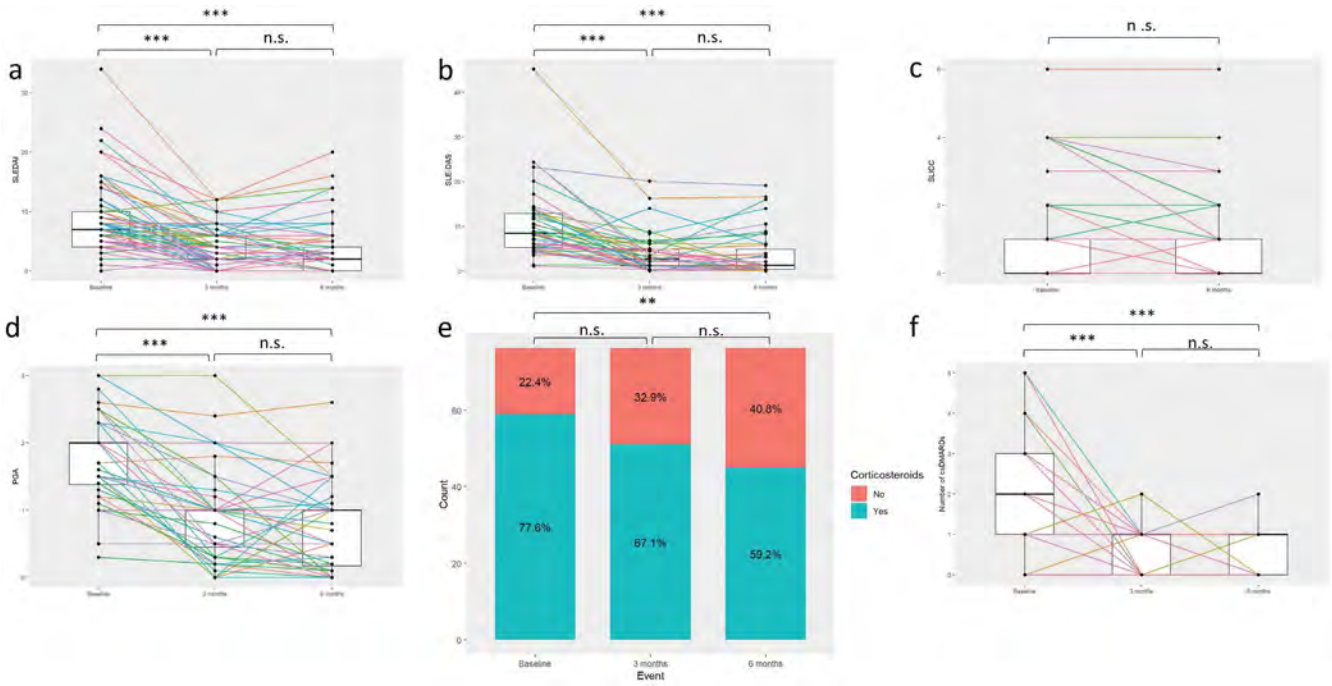


Figure 1: Statistically significant differences in disease indices between the baseline visit and the visits at 3 and 6 months after the start of anifrolumab. p-values significance level: n.s.: > 0.5; * < 0.05–0.01; ** < 0.01–0.001; *** < 0.001. a): SLEDAI – Systemic Lupus Erythematosus Disease Activity Index (n = 77); b) SLE-DAS – Systemic Lupus Erythematosus Disease Activity Score (n = 43); c) SLICC – Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (n = 73); d): PGA – Physician Global Assessment (n = 52); e) Glucocorticoids yes/no (n = 76); f) Number of disease modifying antirheumatic drugs with anifrolumab (n = 76).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

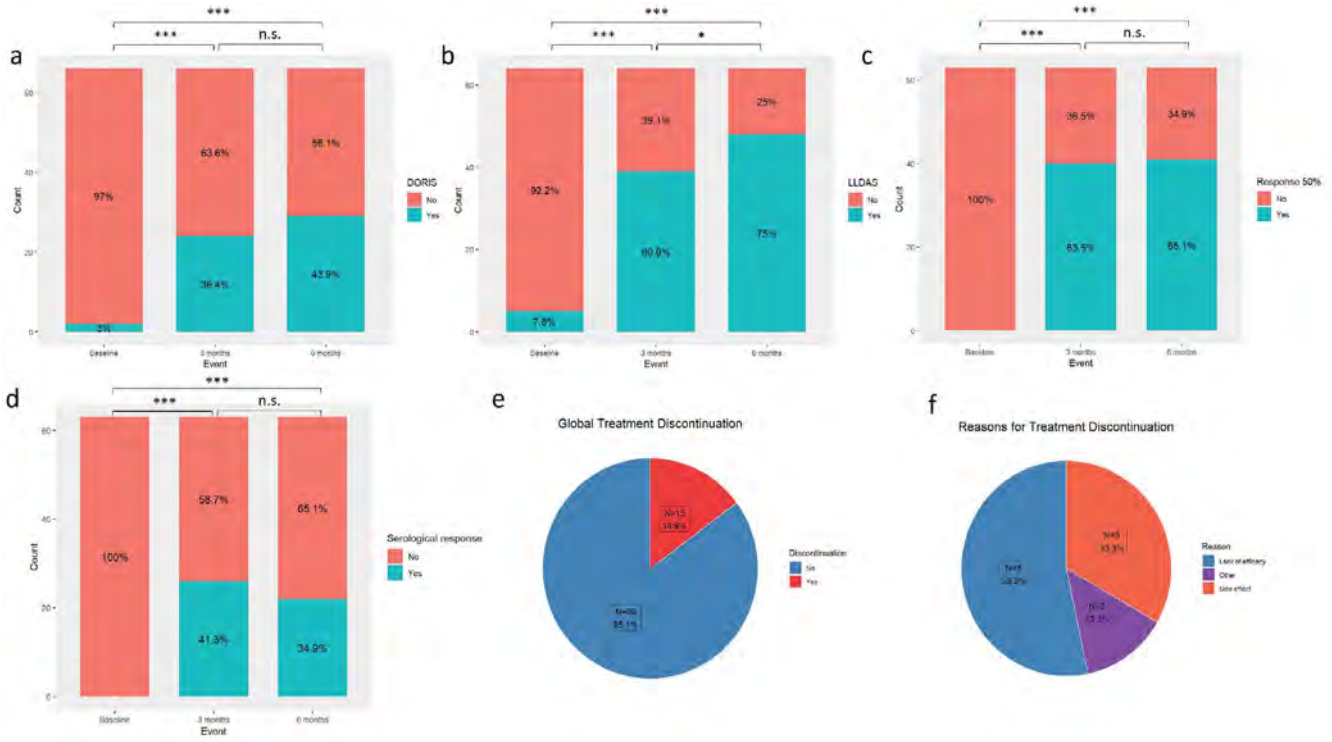


Figure 2: Statistically significant differences in response indices and discontinuation between baseline and the visits at 3 and 6 months after the initiation of anifrolumab. p-values significance level: n.s.: > 0.5; * < 0.05–0.01; ** < 0.01–0.001; *** < 0.001. a) DORIS – Definition of Remission in Systemic Lupus Erythematosus (n = 66); b): LLDAS – Lupus Low Disease Activity State (n = 64); c): 50% response (n = 63); d) Serologic response (n = 63); e) Treatment discontinuation; f) Reasons for treatment discontinuation.

phase reactants (CRP, ESR), response to treatment and medication changes were assessed. Efficacy and security comparisons across visits were done using Friedman's test (adjusted by Holm's method) and Cochran's Q with McNemar's test (Bonferroni correction) for binary outcomes.

Results: Among 133 patients, 100 completed the 3-month visit and 82 the 6-month visit. Median age was 49 years (IQR ±17), and time from diagnosis was 31 years (±16); 87.9% were female, 77.3% Caucasian and 14.4% Hispanic; 56.5% were currently employed and 19.8% were active smokers. Significant improvements at 3 and 6m compared with the baseline visit were observed in SLEDAI, SLEDAS, PGA, the percentage of patients in remission DORIS-21 and in low disease activity (LLDAS), and the number of concomitant disease modifying antirheumatic drugs, and in those receiving glucocorticoids 6m after initiation of anifrolumab vs. the basal visit (Fig. 1-2). Flare counts significantly dropped from 2 (±2) at baseline to 0 (±0 at 3m and ±1 at 6m). Response rates were: physician's criteria 77.1% at 3m and 75.7% at 6m; 50% response in 63.5% and 65.1%; 20% response in 83.6% and 74.5%; serological response in 41.3% and 34.9% (all p = not significant) (Fig. 2).

Discontinuation occurred in 5/95 patients (5%) before 3m and 10/72 (12.2%) between 3–6m. Fourteen hospital admissions (10.5%) occurred during those 6m: 5 due to SLE activity, 2 to infections, 3 to both SLE activity and infection and 4 to other reasons. Five (3.8%) patients presented a COVID-19 and 4 (3%) a herpes zoster infection since anifrolumab onset. One new case of depression and 2 new psychotropic treatments were noted. None of the patients died since starting anifrolumab. There were no differences in either SDI at baseline vs. 6m (0 ± 1 vs. 0 ± 1), or anti-dsDNA titers, C-reactive protein levels or glucocorticoid dose among any of the 3 visits.

Conclusion: In real-life clinical practice, anifrolumab improved multiple SLE activity measures at 3 and 6 months, with a substantial proportion of patients achieving LLDAS or DORIS-defined remission, along with reduced flare rates and background immunosuppressive use, and no new major safety concerns.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: I. Carrión-Barberà: AstraZeneca, 6, GlaxoSmithKlein(GSK), 2; **T. Salman Montes**: None; **L. Triginer**: None; **J. Font-Urgelles**: None; **A. Riveros frutos**: None; **S. Garrote Corral**: None; **M. Garcia-Villanueva**: None; **C. de Frías Polo**: Gebro Pharma, 6; **M. Galindo-Izquierdo**: None; **B. Magallares**: None; **A. Hernández-martín**: None; **J. Fragío Gil**: Quibim, 1; **S. Sandoval Moreno**: None; **C. Ramos Giraldez**: None; **J. Cortés-Hernández**: AstraZeneca, 6, Bristol-Myers Squibb (BMS), 1, GlaxoSmithKline (GSK), 6, Novartis, 1, 5, 6; **E. Díez García**: None; **C. Moriano**: None; **P. Vela Casasempere**: None; **M. Bernabeu Gonzalvez**: None; **I. Altabás-González**: None; **S. Hernández-Baldizón**: Amgen, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 6; **L. Riancho**: None; **I. Ros Vilamajo**: None; **C. Marras Fernández-Cid**: None; **M. Piqueras García**: None; **A. Garcia-Aparicio**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 1, 2, 6, UCB, 6; **m. Garijo Bufort**: None; **J. Gomez-Puerta**: AbbVie/Abbott, 6, AstraZeneca, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **B. Frade Sosa**: Galapagos, 6, GlaxoSmithKlein(GSK), 6; **S. García Cirera**: None; **V. Torrente-Segarra**: None; **L. Sala**: None; **C. Fito-Manteca**: None; **N. del Val del amo**: None; **J. Martínez Barrio**: None; **J. Rosas Gómez de Salazar**: None; **S. Heredia**: None; **a. Urruticoechea-Arana**: None; **A. Brandy**: None; **M. Uriarte**: None; **J. Pego-Reigosa**: AstraZeneca, 1, 5, 6, GlaxoSmithKline (GSK), 1, 5, 6, Otsuka, 1, 6; **I. Rúa-Figueroa**: None.

Abstract Number: 2451

Tofacitinib Lowers Markers of Photosensitivity in Patients with Cutaneous Lupus Erythematosus

Amy Hurst[1], Mehrnaz Gharaee-Kermani[1], Yuli Cai[2], Rachael Bogle[3], Lin Zhang[1], Amber Young[2], Craig Dobry[1], Srilakshmi Yalavarthi[1], Jason S. Knight[1], Johann Gudjonsson[2], Alex Tsoi[3], Patricia Rohan[4], Angela Kibiy[5], Karen Boyle[6], Margie Byron[7], Laura Baird[7] and **J. Michelle Kahlenberg**[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, [3]University of Michigan, Holland, OH, [4]NIH, Bethesda, MD, [5]NIH/NIAID, Rockville, MD, [6]Rho, Inc, Durham, NC, [7]Rho, Inc., Durham, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Photosensitivity lowers quality of life in patients with cutaneous lupus erythematosus (CLE) and puts patients with systemic lupus erythematosus (SLE) at risk of systemic disease flare. Janus kinase (JAK) inhibitors can reduce Type I interferons (IFNs) in the skin, where they are important drivers of photosensitivity. In addition, JAK inhibitors can interrupt neutrophil NETosis, a potentially important cell population in CLE. We thus examined the impact of JAK blockade in patients with a history of CLE.

Methods: We conducted a proof-of-concept mechanistic study in patients with a history of CLE, either in isolation or with associated SLE. Participants underwent phototesting with 0, 10, 20, 30, 40, 50, 60, 70 and 80 mJ/cm^2 UVB prior to initiation of a 3-week course of 11 mg XR tofacitinib PO daily followed by repeat phototesting after drug completion. Biopsies were taken from unexposed skin, the initial minimal erythema dose (MED) site and from the site corresponding to the next highest UVB dose (MED+1) from initial and follow-up phototesting for mechanistic studies. The primary endpoint was the change in percentage of UVB-induced apoptotic epidermal cells from Day 1 (pre-treatment) to Day 26 (post-treatment). Safety and disease activity metrics were assessed.

Results: Seven patients were enrolled and 6 patients completed the study. Participant data can be seen in Table 1. A single grade 2, unrelated adverse event (AE) was reported and no participant withdrew due to an AE. The mean change in percent of apoptotic epidermal cells following tofacitinib treatment was -17.03% (SD 8.355). Analyses of secondary outcomes

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Demographics and Baseline Characteristics
Population: Enrolled

	Tofacitinib (N=7)
Age (years)	
n	7
Mean (SD)	42.7 (6.26)
Median	44.0
Min, Max	34,51
Sex, n(%)	
Female	6 (85.7)
Male	1 (14.3)
Race, n(%)	
White	6 (85.7)
Black or African American	1 (14.3)
Asian	0
Native Hawaiian or Other Pacific Islander	0
American Indian or Alaska Native	0
Hispanic Ethnicity, n(%)	
Hispanic or Latino	2 (28.6)
Not Hispanic or Latino	5 (71.4)
Body Mass Index	
n	7
Mean (SD)	30.31 (10.119)
Median	25.66
Min, Max	17.0,46.9
Fitzpatrick Scale, n(%)	
Type I	1 (14.3)
Type II	2 (28.6)
Type III	1 (14.3)
Type IV	2 (28.6)
Type V	1 (14.3)
Type VI	0
SLEDAI-2K Score (Clinical Criteria)	
n	7
Mean (SD)	0.9 (1.07)
Median	0.0
Min, Max	0,2
CLASI Total Activity Score	
n	7
Mean (SD)	2.4 (3.87)
Median	0.0
Min, Max	0,9
CLASI Total Damage Score	
n	7
Mean (SD)	2.9 (5.40)
Median	0.0
Min, Max	0,14
Lupus Medication Use at Baseline, n(%) [1]	
Corticosteroids (Oral)	0
Anti-malarial	5 (71.4)
Methotrexate	1 (14.3)
Leflunomide	0
MMF/Mycophenolic Acid	0
None	2 (28.6)

Note: Percentages are based on the number of participants with evaluable data.
[1] Participants may be counted more than once if they were taking more than one type of lupus medication at baseline

comparing pre vs. post tofacitinib showed no change in MED, no change in CLASI activity and damage scores, and no change in SLEDAI. A varied response to tofacitinib was observed within and across participants in gene transcripts via bulk RNA sequencing for UVB-mediated cutaneous gene expression for *IL6, IFNB, IFI44, TNFA, IL1B*, and *CXCL9*. However, single cell spatial transcriptomics revealed that following tofacitinib treatment, there was a significant decrease (FDR $\leq$1.0E-03) in UVB-induced type I IFN-regulated genes in many cell populations, including keratinocytes and fibroblasts, and a reduction in genes regulating antigen presentation and cytotoxic T cell activation in myeloid cells, such as *SIGLEC1, CCL5, CD1C, CD207, MX1*, and *IFI44L*. All patients demonstrated a significant reduction from baseline in PMA-stimulated production of neutrophil extracellular traps (NETs) from circulating neutrophils following administration of tofacitinib, and there was a trend towards decreased neutrophil staining in the UVB-treated skin as well.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: A 3-week course of tofacitinib was well-tolerated and reduced epithelial apoptosis after UVB exposure in patients with a history of CLE. Single cell resolution spatial transcriptomics identified cell-specific inflammatory gene reductions in the presence of tofacitinib following UVB exposure. The principal limitation of the trial was the small sample size. Additional studies are needed to investigate whether JAK inhibition is a viable strategy for reduction of photosensitivity and prevention of UVB-mediated skin and systemic disease flares.

Disclosure: A. Hurst: None; **M. Gharaee-Kermani**: None; **Y. Cai**: None; **R. Bogle**: None; **L. Zhang**: None; **A. Young**: None; **C. Dobry**: None; **S. Yalavarthi**: None; **J. Knight**: BioCryst, 2, Ouro Medicines, 2, Roche, 2, Roivant Sciences, 2, Visterra, 2; **J. Gudjonsson**: None; **A. Tsoi**: Galderma, 5, Johnson and Johnson, 5; **P. Rohan**: None; **A. Kibiy**: None; **K. Boyle**: None; **M. Byron**: None; **L. Baird**: None; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5.

Abstract Number: 2452

Preliminary Safety, Efficacy, and Cellular Kinetics of CTA311, a CD19 Targeted Universal CAR-T Therapy, for Active Autoimmune Diseases

Sanbin Wang[1], Heng Mei[2], Dongmei Zhou[3], Wei Xie[2], Songlou Yin[3], Chunmei Liu[3], Hanwei Wang[4], Huan Zhou[5], Yue Xie[6], Lu Han[7], Jiangtao Ren[8], Yali Zhou[8], Wengang Ge[7] and **Jan Davidson-Moncada**[8], [1]920th Hospital of Joint Logistic Support Force, Kunming, China (People's Republic), [2]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (People's Republic), [3]The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China (People's Republic), [4]The Third People's Hospital of Bengbu, Beng bu, China (People's Republic), [5]Clinical Research Hospital of the First Affiliated Hospital of Anhui Medical University, Hefei, China (People's Republic), [6]Bioheng Therapeutics Limited, Nan Jing Shi, China (People's Republic), [7]Bioheng Therapeutics Co., Limited, Nanjing, China (People's Republic), [8]Bioheng Therapeutics Co., Limited, Nan Jing, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) and anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) are autoimmune conditions characterized by B cell activation, autoreactivity, and autoantibody production. CAR-T therapy has emerged as a promising strategy to deplete autoreactive B cells and induce sustained remission. This study

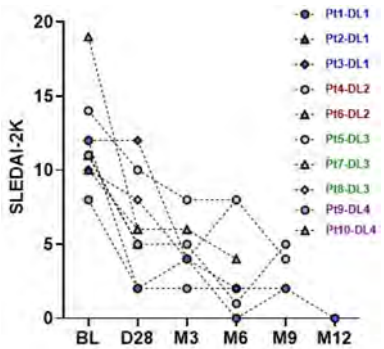


Figure 1. SLEDAI-2K score

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

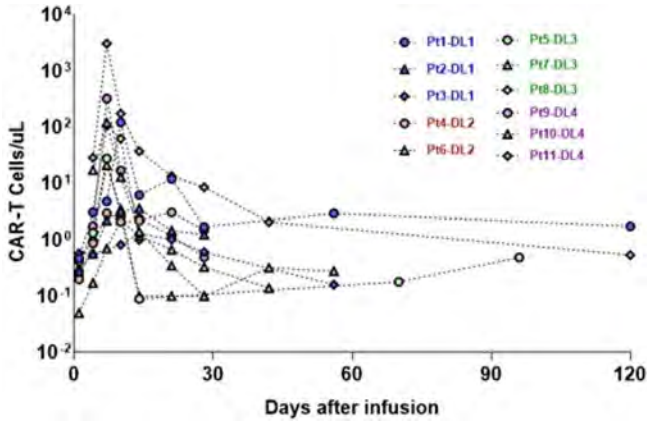


Figure 2. CAR-T cells

evaluates the safety, efficacy and cellular kinetics of CTA311, a CD19 targeted "off-the-shelf" universal CAR-T product, in patients with active autoimmune disease.

Methods: Patients received a single administration of CTA311 treatment at 4 dose levels (DLs): DL1 as 0.2 $\times 10^6$ CAR+T cells/kg, DL2 as 1×10^6 CAR+T cells/kg, DL3 as 3×10^6 CAR+T cells/kg, DL4 as 6×10^6 CAR+T cells/kg following lymphodepletion with cyclophosphamide (300mg/m^2/day×3) and fludarabine (30 mg/m^2/day×3). Clinical activity assessments include disease activity scores (SLEDAI-2K) and Physician's Global Assessment (PGA).

Results: As of April 30, 2025, eleven patients (10 SLE and 1 AAV) received CTA311 at various doses, DL1 (n=3), DL2 (n=2), DL3 (n=3), and DL4 (n=3). Ten (91%) patients were female, median age 31 (range 25-55) years, median disease duration 6 (range 1-23) years. All had previously been treated with steroids and immunosuppressants, and 6 patients received biological agents (3 telitacicept, 1 belimumab, and 2 both).

Treatment was well tolerated; CRS events occurred in 82% (n=9), all low grade (G) (7 G1 and 2 G2). No neurotoxicity was reported. Transient lymphodepletion-related cytopenia (< 28 days) were observed in all patients. Three patients experienced infections deemed to be treatment related (1 pt with pneumonia (G3) and CMV reactivation (G1), 1 pt with fungal infection (G2), and 1 pt with infection NOS (G1)), which all completely resolved within 2 months.

Preliminary efficacy indicated reductions in SLEDAI-2K and PGA accompanied by improvements in autoantibodies, C3, and proteinuria. All 10 patients achieved a Systemic Lupus Erythematosus Responder Index-4 (SRI-4) response, and Lupus Low Disease Activity State (LLDAS) was attained in 4 patients. Two patients achieved DORIS remission. The AAV patient's BVAS score improved from 8 at baseline to 0 at M3 and M4. However, patient resurgence of mild arthritis) M6. All patients discontinued immunosuppressants and decreased/stopped steroid (≤10 mg/d).

PK analysis revealed median peak expansion (C_{max}) of 93,679 (range 84-1,091,116) copies/ug DNA approximately 7-11 days post-infusion. Complete B cell depletion was observed by Day 4 post-infusion and persisted for about 1-3 months. In pts that achieved dsDNA Ab eradication, the Ab remained undetected up to 12 months, and ongoing, despite B-cell recovery.

Conclusion: Preliminary data suggest favorable safety, CAR-T cell expansion, B cell depletion and promising efficacy of CTA311 in B cell-mediated autoimmune diseases. Ongoing follow up and enrollment in additional indications will provide insights into long-term safety and efficacy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Wang: None; **H. Mei**: None; **D. Zhou**: None; **W. Xie**: None; **S. Yin**: None; **C. Liu**: None; **H. Wang**: None; **H. Zhou**: None; **Y. Xie**: None; **L. Han**: None; **J. Ren**: None; **Y. Zhou**: None; **W. Ge**: None; **J. Davidson-Moncada**: None.

Abstract Number: 2453

Belimumab Is Associated with Lower Risk of Progression to LN Compared with Standard of Care in Patients with SLE

Maral DerSarkissian[1], Yan Chen[1], Ariel Chao[1], Shumin Rui[1], Bronwyn Moore[2], Karen Worley[3], Daniel Moldaver[4], **Jeffrey J. Ellis**[3] and Aarat M Patel[5], [1]Analysis Group, Los Angeles, CA, [2]Analysis Group, Montreal, QC, Canada, [3]GSK, Global Real-World Evidence & Health Outcomes Research, Collegeville, PA, [4]GSK, Global Real-World Evidence & Health Outcomes Research, Toronto, ON, Canada, [5]GSK, US Medical Affairs, Durham, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table. Select ATT-weighted baseline characteristics. *Imbalanced after ATT weighting; †the most recent eGFR measurement prior to the index date was used; if multiple measurements were available on the same day, the median value of these measurements was used; ‡eGFR was calculated based on the 2021 CKD-EPI creatinine equation (Inker LA et al. N Engl J Med 2021;385:1737–49); §evaluated among patients with non-missing values during baseline period; ¶CCI was calculated per the Quan study (Quan H et al. Med Care 2005;43:1130–9). Mean (SD) treatment episode duration was 25.9 (20.5) months for belimumab and 36.0 (23.6) months for SOC; SMR 0.67*. ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCI, Charlson Comorbidity Index; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; IQR, interquartile range; SD, standard deviation; SGLT2is, sodium-glucose co-transporter-2 inhibitors; SMD, standardized mean difference; SMR, standardized mortality ratio; SOC, standard of care; UPCR, urine protein-to-creatinine ratio.

Characteristic	Belimumab N=3727	SOC N=3621	SMD
Age, years, mean (SD)	46.9 (13.0)	47.2 (14.1)	0.03
Female, n (%)	3513 (94.3)	3409 (94.1)	0.01
Race, n (%)			
African American	717 (19.2)	692 (19.1)	0.00
Asian	77 (2.1)	72 (2.0)	0.01
Caucasian	2325 (62.4)	2266 (62.6)	0.00
Other/unknown	608 (16.3)	591 (16.3)	0.00
SLE disease severity, n (%)			
Mild	706 (18.9)	712 (19.7)	0.02
Moderate	1993 (53.5)	1914 (52.8)	0.01
Severe	1028 (27.6)	996 (27.5)	0.00
eGFR[†,‡], ml/min/1.73 m², mean (SD)	94.0 (21.2)	92.7 (22.8)	0.06
Serum creatinine[§], mg/dl, mean (SD)	1.0 (4.0)	1.0 (3.4)	0.01
UPCR[§], mg/g, median (IQR)	113.7 (77.4, 187.1)	118.4 (78.8, 203.0)	0.10
Blood urea nitrogen[§], mg/dl, mean (SD)	13.4 (5.9)	13.8 (6.8)	0.06
Serum potassium[§], mmol/l, mean (SD)	4.1 (0.4)	4.1 (0.4)	0.12*
Unique therapies within each class during baseline period, mean (SD)	0.5 (0.5)	0.1 (0.3)	0.97*
Immunosuppressants	0.8 (0.4)	0.7 (0.4)	0.20*
Oral GC	0.0 (0.1)	0.0 (0.1)	0.03
Biologics	0.7 (0.5)	0.6 (0.5)	0.36*
Antimalarials			
Concomitant medications, n (%)			
NSAIDs	1888 (50.7)	1814 (50.1)	0.01
Diuretics	694 (18.6)	672 (18.6)	0.00
Beta-blockers	716 (19.2)	691 (19.1)	0.00
Calcium channel blockers	644 (17.3)	614 (17.0)	0.01
ACEis	389 (10.4)	381 (10.5)	0.00
ARBs	332 (8.9)	323 (8.9)	0.00
SGLT2is	28 (0.8)	27 (0.7)	0.00
Quan-CCI score[¶], mean (SD)	2.1 (1.7)	2.1 (2.0)	0.03

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: LN develops in ~40% of patients with SLE and is associated with increased risk of morbidity, including end-stage kidney disease, and mortality. Belimumab, a B-cell modulator that targets the central immunopathogenic pathway in SLE by selectively inhibiting B-lymphocyte stimulator, has been shown to prevent organ damage progression in SLE and preserve kidney function in LN. This study evaluated whether belimumab is associated with a protective effect and lower risk of progression to LN among patients with SLE versus standard of care (SOC) in real-world clinical practice, by comparing time to initiation of LN therapy.

Methods: A retrospective, longitudinal cohort study (GSK Study 217533) was conducted using claims linked with electronic health record data from the Optum Market Clarity database. Index was defined as the date of initiation of belimumab or SOC (immunosuppressant [IS, except for use in LN initial therapy], intravenous glucocorticoids [GCs], or oral GC escalation to ≥20 mg/day prednisone-equivalent) between Jan 1, 2017, and Mar 31, 2023. The unit of analysis was treatment episode and patients could be included in both study cohorts if they received both belimumab and SOC during the study period. Patients were ≥18 years old with an SLE diagnosis and had ≥12 months continuous enrollment pre-index. Those with LN diagnosis or LN induction therapy prior to the index date were excluded. Initiation of LN induction therapy served as a proxy for incident LN and was defined as earliest use of: subcutaneous belimumab 400 mg once-weekly for four doses; voclosporin; cyclophosphamide (either monotherapy or combined with MMF or azathioprine); high-dose MMF. For each treatment episode, the observation period spanned from index to the earliest of: end of continuous enrollment, end of data availability, death, or treatment switch. Time to initiation of LN induction therapy was assessed using a Cox proportional hazards (PH) model with a robust (Huber-White sandwich) variance estimator, weighted by average treatment effect among the treated weights (ATT-weights) based on propensity-score, and with covariates that remained imbalanced after weighting included in the model for a doubly robust approach.

Results: In total, 1408 belimumab and 74,288 SOC patients were included and contributed 3727 belimumab and 3621 SOC treatment episodes to the analysis. Prior to weighting, belimumab patients were younger (median age 47 vs 53 years) and more likely to have moderate (53.5% vs 31.0%) than mild (18.9% vs 42.9%) SLE severity and a greater number of SLE treatment types at baseline. ATT-weighted baseline characteristics (**Table**) were similar between treatment cohorts. The number of IS, oral GC, and antimalarial therapies remained imbalanced after weighting and were further adjusted in the Cox PH model. Patients receiving belimumab had a significantly lower hazard of initiating LN induction therapy versus SOC (hazard ratio [95% CI]: 0.77 [0.62, 0.95]).

Conclusion: Belimumab use was associated with a lower risk of initiating LN induction therapy versus SOC among patients with SLE, suggesting a potential renal protective effect through which belimumab may prevent progression to LN.

Funding: GSK

Disclosure: M. DerSarkissian: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **Y. Chen**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **A. Chao**: Analysis Group, 3, GSK, 12, I am an employee of Analysis Group, which received funding for this study from GSK.; **S. Rui**: Analysis Group, 3, GSK, 12, Employee of Analysis Group, which received funding from GSK for this study.; **B. Moore**: Analysis Group, 3, GSK, 12, I am an employee of Analysis Group, which received funding for this study from GSK.; **K. Worley**: GSK, 12,, 3; **D. Moldaver**: GSK, 3, 8; **J. Ellis**: GSK, 12,, 3, 8; **A. Patel**: GSK, 12,, 3, University of Virginia, 3, 12, Volunteer Faculty at the University of Virginia, Virginia Society of Rheumatology and The Paediatric Society of the African League Against Rheumatism, 4.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2454

Longitudinal Analysis of B cell Remodeling in Systemic Lupus Erythematosus Following iPSC-Derived CAR T-cell Therapy

Jonatan Tuncel[1], Trever Greene[2], Nicholas Brookhouser[2], Sandeep Kothapally Hanok[1], Seth Peng[1], Alison O'Conor[1], Parastoo Fazeli[3], Jennifer Medlin[4], Cara Bickers[2], Kelsea Hubka[1], Allison Aguilar[1], Wei Zhao[1], Kyla Omilusik[1], John Goulding[1], Tom Lee[2], Jode Goodridge[2], Marie Hu[5], Veronika Bachanova[5], Jeffrey Miller[6], Matthew Lunning[7], Rebecca Elstrom[2], Debra Zack[1], Vaneet Sandhu[2], Bahram Valamehr[8] and Lilly Wong[8], [1]Fate Therapeutics, San Diego, [2]Fate Therapeutics, Inc., San Diego, [3]UMN, ST PAUL, MN, [4]University of Nebraska Medical Center, Omaha, NE, [5]University of Minnesota, Minneapolis, [6]University of Minnesota, Minneaspolis, MN, [7]University of Nebraska Medical Center, Omaha, [8]Fate Therapeutics, Inc., San Diego, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Autologous chimeric antigen receptor (CAR) T-cell therapy is an exciting new potential therapy for autoimmune diseases but limited in scope of application by logistical complexity and cost of treatment. Furthermore, autoimmune patients will benefit from CAR T cell protocols that omit intensive conditioning chemotherapy (CCT) and integrate with their existing treatments. Here, we report 3-12 month follow-up data from our ongoing Phase I trial of FT819, an off-the-shelf iPSC-derived CD19-targeted CAR T-cell therapy, for the treatment of B-cell mediated autoimmune diseases (NCT06308978). FT819 is engineered to improve the safety and efficacy of CAR T cell therapy and incorporates a novel 1XX CAR signaling domain that extends T cell effector function without causing exhaustion. The CAR transgene is integrated into the T cell receptor (TCR) alpha constant locus to promote uniform CAR expression and enhance potency, with bi-allelic disruption of TCR expression to completely prevent graft-versus-host disease.

Methods: All patients enrolled to date were treated with FT819 for moderate to severe systemic lupus erythematosus (SLE) and either received fludarabine-free CCT (bendamustine or cyclophosphamide) or received no CCT and continued their standard-of-care therapy. Blood samples were collected at protocol-specified timepoints for B cell analysis.

Results: At baseline, patients had a mean SLEDAI score of 16 and reduced proportions of naïve B cells compared with healthy controls (HC, 60.2% vs 70.2%), increased proportions of pathogenically associated double-negative (DN) B cells (18.4% vs 8.7%), and circulating plasmablasts (PB, 8.2% vs 2.0%). Clonal architecture, as determined by sequencing of the BCR heavy chain, showed an increase in class-switched BCRs (73.1% vs 45.8%), larger clone sizes (12.3% vs 6.5% of total reads assigned to the top 10 clones), and a less diverse repertoire (Shannon index: 7.5 vs 8.7). Following treatment in patients receiving CCT, and concurrent with the overall resurgence in total B-cell numbers (6-12 mo), proportions of PB and DN B cells returned to the range observed in HC, while naïve B cells expanded to a proportion higher than that seen in HC. Moreover, the average proportion of large clones fell by 73.2%, with 87% of pre-treatment dominant clones absent by 6 months. Repertoire diversity increased from 6.2 to 9.2, and IgG/IgA fractions dropped by 42.6% while IgM rose 2.5-fold. Importantly, these measures paralleled the reduction in SLEDAI in these patients. In the patient treated with FT819 in the absence of CCT, we observed an overall minor reduction in PB (3.3% vs 2.9%) and DN B cells (33.3% vs 25.8%), but no change in naïve B cells at month 3 follow-up. Additionally, we observed a shift toward IgM positivity that, together with observed improvement in SLEDAI, may suggest ongoing rejuvenation of the B-cell compartment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Collectively, these findings demonstrate that FT819 can remodel the B-cell compartment toward a naïve and more diverse repertoire, even without CCT, supporting immune reset as a mechanism of clinical remission. This trial is actively enrolling, and updated patient data will be included at the time of presentation.

Disclosure: J. Tuncel: Fate Therapeutics, 3; **T. Greene**: Fate Therapeutics Inc, 3; **N. Brookhouser**: Fate Therapeutics Inc, 12,, 3; **S. Kothapally Hanok**: Fate Therapeutics, 3; **S. Peng**: Fate Therapeutics, 3; **A. O'Conor**: Fate Therapeutics, 3; **P. Fazeli**: AbbVie/Abbott, 2, Amgen, 6, AstraZeneca, 1, Janssen, 1; **J. Medlin**: None; **C. Bickers**: Fate Therapeutics Inc, 12,, 3; **K. Hubka**: Fate Therapeutics, 3; **A. Aguilar**: Fate Therapeutics, 3; **W. Zhao**: Fate Therapeutics, 3; **K. Omilusik**: Fate Therapeutics, 3; **J. Goulding**: Fate Therapeutics Inc, 12,, 3; **T. Lee**: Fate Therapeutics Inc, 3; **J. Goodridge**: Fate Therapeutics Inc, 3; **M. Hu**: None; **V. Bachanova**: Abvie, 1, ADC, 1, Citius, 5, Incyte, 5; **J. Miller**: Fate Therapeutics, 5, 11; **M. Lunning**: None; **R. Elstrom**: Fate Therapeutics Inc, 12,, 2; **D. Zack**: Fate Therapeutics, 3; **V. Sandhu**: Fate Therapeutics Inc, 3; **B. Valamehr**: Fate Therapeutics, 3; **L. Wong**: Fate Therapeutics, Inc., 12,, 3.

Abstract Number: 2455

Lupus Intervention Fatigue Trial: Preliminary Analysis of Baseline Data

Justin Arnold[1], Linda Ehrlich-Jones[2], Dominique Kinnett-Hopkins[3], Linda Van Horn[4], Grace Whiteford[4], Lutfiyya muhammad[5], Jing Song[6], Joan Chmiel[7], Rowland Chang[5], Pamela Semanik[7], Anh Chung[8], Daniel Erickson[4], Christie Bartels[9] and Rosalind Ramsey-Goldman[5], [1]Northwestern Feinberg School of Medicine, Chicago, IL, [2]Shirley Ryan AbilityLab, Aurora, IL, [3]University of Michigan, Ypsilanti, MI, [4]Feinberg School of Medicine, Chicago, [5]Northwestern University Feinberg School of Medicine, Chicago, IL, [6]Northwestern University Feinberg School of Medicine, Worthington, MN, [7]Feinberg School of Medicine, Chicago, IL, [8]Northwestern University, Chicago, [9]University of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is associated with persistent fatigue. Physical activity (PA) & dietary intake are potential modifiable behaviors that can reduce fatigue in people with SLE. The Lupus Intervention Fatigue Trial, LIFT (NCT02653287), a 12-month, phase II randomized, parallel-group, single-blind study compared motivational interviewing counseling targeting PA & diet with an education-based control program to reduce SLE fatigue. We also assessed neighborhood conditions measured by the Area Deprivation Index (ADI), as a potential factor impacting PA & diet.

Objectives: Present baseline descriptive results of LIFT participants. Assess associations between ADI and PA/diet intake.

Methods: LIFT criteria included age ≥18 yrs, English proficiency, walk household distances, BMI 18–40 kg/m^2, and meeting ACR or SLICC classification criteria for SLE. Accelerometers worn for 7 consecutive days during waking hours captured daily PA: sedentary < 100 counts/min, light PA (LPA) 101–2019 counts/min, and moderate-to-vigorous PA (MVPA) ≥2020 counts/min. Weekly MVPA=daily MVPA average x 7. Diet intake assessed via 24-hour recall from Nutrition Data System for Research (NDSR) generated Healthy Eating Index (HEI) total score (0-100) & food group scores 0-5 or 0-10) with higher scores being healthier. ADI derived from participants' 9-digit ZIP codes (higher ADI values indicate more deprivation, for 17 socioeconomic indicators). Patient-Reported Outcomes (PROs) used Fatigue Severity Score (FSS) & PROMIS measures for Fatigue, Pain Interference, Depression, Anxiety, Sleep Disturbance and Related Impairment, & Physical Function. Descriptive statistics were calculated; Spearman correlations used to assess associations between PA, or HEI and ADI.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics of LIFT Participants (n=167)	
Patient Characteristics	
Age (years), mean (SD)	43.5 (13.0)
Sex, Female (n, %)	152 (91%)
Race (self-reported) (n, %)	
Asian	16 (9.6%)
Black or African American	54 (32.3%)
White	87 (52.1%)
Other/Unknown	9 (5.4%)
Ethnicity (n, %)	
Hispanic or Latino	25 (25%)
Not Hispanic or Latino	136 (81.4%)
Not Reported	6 (3.6%)
Education Level (n, %)	
High School Diploma/GED	9 (5.4%)
Some College	23 (13.9%)
2-Year College Degree	16 (9.6%)
4-Year College Degree	55 (33.1%)
Masters' Degree	42 (25.3%)
Doctoral Degree	12 (7.2%)
Professional Degree	9 (5.4%)
Unknown	1
BMI (kg/m^2), mean (SD)	27.1 (5.1)
Disease Measures	
SLICC DI Score, mean (SD)	1.2 (1.6)
SLEDAI Total Score, mean (SD)	2.9 (3.1)
SLEDAI <6 (n, %)	135 (81%)
SLEDAI >= 6 (n, %)	32 (18%)
Patient-Reported Outcomes	
Fatigue Severity Score (FSS), mean (SD)	4.3 (1.5)
PROMIS-Fatigue, mean (SD)	59.0 (9.0)
PROMIS-Pain Interference, mean (SD)	53.8 (9.9)
PROMIS-Depression, mean (SD)	50.4 (8.7)
PROMIS-Anxiety, mean (SD)	53.8 (9.0)
PROMIS-Sleep Disturbance, mean (SD)	52.6 (8.5)
PROMIS-Sleep Related Impairment, mean (SD)	54.2 (8.9)
PROMIS-Physical Function, mean (SD)	48.7 (7.6)

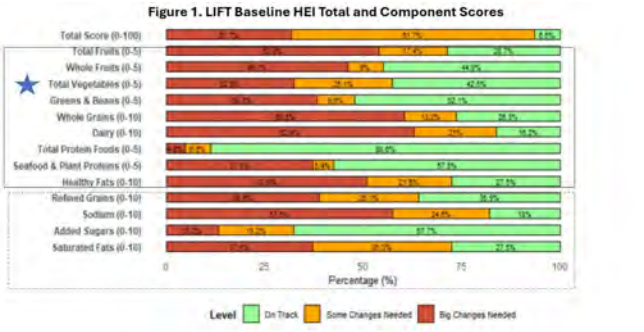
BMI=Body Mass Index; SLICC DI=Systemic Lupus International Collaborating Clinics Damage Index (range 0-53); SLEDAI=Systemic Lupus Erythematosus Disease Activity Index (range 0-105); FSS=Fatigue Severity Score (range 1-7);PROMIS measures (range 10-100, mean [SD] for US population 50 [10]); higher scores for all measures mean worse symptoms except for Physical Function where a lower score is better functioning

Table 2. Baseline Physical Activity (PA) Measures and Neighborhood Resources (ADI); Correlations Between PA and ADI in LIFT Participants (n=167)			
ADI Rank/Average PA Daily Minutes	**Mean (SD)**	**Spearman Correlation Between ADI and PA**	**P-value**
ADI	34.7 (21.4)	NA	NA
Sedentary	582.8 (92.8)	0.09	0.252
LPA	242.2 (75.5)	-0.08	0.299
MVPA*	**19.8 (19.4)**	**-0.20**	**0.009**
Total PA	262.3 (83.4)	-0.13	0.113

ADI=Area Deprivation Index; NA=not applicable; LPA=light physical activity; MVPA=moderate-vigorous physical activity; ***32.5% of LIFT participants met US guidelines of ≥150 minutes/week of MVPA**

Results: Baseline demographics, disease characteristics, PRO's, and HEI for 167 LIFT participants are shown in Table 1; Figure 1. Most participants had low disease activity, low damage scores, low total HEI score (poorer diet quality), and high FSS & PROMIS-Fatigue scores. Most participants lived in less deprived areas, ADI [mean 34.7 (21.4)]. Only 32.5% of participants met U.S. guidelines for PA (≥150 MVPA min/week); MVPA min/week was negatively correlated with ADI suggesting persons living in higher ADI deprivation areas had lower average MVPA minutes (Table 2). Recommended changes based on HEI score are in Figure 1. Modest statistical association was found between ADI (high) and total vegetable intake (low), rho=-0.15, p= 0.049.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Items within dashed box indicate one should eat less from food category, items within solid line indicate one should eat more from food category. Starred item indicates significant relationship between ADI and total vegetable intake, p=.049

Conclusion: Preliminary LIFT baseline data suggest despite low disease activity, LIFT participants have significant fatigue, 1/3rd meet PA guidelines (>150 mins/week of MVPA); lower HEI total and food group scores suggest need for improved diet quality. Mean MVPA minutes/week and total vegetable intake were negatively correlated with ADI rank showing those in higher ADI areas were less physically active and had poorer diet quality. Follow-up analyses will assess change in fatigue between baseline & 6 month visit to compare the intervention and control groups. Tailored interventions to address individual & contextual barriers may be needed to improve PA & HEI impact on fatigue.

NIH P30AR072579, R01AR071091, ULT1R001422, RRF

Disclosure: J. Arnold: None; **L. Ehrlich-Jones**: None; **D. Kinnett-Hopkins**: None; **L. Van Horn**: None; **G. Whiteford**: None; **L. muhammad**: None; **J. Song**: None; **J. Chmiel**: None; **R. Chang**: None; **P. Semanik**: None; **A. Chung**: None; **D. Erickson**: None; **C. Bartels**: None; **R. Ramsey-Goldman**: Ampel Solutions, 2, AstraZeneca, 6, Biogen, 2, Cabaletta, 2, Duke, 2, Exagen Diagnostics, 2, Merck, 2, SUNY Syracuse, 2.

Abstract Number: 2456

Predictors of Real-World Remission in Patients with SLE Initiating Belimumab in the USA

Aarat M Patel[1], Renee L. Gennarelli[2], Temitope Bello[2], Ali Bonakdar[2] and **Karen Worley**[3], [1]GSK, US Medical Affairs, Durham, NC, [2]Cencora, Real-World Evidence, Conshohocken, PA, [3]GSK, Global Real-World Evidence & Health Outcomes Research, Collegeville, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The Definition Of Remission in SLE (DORIS) criteria were developed to align SLE remission definitions.[1,2] Post hoc analyses of clinical trial data demonstrated that belimumab (BEL) plus standard therapy (ST) increases the proportion of patients with SLE in DORIS remission compared with placebo plus ST.[3] As real-world SLE remission data for patients in the USA initiating BEL are scarce and there is a lack of clarity on characteristics of patients achieving remission, this retrospective, observational cohort study (GSK Study 222161) explored predictors of remission in this patient population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

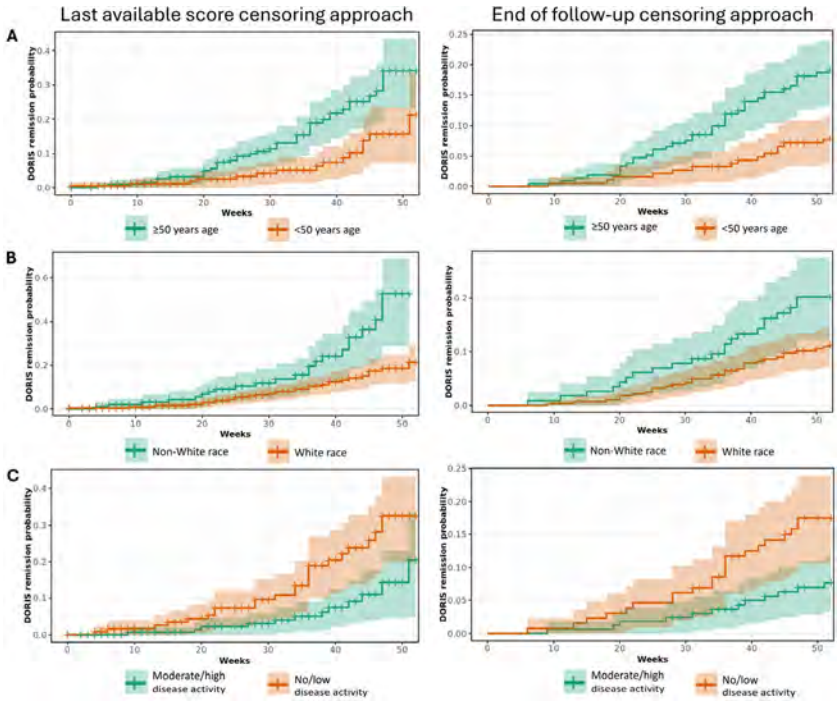


Figure 1. Unadjusted probability estimates of achieving real-world SLE remission (per DORIS proxy) stratified by (A) age, (B) race, and (C) baseline SLEDAI disease activity, as assessed by two censoring approaches. Shaded areas represent confidence bounds.

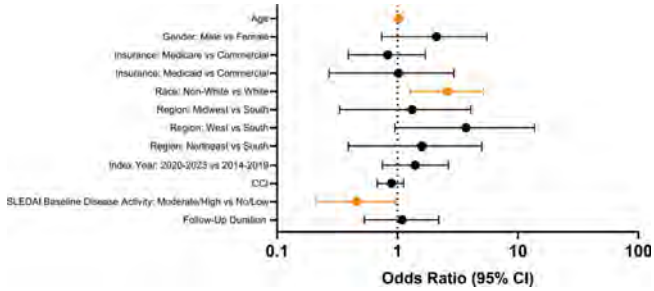


Figure 2. Logistic regression model with real-world SLE remission (per DORIS proxy) by 52 weeks as the event, and baseline patient demographics and clinical characteristics as covariates. Note: No/low disease activity per SLEDAI is not necessarily a complete measure of disease status, as all patients were determined by their physician to need initiation of a new therapy (biologic). CCI, Charlson Comorbidity Index.

Methods: Study period: Jan 1, 2013, to May 31, 2024. Data were derived from the OM1 PremiOM SLE dataset (OM1, Boston, MA, USA). Eligible patients had ≥1 BEL pharmacy/medical encounter during the identification period (Jan 1, 2014, to Oct 31, 2023). Real-world SLE remission was defined per DORIS proxy (SLEDAI/estimated SLEDAI score=0 [no disease activity]; Physician's Global Assessment [PGA] < 2 on the numeric rating scale; prednisone equivalent dose ≤5 mg/day) and assessed up to 52 weeks post-BEL initiation. Kaplan–Meier estimates were used to assess the probability of achieving remission. Two censoring approaches assessed estimate robustness: 1) last available score – earlier of latest available SLEDAI or PGA score in the follow-up period and end of follow-up; 2) end of follow-up – earlier of 52 weeks post-index (first BEL receipt), last activity date, or date of data cutoff. Patient demographics and clinical characteristics associated with remission were identified in a prespecified exploratory analysis using a logistic regression model with remission as the dependent variable; odds ratio (OR), 95% confidence intervals (CI) and p-values were calculated.

Results: Of 398 patients, 94% were female and 71% White, with a mean (standard deviation) age of 51 (14) years at index. Unadjusted probability estimates showed patients aged ≥50 years (vs < 50 years), non-White patients (vs White) and those with no/low (vs moderate/high) disease activity had a slightly higher probability of achieving remission; however, estimates

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

differed by censoring approach and confidence bounds overlapped (**Figure 1**).The adjusted model showed that older patients were significantly more likely to achieve remission by 52 weeks than younger patients (for each year of age OR: 1.03 [95% CI: 1, 1.06], p=0.0248; **Figure 2**). Patients of non-White race were significantly more likely to achieve remission than White patients (2.57 [1.27, 5.19], p=0.0092). Patients with moderate/high disease activity at baseline were significantly less likely to achieve remission than those with no/low disease activity (0.46 [0.21, 0.96], p=0.0378).

Conclusion: Predictors of real-world SLE remission with BEL include non-White race, older age, and no/low baseline disease activity. The association between minimal disease activity and higher remission rates supports the benefit of initiating belimumab treatment earlier in the course of disease.

Funding: GSK

References

[1]van Vollenhoven R et al. *Ann Rheum Dis* 2017;76:554–61
[2]van Vollenhoven RF et al. *Lupus Sci Med* 2021;8:e000538
[3]Parodis I et al. *Lancet Rheumatol* 2024;6(11):e751–61

Disclosure: A. Patel: GSK, 12,, 3, University of Virginia, 3, 12, Volunteer Faculty at the University of Virginia, Virginia Society of Rheumatology and The Paediatric Society of the African League Against Rheumatism, 4; **R. Gennarelli**: Cencora, 3; **T. Bello**: Cencora, 3; **A. Bonakdar**: Cencora, 3; **K. Worley**: GSK, 12,, 3.

Abstract Number: 2457

Maternal, Embryo-Fetal And Neonatal Outcomes Following Belimumab Exposure During Pregnancy In Patients With Systemic Lupus Erythematosus

Kenza El Ouazzani[1], Nathalie Morel[1], Delphine Beghin[2], Gaelle GUETTROT-IMBERT[3], Noémie JOURDE-CHICHE[4], Alban DEROUX[5], Françoise Sarrot-Reynauld[5], Lionel Couzi[1], Vincent Langlois[6], Estibaliz LAZARO[7], Pauline ORQUEVAUX[8], Benjamin DE SAINTE MARIE[9], Kevin Deve[10], christophe Deligny[11], Nicole Ferreira[12], Bertrand Godeau[13], Véronique Le Guern[3], Raphaelle Meunier[14], Elisabeth Pasquier[15], Viviane Queyrel Moranne[16], Laurent Sailler[17], Cécile Saint-Pastou[18], Nathalie Costedoat-Chalumeau[3], Benoit Marin[19], Christophe Richez[1] and the GR2 group study, [1]Bordeaux University Hospital, Bordeaux, France, [2]Paris Pitié-Salpêtrière Hospital, Paris, France, [3]Cochin Hospital, Paris, France, [4]Centre de Néphrologie et Transplantation Rénale, Hôpital de la Conception, Assistance Publique-Hôpitaux de Marseille, Marseille, France., Marseille, France, [5]Grenoble university hospital, Grenoble, France, [6]Le Havre University Hospital, Le Havre, France, [7]Bordeaux University Hospital, Pessac, France, [8]Reims University Hospital, Reims, France, [9]Timone university hospital, Marseille, France, [10]Bayonne hospital, Bayonne, France, [11]Fort-de-France hospital, Fort-de-France, France, [12]Tours University Hospital, Tours, France, [13]Creteil Hospital, Paris, France, [14]Libourne Hospital, Libourne, France, [15]Brest University Hospital, Brest, France, [16]Nice University Hospital, Nice, France, [17]CHU Toulouse, Toulouse, France, [18]Saint-Pierre Hospital, Saint-Pierre, France, [19]Hôpital Pitié-Salpêtrière, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) may be associated with high-risk pregnancies, especially in the presence of specific predisposing factors. While optimal disease control during pregnancy is critical, there is limited evidence on the safety of belimumab exposure in the context of pregnancy (1). This study aimed to assess

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patients characteristics at conception according to belimumab continuation (beli+) or discontinuation (beli -).

	Belimumab continuation (beli+) n=18, n (%)	Belimumab discontinuation (beli-) n=14, n (%)
Maternal age at pregnancy (years, median [min-max])	31 [24-40]	31 [23-35]
Previous SLE features (n=31 patients) *		
- Acute cutaneous lupus	11/15 (73)	9/13 (69)
- Subacute cutaneous or discoid lupus	2/15 (13)	3/13 (23)
- Oral ulcers	5/15 (33)	3/13 (23)
- Non-scarring alopecia	5/15 (33)	4/13 (31)
- Arthritis	14/15 (93)	12/13 (92)
- Serositis	5/15 (33)	7/13 (54)
- Nephritis	12/15 (80)	6/13 (46)
- Neurological involvement	3/15 (20)	0/13 (0)
- Autoimmune hemolysis	2/15 (13)	2/13 (15)
- Anti-dsDNA antibody	12/15 (80)	12/13 (93)
- Anti-Sm antibody	7/15 (47)	4/13 (31)
- Low C3 or low C4	11/15 (73)	10/13 (77)
- Positive Coombs test (MD=4)	4/15 (27)	2/12 (17)
Concomitant treatment (n= 32 pregnancies):		
- Hydroxychloroquine	16/18 (89)	14/14 (100)
- Prednisone (MD=1)	12/17 (71)	11/14 (79)
- Azathioprine	9/18 (50)	7/14 (50)
- Tacrolimus	1/18 (6)	2/14 (14)
- Ciclosporin	1/18 (6)	1/14 (7)

* : in belimumab continuation group, 3 missing data ; in belimumab discontinuation group, 13 patients with 1 twin pregnancy and 2 pregnancies from one mother.

Abbreviation: SLE, systemic lupus erythematosus; MD, missing data

Table 2: Time of belimumab discontinuation, whether or not treatment was continued at the time of conception among the 32 pregnancies.

	Belimumab continuation (beli+) n=18	Belimumab discontinuation (beli-) n=14
Belimumab discontinuation in beli + group:		
- **during the 1st trimester, n (%)** gestational age at discontinuation (median in weeks of gestation [min-max])	10/18 (56) 5.7 [1.1-7.7]	/ /
- **during the 2nd trimester, n (%)** gestational age at discontinuation (weeks of gestation)	1/18 (6) 12.3	/ /
- **during the 3rd trimester, n (%)** gestational age at discontinuation (median in weeks of gestation [min-max])	3/18 (17) 28.6 [24-33.14]	/ /
No discontinuation, n (%)	4/18 (22)	/
Time of belimumab discontinuation before conception (median in months [min-max])	/	4 [2-10]

maternal, embryo-fetal and neonatal outcomes in patients with SLE, exposed to belimumab during the year preceding pregnancy, according to whether treatment was continued or not at time of conception.

Methods: Data were collected from: (1) the GR2 study, a French prospective cohort of pregnancies in women with autoimmune diseases involving 76 centers, (2) the French Teratology Information Service (CRAT) and (3) a national call for observations from the French Rheumatism and Inflammatory Club (CRI). Eligible participants were pregnant women aged ≥ 18 years with SLE according to the 2012 SLICC criteria, treated with belimumab within the year prior conception. Patients were stratified based on belimumab continuation (beli+) or discontinuation (beli-) at conception. Maternal disease activity, obstetrical complications and adverse embryo-fetal and neonatal outcomes were evaluated.

Results: A total of 32 pregnancies from 31 mothers were recorded between March 2016 and December 2024 across 19 French centers (n=19 from the GR2, n=8 from the CRAT and n=5 from the CRI) including 18 pregnancies in beli+ and 14 in beli-. Their characteristics are described in Table 1 and their exposure to belimumab in Table 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Among the 32 pregnancies, 25 resulted in 26 live births including 14 in beli+ and 12 (1 twin pregnancy) in beli-. Pregnancy losses (n=7) included 5 miscarriages (3 in beli+ and 2 in beli-), 1 in utero fetal death due to intervillositis (beli-) and 1 voluntary abortion for non-medical reasons (beli+).

Obstetrical complications occurred in 13/32 pregnancies (9 beli+, 4 beli-), including 3 maternal infections (2 beli+, 1 beli-), 2 preeclampsia (1 beli+, 1 beli-), 2 intrauterine growth restrictions (1 beli+, 1 beli-), 1 small for gestational age (beli +), 1 placenta abruption (beli-), 1 gestational diabetes (beli+), 1 postpartum hemorrhage (beli+) and/or 7 preterm deliveries (5 beli+, 2 beli-). No congenital malformations were identified.

Mild to moderate lupus flares occurred during 8/32 pregnancies (25%, 4 beli+, 4 beli-), at a median gestational age of 10 weeks [5-21] and in 6 during the year post-partum (2 beli+, 4 beli-).

Of the 26 live births, most neonates (n=18, 72%, 1 missing data) had normal Apgar scores. Three neonates (beli+) required hospitalization due to neonatal asphyxia (n=1) and prematurity (n=2). One neonate was suspected of congenital CMV infection (beli +).

No atypical infections were reported within the first year of life of the children in either group.

Conclusion: Adverse maternal and fetal outcomes were observed in both groups, but no specific risk was identified with belimumab continuation at time of conception or during pregnancy. No malformation was reported.

1. Petri M, Landy H et al. Belimumab use during pregnancy: a summary of birth defects and pregnancy loss from belimumab clinical trials, a pregnancy registry and postmarketing reports. Ann Rheum Dis. févr 2023;82(2):217-25.

Disclosure: K. El Ouazzani: None; **N. Morel**: None; **D. Beghin**: None; **G. GUETTROT-IMBERT**: None; **N. JOURDE-CHICHE**: None; **A. DEROUX**: None; **F. Sarrot-Reynauld**: None; **L. Couzi**: None; **V. Langlois**: None; **E. LAZARO**: None; **P. ORQUEVAUX**: None; **B. DE SAINTE MARIE**: None; **K. Deve**: None; **c. Deligny**: None; **N. Ferreira**: None; **B. Godeau**: None; **V. Le Guern**: AstraZeneca, 12, attending meetings and travel., Bristol-Myers Squibb(BMS), 6, Novartis, 2; **R. Meunier**: None; **E. Pasquier**: None; **V. Queyrel Moranne**: None; **L. Sailler**: None; **C. Saint-Pastou**: None; **N. Costedoat-Chalumeau**: None; **B. Marin**: None; **C. Richez**: None.

Abstract Number: 2458

Obecabtagene autoleucel (obe-cel), a CD19-targeting Autologous Chimeric Antigen Receptor T-cell Therapy (CAR T) with a fast off-rate binding domain, in Patients (pts) with Severe, Refractory Systemic Lupus Erythematosus (srSLE): Preliminary Results from the Phase I CARLYSLE Study

Maria Leandro[1], Ruth Pepper[2], Ben Parker[3], Eleni Tholouli[4], David Jayne[5], Ben Uttenthal[6], Josefina Cortés-Hernández[7], Pere Barba[7], José Andrés Román Ivorra[8], Yanqing Hu[9], Wolfram Brugger[10], Silvia Basilico[11], Davide Germano[11] and Claire Roddie[1], [1]University College London and University College London Hospital, London, United Kingdom, [2]University College London, University College London Hospital and Royal Free Hospital NHS Trust, London, United Kingdom, [3]NIHR Manchester CRF, Manchester Royal Infirmary, Manchester, United Kingdom, [4]Manchester Royal Infirmary, Manchester, United Kingdom, [5]University of Cambridge, Cambridge, United Kingdom, [6]Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [7]Hospital Universitari Vall d'Hebron-Universitat Autónoma de Barcelona, Barcelona, Spain, [8]Hospital Universitari i Politècnic La Fe, Valencia, Spain, [9]Autolus Therapeutics, Rockville, MD, [10]Autolus Therapeutics, Munich, Germany, [11]Autolus Therapeutics, Basel, Switzerland

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Pts with srSLE have limited remaining treatment options and represent a population with an unmet need. CD19 CAR Ts have potential for deep depletion of the B-cell lineage, including plasmablasts. Obe-cel is an autologous CD19-directed CAR T with a fast off-rate binding domain designed to reduce immunotoxicity, approved in adult relapsed/refractory B-cell acute lymphoblastic leukemia. We report initial safety and preliminary efficacy results from the single-arm, open-label, dose-finding, Phase I CARLYSLE study (NCT06333483).

Methods: Eligible pts (12–65 years old) had a diagnosis of SLE based on the 2019 EULAR/ACR criteria and a ≥8-point SLEDAI-2K score at screening with ≥1 major SLE-related organ involvement, and were refractory to multiple prior standard-of-care SLE medications. Immunosuppressants were tapered off prior to apheresis. Following lymphodepletion with fludarabine (3×25 mg/m^2) and cyclophosphamide (1x1,000 mg/m^2), obe-cel was administered as a single starting target dose of 50×10^6 (±20%) CAR T-cells. Primary endpoints: incidence of dose limiting toxicities (DLTs) within 28 days of infusion; frequency of adverse events. Secondary endpoints included: SLEDAI-2K; PGA; pharmacokinetics (PK); autoantibody and biomarker levels over time.

Results: As of 17 Mar 2025, seven pts had been enrolled and six had been infused with obe-cel with up to 8 months of follow up. At baseline, all infused pts had severe, refractory, active SLE (SLEDAI-2K score range: 15–28). All infused pts had class III or IV lupus nephritis; four also had class V. Four pts had elevated serum creatinine and an estimated glomerular filtration rate of < 60 mL/min/1.73m^2; six pts had elevated urinary protein-creatinine ratio. Pts were refractory to B-cell targeting agents and immunosuppressants (median: 5 prior medicines; range: 5–6). No DLTs or immune effector cell-associated neurotoxicity syndrome (ICANS) were observed. Three pts experienced Grade (Gr) 1 cytokine release syndrome (CRS) with no Gr ≥2 CRS. Transient hypertension was observed in five pts. All pts had Gr ≥3 neutropenia. Infections were transient and manageable; no life-threatening infections were observed. A ≥10 point reduction in SLEDAI-2K scores was seen in the four pts who had ≥3 months of follow up and all non-renal manifestations completely resolved within 3 months. Steroid doses were tapered to ≤10mg/day post obe-cel infusion; no other SLE medications were administered. Three of six pts had a complete renal response (CRR) at last follow-up, one at Month 1 (M1) and two at M3. Complement C3 normalized and anti-double-stranded DNA antibody decreased in all six pts by M1 compared with baseline levels. PK data indicated robust CAR T-cell expansion; peak expansion was reached at a median of 10 days. Three pts had ongoing CAR T-cell persistence at last follow-up.

Conclusion: Initial findings from the ongoing CARLYSLE study of obe-cel in srSLE show a manageable safety profile, with no DLTs, ICANS or Gr ≥2 CRS. SLEDAI-2K score reduction and clinical benefit were observed in all pts, including three pts who had a CRR. Despite the short follow up and small number of pts, initial findings are promising; further research is warranted. Updated data will be presented at the conference.

Disclosure: M. Leandro: Artiva, 12, PI for Clinical Trials on B cell targeting therapies:, Autolus Therapeutics, 12, PI for Clinical Trials on B cell targeting therapies:, BMS, 12, PI for Clinical Trials on B cell targeting therapies:, Fate Therapeutics, 12, PI for Clinical Trials on B cell targeting therapies:, Roche Basel, 12, PI for Clinical Trials on B cell targeting therapies:, Roche Basel (Co-PI in research grant paid to UCL), 5, Roche Basel/UCB - Advisory board September 2024, 1; **R. Pepper**: Autolus Therapeutics, 1, Roche (Lupus Nephritis) Advisory board, 1, Stada symposium, 6, Vifor (IgA) advisory board, 1; **B. Parker**: Autolus Therapeutics, 1, LUPUS UK, 5, Otsuka, 6, UCB, 12, Conference attendance; **E. Tholouli**: Autolus Therapeutics, 2, 5, Bristol-Myers Squibb(BMS), 2, Janssen, 2, Jazz Pharmaceuticals, 6, Kite/

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Gilead, 2, 5, 6, 12, Travel expenses, Pfizer, 6, Sobi, 6, Takeda, 6, Vertex, 2, 6; **D. Jayne**: Alentis, 2, 11, Amgen, 2, 6, AstraZeneca, 1, 2, 6, Aurinia, 1, 11, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, ChemoCentryx, 2, 6, Chinook, 1, Chugai, 2, 6, CSL Vifor, 2, 6, Fate, 2, GlaxoSmithKlein(GSK), 2, 6, GSK, 1, Hansa, 1, Novartis, 1, 2, 6, Otsuka, 2, Roche, 2, 6, Takeda, 1, 2, 6; **B. Uttenthal**: AbbVie, 12, Sponsorship to attend conference, Analog Devices, 2, Gilead, 12, Sponsorship to attend conference, Jazz, 12, Sponsorship to attend conference, Kite, 6, Kite/Gilead, 1, Kyverna, 1, 12, Sponsorship to attend conference, Novartis, 12, Sponsorship to attend conference, Sartorius, 2, Swarm Oncology, 2, Takeda, 12, Sponsorship to attend conference; **J. Cortés-Hernández**: AstraZeneca, 6, Bristol-Myers Squibb (BMS), 1, GlaxoSmithKline (GSK), 6, Novartis, 1, 5, 6; **P. Barba**: Allogene, 5, Amgen, 5, Bristol-Myers Squibb, 5, Gilead Sciences, 5, InCyte, 5, Jazz Pharmaceuticals, 5, Miltenyi Biomedicine, 5, Nektar, 5, Novartis, 5, Pfizer, 5, Pierre Fabre, 5; **J. Andrés Román Ivorra**: AstraZeneca, 6, GSK, 6, UCB, 6; **Y. Hu**: Autolus Therapeutics, 3, 11; **W. Brugger**: Autolus Therapeutics, 3, 11; **S. Basilico**: Autolus Therapeutics, 3, 11; **D. Germano**: Autolus Therapeutics, 3, 11; **C. Roddie**: Autolus Therapeutics, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Gilead, 2, 6, Janssen, 2.

Abstract Number: 2459

Hydroxychloroquine Discontinuation in Systemic Lupus Erythematosus: A Retrospective Cohort Study with 3-Year Follow-Up

Milena Delai[1], Rachel Simon[1], Eduardo Mantovani Cardoso[2] and Vasileios Kyttaris[3], [1]Beth Israel Deaconess Medical Center, Boston, MA, [2]Beth Israel Deaconess Medical Center, Boston, [3]Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Hydroxychloroquine (HCQ) plays an important role in the immunomodulation of Systemic Lupus Erythematosus (SLE), reducing the risk of flares and overall mortality. However, long-term HCQ use is associated with retinal toxicity, a common reason for discontinuation. The incidence, risk factors, and characteristics of SLE flares post HCQ discontinuation remain unclear. This study aims to identify markers that predict SLE flares in patients who discontinue HCQ.

Methods: Retrospective cohort of adult patients who met the 1997 American College of Rheumatology criteria for SLE and discontinued HCQ at a single center between 2012 and 2023. The index visit was the closest (within 3 months) to HCQ discontinuation, and the follow-up was 36 months from the index visit. Flares were assessed using the SLE Disease Activity Index (SLEDAI) flare rate instrument. We compared variables between patients who experienced flares and those who remained flare-free. Variables a priori identified as potential predictors were analyzed using a Cox regression model.

Results: 42 patients were included in this cohort. The mean age of patients was 50 years, 95% were female, 43% self-identified as White, 33% as Black. The mean duration of SLE was 15.7 years, with the mean HCQ dose before discontinuation being 4 mg/kg/day. The main reason for discontinuation was retinal toxicity (56%). At the index visit, 28% of patients had low complement levels, 39% were positive for anti-dsDNA, 55% were on immunosuppressive or biological treatment, and 26% were using prednisone at baseline (Table 1).

A little over half of the patients flared during the follow-up period. In the first year after HCQ discontinuation, 12 patients (28.6%) flared, while 15 patients (35.7%) flared in the second year, and 14 patients (37.8%) flared in the third year. Five patients were lost to follow-up after 24 months.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Patient characteristics at the index visit. HCQ: hydroxychloroquine; SLE: Systemic Lupus Erythematosus; mg/kg.d: milligrams per kilogram per day; mg/dL: milligrams per deciliter; anti-dsDNA: double-stranded DNA antibody; SLEDAI: SLE Disease Activity Index.

	HCQ discontinuation (N=42)
Age (years, mean ± SD)	50.0±13.2
Sex female, N (%)	40 (95)
Race, N (%)	
White	18 (43)
Black	14 (33)
Asian	6 (14)
Other	4 (10)
Duration of SLE, (years, mean ± SD)	15.7±9.5
HCQ dose (mg/kg.d, mean ± SD)	4.0±1.9
Low complement (C3<90mg/dL or C4<10mg/dL), N (%)	9/32 (28)
Complement C3 (mg/dL, mean ± SD)	107.4±28.3
Complement C4 (mg/dL, mean ± SD)	20.2±10.0
Presence of anti-dsDNA, N (%)	12/31 (39)
Treatment, N (%)	
Immunosuppressive/biological	23 (55)
Mycophenolate Mofetil	9 (21)
Mycophenolate Sodium	3 (7)
Azathioprine	8 (19)
Methotrexate	2 (5)
Belimumab	1 (2)
Abatacept	1 (2)
Prednisone	11 (26)
Clinical SLEDAI score (mean ± SD)	0.5±1.8

Table 2. Comparison of baseline variables between patients with any flare over 3 years versus patients with no flare during follow-up. SLE: Systemic Lupus Erythematosus; HCQ: hydroxychloroquine; mg/kg.d: milligrams per kilogram per day; mg/dL: milligrams per deciliter; anti-dsDNA: double-stranded DNA antibody; SLEDAI: SLE Disease Activity Index.

	Any flare (N=21)	No flare (N=19)	p value
Age (years, mean ± SD)	47.6±13.7	52.0±13.2	0.416
Race, N (%)			0.116
White	6 (29)	12 (63)	
Black	7 (33)	5 (26)	
Asian	5 (24)	1 (5)	
Other	3 (14)	1 (5)	
Duration of SLE (years, mean ± SD)	15±9.4	16.6±10.1	0.714
HCQ dose (mg/kg.d, mean ± SD)	4.5±2	3.5±1.6	0.088
Low complement (C3<90mg/dL or C4<10mg/dL), N (%)	8/16 (50)	1/14 (7)	0.011
Complement C3 (mg/dL, mean ± SD)	91.1±20.1	124.7±27.5	0.001
Complement C4 (mg/dL, mean ± SD)	18.1±7.8	20.3±8.8	0.482
Presence of anti-dsDNA, N (%)	7/15 (47)	4/14 (29)	0.316
Immunosuppressive or biological, N (%)	13 (62)	9 (47)	0.356
Prednisone, N (%)	7 (33)	4 (21)	0.385
Clinical SLEDAI score (mean ± SD)	0.8±2.5	0.3±0.7	1

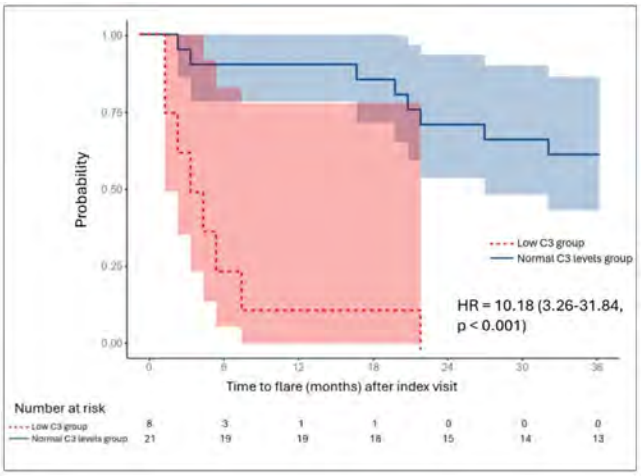


Figure 1: Kaplan-Meier survival analysis stratified by Complement C3 levels (log-rank p-value < 0.001) and Univariate Cox regression analysis with Hazard Ratio (HR).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The comparison of baseline variables between the 21 patients who experienced at least one flare (of any severity) with 19 flare-free patients over the 36 months showed that patients with any flare had lower complement (50% vs. 7%, p = 0.011) and lower mean C3 levels (91.1 ± 20.1 vs. 124.7 ± 27.5 mg/dL, p = 0.001) at the index visit (Table 2).

Kaplan-Meier curve showed that patients with low C3 levels flared more often and sooner than patients with normal C3 at baseline (log-rank p-value < 0.001). Univariate Cox regression analysis revealed that patients with low C3 levels at the index visit had a hazard ratio (HR) of 10.18 (95% CI: 3.26-31.84, p < 0.001) for any flare during follow-up, compared to patients with normal C3 levels (Figure 1).

Conclusion: In this cohort of 42 patients with SLE who discontinued HCQ, 21 patients (50%) experienced at least one flare over the 3 years. All patients with low C3 at baseline flared within the first 24 months, and low C3 was significantly linked to an increased risk of flares, especially in the first year. The use of immunosuppressants or glucocorticoids at the index visit was not associated with flare occurrence during follow-up. These findings suggest that monitoring C3 levels may help identify those at higher risk of complications after HCQ discontinuation. Further studies are needed to develop strategies for flare prevention in this setting.

Disclosure: M. Delai: None; **R. Simon**: None; **E. Mantovani Cardoso**: None; **V. Kyttaris**: AstraZeneca, 2, Biogen, 2, Biopharm Communications, 2, Boehringer-Ingelheim, 2, Cabaletta, 2, Exagen Diagnostics, 5, Fresenius Kabi, 2, Janssen, 2.

Abstract Number: 2460

Comparative Efficacy of Belimumab, Anifrolumab, and Rituximab in SLE: A Retrospective Analysis of Serological and Clinical Outcomes

Pablo Martínez Calabuig[1], Jorge Juan Fragío Gil[2], Roxana González Mazario[3], Laura Salvador Maicas[4], Mireia Sanmartin Martínez[4], Iván Jesús Lorente Betanzos[4], Amalia Rueda Cid[4], Juan José Lerma Garrido[4], Isabel Martínez Cordellat[4], Isabel Balaguer Trull[4], Berta Gómez Correas[4] and Cristina Campos Fernández[3], [1]Hospital General Universitario de Valencia, Spain/ Uversidad Catolica de Valencia San Vicente Martir, Valencia, Spain, Ontinyent, Spain, [2]Hospital General Universitario, Valencia, Spain, [3]Hospital General de Valencia, Valencia, Spain, [4]Hospital General Universitario de Valencia, Valencia, Comunidad Valenciana, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystem involvement and fluctuating activity. Biologic therapies such as Belimumab, Anifrolumab, and Rituximab offer new options for moderate-to-severe or refractory SLE, though comparative data remain limited. This study describes baseline clinical features and compares serologic outcomes over 12 months.

Methods: We conducted a retrospective study of SLE patients meeting 2019 ACR/EULAR criteria treated with Belimumab, Anifrolumab, or Rituximab between 2010–2025 at a university hospital. Clinical data and analytical parameters (anti-dsDNA, C3, C4, hemoglobin, leukocytes, lymphocytes, platelets, creatinine, eGFR) were collected. Linear mixed-effects models assessed treatment, time, and their interaction.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Treatment and clinical manifestations of SLE patients

Table 1.	SLE PATIENTS (N=65)
TREATMENT	
ANIFROLUMAB, N (%)	17 (26.2)
MEDIAN TREATMENT DURATION, MONTHS	6
BELIMUMAB, N (%)	39 (60.0)
MEDIAN TREATMENT DURATION, MONTHS	18
RITUXIMAB, N (%)	9 (13.8)
MEDIAN TREATMENT DURATION, MONTHS	14
CLINICAL MANIFESTATIONS	
CUTANEOUS, N (%)	42 (64.6)
ARTICULAR, N (%)	59 (90.8)
ALOPECIA, N (%)	13 (20.0)
ORAL ULCERS, N (%)	20 (30.8)
NEUROPSYCHIATRIC MANIFESTATIONS, N (%)	33 (50.8)
SEROSITIS, N (%)	26 (40.0)
HEMATOLOGIC MANIFESTATIONS, N (%)	52 (80.0)
GASTROINTESTINAL INVOLVEMENT, N (%)	9 (13.8)
RENAL INVOLVEMENT, N (%)	23 (35.4)

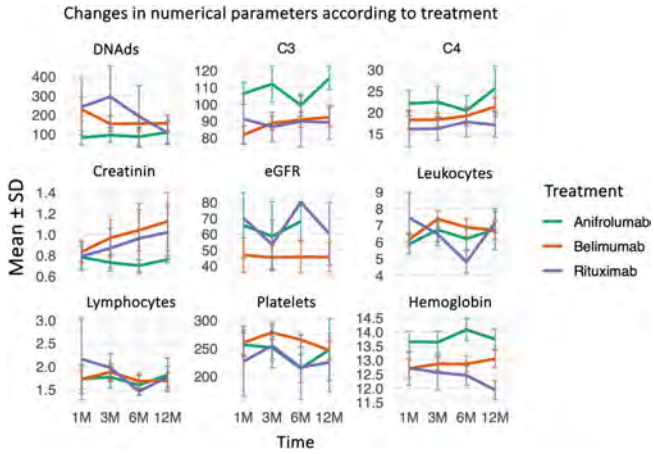


Image 1. Changes in numerical parameters according to treatment.

Results: A total of 65 patients were included (mean age at diagnosis: 36.1 years; 90.8% female). The most frequent baseline manifestations were articular (90.8%), hematologic (80.0%), or cutaneous (64.6%). Biologic therapies included Belimumab (60.0%), Anifrolumab (26.2%), and Rituximab (13.8%) (see Table 1&2).

Therapeutic survival at 12 months was 69.2% for Belimumab, 64.7% for Anifrolumab, and 66.7% for Rituximab. Most discontinuations were due to infections or lack of efficacy. Corticosteroids were used in 88%, 78%, and 83% of Belimumab, Anifrolumab, and Rituximab cases, respectively, with median initial prednisone doses of 7.5, 5, and 10 mg/day.

A significant inter-treatment difference was observed for complement C3 levels ($p=0.032$), with Anifrolumab achieving significantly higher C3 levels than Belimumab at month-1 ($p=0.0091$) and month-3 ($p=0.0097$), suggesting faster complement recovery. Rituximab, did not show significant improvements in C3 levels at any time point (see Image 1).

For anti-dsDNA, overall treatment effect was not statistically significant ($p = 0.13$), though time had a significant impact ($p=0.01$). Belimumab showed a significant intra-group reduction in anti-dsDNA between month 1 and month 12 ($p=0.0058$), while Rituximab was associated with persistently elevated levels.

No statistically significant differences were found between treatments in complement C4 levels ($p=0.26$), although a marginally significant treatment-by-time interaction ($p=0.063$) suggests a possible trend toward different temporal profiles among therapies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Baseline Analytical Characteristics of Patients with SLE

	SLE patients n= 65
Baseline hemoglobin, mean (SD)	12.86 (1.79)
Baseline leukocytes, mean (SD)	6.61 (2.72)
Baseline lymphocytes, mean (SD)	1.49 (0.84)
Baseline platelets, mean (SD)	265.10 (88.41)
Baseline C3, mean (SD)	88.29 (26.93)
Low C3, n (%)	25 (43.1)
Baseline C4, mean (SD)	17.52 (9.78)
Low C4, n (%)	28 (48.3)
Baseline anti-dsDNA, mean (SD)	180.49 (229.11)
Baseline creatinine, mean (SD)	0.86 (0.56)
Baseline eGFR, mean (SD)	81.12 (20.06)
Baseline hematuria, n (%)	5 (8.3)
Baseline proteinuria, n (%)	11 (18.3)

For the remaining analytical parameters no statistically significant differences were observed.

Conclusion: Anifrolumab demonstrated superior early improvement in C3 complement levels, suggesting a rapid modulation of immune activation, while Belimumab was associated with a significant reduction in anti-dsDNA titers over 12 months, indicating effective serologic control over time. Although C4 and anti-dsDNA levels showed trends toward inter-group differences, these were not statistically conclusive in between-treatment comparisons. Rituximab-treated patients, exhibited persistently elevated anti-dsDNA levels and less consistent complement normalization.These findings support individualized SLE treatment based on serologic response and organ involvement.

Disclosure: P. Martínez Calabuig: None; **J. Fragío Gil**: Quibim, 1; **R. González Mazario**: None; **L. Salvador Maicas**: None; **M. Sanmartin Martínez**: None; **I. Lorente Betanzos**: None; **A. Rueda Cid**: None; **J. Lerma Garrido**: None; **I. Martínez Cordellat**: None; **I. Balaguer Trull**: None; **B. Gómez Correas**: None; **C. Campos Fernández**: Hospital General Universitario, 2.

Abstract Number: 2461

Targeting treatment-resistant Systemic Lupus Erythematosus through transcriptome-informed drug repurposing

Alexandra Ainatzoglou[1], Georgia-Savina Moysidou[2], Danae-Mona Nöthling[3], Fanouriakis Antonis[4], George Bertsias[5], **Panagiotis Garantziotis**[3], Georg Schett[6] and Dimitrios Boumpas[7], [1]4th Department of Internal Medicine, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Athens, Greece, [2]Sorbonne université, Service de rhumatologie, groupe hospitalier Pitié-Salpêtrière, Assistance publique-Hôpitaux de Paris, Athens, Greece, [3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [4]National and Kapodistrian University of Athens Medical School, Athens, Greece, Athens, Greece, [5]Rheumatology and Clinical Immunology, University Hospital of Heraklion and University of Crete Medical School and Foundation for Research and Technology-Hellas (FORTH), Infections and Immunity, Institute of Molecular Biology and Biotechnology, Heraklion, Greece, [6]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [7]Joint Rheumatology Program, University of Athens Medical School, Athens, Greece

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) therapies elicit distinct transcriptional responses, yet a subset of patients fails to achieve clinical remission. To guide precision repurposing, we applied a transcriptome-driven strategy to identify compounds that either mimic the molecular effects of standard therapies or reverse gene expression profiles associated with treatment resistance.

Methods: Paired whole-blood transcriptomes from 31 SLE patients treated with rituximab (n=8), belimumab (n=13), or cyclophosphamide (n=10) were analyzed to define drug-specific signatures (absolute $\log_2$FC > 0.58, $p < 0.05$). A "refractory SLE" signature was derived by comparing gene expression at 6 months between responders and non-responders. Signatures were queried against L1000CDS^2 and CMAP2 databases to identify compounds that replicate or reverse these transcriptional patterns. Drug-gene interactions were explored using the DGIdb database.

Results: Transcriptional mimics of standard therapies were largely drug-specific, reflecting distinct modes of action. Rituximab's signature aligned with mTOR blockers (everolimus, dactolisib), PI3K inhibitors (PIK-75, ZSTK474), JAK2 inhibitors (fedratinib) and agents downregulating the p38-MAPK pathway (OXA). Belimumab's mimics included BCL-2 and ERK inhibitors (FR180204). Cyclophosphamide's replicants entailed JNK and NETosis-targeting agents. For refractory SLE, inverse transcriptional alignment was accomplished by several mechanistically diverse compounds including HSP90 inhibitors (geldanamycin, tanespimycin), tyrosine kinase inhibitors (dasatinib, lapatinib), and ferroptosis inducers (CX-5461) Notably, proteasome inhibitors (bortezomib, carfilzomib, ixazomib) emerged as promising agents based on gene interaction mapping, implicating plasma cells in treatment-resistant disease course.

Conclusion: Our analysis delineates molecular correlates of therapeutic response and identifies candidate drugs capable of emulating molecular effects of standard SLE therapies or reversing gene expression patterns associated with treatment failure, offering a framework for drug repurposing in difficult-to-treat SLE.

Disclosure: A. Ainatzoglou: None; **G. Moysidou**: None; **D. Nöthling**: None; **F. Antonis**: None; **G. Bertsias**: AbbVie, 6, AstraZeneca, 2, 5, 6, Eli Lilly, 2, 6, GSK, 2, 5, 6, MSD, 5, Novartis, 2, 6, Otsuka, 6, Pfizer, 6; **P. Garantziotis**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **D. Boumpas**: None.

Abstract Number: 2462

Precision Dosing is Needed to Establish Predictable Exposure to the Active Metabolite of Mycophenolate Mofetil (MMF) in Pediatric Lupus Nephritis (LN)

Pooja Patel[1], Eveline Wu[2], Laura Cannon[3], Kristen Hayward[4], Daryl Okamura[5], Marietta De Guzman[6], Ana Luiza Altaffer[6], Stacy Ardoin[7], Ellen Cody[8], Takanobu Nadai[9], Kei Irie[9], Gabrielle Morgan[10], Carolina Pastrana[3], Angela Merritt[9], Catherine Robben[9], A. Carmela Sagcal-Gironella[11], Junfang Zhao[9], Hermine Brunner[12], Tomoyuki Mizuno[9] and the PLUMM Study Investigators, [1]Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [2]UNC Chapel Hill, Chapel Hill, NC, [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, [4]Seattle Children's Hospital/University of Washington School of Medicine, Seattle, WA, [5]Seattle Children's Hospital, Seattle, WA, [6]Baylor College of Medicine, Houston, TX, [7]Nationwide Children's Hospital, Columbus, OH, [8]Medical College of Wisconsin, Milwaukee, WI, [9]Cincinnati Childrens Hospital Medical Center, Cincinnati, OH, [10]Ann & Robert H. Lurie Children's Hospital, Chicago, IL, [11]Hackensack University Medical Center, Hackensack, NJ, [12]Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION

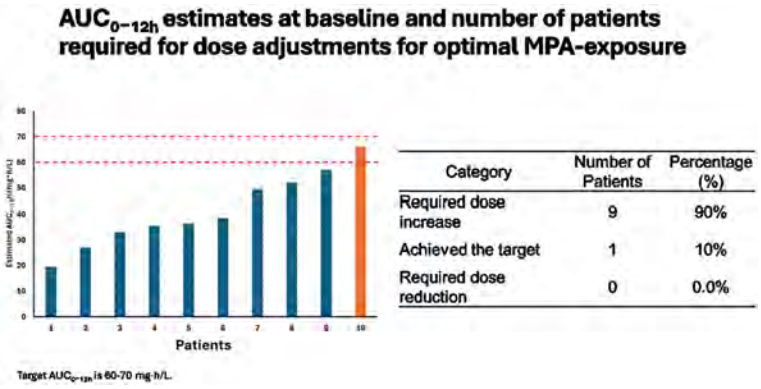
Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Category	Number of Patients	Percentage (%)
Required dose increase	9	90%
Achieved the target	1	10%
Required dose reduction	0	0.0%

Figure 1

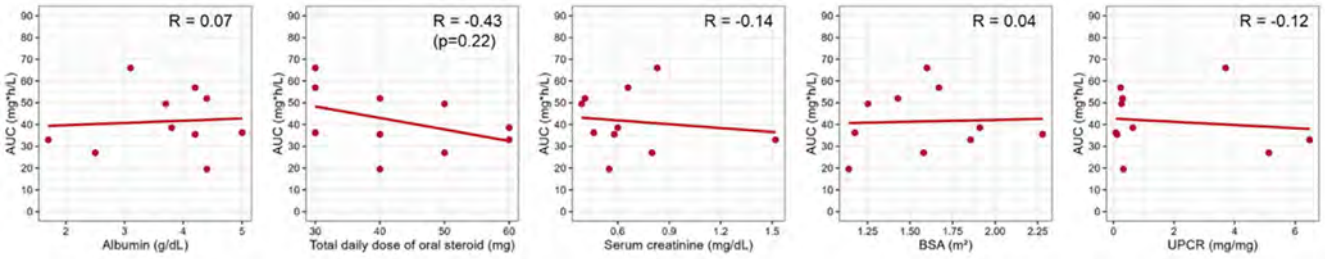


Figure 2

Background/Purpose: The safety and effectiveness of MMF for the treatment of LN have been tested in adult and pediatric patients. MMF, a prodrug, is rapidly converted to the active moiety *mycophenolic acid (MPA)* and is recommended as an immunosuppressive medication for active pediatric LN treatment, usually at a dose of 600 mg/m^2 body surface area (BSA) twice daily (max 3 gram/day). It has been suggested that an area under the concentration-time curve ($AUC_{0\text{-}12h}$) of MPA at $\geq$60-70 mg*h/L is best for reducing proteinuria in LN while levels < 30 mg*h/L are considered ineffective. This is currently being tested in a randomized clinical trial in pediatric LN (PLUMM, NCT05538208). The *objectives* of this analysis were to evaluate (1) the MPA exposures ($AUC_{0\text{-}12h}$) that are achieved with routine dosing of MMF in pediatric LN patients, and (2) associations of MPA exposures with kidney parameters [serum creatinine, albumin, and protein:creatinine ratio (UPCR)] and prednisone use.

Methods: Pediatric patients with biopsy-proven active LN who participated in the PLUMM trial and were on stable therapeutic doses of MMF underwent abbreviated pharmacokinetic profiling (PK; at trough, 20 minutes, 1 hour, and 3 hours) at study entry, using Volumetric Absorptive Microsampling Combined with Mass Spectrometry (PMID: 40132640). MPA exposure was estimated using an established algorithm (PMID: 26143647) and related to kidney parameters and oral prednisone use.

Results: PK profiles were analyzed in 10 enrolled patients receiving stable twice daily doses of MMF for at least 4 days. The median weight and BSA were 56.3 kg and 1.59 m^2, respectively, and the median MMF-dose was 2 g/day, resulting in a median MPA-exposure of 37.4 mg*h/L. There were 2 patients achieving ineffective (< 30) MPA exposures and only 1 patient achieved an MPA exposure considered optimal (Figure 1). Serum creatinine, albumin, UPCR, and BSA were all unrelated to MPA exposure. Conversely, there was a moderately strong inverse relationship (r=–0.43) to prednisone dosage (Figure 2). Data from additional patients enrolled in the PLUMM trial will be shown as they become available.

Conclusion: Current BSA-based dosing of MMF seems to generally result in suboptimal MPA exposure, limiting effective reduction of proteinuria in pediatric LN. Our findings confirm that MPA exposure is negatively associated with daily prednisone dosing (PMIDs: 12164891, 21982386). Given the limited sample size, further studies with larger cohorts are necessary. The impact of precision dosing on clinical outcomes will be evaluated after the completion of the PLUMM study.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Patel: cvs, 11; **E. Wu**: Pharming Healthcare, Inc, 2, 6, Sumitomo Pharma, 2; **L. Cannon**: None; **K. Hayward**: None; **D. Okamura**: None; **M. De Guzman**: None; **A. Altaffer**: None; **S. Ardoin**: None; **E. Cody**: None; **T. Nadai**: None; **K. Irie**: None; **G. Morgan**: None; **C. Pastrana**: None; **A. Merritt**: None; **C. Robben**: None; **A. Sagcal-Gironella**: None; **J. Zhao**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **T. Mizuno**: Chugai Pharmaceutical Co., 6.

Abstract Number: 2463

Allogenic Anti- CD19 CAR-T Cells Induce Remission in Refractory Systemic Lupus Erythematosus

Chunnei Yang[1], Chuanyin Sun[2], Binghe Tan[3], Chao Hu[1], Liyan Wan[2], Changling Xie[3], **Qian Tan**[3], Mingyao Liu[3], Jin Lin[2], Bing Du[3] and Hongyan Tong[1], [1]Department of Hematology, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang, China (People's Republic), [2]Department of Rheumatology, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang, China (People's Republic), [3]BRL Medicine Inc., Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease associated with significant morbidity and mortality. The treatment approach for SLE primarily involves immunomodulation and immunosuppression. However, these drugs have considerable toxicity and are not effective in all patients. Autologous CD19-targeted CAR-T therapies has been explored in several autoimmune diseases and reported promising efficacy in recent studies. In this study, a healthy donor-derived, multiplex genome-edited allogeneic CD19-targeted CAR-T product (BRL-303) was developed for refractory autoimmune diseases patients. Here we report the efficacy and safety profile of BRL-303 in treating patients with systemic lupus erythematosus (SLE).

Methods: This is an investigator-initiated trial evaluated the safety and efficacy of BRL-303 in adult patients with refractory autoimmune diseases (NCT05988216). Participants were screened and underwent lymphodepletion chemotherapy with cyclophosphamide (300 mg/m^2, day -5 to -4) and fludarabine (25 mg/m^2, day -5 to -3), then BRL-303 infusion at day 0 with a dose level of 1×10^6 cells/kg. For Patient SLE-04, the CAR-T cells were directly infused without lymphodepletion. After BRL-303 infusion, each patient underwent safety and efficacy assessment according to protocol.

Results: As of March 16, 2025, 4 patients with refractory systemic lupus erythematosus have been treated. These patients were unable to control disease progression despite treatment with corticosteroids and various immunosuppressants. After BRL-303 infusion, CAR -T cells in all subjects were significantly expanded. Notably, Patient SLE-03 &SLE-04 exhibited the most robust CAR-T cell expansion, with peak CAR copy numbers reaching 13,680 copies/μg on day 14 and 33,171 copies/μg on day 10 post-infusion, respectively . CAR-T cells remained detectable in all patients at 3 months. With expansion of BRL-303, B cells in peripheral blood of patients reached deep and persistent depletion about 1∼3 months. After BRL-303 infusion, all subjects met the Systemic Lupus International Collaborating Clinics (SLICC) criteria for a sustained response (SRI-4) and achieved a SELENA-SLEDAI score of zero and a PGA score<1 at 3 to 6 Months. Moreover, all subjects showed a significant decrease in serum ds-DNA and increase in complements (C3 and C4) within one month. Meanwhile, proteinuria also resolved in all subjects. Importantly,SLE-01 discontinued all immunomodulatory and immunosuppressive medications,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

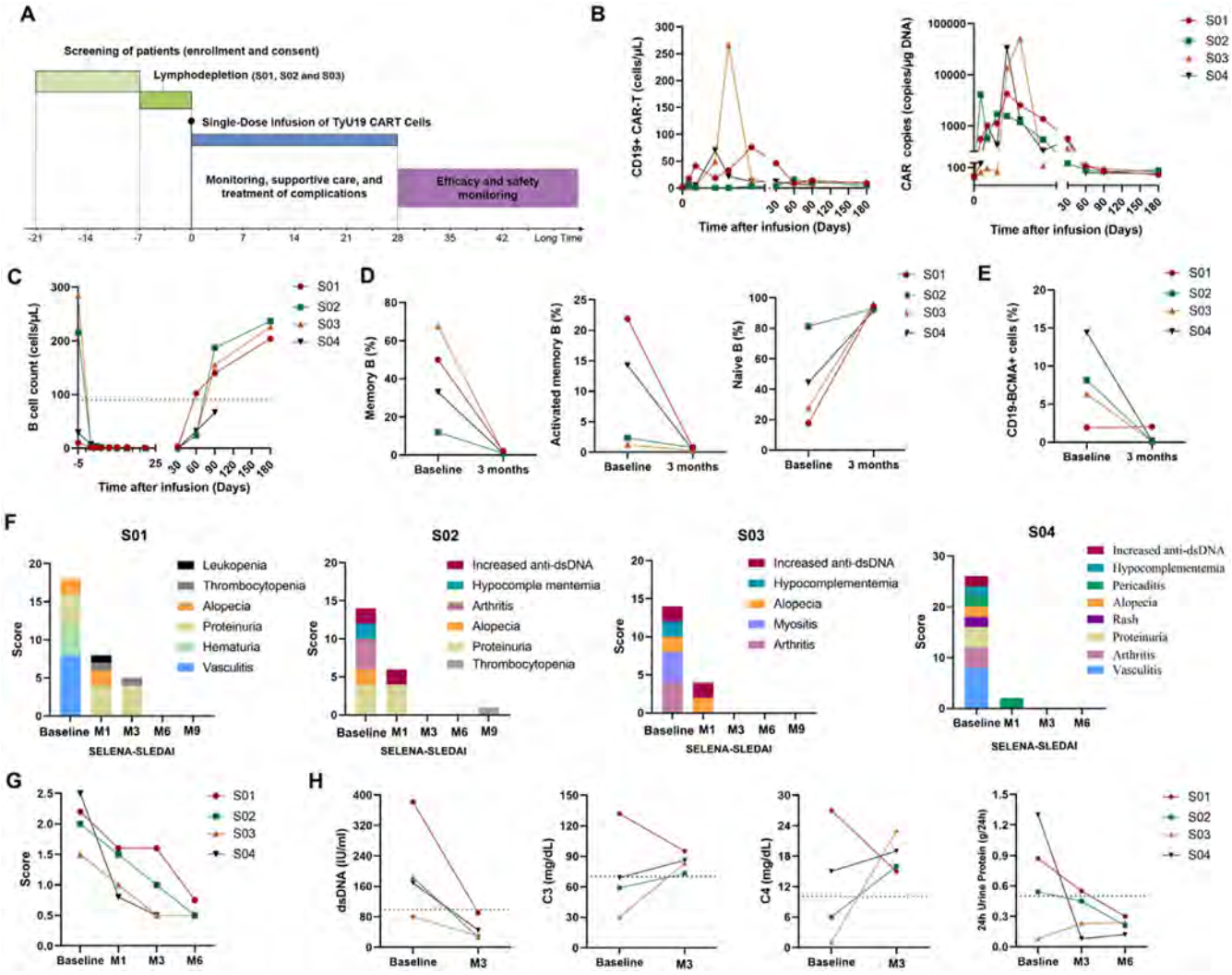


Figure 1. Study process diagram and Effects of BRL-303 for SLE patient (A, Therapeutic timelines; B, BRL-303 detected by flow and qPCR; C, Absolute B cells value; D and E, Changes in the numbers of memory B cells (CD21+CD27+), activated memory B cells (CD11c+CD21lo), naïve B cells (CD21+CD27–) and CD19-BCMA+ plasma cells in PBMC at 3 months after infusion; F and G, SELENA-SLEDAI and PGA change before and after BRL-303 treatment; H, SLEDAI-2K Score changs; C, Serological and 24h urine protein changes)

including glucocorticoids, at 3 months, achieving drug-free remission, while other patients require low-dose glucocorticoid maintenance therapy (≤5mg). All of them developed grade 1 CRS for 2 or 3 days, no ICANS and GvHD observed.

Conclusion: Overall, SLE subjects treated with BRL-303 achieved significant clinical remission, with a controllable safety profile, offering a potential paradigm shift for SLE patients who are refractory to currently available treatments. Further observation of SLE and more autoimmune disorders treated with BRL-303 are ongoing in our study.

Disclosure: C. Yang: None; **C. Sun**: None; **B. Tan**: None; **C. Hu**: None; **L. Wan**: None; **C. Xie**: None; **Q. Tan**: None; **M. Liu**: None; **J. Lin**: None; **B. Du**: None; **H. Tong**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2464

IMC-002 (IMM0306), a First-in-Class Bi-specific Fusion Protein, Demonstrates Improvements in Systemic Lupus Erythematosus (SLE) Disease Activity Measures and Biomarkers in Patients with Moderate to Severe Active SLE in the Open-label Phase 1b/2 Study

Haihong Yao[1], Wenzhi Tian[2], **Qian Zheng**[2], Min Chen[2], Guoping Jiang[3], Zhichun Liu[4], Yingkun Nie[5], Rui Wu[6], Zhaohui Zheng[7] and Zhanguo Li[1], [1]Peking University People's Hospital, Beijing, China (People's Republic), [2]ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd, Shanghai, China (People's Republic), [3]Jilin Province People's Hospital, Changchun, China (People's Republic), [4]The Second Affiliated Hospital of Soochow, Suzhou, China (People's Republic), [5]The Second Affiliated Hospital of Harbin Medical University, Haerbin, China (People's Republic), [6]The First Affiliated Hospital of Nanchang University, Nanchang, China (People's Republic), [7]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Deep B cell depletion has been confirmed to be the main mechanism for complete clinical response of SLE patients. We analyzed the peripheral blood of SLE patients in an in-vitro assay and found that CD47 was expressed in all B cell subtypes especially in plasmablasts which are CD20 negative. IMC-002 (IMM0306) is a mAb-Trap targeting CD20 and CD47, which has been demonstrated to have robust B cells depletion activity in phase I clinical trial for patients with non-

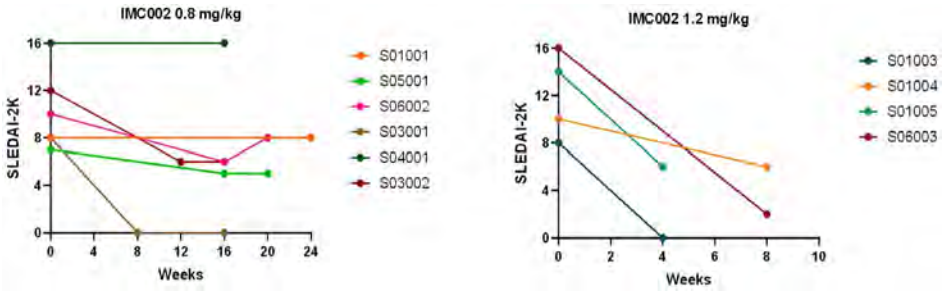


Figure 1. SLEDAI-2K evaluation from first dose to the latest visit at the time of data cutoff

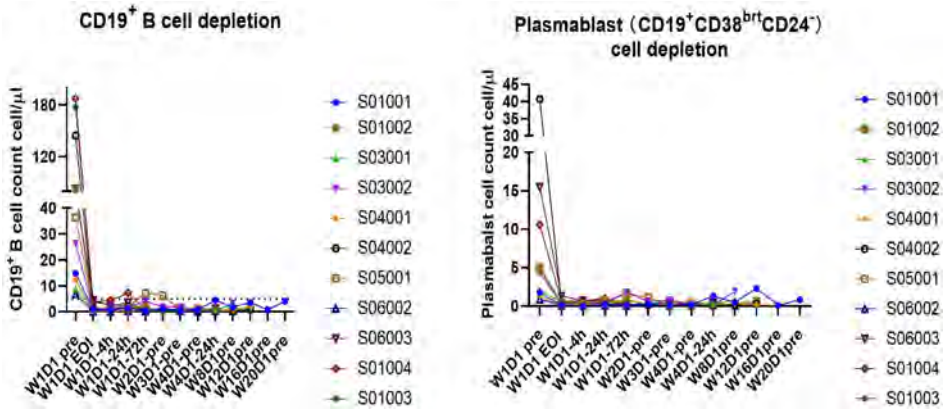


Figure 2. B lymphocyte depletion from first dose to latest available data at the time of data cutoff

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

hodgkin's lymphoma. This study aims to investigate the treatment of IMC-002 on safety, SLE disease activity measures, proteinuria responses and multiple biomarkers in SLE patients who had not previously responded to standard of care.

Methods: As of 14th Apr. 2025 (cut-off date), 11 patients who completed 4-weeks administration (once weekly) of IMC-002 and at least one SLEDAI-2K evaluation in Phase 1b were included in this analysis, 7 patients in 0.8mg/kg dose cohort were followed up for 16-24 weeks, 4 patients in 1.2mg/kg dose cohort were followed up for 4-8 weeks. Moderate to severe active SLE was defined as Class A manifestations in one or more organ systems and/or Class B manifestations in two or more organ systems and SLEDAI≥6, ANA or Anti-dsDNA positive. The efficacy endpoint was SLE Responder Index-4 (SRI-4) evaluation for every 12 weeks in Phase 1b. Other efficacy assessments included BILAG-2004, SLEDAI-2K, PGA and laboratory tests (24-hour urine protein, anti-dsDNA antibody, C3/C4 and IgG/IgA/IgM, B cells count, etc.)

Results: By the data cut-off date, in the 0.8 mg/kg dose cohort, 2 out of 7 patients reached SRI-4 at Week 12, and all patients did not reach 24-week SRI-4 evaluation time; in the 1.2 mg/kg dose cohort, all patients did not reach 12-week SRI-4 evaluation time. 4 patients (57.1%) in the 0.8 mg/kg dose cohort and 4 patients (100%) in 1.2 mg/kg dose cohort showed SLEDAI-2K improvement by≥4 with PGA decrease; 1 patient SLEDAI-2K scored from 8 (baseline) to 0 (W8) in the 0.8 mg/kg dose cohort and 1 patient from 8 (baseline) to 0 (W4) in the 1.2 mg/kg dose cohort (Figure 1). All patients had improvements or no changes in BILAG-2004, and no PGA score worsening in all patients except 1 patient had 0.4 increasement. The 24-hour urine protein were significantly decreased by 32% $\sim$ 62% from baseline during the administration period in all the 5 patients with proteinuria≥0.5g/24h at baseline. Anti-dsDNA antibody in all patients (6/6) showed a significant decrease trend. C3/C4 recovered to normal in 75% patients (3/4) with low complement at baseline. Complete deletion (defined as less than 5 cells/μL) of CD19+ B cells and plasma blasts in all 11 patients was achieved from end of injection (EOI) to latest visit time (up to W20) (Figure 2).

Conclusion: Results of this study suggest that treatment with IMC-002 is effective across multiple organ systems in patients with active SLE. IMC-002 showed deep and persistent B cell depletion in active SLE patients.

Disclosure: H. Yao: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd, 5; **W. Tian**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 3, 8, 11; **Q. Zheng**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 3, 11; **M. Chen**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 3; **G. Jiang**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5; **Z. Liu**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5; **Y. Nie**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5; **R. Wu**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5; **Z. Zheng**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5; **Z. Li**: ImmuneCare Biopharmaceuticals (Shanghai) Co.,Ltd,, 5.

Abstract Number: 2465

CD19/BCMA Dual-Targeting FasTCAR-T Cells GC012F (AZD0120) in patients with refractory Systemic Lupus Erythematosusm: an open-label, single-center Phase I study

chunmei Wu[1], Yakai Fu[2], Jia Liu[3], Yan Ye[4], Ran Wang[5], Xintong Feng[3], Lianjun Shen[6], Peiying Li[5], Shuang Ye[5] and **Qiong Fu**[7], [1]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, China (People's Republic), [2]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China (People's Republic), [3]Astrazeneca, Shanghai, China (People's Republic), [4]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [5]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [6]Astrazeneca, Shanghai, Shanghai, China (People's Republic), [7]Renji Hospital, Shanghai, Shanghai, China

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: GC012F (AZD0120) is a CD19/B cell maturation antigen (BCMA) dual-targeting chimeric antigen receptor T-cell (CAR-T) developed on the novel FasTCAR-T platform with next-day manufacturing, designed to improve depth and duration of B-cell depleting response. We present interim results here from a dose escalation investigator initiative trial (IIT) (NCT05858684) to evaluate the safety and efficacy of GC012F CAR-T cell therapy in resetting humoral immunity in patients with refractory systemic lupus erythematosus (SLE).

Methods: Ten patients with refractory SLE (SLEDAI-2K score range 8-20) were enrolled in this investigator-initiated, open-label, single-center Phase I study. All patients received a single infusion of autologous CD19-BCMA dual chimeric antigen receptor (CAR) T cells at one of three different dose levels following preconditioning with fludarabine and cyclophosphamide. The primary endpoint was safety and tolerability, assessed by the percentage of subjects experiencing dose-limiting toxicity (DLT) within 28 days and the percentage of subjects reporting adverse events (AEs) within 12 weeks. Efficacy was assessed using the SLE Responder Index (SRI-4), the Definition of Remission in SLE (DORIS) criteria and renal response rate. Safety parameters, including cytokine release syndrome and infections, were systematically recorded and evaluated.

Results: The median follow-up duration was 448.5 days (range, 336-612 days), with a mean duration of B-cell aplasia of 126 days (range, 84–168 days). All patients achieved an SRI-4 response in week 24. Five patients met DORIS remission by week 24, six by week 36 and week 48. All patients discontinued immunosuppressive drugs during the follow-up period. One patient experienced a disease flare at week 40. Four patients exhibited residual proteinuria, and repeat kidney biopsies were performed in three of them. The biopsy results primarily showed persistent fibrosis and podocyte injury, with resolution of acute inflammation, significant reduction in immune complex deposition, and absorption or dissipation of electron-dense deposits. No DLTs were observed. Six patients experienced grade 1 CRS, and one patient experienced grade 2 CRS. No cases of immune effector cell-associated neurotoxicity syndrome (ICANS) or grade ≥3 CRS were reported. Other common AEs included hematologic abnormalities, hypogammaglobulinemia, and infections. No fatal adverse events occurred.

Conclusion: GC012F CAR-T cell therapy was well tolerated and demonstrated high efficacy in patients with refractory SLE. A multicenter phase1/2 study (NCT06530849) is ongoing to further evaluate the safety and efficacy of GC012F in a broader range of patients with SLE.

Disclosure: c. Wu: None; **Y. Fu**: None; **J. Liu**: None; **Y. Ye**: None; **R. Wang**: None; **X. Feng**: None; **L. Shen**: None; **P. Li**: None; **S. Ye**: None; **Q. Fu**: None.

Abstract Number: 2466

Efficacy and Safety Results of Zetomipzomib from the PALIZADE Phase 2b Clinical Trial in Patients with Lupus Nephritis

Richard Furie[1], Neel Anand[2], Shraddha Desai[3], Eric Lowe[4], Tony Muchamuel[3], Kiruthi Palaniswamy[2], Rachel Peterson[2], Kathryn Ray[2], Zung To[2], Jennifer Whang[2] and Richard Leff[5], [1]Division of Rheumatology, Northwell Health, Great Neck, NY, [2]Kezar Life Sciences, Inc, South San Francisco, CA, [3]Kezar Life Sciences, Inc, South San Francisco, [4]Kezar Life Sciences, South San Francisco, CA, [5]Richard L Leff MD LLC, Chadds Ford, PA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Zetomipzomib (zeto), a selective immunoproteasome inhibitor, has previously shown anti-inflammatory activity in patients (pts) with SLE and LN in the open-label MISSION study. The PALIZADE trial (NCT05781750) was a global Phase 2b, multi-center, randomized (1:1:1), controlled double-blind study comparing the efficacy and safety of weekly subcutaneous administration of zeto 30 mg or 60 mg with placebo (pbo) in pts with active LN (Class III, IV ± V) on background standard of care therapy of MMF or equivalent plus corticosteroids. An Independent Data Monitoring Committee recommended pausing enrollment and dosing following 4 fatalities (1 - pbo, 2 - 30 mg arm, 1 - 60 mg arm) and additional nonfatal treatment-emergent serious adverse events (TESAE) that showed a common pattern of symptoms or proximity to dosing. PALIZADE was subsequently terminated early by the sponsor for strategic business reasons.

Methods: Planned enrollment was 279 pts, including 249 pts with Class III or IV ± V LN and 30 pts with pure Class V with a planned duration of 52 weeks of treatment and a primary endpoint at Week (W) 37. At the time of termination (October 2024), 84 patients (74 with Class III or IV ± V LN) were enrolled with mean treatment duration of 16.7 weeks. All enrolled pts were included in the safety analysis, and 39 pts with proliferative LN who reached W25 for 24-hour urine protein creatinine ratio (UPCR) evaluation were included in the efficacy analysis. No pt completed the full 52 weeks of treatment.

Table 1. PALIZADE Adverse Events (Safety Population), N=84

	Zeto 30 mg N=27 n (%)	Zeto 60 mg N=29 n (%)	Placebo N=28 n (%)
Participants with at least 1 Treatment Emergent Adverse Event (TEAE)	23 (85.2)	25 (86.2)	17 (60.7)
Treatment Emergent Serious Adverse Event	5 (18.5)	8* (27.6)	3 (10.7)
Deaths	2 (7.4)	1 (3.4)	1 (3.6)
Most common TEAEs:			
Systemic injection reaction (SIR)	14 (51.9)	20 (69.0)	3 (10.7)
Injection site reaction (ISR)	6 (22.2)	13 (44.8)	2 (7.1)
TEAE leading to study drug discontinuation	4 (14.8)	4 (13.8)	1 (3.6)
Grade 3 or 4 TEAE	4 (14.8)	8 (27.6)	3 (10.7)
Grade ≥3 Infectious TEAE†	2 (7.4)	3 (10.3)	0 (0)
Opportunistic Infections‡	0 (0)	0 (0)	0 (0)

*Four participants randomized to zeto 60 mg arm but received zeto 30 mg before the TESAE (2 were after first dose)
†Zeto 30 mg arm: Grade 3 pseudomonas infection (related, recovered), Grade 3 community acquired pneumonia (related, recovered)
Zeto 60 mg arm: Grade 3 septic shock and Grade 4 urinary tract infection (both unrelated, recovered); Grade 3 unspecified bacterial pneumonia (related, recovered); Grade 3 dengue fever (unrelated, recovered)
‡Opportunistic infections were evaluated by the sponsor through clinical assessment of reported infections

Table 2. Proteinuria Changes in Treatment Evaluable Patients, N=39

	Zeto 30 mg N=23	Zeto 60 mg N=26	PBO N=25
Percent of Patients with UPCR ≤0.5			
n	18	18	21
W13 (%)	11.1	27.8	9.5
n	13	12	14
W25 (%)	7.7	41.7	21.4
Median UPCR			
Baseline	3.1	2.5	2.7
W13	1.5	1.2	1.5
W25	1.3	0.5	1.4
Median % Change in UPCR From Baseline			
n	18	18	21
W13 (%)	-26.3	-66.7	-37.6
n	13	12	14
W25 (%)	-35.1	-78.7	-47.2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Preliminary data on changes in proteinuria, median UPCR, SLEDAI-2K, and key lupus serologic markers at W25 are presented here. Whole blood transcriptomic analysis was performed.

Results: Ninety-three percent of enrolled pts were female with mean age of 32.1 years, mean LN duration of 3.7 years, mean UPCR of 3.5 mg/mg, and a mean SLEDAI-2K score of 11.3. The most common TEAEs were injection site reaction (98% were Grades 1 or 2) and systemic injection reaction (97% were Grades 1 or 2), Table 1. Four fatalities (4.8%) and 16 total TESAEs (in 19% of pts) occurred. Evidence suggestive of co-morbidities immediately prior to study drug administration (e.g., possible systemic infection) and/or possible underlying disease characteristics (e.g., cardiovascular) were present in fatal events.

Among the 39 evaluable pts with Class III/IV ± V LN, 42% (5/12) of those treated with 60 mg zeto achieved a UPCR ≤0.5 at W25. The median percent change in UPCR from baseline was -67% at W13 and -79% at W25, suggesting a rapid improvement in proteinuria with 60 mg zeto administration, Table 2. Additionally, improvements in SLEDAI-2K, serologic markers of SLE including anti-dsDNA, C3 and C4 were observed in both zeto arms.

Conclusion: Safety analysis of enrolled pts indicated overall similar safety profiles between zeto dosed at 30 mg and 60 mg, and these findings are consistent with previous studies of zeto in LN. Preliminary efficacy data from a treatment evaluable population with Class III/IV ± V LN in the PALIZADE trial offer encouraging activity in pts receiving a 60 mg dose of zeto.

Disclosure: R. Furie: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **N. Anand**: Celldex, 12,, Exelixis, 12,, Johnson & Johnson, 12,, Kezar Life Sciences, 12,, 3, Nektar Therapeutics, 12,, Pfizer, 12,; **S. Desai**: None; **E. Lowe**: Kezar Life Sciences, 3, 11; **T. Muchamuel**: Kezar Life Sciences, 3; **K. Palaniswamy**: Kezar Life Sciences, Inc, 3; **R. Peterson**: None; **K. Ray**: Kezar Life Sciences, 3; **Z. To**: None; **J. Whang**: Kezar Life Sciences, 3; **R. Leff**: Kezar Life Sciences, 2, 7.

Abstract Number: 2467

Complete Renal Responses and Safety for Belimumab Versus Placebo in a Post Hoc Mycophenolate Mofetil Subgroup with Active Proliferative Lupus Nephritis

Richard Furie[1], Hans-Joachim Anders[2], George Bertsias[3], Ana Delgado[4], Roger A. Levy[5], Paula Curtis[6], Ciara O'Shea[7], Ryan Tomlinson[8] and Brad Rovin[9], [1]Division of Rheumatology, Northwell Health, Great Neck, NY, [2]Hospital of LMU Munich, Department of Medicine IV, Munich, Germany, [3]Rheumatology and Clinical Immunology, University Hospital of Heraklion and University of Crete Medical School and Foundation for Research and Technology-Hellas (FORTH), Infections and Immunity, Institute of Molecular Biology and Biotechnology, Heraklion, Greece, [4]GSK, Immunology Medical Affairs, London, United Kingdom, [5]GSK, Specialty Care, Global Medical Affairs, Collegeville, PA, [6]GSK, Biostatistics, London, United Kingdom, [7]Global Medical Affairs, GSK, Dublin, Ireland, [8]GSK, Development – R&D, Collegeville, PA, [9]The Ohio State University, Columbus, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Key features of the BLISS-LN study design. AZA, azathioprine; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; IV, intravenous; PERR, primary efficacy renal response.

Study design component	BLISS-LN (Belimumab – NCT01639339)
Key endpoints	Primary endpoint: PERR at Week 104 Key secondary endpoint: CRR at Week 104
PERR definition	uPCR ≤0.7; eGFR no worse than 20% below the pre-flare value or ≥60 ml/min/1.73 m², and prednisone dose ≤10 mg/day at Week 24; and no rescue therapy except for short-term rescue in Weeks 24–76 for reasons other than LN. No GC rescue treatments were allowed in Weeks 76–104
CRR definition	uPCR <0.5; eGFR no worse than 10% below the pre-flare value or ≥90 ml/min/1.73 m², and prednisone dose ≤10 mg/day at Week 24; and no rescue therapy except for short-term rescue in Weeks 24–76 for reasons other than LN. No GC rescue treatments were allowed in Weeks 76–104
Recruitment	N=448; Americas, Europe, China, South Korea, Thailand, Taiwan, Philippines
LN classes	Class III or IV (± concomitant class V), or pure class V LN
Study treatment procedure	Belimumab IV 10 mg/kg every 28 days to Week 100
Standard therapy (excluding GC)	Induction therapy with IV CYC (500 mg every 2 weeks) or MMF (target 3 g/day). Maintenance therapy of AZA (2 mg/kg per day) or MMF (1–2 g/day)
GC use at induction	Oral prednisone (≤60 mg/day) Optional 1–3 IV methylprednisolone pulses (500–1000 mg each) at induction
GC tapering schedule	Mandatory taper to ≤10 mg/day prednisone by Week 24, as part of PERR and CRR endpoints. Permitted short-term rescue treatment between Weeks 24 and 76 for non-LN reasons. Patients violating GC regimen rules considered as treatment failures
Prohibited medications	B-cell therapy and any non-belimumab biologics. CYC induction within 3 months before trial initiation
Premedication	None required

Table 2. BLISS-LN CRR responder data at Weeks 76 and 104 for a subgroup of patients receiving MMF with active class III or IV LN ± concomitant class V. *Data shown are for a post hoc subgroup of patients who received MMF standard therapy (No CYC); †CRR responder rates for the combined subgroups "class III or IV" and "class III or IV + V" were manually calculated using data on the number of responders in each subgroup; ‡OR adjusted for race, baseline uPCR and baseline eGFR. BEL, belimumab; CI, confidence interval; OR, odds ratio; PBO, placebo.

	CRR class III or IV pure proliferative (MMF subgroup)*		CRR class III or IV + V mixed proliferative/ membranous (MMF subgroup)*		CRR† class III or IV ± concomitant class V pure proliferative and mixed proliferative/ membranous (MMF subgroup)*	
	BEL (n=94)	PBO (n= 96)	BEL (n=41)	PBO (n=40)	BEL (n=135)	PBO (n=136)
Week 76						
CRR responders	37.2%	25.0%	29.3%	20.0%	34.8%	23.5%
Treatment difference vs PBO	12.2%		9.3%		11.3%	
Week 104						
CRR responders	35.1%	17.7%	26.8%	17.5%	32.6%	17.6%
Treatment difference vs PBO	17.4% OR: 2.34‡ (95% CI: 1.17–4.69)		9.3% OR: 1.86‡ (95% CI: 0.61–5.66)		14.9%	

Background/Purpose: Belimumab, a human IgG1λ monoclonal antibody that selectively binds B-lymphocyte stimulator, was first approved in 2011. It is the only biologic approved for LN and SLE. With greater than 10 years of real-world experience, EULAR acknowledged early use of belimumab in SLE, and ACR recommends its use in LN.

Reinforcing the central role of B-cells in LN immunopathogenesis, Phase 3 trials successfully investigated belimumab (BLISS-LN; NCT01639339[1]) and obinutuzumab (REGENCY; NCT04221477) in biopsy-proven active LN plus standard therapy (ST). Study differences (e.g. populations, concomitant medications, endpoint timings, and definitions) present challenges in comparing LN trial outcomes. In this regard, BLISS-LN's unique design allowed inclusion of pure ISN/RPS class V

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and cyclophosphamide ST. To better align with the design of the REGENCY and NOBILITY (NCT02550652) trials, we analyzed post hoc a BLISS-LN subgroup of patients with active class III or IV LN ± concomitant class V who received MMF ST (i.e. excluding pure class V and cyclophosphamide ST).

Methods: BLISS-LN was a 104-week global trial of 448 adult patients with active class III or IV (± concomitant class V) or pure class V LN.[1] Key features of the BLISS-LN study design (**Table 1**) included a stringent complete renal response (CRR) definition that differs from other trials (BLISS-LN-CRR defined as urinary protein-to-creatinine ratio [uPCR] < 0.5, eGFR ≤10% below the pre-flare value or ≥90 ml/minute/1.73 m^2, and no rescue therapy).[1] Additionally, BLISS-LN-CRR defined treatment failure as use of prohibited therapy and not achieving mandatory prednisone taper to ≤10 mg/day by Week 24.

Results: Of the overall 448 patients in BLISS-LN, 271 had active class III or IV LN ± concomitant class V and received MMF ST. CRR data for this subgroup (referred to as the "MMF subgroup") using prespecified definitions are shown in **Table 2**. At Week 76 in the MMF subgroup, BLISS-LN-CRR treatment difference between belimumab and placebo was 11.3% for class III or IV ± concomitant class V, and 12.2% for class III or IV only. At Week 104, BLISS-LN-CRR treatment difference was 14.9% for class III or IV ± concomitant class V, and 17.4% for class III or IV only.

Regarding safety, in the BLISS-LN MMF subgroup, serious adverse events up to Week 104 were lower with belimumab (24.4%, n=40/164) than placebo (32.1%, n=53/165).

Conclusion: Building on the extensively demonstrated safety[2] and efficacy profiles of belimumab across SLE and LN, this post hoc subgroup analysis of patients with active class III or IV LN ± concomitant class V receiving MMF in BLISS-LN demonstrated enhanced renal responses with belimumab versus placebo at Weeks 76 and 104. This improved outcome is also observed when compared to the overall BLISS-LN population.[1] Belimumab has additionally been shown to be safe and efficacious in patients with LN in the real world.[3] Benefit/risk profiles, real-world effectiveness and data from extra-renal SLE should be considered to inform LN treatment decisions.

Funding: GSK

References

[1]Furie R et al. N Engl J Med 2020;383:1117–28
[2]Wallace D et al. Arthritis Rheumatol 2019;71:1125–34
[3]Gatto M et al. J Autoimmun 2021;124:102729
Original presentation: LUPUS 2025

Disclosure: R. Furie: Bristol-Myers Squibb(BMS), 2, 12, Investigator, Genentech, Inc., 2, 12, Investigator, GlaxoSmithKline (GSK), 2, 5, Kyverna Therapeutics, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Regeneron, 2; **H. Anders**: AstraZeneca, 2, 6, Boehringer Ingelheim, 5, CSL Vifor, 2, 6, GSK, 2, 6, Novartis, 2, 6, Otsuka, 2, 6, Roche, 6, SOBI, 2, Stada, 2, 6; **G. Bertsias**: AbbVie, 6, AstraZeneca, 2, 5, 6, Eli Lilly, 2, 6, GSK, 2, 5, 6, MSD, 5, Novartis, 2, 6, Otsuka, 6, Pfizer, 6; **A. Delgado**: GSK, 12,, 3; **R. Levy**: GSK, 3, 8; **P. Curtis**: GSK, 12,, 3; **C. O'Shea**: GSK, 12,, 3; **R. Tomlinson**: GSK, 12,, 3; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2468

RESET-SLE: Clinical Trial Evaluating Rese-cel (Resecabtagene Autoleucel), a Fully Human, Autologous 4-1BB CD19-CAR T Cell Therapy in Non-Renal SLE and Lupus Nephritis

Saira Sheikh[1], Vimal Derebail[1], Natalie Grovner[1], Gaurav Gulati[2], Mehrdad Abedi[3], Meghan Sise[4], Matthew Frigault[4], Christopher Palma[5], Patrick Reagan[5], Cuoghi Edens[6], Satya Kosuri[6], Caitlin Elgarten[7], Jon Burnham[8], Jonathan Hogan[9], Yvonne White[9], Carl diCasoli[9], Rebecca Estremera[9], Jenell Volkov[9], Daniel Nunez[9], Fatemeh Hadi-Nezhad[10], Thomas Furmanak[9], Jason Stadanlick[9], Larissa Ishikawa[9], Zachary Vorndran[9], Alexandra Ellis[9], Jazmean Williams[9], Steve Flanagan[9], Quynh Lam[10], Samik Basu[9], Raj Tummala[10] and David Chang[9], [1]University of North Carolina at Chapel Hill, Chapel Hill, NC, [2]University of California, Davis School of Medicine, Davis, CA, [3]University of California, Davis School of Medicine, Davis, [4]Massachusetts General Hospital, Boston, MA, [5]University of Rochester, Rochester, NY, [6]University of Chicago, Chicago, IL, [7]Children's Hospital of Philadelphia, Philadelphia, PA, [8]Children's Hospital of Philadelphia, Bryn Mawr, PA, [9]Cabaletta Bio, Philadelphia, PA, [10]Cabaletta Bio, Philadelphia

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Current goals of treatment for systemic lupus erythematosus (SLE) are to achieve low disease state/remission, prevent flares, minimize organ damage, and decrease long-term morbidity and mortality. Therapies providing durable clinical responses without requiring chronic administration are lacking. Rese-cel (formerly CABA-201) is a fully human, autologous 4-1BB CD19-CAR T cell therapy, designed to deeply and transiently deplete CD19 positive cells following a weight-based, single infusion. This approach may enable an "immune system reset" and durable meaningful clinical responses without chronic therapies. RESET-SLE^{TM} (NCT06121297) is an ongoing Phase 1/2 trial in 2 independent cohorts of non-renal SLE and lupus nephritis (LN).

Methods: Patients were 18 to 65 years with SLE, ANA+ or anti-dsDNA+, and Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI 2K) ≥8 despite standard of care (SOC) therapy (non-renal SLE cohort), or active, biopsy-confirmed class III or IV ± V LN despite SOC (LN cohort). A single infusion of 1x10^6 CAR T cells/kg was administered following preconditioning with fludarabine and cyclophosphamide. All non-glucocorticoid (GC) immunomodulatory (IM) agents were discontinued by Day -5. Adverse events, use of SLE medications, SLEDAI-2K changes, achievement of the definition of remission in SLE (DORIS), lupus low disease activity state (LLDAS), and renal responses were assessed. CAR T cells and B cells were profiled in peripheral blood samples pre- and post-infusion by digital PCR and flow cytometry, respectively. Serum cytokines were measured using the mesoscale discovery platform.

Results: As of 31 March 2025, 7 patients have been infused with rese-cel and have at least 4 weeks of follow-up (Table 1). One additional patient has been infused and is in early follow up.

Rese-cel was well-tolerated with Grade 1 cytokine release syndrome (CRS) reported in 2 patients (SLE-2 and LN-1). As previously reported, LN-1 experienced Grade 4 immune effector cell-associated neurotoxicity syndrome (ICANS), associated with a potential occult infection based on cytokine and TCR clonality profiling, which rapidly resolved following standard management.

Robust clinical improvement has been observed in all 7 patients (Table 2).

CAR T cells expanded rapidly and peaked between days 7 and 16 post-infusion, with LN-1 also having a second peak at day 28, followed by contraction. Serum IFNγ rapidly increased concurrently with or prior to rese-cel expansion. Peripheral

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Characteristics

Cohort	Non-renal SLE				LN		
Patient / Cohort	SLE-1[†]	SLE-2	SLE-3	SLE-4	LN-1	LN-2	LN-3
Age, sex	26 M	36 F	44 F	37 F	24 F	35 F	26 F
Disease duration (y)	~6	~17	~9	~10	~2	~8	~16
Autoantibodies[‡]	dsDNA, Sm	dsDNA	dsDNA	dsDNA, Sm	dsDNA, Sm	dsDNA, Sm	Sm
SLEDAI-2K	26	10	8	8	22	14	16
UPCR (mg/mg)	1.08[†]	N/A	N/A	N/A	7.22	4.85	2.04
Therapies at Screening	HCQ, GC, MMF	GC, AZA	HCQ, MMF, BEL	HCQ[†]	HCQ, GC, MMF, ANI, VOC	MMF	HCQ, MMF
Other prior therapies	CYC, BEL, VOC, TAC	HCQ, MTX, ANI, BEL, MSC, RTX, ADA	GC, MTX	MTX, BEL, GC	BEL, LEF	HCQ, GC, AZA, RTX	MTX, AZA, TOC, UST, RTX, GC, OBI
GC dose at Screening (mg/day)	10	7	N/A	N/A[†]	20	N/A	N/A

*Baseline disease activity = activity before pre-conditioning.
[†]SLE-1 had class V LN; inclusion criteria for LN cohort required class III/IV LN.
[‡]All patients: pre-enrollment antibody positive.
§SLE-4 initiated 35 mg/day of prednisone after screening and before leukapheresis, tapering by week 12.
ANI, anifrolumab; AZA, azathioprine; BEL, belimumab; CYC, cyclophosphamide; dsDNA, double-stranded DNA; GC, glucocorticoid; HCQ, hydroxychloroquine; LEF, leflunomide; LN, lupus nephritis; MMF, mycophenolate mofetil; MSC, mesenchymal stem cell; MTX, methotrexate; N/A, not applicable; OBI, obinutuzumab; RESET, Resetting B/T-Tolerance; RTX, rituximab; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000; Sm, Smith; TAC, tacrolimus; TOC, tocilizumab; UPCR, urinary protein-to-creatinine ratio; UST, ustekinumab; VOC, voclosporin; y, years.
Caballetta, Bin: Data on file.

Table 2: Treatment Responses

Patient	Non-renal SLE				LN		
	SLE-1[†]	SLE-2	SLE-3	SLE-4	LN-1	LN-2	LN-3
Latest follow-up	Week 44	Week 28	Week 20	Week 20	Week 32	Week 16	Week 4
DORIS (at latest follow-up)	–	✓	✓	✓	N/A	N/A	N/A
LLDAS (at latest follow-up)	–	✓	✓	✓	N/A	N/A	N/A
SLEDAI-2K score[‡] (baseline to latest follow-up)	26→5	10→0	8→2	8→2	22→4	14→6	16→12
UPCR[§] (baseline to latest follow-up)	1.08→0.5	N/A	N/A	N/A	7.22→0.47	4.85→2.62	2.04→0.97
CRR[¶] (at latest follow-up)	✓	N/A	N/A	N/A	✓	–	–
GC-free	✓	✓	✓	✓	✓	✓	✓
IM-free[†]	✓	✓	✓	✓	✓	✓	✓

*As of MAY 01, 2025.
[†]Enrollment in the LN cohort required class III/IV +/- V LN. SLE-1 had isolated class V LN and extra-renal SLE disease activity (but met inclusion criteria for the non-renal cohort.
[‡]SLEDAI-2K components at latest follow up: SLE-1, leukopenia-1, complement-2, dsDNA-2; SLE-2, dsDNA-2, SLE-4, dsDNA-2, LN-1, hematuria-4, proteinuria-4, pyuria-4.
[§]SLE-1 is undergoing cyclosporine therapy for a non-SLE-related, non-renal-cell related event at latest follow-up.
CRR, complete renal response; DORIS, definition of remission in SLE; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; IM, immunomodulatory; LLDAS, lupus low disease activity state; LN, lupus nephritis; N/A, not applicable; rese-cel, resecabtagene autoleucel; RESET, Resetting SEB-Tolerance; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; UPCR, urine protein-creatinine ratio.
DORIS = Clinical SLEDAI-2K=0 (irrespective of serology); PGA ≤0.5; antimalarials, low-dose glucocorticoids (prednisone ≤5 mg/day), stable immunosuppressives including biologics. LLDAS = SLEDAI-2K score ≤4, with no activity in major organ systems (renal, central nervous, cardiopulmonary, vasculitis or fever); no new SLEDAI-2K-assessed disease activity compared with the previous visit; PGA score ≤1; prednisone or equivalent dosage ≤7.5 mg/day and no non-standard immunosuppressant dosing; antimalarials allowed. CRR = UPCR ≤0.5 mg/mg, ≥60 mL/min or no confirmed eGFR decrease of >20% from baseline, no receipt of rescue therapy.
Caballetta, Bin: Data on file.

B cells were rapidly reduced within the first 2 weeks and started reconstituting between 8 and 20 weeks in all patients to date. Reemergent B cells presented initially with a transitional naïve phenotype (CD19+CD20+CD38++CD24++).

Conclusion: Data from SLE and LN patients infused with rese-cel shows early clinical responses, including meeting the DORIS remission criteria and complete renal response, and an acceptable safety profile, in the setting of CAR T cell expansion and peripheral B-cell reduction. These initial data suggest the potential for rese-cel to reset the immune system in SLE and LN, allowing patients to achieve meaningful clinical responses off all IM agents.

Disclosure: S. Sheikh: AstraZeneca, 1, Aurinia Pharmaceuticals, 5, Biogen, 1, Cabaletta Bio, 5, GlaxoSmithKlein(GSK), 1; **V. Derebail**: Amgen, 2, Cabaletta Bio, 5, iCell Gene Therapeutics, 2, Novartis, 2, Vera Therapeutics, 2; **N. Grovner**: ADC Therapeutics, 2, Affimed, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta, 5, Genentech, 2, Novartis, 2, Poseida, 5, Regeneron, 2, 5; **G. Gulati**: Cabaletta Bio, 5; **M. Abedi**: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Cabaletta Bio, 5, Cytodyne, 12,, Gilead, 6; **M. Sise**: Alpine Immune Science/Vertex, 1, Angion, 5, Cabaletta Bio, 5, Calliditas, 2, Curio, 6, Gilead, 5, Medibeacon, 2, Merck, 5, Merida Biosciences, 2, No, 2, Novartis, 5, Otsuka, 2, 5, Relay Tx, 2, Roche/Genetech, 5, TD Cowen, 6, Travere, 2, Vera, 2; **M. Frigault**: BMS, 2, Cabaletta Bio, 2, 5, Cytoagents, 2, JnJ/Legend, 2, Kite Pharma (Gilead), 2, Novartis, 2, SOBI, 2; **C. Palma**: Cabaletta Bio, 5; **P. Reagan**: Cabaletta Bio, 5, Caribou Bio, 2, Genentech, 5, Kite Pharma (Gilead), 6, Seagen, 5; **C. Edens**: Cabaletta Bio, 5; **S. Kosuri**: Cabaletta Bio, 5; **C. Elgarten**: Cabaletta Bio, 5; **J. Burnham**: Cabaletta Bio, 5; **J. Hogan**: Cabaletta Bio, 3; **Y. White**: Cabaletta Bio, 3; **C. diCasoli**: Cabaletta Bio, 3; **R. Estremera**: Cabaletta Bio, 3; **J. Volkov**: Cabaletta Bio, 3; **D. Nunez**: Cabaletta Bio, 3; **F. Hadi-Nezhad**: Cabaletta Bio, 3; **T. Furmanak**: Cabaletta Bio, 3; **J. Stadanlick**: Cabaletta Bio, 3; **L. Ishikawa**: Cabaletta Bio, 3; **Z. Vorndran**: Cabaletta Bio, 3; **A. Ellis**: Cabaletta Bio, 3; **J. Williams**: Cabaletta Bio, 3;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

S. Flanagan: Cabaletta Bio, 3; **Q. Lam**: Cabaletta Bio, 3; **S. Basu**: Cabaletta Bio, 12,, 3, 11; **R. Tummala**: Cabaletta Bio, 3; **D. Chang**: Cabaletta Bio, 3.

Abstract Number: 2469

Development of Consensus Statements on Glucocorticoid Use in Systemic Lupus Erythematosus

Heh Shiang Sheu[1], **Wen Nan Huang**[1], Yao-Fan Fang[2], Tai-Ju Lee[3], Ling-Ying Lu[4], Ming-Han Chen[5], Der-Yuan Chen[6], Fu-Chiang Yeh[7], Yu-Wan Liao[1], Chang-Youh Tsai[8], Tsu-Yi Hsieh[1], Song-Chou Hsieh[9], Shue-Fen Luo[2], Yu-Jih Su[10], Yeong-Jian Jan Wu[11] and Chun chi Lu[12], [1]Taichung Veterans General Hospital, Taichung, Taichung, Taiwan (Republic of China), [2]Chang Gung Memorial Hospital, Taoyuan, Taoyuan, Taiwan (Republic of China), [3]National Taiwan University Hospital Hsinchu Branch, Hsinchu City, Taiwan (Republic of China), [4]Kaohsiung Veterans General Hospital, Kaohsiung, Kaohsiung, Taiwan (Republic of China), [5]Division of Allergy, Immunology & Rheumatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, Taipei, Taiwan (Republic of China), [6]China Medical University Hospital, Taichung, Taichung, Taiwan (Republic of China), [7]Tri-Service General Hospital, Taipei, Taipei, Taiwan (Republic of China), [8]Fu Jen Catholic University Hospital, New Taipei, New Taipei, Taiwan (Republic of China), [9]National Taiwan Unuversity Hospital, Taipei City, Taiwan (Republic of China), [10]Chang Gung Memorial Hospital, Kaohsiung, Kaohsiung, Taiwan (Republic of China), [11]Chang Gung Memorial Hospital, Chang Gung University, Taoyuan City, Taiwan (Republic of China), [12]1. Tri-Service General Hospital, Taipei, Taiwan 2. Kaohsiung Veteran General Hospital, Kaohsiung, Taiwan, Taipei, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2437–2469) Systemic Lupus Erythematosus – Treatment Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic glucocorticoid (GC) therapy is indispensable for treating active systemic lupus erythematosus (SLE) and lupus nephritis (LN), while contributing significantly to comorbidities and irreversible damage. The judicious limitation of GC use while effectively managing disease activity represents a critical yet unresolved challenge. This study aimed to formulate pragmatic recommendations for GC utilization in SLE.

Methods: Adhering to established consensus guideline procedures, Taiwan College of Rheumatology (TCR) SLE Special Interest Group (SLE-SIG) formulated a set of recommendations utilizing a systematic literature review and a formalized Delphi process. The literature review group identified the topics of interest and the scope of review, and generated preliminary statements. The selected questions constitute (1) general GC usage, tapering, and targets, (2) GC dosing across organ systems, and (3) special considerations on SLE antiphospholipid syndrome, SLE pulmonary arterial hypertension, and pregnancy. Organ involvements and severities were evaluated based on BILAG-2004 and SLEDAI-2K. The GC doses were

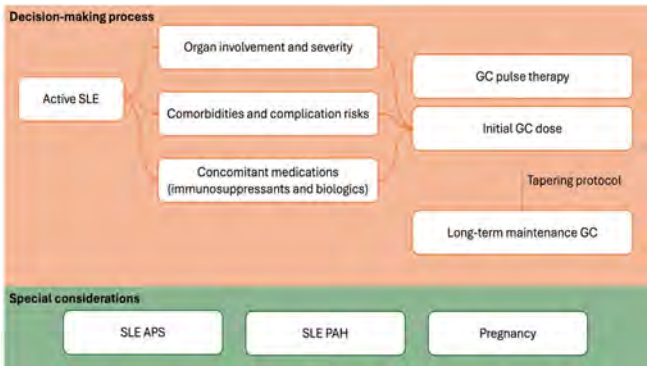


Figure Proposed decision-making process of glucocorticoid dosing in SLE

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table Summary of preliminary recommendations of initial glucocorticoid doses

Statements	Starting dose	MTP pulse
Mild disease and constitutional symptoms	as low as possible	reserved
Mucocutaneous and arthritis	0.3-0.5 mg/kg	reserved
Lupus nephritis: general	0.3-0.5 mg/kg	preferred
	0.5-1.0 mg/kg	optional
Lupus nephritis: high risk	0.5-1.0 mg/kg	preferred
Neuropsychiatric SLE: mild-to-moderate	0.3-0.5 mg/kg	preferred
Neuropsychiatric SLE: severe	0.5-1.0 mg/kg	
Life or organ-threatening, internal organ SLE	0.5-1.0 mg/kg	preferred
Non-life or organ-threatening, internal organ SLE	0.5 mg/kg	optional
SLE-APS and SLE-PAH	preferred over not using GC	
Pregnancy: maternal disease	0.3-0.5 mg/kg, non-fluorinated GC	
Pregnancy: fetal disease	fluorinated GC	

specified in weight-adjusted daily doses (prednisolone equivalent) and the GC pulses were described in daily doses (methylprednisolone equivalent.) A preliminary Delphi round by the expert panel was exercised to deduce the statements based on evidence review and group consensus, and the final statements were modified.

Results: A series of consensus statements encompassed three overarching principles regarding GC utilization in SLE, five general recommendations pertaining to GC initiation, tapering, and therapeutic goals, and eleven organ-specific recommendations. The preliminary evaluation of GC regimens for active SLE involved assessing organ involvement and severity, considering comorbidities and the potential risk of complications, and evaluating concomitant medication regimens, including immunosuppressants and biologics. The initial GC dose and GC pulse therapy were determined based on this evaluation, with the utilization of a tapering protocol to reach the target long-term GC dose at 5 mg/day by week 24 (Figure).

Organ-specific statements delineated the recommended initial GC dose and GC pulses. Organ involvement was categorized as mild disease and constitutional symptoms, mucocutaneous and arthritis, lupus nephritis (LN), neuropsychiatric SLE (NPSLE), and internal organ SLE. The latter three categories were further stratified according to severity for LN and NPSLE, and potential life- or organ-threatening disease for internal organ SLE, respectively. Statements regarding GC use in special considerations, including SLE with anti-phospholipid syndrome (SLE-APS), SLE with pulmonary arterial hypertension (SLE-PAH), and pregnancy, were also provided (Table).

This report presents preliminary consensus statements, subject to a formal Delphi process and subsequent voting by the expert panel to establish agreement levels. The final recommendations will be revised accordingly.

Conclusion: These preliminary statements provide evidence-driven, consensus-based guidance on GC dosing in SLE.

Disclosure: H. Sheu: None; **W. Huang**: None; **Y. Fang**: None; **T. Lee**: None; **L. Lu**: None; **M. Chen**: None; **D. Chen**: None; **F. Yeh**: None; **Y. Liao**: None; **C. Tsai**: None; **T. Hsieh**: None; **S. Hsieh**: None; **S. Luo**: None; **Y. Su**: None; **Y. Wu**: None; **C. Lu**: None.

Abstract Number: 2470

Impaired Myocardial Flow Reserve on 82-Rubidium Positron Emission Tomography in Patients with Systemic Sclerosis

Attila Feher[1], Morgan Emokpae[2], Bindu Koyi[2], Ibolya Csecs[2], Baran Gunes[3], Albert Sinusas[2] and Monique Hinchcliff[4], [1]Yale University School of Medicine - New Haven, CT, New Haven, CT, [2]Yale School of Medicine, New Haven, [3]Yale University School of Medicine, Pompton Plains, NJ, [4]Yale School of Medicine, Westport, CT

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular death ranks as the second leading cause of mortality related to systemic sclerosis (SSc), with coronary microvascular dysfunction (CMVD) likely contributing to this outcome. Positron emission tomography (PET) myocardial perfusion imaging (MPI) has emerged as the noninvasive gold standard for assessing myocardial blood flow (MBF) and myocardial flow reserve (MFR), offering unparalleled accuracy in detecting CMVD. We undertook the present study to explore the relationship between vasodilators, SSc disease-modifying antirheumatic drugs and CMVD in SSc patients.

Methods: We conducted a retrospective study involving patients diagnosed with SSc who underwent 82-rubidium PET MPI from July 2016 to April 2025 for clinical indications. These patients were compared to a control group without connective

Table 1. Baseline and imaging characteristics in systemic sclerosis (SSC) patients and matched controls.

	SSc, n=67	Controls, n=201	p
Age (median [IQR])	61 [56, 68]	62 [54, 72]	0.570
Body mass index (median [IQR])	28.89 [23.85, 34.88]	27.29 [23.13, 34.16]	0.522
Female (%)	58 (86.6)	169 (84.1)	0.769
Cardiovascular comorbidities			
Essential hypertension (%)	34 (50.7)	112 (55.7)	0.571
Dyslipidemia (%)	26 (38.8)	81 (40.3)	0.943
Diabetes (%)	5 (7.5)	19 (9.5)	0.805
Smoking (%)	3 (4.5)	6 (3.0)	0.845
Myocardial infarction (%)	2 (3.0)	5 (2.5)	1.000
Coronary artery bypass surgery (%)	0 (0)	0 (0)	NA
Percutaneous coronary intervention (%)	3 (4.5)	12 (6.0)	0.878
Heart failure (%)	6 (9.0)	29 (14.4)	0.346
Cerebrovascular accident (%)	1 (1.5)	4 (2.0)	1.000
Chronic kidney disease (%)	1 (1.5)	5 (2.5)	1.000
Peripheral artery disease (%)	5 (7.5)	12 (6.0)	0.885
Diffuse cutaneous SSc	14 (20.9)		N/A
Overlap disease	21 (31.3)		N/A
Prior/current digital ulceration	20 (29.8)		N/A
Pulmonary artery hypertension	12 (17.9)		N/A
Interstitial lung disease	34 (50.7)		N/A
Medications			
Calcium channel blocker (n=40)	40 (59.7)	46 (22.9)	<0.001
Angiotensin receptor blocker (n=14)	14 (20.9)	33 (16.4)	0.458
Statin (n=26)	26 (29.9)	94 (46.8)	0.32
Aspirin (n=-16)	16 (23.9)	89 (44.3)	0.004
Beta blocker (n=16)	16 (23.9)	91 (45.3)	0.002
ACE inhibitors (n=7)	7 (10.4)	60 (29.9)	0.103
Methotrexate (n=3)	3 (4.5)	0 (0%)	0.0187
Mycophenolic acid (n=24)	24 (35.8)	0 (0%)	<0.001
Steroids (n=16)	16 (23.9)	0 (0%)	<0.001
PAH therapy (n=16)	16 (23.9)	0 (0%)	<0.001
Regadenoson stress (%)	64 (95.5)	195 (97.0)	0.845
Presenting symptoms (%)			0.953
Abnormal ECG	5 (7.5)	18 (9.0)	
Dyspnea	29 (43.3)	90 (44.8)	
Heart failure	1 (1.5)	5 (2.5)	
Chest pain	25 (37.3)	63 (31.3)	
Pre-operative evaluation	4 (6.0)	15 (7.5)	
Other	3 (4.5)	10 (5.0)	
Abnormal perfusion (%)	11 (16.4)	45 (22.4)	0.386
Ischemic stress ECG response (%)	0 (0.0)	7 (3.0)	0.198
Visual coronary calcium score (median [IQR])	1 [0, 3]	0 [0, 3]	0.365
Stress left ventricular ejection fraction, % (median [IQR])	69 [60, 74]	67 [58.75, 72]	0.160
Follow-up catheterization (%)	12 (18.0)	35 (17.4)	1.000
Obstructive coronary artery disease on follow-up catheterization (%)	1 (1.5)	11 (5.5)	0.305

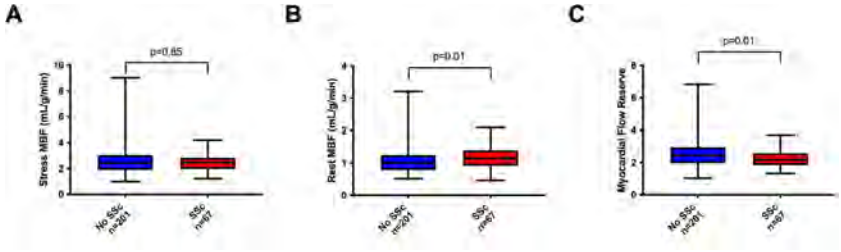


Figure 1. Stress and rest myocardial blood flow (MBF) and myocardial flow reserve in SSc patients and controls

Table 2. Univariable and multivariable logistic regression for prediction of reduced myocardial flow reserve (<2.0)

	Univariable regression		Multivariable regression	
Factor	OR (95% CI)	P value	OR (95% CI)	P value
Female (n=58)	0.76 (0.18-3.37)	0.710		
Disease duration	1.04 (0.99-1.09)	0.093		
dcSSc (n=14)	1.24 (0.36-4.09)	0.727		
Overlap disease (n=21)	1.06 (0.36-3.13)	0.892		
Digital ulceration (n=20)	1.94 (0.67-5.70)	0.223		
Pulmonary artery hypertension (n=12)	0.26 (0.04-1.10)	0.099		
Interstitial lung disease (n=34)	**0.19 (0.06-0.54)**	**0.003**	0.46 (0.09-2.07)	0.310
Medications				
Methotrexate (n=3)	0.78 (0.04-8.56)	0.843		
Mycophenolic acid (n=24)	**0.12 (0.03-0.43)**	**0.002**	**0.09 (0.01-0.56)**	**0.017**
Steroids (n=16)	0.44 (0.11-1.46)	0.201		
Calcium channel blocker (n=40)	**3.50 (1.21-11.23)**	**0.025**	**7.77 (1.93-42.53)**	**0.008**
Angiotensin receptor blocker (n=14)	1.24 (0.36-4.09)	0.727		
PAH therapy (n=16)	0.44 (0.11-1.46)	0.201		
Statin (n=26)	3.72 (1.34-10.86)	0.013	**7.14 (1.86-36.87)**	**0.008**
Aspirin (n=-16)	1.31 (0.41-4.10)	0.642		
Beta blocker (n=16)	2.57 (0.82-8.37)	0.106		
ACE inhibitors (n=7)	1.21 (0.22-5.95)	0.816		

tissue disease, matched 3:1 for age, sex, body mass index (BMI), cardiovascular comorbidities, and presenting symptoms. Differences between groups were analyzed using the Chi-Square test and the Wilcoxon rank-sum test. Univariable and multivariable logistic regression models were used to assess SSc-related predictors of clinically significant reduced MFR (< 2.0). Parameters with p< 0.05 in univariable analysis were included in multivariable model. Statistical analyses were performed with R version 4.4.2.

Results: The final cohort included 67 patients with SSc (87% female, mean age: 61 years, 14 with diffuse cutaneous SSc, disease duration: 12 ± 10 years) and 201 matched controls (Table 1). While stress MBF was not significantly different between SSc patients and controls (2.47 [IQR: 1.99-2.82] vs. 2.43 [IQR: 1.91-3.04] ml/g/min, p=0.85), rest MBF was significantly higher in SSc patients (1.14 [IQR: 0.92-1.37] vs. 1.00 [IQR: 0.78-1.24] ml/g/min, p=0.01) and MFR was significantly lower (2.17 [IQR: 1.84-2.57] vs. 2.44 [IQR: 1.96-2.96], p=0.01, Figure 1). Rates of abnormal perfusion, ischemic ECG changes, stress left ventricular ejection fraction, and visual coronary calcium scores were comparable between SSc patients and controls. In SSc patients, multivariable analysis identified mycophenolate mofetil (MMF) use as associated with significantly reduced odds for abnormal MFR (odds ratio [OR]: 0.09 [95% confidence interval[CI]: 0.01-0.56], p=0.017), whereas calcium channel blocker use (OR: 7.77 [95% CI: 1.93-42.53], p=0.008) and statin use (OR: 7.14 [95% CI: 1.86-36.87], p=0.008) were associated with higher odds of abnormal MFR (Table 2).

Conclusion: Patients with SSc exhibit significantly reduced PET-derived MFR compared to matched controls, indicating higher CMVD prevalence. Our finding of a significant association between calcium channel blocker or statin use and abnormal MFR may reflect more severe systemic microvascular disease. Conversely, the observed association between MMF use and lower incidence of reduced MFR suggests potential benefits through mechanisms such as cytokine suppression, antioxidant activity, or enhanced nitric oxide production. Further studies are warranted to validate these findings and to elucidate the effects of MMF on microvascular function in SSc.

Disclosure: A. Feher: None; **M. Emokpae**: None; **B. Koyi**: None; **I. Csecs**: None; **B. Gunes**: None; **A. Sinusas**: None; **M. Hinchcliff**: AbbVie/Abbott, Boehringer Ingelheim, Kadmon,, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2471

Automated Feedback and Quality Control in Nailfold Capillaroscopy: A Tool for Clinical and Educational Use

Borja del Carmelo Gracia Tello[1], Gema María Lledó Ibáñez[2], Luis Sáez Comet[3], Eduardo Ramos ibáñez[4] and SEMI - GEAS, [1]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [2]Hospital Clínic de Barcelona, Barcelona, Spain, [3]Hospital Universitario Miguel Servet, Zaragoza, Spain, [4]Capillary.io, Zaragoza, Aragon, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Nailfold capillaroscopy is a key tool in the early diagnosis of systemic sclerosis and related disorders. However, incorrect image acquisition can lead to misclassification of capillaroscopic patterns, potentially delaying diagnosis and affecting clinical decisions.

To support clinical reliability we developed a lightweight, real-time system for automatic quality assessment of nailfold capillaroscopy (NFC) images. The system supports exclusion of invalid images from analysis and reporting, provides immediate feedback during image acquisition, and aids clinician training by detecting typical image acquisition problems during a capillaroscopy examination.

Methods: A small and efficient deep learning model based on the ConvNeXt V2 architecture was trained to identify frequent NFC image issues: low magnification, blurring, reflections, incorrect placement, underexposure, and invalid content. For valid images (those without problems), the model also estimates diagnostic usability as low quality or acceptable quality.

Low quality images were defined as diagnostically acceptable but with imperfect focus or suboptimal capillary visibility, while acceptable quality images had clear visualization suitable for confident pattern recognition.

The model was trained on a dataset of 10,866 annotated images. An image may have multiple problem annotations, but quality grading (low or acceptable) was applied only to images without any problems. The number of annotations per annotation type are shown in Table 1.

To ensure clinical reliability, model evaluation metrics were computed at a confidence threshold of 0.85.

Results: The model achieved exceptional performance in detecting low magnification images, with an F1-score of 0.99, and invalid content, with an F1-score of 0.96, two of the most critical categories for ensuring diagnostic image quality. It also showed strong performance in identifying blurry images (F1 = 0.84) and those with excessive reflections (F1 = 0.83).

In terms of quality grading of valid images, the model effectively distinguished between low and acceptable quality among valid images, achieving an F1-score of 0.8316 for low-quality cases. The rest of performance metrics are shown in Table 2.

Conclusion: This real-time model based on ConvNeXt V2 helps ensure that nailfold capillaroscopy examinations are useful and valid. It automatically detects common problems in images and checks whether valid images have enough quality for diagnosis. Because it is fast and lightweight, it can be used during image capture to give immediate feedback, avoid invalid images, and improve the consistency of capillaroscopies. This makes the process more efficient and helps both clinicians and researchers achieve better, more reliable results as well as being a useful tool in the training of new physicians.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Number of annotations per class

Table 1. Number of annotations per class:

Annotation Type	Number of Annotations
Magnification too low	6,251
Too blurry	1,847
Too many reflections	1,189
Incorrect placement	228
Too dark	121
Invalid content	310
Low quality	1,638
Acceptable quality	772

Table 2. Performance metrics per class

Table 2. Performance metrics per class:

Class	Precision	Recall	F1-score
Magnification too low	1.0000	0.9756	0.9876
Invalid content	0.9769	0.9505	0.9635
Too blurry	0.8771	0.8035	0.8387
Too many reflections	0.9170	0.7657	0.8345
Incorrect placement	0.9149	0.6143	0.7350
Too dark	0.8500	0.5862	0.6939
Low quality	0.9145	0.7625	0.8316
Acceptable quality	0.8417	0.6094	0.7069

Disclosure: B. Gracia Tello: None; **G. Lledó Ibáñez**: None; **L. Sáez Comet**: None; **E. Ramos ibáñez**: None.

Abstract Number: 2472

Digesting the data: tracking gastro-intestinal manifestations in systemic sclerosis over time

Cosimo Bruni[1], Jasmin Klöti[2], Aurora Maria Tatu[3], Lea Stamm[2], Rucsandra Dobrota[4], Muriel Elhai[5], Mike Becker[6], Sinziana Muraru[7], Gesa Sauer[8], Anna-Maria Hoffmann-Vold[9], Oliver Distler[10] and **Carina Mihai**[11], [1]University of Zurich, Zurich, Switzerland, [2]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [3]Department of Gastroenterology, University Hospital Zurich, University of Zurich, 8091, Switzerland, [4]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [5]University Hospital zurich, Zurich, Switzerland, [6]Dept. of Rheumatology, University Hospital Zurich, Zurich, Switzerland, [7]University of Zurich, University Hospital Zurich, Zurich, Switzerland, [8]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, zurich, Switzerland, [9]Oslo University Hospital, Oslo, Norway, [10]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [11]University Hospital Zurich, University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Gastrointestinal (GI) involvement is among the most frequent organ manifestations in systemic sclerosis (SSc), yet the timing of presentation of GI manifestations remains incompletely understood. In this retrospective analysis, we aimed to describe the baseline prevalence and the incidence of new GI disease manifestations over time in a real-life, large SSc cohort.

Methods: We included patients from our center's cohort fulfilling the ACR/EULAR 2013 criteria for SSc or the VEDOSS criteria. Electronic medical records were searched for data regarding the presence and the time of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of the included population stratified by severity of the GI involvement based on UCLA GIT 2.0 score.

	Overall (n= 656)	None-mild (n=434)	Moderate (n=102)	Severe-very severe (n=30)
2013 ACR/EULAR criteria fulfilled	544 (82.7)			
Age at first GI diagnosis (years)	55.01 (±14.79)	55.29 (±15.00)	54.15 (±13.68)	55.56 (±11.49)
Age at enrollment (years)	55.43 (±14.96)	55.24 (±15.23)	55.96 (±13.80)	57.20 (±10.48)
Sex (female)	550 (83.8%)	358 (82.0%)	83 (81.4%)	27 (90.0%)
Smoking status				
Former	118 (17.9%)	79 (18.2%)	21 (20.6%)	7 (23.3%)
Current	106 (16.1%)	65 (15.0%)	20 (19.6%)	6 (20.0%)
Cutaneous subset				
Limited	377 (57.3%)	263 (60.6%)	55 (53.9%)	21 (70.0%)
Diffuse	108 (16.4%)	72 (16.6%)	19 (18.6%)	7 (23.3%)
VEDOSS/Sine scleroderma	173 (26.3%)	99 (22.8%)	28 (27.5%)	2 (6.7%)
Autoantibody status				
ANA +	634 (96.4%)	422 (97.2%)	98 (96.1%)	28 (93.3%)
Anti-Topoisomerase I +	133 (19.1%)	99 (22.4%)	17 (16.7%)	6 (19.4%)
Anti-Centromere +	309 (44.3%)	208 (47.1%)	47 (46.1%)	14 (45.2%)
Anti-RNA Polymerase III +	71 (10.2%)	45 (10.2%)	14 (13.7%)	4 (12.9%)
Clinical characteristics				
Current digital ulcers	67 (10.2%)	41 (9.4%)	12 (11.8%)	6 (20.0%)
Previous digital ulcers	102 (15.5%)	73 (16.8%)	13 (12.7%)	7 (23.3%)
Calcinosis	55 (8.4%)	33 (7.6%)	10 (9.8%)	6 (20.0%)
Telangiectasia	318 (48.3%)	204 (47.0%)	55 (53.9%)	21 (70.0%)
Renal crisis	8 (1.2%)	7 (1.6%)	1 (1.0%)	0 (0.0%)
Interstitial lung disease	302 (43.4%)	199 (46.0%)	58 (56.9%)	14 (48.7%)
Pulmonary arterial hypertension	27 (4.1%)	16 (3.7%)	8 (7.8%)	0 (0.0%)
GI manifestation	**318 (48.3%)**	**186 (42.5%)**	**71 (69.6%)**	**24 (80.0%)**
Esophageal disease	296 (45.0%)	173 (39.9%)	66 (64.7%)	23 (76.7%)
Barrett's esophagus	25 (3.8%)	13 (3.0%)	7 (6.9%)	4 (13.3%)
GAVE	9 (1.4%)	5 (1.2%)	2 (2.0%)	0 (0.0%)
Gastroparesis	4 (0.6%)	1 (0.2%)	3 (2.9%)	0 (0.0%)
SIBO	5 (0.8%)	3 (0.7%)	2 (2.0%)	0 (0.0%)
CIPO	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic constipation	17 (2.6%)	5 (1.2%)	5 (4.9%)	3 (10.0%)
Chronic diarrhea	8 (1.2%)	2 (0.5%)	4 (3.9%)	1 (3.3%)
Anal incontinence/dyssinergy	15 (2.3%)	5 (1.2%)	4 (3.9%)	2 (6.7%)
GI Bleeding	12 (1.8%)	9 (2.1%)	2 (2.0%)	1 (3.3%)
UCLA SCTC GIT 2.0 total score	0.29 (±0.33)	0.14 (±0.14)	0.59 (±0.13)	1.30 (±0.29)

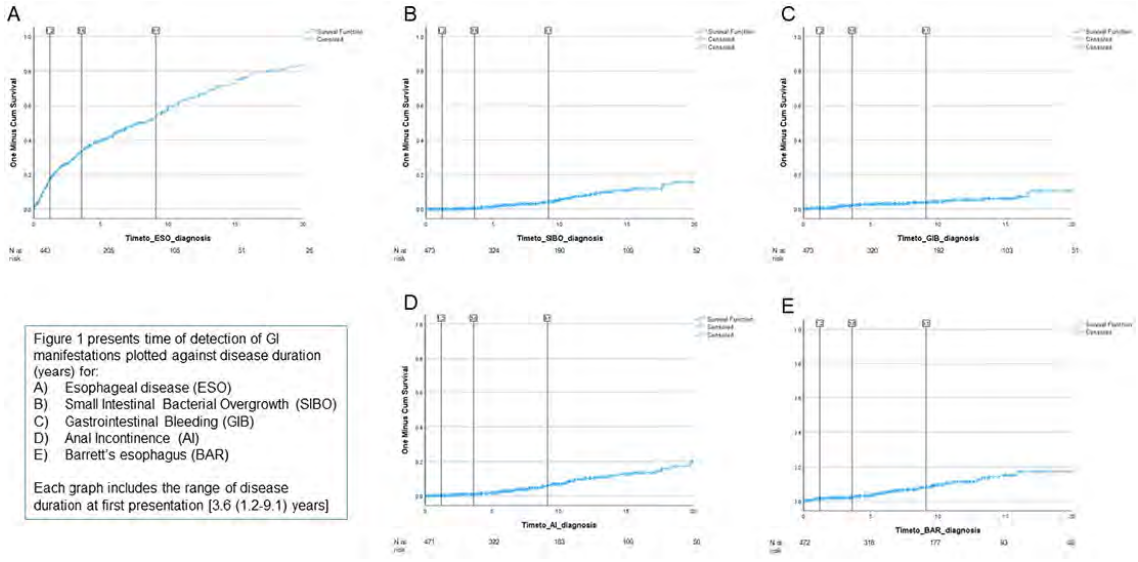


Figure 1 presents time of detection of GI manifestations plotted against disease duration (years) for:
A) Esophageal disease (ESO)
B) Small Intestinal Bacterial Overgrowth (SIBO)
C) Gastrointestinal Bleeding (GIB)
D) Anal Incontinence (AI)
E) Barrett's esophagus (BAR)

Each graph includes the range of disease duration at first presentation [3.6 (1.2-9.1) years]

Figure 1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

detection of specific GI diagnoses. We focused on esophageal disease (defined as at least one of: reflux, dysphagia, or aperistalsis), gastroparesis, gastric antral vascular ectasia (GAVE), small intestinal bacterial overgrowth (SIBO), chronic intestinal pseudo-obstruction (CIPO), chronic constipation, and chronic diarrhea. In addition, data of the University of California at Los Angeles/Scleroderma Clinical Trials Consortium Gastro-Intestinal Tract instrument 2.0 (GIT 2.0) questionnaire were also collected at each annual visit, when available. Based on the GIT 2.0 score, GI disease burden was categorized at baseline into 3 groups: (1) none to mild, (2) moderate, and (3) severe-to-very severe symptoms (Khanna D. et al, Arthritis Rheum 2009). We assessed baseline prevalence of GI diagnoses and used survival curves to investigate the timing of GI diagnoses from disease onset, defined as time from the first non-Raynaud's sign or symptom.

Results: We included 658 patients: 83.6% females, mean age 55.4 (SD 15.0) years, 566 (86%) with available GIT 2.0; additional baseline clinical data are displayed in Table 1. At the first visit, 318 (48.3%) patients already presented with GI manifestations or diagnoses. Of these, the most common was esophageal disease (45.0%), while all other clinically relevant GI manifestations had an initial prevalence of < 4%. According to the GIT 2.0 categories, most patients had none to mild symptoms, while 102 (15.5%) had moderate and 30 (4.6%) had severe-to-very severe GI disease.

Over a mean follow-up time of 3.3 (SD 3.2) years, additional patients developed new GI complications, with the cumulative prevalence increasing to 65% at last follow-up. In particular, esophageal disease increased to 61.1%, Barrett's esophagus from 3.8% to 7.9%, GAVE from 1.4% to 4.3%, SIBO from 0.8% to 7.0%, anal incontinence from 2.3% to 7.6% and GI bleeding from 1.8% to 5.3%. Only 4 patients, already diagnosed with SIBO, developed CIPO during follow-up.

Focusing on patients with known disease duration from SSc onset [n=476 (72%), median 3.6 (IQR 1.2-9.1 years)], we observed that esophageal involvement tended to appear earlier (median time from disease onset: 7.5 years), while others like Barrett's esophagus or SIBO occurred later (Figure 1 A to E).

Conclusion: GI involvement in SSc is frequent and dynamic, with distinct time patterns for individual complications. Early manifestations such as esophageal disease precede more severe complications like GAVE and SIBO. Longitudinal tracking of GI disease in SSc provides important insights into its natural history and may inform anticipatory management strategies.

Disclosure: C. Bruni: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5; **J. Klöti**: None; **A. Tatu**: None; **L. Stamm**: None; **R. Dobrota**: Actelion, 5, 6, Amgen, 6, Boehringer-Ingelheim, 6, Iten-Kohaut, 5, Otsuka, 6, Pfizer, 5, Walter und Gertrud Siegenthaler Fellowship, 5; **M. Elhai**: Astrazeneca, 12, congress support, Boehringer Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5, Iten Kohaut foundation, 5, Janssen, 12, congress support, Kurt und Senta Herrmann foundation, 5, Novartis Foundation for Bio-Medical Research, 5, pfizer, 5, University Zurich, 5; **M. Becker**: Foundation for research in Rheumatology (FOREUM), 5, GSK, 6, 12, congress support, Novartis Foundation for Medical-biological Research, 5, 6, Vifor, 6, 12, congress support; **S. Muraru**: AstraZeneca, 12, congress support; **G. Sauer**: Schweizerische Gesellschaft für Rheumatologie, 12, Congress support EULAR 2023; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6; **C. Mihai**: Boehringer Ingelheim, 2, 12, congress support, Janssen, 2, MED Talks Switzerland, 6, Medbase, 6, MedTrix, 6, Mepha, 6, Novartis, 6, PlayToKnow, 6.

Abstract Number: 2473

Nailfold Capillaroscopy Improves Cardiovascular Risk Stratification in Systemic Sclerosis: An Adjustment to the SCORE2 Algorithm

Carlos Valera Ribera[1], Javier Narváez[2], Joaquin Lacasa Molina[3], Adrián Mayo-Juanatey[4], Paula Mencio[5], Patricia Leon Torralba[5], Pablo Andujar Brazal[5], Ignacio Vázquez Gómez[6] and JUAN JOSE ALEGRE SANCHO[7], [1]Hospital Universitario Doctor Peset, Valencia, Spain, [2]Hospital Universitario de Bellvitge, Barcelona, Spain, [3]Hospital Universitario Doctor Peset, Valencia, Spain, [4]Hospital Universitario Doctor Peset, Valencia, Comunidad Valenciana, Spain, [5]Hospital Universitario Doctor Peset, València, Comunidad Valenciana, Spain, [6]H.U. Doctor Peset, Valencia, [7]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is associated with both micro- and macrovascular damage, increasing cardiovascular (CV) risk. The SCORE2 algorithm estimates CV event risk in the general population but may underestimate it in SSc. Nailfold capillaroscopy (NFC) detects microangiopathy typical of SSc, which may improve CV risk prediction in this population.

To evaluate the predictive value of NFC findings for CV events and assess whether incorporating these into the SCORE2/SCORE2-OP algorithms improves risk stratification.

Methods: We conducted a multicenter retrospective study of 276 SSc patients without prior CV events. SCORE2 was applied to patients aged 40–69, and SCORE2-OP to those ≥70. NFC was performed at diagnosis. A Cox regression identified NFC variables associated with incident MCE during follow-up. Based on these results, a modified SCORE2 was calculated by applying hazard ratios (HRs) of the baseline NFC findings, to the original SCORE2 score. ROC curves assessed the discrimination of original versus the modified model. Patients were categorized into standard risk levels (low, moderate, high, very high), and the Net Reclassification Index (NRI) was calculated.

Results: Over a median follow-up of 9.5 years, 45 patients (16.3%) experienced a CV event. Baseline characteristics are summarized in Table 1. Hemorrhages ($p = 0.002$) and avascular areas ($p < 0.001$) at diagnosis were significantly associated with subsequent CV events. In multivariate Cox analysis, hemorrhages showed an independent protective effect (HR = 0.333, $p = 0.01$), while avascular areas were independently associated with increased risk (HR = 2.238, $p = 0.034$) (Table 2).

The modified SCORE2 showed improved discrimination (AUC 0.767) compared to the original (AUC 0.680) (Figure 1). At the optimal threshold (1.83%), the modified SCORE2 yielded a sensitivity of 85.2% and specificity of 58.4%, versus 74.1% and 59.4% for the original model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Demographic, clinical and laboratory data from the cohort

	N = 276 (%)
Female / Male	248 (89.9) / 28 (10.1)
Age at time of diagnosis, mean (SD)	62.83 ±15.66
Body mass index, mean (SD)	25.28± 4.92
Cardiovascular risk factors	
Smoking history	44 (15.9)
Alcohol consumption	55 (19.9)
Arterial hypertension	90 (32.6)
Systolic arterial pressure, mmHg, mean (SD)	129.85 (20.46)
Diabetes mellitus	25 (9.1)
Dyslipidemia	106 (38.4)
Colesterol total, mg/dL, mean (SD))	196.04 (37.43)
HDL, mg/dL, mean (SD))	53.94 (15.2)
LDL, mg/dL, mean (SD)	122.27 (34.57)
Atheroma plaque	82 (29.7)
Disease duration, years, median, (IQR 25th - 75th)	9.5 (5-14)
SSc cutaneous involvement	
Diffuse	42 (15.2)
Limited	180 (65.2)
Sine esclerodermia	45 (16.3)
Telangiectasias	78 (28.3)
Digital ulcers	76 (27.5)
Calcinosis	46 (16.7)
Oesophageal involvement	110 (39.9)
interstitial lung disease	68 (24.6)
Pulmonary hypertension	34 (12.3)
Cardiac involvement	51 (18.5)
Renal involvement	11 (4)
Arthritis	63 (22.8)
ANA	218 (79)
ATA positive	42 (15.2)
ACA positive	102 (37)
RNA polimerase III positive	7 (2.5)
Cardiovascular event during follow-up	45 (16.3)
Type of event	
Myocardial infarction	21 (46.67)
Peripheral vascular disease (ischemia o thrombosis)	15 (33.33)
Ictus	9 (20)
Deaths	
Total	57 (20.7)
Attributable to cardiovascular events	13 (22.81)

Some patients suffered more than one cardiovascular event during follow-up

Results are presented as the number of cases with percentage, mean ± standard deviation (SD), or median with interquartile range (IQR) for the 25th–75th percentile.

Table 2. Multivariate Cox-regression analysis of predictors for cardiovascular events

Table 2. Multivariate Cox-regression analysis of predictors for cardiovascular events

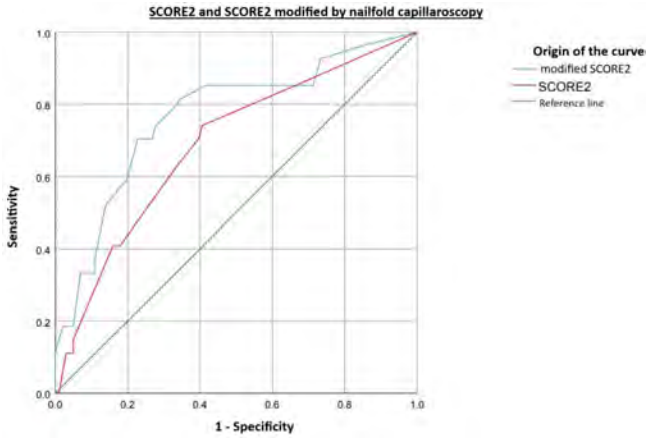
	Hazard ratio	95% Confidence interval	p
Age	0.995	0.959 – 1.033	0.789
Arterial hypertension	1.219	0.262 – 2.469	0.759
Dyslipidemia	1.050	0.400 – 2.756	0.920
Digital ulcers	1.644	0.663 – 4.074	0.283
Interstitial lung disease	**3.815**	**1.560 – 9.330**	**0.003**
Pulmonary hypertension	1.848	0.689 – 4.956	0.222
Cardiac involvement	1.496	0.549 – 4.072	0.431
Haemorrhages in baseline NFC	**0.333**	**0.144 – 0.773**	**0.010**
Avascular areas in baseline NFC	**2.238**	**1.061 – 4.723**	**0.034**

ABBREVIATIONS: NFC = nailfold capillaroscopy

Among patients with CV events, 33% were correctly reclassified to higher risk and 7% incorrectly to lower risk. Among non-event patients, 3% were correctly reclassified to lower risk and 5% incorrectly to higher risk. The total NRI was +0.239, indicating improved net reclassification.

Conclusion: Adjusting the SCORE2 algorithm using NFC findings at the time of diagnosis improves cardiovascular risk prediction in patients with systemic sclerosis. Avascular areas confer increased risk, while hemorrhages appear protective. These microvascular markers may support more personalized cardiovascular prevention strategies in this high-risk population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



SCORE2 and SCORE2 modified by nailfold capillaroscopy

Disclosure: C. Valera Ribera: None; **J. Narváez**: None; **J. Lacasa Molina**: None; **A. Mayo-Juanatey**: None; **P. Mencio**: None; **P. Leon Torralba**: None; **P. Andujar Brazal**: None; **I. Vázquez Gómez**: None; **J. ALEGRE SANCHO**: None.

Abstract Number: 2474

Unveiling the clinical spectrum of ACA-positive SSc-ILD: not as benign as expected

Carlos Valera Ribera[1], JUAN JOSE ALEGRE SANCHO[2], Ivan Castellvi[3], Marta Ibañez[4] and Javier Narváez[5], [1]Hospital Universitario Doctor Peset, Valencia, Spain, [2]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain, [3]Hospital Universitari de la Santa Creu i Sant Pau, Sant Just Desvern, Spain, [4]Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Catalonia, Spain, [5]Hospital Universitario de Bellvitge, Barcelona, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1: Comparative analysis of the characteristics of interstitial lung disease in patients ACA positive, ATA positive and ACA-ATA negative.

	ACA positive N=79 (27.4%)		ATA positive N=54 (19.5%)		ACA-ATA negative N=147 (53.1%)		p-value
Time since the diagnosis of SSc, years, mean ± SD	2.55 ± 5.65		5.63 ± 5.1		3.52 ± 6.02		0.389
HRCT pattern of ILD							
NSIP	48 (61.2%)		43 (79.6%)		108 (73.5%)		0.403
UIP	11 (14.5%)		5 (9.3%)		17 (11.6%)		
Other patterns	17 (22.3%)		6 (11.1%)		22 (14.9%)		
PFT parameters at ILD diagnosis, mean±SD							
%pFEV1	94.1 ± 23.1		86.5 ± 23.4		83.5 ± 23		0.071
%pFVC	96.3 ± 26.2		89.5 ± 22.9		86.9 ± 23.3		**0.013**
FEV1/FVC	91.6 ± 14.3		99.2 ± 8.3		98.8 ± 10.2		**0.004**
DLCO	60.2 ± 24.6		60.9 ± 18.1		65.7 ± 18.1		0.769
KCO	71.7 ± 25.6		85.1 ± 18.5		77.4 ± 9.9		**0.008**
TLC	91.5 ± 20.6		83.4 ± 15.8		86.2 ± 20.3		0.343
FVC/DLCO	1.8 ± 0.8		1.4 ± 0.4		1.5 ± 0.5		**0.016**
NYHA class							
Class I	13 (17.1%)		10 (18.5%)		33 (22.4%)		**0.017**
Class II	52 (68.4%)		21 (38.9%)		97 (45.6%)		
Class III	6 (8%)		14 (25.9%)		31 (21.1%)		
Class IV	5 (6.5%)		9 (16.7%)		16 (10.9%)		
6-minute walking test at ILD diagnosis, meters, mean (SD)	383 (121)		385,5 (79,5)		395.53(96)		0.859
Treatments	Yes (%)	No (%)	Yes (%)	No (%)	Yes (%)	No (%)	
MMF	29 (38.1%)	47 (61.9%)	28 (51.8%)	26 (48.2%)	91 (61.9%)	56 (38.1%)	**0.001**
RTX	15 (19.7%)	61 (80.3%)	8 (14.8%)	46 (85.2%)	26 (17.7%)	121 (82.3%)	0.769
TCZ	4 (5.2%)	72 (94.8%)	0 (0%)	54 (100%)	4 (2.7%)	143 (97.3%)	0.393
AZA	4 (5.2%)	72 (94.8%)	1 (1.8%)	53 (98.2%)	6 (4.1%)	141 (95.9%)	0.770
CYC	6 (7.9%)	70 (92.1%)	2 (3.7%)	52 (96.3%)	13 (8.8%)	134 (91.2%)	0.670
Antifibrotic agents	8 (10.5%)	68 (89.5%)	7 (12.9%)	47 (87.1%)	19 (12.9%)	128 (87.1%)	0.862
Pulmonary transplant	2 (2.6%)	74 (97.4%)	0 (0%)	54 (100%)	2 (1.4%)	145 (98.6%)	0.549
AHSCT	2 (2.6%)	74 (97.4%)	0 (0%)	54 (100%)	5 (3.4%)	142 (96.6%)	0.592
Deaths	16 (21%)		10 (18.5%)		18 (12.2%)		0.188
Survival since ILD diagnosis, years, mean (SD)	11.2 (8.01)		14.12 (8.96)		14.29 (9.59)		0.163

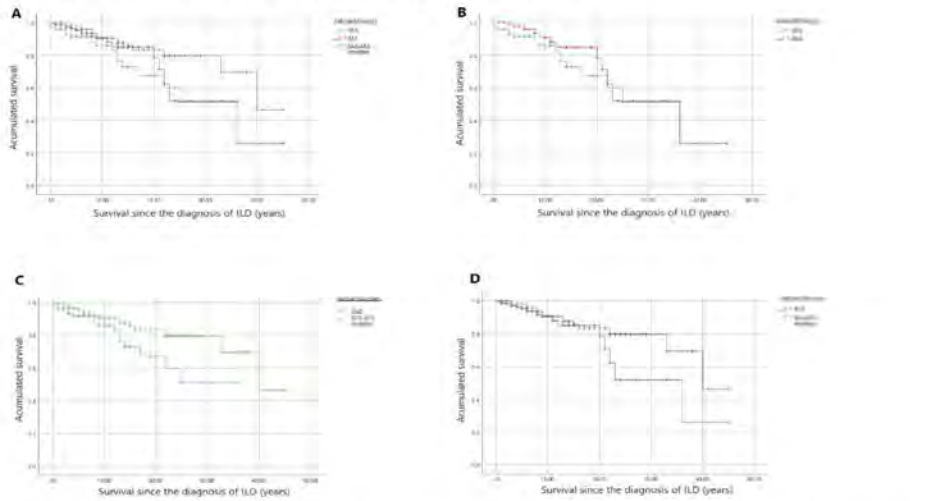
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Characteristics of the 76 patients with ACA-positive SSc-ILD

	N = 76
Women / Men	62 (81.6%) / 14 (18.4%)
Age at diagnosis, years, mean (SD)	58 ± 17
Body mass index, mean (SD)	26.1 ± 5
Ethnicity	Caucasian 69 (90.8%) / Hispanic 6 (7.9%) / Arabic 1 (1.3%)
Disease duration at study inclusion, years, median (IQR 25th-75th)	11 (7 – 15)
Traditional cardiovascular risk factors	
Arterial hypertension	39 (51.5%)
Dyslipidemia	37 (48.7%)
Diabetes mellitus	9 (11.8%)
Smoking history	20 (26.3%)
Clinical manifestations	
Cutaneous subset	
Diffuse	7 (9.2%)
Limited	54 (71.1%)
Sine scleroderma	15 (19.7%)
mRSS, mean (SD)	4.6 (4)
Raynaud's phenomenon	75 (98.7%)
Telangiectasias	59 (77.6%)
Digital ulcers	13 (17.1%)
Calcinosis	9 (11.8%)
Arthritis	15 (19.7%)
Myositis	2 (2.6%)
Esophageal involvement	56 (73.7%)
Intestinal involvement	5 (6.6%)
Anorectal involvement	7 (9.2%)
Scleroderma renal crisis	1 (1.3%)
Primary cardiac involvement	20 (26.3%)
Pulmonary hypertension	14 (18.4%)
Primary biliary cholangitis	4 (5.2%)
Autoantibodies	
ANA positive	75 (98.7%)
Ro-52 positive	14 (18.4%)
ILD characteristics	
Time since the diagnosis of SSc, years, mean ± SD	2.55 ± 5.65
HRCT pattern of ILD	
NSIP	48 (63.2%)
UIP	11 (14.5%)
Other patterns	17 (22.3%)
PFT parameters at ILD diagnosis, mean ± SD	
%pFEV1	94.1 ± 23.1
%pFVC	96.3 ± 26.2
FEV1/FVC	91.6 ± 14.3
DLCO	60.2 ± 24.6
KCO	71.7 ± 25.6
TLC	91.5 ± 20.6
FVC/DLCO	1.8 ± 0.8
NYHA class	
Class I	13 (17.1%)
Class II	52 (68.4%)
Class III	6 (7.9%)
Class IV	5 (6.5%)
Mean distance covered in 6MWT at diagnosis, meters, mean ± SD	383.1 ± 121
Treatments	
Mycophenolate mofetil	29 (38.1%)
Cyclophosphamide	6 (7.9%)
Azathioprine	4 (5.2%)
Rituximab	15 (19.7%)
Tocilizumab	4 (5.2%)
Antifibrotic agents (nintedanib or pirfenidone)	8 (10.5%)
Total follow-up time since ILD diagnosis, years, median (IQR 25th-75th)	10.2 (5.1 – 14.1)
PFT parameters at last follow-up, mean ± SD	
%pFEV1	92.1 ± 25.6
%pFVC	94.4 ± 27.7
FEV1/FVC	91.5 ± 14
DLCO	54.7 ± 21
KCO	82.2 ± 20
TLC	85 ± 22
Pulmonary transplant	2 (2.6%)
AHSCT	2 (2.6%)
Deaths	16 (21%)
Survival since ILD diagnosis, years, mean (SD)	11.2 (8.01)

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan–Meier survival curves in SSc-ILD patients according to autoantibody subsets.



A) Overall survival from ILD diagnosis stratified by serological subgroups: anticentromere antibody-positive (ACA), anti-topoisomerase I antibody-positive (ATA), and ACA/ATA-negative groups. No statistically significant difference was observed (log-rank p=0.164).
B) Pairwise comparison between ACA- and ATA-positive groups showed no significant survival difference (log-rank p=0.471).
C) ACA-positive patients showed significantly worse survival than ACA/ATA-negative patients (log-rank p=0.041).
D) Survival comparison between ATA- and ACA/ATA-negative groups was not statistically significant (log-rank p=0.305).

Note: Survival curves reflect follow-up from ILD diagnosis. Tick marks represent censored observations. Group comparisons were assessed using the log-rank test.

Background/Purpose: Anticentromere antibody (ACA)-positive interstitial lung disease (ILD) in systemic sclerosis (SSc) is traditionally considered less aggressive than anti-topoisomerase I (ATA)-positive ILD. However, its clinical profile and prognosis remain poorly defined. We aimed to characterise ACA-associated SSc-ILD and compare it with other serological subsets.

Methods: Multicentre cross-sectional observational study including 76 ACA-positive SSc-ILD patients, who were compared with ATA-positive (n=54) and ACA/ATA-negative (n=147) groups.

Results: ACA-positive SSc-ILD patients developed ILD earlier than ATA-positive and ACA/ATA-negative individuals (2.5 vs. 5.6 and 3.5 years), although this difference was not statistically significant (p=0.389). Compared with the other groups, ACA-positive patients had higher %pFVC (96.3% vs. 83.5% and 86.9%; p=0.013), lower FEV1/FVC ratio (91.6% vs. 99.2% and 98.8%; p=0.004), and better functional capacity at ILD diagnosis, with fewer patients classified as NYHA class III–IV (14.5% vs. 42.6% and 32%; p=0.017). They also showed lower %pKCO (p=0.008) and a higher FVC/DLCO ratio (p=0.016), reflecting indolent microvascular damage and increased pulmonary vascular resistance. The different characteristics of the three serological groups are presented in table 1.

Worsening of ILD according to ATS criteria was observed in 14.5% of ACA-positive patients. Although no significant differences were found in antifibrotic therapy indication or advanced interventions, 2.6% of ACA-positive patients underwent lung transplantation and 2.6% received autologous haematopoietic stem cell transplantation. The characteristics of ACA-positive SSc-ILD patients are presented in table 2.

Overall survival analysis revealed no significant differences across the three groups (p=0.164), although ACA/ATA-negative patients showed better survival than ACA-positive patients (p=0.041; HR 0.498, p=0.045). The survival analysis is presented in Figure 1.

Conclusion: ACA-positive SSc-ILD does not seem to have a more favourable long-term prognosis compared with other serological subsets.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Valera Ribera: None; **J. ALEGRE SANCHO**: None; **I. Castellvi**: None; **M. Ibañez**: None; **J. Narváez**: None.

Abstract Number: 2475

GERD Severity, Proton Pump Inhibitor Use, and Longitudinal Forced Vital Capacity in the CONQUER Registry

Carrie Richardson[1], Shervin Assassi[2], Flavia Castelino[3], Lorinda Chung[4], Luke Evnin[5], Tracy Frech[6], Jessica Gordon[7], Faye Hant[8], Laura Hummers[9], Dinesh Khanna[10], Kimberly Lakin[7], Dorota Lebiedz-Odrobina[11], Yiming Luo[12], Ashima Makol[13], Maureen Mayes[14], Zsuzsanna McMahan[15], Jerry Molitor[16], Duncan Moore[17], Nora Sandorfi[18], Ami Shah[9], Ankoor Shah[19], Brian Skaug[20], Virginia Steen[21], Elizabeth Volkmann[22], Carleigh Zahn[23], John VanBuren[11] and Elana Bernstein[24], [1]Northwestern University, Chicago, IL, [2]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [3]Massachusetts General Hospital, Boston, MA, [4]Stanford University, Stanford, CA, [5]Scleroderma Research Foundation, Brisbane, CA, [6]Vanderbilt University Medical Center, Nashville, TN, [7]Hospital for Special Surgery, New York, NY, [8]Medical University of South Carolina, Charleston, SC, [9]Johns Hopkins Rheumatology, Baltimore, MD, [10]University of Michigan, Ann Arbor, MI, [11]University of Utah, Salt Lake City, UT, [12]Columbia University Irving Medical Center, New York, [13]Mayo Clinic, Rochester, MN, [14]UT Health Houston Division of Rheumatology, Houston, TX, [15]UT Health Houston, Houston, TX, [16]University of Minnesota, Minneapolis, MN, [17]Northwestern University, Chicago, [18]University of Pennsylvania, Philadelphia, PA, USA, Philadelphia, [19]Duke University, Durham, NC, [20]UTHealth Houston Division of Rheumatology, Houston, TX, [21]Georgetown University School of Medicine, Washington, DC, [22]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA, [23]University of Michigan, Ann Arbor, [24]Columbia University Irving Medical Center, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Gastroesophageal reflux disease may contribute to the progression of interstitial lung disease in systemic sclerosis (SSc). However, it is unclear whether reflux severity or treatment with proton pump inhibitors (PPIs) impacts longitudinal pulmonary function. The purpose of this study was to examine whether either reflux severity as measured by a validated gastrointestinal symptom questionnaire (UCLA SCTC GIT 2.0) or PPI use is associated with longitudinal pulmonary function in SSc.

Methods: Patients were included if they were enrolled in the CONQUER registry, met 2013 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for SSc, completed at least one UCLA SCTC GIT 2.0, and were not pregnant at CONQUER enrollment or during follow-up. We included patients who completed at least 1 pulmonary function test (PFT) for the baseline analysis and at least 2 PFTs for the longitudinal analysis. Baseline missingness and univariate mixed-effect longitudinal regression were used for variable selection to create a mixed-effect longitudinal regression model predicting longitudinal ppFVC using reflux severity on UCLA GIT 2.0 (none or mild, moderate, severe or very severe), PPI use, the interaction between PPI use and GERD severity, as well as appropriate adjustment variables (age, sex, race, disease duration at baseline, follow-up time, baseline modified Rodnan skin score, smoking status, SSc subtype [limited or diffuse], modified Rodnan skin score, scleroderma autoantibodies [Scl70, centromere, RNA Polymerase III, two subserologies, ANA negative, ANA only], and the presence of traumatic ulcers).

Results: One-thousand thirty-nine patients were included, of whom 187 (18.0%) had severe or very severe reflux and 255 (24.5%) had moderate reflux (Table 1). Baseline ppFVC was lower in patients with severe or very severe reflux compared to those with mild or no reflux (81.6% vs. 88.4%). Severe or very severe reflux was significantly associated with longitudinal ppFVC decline in the univariate analysis (-6.1, 95% CI -9.5 to -2.8; p=-0.002; Table 2) but not in the multivariable-adjusted analysis. PPI use was greatest in those with severe-very severe reflux and was independently associated with longitudinal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline patient demographics and clinical characteristics*

	Overall (N = 1019)	Reflux: None to Mild (N = 516)	Reflux: Moderate (N = 255)	Reflux: Severe to Very Severe (N = 187)
Age at baseline visit (years)	52.7 (13.5)	54.8 (13.7)	52.4 (12.7)	48.8 (12.8)
Female Sex	860 (82.8%)	417 (80.8%)	213 (83.5%)	167 (89.3%)
Race/ethnicity				
Hispanic	106 (10.2%)	40 (7.8%)	20 (7.8%)	33 (17.6%)
Non-Hispanic White	730 (70.3%)	379 (73.4%)	187 (73.3%)	113 (60.4%)
Non-Hispanic Black or African American	112 (10.8%)	46 (8.9%)	27 (10.6%)	31 (16.6%)
Non-Hispanic Asian	63 (6.1%)	39 (7.6%)	13 (5.1%)	7 (3.7%)
Years since first non-Raynaud's symptom at baseline	2.5 (1.4)	2.4 (1.4)	2.5 (1.4)	2.5 (1.3)
Years of follow-up since baseline visit				
No follow-up visits	170 (16.4%)	84 (16.3%)	43 (16.9%)	31 (16.6%)
6 months	120 (11.5%)	53 (10.3%)	37 (14.5%)	20 (10.7%)
1 - <2 years	189 (18.2%)	93 (18.0%)	35 (13.7%)	40 (21.4%)
2+ years	466 (44.9%)	243 (47.1%)	111 (43.5%)	78 (41.7%)
Diffuse cutaneous disease	683 (65.7%)	338 (65.5%)	171 (67.1%)	124 (66.3%)
Body Mass Index (BMI) (kg/m^2)	26.6 (6.0)	25.8 (5.2)	27.1 (6.4)	28.4 (7.1)
Never Smoker	698 (67.2%)	353 (68.4%)	172 (67.5%)	124 (66.3%)
Former Smoker	301 (29.0%)	153 (29.7%)	69 (27.1%)	55 (29.4%)
Current Smoker	40 (3.8%)	10 (1.9%)	14 (5.5%)	8 (4.3%)
Autoantibodies				
Centromere	190 (18.3%)	86 (16.7%)	46 (18.0%)	41 (21.9%)
Scl 70	259 (24.9%)	134 (26.0%)	59 (23.1%)	46 (24.6%)
RNA Polymerase III	226 (21.8%)	123 (23.8%)	50 (19.6%)	33 (17.6%)
Modified Rodnan Skin Score (mRSS)	12.1 (10.9)	12.4 (11.2)	12.0 (10.8)	12.1 (10.4)
ppFVC (from GLI calculator)	86.3 (18.9)	88.4 (17.9)	86.0 (18.4)	81.6 (20.6)
ppDLCO (from GLI calculator)	79.2 (26.2)	80.3 (24.8)	78.7 (24.6)	77.5 (32.0)
C-reactive protein (CRP)	2.4 (5.3)	2.1 (3.9)	2.6 (6.6)	3.3 (6.6)
ILD (ever)	512 (49.3%)	258 (50.0%)	125 (49.0%)	94 (50.3%)
Medications at baseline				
Immunomodulatory use	669 (64.4%)	310 (60.1%)	174 (68.2%)	129 (69.0%)
No prednisone	921 (88.6%)	468 (90.7%)	227 (89.0%)	155 (82.9%)
Prednisone <10 mg daily	58 (5.6%)	26 (5.0%)	16 (6.3%)	15 (8.0%)
Prednisone ≥10 mg daily	32 (3.1%)	10 (1.9%)	5 (2.0%)	12 (6.4%)
Prednisone no dose provided	28 (2.7%)	12 (2.3%)	7 (2.7%)	5 (2.7%)
Hydroxychloroquine	180 (17.3%)	84 (16.3%)	37 (14.5%)	43 (23.0%)
Mycophenolate	477 (45.9%)	211 (40.9%)	129 (50.6%)	98 (52.4%)
Methotrexate	78 (7.5%)	42 (8.1%)	21 (8.2%)	11 (5.9%)
Azathioprine	12 (1.2%)	8 (1.6%)	1 (0.4%)	2 (1.1%)
Tocilizumab	28 (2.7%)	10 (1.9%)	9 (3.5%)	5 (2.7%)
Rituximab	14 (1.3%)	7 (1.4%)	4 (1.6%)	3 (1.6%)
Cyclophosphamide	3 (0.3%)	1 (0.2%)	2 (0.8%)	0 (0.0%)
Anti-fibrotics (nintedanib or pirfenidone)	20 (1.9%)	7 (1.4%)	7 (2.7%)	4 (2.1%)
PPI use	496 (47.7%)	186 (36.0%)	150 (58.8%)	120 (64.2%)
H2 blocker use	138 (13.3%)	47 (9.1%)	42 (16.5%)	39 (20.9%)
Prometility use	23 (2.2%)	7 (1.4%)	3 (1.2%)	12 (6.4%)

*Results are listed as N/Total (%) or mean (SD)
ppFVC= forced vital capacity percent predicted, GLI=Global Lung Initiative, ppDLCO=diffusing capacity for carbon monoxide percent predicted

Table 2: Mixed-effect regression model estimates predicting longitudinal FVC percent predicted

	Univariate		Multivariable*	
	Effect (95% CI)	P-value	Effect (95% CI)	P-value
Age at baseline visit (years; odds ratio is for an increase of 10)	1.5 (0.6,2.4)	0.001	0.5 (-0.5, 1.5)	0.31
Follow up time since baseline (years)	-0.3 (-0.5, -0.2)		-0.4 (-0.6, -0.2)	<0.001
Disease duration from date of first non-Raynaud's symptom to baseline visit (years)	-0.1 (-1.0, 0.7)		-0.0 (-1.0, 0.9)	0.92
Sex		<0.001		0.040
Male	Reference		Reference	
Female	7.3 (4.0, 10.5)		3.6 (0.2, 6.9)	
Baseline reflux		0.002		0.22
None to Mild	Reference		Reference	
Moderate	-2.1 (-5.1, 0.8)		-0.9 (-5.3, 3.5)	
Severe to Very Severe	-6.1 (-9.5, -2.8)		-4.7 (-10.0, 0.6)	
Baseline PPI use	-4.9 (-7.4, -2.5)	<0.001	-4.2 (-7.7, -0.7)	0.018
Interaction between baseline PPI status and baseline reflux category		<0.001		>0.99
PPI use and Reflux: None to Mild/ No PPI use	Reference		Reference	
PPI use and Reflux: Moderate	-3.4 (-6.8, 0.0)		-0.1 (-6.0, 5.8)	
PPI use and Reflux: Severe to Very Severe	-7.5 (-11.3, -3.8)		0.3 (-6.5, 7.0)	

Includes a random intercept for each participant.
Predicting longitudinal FVC percent predicted using the baseline variables. All variables are either subject level or at baseline, with the exception of time to FVC measure.
FVC=forced vital capacity
*The multivariable model was also adjusted for baseline modified Rodnan skin score, baseline smoking status (never, former, or current), baseline body mass index, presence of trauma-associated digital ulcerations, SSc subtype (limited cutaneous SSc or diffuse cutaneous SSc), and scleroderma autoantibodies (ANA negative, two subserologies, anti-centromere antibodies, anti-Scl70 antibodies, RNA Polymerase III antibodies, ANA only)

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ppFVC decline in both the univariate (-4.9, 95% CI -7.5 to -2.5, p< 0.001) and multivariable-adjusted models (-4.2, 95% CI -7.7 to -0.7; p=0.018). The interaction between PPI use and GERD severity was significant in the unadjusted model (-7.5, 95% CI -11.3, -3.8; p< 0.001) but not in the multivariable-adjusted model.

Conclusion: Severe or very severe reflux was associated with longitudinal ppFVC decline in univariate analysis, but the association was not statistically significant after adjustment for other variables. PPI use was an independent risk factor for ppFVC decline even after adjustment for GERD symptom severity. Use of PPI in patients with SSc may reflect greater esophageal dysmotility or aspiration risk, independent of GERD symptom severity. Alternatively, PPI use may directly contribute to ppFVC decline, possibly by reducing the concentrations and effectiveness of immunosuppressive medications or increasing pulmonary infection risk.

Disclosure: C. Richardson: Cabaletta Bio, 2; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **L. Evnin**: None; **T. Frech**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **F. Hant**: None; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **K. Lakin**: None; **D. Lebiedz-Odrobina**: None; **Y. Luo**: None; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **J. Molitor**: None; **D. Moore**: AstraZeneca, 5; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 1, Johnson & Johnson, 1, 2, Novartis, 1; **A. Shah**: None; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **B. Skaug**: None; **V. Steen**: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **C. Zahn**: None; **J. VanBuren**: None; **E. Bernstein**: AstraZeneca, 5, aTYR, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2.

Abstract Number: 2476

Blinatumomab in rapid progressive systemic sclerosis

Christina Gebhardt[1], Franziska Szelinski[2], Hector Rincon-Arevalo[2], Giulia Magno[3], Veit Buecklein[3], Gerulf Haenel[4], Gerhard Zugmaier[5], Michael von Bergwelt[3], Marion Subklewe[3], Thomas Dörner[6], Alla Skapenko[7] and Hendrik Schulze-Koops[7], [1]LMU Hospital, Division for Rheumatology and Clinical Immunology, München, Germany, [2]Charite Universitätsmedizin Berlin, Germany, Berlin, Germany, [3]LMU Klinikum, Med. Klinik und Poliklinik III, Munich, Germany, [4]LMU Gene Center, Munich, Germany, [5]Amgen, Munich, Germany, [6]Charite Universitätsmedizin Berlin, Germany and DRFZ, Berlin, Berlin, Germany, [7]LMU Hospital, Division for Rheumatology and Clinical Immunology, Munich, Bayern, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic sclerosis is a severe, potentially fatal disease, characterized by progressive fibrosis of skin and internal organs. Blinatumomab is a bispecific CD3/CD19-T-cell engager (BiTe) approved for treatment of relapsing/refractory Philadelphia chromosome negative, CD19-positive B-precursor-acute lymphocytic leukemia.

Methods: After our first case of blinatumomab for acute progressive systemic sclerosis despite conventional therapy, we now report of our cohort of up to date four BiTe treated patients.

Results: All patients showed rapidly progressive skin fibrosis as well as internal organ involvement, namely myocardial fibrosis in our first patient and pulmonary fibrosis in the other three. We administered four cycles of blinatumomab in our first two patients and two cycles with higher daily dose in the other two patients due to good initial results and low grade toxicity. All patients reported of rapid improvement of skin symptoms with a decrease of the Rodnan Skin Score score from (range) 20 to 5 at our last follow-up. Furthermore we could demonstrate receding cardial as well as pulmonary fibrosis, as seen in imaging (cardiac MRI) and lung function tests (increase of DLCOs by up to 11 %). In all patients, peripheral B cell counts declined completely from the first day of treatment with recovery to normal levels within weeks after treatment. Peripheral T cells were significantly reduced on the first day of treatment, but quickly recovered to normal levels and remained stable during subsequent cycles. IgG and Scl 70 ab levels temporarily decreased after treatment. Remarkably, with the exception of a transient neutropenia in one of the four patients, there were no significant adverse events, in particular ICANs, CRS or infections.

Conclusion: Blinatumomab resulted in profound B-cell depletion and a significant decrease in serum IgG with no increased susceptibility to infections. Clinically, the therapy led to a rapid and sustained improvement in symptoms. Further studies are needed to determine the value of B-cell depleting therapy with blinatumomab in systemic sclerosis.

Disclosure: C. Gebhardt: AbbVie/Abbott, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 2, 6, Janssen, 6, UCB, 1, 6; **F. Szelinski**: None; **H. Rincon-Arevalo**: None; **G. Magno**: None; **V. Buecklein**: None; **G. Haenel**: None; **G. Zugmaier**: Amgen, 3; **M. von Bergwelt**: None; **M. Subklewe**: None; **T. Dörner**: AbbVie, 5, 12, Consulting fees, Celgene, 5, 12, Consulting fees, Deutsche Forschungsgemeinschaft, 5, Eli Lilly, 5, 12, Consulting fees, EMD Merck Serono, 5, 12, Consulting fees, EU Horizon2020 Harmonic SS, 5, Gilead/Galapagos, 12, Consulting fees, GlaxoSmithKlein(GSK), 5, 12, , EMD Merck Serono, Janssen, 5, 12, EMD Merck Serono, Novartis, 5, 12, , EMD Merck Serono, Roche, 5, 12, EMD Merck Serono, Sanofi, 5, UCB, 5; **A. Skapenko**: None; **H. Schulze-Koops**: AbbVie, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Amgen, 12, Research support and principal investigator (clinical trials funds to institution), Biogen Idec, 12, Research support and principal investigator (clinical trials funds to institution), Boehringer Ingelheim, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Bristol Myers Squibb, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Eli Lilly, 6, 12, Research support and principal investigator (clinical trials funds to institution), Galapagos, 2, GSK, 12, Research support and principal investigator (clinical trials funds to institution), Janssen, 6, Janssen-Cilag, 12, Research support and principal investigator (clinical trials funds to institution), Merck Sharp & Dohme, 6, 12, Research support and principal investigator (clinical trials funds to institution), Novartis, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Pfizer, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution), Roche, 12, Research support and principal investigator (clinical trials funds to institution), Sandoz-Hexal, 6, 12, Research support and principal investigator (clinical trials funds to institution), Sanofi, 6, 12, Research support and principal investigator (clinical trials funds to institution), UCB, 2, 6, 12, Research support and principal investigator (clinical trials funds to institution).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2477

Current treatment Strategies in Systemic Sclerosis- Interstitial Lung Disease Patients: Real-World Insights from the EUSTAR Cohort (CP138)

Corrado Campochiaro[1], Marie-Elise Truchetet[2], Madelon Vonk[3], Giacomo De Luca[4], Giovanna Cuomo[5], Lidia P Ananieva[6], Eric Hachulla[7], Vanessa Smith[8], Ana Maria Gheorghiu[9], Radim Bečvář[10], Patricia E. Carreira[11], Nicolas Hunzelmann[12], Daniel Furst[13], Vera Ortiz-Santamaria[14], Francesco Del Galdo[15], Marco Matucci-Cerinic[16], Anna-Maria Hoffmann-Vold[17] and EUSTAR, [1]IRCCS San Raffaele Hospital. Vita-Salute San Raffaele University, Milan, Milan, Italy, [2]Bordeaux University Hospital, Bordeaux, France, [3]Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, [4]Vita-Salute San Raffaele University & IRCCS San Raffaele Hospital, Milan, Italy, [5]Department of Precision Medicine, University Hospital Luigi Vanvitelli, Naples, Italy, Naples, Italy, [6]A Nasonova Institute of Rheumatology, Moscow, Russian Federation, Moscow, Russia, [7]University of Lille, LILLE, France, [8]Ghent University Hospital, Gent, Belgium, [9]Spitalul Clinic Dr. Ion Cantacuzino, Bucharest, Romania, [10]Department of Internal Medicine, Charles University, Prague, Czech Republic, [11]Hospital Universitario 12 de Octubre, Madrid, Spain, [12]Department of Dermatology and Venereology, University Hospital Cologne, Cologne, Germany, [13]Southern California Scleroderma and Rheumatology Center, Los Angeles, CA, [14]HOSP. GENERAL DE GRANOLLERS, Barcelona, Spain, [15]University of Leeds, Leeds, United Kingdom, [16]University San Raffaele Milano, Milano, Milan, Italy, [17]Oslo University Hospital, Oslo, Norway

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The therapeutic landscape for systemic sclerosis- interstitial lung disease (SSc-ILD) has rapidly evolved over the past decade, with increasing adoption of immunosuppressive (IST) and anti-fibrotic therapies. However, real-world data on current treatment strategies, including combination regimens, treatment switches, and clinical predictors for treatment decisions, remain limited. This study aims to characterize treatment patterns and their clinical drivers in the contemporary era using the EUSTAR database.

Methods: We analyzed SSc-ILD patients from the EUSTAR registry first assessed since ^{3} 2017. Treatment courses were defined as any use of IST and/or anti-fibrotic drugs ^{3}3 months. Treatment strategies were classified as: (1) switch: change from one therapy to another during follow-up; (2) discontinuation: stopping a primary therapy without initiating another; (3) unmodified: no changes during follow-up; (4) combination: concurrent use of ^{3} 2 drugs. Frequency and combinations of therapies were described. Logistic regression analyses were used to identify clinical factors associated with treatment strategies.

Results: Among 277 patients, 159 (57%) received IST and/or anti-fibrotic therapy since their first evaluation, Table 1. Multivariable analysis showed that shorter disease duration (OR 0.991, 95% CI 0.987–0.996, p< 0.001) and presence of myositis (OR 9.93, 95% CI 1.94–51.76, p=0.006) were associated with treatment initiation. The different treatment courses are summarized in Figure 1 and grouped according to the 4 most used IST: mycophenolate mofetil (total courses 377, panel A), methotrexate (total courses 187, panel B), rituximab (total courses 257, panel C) and tocilizumab (total courses 122, panel D). A total of 213 treatment switches occurred (see Figure 2). Higher mRSS (OR 1.031, 95% CI 1.002 – 1.062, p = 0.035) and arthritis (OR 3.034, 95% CI 1.551 – 5.936, p = 0.001) were associated with treatment switching in multivariable logistic regression. Younger age (OR 0.968, 95% CI 0.953 – 0.985, p < 0.001), higher dyspnea class (OR 1.557, 95% CI 1.189 – 2.039, p = 0.001), and inflammatory arthritis (OR 2.560, 95% CI 1.354 – 4.840, p = 0.004) were associated with combination therapy. No predictor was associated with treatment discontinuation.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical features of SSc-ILD patients treated at first-time assessment in year ≥ 2017.

Time Period	≥ 2017 (n = 159)
Age (SD)	55.8 (11.8)
Male (%)	45 (28.3)
Disease Duration (months), median (IQR)	53.5 (18.0 – 95.0)
%pDLCO (SD)	59.4 (19.1)
%pFVC (SD)	81.4 (21.0)
Known smoking status	128
Ever smoker (%)	47 (36.7)
Known skin involvement status	79
Sine scleroderma (%)	6 (7.6)
Limited cutaneous (%)	27 (34.2)
Diffuse cutaneous (%)	46 (58.2)
Esophageal symptoms (%)	106/157 (67.5)
Stomach symptoms (%)	35/156 (22.4)
Intestinal symptoms (%)	33/156 (21.1)
Scleroderma Renal Crisis (%)	1 (0.6)
Digital Ulcers (%)	69/155 (44.5)
Inflammatory Arthritis (%)	19/156 (12.2)
Myositis (%)	23/158 (14.5)
PAH (%)	0/33 (0)
Known antibodies status	148
Anti-centromere (%)	8 (5.4)
Anti-topoisomerase (%)	94 (63.5)
Anti-RNA-polymeraseIII (%)	13 (8.7)

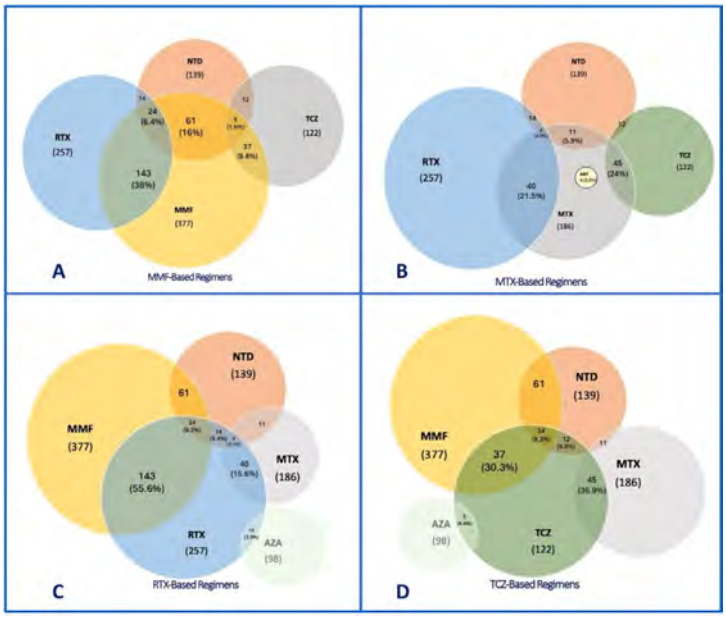


Figure 1. Treatment courses according to the DMARD-based regimen (panel A mycophenolate mofetil-based courses; panel B methotrexate-based courses; panel C rituximab-based courses and panel D tocilizumab-based courses).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

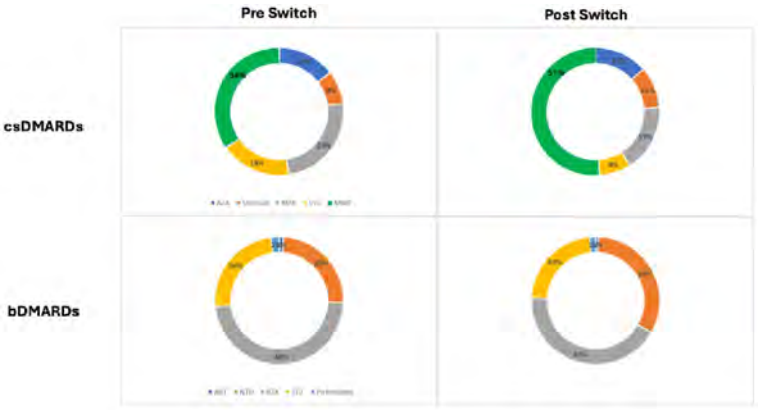


Figure 2. The use of csDMARD and bDMARDs in SSc-ILD patients switching therapies.

Conclusion: In current clinical practice, a considerable amount of SSc-ILD patients is treated. Treatment decisions are influenced not only by lung function but also by systemic features such as arthritis and myositis. Combination strategies and treatment modifications are frequently used in SSc-ILD, reflecting a more individualized approach. These findings have important implications for future trial design and highlight the urgent need for evidence-based guidance on combination and sequential therapies.

Disclosure: C. Campochiaro: Boehringer-Ingelheim, 6, Janssen, 6, Novartis, 6; **M. Truchetet**: AbbVie/Abbott, 2, 12, travel grants, Boehringer-Ingelheim, 2, Eli Lilly, 2, 6, Galapagos, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 2, UCB, 2; **M. Vonk**: Boehringer-Ingelheim, 2, 6, 12, Travel grants, Janssen, 2, 6, 12, travel grants, Merck/MSD, 6; **G. De Luca**: Boehringer-Ingelheim, 6, Janssen, 6; **G. Cuomo**: None; **L. Ananieva**: None; **E. Hachulla**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, Pfizer, 5, Roche-Chugai, 5, Sanofi-Genzyme, 2, 5, Sobi, 5; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **A. Gheorghiu**: Boehringer-Ingelheim, 6, Foundation for research in Rheumatology (FOREUM), 5; **R. Bečvář**: None; **P. Carreira**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, Emmerald Health Pharmaceuticals, 2, 6, Janssen, 2, 6, Mitsubishi Tanabe, 2, 6, Novartis, 2, 6, Prometheus, 2, 6; **N. Hunzelmann**: None; **D. Furst**: AbbVie/Abbott, 2, 5, Actelion, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cytori, 2, NIH, 5, Novartis, 2, 5, Pfizer, 2, 2, 5, 5, Roche-Genentech, 2, 5; **V. Ortiz-Santamaria**: None; **F. Del Galdo**: AbbVie/Abbott, 2, 5, argenx, 2, 5, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Calluna, 2, 5, Deepcure, 2, 5, Engitix, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Merck/MSD, 2, 5, Miltenyi, 2, 5, Mitsubishi-Tanabe, 2, 5, Novartis, 2, 5, Ono, 2, 5, Quell, 2, 5, RelationX, 2, 5, Serono, 2, 5, Syntara, 2, 5, Ventus, 2, 5, ZuraBio, 2, 5; **M. Matucci-Cerinic**: None; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2.

Abstract Number: 2478

Endothelial Cell Biomarker Expression Suggests Increased Cell Adhesion in Juvenile SSc, Increased Cytokine Expression in JDM, and an Intermediate Phenotype in Overlap Syndrome Patients

Daniel Barnett[1], Alyssa Rosek[2], Yi-Chen Chen[3], Alexander Cai[4], Deren Esencan[5], Sophia Matossian[6], Christine Goudsmit[7], Haley Havrilla[8], Anwesha Sanyal[9], Julie Sturza[10], Pei-Suen Tsou[6], Kathryn Torok[9] and Jessica Turnier[11], [1]Division of Pediatric Rheumatology, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, Pittsburgh, PA, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, ANN ARBOR, MI, [4]Division of Rheumatology,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [5]1. Division of Pediatric Rheumatology, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, Pittsburgh, PA, [6]University of Michigan, Ann Arbor, MI, [7]University of Michigan, Ann Arbor, [8]Division of Pediatric Rheumatology, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, Pittsburgh, PA, [9]University of Pittsburgh, Pittsburgh, PA, [10]Division of Pediatric Rheumatology, CS Mott Children's Hospital, University of Michigan, Ann Arbor, MI, Ann Arbor, MI, [11]University of Michigan, Saline, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Vasculopathy is a central driving clinical, histopathologic and pathogenic feature of juvenile systemic scleroderma (jSSc), juvenile dermatomyositis (JDM) and juvenile scleroderma-overlap syndrome (jOverlap). While we recognize distinct clinical patterns of vasculopathy between diseases and disease states, we lack a complete understanding of underlying pathomechanisms driving vasculopathy. In this study, we evaluated endothelial cell (EC) dysregulation markers in a cohort of jSSc, JDM and Overlap patients to identify common and disease-specific biomarkers of vasculopathy that may reflect underlying pathophysiology and disease activity.

Methods: Sixteen biomarkers of EC dysregulation were assessed in plasma from patients with jSSc (n=39), JDM (n=50), jOverlap (n=22) and age-matched controls (n=41) using customized LegendPlex kits from Biolegend, and collected via flow cytometry using Sony ID7000 and Cytek Aurora instruments. The Ang 1/2 ratio was calculated as a surrogate marker of vascular health. Clinical data were obtained from the National Registry of Childhood Onset Scleroderma (NRCOS) and the University of Michigan JDM cohort, including disease activity outcomes in jSSc (clinical assessment and modified Rodnan skin score-mRSS), disease-associated antibody status, and disease type. Biomarker levels were normalized using Z-scores with group differences analyzed by ANOVA, Tukey's tests, and Kruskal-Wallis, and mRSS correlations assessed via Spearman's rho.

Results: Angiogenesis signaling markers Ang1 and Ang 1/2 ratio were significantly elevated in jSSc, while Ang2 and Tie2 were increased in JDM (Fig 1, Table 1). Inflammatory cytokine CXCL10 was significantly higher in JDM and jOverlap patients compared to jSSc and controls. Glycan-binding Gal-9 levels were highest in JDM, followed by jOverlap and then jSSc, while E-selectin showed a similar but less pronounced pattern. Cell adhesion molecules PECAM-1 and VCAM-1 were elevated in jSSc and jOverlap patients, as was ICAM-1, which was particularly elevated in active relative to inactive jSSc samples.

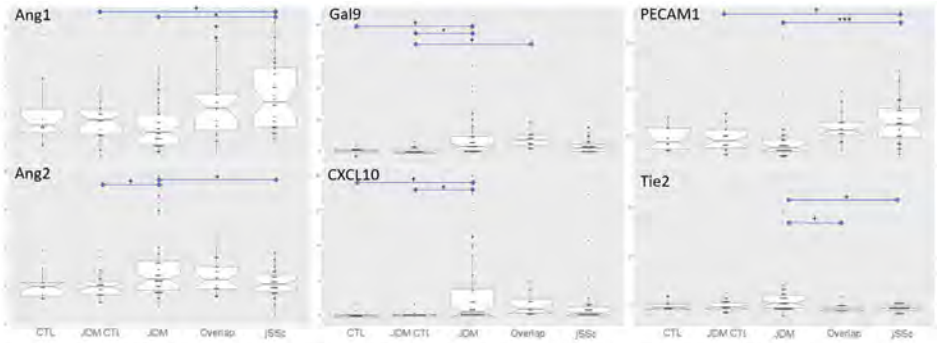


Figure 1. Angiogenesis-related markers show significant changes in the Ang1/2-Tie2 axis. Ang1 is significantly increased in jSSc vs JDM and control, while Ang2 shows a significant increase in JDM vs. jSSc. Gal9 shows significant increases in JDM and overlap patients. IFN-mediated CXCL10 shows significant increase in JDM with trended increases in overlap and jSSc. Cell-cell adhesion molecule PECAM1 was significantly increased in jSSc over JDM with overlap showing an intermediate expression. Tie2 (Ang2 receptor) shows a significant increase in JDM vs overlap and jSSc patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

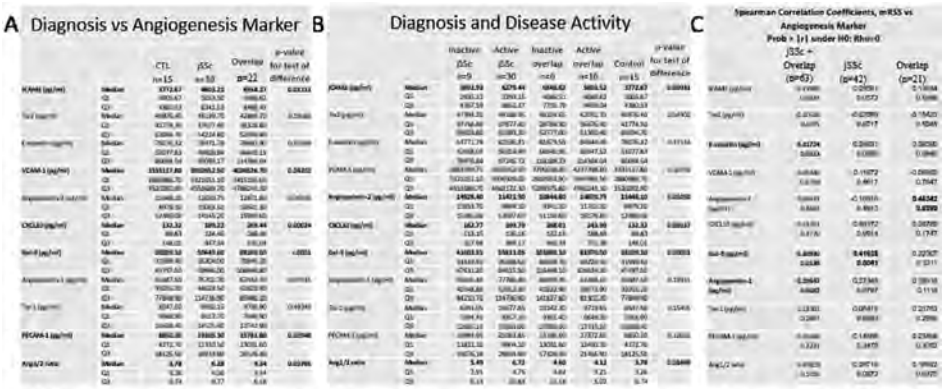


Table 1. Angiogenesis biomarker expression by diagnosis and physician-assessed global and skin-scored disease activity. A. Juvenile systemic scleroderma (jSSc, n=42) and overlap syndrome (n=21) show significant differences from age-matched controls (n=15) for expression of ICAM1, VCAM-1, CXCL10, Gal-9, PECAM-1, and Ang1/2 ratio. PECAM-1 and Ang1/2 ratio show greater expression in jSSc than overlap, while the remaining markers show greater increase in overlap patients. B. Similar changes are observed in physician-assessed inactive vs active samples, particularly CXCL10 and Gal-9 that show greater increase in overlap patients than jSSc, while Ang1/2 ratio shows greater increase in both active and inactive jSSc patients. Ang-2 demonstrates greater increase in inactive jSSc and active overlap disease. C. Spearman's Correlation Coefficients were tested for mRSS (i.e. a disease activity measure) association with angiogenesis biomarkers showing association with Gal-9 in jSSc and pooled patients, Ang-2 in overlap patients, and Ang-1 in pooled patients. E-Selectin also showed significant association with pooled patients.

Myositis Associated Antibodies

		negative	anti-RNP	anti-PM/Scl	anti-topoisomerase (Scl-70)	ANA	P-value for test of difference
ICAM1 (pg/ml)	Median	3655.94	4336.98	6061.83	4710.04	4160.16	0.25941
	Q1	2319.62	2656.33	4714.53	3114.19	3692.93	
	Q3	6612.99	6341.70	10634.13	7524.72	4367.59	
Tie2 (pg/ml)	Median	41180.05	49310.60	45495.90	43120.35	56828.80	0.83420
	Q1	31811.50	31855.50	39213.00	36653.05	48374.50	
	Q3	54921.70	52777.00	60445.10	55895.80	56828.80	
E-selectin (pg/ml)	Median	64979.36	98099.17	87834.36	67140.60	59436.75	0.27601
	Q1	49389.10	78723.42	66843.15	37729.54	54771.79	
	Q3	86825.52	114384.04	116189.23	104304.37	78976.84	
VCAM-1 (pg/ml)	**Median**	**2667571.25**	**3415155.60**	**4482111.45**	**4321453.85**	**3121051.10**	**0.00284**
	Q1	1939966.65	2327030.80	3648519.70	3677768.50	3135485.50	
	Q3	3162291.60	3845088.00	5293975.80	4703958.50	4213817.40	
Angiopoietin-2 (pg/ml)	Median	10829.20	13292.80	13556.25	12269.45	14405.20	0.52262
	Q1	9924.65	11048.30	10880.60	10919.70	14145.20	
	Q3	12839.30	17846.20	15994.60	14757.85	15395.60	
CXCL10 (pg/ml)	**Median**	**242.11**	**121.29**	**553.73**	**179.99**	**317.98**	**0.00951**
	Q1	114.89	100.82	246.19	129.58	250.42	
	Q3	404.88	218.52	1011.57	237.75	317.98	
Gal-9 (pg/ml)	**Median**	**44085.65**	**55674.30**	**106385.75**	**51557.20**	**47340.30**	**0.01455**
	Q1	37524.80	36906.20	70846.20	45851.95	47340.30	
	Q3	111588.00	71072.80	113624.00	61621.85	54684.80	
Angiopoietin-1 (pg/ml)	Median	59112.50	113763.50	63434.15	66768.40	94210.70	0.7753
	Q1	42674.75	94829.80	46487.40	41045.55	78246.10	
	Q3	92194.45	120984.30	85980.20	96769.65	94210.70	
Tie-1 (pg/ml)	Median	9484.05	7861.80	11751.45	9521.60	10665.10	0.93642
	Q1	6440.40	5815.30	8298.50	6648.20	4764.00	
	Q3	29546.60	22851.30	16189.80	14857.55	15595.00	
PECAM-1 (pg/ml)	Median	11182.80	26552.20	19850.70	18981.50	11821.10	0.34160
	Q1	3690.75	19076.10	13081.60	11012.30	11821.10	
	Q3	29615.60	51579.10	29082.30	29533.75	18885.10	
Ang1/2 ratio	Median	5.34	7.50	4.48	5.19	6.12	0.70787
	Q1	3.68	4.89	4.02	2.71	4.86	
	Q3	8.67	9.76	6.10	9.08	6.12	

Table 2. Myositis-associated Antibodies were associated with angiogenesis biomarker changes. VCAM-1, CXCL10, and Gal-9 were all significantly increased in PM/Scl+ patients and each except CXCL10 was also significantly increased in Scl-70+ patients.

Among antibody-defined subsets, PM-Scl+ and Scl-70+ patients showed notable increases in Gal-9 and VCAM-1, and PM-Scl+ patients also showed increased CXCL10 expression.

Conclusion: Distinct angiogenic patterns are observed in JDM and jSSc patients, with jOverlap having a unique profile between both conditions. The Ang1/2-Tie2 axis is inverse between JDM and jSSc, and differs from prior adult scleroderma data. This may suggest earlier disease or unique disease progression in pediatric patents. Increased Gal-9 and CXCL10 expression in JDM and overlap patients, versus prominent cell adhesion molecule expression in jSSc, may define differential biomarker signatures and offer new tools for assessing disease activity and therapeutic response.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: D. Barnett: None; **A. Rosek**: None; **Y. Chen**: None; **A. Cai**: None; **D. Esencan**: None; **S. Matossian**: None; **C. Goudsmit**: None; **H. Havrilla**: None; **A. Sanyal**: None; **J. Sturza**: None; **P. Tsou**: None; **K. Torok**: None; **J. Turnier**: Cabaletta Bio, 2.

Abstract Number: 2479

REMS technology 5-y Imminent Fracture Risk in Systemic Sclerosis.

Fiorella Anna Lombardi[1], **Edmund J MacLaughlin**[2], Marco Di Paola[1], Maurizio Muratore[3], Kathleen Methric[4], Gianmarco Del Vecchio[5], Giusy Peluso[6], Ernesto Casciaro[1], Andrea Claudio Ştețco[7], Francesco Conversano[1], Paola Pisani[1] and Sergio Casciaro[1], [1]Institute of Clinical Physiology, National Research Council, Lecce, Puglia, Italy, [2]Rheumatology Associates of Delmarva and BoneVue Diagnostics, Easton, MD, [3]ASL- LE, "Vito Fazzi" Hospital, Lecce, Puglia, Italy, [4]BoneVue Diagnostics, Catonsville, MD, [5]Department of Research and Development, Echolight S.p.a., Lecce, Puglia, Italy, [6]Department of Innovative Engineering, University of Salento, Lecce, Puglia, Italy, [7]Department of Biological and Environmental Sciences and Technologies, University of Salento, Lecce, Puglia, Italy

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SS) is a rare connective tissue disorder characterized by progressive fibrosis of the skin and internal organs, including lungs, heart and kidneys. Furthermore, SS may increase osteoporosis risk due to chronic inflammatory state, malabsorption/malnutrition, limited mobility and use of corticosteroids therapy. Currently, emerging evidences suggest that SS might represent an independent factor for low BMD, further compromising skeletal health. Additionally, SS patients generally present with overlapping comorbidities, such as rheumatoid arthritis, hypercholesterolemia, hypothyroidism, etc., which may further exacerbate fracture risk (FR) and overall health outcomes. Given the fragile health status of this population, early identification of skeletal fragility is essential for optimal patient management and improved quality life. For this, the present study aims to assess the impact of SS on imminent (within 5 y) FR using Radiofrequency Echographic Multi Spectrometry (REMS) technology, by comparing patients either with SS alone and with SS plus additional comorbidities. A secondary aim is to explore the contribution of comorbidities to increased FR.

Methods: The 5-y FR analysis was assessed by combining both quantitative (BMD, T- and Z-score) and qualitative (bone microarchitecture via Fragility Score, FS) data. REMS technology automatically provides a risk classification system consisting of 7 increasing risk levels, named from R1 to R7, each corresponding to a defined probability of imminent FR. To ascertain the impact of comorbidities on the likelihood of experiencing an incident fracture, a logistic regression was performed.

Results: A cohort of 91 Caucasian patients (both genders) either affected by SS (n = 64, median age: 64.3 yo, 42.2% women < 65 yo) or by SS + other comorbidities (n = 27, median age: 69 yo, and 33.3% women < 65 yo) underwent spinal REMS scan. The FR analysis at major osteoporotic fracture showed that SS patients were classified as follows: R1 (9.3%), R3 (42.2%), R4 (1.6%), R5 (20.3%), R6 (6.3%) and R7 (20.3%). Likewise, SS + comorbidities showed a similar distribution across the 7 classes: 3.7% (R1), 48.2% (R3), 7.4% (R4), 18.5% (R5), 3.7% (R6) and 18.5% (R7). Likewise, the T-score and FS analyses showed similar values between the SS (T-score: -2.2 ± 0.8 and FS: 41.4 ± 19.9; mean ± SD) and SS + comorbidities (T-score: -2.3 ± 0.7 and FS: 43.8 ± 20.4; mean ± SD). Logistic regression did not show any significant association between SS or SS + comorbidities and increased FR, thus indicating that the overlap of other pathological conditions does not exacerbate an already altered skeletal health status.

Conclusion: In conclusion, in our study SS alone appeared to be the primary factor contributing to compromised bone quality and quantity. These findings underscore the importance of early bone health assessment and monitoring in SS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

patients through REMS technology, particularly given the potential for skeletal fragility even in the absence of additional comorbidities. Clinical studies focusing also on exploring the impact of a single comorbidity rather than grouped multiple factors are ongoing to assess how each comorbidity influences fracture skeletal risk in SS patients.

Disclosure: F. Lombardi: None; **E. MacLaughlin**: None; **M. Di Paola**: None; **M. Muratore**: None; **K. Methric**: None; **G. Del Vecchio**: None; **G. Peluso**: None; **E. Casciaro**: None; **A. Şteţco**: None; **F. Conversano**: None; **P. Pisani**: None; **S. Casciaro**: None.

Abstract Number: 2480

Respiratory Muscle Weakness in a Systemic Sclerosis Cohort

Fabian Mendoza[1], Wendy Perdomo[2], Timothy Wilson[1] and Sergio Jimenez[1], [1]Thomas Jefferson University, Philadelphia, PA, [2]Thomas Jefferson University Hospital, Philadelphia, PA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a complex autoimmune disorder marked by vascular damage, immune dysregulation, and fibrosis. Lung involvement, particularly interstitial lung disease (ILD), carries high morbidity and mortality. Respiratory muscle weakness (RMW), though underrecognized in SSc, may contribute to pulmonary function decline independent of parenchymal involvement. Standard pulmonary function tests (PFT) measurements, such as forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO), may decline in patients with RMW, complicating ILD assessment. Diagnostic tools, including maximal inspiratory pressure (MIPs) and diaphragmatic ultrasound, are used to diagnose RMW. This study aims to investigate the prevalence of RMW in a SSc US population, describe the phenotype of patients with RMW, and examine the association of the proposed measurement of RMW with lung volumes and DLCO consecutive patients with SSc. We also correlate RMW with other measurements of sarcopenia in a subpopulation.

Methods: We examined PFTs measurements of RMW in 100 consecutive patients at the Jefferson Scleroderma Center at Thomas Jefferson University. Clinical phenotype, SSc-specific antibodies, MIPs, MEPs, FVC, DLCO, and the presence of ILD at HRCT were studied. We defined RMW as a MIP of less than 50%. Measurements of sarcopenia, including hand dynamometer, fast walking test, and bioimpedance, were correlated in a subgroup of patients.

Chi-square was used to compare categorical variables. Spearman's rho correlation was used to test for significant associations amongst the parameters of interest. Statistical significance was assumed at an alpha value of 0.05.

Results: From 100 SSc patients, 86 had complete PFTs data and were included for analysis. Nine patients (10.47%) were identified to have RMW at the predetermined value. In these patients, 40% displayed limited phenotype, 40% diffuse, and 10%. Sine Scleroderma versus a 25.9% of diffuse phenotype in the patients without RMW (p=0.07). Creatine Kinase value was (120.4 ±89.8 U/L) [20-458] with no difference with SSc patients with no RMW. Only one patient in the RMW group had the diagnosis of myositis. SSA/RO-52 was the most prevalent autoantibody in patients with RMW (3/9). 33.3% of the RMW-SSc patients (3/9) did not have ILD, and 44.4% (4/9) presented less than 10% of parenchymal involvement at HRCT. MIP values directly correlate with MEP (rs = 0.31, p = 0.031), and FVC (rs = 0.29, p = 0.043). No conclusive correlation was found with measurements of generalized sarcopenia.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: RMW is prevalent in more than 10% of patients with SSc in this cohort. Diffuse phenotype and +Ro52 are more prevalent in SSc-RMW. The myositis phenotype was not commonly seen in these patients. A direct correlation between MIPs values and FVC was found. Raising awareness and identifying this phenotype opens the possibility for pharmacological and non-pharmacological therapeutic interventions. Correlation with FVC is of particular importance and requires further study since it is one of the most used values for disease progression in clinical practice and clinical research.

Disclosure: F. Mendoza: None; **W. Perdomo**: None; **T. Wilson**: None; **S. Jimenez**: None.

Abstract Number: 2481

Prevalence and Trends of Suicidal Ideation Among Hospitalized Adults with Systemic Lupus Erythematosus (SLE): A National Inpatient Sample Analysis (2016–2020)

Fatima Khdeir and Aysheh Khdeir, ECU Health Medical Center, Greenville, NC

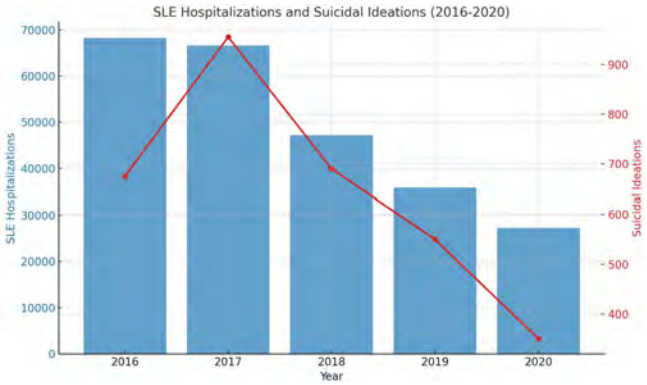
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease associated with psychiatric comorbidities, including depression and suicidal ideation. However, national trends over time have not been fully characterized.

Methods: We conducted a retrospective cross-sectional analysis using NIS data from 2016–2020. Adult patients (age ≥18) diagnosed with SLE were identified using ICD-10 codes. Suicidal ideation was detected using diagnosis code R45.851. Weighted survey procedures were applied for national estimates. Secondary outcomes included age, sex, race, and psychiatric comorbidities such as generalized anxiety disorder, depression, bipolar disorder, and psychotic disorders.

Results: The total weighted number of SLE hospitalizations from 2016 to 2020 was approximately 245,300 patients. Among these, 1.31% had documented suicidal ideation. Patients with suicidal ideation were notably younger, with a mean age of 42.1 years, compared to 47.3 years among those without ($p < 0.001$). No significant differences were observed between males and females. However, there were clear racial disparities, with White patients accounting for the highest



SLE hospitalizations (blue bars) Suicidal ideations (red line) From 2016 to 2020.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

proportion of suicidal ideation cases (53.6%). Psychiatric comorbidities—including anxiety disorders, bipolar disorder, psychotic disorders, and substance abuse—were all significantly associated with increased suicidal ideation ($p < 0.001$). Trend analysis revealed that suicidal ideation cases rose from 675 in 2016 to a peak of 955 in 2017, before steadily declining to 350 in 2020. During the same period, overall SLE hospitalizations also showed a decreasing trend.

Conclusion: Although the overall rate of suicidal ideation among hospitalized SLE patients remains low, psychiatric comorbidities significantly increase risk. After a peak in 2017, a decreasing trend was observed through 2020, likely due to improved psychiatric screening, advances in SLE treatment, multidisciplinary care approaches, and increased recognition of neuropsychiatric risk factors.

Disclosure: F. Khdeir: None; **A. Khdeir**: None.

Abstract Number: 2482

Characterizing Gastrointestinal Involvement in Systemic Sclerosis: Insights from the National Systemic sclerosis Progression INvestiGation (SPRING) Registry of the Italian Society of Rheumatology

Francesco Bonomi[1], Cosimo Bruni[2], Silvia Laura Bosello[3], Fabio Cacciapaglia[4], Corrado Campochiaro[5], Roberto Caporali[6], Veronica Codullo[7], Maria Antonietta D'Agostino[8], Lorenzo Dagna[9], Rossella De Angelis[10], Giacomo de Luca[11], Dilia Giuggioli[12], Serena Guiducci[13], Florenzo Iannone[14], Francesca Ingegnoli[15], Carlomaurizio Montecucco[7], Valeria Riccieri[16], Clodoveo Ferri[17], Marco Matucci-Cerinic[18], Silvia Bellando Randone[19], on behalf of the SPRING-SIR Group, [1]University Hospital Careggi, Florence, Florence, Toscana, Italy, [2]University of Zurich, Zurich, Switzerland, [3]Division of Rheumatology and Clinical Immunology - Catholic University of the Sacred Heart, Rome, Italy, Rome, Italy, [4]Rheumatology Unit DiMePRe-J, University and AOU Policlinico of Bari & Department of Medicine LUM \"G. De Gegnnaro\" University, Casamassima (Bari) - Italy, Bari, Italy, [5]IRCCS San Raffaele Hospital. Vita-Salute San Raffaele University, Milan, Milan, Italy, [6]University of Milan and ASST Gaetano Pini-CTO, Milano, Italy, [7]Policlinico San Matteo, Pavia, Pavia, Italy, [8]Catholic University of the Sacred Heart, Rome, Rome, Italy, [9]Ospedale San Raffaele, Milano, Italy, [10]Polytechnic University of Marche, Ancona, Ancona, Italy, [11]Vita-Salute San Raffaele University. Unit of Immunology, Rheumatology, Allergy and Rare Diseases, IRCCS San Raffaele Hospital, Milan, Italy, [12]Rheumatology Unit, Department of Medical and Surgical Sciences for Children and Adults, University Hospital of Modena and Reggio Emilia School of Medicine, Italy., Modena, Emilia-Romagna, Italy, [13]Division of Rheumatology, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, Florence, Italy, [14]Rheumatology DiMePReJ, University of Bari, School of Medicine, Bari, Italy, Bari, Italy, [15]Clinica Reumatologica, Dipartimento di Reumatologia e Scienze Mediche, ASST Gaetano Pini-CTO, Dipartimento di Scienze Cliniche e di Comunità, Dipartimento di Eccellenza 2023-2027, Università degli Studi di Milano, Milan, Italy, Milan, Italy, [16]Sapienza University of Rome, Rheumatology Clinic, Rome, Italy, Roma, Italy, [17]University of Modena and Reggio Emilia, Modena, Modena, Italy, [18]University San Raffaele Milano, Milano, Milan, Italy, [19]University of Florence, Florence, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Gastrointestinal (GI) involvement affects over 80% of patients with systemic sclerosis (SSc), contributing significantly to morbidity and representing the third leading cause of disease-related mortality. Symptoms can affect any GI tract segment and often appear early in the disease course. To date, no disease-specific treatment exists, and management remains symptomatic. The underlying mechanisms are not fully understood, and the clinical course is highly variable.

This study aimed to identify SSc endotypes associated with GI involvement, determine clinical predictors of GI symptoms, and explore the relationship between disease duration and GI manifestations using data from the SSc Progression INvestiGation (SPRING) registry of the Italian Society of Rheumatology.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of demographical data and symptoms in SSc patients with different extent of GI involvement.

	GI extent			Total 1917	
	No GI symptoms	Upper GI symptoms	Upper and Lower GI symptoms	Missing	p value
	844 (45.8)	704 (38.2)	293 (15.9)	76	
Female sex, n (%)	742 (88.1)	619 (88,1)	265 (91.1)	81	0.345
Age, mean, (SD)	58.09 (14.05)	59.31 (13.16)	59.45 (12.92)	78	0.147
Disease duration, mean (SD)	8.81 (7.68)	10.77 (8.60)	11.55 (9.48)	264	**<0.001**
Tobacco exposure, n (%)	223 (29.3)	218 (35.3)	98 (37.1)	274	**0.015**
Diffuse cutaneous involvement, n (%)	111 (13.2)	159 (22.6)	82 (28)	76	**<0.001**
Sclerodactyly, n (%)	506 (60.1)	539 (76.6)	225 (76.8)	78	**<0.001**
Puffy fingers, n (%)	442 (52.4)	358 (50.9)	142 (48.6)	78	0.531
Digital pitting scars, n (%)	303 (36)	377 (53.6)	174 (59.4)	78	**<0.001**
Digital ulcers, n (%)	132 (15.6)	164 (23.3)	96 (32.8)	76	**<0.001**
Telangectasias, n (%)	414 (49.1)	455 (64.6)	217 (74.6)	78	**<0.001**
Calcinosis, n (%)	56 (6.7)	88 (12.5)	65 (22.2)	79	**<0.001**
Joints contractures, n (%)	70 (8.3)	95 (13.5)	75 (25.6)	77	**<0.001**
Tendon friction rubs, n (%)	40 (4.7)	62 (8.8)	51 (17.5)	77	**<0.001**
Arthritis, n (%)	76 (9.1)	89 (12.7)	42 (14.5)	88	**0.014**
Anti topoisomerase I, n (%)	286 (34.3)	239 (34.3)	100 (35.1)	100	0.970
Anti RNApolimerase III, n (%)	12 (1.8)	10 (1.8)	6 (2.7)	461	0.685
Anti Centromere, n (%)	264 (34.1)	196 (29.9)	93 (34.2)	215	0.190
Nailfold videocapillaroscopy pattern Late, n (%)	151 (19.8)	177 (28.1)	91 (33.8)	257	**<0.001**
Interstitial lung disease, n (%)	262 (31)	298 (42.3)	138 (47.1)	76	**<0.001**
Dyspnea, n (%)	218 (26)	305 (43.3)	173 (59.5)	83	**<0.001**
DLCO, mean (SD)	72.64 (19.85)	66.23 (19.85)	64.44 (21.49)	618	**<0.001**

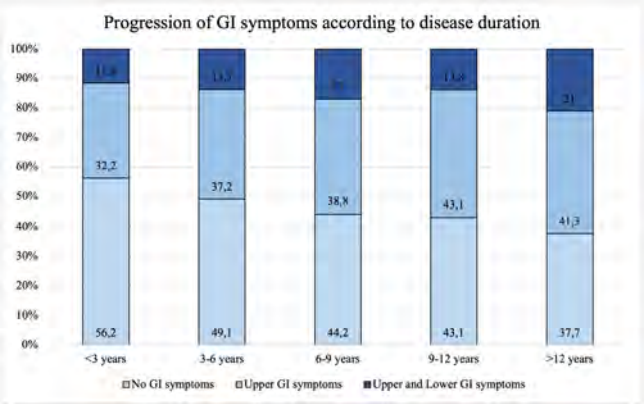


Figure 1. Stratification of GI extent according to disease duration.

Methods: Patients fulfilling the 2013 ACR/EULAR classification criteria and with available GI symptom data were included. GI involvement was defined by the presence of symptoms in at least one of the esophageal, gastric, or intestinal tracts. GI manifestations were classified as "upper GI involvement" (esophageal/gastric symptoms only) or "lower GI involvement" (intestinal symptoms regardless of upper GI symptoms). Chi-square and Student's t-test were used for descriptive comparisons. Logistic regression was used to identify predictors of GI involvement; ordinal regression assessed predictors of increasing GI disease extent.

Results: Among 2178 patients, 1917 met inclusion criteria. Of these, 1073 (56%) reported GI symptoms. Patients with GI involvement had longer disease duration ($p< 0.001$) and more severe disease features, including diffuse cutaneous SSc (dcSSc), interstitial lung disease (ILD), and digital ulcers (DU) (all $p< 0.001$). Autoantibody status, sex, and age were similar across groups. GI involvement increased with longer disease duration, peaking in those with >12 years of disease (62.3%, Figure 1). Logistic regression identified telangiectasias, tobacco exposure, dcSSc, ILD, DU, and longer disease duration as independent predictors of GI symptoms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patients with more extensive GI involvement (both upper and lower) had higher prevalence of severe disease markers, including dyspnea, lower DLCO, and telangiectasias (all p< 0.001, Table 1). Ordinal regression confirmed disease duration, female sex, ILD, DU, dcSSc, telangiectasias, and tobacco exposure as predictors of increasing GI extent. However, in a separate analysis focused on progression from upper to lower GI involvement, only DU, telangiectasias, and anti-centromere antibodies emerged as significant predictors, while disease duration was not.

Conclusion: A more severe SSc phenotype is associated with both the presence and the extent of GI involvement. Key independent risk factors include disease duration, dcSSc, ILD, DU, and tobacco exposure. While disease duration plays a central role in the onset of GI symptoms, it does not appear to drive progression from upper to lower tract involvement, suggesting different mechanisms for initiation versus extension of GI disease.

Disclosure: F. Bonomi: Boehringer-Ingelheim, 6; **C. Bruni**: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5; **S. Bosello**: None; **F. Cacciapaglia**: None; **C. Campochiaro**: Boehringer-Ingelheim, 6, Janssen, 6, Novartis, 6; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Eli Lilly & Co., 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **V. Codullo**: None; **M. D'Agostino**: None; **L. Dagna**: None; **R. De Angelis**: None; **G. de Luca**: None; **D. Giuggioli**: None; **S. Guiducci**: None; **F. Iannone**: None; **F. Ingegnoli**: None; **C. Montecucco**: None; **V. Riccieri**: None; **C. Ferri**: None; **M. Matucci-Cerinic**: None; **S. Bellando Randone**: Boehringer-Ingelheim, 2, 6.

Abstract Number: 2483

Is There a Seasonal Variation in Raynaud's Phenomenon Severity in Patients with Systemic Sclerosis?

Gulsen Ozen[1], Lan Yu[2], Maureen Lauffoon[2], John Pauling[3] and Robyn Domsic[2], [1]University of Iowa Carver College of Medicine, Coralville, IA, [2]University of Pittsburgh, Pittsburgh, PA, [3]North Bristol NHS Trust, Bristol, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Raynaud's phenomenon (RP) is the most common manifestation of systemic sclerosis (SSc) leading to substantial pain and impaired hand function. Establishing treatment efficacy for SSc-RP in clinical trials has been challenging, not least because of the expected seasonal variation in RP severity experienced by patients. There is very limited data on seasonal variation of SSc-RP severity. We aimed to assess how the SSc-RP severity varies throughout the year using the Assessment of SSc–Associated RP (ASRAP) questionnaire, a novel validated patient-reported instrument capturing the severity and impact of SSc-RP.

Methods: SSc patients fulfilling the 2013 ACR/EULAR classification criteria from a single Scleroderma Center completed the ASRAP questionnaire during their regular follow-up visits between October 2022 and September 2024. Data on patients' disease characteristics, comorbidities and medications were collected. Monthly and seasonal changes in ASRAP scores (derived from calibrated items, range 20-80, cohort range 31-75), RP attack duration and frequency were assessed by disease features. Patients with ≥2 questionnaires in the follow-up were assessed for intra-individual seasonal variability of SSc-RP severity.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of the SSc patients

Variables	SSc patients (N=243)
Age at enrollment, mean (SD) years	61.2 (12.5)
Female, %	86.7
White, %	88.9
Disease duration from 1st SSc symptom, median (IQR) years	12.2 (6.7-19.0)
SSc type, %	
Limited cutaneous	59.2
Diffuse cutaneous	40.8
Autoantibody profile, %	
ACA	32.9
ATA	16.0
RNApol3	18.5
Pm-Scl	5.3
U1RNP	5.7
U3RNP	4.9
Th/To	9.0
SSA	10.7
Others	1.2
Overlap syndromes, %	8.6
Disease manifestations (ever), %	
Digital pitting	55.6
Digital ulcers	37.2
Ischemic digital amputations	6.9
Acroosteolysis	12.2
Calcinosis	28.6
Pulmonary hypertension	19.3
Smoking status, %	
Never smoker	69.9
Current smoker	9.7
Former smoker	20.4
Cardiovascular disease, %	5.7
Vasodilators, %	55.9
CCBs	20.5
ARB/ACEi	13.2
PDE5i	20.2
ERA	4.9
PGA	2.5
Others*	18.9
Combination vasodilatory use	22.6
ASRAP score, mean (SD)	48.2 (10.4)

*Others include fluoxetine, prazosin, pentoxifylline, cilastazol and topical nitroglycerin

Table 2. Monthly changes in SSc-RP severity by ASRAP in the entire cohort and by disease features

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	P value
Entire cohort	50.6 (10.5)	50.3 (9.7)	49.9 (9.9)	48.1 (11.0)	45.4 (12.1)	47.0 (9.3)	45.9 (9.6)	46.9 (10.7)	45.9 (10.6)	48.3 (12.6)	48.9 (9.9)	48.4 (9.9)	0.523
Digital pitting/ulcers													
Yes	55.6 (6.6)	52.1 (11.1)	50.1 (11.1)	47.4 (11.1)	48.2 (12.1)	48.0 (11.3)	46.3 (9.6)	45.9 (12.2)	45.4 (10.8)	48.9 (12.9)	47.7 (10.3)	50.8 (9.9)	0.418
No	45.3 (11.6)	49.0 (9.5)	48.6 (7.6)	49.4 (11.4)	43.5 (12.1)	46.0 (8.1)	45.6 (10.0)	47.6 (8.2)	43.1 (10.8)	46.7 (13.1)	44.8 (9.4)	43.3 (8.3)	0.861
RP VAS (0-15)													
<4	44.0 (6.9)	43.7 (7.5)	46.3 (8.7)	42.9 (6.7)	38.8 (6.8)	43.9 (8.1)	41.2 (7.9)	42.4 (6.9)	40.2 (6.4)	40.6 (8.2)	43.3 (7.2)	42.9 (8.2)	0.329
≥4	55.9 (10.4)	56.5 (7.0)	52.3 (10.1)	53.7 (12.2)	52.9 (12.6)	50.4 (9.6)	49.7 (9.3)	51.3 (11.9)	51.7 (11.1)	55.6 (12.3)	50.1 (10.9)	53.8 (8.5)	0.571
Pulmonary hypertension													
Yes	53.1 (5.6)	47.9 (6.6)	49.8 (11.2)	50.5 (12.4)	53.3 (13.6)	42.6 (13.3)	42.8 (8.4)	43.1 (14.1)	31.3 (-)	56.9 (19.6)	44.4 (7.6)	49.8 (13.1)	0.425
No	50.0 (11.4)	50.8 (9.9)	50.0 (9.8)	46.4 (10.1)	43.4 (11.2)	47.8 (8.1)	46.3 (9.7)	47.1 (10.3)	46.7 (10.3)	47.2 (11.7)	47.7 (10.5)	47.4 (8.8)	0.484
SSc cutaneous type													
Diffuse	50.8 (9.3)	48.1 (10.0)	50.4 (9.2)	49.4 (14.1)	46.2 (14.3)	45.2 (10.8)	43.9 (9.6)	46.4 (11.2)	47.8 (12.5)	46.9 (12.9)	43.9 (10.5)	49.3 (11.8)	0.791
Limited	50.9 (12.0)	53.2 (9.3)	49.8 (11.2)	47.5 (10.0)	43.7 (10.3)	48.5 (8.6)	47.4 (9.3)	47.6 (10.6)	45.8 (10.5)	49.9 (12.9)	48.1 (9.7)	48.3 (8.0)	0.628
Vasodilatory use													
Yes	52.8 (10.9)	50.9 (9.6)	50.9 (10.0)	49.3 (12.2)	46.9 (12.3)	46.9 (9.3)	47.1 (10.0)	48.2 (11.9)	45.7 (14.9)	48.3 (14.9)	48.3 (10.3)	48.1 (9.9)	0.755
No	46.3 (8.6)	49.6 (10.2)	47.6 (9.6)	46.1 (9.2)	42.8 (11.9)	47.1 (9.7)	44.8 (9.3)	45.3 (8.9)	47.2 (2.2)	48.2 (9.8)	44.5 (9.1)	48.6 (10.2)	0.886
Smoking													
Never	49.9 (9.9)	44.4 (7.5)	46.4 (8.7)	48.1 (11.9)	46.4 (11.1)	46.6 (8.5)	47.2 (8.7)	45.1 (10.1)	45.6 (9.2)	44.3 (13.8)	46.0 (8.9)	47.2 (9.2)	0.957
Former	46.0 (7.9)	60.4 (0.5)	45.2 (10.8)	54.4 (2.8)	45.2 (13.6)	56.2 (6.9)	39.6 (6.0)	50.5 (11.2)	40.5 (10.0)	53.0 (8.8)	45.2 (7.5)	48.5 (11.3)	0.040
Current	56.4 (14.2)	52.6 (10.7)	55.8 (10.0)	46.5 (3.4)	31.3 (-)	37.6 (8.8)	52.0 (6.3)	41.5 (15.4)	66.3 (-)	47.6 (5.0)	53.2 (13.6)	66.8 (-)	0.242

Results: A total of 243 SSc patients completed 407 ASRAP questionnaires. Most of the patients were Caucasian (89%) and females (87%) with limited cutaneous SSc (59%) and a median (IQR) disease duration of 12.2 (6.7-19.0) years. Digital pitting (DP) and ulcer (DU) were noted in 55% and 36% of the patients, respectively (*Table 1*). Mean ASRAP scores ranged from

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure. ASRAP score, RP attack daily frequency and duration by disease features throughout the year in patients with SSc

45.4 to 50.6 throughout the year (patient-acceptable symptom state threshold=45.3), lowest in July and highest in January (*Table 1, Figure*). Although the difference between July and January (delta 4.7) did not reach statistical significance, this level was consistent with previously noted preliminary "Minimally important clinical difference of 4.17" (*Table 2, Figure*). Patients with a history of DP/DU, pulmonary hypertension (PH) had more variation in RP severity by ASRAP (higher scores in cold months than warm months) throughout the year compared to those without these conditions (*Table 2, Figure*). Smokers had more RP severity, as did those prescribed vasodilators. Similarly, by seasons, patients with DP/DU had significantly higher scores in winter compared to summer (52.7 [9.3] vs. 46.6 [10.9], P=0.04) unlike those without DP/DU (46.1 [8.1] vs. 46.1 [10.8], P=0.997) (*Figure*). Although the average daily RP attacks were more frequent and RP attack duration were longer in cold months than warms months, neither reached statistical significance (*Figure*). At individual patient level among those with ≥2 ASRAP questionnaires (N=102), a similar pattern noted with more variation in those with DU/DP and vasodilator use.

Conclusion: SSc patients with evidence of more severe SSc vasculopathy (DP, DU or PH) exhibited more seasonal variation of SSc-RP severity, as did active smokers. ASRAP scores are highest (worse) in winter and lowest in summer. These findings may help SSc-RP clinical trial design informing physicians about recruitment timing, stratification by more severe vasculopathy and anticipated effect size between winter and summer.

Disclosure: G. Ozen: None; **L. Yu**: None; **M. Lauffoon**: None; **J. Pauling**: AstraZeneca, 2, Boehringer-Ingelheim, 2, IsoMab, 2, Janssen, 2, Permeatus Inc, 2, Sojournix Pharma, 2; **R. Domsic**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2484

Phenotype of systemic sclerosis patients with positive anti–NOR-90 antibodies

Javier Narváez[1], Santos Castañeda[2], Montserrat Roig Kim[3], Martí Aguilar-Coll[4], Laia De Daniel Bisbe[3], Marina Dueñas[5], Cristina Valero[6], Francisco Morandeira[7], Miguel A. González-Gay[8] and Joan Miquel Nolla[3], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [3]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [4]Department of Rheumatology. Hospital Universitario de Bellvitge, Barcelona, Spain, [5]Department of Rheumatology.Hospital Universitario de la Princesa, Madrid, Spain, [6]Hospital de la Princesa, Madrid, Spain, [7]Department of Immunology. Hospital Universitario de Bellvitge, Barcelona, Spain, [8]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Comparative study between systemic sclerosis patients with or without anti–NOR-90 antibodies.

	Positive anti–NOR-90 antibodies N=21	Negative anti–NOR-90 antibodies N=293	p
Women / Men	20 (95%) / 1 (5%)	260 (89%) / 33 (11%)	0.713
Age at diagnosis, mean (SD)	61±13	61±13	0.882
History of cancer, mean (SD)	3 (14%)	44 (15%)	0.928
Overlap syndrome with another autoimmune disease	8 (38%)	109 (37%)	0.935
Rheumatoid arthritis	1		
Sjögren syndrome	4		
Inflammatory myopathy	1		
Thyroid diseases	2		
SSc cutaneous subset			
Diffuse	3 (14%)	60 (20.5%)	0.135
Limited	14 (67%)	200 (68%)	
Sine esclerodermia	0 (0%)	14 (5%)	
Initial (early)	1 (5%)	17 (6%)	
Pre-scleroderma	3 (14%)	2 (0.5%)	
Raynaud	21 (100%)	284 (97%)	0.415
NFC pattern			
Normal	6 (28.5%)	30 (10%)	**0.022**
Non-specific	6 (28.5%)	29 (10%)	
Early	3 (14%)	70 (24%)	
Active	4 (19%)	105 (36%)	
Late	2 (10%)	59 (20%)	
Telangiectasia	9 (43%)	211 (72%)	**0.005**
Digital ulcers	0 (0%)	54 (18%)	**0.032**
Calcinosis	0 (0%)	59 (20%)	**0.018**
Acroosteolysis	0 (0%)	28 (10%)	0.236
Arthralgias	6 (28.5%)	157 (46%)	**0.027**
Arthritis	2 (10%)	82 (28%)	0.065
Myopathy	1 (5%)	27 (9%)	0.706
Esophageal involvement	17 (81%)	245 (84%)	0.675
Gastroparesis or GAVE	3 (14%)	87 (30%)	**0.024**
Intestinal involvement	5 (24%)	142 (48.5%)	**0.029**
Hepatic involvement (PBC or AIH)	3 (14%)	30 (10%)	0.472
Interstitial lung disease	8 (38%)	108 (37%)	0.514
Pulmonary arterial hypertension	0 (0%)	29 (10%)	**0.012**
Renal involvement	0 (0%)	5 (2%)	0.706
Sicca syndrome	8 (38%)	106 (36%)	0.860
Autoantibodies			
Positive ANA	21 (100%)	273 (93%)	0.380
Positive Scl-70	0 (0%)	43 (15%)	0.059
Positive ACA	13 (62%)	135 (46%)	0.165
Anti CENPA	12 (57%)	134 (45.5%)	0.318
Anti CENPB	13 (62%)	135 (46%)	0.160
Positive RNA polymerase III	3 (14%)	23 (8%)	0.399
Positive Pm/Scl	1 (5%)	19 (6.5%)	0.752
Positive antifibrillarin	2 (10%)	5 (2%)	0.073
Positive Th/To	1 (5%)	8 (3%)	0.468
Positive Ku	2 (10%)	9 (3.1%)	0.163
Positive Ro52	5 (24%)	69 (23.5%)	0.985

Abbreviations. ACA = anticentromere antibodies; AIH = Autoimmune Hepatitis; GAVE = Gastric Antral vascular Ectasia; NFC = Nailfold Capillaroscopy; PBC = Primary Biliary Cholangitis; SD= standard deviation

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: To analyze the clinical associations of anti-Nucleolar Organizer Region 90 antibodies (NOR90) antibodies in patients with systemic sclerosis (SSc)

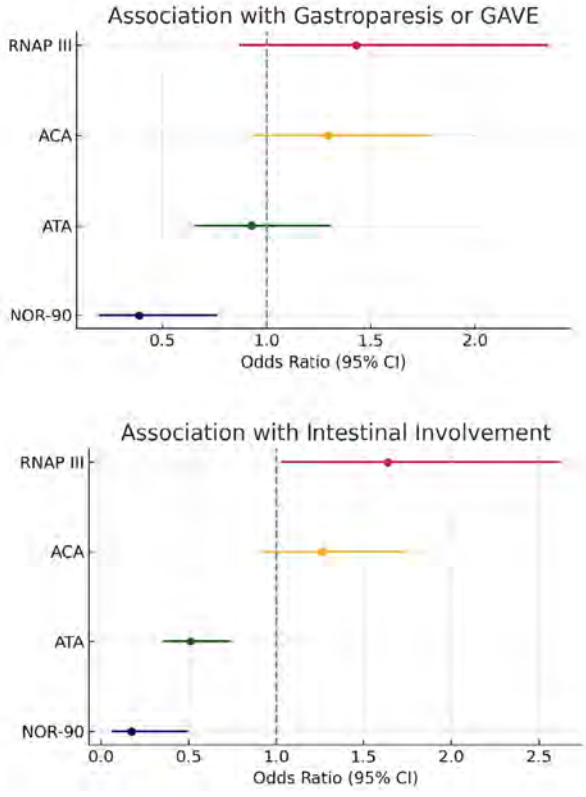
Methods: Cross-sectional study of NOR90-positive SSc patients from two tertiary hospitals. Anti–NOR90 antibodies were detected using the EUROLINE SSc profile (IgG) kit (Euroimmun, Germany). Only patients with repeated moderate or strong positivity were included.

Results: Among the 21 patients with anti–NOR-90 antibodies (95% women), the limited cutaneous subset of SSc was the most prevalent (67%), followed by early disease (5%). Their main characteristics are summarised in Table 1. Nailfold capillaroscopy most frequently revealed normal (28.5%) or non-specific (28.5%) patterns, with only 43% exhibiting one of the three Cutolo patterns.

All patients presented with Raynaud's phenomenon (100%), and the most frequent manifestations included telangiectasias (43%), upper and lower gastrointestinal (GI) symptoms (oesophageal: 81%; gastric: 14%, predominantly gastroparesis; intestinal: 24%), interstitial lung disease (ILD) (38%), and arthralgias (28.5%).

Among the 8 patients with ILD, 63.5% were asymptomatic at diagnosis. Pulmonary function tests at that time were preserved, with a mean (± SD) predicted %CVF of 107 ± 19 (interquartile range [IQR], 95.5–115) and a predicted %DLCO of 80 ± 18 (IQR, 72.5–91). No cases required rescue biologic or antifibrotic therapy, progressed to progressive pulmonary fibrosis, or underwent lung transplantation.

Figure 1. Association of NOR90 and SSc-criteria abs (ATA; ACA; RNAP III) with gastric and intestinal involvement



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fourteen patients (67%) were also positive for at least one SSc-criteria antibody: anti-centromere (62%), including CENP-A (57%) and CENP-B (62%), and RNA polymerase III (14%). None tested positive for ATA/Scl70 antibodies.

Compared with the 293 patients lacking these antibodies (see Table 1), individuals in the anti–NOR-90 group showed significantly less microvascular involvement, with lower frequencies of telangiectasias (43% vs 72%; p=0.005), absence of digital ulcers (0% vs 18%; p=0.032), and a reduced prevalence of calcinosis (0% vs 20%; p=0.018). They also had less frequent gastrointestinal involvement (gastric: 14% vs 30%; p=0.024; intestinal: 24% vs 48.5%; p=0.029) and a lower prevalence of pulmonary arterial hypertension (0% vs 10%; p=0.012). No significant differences were observed in other disease domains. This group also exhibited lower rates of RNAP III positivity.

The association of anti–NOR-90 antibodies with a lower prevalence of intestinal involvement remained significant in multivariable logistic regression adjusted for ATA/Scl70, ACA, and RNAP III, with an OR of 0.332 (95% CI: 0.119–0.931; p=0.036; see Figure 1). The OR for gastric involvement (gastroparesis or GAVE) was 0.395 (95% CI: 0.113–1.374; p=0.144).

Conclusion: Patients with anti–NOR90 antibodies exhibit a distinct systemic sclerosis phenotype, primarily characterized by limited cutaneous involvement, less frequent microvascular and gastrointestinal manifestations, non-severe ILD when present, and absence of pulmonary arterial hypertension. These findings suggest a potentially milder burden of visceral involvement compared to patients without anti–NOR90 antibodies.

Disclosure: J. Narváez: None; **S. Castañeda**: None; **M. Roig Kim**: None; **M. Aguilar-Coll**: None; **L. De Daniel Bisbe**: None; **M. Dueñas**: None; **C. Valero**: None; **F. Morandeira**: None; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2; **J. Nolla**: None.

Abstract Number: 2485

Prevalence of progressive pulmonary fibrosis in systemic sclerosis-associated interstitial lung disease

Javier Narváez[1], Irene Carrión-Barberà[2], Carlos Valera Ribera[3], Alfredo Guillen del Castillo[4], Laura Tio[5], Laura Triginer[6], Lidia Montala-Valencia[7], Carmen Pilar Simeon[8], Anna Pros[2], JUAN JOSE ALEGRE SANCHO[9] and Joan Miquel Nolla[10], [1]Hospital Universitario de Bellvitge, Barcelona, Spain, [2]Department of Rheumatology. Hospital del Mar, Barcelona, Spain, [3]Hospital Universitario Doctor Peset, Valencia, Spain, [4]Departmend of Internal Medicine. Hospital Universitario Vall d´Hebron, Barcelona, Spain, [5]Hospital del Mar Research Institute, Barcelona, Spain, [6]Vall d´Hebron Institut de Recerca (VHIR), Barcelona, Spain, [7]Department of Rheumatology. Hospital Universitario de Bellvitge, Barcelona, Spain, [8]Department of Internal Medicine, Hospital Universitario Vall d'Hebron, Barcelona, Spain, [9]Department of rheumatology. Hospital Universitario Doctor Peset, Valencia, Spain, [10]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: To estimate the prevalence of the progressive pulmonary fibrosis (PPF) phenotype among patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) and identify risk factors that may predict its development.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Results of the Ridge Logistic Regression Model

Predictor	Coefficient	Odds_Ratio	95% Confidence Interval (CI)
(Intercept)	-1.091	0.33	0.19 – 0.53
Age at diagnosis	-0.060	0.94	0.76 – 1.17
Presence of symptomatic ILD	0.029	1.02	0.80 – 1.30
%pFVC <70	0.375	1.45	1.16 – 1.84
%pDLCO <60	0.2271	1.25	1.02 – 1.56
Esophageal involvement	-0.104	0.90	0.70 – 1.15
Pulmonary hypertension	0.1781	1.19	0.94 – 1.49

Methods: A multicentric ambispective study was conducted in four tertiary Spanish hospitals. The diagnosis of PPF was based on the 2022 ATS/ERS/JRS/ALAT criteria for progressive pulmonary fibrosis, requiring at least two of the following three criteria: (1) increased fibrosis on HRCT; (2) worsening respiratory symptoms; and (3) an absolute decline in predicted FVC% by ≥5% or in DLCO% by ≥10% within one year of follow-up

Results: The series included 168 patients with SSc-ILD confirmed by thoracic HRCT. All patients fulfilled the 2013 ACR/EULAR classification criteria for SSc. Based on radiological findings, 70.8% (119) had an NSIP pattern, 11.3% (19) a UIP pattern, 3.6% (6) an OP pattern, 5.4% (9) mixed patterns, and 8.9% (15) an indeterminate pattern.

Of the 168 patients, 37 (22.0%) exhibited radiological worsening, 27 (16.1%) experienced clinical worsening, and 37 (22.0%) showed functional decline. Of these, 31 (18.5%) met the criteria for PPF.

In the comparative analysis, PPF patients were more often men (39% vs. 11.4%; p=0.001) and had a higher prevalence of oesophageal involvement (89.3% vs. 63.6%; p=0.010). Pulmonary arterial hypertension was also significantly more frequent (32.1% vs. 12.5%; p=0.023).

The median time from ILD diagnosis to the evaluation visit was similar between groups: 81.5±84 months (IQR 47–180) in patients with PPF and 71±73 months (IQR 25–131) in those without PPF (p=0.126). PPF patients had lower baseline %pFVC (69.1±18 vs. 88.5±24; p< 0.001) and %pDLCO (51.8±14 vs. 62.9±17; p=0.004), and a higher proportion of %pFVC < 70 (57.1% vs. 19.3%; p=0.001) and %pDLCO < 60 (64.3% vs. 19.3%; p=0.001). Their 6MWT distance was also shorter (356±97 m vs. 409±102 m; p=0.028). As expected, lung transplantation was exclusive to the PPF group (42.8%; p< 0.0001), and mortality was significantly higher (14.3% vs. 2.3%; p=0.014), despite the greater use of biologic agents as rescue therapy (37.3% vs. 0.7%; p=0.001).

A multivariable logistic regression analysis with Ridge penalisation was performed to assess predictors of PPF. The model included six variables: age at diagnosis, oesophageal involvement, PAH, symptomatic ILD, %pFVC < 70, and %pDLCO < 60 (see Table 2). Younger age at diagnosis (coefficient = –1.72), oesophageal involvement (+0.17), PAH (+0.10), and %pFVC < 70 (+0.17) were positively associated with PPF development, whereas symptomatic ILD (+0.08) and %pDLCO < 60 (–0.17) showed weaker associations (See Table 1).

Conclusion: In our series, the prevalence of PPF in SSc-ILD reaches 18.5%. Factors such as %pFVC < 70 at ILD diagnosis, esophageal involvement, and the development of PAH appear to increase the risk of PPF.

Disclosure: J. Narváez: None; **I. Carrión-Barberà**: AstraZeneca, 6, GlaxoSmithKlein(GSK), 2; **C. Valera Ribera**: None; **A. Guillen del Castillo**: None; **L. Tio**: None; **L. Triginer**: None; **L. Montala-Valencia**: None; **C. Simeon**: None; **A. Pros**: None; **J. ALEGRE SANCHO**: None; **J. Nolla**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2486

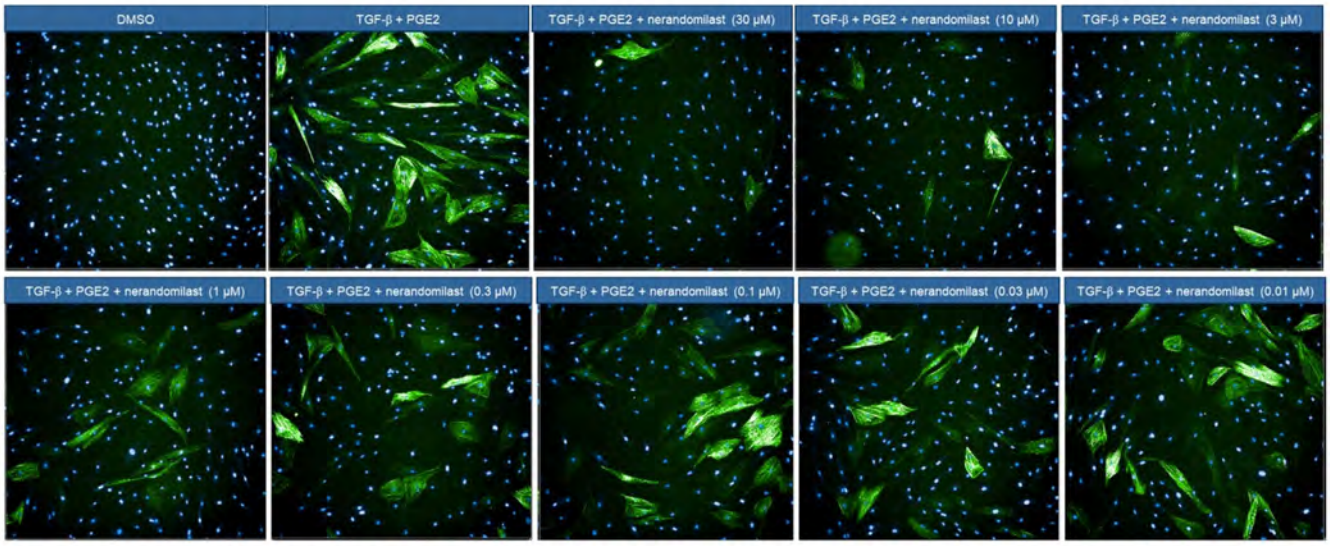
In Vitro Antifibrotic Effects of Nerandomilast on Cell Types Relevant to Intestinal Remodeling and Fibrosis in Systemic Sclerosis

Chang Zeng[1], Leslie Amador[1], Daniela Schloesser[1], Chantelle Simone-Roach[1], Kristen Hall[1], LeeAnne Daley[1], Andrew Mikosz[1], **Jochen Schmitz**[1], David Ebenezer[1], Peter Nickolaus[2], Kremena Simitchieva[3] and Karim El Kasmi[1],
[1]Immunology & Respiratory Disease Research, Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, CT,
[2]Immunology & Respiratory Disease Research, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany,
[3]Inflammation Medicine, Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, CT

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disorder marked by immune dysregulation, vasculopathy, and progressive fibrosis affecting the skin and multiple internal organs, including the gastrointestinal (GI) tract.[1] GI manifestation is the most prevalent complication of SSc, affecting up to 90% of patients.[2] The pathophysiology for SSc GI manifestations is not fully elucidated and may vary across patients; however, it involves myopathy, neuropathy and fibrosis.[1] Animal studies confirm that fibroblast dysfunction has a role in structural or motility abnormalities seen in SSc GI manifestations.[1] Small intestinal dysmotility occurs in 40–88% of patients with SSc, and approximately 20–50% of patients experience GI manifestations involving the colon or large intestine;[3-4] this high prevalence underscores the need for effective therapies.

Phosphodiesterase 4B (PDE4b) inhibition is associated with antifibrotic and immunomodulatory effects.[5-6] Nerandomilast, an oral preferential inhibitor of PDE4B, has shown antifibrotic effects *in vitro* by inhibiting extracellular matrix (ECM) production in both smooth muscle cells and intestinal fibroblasts, suggesting potential benefits in reducing tissue remodeling and intestinal fibrosis. This study investigated the effects of nerandomilast on primary intestinal smooth muscle cells and fibroblasts using *in vitro* models.



αSMA is shown in green and cell nuclei in blue. Abbreviations: αSMA, alpha-smooth muscle actin; DMSO, dimethyl sulfoxide; PGE2, prostaglandin E2; TGF-β, transforming growth factor-β.

Figure. Fluorescent microscope cell images showing the effect of nerandomilast inhibition on expression of αSMA (fibrotic marker) induced by TGF-β in muscle cells of human fibrostenotic Crohn's disease (n=4 donors)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Normal primary human-derived intestinal fibroblasts and smooth muscle cells were treated with nerandomilast following cytokine stimulation. The effects of nerandomilast on smooth muscle cell proliferation, mediated by interleukin-1 beta and basic fibroblast growth factor, were measured using a 5-ethynyl-2'-deoxyuridine assay. Total nuclei number was calculated for transforming growth factor beta and prostaglandin E2-stimulated intestinal fibroblasts. Antifibrotic effects of nerandomilast were determined using an *in vitro* fibrosis model and by measuring the fibrosis markers alpha-smooth muscle actin (αSMA) and ECM protein collagen type I alpha 1 chain (Col1α1) in smooth muscle cells and fibroblasts, respectively.

Results: Nerandomilast reduced the proliferation of intestinal smooth muscle cells and fibroblasts. Additionally, nerandomilast significantly decreased the levels of αSMA in smooth muscle cells (Figure) and reduced Col1α1 expression in fibroblasts.

Conclusion: This study demonstrates the potential of nerandomilast as a therapeutic option for GI manifestations in SSc. *In vitro*, nerandomilast had significant antifibrotic effects on cell types relevant to intestinal remodeling and fibrosis present in SSc. These findings support further investigation of PDE4B inhibition as a targeted approach to managing intestinal fibrosis in SSc.

References:

1. Shreiner AB et al. J Scleroderma Relat Disord 2016;1(3):247.
2. Luquez-Mindiola A et al. World J Clin Cases 2021;9(22):6201.
3. Nassar M et al. Medicine (Baltimore) 2022;101(45):e31780.
4. Volkmann ER, McMahan Z. Curr Opin Rheumatol 2022;34(6):328.
5. Herrmann FE et al. Front Pharmacol 2022;13:838449.
6. Reininger D et al. Br J Pharmacol 2024;181(23):4766.

Disclosure: C. Zeng: Boehringer-Ingelheim, 3; **L. Amador**: Boehringer-Ingelheim, 3; **D. Schloesser**: Boehringer-Ingelheim, 3; **C. Simone-Roach**: Boehringer-Ingelheim, 3; **K. Hall**: Boehringer-Ingelheim, 3; **L. Daley**: Boehringer-Ingelheim, 3, Eli Lilly, 8; **A. Mikosz**: Boehringer-Ingelheim, 3; **J. Schmitz**: Boehringer-Ingelheim, 3, Dynavx, 12,, Eli Lilly, 12,, Merck, 12,; **D. Ebenezer**: Boehringer-Ingelheim, 3; **P. Nickolaus**: Boehringer-Ingelheim, 3; **K. Simitchieva**: Boehringer-Ingelheim, 3; **K. El Kasmi**: Boehringer-Ingelheim, 3.

Abstract Number: 2487

Cardiovascular and venous thromboembolic events in systemic sclerosis: Epidemiological analysis of the Clinical Practice Research Datalink

John Pauling[1], Rachel Charlton[2], Laura Ross[3], Neil McHugh[4] and Anita McGrogan[2], [1]North Bristol NHS Trust, Bristol, United Kingdom, [2]University of Bath, Bath, [3]St. Vincent's Hospital Melbourne, Fitzroy, Victoria, Australia, [4]University of Bath, Bath, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Cardiovascular disease is a leading cause of mortality in systemic sclerosis (SSc). We investigated the association between SSc and the occurrence of both cardiovascular and thromboembolic events using the Clinical Practice Research Datalink (CPRD).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A validated case-ascertainment strategy identified SSc patients in the CPRD. A cohort study design examined rates of coronary arterial disease (CAD), cerebrovascular disease, peripheral artery disease (PAD) and venous thromboembolism (VTE) in SSc patients matched to non-SSc comparators by age, sex and location in a 1:6 ratio. Prevalent and incident cases of SSc were analysed separately. Cox regression analysis was used to determine hazard ratios for event occurrence, adjusted for traditional cardiovascular risk factors.

Results: We identified 877 eligible incident cases of SSc who were matched to 5262 patients without SSc (83.7% female), with a mean follow-up of 8 years. We identified a higher background prevalence of CAD, PAD and VTE at baseline (predating diagnosis) in the SSc cohort (Table 1). The incidence of CAD events in SSc males was 122.3 per 10,000 cases compared to 51.4 per 10,000 non-SSc males; whereas corresponding rates in females were lower for both groups at 43.7 and 28.8 per 10,000 in SSc and non-SSc females respectively (Table 2). Both the unadjusted and adjusted HRs for cardiovascular and VTE events are presented in Table 3. The overall adjusted HR for CAD events was 1.86 (95%CI 1.21-2.87), p=0.005. A similar but stronger association was present for PAD, with an overall adjusted HR of 2.37 (95%CI 1.42-3.95, p=0.001), which was again influenced by high incidence rates in SSc males (139.2 per 10,000 (95% CI 77.1-251.4)) compared with non-SSc male comparators (29.0 per 10,000 (95% CI 17.8-47.4)). In contrast to CAD and PAD, there was no

Table 1. Background proportion of subjects with cardiovascular disease and venous thromboembolism at baseline for the SSc and non-SSc groups

	SSc group			Non-SSc group		
	Males	Females	Overall	Males	Females	Overall
N	144	736	880	864	4416	5280
Coronary artery disease, n (%)						
	8 (5.6)	29 (3.9)	37 (4.2) *	44 (5.1)	84 (1.9)	128 (2.4)
Cerebrovascular disease, n (%)						
	6 (4.2)	23 (3.1)	29 (3.3)	26 (3.0)	118 (2.7)	144 (2.7)
Peripheral arterial disease, n (%)						
	9 (6.3)	22 (3.0)	31 (3.5) *	21 (2.4)	44 (1.0)	65 (1.2)
Venous thrombosis, n (%)						
	<5	14 (1.9)	17 (1.9)	10 (1.2)	72 (1.6)	82 (1.6)
Pulmonary embolism/thrombosis, n (%)						
	<5	13 (1.8)	17 (1.9) *	6 (0.7)	28 (0.6)	34 (0.6)

IHD, ischaemic heart disease; TIA, transient ischaemic attack;

*=p<0.01

Table 2. Incidence of outcomes of cardiovascular disease for the SSc and non-SSc groups over mean of 8 years of follow up stratified for sex

	SSc group			Matched non-SSc group		
	Cases (N)	Person years	Incidence per 10,000 (95% CI)	Cases (N)	Person years	Incidence per 10,000 (95% CI)
Coronary Artery Disease						
Male	10	818	122.3 (65.8-227.3)	27	5252	51.4 (35.3-75.0)
Female	21	4808	43.7 (28.5-67.0)	83	28815	28.8 (23.2-35.7)
Overall	31	5625	55.1 (38.8-78.4)	110	34067	32.3 (26.8-38.9)
Cerebrovascular disease						
Male	<5			27	5537	48.8 (33.4-71.1)
Female	25	4756	52.6 (35.5-77.8)	129	28912	44.6 (37.6-53.0)
Overall	27	5619	48.1 (33.0-70.1)	156	34449	45.3 (38.7-53.0)
Peripheral arterial disease						
Male	11	790	139.2 (77.1-251.4)	16	5516	29.0 (17.8-47.4)
Female	13	4793	27.1 (15.8-46.7)	51	29497	17.3 (13.1-22.8)
Overall	24	5584	43.0 (28.8-64.1)	67	35013	19.1 (15.1-24.3)
Peripheral venous thrombosis						
Male	<5			6	5821	10.3 (4.6-22.9)
Female	16	4809	33.3 (20.4-54.3)	53	29699	17.9 (13.6-23.4)
Overall	19	5686	33.4 (21.3-52.4)	59	35520	16.6 (12.9-21.4)
Pulmonary embolism/thrombosis						
Male	5	833	60.0 (25.0-144.2)	5	5663	8.8 (3.7-21.2)
Female	11	4859	22.6 (12.5-40.9)	33	30221	10.9 (7.8-15.4)
Overall	16	5692	28.1 (17.2-45.9)	38	35885	10.6 (7.7-14.6)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Unadjusted and adjusted hazard ratios of cardiovascular events for SSc patients compared with non-SSc patients

	Unadjusted			Adjusted		
	HR	95% CI	p-value	HR	95% CI	p-value
Coronary Artery Disease						
Male	3.06	(1.36-6.87)	*0.007*	3.56	(1.36-9.34)	*0.010*
Female	1.61	(0.98-2.65)	*0.059*	1.61	(0.96-2.71)	*0.070*
Overall	**1.90**	**(1.25-2.88)**	***0.003***	**1.86**	**(1.21-2.87)**	***0.005***
Cerebrovascular disease						
Male	0.54	(0.13-2.35)	0.414	0.54	(0.12-2.48)	0.430
Female	1.14	(0.73-1.78)	0.555	1.13	(0.72-1.80)	0.590
Overall	**1.05**	**(0.69-1.61)**	**0.805**	**1.02**	**(0.66-1.58)**	**0.912**
Peripheral arterial disease						
Male	5.14	(2.22-11.91)	0.000	4.28	(1.64-11.19)	0.003
Female	1.65	(0.88-3.09)	0.115	1.67	(0.86-3.27)	0.133
Overall	**2.40**	**(1.48-3.90)**	**0.000**	**2.37**	**(1.42-3.95)**	**0.001**
Peripheral venous thrombosis						
Male	2.65	(0.66-10.68)	0.171		NA	
Female	1.85	(1.04-3.30)	0.037	1.83	(0.99-3.37)	0.053
Overall	**1.94**	**(1.14-3.31)**	**0.015**	**1.84**	**(1.05-3.23)**	**0.033**
Pulmonary embolism/thrombosis						
Male	6.89	(1.85-25.75)	0.004		NA	
Female	2.16	(1.05-4.45)	0.035	2.33	(1.01-5.36)	0.047
Overall	**2.80**	**(1.50-5.19)**	**0.001**	**3.01**	**(1.49-6.07)**	**0.002**

NA, event rates too low to run adjusted model for male patients.
* CAD, cerebrovascular disease and venous/pulmonary embolism/thrombosis were adjusted for BMI, smoking, prior history of treated hypertension, prior history of hypercholesterolaemia and/or statin prescribing, aspirin prescribing in the year before index date, NSAID prescribing in the year before index date. PAD was adjusted for BMI, smoking, prior history of treated hypertension, prior history of hypercholesterolaemia and/or statin prescribing.

apparent difference between the incidence of cerebrovascular disease events in SSc and non-SSc subjects, and no apparent sex-difference was observed (Tables 2 and 3). The incidence of peripheral venous thrombosis was higher than pulmonary embolism (33.4 vs. 28.1 per 10,000 SSc subjects). The risk of DVT was almost twice that found in non-SSc controls (adjusted HR: 1.84, 95%CI 1.05-3.23, p=0.033), with no sex difference in incidence rates noted. The increased risk of pulmonary thromboembolic disease was even higher with an adjusted HR of 3.01 (95%CI 1.49-6.07, p=0.002) and was increased for both sexes.

Conclusion: To our knowledge, this is the first study to demonstrate an excess risk of cardiovascular events prior to the diagnosis of SSc, in a cohort matched by age, sex and diabetes status. We have identified an increased risk of cardiovascular events and VTE, both prior to a diagnosis of SSc and within 8 years of SSc diagnosis. Work is needed to establish the mechanism of arterial/venous thrombotic events in SSc. Such insight will facilitate more targeted and effective preventative strategies and improve outcomes in SSc.

Disclosure: J. Pauling: AstraZeneca, 2, Boehringer-Ingelheim, 2, IsoMab, 2, Janssen, 2, Permeatus Inc, 2, Sojournix Pharma, 2; **R. Charlton**: None; **L. Ross**: None; **N. McHugh**: None; **A. McGrogan**: None.

Abstract Number: 2488

Efficacy and Safety of Rituximab for Skin Involvement in Systemic Sclerosis: A Single-Center Study

Kanako Chujo[1], Taichi Miyagi[1], Hiromi Shimada[2], Shusaku Nakashima[2], Yusuke Ushio[1], Koichi Sugihara[2], Mao Mizusaki[2], Naoto Manabe[1], Mayuko Wada[2], Risa Wakiya[3] and Hiroaki Dobashi[2], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan, [2]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa, Japan, [3]Division of Rheumatology, Departent of Internal Medicine, Toho University School of Medicine, Tokyo, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

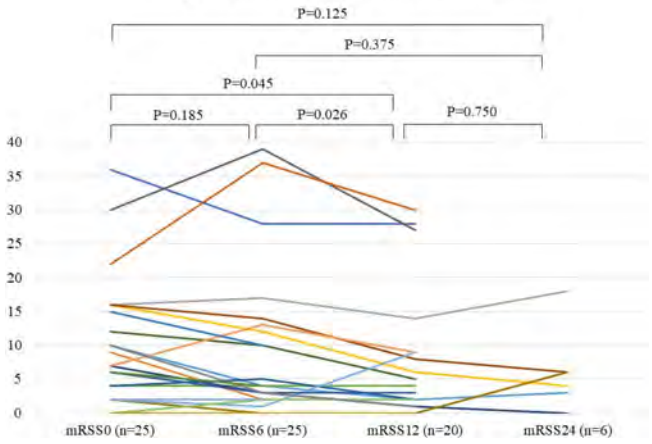
Background/Purpose: Rituximab (RTX) was approved in Japan as a new treatment strategy for systemic sclerosis (SSc). Intravenous rituximab (375mg/m^2) is administered once a week for 4 weeks, every 6 months. This RTX regimen is unique compared to those used in other countries. However, there are few studies on the long-term efficacy and safety of this RTX treatment strategy.

Table1. Patients' characteristics at baseline

	Total (n=25)
Age (years old)	59.28 ± 11.56
Male/female (n)	3/22
dcSSc/lcSSc (n)	10/15
Anti-topoisomerase I (n)	6
Anti-centromere (n)	6
Anti-RNA polymerase III (n)	3
Disease duration (years)	10.26 ± 9.63
mRSS	9.36 ± 9.41
Interstitial lung disease (n)	18
Gastrointestinal disease (n)	12
Pulmonary hypertension (n)	5
Active digital ulcers (n)	3
Concomitant glucocorticoid (n)	12
Concomitant immunosuppressant (n)	4

Values are presented as mean ± standard deviation or number(n).

Figure 1. mRSS after administered RTX



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adverse events on 0-12 month and 12-24 month after RTX administration

0-12 month (n=25)	n	12-24 month (n=20)	n
Total adverse events	13	Total adverse events	8
Death related to adverse events	0	Death related to adverse events	0
Hospitalization related to adverse events	6	Hospitalization related to adverse events	5
Types of adverse events*		Types of adverse events*	
Infectrons	9	Infections	8
COVID-19	6	COVID-19	2
Bacterial pneumonia	1	Bacterial pneumonia	3
Influenza	1	Upper respiratory tract inflammation	1
Diverticulitis	1	Cystitis	1
Lower urinary tract infection	1	Gastroenteritis	1
Liver injury	1	Genital herpes	1
Thrombocytopenia	1	Catheter-related infection	1
Renal limited TMA	1	≥2 episodes of infection	1
Compression fracture	1	Acute heart failure	1
Paralytic ileus	1	Agranulocytosis	1
Cat-scratch disease	1	Subacute ileus	1
		Electrolyte imbalance	1

*Some cases have experienced multiple events

This study aimed to evaluate the real-world efficacy of RTX for skin involvement and its safety up to 2 years in SSc patients treated at our institution.

Methods: We retrospectively analyzed the efficacy of RTX treatment for skin involvement at 0, 6, 12 and 24 months in SSc patients at our hospital from August 2021 to April 2025. Efficacy for skin lesions was evaluated using the modified Rodnan's total skin thickness score (mRSS). Safety was evaluated based on adverse events after RTX administration, with particular attention to infections.

Results: Twenty-five SSc patients who could be evaluated at 6 months after administered RTX were included in our analysis. There were 10 cases with diffuse cutaneous systemic sclerosis and 15 cases with limited cutaneous systemic sclerosis (Table 1). The mean disease duration prior to the initiation of RTX was 10.26 ± 9.63 years. Figure 1 showed mRSS trend after RTX administration. The mean mRSS at the initiation of RTX was 9.36 ± 9.41, and at 6 months average score of 8.68 ± 11.01 was not significantly reduced (p=0.185). However, the average mRSS at 12 months was 7.65 ± 9.64, which was significantly lower compared to 0 and 6 months respectively (p=0.045 and 0.026)(n=20). On the other hand, the mean mRSS at 24 months were 6.17 ± 6.21, which was not significantly different from 0, 6, 12 months respectively (P=0.125, 0.375, and 0.750)(n=6).

Table 2 showed the adverse events after RTX therapy. Infections were the most common adverse events during the 24-month period. Notably, the frequency of infections tended to increase in the latter 12 months. The most frequently observed infections were COVID-19 in the first 12 months and bacterial pneumonia in the second 12 months.

Conclusion: RTX therapy for SSc improved skin stiffness up to 12 months after initiation of treatment. However, there was a trend toward increased adverse events such as infection after 12 months. Further study is needed to determine the long-term efficacy and safety of RTX therapy for SSc.

Disclosure: K. Chujo: None; **T. Miyagi**: None; **H. Shimada**: None; **S. Nakashima**: None; **Y. Ushio**: None; **K. Sugihara**: None; **M. Mizusaki**: None; **N. Manabe**: None; **M. Wada**: None; **R. Wakiya**: None; **H. Dobashi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2489

Unraveling IPAF, VEDOSS and connective tissue diseases classifications through the mixed connective tissue disease spectrum

Kevin Chevalier[1], Benjamin Torreau[2], Marc Michel[3], Bertrand Godeau[3], Christian AGARD[4], Thomas Papo[5], Karim Sacré[6], Brigitte Bader-Meunier[7], Raphaele Seror[8], Xavier Mariette[9], Cacoub Patrice[10], Ygal Benhamou[11], Hervé Levesque[12], Cécile goujard[13], Olivier Lambotte[14], Bernard Bonnotte[15], Maxime Samson[16], Félix Ackermann[17], Jean Schmidt[18], Pierre Duhaut[18], Isabelle Kone-Paut[14], Jean-Emmanuel Kahn[19], Thomas Hanslik[19], Nathalie Costedoat-Chalumeau[20], Benjamin Terrier[20], Alexis REGENT[21], bertrand Dunogue[22], Pascal Cohen[23], Véronique Le Guern[20], Eric HACHULLA[24], Benjamin Chaigne[22] and Luc Mouthon[22], [1]Universitä Paris Cité, Montrouge, France, [2]Internal Medicine and Immunology, CHU Tours, Tours, France, [3]Henri Mondor hospital, Créteil, France, [4]Internal medicine, Nantes University Hospital, Nantes, France, [5]Bichat hospital, Paris, France, [6]Department of Internal Medicine, Bichat University Hospital, Université Paris Cité, AP-HP, Paris, France, Paris, France, [7]Necker hospital, Paris, France, [8]Department of Rheumatology, National referral center for auto immune disease and Sjogren disease, Université Paris-Saclay, INSERM UMR1184: Centre for Immunology of Viral Infections and Autoimmune Diseases, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Le Kremlin Bicêtre, Paris, France., le kremlin bicetre, France, [9]Universitä Paris-Saclay, Le Kremlin Bicetre, France, [10]Department of Internal Medicine and Clinical Immunology, Sorbonne Universités, AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Centre national de références Maladies Autoimmunes et systémiques rares, Centre national de références Maladies Autoinflammatoires rares et Amylose inflammatoire (CEREMAIA), INSERM, UMR S959, Immunology-Immunopathology-Immunotherapy (I3), Paris, France, Paris, France, [11]Internal Medicine, CHU Rouen, Rouen, France, [12]Rouen hospital, Rouen, France, [13]Université Paris Saclay, Department of Internal Medicine and Clinical Immunology, Bicêtre Hospital, APHP, UMR1184 Inserm, CEA, Le Kremlin Bicêtre, France, Kremlin Bicêtre, France, [14]Bicêtre hospital, Kremlin Bicêtre, France, [15]Internal medicine and clinical immunology, Université Bourgogne Europe , CHU Dijon Bourgogne, Dijon, France, [16]CHU Dijon Bourgogne, Dijon, France, [17]Foch hospital, Suresnes, France, [18]Amiens hospital, Amiens, France, [19]Ambroise Paré hospital, Boulogne, France, [20]Cochin hospital, Paris, France, [21]Hopital Cochin, Paris, France, [22]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [23]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [24]CHU Lille, Département de Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Auto-Immunes et Auto-Inflammatoires Rares du Nord, Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille, France, Lille, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Mixed connective tissue disease (MCTD) is a rare systemic disorder that belongs to connective tissue diseases (CTD). Approximately 25% of MCTD patients will meet the classification criteria for at least one other CTD after a median follow-up of 8 years. MCTD has long been debated as an early nonspecific phase/symptom of differentiated connective tissue diseases (dCTD), similarly as others "pre-CTD" states described in literature such as interstitial pneumonia with autoimmune features (IPAF) or very early diagnosis of systemic sclerosis (SSc) (VEDOSS).

Methods: We aimed to evaluate the predictive value of dCTD classification, IPAF, and VEDOSS criteria in MCTD patients. We conducted an observational study within the French MCTD cohort. This cohort includes patients diagnosed with MCTD in 15 rare disease reference and competence centers, including two pediatric centers, across France, according to at least one of the four diagnostic criteria for MCTD and who, at disease onset, did not fulfill classification criteria for SSc, systemic lupus erythematosus, Sjögren's disease (SjD), idiopathic inflammatory myopathies, nor rheumatoid arthritis. IPAF, VEDOSS and current dCTD classification criteria were used to classify patients.

Results: Three hundred and twenty-four patients were included and followed for a median [IQR] duration of 101 [48-176] months. Two hundred and eighty-four (87.7%) patients were females, with a median age at diagnosis of 34 [24-45] years. Among them, 111 (34.3%) progressed into a dCTD, *i.e.* 50 (15.4%) SSc, 40 (12.3%) systemic lupus erythematosus (SLE),

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 – Comparison between MCTD patients fulfilling IPAF criteria (MCTD-IPAF$^+$) or not (MCTD-IPAF$^-$)

	All (N=324)	MCTD-IPAF$^-$ (N=286)	MCTD-IPAF+ (N=38)	p-value
ILD	38 (11.7)	0 (0)	38 (100)	< 0.0001
A. Clinical domain	318 (98.1)	283 (99.0)	35 (92.1)	0.02
1. Distal digital fissuring (*i.e.* "mechanic hands")	0 (0)	0 (0)	0 (0)	-
2. Distal digital tip ulceration	8 (2.5)	8 (2.8)	0 (0)	0.6
3. Inflammatory arthritis or polyarticular morning joint stiffness ⩾ 60 min	217 (67)	194 (67.8)	23 (60.5)	0.4
4. Palmar telangiectasia	3 (0.9)	3 (1.0)	0 (0)	> 0.99
5. Raynaud's phenomenon	293 (90.4)	265 (92.7)	28 (73.7)	0.001
6. Unexplained digital oedema	141 (43.5)	129 (45.1)	12 (31.6)	0.1
7. Unexplained fixed rash on the digital extensor surfaces (Gottron's sign)	0 (0)	0 (0)	0 (0)	-
B. Serologic domain	324 (100)	286 (100)	38 (100)	-
1. ANA ⩾1:320 titer, diffuse, speckled, homogeneous patterns or	277 (85.5)	241 (84.3)	36 (94.7)	0.09
a. ANA nucleolar patterns (any titer) or	-	-	-	-
b. ANA centromere pattern (any titer)	1 (0.3)	1 (0.3)	0 (0)	-
2. Rheumatoid factor ⩾ 2× upper limit of normal	54/210 (25.7)	45/186 (24.2)	9/24 (37.5)	0.2
3. Anti-CCP	3/169 (1.8)	1/149 (0.7)	2/20 (10.0)	0.04
4. Anti-dsDNA	1 (0.3)	1 (0.3)	0 (0)	> 0.99
5. Anti-Ro (SSA)	51/320 (15.9)	35/282 (12.4)	16 (42.1)	< 0.0001
6. Anti-La (SSB)	8 (2.5)	2 (0.7)	6 (15.8)	< 0.0001
7. Anti-ribonucleoprotein	324 (100)	286 (100)	38 (100)	-
8. Anti-Smith	7 (2.2)	5 (1.7)	2 (5.3)	0.2
9. Anti-topoisomerase (Scl-70)	0 (0)	0 (0)	0 (0)	-
10. Anti-tRNA synthetase	1 (0.3)	0 (0)	1 (2.6)	0.1
11. Anti-PM-Scl	0 (0)	0 (0)	0 (0)	-
12. Anti-MDA-5	0 (0)	0 (0)	0 (0)	-
C. Morphologic domain	59 (18.2)	21 (7.3)	38 (100)	< 0.0001
1. Suggestive radiology patterns by HRCT	38 (11.7)	0 (0)	38 (100)	< 0.0001
2. Histopathology patterns or features by surgical lung biopsy	-	-	-	-
3. Multi-compartment involvement (in addition to interstitial pneumonia):	28 (8.6)	21 (7.3)	7 (18.4)	0.02
a. Unexplained pleural effusion or thickening	5 (1.5)	5 (1.7)	0 (0)	> 0.99
b. Unexplained pericardial effusion or thickening	12 (3.7)	11 (3.8)	1 (2.6)	> 0.99
c. Unexplained intrinsic airways disease	7/115 (6.1)	6/84 (7.1)	1/31 (3.2)	0.7
d. Unexplained pulmonary vasculopathy	10 (3.1)	5 (1.7)	5 (13.2)	< 0.0001
Evolution towards dCTD	90 (27.8)	75 (26.2)	15 (39.5)	0.09
Evolution towards SSc*	50 (15.4)	42 (14.7)	8 (21.1)	0.3
Evolution towards SLE£	40 (12.3)	34 (11.9)	6 (15.8)	0.5
Evolution towards SjD£	11 (3.4)	10 (3.5)	1 (2.6)	> 0.99

* According to ACR/EULAR 2013 criteria for SSc
$ According to ACR/EULAR 2019 criteria for SLE
£ According to ACR/EULAR 2016 criteria for SjD
Data are presented as number (percentage). P-value were calculated using Chi-square test or Fisher's exact test for qualitative variables as appropriate
ACR: American college of rheumatology, ANA: antinuclear antibodies, CCP: cyclic citrullinated peptides, EULAR: European alliance of associations for rheumatology, dCTD: differentiated connective tissue disease; HRCT: High-resolution computed tomography-scan, ILD: Interstitial lung disease, IPAF: Interstitial pneumonia with autoimmune features, MCTD: Mixed connective tissue disease, MCTD-IPAF$^+$: patients with MCTD who fulfilled IPAF criteria, MCTD-IPAF$^-$: patients with MCTD who do not fulfill IPAF criteria, MDA5: Melanoma differentiation-associated protein 5, N: Number, PM-Scl : polymyositis scleroderma, RNA: ribonucleic acid, SjD: Sjögren's disease, SLE: Systemic lupus erythematosus, SSc: Systemic sclerosis.

Table 2 – Comparison between MCTD patients fulfilling VEDOSS criteria (MCTD-VEDOSS$^+$) and other MCTD patients (MCTD-VEDOSS$^-$) and comparison between MCTD-VEDOSS$^+$ patients who progressed to systemic sclerosis (MCTD-VEDOSS$^+$-SSc$^+$) or not (MCTD-VEDOSS$^+$-SSc$^-$)

	MCTD-VEDOSS$^-$ (N=31)	MCTD-VEDOSS$^+$ (N=293)	p-value	Number of VEDOSS criteria fulfilled			Comparison within MCTD-VEDOSS$^+$ group		
				2 criteria (N=130)	3 criteria (N=125)	4 criteria (N=38)	MCTD-VEDOSS$^+$-SSc$^-$ (N=247)	MCTD-VEDOSS$^+$-SSc$^+$ (N=46)	p-value
Puffy fingers	10 (32.3)	132 (45.1)	0.02	0 (0)	94 (75.2)	38 (100)	110 (44.5)	22 (47.8)	0.7
Sclerodactyly	3 (9.7)	7 (2.4)	0.06	3 (2.3)	3 (2.4)	1 (2.6)	6 (2.4)	1 (2.2)	> 0.99
Skin thickening extending proximal to MCP joints	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	0 (0	0 (0)	-
Digital tip ulcers	0 (0)	8 (2.7)	> 0.99	5 (3.8)	3 (2.4)	0 (0)	6 (2.4)	2 (4.3)	0.6
Pitting scars	0 (0)	1 (0.3)	-	0 (0)	0 (0)	0 (0)	1 (0.4)	0 (0)	-
Telangiectasia	0 (0)	3 (1.0)	-	2 (1.5)	1 (0.8)	0 (0)	1 (0.4)	2 (4.3)	0.07
Abnormal nailfold capillaries	3/5 (60.0)	68/146 (46.6)	0.1	0 (0)	30/68 (44.1)	38/38 (100)	49/118 (41.5)	19/28 (67.9)	0.01
Lung involvement	10 (32.3)	36 (12.3)	0.002	15 (11.5)	19 (15.2)	2 (5.3)	27 (10.9)	9 (19.6)	0.1
ILD	10 (32.3)	28 (9.6)	< 0.001	13 (10.0)	15 (12.0)	0 (0)	22 (8.9)	6 (13.0)	0.3
PAH	1 (3.2)	9 (3.1)	> 0.99	3 (2.3)	5 (4.0)	1 (2.6)	9 (3.2)	1 (2.2)	> 0.99
Raynaud's phenomenon	0 (0)	293 (100)	< 0.0001	130 (100)	125 (100)	38 (100)	247 (100)	46 (100)	-
Antinuclear antibodies	31 (100)	293 (100)	-	130 (100)	125 (100)	38 (100)	247 (100)	46 (100)	-
SSc-related antibodies*	0 (0)	1 (0.3)	-	0 (0)	1 (0.8)	0 (0)	1 (0.4)	0 (0)	-
Evolution towards SSc$	4 (12.9)	46 (15.7)	0.8	15 (11.5)	21 (16.8)	10 (26.3)	-	-	-

*Anti-centromere, anti-Scl70, anti-RNA polymerase III antibodies
$ According to ACR/EULAR 2013 criteria for SSc
Data are presented as number (percentage). P-value were calculated using Chi-square test or Fisher's exact test for qualitative variables as appropriate
ACR: American College of Rheumatology, EULAR: European alliance of associations for rheumatology, ILD: Interstitial lung disease, MCP: Metacarpophalangeal, MCTD: Mixed connective tissue disease, MCTD-VEDOSS$^+$: patients with MCTD who fulfilled VEDOSS criteria, MCTD-VEDOSS$^-$: patients with MCTD who do not fulfilled VEDOSS criteria, MCTD-VEDOSS$^+$-SSc$^+$: patients with MCTD fulfilling VEDOSS criteria with progression to SSc, MCTD-VEDOSS$^+$-SSc$^-$: patients with MCTD fulfilling VEDOSS criteria without progression to SSc, N: Number, PAH: Pulmonary arterial hypertension, VEDOSS: Very early diagnosis of systemic sclerosis, SSc: Systemic sclerosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 – Comparison of patients' characteristics at MCTD disease diagnosis according to progression to systemic lupus erythematosus (MCTD-SLE$^+$) or not (MCTD-SLE$^-$)

	All (N=324)	MCTD-SLE$^-$ (N=284)	MCTD-SLE$^+$ (N=40)	p-value
Time between first manifestation and diagnosis	9 [3-26.5]	9 [3-27]	11 [3-24]	0.2
Fever	25 (7.7)	22 (7.7)	3 (7.5)	> 0.9
Leukopenia	45/290 (15.5)	40/255 (15.7)	5/35 (14.3)	> 0.99
Thrombocytopenia	3/289 (1.0)	3/254 (1.2)	0/35 (0)	> 0.99
Non-scarring alopecia	10 (3.1)	9 (3.2)	1 (2.5)	> 0.99
Acute cutaneous lupus	6 (1.9)	6 (2.1)	0 (0)	> 0.99
Pleural or pericardial effusion	10 (3.1)	7 (2.5)	3 (7.5)	0.1
Joint involvement	217 (67.0)	187 (65.8)	30 (75.0)	> 0.99
Proteinuria > 0.5 g/24h	5 (1.5)	5 (1.8)	0 (0)	> 0.99
Antiphospholipid antibodies*	12/186 (6.5)	8/164 (4.9)	4/22 (18.2)	0.04
Low C3 and/or low C4	12/163 (7.4)	8/145 (5.5)	4/18 (22.2)	0.03
SLE-specific antibodies$	8 (2.5)	7 (2.5)	1 (2.5)	> 0.99
ACR/EULAR 2019 SLE score ≥ 7	69 (21.3)	55 (19.4)	14 (35.0)	0.02

* Anti-cardiolipin antibodies or anti-ß2GP1 antibodies or lupus anticoagulant
$ Anti-dsDNA antibody or anti-Smith antibody
Data are presented as number (percentage) or median with interquartile range. P-value were calculated using Chi-squared test or Fisher's exact test for qualitative variables and t test for quantitative variables.
ACR: American college of rheumatology, C3: complement component 3, C4: complement component 4, EULAR: European alliance of associations for rheumatology, MCTD: Mixed connective tissue disease, MCTD-SLE$^+$: patients with MCTD who progress to SLE, MCTD-SLE$^-$: patients with MCTD who did not progress to SLE, N: Number, SLE: Systemic lupus erythematosus

and 11 (3.4%) SjD. At MCTD diagnosis, 38 (11.7%) patients had ILD, and all of them fulfilled the IPAF criteria; among which 15 (39.5%) progressed into a dCTD (*vs*. 75 (26.2%) in patients who did not fulfill IPAF criteria; p=0.09) (**Table 1**). At diagnosis, 293 (90.4%) patients fulfilled VEDOSS criteria (MCTD-VEDOSS$^+$) (**Table 2**). All of them had Raynaud's phenomenon and antinuclear antibodies. After a median follow-up of 101 [48-176] months, 46 (15.7%) of the 293 MCTD-VEDOSS$^+$ patients progressed to SSc, compared to 4 (12.9%) of patients not fulfilling VEDOSS criteria (p=0.8). Among MCTD-VEDOSS$^+$ patients, an abnormal nailfold capillaroscopy at MCTD diagnosis was significantly associated with progression toward SSc (p=0.01). At baseline, SSc classification criteria did not predict evolution toward SSc, whereas antiphospholipid antibodies and low C3 and/or low C4 were predictive of an evolution toward SLE (p=0.01 and p=0.04, respectively) (**Table 3**).

Conclusion: At MCTD diagnosis, fulfillment of IPAF and/or VEDOSS classification criteria was not predictive of evolution toward SSc, whereas antiphospholipid antibodies and low C3 and/or low C4 were predictive of an evolution toward SLE. This suggests that MCTD patients should be excluded from IPAF and VEDOSS.

1. Chevalier K, et al. J Intern Med. 2023

Disclosure: K. Chevalier: None; **B. Torreau**: None; **M. Michel**: None; **B. Godeau**: None; **C. AGARD**: None; **T. Papo**: None; **K. Sacré**: None; **B. Bader-Meunier**: None; **R. Seror**: Amgen, 6, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKlein(GSK), 2, 6, Janssen, 2, Kiniska, 2, Novartis, 2, 6; **X. Mariette**: Galapagos, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2, Ose Pharmaceuticals, 5, Pfizer, 2, UCB, 2; **C. Patrice**: None; **Y. Benhamou**: None; **H. Levesque**: None; **C. goujard**: None; **O. Lambotte**: None; **B. Bonnotte**: Boehringer-Ingelheim, 2, Chugai, 2, Novartis, 2, Vifor Pharma, 2; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2; **F. Ackermann**: None; **J. Schmidt**: None; **P. Duhaut**: None; **I. Kone-Paut**: None; **J. Kahn**: None; **T. Hanslik**: None; **N. Costedoat-Chalumeau**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2; **A. REGENT**: Novartis, 2; **b. Dunogue**: None; **P. Cohen**: Roche, 5; **V. Le Guern**: AstraZeneca, 12, attending meetings and travel., Bristol-Myers Squibb(BMS), 6, Novartis, 2; **E. HACHULLA**: None; **B. Chaigne**: None; **L. Mouthon**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2490

Unmasking Mortality Risk: The Impact of Systemic Sclerosis in Stress-Induced Cardiomyopathy

Suryakumar Balasubramanian[1], **Laura Rojo Grajales**[2], Ashlyn Narman[3], Veera Durga Vaishnavi Kurra[4], Ramses Ramirez Damera[2], Alejandro Alvarez Betancourt[2], Abdul Qudoos Iqbal Mohammed[2], Hai Ofek[2], Prachi Anand[2], Roman Zeltser[5] and Amgad N. Makaryus[5], [1]Nassau university Medical center, new york, [2]Nassau University Medical Center, East Meadow, NY, [3]American University of the Caribbean, East Meadow, NY, [4]University of Oklahoma Health Sciences Center, Oklahoma City, OK, [5]Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Stress-induced cardiomyopathy (SIC), also known as Takotsubo cardiomyopathy (TCM), is characterized by acute left ventricular dysfunction, often triggered by emotional or physical stress. In recent years, SIC has been increasingly recognized in patients with underlying systemic inflammatory disorders. Systemic sclerosis (SSc), a chronic autoimmune disease, is known to affect the heart through mechanisms such as myocardial fibrosis and arrhythmias. However, data on the intersection of SIC and SSc are limited, and the clinical outcomes of this rare overlap remain poorly defined.

Methods: We conducted a retrospective analysis of the National Inpatient Sample (2017–2022), identifying adult hospitalizations with a primary diagnosis of stress-induced cardiomyopathy. We initially evaluated several autoimmune diseases for their association with clinical outcomes; systemic sclerosis showed a potentially important association, justifying further evaluation. Patients were then stratified into two groups: those with and without coexisting systemic sclerosis. Outcomes included in-hospital mortality, length of stay, and total hospital charges. Survey-weighted logistic and linear regression models were used to assess associations, adjusting for demographics, comorbidities, and hospital characteristics. Firth logistic regression was employed to address rare-event bias in mortality analyses.

Results: Among 51,415 patients hospitalized with stress-induced cardiomyopathy, only ~70 (0.14%) had a comorbid diagnosis of systemic sclerosis, highlighting the rarity of this overlap. Patients with SSc were predominantly female (100% vs. 89.6%, $p = 0.20$), more likely to be Black (35.7% vs. 6.0%, $p < 0.001$), and had a higher comorbidity burden (Charlson category 3: 71.4% vs. 28.3%, $p = 0.004$). There was no significant difference in mean age (66.8 vs. 67.3 years, $p = 0.82$). In adjusted logistic regression, SSc was independently associated with increased odds of in-hospital mortality (OR 7.39, 95% CI: 1.54–35.56, $p = 0.013$). These findings were consistent in Firth logistic regression (OR 8.61, 95% CI: 1.92–38.58, $p = 0.005$), reinforcing the robustness of the association.

Patients with SSc also had a longer mean LOS (6.29 vs. 3.61 days; 95% CI: 2.18–10.39 vs. 3.52–3.69) and higher mean hospital charges ($77,652 vs. $58,425; 95% CI: $40,356–$114,948 vs. $56,444–$60,407). Although unadjusted comparisons showed higher LOS and charges in the SSc group, these differences were not statistically significant in adjusted models (LOS $\beta = 2.13$, $p = 0.322$).

Conclusion: Systemic sclerosis was associated with significantly higher in-hospital mortality among patients with stress-induced cardiomyopathy (Takotsubo cardiomyopathy), despite its rarity. Both survey-weighted and Firth logistic regression analyses consistently demonstrated this association, reinforcing the robustness of the findings and minimizing the influence

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of confounding and small-sample bias. These results highlight a clinically vulnerable subgroup that warrants closer monitoring. This rare overlap warrants further prospective studies to elucidate underlying immunologic mechanisms and enhance risk stratification.

Disclosure: S. Balasubramanian: None; **L. Rojo Grajales**: None; **A. Narman**: None; **V. Kurra**: None; **R. Ramirez Damera**: None; **A. Betancourt**: None; **A. Iqbal Mohammed**: None; **H. Ofek**: None; **P. Anand**: None; **R. Zeltser**: None; **A. N. Makaryus**: None.

Abstract Number: 2491

High Prevalence of Autoimmunity and Cancer in Anti-NOR90-positive Patients: A Multicenter Observational Study

Marina Dueñas-Ochoa[1], Cristina Valero[2], Francisco Morandeira[3], Juan Carlos Sáez[1], Maryia Nikitsina[4], Montserrat Roig Kim[5], Laia De Daniel Bisbe[5], Esther Vicente-Rabaneda[6], Arantza Alfranca[1], Miguel A. González-Gay[7], Martí Aguilar Coll[8], Rosario Garcia Vicuña[6], Javier Narváez[9] and Santos Castañeda[10], [1]Hospital La Princesa, Madrid, Spain, [2]Hospital de la Princesa, Madrid, Spain, [3]Department of Immunology. Hospital Universitario de Bellvitge, Barcelona, Spain, [4]University Hospital La Princesa, Madrid, Madrid, Madrid, Spain, [5]Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain, [6]Hospital Universitario de La Princesa, Madrid, Spain, [7]Department of Rheumatology and Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, and Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, and Medicine and Psychiatry Department, University of Cantabria, Santander, Spain, [8]Hospital Bellvitge, Barcelona, Spain, [9]Hospital Universitario de Bellvitge, Barcelona, Spain, [10]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-Nucleolar Organizer Region 90 (anti-NOR90) antibodies target nucleolar proteins involved in ribosomal RNA transcription and processing, key steps in protein synthesis. These antibodies have been identified in a wide range of systemic autoimmune rheumatic diseases (SAD), particularly systemic sclerosis (SSc) and Sjögren's syndrome (SS), but also in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA)(1). Some studies have suggested an increased incidence of malignancy in anti-NOR90–positive patients, although findings are inconsistent (2)(3). Our aim was to characterize the clinical profile and frequency of autoimmune diseases and cancer in patients with anti-NOR90.

Methods: We carried out a retrospective, observational and multicenter study including anti-NOR90–positive patients attended at two tertiary hospitals in Spain between January 2013 and April 2025. Antibody detection was performed using the EUROLINE SSc Profile IgG autoAb kit (Euroimmun, Germany). Demographic, clinical, and diagnostic data were collected through electronic medical record review. Descriptive analyses were conducted using measures of central tendency (mean or median) and dispersion (standard deviation-SD or interquartile range-IQR) for continuous variables, and frequencies and percentages for categorical variables.

Results: Seventy-nine anti-NOR90–positive patients were identified (Table 1), mostly females (82%), with a mean age of 63.2±15.6 years. Median follow-up time since anti-NOR90 detection was 38 [17–59.5] months. Over half of the patients were diagnosed with a SAD, most frequently SSc (48.8%), followed by SS (29.2%). Twenty of them (48.8%) showed visceral involvement, predominantly pulmonary in the form of interstitial lung disease (ILD).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical features of anti-NOR90 positive patients (part 1).

Table 1. Clinical features of anti-NOR90 positive patients.

Patients	N=79
Sex (n, %)	65 women (82), 14 men (18)
Age (mean, SD)	63.2 (15.6)
Age, (median, IQR)	64 (54-73)
Time of follow-up, months (median, IQR)	38 (17-59.5)
ANA >1/160 (n, %)	76 (96)
SSc-specificAbs (n, %)	
CENP A/B	16 (20)/26 (33)
RNA pol III	10 (12.6)
PM-Scl	6 (7.6)
Fibrilarin	7 (8.9)
Th/To	4 (5)
Scl70	2 (2.5)
PDGFR	1 (1.3)
Other Abs (n, %)	
DNAds	5 (6.3)
Sm	4 (5)
RNP	2 (2.5)
Ro60/Ro52	7 (8.9)/ 16 (20)
La	3 (3.8)
FR/ACPA	5 (6.3)/ 7 (8.9)
Nucleosomes	7 (8.9)
Mi2α	2 (2.5)
Ku	10 (12.6)
PL7	PL7 1 (1.3)
Patients with SAD (n, %)	41/79 (52)
SAD	
SSc	**20 (48.8)**
lcSSc*	14 (34.1)
dsSSc	1 (2.4)
Pre-scleroderma	3 (7.3)
SSc sine scleroderma	1 (2.4)
Scleromyositis	1 (2.4)
SS	**12 (29.2)**
Primary/ Secondary	6 (14.6)/ 6 (14.6)
RA	6 (14.6)
SLE	4 (9.8)
UCTD	3 (7.3)
Anti-synthetase syndrome	2 (4.9)
ANCA- associated vasculitis	1 (2.4)
*3 overlap with SS, 1 with RA	
Other diagnosis	
GVHD (%)	4 (5)
IPAF (%)	5 (6.3)
Visceral involvement in patients with SAD (n, %)	**20 (48.8)**
Pulmonary	16 (39)
ILD	15 (36.6)
Cardiac	3 (7.3)
Renal	3 (7.3)
Hepatic	3 (7.3)
PBC	2 (4.9)
AIH	1 (2.4)
Cancer (n, %)	16 (20)
Isolated NOR positivity in cancer patients (n, %)	4 (25)

The frequency of malignancy was 20%, distributed among hematologic malignancies (43.75%), non-melanoma skin cancers (18.75%), and solid tumors (37.5%). Within these cases, only one third (31.2%) had a concurrent SAD diagnosis: one limited SSc, one scleromyositis, one undifferentiated connective tissue disease and two overlap syndromes (one with SLE and one with SSc plus SS).

Additionally, other autoantibodies were detected in 75% of cancer cases, most commonly anti-CENP B (41.6%), anti-Ro52 (41.6%), and anti-Ku (33.3%). Overall mortality during the follow-up was 16.4%, with 46% of deaths occurring in patients with cancer.

Conclusion: In our patients, anti-NOR90 antibodies were frequently associated with SAD and showed a notable incidence of malignancies, particularly hematologic. The presence of these antibodies may warrant closer clinical monitoring in routine practice, and larger studies should be conducted to further investigate their potential role as biomarkers for cancer risk and their clinical implications in SAD.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical features of anti-NOR90 positive patients (part 2).

Most frequent autoantibodies in cancer patients	
CENP B	5 (31.25)
Ro52	5 (31.25)
Ku	4 (25)
Types of cancer	
Skin (n, %)	**3 (18.8)**
Basal cell carcinomas	3 (18.8)
Solid organ (n, %)	**6 (37.5)**
Bladder cancer	1 (6.3)
Renal cancer	1 (6.3)
Lung cancer	1 (6.3)
Colon cancer	1 (6.3)
Craniopharyngioma	1 (6.3)
Breast cancer	1 (6.3)
Hematologic (n, %)	**7 (43.8)**
Multiple Myeloma	1 (6.3)
AML	2 (12.5)
ALL	1 (6.3)
Lymphomas	3 (18.8)
Visceral involvement in patients with both cancer and SAD	
ILD (n, %)	2 (40)
Non visceral involvement (n, %)	3 (60)
Deaths (n, %)	13 (16.4)

Abbreviations: SD: standard deviation; IQR: interquartile range; *ANA*: antinuclear antibodies; SSc: systemic sclerosis; Abs: autoantibodies; SAD: systemic autoimmune diseases; lcSSc: limited cutaneous systemic sclerosis; dcSSc: diffuse cutaneous systemic sclerosis; SS: Sjögren's syndrome; RA: rheumatoid arthritis; UTCD: undifferentiated connective tissue disease; GVHD: graft-versus-host disease; IPAF: interstitial pneumonia with autoimmune features; ILD: interstitial lung disease; PBC: primary biliary cholangitis; AIH: autoimmune hepatitis; AML: acute myeloid leukemia; ALL: acute lymphoblastic leukemia

References:

1. Martínez de Victoria Carazo J, et al. Rev Clin Esp(English Ed [Internet]. 2025;225(1):51–5. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2254887424001383
2. Yamashita Y, et al. Rheumatol (United Kingdom). 2022;61(4):1709–16.
3. Hoa S, et al. Rheumatol (United Kingdom). 2022;61(7):2905–14.

Disclosure: M. Dueñas-Ochoa: None; **C. Valero**: None; **F. Morandeira**: None; **J. Sáez**: None; **M. Nikitsina**: None; **M. Roig Kim**: None; **L. De Daniel Bisbe**: None; **E. Vicente-Rabaneda**: None; **A. Alfranca**: None; **M. González-Gay**: Amgen, 2, GlaxoSmithKlein(GSK), 6, Novo Nordisk, 6, Otsuka, 5, Sanofi, 2; **M. Aguilar Coll**: None; **R. Garcia Vicuña**: None; **J. Narváez**: None; **S. Castañeda**: None.

Abstract Number: 2492

Autoantibody Profiles and Disease Trajectories in Early Systemic Sclerosis: Insights from a Prospective Cohort

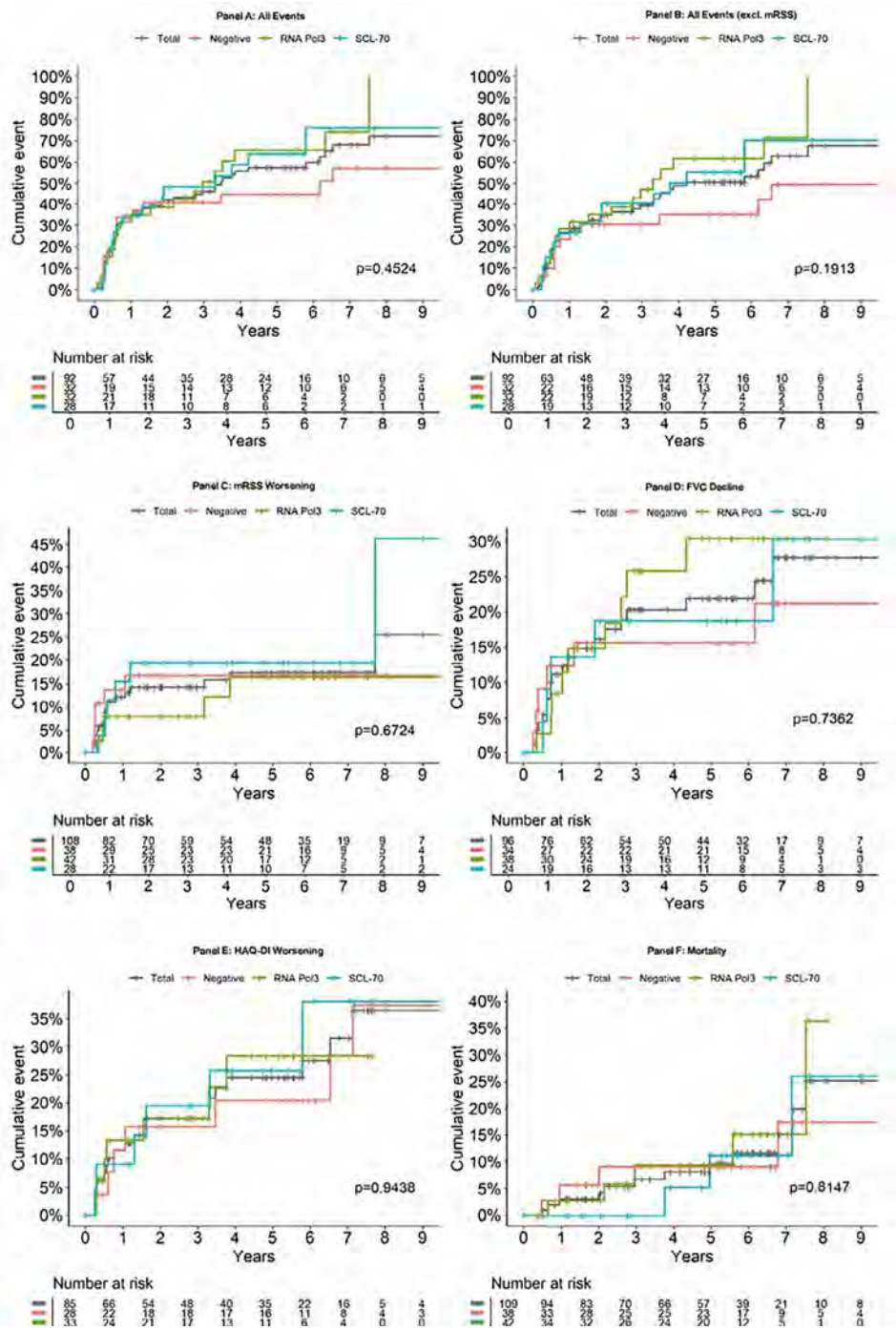
Marzieh Jamali[1], Amisha Kaur[1], Suiyuan Huang[1], James St. Clair[2], John Varga[1], Carleigh Zahn[2], Erica Mulcaire-Jones[1], Alain Lescoat[1] and Dinesh Khanna[1], [1]University of Michigan, Ann arbor, MI, [2]University of Michigan, Ann Arbor

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disease with high mortality. Early stratification by autoantibody (SSc-Ab) profile may inform prognosis and management, but data in early SSc remain limited. This study evaluated clinical features, treatment, and outcomes by SSc-Ab subtype in early SSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Cumulative incidence curves for the whole group and by SSc-Ab subtype. The data should be interpreted as time to the first clinical event. For Panel A, time to first event was assessed by meeting any of the following- mRSS worsening defined as as 5-unit absolute increase or 25% relative increase compared to baseline; FVC % absolute 10% decline compared to baseline; HAQ-DI as 0.5-unit absolute increase compared to baseline; Pulmonary hypertension as mean PAP ≥ 25 mmHg on right heart catheterization; Scleroderma renal crisis; Left heart failure defined as left ventricular ejection fraction ≤ 45%; and mortality. Panel A: Composite clinical events, including mRSS; Panel B: Composite events excluding mRSS; Panel C: Skin progression (mRSS worsening); Panel D: Lung function decline (FVC ≥10%); Panel E: Functional disability (HAQ-DI progression); Panel F: All-cause mortality.

Methods: We analyzed data from 116 patients (pts) enrolled in a prospective registry at a scleroderma center who had diffuse cutaneous SSc (dcSSc) or at-risk for progression based on serologic and clinical features. The at-risk group included those with swollen hands or sclerodactyly with anti-Scl-70 (Scl70) or anti-RNA polymerase 3 (RNAP3) Abs, and/or tendon friction rubs(1). Patients were classified into three groups: RNAP3, Scl70, or Triple Negative (negative for RNAP3, Scl70,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline Characteristics and Treatment for the Total Cohort and by SSc Autoantibody Status (N = 109)

Variables	Total (N=109)	Triple-Negative (N=38)	RNAP3 (N=42)	SCL70 (N=29)	p-value
Demographics					
Age, mean (SD), N=109	51.1 (14.7)	48.7 (13.5) n=38	56.0 (12.1) n=42	47.0 (17.8) n=29	0.0169[a]
Sex, n (%), N=109					
Female	71/109 (65.1%)	27/38 (71.1%)	25/42 (59.5%)	19/29 (65.5%)	0.5571[b]
Race, n (%), N=109					
White	84/109 (77.1%)	28/38 (73.7%)	37/42 (88.1%)	19/29 (65.5%)	0.2097[c]
Black	18/109 (16.5%)	7/38 (18.4%)	4/42 (9.5%)	7/29 (24.1%)	
Other	7/109 (6.4%)	3/38 (7.9%)	1/42 (2.4%)	3/29 (10.3%)	
SSc Type, n (%), N=109					
Diffuse SSc	93/109 (85.3%)	31/38 (81.6%)	41/42 (97.6%)	21/29 (72.4%)	0.0093[b]
Limited SSc	16/109 (14.7%)	7/38 (18.4%)	1/42 (2.4%)	8/29 (27.6%)	
Disease duration from 1st non-Raynaud's phenomenon, median (Q1, Q3), N=109	1.0 (0.7, 1.5)	1.1 (0.9, 1.7) n=38	1.0 (0.7, 1.3) n=42	1.0 (0.8, 1.5) n=29	0.2662[d]
mRSS, mean (SD), N=108	20.3 (10.4)	19.2 (7.9) n=38	24.9 (9.5) n=42	14.9 (11.7) n=28	0.0002[a]
HAQ-DI, mean (SD), N=85	1.00 (0.76)	0.94 (0.67) n=28	1.20 (0.77) n=33	0.80 (0.82) n=24	0.0981[d]
Patient Global Assessment, mean (SD), N=101	6.0 (1.7)	6.0 (1.5) n=36	6.3 (1.6) n=39	5.6 (2.1) n=26	0.2951[a]
Musculoskeletal					
Large joint contracture, n (%), N=107	32/107 (29.9%)	7/38 (18.4%)	16/40 (40.0%)	9/29 (31.0%)	0.1134[b]
Other antibodies					
SSA+, n (%), N=109	17/109 (15.6%)	4/38 (10.5%)	3/42 (7.1%)	10/29 (34.5%)	0.0043[b]
SSB+, n (%), N=109	3/109 (2.8%)	2/38 (5.3%)	0/42 (0.0%)	1/29 (3.4%)	0.3641[c]
SSA+ or SSB+, n (%), N=109	18/109 (16.5%)	5/38 (13.2%)	3/42 (7.1%)	10/29 (34.5%)	0.0075[b]
RNP+, n (%), N=109	16/109 (14.7%)	8/38 (21.1%)	2/42 (4.8%)	6/29 (20.7%)	0.0683[b]
PFT					
FVC % predicted, mean (SD), N=96	82.6 (17.5)	82.5 (18.7) n=34	86.2 (15.0) n=38	77.2 (18.5) n=24	0.1399[a]
DLCO % predicted, mean (SD), N=89	75.6 (22.6)	75.9 (22.1) n=31	79.4 (21.3) n=36	69.0 (24.7) n=22	0.2350[a]
ILD on HRCT at any time during the study, N=109	58/109 (53.2%)	21/38 (55.3%)	18/42 (42.9%)	19/29 (65.5%)	0.1623[b]
Tendon friction rubs, n (%), N=105	26/105 (24.8%)	4/37 (10.8%)	16/39 (41.0%)	6/29 (20.7%)	0.0080[b]
Medications					
Prednisone (current/within 6 months), n (%), N=109	25/109 (22.9%)	6/38 (15.8%)	11/42 (26.2%)	8/29 (27.6%)	0.4265[b]
Any DMARD, n (%), N=109	67/109 (61.5%)	25/38 (65.8%)	24/42 (57.1%)	18/29 (62.1%)	0.7277[b]
Cyclophosphamide, n (%), N=109	5/109 (4.6%)	2/38 (5.3%)	2/42 (4.8%)	1/29 (3.4%)	1.0000[c]
MMF, n (%), N=109	44/109 (40.4%)	17/38 (44.7%)	16/42 (38.1%)	11/29 (37.9%)	0.7934[b]
Methotrexate, n (%), N=109	14/109 (12.8%)	5/38 (13.2%)	5/42 (11.9%)	4/29 (13.8%)	1.0000[c]
Medications at any time during the study					
Prednisone (current/within 6 months), n (%), N=109	48/109 (44.0%)	17/38 (44.7%)	17/42 (40.5%)	14/29 (48.3%)	0.8045[b]
Any DMARD, n (%), N=109	101/109 (92.7%)	38/38 (100.0%)	36/42 (85.7%)	27/29 (93.1%)	0.0361[c]
Cyclophosphamide, n (%), N=109	11/109 (10.1%)	5/38 (13.2%)	3/42 (7.1%)	3/29 (10.3%)	0.6686[c]
MMF, n (%), N=109	86/109 (78.9%)	32/38 (84.2%)	30/42 (71.4%)	24/29 (82.8%)	0.3149[b]
Methotrexate, n (%), N=109	21/109 (19.3%)	8/38 (21.1%)	8/42 (19.0%)	5/29 (17.2%)	0.9251[b]
Hydroxychloroquine, n (%), N=109	17/109 (15.6%)	5/38 (13.2%)	6/42 (14.3%)	6/29 (20.7%)	0.6710[b]

[a] ANOVA
[b] Chi-squared test
[c] Fisher's exact test
[d] Kruskal-Wallis test
SSc: Systemic Sclerosis, mRSS: Modified Rodnan Skin Score, HAQ-DI: Health Assessment Questionnaire-Disability Index, PFT: Pulmonary Function Test, FVC: Forced Vital Capacity, DLCO: Diffusing Capacity of the Lung for Carbon Monoxide, ILD: Interstitial Lung Disease, HRCT: High-Resolution CT, RP: Raynaud's Phenomenon

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Number of Events for the Whole Group and by SSc-Ab during Follow-Up Period

Variables	Total n=92	Negative n=32	RNA Pol3 n=32	SCL-70 n=28	P-value
Any events	51 (55.4%)	15 (46.9%)	20 (62.5%)	16 (57.1%)	0.4429
mRSS worsening[1]	12 (13.0%)	6 (18.8%)	3 (9.4%)	3 (10.7%)	0.5447
FVC-% worsening[2]	12 (13.0%)	4 (12.5%)	5 (15.6%)	3 (10.7%)	0.9270
HAQ-DI worsening[3]	15 (16.3%)	5 (15.6%)	5 (15.6%)	5 (17.9%)	0.9651
Scleroderma renal crisis	5 (5.4%)	0 (0.0%)	4 (12.5%)	1 (3.6%)	0.0778
Pulmonary hypertension on RHC[4]	5 (5.4%)	0 (0.0%)	2 (6.3%)	3 (10.7%)	0.1907
LVEF ≤ 45%[5]	1 (1.1%)	1 (3.1%)	0 (0.0%)	0 (0.0%)	1.0000
Mortality	4 (4.3%)	0 (0.0%)	3 (9.4%)	1 (3.6%)	0.2075

Multiple events might occur at the same time as the first event, so the sum of individual events may exceed the number of any events. Each organ row denotes the first event in the participating subject
[1]mRSS: Modified Rodnan Skin Score, defined as a 5-unit absolute increase or 25% relative increase in mRSS compared to baseline.
[2]FVC-%: Forced Vital Capacity percentage, defined as an absolute 10% decline in FVC-% compared to baseline.
[3]HAQ-DI: Health Assessment Questionnaire-Disability Index, defined as a 0.5-unit absolute increase in HAQ-DI compared to baseline.
[4]Pulmonary hypertension on Right Heart Catheterization, defined as mean PAP ≥ 25 mmHg.
[5]LVEF: Left Ventricular Ejection Fraction, with left heart failure defined as LVEF ≤ 45%.

and anti-centromere). We analyzed longitudinal data including change in modified Rodnan skin score (mRSS), forced vital capacity (FVC), HAQ-DI, organ complications, and mortality. Time-to-event analyses stratified by SSc-Ab group were conducted using cumulative incidence curves and the log-rank test.

Results: A total of 116 pts had a median follow-up of 5.3 years (IQR: 2.1, 6.7); 109 (93.9%) had SSc-Ab data available (Table 1). The mean age was 51.1 years and 65.1% were female. Median disease duration from non-Raynaud phenomenon was 1.0 year . Of the 109, 38.5% were RNAP3+, 26.6% were Scl70+,and 34.8% were Triple Negative. dcSSc was present in 85.3%; 14.7% had at-risk features. RNAP3+ were older (mean 56 years), had the highest mRSS (mean 24.9 units), and the highest predicted FVC (mean 86.2%). At baseline, 61.5% of patients were receiving DMARDs, most commonly mycophenolate mofetil (40.4%), followed by methotrexate (12.8%) and cyclophosphamide (4.6%), while prednisone was used in 22.9%. During follow-up, immunosuppressive therapy was initiated or continued in 92.7% of patients, with variation across Ab subtypes (100% in Triple Negative, 85.7% in RNAP3+, and 93.1% in Scl70+; p=0.03). Mycophenolate mofetil remained the most frequently used agent (78.9%), followed by methotrexate (19.3%).

Of 109 pts, 17 had an event before registry entry and were not included in the time to composite event analysis. Overall, 55.4% experienced ≥1 new clinical event (Table 2), with the majority having mRSS worsening (13%), FVC decline ≥10% (13%), and HAQ-DI worsening (16.3%) as the first event; mortality occurred in 4 (4.3%) pts.

Cumulative incidence curves (Figure Panels A and B) show a trend toward a lower incidence of first events over time in the Triple Negative. mRSS worsening happened predominantly in the first 2 years, whereas FVC decline, HAQ-DI disability, and mortality continued over several years. Panels C-D show a trend toward higher incidence for mRSS worsening in pts with SCL70 and FVC decline in both RNAP3 and SCL70. Panel E-F show the impact of different SSc-Ab on HAQ-DI worsening and mortality. None of these trends were statistically significant.

Conclusion: Distinct SSc-Ab in early SSc are linked to distinct organ involvement and clinical trajectories. Pts continue to have progressive organ involvement and high mortality despite current management strategies.

Disclosure: M. Jamali: None; **A. Kaur**: None; **S. Huang**: None; **J. St. Clair**: None; **J. Varga**: None; **C. Zahn**: None; **E. Mulcaire-Jones**: None; **A. Lescoat**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2493

Investigating scoring systems to measure clinically relevant changes in systemic sclerosis-related finger acro-osteolysis over time, as assessed in serial hand radiographs

Michael Hughes[1], Graham Dinsdale[2], Aayushi Agnihotri[3], Joanne Manning[2], Muditha Samaranayaka[4], Jonathan Harris[2] and Ariane Herrick[5], [1]The University of Manchester, Manchester, England, United Kingdom, [2]Northern Care Alliance NHS Foundation Trust, Salford, United Kingdom, [3]The University of Manchester, Manchester, United Kingdom, [4]Salford Royal Hospital, Salford, United Kingdom, [5]The University of Manchester, UK, Aberdeen, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Acro-osteolysis (A-O, terminal tuft digit resorption) is characteristic of systemic sclerosis (SSc), occurring in 20-25% of patients (1). Outcome measures are much needed. Following our previous work (2) that developed a scoring system for A-O, our objective was to examine different methods of scoring A-O over time, specifically comparing subjective clinician opinion to more formal digit-by-digit scoring, to investigate their potential as outcome measures.

Methods: Patients identified from a tertiary referral centre for SSc who had a first visit between 2006-2018, who had suitable radiographs (both hands, two time points). The final image set contained 180 image pairs from 90 patients.

Radiographs were presented to a single observer for assessment:

1. 180 single (blinded) images; 10 fingers/digits scored: 0 (normal) to 4 (complete terminal tuft resorption); total (sum of all digits), maximum, and Johnstone scores (2) calculated.

2. 90 image pairs presented (left vs right) in a randomised order. Images reviewed answering "is the acro-osteolysis status of the right-hand image more or less severe than the left-hand image?": 5-point ordinal scale: much less severe (-2) to much more severe (+2).

Images with fewer than 3 classifiable digits per hand were excluded. Missing values in included images were replaced with the average score (mean of all other digits).

For paired images the clinician change scores were used to dichotomise: ‘‘changers’’ (patients assessed as changing over time) who were scored ‘‘much more severe’’ (+2) or ‘‘more severe’’ (+1) and ‘‘no change’’ scoring ‘‘same’’ (0), ‘‘less severe’’ (-1), or much less severe (-2). We derived ‘‘change over time’’ data between pairs of images – with change calculated in (1) total score, (2) maximum score, and (3) Johnstone score.

We investigated differences in scoring between the ‘‘changers’’ vs. ‘‘no change’’ groups using T-tests (total) or Mann-Whitney tests (maximum, Johnstone).

Results: Patient demographics (n=90) are presented in Table 1. No score could be given in 102/1800 digits assessed due to amputation (n=17, 17%) or obscured digit (n=85, 83%). 10/180 images, and 9/90 pairs were excluded due to missing data. 81 image pairs were analysed after meeting our criteria, with 25 ultimately labelled as ‘‘changers’’, and 56 labelled as ‘‘no change’’. Figure 1: box plots comparing change-over-time data (total, max, or Johnstone) between the two groups from

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Patient demographics.

Median (IQR) age, years	53 (44-63)
Sex (female), n (%)	75 (83%)
Subtype limited cutaneous SSc, n (%)	66 (73%)
Smoking (never smokers), n (%)	67 (74%)
Median (IQR) disease duration (since 1st non-Raynaud's manifestation), years	3.7 (1.0-8.5)
History of digital ulceration, n (%)	59 (66%)
History of amputation, n (%)	6 (7%)
Presence of calcinosis (clinical), n (%)	43 (48%)
Presence of calcinosis (radiographic), n (%)	52 (58%)
Positive ANA, n (%)	73 (81%)
Positive anti-centromere, n (%)	32 (36%)
Positive anti-PMScl, n (%)	1 (1%)
Positive anti-RNA Polymerase III, n (%)	8 (9%)
Positive anti-RNP, n (%)	8 (9%)
Positive anti-Scl70, n (%)	18 (20%)

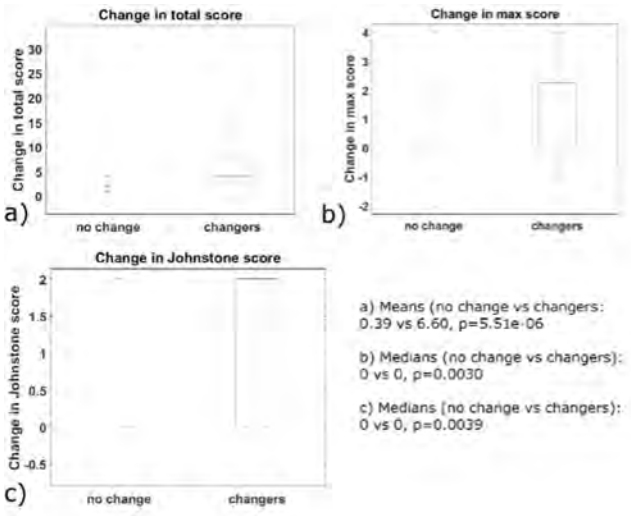


Figure 1. Boxplots comparing changers and no change groups as defined by clinician opinion (paired image assessment): a) Change in total score, b) change in maximum score, and c) change in Johnstone score. Comparisons of means/medians for a, b and c are shown bottom right, with p-values from T-test or Mann-Whitney tests as appropriate.

the dichotomised subjective clinician change score. A significant difference in change in total score of >6 points is identified between the two groups.

Conclusion: Total score appears to show promise for measuring clinically relevant change in A-O. Maximum and Johnstone scores are less sensitive with no obvious difference in group medians (despite statistical significance), likely due to the relatively large number of cases with zero change in both groups. We have explored pragmatic options for quantifying clinically relevant change in A-O with relevance to future longitudinal studies including impact of treatment.

References

1. Avouac, et al. Ann Rheum Dis 2006:1088–92.
2. Johnstone, et al. Rheumatology 2012;:2234–8.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Hughes: Janssen, 5, 6; **G. Dinsdale**: None; **A. Agnihotri**: None; **J. Manning**: None; **M. Samaranayaka**: None; **J. Harris**: None; **A. Herrick**: Abbvie, 2, Boehringer-Ingelheim, 2, Janssen, 2, 6, Zura Bio, 2.

Abstract Number: 2494

Abatacept Reduces CD319+ (SLAM-F7) Cytotoxic T Cells and Cytokine Production in Systemic Sclerosis

Mikel Gurrea-Rubio[1], Kohei Maeda[2], Qi Wu[3], Phillip L Campbell[2], Camila I Amarista[2], Alexander Stinson[4], Ray Ohara[5], Laura Cooney[6], Michael Whitfield[7], Pei-Suen Tsou[8], Dinesh Khanna[8] and David Fox[9], [1]University of Michigan - Ann Arbor, Ann Arbor, MI, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, MI, [3]Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, [4]University of Michigan, Department of Internal Medicine, Division of Rheumatology, Ann Arbor, MI, [5]University of Michigan, Department of Internal Medicine, Division of Rheumatology, West Bloomfield, MI, [6]Immune Tolerance Network, Ann Arbor, MI, [7]Geisel School of Medicine, Lebanon, NH, [8]University of Michigan, Ann Arbor, MI, [9]University of Michigan, Dexter, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: While the ASSET clinical trial (placebo-controlled blinded trial of abatacept) in patients with diffuse cutaneous systemic sclerosis (dcSSc) did not meet its primary endpoint of statistically significant improvement in the modified Rodnan skin score (mRSS), patients with early disease (≤ 5 years) and inflammatory subtype, showed meaningful clinical improvement compared with the placebo group[1-2]. We also found that SSc patients have increased percentages of CD4+ T cells and B cells, but a lower percentage of CD8+ T cells compared to healthy control subjects. Importantly, a robust expansion of CD319+ T cells was seen among the CD4+ cells, whereas they were barely detectable in healthy subjects[3]. We now know that these CD4+CD319+ (also known as SLAM-F7+) cells are highly cytotoxic and are

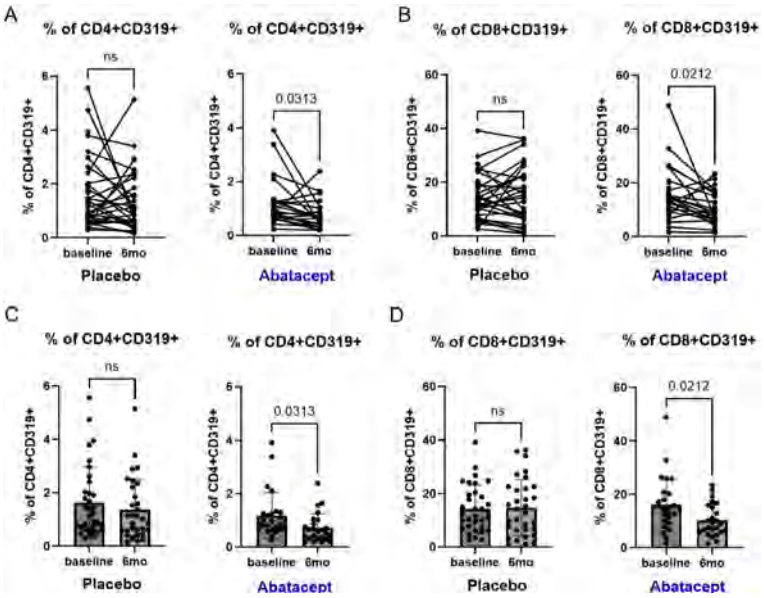


Figure 1. Abatacept reduces cytotoxic CD4+CD319+ and CD8+CD319+ cell populations in systemic sclerosis. (A): CD4+CD319+ and (B): CD8+-CD319+ cells were examined at baseline and 6 months after abatacept or placebo treatment. Patients treated with abatacept showed a significant decrease of CD319+ T cells within CD4+ cells and CD8+ (*p<0.05, paired t-test). (C) and (D): Data presented in boxplots.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

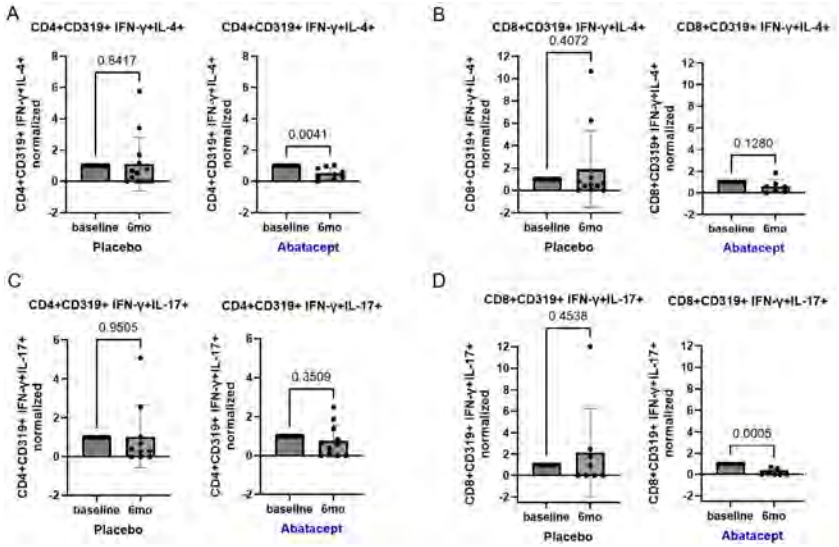


Figure 2. Abatacept reduces the percentage of IL-4/IFN-γ producing CD4+CD319+ and CD8+CD319+ cells in systemic sclerosis. Frequencies of IFN-γ, IL-4 and IL-17 cells within CD4+CD319+ and CD8+CD319+ cells were assessed 1, 3 and 6 months after treatment. Similarly, dual IFN-γ/IL-4, IFN-γ/IL-17 and IL-4/IL-17 production was also assessed at the same time-points. (A): Reduction of dual IL-4/IFN-γ producing CD4+ CD319+ cells was observed in abatacept treated patients at 6 months ($p<0.05$), but not in the placebo group (n.s.). (B): A decrease in IL-4/IFN-γ producing CD8+ CD319+ cells was seen in the abatacept group, although differences did not reach statistical significance ($p=0.0128$). Similarly, abatacept lowered IL-17/IFN-γ production in CD8+ CD319+ cells ($p=0.0005$), but not in CD4+ CD319+ cells at 6 months (C and D). Other analyses of single cytokine production and dual IL-4/IL-17 production did not reach statistical significance (data not shown). Data was normalized to baseline (*$p<0.05$, paired t-test).

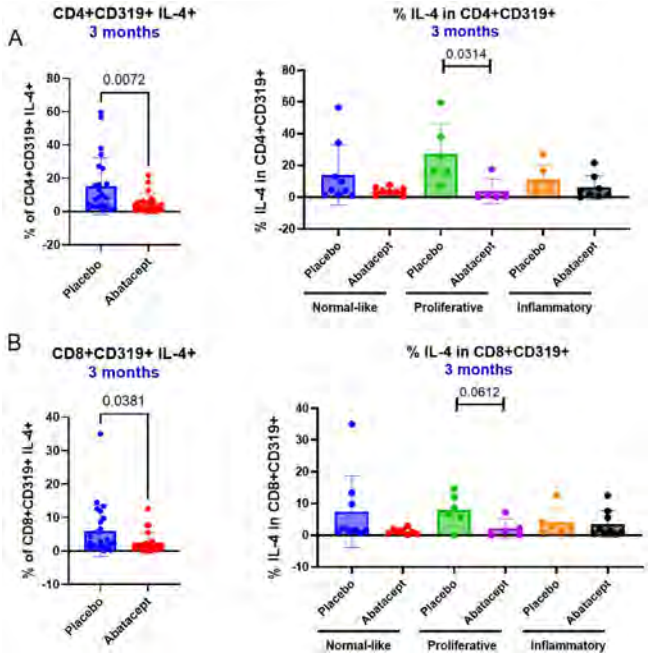


Figure 3. Abatacept decreases IL-4 producing CD4+CD319+ and CD8+CD319+ cells in proliferative subtype patients. (A): IL-4 producing CD4+-CD319+ and CD8+CD319+ cells were statistically decreased in the abatacept group at 3 months ($p=0.0072$). When comparing subtypes of SSc based on their gene signature, we observed a statistically significant reduction in IL-4-producing CD4+CD319+ cells after among the proliferative subtype ($p=0.0314$). (B): Abatacept decreases IL-4 producing CD8+CD319+ cells ($p=0.0381$). A reduction was also seen when comparing abatacept vs placebo in the proliferative subgroup at 3 months. Significant differences between abatacept vs placebo were assessed by a paired-t test. Differences between normal-like, proliferative and inflammatory subsets were assessed using one-way ANOVA with Tukey's multiple comparison test (*$p<0.05$).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

a dominant T cell population in perivascular lymphocytic infiltrates in SSc skin. In this new study, we analyzed the effects of abatacept on both CD4+CD319+ and CD8+CD319+ cells in peripheral blood of 67 dcSSc patients enrolled in the ASSET trial.

Methods: All SSc patients were participants in the ASSET study where longitudinal blood was available. Lymphocyte subsets were characterized by multi-parameter flow cytometry of peripheral blood mononuclear cells at times 0, 1, 3 and 6 months of the ASSET study. Patients were stratified according to their pattern of gene expression on baseline skin biopsies, into three predefined distinct subgroups: inflammatory, fibroproliferative and normal-like. Cytotoxic CD319+ T cells and production of the cytokines INF-γ, IL-4 and IL-17 were measured by intracellular flow cytometry, in both unstimulated cells and following T cell activation in overnight cultures.

Results: A profound decrease of CD319+ T cells was seen within CD4+ cells and CD8+ cells at 6 months (p=0.0313 and p=0.0212 respectively) in patients treated with abatacept compared with placebo **(Figure 1)**. Frequencies of IL-4+ cells within CD4+CD319+ and CD8+CD319+ cells were significantly reduced at 3 months (p=0.0072 and p=0.0381 respectively) but significance was not reached at 6 months. Reduction of dual IL-4/IFN-γ producing CD319+ cells was observed in abatacept treated patients at 6 months, but not in the placebo group **(Figure 2)**. Among normal-like, proliferative and inflammatory SSc subtypes, we found a statistically significant decrease in IL-4 producing CD4+CD319+ cells in the proliferative subtype at 3 months when compared to placebo **(Figure 3)**.

Conclusion: Abatacept has shown promise as a therapy in a subset of early dcSSc patients, emphasizing the need to explore its effects on abnormal and potentially pathogenic immune cell subsets. Here, we demonstrate that abatacept effectively reduces CD319+T cell numbers systemically and also decreases the proportion of CD4+CD319+ cells that are engaged in IL-4 and IL-4/IFN-γ production. Given the fact that CD319 is aberrantly expressed on both CD4+ and CD8+T cells in dcSSc patients, targeting these cells might hold great promise for therapeutic adjustment of lymphocyte balance and function in dcSSc.

Disclosure: M. Gurrea-Rubio: None; **K. Maeda**: None; **Q. Wu**: None; **P. Campbell**: None; **C. Amarista**: None; **A. Stinson**: None; **R. Ohara**: None; **L. Cooney**: None; **M. Whitfield**: Boehringer Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 2, Celdara Medical LLC, 2, 5, 10, 12, Scientific Founder; **P. Tsou**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **D. Fox**: None.

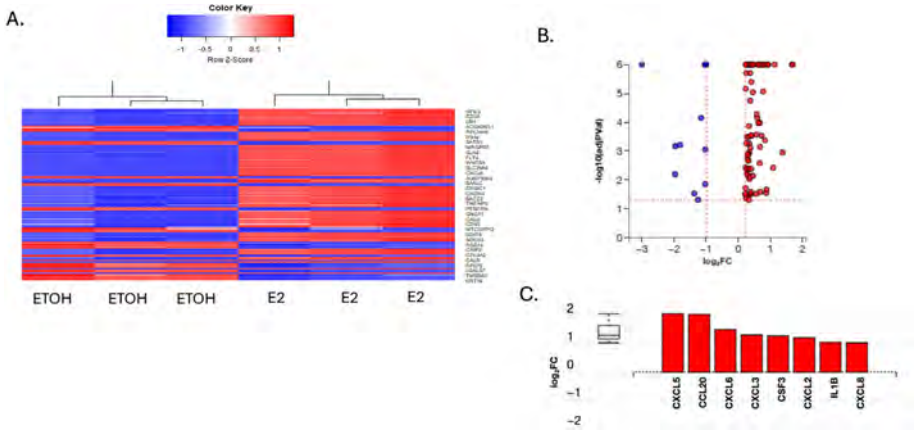
Abstract Number: 2495

IL-6/STAT3 Signaling is Central for Chemokine Production in E2-Induced Dermal Inflammation

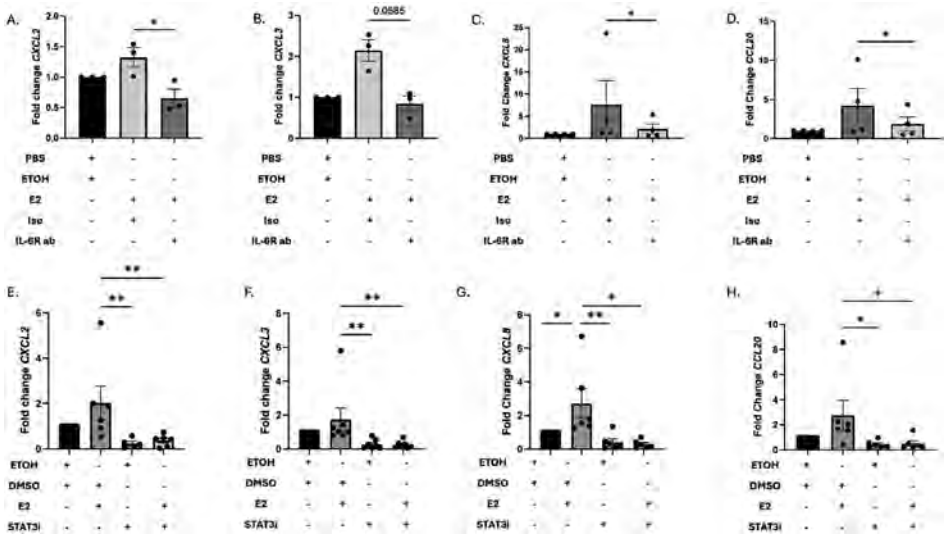
Nicolas Ancona[1], Yucui Li[2], Ludivine Renaud[3], Carol Feghali-Bostwick[3] and DeAnna Baker Frost[3], [1]MUSC Rheumatology & Immunology, Charleston, SC, [2]Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi, Medical University Taiyuan, Shanxi, China (People's Republic), [3]Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

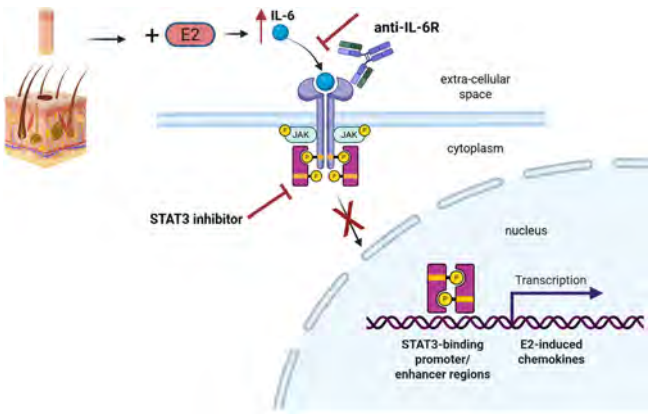
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



A. Heatmap (A), volcano plot (B), and gene measured expression bar plot of the top associated genes (C) in dermal tissues treated with estradiol (E2) compared to vehicle (ethanol, ETOH).



Estradiol-induced chemokine production in human dermal tissue pretreated with an IL-6 receptor antibody (IL-6R ab, A-D), or a STAT3 inhibitor (STAT3i, E-H) prior to estradiol (E2) or vehicle (ethanol, ETOH) .



Schematic describing the relationship between estradiol (E2), IL-6 and STAT3 signaling in E2-induced chemokine production

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Scleroderma (SSc) is an autoimmune disease characterized by dermal inflammation and fibrosis. Patients with SSc have high systemic levels of estradiol (E2), a form of estrogen, compared to age-matched controls, and worse mortality. E2 also contributes to dermal fibrosis in SSc, but we are unsure of its role in dermal inflammation. Using bulk RNA sequencing (RNA seq), we investigated inflammatory pathways in E2-treated dermal tissue.

Methods: We isolated total RNA from human skin tissue treated with ethanol (ETOH, vehicle) or E2 for 48 hours for bulk RNA seq. Using bioinformatics software, we identified statistically significant inflammatory genes and pathways. We confirmed transcript and protein levels using qPCR and ELISA, respectively. Primary human skin dermal fibroblasts from healthy donors treated with ETOH or E2, and dermal fibroblasts from patients with SSc were used for mechanistic studies. Statistical significance was defined as $p< 0.05$.

Results: We detected and confirmed that *CXCL2*, *CXCL3*, *CXCL5*, *CXCL8*, and *CCL20* chemokines are significantly increased in E2 treated skin tissue compared to ETOH. Additionally, these chemokines are induced by E2 in primary human dermal fibroblasts, with E2-induced CXCL5 and CCL20 transcript and secreted protein levels dependent on the MAPK pathway. We detected an association between E2-induced *IL-6* and *CXCL8* and *CCL20* ex vivo transcripts. Using inhibitors to prevent IL-6 and STAT3 signaling prior to E2 stimulation prevented E2-induced *CXCL2*, *CXCL3*, *CXCL8*, and *CCL20* transcripts ex vivo. While SSc dermal fibroblasts treated with anastrozole to prevent E2 generation produced significantly less *CXCL3*, *CXCL5* and *CXCL8*, but not *CXCL2* or *CCL20* transcripts, treatment with bazedoxifene, a selective estrogen receptor modulator and IL-6/STAT3 inhibitor, produced less CXCL5 and CXCL8 secreted protein.

Conclusion: E2 increases *CXCL2*, *CXCL3, CXCL5*, *CXCL8*, and *CCL20* chemokines in dermal tissue and fibroblasts. Although the MAPK pathway is important in their E2-induced expression, IL-6/STAT3 signaling is paramount to E2-induced chemokine expression. Our data suggests E2 production and estrogen receptor signaling through IL-6/STAT3 signaling is responsible, in part, for increased CXCL5 and CXCL8 in SSc. Therefore, E2 augments highly active inflammatory pathways in SSc.

Disclosure: N. Ancona: None; **Y. Li**: None; **L. Renaud**: None; **C. Feghali-Bostwick**: None; **D. Baker Frost**: Allogene, 2, Boehringer-Ingelheim, 2.

Abstract Number: 2496

Comparing Long-term Outcome Across Systemic Sclerosis Subgroups Using a Multi-Organ Disease Progression Score

Philip Yee[1], medha kanitkar[2], stefano rodolfi[3], Voon H. Ong[2] and Christopher Denton[4], [1]Division of Medicine, Centre for Rheumatology, University College London, London, England, United Kingdom, [2]Division of Medicine, Centre for Rheumatology, University College London, London, United Kingdom, [3]University College London, London, United Kingdom, [4]University College London, UK, London, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Evaluating disease modification in systemic sclerosis (SSc) is challenging and requires long term studies. This is especially relevant to limited cutaneous (lc)SSc where severe organ involvement occurs later and less frequently than in diffuse cutaneous (dc)SSc. We have tested a novel composite "time to clinically meaningful progression"

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of the cohort divided according to cutaneous phenotype and ACA status

	DcSSc (n=920)	LcSSc (n=1937)	P value
Age of onset	45 (35-55)	47 (36-57)	0.0024
Female sex	692 (75.2%)	1691 (87.3%)	<0.0001
ILD	395 (42.9%)	514 (26.5%)	<0.0001
PAH	43 (4.7%)	161 (8.3%)	<0.0001
SRC	81 (8.8%)	16 (0.8%)	<0.0001
Severe gut	15 (1.6%)	74 (3.8%)	<0.0001
Severe heart	46 (5%)	39 (2%)	<0.0001
ACA+	28 (3%)	852 (44%)	<0.0001
Limited cutaneous subset			
	ACA+ (n=852)	**ACA- (n=926)**	
Age of onset	50 (39-59)	45 (33-55)	<0.0001
Female sex	787 (92.3%)	767 (82.8%)	<0.0001
ILD	62 (6.3%)	427 (46.1%)	<0.0001
PAH	88 (10.3%)	65 (7%)	0.008
SRC	1 (0.1%)	15 (1.6%)	<0.0001
Severe gut	56 (6.6%)	18 (1.9%)	<0.0001
Severe heart	10 (1.2%)	27 (2.9%)	0.007

endpoint (termed MINIMISE) in a large cohort of SSc to evaluate potential as a clinical trial endpoint for long term interventional or observational research across SSc subsets. We have also explored differences in long term outcome between ACA positive and ACA negative lcSSc, reasoning that ACA negative may show greater progression, and be especially informative in clinical trials.

Methods: Demographic, clinical, and serological data were explored in 2894 well characterized patients followed in our centre. We tested performance of the MINIMISE endpoint that assessed time to first development of new diagnosis of pulmonary arterial hypertension at right heart catheterization (according to current haemodynamic definition at time of diagnosis), new evidence of interstitial lung disease (ILD) with forced vital capacity (FVC) < 70% predicted or worsening of established ILD (reduction in FVC ≥10% in 12 months or between 5 and 9% with contemporary reduction in DLCO ≥15%), new onset severe cardiac involvement attributed to SSc (systolic ejection fraction drop to < 45% or pericardial effusion impairing cardiac function or arrhythmia requiring antiarrhythmic therapy or need for a cardiac device), new onset severe gastrointestinal (GI) involvement (enteral nutrition supplementation for ≥3 weeks or any parenteral feeding or hospital admission for intestinal pseudo-obstruction or obstruction), new onset scleroderma renal crisis, new onset severe digital vasculopathy requiring hospitalization, absolute increase of ≥5 modified Rodnan skin score units, or all-cause mortality.

We performed a time to event analysis for the MINIMISE composite outcome from disease onset, defined by first non-Raynaud SSc manifestation. Kaplan Meier survival failure estimates curves and Cox proportional hazards regression analysis compared disease and ACA subsets. P< 0.05 were considered statistically significant.

Results: Baseline characteristics of the cohort are summarised in **Table 1**. Around one third of cases had dcSSc and as expected this was associated with more frequent disease complications except for PAH and severe GI involvement that were most frequent in lcSSc. A total of 902 (31.6%) patients met the outcome in the first 10 years of the disease; 543 in the lcSSc group. Survival analysis revealed a significantly lower frequency of MINIMISE events in lcSSc vs DcSSc (**Figure 1**). Moreover, when considering only lcSSc, ACA negative patients had significantly more events over time (**Figure 2**).

Conclusion: In lcSSc, clinically meaningful progression, defined by the MINIMISE endpoint, is more frequent in ACA-negative patients. This subgroup may have greatest need and benefit from disease-modifying treatment, and this could be explored in a long-term event driven study although our data suggest that a large cohort and long term follow up will be essential to show benefit in lcSSc.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1 Time to MINIMISE event for lcSSc and dcSSc

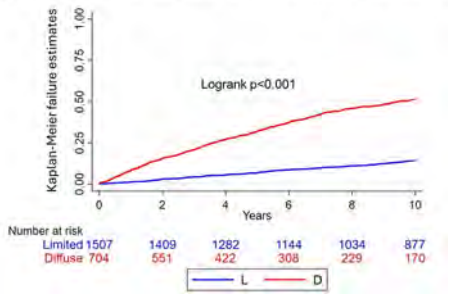
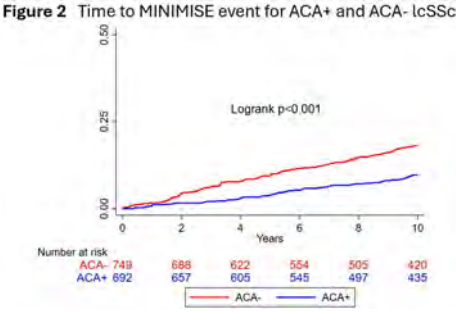


Figure 2 Time to MINIMISE event for ACA+ and ACA- lcSSc



Disclosure: P. Yee: None; **m. kanitkar**: None; **s. rodolfi**: None; **V. Ong**: Boehringer-Ingelheim, 6; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2.

Abstract Number: 2497

Unraveling the Complexity of Interferon Responses in Peripheral Blood Mononuclear Cells in Systemic Sclerosis at Single-Cell Resolution

Pietro Bearzi[1], Elena Pachera[2], Astrid Hofman[3], Laura Much[4], Lumeng Li[1], Kristina Bürki[3], Cosimo Bruni[5], Mike Becker[6], Anna-Maria Hoffmann-Vold[7], Roberto Giacomelli[8] and Oliver Distler[9], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [2]University Hospital Zurich, Zurich, Switzerland, [3]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, the LOOP Zurich, Zurich, Switzerland, [4]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [5]University of Zurich, Zurich, Switzerland, [6]Dept. of Rheumatology, University Hospital Zurich, Zurich, Switzerland, [7]Oslo University Hospital, Oslo, Norway, [8]i) Clinical and Research Section of Rheumatology and Clinical Immunology, Fondazione Policlinico Campus Biomedico; ii) Rheumatology and Clinical Immunology, Department of Medicine, School of Medicine, University of Rome "Campus Bio-Medico", Rome, Italy, [9]Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

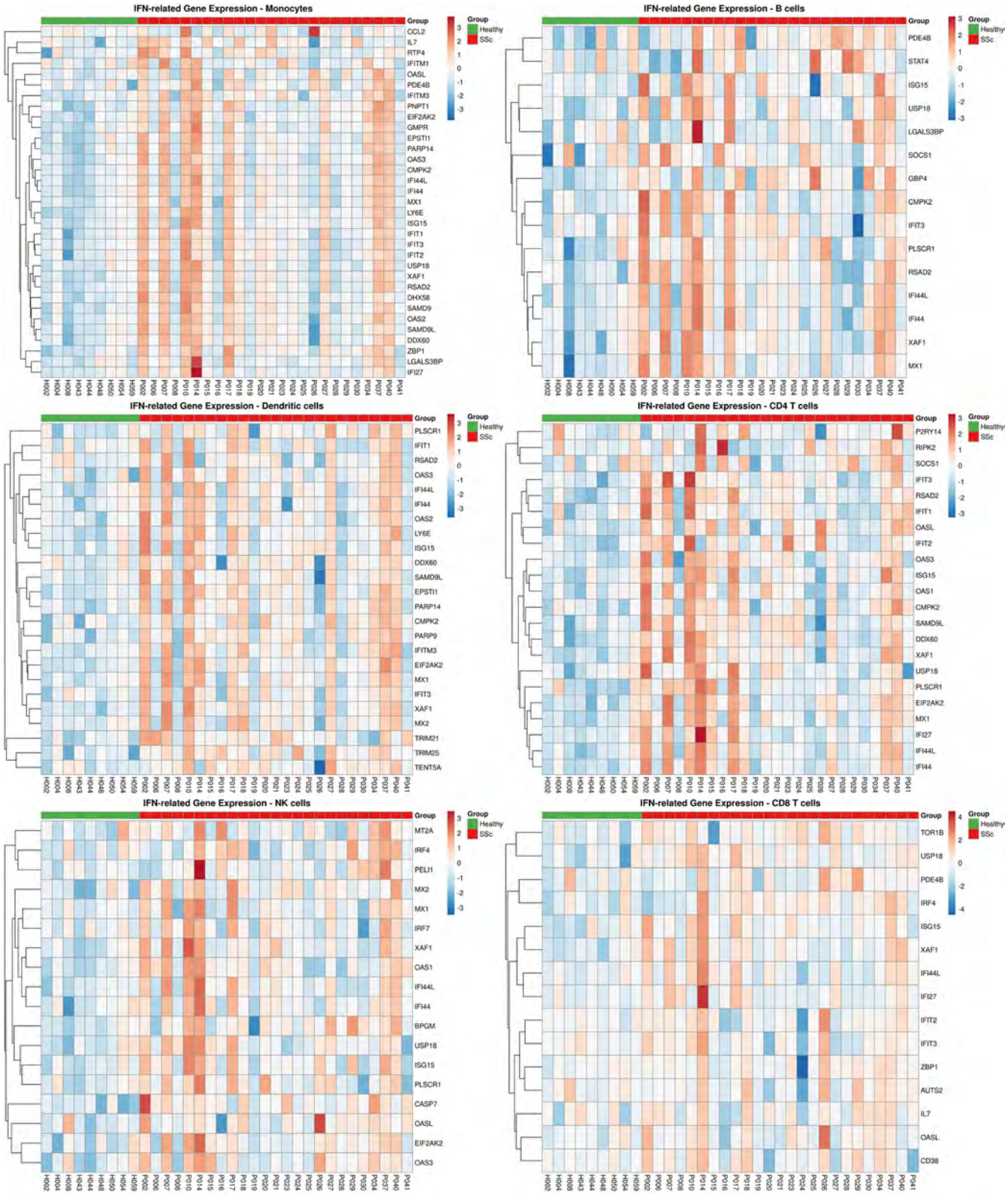


Figure 1. IFN-related DEGs across the different PBMCs subtypes. For each subtype (Monocytes, dendritic cells, NK cells, B cells, CD4 T cells and CD8 T cells), pathway analysis showed significant upregulation of the IFN type I and type II related pathways. Monocytes displayed the highest number of IFN-related DEGs (n = 33). Columns represent subjects (P = Patient, H = Healthy control), rows represent genes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

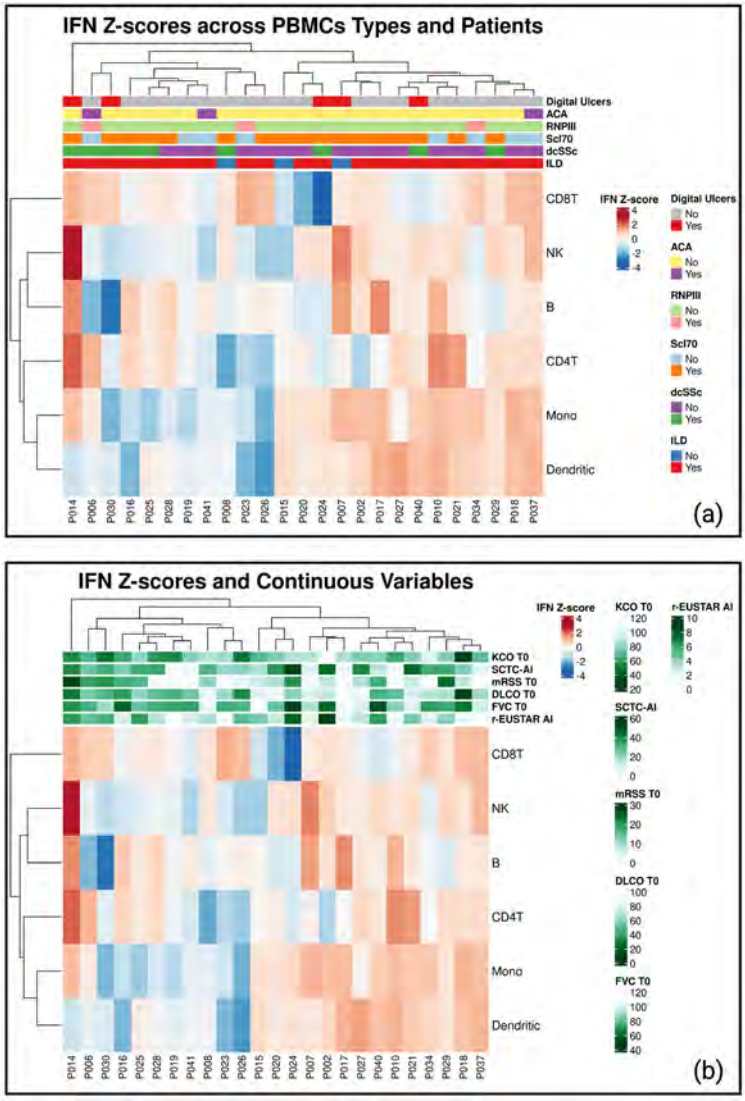


Figure 2. IFN Z scores across different patients (P) (columns) and PBMC subtypes (rows). The heatmap evidences the strong heterogeneity of IFN Z scores both among different patients (columns) and within each patient among different celltypes(rows). For each cell type, the Z-score was calculated using only the IFN-related DEGs specific to that cell type (Figure 1). We assessed for association between categorical (a) and continuous (b) clinical variables. Anti-centromere antibodies (ACA), anti-RNA polymerase III antibodies (RNPIII), anti-topoisomerase I antibodies (Scl70), Revised EUSTAR Activity Index (r-EUSTAR AI), Scleroderma Clinical Trials Consortium Activity Index (SCTC-AI), modified Rodnan Skin Score (mRSS), Functional Vital Capcity (FVC), Diffusing Capacity of the Lung for Carbon Monoxide (DLCO), Carbon monoxide transfer coefficient (KCO).

Background/Purpose: Autoimmunity is a hallmark of SSc pathogenesis. Emerging evidence suggests that interferon (IFN) signaling plays a role in predicting SSc patients at risk of progression. Understanding the alterations in the transcriptome of SSc Peripheral Blood Mononuclear Cells (PBMCs) may provide key insights into the role of IFN signaling and improve patient stratification.

Methods: We performed single cell RNA sequencing of PBMCs from 25 early (≤ 5 years from diagnosis), active SSc (ACR/EULAR 2013) patients and 9 age-matched healthy controls using the Chromium Next GEM protocol. Active SSc was defined by progression of skin or lung fibrosis and/or arthritis. Cellranger was used for read alignment, Seurat v5 for analysis. PBMCs were annotated via Azimuth. Differentially expressed genes (DEGs) were identified using FindMarkers ($|\log2FC| \geq 0.5$, FDR ≤ 0.05). Pathway analysis (MSigDB Hallmark, Reactome) was performed on upregulated DEGs (adj p ≤ 0.05).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

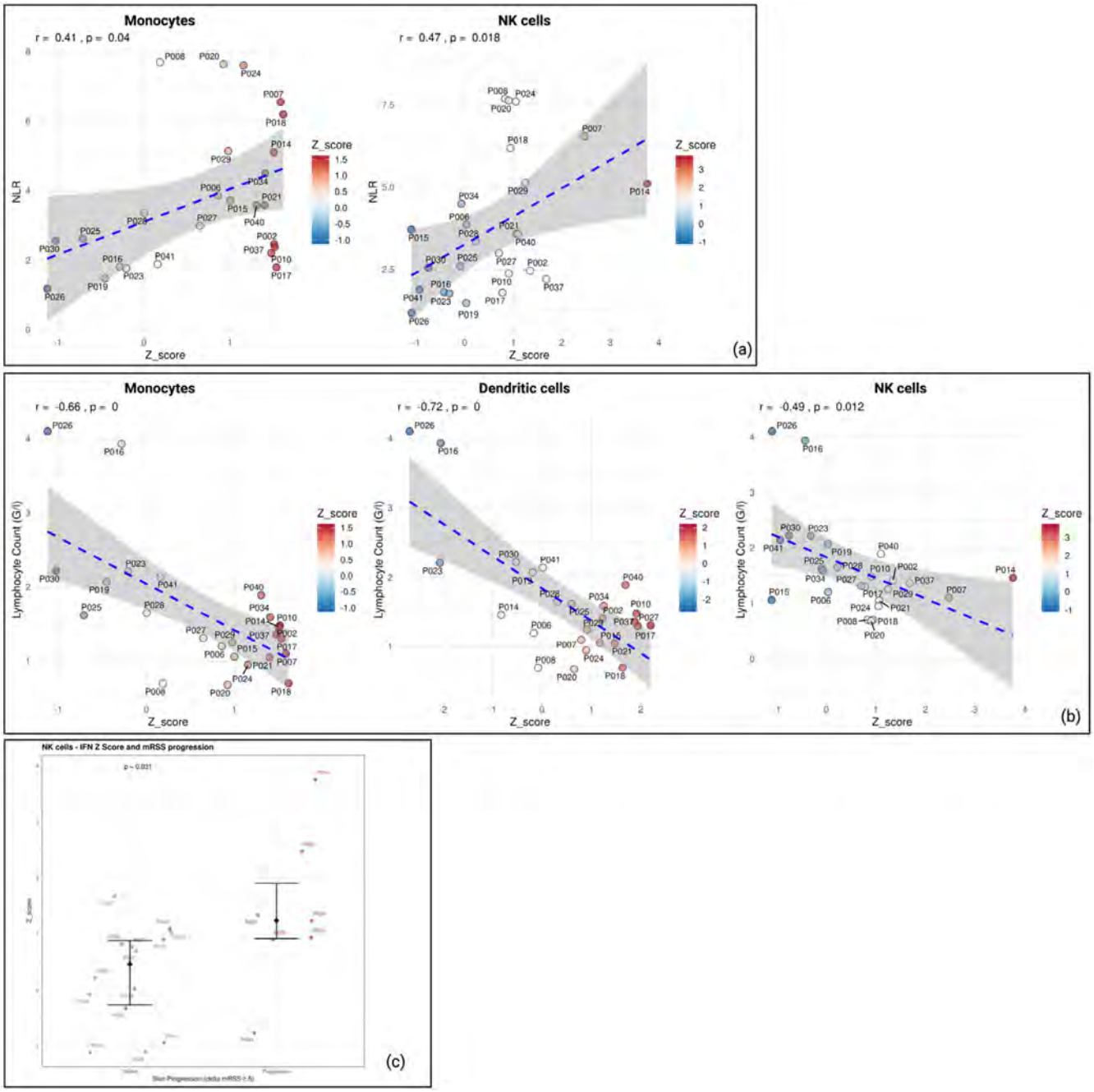


Figure 3. Significant linear regression analysis between celltypes IFN Z scores and NLR (a), lymphocyte count (b). NK cells IFN Z Score grouped by skin fibrosis (mRSS) progression at 1 year (c).

Z-scores for selected DEGs were calculated from count-per-million normalized pseudocounts. Clinical data included autoantibody status, dcSSc, Interstitial Lung Disease (ILD), disease activity indices, CRP, ESR, mRSS, lung function test, neutrophil (N)/lymphocyte (L) counts, and NL Ratio (NLR). Association between Z-scores and continuous clinical variables were assessed using linear regression. Differences in Z scores between patient groups were tested using Mann–Whitney U test.

Results: In the SSc cohort, 88% had ILD, 36% dcSSc, with a median disease duration of 12 [3-22] months. PBMCs (n = 108'138) were annotated as monocytes, dendritic, NK, B, CD4 T and CD8 T cells. Upregulated DEGs related to IFN-α and γ pathways were detected in all cell types (Figure 1) with overall significantly increased expression of *IFI44L, ISG15, EIF2AK2*, and *XAF1*. A prominent heterogeneity in the expression of IFN-related DEGs was observed between SSc samples

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

across all cell types (Figure 1). IFN Z scores further confirmed the substantial heterogeneity between different cell types and individual patients (Figure 2).

Linear regression analysis revealed no significant association between IFN Z-scores and disease activity (r-EUSTAR and SCTC activity indices). In contrast, the IFN Z-scores of monocytes (r = 0.41, p = 0.04) and NK cells (r = 0.47, p=0.018) showed a positive, significant association with NLR (Figure 3a). A significant negative association with L counts and the IFN Z scores was found in monocytes (r = -0.66, p = < 0.001), dendritic cells (r = -0.72, p = < 0.001), and NK cells (r = -0.49, p = 0.012) (Figure 3b). Baseline IFN Z-scores in NK cells were higher in skin progressors (n = 5) at one year (p = 0.031) (Figure 3c). No other clinical parameter was predicted by celltype IFN Z score (Figure 2a-b).

Conclusion: Our data highlight the heterogeneity of IFN response both among patients with active SSc and across different PBMC types within the same patient. IFN response associated with NLR — a predictor of organ involvement and poor prognosis — specifically in monocytes and NK cells.

Other clinical parameters, including disease activity, did not associate with the IFN response signatures in PBMCs.

Disclosure: P. Bearzi: None; **E. Pachera**: None; **A. Hofman**: None; **L. Much**: None; **L. Li**: None; **K. Bürki**: None; **C. Bruni**: Boehringer-Ingelheim, 1, 2, 12, Congress support, EMDO foundation, 5, Iten-Kohaut foundation, 5, Novartis foundation for medical-biological research, 5, Scleroderma Clinical Trial Consortium (SCTC), 5, Scleroderma Research Foundation, 5; **M. Becker**: Foundation for research in Rheumatology (FOREUM), 5, GSK, 6, 12, congress support, Novartis Foundation for Medical-biological Research, 5, 6, Vifor, 6, 12, congress support; **A. Hoffmann-Vold**: AbbVie, 2, Avalyn, 2, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard., Bristol-Myers Squibb, 2, Calluna Pharma, 2, Genentech, 2, Janssen, 2, 5, 6, Medscape, 2, 6, Merck Sharp & Dohme, 2, 6, Novartis, 6, Pliant Therapeutics, 2, Roche, 2, 6, Werfen, 2; **R. Giacomelli**: None; **O. Distler**: 4P-Pharma, 2, 6, AbbVie/Abbott, 2, 6, Acceleron, 2, 6, Acepodia Biotech, 2, 6, Aera, 2, 6, AnaMar, 2, 6, Anaveon AG, 2, 6, Argenx, 2, 6, AstraZeneca, 2, 6, BMS, 2, 5, 6, Calluna (Arxx), 2, 6, Cantargia AB, 2, 6, CITUS AG, 8, CSL Behring, 2, 6, EMD Serono, 2, 6, Galapagos, 2, 6, Galderma, 2, 6, Gossamer, 2, 6, Hemetron, 2, 5, 6, Innovaderm, 2, 5, 6, Janssen, 2, 6, Mediar, 2, 5, 6, mir-29 for the treatment of systemic sclerosis, 10, Mitsubishi Tanabe, 2, 5, 6, MSD Merck, 2, 6, Nkarta Inc., 2, 6, Novartis, 2, 6, Orion, 2, 6, Pilan, 2, 6, Prometheus, 2, 6, Quell, 2, 6, Sumitomo, 2, 5, 6, Topadur, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2498

Effect of autologous myeloablative hematopoietic stem cell transplantation on skin and peripheral blood mononuclear cells in systemic sclerosis patients with interstitial lung disease

Poulami Dey[1], Rachael Bogle[2], Qinmengge Li[3], Olesya Plazyo[4], Rosemary Gedert[4], Carleigh Zahn[4], Pei-Suen Tsou[4], John Varga[4], Lam Tsoi[4], Johann Gudjonsson[4] and Dinesh Khanna[4], [1]Michigan Medicine, Ann Arbor, MI, [2]University of Michigan, Holland, OH, [3]University of Michigan, Ypsilanti, MI, [4]University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

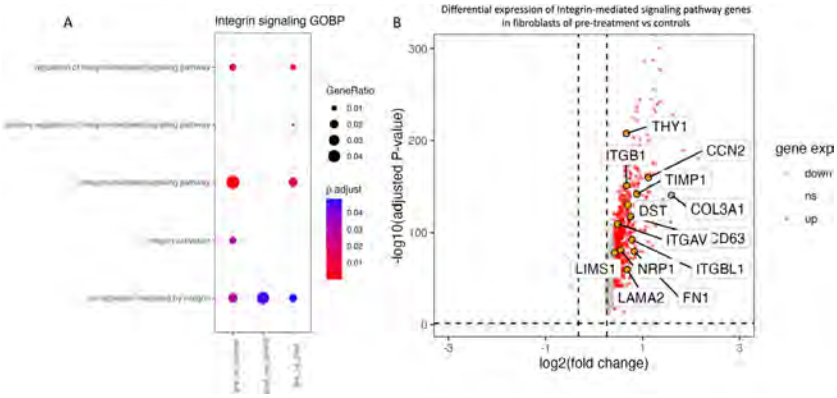


Figure 1: A. Integrin-mediated signaling pathway enriched in the fibroblasts of only pre-treatment skin (pre_vs_control), and not of the post-treatment skin biopsies (post_vs_control). B. Integrin-mediated signaling pathway genes up-regulated in fibroblasts of pre-treatment skin compared to the control skin

Background/Purpose: Systemic sclerosis (SSc) is characterized by skin fibrosis, dysregulated immune response, and vascular system dysfunction. Interstitial lung disease (ILD) is one of the leading causes of SSc-related deaths (Cottin 2019). SSc, associated with ILD, severely affects the immune system and contributes to skin and lung fibrosis. Hematopoietic stem cell transplantation (HSCT) works by resetting the immune system and is emerging as a potential therapeutic strategy for patients with severe SSc-ILD. However, in skin and in peripheral blood mononuclear cells (PBMC) of these patients, the molecular mechanisms and the cell populations that are impacted by the transplant are yet to be identified.

Methods: Single-cell RNA sequencing (scRNA-seq) and assay for transposase-accessible chromatin using sequencing (ATAC-seq) of skin biopsies and PBMCs were performed from four human healthy controls and three SSc-ILD patients before and one year after transplantation. The R packages Seurat (v4.3.0) and Signac (v1.11.0) were used to analyze the scRNA-seq and ATAC-seq data. Cell-cell communication analysis was performed using the R package CellChat (v2.1.2).

Results: Three patients (mean age 54 (range 37-63), 2 men and 1 woman) underwent myeloablative autologous stem cell transplant. The pre (mean 24, SD 5) and post one year (mean 6.33, SD 6.66) modified Rodnan skin score (mRSS) and pre (mean 70, SD 13.45) and post (mean 82, SD 12.12) forced vital capacity percent improved in all patients. A total of 41,181 skin cells were annotated into 10 major cell types and a total of 38,236 PBMCs were annotated into 5 major cell types from the sequencing data. 11,293 skin fibroblasts (FB) were sub-clustered into 7 FB subtypes, with COL11A1+, LTBP2+, and myofibroblasts (CILP_COL8A1+ FBs) showing diminished expression of the pro-fibrotic genes CTGF (CCN2), TAGLN, and VGLL3 post-transplantation at the levels comparable to healthy controls. Enriched cell-cell communication of the CD6/ALCAM pathway was noted only in pre-treatment skin biopsies but neither in post-treatment nor in controls. Additionally, integrin-mediated signaling pathway was found to be enriched in the fibroblasts of pre-treatment skin, and not in the post-treatment skin biopsies (Figure 1). In PBMCs, CD4 T cell proportion was similar in controls and pre-treatment samples but reduced in post-treatment biopsies. LCK pathway, involved in activation of T cell signaling, was found to be associated with cell-cell communication only in pre-treatment PBMC samples but absent in both post-treatment and healthy control.

Conclusion: Our data identify a reduction in expression of pro-fibrotic genes in FB subtypes and diminished signaling of pathways involved in mediating inflammation in SSc-ILD patients who underwent HSCT therapy.

Cottin, V., Brown, K.K. Interstitial lung disease associated with systemic sclerosis (SSc-ILD). *Respir Res* **20**, 13 (2019). https://doi.org/10.1186/s12931-019-0980-7

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: P. Dey: None; **R. Bogle**: None; **Q. Li**: None; **O. Plazyo**: None; **R. Gedert**: None; **C. Zahn**: None; **P. Tsou**: None; **J. Varga**: None; **L. Tsoi**: Galderma, 5, Janssen, 5; **J. Gudjonsson**: None; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2.

Abstract Number: 2499

Concomitant Anti-Ro/SSA Antibodies in Systemic Sclerosis Patients is Associated with Risks Beyond Dryness

Rachael Gordon[1], Leah Wunsch[2], Maureen Lauffoon[1], Thomas Medsger, Jr[3] and Robyn Domsic[1], [1]University of Pittsburgh, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, [3]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, Verona, PA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Sjogren's disease (SjD) is a common systemic autoimmune disorder characterized by progressive inflammation of the exocrine glands, resulting in dry eyes and dry mouth. Anti-Ro/SSA antibodies are the prototypical serologic marker of SjD, but they are also detected in other systemic autoimmune diseases, including systemic sclerosis (SSc). The prevalence and clinical implications of anti-Ro/SSA antibodies in SSc remain poorly understood. We hypothesized that

Table 1: SSc Cohort Baseline Characteristics and Clinical Organ Manifestations at First Visit

	Ro/SSA positive (n=273)	Ro/SSA negative (n=1712)	Not tested (n=1131)	p-value
Demographic variables				
Age at 1st visit (mean ± SD)	52.8 (+/-14.8)	52.1 (+/-14.2)	52.8 (+/- 14.1)	0.43
Age at 1st symptom (mean ± SD)	43.4 (+/-15.9)	44.6 (+/- 15.3)	43.9 (+/- 15.5)	0.16
Disease duration, median (IQR)	4.9	3.4	4.9	**<0.0001**
Female (%)	80.6	81.7	76.7	**0.006**
Race (%)				**0.01**
Caucasian	83.5	90.6	89.4	
Black	11.4	6.3	6.1	
Asian	1.5	0.8	0.4	
Other	3.6	2.3	4.1	
Active smoker	10	13.2	14.4	0.17
Disease symptoms and complications				
Diffuse skin (%)	41.1	41.3	45.6	0.067
Dry eyes (%)	39.7	30.9	21.5	**<0.0001**
Dry mouth (%)	43.4	34.8	30.8	**<0.0001**
Fatigue (%)	76.2	79.9	78.1	0.279
Pulmonary Hypertension (%)	15.8	10.3	12.47	**0.0006**
PH WHO Group (%)				0.002
PAH*	9.8	7.7	8.6	
2	1.2	1.0	0.9	
3	6.5	2.9	4.6	
Exercise-induced	0	0	0.4	
Fibrosis on chest imaging (%)	51.35	37.6	41.0	**0.02**
Esophageal dysmotility ᵠ (%)	30.2	30.0	31.5	0.71
Muscle[ᵖ] (%)	6.6	3.7	3.7	0.07
Joint Swelling (%)	11.4	11.2	9.02	0.15
Tender joints to palpation	9.9	10.0	12.2	0.16
SSc associated autoantibodies (%)				
Anti-Centromere	18.5	26.3	24.9	0.03
Anti-SCL70	22.7	19.4	20.3	0.47
Anti-RNA polymerase III	13.1	21.0	24.4	**0.0004**
Anti-Th/To	7.8	7.6	8.9	0.47
Anti-U3RNP	6.17	4.3	3.3	0.10
Anti-U1RNP	11.9	7.5	5.7	**0.003**
Anti-U11RNP	0.8	1.8	1.9	0.51
Anti-U2RNP	1.6	1.6	1.2	0.84
Anti-Ku	2.0	1.5	0.9	0.26
Anti-RUV/BL12	1.3	2.0	0.6	0.09

*PAH = pulmonary arterial hypertension; PH=pulmonary hypertension, WHO = World Health Organization; ᵠgastrointestional = heartburn plus dysphagia or abnormal esophagram or manometry; [ᵖ]muscle = total CPK ≥ 2 times normal plus proximal weakness or abnormal EMG or abnormal MRI.

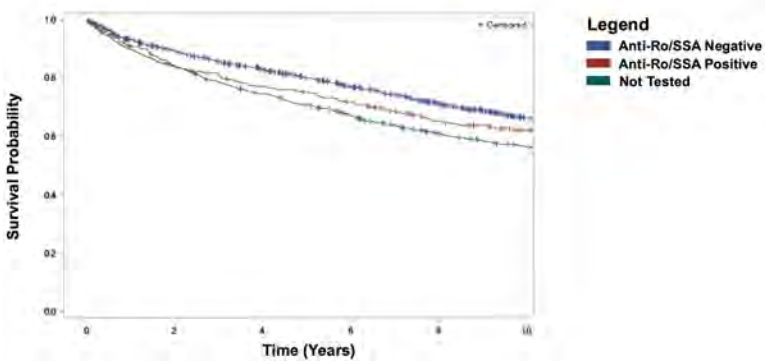
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: SSc Cohort Clinical Organ Manifestations as of Last Follow-Up

	Ro/SSA positive	Ro/SSA negative	Not tested	p-value
Dry eyes (%)	46.7	38.3	27.9	**<0.0001**
Dry mouth	44.5	41.4	37.5	**0.04**
Fatigue	88.6	88.9	86.0	**0.074**
Fibrosis on chest imaging	55.4	43.0 (637)	42.5	**0.0007**
Lowest FVC% pred (Mean ± SD)	70.6 (+/- 22.3)	77.6 (+/-22.6	75.1 (+/-22.9)	**<0.0001**
Pulmonary Hypertension (PH,%)	27.1 (74)	18.2 (312)	24.2	**0.0001**
PH by WHO Group				**0.01**
PAH (1)	47.3 (35)	53.5 (167)	54.0	
2	5.4 (4)	9.9 (31)	6.57	
3	37.8 (28)	26.3 (82)	33.2	
Exercise-induced	4.1 (3)	7.7 (24)	1.82	
Esophageal dysmotility[¶]	57.2 (155)	60.7 (1032)	60.3 (676)	0.06
Malignancy	18.6 (47)	18.5 (286)	16.13 (174)	0.267
Muscle involvement[▽]	12.1 (33)	7.1 (122)	7.1 (80)	**0.01**
Joint Swelling	26.7 (73)	24.8 (425)	17.9 (202)	**<0.0001**
Tender Joints	28.2 (77)	29.6 (507)	27.3 (309)	0.410

*PAH = pulmonary arterial hypertension; PH=pulmonary hypertension, WHO = World Health Organization; [¶]gastrointestional = heartburn plus dysphagia or abnormal esophagram or manometry; [▽]muscle = total CPK ≥ 2 times normal plus proximal weakness or abnormal EMG or abnormal MRI.

Figure 1: 10-Year Survival of SSc patients By Anti-Ro/SSA antibody status



anti-Ro/SSA antibodies confer distinct prognostic risk factors beyond sicca symptoms in patients with SSc. Our objective was threefold: 1) establish Ro/SSA seropositivity prevalence in SSc, 2) determine the frequency of sicca symptoms, and 3) assess if increased frequencies of specific organ complications were associated with Ro/SSA positivity.

Methods: We evaluated all new patients presenting with systemic sclerosis between 1980 and 2024 at a single university-dedicated scleroderma center. Participants underwent comprehensive serologic testing, including ANA, immunodiffusion, protein, and RNA immunoprecipitation (IP). Dedicated ELISA or IP screening for Ro/SSA antibodies was performed as clinically indicated. Demographics, clinical features, and survival were compared over long-term follow-up among patients who were anti-Ro/SSA positive, anti-Ro/SSA negative, or not tested.

Results: There were 3,116 patients seen for an initial visit during this time period. In the cohort, 1,985 underwent anti-Ro/SSA testing. Amongst those tested, 13.8% (273/1,985) were anti-Ro/SSA positive. Amongst the concomitant SSc antibodies, SSA/Ro positivity occurred significantly more frequently with anti-U1RNP positivity, and significantly less with anti-RNA polymerase III antibodies (Table 1), even after correcting for multiple comparisons amongst the antibodies.

Despite the presence of anti-Ro/SSA antibodies, only 47% of patients had objective dry eyes and 45% reported dry mouth, suggesting these antibodies may occur in the absence of a full SjD phenotype.

SSA positivity was not associated with a difference in cutaneous subtype. It was, however, associated with significantly higher rates of pulmonary fibrosis by imaging Table 1& 2). Not surprisingly, the lowest mean FVC was lower in Ro/SSA positive patients. Interestingly, there were higher rates of pHTN (Table 1 & 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kaplan-Meier survival analyses showed reduced 5- and 10-year survival among anti-Ro/SSA positive and untested patients compared to anti-Ro/SSA negative individuals (Figure 1).

Conclusion: Here, we show that 14% of SSc tested patients had Ro/SSA antibodies. As expected, anti-Ro/SSA patients were more likely to have sicca symptoms. Notably, anti-Ro/SSA positive patients had significantly increased rates of pulmonary fibrosis and pHTN. Anti-Ro/SSA positive patients also demonstrated reduced survival at 5 and 10 years. Untested individuals showed a similar survival decrement. Taken together, these data show that anti-Ro/SSA positivity identifies a clinically meaningful SSc phenotype with increased pulmonary involvement and worse prognosis, highlighting its potential role in clinical care and future research.

Disclosure: R. Gordon: Novartis, 1; **L. Wunsch**: None; **M. Lauffoon**: None; **T. Medsger, Jr**: None; **R. Domsic**: None.

Abstract Number: 2500

Greater Economic Burden and Healthcare Resource Utilization in Patients with Systemic Sclerosis With Versus Without Interstitial Lung Disease: Results from a Systematic Literature Review

Emily Glowienka[1], Sarah Nickolls[2], Kevin Coady[1], Eesha Kodi[3], Ian Steinfield[1], Florence Wilson[3], Alicia N. Pepper[3], Svetlana I. Nihtyanova[4], **Roger A. Levy**[5] and Daniel Moldaver[6], [1]Precision AQ, Boston, MA, [2]GSK, Research & Development, Stevenage, United Kingdom, [3]Precision AQ, Vancouver, BC, Canada, [4]GSK, Clinical Sciences, Research & Development, London, United Kingdom, [5]GSK, Specialty Care, Global Medical Affairs, Collegeville, PA, [6]GSK, Global Real-World Evidence & Health Outcomes Research, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: SSc is a rare autoimmune connective tissue disorder; up to 64% of patients with SSc develop interstitial lung disease (ILD), which can result in loss of lung function, diminished quality of life, and premature death. It also contributes a substantial economic burden through healthcare resource use (HCRU), medical expenses, and loss of productivity. This systematic literature review (SLR) evaluated the economic burden and HCRU associated with SSc in patients with ILD (SSc-ILD) and without ILD.

Methods: This SLR (GSK Study 222155) identified eligible studies (patients of any age with SSc, irrespective of severity and subtype) through database searches, with manual searches of recent peer-reviewed SLRs, meta-analyses, and health technology assessment reports. SLR conduct and reporting followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Only cost of illness and HCRU studies published as full text articles, conducted in key countries of interest (United States [US], Canada, United Kingdom, France, Germany, Spain, Japan, and China), with an observation period ending between 2013 and 2023 were selected for data extraction. Cost outcomes included total healthcare, direct, and indirect costs. HCRU outcomes included hospitalization data and length of inpatient (IP) stays. Treatments received for SSc (any use) were also assessed. The Newcastle-Ottawa Scale was used to assess the quality of studies.

Results: Out of 3042 records identified, 54 studies were considered eligible and a total of 17 studies (data reported from US, Canada, England, France, and Spain with sample sizes from 24 to 95,515) were extracted (**Figure**); all were determined to have an overall low risk of bias.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

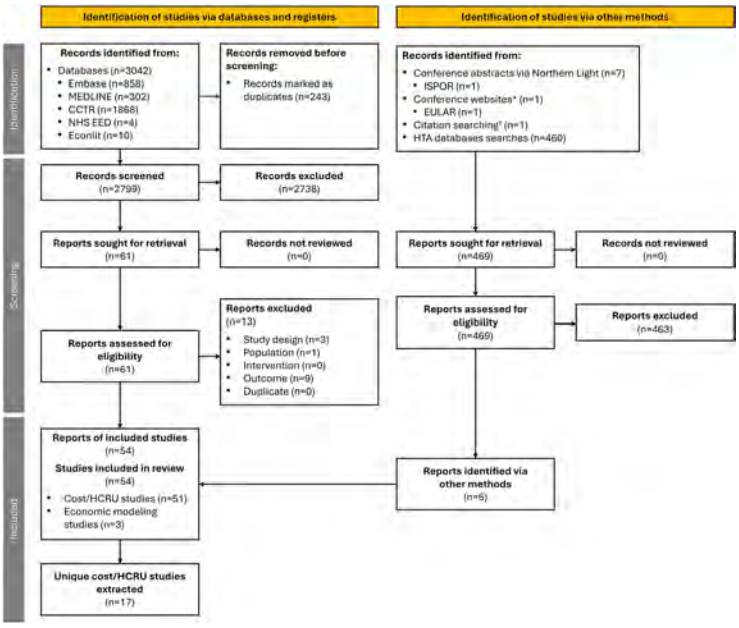


Figure. Flow diagram to summarize identification, screening, inclusion, and extraction of studies. *Hand-searching of conference databases included searches of EULAR to identify any additional abstracts of interest not captured by Northern Light; †citation searching included studies identified via reference checks and Google search engine queries. CCTR, Cochrane Central Register of Controlled Trials; Embase, Excerpta Medica DataBASE; Econlit, Essential Reference Tool for Economic Literature; EULAR, European Alliance of Associations for Rheumatology; HTA, Health Technology Assessment; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; MEDLINE, Medical Literature Analysis and Retrieval System Online; NHS EED, National Health Service Economic Evaluation Databases.

Table 1. Summary of cost outcomes (total direct and indirect healthcare costs; studies reporting values per patient per year only). Note that five studies that were suitable for data extraction are excluded from the table due to not reporting total direct/indirect healthcare costs, or per patient per year data. Mean costs are not adjusted for inflation. *Costs reported after 12-month follow-up; †no studies evaluating SSc without ILD reported total indirect costs or total healthcare costs incorporating direct and indirect; ‡not including medication; §median reported in lieu of mean. OOP, out of pocket.

Study	Country	Cost category	Mean cost
SSc overall			
Total direct healthcare costs			
Khanna 2023	US	Total direct healthcare	$47,095
Zhou 2019a*	US	Total direct healthcare	$22,016
Gayle 2020	England	Total direct all-cause healthcare, age-adjusted‡	£3180§
Lopez-Bastida 2016	England	Direct healthcare	€7925
Lopez-Bastida 2016	France	Direct healthcare	€8452
Chevreul 2015	France	Subtotal, direct healthcare	€8452
Lopez-Bastida 2014	Spain	Direct healthcare	€8235
Lopez-Bastida 2016	Spain	Direct healthcare	€8433
Total indirect costs			
Zhou 2019a*	US	Total indirect	$5170
Chevreul 2015	France	Subtotal, indirect	€10,526
Total healthcare costs, incorporating direct and indirect			
Trenaman 2023	Canada	Total direct and indirect (OOP)	CAD$3357
Lopez-Bastida 2016	England	Total (direct and indirect)	€26,542
Lopez-Bastida 2016	France	Total (direct and indirect)	€21,557
Chevreul 2015	France	Total (direct and indirect)	€22,459
Lopez-Bastida 2014	Spain	Total (direct and indirect)	€21,041
Lopez-Bastida 2016	Spain	Total (direct and indirect)	€21,640
SSc-ILD			
Total direct healthcare costs			
Zhou 2019b*	US	Total direct healthcare	$37,505
Gayle 2020	England	Total direct all-cause healthcare, age-adjusted‡	£6375§
Total indirect healthcare costs			
Zhou 2019b*	US	Total indirect	$6763
Total healthcare costs, incorporating direct and indirect			
Cottin 2021	France	Total annual	€25,753
SSc without ILD†			
Total direct healthcare costs			
Gayle 2020	England	Total direct all-cause healthcare, age-adjusted‡	£1496§

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Summary of HCRU outcomes (focus on hospitalization, ED visits, and length of IP stays). Note that two studies that were suitable for data extraction are excluded from the table due to not reporting data on hospitalization or length of IP stays, or for only evaluating incident SSc. *Data reported after 12-month follow-up; †all scleroderma-related; ‡all services consider individual days, which may include multiple service types; §population comprised patients with at least one visit; estimates reported: ‖per 100 person-years; ¶per person per year (where footnotes not included, such estimates were not reported); values at baseline: **0.30 (1.20), ††0.40 (1.00). CI, confidence interval; ED, emergency department; ICU, intensive care unit; IQR, interquartile range; SD, standard deviation.

Study	Country	Category reported	Unit, estimate type	Estimate reported
SSC overall				
Hospitalization				
Coffey 2021	US	Hospitalizations	Rate, n (rate)	278 (31.90)‖
Khanna 2023	US	ED visits	Visits§, mean (SD)	0.30 (0.00)¶
Ram Poudel 2018	US	ED admissions	Proportion of admissions, %	83.3
Sankar 2021	US	Total admissions	Proportion of admissions, n (%)	382 (60.2)
Zhou 2019a*	US	ED visits	Proportion of patients, n (%)	698 (31.8)**
Gayle 2020	England	ED visits	Count, n	1231
Chevreul 2015	France	Hospitalizations	Visits, mean	1.60¶
Length of stay				
Coffey 2021	US	Length of IP stays	Days, median (IQR)	4.00 (2.00, 6.00)
Potera and Manadan 2022	US	Length of IP stays	Days, mean	6.10
Sankar 2021	US	Length of IP stays	Days, mean (SD)	5.50 (6.40)
Zhou 2019a*	US	Length of IP stays	Days, mean (SD)	3.70 (12.7)
Gayle 2020	England	Length of IP stays	Days, median (IQR)	0.00 (0.00–2.00)
Chevreul 2015	France	Length of IP stays	Days, mean	5.00
SSc-ILD				
Hospitalization				
Sankar 2021	US	Total admissions†	Count, n	231
Zhou 2019b*	US	ED visits	Proportion of patients, n (%)	189 (39.5)††
Gayle 2020	England	ED visits	Count, n	296
Cottin 2021	France	All-cause hospitalization	Proportion‡, n (%)	3289 (98.7)
Cottin 2021	France	ICU admissions	Visits, mean (SD)	3.00 (15.40)¶
Length of stay				
Odion 2021	US	Length of IP stays	Days, mean (adjusted mean difference vs SSc without ILD [95% CI; p-value])	8.38 (1.81; 0.98–2.64; p<0.0001)
Zhou 2019b*	US	Length of IP stays	Days, mean (SD)	7.20 (19.0)
Gayle 2020	England	Length of IP stays	Days, median (IQR)	0 (0–3.00)
SSc without ILD				
Hospitalization				
Sankar 2021	US	Total admissions†	Count, n	151
Gayle 2020	England	ED visits	Count, n	190
Length of stay				
Odion 2021	US	Length of IP stays	Mean	5.97
Gayle 2020	England	Length of IP stays	Days, median (IQR)	0.00 (0.00–1.00)

Marked variation in costs associated with SSc overall and SSc with or without ILD were observed across studies (**Table 1**). Total direct healthcare costs up to $47,095 per patient per year were reported for SSc overall in the US. Where reported, direct healthcare costs were notably higher for SSc-ILD versus SSc without ILD. Patients with SSc-ILD generally had longer IP stays than those without ILD, while data on hospitalization/emergency room visits were limited (**Table 2**).

Treatment rates varied across studies. Glucocorticoids were the most common treatment for SSc/SSc-ILD (global usage: 24.0–74.1%; US rates: 24.0–44.7%), followed by mycophenolate mofetil, while less than 4% of patients received biologics.

Conclusion: These data demonstrate the substantial economic burden and HCRU with SSc and suggest that SSc-ILD has a greater impact on these measures than SSc without ILD, likely due to greater disease severity and associated impairments. However, cost/HCRU estimates varied widely, which may be partially attributable to differences in population criteria and study methodologies. Findings were restricted to five countries reporting scarce indirect cost data. Therefore, there is a need for more comprehensive studies that evaluate a broader range of cost/HCRU outcomes across diverse settings for patients with SSc-ILD, which will help validate and expand upon existing evidence to better characterize the economic burden of SSc-ILD.

Funding: GSK

Disclosure: E. Glowienka: GSK, 5, Precision AQ, 3; **S. Nickolls**: GSK, 3, 8, Pfizer, 8; **K. Coady**: GSK, 5, Precision AQ, 3; **E. Kodi**: GSK, 5, Precision AQ, 3; **I. Steinfield**: GSK, 5, Precision AQ, 3; **F. Wilson**: GSK, 5, Precision AQ, 3; **A. Pepper**: GSK, 5, Precision AQ, 3; **S. Nihtyanova**: GSK, 3, 8; **R. Levy**: GSK, 3, 8; **D. Moldaver**: GSK, 3, 8.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2501

Microvascular dysfunction contributes to hand bone deterioration in SSc patients

Rosanna Campitiello[1], Sabrina Paolino[2], Andrea Casabella[3], Giulia Davoli[2], Elisa Caratto[4], Emanuele Gotelli[1], Elvis Hysa[5], Carmen Pizzorni[2], Vanessa Smith[6], Alberto Sulli[2] and Maurizio Cutolo[7], [1]University of Genoa, Genoa, Liguria, Italy, [2]University of Genoa, Genova, Italy, [3]IRCCS Ospedale Policlinico San Martino, Genova, Italy, [4]Univeristy of Genoa, Alessandria, Italy, [5]University of Genoa, Genoa, Italy, [6]Ghent University Hospital, Gent, Belgium, [7]University of Genova, Genova, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disease characterized by endothelial dysfunction, self-reactive immune response and progressive systemic fibrosis[1]. It is well established that bone micro- and macroarchitectural damage is more prevalent in patients (pts) with SSc compared to healthy subjects(HS)[2]. Moreover, in SSc pts severe microvascular damage exhibit significant alterations in bone health, indicating a strong connection between microvascular

Table I. Statistically significant Spearman correlations between hand BMD and BMC and clinical features, antibody profiles, and NVC parameters in SSc patients. Abbreviations: BMD: bone mineral density; BMC: bone mineral content; SSc: systemic sclerosis; GI: gastrointestinal involvement; mRSS: modified Rodnan skin score; NVC: nailfold videocapillaroscopy; ACA: anticentromere antibodies; SCL70: anti-topoisomerase I antibodies.

Table I

Variables	r	df	p-value
Hand BMD and Skin fibrosis	-0.3836	28	0.036
Hand BMD and GI	-0.3899	28	0.033
Hand BMD and mRSS	-0.5811	23	0.002
Hand BMC and mRSS	-0.4027	23	0.046
Hand BMC and GI	-0.3628	28	0.049
Hand BMD and Numerosity (abs. cap/mm)	0.6893	28	<0.001
Hand BMC and Numerosity (abs. cap/mm)	0.6592	28	<0.001
Hand BMD and Numerosity (semi-quant)	-0.5658	28	0.001
Hand BMC and Numerosity (semi-quant)	-0.5006	28	0.005
Hand BMD and Ramifications	-0.4144	28	0.023
Hand BMC and Ramifications	-0.3892	28	0.034
Hand BMD and Architecture	-0.6749	28	<0.001
Hand BMC and Architecture	-0.7023	28	<0.001
Hand BMD and Late pattern	-0.5752	28	0.001
Hand BMC and Late pattern	-0.4709	28	0.009
Hand BMD and ACA	0.3976	26	0.036
Hand BMD and SCL70	-0.4522	26	0.016

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

dysfunction and muscle/bone impairment[3]. Consequently, the impaired peripheral microcirculation may contribute to the development of localized hand osteoporosis in SSc. The aim of this study was to assess the hand bone quality in SSc pts in correlation with peripheral microcirculatory status assessed with NVC analysis.

Methods: Hand (left and right) and total BMD and BMC were assessed by DXA and a dedicated software (GE Lunar, USA) in 32 SSc pts (age 61 ± 14 years, 94% women) affected by limited or diffuse cutaneous (dcSSc 47%) according to the 2013 EULAR/ACR criteria and 30 age-matched HS. Progressive peripheral microvascular damage, assessed by validates nailfold capillaroscopy (NVC)[4]. Statistical analysis was carried out by non-parametric tests and logistic regression analysis was performed to examine the influence of the capillary loss and hand bone status.

Results: Data revealed significantly lower hand BMD and BMC values (mean±SD) in SSc pts and age matched HS (BMD 0.31 ± 0.07vs 0.39 ± 0.06, $p < 0.01$; BMC 21.27±7.32 vs 30.09 ± 7.8, p< 0,01). The presence of SSc was associated with lower hand BMD compared with HS (adjusted for age, gender, BMI and history of osteoporosis; Beta= -0.2234, $p = 0.025$). In SSc pts a positive correlation was observed between hand and both spine vertebral bodies values ($r(30) = 0.4671$, $p = 0.007$) and femoral bone status (Neck $r(30) = 0.3866$, $p = 0.029$; total $r(30) = 0,354$, $p = 0,047$). Clinical, laboratory and NVC correlations have been performed (Table I). The regression analysis revealed that reduced capillary count significantly accounted for 38.26% of the variance in BMD values ($R^2 = 0.3826$, $F = 17.35$, $p < 0.001$).

Conclusion: In conclusion, hand bone status in SSc pts was found significantly lower compared to spine and femor bone and HC as well as associated with disease severity. The hand bone damage seems linked to the microvascular insufficiency. Therefore, care to the bone status should be taken as consequence of the progressive microvasculatory damage/ insufficiency in SSc.

References: 1) Volkmann, E. R. et al. (2023). Systemic sclerosis. The Lancet, 401(10371), 304–318. 2) Omair, M. A. et al. (2013). Low bone density in systemic sclerosis: A systematic review. The Journal of Rheumatology, 40(11), 1881–1890. 3) Paolino, S. et al. (2021). Body composition and bone status in relation to microvascular damage in systemic sclerosis patients. Journal of Endocrinological Investigation, 44(2), 255–264. 4) Smith, V. et al. (2020). Standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis. Autoimmunity Reviews, 19(3), 102458.

Disclosure: R. Campitiello: None; **S. Paolino**: None; **A. Casabella**: None; **G. Davoli**: None; **E. Caratto**: None; **E. Gotelli**: None; **E. Hysa**: None; **C. Pizzorni**: None; **V. Smith**: Argenx, 2, Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, 5, 6; **A. Sulli**: None; **M. Cutolo**: None.

Abstract Number: 2502

Deciphering Systemic Sclerosis Phenotypes: A Novel Approach Using Clustering Algorithms and Proteomic Insights. Results from the PRECISESADS Study

Santiago Dans Caballero[1], Rafaela Ortega-Castro[2], Chary López pedrera[3], Alejandro Escudero[4], Beatriz Vellón-García[5], Carlos Pérez Sánchez[6] and Clementina López Medina[7], [1]Reina Sofia University Hospital, Lebrija, Andalucia, Spain, [2]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [3]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [4]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Andalucia, Spain, [5]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain/Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Córdoba, Córdoba, Spain, Cordoba, Spain, [6]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [7]Department of Medicine, Hospital Universitario Reina Sofia, University of Cordoba, IMIBIC, Cordoba, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic sclerosis (SSc) is a clinically and biologically heterogeneous autoimmune disease characterized by multiorgan involvement, substantial morbidity, and high mortality. Traditional classification systems (based on the extent of cutaneous involvement or autoantibody status) fail to fully capture the complexity of disease expression and progression. There is a growing need for more precise patient stratification strategies that reflect underlying pathophysiology and can guide therapeutic decisions. Molecular approaches such as proteomic profiling may enable a shift from descriptive to mechanism-based classification frameworks in SSc.

Our objective was to identify biologically and clinically distinct subgroups of SSc patients through unsupervised clustering of clinical and serological data, combined with high-throughput serum proteomic analysis.

Table 1. Comparison of clinical and serological characteristics between the two identified clusters of SSc patients (PRECISESADS cohort). ¶: variables included in the clustering algorithm. ILD: interstitial lung disease; PAH: pulmonary arterial hypertension; GERD: gastroesophageal reflux disease; bDMARD: biologic disease-modifying antirheumatic drug.

Variable	PRECISESADS cohort (n=402)	Cluster 1 (n=221)	Cluster 2 (n=181)	p-value
Age (years), mean (SD)¶	58.1 (12.9)	57.2 (13.2)	59.2 (12.4)	0.12
Disease duration (years), mean (SD)	10.8 (8.7)	10.2 (9.6)	11,6 (7.5)	0.10
Sex (female), n (%)¶	339 (84.3)	188 (85.1)	151 (83.4)	0.75
ILD, n (%)¶	140 (34.8)	32 (14.5)	108 (59.7)	**< 0.01**
Sclerodactyly, n (%)¶	288 (71.6)	118 (53.4)	170 (93.9)	**< 0.01**
PAH, n (%)¶	76 (18.9)	20 (9)	56 (30.9)	**< 0.01**
Limited cutaneous phenotype, n (%)	216 (53.7)	133 (60.2)	83 (45.9)	**< 0.01**
Raynaud phenomenon, n (%)¶	389 (96.8)	209 (94.6)	180 (99.4)	**0.01**
Ever smoking, n (%)¶	55 (13.7)	32 (14.5)	23 (1.7)	0.71
Hypertension, n (%)	129 (32.1)	72 (32.6)	57 (31.5)	0.90
Centromere positivity, n (%)	149 (37.1)	96 (43.4)	53 (29.3)	**< 0.01**
Scl-70 positivity, n (%)	114 (28.4)	44 (19.9)	70 (38.7)	**< 0.01**
Arthritis, n (%)¶	118 (29.4)	46 (20.8)	72 (39.8)	**< 0.01**
Calcinosis, n (%)¶	93 (23.1)	15 (6.8)	78 (43.1)	**< 0.01**
Digital ulcers, n (%)¶	39 (9.7)	11 (5)	28 (15.5)	**< 0.01**
Telangiectasias, n (%)¶	239 (59.5)	88 (39.8)	151 (83.4)	**< 0.01**
GERD, n (%)¶	267 (66.4)	117 (52.9)	150 (82.9)	**< 0.01**
Dyslipidemia, n (%)	98 (24.4)	57 (25.8)	41 (22.6)	0.54
Pitting scars, n (%)¶	198 (49.3)	65 (29.4)	133 (73.5)	**< 0.01**
Current bDMARD, n (%)	10 (2.5)	2 (0.9)	8 (4.4)	**0.04**
Current immunosuppressants, n (%)	106 (26.4)	32 (14.5)	74 (40.9)	**< 0.01**
Obesity, n (%)	39 (9.7)	23 (10.4)	16 (8.8)	0.72
Esophageal dysmotility, n (%)¶	200 (49.7)	77 (63.6)	123 (68)	**< 0.01**
Statins use, n (%)	84 (20.9)	42 (19)	42 (23.2)	0.36
Puffy fingers, n (%)	225 (56)	116 (52.5)	109 (60.2)	0.14
Muscle weakness, n (%)¶	72 (17.9)	21 (9.5)	51 (28.2)	**< 0.01**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

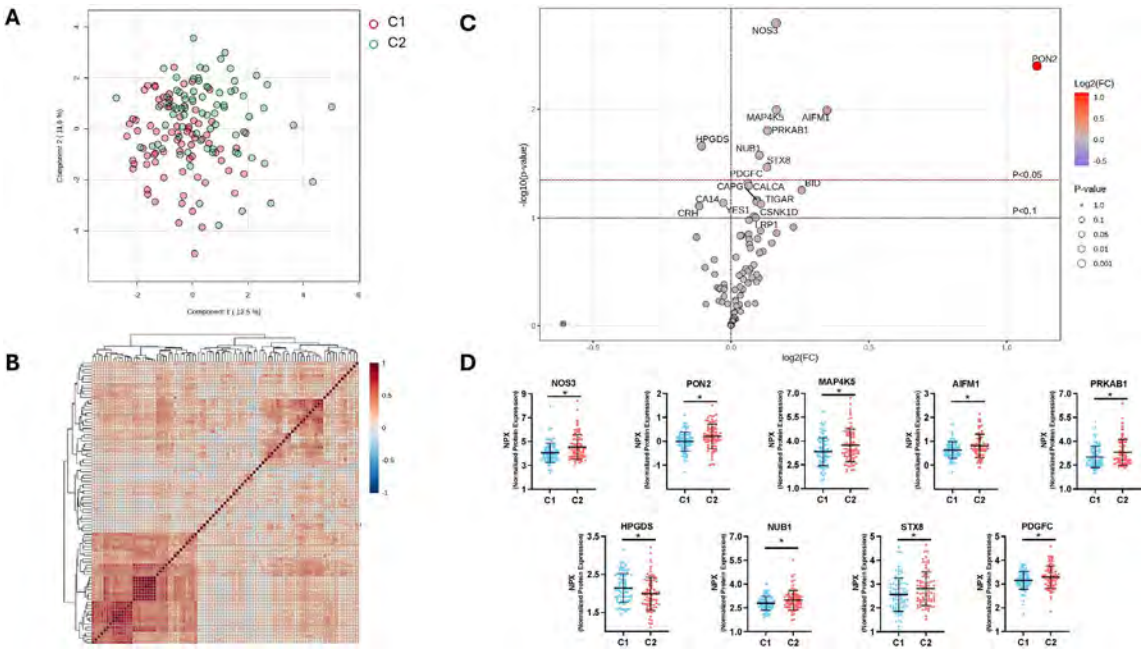


Figure 1. Proteomic analysis of organ damage markers in SSc. (A) Principal component analysis (PCA) of SSc patient clusters based on organ damage-related proteomic markers. (B) Heatmap showing correlations among protein levels across all patients. (C) Volcano plot of differentially expressed proteins between SSc clusters. (D) Circulating levels of statistically significant proteins differentiating cluster 1 and cluster 2.

Methods: Clinical and serological data from 402 patients in the multicenter PRECISESADS cohort were analyzed using k-means clustering to define SSc subtypes. Internal validity was assessed using statistical indices; external validation was performed in an independent Spanish cohort (n=213). Proteomic profiling was conducted on a representative subset of 154 patients using a targeted 92-protein OLINK® panel focused on organ damage. Functional validation was carried out

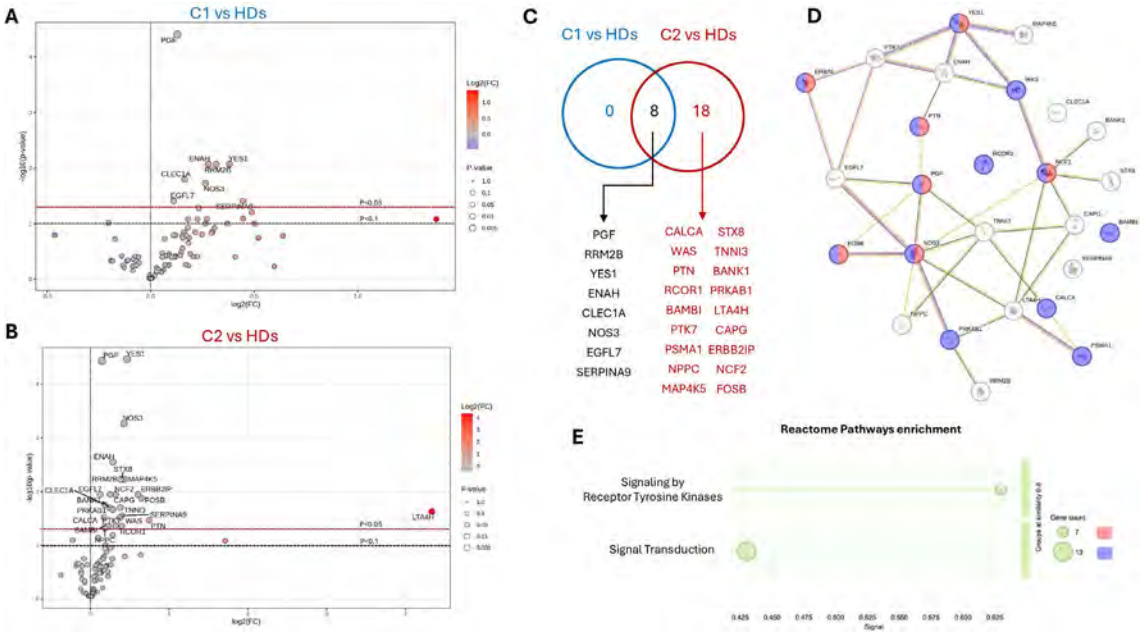


Figure 2. Comparative volcano plots and functional interaction network of differentially expressed proteins in SSc patient clusters vs healthy donors. (A) Volcano plot comparing protein expression between healthy controls and patients in Cluster 1. (B) Volcano plot showing the comparison between healthy controls and Cluster 2 patients, with a greater number of significantly upregulated proteins. (C) Venn diagram showing the overlap of differentially expressed proteins in clusters 1 and 2 compared to healthy donors. (D, E) Functional interaction network of the differentially expressed proteins compared to healthy controls, constructed using the STRING platform The analysis reveals a dysregulation of the Signaling by Receptor Tyrosine Kinases pathway (proteins in red) and signal transduction (proteins in purple).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

by treating immortalized fibroblasts with serum from patients in each cluster, followed by RT-qPCR analysis of fibrotic and inflammatory gene expression.

Results: Two robust and clinically distinct clusters were identified and independently validated. Cluster 2 was associated with a more severe phenotype, including a higher prevalence of interstitial lung disease (59.7% vs. 14.5%), pulmonary arterial hypertension (30.9% vs. 9%), and musculoskeletal involvement. A detailed comparison of demographic and clinical characteristics between clusters is provided in Table 1.

Proteomic analysis revealed 26 upregulated proteins in Cluster 2, including PDGFC, NOS3, and PRKAB1 (linked to fibrosis, endothelial injury, and metabolic stress (Figures 1A-D)). Compared to healthy donors, Cluster 2 showed greater proteomic dysregulation than Cluster 1 (Figures 2A-E), and pathway enrichment highlighted alterations in receptor tyrosine kinase signaling and immune activation. Functional assays confirmed that serum from Cluster 2 patients induced upregulation of profibrotic (PDGFRB, WNT3A) and proinflammatory (TNF, IL1B) genes in fibroblasts. Several proteins also correlated with clinical features such as pulmonary hypertension and esophageal dysmotility.

Conclusion: This integrative approach combining unsupervised clustering, proteomics, and functional validation identifies molecularly and clinically meaningful SSc subgroups. The findings support the use of circulating protein profiles to refine patient stratification and move toward personalized management in SSc.

Disclosure: S. Dans Caballero: None; **R. Ortega-Castro**: None; **C. López pedrera**: None; **A. Escudero**: None; **B. Vellón-García**: None; **C. Pérez Sánchez**: None; **C. López Medina**: None.

Abstract Number: 2503

Validation of a Composite Biomarker Score To Predict Modified Rodnan Skin Score: Insight From Autologous Stem Cell Transplantation International Scleroderma trial

stefano rodolfi[1], kristina clark[2], bahja Ahmed Abdi[1], medha kanitkar[3], Voon H. Ong[3], Alexandre Voskuijl[4], Jeska de Vries-Bouwstra[5], Jacob M. van Laar[6], Christopher Denton[7] and julia Spierings[8], [1]University College London, London, United Kingdom, [2]Kennedy Institute of Rheumatology, University of Oxford, London, United Kingdom, [3]Division of Medicine, Centre for Rheumatology, University College London, London, United Kingdom, [4]Amsterdam University Medical Center, Amsterdam, Netherlands, [5]Leiden University Medical Center, Leiden, Netherlands, [6]UMC Utrecht, Utrecht, Netherlands, [7]University College London, UK, London, United Kingdom, [8]Department of Rheumatology & Clinical Immunology, University Medical Center, Ultrecht, The Netherlands, Utrecht, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2470–2503) Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Skin fibrosis is a cardinal manifestation of diffuse cutaneous systemic sclerosis (dcSSc) and is routinely measured via the modified Rodnan skin score (mRSS); however, mRSS is limited by its operator-dependence and may not reflect the complex disease biology at the cutaneous compartment. A recent high dimensional multi-omic analysis identified 3 serum proteins independently associated with mRSS: tenascin C (TNC), cartilage oligomeric matrix protein (COMP), and collagen type IV alpha 1 (COL4A1). Integrating their serum concentrations, a composite biomarker score to reflect skin involvement was derived and tested in 2 cohorts from a single centre. Whilst there was correlation of the composite marker

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

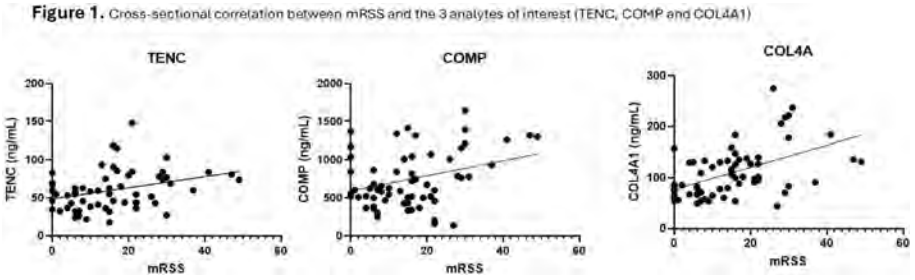


Figure 1. Cross-sectional correlation between mRSS and the 3 analytes of interest (TENC, COMP and COL4A1)

and its components with mRSS and some association with underlying treatment, the results of these studies were inconclusive, potentially due to the narrow range of mRSS and modest impact of standard immunosuppressive treatment in the SSc cohorts. The aim of the present study was to validate this composite biomarker score in a cohort with a greater dynamic range of mRSS and high percentage of patients receiving intensive immunosuppressive treatment.

Methods: We selected patients from 2 centres in the Netherlands who participated in the Autologous Stem Cell Transplantation International Scleroderma (ASTIS) trial. Serum concentrations of TNC, COMP and COL4A1 were measured via commercially available enzyme linked immunosorbent assay (ELISA) kits on samples at baseline, 12 months and 24 months. Serum levels of target analytes were correlated with mRSS data cross-sectionally and longitudinally. Spearman's test, Bland Altman test, univariable and multivariable linear regression were used to test for correlation. A p value < 0.05 was considered statistically significant.

Results: We included 21 patients: 11 treated with cyclophosphamide (CYC), and 10 subjected to autologous haematopoietic stem cell transplant (HSCT). Median mRSS was 21 at baseline, 12 at 12 months, and 6 at 24 months. The concentrations of all 3 analytes showed a significant correlation with mRSS when evaluated cross-sectionally at all the timepoints (**Figure 1**), with COL4A1 maintaining statistical significance at multivariable analysis (r=0.0952, p=0.001). From these data, we derived a refined composite serum biomarker score to predict actual mRSS (**Figure 2**). Next, we assessed the performance of the analytes as dynamic biomarkers of mRSS, however only changes in COMP were associated with mRSS variation (r= 0.013; p= 0.012). Finally, although both treatment arms had the same degree of mRSS variation from baseline to 24 months (i.e. 15 points), the change in COL4A1 concentration was significantly larger in the HSCT group than in the CYC group (**Figure 3**).

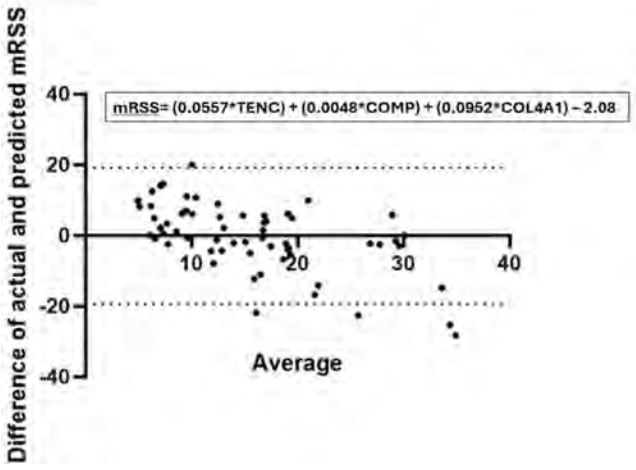
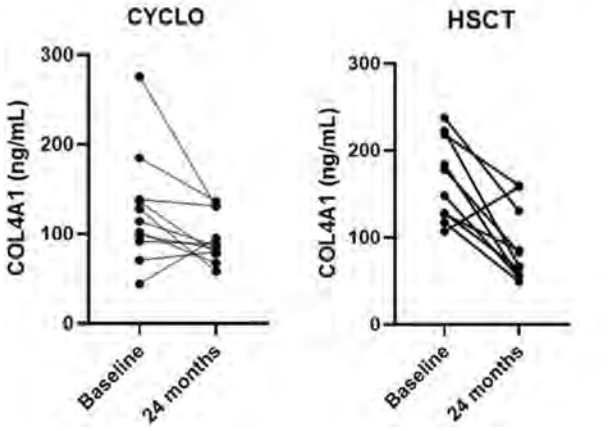


Figure 2. Bland-Altman plot of predicted and actual mRSS, including a refined formula to predict mRSS

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3. Change in COL4A1 concentrations from baseline to 24 months across the 2 treatment groups



Conclusion: Our refined composite biomarker score predicts mRSS score cross-sectionally, however the performance of these analytes as dynamic markers of cutaneous involvement is poor.

The differences for serum COL4A1 across treatment groups, with greater reduction in the HSCT group, was associated with a long-term survival advantage in the ASTIS trial which warrants further evaluation of the role of this protein as a predictive marker in dcSSc

Disclosure: s. rodolfi: None; **k. clark**: None; **b. Ahmed Abdi**: None; **m. kanitkar**: None; **V. Ong**: Boehringer-Ingelheim, 6; **A. Voskuijl**: None; **J. de Vries-Bouwstra**: AbbVie/Abbott, 2, 6, Boehringer-Ingelheim, 2, 6, Jannsen-Cilag, 5, Janssen, 2, 6, Roche, 5; **J. van Laar**: None; **C. Denton**: AbbVie/Abbott, 2, Boehringer-Ingelheim, 2, Certa Pharmaeuticals, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Novartis, 2; **j. Spierings**: None.

Abstract Number: 2504

Variables Associated with In-Hospital Mortality in Adult Eosinophilic Granulomatosis with Polyangiitis from the National Inpatient Sample Database 2017-2021

Anuya Natu[1], Isadora Small[2], Shilpa Arora[3] and Augustine Manadan[4], [1]John H Stroger, Jr. Hospital of Cook County, Chicago, IL, [2]The Latin School of Chicago, Chicago, IL, [3]Cook County Hospital, Chicago, IL, [4]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare systemic vasculitis that can lead to significant morbidity and mortality. This study aims to evaluate the demographic, clinical, and hospital-related characteristics associated with in-hospital mortality among EGPA hospitalizations using a claims-based US national database.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Descriptive Characteristics of Adult Hospitalizations with EGPA from the National Inpatient Sample Database 2017-2021 (n=9,095). Abbreviations: AKI= Acute Kidney Injury; CCI= Charlson Comorbidity Index; EGPA=Eosinophilic Granulomatosis with Polyangiitis; HLH= Hemophagocytic Lymphohistiocytosis; HF= Heart Failure; IQR=interquartile range; LOS=Length of Stay; n=number; NIS= National Inpatient Sample Database; NR = not reported as below permitted reporting threshold (≤10 cases); PI=Pacific Islander.

Hospital Admission Characteristics	Discharged Alive (n=8,830)	In-hospital death (n=265)	P-value
Age, median (IQR), years	63 (50-73)	69 (61-77)	0.018
Male	42.5%	54.7%	0.075
Race/Ethnicity			
White	71.3%	73.6%	0.713
African American	11.3%	7.5%	0.399
Hispanic	7.2%	9.4%	0.528
Asian/PI	4.1%	NR	0.909
Native American	0.6%	0%	0.581
Other Race	3.1%	NR	0.625
Insurance type			
Medicare	53.1%	67.9%	0.034
Medicaid	10.8%	20.8%	0.024
Private Insurance	31.8%	9.4%	<0.001
Self-Pay	2.1%	0%	0.283
No Charge	NR	0%	0.806
Other Insurance	2.1%	NR	0.917
Household Income			
Quartile 1	19.5%	20.8%	0.826
Quartile 2	23.4%	20.8%	0.655
Quartile 3	25.3%	28.3%	0.623
Quartile 4	30.5%	28.3%	0.728
CCI	2 (1-3)	3 (2-5)	0.010
AKI	19.9%	66.0%	<0.001
Alveolar Hemorrhage	0.8%	5.7%	<0.001
Infection	46.2%	79.2%	<0.001
HF (systolic or diastolic)	22.9%	37.7%	0.012
HLH	NR	NR	0.002
Myocardial Infarction	4.0%	7.5%	0.193
Myocarditis	1.2%	0	0.426
LOS, median (IQR), days	4 (2-8)	10 (4-16)	<0.001
Total charges, median (IQR)	$43,916 (24,354-84,791)	$154,087 (74,249-268,624)	<0.001

Methods: A retrospective analysis of the National Inpatient Sample (NIS) database from 2017 - 2021 was conducted to identify adult hospitalizations with a primary or secondary diagnosis of EGPA (ICD 10: M30.1). Descriptive statistics were used to compare patients discharged alive and those who suffered in-hospital mortality. All variables with $p \leq 0.2$ in the univariable screen were included in a multivariable logistic regression model to assess independent predictors of in-hospital death. $p \leq 0.05$ was considered significant in multivariable analysis. Cells of data containing hospitalization records with a value of 1 to 10 were not reported to protect hospital privacy as per the Healthcare Cost and Utilization Project (HCUP) data service agreement.

Results: A total of 9,095 hospitalizations for EGPA were identified, with an in-hospital mortality rate of 2.9% (n = 265) (Table 1). Patients who died in-hospital were older (median age 69 vs. 63 years ; $p = 0.018$), had a higher median Charlson Comorbidity Index (CCI) (3 vs. 2; $p = 0.01$), higher acute kidney injury (AKI) (66.0% vs. 19.9%; $p < 0.001$), higher alveolar hemorrhage (5.7% vs. 0.8%; $p < 0.001$), higher concurrent infection (79.2% vs. 46.2%; $p < 0.001$), higher heart failure

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Univariable Logistic Regression for In-hospital Death for EGPA from NIS 2017-2021. Abbreviations: AKI= Acute Kidney Injury; CCI= Charlson Comorbidity Index; EGPA=Eosinophilic Granulomatosis with Polyangiitis; HLH= Hemophagocytic Lymphohistiocytosis; HF= Heart Failure; NIS= National Inpatient Sample Database. *Univariable analysis was not conducted for Native American, Self Pay, No Charge and Myocarditis as there were no observed deaths in that category.

Variable	OR	P value	95% C.I.
Age	1.03	0.001	1.01 - 1.05
Male	1.64	0.078	0.95 - 2.83
White	1.12	0.713	0.61 - 2.07
African American	0.64	0.402	0.23 - 1.81
Hispanic	1.34	0.529	0.53 - 3.38
Asian/PI	0.92	0.909	0.23 - 3.68
Other Race	0.61	0.628	0.08 - 4.52
Medicare	1.87	0.036	1.04 - 3.37
Medicaid	2.16	0.027	1.09 - 4.28
Private Insurance	0.22	0.001	0.09 - 0.56
Other Insurance	0.90	0.917	0.12 - 6.68
Income Q1	1.08	0.826	0.55 - 2.12
Income Q2	0.86	0.655	0.44 - 1.68
Income Q3	1.16	0.623	0.63 - 2.14
Income Q4	0.90	0.728	0.49 - 1.64
CCI	1.30	<0.001	1.15 - 1.46
AKI	7.84	<0.001	4.38 - 14.02
Alveolar Hemorrhage	7.51	0.002	2.09 - 26.93
HF (Systolic or Diastolic)	2.04	0.013	1.16 - 3.59
HLH	16.96	0.022	1.51 - 189.83
Infection	4.45	<0.001	2.27 - 8.69
Myocardial Infarction	1.98	0.202	0.69 - 5.63

Table 3: Multivariable Logistic Regression for In-hospital Death for EGPA from NIS 2017-2021. Abbreviations: AKI= Acute Kidney Injury; CCI= Charlson Comorbidity Index; EGPA= Eosinophilic Granulomatosis with Polyangiitis; HLH= Hemophagocytic Lymphohistiocytosis; HF= Heart Failure; NIS= National Inpatient Sample Database.

Variable	Odds Ratio	P value	95% C.I.
Age	1.03	0.071	1.00 - 1.05
Male	1.58	0.131	0.87 - 2.87
Medicare	1.77	0.617	0.19 - 16.44
Medicaid	6.17	0.117	0.63 - 60.07
Private Insurance	0.76	0.814	0.07 - 7.70
CCI	1.16	0.137	0.95 - 1.40
AKI	4.81	<0.001	2.50 - 9.25
Alveolar Hemorrhage	6.92	0.014	1.47 - 32.46
HF (Systolic or Diastolic)	1.03	0.935	0.48 - 2.22
HLH	6.10	0.062	0.91 - 40.73
Infection	3.56	<0.001	1.81 - 7.01
Myocardial Infarction	1.24	0.745	0.34 - 4.42

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(37.7% vs. 22.9%; $p = 0.012$), longer median hospital length of stay (10 vs. 4 days; $p < 0.001$), and higher median total hospital charges ($154,087 vs. $43,916; $p < 0.001$). The variables from the univariable screen showing an association with in-hospital mortality were age, male sex, Medicare insurance, Medicaid insurance, private insurance, CCI, AKI, alveolar hemorrhage, heart failure, hemophagocytic lymphohistiocytosis, infection, and myocardial infarction (Table 2).

In multivariable regression analysis, independent predictors of in-hospital mortality included AKI (OR 4.81; 95% CI 2.50 - 9.25), alveolar hemorrhage (OR 6.92; 95% CI 1.47 - 32.46), and infection (OR 3.56; 95% CI 1.81 - 7.01) (Table 3). Age, sex, insurance type, and comorbidity burden were not independent predictors of in-hospital death in EGPA.

Conclusion: In this large, nationally representative cohort, EGPA hospitalizations had a 2.9% in-hospital mortality rate. AKI, alveolar hemorrhage, and infection were strong independent predictors of mortality. These findings highlight the need for early recognition and management of these complications to improve outcomes in hospitalized EGPA patients.

Disclosure: A. Natu: None; **I. Small**: None; **S. Arora**: None; **A. Manadan**: None.

Abstract Number: 2505

Avacopan is Not Associated With An Increased Risk of Infection Compared to Glucocorticoids in Patients with ANCA-Associated Vasculitis

BEATRIZ MARIA FRANCO HONDERMANN, LOYOLA UNIVERSITY MEDICAL CENTER, OAK PARK

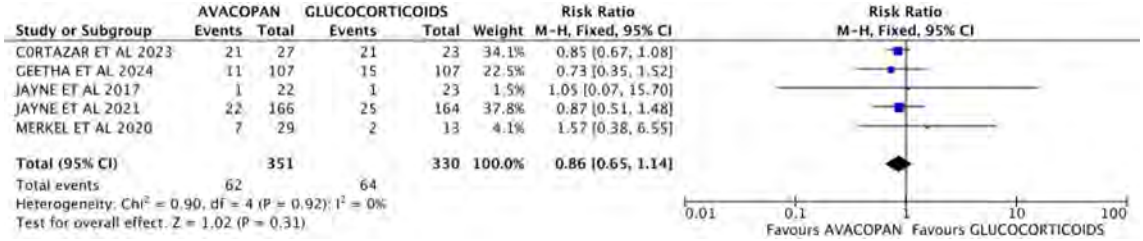
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Avacopan is a novel C5a receptor inhibitor recently approved for treatment of ANCA-associated vasculitis as an alternative to glucocorticoids, It has demonstrated superior efficacy in achieving remission and improving renal outcomes. However, limited studies have compared the safety profiles, particularly the risk of severe infections, between avacopan and glucocorticoids in AAV patients. This meta-analysis aims to evaluate the combined risk of severe infections in patients treated with avacopan compared to those treated with glucocorticoids.

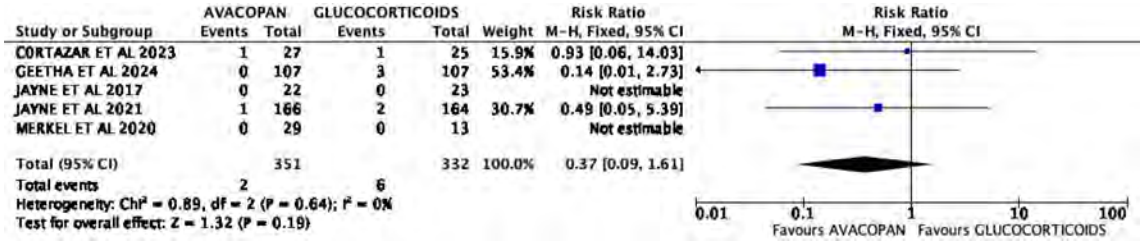
Methods: A comprehensive literature search was performed on Pubmed, Cochrane and Embase databases for randomized controlled trials (RTCs) comparing risk of infection in patients with ANCA-related vasculitis treated with Avacopan versus Glucocorticoids. Severe infection were defined as pneumonia, UTI, neutropenic sepsis, sepsis, fungal infection, reactivation of HSV, meningitis or others as specified by each study. Statistical analysis was performed using Review Manager 5.17. Heterogeneity was assessed by I^2 statistics.

Results: A total of 681 patients from 5 RCTs were included, with 351 (51.5%) receiving avacopan. The mean age was 60.5 years (±14.5), and 46% were female. The follow-up duration ranged from 12 to 52 weeks. Pneumonia was the most commonly reported severe infection. Eight deaths due to severe infections were reported across the studies. The pooled relative risk (RR) for severe infections was 0.84 (RR 0.84; 95% CI: 0.62–1.15; p=0.9; I^2=0%), indicating no statistically significant difference between the avacopan and glucocorticoid groups (Forest Plot 1). Similarly, the RR for death due to infection was 0.37 (RR 0.37; 95% CI: 0.09–1.61; p=0.64; I^2=0%), showing no significant difference between the two treatment groups (Forest Plot 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Forest Plot 1



Forest Plot 2

Conclusion: In conclusion, treatment with Avacopan does not increase the risk of severe infection compared to glucocorticoid treatment in patients with ANCA-associated vasculitis. These results support current literature suggesting better overall outcomes of patients with ANCA-vasculitis treated Avacopan without an increased risk of infection.

Disclosure: B. FRANCO HONDERMANN: None.

Abstract Number: 2506

Timing, Management, and Outcomes of Venous Thromboembolic Events in ANCA-Associated Vasculitis: A Retrospective Cohort Study

Bruno Marchetti[1], Michele Iudici[2], Yann Nguyen[3], Pascal Cohen[4], Loic Guillevin[4], Xavier Puéchal[5] and Benjamin Terrier[6], [1]Department of Internal Medicine, University of Turin, Mauriziano Hospital, Torino, Italy, [2]Division of Rheumatology, Department of Internal Medicine Specialties, Geneva University Hospitals, Geneva, Switzerland, [3]Department of Internal Medicine, Beaujon Hospital, AP-HP Nord, Université Paris Cité, Clichy, France, Clichy, France, [4]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, Paris, France, [5]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [6]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA-associated vasculitis (AAV) has been associated with an increased risk of venous thromboembolic events (VTE). However, limited data are available regarding the precise timing, nature, severity, management, and recurrence of VTE in this population. This study aimed to characterize the clinical features of VTE in AAV patients and assess the impact of immunosuppressive and antithrombotic therapy on outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We conducted a retrospective monocentric cohort study including patients diagnosed with AAV according to the 2022 ACR/EULAR classification criteria who experienced at least one VTE. VTE types, timing in relation to AAV diagnosis and disease activity, therapeutic strategies (including anticoagulation duration and immunosuppression), and VTE-related outcomes were recorded. Recurrence rates and their association with vasculitis flares were also analyzed.

Results: Among 34 patients with AAV and VTE, 28 (82%) had granulomatosis with polyangiitis, 2 (6%) microscopic polyangiitis, and 4 (12%) eosinophilic granulomatosis with polyangiitis. The most common VTEs were pulmonary embolism (n=21, 62%), deep vein thrombosis (n=20, 59%), with 9 patients (26%) experiencing both, and deep vein thrombosis of atypical sites (n=2, 6%).

VTE occurred within the first 6 months of AAV diagnosis in 16 cases (47%), or following a vasculitis flare in 9 patients (26%). In these patients, the median time from diagnosis of vasculitis to VTE was 30 days (IQR 11–96). In the remaining 9 patients, VTE occurred at a median of 69 days (IQR 50–82) after AAV flare. Median Birmingham Vasculitis Activity Score (BVAS) at VTE onset was 5.5 [IQR 0–15].

At the time of VTE, 88% of patients (n=30) were under immunosuppressive treatment and 29 were receiving systemic glucocorticoids with a median prednisone dose of 32.5 mg/day (IQR 9–60). Anticoagulation therapy was administered for a median duration of 6 months [IQR 3–8.25]; 43% received < 6 months, 43% between 6–12 months, and 14% >12 months.

Recurrent VTE occurred in 6 patients (19%) after anticoagulant discontinuation, of whom 3 experienced recurrence concomitant with vasculitis relapse. Two patients (6%) died as a direct consequence of thromboembolic complications.

Conclusion: VTEs in AAV patients frequently occur during periods of active disease and predominantly manifest as pulmonary embolism or deep vein thrombosis. Despite immunosuppressive treatment, thrombotic events still occur. Recurrence was observed in 20% of patients, particularly during relapse. These findings underscore the importance of considering VTE when clinically suspected, especially during AAV onset or relapse.

Disclosure: B. Marchetti: None; **M. Iudici**: Boehringer-Ingelheim, 6; **Y. Nguyen**: None; **P. Cohen**: Roche, 5; **L. Guillevin**: Roche, 5; **X. Puéchal**: Roche, 5; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 2507

Reporting of infectious and hepatic adverse events with avacopan: insights from the World Health Organization pharmacovigilance database (VigiBase)

Camille Mettler[1], Laurent Chouchana[2] and Benjamin Terrier[3], [1]Département de Médecine interne, Hôpital Bichat-Claude-Bernard, Paris, France, [2]Département de Pharmacologie, Centre Régional de Pharmacovigilance, Hôpital Cochin, Paris, France, [3]Cochin Hospital, Paris, France

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of infectious, gastrointestinal and hepatic cases in patients receiving avacopan reported in the WHO global safety database.

Number of cases	All AE n=2775	Infectious AE n=438	Hepatic AE n=79
Sex, female	1121 (40.4%)	169 (38.6%)	35 (44.3%)
Age (years)	62 [50-72]	61 [48-71.2]	68 [61.5-77]
Completeness score	0.3 [0.2-0.3]	0.3 [0.2-0.3]	0.3 [0.2-0.5]
Reporter qualification			
Consumer/Non Health Professional	1601 (57.7%)	257 (58.7%)	22 (27.8%)
Physician	920 (33.2%)	159 (36.3%)	50 (63.3%)
Unknown	254 (9.2%)	22 (5.0%)	7 (8.9%)
Continent of reporting			
North America	2449 (88.3%)	359 (82%)	44 (55.7%)
Europe	305 (11%)	74 (16.9%)	33 (41.8%)
Oceania	20 (0.7%)	5 (1.1%)	2 (2.5%)
Middle East	1 (0%)	0 (0%)	0 (0%)
Asia	0 (0%)	0 (0%)	0 (0%)
Delay (days)	NA	28 [6-78] n=41	47 [40-63] n=21
Serious	1292 (46.6%)	262 (59.8%)	58 (73.4%)
Seriousnes criteria			
Death	174 (6.3%)	41 (9.4%)	3 (3.8%)
Life threatening	22 (0.8%)	4 (0.9%)	2 (2.5%)
Caused/Prolonged hospitalization	639 (23.0%)	130 (29.7%)	17 (21.5%)
Disabling/Incapaciting	2 (0.1%)	0 (0%)	0 (0%)
Other relevant medical condition	454 (16.4%)	87 (19.9%)	35 (44.3%)
Co-reported drug			
Rituximab[a]	239 (8.6%)	84 (19.2%)	9 (11.4%)
Cyclophosphamide[a]	92 (3.3%)	31 (7.1%)	5 (6.3%)
Glucorcoticoids[a]	354 (12.8%)	99 (22.6%)	11 (13.9%)

Note: Data are presented as N (%) or median [IQR]. Abbreviations: AE Adverse event; a Patients could enter different categories.

Background/Purpose: Avacopan, an oral C5aR antagonist, is approved for the treatment of ANCA-associated vasculitis (AAV) as a steroid-sparing alternative. While clinical trials demonstrated a positive benefit/risk ratio, post-marketing surveillance remains essential to assess its real-world safety. Based on its pharmacological activity and on case reports from the literature, we sought to evaluate infectious and hepatic adverse events (AEs) associated with avacopan.

Table 2. Details of infectious and hepatic adverse events reported with avacopan in the WHO global safety database.

Reporting characteristics	Avacopan n=2,775
Infection adverse event	438 (15.8%)
Respiratory tract infection[a]	206 (47.0%)
Pneumonia[a]	118 (26.9%)
COVID-19 infection[a]	96 (21.9%)
Urinary tract infection[a]	45 (10.3%)
Ear, nose and throat infection[a]	43 (9.8%)
Sepsis[a]	30 (6.8%)
Digestive infection[a]	21 (4.8%)
Other fungal infection[a]	15 (3.4%)
VZV infection[a]	11 (2.5%)
Abscess[a]	7 (1.6%)
Cutaneous infection[a]	7 (1.6%)
Invasive fungal infection[a]	5 (1.1%)
CMV infection[a]	4 (0.9%)
Pneumocystis jirovecii infection[a]	2 (0.5%)
Hepatic adverse event	79 (2.8%)
Cytolytic hepatitis[a]	58 (73.4%)
Cholestatic hepatitis[a]	12 (15.2%)
Biliary tract pathology[a]	4 (5.1%)
Fulminant hepatitis[a]	1 (1.3%)

Note: Data are presented as N (%). Abbreviations: a Patients could enter different categories.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Reporting odds ratio of infection with avacopan as compared with immunosuppressants.

Adverse event	Drugs	Cases	Non-Cases	ROR [95% CI]
SOC « infection and infestation »	Avacopan	438	2,337	**2.50 [2.25-2.76]**
	All drugs	2,247,893	30,042,962	Ref.
	Avacopan	438	2,337	**0.78 [0.70-0.86]**
	Immnosuppressant	921,686	3,839,956	Ref.
SMQ « sepsis »	Avacopan	35	2,740	**2.37 [1.69-3.30]**
	All drugs	173,068	32,117,787	Ref.
	Avacopan	35	2,740	1.02 [0.73-1.42]
	Immnosuppressant	58,696	4,702,946	Ref.

Footnote: "Cases" were safety reports including an infectious adverse reaction identified using the System Organ Class (SOC) "Infections and infestations", and Standardised MedDRA Queries (SMQ) "Sepsis" (MedDRA, https://www.meddra.org/). Comparators were all drugs and immunosuppressants drugs (ATC code L04). ROR (95% CI) were calculated as adbc (adbc. e ±1.961a+1b+1c+1d), where a is the number of cases reported with avacopan, b is the number of non-cases (i.e., all other adverse drug reactions reports) reported with avacopan, c is the number of cases reported with all other drugs and d is the number of non-cases reported with all other drugs. Threshold for signal detection is defined as a ROR lower boundary 95% confidence interval ≥1 and a number of cases ≥3. Significant associations (adverse event-drug combination) are presented in bold. Abbreviations: Ref., reference; ROR, reporting odds ratio; SMQ, Standardised MedDRA Queries; SOC, System Organ Class,

Methods: We used VigiBase, the WHO global pharmacovigilance database, up to April 30, 2025. We analyzed and described individual case safety reports related to infectious and hepatic AEs. Disproportionality analyses were performed using reporting odds ratios (RORs) and 95% confidence intervals (CI). A signal was considered significant if the lower CI limit exceeded 1.

Results: Of 32.3 million individual case safety reports, 2,775 involved avacopan (median age 62 years, 40.4% female), with 88.3% from North America (**Tables 1 and 2**). Infectious AEs occurred in 438 cases (15.8%). The median time to onset of infection was 28 days (IQR 7-78). Most cases were considered serious (262, 59.8%), including 130 (29.7%) with hospitalization or prolonged hospitalization, and 41 (9.4%) were fatal. Most frequent reported infections were respiratory tract infections (47%), with COVID-19 (21.9%) and pneumonia (26.9%), urinary tract infections (10.3%) and ENT infections (9.8%). Invasive fungal, CMV and *Pneumocystis jiroveci* infections were reported in 1.1%, 0.9% and 0.5%, respectively. Hepatic events occurred in 77 cases (2.8%), mainly cytolytic hepatitis (24.1%), with a median time to onset of 47 days (IQR 40-63), and 3 were fatal. No vanishing bile duct syndrome was reported. Disproportionality analysis revealed a significant overreporting of infections (ROR 2.50 [2.25-2.76]) or sepsis (ROR 2.37 [1.69-3.30]) compared to all treatments in VigiBase, but not compared to immunosuppressants (ROR 0.78 [0.70-0.86] and ROR 1,02 [0,73-1,42], respectively), with even a significant underreporting of infections with avacopan (**Table 3**).

Conclusion: This study based on VigiBase characterizes the profile of infectious AEs reported with avacopan, which does not appear to differ from the known profile of infections in AAV patients. Avacopan was not associated with an increased risk of reporting of infections compared to immunosuppressants. These data, while reassuring, are preliminary and highlight the need for continued post-marketing surveillance to confirm the long-term safety profile of avacopan.

Disclosure: C. Mettler: None; **L. Chouchana**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 2508

Patient-Reported Outcomes in ANCA-Associated Vasculitis: Early Findings from a Prospective Real-World Cohort

Colebrooke Johnson[1], Nora Shepherd[2], David O'Dea[1], Andrew King[2], Guy Katz[1], Belen Arevalo Molina[1], Zachary Williams[3], Madison Negron[4], Naomi Patel[1] and Sebastian H Unizony[5], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]Massachusetts General Hospital, Nancy, KY, [4]Harvard Extension School, Medford, MA, [5]Massachusetts General Hospital, Harvard Medical School, Boston, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA-associated vasculitis (AAV) imposes a high morbidity burden, both from the disease itself and from treatment-related side effects, often compromising patients' quality of life (QoL). Despite this, patient-reported outcomes (PRO) remain insufficiently studied compared to physician-reported measures. We present initial PRO data from a prospective, longitudinal cohort of individuals with AAV.

Methods: The Mass General Brigham AAV Prospective Registry (AAVPR) enrolls patients with GPA, MPA and EGPA at any stage of disease and regardless of disease activity status. Participants complete surveys every 6 months capturing treatments, comorbidities, and PROs, including the SF-12 and the AAV-PRO, among other variables. The SF-12 gathers physical and mental healthdata in 8 domains and provides physical and mental component summaries (PCS, MCS; 0-100 with lower scores indicating worse QoL). The AAV-PRO collects information in 6 domains (0-100 with higher scores indicating worse QoL and disease burden), including organ-specific symptoms (OSS), systemic-symptoms (SS), treatment side-effects (TSE), social and emotional impact (SEI), concerns about the future (CAF) and physical function (PF). We performed multivariable-adjusted regression to identify factors associated with PROs at baseline and multivariable-adjusted difference-in-difference (DID) regression to identify factors associated with change in PROs from baseline to 6 months. Covariates considered included age, sex, disease duration, glucocorticoid (GC) and immunosuppression use within 6 months prior to baseline, ANCA type and multimorbidity.

Table 1: Patient Characteristics at the Time of Enrollment in the AAV Prospective Registry

	Individuals with AAV (N=92)
Age	59.9 (14.5)
Sex, female	64 (69.8)
Race, White	87 (94.6)
ANCA type	
PR3	39 (42.4)
MPO	35 (38.0)
Dual positive	2 (2.2)
Negative	16 (17.4)
Disease duration, months, median (IQR)	38 (4; 79.5)
AAV treatment within 6 months	
Glucocorticoids	40 (43.5)
Immunosuppression	
Rituximab	50 (54.4)
Cyclophosphamide	7 (7.6)
Azathioprine	3 (3.3)
Methotrexate	10 (10.9)
Mycophenolate mofetil	3 (3.3)
Avacopan	16 (17.4)
Comorbidities	
Pulmonary*	44 (47.8)
Cardiovascular#	52 (56.5)
Diabetes	9 (9.8)
End-stage renal disease	3 (3.3)
Malignancy‡	20 (21.7)
Multimorbidity^	52 (56.5)

Values are n (%) for categorical variables and mean (SD) for continuous variables unless otherwise specified. *Including chronic obstructive pulmonary disease, sleep apnea, bronchiectasis, interstitial lung disease and/or asthma. #Including hypertension, myocardial infarction, coronary artery disease undergoing revascularization, carotid artery stenosis, peripheral artery disease, atrial fibrillation, heart failure and/or stroke. Including gastrointestinal, lung, breast, urogenital, hematologic, bone and soft tissue, brain, skin, and/or thyroid malignancy. ^≥1 Comorbidity. AAV, ANCA-associated vasculitis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. AAV-PRO and SF-12 at Baseline and 6 Months

	Individuals with AAV (N=92)			
	Baseline	6 months	Difference	P values
AAV-PRO domain				
Organ-specific symptoms	24.4 (22.3)	22.3 (19.7)	-2.1 (14.9)	0.178
Systemic symptoms	28.3 (22.9)	27.5 (21.8)	-0.8 (16.5)	0.637
Treatment side-effects	24.6 (18.1)	23.1 (16.3)	-1.5 (14.9)	0.275
Social and emotional impact	29.1 (23.4)	23.8 (20.9)	-5.3 (16.0)	0.002
Concerns about the future	32.7 (25.8)	29.2 (23.4)	-3.5 (18.1)	0.069
Physical function	16.9 (21.1)	14.6 (20.0)	-2.3 (14.9)	0.139
12-Item Short Form Inventory Survey				
Physical component summary	44.6 (10.7)	43.9 (10.1)	-0.7 (8.3)	0.423
Mental component summary	49.9 (10.1)	51.2 (8.9)	-1.3 (9.2)	0.185

Values are mean (SD). The AAV-PRO ranges 0-100 with higher scores indicating worse quality of life and disease burden. The SF-12 ranges 0-100 with lower scores indicating worse quality of life. AAV, ANCA-associated vasculitis; PRO, patient-reported outcome

Results: Among 92 participants with ≥6 months of follow-up, the mean (SD) age was 59.9 (14.5) years, and the median (IQR) duration of disease at baseline was 38 (4-79.5) months. The cohort was predominantly female (69.6%) and White (94.6%), with 38% MPO-ANCA positive patients. Most common AAV treatments within 6 months prior to baseline included GCs (43.5%) and rituximab (54.4%). Additional baseline features are in **Table 1**. Over 6 months, the SF-12 PCS and MCS, and most AAV-PRO domains remained relatively stable, except for SEI scores, which significantly improved (**Table 2**). At baseline (**Table 3**), females reported worse AAV-PRO OSS and TSE scores compared to males. Patients with disease duration ≥6 months had better baseline AAV-PRO OSS, TSE, and PF scores than those with shorter disease duration. Over a 6-month period (**Table 3**), PR3-positive patients showed improvement in AAV-PRO SS, whereas MPO-positive patients worsened (baseline to 6 months mean difference -5.8 for PR3 vs 5.9 for MPO). Additionally, patients with disease duration ≥6 months experienced less improvement in AAV-PRO SEI (baseline to 6 months mean difference -2.8 for ≥6 months vs -11.7 for < 6 months) and a decline in SF-12 MCS (baseline to 6 months mean difference -0.3 for ≥6 months vs 5.3 for < 6 months) compared to those with shorter disease duration. No other statistically significant associations were found.

Table 3. Associations of Patient Characteristics and Selected AAV-PRO Domains and SF-12 MCS

OLS regression-based associations of patient characteristics and PRO at baseline												
	AAV-PRO OSS		AAV-PRO SS		AAV-PRO TSE		AAV-PRO SEI		AAV-PRO PF		SF-12 MCS	
Predictors included in the model	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Female sex	**10.5**	**0.8, 20.1**	3.9	-6.5, 14.4	**8.4**	**0.8, 16.0**	5.2	-5.1, 15.4	-1.5	-11.1, 8.1	-0.6	-5.1, 3.9
Age (in deciles)	1.4	-1.9, 4.7	1.0	-2.6, 4.6	-1.8	-4.4, 0.8	-2.1	-5.6, 1.4	0.5	-2.8, 3.8	1.1	-0.4, 2.7
PR3 ANCA	-0.4	-10.9, 10.1	4.8	-6.6, 16.2	0.3	-8.0, 8.5	5.0	-6.2, 16.1	-0.6	-11.0, 9.9	-1.3	-6.2, 3.6
GC use ▲	-6.2	-18.0, 5.6	-0.1	-12.9, 12.7	-2.3	-11.6, 7.0	6.3	-6.2, 18.9	-1.9	-13.6, 9.9	-0.2	-5.6, 5.3
Immunosuppression ▲	7.8	-2.3, 17.8	4.6	0.407	7.3	-0.6, 15.2	3.8	-6.8, 14.5	3.6	-6.3, 13.6	-4.0	-8.7, 0.6
Disease duration ≥6 months	**-16.5**	**-29.3, -3.7**	-12.0	-25.8, 1.9	**-12.0**	**-22.0, -2.0**	-7.9	-21.4, 5.7	**-13.5**	**-26.2, -0.9**	3.6	-2.4, 9.5
Multimorbidity	6.7	-3.3, 16.8	5.9	-5.0, 16.8	3.7	-4.2, 11.6	8.5	-2.1, 19.2	7.8	-2.2, 17.8	-1.3	-6.0, 3.3
Difference-in-difference OLS regression-based associations of patient characteristics and changes in PROs from baseline to 6 months												
	AAV-PRO OSS		AAV-PRO SS		AAV-PRO TSE		AAV-PRO SEI		AAV-PRO PF		SF-12 MCS	
Predictors included in the model	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Female sex	-0.4	-7.4, 6.6	1.1	-6.2, 8.4	0.3	-5.7, 6.4	-4.6	-11.6, 2.3	-4.2	-10.9, 2.5	2.1	-2.0, 6.2
Age (in deciles)	0.4	-2.0, 2.7	-0.2	-2.7, 2.2	0.0	-2.0, 2.0	0.5	-1.9, 2.8	1.1	-1.2, 3.3	-0.6	-1.9, 0.8
Disease duration ≥6 months	3.1	-4.1, 10.3	5.6	-1.9, 13.2	4.4	-1.9, 10.7	**7.7**	**0.5, 14.9**	6.0	-0.9, 13.0	**-5.2**	**-9.4, -0.9**
PR3 ANCA	-1.4	-9.0, 6.2	**-11.6**	**-19.5, -3.7**	1.1	-5.5, 7.7	-2.0	-9.6, 5.5	-4.0	-11.4, 3.3	-1.0	-5.5, 3.4
Multimorbidity	-2.8	-9.5, 4.4	1.0	-6.2, 8.3	-0.2	-6.2, 5.8	-5.3	-12.2, 1.7	0.1	-6.6, 6.8	1.8	-2.2, 5.9

▲Within 6 months prior to baseline. β, linear regression beta coefficient. Bolded estimates indicate P values <0.05. AAV, ANCA-associated vasculitis; PRO, patient-reported outcome; OLS, ordinary least squares; SF-12, 12-Item Short Form Inventory Survey; MCS, mental component summary. AAV-PRO domains: OSS, organ-specific symptoms; SS, systemic symptoms; TSE, treatment side-effects; SEI, social and emotional impact; PF, physical function.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this prospective cohort of patients with AAV, sex, disease duration, and ANCA type demonstrated independent effects on PRO including the AAV-PRO and the SF-12

Disclosure: C. Johnson: None; **N. Shepherd**: None; **D. O'Dea**: None; **A. King**: None; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **B. Arevalo Molina**: Amgen, 2; **Z. Williams**: None; **M. Negron**: None; **N. Patel**: Amgen, 5; **S. Unizony**: Harvard Pilgrim Healthcare, 2, IQVIA, 2, Sanofi, 2.

Abstract Number: 2509

Predicting future relapse with proteomics in ANCA-Associated Vasculitis

Evan Barnes[1], Nora Shepherd[2], Colebrooke Johnson[1], David O'Dea[1], Bohang Jiang[3], Emily Hyle[2], Zachary Williams[4], Zachary Wallace[5] and Gary Reynolds[6], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Boston, [3]MGH, Boston, MA, [4]Massachusetts General Hospital, Nancy, KY, [5]Massachusetts General Hospital, Newton, MA, [6]Massachusetts General Hospital, Newcastle upon Tyne, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Outcomes for ANCA associated vasculitis (AAV) have been transformed in recent years with many patients achieving prolonged periods of remission. Guidelines advise continuing maintenance therapy following initial treatment for at least 24-48 months but beyond this there is debate in balancing the risks of disease relapse against those of prolonged immunosuppression. These decisions could be guided by biomarkers to identify patients who are likely to remain in remission or could predict incipient flare at an early stage. In this study we explored the utility of serum proteomics measured from patients in clinical remission to predict their risk of future relapse.

Methods: Serum samples and matched clinical data from participants with MPO- or PR3-ANCA+ AAV were retrieved from an ongoing prospective cohort study at Mass General Brigham. The levels of 92 circulating proteins were measured using the Olink inflammation proteomic assay. Relapse was defined as a change in clinical symptoms prompting new or modified treatment after achieving initial remission, and for those patients, additional information was collected including creatinine, presence of sinopulmonary symptoms, and treatment provided during relapse. Proteomic data from the population who experienced relapse was compared to control populations those who did not experience relapse to identify significant changes in protein expression as compared via unpaired t-tests. Adjustment for multiple comparisons was based on the 10% false discovery rate (FDR) procedure.

Results: We identified 44 patients who were in remission when serum was sampled for proteomic analysis. This cohort was balanced for sex (55% female) and ANCA specificity (50% MPO-ANCA) (**Table 1**). Over the follow-up period 29.5% of patients (n=13) experienced at least one flare. The commonest manifestation of flare was sinopulmonary involvement (77%) (**Table 2**). The only baseline clinical predictor of future flare was male sex (p=0.04), whereas neither age (p=0.12) nor ANCA subtype (p=0.90) was predictive. There were higher rates of relapse in those who received cyclophosphamide (46% vs 29%) and lower levels in those who received Rituximab (55% vs 15%), but neither was statistically significant (**Table 2**). Proteomic analysis revealed that elevated levels of the IL6-family cytokine Oncostatin M (OSM) during remission was significantly associated with future risk of flare (adjusted p value < 0.001) (**Figure 1**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of total sample population

Characteristic	N = 44[1]
Age at Diagnosis	53 (17)
Gender	
Female	24 (55%)
Male	20 (45%)
Diagnosis (ANCA type)	
MPO	22 (50%)
Negative	2 (4.5%)
PR3	20 (45%)
Initial Treatment (CYC/RTX/DMARD)	
CYC	15 (34%)
MTX	6 (14%)
Other	4 (9.1%)
RTX	15 (34%)
RTX/CYC	4 (9.1%)
Time from initial diagnosis to sample (months)	72 (64)
Unknown	8

[1] Mean (SD); n (%)

Table 2: Comparison of patients who experienced relapse versus those with sustained remission

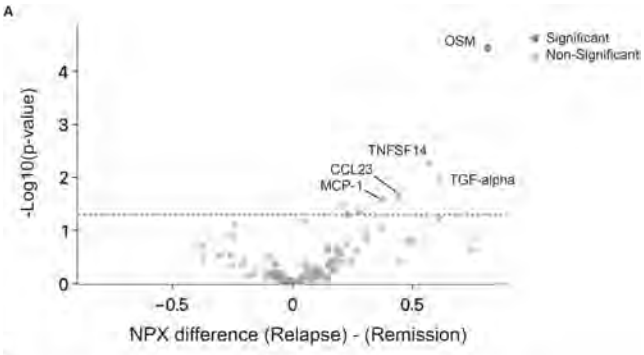
	Experienced Relapse		
Characteristic	N N = 31[1]	Y N = 13[1]	p-value[2]
Age at Diagnosis	55 (42, 72)	46 (37, 59)	0.12
Gender			0.040
Female	20 (65%)	4 (31%)	
Male	11 (35%)	9 (69%)	
Diagnosis (ANCA type)			0.9
MPO	16 (52%)	6 (46%)	
Negative	2 (6.5%)	0 (0%)	
PR3	13 (42%)	7 (54%)	
Initial Treatment (CYC/RTX/DMARD)			0.2
CYC	9 (29%)	6 (46%)	
MTX	3 (9.7%)	3 (23%)	
Other	2 (6.5%)	2 (15%)	
RTX	13 (42%)	2 (15%)	
RTX/CYC	4 (13%)	0 (0%)	

[1] Median (Q1, Q3); n (%)

[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: (A) Volcano plot of proteomic expression data of Olink inflammatory panel proteins. (B) Table summarizing the top 5 differentially expressed proteins between the population experiencing relapse versus the population maintaining prolonged remissions with uncorrected p values and FDR adjusted p-values



B

Protein	NPX difference	P-value	Adjusted p-value
OSM	0.814	0.00003605	0.003316
TNFSF14	0.5679	0.005369	0.247
TGF-alpha	0.6096	0.01124	0.3446
CCL23	0.4425	0.02249	0.4812
MCP-1	0.3767	0.02615	0.4812

Conclusion: For many patients with AAV the most pressing clinical dilemma is identifying when treatment can safely be withdrawn. In deriving a biomarker serum proteomics are an attractive modality because sampling is minimally invasive, assays are robust and can be captured longitudinally. In this preliminary study we identify the IL-6 family cytokine OSM as being predictive of future flare. This is consistent with our previous analysis that has found that OSM is significantly raised in active AAV. While the number of patients in our cohort who flared was low, this study supports the potential of this approach. Our future work will expand this cohort and explore the effect of treatment and whether longitudinal changes can enhance its predictive power.

Disclosure: E. Barnes: None; **N. Shepherd**: None; **C. Johnson**: None; **D. O'Dea**: None; **B. Jiang**: None; **E. Hyle**: None; **Z. Williams**: None; **Z. Wallace**: Amgen, 3; **G. Reynolds**: None.

Abstract Number: 2510

Impact of ANCA specificity on risk of severe infection occurrence in ANCA-associated vasculitis.

Clara Rouane[1], Jon Idoate[1], Morgane Mourguet[1], Thomas Villeneuve[1], Grégoire Prevot[1], Laurent Guilleminault[2], Stan Faguer[1], Antoine Huart[1], David Ribes[1], Dominique Chauveau[1], Martin Michaud[1], Laurent Sailler[1], Sébastien De Almeida Chaves[1], Emmanuelle Mouchon[1], Guillaume De Bonnecaze[1], Margaux Lafaurie[1], Guillaume Moulis[1] and **Grégory Pugnet**[3], [1]CHU Toulouse, Toulouse, France, [2]CHU Toulouse, Toulouse University, Toulouse, France, [3]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: ANCA specificity has shown an association with patients' genetic profile, cytokine profile, certain clinical presentations, serologic response to treatment, and risk of recurrence.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Severe infections occur in approximately 35% of patients with ANCA-associated vasculitis, with a 4.4-fold increased risk compared to the general population. This risk is highest during the first year of the disease, during which infections represent the leading cause of death

The aim of this study is to investigate the relationship between ANCA specificity and the risk of severe infection occurrence during the course of AAV.

Methods: This retrospective, observational study included patients diagnosed with AAV meeting the Chapel Hill Consensus Conference classification criteria who were treated at two hospital centers in southern France between January 1st 2010 and March 30th 2024.•The population was divided in two groups based on the presence or absence of anti-PR3 and anti-MPO ANCA. Patients without ANCA or with non-specific ANCA were excluded. The occurrence of severe infections—defined as those requiring hospitalization, surgical intervention, intravenous antibiotic therapy, or resulting in death—was assessed within three years following inclusion in patients enrolled during either a first onset or a relapse of vasculitis. We compared severe infection occurrence between the groups and conducted a proportional hazards Cox regression model adjusted for sex, age >65 years, FFS ≥1, respiratory involvement, relapse versus first onset status, and for induction therapy (with or without cyclophosphamide).

Results: Of the 529 screened patients, 270 were included in the analysis: 117 with PR3-ANCA vasculitis and 153 with MPO-ANCA vasculitis, of which 142 were GPA, 95 MPA, and 23 EGPA cases. The median age was 65.5 years [IQR: 57-75], and 48% were female. During follow-up, 89 patients (32.9%) developed a severe infection—57 (64.1%) in the MPO group and 32 (35.9%) in the PR3 group—corresponding to cumulative incidences of 7.34 and 4.12 cases per 100 person-years, respectively. Most infections occurred within the first year of follow-up, coinciding with the period of highest immunosuppressive burden. The median time to onset of severe infection was 8 months [range 1–19]; it was shorter in the MPO-ANCA group (4 months [range 1–18]) compared to the PR3-ANCA group (11 months [range 1.5–24]) (p=0.048). Bacterial pneumonia was the most frequently observed infection.

The adjusted proportional hazards Cox regression model found an trend between the presence of anti-MPO ANCA and the risk of severe infection with a HR of 1.55 (95% CI: 0.97 – 2.48; p=0.06).

Conclusion: Our findings showed that MPO-ANCA specificity is associated with an increased risk of severe infections in patients with ANCA-associated vasculitis. Consistent with prior observations, most infections occurred within the first year of follow-up, with no significant difference in infection risk between cyclophosphamide and rituximab treatment arms. These results underscore the prognostic relevance of ANCA specificity in AAV.

Disclosure: C. Rouane: None; **J. Idoate**: None; **M. Mourguet**: None; **T. Villeneuve**: None; **G. Prevot**: None; **L. Guilleminault**: None; **S. Faguer**: None; **A. Huart**: None; **D. Ribes**: None; **D. Chauveau**: None; **M. Michaud**: None; **L. Sailler**: None; **S. De Almeida Chaves**: None; **E. Mouchon**: None; **G. De Bonnecaze**: None; **M. Lafaurie**: None; **G. Moulis**: None; **G. Pugnet**: None.

Abstract Number: 2511

The SHIPE index: A tertile-based approach to predict end-stage kidney disease in ANCA-associated vasculitis

HYUNSUE DO[1], Lucy Eunju Lee[2], Jang Woo Ha[3], Jason Jungsik Song[4], Yong-Beom Park[5] and Sang-Won Lee[6], [1]Kangwon national university hospital, Seoul, South Korea, [2]Yonsei University, Seoul, Republic of Korea, [3]Division of Rheumatology, Department of Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, Seodaemun-gu,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Seoul, Republic of Korea, [4]Yonsei University College of Medicine, Seoul, Republic of Korea, [5]Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, [6]Yonsei university college of medicine, Seoul, South Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Characteristics of 239 AAV patients

Variables	Values
Variables at diagnosis	
Demographic data	
Age (years)	59.0 (49.0-69.0)
Male sex (n, (%))	82 (34.3)
AAV subtypes (n, (%))	
MPA	128 (53.6)
GPA	59 (24.7)
EGPA	52 (21.8)
ANCA positivity (N, (%))	
MPO-ANCA (or P-ANCA) positive	160 (66.9)
PR3-ANCA (or C-ANCA) positive	40 (16.7)
Both ANCA positive	10 (4.2)
ANCA positivity	190 (79.5)
AAV-specific indices	
BVAS	12.0 (7.0-18.0)
FFS	1.0 (1.0-2.0)
Acute phase reactants	
ESR (mm/hr)	59.0 (22.0-96.0)
CRP (mg/L)	13.8 (1.6-71.0)
Laboratory results	
White blood cell count (/mm^3)	9,040.0 (6,400.0-12,660.0)
Haemoglobin (g/dL)	11.4 (9.5-13.3)
Platelet count (× 1000/mm^3)	301.0 (228.0-393.0)
Fasting glucose (mg/dL)	102.0 (91.0-124.0)
Blood urea nitrogen (mg/dL)	17.6 (12.3-31.0)
Serum creatinine (mg/dL)	0.9 (0.7-1.8)
Total protein (g/dL)	6.7 (6.1-7.2)
Serum albumin (g/dL)	3.7 (3.1-4.2)
Comorbidities (n, (%))	
Type 2 diabetes mellitus	60 (25.1)
Hypertension	98 (41.0)
Dyslipidaemia	44 (18.4)
During follow-up	
ESKD (n, (%))	41 (17.2)
Follow-up duration based on ESKD (months)	33.7 (10.2-74.0)
Medications (n, (%))	
Glucocorticoids	224 (93.7)
Cyclophosphamide	128 (53.6)
Rituximab	41 (17.2)
Mycophenolate mofetil	37 (15.5)
Azathioprine	131 (54.8)
Tacrolimus	22 (9.2)
Methotrexate	23 (9.6)
Plasma exchange	21 (8.8)

Values are expressed as a median (interquartile range, IQR) or n (%).
AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polya MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; C: cytoplasmic; BVAS: Birmingham vas activity score; FFS: five-factor score; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein end-stage kidney disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

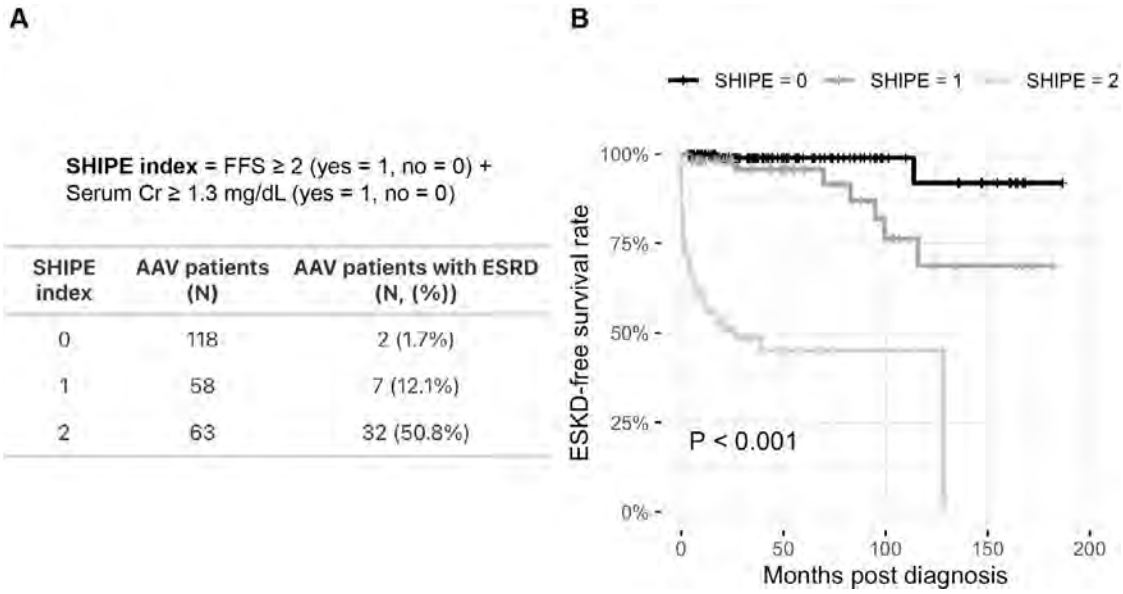


Figure 1. The SHIPE index for AAV patients

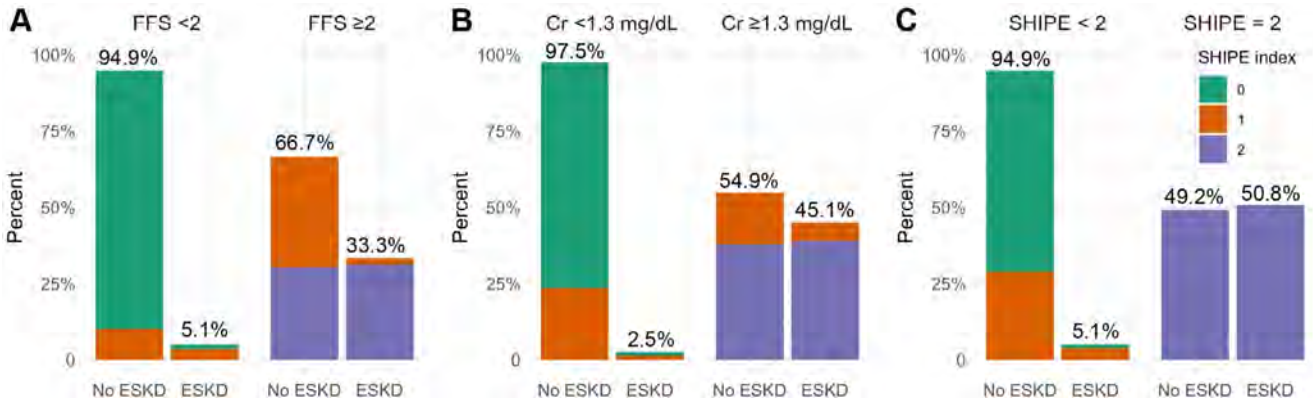


Figure 2. Comparison of three predictors — FFS, serum creatinine, and SHIPE index — for ESKD

Background/Purpose: This study aimed to develop a simple, robust, and ethnoregion-specific index for predicting progression to end-stage kidney disease (ESKD) in Korean patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods: Baseline data from 239 Korean patients with AAV enrolled in a tertiary hospital cohort were analyzed to identify independent predictors of ESKD using univariable and multivariable Cox proportional hazards models. The SHIPE index was constructed by summing the highest tertiles of the identified predictors: Five-Factor Score (FFS ≥2) and serum creatinine (≥1.3 mg/dL), with 1 point assigned to each criterion met. Cumulative ESKD-free survival rates across SHIPE index scores were compared using Kaplan-Meier analysis.

Results: A SHIPE index score of 2 was significantly associated with lower cumulative ESKD-free survival rate compared to scores of 0 or 1 ($P < 0.001$). By integrating two independent predictors, the SHIPE index provides a simple yet effective tool for risk stratification, demonstrating greater robustness against variability in single predictors such as serum creatinine. This index demonstrated clinical utility, providing a straightforward method for identifying high-risk patients in real-world settings.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The SHIPE index is a novel, robust, and convenient tool for predicting ESKD progression in Korean patients with AAV. This study introduces a practical framework for developing tailored prediction indices that can be adapted for diverse ethnic and regional populations. Its simplicity and practical applicability make it well-suited for routine clinical use. Future prospective studies are needed to validate the SHIPE index in larger, multi-ethnic cohorts and ensure its broader applicability.

Disclosure: H. DO: None; **L. Lee**: None; **J. Ha**: Samsung Bioepis, 5; **J. Song**: None; **Y. Park**: Samsung Bioepis, 5; **S. Lee**: None.

Abstract Number: 2512

Contribution of the CALLY index at diagnosis to early prediction of all-cause mortality in patients with ANCA-associated vasculitis

Jang Woo Ha[1] and Sang-Won Lee[2], [1]Division of Rheumatology, Department of Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, Seodaemun-gu, Seoul, Republic of Korea, [2]Yonsei university college of medicine, Seoul, South Korea

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: This study retrospectively investigated whether the initial C-reactive protein (CRP)-albumin-lymphocyte (CALLY) index at diagnosis can contribute to early prediction of all-cause mortality during follow-up in patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods: This study included 323 patients with AAV. Clinical data at AAV diagnosis and those during follow-up were collected. The CALLY index was calculated using the following equation: serum albumin (g/L) × lymphocyte count (/mm3) / CRP (mg/L) /10,000. The parameter of serum albumin (g/L) of an equation of the CALLY index was corrected by multiplying the measured serum albumin (g/dL) by 10.

Results: The median age was 61.0 years (36.2% male and 63.8% female). The median CALLY index was calculated as 0.48. Of the 323 patients, 45 (13.9%) died during the follow-up period of 53.7 months. In ROC curve analysis, the optimal cut-off of the CALLY index for all-cause mortality was determined as 0.55 (area 0.715). Patients with the CALLY index ≤0.55 at AAV diagnosis had a significantly higher risk for death (relative risk 7.294), and exhibited a significantly lower cumulative patients' survival rate than those with the CALLY index >0.55. In multivariable Cox proportional hazard analysis, the CALLY index ≤0.55 (hazard ratio [HR] 3.913), age (HR 1.037) and male sex (HR 2.326) were independently associated with all-cause mortality during follow-up in patients with AAV.

Conclusion: This is the first study to demonstrate that the initial CALLY index at diagnosis could be useful in predicting all-cause mortality during follow-up in patients with AAV.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with AAV (N=323)

Variables	Values
At diagnosis	
Demographic data	
Age (years)	61.0 (50.0–69.0)
Male sex (N, (%))	117 (36.2)
Female sex (N, (%))	206 (63.8)
BMI (kg/m^2)	22.5 (20.3–24.8)
Ex-smoker (N, (%))	9 (2.8)
AAV subtype (N, (%))	
MPA	184 (57.0)
GPA	76 (23.5)
EGPA	63 (19.5)
ANCA type and positivity (N, (%))	
MPO-ANCA (or P-ANCA) positivity	226 (70.0)
PR3-ANCA (or C-ANCA) positivity	51 (15.8)
Both ANCA positivity	14 (4.3)
ANCA negativity	60 (18.6)
AAV-specific indices	
BVAS	12.0 (7.0–18.0)
FFS	1.0 (0–2.0)
Laboratory results	
White blood cell count (/mm^3)	9,240.0 (6,430.0–12,920.0)
Haemoglobin (g/dL)	11.5 (9.6–13.3)
Platelet count (× 1000/mm^3)	295.0 (227.0–387.0)
Fasting glucose (mg/dL)	101.0 (90.0–121.0)
Blood urea nitrogen (mg/dL)	17.6 (12.6–30.9)
Serum creatinine (mg/dL)	0.9 (0.7–1.7)
Serum total protein (g/dL)	6.8 (6.1–7.3)
Serum albumin (g/dL)	3.7 (3.1–4.3)
AST (IU/L)	19.0 (15.0–25.0)
ALT (IU/L)	17.0 (12.0–26.0)
Acute phase reactants	
ESR (mm/hr)	59.0 (22.0–96.0)
CRP (mg/L)	11.9 (1.6–61.0)
Comorbidities (N, (%))	
Hypertension	81 (25.1)
Type 2 diabetes mellitus	132 (40.9)
Dyslipidaemia	53 (16.4)
CALLY index-related variables	
Serum albumin (g/L)*	37.0 (31.0–43.0)
Lymphocyte (/mm^3)	1,510.0 (1,010.0–1,990.0)
CRP (mg/L)	11.9 (1.6–61.0)
CALLY index	0.48 (0.06–3.71)
During follow-up	
Mortality (N, (%))	
All-cause mortality	45 (13.9)
Follow-up duration based on all-cause mortality	53.7 (18.6–89.4)
Medications (N, (%))	
Glucocorticoids	305 (94.4)
Cyclophosphamide	167 (51.7)
Rituximab	59 (18.3)
Mycophenolate mofetil	79 (24.5)
Azathioprine	164 (50.8)
Tacrolimus	24 (7.4)
Methotrexate	39 (12.1)

Values are expressed as a median (25-75 percentile) or N (%).

*Serum albumin (g/L) = serum albumin (g/dL) × 10 AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; BMI: body mass index; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; C: cytoplasmic; BVAS: the Birmingham vasculitis activity score; FFS: the five-factor score; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; CALLY: C-reactive protein-albumin-lymphocyte.

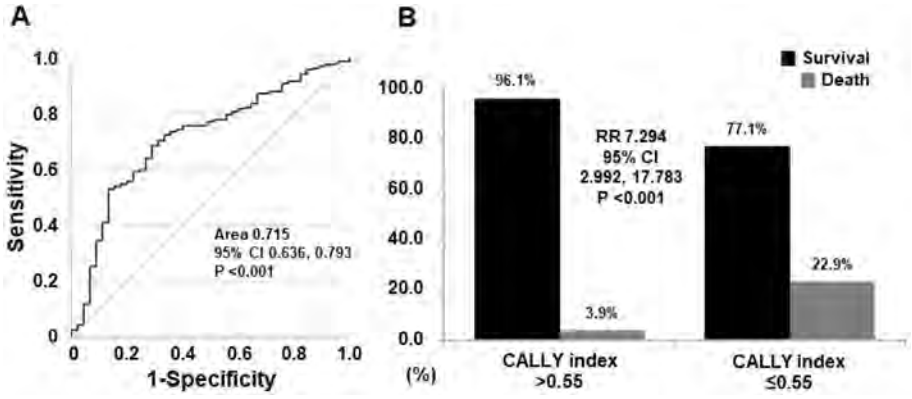


Fig. 1 Relative risk of the initial CALLY index for all-cause mortality (A) The cut-off of the CALLY index was determined as 0.55 using ROC curve analysis. (B) Patients with the CALLY index ≤0.55 at AAV diagnosis had a higher risk for death than those without. CALLY: C-reactive protein-albumin-lymphocyte; ROC: receiver operating characteristic; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; RR: relative risk; CI: confidence interval.

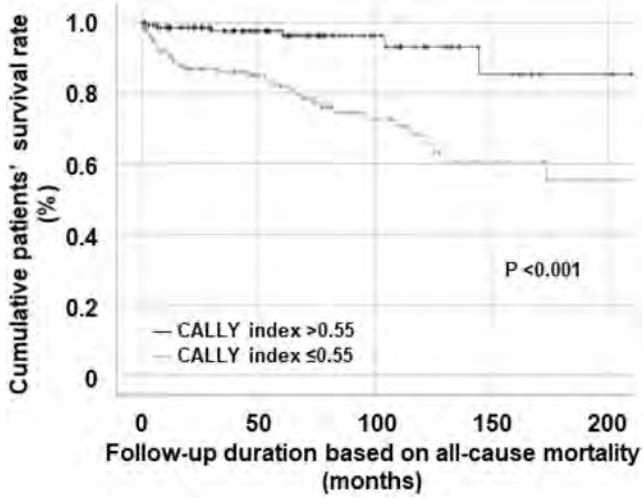


Fig. 2 Cumulative survival rates Patients with the CALLY index ≤0.55 at AAV diagnosis exhibited a significantly lower cumulative patients' survival rate than those without. CALLY: C-reactive protein-albumin-lymphocyte; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody.

Disclosure: J. Ha: Samsung Bioepis, 5; **S. Lee**: None.

Abstract Number: 2513

Beyond Clinical trials in Eosinophilic Granulomatosis with Polyangiitis: A Systematic Review of effectiveness and safety data derived from real-world evidence of Mepolizumab 300 mg

Iñigo Rúa-Figueroa[1], Beatriz Velasco[2] and **Maria Cid**[3], [1]Hospital de Gran Canaria Doctor Negrin, Las Palmas GC, Spain, [2]GSK, Madrid, Spain, [3]Department of Autoimmune Diseases (member of European Reference Network RITA), Hospital Clinic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is characterized by systemic necrotizing vasculitis affecting small and medium-sized vessels, and defined by the presence of eosinophilia, extravascular granulomas, and eosinophil tissue infiltration.

Mepolizumab (MPZ), the first anti-interleukin-5 monoclonal antibody proven effective and safe in the MIRRA clinical trial, has been widely used to treat patients with EGPA.

Therefore, it is pertinent to analyze all published data from real world studies to better understand the effectiveness and safety of MPZ in clinical practice setting.

We aimed to conduct a systematic review of all published clinical research on the real world effectiveness and safety of 300 mg MPZ treatment in patients with EGPA

Methods: A systematic literature review was conducted to identify studies reporting data on the effectiveness and safety of MPZ in patients with EGPA in a real world setting, included in OVID, Medline, and EMBASE databases, covering articles published by November 2024.

This review encompassed studies that reported data on MPZ at the Food and Drug Administration and European medicines Agency approved dose of 300 mg.

Results: Involving a total of 2,639 patients, 14 studies provided specific data on those receiving 300 mg of MPZ, including prospective, ambispective, or retrospective designs, with follow-up periods from 3 to 48 months. Remission rates ranged from 37.9% to 82.0% at 12 months, from 58,3% to 72.7% at 24 months, and stabilized 64% at 48 months.

Treatment with 300 mg MPZ led to a significant reduction in disease activity, as assessed by BVAS, which decreased from 17 to 0 at both 3 and 6 months in one study, and from 4 to 0 at 6, 12, and 24 months in another study. The annualized rate of EGPA-related hospitalizations decreased from 0.54 to 0.02 events/person-year at 48 months. The proportion of patients without immunosuppressive therapy rose to 79% during the 48 months follow up period. No significant differences in Vascular Damage Index score at 12 months were observed, suggesting that MPZ therapy was effective in controlling organ damage progression. Additionally, there was a reduction in glucocorticoid (GC) use, with GC discontinuation rates of up to 41.7% at 24 months and a reduction in GC doses to ≤ 4 mg/day in up to 68% in all the identified articles. The blood eosinophil counts decreased significantly, reaching counts ranging 55-100 cell/μl. A significant reduction in the proportion of ANCA-positive patients was also observed after treatment with MPZ 300 mg.

In terms of safety, MPZ was well-tolerated with adverse events reported primarily as mild to moderate upper respiratory tract infections. The overall rate of MPZ retention was 100% at 6 months and ranged from 90% to 100% at 12 months.

Conclusion: This systematic review of the published evidence on MPZ 300 mg in real-world clinical practice confirms significant clinical benefits from patients with EGPA by improving remission rates, reducing GC dependence, and decreasing disease activity, maintaining a favorable safety profile. These results complement data from clinical trials

Disclosure: I. Rúa-Figueroa: None; **B. Velasco**: GlaxoSmithKlein(GSK), 3; **M. Cid**: AbbVie, 2, 6, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL-Vifor, 2, 6, GSK, 2, 6, Kiniksa Pharmaceuticals, 5, UpToDate, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2514

Comparison of Demographics and Outcomes of Inpatient Hospitalization of Severe Asthma Patients with Eosinophilic Granulomatosis with Polyangitis. A Study on the National Inpatient Sample Database

Prakriti Subedi[1], Anil Regmi[2], Karun Shrestha[3], Manoj Ghimire[4], Sajana Poudel[5], Kalpana Ghimire[1], Oshna Pandey[1] and Clement Tagoe[6], [1]St. Barnabas Hospital, Bronx, NY, [2]Parkview Health, Fort Wayne, IN, [3]St. Barnabas Hospital Internal Medicine Residency, Bronx, NY, [4]St Barnabas Hospital, BRONX, NY, [5]Cook County Health, CHICAGO, NY, [6]Albert Einstein College of Medicine, FRESH MEADOWS, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare vasculitis marked by asthma and eosinophilia, often leading to severe, persistent respiratory symptoms. Unlike severe asthma without EGPA, patients with EGPA typically have longstanding asthma prior to vasculitis onset and show widespread eosinophilic inflammation. These differences necessitate distinct treatment approaches. This study compares the demographic and clinical characteristics of patients with severe asthma with and without EGPA using data from the National Inpatient Sample Database.

Table 1: Patient Demographics

Patient characteristics	Severe asthma with EGPA (n=775)	Severe asthma without EGPA (n=201,765)	p-value
Age(years), SD	52.06 +/- 16.28	51.75 +/- 17.29	0.82
Gender			
Female (%)	470(60.64)	144120(71.43)	0.004
Race			
White	520(68.87)	101830(50.47)	0.0006
Black	130(17.72)	60489(29.98)	
Hispanic	65(0.86)	27076(13.42)	
Asian	30(0.03)	4800(2.44)	
Other	0	1505(0.76)	
Native American	10(1.32)	5775(2.93)	
Income Quartile			
0-25th	155(20.26)	70718(35.05)	0.0005
26th-50th	210(27.45)	51470(25.51)	
51st-75th	190(24.84)	46002(22.8)	
76th-100th	210(27.45)	33492(16.64)	
Bed Size			
Small	165(21.29)	44590(22.1)	0.17
Medium	170(21.94)	57422(28.46)	
Large	440(56.77)	99752(49.44)	
Location/teaching			
Rural, non teaching	25(3.23)	12650(6.27)	0.06
Urban, non teaching	95(12.26)	36297(17.99)	
Urban, teaching	655(84.52)	152816(75.74)	
Hospital Region			
Northeast	115(14.84)	46890(23.24)	
Midwest	255(32.9)	54759(27.14)	
South	190(24.52)	62547(31)	
West	215(27.74)	37588(18.63)	0.003

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Co-morbidities and Complications

Co-morbidities, n(%)	Severe asthma with EGPA (n=775)	Severe asthma without EGPA (n=201,765)	p-value
CHF	140(18.06)	38779(19.22)	0.73
Peripheral vascular disease	30(3.87)	7450(	0.9
Cerebrovascular disease	15(1.94)	4155(2.06)	0.91
Hypertension	245(31.61)	71061(35.22)	0.39
Diabetes	65(8.39)	38819(19.24)	0.0006
DM with complications	95(12.26)	21649(10.73)	0.58
COPD	45(5.81)	24575(12.18)	0.01
Renal disease	90(11.61)	2213(10.96)	0.8
Cancer	15(1.94)	3770(1.87)	0.95
Mod/Severe Liver Disease	0	830(0.41)	0.45
Metastatic Cancer	0	1430(0.71)	0,32
HIV/AIDS	5(0.65)	785(0.39)	0.41
Depression	145(18.71)	40897(20.27)	0.65
Smoking	50(6.45)	33393(16.55)	0.0008
Alcohol	45(5.81)	21931(10.87)	0.44
Complications, n(%)			
Acute MI	85(10.97)	11097(5.5)	**0.002**
AKI	10(1.29)	2355(1.17)	0.88
Pnemothorax	5(0.65)	1340(0.66)	0.97
Ventilator associated pneumonia	0	410(0.2)	0.57
Critical illness Myopathy	5(0.65)	665(0.33)	0.49
Cardiac arrest	5(0.65)	2235(1.11)	0.58
Arrythmia	75(9.68)	17157(13.46)	0.19
Mechanical ventilation	55(7.1)	16585(8.22)	0.61
severe sepsis/septic shock	25(3.23)	6090(3.02)	0.87
Acute respiratory failure	335(43.23)	92428(45.81)	0.54

Methods: A retrospective cross-sectional study was conducted using data from NIS (2016 to 2021). Primary and secondary diagnoses were identified using International Classification of Diseases (ICD-10) codes. All patients aged >18 years with severe asthma were included in the study. Patients were divided into two groups: those with severe asthma and EGPA (n=775) and those with severe asthma without EGPA (n=201,765). Demographics, hospital region, comorbidities, complications, and outcomes, including mortality, length of stay, and hospitalization charges, were compared between the 2 groups. Statistical analysis was done using STATA v.17.

Results: The mean age of patients with severe asthma and EGPA was 52.06 years compared to 51.75 years in those without EGPA (p=0.82). A significantly lower proportion of females was observed in the EGPA group (60.64%) compared to the non-EGPA group (71.43%) (p=0.004). In the EGPA group, there was a higher percentage of White patients (68.87% vs. 50.47%) and a lower percentage of African American patients (17.72% vs. 29.98%). A higher proportion of EGPA patients were treated in urban teaching hospitals (84.52% vs. 75.74%, p=0.06). Comorbidities such as diabetes (8.39% vs. 19.24%, p=0.0006) and chronic obstructive pulmonary disease (5.81% vs. 12.18%, p=0.01) were less common in the EGPA group. However, the incidence of acute myocardial infarction (10.97% vs. 5.5%, p=0.002) was higher in the EGPA group. Notably, there was no significant difference in terms of complications like pneumothorax, acute respiratory failure and mechanical ventilation. There were no statistically significant differences in the outcomes, including mortality, hospital stay, and total costs, between the 2 groups.

Table 3: Primary Outcomes

Outcomes	Severe asthma with EGPA (n=775)	Severe asthma without EGPA (n=201,765)	p-value
Mortality, n(%)	10(1.29)	3070(1.52)	0.81
Length of Stay (LOS) in days, mean (95% CI)	5.6(4.61-6.69)	4.84(4.78-4.9)	0.12
Total charges,$,mean (95% CI)	67676(49920-85433)	54533(53361-55745)	0.14

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study demonstrates that patients hospitalized with severe asthma and concomitant eosinophilic granulomatosis with polyangiitis (EGPA) exhibit distinct demographic and clinical profiles compared to those without EGPA. Importantly, the presence of EGPA does not appear to increase the risk of acute respiratory complications such as pneumothorax, acute respiratory failure, or the need for mechanical ventilation. Moreover, no significant differences were observed in key hospital outcomes—including mortality, length of stay, or total hospitalization costs. These findings suggest that although EGPA defines a unique subset within the severe asthma population, it does not independently contribute to worse short-term inpatient outcomes.

Disclosure: P. Subedi: None; **A. Regmi**: None; **K. Shrestha**: None; **M. Ghimire**: None; **S. Poudel**: None; **K. Ghimire**: None; **O. Pandey**: None; **C. Tagoe**: None.

Abstract Number: 2515

The Association Between Neurologic Involvement and Cumulative Damage in ANCA-Associated Vasculitis

Ruoning Ni[1], Jessica L. Bloom[2], Kaci Pickett-Nairne[2], Lori Silveira[3], Chao Zhang[4], David Cuthbertson[5], Thomas corbridge[6], Nader Khalidi[7], Curry Koening[8], Carol McAlear[9], Paul Monach[10], Larry Moreland[11], Christian Pagnoux[12], Rennie Rhee[9], Philip Seo[13], Jared Silver[6], Ulrich Specks[14], Kenneth Warrington[14], Michael Wechsler[15], Carol Langford[16], Peter Merkel[9] and Rula Hajj-Ali[1], [1]Cleveland Clinic, Cleveland, [2]University of Colorado, Denver, [3]University of Colorado, Aurora, CO, [4]Cleveland Clinic, Cleveland Heights, OH, [5]University of South Florida, Tampa, [6]US Medical Affairs Respiratory GSK, Durham, [7]Department of Medicine, McMaster University and St. Joseph's Healthcare, Hamilton, Canada, [8]University of Texas Dell Medical School, Austin, TX, [9]University of Pennsylvania, Philadelphia, PA, [10]VA Boston Healthcare System, Boston, MA, [11]University of Colorado, Denver, CO, [12]Mount Sinai Hospital, University Health Network, Toronto, and Canadian Vasculitis Research Network (CanVasc), Toronto, ON, Canada, [13]Johns Hopkins University, Baltimore, MD, [14]Mayo Clinic, Rochester, MN, [15]Department of Medicine, National Jewish Health, Denver, [16]Cleveland Clinic, Moreland Hills, OH

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Neurologic involvement (NI) is common in ANCA-associated vasculitis (AAV) and often irreversible. It is unknown whether patients with AAV and NI accumulate more damage than those without NI. The objective of this study was to evaluate the association between NI and cumulative damage in patients with AAV.

Methods: Data from adults with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic GPA (EGPA) participating from 2006 to 2021 in a multicenter longitudinal observational study were analyzed. Cohorts were divided by the presence of NI at any point in their disease course. Neurologic damage items (NDI) were classified as disease-specific (cranial nerve lesion, chronic pachymeningitis, neuropathy, and neuropathic pain) and non-disease specific (strokes, seizures, transverse myelitis, and neurologic mass). Group differences were tested using Kruskal-Wallis test for continuous variables and Fisher's exact test for categorical. General and robust linear regression models were generated to estimate the differences in Vasculitis Damage Index (VDI), ANCA Vasculitis Index of Damage (AVID), AAV-Disease-Specific Damage (AAV-DSD), and AAV-Non-DSD scores. We also estimated the differences in AAV-DSD and Non-DSD scores with NDI removed. These models were adjusted for sex, age at diagnosis, and time from diagnosis to last damage assessment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with ANCA-associated vasculitis stratified by neurologic involvement

Characteristics	All (N=1322)	Without NI (N=796)	With NI (N=526)	*p*-Value
Age at diagnosis (years) (Mean (SD))	48.7 (16.4)	46.8 (16.9)	51.4 (15.4)	< 0.001
Sex (female)	731 (55.3%)	450 (56.5%)	281 (53.4%)	0.283
Self-reported ancestry				0.430
Asian	59 (4.5%)	32 (4.0%)	27 (5.1%)	
Black/African American	25 (1.9%)	17 (2.1%)	8 (1.5%)	
White	1192 (90.2%)	722 (90.7%)	470 (89.4%)	
Other	16 (1.3%)	7 (0.8%)	9 (1.7%)	
Missing	30 (2.3%)	18 (2.3%)	12 (2.3%)	
Ethnicity				0.288
Hispanic	32 (2.4%)	15 (1.9%)	17 (3.2%)	
Non-Hispanic	1194 (90.3%)	723 (90.8%)	471 (89.5%)	
Missing	96 (7.3%)	58 (7.3%)	38 (7.2%)	
Follow-up time (years) (Median (Q1, Q3))	6.9 (3.3, 12.0)	7.0 (3.5, 12.2)	6.7 (3.2, 11.9)	0.307
Disease category				< 0.001
GPA	871 (65.9%)	580 (72.9%)	291 (55.3%)	
MPA	168 (12.7%)	127 (16.0%)	41 (7.8%)	
EGPA	283 (21.4%)	89 (11.2%)	194 (36.9%)	
ANCA type (ELISA)				< 0.001
MPO-ANCA	336 (25.4%)	199 (25.0%)	137 (26.0%)	
PR3-ANCA	648 (49.0%)	425 (53.4%)	223 (42.4%)	
Both	11 (0.8%)	7 (0.9%)	4 (0.8%)	
ANCA negative	327 (24.7%)	165 (20.7%)	162 (30.8%)	

Abbreviations: AVID, ANCA-Associated Vasculitis Index of Damage; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; NI, neurologic involvement; SD, standard deviation; VDI, Vasculitis Damage Index.

Results: Data from 1322 patients [65.9% GPA, 12.7% MPA, 21.4% EGPA] were analyzed: 526 (39.8%) had NI and 796 (60.2%) did not. Of those with ANCA results, 995 (75.3%) were ANCA positive (49.0% PR3-ANCA, 25.4% MPO-ANCA, 0.8% both). Older patients had more NI. Two-thirds of adults with EGPA had NI (**Table 1**). Among all AAV, patients with NI were estimated to have higher VDI (0.6 points; 95% CI: [0.35, 0.86], $p < 0.0001$), AVID (1.1 points; 95% CI: [0.66, 1.54], $p < 0.0001$), and AAV-DSD (0.91 points; 95% CI: [0.71, 1.12], $p < 0.0001$) scores than those without NI. The AAV-DSD score remained higher in those with NI even when NDI were removed. The AAV Non-DSD score was not different between NI groups. Among patients with GPA, those with NI had higher damage scores than those without, even with NDI removed. For MPA, those with NI only had higher AAV-DSD scores than those without. For EGPA, those with and without NI had no difference in scores. For both types of ANCA damage scores were higher among patients positive ANCA vs. those negative, even with NDI removed. Among patients negative for ANCA, those with NI only had higher AAV-DSD scores than those without (**Table 2**). Among patients with NI, those with GPA had more damage than those with MPA or EGPA. There were no differences in damage scores between PR3-ANCA, MPO-ANCA, and ANCA-negative groups (**Table 3**). Damage scores among patients with NI did not differ based on presence or absence of central vs. peripheral nervous system disease manifestations.

Conclusion: Patients with AAV and NI experience greater neurologic and non-neurologic cumulative damage than those without NI. The differences are driven by disease-specific items of damage. Of patients with NI, those with GPA, PR3-ANCA, or MPO-ANCA accumulate the most damage. These results highlight the importance and burden of NI in AAV.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Differences in damage scores based on presence of neurologic involvement among all patients with AAV, AAV subtypes and ANCA status

Outcome	Estimate (95% CI)	*p*-Value
All AAV: NI vs. No-NI *N = 1251*		
Vasculitis Damage Index	0.6 (0.35, 0.86)	<0.001
ANCA-Vasculitis Index of Damage	1.1 (0.66, 1.54)	<0.001
AAV Disease-Specific Damage	0.91 (0.71, 1.12)	<0.001
AAV Non-Disease-Specific Damage	0.08 (-0.17, 0.32)	0.532
MPO-ANCA Positive: NI vs. No-NI *N = 316*		
Vasculitis Damage Index	0.46 (-0.03, 0.95)	0.065
ANCA-Vasculitis Index of Damage	0.95 (0.19, 1.72)	0.015
AAV Disease-Specific Damage	1.1 (0.74, 1.46)	<0.001
AAV Non-Disease-Specific Damage	0.07 (-0.41, 0.56)	0.773
PR3-ANCA Positive: NI vs. No-NI *N = 615*		
Vasculitis Damage Index	0.84 (0.47, 1.22)	<0.001
ANCA-Vasculitis Index of Damage	1.4 (0.7, 2.09)	<0.001
AAV Disease-Specific Damage	0.86 (0.54, 1.18)	<0.001
AAV Non-Disease-Specific Damage	0.28 (-0.08, 0.64)	0.128
Negative ANCA: NI vs. No-NI *N = 310*		
Vasculitis Damage Index	0.23 (-0.26, 0.72)	0.358
ANCA-Vasculitis Index of Damage	0.53 (-0.29, 1.36)	0.205
AAV Disease-Specific Damage	0.71 (0.32, 1.1)	<0.001
AAV Non-Disease-Specific Damage	-0.33 (-0.79, 0.14)	0.167
GPA: NI vs. No-NI *N = 817*		
Vasculitis Damage Index	0.86 (0.53, 1.2)	<0.001
ANCA-Vasculitis Index of Damage	1.53 (0.92, 2.15)	<0.001
AAV Disease-Specific Damage	0.91 (0.63, 1.19)	<0.001
AAV Non-Disease-Specific Damage	0.34 (0.02, 0.66)	0.039
MPA: NI vs. No-NI *N = 156*		
Vasculitis Damage Index	-0.14 (-0.9, 0.63)	0.726
ANCA-Vasculitis Index of Damage	0.15 (-0.83, 1.14)	0.761
AAV Disease-Specific Damage	0.72 (0.35, 1.09)	<0.001
AAV Non-Disease-Specific Damage	-0.49 (-1.22, 0.24)	0.189
EGPA: NI vs. No-NI *N = 278*		
Vasculitis Damage Index	-0.04 (-0.54, 0.47)	0.892
ANCA-Vasculitis Index of Damage	0.48 (-0.27, 1.23)	0.206
AAV Disease-Specific Damage	0.35 (-0.08, 0.78)	0.115
AAV Non-Disease-Specific Damage	-0.3 (-0.79, 0.19)	0.225

Abbreviations: AAV, ANCA-associated vasculitis; CI, confidence interval; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; NDI, neurologic damage items; NI, neurologic involvement

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Differences in damage scores within subgroups among patients with ANCA-associated vasculitis and neurologic involvement based on disease subtypes and ANCA status.

	VDI		AVID		DSDS		Non-DSDS	
	Estimate (95% CI)	P-Value	Estimate (95% CI)	P-Value	Estimate (95% CI)	P-Value	Estimate (95% CI)	P-Value
N = 506								
GPA vs. EGPA	0.68 (0.05, 1.31)	0.034	2.15 (1.09, 3.21)	< 0.001	0.28 (-0.24, 0.8)	0.297	0.89 (0.3, 1.49)	0.003
MPA vs. EGPA	-0.57 (-1.41, 0.26)	0.178	-0.55 (-1.98, 0.88)	0.449	-1.01 (-1.7, -0.32)	0.004	-0.2 (-0.99, 0.59)	0.619
MPA vs. GPA	-1.25 (-2.17, -0.34)	0.007	-2.7 (-4.27, -1.13)	0.001	-1.28 (-2.04, -0.53)	0.001	-1.09 (-1.96, -0.23)	0.013
N = 502								
MPO+ vs. PR3+	0.47 (-0.2, 1.15)	0.170	1 (-0.14, 2.15)	0.086	0.4 (-0.16, 0.95)	0.164	0.56 (-0.08, 1.19)	0.086
ANCA negative vs. PR3+	0.08 (-0.59, 0.76)	0.808	0.61 (-0.53, 1.74)	0.292	0.32 (-0.24, 0.88)	0.267	0.27 (-0.37, 0.9)	0.412
ANCA negative vs. MPO+	-0.39 (-0.95, 0.17)	0.176	-0.39 (-1.35, 0.56)	0.419	-0.08 (-0.54, 0.39)	0.739	-0.29 (-0.82, 0.24)	0.282

Abbreviations: AVID, ANCA-Associated Vasculitis Index of Damage; CNS, central nervous system; DSDS, AAV, ANCA-associated vasculitis; AAV Disease-Specific Damage Score; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; NI, neurologic involvement; Non-DSDS, AAV Non-Disease-Specific Damage Score; PNS, peripheral nervous system; VDI, Vasculitis Damage Index.

Disclosure: R. Ni: None; **J. Bloom**: None; **K. Pickett-Nairne**: None; **L. Silveira**: None; **C. Zhang**: None; **D. Cuthbertson**: None; **T. corbridge**: GSK, 3, 11; **N. Khalidi**: AbbVie/Abbott, 2, 5, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 5, GlaxoSmithKlein(-GSK), 2, 6, Mallinckrodt, 2, NS Pharma, 5, Otsuka, 2, 6, Roche, 2, 6, Sanofi, 2, 5; **C. Koening**: Amgen, 1, Boehringer-Ingelheim, 1; **C. McAlear**: None; **P. Monach**: Boehringer-Ingelheim, 2; **L. Moreland**: None; **C. Pagnoux**: amgen, 1, 2, 6, Astra zeneca, 1, 6, csl vifor, 1, 2, 6, gsk, 1, 2, 6, Novartis, 2, ns pharma, 1, otsuka, 1, 2, 5, 6, Pfizer, 2, 6; **R. Rhee**: None; **P. Seo**: None; **J. Silver**: Amgen, 3, GSK, 3; **U. Specks**: Amgen, 1, 2, 5, Argenx, 2, AstraZeneca, 1, 5, Boehringer-Ingelheim, 1, 2, Bristol-Myers Squibb(BMS), 5, CSL Vifor, 1, Genentech, 5, GlaxoSmithKlein(GSK), 5, Mayo Foundation for Education and Research, 9, Melodia Therapeutics, 2, NorthStar Medical Radioisotopes, 5, Novartis, 1, 2, 5, NS Pharma, 5, UpToDate, 9; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **M. Wechsler**: allakos, 1, 2, 6, Amgen, 1, 2, 6, Areteia Therapeutics, 1, 2, 6, Arrowhead Pharmaceuticals, 1, 2, 6, AstraZeneca, 1, 2, 6, Avalo Therapeutics, 1, 2, 6, Celldex, 1, 2, 6, Connect Biopharma, 1, 2, 6, Eli Lilly, 1, 2, 6, Equillium, 1, 2, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Incyte, 1, 2, 6, Kinaset, 1, 2, 6, Kymera, 1, 2, 6, Merck, 1, 2, 6, Phylaxis, 1, 2, 6, Pulmatrix, 1, 2, 6, Rapt Therapeutics, 1, 2, 6, Recludix Pharma, 1, 2, 6, Regeneron Pharmaceuticals, 1, 2, 6, Roche/Genentech, 1, 2, 6, Sanofi/Genzyme, 1, 2, 6, Sentien, 1, 2, 6, Sound Biologics, 1, 2, 6, Tetherex Pharmaceuticals, 1, 2, 6, Uniquity Bio, 1, 2, 6, Upstream Bio, 1, 2, 6, Verona Pharma, 1, 2, 6, Zurabio, 1, 2, 6; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **R. Hajj-Ali**: AbbVie/Abbott, 2, Amgen, 2, UpToDate, 9.

Abstract Number: 2516

Mortality Trends in Primary Systemic Vasculitis in the United States (1999–2023)

Rameez Qasim[1], **Sabah Mohib**[2], Muhammad Ali[3] and Khadija Mohib[4], [1]Allama Iqbal Medical College Lahore, Lahore, Pakistan, [2]N/A, Reseda, CA, [3]Dow International Medical College, Karachi, Sindh, Pakistan, [4]Kirk Kerkorian School of Medicine at UNLV, Las Vegas, NV

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

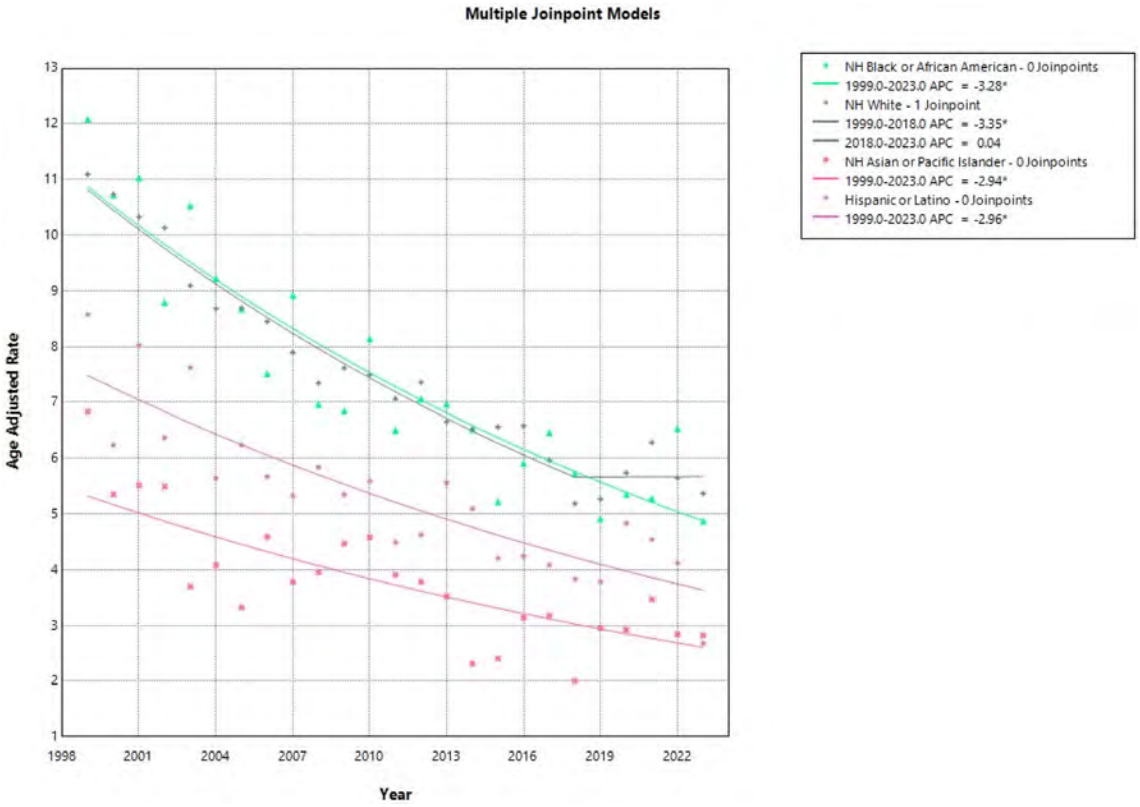
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Primary systemic vasculitides comprise a group of immunological disorders that inflame blood vessel walls and are categorized by the size of the blood vessels involved (small, medium, and large vessel vasculitis). This group of disorders has an elevated mortality rate among rheumatologic diseases, as prior studies have suggested. While earlier analyses have studied mortality trends related to this group of disorders, newer, more updated research is limited, especially concerning trends beyond 2019.

Methods: Datasets from the CDC WONDER Multiple Cause-of-Death public use records from 1999 to 2023 were used to analyze deaths in adults ≥25 years old, assigning ICD-10 codes (M30 and M31 series) to primary systemic vasculitis by year and place of death, as well as by demographic (sex, age group, race) and regional (state, census region, rural-urban) stratifications. Age-adjusted mortality rates (AAMR) were calculated per 1,000,000 with 95% confidence intervals by standardizing crude mortality rates (CMR). Annual percent change (APC) and average annual percent change (AAPC) were evaluated using Joinpoint regression software.

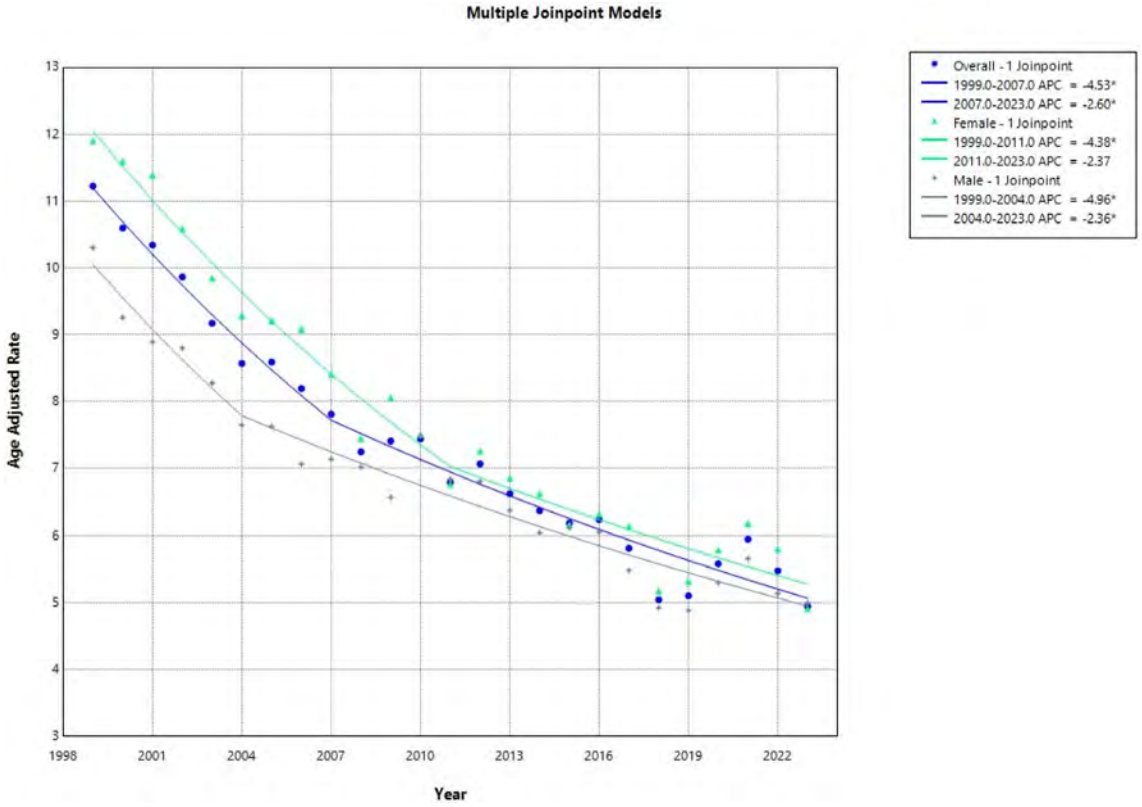
Results: A total of 39,093 deaths occurred from 1999 to 2023, mostly in medical facilities (61.8%). The AAMR declined from 11.2 in 1999 to 4.9 in 2023 (AAPC: -3.3; 95% CI: -3.6 to -2.9). Women had a higher average AAMR compared to men, along with a higher rate of decrease (AAPC women: -3.4; 95% CI: -3.8 to -3.0; men: -2.9; 95% CI: -3.3 to -2.4). Adults aged ≥65 years had the highest average AAMR, along with the highest rate of decrease among the age groups (AAPC ≥65 years: -3.4; 95% CI: -3.7 to -3.0; 45–65 years: -2.9; 95% CI: -3.5 to -2.4; 25–44 years: -2.2; 95% CI: -3.2 to -1.3).

Racially, non-Hispanic (NH) White populations had the highest average AAMR, along with the highest rate of decrease (AAPC NH White: -2.7; 95% CI: -3.3 to -2.2; NH Asian/Pacific Islander: -2.9; 95% CI: -3.8 to -2.0; Hispanic/Latino: -3.0; 95% CI: -3.7 to -2.1; NH Black/African American: -3.3; 95% CI: -4.0 to -2.6).

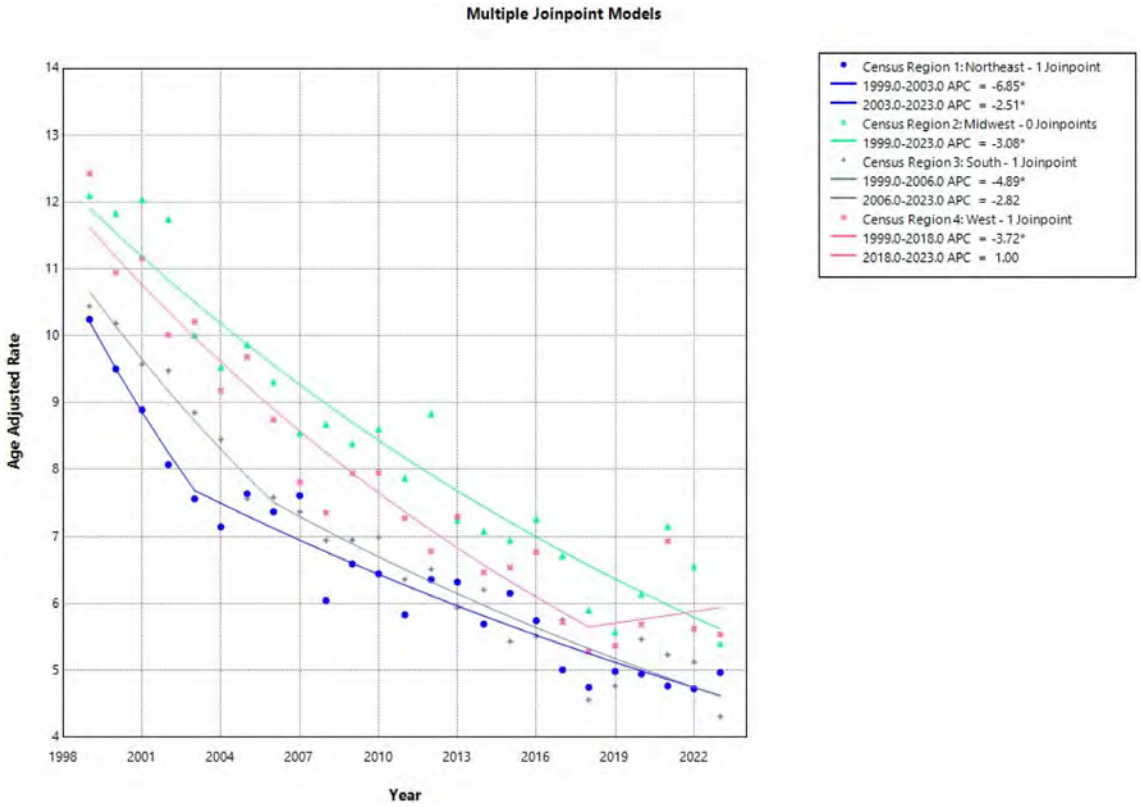


Trends in Vasculitis-Related Mortality by Race, United States (1999–2023)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Primary Systemic Vasculitis Mortality by Sex (1999–2023)



Primary Systemic Vasculitis Mortality by Census Region (1999–2023)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Regionally, the Midwest had the highest average AAMR, though the South had the highest rate of decrease (AAPC South: -3.4; 95% CI: -3.8 to -3.0; West: -2.8; 95% CI: -3.6 to -2.1; Midwest: -3.1; 95% CI: -3.6 to -2.6; Northeast: -3.2; 95% CI: -3.7 to -2.7).

From 1999 to 2020, state-wise AAMRs ranged from 5.1 in Hawaii to 12.6 in Vermont. From 2021 to 2023, AAMRs ranged from 3.7 in Louisiana to 11.8 in Minnesota. From 1999 to 2020, rural areas had a higher average AAMR, though urban areas had a higher rate of decrease (AAPC urban: -3.8; 95% CI: -4.1 to -3.4; rural: -2.5; 95% CI: -3.0 to -2.0).

Conclusion: Though primary systemic vasculitis-related mortality rates in adults declined from 1999 to 2023, disparities across demographic and regional groups remain, highlighting the need for targeted prevention and support systems to improve outcomes in at-risk communities.

Disclosure: R. Qasim: None; **S. Mohib**: None; **M. Ali**: None; **K. Mohib**: None.

Abstract Number: 2517

Predictors for Mortality in Patients Who Received Plasmapheresis for Diffuse Alveolar Hemorrhage in ANCA-Associated Vasculitis

Sai Shanmukha Sreeram Pannala[1], Medha Rajamanuri[2], Srikar Sama[3], Fares Saliba[4], Omar Mourad[5], Koushik Varma Sangaraju[6], Veena Katikineni[7] and Anastasia Slobodnick[8], [1]Zucker School of Medicine at Hofstra/Northwell at Staten Island University Hospital, staten island, new york city, NY, [2]Southern Illinois University School of Medicine, Springfield, IL, [3]University of California San Francisco Fresno, Fresno, CA, [4]Staten Island University Hospital, Staten Island, NY, [5]Zucker School of Medicine at Hofstra/Northwell at Staten Island University Hospital, Staten Island, NY, [6]St. Luke's University Health Network, Bethlehem, PA, [7]Desert Orthopaedic and Rheumatologic Institute, Apple Valley, CA, [8]Northwell, Staten Island, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Plasmapheresis (PLEX) has a compelling rationale in its ability to remove pathogenic ANCAs, in the management of ANCA-associated vasculitis (AAV), particularly in patients with severe manifestations such as diffuse alveolar hemorrhage (DAH). Despite its theoretical benefits, the role of PLEX in AAV + DAH remains debated, and inconsistent evidence regarding its long-term effects on mortality and organ function raises important questions. Our study aims to compare the risk of in-hospital mortality in patients with AAV + DAH who received PLEX to those who did not, seeking to clarify the role of PLEX in improving clinical outcomes and addressing current uncertainties regarding its efficacy in this context.

Methods: Using the National Inpatient Sample database from January 2020 to December 2022, we extracted data on AAV + DAH (AAVDAH), categorizing patients into two groups: those who received plasmapheresis (AAVDAHpl) and those who did not (AAVDAH). We analyzed key demographic, clinical, and hospital-related factors, including gender, age, race, Charlson Comorbidity Index (CCI), income, payer, region, and bed size. The primary outcome was in-hospital mortality, with secondary outcomes including LOS, total charges, sepsis, mechanical ventilation, and pressor requirements. Adjusted odds ratios for mortality and complications were calculated using logistic regression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

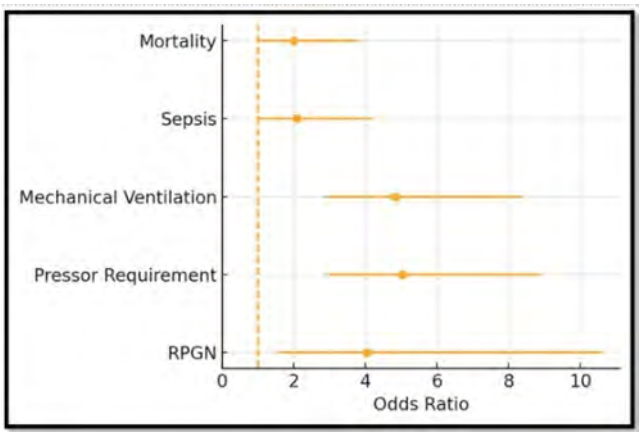


Figure 1: Odds ratios (ORs) with 95% confidence intervals (CIs) for outcomes comparing AAVDAH with plasmapheresis (AAVDAHpl) and AAVDAH without plasmapheresis.

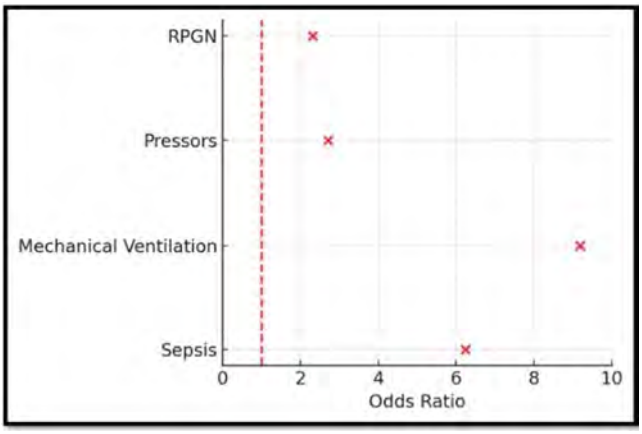


Figure 2: Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) for mortality, adjusting for complications, in patients with AAVDAH who received plasmapheresis (AAVDAHpl).

Table 1: Baseline Characteristics Comparison Between AAVDAH and AAVDAH with Plasmapheresis (AAVDAHpl).

Characteristic	AAVDAH (No Plasmapheresis)	AAVDAH (Plasmapheresis)
Females	44.29%	49.33%
Mean Age	54.45 years	56.65 years
Race Distribution (White)	63.40%	58.33%
Race Distribution (Black)	11.39%	15.28%
Race Distribution (Hispanic)	17.08%	20.83%
Charlson Comorbidity Index (Category 0)	22.45%	16.00%
Charlson Comorbidity Index (Category 1)	12.93%	14.67%
Charlson Comorbidity Index (Category 2)	25.85%	24.00%
Charlson Comorbidity Index (Category 3)	38.78%	45.33%
Household Income (Quartile 1)	27.99%	30.67%
Household Income (Quartile 2)	26.28%	20.00%
Household Income (Quartile 3)	25.26%	30.67%
Household Income (Quartile 4)	20.48%	18.67%
Primary Payer (Medicare)	41.50%	45.33%
Primary Payer (Private Insurance)	18.37%	13.33%
Hospital Region (Northeast)	19.05%	32.00%
Hospital Region (South)	27.55%	29.33%
Hospital Region (Midwest)	29.59%	20.00%
Hospital Region (West)	23.81%	18.67%
Hospital Bed Size (Small)	11.90%	9.33%
Hospital Bed Size (Medium)	27.21%	29.33%
Hospital Bed Size (Large)	60.88%	61.33%

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 1,470 AAVDAH patients were identified, with 375 receiving PLEX (AAVDAHpl). The mean age was 54.45 years in the AAVDAH group and 56.65 years in the AAVDAHpl group. Regarding comorbidity burden (CCI), 25.85% of AAVDAH patients had moderate, compared to 24.00% in AAVDAHpl, and 38.78% had severe burden, compared to 45.33% in AAVDAHpl. AAVDAHpl patients were more likely to be admitted to hospitals in the Northeast (32.00% vs. 19.05%) (Table 1).

The mean LOS was significantly longer in the AAVDAHpl group (23.59 days) vs. 13.79 days ($p < 0.001$), and total charges were higher ($424,256.7 vs. $220,514.1, $p < 0.001$).

The odds of death in the AAVDAHpl group was 1.99 (95% CI: 1.03 - 3.85) ($p = 0.0415$). Significant associations were found between PLEX and various complications, including sepsis (OR = 2.08, $p = 0.041$), mechanical ventilation (OR = 4.82, $p < 0.001$), and pressor requirement (OR = 5.04, $p < 0.001$). RPGN was significantly associated with PLEX (OR = 4.06, $p = 0.0044$) (Fig 1).

Adjusted analyses revealed that mechanical ventilation, sepsis, and pressor requirement were strongly associated with increased mortality in the AAVDAHpl group ($p < 0.001$ for all), while RPGN was not statistically significant ($p = 0.120$) (Fig 2).

Conclusion: This study indicates that PLEX treatment in AAV + DAH may be linked to higher mortality and more severe complications, highlighting the need for a cautious and individualized approach to its use. However, our results are limited by the lack of data on other treatments received by patients for their AAV. The increased risk of complications associated with PLEX further complicates its role in management. Therefore, further research is essential to identify when PLEX is most beneficial, especially in patients with DAH, and to clarify its optimal application in clinical practice.

Disclosure: S. Pannala: None; **M. Rajamanuri**: None; **S. Sama**: None; **F. Saliba**: None; **O. Mourad**: None; **K. Sangaraju**: None; **V. Katikineni**: None; **A. Slobodnick**: None.

Abstract Number: 2518

Impact of psychiatric comorbidity on disease outcomes in ANCA-associated vasculitis: A multi-center retrospective cohort study

Saloni Patel[1], Brendan Denvir[2], Maria Kaltchenko[1], Aaron Bao[3], Varsha Simha[1], Michael Cammarata[4] and Jun Kang[5], [1]Johns Hopkins University School of Medicine, Baltimore, [2]Johns Hopkins, Baltimore, MD, [3]Johns Hopkins School of Medicine, Baltimore, MD, [4]Johns Hopkins, Phoenix, MD, [5]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic small vessel vasculitis associated with significant morbidity and complex care needs across a broad demographic spectrum. While prior studies have demonstrated an increased prevalence of mental health disorders among patients with AAV, the impact of pre-existing psychiatric conditions on disease outcomes remains insufficiently characterized. Given the potential interplay between psychiatric comorbidities and systemic inflammation, further investigation is warranted. This study aims to evaluate the influence of pre-existing psychiatric disorders on clinical outcomes and treatment patterns in adult patients diagnosed with AAV.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. ICD10 and RxNorm codes of outcomes of interest in TriNetX

Outcome	ICD10 Code
Renal	
Acute kidney failure	N17
Chronic kidney disease	N18
End-stage renal disease	N18.6
Pulmonary	
Hemorrhage from respiratory passages	R04
Interstitial lung diseases	J84
Pulmonary embolism	I26
Respiratory failure	J96
Dependence on supplemental oxygen	Z99.81
Dependence on a respirator	Z99.1
Infection	
Pneumonia	J12-J18
Urinary tract infections	N39.0
Skin and soft tissue infections	L00-L08
Sepsis	A41
Bacterial infections	A30-A49
Viral infections	B00-B09, B15-B20, B25-B34
Complications of glucocorticoid use	
Essential hypertension	I10
Diabetes mellitus	E08-E13
Osteoporosis	M80, M81
Cataracts	H25, H26
Glaucoma	H40-H42
Venous thromboembolism	I82
Prescription of glucocorticoids	**RxNorm code**
Prednisone	8640
Methylprednisolone	6902
Prescription of steroid-sparing immunosuppressants	
Cyclophosphamide	3002
Rituximab	121191
Azathioprine	1256
Methotrexate	6851
Mycophenolate mofetil	68149

Methods: We conducted a retrospective cohort study using the TriNetX network, comparing adult AAV patients with and without pre-existing psychiatric diagnoses (schizophrenia, schizoaffective disorder, bipolar disorder, major depressive disorder, or persistent mood disorder). Propensity score matching was performed for age, sex, race, and smoking status. Five-year incident risk of chronic renal disease, pulmonary disease, infections, venous thromboembolism, glucocorticoid use, and glucocorticoid-associated toxicities were compared using relative risk (RR) with 95% confidence intervals (CI). The ICD-10 and RxNorm codes corresponding to these outcomes, as defined within the TriNetX database, are presented in Table 1.

Results: A total of 1,121 AAV patients with preexisting psychiatric disorders and 17,465 without were included, with 1,116 patients in each cohort after matching (Table 2). Before matching, psychiatric comorbidity was associated with higher risks of acute kidney failure (RR 1.31, 95% CI 1.04–1.64), respiratory failure (1.59, 1.29–1.95), venous thromboembolism (1.37, 1.02–1.86), and infections. After matching, psychiatric comorbidity remained associated with increased risks of pneumonia (1.45, 1.09–1.94), skin infections (1.93, 1.40–2.67), sepsis (1.41, 1.01–1.96), and viral infections (1.55, 1.13–2.13). In unmatched analyses, patients with psychiatric disorders were more likely to be prescribed glucocorticoids (1.13, 1.09–1.18) and less likely to receive glucocorticoid-sparing immunosuppressants (0.81, 0.71–0.92); the latter association persisted after matching (Figure 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Tables

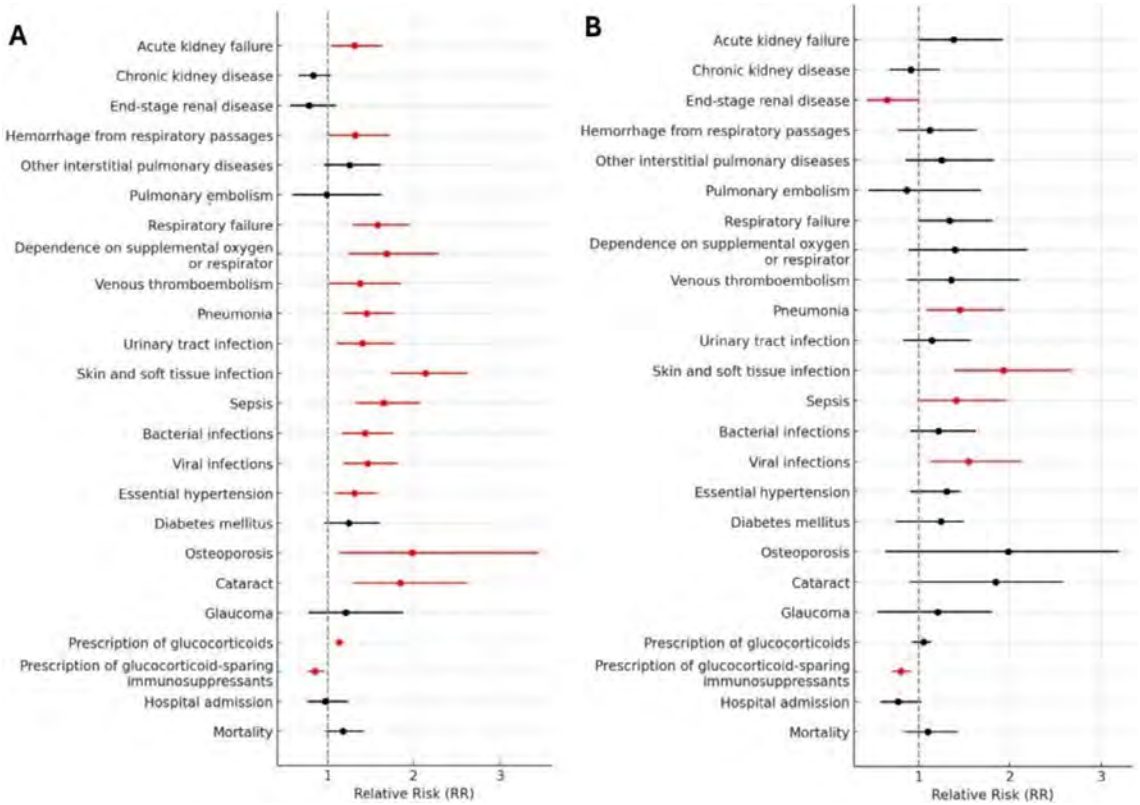
Table 2. Baseline cohort characteristics before and after propensity-score matching

	Before matching					After matching				
	AAV with psychiatric comorbidity		AAV without psychiatric comorbidity			AAV with psychiatric comorbidity		AAV without psychiatric comorbidity		
	N	Value	N	Value	p-value	N	Value	N	Value	p-value
Age at Index (years)*	1,121	56.2	17,465	57.4	0.0213	1,116	56.1	1,116	55.8	0.6157
Sex										
Female	721	64.35%	9422	53.95%	<0.0001	720	64.56%	729	65.33%	0.7137
Male	349	31.17%	7629	43.68%	<0.0001	350	31.32%	349	31.27%	0.9624
Ethnicity*										
Not Hispanic or Latino	954	85.10%	15,259	87.37%	0.0124	954	85.48%	960	86.02%	0.7635
Hispanic or Latino	167	14.90%	2,206	12.63%	0.4854	162	14.52%	156	13.98%	0.897
Race*										
American Indian or Alaska Native	10	0.89%	76	0.44%	0.0289	10	0.90%	10	0.90%	1.0000
Asian	23	2.05%	624	3.57%	0.0071	23	2.06%	19	1.70%	0.5332
Black or African American	152	13.56%	2682	15.36%	0.2965	152	13.62%	158	14.16%	0.6688
Native Hawaiian or Other Pacific Islander	18	1.61%	84	0.48%	<0.0001	13	1.17%	14	1.25%	0.8465
White	918	81.89%	13,999	80.16%	0.7190	918	82.25%	915	81.99%	0.3748
Nicotine dependence*	308	27.48%	1,482	8.49%	<0.0001	303	27.15%	293	26.25%	0.6323
AAV										
GPA	724	64.59%	11,343	64.95%	0.8973	720	64.52%	719	64.43%	0.7879
EGPA	283	25.25%	4,250	24.33%	0.2357	282	25.27%	288	25.81%	0.5811
MPA	108	9.63%	1,872	10.72%	0.7757	108	9.68%	109	9.77%	0.4951
Psychiatric comorbidity										
Bipolar disorder	219	19.54%				218	19.53%			
Persistent mood disorder	278	24.80%				279	25.00%			
Major depressive disorder	525	46.83%				520	46.59%			
Schizoaffective disorder	40	3.57%				40	3.58%			
Schizophrenia	59	5.26%				59	5.29%			

Abbreviations: AAV=ANCA-associated vasculitis, GPA=Granulomatosis with polyangiitis, MPA=Microscopic polyangiitis, EGPA=Eosinophilic granulomatosis with polyangiitis.

*Covariates included in the propensity-score matched analysis

Abbreviations: AAV=ANCA-associated vasculitis, GPA=Granulomatosis with polyangiitis, MPA=Microscopic polyangiitis, EGPA=Eosinophilic granulomatosis with polyangiitis. *Covariates included in the propensity-score matched analysis



Relative risk of 5-year incident outcomes in adult ANCA-associated vasculitis (AAV) patients with a pre-existing psychiatric comorbidity. The reference group for both plots is the cohort of adult patients with AAV and no documented psychiatric disorder (schizophrenia, schizoaffective disorder, bipolar disorder, major depressive disorder, or persistent mood disorder) at any time point. Plot A shows the unadjusted analyses and plot B displays the adjusted analyses after propensity-score matching for age at AAV diagnosis, sex, race, and nicotine dependence in a 1:1 ratio between the cohort of interest and the reference cohort. The dashed gray vertical line in both plots represents no difference in relative risk between the cohorts. Plots highlighted in red indicate a statistically significant difference between cohorts.

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In AAV, pre-existing psychiatric disorders are associated with increased infectious complications and decreased prescription of glucocorticoid-sparing therapies. Future research should investigate potential co-inflammatory interactions between psychiatric disorders and AAV, and socioenvironmental factors influencing medication adherence and access to care.

Disclosure: S. Patel: None; **B. Denvir**: None; **M. Kaltchenko**: None; **A. Bao**: None; **V. Simha**: None; **M. Cammarata**: None; **J. Kang**: AstraZeneca, 12, 5.

Abstract Number: 2519

A Disproportionality Analysis of FDA Adverse Event Reporting System (FAERS) Events for Avacopan

Shiamak Cooper[1], Asim Khanfar[2], Yousef al-mabrouk[3], Omar Hamdan[4] and Anthony Ocon[5], [1]Rochester General Hospital, Irondequoit, NY, [2]Rochester General Hospital, Rochester, NY, [3]Prince Hanza Hospital, Amman, Jordan, [4]University of Jordan, Az-Zarqa, Jordan, [5]Rochester Regional Health, Fairport, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

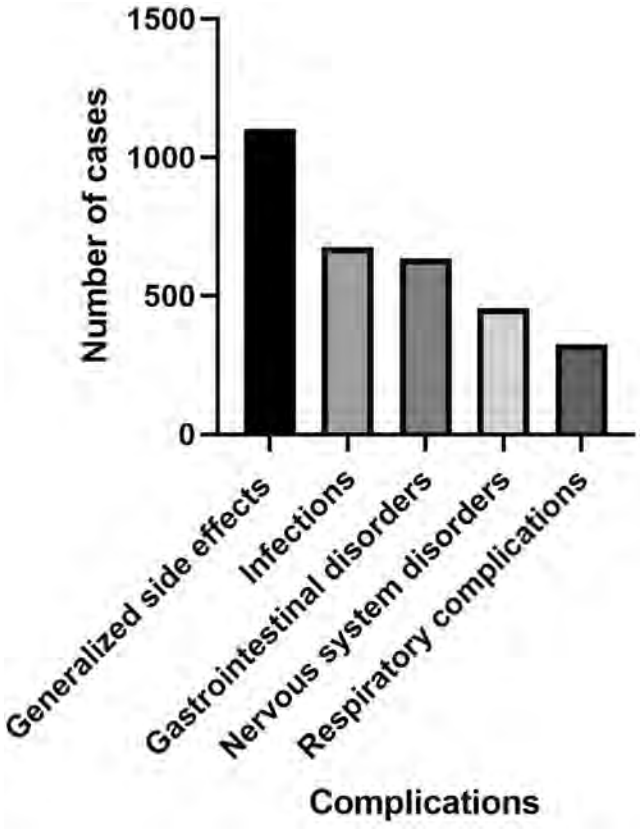


Figure 1. Frequency of adverse events

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Reported Odds Ratio (ROR) and Proportional Reporting Ratio (PRR) of Adverse Events

Adverse reaction	Frequency	ROR	95% Confidence Interval	PRR
Fatigue	202	2.422	2.101 – 2.791	2.343
Diarrhea	191	2.611	2.257 – 3.021	2.527
Nausea	188	2.028	1.751 – 2.349	1.975
Headache	140	1.824	1.541 – 2.160	1.793
Covid-19	127	6.698	5.611 – 7.995	6.500
Drug Ineffective	96	0.5857	0.4782 – 0.7173	0.5966
Pneumonia	96	2.440	1.993 – 2.989	2.403
Dizziness	88	1.398	1.132 – 1.728	1.389
Rash	85	1.723	1.389 – 2.136	1.706
Infection	83	5.009	4.029 – 6.227	4.918
Abdominal Discomfort	81	4.459	3.577 – 5.557	4.382
Vomiting	79	1.342	1.073 – 1.677	1.334
Dyspnea	76	1.075	0.8568 – 1.350	1.074
Infection	76	4.080	3.251 – 5.121	4.016
Dialysis	70	37.41	29.51 – 47.42	36.71
Hypertension	69	2.574	2.028 – 3.267	2.544
Liver Disorder	67	13.38	10.51 – 17.04	13.16
Hepatic Function Abnormal	64	8.930	6.973 – 11.44	8.791
Therapy Interrupted	63	7.863	6.128 – 10.09	7.745
Hepatic Enzyme Increased	56	7.789	5.982 – 10.14	7.686
Abdominal Pain Upper	54	2.365	1.807 – 3.094	2.344
Malaise	53	1.257	0.9587 – 1.649	1.254
Alopecia	53	2.051	1.563 – 2.689	2.035
Peripheral Swelling	52	2.974	2.261 – 3.910	2.945
Drug-Induced Liver Injury	52	17.59	13.37 – 23.14	17.35

Background/Purpose: Avacopan, a C5a receptor inhibitor, is used as an adjunctive treatment for ANCA-associated vasculitis. Previous studies have highlighted its efficacy in reducing glucocorticoid use and improving renal outcomes. However, concerns regarding its safety profile, particularly hepatotoxicity and serious infections, remain significant. This study aims to investigate the incidence and characteristics of adverse events associated with Avacopan using the FDA Adverse Event Reporting System (FAERS) database. By analyzing real-world pharmacovigilance data, this study seeks to provide a comprehensive assessment of the risks posed by Avacopan, thereby informing clinical practice and enhancing patient safety.

Methods: The FAERS database was searched for adverse events related to avacopan. Data were reported as frequencies, proportional reporting ratio (PRR), and as reporting odds ratios (ROR) with a 95% confidence interval (95% CI).

Results: We analyzed 30,179,725 adverse event reports from the FAERS database. A total of 3,658 reports were associated with the use of avacopan. 39.15% of patients were females, whereas 32.34% had an unspecified sex. The most common group of adverse reactions was generalized side effects (1,103), followed by infections (675) and gastrointestinal disorders (635) (Figure 1). Patients on avacopan had a higher ROR of getting fatigue compared to all other drug users (ROR=2.422; 95% CI: 2.101-2.791). In addition, gastrointestinal disorders, including diarrhea and nausea, were higher

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

among avacopan users compared to other drug users (ROR= 2.611 and 2.028, respectively). Drug-induced liver injury was reported in 52 patients on avacopan, and patients who were taking the medications were significantly more likely to get this complication (ROR=17.59; 95% CI: 13.37-23.14) (Table 1).

Conclusion: In this large pharmacovigilance analysis, avacopan use was associated with a distinct adverse event profile, most notably fatigue, gastrointestinal symptoms, and a markedly increased reporting odds of drug-induced liver injury. While these findings underscore known risks observed in clinical trials, the elevated RORs for hepatic events warrant continued surveillance and caution in clinical use. Real-world safety data such as these are critical for guiding risk mitigation strategies and optimizing patient outcomes in ANCA-associated vasculitis.

Disclosure: S. Cooper: None; **A. Khanfar**: None; **Y. al-mabrouk**: None; **O. Hamdan**: None; **A. Ocon**: Amgen, 2, 6.

Abstract Number: 2520

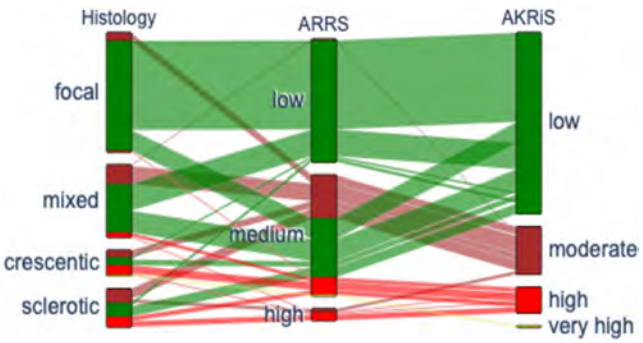
Evolution in Risk Stratification for Renal Outcomes in ANCA-Associated Vasculitides Using Established Scores and Histopathological Criteria in a Large European Cohort

Stefan Krämer[1], Kristian Vogt[2], Martin Busch[3], Tobias Schmitt[4], Raoul Bergner[5], Sebastian Mosberger[5], **Thomas Neumann**[6], Teresa Schreibing[1], Fabian Schumbrink[1] and Thomas Rauen[2], [1]Department of Internal Medicine II, RWTH University Hospital Aachen, Aachen, Germany, [2]Department of Internal Medicine II, RWTH University Hospital AachenMedicine II, Aachen, Germany, [3]Department of Internal Medicine III, University Hospital, Friedrich-Schiller University, Jena, Jena, Germany, [4]University Hospital Jena, Friedrich-Schiller University, Department of Internal Medicine III, Jena, Germany, [5]Department of Internal Medicine A, Nephrology and Rheumatology, Municipal Hospital Ludwigshafen, Ludwigshafen, Germany, [6]Department of Rheumatology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Glomerulonephritis is a common and threatening manifestation in ANCA-associated vasculitis (AAV). To assess the risk of end-stage kidney disease (ESKD), various scores have been developed, with the ANCA renal risk score (ARRS) and the improved ANCA kidney risk score (AKRiS) [1] being introduced most recently. We aim to investigate its performance in granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) separately in comparison to histological finding.



Distribution of histological classification and their transformation into risk classes, color is taken from final AKRiS class to illustrate their origin and flow.

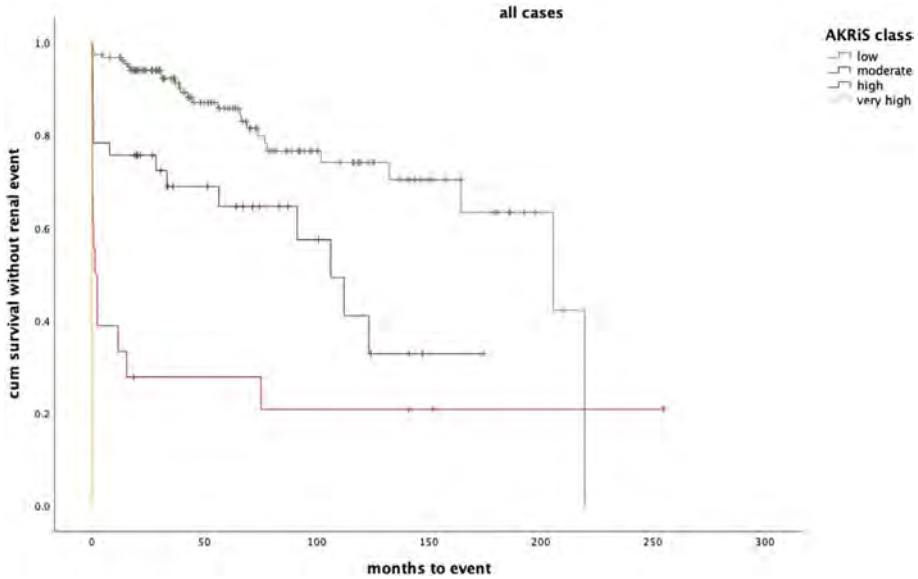
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Risk Classification					
ARRS	**Low**	**Medium**	**High**		**p**
n, (%)	106 (48.2)	104 (47.3)	10 (4.5)		
Composite end point, n (%)	19 (17.9)	44 (42.3)	6 (60)		<0.001
AUC	0.70*				
AAV-depended AUC	MPA: 0.724**, GPA: 0.678***				
AKRiS	**Low**	**Moderate**	**High**	**Very high**	
n, (%)	156 (70.9)	41 (18.6)	22 (1)	1 (0.5)	
Composite end point, n (%)	30 (19.2)	20 (48.8)	18 (81.8)	1 (100)	<0.001
AUC	0.76*				
AAV-depended AUC	MPA: 0.778**, GPA: 0.745***				
Changes ARRS -> AKRiS	up, n (%)				17 (7.7)
	down, n (%)				54 (24.5)
	same, n (%)				149 (67.7)

Histopathological findings and risk scores at diagnosis and outcomes of 220 patients having AAV with renal involvement.

Methods: We retrospectively analyzed 220 AAV cases between 1998 and 2021 who underwent renal biopsies and could be classified according to the 2020 ACR/EULAR criteria as either GPA or MPA. Follow-up visits were recorded every 6 months. The entire follow-up period was screened for the composite renal endpoint, which included death, dialysis, renal transplantation or the development or ESKD persistence with an eGFR < 15 ml/min/1.73 m^2 at or after six months of follow-up. The cases were analyzed according to histology and different risk scores. Comparison was done by Kaplan-Meier Curves, log-rank test and Herrell's C.

Results: Histological analysis revealed that renal biopsies from MPA patients showed significantly more sclerosis, interstitial fibrosis and tubular atrophy. In terms of histological classification, most cases fell into focal and mixed classes, which mainly transitioned into low- and medium-risk AKRiS categories. Higher risk classifications predominantly derived from crescentic and sclerotic classes (Fig. 1). The substantial group categorized as medium risk most frequently transitioned to lower risk scores within AKRiS. Kaplan-Meier-plots document a clear stratification for the chosen renal end-point. The comparison of ARRS and AKRiS by ROC and the AUC analyzes revealed slightly higher values of the new AKRiS score with an AUC of 0.76 as opposed to ARRS with an AUC of 0.70 (Tabl. 1). The AUC was consistently slightly higher for MPA than for GPA in both risk scores and generally higher for AKRiS than for ARRS. AKRiS stratification proved effective for predicting the composite renal endpoint (area under the curve ≥0.7, C-Index 0.899). ARRS and AKRiS classified 67.7% of cases into the same risk category, while AKRiS assigned a lower risk category in 24.5% of cases and upgraded to a higher risk category in only 7.7% of cases.



Kaplan-Meier-plot of the composite renal endpoint for each risk group .

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The new AKRiS score was found to be effective not only in predicting ESKD but also in assessing a strong composite renal endpoint in a large European AAV cohort, despite slight differences in histological and event patterns between GPA and MPA under comparable treatment regimen.

Disclosure: S. Krämer: None; **K. Vogt**: None; **M. Busch**: Alexion, 6, AstraZeneca, 6, Boehringer-Ingelheim, 1, 6, Bristol-Myers Squibb(BMS), 6, CSL Vifor, 1, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 1, 6, Otsuka, 1, Pfizer, 1, 6, Pharmacosmos, 6; **T. Schmitt**: None; **R. Bergner**: AbbVie, 1, 6, Alfasigma, 1, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 6, Eli Lilly, 6, German Rheumatology Society, 12, unpaid board member for Commission für student education, GlaxoSmithKlein(GSK), 1, 6, Janssen, 6, Merck/MSD, 6, Novartis, 1, 6, Vifor, 1, 5; **S. Mosberger**: None; **T. Neumann**: Amgen Switzerland AG, 1, AstraZeneca, 1, Boehringer-Ingelheim, 1, Celgene Switzerland, 1, CSL Vifor Switzerland, 1, 6, GlaxoSmithKlein(GSK), 1, 6, Janssen-Cilag AG, 1, Novartis Pharma Schweiz AG, 1, 6, UCB-Pharma AG, 1; **T. Schreibing**: None; **F. Schumbrink**: None; **T. Rauen**: CSL Vifor, 1.

Abstract Number: 2521

DANGER Score as Predictor of Mortality in ANCA-Associated Vasculitis with or without Glomerulonephritis: Data from the Almenara Vasculitis Cohort

Victor Pimentel-Quiroz[1], Alvaro Oyarce-Calderón[2], Allison Figueroa-Sánchez[3], Leonor León-Yaurimucha[3], Rocío Gamboa-Cárdenas[4], Zoila Rodríguez-Bellido[5], Risto Perich-Campos[6], Graciela Alarcón[7] and Manuel Ugarte-Gil[8], [1]Universidad Científica del Sur, San Isidro, Peru, [2]Hospital Nacional Guillermo Almenara Irigoyen, San Miguel, Peru, [3]Universidad Científica del Sur, Lima, Peru, [4]Universidad Científica del Sur, Lima, Peru, [5]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, Lima, Peru, [6]Hospital Nacional Guillermo Almenara Irigoyen; Universidad Nacional Mayor de San Marcos, La Molina, Peru, [7]The University of Alabama at Birmingham, Oakland, CA, [8]Universidad Cientifica del Sur, Lima, Peru

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The DANGER score can predict mortality in patients with ANCA-associated vasculitis (AAV) with glomerulonephritis (GN). However, this score has not been widely validated and, moreover, there is no evidence of its use in AAV patients without GN. The aim of this study was to evaluate the performance of this score in AAV patients with or without GN from a Latin American cohort.

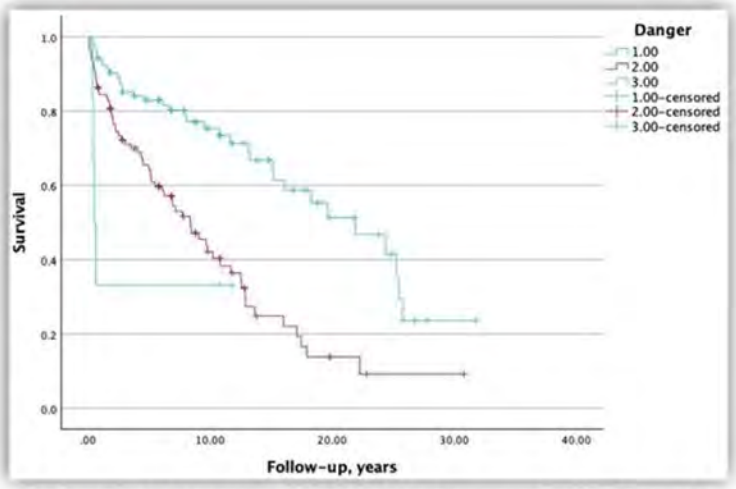
Methods: This was a medical records review study which included patients from the Almenara Vasculitis Cohort who had at least one visit between January 1990 and December 2024. Diagnosis of either microscopic polyangiitis (MPA) or granulomatosis with polyangiitis were included. Mortality was determined as the vital status according to the official information from the

Table 1. Unadjusted and adjusted analyses.

Levels of risk according to the DANGER score	Unadjusted HR (95% CI)	*p* value	Adjusted* HR (95% CI)	*p* value
Low	Ref.		Ref.	
Intermediate	2.71 (1.79 – 4.12)	**<0.001**	3.25 (1.87 – 5.65)	**<0.001**
High	5.04 (1.77 – 14.38)	**0.002**	8.91 (2.43 – 32.75)	**<0.001**

*Adjusted for age at diagnosis, sex and type of diagnosis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Line 1 (blue): Low risk. Line 2 (red): Intermediate risk. Line 3 (green): High risk.

Figure 1. Kaplan-Meier plot of survival according to categories by the DANGER score.

Peruvian Department of Health. Sociodemographic and clinical features were obtained. The DANGER score includes four variables: age at diagnosis, history of hypertension or cardiac disease, and creatinine and hemoglobin levels at diagnosis. This score stratifies the risk of mortality in low, intermediate and high. Unadjusted and adjusted Cox regression models were done to assess the impact of the DANGER score. The model was adjusted for age at diagnosis, gender and type of diagnosis.

Results: Two hundred twenty-five patients were enrolled; most of them were female [154 (68.4%)]. Mean of age and time of follow-up were 59.4 (12.6) and 7.7 (7.1) years, respectively. MPA was the most frequent diagnosis [177 (78.7%)]. During the follow-up, 110 (48.9%) patients died. As to the DANGER score, 105 (46.7%), 113 (50.2%) and 7 (3.1%) patients had low, intermediate and high risk of mortality, respectively. Furthermore, each risk category was predictive of mortality in the unadjusted and adjusted analyses (Table 1). Overall survival according to the stratification is depicted in Figure 1.

Conclusion: The DANGER score had good performance in AAV patients with or without GN in a Latin American cohort. More studies in other populations are necessary to validate these findings.

Disclosure: V. Pimentel-Quiroz: Biopas, 6, Pfizer, 6, Roche, 6, technofarm, 6; **A. Oyarce-Calderón**: None; **A. Figueroa-Sánchez**: None; **L. León-Yaurimucha**: None; **R. Gamboa-Cárdenas**: None; **Z. Rodríguez-Bellido**: None; **R. Perich-Campos**: None; **G. Alarcón**: None; **M. Ugarte-Gil**: AstraZeneca, 1, 6, Ferrer, 1, GlaxoSmithKlein(-GSK), 6, Janssen, 5, technofarma, 1.

Abstract Number: 2522

Clinical Outcomes and Prognostic Impact of Cardiac and Cerebrovascular Involvement in Eosinophilic Granulomatosis with Polyangiitis: A Retrospective Study

Yuko Shirota[1], Misa Oguma[2], MIki Kubota[2], Kei Soeda[2], Yumi Tajima[2], Ryo Kuwata[3], Yumiko Oka[2], Miki Takeshita[2], Takao Kodera[2] and Tomonori Ishii[2], [1]Tohoku Medical and Pharmaceutical University / Department of Hematology and Rheumatology, Sendai, [2]Tohoku Medical and Pharmaceutical University / Department of Hematology and Rheumatology, Sendai, Japan, [3]AIDS Clinical Center of the National Center for Global Health and Medicine, Shinjyuku, Japan

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) is a vasculitis characterized by eosinophilia and granuloma formation, affecting multiple organs. The Five-Factor Score (Medicine, 2011) identifies key prognostic factors, including severe cardiac or gastrointestinal involvement, renal failure, age ≥65, and absence of ENT symptoms. Among

Table. Baseline characteristics of the study population.Clinical manifestations, laboratory parameters, organ involvement, comorbid lifestyle-related diseases, and treatment modalities are presented for the entire cohort, and stratified by survival status (surviving and fetal cases). Proportions within each group are shown in parentheses.

		Total cases	Surviving cases	Fetal cases
Total number of patients, n (%)		51 (100)	47 (100)	4 (100)
Female, n (%)		31 (61)	29 (62)	2 (50)
Age at diagnosis, mean ± SD , years		**60.1 ± 12.1**	**59.3 ± 12.1**	**69.5 ± 8.3**
Items related to the 2022 ACR/EULAR classification criteria for AAV				
Clinical manifestations, n (%)	Obstructive airway disease	46 (90)	42 (89)	4 (100)
	Allergic rhinitis	10 (20)	10 (21)	0 (0)
	Nasal polyps	2 (4)	2 (4)	0 (0)
	Mononeuritis multiplex	31 (61)	30 (64)	1 (25)
	Nasal involvement (discharge, ulcers, crusting, congestion, septal defect/perforation)	29 (57)	27 (57)	2 (50)
	Cartilaginous involvement	0 (0)	0 (0)	0 (0)
	Conductive or sensorineural hearing loss	12 (24)	11 (23)	1 (25)
Laboratory/imaging/histological findings, n (%)	PR3-ANCA (or C-ANCA) positivity	2 (4)	2 (4)	0 (0)
	MPO-ANCA (or P-ANCA) positivity	17 (33)	16 (34)	1 (25)
	Serum eosinophil count ≥ $1x10^9$/liter	51 (100)	47 (100)	4 (100)
	Extravascular eosinophilic-predominant inflammation on biopsy	9 (18)	9 (19)	0 (0)
	Fibrosis or interstitial lung disease on chest imaging	18 (35)	17 (36)	1 (25)
	Pulmonary nodules, mass or cavitation on chest imaging	2 (4)	2 (4)	0 (0)
	Hematuria	7 (14)	7 (15)	0 (0)
	Pauci-immune glomerulonephritis on biopsy	3 (6)	3 (6)	0 (0)
	Nasal/paranasal sinusitis or mastoiditis on imaging	29 (57)	27 (57)	2 (50)
	Granuloma, granulomatous inflammation, or giant cells on biopsy	0 (0)	0 (0)	0 (0)
Organ involvement				
ENT, n (%)		32 (63)	30 (64)	2 (50)
	Chronic sinusitis	29 (57)	27 (57)	2 (50)
	Chronic otitis media	11 (22)	9 (19)	2 (50)
	Nasal polyps	2 (4)	2 (4)	0 (0)
Eye and orbit, n (%)		0 (0)	0 (0)	0 (0)
Central nervous system, n (%)		**12 (24)**	**11 (23)**	**1 (25)**
	Cerebrovascular disease	**11 (22)**	**10 (21)**	**1 (25)**
	Cerebral pachymeningitis	0 (0)	0 (0)	0 (0)
	Cerebral granulomatous lesions/cerebral nodules	0 (0)	0 (0)	0 (0)
	Cranial nerve palsy	1 (2)	1 (2)	0 (0)
Peripheral nervous system, n (%)	Sensory/ motor peripheral neuropathy	30 (59)	29 (62)	1 (25)
Pulmonary, n (%)		46 (90)	42 (89)	4 (100)
	Obstructive airway disease	46 (90)	42 (89)	4 (100)
	Pulmonary nodules, mass or cavitation	0 (0)	0 (0)	0 (0)
	Fibrosis or interstitial lung disease	18 (35)	17 (36)	1 (25)
	Alveolar hemorrhage	0 (0)	0 (0)	0 (0)
	Endobronchial disease	0 (0)	0 (0)	0 (0)
	Pleural effusion	6 (12)	3 (6)	3 (75)
Renal , n (%)		9 (18)	8 (17)	1 (25)
	Pauci-immune glomerulonephritis on biopsy	3 (6)	3 (6)	0 (0)
	Hematuria	9 (18)	8 (17)	1 (25)
Cardiovascular, n (%)		**8 (16)**	**8 (17)**	**0 (0)**
Cutaneous, n (%)		27 (53)	24 (51)	3 (75)
	Purpura/ulcers	27 (53)	24 (51)	3 (75)
	Nodules	0 (0)	0 (0)	0 (0)
Gastrointestinal, n (%)		10 (20)	10 (21)	0 (0)
Lifestyle-related diseases				
	Smoking	14 (27)	12 (26)	2 (50)
	Diabetes	20 (39)	10 (21)	0 (0)
	hyperlipidemia	5 (10)	2 (4)	0 (0)
	hypertension	14 (27)	30 (64)	1 (25)
Treatment				
Glucocorticoid				
	initial dose	46.1 ± 13.9	47.0 ± 13.3	35 ± 17.3
	maintenance dose	4.5 ± 2.3	3.9 ± 1.4	9.6 ± 2.7
Cyclophosphamide		9 (17)	9 (19)	0 (0)
Rituximab		2 (4)	2 (5)	0 (0)
High-dose intravenous immunoglobulin		17 (33)	14 (30)	3 (75)
Mepolizumab		35 (69)	32 (68)	3 (75)
Azathioprine		24 (47)	22 (47)	2 (50)
Mycophenolate mofetil		7 (13)	6 (13)	1 (25)
Methotrexate		7 (13)	6 (13)	1 (25)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

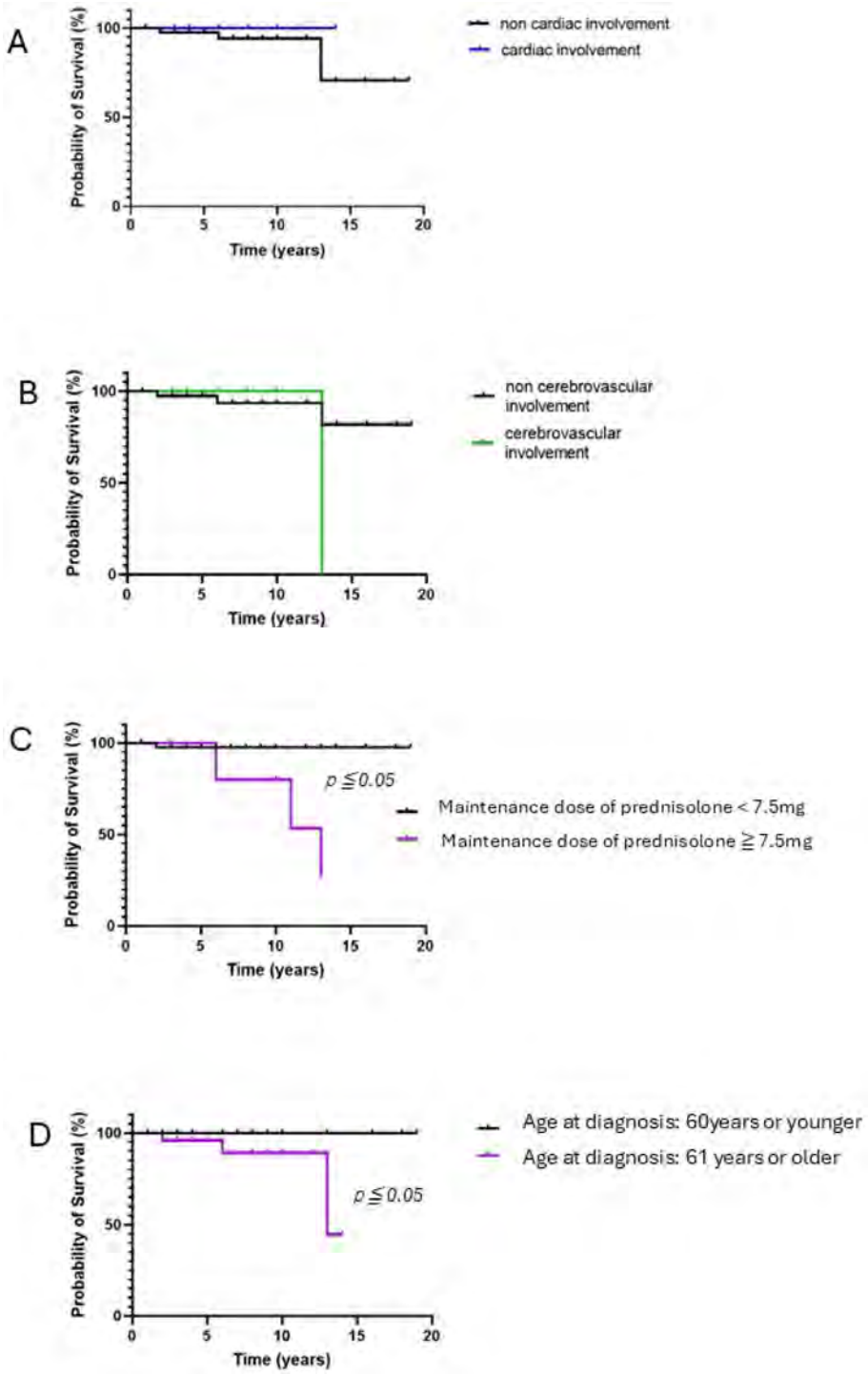


Figure. Kaplan–Meier survival curves. A: Comparison of overall survival between patients with and without cardiac involvement showed no significant difference. B: No significant difference in survival was observed between patients with and without cerebrovascular involvement. C: Patients receiving maintenance prednisolone doses ≥7.5 mg/day demonstrated significantly reduced survival compared to those receiving <7.5 mg/day. D: Patients with disease onset at age ≥61 years had significantly lower survival rates than those with onset at ≤60 years.

these, cardiac involvement is most closely linked to poor outcomes. Although CNS involvement is rare and not included in the score, it may still affect prognosis. Major causes of death in EGPA include cardiac and CNS complications, gastrointestinal perforation, respiratory failure, and infections. Treatment typically includes glucocorticoids and cyclophosphamide, with newer agents like anti–IL-5/IL-5R monoclonal antibodies and rituximab for refractory cases. This study evaluated treatment and outcomes in patients with organ involvement affecting survival.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We retrospectively analyzed 51 patients with EGPA treated at our hospital from 2000 to 2024. The mean age at onset was 60.1±12.1 years. We focused on cardiac and cerebrovascular involvement. CNS lesions were included only if they occurred during the active disease phase. We also assessed the presence of lifestyle-related diseases (e.g., smoking, hypertension, dyslipidemia, diabetes) and ANCA status. Treatments used for remission induction and maintenance were reviewed. Prognosis was analyzed according to presence of cardiac and CNS involvement. In fatal cases, we examined causes of death, treatment regimens, and glucocorticoid dosages. Relative risk with 95% confidence intervals was used for analysis.

Results: All patients received glucocorticoids. Cyclophosphamide was used in 9 cases, rituximab in 2, IVIG in 17, mepolizumab in 35, azathioprine in 24, mycophenolate mofetil in 7, and methotrexate in 7. Mepolizumab was effective in reducing prednisolone doses.

Cardiac involvement was observed in 8 patients, all presenting during the initial phase. None relapsed after treatment. Cardiac function was evaluated over time using echocardiography, focusing on wall motion abnormalities and pericardial effusion. Two patients showed marked improvement with immunosuppressive therapy. One had pre-existing arteriosclerosis and responded poorly. However, all 8 survived beyond 12 months with no cardiac deterioration.

Cerebrovascular events occurred in 11 cases—9 cases at initial presentation, 2 cases at 3- and 11-years post-onset. Lifestyle diseases were not significant risk factors for cardiac or CNS lesions.

Four patients died (mean age 78±4 years). One died of liver cancer; three had refractory disease with persistent glucocorticoid dependency. Of these, two died from pneumonia and one from CNS involvement. Cardiac and CNS involvement were not significant prognostic factors. However, age ≥61 at onset and maintenance prednisolone doses ≥7.5 mg/day were significant risk factors.

Conclusion: Cardiac and cerebrovascular involvement in EGPA may be controlled long-term with appropriate early treatment. In contrast, older-onset patients with glucocorticoid-dependent disease require careful management to prevent fatal infections and poor outcomes.

Disclosure: Y. Shirota: None; **M. Oguma**: None; **M. Kubota**: None; **K. Soeda**: None; **Y. Tajima**: None; **R. Kuwata**: None; **Y. Oka**: None; **M. Takeshita**: None; **T. Kodera**: None; **T. Ishii**: None.

Abstract Number: 2523

Predictors of Glucocorticoid-Free Clinical Remission at Week 48 in Newly Diagnosed Microscopic Polyangiitis and Granulomatosis with Polyangiitis: from nation-wide registry in Japan (J-CANVAS)

Yusuke Ushio[1], Satoshi Omura[2], Daiki Nakagomi[3], Yoshiyuki Abe[4], Makoto Wada[5], Naoho Takizawa[6], Atsushi Nomura[7], Yuji Kukida[8], Naoya Kondo[9], Hirosuke Takagi[10], Koji Endo[11], Shintaro Hirata[12], Naoto Azuma[13], Tohru Takeuchi[14], Shoichi Fukui[15], Kazuro Kamada[16], Ryo Yanai[17], Yusuke Matsuo[18], Yasuhiro Shimojima[19], Ryo Nishioka[20], Ryota Okazaki[21], Tomoaki Takata[22], Mayuko Moriyama[23], Ayuko Takatani[24], Yoshia Miyawaki[25], Tsuyoshi Shirai[26], Takafumi Ito[27], Isao Matsumoto[28], Toshihiko Takada[29], Toshiko Ito-Ihara[30], Takashi Kida[31], Nobuyuki Yajima[17], Takashi Kawaguchi[32], Yutaka Kawahito[31] and Hiroaki Dobashi[33], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita District, Kagawa, Japan, [2]Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465, Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto, Japan, [3]Department of Rheumatology, University of Yamanashi Hospital, Chuo-shi, Yamanashi, Japan, [4]Department of Internal Medicine and Rheumatology, Juntendo University, Bunkyo-Ku, Tokyo, Japan, [5]Center for Rheumatic Disease, Japanese Red Cross Society Kyoto Daiichi Hospital,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kyoto-shi, Kyoto, Japan, [6]Department of Rheumatology, Chubu Rosai Hospital, Nagoya city, Aichi, Japan, [7]Immuno-Rheumatology Center, St. Luke's International Hospital, Chuo-ku, Tokyo, Japan, [8]Department of Rheumatology, Japanese Red Cross Society Kyoto Daini Hospital, Kamigyou, Kyoto, Japan, [9]Department of Nephrology, Kyoto Katsura Hospital, Nishikyo-ku, Kyoto, Japan, [10]Department of Hematology and Rheumatology, Kagoshima University Hospital, Kagoshima, Kagoshima, Japan, [11]Department of General internal medicine, Tottori Red Cross Hospital, Tottori-city, Tottori, Japan, [12]Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan, [13]Department of Diabetes, Endocrinology and Clinical Immunology, Hyogo Medical University School of Medicine, 1-1 Mukogawa-cho, Nishinomiya-shi, Hyogo, Japan, [14]Department of Internal Medicine (IV), Osaka Medical and Pharmaceutical University, Takatsuki, Japan, [15]Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Nagasaki, Japan, [16]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [17]Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Shinagawa-ku, Tokyo, Japan, [18]Department of Rheumatology, Tokyo Kyosai Hospital, Meguro-ku, Tokyo, Japan, [19]Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Matsumoto, Nagano, Japan, [20]Department of Nephrology and Rheumatology, Graduate School of Medical Science, Kanazawa University, Kanazawa, Ishikawa, Japan, [21]Division of Respiratory Medicine and Rheumatology, Department of Multidisciplinary Internal Medicine, Faculty of Medicine, Tottori University, Yonago, Tottori, Japan, [22]Division of Gastroenterology and Nephrology, Tottori University, Yonago, Tottori, Japan, [23]Department of Rheumatology, Shimane University Faculty of Medicine, Izumo-shi, Shimane, Japan, [24]Rheumatic Disease Center, Sasebo Chuo Hospital, Sasebo-shi, Nagasaki, Japan, [25]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Okayama, Japan, [26]Department of Rheumatology, Tohoku University Hospital, Sendai, Miyagi, Japan, [27]Division of Nephrology, Department of Internal Medicine, Teikyo University Chiba Medical Center, Ichiharashi, Chiba, Japan, [28]Department of Rheumatology, Institute of Medicine, University of Tsukuba, Tsukuba-city, Ibaraki, Japan, [29]Department of General Medicine, Shirakawa Satellite for Teaching And Research (STAR) Fukushima Medical University, Shirakawa, Fukushima, Japan, [30]The Clinical and Translational Research Center, University Hospital, Kyoto Prefectural University of Medicine, Kyoto-city, Kyoto, Japan, [31]Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto-city, Kyoto, Japan, [32]Department of Clinical Assessment, Tokyo University of Pharmacy and Life Sciences, Hachioji-city, Tokyo, Japan, [33]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2504–2523) Vasculitis – ANCA-Associated Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Glucocorticoids (GCs) are a cornerstone of remission induction therapy in microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), but long-term GC use is associated with serious adverse effects. Therefore, minimizing GC exposure while maintaining disease control is a major therapeutic goal. However, the frequency and predictors of glucocorticoid-free clinical remission (GFCR) within the first year after treatment initiation remains unclear in patients with newly diagnosed MPA/GPA. This study aimed to investigate the rate and predictors of GFCR at week 48 in patients with newly diagnosed MPA or GPA, and to examine long-term outcomes up to week 96.

Methods: We conducted a retrospective cohort study using a multicenter, nationwide registry in Japan (J-CANVAS). Patients with newly diagnosed MPA or GPA and at least 48 weeks of follow-up were included. GFCR was defined as Birmingham Vasculitis Activity Score (BVAS) of 0 with complete GC withdrawal at week 48. Univariable and multivariable logistic regression analyses were used to identify factors associated with GFCR. Given the limited prior evidence regarding predictors of GFCR, variables for multivariable models were selected based on clinical relevance and statistical trends in univariable analysis (Model 1: $p < 0.05$, Model 2: $p < 0.20$).

Results: Among 728 patients with newly diagnosed MPA/GPA enrolled in the registry, 544 were included in the analysis. At week 48, 29 patients (5.3%) achieved GFCR. Baseline characteristics are shown in Figure 1, and treatment details and outcomes up to week 48 are summarized in Figure 2. In multivariable analysis, the use of rituximab (RTX) and avacopan within

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

	All patients (n = 544)	With GFCR (n = 29)	Without GFCR (n = 515)	p
Age, years	74.0 [68.0–80.0]	74.0 [68.0–79.5]	74.0 [68.0–80.0]	0.74
Sex, Female, n (%)	327 (60.1)	16 (55.2)	311 (60.4)	0.566
Newly diagnosed, n (%)	544 (100)	29 (100.0)	515 (100)	-
Type of vasculitis				
MPA, n (%)	399 (73.3)	24 (82.8)	375 (72.8)	0.286
GPA, n (%)	145 (26.7)	5 (17.2)	24 (27.2)	0.286
ANCA status				
MPO-ANCA positive, n (%)	475 (87.3)	28 (96.6)	447 (86.8)	0.157
PR3-ANCA positive, n (%)	60 (11.0)	1 (3.5)	59 (11.5)	0.236
negative, n (%)	9 (1.7)	0 (0)	9 (1.8)	1.000
Comorbidity				
Hypertension, n (%)	242 (44.5)	14 (48.3)	228 (44.3)	0.704
Diabetes, n (%)	119 (21.9)	5 (17.2)	114 (22.1)	0.649
Chronic kidney disease, n (%)	78 (14.3)	4 (13.8)	74 (14.4)	1.000
Cardiac disease, n (%)	71 (13.1)	2 (6.9)	69 (13.4)	0.407
Cancer, n (%)	76 (14.0)	1 (3.5)	75 (14.6)	0.104
Birmingham Vasculitis Activity Score (BVAS)	14.0 [10.0–19.0]	14.0 [8.0–20.0]	14.0 [10.0–19.0]	0.889
Organ involvement (BVAS ≥ 1) †				
General	373 (68.6)	19 (65.5)	354 (68.7)	0.686
Cutaneous	105 (19.3)	7 (24.1)	98 (19.0)	0.473
Mucous Membranes/eyes	63 (12.1)	3 (10.3)	63 (12.2)	1.000
Ear, nose, and throat	157 (28.9)	9 (31.0)	148 (28.7)	0.834
Chest	245 (45.0)	15 (51.7)	230 (44.7)	0.566
Cardiovascular	17 (3.1)	0 (0)	17 (3.3)	1.000
Abdominal	6 (1.1)	0 (0)	6 (1.2)	1.000
Renal	383 (70.4)	22 (75.9)	361 (70.1)	0.676
Nervous system	146 (26.8)	7 (24.1)	139 (27.0)	0.832
Laboratory data at diagnosis				
S-albumin, mg/dL (n = 28, n = 505)	2.6 [2.2–3.2]	2.6 [2.0–3.2]	2.6 [2.3–3.2]	0.357
S-creatinine, mg/dL	0.87 [0.64–1.43]	0.89 [0.73–1.72]	0.87 [0.64–1.43]	0.483
eGFR, ml/min/1.73m2	55.5 [32.5–76.4]	54.0 [29.7–75.3]	55.6 [33.4–76.5]	0.608
Hemoglobin, mg/dL (n = 29, n = 512)	10.4 [9.2–11.8]	10.6 [9.2–12.1]	10.4 [9.2–11.8]	0.451
Neutrophil, /μL (n = 29, n = 507)	8331 [5817–11920]	9870 [5099–11690]	8310 [5840–11920]	0.686
Lymphocyte, /μL (n = 29, n = 507)	1254 [930–1690]	1110 [800–1645]	1260 [939–1692]	0.355
Serum IgG, mg/dL (n = 27, n = 474)	1627 [1323–2024]	1669 [1351–2074]	1623 [1320–2014]	0.714
CRP, mg/dL (n = 29, n = 513)	8.2 [2.5–13.2]	7.6 [0.6–14.5]	8.2 [2.7–13.1]	0.585

Data are presented as median [IQR] or as n (%), unless otherwise indicated. GFCR, glucocorticoid-free clinical remission; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; ANCA, anti-neutrophil cytoplasmic antibody; MPO, anti-myeloperoxidase; PR3, anti-proteinase 3; BVAS, Birmingham Vasculitis Activity Score; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein. For statistical analyses, $^{*}p < 0.05$, $^{**}p < 0.01$. *P*-value: Wilcoxon rank sum test, Fisher's exact test † Organ involvement was based on BVAS ≥ 1.

Figure 1. Comparison of baseline characteristics between patients with and without GFCR at week 48

the first 24 weeks was independently associated with achieving GFCR, whereas methylprednisolone pulse therapy was negatively associated (RTX: odds ratio [OR] 5.16, 95% confidence interval [CI] 2.37–11.22; avacopan: OR 14.67, 95% CI 4.81–44.70; methylprednisolone pulse: OR 0.14, 95% CI 0.03–0.61). Baseline characteristics including age, sex, ANCA serotype, disease activity (BVAS), and organ involvement were not significantly associated (Figure 3). Patients who achieved

	All patients (n = 544)	With GFCR (n = 29)	Without GFCR (n = 515)	p
Year in which remission induction therapy was initiated, n (%)				
2017–2018	196 (36.0)	13 (44.8)	183 (35.5)	0.325
2019–2020	182 (33.5)	6 (20.7)	176 (34.2)	0.159
2021–2023	166 (30.5)	10 (34.5)	156 (30.3)	0.68
Daily GC dose (prednisolone-equivalent) at each time point				
Initial dose, mg	40.0 [30.0–50.0]	35.0 [30.0–50.0]	40.0 [30.0–50.0]	0.051
at week 1, mg	40.0 [30.0–50.0]	30.0 [27.5–50.0]	40.0 [30.0–50.0]	0.048*
at week 2, mg	40.0 [30.0–45.0]	30.0 [15.0–40.0]	40.0 [30.0–45.0]	0.001**
at week 4, mg	30.0 [25.0–40.0]	20.0 [7.5–30.0]	30.0 [25.0–40.0]	< 0.001**
at week 8, mg	20.0 [17.0–27.0]	15.0 [4.0–20.0]	20.0 [17.5–27.0]	< 0.001**
at week 12, mg	17.5 [12.5–20.0]	7.5 [2.0–15.0]	17.5 [12.5–20.0]	< 0.001**
at week 16, mg	15.0 [10.0–17.5]	5.0 [0–10.0]	15.0 [10.0–17.5]	< 0.001**
at week 20, mg	12.5 [9.0–15.0]	2.5 [0–7.3]	12.5 [10.0–15.0]	< 0.001**
at week 24, mg	10.0 [8.0–14.0]	1.0 [0–5.0]	10.0 [8.0–14.0]	< 0.001**
at week 48, mg	7.0 [5.0–9.0]	0 [0–0]	7.0 [5.0–10.0]	< 0.001**
Treatment up to week 24				
Induction therapy (RTX / IVCYC)				
Both RTX and IVCYC, n (%)	19 (3.5)	0 (0)	19 (3.7)	0.616
RTX without IVCYC, n (%)	142 (26.1)	18 (62.1)	124 (24.1)	< 0.001**
IVCYC without RTX, n (%)	198 (36.4)	4 (13.8)	194 (37.7)	0.009**
Neither RTX nor IVCYC, n (%)	185 (34.0)	7 (24.1)	178 (34.6)	0.315
Other immunosuppressive agents				
AZA, n (%)	182 (33.5)	5 (17.2)	177 (34.4)	0.068
MTX, n (%)	20 (3.7)	1 (3.5)	19 (3.7)	1.000
Adjunctive therapy				
Methylprednisolone pulse, n (%)	177 (32.5)	2 (6.9)	175 (34.0)	0.002**
PLEX, n (%)	29 (5.3)	0 (0)	29 (5.6)	0.391
Avacopan, n (%)	15 (2.8)	6 (20.7)	9 (1.8)	< 0.001**
Treatment from week 24 to 48				
Maintenance therapy				
RTX, n (%)	71 (13.1)	7 (24.1)	64 (12.4)	0.085
AZA, n (%)	222 (40.8)	7 (24.1)	215 (41.8)	0.079
MTX, n (%)	29 (5.3)	1 (3.5)	28 (5.4)	1.000
Adjunctive therapy				
Avacopan, n (%)	10 (1.8)	4 (13.8)	6 (1.2)	0.001**
Outcomes up to week 48				
Death or Major relapse, n (%)	0 (0)	0 (0)	0 (0)	-
Minor relapse, n (%)	31 (5.7)	0 (0)	31 (6.0)	0.399
Severe infection, n (%)	41 (7.5)	0 (0)	41 (8.0)	0.156

Data are presented as median [IQR] or as n (%), unless otherwise indicated. GFCR, glucocorticoid-free clinical remission; GC, glucocorticoid; RTX, rituximab; IVCYC, intravenous cyclophosphamide; AZA, azathioprine; MMF, mycophenolate mofetil; MTX, methotrexate; MZR, mizoribine. For statistical analyses, $^{*}p < 0.05$, $^{**}p < 0.01$. *P*-value: Wilcoxon rank sum test, Fisher's exact test.

Figure 2. Comparison of treatment details and outcomes up to week 48 between patients with and without GFCR at week 48

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Factors	Univariable analysis		Multivariable models†		Multivariable models‡	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age	1.00 (0.97 to 1.03)	0.798				
Female	0.81 (0.38 to 1.71)	0.577				
MPA	1.79 (0.67 to 4.79)	0.245				
MPO-ANCA positive	4.26 (0.57 to 31.82)	0.158			3.86 (0.50 to 29.9)	0.196
BVAS	1.01 (0.96 to 1.06)	0.758				
Organ involvement (BVAS ≥ 1) †						
General	0.86 (0.39 to 1.90)	0.716				
Cutaneous	1.35 (0.56 to 3.26)	0.499				
Mucous Membranes or eyes	0.83 (0.24 to 2.81)	0.762				
Ear, nose, and throat	1.12 (0.50 to 2.51)	0.791				
Chest	1.33 (0.63 to 2.81)	0.458				
Renal	1.34 (0.56 to 3.20)	0.51				
Nervous system	0.86 (0.36 to 2.06)	0.736				
Laboratory data at diagnosis						
S-albumin, mg/dL	0.82 (0.46 to 1.46)	0.499				
eGFR, ml/min/1.73m^2	1.00 (0.98 to 1.01)	0.582				
CRP, mg/dL	0.98 (0.93 to 1.04)	0.545				
Treatment up to 24 weeks						
RTX without IVCYC	5.16 (2.37 to 11.22)	< 0.001**	4.02 (1.56 to 10.38)	0.004**	3.59 (1.29 to 10.02)	0.015*
IVCYC without RTX	0.26 (0.09 to 0.77)	0.015*	0.61 (0.16 to 2.30)	0.469	0.67 (0.17 to 2.60)	0.562
Neither RTX nor IVCYC	0.60 (0.25 to 1.44)	0.253				
Methylprednisolone pulse	0.14 (0.03 to 0.61)	0.009**	0.08 (0.02 to 0.44)	0.004**	0.08 (0.02 to 0.44)	0.003**
Avacopan	14.67 (4.81 to 44.70)	< 0.001**	14.6 (1.63 to 130.62)	0.017*	13.0 (1.43 to 118.5)	0.023*
Treatment from 24 to 48 weeks						
RTX	2.24 (0.92 to 5.46)	0.075			1.18 (0.39 to 3.54)	0.768
AZA	0.44 (0.19 to 1.06)	0.067			0.67 (0.24 to 1.86)	0.446
Avacopan	13.6 (3.60 to 51.2)	< 0.001**	2.22 (0.16 to 30.04)	0.548	2.44 (0.18 to 34.0)	0.507

Logistic regression models were applied for univariate and multivariate analysis.
† P-values are from a multivariable logistic regression model including factors with p-values < 0.05 in univariable analysis.
‡ P-values are from a multivariable logistic regression model including factors with p-values < 0.20 in univariable analysis.
MPA, microscopic polyangiitis; MPO, anti-myeloperoxidase; ANCA, anti-neutrophil cytoplasmic antibody; BVAS, Birmingham Vasculitis Activity Score; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; RTX, rituximab; IVCYC, intravenous cyclophosphamide; AZA, azathioprine.
For statistical analyses, *p < 0.05, **p < 0.01.

Figure 3. Univariable and multivariable logistic regression analyses for predictors of GFCR at week 48

GFCR at week 48 were more likely to maintain GFCR at week 96 (58.6% vs. 4.5%, p < 0.001). Between weeks 48 and 96, the rates of death, relapse, and serious infection were similar regardless of GFCR status at week 48.

Conclusion: In this real-world cohort, the use of RTX and avacopan was independently associated with achieving GFCR at week 48, supporting their role in GC-sparing therapeutic strategies for AAV. Prospective studies are needed to validate these findings and guide individualized treatment approaches.

Disclosure: Y. Ushio: None; **S. Omura**: Janssen, 6, UCB, 6; **D. Nakagomi**: None; **Y. Abe**: None; **M. Wada**: None; **N. Takizawa**: None; **A. Nomura**: None; **Y. Kukida**: None; **N. Kondo**: None; **H. Takagi**: None; **K. Endo**: None; **S. Hirata**: AbbVie/Abbott, 6, Asahi-Kasei Pharma, 5, 6, Astellas, 6, AstraZeneca, 6, Ayumi, 6, Boehringer-Ingelheim, 6, Bristol-Myers Squibb(BMS), 6, Chugai, 5, 6, Daiichi-Sankyo, 6, Eisai, 1, 6, Eli Lilly, 6, Gilead, 6, GlaxoSmithKlein(-GSK), 6, Janssen, 6, Nihon-Shinyaku, 6, Novartis, 6, Otsuka Pharmaceutical, 5, 6, Pfizer, 6, Sandoz, 6, Taisho, 5, 6, Tanabe-Mitsubishi, 6, UCB, 6; **N. Azuma**: Asahi-Kasei Pharma, 5, 6, Eli Lilly, 5, 6; **T. Takeuchi**: None; **S. Fukui**: None; **K. Kamada**: None; **R. Yanai**: None; **Y. Matsuo**: None; **Y. Shimojima**: None; **R. Nishioka**: None; **R. Okazaki**: None; **T. Takata**: None; **M. Moriyama**: None; **A. Takatani**: None; **Y. Miyawaki**: None; **T. Shirai**: AbbVie/Abbott, 6, Asahi Kasei, 6, Astellas, 6, AstraZeneca, 6, Chugai, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Novartis, 6, Pfizer, 6, Sanofi, 6; **T. Ito**: None; **I. Matsumoto**: None; **T. Takada**: None; **T. Ito-Ihara**: None; **T. Kida**: None; **N. Yajima**: None; **T. Kawaguchi**: None; **Y. Kawahito**: None; **H. Dobashi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2524

Rituximab in the Treatment of Susac Syndrome: Single Center Descriptive Study with a Large Susac Cohort

Adam Brown[1], Leonard Calabrese[2] and Rula Hajj-Ali[3], [1]Cleveland Clinic, Shaker Heights, OH, [2]Cleveland Clinic, Cleveland, OH, [3]Cleveland Clinic, Cleveland

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Susac Syndrome is a rare autoimmune condition causing microvascular occlusions in the brain, retina and inner ear leading to the characteristic triad of encephalopathy, branch retinal artery occlusion (BRAO), and sensorineural hearing loss, potentially leading to permanent disability and death if untreated. Approximately 400 cases of Susac Syndrome have been reported since its initial description in the 1970s. Only a handful of cases of Rituximab use in Susac Syndrome have been reported in the literature. The goal of this descriptive study is to highlight our experience with Rituximab from one of the largest cohorts of Susac Syndrome in the world.

Methods: A retrospective chart review of sixty-eight patient meeting the European Susac Consortium criteria was performed identifying all patients treated with Rituximab. The following were recorded: patient demographics, presenting signs/symptoms, whether the full triad of encephalopathy, vision and hearing loss were present, as well as immunosuppressive medications initiated, length of follow up and whether a patient had a flare while on immunosuppression. Rituximab initiation was divided into induction and rescue therapy. Rituximab was considered an induction therapy if it was given when Susac Syndrome was first diagnosed and rescue therapy if it was used after a patient flared while on another immunosuppressive agent. Flares were defined by objective changes in brain MRI, fluorescein angiography or audiometry in addition to clinical symptoms. Flares were considered to have occurred during maintenance therapy if the flare occurred after three months from the first infusion of Rituximab.

Results: Rituximab was used as either induction or rescue therapy in forty patients (58%) within the Susac Syndrome cohort. Twenty-nine patients (72%) receiving Rituximab had the full triad of Susac present at the time of diagnosis. Twenty-eight patients (70%) on Rituximab were followed at least twelve months. Rituximab was utilized either as monotherapy or in combination with other therapeutics such as IVIG or Mycophenolate Mofetil (MMF). Rituximab was used for induction therapy in nineteen patients and rescue therapy in twenty patients. Three patients out of forty flared (7%) while on Rituximab, all were on maintenance therapy at the time of the flare (3/29 flared when isolating to only those patients followed for at least a year (11%)). Flares were a mix of ocular (2) and brain (1). One patient flared while on Rituximab as monotherapy, another was on a combination with MMF 1,000 mg and another on IVIG. The average length of follow up was 3.5 years.

Conclusion: This is the largest cohort of patients with Susac Syndrome treated with Rituximab. The majority of patients did well with only three (7%) flaring while on Rituximab. In the literature, the triad of Susac Syndrome is present in less than twenty percent of patients. In our cohort of patients on Rituximab, the triad was present in seventy-two percent of patients at diagnosis indicating more serious disease. Rituximab has been utilized for multiple decades and considered a well-tolerated therapy, it's use in the treatment for Susac Syndrome should be further explored.

Disclosure: A. Brown: AbbVie/Abbott, 2, Amgen, 2, Sanofi, 2; **L. Calabrese**: AbbVie, 2, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, Fate Therapeutics, 2, Galvani, 2, Genentech, 2, GlaxoSmithKlein(GSK), 2, Janssen,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2, 6, Mymee, 2, Open Evidence, 2, PPD, 2, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6; **R. Hajj-Ali**: AbbVie/Abbott, 2, Amgen, 2, UpToDate, 9.

Abstract Number: 2525

Point-of-Care Risk Factors for Systemic Disease in Patients Presenting with Small Vessel Vasculitis of the Skin

Arjun Mahajan[1], William Song[2], Andrew Walls[3], Arash Mostaghimi[3], Robert Micheletti[2] and Evan Piette[3], [1]Harvard Medical School, Boston, [2]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [3]Brigham and Women's Hospital, Harvard Medical School, Boston

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Table 1. Point-of-Care Risk Factors Associated with Systemic Disease in Patients with SVV of the Skin

	Univariate Analysis		Multivariate Analysis	
Variable	Odds Ratio (95% CI)	P-Value	Odds Ratio (95% CI)	P-Value
Nausea/vomiting	4.507 (2.060 - 9.861)	<0.001	**3.920 (1.580 - 9.770)**	0.003
Fatigue/malaise/lethargy	2.989 (1.627 - 5.491)	<0.001	**2.610 (1.280 - 5.320)**	0.008
Hematuria (dipstick, 3+)#	2.302 (1.303 - 4.069)	0.004	**2.40 (1.23 - 4.68)**	0.010
Ulcerating or necrotic lesions	1.863 (0.817 - 4.251)	0.139	**3.260 (1.240 - 8.590)**	0.017
Abdominal pain/cramping	4.449 (2.220 - 8.914)	<0.001	**2.710 (1.190 - 6.180)**	0.018
Lesions on upper extremities	0.744 (0.464 - 1.195)	0.222	0.590 (0.340 - 1.030)	0.065
Antibiotic use (up to 2 weeks preceding)‡	0.461 (0.280 - 0.758)	0.002	0.580 (0.320 - 1.020)	0.060
Age	0.735 (0.580 - 0.931)	0.011	0.780 (0.590 - 1.030)	0.080
Shortness of breath	1.800 (0.875 - 3.704)	0.110	1.990 (0.890 - 4.460)	0.094
Skin pain	0.683 (0.342 - 1.362)	0.279	0.520 (0.230 - 1.170)	0.112
Lesions on the legs that extend on to buttocks or above the waist on to the trunk	1.352 (0.839 - 2.180)	0.215	1.560 (0.900 - 2.710)	0.114
Fever	0.951 (0.549 - 1.645)	0.857	0.650 (0.330 - 1.250)	0.194
Joint pain (arthritis or arthralgia)	2.540 (1.487 - 4.339)	<0.001	1.520 (0.800 - 2.870)	0.200
Proteinuria (dipstick, trace)#	1.390 (0.739 - 2.614)	0.306	1.60 (0.78 - 3.28)	0.199
Female sex	1.045 (0.651 - 1.678)	0.854	0.830 (0.490 - 1.420)	0.501
Proteinuria (dipstick, 3+)#	2.799 (1.196 - 6.554)	0.018	---	---
Gross hematuria	6.089 (1.001 - 37.025)	0.050	---	---
Diarrhea	2.213 (0.951 - 5.150)	0.065	---	---
Paresthesias/pins and needles, numbness	3.258 (0.856 - 12.399)	0.083	---	---
Proteinuria (dipstick, 2+)#	1.672 (0.829 - 3.372)	0.151	---	---
Unexplained weight loss	2.030 (0.676 - 6.102)	0.207	---	---
Anorexia/loss of appetite	2.414 (0.566 - 10.304)	0.234	---	---
Sore throat	0.295 (0.038 - 2.288)	0.243	---	---
Cough/wheeze	1.478 (0.634 - 3.443)	0.366	---	---
Headache	0.387 (0.049 - 3.066)	0.369	---	---
Nasal symptoms (runny/stuffy nose, sinus pain)	0.432 (0.054 - 3.453)	0.428	---	---
Proteinuria (dipstick, 1+)#	0.799 (0.429 - 1.489)	0.480	---	---
Hematuria (dipstick, 1+)#	0.784 (0.350 - 1.757)	0.554	---	---
Pruritus	0.844 (0.475 - 1.500)	0.563	---	---
Tarry stools/melena	1.983 (0.178 - 22.120)	0.578	---	---
Illicit drug use (excluding marijuana)	1.591 (0.303 - 8.340)	0.583	---	---
Chest pain	1.591 (0.303 - 8.340)	0.583	---	---
Viral syndrome (up to one month prior)	1.322 (0.262 - 6.664)	0.736	---	---
Pneumonia (up to one month prior)	0.870 (0.287 - 2.640)	0.806	---	---
Night sweats	0.786 (0.091 - 6.816)	0.827	---	---
Hematuria (dipstick, 2+)#	0.959 (0.482 - 1.909)	0.906	---	---
Sore throat (up to one month prior)	1.078 (0.294 - 3.951)	0.910	---	---
Hematuria (dipstick, trace)#	0.972 (0.406 - 2.325)	0.949	---	---
URI (up to one month prior)	1.024 (0.430 - 2.436)	0.957	---	---
Limb weakness	0.985 (0.109 - 8.930)	0.990	---	---

Analyses are of the full 430 patient cohort with complete clinical and no urinalysis data, unless otherwise noted.

Results from univariate and multivariate analysis of subset cohort with urinalysis data (n=388), see Supplement 1

‡ Variable with differing statistical significance in multivariate analysis of sub-cohort with urinalysis data, see Supplement 1

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Small vessel vasculitis (SVV) presenting in the skin may be skin-limited or a manifestation of systemic vasculitis or an underlying autoimmune disease. However, no evidence-based protocols exist to identify patients at risk for systemic involvement. This study aimed to identify clinical features present at the time of initial evaluation that predict systemic disease in patients with SVV of the skin, to support early risk stratification and management.

Methods: This multi-center case-control study included 430 adults with biopsy-confirmed SVV of the skin, identified from pathology databases at Massachusetts General Hospital, Brigham and Women's Hospital, and the Hospital of the University of Pennsylvania. In accordance with Chapel Hill consensus criteria, cases were considered to have systemic disease if the SVV was associated with systemic vasculitis or connective tissue disease, or if the SVV caused objective organ dysfunction. Demographic, clinical, and laboratory features at initial presentation were assessed.[1] Univariate and multivariate logistic regression analyses were performed to estimate odds ratios (ORs) and 95% confidence intervals (CIs), with variable selection guided by elastic net regression and 10-fold cross-validation. Significance was set at $P < 0.05$.

Results: Among 430 patients (mean [SD] age, 55 [17.7] years; 55.5% male), 87 had systemic disease and 343 had skin-limited SVV. Multivariate analysis identified nausea/vomiting (OR 3.92; 95% CI 1.58–9.77), ulcerating or necrotic skin lesions (OR 3.26; 95% CI 1.24–8.59), abdominal pain/cramping (OR 2.71; 95% CI 1.19–6.18), and fatigue/malaise/lethargy (OR 2.61; 95% CI 1.28–5.32) as significantly associated with systemic disease. In a subset with urinalysis data (n=388), dipstick hematuria (3+) was associated (OR 2.40; 95% CI 1.23–4.68) and recent antibiotic use was inversely associated (OR 0.54; 95% CI 0.29–0.98) with systemic disease. Joint pain (OR 2.54; 95% CI 1.49–4.34) and younger age (OR 0.74 per SD increase; 95% CI 0.58–0.93) were associated in univariate but not multivariate analysis.

Conclusion: In this multi-institutional study of biopsy-proven SVV, we identified constitutional and gastrointestinal symptoms, necrotic or ulcerating lesions, and dipstick hematuria (3+) as predictors of systemic involvement. These point-of-care features may aid in identifying high-risk patients requiring further evaluation and closer monitoring.

Disclosure: A. Mahajan: None; **W. Song**: None; **A. Walls**: None; **A. Mostaghimi**: None; **R. Micheletti**: Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Cabaletta Bio, 2, 5, 6, InflaRx, 2, 5, 6, Vertex, 2, 5, 6; **E. Piette**: None.

Abstract Number: 2526

Infection Risk Associated with Steroid-Sparing Therapies in GCA, PMR, and ANCA-Associated Vasculitis: A Systematic Review

Divya Sudireddy[1], Brent Leung[2], Jean Liew[3], Tuhina Neogi[4], David Felson[3], Michael LaValley[5] and David Flynn[2], [1]Boston Medical Center, Westborough, MA, [2]Boston University, Boston, [3]Boston University, Boston, MA, [4]Boston University School of Medicine, Boston, MA, [5]Boston University School of Public Health, Arlington, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Giant cell arteritis (GCA), polymyalgia rheumatica (PMR), and ANCA-associated vasculitis (AAV) often require long-term glucocorticoid (GC) therapy, increasing the risk of infections, particularly in older adults with GCA and PMR. Biologics and small molecule therapies are increasingly used to reduce GC exposure but may also increase infection risk through immunosuppression. This systematic review aimed to evaluate the infection risk associated with these therapies along with concomitant GC treatment, as compared to GC treatment alone, in vasculitis clinical trials.

Methods: A comprehensive search of PubMed, Embase, and Cochrane, supplemented by ClinicalTrials.gov was conducted using terms related to GCA, PMR, AAV, biologic therapies (tocilizumab, sarilumab), small molecule therapies (upadacitinib, avacopan), glucocorticoids, and infections. We included randomized controlled trials (RCTs) published in English comparing biologics or small molecules with concomitant GC dosing (active intervention) compared to GC monotherapy (comparator), and reporting infection outcomes. Two independent reviewers screened titles and abstracts, conducted full-text reviews, and extracted data, including study characteristics, details about the intervention and comparator, mean cumulative glucocorticoid use, and overall infection outcomes. We calculated the difference in GC dose between the comparator and active intervention groups and relative risk of infection (active intervention versus comparator group).

Results: The initial search yielded 1,154 studies (Figure 1). We included 10 eligible phase II or III RCTs (1,487 patients total; Table 1). 4 trials evaluated tocilizumab, 2 sarilumab, 1 upadacitinib, and 3 avacopan among patients with GCA, PMR and AAV. All studies reported infection outcomes and included populations with mean age ≥50 years. Follow-up durations ranged from 6 to 18 months. Despite steroid-sparing protocols, cumulative GC use was greater than anticipated in both intervention and comparator groups. In most trials, the intervention group had lower cumulative GC exposure than the comparator group. The frequency of infection varied. When the comparators had much higher GC dosing than the active intervention, the RR for infection was either close to 1 or < 1 (Figure 2). When the active intervention GC dose was comparable to the comparator dose, the RR for infection was >1.

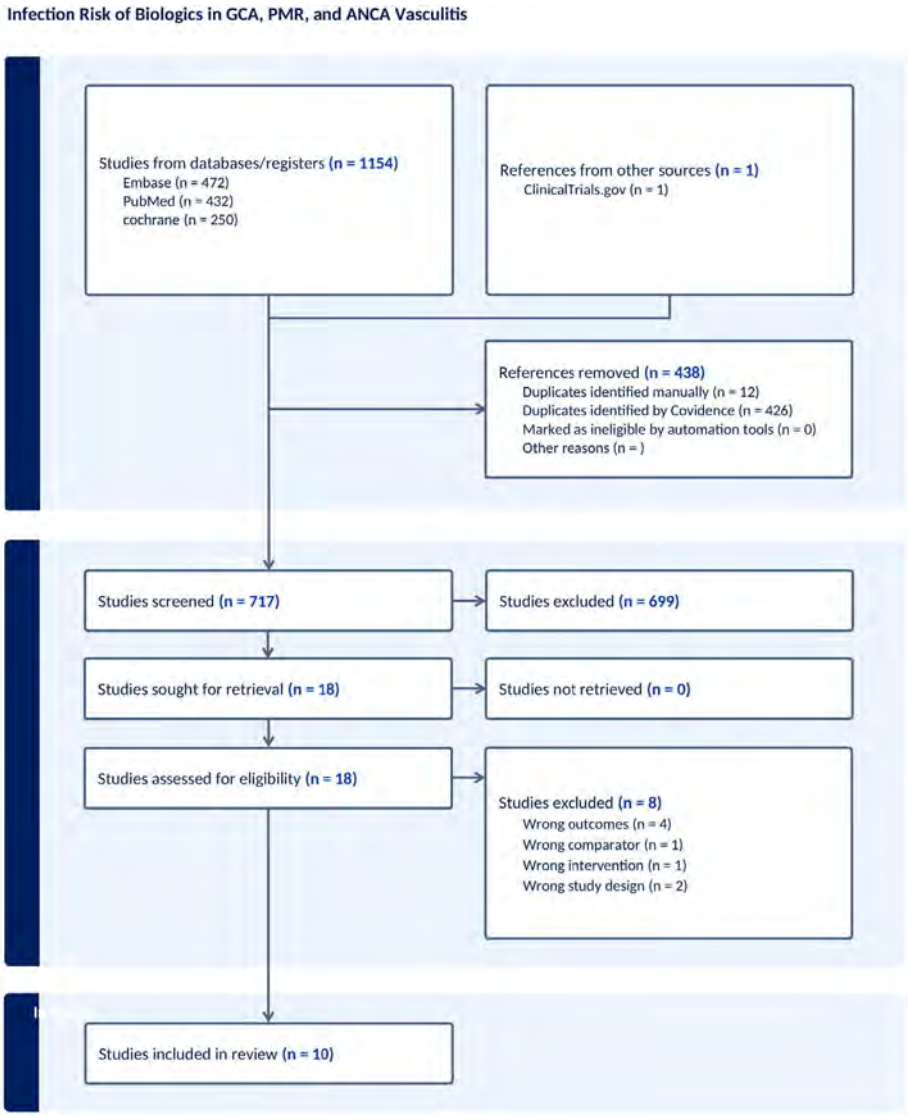


Figure 1. PRISMA flow diagram of study inclusion and exclusion

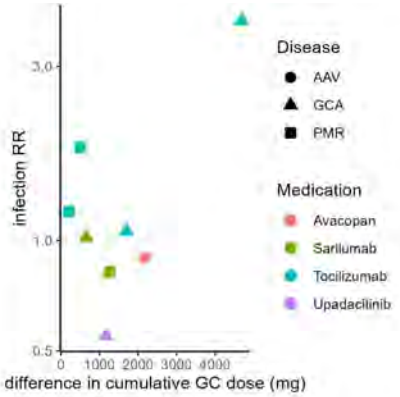
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of included studies, including glucocorticoid exposure and infection outcomes by intervention versus comparator arms

Disease	Trial	Trial Year	Intervention/ Comparator	Dose	Sample Size	Mean age, % female	Cumulative GC dose	% infections	Trial duration
GCA	1	2016	Tocilizumab	8mg/kg q 4 w	20	68; 56%	43 mg/kg	40	52 weeks
			Placebo	Q 4 w	10	67; 58%	110 mg/kg	10	
	2	2017	Tocilizumab	162 mg q w	100	69.5; 78%	1862 mg	75	52 weeks
			Tocilizumab	162 mg q 2 w	50	69.4; 70%	1862 mg	73	
			Placebo	Weekly	50	69.3; 76%	3296 mg	76	
			Placebo	Weekly	51	67.8; 73%	3818 mg	65	
	3 **	2023	Sarilumab	200 mg q 2 w	27	73.4; 85%	1643.1 mg	7	52 weeks + 24 week follow up phase
			Sarilumab	150 mg q 2 w	14	67.1; 93%	2177.1 mg	0	
			Placebo	Q 2 w	28	71.4; 79%	2577.3 mg	3.5	
			Placebo	Q 2 w	14	69.5; 64%	2270.7 mg	7	
	4 **	2025	Upadacitinib	15 mg daily	209	70.8; 74.6%	1615 mg	5.7	52 weeks
			Upadacitinib	7.5 mg daily	107	71; 74.8%	1905 mg	5.6	
			Placebo	daily	112	71.6; 68.8%	2882 mg	10.7	
PMR	5	2022	Tocilizumab	8mg/kg q 4w	49	68; 69.4%	1380 mg	46.9	24 weeks
			Placebo	Q 4 w	51	67; 64.7%	1591 mg	39.2	
	6	2022	Tocilizumab	162 mg q w	19	68.8; 52.6%	781 mg	63	24 weeks
			Placebo	weekly	17	71; 52.9%	1290 mg	35	
	7	2023	Sarilumab	200mg q 2 w	60	69; 75%	777 mg	8.4 *	52 weeks
			Placebo	Q 2 w	58	70; 63.8%	2044 mg	10.3 *	
ANCA	8 **	2017	Avacopan	30 mg BID	22	57; 36.36%	NR	4	24 weeks
			Avacopan	30 mg BID	22	57.4;27.27%	NR	4	
			Placebo/Pred	BID	23	59.1;26.09%	NR	4.3	
	9	2020	Avacopan	10 mg BID	13	60; 38%	NR	24	12 weeks
			Avacopan	30 mg BID	16	55.3; 56%	NR		
			Placebo	BID	13	58.5; 69%	NR	15	
	10	2021	Avacopan	30 mg BID	166	61.2; 41%	1675.5 mg	68.1	52 weeks
			Prednisone	Weight based taper	165	60.5; 46.3%	3846.9 mg	75.6	

** These studies only reported serious infections
* These studies reported number of events

Q = every
BID = twice daily
NR = Data not reported



Abbreviations: AAV, ANCA associated vasculitis; GCA, giant cell arteritis; PMR, polymyalgia rheumatic; RR, risk ratio; GC, glucocorticoid

Infection RR is the risk of infection for the active intervention versus the comparator

The difference in cumulative GC dosing is the difference for the comparator group minus the active intervention group

Figure 2: Infection risk ratios versus difference in mean cumulative glucocorticoid dosing between active intervention and comparator

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Although biologics and small molecules had lower overall cumulative GC exposure, they did not consistently lead to a lower infection risk. When GC exposure was notably higher in the comparator group, infection risk was lower in the intervention group suggesting a possible protective effect of reducing GC. However, when GC doses were more comparable between groups, infection risk was higher in the active intervention arm, likely due to the immunosuppressive effects of combining biologic and small molecules with GC. These findings emphasize the importance of carefully considering infection risk in the management of patients, particularly in older adult populations.

Disclosure: D. Sudireddy: None; **B. Leung**: None; **J. Liew**: None; **T. Neogi**: None; **D. Felson**: None; **M. LaValley**: None; **D. Flynn**: None.

Abstract Number: 2527

Safety Profile and Impaired Humoral Response to the Recombinant Herpes Zoster Vaccine in Behçet's Syndrome Patients under Immunosuppression: a Prospective, Randomized, Placebo-Controlled Trial

Eduardo Borba[1], Caio Carvalho[2], Nadia E Aikawa[3], Ana C Medeiros-Ribeiro[2], Sandra G Pasoto[2], Carla Saad[4], Henrique Giardini[5], Thiago Freitas[5], Rafael Cordeiro[6], Eloisa Bonfa[1] and Clovis Artur Silva[7], [1]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [3]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas HCFMUSP, Sao Paulo, Brazil., Sao Paulo, Sao Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Sao Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [6]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil, [7]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Although rare, new-onset Behçet's syndrome (BS) and disease flares have been reported following vaccination. In this context, the recommendation of the Recombinant Herpes Zoster Vaccine (RVZ) for immunosuppressed patients raises important questions regarding its safety and immunogenicity in BS under immunosuppressive (IS) therapy.

Methods: This prospective, randomized, placebo-controlled, single-center trial included 46 BS patients under IS, randomized 1:1 into: P1 (RZV) and P2 (placebo) groups. A healthy control group (CG) of 138 subjects was included at a 3:1 ratio and age-paired to BS patients (±3 years for patients ≥50 years; 50–55 years for BS patients < 50 years). P1 and CG received two intramuscular RZV doses on D0 and D42, while P2 received placebo. At D84, blinding was opened and P2 received RZV following the same schedule. Blood samples were collected at baseline and 6-weeks after the second dose. Humoral immunogenicity was assessed by ELISA for anti-gE antibodies, with a positive response defined as a ≥4-fold increase above the baseline level. Geometric mean titers (GMTs) and factor increase (FI) were calculated. Local and systemic side-effects were recorded in a diary after RZV for both groups. BS patients recorded new oral/genital ulcers and disease activity was assessed at each visit with the Behçet's Disease Current Activity Form (BDCAF).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: BS patients were younger than controls [41(18–62) *vs*. 52(50–63)years, p=0.001], with 82.6% aged< 50 years *vs*. 100% of controls aged≥50 years (p=0.001).Percentage of female gender was lower in BS (39.1% *vs*. 65%;p=0.002).BS patients were using: azathioprine (54%), prednisone (37%), tumor necrosis factor inhibitors (30%), mycophenolate mofetil (22%), colchicine (13%), methotrexate (11%), tocilizumab (4%), cyclosporine (4%). Seroconversion was achieved by all BS patients (100%) and 99.3% of CG (p >0.999). A significant increase of GMT from baseline was observed in BS [0.12 (0.08-0.18) *vs*. 7.96(5.76-11.0), p< 0.001) and in CG [0.25(0.20-0.30) *vs*. 13.32(11.98-14.82), p< 0.001]. The increase in GMT of BS was lower than CG (7.96 *vs*. 13.32, p=0.02). FI in GMT was similar in BS and CG [66.3(41.0-107.2) *vs*. 53.8 (43.3-66.8), p=0.316]. Demographics and current therapy (including biologics and IS) did not influence antibody titers (p >0.05). Higher local (92% *vs*. 80.4%, p=0.028) and systemic (78% *vs*. 60.8%, p=0.0147) reactions were observed in CG compared to BS. Regarding disease safety, no significant differences in the percentage of new oral (p=0.622) and genital (p=0.608) ulcers, or in BDCAF scores (p=0.787) were observed.

Conclusion: Our study is the first to demonstrate that RVZ appears safe in immunosuppressed BS patients, without evidence of flares using standardized measures. Despite the universal vaccine response in younger BS, antibody titers were lower than in older healthy controls, who would normally predict a weaker response. Further studies are necessary to determine whether the lower antibody levels will compromise long-term protection. (ClinicalTrials NCT05879419).

Disclosure: E. Borba: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **C. Carvalho**: None; **N. Aikawa**: GlaxoSmithKlein(GSK), 5; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **C. Saad**: GlaxoSmithKlein(GSK), 5; **H. Giardini**: None; **T. Freitas**: None; **R. Cordeiro**: None; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

Abstract Number: 2528

Broad Screening of the Human Proteome Identifies a Cassette of Six Autoantigens that Distinguishes IgG4-Related Disease

Federica Bonaso[1], Zhenrui Zhang[2], Mahilan Guha[3], Ian Doyle[4], Jesse Akaa[4], Grace McMahon[5], Isha Jha[5], Sydney Montesi[5], Thomas Guy[6], Guy Katz[5], Zachary Wallace[7], John Stone[8], Vinay S. Mahajan[9], Shiv Pillai[10] and Cory Perugino[11], [1]University of Brescia, ASST Spedali Civili of Brescia, Massachusetts General Hospital, Monza, Italy, [2]Ragon Institute of Mass General Brigham, MIT, and Harvard, Boston, [3]Montgomery Blair High School, Brigham and Women's Hospital, Boston, [4]Massachusetts General Hospital (MGH - Mass General) (MGB), Boston, MA, [5]Massachusetts General Hospital, Boston, MA, [6]Ragon Institute of MGH, MIT and Harvard/ Royal Prince Alfred Hospital Sydney, Sydney, Australia, [7]Massachusetts General Hospital, Newton, MA, [8]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [9]Brigham and Women's Hospital, Boston, MA, [10]Harvard Medical School, Cambridge, MA, [11]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

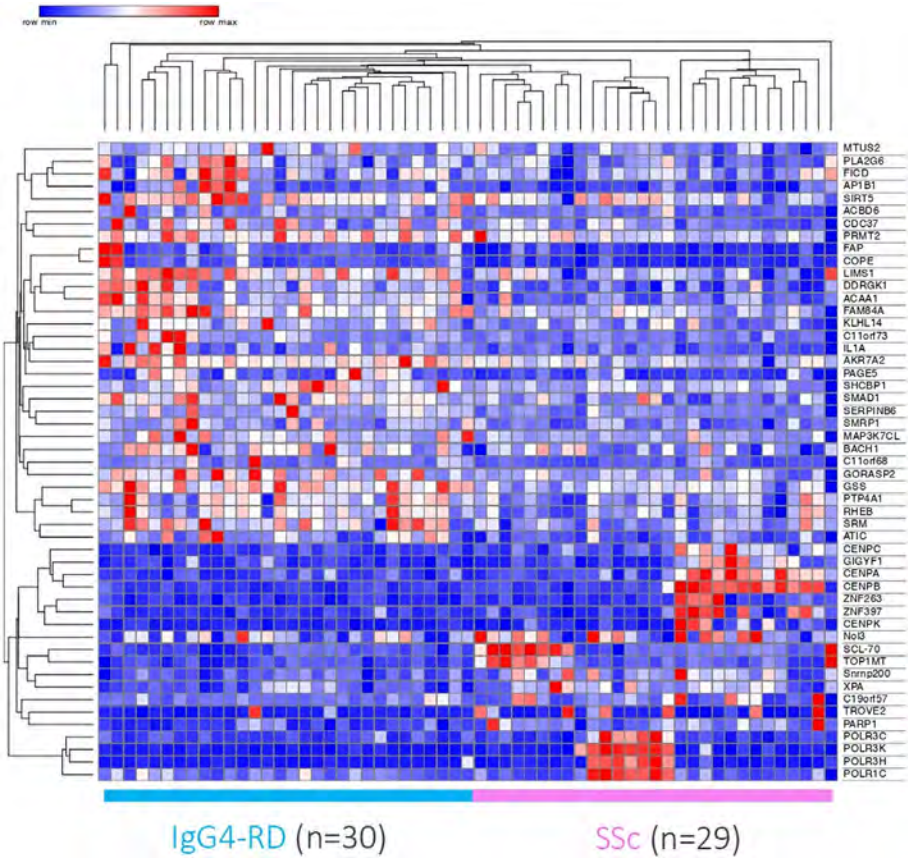


Figure 1. 51 differentially bound self antigens separate IgG4-RD from SSc patients by unsupervised hierarchical clustering. Heatmap with hierarchical clustering of differentially bound autoantigens between IgG4-RD (n=30) and SSc (n=29, 1 SSc patient was excluded.)

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic immune-mediated disease typified by mass-forming lesions. Self-antigens driving the oligoclonal expansion of plasmablasts have previously been reported. However, broad screening of the IgG repertoire from IgG4-RD patients for reactivity across the human proteome has yet to be done. The goal of this study was to identify novel, potentially causal, disease-specific autoantigens by broadly screening the human proteome.

Methods: The HuProt microarray, displaying 21,216 proteins in total, including 15,889 unique human proteins, was used to screen plasma samples from IgG4-RD patients and controls across discovery and validation batches. The discovery batch included IgG4-RD (N=30) and systemic sclerosis (SSc, N=30). The validation batch included IgG4-RD (N=42, 28 of which were not included in the initial batch), idiopathic pulmonary fibrosis (N=20), sarcoidosis (N=20), and healthy donors (N=20). Microarray data was normalized and analyzed for autoantigens selectively bound by IgG4-RD samples after adjusting for false discovery rate. Autoantibodies with frequencies >15% among IgG4-RD were selected for unsupervised hierarchical clustering. A separate analysis focused on the highest titer autoantibodies across cohorts was also conducted. Selected autoantigens were validated using a luciferase immunoprecipitation system (LIPS) assay.

Results: FAM84A and LIMS1 were the two autoantigens that most accurately distinguished IgG4-RD from SSc in the discovery batch, while expected autoantigens distinguished SSc including those against centromeric proteins, RNA polymerase III subunits, and topoisomerase **(Figure 1)**. Anti-FAM84A was present in 9/30 (30%) and anti-LIMS1 in 6/30 (20%) of the IgG4-RD cohort versus 0% in SSc and 1/30 (3%), respectively. The validation batch confirmed the presence of FAM84A and LIMS1 autoantibodies and identified four additional proteins to form a cassette of 6 autoantigens distinguishing IgG4-RD from HD. The additional four autoantigens included CCDC97, MAGEE1, ISM2 and SCG2. The nine anti-FAM84A samples from the discovery batch were reproducibly reactive to FAM84A in the validation batch. After excluding all

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

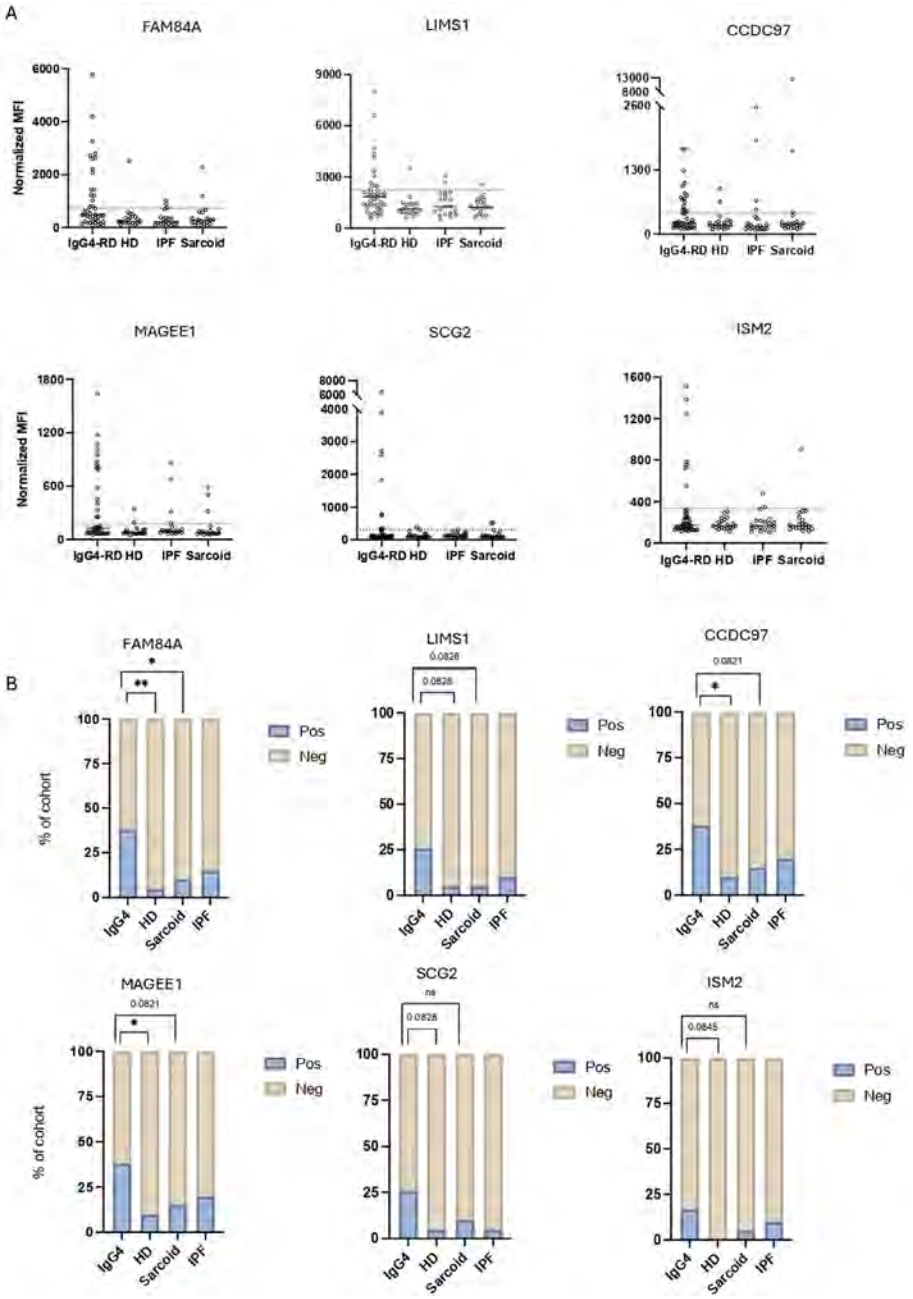


Figure 2 Granularly selected cassette of 6 autoantigens distinguish IgG4-RD patients (n=42) from healthy donors (n=20), IPF (n=20) and Sarcoidosis (n=20). (A) Dot plots showing normalized mean flourescent intensity (MFI) values for each selected autoantibody, dotted red line represents cutoff value computed based on healthy donor cohort by the 1.5*interquartaile range (IQR) rule. (B) Bar charts representing % of subjects in each cohort with MFI values for each selected autoantigen that is above the cutoff described in Figure 1A. P value comparing frequencies between IgG4-RD with healthy donors and sarcoidosis patients was computed by Fisher's exact test. Symbols: ns p value >0.05, *p ≤0.05, ** p≤ 0.01, *** p≤0.001, **** p≤0.0001.

overlapping samples between batches, frequencies of these autoantibodies were 7/28 (25%), 7/28 (25%), 14/28 (50%), 12/28 (43%), 7/28 (25%) and 5/28 (18%), respectively **(Figure 2)**. Reactivity to at least one of these 6 autoantigens was observed in 35 of the 42 (83%) IgG4-RD patients and the IgG4-RD cohort additionally clustered into three distinct groups based on antigen specificity **(Figure 3)**. Analysis focused on the highest titer autoantibodies identified ANXA11, as has been previously reported, and FAM84A. ANXA11 and FAM84A were validated by LIPS, with anti-FAM84A responses observed in 12% (23 of 192) of IgG4-RD patients and anti-ANXA11 in 12.5% (24 of 192). Anti-FAM84A patients showed enrichment for Mikulicz phenotype while anti-ANXA11 was linked to pancreatobiliary involvement.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

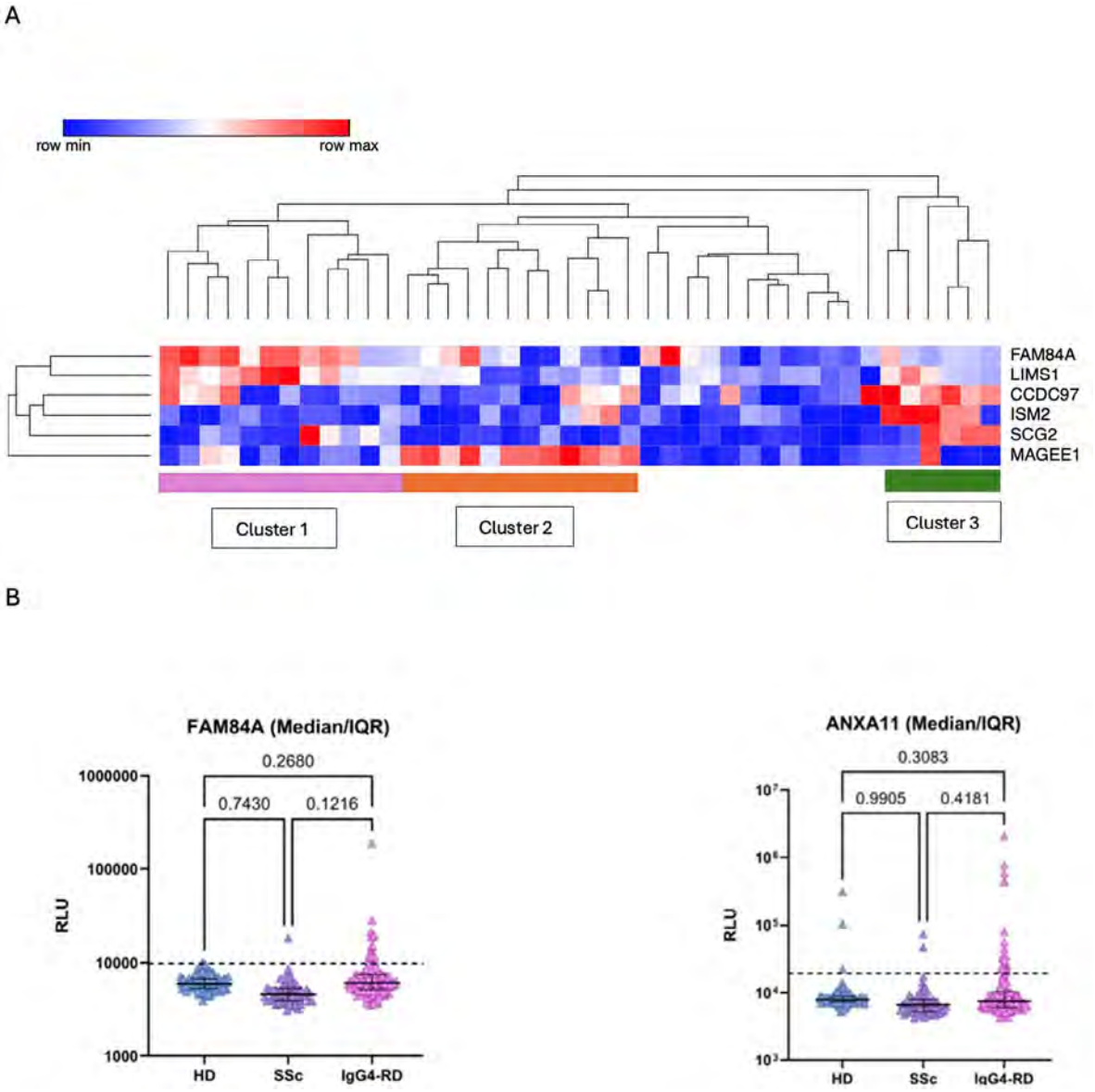


Figure 3. The casette of 6 novel autoantigens segregates the IgG4-RD cohort into 3 clusters and enrich for specific organd manifestations. (A) Heatmap with hierarchical clustering depicting the 6 selected autoantigens in the validation batch . Three main clusters are identified by the unsupervised clustering. (B) Dot plot showing relative light unit (RLU) values from LIPS assay validating FAM84A in a larger cohort IgG4-RD (n=192) compared to healthy donors (n=121) and SSc (n=56). Dashed line represents the cutoff based on mean + 3*standard deviations of the healthy donor cohort. P values were computed with Mann-Whitney U test. Among FAM84A positive IgG4-RD patients, 52% showed lacrimal gland involvement and 39% showed parotid gland involvement. Among ANXA11 positive IgG4-RD patients 70% showed pancreatic involvement.

Conclusion: The novel cassette of 6 autoantigens including FAM84A, LIMS1, CCDC97, MAGEE1, ISM2, and SCG2 distinguished IgG4-RD from controls. Further efforts to validate these findings are needed.

Disclosure: F. Bonaso: None; **Z. Zhang**: None; **M. Guha**: None; **I. Doyle**: None; **J. Akaa**: None; **G. McMahon**: None; **I. Jha**: None; **S. Montesi**: Accendatech USA, 2, Boehringer-Ingelheim, 5, Mediar Therapeutics, 1, 2, Pliant Therapeutics, 5, Wolters Kluwer, 9; **T. Guy**: None; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **Z. Wallace**: Amgen, 3; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **V. Mahajan**: None; **S. Pillai**: Abpro Inc, 4, BeBio, 4, Octagon Therapeutics, 4, Paratus Biosciences, 2; **C. Perugino**: Acepodia, 2, Amgen, 1, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Zenas Biopharma, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2529

IgG4-Related Disease Paravertebral and Ureteropelvic Mass Presentations are Linked to Specific Disease Features

Federica Bonaso[1], Grace McMahon[2], Isha Jha[2], Guy Katz[2], Zachary Wallace[3], John Stone[4] and Cory Perugino[5], [1]University of Brescia, ASST Spedali Civili of Brescia, Massachusetts General Hospital, Monza, Italy, [2]Massachusetts General Hospital, Boston, MA, [3]Massachusetts General Hospital, Newton, MA, [4]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [5]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic immune-mediated disease characterized by mass-forming fibrotic lesions. The aim of this work was to characterize the overall clinical and serological findings of paravertebral (PV) and ureteropelvic junction (UPJ) involvement as two uncommon manifestations that are nevertheless regarded as strongly suggestive of IgG4-RD.

Table 1. Demographics and Laboratory Values for patients with paravertebral (PV) mass, ureteropelvic junction (UPJ) involvement, and remainder of the IgG4-RD cohort. P-values were calculated by comparing the UPJ and PV groups with the remainder of the cohort by applying Mann-Whitney U test for continuous variables, and Fisher's exact test for categorical variables. Statistically significant p-values ($p < 0.05$) are shown in bold.

	Comparison Group: Fulfill ACR/EULAR Classification Criteria but do not have UPJ or PV masses	PV Mass	*P value PV vs. Comparison Group*	UPJ Mass	*P value UPJ vs. Comparison Group*
Demographics					
Subjects – N	382	7		11	
Age at Diagnosis (median, IQR)	61.6 (52.12 – 71.17)	85.1 (58.05 -89.7)	*0.748*	65.4 (59.55 – 75.2)	*0.130*
Age at Diagnosis, N (%)					
<40	38 (9.95)	0 (0)	*>0.999*	0 (0)	*0.610*
40- <50	48 (12.56)	0 (0)	*0.604*	1 (9)	*>0.999*
50- <60	81(21.20)	3 (42.8)	*0.175*	3 (27.3)	*0.708*
60- <70	105 (27.5)	2 (28.6)	*>0.999*	2 (18.2)	*0.734*
≥ 70	110 (28.79)	2 (28.6)	*>0.999*	5 (45.5)	*0.311*
Sex N (%)					
Male	261 (68.33)	7 (100)	*0.104*	10 (90.9)	*0.184*
Female	121 (31.67)	0 (0)	*0.104*	1 (9.1)	*0.184*
Race N (%)					
White	274 (71.73)	4 (57.1)	*0.412*	8 (72.73)	*>0.999*
Asian	52 (13.61)	0 (0)	*0.600*	3 (27.27)	*0.189*
Black or African American	18 (4.71)	1 (14.3)	*0.298*	0 (0)	*>0.999*
Other	38 (9.95)	2 (28.6)	*0.156*	0 (0)	*0.610*
Ethnicity					
Not Hispanic or Latino	308 (80.10)	6 (85.7)	*>0.999*	11 (100)	*0.133*
Hispanic or Latino	47 (12.3)	1 (14.3)	*>0.999*	0 (0)	*0.375*
Unknown or Not Reported	29 (7.6)	0 (0)	*>0.999*	0 (0)	*>0.999*
Laboratory Values – Median (IQR)					
IgG4 (3.9-86.4 mg/dl)	158.6 (67 – 407.5) (N=325)	891 (463.45 – 1785.5) (N=7)	***0.011***	317 (112.7 – 676.1) (N=9)	*0.274*
IgG1 (382.4-928.6 mg/dl)	627.5 (467-861) (N=327)	1045.8 (596.5 – 1229.1) (N=7)	*0.096*	539.7 (417 – 622) (N=9)	*0.308*
IgE (0-100 IU/ml)	127.5 (35-367.75) (N=290)	693 (175 – 949) (N=7)	*0.116*	305 (22-932) (N=9)	*0.341*
C3 (81-157 mg/dl)	120 (97-145) (N=277)	94 (69 -137) (N=7)	*0.301*	111.5 (102-132.75) (N=8)	*0.698*
C4 (12-39 mg/dl)	24 (18-31) (N=279)	22 (9-27.5) (N=7)	*0.374*	22.5 (19-28) (N=8)	*0.762*
Eosinophils (0-8%)	2.65 (1.1-4.925) (N=300)	5.7 (3.65 -9.15) (N=7)	***0.015***	1.6 (0.7-2.7) (N=7)	*0.421*
Abs Eosinophils (cells/uL)	180 (80-340) (N=298)	530 (240-730) (N=7)	***0.015***	100 (55-140) (N=7)	*0.242*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Organ Involvement distribution across the three groups. P-values were calculated by comparing the UPJ and PV groups with the remainder of the cohort by applying Fisher's exact test. Statistically significant p-values ($p < 0.05$) are shown in bold.

	Comparison Group: Fulfill ACR/EULAR Classification Criteria but do not have UPJ or PV masses (N=382)	PV Mass (N=7)	*P value PV vs. Comparison Group*	UPJ Mass (N=11)	*P value UPJ vs. Comparison Group*
Classification criteria inclusion points (median, IQR)	32 (26-42)	62 (40-78)		35 (27.5 -45)	
Organ involvement N (%)					
Pancreas	165 (43.19)	2 (28.57)	*0.704*	4 (36.36)	*0.764*
Bile Ducts	77 (20.16)	0 (0)	*0.353*	2 (18.18)	*>0.999*
Submandibular Gland	157 (41.10)	6 (85.71)	***0.023***	7 (63.64)	*0.213*
Lacrimal Gland	119 (31.15)	5 (71.43)	***0.036***	4 (36.36)	*0.746*
Parotid Gland	80 (20.94)	3 (42.86)	*0.170*	5 (45.45)	*0.065*
Kidney	114 (29.84)	2 (28.57)	*>0.999*	4 (36.36)	*0.740*
Retroperitoneal fibrosis	64 (16.75)	4 (57.14)	***0.020***	3 (27.27)	*0.409*
Prostate	28 (10.73) (N=261)	2 (28.57) (N=7)	*0.178*	4 (40) (N=10)	***0.020***
Vascular	36 (9.42)	1 (14.29)	*0.506*	3 (27.27)	*0.085*
Lungs	80 (20.94)	4 (57.14)	***0.042***	4 (36.36)	*0.258*
Orbits Lesion	53 (13.87)	2 (28.57)	*0.259*	2 (18.18)	*0.657*
Liver	22 (5.76)	0 (0)	*>0.999*	2 (18.18)	*0.140*
Sinuses	33 (8.64)	2 (28.57)	*0.124*	1 (9.09)	*>0.999*
Pericardium	8 (2.09)	1 (14.29)	*1.522*	2 (18.18)	***0.028***

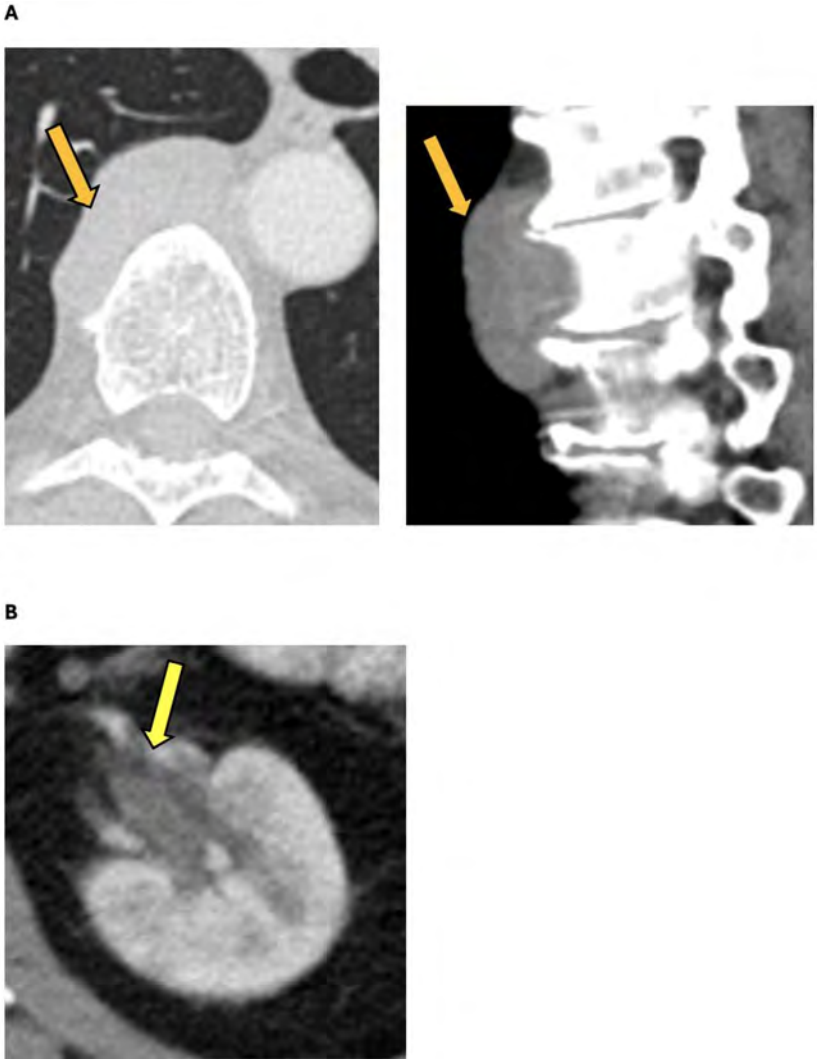


Figure 1. PV mass (A) and UPJ mass (B) imaging from two subjects of our cohort. (A) Computed tomography (CT) scan showing 4.3 x 1.7 cm soft tissue mass spanning the visceral and paravertebral mediastinum at the T6-T8 level (orange arrow), from left to right axial and sagittal sections. (B) CT scan showing 2.6 cm ill-defined parapelvic soft tissue mass within the left kidney (yellow arrow).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Patients with IgG4-RD were recruited from the Massachusetts General Hospital (MGH) Rheumatology Unit from 2008 to 2025. All patients included fulfilled the 2019 ACR/EULAR Classification Criteria for IgG4-RD. The presence of a PV or UPJ mass was determined by chart and imaging review. Demographics, age at diagnosis, organ involvement, and laboratory values were extracted from the medical record. Patients with PV or UPJ masses were compared to all other IgG4-RD patients in the registry.

Results: Among the 400 patients who fulfilled classification criteria in the MGH IgG4-RD registry, 7 (2%) had a PV mass and 11 (3%) had a UPJ mass. No patient had masses in both the PV and UPJ regions. PV masses were typically located anterolateral to the thoracic spine, abutting the vertebral bodies, and forming a band-like structure **(Figure 1A)**. UPJ masses were typically extrinsic to the kidney and abutting the renal vasculature and ureter but generally not causing hydronephrosis (82%, only two patients presented with hydronephrosis one of whom with concomitant retroperitoneal fibrosis) **(Figure 1B)**. All 7 patients with PV masses and 10 of 11 with UPJ masses were male. In contrast, the percentage of patients in the remainder of the cohort who were male was 68% (261 of 382). The median age of diagnosis for patients with PV masses, UPJ masses, and the IgG4-RD comparison group were 65.1, 65.4 and 61.8 years, respectively. Compared to all other IgG4-RD patients, those with PV masses had significantly higher median serum IgG4 values (891 vs 159 mg/dL, p=0.011) and median absolute and relative eosinophil counts (530 vs 180 cells/uL, p=0.015; 5.7 vs 2.7, p=0.015) **(Table 1)**. IgG4-RD patients with PV masses were more likely to have lacrimal gland (71% vs 31%, p=0.036), submandibular gland (86% vs 41%, p=0.023), retroperitoneal (57% vs 17%, p=0.020), and lung involvement (57% vs 21%, p=0.042). In contrast, patients with UPJ masses were more likely to have prostate (40% vs 11%, p=0.02) and pericardial (18% vs 2%, p=0.028) involvement **(Table 2)**.

Conclusion: Although masses in the PV and UPJ regions are considered highly suggestive of IgG4-RD, they occur in only a small minority of cases. Patients with either PV or UPJ masses tend overwhelmingly to be male, and those with PV masses have more exuberant immunologic disease activity (higher serum IgG4, more frequent peripheral eosinophilia) and more extensive organ involvement (higher frequency of lacrimal gland, submandibular gland, retroperitoneal, and lung involvement) compared to all other patients with IgG4-RD. In contrast, IgG4-RD patients presenting with UPJ masses are more likely to have prostate and pericardial involvement. Further studies incorporating imaging, histopathology, and treatment response among larger cohorts of IgG4-RD are needed to characterize these specific disease features further.

Disclosure: F. Bonaso: None; **G. McMahon**: None; **I. Jha**: None; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **Z. Wallace**: Amgen, 3; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **C. Perugino**: Acepodia, 2, Amgen, 1, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Zenas Biopharma, 2.

Abstract Number: 2530

Broad Screening of Inflammation-Associated Proteins Identifies Serum CCL19 and CCL2 as Versatile Biomarkers of Disease Activity in IgG4-Related Disease

Federica Bonaso[1], Bohang Jiang[2], Laura J. Yockey[3], Jesse Akaa[4], Ian Doyle[4], Evan Hsu[5], Courtney Leson[6], Grace McMahon[7], Isha Jha[7], Sydney Montesi[7], Guy Katz[7], Shiv Pillai[8], Pui Lee[5], John Stone[9], Zachary Wallace[10] and Cory Perugino[11], [1]University of Brescia, ASST Spedali Civili of Brescia, Massachusetts General Hospital, Monza, Italy, [2]MGH, Boston, MA, [3]MGH, Charlestown, MA, [4]Massachusetts General Hospital (MGH - Mass General) (MGB), Boston, MA, [5]Boston Children's Hospital, Newton, MA, [6]Boston Children's Hospital, Boston, [7]Massachusetts General Hospital, Boston, MA, [8]Harvard Medical School, Cambridge, MA, [9]Massachusetts General Hospital , Harvard Medical School, Concord, MA, [10]Massachusetts General Hospital, Newton, MA, [11]Massachusetts General Hospital, Harvard Medical School, Boston, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic immune-mediated disease characterized by mass-forming lesions and organ dysfunction. The smoldering tempo and often asymptomatic nature of IgG4-RD pose challenges in the monitoring of disease activity. At least fourteen protein biomarkers have been reported, including serum IgG4.

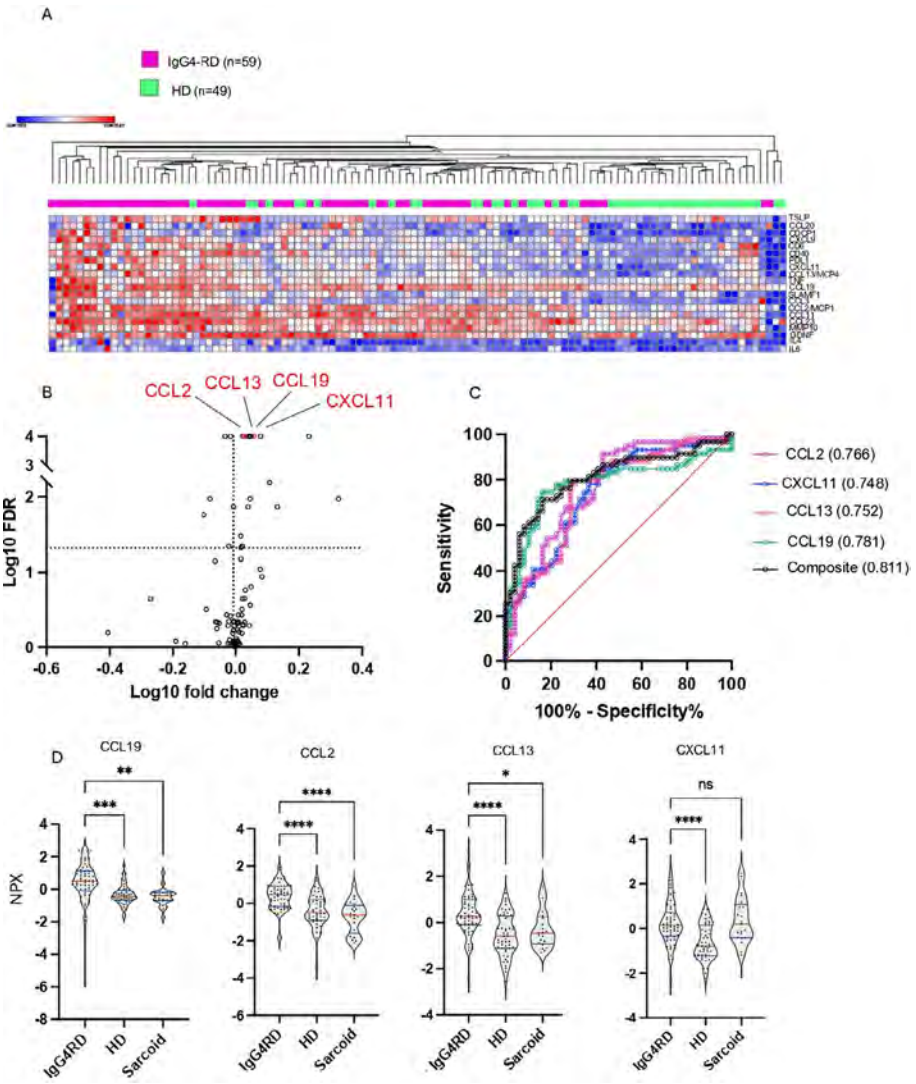


Figure 1. Screening of 92 inflammation associated proteins identifies a cassette of 20 proteins that distinguishes IgG4-RD. (A) Heatmap with hierarchical clustering of differentially abundant plasma proteins between IgG4-RD and healthy donors. (B) Volcano plot displaying log10 false discovery rate (FDR) values on the y-axis and log10 fold change values on the x-axis for all proteins included in the O-link 96 inflammation panel comparing untreated IgG4-RD (N=59) to age- and sex-matched healthy donors without immune mediated disease (N=49). Dashed line represents FDR adjusted p-value cut-off of 0.05 for significantly enriched proteins after controlling for multiple comparisons, age, and sex across cohorts. Red dots represent the four selected proteins positively enriched in IgG4-RD with FDR adjusted p-values <0.05. The 20 dots in the right upper quadrant represent proteins enriched in IgG4-RD patients. (C) Receiver operating characteristic (ROC) curve displays the ability of selected proteins to distinguish IgG4-RD from healthy donors. Areas under the curve are displayed parenthetically after each protein name in the legend. (D) Dot and violin plots displaying individual normalized protein expression (NPX) values for the CCL19, CCL2, CCL13 and CXCL11 in IgG4-RD, HD and sarcoidosis; blue lines represent interquartile range and red line represents median; p value was calculated by ordinary ANOVA. Symbols: ns p value >0.05, *p ≤0.05, ** p≤ 0.01, *** p≤0.001, **** p≤0.0001.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

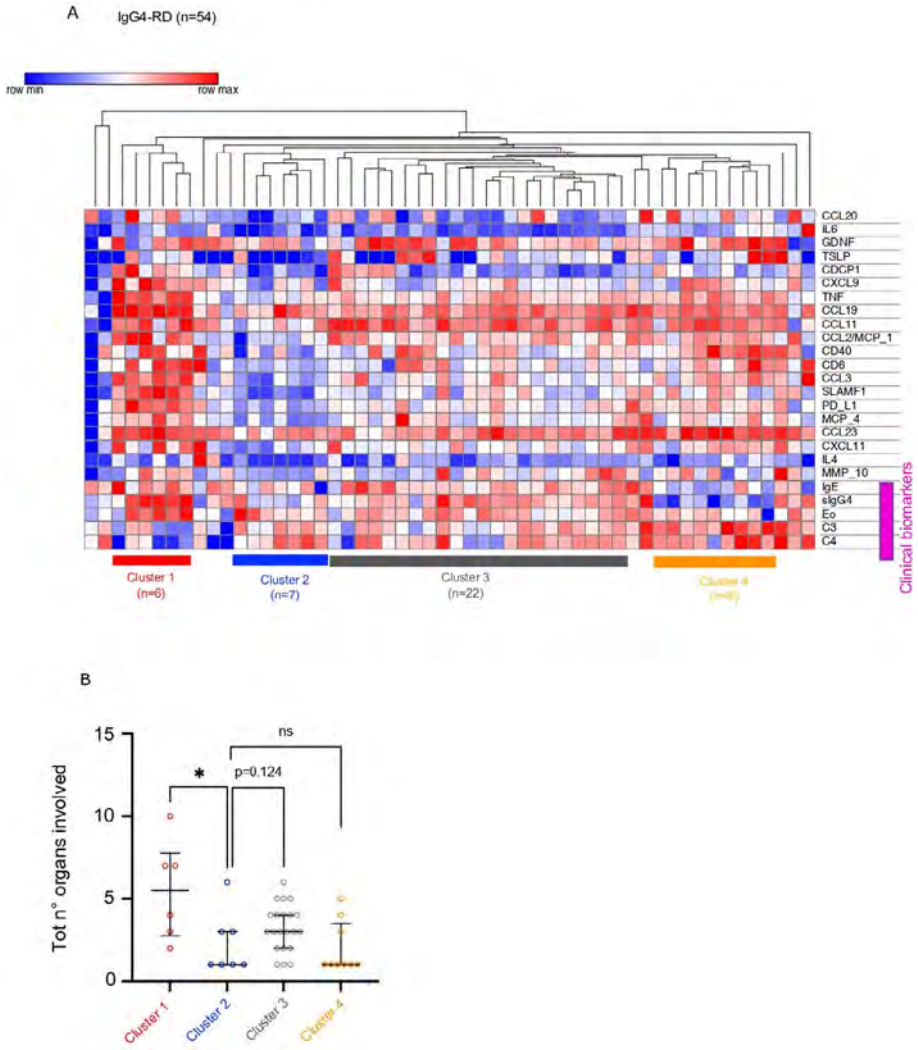


Figure 2. Novel biomarkers, including CCL19 and CCL2, correlate with extensive organ involvement and clinical biomarkers of severe disease. (A) Heatmap with hierarchical clustering of 20 IgG4-RD defining plasma proteins plotted with clinical biomarkers of severe disease including serum IgG4, IgE, absolute eosinophil count, C3, and C4 values. Only 54 patients had all clinical biomarkers available at time of blood draw. For hierarchical clustering the metric used was Euclidian distance and the linkage method was the average. (B) Dot plots showing total number of organs involved in each of the four clusters identified by hierarchical clustering, each dot corresponds to a patient belonging to one of the clusters. Bars represent median and interquartile range. P value the was calculated with Mann-Whitney U test. Symbols: ns p value >0.05, *p ≤0.05, ** p≤ 0.01, *** p≤0.001, **** p≤0.0001.

However, all reported biomarkers have been studied in relative isolation without direct comparison, and none have been demonstrated to correlate with relapsing disease. The goal of this study was to comprehensively screen inflammation associated proteins to identify novel biomarkers of disease activity in IgG4-RD that correlate with relapsing disease.

Methods: Ninety-two inflammation related proteins were measured across 59 patients with IgG4-RD, 49 healthy donors (HD), and 21 patients with sarcoidosis. Six IgG4-RD patients had pre- and post-prednisone samples available that were also studied. Statistical analyses were adjusted for age, sex, and multiple comparisons. Biomarkers that distinguished IgG4-RD were studied by receiver operating characteristic curves, hierarchical clustering, and linear regression. Flow cytometry was performed in a subset of patients to quantify activated $CD4^+$ T cells, activated B cell subsets, and plasmablasts.

Results: A cassette of 20 inflammation-associated proteins was identified that distinguished IgG4-RD from healthy donors **(Figures 1A-B)**. Among these, CCL19, CCL2, CCL13, and CXCL11 were the most accurate and non-redundant in defining IgG4-RD showing a composite area under the curve of 0.811**(Figure 1C)**. CCL19, CCL2 and CCL13 increased

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

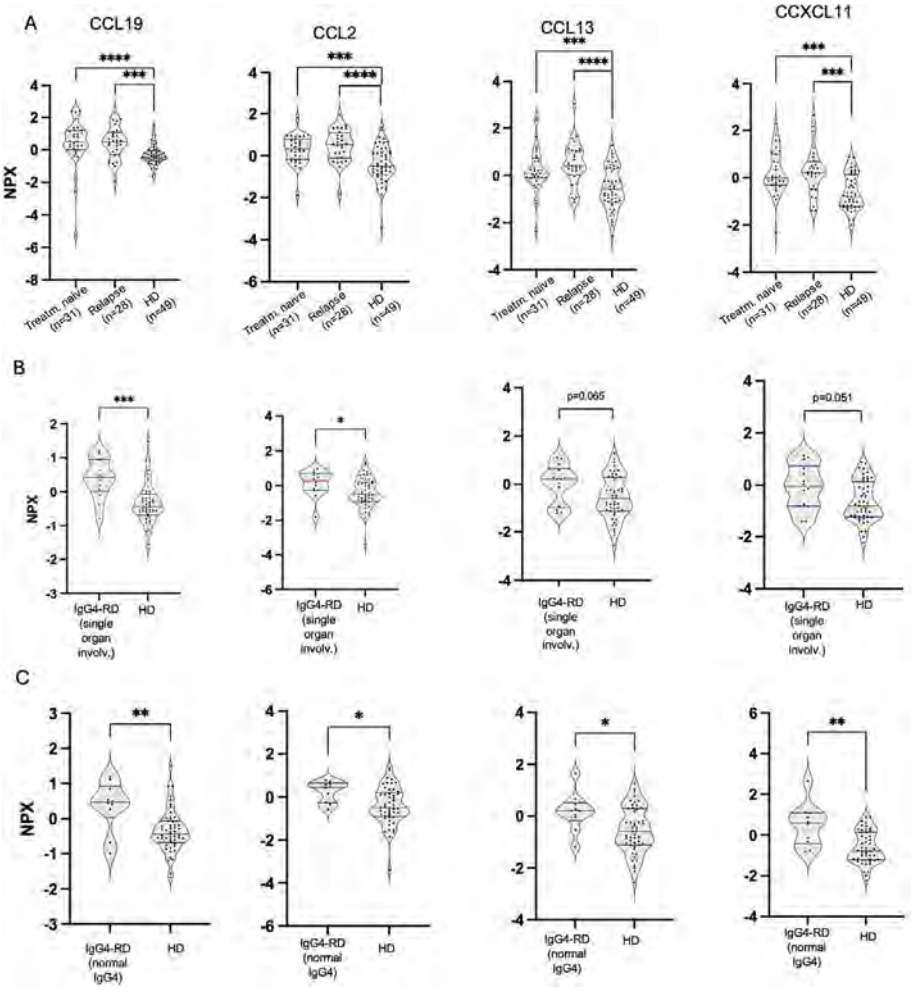


Figure 3. CCL19, CCL2, CCL13, CXCL11 may provide utility in difficult to monitor cases. (A) Dot and violin plots displaying individual normalized protein expression (NPX) values for the CCL19, CCL2, CCL13, and CXCL11 comparing treatment naïve and relapsing cohorts with healthy donors (HD). (B) Dot and violin plots displaying individual NPX values for the CCL19, CCL2, CCL13, and CXCL11 comparing IgG4-RD patients with single organ involvement (n=14) vs. HD. (C) Dot and violin plots displaying individual NPX values for the CCL19, CCL2, CCL13, and CXCL11 comparing IgG4-RD patients with normal serum IgG4 values (4-86mg/dl) (n=10) vs. healthy donors (HD). Blue lines represent interquartile range and red line represents median; p values computed by Mann-Whitney U test. Symbols: * p ≤0.05, ** p≤ 0.01, *** p≤0.001, **** p≤0.0001.

distinguished IgG4-RD from sarcoidosis whereas CXCL11 did not **(Figure 1D)**. These four biomarkers correlated with disease severity based on number of organs involved and clinical laboratory parameters of disease activity, including serum IgG4, IgE, absolute eosinophil count, and complement proteins C3 and C4 **(Figure 2)**. Furthermore, these four biomarkers showed the capacity to predict underlying states of $CD4^+$ T cell and B cell activation based on correlations with flow cytometry data. CCL19, CCL2, and CCL13 showed trends of decline following treatment with prednisone suggesting dynamic changes in response to immunosuppressive therapy and values declining in conjunction with remission. CCL19 and CCL2 were able to distinguish IgG4-RD patients with relapsing disease, single organ involvement, and normal baseline serum IgG4 levels from healthy donors **(Figure 3)**, suggesting promise in the clinical utility of these biomarkers.

Conclusion: CCL19, CCL2, CCL13, and CXCL11 are markedly upregulated in IgG4-RD. CCL19 and CCL2 may be particularly impactful in the longitudinal monitoring of disease activity while CCL19, CCL2, and CCL13 may also distinguish IgG4-RD from the mimicking condition sarcoidosis. Additional studies comparing other IgG4-RD mimickers and paired longitudinal samples are needed.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: F. Bonaso: None; **B. Jiang**: None; **L. Yockey**: None; **J. Akaa**: None; **I. Doyle**: None; **E. Hsu**: None; **C. Leson**: None; **G. McMahon**: None; **I. Jha**: None; **S. Montesi**: Accendatech USA, 2, Boehringer-Ingelheim, 5, Mediar Therapeutics, 1, 2, Pliant Therapeutics, 5, Wolters Kluwer, 9; **G. Katz**: Acepodia, 1, Amgen, 1, 2, 5, Sana, 5, Sanofi, 5, Zenas, 5; **S. Pillai**: Abpro Inc, 4, BeBio, 4, Octagon Therapeutics, 4, Paratus Biosciences, 2; **P. Lee**: Pfizer, 2; **J. Stone**: Acepodia, 2, Amgen, 1, 2, argenx, 2, Bristol-Myers Squibb, 2, Novartis, 2, Q32 Bio, 2, Sanofi, 2, Zenas, 2; **Z. Wallace**: Amgen, 3; **C. Perugino**: Acepodia, 2, Amgen, 1, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Zenas Biopharma, 2.

Abstract Number: 2531

Coronary periarteritis in IgG4-Related Disease

Georges El Hasbani[1], Daniel Larson[2], Matthew Koster[1] and Kenneth Warrington[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

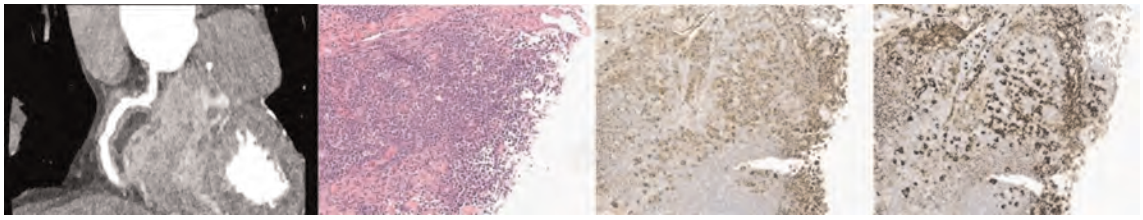
Background/Purpose: IgG4-related disease (IgG4-RD) is characterized by chronic inflammation and fibrosis, which can affect multiple organs, especially the pancreas, salivary glands, and retroperitoneum (1). It may lead to periaortitis, affecting up to 20% of patients, and in rare cases, coronary periarteritis, which can cause severe complications like myocardial infarction (2). This case series aims to explore the clinical and radiological features of coronary periarteritis in IgG4-RD and discuss complications and treatment options.

1. Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med. 2012;366(6):539-51.

2. Katz G, Hedgire SH, Stone JR, Perez-Espina S, Fernandes A, Perugino CA, et al. IgG4-related disease as a variable-vessel vasculitis: A case series of 13 patients with medium-sized coronary artery involvement. Semin Arthritis Rheum. 2023;60:152184.

Methods: A review of the electronic health records was conducted using keywords related to IgG4-RD and coronary involvement. Out of 146 patients reviewed, 9 patients had confirmed IgG4-RD with coronary involvement. Data extracted included diagnosis date, serum IgG4 and C-reactive protein levels, imaging findings, cardiac complications, and treatment details.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CT cardiac demonstrating thickening of the wall of the right coronary artery. H&E, pelvic lymph node biopsy with plasmacytosis. IgG shows most plasma cells express IgG. IgG4 shows 30-40% of plasma cells are IgG4-postive, with over 100/hpf.

Results: All 9 patients were male, with a mean age of 55.5 ± 5.7 years at diagnosis. The mean serum IgG-4 level was 738 ± 1280 mg/dL, while the mean C-reactive protein value was 39.9 ± 54.8 mg/L. The average time between diagnosis of IgG4-RD and coronary involvement was 2 years and 6 months. A tissue biopsy showed IgG4-positive plasma cells in all cases. Coronary artery involvement was primarily detected through CT angiography, showing thickening of vessel walls (Table) . The right coronary artery (RCA) was affected in 5 patients, the left anterior descending artery (LAD) in 4, and the left main coronary artery in 1. In 5 patients, the periarteritis involved the entire length of the coronary artery, and 1 patient had an aneurysm of the LAD. Regarding treatment, all patients received glucocorticoids, and 7 patients were additionally treated with rituximab (RTX). Two patients received RTX for induction only, while 4 patients had induction and maintenance RTX infusions. One patient developed ischemic heart disease, and one progressed to heart failure. Follow-up imaging showed partial or complete resolution of vessel thickening in 7 patients.

Conclusion: Coronary artery involvement in IgG4-RD is rare but significant, leading to periarteritis, and subsequently coronary aneurysm formation. The RCA and LAD appear to be most affected in this condition, with imaging techniques such as cardiac CT being effectively used as diagnostic tool. Rituximab has shown promising data in managing coronary involvement, though its use in this context remains limited, ultimately necessitating larger studies.

Disclosure: G. El Hasbani: None; **D. Larson**: None; **M. Koster**: Amgen, 2; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2.

Abstract Number: 2532

Temporal arteritis revealing eosinophilic diseases: A multicenter retrospective study, literature review, and combined cluster analysis

Julie Merindol[1], Benjamin Torreau[2], Matthieu Groh[3], Amy Klion[4], Paolo Delvino[5], Olivier Espitia[6], Jean-Benoit Arlet[7], Sarah Lechtman[8], Jean-sébastien Allain[9], Federica Bello[10], Anaelle Boucaud[11], Florian Catros[12], Julien Campagne[13], Anne Coutard[14], Cecile-Audrey DUREL[15], Mikael Ebbo[16], Georgina Espigol-Frigole[17], Giacomo Emmi[18], Yanis Kouchit[19], Guillaume Lefevre[20], François Lifermann[21], PAUL LEGENDRE[22], Eric Liozon[23], Francois Maurier[24], Sara Melboucy Belhkir[25], Sébastien Miranda[26], Simon Parreau[23], Paola Parronchi[27], Jacques Pouchot[28], Vincent Pestre[29], Sophie Rosenstingl[30], Jan Willem Cohen Tervaert[31], Odile Souchaud Debouverie[32], Xavier Puéchal[33], Benjamin Terrier[34] and French Vasculitis Study Group, European EGPA Study Group, [1]CHU de Nice, Nice, France, [2]Internal Medicine and Immunology, CHU Tours, Tours, France, [3]Hôpital Foch, paris, France, [4]NIAID/NIH, Bethesda, MD, [5]University of Milano-Bicocca, Monza, Monza and Brianza, Italy, [6]CHU de Nantes, Nantes, France, [7]APHP, Paris, [8]CHU de Nice, Nixe, France, [9]Scorff-Lorient Hospital, Lorient, France, [10]Université de Florence, Florence, Italy, [11]CHU de Tours, Tours, France, [12]CHI VAL, Ariège, France, [13]Hopital Robert Schuman, Metz, France, [14]Groupe Hospitalier de Bretagne Sud, Lorient, France, [15]CHU de Lyon, Lyon, France, [16]Internal Medicine, Marseille-APHM, hôpital La Timone, Marseille, France, [17]Hospital Clnic de Barcelona, Barcelona, Spain, [18]Department of Medical, Surgery and Health Sciences, University of Trieste, Italy and Clinical Medicine and Rheumatology Unit, Cattinara University Hospital, Trieste, Italy, Trieste, Italy, [19]CH de Cannes, Cannes, France, [20]CHU de Lille, Lille, France, [21]Internal Medicine, CH de Dax, Dax, France, [22]CH LE MANS, Le Mans, France, [23]CHU de Limoges, Limoges, France, [24]HOPITAUX PRIVES DE METZ, Vaux / Frankreich, France, [25]CH de Saint Quentin, Saint Quentin, France, [26]Internal Medicine, CHU Rouen, Rouen, France, [27]CHU de Florence, Florence, Italy,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[28]AP-HP, Rueil Malmaison, France, [29]CH d'Avignon, Avignon, France, [30]CH de Compiegne, Compiegne, France, [31]University of Alberta, Edmonton, AB, Canada, [32]CHU de Poitiers, Poitiers, France, [33]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [34]Cochin Hospital, Paris, France

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Temporal arteritis (TA) classically presents as a large-vessel vasculitis in older adults with cranial ischemic symptoms. However, in younger patients or in the presence of eosinophilia, alternative etiologies must be considered.

Methods: We conducted a retrospective, multicenter, descriptive study that included patients with 1) confirmed temporal arteritis, either by histologic confirmation or by the presence of typical clinical symptoms combined with imaging abnormalities, and 2) pretreatment blood eosinophilia >1000/mm^3. We also performed a literature review to identify additional cases of eosinophilia-associated temporal arteritis (EoTA). Finally, unsupervised hierarchical clustering was used to classify patients into subgroups to capture the full spectrum of EoTA.

Results: A total of 78 patients were included, i.e. 40 original cases and 38 from the literature review. The median age was 59 years [IQR 41.2-69.8] and 73% were male. The diagnosis of TA was based on histology in 85% of patients, while 33% also had imaging abnormalities.

Constitutional symptoms were reported in 63%, headache in 42%, TA induration in 29%, jaw claudication in 26%, and ocular ischemic events in 10%. Other manifestations included pulmonary (47%) and sinonasal (32%) involvement, and peripheral neuropathy (28%). Median eosinophil count was 3500/mm^3 [IQR 1800–7370], CRP was 28.8 mg/L [5.0–94.8], and 33% were ANCA positive, predominantly MPO-ANCA. Temporal artery biopsies showed eosinophilic and mononuclear cell infiltration in 69% and 53%, respectively, giant cells in 25%, and internal elastic lamina fragmentation in 40%.

Overall, 71% of patients met EGPA criteria, 53% met GCA criteria and 32% met both criteria according to the 2022 ACR/EULAR classification. In addition, 29% of patients were classified as hypereosinophilic syndrome (SHE).

First-line therapy consisted of glucocorticoids (GC) in 87%, in combination with immunosuppressive agent in 32% (conventional synthetic DMARDs in 18, biologic DMARDs in 5, eosinophil-targeting biologics in 4). At 6 months, 16 (27%) were in remission, 36 (61%) were GC-dependent, 2 (3%) were refractory, 5 (8.5%) had relapsed, while 19 (24%) did not reach the 6-month follow-up.

Cluster analysis identified four distinct groups. Cluster 1 (23%) included young men with isolated TA, low acute phase reactants, consistent with juvenile TA and Kimura disease, and had the highest remission rate (58%). Cluster 2 (32%) included middle-aged patients with systemic involvement, mainly cardiovascular, moderate CRP levels, consistent with HES, and showed frequent GC dependence (82%) and relapses (9%). Cluster 3 (15%) was characterized by older patients with typical features of GCA, with frequent GC dependence (78%). Cluster 4 (29%) included patients with sinonasal involvement, asthma and mononeuritis multiplex, high eosinophil counts and positive MPO-ANCA, consistent with EGPA and showed frequent GC dependence (82%).

Conclusion: Eosinophilia-related TA is a heterogeneous entity at the intersection of GCA, EGPA, HES, and localized TA. While systemic forms resemble EGPA or SHE, others, especially in younger patients, represent benign forms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Merindol: None; **B. Torreau**: None; **M. Groh**: None; **A. Klion**: None; **P. Delvino**: None; **O. Espitia**: Novartis, 2; **J. Arlet**: None; **S. Lechtman**: None; **J. Allain**: None; **F. Bello**: None; **A. Boucaud**: None; **F. Catros**: None; **J. Campagne**: None; **A. Coutard**: None; **C. DUREL**: None; **M. Ebbo**: None; **G. Espigol-Frigole**: None; **G. Emmi**: None; **Y. Kouchit**: None; **G. Lefevre**: None; **F. Lifermann**: None; **P. LEGENDRE**: None; **E. Liozon**: None; **F. Maurier**: None; **S. Melboucy Belhkir**: None; **S. Miranda**: None; **S. Parreau**: None; **P. Parronchi**: None; **J. Pouchot**: None; **V. Pestre**: None; **S. Rosenstingl**: None; **J. Cohen Tervaert**: AbbVie/Abbott, 6, GlaxoSmithKlein(-GSK), 6, Hoffmann-La Roche, 6, IDMC InflaRx, 12, Chair, Mallinckrodt Pharmaceuticals, 2, Medexus, 6, Merck/MSD, 2, Novartis, 2, Pfizer, 6, Sanofi, 6; **O. Souchaud Debouverie**: None; **X. Puéchal**: Roche, 5; **B. Terrier**: Amgen, 1, Astra-Zeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 2533

Patterns of skin lesion transcriptomics in different forms of vasculitis

Karyssa Stonick[1], Luciana Yamamoto de Almeida[2], Seolkyoung Jung[3], Faiza Naz[4], Alice Fike[4], Kaitlin Quinn[4], Shubhasree Banerjee[5], Christopher Hansen[6], David Cuthbertson[7], Anthony Fernandez[8], Nader Khalidi[9], Tanaz Kermani[10], Carol Langford[11], Carol McAlear[5], Christian Pagnoux[12], Rennie Rhee[5], Peter Merkel[5], Robert Micheletti[13], Peter Grayson[14] and Vascultis Clinical Research Consortium, [1]National Insitute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [2]National Institutes of Health, Bethesda, MD, [3]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [5]University of Pennsylvania, Philadelphia, PA, [6]University of Utah, Salt Lake City, UT, [7]University of South Florida, Tampa, [8]Cleveland Clinic Foundation, Westlake, OH, [9]McMaster University, Hamilton, ON, Canada, [10]University of California Los Angeles, Santa Monica, CA, [11]Cleveland Clinic, Moreland Hills, OH, [12]Mount Sinai Hospital, Toronto, ON, Canada, [13]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [14]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The systemic vasculitides are a family of rare diseases defined by immune-mediated inflammation and destruction of vasculature. Causal etiologies of most forms of vasculitis are unknown. Classification schemes to distinguish between forms of vasculitis typically rely on the clinical pattern of disease and do not incorporate biologic data about immune dysregulation. This study aimed to determine the relationship between tissue transcriptomics and clinical diagnoses by profiling skin lesions from patients with different types of vasculitis.

Methods: Patients with skin lesions attributed to one of nine pre-specified vasculitides were recruited into a multi-center prospective observational cohort. Bulk RNA was extracted from 4-6 mm punch biopsies of affected skin using a TRIzol-cholorform method (New England Biolabs Next Ultra II RNA library kit) and sequenced on a Nextseq 2000/NovaseqXPlus (Illumina).

Results: 70 patients underwent punch biopsies of vasculitic skin lesions. The cohort included patients with isolated cutaneous small-vessel vasculitis (CSVV) (n=18), IgA vasculitis (IgAV) (n=15), VEXAS (Vacuoles, E1-enzyme, X-linked, Autoinflammatory, Somatic) syndrome (n=10), granulomatosis with polyangiitis (GPA) (n=7), eosinophilic granulomatosis with polyangiitis (EGPA) (n=6), polyarteritis nodosa (PAN) (n=6), microscopic polyangiitis (MPA) (n=3), urticarial vasculitis (UV) (n=4), or cryoglobulinemic vasculitis (CryoV) (n=1) . The skin lesion morphology included purpuric macules (PM, n = 20), purpuric papules (PP, n=20), urticarial lesions (U, n=10), nodules (N, n=9), plaques (P, n=5), retiform purpura (RP, n=5), and one patient with unknown morphology. Plotting of principal component analysis eigen scores revealed that VEXAS

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

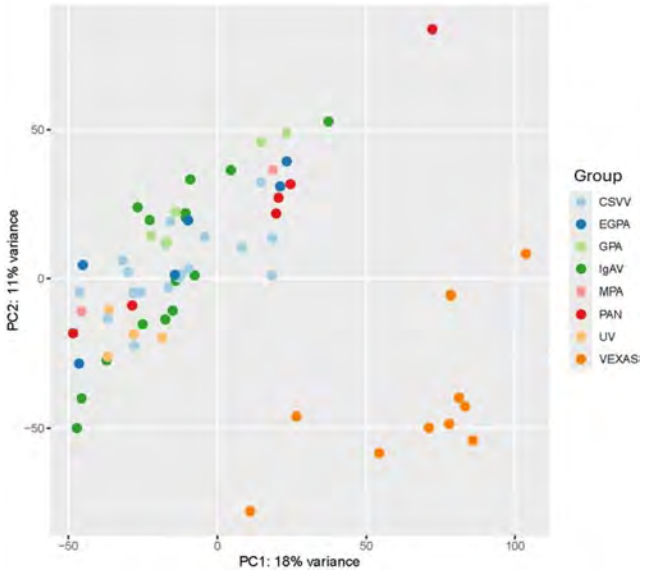


Figure 1: Principal component analysis grouping by type of vasculitis. Patients with cryoglobulinemic vasculitis and outliers were excluded from this analysis. PC: Principal component. CSVV: isolated cutaneous small-vessel vasculitis (n=18), EGPA: eosinophilic granulomatosis with polyangiitis (n=6), GPA: granulomatosis with polyangiitis (n=7), IgAV: IgA vasculitis (n=15), MPA: microscopic polyangiitis (n=3), PAN: polyarteritis nodosa (n=6), UV: urticarial vasculitis (n=4), and VEXAS: Vacuoles, E1-enzyme, X-linked, Autoinflammatory, Somatic syndrome (n=10).

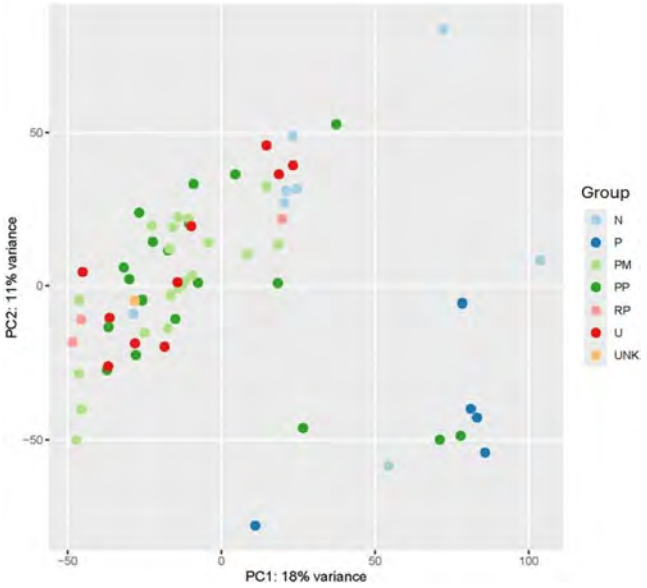


Figure 2: Principal component analysis grouping by skin lesion morphology among patients with skin manifestations of vasculitis. Patients with cryoglobulinemic vasculitis and outliers were excluded from this analysis. PC: Principal component. N: nodules (n=9), P: plaques (n=5), PM: purpuric macules (n = 20), PP: purpuric papules (n=20), RP: retiform purpura (n=5), U: urticarial lesions (n=10), and UNK: unknown (n=1).

samples clustered independently from the other forms of vasculitis in this cohort (**Figure 1**). There was no clear clustering based on skin morphology (**Figure 2**). Differential gene expression analysis revealed a substantial number of significantly differentially expressed genes (DEGs) between VEXAS and the other forms of vasculitis. Gene Ontology enrichment analysis identified a relative upregulation of interferon response genes in VEXAS. The top DEGs that defined this upregulation of the interferon pathway in VEXAS relative to the other forms of vasculitis were *XAF1* (log2 fold change = 4.132), *ISG15* (log2 fold change = 3.494), and *IFIT3* (log2 fold change = 3.453).

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Direct profiling of affected tissue across different forms of vasculitis reveals shared and divergent pathophysiology. For example, tissue transcriptomics confirm that VEXAS has a strong interferon signature relative to other types of vasculitis. Clinical assessment of morphology without incorporation of biological data about immune dysregulation misses critical information. Our data supports that future classification schema for systemic vasculitides would benefit from the incorporation of biologic data with clinical features for the characterization of disease. This has the potential to lead to novel and personalized approaches to treatment.

Disclosure: K. Stonick: None; **L. Yamamoto de Almeida**: None; **S. Jung**: None; **F. Naz**: None; **A. Fike**: None; **K. Quinn**: None; **S. Banerjee**: None; **C. Hansen**: None; **D. Cuthbertson**: None; **A. Fernandez**: AbbVie/Abbott, 2, 6, Amgen, 6, AstraZeneca, 12, 5, Biogen, 2, Bristol-Myers Squibb(BMS), 6, Merck/MSD, 2, Pfizer, 12, 5; **N. Khalidi**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 6, Mallinckrodt, 6, NS Pharma, 5, Otsuka, 6, Roche, 2, Sanofi, 5; **T. Kermani**: None; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **C. McAlear**: None; **C. Pagnoux**: AstraZeneca, 1, ChemoCentryx, 1, GlaxoSmithKlein(GSK), 1, 5, InflaRx GmbH, 1, otsuka, 1, 5, Pfizer, 1, 5, Roche, 1, 5; **R. Rhee**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **R. Micheletti**: Amgen, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Cabaletta Bio, 2, 5, 6, InflaRx, 2, 5, 6, Vertex, 2, 5, 6; **P. Grayson**: None.

Abstract Number: 2534

Frequency of Ocular and Gastrointestinal Lesions Is Increased in Japanese Behçet's Disease Patients with HLA-B61

Koichi Sugihara[1], Risa Wakiya[2], Hiromi Shimada[1], Taichi Miyagi[3], Yusuke Ushio[3], Mao Mizusaki[1], Kanako Chujo[3], Naoto Manabe[3], Mayuko Wada[1], Shusaku Nakashima[1] and Hiroaki Dobashi[1], [1]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa, Japan, [2]Division of Rheumatology, Department of Internal Medicine, Toho University, Ota City Tokyo, Japan, [3]Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Japan

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: The associations of HLA-B51 and HLA-A26 with the onset of Behçet's disease (BD) are well established. Although BD manifests with a variety of clinical lesions, the relationships between specific HLA types and individual disease manifestations—especially HLA types beyond B51 and A26—remain unclear.

This study aimed to investigate the associations between HLA-A and HLA-B alleles and clinical lesions in Japanese patients with BD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. HLA-A type of study participants.

HLA-A type	BD N=36	HC N=5308	*p*-value
A1	2.8%	1.0%	0.3071
A2	38.9%	43.4%	0.6173
A11	16.7%	16.8%	1.0000
A24	58.3%	61.1%	0.7345
A25	2.8%	NA	NA
A26	44.4%	20.7%	0.0014*
A31	11.1%	17.6%	0.3844
A33	11.1%	14.5%	0.8114

P values were determined by Fisher's exact test.
*Data were considered significant at $p < 0.05$.
HLA: Human Leukocyte Antigen; BD: Behcet's disease; HC: healty control; NA: not available.

Table 2. HLA-B type of study participants.

HLA-B type	BD N=36	HC N=5308	*p*-value
B7	8.3%	10.6%	1.0000
B27	2.8%	0.8%	0.2531
B35	13.9%	15.5%	1.0000
B39	2.8%	7.0%	0.5134
B44	11.1%	13.3%	1.0000
B46	8.3%	9.6%	1.0000
B48	8.3%	5.6%	0.4531
B51	36.1%	17.6%	0.0074*
B52	16.7%	21.8%	0.5477
B54	16.7%	14.0%	0.6289
B56	5.6%	1.8%	0.1406
B60	5.6%	10.8%	0.4244
B61	36.1%	25.5%	0.1777
B62	8.3%	16.3%	0.2584
B70/71/72	5.6%	3.1%	0.3109
B75	5.6%	2.0%	0.1641

P values were determined by Fisher's exact test.
*Data were considered significant at $p < 0.05$.
HLA: Human Leukocyte Antigen; BD: Behcet's disease; HC: healty control; NA: not available.

Methods: This retrospective study included patients with BD who visited Kagawa University Hospital in 2024 and whose HLA-A and HLA-B types had been analyzed. All patients were ≥18 years and met the International Criteria for Behçet's Disease. The frequency of HLA-A and HLA-B alleles in BD patients was compared with that in healthy Japanese individuals.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Comparison of demographic and disease characteristics between HLA-B61-positive and HLA-B61-negative patients with Behcet's disease.

	Total	HLA-B61 positive	HLA-B61 negative	*p*-value
N	36	13	23	NA
Age, year	44.3 ± 12.2	41.0 ± 9.7	46.1 ± 13.2	0.3226
Female, n(%)	27 (75.0)	8 (61.5)	19 (82.6)	0.2347
Disease duration, year	8.6 ± 7.7	9.9 ± 6.3	7.8 ± 8.4	0.1143
HLA-B51 positive, n(%)	13 (36.1)	3 (23.1)	10 (43.5)	0.2920
HLA-A26 positive, n(%)	16 (44.4)	6 (46.2)	10 (43.5)	1.0000
Major lesions ever observed				
Oral ulcer, n(%)	36 (100)	13 (100)	23 (100)	NA
Genital ulcer, n(%)	32 (88.9)	12 (92.3)	20 (87.0)	1.0000
Skin lesion, n(%)	30 (83.3)	13 (100)	17 (73.9)	0.0679
Erythema nodosum, n(%)	11 (30.6)	6 (46.2)	5 (21.7)	0.1525
Thrombophlebitis, n(%)	2 (5.6)	0 (0)	2 (8.7)	0.5254
Papulopustular skin lesions, n(%)	29 (80.6)	13 (100)	16 (69.6)	0.0343*
Arthritis, n(%)	27 (75.0)	9 (69.2)	18 (78.3)	0.6933
Ocular involvement, n(%)	13 (36.1)	8 (61.5)	5 (21.7)	0.0298*
Epididymitis, n(%)	2 (5.6)	1 (7.7)	1 (4.4)	1.0000
Gastrointestinal involvement, n(%)	5 (13.9)	4 (30.8)	1 (4.4)	0.0470*
Nervous system involvement, n(%)	6 (16.7)	2 (15.4)	4 (17.4)	1.0000
Vascular involvement, n(%)	1 (2.8)	0 (0)	1 (4.4)	1.0000

P values were determined by Mann–Whitney U test and Fisher's exact test.
*Data were considered significant at $p < 0.05$.
HLA: Human Leukocyte Antigen; NA: not applicable.

Additionally, the prevalence of specific BD manifestations was analyzed according to HLA alleles. Statistical analyses were performed using the Mann–Whitney U test and Fisher's exact test.

Results: A total of 36 patients were included (mean age 44.3 years; 75.0% female; mean disease duration 8.6 years). As previously reported, HLA-B51 and HLA-A26 were significantly more prevalent in BD patients than in healthy controls (36.1% vs. 17.6%, p = 0.0074; 44.4% vs. 20.7%, p = 0.0014, respectively). No significant differences were found for other HLA alleles.

Among BD patients, those with HLA-B61 had significantly higher frequencies of ocular and gastrointestinal involvement compared to those without HLA-B61 (61.5% vs. 21.7%, p = 0.0298; 30.8% vs. 4.4%, p = 0.0470, respectively). No significant differences in age, sex, or disease duration were observed between HLA-B61–positive and –negative groups. Additionally, patients with HLA-A2 were significantly less likely to present with arthritis (p = 0.0144).

Conclusion: While HLA-B61 has been previously linked to ankylosing spondylitis and Crohn's disease, this study suggests a novel association between HLA-B61 and ocular and gastrointestinal manifestations in Japanese patients with Behçet's disease. Further studies with larger cohorts are warranted to confirm these findings.

Disclosure: K. Sugihara: None; **R. Wakiya**: None; **H. Shimada**: None; **T. Miyagi**: None; **Y. Ushio**: None; **M. Mizusaki**: None; **K. Chujo**: None; **N. Manabe**: None; **M. Wada**: None; **S. Nakashima**: None; **H. Dobashi**: None.

Abstract Number: 2535

Behçet's syndrome: distinct features in 344 pediatric and adult patients in a non-endemic region

Ricardo Machado[1], Thales Souza[2], Matheus França[3], Vinicius Matias[4], Sylvia Farhat[1], Carolina Siqueira[4], Maria Carolina Santos[4], Lia Steuer[1], Luisa Forero[1], Rafael Bassara Macedo[5], Thiago Freitas[6], barbara Bayeh[7], Carolina Ejnisman[8], Pedro Araujo[9], Rafael Cordeiro[10], Fabio Specian[5], Verena Balbi[1], Nadia Emi Aikawa[11], Katia Kozu[1], Clovis Artur Silva[12], **Lucia Maria Campos**[13], Adriana Elias[14] and Henrique Giardini[6], [1]Instituto da Criança e do Adolescente, Hospital das Clinicas,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sao Paulo, Sao Paulo, Brazil, [2]Faculdade de Medicina da Universidade de Brasilia, Brasilia, Distrito Federal, Brazil, [3]Instituto da Criança e do Adolescente, Hospital das Clinicas, University of Sao Paulo Medical School, Sao Paulo, Sao Paulo, Brazil, [4]Faculdade de Ciências Medicas da Santa Casa de Sao Paulo, Sao Paulo, Sao Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (USP), Sao Paulo, Sao Paulo, Brazil, [6]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [7]Hospital das Clínicas, University of Sao Paulo Medical School, Sao Paulo, Sao Paulo, Brazil, [8]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [9]Universidade de São Paulo, Sao Paulo, São Paulo, Brazil, [10]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil, [11]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [12]University of São Paulo, São Paulo, São Paulo, Brazil, [13]Instituto da Criança e do Adolescente, São Paulo, São Paulo, Brazil, [14]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas, University of Sao Paulo Medical School, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's syndrome (BS) is a chronic inflammatory disorder characterized by a heterogeneous clinical presentation, occurring primarily in young adults and very rarely in children and adolescents. In addition, there are few studies that compared childhood-onset BS (cBS) and adult-onset BS (aBS), especially in non-endemic regions. Therefore, the objectives of the present study were to evaluate demographic, clinical and therapeutic data in cBS and aBS.

Methods: Medical records of 344 patients [99 cBS (≤ 18 years-old) and 245 aBS] from three tertiary Brazilian Rheumatology centers were reviewed in order to compare clinical and therapeutic features. cBS and aBS were classified according to International Study Group and/or the International Criteria for Behçet's Disease.

Results: The median age at diagnosis was 11(0.5-17) years in cBS and 30(18-76) years in aBS. The median follow-up time was significantly reduced in cBS compared to aBD [7(0-23) vs. 10(0-27) years, p=0.014], with similar female sex in both groups (56% vs. 62%, p=0.14). Classification criteria were fulfilled in 82% of cBS and 100% of aBS patients. Fever (30% vs. 15%, p=0.002), gastrointestinal involvement (55% vs. 14%, p=0.003), and a family history of autoimmune diseases (22% vs. 16%, p=0.001) were significantly higher in cBS compared to aBS. In contrast, genital ulcers (67% vs. 81%, p=0.01), cutaneous lesions (47% vs. 68%, p=0.001), including pseudofolliculitis (34% vs. 53%, p=0.001) and erythema nodosum (24% vs. 36%, p=0.03), uveitis (32% vs. 44%, p=0.03), corticosteroids (68% vs. 88%, p< 0.001), azathioprine (56% vs. 70%, p=0.01), cyclosporine (9% vs. 22%, p=0.004), cyclophosphamide (19% vs. 34%, p=0.001), and intravenous immunoglobulin use (9% vs. 18%, p=0.03) were significantly lower in the former group. Frequencies of oral and cutaneous ulcers, articular or central nervous system involvement, retinal vasculitis, colchicine, mycophenolate mofetil, and methotrexate use were similar in both groups (p >0.05).

Conclusion: cBS was rarely observed in our non-endemic region, potentially due to under recognition, as it often presented with nonspecific symptoms such as fever and gastrointestinal involvement. The broader spectrum of symptoms in aBS patients might account for the more extensive use of immunosuppressive agents.

Disclosure: R. Machado: None; **T. Souza**: None; **M. França**: None; **V. Matias**: None; **S. Farhat**: None; **C. Siqueira**: None; **M. Santos**: None; **L. Steuer**: None; **L. Forero**: None; **R. Bassara Macedo**: None; **T. Freitas**: None; **b. Bayeh**: None; **C. Ejnisman**: None; **P. Araujo**: None; **R. Cordeiro**: None; **F. Specian**: None; **V. Balbi**: None; **N. Aikawa**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

K. Kozu: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Campos**: None; **A. Elias**: None; **H. Giardini**: None.

Abstract Number: 2536

High Levels of Fatigue and Poor Sleep Quality in Behçet Disease: a Cross-sectional Study from a Non-endemic Area

Mateus Augusto Rangel Nunes, Carlos Teixeira, Laurie Kumano, Gabriela Gutierrez, Vitor Grotti, Ana Paula Toledo Del Rio, Ibsen Coimbra, Alisson Pugliesi and Zoraida Sachetto, UNICAMP, Campinas, Brazil

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet's disease (BD) is a chronic systemic inflammatory disease classified as a variable vessel vasculitis of unknown etiology. It is marked by recurrent oral and genital aphthous lesions, skin lesions, and potential involvement of ocular, articular, intestinal, neurological, and vascular systems. In endemic areas, fatigue is a common symptom in BD patients, often associated with sleep disorders and reduced quality of life. This study aimed to assess fatigue and sleep disorders in patients with BD from a non-endemic area and correlate these symptoms with sociodemographic features.

Methods: This cross-sectional study involved patients with BD from a tertiary university hospital, all patients met the International Study Group (ISG) and International Criteria for Behçet's Disease (ICBD). Patients consented to participate in the study and provided data on age, sex, and socio-demographic characteristics. Also, patients were categorized based on the presence of fatigue. Fatigue was assessed with FACIT-Fatigue score (FFS). Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). Statistical analyses included Fisher's exact test for categorical variables and Student's t-test for continuous variables, with significance set at $p < 0.05$.

Results: The study included 42 patients, 22 of whom were female (52.3%), with a mean age of 47.6±14.1 years, and a low predominance of the white race (52.4%). Mean FFS was 32.4±10.8 and PSQI 9.09±4.79. A significant inverse relationship was found between FFS and PSQI (Pearson $r = -0.470$; $p < 0.01$). Patients with higher body mass index presented more fatigue (p=0.005). There were no significant differences regarding sex, ethnicity, smoking history, alcohol use, physical activity or marital status. A high frequency of poor sleep quality was present in patients with fatigue (51.6%; p=0.016). Additionally, patients with fatigue presented higher scores in PSQI global score (p=0.001) and its subdomains such as sleep onset latency (p=0.026) and sleep duration (p=0.040).

Conclusion: This study shows a high frequency of fatigue and poor sleep quality in BD patients from a non-endemic region. Our findings underscore the importance of recognizing these factors, suggesting the need for a multidisciplinary therapeutic approach to enhance the overall well-being of BD patients.

Disclosure: M. Nunes: None; **C. Teixeira**: None; **L. Kumano**: None; **G. Gutierrez**: None; **V. Grotti**: None; **A. Del Rio**: None; **I. Coimbra**: None; **A. Pugliesi**: AbbVie/Abbott, 6, Boehringer-Ingelheim, 6, Johnson, 6, Pfizer, 6, UCB, 6; **Z. Sachetto**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2537

Variation in Treatment Approaches in IgA-Vasculitis Among Pediatricians and Pediatric rheumatologists: A Cross-Sectional International Survey

Merav Heshin Bekenstein[1], Tali Elbaz[2], Yael Illous[2] and Barak Kandell[3], [1]Tel Aviv Medical Center Israel, Binyamina, Tel Aviv, Israel, [2]School of Medicine, Faculty of Medical and Health Sciences, Tel Aviv, Israel, [3]The Academic College of Tel Aviv-Yafo, Tel Aviv, Israel

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

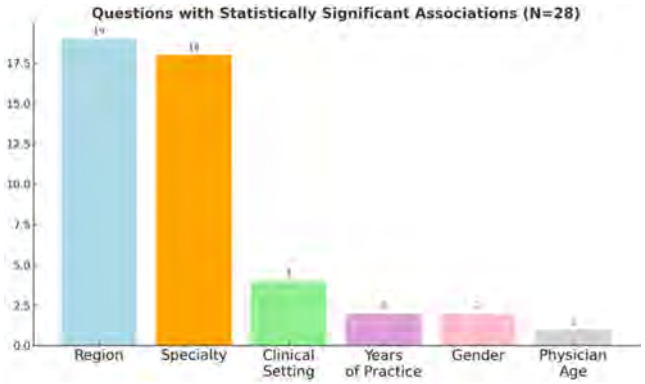
Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: IgA Vasculitis (IgAV) is the most common small-vessel vasculitis in children. Although there is no evidence-based recommendations for treating IgAV, the European SHARE recommendations published in 2019 provided international expert consensus for its treatment1. This study aims to explore the treatment and disease follow-up approaches in IgA Vasculitis among pediatricians and pediatric rheumatologists throughout the world, based on the disease presentation, including organ involvement and severity.

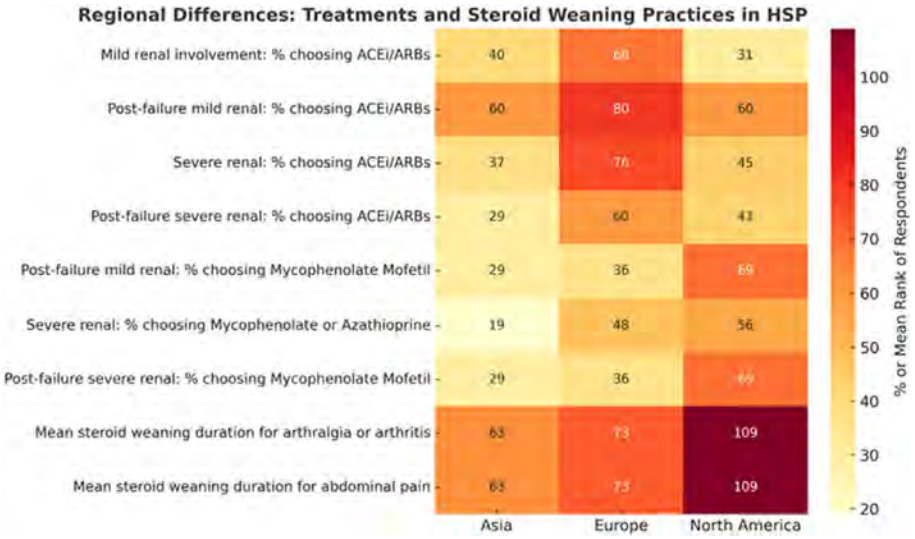
Methods: A 24-question electronic, cross sectional international survey was sent to pediatricians and pediatric rheumatologists through electronic platforms. Responses were anonymous and voluntary. Responses were analyzed for variability by geographic location, gender, experience, subspecialty and practice setting (hospital vs. clinic). 196 pediatricians were included in the analysis, of which 123 were pediatric rheumatologists.

Results: Geographic variability, gender, subspecialty, practice setting and clinical experience were all found to significantly affect the choice of treatment for HSP (Figure 1). Geographic location showed the greatest variability (Figure 2), followed by subspecialty (Figure 3). For example, in cases of severe gastrointestinal (GI) symptoms, the administration of high-dose Methylprednisolone IV at 30 mg/kg/day for three days, followed by tapering was more common in North America compared to Asia and Europe (p=0.043). For mild GI symptoms, pediatric rheumatologists were less likely to choose NSAIDs compared to general pediatricians (p=0.024) and preferred hydration and rest (p=0.024). Practice setting influenced treatment choices, with hospital-based physicians favoring IV steroids for severe GI and renal involvement more than clinic-based physicians (p=0.032). Gender was shown to have a limited impact, with minor differences noted in specific GI treatments. Clinical experience primarily affected steroid tapering duration, with more experienced physicians favoring shorter tapering periods (p=0.03).

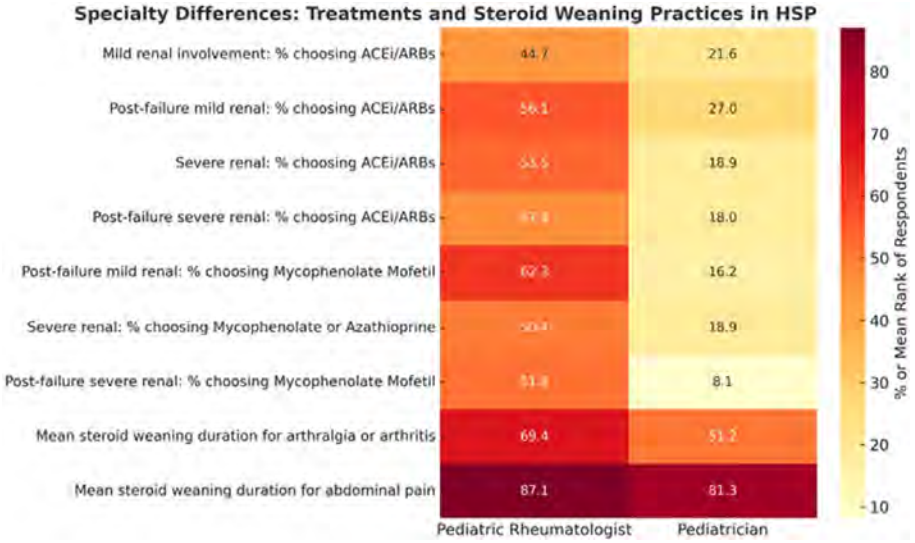


The Statistically significant associations identified for each physician characteristic (out of 28 analyses). Geographic region (19/28) and medical specialization (18/28) showed the strongest effect on the treatment choices, while gender, experience, practice setting, and age had minimal impact.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Selected treatment questions demonstrating significant differences between geographic regions of the replying physicians. In cases of renal involvement, European physicians showed higher preference for ACE inhibitors/ARBs, while North American physicians preferred MMF and longer steroid tapering.



Selected treatment questions demonstrating significant differences between rheumatologists and general pediatricians. Rheumatologists reported higher use of ACE inhibitors/ARBs and MMF, along with a tendency toward longer steroid tapering.

Conclusion: To the best of our knowledge, this is the first international study to assess real-world treatment approaches to IgA vasculitis in children. The study reveals significant variability in the treatment preferences for IgAV, affected primarily by geographic location and subspecialty, with lesser contribution of clinical setting, years of practice and gender. These findings highlight the need to develop standardized, evidence-based clinical guidelines to the treatment approach for IgAV, in order to reduce variability and improve the care of children with IgA-Vasculitis.

References: [1]Ozen S, Marks SD, Brogan P, Groot N, de Graeff N, Avcin T, Bader-Meunier B, Dolezalova P, Feldman BM, Kone-Paut I, Lahdenne P. European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative. Rheumatology. 2019 Sep 1;58(9):1607-16.

Disclosure: M. Heshin Bekenstein: None; **T. Elbaz**: None; **Y. Illous**: None; **B. Kandell**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2538

Comparative Study of Two Classification Criteria Sets in Real Clinical Practice in Behçet's Disease

Rafael Gálvez Sánchez[1], José Luis Martín-Varillas[2], Lara Sánchez Bilbao[3], Ivan Ferraz Amaro[4], Carmen Lasa Teja[5], Elena Aurrecoechea[6], Diana Prieto-Peña[7] and Ricardo Blanco[3], [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander , Spain, Santander, Spain, [2]Rheumatology Division, Hospital de Laredo. IDIVAL, Immunopathology Group. Santander, Spain., Laredo, Spain, [3]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain, [4]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [5]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Riotuerto, Cantabria, Spain, [6]Hospital Sierrallana, CANTABRIA, Spain, [7]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet´s Disease (BD) was traditionally classified according to the International Study Group (ISG) in which oral ulcers were mandatory. International Team for the Revision of the International Criteria for BD (ITR-ICBD)are based on a scoring system. Our aim was to assess **a)** the sensitivity and **b)** the concordance between ISG and the ICDB criteria in global and severe ocular, vascular and neurological) BD.

Methods: Patients diagnosed with BD by expert rheumatologists in a well-defined population in Northern Spain between January 1980-November 2023 were studied. Both ISG and ICBD criteria were compared. Sensitivity and concordance were evaluated using two statistical methods: the Prevalence-Adjusted and Bias-Adjusted Kappa (PABAK), which accounts for the effects of prevalence and bias, and the unadjusted Cohen's Kappa coefficient.

Results: We studied 142 patients diagnosed with BD by expert rheumatologists (73 men, mean age: 36.4±13.9 years). Among them, 84 fulfilled the ISG criteria and 116 met the ICBD criteria, **figure 1** shows the overlap between expert diagnosis and the two classification systems. **a)** The sensitivity of the ISG and ICBD criteria in the overall cohort was 59.1% and 81.6%, respectively. Among patients with severe manifestations (ocular, vascular, or neurological), sensitivity increased to 71.2% for ISG and 92.5% for ICBD as shown in **figure 2**. **b)** The overall concordance between the two criteria was moderate, with a Kappa of 0.490 (95% CI: 0.356–0.623), and 70.4% of patients classified identically. When adjusting for prevalence and bias, concordance improved slightly (PABAK = 0.549). The highest agreement between classification criteria was observed when ocular involvement was deliberately added to all patients in the cohort (PABAK = 0.788; Kappa = 0.405), whereas the lowest agreement occurred when vascular involvement was added (PABAK = 0.338; Kappa = 0.216) (**figure 3**).

Conclusion: Sensitivity of the ICBD criteria was higher than the traditional ISG criteria in classifying BD, particularly in severe cases. Greater differences in concordance between both diagnostic criteria for BD were found when modifying the ocular involvement variable.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

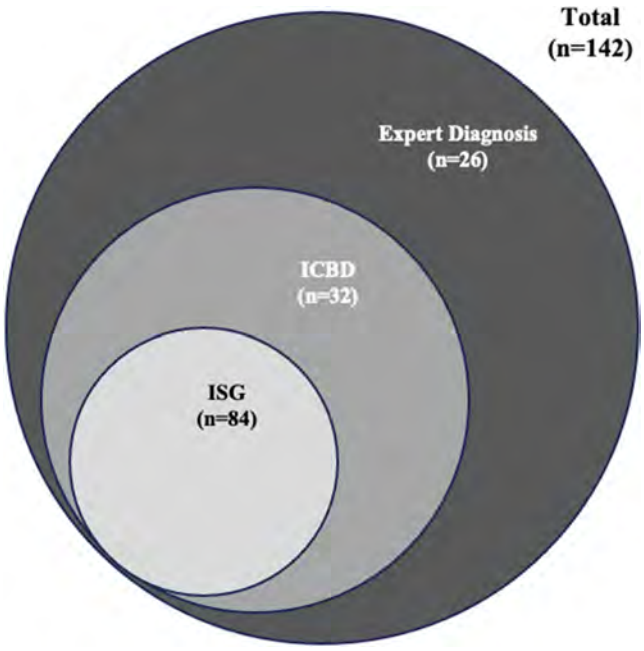


Figure 1: Overlap of Behçet's Disease cases detected by Expert Diagnosis, ICBD, and ISG criteria. The Venn diagram shows the unique and shared cases among the three methods.

	ISG	ICBD
Sensitivity (%)	59.1	81.6
Sensitivity in Severe BD (%)	71.2	92.5
Specific agreement + (%)	84.0 (78.3 - 88.4)	
Specific agreement - (%)	61.9 (51.2 - 71.6)	
Global agreement (%)	77.5 (69.9 - 83.6)	
Kappa (95% CI)	0.490 (0.356 - 0.623)	
PABAK	0.549	

Figure 2: Comparison of ISG and ICBD classification criteria performance in Behçet's Disease.

Condition	Kappa (95% CI)	PABAK
Ocular (added)	0.405 (0.176 - 0.634)	0.788
Ocular (removed)	0.443 (0.326 - 0.561)	0.408
Vascular (added)	0.216 (0.103 - 0.330)	0.338
Vascular (removed)	0.559 (0.427 - 0.690)	0.605
Neurological (added)	0.235 (0.118 - 0.353)	0.352
Neurological (removed)	0.507 (0.374 - 0.640)	0.563

Figure 3. Variation in concordance between ISG and ICBD classification criteria when each severe manifestation is systematically added to or removed from all 142 patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: R. Gálvez Sánchez: None; **J. Martín-Varillas**: AbbVie, Pfizer, Lilly, Celgene, Janssen, and UCB Pharma, 5; **L. Sánchez Bilbao**: AbbVie/Abbott, 6, Eli Lilly, 6, Janssen, 6, UCB, 6; **I. Ferraz Amaro**: None; **C. Lasa Teja**: None; **E. Aurrecoechea**: None; **D. Prieto-Peña**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2539

Patient-reported outcomes in patients with polymyalgia rheumatica under rheumatology care: baseline data from the ENRICH-PMR cohort

Sebastian E Sattui[1], Amy Mudano[2], Yujie Su[2], Sandeep Sodhi[3], Fenglong Xie[4], Iris Navarro-Millan[5], Robyn Domsic[6] and Jeffrey Curtis[7], [1]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, [2]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [3]Illumination Health, Hoover, AL, [4]The University of Alabama at Birmingham, Birmingham, AL, [5]Weill Cornell Medicine, Hospital for Special Surgery, Poughkeepsie, NY, [6]University of Pittsburgh, Pittsburgh, PA, [7]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Worse health-related quality of life has been reported in individuals with polymyalgia rheumatica (PMR), yet the factors contributing to this burden – including the impact of glucocorticoids (GC) and GC-sparing agents – remain poorly understood. Longitudinal cohort studies incorporating patient-reported outcomes (PROs) can provide valuable insights to guide more patient-centered treatment. The objective of this study was to describe the baseline characteristics and PROs of patients in the ENRICH-PMR cohort, an ongoing longitudinal cohort of patients with PMR under rheumatology care.

Methods: A prospective cohort of patients with PMR was created within the Excellence Network in Rheumatology to Innovate Care and High-impact research (ENRICH), the largest US community-based, embedded, practice-based research network. Patients with a diagnosis of PMR routinely cared for in offices with access to a customizable in-office tablet app (I-PRO) deployed at routinely scheduled visits were invited to participate. The baseline I-PRO survey included information on date of diagnosis and current dose of GC use. Demographics, body mass index, and GC-sparing agent use was collected from electronic medical records. Comorbidities were identified using the RxRisk index, a validated medication-based measure of comorbidity.

PROs collected quarterly included 3 PROMIS measures: physical function, pain interference, and fatigue; PROMIS sleep and depression were collected annually. RAPID-3 was used to assess disease activity, and data on Patient Acceptable Symptom State (PASS) was collected to assess patients' perception of their health state. For this analysis, the most recent PROs available (i.e., closest to the time of enrollment) were included. Descriptive statistics were used to summarize the cohort and compare PROs by sex, using standardized mean differences (SMD) >0.10 to identify those that are likely clinically relevant.

Results: Between April and October 2024, 1,182 PMR patients completed the baseline survey. Most were female (64.8%), white (82.05), with mean (SD) age of 73.7 (9.1); nearly half were age ≥75. Over one-quarter (28.8%) were within two years of PMR diagnosis. The mean (SD) number of comorbidities was 7.8 (3.7). More than half (56.6%) were receiving GCs, and a majority (xx%) were on a GC-sparing agent, most commonly methotrexate.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with PMR in the ENRICH-PMR cohort with PRO data available

Characteristic	Total (n = 1,182)
Age, mean (SD)	73.7 (9.1)
Age, categories,	
<50	1 (0.1%)
50-64	195 (16.5%)
65-75	399 (33.8%)
≥75	587 (49.7%)
Sex, female	766 (64.8%)
Ethnicity/Race	
Hispanic	39 (3.3%)
White	969 (82.0%)
Black or African American	49 (4.1%)
Other/Unknown	125 (10.6%)
BMI, kg/m^2	
<18.5	15 (1.3%)
18.5-24.9	351 (30.4%)
25.0-29.9	400 (34.6%)
30.0-34.9	244 (21.1%)
≥35.0	146 (12.6%)
Census Region	
Midwest	147 (12.4%)
Northeast	35 (3.0%)
South	742 (62.8%)
West	258 (21.8%)
Years of EHR observation, median (Q1, Q3)	
Index date (recruitment) to last visit, median (IQR)	0.5 (0.2, 0.8)
First visit to last visit in the data, median (IQR)	3.2 (1.7, 5.4)
Time since PMR diagnosis, years	
<1	105 (8.9)
1-2	235 (19.9)
2-5	427 (36.1)
5-10	307 (26.0)
>10	108 (9.1)
Health Insurance	
Medicare	401 (37.4)
Medicare Advantage	138 (12.9)
Medicaid	3 (0.3)
Commercial	510 (47.5)
VA/Other Government	16 (1.5)
None	5 (0.5)
Area deprivation index (ADI)	
Mean (SD)	40.2 (25.2)
ADI ≥80th percentile (i.e. most deprived)	105 (9.3)
Number of comorbidities, RxRisk Categories, mean (SD)	7.8 (3.7)
Comorbidities	
Osteoporosis/Paget's	356 (30.1)
Hypertension	463 (39.2)
Hyperlipidemia	615 (52.0)
Diabetes	227 (19.2)
Ischemic heart disease	505 (42.7)
Heart failure	649 (54.9)
Malignancy	114 (9.6)
Chronic Pulmonary Disease	217 (18.4)

Data presented as n(%), unless specified otherwise.
SD = standard deviation, VA = Veterans affair

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Current treatment in patients with PMR at time of inclusion in cohort (n=1182)	
Medication	N (%)
Glucocorticoids, any use	669 (56.6%)
Current glucocorticoid dose (mg/day) [among users]	
<2.5	174 (26.0%)
2.5 - <5	187 (28.0%)
5 - <7.5	151 (22.6%)
7.5 - <10	56 (8.4%)
10 - <15	63 (9.4%)
15 - <20	21 (3.1%)
≥20	17 (2.5%)
Conventional immunosuppressive medication	
Methotrexate	297 (24.2%)
Hydroxychloroquine	201 (16.4%)
Leflunomide	67 (5.5%)
Sulfasalazine	30 (2.4%)
Azathioprine	16 (1.3%)
Biologics	
Sarilumab	79 (6.4%)
Tocilizumab	58 (4.7%)
Rituximab	6 (0.5%)
Janus Kinase Inhibitors*	19 (1.6)
*Included tofacitinib and upadacitinib.	

Compared to males, female patients had a worse RAPID-3. Similarly, female patients reported lower physical function (41.3 (9.2) vs 44.9 (9.3), respectively) and greater pain interference (56.4 (9.2) vs 53.3 (8.3), respectively) as measured by PROMIS scores. This difference was clinically relevant based on SMDs >0.10. Overall, 37.0% of the cohort reported their current health state, as affected by PMR, to not be acceptable.

Conclusion: This baseline data from a large, prospective cohort of patients with PMR under rheumatology care shows that PMR patients experience a substantial impact of their disease across multiple PRO domains, and more than one-third express dissatisfaction with their current symptom state. Ongoing analyses will examine factors associated with worse PROs to inform more personalized PMR management strategies.

Table 3. Patient-reported outcomes by sex				
PRO (n)	All PMR patients, mean (SD)	Female, mean (SD)	Male, mean (SD)	SMD (95% CI)*
RAPID-3 (n = 1,182)	10.2 (6.3)	11.1 (6.2)	8.4 (6.1)	0.45 (0.33, 0.58)
Patient Global Scale (n = 1,182)	4.1 (2.6)	4.5 (2.6)	3.5 (2.6)	0.38 (0.26, 0.50)
PASS* (n = 1,182)	745 (63.0%)	467 (61.0%)	278 (66.8%)	-0.12 (-0.24, 0.00)
PROMIS domains**				
Physical function (n = 1,020)	42.6 (9.4)	41.3 (9.2)	44.9 (9.3)	-0.39 (-0.52, -0.26)
Pain interference (n = 508)	55.4 (9.0)	56.4 (9.2)	53.3 (8.3)	0.36 (0.17, 0.54)
Fatigue (n = 256)	50.5 (10.4)	52.0 (10.6)	47.7 (9.4)	0.43 (0.17, 0.69)
Depression (n = 1,117)	47.6 (9.5)	48.7 (9.8)	45.7 (8.5)	0.33 (0.20, 0.45)
Sleep Disturbance (n = 880)	50.2 (8.4)	50.9 (8.8)	49.0 (7.5)	0.23 (0.09, 0.37)

PASS = Patient acceptable symptom state; PROMIS = Patient-Reported Outcomes Measurement Information System; SMD = Standardized Mean Difference; CI = confidence interval
*SMDs > 0.10 indicate differences that are likely clinically relevant
** PROMIS domains are scored on a 1-100 scale and have mean of 50 and SD of 10. Scores within 5 units (i.e. ≥45 for PROMIS Physical function) and ≤55 for all other PROMIS domains, are considered normal.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: S. Sattui: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2; **A. Mudano**: None; **Y. Su**: None; **S. Sodhi**: None; **F. Xie**: None; **I. Navarro-Millan**: None; **R. Domsic**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, Bendcare, 5, Bristol-Myers Squibb(BMS), 5, Corrona, 2, 5, Crescendo, 2, 5, Eli Lilly, 2, 5, FASTER, 2, 4, Genentech, 2, 5, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, 5, Moderna, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2540

Monocyte-to-High-Density Lipoprotein Cholesterol Ratio as a Clinical Marker of Gastrointestinal Involvement in Behçet Syndrome

Hansun Song, **Seong-Ryul Kwon** and Mie Jin Lim, College of Medicine, Inha University, Incheon, Republic of Korea

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Behçet syndrome (BS) is a chronic multisystem vasculitis marked by recurrent mucocutaneous and ocular inflammation, and in a subset of patients, gastrointestinal (GI) involvement. Gastrointestinal BS (GIBS) is a clinically important phenotype due to its potential for severe morbidity and its diagnostic overlap with other inflammatory bowel disorders. Timely identification of GIBS remains a clinical challenge, often requiring invasive procedures such as colonoscopy. Thus, there is growing interest in identifying noninvasive biomarkers that can aid in risk stratification and guide diagnostic decision-making. The monocyte-to-high-density lipoprotein cholesterol ratio (MHR), reflecting both systemic inflammation and lipid-related oxidative stress, has emerged as a potential biomarker in several immune-mediated diseases. However, its utility in Behçet syndrome, particularly in detecting GI involvement, has not been established. This study aimed to evaluate the clinical significance of MHR in identifying gastrointestinal involvement in BS patients.

Table 1. Comparison of Inflammatory Parameters Between Behçet Syndrome Patients With and Without Gastrointestinal Involvement This table summarizes the results of independent t-tests comparing inflammatory markers between patients with gastrointestinal involvement (GI BS) and those without. Monocyte count and monocyte-to-high-density lipoprotein cholesterol ratio (MHR) were significantly higher in GI BS patients. HDL levels and monocyte percentage showed trends toward significance. Statistical significance was set at $p<0.05$. CI: confidence interval; HDL: high-density lipoprotein; MHR: monocyte-to-HDL ratio; WBC: white blood cell count.t-test results comparing GI BS and non-GI BS patients

GI BS	P-value	95% C.I	
WBC	0.113	-235.3	2154.83
Monocyte ratio in %	0.062	-0.045	1.81
Monocyte count	**0.011**	**25.06**	**180.73**
HDL	0.073	-14.4	0.66
MHR	**0.002**	**1.56**	**6.44**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We retrospectively analyzed 2,074 patients with BS registered in the Clinical Data Warehouse of Inha University Hospital from January 1997 to December 2024. Diagnosis was based on the ISG (1990) and ICBD (2013) criteria. Patients were included if they underwent colonoscopy at or after diagnosis and had HDL cholesterol measured at a time point close to the colonoscopy. Exclusion criteria were infectious colitis, malignancies, or MHR data obtained outside the clinically relevant time window. MHR was calculated by dividing absolute monocyte count (/mm^3) by HDL cholesterol (mg/dL). Statistical analysis was performed using independent t-tests, with $p< 0.05$ considered significant.

Results: Among 86 eligible patients, 34 (39.5%) exhibited GI involvement. MHR was significantly higher in GIBS patients than in those without GI involvement (p=0.002, 95% CI: 1.56–6.44, Table1). Monocyte counts were also elevated in the GIBS group (p=0.011), particularly among males (p=0.021), while no significant difference was observed in females (p=0.081). HDL levels alone were not significantly different. These findings suggest that MHR, rather than its individual components, more accurately reflects the inflammatory burden associated with GI manifestations in BS.

Conclusion: MHR was associated with gastrointestinal involvement in Behcet syndrome patients. It can be utilized as a marker for identifying high-risk patient group in Behcet syndrome patients.

Elevated MHR is significantly associated with gastrointestinal involvement in Behçet syndrome and may serve as a clinically relevant, noninvasive marker for identifying high-risk patients. Given its accessibility, cost-effectiveness, and correlation with inflammatory burden, MHR may aid in early detection and risk-based decision-making in the management of GIBS. Validation in prospective studies could support its integration into clinical practice as a screening and monitoring tool.

Disclosure: H. Song: None; **S. Kwon**: None; **M. Lim**: None.

Abstract Number: 2541

Development of Severity Classification Criteria for Introduction of Infliximab for Chronic Pogressive Neuro-Behçet's Disease

Shunsei Hirohata[1], Hirotoshi Kikuchi[2], Tetsuji Sawada[3], Toshihiro Tono[4], Mitsuhiro Takeno[5] and Izumi Kawachi[6], [1]Nobuhara Clinic, Tokyo, Japan, [2]Teikyo University School of Medicine, 3-12-1 1308, Japan, [3]Tokyo Medical University, Tokyo, Japan, [4]Kitasato University School of Medicine, Kanagawa, Japan, [5]Nippon Medical School Musashi Kosugi Hospital, Kawasaki, Japan, [6]Niigata University Graduate School of Medicine and Dental Sciences and Niigata University Brain Institute, Niigata, Japan

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Chronic progressive neuro-Behçet's disease (CPNB) is characterized by progressive deterioration leading to disability and death. It has been appreciated that methotrexate (MTX) has beneficial effects for CPNB. Moreover, recent studies have demonstrated that infliximab (IFX) is effective for patients who had inadequate responses to MTX. However, it is unclear which patients should be treated and how, especially on the initiation of treatment. Thus, clinical markers of the severity would be helpful for decisions on treatment strategies. We therefore tried to determine severity classification criteria for introduction of IFX in patients with CPNB.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

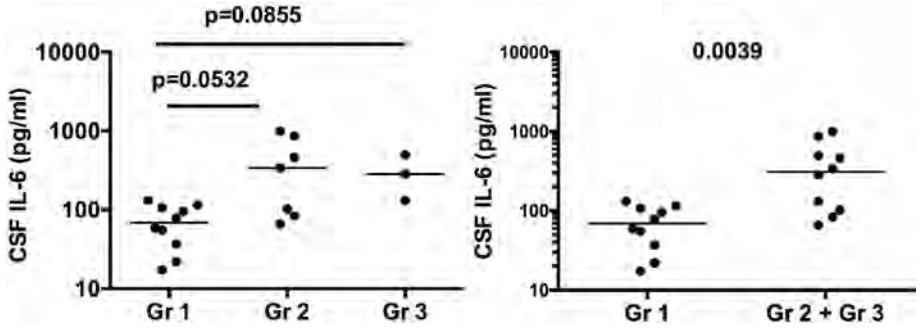


Figure 1 CSF IL-6 in 3 provisional severity groups.

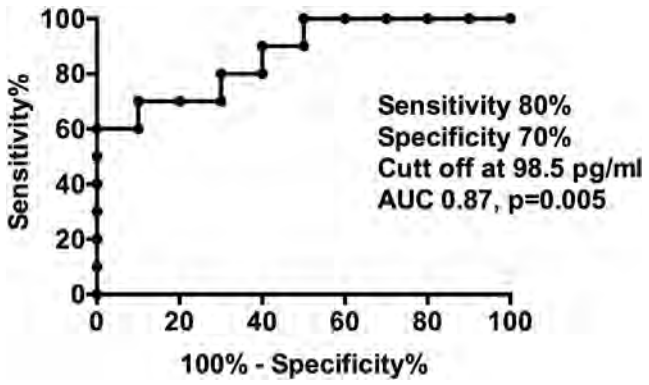


Figure 2 ROC analysis for CSF IL-6 between Gr 1 and combined Gr 2 + Gr 3.

Methods: Twenty-six patients with CPNB (19 males, 7 females, ages 47.7±15.6 years [mean±SD]), who had been collected in a multicenter study by the Japanese Research Committee from 2011 to 2013, were followed up for 6-216 months (median 93.0 months). The provisional severity levels were retrospectively determined according to treatment regimens and responses of the patients, such as - Group (Gr)1: no progression with MTX alone, Gr 2: no progression with combined MTX and IFX, Gr 3: progression even with combination of MTX and IFX. Cerebrospinal fluid (CSF) IL-6 levels and brain MRI findings before starting treatment, and progressions of neurobehavior manifestations after treatment were evaluated. The relationship between these parameters and provisional severity levels was examined retrospectively. Based on the results, new severity criteria were established.

Results: CSF IL-6 was significantly lower in Gr 1 than in combined Gr 2+ Gr 3 (p=0.0039), despite no significant difference among the 3 groups (**Figure 1**). ROC analysis disclosed that a cut-off of 98.5 pg/ml of CSF IL-6 discriminated between Gr 1 and combined Gr 2+ Gr 3 with 80% sensitivity and 70% specificity (AUC 0.87, p=0.005) (**Figure 2**). On the other hand, 3 patients among the 26 patients lacked brainstem atrophy on MRI, in whom no progression of symptoms was observed. Thus, the severity of CPNBD (stage 1-3) was formulated according to the presence of brainstem atrophy and the elevation CSF IL-6 over 99.0 pg/ml (**Table**). The higher stage tended to be associated with the progression in the 26 patients (p=0.0925).

Table Suggested severity criteria for CPNBD

Stage 1: brainstem atrophy (-)
Stage 2: brainstem atrophy (+) and CSF IL-6 below 99.0 pg/ml
Stage 3: brainstem atrophy (+) and CSF IL-6 over 99.0 pg/ml

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The severity classification criteria for CPNB, developed based on the presence of brainstem atrophy and the elevation of CSF IL-6 (over 99.0 pg/ml), were considered useful in determining treatment strategy. Thus, MTX alone would be recommended in stage 1, whereas combination of MTX and IFX should be considered in Stage 3. As for patients in stage 2, IFX should be considered for patients with persistent CSF IL-6 over 99.0 pg/ml despite increased doses of MTX.

Disclosure: S. Hirohata: None; **H. Kikuchi**: None; **T. Sawada**: None; **T. Tono**: None; **M. Takeno**: None; **I. Kawachi**: None.

Abstract Number: 2542

A Rule Based NLP Pipeline for Glucocorticoid Exposure

Simran Nimal[1], Megan Sullivan[1], Christopher Conyers[2], Joseph Rosen[1], Christopher Grilli[1], Kenneth Warrington[3] and Victor E Ortega[1], [1]Mayo Clinic Arizona, Scottsdale, AZ, [2]Mayo Clinic Arizona, Scottsdale-85259, AZ, [3]Mayo Clinic, ROCHESTER, MN

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

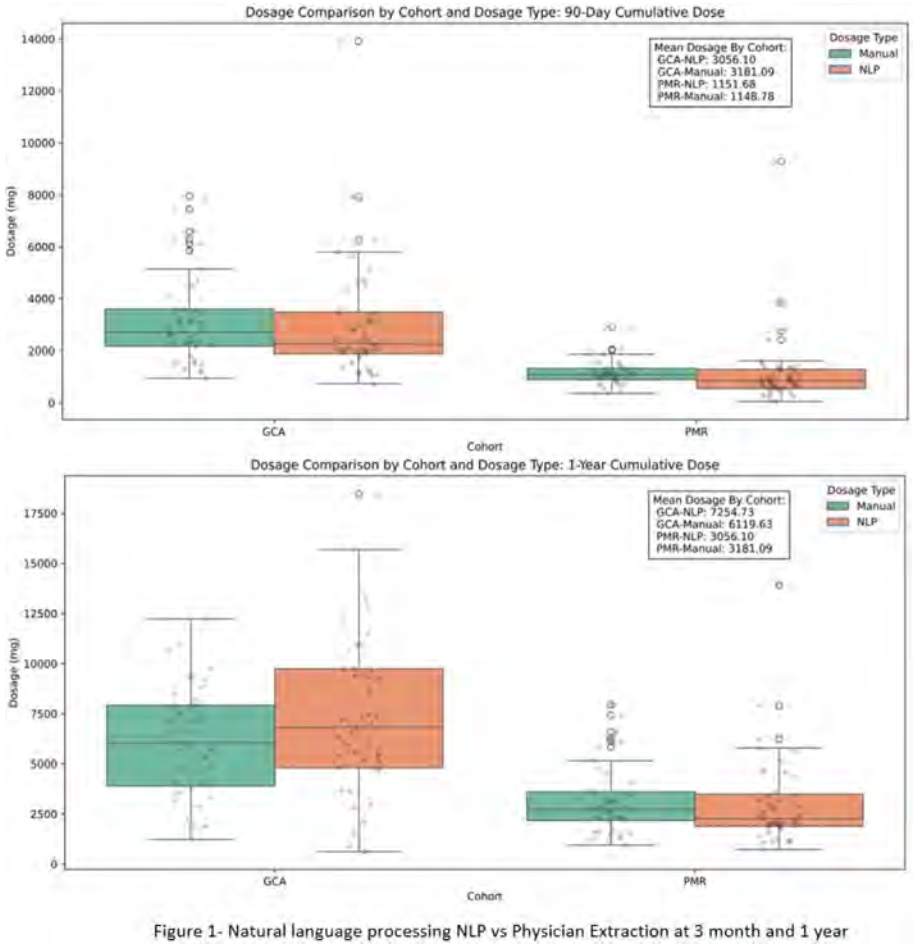


Figure 1- Natural language processing NLP vs Physician Extraction at 3 month and 1 year

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

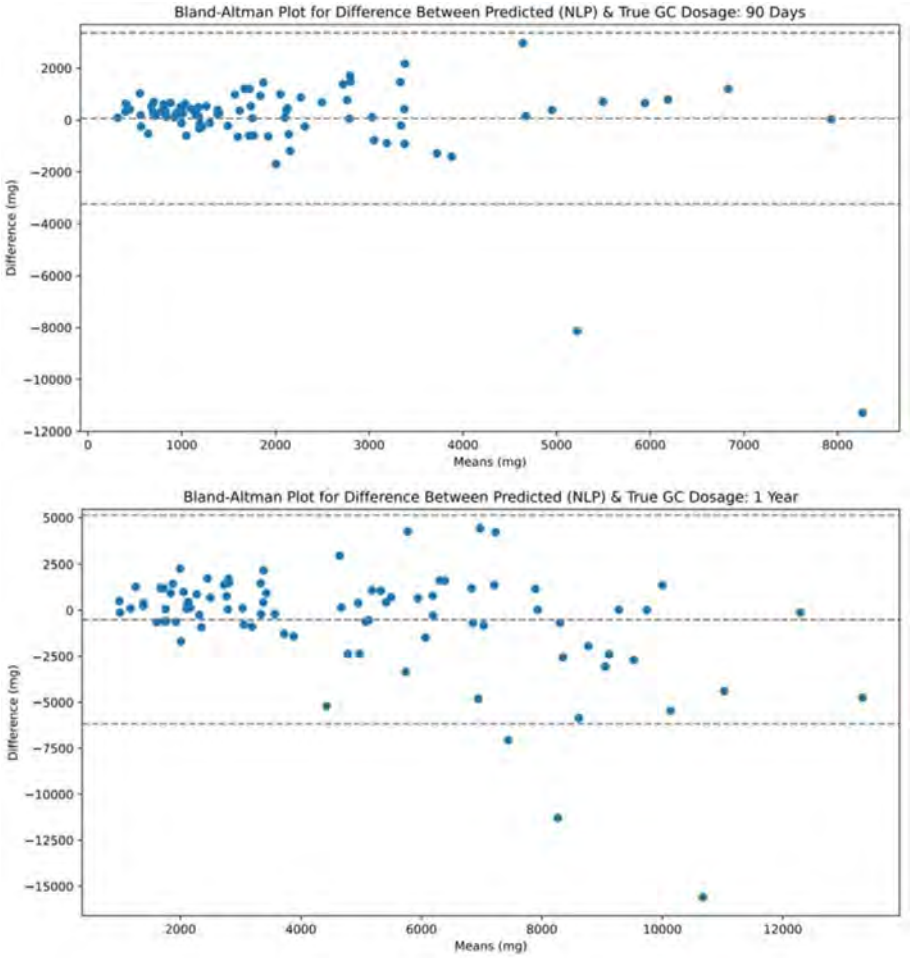


Figure 2 - Bland Altman Plot of NLP model vs physician-extracted data at 3 months and 1 year

Figure 2 - Bland Altman Plot of NLP model vs physician-extracted data at 3 months and 1 year

Background/Purpose: Glucocorticoids (GCs) are essential for managing giant cell arteritis (GCA) and polymyalgia rheumatica (PMR), but prolonged use poses risk due to cumulative dosing and side effects. (1) Accurate tracking of GC exposure is vital, yet electronic medical record (EMR) documentation is often inconsistent. (2) A meta-analysis of 25 studies found that the mean cumulative GC dose over one year was up to 5600 mg for PMR and 8200 mg for GCA patients. (3) We propose a natural language processing (NLP) tool to standardize GC data extraction from EMRs, an advancement over prior tools to improve care and research. (4)

Methods: Patients > 50 years of age with an ICD code for GCA or PMR were identified. Individuals without prescription GC coverage for > 75% of the first year, defined as 365 days following the initial ICD code entry, were excluded. A rule-based NLP model was created using EMR data to calculate systemic prednisone and methylprednisolone doses over time. Methylprednisolone doses were transitioned into prednisone equivalent doses at a 4:5 ratio. A validation cohort of 89 patients was created where a clinician performed chart review and documented dosage changes over time. Cumulative GC dose was estimated at 3 months and 12 months and model error recorded. The model was then applied to the entire cohort to record the average 90 day and 1-year cumulative GC dose.

Results: 956 patients met inclusion criteria. Of these, 714 had isolated PMR and 242 had GCA. 89 patients (45 GCA and 44 isolated PMR) were included for comparison of the model to physician-extracted data. The NLP-driven model compared to EMR data extracted by a physician revealed a mean relative error rate of 0.25% and 3.93% at 3 and 12 months for isolated PMR, respectively, with rates of 11.89% and 18.55% for GCA (**Figure 1)**. Bland-Altman plots in **Figure 2** showed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

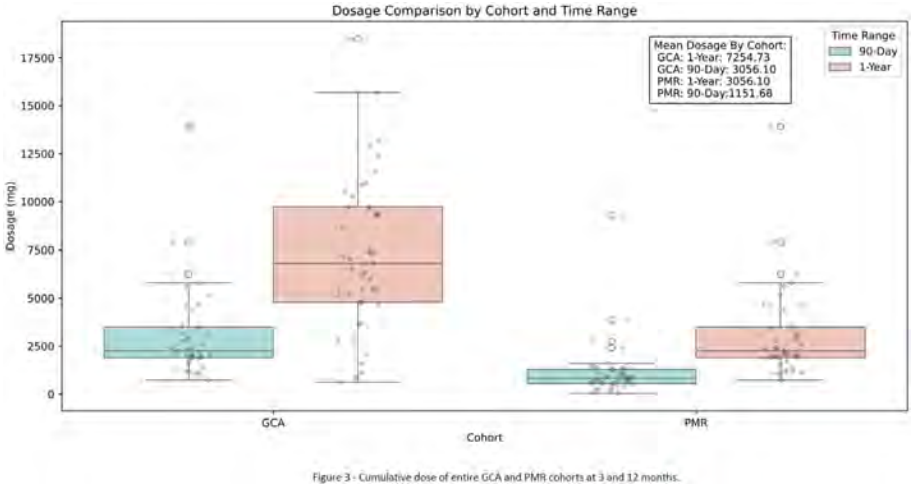


Figure 3 - Cumulative dose of entire GCA and PMR cohorts at 3 and 12 months.

low systemic bias (90 day mean difference 61.0, 95% CI -295.4 to 417.47; 1 year mean difference -512.1, 95% -1119.1 to 94.8). The mean cumulative full cohort dose is described in **Figure 3**.

Conclusion: The mean 1-year cumulative GC doses observed in our cohort for GCA and PMR are consistent with previous studies. An NLP-based model is a valid approach for estimating GC exposure over time. This can have relevance in large datasets and EMR's where GC doses have been difficult to calculate.

References:

1. González-Gay MA BR, Rodríguez-Valverde V, Martínez-Taboada VM, Delgado-Rodriguez M, Figueroa M, Uriarte E. Permanent visual loss and cerebrovascular accidents in giant cell arteritis: predictors and response to treatment. 1998.
2. Cohen GR FC, Ryan AM, Richardson CR, Adler-Milstein J. Variation in Physicians' Electronic Health Record Documentation and Potential Patient Harm from That Variation. J Gen Intern Med. 2019.
3. Lai LYH HE, West RM, Mackie SL. Association between glucocorticoid therapy and incidence of diabetes mellitus in polymyalgia rheumatica and giant cell arteritis: a systematic review and meta-analysis. RMD Open. 2018.
4. Hannah L Weeks CB, Elizabeth McNeer, Michael L Williams, Cosmin A Bejan, Joshua C Denny, Leena Choi. medExtractR: A targeted, customizable approach to medication extraction from electronic health records. Journal of the American Medical Informatics Association.

Disclosure: S. Nimal: None; **M. Sullivan**: None; **C. Conyers**: None; **J. Rosen**: None; **C. Grilli**: None; **K. Warrington**: Bristol-Myers Squibb(BMS), 5, Sanofi, 2; **V. Ortega**: None.

Abstract Number: 2543

Severe Visual Impairment in Behçet Syndrome in Time: A Comparison of Four Time Periods

Mustafa Erdogan[1], Koray Tascilar[2], Yagmur Ersoya[3], Alp Ozcan[4], Mert Gurcan[4], Talal Ammar[4], **Sinem Nihal Esatoglu**[5], Yesim Ozguler[5], Gulen Hatemi[5] and Hasan Yazici[6], [1]Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine, Department of Internal Medicine, Division of Rheumatology / Marmara University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [2]Friedrich Alexander University of Erlangen Nuremberg, Universitätsklinikum Erlangen Department of Medicine 3, Rheumatology and Immunology, Erlangen, Germany, [3]Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine, Department of Internal Medicine, Istanbul, Turkey,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[4]Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine, Istanbul, Turkey, [5]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey, [6]Academic Hospital, Istanbul, Turkey

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: There is consensus that the visual prognosis in Behçet syndrome (BS) uveitis has considerably improved in time (1-3). We wanted to better quantitate this impression. To tabulate the prognosis of Behçet syndrome uveitis in the previous four decades in a dedicated BS outpatient clinic by utilizing a severe and irreversible visual acuity impairment definition as the main outcome measure.

Methods: Medical records of 9289 BS patients registered between the years 1976 and 2019 were screened for the presence of uveitis and severe visual impairment (SVI). SVI was defined as an irreversible visual acuity of ≤20/200 for at least 3 months. A standard form was used for retrieving data on demographics, clinical features, visual acuity, and treatments. Records with no or inadequate data (n=527) were excluded. The remaining 8762 patients were analyzed in 4 different time

Table 1. Visual outcome in male patients with Behçet uveitis

	GROUP 1 (1972-1989)	GROUP 2 (1990- 1999)	GROUP 3 (2000-2009)	GROUP 4 (2010-2019)
Number of BS patients	778	1518	1830	1152
Patients with uveitis, n/N (%)	524/778 (67.4)	819/1518 (54)	970/1830 (53)	630/1152 (54.7)
Number of patients without uveitis at registration	3/524	3/819	1/970	0/630
Patients with bilateral SVI at registration n/N (%)	50/524 (9.5)	59/819 (7.2)	43/970 (4.4)	24/630 (3.8)
Patients with initial unilateral SVI who developed bilateral SVI during follow up, n/N (%)	30/474 (6.3)	34/760 (4.5)	14/927 (1.5)	5/606 (0.8)
*at first year, n/N (%)**	*17/467 (3.6)*	*20/752 (2.7)*	*9/921 (1)*	*3/603(0.5)*
*at third year, n/N (%)***	*25/450 (5.6)*	*26/739 (3.5)*	*13/907 (1.4)*	*3/595 (0.5)*
Patients without SVI in either eye who developed bilateral SVI during follow-up, n/N (%)	24/474 (5.1)	18/760 (2.4)	6/927 (0.6)	1/606 (0.2)
*at first year, n/N (%)**	*10/467 (2.1)*	*8/752 (1.1)*	*2/921 (0.2)*	*1/603 (0.2)*
*at third year, n/N (%)***	*15/450 (3.3)*	*13/739 (1.8)*	*2/907 (0.2)*	*1/595 (0.2)*

All percentages were calculated among the patients without initial bilateral SVI
* Patients who were followed for less than a year were excluded from the analysis ** Patients who were followed for less than 3 years were excluded from the analysis

Table 2. Visual outcome in female patients with Behçet uveitis

	GROUP 1 (1972-1989)	GROUP 2 (1990- 1999)	GROUP 3 (2000-2009)	GROUP 4 (2010-2019)
Number of BS patients	416	899	1244	925
Patients with uveitis, n/N (%)	238/416 (57)	327/899 (36)	537/1244 (43)	364/925 (39)
Number of patients without uveitis at registration	3/238	3/327	1/537	0/364
Patients with bilateral SVI at registration n/N (%)	9/238 (3.8)	11/327 (3.4)	10/537 (1.9)	2/364 (0.5)
Patients with initial unilateral SVI who developed bilateral SVI during follow up, n/N (%)	1/229 (0.4)	4/316 (1.3)	8/527 (1.5)	3/362 (0.8)
*at first year, n/N (%)**	*0*	*2/315 (0.6)*	*5/526 (1.1)*	*2/361 (0.6)*
*at third year, n/N (%)***	*1/228 (0.4)*	*4/311 (1.3)*	*7/524 (1.3)*	*2/361 (0.6)*
Patients without SVI in either eye who developed bilateral SVI during follow-up, n/N (%)	2/229 (0.9)	2/316 (0.6)	1/527 (0.2)	1/362 (0.3)
*at first year, n/N (%)**	*1*	*0*	*0*	*0*
*at third year, n/N (%)***	*1*	*0*	*0*	*0*

All percentages were calculated among the patients without initial bilateral SVI
* Patients who were followed for less than a year were excluded from the analysis ** Patients who were followed for less than 3 years were excluded from the analysis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

periods according to the first registration year (G1:< 1990, G2: 1990- 1999, G3:2000-2009, G4:2010-2019). Men and women were analyzed separately.

Results: A total of 4409/8762 (50.3%) BS patients had uveitis during their disease course, and 776 /4409 (17.6%) of whom had SVI in either or both eyes. Among the patients who had SVI, 767 had uveitis at the time of the registration, as shown in Tables 1 and 2. They show that males had more frequent and severe uveitis in all time periods. Since there were a relatively small number of female patients with SVI, the results were formally analyzed only for males. The frequency of SVI decreased in time. This was true both among the patients with no SVI in either eye at the time of registration or the development of the presence of SVI only in one eye at the time of registration. Of particular note is that this decrease was considerably more pronounced among the male BS uveitis patients initially with no SVI, as seen in Table 1. In men, the proportion of patients progressing from unilateral to bilateral SVI was higher in the before-2000 group (64/199, 32%) compared to the after-2000 group (19/118, 16%) [$\chi^2 = 9.8$, $p = 0.002$]. Azathioprine was the most frequently used immunosuppressive, with 46% in G1 and 80-89% among the G2-4 patients. Similarly, no patients had used a-TNF agents in G1, 3 patients in G2, 12% of the patients in G3, and 38% in G4.

Conclusion: These data further emphasize the strikingly different disease course of BS uveitis between males and females. They also confirm the contention that we can currently much more effectively manage BS uveitis. We propose that the SVI definition we use strongly reflects better medical management rather than a milder natural disease course at recent times. This is supported by the more pronounced decrease in the frequency of bilateral SVI over time among BS uveitis patients who initially had no SVI, compared to those with unilateral SVI at the time of their registration in our clinic. Finally, our observations also emphasize that formal drug trials in BS uveitis should either be conducted separately in either sex or include enough patients of either sex to allow a meaningful analysis of the trial outcomes.

Disclosure: M. Erdogan: None; **K. Tascilar**: None; **Y. Ersoya**: None; **A. Ozcan**: None; **M. Gurcan**: None; **T. Ammar**: None; **S. Esatoglu**: None; **Y. Ozguler**: None; **G. Hatemi**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 2, Novartis, 6, Pfizer, 6, UCB, 6; **H. Yazici**: None.

Abstract Number: 2544

Diagnostic value of vein wall thickness measurement for patients with suspected Behçet syndrome

ruken Alcin Bayraktar[1], Yasemin Kayadibi[2], Aysenur Kahveci[2], **Sinem Nihal Esatoglu**[3], Ibrahim Adaletli[2], Yesim Ozguler[3], Melike Melikoglu[3] and Gulen Hatemi[3], [1]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Radiology, Istanbul, Turkey, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Several studies have demonstrated increased venous wall thickness (VWT) in patients with Behçet's syndrome (BS) compared to healthy and diseased control groups. Ultrasonographic measurement of VWT has been proposed as a potential diagnostic tool to differentiate BS from other diseases. However, the diagnostic utility of this method remains controversial. An optimal approach to evaluate the diagnostic value of VWT measurement would be to perform

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics, clinical characteristics, and common femoral vein wall thickness of the patients and the controls

	BS (n=45)	Non-BS (n=39)	Vascular BS (n=30)	Healthy controls (n=36)
Male, n (%)	19 (42)	22 (56)	27 (90)	17 (47.2)
Mean (SD) age, yrs	38.1±11.1	38.9±10.9	42.3 ± 10.9	31.4 ± 7.9
Mean (SD) BMI	26.0 ± 5.1	26.4 ± 5.4	26.1 ± 3.8	24.4 ± 2.9
Smoking history, n (%)	26 (57.8)	20 (51.3)	22 (73.3)	7 (19.4)
Oral ulcer, n (%)	45 (100)	23 (59)	30 (100)	N/A
Genital ulcer, n (%)	33 (73.3)	0	16 (53.3)	N/A
PPL, n (%)	37 (82.2)	16 (431)	20 (66.7)	N/A
Erythema nodosum, n (%)	17 (37.8)	0	11 (36.7)	N/A
Arthritis/arthralgia, n (%)	12 (26.7)	5 (12.8)	3 (10)	N/A
Uveitis, n (%)	19 (42.2)	5 (12.8)	9 (30)	N/A
Lower extremity DVT, n (%)	5 (11.1)	2 (5.1)	30 (100)	N/A
Pathergy, n (%)	13/40 (32.5)	2/38 (5.3)	9/25 (36)	N/A
Median (Q1-Q3) right CFVWT, mm	0.59 (0.53-0.69)	0.57 (0.50-0.66)	0.76 (0.63-0.87)	0.49 (0.47-0.53)
Median (Q1-Q3) left CFVWT, mm	0.60 (0.50-0.68)	0.57(0.49-0.67)	0.71 (0.62 -0.86)	0.48 (0.43 -0.50)

BS: Behçet's syndrome; BMI: Body mass index; CFVWT: Common femoral vein wall thickness; DVT: Deep vein thrombosis; PPL: Papulopustular lesions; Q1-Q3: First-third quartile, SD: Standard deviation

Doppler ultrasonography in patients referred for screening with a suspicion of BS, and determining the sensitivity and specificity based on the measurements of those who are and who are not diagnosed with BS after a multidisciplinary diagnostic work-up.

Methods: All individuals who presented to our clinic for BS screening between May 2023 and December 2023 were included. Additionally, 30 patients with vascular BS and deep vein thrombosis (DVT) and 36 healthy individuals were also enrolled. Two radiologists, blinded to the clinical diagnoses, independently measured the wall thickness of the common femoral vein (CFV), great saphenous vein (GSV), and small saphenous vein (SSV). Results were presented as medians and interquartile ranges, and intergroup comparisons were conducted using the Kruskal–Wallis test.

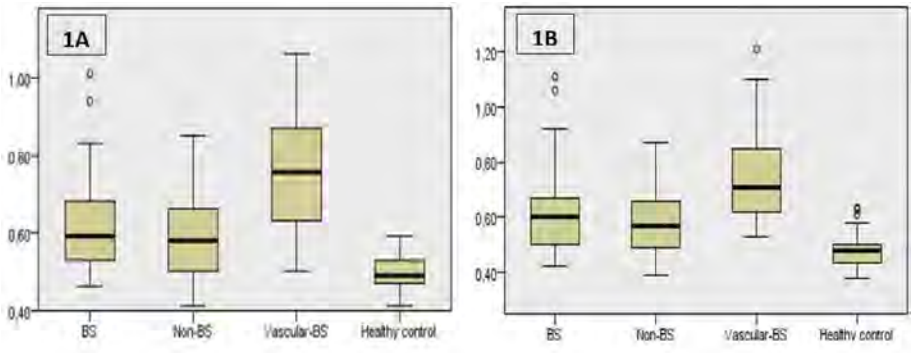


Figure 1. Right and left common femoral vein wall thickness across diagnostic groups

Right (1A) and left (1B) common femoral vein wall thickness in patients diagnosed with Behçet's syndrome after screening, patients diagnosed with non-BS inflammatory conditions, patients with vascular BS under follow-up, and healthy controls.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Among 84 screened individuals, BS was diagnosed in 45 patients, while 39 were found to have non-BS conditions. Lower extremity DVT was present in 5 of the BS patients and in 2 of the non-BS patients. The non-BS group were diagnosed with other conditions including spondyloarthritis, uveitis, inflammatory bowel disease, recurrent aphthous stomatitis, connective tissue diseases, systemic autoinflammatory disorders, and chronic thromboembolic pulmonary hypertension. Compared to other groups, healthy controls were younger, had lower body mass index (BMI), and were less frequently smokers. The highest median CFV thickness was observed in vascular BS patients [right: 0.76 mm (0.63–0.87), left: 0.71 mm (0.62–0.86)], followed by patients diagnosed with BS after screening [right: 0.59 mm (0.53–0.69), left: 0.60 mm (0.50–0.68)], non-BS patients diagnosed after screening [right: 0.58 mm (0.50–0.66), left: 0.57 mm (0.49–0.67)], and healthy controls [right: 0.49 mm (0.47–0.53), left: 0.48 mm (0.43–0.50)]. CFV thickness was significantly higher in vascular BS patients and significantly lower in healthy controls ($p < 0.001$ for all comparisons). However, there was no significant difference between BS and non-BS patients, and this pattern was consistent across other examined veins. This pattern remained unchanged after excluding the 7 patients with a history of lower extremity DVT. Inter-observer reliability between the radiologists was excellent (ICC for right CFV: 0.97; left CFV: 0.96).

Conclusion: Venous wall thickness was higher in both BS and non-BS patients compared to healthy individuals. However, VWT measurement did not aid in differentiating BS from other inflammatory diseases in patients referred for BS evaluation. The significantly increased VWT in vascular BS raises the question of whether this finding reflects vascular inflammation or vascular remodeling.

Disclosure: r. Alcin Bayraktar: None; **Y. Kayadibi**: None; **A. Kahveci**: None; **S. Esatoglu**: None; **I. Adaletli**: None; **Y. Ozguler**: None; **M. Melikoglu**: None; **G. Hatemi**: AbbVie/Abbott, 6, Amgen, 6, Boehringer-Ingelheim, 2, Novartis, 6, Pfizer, 6, UCB, 6.

Abstract Number: 2545

Prevalence, Clinical Correlations and Outcomes of Cryoglobulinemic Vasculitis: a Retrospective Monocentric Study (2013–2023)

Valeria Manfrè[1], elena treppo[2], Maria Pillon[3], Maria De Martino[4], Cinzia Fabro[5], Miriam Isola[4], Martina Fabris[6], Francesco Curcio[6] and Luca Quartuccio[1], [1]Division of Rheumatology, Department of Medicine (DMED), Academic Hospital "Santa Maria della Misericordia", ASUFC, University of Udine, Udine, Italy, Udine, Italy, [2]Division of Rheumatology, Department of Medicine, University of Udine, Udine, Italy, [3]Division of Rheumatology, Department of Medicine, University of Udine, Udine, Italy, Udine, Italy, [4]Institute of Statistics, Department of Medicine, University of Udine, Udine, Italy., Udine, Italy, [5]Division of Rheumatology, Department of Medicine, University of Udine, Udine, Italy., Udine, Italy, [6]Institute of Clinical Pathology, Department of Medicine, University of Udine, Udine, Italy., Udine, Italy

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III

Session Type: Poster Session C

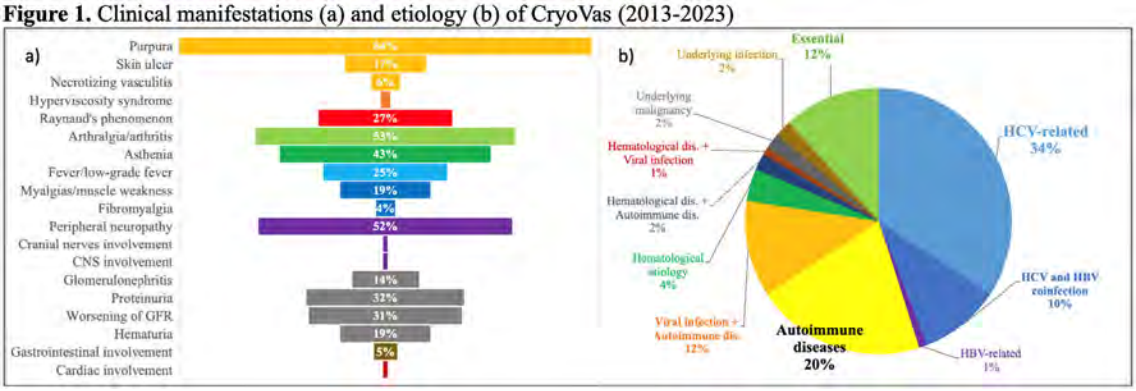
Session Time: 10:30AM–12:30PM

Background/Purpose: Cryoglobulinemic vasculitis (CryoVas) is a rare immune-complex-mediated disorder, often associated with hepatitis C virus (HCV) infection, autoimmune diseases (ADs), or other etiologies. Despite its clinical relevance, data on the prevalence and diagnostic yield of cryoglobulin testing remain scarce.

This study aims to evaluate the prevalence, clinical manifestations, outcomes, and underlying etiologies of CryoVas among patients with positive cryoglobulin tests over a 10-year period in a specialized laboratory.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Clinical manifestations (a) and etiology (b) of CryoVas (2013-2023)



Methods: We conducted a retrospective monocentric study analyzing all cryoglobulin tests performed in a specialized laboratory from 2013 to 2023. A total of 13,607 tests were performed, of which 1,593 (11.7%) yielded positive results, corresponding to 596 individual patients. Medical records were reviewed to confirm CryoVas diagnoses per classification criteria.

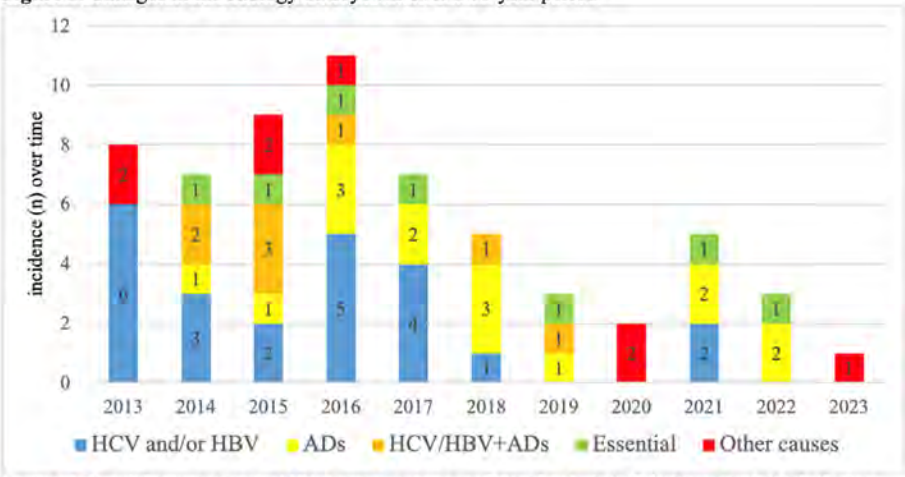
Results: Among 596 patients, 102 (17%) were diagnosed with CryoVas. Median age at onset was 65 years (IQR 56–73), with females comprising 65%. HCV-related CryoVas accounted for 34%, AD-related for 20% (mainly Sjögren's disease, 67%), and essential CryoVas for 12%.

CryoVas was diagnosed before 2013 in 40% of cases, 66% of whom had HCV/HBV. After 2017, with pan-genotypic HCV treatments, CryoVas incidence declined significantly (from 8.4 ± 1.7 to 3 ± 1.6 cases/year; ***p*=0.001**).

At onset of CryoVas, median BVASv3 was 6 (IQR 2–9). Type I CryoVas more often presented with ulcers, necrotizing vasculitis (***p*=0.001**), and hyperviscosity. Raynaud's was more frequent in AD-related CryoVas (***p*=0.025**). Glomerulonephritis and GI involvement were more common in essential CryoVas (***p*=0.011** and *p*=0.380, respectively). RF levels were higher in essential CryoVas (median 473 IU/L; ***p*=0.010**).

Two-thirds of AD-related CryoVas patients received Rituximab (RTX), while Belimumab (BEL) was used exclusively in AD-related and essential CryoVas.

Figure 2. Changes in the etiology of CryoVas over a 10-year period



Legend: ADs, autoimmune diseases; "Other causes" include malignancies, bacterial infections, hematologic diseases

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Over a median 7-year follow-up (IQR 3–11), relapse occurred in 71% of AD-related CryoVas vs. 42% of others (***p*=0.097**). Nearly one-quarter of AD-related patients were still on RTX at last follow-up. Although 94% achieved clinical remission, cryoglobulin clearance occurred in only 60%.

Conclusion: CryoVas remains a significant clinical condition, with its etiology progressively evolving in recent years.

Treatment approaches varied by etiology, with RTX serving as a cornerstone for CryoVas associated with ADs, while BEL demonstrated potential in select cases.

Despite advancements in treatment and high rate of complete clinical response, relapse rates remain high, particularly in autoimmune-related CryoVas. Additionally, cryoglobulin clearance was achieved in approximately 60% of patients during follow-up, reflecting a partial immunological response.

Disclosure: V. Manfrè: None; **e. treppo**: None; **M. Pillon**: None; **M. De Martino**: None; **C. Fabro**: None; **M. Isola**: None; **M. Fabris**: None; **F. Curcio**: None; **L. Quartuccio**: None.

Abstract Number: 2546

Diagnostic Journey, Clinical Burden, And Quality Of Life Of Patients With IGg4-Related Disease: Results Of A Cross-Sectional Survey Of Patients And Physicians In The United States

Yasmin Hernandez-Barco[1], Jenny Y. Park[2], Rajvi Wani[3], Andrea Meyers[4], Matthew Charles Baker[5], Leonard Calabrese[6], Kristina Patterson[2], Hannah Connolly[7], Shiva Lauretta Birija[7] and Emma Culver[8], [1]Massachusetts General Hospital; Harvard Medical School, Boston, MA, [2]Amgen Inc., Thousand Oaks, CA, [3]Amgen Canada Inc., Mississauga, ON, Canada, [4]Amgen Canada Inc., Thousand Oaks, ON, Canada, [5]Stanford University, Menlo Park, CA, [6]Cleveland Clinic, Cleveland, OH, [7]Adelphi Real World, Bollington, United Kingdom, [8]John Radcliffe Hospital; University of Oxford, Oxford, United Kingdom

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2524–2546) Vasculitis – Non-ANCA-Associated & Related Disorders Poster III
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: IgG4-related disease (IgG4-RD) is a chronic immune-mediated fibroinflammatory condition characterized by fibrosis and organ damage. Although IgG4-RD is increasingly recognized, real-world clinical burden remains poorly understood. This study aims to characterize the US IgG4-RD population, their diagnostic journey, clinical characteristics, treatment patterns, and burden of illness.

Methods: Data were derived from the Adelphi IgG4-RD Disease Specific Programme (DSP)™, a cross-sectional survey of patients with IgG4-RD and their providers in the United States, collected from 2023 to 2024. Physicians provided data on patient demographics, symptomology, treatment and clinical outcomes. Patient reported outcomes (PROs) including, Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, EuroQol 5-dimension 5-level (EQ-5D-5L), and Work Productivity and Activity Impairment (WPAI) were collected from patients.

Results: In total, 41 physicians returned data on 161 patients, and 27 patients completed surveys. Mean patient age was 55.4 ± 13.0 years, 62.1% were male and 71.4% were White (**Table 1)**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 – Patient demographics

Patient age, years	n=161
Mean ± SD	55.4 ± 13.0
Patient sex, n (%)	n=161
Male	100 (62.1)
Ethnicity, n (%)	n=161
White	115 (71.4)
Other	46 (28.6)
Employment status, n (%)	n=156
Working full time	86 (55.1)
Not working due to retirement	28 (17.9)
Working part time	21 (13.5)
Other	21 (13.5)
Not working full-time due to IgG4-RD, n (%)	n=50
Yes	9 (18.0)

Mean age at symptom onset was 50.1 ± 13.2 years and time to diagnosis was 11.5 ± 21.8 months. Fatigue (41.6%), joint pain (23.0%), and weight loss (22.4%) were the most commonly reported symptoms at first consultation. The pancreas (31.7%), parotid glands (22.4%) and retroperitoneal fibrosis (19.3%) were the most commonly reported organ manifestations (**Table 2)**.

Primary care physicians (47.4%), gastroenterologists (20.4%) and rheumatologists (11.2%) were most commonly consulted about initial symptoms. Patients required a mean of 3.3 ± 2.0 consultations and providers, on average, used 13.4 ± 7.8 assessments to aid diagnosis. A different diagnosis than IgG4-RD was initially suspected for 90.2% of patients, most commonly conditions such as pancreatitis (15.4%), chronic fatigue syndrome (14.7%) and vasculitis (14.0%).

Treatment initiation was, on average, 8.9 ± 13.3 months following diagnosis. Rheumatologists (70.2%), gastroenterologists (41.0%) and primary care physicians (29.2%) primarily managed patients' treatment regimens. Prednisone was the most common first line therapy (66.3%), followed by rituximab (16.9%) and azathioprine (10.6%).

Table 2 – Patient diagnostic journey

Symptoms at first consultation, n (%)	n=161
Fatigue	67 (41.6)
Joint pain	37 (23.0)
Weight loss	36 (22.4)
Organ site manifestations at first consultation, n (%)	n=162
Pancreas	51 (31.7)
Parotid Glands	36 (22.4)
Retroperitoneal Fibrosis	31 (19.3)
Physician for first consultation	n=152
Primary care physician	72 (47.4)
Gastroenterologist	31 (20.4)
Rheumatologist	17 (11.2)
Physician making IgG4-RD diagnosis, n (%)	n=156
Rheumatologist	67 (42.9)
Gastroenterologist	55 (35.3)
Primary care physician	10 (6.4)
Ear, nose and throat specialist	7 (4.5)
Assessments conducted as part of IgG4-RD diagnosis, n (%)	n=161
Tissue Biopsy	142 (88.2)
Serum IgG4 levels	128 (79.5)
Physical examination	125 (77.6)
Computed tomography	119 (73.9)
C-reactive protein	111 (68.9)
Erythrocyte sedimentation rate	95 (59.0)
Serum IgG levels	88 (54.7)
Complete blood count	85 (52.8)

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3- Patient-reported outcomes

FACIT Fatigue score (normal range ~40-45)	n=27
Mean ± SD	34.0 ± 13.7
EQ-5D-5L Score	n=27
Mean ± SD	0.8 ± 0.2
WPAI: Percent overall work impairment due to problem	n=14
Mean ± SD	20.1 ± 22.7
WPAI: Percent work time missed due to problem	n=15
Mean ± SD	10.9 ± 26.9
WPAI: Percent impairment while working due to problem	n=14
Mean ± SD	17.9 ± 18.9
WPAI: Percent activity impairment due to problem	n=27
Mean ± SD	34.1 ± 27.9

Hospitalizations due to IgG4-RD were reported for 14.3% of patients in the 12 months prior to the survey. Among those hospitalized, 68.4% were admitted via the emergency room. Patients reported impact to quality of life as characterized by PROs presented in **Table 3**.

Conclusion: Patients face delays in receiving a correct IgG4-RD diagnosis, with the diagnostic journey often involving multiple consultations and tests. IgG4-RD presents heterogeneously, and the majority of patients reported substantial burden of illness and impact to daily lives. Earlier clinical diagnosis and effective management may improve health outcomes and quality of life among patients with IgG4-RD.

Disclosure: Y. Hernandez-Barco: Amgen, 2, Nestlé Health Science, 1; **J. Park**: Amgen, 3, 11; **R. Wani**: Amgen, 3, 11; **A. Meyers**: Amgen, 3, 11; **M. Baker**: Amgen, 2, Sanofi, 2, Zenas BioPharma, 2; **L. Calabrese**: AbbVie, 2, Amgen, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, Fate Therapeutics, 2, Galvani, 2, Genentech, 2, GlaxoSmithKlein(-GSK), 2, Janssen, 2, 6, Mymee, 2, Open Evidence, 2, PPD, 2, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6; **K. Patterson**: Amgen, 3, 11; **H. Connolly**: Adelphi Real World, 3; **S. Birija**: Adelphi Real World, 3; **E. Culver**: Amgen, 1, 2, Zenus, 2.

Abstract Number: 2548

Management of Uncontrolled Gout Among Rheumatologists: Findings from a Medical Chart Audit

Hyon K. Choi[1], Nana Kragh[2], Amod Athavale[3], **Bhavisha Desai**[4], Amal Gulaid[3], Abiola Oladapo[5], Brittany Smith[3] and Kenneth Saag[6], [1]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [2]Sobi, Kongens Lyngby, Denmark, [3]Trinity Life Sciences, Waltham, MA, [4]Sobi, Glastonbury, CT, [5]Sobi INC, Waltham, MA, [6]The University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Uncontrolled gout (UG) is defined by persistently high sUA levels, despite the use of oral urate lowering treatments (ULT), resulting in gout-related manifestations. Current ACR guidelines recommend a treat-to-target approach with routine sUA monitoring and a sUA goal of < 6mg/dL with the use of ULTs. The aim of this study was to assess current UG management, treatment practices and perceptions among rheumatologists.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Physician Demographics and Patient Demographics and Clinical Characteristics

Physician Demographics (N = 175)	
Number of Years as a Practicing Physician	
Mean (SD)	14.9 years (6.9)
Primary Practice Setting (% of physicians)	
Single-specialty group practice	38%
Multi-specialty group practice	29%
Academic / Teaching Hospital	11%
Solo private practice	13%
Local or Community Hospital	8%
Primary Practice Location (US) (% of physicians)	
Urban	72%
Suburban	27%
Rural	1%
Number of Gout Patients Managed per Physician in the Last 12 Months	
Mean (SD)	149.0 (97.9)
Number of UG Patients Managed per Physician in the Last 12 Months	
Mean (SD)	67.7 (39.3)
Patient Demographics and Clinical Characteristics (N = 409)*	
Age (Mean (SD))	
At initial gout diagnosis	46.3 (10.6)
Current age	53.3 (10.4)
Sex (% of patients)	
Male	91%
Female	9%
Ethnicity (% of patients)	
Hispanic/Latino	14%
Not Hispanic/Latino	82%
I do not know	4%
Race+(% of patients)	
White	73%
Black or African American	11%
Asian	7%
Native Hawaiian or other Pacific Islander	2%
Other	4%
I do not know	2%
Number of Years from Gout Diagnosis to Most Recent Visit	
Mean (SD)	6.3 years (5.9)
Number of Years on Most Recent ULT	
Mean (SD)	4.2 years (4.2)
sUA Level (Mean (SD))	
At initial gout diagnosis	9.2 mg/dL (1.3)
At initiation of most recent ULT	8.8 mg/dL (1.2)
Most Common Symptoms at Initial Gout Diagnosis (% of patients)	
Swollen joints	78%
Gout flares	76%
Visible tophi	75%
Joint pain	72%
Joint discomfort	69%
Most Common Symptoms at Initiation of Most Recent ULT (% of patients)	
Visible tophi	76%
Swollen joint	73%
Gout flares	67%
Joint pain	67%
Joint discomfort	61%

* UG is defined as the following: a) Inadequate control of symptoms and failure to normalize sUA with xanthine oxidase inhibitors, or where these drugs are contraindicated for the patient b) Serum uric acid (sUA) > 6 mg/dL c) A history of symptomatic gout (> 2 gout flares within 12 months, and/or presence of > 1 gout tophus, and/or current diagnosis of gouty arthritis)

Methods: A retrospective medical chart audit was conducted in the US from March to June 2024, via a web-enabled case report form, among board-certified rheumatologists with ≥3 years of clinical practice experience recruited via a panel. Respondents were required to have treated ≥25 patients with gout and ≥10 patients with UG in the last year. Data were abstracted from medical records of patients who met the following criteria: Diagnosed with UG, experienced gout related symptoms in the last year and have a sUA >6 mg/dL. Key variables included patient demographics, treatment history, adherence and healthcare resource utilization. Rheumatologists also completed an online survey related to their perceptions of UG management using a 1-7 Likert scale. Scores ≥6 indicates higher/strong level of satisfaction or agreement, while scores < 6 indicates the contrary.

Results: A total of 175 rheumatologists abstracted 409 records of patients with UG (**Table 1**). In the past year, on average (SD), physicians managed 149 (98) patients with gout, with 68 (39) classified as having UG. Most commonly reported comorbidities were renal impairment (71%), hypertension (47%) and obesity (36%). At most recent visit, most patients had visible tophi (90%; 39% considered very severe), gout flares (58%; 61% very severe), swollen joints (47%; 54% very severe), joint pain (47%; 48% very severe) and joint discomfort (47%; 49% very severe). Rheumatologists reported measuring sUA at every visit in a majority (90%) of their patients, with patients having on average (SD), 3.9 (2.6) routine visits in the past year. As

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Rationale for Treatment Selection

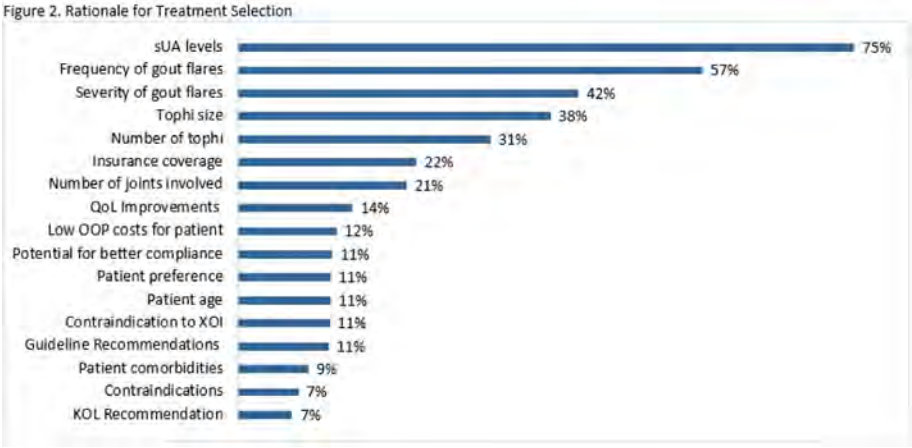
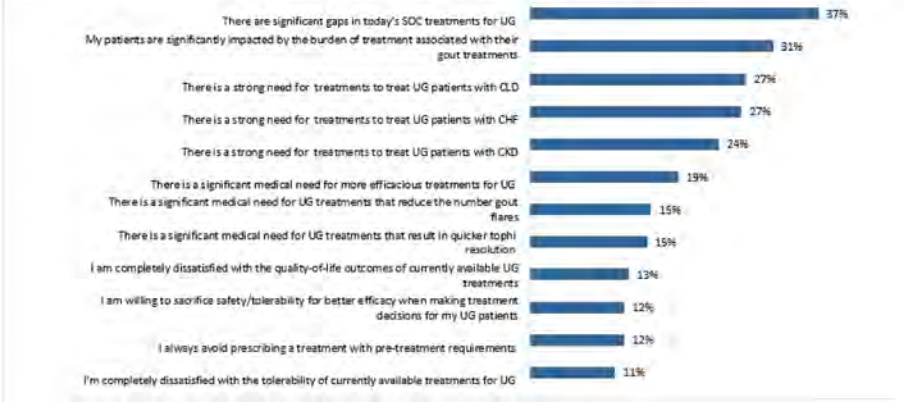


Figure 3. Rheumatologist Perceptions on Gout Treatment and Management
(% of HCPs that rated their level of agreement to the following statements as rated 6-7 on a scale from 1-7)



of the most recent visit, mean (SD) sUA level was 8.2 mg/dL (1.3). Clinical manifestations and sUA drive treatment choice, with treatments chosen due to sUA levels (75%), frequency of gout flares (57%) and severity of gout flares (42%) (**Figure 2**).

Patients with UG most recently received allopurinol (72%), with a median (IQR) dose of 300 mg/day (300-400) and 32% prescribed >300 mg/day. Other patients most recently received febuxostat (24%), colchicine (18%) and pegloticase (4%). Only 25% of patients were considered adherent (i.e., taking medication >75% of the time) with lack of compliance, most commonly attributed to forgetfulness (68%), lack of health literacy around medication (46%) or gout (35%). Rheumatologists were extremely satisfied with allopurinol in 60% of their patients, febuxostat in 50%, pegloticase in 22%. About 37% of rheumatologists indicated that unmet needs exist in current management of UG and 31% believed their patients are impacted by the burden of current gout treatments (**Figure 3**).

Conclusion: This study highlights the challenges rheumatologists face in managing UG and unmet needs in gout treatments as evidenced by high sUA levels, frequent flares and tophi presence and low adherence rates to current ULTs.

Disclosure: H. Choi: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **N. Kragh**: Sobi, 3; **A. Athavale**: Sobi, 2, Trinity Life Sciences, 3, 8; **B. Desai**: Sobi, 3, 11; **A. Gulaid**: Sobi, 2, Trinity Life Sciences, 3; **A. Oladapo**: Sobi Inc, 3; **B. Smith**: Sobi, 2, Trinity Life Sciences, 3; **K. Saag**: Arthrosi, 2, 5, Atom Bioscience, 2, Cyrstalys, 2, Inventis, 5, LG Pharma, 2, 5, Novo Nordisc, 2, Olatec, 5, Shanton, 2, Sobi, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2550

Development of a 'Training Toolkit' to Support Advanced Practice Providers (APPs) Entry into a Rheumatology Musculoskeletal Ultrasound Subspecialty Clinic

Christopher Estes[1], Janeth Yinh[1], Mark Matza[2], Marcy Bolster[3] and Minna Kohler[4], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Newton, MA, [3]Massachusetts General Hospital, Concord, MA, [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: The integration of advanced practice providers (APPs) into rheumatology practice may help address increasing demand and long wait times.[1] However, outcome data on APP involvement, particularly in procedural roles, remain limited. We report how ultrasound (US)-guided procedures performed by a newly hired APP in a high-volume, procedure-focused rheumatology musculoskeletal (MSKUS) clinic can enhance patient access to diagnostic and therapeutic interventions.

Methods: CPT codes for US-guided procedures performed by a newly hired APP were tracked over a 7-month period (8/2023–3/2024). Prior to this period, the APP had 1 year of experience performing palpation-guided injections and completed a rheumatologic MSKUS training program emphasizing procedural guidance. The APP performed over 100 US-guided procedures under direct supervision before transitioning to independent practice. Procedures included US-guided aspiration and/or corticosteroid injection. CPT codes were used to classify procedures sites with US-guidance: large joint/bursa (20611), intermediate joint/bursa (20606), small joint (20604), tendon sheath (20550), and carpal tunnel (20526). Data were analyzed by frequency and percentage of total procedures performed. Associated clinical diagnoses were also collected.

Results: Over the 7-month period, the APP performed a total of 284 US guided procedures during independently scheduled procedure clinics. Of these, 59% (n=167) were large joints/bursae, 11% (n=32) involved intermediate joints/bursae, 25% (n=70) were small joint injections, 2% (n=7) involved tendon sheaths, and 3% (n=8) were carpal tunnel injections (Fig. 1). Indications for procedures included joint effusion, synovitis, bursitis, tendinitis and carpal tunnel syndrome.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1

Rheumatology APP 'Training Toolkit' *	
In-Person	Conferences: - ACR Convergence 2023 - SOTA 2024 Rheumatology MSKUS CME Courses: -2023 NYU Langone Health Ultrasound for Rheumatologists and Other Musculoskeletal Providers Course -2024 USSONAR Multi-Track Ultrasound in Rheumatology Conference Seminars through employer: - Musculoskeletal US Fellows' Conference - Weekly Grand Rounds
Online	ACR: -Rheum2Learn -ACR's Advances Rheumatology Course -ACR on Air Podcast
Textbooks	General Rheumatology - Cellular and Molecular Immunology, 10th ed.[1] - Rheumatology, 8th ed. [4] - Rheumatology Secrets, 4th ed.[6] Musculoskeletal Ultrasound: - Ultrasound Guided Musculoskeletal Injections[2] - Diagnostic Ultrasound: Musculoskeletal, 2nd ed.[3] - Musculoskeletal Ultrasound in Rheumatology, 2nd ed.[5]
Financial	- RRF Mentored Nurse Practitioner/Physician Assistant Award for Workforce Expansion grant - Institutional Funds

ACR – American College of Rheumatology; CME – Continuing Medical Education; MGH – Massachusetts General Hospital; RRF – Rheumatology Research Foundation; USSONAR - Ultrasound School of North American Rheumatologists

1. Abbas AK, Lichtman, AH, Pillai S. *Cellular and Molecular Immunology*. 10th ed. Elsevier, Inc; 2022.
2. Allen GM, Wilson DJ. *Ultrasound Guided Musculoskeletal Injections*. Elsevier, Inc; 2018
3. Griffith J. *Diagnostic Ultrasound: Musculoskeletal*. 2nd ed. Elsevier, Inc; 2019.
4. Hochberg M, Gravallese E, Smolen J, van der Heijde D, Weinblatt M, Weisman M. *Rheumatology*. 8th ed. Elsevier, Inc; 2023.

Underlying diagnoses among patients included inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, spondylarthritis), crystalline arthritis (gout, calcium pyrophosphate deposition disease), osteoarthritis, and mechanical overuse syndromes. Patient access improved to less than 2 weeks.

Conclusion: In an early implementation phase, the majority of US-guided procedures performed by a novice APP involved large joints (e.g. shoulders, hips, and knees) and small joints (e.g. MCP, MTP, PIP), with large joints comprising over half of all procedures. These findings guide referral planning and scope expectations for APPs new to a rheumatology MSKUS procedure clinic. Ongoing assessments will evaluate the evolution of procedure types and volumes over time as the APP gains experience, providing further insight into the scope and capacity of APPs in performing US-guided procedures within rheumatology practice demonstrating impact on rheumatology workforce expansion and patient access.

Disclosure: C. Estes: None; **J. Yinh**: Janssen, 2, Springer, 9; **M. Matza**: Expert Review, 12, Novartis, 1, Summus Global, Inc, 2, USSONAR, 6; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2551

Integrating Advanced Practice Providers into a Rheumatology Musculoskeletal Ultrasound Clinic: Enhancing Patient Access and Procedural Expertise

Christopher Estes[1], Janeth Yinh[1], Mark Matza[1], Marcy Bolster[2] and Minna Kohler[3], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Concord, MA, [3]Massachusetts General Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Point-Of-Care Ultrasound (POCUS) use among Advanced Practice Providers (APPs) is expanding across health care, yet formal rheumatology-specific POCUS training remains limited. Existing POCUS curricula for APPs in emergency medicine and critical care are not tailored to rheumatology needs[1,2]. The American College of Rheumatology Musculoskeletal Ultrasound Certification (RhMSUS)[3] is a recognized marker of competence, attainable by APPs, though

Table 1

Self-Directed Study & Educational Resources*	
In-Person	14-hour Hands-On CME Courses: -2023 NYU Langone Health Ultrasound for Rheumatologists and Other Musculoskeletal Providers Course -2024 USSONAR Multi-Track Ultrasound in Rheumatology Conference Didactics and Hands-on Workshop (Massachusetts General Hospital) - monthly Musculoskeletal Ultrasound Fellows Conference
Online	USSONAR: - The Rheumatologists Guide to Musculoskeletal Ultrasound Normal Anatomy - Membership learning curriculum
Textbooks	Musculoskeletal Ultrasound: - Ultrasound Guided Musculoskeletal Injections[1] - Diagnostic Ultrasound: Musculoskeletal, 2nd ed.[2] - The Rheumatologists Guide to Musculoskeletal Ultrasound Normal Anatomy[3] - Musculoskeletal Ultrasound in Rheumatology, 2nd ed.[4]

ACR – American College of Rheumatology; CME – Continuing Medical Education; MGH – Massachusetts General Hospital; NYU - New York University; USSONAR - Ultrasound School of North American Rheumatologists

1. Allen GM, Wilson DJ. *Ultrasound Guided Musculoskeletal Injections*. Elsevier, Inc; 2018.
2. Griffith J. *Diagnostic Ultrasound: Musculoskeletal*. 2nd ed. Elsevier, Inc; 2019.
3. Kissin E. *The Rheumatologists Guide to Musculoskeletal Ultrasound Normal Anatomy*. USSONAR; 2018.
4. Kohler MJ. *Musculoskeletal Ultrasound in Rheumatology Review*. 2nd ed. Springer Nature Switzerland AG; 2021.

* Not intended to endorse or sponsor any product, service, or activity

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

only two currently hold this designation4. We developed a rheumatologic POCUS curriculum to support APP integration into an outpatient rheumatology musculoskeletal ultrasound (MSKUS) clinic and patient care access expansion.

Methods: We developed a training program for a newly hired APP within a rheumatology MSKUS clinic at an academic center. In this model, the APP was precepted by 3 RhMSUS-certified rheumatologists, starting with clinical observation, progressing to supervised image acquisition, and MSKUS-guided procedures. Procedural competence progressed from large joints to small joints, then peri-articular structures. Protected time for the APP for both in-person and online POCUS education was included, supported by a Rheumatology Research Foundation workforce expansion grant, institutional funds, and APP personal funds. Competency was assessed through objective structured clinical examinations by supervisors and attainment of RhMSUS certification. APP clinics were limited to procedural applications and were conducted adjacent to supervising physicians' clinics for direct feedback.

Results: Together with general rheumatology training, MSKUS training was completed over eight months prior to launching independent APP clinics. The APP completed two 14-hour hands-on CME courses in rheum POCUS, attended MSKUS didactics and workshops alongside rheumatology fellows, accessed online, self-paced modules through the Ultrasound School of North American Rheumatologists (USSONAR), and reviewed MSKUS textbooks (Table 1). During this time, the APP had direct supervision of MSKUS-guided procedures in clinic. The APP achieved RhMSUS certification 10 months after starting independent practice, and 16 months after hire. Urgent patient access to the rheumatology MSKUS clinic improved to less than 2 weeks.

Conclusion: Integrating an APP into a rheumatology MSKUS practice can improve patient access and is supported by structured supervision, multimodal education, and educational funding. This framework offers a model for developing novice APPs into autonomous RhMSUS-certified rheumatology POCUS providers with procedural expertise.

Disclosure: C. Estes: None; **J. Yinh**: Janssen, 2, Springer, 9; **M. Matza**: Expert Review, 12, Novartis, 1, Summus Global Inc., 2, USSONAR, 6; **M. Bolster**: Genentech, 5, Mitsubishi, 5, Prometheus, 5; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9.

Abstract Number: 2552

Effects of 360° Virtual Reality Embodiment Videos on Pain in Hand Osteoarthritis: A Within-Subject Pre-Post Study

David Vo[1], Robert Edwards[2] and Nancy Baker[3], [1]Tufts University, Huntington Beach, CA, [2]Brigham and Womens Hospital, Chestnut Hill, MA, [3]Tufts University, Medford, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoarthritis (OA) is associated with chronic pain in the joints, which affects many individuals' daily function and quality of life. The sense of embodiment (SoE) is an illusory perception that an artificial body belongs to the real one and has been suggested to have analgesic effects for chronic pain (Baker et al, 2022). SoE can be facilitated through virtual reality (VR) and spherical video-based virtual reality (SVVR) (Serino et al., 2023). These studies suggest pre-recorded SVVR can be used as a non-pharmacological approach for pain modulation. This study evaluates the analgesic effects of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Participant changes in pain pre and post 5-minute SVVR intervention

		Mean(SD)	*p*	*r*
Pre-SVVR	NRS (Pre-SVVR)	1.9(1.5)		
Post-SVVR	NRS (During-SVVR)	1.0(1.2)	0.02	0.74
	NRS (Post-SVVR)	0.9(1.1)	0.01	0.80
	NRS (End-of-visit)	1.2(1.1)	0.16	0.44
	EQ	3.9(1.1)		
	IPQ	4.3(0.8)		

NRS= numeric rating scale for pain; EQ= embodiment questionnaire; IPQ= igroup presence questionnaire

embodiment-inducing SVVR in people with hand OA. We hypothesized that people with pain due to hand OA would have significantly reduced pain after SVVR.

Methods: We recruited 10 individuals with hand OA who completed the study in a single visit. We used a within-subjects pre-post design to evaluate the analgesics effects of a 5-minute SVVR intervention delivered through the Meta Quest 2 VR headset. Participants' subjective pain intensity ratings were recorded using a standard (0-10) numeric rating scale (NRS) before, during, and after the intervention. We measured the level of embodiment and presence the participants experienced from the SVVR using the Embodiment Questionnaire (EQ) and the Igroup Presence Questionnaire (IPQ).

Data analysis: We used a Wilcoxon Signed-Rank test to determine the significance of change scores. We calculated the effect size *r* with the following criteria: small 0.10-0.29; moderate 0.30-0.49; large ≥ 0.50.

Results: The SVVR significantly reduced pain intensity in people with hand OA during (p= .02; r= .82) and immediately following (p= .01; r= .90) the intervention with large effect sizes. Pain intensity was no longer significantly reduced (from baseline) at the end of the study visit (p= .16; r= 50). The SVVR was moderately effective in facilitating a sense of embodiment and presence in the participants (EQ= 3.9, IPQ= 4.3; out of a seven-point Likert scale). (See Table)

Conclusion: The SVVR intervention significantly reduced pain intensity in people with Hand OA during a single brief treatment. However, the acute analgesic effects were not sustained throughout of the full study visit, suggesting that additional (or longer) treatments might be required in order to maintain the reductions in pain. EQ and IPQ levels show moderate embodiment-inducing effects, suggesting that mechanisms such as distraction may be contributing to the intervention's pain-relieving effects.

Baker, N. A., Polhemus, A. H., Ospina, E. H., Feller, H., Zenni, M., Deacon, M., DeGrado, G., Basnet, S., & Driscoll, M. (2022). The state of science in the use of virtual reality in the treatment of acute and chronic pain. *The Clinical Journal of Pain*, *38*(6), 424–441. https://doi.org/10.1097/ajp.0000000000001029

Serino, S., Sansoni, M., Di Lernia, D., Parisi, A., Tuena, C., & Riva, G. (2023). 360-degree video-based body-ownership illusion for inducing embodiment: Development and feasibility results. *Virtual Reality, 27*, 2665–2672. https://doi.org/10.1007/s10055-023-00836-6

Disclosure: D. Vo: None; **R. Edwards**: None; **N. Baker**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2554

Real-World Observations on Symptom Response and Tolerability of Intravenous Immunoglobulin in Patients with Inflammatory Myopathies through a Nurse-Led Outcomes Monitoring Program in a Home Infusion Setting

Didem Saygin[1], **Elizabeth Neal**[2], Edward O'Bryan[3], Alisha Smith, PharmD[3], Leslie Myers[3] and Timothy Walton[3], [1]Rush University Medical Center, Chicago, IL, [2]CSI Pharmacy, Nash, TX, [3]CSI Pharmacy, Nash

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: (2547–2566) ARP Posters II

Session Type: Poster Session C

Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are autoimmune diseases typically characterized by muscle weakness. Intravenous Immunoglobulin (IVIg) is an effective immunomodulatory therapy in patients with refractory IIM. However, data is limited regarding trajectory of patient reported symptom response and tolerability of IVIg among patients

Table 1. Baseline characteristics of the patients with IIM who receive IVIg through home infusion.

Variable	Patients with IIM (n =14)
Sex	
Female	8 (57%)
Male	6 (43%)
Age	63 [47-49]
45-64 years	7 (50%)
65-74 years	6 (43%)
≥75 years	1 (7%)
Race	
African American	4 (29%)
Caucasian	10 (71%)
IIM Subtype	
Dermatomyositis	7 (50%)
Immune Mediated Necrotizing Myopathy	2 (14%)
Polymyositis	5 (36%)
Number of monthly infusions	
1-2	14 (100%)
3	12 (85.7%)
4-5	9 (64.3%)
6	6 (42.9%)
7	5 (35.7%)
8	4 (28.6%)
9	2 (14.3%)
Disease duration (yrs)	4 [2-13]
1 - 5 years	8 (57%)
6 - 10 Years	1 (7%)
11 - 20 Years	4 (29%)
20+ years	1 (7%)
Clinical manifestations at the time of 1st infusion	
Muscle weakness	14 (100%)
Muscle pain	9 (64%)
Joint pain	7 (50%)
Joint swelling	6 (43%)
Rash	7 (50%)
Raynaud phenomenon	3 (21%)
Dyspnea	6 (43%)
Pulmonary arterial hypertension	2 (14%)
Interstitial lung disease	1 (7%)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Adverse reactions during IVIg infusions.

	1st IVIg	2nd IVIg	3rd IVIg	4th IVIg	5th IVIg	6th IVIg	7th IVIg	8th IVIg	9th IVIg
Adverse Reactions									
Moderate, Severe, Critical	0	0	0	0	0	0	0	0	0
Mild Side Effect*									
Headache	4	1	0	0	0	0	0	0	0
Nausea	0	1	0	0	0	0	0	0	0
Itching	1	0	0	0	0	0	0	0	0
Swelling	1	0	0	0	0	0	0	0	0
Dizziness	1	0	0	0	0	0	0	0	0
Fever	1	0	0	0	0	0	0	0	0
Tingling	1	0	0	0	0	0	0	0	0
Pain	1	0	0	0	0	0	0	0	0
Total	10	2	0	0	0	0	0	0	0

*5 out of 14 patients reported a side effect during their infusion

with IIM. This study aims to report the symptom change and treatment tolerance of IVIg naïve adults with IIM through implementation of a structured outcomes monitoring program within a home infusion and specialty pharmacy model.

Methods: As part of a proprietary clinical outcomes program, an IIM clinical care and patient-reported outcomes monitoring program was developed by a multidisciplinary team within a home infusion and specialty pharmacy organization. The patients with confirmed IIM diagnosis who were IVIg treatment naïve and had ≥2 IVIg infusions, were recruited between 5/2024 – 3/2025. The program integrated clinical safety assessments and structured collection of patient symptoms via Health Assessment Questionnaire (HAQ), Patient Global Disease Activity (PTGD), and Patient-Reported Outcomes Measurement Information System (PROMIS®) Physical Function (v2, 8b), Fatigue (v1, 7a), and Pain Interference (v1.1; 6a) and Brief Pain Inventory (BPI). Patients also responded to anchor questions regarding their symptoms. All data was collected

Figure 1. Change in patient reported outcome measures of patients with IIM at each IVIg infusion.

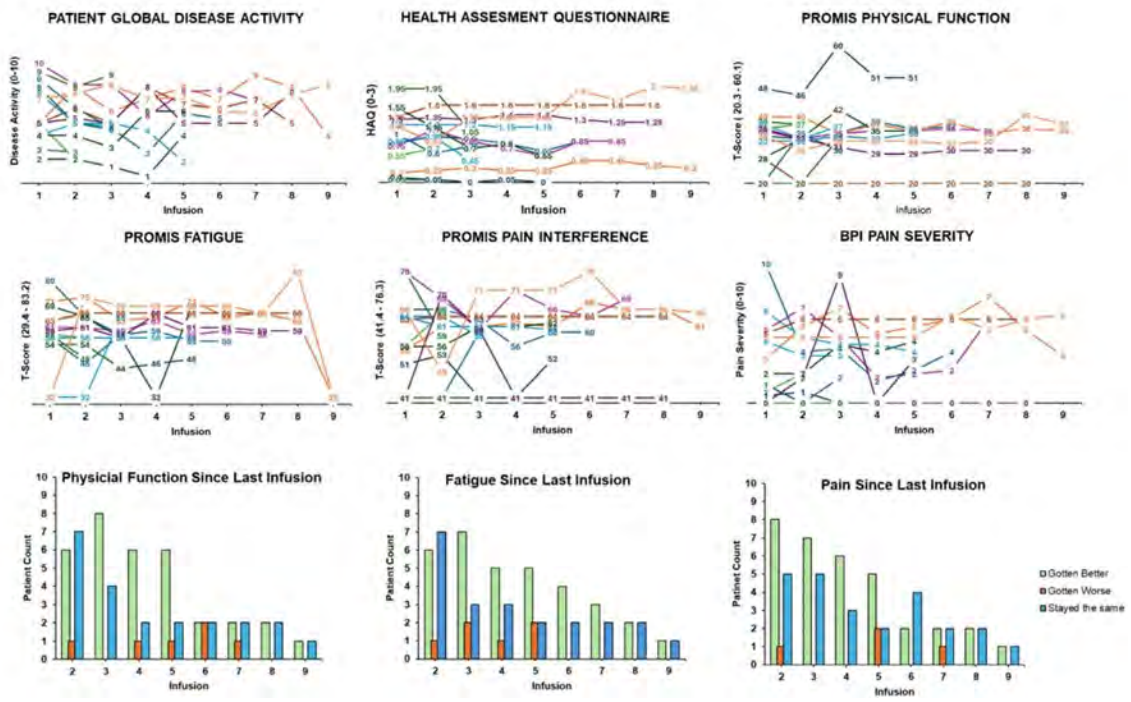


Figure 1. Change in patient reported outcome measures of patients with IIM at each IVIg infusion.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

by specialty pharmacy nurses prior to each IVIg infusion. Adverse drug reactions (ADRs) were identified through pharmacist-led patient interviews and review of nursing infusion documentation. Descriptive statistical analyses were conducted to summarize key findings.

Results: A total of 21 patients with IIM were enrolled in the program, of whom 14 (7 DM, 2 IMNM, and 5 PM; median age of 63 [47-49]) met the inclusion criteria and received their monthly IVIg infusions through a national home infusion service (**-Table 1**). Seventy-five infusion-related assessments were collected, with a mean 5 monthly IVIg infusions per patient (range 2-9). Baseline organ involvement of patients included muscle in 100% (n=14), joint in 57% (n=8), skin in 57% (n=8), and lung in 43% (n=6). One month after the 1st infusion, 6 patients (42.9%) reported improvement in their physical function and fatigue, 7 (50%) reported staying the same, and 1 reported worsening (7%) **(Figure 1)**. Most patients continued to report improvement at each infusion after 2nd, 3rd, and 4th infusions. Similar trends were observed for PTGD, pain intensity and interference. No severe ADRs were reported during the first 9 infusions. The most common side effect was headache (28.6%) and other mild side effects were within reported incidence rates **(Table 2)**.

Conclusion: This study demonstrated that IVIg-naïve IIM patients can be effectively monitored through a nurse-led, structured outcomes program which could represent a scalable approach for managing complex immunotherapy in decentralized environments. Approximately half of the patients reported improvement after one IVIg infusion. Symptomatic improvement and lack of serious adverse events suggest that the IVIg is well tolerated and may offer meaningful benefits to patients with IIM.

Disclosure: D. Saygin: None; **E. Neal**: None; **E. O'Bryan**: None; **A. Smith, PharmD**: None; **L. Myers**: None; **T. Walton**: None.

Abstract Number: 2558

Impact of Social Determinants of Health on Patient Perceptions of Home Infusion Therapy in the Treatment of Rheumatologic Conditions

Leslie Myers[1], Elizabeth Neal[2], Edward O'Bryan[1], Michele Way[3] and Timothy Walton[1], [1]CSI Pharmacy, Nash, [2]CSI Pharmacy, Nash, TX, [3]CSI Pharmacy, Olathe, KS

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Home infusion therapy is an established alternative site of care for patients requiring administration of infusion medications through a needle or catheter. Supported by clinically trained pharmacists and nurses, this model allows patients to receive therapy in their homes and has been associated with improved quality of life, reduced disruption to daily activities, and comparable clinical outcomes to traditional care settings. This study assessed patient perceptions of home infusion therapy, across diverse rheumatologic demographics, clinical status, race, level of education, and geographical location. The survey evaluated clinical experiences and Social Determinants of Health (SDoH) domains (e.g., financial impact, access to care, cultural sensitivity, emotional well-being, and safety).

Methods: A cross-sectional survey was conducted in a random 10% sample (N=300) of a national home infusion provider's patient population. From that sample, 24 rheumatologic patients completed the nurse-administered survey between April and July 2024. Inclusion criteria required active infusion under company-employed nurses. Patient conditions included

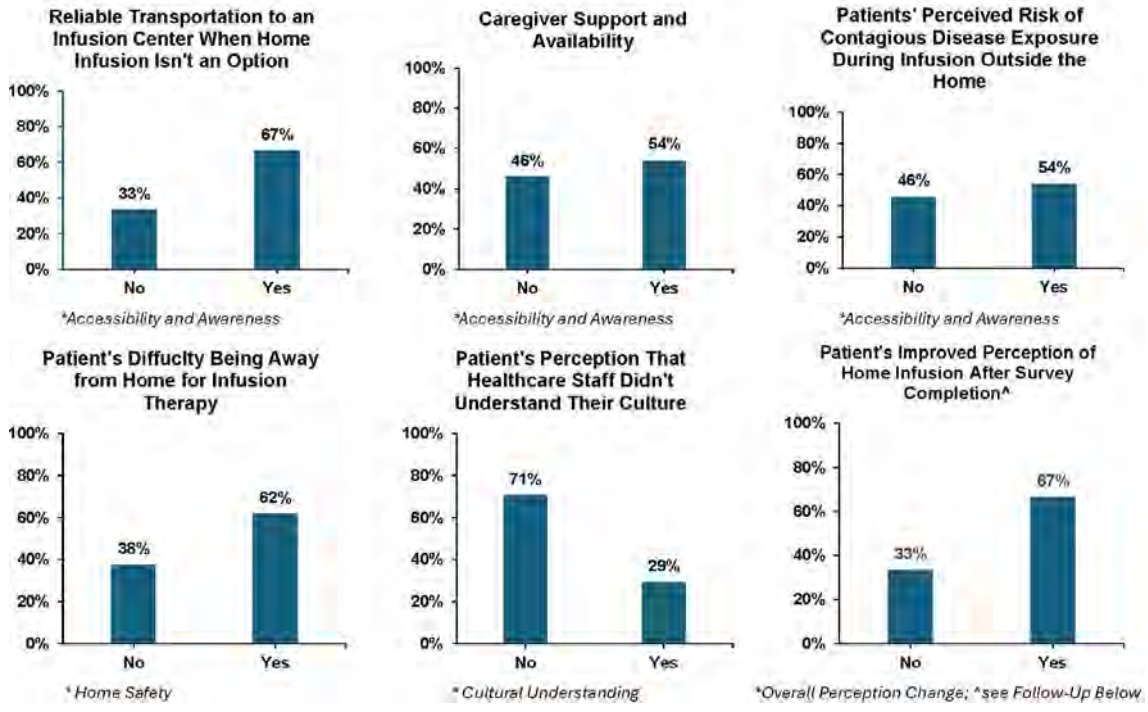
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics of patients

Variable	Rheumatology Patients (n =24)
Sex	
Female	20 (83%)
Male	4 (17%)
Age	54 [18-83]
18-44 years	5 (21%)
45-64 years	13 (54%)
65-85 years	6 (25%)
Race	
African American	4 (17%)
Asian	1 (4%)
Caucasian	19 (79%)
Diagnosis	
Dermatomyositis	2 (8%)
Dermatopolymyositis	5 (21%)
Drug-induced myopathy	1 (4%)
Inclusion Body Myositis	1 (4%)
Juvenile Dermatomyositis	1 (4%)
Lupus	1 (4%)
Myositis	1 (4%)
Other Symptoms and Signs Involving the Musculoskeletal System	1 (4%)
Polymyositis	8 (33%)
Rheumatoid Arthritis	2 (8%)
Sjögren's Syndrome	1 (4%)
Medication Administered	
Immunoglobulin	23 (96%)
Intravenous Immunoglobulin	21 (91%)
Subcutaneous Immunoglobulin	2 (9%)
Tumor Necrosis Factor (TNF) Blocker	1 (4%)
Highest Level of Education	
Bachelor's Degree	7 (29%)
Doctoral Degree	1 (4%)
High School/GED	6 (25%)

Demographics of patients

Figure 1. Percentages of Survey Responses



Percentages of Survey Responses

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Myositis (N= 19), Myopathy (N =1), Lupus (N=1), Rheumatoid Arthritis (N=2), Sjögren's Syndrome (N=1). Survey responses were captured using Likert-scale and binary ("Yes/No") formats, with Likert-scale results summarized using median, interquartile range (IQR), and % of top anchor. The survey assessed accessibility, awareness, safety, financial impact, cultural awareness, mood improvement, and overall impression of home infusion therapy.

Results: The cohort included 83% females and 17% males, with a mean age of 54 (18-83). Immunoglobulin therapy represented 96% of patients and biologic therapies 4% (**Table 1**). Patients overwhelmingly perceived home infusion as cost- and timesaving (median = 10, IQR (1,3): 10,10), with 88% citing strong financial benefits. Accessibility barriers, such as transportation or caregiver availability, were noted by a minority. Patients reported high confidence in the safety of home infusions (median = 10, IQR (1,3): 10,10), and 83% found the therapy easy to access. Mood improvement was substantial when home infusion was compared to traveling to a hospital/infusion center for treatment (median = 10, IQR (1,3): 10,10), and 92% "very much so" felt home infusion positively impacted their emotional well-being. Cultural understanding by healthcare staff was rated variably; while 71% felt culturally understood, 29% did not. While 75% reported that home infusion "very much so" helped with the understanding of one's culture.

Table 2. Median Values and % of Top Anchor Reponses

Accessibility and Awareness	Median (IQR 1,3)	% of Top Response Anchor
Patient Difficulty to Afford Transportation to Infusion Therapy Outside of The Home 1 = Not Hard At All 10 = Very Hard	6 (2,10)	29
Patients Sureness Their Home Provided a Safe and Clean Environment for Infusion Therapy 1 = Not Sure 10 = Very Sure	10 (10,10)	92
Patients Sureness the Hospital/Infusion Center Was a Safe and Clean Place to Get Their Infusion Therapy 1 = Not Sure 10 = Very Sure	4 (1,6)	21
Patients Found it Easy to Receive Home Infusion Therapy When Needed 1 = Very Hard 10 = Very Easy	10 (10,10)	83
Financial and Time Impact	**Median (IQR 1,3)**	**% of Top Response Anchor**
Patients Felt the Option of Home Infusion Therapy Provided a Time and Cost Savings 1 = Not At All 10 = Yes A Lot	10 (10,10)	88
Patients Felt the Option of Home Infusion Therapy Helped Balance Their Work Schedule 1 = Not At All 10 = Yes A Lot	10 (10,10)	83
Patients Felt T heir Job, or Lack of One, Made it Difficult for Home Infusion Therapy 1 = Not At All 10 = Yes A Lot	3 (1,7)	21
Mood	**Median (IQR 1,3)**	**% of Top Response Anchor**
Patients Who Received Home Infusion Therapy Improved Their Mood When Compared to Traveling to a Hospital/Infusion Center for Treatment 1 = Not Really 10 = Very Much So	10(10,10)	92
Cultural Understanding	**Median (IQR 1,3)**	**% of Top Response Anchor**
Patients Felt Home Infusion Helped with the Understanding of a Their Culture 1 = Not Really 10 = Very Much So	10 (10,10)	75
Overall Perception Change of Home Infusion Therapy	**Median (IQR 1,3)**	**% of Top Response Anchor**
^ If Positive Perception Noted, Ranking of Perception Change 1 = Slightly Changed 10 = Greatly Changed	9 (8,10)	33

Median Values and % of Top Anchor Reponses

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patients reported a strong preference for home infusion due to convenience and reduced exposure risk compared to infusion centers (**Figure 1 and Table 2**).

Conclusion: Home infusion therapy is highly valued by rheumatology patients, for its financial, work-life balance, mental health, and safety-related advantages. These findings support the need for broader adoption and education about home infusion as a patient-centered care model aligned with holistic health outcomes in rheumatologic patients.

Disclosure: L. Myers: None; **E. Neal**: None; **E. O'Bryan**: None; **M. Way**: None; **T. Walton**: None.

Abstract Number: 2559

Increasing Clinical Trial Awareness in Sample of Underrepresented Systemic Lupus Erythematosus Patients

Leslie Ranken[1], Kyle Osborne[2], Robert Fairman[3], Gregory Russell[4], Sara Ohl[2] and Jessica Kearney-Bryan[5], [1]Atrium Health Carolinas Medical Center Wake Forest School of Medicine Charlotte, Charlotte, NC, [2]Atrium Health, Charlotte, NC, [3]Wellstar Health, Marietta, GA, [4]Wake Forest School of Medicine, Winston-Salem, NC, [5]Atrium Health Carolinas Medical Center, Charlotte, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Underrepresented Systemic Lupus Erythematosus (SLE) patients are greatly underrepresented in SLE clinical trials. We aimed to increase clinical trial awareness with various interventions in our community practice with a small sample of patients.

Methods: The primary investigator's underrepresented SLE patients meeting ACR classification for the disease aged 18 and over were offered an electronic survey to assess their knowledge of clinical trials. They were given material about clinical trials and information from the Lupus Foundation and encouraged to contact them for support groups, etc. At year two, surveys were given to the same patients to see if they have increased knowledge of clinical trials in SLE, or to see if any of them have joined a clinical trial in the study period.

Results: At the end of year one, 86 patients filled out the demographics portion of the survey. Of these, 81% (n=70) % were Black, 14 % (n=12) were Hispanic/Latinx, 2% (n=2) were White, with 1% (n=1) Asian and 1% (n=1) not choose not to report race. Two (2%) of those 86 did not answer the questions regarding resources and could not be included; of those

Question	Baseline, N=58	Follow-up, N=58	*p* value*
1. Do you know that there are clinical trials for lupus patients?	27 (47%)	38 (66%)	**0.016**
If yes, do you know how to find them?	8/25 (32%)	18/36 (50%)	0.16
2. Have you ever been in a clinical trial for lupus?	2 (3%)	7 (12%)	0.096
3. If you qualified for a clinical trial for lupus, would you enroll?	30 (52%)	37 (64%)	0.090
4. Have you utilized the Lupus Foundation?	2 (3%)	5 (9%)	0.26

Survey Response Data

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

84, 58 (69%) completed a follow-up questionnaire. One had follow-up data but no baseline data. The 58 who provided data at both visits comprise the sample for analysis, as the goal was to compare baseline and follow-up responses to the same questions. Significant change was observed in the rate of awareness from baseline visit to the follow-up visit. Sixteen additional participants reported being aware of clinical trials at follow-up compared to baseline (while 5 changed from being aware at baseline to not at follow-up). This change is significant, p=0.016. As noted in the table, other areas (such as willingness to participate in a clinical trial if qualified to do so) also observed improved rates at follow-up, but no other changes were significant at the pre-established value of $p< 0.05$.

Conclusion: SLE is a serious chronic illness and clinical trials are necessary to get more drugs approved for treatment. Underrepresented populations are most severely affected, and yet there are barriers to clinical trial interest and entry. Our data showed that our intervention did increase clinical trial awareness in our small sample of patients. There was a trend for patients to say they would be willing to participate in a clinical trial if qualified to do so, but it did not become clinically significant. This could have been due to a small sample size. We do believe education is key to increasing underrepresented patients in SLE clinical trials.

Disclosure: L. Ranken: None; **K. Osborne**: None; **R. Fairman**: None; **G. Russell**: None; **S. Ohl**: None; **J. Kearney-Bryan**: None.

Abstract Number: 2563

Factors Associated With Medication Use in the Preconception and Perinatal Period Among Women With Autoimmune Disorders: A Systematic Review

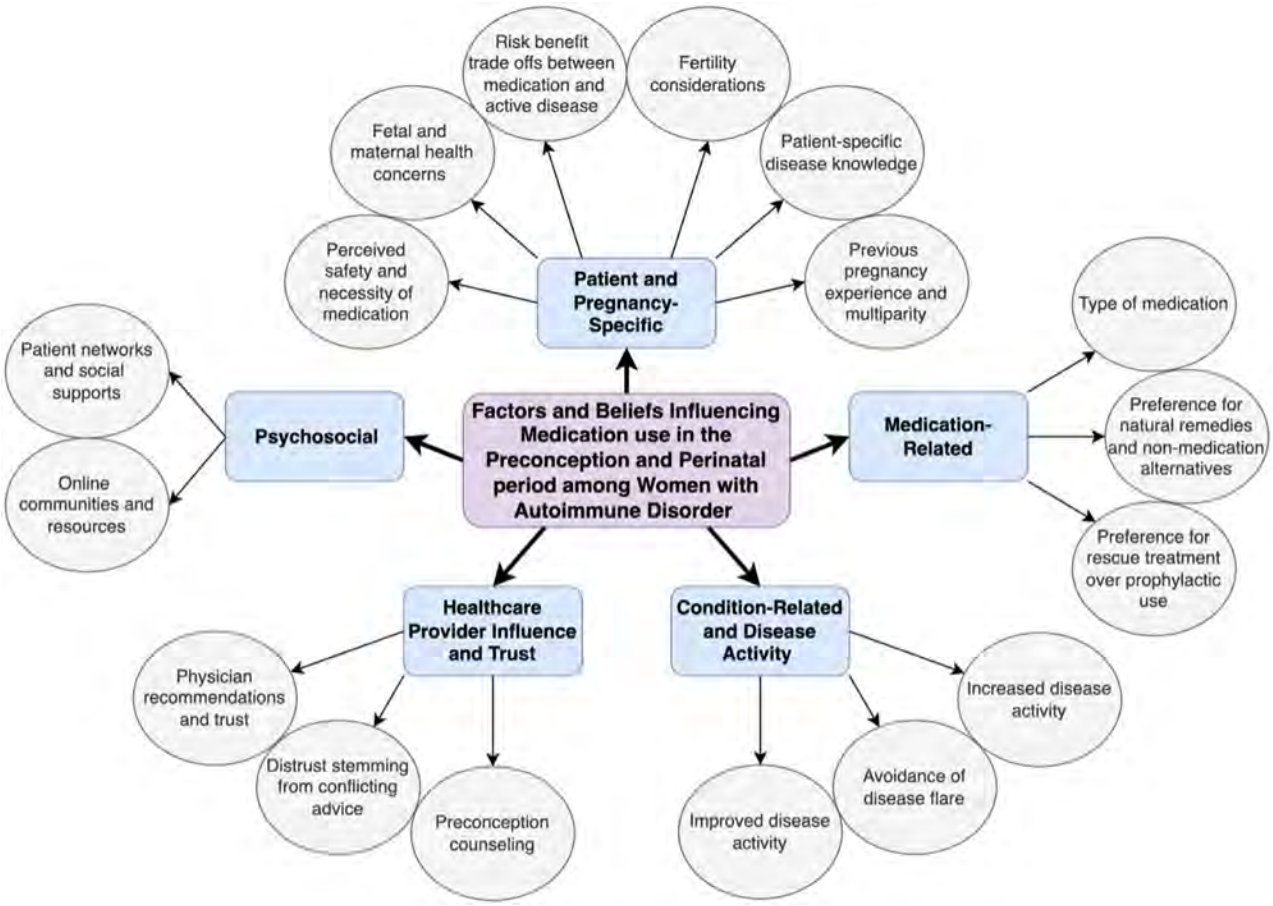
Olivia Novosel[1], Sabrina Chiodo[1], Yanara Marks[1], Lux Li[1], Renee Gabrielle Fajardo[1], Lauren Tailor[1], Lucy Zhao[1], Jessie Cunningham[2], Cristina Longo[3] and Sonia Grandi[1], [1]Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, ON, Canada, Toronto, ON, Canada, [2]Health Sciences Library, The Hospital for Sick Children, Toronto, ON, Canada, Toronto, ON, Canada, [3]Faculty of Pharmacy, University of Montreal, Montréal, QC, Canada, Montreal, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Autoimmune disorders (AD) disproportionately affect women of reproductive age, presenting challenges for disease management during the preconception and perinatal periods. Treatment decisions are complicated by the need to balance disease activity with potential risks to maternal and fetal health. Concerns about medication safety, teratogenicity, and disease severity often influence whether treatments are continued, discontinued, or switched. The objective of this review is to identify factors influencing medication use among women with AD who are attempting to conceive or are pregnant.

Methods: We conducted a systematic search in Ovid MEDLINE, Embase, CINAHL, and Cochrane Central for studies published from database inception until July 2024. Studies were included if they examined women with AD (e.g., inflammatory bowel disease (IBD), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), multiple sclerosis (MS), vasculitis) in the preconception or perinatal periods, reported on medication use or decision-making, and were published in English. Both qualitative and quantitative studies were eligible for inclusion. Data on medication use were extracted and categorized using

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Factors and beliefs influencing medication use in the preconception and perinatal period among women with autoimmune disorders

the WHO Multidimensional Adherence Model. Themes were synthesized using a narrative approach. Study quality was assessed using JBI (formerly Joanna Briggs Institute) critical appraisal tools.

Results: Our search identified 6415 articles, of which 20 studies met the inclusion criteria. Factors influencing medication use included patient- and pregnancy-specific beliefs (e.g., safety concerns, perceived necessity, and disease knowledge), medication-related (type and preference), condition-related (disease severity and activity), healthcare provider influence and trust, and psychosocial factors such as social support and involvement in online communities. Factors contributing to the continuation of medications included trust in healthcare providers and knowledge surrounding disease management, while discontinuation was found to be influenced by concerns about fetal harm and distrust in medical advice. Notably, inconsistent messaging from providers emerged as a recurrent barrier to medication use.

Conclusion: Decisions surrounding medication use in women with AD during the preconception and perinatal periods are shaped by complex, multifactorial influences. Addressing gaps in provider consensus, improving patient education, and increasing patient supports could improve informed decision-making and management of disease. Future research should focus on including underrepresented AD subtypes beyond IBD and RA to better understand the experiences of women with these conditions.

Disclosure: O. Novosel: None; **S. Chiodo**: None; **Y. Marks**: None; **L. Li**: None; **R. Fajardo**: None; **L. Tailor**: None; **L. Zhao**: None; **J. Cunningham**: None; **C. Longo**: None; **S. Grandi**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2564

An Illustration-based Patient-reported Outcome Measure Reveals Concealed Symptoms in Patients with Rheumatoid Arthritis and the Factor Contributing to the Discrepancy Between Patient and Evaluator Global Assessments

Mie Fusama[1], Hideko Nakahara[2], Megumi Okada[3], Kayoko Sakagami[4], Ikuyo Noguchi[5], Harumi Matsumura[6], Hiroaki Ito[4], Kosaku Oda[5], Yoshitaka Shinto[3], Kenshi Higami[6], Satomi Higami[6] and **Tetsuya Tomita**[7], [1]Kansai University of International Studies, Miki, Japan, [2]Osaka Yukioka College of Health Science, Ibaraki, Osaka, Japan, [3]Shinto Orthopaedics and Rheumatology Clinic, Osaka, Japan, [4]Infusion Clinic, Osaka, Japan, [5]Oda Orthopedic Surgery Rheumatology Clinic, Nishinomiya, Japan, [6]Higami Clinic of Rheumatology and Diabetology, Kashihara, Japan, [7]Morinomiya University of Medical Sciences, Osaka, Japan

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: RA patients frequently encounter challenges in effectively communicating their symptoms to medical professionals. Recently, the "Okomarigoto Sheet" (OS), an illustration-based patient-reported outcome measure for RA patients, was developed and has been widely used in Japan. However, the OS's correlation with the conventional patient-reported outcome (PRO) has not been sufficiently evaluated. This study aims to investigate whether items on the OS are related to conventional measures of disease activity and PRO, and assess its effectiveness in facilitating patients' expression of their symptoms.

Methods: Participants were recruited from four clinics. The OS consists of three symptom scales - morning stiffness duration, the Visual Analogue Scale (VAS) for joint pain and fatigue (0 = none, 100 mm = very severe). Illustrations depicting symptoms in five different situations were also provided for each symptom. Each illustration is scored as follows: no symptoms = 0, mild-moderate symptoms = 1, severe symptoms = 2. The total score of 5 illustrations for each symptom ranges from 0-10, with the total score of whole illustrations ranges from 0 to 30; indicating symptom severity. The correlations between the total illustration score and disease activity and QOL (SF-12) were evaluated. The correlations between patient global assessment (PGA), evaluator global assessment (EGA), and swollen joint count (SJC) and the total score of 5 illustrations for each symptom were also analyzed. Statistical analysis was conducted using Spearman's rank correlation coefficient.

Results: 80 patients (mean age: 61 years old) responded to the questionnaire. The total score of whole illustrations was positively correlated with DAS28 (rs= 0.538) and CDAI (0.648), and negatively correlated with Physical Component Summary (-0.534) and Mental Component Summary (-0.417) of SF-12. Stiffness duration, pain and fatigue VAS were positively correlated with total score of 5 illustrations for each symptom. Of the patients who scored 0 on stiffness duration, pain and fatigue VAS, 9 patients had symptoms in the illustrations (5 for stiffness; 1 for pain; 4 for fatigue). In addition, PGA was significantly correlated with all of total score of 5 illustrations for each symptom (stiffness: rs=0.551, pain: rs=0.651, fatigue: rs= 0.353, respectively). However, EGA was significantly associated with the total scores of 5 illustrations for stiffness (rs=0.476) and pain (rs=0.449), but not fatigue (rs= 0.164). SJC was also associated with the total scores of 5 illustrations for stiffness (rs=0.263) and pain (rs=0.379), but not fatigue (rs= 0.083).

Conclusion: The illustration-based OS reflected the findings obtained using standard measures of disease activity and QOL. It has also the potential to clarify symptoms that are not adequately captured by VAS. Furthermore, total score of 5 illustrations for fatigue was associated with PGA but not with EGA and SJC. It was reported that EGA is most closely

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

associated with SJC. Therefore, utilizing OS not only clarifies patients' symptoms in greater detail, but also suggests that fatigue may be one of the factors contributing to the discrepancy between PGA and EGA.

Disclosure: M. Fusama: None; **H. Nakahara**: None; **M. Okada**: None; **K. Sakagami**: None; **I. Noguchi**: None; **H. Matsumura**: None; **H. Ito**: None; **K. Oda**: None; **Y. Shinto**: None; **K. Higami**: None; **S. Higami**: None; **T. Tomita**: None.

Abstract Number: 2566

Using Abdominal CT-Derived Bone Mineral Density and Psoas Volume for Opportunistic Osteoporosis Screening and Fracture Risk Assessment

Ye Liu[1], Hongke Wu[1], Amy Mudano[2], Omar Safarini[1], John Eddins[1], Carlos Cardenas[1], Lesley Jackson[1], Jeffrey Curtis[3] and Steven Rothenberg[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Foundation for Advancing Science, Technology, Education and Research (FASTER), Hoover, AL, [3]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (2547–2566) ARP Posters II
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Osteoporosis (OP) is assessed by dual-energy X-ray absorptiometry (DXA) for bone mineral density (BMD). Computed tomography (CT) offers an alternative for "opportunistic" screening. This study evaluated the performance of CT-derived BMD alone and combined with psoas muscle mass to classify OP based on DXA and predict major osteoporotic fracture (MOF) risk based on FRAX.

Methods: Consecutive abdominal CT scans (2015–2018) of women with DXA available within 1 year of the CT exam were processed to quantify L1 vertebral attenuation and psoas muscle volume. T-scores and EHR data were extracted for age, race, and BMI. We obtained the lowest T score among lumbar spine, femoral neck, or total hip. OP was defined as the lowest T-score ≤ -2.5. CT BMD was defined as L1 attenuation in Hounsfield units. We fit 4 probit models to evaluate the discrimination ability of identifying OP: CT BMD alone (Model 1), CT BMD + psoas volume (Model 2), CT BMD + age + race + BMI (Model 3), and CT BMD + psoas volume + age + race + BMI (Model 4). AUROCs were used to compare discrimination.

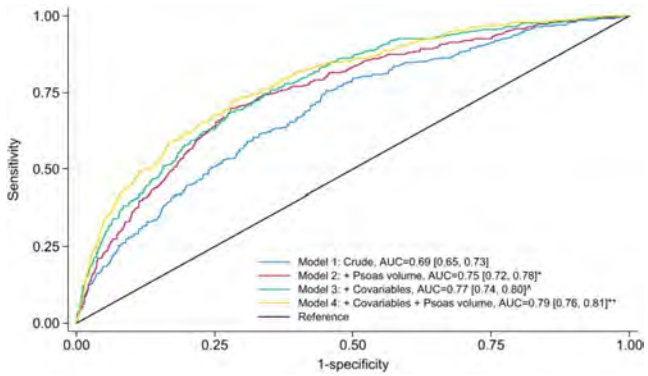


Figure 1. Abdominal CT-derived BMD and psoas volume in osteoporosis assessment: ROC curve comparison between models for osteoporosis classification (lowest T-score <=-2.5 vs. > -2.5) ROC curve comparison between models for osteoporosis classification (*: p<0.001 vs. Model 1. ^: p=0.18 vs. Model 2. **: p=0.039 vs. Model 3. N=1,442 women)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

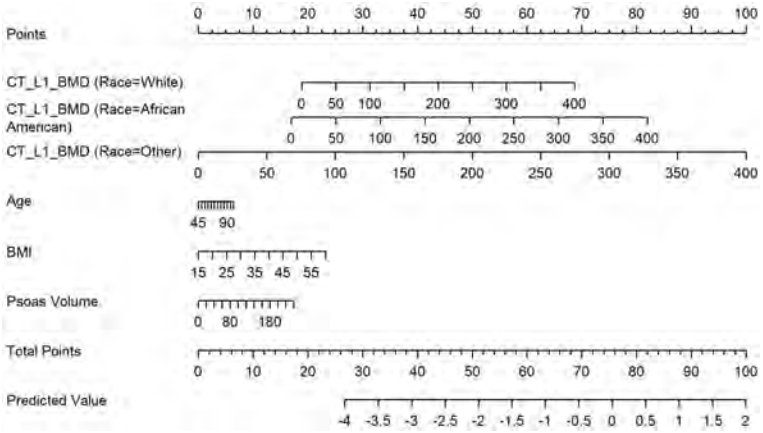


Figure 2. Regression-based nomogram for linear model predicting lowest T-score among lumbar spine, femoral neck, or total hip based on CT L1 BMD, psoas volume, and clinical variables (age, BMI, race)

Clustered bootstrap was used to calculate 95% CI and compare AUROC, accounting for repeated scans. We then built a linear model to predict the lowest T-score from CT BMD, psoas volume, age, race, and BMI by 5-fold cross-validation, with results visualized in a nomogram. A subgroup analysis of women with full FRAX risk factor data available was performed, modeling MOF risk ≥20% as the outcome, using similar analytical approaches.

Results: A total of 1,761 CT scans linked with DXA were analyzed(mean age: 67.5 ± 9.7). ROC curves and AUROCs are shown in Figure 1. Discrimination was modest (AUROC 0.69) using the CT L1 BMD alone and appreciably improved after adding psoas volume (AUROC 0.75). The AUROC for CT L1 BMD, independent of age, BMI, and race, was 0.67 [0.63–0.71], and for psoas volume was 0.62 [0.59–0.66] (p = 0.11). The linear model predicting lowest T-score showed good discrimination (g-index=0.84) and calibration (slope=0.996; see nomogram in Figure 2). However, neither CT BMD alone (AUROC = 0.66 [0.55–0.76]) nor combined with psoas volume (AUROC = 0.66 [0.56–0.76], p = 0.69) effectively identified high MOF risk.

Conclusion: Adding psoas muscle volume to L1 CT BMD from abdominal CT performed for other purposes significantly improved OP classification compared to CT L1 attenuation alone. Combining muscle volume and BMD measures may improve incidental OP diagnosis accuracy for targeted interventions.

Disclosure: Y. Liu: Amgen, 5; **H. Wu**: None; **A. Mudano**: None; **O. Safarini**: None; **J. Eddins**: None; **C. Cardenas**: None; **L. Jackson**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **S. Rothenberg**: None.

Abstract Number: 2567

Temporal Trends in Cardiometabolic Multimorbidity Risk in Rheumatoid Arthritis: A National, Matched Cohort Study

Tate Johnson[1], Joshua Baker[2], Punyasha Roul[3], Grant Cannon[4], Gary Kunkel[5], Brian Sauer[6], Ted Mikuls[1] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pennsylvania, Philadelphia, PA, [3]UNMC, Omaha, NE, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [6]Salt Lake City VA/University of Utah, Salt Lake City, UT

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Epidemiology & Public Health II (2567–2572)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Multimorbidity, the presence of multiple chronic conditions, is over-represented in RA. A cardiometabolic multimorbidity (CMM) phenotype has emerged in the general population, but is not well studied in RA despite cardiovascular disease (CVD) being the leading cause of death in RA. We evaluated the risk of CMM in RA and whether CMM risk has improved with advances in RA management.

Methods: Using national Veterans Affairs (VA) data, we identified incident RA patients (≥2 RA ICD codes, rheumatologist diagnosis, positive autoantibody or DMARD fill, plus ≥365 days in VA care before a DMARD fill or RA ICD code) matched up to 10 non-RA controls on age, sex, and VA enrollment year. Cohort entry was the date the RA algorithm was fulfilled. A traditional CMM outcome included coronary artery disease (CAD), stroke, and diabetes (DM). Given the growing recognition of Cardiovascular-Kidney-Metabolic (CKM) syndrome and its impact on both atherosclerotic CVD and heart failure (HF), an expanded CMM outcome was defined, informed by CKM syndrome components (CAD, stroke, HF, DM, hypertension [HTN], hyperlipidemia [HPL], chronic kidney disease [CKD], and obesity). Individual conditions were identified by ≥2 ICD codes ≥30 days apart. CMM onset was the date ≥2 conditions developed. We additionally defined more severe CMM phenotypes, requiring ≥3 and ≥5 (expanded CMM only) conditions. Patients meeting CMM outcomes prior to cohort entry were excluded. We examined the RA-related risk of CMM using Cox regression, stratified on matched sets and adjusting for age, sex, race, ethnicity, smoking status, BMI, rurality, and healthcare utilization. Censoring occurred at death or end of study period (1/2023). Temporal trends in CMM risk were evaluated in models stratified on RA diagnosis year (2000-2005, 2006-2011, 2012-2017), testing the linear interaction of RA status and time-period. Secondary analyses evaluated CMM risk stratified by seropositivity (RF and/or anti-CCP) and elevated inflammation (ESR and/or CRP) at baseline.

Results: We matched 28,537 RA patients (mean age 63, 85% male) to 252,602 non-RA controls. Over 2,522,982 person-years, 25,474 patients developed the traditional CMM outcome. The incidence of all CMM outcomes was higher in patients with RA (range aHR 1.14-1.31) in fully adjusted models (**Table 1**). The RA-related risk of CMM was higher in more recent time periods (p-for-trend < 0.001 for all CMM outcomes; **Figure 1**). The expanded CMM outcome severe phenotype (≥5 conditions) in the most recent time-period (RA diagnosis year 2012-17) was the most over-represented outcome in RA (aHR 1.42 [1.34-1.51]; **Figure 1**). CMM risk compared to controls was similar regardless of serostatus, while risk was typically accentuated in those with elevated inflammation (range aHR 1.13-1.48) at baseline compared to those with normal inflammatory measures (range aHR 1.12-1.18) (**Table 2**).

Table 1. Risk of cardiometabolic multimorbidity development in RA vs. matched controls

	RA (N=28,537)		Controls (N=252,602)		
	N	IR (95% CI)*	N	IR (95% CI)*	aHR (95% CI)**
Traditional Cardiometabolic Multimorbidity (CAD, Stroke, DM)					
≥2 cond.	4,051	17.9 (17.4-18.5)	21,423	9.3 (9.2-9.5)	1.23 (1.19-1.28)
≥3 cond.	1,120	4.2 (4.0-4.4)	6,186	2.1 (2.1-2.2)	1.21 (1.13-1.29)
Expanded Cardiometabolic Multimorbidity (CAD, Stroke, HF, DM, HTN, HPL, Obesity)					
≥2 cond.	5,941	84.7 (82.5-86.8)	23,994	42.6 (42.1-43.2)	1.14 (1.10-1.18)
≥3 cond.	7,334	56.8 (55.6-58.2)	34,258	29.0 (28.7-29.3)	1.20 (1.17-1.24)
≥5 cond.	4,499	18.9 (18.4-19.5)	23,194	9.1 (9.0-9.2)	1.31 (1.27-1.36)

* Incidence rate (IR) calculated per 1,000 person-years

**Adjusted hazard ratios (aHR) estimated in multivariable Cox regression models, stratified on matched pairs, and adjusted for age, sex, race, ethnicity, BMI, smoking status, rurality, and healthcare utilization.

Abbreviations: CAD, coronary artery disease; CI, confidence interval; Cond, condition; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; HPL, hyperlipidemia; RA, rheumatoid arthritis

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

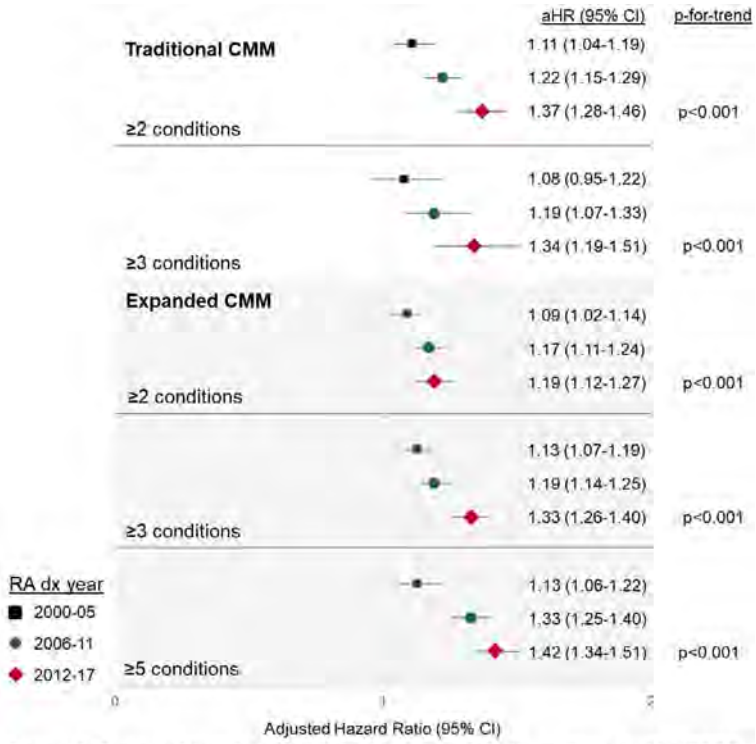


Figure 1. Temporal trends in the risk of cardiometabolic multimorbidity (CMM) in RA vs. matched controls. Adjusted hazard ratios (aHR) and 95% confidence intervals (CI) estimated in Cox regression models, stratified on matched sets and adjusted for age, sex, race, ethnicity, BMI, smoking status, rurality, and healthcare utilization. Models stratified by RA diagnosis year in sequential 5-year time periods, testing the interaction of RA and time-period in a linear manner.

Conclusion: RA-related wrisk of CMM is worsening over the past two decades despite advances in RA disease activity management. The burden of CMM highlighted by these data underscores the need for additional RA-specific strategies paired with disease activity control to reduce cardiometabolic risk and improve CVD-related outcomes in this high-risk population.

Table 2. Risk of cardiometabolic multimorbidity development in RA vs. matched controls, stratified by seropositivity and baseline acute phase reactants

	Seropositive RA	Seronegative RA
Traditional CMM	aHR (95% CI)	aHR (95% CI)
≥2 cond.	1.22 (1.17-1.28)	1.25 (1.18-1.32)
≥3 cond.	1.13 (1.04-1.24)	1.33 (1.20-1.47)
Expanded CMM		
≥2 cond.	1.12 (1.08-1.17)	1.17 (1.11-1.24)
≥3 cond.	1.17 (1.13-1.22)	1.24 (1.18-1.30)
≥5 cond.	1.31 (1.25-1.36)	1.32 (1.25-1.40)
	Elevated ESR/CRP	**Normal ESR/CRP**
Traditional CMM	aHR (95% CI)	aHR (95% CI)
≥2 cond.	1.31 (1.24-1.38)	1.17 (1.11-1.23)
≥3 cond.	1.31 (1.19-1.44)	1.12 (1.02-1.23)
Expanded CMM		
≥2 cond.	1.13 (1.08-1.19)	1.14 (1.09-1.19)
≥3 cond.	1.27 (1.21-1.32)	1.15 (1.11-1.20)
≥5 cond.	1.48 (1.40-1.55)	1.18 (1.13-1.24)

Adjusted hazard ratios (aHR) estimated in multivariable Cox regression models, stratified on matched pairs, and adjusted for age, sex, race, ethnicity, BMI, smoking status, rurality, and healthcare utilization.

Abbreviations: CMM, cardiometabolic multimorbidity; Cond, condition; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RA, rheumatoid arthritis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: T. Johnson: None; **J. Baker**: Amgen, 5; **P. Roul**: None; **G. Cannon**: None; **G. Kunkel**: None; **B. Sauer**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 2568

Cardiovascular Risk Prediction in Systemic Lupus Erythematosus: Comparing the PREVENT and SLECRISK Models

Youngmin Kim[1], Hongshu Guan[2], Emily Oakes[1], Katherine Zhong[3], Misti Paudel[4], May Choi[5], Katherine Liao[1], Brittany Weber[6] and Karen H. Costenbader[7], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital/Harvard Medical School, Boston, [3]Brigham and Women's Hospital, Short Hills, NJ, [4]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [5]University of Calgary, Calgary, AB, Canada, [6]Brigham and Women's Hospital, DEDHAM, MA, [7]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Epidemiology & Public Health II (2567–2572)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have increased risk for atherosclerotic cardiovascular disease (CVD) events, often underrepresented in traditional risk models. We previously developed an SLE-specific 10-year CVD risk model, SLECRISK, incorporating SLE-specific variables (Choi et al., 2024). The American Heart Association (AHA) recently introduced the PREVENT (Predicting Risk of cardiovascular disease EVENT) algorithm to assess CVD risk (Khan et al., 2024). We compared the predictive performance of SLECRISK and PREVENT in our SLE cohort.

Methods: Adult SLE patients meeting ACR 1997 and/or EULAR criteria from our academic center were included. SLECRISK and PREVENT estimated 10-year risk of myocardial infarction, stroke, or cardiac death. Outcomes were adjudicated by two cardiologists. Discrimination was assessed using c-statistics. Model performance was compared by sensitivity, specificity, and AIC. Calibration was evaluated by decile-based observed vs. predicted risk plots. Risk categories were defined as ≤7.5% (low), 7.5–20% (moderate), or ≥20% (high). Demographics and clinical features of patients classified as moderate/high risk by SLECRISK vs. PREVENT were analyzed using t-tests and chi-square tests.

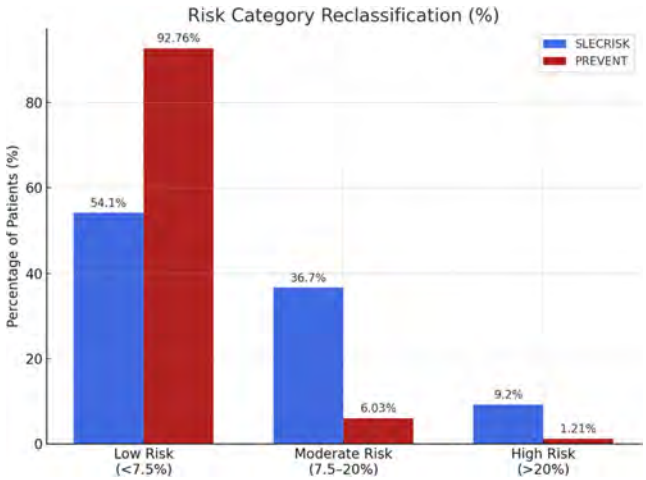


Figure 1. Risk Category Classification of SLECRISK and PREVENT in definite (adjudicated) and probable MACE.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In this cohort of 1,243 patients, PREVENT and SLECRISK yielded similar discrimination (AUC: 0.756 vs. 0.744; p = 0.68), but SLECRISK showed better model fit (AIC: 592.2 vs. 611.1). **Figure 1** shows proportions of patients categorized into low, moderate, and high CVD risk by each model. Using a ≥7.5% cutoff, 581 patients (46.7%) were classified as moderate/high risk by either model: 491 by SLECRISK only, 11 by PREVENT only, and 79 by both. Patients flagged by SLECRISK alone were significantly younger (mean 42.5 vs. 57.5 years, p < 0.0001), had lower systolic BP (122.0 vs. 145.3 mmHg, p < 0.0001), creatinine (0.93 vs. 2.55 mg/dL, p < 0.0001), and LDL (101.9 vs. 110.4 mg/dL, p = 0.02), but higher prevalence of SLE autoantibodies, including anti-dsDNA (78.6% vs. 36.7%) and anti-RNP (55.7% vs. 27.8%), all significant (**Table 1**). Calibration analysis showed better concordance between predicted and observed CVD with SLECRISK (**Fig. 2**).

Conclusion: SLECRISK identified more at-risk SLE patients, effectively capturing younger individuals with greater immunologic activity and lower traditional cardiovascular burden. Despite similar AUCs, SLECRISK showed better calibration and model fit. These findings support integration of SLECRISK into clinical care and guidelines for CVD risk stratification in SLE.

Table 1. Comparison of baseline characteristics between patients classified as moderate/high cardiovascular risk (7.5% and greater) by SLECRISK only versus by PREVENT only or by both models among 1,243 patients

Baseline Characteristics	SLECRISK (n=491)	PREVENT (n=90)	p-value
Age, years	42.5 (12.6)	57.5 (17.2)	<0.0001
Female, %	92.1	92.2	0.96
Total Cholesterol, mg/dL	182.7 (38.2)	204.6 (111.9)	0.001
LDL, mg/dL	101.9 (27.6)	110.4 (42.1)	0.02
SBP, mmHg	122.0 (16.6)	145.3 (24.4)	<0.0001
DBP, mmHg	76.0 (11.1)	82.2 (16.4)	0.001
Smoking, %	9.4	7.8	0.91
Diabetes, %	5.3	32.2	<0.0001
Mean SLE Duration, years	14.9 (10.2)	14.0 (10.7)	0.48
Creatinine, mg/dL	0.93 (0.68)	2.55 (2.83)	<0.0001
Anti-dsDNA, %	78.6	36.7	<0.0001
Anti-RNP, %	55.7	27.8	<0.0001
Anti-Ro, %	57.6	29.0	<0.0001
Anti-La, %	40.5	25.6	0.01
Lupus anticoagulant, %	19.8	24.4	0.38
Anti-cardiolipin IgG, %	21.0	13.3	0.05
Anti-β2 Glycoprotein I IgG, %	2.4	7.8	0.05
Low C3, %	61.9	44.4	<0.0001
Low C4, %	56.2	48.9	0.01

Abbreviations: IgG, immunoglobulin G; C3, complement component 3; C4, complement component 4; DBP, diastolic blood pressure; dsDNA, double-stranded DNA; LDL, low-density lipoprotein; RNP, ribonucleoprotein; SBP, systolic blood pressure; SLE, systemic lupus erythematosus.

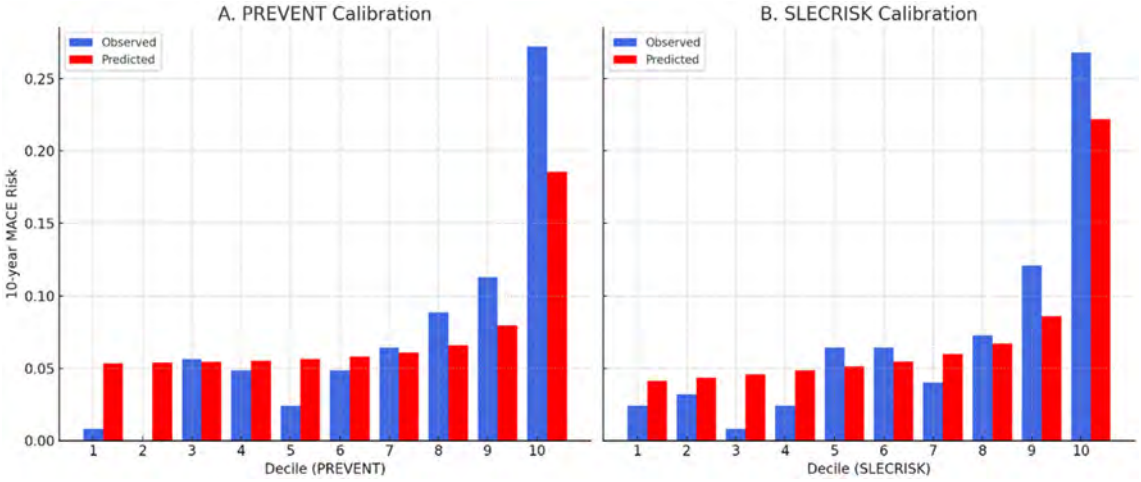


Figure 2. Calibration plot of PREVENT and SLECRISK Models.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: Y. Kim: None; **H. Guan**: None; **E. Oakes**: None; **K. Zhong**: None; **M. Paudel**: None; **M. Choi**: AstraZeneca, 2, 5, 6, Celltrion, 2, MitogenDx, 2, Organon, 6, Werfen, 2; **K. Liao**: Merck/MSD, 2, UCB, 2; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 2569

Performance of the PREVENT Heart Failure General Population Risk Score in Patients with Rheumatoid Arthritis

Ilana Usiskin[1], Katherine Zhong[2], Ying Qi[3], Lauren rusnak[1], Andrew Cagan[1], Yumeko Kawano[1], Tianrun Cai[1], Daniel Solomon[4], Jennifer Ho[5], Brittany Weber[6] and Katherine Liao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Short Hills, NJ, [3]Brigham and Women's Hospital, Boston, [4]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [5]Beth Israel Deaconess Medical Center, Boston, MA, [6]Brigham and Women's Hospital, DEDHAM, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Epidemiology & Public Health II (2567–2572)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of heart failure (HF) compared to the general population, and HF with preserved ejection fraction (HFpEF) is the predominant subtype in RA. The 2023 Predicting Risk of Cardiovascular Disease Events (PREVENT) risk equations include estimates of 10-year risk for HF (PREVENT-HF) in the general population. As inflammation is important in HF, particularly HFpEF, the ability to estimate HF risk in the RA population may open opportunities for earlier intervention with anti-inflammatory therapy. We aimed to study the performance of the PREVENT-HF risk equation for incident HF among patients with RA.

Methods: We studied a multi-institution electronic health record (EHR)-based longitudinal RA cohort. The study applied validated definitions for RA diagnosis, and patients were followed for incident HF, and HF subtype [HFpEF (EF≥50%) vs HF with reduced EF (HFrEF, EF< 50%)] using a combination of ICD codes and clinical information extracted using natural language processing. RA diagnosis date was the index date, and subjects with prevalent HF were excluded. Covariates for PREVENT-HF and other known HF risk factors were extracted from the EHR 1 year prior and 3 months after the index date. The PREVENT-HF score was calculated at the index date. Subjects were followed until their 1st HF diagnosis, loss to follow-up, or through 10 years, whichever occurred earlier. Discrimination of PREVENT-HF was evaluated by calculating the area under the curve (AUC), and calibration was tested using a calibration plot and the Hosmer-Lemeshow test.

Results: We studied 2,209 patients with RA, and 150 (6.8%) developed HF within 10 years after the index date. RA patients with HF were older, more likely to be male, with higher BMI, lower eGFR, and a higher burden of cardiovascular risk factors than patients without incident HF (Table 1). Those with incident HF also had higher C-reactive protein (CRP) and were less likely to be on methotrexate or TNF inhibitor than patients without incident HF. Of those with incident HF, 72% had HFpEF (EF≥50%) and 28% HFrEF (EF< 50%). The PREVENT-HF estimated median 10-year HF risk was 8.2% (IQR 4.5-16.1) among those who developed HF and 2.4% (IQR 0.9-5.4) among those who did not. The AUC of PREVENT-HF was 0.78, and the calibration plot showed overall underestimation of HF risk (Hosmer-Lemeshow p-value < 0.001; Figure 1). Underestimation was more prominent in the borderline and intermediate risk categories, which were predominantly HFpEF (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of RA cohort stratified by incident heart failure within 10 years of RA diagnosis date

Characteristic	Overall (n=2,209)*	Heart Failure (n=150)*	No Heart Failure (n = 2,059)*	p-value
PREVENT-HF Components				
Age	56 (47, 65)	65 (57, 73)	56 (47, 64)	<0.001
Female	75%	57%	76%	<0.001
BMI (mg/kg2)	28 (24, 32)	31 (26, 36)	28 (24, 32)	<0.001
Current smoker	10%	13%	10%	0.4
SBP (mmHg)	128 (118, 140)	130 (118, 142)	128 (118, 140)	0.2
eGFR	90 (75, 103)	76 (58, 92)	91 (77, 103)	<0.001
Antihypertensive medication	38%	77%	36%	<0.001
Diabetes	12%	24%	11%	<0.001
Self- reported race				0.11
Asian	3%	1%	3%	
Black	7%	10%	7%	
Hispanic	7%	3%	7%	
White	78%	82%	78%	
Unknown/Other	5%	4%	5%	
Established HF Risk Factors				
Atrial Fibrillation	2%	4%	2%	0.016
Coronary Artery Disease	8%	23%	7%	<0.001
Hyperlipidemia	24%	33%	24%	0.011
Hypertension	32%	50%	31%	<0.001
Prior Stroke	4%	11%	4%	<0.001
Chronic Kidney Disease	3%	9%	2%	<0.001
C-Reactive Protein**	6.8 (2.2, 18.0)	13.9 (4.8, 29.2)	6.6 (2.2, 17.2)	<0.001
RA treatments				
Methotrexate	30%	9%	32%	<0.001
TNFi	10%	4%	10%	0.016
Any DMARD	40%	17%	42%	<0.001
Steroids	45%	38%	45%	0.090
Ejection Fraction***				
HFpEF (EF ≥50%)	-	72%	-	
HFrEF (EF < 50%)	-	28%	-	
PREVENT Heart Failure Score	2.6 (0.9, 6.0)	8.2 (4.5, 16.1)	2.4 (0.9, 5.4)	<0.001

*Median (IQR) or %
** n=751(34%) overall cohort without CRP data
***n=6 (4%) HF subjects without EF data

Conclusion: The PREVENT-HF equation is a promising tool to identify RA patients at increased HF risk, however it generally underestimates HF risk particularly among subjects with borderline and intermediate risk. Further work is needed to determine factors that may enhance prediction for HF, particularly HFpEF, in RA.

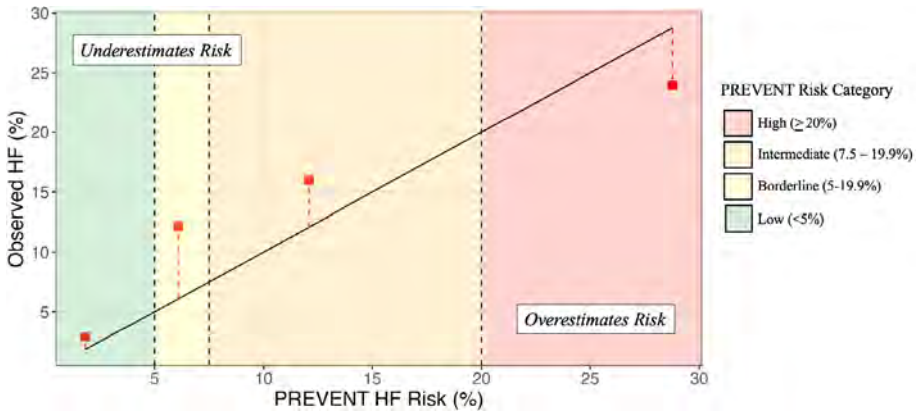


Figure 1. Calibration plot of predicted HF risk by PREVENT-HF compared to observed incident HF events [red squares denote predicted vs observed by PREVENT-HF risk category].

Table 2. Comparison of the predicted HF risk by PREVENT-HF to observed incidence of HF, categorized by risk category.

PREVENT-HF Risk Category	Total (n)	Average predicted incident HF (%)	Observed incident HF, (%)	HF subtypes within each category (%)	
				HFpEF	HFrEF
Low (<5%)	1536	2	3	59	41
Borderline (5-7.4%)	239	6	12	72	24
Intermediate (7.5 - 19.9%)	338	12	16	72	20
High (≥20%)	96	29	24	72	22

Disclosure: I. Usiskin: None; **K. Zhong**: None; **Y. Qi**: None; **L. rusnak**: None; **A. Cagan**: None; **Y. Kawano**: None; **T. Cai**: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9; **J. Ho**: Eli Lilly, 2, Pfizer, 8; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **K. Liao**: Merck/MSD, 2, UCB, 2.

Abstract Number: 2570

Accelerometer-derived 'weekend Warrior' Physical Activity, Genetic Susceptibility, and Incident Rheumatoid Arthritis: A Prospective Cohort Study

Zihao Xu[1] and **Zhixiu Li**[2], [1]Southern University of Science and Technology, ShenZhen, China (People's Republic), [2]Southern University of Science and Technology, ShenZhen, Guangdong, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Epidemiology & Public Health II (2567–2572)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Physical activity is associated with a reduced risk of rheumatoid arthritis (RA). However, it is unclear whether the 'weekend warrior' (WW) pattern, characterized by achieving the majority moderate-to-vigorous PA (MVPA) with 1-2 days, offers similar benefits for incident RA to a more evenly distributed pattern. This study aimed to explore the association of accelerometer-deviced WW and other patterns patterns with incident RA, and the modification effect by genetic susceptibility.

Methods: A total of 89,241 participants from the UK Biobank without a prior diagnosis of RA and with a complete week of accelerometer-based physical activity data (collected between 2013 and 2015) were included. Participants were categorized according to guideline-based thresholds: inactive (< 150 min/week), active WW (≥150 min/week with ≥50% of total MVPA accrued in 1–2 days), and regularly active (≥150 min/week but not meeting the active WW criteria). A polygenic risk score for RA was was used for further assessing the interactions and joint effects of genetic risk and activity pattern. The associations between different activity patterns and incident RA were evaluated using multivariable Cox proportional hazards models, adjusting for potential confounders.

Results: During a mean follow-up of 7.8 years, 675 individuals developed RA. Overall, a nonlinear inverse relationship was observed between total MVPA and incident RA (P for nonlinearity = 0.003). Compared to inactive group, both the active WW (HR = 0.60, 95%CI, 0.50-0.71) and regular active (HR = 0.62, 95%CI, 0.50-0.77) group exhibited a similarly reduced risk of RA. When WW and regular activity were compared directly, there were no statistically significant difference. Similar

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

findings were observed when applying the median MVPA threshold of ≥230.4 min/week. No significant interaction between genetic risk of RA and activity pattern was observed. Moreover, participants with an active WW pattern and low genetic risk had the lowest risk of incident RA (HR = 0.33, 95%CI, 0.23-0.46) compared with inactve individuals with low genetic risk.

Conclusion: Both concentrated MVPA accumulated over 1 to 2 days and evenly distributed physical activity were associated with a reduced risk of developing RA, even in the high and middle genetic risk group. These findings suggest that meeting MVPA guidelines—whether through a WW or regular pattern—may mitigate RA risk even in individuals with elevated genetic predisposition.

Disclosure: Z. Xu: None; **Z. Li**: None.

Abstract Number: 2571

Rare Clinically Significant Methotrexate Toxicity Despite Frequent Laboratory Abnormalities: A Population-Based Study of Methotrexate Monitoring

Griffin Reed[1], Jeffrey Yang[1], Georges El Hasbani[1], Cynthia Crowson[2], Hannah Langenfeld[1], Jeffrey Sparks[3], Bryant England[4], gabriela Schmajuk[5], Kaleb Michaud[4], John Davis[1] and Vanessa Kronzer[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Stewartvillle, MN, [3]Brigham and Women's Hospital, Boston, MA, [4]University of Nebraska Medical Center, Omaha, NE, [5]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Epidemiology & Public Health II (2567–2572)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Methotrexate laboratory monitoring is highly resource intensive, and recent evidence questions whether the true toxicity of methotrexate has been over-estimated. Therefore, we aimed to determine the incidence of clinically significant methotrexate toxicity.

Methods: We leveraged a population-based cohort in a geographically defined area. We screened these 1.4 million individuals for adults with ≥2 diagnostic codes for systemic rheumatic disease and new initiation of low-dose (≤25 mg/week) methotrexate between January 1, 2012 and December 31, 2024. We manually confirmed incident methotrexate use, recorded covariates including frequency of methotrexate laboratory monitoring as compared to ACR guidelines (≥3 in the first 3 months, ≥3 in the next 3-12 months, and at least every 3 months thereafter), determined whether each potential methotrexate-related abnormality [AST (high), ALT (high), creatinine (high), hemoglobin (low), platelets (low), or white blood cells (low)] was clinically significant (defined as temporary or permanent methotrexate dose reduction and/or discontinuation), and quantified healthcare resources used as a result of any abnormalities. We calculated the incidence of clinically significant methotrexate toxicity per 100 person-years.

Results: Of the 3,558 individuals reviewed, we included all 2,606 who met the above inclusion criteria (mean age 58 years, 65% female, mean 4.3 [SD 3.1] years methotrexate use spanning 11,169 total person-years, 324 [12%] meeting ACR monitoring guidelines across all time points, **Table 1**). Many patients developed laboratory abnormalities (**Table 2**). However, only 97 of 4,847 (2.0%) of these abnormalities were clinically significant (0.9 per 100 person-years). Of those, 31 (32%) resulting in a reduced dose of methotrexate, and 66 (68%) resulting in permanent discontinuation, mostly for elevated AST

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of the 2,606 individuals with systemic rheumatic disease and incident low-dose methotrexate use 2012-2024

Characteristic	N=2,606
Age, mean (SD), years	58 (16)
Female sex, (%)	65%
White race, (%)	92%
BMI, mean (SD), kg/m²	31 (8)
Smoking history, (%)	
Never	53%
Former	38%
Current	9%
Alcohol drinks per week, (%)	
0-2	89%
3-7	10%
8 or more	1%
Rheumatic disease diagnosis, (%)	
Ankylosing spondylitis	1%
Large vessel vasculitis	1%
Polymyalgia rheumatica	6%
Psoriasis/ psoriatic arthritis, or other spondyloarthritis	21%
Rheumatoid arthritis	64%
Sjögren's disease	1%
Systemic sclerosis, limited or diffuse	1%
Other/unknown	6%
Methotrexate use duration during follow-up, (%)	
<3 months	6%
3 to <6 months	6%
6 months to <1 year	7%
1 to <5 years	41%
5+ years	39%
Formulation of the first methotrexate prescription, (%)	
Oral	93%
Subcutaneous	7%
Met ACR methotrexate monitoring guidelines, N (%)	
Months 0-3	1,507 (58%)
Months 3-12	1,566 (63%)
≥12 months	420 (18%)
All time points	324 (12%)

BMI = body mass index, SD = standard deviation

Table 2. Incidence of abnormal methotrexate monitoring labs and their clinical significance

Laboratory measure	Patients ever abnormal N (%)	Abnormal/total monitoring tests N (%)	Clinically significant abnormalities N tests (rate per 100 py)
AST or ALT	871 (33%)	1223/25863 (5%)	59 (0.53)
Creatinine	688 (26%)	1114/25863 (4%)	5 (0.05)
Hemoglobin	1065 (41%)	1697/25863 (7%)	11 (0.10)
Platelets	357 (14%)	514/25863 (2%)	13 (0.12)
White blood cells	226 (9%)	299/25863 (1%)	9 (0.08)
Total	1743 (67%)	4847/129315 (4%)	97 (0.87)

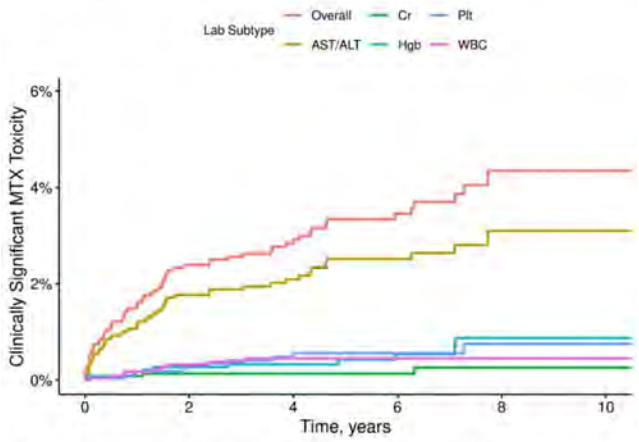
ALT = alanine Aminotransferase, AST = aspartate aminotransferase, py = person years

and/or ALT (**Table 2, Figure 1**). On the other hand, the methotrexate monitoring abnormalities led to an additional 4,546 blood draws, 84 healthcare visits, 104 imaging studies, 16 bone marrow biopsies, and 2 liver biopsies.

Conclusion: This first population-based study of manually-validated methotrexate toxicity events found that the incidence of clinically significant methotrexate toxicity was low, and healthcare resource utilization in response to abnormal labs was high. These results suggest that less frequent methotrexate monitoring may be justified. Future work will elucidate the populations that most benefit from less frequent monitoring and identify the optimal monitoring protocols.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Time to clinically significant methotrexate monitoring abnormality with subclassification by abnormality type



ALT = alanine Aminotransferase, AST = aspartate aminotransferase, Cr = serum creatinine, Hgb = hemoglobin, Plt = platelets, WBC = white blood count

Disclosure: G. Reed: None; **J. Yang**: None; **G. El Hasbani**: None; **C. Crowson**: None; **H. Langenfeld**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **B. England**: Boehringer-Ingelheim, 2, 5; **g. Schmajuk**: None; **K. Michaud**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **V. Kronzer**: None.

Abstract Number: 2572

Multi-Modal Machine Learning Prediction and Phenotyping of Systemic Lupus Erythematosus Using Longitudinal EHR and Genomic Data from the *All of Us* Program

Hunter Sporn[1], Roshni Parulekar-Martins[1], Haopeng Wang[1], Xinran Yu[1], Jeong Yee[2], Youngmin Kim[3], Jing Cui[4] and Karen H. Costenbader[5], [1]Massachusetts Institute of Technology, Boston, [2]Sungkyunkwan University, Suwon, MA, South Korea, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham and Women's Hospital/ Harvard Medical School, Boston, [5]Harvard Medical School and Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Epidemiology & Public Health II (2567–2572)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Timely diagnosis and clinically meaningful stratification of systemic lupus erythematosus (SLE) remain major unmet needs. Existing risk models rely on limited genetic or lifestyle predictors and are often built on non-representative cohorts. Phenotyping studies, meanwhile, typically use curated registries that fail to capture the real-world complexity of SLE presentations. The NIH All of Us program, a US-wide cohort, offers an unprecedented opportunity to integrate genetic risk scores (GRS), structured electronic health record (EHR) data, using unsupervised learning at scale to address both challenges.

Methods: Within All of Us (version 8), we identified SLE cases (≥2 ICD-10 codes on separate days) and matched controls by age, sex, and genetically inferred ancestry. Supervised models (logistic regression, random forest, XGBoost) were trained using 5-year pre-diagnosis features: GRS, medications, symptoms, reproductive, and self-reported lifestyle factors. Performance was assessed across time windows on a held-out test set.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

For phenotyping, we implemented two unsupervised clustering pipelines. Approach A used normalized immune, renal, and metabolic lab data during flare and non-flare periods. Approach B integrated post-diagnosis lab values, medication classes, and grouped conditions (6-18 months post-index). Dimensionality reduction (PCA, UMAP) preceded clustering (k-means, HDBSCAN). Clusters were interpreted based on lab profiles, treatment exposure, and organ-specific manifestations.

Results: 1526 SLE cases were matched to 3942 non-SLE controls. (**Table 1**) Prediction models yielded AUCs 0.61–0.64. GRS, joint pain, depression, and obesity were consistent predictors. Accuracy peaked near diagnosis (AUC 0.71), though at the cost of recall—highlighting the challenge of early signal detection.

Clustering revealed distinct, interpretable phenotypes (**Figures 1-2**). A flare-associated cluster had concurrent dsDNA elevation, proteinuria, and transaminitis (renal/hepatic flare). A non-flare cluster featured persistent hypocomplementemia and hypertriglyceridemia, consistent with systemic inflammation and metabolic dysregulation. A 3rd group had high psychiatric and musculoskeletal burden with minimal serologic activity or immunosuppressant exposure—suggesting a care-intensive, serologically quiescent phenotype. Clusters demonstrated high clinical interpretability and mapped to established organ-domain patterns, with approach-specific silhouette scores from 0.27–0.49.

Conclusion: This is among the 1st studies to apply integrated machine learning across genomic and EHR and self-reported data to model both SLE risk and phenotypic heterogeneity. While predictive performance remains limited, phenotyping revealed actionable, domain-aligned subtypes with potential to inform prognosis, treatment, and clinical trial design. These findings highlight the promise of real-world, multimodal data to advance precision medicine in rheumatology.

Table 1. Selected Demographic and Clinical Characteristics of the SLE Cases and their Matched Controls for 5 year - 1 year Pre-Diagnosis (SLE Diagnosis Index Date) in the All of Us Cohort, version 8

Feature	SLE Cases (n=1526)	Controls (n=3942)
Demographics		
Age (mean, SD)	55.305 (14.677)	56.557 (14.348)
Sex at Birth – Female	1371 (89.84%)	3560 (90.29%)
Sex at Birth – Male	141 (9.24%)	374 (9.49%)
Race – European	687 (45.02%)	2047 (51.91%)
Race – African	517 (33.88%)	1183 (30.00%)
Race – Admixed American	266 (17.43%)	643 (16.31%)
Race – East Asian	30 (1.97%)	47 (1.19%)
Race – South Asian	20 (1.31%)	22 (0.56%)
Clinical Score		
Score (mean, SD)	42.747 (1.676)	42.251 (1.654)
Survey: Alcohol Use		
No response (nan)	1458 (95.54%)	3759 (95.33%)
1–2 drinks/day	49 (3.21%)	141 (3.58%)
Medical Record Frequency		
Obesity	0.106 (0.307)	0.142 (0.349)
Depressive symptoms	0.083 (0.275)	0.109 (0.312)
Joint pain	0.181 (0.385)	0.200 (0.400)
Rheumatism	0.004 (0.063)	0.003 (0.057)
Hydroxychloroquine use	0.093 (0.291)	0.030 (0.170)
Ibuprofen use	0.139 (0.346)	0.177 (0.382)
Capsaicin use	0.003 (0.057)	0.008 (0.091)
Estradiol use	0.058 (0.233)	0.084 (0.277)
Naproxen use	0.071 (0.258)	0.081 (0.273)
Diclofenac use	0.042 (0.201)	0.055 (0.229)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

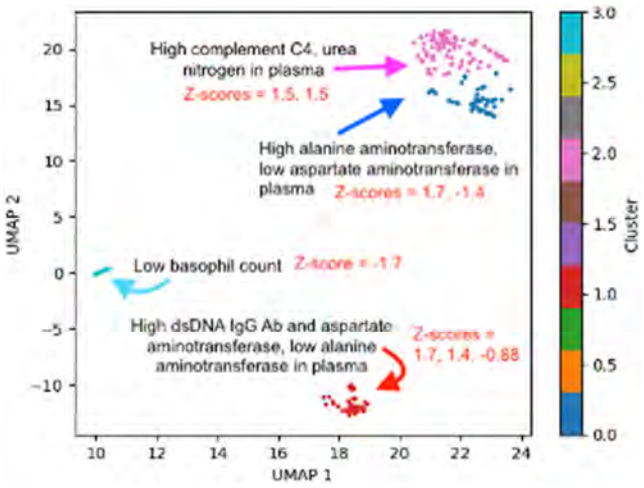


Figure 1. SLE Patient Phenotypes for New Onset SLE Cases in the All of Us Program (version 8) using Genomic, EHR and Self-reported data (Flare-State Patients, Phenotyping Approach A)

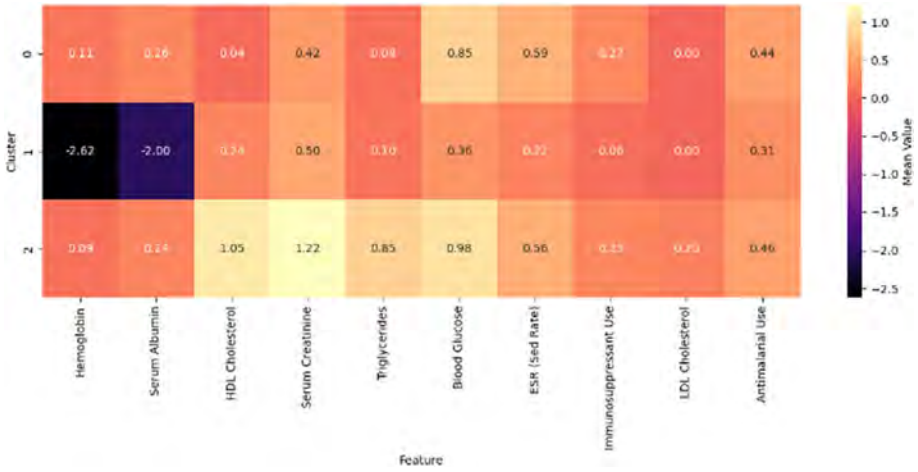


Figure 2. Top 10 Differentiating Features by Patient Type/Cluster (Phenotyping Approach B)

Disclosure: H. Sporn: None; **R. Parulekar-Martins**: None; **H. Wang**: None; **X. Yu**: None; **J. Yee**: None; **Y. Kim**: None; **J. Cui**: None; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5.

Abstract Number: 2573

Impaired Humoral Response to Recombinant Herpes Zoster Vaccine in Rituximab Treated Autoimmune Rheumatic Diseases Patients: A Prospective Controlled Phase 4 Study

Nadia Emi Aikawa[1], Henrique Dalmolin[2], Sandra G Pasoto[3], Ana C Medeiros-Ribeiro[3], Luciana Parente Costa Seguro[4], Emily Figueiredo Neves Yuki[5], Carlos Emilio Insfran Echauri[3], Clovis Artur Silva[6] and Eloisa Bonfa[4], [1]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [2]Santa Casa de Sao Paulo and Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [5]Faculdade de Medicina da USP, São Paulo, São Paulo, Brazil, [6]University of São Paulo, São Paulo, São Paulo, Brazil

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

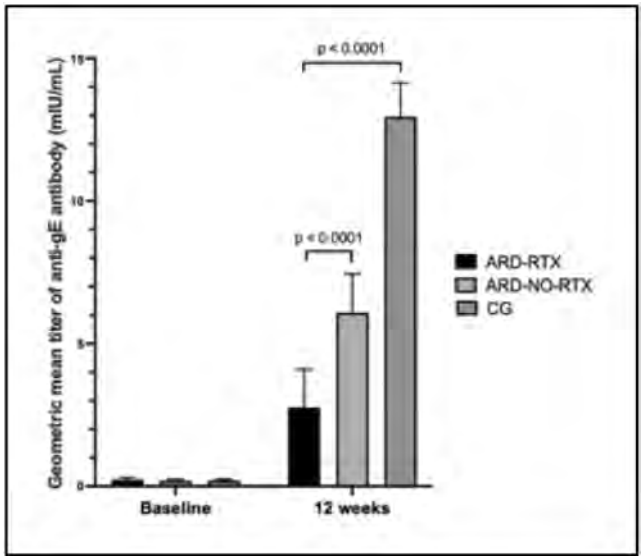
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Infection-related Rheumatic Disease (2573–2578)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Patients with autoimmune rheumatic diseases (ARDs) are at increased risk for herpes zoster (HZ), especially those treated with B-cell depleting agents. Although the recombinant zoster vaccine (RZV) has demonstrated high efficacy in healthy individuals, its immunogenicity in rituximab (RTX)-treated ARD patients remains poorly defined. This study aims to assess humoral immunogenicity to the RZV in ARD patients treated with RTX (ARD-RTX group), compared to both healthy control group (CG) and immunosuppressed ARD patients not exposed to RTX (ARD-NO RTX). Secondarily, to evaluate the influence of demographic variables, disease, and concomitant immunosuppressive drugs on RZV immune response in RTX-treated ARD patients.

Methods: This prospective controlled phase 4 study included adult ARD patients who had received at least one cycle of RTX 22–28 weeks prior to enrollment (ARD-RTX group). Two comparator groups were included: a CG of non-immunosuppressed individuals (1:3 ratio) and ARD-NO RTX group (1:3 ratio). All participants received two intramuscular doses of RZV six weeks apart. Anti-glycoprotein E (anti-gE) antibody levels were measured before the first dose and six weeks after the second dose. Anti-gE geometric mean titers (GMTs) were calculated and humoral response/seroconversion (SC) was defined as a 4-fold increase in titers. Adverse events were assessed.

Results: 76 patients ARD-RTX and 228 CG subjects were enrolled. The ARD-RTX included rheumatoid arthritis (36%), systemic lupus erythematosus (26%), Sjögren disease (13%), systemic sclerosis (11%), systemic autoimmune myopathy (17%), and ANCA-associated vasculitis (4%). Seventy-two ARD-RTX patients were compared to 216 ARD-NO RTX group with similar mean age, sex distribution and diagnoses ($p > 0.05$). Glucocorticoids use was higher in ARD-RTX (50% vs. 29.2%, p=0.001), whereas ARD-NO RTX used more leflunomide, iTNF, tocilizumab and belimumab ($p < 0.05$). Baseline GMTs were comparable between the three groups (p=0.487). Following full vaccination, ARD-RTX group had lower GMT compared to ARD-NO RTX group and CG [2.77 (95%CI 1.87–4.1) vs. 6.1 (95%CI 5.0–7.44) vs. 12.96 (95%CI 11.87–14.15) mUI/mL, $p < 0.001$] (Figure 1). Similarly, factor increase in GMT was reduced in ARD-RTX compared to ARD-NO RTX and CG [12.3 (95%CI 7.6-19.8) vs. 31.4 (95%CI 24.6-40.0) vs. 64.6 (95%CI 54.3-76.8), $p< 0.001$]. ARD-RTX patients



Comparison of humoral immunogenicity after RZV between autoimmune rheumatic diseases (ARD) patients under rituximab (RTX) with ARD without RTX and healthy control group (CG)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

also demonstrated a lower SC compared to ARD-NO RTX and CG group (66% vs. 85.6% vs. 99%, p< 0.001). There was no association of SC in ARD-RTX with age, ARD diagnosis, glucocorticoid, or immunosuppressive therapies (p >0.05). Regarding safety, no severe adverse events were reported. Local reactions (60.5% vs. 84.6%, p< 0.0001) and systemic reactions (39.5% vs. 63.2%, p< 0.0001) following first vaccine dose were significantly lower in ARD-RTX group compared to CG.

Conclusion: RTX significantly impairs humoral response to RZV in ARDs, independent of age, diagnosis, or concomitant immunosuppression. These findings highlight a possible vulnerability in vaccine protection and support the consideration of RZV before RTX use to optimize immune response (ClinicalTrials NCT05879419).

Disclosure: N. Aikawa: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **H. Dalmolin**: None; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Costa Seguro**: AstraZeneca, 6, GlaxoSmithKlein(-GSK), 5, 6; **E. Figueiredo Neves Yuki**: GlaxoSmithKlein(GSK), 5; **C. Insfran Echauri**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

Abstract Number: 2574

Differences in SARS-CoV-2 Antigen Persistence in Individuals with Systemic Autoimmune Rheumatic Diseases Compared to the General Population

Naomi Patel[1], Zoe Swank[2], Jiaqi Wang[1], Xiaosong Wang[3], Lauren O'Keeffe[2], Madison Negron[4], Liya Sisay Getachew[5], Louise Hansen[6], Grace Qian[2], Alene Saavedra[2], Kevin Mueller[2], Natalie Davis[7], Kathleen Vanni[5], Zachary Wallace[8], David Walt[2], Jeffrey Sparks[5] and RECOVER-Adult, [1]Massachusetts General Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, Natick, MA, [4]Harvard Extension School, Medford, MA, [5]Brigham and Women's Hospital, Boston, MA, [6]Brigham and Women's Hospital, B, [7]Brigham and Women's Hospital, Brookline, MA, [8]Massachusetts General Hospital, Newton, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Infection-related Rheumatic Disease (2573–2578)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Individuals with systemic autoimmune rheumatic diseases (SARDs) are at risk for worse acute and post-acute COVID-19 outcomes due to use of immunosuppressive medications and possibly prolonged viral shedding. Whether individuals with SARDs have higher levels of viral antigens and/or longer persistence of viral antigens after COVID-19 has not been studied.

Methods: We evaluated differences between an immunocompromised state and prolonged SARS-CoV-2 antigen (spike, S1 [Spike protein that contains the receptor binding domain], and nucleocapsid) positivity after COVID-19 in two prospective cohorts. We studied immunosuppressed individuals with SARDs in the RheumCARD study at a large US healthcare system and immunocompetent individuals in the RECOVER study. SARS-CoV-2 antigens were measured in collected plasma or

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Baseline characteristics at the time of sample collection for post COVID-19 cases in the RheumCARD and RECOVER cohorts

Characteristic	Immunosuppressed individuals with SARDs in RheumCARD (n = 210)	Immunocompetent individuals in RECOVER (n = 429)
Mean age at sample collection, years (SD)	56.3 (14.3)	45 (15.5)
Female, n (%)	170 (81.0)	285 (66.4)
Race, n (%)		
Asian	5 (2.4)	20 (4.7)
Black	6 (2.9)	81 (18.9)
White	172 (81.9)	262 (61.1)
Other, multiple, or unknown	27 (12.9)	66 (15.4)
Comorbidities		
Cancer	21 (10.0)	9 (2.1)
Cardiopulmonary disease	59 (28.1)	61 (14.2)
Diabetes	11 (5.2)	48 (11.2)
Time to collection		
Before 45 days	8 (3.8)	0 (0)
3 months +/- 45 days	60 (28.6)	348 (81.1)
6 months +/- 45 days	62 (29.5)	81 (18.9)
Beyond 6 months and 45 days	80 (38.1)	0 (0)
Calendar time of COVID-19, n (%)		
3/1/2020-12/16/2021 (pre-Omicron)	79 (37.6)	145 (33.8)
12/17/2021-3/7/2023 (Omicron)	131 (62.4)	284 (66.2)
Vaccinated at COVID-19 onset	154 (73.1)	382 (89.0)
SARD type, n (%)		
Inflammatory arthritis	128 (61.0)	-
Connective tissue disease	48 (22.9)	-
Vasculitis	17 (8.1)	-
Other	10 (4.8)	-
Multiple	7 (3.3)	-
DMARD use, n (%)		
No DMARD	27 (12.9)	-
csDMARDs only	66 (31.4)	-
bDMARD	107 (51.0)	
JAK inhibitors	10 (4.8)	-
Glucocorticoid use, n (%)	33 (15.7)	-
Disease activity		
Remission	33 (15.7)	-
Low disease activity	113 (53.8)	-
Moderate disease activity	43 (20.5)	-
Severe disease activity	4 (1.9)	-
Unknown or missing	17 (8.1)	-

csDMARD, conventional synthetic DMARD; bDMARD, biologic DMARD; JAK, Janus Kinase

serum samples using previously validated ultra-sensitive single molecule array, a digital enzyme-linked immunosorbent assay that uses antibody-coated magnetic beads to capture antigen molecules, which are then detected and loaded into microwell arrays through the enzymatic cleavage of a fluorescent substrate. We used logistic regression to evaluate unadjusted and adjusted (for age, sex, calendar year of infection, and vaccination status at the time of infection) odds ratios for SARS-CoV-2 antigen positivity comparing RheumCARD vs. RECOVER at 3 and 6-months following COVID-19.

Results: Among 210 immunocompromised individuals with SARDs in RheumCARD and 429 immunocompetent individuals in RECOVER (**Table**), the mean age was 56.3 vs. 45.0 years, respectively, and 81.0% vs. 66.4% were female in each cohort. COVID-19 occurred in pre-Omicron variants (before 12/16/2021) in 37.6% of RheumCARD vs. 33.8% of RECOVER. Most individuals were vaccinated at the time of infection (73.3% in RheumCARD vs. 89.0% in RECOVER). Among those with SARDs, the most common SARD type was inflammatory arthritis (61.0%) and most (53.8%) had low disease activity. Many patients (31.4%) were receiving conventional synthetic DMARDs only, with 25.2% receiving TNF inhibitors and 8.6% receiving CD20 inhibitors. A minority (15.7%) were receiving glucocorticoids at the time of infection.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

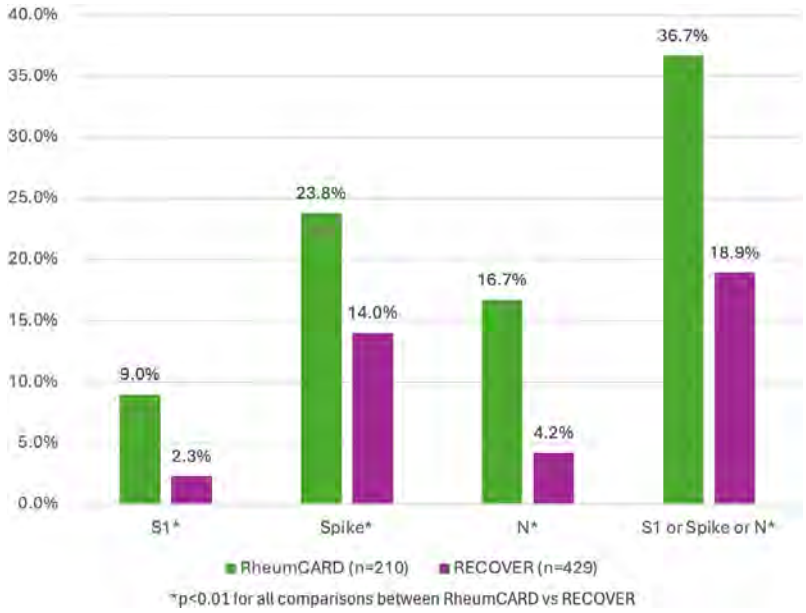


Figure 1. Frequency of positive SARS-CoV-2 antigens (S1 [spike protein that contains the receptor binding domain], spike, or nucleocapsid [N]) after COVID-19 in the RheumCARD vs. RECOVER cohorts at time of blood draw

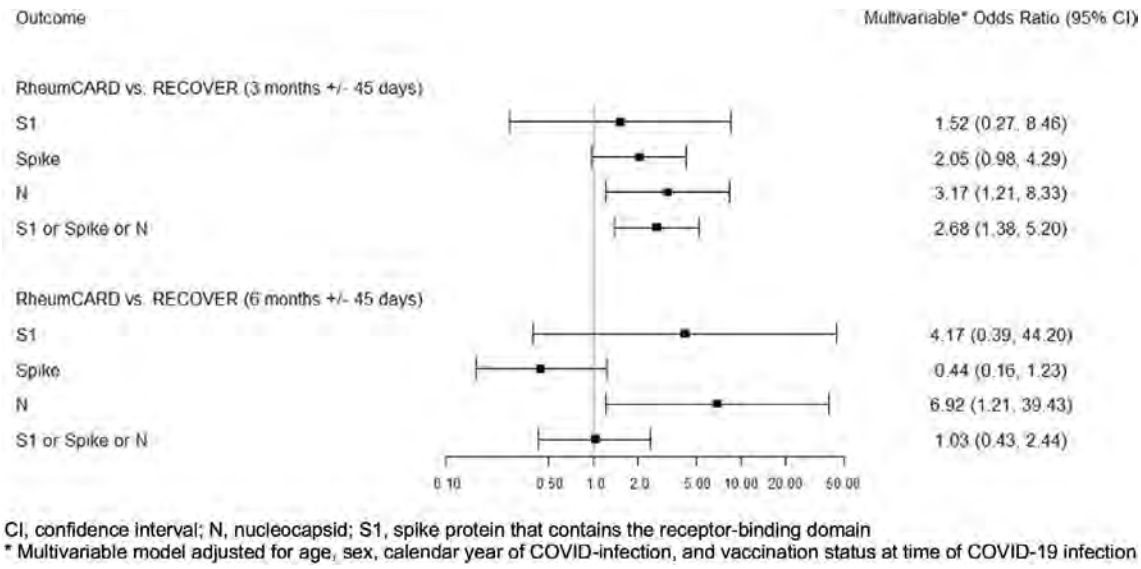


Figure 2. Differences in antigen positivity in the RheumCARD vs. RECOVER cohorts at 3 and 6 months following COVID-19 infection

At the time of blood draw, any SARS-CoV-2 antigen positivity was more common in those with SARDs (36.7% in RheumCARD vs. 18.9% in RECOVER; p< 0.001) (**Figure 1**). Those with SARDs had higher odds of nucleocapsid antigen positivity (adjusted OR 3.17, 95%CI 1.21-8.33) or any antigen positivity (adjusted OR 2.68, 95%CI 1.38-5.20) 3 months after COVID-19 (**Figure 2**). At 6 months following COVID-19 infection, nucleocapsid antigen positivity remained significantly higher among those with SARDs (adjusted OR 6.92, 95%CI 1.21-39.43).

Conclusion: Individuals with SARDs were more likely to have SARS-CoV-2 antigen positivity at 3 and 6 months following COVID-19 infection compared with immunocompetent individuals, not explained by demographics, variant, or vaccination. Persistent nucleocapsid antigen positivity, a marker of viral shedding rather than vaccination, was the greatest driver of differences between groups, suggesting that an immunocompromised state may result in prolonged antigenemia.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Patel: Amgen, 5; **Z. Swank**: None; **J. Wang**: None; **X. Wang**: None; **L. O'Keeffe**: None; **M. Negron**: None; **L. Getachew**: None; **L. Hansen**: None; **G. Qian**: None; **A. Saavedra**: None; **K. Mueller**: None; **N. Davis**: None; **K. Vanni**: None; **Z. Wallace**: Amgen, 3; **D. Walt**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 2575

Influenza and COVID-19 Vaccination Uptake Among Women with Systemic Rheumatic Diseases in New York City Assessed Between 2022 and 2024

Yongjay Kim[1], Sandhya Kannayiram[2], Amaya Smole[3], Lucy Masto[4], Neha Nagpal[5], Naiva Manuela Piatchou Donfack[5], Deanna Jannat-Khah[5], Lisa Mandl[5], Caroline Siegel[5], Sarah Lieber[5], Michael Lockshin[5], Lisa Sammaritano[5] and Medha Barbhaiya[5], [1]Hospital for Special Surgery, Englewood Cliffs, NJ, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, [3]Hospital for Special Surgery, Brooklyn, NY, [4]Hospital for Special Surgery, San Francisco, CA, [5]Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Infection-related Rheumatic Disease (2573–2578)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Women with systemic rheumatic diseases (SRDs), and particularly those on immunosuppressive medications, are at increased risk for serious infections such as influenza and COVID-19. While current guidelines recommend vaccination with non-live vaccines for patients with SRDs, patient uptake of vaccines in real-world settings remain unclear.

Methods: Women aged 18-65 evaluated at least twice by a rheumatologist at the Hospital for Special Surgery (HSS) who were enrolled in the HSS Rheumatology Women's Reproductive Health and Wellness Cohort between 2022-2024 were included. All subjects had an SRD diagnosis by ICD-10 code-based algorithms and completed demographic, medical history, and vaccination questionnaires. Bivariate analyses compared demographic, socioeconomic, lifestyle, and clinical factors of patients ever versus never vaccinated for influenza or COVID-19. Multivariable models evaluated factors associated with ever versus never vaccination for COVID-19 and influenza vaccination separately.

Results: Of 740 participants (mean age 47.4±12.4 years, 538 [72.7%] White, 98 [13.2%] Hispanic or LatinX, 668 (84.6%) self-reported ever receiving influenza vaccination and 719 (97.2%) reported receiving COVID-19 vaccination. Compared to unvaccinated patients, women vaccinated for influenza more frequently had a Bachelor's degree or higher (88.0% vs 75.0%), were married/partnered (67.1% vs 48.6%), on immunosuppressive medications (60.2% vs 47.9%), saw a primary care physician (PCP) (78.0% vs 56.9%) or gynecologist (75.5% vs 54.2%) at least yearly, and had an inflammatory arthritis (IA) diagnosis (62.2% vs 44.1%), but were less frequently on corticosteroids (12.0% vs 20.8%). Participants ever vs. never vaccinated for COVID-19 were more frequently married/partnered (66.0% vs 42.9%), privately insured (88.4% vs 70.0%), employed (71.1% vs 38.1%), ever used alcohol (83.8% vs 61.9%), and saw a PCP (76.6% vs. 52.4%) or gynecologist (74.0% vs 52.4%) at least yearly, but were less frequently on corticosteroids (12.2% vs 33.3%) [**Table 1, p< 0.05**]. Among patients never vaccinated for influenza, participants with IA versus connective tissue diseases were more likely to cite vaccine side effects as a reason for not getting vaccinated (19.2% vs 0.0%). In multivariable analyses, the odds of never receiving influenza vaccination were greater among individuals with < 1 PCP visit per year (OR 2.78, 95% CI [1.52–5.06]), but lower among those taking immunosuppressive medications (OR 0.45, 95%CI [0.24–0.84]) [**Table 2**]. For COVID-19, the

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic, Rheumatologic, and Lifestyle Characteristics Among 740 Women with Systemic Rheumatic Diseases in New York City, by Influenza and COVID-19 Vaccination Status Assessed Between 2022-2024

	Influenza			*COVID-19*		
	Never Vaccinated (N=72)	Ever Vaccinated (N=660)	p-value	Never Vaccinated (N=21)	Ever Vaccinated (N=719)	p-value
Demographics (N,%, except age)						
Age (mean, ± SD)	49.3 (±11.1)	47.1 (±12.5)	0.11	46.9 (±10.9)	47.4 (±12.4)	0.80
Race*			0.20			0.06
• White	44 (66.7%)	494 (75.5%)		10 (55.6%)	528 (75.2%)	
• Black or African American	9 (13.6%)	51 (7.8%)		4 (22.2%)	56 (8.0%)	
• Other	13 (19.7%)	109 (16.7%)		4 (22.2%)	118 (16.8%)	
Ethnicity*			0.11			>0.90
• Hispanic/LatinX	14 (19.4%)	84 (12.6%)		2 (9.5%)	96 (13.4%)	
• Not Hispanic/LatinX	58 (80.6%)	581 (87.4%)		19 (90.5%)	620 (86.6%)	
Highest Level of Education*			**<0.01**			0.50
• Bachelor's Degree or Higher	54 (75.0%)	587 (88.0%)		17 (81.0%)	624 (86.9%)	
• No Bachelor's Degree or Higher	18 (25.0%)	80 (12.0%)		4 (19.1%)	94 (13.1%)	
Relationship Status*			**<0.01**			**0.04**
• Married or partnered	34 (48.6%)	446 (67.1%)		9 (42.9%)	471 (66.0%)	
• Single/divorced/separated/widowed	36 (51.4%)	219 (32.9%)		12 (57.1%)	243 (34.0%)	
Insurance Status*			0.30			**0.03**
• Commercial or private insurance	58 (84.1%)	587 (88.3%)		14 (70.0%)	631 (88.4%)	
• Medicare, Medicaid, or other	11 (15.9%)	78 (11.7%)		6 (30.0%)	83 (11.6%)	
Employment Status*			0.30			**<0.01**
• Working for compensation	47 (65.3%)	466 (70.7%)		8 (38.1%)	505 (71.1%)	
• Not working[1]	25 (34.7%)	193 (29.3%)		13 (61.9%)	205 (28.9%)	
Living Situation*			0.20			>0.90
• Own or partner's apartment	65 (92.9%)	626 (93.9%)		19 (95.0%)	672 (93.7%)	
• With family or friends	3 (4.3%)	37 (5.6%)		1 (5.0%)	39 (5.4%)	
• Other	2 (2.9%)	4 (0.6%)		0 (0.0%)	6 (0.8%)	
Smoking Status*			0.30			0.60
• Ever smoked	19 (27.5%)	143 (21.7%)		3 (15.0%)	159 (22.5%)	
• Never smoked	50 (72.5%)	515 (78.3%)		17 (85.0%)	548 (77.5%)	
Alcohol Status*			0.30			**0.02**
• Ever used alcohol	56 (78.8%)	551 (83.6%)		13 (61.9%)	594 (83.8%)	
• Never used alcohol	15 (21.1%)	108 (16.4%)		8 (38.1%)	115 (16.2%)	
Medication History (N,%)**						
• Any immunosuppressive meds*[2]	34 (47.9%)	399 (60.2%)	**<0.05**	9 (42.9%)	424 (59.5%)	0.13
• No immunosuppressive meds	37 (52.1%)	264 (39.8%)		12 (57.1%)	289 (40.5%)	
• Steroids*	15 (20.8%)	80 (12.0%)	**0.03**	7 (33.3%)	88 (12.2%)	**0.01**
• No steroids	57 (79.2%)	588 (88.0%)		14 (66.7%)	631 (87.8%)	
• Antimalarials*	32 (45.1%)	241(36.35%)	0.20	5 (23.8%)	445 (62.4%)	0.30
• No antimalarials	39 (54.9%)	422(63.65%)		16 (76.2%)	268 (37.6%)	
SRD Medical History (N,%)						
Timing of most recent flare*			0.30			0.30
• Current Flare	15 (21.4%)	158 (24.2%)		6 (28.6%)	167 (23.8%)	
• Within the last 3 months	24 (34.3%)	192 (29.5%)		9 (42.86%)	207 (29.5%)	
• 3 months – 1 year	8 (11.4%)	120 (18.4%)		2 (9.5%)	126 (18.0%)	
• Greater than 1 year ago	12 (17.1%)	122 (18.7%)		1 (4.8%)	133 (19.0%)	
• No flares or don't recall	11 (15.7%)	60 (9.2%)		3 (14.3%)	68 (9.7%)	
SRD Diagnoses			**<0.01**			0.06
• Inflammatory Arthritis[3]	26 (44.1%)	369 (62.2%)		7 (38.9%)	388 (61.2%)	
• Connective Tissue Disease[4]	33 (55.9%)	224 (37.8%)		11 (61.1%)	246 (38.8%)	
Health Maintenance History (N,%)						
Primary Care Physician Visits			**<0.01**			**0.01**
• At least once a year	41 (56.9%)	521 (78.0%)		11 (52.4%)	551 (76.6%)	
• <1 visit per year	31 (43.1%)	147 (22.0%)		10 (47.6%)	168 (23.4%)	
Gynecologist Visits			**<0.01**			**0.03**
• At least once a year	39 (54.2%)	504(75.45%)		11 (52.4%)	532 (74.0%)	
• <1 visit per year	33 (45.8%)	164(24.55%)		10 (47.6%)	187 (26.0%)	

P-value <0.05=statistically significant. *Column values within each category may not add up due to individuals who preferred not to answer the specific question. **Current medication use at the time of data collection. 1. Includes individuals with disability, retired, unemployed, and students; 2. Includes Abatacept, Adalimumab, Anakinra, Anifrolumab, Belimumab, Canakinumab, Certolizumab, Denosumab, Etanercept, Golimumab, Guselkumab, Infliximab, Ixekizumab, Mepolizumab, Rilonacept, Risakizumab, Rituximab, Sarilumab, Secukinumab, Tocilizumab, Ustekinumab, Azathioprine, Cyclophosphamide, cyclosporine, leflunomide, methotrexate, mycophenolate, sulfasalazine, tacrolimus, thalidomide, voclosporin, baricitinib, tofacitinib, upadicitinib; 3. Includes Ankylosing spondylitis, JRA, PSA, Spondyloarthritis, Enteropathic arthritis, PMR, Polyarthritis; 4. Includes APS, SLE, Overlap CTDs, UCTD, Myositis, Systemic Sclerosis, Eosinophilic fasciitis.

Table 2. Logistic Regression Model Results Evaluating the Association Between Demographic and Clinical Characteristics with Influenza Vaccination Status (Never vs. Ever Vaccination) Among 740 Women with SRDs

Variable	Odds Ratio	95% Confidence Interval	p-value
Demographics			
Age	1.02	1.00 – 1.05	0.07
Race			
• White	*Referent*		
• Black or African American	1.61	0.61 – 3.76	0.30
• Other	1.38	0.62 – 2.87	0.40
Ethnicity			
• Not Hispanic/Latino	*Referent*		
• Hispanic/Latino	1.10	0.47 – 2.36	0.80
Clinical Characteristics			
Immunosuppressive medications			
• No immunosuppressive medications	*Referent*		
• Any immunosuppressive medications	0.45	0.24 – 0.84	**0.01**
Steroids			
• No steroids	*Referent*		
• Steroids	1.80	0.79 – 3.79	0.14
Primary Care Physician Seen ≥1x per Year			
• Yes	*Referent*		
• No	2.78	1.52 – 5.06	**<0.01**
Rheumatology Diagnosis			
• Inflammatory Arthritis	*Referent*		
• Connective Tissue Disease	1.31	0.72 – 2.41	0.4

A p-value of <0.05 was considered statistically significant. Patients who chose not to respond were excluded from the model.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Logistic Regression Model Results Evaluating the Association Between Demographic and Clinical Characteristics with COVID-19 Vaccination Status (Never vs. Ever Vaccination) among 740 Women with SRDs

Variable	Odds Ratio	95% Confidence Interval	p-value
Demographics			
Age	0.99	0.95 – 1.04	0.80
Race			
• White	*Referent*		
• Black or African American	4.15	1.04 – 14.30	**0.03**
• Other	1.50	0.32 – 5.44	0.60
Clinical Characteristics			
Steroids			
• No steroids	*Referent*		
• Steroids	2.80	0.73 – 8.93	0.10
Primary Care Physician Seen ≥1x per Year			
• Yes	*Referent*		
• No	2.38	0.79 – 6.99	0.11
Rheumatology Diagnosis			
• Inflammatory Arthritis	*Referent*		
• Connective Tissue Disease	1.66	0.56 – 5.21	0.4

A p-value of <0.05 was considered statistically significant. Patients who chose not to respond were excluded from the model.

odds of never receiving vaccination were greater among those who were Black versus White (OR 4.15, 95% CI [1.04-14.3]) [**Table 3**].

Conclusion: Influenza and COVID-19 vaccination uptake was overall high in this cohort of women with SRDs, with notable associations between black race, immunosuppressive medication use, and frequency of PCP visits with vaccination status. Factors associated with COVID-19 vaccination should be interpreted cautiously due to few unvaccinated women in the current study. Addressing concerns about side effects and improving access to routine care may further optimize vaccination uptake.

Disclosure: Y. Kim: None; **S. Kannayiram**: None; **A. Smole**: None; **L. Masto**: None; **N. Nagpal**: None; **N. Piatchou Donfack**: EMD Serono, 3; **D. Jannat-Khah**: AstraZeneca, 11, CytoDyn, 11; **L. Mandl**: ACP, 12, Associate Editor Annals of Internal Medicine, Wolters, 9; **C. Siegel**: None; **S. Lieber**: None; **M. Lockshin**: None; **L. Sammaritano**: None; **M. Barbhaiya**: None.

Abstract Number: 2576

Methotrexate Treatment of Arthritis Caused by Chikungunya Virus (MARCH) Study: Anti-inflammatory cytokine signals related to decreased arthritis disease activity over time

Alfonso Sucerquia[1], Jose Forero[2], Juan Alzate[1], Adrienne Poon[3], Gary Firestein[4], Larry Moreland[5], Andres Cadena[6], Jose Lara[6], Octavio pizarro[6], Jesus Godoy[6], Liliana Encinales[7], David Boyle[8], Evelyn Mendoza[9], Carlos Herrera[10] and Aileen Chang[3], [1]The George Washington University, Arlington, [2]The George Washington University, Arlington, VA, [3]The George Washington University, Washington, [4]University of California, San Diego, San Diego, CA, [5]University of Colorado, Denver, CO, [6]Clinica de la Costa, Barranquilla, Colombia, [7]Allied Research Society, Barranquilla, Colombia, [8]University of California, San Diego, San Diego, [9]Universidad Libre de Barranquilla, Barranquilla, Colombia, [10]The George Washington University, Alexandria

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Infection-related Rheumatic Disease (2573–2578)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: The MARCH study evaluates the efficacy of methotrexate monotherapy in patients with chikungunya-associated arthritis and aims to elucidate its pathologic mechanism via cytokine analysis. As of May 05, 2025, 140 of the targeted 162 participants have been enrolled, with recruitment ongoing.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

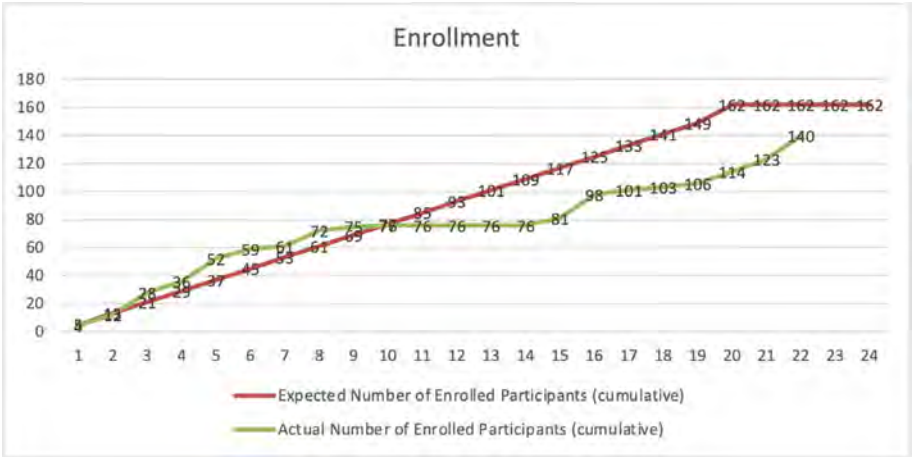


Figure 1. Cumulative enrollment of participants over time in the MARCH trial. The green line represents the actual number of participants enrolled each month, while the red line indicates the expected cumulative enrollment target. As of Month 22, 140 participants have been enrolled out of the planned 162, with final enrollment expected to be completed by June.

Methods: Enrollment began on July 18, 2023, in Barranquilla, Colombia. This randomized, placebo-controlled, double-blind, parallel-design Phase 3 clinical trial investigates six months of methotrexate/placebo randomized 2:1 in adult volunteers with a history of Chikungunya Arthritis. An optional dose escalation from 15 mg/week to 20 mg/week is permitted at six weeks, followed by an optional open-label extension from six to 12 months, with follow-up until 24 months. Immunological profiling was performed using a Meso Scale Discovery (MSD) multiplex immunoassay platform, which enables the simultaneous, high-sensitivity quantification of multiple cytokines and chemokines in serum samples.

Results: Of 245 screened participants, 140 were enrolled (111 females, 29 males), and 132 remain actively in treatment (Figure 1). The mean age of the cohort is 55.54 +/- 12.93 years, with 53% having completed elementary education. Over six months, there was a significant reduction ($p < 0.001$) in disease severity, as measured by arthritis disease activity by the disease activity score-28 (DAS-28), disability by the health assessment questionnaire (HAQ), and arthritis flare activity by the flare score, indicating a shift from moderate/severe to mild disease activity, improved functional capacity, and less flare intensity (Figure 2). Immunological analysis revealed statistically significant increases in wound healing cytokines including Eotaxin, B-NGF, TGFB-2, TGFB-3, and HGF, while inflammatory and pain cytokines such as RANKL/TNFSF11, GM-CSF, IL-10, IL-17, IL-1B, IL-4, IL-6, IL-8, and Substance P showed significant decreases over time. TNF-α, TGFB-1, and IL-2 exhibited slight, non-significant increases, whereas IFN-γ demonstrated a non-significant decrease (Figure 3).

Conclusion: Interim analysis indicates that methotrexate is generally well-tolerated in treating chikungunya-related arthritis. The study's cohort, with a mean arthritis duration post-infection of approximately ten years, provides valuable insights into the chronic impact of the disease. The evolving immunological profile suggests transitioning from an acute

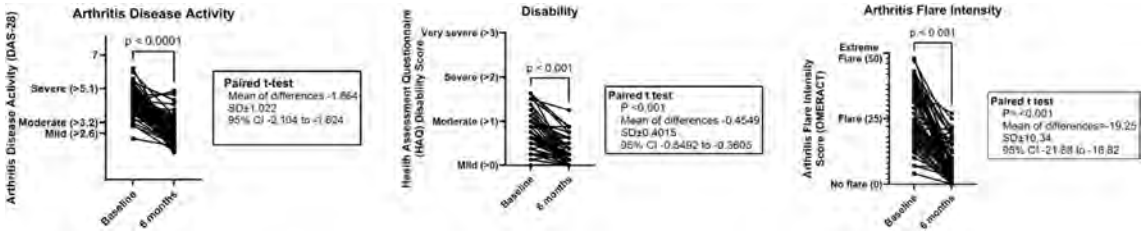


Figure 2. Patient reported outcomes. 2a) Arthritis disease activity measured by the Disease Activity Score-28 2b) Disability measured by the Health Assessment Questionnaire 2c) Arthritis Flare Intensity measured by the Arthritis Flare Intensity Score adapted for use in Chikungunya arthritis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

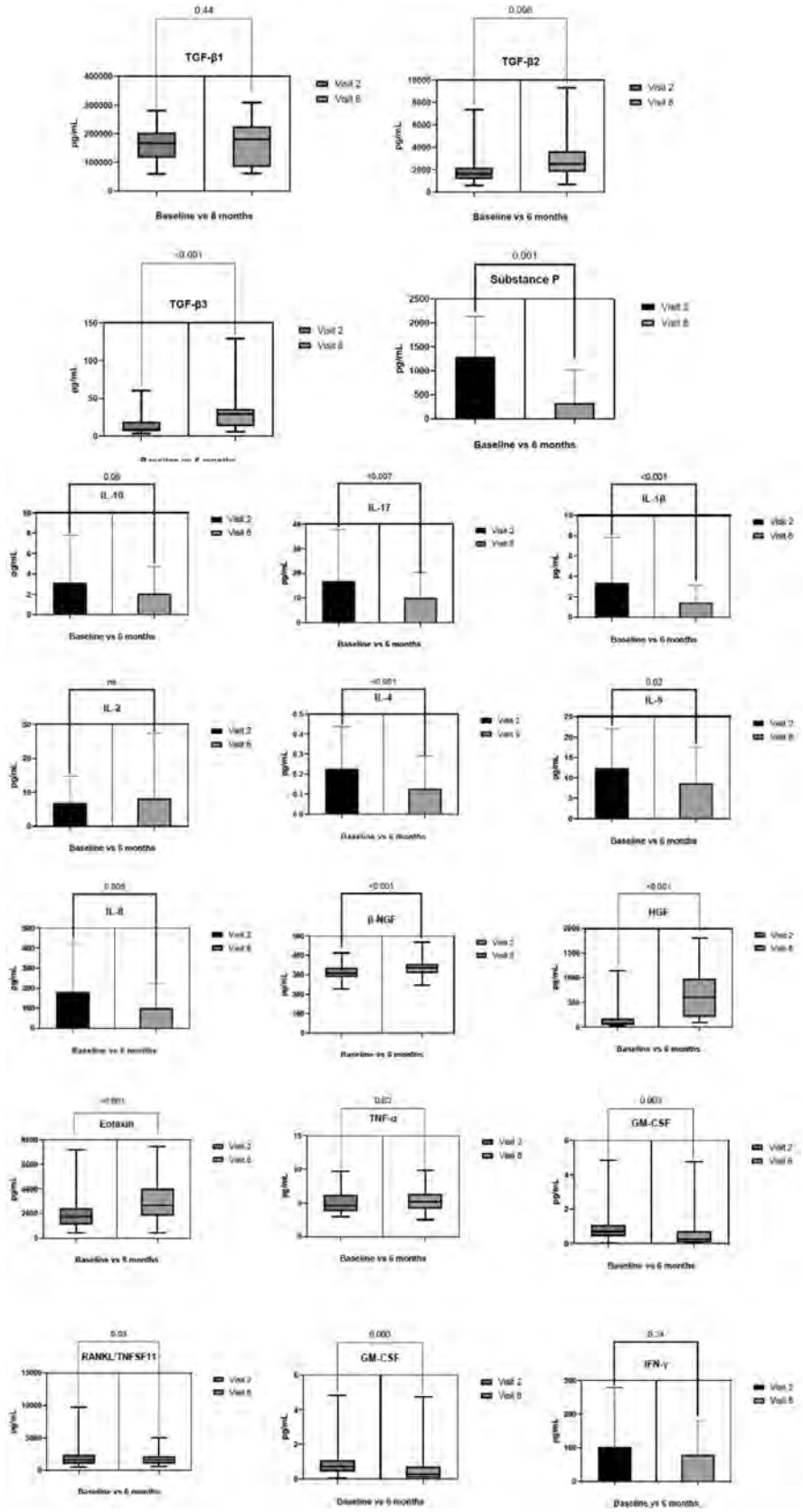


Figure 3. Cytokine measurement comparison between enrollment vs. 6 months after treatment with MTX/Placebo.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

pro-inflammatory state to a reparative state. These findings underscore the complex interplay between inflammatory and regulatory mechanisms in chronic alphaviral arthritis and are expected to inform future treatment guidelines. The study remains blinded, with most enrolled participants having completed the closed-label phase and currently in the open-label follow-up stage. As the study is still blinded, it remains unclear whether the observed clinical and immunological changes are attributable to the therapeutic effect of methotrexate or reflect the natural course of disease improvement.

Disclosure: A. Sucerquia: None; **J. Forero**: None; **J. Alzate**: None; **A. Poon**: None; **G. Firestein**: Eli Lilly, 5; **L. Moreland**: None; **A. Cadena**: None; **J. Lara**: None; **O. pizarro**: None; **J. Godoy**: None; **L. Encinales**: None; **D. Boyle**: None; **E. Mendoza**: None; **C. Herrera**: None; **A. Chang**: None.

Abstract Number: 2577

Duration of SARS-CoV-2 Viral Shedding After Acute Infection in Patients with Rheumatic Diseases Using B Cell Depletion or Tumor Necrosis Factor Inhibitors

Liya Sisay Getachew[1], Xiaosong Wang[2], Zachary Wallace[3], Naomi Patel[4], Lauren O'Keeffe[5], Madison Negron[6], Grace Qian[5], Alene Saavedra[5], Kevin Mueller[5], Natalie Davis[7], Yijia Li[8], Manish Choudhary[5], Julie Boucau[3], Brooke Leeman[5], Gregory Edelstein[5], Owen Glover[3], Yumeko Kawano[5], Rinki Deo[5], Caitlin Marino[3], Zahra Reynolds[3], Karry Su[3], Chase Mandell[3], Eliza Passell[3], Mamadou Barry[3], Andrew Alexandrescu[3], Dibya Ghimire[3], Mriganka Mandal[9], Tammy Vyas[3], Sarah Hammond[3], Jatin Vyas[3], Jacob Lemieux[3], Mark Siedner[3], Amy Barczak[3], Jonathan Li[3] and Jeffrey Sparks[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Natick, MA, [3]Massachusetts General Hospital, Boston, [4]Massachusetts General Hospital, Boston, MA, [5]Brigham and Women's Hospital, Boston, [6]Harvard Extension School, Medford, MA, [7]Brigham and Women's Hospital, Brookline, MA, [8]University of Pittsburgh, Pittsburgh, [9]Dana-Farber Cancer Institute, Boston

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Infection-related Rheumatic Disease (2573–2578)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: People with rheumatic diseases are at risk for acute and post-acute COVID-19 outcomes in part due to immunosuppressive medications. Those on B-cell depleting therapies (BCD) tend to have worse outcomes, and some uncontrolled retrospective case reports and case series showed prolonged viral shedding. Recent data suggest that tumor necrosis factor inhibitors (TNFi) have less impact on COVID-19 severity. We aimed to prospectively investigate duration of SARS-CoV-2 viral shedding in rheumatic patients using BCD or TNFi

Methods: We conducted a matched cohort study among participants in POSITIVES, a prospective study enrolling outpatients with acute COVID-19 infection within 5 days of diagnosis. Anterior nasal swabs were self-collected three times weekly over 2 weeks and then weekly until two negative PCR results. Viral PCR and culture were performed on each sample. In this analysis, we evaluated people who were on BCD or TNFi at COVID-19 onset. For each case, immunocompetent comparators with acute COVID-19 were matched (1:2) using propensity scores based on age, sex, race, ethnicity, number of prior COVID-19 vaccinations, calendar time, and use of antivirals. We used Cox regression and linear mixed-effects models to compare each immunocompromised group with their immunocompetent comparator for time to negative PCR (primary), time to negative viral culture, and viral load trajectories.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics at enrollment for TNFi users, B cell depletion users, and match immunocompetent comparators.

	TNFi users (n=30)	Immunocompetent comparators matched to TNFi users (n=53)	B cell depletion users (n=16) *	Immunocompetent comparators matched to B cell depletion users (n=33)
Mean age, years (SD)	51.3 (15.1)	51.2 (19.0)	50.1 (16.8)	51.6 (16.5)
Female	24 (80)	42 (79)	12 (75)	21 (64)
Race				
-Asian	2 (7)	2 (4)	0 (0)	2 (6)
-Black	1 (3)	5 (9)	2 (13)	1 (3)
-Other	1 (3)	6 (11)	1 (6)	1 (3)
-White	26 (87)	40 (76)	13 (81)	29 (88)
Ethnicity				
-Hispanic	0 (0)	6 (11)	1 (6)	1 (3)
-Not Hispanic	26 (87)	40 (76)	15 (94)	27 (82)
-Unknown	4 (13)	7 (13)	0 (0)	5 (15)
Mean number of prior COVID-19 vaccines (SD)	4.3 (1.3)	4.2 (1.3)	4.2 (1.7)	3.7 (1.8)
Unvaccinated	1 (3)	1 (2)	1 (6)	3 (9)
Nirmatrelvir-ritonavir use n (%)	23 (77)	40 (76)	11 (69)	20 (61)
Autoimmune disease n (%)				
-Rheumatoid arthritis	16 (53)	-	5 (31)	-
-Other inflammatory arthritis	9 (30)	-	0 (0)	-
-Systemic vasculitis	3 (10)	-	4 (25)	-
-IgG4-related disease	0 (0)	-	1 (6)	-
-Multiple sclerosis	0 (0)	-	3 (19)	-
-Sjögren disease	0 (0)	-	1 (6)	-
-Sarcoidosis	1 (3)	-	0 (0)	-
Concomitant Immunosuppression n (%)				
-Methotrexate	13 (43)	-	5 (31)	-
-Leflunomide	1 (3)	-	2 (13)	-
-Sulfasalazine	0 (0)	-	1 (6)	-
-Glucocorticoids	8 (27)	-	4 (25)	-

*All participants with B cell depletion were taking rituximab

TNFi, tumor necrosis factor inhibitors; SD, standard deviation

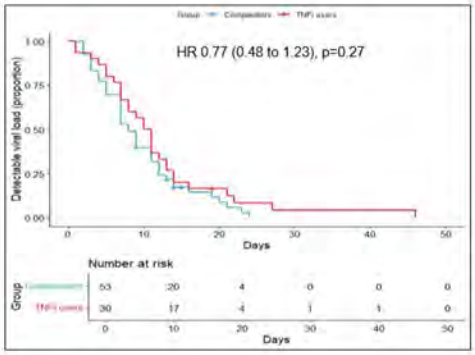
Results: We analyzed 30 TNFi and 16 BCD users, each matched to 53 and 33 immunocompetent comparators, respectively. The most common rheumatic disease was RA (53% among TNFi; 30% among BCD). More than 60% were using an antiviral and the mean number of COVID-19 vaccinations was 4.3 (**Table 1**). The median time to undetectable viral load was similar between TNFi users and comparators (HR 0.77, 95%CI 0.48 to 1.23, p=0.27; **Figure 1**). In contrast, there was a significant difference in the median (IQR) days to undetectable viral load between BCD users 15 (7, 23) vs. their comparators 7 (3, 13; HR 0.43, 95%CI 0.22 to 0.86; p=0.017). Results were similar when examining time to negative viral culture. When analyzing the difference in viral decay trajectories, the BCD group had significantly different trajectory than their immunocompetent comparators (p=0.008), while TNFi and their comparators had similar trajectory (p=0.19, **Figure 2**).

Conclusion: In this prospective study of viral shedding during acute COVID-19, BCD users had longer SARS-CoV-2 viral persistence than immunocompetent comparators. While BCD users had about 8 days longer median duration of viral shedding, nearly all had negative PCR after one month of follow-up. Studies are ongoing to evaluate whether BCD may be associated with in-host viral evolution and the impact of prolonged viral shedding on patient outcomes.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Kaplan-Meier curves and hazard ratios for undetectable viral load for A) TNFi users and their immunocompetent comparators, B) B cell depletion users and their immunocompetent comparators.

A.



B.

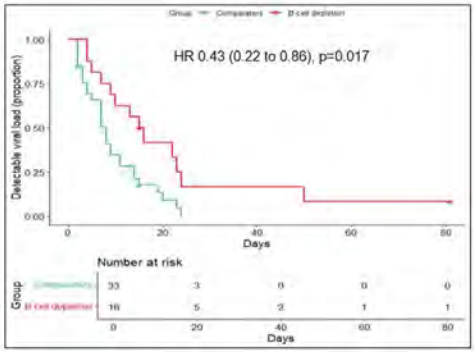
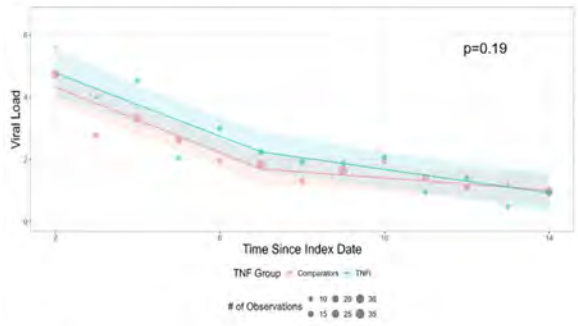
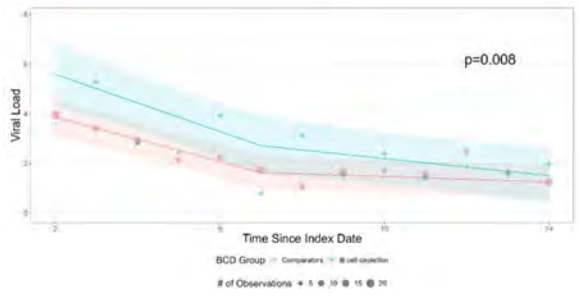


Figure 2. Virologic decay over time for A) TNFi users and their immunocompetent comparators, B) B cell depletion users and their immunocompetent comparators.

A.



B.



23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: L. Getachew: None; **X. Wang**: None; **Z. Wallace**: None; **N. Patel**: Amgen, 5; **L. O'Keeffe**: None; **M. Negron**: None; **G. Qian**: None; **A. Saavedra**: None; **K. Mueller**: None; **N. Davis**: None; **Y. Li**: None; **M. Choudhary**: None; **J. Boucau**: None; **B. Leeman**: None; **G. Edelstein**: None; **O. Glover**: None; **Y. Kawano**: None; **R. Deo**: None; **C. Marino**: None; **Z. Reynolds**: None; **K. Su**: None; **C. Mandell**: None; **E. Passell**: None; **M. Barry**: None; **A. Alexandrescu**: None; **D. Ghimire**: None; **M. Mandal**: None; **T. Vyas**: None; **S. Hammond**: None; **J. Vyas**: None; **J. Lemieux**: None; **M. Siedner**: None; **A. Barczak**: None; **J. Li**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5.

Abstract Number: 2578

Association of Oral Outpatient Antiviral Medications for COVID-19 with the Risk of Post-acute Sequelae of COVID-19 in Individuals with Systemic Autoimmune Rheumatic Diseases

Madison Negron[1], Jiaqi Wang[2], Xiaosong Wang[3], Lauren O'Keeffe[4], Grace Qian[4], Kevin Mueller[4], Alene Saavedra[4], Natalie Davis[5], Liya Sisay Getachew[6], Jeffrey Sparks[6] and **Naomi Patel**[7], [1]Harvard Extension School, Medford, MA, [2]Massachusetts General Hospital, BOston, [3]Brigham and Women's Hospital, Natick, MA, [4]Brigham and Women's Hospital, Boston, [5]Brigham and Women's Hospital, Brookline, MA, [6]Brigham and Women's Hospital, Boston, MA, [7]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Infection-related Rheumatic Disease (2573–2578)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Prior studies have evaluated the efficacy of antiviral medications on acute outcomes of COVID-19 infection as well as the risk of post-acute sequelae of COVID-19 (PASC, i.e., "long COVID") in the general population. However, there are little data regarding the effectiveness of these agents for reducing the risk of PASC in individuals with systemic autoimmune rheumatic diseases (SARDs).

Methods: We consecutively enrolled individuals with SARDs into the prospective RheumCARD study at a large US healthcare system following their COVID-19 infection from December 16, 2021 (following the start of the Omicron era and availability of oral outpatient therapy) until January 30, 2024. Individuals who were hospitalized for acute COVID-19 and/or who received COVID-19 monoclonal antibodies or remdesivir were excluded. Individuals completed surveys at least 28 days following COVID-19 infection regarding the presence vs. absence of persistent symptoms as well as the duration of symptoms. We assessed the odds of PASC at both 28 and 90 days following COVID-19 infection and used multivariable logistic regression to compare those who did versus did not receive oral outpatient antiviral medication (either nirmatrelvir/ritonavir or molnupiravir) for acute COVID-19 infection. The multivariable model was adjusted for age, sex, and race.

Results: Among 430 patients (49% treated with nirmatrelvir/ritonavir or molnupiravir and 51% not treated with antiviral medications), the mean age at COVID-19 onset was 56.2 years, 82% were female, and 91% were White (**Table**). The most common SARD category was inflammatory arthritis (37%), followed by connective tissue disease (11%). Many were using conventional synthetic DMARDs (49%), biologic DMARDs (41%); 7% were using CD20 inhibitors) and 15% were using systemic glucocorticoids at the time of COVID-19 infection. Nearly all (97%) were vaccinated at the time of COVID-19 infection. The prevalence of PASC at 28 days in those who did vs. did not receive antiviral therapy was 33% vs. 31% (p=0.77). However, the prevalence of PASC at 90 days in those who did vs. did not receive antiviral therapy was 5% vs. 11% (p=0.02). Compared to those who did not receive antiviral medications (n=221), those prescribed antiviral therapy (n=209) had

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics in individuals with rheumatic disease and COVID-19 who did vs. did not receive oral outpatient antiviral therapy for acute COVID-19 infection.

	All patients (n=430)	Received antiviral therapy (n=209)	No antiviral therapy (n=221)
Age, years, mean, (SD)	56.2 (14.9)	58.1 (14.6)	54.3 (14.9)
Female, n (%)	352 (81.9)	169 (80.9)	183 (82.8)
Race, n (%)			
Asian	16 (3.8)	8 (3.9)	8 (3.7)
Black or African American	9 (2.1)	3 (1.5)	6 (2.8)
Multiple	3 (0.7)	2 (1.0)	1 (0.5)
White	386 (91.0)	191 (92.3)	195 (89.9)
Other or unknown	17 (4.0)	5 (2.4)	12 (5.4)
Hispanic, n (%)	21 (5.2)	8 (4.0)	12 (5.8)
Vaccinated, n (%)	419 (97.4)	206 (98.6)	213 (96.4)
Systemic Autoimmune Rheumatic Disease Category, n (%)			
Inflammatory arthritis	183 (42.6)	96 (45.9)	87 (39.3)
Connective tissue disease	50 (11.6)	10 (4.8)	40 (18.1)
Vasculitis	36 (8.4)	22 (10.5)	14 (6.39)
Multiple	118 (27.4)	63 (30.1)	55 (24.9)
Other	43 (10.0)	18 (8.6)	25 (11.3)
Immunomodulatory therapy at time of COVID-19, n (%)			
csDMARD	209 (48.6)	110 (52.6)	99 (44.8)
CD20 inhibitor	29 (6.7)	20 (9.6)	9 (4.1)
Other bDMARD	146 (34.0)	84 (40.2)	62 (28.1)
tsDMARD	15 (3.5)	10 (4.8)	5 (2.3)
No DMARD	82 (19.1)	22 (10.5)	60 (27.2)
Systemic glucocorticoid use, n (%)	65 (15.2)	36 (17.2)	29 (13.1)
Prednisone-equivalent daily dose, mg, median (IQR)	5.0 (3.5, 12.5)	5.0 (3.0, 11.0)	7.0 (5.0, 20.0)

csDMARD, conventional synthetic DMARD; bDMARD, biologic DMARD; tsDMARD, targeted synthetic DMARD

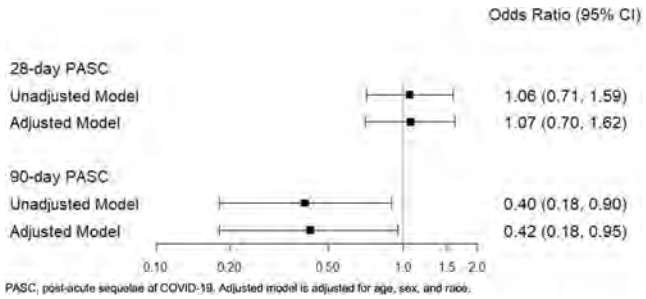


Figure. Odds of PASC at 28 and 90 days in individuals with rheumatic diseases and COVID-19 who did vs. did not receive antiviral therapy for acute COVID-19 infection

significantly lower odds of PASC at 90 days (adjusted OR 0.42, 95% CI: 0.18-0.95), while there was no difference in odds of PASC between groups at 28 days (**Figure**).

Conclusion: In this prospective contemporary cohort, individuals with SARDs who received oral outpatient antiviral therapy had significantly lower odds of PASC lasting at least 90 days following COVID-19 infection than those who did not receive antiviral therapy, while odds of PASC lasting at least 28 days did not differ between groups. These findings support additional potential benefits of oral outpatient antiviral treatment for PASC risk among individuals with SARDs who are eligible and do not have contraindications.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Negron: None; **J. Wang**: None; **X. Wang**: None; **L. O'Keeffe**: None; **G. Qian**: None; **K. Mueller**: None; **A. Saavedra**: None; **N. Davis**: None; **L. Getachew**: None; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **N. Patel**: Amgen, 5.

Abstract Number: 2579

Mutant COPA Permits Aberrant NETosis and Exacerbates Autoimmune Lung Disease

Richard Moore[1], Lihong Huo[1], Colin Koziel[1], Barry Stripp[2], Tiphanie Vogel[3], Daniel Wallace[4] and Caroline Jefferies[5], [1]Cedars-Sinai, Beverly Hills, CA, [2]Women's Guild Lung Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [3]Baylor College of Medicine, Houston, TX, [4]Cedars Sinai Medical Center, Studio City, CA, [5]Cedars-Sinai Medical Center, Beverly Hills, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Innate Immunity (2579–2584)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: COPA syndrome is an autosomal dominant disease caused by missense mutations within the *COPA* gene. Typical onset begins during childhood with patients developing lung disease such as diffuse alveolar hemorrhage (DAH). Despite its severity, the cause of lung involvement in COPA syndrome is unknown. Here, we find that mutant COPA worsens and prolongs disease in a murine model of DAH and permits aberrant NETosis in humans and mice, offering a route by which lung disease may progress in patients with COPA syndrome.

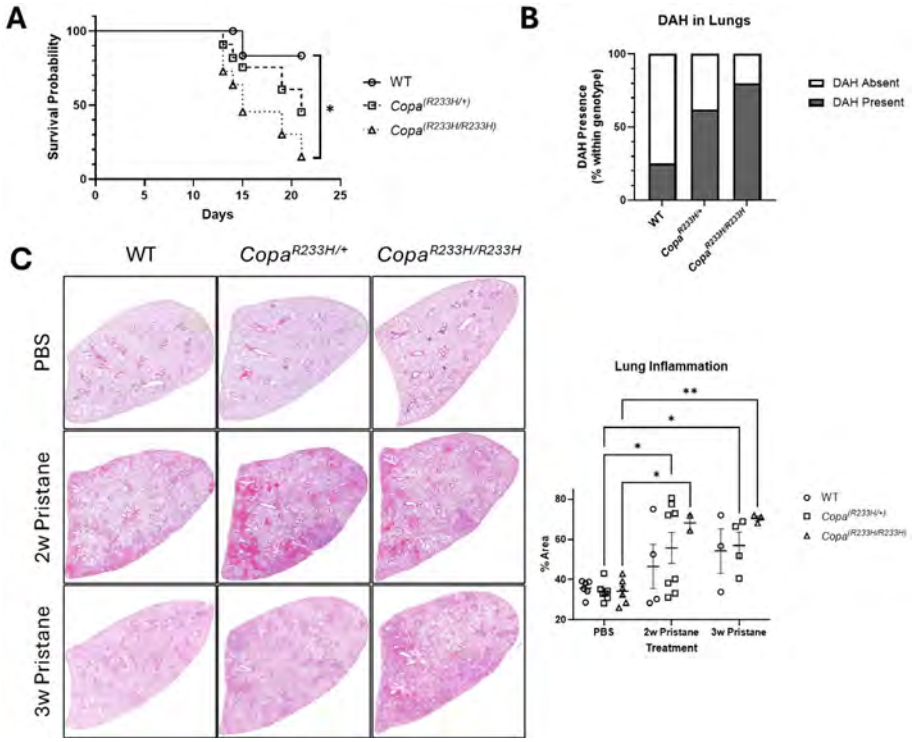


Figure 1: Mice bearing the Copa-R233H allele develop worsened and protracted disease in response to pristane. A) Survival of mice in response to a single intraperitoneal dose of pristane. B) Presence of diffuse alveolar hemorrhage in lungs 2 weeks after pristane injection. C) H&E-stained left lung lobes from PBS- or pristane-treated mice 2 or 3 weeks after i njection (left) as quantified by relative stained area (right). Values are mean +/- SEM. Statistical significance was determined using Log-rank (Mantel-Cox) or Two-Way ANOVA tests. *p<0.05, **p<0.01.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

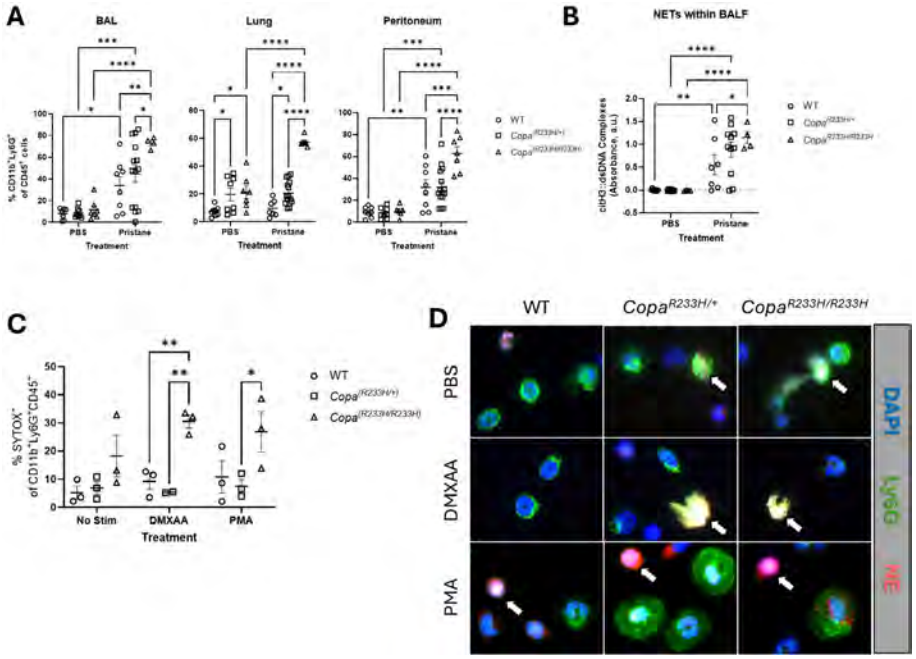


Figure 2: Copa-R233H promotes neutrophil infiltration into inflamed tissue and allows spontaneous and STING-dependent NETosis. A) Neutrophils as a percentage of CD11b+Ly6G+ of CD45+ cells within inflamed tissues 2 weeks after pristane injection. B) Presence of NETs, as measured by citH3::dsDNA complexes, within BAL fluid 2 weeks after pristane injection. C, D) Ability of peritoneal neutrophils to undergo NETosis in response to the STING agonist DMXAA or PMA, as measured by SYTOX+ via flow cytometry (C) and visualized via immunofluorescence (D, arrows). Values are mean +/- SEM. Statistical significance was determined using Two-Way ANOVA. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Methods: *Copa*$^{+/+}$ (WT), *Copa*$^{R233H/+}$, and *Copa*$^{R233H/R233H}$ C57BL/6 mice were generated and treated with pristane to induce DAH. Tissues were isolated at 4, 14, or 21 days and analyzed by flow cytometry, ELISA, qPCR, immunofluorescence (IF), and H&E. Circulating whole blood, neutrophils, and plasma were isolated from healthy control (HC) and COPA patients and analyzed by IF, ELISA, and scRNA-seq. Primary lung basal epithelial cells (BECs) isolated from COPA lung explants and immortalized HC BECs were transfected with dsDNA and analyzed via qPCR.

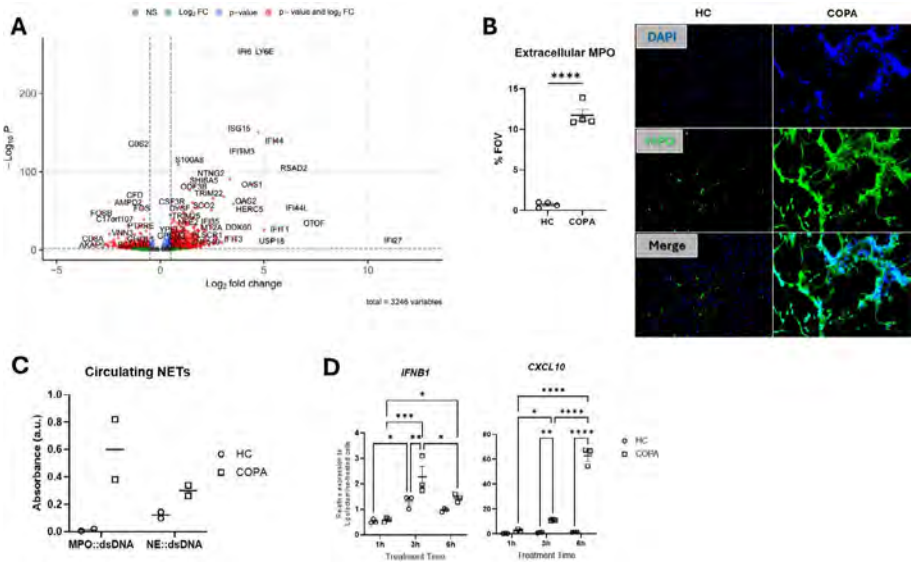


Figure 3: COPA-R233H fails to restrain inflammation in patient neutrophils and epithelial cells. A) Neutrophils from patients with COPA syndrome display a dramatic inflammatory signature as determined via scRNA-seq. B, C) Patient neutrophils undergo spontaneous NETosis after 4 hours in culture (B), and patients have elevated circulating NETs as measured by MPO::dsDNA and NE::dsDNA complexes (C). D) COPA patient-derived basal epithelial cells fail to curb IFNB1 and CXCL10 transcript production in response to dsDNA transfection. Values are mean +/- SEM. Statistical significance was determined using Two-Way ANOVA. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Unlike WT, mutant mice failed to recover from pristane-induced disease as observed by survival, development of DAH, and lung inflammation (Fig 1A-C). Mutant mice underwent dramatic granulopoiesis reflected in dominant neutrophil infiltrates within the BAL, lung, and peritoneum versus WT (Fig 2A). We found elevated neutrophil extracellular traps (NETs) within mutant BAL, and mutant neutrophils underwent increased NETosis compared to WT (Fig 2B-D). Additionally, scRNA-seq of human neutrophils revealed a highly elevated inflammatory signature in COPA versus HC, corroborated by increased NETosis and circulating NETs in these patients (Fig 3A-C).

To ask how neutrophils may be recruited into the lung during COPA, we exposed human BECs to dsDNA to simulate alveolar NETs. COPA BECs generated a robust and prolonged inflammatory response compared to HC, specifically *IFNB1* and the neutrophil chemoattractant *CXCL10*, suggesting an amplified capacity to recruit neutrophils (Fig 3D).

Conclusion: In summary, we found that COPA^{R233H} exacerbates pristane-induced lung disease, is associated with increased NETosis, and permits excessive *CXCL10* production in epithelial cells. Taken together, our data detail a route by which lung inflammation in COPA syndrome may be promoted in a feed-forward manner via aberrant NETosis and inflamed alveolar epithelium.

Disclosure: R. Moore: None; **L. Huo**: None; **C. Koziel**: None; **B. Stripp**: None; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6; **D. Wallace**: PPD, 2; **C. Jefferies**: None.

Abstract Number: 2580

Estrogen Modulates Neutrophil Biology: Implications for Autoimmunity

William Ambler[1], Eduardo Patino-Martinez[1], Gustaf Wigerblad[1], Shuichiro Nakabo[2], Jorge Romo-Tena[3], Norio Hanata[4], James Simone[1], Stephen Brooks[1], Kan Jiang[5], Hong-wei Sun[1], Faiza Naz[6], Shamima Islam[6], Gustavo Gutierrez-Cruz[1], Stefania Dell'Orso[1], Anshu Deewan[7], Vicky Chen[7], Paul Schaughency[8], Carmelo Carmona-Rivera[4], Sarfaraz Hasni[1], Veronica Gomez-Lobo[9] and Mariana Kaplan[4], [1]NIH/NIAMS, Bethesda, MD, [2]NIAMS, NIH, Bethesda, MD, [3]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [4]Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, MD, [5]Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, Bethesda, [6]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [7]NIH/NIAID, Bethesda, MD, [8]NIAID, NIH, Bethesda, MD, [9]NIH/NICHD, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Innate Immunity (2579–2584)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Neutrophils are essential for inflammation and host defense against infections. Our group has previously highlighted their key roles in the pathogenesis of diseases that are more common in women, such as systemic lupus erythematosus (SLE) and other systemic rheumatic conditions. We have also reported sex-based differences in neutrophil biology that affect key biologic processes and may influence this differential predisposition to systemic autoimmune disease and response to infections. These differences include variations in sensitivity to type I interferons (IFN-I), immunometabolic activity, and maturation status of neutrophils, all with significant functional and pathogenic implications. Our previous work suggests that sex hormones may contribute to these differences, although the exact mechanisms remain unclear. We hypothesize that estrogen influences neutrophil gene expression and chromatin structure during granulopoiesis, ultimately shaping neutrophil function.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We used single cell transcriptomics (sc-RNAseq), as well as flow cytometry, to analyze neutrophils. In mouse models, we performed oophorectomy (Oop) and sham surgeries, with or without administration of exogenous estradiol, to manipulate levels of gonadal hormones. Neutrophil extracellular trap (NET) formation was assessed by immunofluorescence microscopy. Human biospecimens were collected at the NIH Clinical Center for similar sc-RNAseq and NET assessments.

Results: Single-cell RNAseq, revealed that Oop significantly reduced a neutrophil subset characterized by high expression of by IFN-I stimulated genes (the "IFN-I cluster"). Neutrophils from Oop mice also showed reduced NET formation in response to danger signals. In contrast, treatment with exogenous estradiol restored IFN-I cluster prevalence and enhanced granulopoiesis in bone marrow and spleen. To translate these findings into humans, we studied individuals with androgen insensitivity syndrome (AIS; XY karyotype) who have higher levels of circulating estrogen compared to healthy volunteer (HV) males. Neutrophils from AIS individuals were more mature, had an expanded IFN-I cluster, and expressed higher IFN-I signatures than neutrophils from healthy men. Functionally, AIS neutrophils resembled those from women, showing enhanced NET formation and different bioenergetics.

In SLE, sex differences in neutrophil biology are also observed. Female SLE patients had more IFN-I cluster- neutrophils and a stronger IFN-I-gene signature compared to male patients, though this difference diminished after menopause, further supporting the role for estrogen.

Conclusion: Our findings demonstrate that estrogen modulates neutrophil development and function in both mice and humans. Estrogen promotes granulopoiesis, drives the formation of an IFN-I-responsive neutrophil subset, and enhances neutrophil effector functions such as NET formation. These sex hormone-mediated differences in neutrophil biology may help explain the increased prevalence of autoimmune diseases in women.

Disclosure: W. Ambler: None; **E. Patino-Martinez**: None; **G. Wigerblad**: None; **S. Nakabo**: None; **J. Romo-Tena**: None; **N. Hanata**: None; **J. Simone**: None; **S. Brooks**: None; **K. Jiang**: None; **H. Sun**: None; **F. Naz**: None; **S. Islam**: None; **G. Gutierrez-Cruz**: None; **S. Dell'Orso**: None; **A. Deewan**: None; **V. Chen**: None; **P. Schaughency**: None; **C. Carmona-Rivera**: None; **S. Hasni**: None; **V. Gomez-Lobo**: None; **M. Kaplan**: None.

Abstract Number: 2581

From Skin to Kidney: Neutrophil-Mediated Crosstalk Links Cutaneous Injury to Renal Inflammation and Vascular Remodeling in Lupus

Angelique Cortez[1], Lindsay Mendyka[2], Paola Garcia[3], Elizabeth Nowak[1], Fred Kolling[4], Lucas Salas[1], Christopher Burns[5], Andrea Fava[6] and Sladjana Skopelja-Gardner[7], [1]Dartmouth College, Lebanon, NH, [2]Dartmouth College, Lyme, NH, [3]St. Mary's University, San Antonio, TX, [4]Geisel School of Medicine at Dartmouth, Lebanon, NH, [5]Dartmouth Health, Lebanon, NH, [6]Johns Hopkins University, Baltimore, MD, [7]Dartmouth Geisel School of Medicine, Lebanon, NH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Innate Immunity (2579–2584)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: The majority of SLE patients are sensitive to ultraviolet light (UV), which can lead to local and systemic inflammation, including lupus nephritis (LN) flares. While we previously showed that neutrophils remigrate from UV-exposed skin to the kidney, how these neutrophils impact renal structural cells remains unclear. We hypothesize that neutrophils play a reparative role in healthy kidneys but exert pro-inflammatory effects in lupus-like kidneys.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: ScRNA-seq was performed by 10X Genomics on saline-perfused, digested kidneys and enriched neutrophils from 3-month-old female B6 mice before and 2 days after a single UVB exposure (500 mJ/cm^2). Clustering (Seurat), pathway analysis (clusterProfiler), and ligand-receptor analysis (CellChat) were used. Neutrophils were profiled by flow cytometry 6 days post-UVB in 3-month-old female B6 and MRL-lpr mice. Spatial transcriptomics (Visium) was performed on class III/IV LN kidneys, and urinary immune cells were quantified by DNA methylation deconvolution.

Results: Acute skin exposure to UV in B6 mice resulted in the expansion of renal glomerular endothelial cells, confirmed by increased CD31 staining. Of the most highly upregulated pathways in the expanded glomerular endothelial cluster were *regulation of angiogenesis* and *vascular development*, which were validated by increased angiogenesis transcriptional scores and expression of *Angpt2, Angptl1*, and *Angptl4*. Ligand-receptor analysis of the structural cells and enriched neutrophils showed significant increase in neutrophil-endothelial interactions (Cd177-Pecam-1). Neutrophil scRNAseq and flow cytometry at D2 showed UV skin exposure recruits CD177hi neutrophils that infiltrate the kidney. On day 6 post-UV, neutrophils in B6 kidneys had increased surface expression of CXCR4 and the inhibitory receptor CD371 (Clec12a). In contrast, CD371 levels were significantly decreased on the kidney infiltrating neutrophils of MRL-lpr mice after UV and no change in CXCR4 was seen. Spatial transcriptomics analysis of LN patient kidney biopsies revealed increased intra-glomerular neutrophil signature in patients with active skin disease and increased angiogenesis pathway score. In support of neutrophil-mediated skin-kidney crosstalk in SLE, intrarenal neutrophil levels were higher in lupus nephritis (LN) patients with active skin disease at the time of kidney biopsy than in LN patients without cutaneous involvement. In a subset of SLE patients without clinical signs of LN, high urinary neutrophils were associated with active skin disease, suggesting distal inflammation in the skin could contribute to subclinical renal processes in SLE.

Conclusion: Our findings reveal that UV exposure triggers glomerular endothelial expansion and pro-angiogenic signaling in the kidney, accompanied by increased recruitment of CD177$^+$ neutrophils. The regulatory phenotype of renal neutrophils post-UV in health kidneys is lost in lupus-like kidneys. Spatial and urinary profiling in LN and SLE patients supports a model of neutrophil-mediated skin-to-kidney crosstalk, implicating cutaneous flares in both clinical and subclinical renal involvement.

Disclosure: A. Cortez: None; **L. Mendyka**: None; **P. Garcia**: None; **E. Nowak**: None; **F. Kolling**: None; **L. Salas**: None; **C. Burns**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **S. Skopelja-Gardner**: None.

Abstract Number: 2582

Inflammatory Cell Death and Impaired Efferocytosis Drive Monocyte and Macrophage Dysfunction in VEXAS Syndrome.

Paul Breillat[1], Samuel Magaziner[2], Stéphane Camus[3], Lea Dionet[4], Quentin Delcros[5], Federica Pallotti[6], Kevin Chevalier[5], Margot Poux[7], Olivia Lenoir[8], Pierre-Louis Tharaux[5], Olivier Kosmider[9], David Beck[10] and Benjamin Terrier[11], [1]INSERM, PARIS 17, Ile-de-France, France, [2]Center for Human Genetics and Genomics, NYU Grossman School of Medicine, New York, NY, USA., New York, NY, [3]Université de Paris, INSERM UMR970, Paris Cardiovascular Research Center, Paris, France., PARIS, France, [4]INSERM, Paris, France, [5]Paris Cardiovascular Research Center, Université Paris Cité, INSERM U970, Paris, France, PARIS, France, [6]Internal Medicine and Clinical Immunology, Rennes, France, [7]Universitä de Paris, PARIS 04EME, France, [8]Paris Cardiovascular Research Center, Université Paris Cité, INSERM U970, Paris, France, PARIS, Ile-de-France, France, [9]AP-HP, Hopital Cochin, Institut Cochin, CNRS UMR8104, INSERM U1016 Université Paris Cité Paris France., PARIS, France, [10]Center for Human Genetics and Genomics, NYU Grossman School of Medicine. Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine. Department of Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, New York, NY, USA, New York, NY, [11]Cochin Hospital, Paris, France

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Innate Immunity (2579–2584)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is a life-threatening systemic disorder characterized by inflammation and increased risk of opportunistic infections. VEXAS results from somatic mutations in the ubiquitin-activating enzyme 1 (*UBA1)* gene that abolish UBA1 function in hematopoietic stem cells and peripheral myeloid cells. Monocytes from VEXAS patients are numerically and functionally impaired and display an inflammatory signature. However, the relationship between the *UBA1* mutation and the clinical manifestations of the disease remains elusive. We investigated the functional consequences of *UBA1* inactivation in VEXAS monocytes/macrophages.

Methods: We generated human monocytic THP-1 cells with a conditional Cas9-mediated knockout of endogenous *UBA1* in parallel with constitutive expression of wild-type ($UBA1^{WT}$) or VEXAS-associated ($UBA1^{M41V}$) *UBA1* gene. We assessed spontaneous and TNFα-induced inflammatory cell death using flow cytometry, Western blotting and live cell imaging. We also analyzed inflammatory cell death pathways in VEXAS skin biopsies. Next, we assessed pathogen-driven immune responses by measuring cytokine production after TLR stimulation of both whole blood from VEXAS patients (TruCulture system) and $UBA1^{WT}$ and $UBA1^{M41V}$ THP-1. THP-1-derived macrophages were assessed for differentiation, polarization, cytokine production by Luminex, transcriptome, and efferocytosis process by flow cytometry, Western blot and immunofluorescence.

Results: The $UBA1^{M41V}$ THP-1 monocytes exhibited poly-ubiquitination defects, an inflammatory transcriptional profile and increased spontaneous cell death. Specifically, $UBA1^{M41V}$ THP-1 cells were more susceptible to TNFα-induced cell death via RIPK1 activation, which was rescued by caspase- and RIPK1-specific inhibitors. These observations were confirmed in $CD14^+$ sorted cells from peripheral blood and in $CD68^+$ cells in skin biopsies from VEXAS patients. TLR-induced cytokine production was defective in $UBA1^{M41V}$ THP-1 cells, which correlated with impaired NF-κB signaling. Similar results were obtained in whole blood from patients after stimulation with TLR agonists.

$UBA1^{M41V}$ THP1-derived macrophages displayed an inflammatory phenotype with increased secretion of pro-inflammatory cytokines (IL-1β, IL-6, IFN-γ, TNF-α) and increased spontaneous cell death. They also exhibited defective efferocytosis, with decreased MERTK expression and impaired lysosomal degradation of engulfed cells. This was associated with decreased expression of LAMP-1 and cathepsins.

Conclusion: Our results show that the $UBA1^{M41V}$ mutation disrupts TLR-induced monocyte cytokine production and increases cell death, which may explain the severe monocytopenia and susceptibility to serious infections in VEXAS. In addition, the $UBA1^{M41V}$ mutation skews macrophages toward an inflammatory phenotype with an impaired efferocytosis, which likely contributes to chronic inflammation and susceptibility to intracellular pathogen infections. Overall, we provide new insights into the pathophysiology of VEXAS.

Disclosure: P. Breillat: None; **S. Magaziner**: None; **S. Camus**: None; **L. Dionet**: None; **Q. Delcros**: None; **F. Pallotti**: None; **K. Chevalier**: None; **M. Poux**: None; **O. Lenoir**: None; **P. Tharaux**: None; **O. Kosmider**: None; **D. Beck**: Alexion, 2, Genesis Therapeutics, 2, GSK, 2, Novartis, 2, Sobi, 2; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2584

Spatially Resolved Transcriptomics Reveal Macrophage Heterogeneity in Giant Cell Arteritis

Lea Dionet[1], Federica Pallotti[2], Margot Poux[3], Quentin Delcros[4], Nader Yatim[5], Brian Soong[6], Paul Breillat[7], Kevin Chevalier[8], claudie Cladière[9], Patrick Bruneval[10], Benoit Terris[4], Alexis REGENT[11], Xavier Puéchal[12], Luc Mouthon[13], Miriam Merad[6], Olivia Lenoir[14], Pierre-Louis Tharaux[15], Maxime Samson[16] and Benjamin Terrier[17], [1]INSERM, Paris, France, [2]Internal Medicine and Clinical Immunology, Rennes, France, [3]Universitä de Paris, PARIS 04EME, France, [4]AP-HP, Paris, France, [5]University of Paris-Cite, New York, NY, [6]Mount Sinai School of Medicine, New York, [7]INSERM, PARIS 17, Ile-de-France, France, [8]Universitä Paris Cité, Montrouge, France, [9]Marie et Louis Pasteur University, EFS, INSERM, UMR RIGHT, Besançon, France, Dijon, France, [10]AP-HP, Paris, [11]Hopital Cochin, Paris, France, [12]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Hospital Cochin, and Université Paris Cité, Paris (75014), Ile-de-France, France, [13]Department of Internal Medicine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin University Hospital, Université Paris Cité, AP-HP, Paris, France, [14]Paris Cardiovascular Research Center, Université Paris Cité, INSERM U970, Paris, France, PARIS, Ile-de-France, France, [15]Paris Cardiovascular Research Center, Université Paris Cité, INSERM U970, Paris, France, PARIS, France, [16]CHU Dijon Bourgogne, Dijon, France, [17]Cochin Hospital, Paris, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Innate Immunity (2579–2584)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Giant cell arteritis (GCA) is a large-vessel vasculitis affecting individuals over 50 years of age. Current models implicate genetic susceptibility, immune senescence, activation of vascular dendritic cells, and recruitment of CD4+ T cells driving inflammation via IFN-γ and IL-17. These cytokines stimulate vascular resident cells and recruit monocytes that differentiate into macrophages. While macrophages are consistently present in GCA lesions, their phenotypic heterogeneity and molecular drivers remain poorly characterized. Here, we explore macrophages landscape and heterogeneity in human temporal artery biopsies (TAB) from GCA patients to identify key regulators of myeloid cell response in GCA.

Methods: We analyzed blood and TAB from patients with biopsy-proven GCA and age-matched controls. Spatial transcriptomic profiling of TAB was performed using GeoMx and Visium HD plateforms. TREM-1 and TREM-2 protein expression was assessed by multiplex immunofluorescence (IF). Flow cytometry analyzed TREM-1 and TREM-2 expression on circulating monocytes, and serum soluble TREM-1 (sTREM-1) and sTREM-2 were measured by ELISA. *In vitro* functional analyses included THP-1-derived macrophages cultured and a TREM-1 inhibition assay using nangibotide.

Results: Spatial transcriptomics showed TREM-1 signaling among top upregulated pathways in media-infiltrating $CD68^+$ macrophages from GCA lesions, alongside Th1, IL-6, and interferon signaling pathways, and identified IFN-γ and TLR activation as major upstream regulators using Ingenuity Pathway Analysis. The intima showed upregulation of myofibroblast-related genes, with causal network analysis predicted TREM-2 activation. High-resolution spatial transcriptomics (Visium HD) revealed $SPP1^+$ $TREM1^+$ inflammatory macrophages in the media, and $MERTK^+$ $FOLR2^+$ $GPNMB^+$ $TREM2^+$ macrophages in proximity to myofibroblasts. IF confirmed TREM-1 protein expression by most media-infiltrating $CD68^+$ macrophages, while a smaller subset expressed TREM-2.

Circulating monocytes expressed high TREM-1 and low TREM-2 in both GCA and controls. In contrast, serum sTREM-1 and sTREM-2 were significantly elevated in GCA patients (sTREM-1: 419.3 ± 30.5 vs. 224.9 ± 17.1 pg/mL, $p< 0.0001$; sTREM-2: 829.2 ± 106.4 versus 284.7 ± 26.6 pg/mL, $p< 0,0001$, for TREM-2), and sTREM-1 correlated with CRP ($r=0.55$, $p< 0.01$) and IL-6 (**$r=0.58$, $p< 0.01$**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In vitro, culture with IFN-γ/LPS increased proinflammatory genes and *TREM1* in THP-1-derived macrophages, while IL-4/IL-13 - associated with an anti-inflammatory and pro-resolving phenotype - induced both TREM1 and TREM2 expression, suggesting a homeostatic role for TREM-2. Finally, nangibotide, a TREM-1 inhibitor, reduced THP-1 monocyte migration and decreased NFkB activation when added to IFN-γ/LPS-polarized THP-1-derived macrophages, suggesting a role for TREM-1 in macrophage recruitment and activation.

Conclusion: TREM-1 and TREM-2 define distinct macrophage subsets in GCA. TREM-1 is associated with inflammation and monocyte recruitment, while TREM-2 may mediate homeostatic functions. These findings position TREM-1 as a promising therapeutic target.

Disclosure: L. Dionet: None; **F. Pallotti**: None; **M. Poux**: None; **Q. Delcros**: None; **N. Yatim**: None; **B. Soong**: None; **P. Breillat**: None; **K. Chevalier**: None; **c. Cladière**: None; **P. Bruneval**: None; **B. Terris**: None; **A. REGENT**: Novartis, 2; **X. Puéchal**: Roche, 5; **L. Mouthon**: None; **M. Merad**: None; **O. Lenoir**: None; **P. Tharaux**: None; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 2585

The effect of prophylactic colchicine use on gene expression in gout

Austin Wheeler[1], Guanqi Lu[2], Ana Vazquez[3], Jeffrey Edberg[4], Angelo Gaffo[5], Tate Johnson[1], Michael Duryee[1], James O'Dell[1], Jeff Newcomb[1], Michael Pillinger[6], Robert Terkeltaub[7], Ryan Ferguson[8], Mary Brophy[8], Tuhina Neogi[9], Bryant England[1], Ted Mikuls[1], Tony Merriman[10] and Richard Reynolds[4], [1]University of Nebraska Medical Center, Omaha, NE, [2]Michigan State University, East Lansing, MI, [3]Michigan State University, Miami, FL, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [6]New York University Grossman School of Medicine, New York, NY, [7]Retired, San Diego, CA, [8]VA Cooperative Studies Program Coordinating Center, Boston, MA, [9]Boston University School of Medicine, Boston, MA, [10]University of Alabama at Birmingham, Homewood, AL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (2585–2590)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Colchicine is recommended for the treatment and prophylaxis of gout flares and approved for secondary prevention of ischemic cardiovascular disease (CVD). While its primary anti-inflammatory mechanism is thought to be tubulin disruption, other biological pathways are likely impacted. This study evaluated the effect of prophylactic colchicine on gene expression among individuals with gout enrolled in the 72-week STOP Gout clinical trial (O'Dell JR et al. NEJM Evid 2022).

Methods: STOP Gout participants (N=940) met classification criteria for gout, were randomized to treat-to-target allopurinol or febuxostat, and received anti-inflammatory prophylaxis (90% colchicine). Prophylaxis was stopped at 24 weeks but could be continued or resumed up to week 48 if desired or clinically indicated. This study limited to those with whole blood RNA PaxGene (BD Biosciences) tube samples at 24 and/or 48 weeks (N = 259). Those identified as in active flare or with 0-10 pain score >3 at the time of lab draw were excluded (N = 45). Sequencing libraries were prepared from extracted RNA using Illumina Stranded Total RNA Prep with Ribo-Zero™ Plus rRNA Depletion + Globin Reduction. Sequence reads were aligned and counted via STAR aligner software. Normalized counts were generated using DESeq2. Differential expression was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

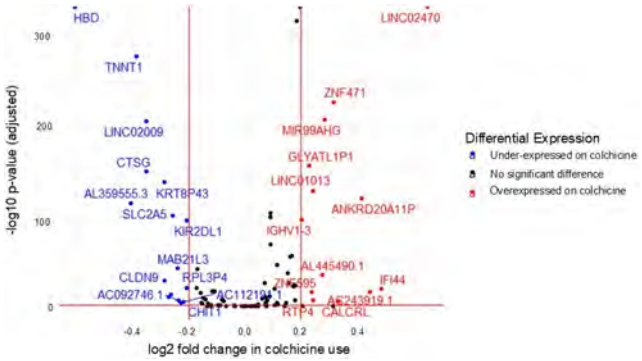


Figure 1. Gene expression differences by colchicine use among STOP Gout participants at 24 and 48 weeks. Cut-offs for significance defined as absolute log2 fold change >0.2 and adjusted p-value <0.1.

evaluated using mixed effects negative binomial regression with subject-specific random intercepts accounting for repeated measures in the GLMMseq package (R 4.4.1). For each gene, hypothesis tests of fixed effects were made for colchicine use status, timepoint, and colchicine:time interaction. Genes were filtered for false discovery rate-adjusted p-value < 0.1, |log2 fold change| >0.2, and absence of time interaction.

Table 1. Description of genes differentially expressed on colchicine with functional classification. Abbreviations: fold change (FC) Negative log2 fold change (grey) is under-expressed on colchicine. Positive log2 fold change (orange) is overexpressed on colchicine. Functional classification of "-" denotes none established.

Gene	Log2 FC On colchicine	Functional Classification
LINC02470	0.653	Innate Immune Response
IFI44	0.489	Innate Immune Response
AC243919.1	0.446	-
ANKRD20A11P	0.417	-
CALCRL	0.336	Cell Signaling
ZNF471	0.318	Transcription Factor
MIR99AHG	0.285	Cell Signaling
AL445490.1	0.277	-
LINC01013	0.245	Cell Signaling
RTP4	0.244	Other
ZNF595	0.238	-
GLYATL1P1	0.230	-
IGHV1-3	0.204	Adaptive Immune Response
HBD	-0.608	Hematologic
AL359555.3	-0.408	-
TNNT1	-0.387	Cardiovascular System
CTSG	-0.352	Innate Immune Response
LINC02009	-0.352	-
CLDN9	-0.289	Cell Signaling
KRT8P43	-0.288	-
GRB10	-0.272	Cell Signaling
SHE	-0.263	Cell Signaling
SLC2A5	-0.260	Cardiovascular System
MAB21L3	-0.242	Other
AC092746.1	-0.237	Transcription factor
CHIT1	-0.230	Innate Immune Response
AC112191.1	-0.221	-
KIR2DL1	-0.209	Innate Immune Response
RPL3P4	-0.209	-

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of 214 gout participants included, 165 had samples at one timepoint and 49 at both (total 263 samples). At 24 weeks, 98 of 132 samples (74.2%) were on colchicine, whereas 33 of 131 (25.1%) were on colchicine at 48 weeks. There were 29 genes associated with colchicine use (**Figure 1**; 16 under-expressed and 13 overexpressed). Nineteen had a described physiologic function on NIH Gene and literature review and were descriptively classified, most commonly as related to innate immunity (**Table 1**). Delta hemoglobin (HBD) was suppressed on colchicine, consistent with its known potential for anemia. Long non-coding RNA LINC02470, previously described as a correlate of transforming growth factor (TGF)-β-mediated inhibition of the innate immune response, was the most overexpressed gene on colchicine. SLC2A5, a requisite gene in dietary fructose-induced hypertension, and TNNT1, a troponin subunit that regulates myocardial contraction, were under-expressed on colchicine.

Conclusion: This study identifies potential mechanisms underlying the systemic impact of colchicine in individuals with gout. The most overexpressed gene, LINC02470, is a novel finding in gout but has been shown to correlate with innate immune inhibition and is also in close proximity to CLEC12A, which is known to bind monosodium urate crystals and suppress immune response. SLC2A5 is essential for fructose-induced hypertension, and its reduced expression with colchicine suggests one potential link to CVD risk reduction.

Disclosure: A. Wheeler: None; **G. Lu**: None; **A. Vazquez**: None; **J. Edberg**: None; **A. Gaffo**: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **T. Johnson**: None; **M. Duryee**: None; **J. O'Dell**: None; **J. Newcomb**: None; **M. Pillinger**: Amgen, Federation Bio, Fortress Biotech, Scilex, and SOBI, 2, Convergence Bio, 2; **R. Terkeltaub**: Atom Bioscience, 2, BPG Bio, 2, Crystalys, 2, Novartis, 2, Shanton, 2; **R. Ferguson**: None; **M. Brophy**: None; **T. Neogi**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **T. Merriman**: None; **R. Reynolds**: None.

Abstract Number: 2586

Estimated Carrier Prevalence of HLA-B*58:01 Across Diverse Populations in the US and Globally

Qiping Xu[1], Joan Bathon[2] and Yiming Luo[2], [1]Mayo Clinic, Mankato, [2]Columbia University, NEW YORK, NY

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (2585–2590)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: The HLA-B*58:01 is strongly associated with allopurinol-induced severe cutaneous adverse reactions. The 2020 American College of Rheumatology (ACR) Guideline for the Management of Gout conditionally recommends HLA-B*58:01 testing prior to initiating allopurinol in patients of certain Asian or African descent, while advising against routine testing in other ethnic groups. These recommendations are based on reported carrier prevalence and cost-effectiveness analyses. However, data remain limited for populations such as Native American, South Asian, and Middle Eastern groups. This study aimed to estimate the prevalence of HLA-B*58:01 carriers across diverse U.S. and global populations.

Methods: We performed a descriptive analysis of HLA-B*58:01 carrier prevalence across diverse populations using two data sources: (1) the National Marrow Donor Program (NMDP) , a large U.S. hematopoietic cell registry of approximately 2.9 million individuals. Allele frequencies, estimated via a modified expectation–maximization algorithm from mixed-resolution HLA typing data, were publicly available (Gragert et al., 2013). Carrier prevalence was inferred assuming Hardy-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

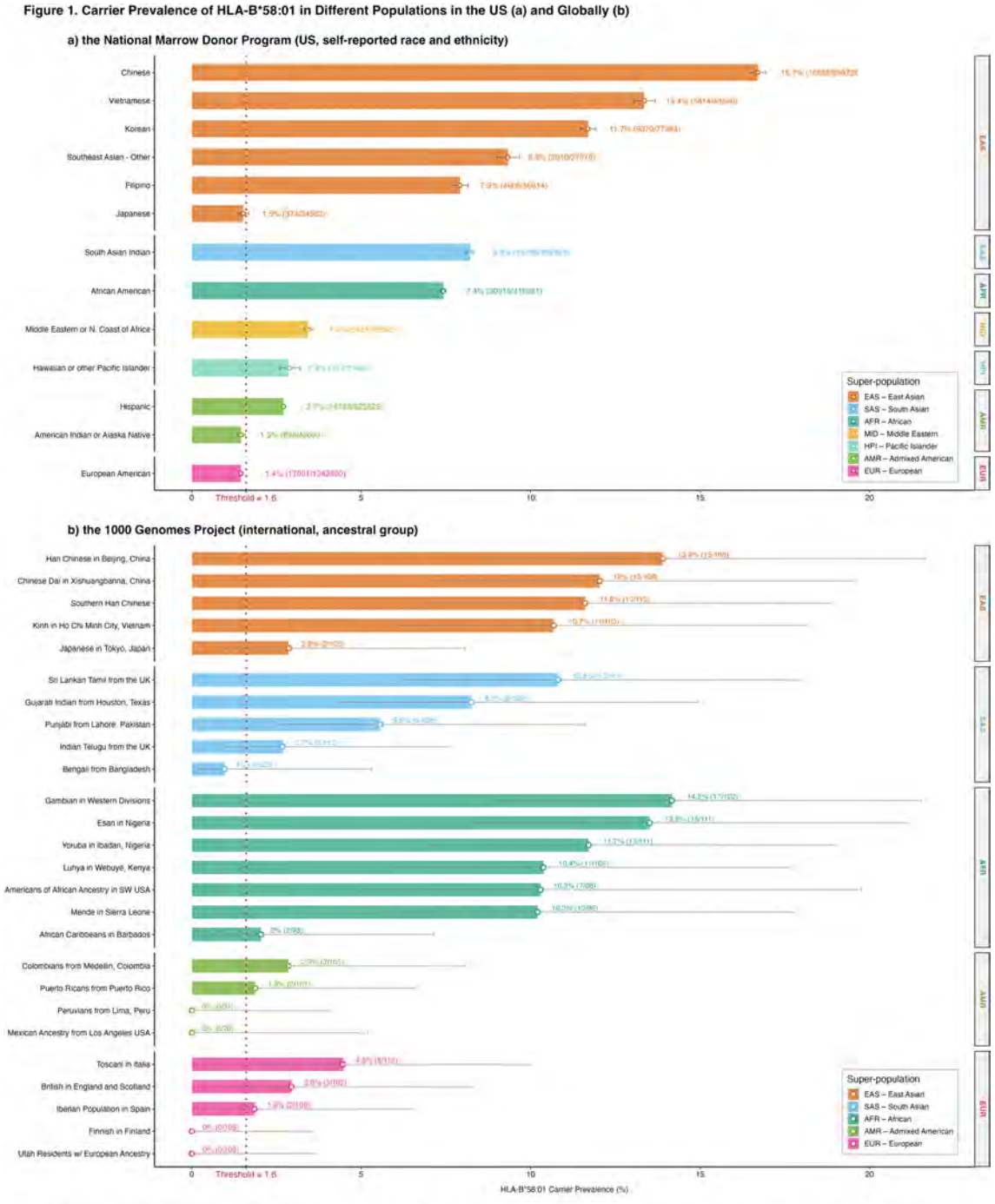


Figure 1. Carrier prevalence of HLA-B*58:01 across U.S. populations from the National Marrow Donor Program registry (NMDP, panel a) and global populations from the 1000 Genomes Project (1KG, panel b). In NMDP data, carrier prevalence was estimated from allele frequencies under the assumption of Hardy-Weinberg equilibrium. In 1KG data, carrier prevalence was directly calculated from individual-level HLA genotyping. Carrier prevalence (%) and carrier counts (carrier number/sample size) are shown for each population. Error bars represent 95% confidence intervals calculated using the Wilson score method. The 1.6% threshold for cost-effective testing is indicated for reference.

Weinberg equilibrium; and (2) the 1000 Genomes Project (1KG) , an international consortium that includes 2,693 individuals with publicly available four-digit HLA typing data. In the NMDP, population categories are based on self-reported race and ethnicity, whereas 1KG populations were sampled by self-identified ancestry and are widely used as genetic ancestry reference groups. We compared carrier prevalence to 1.6%, the threshold for cost-effective testing based on a prior modeling study cited in the ACR guideline (Jutkowitz et al., 2017).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: In the NMDP, estimated HLA-B*58:01 carrier prevalence exceeded the 1.6% threshold for cost-effective testing in individuals self-identifying as Chinese (16.7%, 95%CI 16.5%-16.9%), Vietnamese (13.4%, 95%CI 13.0%-13.7%), Korean (11.7%, 95%CI 11.5%-11.9%), other Southeast Asian (9.3%, 95%CI 9.0%-9.7%), Filipino (7.9%, 95%CI 7.7%-8.1%), South Asian Indian (8.2%, 95%CI 8.1%-8.3%), African American (7.4%, 95%CI 7.3%-7.5%), Middle Eastern or North African (3.4%, 95%CI 3.3%–3.6%), Hawaiian or other Pacific Islander (2.9%, 95%CI 2.6%-3.2%), and Hispanic (2.7%, 95% CI 2.7%-2.8%) (Figure 1a). In contrast, the estimated prevalence was below the 1.6% threshold for cost-effective testing among Japanese (1.5%, 95%CI 1.4%-1.7%), American Indian or Alaska Native (1.5%, 95%CI 1.4%-1.6%), and European American (1.4%, 95%CI 1.4%-1.5%). Carrier frequencies in ancestry-based populations from 1KG were largely consistent with NMDP estimates (Figure 1b).

Conclusion: Estimated HLA-B*58:01 carrier prevalence varies by race and ethnicity, with most groups exceeding the 1.6% threshold for cost-effective testing. Among those below the threshold, prevalence was only marginally lower. These findings raise the possibility that broader HLA-B*58:01 testing than recommended by the 2020 ACR guideline could be considered prior to allopurinol initiation.

Disclosure: Q. Xu: None; **J. Bathon**: AbbVie/Abbott, 2, Merck, 2, Ono Pharma, 2; **Y. Luo**: None.

Abstract Number: 2587

Nanoencapsulated Sirolimus Plus Pegadricase Reduced Disease Burden in Patients With Uncontrolled Gout: Results From the Phase 3 DISSOLVE Trials

Puja Khanna[1], Amar Majjhoo[2], Rehan Azeem[3], Ben Peace[4], Bhavisha Desai[5] and Vibeke Strand[6], [1]Division of Rheumatology, University of Michigan, Ann Arbor, MI, [2]Shores Rheumatology, St. Clair Shores, MI, [3]Global MACD, Sobi Inc., Waltham, MA, [4]Statistical Science, Sobi, Stockholm, Sweden, [5]Sobi, Glastonbury, CT, [6]Division of Immunology/ Rheumatology, Stanford University, Palo Alto, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (2585–2590)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Patients (pts) with uncontrolled gout (UG; persistent elevation in serum uric acid [sUA] levels and clinical manifestations despite oral urate-lowering therapy) have poor health-related quality-of-life (HRQOL) outcomes. The global UG disease burden is substantial and increasing. NASP (formerly SEL-212) is an investigational, novel, every 4-wk (Q4W), sequential 2-component infusion therapy consisting of targeted nanoencapsulated sirolimus (NAS, formerly SEL-110), which mitigates the formation of antipegadricase antibodies, and a uricase (pegadricase [P]; formerly SEL-037), which reduces sUA. Here, we report sUA levels, joint exam findings, and HRQOL outcomes in pts with UG who received 6 doses of NASP or placebo (PBO) in the phase 3 DISSOLVE I and II (NCT04513366, NCT04596540) studies.

Methods: Eligible pts had a history of symptomatic gout (≥3 gout flares within 18 mo of screening, ≥1 tophus, or current gouty arthritis), inability to normalize sUA and control symptoms with treatment, and screening sUA ≥7 mg/dL, which aligned with ACR diagnostic criteria for gout (Neogi *et al. Arthritis Rheumatol* 2015). Pts were randomized 1:1:1 to receive high-dose (HD) NASP (0.15 mg/kg NAS; 0.2 mg/kg P), low-dose (LD) NASP (0.10 mg/kg NAS; 0.2 mg/kg P), or PBO Q4W; those who received 6 doses were included in this post hoc analysis. Pt-reported outcomes (PROs) included the 36-Item Short Form

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

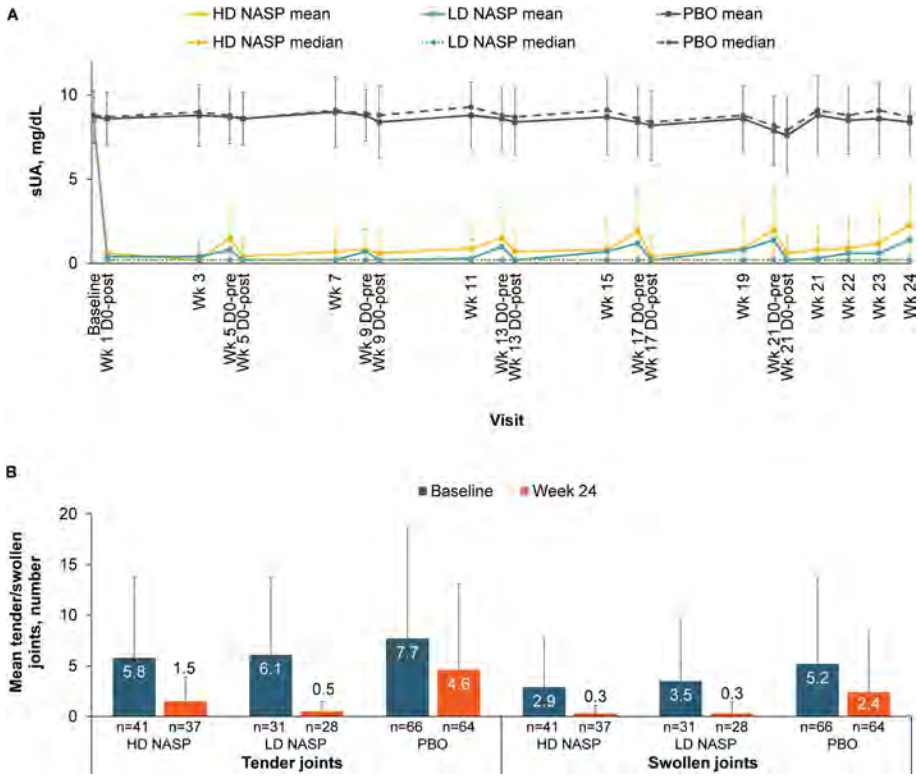


Figure 1: (A) sUA Over Time and (B) Number of Tender/Swollen Joints at Baseline and Week 24. Error bars show standard deviation for both panels. In panel A, n values were 42 at baseline and 37 at week 24 for HD NASP, 35 at both time points for LD NASP, and 67 at both time points for PBO. D, day; HD NASP, high-dose NASP; LD NASP, low-dose NASP; n, number of patients; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; post, post-dose; pre, pre-dose; sUA, serum uric acid; Wk, week.

Health Survey (SF-36) physical component summary (PCS) score (minimal clinically important difference [MCID], 5) and Health Assessment Questionnaire-Disability Index (HAQ-DI) pain score (MCID, 16).

Results: In pts receiving HD NASP (n=42), LD NASP (n=35), or PBO (n=67), mean sUA changes of –88%, –94%, and –0.3% (median: –97%, –98%, and 1.5%) were observed from baseline (mean [standard deviation (SD)]: 8.5 [1.4], 8.5 [1.3], and 8.7 [1.6] mg/dL) to wk 24 (mean [SD]: 1.1 [2.0], 0.5 [0.8], and 8.5 [2.0] mg/dL), respectively. In the NASP arms, sUA reduction was noted immediately after the first dose, and mean sUA generally remained ≤2.0 mg/dL throughout the study (**Figure 1A**). Pts receiving HD NASP, LD NASP, and PBO had mean reductions in the number of tender (–74%, –92%, and –40%) and swollen (–90%, –91%, and –54%) joints from baseline (mean number of tender/swollen joints:

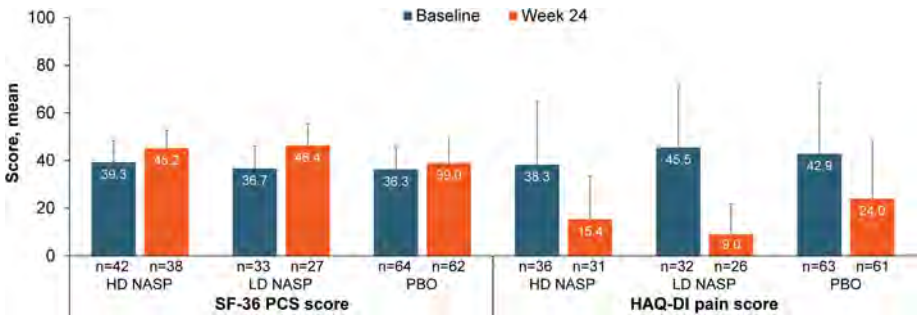


Figure 2: SF-36 PCS Score and HAQ-DI Pain Score at Baseline and Week 24. Error bars show standard deviation. Higher SF-36 scores indicate greater improvement in health-related quality of life; lower HAQ-DI scores indicate greater improvement in functional ability and less disability. HAQ-DI, Health Assessment Questionnaire-Disability Index; HD NASP, high-dose NASP; LD NASP, low-dose NASP; n, number of patients; NASP, nanoencapsulated sirolimus plus pegadricase; PBO, placebo; PCS, physical component summary; SF-36, 36-Item Short Form Health Survey.

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

5.8/2.9, 6.1/3.5, and 7.7/5.2) through wk 24 (mean number of tender/swollen joints: 1.5/0.3, 0.5/0.3, and 4.6/2.4). HD and LD NASP generally led to an approximately 2-fold reduction in the mean number of tender and swollen joints vs PBO (**-Figure 1B**). NASP-treated pts showed improvement in mean SF-36 PCS scores (HD NASP: 5.9; LD NASP: 9.7) that exceeded the MCID and was >2-fold higher than the change for PBO-treated pts by wk 24 (2.8); NASP-treated mean SF-36 PCS scores (HD NASP: 45.2; LD NASP: 46.4) were comparable to the US general population (49.2; Maglinte *et al*. *J Clin Epidemiol* 2012). By wk 24, a greater mean HAQ-DI pain score reduction was seen with NASP (HD NASP: –60%; LD NASP: –80%) vs PBO (–44%; **Figure 2**).

Conclusion: NASP-treated pts had meaningful reductions in disease burden and key clinical manifestations, as reflected by improvements in sUA levels and PROs. This therapy has a noteworthy impact on resolving acute gout symptoms over 6 treatments and shows promise for improving HRQOL.

Disclosure: P. Khanna: Arthrosi, 5, Olatec, 5, Selecta Biosciences, 5, Sobi, 2; **A. Majjhoo**: AbbVie, 2, 6, Amgen, 2, 6, Cipher, 2, 6, Exagen, 2, 6, Janssen Innovative Medicine, 2, 6, UCB, 2, 6; **R. Azeem**: Selecta Biosciences, 11, Sobi, 3, 12, Shareholder; **B. Peace**: Sobi, 7, Veramed, 3; **B. Desai**: Sobi, 3, 11; **V. Strand**: AbbVie, 2, Alumis, 2, Amgen, 2, Arthrosi, 2, Artiva Biotherapeutics, 2, AstraZeneca, 2, Bayer, 2, Blackrock, 2, Boehringer-Ingelheim, 2, Bristol Meyers Squibb, 2, Catalyst, 2, Cipher, 2, CitryII, 2, Contura, 2, Cullinan, 2, Fate Therapeutics, 2, Fortress Biotech, 2, Gate Bioscience, 2, Genascence, 2, GlaxoSmithKlein(GSK), 2, Inmedix, 2, Kiniksa, 2, Lipum, 2, Longitude Capital, 2, MED Institute, 2, Novartis, 2, Omeros, 2, RAPT, 2, Royalty Pharma, 2, Sanofi, 2, SetPoint, 2, Sobi, 2, Spherix, 2, SynAct, 2, Takeda, 2, Topography, 2, Zoe, 2.

Abstract Number: 2588

Nanoencapsulated Sirolimus plus Pegadricase (NASP) Demonstrates a Reduction in Gout Flares: Results from the Phase 3 DISSOLVE Studies

Angelo Gaffo[1], Herbert Baraf[2], Anand Patel[3], Tuhina Neogi[4], Rehan Azeem[5], Wesley DeHaan[6], Ben Peace[7], Hugues Santin-Janin[8], Bhavisha Desai[9] and Naomi Schlesinger[10], [1]Division of Rheumatology and Clinical Immunology, University of Alabama, Birmingham, AL, USA; Birmingham VA Medical Center, Birmingham, AL, USA, Birmingham, AL, [2]The Center for Rheumatology and Bone Research, Rheumatology, Wheaton, Maryland, USA; Division of Rheumatology, The George Washington University, Washington, DC, [3]Conquest Research, Winter Park, FL, USA, Winter Park, FL, [4]Boston University School of Medicine, Boston, MA, [5]Global MACD, Sobi Inc., Waltham, MA, [6]Sobi, Inc, Waltham, MA, [7]Statistical Science, Sobi, Stockholm, Sweden, [8]Sobi, BASEL, Switzerland, [9]Sobi, Glastonbury, CT, [10]Spencer Fox Eccles School of Medicine, University of Utah, Salt Lake City, UT, USA, Salt Lake City, UT

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (2585–2590)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Urate-lowering therapy is recommended to lower serum urate (sUA) and for long-term prevention of gout flares (FitzGerald *et al. Arthritis Care Res (Hoboken)* 2020; Dalbeth *et al. Lancet* 2021), though an initial increase in gout flares after ULT initiation has been documented (Feng *et al. Int J Clin Exp Med* 2015; Schlesinger *et al. Nat Rev Rheumatol* 2023). NASP (formerly SEL-212) is an investigational, every 4-week, sequential infusion therapy designed to reduce sUA levels in patients (pts) with uncontrolled gout (UG), consisting of targeted immunomodulating, nanoencapsulated sirolimus (NAS; formerly SEL-110), sequentially administered with pegadricase (a pegylated uricase; formerly SEL-037). Gout flare incidence in pts receiving NASP has been previously reported (Baraf *et al. British Society for Rheumatology (BSR) 2024 Annual Meeting;* Poster P084). Here, we report gout flare outcomes in pts who received 6 doses of NASP or placebo (PBO).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

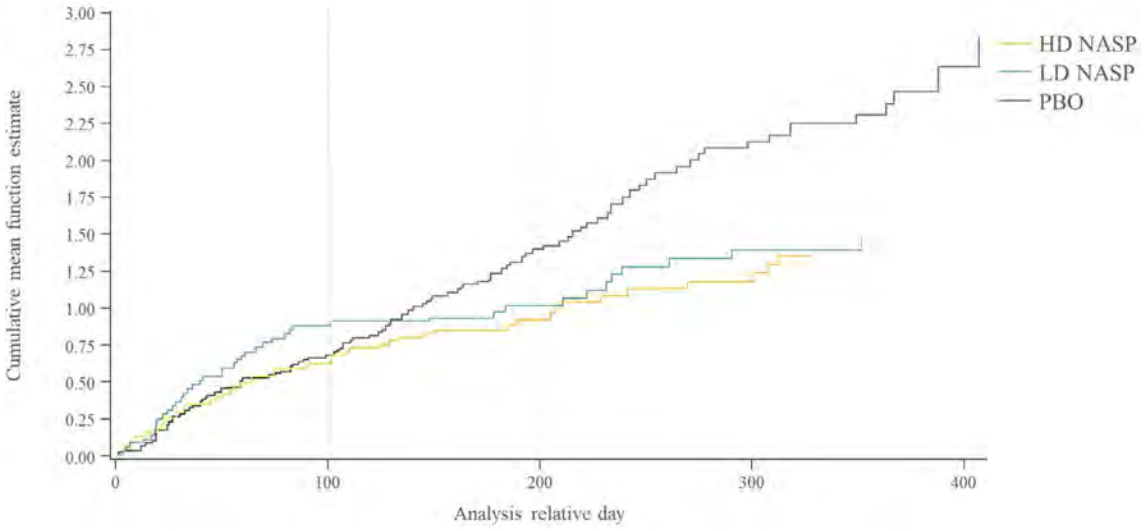


Figure 1. Cumulative mean estimate of gout flares in patients who completed 6 doses of study drug. Cumulative mean function estimate of gout flares per patient is shown for patients receiving 6 doses of HD NASP (yellow), LD NASP (teal) or PBO (dark gray). The event of interest is gout flare, and multiple gout flares are taken into consideration in the cumulative mean function. The analysis relative day is the number of days since the first dose of treatment. HD NASP, sequential infusions of 0.15 mg/kg nanoencapsulated sirolimus and 0.2 mg/kg pegadricase, LD NASP, sequential infusions of 0.10 mg/kg nanoencapsulated sirolimus and 0.2 mg/kg pegadricase; PBO, placebo.

Methods: This *post hoc* analysis of pooled data from DISSOLVE I (NCT04513366) and DISSOLVE II (NCT04596540) focuses on gout flare outcomes in pts who received 6 doses of NASP (high-dose [HD]: sequential infusions, 0.15 mg/kg NAS and 0.2 mg/kg pegadricase; low-dose [LD]: sequential infusions, 0.10 mg/kg NAS and 0.2 mg/kg pegadricase) or PBO every 4 weeks. Flares were assessed using a validated definition in pts with gout (Gaffo *et al. Arthritis Rheumatol* 2018).

Results: Overall, 42, 35 and 67 pts received 6 doses in the HD, LD, and PBO groups, respectively. At treatment initiation (weeks 1–4), the proportion of pts who experienced a gout flare was similar in the three treatment arms: 23.8%, 28.6% and 20.9% in pts treated with HD NASP, LD NASP and PBO, respectively. Over the study period (up to week 24), the proportion of pts experiencing flares decreased for NASP and remained consistent for PBO: 4.8%, 5.7% and 22.4% of pts in the HD, LD, and PBO arms, respectively, experienced a flare during weeks 21-24. During weeks 13–24, the average number of gout flares per patient was 2.3 and 5.7 times fewer on HD and LD, respectively, vs PBO (HD: 12 flares in 42 pts, rate of 0.29 gout flares per patient; LD: 4 in 35 pts, rate of 0.11; PBO: 44 in 67 pts, rate of 0.66). Cumulative gout flare rates over time were similar between NASP- and PBO-treated pts through Day 100. Between days 100–200, cumulative gout flare rates plateaued in NASP-treated pts but continued to increase in PBO-treated pts (**Figure 1**). Across all treatment arms, most flares ranged from mild to moderate intensity.

Conclusion: The proportion of pts with flares and number of flares decreased with NASP compared to PBO over the course of the study, with 95.2% and 94.3% of HD and LD-treated pts being flare-free during weeks 21–24. These results highlight the potential of NASP as an effective therapy for reducing disease burden and improving a key clinical outcome in pts with UG.

Disclosure: A. Gaffo: Atom, 2, Avalo Therapeutics, 2, PK Med, 2, Scilex, 2, Sobi, 2; **H. Baraf**: Arthrosi, 2, Olatec, 2, Otsuka, 3, Pacira, 2, Selecta Biosciences, 2, Sobi, 2; **A. Patel**: None; **T. Neogi**: None; **R. Azeem**: Selecta Biosciences, 11, Sobi, 3, 12, Shareholder; **W. DeHaan**: Selecta Biosciences Inc., 11, Sobi, 3; **B. Peace**: Sobi, 7, Veramed, 3; **H. Santin-Janin**: Sobi, 3; **B. Desai**: Sobi, 3, 11; **N. Schlesinger**: Amgen, 1, Arthrosi, 1, Olatec, 1, Protalix, 1, Scilex, 1, Shanton, 1, Sobi, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2589

Multi-omics Integration Reveals Gut Microbiota–Metabolite Dysregulation in Gout with Metabolic Syndrome

Yuanpiao Ni[1], Fanxin Zeng[2], Yufeng Qing[3] and Quanbo Zhang[3], [1]Affiliated Hospital Of North Sichuan Medical College, Nanchong, Sichuan, China (People's Republic), [2]Dazhou Central Hospital, Dazhou, Sichuan, China (People's Republic), [3]The Affiliated Hospital of North Sichuan Medical College, Nanchong, Sichuan, China (People's Republic)

SESSION INFORMATION

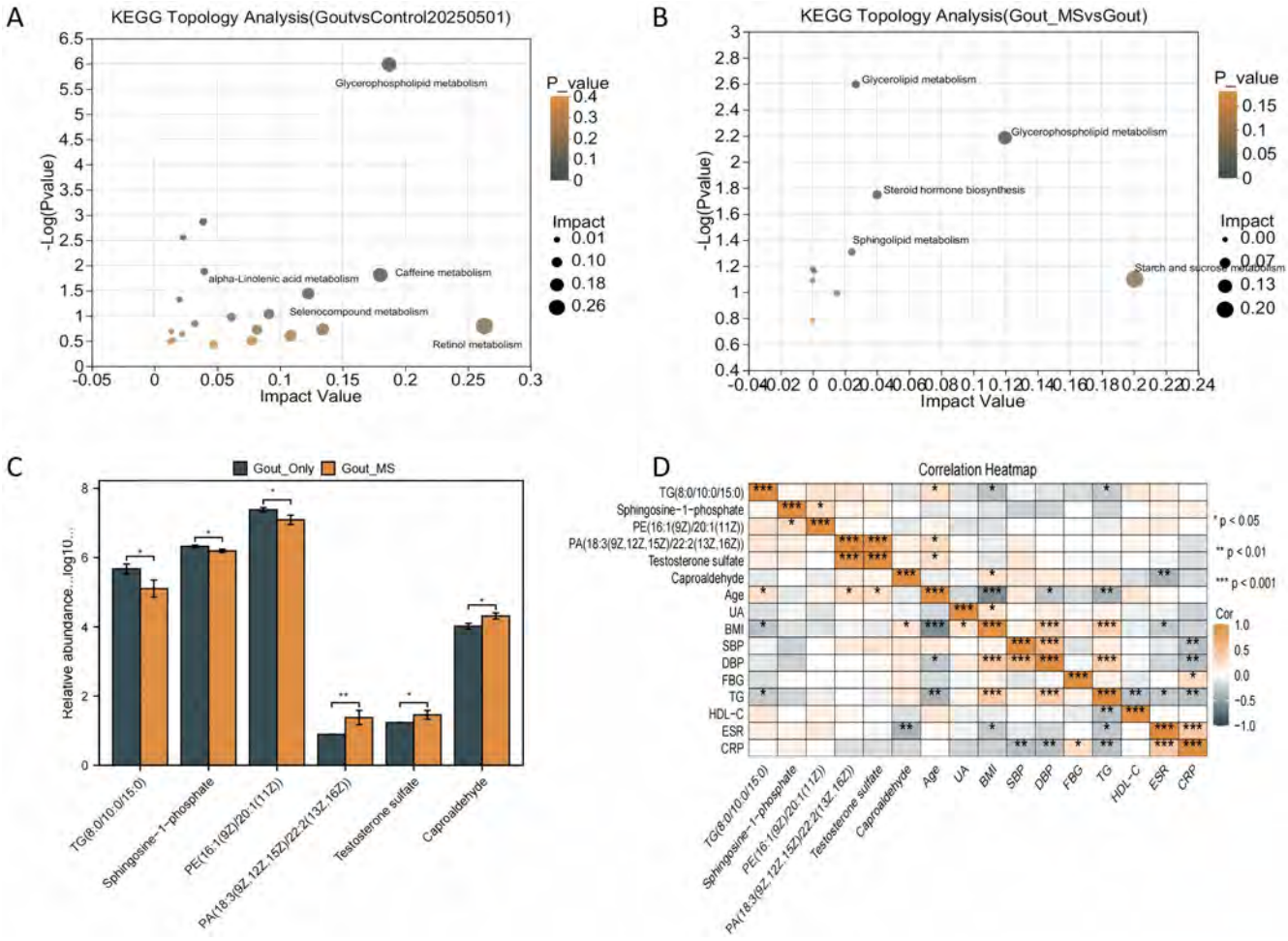
Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (2585–2590)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Gout is a metabolic disorder driven by abnormalities in urate metabolism and chronic inflammation. Recent studies suggest that gout is not limited to joint involvement but is also closely associated with various systemic metabolic disturbances, particularly metabolic syndrome (MS), which comprises central obesity, insulin resistance, hypertension, and dyslipidemia. MS significantly increases the risk of cardiovascular disease, type 2 diabetes, and mortality. The comorbidity between gout and MS suggests that the two conditions may share common pathophysiological mechanisms. As a critical interface between environment, immunity, and metabolism, the gut microbiome may play a key role in the



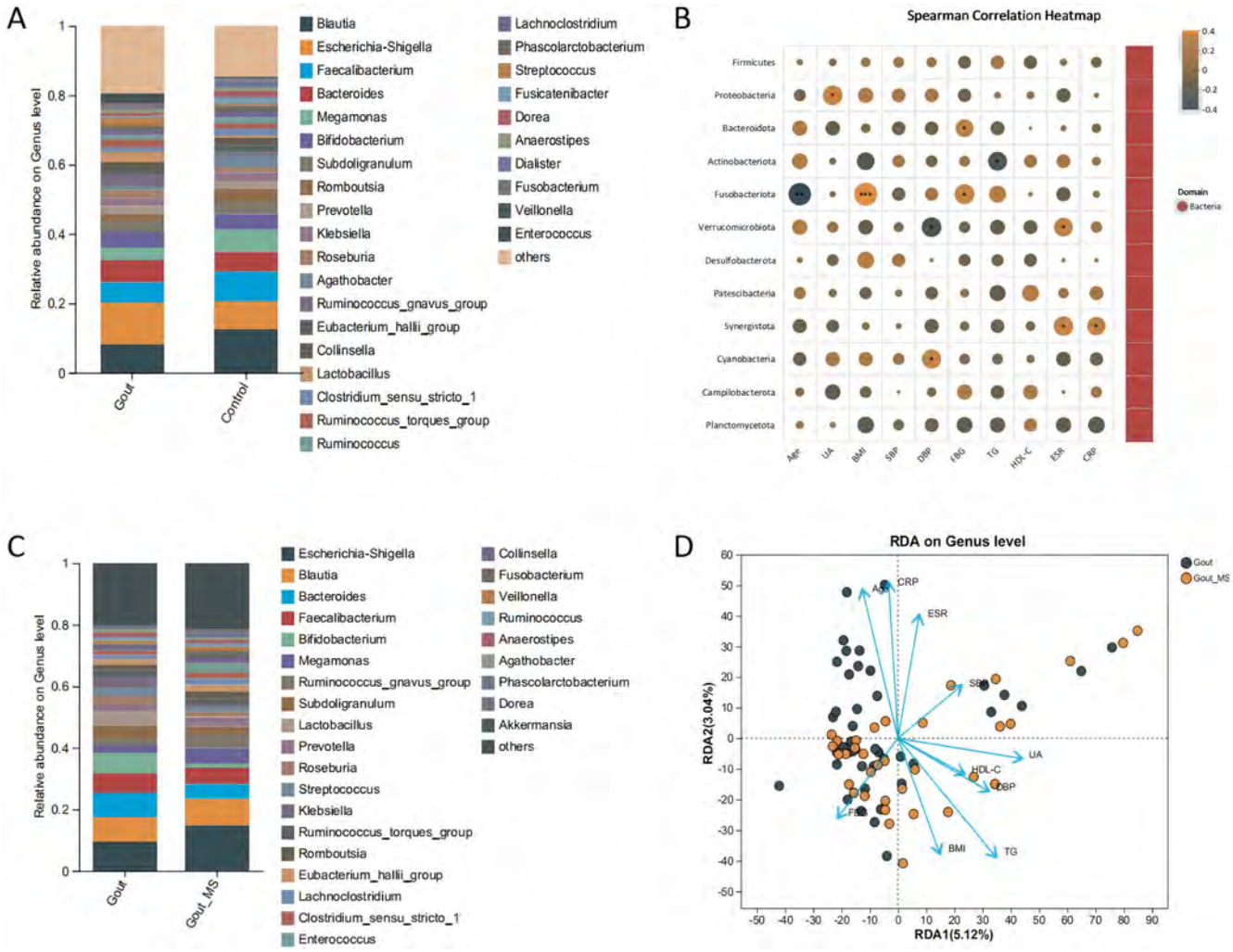
Key Pathways and Metabolites Revealed by Metabolomics and Their Correlation with Clinical Indicators

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

interaction between gout and MS. However, there is currently a lack of systematic multi-omics research elucidating the characteristics of microbiota–metabolite interactions, which hinders the development of personalized prevention and treatment strategies.

Methods: This study included 77 patients with gout, stratified into two subgroups based on the presence of MS: gout + MS group (n = 34) and gout-only group (n = 43). Additionally, healthy controls (n = 73) were recruited for microbiome (n = 73) and metabolomics (n = 50) comparisons. We applied 16S rRNA sequencing, metagenomics, and untargeted metabolomics to characterize gut microbial composition and metabolic profiles. Multi-omics integration was used to construct a microbiota–metabolite interaction network.

Results: Metabolomic analysis revealed significant disturbances in short-chain fatty acid, purine, and bile acid metabolism pathways in gout patients, along with marked alterations in glycerophospholipid levels. The presence of MS further exacerbated abnormalities in glycerolipid, sphingolipid, steroid hormone biosynthesis, and carbohydrate metabolism, leading to the identification of six key differential metabolites. Microbial analysis showed a depletion of beneficial taxa such as Actinobacteria and Firmicutes, along with an enrichment of potentially pathogenic Bacteroidetes, particularly in the gout + MS group. These microbial changes were closely associated with metabolic indices. Multi-omics integration identified microbiota–metabolite modules specific to the gout + MS group. A random forest model based on differential taxa and metabolites demonstrated strong discriminative performance (AUC = 0.81).



Analysis of Gut Microbiota Structure in Gout and Its Correlation with Clinical Indicators

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This study provides a comprehensive characterization of gut microbiota and metabolic alterations in gout patients with and without MS, offering new insights into the microbiota–metabolite interaction networks underlying these conditions. These findings enhance our understanding of disease heterogeneity and may inform future biomarker-based stratified management strategies.

Disclosure: Y. Ni: None; **F. Zeng**: None; **Y. Qing**: None; **Q. Zhang**: None.

Abstract Number: 2590

Translating findings on urate-metabolizing bacterial genes and urate levels at the human population level: a gut microbiome analysis of three independent cohorts of men and women

Sharan Rai[1], Natalie McCormick[2], Xochitl Morgan[3], Matthew Nayor[4], Robert Terkeltaub[5], Dylan Dodd[6], Lama Nazzal[7], Huilin Li[7], Gary Curhan[8], Curtis Huttenhower[3] and Hyon K. Choi[9], [1]Massachusetts General Hospital/Harvard Medical School, Boston, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Harvard T.H. Chan School of Public Health, Boston, [4]Boston University, Boston, [5]Retired, San Diego, CA, [6]Stanford University, Palo Alto, CA, [7]NYU Langone, New York, NY, [8]Brigham and Women's Hospital, Boston, [9]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (2585–2590)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Approximately 21% of US adults have hyperuricemia, the causal precursor for gout. Human cells do not degrade urate (due to uricase gene inactivation). However, a cluster of 7 bacterial genes in ~15-20% of commensal human gut purine degrading bacteria (PDB) encodes high capacity anaerobic uricolysis [1], distinct from strictly aerobic microbial uricase activity. Moreover, the majority of gut bacteria reside in the deeply anaerobic colonic lumen. By converting urate to xanthine, lactate, and short-chain fatty acids (SCFAs), PDB compensate for murine uricase knockout, thereby maintaining lower serum and cecal urate levels. Here, we seminally tested the association between gut PDB uricolytic genes and urate levels in humans.

Methods: We analyzed available blood and stool metagenomic (Illumina) data collected contemporaneously from men and women enrolled in three independent, prospective, nationwide cohort studies: Framingham Heart Study (FHS; N=1129 men and women), Men's Lifestyle Validation Study (MLVS; N=296 men), and Mind Body Study (MBS; N=207 women). The sequences of previously characterized urate-metabolizing genes (i.e., *ygeX*, *ygeY*, *ygeW*, *ygfK*, and *ssnA*) [1] were mapped to Uniref90 sequences and their corresponding species-level genomic bins, using HUMAnN and diamond [2-4]. We calculated the Spearman correlation between urate levels and each putative urate-metabolizing gene / Uniref90. These were visualized as undirected networks using the igraph and ggraph R packages.

Results: We identified 15 human gut-associated species-level genomic bins containing at least five urate-metabolizing genes in their pangenomes, corresponding to commensal gut species **(Figure 1)**. These included *Flavonifractor plautii*, *Enterocloster bolteae*, and *Ruminococcus torques*. **Figure 1** shows undirected associations between species-level genomic bins and their corresponding urate-metabolizing genes. In all, 12 of 48 identified urate-metabolizing genes significantly correlated with urate (spearman rho $q < 0.1$) in at least two studies, and 31 significantly correlated in at least one study **(Figure 2)**. Additionally, 6 urate-metabolizing genes significantly correlated with urate only among participants in the MBS (i.e., women-only cohort) but not FHS or MLVS **(Figure 2)**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

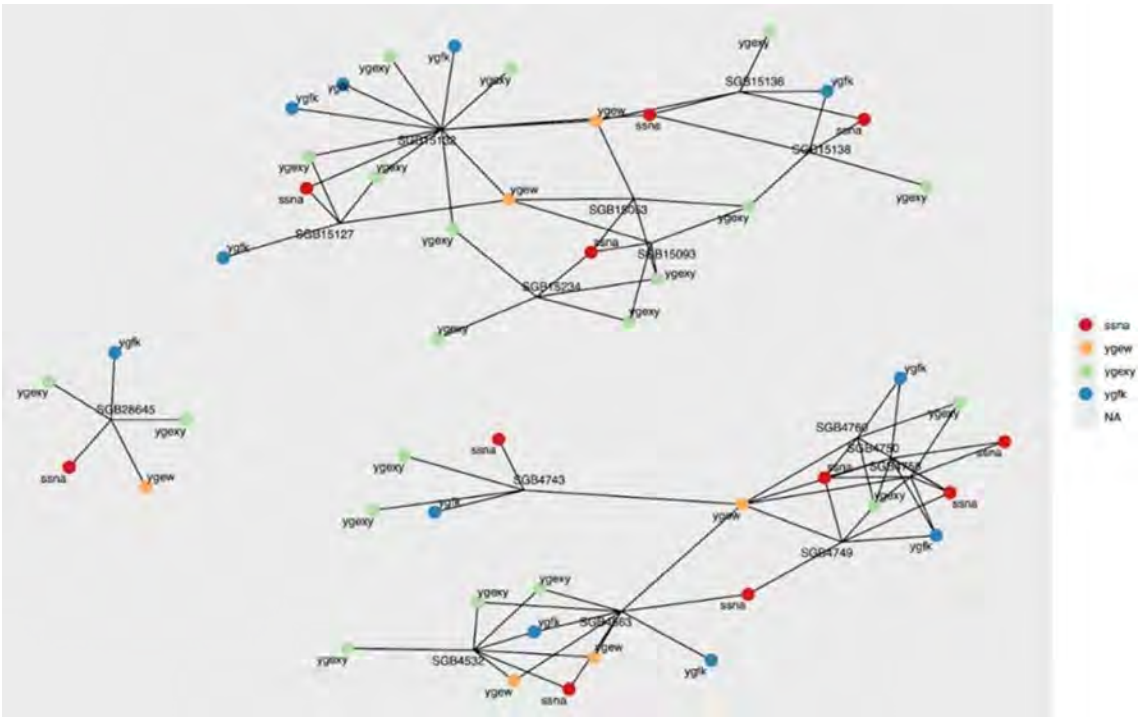


Figure 1. Undirected network diagram illustrating the associations between species-level genomic bins and corresponding urate-metabolizing genes.

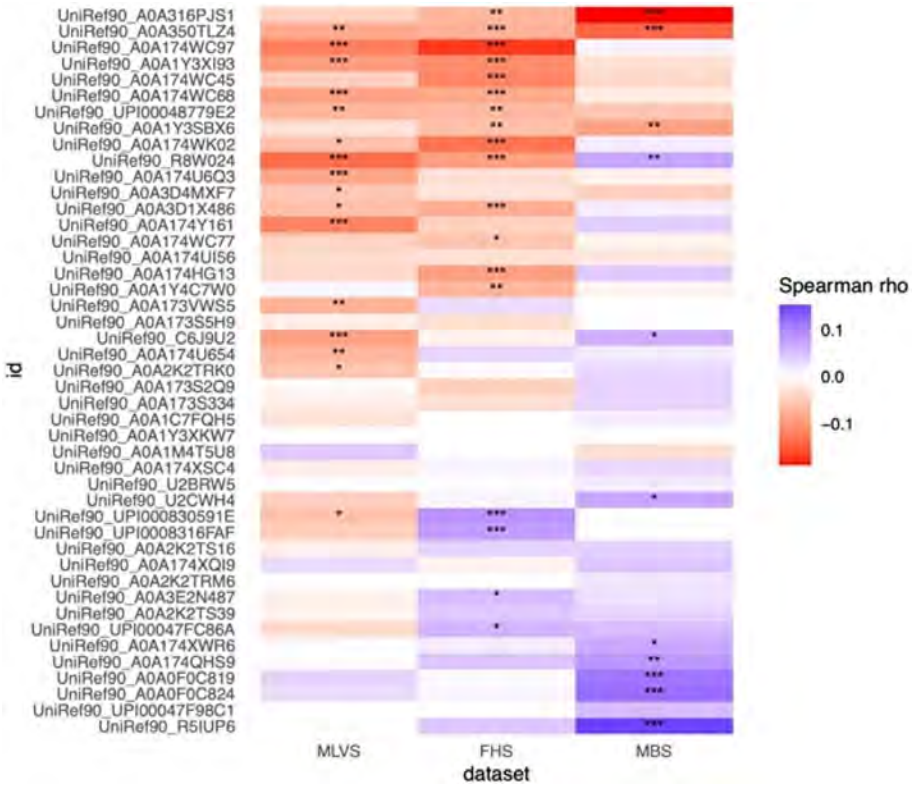


Figure 2. Correlations between network Uniref90 genetic sequences and urate levels in each of the three cohorts. Symbols: *qval < 0.1, **qval < 0.05, ***qval < 0.01.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: The abundance of putative urate-metabolizing genes is significantly correlated with urate in 3 human cohorts, and some may be sex-influenced. The commensal gut species identified may be particularly relevant to hyperuricemia and gout, including capacity for anti-inflammatory SCFA production (e.g., butyrate) and documented associations with other inflammatory conditions. These results, superimposed on known gut dysbiosis in gout [5], support actual modulation of urate by the gut microbiome in humans, and suggest a novel potential therapeutic target for prevention and treatment of gout.

References:

1. PMID: 37541197
2. PMID: 33944776
3. PMID: 36823356
4. PMID: 33828273
5. PMID: 39829115

Disclosure: S. Rai: None; **N. McCormick**: None; **X. Morgan**: None; **M. Nayor**: None; **R. Terkeltaub**: Atom Bioscience, 2, BPG Bio, 2, Crystalys, 2, Novartis, 2, Shanton, 2; **D. Dodd**: None; **L. Nazzal**: None; **H. Li**: None; **G. Curhan**: None; **C. Huttenhower**: None; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2.

Abstract Number: 2591

Association Between Changes in Bone Quality Parameters and Inflammatory Ratios in Postmenopausal Women Treated with Romosozumab: A Retrospective Observational Study

Montserrat Robustillo-Villarino[1], Andres Zuniga-Vera[1] and Marile Sanabria-Hernández[2], [1]Department of Rheumatology, Hospital Universitario de la Plana, Vila-real, Castellón, Spain, Vila-real, Castellón, Spain, [2]Hospital Universitario de la Plana, Vila-Real, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (2591–2596)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Osteoporosis (OP) is characterized by low bone mass and microarchitectural deterioration, increasing fracture risk. Bone Mineral Density (BMD), T-score, and Trabecular Bone Score (TBS) are key diagnostic and monitoring tools. Systemic inflammatory markers linked to cardiovascular risk such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) have been proposed as potential indicators of and other cardiovascular events. Romosozumab (ROMO), a sclerostin inhibitor with dual anabolic and antiresorptive action, is approved for high-risk postmenopausal OP patients. This study evaluated the association between changes in TBS, T-score, BMD, and inflammatory ratios in women treated with ROMO.

Methods: We conducted a retrospective observational study of postmenopausal women with OP treated with ROMO. Pre- and post-treatment measurements of TBS, T-score, BMD, NLR, PLR, and MLR were analyzed. Delta changes (post-treatment minus baseline) were calculated for each parameter. Correlation analyses and linear regression models assessed the predictive value of inflammatory ratios on bone parameter changes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

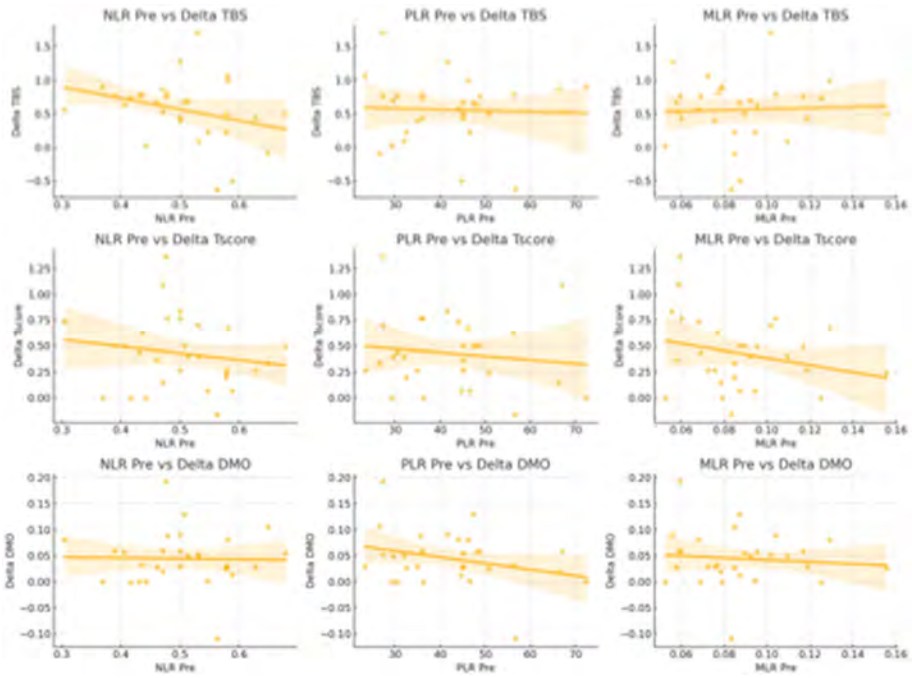


Figure 1. Relationships Between Baseline Inflammatory Ratios (NLR, PLR, MLR) and Changes in Trabecular Bone Score (TBS), T-score, and Bone Mineral Density (BMD) in Postmenopausal Women Treated With Romosozumab. Regression analyses show no significant predictive capacity (R^2 < 0.1) across all models.

Results: Thirty-seven postmenopausal women (mean age 46.0 years) completed ROMO therapy and follow-up. Fracture history included single (62%), multiple (32%), or no fractures (5%). Comorbidities included inflammatory diseases (8%), COPD (14%), dyslipidemia (38%), hypertension (43%), and smoking (14%).

Significant improvements were observed in TBS (mean +0.85 units, p< 0.001), T-score (mean +0.61 units, p< 0.001), and BMD (mean +0.06 g/cm^2, p< 0.001). A moderate positive correlation was found between NLR change and TBS improvement (r=0.45, p< 0.05). No significant associations were found for PLR or MLR. Regression models showed low predictive capacity of NLR, PLR, or MLR on changes in TBS, T-score, or BMD (R^2< 0.1 in all models). Baseline ratios also showed negligible predictive value (R^2 TBS=-0.75, T-score≈0.00, BMD≈0.005).

Conclusion: Romosozumab significantly improves bone quality and density in postmenopausal women with OP. While NLR changes moderately correlate with TBS improvement, inflammatory ratios NLR, PLR, and MLR lack predictive utility for treatment response. Additionally, ROMO treatment did not significantly alter these inflammatory markers of cardiovascular risk in various clinical contexts, supporting a neutral effect on subclinical systemic inflammation linked to cardiovascular risk. These findings may be relevant in the context of cardiovascular safety discussions surrounding ROMO.

References:

McClung MR, Betah D, Leder BZ, et al. Romosozumab improves microarchitecture as assessed by tissue thickness-adjusted trabecular bone score in postmenopausal women with osteoporosis. J Bone Miner Res. 2025 Feb;40(2):193–200.

Liu YC, Yang TI, Huang SW, et al. Associations of the Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio with Osteoporosis: A Meta-Analysis. Diagnostics (Basel). 2022 Nov 28;12(12):2968.

Disclosure: M. Robustillo-Villarino: None; **A. Zuniga-Vera**: None; **M. Sanabria-Hernández**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2592

Romosozumab and Denosumab Combination Therapy in Postmenopausal Osteoporosis

Giovanni Adami[1], Francesco Pollastri[2], Angelo Fassio[2], Camilla Benini[2], Davide Gatti[2], Ombretta Viapiana[2] and Maurizio Rossini[2], [1]University of Verona, Italy, Verona, Italy, [2]University of Verona, Verona, Italy

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (2591–2596)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Transition from long-term denosumab to PTH-analogs or romosozumab might expose patients to the risk of the so-called rebound phenomenon. Adding romosozumab to denosumab might represent an option in patients experiencing a fracture while on denosumab. The aim of this study was to investigate the effects of the combination of romosozumab to denosumab in post-menopausal osteoporosis.

Methods: We did a 36-month prospective, quasi-experimental, study. Post-menopausal women were divided into two groups: patients on denosumab who added romosozumab to denosumab (Dmab from M-24 to M0 à Dmab+Romo from M0 to M+12), and matched controls on denosumab continuing denosumab (Dmab from M-24 to M0 à Dmab from M0 to M+12). Patients for this group were selected from the overall pool of post-menopausal women treated with denosumab referring to our outpatient clinic who had available baseline (M-24) and follow-up DXA scans and serum samples collected (n=388). Patients were then matched through propensity score matching to balance baseline characteristics between the treated and control groups. Bone mineral density (BMD) and bone turnover markers (CTX, P1NP) were assessed at follow-up time points.

Results: A total of 50 women were included in the study. Twenty-five patients in the Dmab à Dmab+Romo group and 25 matched controls in the Dmab à Dmab group. Overall, lumbar spine BMD increased more in the Dmab à Dmab+Romo group (11.6% SE 3.0, p 0.010) compared to the Dmab à Dmab group (8.3% SE 3.3, p NS). Adding romosozumab to denosumab increased P1NP significantly between M0 and M+3 (+22.5 ng/mL SE 8.7, p 0.028). **Figure 1** shows the bone markers trends in the two groups, **Figure 2** shows the BMD trends in the two groups.

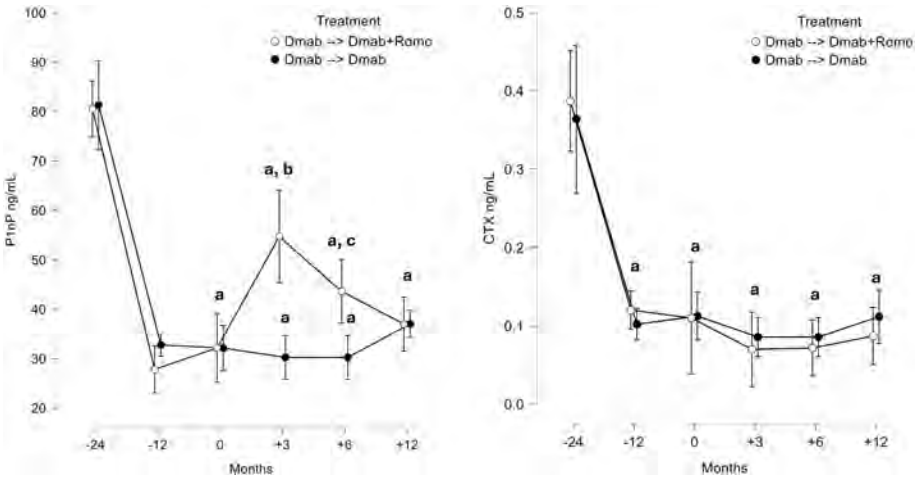


Figure 1. Bone turnover markers (BTMs) changes over the study period

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

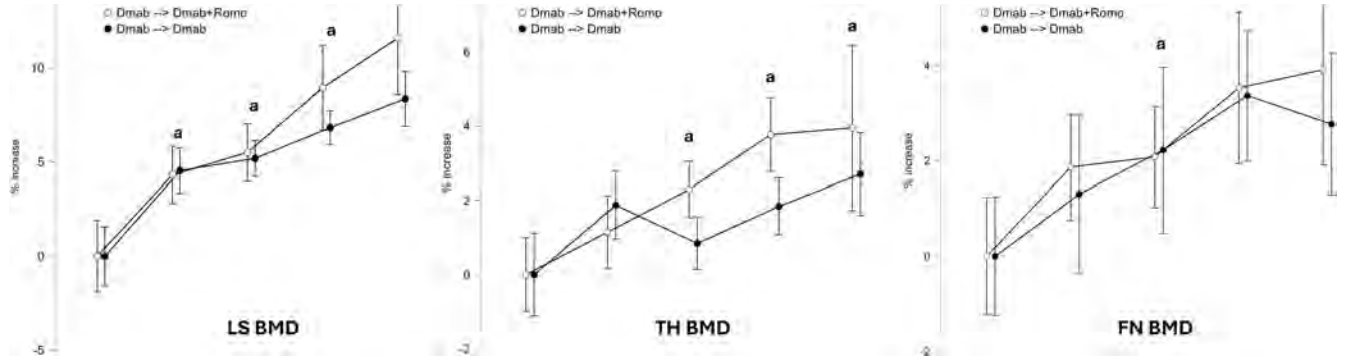


Figure 2. Bone mineral density (BMD) changes over the study period

Conclusion: Ongoing treatment with denosumab did not blunt the anabolic response of romosozumab, indicating sustained modeling-based bone formation activity. Adding romosozumab in patients failing denosumab might be a valuable option.

Disclosure: G. Adami: AbbVie/Abbott, 2, 6, Amgen, 2, 6, Eli Lilly, 2, 6, UCB, 2, 6; **F. Pollastri**: None; **A. Fassio**: None; **C. Benini**: None; **D. Gatti**: None; **O. Viapiana**: None; **M. Rossini**: None.

Abstract Number: 2593

Single Switch from Reference Denosumab to TVB-009 in Women with Postmenopausal Osteoporosis: Analysis of the Phase 3, Randomized, Double-Blind, Multinational, Multicenter Study

Karel Pavelka[1], Frank Schneider[2], Deepak S[3], Bracha Timan[4], Hadas Barkay[4] and Anton Buchner[2], [1]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, [2]Teva GmbH, Ulm, Germany, [3]Teva Pharma India Private Limited, Bangalore, India, [4]Teva Pharmaceutical Industries Ltd., Netanya, Israel

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (2591–2596)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: TVB-009 is being developed as a proposed biosimilar candidate to the reference denosumab. Biosimilarity of TVB-009 to US-licensed denosumab (US-denosumab) and EU-approved denosumab was demonstrated in healthy participants in a Phase 1 pharmacokinetic/pharmacodynamic study. No clinically relevant differences in efficacy or safety between TVB-009 and US-denosumab were demonstrated in women with postmenopausal osteoporosis (PMO) in the 52-week main treatment (tx) period of a 78-week Phase 3 study (NCT04729621). The objective of this analysis was to evaluate the impact of a single switch from US-denosumab to TVB-009 on safety, immunogenicity, and efficacy in women with PMO during the subsequent 26-week transition period.

Methods: Eligible participants included postmenopausal women aged 60–90 years with a diagnosis of osteoporosis and a lumbar spine bone mineral density (LS-BMD) measurement T-score of ≥–4.0 to < –2.5 at screening. At baseline, participants were randomized 1:1 to receive 60 mg of TVB-009 or US-denosumab by subcutaneous injection on Day 1 and at Week 26 in the main tx period. In the transition period, participants in the US-denosumab arm were re-randomized 1:1 to

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. TEAEs in the Transition Period of the Phase 3 Study in Women with PMO

TEAE, n (%)	TVB-009/ TVB-009 (n=148)	US-denosumab/ US-denosumab (n=72)	US-denosumab/ TVB-009 (n=71)
Any TEAE	50 (33.8)	20 (27.8)	26 (36.6)
TEAEs related to study drug	2 (1.4)[a]	0	0
Serious TEAEs	5 (3.4)[b]	0	1 (1.4)[c]
TEAEs leading to discontinuation	0	0	0
TEAEs leading to death	0	0	0
Most frequent adverse events (≥ 2%)			
Headache	4 (2.7)	1 (1.4)	3 (4.2)
Hypercalcemia	4 (2.7)	2 (2.8)	2 (2.8)
Dyslipidemia	0	0	2 (2.8)
COVID-19	3 (2.0)	0	1 (1.4)
Upper respiratory tract infection	3 (2.0)	2 (2.8)	1 (1.4)
Nasopharyngitis	4 (2.7)	5 (6.9)	0
Arthralgia	4 (2.7)	4 (5.6)	0
Pain in extremity	3 (2.0)	3 (4.2)	0
Back pain	8 (5.4)	2 (2.8)	0
Spinal pain	3 (2.0)	2 (2.8)	0

PMO, postmenopausal osteoporosis; TEAE, tx-emergent adverse event; tx, treatment.
Safety was analyzed in all participants who received the third dose of the study drug. [a]A total of 3 TEAEs related to the study drug were reported for 2 participants in the TVB-009/TVB-009 group: periorbital hemorrhage, low-density lipoprotein increased, and back pain; all were mild in severity. [b]Serious TEAEs included bone cancer, chronic obstructive pulmonary disease, urinary incontinence, COVID-19 pneumonia, helicobacter infection, and malaise in 1 participant each; none of these serious TEAEs had a reasonable possible relationship to the study drug. [c]Serious TEAEs included cholelithiasis, which was mild in intensity with no reasonable possible relationship to the study drug.

receive a single dose of TVB-009 or a third dose of US-denosumab at Week 52, while participants in the TVB-009 arm received a third dose of TVB-009.

Results: Of 332 participants initially randomized, 291 completed the main tx period and were randomized in the transition period (TVB-009/TVB-009, n=148; US-denosumab/US-denosumab, n=72; US-denosumab/TVB-009, n=71). In the transition period, comparable proportions of participants experienced tx-emergent adverse events (TEAEs) across the 3 tx groups (**Table 1**). One participant in the US-denosumab/TVB-009 group experienced a serious TEAE of cholelithiasis, which was mild and not related to the study drug. Five (3.4%) participants in the TVB-009/TVB-009 tx group experienced serious TEAEs that were unrelated to tx; none were reported in the US-denosumab/US-denosumab group. TEAEs reported in ≥5% of participants in either tx group were back pain (5.4% vs 2.8%), nasopharyngitis (2.7% vs 6.9%), and arthralgia (2.7% vs 5.6%) in the TVB-009/TVB-009 vs US-denosumab/US-denosumab groups, respectively. Notably, no TEAEs in ≥5% of participants were reported in the US-denosumab/TVB-009 group (**Table 1**). Similar proportions of participants in US-denosumab/US-denosumab and US-denosumab/TVB-009 were anti-drug antibody (ADA)-positive (7.1% vs 5.7%) and ADA-positive, not tx related (5.7% vs 1.4%; **Table 2**). None of the participants developed hypersensitivity reactions. The mean (standard deviation) percent change in LS-BMD from Week 52 to Week 78 was comparable between the US-

Table 2. Immunogenicity in the Transition Period of the Phase 3 Study in Women with PMO

	TVB-009/ TVB-009 (n=148)				US-denosumab/ US-denosumab (n=72)				US-denosumab/ TVB009 (n=71)			
	W54	W65	W78	Total	W54	W65	W78	Total	W54	W65	W78	Total
Number of participants with assessment at visit	146	143	140	**147**	67	69	67	**70**	70	69	69	**70**
ADA-positive, n (%)	6 (4.1)	3 (2.1)	6 (4.3)	**7 (4.8)**	5 (7.5)	3 (4.3)	3 (4.5)	**5 (7.1)**	2 (2.9)	3 (4.3)	3 (4.3)	**4 (5.7)**
ADA-positive, NTR,[a] n (%)	6 (4.1)	4 (2.8)	3 (2.1)	**7 (4.8)**	4 (6.0)	4 (5.8)	4 (6.0)	**4 (5.7)**	1 (1.4)	1 (1.4)	1 (1.4)	**1 (1.4)**
ADA titer, median (min, max)	2.11 (1.7, 3.6)	2.96 (2.4, 3.2)	2.25 (1.3, 2.8)	—	2.21 (1.6, 2.4)	2.36 (2.0, 2.5)	2.43 (2.3, 2.5)	—	1.72 (1.6, 1.8)	1.72 (1.5, 2.1)	1.92 (1.4, 2.4)	—
Neutralizing ADA, n	1	1	1	**1**[b]	0	0	0	**0**	0	0	0	**0**

ADA, anti-drug antibody; max, maximum; min, minimum; NTR, not tx related; PMO, postmenopausal osteoporosis; tx, treatment; W, Week.
Immunogenicity was analyzed in all participants who received the third dose of the study drug.
[a]Participants who initially were screened to be ADA-positive from baseline with no change or increase in optic density signal and in percent inhibition signal in the confirmatory titer at further tested time points were marked as not tx-emergent ADA. [b]The participant from the TVB-009 tx group who tested positive for neutralizing ADA in the main tx period remained on TVB-009 during the transition period and tested positive for neutralizing ADA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

denosumab/US-denosumab and US-denosumab/TVB-009 groups (1.15 [3.44] and 1.24 [3.07]); similar trends were observed for femoral neck and total hip BMD.

Conclusion: Women with PMO who single-switched from reference US-denosumab to TVB-009 demonstrated a comparable safety, immunogenicity, and efficacy profile to those who remained on US-denosumab. Our results demonstrate that a single switch from reference denosumab to TVB-009 does not affect safety and efficacy in this population.

Disclosure: K. Pavelka: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **F. Schneider**: Teva, 3, 11; **D. S**: Teva, 3, 11; **B. Timan**: Teva, 3, 11; **H. Barkay**: Teva, 3, 11; **A. Buchner**: Teva, 3, 11.

Abstract Number: 2594

Comparing Immunogenicity Between TVB-009 and Reference Denosumab in Healthy Adults and Participants with Postmenopausal Osteoporosis

Karel Pavelka[1], **Frank Schneider**[2], Deepak S[3], Bracha Timan[4], Hadas Barkay[4] and Anton Buchner[2], [1]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, [2]Teva GmbH, Ulm, Germany, [3]Teva Pharma India Private Limited, Bangalore, India, [4]Teva Pharmaceutical Industries Ltd., Netanya, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (2591–2596)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: TVB-009 is being developed as a proposed biosimilar candidate to the reference denosumab. Denosumab is a human IgG2 monoclonal antibody that binds to the human receptor activator of nuclear factor kappa-B ligand to inhibit osteoclast formation and activation, thus reducing the risk of fracture in conditions such as osteoporosis. Biosimilarity of TVB-009 to US-licensed denosumab (US-denosumab) and EU-approved denosumab (EU-denosumab) was demonstrated in a 36-week Phase (Ph) 1 pharmacokinetic/pharmacodynamic (PK/PD) study, and no clinically relevant differences in efficacy or safety between TVB-009 and US-denosumab were demonstrated in a Ph 3 study (NCT04729621). The objective of our analysis was to demonstrate that there are no clinically meaningful differences in immunogenicity between TVB-009 and US-/EU-denosumab in the Ph 1 and Ph 3 (52-week main treatment period) studies.

Methods: In the Ph 1 study, healthy participants aged 28–55 years were randomized 1:1:1 to receive a single 60-mg subcutaneous injection of TVB-009, US-denosumab, or EU-denosumab on Day 1. In the Ph 3 main treatment period, postmenopausal women aged 60–90 years with a diagnosis of osteoporosis were randomized 1:1 to receive TVB-009 or US-denosumab on Day 1 and Week 26. Safety and immunogenicity were evaluated similarly in both studies. Blood samples for anti-drug antibody (ADA) testing were collected predose on Day 1 and throughout each study. All samples were screened for ADA using bridging ELISA; ADA-positive (ADA+) samples were then analyzed in a confirmatory assay, and confirmed samples were tested for antibody titer determination and neutralization potential.

Results: In the Ph 1 study, 345 participants were randomized and included in the safety population (n=115 per treatment group). In the Ph 3 study, 331 of 332 participants randomized in the main treatment period were included in the safety population (TVB-009, n=166; US-denosumab, n=165). Baseline characteristics were similar between treatment groups in both studies. In Ph 1, no ADAs against TVB-009 were observed, and therefore there was no impact on PK, PD, or safety related

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

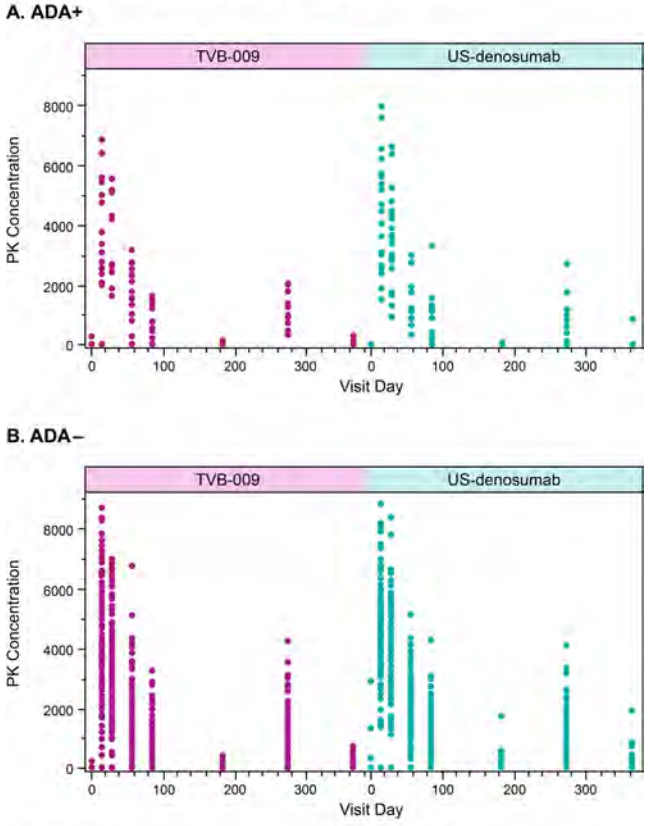
Table 1. Immunogenicity in the Main Treatment Period of the Ph 3 Study in Women with Postmenopausal Osteoporosis

	TVB-009 (n=166)						US-denosumab (n=165)					
	Day 1	Day 15	W4	W39	W52	Total	Day 1	Day 15	W4	W39	W52	Total
Number of participants with assessment at visit	166	163	163	155	152	**166**	165	164	161	153	147	**165**
ADA-positive, n (%)	3 (1.8)	9 (5.5)	5 (3.1)	5 (3.2)	5 (3.3)	**11 (6.6)**	1 (0.6)	17 (10.4)	12 (7.5)	10 (6.5)	9 (6.1)	**25 (15.2)**
ADA-positive, NTR,[a] n (%)	8 (4.8)	7 (4.3)	8 (4.9)	7 (4.5)	7 (4.6)	**8 (4.8)**	11 (6.7)	7 (4.3)	7 (4.3)	7 (4.6)	6 (4.1)	**11 (6.7)**
ADA titer, median (min, max)	1.69 (1.6, 2.0)	2.01 (1.6, 2.9)	2.01 (1.9, 2.5)	1.98 (1.7, 2.6)	2.16 (1.7, 2.6)	—	2.60 (2.6, 2.6)	2.40 (1.3, 3.4)	1.69 (1.3, 3.4)	1.94 (1.3, 2.4)	1.75 (1.3, 2.2)	—
Neutralizing ADA, n	0	0	0	1	1	**1**	0	1	0	1	0	**2**

ADA, anti-drug antibody; max, maximum; min, minimum; NTR, not treatment related; Ph, Phase; W, Week.
[a]Participants who initially were screened to be ADA-positive from baseline with no change or increase in optic density signal and in percent inhibition signal in the confirmatory titer at further tested time points were marked as not treatment-emergent ADA.

to ADA presence. In the Ph 3 main treatment period, a comparable proportion of participants on TVB-009 and US-denosumab were ADA+ (**Table 1**). One participant on TVB-009 and 2 participants on US-denosumab tested positive for neutralizing ADAs. However, ADA+ participants had a similar PD response as ADA-negative (ADA–) participants and experienced an increase in lumbar spine bone mineral density from baseline. Serum concentrations after TVB-009 and US-denosumab treatment showed high intersubject variability regardless of ADA presence, and the range of concentrations overlapped between ADA+ and ADA– participants for both treatment groups (**Figure 1**).

Figure 1. PK Concentrations in the Main Treatment Period of the Ph 3 Study by ADA Status for TVB-009 and US-denosumab in Women with Postmenopausal Osteoporosis: (A) ADA+ and (B) ADA–



ADA, anti-drug antibody; ADA+, ADA-positive; ADA–, ADA-negative; Ph, Phase; PK, pharmacokinetic.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Immunogenicity profiles of TVB-009 and US-denosumab were similar in healthy participants and women with postmenopausal osteoporosis, with no detectable impact of ADA or neutralizing ADA on PK, PD, efficacy, and safety, further confirming that there are no clinically meaningful differences between TVB-009 and the reference denosumab.

Disclosure: K. Pavelka: AbbVie, 6, Eli Lilly, 6, Janssen, 6, Medac, 6, Novartis, 6, Sandoz, 6, UCB, 6; **F. Schneider**: Teva, 3, 11; **D. S**: Teva, 3, 11; **B. Timan**: Teva, 3, 11; **H. Barkay**: Teva, 3, 11; **A. Buchner**: Teva, 3, 11.

Abstract Number: 2595

Impact of Different Types of Physical Activity on Bone Health in Patients with Inflammatory Rheumatic Diseases: a Cross-Sectional Analysis from a Prospective Cohort Study

Edgar Wiebe[1], Claire-Felicia Liebich[2], Dörte Huscher[3], Lien Meerkatt[4], Andriko Palmowski[5], Sandra Hermann[1], Burkhard Muche[5], Zhivana Boyadzhieva[2], Gerhard Krönke[6], Bernd Wolfarth[2] and FRANK BUTTGEREIT[7], [1]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany, Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Berlin, Germany, [5]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [6]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Berlin, Germany, [7]Charité University Medicine Berlin, Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (2591–2596)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: Physical exercise helps maintain bone mineral density (BMD), prevent falls, and reduce fracture risk. Strength and weight-bearing exercises are particularly effective. However, individuals with inflammatory rheumatic diseases often face disease-related functional impairments that limit their ability to engage in such activities. The interactions between rheumatic diseases, exercise, and bone health remain underexplored.

This study aimed to assess the impact of different types of physical activity on BMD in patients with inflammatory rheumatic diseases.

Methods: We analyzed data from the Rh-GIOP cohort, a prospective observational study of patients with immune-mediated inflammatory diseases. Participants underwent dual-energy X-ray absorptiometry (DXA) and systematic bone health assessments. Self-reported physical activity was categorized as any exercise, weight-bearing, high-impact, and low-impact. Frequency-based classifications (strength, aerobic, balance training ≥65 years) followed WHO criteria.

Multivariable linear regression models assessed clinical, serological, and treatment-related predictors of lumbar spine and femoral T-score, trabecular bone score (TBS), and 3D-DXA-based femoral structure (3D-Shaper v2.12). Physical activity types were then added to these models. Missing data were handled via multiple imputation (10 replications).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We included 1,870 patients (mean age 63 ± 13; 75% female, 90% postmenopausal) with rheumatoid arthritis (n=631), connective tissue diseases (n=424), vasculitides (n=274), and spondyloarthropathies (n=240). Median disease duration was 9.5 years (IQR 3.6–17.4). Regular exercise was reported by 63%; 59% performed low-impact, 52% weight-bearing, 34% aerobic, 23% strength, and 18% high-impact activities.

Positive associations with lumbar spine T-score were found for weight-bearing (+0.16 [0.02;0.30], p=0.03), high-impact (+0.27 [0.09;0.45], p=0.003), strength (+0.19 [0.02;0.37], p=0.033), and balance training (+0.002 [0.00;0.04], p=0.013). Only high-impact activity was associated with femoral T-score (+0.16 [0.03;0.28], p=0.017). TBS at the spine was positively linked to weight-bearing exercise (+0.018 [0.003;0.033], p=0.022). High-impact activity was associated with femoral trabecular parameters (+4.62 [0.22;9.02], p=0.040), while endurance training benefited cortical structure (+0.01 [0.00;0.03], p=0.049). Trends toward benefit were observed for strength, weight-bearing, and low-impact activities. No exercise type was negatively associated with bone outcomes.

Conclusion: In patients with inflammatory rheumatic diseases, mechanical loading activities such as weight-bearing, strength, and high-impact exercises are most beneficial for improving BMD and microarchitecture. These findings support the development of tailored exercise programs based on individual capabilities to optimize bone health. Longitudinal studies with fracture outcomes will further clarify long-term benefits.

Disclosure: E. Wiebe: Sobi, 6; **C. Liebich**: None; **D. Huscher**: None; **L. Meerkatt**: None; **A. Palmowski**: Novartis, 1; **S. Hermann**: None; **B. Muche**: AbbVie/Abbott, 6, Amgen, 6, Celltrion, 6, Theramex, 6, UCB, 6; **Z. Boyadzhieva**: None; **G. Krönke**: None; **B. Wolfarth**: None; **F. BUTTGEREIT**: Abbvie, 2, 5, 6, Biogen, 5, 6, Eli Lilly, 5, 6, Galapagos, 5, 6, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, 12, grant support, consultancy fees, honoraria and travel expenses from Abbvie, Pfizer, Gruenenthal, and Horizon Therapeutics, all unrelated, Janssen, 6, Medac, 5, 6, Novartis, 1, 6, pf, 5, 6, Roche, 6, Sanofi, 5, 6.

Abstract Number: 2596

Predicting Osteoporosis Using Routine Clinical Data: A Machine Learning Approach

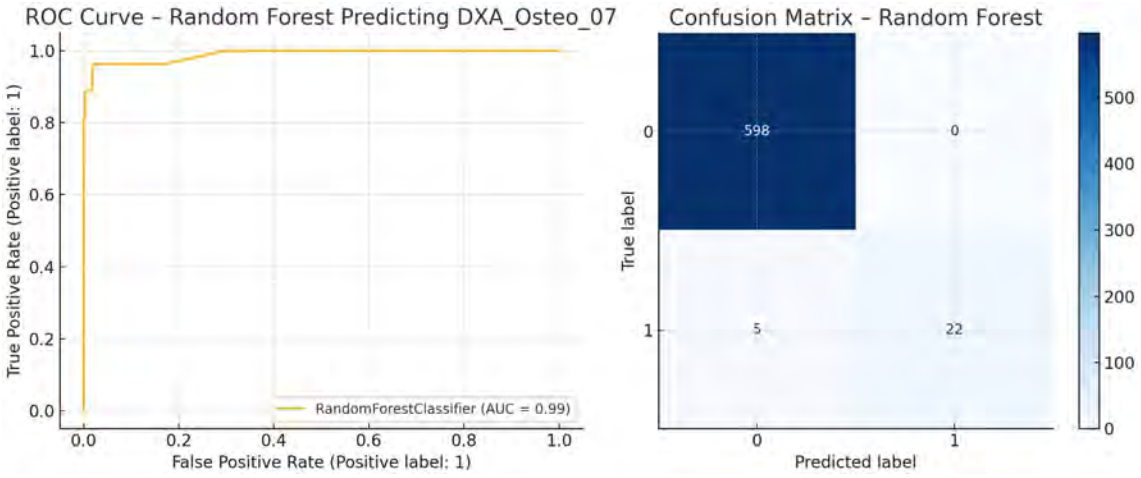
Shiza sarfraz and Hassam Ali, East Carolina University Brody School of Medicine, Greenville, NC

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (2591–2596)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Dual-energy X-ray absorptiometry (DXA) is the gold standard for diagnosing osteoporosis but is underutilized due to access, cost, and referral barriers. We aimed to develop and evaluate a machine learning model to predict DXA-defined osteoporosis using only non-imaging clinical and lifestyle variables available in routine care.

Methods: Data were drawn from the 2021–2022 National Health and Nutrition Examination Survey (NHANES(. Adults ≥20 years with complete DXA data (femoral and spine bone mineral density [BMD]) and clinical/laboratory variables were included. Osteoporosis was defined as minimum BMD < 0.7 g/cm^2 at either site. Predictors included demographics (age,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Model Performance in Predicting DXA-Defined Osteoporosis. ROC curve (left) shows excellent discrimination (AUC = 0.99), and the confusion matrix (right) confirms strong sensitivity and perfect specificity using non-DXA features.

sex, race/ethnicity), anthropometrics (BMI, waist circumference), lifestyle (smoking, alcohol, physical activity), diet (calcium, vitamin D intake), biomarkers (serum vitamin D, CRP, cholesterol), and weight change. DXA variables were excluded from predictors. A random forest classifier was trained on a 70% split and evaluated on a 30% held-out test set. Logistic regression using the same inputs served as a comparator.

Results: Among 2,083 eligible adults, 90 (4.3%) met the DXA-defined osteoporosis threshold (minimum BMD < 0.7 g/cm^2 at spine or femur). The random forest model, trained without DXA data, achieved an AUC of 0.99 on the test set (n=625), with sensitivity of 81.5%, specificity of 100%, and F1-score of 0.90. Model accuracy was 99.2%, and all predicted positives were true positives (PPV: 100%). In contrast, logistic regression using the same features yielded an AUC of 0.87, but failed to reliably detect positive cases (sensitivity: 11.1%, F1-score: 0.18). The random forest model identified age, BMI, serum vitamin D, CRP, smoking history, physical activity, and calcium intake as the most influential predictors (Figure 2). Feature importance analysis revealed strong nonlinear effects of inflammatory and nutritional biomarkers, alongside classical osteoporosis risk factors. Notably, the model detected subtle combinations of risk even in participants without overt clinical suspicion. ROC and confusion matrix plots demonstrated excellent calibration and discrimination (Figure 1).

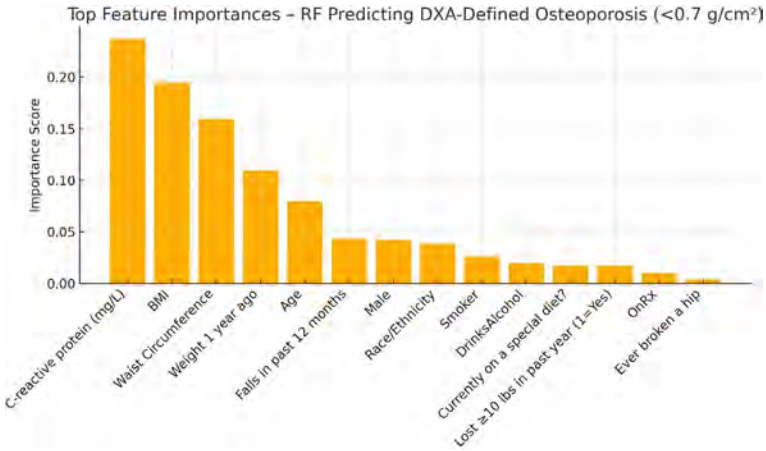


Figure 2. Top Predictors of DXA-Defined Osteoporosis. Feature importance plot from the random forest model highlights age, BMI, vitamin D, CRP, smoking, and physical activity as leading contributors.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: A random forest model using non-imaging data accurately identified individuals with DXA-defined osteoporosis, outperforming traditional regression approaches. This approach may assist in screening and triage, particularly in settings where DXA access is limited or underused.

Disclosure: S. sarfraz: None; **H. Ali**: None.

Abstract Number: 2597

Altered Tryptophan Metabolism in Neuropsychiatric Lupus: A Cluster Analysis to Identify Distinct Subgroups

Yang Wu[1], Shangzhu Zhang[2], Mengtao Li[3], Christian Lood[4] and Xiaofeng Zeng[5], [1]1. Chinese Academy of Medical Sciences & Peking Union Medical College; 2. Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China; 3. University of Washington, Division of Rheumatology, Seattle, WA, USA, Beijing, China (People's Republic), [2]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Beijing, China (People's Republic), [3]Peking Union Medical College Hospital, Beijing, Beijing, China (People's Republic), [4]University of Washington, Division of Rheumatology, Seattle, [5]Peking Union Medical College Hospital Department of Rheumatology and Clinical Immunology, Beijing, Beijing, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis (2597–2602)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Patients with neuropsychiatric systemic lupus erythematosus (NPSLE) experience impaired quality of life, whereas the underlying cause(s) remain unclear. The heterogeneity within NPSLE subtypes poses challenges for diagnosis, treatment, and research into disease pathogenesis[1]. While altered tryptophan metabolism has been reported in SLE[2], this study focuses on measuring tryptophan metabolites in specific NPSLE patients to identify clinically relevant subgroups.

Methods: Serum levels of tryptophan (TRP), kynurenine (KYN), and serotonin were measured by ELISA in two independent cohorts. The Peking Union Medical College Hospital (PUMCH) cohort included patients with NPSLE (n=46), lupus nephritis (LN, n=15), SLE without major organ involvement (WMOI, n=30), and healthy controls (HC, n=45). The University of Washington (UW) cohort consisted of patients with NPSLE (n=9), non-NPSLE (n=10), and HC (n=20). IDO activity was assessed indirectly via the KYN/TRP ratio. Unsupervised hierarchical clustering was performed using R4.4.0 and the cluster quality was assessed using the Hopkins's statistic. Statistical analysis utilized Mann-Whitney U tests and Spearman's correlation.

Results: TRP metabolite patterns were similar between two cohorts. TRP and serotonin levels were significantly decreased in NPSLE compared to WMOI and HC (Figs. 1, 2A-B), while KYN/TRP ratios were significantly elevated in NPSLE compared to non-NPSLE and HC (Figs. 1, 2C-D). Lower serotonin levels were correlated with higher SLE disease severity and activity (Figs. 2E-F). Clustering of 13 neuropsychiatric symptoms and 4 tryptophan metabolism biomarkers yielded three distinct patient subgroups (Hopkins=0.757). Cluster 1 (n=26) was characterized by the highest prevalence of seizure, cerebrovascular disease, and headaches, alongside the lowest KYN levels and KYN/TRP ratio. Cluster 2 (n=7) exhibited markedly elevated KYN and KYN/TRP ratio and high rates of cognitive impairment, psychosis, and delirium, accompanied by decreased TRP and serotonin levels. Cluster 3 (n=4) featured myelopathy, demyelination, and cranial neuropathy symptoms with the highest KYN levels and increased KYN/TRP ratios, combined with reduced serotonin levels.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

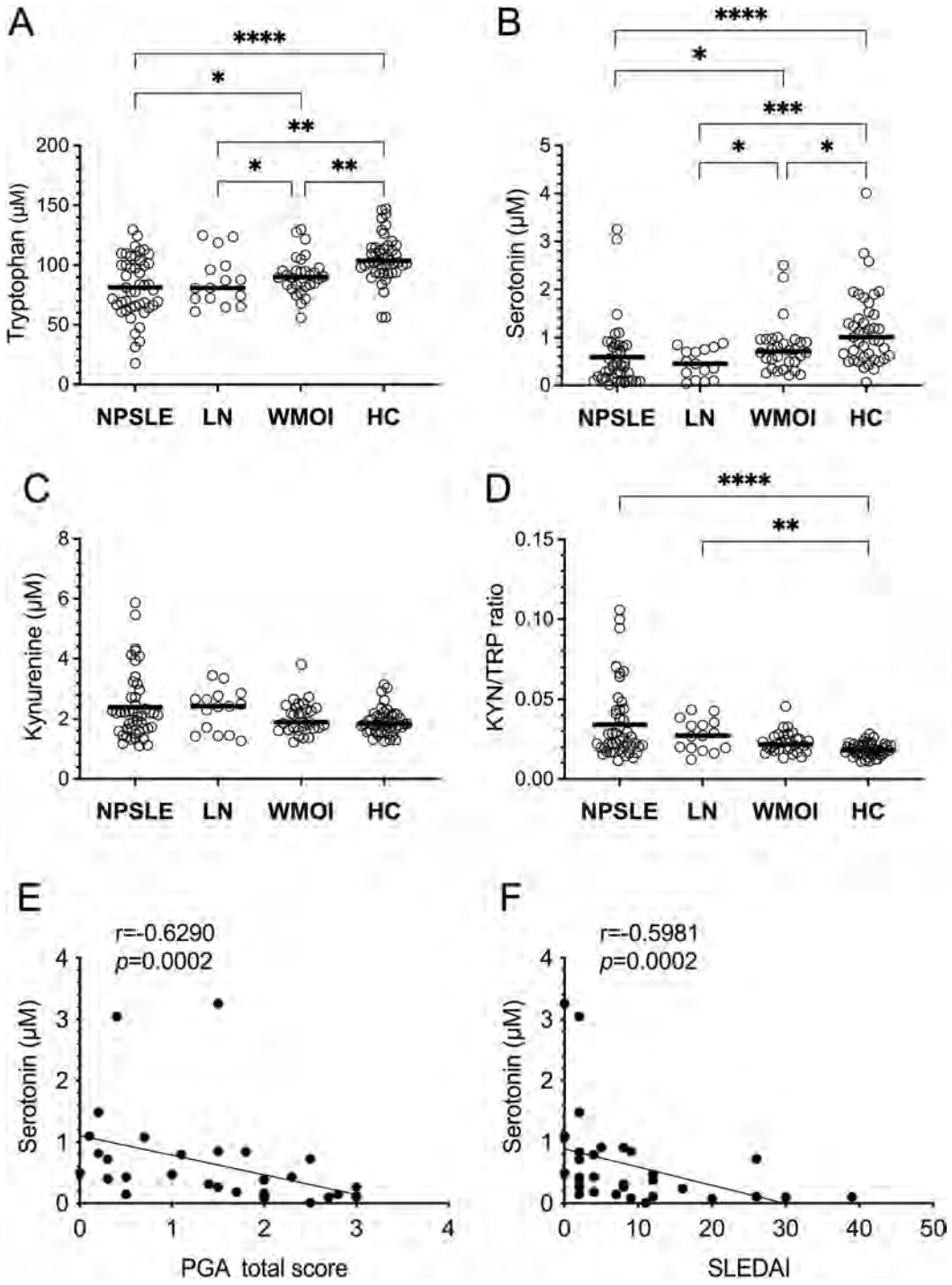


Figure 1. Serum levels of tryptophan metabolites and correlations between serotonin and clinical scores in patients from PUMCH cohort. Serum levels of (A) Tryptophan; (B) Serotonin; (C) Kynurenine; (D) the Kynurenine/Tryptophan ratio were analyzed in patients with Neuropsychiatric Systemic Lupus Erythematosus (NPSLE, n=46), lupus nephritis (LN, n=15), SLE without major organ involvement (WMOI, n=30), and healthy controls (HC, n=45). Correlations between serotonin and (E) Physician Global Assessment (PGA) total scores; (F) Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). For statistical analyses, *p<0.05, **p<0.01, ***p<0.001, **** p<0.0001.

Conclusion: Our study is the first to classify NPSLE into three main subgroups based on differential expression of tryptophan metabolites, which simultaneously influence the mental health, nervous, and immune systems[3]. Variations in biomarker profiles among subgroups can inform clinical diagnosis and treatment strategies. Further studies are needed to determine whether subtypes within each subgroup share similar pathogenic mechanisms.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

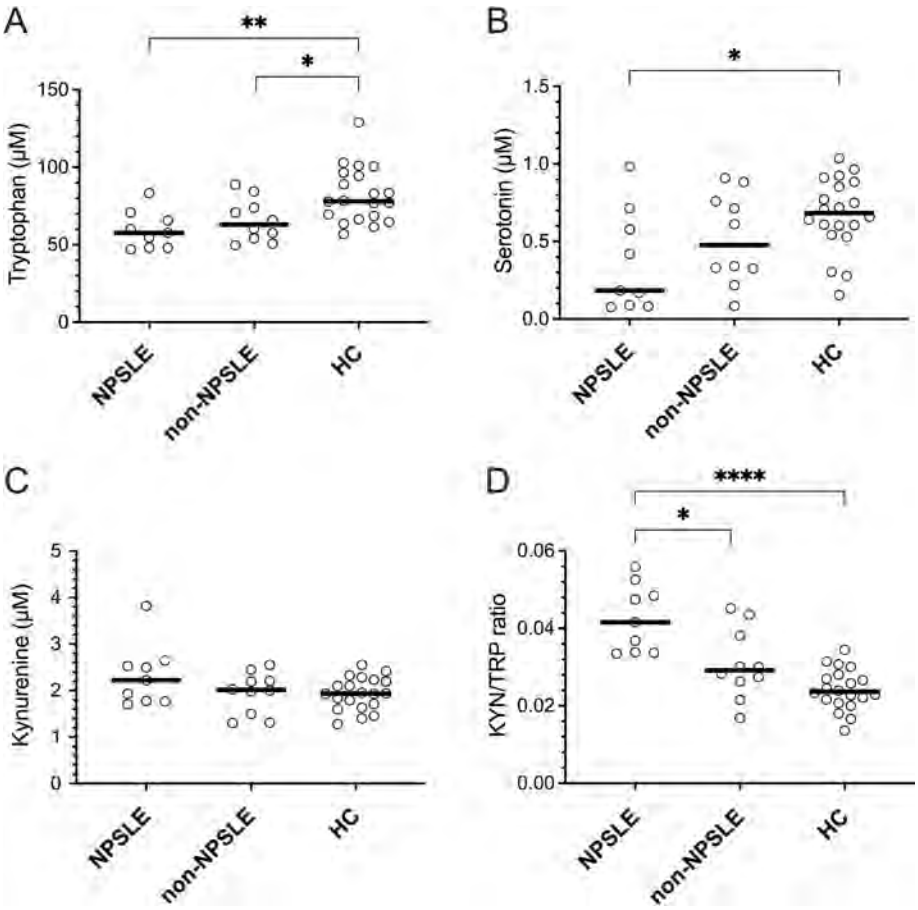


Figure 2. Serum levels of tryptophan metabolites in patients from UW cohort. Serum levels of (A) Tryptophan; (B) Serotonin; (C) Kynurenine; (D) the Kynurenine/Tryptophan ratio were analyzed in patients with Neuropsychiatric Systemic Lupus Erythematosus (NPSLE, n=9), non-NPSLE (n=10), and healthy controls (HC, n=20).

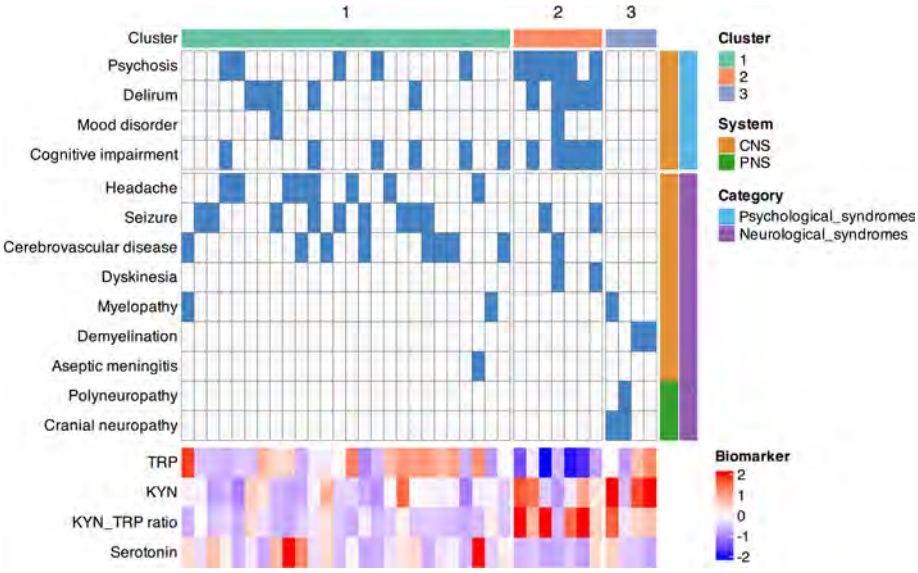


Figure 3. Different tryptophan metabolism biomarkers and clinical symptoms of the patients in three clusters TRP: tryptophan; KYN: kynurenine; CNS: central nervous system; PNS: peripheral nervous system.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References:

1. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum. 1999;42:599-608.
2. Lood C, Tyden H, Gullstrand B, et al. Type I interferon-mediated skewing of the serotonin synthesis is associated with severe disease in systemic lupus erythematosus. PLoS One. 2015;10:e0125109.
3. Cervenka I, Agudelo LZ, Ruas JL. Kynurenines: Tryptophan's metabolites in exercise, inflammation, and mental health. Science. 2017;357.

Disclosure: Y. Wu: None; **S. Zhang**: None; **M. Li**: None; **C. Lood**: Archon, 5, Boehringer-Ingelheim, 5, Citryll, 2, Gilead Sciences, 5, Neutrolis, 5, Pfizer, 5, Redd Pharma, 1, 2, 5, 11; **X. Zeng**: None.

Abstract Number: 2598

Keratinocyte-Secreted Leukemia Inhibitory Factor Counteracts Type I IFN-Induced Antigen-Presenting Phenotype in Melanocytes: Utility in Cutaneous Lupus Skin

Rezvan Moallemian[1], Lin Zhang[2], Mehrnaz Gharaee-Kermani[1], Rachel Holle[3] and J. Michelle Kahlenberg[1], [1]University of Michigan, Ann Arbor, MI, [2]Michigan Medicine, Ann Arbor, MI, [3]University of Michigan, Ann Arbor

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis (2597–2602)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Current therapies for cutaneous lupus erythematosus (CLE) are limited, highlighting the need for novel approaches. CLE lesions commonly exhibit photosensitivity and heightened type I interferon (IFN) activity. Persistent type I IFN exposure amplifies the inflammatory response of keratinocytes (KCs) to ultraviolet (UV) radiation, triggering further IFN production and worsening skin lesions. Interactions between KCs and other skin cells, such as melanocytes, are key to modulating inflammation and providing protection against environmental stressors. In this study, we investigated novel regulatory pathways between KCs and melanocytes.

Methods: We performed single-cell RNA sequencing (scRNA-seq) to characterize gene expression in melanocyte populations derived from skin biopsies of systemic lupus erythematosus (SLE) patients and healthy individuals, both with and without UV exposure. To investigate keratinocyte–melanocyte interactions, primary keratinocytes were treated with UV radiation, IFN-α, or a combination of both. The resulting conditioned media were applied to primary melanocytes along with specific inhibitors targeting JAK1 (Baricitinib), STING (H151), or cGAS (G140). MHC class II and pro-inflammatory cytokine expression in melanocytes were assessed via RT-qPCR. In parallel, cytokine profiles of the keratinocyte supernatants were analyzed using the Luminex Human Discovery Assay to identify soluble factors that may contribute to melanocyte activation.

Results: Analysis of single-cell RNA sequencing data identified leukemia inhibitory factor (LIF) as a key upstream regulator in SLE keratinocytes, with elevated LIF expression observed in primary keratinocytes. Supernatants from UV-treated keratinocytes induced upregulation of antigen-presenting markers in melanocytes in a JAK1-dependent manner. Given that LIF signals through the LIF receptor to activate the JAK-STAT pathway, we hypothesized that LIF would promote inflammatory responses in melanocytes. Unexpectedly, however, the addition of LIF to keratinocyte supernatants significantly reduced MHC-II expression in primary melanocytes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

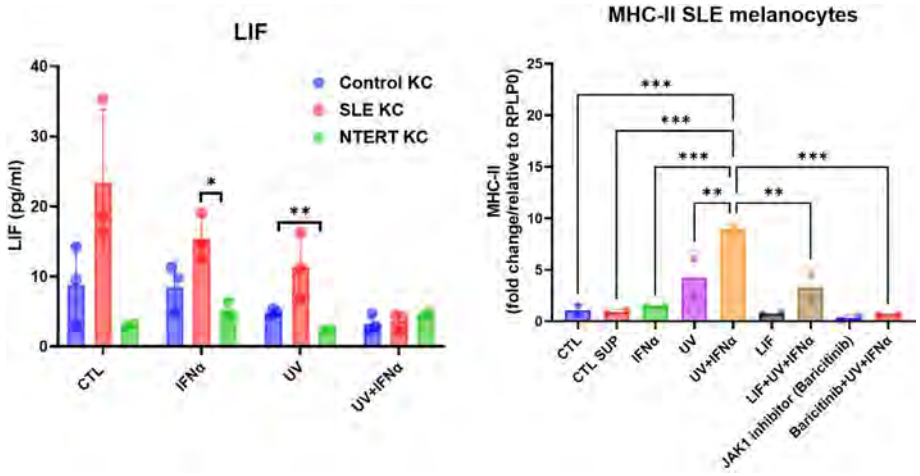


Figure 1. LIF attenuates MHC-II expression in melanocytes stimulated with UV/IFN-α–treated keratinocyte supernatants. (a) Primary keratinocytes from healthy controls (HC), SLE patients, and NTERT KC cells were exposed to IFN-α, UV, or UV+IFN-α. LIF levels in the supernatants were quantified using the Luminex Human Discovery Assay. SLE keratinocytes showed a significant reduction in LIF secretion following UV+IFN-α treatment. (b) Primary melanocytes were stimulated with keratinocyte-conditioned media from the indicated treatments. Supernatants from UV+IFN-α–treated KCs strongly induced MHC-II expression in melanocytes, which was significantly reduced by the addition of LIF (250ng/ml) or JAK1 inhibitor (5uM). MHC-II levels were measured by RT-qPCR. *P ≤ 0.05, **P ≤ 0.01, **P ≤ 0.001.

Conclusion: Melanocytes isolated from SLE lesions exhibit abnormal features, including heightened type I interferon exposure and upregulation of MHC class II molecules. Our data suggest that type I IFNs drive this upregulation and may shift melanocyte function away from pigmentation and keratinocyte support toward immune activation. Importantly, we show that the addition of LIF or JAK1 inhibitor significantly suppresses MHC-II expression in melanocytes, revealing potential regulatory pathways that may limit aberrant immune activation in CLE. Cytokine profiling confirmed that LIF is actively secreted by keratinocytes and modulated in inflammatory conditions. These findings support a model in which LIF acts as a brake on IFN-driven immune activation, a function that may be compromised in lupus skin, contributing to aberrant immune activation. Ongoing studies aim to further define the role of LIF in CLE.

Disclosure: R. Moallemian: None; **L. Zhang**: None; **M. Gharaee-Kermani**: None; **R. Holle**: None; **J. Kahlenberg**: AstraZeneca, 1, Aurinia Pharmaceuticals, 1, Avion Pharmaceuticals, 1, Biogen, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Danger Bio, 1, Eli Lilly, 1, Exo Therapeutics, 2, GlaxoSmithKlein(GSK), 2, Janssen, 5, Provention Bio, 1, Q32 Bio, 5, Rome Therapeutics, 2, 5, Ventus, 2, 5.

Abstract Number: 2599

Identification of a New Pathogenic Axis in Antiphospholipid Syndrome Linking Antiphospholipid Antibodies, Liver Function, and Circulating Proatherogenic Metabolites

Beatriz Vellón-García[1], Sagrario Corrales-Díaz-Flores[2], MARIA ANGELES AGUIRRE ZAMORANO[3], Ismael Sanchez-Pareja[3], Laura muñoz-Barrera[3], Tomás Cerdó[3], Pedro Seguí-Azpilcueta[4], Christian Merlo[2], Maria del carmen abalos-aguilera[2], Nuria Barbarroja[5], Rafaela Ortega-Castro[6], José-Antonio Gonzalez-Reyes[7], Alejandro Escudero-contreras[2], Chary López pedrera[8], Jose manuel Villalba[9] and Carlos Pérez Sánchez[10], [1]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain/ Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Córdoba, Córdoba, Spain, Cordoba, Spain, [2]Rheumatology Service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/University of Cordoba/ Reina Sofia University Hospital, Córdoba, Spain, Cordoba, Spain, [3]Rheumatology service/Maimonides Institute for Research in

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Córdoba, Spain, [4]Radiology Service, Reina Sofia Hospital/Maimonides Institute for Research in Biomedicine of Cordoba/University of Cordoba, Spain, Córdoba, United Kingdom, [5]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain, [6]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [7]Department of Cell Biology, Immunology and Physiology, University of Cordoba (UCO), Agrifood Campus of International Excellence, (ceiA3)., Cordoba, Spain, [8]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Spain, [9]Department of Cell Biology, Physiology and Immunology, Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Reina Sofia University Hospital, University of Cordoba, Cordoba, Spain, Cordoba, Spain, [10]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain/ CobiomicBioscience S.l, Cordoba, Spain, Cordoba, Spain

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis (2597–2602)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

Background/Purpose: This study aims to:

1- Characterize the circulating metabolomic signature in APS patients; 2- Investigate the role of hepatic involvement in the pathophysiology of APS; 3- Evaluate the direct effects of aPLs on the metabolism of hepatic cells *in vitro*; 4- Examine the short-term impact of ubiquinol (reduced CoQ_{10}) supplementation both *in vivo* and *in vitro* on the disrupted liver–metabolome axis.

Methods: Serum metabolomic profiling of 129 primary APS patients and 43 healthy donors (HDs) was performed using nuclear magnetic resonance (Nightingale), quantifying over 250 metabolites. Longitudinal changes were assessed in a subgroup of 15 APS patients who received ubiquinol supplementation for one month (clinical trial NCT02218476). The involvement of liver function was explored *in vivo* and *in vitro*. Correlations between circulating metabolites, liver-related biomarkers, and aPLs were carried out. *In vitro*, HepG2 cells were treated with purified aPLs, and their functional responses were assessed (Seahorse XF Palmitate Oxidation Stress Test Kit, WB, RT-PCR), both alone and in combination with CoQ_{10}.

Results: Metabolomic profiling revealed 53 significantly altered metabolites in APS patients including decreased atheroprotective lipids (HDL-related lipids) and elevated pro-atherogenic mediators (VLDL, LDL). These alterations were associated with arterial thrombosis, atheroma plaques, and recurrent thrombotic events. Evidence for liver involvement was supported by significant correlations between circulating metabolites, liver transaminases, FIB-4 index, and aPL levels.

In vitro studies reinforced the hypothesis of liver involvement. Exposure of HepG2 cells to purified aPLs increased the secretion of LDL and VLDL and upregulated hepatic injury markers. Functional metabolic assays demonstrated enhanced fatty acid oxidation under metabolic stress, accompanied by increased pACC1/ACC1 ratio and ACAA2 expression. This metabolic shift may promote triglyceride synthesis and facilitate the export of proatherogenic VLDL particles.

Moreover, in APS patients, ubiquinol supplementation partially corrected the altered lipidomic profile by decreasing pro-atherogenic and increasing anti-atherogenic markers. *In vitro*, pre-treatment of hepatocytes with CoQ_{10} effectively prevented the liver alterations induced by aPLs exposure.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: 1- APS patients display a distinct pro-atherogenic serum metabolomic profile
2- Liver involvement in APS is supported by clinical correlations and *in vitro* evidence showing that aPL promote hepatocyte dysfunction, induce metabolic reprogramming and enhance atherogenic lipid export.
3- Ubiquinol supplementation mitigates metabolic and hepatic disturbances in APS both *in vivo* and *in vitro*,
These findings reveal a novel liver–metabolism–autoantibody axis in APS, which appears to be attenuated by ubiquinol supplementation.

Fundings: ISCIII (PI24/00959, CD21/00187, RD24/0007/0019), co-financed by European Union-NextGeneration EU, via PRTR. RYC2021-033828-I. PID2022-141500OA-I00.

Disclosure: B. Vellón-García: None; **S. Corrales-Díaz-Flores**: None; **M. AGUIRRE ZAMORANO**: None; **I. Sanchez-Pareja**: None; **L. muñoz-Barrera**: None; **T. Cerdó**: None; **P. Seguí-Azpilcueta**: None; **C. Merlo**: None; **M. abalos-aguilera**: None; **N. Barbarroja**: None; **R. Ortega-Castro**: None; **J. Gonzalez-Reyes**: None; **A. Escudero-contreras**: None; **C. López pedrera**: None; **J. Villalba**: None; **C. Pérez Sánchez**: None.

Abstract Number: 2600

Deconstructing Lupus Nephritis Kidney Tissue at Single-Cell Resolution

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis (2597–2602)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Lupus nephritis (LN) is a heterogeneous disease driven by diverse immune and tissue cell types. We defined the cell states in the tissue and blood and tested their association with histopathological indices.

Methods: We obtained 538K single-cell and 143K single-nuclear profiles from kidney biopsies of 156 LN patients and 30 controls from pre-implantation transplant biopsies. We also obtained 327K single-cell blood profiles from a subset of 119 cases and 19 controls (**Figure 1**). All LN patients were >18 years, had urine protein/creatinine ratio >0.5 at biopsy, and were International Society of Nephrology (ISN) class III, IV, V, or combined III or IV with V.

Results: We built an atlas of kidney tissue cell types in LN encompassing 55 immune and 36 tissue states. Integrating tissue immune single cell data with blood data enabled classification of tissue-specific immune cell states (**Figure 2**). For example, we identified autoimmune-associated B cells (ABCs, B5) as a cell state shared between tissue and blood while plasma cell populations (P6-8) were tissue-specific. In the myeloid compartment, we identified plasmacytoid dendritic cells (DC20) as a shared population, while macrophage cell states were tissue-specific (M5-14).

Using Covarying Neighborhood Analysis, we identified LN pathological features associated with cell state changes (**-Figure 3**). Increasing chronicity tracked with the most dramatic changes in both tissue and immune states. The proportion of proximal tubule cells that were injured or degenerating (PT0, PT7) expanded with chronicity, reflecting ongoing, irreversible tissue damage. Increasing chronicity was associated with an expansion of tissue-specific CD56 bright NK cells (NK1), GPNMB^{high} NUPR1^{high} Macrophages (M5), and CLEC10A^{low} cDC2 (DC17). Most expanded immune populations were tissue-specific states.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

It was essential to identify activity-associated populations since they may be driving reversible inflammation in LN. Adjusting away chronicity, we identified specific activity-associated cell states in the myeloid compartment. Highly tissue-specific macrophage populations were expanded, including M5, *GPNMB*^{high} *LYVE1*^{low} (M11), *C1Q*^{low} *SPP1*^{high}, SPP1^{high} FABP5^{high} (M7), and MERTK^{high} FABP5^{high} (M9). We speculate that M5 may be a profibrotic pathogenic population that may be targeted for therapeutic benefit.

After adjusting for chronicity and activity, ISN classes were not independently associated with specific changes in cell states. Blood cell states minimally associated with activity or chronicity. We observed case-status associated with interferon signatures in both blood and tissue.

Conclusion: Our results define key cell states in the tissue and immune compartments and argue that profound changes in kidney tissue and immune cell states are associated with increasing chronicity. Specific myeloid compartment changes are associated with activity. These features are not associated with substantial changes in the blood. Our results argue that myeloid populations may be targeted, in addition to B cell therapies, to prevent progression of tissue inflammation and ongoing tissue damage in LN.

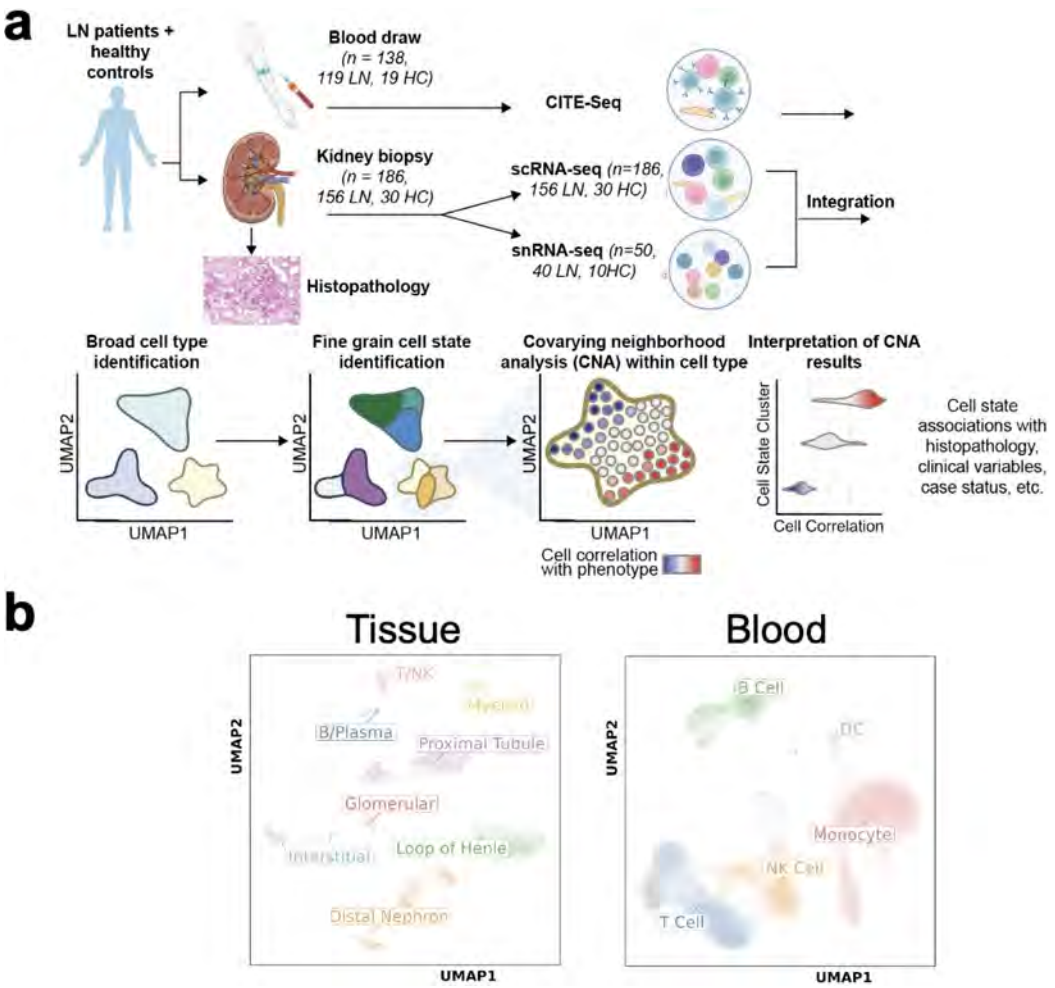


Figure 1. a, Schematic overview of the data collection and analysis pipeline. Blood and kidney samples were collected from LN patients and healthy controls (HC). Histopathology and clinical scoring was performed on renal biopsies. CITE-sequencing was performed on blood samples, and scRNA-sequencing and snRNA-sequencing were performed on tissue samples. Both tissue modalities were integrated with Harmony (PMID: 31740819). Broad cell types were annotated separately in tissue and blood. Fine grain clustering for cell state annotation was performed on each broad cell type. For each tissue, covarying neighborhood analysis was performed within each cell type to define cell state associations with various clinical variables. b, UMAPs of all single cell or single nuclear annotations in tissue (left) and blood (right), colored by broad cell type annotation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

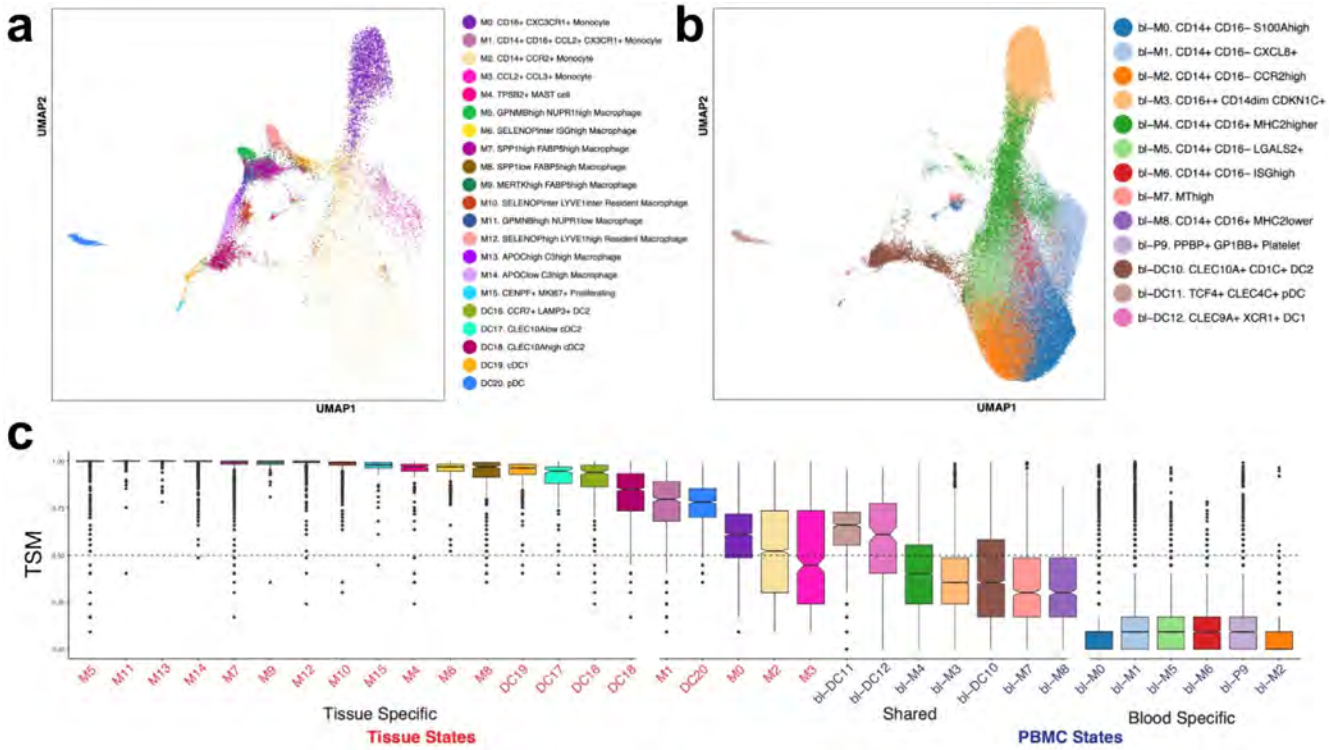


Figure 2. a-b, Joint embedding of tissue (a) and blood (b) myeloid single-cell populations, colored by their original fine-grain annotations obtained in a separate embedding. c, Tissue specificity metric (TSM) scores stratified by cell state annotation. TSM was calculated as the proportion of a given cell's 50 nearest neighbors that are from tissue, weighted to account for larger amount of total myeloid blood than tissue myeloid cells.

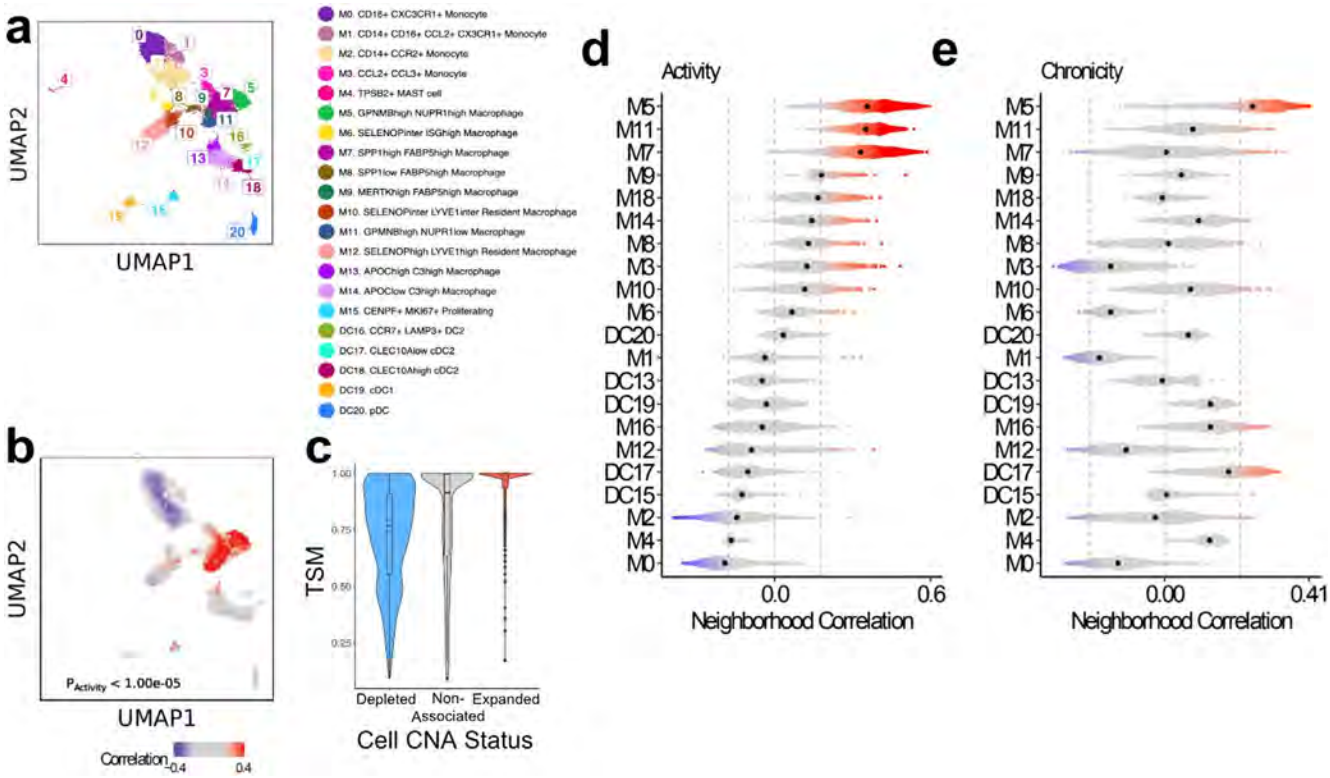


Figure 3. a, UMAP of myeloid cell states in tissue, colored by fine grain cell state annotations. Annotation boxes are located at the centroid (mean) of each cluster. b, UMAP of per-cell correlation coefficient associations with activity index, as quantified in CNA. c, TSM for cells significantly expanded or depleted with activity index in CNA. d-e, CNA correlation coefficients for cells in each myeloid cluster, indicating cell state correlations with activity index (d) and chronicity index (e).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: N. Sugiarto: None; **M. Curtis**: None; **S. Gurajala**: None; **T. Eisenhaure**: None; **Q. Xiao**: None; **J. Mears**: None; **A. Arazi**: None; **P. Hoover**: None; **C. Berthier**: None; **S. Sakaue**: None; **A. Fava**: Artiva, 2, AstraZeneca, 1, 2, Bain Capital, 2, Biogen, 1, Bristol-Myers Squibb(BMS), 2, Exagen, 5, 9, Quotient Therapeutics, 2, UCB, 6, Zenas, 2; **D. Hildeman**: None; **E. Woodle**: Biogen, 5, Bristol-Myers Squibb, 5, Eledon, 5, Sanofi, 6; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **J. Barnas**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **C. Putterman**: Cullinan, 1, Progentec, 1; **D. Kamen**: None; **M. McMahon**: Artiva, 2, AstraZeneca, 2, 6, Aurinia, 6, Bristol-Myers Squibb(BMS), 5, GlaxoSmithKlein(GSK), 1, 5, 6, Novartis, 5, Roche, 1; **J. Grossman**: artiva, 5, exact sciences, 11, illumina, 11, iqvia, 11, Merck/MSD, 11, Novartis, 5; **K. Kalunian**: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Genentech, 1, GlaxoSmithKlein(GSK), 1, Merck/MSD, 1, Novartis, 1, Pfizer, 1, Roche, 1; **J. Hodgin**: Genentech, 5, Gilead, 5; **F. Payan Schober**: None; **M. Ishimori**: None; **M. Weisman**: Spyre Therapeutics, 1, 2; **W. Apruzzese**: Pfizer, 3, 12, my contributions to this work occurred prior to my employment at Pfizer; **J. Guthridge**: None; **M. Brenner**: AbbVie/Abbott, 2, Johnson & Johnson, 5, Mestag Therapeutics, 2, 8, Moderna, 2, Ono Pharma, 5, Simcere, 2; **J. Anolik**: None; **D. Wofsy**: None; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2; **A. Davidson**: None; **M. Petri**: Amgen, 2, AnaptysBio, 2, Annexon Bio, 2, AstraZeneca, 2, 5, Atara Biosciences, 2, Aurinia, 2, 5, Autolus, 2, Bain Capital, 2, Baobab Therapeutics, 2, Biocryst, 2, Biogen, 2, Boxer Capital, 2, Cabaletto Bio, 2, Caribou Biosciences, 2, CTI Clinical Trial and Consulting Services, 2, CVS Health, 2, Dualitybio, 2, Eli Lilly, 2, 5, EMD Serono, 2, Emergent, 2, Escient Pharmaceuticals, 2, Exagen, 5, Exo Therapeutics, 2, Gentibio, 2, GlaxoSmithKlein(GSK), 2, 5, iCell Gene Therapeutics, 2, Innovaderm Research, 2, IQVIA, 2, Janssen, 5, Kezar Life Sciences, 2, Kira Pharmaceuticals, 2, Nexstone Immunology, 2, Nimbus Lakshmi, 2, Novartis, 2, Ono Pharma, 2, PPD Development, 2, Proviant, 2, Regeneron, 2, Seismic Therapeutic, 2, Senti Biosciences, 2, Sinomab Biosciences, 2, Steritas, 2, Takeda, 2, Tenet Medicines, 2, TG Therapeutics, 2, UCB, 2, Variant Bio, 2, Worldwide Clinical Trials, 2, Zydus, 2; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **N. Hacohen**: Calico Biosciences, 5, Cytoreason, 1, 11, Danger Bio, 1, 11, Moderna, 5, Repertoire Immune Medicines, 1, 11, Takeda, 5; **B. Diamond**: None; **S. Raychaudhuri**: Bonito, 1, Bristol-Myers Squibb(BMS), 1, Janssen, 1, Mestag, 1, 8, Nimbus, 2, Pfizer, 1, Sonoma, 1, 8, Visterra, 6.

Abstract Number: 2601

Characterisation of immunometabolic reprogramming at the single cell level in patients with systemic lupus erythematosus and preclinical autoimmunity

Antonios Psarras[1], Sinibaldo Arocha[2], Liezel Tamon[2], David Ahern[2], Md Yuzaiful Md Yusof[3], Ed Vital[4] and Alexander Clarke[5], [1]University of Oxford, Oxford, England, United Kingdom, [2]University of Oxford, Oxford, United Kingdom, [3]University of Leeds, Leeds, United Kingdom, [4]University of Leeds, Leeds, England, United Kingdom, [5]Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis (2597–2602)

Session Type: Abstract Session

Session Time: 1:00PM–2:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic lupus erythematosus (SLE) is characterised by innate immune activation and autoantibodies against nucleic self-antigens. The metabolic state of immune cells is emerging as a critical checkpoint of their effector functions, including proliferation, activation, secretion of cytokines, and escalation of inflammation. Previously described transcriptomic data suggested significant alterations in the metabolic profile of SLE immune cells, but there is lack of single-cell data confirming the changes at the protein level. The aim of this study was to create a detailed single-cell immunometabolic map in different stages of lupus disease activity and in ANA-positive individuals at risk of SLE.

Methods: Blood samples were obtained from patients from high disease activity SLE (n = 20), low disease activity SLE (n = 20), primary Sjogren's Syndrome (n = 7), Rheumatoid Arthritis (n = 8), age- and sex-matched healthy donors (n = 20), and at-risk individuals before (n = 23) and after (n = 23) developing SLE. SLE patients met 2012 SLICC classification criteria and disease activity was evaluated using BILAG-2004. Cryopreserved human peripheral blood mononuclear cells (PBMCs) were thawed and subsequently stained with 50 distinct heavy metal-conjugated antibodies before they were processed by mass cytometry (CyTOF). Raw data were normalised using CyTOF software and were subsequently debarcoded using Premessa R package. Clustering, differential abundance, and differential expression was performed by using FlowSOM R package incorporating key clinical and immunological parameters in the data analysis.

Results: Principal analysis identified 36 distinct cellular components (B cell and T cell subsets, monocytes, NK cells, myeloid and plasmacytoid dendritic cells) and 6 key metabolic pathways (glycolysis, OxPHOS, PPP, TCA & ETC, fatty acid metabolism, amino acid metabolism). Cellular composition was significantly different among the patient groups with plasmablast expansion being a key element within the high disease activity SLE and the at-risk individuals who progressed to SLE. There were significant differences in the expression of the metabolic enzymes among different cellular components within the same individual; for instance, monocytes appeared more metabolically active compared to B cell populations. Patients with established autoimmune disease (e.g. SLE and primary Sjogren's syndrome) were characterised by changes in several metabolic enzymes, mainly in glycolysis and OxPHOS pathways. These metabolic changes were correlated with differences in disease activity of SLE patients. Cellular and metabolic changes were observed in at-risk individuals highlighting an early immunometabolic reprogramming prior to the development of clinically overt autoimmune disease.

Conclusion: We identified immunometabolic changes at the single cell level, which can influence immune function, associated with disease activity in SLE and related diseases. Further, this immunometabolic reprogramming preceded clinically overt SLE or therapy suggesting a fundamental role in pathogenesis. Future analysis will explore the effect of these changes on longitudinal immune function and clinical status.

Disclosure: A. Psarras: AstraZeneca, 6; **S. Arocha**: None; **L. Tamon**: None; **D. Ahern**: None; **M. Md Yusof**: GlaxoSmithKlein(GSK), 1, Novartis, 1, 6, UCB, 2, 6; **E. Vital**: AbbVie, 2, 6, Alpine, 2, AstraZeneca, 2, 5, 6, Aurinia, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Idorsia, 6, ILTOO Pharma, 6, Merck, 2, 6, Novartis, 2, 6, 12, Paid instructor, Otsuka, 2, 6, Pfizer, 2, 6, Roche, 2, 5, 6, Sandoz, 5, UCB, 2, 6; **A. Clarke**: None.

Abstract Number: 2602

Cellular and molecular fine mapping in single-cell data pinpoints new immunopathology of systemic lupus erythematosus

Masahiro Nakano[1], Michihiro Kono[1], Kenichiro Asahara[1], Takayuki Katsuyama[2], Eri Katsuyama[3], Takahiro Arakawa[1], Tsugumi Kawashima[1], Hajime Inokuchi[1], Takahiro Nishino[1], Haruka Takahashi[1], Bunki Natsumoto[1], Hiroaki Hatano[1], Yoshinori Matsumoto[2] and Kazuyoshi Ishigaki[1], [1]Laboratory for Human Immunogenetics, Riken Center for Integrative Medical Sciences, Yokohama, Japan, [2]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, [3]Faculty of Health Science, Okayama University Medical School, Graduate School of Health Sciences, Boston, MA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Etiology and Pathogenesis (2597–2602)
Session Type: Abstract Session
Session Time: 1:00PM–2:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease with unknown etiology. While we previously identified key gene signatures of SLE using bulk RNA-seq from 27 immune cell types (*Cell* 2022), we failed to identify more granular disease-relevant cell states within each cell type. Although single-cell RNA-seq (scRNA-seq) can address this problem, recent studies ended up defining ~20 coarse cell types and relied on cell-type-level pseudo-bulk analysis, which has hindered the discovery of new drug targets. Our in-depth investigation strategy for single-cell data, cellular and molecular fine mapping, aimed to identify new disease-relevant cell states in SLE and to perform a detailed functional characterization of them.

Methods: We applied our strategy to the largest-scale single-cell data of SLE with ~1.8 million peripheral blood mononuclear cells from 97 healthy controls and 191 SLE cases (Figure 1). We identified granular cell states that expanded in SLE (cellular fine mapping) and investigated their molecular profile using in silico and experimental approaches (molecular fine mapping).

Results: After we identified 118 granular cell states in 25 cell types with fine-grained clustering, we discovered that previously uncharacterized cell states such as *FAM13A*$^{+}$*ARID5B*$^{+}$ naive CD4^{+} T cells, *ARHGAP15*$^{+}$*CAMK4*$^{+}$ T cells, *GZMK*$^{+}$*GZMH*$^{+}$*HLA-DR*$^{+}$ effector memory CD8^{+} T cells, and *C1Q*$^{+}$ monocytes, expanded especially in clinically active SLE (covarying neighborhood analysis, Figure 2).

Next, our new statistical model, which can decompose conventional pseudobulk-level differential expression into cell state abundance signature genes (quantitative change) and dysregulated signature genes (qualitative change) at single-cell level, showed that classical immunological pathways were more enriched in cell state abundance signature genes rather than dysregulated signature genes. Integrative analysis using genome-wide association studies (SLE-GWAS) with sc-linker pipeline also revealed that SLE polygenic signals were more linked to cell state abundance signature genes, suggesting that these expanded cell states can exert causal effects on SLE pathogenesis.

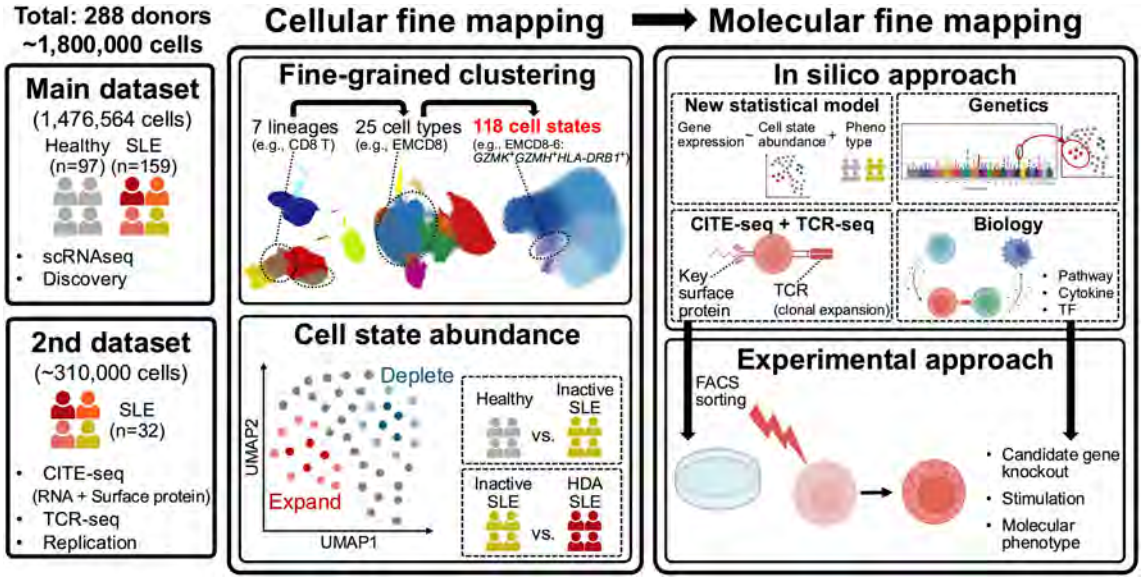


Figure 1. Overview of this study

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

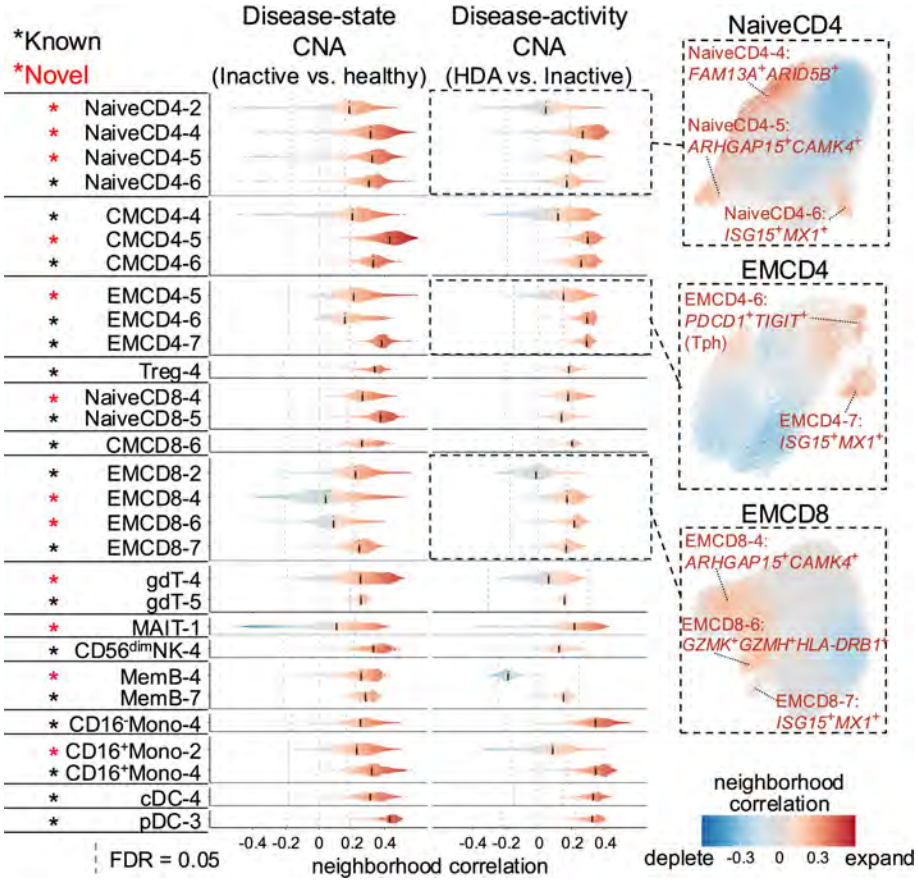


Figure 2. Granular cell states that expanded in SLE

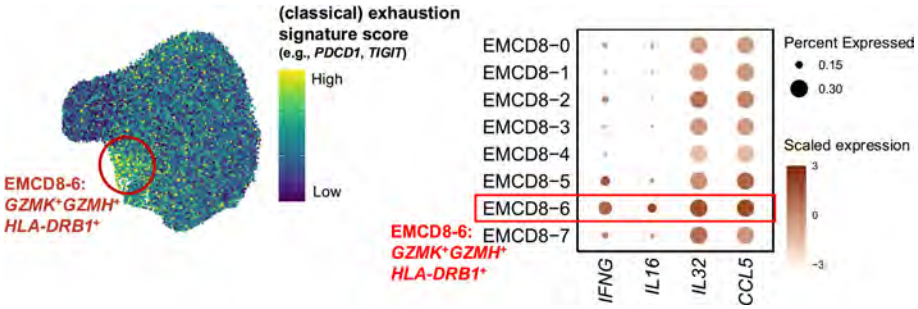


Figure 3. Molecular profiles in GZMK+GZMH+HLA-DR+ effector memory CD8+ T cells

Finally, we investigated detailed molecular profiles of these new disease-relevant cell states. For example, *GZMK*$^{+}$*GZMH*$^{+}$*HLA-DR*$^{+}$ effector memory CD8^{+} T cells exhibited the highest expression of exhaustion signatures (*PDCD1* and *TIGIT*) and key cytokines (*IFNG* and *IL16*, Figure 3). Integrative analysis with 137 cell surface markers identified four key surface markers of this subpopulation, which enabled us to perform in-depth functional characterization through experimental approaches such as in vitro stimulation. Furthermore, CRISPR gene knockout screening also identified several transcriptional regulator candidates of these cell states.

Conclusion: Our intensive cellular and molecular fine-mapping approach successfully pinpointed new disease-relevant cell states in SLE and their key molecules, which could be the next treatment targets.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: M. Nakano: None; **M. Kono**: None; **K. Asahara**: None; **T. Katsuyama**: None; **E. Katsuyama**: None; **T. Arakawa**: None; **T. Kawashima**: None; **H. Inokuchi**: None; **T. Nishino**: None; **H. Takahashi**: None; **B. Natsumoto**: None; **H. Hatano**: None; **Y. Matsumoto**: AbbVie/Abbott, 6, Eli Lilly, 6, GlaxoSmithKlein(GSK), 6, Pfizer, 6; **K. Ishigaki**: None.

Abstract Number: 2603

Evaluating the Feasibility, Acceptability, and Behavioral Impact of Brief Action Planning (BAP) Coaching for Physical Activity in Adults with Chronic Knee Symptoms: A Qualitative Study

Moath Alshahrani[1], Kristin Haglund[2], Miranda McIlheran[2], Rowland Chang[3], Pamela Semanik[4], Sheikh Iqbal Ahamed[2] and Daniel Pinto[5], [1]Marquette University/ King Khalid University, Milwaukee, WI, [2]Marquette University, Milwaukee, WI, [3]Northwestern University Feinberg School of Medicine, Chicago, IL, [4]Rush uUniversity, Chicago, IL, [5]Marquette University, Wauwatosa, WI

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: ARP II: Perception, Prediction, and Prevention (2603–2608)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Physical activity (PA) improves chronic knee symptoms (CKS) by decreasing pain and improving function, yet many interventions to increase PA are resource-intensive or poorly tailored to individual motivation. Brief Action Planning (BAP) offers is a self-management support tool based on motivational interviewing that remains understudied in real-world contexts. This study aimed to explore the feasibility, acceptability, and perceived impact of a computer-supported coaching program to support action planning for physical activity among adults with CKS in workplace

Methods: Employees (N=9) were recruited via health portal to participate in a 12-week randomized controlled trial assessing health coaching plus Fitbit. The coaching program consisted of an initial 30-minute rapport-building session and 10-minute follow-up sessions delivered remotely by trained health coaches. Number of follow-up sessions ranged between 4-11 based on participant preference. Participants were invited to engage in semi-structured interviews post-intervention which were transcribed and analyzed using qualitative content analysis. Codes were developed independently by two trained researchers. Self Determination Theory's (SDT) three psychological needs autonomy, competence, and relatedness were used to interpret the motivational mechanisms supporting behavior change. Data were examined within and across codes to identify three themes and nine sub-themes

Results: Theme 1, value and sustainability of the BAP program included subthemes of acceptability, positive experience with coaching, and anticipated sustainability of behavioral change. Theme 2, active ingredients that facilitated physical activity behavior, included subthemes of coaching accountability, goal-setting structure, and behavioral monitoring. Theme 3, contextual conditions influencing motivation and program fit, included personal motivation, knee pain management, and workplace or lifestyle integration. Participants viewed the coaching relationship as the central driver of behavior change. Coaching enhanced personal accountability, enabled adaptive goal setting, and fostered supportive dialogue. Fitbit use complemented goal adherence but was secondary to interpersonal support. Mapping to SDT, autonomy was supported by individualized goal-setting; competence through iterative plan refinement and feedback; and relatedness through an empathic, nonjudgmental coaching relationship. Internalized motivation and increased self-efficacy supported sustainability of behavior change

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Brief action planning-based coaching paired with Fitbit PA feedback was perceived as feasible, highly acceptable, and impactful for promoting physical activity in employed individuals with chronic knee symptoms

Disclosure: M. Alshahrani: None; **K. Haglund**: None; **M. McIlheran**: None; **R. Chang**: None; **P. Semanik**: None; **S. Ahamed**: None; **D. Pinto**: Coaching Connections, LLC., 8.

Abstract Number: 2604

Cross-Sectional Relationship Between Sarcopenic Obesity and Knee Osteoarthritis: The Johnston County Osteoarthritis Project

David Werner[1], Carolina Alvarez[2], John Batsis[3], Reece Blay[4], Laura Bilek[5], Amanda Nelson[3] and Yvonne Golightly[5], [1]University of Nebraska Medical Center, Mason, OH, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, [4]University of Nebraska Medical Center, Council Bluffs, IA, [5]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: ARP II: Perception, Prediction, and Prevention (2603–2608)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Current consensus for defining sarcopenia (loss of muscle mass and strength with aging) and sarcopenic obesity (SO, sarcopenia with obesity) suggests combining measures of strength and physical function with body composition parameters. Limited evidence suggests that SO is associated with knee osteoarthritis (KOA), moreso than either sarcopenia or obesity alone. However, previous studies often defined SO using only body composition or clinical measures, rather than a combination of both. Therefore, this study examined the relationship between KOA and sarcopenia, obesity, and SO utilizing a definition of sarcopenia, obesity, and SO that combined body composition and clinical definitions.

Methods: The sample was drawn from participants enrolled in the Johnston County Osteoarthritis Project (JoCoOA) with available whole body dual energy x-ray absorptiometry (DXA) scans, along with data on anthropometric, knee symptoms and radiographic, and physical function measures from one visit occurring between 1999-2010. Obesity was defined using cutoffs based on body fat % and either BMI, waist-to-height, or waist circumference (Table 1). Sarcopenia was defined as

Table 1. Normative data for identification of obesity, sarcopenia, and sarcopenic obesity.

Assessment	Definition	PMID
Obesity		
BMI	Compared to sex-matched normative data	36719951
Waist to height	Compared to sex-matched normative data	36719951
Waist circumference	Compared to sex-matched normative data	36719951
Percent body fat	Compared to sex, age, and race-matched normative data	10966886
Sarcopenia		
Chair stand	Compared to sex and age-matched normative data	35000330; 3491815
Hand grip strength	Compared to sex and age-matched normative data	25474696
Appendicular lean mass	Lowest quintile of appendicular lean mass percent	

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

low fat-free mass with either low grip strength or poor chair stand time when compared to age and sex-matched normative values (Table 1). SO was defined as having both obesity and sarcopenia. Outcomes included radiographic KOA (rKOA) defined by a Kellgren-Lawrence grade ≥2 and symptomatic knee OA (sxKOA) defined by rKOA and symptoms (pain, aching, stiffness on most days) in the same knee. Logistic regression models assessed cross-sectional associations among obesity, sarcopenia, and SO and rKOA or sxKOA, adjusting for age, sex, race (Black/White), education level, smoking status(never/former/current), number of chronic conditions, and prior knee injury.

Results: A total of 1878 participants (mean age 63.6±10.4 years, 1/3 male, 1/3 Black) were included (Table 2). Individuals were classified as having neither obesity nor sarcopenia (64%), obesity only (23%), sarcopenia without obesity (2%), and SO (10%). Approximately 1/3 of the sample had rKOA and 2/5 had sxKOA. Compared to the referent group of no obesity or sarcopenia, obesity only and SO were associated with more than double the odds of rKOA and sxKOA (Table 3). Compared to obesity only, SO was related to sxKOA but not rKOA, and compared to sarcopenia only, SO was associated with rKOA and sxKOA.

Table 2. Descriptive statistics for JbCoOA with available DXA, N=1878.

Characteristics	n or mean	% or ±S
Age, mean±SD years, range=45-95	63.6	±10
Male	627	33
Black	636	33
Education < High School (missing=11)	440	23
Smoking status (missing=105)		
never	945	50
past	522	27
current	306	16
Multimorbidities (missing=13)		
0	234	12
1-2	553	29
3+	1078	57
History of knee injury (missing=9)	329	17
Individual anthropometry, physical function, and DXA cutoffs		
BMI=30 kg/m^2	863	46
High Waist Circumference: >88cm for women, >102cm for men	1074	57
High risk Waist-to-Height>0.6	833	44
High Fat Mass %	670	35
Long/abnormal Time to 5 Chair Stands	1004	53
Low/weak Hand Grip Strength	279	14
Lowest quintile ALM%: <23.98% for women, <30.84% for men	376	20
Definitions of Sarcopenia and Obesity		
Obesity	623	33
Sarcopenia	233	12
Sarcopenic Obesity	188	10
Mutually-exclusive definition		
no obesity or sarcopenia	1210	64
obesity only	435	23
sarcopenia only	45	2
sarcopenic obesity	188	10
Outcomes		
rKOA (KLG=2)	639	34
sxKOA (KLG=2 and symptoms in same knee)	386	20

SD=standard deviation; OA=osteoarthritis; rKOA=radiographic knee OA; sxKOA=symptomatic knee OA; symptoms=pain, aching, or stiffness on most days

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Cross-sectional associations between main effect and knee osteoarthritis (KOA) outcomes, adjusted* odds ratios (aOR) and 95% confidence intervals (CI).

	Radiographic KOA	Symptomatic KOA
Main effect	aOR (95% CI)	aOR (95% CI)
Mutually-exclusive comparisons		
obesity only (vs no obesity or sarcopenia)	**2.16 (1.67, 2.79)**	**2.08 (1.56, 2.79)**
sarcopenia only (vs no obesity or sarcopenia)	0.86 (0.42, 1.74)	1.51 (0.69, 3.29)
sarcopenic obesity (vs no obesity or sarcopenia)	**2.40 (1.70, 3.40)**	**3.38 (2.34, 4.88)**
sarcopenic obesity (vs obesity only)	1.11 (0.76, 1.63)	**1.62 (1.08, 2.43)**
sarcopenic obesity (vs sarcopenia only)	**2.81 (1.31, 6.03)**	2.24 (0.98, 5.11)

Using 10 multiple imputed datasets. Logistic regression modeling log odds for KOA outcome.
*Adjusted for: age, sex, race, education, smoking, multimorbidities, and knee injury
Shown **BOLD** when significant at 0.05 level.

Conclusion: These findings suggest that SO is strongly related to sxKOA when compared to obesity only or normal cutoffs of fat-free and fat mass. Both sarcopenia and obesity are related to changes in body composition and metabolic function associated with aging and the combination of sarcopenia and obesity (i.e. SO) works synergistically in its relationship with KOA, as the odds are higher than both conditions in isolation. Future research using current definitions of SO should investigate longitudinal relationships to inform interventions to address SO and KOA.

Disclosure: D. Werner: None; **C. Alvarez**: None; **J. Batsis**: None; **R. Blay**: None; **L. Bilek**: Osteoboost, Inc, 1, 11; **A. Nelson**: Novo Nordisk, 1; **Y. Golightly**: None.

Abstract Number: 2605

Do Patients Recall Their Rheumatic Diagnoses Accurately? A Comparison by Disease Type

Sydney Liles[1], Samantha Namit[2], Jennifer Copson[3], Matthew Librizzi[2], Sophia Baionno[2], Nurten Gizem Tore[2], Yvonne Lee[4] and Daniel K. White[1], [1]University of Delaware, Newark, DE, [2]University of Delaware, Newark, [3]University of Delaware, Wilmington, DE, [4]Northwestern University, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: ARP II: Perception, Prediction, and Prevention (2603–2608)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Rheumatic diseases represent a major public health concern in the United States due to their high prevalence and their association with disability. Observational studies are an essential tool in understanding the distribution and impact of these conditions. Such studies often rely on patients to recall their physician provided diagnosis. However, previous research has shown mixed results on this agreement. The purpose of this study was to assess the preliminary agreement of patient-recalled diagnosis type with a physician diagnosis in an online cohort of adults with rheumatic disease in the United States.

Methods: We used cross-sectional data from the Observational Arthritis Foundation Internet Study. Participants were recruited online using advertisements on Meta. Those who were ≥ 18 years old, lived in the US, and had a patient-recalled rheumatic condition were included in the study. Demographic information was collected using questionnaires. Study

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Percentage of agreement, Kappa values (K) and 95% confidence intervals, sensitivity, specificity for Osteoarthritis, Gout, Fibromyalgia, Rheumatoid Arthritis, Psoriatic Arthritis, Lupus, and other

Rheumatic Disease Type	Percentage of agreement of patient-recalled diagnosis with physician reported diagnosis	K (95% CI)	Sensitivity	Specificity
Osteoarthritis (n = 78*)	88.0%	0.69 (0.53, 0.85)	0.90	0.81
Gout (n = 9*)	98.2%	0.88 (0.71, 1.00)	0.89	0.99
Fibromyalgia (n = 45*)	92.6%	0.85 (0.75, 0.95)	0.91	0.94
Rheumatoid Arthritis (n = 22*)	93.5%	0.80 (0.65, 0.94)	0.86	0.95
Psoriatic Arthritis (n = 8*)	98.2%	0.88 (0.71, 1.00)	0.80	1.00
Lupus (n = 7*)	99.1%	0.93 (0.79, 1.00)	0.88	1.00
Other (n = 8*)	88.0%	0.25 (-0.03, 0.54)	0.27	0.95

*Participants could report more than one diagnosis and be counted in multiple diagnoses

participants were asked what "Type(s) of Arthritis you have been diagnosed with:". Response options included Osteoarthritis (OA), Fibromyalgia, Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Gout, Lupus, and/or Other. We compared patient-recalled diagnoses with health records/provider report. Health record/provider reported diagnoses were collected through uploaded documentation from an electronic medical record or receiving a completed form specifying rheumatic diagnoses completed by a physician. We assessed agreement by calculating percent agreement, kappa coefficients (κ) with 95% confidence intervals (CI), sensitivity, and specificity for each diagnosis. Kappa coefficients were interpreted using 0 no agreement, 0.1-0.2 slight, 0.21-0.4 fair, 0.41-0.6 moderate, 0.61-0.8 substantial, 0.81-0.99 near perfect, and 1.0 perfect agreement.

Results: 108 participants (mean age = 57.3 years old, 85.2% female, mean BMI =34.1 kg/m^2, mean Charleson Comorbidity Index Score 3.4, 18.5% non-White, 78.7% with at least an associate's degree) were included in the analysis. Percentages of agreement between physician diagnoses and patient-recalled ranged from 88% to 99%, with corresponding kappa coefficients ranging from 0.25 to 0.93 (Table 1). Lupus showed the highest agreement (99.1%) and a kappa coefficient of 0.93 95% CI (0.79, 1.00). Osteoarthritis and the "Other" category each had agreement percentages of 88.0% with kappa values of 0.69 (0.53, 0.85) and 0.25 (-0.03, 0.54), reflecting substantial and fair agreement, respectively. Specificity scores ranged from 0.81 to 1.00, while sensitivity scores ranged from 0.80 to 0.90 for all conditions except "Other" (sensitivity 0.27). Examples of reported "Other" diagnoses include ankylosing spondylitis, Sjogren's arthritis, or scleroderma.

Conclusion: We found, in our preliminary study, that patient-recalled diagnoses of specific rheumatic conditions have substantial agreement with physician diagnoses. However, patient-recalled diagnoses of 'Other' have fair agreement with physician report. Patient-recalled diagnoses may serve as a reasonable proxy for provider-confirmed diagnoses. These findings need to be replicated in larger and more diverse samples.

Disclosure: S. Liles: None; **S. Namit**: None; **J. Copson**: None; **M. Librizzi**: None; **S. Baionno**: None; **N. Tore**: None; **Y. Lee**: CVS Health, 12, GE Healthcare, 12, Tonix, 1; **D. White**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2606

The Impact of Social Media and Artificial Intelligence on Illness Perception and Treatment Adherence in Patients with Rheumatic Diseases

Egla Samantha Sanchez-Peralta[1], Pablo Gamez-Siller[1], Angel Kevin Garza-Elizondo[1], Fabiola Alejandra Fuentes-Rios[1], Gemma Alely Garcia-Ramos[1], Derek de Jesus Gauna Leal[1], Ariana Silva-de Leon[1], Nathalia Valdez-Benavides[1], Jesus Alberto Cardenas-de la Garza[2], Margarita Isabel Alarcon-Jarquin[3], Dionicio A. Galarza-Delgado[4] and Diana E. Flores-Alvarado[1], [1]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Nuevo Leon, Mexico, [2]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, México, Monterrey, Mexico, [3]Rheumatology Service, University Hospital "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Monterrey, Nuevo Leon, Mexico, [4]Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Universidad Autónoma de Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: ARP II: Perception, Prediction, and Prevention (2603–2608)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Social media (SM) and Artificial Intelligence (AI) are common sources of health information for patients with chronic diseases. Seeking medical information from unreliable sources can negatively affect the health perspective of patients with rheumatic diseases and their treatment adherence. We aimed to determine the influence of SM and AI on disease perception and treatment adherence in patients with rheumatic diseases.

Methods: We conducted an observational, cross-sectional study at an outpatient rheumatology clinic. Patients >18 years and with at least one rheumatologic diagnosis were included. Electronic health literacy was assessed with eHEALS higher scores indicating better electronic medical understanding. The impact of SM on daily life was evaluated with social media

Table 1. Social Media and Artificial Intelligence perception for rheumatic disease knowledge

	< 45 years n=39	>45 years n=56	p-value
Hours using SM			
< 2 hours	33 (84.6)	47 (83.9)	0.245[a]
2-4 hours	5 (12.8)	6 (10.7)	
Modified treatment based on SM			
Yes	1 (2.6)	9 (16.1)	**0.043[a]**
No	38 (97.4)	47 (83.9)	
Used AI for disease information			
Yes	17 (43.6)	12 (21.4)	**0.047[a]**
No	22 (56.4)	43 (76.8)	
Modified treatment based on AI			
Yes	0	2 (3.6)	0.198[a]
No	39 (100)	53 (94.6)	
Has the internet change your way of thinking about your disease			
Yes	26 (66.7)	28 (50)	0.182[a]
No	13 (33.3)	27 (48.2)	
Would you use SM if your doctor recommended it?			
Yes	38 (97.4)	49 (87.5)	0.135[a]
No	1 (2.6)	7 (12.5)	
Morisky-Green test			
Adherence	17 (43.6)	20 (54.1)	0.439[b]
No adherence	22 (56.4)	36 (64.3)	
eHEALS	28 (25-33)	21 (16-32)	**0.010[c]**
SMEQ	18 (13-26)	11 (7-17)	**<0.001[c]**
AIAS-4	31 (24-37)	30 (15-37)	0.522[c]

a Fisher´s exact test; b Chi-square test; c Mann-Whitney´s U test; SM: Social media; AI: Artificial Intelligence; eHEALS: eHealth literacy scale; SMEQ: Social media engagement questionnaire; AIAS-4: Artificial Intelligence Attitude Scale

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

engagement questionnaire (SMEQ), higher scores indicating more involvement of SM. Morisky-Green test was used to evaluate treatment adherence, with a score > 3 indicating adherence. To assess the perspective of AI, Artificial Intelligence Attitude Scale (AIAS-4) was utilized. A comparison was done between two groups of ages (< 45 and >45 years). Descriptive analysis was performed. Chi-square test and Mann-Whitney´s U test were utilized, as appropriate. A p-value < 0.05 was considered significant.

Results: A total of 95 patients were included, of whom 88 patients were women (92.6%), with a median age of 50 (IQR: 39-60). The most common diagnoses were rheumatoid arthritis (n=46/48.4%) and systemic lupus erythematous (n=27/28.5%). The most common duration of disease was 1-4 years (n=39/41.4%). Most patients use smartphones (96.8%), and 58.9% use computers. In addition, 94.7% of patients use SM daily, with Facebook being the most common (n=68/71.6%) and spending less than two hours seeking information about their disease (n=80/84.3). Regarding the use of AI, 45 patients (47.4%) use AI, and 29 patients (30.5%) have used AI to seek information about their disease. Half of the patients (56.8%) believe that the internet has changed their perspective of their disease, making them more interested in their condition (n=23/24.3%). Most patients consider that their doctor is open to talking about the information found on internet platforms (n=80/84.2%) and would use SM if their doctor recommended it (n=87/91.6%). Patients < 45 years (n=39) were less likely to modify their treatment based on information found on SM and tend to use more AI to seek information about their disease, compared to patients >45 years (n=56) (p= 0.043, p=0.047, respectively). Regarding eHEALS, patients < 45 years have more electronic health literacy than patients > 45 years (p=0.010) and tend to be more involved in SM (p= < 0.001). There were no significant differences between treatment adherence and the perspective of their disease based on the information from SM or AI (Table 1).

Conclusion: More than half of our patients believe that the internet has changed their perspective of their disease, making them more interested in their condition. Younger patients have greater electronic health literacy, are more engaged in social media, and are more likely to use AI for health information. However, they are less prone to modifying their treatment based on this information.

Disclosure: E. Sanchez-Peralta: None; **P. Gamez-Siller**: None; **A. Garza-Elizondo**: None; **F. Fuentes-Rios**: None; **G. Garcia-Ramos**: None; **D. Gauna Leal**: None; **A. Silva-de Leon**: None; **N. Valdez-Benavides**: None; **J. Cardenas-de la Garza**: None; **M. Alarcon-Jarquin**: None; **D. Galarza-Delgado**: None; **D. Flores-Alvarado**: None.

Abstract Number: 2607

ERS-RA as a Tool for Cardiovascular Risk Prediction in Established Rheumatoid Arthritis: An External Validation

Misti Paudel[1], Katherine Liao[2], Jon Giles[3], Joan Bathon[4], Hongshu Guan[5], Brendan Everett[6], Leah Santacroce[7], Nancy Shadick[8], Michael Weinblatt[9], Pamela Rist[6] and Daniel Solomon[10], [1]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [2]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, USA, Boston, MA, [3]Cedars Sinai Medical Center, Los Angeles, CA, [4]Columbia University, NEW YORK, NY, [5]Brigham and Women's Hospital/ Harvard Medical School, Boston, [6]Brigham and Women's Hospital and Harvard Medical School, Boston, [7]Brigham and Women's Hospital, Boston, MA, [8]Brigham & Women's Hospital, Boston, MA, [9]Brigham and Women's Hospital/ Harvard Medical School, Waban, MA, [10]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: ARP II: Perception, Prediction, and Prevention (2603–2608)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: The Expanded Risk Model for Rheumatoid Arthritis (ERS-RA) incorporates traditional CV risk factors and RA-related measures of disease activity and has demonstrated better performance compared to a traditional cardiovascular (CV) risk factor model. Additional external validations are needed to better understand the utility of ERS-RA in different patient groups with RA.

Methods: We used data from the longitudinal Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study (BRASS). We obtained CV endpoints from three data sources: 1) self-reported CV events in BRASS, assessed annually, 2) linkage to Medicare/Medicaid claims, and 3) linkage to electronic health records (EHR). We used validated algorithms to define CV events in claims. We searched for and adjudicated CV events in EHRs with diagnosis and procedure codes. Due to uncertainty in accuracy of self-reported CV events, we included events from claims and EHR in primary analyses (narrow definition) and integrated self-reported events as a third source (broad definition). We defined follow-up as time from enrollment until first CV event or last study visit and truncated at 10 years. For the narrow CV definition, participants were censored at the visit prior to their self-reported CV event. We restricted to participants aged 20-80 years at enrollment and excluded participants with prevalent CV at baseline. We used multiple imputations with fully conditional specification to impute missing covariates. Model performance was assessed by evaluating discrimination (C-statistic) and visual inspection of calibration plots. Additionally, model performance was evaluated by dichotomizing predicted 10-year risk as < 7.5% vs. ≥7.5% and < 10% vs. ≥10%.

Results: We identified 1,332 participants in BRASS without evidence of CV events at baseline. The cohort had a mean age of 54 years; 16% were male; 8% current smokers; 6% diabetes; 22% hyperlipidemia; and 30% hypertension. RA duration was < 5 years in 37%; and 71% were rheumatoid factor positive. The mean follow-up was 81 (SD 41) months [approximately 6.8 (3.4) years]. We observed 71 (5%) participants with a CV event (narrow definition) and 166 (12%; broad definition). We observed c-statistics of 0.659 (broad definition) and 0.810 (narrow definition) (**Table 1)**. Calibration curves (**Figure 1**) indicated slight overprediction of CV risk using the narrow definition, with tighter calibration for lower predicted risk values. Conversely, using the broad definition, we observed slight underprediction of CV risk and less precision. Using a cut-point of <

Table 1. Model Performance of the ERS-RA for Broad and Narrow CV Definitions

Metric	CV Event Definitions	
	Broad definition	Narrow definition
Number of patients with a CV event	166	71
Observed %	12.5	5.3
Predicted %	31.8	31.8
Absolute difference, %	19.4	26.5
C-statistic	0.659	0.810
Predicted 10-year risk: <7.5% vs. ≥7.5% predicted risk		
Participants with ≥7.5% predicted risk, n (%)	424 (31.8)	424 (31.8)
Sensitivity, %	54.2	78.9
Specificity, %	71.4	70.8
Positive Predictive Value, PPV, %	21.2	13.2
Negative Predictive Value, NPV, %	91.6	98.4
Predicted 10-year risk: <10% vs. ≥10% predicted risk		
Participants with ≥10% predicted risk, n (%)	307 (23.1)	307 (23.1)
Sensitivity, %	41.6	63.4
Specificity, %	79.6	79.2
Positive Predictive Value, PPV, %	22.5	14.7
Negative Predictive Value, NPV, %	90.5	97.5

Abbreviations: CV = cardiovascular; Broad CV definition = events from Medicare/Medicaid claims, electronic health records and/or self-reported. Narrow CV definition= events from Medicare/Medicaid and/or electronic health records.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

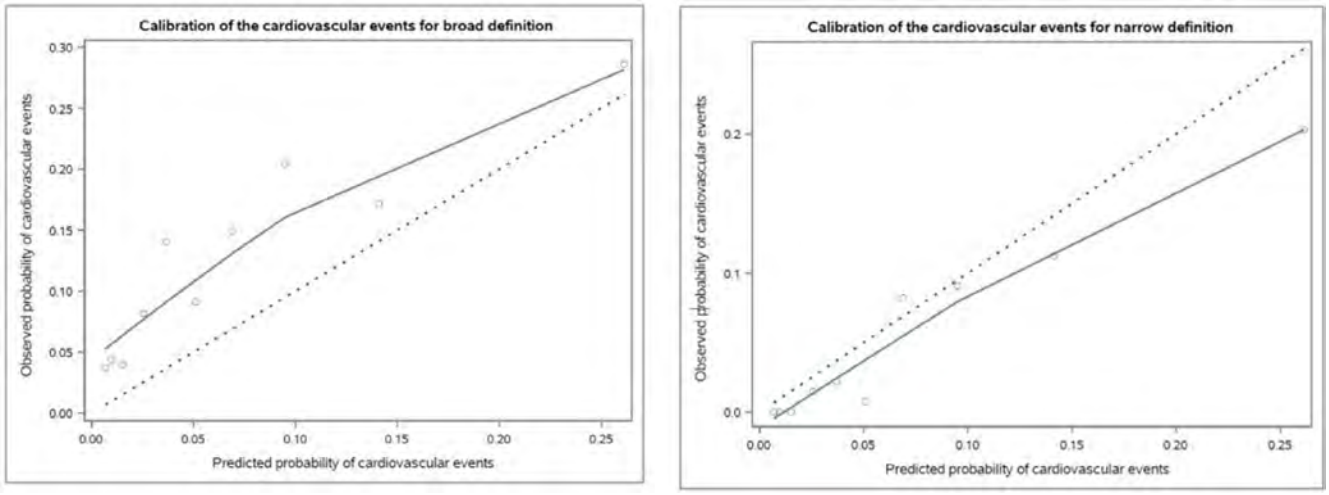


Figure 1. Calibration Curves for Broad and Narrow CV Definitions

7.5% we observed sensitivity (0.542 vs. 0.789), specificity (0.714 vs. 0.708), positive predictive value (PPV, 0.212 vs. 0.132), and negative predictive value (NPV, 0.916 vs. 0.984) for broad and narrow definitions, respectively. Results were similar for a cut-point of 10% predicted risk.

Conclusion: In this cohort of individuals with established RA the ERS-RA generally demonstrated good discrimination and calibration for CV events defined using validated algorithms in claims and EHR; however, its precision was lower when self-reported CV events were included.

Disclosure: M. Paudel: None; **K. Liao**: Merck, 2; **J. Giles**: AbbVie/Abbott, 2, Eli Lilly, 2, Genentech, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Sana, 2; **J. Bathon**: AbbVie/Abbott, 2, Merck, 2, Ono Pharma, 2; **H. Guan**: None; **B. Everett**: American Heart Association, 2, FDA, 2, Kowa, 1, Merck, 2, NIDDK, 2, Novo Nordisk, 2, 5, PCORI, 5, UpToDate, 9; **L. Santacroce**: None; **N. Shadick**: Bristol-Myers Squibb(BMS), 5, Janssen, 5; **M. Weinblatt**: aclaris, 2, amgen, 2, anaptysbio, 2, Artiva Bio, 2, Biohaven, 2, Bristol-Myers Squibb(BMS), 2, 5, Canfite, 11, Curie Bio, 2, Deep Cure, 2, Eli Lilly, 2, Gilead, 2, Ignite, 2, Inmedix, 11, Janssen, 5, Janux Therapeutics, 2, Johnson and Johnson, 2, Lifordi, 2, Marvel Bio, 2, Matchpoint, 2, Merck/MSD, 2, Neutrolis, 2, Novartis, 2, Sana, 2, Santa Ana, 2, Sci Rhom, 2, scipher medcine corp, 11, SetPoint Medical, 2, Surf Therapeutics, 2, Thymmune, 2, Xencorp, 2, ZuraBio, 2; **P. Rist**: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9.

Abstract Number: 2608

Metabolic dysfunction-Associated Steatotic Liver Disease, Cardiometabolic Risk Factors, and Cardiac Manifestations in Psoriasis

Maria Dons[1], Charlotte Näslund-Koch[2], Morten Sengeløv[3], Sofie Bøgh-Sørensen[3], Kristoffer Skaarup[3], Marianne Bengtson Løvendorf[4], Filip Davidovski[3], Anne Marie Reimer Jensen[3], Brittany Weber[5], Lise Lotte Gluud[6], Claus Zachariae[2], Lone Skov[2] and Tor Biering-Sørensen[3], [1]Copenhagen University Hospital Gentofte, Copenhagen, Hovedstaden, Denmark, [2]Dep. of Dermatology and Allergy, Copenhagen University Hospital – Herlev & Gentofte, Copenhagen, Hovedstaden, Denmark, [3]Center for Translational Cardiology and Pragmatic Randomized Trials, Dep. of Cardiology, Copenhagen University Hospital - Gentofte, Copenhagen, Hovedstaden, Denmark, [4]Department of Dermatology and Allergy, Copenhagen University Hospital – Herlev & Gentofte, Copenhagen, Hovedstaden, Denmark, [5]Brigham and Women's Hospital, DEDHAM, MA, [6]Gastro Unit, Copenhagen University Hospital – Hvidovre, Copenhagen, Hovedstaden, Denmark

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

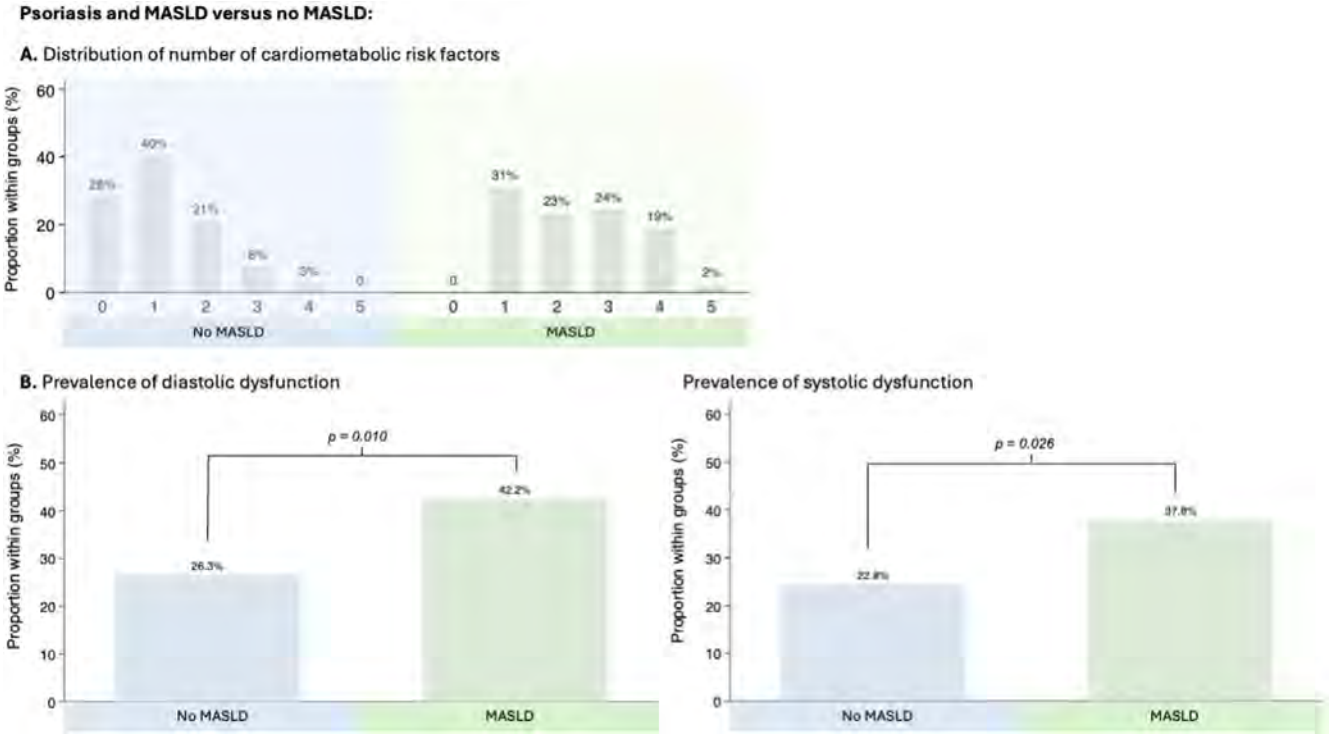
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: ARP II: Perception, Prediction, and Prevention (2603–2608)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Metabolic dysfunction-associated steatotic liver disease (MASLD) is increasingly recognized as a cardiometabolic risk factor. Individuals with psoriasis have a high prevalence of MASLD, yet the association between MASLD and cardiac manifestations in this population remains unclear.

We aimed to evaluate associations between MASLD, cardiovascular risk factors, and cardiac structure and function in adults with psoriasis.

Methods: A total of 261 adults with psoriasis were consecutively enrolled in the PSOCADIA study (Prevalence and risk factors asSOciated with CArdiac comorbiDIty in psoriAsis, ClinTrials.gov: NCT04950218) from the Copenhagen Translational Skin Immunology Biobank and Research Programme (BIOSKIN). Participants underwent clinical assessment, transthoracic echocardiography, transient elastography (TE), and blood withdrawal. MASLD was defined as hepatic steatosis on TE with controlled attenuation parameter ≥ 250 dB and presence of ≥ 1 cardiometabolic risk factor(s), excluding other causes of liver disease. Measures of cardiac structure and function were compared between psoriasis patients with MASLD and those without MASLD. Associations between MASLD, diastolic and systolic dysfunction were assessed in uni- and multivariable regression models.

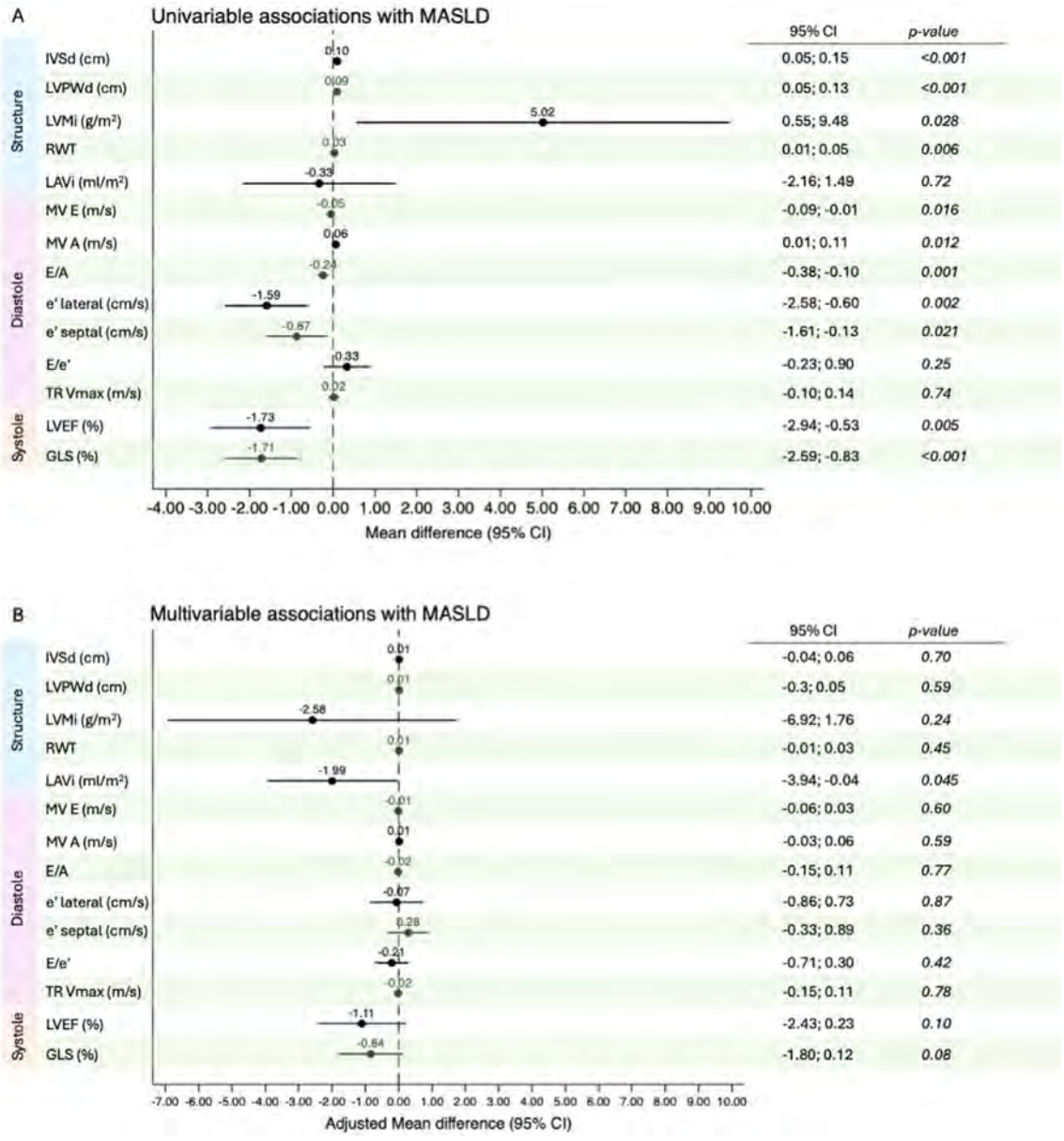
Results: We prospectively enrolled 261 individuals with psoriasis (median age 53.5 years, 46.4% women), whereof 20.7% had psoriatic arthritis. MASLD was present in 90 patients (34.5%) of whom 7 (8%) had possible advanced fibrosis. Compared to individuals without MASLD, those with MASLD exhibited higher blood pressure, higher body mass index (BMI),



Cardiometabolic risk factors and myocardial dysfunction in adults with psoriasis with and without MASLD. A) Distribution of the number of cardiometabolic risk factors and B) Prevalence of diastolic and systolic dysfunction in individuals with psoriasis with and without MASLD. Bars represent the proportion of individuals (%) within each group. Cardiometabolic risk factors included obesity, hypertension, dyslipidemia, diabetes, and metabolic syndrome. Abbreviations: MASLD, metabolic dysfunction-associated liver disease.

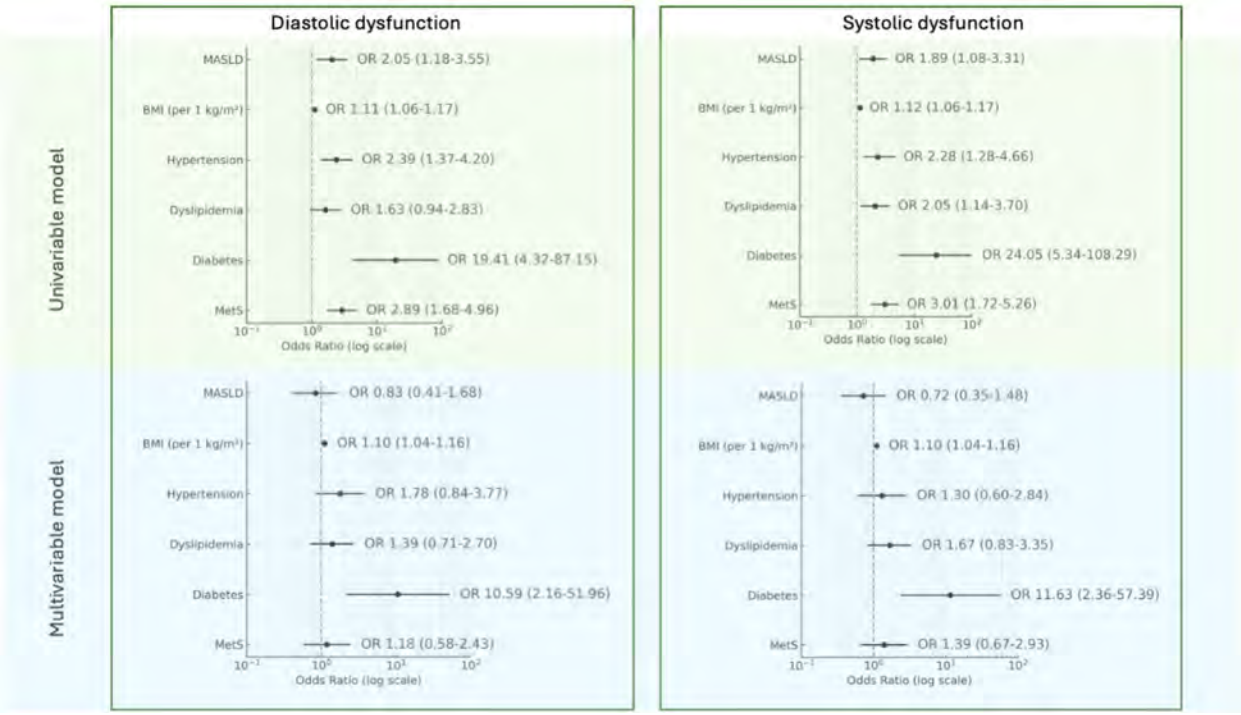
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and more adverse cardiometabolic profiles including more prevalent diabetes (14.4% vs. 1.9%, $p < 0.001$). MASLD was associated with structural measures indicative of cardiac hypertrophy and worse measures of diastolic and systolic function. However, after adjusting for age, sex, and BMI, these associations were no longer statistically significant. In fully adjusted models, MASLD was not associated with diastolic or systolic dysfunction. In contrast, higher BMI and diabetes remained independently associated with myocardial dysfunction.



Association between MASLD and cardiac structure and function in A) uni- and B) multivariable models adjusted for age, sex, and BMI. Mean differences (x-axis) in echocardiographic measures of cardiac structure, diastolic and systolic function (y-axis) in MASLD compared to no MASLD in the study population. Mean differences plotted with 95% confidence intervals in A) univariable linear regression models and B) multivariable linear regression models adjusted for age, sex, and BMI. Abbreviations: IVSd, Interventricular septum diameter; LVPWd, Left ventricular posterior wall diameter; LVMi, Left ventricular mass index; RWT, Relative wall thickness; LAVi, Left atrial volume index; MV E, Mitral valve early filling velocity; MV A, Mitral valve atrial contraction velocity; E/A, Ratio of early to late mitral inflow velocities; e', Early diastolic mitral annular velocity; E/e', Ratio of early mitral inflow to mitral annular velocity; TR Vmax, Tricuspid regurgitation peak velocity; LVEF, Left ventricular ejection fraction; GLS, Global longitudinal strain.

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Associations between MASLD, cardiometabolic risk factors and myocardial dysfunction in psoriasis. Uni- and multivariable associations between risk factors and diastolic and systolic dysfunction. Forest plots display odds ratios (OR) for diastolic dysfunction (left panels) and systolic dysfunction (right panels) on logarithmic scale with 95% confidence intervals for MASLD and other key cardiometabolic risk factors. Top panels show univariable models for each risk factor, while bottom panels show fully adjusted models for age, sex, and all risk factors. Abbreviations: MASLD, metabolic dysfunction-associated steatotic liver disease; BMI, body mass index; MetS, metabolic syndrome.

Conclusion: In adults with psoriasis, associations between MASLD and abnormal cardiac structure and function were attenuated after adjustment for cardiometabolic risk factors, underscoring the importance of risk factor control in individuals with psoriasis and concomitant MASLD. This may also reflect that most adults with psoriasis and MASLD did not have hepatic fibrosis in this cohort.

Disclosure: M. Dons: Karen Elise Jensens Foundation, 5, Lundbeck Foundation, 5; **C. Näslund-Koch**: AbbVie/Abbott, 12, Investigator, CSL Behring, 12, Investigator, Danish National Psoriasis Foundation, 5, Ellab Foundation, 5, Galderma, 12, Investigator, Kgl. Hofbundtmager Aage Bang Foundation, 5, Krista and Viggo Petersens Foundation, 5, LEO foundation, 2, 5, 6, LEO Pharma, 12, Investigator, Novartis, 12, Investigator, Siemens Healthcare, 5, UCB, 6; **M. Sengeløv**: None; **S. Bøgh-Sørensen**: None; **K. Skaarup**: None; **M. Løvendorf**: None; **F. Davidovski**: None; **A. Jensen**: None; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2; **L. Gluud**: AstraZeneca, 1, 2, Beckton Dickinson, 2, Boehringer-Ingelheim, 1, 2, Ipsen, 12, Support for attending meetings and/or travel, Novo Nordisk, 1, 2, 5, 6, Sobi International, 5; **C. Zachariae**: None; **L. Skov**: AbbVie/Abbott, 1, 6, Almirall, 1, 5, Bristol-Myers Squibb(BMS), 1, 5, 6, Eli Lilly, 1, 6, Janssen, 1, 5, 6, Novartis, 1, Pfizer, 6, Sanofi, 1, 5, 6, stada, 1, takeda, 1, 6, UCB, 1, 5, 6; **T. Biering-Sørensen**: Amgen, 2, AstraZeneca, 5, 6, Bayer, 6, Boston Scientific, 5, CSL Seqirus, 2, GE Healtcare, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, IQVIA, 2, Novartis, 5, 6, Novo Nordisk, 2, 5, Parexel, 2, Pfizer, 5, Sanofi Pasteur, 2, 5, 6.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

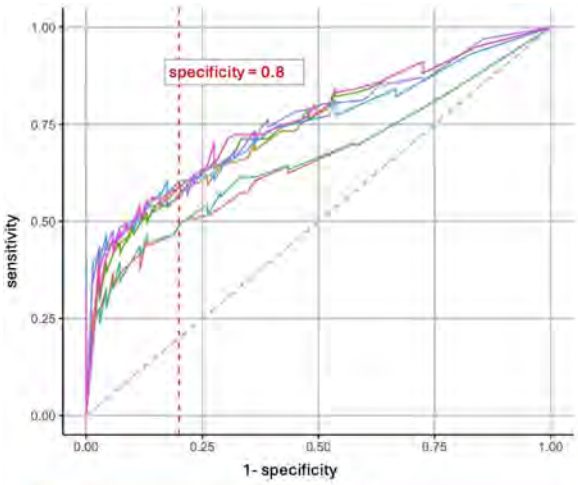
Abstract Number: 2609

Evaluation of the Performance of Candidate Enthesitis Ultrasound Scoring Systems for Psoriatic Arthritis Diagnosis – DUET Study

Nam Nguyen[1], Mu Yang[2], Sibel Aydin[3], Gurjit Kaeley[4], Richard Cook[2] and Lihi Eder[1], [1]University of Toronto, Toronto, ON, Canada, [2]University of Waterloo, Waterloo, Canada, [3]Department of Medicine, University of Ottawa, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [4]UF COM-J, Ponte Vedra Beach, FL

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Imaging of Rheumatic Diseases (2609–2614)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Psoriatic arthritis (PsA) is often diagnosed late, leading to worse outcomes. Enthesitis is a key feature that can aid in early detection, but its clinical assessment is unreliable. Ultrasound (US) offers a more objective method for evaluating enthesitis, yet standardization remains a challenge. The GRAPPA Ultrasound Working Group is developing the Diagnostic Ultrasound Enthesitis Tool (DUET), a PsA-specific sonographic enthesitis scoring system to distinguish PsA from non-inflammatory conditions. While DUET has been derived from a discovery cohort, external validation is needed before its clinical adoption. In this study, we aimed to evaluate the discriminative ability of candidate DUET scores using independent data to inform the selection of a DUET scoring system.

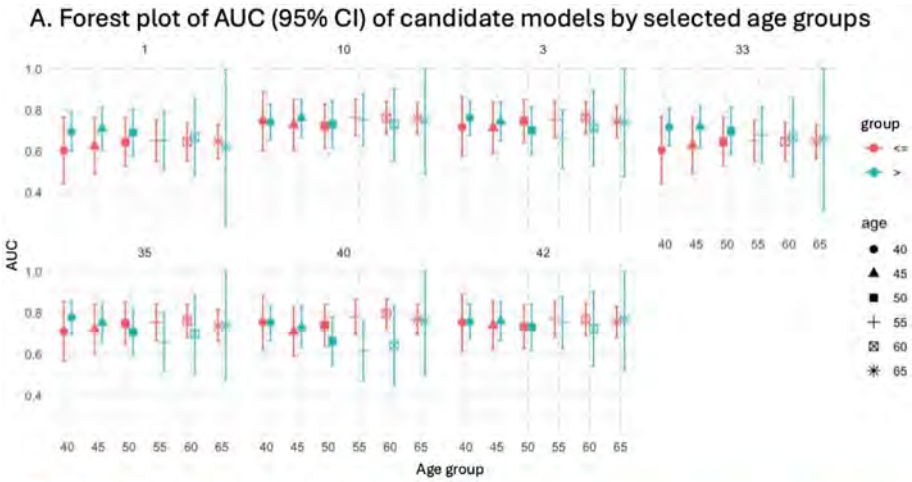


Risk score	Sites included	Formula	AUC
1	Pat, Ach	0.154*(PD+Hypo+Thick)+0.093*(Enth+3*Eros)-0.105	0.66
3	Pat, Ach, Tric	0.109*(PD+Hypo+Thick)+0.069*(Enth+3*Eros)-0.152	0.74
10	Pat, Ach, Tib, Tric	0.082*(PD+Hypo+Thick)+0.061*(Enth+3*Eros)-0.192	0.75
33	Pat, Ach	0.142*(2*PD+Hypo+Thick)+0.091*(Enth+3*Eros)-0.133	0.66
35	Pat, Ach, Tric	0.095*(2*PD+Hypo+Thick)+0.068*(Enth+3*Eros)-0.187	0.75
40	Pat, Ach, Quad, Tric	0.066*(2*PD+Hypo+Thick)+0.037*(Enth+3*Eros)-0.131	0.76
42	Pat, Ach, Tib, Tric	0.066*(2*PD+Hypo+Thick)+0.064*(Enth+3*Eros)-0.204	0.76

Pat: patellar tendon origin at patella; Ach: Achilles tendon; Tric: tricep tendon; Quad: quadricep tendon insertion at patella; Tib: patellar tendon insertion at tibial tuberosity; PD: Power doppler grade (0-3); Hypo: hypoechogenicity (0-1); Thick: Thickening (0-1); Enth: Enthesophyte (0-3); Eros: erosion (0-1).

Figure 1. ROC curve of candidate DUET scores

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



B. AUC of candidate models by age group

Risk score	≤40 (N=49)	>40 (N=121)	≤45 (N=69)	>45 (N=101)	≤50 (N=86)	>50 (N=84)	≤55 (N=110)	>55 (N=60)	≤60 (N=137)	>60 (N=33)	≤65 (N=155)	>65 (N=15)
1	0.60	0.70	0.63	0.71	0.65	0.69	0.65	0.65	0.65	0.67	0.65	0.62
3	0.72	0.76	0.71	0.75	0.75	0.70	0.76	0.66	0.76	0.71	0.75	0.74
10	0.75	0.74	0.73	0.76	0.72	0.73	0.76	0.75	0.76	0.73	0.76	0.75
33	0.61	0.72	0.63	0.72	0.65	0.70	0.65	0.68	0.65	0.67	0.65	0.66
35	0.71	0.78	0.72	0.75	0.75	0.71	0.76	0.66	0.76	0.70	0.74	0.74
40	0.76	0.75	0.71	0.73	0.74	0.66	0.78	0.62	0.80	0.64	0.77	0.76
42	0.75	0.76	0.74	0.76	0.73	0.73	0.77	0.75	0.77	0.72	0.76	0.77

Figure 2. Discriminative ability of candidate DUET scores stratified by age groups

Methods: This retrospective cross-sectional study analyzed US scans from PsA patients and non-psoriatic controls collected in a single centre following standard protocol. All PsA patient met the DUET enrollment criteria including PsA duration < 5 years and were not using biologics. Controls had no psoriasis or other autoimmune disease. Enthesis US scans of the quadriceps, proximal and distal patellar tendons, triceps and Achilles were scored by a single reader blinded to the diagnosis for entheseal elementary lesions including hypoechogenicity, thickening, Doppler signal, enthesophytes, calcifications and erosions. We evaluated seven candidate DUET scores, each incorporating different combinations of entheseal sites and elementary lesions. Models were refitted using coefficients estimated in the discovery cohort. Model performance was also stratified by age group.

Results: In our validation cohort of 102 PsA patients and 69 controls, the seven candidate DUET risk scores yielded areas under the curve (AUCs) ranging from 0.660 to 0.764 (Figure 1). Stratifying the risk scores by age with a cutoff of 55 years enhanced AUCs to 0.781 (under 55) and 0.753 (over 55) (Figure 2).

Conclusion: The candidate DUET scores demonstrated discriminative ability in an external validation cohort, with additional improvement following age stratification. These findings will guide further refinement of the selected DUET score and inform its integration into clinical and research settings.

Disclosure: N. Nguyen: None; **M. Yang**: None; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **G. Kaeley**: AbbVie/Abbott, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Janssen, 5, Novartis, 5; **R. Cook**: None; **L. Eder**: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2610

Imaging remission in aortitis associated with giant cell arteritis. Multicenter study with tocilizumab in monotherapy and combined therapy

Adrian Martin-Gutierrez[1], Javier Loricera[2], Diana Prieto-Peña[3], Vicente Aldasoro Cáceres[4], Olga Maiz[5], Eugenio de Miguel[6], Eva Galíndez Agirregoikoa[7], Ivan Ferraz Amaro[8], Santos Castañeda[9], Ricardo Blanco[10] and Tocilizumab in Giant Cell Arteritis Spanish Collaborative Group, [1]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Renedo de Pilagos, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Spain, [3]Division of Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain., Santander, Spain, [4]Hospital Universitario de Navarra, Pamplona, Spain, [5]Hospital Universitario de Donosti, Donostia, Spain, [6]Hospital Universitario La Paz, Madrid, Spain, [7]BASURTO UNIVERSITY HOSPITAL, BILBAO, Spain, [8]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [9]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [10]Rheumatology Division, Hospital Universitario Marqués de Valdecilla, IDIVAL, Immunopathology Group, Santander, Spain, Santander, Cantabria, Spain

Table 1. Main general features of 196 patients with aortitis associated with Giant Cell Arteritis at tocilizumab initiation.

	Overall n=196	TCZcombo n=60	TCZmono n=136	p
Age, years, mean ± SD	71.3±9.5	70.3±9.5	70.4±9.4	0.3451
Sex, female/male, n (% female)	148/48 (75.5)	43/17 (71.7)	105/31 (77.2)	0.4715
Time from GCA diagnosis to TCZ start (months), median [IQR]	7 [2-18.7]	13 [4-27]	5 [2-14.8]	**0.0120**
Newly Diagnosed/Refractory GCA, n/n (% Newly diagnosed)	33/163 (16.8)	4/56 (6.7)	29/107 (21.3)	**0.0120**
Extracranial phenotype, n (%)	126 (64.3)	24 (40)	46 (33.8)	0.4224
Mixed phenotype, n (%)	70 (35.7)	36 (60)	90 (66.2)	0.4224
CRITERIA				
GiACTA, n (%)	145 (74)	44 (73.3)	101 (77.7)	0.5825
ACR 1990, n (%)	105 (54)	29 (48.3)	76 (55.9)	0.2788
ACR/LVV, n (%)	120 (61.2)	42 (84)	78 (86.6)	0.8016
Cardiovascular risk factors, n (%)				
High blood pressure	112 (57)	36 (64.3)	76 (57.1)	0.3615
Dyslipidaemia	103 (53)	30 (53.6)	73 (54.9)	0.8683
Diabetes	26 (13)	8 (14.3)	18 (13.5)	0.9061
Previous or current smoking history	20 (10)	6 (10.7)	14 (10.4)	0.9999
SYSTEMIC MANIFESTATIONS, n (%)				
PMR	131 (67.2)	45 (75)	86 (63.7)	0.1210
Constitutional syndrome	87 (44.6)	21 (35)	66 (48.9)	0.0717
Fever	24 (12.4)	6 (10)	18 (13.4)	0.6391
ISCHEMIC MANIFESTATIONS, n (%)				
Headache	74 (37.8)	22 (38)	52 (38.2)	0.8057
Jaw claudication	27 (14.4)	5 (8.5)	22 (17.1)	0.1776
Visual impairment	16 (8.2)	5 (8.3)	11 (8.08)	0.5955
Stroke	2 (1)	0 (0)	2 (1.5)	0.9999
LABORATORY				
ESR, mm/1st hour, median [IQR]	32 [14-54]	28 [11.3-50.5]	32 [15-58]	0.1852
CRP, mg/dL, mean (SD)	2.9±3.9	2±1.8	3.3±4.4	**0.0078**
Hb, g/dL, mean (SD)	12.5±1.65)	12.3±1.4	12.6±1.7	0.2323
POSITIVE TEMPORAL ARTERY BIOPSY, n (%)	56 (50)	18 (48.6)	38 (50.7)	0.9999
Previous conventional synthetic DMARDs, n (%)	116 (59.1)	58 (96.7)	57 (41.9)	**<0.0001**
MTX	108 (55.1)	53 (88.3)	55 (40.4)	**<0.0001**
AZA	4 (2)	4 (6.7)	0 (0)	**0.0116**
SSZ	2 (1)	0 (0)	2 (1.4)	0.9999
HCQ/ICQ	1 (0.5)	1 (1.7)	0 (0)	0.9999
MMF	1 (0.5)	1 (1.7)	0 (0)	0.9999
Previous biological therapy, n (%)	2 (1)	1 (1.7)	1 (0.7)	0.9999
GLUCOCORTICOIDS AT TCZ INITIATION				
Prednisone at TCZ initiation, mg/day, median [IQR]	15 [10-30]	10 [7.5-20]	15 [10-30]	**0.0013**
ROUTE OF ADMINISTRATION OF TOCILIZUMAB				
Intravenous /subcutaneous, n/n (% intravenous)	110/86 (56.1)	41/19 (68.3)	69/67 (50.7)	**0.0221**

***Abbreviations**: ACR: American College of Rheumatology; ACR/LVV: Large vessel vasculitis: ACR criteria of GCA with a positive image suggestive for aortitis; AZA: azathioprine; CQ: chloroquine; CRP: C-reactive protein; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; ESR: erythrocyte sedimentation rate; GiACTA: Giant Cell Arteritis Actemra trial; Hb: hemoglobin; HCQ: hydroxychloroquine; IFX: infliximab; IQR: interquartile range; LFN: leflunomide; MMF: mycophenolate mofetil; n: number; PET/CT: positron emission tomography/computed tomography scan; PMR: polymyalgia rheumatica; RTX: rituximab; SD: standard deviation; SSZ: sulfasalazine; TCZ: tocilizumab. The significance of the imaging tests was calculated according to the number of examinations done.*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Imaging of Rheumatic Diseases (2609–2614)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Aortitis is a frequent and potential severe complication of giant cell arteritis (GCA)(GCA-aortitis). Tocilizumab (TCZ) was approved for the treatment of GCA, but its efficacy in GCA-aortitis has not been specifically studied in randomized clinical trials. GCA-aortitis may be more refractory to TCZ than classic cranial GCA phenotype.

Our aim was to assess the effectiveness and safety of TCZ in monotherapy (TCZmono) compared to TCZ combined with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs)(TCZcombo) in GCA-aortitis in clinical practice. To study associative factors associated with imaging remission.

Methods: Comparative multicenter observational study of GCA-aortitis treated with TCZcombo vs TCZmono. Outcomes, at 12 and 24 months, were: clinical, EULAR, and imaging remission (^{18}F-FDG PET/CT vascular uptake lower than liver uptake), glucocorticoid-sparing effect and safety data. Associative factors associated with imaging remission (multivariable logistic regression) were determined at 24 months.

Results: 196 patients (148 female/48 male) with GCA-aortitis treated with TCZ (136 TCZmono/60 TCZcombo) (**Table 1**). After 24 months since the initiation of TCZ, imaging remission (50% vs.15.8%; p=0.026) was higher with TCZcombo (**Figure**). In contrast, there were no differences in EULAR and clinical remission. Prednisone sparing effect was higher in TCZcombo. In addition, a non-statistically lower adverse events rate was observed in TCZcombo (8.7 vs. 13.2 vs. adverse

Table 2. Multivariable analysis through stepwise logistic regression of associative factors with imaging remission at 24 months of initiation of TCZ.

IMAGING REMISSION at 24 month	Univariable		Multivariable	
	OR (CI 95%)	p	OR (CI 95%)	p
Age, years, mean ± SD	1.015 (0.927-1.112)	0.708		
Sex, female/male, n (% female)	0.857 (0.178-4.126)	0.847		
Time from GCA diagnosis to TCZ start (months), median [IQR]	0.947 (0.930-1.020)	0.198	0.959 (0.896-1.026)	0.211
Newly Diagnosed/Refractory GCA: n/n (% Newly diagnosed)	1.250 (0.205-7.615)	0.809		
Extracranial: n (%)	0.476 (0.118-1.929)	0.295		
Cardiovascular risk factors, n (%)				
High blood pressure	1.167 (0.269-5.054)	0.999		
Dyslipidaemia	0.769 (0.185-3.191)	0.717		
Diabetes	846201707 (0-)	0.290		
Previous or current smoking history	0.870 (0.70-10.728)	0.999		
SYSTEMIC MANIFESTATIONS, n (%)				
PMR	3.250 (0.708-14.921)	0.130	1.829 (0.299-11.187)	0.513
Constitutional syndrome	1.056 (0.214-5.211)	0.947		
Fever	0 (0-0)	0.999		
Asthenia	1.071 (0.264-4.341)	0.999		
ISCHEMIC MANIFESTATIONS, n (%)				
Headache	1.062 (0.245-4.599)	0.813		
Jaw claudication	3871533733 (0-)	0.324		
Visual impairment	4038687107 (0-)	0.099		
LABORATORY				
ESR, mm/1st hour, median [IQR]	1.027 (0.997-1.058)	0.080	1.026 (0.996-1.057)	0.096
CRP, mg/dL, mean (SD)	1.111 (0.764-1.617)	0.666		
GLUCOCORTICOIDS AT TCZ INITIATION				
Prednisone at TCZ initiation, mg/day, median [IQR]	1.007 (0.950-1.066)	0.837		
ADMINISTRATION OF TOCILIZUMAB				
Intravenous /subcutaneous, n/n (% intravenous)	0.941 (0.217-4.074)	0.935		
Combination with others DMARDs	**5.333 (1.142-24.899)**	**0.026**	**5.259 (1.030-26.847)**	**0.046**

In this analysis, imaging remission is the dependent variable.

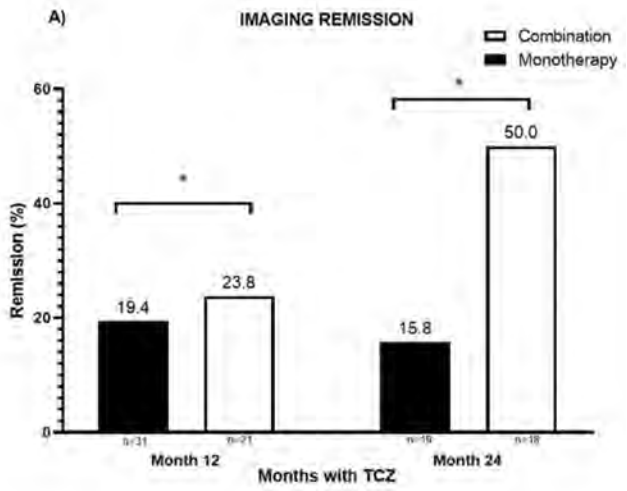
Abbreviations: CI: confidence intervale; ESR: erythrocyte sedimentation rate; Hb: haemoglobin: OR: odds ratio; PMR: polymyalgia rheumatica; TCZ: tocilizumab.

Multivariable analysis is adjusted by "Time from GCA diagnosis to TCZ start", "PMR", "ESR".

Statistical significance (p<0.05) is expressed as **bold** characters.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Imaging remission at 12 and 24 months after initiation of tocilizumab in a wide series of GCA-aortitis patients. Comparison between tocilizumab in monotherapy vs. tocilizumab combined with disease-modifying antirheumatic drugs.



+ No significant differences; *p<0.05
GCA: giant cell arteritis; TCZ: tocilizumab.

events 100 patients/year; p=0.21). In a multivariable logistic study TCZcombo vs TCZmono increases the imaging remission 5.26-fold (OR 5.26 (95% CI: 1.03-26.85; p=0.046) at 24-month follow-up (**Table 2**).

Conclusion: In GCA-aortitis, TCZ therapy combined with csDMARDs may be more effective than TCZmono in imaging remission without increasing adverse events.

Disclosure: A. Martin-Gutierrez: None; **J. Loricera**: AbbVie/Abbott, 5, AstraZeneca, 2, 5, 6, Celgene, 2, 5, 6, Eli Lilly, 5, Janssen, 5, Merck/MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 5, Roche, 2, 5, 6, UCB, 2, 5, 6; **D. Prieto-Peña**: None; **V. Aldasoro Cáceres**: None; **O. Maiz**: None; **E. de Miguel**: AbbVie, 1, 5, 6, BMS, 6, Eli Lilly, 1, 6, Grunenthal, 6, Janssen, 1, 6, MSD, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 5, 6, Sanofi, 6, UCB, 6; **E. Galíndez Agirregoikoa**: None; **I. Ferraz Amaro**: None; **S. Castañeda**: None; **R. Blanco**: AbbVie/Abbott, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck/MSD, 2, 5, 6, Pfizer, 2, 6, Roche, 2, 5, 6.

Abstract Number: 2611

Exploring the Role of a Lung Ultrasound Score in the Assessment of Severity of Connective Tissue Disease-Related Interstitial Lung Disease

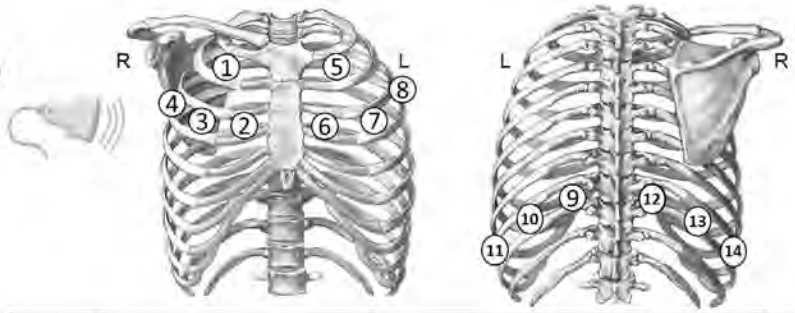
jin ding[1], ying zhang[1], Linxuan Pang[1], ning guo[2] and zhaohui zheng[1], [1]Department of Clinical Immunology, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China (People's Republic), [2]Department of Radiology, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Imaging of Rheumatic Diseases (2609–2614)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A



B

Site	B-line number score 0: none 1: <4 2: 4-6 3: >6 or fully integrated				Pleural line score 0: normal 1: coarse 2: irregular 3: discontinuous, fragmented				Am-line score 0: none 4: exist		Pleural effusion* score 0: none 5: exist	
	0	1	2	3	0	1	2	3	0	4	0	5
1												
2												
3 4												
5												
6												
7												
8												
9												
10												
11												
12												
13												
14												
Total												

Check the corresponding score at each site and then calculate the total score. Total score = Sum of 14 sites scores (B line score+ pleural line score) +Am-line score + pleural effusion score (range 0-93)

*: For the pleural effusion score of 5 to be considered, the presence of either B lines or pleural lines score is required.

Figure 1.The bilateral anterolateral posterior chest wall 14 intercostal lung ultrasound scanning method (A) and a lung ultrasound scoring system (B) for connective tissue disease related interstitial lung disease.

Background/Purpose: The role of lung ultrasound (LUS) in assessing disease severity of interstitial lung disease (ILD) remains unclear. We employed a semiquantitative scoring system to evaluate the ability of a LUS score to assess disease severity in patients with connective tissue disease (CTD) related ILD.

Methods: This study involved individuals from a prospective cohort of patients with CTD exhibiting respiratory symptoms or clinical suspicion of ILD who attended our hospital from December 2023 to December 2024. All patients underwent LUS, high-resolution CT (HRCT), and pulmonary function test (PFT) within one week. LUS was performed using a 14 intercostal scanning protocol, and the total LUS score was calculated using a semiquantitative scoring system (Figure 1). HRCT results were evaluated by two experienced radiologists and analyzed a commercial quantitative computed tomography (QCT) software. According to the Goh staging system, ILD was categorized as limited or extensive if < 20% or >20%, respectively, of the total lung area was affected. Differences in LUS scores across ILD severity groups were compared, and correlations between LUS scores and QCT and PFT results were analyzed. The stratification efficacy of the LUS score was evaluated using the area under of the receiver operating characteristic curve (AUC) with 95% confidence intervals (CI).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

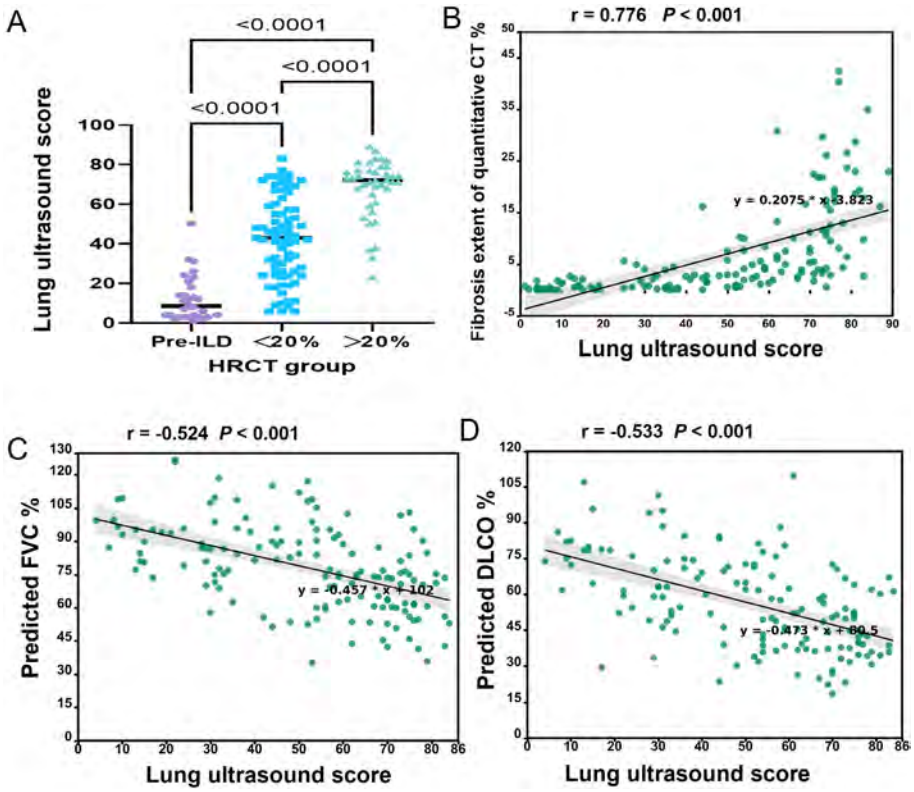
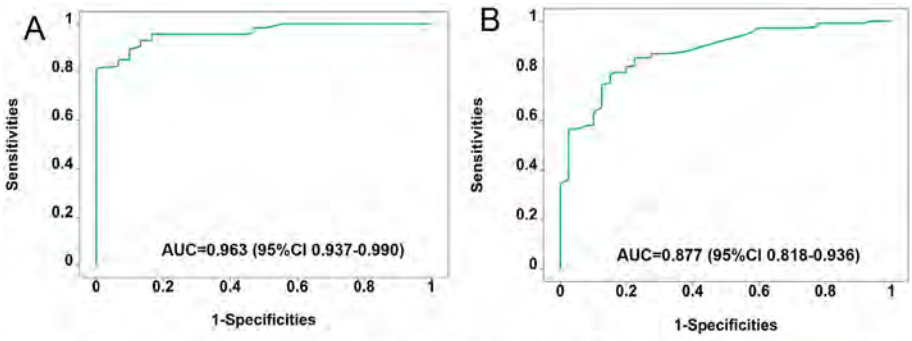


Figure 2. Differences in lung ultrasound scores among patients with connective tissue diseases related interstitial lung diseases of varying HRCT severity grading (A), as well as correlation between lung ultrasound scores and fibrosis extent on quantitative HRCT (B), predicted percentage of forced vital capacity (C), and predicted percentage of diffusing capacity of the lungs for carbon monoxide (D) in patients.

Results: A total of 146 patients with CTD-ILD were enrolled (mean age 56.1 ± 11.7 years; 108 [74.0%] female). Among these patients, 50 (34.2%) were diagnosed with idiopathic inflammatory myopathy; 35 with rheumatoid arthritis; 27 with Sjögren's disease; 20 with systemic sclerosis; 11 with systemic lupus erythematosus; and 3 with mixed connective tissue



C

Predictions of lung ultrasound score versus gradings of HRCT						
ILD		Lung ultrasound score grading			Total	Accuracy
HRCT grading		1(<20)	2(20-55)	3 (>55)		(%)
Preclinical	1	25	5	0	30	83.3
Limited (<20%)	2	5	46	25	76	60.5
Extensive (>20%)	3	0	6	34	40	85.0
	Total	30	57	58	146	71.9

quadratic weighted kappa = 0.736; 95% CI: 0.621–0.850

Figure 3. Receiver operating characteristic curves of lung ultrasound scores for distinguishing between preclinical ILD and ILD (A), as well as between limited and extensive ILD (B); and the predictions of lung ultrasound score versus HRCT gradings (C). AUC: area under the receiver operating characteristic curve.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disease. The cohort comprised 30 individuals classified with preclinical ILD, 76 with limited ILD, and 40 with extensive ILD. Patients with extensive ILD exhibited higher QCT parameters but lower PFT results than those with limited ILD or preclinical ILD. The median LUS scores in patients with extensive ILD were significantly higher (72, IQR 62–77) compared with those in the limited ILD (43, IQR 24.5–58.5) and preclinical ILD groups (8.5, IQR 3.0–18.75) ($P < 0.001$). Furthermore, LUS scores exhibited a positive correlation with fibrosis extent assessed by QCT ($r = 0.776$, $P < 0.001$) and negative correlations with diffusion capacity for carbon monoxide (DLCO) ($r = -0.533$, $P < 0.001$) and forced vital capacity (FVC) ($r = -0.524$, $P < 0.001$) (Figure 2). At cutoffs of 19.5 and 55.5, LUS distinguished preclinical ILD from limited ILD and extensive ILD, with sensitivities of 95.7% and 89.7% and specificities of 83.3% and 73.8%, respectively (AUC 0.963 and 0.877) (Figure 3). The agreement between LUS and HRCT severity stratification was good (quadratic weighted kappa = 0.736; 95% CI: 0.621–0.850), and interoperator consistency was excellent (intra-class correlation coefficient: 0.971, 95% CI: 0.965–0.980, $P < 0.001$).

Conclusion: LUS exhibited favorable sensitivity and specificity for distinguishing between CTD-ILD patients of varying severity grades. Moreover, LUS presents a promising imaging modality for disease severity stratification and longitudinal monitoring of disease progression.

Disclosure: j. ding: None; **y. zhang**: None; **L. Pang**: None; **n. guo**: None; **z. zheng**: None.

Abstract Number: 2612

Automated, Artificial Intelligence-supported Sonographic Examination of the Hands for the Detection and Quantification of Arthritis and Osteoarthritis in the Hand and Finger Joints in Outpatient Rheumatology Care

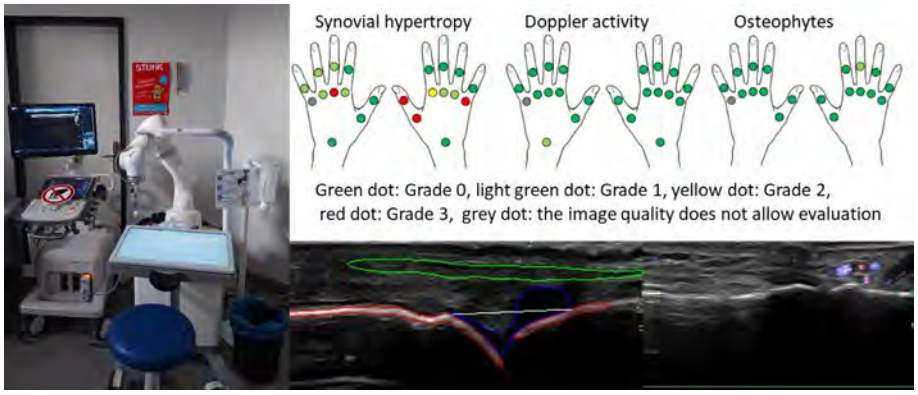
Oliver Sander[1], Lea Ormeloh[1], Laura Grünkewitz[1], Martin Gallmann[1], Benedict Blümel[1], Rishi Adhikari[1], Hasan Acar[1], Gamal Chehab[1], Jörg Distler[2] and Jutta Richter[3], [1]Department of Rheumatology, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University. Hiller Research Center, University Hospital Düsseldorf, Medical Faculty of Heinrich-Heine University., Düsseldorf, Germany, [2]University Hospital Duesseldorf and HHU, Duesseldorf, Germany, [3]Clinic for Rheumatology and Hiller Research Unit, Heinrich-Heine-University Duesseldorf, Medical Faculty, Duesseldorf, Germany, Dösseldorf, Germany

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Imaging of Rheumatic Diseases (2609–2614)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: The integration of artificial intelligence (AI) in combination with robotics into clinical diagnostics has the potential to increase precision and efficiency and relieve increasingly scarce staff. Rheumatoid arthritis (RA), hand osteoarthritis (HOA), and psoriatic arthritis (PsoA) are common or relevant causes of hand complaints and impending functional limitations. The aim of the pilot phase is to introduce and test the safety, reliability, and acceptance of the hand examination using the ultrasound robot ARTHUR and the AI DIANA (both ROPCA Denmark) in an university outpatient clinic.

Methods: ARTHUR and DIANA offer automated scanning and evaluation of the wrists, all MCP, IP/PiP, and the DiP joints for synovial thickening, increased perfusion, and osteophytes based on the OMERACT guidelines. CANON aplio a ultrasound scanner with an 18L7 UHF ultra-wide linear probe was used. Procedures, reasons for discontinuation, and satisfaction were recorded in a standardized manner.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



ARTHUR diagnostic unit and DIANA report

Results: Within the first 12 weeks of use, 10,000 joints in 500 patients were examined (200 patients with RA, 100 PsoA, 50 HOA, 150 with other conditions). 5 examinations were discontinued without data transfer. 16 examinations were transferred but not read; all other examinations were completed successfully. No discontinuations for safety reasons were necessary. The average time for examiation of both hands took 20 minutes. Patient satisfaction was high: 92% reported being "very satisfied," 8% described themselves as "satisfied," and one patient rated the experience as "undecided." No one expressed dissatisfaction. The willingness to participate in a follow-up examination was 99.7%. Five patients reported mild pain during the examination but would still undergo the procedure again.

The figure shows the ARTHUR diagnostic unit on the left, a DIANA report on the top, and the corresponding image documentation below (red bone, blue synovium, green tendon in the example of an MCP joint, and Doppler of an IP joint).

In 91% of joints examined by ARTHUR documentation and recognizability of the joint structures was good or very. Difficulties were encountered with pronounced deformities or extension deficits. In the AI-supported interpretation of the stored images, DIANA shows a fair detection and differentiation of synovitis, with a relevant error rate of < 5%, but the detection of osteophytes is still unsatisfactory.

Conclusion: The implementation of a new AI-supported technology is associated with administrative hurdles and requirements. Technically, the robot demonstrates good performance, including robust image acquisition for synovitis and effusion. The joint-related correction rate for gross deviations exceeding at least 2 score points for synovitis by the experienced rheumatologist was below 5%. Currently, parallel evaluation and approval by experienced examiners is still necessary. Further training of the evaluation AI promises to further increase reliability and thus significantly improve the patient experience. Patient acceptance of the examination was very high.

Disclosure: O. Sander: None; **L. Ormeloh**: None; **L. Grünkewitz**: None; **M. Gallmann**: None; **B. Blümel**: None; **R. Adhikari**: None; **H. Acar**: None; **G. Chehab**: None; **J. Distler**: 4D Science, 8, 11, Actelion, 2, 6, Active Biotech, 2, 6, Anamar, 2, 6, Array Biopharma, 2, 6, ARXX Therapeutics, 2, 6, aTyr Pharma, 2, 6, Bayer Pharma, 2, 6, BMS (Bristol-Myers Squibb), 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, FibroCure, 4, Galapagos, 2, 6, GSK, 2, 6, Inventiva, 2, 6, JB Therapeutics, 2, 6, Medac, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Redx Pharma, 2, 6, RuiYi, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6; **J. Richter**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2613

ga-fapi-04 PET/CT Reveals Increased Fibroblast Activation in Synovial and Enthesial Tissues of Psoriasis Patients with Arthralgia and Predicts the Development of Psoriatic Arthritis

Giulia Corte[1], Koray Tascilar[2], armin Atzinger[3], Alp Temiz[2], Melek Yalcin Mutlu[4], Rita Noversa de Sousa[5], Maria Gabriella Raimondo[6], Andreas Ramming[7], Sara Bayat[2], Michael Sticherling[8], Torsten Kuwert[9], Christian Schmidkonz[9], Georg Schett[10] and Filippo Fagni[11], [1]- Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [2]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [3]Department of Nuclear Medicine, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [4]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, erlangen, [5]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, [6]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [7]Department of Internal Medicine 3, Rheumatology & Immunology, Friedrich-Alexander-University (FAU) & Universitätsklinikum Erlangen, Erlangen, Germany, [8]Department of Dermatology, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [9]Department of Nuclear Medicine, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, [10]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany, [11]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Bayern, Germany

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Imaging of Rheumatic Diseases (2609–2614)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: ^{68}Ga-FAPI-04 PET/CT reveals fibroblast activation in vivo and is increasingly used to assess rheumatic diseases, including inflammatory arthritides. (1,2) We previously demonstrated that the synovio-entheseal ^{68}Ga-FAPI-04 uptake is increased in psoriasis (PsO) patients with arthralgia. (3) We now report the risk of PsA development with ^{68}Ga-FAPI-04 uptake in a longitudinal cohort of PsO patients at risk.

Methods: PsO patients with arthralgia but without arthritis/enthesitis underwent a whole-body ^{68}Ga-FAPI-04 PET/CT scan. We evaluated 34 synovial, 34 enthesial and 5 axial sites for ^{68}Ga-FAPI-04 uptake using the maximal standardized uptake value (SUVmax) and PET/CT Joint Index (PET-JI) (2), both calculated at each site individually and cumulatively at all sites. Patients were considered "^{68}Ga-FAPI-04 positive" when a PET-JI ≥2 was detected at least at one site.

Subsequently, patients were examined by a rheumatologist every 3 months or in case of symptoms worsening or reported joint swelling. Only patients with a ≥6 months of follow-up were included in the evaluation. PsA diagnosis was based on the fulfillment of CASPAR criteria. We described sites and intensity of ^{68}Ga-FAPI-04 uptake, compared the characteristics of ^{68}Ga-FAPI-04 positive vs negative patients and performed survival analyses to estimate the risk of PsA development.

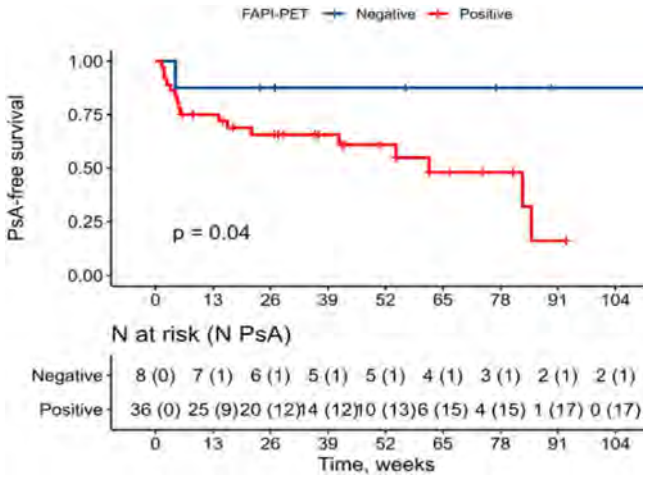
Results: We included 44 patients, 59% were male, the mean age was 50 years (IQR 42-58). Further baseline characteristics are summarized in table 1. We found relevant ^{68}Ga-FAPI-04 uptake in 36 (81.8%) patients with a mean cumulative SUVmax of 22.4 (±23.8) and PET-JI of 13.6 (±13.8), most commonly around mechanically challenged large joints: greater trochanter (n=15), shoulder (n=14), ankle (n=13), knee (n=13) and acromioclavicular joints (n=12), spinous process of the L5 vertebra (n=10). ^{68}Ga-FAPI-04 positive patients had significantly higher BMI (p=0.023) and DAS28-CRP (p=0.04), driven by higher patient global VAS and CRP levels.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and patient characteristics compared by 68Ga-FAPI-04-PET/CT status

	Overall N= 44	Positive N = 36	Negative N= 8	P-value
Age (years), median (IQR)	50 (42, 58)	51 (42, 58)	47 (42, 60)	0.9
Male/Female	26/18	21/15	5/3	> 0.9
PsO involvement, N(%)				
Scalp	23 (52.3%)	19 (52.8%)	4 (50.0%)	>0.9
Nail	13 (29.5%)	9 (25.0%)	4 (50.0%)	0.2
BMI, median (IQR)	27.7 (24.8, 33.4)	27.8 (25.4, 34.3)	24.4 (22.7, 28.5)	0.023*
Tender Joint Count (66/68), median (IQR)	1.00 (0.0 , 4.0)	1.00 (0.0 , 4.0)	0.5 (0.0, 2.0)	0.5
VAS Pain (0 – 100), median (IQR)	35 (20, 60)	40 (30, 60)	20 (10, 30)	0.075
DAS28-CRP, median (IQR)	2.48 (1.70, 3.51)	2.73 (1.89, 3.54)	1.05 (0.77, 2.48)	0.04*
LEI > 0, N (%)	18 (40.9%)	16 (44.4%)	2 (25.0%)	0.4
MASES > 0, N (%)	10 (22.7%)	8 (22.2%)	2 (25.0%)	> 0.9
PASI, N (%)	1.65 (0.7, 3.0)	1.70 (0.80, 3.00)	1.50 (0.00, 1.90)	0.3
HAQ-DI, median (IQR)	0.38 (0.00, 0.88)	0.38 (0.00, 0.89)	0.38 (0.00, 0.63)	>0.9
CRP > 5 mg/dL, N (%)	15 (34.1%)	14 (38.9%)	1 (12.5%)	0.2
mg/dL, mean (SD)	8.0 (6.5)	8.9 (7.5)	5.6 (1.6)	
No therapy	27 (61.4%)	23 (63.9%)	4 (50.0%)	0.7
DMARD Therapy at Baseline, N (%)				
cDMARD	1 (2.3%)	1 (2.8%)	0 (0.0%)	>0.9
bDMARD	13 (29.5%)	10 (27.8%)	3 (37.5%)	0.7
tsDMARD	2 (4.5%)	1 (2.8%)	1 (12.5%)	0.3
Final tratment status, N (%)				0.3
No therapy	13 (29.5%)	11 (30.6%)	2 (25.0%)	
Same therapy	12 (27.3%)	8 (22.2%)	4 (50.0%)	
Start therapy/switched therapy	19 (43.2%)	17 (47.2%)	2 (25.0%)	

bDMARD, biological disease-modifying antirheumatic drugs; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; cDMARD, conventional antirheumatic drugs; CRP, C-reactive protein; DAS28-ESR, Disease Activity Score based on Erythrocyte Sedimentation Rate; HAQ, Health Assessment Questionnaire; LEI, Leeds Enthesitis Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; PASI, Psoriasis Area and Severity Index; VAS, Visual Analogue Scale.



Kaplan-Meyer curves of PsA-free survival in PsO patients with positive 68Ga-FAPI-04-PET/CT scans (blue line) vs. negative 68Ga-FAPI-04-PET/CT scans (red line) at synovial and entheseal sites

During a mean follow-up of 42 (±41) weeks, 18 patients (41%) developed PsA. 17/36 (47%) patients with a ^{68}Ga-FAPI-04 positive scan at baseline were PsA progressors, whereas only 1/8 (13%) without FAPI uptake developed PsA ((HR 6.55, 95%CI 0.85-50.8), log-rank p-value=0.04). Although not statistically significant (p=0.33 and 0.34), PsA progressors had higher mean cumulative SUV-max (27.0 ±26.8) and PET-JI (16.0 ±15.6) compared to non-progressors (SUVmax: 19.4 ± 21.6) (PET-JI: 11.9 ±12.3).

Conclusion: This prospective study shows that fibroblast activation detected by ^{68}Ga-FAPI-04-PET/CT is linked to a 6-fold higher risk of PsA development in PsO patients. Our data suggest that this imaging technique may be useful in identifying PsO patients at risk of PsA development, who may benefit from close monitoring and possible preventive interventions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References:

1. Schmidkonz C, et al. Journal of Nuclear Medicine. 2023.
2. Luo Y, et al. Radiology. 2023;307(3):e222052.
3. Corte G, et al. RMD Open. 2024 Jun 11;10(2):e004294

Disclosure: G. Corte: None; **K. Tascilar**: None; **a. Atzinger**: None; **A. Temiz**: None; **M. Yalcin Mutlu**: None; **R. Noversa de Sousa**: None; **M. Raimondo**: UCB, 6; **A. Ramming**: Boehringer-Ingelheim, 2, Johnson & Johnson, 2, MoonLake Immunotherapeutics AG, 2, 5, Novartis Pharma GmbH, 2, UCB, 2; **S. Bayat**: None; **M. Sticherling**: None; **T. Kuwert**: None; **C. Schmidkonz**: None; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **F. Fagni**: None.

Abstract Number: 2614

Impact of Vagus Nerve-Mediated Neuroimmune Modulation on structural joint damage using Gd-MRI RAMRIS imaging in Biologic-Experienced Patients with Rheumatoid Arthritis

Charles Peterfy, MD, PhD[1], John Tesser[2], Yaakov Levine[3], Melissa Evangelista[4], Vibeke Strand[5], Michael Weinblatt[6] and David Chernoff[7], [1]Spire Sciences, Inc., Boca Raton, FL, [2]Arizona Arthritis & Rheumatology Associates, Phoenix, AZ, [3]SetPoint Medical, Valencia, CA, [4]SetPoint Medical Corporation, Valencia, CA, [5]Stanford University School of Medicine, Palo Alto CA, Portola Valley, CA, [6]Brigham and Women's Hospital/ Harvard Medical School, Waban, MA, [7]SetPoint Medical, Sausalito, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Imaging of Rheumatic Diseases (2609–2614)

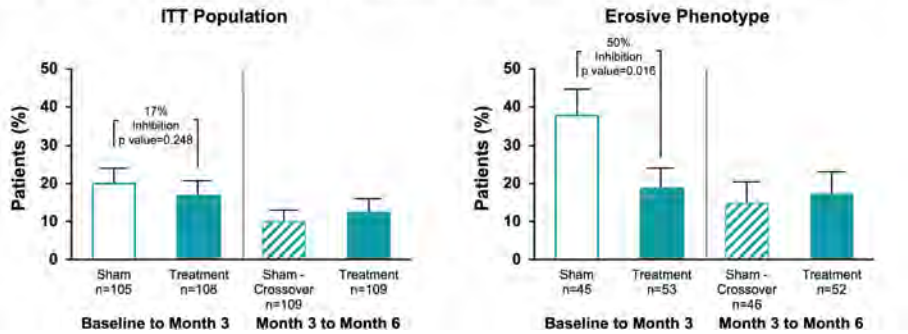
Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Previously reported results from RESET-RA (ClinicalTrials.gov, NCT04539964) showed neuroimmune modulation via electrical stimulation of the left vagus nerve using an implantable device to treat RA provided clinical efficacy compared to sham at 3 months. Further improvement was observed in both groups, after sham crossover to stimulation.

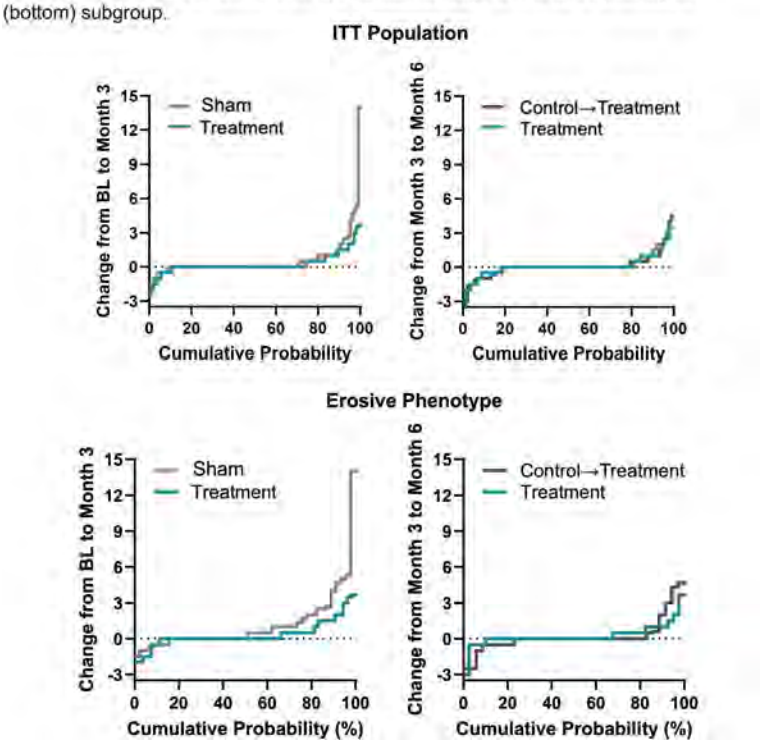
Vagus nerve stimulation may directly impact bone turnover via release of specialized pro-resolving mediators (SPMs) and neurotransmitters that act through ChemR23 receptors, nicotinic acetylcholine receptors and adrenergic receptors on osteoblasts and osteoclasts to reduce RANKL pathways and increase OPG, leading to inhibition of osteoclast activity.

Figure 1: Percentage of patients with bone erosion progression from baseline to Month 3 and Month 3 to Month 6 for ITT population and erosive phenotype subgroup.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2: Cumulative distribution of change in RAMRIS erosion scores from baseline to Month 3 and Month 3 to Month 6 for ITT population (top) and erosive phenotype (bottom) subgroup.



To objectively evaluate treatment effect of neuroimmune modulation on joint erosions, we report results from RESET-RA, which employed an OMERACT-validated imaging method using gadolinium-enhanced MRI of the hand and wrist, called RAMRIS (Rheumatoid Arthritis MRI Scoring system).

Methods: Adults with moderate-to-severe, active RA despite prior exposure to one or more biologic or targeted synthetic DMARDs (b/tsDMARDs) underwent outpatient surgery to implant the integrated neurostimulator, followed by 1:1 randomization to treatment (stimulation) or sham. MRIs were obtained at baseline, 3 months and 6 months after randomization and evaluated to assess progression of bone erosions. Images were scored centrally by two independent radiologists blinded to treatment allocation, clinical information, and the order in which images were acquired to ensure objective, unbiased scoring.

While active synovitis was not required for eligibility, prespecified analyses included an enriched subgroup of patients with erosive phenotype, i.e., patients at higher risk of erosion progression based on active, intra-articular synovitis at baseline (score ≥ 2 on any individual joint, at least 4 joints with a synovitis score of 1, or any joint with osteitis).

Results: Baseline RAMRIS scores were comparable between treatment and sham for both the ITT population and enriched subgroup. The non-enriched, ITT population showed that at 3 months, treatment had fewer patients with erosion progression (>0.5 increase in erosion score) compared to sham, but differences were not statistically significant. However, in the enriched subgroup, the proportion of patients with erosion progression at 3 months was significantly lower for treatment (18.9%) compared to sham (37.8%, p=0.0156) (**Figure 1**). After sham crossed over to treatment and received stimulation for 3 months, the proportion of patients with erosion progression reduced to levels comparable to the treatment group (17.0% treatment, 21.7% sham-crossover, (**Figure 1**). The cumulative distribution of change in erosion scores also showed greater inhibition of erosion progression with stimulation that was more pronounced in the enriched subgroup (**Figure 2**).

Conclusion: Neuroimmune modulation using an implantable device is effective in inhibiting progression of structural damage as early as 3 months in adults with active RA and active synovitis at baseline who previously had inadequate response or intolerance to at least one b/tsDMARD.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: C. Peterfy, MD, PhD: Abbisko, 2, AbbVie/Abbott, 2, Daiichi-Sankyo, 2, Deciphera, 2, Eli Lilly, 2, Genascense, 2, Hutchmed, 2, Istesso, 2, Labcorps, 2, Nimbus, 2, Orthotrophix, 2, Paradigm, 2, Samsung Bioepois, 2, Sarepta, 2, SetPoint, 2, Sonoma, 2, SynOx, 2; **J. Tesser**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, 5, 6, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, 6, Celgene, 5, Eli Lilly, 2, 5, 6, Genentech, 5, Gilead, 5, GlaxoSmithKlein(-GSK), 2, 5, 6, IGM Biosciences, 5, Janssen, 2, 5, 6, Merck/MSD, 5, Novartis, 2, 5, Pfizer, 5, 6, Roche, 5, SetPoint Medical, 2, UCB, 2, 5, 6; **Y. Levine**: SetPoint Medical, 3, 10, 11; **M. Evangelista**: SetPoint Medical, 3, 8; **V. Strand**: AbbVie/Abbott, 2, Alumis, 2, Amgen, 2, Arthrosi, 2, Artiva, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer-Ingelheim, 2, catalys, 2, contura, 2, Cullinan, 2, Fate Therapeutics, 2, Fortress Biotech, 2, genasence, 2, GlaxoSmithKlein(GSK), 2, Inmedix, 2, Lipum, 2, Longitude Capiral, 2, MED institute, 2, Novartis, 2, RAPT, 2, Royalty Pharma, 2, Sanofi, 2, scipher medcine corp, 2, SetPoint Medical, 2, Sobi, 2, Spherix, 2, Synact, 2, Takeda, 2, Topography, 2, Zoe, 2; **M. Weinblatt**: aclaris, 2, amgen, 2, anaptysbio, 2, Artiva Bio, 2, Biohaven, 2, Bristol-Myers Squibb(BMS), 2, 5, Canfite, 11, Curie Bio, 2, Deep Cure, 2, Eli Lilly, 2, Gilead, 2, Ignite, 2, Inmedix, 11, Janssen, 5, Janux Therapeutics, 2, Johnson and Johnson, 2, Lifordi, 2, Marvel Bio, 2, Matchpoint, 2, Merck/MSD, 2, Neutrolis, 2, Novartis, 2, Sana, 2, Santa Ana, 2, Sci Rhom, 2, scipher medcine corp, 11, SetPoint Medical, 2, Surf Therapeutics, 2, Thymmune, 2, Xencorp, 2, ZuraBio, 2; **D. Chernoff**: SetPoint Medical, 12, 3, 8, 10, 11.

Abstract Number: 2615

The Cost of Complexity: Financial Toxicity in Rheumatic Disease, Cancer, and Their Intersection

Manush Sondhi[1], Bhavik Bansal[2], Hemant Khandelia[1], Jiha Lee[3], Sebastian E Sattui[4], Siddharth Singh[5] and Namrata Singh[6], [1]University of Washington, Seattle, WA, [2]UT Southwestern Medical Center, Dallas, [3]University of Michigan, Ann Arbor, MI, [4]Division of Rheumatology and Clinical Immunology, University of Pittsburgh, Pittsburgh, PA, [5]University of California San Diego, San Diego, CA, [6]University of Washington, Bellevue, WA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Measures & Measurement of Healthcare Quality (2615–2620)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Financial toxicity (FT) is the financial burden of accessing health care, well known in cancer and increasingly seen in rheumatic disease (RD). We compared FT among adults with neither condition, RD only, cancer only, and both.

Methods: We used the National Health Interview Survey, a nationally representative sample of US adults from 2019-2023. Adults were categorized by self-reported RD, including arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia, and/or cancer. FT was defined as the presence of one or more of the following: financial distress, difficulty paying bills, delayed or forgone care, cost-related medication non-adherence, and food insecurity. Weighted logistic regressions were used to examine associations between disease groups and FT components, adjusting for demographics, comorbidities, and insurance status. To account for baseline differences and insurance coverage, analyses were stratified by age (< 65 versus ≥65 years). Analyses were conducted in RStudio v4.4.1; significance was set at $p < 0.05$.

Results: A total of 149,905 adults were included, of whom 10,094 (weighted prevalence: 6.3% [95% CI: 6.1%–6.5%]) had cancer only, 30,446 (18.5% [95% CI: 18.2%–18.8%]) had rheumatic disease (RD) only, and 8,713 (4.7% [95% CI: 4.6%–4.9%]) had both RD and cancer. These correspond to approximately 80.5, 235.6, and 59.9 million U.S. adults, respectively. Adults with both RD and cancer were more likely to be aged ≥65 years (70.5%) and had the highest rates of multimorbidity (62.1% with ≥2 comorbidities). Most adults across groups were female and insured, with higher educational attainment in the cancer-only and neither condition **(Table 1)**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Characteristics of Adults with Cancer and/or RD from the National Health Interview Survey, 2019 to 2023

	Neither Rheumatic Disease nor Cancer	Cancer Only	Rheumatic Disease Only	Rheumatic Disease and Cancer
Sample	N = 100,652	N = 10,094	N = 30,446	N = 8,713
Weighted sample	928,897,493[†]	68,736,147[†]	216,267,964[†]	53,352,263[†]
Age category, yrs				
18-39 years	40,418.0 (48.3)	631.0 (8.8)	2,010.0 (9.1)	92.0 (1.6)
40-64 years	41,890.0 (39.5)	3,596.0 (42.2)	12,452.0 (47.1)	1,952.0 (27.9)
65+ years	18,344.0 (12.2)	5,867.0 (49.0)	15,984.0 (43.8)	6,669.0 (70.5)
Sex				
Female	51,691.0 (49.2)	5,480.0 (52.9)	18,783.0 (59.1)	5,394.0 (59.4)
Male	48,946.0 (50.8)	4,614.0 (47.1)	11,662.0 (40.8)	3,319.0 (40.6)
Race				
Asian	7,312.0 (7.1)	185.0 (2.3)	855.0 (3.5)	91.0 (1.5)
Black	11,278.0 (12.3)	591.0 (6.3)	3,749.0 (12.4)	520.0 (6.4)
Hispanic	16,806.0 (19.8)	598.0 (7.7)	2,634.0 (11.0)	362.0 (5.3)
Others	2,655.0 (2.8)	145.0 (1.5)	764.0 (2.6)	182.0 (2.1)
White	62,601.0 (58.0)	8,575.0 (82.1)	22,444.0 (70.6)	7,558.0 (84.6)
Education Category				
High School or less	32,044.0 (37.5)	2,854.0 (32.3)	12,260.0 (44.2)	3,017.0 (38.8)
Some college or higher	68,608.0 (62.5)	7,240.0 (67.7)	18,186.0 (55.8)	5,696.0 (61.2)
Insured				
Insured	90,367.0 (87.6)	9,829.0 (96.2)	29,381.0 (95.5)	8,607.0 (98.5)
Uninsured	10,285.0 (12.4)	265.0 (3.8)	1,065.0 (4.5)	106.0 (1.5)
Region				
North Central/Midwest	21,445.0 (20.1)	2,328.0 (22.4)	7,222.0 (22.7)	2,054.0 (22.4)
Northeast	16,627.0 (17.6)	1,705.0 (17.3)	5,134.0 (17.6)	1,492.0 (17.8)
South	36,144.0 (37.8)	3,631.0 (37.5)	11,366.0 (38.8)	3,196.0 (39.0)
West	26,436.0 (24.5)	2,430.0 (22.7)	6,724.0 (20.9)	1,971.0 (20.9)
Number of Comorbidities				
0	53,752.0 (56.8)	2,884.0 (30.5)	5,910.0 (21.1)	1,146.0 (13.4)
1	27,386.0 (26.6)	2,980.0 (29.6)	8,397.0 (27.7)	2,126.0 (24.6)
>=2	19,514.0 (16.6)	4,230.0 (39.9)	16,139.0 (51.2)	5,441.0 (62.1)

[†] n (unweighted) (%)

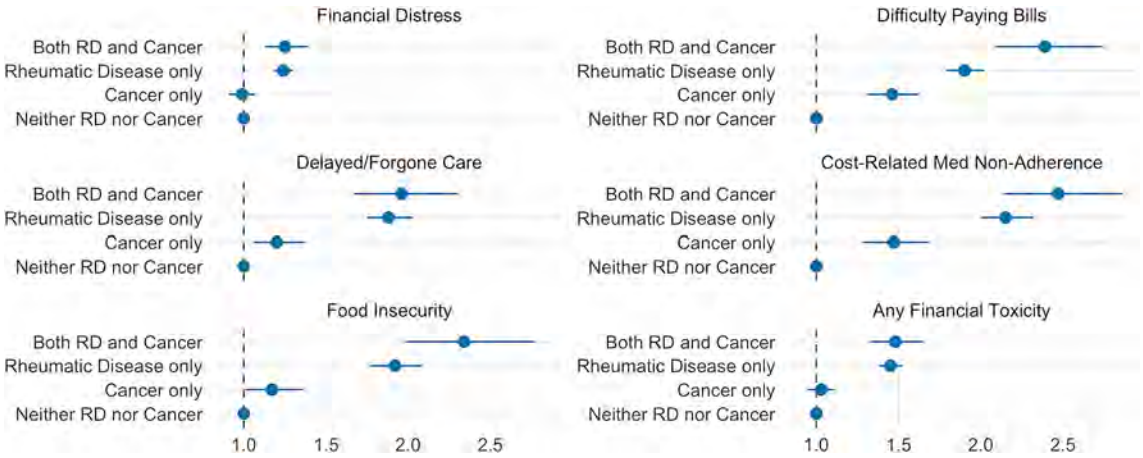


Figure 1: Adjusted Odds Ratios for Financial Toxicity Outcomes Among Younger Adults (<65 years) by Disease Group

In adults under 65, FT was highest in those with RD alone (63.9%) or RD plus cancer (64.3%), compared to 54% in those without either condition. Medication non-adherence was higher in RD groups (16.3% RD only, 19.2% RD with cancer). In adults over 65, FT was most prevalent in those with RD only (41.4%), with financial distress highest in this group (35.1%).

Among adults < 65 years, compared to those with neither RD nor cancer, persons with RD alone or in combination with cancer were consistently associated with increased FT across all domains **(Figure 1)**. Among adults ≥65 years, RD remained associated with higher odds of difficulty paying bills, cost-related medication non-adherence, and food insecurity, while cancer alone was not associated with increased financial toxicity and appeared protective in some domains compared to those with neither condition. The combined burden of RD and cancer conferred a similar level of risk as RD alone **(Figure 2)**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

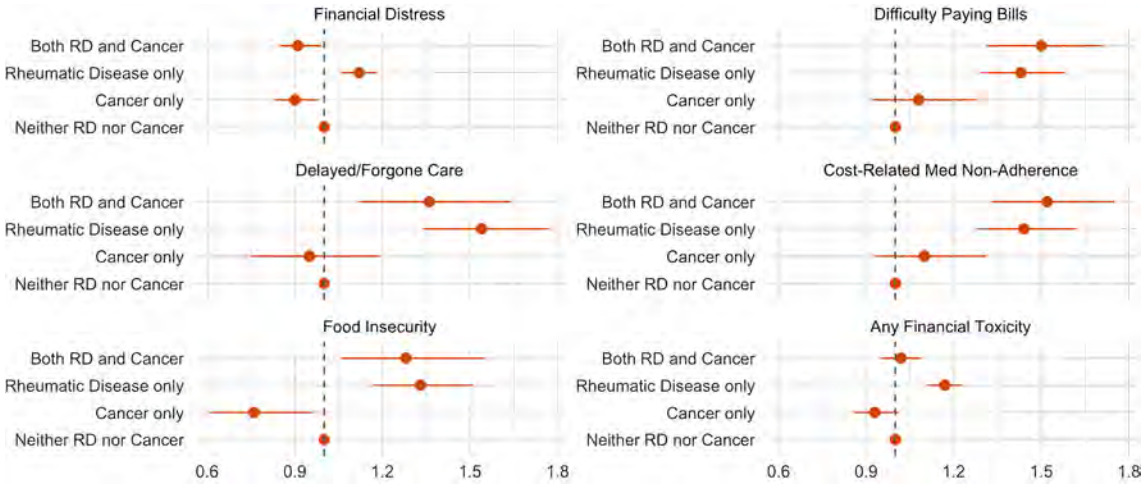


Figure 2: Adjusted Odds Ratios for Financial Toxicity Outcomes Among Older Adults (≥65 years) by Disease Group

Conclusion: Among younger adults, RD had a stronger association with FT than cancer, with the highest burden seen in those with both. Similar trends were observed among older adults, though with more modest effect sizes. While cancer may lead to short-term high costs, RD imposes a chronic financial burden from ongoing treatment and care. Even among Medicare-insured older adults, FT persists. These findings underscore the need for RD-specific FT assessment tools and greater clinical attention to financial burden, particularly as longer life expectancy amplifies the long-term economic impact of chronic RDs.

Disclosure: M. Sondhi: None; **B. Bansal**: None; **H. Khandelia**: None; **J. Lee**: None; **S. Sattui**: Amgen, 1, 2, 5, Fresenius Kabi, 6, Glaxo Smith Kline, 5, National Institute of Aging (grant number R03AG082983), 5, Rheumatology Research Foundation Investigator Award, 5, Sanofi, 1, 2; **S. Singh**: None; **N. Singh**: None.

Abstract Number: 2616

Real-World Implication of Clinical Disease Activity Index (CDAI) Utilization on Treatment Decisions and Clinical Outcomes in Rheumatoid Arthritis

Ryan Clark[1], Sally Almahdawi[1], Carolina Alvarez[2], Rumey Ishizawar[3] and Thuyvan Phan[4], [1]UNC Eshelman School of Pharmacy, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Miami, FL, [3]UNC Division of Rheumatology, Allergy and Immunology and TARC, Chapel Hill, NC, [4]UNC Health, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Measures & Measurement of Healthcare Quality (2615–2620)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: The University of North Carolina (UNC) Hospitals Rheumatology Clinic is utilizing the Clinical Disease Activity Index (CDAI) in patients with rheumatoid arthritis (RA) per the American College of Rheumatology (ACR) recommendation to guide therapeutic decisions in a treat-to-target approach. Through quality initiatives in clinic, approximately 70% of RA encounters now capture CDAI. This study was designed to understand covariables impacting CDAI over time and treatment actions, as well as determine generalizable applicability in clinical practice.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This was a single-center, retrospective cohort study evaluating the use of CDAI to monitor disease activity and treatment response for adult patients (≥18 years) with RA, defined by treating rheumatologist from 10/01/2022 to 09/30/2023. Patients were included if they had three documented CDAI scores within the study period. Analyses included associations between CDAI with sex, race, insurance, income, steroid use, steroid sparing agents (conventional and targeted DMARDs and/or biologics) over time. The utility of the CDAI was examined by assessing whether provider's treatment actions were associated with CDAI scores vs other reasons such as patient's preference, medication side effect profile, or insurance coverage. Mixed linear (random intercept and linear time, other covariables as fixed effects, and unstructured covariance) and population-averaged logistic regression, using generalized estimating equations, were used to produce betas or odds ratios (OR), respectively, and 95% confidence intervals (CI) for these associations.

Results: A total of 234 patients had three CDAI scores within 12 months. Mean baseline CDAI score was 15.5 ± 12. The mean time from visit 1 to visit 2 and 3 was 15.1 weeks and 31.8 weeks, respectively (Table 1). CDAI score significantly decreased over time, on average 2.9 units (95% CI -4.0, -1.8) after 15 weeks and 3.5 units (95% CI -4.8, -2.1) after 30 weeks from baseline. CDAI score was significantly higher for those with no insurance vs private insurance by 3.9 units (95% CI -0.0, 7.8). Patients with Medicare or other government insurances (vs private) had lower odds of escalation or switch in therapy, OR 0.57 (95% CI 0.33, 0.98) and OR 0.50 (95% CI 0.28, 0.90), respectively (Table 2). Patients with moderate or high CDAI

Table 1. Descriptive statistics for RA CDAI utilization, N=234

	Visit 1					
	n or mean or median	*% or ±SD or (IQR)*				
Static variables						
Age at RA diagnosis, mean±SD years (range=17-84)	48.0	±13.6				
Male, n %	41	17.5				
Race/Ethnicity, n %						
White, non-Hispanic	107	45.7				
Black, non-Hispanic	56	23.9				
Hispanic	55	23.5				
Other, non-Hispanic	16	6.8				
Insurance, n %						
Private	75	32.1				
Medicare only	84	35.9				
Other governmental	38	16.2				
None	37	15.8				
	Visit 1		*Visit 2*		*Visit 3*	
Time-varying variables	*n or mean or median*	*% or ±SD or (IQR)*	*n or mean or median*	*% or ±SD or (IQR)*	*n or mean or median*	*% or ±SD or (IQR)*
Time from visit 1, *mean±SD weeks*			15.1	±5.7	31.8	±8.9
CDAI score, *mean±SD (range=0-69)*	15.5	±12.0	12.4	±9.7	12.2	±9.9
CDAI score categories*, n %*						
remission (CDAI≤2.8)	13	5.6	26	11.1	25	10.7
low (2.8<CDAI≤10)	88	37.6	94	40.2	103	44.0
moderate (10<CDAI≤22)	81	34.6	87	37.2	75	32.1
high (22<CDAI)	52	22.2	27	11.5	31	13.2
RA medications*, n %*						
Conventional DMARDs only	84	35.9	92	39.3	87	37.2
Conventional DMARDs and Biologics	71	30.3	74	31.6	78	33.3
Conventional DMARDs and Targeted	10	4.3	8	3.4	9	3.8
Biologics only	32	13.7	38	16.2	38	16.2
Targeted only	7	3.0	6	2.6	6	2.6
None	30	12.8	16	6.8	16	6.8
Steroids*, n %*	63	26.9	58	24.8	51	21.8
Provider actual treatment action*, n %*						
No change in therapy	101	43.2	119	50.9	137	58.5
Escalate or switch therapy	116	49.6	93	39.7	77	32.9
Taper therapy	17	7.3	21	9.0	18	7.7
Other			1	0.4	2	0.9
Reason for actual treatment action*, n %*						
Disease controlled	77	32.9	101	43.2	122	52.1
Continued disease activity	108	46.2	82	35.0	71	30.3
Taper due to remission	7	3.0	8	3.4	7	3.0
Side effects	16	6.8	15	6.4	11	4.7
Patient declined/refused intended treatment plan	13	5.6	14	6.0	10	4.3
Cost/insurance coverage	3	1.3	6	2.6	2	0.9
Other	10	4.3	8	3.4	11	4.7

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Percent of treatment action by CDAI score group

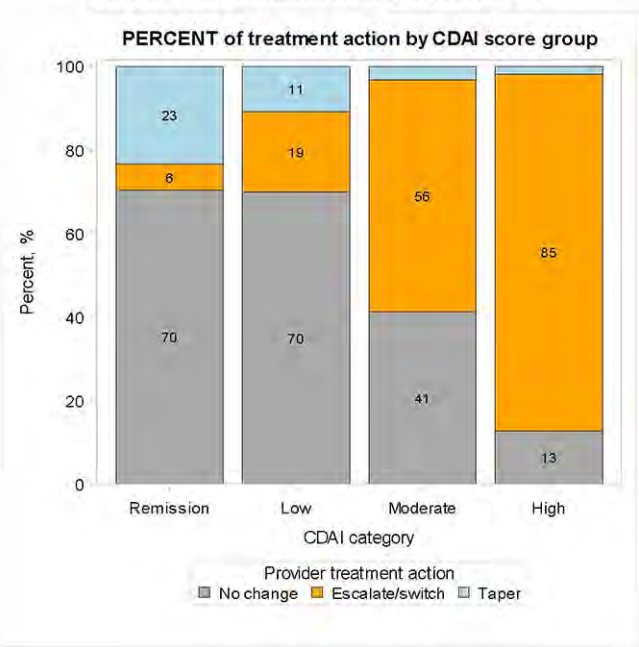


Figure 1 - Percent of treatment action by CDAI score group

(compared to low/remission) had higher odds of escalation or switch in therapy and lower odds of no change or taper therapy (Figure 1, Table 2). Treatment actions guided by CDAI scores had higher odds of escalation or switch in therapy, OR 2.83 (95% CI 1.47, 5.46) and lower odds for tapering therapy, OR 0.15 (95% CI 0.06, 0.33) compared to other reasons (Table 2).

Conclusion: Within the UNC Rheumatology Clinic, treatment changes were guided by CDAI scores. Other factors (e.g., access to insurance or insurance types, income, and race/ethnicity) may also play a role in treatment decisions and degree of disease activity. Therefore, other clinic resources may need to be utilized to bridge gaps between these disparities

Table 2. Adjusted associations between covariables and treatment action over time, RA CDAI Utilization, N=234

		No change in therapy *(vs taper or escalate/switch)*	Escalate / switch therapy *(vs no change or taper)*	Taper therapy[1] *(vs no change or escalate/switch)*
Covariable	*Unit of change or comparison*	*OR (95% CI)*	*OR (95% CI)*	*OR (95% CI)*
Insurance	Medicare only (vs Private)	1.39 (0.83, 2.31)	**0.57 (0.33, 0.98)**	1.74 (0.64, 4.68)
	Other governmental (vs Private)	1.31 (0.72, 2.36)	**0.50 (0.28, 0.90)**	2.25 (0.71, 7.13)
	None (vs Private)	0.83 (0.43, 1.62)	1.45 (0.72, 2.90)	0.36 (0.08, 1.64)
DMARDs	Conventional and Biologics (vs Conventional only)	**2.18 (1.34, 3.53)**	**0.27 (0.16, 0.47)**	1.94 (0.61, 4.63)
	Conventional and Targeted (vs Conventional only)	0.81 (0.25, 2.57)	**0.36 (0.13, 0.96)**	**8.29 (1.68, 40.9)**
	Biologics only (vs Conventional only)	1.58 (0.93, 2.69)	0.54 (0.29, 1.01)	1.45 (0.55, 3.80)
	Targeted only (vs Conventional only)	1.79 (0.61, 5.22)	**0.60 (0.20, 1.81)**	ne
	None (vs Conventional only)	**0.38 (0.18, 0.77)**	**4.29 (2.10, 8.74)**	0.10 (0.01, 1.67)
Steroid	5 mg dose higher	**0.56 (0.33, 0.95)**	1.19 (0.96, 1.46)	1.51 (0.83, 2.76)
CDAI category	moderate (vs low or remission)	**0.33 (0.22, 0.50)**	**6.49 (4.13, 10.2)**	**0.15 (0.05, 0.39)**
	high (vs low or remission)	**0.08 (0.04, 0.16)**	**26.8 (13.7, 52.4)**	**0.07 (0.01, 0.74)**
CDAI treatment action reason	CDAI reason (vs other type)	0.96 (0.54, 1.73)	**2.83 (1.47, 5.46)**	**0.15 (0.06, 0.33)**

CI=confidence interval; ne=not estimable due to cells<5
Effects shown **BOLD** if significant at 0.05 alpha level.
Three population averaged logistic models (by column) using GEE with unstructured covariance matrix. All models additionally adjusted for age at visit 1, time since RA diagnosis, time since last therapeutic change, sex, race/ethnicity, and income.
[1]Model excludes instances of targeted only DMARDs due to convergence

to provide equitable care to all patients. Further quality improvement studies are needed to see if treatment decisions and outcomes are different in patients with RA who are seen without a CDAI score.

Disclosure: R. Clark: None; **S. Almahdawi**: None; **C. Alvarez**: None; **R. Ishizawar**: None; **T. Phan**: None.

Abstract Number: 2617

Design and Initial Results from a Cluster Randomized Trial of a Provider-Facing Immunization Dashboard to Improve Shingrix Vaccination in the Veterans Health Administration

Jing Li[1], Cherish Wilson[2], Gary Tarasovsky[3], Sooyeon Kwon[4], Mary Whooley[3] and **gabriela Schmajuk**[5], [1]University of California, San Francisco, San Francisco, CA, [2]UCSF / SFVA, San Francisco, CA, [3]SFVA, San Francisco, [4]Albany Stratton VAMC, Loudonville, NY, [5]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Measures & Measurement of Healthcare Quality (2615–2620)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Patients prescribed immunosuppressive medications are at increased risk for herpes zoster and related complications, and the American College of Rheumatology recommends the recombinant zoster vaccine (Shingrix) for most patients receiving these treatments. However, fewer than half of Veterans in the VHA receiving immunosuppressive therapy have received even one dose of the Shingrix vaccine. To address this gap, we developed a national EHR-based dashboard to promote guideline-concordant Shingrix vaccination across the VHA and deployed it using a wait-list randomized control trial design.

Methods: Using data from the VHA Corporate Data Warehouse, we identified patients eligible for Shingrix according to ACR vaccination guidelines. A PowerBI dashboard was created to display patient-level information (immunosuppressant use, vaccination status) and facility-level vaccination rates (**Figure 1**).

All 131 VHA facilities were invited to participate in a waitlist-randomized trial of dashboard access. Seventy-three facilities responded to the invitation, and they were randomized to either "early access" (September 2024) or "late access" (Summer 2025), stratified by facility size and baseline percentage of patients vaccinated. Dashboard use was tracked using PowerBI user logs. The main outcome was the percentage of eligible patients with at least one dose of Shingrix, calculated weekly between June 2024 and March 2025 (38 weeks). A two-group interrupted time series (ITS) analysis was conducted to compare rates of improvement in early-access vs. late-access (control) sites.

Table. Percentage of patients with at least one Shingrix vaccine, overall and by groups at the beginning and the end of the study period

	All facilities included in the study (N=79357 pts)	Early-access facilities (38 facilities) (n=41191 pts)	Late-access (control) facilities (35 facilities) (n= 38166 pts)
Beginning of the study period (Week 1), mean (SD)	57.1 (8.1)	57.0 (8.1)	57.2 (8.1)
End of the study period (Week 38), mean (SD)	59.5 (7.8)	59.5 (7.7)	59.5 (7.6)
Post-linear trends from Interrupted Time Series analysis, coef. (95%CI)	-	0.07 (0.04, 0.09)	0.05 (0.03, 0.07)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The 73 participating facilities served 79,357 Veterans prescribed immunosuppressive medications at baseline; 87% were age ≥50, 88% male, 73% white, and 89% non-Hispanic. The most common regimens were csDMARD monotherapy (37%) and biologic monotherapy (20%).

Most facilities (79%) were high-complexity sites located in the North Atlantic (23%) or Southeast (25%) regions. At the 38 early-access sites, 71% (27/38) had at least one clinician access the dashboard at least once during the study period. Access peaked in the first month after launch and was more sporadic thereafter (median (IQR) number of sessions over the study period: 38 (38 – 114)).

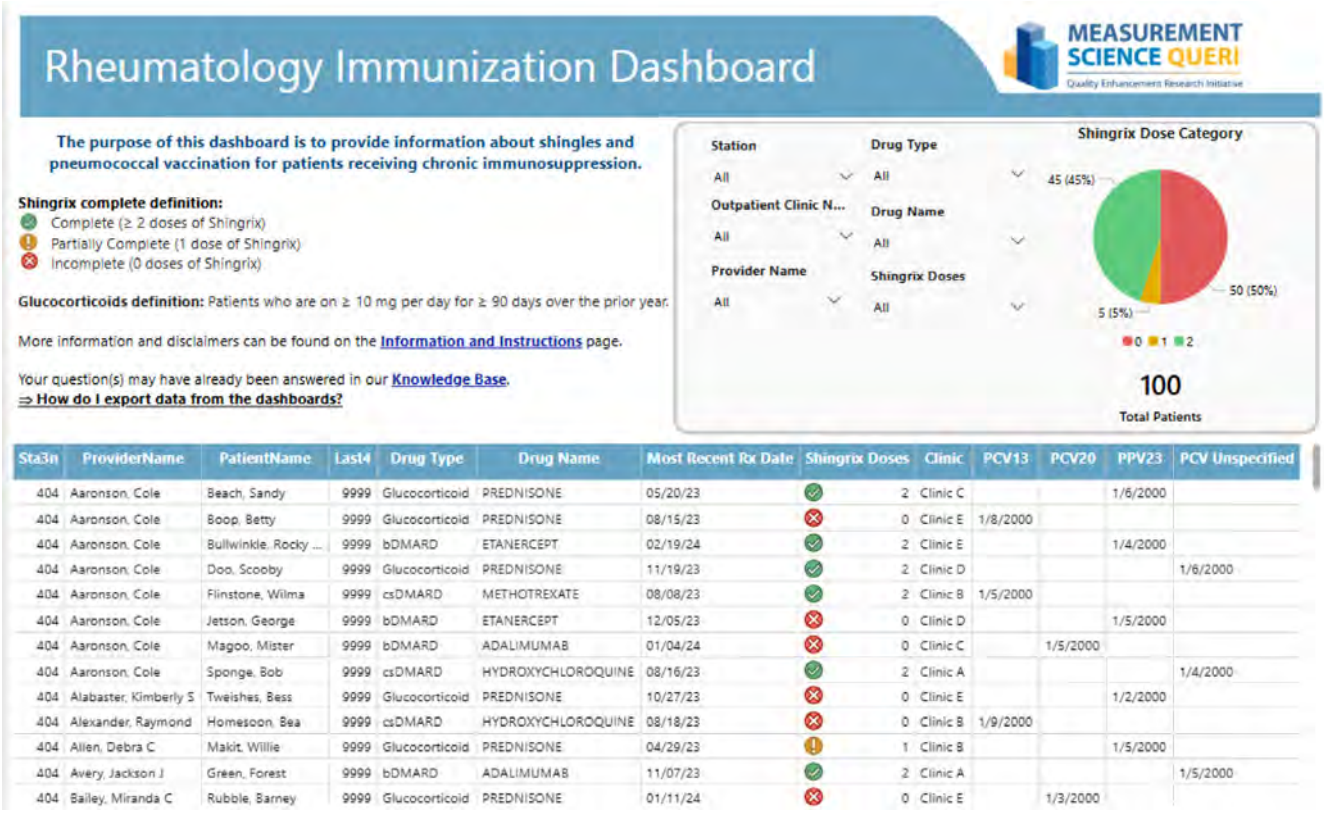


Figure 1. Screenshot of the Shingrix immunization dashboard (fictitious data)

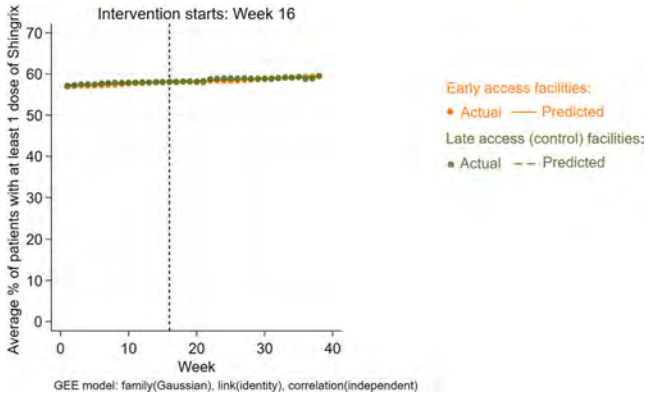


Figure 2. Interrupted time series (ITS) analysis assessing Shingrix vaccination pre- and post-dashboard access for "early access" versus "late access" (control) facilities

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

In this analysis of the first 38 weeks post-launch, Shingrix vaccination increased modestly from 57.1% to 59.5% across all sites. Early-access facilities saw a post-intervention increase of 0.07 percentage points (pp) per week, compared to 0.05 pp/week at control sites. The difference in trends was not statistically significant (difference: 0.02 pp/week; 95% CI: –0.01 to 0.05) (**Table; Figure 2**).

Conclusion: We designed an innovative wait-list randomized control trial of a provider-facing immunization dashboard to improve Shingrix vaccination. After 4 months of implementation, we observed no significant difference in Shingrix vaccination rates between early-access and control sites. This may reflect the typical 3–4 month interval between rheumatology visits. Longer follow-up, enhanced promotion of the dashboard, and additional clinician and patient education may be needed to realize te full impact of this intervention.

Disclosure: J. Li: None; **C. Wilson**: None; **G. Tarasovsky**: None; **S. Kwon**: None; **M. Whooley**: None; **g. Schmajuk**: None.

Abstract Number: 2618

Effect of Implementing a Dashboard with or without a Best Practice Alert on HLA-B*58:01 Testing Rates among Allopurinol Users at VA Medical Centers

Abimbola Fadairo-Azinge[1], gabriela Schmajuk[2], Sristi Sharma[3], Colleen Flanagan[4], Sara Faghihi-Kashani[5] and Mary Whooley[6], [1]UNIVERSITY OF CALIFORNIA SAN-FRANCISCO, SAN FRANCISCO, [2]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [3]UNIVERSITY OF CALIFORNIA SAN FRANCISCO, SAN FRANCISCO, [4]UNIVERSITY OF CALIFORNIA SAN FRANCISCO, SAN FRANCISO, [5]UCSF, Mountain View, CA, [6]SFVA, San Francisco

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Measures & Measurement of Healthcare Quality (2615–2620)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: The American College of Rheumatology recommends HLA-B*58:01 allele testing before the initiation of allopurinol, specifically among Asian and Black/African American patients, due to their increased risk for severe hypersensitivity reactions. However, testing rates remain low at many healthcare facilities. This study aimed to determine whether the introduction of a clinician-facing dashboard, with or without a Best Practice Alert (BPA), would increase HLA-B*58:01 testing rates among eligible patients at two Veterans Health Administration (VA) medical centers.

Methods: In October 2022, we launched a clinician-facing dashboard that displayed HLA-B*58:01 testing results for all patients prescribed allopurinol at two VA Medical Centers. In January 2023, we added a synchronous BPA that appeared at one of the two medical centers whenever a provider entered a prescription for allopurinol. The BPA was presented as blue text on the medication order entry form and stated "HLA-B*58:01 genotyping recommended before rx for Asian or African American." Using data from the electronic health record, we compared the change in proportion of patients receiving allopurinol prescriptions who had HLA-B*58:01 genotype testing done after implementation of the dashboard (± BPA) at the two VA medical centers.All statistical analyses were conducted using R (R Foundation for Statistical Computing, Vienna, Austria). A p-value of < 0.05 was considered statistically significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of Asian and Black patients prescribed allopurinol and characteristics of two VA medical centers.

Characteristics	Dashboard + BPA (n=448)	Dashboard alone (n=499)	p value
Mean age of patients ± SD	71 ± 13	69 ± 14	0.037
Male sex	443 (99%)	499 (100%)	0.044
Race - Black	228 (51.0 %)	199 (40.0%)	0.002
Race - Asian	220 (49.0%)	300 (60.0%)	
Ethnicity - Hispanic	12 (2.6%)	52 (10.4%)	<0.0001
HLA-B*58:01 testing prior to 10/2022	13.1%	1.0%	<0.0001
Facility characteristics	**Dashboard + BPA**	**Dashboard alone**	
# Unique non-rheumatologists prescribing allopurinol 10/2022-12/2023	331	161	0.95
# Unique rheumatologists prescribing allopurinol 10/2022-12/2023	18	9	0.95
Academic affiliation with a university	yes	yes	N/A
Services available	Primary care, specialty care, and tertiary care	Primary care, specialty care, and tertiary care	N/A
Location	SF Bay Area	SF Bay Area	N/A
# Unique patients receiving care in 2023	28,905	29,094	N/A
Outcomes (10/2022-12/2023)	**Dashboard + BPA**	**Dashboard alone**	
# Unique non-rheumatologists who ordered one or more tests	56 (16.9%)	9 (5.59%)	0.0004
# Unique rheumatologists who ordered one or more tests	15 (83.3%)	8 (88.9%)	0.70
# Unique prescribers who ordered one or more tests	71 (20.3%)	17 (10.0%)	0.003
# Unique patients who had HLA-B*58:01 testing	165 (36.8%)	19 (3.8%)	<0.0001

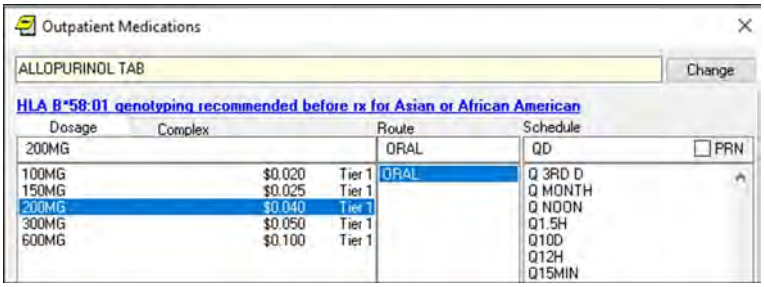
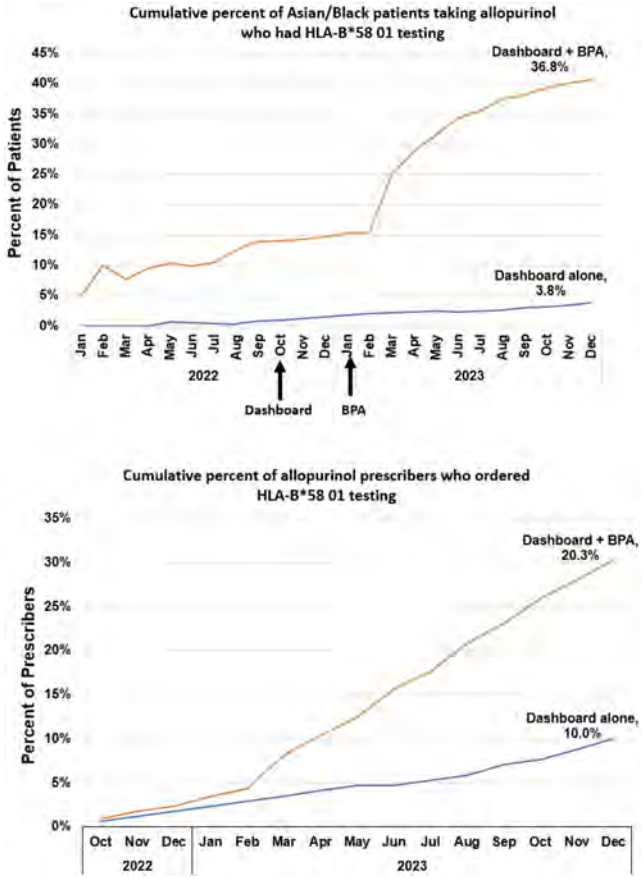


Figure 1. Interventions: Blue Text alert encountered by providers when entering an order for allopurinol at the BPA+DASHBOARD SITE

Results: From October 2022 through December 2023, the number of Asian or African American/Black patients who filled one or more prescriptions for allopurinol was 448 at the BPA + dashboard site and 499 at the dashboard only site. The two sites were similar in complexity, patient volume, location, and academic affiliation (Table 1). Between October 2022 and December 2023, the cumulative percentage of patients who had HLA-B*58:01 testing increased from 13.1% to 36.8% at the dashboard + BPA site and from 1.0% to 3.8% at the dashboard only site (Figure 2A, $p< 0.05$). Between January and December 2023, the number of Asian or African American/Black patients who had HLA-B*58:01 testing during a single month increased from an average of three per month to ten per month at the dashboard + BPA medical center and from one to three patients per month at the dashboard only medical center ($p< 0.05$). Allopurinol prescribers at the dashboard + BPA facility were more likely to order at least one HLA-B*58:01 test during the observation period than those at the dashboard only medical center (Figure 2B, 20.3% vs. 10.0%; $p=0.003$). However, this varied by provider type. Although

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



2a. Percent of Asian or African American/Black patients prescribed allopurinol who had HLA-B*58:01 testing 2b. Percent of prescribers who ordered one or more HLA-B*58:01 tests for Asian or African American/Black patients on allopurinol

there was a significant difference in the proportion of non-rheumatologists who ordered genotyping at the dashboard + BPA vs. dashboard alone facilities (15.4% vs. 4.3%; p=0.0004), there was no significant difference in the proportion of rheumatologists who ordered HLA-B*58:01 testing at the two facilities (83.3% vs. 88.9%; p=0.70).

Conclusion: Implementing a dashboard plus simple text BPA was associated with a greater increase in the proportion of patients who completed guideline-recommend HLA-B*58:01 testing compared to implementing a dashboard alone.

Disclosure: A. Fadairo-Azinge: None; **g. Schmajuk**: None; **S. Sharma**: None; **C. Flanagan**: None; **S. Faghihi-Kashani**: None; **M. Whooley**: None.

Abstract Number: 2619

What Works? A Consolidated Framework for Implementation Research-Guided Exploration of Patient Safety in Rheumatology Practices

Catherine Nasrallah[1], Cherish Wilson[2], Christine Hariz[3], Alicia Hamblin[4], Cammie Young[5], gabriela Schmajuk[6] and Jinoos Yazdany[4], [1]University of California San Francisco (UCSF), San Francisco, CA, [2]UCSF / SFVA, San Francisco, CA, [3]University of California San Francisco (UCSF, San Francisco, CA, [4]UCSF, San Francisco, CA, [5]University of California, San Francisco, Oakland, CA, [6]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Measures & Measurement of Healthcare Quality (2615–2620)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Despite widespread recognition of persistent patient safety challenges in the U.S. health care system, the development of feasible and scalable solutions has lagged, particularly for ambulatory patients receiving immunosuppressive therapies. In this qualitative study we interviewed stakeholders across a diverse group of rheumatology practices to identify barriers and facilitators of high performance on four national patient safety measures, including screening for Hepatitis B and Tuberculosis prior to initiating immunosuppressive therapy, recommended Hydroxychloroquine dosing, and osteoporosis assessment for high-risk populations.

Table 1: Characteristics of Practices Interviewed

Type of Practice	**N (%)**
Single Specialty group	7 (37)
Academic Medical Center	5 (26)
VA Medical Center	3 (16)
Multi-specialty group	2 (11)
Large Non-academic Health System	1 (5)
Solo practice	1 (5)
Number of People Employed at Practice	
<10	2 (11)
11-30	6 (32)
31-50	4 (21)
51-100	4 (21)
>100	3 (16)
Total Number of Clinicians at Practice	
1–5	6 (32)
6–10	4 (21)
11–20	5 (26)
21–50	2 (11)
>50	2 (11)
Type(s) of Patient Insurance Accepted (not mutually exclusive)	
Private	16 (84)
Public	16 (84)
Medicare and Medicaid	13 (68)
Medicare only	3 (16)
VA	6 (32)
Number of Visits Per Week	
<100	2 (11)
100-200	5 (26)
201-400	6 (32)
401-700	3 (16)
>700	2 (11)
Unknown	1 (5)
Proportion of Visits that are In-Person	
<50%	2 (11)
50-70%	0 (0)
71-90%	5 (26)
91–100%	12 (63)
EHR Vendor	
Epic	6 (32)
NextGen	5 (26)
CPRS	3 (16)
Athena Practice	1 (5)
Amazon Web Services (AWS)	1 (5)
Cerner	1 (5)
CGM Aprima	1 (5)
E-ClinicalWorks	1 (5)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Key Opportunities, Innovations, and Best Practices aligned with CFIR, with Supporting Quotes.

CFIR Domain	Opportunities	Exemplary Quotes
Process	1. Preventive care protocol 2. Risk screening	"I made a letter template that anyone in the health system can use for vaccination recommendations for immunosuppressed patients. I fill it out and send it to the patient. Or fax it into the pharmacy or the PCP." (P150)
Intervention characteristics	1. Medication monitoring system 2. EHR based alerts and reminders 3. Automatic data integration 4. EHR synopsis and customization	"Wherever we start immunosuppressives or biologic .... it's a communication order embedded within MyChart... It automatically takes it to my enrollment team and that will give them clear instructions on whether I need pre-labs." (P149) "If they're on HCQ, we have a pop-up on the side that reminds them to do their eye exams every six months." (P58) "Labs get sent out. They automatically flow in with a HL7 message, then they just flow right into the chart." (P25)
Individual characteristics	1. Commitment to safety and quality improvement	"It happened because I'm interested in quality of care and I like standardization. I like things to be easier and to be efficient." (P142)
Inner Setting	1. Staff training and education 2. Interdisciplinary collaboration 3. Monitoring and evaluation	"I created a laminated Excel spreadsheet, and it'll say the name of the measure, and then what is required of the measure, and what they're needing to do." (P5) "We have a close relationship with our pharmacy team, and I appreciated the Swiss cheese model that they provide. 'Hey, you ordered this, but they haven't had this test in quite a long time. Consider repeating the latent TB test.'" (P144)
Outer Setting	1. External reporting and compliance 2. Regular performance review	"I take a look and see how I'm performing, where I'm performing, and what's going on, and then try to look and do the deeper dive." (P13)

Methods: We identified 139 practices participating in the ACR's RISE registry with above-average performance on ≥1 of the 4 patient safety measures for interviews. Since RISE practices are largely community-based, we also invited 6 academic (AMCs) and 5 Veterans Affairs (VA) medical centers. Rheumatologists and key staff members involved in patient safety measure workflows were invited to take part in virtual semi-structured interviews. Guided by the concepts of the Consolidated Framework for Implementation Research (CFIR), the recorded interviews were transcribed verbatim and analyzed thematically using deductive and inductive techniques to generate themes.

Table 3: Major Challenges Faced by Practices Aligned with CFIR, with Supporting Quotes

CFIR Domain	Barriers	Exemplary Quotes
Process	1. Cumbersome workflow 2. Documentation gaps	"There are instances where there's a weight missing, was incorrectly entered, kilograms are put in for pounds. That's the biggest thing for the hydroxychloroquine– the absence of a reliable or recent weight." (P145)
Innovation	1. Limited EHR data integration 2. Unstructured EHR fields	"Part of the problem is, if it's not discrete data, it doesn't get counted." (P7) "PPD results, we've saved in many different fields, we don't have a great one-stop solution. We have some on the problem list...some saved in notes and carried forward with the date. That's been a challenge." (P140)
Individual characteristics	1. Clinician/staff noncompliance with workflow 2. Patient health literacy	"We're not part of a bigger clinic system. Our doctors are the board members, and they are all very independent and kind of stubborn. So, each one of them does things the way that they want to." (P108) "Another barrier is health literacy in patients. So I often have to find words on how I describe these situations so that the patient can understand at their level." (P150)
Inner Setting	1. Time constraints 2. Structural and logistics barriers 3. Increased workload	"We used to have a DEXA scanner in-house. We haven't had that for several years. So, we send the patient out." (P108) "It's one of my jobs, along with 27,000 others. If I tried to give it to a clinician, it would never get done either." (P58)
Outer Setting	1. Inaccurate data in RISE 2. Insurance and financial constraints	"Our measure is around 40% for Plaquenil, but there's no way it's 40% because most of my patients, regardless of weight, are on 200 mg daily at this point... It's closer to 70." (P14) "Your insurance company doesn't want to pay it but once a year. All of a sudden, we need to put in an order. Sometimes those don't coincide, so a little problematic." (P24)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: We conducted 19 interviews with 21 participants across 11 RISE practices, 5 AMCs, and 3 VAs. Participants included 11 rheumatologists, 6 practice managers, 2 pharmacists, 1 nurse, and 1 quality and compliance manager (Table 1). Practices described several innovative workflows that supported high performance on quality measures. These included standardized screening protocols and safety monitoring tools, often incorporating EHR-based alerts, integrated screening data, performance dashboards, and customized EHR fields for documentation. High performance was commonly attributed to clinicians' strong commitment to patient safety, ongoing staff training on clinical guidelines, and interdisciplinary collaboration, particularly with pharmacists (Table 2).

Respondents also identified persistent challenges including inefficient workflows for repatriating external lab data, inconsistent or missing documentation of screening information in structured EHR fields, non-standardized workflows and logistical difficulties in tracking the implementation and performance of safety measures (Table 3).

Conclusion: This study provided critical insights into key barriers and facilitators affecting rheumatology practices' performance on patient safety measures. Qualitative interviews revealed strategies associated with higher performance on safety measures, such as EHR-supported protocols and collaboration with pharmacists, but also highlighted challenges like inefficient workflows for data entry and data integration issues. These findings have laid the foundation for the development of the Rheum Safe Patient Safety Toolkit, currently in development. The toolkit will guide RISE practices in implementing patient safety measures and optimizing workflows for scalable and sustained improvement.

Disclosure: C. Nasrallah: None; **C. Wilson**: None; **C. Hariz**: None; **A. Hamblin**: None; **C. Young**: None; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, Aurinia, 5, Gilead, 5.

Abstract Number: 2620

Transition Success of Pediatric Rheumatology Patients: A Novel Scoring System

Kyla Blasingame[1], David McDonald[1], Karissa Chesky[1], Jimin Kim[1], charles lee[1], Constance Wiemann[1], Blanca Sanchez-Fournier[1], Miriah Gillispie-Taylor[2] and Tiphanie Vogel[1], [1]Baylor College of Medicine, Houston, TX, [2]Baylor College of Medicine/Texas Children's Hospital, Houston, TX

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Measures & Measurement of Healthcare Quality (2615–2620)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Success of transition from pediatric to adult care depends on many factors. Various scores for transition readiness have been developed, including some designed to capture patient self-reported readiness and others that focus on program specific parameters. However, few patient-level transition success scores exist. Without such a score, it is difficult to assess the impact of programmatic interventions to improve the process of transition on transition outcomes. We created a novel transition success score for pediatric rheumatology patients.

Methods: Pediatric rheumatologists and adolescent health experts were consulted. Four components were included in the score: attending the first adult appointment in the time frame designated by the pediatric rheumatologist (component 1), refilling medications within 3 months of the first adult appointment (component 2), attending a second adult appointment (component 3), and no rheumatology-related emergency department visits in the first year after transition (component 4).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Scores were determined via electronic medical record (EMR) review. Each component was weighted as one-quarter of the total transition success score. The few patients who transitioned off medications were scored successfully for component 2.

Results: From 2017-2024, we identified 357 patients with a final visit to pediatric rheumatology using direct provider notification of transition to adult rheumatology clinic and EMR review. Of those, 199 were able to be scored for transition success. Some patients were unable to be scored due to subsequent healthcare details being inaccessible via EMR (n=73), others because it was still < 1 year since the final pediatric appointment (n=59), and others for various reasons such as dismissal from the need for future rheumatology followup (n=26). The average age at transition was 18.6 years. 73/199 (37%) patients scored 100 (ie achieved all 4 components of successful transition) and 77/199 (39%) scored 75. Only 3 patients (1.5%) scored 0. The average score was 74.3%. When considered by component, 114 patients (57%) met component 1, 151 (76%) met component 2, 160 (80%) met component 3, and 166 (83%) met component 4.

Conclusion: We developed a transition success score and applied it to patients who had transitioned from our pediatric rheumatology clinic. Although 150/199 patients (75%) fulfilled 3 or 4 out of 4 components of successful transition, we were unable to document attendance at a second adult rheumatology appointment for a surprising 20% of transitioned patients. Our next steps include correlating components of our transition program, including demographics, transition planning, self-reported transition readiness, and receipt of a transition summary letter, with the transition success score to better understand what factors predict successful transition.

Disclosure: K. Blasingame: None; **D. McDonald**: None; **K. Chesky**: None; **J. Kim**: None; **c. lee**: None; **C. Wiemann**: None; **B. Sanchez-Fournier**: None; **M. Gillispie-Taylor**: None; **T. Vogel**: AstraZeneca, 5, moderna, 2, Pfizer, 2, SOBI, 1, 2, takeda, 6.

Abstract Number: 2621

Erosive Hand Osteoarthritis Is Associated With Increased Risk of Incident Osteoporotic Fractures In Post-menopausal Women (QUALYOR Cohort)

MAXIME AUROUX[1], MERCIER-GUERY Alexandre[1], PIOT Anne[2], MERLE Blandine[3], PRORIOL Mathilde[1], FONTANGES Elisabeth[1], DUVERT Florence[1], Eric LESPESSAILLES[4] and CHAPURLAT Roland[1], [1]Hospices Civils de Lyon, LYON, France, [2]Centre Hospitalier Lucien Hussel, VIENNE, France, [3]INSERM U1033, LYON, France, [4]University Hospital of Orléans, Orleans, France

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis – Clinical (2621–2626)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Erosive hand osteoarthritis (ErHOA) is a severe form of hand osteoarthritis (HOA) characterized by greater inflammation and higher burden of disease. In this more inflammatory form of HOA, we wanted to explore bone loss and fracture

Methods: We used data from the prospective QUALYOR study that enrolled 1575 postmenopausal women, aged at least 55 years, followed prospectively for 12 years.

At the 5-year visit (baseline of this work), we evaluated HOA using hand radiographs and clinical examination. HOA status was defined as follows:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

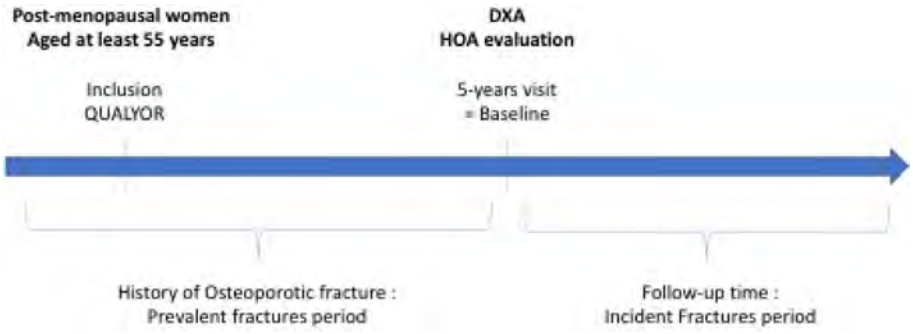


Figure 1. Study design

- No HOA : no pain AND no radiographic sign
- Radiographic HOA (RxHOA) : at least 2 joints graded KL ≥ 2 AND no symptoms
- Symptomatic HOA (SyHOA) : ACR criteria for HOA (no eroded joints)
- Erosive HOA (ErHOA) : SyHOA with at least one eroded joint

Osteoporotic (OP) status was evaluated at the 5-year visit by DXA (BMD at lumbar spine and hip) and history of fractures (medically confirmed) was recorded. Incident OP fractures at each subsequent follow-up visit were medically ascertained. OP status was defined as follows:

- No OP: All T-scores above -2.5 AND no history of OP fractures
- OP DXA: At least one T-score bellow -2.5 AND no history of OP fracture
- OP fracture: History of at least one OP fracture (regardless of T-scores)

Table 1. Characteristics of the total population and according to HOA status

Population		Total Population	No HOA	RxHOA	Sy HOA no Er	ErHOA	p-value
Effectives	n	**1180**	**364**	**335**	**340**	**141**	
Mean Follow-up time (SD)	years	4.66 (0.85)	4.72 (0.79)	4.64 (0.87)	4.68 (0.83)	4.48 (0.98)	n.s
Mean age (SD)	years	71.73 (6.41)	69.24 (5.58)	72.37 (6.43)	72.10 (6.03)	75.77 (6.65)	<0.001
Mean BMI (SD)	kg/m2	24.95 (4)	24.79 (4.38)	24.63 (3.58)	25.27 (3.91)	25.36 (4.11)	n.s
Mean T-score Hip (SD)	D.S	-1.51 (0.73)	-1.45 (0.75)	-1.60 (0.71)	-1.49 (0.73)	-1.48 (0.73)	n.s
Mean T-score neck (SD)	D.S	-1.71 (0.62)	-1.66 (0.63)	-1.79 (0.57)	-1.70 (0.64)	-1.71 (0.63)	<0.05
Mean T-score lumbar spine (SD)	D.S	-1.4 (0.97)	-1.55 (0.90)	-1.44 (0.86)	-1.27 (1.07)	-1.20 (1.11)	<0.001
OP statuts							
No OP	n (%)	827 (70.1%)	242 (66.5%)	237 (70.7%)	248 (72.9%)	100 (70.9%)	
OP DXA	n (%)	201 (17%)	59 (16.2%)	58 (17.3%)	57 (16.8%)	17 (12.1%)	n.s
OP fracture	n (%)	152 (12.9%)	63 (17.3%)	40 (11.9%)	35 (10.3%)	24 (17%)	
Bone treatment at baseline	n (%)	57 (4.8%)	24 (6.6%)	15 (4.5%)	11 (3.2%)	7 (5%)	n.s
Mean treatment duration at baseline	years	2.43 (1.52)	2.40 (1.44)	2.09 (1.57)	3.17 (1.71)	2.12 (1.28)	n.s
Type of treatment							
Bisphosphonate	n	45	17	13	10	5	-
Denosumab	n	8	4	2	1	1	-
Teriparatide	n	2	2	0	0	0	-
Raloxifene	n	2	1	0	0	1	-
Calcium supplémentation	n (%)	209 (17.7%)	58 (15.9%)	72 (21.5%)	53 (15.6%)	26 (18.4%)	n.s
Vitamin D supplementation	n (%)	1061 (89.9%)	325 (89.3%)	296 (88.4%)	311 (91.5%)	129 (91.5%)	n.s
Prevalent fracture	n (%)	152 (12.9%)	53 (14.6%)	40 (11.9%)	35 (10.3%)	24 (17%)	n.s
Time from 1st fracture to baseline	years	3.01 (1.81)	3.09 (1.89)	2.85 (1.92)	3.34 (1.73)	2.59 (1.53)	n.s
Number of prevalent fractures at baseline	n	190	66	47	43	34	-
1 fracture	n	123	45	34	27	17	-
2 fractures	n	24	6	5	8	5	-
3 fractures	n	2	0	1	0	1	-
4 fractures	n	2	1	0	0	1	-
5 fractures	n	1	1	0	0	0	-
Incident fracture	n (%)	131 (11.1%)	38 (10.4%)	31 (9.3%)	37 (10.9%)	25 (17.7%)	0.05
Time from baseline to 1st incident fracture	years	2.2 (1.42)	2.31 (1.38)	2.22 (1.51)	2.20 (1.38)	2.04 (1.48)	n.s
Number of incident fractures	n	166	43	39	54	30	-
1 incident fracture	n	106	33	27	25	21	-
2 incident fractures	n	19	5	2	9	3	-
3 incident fractures	n	3	0	0	2	1	-
4 incident fractures	n	2	0	2	0	0	-
5 incident fractures	n	1	0	0	1	0	-
Comorbidities							
Diabete	n (%)	52 (4.4%)	12 (3.3%)	16 (4.8%)	14 (4.1%)	10 (7.1%)	n.s
HTA	n (%)	416 (35.3%)	110 (30.2%)	119 (35.5%)	124 (36.5%)	63 (44.7%)	n.s
Hypercholesterolemia	n (%)	282 (23.9%)	73 (20.1%)	78 (23.3%)	91 (26.8%)	40 (28.4%)	n.s
Obesity	n (%)	127 (10.8%)	37 (10.2%)	26 (7.8%)	39 (11.5%)	25 (17.7%)	0.05

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

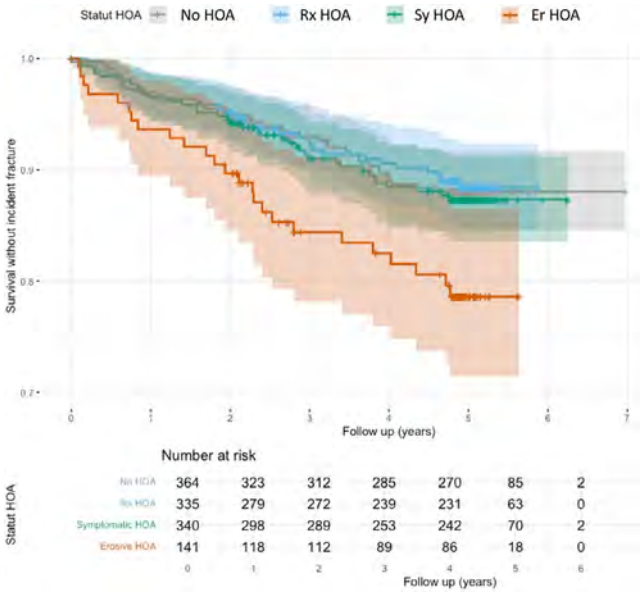


Figure 2. Kaplan-Meier curves representation the survival without incident fracture according to HOA status

We investigated the association between HOA status and incidence of OP fractures using a Cox model with adjustment for age, history of fractures, T-scores and obesity. Kaplan Meier curves representing survival without incident fractures were obtained according to HOA status. We also conducted a subgroup analysis stratifying patient by prevalent fracture at baseline combined with HOA status.

Results: We have analyzed data from 1180 patients. The mean age was 71.7(± 6.41) years and the mean follow-up time was 4.6 (±0.85) years. Among them, 364 (30.8%) had no HOA, 335 (28.4%) had RxHOA, 340 (28.8%) had SyHOA and 141 (11.9%) had ErHOA. Patients with HOA were older than patients without HOA (Table 1)

During follow-up, 131 patients (11.1%) experienced 166 incident OP fractures with a mean follow-up time to event of 2.2 (±1.42) years. Patients with incident OP fractures were older and had lower BMD. Among them 19.1% had ErHOA compared to 11.1% in those without incident OP fracture ($p< 0.05$). Kaplan-Meier curves depicting the survival without incident fracture according to HOA status is provided in Figure 2. The HR for incident fracture in patients with ErHOA compared to patients without HOA was 1.93 (CI95% 1.12-3.32, $p< 0.05$), whereas the HR was 1.1 (CI95% 0.69-1.77) for SyHOA and HR 0.95 (CI95% 0.59-1.57) for RxHOA compared with patients without HOA.

Patients with ErHOA and no history of OP fracture had an increased risk of incident fractures with a HR of 1.95 (CI95% 1.07-3.5, $p< 0.05$) compared to patient without HOA and no history of fracture. Of note, patients without HOA but prevalent OP fracture – a recognized strong risk factor for fracture – had a HR of 1.41 (CI95% 0.62-3.23) when compared with those without prevalent fracture.

Conclusion: In conclusion, erosive HOA is a strong predictor of incident osteoporotic fracture, in postmenopausal women, independently of various classical risk factors for fracture. Exploring the sources of bone loss distinguishing erosive HOA from other types of HOA is warranted.

Disclosure: M. AUROUX: None; **M. Alexandre**: None; **P. Anne**: None; **M. Blandine**: None; **P. Mathilde**: None; **F. Elisabeth**: None; **D. Florence**: None; **E. LESPESSAILLES**: AbbVie, 5, 6, Amgen, 2, 5, 6, Eli Lilly, 2, 5, 6, Expanscience, 2, 6, Galapagos, 6, MSD, 2, 5, 6, Novartis, 5, UCB, 5; **C. Roland**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2622

Oral Microbiome Dysbiosis and Oral-gut Microbial Network Disruption in Hand Osteoarthritis: Data from the Xiangya Osteoarthritis Study

Jiatian Li[1], Yadan Xiao[2], Tuo Yang[1], david Hunter[3], Weiya Zhang[4], Michael Doherty[4], Yuqing Zhang[5], Zidan Yang[1], Yilun Wang[1], Dongxing Xie[1], Changjun Li[1], Wei Li[1], Zeqin Wen[1], Chao Zeng[1], Guanghua Lei[1] and **Jie Wei[1]**, [1]Xiangya Hospital, Central South University, Changsha, Hunan, China (People's Republic), [2]Xiangya School of Public Health, Central South University, Changsha, Hunan, China (People's Republic), [3]Sydney Musculoskeletal Health, University of Sydney, St Leonards, New South Wales, Australia, [4]School of Medicine, University of Nottingham, Nottingham, United Kingdom, [5]Massachusetts General Hospital, Quincy, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis – Clinical (2621–2626)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: The oral microbiome plays a critical role in modulating systemic inflammation and maintaining immune homeostasis, partly through its interactions with the gut microbiome. Although gut microbiome dysbiosis has been implicated in symptomatic hand osteoarthritis (SHOA), the role of oral microbiome dysbiosis in SHOA and its potential correlation with gut microbiome remains unclear. Elucidation these relationships may provide novel insights into the pathogenesis of SHOA and inform future treatment strategies.

Methods: Participants were recruited from the Xiangya Osteoarthritis (OA) Study, a community-based cohort study. SHOA was defined as the presence of both self-reported pain and radiographic OA in at least one hand. The control group comprised participants without hand pain or radiographic OA. Among the 764 participants included in this study, 52 (6.8%) had SHOA. Saliva samples were analyzed using 16S rRNA gene sequencing. Oral microbial richness (α-diversity, measured by Shannon index) and composition (β-diversity, measured by Bray-Curtis distance) were compared between SHOA and control groups. Associations of the relative abundance of oral microbiome genera with SHOA and its severity were examined. Functional alterations in the oral microbiome were inferred using Kyoto Encyclopedia of Genes and Genomes (KEGG) level 3 pathways analysis. Gut microbiome data from a previous study conducted within the same cohort were

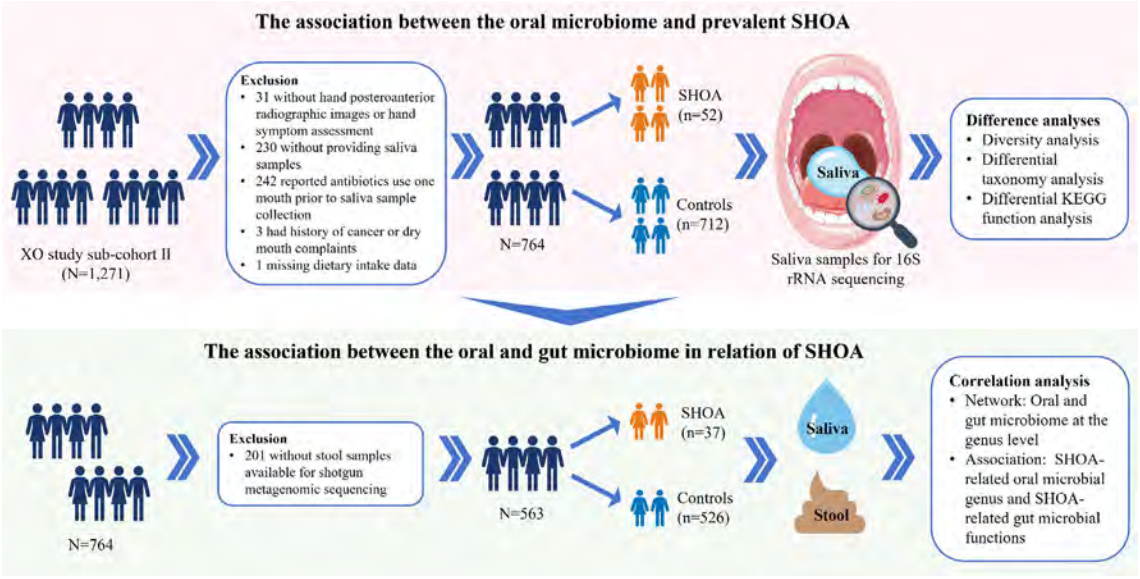


Figure 1. Summary of the present study. SHOA, symptomatic hand osteoarthritis; KEGG, Kyoto Encyclopedia of Genes and Genomes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

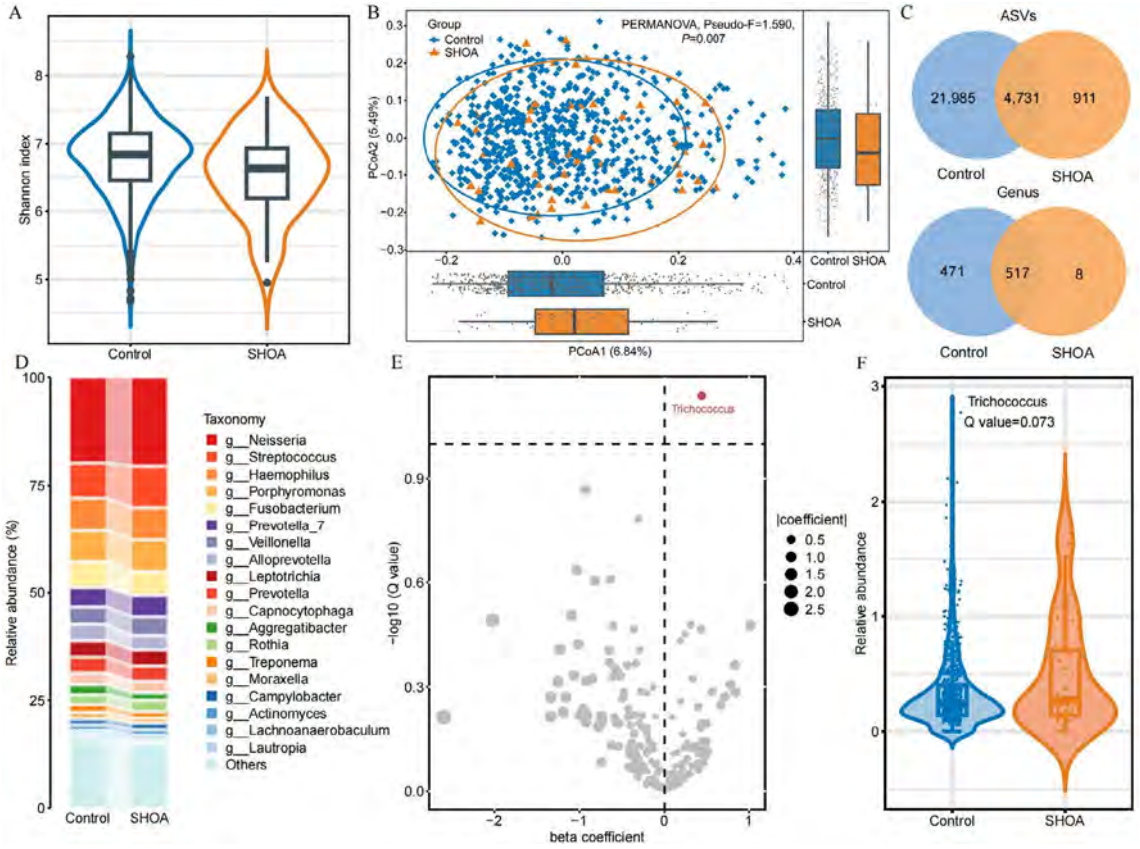


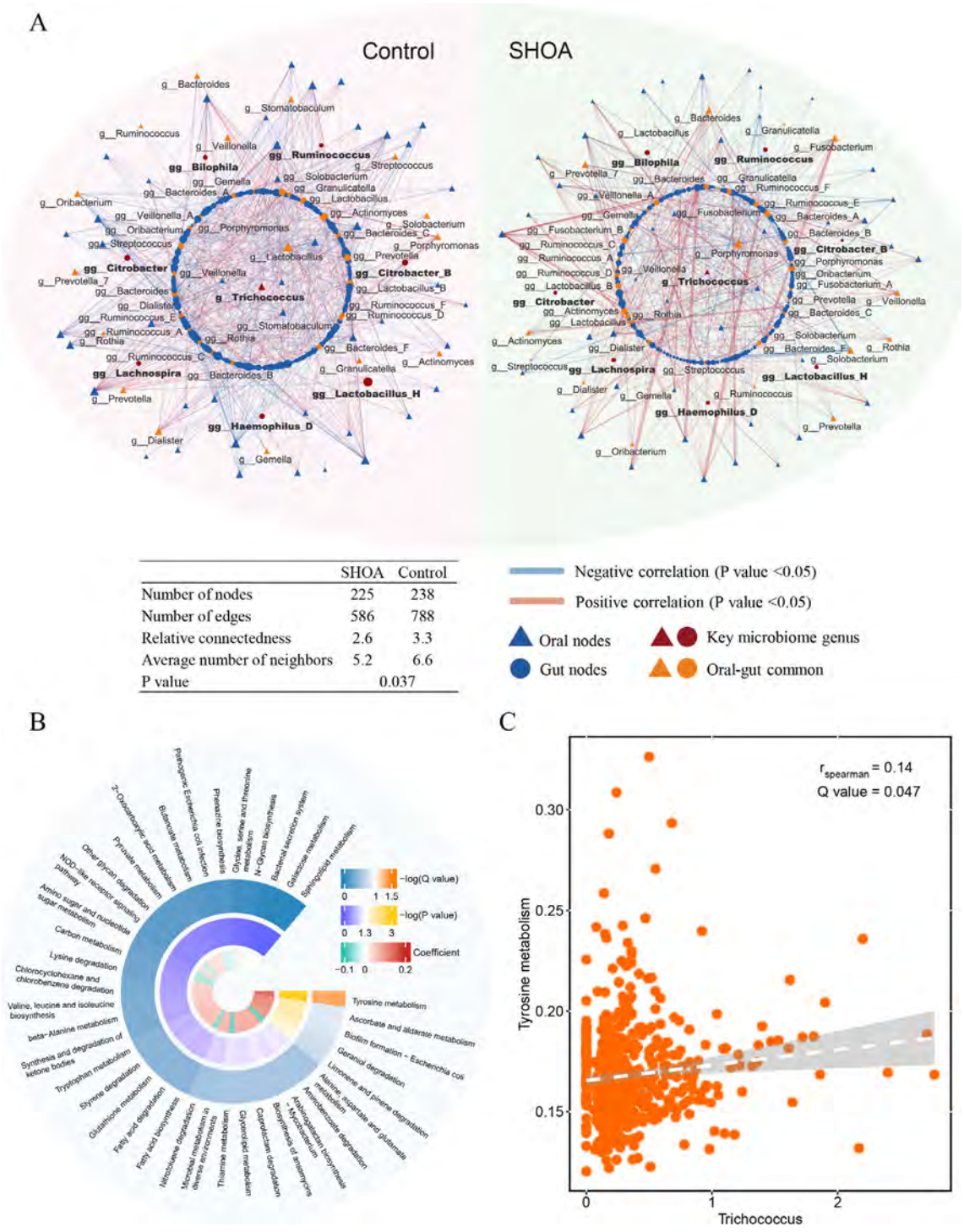
Figure 2. Comparison of oral microbiome diversity and composition between participants with SHOA and controls. (A) Violin plots showing α-diversity measured by the Shannon index between participants with SHOA and controls. (B) PCoA plots comparing β-diversity measured by Bray-Curtis distance between participants with SHOA and controls. (C) Venn diagram illustrating shared and exclusive ASVs and microbial genera between participants with SHOA and controls. (D) Relative abundance of the top 20 microbial genera in the oral microbiome composition of participants with SHOA and controls. (E) Volcano plot depicting differences in the microbial genera between participants with SHOA and controls. The red region indicates statistically significant differences (Q<0.1). (F) Relative abundance of differential microbial genus between participants with SHOA and controls. SHOA, symptomatic hand osteoarthritis; PCoA, principal coordinates analysis; ASVs, amplicon sequence variants.

integrated to examine ecological links between the oral and gut microbiomes.[1] Correlations between SHOA-associated oral microbial genera and SHOA-associated gut microbial functions were also assessed. A workflow is presented in **Fig. 1**.

Results: Compared with controls, participants with SHOA exhibited significantly lower oral microbial α-diversity (P=0.007, **Fig. 2A**) and altered β-diversity (P=0.007, **Fig. 2B**). A total of 911 amplicon sequence variants and eight genera were uniquely identified in the SHOA group (**Fig. 2C**). In both the SHOA and control groups, the oral microbiome was predominantly composed of the genera *Neisseria*, *Streptococcus*, *Haemophilus*, *Porphyromonas*, *Fusobacterium***(Fig. 2D)**. The relative abundance of the genus *Trichococcus* was significantly higher in SHOA participants (P=0.001, Q=0.073, **Fig. 2E-F**), and was positively correlated with SHOA severity. Oral microbiome KEGG level 3 pathways involved in tropane, piperidine, and pyridine alkaloid biosynthesis (P=0.006, Q=0.084), as well as indole alkaloid biosynthesis (P=0.006, Q=0.090), were significantly inversely associated with SHOA. Furthermore, the number of correlations in the oral-gut microbiome network was significantly reduced in SHOA participants compared with controls (**Fig. 3A)**. Additionally, a positive correlation was observed between oral microbiota *Trichococcus* and the gut microbiome KEGG pathway of tyrosine metabolism, both of which were significantly associated with SHOA (P=0.001, Q=0.047, **Fig. 3B-C**).

Conclusion: Oral microbiome dysbiosis and the disrupted oral-gut microbiome network are associated with prevalent SHOA, suggesting a potential role for oral-gut microbiome interactions in disease pathogenesis.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



	SHOA	Control
Number of nodes	225	238
Number of edges	586	788
Relative connectedness	2.6	3.3
Average number of neighbors	5.2	6.6
P value	0.037	

Figure 3. Oral-gut microbiome correlation networks at the genus level in SHOA group and control group and the association between SHOA-related oral microbial genus and SHOA-related gut microbial functions. (A) Only genera with a relative abundance >0.01 and present in >70% of samples were considered. Solid lines indicate significant correlations (P<0.05) between oral and gut microbial genera, with line width indicating correlation magnitude. Red and blue edges represent positive and inverse correlations, respectively. Red triangles (circles) denote oral (gut) microbial genera with significant differences in relative abundance between the SHOA group and the control group. Yellow triangles (circles) represent oral (gut) microbial genera with no significant differences in relative abundance between the two groups. (B) Heatmap-circle showing correlations between SHOA-related oral microbial genus (i.e., Trichococcus) and SHOA-related gut microbial KEGG pathways. (C) Scatter plot illustrating the correlation between the SHOA-related oral microbial genus (i.e., Trichococcus) and the SHOA-related KEGG pathway (i.e., tyrosine metabolism), which was identified as a significant association. SHOA, symptomatic hand osteoarthritis; KEGG, Kyoto Encyclopedia of Genes and Genomes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

REFERENCES
1. Wei J, et al. EBioMedicine 2023;98:104892.

Disclosure: J. Li: None; **Y. Xiao**: None; **T. Yang**: None; **d. Hunter**: None; **W. Zhang**: None; **M. Doherty**: None; **Y. Zhang**: None; **Z. Yang**: None; **Y. Wang**: None; **D. Xie**: None; **C. Li**: None; **W. Li**: None; **Z. Wen**: None; **C. Zeng**: None; **G. Lei**: None; **J. Wei**: None.

Abstract Number: 2623

Disease Activity is a Novel Imaging Biomarker Associated with Knee Pain: Data from the Osteoarthritis Initiative

Jeffrey Driban[1], Jonggyu Baek[2], Julieann Patarini[2], Emily Kirillov[3], Nhung Vo[3], Michael Richard[3], Ming Zhang[4], Matthew Harkey[5], Grace Lo[6], Kate Lapane[2], Shao-Hsien Liu[2], Charles Eaton[7], James Mackay[8], Joshua Harvey[2] and Timothy McAlington[9], [1]University of Massachusetts Chan Medical School, Marlborough, NH, [2]UMass Chan Medical School, Worcester, MA, [3]Tufts Medical Center, Boston, MA, [4]Boston University, Westford, MA, [5]Michigan State University, East Lansing, MI, [6]Baylor College of Medicine / MEDVAMC, Houston, TX, [7]Brown University, Pawtucket, RI, [8]University of Cambridge; Norwich Medical School, San Diego, CA, [9]UMass Chan School of Medicine, Arlington, MA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis – Clinical (2621–2626)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Barriers to developing effective osteoarthritis (OA) therapies include the lack of standardized definitions for disease progression and structural endpoints that reliably predict changes in symptoms (e.g., pain). We recently developed a "disease activity" composite metric that combines bone marrow lesion (BML) and effusion-synovitis volumes on magnetic resonance (MR) imaging into a standardized definition of disease progression related to pain. While many imaging biomarkers are associated with pain, the clinically meaningful magnitude of change in these measures remains unclear. We aimed to examine the association between 2-year changes in disease activity and 2-year changes in knee pain and quantify thresholds of clinically meaningful change for our novel disease activity composite metric.

Methods: We conducted a longitudinal nested cohort study within the Osteoarthritis Initiative, including participants with at least possible radiographic knee OA (Kellgren-Lawrence grade ≥ 1) and mild knee pain (WOMAC pain score ≥ 10/100). We measured BML and effusion-synovitis volumes on MR images (intraclass correlation coefficients > 0.95). We assessed 4 methods to calculate the disease activity metric: 1) sum of standardized volumes, 2) z-score, 3) percentile, and 4) adjusted

Table. The distribution and association of 2-year changes in disease activity (DA) metrics with categories of 2-year changes in knee pain.

	2-year changes of WOMAC				
2-year change	Pain Improvement < -20 (n = 139) median (25th, 75th)	No Change -20 to 20 (Reference) (n = 1081) median (25th, 75th)	Pain Worsening > 20 (n = 75) median (25th, 75th)	OR (95% CI)* Pain Improvement	OR (95% CI)* Pain Worsening
DA	-0.07 (-1.26, 0.86)	0.32 (-0.33, 1.24)	1.18 (-0.06, 2.64)	0.87 (0.82, 0.93)	1.16 (1.05, 1.27)
DA z-score	-0.05 (-0.43, 0.32)	0.15 (-0.13, 0.46)	0.43 (-0.03, 0.88)	0.46 (0.34, 0.63)	2.09 (1.32, 3.32)
DA percentile	-0.73 (-10.84, 8.85)	3.21 (-3.18, 13.17)	11.81 (-1.00, 27.78)	0.79 (0.72, 0.87)	1.29 (1.13, 1.47)
Adjusted DA percentile	-1.11 (-14.86, 8.57)	2.53 (-4.14, 12.81)	11.05 (-1.06, 27.66)	0.79 (0.72, 0.87)	1.30 (1.14, 1.48)

* Footnote: Odds ratio (OR) per unit increase of DA and DA z-score; OR per 10 percent increase of percentiles.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

percentile. We used established cut-points to categorize 2-year change in pain: 1) pain improvement (< - 20), 2) minimal change (-20 to 20), and 3) worsening (> 20). We calculated the distribution of each disease activity metric across categories of changes in WOMAC knee pain. We then used multinomial logistic regression to explore the association between 2-year changes in disease activity and categories of changes in WOMAC knee pain (3-level outcome, reference = minimal change).

Results: Among 1,295 knees (641 participants), 139 knees had meaningful pain improvement (71% female, 53% obese, 81% radiographic knee OA), 75 knees had worsening (70% female, 62% obese, 79% radiographic knee OA), and 1,081 had no meaningful change (58% female, 45% obese, 79% radiographic knee OA). Changes in each disease activity metric were associated with both pain improvement (OR= 0.46 to 0.87; Table) and pain worsening (OR= 1.16 to 2.09; Table). Among knees with minimal change in pain, most knees experienced worsening disease activity scores (Table). Median disease activity changes among participants with pain improvement or worsening may serve as a threshold for defining minimally clinically important changes to effectively distinguish most knees with minimal pain changes as having minimal disease activity changes (Table, Figure).

Conclusion: All disease activity metrics were associated with knee pain, underscoring their utility in monitoring disease activity as an indicator of pain. Most knees with minimal changes in pain had subtly worsening disease activity, which reflects the natural history of OA progression. Most knees showing clinically meaningful improvement in pain experienced improved

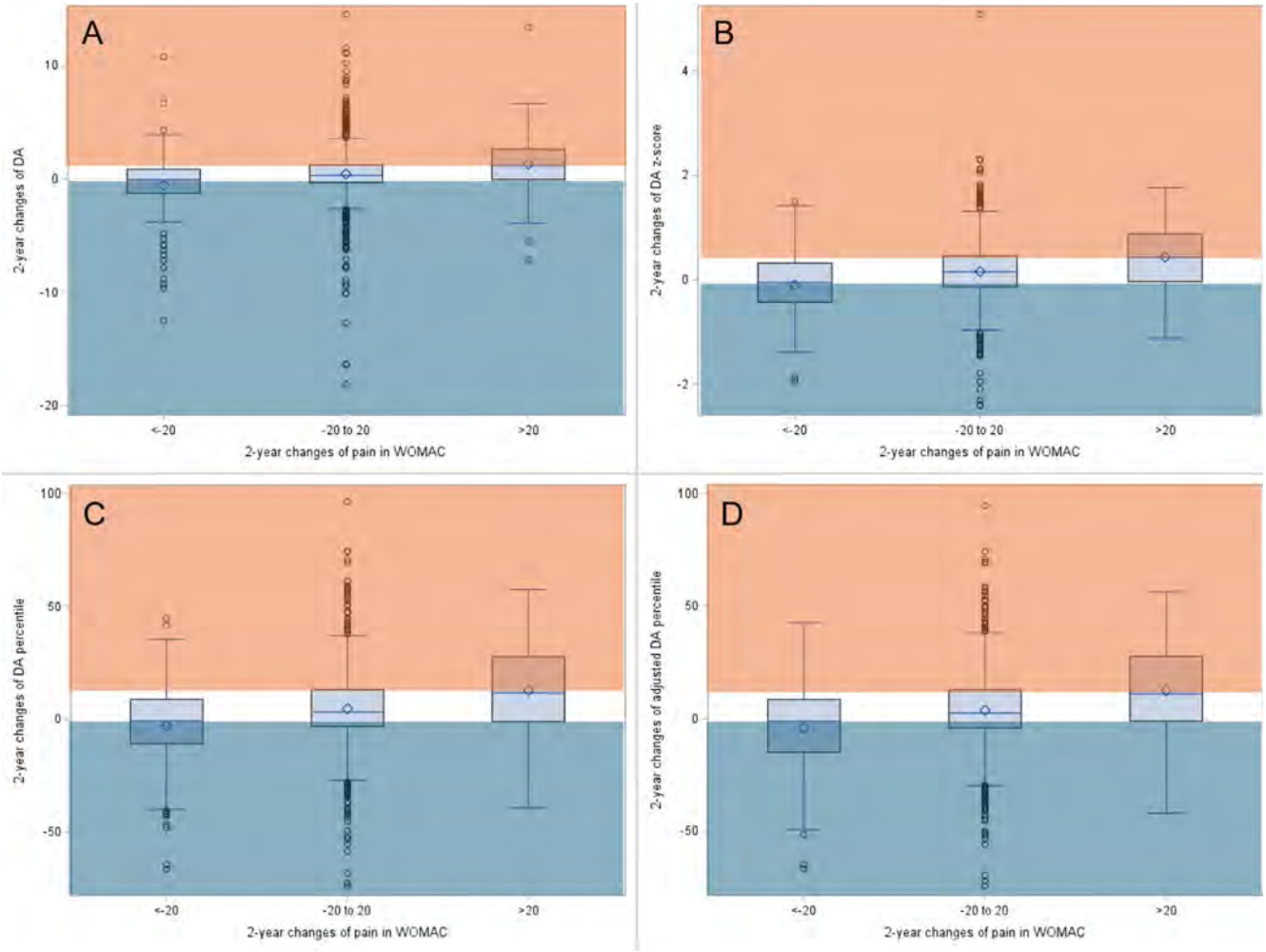


Figure. The distribution of 2-year changes in disease activity (DA) metrics across categories of 2-year changes in WOMAC knee pain scores, with orange reflecting clinically meaningful worsening in disease activity and blue representing clinically meaningful improvement in disease activity. Note. A. Disease activity score, B. Disease activity z-score, C. Disease activity percentile, and D. Disease activity adjusted percentile.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disease activity; in contrast, knees with worsening knee pain had worsening disease activity. Our composite disease activity metric shows promise as a biomarker for defining structural progression in knee OA that is clinically relevant to pain outcomes.

Disclosure: J. Driban: None; **J. Baek**: None; **J. Patarini**: None; **E. Kirillov**: None; **N. Vo**: None; **M. Richard**: None; **M. Zhang**: None; **M. Harkey**: None; **G. Lo**: None; **K. Lapane**: None; **S. Liu**: None; **C. Eaton**: None; **J. Mackay**: AstraZeneca, 3, Blue Earth Diagnostics, 3; **J. Harvey**: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2.

Abstract Number: 2624

Results of Large Multi-Site Pragmatic Clinical Trial Comparing Corticosteroids or Blinded Lidocaine-only Injections in Treating Osteoarthritis of the Knee

Joshua Baker[1], Katherine Wysham[2], Mercedes Quinones[3], Bryant England[4], Kaitian Jin[1], Marianna Olave[5], Sarah Wetzel[6], Rachel Gillcrist[7], Criswell Lavery[1], Natalie Keller[8], Kimberly Hayes[9], Bridget Kramer[4], Hannah Brubeck[10], Bibiana Ateh[11], Daniel K. White[12], Alexis Ogdie[13], Rui Xiao[1], Tuhina Neogi[14] and Carla Scanzello[1], [1]University of Pennsylvania, Philadelphia, PA, [2]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [3]Washington DC VA Medical Center, Bethesda, MD, [4]University of Nebraska Medical Center, Omaha, NE, [5]Brown University, Philadelphia, PA, [6]Drexel University, Pittsburgh, PA, [7]Dartmouth College, Lebanon, NH, [8]University of Oklahoma, Philadelphia, PA, [9]Teachers College, Columbia University, Philadelphia, PA, [10]VA Puget Sound Health Care System, Seattle, WA, [11]Washington VA Medical Center, Washington, District of Columbia, [12]University of Delaware, Newark, DE, [13]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE, [14]Boston University School of Medicine, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis – Clinical (2621–2626)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Intra-articular corticosteroids are widely used for routine management of chronic pain from knee osteoarthritis (KOA), though estimates of their benefit vary widely. We aimed to quantify the short-term benefit of corticosteroid injections in reducing symptoms of KOA in a large, pragmatic, multi-site clinical trial.

Methods: This was a factorially-designed crossover randomized trial among patients with KOA across 4 Veteran Affairs Medical Centers. Participants were 40-80 years of age, had a clinical diagnosis of KOA, a Kellgren-Lawrence X-ray grade > or = 1, and a clinical indication for joint injection according to the treating provider. Participants were randomized to an incentive arm to promote physical activity, or an attention control. Within these arms, participants were further randomized to receive blinded injections with corticosteroid plus lidocaine (40 mg methylprednisolone) or lidocaine-only in a crossover design over 28 weeks. The primary outcome was the change in the Knee Osteoarthritis Outcome Score (KOOS) (range 0-100). A change of $\geq$10 was considered the minimal clinically important difference (MCID). Linear or generalized mixed-effects models were used to evaluate the effect of the corticosteroid injection over all outcomes between 2-12 weeks. We also performed a crossover analysis among 196 participants that received a second injection at week 16 (N=392). Sensitivity analyses included a last-observation-carried-forward approach to account for missingness as well as sub-group analyses.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

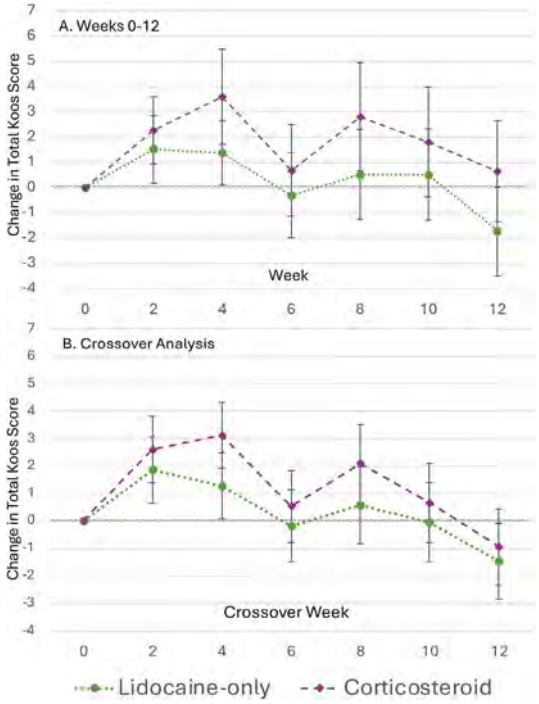


Figure 1: Changes in total KOOS (with 95% confidence intervals) in the corticosteroid plus lidocaine (purple) and lidocaine-only (green) arms over 12 weeks of follow up for A) the primary analysis between weeks 0-12, and B) the crossover analysis. An increase in KOOS indicates an improvement/reduction in KOA symptoms.

Table 1: Time-averaged change from baseline among those receiving corticosteroid plus lidocaine compared to those receiving lidocaine only over all time-points between 2 and 12 weeks. The standardized effect size (or risk difference for binary outcomes) are also shown.

	Corticosteroid N=110	**Lidocaine-only N=111**		
First Injection (2-12 Weeks)	*Mean (SE)*	*Mean (SE)*	*Effect Size/ Risk Difference*	*p-value*
Primary Outcome				
Change in Total KOOS	1.69 (1.01)	-0.034 (1.02)	0.25	0.23
Secondary Outcomes				
Probability of KOOS MCID	20.9%	16.8%	0.041	0.31
KOOS Pain	2.15 (1.22)	0.084 (1.22)	0.22	0.23
KOOS Symptoms	-1.68 (0.95)	-3.37 (0.96)	0.15	0.21
KOOS ADL	1.41 (1.25)	1.30 (1.25)	0.012	0.96
KOOS Sports/Rec	1.53 (1.81)	-2.83 (1.82)	0.36	0.09
KOOS QOL	4.42 (1.23)	4.85 (1.24)	0.046	0.81
PROMIS Pain Intensity	-1.21 (0.56)	-0.90 (0.56)	0.077	0.70
PROMIS Pain Interference	-1.86 (0.51)	-0.71 (0.52)	0.29	0.12
PROMIS Pain Behavior	-0.62 (0.39)	-0.71 (0.39)	0.027	0.87
	Corticosteroid N=196	**Lidocaine-only N=196**		
Crossover (2-12 weeks)	*Mean (SE)*	*Mean (SE)*	*Effect Size/ Risk Difference*	*p-value*
Change in Total KOOS	0.86 (0.94)	0.48 (0.94)	0.045	0.29
Probability of KOOS MCID	19.7%	15.3%	0.044	0.10
KOOS Pain	1.64 (1.06)	0.98 (1.06)	0.06	0.15
KOOS Symptoms	-1.92 (0.69)	-2.52 (0.69)	0.050	0.24
KOOS ADL	1.53 (1.17)	1.30 (1.17)	0.022	0.61
KOOS Sports/Rec	0.42 (1.48)	0.062 (1.48)	0.029	0.50
KOOS QOL	2.46 (1.06)	2.81 (1.05)	0.030	0.43
PROMIS Pain Intensity	-1.05 (0.40)	-0.43 (0.40)	0.13	0.03
PROMIS Pain Interference	-1.04 (0.38)	-0.33 (0.38)	0.15	0.02
PROMIS Pain Behavior	-0.68 (0.28)	-0.60 (0.28)	0.021	0.74

Footnote: Changes are predicted from mixed effects models that incorporate all bi-weekly time-points between 2 and 12 weeks and are adjusted for the baseline value.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

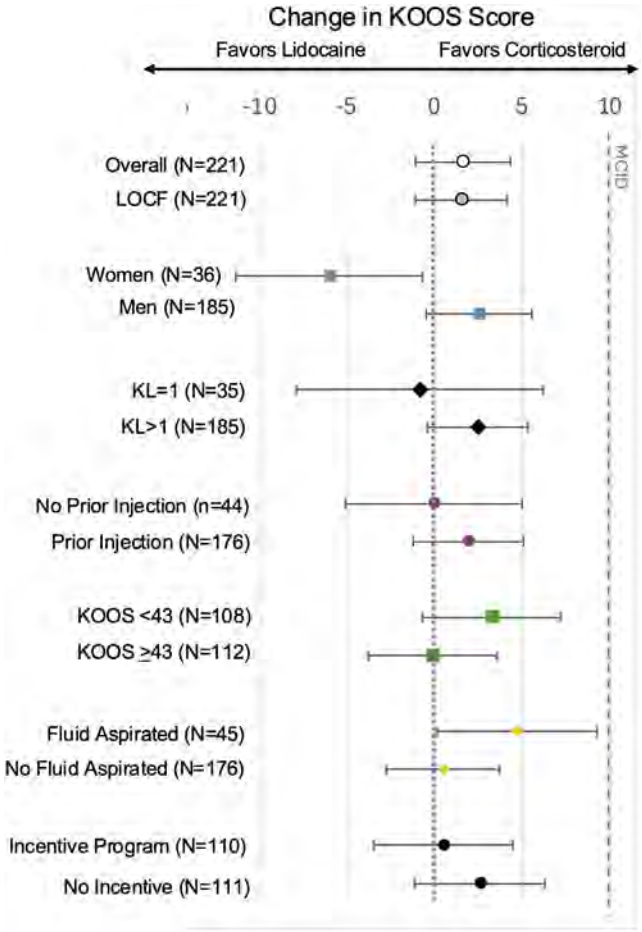


Figure 2: Subgroup analyses for primary outcome comparing corticosteroid plus lidocaine to lidocaine-only. Point estimates and confidence intervals shown are the estimates of difference betweenc corticosteroid and lidocaine-only groups from time-averaged mixed-effects models within each subgroup of interest. Abbreviations: KL, Kellgren-Lawrence; KOOS, Knee Osteoarthritis Outcome Score; LOCF, last observation carried forward.

Results: Of 231 enrolled, 221 were randomized (mean age 64 years; 84% male, median K-L grade of 3). 176 (80%) had received a prior injection. Those randomized to initial corticosteroids showed no improvement in total KOOS scores compared to lidocaine-only at any time point or when evaluating all outcomes over 12-weeks [B: 1.72 (95% CI: -1.08, 4.52) p=0.23] (**Figure 1a**, **Table 1**). The probability of achieving KOOS MCID was 20.9% v. 16.8% for the lidocaine-only arm (Risk Difference [RD] = 0.041 (95% CI: -4.1, 12.3); Number Needed to Treat [NNT] = 24 (95% CI: 8, ∞). A crossover analysis comparing 196 participants to themselves demonstrated no benefit over 12-weeks [B: 0.36 (95% CI: -1.17, 1.90) p=0.29] (**Figure 1b**). The probability of achieving MCID was 19.7% v. 15.3% for lidocaine-only (RD=0.044 [95% CI: -0.011, 0.10]; NNT=23 [95% CI: 10, ∞]). There were no carryover effects. Results were similar for secondary outcomes, in sensitivity analysis, and across subgroups (**Table 1; Figure 2**). There was no interaction with the exercise incentive arm. Among those receiving both injections, only 55% correctly guessed the order of their injections. Rescue injections were infrequent (n=6 during lidocaine-only; n=7 during corticosteroid).

Conclusion: In this well-powered, blinded, pragmatic, randomized trial, corticosteroid injections provided no significant benefit over 12 weeks compared to lidocaine-only injections. These findings, in the context of the existing literature, suggest limited benefit of this commonly performed procedure in real-world practice and raise new questions about whether this intervention should be widely used for routine management of KOA symptoms.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: J. Baker: Amgen, 5; **K. Wysham**: None; **M. Quinones**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **K. Jin**: None; **M. Olave**: None; **S. Wetzel**: None; **R. Gillcrist**: None; **C. Lavery**: None; **N. Keller**: None; **K. Hayes**: None; **B. Kramer**: None; **H. Brubeck**: None; **B. Ateh**: None; **D. White**: None; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11; **R. Xiao**: None; **T. Neogi**: None; **C. Scanzello**: COMPOSITIONS AND METHODS FOR TREATING OSTEOARTHRITIS USING A CD14 INHIBITOR, 10.

Abstract Number: 2625

Early Detection of Knee Osteoarthritis – The Role of a Composite Disease Activity Metric: Data from the Osteoarthritis Initiative

Julieann Patarini[1], Timothy McAlington[2], Jonggyu Baek[1], Emily Kirillov[3], Nhung Vo[3], Michael Richard[3], Ming Zhang[4], Matthew Harkey[5], Grace Lo[6], Shao-Hsien Liu[1], Kate Lapane[1], Charles Eaton[7], James Mackay[8] and **Jeffrey Driban**[9], [1]UMass Chan Medical School, Worcester, MA, [2]UMass Chan School of Medicine, Arlington, MA, [3]Tufts Medical Center, Boston, MA, [4]Boston University, Westford, MA, [5]Michigan State University, East Lansing, MI, [6]Baylor College of Medicine / MEDVAMC, Houston, TX, [7]Brown University, Pawtucket, RI, [8]University of Cambridge; Norwich Medical School, San Diego, CA, [9]University of Massachusetts Chan Medical School, Marlborough, NH

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis – Clinical (2621–2626)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Bone marrow lesions (BMLs) and effusion-synovitis are frequent and dynamic disease processes detected from early- to late-stage knee OA. These processes are associated with knee symptoms, representing the primary clinical manifestations of OA. Through a systematic and iterative process, we previously developed and validated a composite biomarker – the disease activity metric – that combines BML and effusion-synovitis volumes throughout a knee into an efficient continuous single score. It remains unclear whether this composite score represents clinically meaningful pathways to early stages of OA and if it could detect people early, before the onset of OA. We evaluated whether these dynamic disease processes (effusion-synovitis volume and BMLs), summarized by a validated efficient continuous composite score, are present in early OA and prognostic of incident symptomatic knee OA over the subsequent three years.

Methods: We analyzed a convenience sample within the Osteoarthritis Initiative (OAI) of participants without symptomatic knee OA. Pain assessments and radiographs were collected annually. Using magnetic resonance images from the initial visit, we combined effusion-synovitis and BML volumes (intra-reader ICCs ≥ 0.95) to calculate a composite score, referred to as the disease activity metric. A disease activity metric of 0 corresponded to the average in a reference sample (n=197, 53% with moderate-severe radiographic knee OA, average [SD] WOMAC pain score = 5.0 [3.6]); lower (negative) values indicate milder disease, while greater values indicate worse disease. The outcome was incident symptomatic knee OA (the combined state of frequent knee pain and radiographic OA [Kellgren-Lawrence Grade ≥ 2]) within three years after the disease activity measurement. We used logistic regression with repeated measures to examine the association between disease activity (continuous and tertiles) and incident symptomatic knee OA, adjusting for gender, age, and body mass index.

Results: Among 913 knees (n=572 participants), most were female (56%), white (82%), and had a mean age of 61 (SD=9) and body mass index of 29.4 (SD=4.5) kg/m^2. Disease activity ranged from -3.8 to 24.8 (lower values = smaller effusion-synovitis and BML volumes). Knees that developed incident symptomatic OA had a greater mean disease activity metric compared to those that did not (-0.3 [2.7] vs. -1.4 [2.7]). The adjusted relative risk of incident symptomatic OA per 1 unit

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Worse Disease Activity is Associated with a Greater Chance of Incident Symptomatic or Radiographic OA

	Incident Symptomatic OA			
Overall Study Sample	Absent n= 630	Present n = 283	Unadjusted Relative Risk (RR) (95% CI)	Adjusted RR[a] (95% CI)
Disease Activity (mean (SD))	-1.37 (2.68)	-0.30 (2.66)	**1.07 (1.03 - 1.11)**[b]	**1.08 (1.04 - 1.11)**[b]
Disease Activity –Tertiles Low (-3.83 to -2.46)	253 (40%)	48 (17%)	REFERENCE	
Moderate (-2.44 to -1.05)	207 (33%)	99 (35%)	**2.05 (1.50 - 2.80)**	**1.99 (1.46 - 2.71)**
High (-1.04 to 24.79)	170 (27%)	136 (48%)	**2.89 (2.14 - 3.91)**	**2.79 (2.06 – 3.78)**
No Symptoms, No Radiographic OA (n = 277)	Incident Symptomatic OA			
	Absent n= 259	Present n = 18	Unadjusted RR* (95% CI)	
Disease Activity (continuous)	-1.94 (1.96)	-1.77 (1.29)	1.05 (0.93 - 1.19)	
Disease Activity –Tertiles Low (-3.83 to -2.46)	128 (49%)	7 (39%)	REFERENCE	
Moderate (-2.44 to -1.05)	84 (32%)	7 (39%)	1.23 (0.50 - 3.03)	
High (-1.04 to 24.79)	47 (18%)	4 (22%)	1.49 (0.50 - 4.42)	
Radiographic OA Only (No Symptoms) (n = 459)	Incident Symptomatic OA			
	Absent n= 211	Present n = 248	Unadjusted RR* (95% CI)	
Disease Activity (continuous)	-0.62 (3.43)	-0.22 (2.71)	1.02 (0.99 - 1.05)	
Disease Activity –Tertiles Low (-3.83 to -2.46)	58 (27%)	38 (15%)	REFERENCE	
Moderate (-2.44 to -1.05)	70 (33%)	87 (35%)	**1.42 (1.07 - 1.89)**	
High (-1.04 to 24.79)	83 (39%)	123 (50%)	**1.56 (1.19 - 2.05)**	
Symptoms Only (No Radiographic OA) (n = 175)	Incident Symptomatic OA			
	Absent n= 158	Present n = 17	Unadjusted RR* (95% CI)	
Disease Activity (continuous)	-1.43 (2.34)	0.03 (2.64)	**1.16 (1.05 - 1.29)**	
Disease Activity –Tertiles Low (-3.83 to -2.46)	66 (42%)	3 (18%)	REFERENCE	
Moderate (-2.44 to -1.05)	53 (34%)	5 (29%)	2.04 (0.78 - 45.37)	
High (-1.04 to 24.79)	39 (25%)	9 (53%)	**5.65 (1.85 - 17.30)**	

Notes. (a). Relative risks adjusted for age, gender, and body mass index. (b). Relative risks for disease activity as a continuous measurement are per 1 unit. Bold = statistically significant associations. * Only unadjusted relative risks are reported because of the limited sample size within each stratum.

increase in disease activity was 1.08 (95% confidence interval: 1.04-1.11). Stratified analyses suggested that the association was driven by knees with either radiographic OA only or symptoms only at baseline.

Conclusion: Our findings underscore the critical role of the composite disease activity metric in the early detection of knee OA. By integrating BMLs and effusion-synovitis volumes, this metric provides a powerful prognostic tool, enabling earlier detection and potential intervention to alter disease progression. These results also support the development of targeted therapies that address inflammation and bone turnover in early OA.

Disclosure: J. Patarini: None; **T. McAlington**: Anika, 2, Grunenthal, 2, Kiniksk, 2, Kolon TissueGene, Inc., 2, Medipost, 2, Novan, 2, Organogenesis, 2, Regeneron, 2, Remedium-Bio, 2, Samumed, 2, Sanofi, 2, Scarcell, 2, Visor, 2; **J. Baek**: None; **E. Kirillov**: None; **N. Vo**: None; **M. Richard**: None; **M. Zhang**: None; **M. Harkey**: None; **G. Lo**: None; **S. Liu**: None; **K. Lapane**: None; **C. Eaton**: None; **J. Mackay**: AstraZeneca, 3, Blue Earth Diagnostics, 3; **J. Driban**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2626

Lorecivivint Delayed Time to Pain and Function Worsening Compared to Placebo: Evaluation of Knee OA Symptom Progression Outcomes in a Phase 3 Trial (OA-07)

Yusuf Yazici[1] and Christopher Swearingen[2], [1]NYU Grossman School of Medicine, La Jolla, CA, [2]Biosplice Therapeutics, Inc, San Diego, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Osteoarthritis – Clinical (2621–2626)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Increased pain and decreased function are hallmarks of knee OA progression. Lorecivivint (LOR), an intra-articular CLK/DYRK inhibitor thought to modulate inflammatory and Wnt pathways, appeared safe, improved pain and function outcomes and maintained radiographic medial joint space width (JSW) compared with placebo (PBO) in clinical trials to date. A Phase 3 trial, OA-07 (NCT04520607), evaluated LOR's safety and assessed WOMAC Pain and Function and JSW outcomes. A post-hoc analysis assessed whether LOR could delay pain and function worsening, proposed predictors of future knee replacement surgery[1].

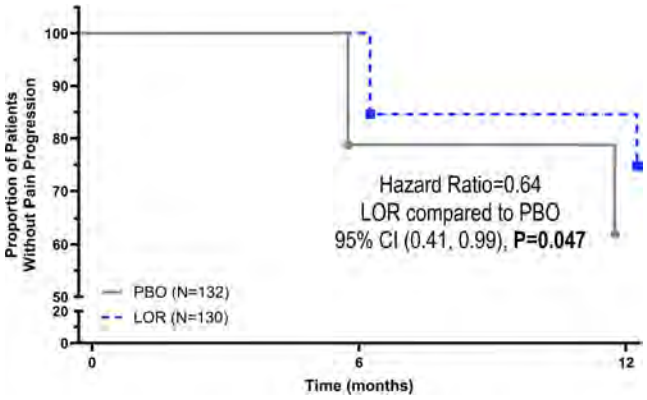


Figure 1. Analysis of LOR compared to PBO in Time to Progression in WOMAC Pain [0-100]

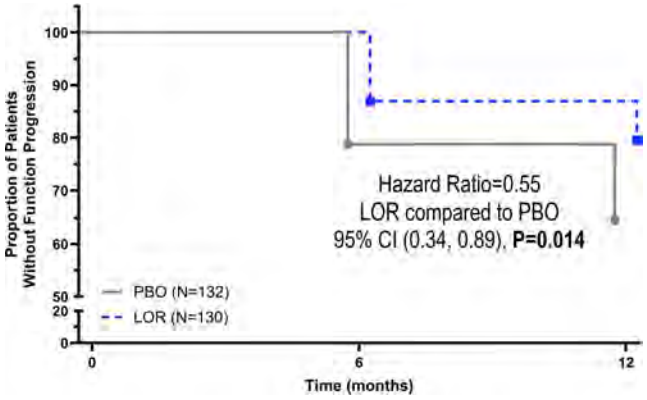


Figure 2. Analysis of LOR compared to PBO in Time to Progression in WOMAC Function [0-100]

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

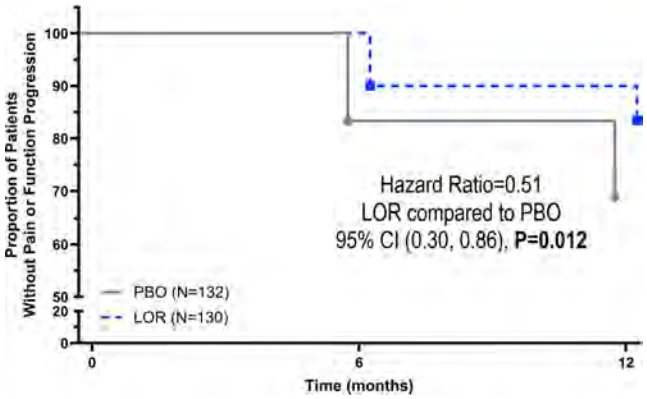


Figure 3. Analysis of LOR compared to PBO in Time to Coincident Progression of WOMAC Pain and Function

Methods: Patients who had completed the year-long, single-injection LOR trial Study OA-11 (NCT03928184), were invited to enroll into Study OA-07. At OA-07 baseline, patients received the same randomized study injection originally received in Study OA-11 and patients and investigators remained blind to treatment allocation. At the end of OA-07's first year, all patients were treated with open-label LOR.

In this post-hoc analysis, worsening in WOMAC Pain (WOMAC Pain [0-100] increase by 10+ points), worsening in WOMAC Function (> 9 points), and worsening in coincident WOMAC Pain and Function were explored using multivariable Logistic and Cox regression to assess differences between LOR and PBO in the first year of OA-07 in the Full Analysis Set. Progression in PBO patients during the first year was analyzed compared to their second year after cross-over to LOR, so that each patient served as their own control. The PBO-LOR crossover analysis was analyzed using repeated measures multivariable logistic and Cox regression in the Per-Protocol Analysis Set for complete Year 1 and Year 2 assessments.

Results: 276 patients were enrolled (LOR N=138, PBO N=138, 62.7% female, mean age 61.0 ± 8.2 years, mean BMI 31.8 ± 4.9 kg/m^2, 45.3% Kellgren-Lawrence Grade 3, average medial JSW 2.63 ± 0.69 mm). LOR appeared safe and well-tolerated with no adverse event rate differences compared to PBO.

Significant reduction in the progression of WOMAC Pain (LOR n=38 [29.2%], PBO n=57 [43.2%], OR=1.86, 95% CI [1.12, 2.12], P=0.018), progression of WOMAC Function (LOR n=35 [26.9%], PBO n=52 [39.4%], OR=1.82, 95% CI [1.07, 3.08], P=0.026), and progression in composite Pain and Function (n=28 [21.5%]) PBO (n=45 [34.1%]) (OR=1.90, 95% CI [1.09, 3.31], P=0.023), adjusting for age and KL Grade, were seen with LOR compared to PBO. Time to progression was also significantly reduced in LOR compared to PBO for WOMAC Pain (**Figure 1**), WOMAC Function (**Figure 2**), the combined Pain and Function progression (**Figure 3**). LOR also reduced progression in WOMAC Pain (OR=1.73, 95% CI (0.88, 3.04), P=0.054) and WOMAC Function (OR=2.12, 95% CI (1.16, 3.87), P=0.015) in PBO patients crossed over to LOR.

Conclusion: LOR was shown to be safe and efficacious in Study OA-07. Significant reduction in pain and function progression was seen for LOR compared to PBO, with LOR delaying time to progression. PBO patients who crossed to LOR treatment also demonstrated reduced progression. LOR continues to show promise as a safe, disease-modifying knee OA treatment.

References: 1. Kim Y et al. *Arthritis Care Res* 2022;74(7):1154-1162

Disclosure: Y. Yazici: Biosplice Therapeutics, Inc., 3, 10, 11; **C. Swearingen**: Biosplice Therapeutics, Inc, 3, 10, 11.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2627

Risk of Adverse Pregnancy Outcomes in Individuals with Rheumatic Diseases Using Prenatal Antirheumatic Drugs: a Population-Based Cohort Study

Shenthuraan Tharmarajah[1], Dharini Mahendira[2], Swaleh Hussain[1], Howard Berger[3], Sara Guilcher[4], Lisa McCarthy[4] and Mina Tadrous[1], [1]University of Toronto, Toronto, ON, Canada, [2]St Michael's Hospital, Toronto, Canada, [3]St. Michael's Hospital, Toronto, Canada, [4]University of Toronto, Toronto, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (2627–2632)
Session Type: Abstract Session
Session Time: 3:00PM–4:30PM

Background/Purpose: Disease-modifying antirheumatic drugs (DMARDs) are the primary class of drug therapies generally used to treat rheumatic diseases, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). However, the safety effects of DMARD use during pregnancy remain largely understudied, despite many individuals continuing some form of DMARD therapy during pregnancy to control maternal disease activity. Within Canada, past observational studies have leveraged claims data from the provinces of Quebec and British Columbia to study DMARD safety in pregnancy. This study aimed to assess the risk of severe maternal morbidity (SMM) and severe neonatal morbidity (SNM) in individuals with rheumatic diseases using DMARDs during pregnancy in Ontario, Canada's most populous province.

Methods: Leveraging routinely collected population-based healthcare administrative claims data at ICES in Ontario, Canada, we included pregnant individuals with RA, SLE, PsA, and/or AS who delivered a liveborn or stillborn singleton infant after 20 weeks of gestation between April 1, 2006, and March 31, 2021. DMARD exposure was defined as having at least one conventional synthetic or biological DMARD dispensation reimbursed from estimated conception to delivery. To adjust for confounders such as maternal age, rheumatic conditions and comorbidities, healthcare utilization, and concomitant medication use, propensity scores were calculated to estimate the probability of DMARD exposure. Stabilized inverse probability of treatment weights were derived from propensity scores and used in logistic regression modelling to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) for SMM and SNM in the DMARD-exposed cohort versus unexposed comparators.

Results: There were 836 pregnant individuals with rheumatic conditions, with 302 exposed to DMARDs and 534 unexposed. Most individuals had a diagnosis of RA (n=396, 47.4%), followed by SLE (n=357, 42.7%), AS (n=86, 10.3%), and PsA (n=48, 5.7%), with 49 (5.9%) individuals having more than one of these conditions. In unadjusted analyses, DMARD exposure was associated with SMM (OR: 1.81, 95% CI: 1.11–2.96) but not associated with SNM (OR: 0.97, 95% CI: 0.62–1.51). After adjusting for confounders, DMARD exposure was not associated with SMM (OR: 1.47, 95% CI: 0.86-2.51) or SNM (OR: 0.94, 95% CI: 0.59-1.49). Sensitivity analyses using overlap weights, entropy weights, and a longer exposure window from six months before estimated conception to delivery did not yield significant changes in point estimates and confidence intervals.

Conclusion: These findings suggest that DMARD use before and during pregnancy is not associated with an increased risk of SMM or SNM. Further studies with larger sample sizes are needed to better understand the long-term maternal and neonatal outcomes associated with prenatal DMARD use and develop real-world evidence-based clinical guidelines for safe prescribing during pregnancy.

Disclosure: S. Tharmarajah: None; **D. Mahendira**: None; **S. Hussain**: None; **H. Berger**: None; **S. Guilcher**: None; **L. McCarthy**: None; **M. Tadrous**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2628

Calprotectin and Anti-CCP Antibodies Predict Development of Preeclampsia

Daniele Marcy[1], Nanette Santoro[2], Claudia Lugo[3], Kristin Sturm[2] and Kristen Demoruelle[4], [1]University of Colorado, Northglenn, CO, [2]University of Colorado Anschutz Medical Campus, Aurora, CO, [3]University of Colorado, Denver, CO, [4]University of Colorado Anschutz Medical Campus, Golden, CO

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (2627–2632)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Several systemic autoimmune diseases are associated with an increased risk of preeclampsia. Preeclampsia is a pregnancy complication characterized by new-onset hypertension after 20 weeks of gestation. Neutrophil extracellular trap (NET) formation is a process during which activated neutrophils externalize nuclear and cytoplasmic proteins in net-like structures. NETosis is increased in several systemic autoimmune diseases and has also been implicated in the pathogenesis of preeclampsia. Yet, there are limited data examining whether peripheral blood measures of NETosis can serve as predictive biomarkers for preeclampsia. In addition, autoantibodies to cyclic citrullinated peptide (anti-CCP) can target proteins externalized during NETosis, and preeclampsia is a risk factor for future development of rheumatoid arthritis (RA). In this study, we evaluated the relationship between preeclampsia, NETosis and anti-CCP antibodies in pregnant women without a history of autoimmune disease.

Methods: We included stored serum from Baby Blanket, a single-center, prospective pregnancy cohort (2011-2013) that collected maternal blood during pregnancy and obtained delivery outcomes by medical chart review. We included samples collected after 20 weeks gestation (median 33.4, IQR 27.0-35.5 weeks) in all women who later developed preeclampsia (N=35) and in 35 controls matched on age, parity, and history of diabetes who did not develop preeclampsia. No women had an underlying history of RA or lupus. Serum was tested for calprotectin (Werfen), anti-CCP-IgG (CCP3, Werfen), and anti-CCP-IgA (CCP3.1 plate with research modification to detect IgA only). Calprotectin is an S100A8/A9 heterodimer released from neutrophils upon NET formation and can be used to quantify NETosis. Levels were compared between women who did vs. did not develop preeclampsia by Wilcoxon ranked sum test.

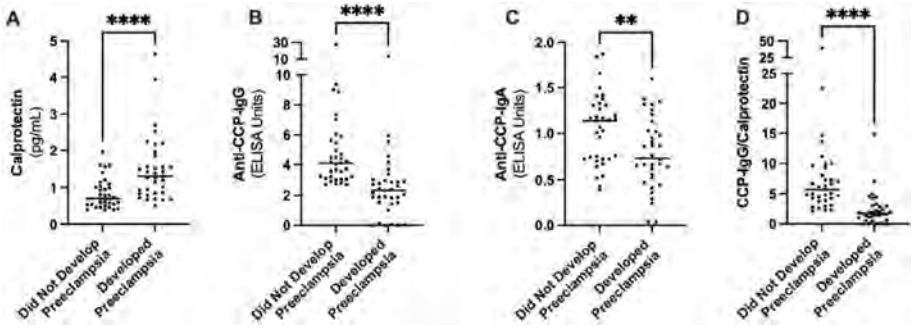


Figure 1. Serum levels of Calprotectin and Anti-CCP in pregnant women. The figure depicts serum levels of calprotectin (A), anti-CCP-IgG (B), anti-CCP-IgA (C) and that ratio of anti-CCP-IgG/calprotectin in pregnant women after 20 weeks gestation who either did or did not later develop preeclampsia. P-values calculated by Wilcoxon ranked sum test.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Serum calprotectin levels were significantly higher in individuals who later developed preeclampsia compared to control pregnancies (p=0.008, Figure 1A). Paradoxically, serum anti-CCP-IgG and anti-CCP-IgA levels were significantly lower in individuals who later developed preeclampsia compared to controls (p< 0.001, Figure 1B-C). Notably, an anti-CCP-IgG/calprotectin ratio < 2 was 62.8% sensitive and 100% specific for developing preeclampsia.

Conclusion: Higher serum calprotectin and lower serum anti-CCP levels were strongly associated with increased risk of preeclampsia in women without autoimmune disease and may serve as novel clinical biomarkers for risk prediction. The finding that women who developed preeclampsia had lower anti-CCP levels and lower anti-CCP-IgG/calprotectin ratios suggests a potential protective effect of anti-CCP antibodies during pregnancy, perhaps buffering pathogenic effects of NET-associated proteins. While most anti-CCP levels in this study were not above the diagnostic level of positivity used in RA, low levels of anti-CCP antibodies can still be biologically relevant. Future studies are needed to determine whether anti-CCP could also be a predictive biomarker for preeclampsia in women with autoimmune diseases, particularly RA.

Disclosure: D. Marcy: None; **N. Santoro**: None; **C. Lugo**: None; **K. Sturm**: None; **K. Demoruelle**: Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Gilead, 5, Merck/MSD, 2, Pfizer, 5.

Abstract Number: 2629

Predictors of 30-day Readmissions in Pregnant Patients with Systemic Lupus Erythematosus: The Impact of Social Determinants of Health.

Sandhya Kannayiram[1], Yiyuan Wu[2], Lisa Sammaritano[3], Michael Lockshin[4], Rich Caruana[5], Ware Branch[6], Jane Salmon[3] and Bella Mehta[7], [1]Hospital for Special Surgery, Weill Cornell Medicine, New York, [2]Weill Cornell Medicine, New York, NY, [3]Hospital for Special Surgery, New York, NY, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [5]Microsoft, Redmond, WA, [6]University of Utah Health Sciences Center, Salt Lake City, UT, [7]Hospital for Special Surgery, Weill Cornell Medicine, Jersey City, NJ

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (2627–2632)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Social Determinants of Health (SDOH) are increasingly recognized as significant contributors to adverse outcomes in pregnant patients with SLE. This study aims to evaluate the impact of SDOH on 30-day readmissions during pregnancy- and delivery-related hospitalizations in SLE patients, hypothesizing that incorporating SDOH into predictive models will enhance understanding of readmission risks and outcomes.

Methods: We conducted a retrospective analysis using the National Readmissions Database (NRD) from 2011 to 2021, which covers 28 states and represents 60% of U.S. hospitalizations. We identified adult pregnant patients with SLE using ICD-9 and 10 codes and categorized them into pregnancy- and delivery-related hospitalizations, including delivery cases within the pregnancy cohort. Our primary outcome was 30-day all-cause readmissions, and secondary outcomes included length of stay(LOS) and total hospitalization charges(THC). The SDOH evaluated in the study consists of income by zip code and insurance type. Descriptive analyses compared age, SDOH, clinical factors, LOS, and THC between initial hospitalizations and 30-day readmissions. We employed an Explainable Boosting Machine (EBM) model, using a 70-30 train-test split to predict readmissions based on features including comorbidities and SDOH. Weighted Mean absolute scores were aggregated globally to measure variable importance.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table : A Comparative Analysis of Demographics and Social Determinants of Health for Pregnant Patients with Systemic Lupus Erythematosus during Initial Hospitalizations and 30-Day Readmissions.

Variables	Pregnancy including delivery related hospitalizations in SLE		Delivery related hospitalizations in SLE	
	Initial admission N (%) = 66,301	Readmission within 30 days N (%) = 2,469	Initial admission N (%) = 57,820	Readmission within 30 days N (%) =1,267
Age in years [Median (IQR)] *	30 (26, 34)	29 (25, 33)	31 (27, 34)	30 (26, 35)
Median household income by zip code (Qnartiles)*				
• 0-25th	18,848 (29%)	876 (36%)	15,249 (27%)	439 (35%)
• 26-50th	16,032 (24%)	608 (25%)	13,565 (24%)	313 (25%)
• 51-75th	16,266 (25%)	572 (23%)	14,138 (25%)	309 (25%)
• 76-100th	14,552 (22%)	391 (16%)	13,078 (23%)	194 (15%)
Insurance*				
• Medicaid	3,950 (6.0%)	307 (12%)	2,906 (5.1%)	127 (10%)
• Medicare	25,452 (38%)	1,160 (47%)	20,775 (37%)	560 (44%)
• Private/Self-pay	33,466 (51%)	865 (35%)	30,112 (53%)	506 (40%)
• Others	3,319 (5.0%)	136 (5.5%)	2,666 (4.7%)	73 (5.8%)
Discharge location*				
• Home discharge	64,075 (97%)	2,209 (89%)	55,246 (98%)	1,163 (92%)
• Location other than Home	2,226 (3.4%)	261 (11%)	1,307 (2.3%)	104 (8.2%)
Hospital Location+				
• Large metropolitan areas (≥ 1million residents)	43,648 (66%)	1,675 (68%)	36,779 (65%)	858 (68%)
• Small metropolitan areas (< 1 million residents)	19,792 (30%)	717 (29%)	17,200 (30%)	370 (29%)
• Micropolitan and non-urban residual areas	2,861 (4.3%)	77 (3.1%)	2,574 (4.6%)	39 (3.1%)
Hospital Bed size*				
• Large	44,760 (68%)	1,812 (73%)	37,572 (66%)	928 (73%)
• Medium	14,735 (22%)	489 (20%)	12,856 (23%)	251 (20%)
• Small	6,806 (10%)	169 (6.8%)	6,125 (11%)	87 (6.9%)
Length of Stay in days [Median (IQR)] *	3 (2, 4)	3 (2, 6)	3 (2, 4)	3 (2, 6)
Total Hospitalization charges [Median (IQR)] *	$19,408 (12,157- 32,338)	$22,952 (12,422- 45,499)	$19,497 (12,403-31,876)	$24,767 (13,286- 48,413)

*P value <0.05 was considered statistically significant; + - non-significant p value. Statistical analysis with Wilcoxon rank-sum test for complex survey samples; chi-squared test with Rao & Scott's second-order correction.

Results: Among pregnancy- and delivery-related hospitalizations, 3.6% resulted in readmissions, while 2.2% of delivery-related hospitalizations led to readmissions. Patients in the lowest income quartile (0–25th percentile) faced nearly double the readmission rates compared to the highest quartile (36% vs. 16% for pregnancy and delivery; 35% vs. 15% for delivery-related hospitalizations). Similarly, patients with public insurance (Medicare/Medicaid) were more likely to be readmitted, while those with private insurance/self-pay were less likely, underscoring systemic inequities **(Table)**.

SLE patients with thrombocytopenia (8.6% vs. 6.2%), hypertension (11% vs. 3.8%), pre-eclampsia/eclampsia (19% vs. 15%), or Acute kidney injury (6.4% vs. 1.7%) during pregnancy and those with pre-eclampsia/eclampsia (24% vs. 15%), renal failure (19% vs. 9.5%), pulmonary edema (3.9% vs. 1.1%), sepsis (3.6% vs. 1.1%), or thromboembolism (4.9% vs. 2.9%) during delivery had higher 30-day readmission rates[p value < 0.05].

Importance analysis **(AUROC ≃0.68)** identified LOS, insurance type, comorbidities, hospital characteristics, income, and age as key predictors for pregnancy and delivery-related readmissions, with LOS and insurance showing the highest predictive value. Comorbidities, LOS, insurance, hospital characteristics, income, and age were top predictors for delivery-related admissions.

Conclusion: SDOH are an important predictor of readmissions in SLE patients during pregnancy and delivery. Targeted strategies focusing on improving access to resources and healthcare and addressing income disparities within disadvantaged communities may help reduce readmission rates and improve outcomes for this high-risk group.

Acknowledgements: K23 Grant Award Number - 1K23AR082991-01A1

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

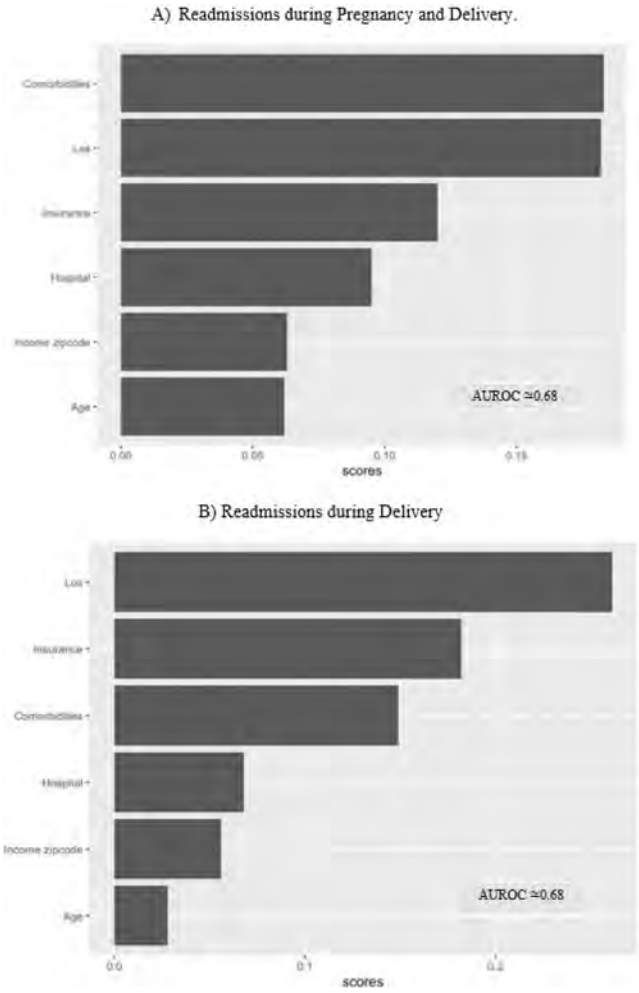


Figure: Feature Importance Scores for predicting 30-Day Readmissions in SLE patients during pregnancy and delivery-related hospitalizations.

Disclosure: S. Kannayiram: None; **Y. Wu**: None; **L. Sammaritano**: None; **M. Lockshin**: None; **R. Caruana**: None; **W. Branch**: UCB, 5; **J. Salmon**: UCB, 1, 5; **B. Mehta**: Amgen, 1, Horizon, 1.

Abstract Number: 2630

The Absence of DORIS Remission Is Associated with Greater Risk of Preterm Birth and Preeclampsia in SLE Pregnancies

Camila Hernández-Blanco[1], Philip Carlucci[2], Peter Izmirly[3], Jessica Dai[4], Mala Masson[5], Michael Belmont[1], Amit Saxena[6], Jane Salmon[7], Justin Brandt[1] and Jill Buyon[8], [1]NYU Langone Health, New York, NY, [2]New York University School of Medicine, New York, NY, [3]New York University Grossman School of Medicine, New York, NY, [4]New York University Grossman School of Medicine, Tenafly, NJ, [5]NYU Langone Medical Center- Division of Rheumatology, New York, NY, [6]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [7]Hospital for Special Surgery, New York, NY, [8]NYU Grossman School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (2627–2632)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Systemic Lupus Erythematosus (SLE) primarily affects females of childbearing age and increases the risk of adverse pregnancy outcomes (APOs), particularly in non-White individuals and those with active disease. This study leveraged an urban multi-ethnic longitudinal SLE pregnancy cohort to evaluate predictors of APOs, with a focus on DORIS remission and outcomes across multiple pregnancies—two underexplored areas in SLE pregnancy research. The incidence of intrahepatic cholestasis of pregnancy, a rare condition not well-characterized in SLE that may increase the risk of preeclampsia, was also assessed.

Table 1. Characteristics and Outcomes in the Pregnancy Cohort. A. N is specified where it differs from the overall sample size. Data is represented as N (%) for categorical variables and median (IQR) for continuous variables. *Low complements, thrombocytopenia, anti-dsDNA (crithidia), DORIS, and cholestasis were considered if present at any time during pregnancy. **The highest SELENA SLEPDAI during pregnancy is represented as well as the measure taken during each trimester. Medications include those taken at any time during pregnancy. B. Pregnancy outcomes in the SLE cohort (N=95), also stratified by DORIS remission status.

A

Patient Characteristics, N=95 (%)		APO, n=54	No APO, n=41
Age (years)	32 (29-36)	33 (30-37)	31 (28-34)
Gestational age at delivery (weeks)	38 (36-39)	37 (34-38)	38 (37-39)
BMI, kg/m2 (n=86)	25 (23-29)	25 (23-29)	25 (23-30)
Nulliparous (n=92)	46 (50)	26 (48)	20 (49)
ACR criteria ever			
Cutaneous	70 (74)	40 (74)	30 (73)
Arthritis	65 (68)	38 (70)	27 (66)
Serositis	21 (22)	15 (28)	6 (15)
Lupus Nephritis	42 (44)	29 (54)	13 (32)
CNS	3 (3)	3 (100)	0 (0)
Hematological disorder	57 (60)	33 (61)	24 (59)
Immunological disorder	81 (85)	48 (89)	33 (80)
Anti-SSA (anti-Ro)	46 (48)	25 (46)	21 (51)
Anti-SSB (anti-La)	17 (18)	11 (20)	6 (15)
Anti-Sm	32 (34)	24 (44)	8 (20)
Antiphospholipid antibodies	26 (27)	15 (28)	12 (29)
Anti-cardiolipin	19 (20)	9 (17)	10 (24)
Anti- β2GP1	19 (20)	10 (19)	9 (22)
Lupus anticoagulant (LAC)	16 (17)	8 (15)	8 (20)
Anti-dsDNA (n=76)*	27 (36)	16 (30)	11 (27)
Low C3 (n=93)*	20 (22)	12 (22)	8 (20)
Low C4 (n=93)*	36 (39)	18 (33)	18 (44)
Low complements (n=93)*	41 (44)	22 (41)	19 (46)
Thrombocytopenia (n=93)*	2 (2)	2 (4)	0 (0)
SELENA SLEPDAI (n=94)**	2 (0-6)	2 (0-8)	2 (0-4)
First trimester (n=63)	2 (0-5)	2 (0-6)	2 (0-4)
Second trimester (n=74)	2 (0-4)	2 (1-6)	2 (0-4)
Third trimester (n=65)	2 (0-4)	2 (0-4)	2 (0-4)
Maternal flares during pregnancy	20 (21)	14 (30)	6 (15)
DORIS remission (n=93)*	60 (65)	30 (56)	30 (73)
Medications during pregnancy			
Hydroxychloroquine	84 (88)	49 (91)	35 (85)
Azathioprine	26 (27)	19 (35)	7 (17)
Prednisone	31 (33)	22 (41)	9 (22)
Lovenox	14 (15)	8 (15)	6 (15)
Aspirin	86 (91)	48 (89)	38 (93)
Anti-hypertensives	12 (13)	11 (20)	1 (2)
Cholestasis of pregnancy (n=114)*	8 (7)	1 (2)	7 (17)

B

Outcomes in NYU Cohort, N=95 (%)		DORIS Remission, n=60	Non-Remission, n=33
Fetal Death	5 (5)	3 (5)	2 (6)
Neonatal Death	4 (4)	0 (0)	4 (12)
Preterm Birth	17 (18)	5 (8)	10 (30)
Preeclampsia	26 (27)	11 (18)	14 (42)
SGA 5th – 10th percentile	10 (11)	5 (8)	3 (9)
SGA < 5th percentile	19 (20)	10 (17)	9 (27)
PPROM	11 (12)	5 (8)	6 (18)
APO	54 (57)	30 (50)	22 (67)
Healthy	41 (43)	30 (50)	11 (33)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Predictors of Adverse Pregnancy Outcome. Characteristics of interest are shown in the left most column. The proportion of patients with each characteristic who had the defined APOs is represented. A logistic regression analysis was used to associate each characteristic with APOs. Significant associations are highlighted in red.

Characteristic		No APO	Any APO		Fetal Death	Neonatal Death	Preterm Birth	SGA <5th	SGA 5th-10th	PPROM	Preeclampsia
	Total n	n	OR (CI)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Hispanic	27	11	1.15 (0.47-2.89)	16 (59)	3 (11)	2 (7)	5 (19)	6 (22)	2 (7)	4 (15)	6 (22)
Black Race	30	8	2.84 (1.14-7.64)	22 (73)	1 (3)	3 (10)	8 (27)	10 (33)	3 (10)	5 (17)	13 (43)
Non-White Race	51	17	2.4 (1.05-5.60)	34 (67)	2 (4)	3 (6)	10 (20)	11 (22)	7 (14)	6 (12)	20 (39)
Previous Renal Disease	42	23	2.50 (1.08-5.96)	29 (69)	3 (7)	3 (7)	10 (24)	11 (26)	4 (10)	3 (7)	19 (45)
Anti-SSA (Ro)	46	21	0.82 (0.36-1.85)	25 (54)	3 (7)	3 (7)	5 (11)	10 (22)	5 (11)	7 (15)	9 (20)
Anti-SSB (La)	17	6	1.49 (0.51-4.70)	11 (65)	2 (12)	2 (12)	2 (12)	4 (24)	2 (12)	2 (12)	5 (29)
Lupus Anticoagulant	16	7	0.83 (0.34-2.02)	9 (56)	0 (0)	2 (13)	4 (25)	3 (19)	2 (13)	3 (19)	4 (25)
Anti-Cardiolipin	19	10	0.62 (0.22-1.71)	9 (47)	1 (5)	1 (5)	4 (21)	1 (5)	1 (5)	3 (16)	4 (21)
Anti-Beta Glycoprotein	19	9	0.8 (0.29-2.25)	10 (53)	0 (0)	1 (5)	5 (26)	4 (21)	2 (11)	2 (11)	5 (26)
Any APL	26	12	0.85 (0.34-2.12)	14 (54)	1 (4)	2 (8)	5 (19)	3 (12)	2 (8)	5 (19)	6 (23)
Anti-dsDNA	27	11	1.51 (0.59-4.0)	16 (59)	0 (0)	0 (0)	5 (19)	5 (19)	6 (22)	1 (4)	10 (37)
Anti-Sm	32	8	3.3 (1.33-8.88)	24 (75)	0 (0)	2 (6)	10 (31)	12 (38)	4 (13)	7 (22)	11 (34)
Previous Pregnancy	46	19	1.16 (0.51-2.63)	27 (59)	3 (7)	4 (9)	8 (17)	8 (17)	3 (7)	7 (15)	14 (30)
Previous Pregnancy Morbidity	8	1	5.96 (1-114)	7 (88)	0 (0)	1 (14)	2 (29)	2 (29)	0 (0)	2 (29)	5 (71)
SLEPDAI	2 (0-6)		1.11 (1.02-1.23)			0.04	0.03				0.02
DORIS Non-remission	33	11	1.93 (0.81-4.81)	22 (67)	2 (6)	4 (12)	10 (30)	9 (27)	3 (9)	6 (18)	14 (42)
Maternal Flares	20	6	2.04 (0.73-6.29)	14 (70)	2 (10)	2 (10)	6 (30)	5 (25)	2 (10)	5 (25)	9 (45)
Low C3	23	11	1.18 (0.44-3.32)	12 (52)	2 (9)	2 (9)	4 (17)	3 (13)	3 (13)	4 (17)	4 (17)
Low C4	36	18	0.64 (0.27-1.48)	18 (50)	2 (6)	2 (6)	4 (11)	6 (17)	4 (11)	3 (8)	7 (19)
Low complements	41	19	1.81 (0.80-0.35)	22 (54)	2 (5)	3 (7)	6 (15)	8 (20)	5 (12)	5 (12)	9 (22)
Anti-hypertensives	12	1	10.23 (1.86-191)	11 (92)	0 (0)	2 (17)	5 (42)	7 (58)	9 (0)	1 (8)	8 (67)
Glucocorticoids	31	9	2.44 (1-6.36)	22 (71)	1 (3)	2 (6)	8 (26)	6 (19)	5 (16)	5 (16)	13 (42)
Lovenox	14	6	1.01 (0.32-3.33)	8 (57)	0 (0)	1 (7)	4 (29)	2 (14)	1 (7)	2 (14)	6 (43)
Azathioprine	26	7	2.64 (1.02-7.49)	19 (73)	0 (0)	2 (8)	4 (15)	2 (8)	1 (4)	2 (8)	6 (23)
Cholestasis	8	7	0.13 (0.01-0.76)	1 (13)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)

Methods: The cohort includes 114 pregnancies in 95 consecutively consented SLE patients classified by ACR, SLICC and/or EULAR criteria. Clinical and laboratory data were collected during routine rheumatology visits. The primary outcome was a composite of APOs using modified PROMISSE definitions, which included preeclampsia, preterm premature rupture of membranes (PPROM), preterm birth (PTB) < 36 weeks, small for gestational age (SGA) birth, fetal death >10 weeks' gestation, and neonatal death within 28 days of birth. Logistic regression assessed predictors including race/ethnicity, history of lupus nephritis, autoantibodies, disease activity measured by SLEPDAI, DORIS remission, and medications. For patients with >1 pregnancy, only the first was included in regression analyses; a descriptive analysis examined the impact of prior APOs on future pregnancy outcomes.

Results: Among 95 pregnant SLE patients, 28% were Hispanic, 44% White, 32% Black, and 13% Asian. APOs occurred in 57%, most commonly preeclampsia (27%), SGA < 5th percentile (20%), and PTB (18%) (Table 1A). Significant predictors included antihypertensive use (OR 10.2, p=0.029), prior lupus nephritis (OR 2.5, p=0.034), non-White race (OR 2.4, p=0.039), Black race (OR 2.8, p=0.003), higher SLEPDAI (OR 1.11, p=0.022), and anti-Sm positivity (OR 3.3, p=0.01) (Table 2). LAC was associated with neonatal death. All APOs occurred with higher frequency in those who were not in sustained DORIS remission and significantly associated with PTB and preeclampsia (Tables 1B, 2). Notably, all 4 neonatal deaths occurred in patients not in DORIS remission. In the 16 patients with multiple pregnancies, the proportion in DORIS remission improved from 62% in the first pregnancy to 81% in the second pregnancy. While 8 of these 16 (50%) had an APO in the first pregnancy, only 3 had recurrent APOs, and 1 developed a new APO in pregnancy 2 (Figure 1A-B). Compared to the reported frequency of intrahepatic cholestasis in 0.2 to 2% percent of healthy pregnancies, it occurred in 8/114 pregnancies (7%, one patient twice, one with APO).

Conclusion: In this diverse SLE cohort, known predictors of APOs – including antihypertensive use, prior nephritis and active disease – were confirmed. The absence of DORIS remission was associated with preeclampsia and PTB. Prior pregnancy morbidity did not predict future APOs. These findings highlight the relevance of DORIS remission to maternal-fetal outcomes. The high prevalence (7%) of cholestasis of pregnancy in this cohort warrants further attention given its known fetal risks.

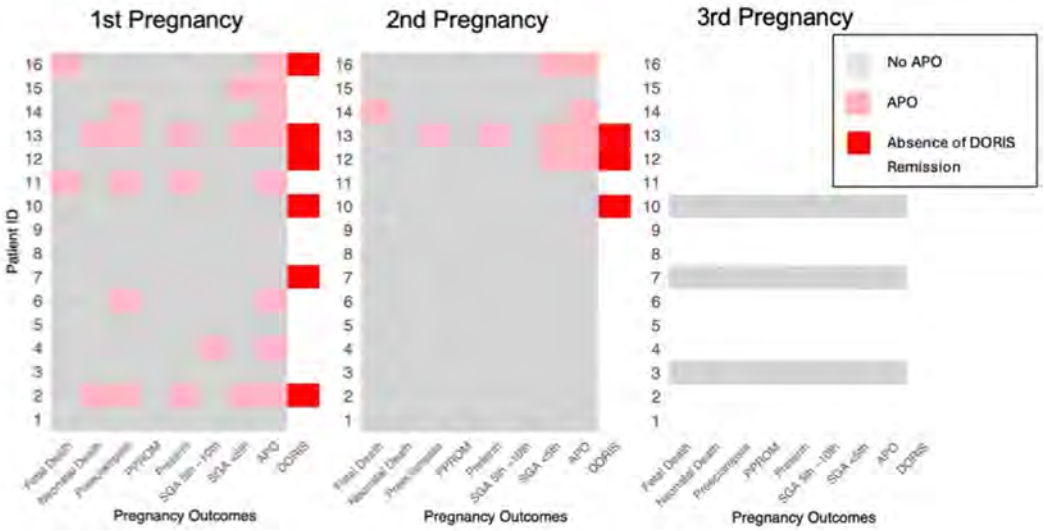
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: A. Table describing the characteristics of patients with multiple pregnancies. B. Map showing the pregnancy outcomes and DORIS remission of 16 patients with multiple pregnancies in the lupus pregnancy cohort. Pink colored boxes indicate the presence of that outcome. Grey boxes indicate the absence of that outcome. Only 3 patients had a third pregnancy represented.

A

Characteristic	1st Pregnancy, N=16 (%)	2nd Pregnancy N=16 (%)
Hispanic	5 (31)	5 (31)
White	9 (60)	9 (60)
Black	4 (25)	4 (25)
Asian	1 (6)	1 (6)
Non-white	7 (44)	7 (44)
Previous Renal Disease	9 (56)	9 (56)
Anti-SSA (Ro)	9 (56)	9 (56)
Anti-SSB (La)	6 (38)	6 (38)
Lupus Anticoagulant	3 (19)	4 (25)
Anti-Cardiolipin	5 (31)	4 (25)
Anti-Beta Gly	4 (25)	4 (25)
Anti-Sm	3 (19)	3 (19)
Anti-dsDNA (n=12, 11)*	6 (50)	5 (45)
Previous Pregnancy	5 (31)	16 (100)
SLEPDAI **	2 (0-4.75)	2.5 (0-4)
DORIS Remission	10 (63)	13 (81)
Maternal Flares	3 (19)	3 (19)
Thrombocytopenia (n=15)*	1 (6)	1 (6)
Low C3*	5 (31)	5 (31)
Low C4*	8 (50)	8 (50)
Anti-hypertensives	2 (13)	1 (6)
Glucocorticoids	7 (44)	4 (25)
Lovenox	3 (19)	4 (25)
Azathioprine	6 (38)	6 (38)
Hydroxychloroquine	15 (94)	16 (100)
Aspirin	14 (88)	15 (94)

B



Disclosure: C. Hernández-Blanco: None; **P. Carlucci**: None; **P. Izmirly**: Hansoh Bio, 2; **J. Dai**: None; **M. Masson**: None; **M. Belmont**: None; **A. Saxena**: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **J. Salmon**: UCB, 1, 5; **J. Brandt**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2631

Dapirolizumab Pegol, a Novel CD40L Inhibitor, Showed No Adverse Outcomes in an *In Vivo* Non-Human Primate Reprotoxicity Study and Displayed Minimal to No Human Placental Transfer in an *Ex Vivo* Study

Lewis Renshall[1], Birgit Hirschmugl[2], Bernd Potthoff[3], Emmanuel Goursaud[3], Pierre Bonnaillie[3], Sarah Kettell[3], Veerle Snoeck[3], Emma Smith[4], Farnaz Fallah-Arani[4], **Anthony Shock**[4], Alison Wolfreys[4], Christian Wadsack[2] and Paul Brownbill[1], [1]Maternal and Fetal Health Research Centre, University of Manchester, Manchester, United Kingdom, [2]Department of Obstetrics and Gynecology, Medical University of Graz, Graz, Austria, [3]UCB, Braine-l'Alleud, Belgium, [4]UCB, Slough, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (2627–2632)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Dapirolizumab pegol (DZP) is a novel CD40L inhibitor with broad modulatory effects on SLE immunopathology;[1,2] it consists of a polyethylene glycol (PEG)-conjugated antigen-binding fragment (Fab'), which lacks an Fc domain. DZP demonstrated efficacy in the phase 3 PHOENYCS GO trial (NCT04294667).[3] SLE predominantly affects women of childbearing age, conferring potential maternal and fetal risks.[4] Here, DZP reprotoxicity was studied *in vivo* in non-human primates (NHPs; cynomolgus monkeys), and DZP transfer across human placentas was evaluated *ex vivo*.

Methods: In an enhanced pre/postnatal development (ePPND) study, pregnant NHPs (N=14) received weekly intravenous DZP 27 or 50 mg/kg from gestation Day 20 to birth. Infant development was monitored for 9 months. *Ex vivo* dual perfusion of human placentas (N=22) assessed DZP and control IgG full monoclonal antibody transfer over up to 6 hours.

Results: In the ePPND study, pregnancy outcomes, embryofetal development, and infant postnatal development to 9 months post-birth were not affected by DZP. DZP induced expected decreases in B cells, IgG, and IgM in pregnant mothers, with no evidence of these effects in infants, nor altered development of infant immune systems to 9 months post-birth. Post-birth, DZP transfer from mother to infant (< 0.3% infant:mother plasma ratio) and mother plasma to milk (< 0.08% mother milk:plasma ratio) were very low. In the human *ex vivo* placental model, DZP was below quantification (minimal to none) in human placental fetal perfusate, in contrast to IgG full antibody control.

Conclusion: DZP showed no adverse outcomes on pregnancy or infant development post-birth in NHPs. In the *ex vivo* human placental model, DZP transfer was below the level of detection. These data align with lack of active placental transfer via the neonatal Fc receptor, causing minimal to no DZP transfer from mother to fetus, and suggest DZP may not be anticipated to cross the placenta to significant levels. These findings support further investigation of DZP in the setting of human pregnancy.

References: 1. Cutcutache I. Arthritis Rheumatol 2023;75 (suppl 9); **2**. Powlesland AS. Annals Rheum Dis 2024;83 (suppl 1):261; **3**. Clowse M. Arthritis Rheumatol 2024;76 (suppl 9); **4**. Gamba A. J Clin Med 2024;13(12):3454.

Disclosure: L. Renshall: None; **B. Hirschmugl**: None; **B. Potthoff**: UCB, 3, 12, Shareholder; **E. Goursaud**: UCB, 3, 12, Shareholder; **P. Bonnaillie**: UCB, 3, 12, Shareholder; **S. Kettell**: UCB, 3, 12, Shareholder; **V. Snoeck**: UCB, 3; **E. Smith**: UCB, 3, 12, Shareholder; **F. Fallah-Arani**: UCB, 3, 12, Shareholder; **A. Shock**: UCB, 3, 12, Shareholder; **A. Wolfreys**: UCB, 3, 12, Shareholder; **C. Wadsack**: None; **P. Brownbill**: AstraZeneca, 5, UCB, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2632

Maternal vascular malperfusion: association with adverse perinatal outcomes in lupus pregnancies

ANA JIMENA LOPEZ DIAZ[1], **MARIA DEL CARMEN ZAMORA MEDINA**[2], Mario Isaac Lumbreras Márquez[1], Diana Yazmin Copado mendoza[1], Oralia Alejandra Orozco Guillén[1], Maria José rodríguez Sibaja[1], Martha Leticia Palafox Vargas[1] and Sandra Acevedo gallegos[1], [1]Instituto Nacional de Perinatología, Mexico City, Distrito Federal, Mexico, [2]Instituto Nacional de Perinatologia, Mexico City, Distrito Federal, Mexico

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (2627–2632)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with increased risk of adverse perinatal outcomes (APOs), including preeclampsia, preterm birth, fetal growth restriction, and stillbirth. Placental findings of maternal vascular malperfusion (MVM), particularly intervillous fibrin deposition (IVFD), are more frequently observed in patients with SLE and antiphospholipid syndrome (APS). While IVFD has been linked to small-for-gestational-age (SGA) neonates in SLE pregnancies, its association with other severe APOs remains poorly characterized. The aim of our study is t compare the incidence of high-grade MVM between pregnant individuals with and without SLE and to evaluate the association between these placental lesions and APOs.

Methods: We included women aged ≥18 years with singleton pregnancies and a preexisting diagnosis of SLE (2012 SLICC criteria), managed at the National Institute of Perinatology between January 2016 and May 2024, with available placental histopathology. Placental lesions were assessed using the 2016 Amsterdam Working Group criteria and classified based on Freedman's phenotypes incorporating lesion severity. Exclusion criteria included other autoimmune diseases (except APS), pregnancies in women ≤18 years, multiple gestations, assisted reproduction, absence of prenatal care, or SLE diagnosed during pregnancy. The control group comprised healthy pregnant women matched 1:1 by maternal and gestational age. The primary outcome was the frequency of high-grade MVM. Associations between high-grade MVM and APOs—fetal or neonatal death, preterm birth < 37 weeks due to placental insufficiency (i.e., preeclampsia, hypertension, fetal growth restriction), and SGA neonates (birthweight < 10th percentile)—were assessed using univariable logistic regression, with odds ratios (ORs) and 95% confidence intervals (CIs). $P < 0.05$ was considered statistically significant.

Results: Among 130 SLE patients (mean age 28.0 ± 5.5 years; gestational age 36.5 ± 3.4 weeks), 25.4% had APS and 23.8% experienced an SLE flare during pregnancy. APOs occurred in 31.5%, including SGA (19%), fetal/neonatal death (3.8%), and preterm birth (19.2%). Placental weight was significantly lower in SLE patients compared to controls (388.9 ± 102.7 g vs. 440.4 ± 81.1 g; $P < 0.001$), particularly in those with flares ($P = 0.014$). High-grade MVM was significantly more

Table 1. Placental morphological characteristics and histopathological lesions.

Characteristic	Total N = 130	Flare during pregnancy N = 31	No flare during pregnancy N = 99	P value
Placental weight, grams, mean, SD	388.89 ± 102.66	**349.84 ± 109.69**	**401.63 ± 97.51**	**0.014**
MVM, n (%)	100 (76.9)	26 (83.9)	74 (74.7)	0.339
IVFD, n (%)	12 (9.2)	3 (9.7)	9 (9.1)	0.999
FVM, n (%)	35 (26.9)	9 (29.0)	26 (26.3)	0.818
Corioamnionitis, n (%)	13 (10.0)	3 (9.7)	10 (10.1)	0.999

MVM = maternal vascular malperfusion,
IVFD= intervillous fibrin deposits
FVM = fetal vascular malperfusion

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Placental morphological characteristics and histopathological lesions

Caractheristic	SLE cohort N = 130	No SLE cohort N = 130	*P value*
Placental weight, grams, mean, SD	388.89 ± 102.66	440.39 ± 81.12	*P* <0.001
High-grade MVM, n (%)	44 (33.8)	5 (3.8)	*P*=0.001

Table 2. Placental histopathologic lesions and their association with APO

Placental lesion	Neonatal/fetal loss OR (95% CI)	Birthweight <10th centile OR (95% CI)	Birth <37 weeks due to placental insufficiency OR (95% CI)
High-grade MVM	6.81 (1.10,41.95)	5.81 (2.86, 11.79)	4.07 (1.71, 9.65)

frequent in SLE patients (33.8% vs. 3.8%; P = 0.001) and was associated with increased odds of fetal/neonatal death (OR 6.81; 95% CI: 1.10–41.95), preterm birth < 37 weeks due to placental insufficiency (OR 4.07; 95% CI: 1.71–9.65), and SGA neonates (OR 5.81; 95% CI: 2.86–11.79).

Conclusion: High-grade MVM is significantly more prevalent in pregnancies complicated by SLE and is strongly associated with increased odds of fetal/neonatal death, preterm birth due to placental insufficiency, and SGA neonates.

Disclosure: A. LOPEZ DIAZ: None; **M. ZAMORA MEDINA**: None; **M. Lumbreras Márquez**: None; **D. Copado mendoza**: None; **O. Orozco Guillén**: None; **M. rodríguez Sibaja**: None; **M. Palafox Vargas**: None; **S. Acevedo gallegos**: None.

Abstract Number: 2633

Comparative 3-year Safety Outcomes in Patients with Ankylosing Spondylitis Initiating JAK Inhibitor or TNF Inhibitor Therapy

Hsin-Hua Chen, Taichung Veterans General Hospital, Taichung, Taiwan (Republic of China)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondyloarthritis (2633–2638)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: To compare safety outcomes in patients with ankylosing spondylitis (AS) initiating Janus kinase inhibitors (JAKi) versus tumor necrosis factor inhibitors (TNFi).

Methods: This retrospective cohort study utilized data from the TriNetX Global Collaborative Network, comparing patients initiating JAKi (n=299) versus TNFi (n=299) after propensity score matching for age, sex, race, diabetes mellitus, hypertension, psoriasis, inflammatory bowel disease, uveitis, and hyperlipidemia, . Patients were followed for up to three years.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline Characteristics Before and After PSM (JAKi vs TNFi).

Table 1. Baseline Characteristics before and after propensity score matching in patients with ankylosing spondylitis initiating JAK inhibitors or TNF inhibitors (JAKi vs TNFi).

Baseline Variable	Pre-match JAKi (n=300)	Pre-match TNFi (n=12,443)	p-value	Std diff.	Post-match JAKi (n=299)	Post-match TNFi (n=299)	p-value	Std diff.
Age at index, years	49.0 ± 15.9	42.8 ± 15.5	<0.001	0.390	48.9 ± 15.9	49.0 ± 14.8	0.915	0.009
White race	74.7%	66.0%	0.002	0.191	74.9%	75.3%	0.925	0.008
Female	55.0%	38.2%	<0.001	0.342	54.8%	52.5%	0.566	0.047
Diabetes mellitus	8.0%	5.5%	0.064	0.099	8.0%	8.0%	1.000	<0.001
Hypertension	23.7%	14.5%	<0.001	0.234	23.4%	26.1%	0.448	0.062
Psoriasis	10.3%	4.6%	<0.001	0.220	10.0%	9.4%	0.782	0.023
Inflammatory bowel disease	17.0%	8.3%	<0.001	0.263	16.7%	17.4%	0.828	0.018
Uveitis (iritis)	3.3%	8.5%	0.001	0.220	3.3%	3.3%	1.000	<0.001
Hyperlipidemia	16.3%	10.8%	0.003	0.161	16.1%	16.7%	0.825	0.018

Footnotes: PSM – propensity score matching; JAKi – Janus kinase inhibitor; TNFi – tumor necrosis factor inhibitor. Values are presented as mean ± standard deviation or % of patients. *Std diff.* – standardized difference (absolute difference in means or percentages divided by pooled standard deviation), used to assess balance between groups (imbalances defined by |Std diff.| > 0.10). Pre-match columns reflect the original unmatched cohorts (JAKi n=300, TNFi n=12,443), while post-match columns reflect the propensity score-matched sample (n=299 in each group).

Table 2. Three-year safety outcomes in patients with ankylosing spondylitis initiating JAK inhibitors or TNF inhibitors after propensity score matching shown as hazard ratios with 95% confidence intervals (JAKi vs. TNFi)

Outcomes included mortality, major adverse cardiovascular events (MACE), venous thromboembolism (VTE), malignancy, gastrointestinal bleeding, hepatitis (non-infectious), serious infections (sepsis, pneumonia, herpes zoster), dermatologic events, and neuropsychiatric disorders. Kaplan–Meier analysis provided hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: JAKi initiation was associated with significantly increased all-cause mortality (4.3% vs. 3.3%; HR 4.94, 95% CI 1.59–15.37) and gastrointestinal bleeding (3.4% vs. 0%; p=0.002). Conversely, malignancy occurred exclusively among TNFi initiators (3.4% vs. 0%; p=0.001). Herpes zoster infection showed a non-significant trend toward higher incidence in JAKi users (6.0% vs. 5.0%; HR 1.90, 95% CI 0.95–3.83). No significant differences emerged in MACE, VTE, serious bacterial infections (including pneumonia and sepsis), dermatologic events, or hepatitis. Anxiety/insomnia diagnoses were numerically lower with JAKi (14.3% vs. 24.1%), but without statistical significance.

Conclusion: Compared with TNFi, JAKi therapy in AS was associated with increased mortality and gastrointestinal bleeding, but lower short-term malignancy incidence. Infection-related outcomes were similar, aside from a potential herpes zoster risk. These findings highlight distinct safety trade-offs, underscoring the need for individualized treatment choices in AS.

Disclosure: H. Chen: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2634

Sex differences in medication discontinuation in axial spondyloarthritis

Rachael Stovall[1], Cinthia Blat[2], Eric Roberts[3], Jean Liew[4], Katherine Wysham[5], Namrata Singh[1], Janna Friedly[1], Lianne S. Gensler[6], gabriela Schmajuk[7] and Jinoos Yazdany[8], [1]University of Washington, Seattle, WA, [2]University of California San Francisco, San Francisco, CA, [3]University of California, San Francisco, SF, CA, [4]Boston University School of Medicine, Boston, MA, [5]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [6]Department of Medicine/Rheumatology, University of California, San Francisco, San Francisco, CA, [7]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [8]UCSF, San Francisco, CA

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondyloarthritis (2633–2638)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Women with axial spondyloarthritis (axSpA) tend to report worse outcomes and greater functional impairment than men. They may also respond less favorably to medication, though most data focus on tumor necrosis factor inhibitors (TNFi). Less is known about their response to interleukin-17 inhibitors (IL-17i) and Janus kinase inhibitors (JAKi), particularly in real-world settings. We assessed sex differences in medication discontinuation among U.S. adults with axSpA using the Rheumatology Informatics System for Effectiveness (RISE) registry.

Methods: We conducted a retrospective cohort study using RISE from 2000–2022, identifying new users of TNFi, IL-17i, and JAKi with axSpA. Patients had ≥2 consecutive prescriptions for the same drug. Discontinuation was defined as a stop date or ≥90-day gap without prescription (≥60 days for infliximab). Cox proportional hazards models assessed sex differences in discontinuation, adjusting for demographics, body mass index, area deprivation index, insurance type, and visit frequency. Multiple imputation addressed missingness. Sensitivity analyses included requiring only 1 prescription, requiring medication stop dates, and adjusting for disease activity using the Multi-Dimensional Health Assessment Questionnaire (MDHAQ). We also examined drug continuation by sex and age (18–64 vs ≥65) using Kaplan Meier curves.

Results: Among 4,799 axSpA patients (mean age 49.7 years; 54.3% female), 90% used TNFi, 7.4% IL-17i, and 2.6% JAKi (**Table 1**). Women had a higher adjusted risk of TNFi discontinuation than men (N=4,320, aHR 1.24, 95% CI: 1.15–1.35), which persisted across sensitivity models (**Table 2**). Adjustment for MDHAQ attenuated the association (aHR 1.16, 95% CI: 0.92–1.46). No significant sex differences were seen for IL-17i (N=356, aHR 1.21, 95% CI: 0.92–1.60) or JAKi (N=123, aHR 0.89, 95% CI: 0.47–1.66), though sample sizes were small. Among TNFi users, women under 65 had the lowest probability of medication continuation (**Figure**). There were no differences by sex and age in the IL17i and JAKi groups.

Conclusion: In this national axSpA cohort, women were more likely than men to discontinue TNFi therapy. This was not observed for IL-17i or JAKi, and larger studies are needed to confirm these results. These findings highlight the importance of investigating sex-based differences in axSpA treatment response.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics in patients with axSpA prescribed a TNFi, IL17i or JAKi.

Characteristic	Overall N = 4,799 (%)	Female N = 2,605 (%)	Male N = 2,194 (%)
Age (years) +/- SD	49.7 (14.5)	49.3 (14.0)	50.0 (15.0)
18-29	451 (9.4)	218 (8.4)	233 (10.6)
30-40	892 (18.6)	502 (19.3)	390 (17.8)
41-50	1,169 (24.4)	683 (26.2)	486 (22.2)
51-60	1,159 (24.2)	649 (24.9)	510 (23.2)
61-70	739 (15.4)	366 (14.0)	373 (17.0)
71-80	340 (7.1)	157 (6.0)	183 (8.3)
>80	49 (1.0)	30 (1.2)	19 (0.9)
Race and ethnicity			
African American	204 (4.3)	125 (4.8)	79 (3.6)
Asian	92 (1.9)	43 (1.7)	49 (2.2)
Hispanic	229 (4.8)	136 (5.2)	93 (4.2)
Non-Hispanic White	3,360 (70.0)	1,815 (69.7)	1,545 (70.4)
Other or mixed	178 (3.7)	99 (3.8)	79 (3.6)
Unknown	736 (15.3)	387 (14.9)	349 (15.9)
Body mass index (kg/m2)			
Underweight: <18.5	52 (1.1)	37 (1.4)	15 (0.7)
Normal weight: 18.5-24.9	909 (18.9)	578 (22.2)	331 (15.1)
Overweight: 25-29.9	1,176 (24.5)	522 (20.0)	654 (29.8)
Obese: 30+	1,775 (37.0)	1,075 (41.3)	700 (31.9)
Unknown	887 (18.5)	393 (15.1)	494 (22.5)
Ever smoker			
Ever	837 (17.4)	421 (16.2)	416 (19.0)
Never	1,524 (31.8)	890 (34.2)	634 (28.9)
Unknown	2,438 (50.8)	1,294 (49.7)	1,144 (52.1)
National area deprivation index*, Median (Q1, Q3)	43.9 (25.8)	46.2 (26.0)	41.1 (25.4)
Quintile 1 (1-19)	943 (19.6)	453 (17.4)	490 (22.3)
Quintile 2 (20-33)	861 (17.9)	438 (16.8)	423 (19.3)
Quintile 3 (34-49)	886 (18.5)	478 (18.3)	408 (18.6)
Quintile 4 (50-70)	905 (18.9)	512 (19.7)	393 (17.9)
Quintile 5 (71-100)	875 (18.2)	541 (20.8)	334 (15.2)
Unknown	329 (6.9)	183 (7.0)	146 (6.7)
Insurance category			
Private	2,855 (59.5)	1,503 (57.7)	1,352 (61.6)
Medicare	1,228 (25.6)	636 (24.4)	592 (27.0)
Medicaid	209 (4.4)	144 (5.5)	65 (3.0)
Other insurance	111 (2.3)	73 (2.8)	38 (1.7)
Unknown	396 (8.3)	249 (9.6)	147 (6.7)
MDHAQ**, Mean (SD)	2.5 (2.5)	2.8 (2.5)	2.2 (2.5)
Unknown	4,126	2,207	1,919
Visit count during baseline period, Median (Q1, Q3)	2.00 (1.0, 3.0)	2.00 (1.0, 3.0)	1.00 (1.0, 2.0)
Oral glucocorticoid use	1,145 (23.9)	711 (27.3)	434 (19.8)
Opioid use	471 (9.8)	283 (10.9)	188 (8.6)
TNFi	4,320 (90.0)	2,304 (88.4)	2,016 (91.9)
IL17i	356 (7.4)	221 (8.5)	135 (6.2)
JAKi	123 (2.6)	80 (3.1)	43 (2.0)

Values are expressed as N (%) unless otherwise indicated.
*range 1-100, lower to higher disadvantage
**range 0-10, higher to lower health status

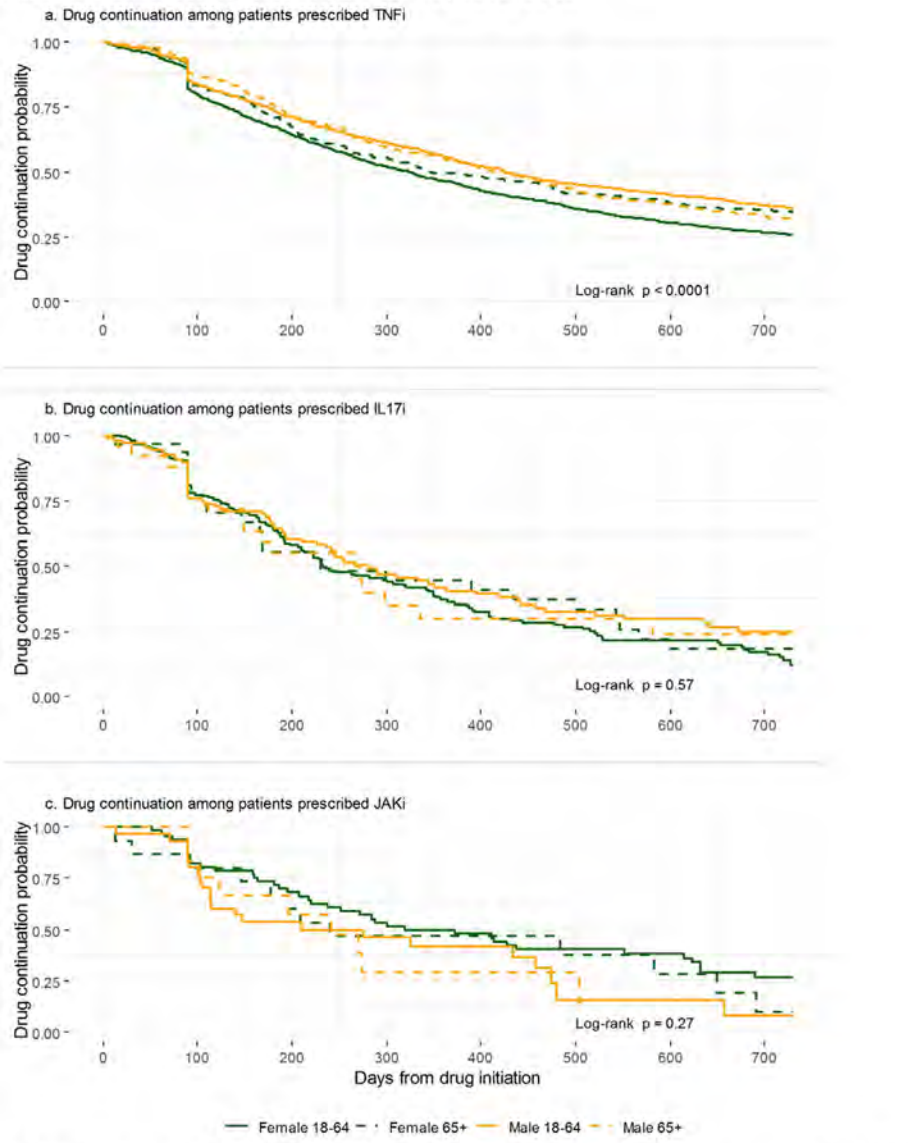
Table 2. Adjusted risk of drug discontinuation in patients with axSpA prescribed a TNFi, IL17i or JAKi*.

Characteristic	TNFi‡				IL17i**,‡				JAKi**,‡			
	N	aHR	95% CI	p-value	N	aHR	95% CI	p-value	N	aHR	95% CI	p-value
Primary analysis: 2 or more medication records												
Sex	4,320				356				123			
Female		**1.24**	**1.15, 1.35**	**<0.001**		1.21	0.92, 1.60	0.17		0.89	0.47, 1.66	0.70
Male		—	—			—	—					
Sensitivity analysis 1: Full cohort (1 or more medication records)												
Sex	7,224				749				264			
Female		**1.19**	**1.12, 1.28**	**<0.001**		1.08	0.87, 1.33	0.48		0.95	0.64, 1.41	0.80
Male		—	—			—	—			—	—	
Sensitivity analysis 2: Documented stop dates only					197				47			
Sex	1,659					1.29	0.88, 1.90	0.20		—	—	
Female		**1.23**	**1.09, 1.40**	**0.001**		—	—			—	—	
Male		—	—									
Sensitivity analysis 3: Primary analysis + adjustment for MDHAQ												
Sex	594								21			
Female		1.16	0.92, 1.46	0.22	58	—	—			—	—	
Male		—	—			—	—			—	—	

*All models were adjusted for age, race/ethnicity, national area deprivation index, insurance, BMI, visit count during baseline period, oral glucocorticoid use, and opioid use; sensitivity analysis 3 also included MDHAQ as a covariate
**Sample sizes were too small to conduct sensitivity analysis 3 among patients prescribed an IL17i or sensitivity analyses 2 and 3 among patient prescribed a JAKi
‡For the primary analysis and sensitivity analyses 1 and 2, missing covariates were imputed through multiple imputation by iterative chained equations using 165 datasets; for sensitivity analysis 3, only patients with observed values for MDHAQ were included in the model, missing values for all other covariates were imputed

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure. Probability of medication continuation by sex and age.



Disclaimer: Data collection was supported by the ACR's RISE Registry. The views expressed represent those of the authors, not necessarily those of ACR.

Disclosure: R. Stovall: None; **C. Blat**: None; **E. Roberts**: None; **J. Liew**: None; **K. Wysham**: None; **N. Singh**: None; **J. Friedly**: None; **L. Gensler**: Acelyrin, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2, 5; **g. Schmajuk**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2.

Abstract Number: 2635

Differences in structural lesions of the spine between patients with early axSpA and non-axSpA chronic back pain: 2-year results of the SPACE Cohort

Gizem Ayan[1], Liese de Bruin[2], Miranda van Lunteren[2], Manouk de Hooge[3], Ana Bento da Silva[2], Mary Lucy Marques[4], Monique Reijnierse[5], Victoria Navarro-Compan[6], Marleen van de sande[7], Inger Jorid Berg[8], Roberta Ramonda[9], Sofia Exarchou[10], Désirée Van Der Heijde[2], Floris A. van Gaalen[2] and **Sofia Ramiro**[11], [1]Ankara Research and Training Hospital,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ankara, Turkey, [2]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands, [3]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [4]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; and Coimbra Local Health Unit, Coimbra, Portugal, [5]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands, [6]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain, [7]The Department of Rheumatology and Clinical Immunology, Amsterdam University Medical Center, Amsterdam, Netherlands, [8]Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway, [9]Rheumatology Unit-DIMED-University of Padova ITALY, Padova, Padua, Italy, [10]Lund University, Skarp, Skane Lan, Sweden, [11]Leiden University Medical Center, Bunde, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondyloarthritis (2633–2638)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: The difference in spinal structural lesions and their progression over time between chronic back pain (CBP) patients with and without early axSpA is unknown. We aimed to compare structural lesions of the spine on conventional radiographs (CR) and magnetic resonance imaging (MRI) over 2 years (2Y), as well as their 2Y-change, between patients with early axSpA and non-axSpA CBP.

Methods: Patients included in the Spondyloarthritis Caught Early cohort (CBP ≥3 months and ≤2 years, starting < 45 years), were diagnosed with axSpA or non-axSpA CBP by their rheumatologist at 2Y follow-up (1). Only patients with available imaging (CR or MRI) at both baseline (BL) and 2Y were included. Spinal lesions on CR were assessed by three central readers using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Structural lesions on spinal MRIs were assessed by two central readers using the Canada-Denmark scoring system. Readers made assessments independently, and they were blinded to demographic, clinical data and to the chronological order. BL spinal structural lesions and 2Y changes were compared between axSpA and non-axSpA. Generalized Estimating Equations models were used to assess the progression of structural lesions over 2Y, adjusting for age, sex, NSAID use, and diagnosis.

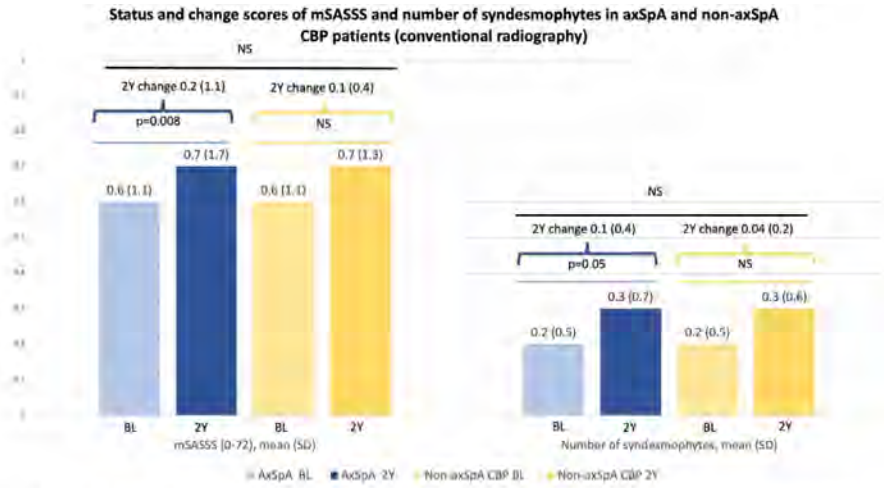


Figure 1. Status and change scores of mSASSS and number of syndesmophytes in axSpA and non-axSpA CBP patients.

- *Lines indicate p-values for BL to 2Y differences within groups and between-group differences in 2Y change scores. No significant difference was observed at BL and 2Y between axSpA and non-axSpA. BL, Baseline; 2Y, 2-years; CBP, Chronic back pain; NS, Non-significant*

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

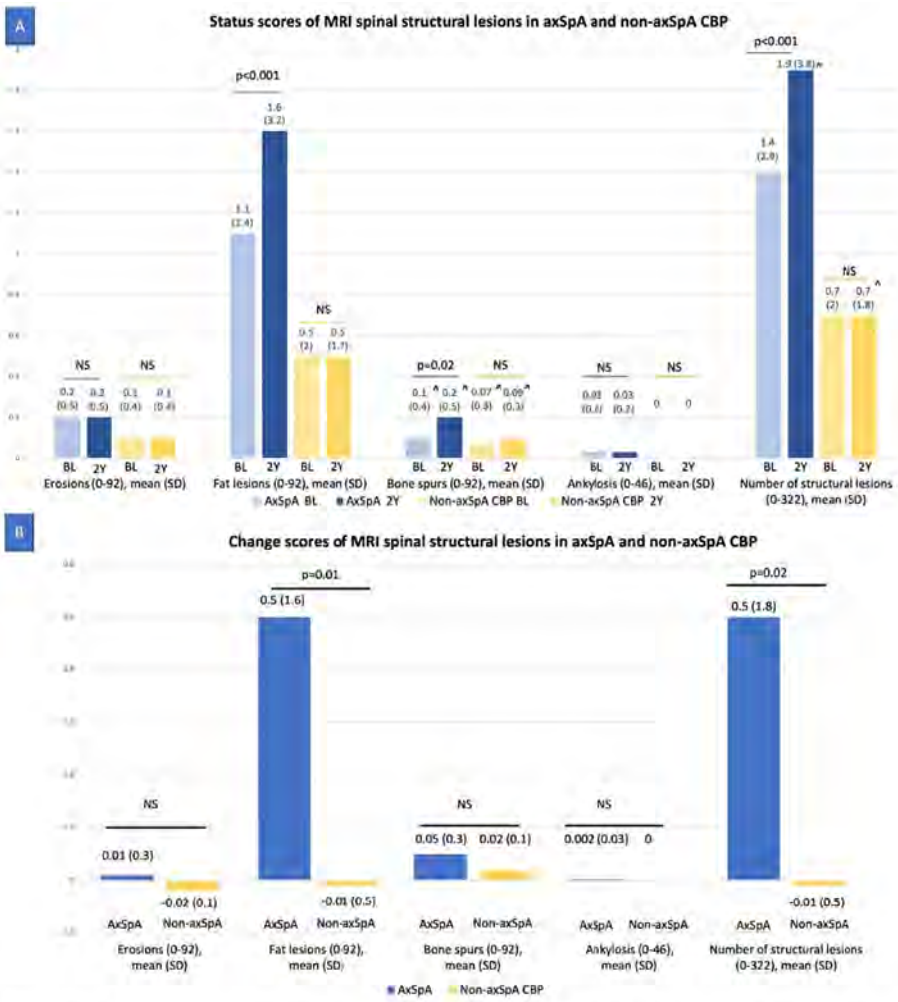


Figure 2. A. Status scores of MRI spinal structural lesions in axSpA and non-axSpA CBP. **B.** 2Y change scores of MRI spinal structural lesions in axSpA and non-axSpA CBP.

- *In Figure 2A, Lines indicate p-values for BL to 2Y differences within groups. Significant differences between the axSpA and non-axSpA groups at BL or 2Y for individual lesions are marked with a superscript (^).*
- *In Figure 2B, lines indicate p-values between the axSpA and non-axSpA -. BL, Baseline; 2Y, 2-years, Chronic back pain; NS, Non-significant*

Results: CR data from 318 patients (67% axSpA) and MRI data from 351 patients (69% axSpA) were included. Overall, 278 patients had both CR and MRI available at BL and 2Y [mean (SD) age 30 (8) years, 46% males, 61% HLA-B27+]. On CR, the mean (SD) BL mSASSS was 0.6 (1.1) for both axSpA and non-axSpA (Figure 1). Over 2Y, the progression of spinal structural lesions was similar between the axSpA and non-axSpA groups on CR, with overall mSASSS progression being minimal, specifically 0.01 mSASSS units per year. Mean number of syndesmophytes at BL and 2Y change scores between patients with axSpA and non-axSpA were similar. On MRI, axSpA patients had a mean of 1.4 (2.9) total structural lesions compared to 0.7 (2) in non-axSpA at BL (p=0.12) (Figure 2A). The 2Y increase in the mean total number of structural lesions [0.5 (1.8)] was mainly driven by the increase in fat lesions [0.5 (1.6)] in the axSpA group and was significantly higher than in non-axSpA (Figure 2B). The proportion of patients with ≥3 fat lesions both at BL and 2Y was higher in the axSpA group (BL: 9% vs 1%, p=0.004, 2Y: 15% vs 1%, p< 0.001). On MRI, fat lesions progressed at a rate of 0.16 units/year in axSpA (p=0.002) and -0.02 units/year in non-axSpA (p=0.7). The remaining lesions showed no significant progression.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Over 2 years, there is minimal progression of spinal structural damage typical for axSpA on CR in both early axSpA and non-axSpA CBP. On MRI, there is a significant increase in the number of fat lesions in axSpA, contrasting with non-axSpA in which no progression is observed. Fat lesions may be important to assess spinal disease progression from early disease onwards.

References: (1) Marques et al. Ann Rheum Dis. 2024;83(5):589-598

Disclosure: G. Ayan: None; **L. de Bruin**: None; **M. van Lunteren**: None; **M. de Hooge**: UCB pharma, 2; **A. Bento da Silva**: None; **M. Marques**: Novartis, 2, 6; **M. Reijnierse**: None; **V. Navarro-Compan**: AbbVie, 2, 5, 6, Alfasigma, 2, Bristol Myers Squibb, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, MoonLake, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **M. van de sande**: AbbVie/Abbott, 2, Benecke, 6, Eli Lilly, 6, Janssen, 2, 5, 6, Novartis, 2, 6, Ucb, 2, 6; **I. Jorid Berg**: None; **R. Ramonda**: None; **S. Exarchou**: AbbVie/Abbott, 1, 5, Amgen, 1, 5, Eli Lilly, 1, 5, Janssen, 1, Novartis, 1, 5, 6, Pfizer, 5, UCB, 1, 6; **D. Van Der Heijde**: AbbVie, 2, Alfasigma, 2, Annals of the Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly and Company, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, RMD Open, 12, Editoral board member, Takeda, 2, UCB, 2; **F. van Gaalen**: AbbVie, 2, BMS, 2, Eli Lilly, 2, Jacobus Stichting, 5, MSD, 2, Novartis, 2, 5, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, UCB, 5; **S. Ramiro**: AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos/Alfasigma, 2, 5, Janssen, 2, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 2636

Autoantibodies to 14-3-3 eta: A Novel Diagnostic Biomarker for Axial Spondyloarthritis

Raj Sengupta[1], Anthony Marotta[2], Walter P. Maksymowych[3], Charlotte Cavill[4], Stephen Bleakley[2] and Norma Biln[5], [1]Royal National Hospital for Rheumatic Diseases, Bath, England, United Kingdom, [2]Augurex Life Sciences Corp, Vancouver, BC, Canada, [3]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [4]Royal United Hospitals Bath NHS Foundation Trust, Bath, England, United Kingdom, [5]Augurex Life Sciences, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondyloarthritis (2633–2638)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: People with axial spondyloarthritis (axSpA), typically present with persistent back pain and experience up to a 10-year diagnostic delay that may lead to irreversible spinal damage. Earlier diagnosis and treatment may prevent this damage. As such, there is a high clinical unmet need in primary care, to differentiate patients with axSpA who require a referral to a rheumatologist from those with mechanical backpain (MBP). According to the Spondyloarthritis Research and Treatment Network (SPARTAN), identifying 1 axSpA patient of 3 referred, could meaningfully reduce diagnostic delay. This study examines the discriminative performance of 14-3-3η AAbs in patients with axSpA, including those with radiographic (r-) and non-radiographic (nr-) disease, compared to people with MBP.

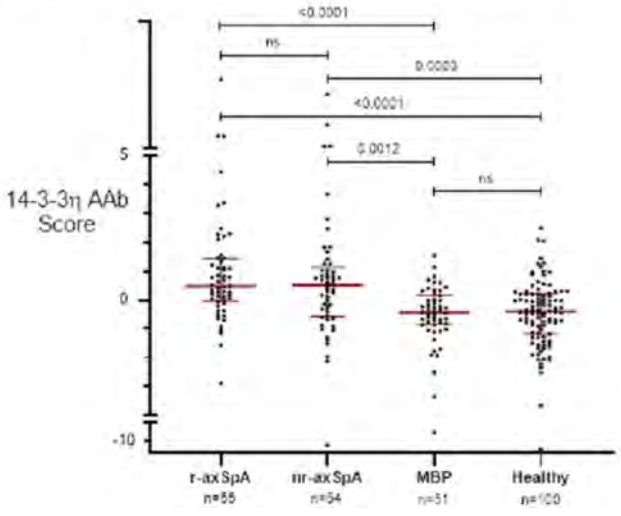
Methods: Patient serum (n=160) from the Bath Spondyloarthritis Biobank, a repository collected during routine clinical visits, were selected based on sample availability. Patients had a rheumatologist confirmed diagnosis and met classification criteria for r-axSpA (modified New York criteria, n=55), nr-axSpA (ASAS 2009 criteria, n=54) or MBP (n=51). 14-3-3η AAb levels were measured using the Health Canada and UKCA approved multiplex assay.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. 14-3-3η AAb Model Performance by axSpA Subset

Models	14-3-3η AAbs alone	14-3-3η AAbs + Age, Sex	14-3-3η AAb + (Age, Sex, CRP)	14-3-3η AAb + (Age, Sex, CRP, HLA-B27)
all axSpA versus MBP axSpA (n=109), MBP (n=51)				
AUC (95% CI)	0.77 (0.69-0.84)	0.88 (0.83 - 0.93)	0.89 (0.84 – 0.94)	0.93 (0.88 – 0.98)
SP/SN	90%, 42%	90%, 67%	90%, 72%	90%, 88%
PPV	88%	94%	94%	95%
NPV	42%	56%	60%	78%
DxOR (95% CI)	5.4 (2.1 - 13.6)	18.4 (6.74 - 50.2)	23.4 (8.5 – 64.6)	63.7 (21.4 – 189.5)
r-axSpA versus MBP r-axSpA (n=55), MBP (n=51)				
AUC (95% CI)	0.78 (0.69-0.87)	0.91 (0.85 - 0.97)	0.92 (0.86 – 0.98)	0.94 (0.89 – 0.99)
SP/SN	92%, 47%	92%, 75%	92%, 81%	90%, 90%
PPV	83%	89%	92%	90%
NPV	69%	77%	82%	90%
DxOR (95% CI)	10.6 (7.4 – 15.3)	26.9 (8.9 – 81.2)	51.8 (15.1 – 177.1)	84.6 (22.9 – 312.7)
nr-axSpA versus MBP nr-axSpA (n=54), MBP (n=51)				
AUC (95% CI)	0.73 (0.63-0.82)	0.88 (0.81 - 0.95)	0.87 (0.80 – 0.94)	0.93 (0.87 – 0.99)
SP/SN	92%, 38%	90%, 62%	90%, 66%	90%, 83%
PPV	83%	87%	88%	90%
NPV	59%	70%	71%	83%
DxOR (95% CI)	7.12 (2.2 – 22.7)	14.6 (5.3 – 40.4)	17.5 (5.9 – 51.9)	44.0 (13.6 – 141.7)

Figure 1. 14-3-3η AAb Score Distribution r-axSpA versus MBP Model



Nominal regression was performed to model the relationship between predictor variables and diagnosis. The probability formula generated from this regression was used to calculate a linear score for three models alongside variables of age, sex, CRP and HLA-B27: 1) all patients with axSpA (n=109), 2) r-axSpA, and 3) nr-axSpA versus MBP as a control group. This score quantifies the likelihood of a diagnosis based on model predictors. The r-axSpA versus MBP regression was used to calculate 14-3-3η AAb scores in banked serum samples from healthy individuals (n=100) for comparison. Statistical significance was set at $p < 0.05$.

Results: Mean age (SD) was 55 (23) yrs for r-axSpA, 42 (14) yrs for nr-axSpA, and 30 (14) yrs for MBP. Gender distribution (% male) was respectively 67%, 41%, and 59%. Disease duration (SD) was 13 (27) yrs for r-axSpA, and 5 (5) yrs for nr-axSpA. HLA-B27+ status was: 69% for r-axSpA, 72% for nr-axSpA, and 18% for MBP. 14-3-3η AAb predictive model

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ROC AUCs for all axSpA versus MBP were 0.77, r-axSpA of 0.78 and nr-axSpA 0.73 (Table 1). Selecting the best sensitivity (SN) for ~90% specificity (SP) returned SP & SN for all axSpA of 90% & 42%, r-axSpA of 92% & 47% and nr-axSpA of 92% & 38%. Corresponding Positive Predictive Values (PPV) were 88%, 83% and 83%, exceeding the SPARTAN target 33.3% PPV. In the All axSpA model, adding age and sex variables to the 14-3-3η AAb score, improved the diagnostic odds ratio (DxOR) from 5.4 to 18.4 and increased to 23.4 with CRP added and to 63.7 with HLA-B27 added. Scores for healthy controls were similar to patients with MBP, p >0.99 (Figure 1).

Conclusion: The 14-3-3η AAb biomarker differentiates radiographic and non-radiographic-axSpA from MBP, achieves a high PPV and its discrimination improves when age, sex, CRP, and HLA-B27 are added. Alongside these easily accessible patient variables at primary care, 14-3-3η AAb may reduce diagnostic delay and complement HLA-B27.

Disclosure: R. Sengupta: AbbVie, 6, Eli Lilly and Company, 6, Novartis, 5, 6, Pfizer, 6, UCB Pharma, 5, 6; **A. Marotta**: Augurex Life Sciences Corp., 12, 2; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **C. Cavill**: None; **S. Bleakley**: Augurex Life Sciences Corp., 3, 11; **N. Biln**: Augurex Life Sciences Corp., 3, 4, 8, 11.

Abstract Number: 2637

Initial Phospholipid Transferase Activity Is Predictive of Five-Year Sacroiliac Radiographic Progression in Axial Spondyloarthritis: Findings From the DESIR Cohort

Frank Verhoeven[1], Olivier Fakih[1], Sophie Hecquet[2], anne tournadre[3], jean Paul Pais de Barros[4], Céline Delougeot[5], Clément Prati[1] and WENDLING Daniel[1], [1]CHU de Besançon, Besançon, Franche-Comte, France, [2]Rheumatology department, Cochin hospital, Paris, France, [3]CHU Clermont ferrand, Clermont-Ferrand, France, [4]Labex lipstick, Dijon, France, [5]université Marie et Louis Pasteur, Besancon

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondyloarthritis (2633–2638)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: The pathophysiology of axial spondyloarthritis (axSpA) involves the gut-joint axis. Recent studies suggest more active disease in cases of gut involvement.

The objective of this study is to evaluate the impact of bacterial translocation levels at baseline in the DESIR cohort on 5-year outcomes in patients.

Methods: We included patients from the DESIR cohort meeting the 2009 ASAS criteria, for whom serum samples at baseline and 5-year follow-up data were available. Gut permeability was assessed by measuring serum zonulin levels using ELISA. Bacterial translocation was evaluated by quantifying serum levels of lipopolysaccharides (LPS) and their esterified free fatty acid components (3OHC10, 12, 14, 16, and 18) using liquid chromatography coupled with mass spectrometry. Phospholipid transfer protein (PLTP) activity, which plays a role in LPS transfer, was also measured. We analyzed these biomarkers concerning the occurrence of extra-articular manifestations (psoriasis, IBD, and uveitis), radiographic spinal

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Univariate analysis of the impact of different levels of LPS, Zonuline and PLTP activity on the radiographic progression of the sacroiliac after 5 years

	5 years Sacroiliac radiographic progression		Transition to radiographic form at 5 years	
	YES	NO	YES	NO
LPS	***656 ± 200***	***716 ± 199 ****	681 ± 200	710 ± 194
3OHC10 (pmol/ml)	88 ± 44	85 ± 39	93 ± 38	85 ± 38
3OHC12 (pmol/ml)	38 ± 30	42 ± 35	42 ± 23	40 ± 34
3OHC14 (pmol/ml)	46 ± 15	47 ± 20	43 ± 10	47 ± 19
3OHC16 (pmol/ml)	277 ± 77	288 ± 71	***252 ± 48***	***290 ± 71 ****
3OHC18 (pmol/ml)	***206 ± 119***	***253 ±116 *****	249 ± 149	248 ±115
Zonuline (ng/ml)	***104 ± 103***	***147 ±155 *****	***72 ± 84***	***156 ±157 *****
Activité PLTP (nmol/h/ml)	***5,8 ± 1,7***	***5,2 ± 1,6 ****	5,6 ± 1,8	5,2 ± 1,7

* P < 0,05 ; ** p<0,01

progression assessed by mSASS, sacroiliac joint radiographic progression evaluated by the change in sacroiliitis grade (NYm), and the transition from non-radiographic to radiographic axSpA over 5 years.

Results: Out of 708 patients in the DESIR cohort, 319 met the inclusion criteria. The mean age was 31.7 (±7.3) years, with 49.2% male, 82% HLA-B27 positive, 27% with radiographic axial involvement, and symptom duration of 1.6 (±0.9) years. The cohort included 15% with psoriasis, 6% with IBD, 9% with uveitis, 55% with enthesitis, and 12% with dactylitis. Baseline disease activity scores included a BASDAI of 42 (±20), an ASDAS-CRP of 2.6 (±1), and a CRP of 8.4 (±13) mg/L. At baseline, LPS levels (and their fatty acid subgroups), zonulin levels, and PLTP activity were not associated with the presence of extra-musculoskeletal manifestations or disease activity. These levels also did not differ between patients who developed extra-musculoskeletal manifestations at 5 years and those who did not. In patients with sacroiliac progression, lower total LPS levels (716 ± 199 pmol/mL vs. 656 ± 200 pmol/mL; p = 0.036), lower 3OHC18 levels (252.5 ± 116.8 pmol/mL vs. 205.9 ± 119 pmol/mL; p = 0.007), and lower zonulin levels (147 ± 155 ng/mL vs. 104 ± 103 ng/mL; p = 0.01) were observed. PLTP activity was higher in patients with sacroiliac progression (5.2 ± 1.6 nmol/h/mL vs. 5.8 ± 1.7 nmol/h/mL). In multivariate analysis accounting for age, sex, smoking, and ASDAS-CRP, PLTP activity remained significantly associated with sacroiliac progression (p = 0.028). Finally, in patients transitioning from non-radiographic to radiographic axSpA, lower 3OHC16 levels (290 ± 71 pmol/mL vs. 252 ± 48 pmol/mL) and lower zonulin levels (156 ± 157 ng/mL vs. 72 ± 84 ng/mL; p = 0.003) were noted.

Conclusion: In early axial spondyloarthritis, baseline PLTP activity was associated with sacroiliac radiographic progression at 5 years

Disclosure: F. Verhoeven: None; **O. Fakih**: None; **S. Hecquet**: None; **a. tournadre**: None; **j. Pais de Barros**: None; **C. Delougeot**: None; **C. Prati**: None; **W. Daniel**: None.

Abstract Number: 2638

Asemblenet: A Hybrid AI Model for Mri-based Classification of Ankylosing Spondylitis

Miral Gharib[1], Amith Khandakar[2], Mohamed Arselene Ayari[3] and Samar Al emadi[4], [1]hamad medical corporation, Doha, Qatar, [2]Department of Electrical Engineering, College of Engineering, Qatar University, Doha, Qatar, Doha, Qatar, [3]Department of Civil and Environmental Engineering, College of Engineering, Qatar University, Doha, Qatar, [4]Hamad medical corporation, Doha, Qatar

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025

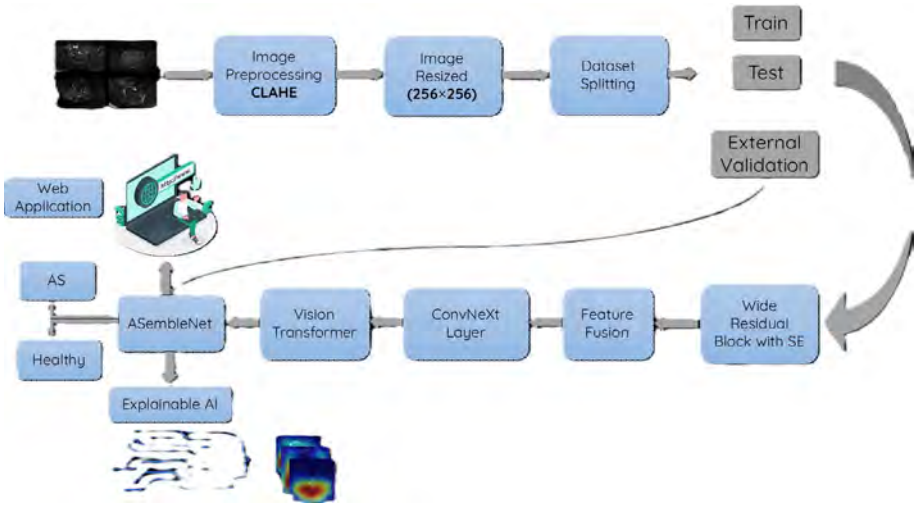
Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II: Advances in Axial Spondyloarthritis (2633–2638)

Session Type: Abstract Session

Session Time: 3:00PM–4:30PM

Background/Purpose: Ankylosing spondylitis (AS) is a progressive inflammatory disease with delayed diagnosis due to subtle early imaging findings. We present ASembleNet, a deep learning model integrating convolutional and transformer-based architectures for accurate AS classification on MRI. The model was developed using multi-institutional, publicly available datasets and externally validated with expert-reviewed cases.

Methods: Three datasets were used for model development. Dataset 1 consisted of 4,115 axial and coronal MRI images from AS patients and healthy controls collected at Elazığ Fethi Sekin City Hospital (2018–2023). Dataset 2 included 213 expert-annotated MRI images from the Assessment of Spondyloarthritis International Society (ASAS) Online Case Library for external validation. Dataset 3 comprised 102 normal MRIs sourced from Radiopaedia.org to augment healthy control data. All images underwent standardized preprocessing: cropping of artifacts, resizing to 256×256 pixels, and contrast enhancement via CLAHE. ASembleNet architecture (Figure 1) combines wide residual blocks, ConvNeXt layers, and



Methodology of our proposed model

Table 1: Dataset distribution for axial and coronal MRI from three public sources.

Dataset	Category	Source	Training Set	Validation Set	Total
Axial MRI	Ankylosing Spondylitis	Dataset 1	1000 images	-	1000 images
	Ankylosing Spondylitis	ASAS Online Case Library	56 images (5 cases)	56 images (4 cases)	112 images
	Healthy Controls	Dataset 1	1110 images	-	1110 images
	Healthy Controls	Radiopaedia.org	-	51 images	51 images
Coronal MRI	Ankylosing Spondylitis	Dataset 1	1000 images	-	1000 images
	Ankylosing Spondylitis	ASAS Online Case Library	51 images (5 cases)	50 images (5 cases)	101 images
	Healthy Controls	Dataset 1	1005 images	-	1005 images
	Healthy Controls	Radiopaedia.org	-	51 images	51 images

Axial MRI Dataset Coronal MRI Dataset

Table: Dataset distribution across training and validation sets used in the development of ASembleNet. MRI images were sourced from Dataset 1, the ASAS Online Case Library, and Radiopaedia.org.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Performance comparison of ASembleNet and other deep learning models.

Model	Accuracy (Axial)	Precision (Axial)	F1-score (Axial)	Recall (Axial)	Accuracy (Coronal)	Precision (Coronal)	F1-score (Coronal)	Recall (Coronal)
IRv2	96.26%	96.26%	96.26%	96.26%	95%	95%	95%	95%
InceptionV3	98.13%	98.13%	98.13%	98.13%	96%	96%	96%	96%
Xception	98.13%	98.13%	98.13%	98.13%	98%	98%	98%	98%
ResNet50	97.19%	97.19%	97.19%	97.19%	97%	97%	97%	97%
ASembleNet	98.13%	98.13%	98.13%	98.13%	99%	99%	99%	99%

Table: Performance comparison of ASembleNet and benchmark deep learning models on Axial and Coronal MRI images. Metrics include Accuracy, Precision, Recall, and F1-score. ASembleNet demonstrates superior performance.

Axial MRI Metrics Coronal MRI Metrics

Vision Transformer encoders with Squeeze-and-Excitation modules for attention calibration and Grad-CAM for interpretability. The dataset distribution is detailed in Table 1. Training-validation split ensured ASAS cases were used solely for external testing. Performance metrics included accuracy, precision, recall, F1-score, AUC, and confusion matrix analysis.

Results: ASembleNet achieved 99% classification accuracy for coronal MRI and 98.13% for axial MRI, outperforming Xception, ResNet50, and InceptionV3 models. The model consistently showed high sensitivity and specificity across all classes. External validation on ASAS cases confirmed generalizability. Model performance across architectures is summarized in Table 2. Grad-CAM visualizations demonstrated clinically relevant feature localization, aligning with expert interpretations. A publicly accessible web-based platform was developed to facilitate real-time AS classification by clinicians.

Conclusion: ASembleNet demonstrates high accuracy in detecting AS on MRI using a hybrid deep learning approach trained on diverse, real-world datasets. Its strong performance on external validation and integration with explainable AI tools underscore its potential as a reliable clinical decision-support tool for early AS diagnosis.

Disclosure: M. Gharib: None; **A. Khandakar**: None; **M. Ayari**: None; **S. Al emadi**: None.

Abstract Number: 2639

Gut Microbiome Signatures Forecast Clinical Response to Methotrexate in Treatment-Naïve Early Rheumatoid Arthritis

VINOD GUPTA[1], Adam Koller[1], Benjamin Hur[1], Marissa Bailey[1], Kara Delger[2], Elena myasoedova[1], Vanessa Kronzer[1], John Davis[1] and Jaeyun Sung[1], [1]Mayo Clinic, ROCHESTER, MN, [2]Mayo Clinic, St Charles, MN

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization (2639–2644)
Session Type: Abstract Session
Session Time: 9:30AM–11:00AM

Background/Purpose: Oral methotrexate (MTX) is the cornerstone treatment for newly diagnosed rheumatoid arthritis (RA), yet up to 50% of patients do not respond adequately. Early prediction of MTX response is crucial to prevent disease progression and promptly initiate alternative therapies. Recent studies suggest a link between the gut microbiome and MTX efficacy in treatment-naïve RA patients. However, the use of 16S rRNA sequencing in these studies limits taxonomic resolution in identifying gut microbial relationships with treatment response; and the response criteria applied were arbitrary, as

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographic and clinical characteristics of the study population.

Patient characteristics	Visit 1 (Baseline)			Visit 2 (Follow-up)		
	Patient groups categorized by their response to methotrexate (MTX), based on the EULAR response criteria		*P*-value[e]	Patient groups categorized by their response to methotrexate (MTX), based on the EULAR response criteria		*P*-value[e]
	Responder (n = 37)	Non-responder (n = 23)		Responder (n = 37)	Non-responder (n = 23)	
Duration between visits (days), median [Q1, Q3][a]	N/A	N/A	N/A	99 [91.0, 109.0]	97 [88.5, 108.5]	0.08
Age (years), median [Q1, Q3]	49.8 [42.2, 60.5]	50.6 [45.6, 59.1]	0.67	50.1 [42.5, 60.8]	50.9 [45.9, 59.4]	0.67
BMI (kg/m^2), median [Q1, Q3]	27.7 [24.0, 32.0]	31.7 [26.5, 34.7]	0.13	N/A	N/A	N/A
Smoker (current), n (%)	3 (8.1)	3 (13)		N/A	N/A	
DAS28-CRP[b], median [Q1, Q3]	4.5 [3.7, 5.7]	3.8 [3.0, 5.0]	0.05	2.6 [1.9, 3.3]	4.4 [3.1, 5.3]	1.9×10^{-5}
ΔDAS28-CRP, median [Q1, Q3]	N/A	N/A	N/A	−1.7 [−2.5, −1.2]	−0.1 [−0.3, 0.8]	N/A
CRP[c] (mg/L), median [Q1, Q3]	4.8 [2.9, 15.7]	4.5 [2.9, 12.0]	0.63	2.9 [2.9, 4.7]	6.3 [2.9, 9.7]	0.02
ESR[d] (mm/h), median [Q1, Q3]	16 [5.0, 31.0]	11 [5.0, 20.5]	0.34	8 [5.0, 16.0]	8 [5.0, 14.0]	0.65
Rheumatoid factor (RF)			1			N/A
positive, n (%)	22 (59.5)	13 (56.5)		N/A	N/A	
negative, n (%)	15 (40.5)	9 (39.1)		N/A	N/A	
not available	0 (0.0)	1 (4.3)		N/A	N/A	
Anti-citrullinated protein antibodies (ACPA)			0.15			N/A
positive, n (%)	28 (75.7)	12 (52.2)		N/A	N/A	
negative, n (%)	9 (24.3)	10 (43.5)		N/A	N/A	
not available	0 (0.0)	1 (4.3)		N/A	N/A	
Methotrexate use						
User, n (%)	0	0	N/A	37 (100)	23 (100)	1
Dose[e] (mg or mg/L), median [Q1, Q3]	15 [12.5, 15.0][f]	15 [15.0, 15.0][f]	0.36	15 [15.0, 20.0][g]	15 [15.0, 20.0][g]	0.72
Frequency	Weekly	Weekly	N/A	Weekly	Weekly	N/A
Prednisone use						
User, n (%)	7 (18.9)	7 (30.4)	0.36	13 (35.1)	5 (21.7)	0.38
Dose (mg), median [Q1, Q3]	10 [10.0, 20.0]	20 [17.5, 20.0]	0.35	5 [5.0, 10.0]	5 [5.0, 5.0]	0.96
Frequency	Daily	Daily	N/A	Daily	Daily	N/A

[a]Upper and lower quartiles; [b]DAS28-CRP, Disease Activity Score on 28 joints; [c]CRP, C-reactive protein; [d]ESR, Erythrocyte sedimentation rate; [e]Methotrexate dose was measured in milligrams (mg) if administered by oral route or mg/L if administered by intravenous; [f]Stool samples were collected before prescribing the methotrexate to early arthritis patients; [g]All 60 patients continued to use methotrexate during their follow-up visit; [h]Fisher's exact test and Mann-Whitney *U* test was used to test for statistical significance amongst categorical and continuous variables, respectively; N/A, not applicable or not available.

acknowledged by the investigators. To enhance clinical applicability, our study used whole genome shotgun metagenome sequencing and the standardized EULAR response criteria to rigorously investigate associations between pre-treatment gut microbiome and MTX response.

Methods: A cohort of 60 treatment-naïve RA patients (mean age 51.2 years) initiated treatment with oral MTX at a low dose (15 mg/week). Of these, 43 were female, 6 were current smokers, and 14 were on prednisone (**Table 1**). Stool samples collected at baseline and after 3–3.5 months of treatment underwent metagenomic sequencing. Patients were classified as MTX responders (n = 37) or non-responders (n = 23) based on the EULAR response criteria. Response was defined as a decrease in DAS28-CRP (ΔDAS28-CRP) > 1.2, or ΔDAS28-CRP > 0.6 with a follow-up DAS28-CRP ≤ 5.1. Differential abundance and prevalence analyses identified microbiome features distinguishing the two groups. A gradient-boosting linear regression model using baseline gut microbiome and clinical data (BMI, DAS28-CRP, ACPA status, and prednisone dose) was developed to predict MTX response.

Results: Baseline microbiome analysis revealed significant differences between responders and non-responders, with five species and nine metabolic pathways having differential abundance (**Fig. 1**). Additionally, clinical response correlated strongly with the presence of specific species, such as *Bacteroides fragilis* and *Eubacterium* sp. AF16-48 (**Fig. 1**). Additionally, the odds of MTX response increased ten-fold in patients harboring any of the top ten differentially prevalent gut microbial species (OR = 10.4). Moreover, genes of the dihydrofolate reductase (DHFR) enzyme were significantly less abundant in responders (P = 0.031). Finally, our machine learning model using baseline gut microbiome and clinical data demonstrated an AUC of 0.83 in leave-one-out cross-validation, outperforming an AUC of 0.72 from clinical data alone. Our model achieved an AUC of 0.77 in an external validation cohort of 38 treatment-naïve RA patients (**Fig. 2**).

Conclusion: We identified gut microbiome features associated with MTX response in early RA patients. Our machine learning model suggests the potential of gut microbiome profiling as a personalized predictive tool for MTX outcomes.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

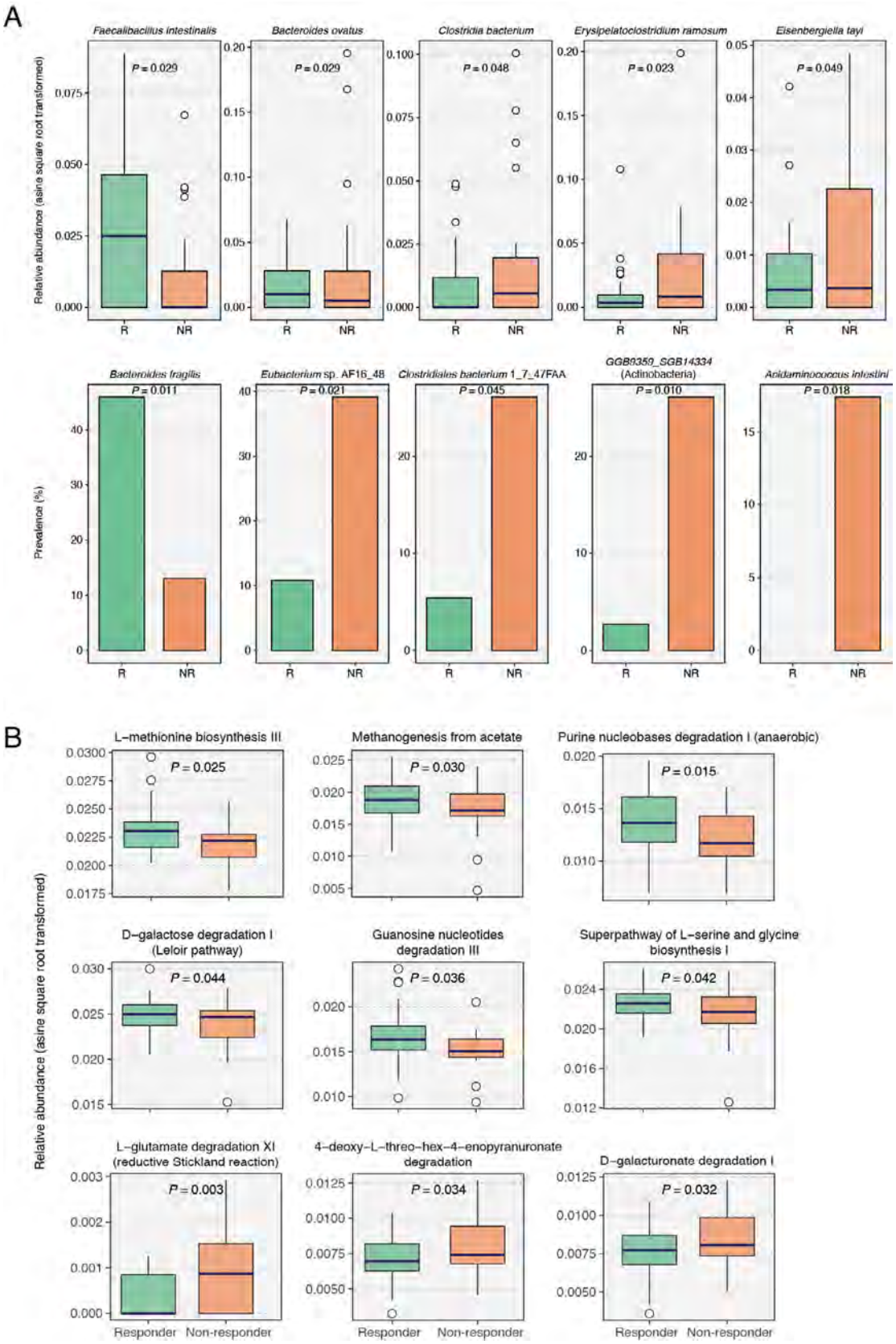


Figure 1. Differences in baseline gut microbial species (A) and MetaCyc pathways (B) between responders and non-responders. Multiple linear regression models adjusted for age and BMI were used to test for the statistical significance to identify the differentially abundant microbiome features between both patient groups. Differentially prevalent species were identified using Fisher's exact test. R, Responder; NR, Non-responder.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

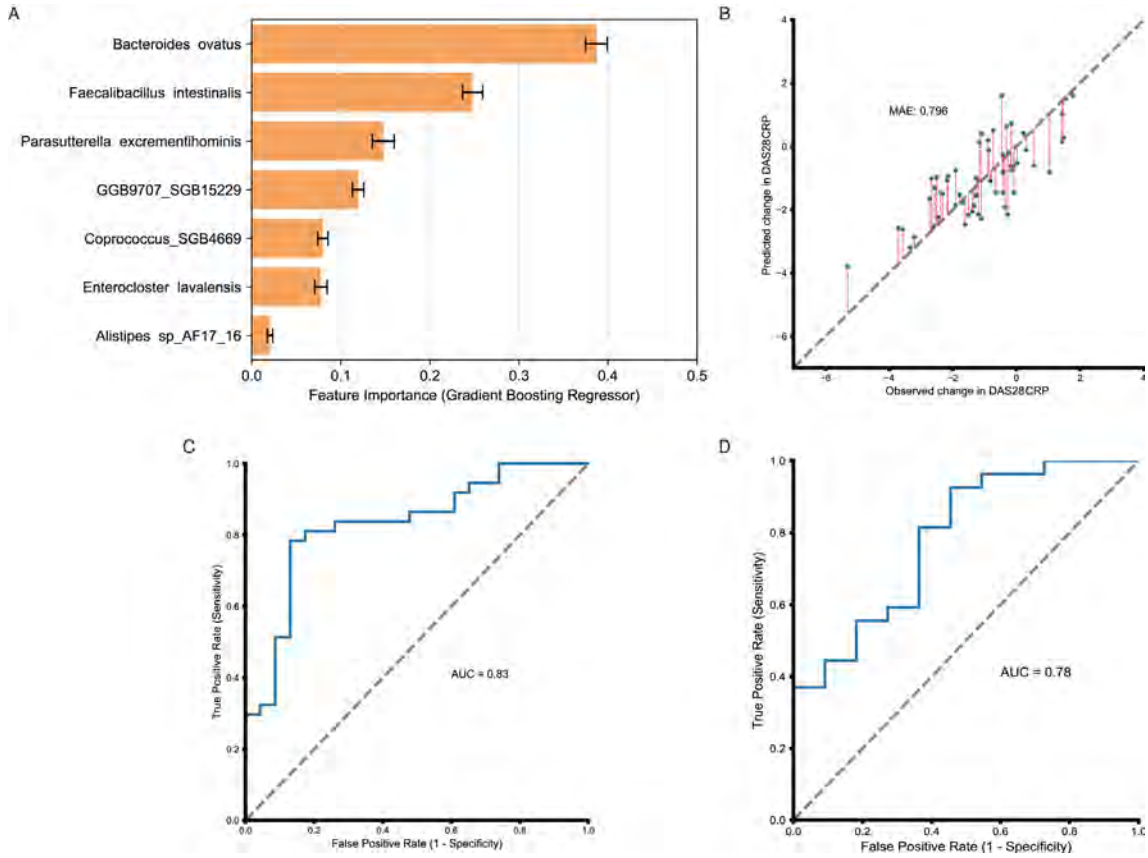


Figure 2. Performance of microbiome-based gradient-boosting linear regression model in predicting the MTX response. (A) Feature importance of microbial species that were used in the model. (B) Scatter plot between predicted ΔDAS28CRP and actual ΔDAS28CRP values. (C) Leave-one-out cross-validation receiver operating characteristic (ROC) curve of the gradient boosting machine-learning model predicting response to MTX from the training dataset. (D) ROC curve of the gradient boosting machine-learning model predicting response to MTX from an external validation cohort.

Disclosure: V. GUPTA: None; **A. Koller**: None; **B. Hur**: None; **M. Bailey**: None; **K. Delger**: None; **E. myasoedova**: None; **V. Kronzer**: None; **J. Davis**: Pfizer, 5, Remission Medical, 1, 9, 10, Rheumasense, 1, 9, 10; **J. Sung**: Rheumasense, 1, 9, 10.

Abstract Number: 2640

Effectiveness of Biological and Target-Synthetic Treatment in Patients with Rheumatoid Arthritis and Kidney Dysfunction: A Large Prospective Registry Study

Sho Fukui[1], Hilde Ørbo[2], Sara Tedeschi[1], Hongshu Guan[3], Leslie Harrold[4], Heather Litman[5] and Daniel Solomon[1], [1]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [2]Diakonhjemmet Hospital, Oslo, Norway, [3]Brigham and Women's Hospital/ Harvard Medical School, Boston, [4]CorEvitas, Northborough, MA, [5]Corrona, LLC, Waltham, MA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization (2639–2644)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline characteristics of RA patients by baseline eGFR before weighting

		N (%) or median (IQR)	
		Non-reduced eGFR (≥60 mL/min/1.73m^2) N=10,813	Reduced eGFR (<60 mL/min/1.73m^2) N=1,263
Initiated bDMARDs	TNFi	4,787 (44.3%)	531 (42.0%)
	CTLA4-Ig	1,996 (18.5%)	269 (21.3%)
	IL-6i	1,504 (13.9%)	175 (13.9%)
	BCDT	940 (8.7%)	119 (9.4%)
	JAKi	1,586 (14.7%)	169 (13.4%)
Age, years		58.0 (49.0, 66.0)	69.0 (62.0, 76.0)
Gender	Female	8,620 (79.7%)	1,059 (83.8%)
	Male	2,193 (20.3%)	204 (16.2%)
Race	Non-Hispanic white	8,818 (81.5%)	1,052 (83.3%)
	Hispanic	953 (8.8%)	61 (4.8%)
	Black	595 (5.5%)	120 (9.5%)
	Asian	176 (1.6%)	10 (0.8%)
	Others	271 (2.5%)	20 (1.6%)
Body mass index, kg/m^2		29.2 (24.8, 34.4)	29.5 (25.0, 35.2)
Current smoker		1,956 (18.1%)	165 (13.1%)
eGFR, mL/min/1.73m^2		92.8 (79.3, 103.4)	52.3 (43.9, 56.6)
Hypertension		4,760 (44.0%)	894 (70.8%)
on medication		2,767 (25.6%)	526 (41.6%)
Hyperlipidemia		2,124 (19.6%)	408 (32.3%)
on medication		1,280 (11.8%)	252 (20.0%)
Diabetes mellitus		1,435 (13.3%)	282 (22.3%)
on medication		812 (7.5%)	149 (11.8%)
Fibromyalgia		638 (5.9%)	98 (7.8%)
Duration of RA, years		7.0 (2.3, 15.0)	9.3 (3.4, 18.7)
Seropositive [a]		5,691 (52.6%)	629 (49.8%)
Secondary Sjogren Syndrome		2,189 (20.2%)	290 (23.0%)
CDAI		21.0 (15.0, 30.5)	20.7 (14.6, 30.2)
mHAQ (>=6 domain)		0.6 (0.2, 1.0)	0.6 (0.2, 1.0)
NSAIDs use		4,984 (46.1%)	415 (32.9%)
Glucocorticoid use		4,124 (38.1%)	483 (38.2%)
Dose among users, mg/day		6.0 (5.0, 10.0)	6.0 (5.0, 10.0)
Methotrexate use		5,785 (53.5%)	611 (48.4%)
Dose among users, mg/week		17.5 (12.5, 20.0)	15.0 (12.5, 20.0)
Use of non-methotrexate csDMARDs		3,453 (31.9%)	413 (32.7%)
Previous use of bDMARDs			
History of TNFi use		4,761 (44.0%)	537 (42.5%)
History of CTLA4-Ig use		1,729 (16.0%)	225 (17.8%)
History of IL-6i use		995 (9.2%)	115 (9.1%)
History of BCDT use		622 (5.8%)	89 (7.0%)
History of JAKi use		837 (7.7%)	113 (8.9%)

[a] positive rheumatoid factor or anti-citrullinated cyclic peptide antibody

Number (%) or median (interquartile range) are reported. RA, rheumatoid arthritis; eGFR, estimated glomerular filtration rate; bDMARDs, biologic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; TNFi, tumor necrosis factor inhibitors; CTLA4-Ig, cytotoxic T-lymphocyte-associated protein 4 immunoglobulin; IL-6i, interleukin-6 inhibitors; BCDT, B cell depletion therapy; JAKi, Janus kinase inhibitors; BMI, body mass index; NSAIDs, nonsteroidal anti-inflammatory drugs; CDAI, Clinical Disease Activity Index; mHAQ, modified Health Assessment Questionnaire.

Background/Purpose: Kidney dysfunction is common in patients with rheumatoid arthritis (RA). However, there has been limited and conflicting evidence on the effectiveness of biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) in RA patients with kidney dysfunction.

Methods: This study used the CorEvitas RA registry, a large prospective registry of RA patients from multiple US institutions. We included patients with moderate-to-high clinical disease activity index (CDAI) who newly initiated each class of b/tsDMARDs (TNFi, CTLA4-Ig, IL-6i, BCDT, or JAKi) during the registry follow-up from Oct 2001 to Dec 2023. The index date was set at the b/tsDMARDs initiation. The exposure of interest was a reduced estimated glomerular filtration rate (eGFR < 60 mL/min/1.73m^2) at the index date, in comparison to non-reduced eGFR (≥60 mL/min/1.73m^2). Outcomes included CDAI remission (REM), CDAI-remission or low disease activity (REM/LDA), and each outcome without concomitant glucocorticoid (GC) use. The patients were followed until the first occurrence of an outcome or the last study visit. Propensity scores (PS) for baseline reduced eGFR were used for overlap weighting. Kaplan-Meier curves and Cox proportional hazards models before and after weighting examined the association between baseline reduced eGFR and treatment outcomes. Sensitivity analysis using an alternative exposure of chronic kidney disease (CKD) G3a or worse (eGFR ≤ 60 mL/min/1.73m^2 for ≥3 months) was also performed. Given that low eGFR may potentially lead to more MTX discontinuation, four-way decomposition causal mediation analysis evaluated whether MTX discontinuation mediated the association among those who used MTX at baseline.

Results: We identified 12,076 new b/tsDMARDs treatment courses (TNFi 5,318; CTLA4-Ig 2,265; IL-6i 1,679; BCDT 1,059; JAKI 1,755) among 9,569 patients. At baseline, median age was 59.0 years, 80.2% were female, and median eGFR was 52.3 mL/min/1.73m^2 in the reduced eGFR group and 92.8 mL/min/1.73m^2 in the non-reduced eGFR group. Patients with low eGFR were older, had more comorbidities, and used NSAIDs less often (**Table 1**). After PS overlap weighting, patient

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

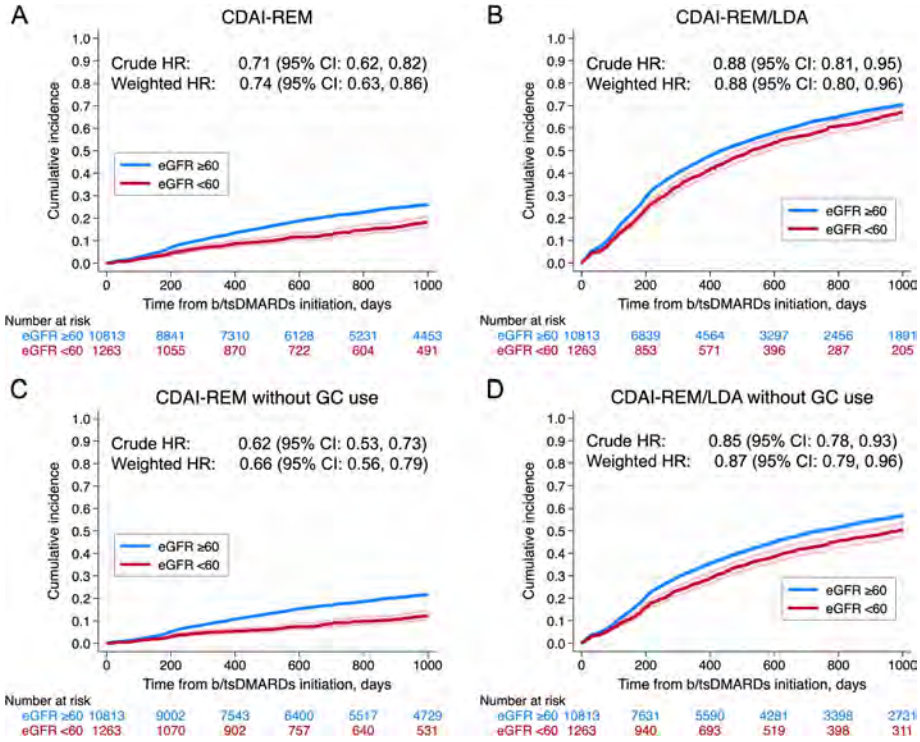


Figure 1. Achievement of CDAI-REM and CDAI-REM/LDA after initiating b/tsDMARDs by baseline eGFR: Kaplan–Meier cumulative incidence curves (95% CI) for (A) CDAI-REM, (B) CDAI-REM/LDA, (C) CDAI-REM without GC use, and (D) CDAI-REM/LDA without GC use are visualized by reduced eGFR (<60) versus non-reduced eGFR (≥60) at baseline. Time zero represents initiation of b/tsDMARDs. Crude HR (95% CI) and HR (95% CI) after propensity-score overlap weighting (weighted HR) of reduced eGFR for achieving outcomes are described. CDAI, Clinical Disease Activity Index; REM, remission; REM/LDA, remission or low disease activity; GC, glucocorticoid; b/tsDMARDs, biologic or targeted synthetic disease-modifying antirheumatic drugs; eGFR, estimated glomerular filtration rate; HR, hazard ratio; CI, confidence interval

characteristics were well-balanced. Reduced eGFR was associated with less achievement of CDAI-REM (crude HR 0.71 [95% CI: 0.62, 0.82]) and CDAI-LDA/REM (crude HR, 0.88 [95% CI: 0.81, 0.95]). Restricting the outcomes to those without GC use modestly strengthened these associations. These results were similar after weighting (**Figure 1**). Sensitivity analyses using CKD G3a as the exposure demonstrated comparable results. Among baseline MTX users, MTX discontinuation did not completely explain the association between kidney dysfunction and less CDAI-REM achievement.

Conclusion: Although b/tsDMARDs remain effective treatments for RA with kidney dysfunction, patients with reduced eGFR are approximately 30% less likely to achieve remission. Tailored treatment strategies are therefore required to optimize disease control in this high-risk population.

Disclosure: S. Fukui: None; **H. Ørbo**: None; **S. Tedeschi**: Alexion, 5, Amgen, 2, Avalo Therapeutics, 2, Fresenius Kabi, 2, Kyowa Kirin, 2, Merck/MSD, 2, Novartis, 2; **H. Guan**: None; **L. Harrold**: CorEvitas, 3, Pfizer, 2; **H. Litman**: CorEvitas, 3; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9.

Abstract Number: 2641

Cizutamig, a BCMA T-cell engager: preclinical to clinical translation of design optimization for the treatment of autoimmune diseases

Ricardo Grieshaber-Bouyer[1], Jamie Haddon[2], Maria Gabriella Raimondo[3], Carlo Tur[3], Sebastian Böltz[3], Tobias Dashi[4], Melanie Hagen[5], Andreas Wirsching[3], Tobias Rathe[4], Xuan Wu[6], Peter Wung[2], Francis Kim[2], Yonghong Zhu[6], Ken Song[2], Timothy Lu[7] and Georg Schett[8], [1]University Hospital Erlangen, Erlangen, Germany, [2]Candid Therapeutics, San Diego, CA,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

[3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [4]Department of Internal Medicine 3- Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [5]Friedrich-Alexander-University Erlangen-Nuremberg, Department of Internal Medicine 3 - Rheumatology and Immunology, Erlangen, Germany, [6]EpimAb Biotherapeutics, Shanghai, China (People's Republic), [7]Candid Therapeutics, San Diego, [8]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization (2639–2644)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Emerging data show the potential of T-cell engagers (TCEs) for deep B cell depletion to treat autoimmune diseases. Cizutamig is a purposefully designed BCMAxCD3 TCE based on the FIT-Ig® platform and an optimized CD3 binding affinity to reduce cytokine release while maintaining killing of BCMA-expressing B cells, plasmablasts and plasma cells. This study aimed to evaluate the translatability of TCE design from preclinical data to clinical activity in patients.

Methods: Previous in vitro methods on plasma cell killing, T cell activation, and cytokine release comparing cizutamig to benchmark BCMA TCEs have been previously described. To assess in vivo preclinical activity, immunodeficient mice reconstituted with peripheral blood mononuclear cells (PBMCs) from a patient with systemic lupus erythematosus (SLE) were treated with 3 weekly doses of vehicle, isotype (1 mg/kg), or 0.1, 0.3, or 1 mg/kg of cizutamig (n=10 per group). Levels of human serum IgG, anti-dsDNA antibodies, splenic B cells and kidney immune complexes were measured. A Phase 1 dose

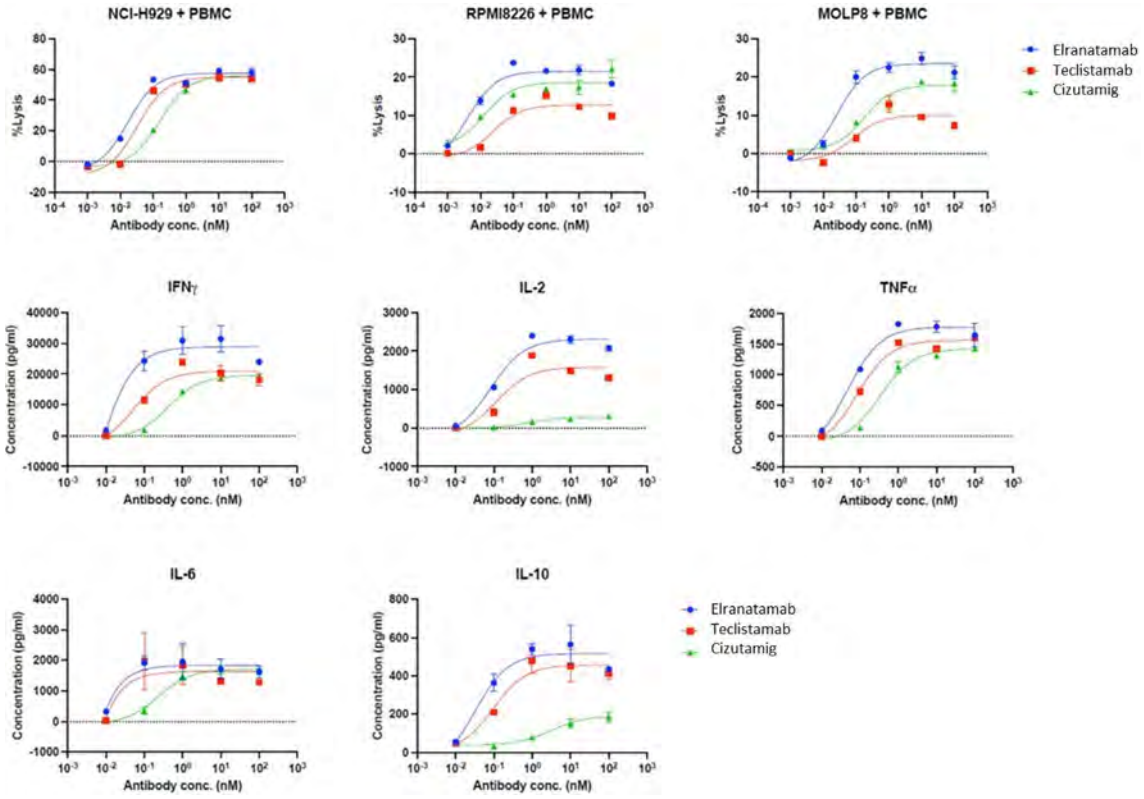


Fig 1. T cell mediated killing and cytokine release by healthy donor PBMCs co-cultured with BCMA-expressing cell lines in the presence of cizutamig or benchmark BCMAxCD3 TCEs (elranatamab, teclistamab).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

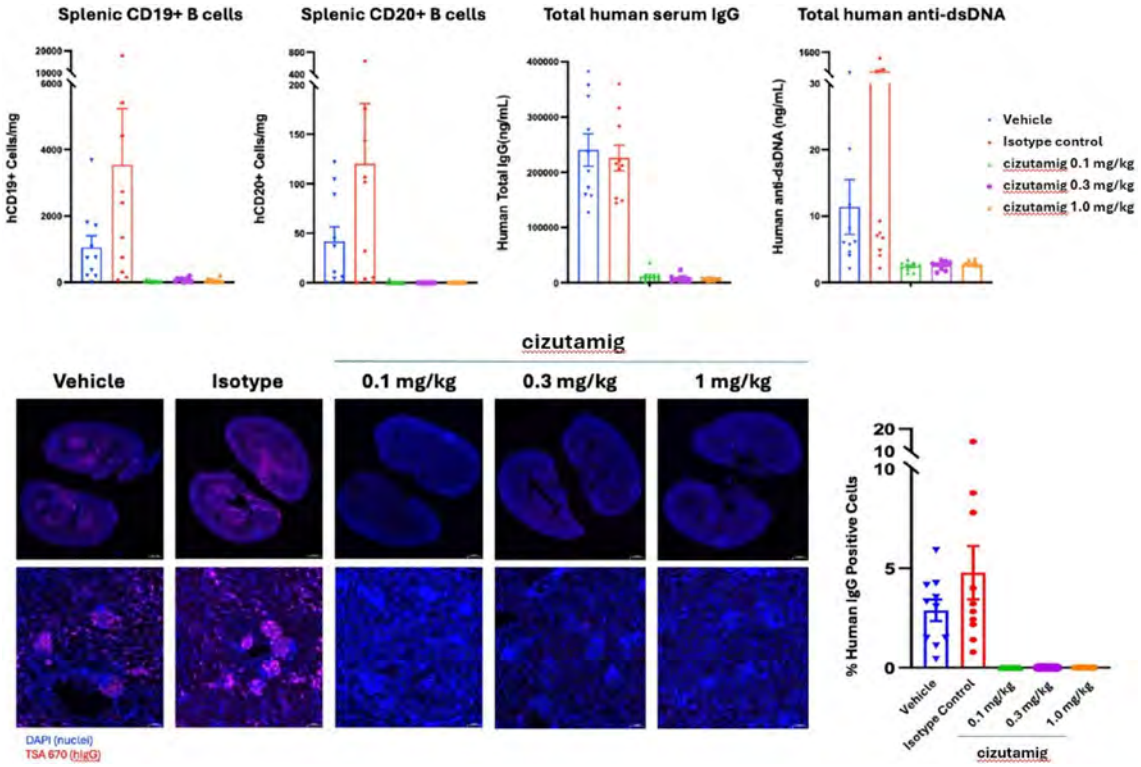


Fig 2. Cizutamig mediated elimination of human splenic B cells, serum IgG, anti-dsDNA, and glomerular immune deposits in SLE patient PBMC humanized mouse model.

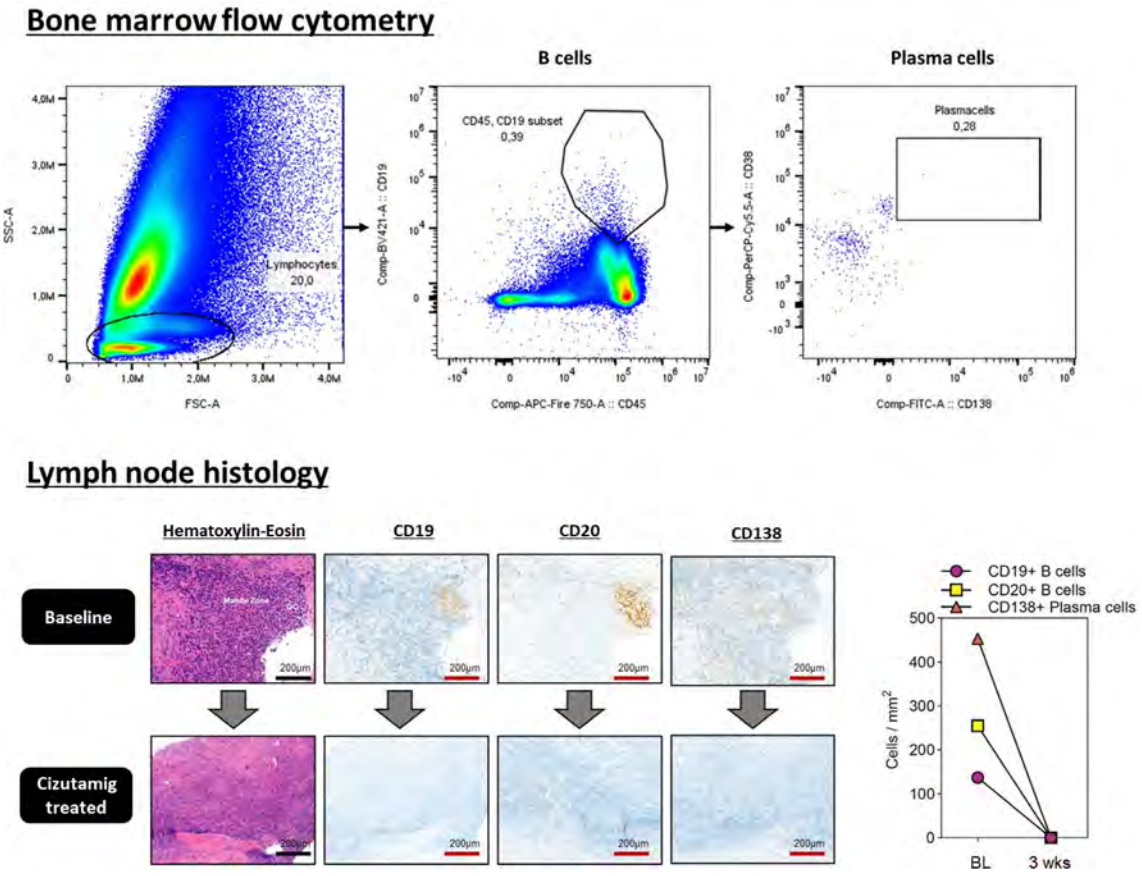


Fig 3. Cizutamig mediated depletion of B cells and plasma cells in the bone marrow and lymph node 3 weeks from start of treatment (BL: baseline, FSC-A: forward scatter area, SSC-A: side scatter area).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

escalation study to assess safety and efficacy was completed in patients with relapsed/refractory multiple myeloma (RRMM) in which cizutamig was administered weekly with step-up dosing. A patient with rheumatoid arthritis (RA) refractory to 5 targeted synthetic and biologic DMARDs including rituximab was the first non-oncology patient treated with weekly doses of cizutamig.

Results: In vitro, cizutamig showed comparable T cell dependent cytotoxicity of BCMA-expressing cell lines with lower cytokine release compared to benchmark BCMA TCEs (Fig 1). In the SLE mouse model, cizutamig showed complete depletion of serum IgG and anti-dsDNA antibodies, splenic B cells, and IgG deposits in the kidneys (Fig 2). In the Phase 1 study, 40 RRMM patients were treated with cizutamig at doses from 0.2 mg to 300 mg. For those who received ≥ 60mg dose, the objective response rate was 66% (12 of 18 patients) with minimal residual disease achieved in 42% of responders. Across all doses, only Grade 1 (18%) or Grade 2 (8%) cytokine release syndrome (CRS) per ASTCT criteria was seen with a median onset time and duration of 1 day (range 1-2) and 3 days (range 1-6), respectively. No immune effector cell-associated neurotoxicity syndrome (ICANS) was observed. In the refractory RA patient, after 3 weeks of treatment, near complete depletion of serum plasma light chains, bone marrow CD138+ plasma cells, and lymph node CD19+ and CD20+ B cells and CD138+ plasma cells were observed (Fig 3). Clinical response was achieved with DAS28 score decreasing from 6.3 to 2.7 units 5 weeks after treatment initiation. No CRS or ICANS was observed.

Conclusion: Cizutamig was designed to mitigate cytokine release while preserving cytotoxicity of BCMA-expressing cells. Preclinical and clinical data demonstrate a differentiated safety profile with signs of clinical activity in RRMM patients and a patient with refractory RA. Further clinical evaluation of cizutamig in autoimmune diseases is being explored.

Disclosure: R. Grieshaber-Bouyer: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6; **J. Haddon**: BigHat Biosciences, 12, 3, Candid Therapeutics, 3, 11; **M. Raimondo**: UCB, 6; **C. Tur**: Sanofi, 2; **S. Böltz**: None; **T. Dashi**: None; **M. Hagen**: None; **A. Wirsching**: None; **T. Rathe**: None; **X. Wu**: EpimAb Biotherapeutics, 3; **P. Wung**: AbbVie/Abbott, 12, 3, 11, Candid Therapeutics, 3, 11, Kyverna, 3; **F. Kim**: Candid Therapeutics, 3, Kyverna Therapeutics, 3; **Y. Zhu**: EpimAb Biotherapeutics, 3, 4; **K. Song**: Candid Therapeutics, 3, 4, 11, Perceptive Capital Solutions Corp, 4, 11; **T. Lu**: Candid Therapeutics, 3, 11; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6.

Abstract Number: 2642

Impact of Rheumatoid Arthritis Therapeutic Classes on Risk of Major Adverse Cardiovascular Events and Venous Thromboembolism: A Population-Based Cohort Study

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization (2639–2644)
Session Type: Abstract Session
Session Time: 9:30AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of major adverse cardiovascular events (MACE) and venous thromboembolism (VTE). Inflammation is a driver of vascular risk, but specific RA therapeutic classes may differentially influence this risk, especially among older patients with additional risk factors. We aimed to evaluate the association between RA medications and advanced therapy (AT) classes and the incidence of MACE and VTE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Adjusted hazard ratios (HR) and 95% confidence intervals for healthcare utilization due to major adverse cardiovascular events (MACE) or venous thromboembolism (VTE) by RA therapeutic class and baseline cardiovascular (CVD) risk.

	High Risk CVD cohort	Low Risk CVD cohort
	N=8,016 (person-years 69,638)	N=2,004 (person-years 20,353)
MACE		
csDMARD prescription (reference)		
No csDMARD/AT prescription	13.3 (11.9, 14.8)	17.2 (12.9, 23.0)
Oral GC prescription	1.54 (1.26, 1.88)	2.05 (1.14, 3.69)
AT prescription	0.63 (0.41, 0.99)	0.36 (0.11, 1.26)
VTE		
csDMARD prescription (reference)		
No csDMARD/AT prescription	25.8 (19.2, 34.8)	23.0 (14.0, 38.1)
Oral GC prescription	3.20 (1.81, 5.65)	3.60 (1.56, 8.32)
AT prescription	2.11 (0.88, 5.03)	0.39 (0.04, 4.10)

csDMARD: conventional synthetic disease modifying antirheumatic drug; AT: advanced therapy; GC: glucocorticoid.

Methods: RA patients were identified from the Ontario Rheumatoid Arthritis Database, a population-based registry derived using a validated algorithm and maintained at ICES. We included patients aged >67 years diagnosed between January 1, 2008, and December 30, 2013, and followed them through to December 30, 2023, with a minimum of 6 months follow-up. The primary outcome was healthcare utilization related to MACE (composite of myocardial infarction, stroke, congestive heart failure, and coronary artery bypass grafting) and/or VTE (deep vein thrombosis or pulmonary embolism), requiring hospital admission, emergency department (ED) visits, or physician encounters. RA therapeutic class was obtained from prescription data (Ontario Drug Benefit) and treated as a time-varying exposures into 4 mutually exclusive groups: (1) No csDMARDs or AT, (2) oral glucocorticoid (GC), (3) csDMARDs only (reference), or (4) b/tsSMARD (AT). The cohort was stratified by CVD risk, with high-risk individuals defined by the presence of established CVD, diabetes mellitus, or hypertension at RA diagnosis. The association between therapeutic class and recurrent healthcare encounters was assessed using the Andersen-Gill, an extension of the Cox model, adjusted for baseline covariates including concomitant csDMARD.

Results: A total of 10,020 RA patients were included and 80% had high CVD risk (n= 8,016). Over a median follow-up of 10.9 (IQR: 5.9-12.7) years, 16,468 MACE and 2,326 VTE events occurred in the high-risk group, compared to 2,965 MACE and 495 VTE events in the low CVD risk cohort. Compared to csDMARDs, there was a significant positive association between no csDMARD/AT (adjusted hazard ratio [aHR]: 13.3; 95% CI: 11.9, 14.8), oral GC (HR: 1.54; 95% CI: 1.26, 1.88), and higher hazard of MACE in the high-risk CVD cohort, while AT was associated with a lower hazard (adj HR: 0.63; 95% CI: 0.41, 0.99) (Table). Similar results were observed for no csDMARD/AT and oral GC in the low-risk CVD cohort. No csDMARD/AT and oral GC prescription were significantly associated with higher hospitalization/ED or physician visits for VTE compared to csDMARDs in both low and high CVD risk cohorts (Table). VTE events were numerically higher for AT users in the high CVD risk cohort, but this was not statistically significant.

Conclusion: In this study, therapeutic choice significantly influenced MACE and VTE outcomes. Compared to csDMARDs, advanced therapies were associated with a lower hazard, while GC and lack of RA treatment were associated with a higher hazard. These findings highlight the importance of integrating cardiovascular and thrombotic risk assessment into RA treatment decisions to optimize both disease and safety outcomes.

Disclosure: M. Movahedi: None; **A. Cesta**: None; **S. Aydin**: AbbVie/Abbott, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6; **P. Akhavan**: AbbVie/Abbott, 1, Fresenius-Kabi, 1, Janssen, 1, Sandoz, 6; **T. Kendzerska**: None; **C. Bombardier**: None; **B. Kuriya**: AbbVie/Abbott, 1, Pfizer, 1, UCB, 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2643

Microbiome Signatures in RA Treatment: Personalizing Methotrexate Therapy

Rahul Bodkhe[1], Kai Trepka[1], Diego Orellana[1], Rebecca Blank[2], Peter Turnbaugh[3], Jose Scher[4] and **Renuka Nayak**[5], [1]University of California San Francisco, San Francisco, CA, [2]NYU Langone Health, New York, NY, [3]University of California, San Francisco, San Francisco, CA, [4]New York University School of Medicine, New York, NY, [5]University of California, San Francisco (UCSF), San Francisco, CA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization (2639–2644)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a common systemic autoimmune disease that targets the joints, causing persistent pain and swelling. Oral methotrexate (MTX) remains first-line therapy and an anchor drug for RA. However, up to 50% of patients do not achieve a clinically adequate outcome, and there is a lack of prognostic tools to predict MTX response. Variations in clinical outcomes may stem from interindividual differences in the gut microbiome. We and others have found differences in the pre-treatment microbiome of MTX responders (MTX-R) and non-responders (MTX-NR). However, whether there are consistent microbiome features associated with response in multiple cohorts remains unknown. Identification of cross-cohort features would enable development of a generalizable predictive model. Here, we investigate the microbiomes of 3 diverse patient cohorts and their associations with MTX response.

Methods: Three metagenomic datasets comprising fecal samples from 86 treatment-naïve RA subjects were analyzed. Two cohorts (Cohort 1, n=32; Cohort 2, n=25) were recruited from rheumatology clinics at New York University and University of California, San Francisco. Data for a third cohort (Cohort 3, n=29) was publicly available from Sequence Read Archive. Participants were new-onset RA patients. MTX response was defined as an improvement of ≥1.8 in the DAS28 at 12 to 16 weeks post-MTX monotherapy. MMUPHin was employed for metagenomic batch correction and data harmonization. Microbiome differences were assessed using PERMANOVA.

Results: After batch correction, when examining all three cohorts, we confirmed that the pretreatment gut microbiome community composition differed between MTX-R and MTX-NR patients. Of 2,386 strains observed, 95 were differentially abundant ($p_{unadj} < 0.05$), with 24 increased and 71 decreased in MTX-NR. Key gut commensal strains were decreased in MTX-NR, including multiple strains from the *Faecalibacterium*, *Clostridium*, and *Bacteroides* genera. Functional profiling of the microbiome identified 8,895 KEGG Orthologs (KOs), of which 252 were associated with response. Intriguingly, we observed decreased abundance of 231 KOs in MTX-NR that are likely direct and indirect targets of MTX, including dihydrofolate reductase (K00287), methylenetetrahydrofolate dehydrogenase (K01491), and genes associated with metabolism of pyrimidines (K01591), purines (K01939), and histidine (K00013) ($p_{unadj} < 0.05$). Of 601 pathways examined, 19 differed by MTX response status. Biosynthesis pathways for L-histidine, L-tyrosine, L-lysine, and inosine-5'-phosphate and the superpathway for pyrimidine salvage were reduced in MTX-NR ($p_{unadj} < 0.05$). Finally, we applied machine learning techniques to the metagenomic data, resulting in a model that predicted response to MTX.

Conclusion: Our study confirms that the pretreatment gut microbiome is associated with response to MTX in new-onset RA across multiple diverse cohorts. We identify multiple taxa, microbial functions, and pathways that are reproducibly associated with clinical response in patients. Development of a robust predictive model will bring us closer to the goal of advancing precision medicine for patients with RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

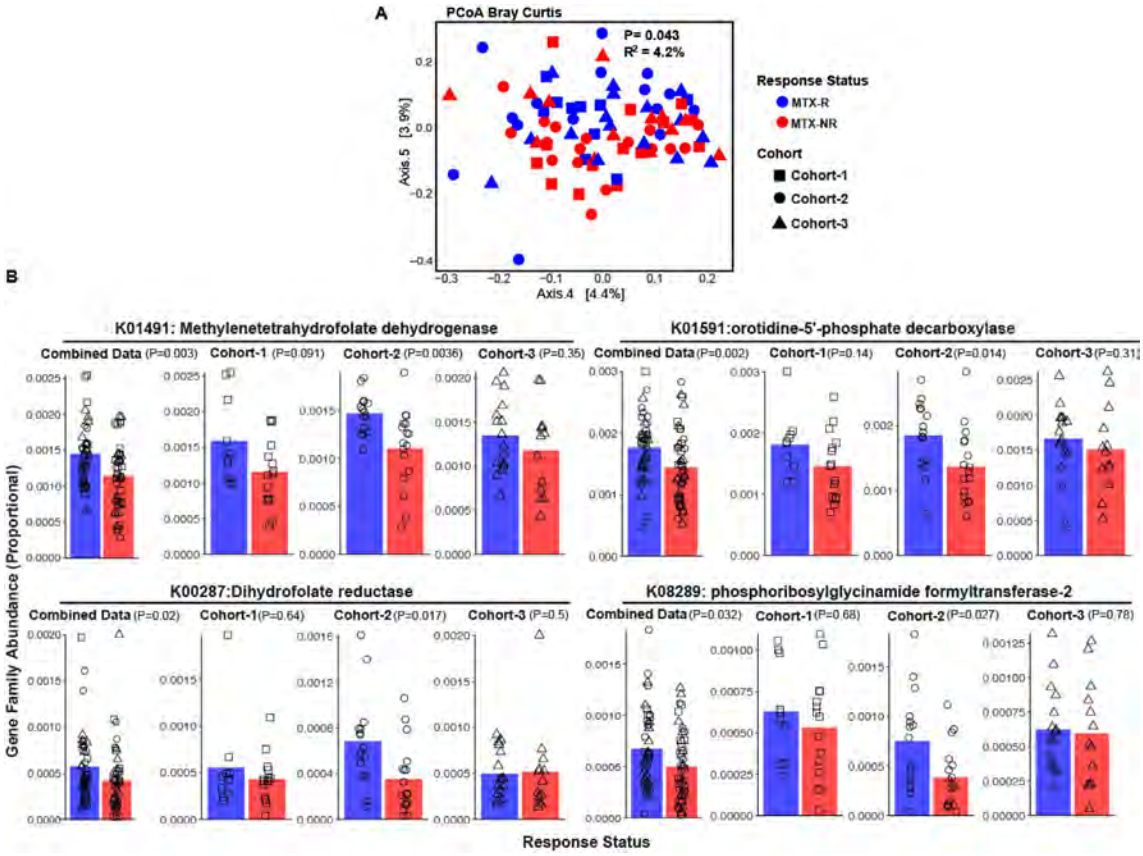


Figure 1. Pretreatment gut microbiome differs between methotrexate responders (MTX-R) and non-responders (MTX-NR) in patients with new-onset rheumatoid arthritis (RA). A. Principal coordinates analysis (PCOA) of pretreatment microbiota composition from MTX-R and MTX-NR groups, based on Bray-Curtis distances (p=0.046, R2 = 0.042). B. Differentially abundant KEGG orthologs that are likely to be direct or indirect targets of MTX identified using a mixed-effects model on combined data and Wilcoxon tests within individual cohorts.

Disclosure: R. Bodkhe: None; **K. Trepka**: None; **D. Orellana**: None; **R. Blank**: None; **P. Turnbaugh**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **R. Nayak**: None.

Abstract Number: 2644

Single Cell RNA-seq Profiling Reveals a Blood Monocyte Phenotype Associated with Response to TNF Inhibitor Therapy in RA Patients

Kathryne Marks[1], Alice Horisberger[2], Ifeoluwakiisi Adejoorin[1], Leah Santacroce[1], Mehreen Elahee[3], Joan Bathon[4], Kevin Wei[5], Daniel Solomon[6] and Deepak Rao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Lausanne University Hospital (CHUV), Lausanne, Switzerland, [3]Brigham and Women's Hospital, Wexford, PA, [4]Columbia University, NEW YORK, NY, [5]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [6]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Treatment II: Phenotyping and Personalization (2639–2644)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: TNF inhibitors (TNFi) are the most common biologic DMARD used to treat RA; however, no robust biomarkers have been established to predict likelihood of a good response to them. We hypothesized that detailed cellular profiling on blood samples from RA patients can identify specific immune cell features in baseline samples that are associated with TNFi treatment response. We assessed blood samples from 97 RA patients from a randomized trial to identify cellular features associated with response to TNFi or triple therapy.

Methods: We utilized PBMCs collected as part of the TARGET trial (Solomon et al., Ann Rheum Dis, 2023), which randomized RA patients with an inadequate response to methotrexate to either TNFi (adalimumab or etanercept; n=51) or triple therapy (sulfasalazine and hydroxychloroquine; n = 47). Patients were 72% female with a median age of 60. Treatment response was determined by DAS28 EULAR response criteria at 24 weeks (66% responders in TNFi arm, 69% responders in triple therapy arm). We performed scRNA-seq on PBMCs from baseline and week 24 followed by unsupervised clustering. Data were analyzed using covarying neighborhood analysis (CNA), mixed effects association of single cell analysis (MASC), Wilcoxon paired tests, and differential gene expression analyses.

Results: To define cellular phenotypes affected by TNFi therapy, we compared baseline and week 24 samples. TNFi induced substantial changes in phenotypes of every major immune cell lineage (Fig1). Our analyses highlighted shifts in phenotypes of classical CD14+ CD16- monocytes comparing baseline and week 24 TNFi samples. These changes were observed in TNFi treated patients and not in the triple therapy group (Fig2A-B). To identify cellular features in baseline samples associated with subsequent response to TNFi, we compared immune profiles of baseline samples from TNFi responders and non-responders. Abundance of a monocyte phenotype which corresponded precisely to the monocytes strongly reduced by TNFi in longitudinal analyses differed significantly between TNFi responders and non-responders (Fig2C). These monocytes express inflammatory factors including IL1b and CCL2 and several chemokines are more highly

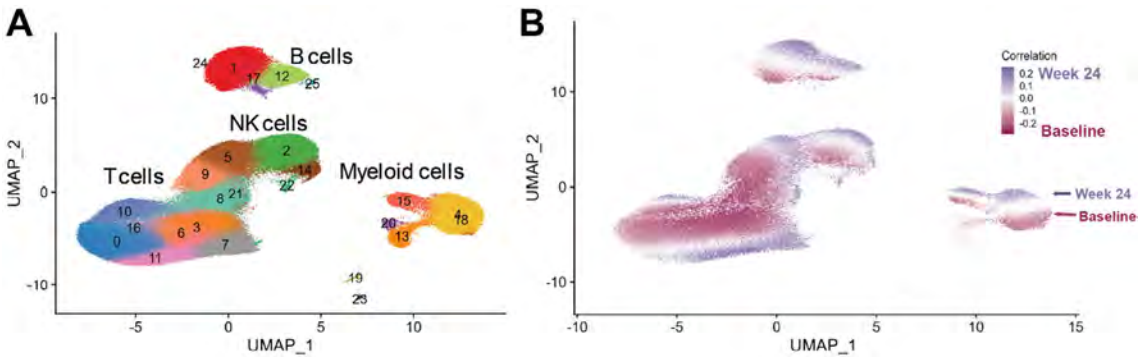


Figure 1. A) scRNAseq of PBMCs from TNFi-treated RA patients, including cells from baseline (pre-treatment) and week 24 post-treatment samples (~355K cells). B) Covarying neighborhood analysis (CNA) showing changes in all major PBMC populations associated with TNFi therapy. p <0.01 and FDR < 0.1 and adjusted for age and sex.

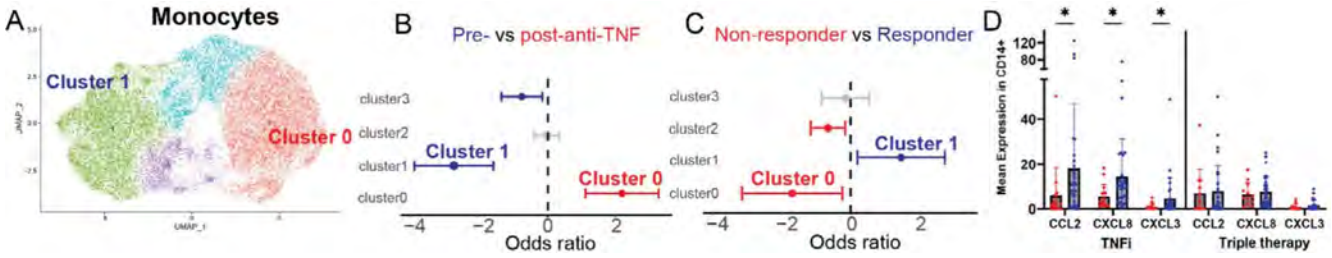


Figure 2. Identification of a monocyte population associated with TNFi treatment response. A) UMAP of monocytes from scRNAseq of TNFi-treated patients in TARGET. B) MASC analysis demonstrating clusters associated with baseline (pre-treatment) or week 24 (post-treatment) samples in the TNFi treated cohort. C) MASC analysis demonstrating clusters in baseline (pre-treatment) samples associated with responders or non-responders to TNFi therapy. D) Mean expression of CCL2, CXCL8 and CXCL3 at baseline in responders and non-responders to TNFi or triple therapy.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

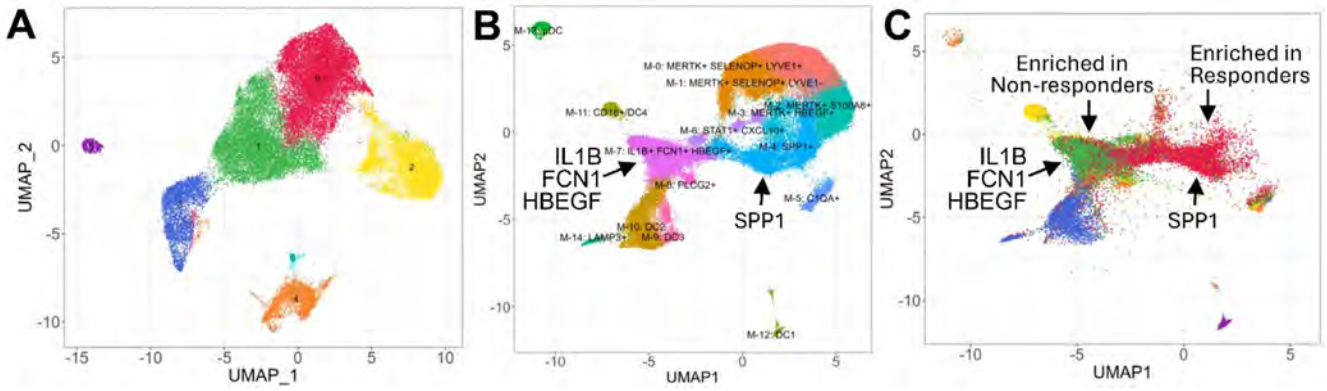


Figure 3. Mapping TNFi treatment-response associated monocytes in blood to RA synovial myeloid populations. A) Myeloid cells from TARGET PBMCs. The red cluster indicates the cluster associated with TNFi response. B) UMAP of RA synovial myeloid cells from synovial tissue generated through AMP (Zhang et al, Nature, 2023). C) Mapping of TARGET myeloid cells to AMP synovial myeloid cells. The colors match the cluster source of each cell shown in A.

expressed in baseline monocytes of TNFi responders as compared to non-responders (Fig2D). Transcriptomic mapping of myeloid cells from this blood scRNA-seq to myeloid cells from RA synovial tissue revealed similarities of the TNFi response-associated monocytes to inflammatory macrophages in RA synovial tissue (Fig3). Analysis of differentially expressed genes encoding surface proteins yielded a candidate list of surface factors, which we validated by flow cytometry. Cytometry quantification of these markers correlated with change in DAS28 in TNFi treated patients and successfully reproduced the discrimination of TNFi responders and non-responders in a subset of TARGET patients (n=18).

Conclusion: Immune profiling of blood from RA patients by scRNA-seq has identified monocytes in blood that are expanded pre-treatment in responders to TNFi. These monocytes can be quantified in blood using a simple cytometry test, which may facilitate translation of a predictive biomarker test to clinical application.

Disclosure: K. Marks: None; **A. Horisberger**: None; **I. Adejoorin**: None; **L. Santacroce**: None; **M. Elahee**: None; **J. Bathon**: AbbVie/Abbott, 2, Merck/MSD, 2, SetPoint, 2; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2.

Abstract Number: 2645

Age-specific Incidence of Systemic Lupus Erythematosus in the United States: A Meta-analysis of Data from the Centers for Disease Control and Prevention Lupus Registries

Peter Izmirly[1], Elizabeth Ferucci[2], Aimee Hersh[3], Mary Beth Son[4], Cristina Drenkard[5], S. Sam Lim[6], Cynthia Crowson[7], Ali Duarte-Garcia[8], Jill Buyon[9], Heather Gold[9], Maria Dall'Era[10], Patti Katz[11], Laura Plantinga[12], Jinoos Yazdany[13], Jennifer Reihm[14], Emily Somers[15] and Hilary Parton[16], [1]New York University Grossman School of Medicine, New York, NY, [2]Alaska Native Tribal Health Consortium, Anchorage, AK, [3]University of Utah, Salt Lake City, UT, [4]Boston Children's Hospital, Boston, MA, [5]Rollins School of Public Health, Emory University, Atlanta, Georgia, USA, Acworth, GA, [6]Emory University School of Medicine, Atlanta, GA, [7]Mayo Clinic, Stewartvillle, MN, [8]Mayo Clinic, Rochester, MN, [9]NYU Grossman School of Medicine, New York, NY, [10]Division of Rheumatology, University of California, San Francisco, CA, [11]UCSF, San Rafael, CA, [12]University of California, San Francisco, San Francisco, CA, [13]UCSF, San Francisco, CA, [14]University of California, San Francisco, San Francisco, [15]University of Michigan, Ann Arbor, MI, [16]New York City Department of Health and Mental Hygiene, New York

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III (2645–2650)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Current estimates for age of SLE onset are limited, particularly for males and racial/ethnic groups in the United States. Leveraging five Centers for Disease Control and Prevention population-based SLE surveillance registries, which were developed to provide epidemiologic data for SLE across diverse regions of the US, we performed meta-analyses to estimate the age-specific incidence of SLE, overall and by sex and race/ethnicity.

Methods: The registries in Georgia, California, New York and the Indian Health Service (IHS) used the 1997 revised ACR classification criteria while the registry in Minnesota used the EULAR/ACR classification criteria for SLE as their primary case definitions. The surveillance periods ranged from 2002 to 2018. Age-specific incidence of SLE stratified by sex and race/ethnicity was obtained from each registry. Given the small number of registries and near-complete case ascertainment from each site, we performed a fixed-effects meta-analysis to estimate the pooled incidence using inverse-variance weighting, stratified by sex and race/ethnicity (females only due to small sample sizes for males), across the four state sites. Given the IHS registry focused solely on the American Indian/Alaska Native (AI/AN) population, their data was included separately in the female racial/ethnic estimates and not as part of the pooled estimates. To examine age-specific patterns of diagnoses, we then estimated the percentage of all SLE patients diagnosed among each age group, 0-19, 20-29, 30-39, 40-49, 50-59, 60-69, ≥70 years, from all the registries, weighted by the number of person-years contributed by the five sites.

Results: The registries contributed 939 incident classified cases of SLE from a mix of urban and rural areas. The fixed-effects model yielded overall incidence rates of 9.6 (95%CI: 8.9-10.3) and 1.7 (95%CI: 1.4-2.0) per 100,000 person-years among females and males, respectively, Figure 1. Incidence rates among females were highest for those aged 30-39 (13.8, 95%CI: 12.0-16.0), while rates among males were highest for those aged 60-69 (3.1, 95%CI: 1.9-5.0). Black females aged 20-39 and 40-59 had the highest SLE incidence rates (24.2, 95%CI: 20.5-28.6) and (24.3, 95% CI: 20.3-29.3), Figure 2. Among females diagnosed with SLE before age 20, incidence was highest among Asian (7.2, 95%CI: 3.8-13.5) and Black (6.4, 95%CI: 4.5-9.1) individuals. Among females diagnosed with SLE after age 60, incidence was highest among Black (13.8, 95%CI: 9.5-20.0) and AI/AN (9.4, 95%CI: 3.4-15.4) individuals. Weighted percentages (Table 1) show that 7.8% of those with SLE were diagnosed before age 20, while 17.9% were diagnosed after age 60. The largest proportion of individuals with SLE, 22.2%, were diagnosed between 30 and 39 years.

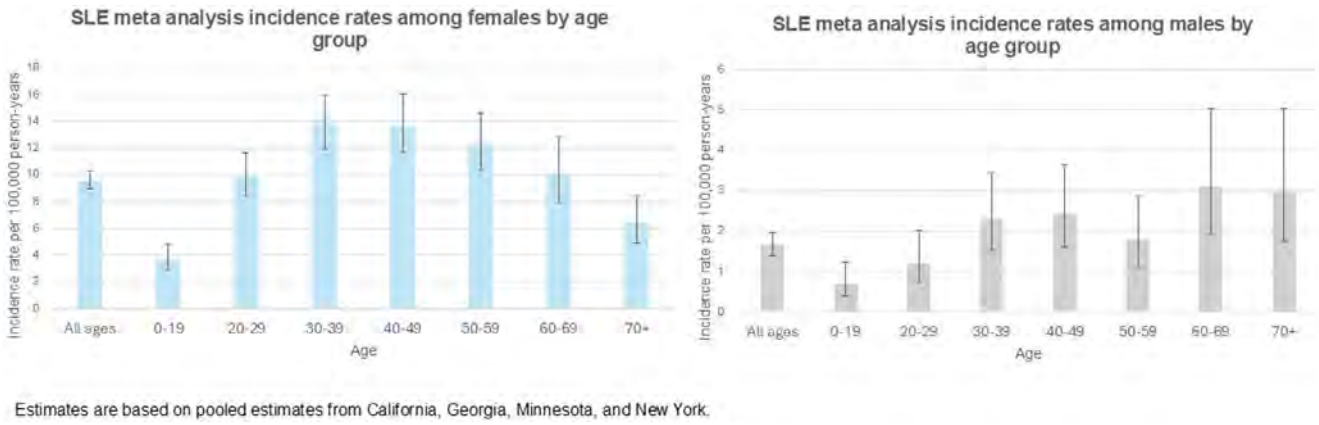


Figure 1. SLE meta analysis incidence rates among females and males by age group.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

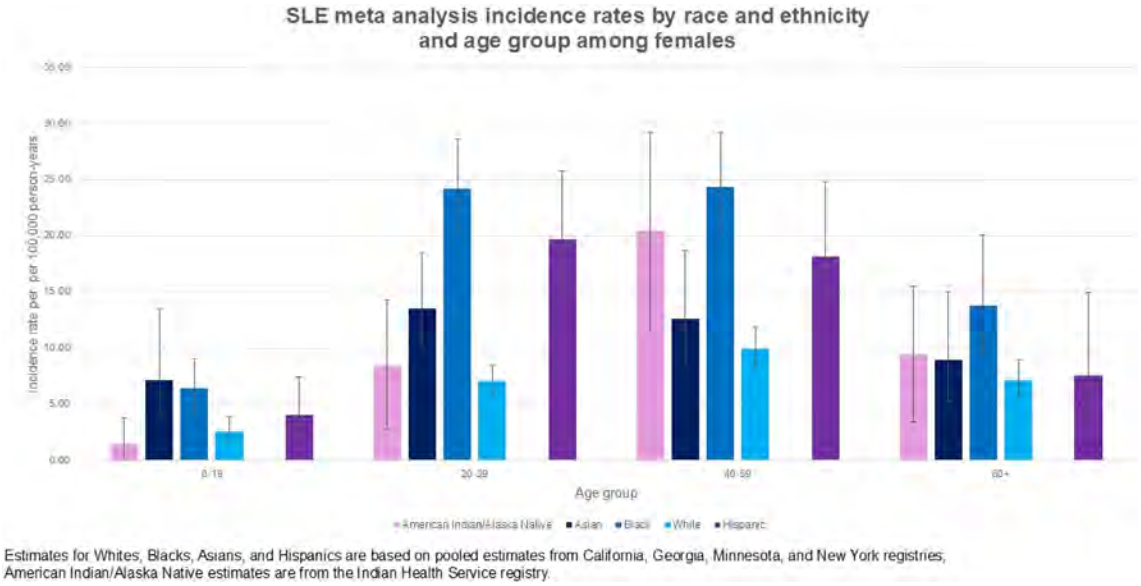


Figure 2. SLE meta-analysis incidence rates by race and ethnicity and age group among females.

Age range	Weighted Average by Person-Years (%)
0-19 years	7.8
20-29 years	17.7
30-39 years	22.2
40-49 years	19.9
50-59 years	16.0
60-69 years	9.7
≥70 years	8.3

Age-Specific Patterns of Diagnoses

Conclusion: In this coordinated network of population-based SLE registries, age-specific incidence rates were obtained, and data were provided on males and previously understudied age groups. While female incidence rates were highest during the reproductive years, the incidence rates for males increased with age with the highest rates at ages 60-69. Overall, 18% of patients with SLE were diagnosed after age 60 and nearly 8% before age 20.

Disclosure: P. Izmirly: Hansoh Bio, 2; **E. Ferucci**: None; **A. Hersh**: None; **M. Son**: None; **C. Drenkard**: None; **S. Lim**: Accordant, 2, AstraZeneca, 2, Biogen, 5, BMS, 5, Genentech, 2, Gilead, 5, GSK, 2, Novartis, 5, UCB, 5; **C. Crowson**: None; **A. Duarte-Garcia**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **H. Gold**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **P. Katz**: None; **L. Plantinga**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **J. Reihm**: None; **E. Somers**: None; **H. Parton**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2646

DNA methylation-based clustering reveals clinically distinct subtypes of systemic lupus erythematosus

Meghan Nelson[1], Mary Horton[2], Joanne Nititham[2], Jinoos Yazdany[3], Maria Dall'Era[4], Cristina Lanata[5] and Lindsey Criswell[2], [1]NIH/NIAMS/NHGRI, Bethesda, MD, [2]NIH/NHGRI, Bethesda, MD, [3]UCSF, San Francisco, CA, [4]Division of Rheumatology, University of California, San Francisco, CA, [5]NIH/NHGRI, Bethesda

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III (2645–2650)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disease with significant variability in clinical presentation. DNA methylation has been associated with lupus risk and heterogeneity. In order to identify biologically relevant molecular subtypes, we leveraged genome-wide methylation profiles to cluster patients and evaluate associations between methylation-based clusters and SLE clinical characteristics.

Methods: We analyzed methylation profiles from 1,882 multi-ancestry SLE patients. Clinical data was collected at enrollment and time of peripheral blood collection. Genome-wide methylation profiles were generated using Illumina's EPICv2 BeadChip (n= 937,690 CpG sites). Normalization and quality control were performed using *minfi*. CpGs with high detection p-values and cross-reactive probes were excluded, and missing methylation values imputed using methyLImp2. We selected the top 5% most variable CpGs (~60,000) by beta value standard deviation and performed unsupervised k-means clustering using *ConsensusClusterPlus* across multiple CpG sets (n = 5,000; 10,000; 25,000; 60,000 CpGs). The most distinct clustering was observed with 60,000 CpGs and k=4. Differentially methylated positions (DMPs) by cluster

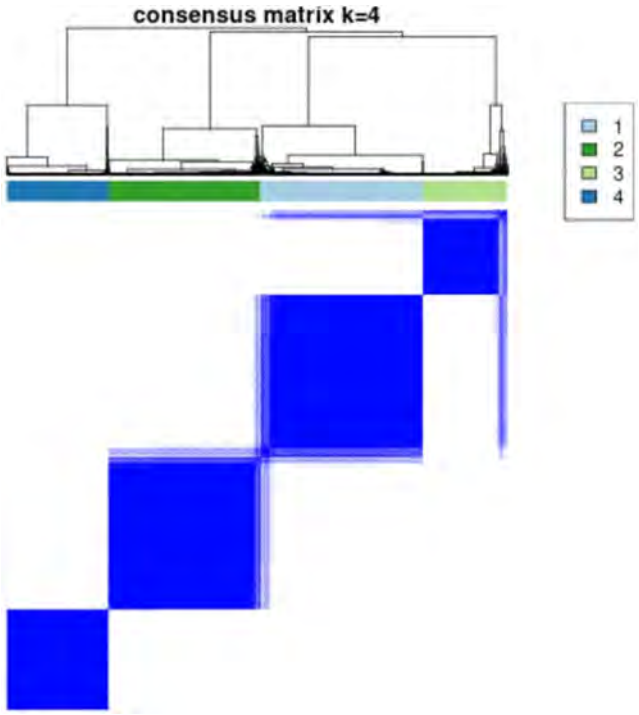
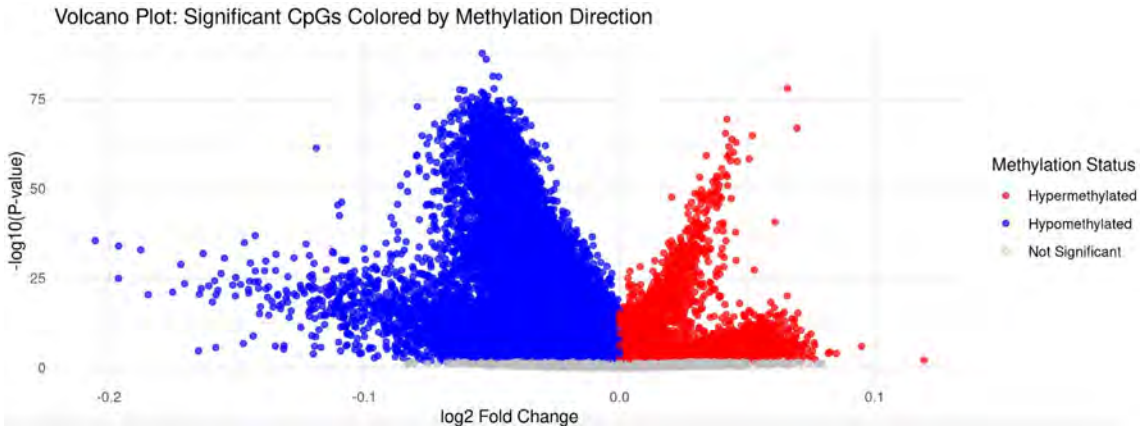


Figure 1. Consensus Plot (k=4) of Patient Clusters based off methylation beta values.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



were identified using *limma*, with beta values used for coefficient interpretation and M values to determine statistical significance. Models adjusted for genetic principal components, Houseman estimated blood cell proportions, batch, age, disease duration, sex. DMPs with FDR q< 0.05 were considered statistically significant.

Results: We identified 4 distinct clusters based on methylation beta values (Figure 1). Clusters 1 and 2 reflected milder disease with discoid rash (p=0.002); Cluster 3 exhibited older age at enrollment (p=0.001); Cluster 4 was associated with more severe disease as reflected by younger age of diagnosis (p=0.006), serositis (p< 0.001), nephritis (p< 0.001), higher proportion of males (p=0.006) and hematologic abnormalities (p< 0.001). 2,569 CpGs with FDR q< 0.05 were identified across all cross-comparisons between clusters (Figure 2). Significant CpGs annotated to *ZFP36L1* (an RNA-binding protein that plays a role in post-transcriptional gene regulation), *DOCK9* (involved in intracellular signaling networks), and *NEK8* (protein kinase involved in cell cycle regulation, DNA damage response, and mitosis). Of the significant CpG sites, the absolute change in methylation between clusters ranged from -4.6% to 3.8 %. A majority of these were hypomethylated; 267 were located within genes, and 322 were in promoter regions. Gene set enrichment analysis (GSEA) revealed cluster-specific enrichment: Cluster 1 in leukocyte cell adhesion (FDR q=0.025) and leucocyte activation involved in immune response (FDR q=0.025); Cluster 2 in positive regulation of *MAPK* (FDR q=0.0003); Cluster 3 in neutrophil degranulation (FDR q=0.001); and Cluster 4 in pattern specification (FDR q=1e-5) and cell adhesion (FDR q=1e-5).

Conclusion: We identified 2,569 differentially methylated CpGs across 4 distinct SLE clusters. These results support the potential of DNA methylation profiling to reveal molecular subtypes of SLE and improve risk stratification.

Disclosure: M. Nelson: None; **M. Horton**: None; **J. Nititham**: None; **J. Yazdany**: AstraZeneca, 2, 5, Aurinia, 5, BMS Foundation, 5, 12, BMS Foundation, Gilead, 5, Pfizer, 2, UCB, 2; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **C. Lanata**: None; **L. Criswell**: None.

Abstract Number: 2647

Unlinked Paths to SLE: Divergent Associations of DNA Methylation and Polygenic Risk Scores with SLE Features

Holme Vestin[1], Nina Oparina[1], Elisabeth Skoglund[1], Maija-Leena Eloranta[1], Martina Frodlund[2], Iva Gunnarsson[3], Chrisopher Sjöwall[2], Elisabet Svenungsson[4], Lars Rönnblom[1], Juliana Imgenberg-Kreuz[1] and **Dag Leonard**[1], [1]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [2]Department of Biomedical and Clinical Sciences, Division of Inflammation and Infection/Rheumatology, Linköping University, Linköping, Sweden, [3]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, [4]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III (2645–2650)
Session Type: Abstract Session
Session Time: 9:30AM–11:00AM

Background/Purpose: The aetiopathogenesis of SLE encompasses genetic and epigenetic factors, including hypomethylation of type I interferon (IFN) regulated genes (1) and the HLA-DRB1*03:01 haplotype, linked to *C4A* copy numbers and associated with anti-SSA/SSB antibodies (2). Further, a non-HLA SLE polygenic risk score (SLE-PRS) has been linked to a more severe disease (3). This study aimed to investigate the relationship between a methylation-based SLE risk score (MRS), an SLE-PRS, an HLA-DRB1*03:01 tag SNP, serum IFN-α levels and clinical phenotype.

Methods: DNA methylation levels in whole blood from patients fulfilling ≥4 ACR-82 criteria (n=547) and controls matched for age and sex (n=587) were investigated by the Illumina HM450K methylation array. Significant differentially methylated CpGs with a $\Delta\beta$ of ≥0.1 between cases and controls and located at independent genetic loci (n=17) were selected for calculation of the MRS. Clinical data were collected from patient charts. Serum IFN-α2 levels were measured in a subgroup of patients (n=85) using Simoa.

We analysed if the MRS was associated with the SLE-PRS including 57 non-HLA SLE risk loci (3), with the HLA-DRB1*03:01 tag SNP rs1269852 and with levels of IFN-α using linear regression models. Associations between the MRS, SLE-PRS and HLA-DRB1*03:01 tag SNP and clinical variables were assessed applying logistic regression. Models were adjusted for age and sex, $p< 0.05$ was considered significant.

Results: The MRS was associated with high disease activity (SLEDAI >4 or SLAM >6) (OR=1.01, $p=2.0\times10^{-4}$), higher IFNα levels (Exp(B)=1.03, $p=8.1x10^{-13}$) and low complement (OR=1.01, $p=2.2\times10^{-3}$), while the SLE-PRS was not (all $p >0.05$). Further, no significant correlation between the MRS and the SLE-PRS was observed ($p >0.05$).

The MRS was associated with discoid rash (OR=1.02, $p=3.5x10^{-4}$), hematologic criteria (OR=1.02, $1.6x10^{-7}$) and immunologic criteria (OR=1.01, $p=1.4x10^{-4}$), while the SLE-PRS was associated with the nephritis (OR=1.19, p=0.04) and the immunologic criteria (OR=1.40, $p=1.1x10^{-4}$). Further, the MRS, but not the SLE-PRS, associated with anti-SSA and anti-RNP antibodies (OR=1.03, $p=1.1x10^{-12}$ and OR=1.02, $p=8.2x10^{-11}$).

The HLA-DRB1*03:01 tag SNP was significantly associated with higher MRS (B=7.22, $p=8.6x10^{-4}$) and with anti-SSA and anti-SSB antibodies (OR 3.09 and 4.75, both $p< 1x10^{-10}$).

Conclusion: The lack of correlation between the MRS and SLE-PRS suggests that they reflect distinct, yet complementary, aspects of SLE pathogenesis. The association between the MRS, high disease activity, higher levels of IFN-α2 in serum, anti-SSA antibodies and the HLA-DRB1*03:01 tag SNP implies that an epigenetic predisposition for IFN-α signalling might be of particular importance in HLA-DRB1*03:01 positive patients. These results underscore the relevance of integrating epigenetic profiling with genetic data to better understand disease heterogeneity and mechanisms in SLE.

References

1. Araki Y, et al. Int J Mol Sci. 2024
2. Lundtoft C, et al. Arthritis Rheumatol. 2022
3. Reid S, et al. Ann Rheum Dis. 2020

Disclosure: H. Vestin: None; **N. Oparina**: None; **E. Skoglund**: None; **M. Eloranta**: None; **M. Frodlund**: None; **I. Gunnarsson**: None; **C. Sjöwall**: Bristol-Myers Squibb(BMS), 3; **E. Svenungsson**: AstraZeneca, 11, Pfizer, 11; **L. Rönnblom**: AstraZeneca, 6, Biogen, 2; **J. Imgenberg-Kreuz**: None; **D. Leonard**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2648

Transcriptome analysis of quiescent SLE cases uncovers dysregulated pathways associated with disease flares

Lorenzo Beretta[1], Guillermo Barturen[2], Torsten Witte[3], Ignasi Rodriguez-Pinto[4], Ricard Cervera[5], Rafaela Ortega-Castro[6], Falk Hiepe[7], László Kovacs[8], Bohacsi Virag[8], Raquel Faria[9], Dionysis Nikolopoulos[10], Barbara Vigone[11], Marta Alarcon-Riquelme[12] and Ioannis Parodis[13], [1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Milan, Italy, [2]Center for Genomics and Oncological Research (GENYO), Andalusia, Spain, [3]Dept of Rheumatology and Immunology, Hannover, Niedersachsen, Germany, [4]HospitalClínic, Institut d'Investigacions Biomediques August Pi i Sunye, Department of Autoimmune Diseases, Barcelona, Spain, [5]Hospital Clinic Barcelona, Barcelona, Spain, [6]Rheumatology service/Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ Reina Sofia University Hospital/ University of Cordoba, Spain, Cordoba, Andalucia, Spain, [7]Charité - Universitätsmedizin Berlin, Berlin, Germany, [8]University of Szeged, Department of Rheumatology and Immunology, Faculty of Medicine, Szeged, Hungary, [9]UIC, Porto, Portugal, [10]Karolinska Institutet and Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [11]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Referral Center for Systemic Autoimmune Diseases, Milano, Italy, [12]Fundación Progreso y Salud, Andalusian Government, Granada, Spain, [13]Karolinska Institutet and Karolinska University Hospital, Department of Medicine Solna, Division of Rheumatology, Stockholm, Sweden

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III (2645–2650)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Unpredictability is a major challenge in systemic lupus erythematosus (SLE). Routinely used clinical and laboratory parameters fail to predict the risk of and time to flare. We hypothesise that gene signatures may better predict flaring and might thus have merit in disease monitoring.

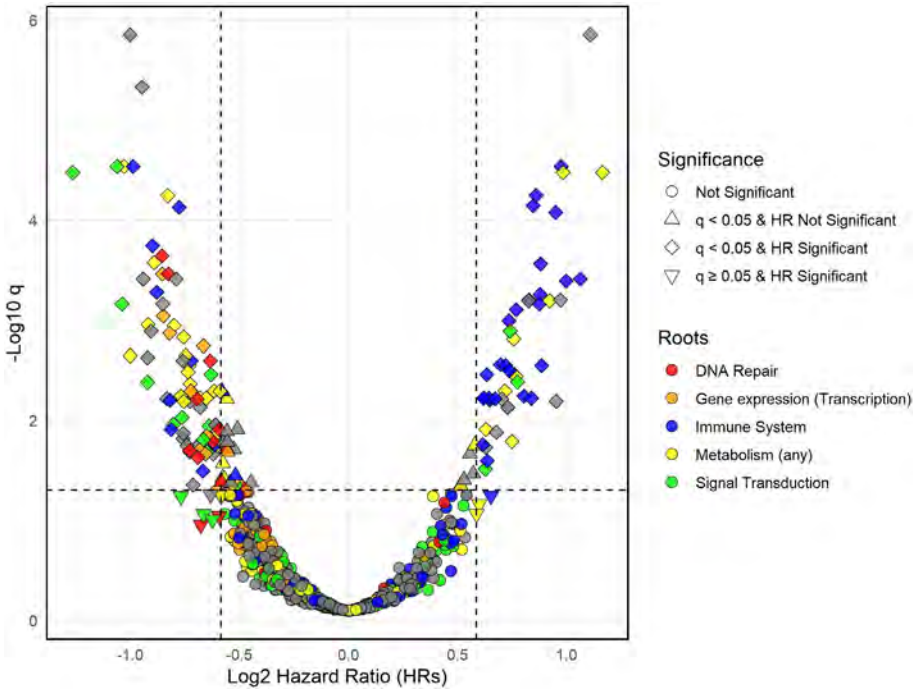
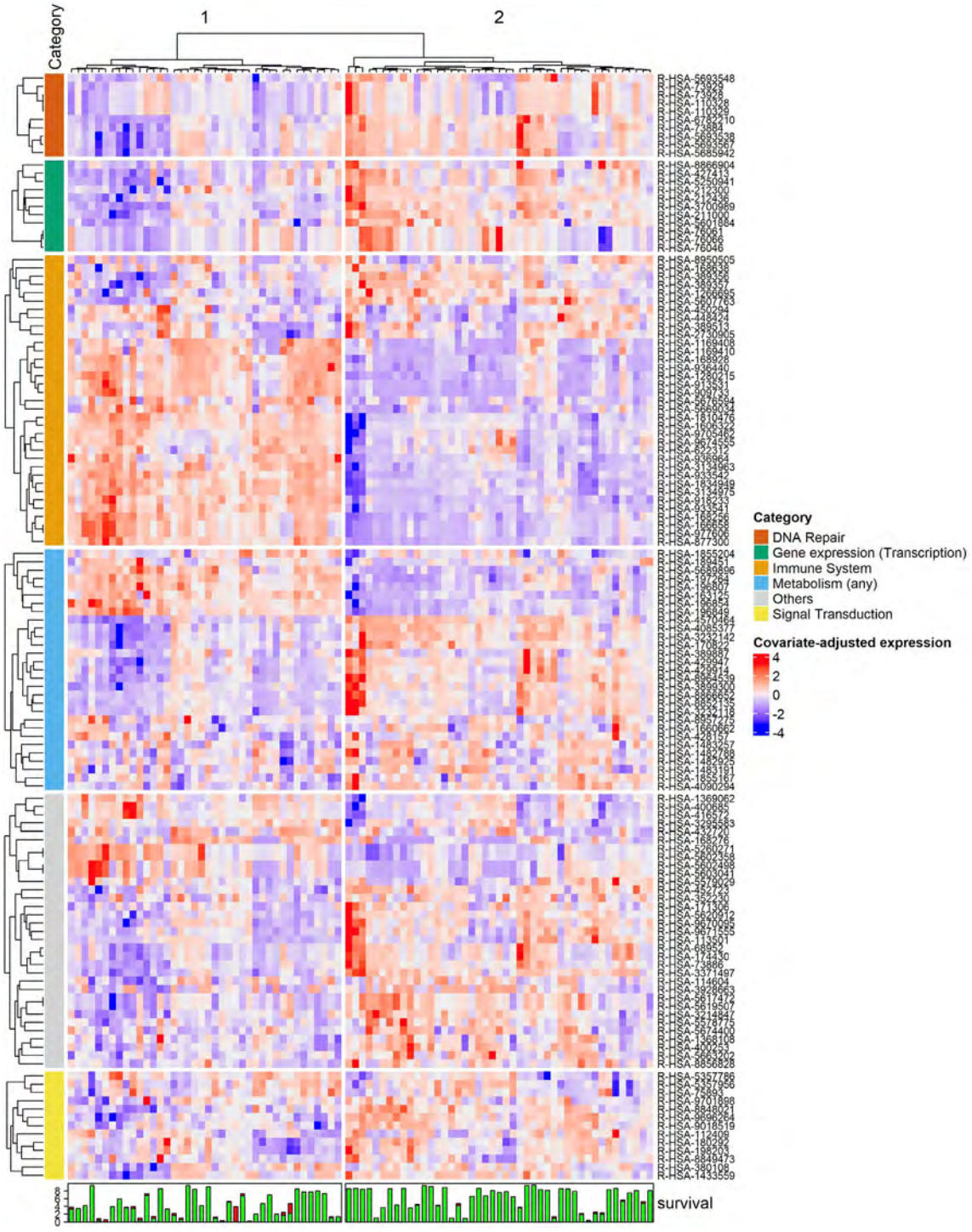


Figure 1

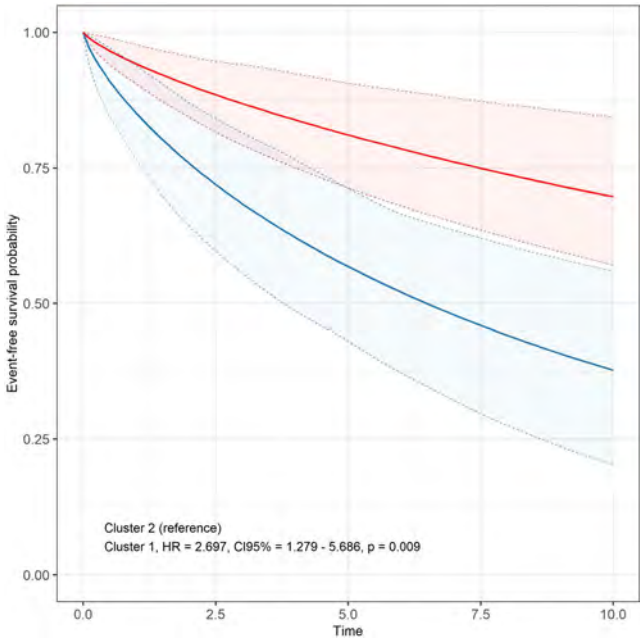
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Heatmap

Methods: Eligible for this analysis were SLE patients from the European multicenter PRECISESADS project (NCT02890121) with available transcriptome data and long-term follow-up including disease flares. The analysis was restricted to patients with quiescent disease at baseline, defined as a clinical SLEDAI-2K score < 6. Flare was defined as any increase in disease activity resulting in a change of therapy. For each patient Reactome pathways according to the Functional Analysis of Individual Microarray Expression (FAIME) algorithm, were calculated. Time-dependent analysis for interval censored data was conducted with parametric models correcting for relevant confounding covariates associated with flares and individual regression weights. Q value < 0.05 and a hazard ratio (HR) >1.5 for causative pathways or < 0.667 for protective ones were considered significant.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Survival Clusters

Results: Long-term data were available in 131 patients, including 85 with quiescent disease at baseline. At the time of blood sampling, those patients had a mean (SD) age of 47.5 (13.9) years and a mean disease duration of 15.7 (9.7) years, and they were mostly women (n=84, 98.8%). The mean clinical SLEDAI-2K was 1.5 (1.5). At baseline, 59 (69.4%) patients were treated with hydroxychloroquine, 25 (29%) with synthetic immunosuppressants, and 36 (42.3%) with glucocorticoids at a mean daily dose of 2.3 (0.5) mg of prednisone equivalent. After a mean observation time of 6.9 (2.6) years, flares occurred in 30 patients (35%).

Among those 30 patients, the first flare was developed after a mean time of 3.0 (2.0) years, and the non-cumulative count of those flares per domain was 18 articular, 9 cutaneous, 5 constitutional, 4 haematological, 3 vascular, and 2 renal.

Overall, 1265 Reactome pathways were explored, of those 83 and 48 pathways were significantly associated with increased or reduced flaring hazards, respectively (Figure 1).

Flaring patients had a reduced capability of DNA repair, increased DNA damage due to impaired telomere function, an increased activity interferon-related pathways, an increased activity of the complement system, an increased inflammasome, reduced CTLA4 and CD28 inhibitory mechanisms, a disrupted circadian clock and several metabolic alterations.

Conclusion: Our findings reveal that specific pathway deregulations linked to SLE pathogenesis may herald the occurrence of flares in quiescent patients. Impaired DNA repair, increased interferon signaling, complement activation, inflammasome upregulation, and reduced CTLA4/CD28 inhibitory mechanisms suggest a predisposition to immune dysregulation preceding clinical flares. These insights highlight potential molecular predictors of flaring and suggest that targeted immunomodulation or specific interventions may be warranted in selected patients to prevent flares and mitigate the risk of long-term damage accrual, ultimately improving disease monitoring strategies in SLE.

Disclosure: L. Beretta: None; **G. Barturen**: None; **T. Witte**: None; **I. Rodriguez-Pinto**: None; **R. Cervera**: None; **R. Ortega-Castro**: None; **F. Hiepe**: None; **L. Kovacs**: None; **B. Virag**: None; **R. Faria**: None; **D. Nikolopoulos**: None; **B. Vigone**: None; **M. Alarcon-Riquelme**: None; **I. Parodis**: Amgen, 5, 6, AstraZeneca, 5, 6, Aurinia, 5, BMS, 5, Eli Lilly, 5, F. Hoffman-La Roche Ltd, 5, 6, Gilead, 6, GSK, 5, 6, Janssen, 6, Novartis, 6, Otsuka, 5, 6, UCB, 2, 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2649

Simultaneous Assessment of Complementary Lupus-Specific Immune Mediator-Informed Indexes Improves Their Ability to Concurrently Discern Current Disease Activity And Future Flare Risk In Systemic Lupus Erythematosus

Melissa Munroe[1], Derek Blankenship[2], Daniele DeFreese[2], Adrian Holloway[2], Bernard Rubin[2], Mohan Purushothaman[2], Wade DeJager[3], Susan Macwana[4], Joel Guthridge[4], Stan Kamp[4], Nancy Redinger[4], Teresa Aberle[4], Eliza Chakravarty[4], Cristina Arriens[4], Yangfen Li[5], Hu Zeng[5], Stephanie Dezzutti[6], Peter Izmirly[7], Uma Thanarajasingam[5], Diane Kamen[8], Jill Buyon[9], Judith James[4] and Eldon Jupe[2], [1]Oklahoma Medical Research Foundation; Progentec Diagnostics, Inc., Oklahoma City, OK, [2]Progentec Diagnostics, Inc., Oklahoma City, OK, [3]Oklahoma Medical Research Foundation, Oklahoma City, [4]Oklahoma Medical Research Foundation, Oklahoma City, OK, [5]Mayo Clinic, Rochester, MN, [6]Medical University of South Carolina, Charleston, SC, [7]New York University Grossman School of Medicine, New York, NY, [8]Medical University of South Carolina, Johns Island, SC, [9]NYU Grossman School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III (2645–2650)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Immune dysregulation propels systemic lupus erythematosus (SLE) pathogenesis. Capturing it as lab-based screening tests could help prioritize SLE patients for early intervention and proactive disease management. This study ascertained the usefulness of simultaneous Lupus Flare Risk Index (L-FRI) and Lupus Disease Activity Index (L-DAI) assessment to determine parallel risk of *future* clinical disease flare and *concurrent* disease activity.

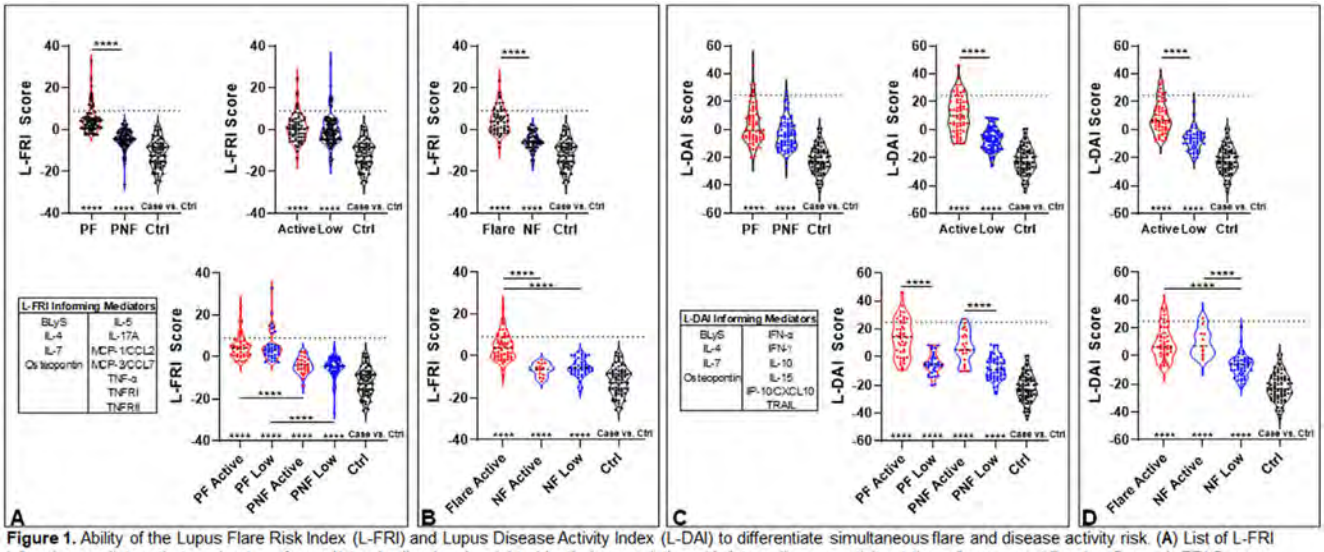


Figure 1. Ability of the Lupus Flare Risk Index (L-FRI) and Lupus Disease Activity Index (L-DAI) to differentiate simultaneous flare and disease activity risk. (**A**) List of L-FRI informing mediators that are log-transformed/standardized and weighted by their association with future disease activity at time of concurrent flare/nonflare + L-FRI Scores comparing Pre-flare (PF) vs. Pre-Nonflare (PNF), Active (hSLEDAI ≥ 4) vs Low (hSLEDAI < 4) disease activity, and comparisons of flare/disease activity risk status, each vs. healthy controls (Ctrl). (**B**) L-FRI scores comparing concurrent SFI-defined Flare vs. Nonflare (NF), and comparisons of flare/disease activity status, each vs. Ctrls. **A-B**. Visits above the dashed line are in the "high" risk category and are enriched for severe pre-flare/flare status. (**C**) List of L-DAI informing mediators that are log-transformed/standardized and compositely weighted by their association with concurrent disease activity and SLE-associated autoantibody specificities + L-DAI Scores comparing PF vs. PNF, Active vs Low disease activity, and comparisons of flare/disease activity risk status, each vs. Ctrl. (**D**) L-DAI scores comparing Active vs. Low disease activity at time of concurrent SFI-defined Flare/NF, and comparisons of flare/disease activity status, each vs. Ctrl. **C-D**. Visits above the dashed line are in the "high" risk category and are enriched for active disease with renal features. ****p<0.0001 Kruskal-Wallis test with Dunn's multiple comparison. Graphs = mean ± SEM.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

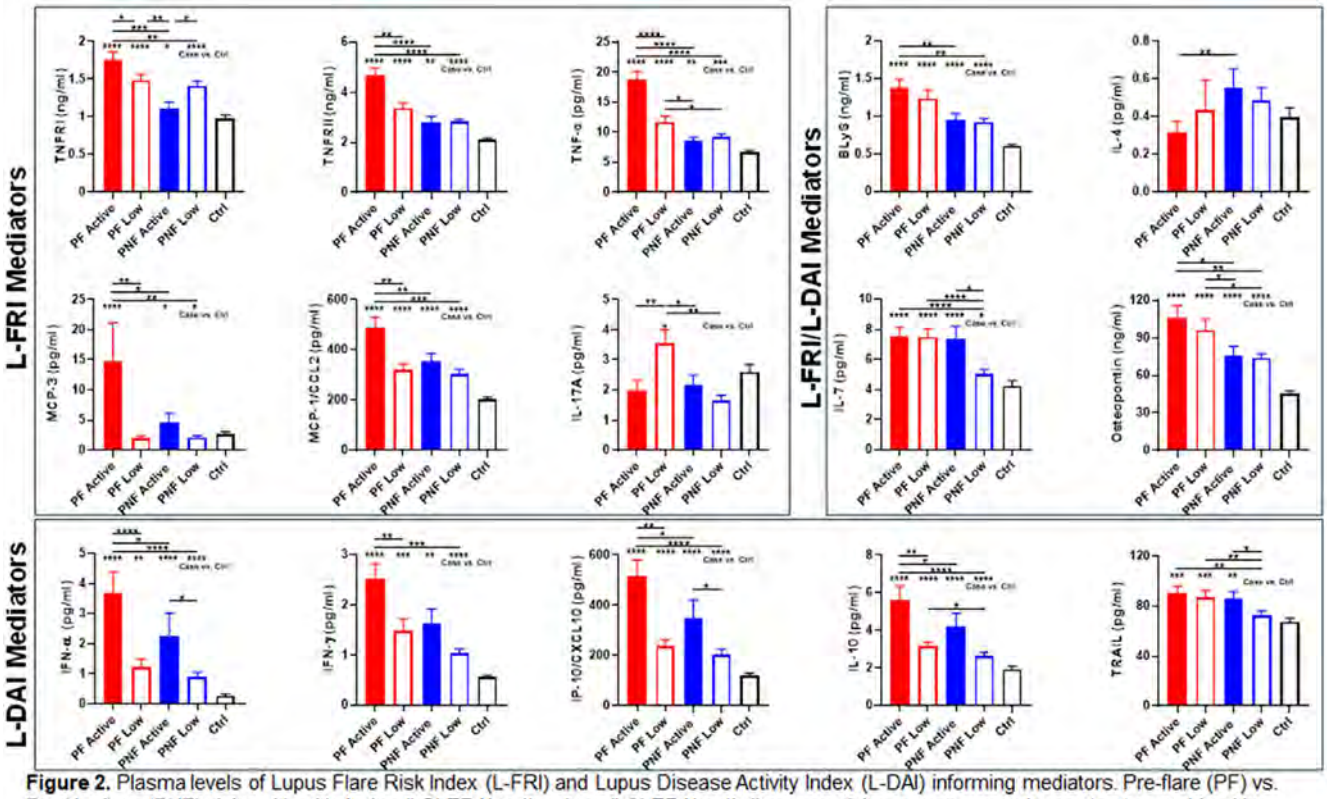


Figure 2. Plasma levels of Lupus Flare Risk Index (L-FRI) and Lupus Disease Activity Index (L-DAI) informing mediators. Pre-flare (PF) vs. Pre-Nonflare (PNF) visits with with Active (hSLEDAI ≥ 4) or Low (hSLEDAI < 4) disease activity were compared to each other and healthy controls (Ctrl). *$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$ Kruskal-Wallis test with Dunn's multiple comparison. Graphs = mean ± SEM.

Methods: L-FRI and L-DAI scores were calculated from 11 and 10 informing plasma mediators, respectively (**Fig. 1**) in 86 preflare (PF) vs. 87 prenonflare (PNF) visits, and 60 flare vs. 62 nonflare (NF) follow-up visits with available samples from a unique cohort of prospectively followed SLE patients. The algorithms reflect the sum of log-transformed/standardized informing immune mediators, weighted by their association with either ensuing disease activity at the time of *future* flare/NF (L-FRI) or a composite of *current* disease activity and SLE-associated autoantibody specificities (L-DAI). Hybrid SLEDAI (hSLEDAI) scores, clinical features, medication usage, and the presence of autoantibody specificities to dsDNA, chromatin, Ro/SSA, La/SSB, Sm, SmRNP, and RNP were also determined.

Results: Forty-three of 86 (50%) PF vs. 26 of 87 (30%) PNF visits were associated with active disease (hSLEDAI≥4; *p=0.0084*). The 43 PF and 61 PNF visits with low disease activity included 16 (PF)/10 (PNF) LLDAS and 14 (PF)/30 (PNF) in DORIS remission. The L-FRI did not differentiate disease activity itself (**Fig 1A**), but discerned flare risk in PF vs. PNF (**Fig. 1A**) and Flare vs. NF visits (**Fig. 1B**), irrespective of disease activity state. The L-DAI did not differentiate flare risk itself (**Fig. 1C**), but differentiated concurrent active vs. low (hSLEDAI< 4) disease activity, irrespective of flare risk status (**Fig.1C-D**). All SLE scores were higher than matched controls (*p< 0.0001*, **Fig. 1**). Plasma levels of osteopontin and BLyS (L-FRI, L-DAI), as well as other L-FRI informing mediators TNF-α, TNFRI, TNFRII, MCP-1, and MCP-3, were highest in PF visits with active disease (*p< 0.05*), while IL-17A levels were highest in PF visits with low disease activity and IL-4 highest in PNF visits with active disease (*p< 0.05*), **Fig. 2**. IL-7 (L-FRI, L-DAI) and TRAIL (L-DAI) levels were increased with both flare and disease activity risk (*p< 0.05*), while L-DAI informing mediators IFN-α, IFN-γ, IP-10, and IL-10 were highest in active disease (PF >PNF levels, *p< 0.05*), **Fig 2**. Of note, the L-FRI and L-DAI performed well at assessing flare and disease activity risk, respectively (AUC >0.8), yet parallel assessment of L-FRI and L-DAI performed better than either alone to identify simultaneous risk of concurrent active disease and imminent flare risk, **Table 1**.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Combination of L-FRI and L-DAI Tests Optimally Informs *Future* Flare and *Concurrent* Disease Activity Risk

Comparison	Variables	Test	AUC	95% CI	p-value
Flare Risk Status	Pre-Flare (PF) vs. Pre-Nonflare (PNF)[a]	L-FRI[b]	0.942	0.910-0.974	***<0.0001***
		L-DAI[c]	0.646	0.558-0.734	***0.0023***
		L-FRI + L-DAI	0.951	0.921-0.981	***<0.0001***
Disease Activity Risk Status	Active (Act) vs. Low Disease Activity[d]	L-FRI	0.569	0.480-0.657	*0.1315*
		L-DAI	0.884	0.831-0.937	***<0.0001***
		L-FRI + L-DAI	0.899	0.849-0.949	***<0.0001***
Pre-Flare Disease Activity Risk	PF/Act vs. PNF/Act	L-FRI	0.527	0.398-0.656	*0.6769*
		L-DAI	0.891	0.821-0.961	***<0.0001***
		L-FRI + L-DAI	0.925	0.868-0.981	***<0.0001***
Pre-Nonflare Disease Activity Risk	PF/Low vs. PNF/Low	L-FRI	0.530	0.395-0.666	*0.6586*
		L-DAI	0.865	0.775-0.955	***<0.0001***
		L-FRI + L-DAI	0.868	0.780-0.956	***<0.0001***
Active Disease Flare Risk	PF/Act vs. PNF/Act	L-FRI	0.931	0.871-0.990	***<0.0001***
		L-DAI	0.651	0.515-0.786	***0.0459***
		L-FRI + L-DAI	0.930	00.868-0.992	***<0.0001***
Low Disease Activity Flare Risk	PF/Low vs. PNF/Low	L-FRI	0.943	0.901-0.985	***<0.0001***
		L-DAI	0.607	0.489-0.725	*0.0874*
		L-FRI + L-DAI	0.956	0.919-0.994	***<0.0001***
Moderate Flare/Disease Activity Risk	PF/Low vs. PNF/Act	L-FRI	0.924	0.862-0.986	***<0.0001***
		L-DAI	0.794	0.669-0.920	***0.0002***
		L-FRI + L-DAI	0.950	0.891-1.000	***<0.0001***
Highest vs. Lowest Flare/Disease Activity Risk	PF/Act vs. PNF/Low	L-FRI	0.953	0.917-0.990	***<0.0001***
		L-DAI	0.921	0.871-0.973	***<0.0001***
		L-FRI + L-DAI	0.989	0.974-1.000	***<0.0001***

[a]Pre-Flare/Pre-Nonflare visits occurred within 12 weeks of SELENA-SLEDAI Flare Index (SFI) defined Flare/Comparable Nonflare

[b]Lupus Flare Risk Index (L-FRI) informs flare risk within next 12 weeks

[c]Lupus Disease Activity Index (L-DAI) informs concurrent SLE disease activity risk

[d]Disease Activity: Active (hSLEDAI≥4); Low (hSLEDAI<4)

Conclusion: Simultaneous use of the L-FRI and L-DAI optimally identified risk of imminent lupus disease flare and concurrent active disease to identify SLE patients who may benefit from early intervention strategies. Such an approach would improve disease management and be advantageous in prospective clinical trials for study participant recruitment and assessment.

Disclosure: M. Munroe: Progentec Diagnostics, Inc., 3, 4, 5, 10; **D. Blankenship**: Progentec Diagnostics, Inc., 2; **D. DeFreese**: Progentec Diagnostics, Inc., 3; **A. Holloway**: Progentec Diagnostics, Inc., 3; **B. Rubin**: Progentec Diagnostics, Inc., 3, 4; **M. Purushothaman**: Progentec Diagnostics, Inc., 3, 4, 10; **W. DeJager**: None; **S. Macwana**: None; **J. Guthridge**: None; **S. Kamp**: None; **N. Redinger**: None; **T. Aberle**: None; **E. Chakravarty**: None; **C. Arriens**: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **Y. Li**: None; **H. Zeng**: None; **S. Dezzutti**: None; **P. Izmirly**: Hansoh Bio, 2; **U. Thanarajasingam**: None; **D. Kamen**: None; **J. Buyon**: Artiva Biotherapeutics, 2, Biogen, 2, Bristol-Myers Squibb(BMS), 2, Celgene, 2, CLIMB Bio Operating, 2, GlaxoSmithKlein(GSK), 2, Janssen, 2, Related Sciences, 2, UCB, 2; **J. James**: GlaxoSmithKlein(GSK), 2, Progentec, 5; **E. Jupe**: Progentec Diagnostics, Inc., 3, 4, 10.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2650

LFA-REAL Outperforms SLEDAI and BILAG in Detecting Clinical Change in Lupus Activity

Alberto Nordmann-Gomes[1], Leila Khalili[2], Cynthia Aranow[3], Meghan mackay[4], Mimi Kim[5], Diane Kamen[6], Cristina Arriens[7], Maya Souvignier[8], Wei Tang[9], Stephen Suh[8], Maria Dall'Era[10], Joan Merrill[11] and Anca Askanase[2], [1]Columbia University Irving Medical Center, New York, NY, [2]Columbia University Medical Center, New York, NY, [3]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [4]Feinstein Institutes for Medical Research, Manhasset, NY, [5]Albert Einstein College of Medicine, Bronx, NY, [6]Medical University of South Carolina, Johns Island, SC, [7]Oklahoma Medical Research Foundation, Oklahoma City, OK, [8]Columbia University Irving Medical Center, New York City, NY, [9]Westchester Medical Center, Valhalla, NY, [10]Division of Rheumatology, University of California, San Francisco, CA, [11]Oklahoma Medical Research Foundation, Oklahoma

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Diagnosis, Manifestations, & Outcomes III (2645–2650)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Disease activity measures in SLE have important limitations that restrict their performance in clinical practice and research. The Lupus Foundation of America-Rapid Evaluation of Activity in Lupus (LFA-REAL) is a novel and simple SLE disease activity instrument. Each organ and active symptom/sign receives a unique visual analog score (0-100mm each), allowing sensitive detection and granular understanding of disease fluctuations. The system allows rapid yet versatile evaluation of progress at the level of symptoms, organs, or overall disease, and addresses pitfalls in glossary defined cutoffs for scoring that limit the utility of the SLE Disease Activity Index (SLEDAI) and British Isles Lupus Assessment Group Index (BILAG). Here, we evaluate the sensitivity of the LFA-REAL to detect changes in the clinician's global Impression of clinically significant change (CGIC) compared to the SLEDAI and BILAG.

Methods: An observational, longitudinal, prospective study of SLE patients was conducted at four lupus centers. Each study participant was evaluated at a baseline and follow-up visit. The same clinician scored the SLEDAI, BILAG, and LFA-REAL. At the follow-up visit, the physician also rated the CGIC, which rates no change vs clinically significant change compared to the previous visit. Agreement between changes in disease activity scores and CGIC was analyzed, generating ROC curves to assess the accuracy of each instrument to detect the clinician's overall conclusion about the degree of change.

Results: Of 163 patients enrolled, 145 completed follow-up visits, 124 (85%) were women, mean age was 41.4 +/- 12.9 years (Table 1). Among the 145 patients with follow-up, 33 (23%) had CGIC clinically significant disease improvement, 25 (17%) worsening, and 87 (60%) no change. For the CGIC improvement group the median change in LFA-REAL from visit 1 to visit 2 (V2-V1) (ΔLFA-REAL) was -36 (IQR: -62 ; -20), for the group with no change in CGIC the median change in LFA-REAL was 0 (IQR: -20 ; 10), and for those who worsened: 27 (6 ; 34) (Figure 1). Compared to BILAG and SLEDAI, LFA-REAL demonstrated the greatest sensitivity for clinical change in either direction, with area under the curve (AUC) of 0.8385 for improvement and 0.8305 for worsening. BILAG AUCs were 0.7461 and 0.7553, and SLEDAI AUCs were 0.7385 and 0.7362, respectively (Figure 2). Using DeLong's test, the AUC for LFA-REAL was significantly greater than that of SLEDAI for detecting improvement ($p = 0.042$) and trended towards greater sensitivity than BILAG ($p = 0.073$). Detection of worsening was similar compared to SLEDAI ($p = 0.093$) and BILAG ($p = 0.188$). Of the 25 patients classified as having clinical worsening by CGIC, 8 (32%) required a change in treatment. LFA-REAL identified all 8 of these patients as having clinically significant worsening, compared to 4 (50%) detected by BILAG and 2 (25%) by SLEDAI.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Baseline demographic and clinical characteristics of the participants.

	Participants (N=145)
Sex	
Female, n (%)	124 (85)
Male, n (%)	21 (15
Age, median years (IQR)	40 (32-49)
Race	
White, n (%)	60 (42)
Black, n (%)	58 (40)
Asian, n (%)	18 (12)
Other, n (%)	9 (6)
Ethnicity	
Hispanic, n (%)	37 (26)
Not Hispanic, n (%)	108 (74)
Site	
CUMC, n (%)	49 (33)
MUSC, n (%)	42 (29)
FIMR, n (%)	27 (19)
OMRF, n (%)	27 (19)
SLE disease duration, median years (IQR)	17 (12-23)
Physician's assessment of overall disease activity	
Asymptomatic, n (%)	31 (21)
Mild/moderate, n (%)	96 (66)
Severe, n (%)	18 (13)
Disease activity scores at baseline	
Mean SLEDAI (SD)	5.1 (4.5)
Mean BILAG (SD)	6.7 (6.8)
Mean LFA-REAL (SD)	51.0 (52.9)
Bivariate correlations LFA-REAL and disease activity	
SLEDAI r (p)	0.657 (<0.001)
BILAG r (p)	0.782 (<0.001)
PGA r (p)	0.824 (<0.001)
Active organ system involvement at baseline	
Musculoskeletal, n (%)	84 (58)
Mucocutaneous, n (%)	66 (46)
Vasculitis, n (%)	4 (3)
Cardiorespiratory, n (%)	3 (2)
Renal, n (%)	23 (16)
Neuropsychiatric, n (%)	0 (0)
Constitutional, n (%)	6 (4)
Hematologic, n (%)	44 (30)

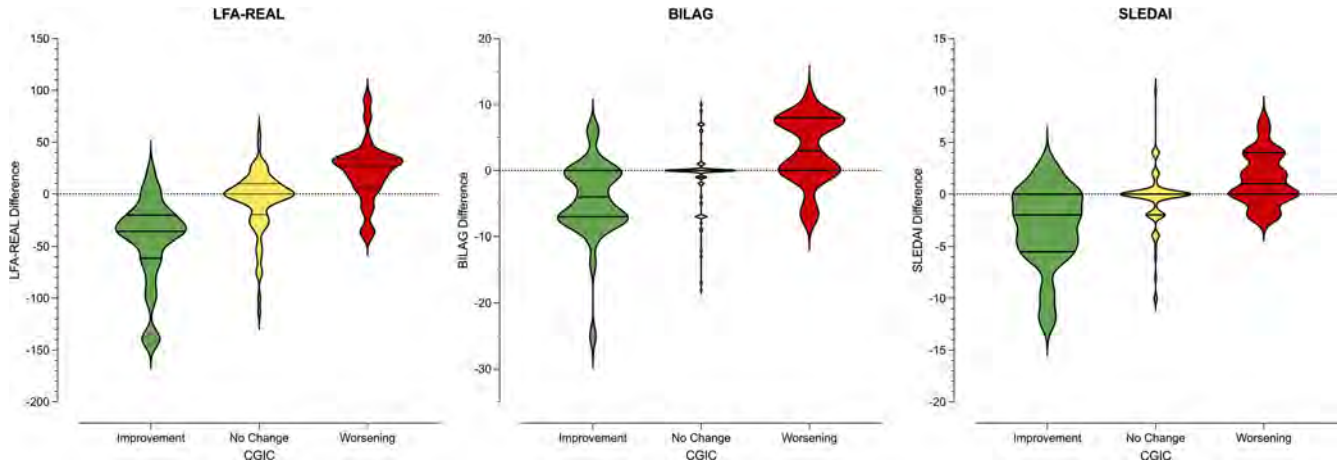
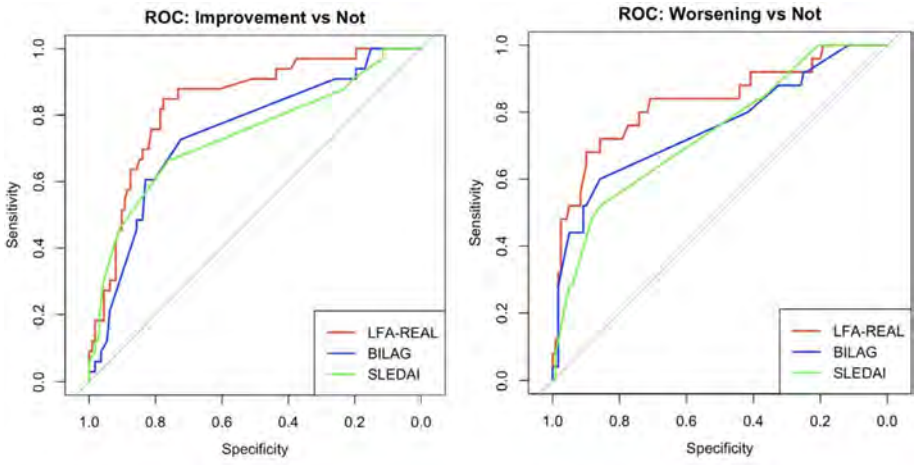


Figure 1. Change in disease activity scores according to CGIC group

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



Disease activity Score	AUC
LFA-REAL	0.8385
BILAG	0.7461
SLEDAI	0.7385

Disease activity Score	AUC
LFA-REAL	0.8305
BILAG	0.7553
SLEDAI	0.7362

Figure 2. ROC curves: Ability of disease activity scores to identify clinical improvement or worsening according to CGIC

Conclusion: LFA-REAL demonstrated greater accuracy than SLEDAI and BILAG in detecting clinically significant disease changes in SLE. These findings support the potential utility of this easy to score instrument for monitoring disease activity in both clinical practice and research.

Disclosure: A. Nordmann-Gomes: None; **L. Khalili**: None; **C. Aranow**: Alumis Inc., 2, Ampel Solutions, 2, AstraZeneca, 2, BMS, 2, GSK, 2, Kezar Life Sciences Inc., 2, Merck Sharp & Dohme, 2; **M. mackay**: None; **M. Kim**: None; **D. Kamen**: None; **C. Arriens**: AstraZeneca, 5, Aurinia, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, Health and Wellness Partners, 1, Synthekine, 1, UCB, 1; **M. Souvignier**: None; **W. Tang**: None; **S. Suh**: None; **M. Dall'Era**: AstraZeneca, 2, Aurinia, 2, Biogen, 2, Genentech, Inc., 2, GlaxoSmithKline (GSK), 2, Janssen, 2; **J. Merrill**: None; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5.

Abstract Number: 2651

Development and Validation of the Scleroderma Clinical Trials Consortium Classification Criteria for Systemic Sclerosis Heart Involvement

Laura Ross[1], Andrew Burns[2], Andre La Gerche[3], Dylan Hansen[4], Gerry Coghlan[5], Wendy Stevens[6], David Prior[7], Alan Pham[8], Penelope McKelvie[4], Chiara Bellocchi[9], Yolanda Braun Moscovici[10], Cosimo Bruni[11], Patricia E. Carreira[12], Tracy Frech[13], Sabrina Hoa[14], Marie Hudson[15], Vivien Hsu[16], Marco Matucci-Cerinic[17], Benjamin Medina Fonseca[18], Andrea Low[19], Sue-Ann Ng[19], Tatiana Rodriguez-Reyna[20], Joanne Sahhar[21], Mohamed Talaat[22], Susanna Proudman[23], Alessandra Vacca[24], Murray Baron[25], Mandana Nikpour[26] and SCTC Cardiac Working Group, [1]The University of Melbourne, Melbourne, Victoria, Australia, [2]St Vincent's Hospital Melbourne, Fitzroy, Australia, [3]St Vincent's Institute of Medical Research, Melbourne, Victoria, Australia, [4]St Vincent's Hospital Melbourne, Melbourne, Victoria, Australia, [5]Royal Free Hospital, London, United Kingdom, [6]St Vincent's Hospital Melbourne & University of Melbourne, Fitzroy, Australia, [7]University of Melbourne, Parkville, Australia, [8]Alfred Hospital, Melbourne, Australia, [9]University of Milan, Milan, Italy, [10]Rambam Heath Care Campus, Haifa, Israel, [11]Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [12]Hospital Universitario 12 de Octubre, Madrid, Spain, [13]Vanderbilt University

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Medical Center, Nashville, TN, [14]University of Montreal, Brossard, QC, Canada, [15]McGill University, Montral, QC, Canada, [16]Rutgers- RWJ Medical School, South Plainfield, NJ, [17]University San Raffaele Milano, Milano, Milan, Italy, [18]Universidad Nacional Autonoma de Mexico, Monterry, Mexico, [19]Singapore General Hospital, Singapore, Singapore, [20]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [21]Monash Health, Melbourne, Victoria, Australia, [22]Augusta Health, Charlottesville, VA, [23]Royal Adelaide Hospital and University of Adelaide, Medindie, South Australia, Australia, [24]University and AOU of Cagliari, Monserrato, Italy, [25]McGill University, Montreal, Canada, [26]University of Sydney, School of Public Health, Faculty of Medicine and Health, Sydney, New South Wales, Australia; St Vincent's Hospital Melbourne, Department of Rheumatology, Fitzroy, Victoria, Australia, Melbourne, Victoria, Australia

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical III (2651–2656)

Session Type: Abstract Session

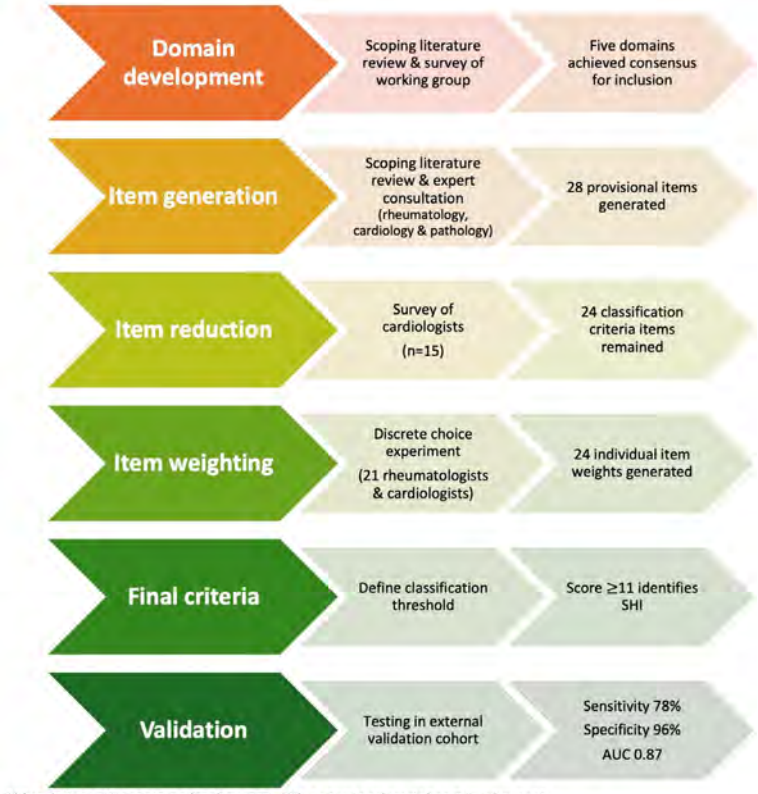
Session Time: 9:30AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) heart involvement (SHI) is a serious disease manifestation associated with high mortality. This study presents newly developed classification criteria to enable standardised identification of SHI in clinical studies.

Methods: An international inter-disciplinary working group including rheumatology, cardiology and anatomical pathology members was assembled. Consensus methods were applied to determine the domains of cardiac disease to be included in the criteria and generate provisional items (Figure 1).

Repeated consensus exercises and a discrete choice experiment were performed to reduce and weight items. A classification threshold was defined in a single centre derivation cohort (n=20), with emphasis placed on the specificity of the

Figure 1: Development of Systemic Sclerosis Heart Involvement Classification Criteria



Abbreviations: AUC: area under the curve; SHI: systemic sclerosis heart involvement

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: SCTC Systemic Sclerosis Heart Involvement Classification Criteria

- A diagnosis of systemic sclerosis heart involvement (SHI) can only be made in the setting of an established diagnosis of systemic sclerosis
- SHI can only be diagnosed when other causes of cardiomyopathy, particularly infiltrative diseases, have been reasonably excluded. Other causes of cardiomyopathy to be excluded include:
  - Cardiac disease secondary to pulmonary vascular disease
  - Ischaemic heart disease
  - Hypertensive heart disease
  - Cardiac disease secondary to renal disease
  - Dilated cardiomyopathy (e.g. genetic, post non-systemic sclerosis myocarditis, alcohol etc)
  - Cardiac sarcoidosis, cardiac amyloidosis, iron overload, Fabry's disease

Classification score ≥11 indicates presence of SHI

Classification criteria item	Item weight
Endomyocardial biopsy	
Perivascular and/or interstitial mononuclear inflammatory infiltrate adjacent to areas of myocyte necrosis and/or degeneration, with or without myocardial fibrosis	6
Perivascular and/or interstitial inflammatory infiltrate without myocyte necrosis	5
Pathological degree of interstitial fibrosis with or without replacement fibrosis	6
Fibrous or fibrinous pericarditis or pericardial adhesions	5
Cardiac magnetic resonance imaging	
Evidence of myocarditis as per Lake Louise Criteria	5
Abnormalities on T2 sequences (including T2 mapping) or post-contrast imaging suggestive of myocardial oedema that do not meet Lake Louise criteria for diagnosis of myocarditis	5
Epicardial or mid-wall late gadolinium enhancement in a non-ischaemic pattern	6
Abnormal T1 mapping time	5
Focal thinning or akinesis of myocardial wall or wall motion abnormalities	4
Evidence of thickened pericardium on either CMR, cardiac CT, TTE	4
Objective evidence of myocardial ischaemia in the absence of epicardial coronary artery disease (e.g. transmural scarring on CMR and patent coronary arteries)	4
Echocardiography	
Acute or subacute onset global or regional left and, or right ventricular dysfunction / reduced ventricular ejection fraction	4
Grade II or Grade III left ventricular diastolic dysfunction, according to ASE/EACVI criteria	4
Chronic non-trivial pericardial effusion	3
Electrocardiography	
Unexplained 2nd degree Mobitz type II conduction defect or complete heart block	4
Multifocal or complex ventricular ectopics	4
Sustained or non-sustained ventricular tachyarrhythmia	5
Right heart catheterisation	
Unexplained post capillary wedge pressure >15mmHg or left ventricular end diastolic pressure >12mmHg	4
Serum biomarkers	
Elevated troponin (above upper limit of normal)	3
Elevated serum BNP / NT-proBNP (above upper limit of normal)	3
Clinical features	
New onset heart failure	3
Signs, symptoms, investigation findings of cardiac constriction	3
Acute pericarditis indicated by clinical symptoms and either typical ECG changes or imaging evidence of pericardial inflammation	4

Note: Patients do not have to complete all investigations to secure a diagnosis of systemic sclerosis heart involvement. If a particular investigation has not been performed or the described abnormality is not observed, the patient scores zero for that item.

Abbreviations: ASE: American Society of Echocardiography; BNP: B-type natriuretic peptide; CMR: cardiac magnetic resonance imaging; CT: computed tomography; EACVI: European Association of Cardiovascular Imaging; ECG: electrocardiography; NT-proBNP: N-terminal pro B-type natriuretic peptide; TTE: transthoracic echocardiography; SCTC: Scleroderma Clinical Trials Consortium; SHI: systemic sclerosis heart involvements

classification criteria. Performance of the criteria were tested against physician-diagnosed SHI, the current diagnostic gold standard.

External validation studies were performed in a multi-centre validation cohort (n=168) to determine the sensitivity, specificity and discriminant validity of criteria by calculating the areas under receiver operator curves (AUC). Logistic regression analysis was performed to calculate the diagnostic odds ratio (OR) of the criteria classifying a patient as positive for SHI.

Results: The working group achieved consensus that criteria should be developed to identify the direct effects of SSc on the heart and discriminate SHI from cardiac complications of other disease manifestations, e.g. pulmonary arterial hypertension, renal disease. It was agreed that criteria should reflect the pathogenic changes of fibrosis, inflammation and vasculopathy known to affect the myocardium and pericardium in SSc.

Five domains of cardiac disease reached the *a priori* threshold of 70% agreement for inclusion in the classification criteria. Twenty-eight provisional items were generated from the results of a literature review and expert consultation. Four items were omitted following item reduction survey, with the remaining 24 items weighted using the results of the discrete choice experiment (Table 1).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A classification criteria score was calculated for each patient in the derivation cohort by summing individual criterion weights. A SHI classification score of ≥11 was chosen as it defined the the presence of SHI with a sensitivity of 100% and specificity of 82%. Application of this score to the validation cohort correctly classified 91% of cases, with a sensitivity of 78% and specificity of 96% and AUC of 0.87 (95%CI 0.80-0.93), compared to physician-diagnosed SHI (the current gold standard). A classification criteria score ≥11 gave an OR 82.60 (95%CI 26.47-257.72) for the presence of SHI.

Conclusion: These newly developed classification criteria are the first clinical criteria that can identify SHI with good sensitivity and excellent specificity. Their implementation in future studies will further validate their use and encourage systematic investigation of this important disease manifestation.

Disclosure: L. Ross: None; **A. Burns**: None; **A. La Gerche**: None; **D. Hansen**: None; **G. Coghlan**: Johnson & Johnson, 2, 5, 6, MSD, 2, 6; **W. Stevens**: Boehringer-Ingelheim, 2, 5, 6, GlaxoSmithKlein(GSK), 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6; **D. Prior**: None; **A. Pham**: None; **P. McKelvie**: None; **C. Bellocchi**: None; **Y. Braun Moscovici**: None; **C. Bruni**: Boehringer Ingelheim, 2, EMDO Foundation, 5, Iten-Kohaut Foundation, 5, Scleroderma Clinical Trials Consortium (SCTC), 5, Scleroderma Research Foundation (SRF), 2; **P. Carreira**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Corbus, 2, 6, Emmerald Health Pharmaceuticals, 2, 6, Janssen, 2, 6, Mitsubishi Tanabe, 2, 6, Novartis, 2, 6, Prometheus, 2, 6; **T. Frech**: None; **S. Hoa**: None; **M. Hudson**: Astra Zeneca, 5, 6, Boehringer-Ingelheim, 5, Merck, 1, Pfizer, 5; **V. Hsu**: None; **M. Matucci-Cerinic**: None; **B. Medina Fonseca**: None; **A. Low**: None; **S. Ng**: None; **T. Rodriguez-Reyna**: None; **J. Sahhar**: Boehringer-Ingelheim, 6; **M. Talaat**: None; **S. Proudman**: Boehringer-Ingelheim, 5, 6, Janssen, 5, 6, Merck/MSD, 1; **A. Vacca**: None; **M. Baron**: None; **M. Nikpour**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, GlaxoSmithKline (GSK), 2, 6, Johnson & Johnson, 2, 6.

Abstract Number: 2652

Anti-mitochondrial Antibodies in Systemic Sclerosis Target Enteric Neurons and Are Associated with GI Dysmotility

Zsuzsanna McMahan[1], Srinivas Puttapaka[2], Livia Casciola-Rosen[3], Timothy Kaniecki[3], Laura Gutierrez[3], Su Hong MIng[2], Philippa Seika[2] and **Subhash Kulkarni**[4], [1]UT Health Houston, Houston, TX, [2]BIDMC/Harvard, Boston, MA, [3]Johns Hopkins University, Baltimore, MD, [4]BIDMC, Boston, MA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical III (2651–2656)
Session Type: Abstract Session
Session Time: 9:30AM–11:00AM

Background/Purpose: Most patients with systemic sclerosis (SSc) experience gastrointestinal (GI) dysmotility. The enteric nervous system (ENS) regulates GI motility, and its dysfunction causes dysmotility. A subset of SSc patients harbor autoantibodies against the M2 mitochondrial antigen (AM2A). Here, we investigate whether M2 is expressed by specific ENS cells, and if AM2A associate with GI dysmotility in SSc patients.

Methods: Patients with SSc were prospectively enrolled from a large Scleroderma Center into the NIH-funded cohort based on ACR/EULAR criteria or CREST features and GI symptomatology. Clinical phenotyping, including Medsger Severity Scores, autoantibody profiles, and overlap diagnoses (e.g., PBC), was performed at enrollment and during routine follow-up. Whole gut transit (WGT) scintigraphy was conducted using radiolabeled meals to evaluate GI motility. AM2A autoantibodies were assessed by ELISA, and their uptake was studied via immunostaining in HepG2 cells, human intestinal tissue, and neural-crest lineage mouse models using confocal microscopy. Functional effects of AM2A were

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

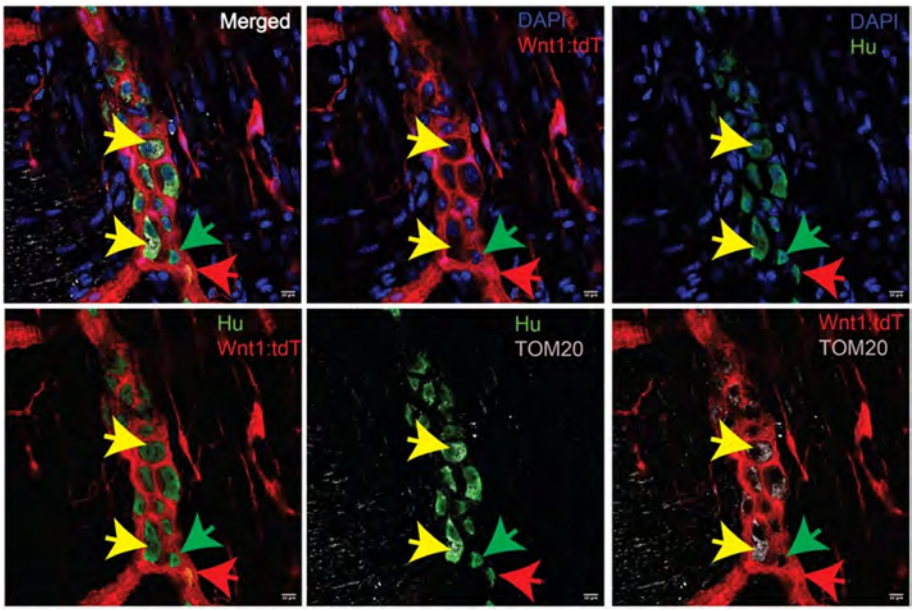


Figure 1. Figure 3: A subset of mesoderm-derived enteric neurons (MENs) are enriched in mitochondria. Immunostaining of adult murine small intestinal longitudinal muscle - myenteric plexus (LM-MP) tissue with ANNA1 antisera containing antibodies against Hu (green) and antibodies against the pan-mitochondrial antigen TOM20 (cyan). LM-MP is derived from an neural crest lineage-specific adult mouse Wnt1-cre:tdTomato, where tdTomato (red) labels neural crest-derived cells. The representative image shows that tdTomato- Hu+ neurons (MENs, yellow arrows) are enriched in TOM20, while the neural crest-derived neurons (NENs, red arrow) and a subset of MENs (green arrow) are not. Nuclei are labeled with DAPI (blue). Scale bar = 10 m.

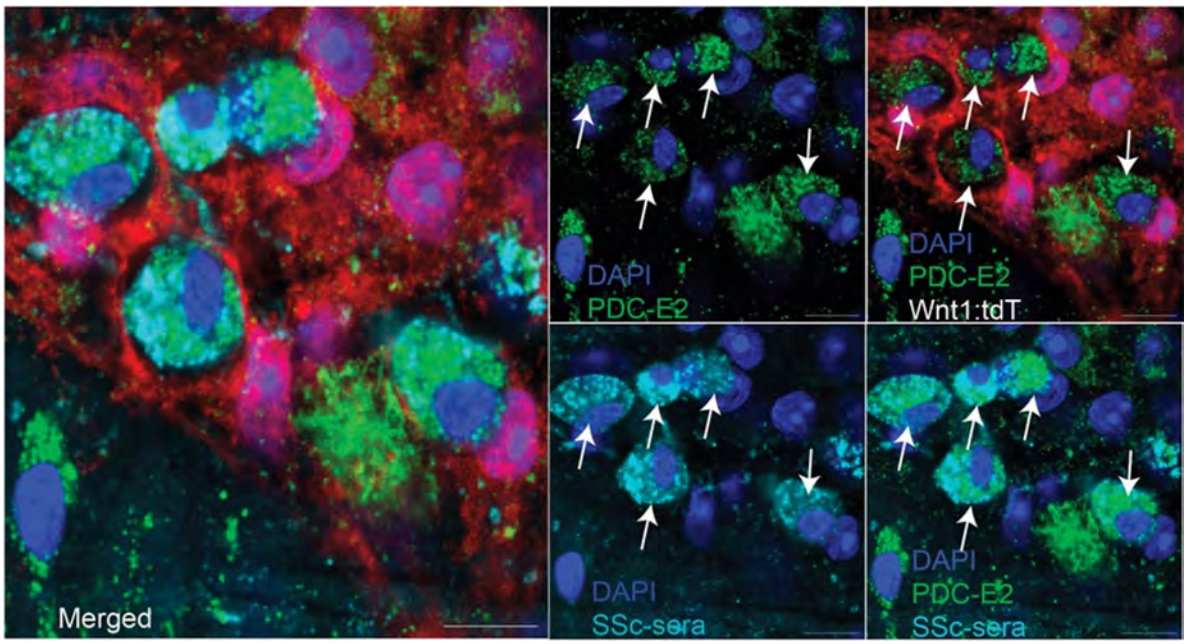


Figure 2. SSc-AM2A penetrate viable MENs ex vivo. Adult murine small intestinal LM-MP tissues from the Wnt1-cre:tdTomato lineage fate mapping mouse when cultured with SSc patient sera containing AM2A (FW-2530), and immunostained with commercially available anti-DLAT antibodies post-culture show that tdTomato-negative myenteric neurons or MENs show presence of SSc autoantibodies (AM2A; cyan) within their soma which co-localizes with the presence of DLAT (green) immunostaining (white arrows). Nuclei are labeled with DAPI (blue). Scale bar = 10 m.

tested with Seahorse assays. Immunoprecipitation and Western blot confirmed antibody-protein interactions. All protocols were IRB-approved, and statistical analyses included t-tests, chi-square, regression, and Spearman correlation, with significance set at $p < 0.05$.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

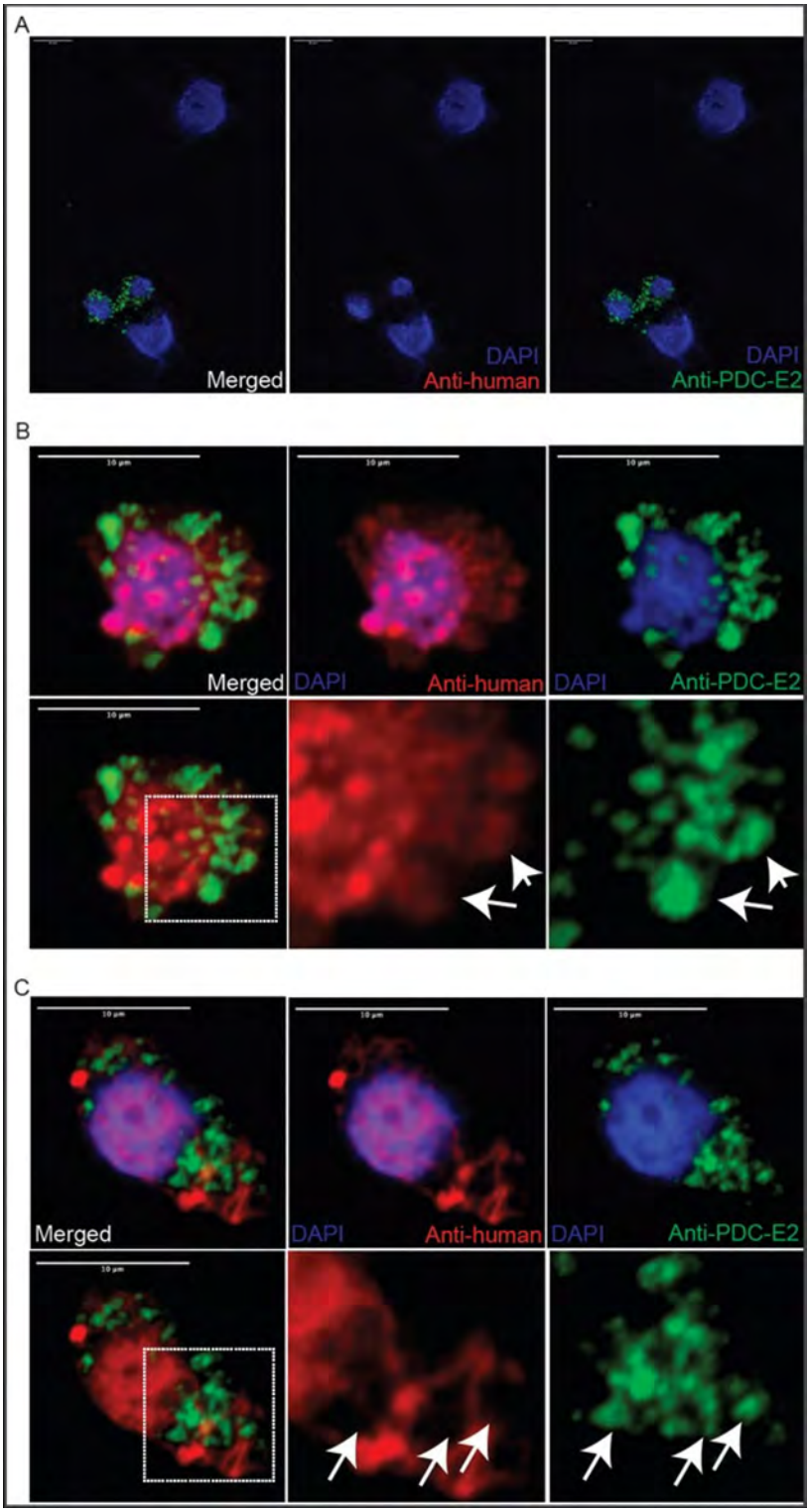


Figure 3. SSc autoantibodies penetrate viable cells and engage intracellular targets upon uptake. HepG2 cells when cultured with and without SSc antisera (red) can be used to test intracellular uptake. Live HepG2 cells cultured (A) without SSc antisera, and with (B) AM2A+ SSc antisera (patient FW-2530), and (C) AM2A- SSc antisera (patient FW-2340), were subsequently fixed and immunostained with commercially available anti-M2/PDC-E2 antibody (green) and imaged to observe that SSc autoantibodies were present within cells cultured with SSc patient antisera. Furthermore, AM2A+ antisera was detected in PDC-E2- expressing mitochondria (B, white arrow), but the AM2A- antisera labeled cellular compartments other than the PDC-E2-expressing mitochondria (C, white arrows). Nuclei are labeled with DAPI (blue). Scale bar = 10 μm.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Nineteen of 147 patients (12.9%) were AM2A positive. AM2A positivity was significantly associated with slower transit in the esophagus (β -14.4, 95%CI -26.2, -2.6) and stomach (β -7.9, 95% CI -14.1, -1.6). Immunostaining demonstrated pan-mitochondrial antigens TOM-20 and M2 enrichment in human ENS neurons, specifically in mesoderm-derived enteric neurons (MENS). Autoantibodies in SSc sera penetrated live adult murine MENs and HepG2 cells, when adult murine longitudinal muscle containing myenteric plexus (LM-MP) tissue and HepG2 cells were cultured with SSc sera. Upon penetrating live cells, AM2A localized to mitochondria, and immunoprecipitation demonstrated binding to the M2 antigen. Seahorse assays show that penetration of HepG2 cells with SSc-AM2A altered cellular respiration suggesting that penetrating AM2A are pathogenic.

Conclusion: AM2A in SSc patients associate with slower GI transit. SSc autoantibodies penetrate live cells in vitro, and SSc-AM2A penetrate live cells to target the mitochondrial M2 antigen and cause functional deficits in cellular respiration. Since a subset of enteric neurons (MENs) is enriched in mitochondria, which are similarly penetrated by SSc-AM2A ex vivo, the presence of GI dysmotility in SSc patients harboring AM2A suggests that SSc-AM2A may penetrate MENs in vivo, driving ENS and GI dysfunction. Further studies are warranted to test how AM2A alter ENS function in vivo to contribute to GI dysmotility in SSc.

Disclosure: Z. McMahan: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **S. Puttapaka**: None; **L. Casciola-Rosen**: None; **T. Kaniecki**: None; **L. Gutierrez**: None; **S. Hong MIng**: None; **P. Seika**: None; **S. Kulkarni**: None.

Abstract Number: 2653

First Prospective Evaluation of Recombinant Herpes Zoster Vaccine in Systemic Sclerosis: Immunogenicity, Safety, and Disease Activity Outcomes

Ana Paula Luppino-Assad[1], Renata P Mello[2], Ana C Medeiros-Ribeiro[3], Nadia E Aikawa[4], Sandra G Pasoto[3], Leonard V Kupa[5], Renata Miossi[6], Percival D Sampaio-Barros[6], Eduardo Borba[7], Eloisa Bonfa[7] and Clovis Artur Silva[8], [1]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, SAO PAULO, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, São Paulo, Sao Paulo, Brazil, [3]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [4]Pediatric Rheumatology Unit, Instituto da Criança e do Adolescente, Hospital das Clinicas HCFMUSP, Sao Paulo, Brazil., Sao Paulo, Sao Paulo, Brazil, [5]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil, [6]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, São Paulo, [7]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil, [8]University of São Paulo, São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical III (2651–2656)
Session Type: Abstract Session
Session Time: 9:30AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) patients are at higher risk of herpes zoster (HZ) due to underlying immune dysregulation and immunosuppressive therapies. Vaccination is a key strategy for preventing HZ. Although the recombinant zoster vaccine (RZV/Shingrix®) is approved for immunocompromised individuals, its immunogenicity, safety, and impact on disease activity (DA) have not been specifically evaluated in SSc patients. This study aimed to evaluate the humoral immune response to RZV in immunosuppressed SSc patients compared to healthy controls, to identify factors influencing vaccine

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Humoral response rates at V3 (D84) and anti-gE IgG titers before (D0) and after two doses (D84) of RZV in SSc patients and CG.

	Humoral response	Geometric mean titer		*p value*	Factor increase in GMT
	D84	D0	D84	D0 vs. D84	
SSc, n=68	63 (92.6)	0.19 (0.14-0.25)	5.81 (4.41-7.65)	**< 0.001**	31.0 (20.64-46.56)
CG, n= 299	298 (99.7)	0.21 (0.18-0.24)	12.56 (11.63-13.56)	**< 0.001**	59.44 (51.37-68.78)
p (SSc vs CG)	**0.001**	0.463	**< 0.001**	-	**< 0.001**

SSc - systemic sclerosis; CG – control group; GMTs – Geometric mean titers (AU/mL); Frequencies of humoral response are presented as number (%) and they were compared using two-sided chi-square test between SSc and CG at D84 (12-week after first vaccine dose). Ig-gE IgG titers and factor increase in GMT are expressed as geometric means with 95% confidence interval (95%CI). Data regarding anti-gE titers were analyzed using ANOVA with repeated measures and 2 factors [2 groups (SSc vs. CG), at 2 time points (D0 and D84)], followed by Bonferroni's multiple comparisons at neperian logarithm (ln)-transformed data. GMT and factor increase in GMT were compared using Mann-Whitney test for intergroup comparisons in ln-transformed data at pre-specified time points (D0 and D84). All analyses were two-side

Table 2. Changes in disease activity metrics in P1 and P2 groups following vaccination or placebo dose.

	Baseline			6 weeks			12 weeks		
	P1 (N=37)	P2 (N=39)	*p value*	P1 (N=36)	P2 (N=39)	*p value*	P1 (N=36)	P2 (N=39)	*p value*
PtGA	5.0 (0.0-7.0)	3.0 (0.0-6.0)	0.290	3.5 (0.0-5.3)	2.0 (0.0-5.5)	0.711	3.0 (0.0-5.3)	3.0 (0.0-6.5)	1.000
PrGA	2.0 (0.0-3.0)	0.0 (0.0-2.0)	0.143	2.0 (0.0-3.0)	0.0 (0.0-2.0)	0.082	1.0 (0.0-3.0)	0.0 (0.0-3.0)	0.688
ScleroID	3.6 (1.6-5.4)	3.0 (1.5-5.4)	0.708	2.8 (1.2-4.8)	2.3 (1.0-5.3)	0.573	2.4 (0.7-5.0)	2.4 (1.2-5.3)	0.890
CDAI	7.0 (2.0-12.0)	4.0 (0.0-10.5)	0.251	5.5 (0.0-10.8)	3.0 (0.0-11.0)	0.523	5.5 (0.0-13.0)	4.0 (0.0-9.5)	0.669
mRSS	3.0 (0.0-7.0)	1.0 (0.0-4.0)	0.250	2.0 (0.0-7.0)	0.0 (0.0-3.0)	0.386	2.0 (0.0-4.0)	1.0 (0.0-3.5)	0.738
mMRC (0-2)	29 (78.4)	31 (79.5)	0.905	33 (91.7)	30 (76.9)	0.117	32 (88.9)	30 (76.9)	0.227
mMRC (3-4)	8 (21.6)	8 (20.5)	0.905	3 (8.3)	9 (23.1)	0.117	4 (11.1)	9 (23.1)	0.227
	Baseline - 6 week			**6 weeks - 12 week**			**Total Baseline - 12 weeks**		
	P1 (N=37)	P2 (N=39)	*p value*	P1 (N=36)	P2 (N=39)	*p value*	P1 (N=75)	P2 (N=78)	*p value*
ΔScleroID ≥ 0.48	7 (18.9)	7 (18.0)	0.883	9 (25.0)	16 (41.0)	0.143	16 (21.3)	23 (29.5)	0.247
ΔCDAI > 6.5	3 (8.1)	3 (7.7)	1.000	4 (11.1)	6 (15.4)	0.738	7 (9.3)	9 (11.5)	0.655
ΔmRSS ≥ 5	1 (2.7)	0 (0.0)	0.486	0 (0.0)	0 (0.0)	1.000	1 (1.3)	0 (0.0)	0.490
ΔmMRC ≥ 1	4 (10.8)	1 (2.6)	0.194	5 (13.9)	2 (5.1)	0.250	9 (12.0)	3 (3.8)	0.075
Worsening in any parameter	15 (40.5)	11 (28.2)	0.257	18 (50.0)	24 (61.5)	0.314	33 (44.0)	35 (44.9)	0.913

PtGA - Patient's Global Assessment; PrGA - Provider's Global Assessment; ScleroID - EULAR Systemic Sclerosis Impact of Disease questionnaire; CDAI - Clinical Disease Activity Index; mRSS - Modified Rodnan Score; mMRC - Modified Medical Research Council Dyspnea Scale. Deterioration in established validated assessment tools were defined: increase in ScleroID of ≥ 0.48; CDAI > 6.5; mRSS ≥ 5; mMRC ≥ 1. Mann-Whitney test was used for intergroup comparison.

response, and to assess RZV safety profile and impact on patient-reported outcome measure (PROM) using validated scores.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: In this randomized, double-blind, placebo-controlled trial, 76 immunosuppressed SSc patients (≥18 years) and 304 healthy individuals (≥50 years) in control group (CG) received two RZV doses. SSc patients were randomized to vaccine (P1) or placebo (P2) at D0 and D42, with unblinding at D84, after which P2 also received RZV (D84, D126). Anti-glycoprotein E antibody (Anti-gE) levels were measured at baseline and 6-week visit after vaccination using an in-house GlaxoSmithKline (GSK)'s enzyme-linked immunosorbent assay (ELISA). A humoral response was defined as ≥4-fold the pre-vaccination concentration. Geometric mean titers (GMTs) and factor increase (FI) were calculated. PROM and DA was assessed by EULAR Systemic Sclerosis Impact of Disease (ScleroID), Modified Medical Research Council (mMRC) Dyspnea Scale, Clinical Disease Activity Index (CDAI), and patient/provider's global assessments

Results: Female sex was similar between groups ($p > 0.05$). SSc patients were younger [53.0 (46.0-61.0) vs 55.0 (52.0-61.0), $p=0.002$] years, more often Black (44.1 vs 19.4%, $p< 0.001$), had lower body mass index ($p=0.005$), and more chronic kidney disease ($p=0.001$). At 6-week visit after the 2nd dose, humoral response was observed in 92.6% of SSc and 99.7% of CG ($p=0.001$). SSc had a significantly lower GMT [5.8 (95% CI 4.4-7.7) vs 12.6 (95% CI 11.6-13.6), $p< 0.001$], and FI at D84 [31.0 (95% CI 20.6-46.6) vs 59.4 (95% CI 51.4-68.8), $p< 0.001$] compared to CG (table 1). No demographic or immunosuppressive therapy predicted impaired vaccine response. Local adverse events were less frequent in SSc patients (73.7 vs 86.5%, $p=0.024$) with significantly low rates of pain, erythema and edema at injection sites ($p< 0.05$). Systemic reactions were comparable overall (59.2 vs 61.5%, $p=0.712$), although dyspnea ($p< 0.001$), tremor ($p=0.018$) and vomiting ($p=0.032$) were more common among SSc patients. DA parameters and PROM (ScleroID, mMRC, CDAI, and patient/provider's global assessments) showed no significant differences between vaccinated (P1) and placebo (P2) groups at baseline, D42, D84 ($p >0.05$). Rates of worsening across validated DA measures were similar between groups at all time points ($p >0.05$) (Table 2).

Conclusion: RZV is safe and highly immunogenic in immunosuppressed SSc patients, without affecting DA as measured by validated scores. However, lower antibody titers raise concerns about long-term protection, underscoring the need for ongoing monitoring in this population (ClinicalTrials NCT05879419).

Disclosure: A. Luppino-Assad: GlaxoSmithKlein(GSK), 5; **R. Mello**: None; **A. Medeiros-Ribeiro**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **N. Aikawa**: GlaxoSmithKlein(GSK), 5; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Kupa**: GlaxoSmithKlein(GSK), 5; **R. Miossi**: None; **P. Sampaio-Barros**: None; **E. Borba**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (303378/2022-0), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

Abstract Number: 2654

Discordance Between Patient and Physician Global Assessments in Early Systemic Sclerosis

Ellen Romich[1], Alexis Ogdie[2], Alisa Stephens Shields[2], Peter Merkel[2], Jessica Alvey[3], Shervin Assassi[4], Elana Bernstein[5], Sonali Bracken[6], Flavia Castelino[7], Lorinda Chung[8], Luke Evnin[9], Tracy Frech[10], Jessica Gordon[11], Faye Hant[12], Monica Harding[13], Laura Hummers[14], Dinesh Khanna[15], Kimberly Lakin[11], Dorota Lebiedz-Odrobina[13], Yiming Luo[5], Ashima Makol[16], Maureen Mayes[17], Zsuzsanna McMahan[18], Jerry Molitor[19], Duncan Moore[20], Carrie Richardson[21], Ami Shah[14], Ankoor Shah[22], Brian Skaug[23], Virginia Steen[24], John VanBuren[13], Elizabeth Volkmann[25], Carleigh Zahn[15], Nora Sandorfi[2]

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

and the CONQUER Investigators, [1]University of Pennsylvania, Media, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Utah Data Coordinating Center, University of Utah, Salt Lake City, UT, [4]Division of Rheumatology, UTHealth Houston, Houston, Texas, USA, Houston, TX, [5]Columbia University, New York, NY, [6]Duke University Medical Center, Durham, NC, USA, Apex, NC, [7]Massachusetts General Hospital, Boston, MA, [8]Stanford University, Stanford, CA, [9]Scleroderma Research Foundation, San Francisco, CA, [10]Vanderbilt University Medical Center, Nashville, TN, [11]Hospital for Special Surgery, New York, NY, [12]Medical University of South Carolina, Charleston, SC, [13]University of Utah, Salt Lake City, UT, [14]Johns Hopkins Rheumatology, Baltimore, MD, [15]University of Michigan, Ann Arbor, MI, [16]Mayo Clinic, Rochester, MN, [17]UT Health Houston Division of Rheumatology, Houston, TX, [18]UT Health Houston, Houston, TX, [19]University of Minnesota, Minneapolis, MN, [20]Northwestern Memorial Hospital, Chicago, IL, [21]Northwestern University, Chicago, IL, [22]Duke University, Durham, NC, [23]UTHealth Houston Division of Rheumatology, Houston, TX, [24]Georgetown University School of Medicine, Washington, DC, [25]Division of Rheumatology, Department of Medicine, University of California, David Geffen School of Medicine, Los Angeles, CA, USA, Los Angeles, CA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical III (2651–2656)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: To determine the frequency and extent of discordance between patient and physician global assessments of disease in early systemic sclerosis and identify factors associated with discordance.

Methods: Adult patients with early systemic sclerosis from the COllaborative National QUality and Efficacy Registry (CONQUER) were included. Global disease assessments by patients and physicians (0-10, higher is worse, 7-day recall), clinical evaluations, and patient-reported outcomes were collected at enrollment and every 6 months. Score concordance was defined as patient and physician global scores within 1 point, and discordance as a difference of ≥ 2 points, creating 3 categories: concordance, patient scores worse, and physician scores worse. The frequency of discordance and correlation between global assessments were determined for the enrollment visit, and factors associated with discordance were assessed using multivariable mixed-effects proportional odds regression with concordance as the reference category.

Results: 956 patients (83% female, 33% limited cutaneous disease, 19% with disease duration < 1 year) with both global assessments available were included **(Table 1)**. The correlation between patient and physician global assessments was weak (Pearson's *r*=0.28) **(Figure 1)**. Discordance between global assessments was present in 510 (53%) of patients (35% patient score worse; 19% physician score worse)**(Figure 2)**. In the multivariable model, compared to score concordance, physicians tended to report global scores worse than patient scores when there was a higher modified Rodnan skin score (mRSS)(odds ratio (OR), [95% confidence interval (CI)]: 1.03 [1.01, 1.05]), worse New York Heart Association (NYHA) functional Class (Class II OR 1.78 [1.20, 2.65]; Class III/IV: 2.83 [1.07, 7.46]), and higher PROMIS Pain Interference (OR 1.03, [1.00, 1.05]), while higher diffusing capacity of the lung for carbon monoxide (DLCO) %-predicted (OR 0.94 [0.90, 0.98]) was associated with lower likelihood of discordance with physician scores worse. Patients tended to report global scores worse than physician scores when there was higher overall pain/discomfort (OR 1.29 [1.18, 1.42]), while decreased likelihood of discordance with the patient scores worse was observed for limited vs. diffuse cutaneous subtype (OR 0.45 [0.28, 0.71]), higher mRSS (OR 0.97 [0.95, 0.99]), and worse NYHA functional Class (Class III/IV OR 0.29 [0.13, 0.66]).

Conclusion: Discordance between global assessments is present in over half of cases in systemic sclerosis, with patients tending to rate their condition worse compared to their physician's rating. Discordance in which physician scores are worse is associated with disease characteristics and measures of severity, while discordance in which patient scores are worse is associated with increased pain and lower likelihood of severe manifestations. Physicians may underestimate disease impact when disease manifestations are less severe. These results highlight differing perceptions of disease severity and emphasize the need for comprehensive approaches to symptom management and measurement of disease burden in this complex disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Characteristics of patients with systemic sclerosis and frequency at enrollment of patient-physician discordance of global assessments

	Patient characteristics	Difference between patient and physician global assessment		
	Overall	Physician score worse	Concordance (+/- 1 point)	Patient score worse
Overall	N = 956	177 (19%)	446 (47%)	333 (35%)
Subgroups				
Age at baseline visit (years)	52.7 (13.5)	53.5 (13.4)	52.9 (14.2)	52.1 (12.7)
Female sex	794 (83%)	134 (17%)	371 (47%)	289 (36%)
Disease duration at enrollment less than 1 year	179 (19%)	36 (20%)	74 (41%)	69 (39%)
Limited cutaneous subtype	318 (33%)	44 (14%)	150 (47%)	124 (39%)
ILD status				
ILD status unknown (no HRCT)	316 (33%)	50 (16%)	155 (49%)	111 (35%)
No ILD	280 (29%)	45 (16%)	123 (44%)	112 (40%)
ILD present	360 (38%)	82 (23%)	168 (47%)	110 (31%)
Abnormal gastrointestinal tract	676 (71%)	113 (17%)	316 (47%)	247 (37%)
Renal crisis	35 (4%)	15 (43%)	15 (43%)	5 (14%)

Values presented as n (%) or mean (standard deviation). Patient characteristics in the overall cohort are displayed as column percentages. The frequency of discordance and concordance is displayed as row percentages to allow comparison of discordance rates by subgroups. Abnormal gastrointestinal tract is based on the Gastrointestinal Medsger Severity Scale. ILD, interstitial lung disease; HRCT, high-resolution computed tomography chest imaging.

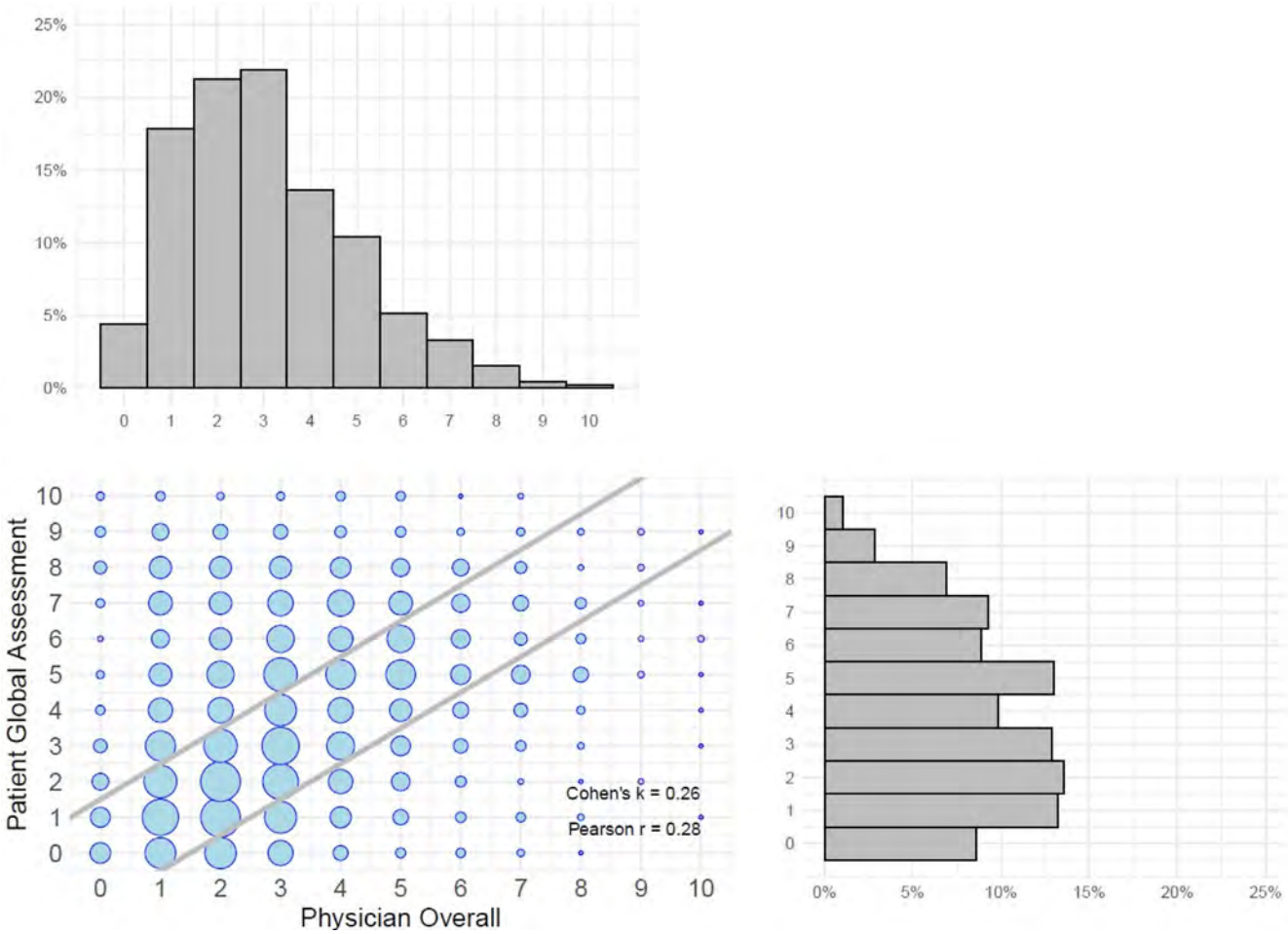


Figure 1. Scatterplot and distributions of patient and physician global assessments of overall disease activity in systemic sclerosis at enrollment visit. The size of the blue circles represents the number of patients with each score combination. Points above the gray lines indicate discordance with the patient score worse, while points below the gray lines indicate discordance with the physician score worse. Points between the gray lines are concordant. Mean (standard deviation) global assessments at enrollment were 4.2 (2.6) and 3.5 (2.0) among patients and physicians, respectively. The distributions demonstrate that patients are more likely to utilize the full range of scores compared to physicians.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

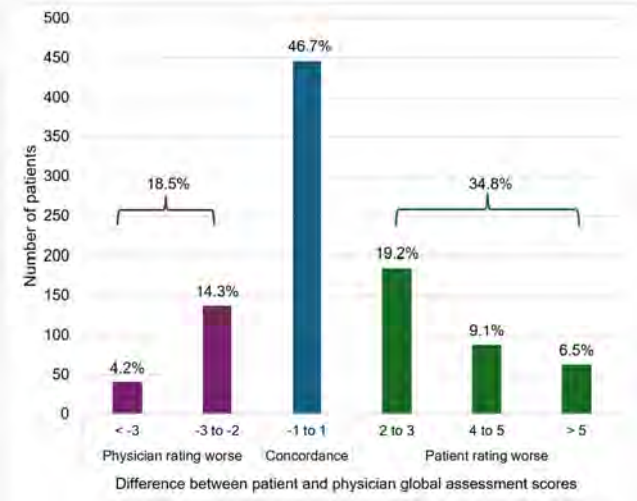


Figure 2. Distribution of differences between patient and physician global assessment scores among patients with systemic sclerosis at enrollment visit. Global assessment score concordance (+/- 1 point) was present in 47% of patient-physician assessments at the enrollment visit (blue). Discordance (≥ 2-point difference) was present in 53%. Patient global assessment scores were worse than the physician scores in 35% (green), while physician global assessment scores were worse than the patient scores in 19% (purple). Patient scores were more likely to show high discordance, with 15% of scores 4 or more points higher than the corresponding physician scores.

Disclosure: E. Romich: Lungpacer Medical, Inc., 11, Teva Pharmaceuticals, 12, Spouse employment; **A. Ogdie**: AbbVie, 2, 5, Amgen, 2, 5, 11, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, CorEvitas, LLC, 2, 5, Eli Lilly, 2, 5, Forward Databank, 5, Gilead, 1, 2, Janssen, 2, 5, Kopa/Twill Health, 2, NIH/NIAMS, National Psoriasis Foundation, 5, Novartis, 2, 5, 11, Pfizer, 2, 5, 11, Rheumatology Research Foundation, 5, Spyre, 2, Takeda, 2, UCB, 2, 5, University of Pennsylvania, 5; **A. Stephens Shields**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **J. Alvey**: None; **S. Assassi**: AbbVie, 2, AstraZeneca, 2, aTyr, 2, 5, Boehringer Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, CSL Behring, 2, Janssen, 5, Merck, 2, Mitsubishi Tanabe, 2, PeerView Institute for Medical Education, 6, Scleroderma Research Foundation, 5, 6, Takeda, 2, TeneoFour, 2; **E. Bernstein**: AstraZeneca, 5, aTyr, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 5, Cabaletta Bio, 5, Synthekine, 2; **S. Bracken**: None; **F. Castelino**: Boehringer-Ingelheim, 2, Genentech, 5, Horizon, 5, Mediar Therapeutics, 1, Takeda, 1; **L. Chung**: AbbVie/Abbott, 1, Boehringer-Ingelheim, 1, CRISPR Therpeutics, 2, Cure Ventures, 2, jade, 2, Kyverna, 6, Mediar, 1, 2; **L. Evnin**: None; **T. Frech**: None; **J. Gordon**: Cumberland, 5, Prometheus/Merck, 5; **F. Hant**: None; **M. Harding**: None; **L. Hummers**: AbbVie/Abbott, 1, AstraZeneca, 5, Biotest, 2, Boehringer-Ingelheim, 1, 5, Cumberland Pharmaceuticals, 5, GlaxoSmithKlein(GSK), 5, Horizon Pharma, 5, Merck/MSD, 5, Mitsubishi Tanabe, 5; **D. Khanna**: Argenx, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Cabaletta, 2, Novartis, 2, UCB, 2, Zura Bio, 2; **K. Lakin**: None; **D. Lebiedz-Odrobina**: None; **Y. Luo**: None; **A. Makol**: Amgen, 12, Site PI for Clinical trial, AstraZeneca, 12, Site PI for Clinical trial, Boehringer-Ingelheim, 1, 12, Site PI for Clinical trial, Sanofi Genzyme, 12, Site PI for Clinical trial; **M. Mayes**: Argenx, 2, AstraZeneca, 5, atyr, 5, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 1, 5, h, 5, Novartis, 2, prometheus merck, 5; **Z. McMahan**: Aera Therapeutics, 2, Allogene, 2, Boehringer-Ingelheim, 2, guidepoint, 2; **J. Molitor**: None; **D. Moore**: AstraZeneca, 5; **C. Richardson**: Cabaletta Bio, 2; **A. Shah**: None; **A. Shah**: Adtium Bio, 2, Cabaletta Bio, 5, Horizon Therapeuatics, 5, Mitsubishi, 2; **B. Skaug**: None; **V. Steen**: None; **J. VanBuren**: None; **E. Volkmann**: AbbVie, 2, Boehringer-Ingelheim, 2, 5, 6, 12, Medical writing support provided by Fleishman Hillard, Bristol-Myers Squibb(BMS), 2, GlaxoSmithKleine, 2, 5, Horizon, 5, Kadmon, 5, Prometheus, 5, The National Heart, Lung and Blood Institute, 5; **C. Zahn**: None; **N. Sandorfi**: Bristol-Myers Squibb(BMS), 2, Immunovant, 2, Janssen, 2, Novartis, 1.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2655

Fetal and maternal outcomes in systemic sclerosis and very early diagnosis of systemic sclerosis pregnancies, a national prospective study

Anne Murarasu[1], lauren beaudeau[2], Véronique Le Guern[3], gaelle guettrot-Imbert[3], claire cazalets[4], cecile durant[5], Cecile Yelnik[6], Céline Roussin[7], Marie-Charlotte Besse[8], Emilie Berthoux[9], Emmanuel Chatelus[10], Eric Hachulla[11], Estibaliz LAZARO[12], Francois Maurier[13], Gaelle leroux[14], Grégory Pugnet[15], Isabelle durieu[16], Loic RAFFRAY[17], Maelle Le Besnerais[18], Mélanie roriz[19], Odile SOUCHAUD-DEBOUVERIE[20], Patrick JEGO[21], Pauline ORQUEVAUX[22], Claire de Moreuil[23], Helene MAILLARD[24], Nathalie Morel[25], Anna Molto[26], Camille Le Ray[27], emmanuelle pannier[27], loic sentilhes[25], Luc Mouthon[28], Nathalie Costedoat-Chalumeau[29], Benjamin Chaigne[30] and the GR2 group study, [1]Tours University Hospital, Tours, France, [2]Centre Hospitalier Ales Les Cevennes, Ales, France, [3]Cochin hospital, Paris, France, [4]Rennes Hospital, Rennes, France, [5]Nantes University Hospital, Nantes, France, [6]lille university, Lille, France, [7]Centre Hospitalier Ouest Réunion, Saint Paul, France, [8]Tours University Hospital, 37000 tours, Ile-de-France, France, [9]Internal Medicine, Saint Luc Saint Joseph Hospital, Lyon, France, [10]Department of Rheumatology, University Hospital Strasbourg, France, Strasbourg, France, [11]University of Lille, LILLE, France, [12]Bordeaux University Hospital, Pessac, France, [13]HOPITAUX PRIVES DE METZ, Vaux / Frankreich, France, [14]Pitié-Salpêtrière University Hospital, Paris, France, [15]CHU Toulouse Rangueil Service de Medecine Interne et Immunologie Clinique, Toulouse, France, [16]Lyon University Hospital, Lyon, France, [17]Félix-Guyon University Hospital of La Réunion, Saint Denis, France, [18]Rouen University Hospital, Rouen, France, [19]Agen hospital, Agen, France, [20]Poitiers University Hospital, Poitiers, France, [21]Rennes University Hospital, Rennes, France, [22]Reims University Hospital, Reims, France, [23]CHU DE BREST, BREST, France, [24]Lille University Hospital, Lille, France, [25]Bordeaux University Hospital, Bordeaux, France, [26]Assistance Publique Hôpitauxde Paris, Paris, France, [27]Cochin Port Royal University Hospital, Paris, France, [28]Hopital Cochin - Paris University, Paris, France, [29]Inserm DR Paris 5, Paris, France, [30]Cochin University Hospital, Paris, France

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical III (2651–2656)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Pregnancy in women with systemic sclerosis (SSc) is considered high-risk due to complications like scleroderma renal crisis and preeclampsia, related to vasculopathy. Prospective data on pregnancy outcomes in SSc are lacking. We aimed to describe adverse pregnancy outcomes (APOs), disease course, and associated factors in SSc pregnancies, and to compare APO rates to the general population.

Methods: We included all pregnancies in women with SSc (ACR/EULAR 2013 criteria) or very early SSc (VEDOSS) enrolled in the French prospective GR2 study (2014–2020). We analyzed pregnancies beyond 22 weeks for APOs: fetal demise, preterm delivery≤34 weeks, placental insufficiency complications (preeclampsia, HELLP, fetal growth restriction [FGR], placental abruption), and small for gestational age (SGA, < 10th percentile using AUDIPOG curves). Disease worsening was defined as the appearance or progression of vascular manifestations (cutaneous ulcers, pulmonary arterial hypertension, or renal crisis), interstitial lung disease, worsening of skin fibrosis, calcinosis, joint involvement, or gastrointestinal tract involvement (excluding gastroesophageal reflux disease). Adverse pregnancy outcome rates were compared to those of age-matched controls from the 2016 French perinatal survey.

Results: Fifty-eight pregnancies (52 women) were included: 16 diffuse SSc (27.5%), 34 limited (58.6%), and 8 VEDOSS (13.8%). None had prior pulmonary arterial hypertension or renal crisis. Among 53 pregnancies beyond 22 weeks, 14 (26.4%) had APOs: 2 preterm deliveries (3.8%), 12 placental complications (22.6%; 7 preeclampsia, 5 FGR), and 6 SGA (11.3%). Six women (11.3%) had severe postpartum hemorrhage. Rates of preeclampsia, preterm birth, birth weight < 2500g, and postpartum hemorrhage were significantly higher than in the general population (13.2% vs 3.0%, p=0.001; 13.2% vs 5.8%, p< 0.047; 21.1% vs 4.3%, p< 0.0001; 11.3% vs 1.4%, p< 0.0001). No factors were significantly associated with APO in univariate analysis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Obstetrical complications in 53 pregnancies ongoing after 22 weeks in women with Systemic sclerosis

	All pregnancies (n=53)	lcSSc (n=32)	dcSSc (n=15)	VEDOSS (n=6)
Pregnancy outcome				
Live birth	53 (100.0%)	32 (100.0%)	15 (100.0%)	6 (100.0%)
Adverse pregnancy outcome	14 (26.4%)	9 (28.1%)	3 (20.0%)	2 (33.3%)
Preterm birth ≤34 weeks	2 (3.8%)	1 (3.1%)	1 (6.7%)	0 (0.0%)
SGA < 10th percentile*	6/52 (11.5%)	3/31 (9.7%)	2 (13.3%)	1 (16.7%)
Fetal/Neonatal death after 22 weeks	0 (0.0%)	-	-	-
Placental insufficiency complications	12 (22.6%)	8 (25.0%)	2 (13.3%)	2 (33.3%)
Preeclampsia	7 (13.2%)	5 (15.6%)	1 (6.7%)	1 (16.7%)
HELLP syndrome	2 (3.8%)	1 (3.1%)	0 (0.0%)	1 (16.7%)
FGR	5 (9.4%)	3 (9.4%)	1 (6.7%)	1 (16.7%)
SGA (MD=1)	6 (11.3%)	3 (9.4%)	2 (13.3%)	1 (16.7%)
Characteristics of delivery Vaginal delivery*	35/49 (71.4%)	22/29 (75.9%)	10/14 (71.4%)	3/6 (50.0%)
Cesarean before labor*	9/49 (18.4%)	6/29 (20.7%)	2/14 (14.3%)	1/6 (16.7%)
Cesarean during delivery*	5/49 (10.2%)	1/29 (3.4%)	2/14 (14.3%)	2/6 (33.3%)
Labor induction*	15/46 (32.6%)	6/27 (22.2%)	6/14 (42.9%)	3/5 (60.0%)
Peripartum complications				
Thrombotic event	3 (5.7%)	2 (6.2%)	1 (6.7%)	0 (0.0%)
Severe haemorrhagic event	6 (11.3%)	1 (3.1%)	3 (20.0%)	2 (33.3%)

Data are n (%), or n/N (%) in cases of missing data
*Data not available for all patients
Abbreviations: dcSSc: diffuse cutaneous SSc; GR2: Prospective observational study of the research group on pregnancy in rare diseases; HELLP: Haemolysis and Elevated Liver enzymes, and Low platelets; FGR: Fetal Growth Restriction; lcSSc: limited cutaneous SSc; SGA: Small for gestational Age; SSc: systemic sclerosis; VEDOSS: very early diagnosis of systemic sclerosis.

Table 2. Adverse pregnancy outcomes in women with systemic sclerosis or very early diagnosis of systemic sclerosis (GR2 study) and in the French general population (ENP 2016 study) – Ongoing pregnancies > 22weeks – univariate analysis using conditional logistic regression

	Systemic sclerosis women (n=53)	Matched 2016 ENP women (n=530)	Crude Odds Ratio (95CIs (%)	p**
Preterm birth (<37 weeks)	7 (13.2%)	31 (5.8%)	**2.4[1.01-5.7]**	**0.047**
Preeclampsia	7 (13.2%)	16 (3.0%)	**5.1[1.9-13.5]**	**0.001**
FGR	5 (9.4%)	20 (3.8%)	2.7 [1.0-7.5]	0.06
Birth weight<2500g*	11/52 (21.1%)	23 (4.3%)	**6.1[2.7-13.7]**	**<0.0001**
Induction of labor*	15/46 (32.6%)	109 (20.6%)	1.9 [1.0-3.6]	0.06
Cesarean*	15/50 (30.0%)	109 (20.6%)	1.7 [0.9-3.2]-	0.115
Severe postpartum haemorrhage §	6 (11.3%)	7 (1.4%)	**9.3[3.0-28.8]**	**<0.0001**

Data are n (%), or n/N (%) in cases of missing data
*Data not available for all patients
** Chi2 test or fisher exact test if needed.
§ Severe postpartum haemorrhage: >1000mL of estimated blood loss, the need for red blood cells transfusion, uterine artery embolization, uterine balloon tamponade, vascular ligation, and/or hysterectomy.

Abbreviations: 95CIs: confidence interval; ENP: French perinatal Survey; GR2: Prospective observational study of the research group on pregnancy in rare diseases; FGR: fetal growth restriction;

Disease worsened in 23 of 58 pregnancies (39.7%), mostly cutaneous vascular events, especially postpartum. Risk factors included absence of anti-centromere antibodies (OR=0.2 [0.1–0.8]), diffuse SSc (OR=3.7 [1.1–12.4]), and prior cutaneous vascular involvement (OR=3.7 [1.2–11.5]).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3. Factors associated with worsening of systemic sclerosis or very early diagnosis of systemic sclerosis during pregnancy and one year postpartum (n=58) – univariate analysis

	Disease worsening (n=23)	No disease worsening (n=35)	Crude Odds Ratio [95%IC]	p**
VEDOSS	1 (4.3%)	7 (20.0%)	0.2 [0.02-1.6]	0.13
dcSSc	10 (43.5%)	6 (17.1%)	**3.7 [1.1-12.4]**	**0.028**
lcSSc	12 (52.2%)	22 (62.9%)	0.6 [0.2-1.9]	0.42
Anti-topoisomerase I Ab	10 (43.5%)	9 (25.7%)	2.2 [0.7-6.8]	0.16
Anti-centromere Ab	4 (17.4%)	17 (48.6%)	**0.2 [0.1-0.8]**	**0.016**
Disease duration < 3 years	14 (60.9%)	14 (40.0%)	2.3 [0.8-6.8]	0.12
Prior cutaneous vascular manifestation**	13 (56.5%)	9 (25.7%)	**3.7 [1.2-11.5]**	**0.018**

Data are n (%)
* Prior cutaneous vascular manifestation: fingertip lesions (digital ulcers, pitting scars), before pregnancy
** Chi2 test or fisher exact test if needed.
Abbreviations: Ab: antibody; dcSSc: diffuse cutaneous systemic sclerosis; lcSSc: limited cutaneous systemic sclerosis; SSc: systemic sclerosis; VEDOSS: very early diagnosis of systemic sclerosis.

Conclusion: In this prospective cohort of 58 pregnancies in women with SSc or VEDOSS and no prior severe organ involvement, 91.4% resulted in live births. Despite a relatively low incidence of severe complications, SSc pregnancies were associated with significantly higher rates of APOs and severe postpartum hemorrhage compared to the general population. Disease progression occurred in nearly 40% of cases, particularly affecting skin vascular manifestations during the postpartum period, and was more frequent in women with diffuse cutaneous SSc, prior vascular involvement, and antibodies other than anti-centromere.

Disclosure: A. Murarasu: GlaxoSmithKlein(GSK), 12, supported by GSK, and Chugai for attending meetings; **I. beaudeau**: None; **V. Le Guern**: AstraZeneca, 12, attending meetings and travel., Bristol-Myers Squibb(BMS), 6, Novartis, 2; **g. guettrot-Imbert**: None; **c. cazalets**: None; **c. durant**: None; **C. Yelnik**: None; **C. Roussin**: None; **M. Besse**: None; **E. Berthoux**: None; **E. Chatelus**: None; **E. Hachulla**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, CSL Behring, 5, GlaxoSmithKlein(GSK), 2, 5, 6, Johnson & Johnson, 2, 5, 6, Novartis, 2, 5, Pfizer, 5, Roche-Chugai, 5, Sanofi-Genzyme, 2, 5, Sobi, 5; **E. LAZARO**: None; **F. Maurier**: None; **G. leroux**: None; **G. Pugnet**: None; **I. durieu**: MYLAN, 12, ATTENDING MEETINGS; **L. RAFFRAY**: None; **M. Le Besnerais**: None; **M. roriz**: None; **O. SOUCHAUD-DEBOUVERIE**: None; **P. JEGO**: None; **P. ORQUEVAUX**: None; **C. de Moreuil**: Roche, 5; **H. MAILLARD**: None; **N. Morel**: None; **A. Molto**: AbbVie/Abbott, 2, 5, 6, BIOGEN, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Janssen, 2, 5, 6, Merck/MSD, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB Pharma France, 1, 6; **C. Le Ray**: None; **e. pannier**: None; **I. sentilhes**: None; **L. Mouthon**: Boehringer-Ingelheim, 6, csl, 5, 6, lfb biotechnologies, 5, Roche, 5; **N. Costedoat-Chalumeau**: Bristol-Myers Squibb(BMS), 6, Roche, 5, UCB Pharma France, 5; **B. Chaigne**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2656

Long-term effect of selexipag in systemic sclerosis-associated digital ulcers: a case control, multicentre, observational study

Claudia Iannone[1], Marco Di Battista[2], Maria Rosa Pellico[3], ilaria Magi[4], Antonina Minniti[5], Giuseppe Armentaro[4], Silvia Cavalli[4], Manuel Sette[4], Laura Giudice[4], Cristina Bochicchio[4], Alessandra Della Rossa[6], Antonio Gaetano Tavoni[7], Fabio Cacciapaglia[8], Stefano Stano[9], Martina Orlandi[10], Dilia Giuggioli[11], Marta Mosca[12], Roberto Caporali[13] and Nicoletta Del pAPA[3], [1]University of Milan, Gaetano Pini CTO, Milano, Milan, Italy, [2]Rheumatology Unit, University of Pisa, Pisa, Italy, [3]ASST Pini-CTO, Clinical Rheumatology Unit, Milano, Italy, [4]ASST Pini-CTO, Clinical Rheumatology Unit, Milan, Italy, [5]ASST Gaetano Pini, milano, Milan, Italy, [6]Rheumatology Unit, University of Pisa, Milan, Italy, [7]Clinical Immunology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Milan, Italy, [8]Rheumatology Unit DiMePRe-J, University and AOU Policlinico of Bari & Department of Medicine LUM \"G. De Gegnnaro\" University, Casamassima (Bari) - Italy, Bari, Italy, [9]6. Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area (DiMePRe-J), University of Bari, Bari, Italy, [10]Rheumatology Unit, Department of Medical and Surgical Sciences for Children and Adults, University Hospital of Modena and Reggio Emilia School of Medicine, Italy., modena, Italy, [11]Scleroderma Unit, Rheumatology Unit, University Hospital of Modena and Reggio Emilia, Modena, Italy, Modena, Italy, [12]University of Pisa, Pisa, Pisa, Italy, [13]University of Milan and ASST Gaetano Pini-CTO, Milano, Italy

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical III (2651–2656)

Session Type: Abstract Session

Session Time: 9:30AM–11:00AM

Background/Purpose: Digital ulcers (DUs) affect approximately 50% of SSc patients, causing significant pain and disability. Current management involves both systemic and local therapies. However, the burden in terms of pain and quality of life due to refractory DUs remains heavy. Indeed, over 67% of SSc patients experience >5 DUs in their disease course, reflecting the high burden of this disease domain. While selexipag, an oral selective IP prostacyclin receptor agonist, is approved for the treatment of SSc-associated pulmonary arterial hypertension (PAH), its potential in healing DUs is largely unexplored. We aimed at evaluating the long-term efficacy of selexipag compared to iloprost in treating SSc-DUs.

Methods: This retrospective multicentre study included 96 SSc patients with refractory DUs, 32 treated with selexipag (median dose of 1600mg/day- IQR1100mg) and 64 with intravenous iloprost (0.5–2ng/kg/min), matched for gender, disease subset, and age at diagnosis (Table 1). Both groups were concomitantly treated with conventional vascular therapies (i.e. calcium channel blockers, endothelin receptor antagonists and phosphodiesterase 5- inhibitors). DUs number, ischemic pain and Raynaud phenomenon (RP) severity were assessed at baseline, 6,12, and 24 months. Pain and RP were evaluated using Likert Pain Scale (LPS) and Raynaud Condition Score (RCS), respectively. Additionally, DUs recurrence and new onset were recorded. Healing rates were estimated using Kaplan-Meier analysis.

Results: DUs healing rate was significantly higher in selexipag-treated patients in comparison with iloprost-treated ones (87% vs 28%) at 96 weeks, with the formers achieving faster healing (75% vs 18% by week 40) ($p< 0.001$) (Figure1). DUs number, RCS and LPS scores showed significant improvement in selexipag-treated group compared to iloprost ($p< 0.001$ for all) throughout the 24-month follow-up (Figure 2 A-B-C). Repeated measures analysis demonstrated significant changes over time for all three outcomes. The difference in treatment effect was supported by Mann-Whitney U analyses, showing comparable baseline measures (DUs: $p=0.901$; RCS: $p=0.561$; LPS: $p=0.708$) significant differences emerged by 6 months (DUs: $p=0.001$; RCS: $p< 0.001$; LPS: $p< 0.001$) and were maintained through 12 and 24 months (all $p< 0.001$). Additionally, selexipag-treated patients experienced significantly lower relapse rates (5% vs 45% at 24 months, $p< 0.001$) (Figure2D). Consistently, DUs formation remained lower with selexipag (5% vs 40% at 24 months, $p< 0.001$)(Figure 2E).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Demographics and clinical characteristics of patients treated with iloprost or selexipag.

	Iloprost N = 64	Selexipag N = 32	*p-value*
Sex, F (n, %)	54 (84.4 %)	27 (84.4 %)	1
SSc variant, lcSSc (n, %)	38 (59.4%)	19 (59.4%)	1
Age, (median, IQR)	59.7 (24.4)	56.9 (29.2)	0.92
Age at diagnosis (median, IQR)	41.5 (23.1)	38.7 (26.0)	0.68
Smoking status (n, %)			
Non-smokers	47 (73.4%)	23 (71.9%)	0.62
Previous smokers	8 (12.5%)	6 (18.8%)	0.62
Active smokers	9 (14.1%)	3 (9.4%)	0.62
Autoimmunity (n, %)			
ANA	64 (100%)	32 (100%)	1
Scl70	33 (51.6%)	15 (46.9%)	0.33
ACA	27 (42.2%)	17 (53.1%)	0.38
DUs-therapy latency (median, IQR)	1.1 (3.4)	5.6 (6.7)	0.14
Age at Therapy (median, IQR)	49.3 (25.2)	54.0 (29.3)	0.07
N° of DUs at baseline (median, IQR)	2 (2)	2 (2)	0.55
PDE5i (n, %)	22 (34.4%)	15 (46.9%)	0.270
ERA (n, %)	34 (53.1%)	22 (68.8%)	0.189
CCB (n, %)	32 (50.0%)	14 (43.8%)	0.666
No vasoactive therapy (n, %)	7 (10.9%)	3 (9.4%)	0.268
Therapy with 1 vasoactive agent (n, %)	27 (42.2%)	10 (31.3%)	0.268
CT with 2 vasoactive agents (n, %)	29 (45.3%)	16 (50.0%)	0.268
CT with 3 vasoactive agents (n, %)	1 (1.6%)	4 (9.4%)	0.268
Anti-platelet therapy (n, %)	29 (19.7%)	10 (31.3%)	0.875
Statin (n, %)	15 (23.4%)	6 (18.8%)	0.430
Immunosuppressive therapy (n, %)	33 (51.6%)	18 (56.3%)	0.664
Methotrexate	11(17.2%)	3 (9.4%)	0.370
Mycophenolate	17 (26.6%)	7 (21.9%)	0.617
Tocilizumab	4 (6.3%)	3 (9.4%)	0.579
Rituximab	6 (9.4%)	4 (12.5%)	0.637

F = Female; SSc = Systemic Sclerosis; lcSSc = limited cutaneous Systemic Sclerosis; IQR = Interquartile Range; ANA = Antinuclear Antibodies; Scl70: Antitopoisomerase-I; ACA = Anticentromere Antibodies; DUs = Digital Ulcers;

Demographics and clinical characteristics of patients treated with iloprost or selexipag.

Conclusion: Our study shows that SSc patients treated with selexipag have a better sustained outcome of DUs compared to those treated with intravenous iloprost over 24 months. Furthermore, oral administration and good tolerability profile make selexipag a promising alternative option to standard therapy for SSc-related DUs, overcoming challenges such as difficult venous access, high hospitalization costs, and lost work productivity associated with IV administration. Prospective studies are needed to confirm a wider use of selexipag other than PAH.

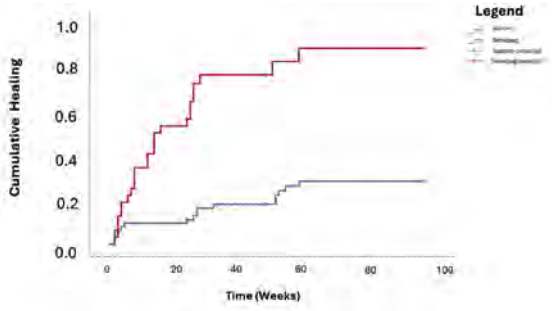


Figure 1. Kaplan-Meier analysis showing cumulative healing rates of DUs in SSc patients treated with selexipag versus iloprost over 96 weeks of follow-up. The vertical dashed line indicates week 40. Censored events are indicated by vertical marks on the curves.

Kaplan-Meier analysis showing cumulative healing rates of DUs in SSc patients treated with selexipag versus iloprost over 96 weeks of follow-up.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

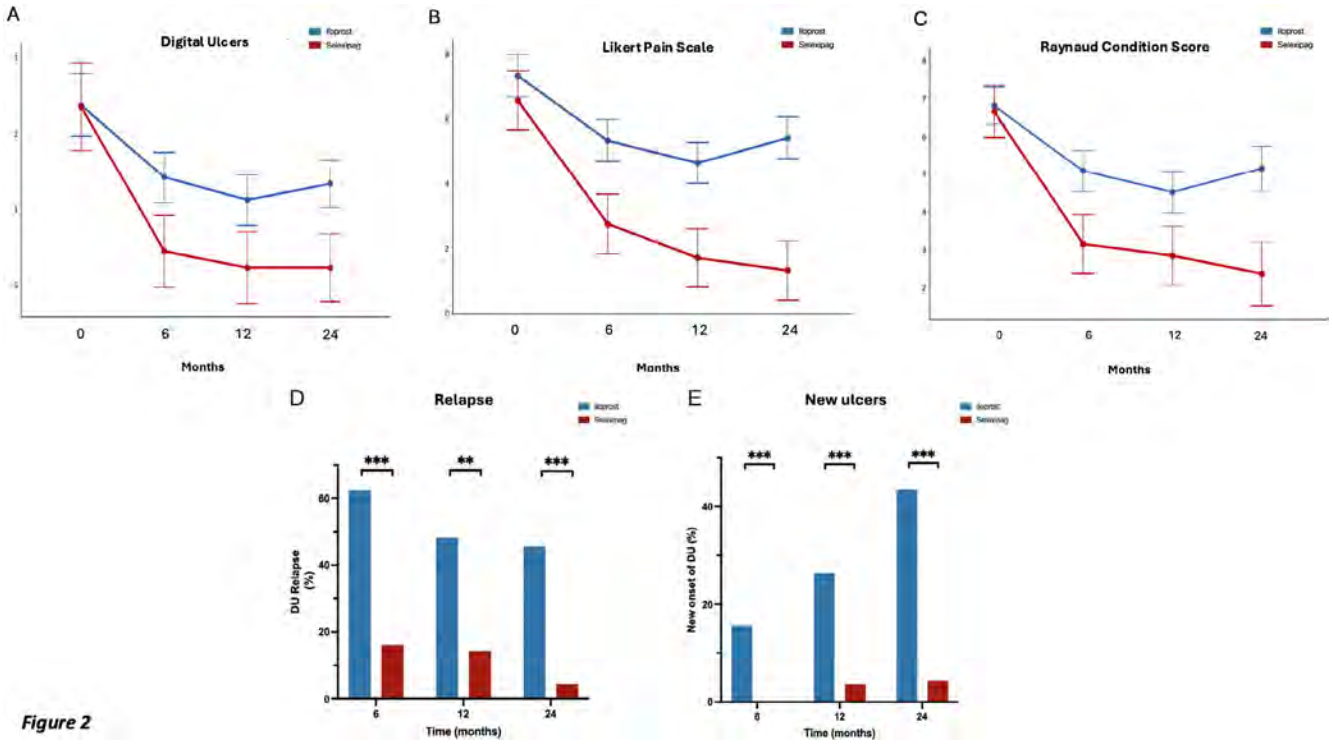


Figure 2

Clinical outcomes comparing Iloprost (blue) versus Selexipag (red) therapies in scleroderma patients over 24 months. Panels show: (A) Digital ulcer reduction, (B) Pain scale improvement, (C) Raynaud condition score decrease, (D) Relapse rates, and (E) New ulcer rates. Error bars represent standard deviation; asterisks indicate statistical significance.

Disclosure: C. Iannone: None; **M. Di Battista**: None; **M. Pellico**: None; **i. Magi**: None; **A. Minniti**: None; **G. Armentaro**: None; **S. Cavalli**: None; **M. Sette**: None; **L. Giudice**: None; **C. Bochicchio**: None; **A. Della Rossa**: None; **A. Tavoni**: None; **F. Cacciapaglia**: None; **S. Stano**: None; **M. Orlandi**: None; **D. Giuggioli**: None; **M. Mosca**: AbbVie, 2, AstraZeneca, 2, 6, Biogen, 2, BMS, 2, Eli Lilly, 6, GSK, 2, 5, 6, Idorsia, 2, Milteny, 2, Novartis, 2, Otsuka, 2, 6, UCB, 2, 6; **R. Caporali**: AbbVie, 2, 6, Amgen, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Eli Lilly & Co., 2, 6, Fresenius Kabi, 2, Galapagos, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, Sandoz, 2, 6, UCB, 2, 6; **N. Del pAPA**: None.

Abstract Number: 2657

Incidence of Rheumatic Diseases Among Patients Receiving GLP-1 Receptor Agonists: A Comparative Analysis with DPP-4 Inhibitors in a Propensity Score-Matched Cohort

Betul Ibis[1], Furkan Bahar[1], Yu-Che Lee[2], Ko-Yun Chang[3], Yu Chang[4] and Cho-Han Chiang[5], [1]Mount Auburn Hospital, Harvard Medical School, Cambridge, MA, [2]University at Buffalo, Buffalo, NY, [3]National Jewish Health, Denver, CO, [4]National Cheng Kung University Hospital, Tainan, Taiwan (Republic of China), [5]Mount Auburn Hospital, Harvard Medical School, Cambridge

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Epidemiology & Public Health I (2657–2662)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: GLP-1 receptor agonists (GLP-1RAs) are increasingly utilized in diabetes mellitus management due to their glucose-lowering and cardiovascular benefits. However, the effect of GLP-1RAs on rheumatic disease incidence is not well defined. This study evaluates the incidence of rheumatic diseases in patients treated with GLP-1RAs, using patients receiving DPP-4 inhibitors (DPP-4i) as a comparator group.

Methods: We conducted a propensity score-matched cohort study utilizing the TriNetX Analytics Network database, comprising anonymized patient data from healthcare institutions worldwide. Adult patients (≥18 years) initiating treatment with GLP-1RAs were matched 1:1 with those initiating DPP-4i therapy based on age, sex, race, hemoglobin A1c levels, BMI, underlying comorbidities, commonly used medications, and diabetes medications to ensure baseline comparability. The primary outcomes included the incidence rates of rheumatoid arthritis, gout, systemic lupus erythematosus, ankylosing

Table 1. Patient baseline characteristics before and after propensity score matching

Variables	Before Matching			After Matching		
	GLP-1RA	DPP-4i	SMD	GLP-1RA	DPP-4i	SMD
Age at Index ,mean	55.6 ± 13.3	63.7 ± 13.5	0.61	59.5 ± 12.5	59.6 ± 13.3	0.01
Male	188533 (46.6)	192470 (53.6)	0.14	110614 (50.9)	111268 (51.2)	0.01
White	243604 (60.2)	144937 (40.4)	0.4	117643 (54.1)	120251 (55.3)	0.02
Black	74337 (18.4)	44801 (12.5)	0.16	35404 (16.3)	36536 (16.8)	0.01
Hispanic	43284 (10.7)	29075 (8.1)	0.09	22505 (10.4)	22696 (10.4)	0
Asian	18033 (4.5)	36365 (10.1)	0.22	13999 (6.4)	13687 (6.3)	0.01
Exam Values						
Hemoglobin A1c ,mean	8.4 ± 2.1	8.3 ± 2.0	0.08	8.4 ± 2.0	8.4 ± 2.1	0
BMI ,mean	35.9 ± 8.1	30.6 ± 7.4	0.68	33.5 ± 7.6	32.7 ± 7.3	0.12
Underlying Comorbidities						
Hypertension	234211 (57.8)	202665 (56.5)	0.03	127959 (58.9)	128142 (59.0)	0
Hyperlipidemia	137333 (33.9)	113992 (31.8)	0.05	74741 (34.4)	75662 (34.8)	0.01
Heart failure	24661 (6.1)	32213 (9.0)	0.11	16086 (7.4)	16466 (7.6)	0.01
Chronic kidney disease	38255 (9.4)	57859 (16.1)	0.2	27164 (12.5)	27498 (12.7)	0
Chronic obstructive pulmonary disease	14495 (3.6)	18578 (5.2)	0.08	9678 (4.5)	9972 (4.6)	0.01
Liver cirrhosis	4197 (1.0)	5013 (1.4)	0.03	2662 (1.2)	2713 (1.2)	0
Connective Tissue Disease	202 (0.0)	134 (0.0)	0.01	84 (0.0)	91 (0.0)	0
Tobacco use	9850 (2.4)	6982 (1.9)	0.03	5161 (2.4)	5307 (2.4)	0
Diabetes Medications						
Metformin	217199 (53.6)	226914 (63.2)	0.2	129626 (59.7)	128330 (59.1)	0.01
Sulfonylureas	76311 (18.8)	105274 (29.3)	0.25	53022 (24.4)	53104 (24.4)	0
Alpha glucosidase inhibitors	1288 (0.3)	6720 (1.9)	0.15	1177 (0.5)	930 (0.4)	0.02
Thiazolidinediones	17414 (4.3)	21800 (6.1)	0.08	11226 (5.2)	11152 (5.1)	0
Sodium-glucose co-transporter 2 (SGLT2) inhibitors	79683 (19.7)	49349 (13.8)	0.16	38551 (17.7)	37382 (17.2)	0.01
Insulin	146180 (36.1)	122003 (34.0)	0.04	78184 (36.0)	78900 (36.3)	0.01
Antiplatelets						
Aspirin	62963 (15.5)	93200 (26.0)	0.26	44465 (20.5)	45020 (20.7)	0.01
Clopidogrel	19725 (4.9)	31604 (8.8)	0.16	14301 (6.6)	14351 (6.6)	0
Prasugrel	1375 (0.3)	1509 (0.4)	0.01	860 (0.4)	831 (0.4)	0
Ticagretor	3704 (0.9)	4226 (1.2)	0.03	2381 (1.1)	2385 (1.1)	0
Medications						
Beta Blocking Agents	104261 (25.7)	125034 (34.8)	0.2	66573 (30.6)	67206 (30.9)	0.01
Statins	207733 (51.3)	214225 (59.7)	0.17	123934 (57.0)	124158 (57.1)	0
Loop diuretics	40255 (9.9)	52573 (14.7)	0.14	26628 (12.3)	27113 (12.5)	0.01
Angiotensin-converting enzyme inhibitor	106146 (26.2)	84672 (23.6)	0.06	60045 (27.6)	61157 (28.1)	0.01
Angiotensin II receptor blockers	88627 (21.9)	104353 (29.1)	0.17	53171 (24.5)	51984 (23.9)	0.01
Other						
Office or Other Outpatient Services	246102 (60.8)	123656 (34.5)	0.55	108194 (49.8)	107820 (49.6)	0
Hospital Inpatient and Observation Care	31866 (7.9)	38145 (10.6)	0.1	21392 (9.8)	22305 (10.3)	0.01
Persons with potential health hazards related to socioeconomic and psychosocial circumstances	5782 (1.4)	4167 (1.2)	0.02	2878 (1.3)	2957 (1.4)	0

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Incidence of rheumatic diseases among patients with GLP-1RA vs DPP-4i group

Table 2. Mortality and incidences of rheumatic disease among patients with GLP-1RA vs DPP-4i group								
Outcomes	GLP1-RA Group			DPP4i Group			Hazard Ratio (CI 95%)	P-value (log rank)
	Cases with outcome	Patient Number at Risk	Incidence rates (per 1000 patient-years)	Cases with outcome	Patient Number at Risk	Incidence rates (per 1000 patient-years)		
Rheumatoid arthritis	485	217,302	2.23	542	217,302	2.49	0.87 (0.77, 0.98)	0.026
Gout	1,827	217,302	8.4	2,157	217,302	9.92	0.82 (0.77, 0.87)	<0.001
SLE	93	217,302	0.42	103	217,302	0.49	0.87 (0.66, 1.16)	0.362
Ankylosing spondylitis	59	217,302	0.27	46	217,302	0.21	1.24 (0.84, 1.83)	0.261
Scleroderma	21	217,302	0.09	23	217,302	0.1	0.88 (0.49, 1.60)	0.693
Psoriatic arthritis	78	217,302	0.35	64	217,302	0.29	1.18 (0.85, 1.64)	0.316
Osteoarthritis	11,700	217,302	53.84	12,367	217,302	56.91	0.91 (0.89, 0.94)	<0.001

spondylitis, scleroderma, psoriatic arthritis, and osteoarthritis within 1 year after the index date. Cox proportional hazards models were employed to assess and compare the risk (hazard ratios [HRs]) of developing various rheumatic diseases between the groups. Statistical significance was set at a p-value < 0.05.

Results: After matching, each group comprised 217,302 patients. Mean age (59.5±12.5 vs. 59.6±13.3 years), sex (50.9% vs. 51.2% males), mean hemoglobin A1c (8.4 ± 2.0 vs. 8.4 ± 2.1), and BMI (33.5 ± 7.6 vs. 32.7 ± 7.3) were similar between groups. Additionally, the GLP-1RA group showed significantly reduced risks of rheumatoid arthritis (HR 0.87; 95% CI 0.77–0.98; p=0.026), gout (HR 0.82; 95% CI 0.77–0.88; p< 0.001), and osteoarthritis (HR 0.92; 95% CI 0.89–0.94; p< 0.001). No significant differences were noted for systemic lupus erythematosus, ankylosing spondylitis, scleroderma, or psoriatic arthritis.

Conclusion: In this propensity score-matched study, GLP-1RA therapy was associated with a significantly reduced incidence of rheumatoid arthritis, gout, osteoarthritis, compared to DPP-4i treatment. These findings suggest beneficial effects of GLP-1RAs on rheumatological outcomes, supporting their broader therapeutic implications in diabetes management.

Disclosure: B. Ibis: None; **F. Bahar**: None; **Y. Lee**: None; **K. Chang**: None; **Y. Chang**: None; **C. Chiang**: None.

Abstract Number: 2658

Risk of Immune-Mediated Inflammatory Diseases and Other Safety Outcomes in Patients with T2DM and Obesity Initiating GLP-1 RA: A Propensity Score-Matched Multi-center Study using the TriNetX Global Network

Hsin-Hua Chen and Wen-Cheng Chao, Taichung Veterans General Hospital, Taichung, Taiwan (Republic of China)

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Epidemiology & Public Health I (2657–2662)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly prescribed for type 2 diabetes mellitus (T2DM) and obesity due to their beneficial metabolic effects. However, real-world evidence on whether GLP-1 RAs affect the incidence of immune-mediated inflammatory diseases (IMIDs), neurologic conditions, psychiatric

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

disorders, or other safety outcomes remains limited. This study evaluated the associations of initiating GLP-1 RAs with the incidence of IMIDs and various clinically important outcomes, including gout, osteoarthritis, and neurodegenerative disorders (dementia, Parkinson disease) in adults with T2DM or obesity.

Methods: We conducted a propensity score-matched retrospective cohort study utilizing data from the global TriNetX federated electronic health records network. Two separate analyses were performed: adults with T2DM (n=793,873) and non-diabetic adults with obesity or overweight (N=79,148). Patients initiating GLP-1 RAs (≥3 prescriptions) were matched 1:1 to comparable patients initiating non-GLP-1 medications based on demographics, BMI, comorbidities, and medication history. Outcomes assessed were new-onset IMIDs, gout, osteoarthritis, and neurodegenerative diseases (dementia, Parkinson's disease). Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using Cox regression. Kaplan-Meier analyses and E-values assessed robustness, and multiple comparison corrections were applied using Bonferroni and False Discovery Rate (FDR).

Results: GLP-1 RA initiation was not associated with increased risk of IMIDs, and musculoskeletal diseases (gout or osteoarthritis) in either cohort. Notably, GLP-1 RA use was associated with significantly lower incidence of all-cause mortality in both T2DM (HR 0.38, 95% CI 0.36-0.40; p< 0.001; E-value=4.70) and obesity cohorts (HR 0.23, 95% CI 0.18-0.30; p< 0.001; E-value=8.16) lower dementia incidence in both T2DM (HR 0.51, 95% CI 0.47–0.55; p< 0.001; E-value=3.33) and obesity cohorts (HR 0.21, 95% CI 0.12–0.36; p< 0.001; E-value=9.99). Parkinson's disease incidence was significantly lower only in the obesity cohort (HR 0.27, 95% CI 0.12–0.58; p< 0.001), but not after adjustment in the T2DM cohort. Use of GLP1 RA was also associated with a lower risk of cardiovascular diseases (heart failure, cerebral infarction and pulmonary embolism/deep vein thrombosis in both T2DM and obesity cohorts.

Conclusion: In patients with T2DM or with overweight/obesity, real-world initiation of GLP-1 receptor agonist therapy was **not associated with an increased risk of autoimmune or inflammatory diseases**. We found no signal that GLP-1 RAs precipitate IMIDs such as RA, lupus, or IBD. Conversely, GLP-1 RA use was linked to significant reductions in all-cause mortality, heart failure, stroke, chronic kidney disease, severe infections, and even dementia, without new safety concerns.

Disclosure: H. Chen: None; **W. Chao**: None.

Abstract Number: 2659

Sodium-Glucose Cotransporter 2 Inhibitors for the Primary Prevention of Systemic Autoimmune Rheumatic Diseases in Patients with Type 2 Diabetes: A Population-Based Target Trial Emulation

Jamie Chieh Lo[1], Karen H. Costenbader[2] and Kevin Sheng-Kai Ma[3], [1]National Taiwan University Hospital, Keelung, Taipei, Taiwan (Republic of China), [2]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [3]Center for Global Health, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States, Philadelphia, PA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Epidemiology & Public Health I (2657–2662)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Treatment with dipeptidyl peptidase-4 inhibitors (DPP4i) have been shown to reduce the risk of systemic autoimmune rheumatic diseases (SARD) in patients with type 2 diabetes (T2D). This study aimed to evaluate the effect of treatment with sodium-glucose cotransporter-2 inhibitors (SGLT2i) on the risk of new-onset SARD.

Methods: This emulated target trial used electronic health records of adults with T2D who initiated either an SGLT2i (canagliflozin, dapagliflozin, empagliflozin, or ertugliflozin) or a DPP4i (alogliptin, saxagliptin, linagliptin, or sitagliptin) between 2016 and 2024 from 101 U.S. healthcare organizations. Propensity score matching was used to balance baseline characteristics. Outcomes included new-onset rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), systemic sclerosis (SSc), Sjögren's syndrome (SjS), mixed connective tissue disease (MCTD), Behcet's disease, polymyalgia rheumatica (PMR), and vasculitis. Patients were followed from initial prescription through incident SARD, end of prescription or switch to the other drug class, death or end of follow-up. Cox proportional hazards models and the log-rank test were used to evaluate the effect of SGLT2i on SARD over time.

Results: A total of 699,1977 pairs of SGLT2i and matched-DPP4i initiators were included. SGLT2i initiators had a significantly lower risk of RA (hazard ratio [HR] 0.77, 95% confidence interval [CI] 0.54-0.58), SLE (HR=0.85, 95% CI 0.79-0.92), SSc (HR 0.80, 95% CI=0.66-0.96), MCTD (HR=0.83, 95% CI=0.80-0.87), PMR (HR=0.67, 95% CI=0.62-0.72), and vasculitis (HR=0.79, 95% CI=0.70-0.89). Risks of Sjögren's and AS were not significantly reduced. Overall risk of any SARD was HR (95%CI). Among the SGLT2i studied, dapagliflozin and empagliflozin showed the most pronounced reductions in the risk of new-onset SARD. Canagliflozin was associated with a reduced risk of new-onset RA and vasculitis.

Conclusion: Treatment with SGLT2i, especially dapagliflozin and empagliflozin, was associated with reduced risks of developing various SARD compared to DPP4i. These findings provide evidence for the broader immunomodulatory effects of SGLT2i. Prospective studies on the roles of SGLT2i in attenuating inflammation and autoimmunity are warranted to validate the finding.

Disclosure: J. Lo: Gilead, 6; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **K. Sheng-Kai Ma**: None.

Abstract Number: 2660

Understanding Gout in Women: Longitudinal Changes in Serum Urate Levels from Pre-menopause through Post-menopause

Shreya Billa[1], Sho Fukui[1], Misti Paudel[2], Takahiro Suzuki[3], Ryosuke Imai[4], Yuntae Kim[5], Takehiro Nakai[6], Hiromichi Tamaki[6], mitsumasa kishimoto[7], Hilde Ørbo[1], Sara Tedeschi[1], Hyon K. Choi[8], Masato Okada[9] and Daniel Solomon[1], [1]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [3]Department of Cardiovascular Medicine, St. Luke's International Hospital, Tokyo, Japan, [4]Department of Pulmonary Medicine, St. Luke's International Hospital, Tokyo, Japan, [5]Department of Gastroenterology, St. Luke's International Hospital, Tokyo, Japan, [6]Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan, [7]Kyorin University School of Medicine, Tokyo, Japan, [8]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [9]Immuno-Rheumatology Center, St. Luke's International Hospital, Tokyo, Japan

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Epidemiology & Public Health I (2657–2662)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Understanding longitudinal changes in serum urate (SU) allows for the development of evidence-based interventions for gout. Post-menopausal women, who are at risk of gout, have increased SU levels. This increase is partially attributed to the loss of estrogen's protective effect on kidney function. While cross-sectional studies have been conducted, longitudinal SU changes during the menopausal transition and interactions with coexisting conditions that modify SU, such as BMI and estimated glomerular filtration rate (eGFR), are not well studied.

Methods: This retrospective longitudinal cohort study included Japanese women who underwent annual medical examinations from April 2004 to September 2024. Each woman had at least one visit before and after a self-report of menopause. Women with possible surgical menopause and those who received hormonal therapy were excluded. The median date between the two consecutive visits before and after menopause was considered the date of menopause for statistical analyses. Menopausal transition stages were temporally categorized as pre-menopause (>5 years before menopause), peri-menopause (from 5 years before up until menopause), and post-menopause (after menopause). Longitudinal changes in SU and hyperuricemia (HU: SU ≥6.8 mg/dL or taking medications for gout/HU) were examined by interrupted time-series

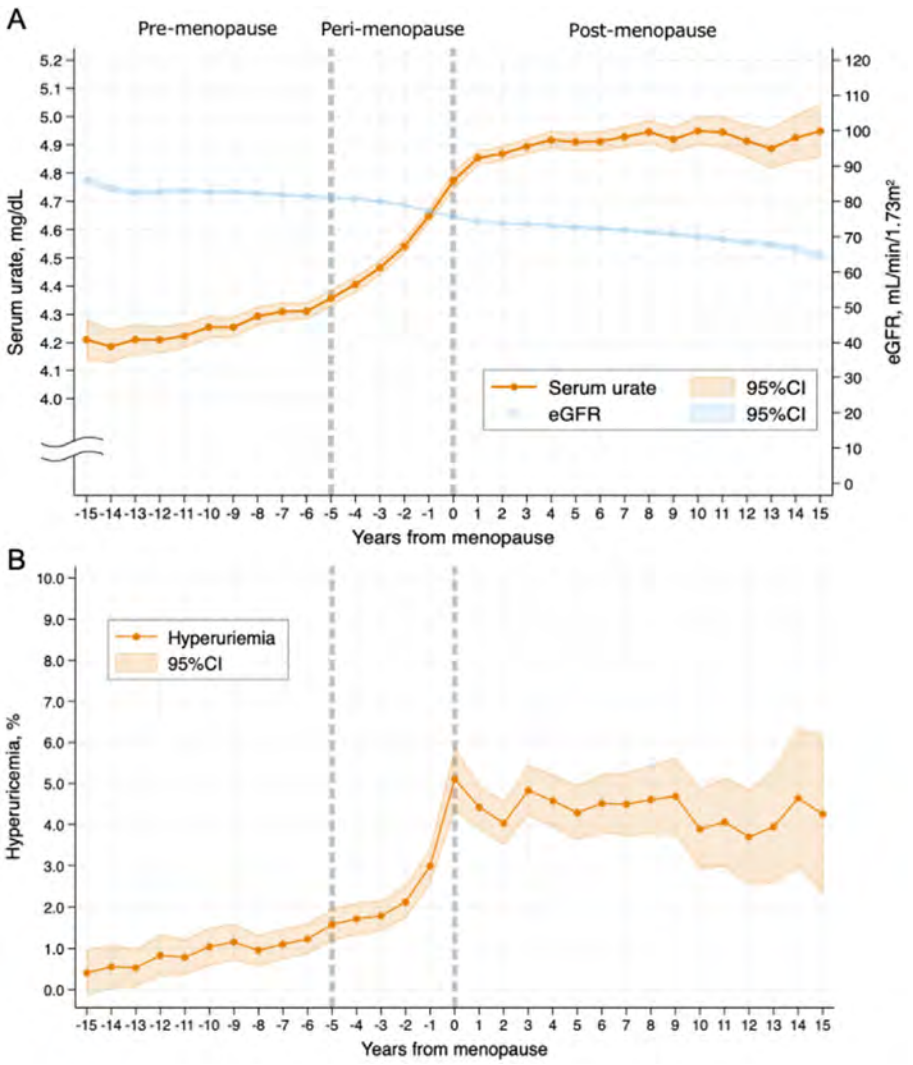


Figure 1. Longitudinal trends in serum urate and hyperuricemia observed in women. Mean serum urate levels (A) and the proportion who had hyperuricemia (B) with a 95% CI were described. The date of menopause was defined as the median date between the two consecutive visits immediately before and after the self-reported menopause occurrence. The time from menopause was calculated for each visit. Participant data was then summarized by years since menopause. eGFR, estimated glomerular filtration rate; CI, confidence intervals

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Result of interrupted time-series analyses for serum urate levels in women

	Model 1 β coefficient (95%CI)	Model 2 β coefficient (95%CI)
*Mean SU level difference by the menopausal stages		
Pre-menopause	Reference	Reference
Peri-menopause	0.286 (0.261, 0.310)	0.334 (0.242, 0.426)
Post-menopause	0.410 (0.387, 0.433)	0.369 (0.267, 0.471)
SU slope in pre-menopausal stage (annual SU change)	0.033 (0.030, 0.035)	0.022 (0.019, 0.025)
**Additional slope change		
Pre-menopause	Reference	Reference
Peri-menopause	0.062 (0.057, 0.067)	0.053 (0.049, 0.058)
Post-menopause	-0.017 (-0.021, -0.014)	-0.022 (-0.025, -0.019)
eGFR, per mL/min/1.73 m^2		-0.011 (-0.012, -0.011)
***Product term of eGFR and menopause stages		
Pre-menopause		Reference
Peri-menopause		-0.002 (-0.003, -0.002)
Post-menopause		-0.003 (-0.004, -0.003)
BMI, per kg/m^2		0.076 (0.072, 0.080)
***Product term of BMI and menopause stages		
Pre-menopause		Reference
Peri-menopause		0.005 (0.001, 0.008)
Post-menopause		0.013 (0.009, 0.017)

Model 1 included time from menopause + menopause stage + time from menopause*menopause stage
Model 2 included model 1 variables + age at menopause + BMI + eGFR + smoking status + alcohol intake + medication use for hypertension, diabetes, and dyslipidemia + eGFR*menopause stage + BMI*menopause stage
CI, confidence interval; eGFR, estimated glomerular filtration rate; BMI, body mass index

*Difference in SU mean relative to the reference (pre-menopausal stage)
**Change in SU relative to the annual change in SU of the reference (pre-menopausal stage)
***Change in SU for each unit of change in eGFR or BMI relative to the reference (pre-menopausal stage)

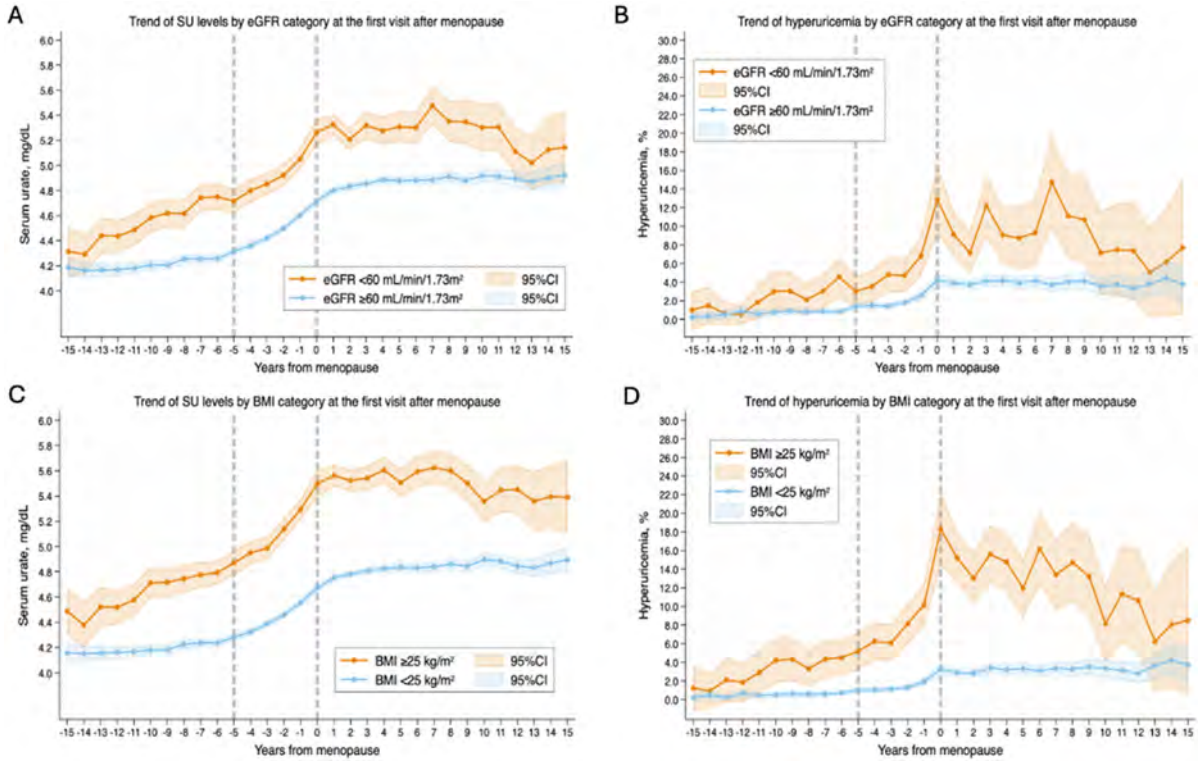


Figure 2. Longitudinal trends in serum urate by subgroups of women. Mean serum urate levels (A, C) and the proportion who had hyperuricemia (B, D) with a 95% CI were described by stratified subgroups of eGFR (A, B) and BMI (C, D) The date of menopause was defined as the median date between the two consecutive visits immediately before and after the self-reported menopause occurrence. The time from menopause was calculated for each visit. Participant data was then summarized by years since menopause. The information at the first visit after menopause was used for stratification. eGFR, estimated glomerular filtration rate; BMI, body mass index; CI, confidence intervals

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

analyses and evaluated across subgroups stratified by median menopausal age, kidney function (eGFR < 60 or ≥ 60 mL/min/1.73 m^2), BMI (< 25 or ≥ 25 kg/m^2), and alcohol intake (≥1 drink/day or no drinks) at the first visit after menopause.

Results: We analyzed 8,169 eligible participants with 93,511 visits over a median follow-up of 13.8 years. SU gradually increased during pre-menopause, rose rapidly during peri-menopause, and stabilized post-menopause (**Figure 1**). Compared to pre-menopause, the mean SU level was 0.41 mg/dL (95% CI: 0.38, 0.43) higher during post-menopause. SU increased by 0.033 mg/dL per year (95% CI: 0.030, 0.035) during pre-menopause. The slope changed to 0.095 mg/dL (+0.062 mg/dL [95% CI: 0.057, 0.067]) during peri-menopause and 0.016 mg/dL (–0.017 mg/dL [95% CI: –0.021, –0.014]) during post-menopause (**Table 1**). HU prevalence was < 1.0% during pre-menopause, began to increase approximately 2-3 years before menopause, and was 4-5% during post-menopause (**Figure 1**). Association of SU levels with eGFR and BMI were also larger during peri-menopause and post-menopause compared to pre-menopause (**Table 1**). Women with an eGFR < 60 mL/min/1.73 m^2 and a BMI ≥ 25 kg/m^2 had a greater rise in SU during peri-menopause: HU was observed in approximately 18% of overweight or obese women at menopause (**Figure 2**).

Conclusion: This longitudinal study found that SU levels and HU prevalence drastically increase several years before menopause and are already elevated by the time of menopause. Maintaining a healthy body weight and preserving kidney function prior to menopause may decrease post-menopausal HU and potentially control subsequent gout in women.

Disclosure: S. Billa: None; **S. Fukui**: None; **M. Paudel**: None; **T. Suzuki**: None; **R. Imai**: None; **Y. Kim**: None; **T. Nakai**: None; **H. Tamaki**: AbbVie/Abbott, 6, Astellas Pharma, 6, Ayumi Pharma, 6, Chugai pharmaceutical, 6, Dai-ichi-Sankyo, 12, Personal Fees, Eisai, 12, Personal Fees, GSK, 12, Personal Fees, Illy-lily, 12, Personal Fees, Kyowa-KIrin, 6, Ono pharmaceutical, 6, Pfizer, 12, Personal Fees, Takeda Pharmaceutical, 6, Tanabe-Mitsubishi, 6; **m. kishimoto**: AbbVie, 2, 6, Amgen, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi, 2, 6, BMS, 2, 6, Celgene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Johnson & Johnson, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Takeda, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **H. Ørbo**: None; **S. Tedeschi**: Alexion, 5, Amgen, 2, Avalo Therapeutics, 2, Fresenius Kabi, 2, Kyowa Kirin, 2, Merck/MSD, 2, Novartis, 2; **H. Choi**: Ani, 2, LG, 2, Shanton, 2, Sobi, 2; **M. Okada**: Astellas, 6, Eli Lilly and Company, 6, GSK, 6, Janssen, 6; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9.

Abstract Number: 2661

Heterogeneity of RA-ILD by Longitudinal Forced Vital Capacity Measurements Is Associated with Survival and Respiratory Hospitalization

Bryant England[1], Yangyuna Yang[1], Punyasha Roul[2], Tate Johnson[1], Scott Matson[3], Grant Cannon[4], Brian Sauer[5], Jeffrey Curtis[6], Joshua Baker[7] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]UNMC, Omaha, NE, [3]University of Kansas, Kansas City, MO, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]Salt Lake City VA/University of Utah, Salt Lake City, UT, [6]Foundation for Advancing Science, Technology, Education and Research, Birmingham, AL, [7]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Epidemiology & Public Health I (2657–2662)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

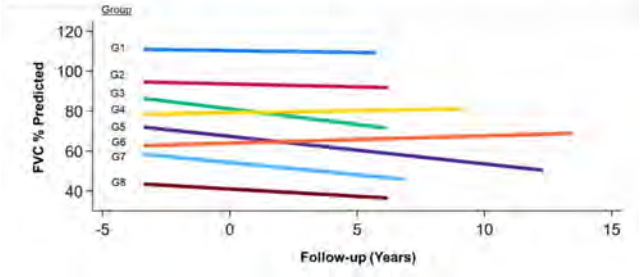
Background/Purpose: Forced vital capacity (FVC) is one of the primary disease measures monitored in RA-associated interstitial lung disease (RA-ILD). While prior studies have suggested a minority of RA-ILD patients fulfill a progressive phenotype specified for inclusion in antifibrotic clinical trials, the trajectories of FVC over time in large, real-world RA-ILD populations are not well described. We investigated FVC trajectories among RA-ILD patients within the Veterans Health Administration, the largest integrated healthcare system in the U.S.

Methods: We performed a cohort study of RA-ILD patients within the Veterans Health Administration between 1999 and 2021. RA-ILD patients were identified using validated RA and ILD algorithms (>80% PPV for RA-ILD), then followed until death or end of study. FVC values were obtained from VA databases of pulmonary function test (PFT) results and also extracted from clinical notes (when primary PFT results were not available) using a validated natural language processing tool. All available FVC values were utilized. Group based trajectory modeling was utilized to derive unique longitudinal trajectories of FVC values, with selection of the optimal numbers of trajectories determined by model fit characteristics (AIC/BIC), group size, and clinical interpretability. Trajectory group membership was used to predict survival and respiratory hospitalization following RA-ILD index date in Cox regression models that included age, sex, race, smoking status, comorbidity burden, and calendar year.

Results: We studied 5,172 RA-ILD patients (92.3% male, mean age 68.8 years) with 18,007 FVC values and identified eight unique FVC trajectories (**Figure 1**). While initial FVC values were a major determinant of group membership, four of eight trajectory groups (54% of patients) were characterized by a mean FVC % predicted decline >0.7%/year during follow-up (range -0.73 to -1.56%/year). Over 24,780 patient-years of follow-up, 3,400 deaths and 2,763 respiratory hospitalizations occurred. Survival significantly differed across FVC trajectory groups, with trajectory groups characterized by greater FVC decline being associated with poorer survival (adjusted HR 1.56 [1.45-1.67] for groups 3, 5, 7, and 8 combined progressive vs. groups 1, 2, 4, and 6 combined non-progressive) (**Figure 2A-B**). Progressive trajectory groups were also associated with respiratory hospitalization risk (**Figure 3A**) with the combined progressive FVC trajectory groups having a >1.6-fold higher risk than the combined non-progressive groups (**Figure 3B**). Findings persisted when adjusting for baseline FVC (not shown).

Conclusion: Within a large, national RA-ILD population, we identified eight unique trajectories of the RA-ILD disease course characterized by differing patterns of longitudinal FVC values. A progressive RA-ILD disease course (mean decline in FVC % predicted of 0.7 to 1.6 per year) occurred amongst 54% of RA-ILD patients and was predictive of poorer survival and respiratory hospitalization. These findings highlight RA-ILD heterogeneity and the prognostic value of monitoring disease trajectories with longitudinal FVC measurements.

Figure 1. Unique trajectories of forced vital capacity measurements among patients with RA-ILD.



Group	% of RA-ILD patients	FVC % pred. Intercept	ΔFVC%/year (Std. Error)
1	2.3	110.3	-0.19 (0.11)
2	20.5	93.5	-0.29 (0.08)
3*	8.7	81.1	**-1.56 (0.14)**
4	20.1	79.1	0.21 (0.09)
5*	23.9	67.3	**-1.38 (0.09)**
6	3.2	63.9	0.36 (0.09)
7*	18.1	54.2	**-1.22 (0.07)**
8*	3.3	40.9	**-0.73 (0.11)**

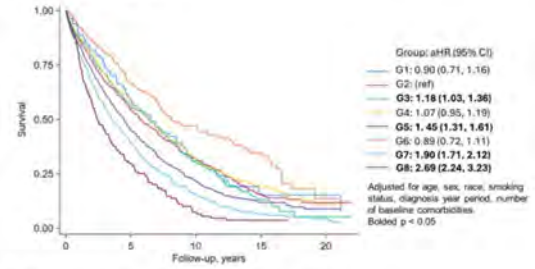
*Denotes groups considered progressive

Abbreviations: FVC, forced vital capacity; RA-ILD, rheumatoid arthritis-associated interstitial lung disease

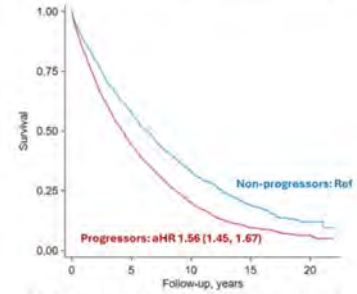
23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Kaplan-Meier curves depicting survival among RA-ILD patients by FVC trajectory group assignment.

A. All FVC trajectory groups.



B. Progressive vs. non-progressive FVC trajectory groups.

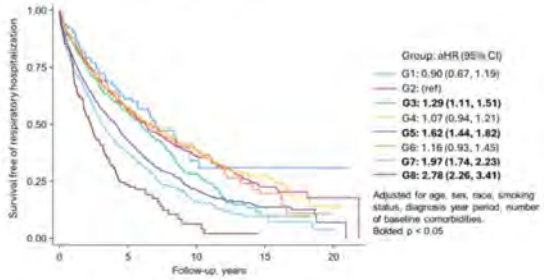


Adjusted for age, sex, race, smoking status, diagnosis year period, number of baseline comorbidities.

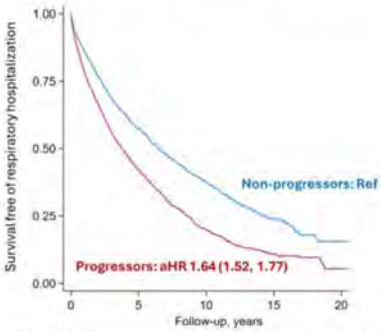
Progressors = groups 3, 5, 7, 8
Non-progressors = groups 1, 2, 4, 6

Figure 3. Kaplan-Meier curves depicting survival free of respiratory hospitalization by forced vital capacity trajectory groups.

A. All FVC trajectory groups.



B. Progressive vs. non-progressive FVC trajectory groups.



Adjusted for age, sex, race, smoking status, diagnosis year period, number of baseline comorbidities

Progressors = groups 3, 5, 7, 8
Non-progressors = groups 1, 2, 4, 6

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: B. England: Boehringer-Ingelheim, 2, 5; **Y. Yang**: None; **P. Roul**: None; **T. Johnson**: None; **S. Matson**: None; **G. Cannon**: None; **B. Sauer**: None; **J. Curtis**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bendcare, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Glaxo Smith Kline, 2, 5, Horizon, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sanofi, 2, 5, Scipher medicine, 2, 5, SetPoint, 2, 5, UCB, 2, 5; **J. Baker**: None; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1.

Abstract Number: 2662

Target trial emulation of biologic and targeted synthetic disease-modifying antirheumatic drugs in rheumatoid arthritis-associated interstitial lung disease

Gregory McDermott[1], Daniel Solomon[2], Jeffrey Sparks[3] and Rishi Desai[3], [1]Brigham and Women's Hospital, Brookline, MA, [2]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Epidemiology & Public Health I (2657–2662)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: RA-ILD is associated with high mortality, but the optimal treatment approach is unclear. While immunosuppressants may treat inflammatory components of ILD, there are concerns about pro-fibrotic effects and increased infection risk. Prior studies investigating specific biologic or targeted synthetic DMARDs (b/tsDMARDs) in RA-ILD had small sample size, and no randomized trials have been performed. Despite this limited evidence, the 2023 ACR/CHEST guideline conditionally recommended rituximab as initial RA-ILD therapy.

Methods: Nationwide data from Medicare Parts A/B/D from 1/1/2006 to 12/31/2019 (n=7,993,101 patients) served as the data source. We identified patients with RA-ILD to emulate target trials comparing b/tsDMARDs. RA-ILD patients had ≥2 RA ICD-9/10 codes, ≥1 DMARD prescription 7-365 days after RA ICD code, and ≥2 ILD ICD codes, including ≥1 ILD ICD code from a pulmonologist (PPV 81%). We emulated target trials comparing patients with RA-ILD initiating abatacept, tocilizumab, JAK inhibitors, or TNF inhibitors, each compared to rituximab. The index date was first b/tsDMARD after RA-ILD diagnosis. The primary outcome was a composite of respiratory hospitalization (including respiratory infections), lung transplant, or death. We constructed propensity scores (PS) for treatment selection using 46 pre-exposure variables including year of enrollment, demographic factors, RA-related factors (including line of therapy and oral glucocorticoids), pulmonary factors, comorbidities, medications, healthcare utilization, and Medicare low-income subsidy eligibility. After 1:1 PS matching and using an intention-to-treat follow up, we constructed Kaplan-Meier curves and used Cox regression to estimate hazard ratios for the composite outcome and its components.

Results: After PS matching, we analyzed RA-ILD patients (mean age 74 years, 70% female) initiating abatacept (n=701), JAK inhibitor (n=152), tocilizumab (n=390), or TNFi (n=773), each compared to an equal number of rituximab initiators. Separate emulated target trials were used for each two-way comparison. PS matching successfully achieved balance in baseline covariates between treatment groups. Comparing each b/tsDMARD to rituximab, there were no significant differences in the risk of the composite outcome of respiratory hospitalization, lung transplant, or death: abatacept (HR 0.88 95%CI 0.76-1.02), JAK inhibitor (HR 0.75 95%CI 0.51-1.11), tocilizumab (HR 1.03 95%CI 0.84-1.28), or TNF inhibitor (HR 1.01 95%CI 0.88-1.16), each compared to rituximab (**Figure 1**). Separate analyses found no statistically significant differences between b/tsDMARDs and rituximab for respiratory hospitalization or death (**Figure 2**).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1: Kaplan-Meier curves showing event-free survival of respiratory hospitalization, death, or lung transplant among RA-ILD patients after initiation of abatacept, JAK inhibitor, tocilizumab, or TNF inhibitors compared to rituximab in propensity score-matched analyses.

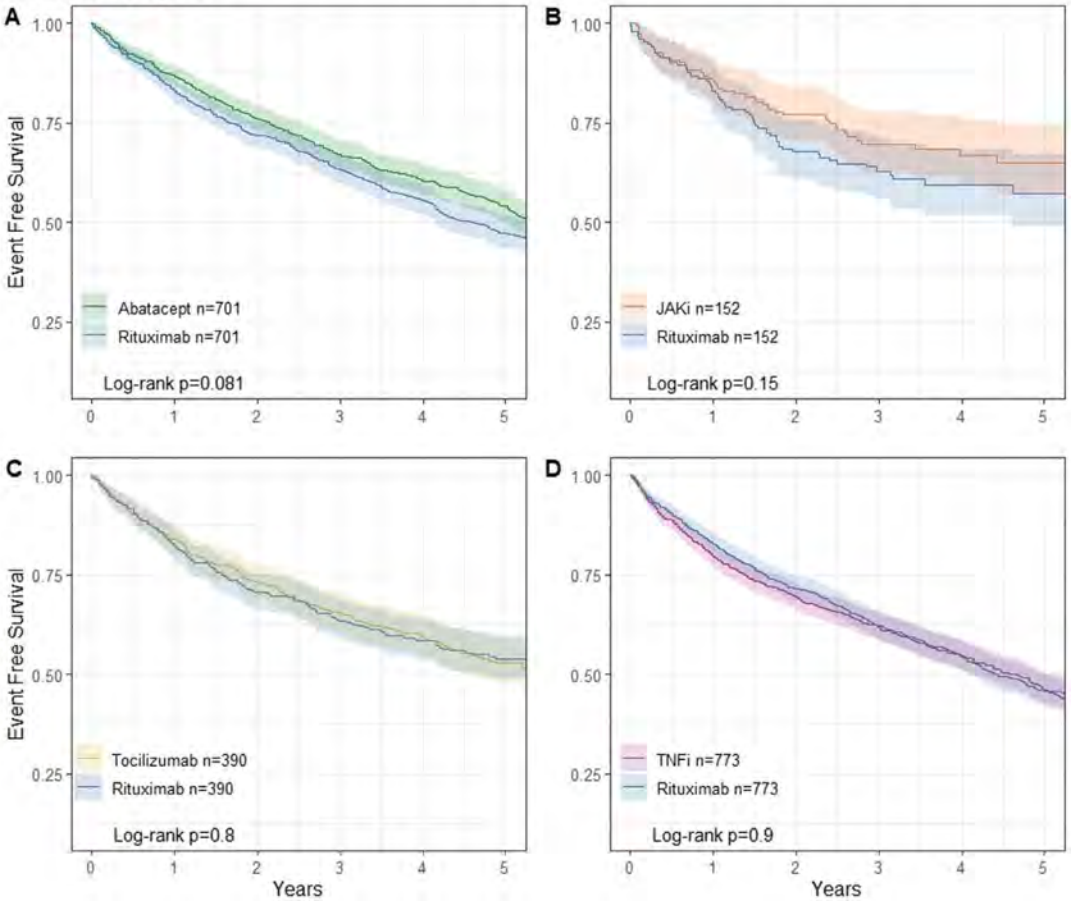
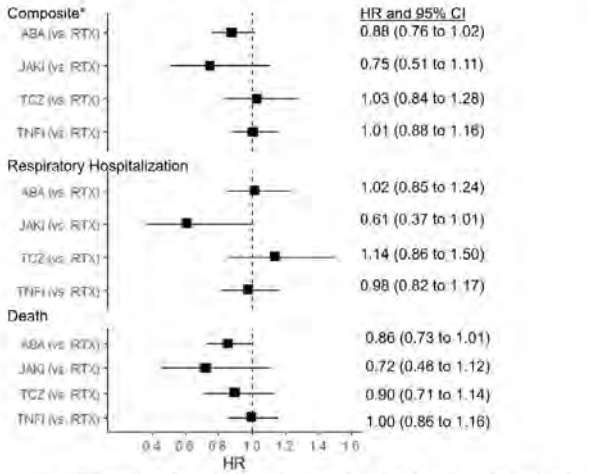


Figure 2: Hazard ratios for composite outcome of respiratory hospitalization, lung transplant, or death among RA-ILD patients initiating abatacept, JAK inhibitors, tocilizumab, TNF inhibitors, or rituximab in propensity-score matched analyses



* Composite outcome of respiratory hospitalization, lung transplant, or death (There were an insufficient number of lung transplants to model separately)

ABA = abatacept, JAKi = janus kinase inhibitor, TNFi = tumor necrosis factor inhibitor, TCZ = tocilizumab

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Despite rituximab being conditionally recommended as first line treatment for RA-ILD in the recent ACR/CHEST guideline, we found no significant differences between rituximab and other b/tsDMARDs in the risk of respiratory hospitalization, lung transplant, or death. There were nonsignificant findings of decreased mortality in RA-ILD patients treated with abatacept or JAK inhibitors compared to rituximab. These findings highlight the need for randomized controlled trials in RA-ILD.

Disclosure: G. McDermott: None; **D. Solomon**: Amgen, 5, CorEvitas, 5, GreenCape Health, 8, Janssen, 5, UpToDate, 9; **J. Sparks**: Boehringer Ingelheim, 5, Bristol-Myers Squibb (BMS), 5, Janssen, 5; **R. Desai**: Bayer, 5, Novartis, 5, Vertex, 5.

Abstract Number: 2663

PAXIS: A Randomized, Double-Blind, Placebo-Controlled, Dose Finding Phase 2 Study (Part 1) Followed by an Open-Label Period (Part 2) to Assess the Efficacy and Safety of Pacritinib in Patients with VEXAS Syndrome

David Beck[1], Mael Heiblig[2], Sinisa Savic[3], Marcela ferrada[4], Arsène Mekinian[5], Onima Chowdhury[6], Danielle Hammond[7], Lachelle D. Weeks[8], Carmelo Gurnari[9], Yohei Kirino[10], Sophie georgin-Lavialle[11], Sarah A. Buckley[12], Bryan G. harder[12], Sandra Goble[12] and Matthew Koster[13], [1]Center for Human Genetics and Genomics, NYU Grossman School of Medicine. Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine. Department of Biochemistry and Molecular Pharmacology, NYU Grossman School of Medicine, New York, NY, USA, New York, NY, [2]Lyon-Sud Hospital, Hospices Civils de Lyon, Paris and Université Claude Bernard, Lyon, France, [3]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [4]University of Maryland, Bethesda, MD, [5]Department of Internal Medicine, Inflammation-Immunopathology-Biotherapy Department (DMU i3), Saint-Antoine University Hospital, 75012 Paris, France, Paris, France, [6]Oxford University Hospitals' NHS Foundation Trust and Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, United Kingdom, [7]The University of Texas MD Anderson Cancer Center, Houston, TX, [8]Dana Farber Cancer Institute, Boston, MA, [9]Department of Biomedicine and Prevention, University of Rome Tor Vergata and Translational Hematology and Oncology Research Department, Taussig Cancer Center, Cleveland Clinic, Clevland, OH, Rome, Italy, [10]Yokohama City University Graduate School of Medicine, Yokohama, Japan, [11]Sorbonne university, Tenon hospital, DMU3ID, CEREMAIA, ERN RITA, Paris, France, [12]Sobi Inc., Waltham, MA, [13]Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye (2663–2668)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: VEXAS syndrome (Vacuoles, E1 ubiquitin-activating enzyme, X-linked, Autoinflammatory, Somatic) is a systemic disorder characterized by an overlap of hematologic and inflammatory features. Treatment poses a challenge, as most immunomodulators fail to control the disease, resulting in a requirement for moderate to high doses of glucocorticoids (GCs). Pacritinib, an oral inhibitor of IRAK1, JAK2, and ACVR1, is FDA-approved for myelofibrosis with severe thrombocytopenia (platelets < 50 x 10^9/L) and has emerged as a potential treatment for VEXAS syndrome.

Methods: PAXIS is an international, randomized, multicentre, double-blind, placebo-controlled phase 2 dose finding trial. It is designed to assess pacritinib in adult patients with VEXAS syndrome. Inclusion criteria include documented evidence of past inflammatory involvement and ongoing GCs for ≥4 consecutive weeks at a baseline dose of 15-45 mg/day. Previous exposure to non-GC therapies is allowed, but patients must undergo a washout period. Exclusion criteria include prior allogeneic hematopoietic stem cell transplantation, receiving ≥9 units of red blood cell transfusion in the prior 90 days,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

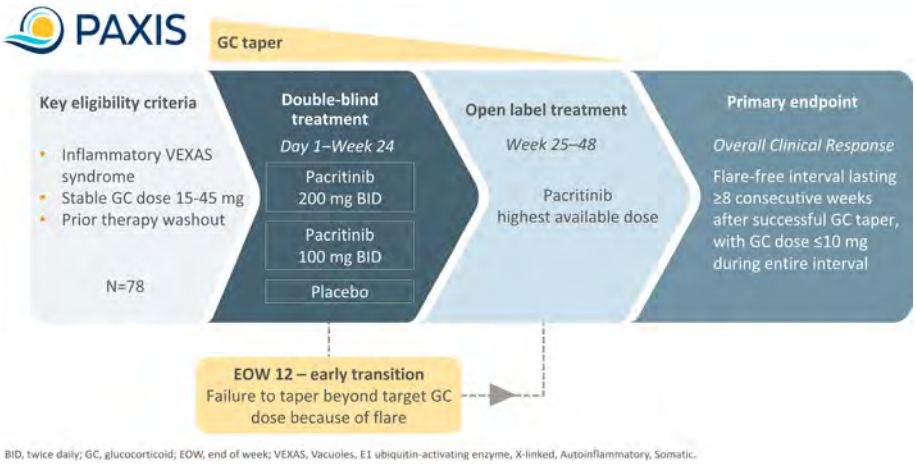


Figure 1: PAXIS Study Design

concurrent myelodysplastic syndrome requiring antineoplastic treatment, and exposure to any HMAs in the previous 6 months or exposure to more than 4 cycles of HMAs at any time.

The study will consist of a screening period, a double-blind period (up to end of week 24), an open-label period (up to end of week 48), and a 30-day post-end of treatment period (**Figure 1**). Patients (n=78) will be randomized 1:1:1 to receive pacritinib 200 mg twice daily (BID), pacritinib 100 mg BID, or placebo (26 per arm). All patients will follow a fixed GC taper.

Results: The primary endpoint (assessed during the double-blind period) is the proportion of patients who achieve Overall Clinical Response, defined as having a flare-free interval lasting ≥8 weeks following a GC taper, and a GC dose during the interval of ≤10 mg/day. Secondary endpoints include number of flare free days with GC dose < 10 mg/day, hematologic improvement (in platelets and hemoglobin), change in quality-of-life measures, and safety. Exploratory endpoints include change in symptoms based on the VEXAS-symptom assessment form (VEXAS-SAF), change in disease activity measured by the Clinical Global Impression of Change (CGI-C) and the VEXAS-disease activity index (VEXAS-DAI), change in variant allele frequency (VAF) of *UBA1* by next generation sequencing (NGS), and improvement in GC toxicity as measured by the glucocorticoid toxicity index (GTI). PAXIS is anticipated to enroll at 40 sites across 8 countries.

Conclusion: The PAXIS study represents a significant step forward in the treatment of VEXAS syndrome. As the first randomized, double-blind placebo-controlled pharmacotherapy trial for this disease, it has the potential to redefine treatment and address unmet needs for this complex, refractory, and sometimes fatal condition.

This abstract has been accepted for publication by the European Alliance of Associations for Rheumatology (EULAR). The definitive copyedited version is available online at: www.ard.eular.org

Disclosure: D. Beck: Alexion, 2, Genesis Therapeutics, 2, GSK, 2, Novartis, 2, Sobi, 2; **M. Heiblig**: AbbVie, 2, Astellas, 2, Blueprint, 2, BMS/Celgebe, 2, Jazz Pharmaceuticals, 2, Servier, 2; **S. Savic**: BioCryst, 2, Celldex, 2, CSL Behring, 2, 5, KalVista, 2, 6, Novartis, 2, 5, 6, Pharming, 2, 6, Phavaris, 2, Sobi, 2, Takeda, 2, 6; **M. ferrada**: UpToDate, 9; **A. Mekinian**: Roche, 5; **O. Chowdhury**: Jazz Pharmaceuticals, 6, Novartis, 6; **D. Hammond**: None; **L. Weeks**: AbbVie, 2, Sobi, 2, Vertex, 2; **C. Gurnari**: Alexion, 5, Genesis Therapeutics, 2; **Y. Kirino**: Amgen, 6, Novartis, 2, 6, Sobi, 2; **S. georgin-Lavialle**: Novartis, 2, Sobi, 2; **S. Buckley**: Sobi, Inc., 3; **B. harder**: Sobi, Inc., 3; **S. Goble**: Sobi, Inc., 3; **M. Koster**: Amgen, 2.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2664

Neutrophil-to-Lymphocyte Ratio (NLR) as a Clinically Accessible Marker for Interferon Signatures in Autoimmune Diseases

YOSHINOBU KOYAMA[1], KENTA SHIDAHARA[2], YU NAKAI[2], YOSHIHARU SATO[3] and YOSHINORI NISHIURA[2], [1]Japanese Red Cross Okayama Hospital, Okayama, Okayama, Japan, [2]Japan Red Cross Okayama Hospital, Okayama-shi, Okayama, Japan, [3]DNA Chip Research Inc., Kawasaki-shi, Kanagawa, Japan

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye (2663–2668)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Interferons (IFNs) play critical roles in systemic autoimmune diseases, particularly systemic lupus erythematosus (SLE), where heightened type I IFN signaling is a hallmark. Elevated IFN activity is also observed in rheumatoid arthritis (RA), systemic sclerosis (SSc), and idiopathic inflammatory myopathy (IIM), making IFNs promising therapeutic targets. However, their pathogenic involvement varies among patients. In the TULIP trial, anifrolumab showed greater efficacy in SLE patients with elevated type I IFN signatures. Although IFN signatures derived from transcriptomic profiles are valuable biomarkers, their clinical utility is limited by cost. At ACR 2024, we reported a strong correlation between the neutrophil-to-lymphocyte ratio (NLR) and IFN signatures in patients with SLE. This study investigated whether the NLR can serve as a practical surrogate for IFN signatures in SLE, RA, SSc, and IIM patients.

Methods: We enrolled 236 patients with autoimmune diseases: 36 with SLE, 31 with RA, 95 with SSc, and 74 with IIM. Whole-blood RNA was subjected to transcriptome analysis. Seventy-three genes were assigned as type I IFN-related, 94 as type II, and 10 as type III. The IFN signature score was calculated as the sum of the Z scores for each group. The $\log_2$-transformed NLR ($\log_2$NLR) was derived from clinical blood data obtained at the time of RNA sampling. Correlations between the Log_2NLR and type I–III IFN scores were evaluated.

Results: Log_2NLR significantly correlated with all three IFN signatures across diseases.

In **SLE**, strong correlations were observed with type I IFN ($R^2 = 0.40$, $P = 5.99\times10^{-12}$), type II IFN ($R^2 = 0.29$, $P = 2.77\times10^{-8}$), and type III IFN ($R^2 = 0.57$, $P = 1.32\times10^{-7}$).

In **SSc**, the correlations were even stronger: type I IFN ($R^2 = 0.57$, $P = 1.74\times10^{-7}$), type II IFN ($R^2 = 0.36$, $P = 1.74\times10^{-7}$), and type III IFN ($R^2 = 0.63$, $P = 9.79\times10^{-22}$).

In **RA**, the associations were weaker but significant: type I IFN ($R^2 = 0.19$, $P = 0.013$), type II IFN ($R^2 = 0.13$, $P = 0.042$), and type III IFN ($R^2 = 0.44$, $P = 5.00\times10^{-5}$).

In **IIM**, correlations were also significant: type I IFN ($R^2 = 0.17$, $P = 0.0002$), type II IFN ($R^2 = 0.06$, $P = 0.032$), and type III IFN ($R^2 = 0.37$, $P = 1.01\times10^{-8}$).

Conclusion: The NLR was significantly correlated with type I, II, and III IFN signatures in patients with SLE, SSc, RA, and IIM. The strongest associations were observed in SLE and SSc patients, indicating a more consistent IFN-driven pathogenesis in these diseases. In contrast, RA and IIM showed weaker associations, possibly reflecting greater disease heterogeneity and variable IFN involvement. Among the IFN types, the type III IFN signature showed the most consistent and strongest

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

correlation with the NLR. Given its simplicity and availability, the NLR has emerged as a practical and cost-effective surrogate biomarker for IFN activation, with potential utility in clinical decision-making across autoimmune diseases.

Disclosure: Y. KOYAMA: AstraZeneca, 5, Novartis, 5, Ono, 5; **K. SHIDAHARA**: None; **Y. NAKAI**: None; **Y. SATO**: None; **Y. NISHIURA**: None.

Abstract Number: 2665

Preexisting Antibodies Against Vaccine Antigens Are Preserved In Patients With Systemic Lupus Erythematosus and Sjögren's Disease Upon Ianalumab Treatment While Autoantibodies Decline

Thomas Dörner[1], Nan Shen[2], **Thomas Grader-Beck**[3], Caroline Walter[4], Catherine Wioland[4], Celine Rauld[4], Patrick Schmutz[4], Simone Riek[4], Wolfgang Hueber[5], CAROLE SIPS[6], Stephen Oliver[4], Carol Lau[7], Claire Bonal[6] and Isabelle Isnardi[8], [1]Charite Universitätsmedizin Berlin, Germany and DRFZ, Berlin, Berlin, Germany, [2]Shanghai Jiang Tong University School of Medicine, Shanghai, China (People's Republic), [3]Johns Hopkins, Reisterstown, MD, [4]Novartis Pharma AG, Basel, Switzerland, [5]Novartis Pharmaceuticals, Basel, Switzerland, [6]Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland, [7]Novartis Pharmaceuticals Corporation, East Hanover, [8]Novartis, Gueberschwihr, France

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye (2663–2668)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Ianalumab, an afucosylated mAb, depletes B cells via enhanced antibody (Ab)-dependent cellular cytotoxicity and blocks B cell-activating factor (BAFF): BAFF-receptor (BAFF-R) mediated signals.[1] It is currently being assessed for the treatment of immune-mediated diseases. Given its novel mode of action, it is crucial to assess the effects of ianalumab on preexisting Abs against vaccine antigens (Ags). We evaluated the impact of ianalumab treatment vs placebo on pre-existing Ab levels against 7 pathogens in patients with SLE and Sjögren's disease (SjD).

Methods: A retrospective analysis was conducted on serum samples from 2 randomized, double-blind (DB), placebo-controlled, phase 2 studies in patients with SjD (NCT02962895) or SLE (NCT03656562). Patients received either placebo or ianalumab 300 mg subcutaneously monthly for 24 weeks (79 with SjD) or for 28 weeks (40 with SLE). In SjD study, patients on 300 mg ianalumab at Week (W) 24 were re-randomized to receive DB monthly ianalumab 300 mg or placebo until W52. Patients on placebo at W24 were switched to a lower ianalumab dose and were excluded from further analysis. In the SLE study, all the patients switched from DB to open label ianalumab up to W52. Abs (IgG isotypes) to vaccine Ags and auto-Abs were measured at baseline (BL), W24 (SjD) or W28 (SLE), and W52. Changes in Ab levels from BL and proportions of patients maintaining protective levels at W52 were assessed. Three patients (2 SjD and 1 SLE) received booster doses against diphtheria and tetanus toxoid (TTd) under ianalumab treatment.

Results: The proportion of patients with SjD and SLE maintaining protective Ab levels against TTd, measles, mumps, varicella, rubella, diphtheria, and influenza remained stable after 52 weeks of ianalumab treatment. In SjD, changes from BL to W24 were < 6% for all Ags in both groups. In SLE, changes from BL to W28 were < 10% in both groups for all Ags besides diphtheria (**Fig. 1**). For diphtheria, up to 18% changes were seen with ianalumab treatment, likely due to the low preexisting protection (< 50% of patients had protective levels at BL). By contrast, several auto-Abs showed a significant reduction in ianalumab-treated patients (e.g. up to 60% reduction of anti-ribosomal P Abs at W28) compared with placebo (**Fig. 1**). These results align with ianalumab's ability to deplete memory and Ab-producing cells,[2] while likely not affecting the long-

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

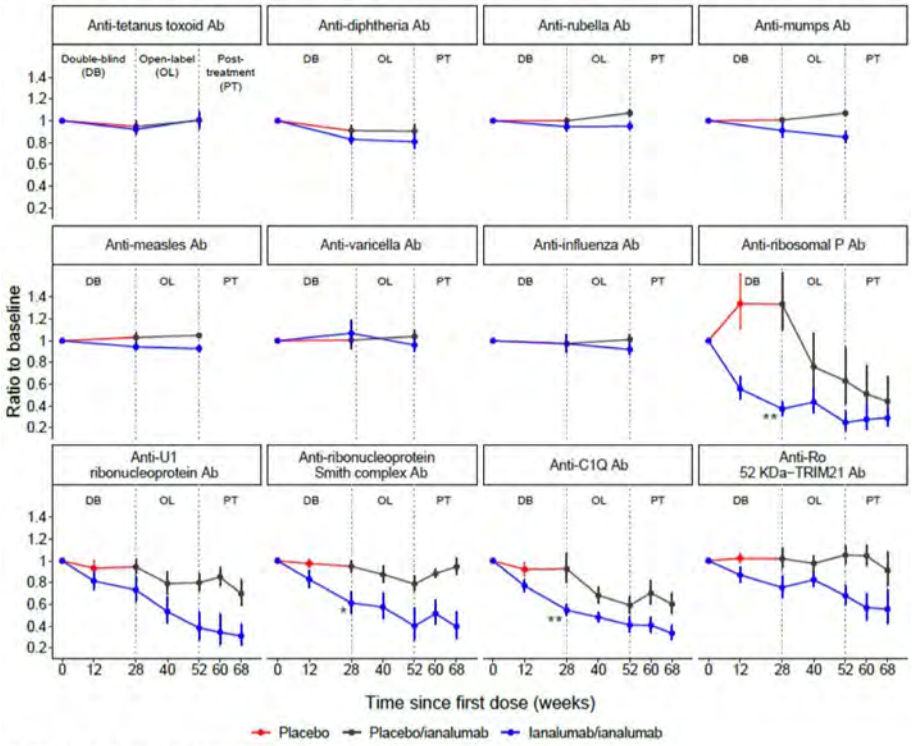


Figure 1. Titers from vaccine antigens and auto-antibody titers following treatment with ianalumab or placebo over time in patients with SLE.
Ratio to baseline of antibodies to vaccine antigens and autoantibodies were measured over time in patients with SLE treated with placebo vs ianalumab. All antibodies measured were IgG.

Significance values were calculated at the end of the double-blind period (28 weeks). *P<0.05; **P<0.01.
Ab, antibody; IgG, immunoglobulin G; SLE, systemic lupus erythematosus.

lived bone marrow plasma cells that do not express BAFF-R.[3] Among the 3 patients who received booster doses against diphtheria and TTd during ianalumab treatment, 2 showed a subsequent increase in corresponding titers, whereas the other patient received the booster only 10 days before W52 sampling, which explains no increase in titers.

Conclusion: Treatment with ianalumab up to 52 weeks did not result in a reduction of the Ab titers to previous immunizations against tetanus, varicella, measles, mumps, rubella, diphtheria, and influenza while having a clear impact on auto-Ab levels.

References

1. McWilliams EM, et al. *Blood Adv* 2019;3(3):447-460.
2. Dörner T, et al. *Ann Rheum Dis* 2024;83:956-957.
3. Darce JR, et al. *J Immunol* 2007;179 (11):7276-7286.

Disclosure: T. Dörner: AbbVie, 5, 12, Consulting fees, Celgene, 5, 12, Consulting fees, Deutsche Forschungsgemeinschaft, 5, Eli Lilly, 5, 12, Consulting fees, EMD Merck Serono, 5, 12, Consulting fees, EU Horizon2020 Harmonic SS, 5, Gilead/Galapagos, 12, Consulting fees, GlaxoSmithKlein(GSK), 5, 12, EMD Merck Serono, Janssen, 5, 12, EMD Merck Serono, Novartis, 5, 12, EMD Merck Serono, Roche, 5, 12, EMD Merck Serono, Sanofi, 5, UCB, 5; **N. Shen**: None; **T. Grader-Beck**: Argenx, 5, 12, Consulting fees, Bristol-Myers Squibb(BMS), 5, 12, Consulting fees, Novartis, 5, 12, Consulting fees; **C. Walter**: Novartis, 3, 12, Shareholder; **C. Wioland**: Novartis, 3, 12, Shareholder; **C. Rauld**: Novartis, 3, 12, Shareholder; **P. Schmutz**: Novartis, 3, 12, Shareholder; **S. Riek**: Novartis, 3, 12, Shareholder; **W. Hueber**: Novartis, 3, 11; **C. SIPS**: Novartis, 3, 11; **S. Oliver**: Novartis, 3, 11; **C. Lau**: Novartis, 3, 12, Shareholder; **C. Bonal**: Novartis, 3, 11; **I. Isnardi**: Novartis, 3, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2666

Rare *TNFAIP3* Hypomorphic Variants are a Massively Underestimated Driver of Human Autoinflammatory Disease

Danica Lee[1], Urekha Karri[2], Yiming Luo[3], Kader Cetin Gedik[4], Manuel Carpio Tumba[5], Prabal Chhibbar[6], Priyamvada Roy[6], Guido Falduto[7], Jishnu Das[5] and Daniella Schwartz[5], [1]University of Pittsburgh School of Medicine, Pittsburgh, PA, [2]School of public health, Pittsburgh, PA, [3]Columbia University, New York, NY, [4]UPMC Children's Hospital of Pittsburgh/ University of Pittsburgh, Pittsburgh, PA, [5]University of Pittsburgh, Pittsburgh, PA, [6]University of Pittsburgh School of Medicine, Pittsburgh, [7]University of Pittsburgh Medical Center, Pittsburgh, PA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye (2663–2668)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: *TNFAIP3* encodes the ubiquitin editing enzyme A20, which inhibits multiple proinflammatory signaling pathways. Heterozygous germline mutations in *TNFAIP3* cause the autoinflammatory disease Haploinsufficiency of A20 (HA20). The prevalence of HA20 is thought to be low, with only 200 reported cases, yet HA20 is clinically heterogeneous and has variable severity. The full spectrum of disease-causing and disease-modifying *TNFAIP3* variants is unknown. Therefore, we hypothesized that HA20 prevalence is underestimated due to ascertainment bias.

Methods: To better understand HA20 prevalence and ascertain its full phenotypic spectrum, we analyzed three large population databases with whole genome sequencing data: gnomad v4 (730,947 exomes; 76,215 genomes), All of Us v7 (244,845 genomes and electronic health records (EHR) data), and UK BioBank (500,000 genomes and EHR data). We identified individuals harboring rare (MAF< 0.01%) predicted loss-of-function (pLOF) variants (frameshift, truncating, splice null) or rare predicted pathogenic missense (pPM) variants (CADD≥30; SIFT=deleterious; PolyPhen=probably damaging). Phenome-wide association studies (PheWAS) determined conditions that were significantly associated with pLOFs and pPMs. We then functionally validated the variants by performing luciferase assays to measure TNF-induced NF-kB activation, Western blot to measure basal A20 expression, and cycloheximide assays to measure protein stability. Lastly, we compared our results from these "virtual" cohorts to a "referral" cohort of patients seen at our medical center who harbor LOF (48 subjects, 17 variants) or missense (14 subjects, 9 variants) *TNFAIP3* mutations.

Results: pLOF variants had a mean prevalence of 1:14,403, while pPM variants had a mean prevalence of 1:2,782, suggesting that ~100,000 to 2.9 million individuals worldwide may suffer from A20-insufficient disease. *TNFAIP3* variants conferred a 164-fold risk of Behcet's disease and a 14-fold to 138-fold risk of other HA20-associated phenotypes like

Table 1. Prevalence estimates of pLOF or missense TNFAIP3 variants in the US (AoU), UK (UKBB), and globally (gnomAD). Number of individuals harboring pLOF variants, or pPM variants (missense variants with CADD^{3}30; SIFT=deleterious; PolyPhen=probably damaging; MAF<0.01%). Mean prevalence of the variants and affected number of individuals were estimated based on the 2024 U.S. Census count of 340.1 million.

	GnomAD v4	All of Us v7	UKBB
Genomes	807,162	244,845	500,000
# of subjects with pLOF variants (# of variants)	34 (30)	17 (11)	7 (7)
Mean prevalence of pLOFs only	1:23,740	1:14,403	1:71,249
95% CI (Wilson-Brown)	1:16,990-1:33,172	1:8,992-1:23,067	1:34,600-1:147,454
Estimated affected US population	14,326	23,613	4,762
# of subjects with pLOF or missense variants (# of variants)	164 (56)	87 (37)	173 (30)
Mean Prevalence of pLOF or missense variants	1:4,922	1:2,782	1:2,2890
95% CI (Wilson-Brown)	1:4,224-1:5,735	1:2,259-1:3,427	1:2,491-1:3,355
Estimated affected US population	69,097	122,250	117,681

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

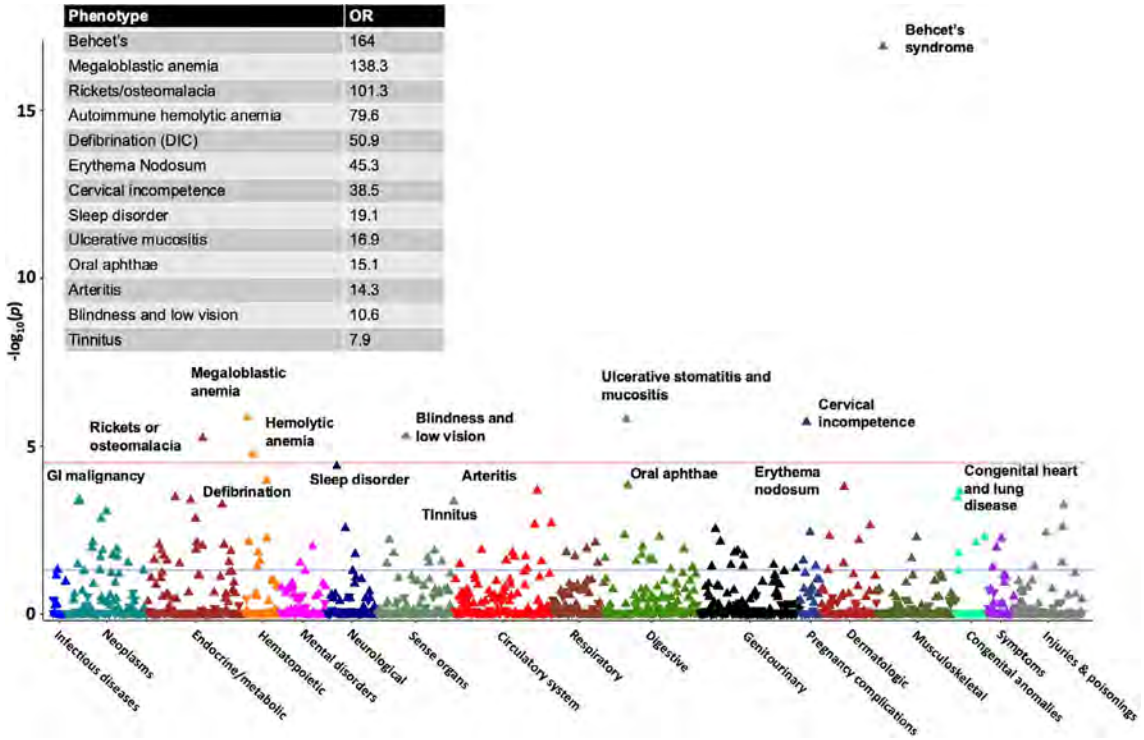


Figure 1. Inflammatory conditions are significantly associated with pathogenic TNFAIP3 variants. Manhattan plot of conditions that are significantly associated with rare pathogenic TNFAIP3 variants in meta-PheWAS of AoU and UKBB data. Each data point represents one condition. Blue line represents uncorrected p-value and red line represents Bonferroni adjusted p-value. The table above reports odds ratio (OR) for top associated conditions compared to control cohort.

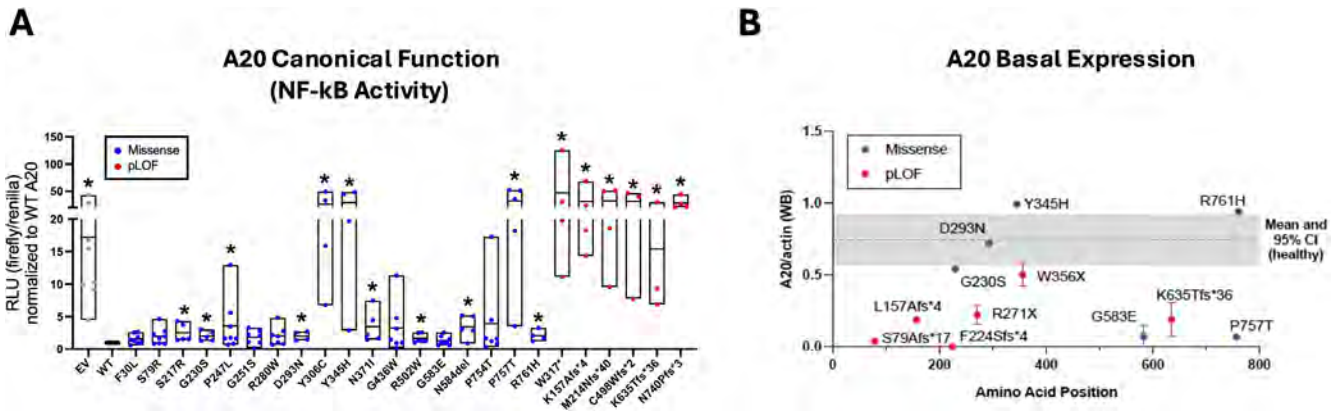


Figure 2. Hypomorphic TNFAIP3 variants can affect A20 function and/or expression. (A) Over-expressed mutant A20 proteins fail to suppress TNF-induced NF-kB activity in A20-deficient HEK293 cells transfected with the luciferase reporter plasmid (*p<0.05, ratio paired t-test); WT = wild-type, EV = empty vector. (B) Basal A20 expression (Western blot) of A20 variants, expression normalized to actin.

stomatitis/mucositis, vasculitis, and autoimmune hemolytic anemia (PheWAS, p < 1e-5, Bonferroni). *In vitro*, variants reduced A20 stability, expression, and/or TNF-induced NF-kB activation. In our Pittsburgh cohort, patients exhibited clinical autoinflammation and/or autoimmunity as well as evidence of basally activated TNF-NFκB, inflammasome-IL-1β, and/or Type I interferon signaling. LOF and missense variants either increased A20 protein degradation, resulted in production of an A20 protein unable to suppress TNF-induced NFkB activation, or reduced both protein stability and function. Patients exhibited >90% response to therapies targeting A20-regulated pathways such as TNF, IL-1, and JAK inhibitors.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Together, these data suggest that hypomorphic *TNFAIP3* variants are a massively underrecognized cause of autoinflammation with high disease burden. Increased recognition and expanded genetic testing could potentially improve health outcomes by directing these patients towards more precise immune-targeting therapies.

Disclosure: D. Lee: None; **U. Karri**: None; **Y. Luo**: None; **K. Cetin Gedik**: None; **M. Carpio Tumba**: None; **P. Chhibbar**: None; **P. Roy**: None; **G. Falduto**: None; **J. Das**: None; **D. Schwartz**: Eli Lilly, 5, Jeffrey Modell Foundation, 5, National Institutes of Health, 5, Samuel and Emma Winters Foundation, 5, Sobi, 1, 5.

Abstract Number: 2667

Amyloidosis Secondary to Familial Mediterranean Fever: Machine Learning Based Prediction Models

Berkay Aktas[1], Enes Azman[1], Yusuf Ecren Oner[2], kadir Kaya[2], husnu Mert Yuksel[3], Ali Hosgel[2], Dilan Karahan[2], Zehra Beyza Coban[2], Kerem parlar[4], Ozgur Can Kilinc[1], Beste Acar[1] and serdal Ugurlu[5], [1]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [2]Istanbul University-Cerrahpasa, Istanbul, Turkey, Istanbul, Turkey, [3]Istanbul University-Cerrahpasa, Istanbul, Turkey, Istanbul, Istanbul, Turkey, [4]Cerrahpasa Faculty of Medicine, Istanbul University-Cerrahpasa, İstanbul, Turkey, [5]Istanbul University-Cerrahpasa, Department of Internal Medicine, Division of Rheumatology, Istanbul, Turkey

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye (2663–2668)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Familial Mediterranean Fever (FMF) is a monogenic autoinflammatory disease caused by MEFV mutations. Amyloidosis remains its most serious complication, with several risk factors reported in the literature. Traditional models, used to identify these factors, are limited by their reliance on linearity and inability to capture complex patterns in high-dimensional datasets. Machine learning ensemble models have not yet been applied to predict amyloidosis in FMF. This study aimed to develop and compare the performance of logistic regression, Random Forest and Gradient Boosting models.

Methods: From a database of 920 FMF patients diagnosed and followed at our rheumatology department between 1990–2022, records were retrieved. Patients without available documents or those followed elsewhere were excluded. Diagnoses were validated using Tel-Hashomer criteria and patients later found to have other diseases were excluded. Biopsy-confirmed amyloid fibrils were required to classify patients as having amyloidosis. Demographic, clinical, genetic, and laboratory data were recorded.

Imputation with MICE method was done in R in respect to alignment of imputed dataset to original dataset. The imputed dataset loaded into Python and training-test sets (0.8:0.2) were created (random state=42). Logistic Regression, Random Forest, Gradient Boosting models were created thereafter. Recursive feature elimination was applied for logistic regression and Synthetic Minority Oversampling Technique (SMOTE) was used to oversample amyloidosis cases and prevent overfitting. Mann-Whitney and chi-squared tests were used for comparisons.

Results: Of 920 FMF patients, 615 with available data were included, 58 (9.4%) of whom had biopsy-confirmed amyloidosis. Variable comparisons between patients with and without amyloidosis are shown in Table 1. Age at symptom onset, diagnostic delay, disease duration, M694V homozygosity, frequent infections, arthritis, erysipelas-like erythema, myalgia, protracted febrile myalgia, and median CRP were significantly associated with amyloidosis ($p < 0.001$).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Characteristics of the Patients with and without Amyloidosis

	FMF (n=557)	FMF with Amyloidosis (n=58)	p value
Age at Symptom Onset, median (IQR)	11 (7-20)	7 (4.5-12.5)	**<0.001**
Diagnostic Delay, years, median (IQR)	3 (0-11)	10 (2.5-18)	**<0.001**
Disease Duration, years, median (IQR)	24 (20-31)	35 (26-43)	**<0.001**
Female Gender, n (%)	347 (62)	27 (47)	**0.028**
Higher Educational Status, n (%)	208 (37)	23 (40)	0.104
M694V Homozygous, n (%)	133 (24)	34 (59)	**<0.001**
Presence of Comorbidity, n (%)	180 (32)	34 (59)	**0.003**
Consanguinity in Parents, n (%)	87 (16)	18 (31)	**0.01**
Family History of FMF, n (%)	311 (56)	41 (71)	0.125
Family History of other rheumatic/inflammatory disease, n (%)	183 (33)	25 (43)	0.27
Malignancy, n (%)	9 (1.6)	3 (5)	0.41
Frequent Infection, n (%)	67 (12)	18 (31)	**<0.001**
Clinical Features, n (%)			
• Fever	433 (78)	50 (86)	0.61
• Abdominal Pain	471 (85)	50 (86)	0.32
• Chest Pain	202 (36)	31 (53)	**0.029**
• Arthralgia	381 (68)	53 (91)	**0.002**
• Arthritis	220 (39)	37 (64)	**<0.001**
• Erysipelas Like Erythema	83 (15)	28 (48)	**<0.001**
• Myalgia	185 (33)	37 (64)	**<0.001**
• Protracted Febrile Myalgia	44 (8)	18 (31)	**<0.001**
Age at Colchicine Initiation, median (IQR)	20 (12-29.5)	21 (14.5-31)	0.23
Regular Follow-up, n (%)	281 (50)	35 (60)	0.59
Irregular Use of Colchicine	238 (43)	21 (36)	0.08
Median CRP, median (IQR)	2.31 (0.77-5.54)	5.34 (1.41-9.27)	**<0.001**

Among the models, Random Forest performed best (AUC: 0.70, F1: 0.3, Precision: 0.375, Recall:0.25), followed by Gradient Boosting (AUC: 0.65, F1: 0.2, Precision: 0.17, Recall:0.25) and Logistic Regression (AUC: 0.60, F1: 0.17, Precision: 0.13, Recall:0.25). AUC curves and Shapley Additive Explanations (SHAP) values for the Random Forest model are shown in Figure 1 and Figure 2, respectively.

Conclusion: To our knowledege, this is the first study showing that ensemble machine learning models outperform logistic regression in predicting amyloidosis in FMF patients. Despite inherently "opaque" machinary and lower interpretability, these ensemble models are valuable given their superior performance. Furhtermore, increasing the Random Forest decision threshold to 0.6 raised precision to 0.75, enabling more efficient patient screening, especially in underserved areas. Advancing these models requires continued collaboration and a multidisciplinary approach. We invite the healthcare community to join in this effort to achieve meaningful progress and improved patient outcomes.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

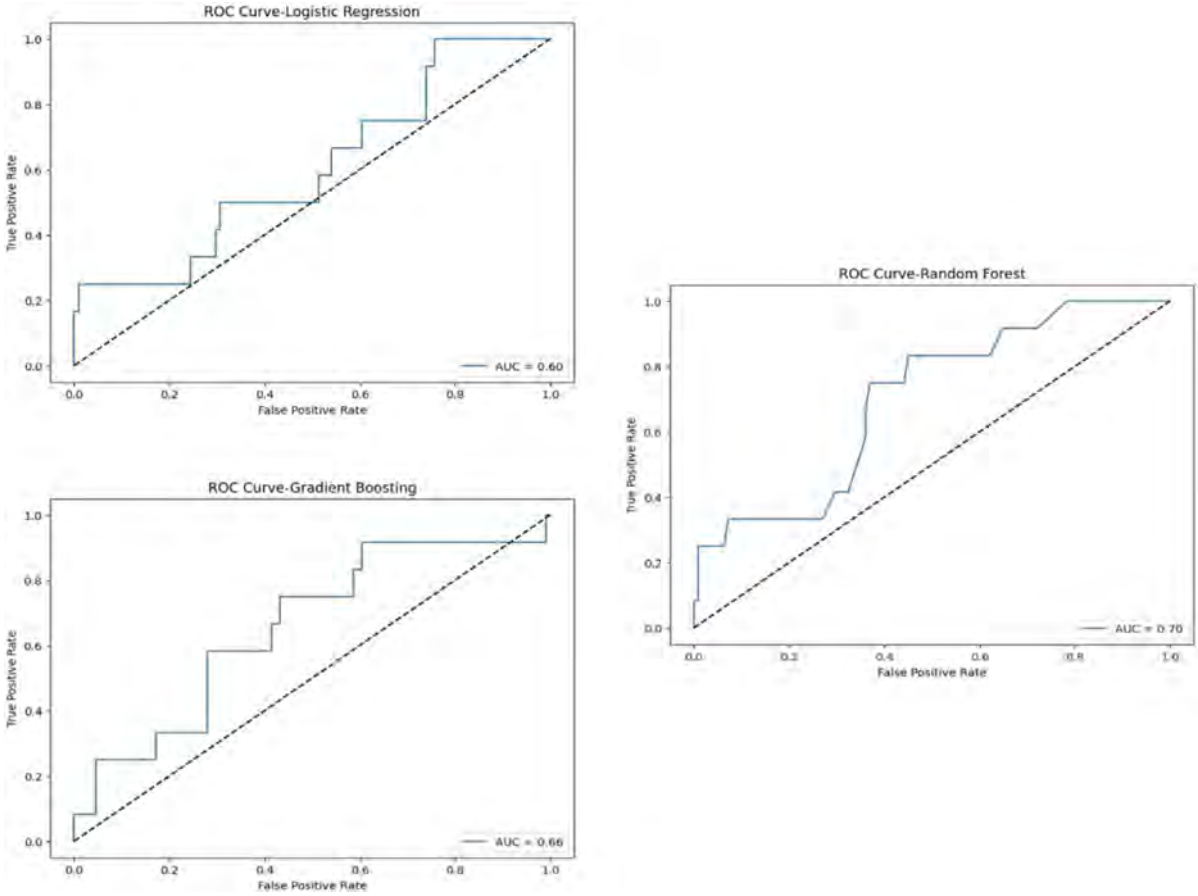


Figure 1: AUC Curves of Models SHAP Values (Random Forest Model)

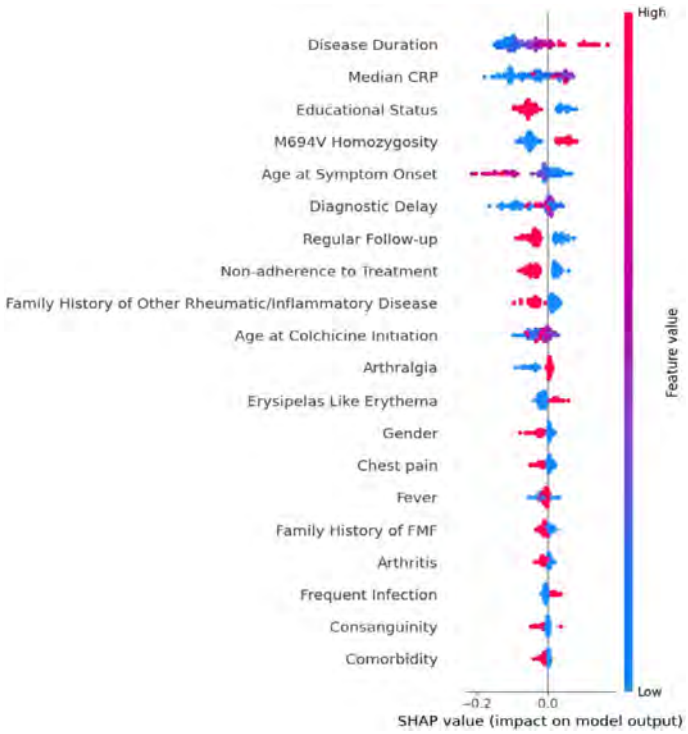


Figure 2: SHAP Values (Random Forest Model)

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: B. Aktas: None; **E. Azman**: None; **Y. Oner**: None; **k. Kaya**: None; **h. Yuksel**: None; **A. Hosgel**: None; **D. Karahan**: None; **Z. Coban**: None; **K. parlar**: None; **O. Kilinc**: None; **B. Acar**: None; **s. Ugurlu**: None.

Abstract Number: 2668

CD14$^+$ Myeloid Cells Mediate UVB Photosensitivity in Autoimmune Skin Disease via a Spatially Resolved Inflammatory Circuit

Nazgol Haddadi[1], Khashayar Afshari[1], Yuqing Wang[1], Carolina S. Lopes[1], Chee-Huat L. Eng[2], Nuria Martinez-Gutierrez[1], Leah Whiteman[1], Kevin Wei[3], Kirsten Frieda[2], Stefania Gallucci[1], Misha Rosenbach[4], Ruth Ann Vleugels[5], John E. Harris[1], Manuel Garber[1] and Mehdi Rashighi[1], [1]UMass Chan Medical School, Worcester, MA, [2]Spatial Genomics, Inc., Pasadena, CA, [3]Brigham and Women's Hospital at Harvard Medical School, Boston, MA, [4]University of Pennsylvania, Philadelphia, PA, [5]Brigham and Women's Hospital, Chestnut Hill, MA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases III: End Organ Focus on Heart, Lung and Eye (2663–2668)

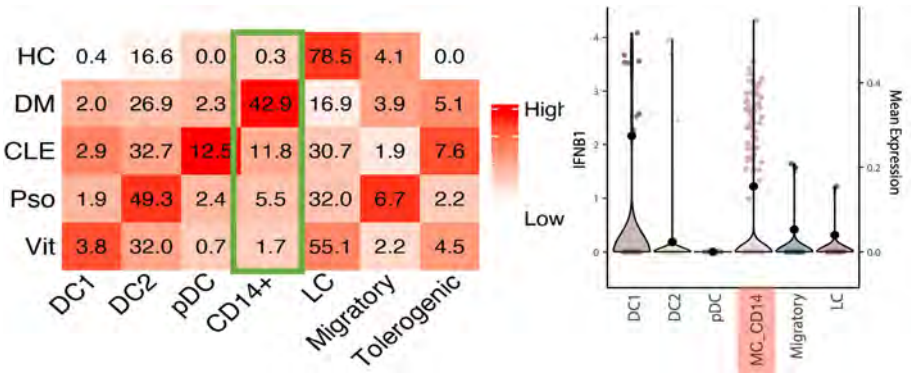
Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Inflammatory skin diseases vary widely in symptoms and causes. While ultraviolet (UV) light helps treat some like vitiligo and psoriasis, in conditions like cutaneous lupus erythematosus (CLE) and dermatomyositis (DM), UV exposure can worsen disease. The biological basis for this photosensitivity remains unclear.

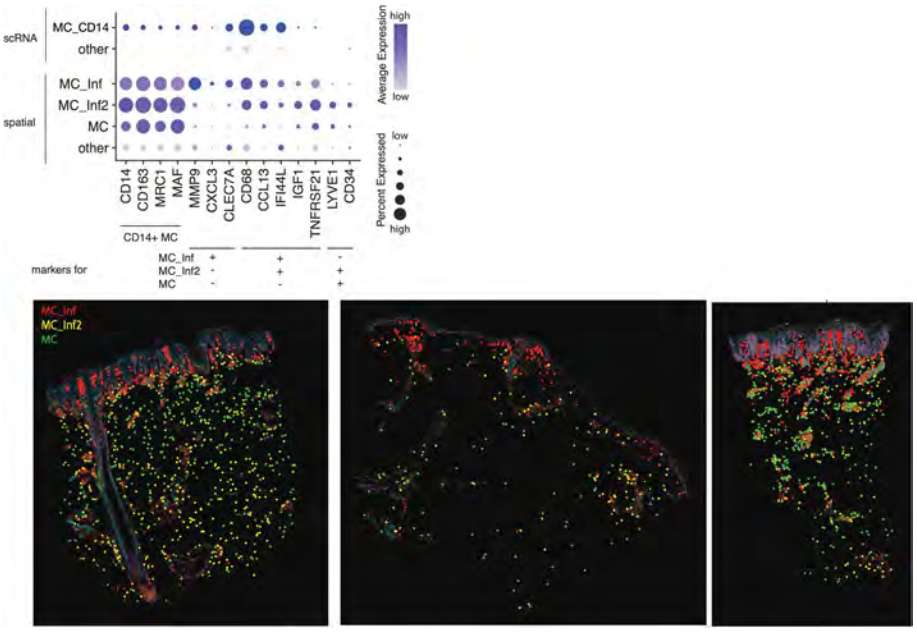
Methods: We used a multi-omics approach—single-cell RNA sequencing (scRNA-seq), spatial transcriptomics, and proteomics—to analyze lesional and non-lesional skin from patients with DM, CLE, vitiligo, psoriasis, and healthy controls. In vivo, a photoprovocation test was performed on sun-protected skin of healthy volunteers, DM, and CLE patients; post-irradiation biopsies were analyzed by flow cytometry and spatial transcriptomics. In vitro, keratinocytes were treated with UVB ± IFN-β. Supernatants were applied to monocyte-derived dendritic cells (moDCs) generated from PBMCs, and their activation was assessed.

Results: CD14$^+$ myeloid cells, which resembled monocyte-derived dendritic cells (moDCs) in culture, were the only immune population distinguishing photosensitive (CLE, DM) from photoresponsive (psoriasis, vitiligo) diseases. These cells were enriched in lesional DM (43%) and CLE (12%) compared to controls (< 0.3%) and localized near the dermo-epidermal junction, adjacent to cytotoxic CD4$^+$ T cells. CD14$^+$ myeloid cells expressed IFNB1 and MMP9, suggesting involvement in IFN-I signaling and tissue remodeling. UVB photoprovocation confirmed increased recruitment of CD14$^+$ myeloid cells to the skin,

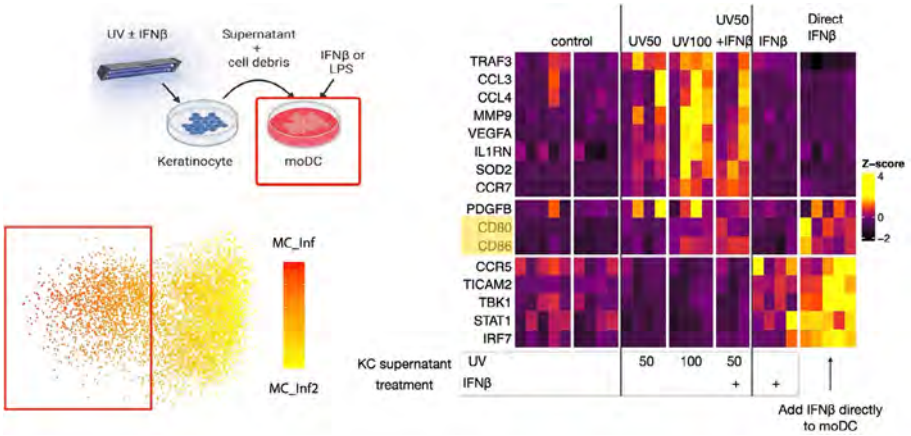


CD14$^+$ myeloid cells (MC_CD14) are expanded in dermatomyositis and lupus skin in our single-cell RNA sequencing dataset (heatmap, left) and show the highest IFNB1 expression among dendritic cell subsets (violin plot, right).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



The dot plot (top) shows shared marker expression between CD14$^+$ myeloid subsets identified by scRNA-seq and spatial single-cell transcriptomics (SeqFISH+). The MC_Inf transcriptional signature aligns with the scRNA-seq-defined CD14$^+$ myeloid profile and maps to cells spatially enriched near the dermo-epidermal junction, as illustrated in the bottom panels.



Schematic and heatmaps showing moDCs stimulated with supernatants from UV-treated keratinocytes. Exposure to supernatants from UVB-damaged keratinocytes, particularly in the presence of IFN-β, induced a transcriptional program enriched for MC_Inf markers (e.g., CD80, CD86, CCL4, MMP9), consistent with acquisition of a pro-inflammatory phenotype.

more so in DM and CLE patients. IFN-β priming sensitized keratinocytes to UVB-induced death and enhanced secretion of TNF-α and IL-6, which activated moDCs. Upon activation, moDCs release chemokines promoting immune cell recruitment, amplified in the presence of IFN-β.

Conclusion: Our findings reveal a UVB-induced inflammatory circuit driven by IFN-β–primed keratinocytes and CD14$^+$ myeloid cells in CLE and DM. By defining this keratinocyte–myeloid interaction, we highlight new opportunities for targeted therapies that may prevent lesion flares in photosensitive patients.

Disclosure: N. Haddadi: None; **K. Afshari**: None; **Y. Wang**: None; **C. Lopes**: None; **C. Eng**: None; **N. Martinez-Gutierrez**: None; **L. Whiteman**: None; **K. Wei**: 10X Genomics, 5, anaptysbio, 2, Gilead, 5, Merck/MSD, 5, Mestag, 2, Pfizer, 2; **K. Frieda**: None; **S. Gallucci**: None; **M. Rosenbach**: None; **R. Vleugels**: None; **J. Harris**: None; **M. Garber**: None; **M. Rashighi**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2669

RESET-Myositis: Clinical Trial Evaluating Rese-cel (Resecabtagene Autoleucel), A Fully Human, Autologous 4-1BB CD19-CAR T Cell Therapy in Idiopathic Inflammatory Myopathies

Erin Wilfong[1], Tahseen Mozaffar[2], Elie Naddaf[3], Nizar Chahin[4], Huifang Lu[5], Iazsmin Bauer Ventura[6], Courtney Little[7], Carl diCasoli[7], Claire Miller[8], Jenell Volkov[7], Daniel Nunez[7], Thomas Furmanak[7], Jason Stadanlick[7], Larissa Ishikawa[7], Zachary Vorndran[7], Alexandra Ellis[7], Jazmean Williams[7], Steve Flanagan[7], Quynh Lam[8], Fatemeh Hadi-Nezhad[8], Raj Tummala[8], Samik Basu[7] and David Chang[9], [1]Vanderbilt University Medical Center, Nashville, TN, USA, Nashville, TN, [2]University of California, irvine, Orange, CA, [3]Mayo Clinic, Rochester, MN, [4]Oregon Health & Science University, Portland, [5]UT MD Anderson Cancer Center, Houston, TX, [6]University of Chicago, Chicago, IL, [7]Cabaletta Bio, Philadelphia, PA, [8]Cabaletta Bio, Philadelphia, [9]Cabaletta Bio, Bryn Mawr, PA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics (2669–2674)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: The goals of treatment for idiopathic inflammatory myopathy (IIM) are to eliminate or reduce inflammation, restore muscle performance, reduce morbidity, and improve a patient's quality of life. Therapies providing durable meaningful clinical responses without requiring chronic administration are lacking. Rese-cel (formerly CABA-201), is a fully human, autologous 4-1BB CD19-CAR T cell therapy, designed to deeply and transiently deplete CD19 positive cells following a weight-based, single infusion with the potential to enable an "immune system reset" with durable responses. RESET-Myositis™ (NCT06154252) is an ongoing Phase 1/2 trial evaluating rese-cel in 3 independent cohorts of adults with dermatomyositis [DM], antisynthetase syndrome [ASyS] and immune mediated necrotizing myopathy [IMNM].

Methods: Patients were 18 to 75 years with refractory IIM per 2017 ACR/EULAR classification criteria, with myositis specific autoantibody (MSA), manual muscle test ≤142, at least moderate disease activity on 2 or more core set measures (CSMs). A weight-based infusion of $1x10^6$ CAR T cells/kg was given following preconditioning with fludarabine and cyclophosphamide. All non-glucocorticoid (GC) IM agents were discontinued by Day –5. Adverse events, use of IM medications and efficacy

Table 1. Baseline Characteristics

	RESET-Myositis					
Cohort	**IMNM**			**DM**	**ASyS**	
Patient	**IMNM-1**	**IMNM-2**	**IMNM-3**	**DM-1**	**ASyS-1**	**ASyS-2**
Age, sex	33 M	60 M	55 M	57 M	39 M	48 F
Disease duration (y)	~2	~4	~1	~4	~4	~15
Antibodies	SRP	HMGCR	SRP	SAE	Jo-1	Jo-1
Baseline disease activity*	**MMT-8**					
	130	126	105	131	119	140
	CK (U/L)					
	617	4725	1447	94	502	121
Therapies at Screening	GC, MTX	GC, IVIg	MTX, AZA	GC, MMF, HCQ	GC, IVIg, TAC	GC, IVIg, MMF, TAC
Other prior therapies	RTX, IVIg	RTX, MMF, MTX	GC	IVIG	RTX, MMF, TOC, AZA	RTX, MTX, MMF, AZA
GC dose at Screening (mg/day)	5	5	NA	20	10	5

As of 31 March 2025
*Baseline disease activity = activity before preconditioning.
AZA, azathioprine; CK, creatinine kinase; ASyS - Anti-Synthetase; DM, dermatomyositis; GC, glucocorticoid; HCQ, hydroxychloroquine; HMGCR, 3-hydroxy-3-methylglutaryl-coenzyme A reductase; IMNM, immune-mediated necrotizing myopathy; IVIg, intravenous immunoglobulin; MMF, mycophenolate mofetil; MMT-8, manual muscle testing 8; MTX, methotrexate; RESET, REstoring SElf-Tolerance; RTX, rituximab; SAE, small ubiquitin-like modifier activating enzyme; SRP, signal recognition particle; TAC, tacrolimus; TOC, tocilizumab; U/L, units per liter; y, years.
Cabaletta Bio: Data on file.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Treatment Responses

	IMNM			DM	ASyS	
Patient	IMNM-1	IMNM-2	IMNM-3	DM-1	ASyS-1	ASyS-2
Latest follow-up	52 weeks	24 weeks	12 weeks	24 weeks	8 weeks	4 weeks
TIS Response	Minimal to moderate†	No response	Moderate	Major	Major	Moderate
GC-free	✓	✓	✓	✓	✓	✓
IM-free	✓	-	✓	✓	✓	✓

As of 31 March 2025.
† Minimal to moderate improvement at all timepoints from Week 20 to 52, except Week 48.
ASyS, antisynthetase syndrome; DM, dermatomyositis; GC, glucocorticoids; IM, immunomodulatory medication; IMNM, immune-mediated necrotizing myopathy; IVIG, intravenous immunoglobulin; rese-cel, resecabtagene autoleucel; RESET, REstoring SElf-Tolerance; TIS, total improvement score.
Cabaletta Bio; Data on file

measurements to calculate the TIS were collected. CAR T cells and B cells were profiled in peripheral blood pre- and post-infusion by digital PCR and flow cytometry, respectively. Serum cytokines were measured using the mesoscale discovery platform.

Results: As of 31 March 2025, 6 patients have been infused with rese-cel and have at least 1 month of follow-up (Table 1). Additional patients were recently infused and are in early follow-up.

Rese-cel was well-tolerated in all 6 patients with Grade 1 cytokine release syndrome (CRS) in 3 of 6 patients, and no Grade 2 or higher CRS, dose-limiting toxicity or immune effector cell-associated neurotoxicity syndrome (ICANS). IMNM-2 with multiple risk factors, experienced a pulmonary embolism (PE) on Day 38, which was assessed as unrelated to rese-cel.

Five out of 6 patients achieved a drug-free clinical response on TIS (Table 2).

Rese-cel expanded rapidly in all patients and peaked between days 8 and 14 after infusion. Serum IFNγ levels increased post-infusion and peaked prior to rese-cel peak expansion. Rese-cel contracted quickly and was undetectable peripherally within the first 8 weeks in most patients. B cells ($CD19^{+}CD20^{+}$) were rapidly reduced to undetectable levels by 14 days and through the first month post rese-cel infusion in all patients. B cell reconstitution occurred as early as 8 weeks after infusion in 4 patients and 12 weeks in 1 patient. Reemergent B cells had predominantly transitional naïve phenotype (CD19+CD20+CD38++CD24++).

Conclusion: Data from IIM patients infused with rese-cel show early drug-free clinical responses in most patients and acceptable safety in the setting of rese-cel expansion and peripheral B cell depletion. DM & ASyS patients achieved a higher threshold of response than IMNM which is not unexpected. These initial data suggest the potential for rese-cel to reset the immune system, allowing patients to achieve meaningful drug-free clinical responses.

Disclosure: E. Wilfong: Allogene, 2, AstraZeneca, 2, Boehringer Ingelheim, 1, 5, 12, Medical writing support provided by Fleishman Hillard, Capstan Therapeutics, 2, Merck, 1, UpToDate, 9; **T. Mozaffar**: Amicus, 2, 5, AnnJi, 2, 5, Argenx, 2, 5, Arvinas, 2, AskBio, 2, Astellas Gene Therapy, 2, 5, AstraZeneca, 2, 5, Bristol-Myers Squibb(BMS), 5, Cartesian Therapeutics, 5, Fate, 2, Grifols, 5, Horizon Therapeutics, 2, Janssen, 2, 5, Maze Therapeutics, 2, ML-Bio, 5, Sanofi, 2, 5, Sarepta, 2, Spark Therapeutics, 2, 5, UCB, 2, 5, Valerion, 5; **E. Naddaf**: Abcuro, 5, Cabaletta Bio, 5, Fulcrum, 5, Janssen, 2, Johnson and Johnson, 1; **N. Chahin**: Cabaletta Bio, 5; **H. Lu**: None; **I. Bauer Ventura**: Boehringer-Ingelheim, 1; **C. Little**: Cabaletta Bio, 3; **C. diCasoli**: Cabaletta Bio, 3; **C. Miller**: Cabaletta Bio, 3; **J. Volkov**: Cabaletta Bio, 3; **D. Nunez**: Cabaletta Bio, 3; **T. Furmanak**: Cabaletta Bio, 3; **J. Stadanlick**: Cabaletta Bio, 3; **L. Ishikawa**:

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cabaletta Bio, 3; **Z. Vorndran**: Cabaletta Bio, 3; **A. Ellis**: Cabaletta Bio, 3; **J. Williams**: Cabaletta Bio, 3; **S. Flanagan**: Cabaletta Bio, 3; **Q. Lam**: Cabaletta Bio, 3; **F. Hadi-Nezhad**: Cabaletta Bio, 3; **R. Tummala**: Cabaletta Bio, 3; **S. Basu**: Cabaletta Bio, 12, 3, 11; **D. Chang**: Cabaletta Bio, 3.

Abstract Number: 2670

Real-World Experience of Anifrolumab in 24 Patients with Refractory Dermatomyositis: A Multicenter Retrospective Study.

Miriam Retuerto Guerrero[1], Clara Moriano[2], Ana Pareja-Martínez[3], Natalia Molina-Esteban[4], Jose Puig-Buendia[5], Concepción Postigo-Llorente[5], Ana Lopez-Ceron Cofiño[6], Julia Martínez Barrio[7], Paola Vidal-Montal[8], Elena Sendagorta Cudos[9], GUILLERMO GONZALEZ ARRIBAS[10], Jaime Calvo[11], Juan Ramon De Dios[12], Juan María Blanco-Madrigal[13], Paloma Vela Casasempere[14], Javier Bachiller[15], Concepción Fito-Manteca[16], Carmen Ordas calvo[17], Luisa Martos Cabrera[18], Alejandro Sanchez Herrero[19], Luis Ortega-Valin[20] and Elvira Diez Alvarez[21], [1]Complejo Asistencial Universitario de León, Leon, Castilla y Leon, Spain, [2]Hospital León, LEON, Castilla y Leon, Spain, [3]Rheumatology. Hospital Universitario Infanta Leonor, Madrid, Madrid, Spain, [4]Rheumatology. Hospital Universitario 12 de octubre, Madrid, Madrid, Spain, [5]Dermatology. Hospital universitario 12 de octubre, Madrid, Madrid, Spain, [6]Rheumatology. Complejo Asistencial Universitario de Soria, Soria, Castilla y Leon, Spain, [7]Department of Rheumatology, Hospital Gregorio Marañón, Madrid, Spain, Madrid, Madrid, Spain, [8]Rheumatology. Hospital Universitari de Bellvitge, Barcelona, Catalonia, Spain, [9]Dermatology. Hospital universitario La Paz, Madrid, Madrid, Spain, [10]Facultativo especialista, PALMA DE MALLORCA, Galicia, Spain, [11]Department of Rheumatology, Hospital Universitario Araba, School of Medicne, Universidad del País Vasco, BIOARABA Health Research Institute, Vitoria, Spain, Vitoria, Pais Vasco, Spain, [12]Department of Rheumatology. Hospital Universitario Araba. Instituto de Investigación Sanitaria BIORABA., Vitoria, Pais Vasco, Spain, [13]Rheumatology. Hospital Universitario Araba., Vitoria, Pais Vasco, Spain, [14]Hospital General Universitario Alicante, Alicante, Comunidad Valenciana, Spain, [15]Hospital Ramon y Cajal, Madrid, Madrid, Spain, [16]Rheumatology. Hospital Universitario de Navarra., Pamplona, Navarra, Spain, [17]Rheumatology. Hospital Universitario de Cabueñes., Gijon, Asturias, Spain, [18]Dermatology. Hospital Universitario de La Princesa, Madrid, Madrid, Spain, [19]Dermatology. Complejo Asistencial Universitario de Leon, Leon, Castilla y Leon, Spain, [20]Pharmacy. Complejo Asistencial Universitario de Leon, Leon, Castilla y Leon, Spain, [21]Rheumatology. Complejo Asistencial Universitario de Leon, Leon, Castilla y Leon, Spain

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics (2669–2674)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Dermatomyositis (DM) is a systemic autoimmune disease marked by muscle weakness and characteristic cutaneous manifestations. Dysregulation of the Type I interferon (IFN-I) pathway plays a crucial role in its pathogenesis. Anifrolumab (ANI), an anti-IFNAR1 monoclonal antibody approved for the treatment of lupus, is a potential treatment for IFN-I–mediated diseases. This study aims to assess the efficacy and safety of ANI in patients with refractory DM.

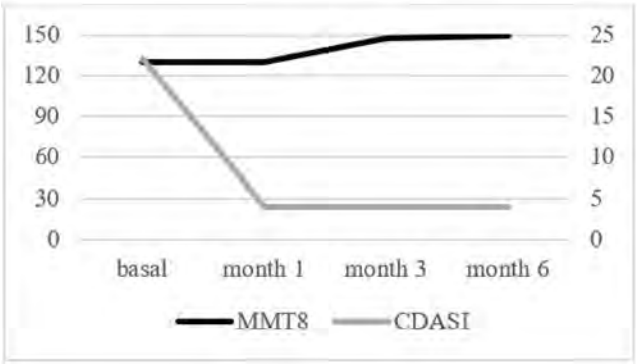


Figure 1. Evolution of CDASI and MMT8 after initiation of anifrolumab over a 6-month follow-up period.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We performed a multicenter, multidisciplinary, retrospective study involving 24 DM patients treated with ANI under compassionate use. Data collected included demographics, clinical features, serology, prior treatments, and concomitant medications. Efficacy was measured using the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) and the Manual Muscle Test 8 (MMT8). Safety was evaluated based on adverse events (AEs).

Results: Of the 24 patients, 83% were female, with a mean age of 58.1±21.1 years at DM diagnosis and 53.9±19.8 years at ANI initiation. The majority were Caucasian (79%). DM subtypes included classic (9), amyopathic (10), juvenile (3), and antisynthetase syndrome (2); 21% had a paraneoplastic origin. Common cutaneous manifestations included Gottron's papules (100%), pruritus (92%), periorbital erythema (83%), periungual erythema (79%), alopecia (46%), and calcinosis (38%). Musculoskeletal involvement was observed in 58%, dysphagia in 42%, arthritis in 50%, and interstitial lung disease in 21%. Myositis-specific antibodies were detected in 19 patients: anti-TIF1γ (8), anti-MDA5 (3), anti-SAE (4), anti-ARS (3), anti-Mi-2 (1); 5 patients were seronegative. Anti-Ro52 was present in 9 (38%). Prior treatments included oral CS (100%), HCQ (88%), MTX (88%), AZA (25%), TAC (21%), MMF (67%), IVIG (79%), RTX (29%), TOFA (42%), BARI (8.3%), RUXO (4.1%), and others.

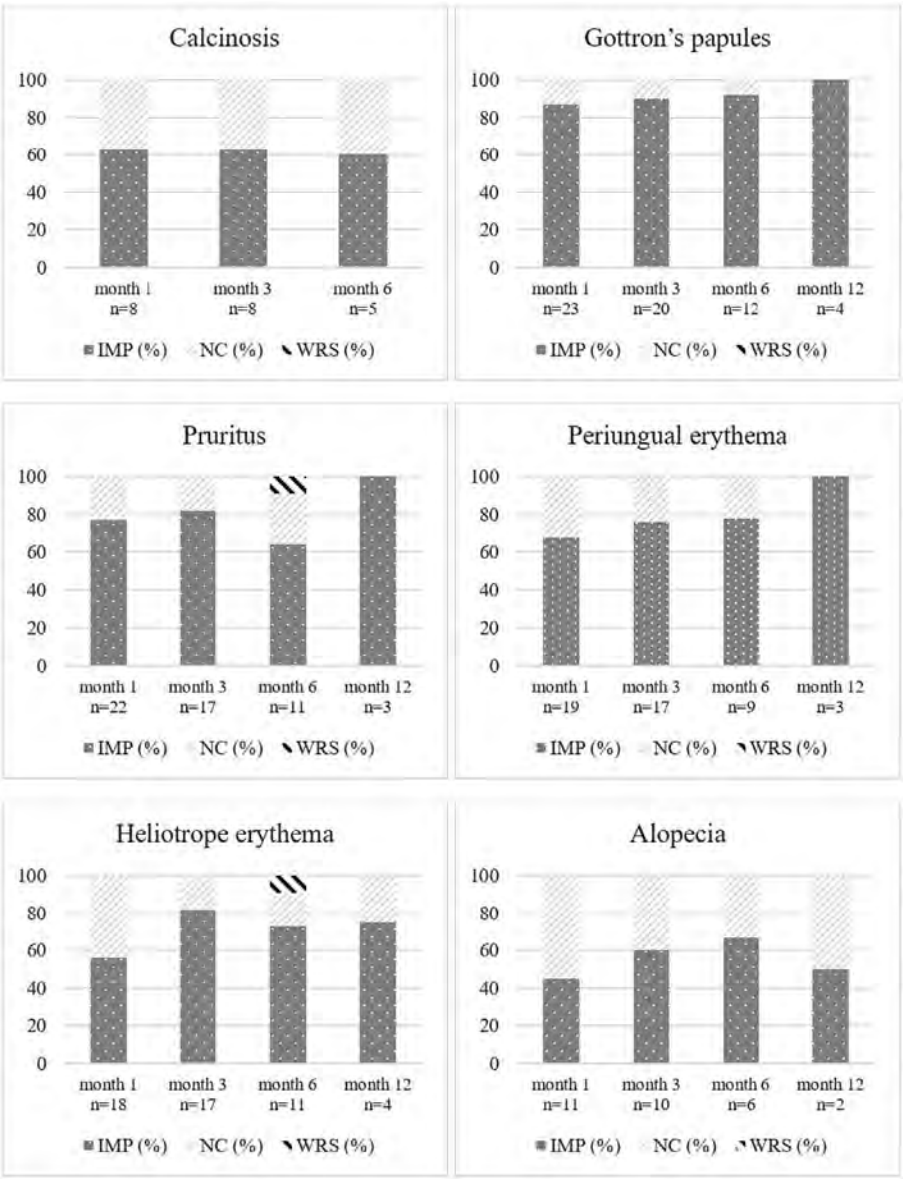


Figure 2. Impact of anifrolumab on different cutaneous manifestations over 12 months of follow-up.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 3. Significant improvement in facial and upper chest erythema observed following three doses of anifrolumab.

ANI was initiated mainly for cutaneous refractoriness (91.6%) and musculoskeletal activity (8.4%). It was administered at 300 mg every 4 weeks, except in one juvenile DM patient, who received 150 mg every 4 weeks. Half of the patients received concomitant csDMARDs: MTX (4), MMF (4), TAC (2), AZA (1), and TAC + MMF (1). After a mean follow-up of 7.5±4.2 months, most patients showed marked cutaneous improvement (CDASI) and muscle stability (MMT8) (Figure 1). The impact of ANI on cutaneous manifestations over 12 months is shown in Figure 2. In two patients, the IVIG intervals were successfully spaced due to clinical improvement. One juvenile DM patient had a flare, with CK elevation (450 UI/L) and a positive Gowers' sign after discontinuing MTX. AEs included impetigo (1), arthralgia/myalgia (1), urinary tract infections (2), and herpes zoster (1). No AEs led to ANI discontinuation, although one patient stopped treatment due to loss to follow-up.

Conclusion: Anifrolumab demonstrated early efficacy in dermatomyositis, with a favorable safety profile in refractory DM. This is the largest real-world series of DM patients treated with ANI to date, supporting its role in IFN-I–mediated dermatomyositis.

Disclosure: M. Retuerto Guerrero: None; **C. Moriano**: None; **A. Pareja-Martínez**: None; **N. Molina-Esteban**: None; **J. Puig-Buendia**: None; **C. Postigo-Llorente**: None; **A. Lopez-Ceron Cofiño**: None; **J. Martínez Barrio**: None; **P. Vidal-Montal**: None; **E. Sendagorta Cudos**: None; **G. GONZALEZ ARRIBAS**: None; **J. Calvo**: None; **J. De Dios**: None; **J. Blanco-Madrigal**: None; **P. Vela Casasempere**: None; **J. Bachiller**: None; **C. Fito-Manteca**: None; **C. Ordas calvo**: None; **L. Martos Cabrera**: None; **A. Sanchez Herrero**: None; **L. Ortega-Valin**: None; **E. Diez Alvarez**: None.

Abstract Number: 2671

Effect of Efgartigimod PH20 SC on Total Improvement Score, its Core Set Measures, and Patient/Clinician Impressions of Change: Results from the Phase 2 ALKIVIA Study of Adults with Active Idiopathic Inflammatory Myopathy

Rohit Aggarwal[1], Sebastian Rodriguez-Garcia[2], Agna Neto[3], Despoina Papadopoulou[4], Ben Van Baelen[3], Paul Duncombe[3], Leentje De Ceuninck[5], Bas van der Woning[6] and Hector Chinoy[7], [1]University of Pittsburgh, Rheumatology and Clinical Immunology, Pittsburgh, United States of America, Pittsburgh, PA, [2]Hospital Universitario de La Princesa, Madrid, Spain, [3]argenx, Ghent, Belgium, [4]argenx, Alimos Attikis, Greece, [5]argenx, Issy-les-Moulineaux, France, [6]argenx BV, Boston, MA, [7]The University of Manchester, Manchester, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics (2669–2674)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Idiopathic inflammatory myopathy (IIM) is a rare, systemic, autoimmune, rheumatic disease, with different subtypes, characterized by muscle weakness and extra-muscular involvement. There are no approved targeted treatments indicated for multiple IIM subtypes. Efgartigimod is an IgG1 antibody Fc fragment engineered for high neonatal Fc receptor (FcRn) affinity. ALKIVIA evaluates the safety and efficacy of subcutaneous (SC) efgartigimod PH20 (coformulation of efgartigimod and recombinant human hyaluronidase PH20; EFG) plus standard of care (SOC) vs placebo PH20 (PBO) plus SOC in patients with IIM.

Methods: ALKIVIA (NCT05523167) is an operationally seamless phase 2/3, randomized, double-blinded, PBO-controlled, parallel-group, multicenter study in adults with IIM. The completed phase 2 randomized 89 patients (1:1) with immune-mediated necrotizing myopathy, dermatomyositis, polymyositis, or anti-synthetase syndrome, meeting ACR/EULAR classification criteria to receive weekly EFG or PBO alongside SOC for IIM. The primary endpoint was the 2016 ACR/EULAR Total Improvement Score (TIS) at Week 24, a composite endpoint based on improvement in Physician's Global Disease Activity (MDGA), manual muscle testing-8 (MMT8), muscle enzymes, Patient Global Disease Activity (PGA), Health Assessment Questionnaire Disability Index (HAQ-DI), and Extra-muscular Global Disease Activity. Key secondary endpoints were time to TIS, proportion of patients with TIS ≥20 and ≥40, changes in MMT8, PGA, and MDGA at Week 24.

Results: Of the 89 participants, 76.4% were female and 71.8% white, with a mean (SD) age of 56.6 (13.3) years. Least-squares mean TIS at Week 24 was statistically significantly higher in the EFG than the PBO arm (50.45 vs 35.65; *P*=0.0004). EFG-treated participants showed significant improvement in all key secondary endpoints compared with PBO, including the proportion of participants with minimal (≥20) and moderate (≥40) TIS, and the exploratory endpoint of major (≥60) TIS (91.5 vs 73.8%; 78.7 vs 47.6%, *P*=0.0029; and 34.0 vs 9.5%, *P*=0.0055, respectively) (**Figure 1**). Median times to TIS ≥20 and ≥40 were shorter with EFG compared to PBO (30 vs 71.5 days, *P*=0.0020; 113 days vs not estimable, *P*=0.0293). EFG treatment improved all 6 core set measures (**Figure 2A**). Both Patient and Clinician Global Impression of Change "much/moderately better" were improved at Week 24 with EFG vs PBO (54.4% vs 40.4%, and 60.8% vs 38.1%, respectively; **Figure 2B**). Significant improvements were seen in MMT8 (LSM 15.16 vs 7.60, *P*=0.0011), PGA (LSM –2.72 vs –1.03, *P*=0.0015), and MDGA (LSM –2.88 vs –1.94, *P*=0.0379). Safety was comparable between treatment arms (**-Table 1**), with the most common AEs in the EFG arm being injection site erythema (23.4%), rash (17.0%), bruising (10.6%) or reaction (10.6%), and diarrhea (12.8%). Two deaths occurred in the EFG arm (both unrelated to study drug) and none in the PBO arm.

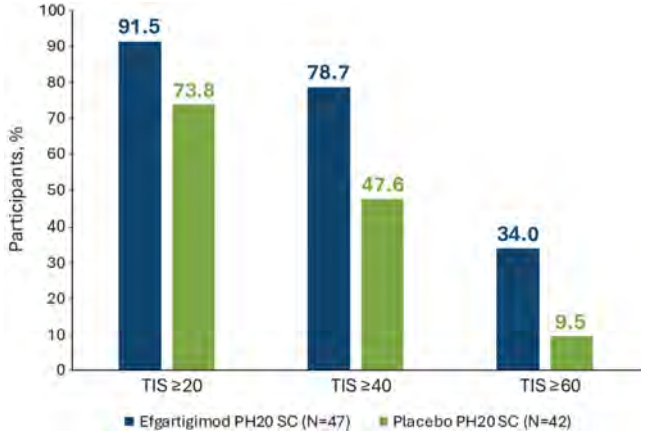
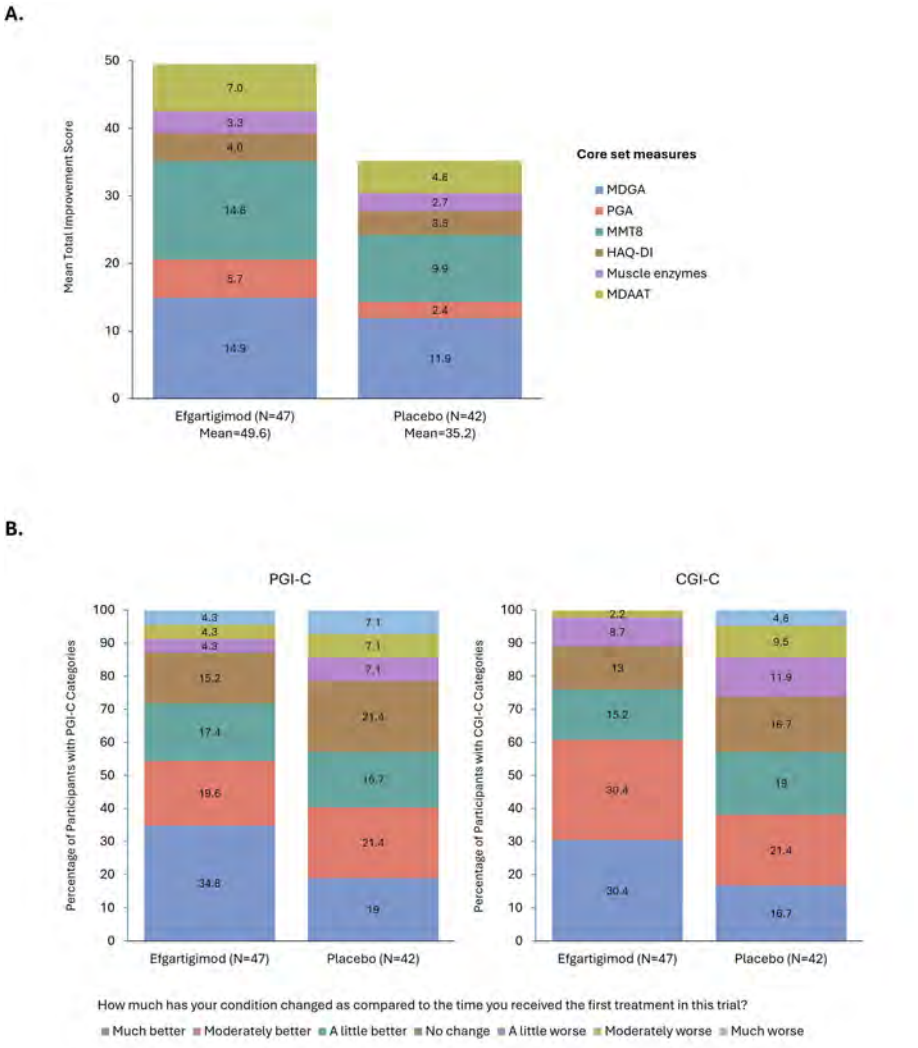


Figure 1. Proportion of participants with TIS ≥20, ≥40, and ≥60 at Week 24

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



CGI-C, Clinician Global Impression of Change; HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intent-to-treat; MDAAT, Myositis Disease Activity Assessment Tool; MDGA, Physician Global Assessment of Disease Activity; MMT8, manual muscle testing-8; PGA, Patient Global Assessment of Disease Activity; PGI-C, Patient Global Impression of Change.

Figure 2. (A) Percentage contribution of core set measures to total improvement score (TIS) at Week 24 in efgartigimod vs. placebo (ITT analysis set) (B) PGI-C and CGI-C at last assessment before or at Week 24.

Table 1. Safety summary

	Efgartigimod PH20 SC (N=47, PYFU=22)			Placebo PH20 SC (N=42, PYFU=18)		
	n (%)	m	ER/100 PYFU	n (%)	m	ER/100 PYFU
≥1 AE	41 (87.2)	320	1474.1	37 (88.1)	168	916.7
≥1 study drug-related AE	21 (44.7)	147	677.2	14 (33.3)	53	289.2
≥1 SAE	8 (17.0)	11	50.7	9 (21.4)	10	54.6
≥1 study drug-related SAE	0	0	0	2 (4.8)	2	10.9
≥1 Grade ≥3 AE	7 (14.9)	10	46.1	12 (28.6)	13	70.9
≥1 AE leading to study drug discontinuation	3 (6.4)	3	13.8	4 (9.5)	4	21.8
≥1 AESI (infection)	20 (42.6)	24	110.6	20 (47.6)	31	169.1
≥1 injection-site reaction	21 (44.7)	155	714.0	9 (21.4)	41	223.7
≥1 fatal AE	2 (4.3)	2	9.2	0	0	0

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: ALKIVIA, the first FcRn inhibitor study in IIM, established proof of concept and highlights the mechanistic relevance of FcRn inhibition in IIM. Results support further evaluation of efgartigimod PH20 SC in patients with IIM in the ongoing phase 3 part of the study.

Disclosure: R. Aggarwal: Alexion, 2, ANI Pharmaceuticals, 2, Argenx, 2, Artasome, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, CabalettaBio, 2, Capella, 2, Capstanx, 2, CSL Behring, 2, EMD Serono, 2, 5, Galapagos, 2, Horizon Therapeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Kezar, 2, Kyverna, 2, Lilly, 2, Manta Medicines, 2, Nkarta, 2, Novartis, 2, Octapharma, 2, Pfizer, 2, 5, Priovant, 2, 5, Teva, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2; **S. Rodriguez-Garcia**: argenx, 2; **A. Neto**: argenx, 2, PPD, 3; **D. Papadopoulou**: argenx, 3, 11; **B. Van Baelen**: argenx, 3, 11; **P. Duncombe**: argenx, 3, 11; **L. De Ceuninck**: argenx, 3, 11; **B. van der Woning**: argenx, 3, 11; **H. Chinoy**: argenx, 2, AstraZeneca, 1, Pfizer, 2, 5.

Abstract Number: 2672

Safety and efficacy of Upadacitinib in melanoma differentiation-associated gene 5-positive dermatomyositis with interstitial lung disease: a single-centre, retrospective, propensity score-matched cohort study

Can Xia[1], Wanlong Wu[1], Yan Ye[1], Jingjing Li[2], Runci Wang[1], Wenwen Xu[3], Zhiwei Chen[1], Yakai Fu[2], Xia Lyu[1], Kaiwen Wang[1], Wei Fan[1], Jia Li[1], Xiaodong Wang[2], Shuang Ye[4] and **Qiong Fu**[5], [1]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [2]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, Shanghai, China (People's Republic), [3]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [4]Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, Shanghai, Shanghai, China (People's Republic), [5]Renji Hospital, Shanghai, Shanghai, China

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics (2669–2674)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Anti-melanoma differentiation-associated protein 5 (MDA5) antibody-positive dermatomyositis (MDA5+DM) is a distinct and severe subtype of dermatomyositis, frequently complicated by interstitial lung disease (ILD). Among these patients, rapid progressive ILD (RP-ILD) is the leading cause of high mortality, often resulting in severe respiratory failure within a short time frame. Despite available treatments, managing MDA5+ DM-associated ILD (MDA5+DM-ILD) remains a significant clinical challenge, with first-year mortality rates reported as high as 40%. Therefore, exploring effective therapeutic options is crucial. This cohort study aims to evaluate the efficacy and safety of Upadacitinib (UPA) in patients with MDA5+ DM-ILD, assessing its potential to improve clinical outcomes.

Methods: All patients with MDA5+DM-ILD who were admitted to Renji Hospital, affiliated with Shanghai Jiao Tong University School of Medicine, between 2013 and 2024 were included in the study. The primary efficacy endpoint was the 1-year survival rate. Secondary efficacy endpoints included the dosage of glucocorticoid usage, changes in lung function, and relevant laboratory parameters. Propensity score matching (PSM) was applied to minimize confounding biases and enhance intergroup comparability.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Demographic data in the UPA group and the non-UPA group before and after PSM. PSM, propensity score matching; UPA, Upadacitinib; SMD, standard mean difference; ILD, interstitial lung disease; RP-ILD, rapidly progressive interstitial lung disease; FVC, forced vital capacity. *p<0.05

	Before PSM				After PSM		
Characteristics	UPA(n=49)	non-UPA(n=377)	P value	SMD	non-UPA(n=147)	P value	SMD
Age, years	55(48, 63)	52(44, 59)	0.022*	0.32	55(49, 61)	0.819	0.017
Male, n (%)	21(42.9)	126(33.4)	0.251	0.195	58(39.5)	0.801	0.069
Course of ILD, months	1(1, 2)	1(1, 2)	0.466	0.064	1(1, 2)	0.199	0.031
Spontaneous Pneumomediastinum, n (%)	9(18.4)	41(10.9)	0.195	0.213	27(18.4)	1	< 0.001
Non-invasive assisted ventilation, n (%)	7(14.3)	34(9.0)	0.358	0.165	21(14.3)	1	< 0.001
Invasive mechanical ventilation, n (%)	7(14.3)	86(22.8)	0.24	0.221	21(14.3)	1	< 0.001
RP-ILD, n (%)	30(61.2)	213(56.5)	0.635	0.096	84(57.1)	0.738	0.083
PaO2/FiO2, mmHg	309(242, 352)	338(237, 405)	0.079	0.19	319(217, 385)	0.413	0.056
Neutrophil-to-lymphocyte ratio	8.4(5.1, 12.9)	7.4(4.3, 12.8)	0.188	0.053	7.9(4.5, 14.2)	0.54	0.086
Lactate dehydrogenase level, U/l	381(325, 474)	319(249, 424)	0.001*	0.3	332(23, 452)	0.028*	0.086
Serum ferritin, ng/ml	1326(663, 2121)	1099(451, 1941)	0.181	0.005	1141(520, 1868)	0.309	0.032
C-reactive protein level, mg/l	2.8(0.8, 8.3)	3.3(0, 10.1)	0.951	0.273	2.2(0, 6.6)	0.197	0.086
Alanine aminotransferase, IU/l	66(38, 124)	60(36, 111)	0.679	0.01	60(38, 104)	0.694	0.136
Creatine kinase, U/l	54(29, 125)	46(26, 92)	0.234	0.069	47(26, 99)	0.39	0.113
FVC, %of predicted value	56.6±21.4	64.3±20.9	0.032*	0.366	61.7±21.4	0.16	0.238
unable to perform, n (%)	10(20.4)	92(24.4)	0.661	0.096	37(25.2)	0.629	0.114
FVC% < 50% or unable to perform, n (%)	25(51.0)	173(45.9)	0.599	0.103	74(50.3)	1	0.014
Combined treatment							
Maximum prednisone dosage, mg/day	150(100, 200)	100(100, 200)	0.216	0.034	125(100, 238)	0.626	0.028
Immunoadsorption, n (%)	14(28.6)	15(4.0)	< 0.001*	0.707	6(4.1)	< 0.001*	0.702
Tofacitinib, n (%)	0(0)	296(78.5)	< 0.001*	2.703	119(81.0)	< 0.001*	2.915
Intravenous immunoglobulin, n (%)	26(53.1)	210(55.7)	0.844	0.053	89(60.5)	0.451	0.151
Plasma exchange, n (%)	0(0)	3(0.8)	1	0.127	2(1.4)	1	0.166
Use of ⩾2 immunosuppressants, n (%)	10(20.4)	159(42.2)	0.006*	0.483	68(46.3)	0.002*	0.57
1 year survival rate, n (%)	39(79.6)	228(60.5)	0.026*		86(58.5)	0.031*	

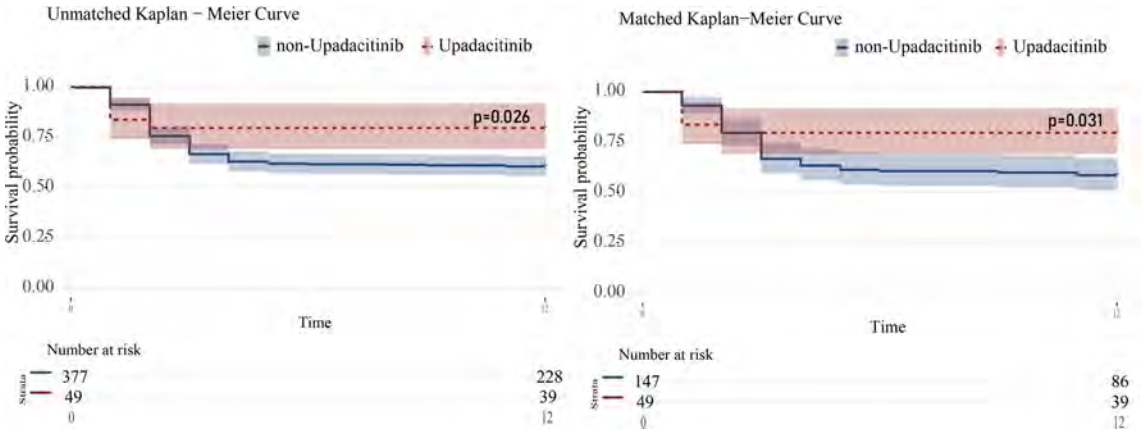


Figure 1 Kaplan-Meier survival curves comparing UPA group and non-UPA group patients before and after PSM.

Results: In the eligible cohort, a total of 49 patients received UPA treatment, while 377 patients were in the non-UPA group, of whom 78.5% received tofacitinib. After propensity score matching (PSM), baseline differences between the two groups were reduced (Table 1). The 1-year survival rates were 79.6% (39/49) in the UPA group and 60.5% (228/377) in the non-UPA group. Following PSM, the 1-year survival rate of the non-UPA group was 58.5%, with the difference remaining statistically significant (P=0.031) (Figure 1). Multivariate Cox regression analysis after PSM indicated that UPA treatment was associated with a significantly lower mortality risk, with a hazard ratio (HR) of 0.491 (95% confidence interval: 0.251-0.960) compared to the non-UPA group (Figure 2A). Subgroup analyses further demonstrated that UPA provided greater therapeutic benefits in patients with PaO_2/FiO_2 ratios between 200-300 mmHg (Figure 2B).

Conclusion: In this cohort study, UPA demonstrated a superior ability to improve the survival of patients with MDA5+DM-ILD compared to the non-UPA treatment regimen.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

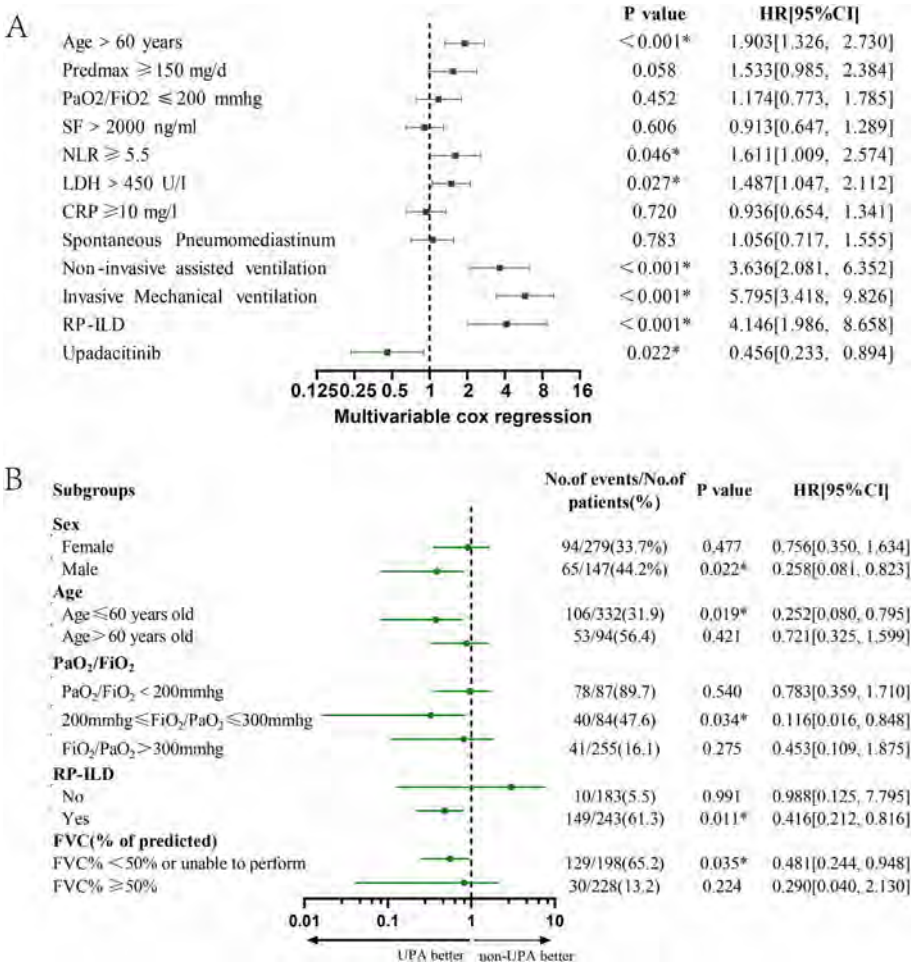


Figure 2 Prognostic analysis and subgroup treatment outcomes of UPA in MDA5+DM-ILD Patients. (A) Multivariate Cox regression forest plots for prognostic factors. (B) Subgroup analysis of treatment outcomes. Predmax, maximum prednisone dose; SF, serum ferritin; NLR, neutrophil-to-lymphocyte ratio; LDH, lactate dehydrogenase; CRP, C-reactive protein; RP-ILD, rapidly progressive interstitial lung disease; FVC, forced vital capacity. *P < 0.05.

Disclosure: C. Xia: None; **W. Wu**: None; **Y. Ye**: None; **J. Li**: None; **R. Wang**: None; **W. Xu**: None; **Z. Chen**: None; **Y. Fu**: None; **X. Lyu**: None; **K. Wang**: None; **W. Fan**: None; **J. Li**: None; **X. Wang**: None; **S. Ye**: None; **Q. Fu**: None.

Abstract Number: 2673

Quantitative 18F-FDG PET/CT analysis reveals new patterns of muscle involvement and prognostic indicators in idiopathic inflammatory myopathies: beyond proximal muscle weakness

Fatma Basibuyuk[1], Melih Yigithan Bahadir[2], Gokce Kenar Artin[2], Amac Kiray[2], Recep Bekis[2] and İsmail Sari[2], [1]Dokuz Eylul University, Izmir, Turkey, [2]Dokuz Eylül University, İzmir, Izmir, Turkey

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics (2669–2674)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Distribution of Muscle Involvement by Muscle Groups in Idiopathic Inflammatory Myopathy Patients as Assessed by 18F-FDG PET/CT (SUVmax, MLV, and TLG).

		SUV max	MLV	TLG
		Median (n)	Median (n)	Median (n)
HEAD-NECK MUSCLES	SCM	1.87 (13)	2.29 (13)	5.51 (11)
	Suboccipital	2.04 (13)	2.24 (13)	3.10 (11)
	Scalene	1,38 (13)	1.23 (9)	1.74 (8)
	TOTAL	1.76 (16)	3.52 (16)	4.48 (16)
THORAX MUSCLES	Autochthonous back muscles cervical	2.58 (13)	21.41 (13)	35.74 (13)
	Autochthonous back muscles thoracal	2.47 (16)	29.26 (17)	52.27 (17)
	Autochthonous back muscles lumbar	1.89 (16)	15.87 (16)	26.56 (16)
	Thoracic wall muscles	2.43 (16)	32.74 (16)	54.98 (16)
	Superficial thoracic muscles	2.58 (14)	23.61 (14)	44.46 (14)
	TOTAL	3.02 (17)	77.58 (17)	115.99 (17)
ABDOMEN MUSCLES	Abdominal wall	1.91 (11)	9.25 (11)	10.80 (11)
	TOTAL	1.25 (11)	0,33 (11)	0.65 (11)
UPPER EXTREMITY MUSLES	Shoulder	2,79 (17)	41.31 (17)	56.22 (17)
	Anterior arm muscles	2,47 (15)	23.13 (15)	39.32 (15)
	Posterior arm muscles	1,85 (14)	5.34 (14)	5.39 (14)
	TOTAL	3.00 (18)	54.28 (18)	103.52 (18)
LOWER EXTREMITY MUSCLES	Anterior pelvic arch	2.08 (17)	10.8 (17)	17.77 (17)
	Posterior pelvic arch	2.07 (17)	14.77 (17)	25.19 (17)
	Short lateral thigh muscle	2.17 (17)	11.30 (17)	16.81 (17)
	Anterior compartment of the thigh	2.08 (14)	16.70 (14)	27.52 (14)
	Medial compartment of the thigh	2.29 (14)	30.53 (14)	51.125 (14)
	Posterior compartment of the thigh	2,06 (9)	3.54 (9)	5.59 (9)
	TOTAL	2.99 (18)	79.75 (18)	127.50 (18)

SUVmax: Maximum Standardized Uptake Value, **MLV:** Metabolic Lesion Volume, **TLG:** Total Lesion Glycolysis, **SCM:** Sternocleidomastoid Muscle

Background/Purpose: To characterize muscle involvement in idiopathic inflammatory myopathies (IIMs) using detailed anatomical segmentation and volumetric 18F-FDG PET/CT analysis, and to evaluate the prognostic value of global metabolic burden compared to SUVmax.

Methods: Patients with IIMs undergoing baseline 18F-FDG PET/CT were retrospectively analyzed. Clinical and laboratory data (CK, AST, LDH, CRP, ESR) were collected. Severe or refractory disease was defined clinically. Each muscle group was individually assessed, then categorized into five regions (head/neck, thorax, abdomen, upper and lower extremities) based on anatomical curricula. PET parameters included SUVmax (peak activity), metabolic lesion volume (MLV), and total lesion glycolysis (TLG; SUVmean × MLV). Log-transformation normalized data. Pearson correlations and nonparametric tests assessed associations. ROC analysis after logistic regression evaluated prognostic performance.

Results: Twenty-one patients [median age 62 (range 22–77); 76.2% female] were included. Diagnoses were dermatomyositis (71.4%), polymyositis (23.8%), and antisynthetase syndrome (4.8%). Median follow-up was 11.5 months. Detailed anatomical segmentation (Table 1) revealed that thoracic muscles, particularly autochthonous thoracic and thoracic wall muscles, had the highest MLV and TLG values (median TLG: 115.99 thorax vs. 127.5 lower extremities). Lower extremities also showed significant burden, whereas abdominal and head/neck muscles were less involved (Figure 1). At follow-up, 33.3% (7/21) developed severe disease and 42.9% (9/21) were refractory. SUVmax did not correlate significantly with baseline laboratory markers or outcomes. In contrast, TLG demonstrated strong correlations with AST (r=0.657, p=0.003), LDH (r=0.663, p=0.003), CRP (r=0.598, p=0.009), and ESR (r=0.549, p=0.018). ROC analysis showed that TLG (AUC 0.821) and MLV (AUC 0.803) outperformed SUVmax (AUC 0.652) in predicting severe/refractory disease (Figure 2).

Conclusion: This study provides the first detailed volumetric map of muscle inflammation in IIMs using 18F-FDG PET/CT.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

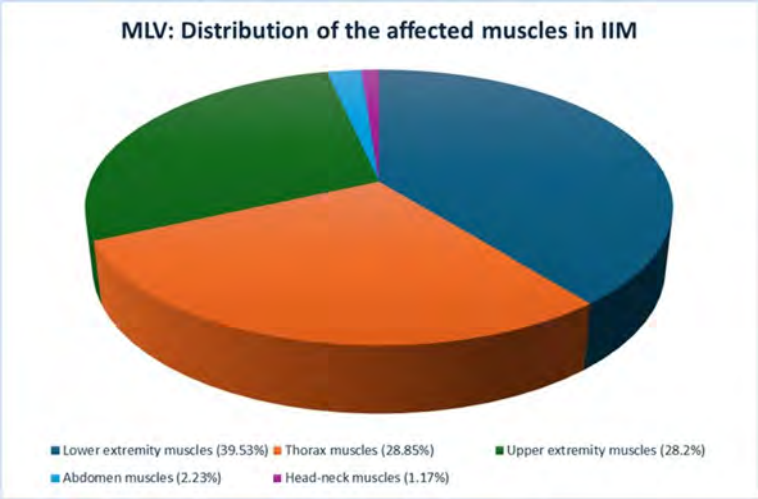
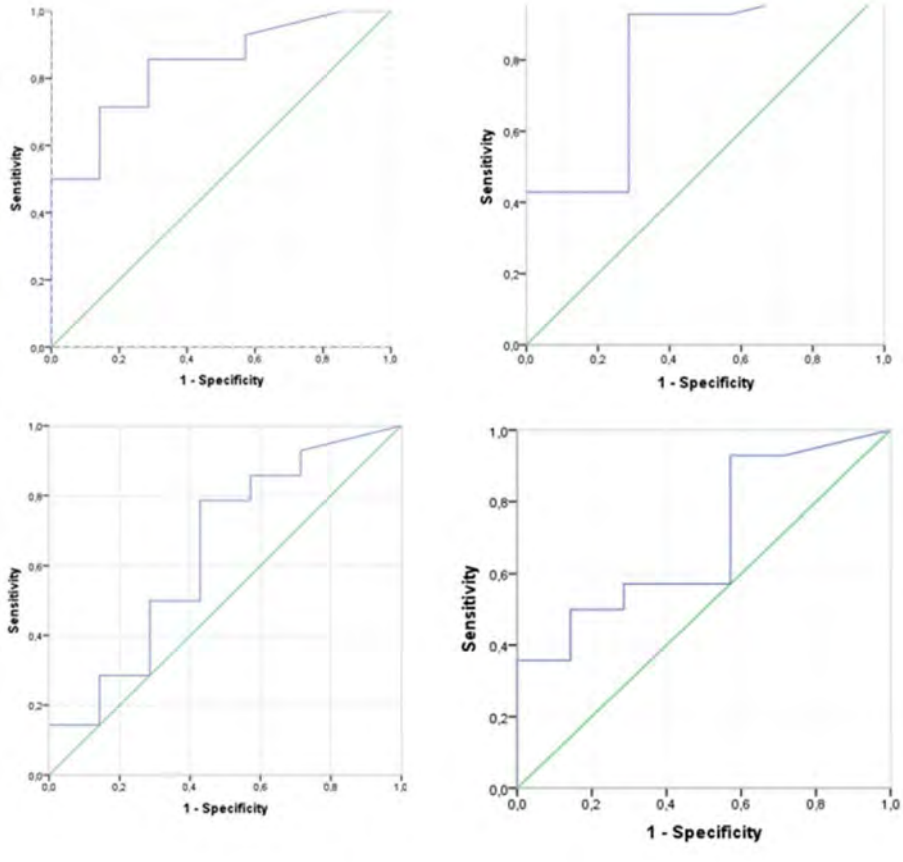


Figure 1.Graphical Distribution of Muscle Group Involvement in IIM Patients Based on MLV and TLG Measurements.



Graph 1. AUC: 0.837 (CI: 0.661-1.000), p: 0.014 (SUVmax, MLV, TLG)
Graph 2. AUC: 0.806 (CI: 0.594-1.000), p: 0.025 (MLV, TLG)
Graph 3. AUC: 0.643 (CI: 0.375-0.910), p: 0.296 (MLV, SUVmax)
Graph 4. AUC: 0.694 (CI: 0.457-0.931), p: 0.156 (SUVmax, TLG)

Figure 2. ROC Curves Comparing the Discriminative Ability of SUVmax, MLV, and TLG for Predicting Severe or Refractory Disease.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Thoracic and paraspinal muscles were major sites of involvement, challenging the classical focus on proximal muscles. Volumetric PET parameters, particularly TLG and MLV, more effectively captured the global inflammatory load and correlated with severe or refractory disease. These findings suggest that comprehensive volumetric PET/CT analysis may enhance diagnostic precision and risk stratification in IIMs.

Disclosure: F. Basibuyuk: None; **M. Bahadir**: None; **G. Kenar Artin**: None; **A. Kiray**: None; **R. Bekis**: None; **İ. Sari**: None.

Abstract Number: 2674

Pulmonary ultrasound findings and their relationship with clinical characteristics and myopathy antibodies in a cohort of patients with myositis

Ana Mora[1], Carina Soto-Fajardo[2], Jiram Torres-Ruiz[3], Diana Gómez-Martín[4], Fabian Carranza[5], Tabata Cano[6], Elena Cervantes Ramírez[7], Alejandra Espinosa[5], Yatzil Reyna Juarez[8] and Carlos Pineda[2], [1]National Rehabilitation Institute "Luis Guillermo Ibarra Ibarra", Mexico, Mexico, [2]National Rehabilitation Institute "Luis Guillermo Ibarra Ibarra", Mexico City, Mexico, [3]INCMNSZ, Ciudad de México, Mexico, [4]INCMNSZ, Mexico city, Federal District, Mexico, [5]National Rehabilitation Institute "Luis Guillermo Ibarra Ibarra", Ciudad de México, Mexico, [6]National Rehabilitation Institute "Luis Guillermo Ibarra Ibarra", Huixquilucan, Mexico, [7]National Rehabilitation Institute "Luis Guillermo Ibarra Ibarra", Mexico, [8]Instituto Politècnico Nacional, Tultitán de Mariano Escobedo, Mexico State, Mexico

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies – Basic & Clinical Science I: Diagnostics & Therapeutics (2669–2674)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of diseases characterized by muscular and systemic involvement, with interstitial lung disease (ILD) being a challenging problem. High-resolution tomography (HRCT) is the current reference standard for diagnosing ILD; however, there are limitations related to its cost, accessibility, and the use of ionizing radiation. Lung ultrasound (LUS) has recently been used to detect ILD associated with other rheumatic diseases, which may justify its use as a screening method for clinical suspicion of ILD. However, evidence on using LUS in ILD associated with IIM is limited. We aimed to characterize the LUS findings in patients with IIM and their relationship with clinical features and antibodies.

Methods: Patients diagnosed with IIM according to the ACR/EULAR 2017 Classification Criteria were included, and they underwent HRCT, LUS, and pulmonary function tests (PFT). The Warrick score was used to assess the severity and extent of ILD. Ultrasound was performed using a LOGIQTMe device with a 4-12 MHz linear probe, applying two scanning methods (14 predetermined intercostal space (ICS) and 12 posterior-basal ICS). "B" lines (BL) and pleural abnormalities (PA) were documented for each ICS. Descriptive statistics were used based on the distribution of the variables, ROC curve analysis was conducted, and the sensitivity and specificity of LUS for detecting ILD compared to HRCT were calculated. Correlations were analyzed using the Spearman correlation coefficient between the ultrasound findings, the Warrick score, and the PFT.

Results: We included 59 patients diagnosed with IIM, mostly women (79.7%). The median and interquartile range (IQR) of age enrolment was 52 years (39.0-60.5). The most common diagnoses were dermatomyositis (72.9%) and antisynthetase syndrome (15.3%). The most frequent antibodies in the recruited patients were Ro-52 (30.5%), Mi-2 (23.7%), and MDA-5 (16.9%). The prevalence of ILD was 64.4%. Relevant baseline characteristics are shown in Table 1.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. General Characteristics

Table 1. General Characteristics			
Variable	**ILD n = 38 (64.4 %)**	**w/o ILD n = 21 (35.6 %)**	**p**
Age	60 (51 - 63)	46 (34.75 – 55.0)	0.06
Gender (Female)	18 (38.3)	29 (61.7)	0.3
Diagnosis			
DM	12 (27.9)	31 (72.1)	
ASyS	8 (88.9)	1 (11.1)	.003
PM	1 (25)	3 (75)	
SP	0 (0)	3 (100)	
Jo-1	4 (100)	0 (0)	0.005
Ro -52	10 (55.6)	8 (44.4)	
Warrick score	11.00 (10.00 – 17.00)	0 (0 – 4)	< 0.001
B-line count in 14 ICS	10.00 (4.00 – 24.00)	0 (0 - .25)	< 0.001
B-line count in 12 ICS	5.00 (1.00 – 14.00)	0 (0 – 0)	< 0.001
Pleural line abnormalities (22 ICS)	8.0 (4.00 – 12.00)	0 (0 – 2)	< 0.001
FVC	84 (68 – 111)	95.5 (82 – 104.7)	0.13
FEV1	80 (71 – 115)	93.0 (83.5 -101.5)	0.09
FEV1 / FVC	100 (94 – 103)	98.50 (94.2-104.50)	0.86

Continous variables: Mean ± DE, Median (25–75), Categorical variables: Frequency (%)

ILD: Interstitial Lung Disease, Intercostal spaces: ICS, DM: Dermatomyositis , ASyS: antisynthetase syndrome, PM: Polymyositis, SP: superposition, FVC: Forced vital capacity, FEV1: Forced expiratory volume, FEV1/FVC: Ratio FEV1/FVC

Table 2. Correlations between ultrasonographic findings and Warrick score

Table 2			
Variable	**Lines B 14 ICS >5**	**Lines B 12 ICS >2**	**Alteration in the pleural line >1**
Warrick gravity	r = 0.641 p = < 0.0001	r = 0.55 p = < 0.0001	r = 0.60 p = < 0.001
Warrick extension	r = 0.65 p = < 0.0001	r = 0.54 p = < 0.0001	r = 0.59 p = < 0.001
Warrick total	r = 0.64 p = < 0.0001	r = 0.54 p = < 0.0001	r = 0.59 p = < 0.001

Intercostal spaces: ICS

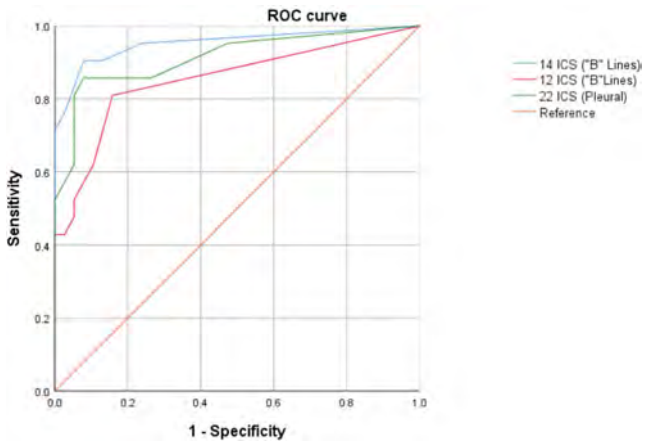


Image 1. ROC curve of ultrasonographic findings

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

A positive, strong correlation was demonstrated between the Warrick score and B-line count in 14 ICS (rho= 0.64, p< 0.0001) and 12 ICS (rho=0.54, p< 0.0001). Also, a positive correlation was observed between pleural line abnormalities and the Warrick score (rho=0.59,p< 0.0001). Table 2.

The AUCs were 0.95 (95% CI, 0.88-1.00), 0.85 (95% CI, 0.74-0.96), and 0.91 (95% CI, 0.82-0.99) for the evaluation of the number of B-lines in 14 ICS, 12 ICS, and the number of ICS with pleural abnormalities (22 EIC), respectively. Image 1

Conclusion: Our study confirms that LUS is a valuable tool for detecting ILD in patients with IIM. It offers real-time visualization and high diagnostic accuracy by quantifying B-lines and evaluating pleural abnormalities using either of the two scanning protocols (14 and 12 ICS). The method demonstrates strong diagnostic performance and a good correlation with the Warrick scores.

Disclosure: A. Mora: None; **C. Soto-Fajardo**: None; **J. Torres-Ruiz**: None; **D. Gómez-Martín**: None; **F. Carranza**: None; **T. Cano**: None; **E. Cervantes Ramírez**: None; **A. Espinosa**: None; **Y. Reyna Juarez**: None; **C. Pineda**: None.

Abstract Number: 2675

RANTES and CXCL10 as Potential Tear-Based Biomarkers Associated with Ocular Damage in Pediatric Chronic Anterior Uveitis

Ilaria Maccora[1], Mariia Pavlenko[2], Mekibib Altaye[3], Hermine Brunner[4], Alexandra Duell[4], Megan Quinlan-Waters[5], Alyssa Sproles[6], Sherry Thornton[4], Grant Schulert[4], Virginia Miraldi Utz[4] and Sheila Angeles-Han[6], [1]Rheumatology Unit, ERN ReCoNNET Center, Meyer Children's Hospital IRCCS, Florence, Italy, Firenze, Florence, Italy, [2]Rheumatology Division, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, Cincinnati, OH, [3]Cincinnati Children's Hospital, Cincinnati, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [5]Cincinnati Children's Hospital Medical Center, CCHMC, [6]Cincinnati Children's Hospital, Cincinnati, OH

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical III (2675–2680)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Pediatric chronic anterior uveitis (CAU) leads to sight-threatening complications in approximately 50% of affected children. Among complications, cataract and glaucoma are among the most common ocular complications of CAU. We aim to identify tear-based biomarkers associated with ocular damage in pediatric CAU.

Methods: This cross-sectional study included children ≥5 years old diagnosed with CAU (juvenile idiopathic arthritis-associated (JIA-U) or idiopathic (iCAU)) from our registry at CCHMC. Tear samples were collected from both eyes by Schirmer strips. Ocular complications included cataract, glaucoma, synechiae, band keratopathy, macular edema, epiretinal membrane, and optic disc oedema. Levels of S100A8, A9, and A12 were measured by ELISA, and IL-18, IL-8, CXCL10 (IP-10), MCP-1, RANTES, and sICAM-1 by Luminex assays. Biomarker levels were compared by the number of ocular complications (0, 1, >1). An exploratory Spearman correlation (ρ) analysis was performed and a Heatmap was developed to identify potential significant associations. A p-value < 0.05 was considered significant.

Results: Forty-one children (29 JIA-U; 12 iCAU) with CAU contributed 121 tear samples (86 JIA-U; 35 iCAU) (Table 1), of whom 77 samples are from eyes with complications (51 by JIA-U and 26 by iCAU, $\chi^2$2.41, p=0.088). We observed significant differences regarding the number of complications between JIA-U vs iCAU (mean 1.88 vs 2.15, p< 0.001).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Clinical Characteristics of Children with Chronic Anterior Uveitis

	All CAU Cohort N (%)	JIA-U N (%)	iCAU N (%)
Number of patients	**41 (100)**	**29 (70.7)**	**12 (29.3)**
Female	30 (73.2)	25 (86.2)	5 (41.7)
Male	11 (26.8)	4 (14.8)	7 (58.3)
Race			
White	37 (90.2)	25 (86.2)	12 (100)
Black and African American	1 (2.4)	1 (3.4)	0
Asian	2 (4.9)	2 (6.9)	0
American Indian or Alaska Native	1 (2.4)	1 (3.4)	0
Ethnicity			
Non-Hispanic	38 (92.7)	26 (89.6)	12 (100)
Hispanic	2 (4.92)	2 (6.9)	0
Unknown	1 (2.4)	1 (3.4)	0
Age at sample collection in years Mean (range)	12 (5-20)	12 (5-19)	12 (7-19)
Time of uveitis course in years Mean (range)	4.8 (0-17)	4.8 (0-17)	4.9 (0-8)
Arthritis characteristics			
Oligoarticular		16 (55.2)	N/A
Polyarticular RF-		13 (44.8)	N/A
Arthritis activity*			
Active		13	N/A
Inactive		21	N/A
Uveitis activity*			
Active	21 (100)	14 (66.7)	7 (33.3)
Inactive	35 (100)	25 (71.4)	10 (28.6)
Medication use for eye at time of visit			
Topical medications			
Corticosteroids	34 (83)	25 (86.2)	9 (75)
Glaucoma medication	10 (24.4)	7 (24.1)	3 (25)
Cyclopentolate	2 (4.9)	2 (6.9)	0
Systemic medications			
Methotrexate	26 (63.4)	19 (65.5)	7 (58.3)
Infliximab	9 (22)	6 (20.7)	3 (25)
Adalimumab	8 (19.5)	7 (24.1)	1 (8.3)
Tocilizumab	5 (12.2)	5 (17.2)	0
Abatacept	1 (2.4)	1 (3.5)	0
Golimumab	1 (2.4)	1 (3.5)	0
Leflunomide	1 (2.4)	1 (3.5)	0

*One patient could contribute to both active and inactive uveitis/arthritis groups; List of abbreviations: JIA-U-Juvenile Idiopathic Arthritis-associated uveitis; CAU - Chronic Anterior Uveitis; iCAU - Idiopathic CAU; N number; N/A not applicable

We observed an increased level of RANTES in children with complications compared to those without complications (0.752 vs 0.389, p=0.028), and when considering the number of complications [0, 1, or >1] (0.389 vs 0.675 vs 0.824 respectively, p=0.022) (Figure 1A). Conversely, CXCL10 was decreased in children with complications (2.82 vs 2.99, p=0.010), and when stratified by the number of complications (2.991 vs 2.881 vs 2.785 respectively, p=0.004, Figure 1B).

As shown in Figure 2, there were several significant correlations between the level of candidate biomarkers and ocular parameters: RANTES was positively correlated with the presence of complications (ρ=271, p=0.005) and glaucoma (ρ=306,p=0.015), while CXCL10 was negatively correlated with the presence of complications(ρ=0.27, p=0.005, the number of complications (ρ=0.31,p=0.006), and the presence of macular oedema/and papillitis (ρ=245,p=0.031). Moreover we found a positive correlation between S100A9 and the presence of cataract (ρ=384,p=0.003) and a negative correlation with uveitis activity (ρ=292,p=0.007).

Conclusion: We identified RANTES, CXCL10 and S100A9 as potential tear-based biomarkers associated with ocular damage in pediatric patients with CAU. RANTES appears to be elevated with ocular complications, whereas CXCL10 is decreased. The role of RANTES has been demonstrated in experimental autoimmune uveitis models and patients with

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

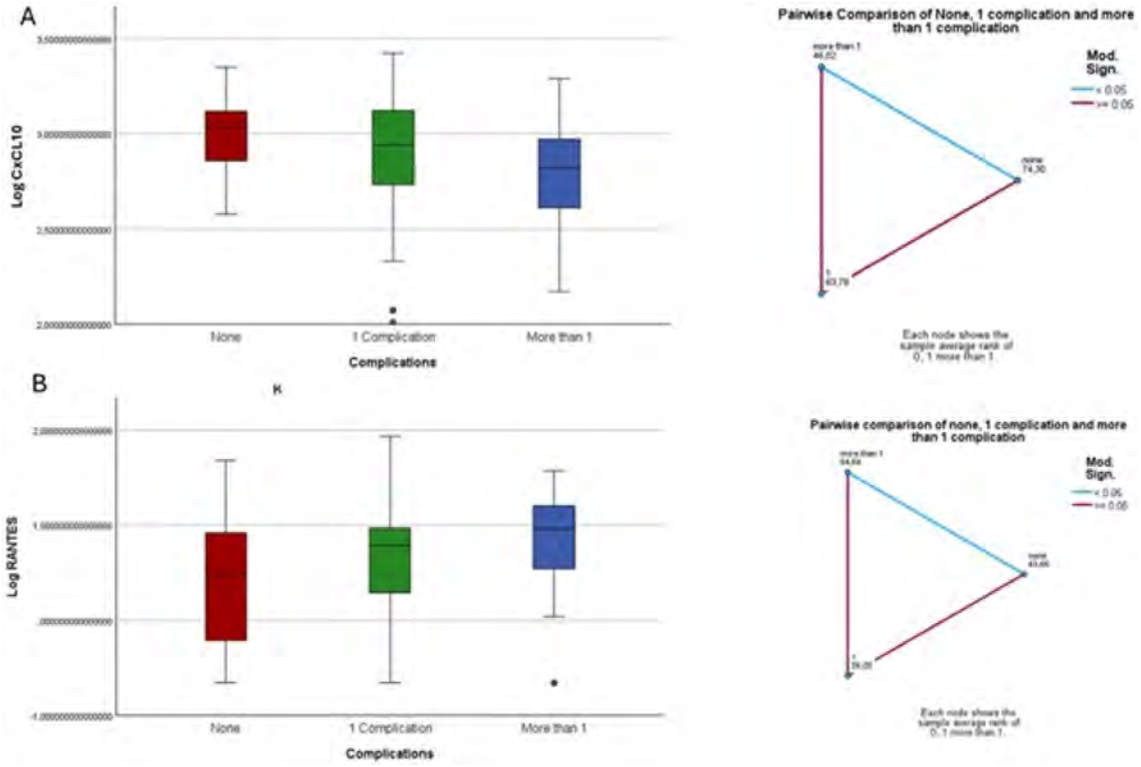


Figure 1: Significant differences in complications and A) CXCL10 and B) RANTES with pairwise comparison that indicate differences.

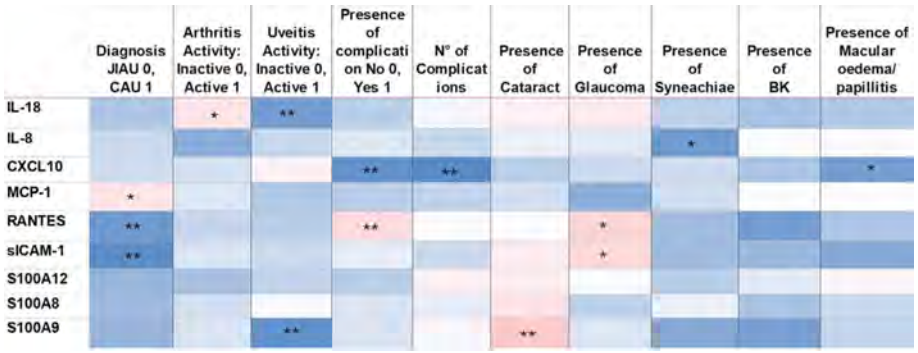


Figure 2: Heatmap representing the correlations among the logarithmic value of cytokines and chemokines and the different variables considered. The significant correlations are identified with one or two stars (0.05 >p>0.009 and p <0.009 respectively). The blue color represents negative correlations, while red color positive correlations

uveitis. It has also been shown to differentiate patients with glaucoma. Further, we identified CXCL10 and S100A9 correlations with specific complications. Next steps are to determine biomarkers that are associated with specific ocular complications and differentiate activity from damage (chronicity).

Disclosure: I. Maccora: None; **M. Pavlenko**: None; **M. Altaye**: None; **H. Brunner**: AbbVie, 2, AstraZeneca-Medimmune, 2, Biogen, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Eli Lilly, 2, EMD Serono, 2, F. Hoffmann-La Roche, 2, Genentech, 5, GlaxoSmithKline, 2, Merck, 2, Novartis, 2, Pfizer, 2, 5, Sanofi, 2, UCB, 2; **A. Duell**: None; **M. Quinlan-Waters**: None; **A. Sproles**: None; **S. Thornton**: None; **G. Schulert**: IpiNovoyx, 5, Novartis, 2, SOBI, 2; **V. Miraldi Utz**: None; **S. Angeles-Han**: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2676

Tofacitinib in Juvenile spondyloarthropathy: clinical efficacy, impact on biomarkers and comparison with Adalimumab

Anu Balakrishnan[1], Asif Khan[2], Shivika Guleria[3], Fareha Umam[4], Naveen R[5], Priyansh Jain[2], Lekshmi Minikumari Rahulan[2], Rudrarpan Chatterjee[6] and **Amita Aggarwal**[7], [1]Sanjay Gandhi Post Graduate Institute, India, Lucknow, Uttar Pradesh, India, [2]Sanjay Gandhi Postgraduate Institute of Medical sciences Lucknow, Lucknow, Uttar Pradesh, India, [3]SGPGIMS, Lucknow, Lucknow, Uttar Pradesh, India, [4]Dept of Clinical Immunology and Rheumatology, SGPGIMS, Lucknow, Uttar Pradesh, India, [5]Sanjay Gandhi Post graduate institute of medical sciences, Lucknow, Uttar Pradesh, India, [6]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow., Lucknow, Uttar Pradesh, India, [7]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Lucknow, Uttar Pradesh, India

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Pediatric Rheumatology – Clinical III (2675–2680)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Tofacitinib is a JAK inhibitor that has been approved for treatment of polyarticular Juvenile idiopathic arthritis. However, data on its use in juvenile spondyloarthropathy including Enthesitis related arthritis is limited. MRP8/14 and MMP3 are good biomarkers of activity in Juvenile spondyloarthropathy[1,2]. Thus, we studied the effect of Tofacitinib on disease activity, biomarkers and compared that with treatment with adalimumab.

Methods: Patients with juvenile spondyloarthropathy (onset < 18 years), and having poor response to NSAIDs and/or methotrexate/Sulphasalazine were included in the study. Patients were given a choice of tofacitinib(tofa) or Adalimumab (ADA) and based on preference, the availability of cold chain to store ADA patients were treated with either ADA or tofacitinib.

Table 1: Baseline characteristics of two groups

Characteristics	Tofacitinib group (n=29)	TNF inhibitor group (n=24)
Male: female	28:1	22:2
Age at the onset of disease	12.6+3.61	11.7+3.57
Age at inclusion (years)	17.8+3.54	17.9+3.81
Duration of disease (years)	5.21+3.25	6.02+3.84
Clinical features (N)		
Arthritis	25	25
Enthesitis	21	21
IBP	20	20
Sacroiliitis	21	21
Uveitis	02	02
Hip disease	19	19
Tarsitis	10	10
HLA B27		13/14
Disease activity parameters		
ESR	46.78+29.28	65.68+41.01
JSpADA	4.12+1.26	5.06+1.18
BASDAI	4.39+1.89	5.76+1.74
BASMI	2.03+1.25	3.58+1.86
BASFI	3.49+2.45	5.77+2.42
ASDAS ESR	3.61+1.04	4.51+0.90

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

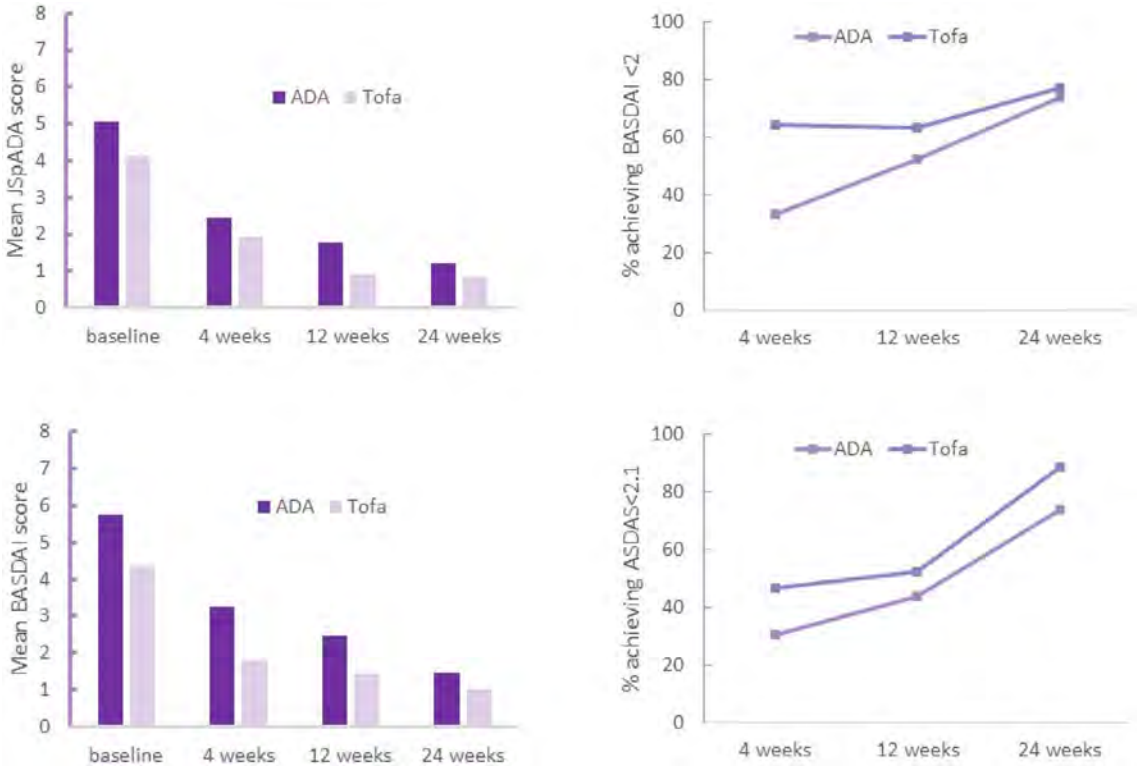


Figure 1: Effect of ADA and Tofa on JSpADA, BASDAI, ASDAS at different time points

Drugs were provided free of cost and were supported by a foundation. The disease activity was assessed using JSpADA, BASDAI, BASFI, BASMI and ASDAS at baseline, 4 weeks, 16 weeks and 24 weeks. ESR, CRP, MMP3, MRP 8/14, were measured at 0 and 4 weeks. The study was approved by institutional ethics committee and consent was taken from patient/guardian.

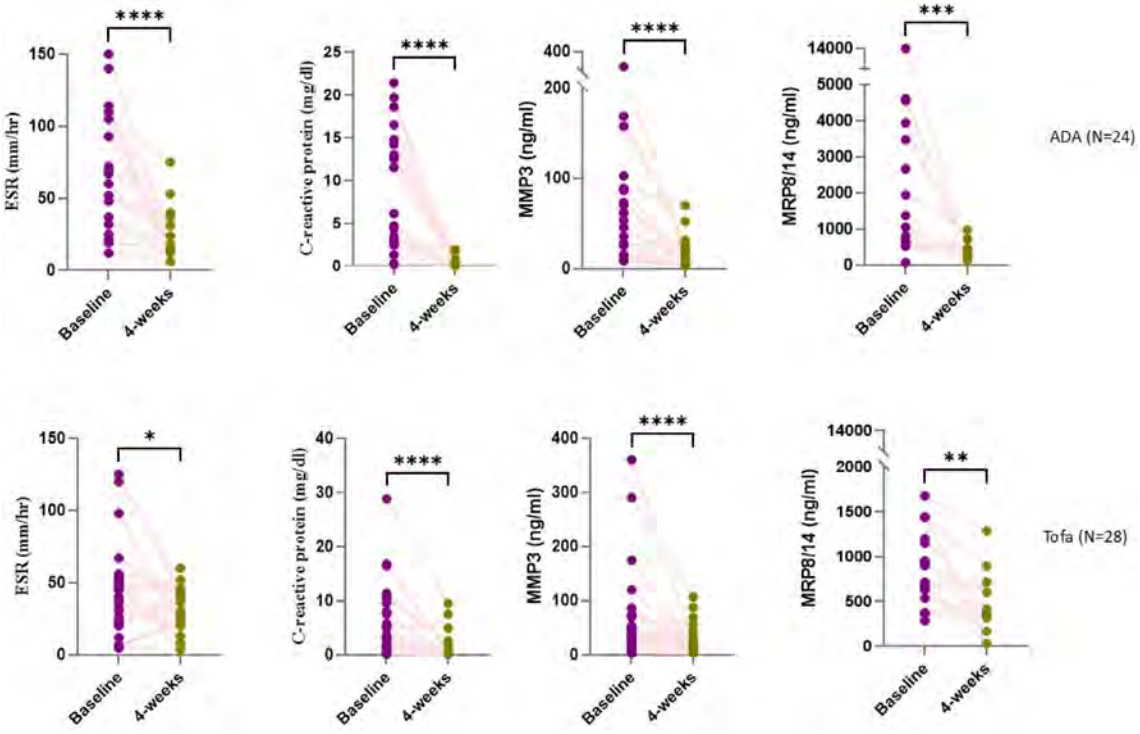


Figure 2: Effect of ADA and Tofa on ESR, CRP, MMP3 and MRP8/14

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: The study included 53 patients with JSpA (29 on Tofacitinib and 24 on ADA). The clinical features of the two groups showed that the mean age of onset, duration of disease and clinical features were similar in both the groups however disease activity was higher in ADA group. (Table 1). In ADA group 1 patient had transaminitis at 12 weeks, 1 had flare after 16 weeks, 1 had anemia and GI infection and one each was lost to follow up at 16 and 24 weeks. In Tofa group 1 patient each was lost to follow up at 4, 12 and 24 weeks thus 26 complete the 24 week follow up.

Both JSpADA score and BASDAI reduced after 4 weeks and over the next 24 weeks there was further reduction of the score (figure 1). Both groups had a similar reduction in scores. BASDAI remission (< 2) was seen in 14/19 (73.7%) in ADA group and 20/26 (76.9%) patients in Tofa group. ASDAS based low disease activity was achieved by 73.6% in ADA group and in 88.4% in tofa group ($p < 0.05$) (figure 1).

The blood biomarkers i.e. ESR, CRP, MMP and MRP8/14 showed a significant fall at 4 weeks, however the degree of fall was similar between ADA and Tofa.(Figure 2)

Conclusion: Tofacitinib shows similar efficacy, reduction in markers of inflammation as adalimumab in JSpA. It has a good safety profile and also has rapid onset of action.

1. J Rheumatol. 2011 Nov;38(11):2482-7. 2. Rheumatology (Oxford). 2014 Feb;53(2):270-4.

The study was funded by an intramural grant to AA

Disclosure: A. Balakrishnan: None; **A. Khan**: None; **S. Guleria**: None; **F. Umam**: None; **N. R**: None; **P. Jain**: None; **L. Minikumari Rahulan**: None; **R. Chatterjee**: None; **A. Aggarwal**: None.

Abstract Number: 2677

Quantified Imaging Response at the Sacroiliac Joints to TNF-Inhibitor Therapy in Youth with Axial Disease

Timothy Brandon[1], Rui Xiao[2], Daniel Lovell[3], Edward Oberle[4], Matthew Stoll[5], Nancy A. Chauvin[6], Michael Francavilla[7], Walter P. Maksymowych[8] and **Pamela Weiss**[9], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]Nationwide Children's Hospital, Columbus, OH, [5]University of Alabama at Birmingham, Birmingham, AL, [6]The Cleveland Clinic, Hummelstown, PA, [7]Department of Pediatric Radiology, Children's Hospital Philadelphia, Philadelphia, PA, [8]Department of Medicine, University of Alberta, 568 Heritage Building, Edmonton, AB, Canada, [9]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical III (2675–2680)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: This study assessed the timeline for the resolution of inflammation, changes in structural lesions at the sacroiliac joints (SIJ), and their correlation with patient-reported outcomes in youth with spondyloarthritis and axial disease (axJSpA) starting tumor necrosis factor inhibitor (TNFi) therapy.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This prospective, observational, multicenter study included youth aged 8 to 18 years with a clinical diagnosis of axJSpA starting TNFi therapy. TNFi therapy continued through the observation window as part of ongoing standard of care. Assessments at baseline and 12 weeks included a questionnaire, clinical exam, and MRI. Those with persistent SIJ inflammation at 12 weeks were invited for repeat MRI and questionnaires at 24 weeks. Imaging was independently assessed by 3 reviewers, blinded to timepoint and clinical details, using the Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ inflammation and structural scores (SIS and SSS). Patient-reported outcomes included PROMIS pain interference and global health scores, self-rated pain (neck/back/hip), and global change assessment (improved, stable, or worsened); Associations between imaging scores and patient-reported outcomes were analyzed using Spearman's correlation.

Results: Seventy-five participants enrolled; 73 (97.3%) completing the baseline visit. Among those, 62 (84.9%) had MRI findings consistent with axJSpA, and 57 of 62 (91.9%) completed the 12-week visit. Subject baseline characteristics are shown in Table 1. The median baseline SIS was 11 (IQR 5-20), and 89% of participants had ≥ 1 structural lesion, most commonly erosion. Change in imaging lesions from baseline to 12 and 24 weeks are illustrated in Figure 1. At 12 weeks, 89% improved in SIS (median change: -8 [IQR -18 to -3]); 63% achieved resolution of inflammation (SIS < 2). Of 26 with persistent inflammation and available global change data, 85% reported at least moderate improvement. At 24 weeks, 14 of 25 (25% of total) had ongoing inflammation with a median SIS of 1 (IQR 0-2). Erosion and sclerosis scores declined, increased or stayed the same in 58/25/17% and 21/9/70% of participants, respectively. Structural changes that reflect a tissue response to resolution of inflammation (fat metaplasia and backfill) demonstrated increased scores in 30% and 28%, respectively at week 12. Correlations between imaging outcomes and patient-reported measures at 12 weeks are shown in Figure 2.

Table 1. Subjects

	Median (IQR) or n (%)
Criteria fulfilled	
ESSG	48 (84.2%)
ILAR ERA	49 (86.0%)
ILAR PsA	3 (5.3%)
Age at baseline, years	15.3 (13.5-16.9)
Sex, male	39 (68.4%)
HLA-B27+	22 (41.5%)
Family history of SpA	5 (9.3%)
Peripheral arthritis	16 (28.1%)
Enthesitis	31 (54.4%)
Psoriasis	6 (10.5%)
Inflammatory Bowel disease	9 (15.8%)
TNFi therapy	
Adalimumab	49 (86.0%)
Etanercept	5 (8.8%)
Infliximab	3 (5.2%)
Inflammation Score (baseline; range 0-72)	11 (5-20)
Structural lesions	
Erosion	51 (89.5%)
Sclerosis	21 (36.8%)
Fat metaplasia	6 (10.5%)
Backfill	6 (10.5%)
Ankylosis	2 (3.5%)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

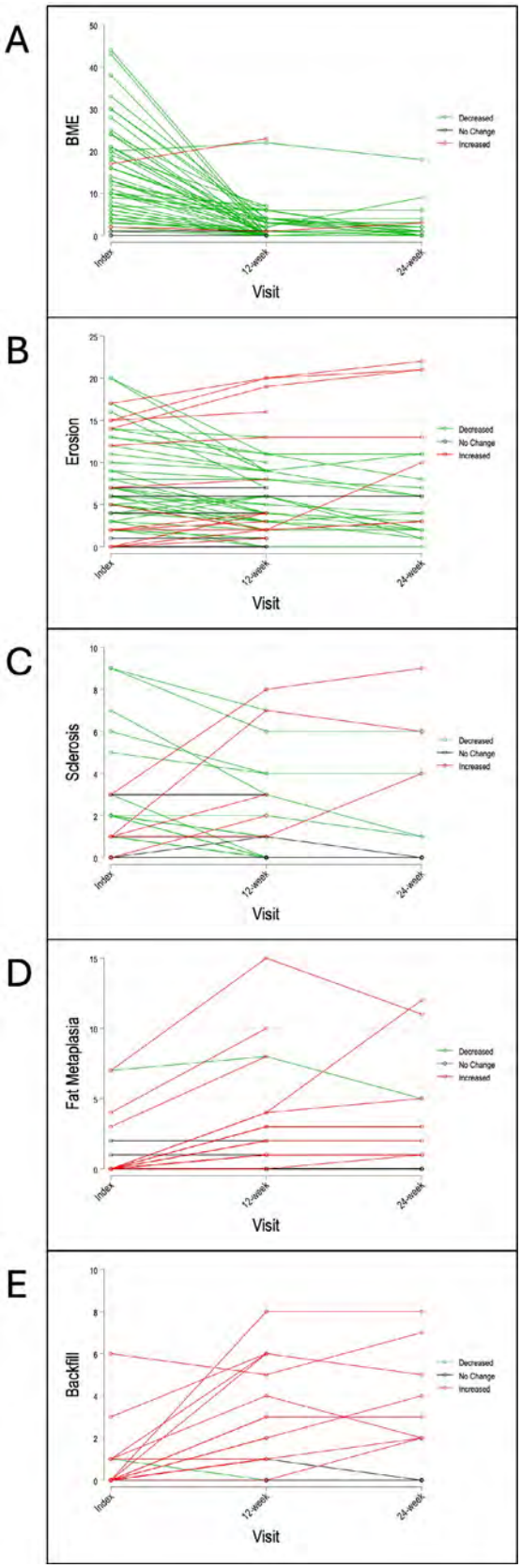


Figure 1. Lesion scores of each participant at baseline, 12 weeks, and 24 weeks for (A) Bone marrow edema (BME), (B) Erosions, (C) Sclerosis, (D) Fat metaplasia, and (E) Backfill. Each line represents a single participant and is color-coded to represent decreased (green), no change (black), or increased (red) in each lesion score from baseline to the final visit (12 or 24 weeks). Fat metaplasia and backfill are structural changes that reflect a tissue response to resolution of inflammation.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

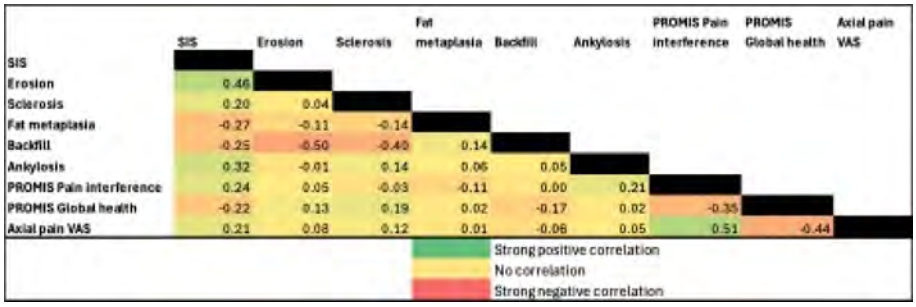


Figure 2. Correlation matrix of patient-reported and imaging outcomes after 12 weeks of TNFi therapy. All raw scores generated from PROMIS instruments are translated into standardized T-scores with a population mean of 50 and standard deviation of 10. Higher scores in a domain represent more of the trait being measured; higher T-scores indicate a worse outcome in pain interference; lower T-scores indicate a worse outcome global health.

Conclusion: Approximately half of participants had persistent SIJ inflammation on MRI at 12 weeks, yet 85% of those reported meaningful clinical improvement. Reductions in certain structural lesion scores were observed, and there was some evidence of early reparative changes, such as fat metaplasia or backfill. These findings underscore variability in therapeutic response to TNFi and indicate that significant clinical and imaging improvements may occur early in treatment, although a subset of patients may continue to exhibit active inflammation beyond 12 weeks. The modest correlations observed between imaging findings and patient-reported outcomes highlight the need for a multimodal approach to assessing treatment response in axJSpA.

Disclosure: T. Brandon: None; **R. Xiao**: None; **D. Lovell**: AbbVie, 2, Bristol-Myers Squibb(BMS), 2, Canadian Arthritis Society, 12, DSMB memberNIH-NIAMS and NIAID, Canadian Arthritis Society, Novartis, 2; **E. Oberle**: Pfizer, 1; **M. Stoll**: None; **N. Chauvin**: None; **M. Francavilla**: None; **W. Maksymowych**: AbbVie, 2, 5, 6, BMS, 2, 5, 6, Boehringer-Ingelheim, 2, Celgene, 2, Chief Medical Officer for CARE ARTHRITIS, 4, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

Abstract Number: 2678

The Association Between Medication Taper Duration and Time to JIA Disease Flare: A Retrospective Cohort Study

Christian-Immanuel Oliveros[1], Kelly Rouster-Stevens[2], Laura Johnson[3] and Sampath Prahalad[4], [1]Emory University / Children's Healthcare of Atlanta, Atlanta, GA, [2]Emory University/Children's Healthcare of Atlanta, Peachtree Corners, GA, [3]Emory University, Atlanta, GA, [4]Emory + Children's Pediatric Institute, Atlanta, GA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical III (2675–2680)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Once clinically inactive, many patients with oligoarticular (oligoJIA) or polyarticular JIA (polyJIA) are interested in de-escalating therapy in a safe and successful manner.

Many studies have attempted to answer questions regarding JIA medication withdrawal such as priority of medication to wean on those using combination therapy or recapturing patients who flare. However, no studies to date have attempted to determine if there is an association between duration of medication taper and time to relapse should it occur.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: This is a single site, retrospective cohort study. Eligible subjects included all pediatric patients with oligoJIA or polyJIA seen between January 1, 2015, and August 31, 2023, who tapered off a unique conventional disease-modifying antirheumatic drug (cDMARD), which included methotrexate or leflunomide, and/or biologic disease-modifying antirheumatic drug (bDMARD), which included adalimumab, infliximab or etanercept, as directed by their rheumatology provider or on their own accord.

The primary objective was to determine if there was an association between length of medication taper and time to disease relapse should it occur. The secondary objective was to identify risk factors for JIA disease relapse.

Kaplan-Meier survival curves were used to illustrate the observed probability of flare-free survival over time. To explore Unadjusted Cox proportional hazards regressions were used to estimate the association between exposures of interest and time to flare, using robust (sandwich) standard errors clustered by participant (due to multiple tapers within certain subjects). Variables that were statistically significant in the unadjusted models were entered into a final multivariable model.

Results: Among oligoJIA subjects (n = 67), there were 60 unique cDMARD tapers, 17 unique bDMARD tapers, and one patient simultaneously tapered cDMARD and bDMARD, who was excluded from the analysis. Risk factors ($p< 0.05$) for oligoJIA flare included tapering off a bDMARD, having more than 1 joint affected, HLA-B27 and RF positivity. Subjects with longer tapers (>6 months, > 12 months) of either medication class demonstrated increased risk for disease relapse compared to shorter taper durations (HR of 2.29 (95%CI: 1.23-4.26, p=0.009) for >6 months, HR of 6.41 (95% CI: 3.47-11.76, $p< 0.001$) for > 12 months).

Among polyJIA subjects (n = 41), there were 41 unique cDMARD tapers and 10 unique bDMARD tapers. Risk factors for polyJIA flare included tapering off a bDMARD and abruptly stopping either JIA medication (versus tapering over time). Subjects with longer taper durations (≥1 day) demonstrated a protective effect against disease relapse compared to subjects who immediately stopped (aHR: 0.41; 95% CI: 0.016-1.07, p=0.035).

Table 1.

Table 1. Oligo JIA Cohort: Results from Multivariable Cox Proportional Hazards Model[1]

	Adj. HR (95% CI)	p-value
Number of Affected Joints		
0-1	Ref	
2-4	2.10 (1.12, 3.95)	**0.021**
Medication Being Tapered		
DMARD	Ref	
Biologic	2.17 (1.05, 4.78)	**0.037**
Taper Time		
< 12 months	Ref	
≥ 12 months	4.57 (2.42, 8.62)	**<0.001**

[1] Cox proportional hazards regression to estimate the association between variables and time to flare, using robust (sandwich) standard errors clustered by patient

Table 2.

Table 2. Poly JIA Cohort: Results from Multivariable Cox Proportional Hazards Model[1]

	Adj. HR (95% CI)	p-value
Medication Being Tapered		
DMARD	Ref	
Biologic	3.05 (1.08, 8.59)	0.069
Taper Time		
0 days	Ref	
≥ 1 day	0.41 (0.16, 1.07)	**0.035**

[1] Cox proportional hazards regression to estimate the association between variables and time to flare, using robust (sandwich) standard errors clustered by patient

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

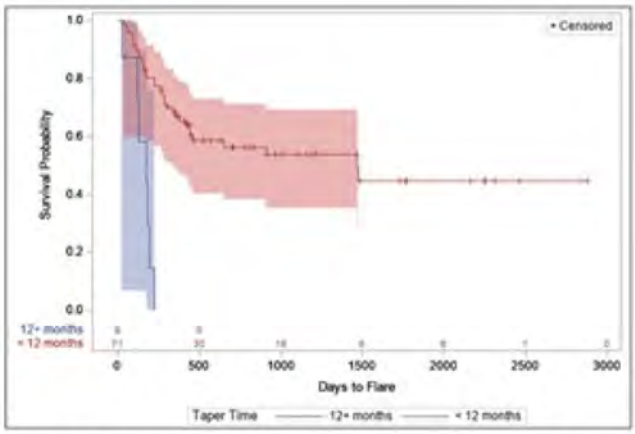


Figure 1a. Oligo JIA Cohort: Kaplan Meier Curve Estimating Survival Curves, Stratified by Taper Time (<12 months vs. 12+ months)

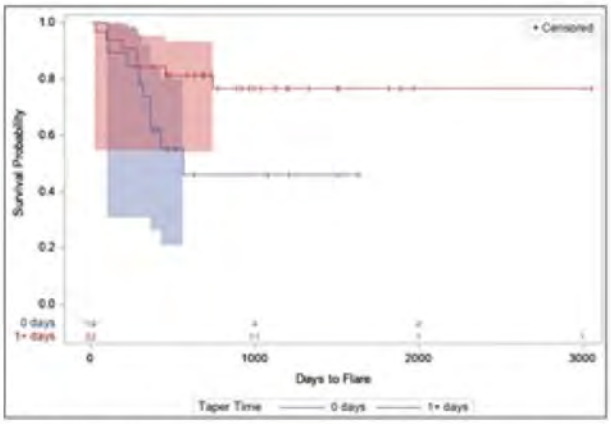


Figure 1b. Poly JIA Cohort: Kaplan Meier Curve Estimating Survival Curves, Stratified by Taper Time (0 days vs. 1+ days)

Figures 1a and 1b.

Conclusion: For oligoJIA patients, there was an inverse association between duration of medication taper and time to relapse. This suggests that children with clinically inactive oligoJIA and particularly those with favorable factors (negative RF or HLA-B27 status, cDMARD monotherapy, only one joint affected) could undergo faster tapers. However, in those with polyJIA, children may benefit from a taper over time versus abruptly stopping their medication.

Disclosure: C. Oliveros: None; **K. Rouster-Stevens**: Accordant, 2; **L. Johnson**: None; **S. Prahalad**: None.

Abstract Number: 2679

Early-Life Nutrition and Gene-Environment Interactions Influencing Juvenile Idiopathic Arthritis Risk: Results from a Pregnancy Cohort

Vilde Øverlien Dåstøl[1], Ida Henriette Caspersen[2], Kristine Løkås Haftorn[3], Sigrid Hestetun[4], Siri Eldevik Håberg[5], Karen H. Costenbader[6], Marin Strøm[7], Sjurdur Frodi Olsen[8], Anne Lise Brantsæter[9], Ketil Størdal[10] and Helga Sanner[1], [1]Oslo University Hospital, Oslo, Norway, [2]Norwegian Institute of Public Health, Centre for Fertility and Health/Oslo University Hospital, Oslo, Norway, [3]Oslo University Hospital, Department of Rheumatology, Oslo, Norway, [4]Oslo University Hospital, Department of Rheumatology/University of Oslo, Oslo, Norway, [5]Norwegian Institute of Public Health, Centre for Fertility and Health/University of Bergen, Oslo, Norway, [6]Harvard Medical School and Brigham and Women's Hospital, Boston, MA, [7]Statens Serum Institut, Department of Epidemiology Research, Copenhagen, Denmark, [8]Statens Serum Institut,Biobank, congenital disorders, and vaccines preparedness/Harvard T.H. Chan School of Public Health, Copenhagen, Denmark, [9]Norwegian Institute of Public Health, Department of Food Safety and Centre for Sustainable Diets, Oslo, Norway, [10]Oslo University Hospital, Department of Pediatric and Adolescent Medicine/University of Oslo, Oslo, Norway

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical III (2675–2680)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Early-life nutrition may influence the risk of immune-mediated diseases like juvenile idiopathic arthritis (JIA). The benefits of breastfeeding are well established, but findings related to JIA have been inconsistent and mainly based on small case-control studies (1). Early introduction of solid food may promote immune tolerance (2), which could reduce the risk of immune-mediated diseases like JIA, but this has not been studied. We aimed to investigate the association

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Results of Analyses of Breastfeeding duration and Age at Introduction of Solid Food, and Child Risk of Developing JIA in the MoBa Cohort

Exposure	JIA/non-JIA (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Full breastfeeding duration			
<4 months	83 (34.7) / 25,050 (34.9)	1.13 (0.85-1.49)	1.10 (0.82-1.46)
4-5 months	113 (47.3) / 36,369 (50.7)	Ref	Ref
≥6 months	43 (18) / 10,342 (14.3)	1.36 (0.94-1.97)	1.41 (0.97-2.05)
Age at introduction of solid foods			
<4 months	17 (7) / 4,272 (6)	1.31 (0.79-2.16)	1.14 (0.68-1.90)
4-5 months	164 (68.6) / 54,027 (75.3)	Ref	Ref
≥6 months	58 (24.3) / 13,462 (18.8)	**1.42 (1.05-1.92)**	**1.48 (1.09-2.00)**

between breastfeeding duration, age at introduction of solid food, and risk of JIA in a large population-based pregnancy cohort, including possible gene-environment interactions.

Methods: We used The Norwegian Mother, Father, and Child Cohort Study (MoBa), a cohort that recruited pregnant women from 1999-2008, with data from >114 000 mother-infant pairs. A JIA case was, as previously validated (3), defined as having at least two ICD-10 codes (M08/M09) by linking the cohort to the Norwegian Patient Registry. At 6 months post-partum, mothers completed a questionnaire reporting infant feeding practices. Full breastfeeding was defined as receiving only breast milk without any formula or solid food. We categorized breastfeeding and age at solid food introduction as: < 4 months, 4–5 months (reference), and ≥6 months.

We used multivariable logistic regression and estimated odds ratios (aORs) adjusted for: maternal history of inflammatory rheumatic disease, age, education, BMI, parity, mode of delivery, preterm birth and gestational smoking. Umbilical cord blood sampling at birth allowed genotyping of a subsample of the children. We calculated polygenic risk scores (PRSs) using summary statistics from a large genome-wide association study (GWAS) to estimate the children's genetic risk of JIA (4). By using these PRSs, we assessed gene-environment interactions.

Results: Our final analytical sample included 239 infants who later developed JIA and 71,761 infants who did not, with genotyping data on 169 cases and 39,488 non-cases. The risk of JIA was non-significantly higher in those with a full breastfeeding duration ≥6 months (aOR 1.39, 95% CI 0.98-1.99) **(Table 1)**. We identified interactions between genetic susceptibility to JIA and both short (< 4 months) and prolonged (≥6 months) breastfeeding (p = 0.02 and 0.04).

Additionally, delayed introduction of solid food (≥6 months) was associated with an increased risk of JIA (aOR 1.48, 95% CI 1.09-2.00) **(Table 1)**, with no evidence of gene-environment interaction.

Conclusion: Our findings suggest that later introduction of solid food is associated with an increased risk of JIA, supporting the hypothesis that earlier dietary exposures may promote immune tolerance. Additionally, we observed interactions between genetic susceptibility to JIA and breastfeeding duration, indicating that genetic predisposition may modify the association between breastfeeding and disease risk, which warrants further investigation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References:

1) Clarke SLN, et al. Rheumatology (Oxford). 2022;61(2)
2) Skjerven HO, et al. Lancet. 2022 Jun 25;399(10344)
3) Hestetun SV, et al. Arthritis Rheumatol. 2025 Apr;77(4)
4) López-Isac E, et al. Ann Rheum Dis. 2021;80(3)

Disclosure: V. Dåstøl: None; **I. Caspersen**: None; **K. Haftorn**: None; **S. Hestetun**: None; **S. Håberg**: None; **K. Costenbader**: AbbVie, 2, 5, Bain, 2, 5, Biogen, 2, 5, Brigham & Women's Hospital, 3, GSK, 2, 5; **M. Strøm**: None; **S. Olsen**: None; **A. Brantsæter**: None; **K. Størdal**: None; **H. Sanner**: None.

Abstract Number: 2680

High Health Care Utilization Preceding Diagnosis of Juvenile Idiopathic Arthritis

Anna Costello[1], Rui Xiao[1], Jahan Jazayeri[1], Timothy Brandon[1], Xuemei Zhang[1], Irit Rasooly[1] and **Pamela Weiss**[2], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Childrens Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Pediatric Rheumatology – Clinical III (2675–2680)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Timely diagnosis of Juvenile Idiopathic Arthritis (JIA) enables early initiation of therapy and improves outcomes, yet JIA patients often experience circuitous pathways to diagnosis. We aimed to characterize the healthcare utilization in the year preceding JIA diagnosis.

Methods: We used deidentified administrative data from the Truven Marketscan commercial and Medicaid databases (2014 to 2022). Inclusion criteria for the study were: (1) age 1-17 years and (2) diagnosis of JIA as defined by (a) ≥2 International Classification of Disease (ICD)-9 or 10 JIA codes within 6 months, (b) ≥1 JIA code from a rheumatologist, or (c) ≥1 JIA

Table 1: Cohort Demographics

	JIA Patients n=10021	Healthy Controls n= 20042
	Median (IQR) or n (%)	
Demographics		
Male, n (%)	3552 (35.4)	7104 (35.4)
Age at Diagnosis, median (IQR)	13 (9-16)	13 (9-16)
Insurance Type		
Commercial	5914 (59.0)	11828 (59.0)
Medicaid	4107 (41.0)	8214 (41.0)
***Geographic region of residence, n (%)**		
Northeast	1070 (18.1)	1213 (10.3)
North Central	1380 (23.3)	2676 (22.6)
South	2275 (38.5)	7093 (59.9)
West	1131 (19.1)	830 (7.0)
Unknown	58 (1.0)	16 (0.1)
Number of Complex Chronic Conditions, n (%)		
0	9392 (93.7)	20042 (100)
1	580 (5.8)	0 (0)
2+	49 (0.4)	0 (0)

Legend. International Classification of Diseases version 9 (696.0, 714.x, 720.0, 720.81, 720.89, and 720.9) and 10 (M05.00, M06.xx, M08.xx, M45.x, M46.0x, M46.8x, M46.9x, and L40.5x) codes were used to determine cohort inclusion.
*Region only available for commercial insurance patients. JIA, Juvenile Idiopathic Arthritis; IQR, Interquartile Range

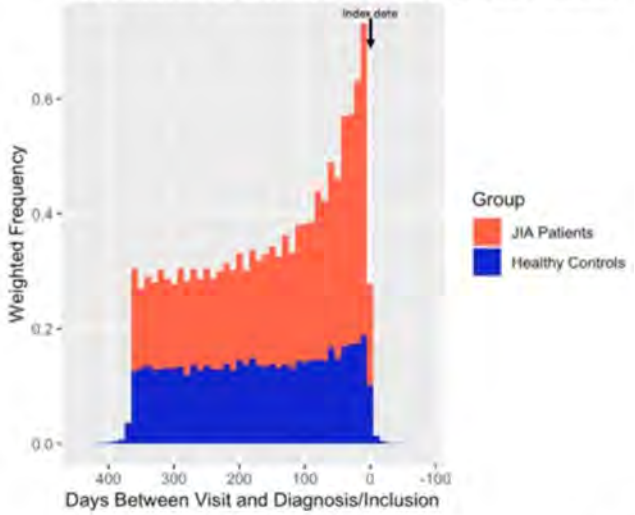
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Healthcare Utilization 12 months prior to index date

	JIA cohort n=10021 Mean (SD)	Healthy Control n=20042 Mean (SD)	Incident Rate Ratio (95% CI)	p-value
Total Healthcare Utilization	13.43 (14.68)	5.26 (8.52)	2.55 (2.53-2.57)	**<0.001**
Number of Outpatient visits	11.78 (13.73)	4.60 (8.21)	2.56 (2.54-2.58)	**<0.001**
Number of ED/Urgent Care visits	1.54 (2.76)	0.64 (1.46)	2.42 (2.36-2.47)	**<0.001**
Number of Inpatient Hospitalizations	0.11 (0.52)	0.02 (0.20)	4.48 (4.04-4.97)	**<0.001**

Legend. The index date for JIA patients was defined as the date of the first JIA code that they received. The index date for healthy controls was defined as the date of an outpatient visit occurring within two months of the index date of the matched JIA patient. Visit numbers presented as mean (standard deviation). p-value calculated using manual Wald test. JIA, Juvenile Idiopathic Arthritis, CI, confidence interval.

Figure 1: Time Between Visits and Diagnosis/Inclusion



Legend. This figure demonstrates the frequency of healthcare utilization in the outpatient, inpatient, or ED settings as patients approach the date of diagnosis (day 0) for JIA patients or inclusion in the cohort for healthy controls. The visit frequencies are weighted to account for the numbers of patients versus controls.

code with a claim for a JIA directed therapy or intraarticular steroid injection within 6 months. Patients were excluded if they did not have continuous enrollment in the database for 12 months prior to the index date or if they had a claim with a JIA code during that period. Age- and sex-matched controls were identified at a 2:1 ratio. The index date for JIA patients was defined as the date of the first JIA code. The index date for controls was defined as the date of a visit occurring within two months of the index date of the matched JIA patient. Healthcare utilization was defined as any inpatient admission, emergency department or urgent care visit, and outpatient claim for a billing visit with a physician or advanced practice provider. Incidence rate ratios (IRRs) were calculated to compare healthcare between JIA patients and controls in the 12 months prior to the index date, and the manual Wald test was used to calculate the relevant p-values.

Results: 10,021 children, ages 1-18 years, had an incident diagnosis of JIA in the years of study. Median age in both JIA patients and controls was 13 (interquartile range 9-16), and there was no significant difference in insurance type or prevalence of chronic conditions between the JIA patients and controls (**Table 1)**. Healthcare utilization in the year preceding

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

the index date was significantly higher for JIA patients versus controls (**p< 0.001**). JIA patients had a median of 10 healthcare encounters (interquartile range [IQR] 5 to 17) while controls had a median of 3 visits (IQR 1 to 7). This increased utilization was consistent for outpatient (IRR 2.56, p< 0.001), inpatient (IRR 4.48, p< 0.001), and emergency room/urgent care encounters (IRR 2.42, p< 0.001) (**Table 2**). Healthcare utilization for JIA patients escalated as the index date approached (**-Figure 1**). JIA outpatient encounters were most frequent with generalists (74.8% of visits) and orthopedists (4.9%) in the pre-diagnosis period. Further, 22.9% of children with JIA saw an orthopedist in the year preceding JIA diagnosis, with most receiving non-specific diagnosis codes for joint pain or effusion.

Conclusion: Children with JIA have significantly higher health care utilization in comparison to age- and sex- matched healthy peers in the 12 months preceding JIA diagnosis. This pattern suggests that there may be opportunities, particularly in primary care and orthopedics, to identify JIA earlier. Understanding the patterns of utilization could help target interventions to improve the time to diagnosis, and ultimately the experiences and outcomes, for these patients.

Disclosure: A. Costello: None; **R. Xiao**: None; **J. Jazayeri**: None; **T. Brandon**: None; **X. Zhang**: None; **I. Rasooly**: None; **P. Weiss**: Bristol-Myers Squibb(BMS), 2, Pfizer, 1.

Abstract Number: 2681

Derivation and Validation of Inflammation-Adjusted Lipid Measures to Improve Cardiovascular Risk Prediction in Rheumatoid Arthritis

Tate Johnson[1], George Reed[2], Joel Kremer[3], Dimitrios Pappas[4], Punyasha Roul[5], Grant Cannon[6], Gail Kerr[7], Andreas Reimold[8], Katherine Liao[9], Michael George[10], Jon Giles[11], Christina Charles-Schoeman[12], Joshua Baker[10], Ted Mikuls[1] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Massachusetts Chan Medical School, Worcester, MA, [3]The Corrona Research Foundation, Delray Beach, FL, [4]CorEvitas, New York, NY, [5]UNMC, Omaha, NE, [6]University of Utah and Salt Lake City VA, Salt Lake City, UT, [7]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [8]Dallas VA Medical Center, Dallas, TX, [9]Brigham and Women's Hospital, Boston, MA, [10]University of Pennsylvania, Philadelphia, PA, [11]Cedars Sinai Medical Center, Los Angeles, CA, [12]UCLA Medical Center, Santa Monica, CA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes) (2681–2686)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Total cholesterol (TC) and low-density lipoprotein (LDL) are critical measures of atherosclerotic cardiovascular disease (ASCVD) risk. However, the lipid paradox in RA, whereby systemic inflammation reduces lipid levels despite an increased risk of ASCVD, renders TC and LDL unreliable. To account for the lipid paradox, we derived and externally validated inflammation adjusted lipid measures in RA and tested the hypothesis that inflammation adjusted lipids would be more strongly associated with incident ASCVD than unadjusted lipid levels.

Methods: Derivation occurred using baseline data in CERTAIN, a prospective cohort of active RA patients initiating or switching a biologic DMARD. Participants with high sensitivity C-reactive protein (hsCRP) and serum lipids available were included. Statin, JAK inhibitor, and IL-6 inhibitor use were exclusion criteria. Linear spline regression with a single knot was executed using log-transformed hsCRP as a predictor of lipid levels, adjusting for age, sex, smoking status, BMI, diabetes, hypothyroidism, and DMARD use. External validation was conducted in the Veterans Affairs RA registry, a multicenter, prospective RA cohort, with identification of ASCVD events (myocardial infarction, stroke) in linked VA, Medicare, and National

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

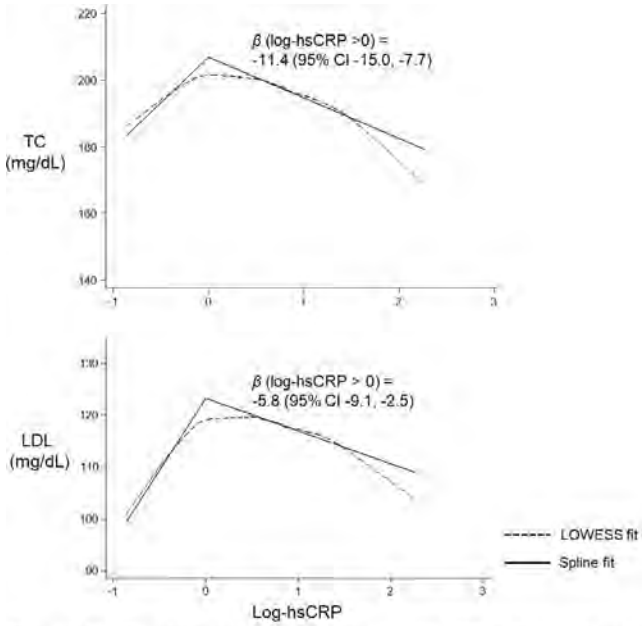


Figure 1. Modeling the association between elevated hsCRP and serum lipids. Linear spline with a knot at hsCRP = 1 illustrating the association (β) between increasing hsCRP (per log unit) with TC and LDL levels in the CERTAIN registry (derivation cohort). The magnitude of the estimated β was used as a correction factor for lipid levels in the VARA registry (validation cohort).
Abbreviations: hsCRP, high sensitivity C-reactive protein; TC, total cholesterol; LDL, low-density lipoprotein;

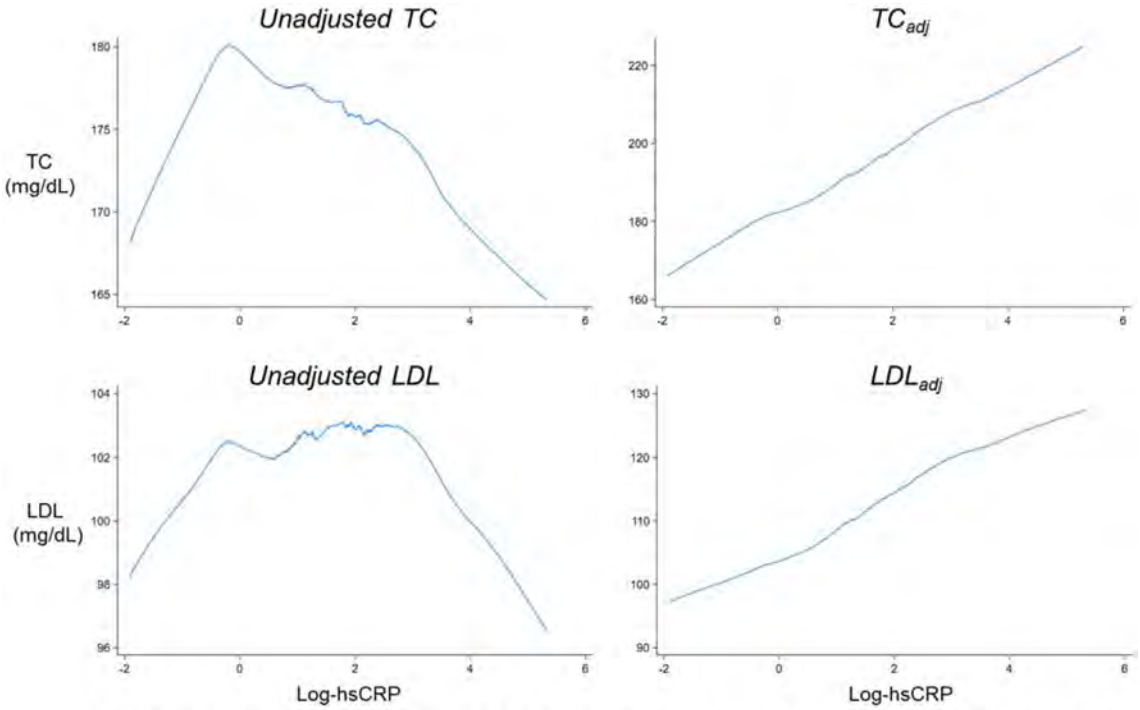


Figure 2. Association of hsCRP with serum lipids before and after inflammation-adjustment. Lowess smoothing illustrating the association between log-hsCRP concentrations with unadjusted (left column) and inflammation-adjusted (right column) TC (top row) and LDL levels (bottom row) in the VARA registry (validation cohort).
Abbreviations: hsCRP, high sensitivity C-reactive protein; TC, total cholesterol; LDL, low-density lipoprotein;

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Validation of Inflammation Adjusted Lipid Measures with Incident Cardiovascular Events in the VA Rheumatoid Arthritis Registry [a]

	Unadjusted TC		TC_{adj} [b]	
Categorical Cutoffs (mg/dL)	*N (%) patients*	*aHR (95% CI)*	*N (%) patients*	*aHR (95% CI)*
<150	522 (24.8)	Ref	256 (12.2)	Ref
150-200	1,065 (50.6)	1.25 (0.96-1.62)	984 (46.7)	1.35 (0.96-1.92)
200-240	408 (19.4)	1.35 (0.98-1.87)	593 (28.2)	1.80 (1.25-2.60)
>240	111 (5.3)	1.21 (0.73-2.01)	273 (13.0)	1.41 (0.91-2.19)
Dichotomous Cutoff (mg/dL)				
<150	522 (24.8)	Ref	256 (12.2)	Ref
>150	1,584 (75.2)	1.29 (1.01-1.66)	1,850 (87.8)	1.49 (1.06-2.07)
	Unadjusted LDL		**LDL_{adj} [c]**	
Categorical Cutoffs (mg/dL)	*N (%) patients*	*aHR (95% CI)*	*N (%) patients*	*aHR (95% CI)*
<100	1,008 (47.9)	Ref	782 (37.1)	Ref
100-130	685 (32.5)	1.18 (0.93-1.51)	720 (34.2)	1.35 (1.04-1.74)
130-160	316 (15.0)	1.48 (1.10-1.99)	445 (21.1)	1.39 (1.04-1.85)
>160	97 (4.6)	1.22 (0.74-2.03)	159 (7.5)	1.48 (1.00-2.21)
Dichotomous Cutoff (mg/dL)				
<100	1,008 (47.9)	Ref	782 (37.1)	Ref
>100	1,098 (52.1)	1.27 (1.02-1.57)	1,324 (62.9)	1.38 (1.10-1.72)

[a] Adjusted hazard ratios (aHR) with 95% confidence intervals (CI) estimated in Cox regression models adjusting for age, sex, race, smoking status, body mass index, and cardiovascular risk factors.
[b] TC_{adj} = Unadjusted TC + (11.4 x log-hsCRP)
[c] LDL_{adj} = Unadjusted LDL + (5.8 x log-hsCRP)
Abbreviations:; Ref, reference; VA, Veterans Affairs

Death Index data. The magnitude of the estimated β for hsCRP was used as a correction factor for baseline TC and LDL levels in VARA (TC_{adj} *[or* LDL_{adj}*]* = *Unadjusted TC [or LDL]* + β**log-hsCRP*). The association between hsCRP and lipid levels, before and after inflammation adjustment, was illustrated with Lowess smoothing. The association of unadjusted lipids, TC_{adj} and LDL_{adj} values (categorical and dichotomous cutoffs) with incident ASCVD were compared using multivariable Cox regression.

Results: Among 1,663 patients in CERTAIN (mean age 54.4, 81.2% female, mean hsCRP 10.7 mg/L), an inverse U-shaped relationship was observed between hsCRP and unadjusted lipids. A linear spline with a knot at log-hsCRP = 0 yielded the best model fit, leading to a correction factor of 11.4 (TC) and 5.8 (LDL) for each log unit increase in hsCRP above 0 (**Figure 1**). Adjusting lipid levels for log-hsCRP >0 among 2,106 VARA registry participants (mean age 61.7, 86.4% male, mean hsCRP 11.1 mg/L) corrected the U-shaped relationship (**Figure 2**) and recategorized a greater proportion of participants into higher TC_{adj} and LDL_{adj} categories (**Table 2**). Over 17,701 person-years, we observed 371 incident ASCVD events. The associations between categorical and dichotomous TC_{adj} (range aHR 1.35-1.80) and LDL_{adj} (range aHR 1.22-1.56) cutoffs with ASCVD events were stronger than for unadjusted lipids (**Table 2**).

Conclusion: Compared to unadjusted lipids, inflammation-adjusted TC and LDL identified a larger number of RA patients with high-risk lipid levels and strengthened the association between serum lipids and ASCVD risk. This approach may identify patients with a statin indication who are otherwise missed using current guidelines. Though a critical first step in overcoming challenges to care posed by the lipid paradox, additional study is required to integrate these results into risk calculators to optimize CVD prevention in RA.

Disclosure: T. Johnson: None; **G. Reed**: CorEvitas (part of ThermoFisher), 2, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 2; **J. Kremer**: CorEvitas (part of ThermoFisher), 1, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4; **D. Pappas**: AbbVie/Abbott, 2, CorEvitas, Part of Thermofisher, 3, 11, Corrona Research Foundation, a not-for-profit 501(c)3 foundation, 4, Novartis, 2, Roche, 2; **P. Roul**: None; **G. Cannon**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2; **A. Reimold**: None; **K. Liao**: Merck/MSD, 2, UCB, 2; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **J. Giles**: AbbVie/Abbott, 2, Eli Lilly, 2, Genentech, 2, Merck/MSD, 2, Novartis, 2, Pfizer, 2, Sana, 2; **C. Charles-Schoeman**: AbbVie/Abbott, 2, 5, Alexion, 5, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, 5, CSL Behring, 5, Galapagos, 2, Immunovant, 2, Janssen, 5, Octapharma, 2, 5, Pfizer, 2, 5, Priovant, 5, Recludix, 2, Sana Biotechnology, 2; **J. Baker**: Amgen, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **B. England**: Boehringer-Ingelheim, 2, 5.

Abstract Number: 2682

Methotrexate use and higher age impair humoral response against the recombinant herpes zoster vaccine (RZV) in Rheumatoid Arthritis: a prospective, randomized, placebo-controlled trial

Ana C Medeiros-Ribeiro[1], Lucas Farias[2], Nadia Emi Aikawa[3], Sandra G Pasoto[1], Leonard V Kupa[2], Carla Saad[1], Andrea Shimabuco[2], Karina Bonfiglioli[4], Diogo Domiciano[4], Andre Franco[4], Clovis Artur Silva[5] and Eloisa Bonfa[6], [1]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Brazil, [2]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, São Paulo, Sao Paulo, Brazil, [3]Rheumatology Division and Pediatric Rheumatology Unit, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, São Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, Brazil, Sao Paulo, Sao Paulo, Brazil, [5]University of São Paulo, São Paulo, São Paulo, Brazil, [6]Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, São Paulo, Brazil

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes) (2681–2686)

Session Type: Abstract Session

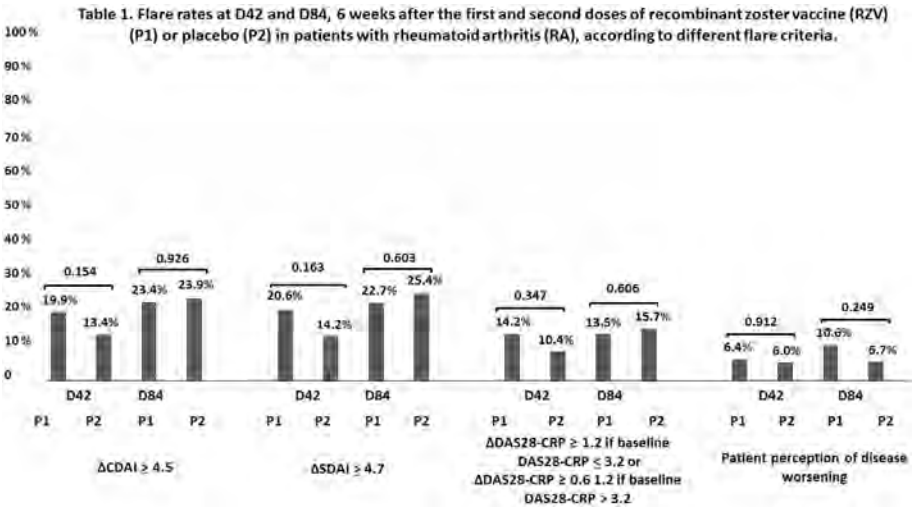
Session Time: 11:30AM–1:00PM

Background/Purpose: The recombinant vaccine against herpes zoster (HZ) (RZV) is recommended by ACR and EULAR for immunocompromised individuals. Short-term observational data from RA cohorts aged ≥50 years supports its overall reactogenicity and possible safety in non-randomized designs. However, the specific impact of different immunosuppressive drugs or combinations on vaccine immunogenicity is limited to small sample sizes or selected groups of patients, hampering conclusions about the effect of specific therapies. Moreover, new flare definition criteria using CDAI/SDAI were recently validated but the effect of vaccination using these new criteria were not evaluated. To address these gaps, we conducted a large prospective, randomized controlled trial to evaluate safety and assess humoral immunogenicity induced by RZV in RA adult (≥18 years) patients.

Methods: RA patients were randomized to receive RZV (P1) or placebo (P2) at D0 and D42. Groups were blindly evaluated for disease activity (CDAI, SDAI and DAS28-CRP) at D0, D42 and D84. P2 group was vaccinated with a similar schedule at D84 and D126. Immunogenicity was evaluated in patients (P1+ P2) and compared to non-immunosuppressed control group (CG) at 1st RZV dose and 6 weeks post-vaccination. Anti-gE antibody concentrations (ELISA) were assessed at 1st RZV dose and six weeks after the second dose. Pre and post vaccination geometric mean titers (GMTs) and soroconversion (SC) were calculated. Adverse events (AE) were monitored for 3 months through scheduled visits and phone contacts.

Results: A total of 320 RA patients were randomized at D0: 165 in P1 and 155 in P2. The groups were balanced for age (p=0.562), sex (p=0.331), previous HZ infections (p=0.580), disease duration (p=0.838), rheumatoid factor (p=0.411) and anti-CCP (p=0.456) positivity, disease-modifying antirheumatic drugs (p >0.05), CDAI (p=0.268), SDAI (p= 0.343)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



For safety analyses, all patients who adhered to protocol were included (n=275: 141 in P1 and 134 in P2). Results are expressed in % and compared with the chi-square or Fisher's exact test, as appropriate, as two-sided analyses; CDAI (Clinical Disease Activity Index), SDAI (Simplified Disease Activity Index), DAS28-CRP (Disease Activity Score using 28-joint count and C-reactive protein) and patient perception of disease worsening at D42 and D84 were compared to baseline status (D0). P1: pacients vaccinated with recombinant zoster vaccine (RZV) at D0 and D42; P2: patients who received placebo at DO and D42.

and DAS28-CRP (p=0.268). After 2 vaccine doses, SC (96.6% vs. 100%, p=0.030) and GMT [8.3 (7.2-9.5) vs 12.9 (11.5-14.5 mUI/mL; p< 0.001] were significantly reduced in patients compared to CG. Linear regression corrected for pre-vaccination GMT linked older age (p=0.032), higher disease activity (p=0.042), MTX (p< 0.001), and prednisone use (p=0.045) with lower post-vaccination GMT. The concomitant use of MTX reduced post-vaccination GMT among bDMARD (p< 0.001) users (mainly TNFi users, p=0.003) and sDMARD users (p< 0.001). In multivariate analysis, higher pre-vaccination GMT persisted associated with higher post-vaccination GMT (p< 0.001), while older age (p=0.033) and MTX use (p< 0.001) remained associated with lower post-vaccination GMT. No HZ cases occurred by D84. Flare rates were comparable (p >0.05) between P1 and P2 (Figure 1) both at D42 and D84. No moderate/severe AEs were observed.

Conclusion: This large study showed that RZV was safe in immunosuppressed RA patients, with no evidence of increased flare rate using validated measures in comparison to placebo. Importantly, we identified MTX and older age as key factors that significantly impair humoral immune response. Although the humoral correlates of protection are not established, new strategies may be recommended for these patients (ClinicalTrials NCT05879419).

Disclosure: A. Medeiros-Ribeiro: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Farias**: None; **N. Aikawa**: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **S. Pasoto**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (305242/2019-9), 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **L. Kupa**: GlaxoSmithKlein(GSK), 5; **C. Saad**: None; **A. Shimabuco**: None; **K. Bonfiglioli**: None; **D. Domiciano**: None; **A. Franco**: None; **C. Silva**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (304984/2020-5), 5, Fundação de Amparo a Pesquisa do Estado de Sao Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5; **E. Bonfa**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) #305242/2019-9, 5, Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) (2022/12925-8), 5, GlaxoSmithKlein(GSK), 5.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2683

Association of Genetic Risk for Pain Intensity with Longitudinal Disease Activity in Rheumatoid Arthritis

Stevie Barry[1], Katie McMenamin[2], Austin Wheeler[3], Bryant England[3], Grant Cannon[4], Brian Sauer[5], Gary Kunkel[6], Katherine Wysham[7], Beth Wallace[8], Andreas Reimold[9], Gail Kerr[10], Isaac Smith[11], John Richards[12], Iris Lee[13], Rui Xiao[1], Sylvanus Toikumo[14], Henry Kranzler[14], Rachel Kember[14], Scott Damrauer[14], Michael Levin[14], Michael George[1], Ted Mikuls[3], Joshua Baker[1] and Thomas Riley[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Boston Medical Center, Boston, MA, [3]University of Nebraska Medical Center, Omaha, NE, [4]University of Utah and Salt Lake City VA, Salt Lake City, UT, [5]Salt Lake City VA/University of Utah, Salt Lake City, UT, [6]University of Utah and George E Wahlen VAMC, Salt Lake City, UT, [7]VA PUGET SOUND/UNIVERSITY OF WASHINGTON, Seattle, WA, [8]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [9]Dallas VA Medical Center, Dallas, TX, [10]Washington DC VAMC/Georgetown and Howard Universities, Washington, DC, [11]Duke University Hospital, Durham, NC, [12]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [13]Washington University in St Louis, Saint Louis, MO, [14]University of Pennsylvania / Corporal Michael J. Crescenz VAMC, Philadelphia, PA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes) (2681–2686)

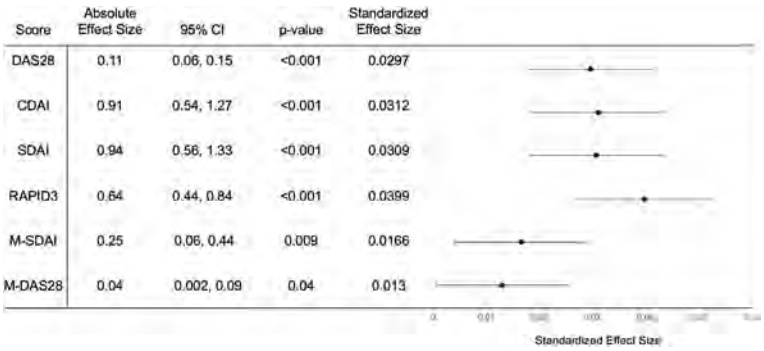
Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Guidelines recommend the use of composite scores to evaluate disease activity in RA and inform a treat-to-target approach. It is recognised that patient-reported components of these scores are influenced by factors unrelated to inflammation such as other chronic pain conditions. We assessed whether those with a higher genetic predisposition to pain had higher disease activity scores and which components of disease activity were most affected.

Methods: Participants from the Veterans Affairs RA registry, a longitudinal cohort of veterans with RA, were genotyped using the Infinium Global Screening Array-24 v2.0; imputation was performed using the TOPMed server. We applied two existing polygenic risk scores (PGS) including: 1) pain intensity (PI-PGS) and 2) chronic back pain (CBP-PGS). Scores were normalized and standardized within participants of similar genetic backgrounds. Disease activity components were recorded by treating providers during routine clinical encounters and extracted from the electronic health record. We

Figure 1: Standardized effect of the pain intensity polygenic score on disease activity scores within VARA. Table and forest plot demonstrating standardised effect size of 1SD increase in PI-PGS on disease activity scores. Similar standardized effects are observed on the traditional disease activity scores; the PI-PGS had a lower standardized effect in the scores modified to remove some patient-reported aspects. Absolute effect sizes are included on the scale of the individual disease activity score. Abbreviations DAS28 – disease activity score-28 CDAI – clinical disease activity index SDAI - simplified disease activity index HAQ – health activity questionnaire RAPID3 – routine assessment of patient index data 3 M-SDAI – modified simplified disease activity index M-DAS28 – modified disease activity score-28 VARA – Veterans Affairs Rheumatoid Arthritis Registry PI-PGS – pain intensity polygenic score



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Absolute effect of pain intensity and chronic back pain polygenic scores on components of disease activity scores grouped by patient-reported and objective aspects of disease activity. The PGS demonstrate statistically significant effects on patient-reported aspects of disease activity. The effect of 1 standard deviation change in the PGS on components of disease activity scores was determined through generalized linear models using all available longitudinal data, adjusting for age, sex, and five principal components of population structure. Abbreviations: PI-PGS – pain intensity polygenic score CBP-PGS – chronic back pain polygenic score TJC – tender joint count (0-28) Pt global – patient global assessment (0-100) Prov global – provider global assessment (0-100) SJC – swollen joint count (0-28) CRP – C-reactive protein, log-transformed ESR – erythrocyte sedimentation rate, log-transformed

Component	PI-PGS (95% CI)	p-value	CBP-PGS (95% CI)	p-value
Subjective				
Pain	0.26 (0.17-0.35)	<0.001	0.14 (0.05-0.22)	0.002
TJC	0.46 (0.29-0.64)	<0.001	0.22 (0.05-0.39)	0.011
Pt global	1.88 (1.07-2.68)	<0.001	1.33 (0.57-2.09)	0.001
Prov global	1.22 (0.59-1.84)	<0.001	0.41 (-0.21-1.03)	0.198
HAQ	0.06 (0.04-0.08)	<0.001	0.03 (0.005 – 0.05)	0.015
Objective				
SJC	0.09 (-0.02-0.2)	0.123	0.06 (-0.06-0.18)	0.32
CRP	0.04 (-0.004-0.08)	0.075	0.04 (0.004-0.09	0.033
ESR	0.04 (0.009-0.08)	0.015	0.04 (-0.0002-0.07)	0.051

assessed common disease activity scores including the DAS28, Clinical Disease Activity Index (CDAI), and Routine Assessment of Patient Index Data 3 (RAPID3), as well as modified disease activity scores (M-DAS28, M-SDAI) that replace patient global assessment with provider global assessment and removes tender joint count (TJC). The effect of PI-PGS and CBP-PGS on disease activity scores and their individual components was evaluated with generalized estimating equations to use all available longitudinal data, adjusted for sex, age, and five principal components of population structure and clustered by participant with an exchangeable correlation structure. We evaluated the effect of the genetic risk as a continuous measure and by quartile.

Results: A 1 standard deviation (SD) higher PI-PGS and CBP-PGS were each associated with significantly higher DAS28, CDAI, SDAI, and RAPID3. The strength of the association was more modest for the M-DAS28 and M-SDAI (Fig. 1). A 1 SD increase in each PGS was associated with significantly higher pain score, TJC, patient global scores and HAQ (Table 1). There was no association between a 1SD increase in either PGS and SJC or CRP. A dose-dependent effect of PI-PGS on disease activity scores was observed; there were significant differences between 1st and 4th quartile of PI-PGS for all disease activity scores (Fig 2). The highest quartile had a 0.29 higher average DAS28 compared to the lowest quartile. This difference represents 24% of the minimal clinically important difference described for the DAS28.

Conclusion: Higher genetic predisposition to pain is associated with higher disease activity scores in a dose dependent manner with an effect size that may have clinical relevance. The consistency of the findings using a risk score developed for back pain suggests an association through mechanisms unrelated to RA inflammation. Our study suggests commonly

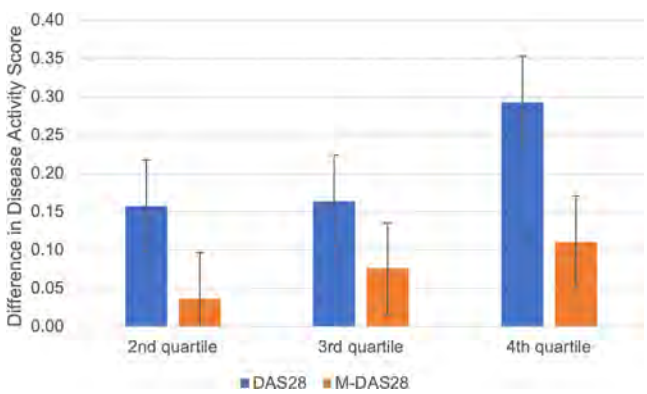


Figure 2. Absolute effect of quartile of pain-intensity polygenic score on DAS28 and M-DAS28. A dose effect is observed from increasing quartile of PI-PGS as compared to 1st quartile on DAS28 and to a more modest extent on M-DAS28. Absolute effect sizes are shown. Abbreviations: DAS28 – disease activity score-28 M-DAS28 – modified disease activity score-28

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

used disease activity scores, especially components related to patient global and TJC, are biased in the setting of chronic pain. Clinicians should interpret disease activity in the context of the presence of other chronic pain conditions and consider using M-DAS28 and M-SDAI in those with chronic pain.

Disclosure: S. Barry: None; **K. McMenamin**: None; **A. Wheeler**: None; **B. England**: Boehringer-Ingelheim, 2, 5; **G. Cannon**: None; **B. Sauer**: None; **G. Kunkel**: None; **K. Wysham**: None; **B. Wallace**: None; **A. Reimold**: None; **G. Kerr**: Amgen, 2, Bristol-Myers Squibb(BMS), 2, CSL-Behring, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2; **I. Smith**: None; **J. Richards**: None; **I. Lee**: None; **R. Xiao**: None; **S. Toikumo**: None; **H. Kranzler**: Aklermes, 5, 12, Medication Supplies, Altimmune, 1, 2, Clearmind Medicine, 1, Dicerna, 5, Eli Lilly, 5, Ethypharm, 5, Imbrium, 5, Indivior, 5, Kinnov, 5, Otsuka, 5, Pear, 5, Sobrera Pharmaceuticals, 2, U.S. Provisional Patent, 10; **R. Kember**: None; **S. Damrauer**: Amgen, 12, Non-financial research support, Novo Nordisk, 12, Non-financial research support, US Department of Veterans Affairs, 10; **M. Levin**: None; **M. George**: Boehringer-Ingelheim, 2, GlaxoSmithKlein(GSK), 5, Janssen, 5, Pfizer, 2, 5; **T. Mikuls**: Amgen, 2, 5, Merck/MSD, 1, Olatech Therapeutics, 1, UCB, 1; **J. Baker**: Amgen, 5; **T. Riley**: None.

Abstract Number: 2684

Multimodal Analysis Revealed Altered Brain Connectivity Patterns and Neuroinflammatory Processes in the Background of Difficult-To-Treat Rheumatoid Arthritis

Lilla Gunkl-Tóth[1], Gergely Orsi[2], Noémi Császár-Nagy[3], Lili Duzsik[4], Gábor Mátay[4], Gábor Kumánovics[5], Gábor Sütő[2], Krisztina Csókási[2], Szabolcs Takács[6], Zoltán Vidnyánszky[7], József Kun[2], Krisztina Takács-Lovász[2], Gellért Karvaly[8], Róbert Farkas[8], Anett Pintér[8], Panna Királyhidi[8], György Nagy[8] and Zsuzsanna Helyes[2], [1]Semmelweis University, Budapest, Budapest, Hungary, [2]University of Pécs, Pécs, Hungary, [3]National University of Public Services, Budapests, Hungary, [4]Psychosomatic Outpatient Clinic, Budapest, Hungary, [5]University of Pecs, Pecs, Hungary, [6]Károli Gáspár University, Budapest, Hungary, [7]Brain Imaging Centre, Research Centre for Natural Sciences, Budapest, Hungary, [8]Semmelweis University, Budapest, Hungary

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes) (2681–2686)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Despite advances in rheumatoid arthritis (RA) treatment, 5–20% of patients experience persistent symptoms, particularly pain, and are classified as difficult-to-treat (D2T). Factors such as treatment resistance, comorbidities, and central pain sensitization may contribute; however, the exact mechanisms remain unclear. This study focused on investigating the underlying factors of the D2T condition and revealing the connections between pain and inflammation with a multimodal approach.

Methods: 31 D2T RA (determined by the 2020 EULAR definition), 18 non-D2T RA patients, and 32 healthy controls (HCs) were included. All participants underwent a clinical assessment, psychological analysis (including in-depth interviews, the Rorschach test, and questionnaires), two resting-state functional MRI (fMRI) scans with standardized heat pain stimulation in between, as well as peripheral blood transcriptomic analysis and plasma metabolomics.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Resting-state fMRI revealed significantly reduced intrinsic connectivity of the posterior cingulate cortex (PCC) in RA patients, especially in D2T RA. Following acute painful stimulation, intrinsic connectivity of the PCC increased in D2T RA, in contrast to the decreased connectivity observed in non-D2T RA patients and healthy controls (HCs). *(Figure 1.)* Seed-based analysis of the postcentral gyrus (PCG) revealed a reduction in connectivity strength across many connections within the somatosensory area, which were significantly altered after pain stimulation in all RA patients compared to HCs. Fractional amplitude of low-frequency fluctuations (fALFF) analysis revealed significantly reduced activity in several brain regions (e.g., lateral occipital cortex, middle frontal gyrus, medial prefrontal cortex, and frontal pole) in RA, with D2T patients showing the most significant reductions. Compared to non-D2T RA, D2T patients also exhibited lower fALFF in additional brain regions, indicating more complex alterations in pain and somatosensory processing, behavior, and cognitive functions, which aligns with our psychological results showing increased relational and decision-making inhibition, reduced motivation, and impaired mental control in RA. *(Figure 2.)* Transcriptomic analysis showed 70 downregulated and 17 upregulated differentially expressed (DE) mRNAs in D2T RA compared to the non-D2T RA group (e.g., neuregulin-1 (NRG1) or S100B). Functional analysis demonstrated a direct link of DE mRNAs to neuronal differentiation processes, neuroinflammation, or neuroplasticity. *(Figure 3.)* Metabolomic analysis revealed significant differences in amino acid and sphingolipid metabolism.

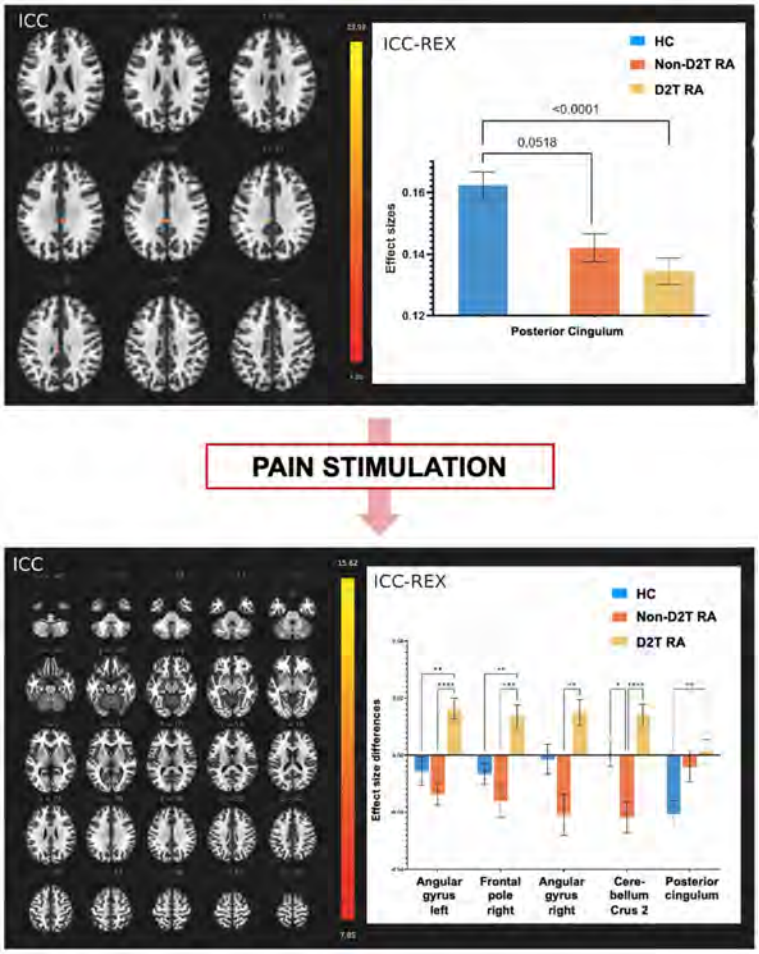


Figure 1. ***Resting-state intrinsic connectivity patterns before and after painful stimulation*** ICC, intrinsic connectivity; HC, healthy controls, D2T, difficult-to-treat; RA, rheumatoid arthritis

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

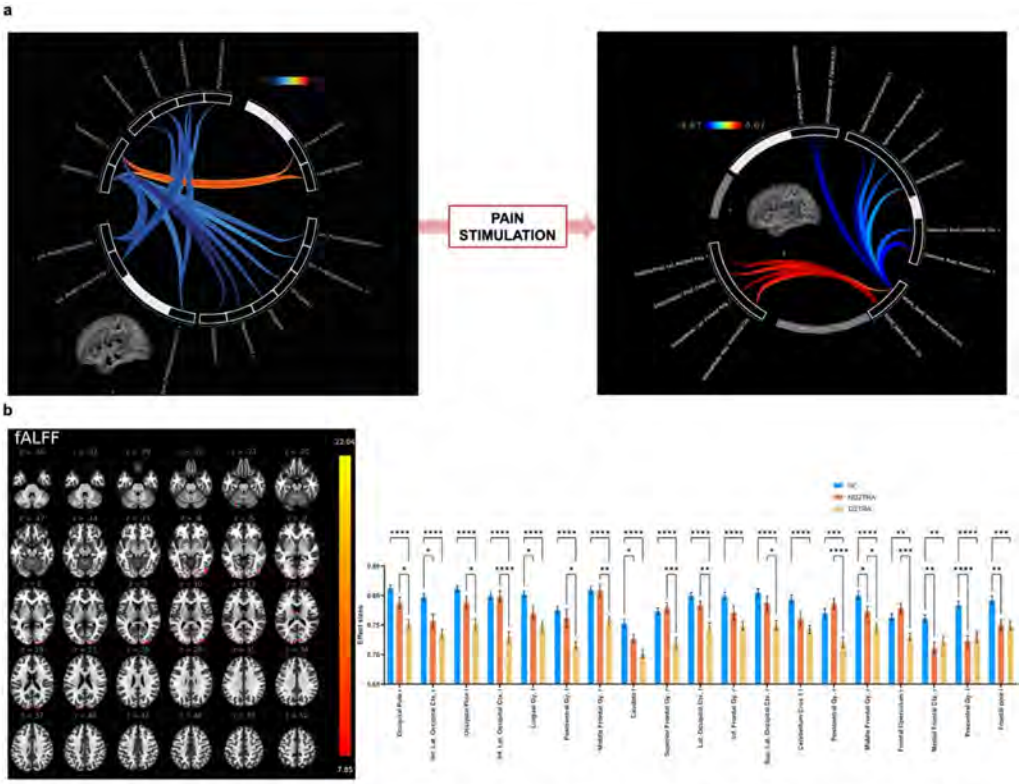


Figure 2. ***Connection of the postcentral gyrus before and after pain stimulation (a) The activity of many brain areas differed significantly in D2T, non-D2T RA patients and HCs based on fALFF analysis*** ***(b)*** fALFF, fractional amplitude of low-frequency fluctuations; HC, healthy controls; D2T, difficult-to-treat; RA, rheumatoid arthritis

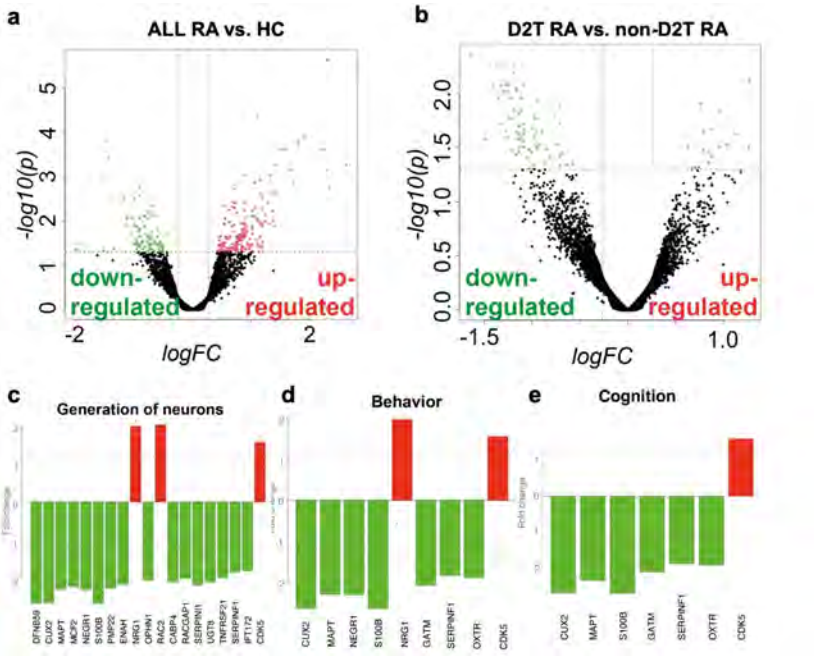


Figure 3. ***Volcano plot of transcriptomic analysis of all RA vs. HC (a) and D2T RA vs. non-D2T RA patients (b); Gene ontology (GO)-based enrichment analysis reveals significantly different pathways in the comparison of D2T RA vs. non-D2T RA (p<0.001) (c-e)***

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Teveal a novel neuroimmune signature of D2T RA, characterized by altered brain connectivity patterns, psychological disturbances, and distinct transcriptomic and metabolomic profiles. These results may lead to new opportunities for patient stratification, biomarker development, and personalized interventions targeting central mechanisms.

Funding: HUN-REN–PTE Chronic Pain Research Group (14017), OTKA K138046 and K131479, TKP2021-EGA-29, National Brain Research Program, Richter Gedeon PhD Scholarship for LGT.

Disclosure: L. Gunkl-Tóth: None; **G. Orsi**: None; **N. Császár-Nagy**: None; **L. Duzsik**: None; **G. Mátay**: None; **G. Kumánovics**: None; **G. Sütő**: None; **K. Csókási**: None; **S. Takács**: None; **Z. Vidnyánszky**: None; **J. Kun**: None; **K. Takács-Lovász**: None; **G. Karvaly**: None; **R. Farkas**: None; **A. Pintér**: None; **P. Királyhidi**: None; **G. Nagy**: None; **Z. Helyes**: None.

Abstract Number: 2685

Assessing for Racial/ethnic Variability in U.s.-frax^{tm} Performance Among Older Adult Women with Rheumatoid Arthritis in the United States

Rachel Elam[1], Jing Li[2], Angel Paul[3], Emma Kersey[4], gabriela Schmajuk[5], William Leslie[6] and Laura Carbone[1], [1]Augusta University, Augusta, GA, [2]University of California, San Francisco, San Francisco, CA, [3]University of California San Francisco, Berkeley, CA, [4]University of California San Francisco, San Francisco, CA, [5]University of California, San Francisco, and San Francisco Veterans Affairs Medical Center, San Francisco, CA, [6]University of Manitoba, Winnipeg, MB, Canada

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes) (2681–2686)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Women with rheumatoid arthritis (RA) have 1.5- and 2-fold higher risk of major osteoporotic fracture (MOF: first of distal forearm, hip, humerus, or clinical vertebral fracture) and hip fracture, respectively. Most fractures occur in women with osteopenia, where fracture risk stratification with FRAX^{TM} guides drug therapy initiation in the United States. U.S.-FRAX was calibrated using mainly White cohorts, and its performance across racial/ethnic groups with RA is uncertain. We assessed racial/ethnic differences in U.S.-FRAX performance in predicting imminent (2-year) MOF and hip fracture risk in older U.S. women with RA.

Methods: We retrospectively analyzed RISE registry data linked to Medicare claims (2016-2018). We included women ≥ 65 years old with RA (≥ 2 RA-coded RISE visits ≥ 30 days apart by 1/1/2017) and Medicare coverage throughout 2016 and extending into 2017. Only participants identified as Asian, Black, Hispanic, or White race/ethnicity in Medicare were included as we used these four race/ethnicity-specific U.S.-FRAX models. We used Fine-Gray competing risk models to assess associations between U.S.-FRAX 10-year MOF and hip fracture probabilities and imminent fracture risk, with separate analyses overall and in each racial/ethnic group. Variables to compute U.S.-FRAX were obtained from RISE and Medicare at or before 1/1/2017. Bone mineral density (BMD) and parental hip fracture were not available. U.S.-FRAX without BMD was used, adjusting with age- and sex-specific estimates of the effect of affirming a parental hip fracture. Incident MOF and hip fracture were identified using validated claims-based definitions starting 1/1/2017. Observed absolute 2-year fracture incidence per 1,000 person-years was compared across FRAX risk categories (low: < 10% MOF, < 1%

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Subhazard ratios from Fine-Gray competing risk models for incident major osteoporotic fracture and incident hip fracture per 10% increase in U.S.-FRAX major osteoporotic fracture or hip fracture probability score, respectively, among women with rheumatoid arthritis[1]

	Overall (n = 14,533)	Asian (n = 159)	Black/African American (n = 1,127)	Hispanic/ Latina (n = 683)	White (n = 12,564)
	sHR (95% CI)	sHR (95% CI)[2]	sHR (95% CI)[2]	sHR (95% CI)[2]	sHR (95% CI)[2]
MOF Probability Score[3]	1.58 (1.52 - 1.64)	2.64 (1.59 - 4.39)	2.21 (1.60 - 3.07)	2.05 (1.64 - 2.57)	1.57 (1.51 - 1.64)
Hip Fracture Probability Score[3]	1.76 (1.66 - 1.88)	1.12 (0.68 - 1.84)	3.81 (2.19 - 6.63)	2.51 (1.80 - 3.50)	1.73 (1.62 - 1.85)

sHR: subhazard ratio; CI: confidence interval; MOF: major osteoporotic fracture

[1]The data presented here was supported by the American College of Rheumatology's RISE Registry. However, the views expressed represent those of the authors and do not necessarily represent the views of the American College of Rheumatology. The study protocol was prepared by Rachel E. Elam, MD. The data analysis was executed by the UCSF Data Analytic Center. Funding for this project was provided by the Rheumatology Research Foundation Scientist Development Award.

[2]For each U.S.-FRAX race/ethnicity group, the subhazard ratios and 95% confidence intervals presented here are derived from a competing risk model fit on just the population of women in that race/ethnicity group (i.e. a separate model was constructed for each race/ethnicity group)

[3]U.S.-FRAX 10-year fracture risk probability score was modeled here in decimal form (range of probability score 0 to 1.0)

Table 2. Areas under the curve (AUCs) for 2-year prediction of incident fracture by site by U.S.-FRAX 10-year site-specific fracture probability score[1] in women with rheumatoid arthritis, overall and by U.S.-FRAX race/ethnicity group

		Number of Fractures[2]	Cross-validated AUC[3] (95% CI)	P value[4]
MOF	Overall (n = 14,533)	1477	0.66 (0.65 - 0.68)	—
	Asian (n = 159)	13	0.71 (0.47 - 0.90)	0.78
	Black/African American (n = 1,127)	55	0.63 (0.57 - 0.66)	0.22
	Hispanic/Latina (n = 683)	69	0.69 (0.64 - 0.76)	0.56
	White (n = 12,564)	1340	0.67 (0.65 - 0.69)	Ref
Hip fracture	Overall (n = 14,533)	419	0.71 (0.69 - 0.73)	—
	Asian (n = 159)	<10	0.48 (0.23 - 0.66)	0.27
	Black/African American (n = 1,127)	<20	0.72 (0.60 - 0.84)	0.81
	Hispanic/Latina (n = 683)	21	0.75 (0.62 - 0.86)	0.51
	White (n = 12,564)	381	0.70 (0.68 - 0.72)	Ref

AUC: Area under the curve; CI: confidence interval; Ref: reference group

[1]U.S.-FRAX 10-year fracture risk probability score was modeled here in decimal form (range of probability score 0 to 1.0)

[2]Cell values and aggregate statistics that correspond to fewer than 10 participants are obscured to protect participant privacy in accordance with RISE policy

[3]Cross-validation was performed using a 10-fold cross-validation method of each AUC estimate

[4]P values are derived from a Z-test for independent AUCs comparing the AUC estimate for each U.S.-FRAX race/ethnicity group to the AUC in White women (reference group), separately for each fracture site (MOF or hip fracture)

hip; moderate: 10-20% MOF, 1-3% hip; high: >20% MOF, >3% hip) using the Cochran-Armitage trend test. Discrimination was measured via cross-validated Areas Under the Curve (AUCs) in racial/ethnic groups, with comparison to White women.

Results: Among 14,533 women with RA (mean age: 73.8±6.4 years; 1% Asian; 8% Black; 5% Hispanic; 86% White), we observed 1,477 MOFs and 419 hip fractures. FRAX scores were statistically significantly associated with corresponding fracture risk at both sites overall, and in Black, Hispanic, and White women (Table 1). FRAX MOF, but not hip fracture, scores were statistically significantly associated with fracture risk in Asian women (Table 1). Observed MOF incidence increased significantly across FRAX risk categories overall and in all racial/ethnic groups ($P \leq 0.01$). For hip fracture, the trend was statistically significant overall and in White women ($P < 0.01$), and approached significance in Black ($P=0.09$) and Hispanic ($P=0.07$) women. FRAX discrimination for imminent MOF and hip fracture was fair, and AUCs did not differ by race/ethnicity (Table 2).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: U.S.-FRAX without BMD predicted imminent MOF and hip fracture risk in older women with RA, and showed similar discrimination across racial/ethnic groups. Future studies with longer follow-up are needed to assess calibration by race/ethnicity and evaluate performance within RA-specific subgroups, such as stratifying by RA disease activity.

Disclosure: R. Elam: None; **J. Li**: None; **A. Paul**: None; **E. Kersey**: None; **g. Schmajuk**: None; **W. Leslie**: None; **L. Carbone**: None.

Abstract Number: 2686

Impact of autoimmunity, disease activity and treatment on the time course of bone density, microstructure and biomechanics in inflammatory arthritis.

Koray Tascilar[1], Alp Temiz[1], Filippo Fagni[2], Arnd Kleyer[3], Louis Schuster[1], Stephan Kemenes[1], Sara Bayat[1], David Simon[4] and Georg Schett[5], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [2]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Bayern, Germany, [3]Charite Universitätsmedizin Berlin, Erlangen, Bayern, Germany, [4]Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin, Germany; Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, Berlin, Germany, [5]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Rheumatoid Arthritis – Diagnosis, Manifestations, and Outcomes III: Long Live (Comorbidity and Outcomes) (2681–2686)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: RA and PsA follow different pathomechanisms and incur disease-specific erosive and osteoproliferative bone changes. We used data from a large cohort of RA and PsA patients who underwent high-resolution peripheral quantitative computed tomography (HR-pQCT) imaging and analyzed the impact of the primary disease, disease activity and exposure to targeted treatments on bone density, structure and biomechanics over time.

Methods: The study included RA patients fulfilling the 2010 ACR/EULAR criteria and PsA patients fulfilling the CASPAR criteria in University Hospital Erlangen with ethics approval (324_16B) and written informed consent of the participants. HR-pQCT of the distal radius and 2nd and 3rd metacarpal heads (MCP) was performed bi/annually measuring volumetric bone density (vBMD), trabecular and cortical microstructure, bone stiffness and failure load. Cohort follow-up started at the earliest HR-pQCT and ended at the latest. Imaging episodes between consecutive imaging dates were classified based on the type of coinciding targeted treatments and using time-weighted average DAS-28 as the disease activity exposed. HR-pQCT measurements at the beginning and end of an episode were the episode baseline and outcome values. We used mixed-effects/additive regression to model episode outcome as a function of the episode baseline, episode duration, gender, age and weight of the patients and calculated adjusted marginal means at yearly intervals by diagnosis, and at fixed DAS-28 ESR values representing continuous remission (2.0) and continuous high disease activity (6.0). btsDMARD effects were summarized using their regression coefficients comparing to no use.

Results: We included 946 radius and 916 MCP scans from 482 patients with PsA (n=175), RA- (n=86) and RA+ (n=221) over a median (IQR) follow-up of 28 months (12 to 50). Glucocorticoid exposure was similar in RA+ and RA- patients (Table-1). Measurements at radius showed a total vBMD deterioration in a similar fashion for both RA and PsA while RA+

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table-1

Table-1 Baseline characteristics

Characteristic	Overall N = 482[1]	PsA N = 175[1]	RA seronegative N = 86[1]	RA seropositive N = 221[1]	p-value[2]
Age (years)	53 ± 13	51 ± 13	58 ± 13	53 ± 12	<0.001
Sex					<0.001
m	188 (39%)	93 (53%)	24 (28%)	71 (32%)	
w	294 (61%)	82 (47%)	62 (72%)	150 (68%)	
Number of radius scans					0.047
1	119 (29%)	48 (32%)	21 (31%)	50 (26%)	
2	141 (34%)	56 (37%)	29 (43%)	56 (29%)	
3	92 (22%)	31 (21%)	12 (18%)	49 (25%)	
≥4	60 (15%)	16 (11%)	6 (8.8%)	38 (20%)	
Number of MCP scans					0.2
1	160 (38%)	66 (42%)	33 (43%)	61 (32%)	
2	141 (33%)	54 (34%)	26 (34%)	61 (32%)	
3	67 (16%)	23 (14%)	10 (13%)	34 (18%)	
≥4	58 (14%)	16 (10%)	8 (10%)	34 (18%)	
Median scan interval (radius, months)	22 (14, 31)	25 (17, 37)	20 (14, 34)	22 (14, 28)	0.033
Median scan interval (MCP, months)	22 (14, 34)	25 (16, 38)	19 (14, 27)	22 (14, 30)	0.090
Disease duration (years)	3 (0, 10)	2 (0, 8)	3 (1, 7)	4 (0, 12)	0.4
Height (cm)	170 ± 9	173 ± 9	168 ± 8	169 ± 9	<0.001
Weight (kg)	80 ± 19	85 ± 17	77 ± 19	77 ± 19	<0.001
DAS28 ESR	2.80 (1.89, 3.93)	2.75 (1.74, 3.76)	2.90 (1.97, 3.90)	2.82 (1.93, 4.02)	0.6
HAQ score	0.63 (0.13, 1.13)	0.25 (0.00, 0.88)	0.88 (0.50, 1.50)	0.69 (0.13, 1.38)	<0.001
Number of csDMARDs					<0.001
0	73 (15%)	45 (26%)	7 (8.1%)	21 (9.5%)	
1	267 (55%)	100 (57%)	36 (42%)	131 (59%)	
2	112 (23%)	27 (15%)	36 (42%)	49 (22%)	
≥3	30 (6.2%)	3 (1.7%)	7 (8.1%)	20 (9.0%)	
Number of tsDMARDs					<0.001
0	367 (76%)	153 (87%)	68 (79%)	146 (66%)	
1	107 (22%)	21 (12%)	18 (21%)	68 (31%)	
2	8 (1.7%)	1 (0.6%)	0 (0%)	7 (3.2%)	
Number of bDMARDs					0.022
0	130 (27%)	31 (18%)	32 (37%)	67 (30%)	
1	161 (33%)	71 (41%)	23 (27%)	67 (30%)	
2	91 (19%)	34 (19%)	15 (17%)	42 (19%)	
≥3	100 (21%)	39 (22%)	16 (19%)	45 (20%)	
Glucocorticoid use	304 (63%)	67 (38%)	65 (76%)	172 (78%)	<0.001

[1]Mean ± SD, Median (Q1, Q3), n (%)

[2]Kruskal-Wallis rank sum test, Pearson's Chi-squared test, Fisher's exact test

patients show lower total vBMD at all timepoints. This separation was prominent in trabecular vBMD (Fig1A) trabecular microstructure (Fig1B) and biomechanics (Fig1C). Patients with PsA showed higher cortical vBMD and a numerically slower rate of cortical bone loss compared to RA (Fig1A) and a stable trabecular count (Fig1B). Patterns at the MCP region were grossly similar. Disease activity comparisons indicate deteriorating radial trabecular vBMD in PsA patients after 1 year under high disease activity and in all vBMDs in RA+ patients after 1 year including stiffness and failure load (Fig2A). TNF blockers, baricitinib and rituximab use improved bone density at the MCP in RA+ patients (Fig2B) , no particular pattern was discernible at the radius and for RA- and PsA.

Conclusion: Seropositive RA patients show worse bone density and microstructure across the board, which is also affected by disease activity, segregating from seronegative RA despite similar glucocorticoid use. Intervention with TNF-blockers, rituximab and baricitinib seem beneficial for bone density at the MCP, possibly indicating interception of local inflammation.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

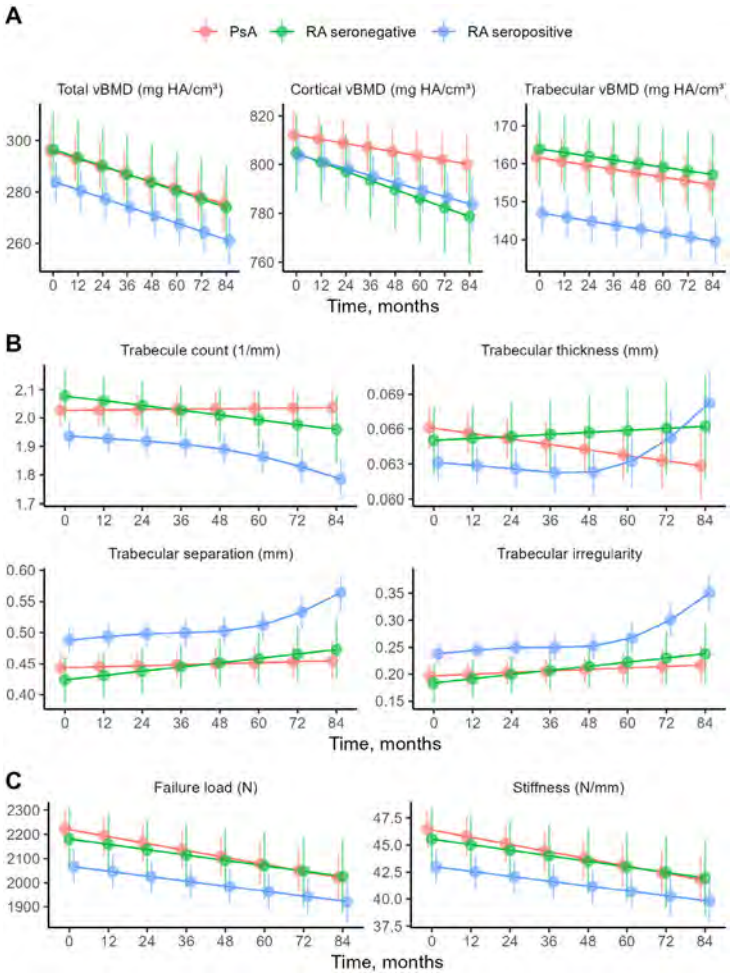


Fig1 Marginal mean HR-pQCT measurements over time adjusted for age, gender and weight by diagnosis showing A) Bone density B) Trabecular microstructure, and C) Bone biomechanics.

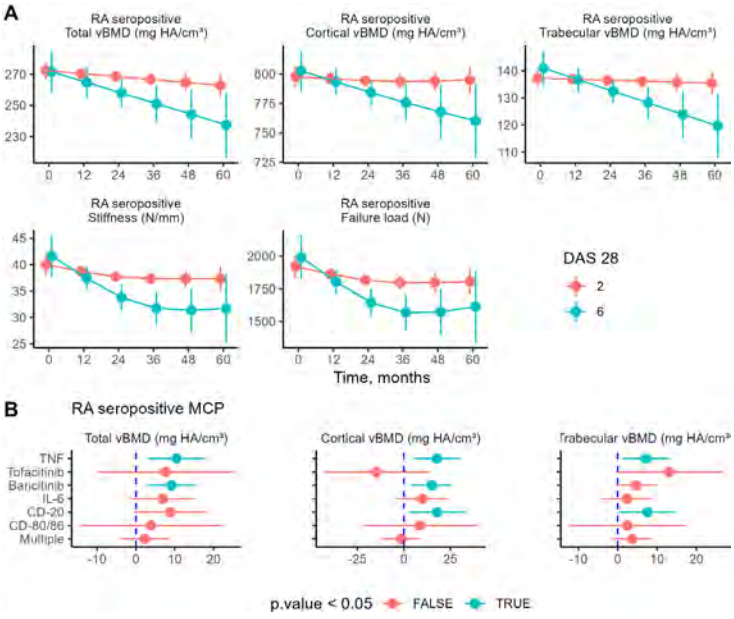


Fig2. A) Bone density and biomechanics at the radius in seropositive RA patients assuming constant DAS-28 remission vs. high disease activity over time. B) Regression coefficients indicating the effect of targeted treatments on bone density at the MCP in seropositive RA patients.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: K. Tascilar: None; **A. Temiz**: None; **F. Fagni**: None; **A. Kleyer**: None; **L. Schuster**: None; **S. Kemenes**: None; **S. Bayat**: None; **D. Simon**: AbbVie, 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, Janssen-Cilag, 2, 6, Kyverna Therapeutics, 12, Financial/Material Study Support, Lilly, 2, 6, Medac, 2, 6, Novartis, 2, 6, UCB, 2, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6.

Abstract Number: 2687

Glucagon-like peptide-1 receptor agonists therapy is associated in improvement in psoriatic arthritis-related and metabolic outcomes: A retrospective analysis of two cohorts

Lihi Eder[1], Uma Scher[2], Kyra Chen[3], Alexandra L. Rice[3], Sydney Thib[4] and Rebecca Haberman[5], [1]University of Toronto, Toronto, ON, Canada, [2]NYU School of Medicine, Scarsdale, NY, [3]NYU Grossman School of Medicine and NYU Langone Health Psoriatic Arthritis Center, New York, [4]Women's College Research Institute, Women's College Hospital, Toronto, Canada, [5]NYU Langone Health, New York, NY

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions (2687–2692)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Obesity is highly prevalent in psoriatic arthritis (PsA) and is associated with reduced therapeutic response, worse disease outcomes, and increased cardiometabolic risk. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are being increasingly used for weight loss and diabetes, but their impact on PsA outcomes remains unclear. We aimed to characterize patients with PsA initiating GLP-1 RAs and assess longitudinal changes in weight, psoriatic disease activity and cardiometabolic parameters.

Methods: We conducted a retrospective analysis of PsA patients from two academic cohorts (Toronto and NYU, PPACMAN sites) who initiated GLP-1 RAs (semaglutide, liraglutide, or tirzepatide) for weight loss or diabetes. Data from clinic visits within 1 year before and after GLP-1 RA initiation were extracted, including joint counts, skin involvement, enthesitis, CRP, and patient-reported outcomes. Disease Activity in PsA (DAPSA) scores were calculated. Cardiometabolic data (weight, blood pressure, lipids) were also collected. Within-patient changes were assessed using the Wilcoxon signed-rank test. Linear regression models, adjusting for baseline outcome values, were used to examine the association between percent weight change and change in outcomes.

Results: A total of 48 patients (18 Toronto, 30 NYU; median age 52.7 years; 60.4% female; median BMI 34.9, **Table 1**) were included. Cardiometabolic and other comorbidities were common: obesity (64.6%), diabetes (35.4%), hypertension (50%), cardiovascular disease (12.5%), fatty liver (20.8%), depression (39.6%), sleep apnea (35.4%), and osteoarthritis (27.1%). Sixty percent had ≥3 comorbidities. Significant weight loss was observed post-treatment (-6.43 kg (95% CI -9.5, -2.0), $p<$ 0.0001, **Table 2**), with 35.4% losing 5–10% and 25% losing >10% of their baseline weight. CRP levels decreased significantly (-1.1 mg/L (95% CI: -2.0, -0.2), p=0.002), as did pain scores (-1.0 (95% CI: -1.75, 0), p=0.01). DAPSA (-3.52, p=0.11) and patient global assessment (-0.5, p=0.08) showed numerical improvements. A significant reduction in triglycerides (-0.35 mmol/L, p=0.02) was also noted. Regression analyses revealed that each 1% reduction in body weight was associated with significant improvements in DAPSA (β=-0.49 (95% CI: -0.94, -0.03), **Table 3**), tender joint count (β=-0.18 (95% CI: -0.32, -0.05)), EQ-5D (β=0.0016 (95% CI: 0.008, 0.023)), LDL (β=-0.05 (95% CI: -0.10, -0.003)), and systolic blood pressure (β=-0.67 (95% CI: -1.18, -0.15)).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 - Patient characteristics prior to initiation of GLP1-RA therapy

Variable	Median (IQR)/Frequency (%)	N
Age	52.7 (42.3, 59)	48
Sex: Female	29 (60.4%)	48
BMI (kg/m²)	34.9 (31, 40.6)	48
Obesity (BMI>30)	31 (64.6%)	48
Diabetes mellitus	17 (35.4%)	48
Hypertension	24 (50%)	48
Fatty liver	10 (20.8%)	48
Sleep apnea	17 (35.4%)	48
Cardiovascular disease*	6 (12.5%)	48
Depression	19 (39.6%)	48
Osteoarthritis	13 (27.1%)	48
Weight (kg)	102.5 (89.9, 119.8)	48
DAPSA	14.5 (9.5, 18.9)	26
Tender joint count (0-68)	1 (0, 3.8)	45
Swollen joint count (0-66)	0 (0, 1)	45
BSA (%)	0 (0, 1)	45
Pain score (0-10)	5 (2.4, 7)	29
Patient global activity (0-10)	6 (3.1, 7)	26
HAQ-DI	0.72 (0.30, 1.25)	18
FACIT-Fatigue	33.1 (22.9, 40.8)	18
EuroQol 5-Dimensions (0-1)	0.61 (0.57, 0.78)	18
Physician global activity (0-10)	2 (1, 3)	35
CRP (mg/L)	3.7 (1.9, 11.0)	38
Cholesterol (mmol/L)	4.6 (3.9, 5.2)	34
Triglycerides (mmol/L)	2.24 (1.5, 3.8)	34
LDL-c (mmol/L)	2.5 (1.9, 3.3)	34
HDL-c (mmol/L)	1.3 (1.0, 1.5)	34
Systolic blood pressure (mmHg)	122 (115, 134)	48
ALT (IU/L)	26.5 (17.9, 51)	46

BSA - Body surface area of psoriasis; CRP- C-reactive protein; DAPSA - Disease activity in psoriatic arthritis; FACIT- Functional Assessment of Chronic Illness Therapy; HAQ-DI - health assessment questionnaire disability index; LDL – low density lipoprotein; HLD- high density lipoprotein; AST- alanine transaminase. Cardiovascular disease includes a history of coronary artery disease, arrhythmia or heart failure

Table 2 - Median changes in PsA and metabolic measure following GLP1-RA therapy

Variable	Median change (95% CI)	p value*	N
Weight (kg)	**-6.43 (-9.50, -2.00)**	**<0.0001**	**48**
DAPSA	-3.52 (-8.62, 2.77)	0.11	21
CRP (mg/L)	**-1.1 (-2.0, -0.2)**	**0.002**	**31**
Tender joint count	0 (-1, 0)	0.29	45
Swollen joint count	**0 (0, 0)**	**0.03**	**45**
Pain (0-10)	**-1.0 (-1.75, 0)**	**0.01**	**25**
Patient global activity (0-10)	-0.5 (-1.67, 0)	0.08	23
HAQ-DI	-0.05 (-0.25, 0.08)	0.27	18
FACIT- Fatigue	2.75 (-3.0, 7.5)	0.14	18
EuroQol 5-Dimensions (0-1)	0.01 (0, 0.14)	0.14	18
BSA (%)	0.01 (0, 1)	0.56	45
Cholesterol (mmol/L)	-0.23 (-0.45, 0.20)	0.10	28
Triglycerides (mmol/L)	**-0.35 (-0.71, -0.13)**	**0.02**	28
ALT	-2.5 (-6, 1)	0.24	42
Systolic BP (mm/Hg)	0 (-4, 5)	0.88	42

*Wilcoxon Signed-Rank test for paired samples

BSA - Body surface area of psoriasis; CRP- C-reactive protein; DAPSA - Disease activity in psoriatic arthritis; FACIT- Functional Assessment of Chronic Illness Therapy; HAQ-DI - health assessment questionnaire disability index; AST- alanine transaminase

Conclusion: In this initial analysis of a real-world study conducted in dual psoriasis-PsA PPACMAN clinics, GLP-1 RA therapy in patients with PsA was associated with clinically meaningful weight loss and improvements in systemic inflammation, pain, and cardiometabolic markers. Improvements in PsA outcomes were proportional to the degree of weight loss. These findings warrant further investigation in prospective controlled studies to evaluate the therapeutic role of GLP-1 RAs in PsA management and its frequent comorbidities.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 3 - The association between body weight reduction (% from baseline) and changes in PsA and metabolic outcomes following GLP1-RA therapy - Linear regression model

Outcome	Adjusted β coefficient for % of body weight change (95% CI)*	p value	N
DAPSA	-0.49 (-0.94, -0.03)	0.04	21
Pain (0-10)	-0.09 (-0.20, 0.02)	0.10	25
CRP (mg/L)	-0.10 (-0.23, 0.04)	0.15	31
Tender joint count (0-68)	-0.18 (-0.32, -0.05)	0.01	45
Swollen joint count	-0.02 (-0.06, 0.02)	0.26	45
BSA (%)	0.01 (-0.02, 0.04)	0.57	45
HAQ-DI	-0.02 (-0.04, 0.00)	0.09	18
EuroQol 5-Dimensions (0-1)	0.016 (0.008, 0.023)	<0.001	18
Cholesterol (mmol/L)	-0.07 (-0.11, -0.03)	0.003	28
Triglycerides (mmol/L)	-0.05 (-0.10, 0.00)	0.07	28
LDL-c (mmol/L)	-0.05 (-0.10, -0.003)	0.04	28
Systolic BP (mm/Hg)	-0.67 (-1.18, -0.15)	0.01	42

* The reported estimates indicate the change in the corresponding outcome for each 1% reduction in body weight adjusted for baseline level of the assessed outcome

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **U. Scher**: None; **K. Chen**: None; **A. Rice**: None; **S. Thib**: None; **R. Haberman**: Johnson and Johnson, 1, 5, Novartis, 1.

Abstract Number: 2688

Single cell RNA-seq immune profiling of blood samples from a psoriatic disease clinical trial reveals a CD4 T cell population associated with response to IL-23 blockade

Kathryne Marks[1], Anina Sun[2], Ifeoluwakiisi Adejoorin[1], Lourdes Perez Chada[3], Anna Perillo[4], Leanne Barrett[2], Michael Garshick[5], James Krueger[6], Joseph Merola[7], Marcelo DiCarli[2], Deepak Rao[1] and Brittany Weber[8], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham And Women's Hospital, Boston, [3]Harvard Medical School, Wayland, MA, [4]The Rockefeller University, New York, NY, USA, New York, NY, [5]NYU Langone Health, Tenafly, NJ, [6]Rockefeller University, New York, NY, [7]UT Southwestern Medical Center, Dallas, TX, [8]Brigham and Women's Hospital, DEDHAM, MA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions (2687–2692)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: The use of IL-23 inhibitors (IL-23i) for psoriatic diseases resulted in significant improvement in disease symptoms for many patients. Whether any blood immune cell profiles can predict clinical response to IL-23 blockade has not been examined, however. Here, we applied single cell RNA-seq immune profiling to blood samples from 27 PsO/A patients to identify cellular features associated with response to IL-23 blockade by tildrakizumab in the setting of a clinical trial.

Methods: PBMCs from psoriasis (n = 21) and psoriatic arthritis (n=6) patients were collected as part of the MINIMA study (NCT04271540) at Brigham and Women's Hospital before (following washout) and after 24 weeks of treatment with tildrakizumab. Patients currently had moderate or severe PsO. PASI scores were recorded before and after treatment, and % improvement of 50% or 70% was calculated. 48% of participants had a PASI improvement of 70% or greater, and 78% PASI improvement of 50% or greater. Table 1 denotes the disease characteristics and demographics of the patients. Single-cell RNA sequencing was conducted on baseline samples before treatment and on follow-up samples, followed by

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Description of patients included in the scRNAseq from the MINIMA trial.

Patients	Pre/Post paired samples	FollowUP	Female median (%)	Age median (range)	PsA	Medication	DeltaPASI median (range)	PASI improved by 50%	PASI improved by 70%
27		26~6mo	10(37%)	63(31-79)	6(22%)	Tildrekizumab (anti-P19)	-7.8 (-0.9--17.7)	21 (78%)	13 (48%)

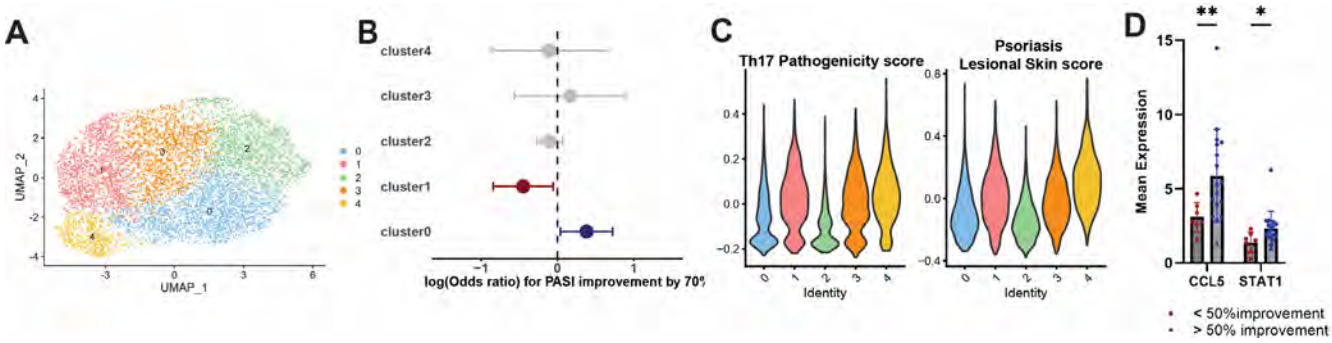


Figure 1. A) scRNAseq of PBMCs from IL-23i-treated patients, including cells from baseline (pre-treatment) and week 24 post-treatment samples (~136K cells). B) Mixed effects association of single cell analysis demonstrates a lack of association of PBMC clusters with pre- or post-IL-23i. C) CD4 T cells subset from PBMCs. D) IL23R, IL17A, and IFN expression in CD4 T cells.

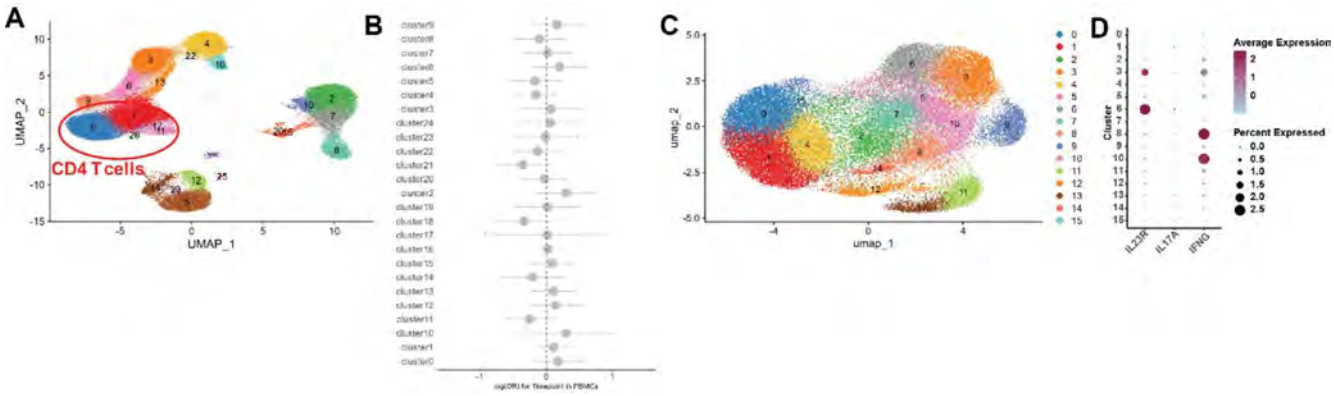


Figure 2. A) Subcluster of CD4+IL23R+ clusters. B) MASC analysis of pre-treatment samples demonstrating CD4+IL23R+ subclusters associated with baseline (pre-treatment) or week 24 (post-treatment). C) Module scores of genes that predict Th17 cell pathogenicity and genes highly expressed in psoriasis lesional skin. Both scores are higher in the better improvement-associated cluster than the lesser improvement-associated cluster. D) Mean expression of CCL5 and STAT1 in pre-treatment samples is higher in those who have greater than 50% improvement from IL-23i at week 24.

QC, batch correction, and unsupervised clustering. Analyses were performed using Wilcoxon paired tests, covarying neighborhood analysis (CNA), mixed effects association of single cell analysis (MASC), and differential gene expression analysis.

Results: We compared baseline samples from patients with greater or less than 70% improvement to identify baseline immune features associated with response. Assessment of PBMCs at a broad level did not reveal associations of any major immune cell populations with better or worse response to IL-23i. We then focused on T cell populations likely to be affected by IL-23i especially IL-23R+ T cells (**Fig 1**). The IL23R+ CD4 T cell had phenotypes consistent with Th17 and Th1 cells, including expression of IFNG, CXCR3, and IL17A, CCR6 and RORC. As a whole, the proportion of these cells in blood did not change following IL-23i. Further subcluster analysis of the IL23R+ CD4 T cell clusters revealed an association of a subcluster of cells with 70% clinical improvement and a separate subcluster of cells associated with lesser clinical improvement (**Fig 2**). Response-associated CD4+ T cells had a gene signature which corresponded to pathogenic Th17 cells (Hu et al,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Nat. Commun. 2017). Additionally, patients with improvement >50% had higher expression of CCL5 and STAT1 in the IL23R+ CD4 T cells. To understand relevance of these cells to cells that are expanded in psoriasis skin, we applied a gene module score of genes associated with IFNg+ IL-17A+ cells from psoriasis skin (Kim et al, J. Allergy Clin. Immunol., 2021). This gene score was also higher in the response-associated cluster.

Conclusion: We have identified a subset of CD4+ T cells whose abundance in circulation before treatment is associated with response to IL-23i in skin disease severity. This T cell population demonstrates transcriptomic features that correspond to those expanded in psoriasis lesional skin. These results suggest that cellular features detectable in blood may be informative in predicting clinical response to IL-23 blockade.

Disclosure: K. Marks: None; **A. Sun**: None; **I. Adejoorin**: None; **L. Perez Chada**: Bristol-Myers Squibb(BMS), 2, 6, Takeda, 2; **A. Perillo**: AbbVie, 2, 5, 6, Allergan, 2, 6, Almirall, 2, 6, Amgen, 2, 5, 6, Aristea, 2, 6, Artax Biopharma, 2, 5, 6, Avillion, 5, Biogen Idec, 2, 5, 6, Boehringer-Ingelheim, 2, 5, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, Bruxelles Biopharma, 5, Calliditas, 2, 6, Eli Lilly, 2, 5, 6, Escalier, 2, 6, Exicure, 5, Immunotherapeutics, 2, 6, Incyte, 2, 5, 6, Innovaderm, 5, Janssen, 2, 5, 6, Kymera Therapeutics, 2, 6, Kyowa Kirin, 2, 5, 6, MC2 Therapeutics, 2, 6, Merck, 2, 6, MoonLake, 2, 6, Novan, 5, Novartis, 2, 5, 6, Nuvig Therapeutics, 2, 6, ONO-Pharma, 5, Oruka Therapeutics, 2, 6, Pfizer, 2, 5, 6, Provectus, 5, Regeneron, 5, Sanofi, 2, 6, SUDO Bio, 5, Sun Pharma, 2, 6, Takeda, 2, 5, 6, Target-Derm, 2, 6, UCB, 2, 5, 6, UNION Therapeutics, 2, 6, Valeant, 2, 6, Ventyx, 2, 6, Vitae Pharmaceuticals, 5; **L. Barrett**: None; **M. Garshick**: Agepha, 2, Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2; **J. Krueger**: AbbVie, Allergan, Almirall, Amgen, Artax, 2, AbbVie, Amgen, Artax Biopharma, Avillion, 5, Aristea, Biogen Idec, Boehringer Ingelheim, 2, Biogen, Boehringer Ingelheim, BMS, 5, Bristol-Myers Squibb, Calliditas, CSL Behring, Eli Lilly, Escalier, Evommune, Incyte, 2, Bruxelles Biopharma, Exicure,Innovaderm, 5, Eli Lilly, Escalier, Evommune, Incyte, 2, Incyte, Janssen, Kyowa Kirin, Eli Lilly, 5, Janssen, Kymera Therapeutics, Kyowa Kirin, 2, MC2 Therapeutics, Merck, MoonLake, 2, Novan, Novartis, ONO-Pharma, Pfizer, 5, Novartis, NuvigTherapeutics, Oruka Therapeutics, 2, Pfizer, Sanofi, Schrodinger, Sun Pharma, 2, Provectus, Regeneron, SUDO Bio ,Takeda, 5, Takeda, Target- Derm, UCB, UNION Therapeutics, 2, UCB, Vitae Pharmaceuticals, 5, Valeant, Ventyx, 2; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **M. DiCarli**: Bayer, 2, Gilead, 5, Janssen, 2, Spectrum, 5; **D. Rao**: Abbvie, 6, Aditum, 2, AnaptysBio, 2, AstraZeneca, 2, Biogen, 2, Dragonfly, 2, Epana, 1, HiFiBio Therapeutics, 2, Janssen, 5, Merck/MSD, 2, 5, Site Tx, 2; **B. Weber**: Bristol-Myers Squibb(BMS), 2, Kiniksa Pharmaceuticals, 2, Novo nordisk, 2, Novo Nordisk, 2, Oruka, 2.

Abstract Number: 2689

Comparison of Incidence of Psoriatic Arthritis in Patients With Psoriasis Treated With Interleukin-17 Inhibitors vs Interleukin-23 Inhibitors, Interleukin-12/23 Inhibitors, and Tumor Necrosis Factor Inhibitors in Real-World Practice: A Retrospective Study

April Armstrong[1], Joseph Merola[2], Gang Wang[3], Ariane Faucher[4], Riley Taiji[4], Francis Vekeman[4], Alexis Shew[5], Tim Nguyen[5] and Laura Coates[6], [1]University of California Los Angeles, Los Angeles, CA, USA, Los Angeles, CA, [2]UT Southwestern Medical Center, Dallas, TX, [3]Department of Dermatology, Xijing Hospital, The Fourth Military Medical University, Xi'an, China (People's Republic), [4]STATLOG, Inc, Montreal, QC, Canada, [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [6]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, England, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions (2687–2692)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Biologic therapies for moderate to severe psoriasis (PsO) include inhibitors of IL-17 (IL-17i), IL-23i, IL-12/23i, and tumor necrosis factor (TNFi). Previous studies that assessed whether biologic treatments can prevent inflammatory arthritis (IA; including PsA) in patients with PsO have not accounted for potential confounders such as PsO severity, PsA/IA-related therapy, and physician preference. This study compared incident PsA/IA among patients with PsO who newly initiated IL-17i, IL-23i, IL-12/23i, or TNFi therapy.

Methods: Adults with ≥2 PsO diagnosis codes (International Classification of Disease [ICD] codes) ≥30 days apart who newly initiated an IL-17i, IL-23i, IL-12/23i, or TNFi between January 1, 2019, and April 17, 2024 (index date = first record), were included in this retrospective cohort analysis of electronic health records (EHR). Exclusion criteria included missing age/sex information, any diagnosis code for IA (PsA or other IA) any time before or within 14 days after the index date, or NSAID prescriptions in 12 months prior to (pre-index period) or on the index date to mitigate protopathic bias. Patient demographics, clinical characteristics, past treatments, and comorbidities in the pre-index period or at index were descriptively reported. We used the Kaplan-Meier (KM) method to estimate the cumulative incidence of PsA or other IA during the follow-up period, and a 2-sample test with Greenwood plug-in estimator for variance to compare the area under the curve (AUC; ie, restricted mean time lost [RMTL]) between cohorts up to the last common time point. Propensity score matching (PSM) was used to attempt to balance covariates for each pairwise comparison. Covariates included key disease and demographic characteristics (including but not limited to those in **Table 1**) from both structured and natural language processing–derived EHR data.

Table 1. Baseline Demographics and Clinical Characteristics of Patients Treated with Interleukin-17, Interleukin-23, Interleukin 12/23, or Tumor Necrosis Factor Inhibitors[a,b]

Characteristic	IL-17i vs IL-23i		IL-17i vs IL-12/23i		IL-17i vs TNFi	
	IL-17i (n=1444)	IL-23i (n=1444)	IL-17i (n=765)	IL-12/23i (n=765)	IL-17i (n=1476)	TNFi (n=1476)
Age, mean (SD), years	51.0 (15.2)	50.9 (15.2)	49.4 (15.5)	50.0 (15.7)	50.5 (15.3)	50.5 (15.2)
Female, n (%)	737 (51.0)	734 (50.8)	409 (53.5)	390 (51.0)	753 (51.0)	763 (51.7)
Race, n (%)						
Asian	48 (3.3)	44 (3.1)	23 (3.0)	21 (2.8)	49 (3.3)	49 (3.3)
Black or African American	68 (4.7)	69 (4.8)	39 (5.1)	32 (4.2)	71 (4.8)	106 (7.2)
White	1203 (83.3)	1224 (84.8)	623 (81.4)	650 (85.0)	1230 (83.3)	1176 (79.7)
Other/unknown	125 (8.7)	107 (7.4)	80 (10.5)	62 (8.1)	126 (8.5)	145 (9.8)
BMI, mean (SD), kg/m²	32.3 (7.6)	32.1 (8.0)	32.0 (7.7)	31.5 (8.0)	32.4 (7.7)	32.0 (7.6)
PsO BSA involvement, n (%)						
Mild (BSA <3%)	34 (2.4)	58 (4.0)	17 (2.2)	23 (3.0)	35 (2.4)	49 (3.3)
Moderate (3%-10%)	61 (4.2)	58 (4.0)	37 (4.8)	32 (4.2)	64 (4.3)	66 (4.5)
Severe (BSA >10%)	48 (3.3)	91 (6.3)	27 (3.5)	32 (4.2)	49 (3.3)	65 (4.4)
Unknown	1301 (90.1)	1237 (85.7)	684 (89.4)	678 (88.6)	1328 (90.0)	1296 (87.8)
PsO special areas of involvement, n (%)[c]						
Scalp	147 (10.2)	136 (9.4)	74 (9.7)	67 (8.8)	152 (10.3)	114 (7.7)
Face	35 (2.4)	25 (1.7)	20 (2.6)	7 (0.9)	37 (2.5)	23 (1.6)
Palm/soles	0	5 (0.4)	0	3 (0.4)	0	6 (0.4)
Nails	25 (1.7)	16 (1.1)	13 (1.7)	12 (1.6)	25 (1.7)	18 (1.2)
Genitals	11 (0.8)	4 (0.3)	4 (0.5)	5 (0.7)	11 (0.8)	3 (0.2)
Charlson-Deyo Comorbidity Index, mean (SD)	1.6 (2.0)	1.6 (2.0)	1.5 (2.0)	1.5 (1.9)	1.6 (2.0)	1.6 (2.0)
Frequent comorbidities (>5%), n (%)						
Diabetes (mild to moderate)	188 (13.0)	187 (13.0)	89 (11.6)	81 (10.6)	193 (13.1)	197 (13.4)
Chronic pulmonary disease	155 (10.7)	160 (11.1)	78 (10.2)	73 (9.5)	157 (10.6)	159 (10.8)
Time from PsO onset to index, mean (SD), years	3.0 (3.2)	3.5 (3.6)	3.1 (3.3)	3.4 (3.5)	3.0 (3.1)	3.0 (3.2)
Treatment history in 1 year prior to index date, n (%)						
csDMARDs	135 (9.4)	107 (7.4)	77 (10.1)	57 (7.5)	136 (9.2)	237 (16.1)
tsDMARDs	166 (11.5)	183 (12.7)	74 (9.7)	89 (11.6)	169 (11.5)	153 (10.4)
Systemic glucocorticoids	609 (42.2)	617 (42.7)	310 (40.5)	303 (39.6)	626 (42.4)	697 (47.2)

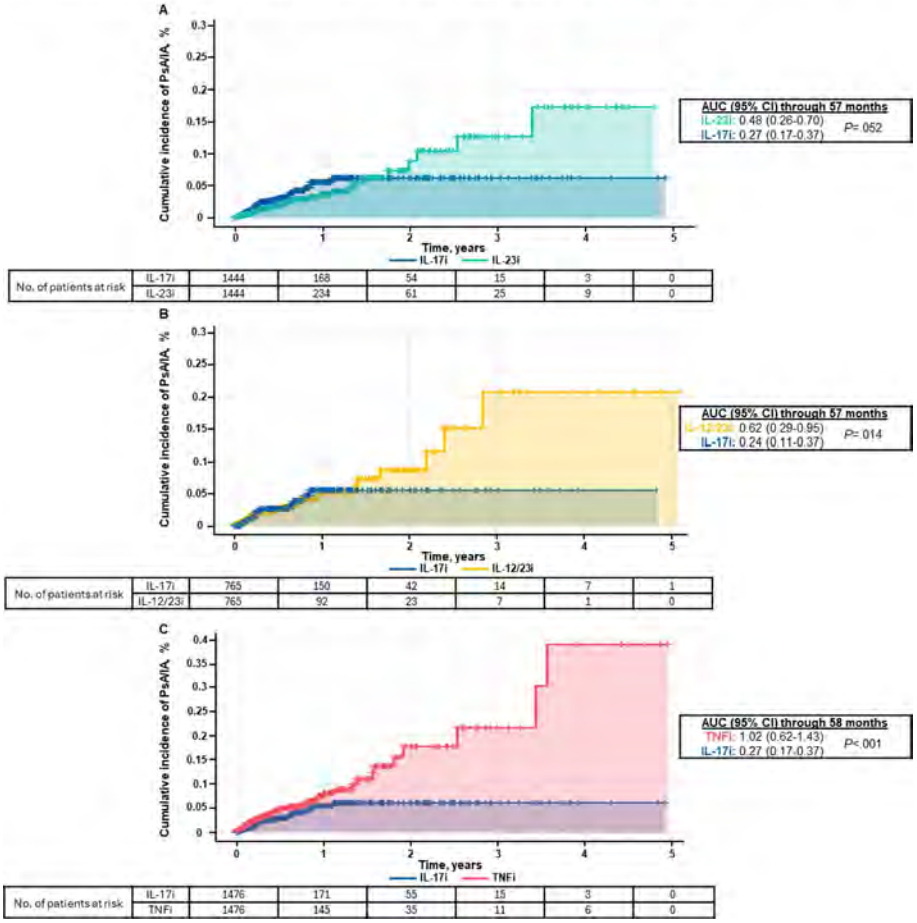
BMI, body mass index; BSA, body surface area; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; IL-12/23i, interleukin 12/23 inhibitor; IL-17i, interleukin 17 inhibitor; IL-23i, interleukin 23 inhibitor; PsO, psoriasis; TNFi, tumor necrosis factor inhibitor; tsDMARD, targeted synthetic disease-modifying anti-rheumatic drug. a Propensity score–matched results. b For each pairwise comparison, standardized mean differences were <0.2 for all patient characteristics. c During 12-month pre-index period. Data are not mutually exclusive.

Table 2. Frequency of Prescriptions by Biologic Class[a]

Biologic treatment	Patients, n (%)
IL-17i	
Secukinumab	851 (57.7)
Ixekizumab	610 (41.3)
Brodalumab	15 (1.0)
IL-23i	
Risankizumab	1363 (60.9)
Guselkumab	812 (36.3)
Tildrakizumab	62 (2.8)
IL-12/23i	
Ustekinumab	781 (100)
TNFi	
Adalimumab	2092 (86.6)
Etanercept	186 (7.7)
Infliximab	75 (3.1)
Certolizumab pegol	57 (2.4)
Golimumab	5 (0.2)

IL-12/23i, interleukin 12/23 inhibitor; IL-17i, interleukin 17 inhibitor; IL-23i, interleukin 23 inhibitor; TNFi, tumor necrosis factor inhibitor. a Before propensity score matching.

Figure 1. Kaplan-Meier curves of cumulative incidence of PsA and other IA[a] in patients with PsO treated with (**A**) IL-17i vs IL-23i, (**B**) IL-17i vs IL-12/23i, and (**C**) IL-17i vs TNFi[b]



AUC, area under the curve; IA, inflammatory arthritis; ICD, International Classification of Diseases; IL-12/23i, interleukin 12/23 inhibitor; IL-17i, interleukin 17 inhibitor; IL-23i, interleukin 23 inhibitor; PsA, psoriatic arthritis; PsO, psoriasis; TNFi, tumor necrosis factor inhibitor. a ICD diagnostic codes for PsA included ICD-9-CM: 696.0 and ICD-10-CM: L40.5x; ICD diagnostic codes for other IA included ICD-9-CM: 718.5, 716.85, 714.9, 714.0, and 720x, and ICD-10-CM: M06.4, M46.1, M45x, M46.9x, M07.6x, and M05x. b Propensity score–matched results.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Before PSM, the most common biologics by class were secukinumab (IL-17i), risankizumab (IL-23i), ustekinumab (IL-12/23i), and adalimumab (TNFi; **Table 2**). After PSM, 1444 patients were included in the IL-17i vs IL-23i cohort, 765 patients were in the IL-17i vs IL-12/23i cohort, and 1476 patients were in the IL-17i vs TNFi cohort (**Table 1**). Patient demographics, past treatment, clinical characteristics, and mean times from PsO onset to index and follow-up were balanced across cohorts. KM analysis revealed a trend toward lower RMTL for time with PsA/IA through 57 months in patients treated with IL-17i vs IL-23i (P=.052; **Figure 1**). RMTL for time with PsA/IA through 57 months was significantly lower in patients treated with IL-17i vs IL-12/23i (P< .05) and in those treated with IL-17i vs TNFi through 58 months(P< .01). On average, patients treated with IL-17i had a 45% reduction in time with PsA/IA vs those treated with IL-23i, a 61% reduction in time with PsA/IA vs those treated with IL-12/23i, and a 74% reduction in time with PsA/IA vs those treated with TNFi over the available follow-up.

Conclusion: In this retrospective cohort analysis of EHR data employing PSM, patients with PsO treated with IL-17i had lower incidence of PsA/IA development through 5 years post-treatment initiation than patients treated with IL-23i, IL-12/23i, or TNFi therapies.

Disclosure: A. Armstrong: AbbVie/Abbott, 1, 6, 12, Research Investigator, Almirall, 1, 6, 12, Research Investigator, Arcutis, 1, 6, 12, Research Investigator, Aslan, 1, 6, 12, Research Investigator, Beiersdorf, 1, 6, 12, Research Investigator, Boehringer-Ingelheim, 1, 6, 12, Research Investigator, Bristol-Myers Squibb(BMS), 1, 6, 12, Research Investigator, Dermavant, 1, 6, 12, Research Investigator, Dermira, 1, 6, 12, Research Investigator, Eli Lilly, 1, 6, 12, Research Investigator, EPI Health, 1, 6, 12, Research Investigator, Incyte, 1, 6, 12, Research Investigator, Janssen, 1, 6, 12, Research Investigator, Leo Pharma, 1, 6, 12, Research Investigator, Mindera Health, 1, 6, 12, Research Investigator, Nimbus, 1, 6, 12, Research Investigator, Novartis, 1, 6, 12, Research Investigator, Ortho Dermatologics, 1, 6, 12, Research Investigator, Pfizer, 1, 6, 12, Research Investigator, Regeneron, 1, 6, 12, Research Investigator, Sanofi, 1, 6, 12, Research Investigator, Sun Pharma, 1, 6, 12, Research Investigator, UCB, 1, 6, 12, Research Investigator; **J. Merola**: AbbVie/Abbott, 2, 12, Investigator, Amgen, 2, 12, Investigator, Arena, 2, Avotres, 2, Biogen, 2, 12, Investigator, Bristol-Myers Squibb(BMS), 2, 12, Investigator, Celgene, 2, Dermavant, 2, 12, Investigator, Eli Lilly, 2, 12, Investigator, EMD Serono, 2, Janssen, 2, 12, Investigator, Leo Pharma, 2, 12, Investigator, Merck/MSD, 2, Novartis, 2, 12, Investigator, Pfizer, 2, 12, Investigator, Regeneron, 2, 12, Investigator, Sanofi, 2, 12, Investigator, Sun Pharma, 2, 12, Investigator, UCB, 2, 12, Investigator; **G. Wang**: AbbVie/Abbott, 1, 6, Eli Lilly, 1, 6, Janssen, 1, 6, Leo Pharma, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, Sanofi, 1, 6; **A. Faucher**: STATLOG Inc., 3, 12, Employee of STATLOG Inc., which has received funding from Novartis Pharmaceuticals Corporation.; **R. Taiji**: STATLOG Inc., 3, 12, Employee of STATLOG Inc., which has received funding from Novartis Pharmaceuticals Corporation.; **F. Vekeman**: STATLOG Inc., 3, 12, Employee of STATLOG Inc., which has received funding from Novartis Pharmaceuticals Corporation.; **A. Shew**: Novartis, 3, 11; **T. Nguyen**: Novartis, 3, 11; **L. Coates**: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, 5, 6, Domain, 2, Eli Lilly and Company, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 5, 6, GSK, 6, Janssen, 2, 5, 6, Medac, 6, MoonLake Immunotherapeutics, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 2690

Dietary interventions in Psoriatic Arthritis: A Randomized controlled clinical trial

Lihi Eder[1], Sohan Shahab[2], Sarah Hopkins Gillespie[3], Laura Bumbulis[4], Helen Emanoilidis[5], Charlene Compher[6], Jose Scher[7], Dafna D. Gladman[8], Richard Cook[4], Vinod Chandran[1] and Alexis Ogdie[9], [1]University of Toronto, Toronto, ON, Canada, [2]Women's College Research Institute, Women's College Hospital, Toronto, Canada, [3]University of Pennsylvania, Philadelphia, PA, [4]University of Waterloo, Waterloo, Canada, [5]Women's College Hospital, Toronto, Canada, [6]University of Pennsylvania School of Nursing and Hospital of the University of Pennsylvania, Philadelphia, [7]New York University School of Medicine, New York, NY, [8]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Division of Rheumatology, Toronto, ON, Canada, [9]Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Wilmington, DE

SESSION INFORMATION

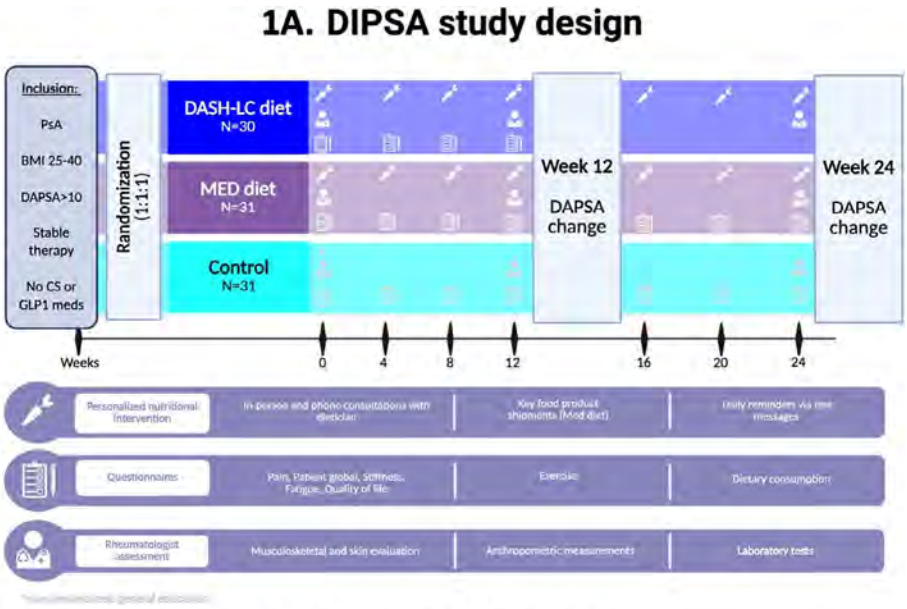
Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions (2687–2692)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: The Dietary Interventions in Psoriatic Arthritis (DIPSA) study is a multicentre randomized controlled trial (RCT) designed to evaluate the efficacy of two personalized dietary interventions in improving clinical outcomes in patients with active psoriatic arthritis (PsA), compared to standard of care.



1B. Baseline variable of study participants

Variable	MED N=31	DASH-LC N=30	Control N=31
Age (mean, SD)	57 (13)	52 (13)	56 (13)
Sex: Female (N, %)	18 (58%)	22 (73%)	24 (77%)
Race: White (N, %)	25 (81%)	26 (87%)	23 (74%)
BMI (mean, SD)	32 (4.5)	34 (4)	32 (4.3)
DAPSA (mean, SD)	17 (7.2)	21 (15)	21 (8.8)
Tender joints (mean, SD)	6.2 (6.6)	8.7 (13)	7.7 (5.9)
Swollen joints (mean, SD)	0.7 (1.3)	1.5 (3.1)	1.7 (3.6)
Patient global (mean, SD)	5.1 (1.7)	5.2 (2.2)	5.4 (2)
Pain (mean, SD)	4.8 (1.9)	5.2 (1.9)	5.5 (2.1)
Physician global (mean, SD)	2.5 (1.3)	2.6 (1.6)	2.4 (1.6)
hsCRP (mg/L) (mean, SD)	4.9 (5.7)	5.1 (4.1)	4.2 (4.3)
PASI (mean, SD)	1.3 (2.4)	1.2 (1.7)	0.5 (0.8)

Figure 1: 1A. DIPSA study design, enrolment criteria and study procedures; 1B. Baseline characteristics by arm. BMI- Body mass area; DAPSA - Disease activity in Psoriatic Arthritis; PASI - Psoriasis Area and Severity Index

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: Adults with moderately active PsA (Disease Activity index for PsA (DAPSA) >10), BMI 25–40, and stable drug therapy were recruited from 3 centres. Participants were randomized to one of 3 arms: (1) a Mediterranean (Med) diet focused on healthy food composition; (2) a low-calorie Dietary Approaches to Stop Hypertension (DASH-LC) diet targeting weight reduction; or (3) a standard-of-care control arm receiving general, non-personalized dietary advice. Interventions were delivered by registered dietitians through 2 in-person consultations and 7 structured telephone sessions. Clinical evaluations were performed at baseline, 12, and 24 weeks by rheumatologists. Patient-reported outcomes were collected from weeks 0 to 24. The primary outcome was change in DAPSA at week 12. Secondary outcomes included DAPSA change at week 24, as well as changes in pain, PROMIS fatigue, Psoriatic Arthritis Impact of Disease (PsAID), tender/swollen joint

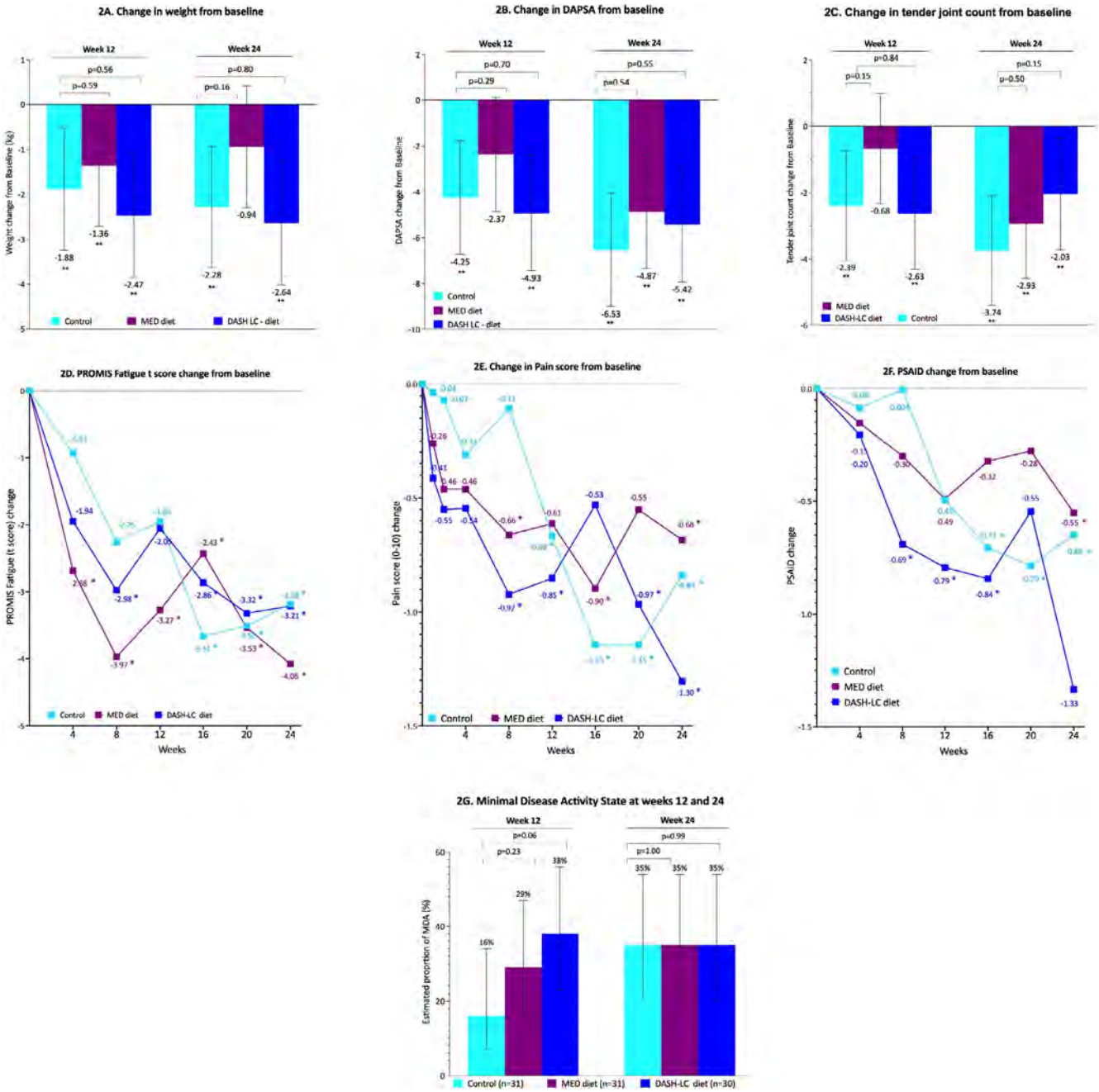


Figure 2: Change in study outcome by study arm. 2A. Weight; 2B. DAPSA; 2C. Tender joint count; 2D. PROMIS Fatigue (t score); Pain score; 2E. PSAID; Minimal Disease Activity state. * indicates p<0.05 compared to baseline. DAPSA - Disease activity in Psoriatic Arthritis; PSAID - Psoriatic Arthritis Impact of Disease.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

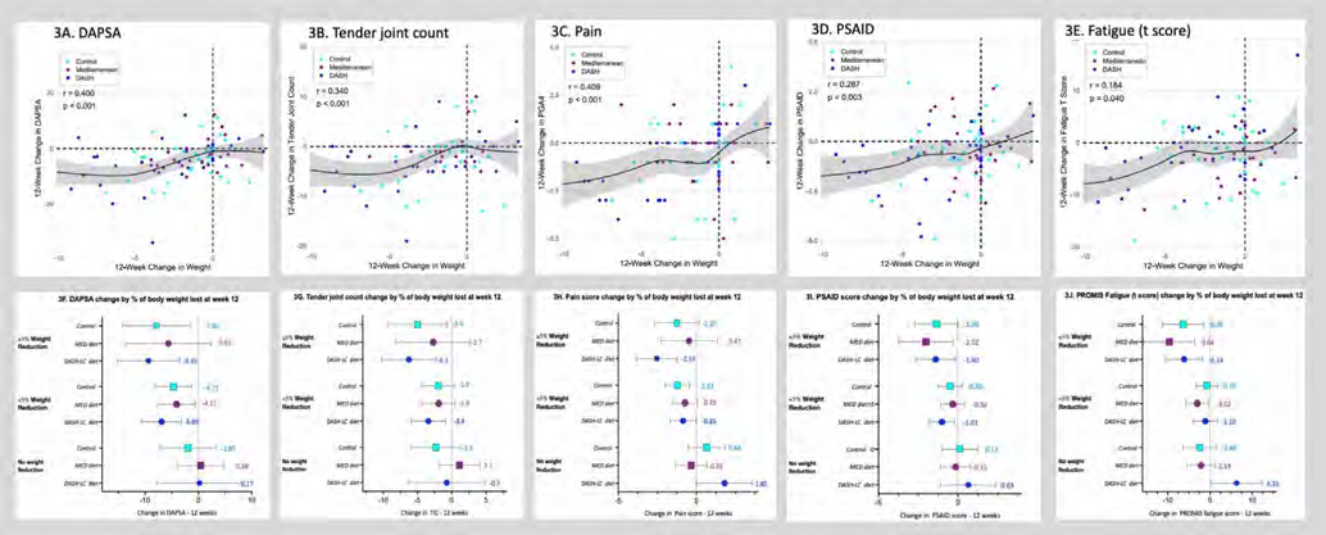


Figure 3. 3A-E. The correlation between study outcomes and weight change from baseline with splines; 3F-3J. The estimated mean change (95% CI) in study outcomes by the extent of weight reduction (none, <5% and >5% reduction in body weight) for each study arm.

counts, anthropometric measures, and inflammatory markers. Missing data were managed using last observation carried forward and multiple imputation. Changes across study arms and from baseline were assessed using random-effects regression models.

Results: Of 92 randomized patients (Med: n=31, DASH-LC: n=30, Control: n=31), 12 withdrew post-randomization. Baseline characteristics were comparable across arms (**Fig. 1**). All groups experienced significant, yet modest, weight loss by week 12 (Med: –1.36 kg; DASH-LC: –2.47 kg; Control: –1.88 kg, **Fig. 2A**), with small additional reductions by week 24. No significant differences in weight loss were observed between arms. At week 12, significant reductions in DAPSA were observed in the DASH-LC (–4.93) and control (–4.25) groups; by week 24, all groups showed improvement (Med: –4.87; DASH-LC: –5.42; Control: –6.53, **Fig. 2B**), without significant between-group differences. Minimal Disease Activity (MDA) was achieved at week 12 by 38% in DASH-LC and 29% in Med versus 16% in control (p=0.23 and p=0.06, respectively), though week 24 rates were similar across groups. Improvements in pain, fatigue, PsAID, and tender joint counts were observed across all arms (**Fig. 2C-G**). Notably, weight loss magnitude was significantly associated with improvement in clinical outcomes—including DAPSA, pain, fatigue, PsAID, and tender joint count—independent of treatment group (**Fig. 3**).

Conclusion: Both personalized dietary interventions and standard dietary advice led to modest weight loss and improvements in PsA disease activity. The degree of weight loss, rather than the specific dietary strategy, was the primary determinant of clinical benefit.

Disclosure: L. Eder: AbbVie, 1, 2, 5, 6, BMS, 1, 2, Eli Lilly, 1, 2, 5, 6, Fresenius Kabi, 1, 5, J&J, 1, 2, 5, Janssen, 1, 5, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, UCB, 1, 2, 5; **S. Shahab**: None; **S. Hopkins Gillespie**: None; **L. Bumbulis**: None; **H. Emanoilidis**: None; **C. Compher**: None; **J. Scher**: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **R. Cook**: None; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **A. Ogdie**: AbbVie, 5, Amgen, 5, 11, Bristol Myers Squibb, 5, Celgene, 5, CorEvitas, 2, Eli Lilly, 5, Novartis, 5, 11, Pfizer, 5, 11.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2691

Understanding the Impact of Overweight and Obesity on Treatment Response in Psoriatic Arthritis: Results from a Longitudinal Cohort Study

Pankti Mehta[1], Mu Yang[2], Virginia Carrizo Abarza[3], Fadi Kharouf[4], Richard Cook[2], Dafna D. Gladman[5], Vinod Chandran[6] and Denis Poddubnyy[7], [1]University of Toronto, Gladman Krembil Psoriatic Arthritis Research Program, Toronto, ON, Canada, [2]University of Waterloo, Waterloo, Canada, [3]University of Toronto, Toronto, [4]University Health Network and University of Toronto, Toronto, ON, Canada, Toronto, ON, Canada, [5]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Division of Rheumatology, Toronto, ON, Canada, [6]University of Toronto, Toronto, ON, Canada, [7]Division of Rheumatology, Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada, and Department of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Berlin, Germany; Department of Epidemiology, German Rheumatism Research Centre, Berlin, Germany

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions (2687–2692)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Overweight and obesity is associated with poor outcomes in Psoriatic Arthritis (PsA), with reduced odds of achieving minimal disease activity (MDA). Whether this effect is mediated by direct inflammation or psychosocial factors such as pain perception and mood remains unclear. This study aimed to assess the influence of body mass index (BMI) on components of treatment response in patients with PsA.

Methods: Patients with available body mass index (BMI) values were selected from a large longitudinally assessed PsA cohort followed from 1978. These patients are followed every six months with comprehensive documentation of demographic data, clinical and patient-reported outcomes, and treatment details.

Generalized estimating equations (GEE) were used to assess the association of BMI with MDA and its subcomponents, adjusting for age, sex, anxiety, depression, fibromyalgia, smoking, radiographic damage (modified Steinbrocker score), and use of TNFi and PDE4i.

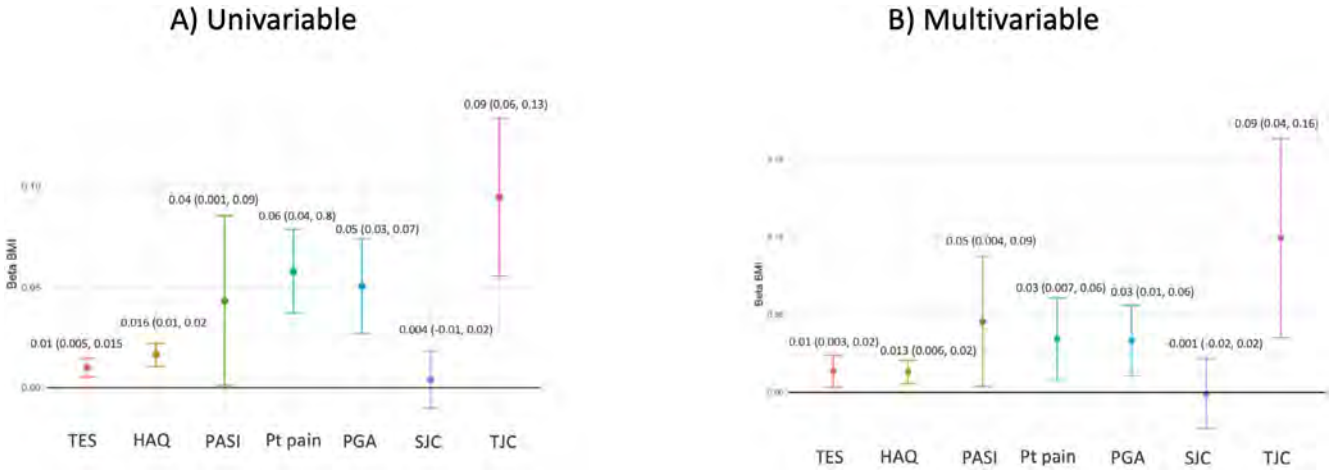


Figure 1: Association of BMI with components of MDA *TES: total entheseal score, HAQ- Health Assessment Questionnaire, Pt- patient, PGA- Patient Global Assessment, SJC_ Swollen Joint Count, TJC- Tender Joint Count

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

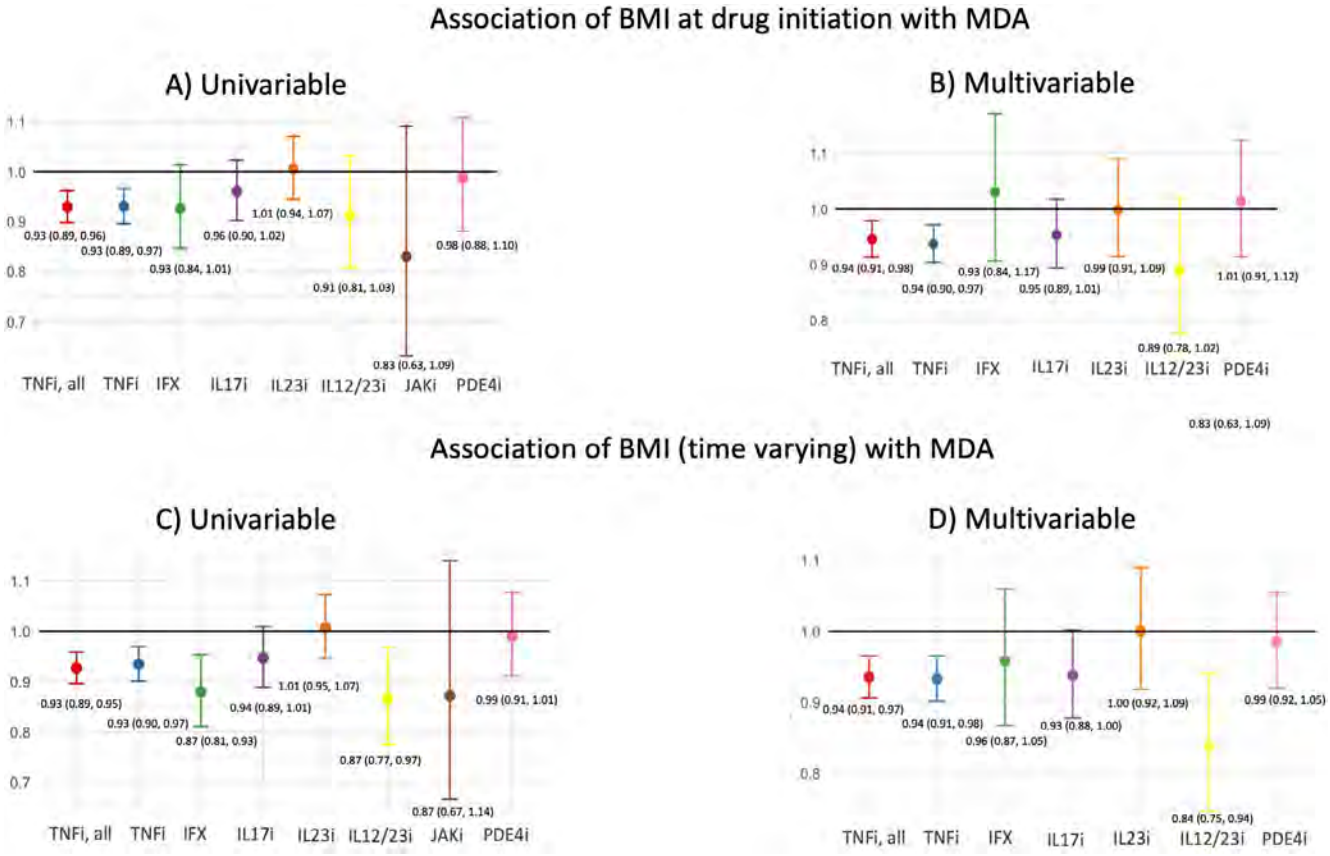


Figure 2: Drug-stratified analyses of BMI at drug initiation and BMI as a time time-varying variable with MDA *TNFi- Tumor Necrosis Factor, i- inhibitor, IL-interleukin, JAK- Janus Kinase, PDE4-Phosphodiesterase 4

We also evaluated the effect of baseline BMI at drug initiation and time-varying BMI (to incorporate effects of drugs on BMI) on treatment response across six drug classes (TNFi, IL-17i, IL-23i, IL-12/23i, JAKi, PDE4i) using univariable and multivariable GEE. The multivariable model was adjusted for age, sex, anxiety, depression, fibromyalgia, smoking, radiographic damage (modified Steinbrocker score), and line of treatment. Missing data were addressed using multiple imputation (MICE).

Results: Of 1291 patients included, the mean age was 44.9 (SD 13.3) years, and 55% were males. The mean BMI was 28.8 (SD 6.34) kg/m2. 428 patients received b- and/or tsDMARDs (40 patients - infliximab, 288 - other TNFis, 113 - IL17i, 36 - IL12/23i, 43 - IL23i, 14 - JAKi, and 30 - PDE4i).

Higher BMI was significantly associated with lower odds of achieving MDA [OR 0.95; 95% CI 0.94–0.97], and worse outcomes across multiple MDA subcomponents, including enthesitis, tender joint count, PASI, patient pain, global assessments, and HAQ, but not swollen joint count (Figure 1).

This association was sustained in the multivariable GEE analyses with reduced odds for MDA with increasing BMI [OR 0.96 (0.93-0.98) with similar effects on the subcomponents (Figure 1).

In drug stratified analyses, BMI at drug initiation was significantly associated with reduced MDA [0.93 (0.89-0.97)] in the TNFi group, and TNFi group excluding infliximab [0.93 (0.89-0.97)]. BMI did not impact the response across other drug groups. This association was sustained also in the multivariable analyses (Figure 2).

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Obesity is independently associated with poorer treatment outcomes and reduced odds of achieving MDA in PsA, largely driven by subjective and skin-related domains. The impact appears most pronounced among patients treated with TNFis. These findings highlight the need for tailored therapeutic strategies in obese PsA patients and the potential importance of addressing psychosocial factors and weight management in clinical care.

Disclosure: P. Mehta: None; **M. Yang**: None; **V. Carrizo Abarza**: None; **F. Kharouf**: None; **R. Cook**: None; **D. Gladman**: AbbVie, 2, 5, Amgen, 2, 5, AstraZeneca, 2, BMS, 2, 5, Eli Lilly, 2, 5, Janssen, 5, Johnson & Johnson, 2, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, UCB, 2, 5; **V. Chandran**: AbbVie/Abbott, 1, 5, AstraZeneca, 12, Spousal employment, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, 5, Fresenius Kabi, 2, Janssen, 1, 5, 6, Novartis, 1, UCB, 1; **D. Poddubnyy**: AbbVie, 2, 5, 6, Biocad, 2, BMS, 6, Eli Lilly, 2, 5, 6, Gilead, 2, GSK, 2, Moonlake, 2, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 6, UCB, 2, 6.

Abstract Number: 2692

Individualized Strength, Mobility and Aerobic Rehabilitation Training in axial Spondyloarthritis (iSMART in axSpA)

Sophie De Mits[1], Tine Willems[2], Lieven Danneels[2], Patrick Calders[2], Gaëlle Varkas[3], Filip Van den Bosch[4], Dirk Elewaut[5] and Philippe Carron[6], [1]Ghent University Hospital, Gent, Belgium, [2]Ghent University, Gent, Belgium, [3]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium, [4]Department of Internal Medicine and Pediatrics, Ghent University and VIB Center for Inflammation Research, Ghent, Belgium, [5]VIB Center for Inflammation Research, and Ghent University Hospital, Department of Rheumatology, Ghent, Belgium, [6]Ghent University and VIB Center for Inflammation Research, Ghent, Belgium

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Pathogenesis, Exercise, and Dietary Interventions (2687–2692)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: AxSpA primarily affects the sacroiliac joints and spine, reducing trunk strength, mobility, and cardiorespiratory fitness. While exercise is a key treatment, few studies have examined combined trunk mobility and strength training with cardiorespiratory training. This prospective interventional study assessed the benefits of a combined and personalized exercise intervention based on baseline physical tests.

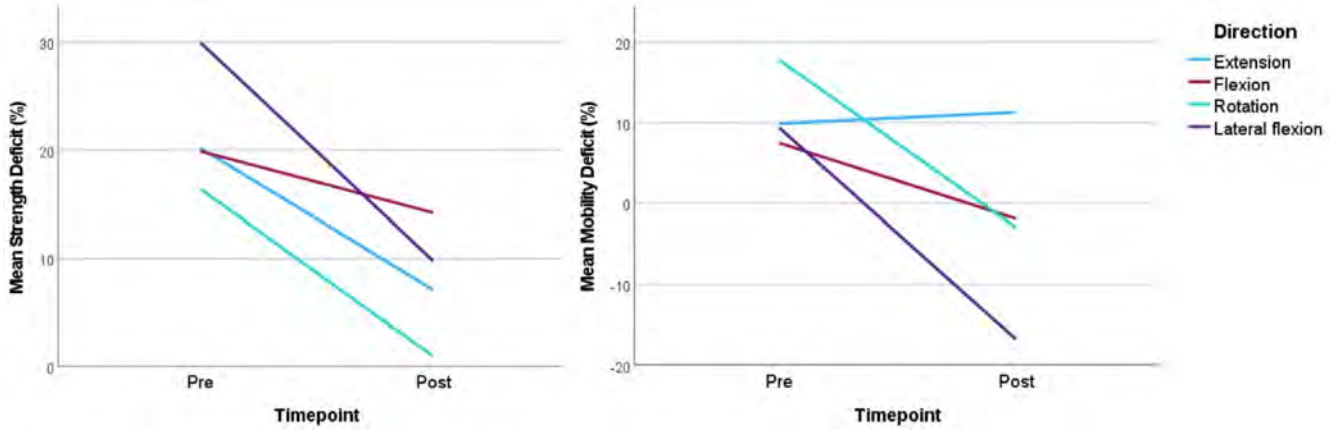


Fig.1: Mean strength (A) and mobility (B) deficit before and after the training program for the different directions.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: cardiorespiratory parameters before and after intervention

	Pre		Post		Estimated time effect		
	Mean	SD	Mean	SD	Mean	95% CI	p-value
anaerobic threshold, % (VO2VT1/VO2pred)	58.1	17.7	72.2	21.6	13.81	5.40 – 22.23	0.002
oxygen pulse, % (VO2/HR)	12.9	3.5	14.4	3.4	1.39	0.48 – 2.31	0.004
ventilatory efficiency (VE/VCO2)	24.7	2.5	26.4	2.5	1.65	0.82 – 2.47	<0.001
respiratory condition, % (PeakVO2/VO2pred)	94.8	22.2	103	25.7	8.37	-2.63 – 19.36	0.13
mechanical efficiency (T2VE-T1VE)/(T2VCO2-T1VCO2)	25.9	3.5	25.5	13.6	1.09	0.18-2.00	0.021

Table 2: clinical parameters before and after intervention

	Pre		Post		Estimated time effect		
	Mean	SD	Mean	SD	Mean	95% CI	p-value
BASFI-score	2.8	2.2	2.4	2.1	-0.448	-0.974 – 0.079	0.092
BASDAI-score	3.5	2.1	2.9	2.2	-0.579	-1.066 – -0.092	0.021
Total BASMI score	2.0	1.1	1.8	1.0	-0.285	-0.574 – 0.004	0.053
Chest expansion	4.5	1.9	5	2.1	0.586	-0.060 – 1.231	0.073

Methods: Participants with AxSpA completed a baseline maximal Cardiopulmonary Exercise Test (CPET) and trunk strength/mobility tests using David Back Concept (DBC) devices. Strength and mobility deficits were calculated as: (Reference – Patient value) × 100 / Reference. BASDAI, BASFI, BASMI, and chest expansion (CE) were registered pre- and post-intervention. The 8-week program consists of two weekly sessions of two 10-minute intervals of cardiorespiratory training at a set heart rate (HR), followed by DBC device exercises. Cardiorespiratory intensity was based on ventilatory threshold 1 (VT1) and monitored via a Polar HR device. Trunk training focused on mobility and resistance using each patient's one-repetition-maximum and maximal range of motion at baseline. All sessions were supervised to ensure correct execution and safety. Post-intervention, CPET and DBC tests were repeated. Linear mixed models analyzed changes over time.

Results: Thirty axSpA patients (14M/16F, age 42±11.2 years; BASDAI 3.5±2.1, BASFI 2.8±2.2, BASMI 2.0±1.1, CE 4.5 ±2.0 cm) participated; 2 patients were lost to follow-up (1: flare, 2: personal reasons). Strength increased on average by 14.1% ($p< 0.001$), and mobility improved by 14.9% ($p< 0.001$) on average, with significant time and direction effects.(See Fig.1) Cardiorespiratory parameters improved significantly: oxygen pulse ($p=0.004$), ventilatory efficiency ($p< 0.001$), anaerobic threshold ($p=0.002$), and mechanical efficiency ($p=0.021$), but not efficiency slope ($p=0.888$). (See Table 1) BASDAI (2.9 ±2.2, $p=0.021$) and CE (5.0±2.1 cm, $p=0.020$) showed significant improvement, while BASMI (1.8±1.0, $p=0.053$) showed a borderline significant decrease and BASFI (2.4±2.1, $p=0.092$) did not differ significantly. (See Table 2)

Conclusion: A combined, individually tailored exercise program, dependent on baseline objectively measured physical parameters, significantly improved cardiorespiratory fitness, trunk strength, and mobility in AxSpA patients. These results support the role of individualized exercise interventions in enhancing patient outcomes and reducing functional limitations.

Disclosure: S. De Mits: None; **T. Willems**: None; **L. Danneels**: None; **P. Calders**: None; **G. Varkas**: AbbVie, 2, 5, 6, Amgen, 2, 6, Celltrion, 2, 5, 6, EG, 5, Eli Lilly, 2, 6, Galapagos, 2, 5, 6, Janssen, 2, 6, MSD, 5, Novartis, 2, 6, Pfizer, 2, 5, 6, Takeda, 5, UCB, 2, 6; **F. Van den Bosch**: AbbVie, 2, 6, Alfasigma, 2, Amgen, 2, 6, Eli Lilly, 2, Galapagos, 2, Grey Wolf Therapeutics, 2, Janssen, 2, 6, Merck, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **D. Elewaut**: AbbVie, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Novartis, 2, 6, UCB, 2, 6; **P. Carron**: AbbVie/Abbott, 2, 6, Alfasigma, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Eli Lilly, 2, 6, Johnson & Johnson, 2, 6, Novartis, 2, 6, UCB, 2, 6.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2693

CAR T-cell Therapy in SLE: A Systematic Review

Alberto Nordmann-Gomes[1], Leila Khalili[2], Wei Tang[3], Laura Geraldino-Pardilla[4], Yevgeniya Gartshteyn[5], Robert Clancy[4], Stephen Suh[6], Maya Souvignier[6], Michel Sadelain[6] and Anca Askanase[2], [1]Columbia University Irving Medical Center, New York, NY, [2]Columbia University Medical Center, New York, NY, [3]Westchester Medical Center, Valhalla, NY, [4]Columbia University, New York, NY, [5]Columbia University Medical Center, Glen Rock, NJ, [6]Columbia University Irving Medical Center, New York City, NY

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment II (2693–2698)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: CAR T-cell therapy is poised to revolutionize the treatment of systemic lupus erythematosus (SLE). Recently, several authors have reported their experience using CAR T-cell therapy for patients with SLE; nonetheless, all studies are limited by a reduced sample size. Here, we review and summarize the available clinical evidence published or presented to date on the use of CAR therapy in SLE.

Methods: We conducted a systematic review to evaluate all clinical studies assessing safety and efficacy outcomes of CAR therapy in SLE. MEDLINE (PubMed), Embase, Scopus, and CENTRAL were consulted, as well as the ACR Convergence 2024 Archives.

Results: The search strategy yielded 4,943 results, of which 14 studies were included in the analysis (including 8 from the consulted databases and 6 from the 2024 ACR Archives). The studies had a combined population of 98 participants. All studies included patients with refractory and active SLE who had failed at least 2 immunosuppressive therapies. Most studies (n=12 [85%]) used a CD19-targetted CAR, with only 2 groups (15%) assessing bispecific CD19-BCMA CAR T-cells. Two studies (15%) evaluated allogeneic CAR products. All groups reported successful B-cell depletion, typically achieved within 1–3 weeks, and B-cell reconstitution was observed after 2-3 months by most groups. Pooled analysis of the 63 individual SLEDAI scores available showed a median decrease in SLEDAI of 6 points (IQR: 3.5 - 8.5) at month 1, 8 points (IQR: 6 -

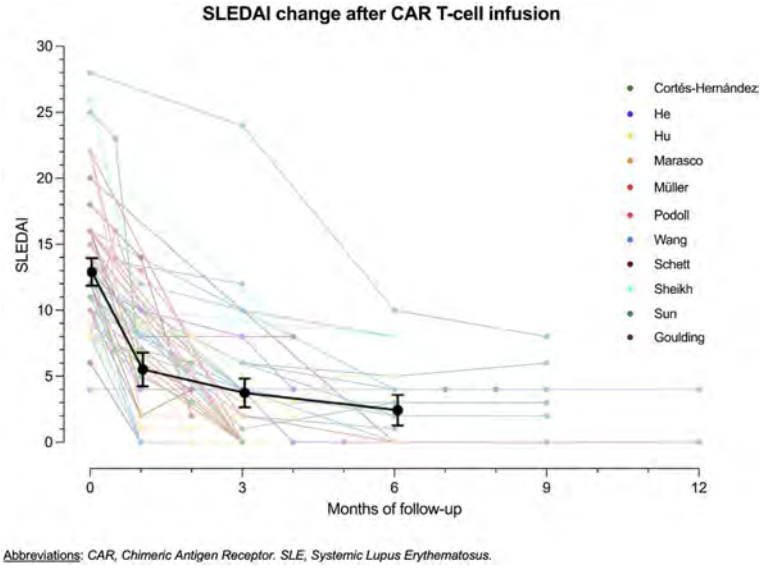


Figure 1. SLEDAI reduction in studies evaluating CAR T-cell therapy in patients with SLE

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

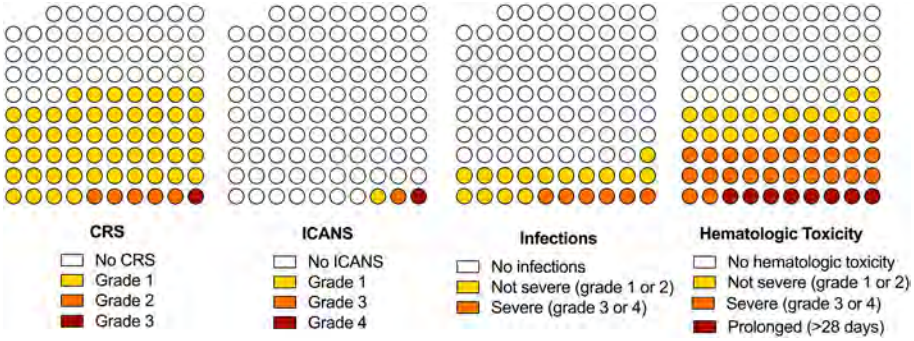


Figure 2. Safety outcomes of CAR T-cell therapy in patients with SLE

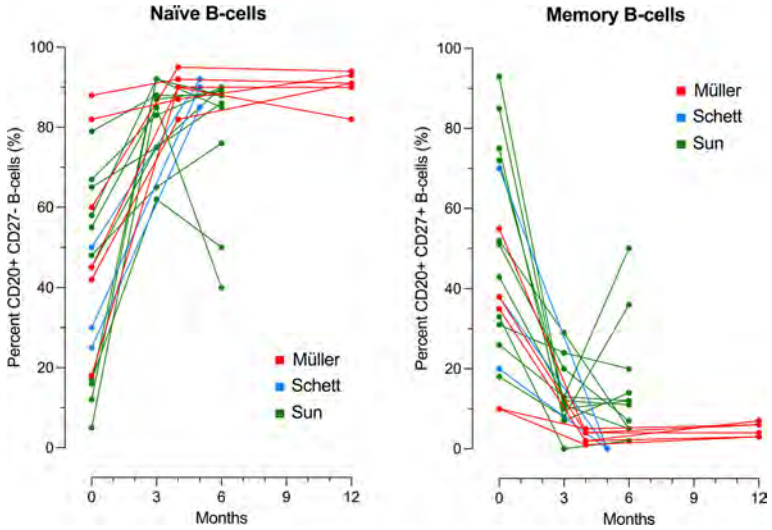


Figure 3. B-cell phenotypes after CAR T-cell infusion in patients with SLE

9.3) at month 3, and 8 points (IQR: 6 - 12) at month 6. The mean baseline SLEDAI of 12.8 (95% CI 11.7-13.8) decreased to 3.6 (95% CI 2.5-4.7), and 2.3 (95% CI 1.1-3.5) after 3 and 6 months; respectively. Thirty-one (48%) patients had a SLEDAI score of 0 at their last follow-up, and 59 (91%) had a score of 4 or less. There was no difference in efficacy between autologous vs allogeneic products, or between CD19-targeted vs CD19- and BCMA-targeted therapies. Cytokine release syndrome (CRS) occurred in 56 (57%) participants, of which 50 (89%) were grade 1, 5 (9%) grade 2, and 1 (2%) grade 3. Immune effector cell-associated neurotoxicity syndrome (ICANS) was reported in 3 patients (3%), 1 grade 1, 1 grade 3, and 1 grade 4. Twenty-one patients (21%) developed infections, of which six (28%) were severe. Severe (grade 3 or 4) and prolonged (>28 days) hematologic toxicity was observed in 17 (17%) and 8 (8%) patients; respectively. Among the 5 studies analyzing B-cell phenotypes, all reported a marked increase in naïve B-cell populations (CD20+, CD27–) alongside a significant reduction in memory B-cells (CD20+, CD27+). Among the 40 patients in which serum biomarkers were measured, anti-dsDNA levels decreased in 36 (90%) patients and normalized in 29 (73%). Complement levels normalized in 37 (93%) patients.

Conclusion: This systematic review showed consistent efficacy with decrease in SLEDAI from 12.8 at baseline to 2.3 at 6 months after CAR T-cell. CRS and ICANS were milder and less frequent than expected from oncology data. The findings further support the efficacy and safety of this treatment modality while highlighting the need for additional research to better define its role in SLE management.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosure: A. Nordmann-Gomes: None; **L. Khalili**: None; **W. Tang**: None; **L. Geraldino-Pardilla**: Aurinia, 2, 6, Bristol-Myers Squibb(BMS), 1, 2, 6; **Y. Gartshteyn**: None; **R. Clancy**: None; **S. Suh**: None; **M. Souvignier**: None; **M. Sadelain**: Alaya.bio, 5, Atara biotherapeutics, 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company, Bristol-Myers Squibb(BMS), 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company, Celgene, 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company, Fate Therapeutics, 5, Juno, 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company, Minerva biotechnologies, 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company, Senescea, 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company, Takeda pharmaceuticals, 12, Memorial Sloan Kettering Cancer Center has licensed Sadelain lab CAR technologies to this company; **A. Askanase**: AbbVie, 2, Amgen, 2, 5, AstraZeneca, 2, 5, Aurinia, 2, 5, BMS, 2, 5, Eli Lilly, 5, Genentech, 2, 5, GSK, 2, 5, Idorsia, 2, 5, Janssen, 2, NKARTA, 5, Pfizer, 2, Sanofi, 5, UCB, 2, 5.

Abstract Number: 2694

Effect of Deucravacitinib Treatment on Renal Dysfunction–Associated Plasma Biomarkers From a Phase 2 Study in Patients With Systemic Lupus Erythematosus

Amit Saxena[1], Chun Wu[2], Brad Rovin[3], Zahi Touma[4], Xueer Chen[5], Ilias Kouris[6] and Jinqi Liu[5], [1]Division of Rheumatology, Department of Medicine, NYU Grossman School of Medicine, New York, NY, [2]Bristol Myers Squibb, Princeton, [3]The Ohio State University, Columbus, OH, [4]University of Toronto, Toronto, ON, Canada, [5]Bristol Myers Squibb, Princeton, NJ, [6]Bristol Myers Squibb, Boudry, Switzerland

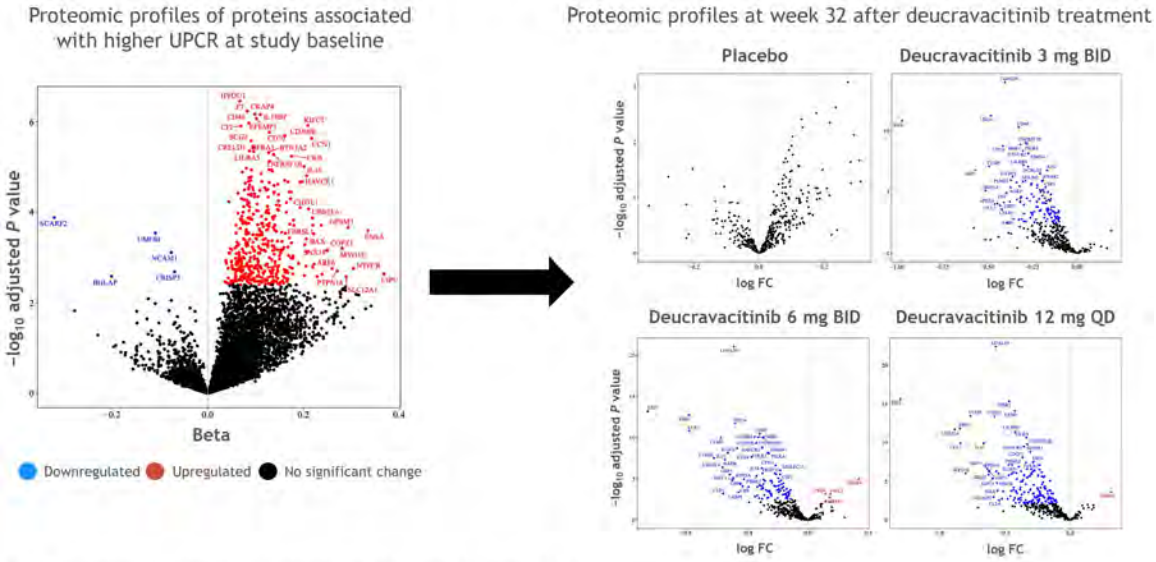
SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment II (2693–2698)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Plasma biomarkers may play a role in understanding kidney health in patients with lupus, particularly in terms of early detection of lupus nephritis (LN), monitoring for disease progression, and predicting treatment responses. Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor that has shown clinical efficacy in the 48-week, double-blind, placebo-controlled, phase 2 PAISLEY SLE study (NCT03252587).[1] In this post hoc analysis, we investigated circulating proteins associated with kidney dysfunction at baseline (BL) by analyzing proteomic profiles of patients with higher BILAG renal scores and urine protein-to-creatinine ratios (UPCRs) in PAISLEY SLE and assessed the impact of deucravacitinib on these biomarkers throughout the course of the study.

Methods: Patients with SLE were randomized 1:1:1:1 to placebo (n = 90) or deucravacitinib 3 mg twice daily (BID; n = 91), 6 mg BID (n = 93), or 12 mg once daily (n = 89). Proteomic profiles of 1187 clinical samples, collected longitudinally from 351 patients at BL and 268 patients at W12, W32, and W48, were evaluated using Olink Explore HT assays. Using DREAM, genome-wide statistical analyses were conducted to identify differentially expressed proteins associated with a higher BILAG renal score and UPCR at BL and W32. Pharmacodynamics in the intent-to-treat population were analyzed using linear mixed-effects models adjusted for stratum and batch. Pathway enrichment analyses using the Gene Ontology database identified biological pathways that were significantly represented among differentially expressed proteins. Protein biomarkers associated with low estimated glomerular filtration rate (eGFR) identified at BL in the phase 3 abatacept LN study (NCT01714817) were also evaluated for changes throughout the PAISLEY SLE study.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Identification of dysregulated plasma proteins associated with higher UPCR at baseline and the effects of deucravacitinib treatment at week 32 for patients treated in the phase 2 PAISLEY SLE study



Cutoff criteria at BL and week 32 were determined by an adjusted $P < 0.05$.
BID, twice daily; BL, baseline; FC, fold change; QD, once daily; UPCR, urine protein-to-creatinine ratio.

Figure 1. B-cell phenotypes after CAR T-cell infusion in patients with SLE

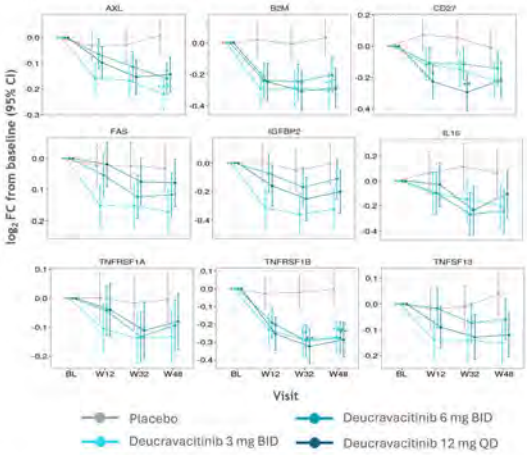
Results: Plasma proteins significantly associated with higher BILAG renal scores (n = 72) or UPCR (n = 420) were identified; pathway analyses indicated dysregulated immune responses, including leukocyte activation, cytokine production, and cell adhesion regulation. At W32, deucravacitinib vs placebo significantly reduced expression of several biomarkers (eg, CD27, AXL, EPHB6, IL-18BP) associated with higher BILAG renal domain score at BL. Similarly, deucravacitinib significantly

Figure 2. Biomarkers associated with abnormal eGFR at baseline in the abatacept phase 3 lupus nephritis study and effects of deucravacitinib treatment on these biomarkers in patients treated in the phase 2 PAISLEY SLE study

Biomarkers associated with abnormal eGFR in patients with LN treated in the abatacept phase 3 trial (NCT01714817)

Analyte	eGFR ρ	eGFR adj *P*	Analyte	eGFR ρ	eGFR adj *P*
CD40	−0.6073	1.10E-23	TRAIL_R3	−0.2775	3.30E-05
Myoglobin	−0.5599	3.30E-19	TNFa	−0.2675	6.80E-05
TNFRI	−0.542	4.10E-18	MMP_10	−0.2593	0.00012
SCF	−0.5098	7.70E-16	Gelsolin	−0.2539	0.00018
FAS	−0.492	5.70E-15	YKL_40	−0.2546	0.00018
B2M	−0.491	1.30E-14	AXL	−0.2503	0.00019
APRIL	−0.469	1.50E-13			
MMP_7	−0.4629	2.70E-13			
CD27	−0.4084	2.80E-10			
Angiogenin	−0.3805	8.20E-09			
IGFBP_7	−0.3666	2.40E-08			
TNFR2	−0.3692	2.60E-08			
OPG	−0.3266	1.20E-06			
HCC_4	−0.3202	1.50E-06			
MPIF_1	−0.3106	3.70E-06			
IL_16	−0.2892	2.00E-05			
PGI	−0.289	2.00E-05			
MIG	−0.2836	2.40E-05			
IGFBP_2	−0.284	3.00E-05			

Reduction of representative LN-relevant biomarkers with deucravacitinib treatment in the phase 2 PAISLEY SLE study



Analytes with eGFR ρ > 0.25 and adjusted $P < 0.05$ are shown. The BH method was used to correct for multiple comparisons for *P* values.
*Adjusted $P < 0.05$; **Adjusted $P < 0.01$; ***Adjusted $P < 0.001$ vs placebo; error bars denote the 95% CI.
BH, Benjamini-Hochberg; BID, twice daily; eGFR, estimated glomerular filtration rate; FC, fold change; LN, lupus nephritis; QD, once daily; SLE, systemic lupus erythematosus; W, week.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

reduced expression of biomarkers associated with increasing UPCR at W32 vs placebo (**Figure 1**). Furthermore, biomarkers negatively associated with eGFR in the abatacept LN study were reduced with deucravacitinib vs placebo (**Figure 2**).

Conclusion: Deucravacitinib treatment demonstrated significant reduction of proteins associated with renal dysfunction in patients treated in the PAISLEY SLE study. Further investigation of the effects of deucravacitinib on renal biomarkers and attenuation of renal disease progression in the phase 3 POETYK SLE-1 and SLE-2 studies is warranted.

Reference:

1. Morand E, et al. *Arthritis Rheumatol* 2023;75:242–252.

Disclosure: A. Saxena: AbbVie, 1, Amgen, 1, AstraZeneca, 1, Aurinia, 1, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Genentech, 1, GSK, 1, Kezar Life Sciences, 1, Synthekine, 1, UCB, 2, 5; **C. Wu**: Bristol Myers Squibb, 3, 11; **B. Rovin**: Alexion, 2, Artiva, 2, 11, AstraZeneca, 2, Aurinia, 2, 5, Biogen, 2, 5, Bristol Myers Squibb, 2, Cabelleta, 2, Century, 2, F. Hoffman-La Roche Ltd/Genentech, Inc., 2, GlaxoSmithKlein(GSK), 2, Novartis, 2; **Z. Touma**: AbbVie, 2, AstraZeneca, 1, 2, 5, GSK, 2, 5, Merck KgaA, 2, Novartis, 1, Roche, 2, Sarkana Pharma Inc, 2, UCB/Biopharma, 1, 2; **X. Chen**: Bristol Myers Squibb, 3, 11; **I. Kouris**: Bristol Myers Squibb, 3, 11; **J. Liu**: Bristol-Myers Squibb (BMS), 3, 11.

Abstract Number: 2695

B-cell depletion and lymphoid follicle disruption upon different B-cell depleting agents

Carlo Tur[1], Markus Eckstein[2], Laura Bucci[1], Janina Auth[3], Christina Bergmann[1], Simon Rauber[4], Melanie Hagen[1], Danae-Mona Nöthling[1], Sebastian Böltz[1], Andreas Wirsching[1], Filippo Fagni[5], Giulia Corte[6], Panagiotis Garantziotis[1], Jule Taubmann[7], jochen wacker[1], Andreas Ramming[8], Maria Antonietta D'Agostino[9], Arndt Hartmann[10], Fabian Müller[11], Andreas Mackensen[12], Ricardo Grieshaber-Bouyer[13], Georg Schett[14], Aline Bozec[1] and Maria Gabriella Raimondo[1], [1]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [2]Institute of Pathology and Comprehensive Cancer Center EMN, Friedrich-Alexander- Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, [3]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Bayern, Germany, [4]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Bayern, Germany, [5]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Bayern, Germany, [6]-Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Germany, Erlangen, Germany, [7]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-Universität Erlangen-Nürnberg and University Hospital Erlangen, Erlangen, Germany, [8]Department of Internal Medicine 3, Rheumatology & Immunology, Friedrich-Alexander-University (FAU) & Universitätsklinikum Erlangen, Erlangen, Germany, [9]Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [10]Institute of Pathology and Comprehensive Cancer Center EMN, Friedrich-Alexander- Universität (FAU) Erlangen-Nürnberg and Uniklinikum Erlangen, Erlangen, Bayern, Germany, [11]University Hospital of Erlangen, Erlangen, Germany, [12]Department of Medicine 5 - Hematology and Oncology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) and Uniklinikum Erlangen, Erlangen, Germany, [13]University Hospital Erlangen, Erlangen, Germany, [14]Uniklinikum Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment II (2693–2698)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Advanced protein-based therapies targeting B-cells, including glycoengineered CD20 monoclonal antibody obinutuzumab (OBI) and the CD19/CD3 T-cell engager blinatumumab (BLI), show promise for managing severe autoimmune diseases (AIDs). These innovative agents are believed to offer more effective B-cell depletion compared to rituximab (RTX), potentially enabling the elimination of B-cells within affected tissues.

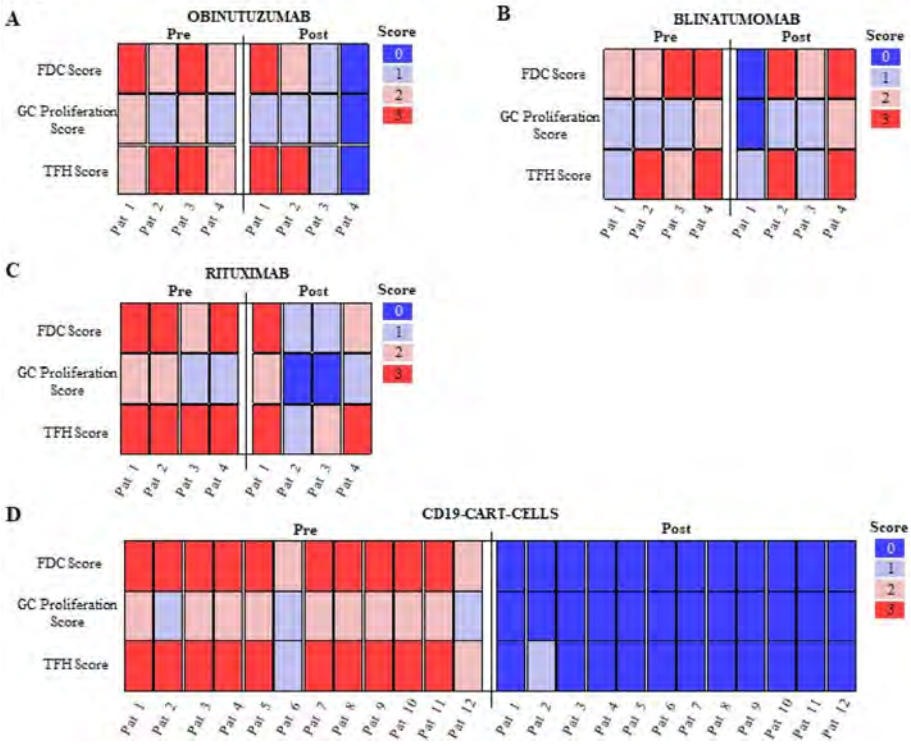
Methods: We performed sequential US-guided inguinal lymph node (LN) biopsies before and after OBI-, BLI-, RTX- and CD19 chimeric antigen receptor T-cell treatment (CAR) in AID patients. Immunohistochemistry (IHC) staining was performed to quantify the number of B cells, plasma cells, follicular dendritic cells (FDCs), follicular T helper cells (TFH), proliferating germinal centre B cells, T cells and macrophages.

Results: Baseline and follow-up LN biopsies from 24 AID patients (7 SLE, 7 SSc, 4 Idiopathic Inflammatory Myositis [IIM], 6 RA) were analysed. Four patients received OBI (3 SLE, 1 IIM), 4 BLI (4 RA), 4 RTX (2 IIM, 2 RA) and 12 CAR (4 SLE, 7 SSc, 1 IIM).

Peripheral blood B-cell depletion occurred in all but one BLI-treated patient.

IHC quantification of B cells in LNs by CD19 and CD20 staining was performed. In all 12 CAR-treated patients, B cells were completely depleted (p-value for CD19+ and CD20+ cell before vs after CAR = 0.0005). In contrast, in all but one (OBI-treated) patients, B cells were not depleted. OBI showed robust (CD20+: -92%; CD19+: -96%) LN reduction of B-cells. Reduction was less pronounced in BLI-treated patients (CD20+: -69%; CD19+: -47%) and RTX- treated patients (CD20+: -86%; CD19+: -86%). CD138+ plasmablast/plasma depletion was incomplete across all treatments: CAR -59%, OBI -54%, RTX -32% and BLI -7%.

Figure 1



Heatmap scoring of follicular dendritic cell (FDC) score, germinal centre proliferation score (GC proliferation score) and the T follicular helper cell score (TFH score) for each treatment.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Changes in the follicular structure in the LNs were also assessed, including the number of CD23+ FDCs, PD-1+ TFH cells and the proliferation rate in the follicles (Ki67+) before and after treatment. These data were integrated into a combined B-cell compartment architecture score (score range 0 – 9). In all CAR-treated patients the follicular LN architecture was completely disrupted (median B-cell compartment score post-treatment [IQR]: 0.0 [0 – 0]). Among patients treated with protein-based B-cell depleting agents, only one (OBI-treated) exhibited dissolution of the follicular architecture in the LNs, while all others retained some degree of follicular structure. In OBI-treated patients the median [IQR] B-cell compartment score was 4.5 [0.75 – 6.75], in the BLI-treated patients 5.5 [1.75 – 7.75] and RTX- treated patients 4.5 [2.25 – 7.5], all showing maintained follicular structures (Figure 1). Neither T-cell nor macrophages numbers were affected by any of the B-cell targeted treatment agents. Complete depletion was associated with stable drug-free remission, while incomplete depletion required re-treatment with immunomodulatory drugs.

Conclusion: Protein-based B-cell depletion reduces but rarely deplete B cells in LNs leaving the follicular architecture intact and being associated with disease recurrence, whereas CAR ensures consistent full B-cell depletion and follicular structural disruption enabling sustained remission.

Disclosure: C. Tur: Sanofi, 2; **M. Eckstein**: None; **L. Bucci**: None; **J. Auth**: None; **C. Bergmann**: Kyverna Therapeutics, Inc., 5; **S. Rauber**: None; **M. Hagen**: None; **D. Nöthling**: None; **S. Böltz**: None; **A. Wirsching**: None; **F. Fagni**: None; **G. Corte**: None; **P. Garantziotis**: None; **J. Taubmann**: None; **j. wacker**: None; **A. Ramming**: Boehringer-Ingelheim, 2, Johnson & Johnson, 2, MoonLake Immunotherapeutics AG, 2, 5, Novartis Pharma GmbH, 2, UCB, 2; **M. D'Agostino**: Bristol-Myers Squibb(BMS), 5; **A. Hartmann**: None; **F. Müller**: AbbVie/Abbott, 6, ArgoBIO, 2, AstraZeneca, 2, 6, Beigene, 6, Bristol-Myers Squibb(BMS), 2, 5, 6, CRISPR Therapeutics, 2, EcoR1, 2, Incyte, 6, Janssen, 2, 6, Kite/Gilead, 2, 5, 6, Merck/MSD, 6, Miltenyi, 2, 6, Novartis, 2, 6, Pfizer, 6, Sobi, 2, 6, Takeda, 6; **A. Mackensen**: None; **R. Grieshaber-Bouyer**: AstraZeneca, 1, Candid Therapeutics, 1, Cullinan Therapeutics, 1, Eli Lilly, 6; **G. Schett**: Cabaletta, 6, Eli Lilly, 6, Janssen, 6, Kyverna, 6, Novartis, 6, UCB, 6; **A. Bozec**: None; **M. Raimondo**: UCB, 6.

Abstract Number: 2696

Biomarker Data From an Open-Label, Phase 1/2 Study for YTB323 (Rapcabtagene Autoleucel, a Rapidly Manufactured CD19 CAR-T Therapy) Suggest Reset of the B Cell Compartment in Severe Refractory SLE

Eric Morand[1], Josefina Cortés-Hernández[2], Zahir AMOURA[3], Julia Weinmann-Menke[4], Britta Maurer[5], Edouard Forcade[6], Stephanie Finzel[7], Jose Alvaro-Gracia[8], Marc Scherlinger[9], Alberta Hoi[10], Yannick Muller[11], Rangi Kandane-Rathnayake[12], Ozana Fischer[13], Beata Kovacs[13], Frédérique Chaperon[13], David Pearson[13], Adrienne Lefeber[14], Chih-Yung Sean Lee[14], Jianping Yuan[14], Vassilis Bitsikas[13], Aditya Mahadevan Iyer[15], Theodoulos Rodosthenous[16], Melissa Fernandes[13], Thomas Calzascia[13], Richard Siegel[13], Peter Gergely[13] and Tamas Shisha[13], [1]Centre for Inflammatory Diseases, Monash University and Monash Health, Melbourne, Victoria, Australia, [2]Hospital Universitari Vall d'Hebron-Universitat Autónoma de Barcelona, Barcelona, Spain, [3]APHP, Paris, France, [4]Department of Nephrology and Rheumatology and Center of Immunotherapy, Medical Center of the Johannes Gutenberg University, Mainz, Germany, [5]Department of Rheumatology & Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [6]CNRS-UMR 5164 Immuno ConcEpT, Bordeaux University and Service d'Hématologie Clinique et Thérapie Cellulaire, CHU Bordeaux, F-33000, Bordeaux, France, [7]Department of Rheumatology and Clinical Immunology, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, [8]Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Department of Rheumatology, Hospital General Universitario Gregorio Marañón and Faculty of Medicine, Complutense University of Madrid, Madrid, Spain, [9]Department of Rheumatology, Hopitaux Universitaires de Strasbourg, Centre National de Référence RESO, Strasbourg, France, [10]Centre for Inflammatory Diseases, Monash University and Department of Rheumatology, Monash Health, Clayton, Victoria, Australia, [11]Division of Immunology and Allergy, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, [12]Center for Inflammatory Diseases, Monash University, Clayton, Victoria, Australia, [13]Novartis Biomedical Research, Basel, Switzerland, [14]Novartis Biomedical Research, Cambridge, MA, [15]Novartis Biomedical Research, Hyderabad, India, [16]Novartis Pharmaceuticals UK Ltd, London, United Kingdom

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment II (2693–2698)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Current evidence suggests that B cell depletion through CD19-directed chimeric antigen receptor T cell (CAR-T) therapies may offer promise in improving outcomes in severe refractory systemic lupus erythematosus (srSLE).[1] YTB323 (rapcabtagene autoleucel) is a rapidly manufactured, autologous CD19 CAR-T therapy that is also being investigated in hematological malignancies.[2] Herein, we report interim biomarker data from a phase 1/2 open-label study investigating YTB323 in patients with srSLE.[3]

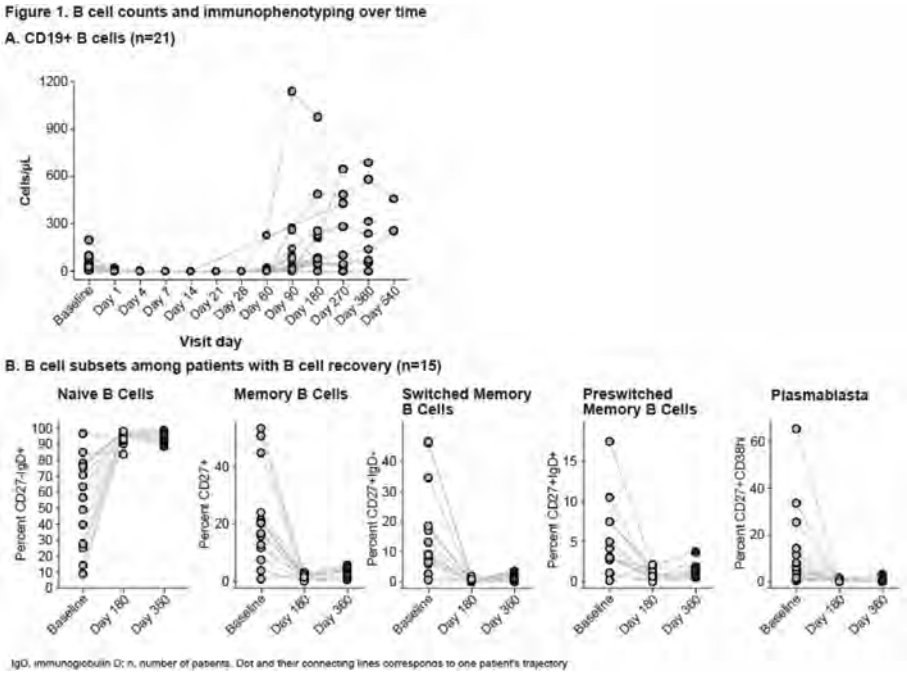
Methods: This ongoing open-label, single-arm, multicenter phase 1/2 study (NCT05798117) assesses the safety, efficacy and cellular kinetics of YTB323 in patients with srSLE (defined as SLE Disease Activity Index 2000 [SLEDAI-2K] ≥8 with major organ involvement, having failed ≥2 standard immunosuppressive therapies and ≥1 biological agent).[3] YTB323 treatment was administered as a single dose of 12.5×10^6 CAR-positive viable T cells, following lymphodepletion. Cellular kinetics, quantified by polymerase chain reaction and flow cytometry, and biomarkers, measured by transcriptome analysis, were assessed. Assessments of B cell counts and B cell subsets after recovery were monitored via flow cytometry.

Table 1. Patient baseline characteristics (n=21)

Age, years, mean (SD)	36.6 (10.60)
Female sex, n (%)	19 (90.5)
SLE duration, years, mean (SD)	13.6 (8.07)
SLEDAI -2K at baseline, mean (SD)	14.1 (5.37)
Duration of follow-up, months, mean (SD)	11.2 (4.50)

n, number of patients; SD, standard deviation; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index 2000

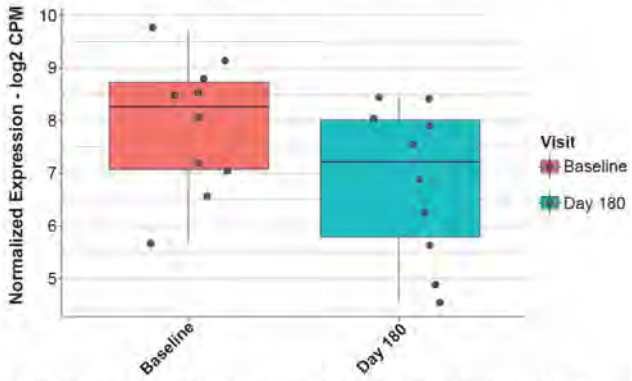
Figure 1. B cell counts and immunophenotyping over time



IgD, immunoglobulin D; n, number of patients. Dot and their connecting lines corresponds to one patient's trajectory

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Changes in type I IFN inducible gene expression (21-IFNGS) after YTB323 treatment, (n=10)



The lower and upper hinges of each box correspond to the first and third quartiles (25th and 75th), respectively; Black horizontal line in each box corresponds to the median 21-IFNGS expression.
The upper whisker extends from the hinge to the largest value no further than 1.5 * IQR from the hinge (where IQR is the inter-quartile range, or distance between the first and third quartiles).
The lower whisker extends from the hinge to the smallest value at most 1.5 * IQR of the hinge.
The individual dots correspond to the median normalized expression of the 21 IFN gene signature.
Each dot corresponds to one patient

CPM, counts per million; FC, fold change; IFN, interferon; IFNGS, interferon gene signature; IQR, interquartile range, n, number of patients

Results: Data from all enrolled patients in the study (n=21) were analyzed. At baseline, mean (standard deviation [SD]) age was 36.6 years (10.6), and 90.5% of patients were female. The mean (SD) duration of follow-up was 11.2 months (4.5; **Table 1**). Cellular kinetics and pharmacodynamics data revealed peak expansion of CAR-T cells (median time to peak concentration [Tmax]) 2 weeks post-infusion and median time of clearance from peripheral blood of 2 months. YTB323 treatment induced a rapid, complete, and sustained depletion of CD19-positive B cells, with subsequent B cell recovery occurring at a median of 90 days post-infusion (**Figure 1A**). Analysis of B cell subsets at days 180 and 360 in patients with B cell recovery (n =15) showed that returning B cells had a predominantly naïve phenotype (CD27-IgD+), with a decrease in the proportion of other B cell subsets (**Figure 1B**). Expression of type I interferon (IFN) inducible genes was downregulated after YTB323 treatment (n =10; **Figure 2**).

Conclusion: Interim biomarker data from this phase 1/2 trial show complete CD19 B cell depletion and IFN pathway suppression, followed by repopulation with a naïve B cell phenotype. These findings support the concept of an immune "reset" of the B cell compartment via CD19 CAR-T therapy in srSLE.

References

1. 1. Müller F et al. *N Eng J Med*. 2024;390(8):687–700.
< ! 2. Barba P et al. Blood. 2022;140(Suppl1):1056–9.
< ! 3. ClinicalTrials.gov. NCT05798117. Accessed April 23, 2025. https://clinicaltrials.gov/study/NCT05798117

Disclosure: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol Meyers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech, 5, GSK, 1, 2, 5, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Quell, 1, 2, 6, Remegen, 1, 2, 6, Takeda, 5, UCB, 1, 2, 5, Zenas, 1, 2, 6; **J. Cortés-Hernández**: AstraZeneca, 6, Bristol-Myers Squibb (BMS), 1, GlaxoSmithKline (GSK), 6, Novartis, 1, 5, 6; **Z. AMOURA**: AstraZeneca, 6, Bristol-Myers Squibb(BMS), 6, GlaxoSmithKlein(GSK), 6, Merck/MSD, 6, Novartis, 6, Roche, 6; **J. Weinmann-Menke**: AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, 6, Diamed, 5, GlaxoSmithKlein(GSK), 2, 6, Miltenyi, 5, Novartis, 2, 6, Otsuka, 2, 6, Takeda, 6, Toray, 5, Vifor, 6; **B. Maurer**: AbbVie/Abbott, 5, Actelion, 12, Congress support, Boehringer-Ingelheim, 1, 5, 6, GlaxoSmithKlein(GSK), 2, Janssen, 2, Medtalk, 12, Congress support, Mepha, 12, Congress support, Merck/MSD, 12, Congress support, Novartis, 2, 5, 6, Otsuka, 6, Pfizer, 12, Congress support, Protogen, 5, Roche, 12, Congress support, UCB, 12, Congress support; **E. Forcade**: Alexion, 6, Astellas, 6, Gilead,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

6, GlaxoSmithKlein(GSK), 6, Jazz, 6, Merck/MSD, 6, Novartis, 6, Sobi, 6; **S. Finzel**: AbbVie/Abbott, 6, Alfasigma/Galapagos, 6, 12, meeting or travel grant, AstraZeneca, 2, Biotest, 6, 12, meeting or travel grant, Celltrion, 6, Chugai, 6, Eli Lilly, 12, meeting or travel grant, GlaxoSmithKlein(GSK), 2, 6, Johnson&Johnson, 2, 6, 12, meeting or travel grant, Novartis, 2, 6, 12, meeting or travel grant, NovoNordisk, 2, Sobi, 12, meeting or travel grant, UCB, 2, 6, 12, meeting or travel grant; **J. Alvaro-Gracia**: AbbVie/Abbott, 2, 6, AstraZeneca, 2, 6, Bristol-Myers Squibb(BMS), 2, 6, Galapagos, 2, 6, GlaxoSmithKlein(GSK), 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **M. Scherlinger**: AbbVie/Abbott, 6, Amgen, 6, AstraZeneca, 6, Biogen, 6, Bristol-Myers Squibb(BMS), 6, Fresenius, 6, Galapagos, 6, GlaxoSmithKlein(GSK), 6, Innate Pharma, 6, Nordic Pharma, 6, Novartis, 6, Roche, 6, Sandoz, 6; **A. Hoi**: AstraZeneca, 1, 5, 12, contract research, Bristol-Myers Squibb(BMS), 5, Eli Lilly, 5, GlaxoSmithKline (GSK), 1, Johnson & Johnson, 1, Merck/MSD, 12, contract research, UCB, 5; **Y. Muller**: AstraZeneca, 1, 5, 6, Blueprint Medicines, 1, 5, 6, GlaxoSmithKlein(GSK), 1, 5, 6, Sanofi, 1, 5, 6, Takeda, 1, 5, 6, Thermofisher, 1, 5, 6, US 2023/0340068 A1, 12, an inventor of a CAR-T licence, Viatris, 1, 5, 6; **R. Kandane-Rathnayake**: Bristol-Myers Squibb(BMS), 5, GlaxoSmithKline (GSK), 5, Novartis, 5; **O. Fischer**: Novartis, 3, 11; **B. Kovacs**: Novartis, 3, 11; **F. Chaperon**: Novartis, 3, 11; **D. Pearson**: Novartis, 3, 11; **A. Lefeber**: Novartis, 3, 11; **C. Sean Lee**: Novartis, 3, 11; **J. Yuan**: Novartis, 3, 11; **V. Bitsikas**: Novartis, 3, 11; **A. Iyer**: Novartis, 3, 11; **T. Rodosthenous**: Novartis, 3, 11; **M. Fernandes**: Novartis, 3, 11; **T. Calzascia**: Novartis, 3, 11; **R. Siegel**: Novartis, 3, 11; **P. Gergely**: Novartis, 3, 11; **T. Shisha**: Novartis, 3, 11.

Abstract Number: 2697

A Prospective Randomized Controlled 96-week Study to Evaluate the Efficacy and Safety of Tacrolimus and Glucocorticoid as Continuous Induction-maintenance Treatment for Class III/IV±V Lupus Nephritis

Sandra Navarra[1], Desmond Yat-Hin Yap[2], Zhaohui Ni[3], Yingyos Avihingsanon[4], Soo Kun Lim[5], Na Jiang[3], Wei Chen[6], Chao Li[7], Helen Zhi[8], Chenzhu Zhang[9], Catherine Chan[2], Susan Yung[2], Tsutomu Takeuchi[10] and Tak Mao Daniel Chan[2], [1]University of Santo Tomas, Manila, Philippines, [2]Department of Medicine, The University of Hong Kong, Hong Kong SAR, Hong Kong, [3]Renji Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, China (People's Republic), [4]King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand, [5]Department of Medicine, University Malaya Medical Centre, Kuala Lumpur, Malaysia, [6]Department of Nephrology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China (People's Republic), [7]Department of Nephrology, Peking Union Medical College Hospital, Beijing, China (People's Republic), [8]School of Public Health, The University of Hong Kong, Hong Kong SAR, Hong Kong, [9]Department of Medicine, University of Hong Kong-Shenzhen Hospital, Shenzhen, China (People's Republic), [10]Saitama Medical University and Keio University, Tokyo, Japan

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment II (2693–2698)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Tacrolimus (TAC) and glucocorticoid as continuous induction-maintenance therapy for lupus nephritis (LN) has never been investigated. We conducted a prospective randomized open-label multicenter study to evaluate its efficacy and safety against standard-of-care mycophenolate mofetil (MMF) and glucocorticoid dual immunosuppression in Asian patients with active severe LN.

Methods: Patients with biopsy-proven Class III/IV±V LN were randomized to receive pulse methylprednisolone (500mg/500mg/150mg) for 3 days followed by oral prednisolone (0.7 mg/kg/day, then taper) in combination with either TAC (initial dose 2 mg bid; target trough level 6-8 ng/mL) or MMF (1 g bid), then followed for 96 weeks. Primary endpoint was sustained renal response (SRR) [defined as proteinuria reduced by $\geq$50% compared with baseline and 24-hr urine protein < 1 g and serum creatinine not higher than 15% above baseline and no disease flare or rescue therapies] at Week 96.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

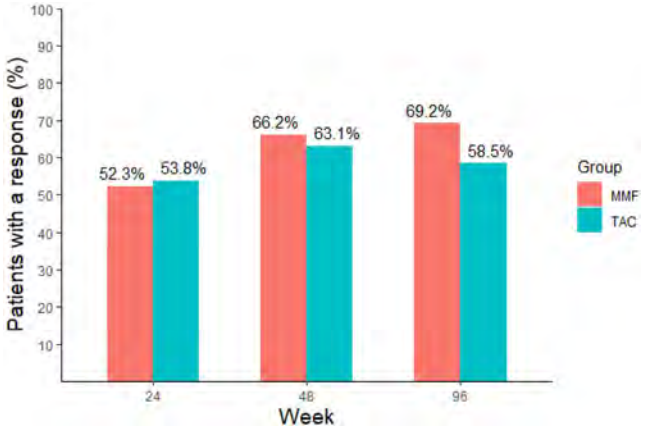


Figure 1. Sustained renal response (SRR) rate in patients with active lupus nephritis treated with tacrolimus (TAC) or mycophenolate mofetil (MMF) in combination with glucocorticoid.

Key secondary endpoints included rates of complete renal response (CR), adverse events, and time-to-renal related adverse events/death.

Results: A total of 130 patients were randomized (65 in each group). TAC and MMF treatment groups showed similar rates of SRR (58.5% vs. 69.2%, OR 0.62; 95% CI 0.29-1.29; p=0.2) and CR (55.4% vs. 63.1%, OR 0.72; p=0.36) at Week 96. SRR rates for TAC and MMF groups were 53.8% vs 52.3% at Week 24, and 63.1% vs. 66.2% at Week 48 respectively (Figure 1). Time-to-renal related adverse events/death were similar in both groups (HR 0.70; 95% CI 0.37-1.35; p=0.29). Overall adverse event rates were 69.2% and 70.8% in TAC and MMF groups respectively (p=1.00), while serious adverse events were more frequent in the MMF group (12.3% vs. 30.8%, p=0.02). Acute kidney injury (16.9% vs. 3.1%) and tremor (16.9% vs. 0%) were more frequent in TAC-treated patients, while leucopoenia (1.5% vs. 12.3%) was more frequent in the MMF group. Three patients in the MMF group died.

Conclusion: Immunosuppressive regimen with TAC combined with glucocorticoid showed comparable efficacy as MMF with glucocorticoid, as continuous induction-maintenance treatment for active LN over 96 weeks, with similar overall adverse event rate but different safety profile between the two treatments.

Disclosure: S. Navarra: Astellas, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, Biogen, 2, 12, Independent Data Monitoring Committee, Viatris (Idorsia), 2, 6; **D. Yap**: None; **Z. Ni**: None; **Y. Avihingsanon**: Astellas, 6, Novartis, 5; **S. Lim**: None; **N. Jiang**: None; **W. Chen**: None; **C. Li**: None; **H. Zhi**: None; **C. Zhang**: None; **C. Chan**: None; **S. Yung**: None; **T. Takeuchi**: AbbVie, 2, 6, Astellas Pharma, 6, AstraZeneca, 6, Chugai Pharmaceutical, 6, Eisai, 6, Eli Lilly, 2, 6, Gilead Sciences, 2, 6, Janssen, 6, Mitsubishi Tanabe Pharma, 2, 6, Pfizer, 6, Taisho Pharmaceutical, 2, 6; **T. Chan**: Astellas Pharm Inc, 5, GlaxoSmithKlein(GSK), 2, Novartis, 2.

Abstract Number: 2698

Comparative Efficacy of Tacrolimus-Based Induction Therapy with and without Mycophenolate Mofetil in Lupus Nephritis: A Target Trial Emulation Study

Yun Kyu Kim[1], Hajeong Lee[2], Jun Won Park[3], Eun Bong Lee[3], You-Jung Ha[4] and Jin Kyun Park[2], [1]Seoul National University, Seoul, Republic of Korea, [2]Seoul National University Hospital, Seoul, Republic of Korea, [3]Seoul National University Hospital, Seoul, South Korea, [4]Seoul National University Bundang Hospital, Seongnam, South Korea

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Systemic Lupus Erythematosus – Treatment II (2693–2698)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: The efficacy of calcineurin inhibitors in the induction treatment of lupus nephritis (LN) has been increasingly supported by recent studies. Based on these findings, current guidelines recommend a combination of tacrolimus (TAC), mycophenolate mofetil (MMF), and glucocorticoids (GC) as an option for the first-line induction therapy. However, several studies have also demonstrated that TAC + GC therapy is effective for induction therapy, with favorable safety profile. Therefore, our study aimed to compare the efficacy of TAC + GC versus TAC + MMF + GC for remission induction in patients with proliferative LN.

Methods: This multicenter retrospective cohort study, designed as a target trial emulation, included patients with biopsy proven proliferative LN who received either TAC + GC or TAC + MMF + GC as induction therapy between September 2007 and July 2023. Based on the induction regimen, patients were classified into the TAC + GC and TAC + MMF + GC groups. The primary outcome was 12-month total renal response, defined as achieving either complete or partial renal response after 12 months. To address the baseline imbalances between the two groups, inverse probability of treatment weighting (IPTW) was applied. The comparative efficacy of TAC + MMF + GC compared to TAC + GC was estimated by

Table 1

Table 1. Baseline characteristics of the study population.

	Original population			IPTW-adjusted population		
	TAC+GC (n=48)	TAC+MMF+ GC (n=67)	SMD	TAC+GC (%)	TAC+MMF+ GC (%)	SMD
Age, year	35.6 ± 12.0	31.5 ± 11.2	0.356	33.4 ± 11.2	33.2 ± 12.6	0.017
Sex, female	43 (89.6)	53 (79.1)	0.291	85.2	83.9	0.037
Diabetes mellitus	3 (6.2)	1 (1.5)	0.249	3.3	2.1	0.077
Duration of LN, year	5.3 ± 5.1	4.0 ± 5.4	0.258	4.9 ± 4.9	4.8 ± 5.9	0.028
Newly diagnosed LN	7 (14.6)	18 (26.9)	0.307	17.8	20.9	0.077
LN class						
III	6 (12.5)	14 (20.9)	0.227	13.4	21.3	0.212
III+V	6 (12.5)	6 (9.0)	0.115	12.7	7.4	0.175
IV	32 (66.7)	40 (59.7)	0.145	66.4	61.8	0.095
IV+V	4 (8.3)	7 (10.4)	0.073	7.6	9.4	0.066
Serum albumin, g/dL	3.3 ± 0.6	3.1 ± 0.6	0.346	3.1 ± 0.6	3.1 ± 0.5	0.060
Serum GFR, mL/min/1.73m^2	80.7 ± 33.5	99.2 ± 30.2	0.580	90.3 ± 31.2	93.0 ± 31.4	0.087
UPCR, g/g	3.2 ± 2.6	3.6 ± 2.4	0.142	3.7 ± 3.0	3.5 ± 2.4	0.076
Anti-dsDNA positivity	34 (70.8)	53 (79.1)	0.192	75.4	74.3	0.026
Baseline GC dose, mg/day	19.7 ± 18.3	29.1 ± 21.3	0.476	27.3 ± 23.8	25.7 ± 20.4	0.074
HCQ use	28 (58.3)	42 (62.7)	0.089	56.7	59.0	0.045
RAAS blockade use	36 (75.0)	44 (65.7)	0.205	70.0	69.3	0.017
TAC dose, mg/day	2.6 ± 1.3	2.7 ± 1.6	0.100	2.6 ± 1.3	2.7 ± 1.5	0.029

Data are in mean ± standard deviation or numbers (%).
CYC, cyclophosphamide; GC, glucocorticoid; GFR, glomerular filtration rate; HCQ, hydroxychloroquine; IPTW, inverse probability of treatment weighting; LN, lupus nephritis; MMF, mycophenolate mofetil; RAAS, renin-angiotensin-aldosterone system; SMD, standardized mean difference; TAC, tacrolimus; UPCR, urine protein/creatinine ratio.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Serial change of albumin, GFR, and UPCR in the study population

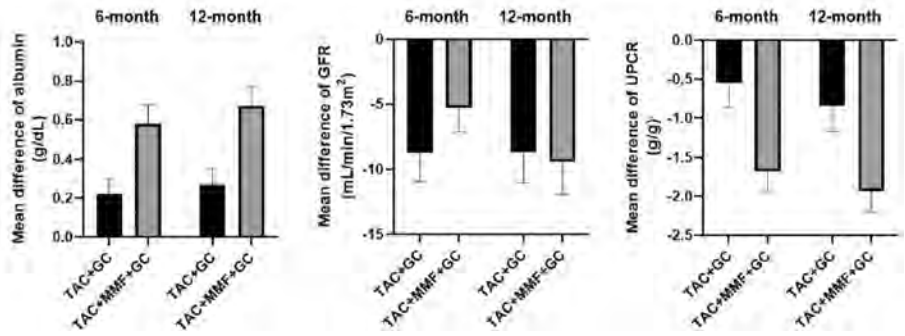


Figure 1

Table 2

Table 2. Comparative efficacy of TAC + MMF + GC regimen compared to TAC + GC regimen

	As-started analysis[a]			On-treatment analysis[b]		
	TAC+GC (n=48)	TAC+MMF+ GC (n=67)	p	TAC+GC (n=40)	TAC+MMF+ GC (n=55)	p
12-month TR, n (%)	16 (33.3)	40 (59.7)	0.009	16 (40.0)	40 (72.7)	0.003
12-month TR, OR[c] [95% CI]						
Crude	2.96 [1.38-6.54]		0.006	4.00 [1.71-9.75]		0.002
IPTW-adjusted	2.85 [1.32-6.33]		0.010	3.01 [1.29-7.23]		0.014

CI, confidence interval; CR, complete renal response; GC, glucocorticoid; IPTW, inverse probability treatment weighting; MMF, mycophenolate mofetil; OR, odds ratio; TAC, tacrolimus; TR, total renal response.
[a], analogous to intention-to-treat approach
[b], analogous to per-protocol approach
[c], OR is calculated using the TAC + GC group as the reference

using binary logistic regression, based on both as-started (corresponding to intention-to-treat) and on-treatment (corresponding to per-protocol) analyses.

Results: A total of 115 patients (48 in TAC + GC group and 67 in TAC + MMF + GC group) were included in the analysis. The baseline characteristics of the study population is shown in Table 1. The 12-month total renal response was achieved in 16 (33.3%) patients in the TAC + GC group and 40 (59.7%) patients in the TAC + MMF + GC group. Both groups showed improvements in serum albumin and proteinuria, while renal function declined (Figure 1). Compared to the TAC + GC group, the TAC + MMF + GC group showed significantly higher 12-month total renal response in both as-started and on-treatment analyses (Table 2). Adverse drug reactions occurred in 7 (14.6%) patients in the TAC + GC group and 11 (16.4%) patients in the TAC + MMF + GC group.

Conclusion: Compared to TAC + GC, TAC + MMF + GC therapy showed significantly higher renal response and comparable adverse drug reactions in patients with proliferative LN. These findings support TAC + MMF + GC as the preferred TAC-based induction regimen for proliferative LN.

Disclosure: Y. Kim: None; **H. Lee**: None; **J. Park**: Samsung Bioepis, 5; **E. Lee**: None; **Y. Ha**: None; **J. Park**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2699

Cutaneous IgA Vasculitis: Emulation of a Target Trial from a European Multicentric Retrospective Study

Elena Biancamaria Mariotti[1], Boris Sorin[2], William Lutz[3], Chloé Grolleau[3], Thomas Bettuzzi[4], Caterina Ricordi[5], Santos Castañeda[6], Luisa Herda[7], Cord Sunderkotter[7], Rodérau Outh[8], Romain Paule[9], Alexandra Audemard-Verger[10], Marzia Caproni[11], Angelo Valerio Marzano[12], Pietro Quaglino[13], Laura Atzori[14], Julien Campagne[15], Mehemt Erkan[16], Nabil Belfeki[17], Marijan Frkovic[18], Nicolas Dupin[19], Raphael Porcher[20], Marie Jachiet[21] and Benjamin Terrier[19], [1]University of Florence, Azienda USL Toscana Centro, Department of Dermatology, Florence, Firenze, Italy, [2]Assistance Publique Hôpitaux de Paris, Paris, France, [3]University Paris Cité, Hospital Saint Louis, Dermatology department, Paris, Paris, France, [4]Université Paris Est Créteil Val de Marne, Hôpital Henri-Mondor (APHP), Service de dermatologie, EpiDermE, Paris, France, [5]AUSL-IRCCS Reggio Emilia, Parma, Italy, [6]Hospital Universitario de La Princesa, IIS-Princesa, Madrid, Madrid, Spain, [7]Department of Dermatology and Venereology, Martin Luther University Halle-Wittenberg, Halle (Saale), Halle, Germany, [8]Department of Internal Medicine, Centre Hospitalier de Perpignan, Perpignan, France., Clermont-Ferrand, France, [9]Hospital Foch, Service de medicine interne, Suresnes, Paris, Suresnes, France, [10]Department of Internal Medicine, Tours University Hospital, Tours, France., Tours, France, [11]University of Florence, Azienda USL Toscana Centro, Department of Dermatology, Florence, Florence, Italy, [12]Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Milan, Italy, [13]University of Turin, Department of Medical Sciences, Section of Dermatology, Turin, Torino, Italy, [14]Dermatology Clinic, Department of Medical Sciences and Public Health, University of Cagliari, Cagliari, Cagliari, Italy, [15]Hospital Robert Schuman, Metz, France, [16]Hacettepe University Faculty of Medicine Department of Pediatric Rheumatology Ankara, Türkiye, Ankara, Turkey, [17]Head of the Internal Medicine and Clinical Immunology Department South Île de France Health Hospital Group, Melun Center, Melun, France, [18]Division for clinical immunology and rheumatology, Department of pediatrics UHC Zagreb / School of Medicine Zagreb Croatia, Zagabria, Croatia, [19]Cochin Hospital, Paris, France, [20]Université Paris Cité and Université Sorbonne Paris Nord, INSERM, INRAE, Center for Research in Epidemiology and StatisticS (CRESS), Paris, France, Paris, France, [21]University Paris Cité, Hôpital Saint-Louis, Dermatology department, Paris, Paris, France

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II (2699–2704)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Immunoglobulin A vasculitis (IgAV) is a small vessel vasculitis marked by IgA, deposition, palpable purpura with lower body predilection and variable joints, kidney and gastrointestinal tract involvement. In 2018, the addendum to the 2012 Chapel Hill Consensus Conference established the recognition of an exclusively or predominantly cutaneous form of the disease, more common in adults. Despite its frequency, standardized management of cutaneous IgA vasculitis remains elusive. The objective of this study was to compare colchicine, dapsone and glucocorticoids (GCs) to induce remission in newly diagnosed or relapsing skin-limited/dominant IgA vasculitis.

Methods: Patients with cutaneous IgAV treated with colchicine, dapsone, or GCs were included between January 1, 2014, and May 1, 2024. Data were collected retrospectively from 38 tertiary centers across eight countries in Europe. Inclusion criteria were age >8 years, biopsy-proven diagnosis of IgAV with evidence of IgA deposition in the skin and/or other organs, newly diagnosed or relapsing IgAV with active skin manifestations; absence of severe organ involvement; and a minimum follow-up of 3 months. The primary endpoint was to evaluate the proportion of patients achieving sustained remission of cutaneous involvement at day 90 (SRD90). Treatments were compared pairwise using inverse probability treatment weighting with the propensity score to adjust for confounders. Variables differing between responders and non-responders and susceptible to be associated with the endpoint were included in the propensity score. Patients receiving multiple therapies were counted per treatment line. Missing data were addressed with multiple imputation by chained equations.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: Of the 407 cases identified, 208 patients (114 males, 89 females; median age 44.9 years) were included in the study. Most were enrolled at initial diagnosis (174). At day 90, 109 patients (52.4%) had achieved sustained remission of cutaneous involvement. A total of 164 patients contributing to 216 therapeutic lines were analysed: 113 corresponded to colchicine, 83 to GCs, 20 to dapsone. Variables included in the propensity score were age at diagnosis, gender, necrotic lesions, myalgia and number of therapeutic lines. In the univariate analysis, no significant difference but trends were observed in the proportion of patients with SRD90 when comparing GCs vs colchicine (odds ratio [OR] 1.77 95% CI [0.97 - 3.20], p=0.059) and GCs vs dapsone (OR 1.82 95%CI [0.67 - 4.93], p=0.235). No difference was observed between colchicine and dapsone (OR 0.55 95% CI [1.68 - 5.15], p=0.360]). After weighting, GCs vs. colchicine showed balanced covariates (standardized mean differences < 0.10) and the proportion of SRD90 in the GCs group was higher (OR 1.88, 95%CI [1.04 - 3.41], p=0.034). No balance was achieved in comparisons involving dapsone due to low sample size.

Conclusion: GCs were significantly associated with a more favorable outcome than colchicine in achieving sustained remission of cutaneous involvement. The efficacy of dapsone versus colchicine or GCs could not be assessed using propensity scores, but suggests a similar response rate to colchicine and a lower efficacy compared to GCs.

Disclosure: E. Mariotti: None; **B. Sorin**: None; **W. Lutz**: None; **C. Grolleau**: None; **T. Bettuzzi**: None; **C. Ricordi**: None; **S. Castañeda**: None; **L. Herda**: None; **C. Sunderkotter**: Boehringer Ingelheim, 6, GSK (Glaxo Smith Klyne), 6, Vifor, 6; **R. Outh**: None; **R. Paule**: None; **A. Audemard-Verger**: None; **M. Caproni**: None; **A. Marzano**: None; **P. Quaglino**: None; **L. Atzori**: None; **J. Campagne**: None; **M. Erkan**: None; **N. Belfeki**: None; **M. Frkovic**: None; **N. Dupin**: None; **R. Porcher**: None; **M. Jachiet**: None; **B. Terrier**: Amgen, 1, AstraZeneca, 1, 2, GlaxoSmithKlein(GSK), 1, 2, Novartis, 1, 2, Roche, 5, Vifor Pharma, 2.

Abstract Number: 2700

Neutrophil Transcriptomics and Maturation Pathways in VEXAS Syndrome

Chloe Palmer[1], Gustaf Wigerblad[2], Tom Hill[3], Benjamin Turturice[1], Urvashi Kaundal[1], Paul Schaughency[3], Bhavisha Patel[4], Emma Groarke[5], Neal Young[5], Stefania Dell'orso[1] and Peter Grayson[6], [1]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]National Institutes of Health, Stockholm, Sweden, [3]NIAID, NIH, Bethesda, MD, [4]National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Beltsville, MD, [5]National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Bethesda, MD, [6]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II (2699–2704)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a severe adult-onset inflammatory disease caused by somatic mutations of the ubiquitin-like modifier activating enzyme 1 (*UBA1*) gene. Expansion of *UBA1* mutated hematopoietic stem cells in the bone marrow of patients produces skewing towards the myeloid compartment. Neutrophils are enriched at sites of inflammation, yet prior functional studies in VEXAS have not focused on neutrophils. The aim of this study was to examine the transcriptomes and maturation of neutrophils in peripheral blood and marrow from patients with VEXAS.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: We collected paired bone marrow and peripheral blood samples from 26 VEXAS patients with somatic pathogenic variants in *UBA1* at p.Met41 for single-cell RNA sequencing (scRNA-seq). Negatively isolated neutrophils were captured using 10X Genomics Chromium 3' Kits. Libraries were sequenced on the Illumina Novaseq 6000/X plus. Reads were aligned and quantified using Cell Ranger v8.0.0; dimensional reduction, clustering, and gene expression analysis was conducted using R package Seurat v5.2.1. Trajectory analysis and lineage differential expression tests were performed by R packages slingshot v3.20 and tradeSeq v1.23.0. Longitudinal analyses were performed in patients who were treated with hypomethylating agents, where one patient achieved molecular remission (i.e. eradication of the mutant clone).

Results: Canonical mutation types were proportional among the cohort (p.Met41Thr (n=10), p.Met41Leu (n=8), and p.Met41Val (n=8)) with median variant allele fraction 74% (range 24-89%). Circulating neutrophil counts were preserved to elevated in patients with VEXAS, while lymphocyte, monocyte, and natural killer cell counts were typically reduced. Immature granulocytes were commonly detected in peripheral blood and confirmed by scRNA-seq. Upregulation of genes related to neutrophil survival and inflammation were seen in neutrophils from patients with VEXAS. In particular, interferon response genes were highly upregulated in VEXAS neutrophils. Trajectory analysis identified two pathways of neutrophil differentiation in VEXAS: traditional development and an atypical pathway where myeloid-committed stem cells rapidly differentiated into mature neutrophils. Over-expression of genes associated with emergency granulopoiesis and immune metabolism defined the atypical pathway. Mutational burden in blood and bone marrow was eradicated in one patients with VEXAS following treatment with azacytidine. Comparing neutrophils before and after molecular remission revealed with significant reduction in interferon response gene expression, elimination of the atypical trajectory in peripheral blood, and normalization of neutrophil maturity subsets relative to healthy controls in both blood and bone marrow.

Conclusion: Neutrophils are critical effector cells in VEXAS syndrome, with distinct inflammatory transcriptomic profiles that normalize in molecular remission. These results are informative about the heterogeneity of neutrophils in VEXAS syndrome and may lead to discovery of novel myeloid-directed therapeutic targets.

Disclosure: C. Palmer: None; **G. Wigerblad**: None; **T. Hill**: None; **B. Turturice**: None; **U. Kaundal**: None; **P. Schaughency**: None; **B. Patel**: None; **E. Groarke**: None; **N. Young**: None; **S. Dell'orso**: None; **P. Grayson**: None.

Abstract Number: 2701

Ophthalmic Manifestations of Relapsing Polychondritis

Akash Gupta[1], Rennie Rhee[2], Kaitlin Quinn[3], Naomi Amudala[2], Nirali Bhatt[4], Carol McAlear[2], Marcela ferrada[5], Peter Grayson[6], Peter Merkel[2] and Shubhasree Banerjee[2], [1]Hospital of University of Pennsylvania, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [4]Scheie Eye Institute, University of Pennsylvania, Philadelphia, PA, [5]University of Maryland, Bethesda, MD, [6]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Chevy Chase, MD

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II (2699–2704)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: The prevalence of ocular involvement (OI) in patients with relapsing polychondritis (RP) has not been well defined. This study aimed to describe ocular manifestations, other clinical features, and use of immunosuppressive agents (IS), in patients with RP with and without OI.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

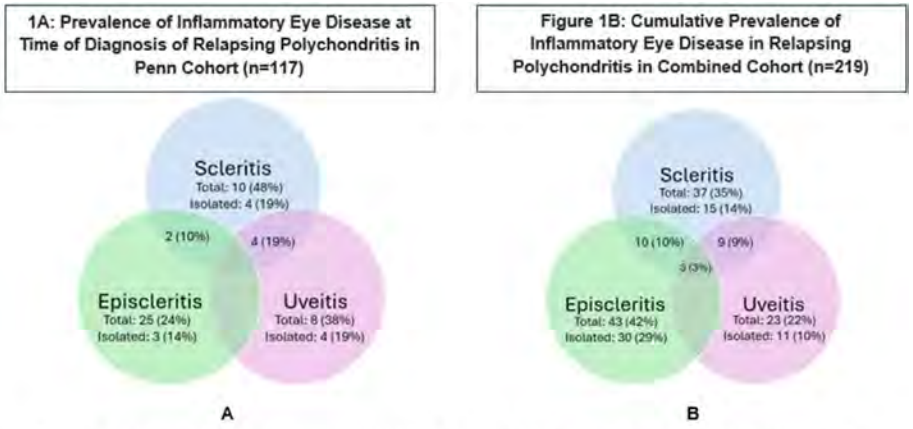


Figure 1. Prevalence of types of inflammatory eye disease in patients with relapsing polychondritis.

Methods: The study included adult patients with physician-diagnosed RP enrolled in a multicenter prospective observational cohort [University of Pennsylvania (Penn) and the National Institutes of Health (NIH)]. Data on demographics, clinical presentations, including OI, and use of IS [glucocorticoids (GC), non-biologic, and biologic IS] were collected. Means with standard deviation (SD) were calculated for continuous variables. Fischer's exact test was used to compare patients with and without OI.

Results: A total of 219 patients with RP (Penn=117; NIH=102) were included; of which, 185 (84%) were female, 194 (89%) were white, average age was 43 (SD 12.9) and average disease duration was 6.9 (SD 10) years. One hundred five (48%) had an OI during their disease course: episcleritis (n=43, 41%), scleritis (n=37, 35%), and uveitis (n=23, 22%), and recorded only in the Penn cohort were conjunctivitis (n=5, 9%) and eyelid swelling (3, 5%). Some patients had more than one OI (**Figure 1**). Clinical data at the time of diagnosis of RP was available in 117 patients (Penn cohort); 21 (18%) patients had an OI at the time of diagnosis, and the remaining 35 (30%) patients developed OI later. Among the patients with OI, scleral thinning and blindness were observed in 3 (7%) and 1 (2%) patients, respectively.

Table 1. Medication use in patients with relapsing polychondritis with and without ocular disease

Medication	Patients with eye involvement ever (n=90)	Patients without eye involvement ever (n=129)	p-value
Glucocorticoid	82 (91%)	121 (94%)	0.560
Non-biologic IS	79 (88%)	95 (74%)	0.011
Biologic IS	53 (59%)	60 (47%)	0.076
Methotrexate	63 (70%)	77 (60%)	0.152
Mycophenolate	22 (24%)	15 (12%)	0.016
Azathioprine	16 (18%)	12 (9%)	0.098
Leflunomide	12 (13%)	2 (2%)	0.001
Cyclophosphamide	5 (6%)	2 (2%)	0.126
Hydroxychloroquine	10 (11%)	18 (14%)	0.681
TNF inhibitors	28 (31%)	26 (20%)	0.080
Infliximab	22 (24%)	10 (8%)	<0.001
Adalimumab	19 (21%)	17 (13%)	0.139
Etanercept	6 (7%)	3 (2%)	0.166
Certolizumab	3 (3%)	3 (2%)	0.691
Golimumab	2 (2%)	3 (2%)	1.0
IL6 inhibitors	10 (11%)	9 (7%)	0.332
Ustekinumab	2 (2%)	2 (2%)	1.0
Secukinumab	2 (2%)	2 (2%)	1.0
Rituximab	5 (6%)	3 (2%)	0.278
Tofacitinib	2 (2%)	6 (5%)	0.476

23265203, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Compared to patients without OI, those with OI had higher rates of fever (n=24, 27%; vs n=15, 12%; p=0.007), arthritis (n=57, 63%; vs n=61, 47%; p=0.020), rash (n=32, 36%; n=15, 12%, p< 0.001), oral ulcers (n=29, 32%; n=25, 19%; p=0.038), genital ulcers (n=20, 22%; n=10, 8%; p=0.003), cough (n=56, 62%; n=58, 45%, p=0.010), and wheezing (n=31, 34%; n=26, 20%, p=0.020). OI was also associated with increased rates of sensorineural hearing loss (SNHL) (n=30, 33%; n=26, 20%, p=0.040), auricular deformity (n=16, 18%; n=7, 5%; p=0.006), and nasal bridge collapse (n=16, 18%; n=8, 6%; p=0.009). Coexisting autoimmune diseases were reported in 32 (27%) patients in the Penn Cohort, with no significant difference between those with and without OI (n=10, 24%; n=22, 29%; p=0.650).

Use of non-biologic IS was significantly higher (n=79, 88%; n=95, 74%; p=0.010) in those with OI compared to those without OI. Patients with OI were more likely to receive infliximab compared to those without OI (n=22, 24%; n=10, 8%; p< 0.001). There was no significant difference in the use of GC in patients with and without OI (n=82, 91%; n=121, 94%, p=0.560). (**Table 1**).

Conclusion: OI is common in RP and often develops after diagnosis, with many patients experiencing multiple ocular manifestations. OI is associated with a higher burden of systemic disease, greater risk of organ damage, and frequent use of non-biologic IS and select biologic IS. These findings underscore the importance of monitoring for OI in RP, which may indicate severe disease and influence treatment decisions.

Disclosure: A. Gupta: None; **R. Rhee**: None; **K. Quinn**: None; **N. Amudala**: None; **N. Bhatt**: None; **C. McAlear**: None; **M. ferrada**: UpToDate, 9; **P. Grayson**: None; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **S. Banerjee**: None.

Abstract Number: 2702

Diagnostic Performance of Vascular Ultrasound in Giant Cell Arteritis – A Single Center Experience

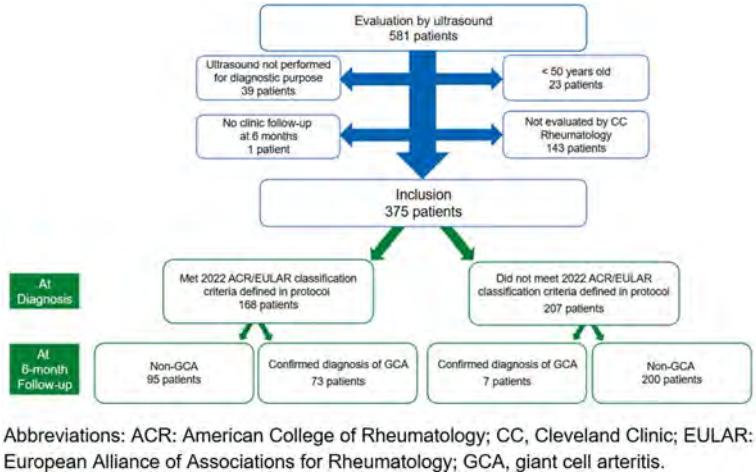
Ruoning Ni[1], Carol Langford[2], Minna Kohler[3], amne Dargham[1], Irene Katzan[1], Chao Zhang[4] and Rula Hajj-Ali[1], [1]Cleveland Clinic, Cleveland, [2]Cleveland Clinic, Moreland Hills, OH, [3]Massachusetts General Hospital, Harvard Medical School, Boston, MA, [4]Cleveland Clinic, Cleveland Heights, OH

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II (2699–2704)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Diagnostic approaches to giant cell arteritis (GCA) differ between the United States (U.S.) and Europe, with Europe favoring rheumatologist-performed ultrasound and the U.S. relying on temporal artery biopsy (TAB). Limited U.S. data on ultrasound use in GCA and lack of vascular ultrasound (VUS) training among U.S. rheumatologists constrains clinical decision-making. We aim to evaluate the diagnostic performance of VUS, including temporal, axillary and vertebral artery ultrasound at Cleveland Clinic (CC) for the diagnosis of GCA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

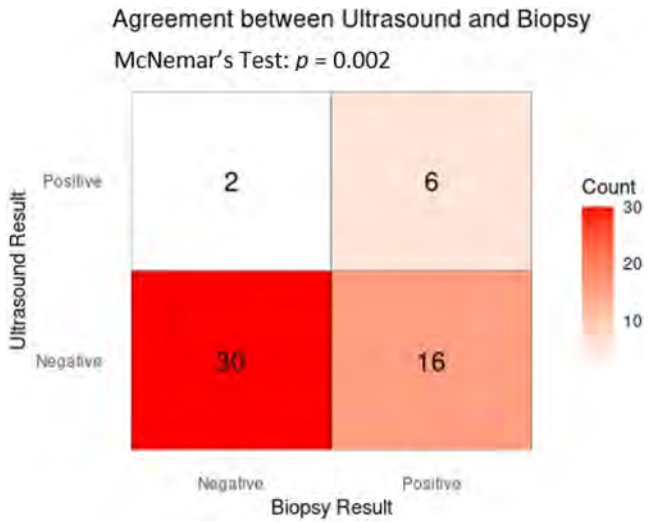


Abbreviations: ACR: American College of Rheumatology; CC, Cleveland Clinic; EULAR: European Alliance of Associations for Rheumatology; GCA, giant cell arteritis.

Algorithm of patient population

Methods: Patients aged ≥ 50 years old with suspected GCA who underwent radiology-performed VUS and were evaluated at the CC rheumatology clinic on at least two visits, with a 6-month interval between visits from 12/2020 to 12/2024, were included in this retrospective cohort analysis. Patient demographics, clinical manifestations, and final diagnosis were extracted. At the 6-month follow-up, a confirmed clinical diagnosis of GCA was established by the clinician based on a combination of clinical symptoms, laboratory markers, imaging and/or pathological findings, exclusion of other potential diagnoses, and treatment response. Operating characteristics of VUS, including sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated and compared to a diagnosis of GCA, using the 2022 ACR/EULAR classification criteria for GCA (as defined in this protocol) and with a confirmed clinical diagnosis of GCA at 6-month follow-up. The correlation coefficient of VUS and TAB was generated in patients with a confirmed diagnosis of GCA at 6-month follow-up.

Results: In total, 581 patients underwent VUS of whom 375 patients met the inclusion criteria. Of these, 168 (44.8%) met the 2022 ACR/EULAR classification criteria and 80 (21.3%) had a confirmed clinical diagnosis of GCA at 6-month follow-up (Table 1). Patients diagnosed with GCA more commonly presented with positive VUS, higher scores on 2022 ACR/EULAR classification criteria, compared to those without GCA, while the occurrence of abrupt headache did not differ



Heatmap for positive temporal, axillary or vertebral artery ultrasound and positive temporal artery biopsy, indicative of a statistically significant asymmetry in the discordant classifications between ultrasound and temporal artery biopsy.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Variables	All (n=375)	Non-GCA (n=295)	Confirmed diagnosis of GCA at 6-month follow-up (n=80)	p-value
Age at diagnosis (years) (Mean (SD))	70.3 [63.4;76.5]	69.6 [62.8;75.9]	70.9 [64.5;77.4]	0.056
Female – n (%)	253 (67.5%)	193 (65.4%)	60 (75.0%)	0.137
Self-reported white ancestry – n (%)	307 (81.9%)	239 (81.0%)	68 (85.0%)	0.511
Abrupt headache – n (%)	283 (75.5%)	216 (73.2%)	67 (83.8%)	0.073
Scalp tenderness – n (%)	123 (32.8%)	80 (27.1%)	43 (53.8%)	<0.001
Abnormal examination of the temporal artery – n (%)	21 (5.60%)	8 (2.71%)	13 (16.2%)	<0.001
Jaw or tongue claudication – n (%)	50 (13.3%)	18 (6.10%)	32 (40.0%)	<0.001
Permanent vision loss – n (%)	36 (9.6%)	22 (7.5%)	14 (17.5%)	0.013
Morning stiffness in shoulders/neck – n (%)	168 (44.8%)	123 (41.7%)	45 (56.2%)	0.028
ESR ≥ 50 mm/hour or CRP ≥ 10 mg/L – n (%)	243 (64.8%)	177 (60.0%)	66 (82.5%)	<0.001
Time from initiation of glucocorticoids to ultrasound (days) [Median (IQR)]	0.0[0.0;6.0]	0.0 [0.0;5.0]	3.0 [1.0;15.5]	<0.001
Positive ultrasound – n (%)	17 (4.53%)	0 (0.00%)	17 (21.3%)	<0.001
Temporal artery biopsy performed – n (%)	135 (36.0%)	81 (27.5%)	54 (67.5%)	<0.001
Time from initiation of glucocorticoids to biopsy (days) [Median (IQR)]	7.0 [3.0;13.0]	5.0 [3.0;12.0]	9.0 [3.0;13.8]	0.183
Giant cell arteritis on biopsy – n (%)	22 (23.9%)	0 (0.00%)	22 (47.8%)	<0.001
*Increased uptake of large vessels on PET-CT – n (%)	3 (10.0%)	2 (7.7%)	1 (25.0%)	0.360
Bilateral axillary involvement – n (%)	7 (1.9%)	0 (0.0%)	7 (8.8%)	<0.001
Scores of 2022 ACR/EULAR criteria (points) [Median (IQR)]	5.0 [4.0;7.0]	5.0 [4.0;6.0]	9.00 [7.0;11.0]	<0.001
2022 ACR criteria met per protocol – n (%)	168 (44.8%)	95 (32.2%)	73 (91.2%)	<0.001

* PET-CTs were performed on a total of 30 patients.
Abbreviations: ACR: American College of Rheumatology; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; EULAR: European Alliance of Associations for Rheumatology; IQR, interquartile range; PET-CT: Positron Emission Tomography - Computed Tomography; SD: standard deviation.

Characteristics of patients with/without confirmed diagnosis of giant cell arteritis at 6-month follow up

between the two groups (Table 1). The sensitivity, specificity, PPV and NPV of VUS compared to the 2022 ACR/EULAR classification criteria were 9.5%, 99.5%, 94.1% and 57.5%, respectively. When compared to the confirmed diagnosis of GCA at 6-month follow-up, the sensitivity, specificity, PPV, and NPV of VUS were 21.3%, 100.0%, 100.0%, and 82.4% respectively. A total of 135 patients (36.0%) underwent TAB, of which 22 biopsies confirmed GCA. The Cohen's Kappa coefficient between VUS and TAB results was 0.64, indicating fair agreement (Figure 2).

Conclusion: In this cohort, VUS demonstrated low sensitivity but high specificity in patients with a confirmed diagnosis of GCA at 6-month follow-up; there was a fair agreement between VUS and TAB. Compared to reported sensitivity rates in existing studies, our findings indicate a lower sensitivity, underscoring the variability of VUS performance across different settings. Future work should aim to refine VUS protocols and acquisition techniques to assess performance across varied settings to ensure more consistent diagnostic outcomes.

Disclosure: R. Ni: None; **C. Langford**: AbbVie/Abbott, 12, Non-paid consultant, AstraZeneca, 5, 12, Non-paid consultant, Bristol-Myers Squibb(BMS), 5, 12, Non-paid consultant, GlaxoSmithKlein(GSK), 5, NS Pharma, 5; **M. Kohler**: Janssen, 5, 12, medical advisory board, Novartis, 12, medical advisory board, Setpoint Medical, 5, Springer Publications, 9; **a. Dargham**: None; **I. Katzan**: None; **C. Zhang**: None; **R. Hajj-Ali**: AbbVie/Abbott, 2, Amgen, 2, UpToDate, 9.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: 2703

Longitudinal Changes on Cranial Magnetic Resonance Imaging in Relapsing Giant Cell Arteritis

Ruoheng Zeng[1], Ryan Rebello[2], Konstanze Guggenberger[3], Joshua Baker[4], Shubhasree Banerjee[4], Robert Kurtz[4], Naomi Amudala[4], Peter Merkel[4] and Rennie Rhee[4], [1]University of Pennsylvania School of Medicine, Philadelphia, PA, [2]St. Joseph's Hospital at McMaster University, Hamilton, ON, Canada, [3]University Hospital of Wuerzburg, Wuerzburg, Germany, [4]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II (2699–2704)

Session Type: Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: There is a need for better tools to monitor disease activity in giant cell arteritis (GCA). Prior studies demonstrated that vascular enhancement on cranial vessel wall magnetic resonance imaging (vw-MRI) decreases with treatment of GCA, but whether enhancement increases during relapse is not well known. This study examined changes on vw-MRI during relapse of cranial GCA.

Methods: Patients were prospectively enrolled in the study after receiving a diagnosis of GCA by a rheumatologist. All patients met the 2022 American College of Rheumatology/EULAR classification criteria for GCA. Enrolled patients underwent cranial vw-MRIs at enrollment, month 1, month 6, and month 12. Additional imaging was acquired in the setting of suspected relapse, defined as recurrence or worsening of symptoms of GCA felt to require escalation of immunosuppressive therapies. Neuroradiologists masked to disease activity and other clinical data graded vw-MRI enhancement for several cranial arteries and ocular structures using a previously-validated semiquantitative scoring system. Changes in MRI scores were compared with clinically-determined disease activity and acute phase reactants (APRs).

Results: Fourteen patients were included in the study, all of whom underwent a temporal artery biopsy (TAB), of which 12 (86%) had histologic evidence of GCA. All patients were treated with both high-dose glucocorticoids and adjunctive immunosuppressive therapies (10 treated with tocilizumab, 2 with tocilizumab and methotrexate, and 2 with trial-related study drug). Over the course of the study 4 patients experienced a cranial or ocular relapse, 2 patients experienced a relapse with polymyalgia rheumatica (PMR) without cranial symptoms, and 8 patients were in sustained remission. All 4 patients with

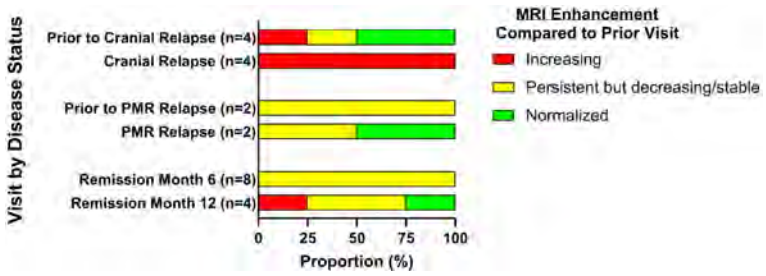


Figure 1. Changes on magnetic resonance imaging prior to and during relapse of giant cell arteritis. Graphs reflect changes in magnetic resonance imaging (MRI) enhancement from most recent visit. MRI enhancement increased during cranial relapse in 4 patients, including 1 patient who experienced increasing enhancement prior to clinical presentation of relapse. MRI enhancement decreased or became normal in 2 patients with a relapse of polymyalgia rheumatica only (non-cranial disease) and in most visits among 8 patients with non-relapsing giant cell arteritis. One patient classified as having non-relapsing giant cell arteritis and who remained in remission during the study period was noted to have increased MRI enhancement at month 12; several months after completion of the study, this patient experienced a relapse, although repeat MRI was not performed at the time of relapse.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

a cranial or ocular relapse had increased vw-MRI enhancement in at least one cranial structure. Two patients experiencing relapse of PMR had persistent, but not increased enhancement, while 7 of 8 patients in sustained remission had decreased or normal enhancement on follow-up. In 2 patients experiencing relapse, increased vw-MRI enhancement was seen months prior to clinical signs of relapsing disease. Cranial structures that showed increased enhancement at relapse included the occipital artery, optic nerve sheath, and maxillary artery. Levels of APRs remained normal in most patients, likely impacted by use of tocilizumab.

Conclusion: This study serves as proof-of-concept that vw-MRI may be potentially useful to monitor for relapse in GCA. Abnormal vw-MRI enhancement of cranial and orbital structures is responsive to change and correlates with clinical disease activity. Moreover, vw-MRI is more sensitive to changes in disease activity compared to APRs, suggesting that vw-MRI provides additive information to current biomarkers of GCA. A non-invasive method for accurately assessing disease activity is imperative for high-quality longitudinal care of patients with GCA. These findings expand the repertoire of imaging modalities to study for use in assessing disease activity for GCA.

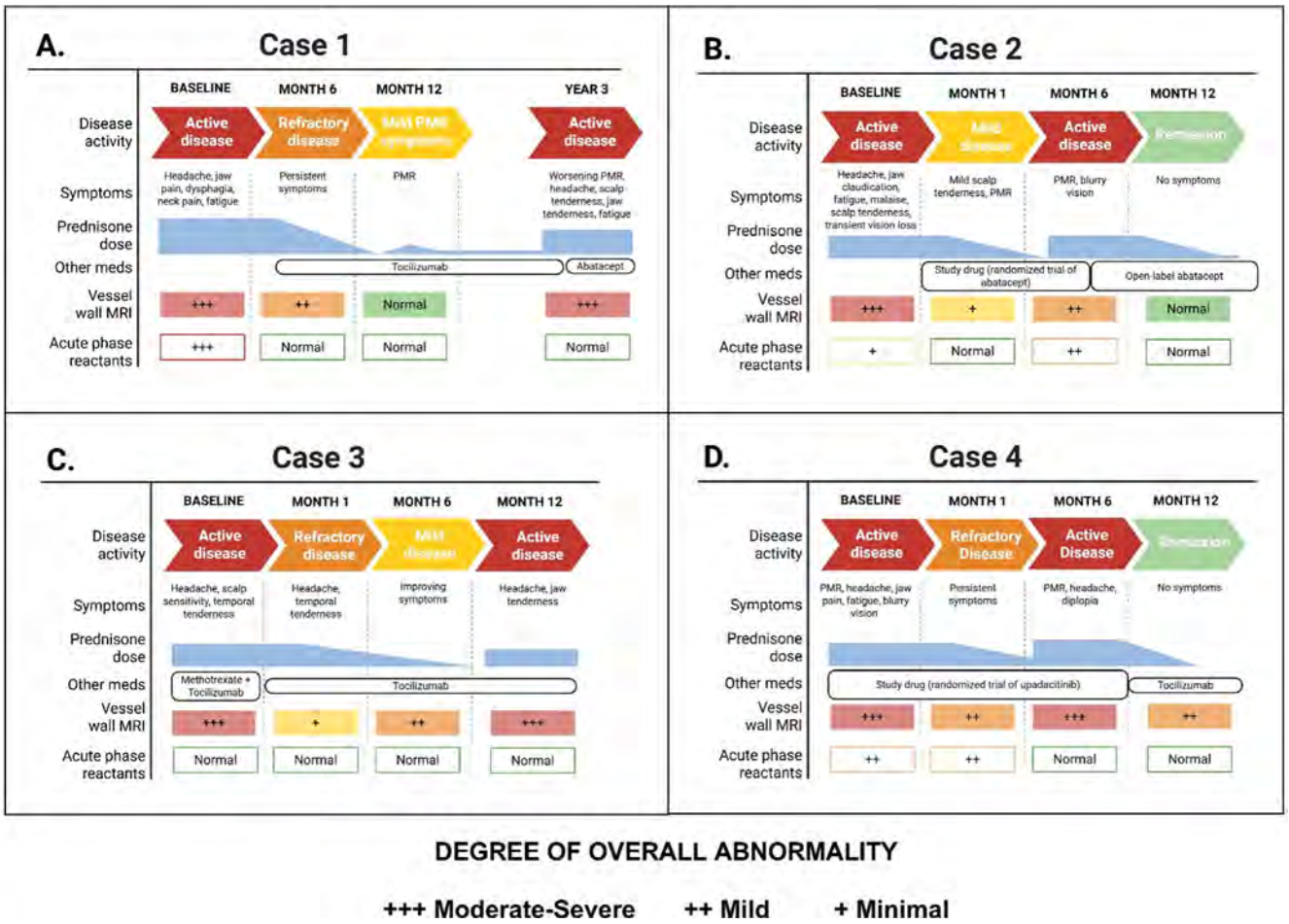


Figure 2. Longitudinal changes in disease activity measures of four patients with relapsing giant cell arteritis (GCA). Figures depict chronological changes in clinical status, medications, combined orbital and cranial vessel wall MRI (vw-MRI), and acute phase reactants (APRs) during enrollment in the 4 patients who experienced cranial or ocular relapse of GCA. (A) In Case 1, although APRs normalized, vw-MRI at month 6 showed persistent abnormal vascular enhancement similar to the patient's refractory clinical symptoms. Then relapse in year 3 was associated with worsening changes on vw-MRI whereas APRs remained normal, likely due to use of tocilizumab. (B) In Case 2, both vw-MRI and APRs tracked with disease activity in patient enrolled in clinical trial of abatacept. (C) In Case 3, worsening changes on vw-MRI were observed at month 6 prior to developing clinical manifestations of relapse at month 12 whereas APRs were normal throughout likely due to use of tocilizumab. (D) In Case 4, relapse at month 6 was associated with worsening changes on vw-MRI whereas APRs were normal.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

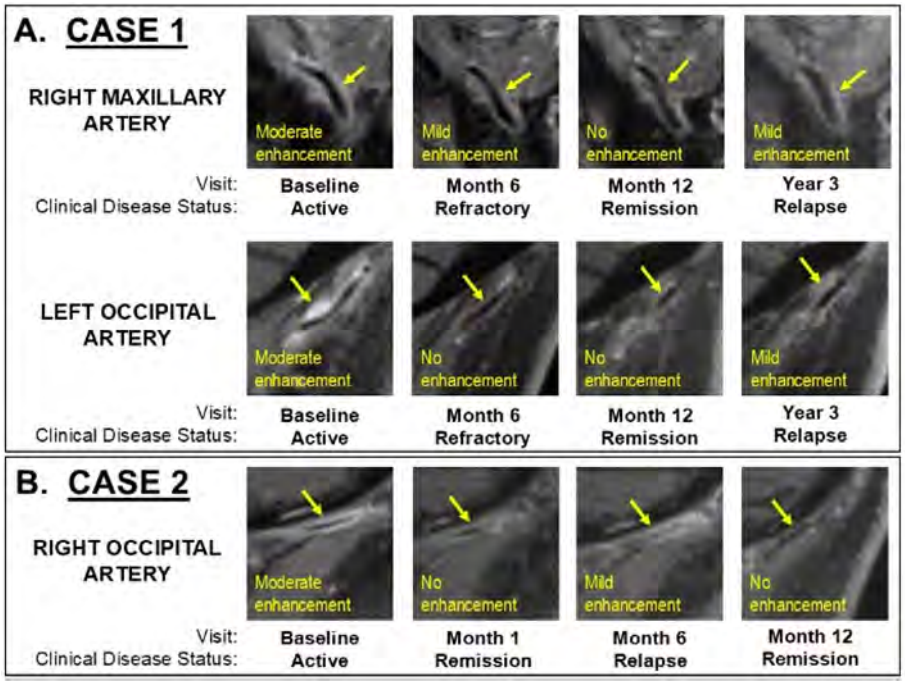


Figure 3. Example images of dynamic changes in vessel wall enhancement on magnetic resonance imaging in two cases of relapsing cranial giant cell arteritis. All magnetic resonance images are sagittal post-contrast T1-weighted black-blood sequences with fat saturation. Visit and clinical disease status are listed below each image. (A) Case 1: right maxillary and left occipital arteries (arrows) at each visit. (B) Case 2: right occipital artery (arrow) at each visit.

Disclosure: R. Zeng: None; **R. Rebello**: None; **K. Guggenberger**: None; **J. Baker**: None; **S. Banerjee**: None; **R. Kurtz**: None; **N. Amudala**: Amgen, 2, 6, J&J, 2, 6; **P. Merkel**: AbbVie, 2, 5, Alpine, 2, Amgen, 2, 5, ArGenx, 2, AstraZeneca, 2, 5, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb (BMS), 2, 5, CSL Behring, 2, Eicos, 5, Electra, 5, GlaxoSmithKlein (GSK), 2, 5, iCell, 2, Interius, 2, Kinevant, 2, Kyverna, 2, 11, Lifordi, 11, Metagenomia, 2, Neutrolis, 2, 5, 11, Novartis, 2, NS Pharma, 2, Otsuka, 2, Q32, 2, 11, Quell, 2, Regeneron, 2, Sanofi, 2, Sparrow, 2, 11, Takeda, 2, 5, UpToDate, 9, Vistera, 2; **R. Rhee**: None.

Abstract Number: 2704

Complete metabolic response on PET/CT in giant-cell arteritis-related large vessel vasculitis : comparison of two strategies using glucocorticoids or glucocorticoids + tocilizumab

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders II (2699–2704)
Session Type: Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Persistent large-vessel vasculitis (LVV) on PET/CT in giant-cell arteritis (GCA) is associated with a higher risk of aortic dilation. Few data are available on complete metabolic response under treatment (i.e., total extinction of vascular uptakes). This study compared the ability of glucocorticoids (GC) alone and GC + tocilizumab (TCZ) to obtain a complete metabolic response on repetitive PET/CT.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Comparison of GC alone and GC+TCZ to obtain a PET/CT extinction in GCA-related LVV

	GC alone (n=76)	GC + TCZ (n=91)	p
Demographics			
Female	55 (72)	64 (70)	0.77
Median age, years	69 [64–74]	69 [66–75]	0.36
Cardiovascular risk factors			
Tobacco use	28 (37)	28 (31)	0.41
Arterial hypertension	26 (34)	39 (43)	0.25
Diabetes mellitus	7 (9)	5 (5)	0.35
Dyslipidemia	18 (24)	24 (26)	0.69
Obesity	17 (22)	7 (8)	**0.003**
Clinical manifestations at baseline			
Body Mass Index, kg/m²	24 [21.5–26.6]	24.2 [21.5–27.1]	0.89
Cranial manifestations	45 (59)	65 (71)	0.10
Ophthalmic involvement	7 (9)	14 (15)	0.25
Polymyalgia rheumatica	25 (33)	50 (55)	**0.004**
Diagnosis of LVV on PET/CT			
GCA and LVV diagnosed concomitantly	50 (66)	65 (71)	0.43
Elapsed time in others, months	43 [23–177]	8.5 [6–15]	**<0.0001**
Laboratory tests, at baseline			
C-reactive protein level, mg/l	78 [54–107]	79 [40–134]	0.92
Hemoglobin, g/dl	10.9 [10.25–11.75]	11.2 [10.4–12.2]	0.28
GC management			
GC doses at onset, mg/day	40 [37.5–60]	45 [40–60]	0.35
GC discontinuation at last follow-up	46 (61)	72 (79)	**0.009**
Elapsed time to GC discontinuation, months	21.5 [17–36]	12 [10–18]	**<0.0001**
Outcomes			
Total follow-up	53 [27–95]	33 [15–53]	**<0.0001**
Time between the first and last PET/CT, months	8 [6–11]	12 [10–20]	**<0.0001**
Total extinction of last PET/CT	31 (41)	69 (76)	**<0.0001**
Any LVV relapse on PET/CT during follow-up	4 (5)	11 (12)	0.17
Any GCA relapse during follow-up	35 (46)	58 (64)	**0.03**
Follow-up after last PET/CT, months	42 [22–67]	12 [2–27]	**<0.0001**

GCA: Giant Cell Arteritis; LVV: Large Vessel Vasculitis; FU: follow-up; TCZ: Tocilizumab; GC: glucocorticoids; PET/CT: positrons emission tomography coupled with a computed tomography

Methods: Through the French Large-Vessel Vasculitis Study Group (GEFA), we retrospectively enrolled all GCA patients who satisfied the following criteria: 1) a LVV was evidenced on PET/CT; 2) all patients were treated either with GC alone or GC+TCZ; and 3) at least a second PET/CT was repeated under the same initial treatment. Patients who received another treatment between the two repeated PET/CT were excluded.

Patients who showed a total vascular extinction on repeated PET/CT without LVV relapse during follow-up were considered as a success. Patients with still positive PET/CT or with LVV relapse during follow-up were considered as failures.

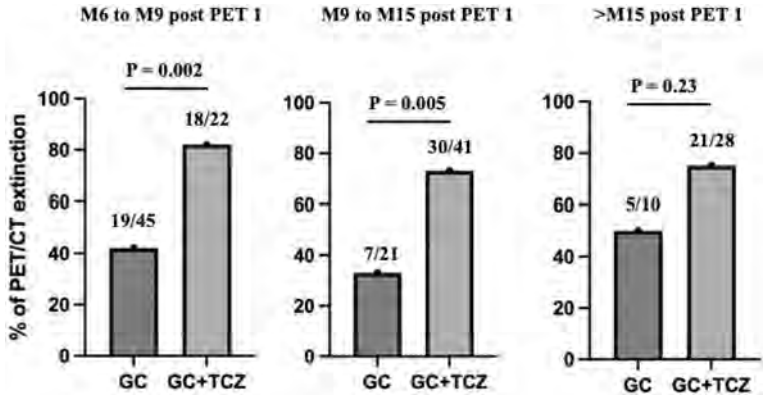


Figure 1. Proportion of negative PET/CT in the two groups according to the time of control.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: A total of 167 patients were enrolled, 76 treated with GC alone and 91 treated with GC + TCZ. Their characteristics at baseline are shown and compared in Table 1. LVV was diagnosed on PET/CT at GCA diagnosis in 66% and 71% (p=ns) of patients in the GC and GC+TCZ groups, respectively. A second PET/CT was repeated at 8 [IQR 25-75, 6–11] months in the GC group and 12 [10–20] months in the GC+TCZ group (p< 0.0001). Under GC alone, 41% of PET/CT showed a total extinction of vascular uptakes versus 76% in the TCZ group (p< 0.0001). Figure 1 shows the proportion of negative PET/CT in the two groups according to the time of control. LVV relapse on a third PET/CT was diagnosed in 5% of patients treated with GC alone and 12% of patients treated with GC+TCZ (p=0.17). At last follow-up, more patients treated with GC+TCZ had discontinued GC (79% vs. 61% in patients treated with GC alone, p=0.009).

Conclusion: This study suggests that the combination of GC+TCZ is more efficient than GC alone to obtain a complete metabolic extinction on repeated PET/CT in GCA-related large vessel vasculitis. A further longitudinal study is required to analyze the impact on the risk of aortic dilation.

Disclosure: H. De Boysson: AbbVie/Abbott, 1, 2, Chugai, 2, Fresenius Kabi, 1, 2, Novartis, 2; **A. Dumont**: None; **T. Orvain**: None; **O. Espitia**: Novartis, 2; **C. Comarmond**: Roche, 5; **S. Deshayes**: None; **L. Sailler**: None; **J. Alexandra**: Chugai France, 2; **M. Samson**: AbbVie/Abbott, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, Chugai, 2, Fresenius Kabi, 2, GlaxoSmithKlein(GSK), 2, Novartis, 2, 5, Vifor Pharma, 2; **A. Aouba**: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Late Breaking (L01-18)

Abstract Number: LB01

Low-dose Interleukin-2 Therapy in Systemic Lupus Erythematosus: a double-blind, randomised, placebo-controlled, phase IIb trial

Xia Zhang[1], Ruiling Feng[1], Zhanguo Li[2] and Jing He[1], [1]Peking University People's Hospital, Beijing, China (People's Republic), [2]Peking Univeristy People's Hospital, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Low-dose Interleukin-2 (Ld-IL2) has shown therapeutic effect in autoimmune diseases, particularly systemic lupus erythematosus (SLE). Various doses from 0.33 to 3.0 million units of IL-2 have been used widely in clinics. As

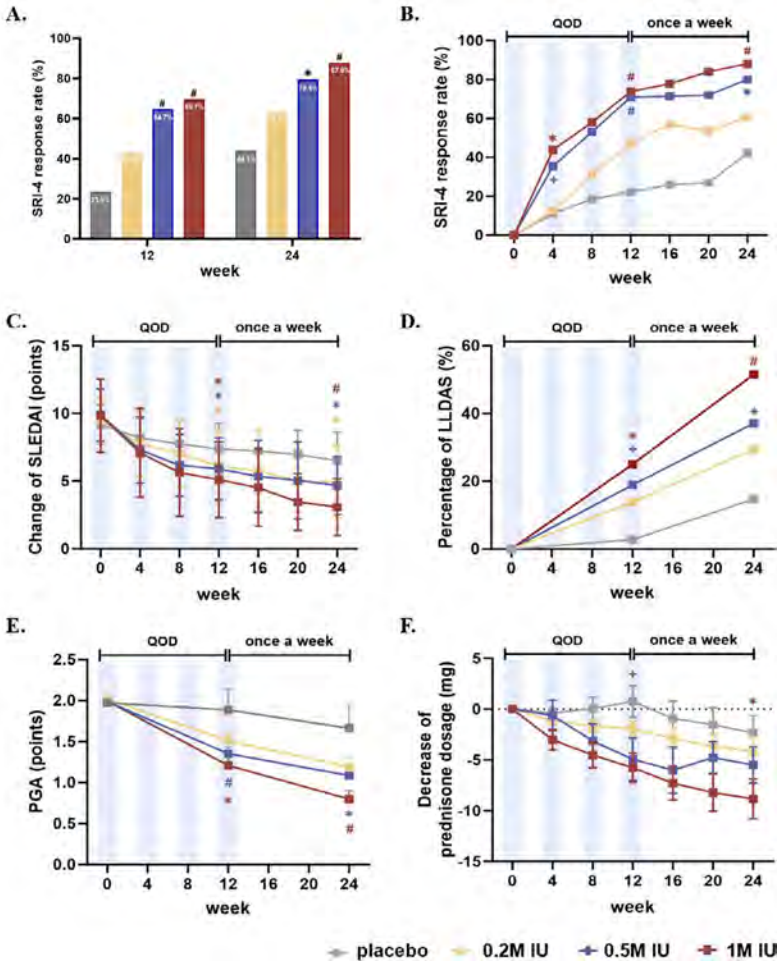


Figure 1. The clinical efficacy through 48 weeks in overall study population (A) Efficacy of Ld-IL2 assessed by SRI-4 during 24 weeks. (B) Percentage of SRI-4 responders at week 12 and 24. (C) Change of SLEDAI from baseline to 24 weeks. (D) Proportion of LLDAS responders at week 12 and 24. (E) Improvement with Ld-IL2 determined by PGA. (F) Change of prednisone dose from baseline to week 24. Red represents Ld-IL2 1M IU versus placebo group; blue Ld-IL2 0.5M IU versus placebo group; yellow represents Ld-IL2 0.2M IU versus placebo group. Ld-IL-2, low-dose interleukin 2. SRI-4: Systemic Lupus Erythematosus Responder Index 4; PGA: physician's global assessment. + P<0.05; *P<0.01; # P<0.001

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

far, the optimal dose in SLE treatment has not been evaluated, which leads to uncertainty of efficacy and causes difficulty of dose decision in practice.

Methods: In this multicenter, randomized, double-blind, Phase IIb trial, 152 active SLE patients were randomized (1:1:1:1) to receive subcutaneous IL2 (0.2, 0.5, or 1.0 million IU) or placebo every other day for 12 weeks, then weekly for further 12 weeks.

Results: At week 12, significantly higher SRI-4 response rates were demonstrated in IL2 1M IU (69.7%), 0.5M IU (64.7%), and 0.2M IU (42.9%) than in placebo (23.5%). Notably, these significant differences proceeded until the end of treatment period at week 24 ($p < 0.001$). Secondary outcomes revealed SLE patients achieving LLDAS at doses of 1M IU, 0.5M, and 0.2M (51.5%, 37.1%, and 28.5% respectively) at week 24. In the 1M IU Ld-IL2 group, significant reductions were observed in PGA scores, anti-dsDNA antibody, and prednisone dosages, accompanied by remarkable increases in serum C3 and C4 levels. Infection rates were lower in IL2 groups compared to placebo. Ld-IL2 drives expansion of Tregs and rebalance of Tregs/Teff ratio.

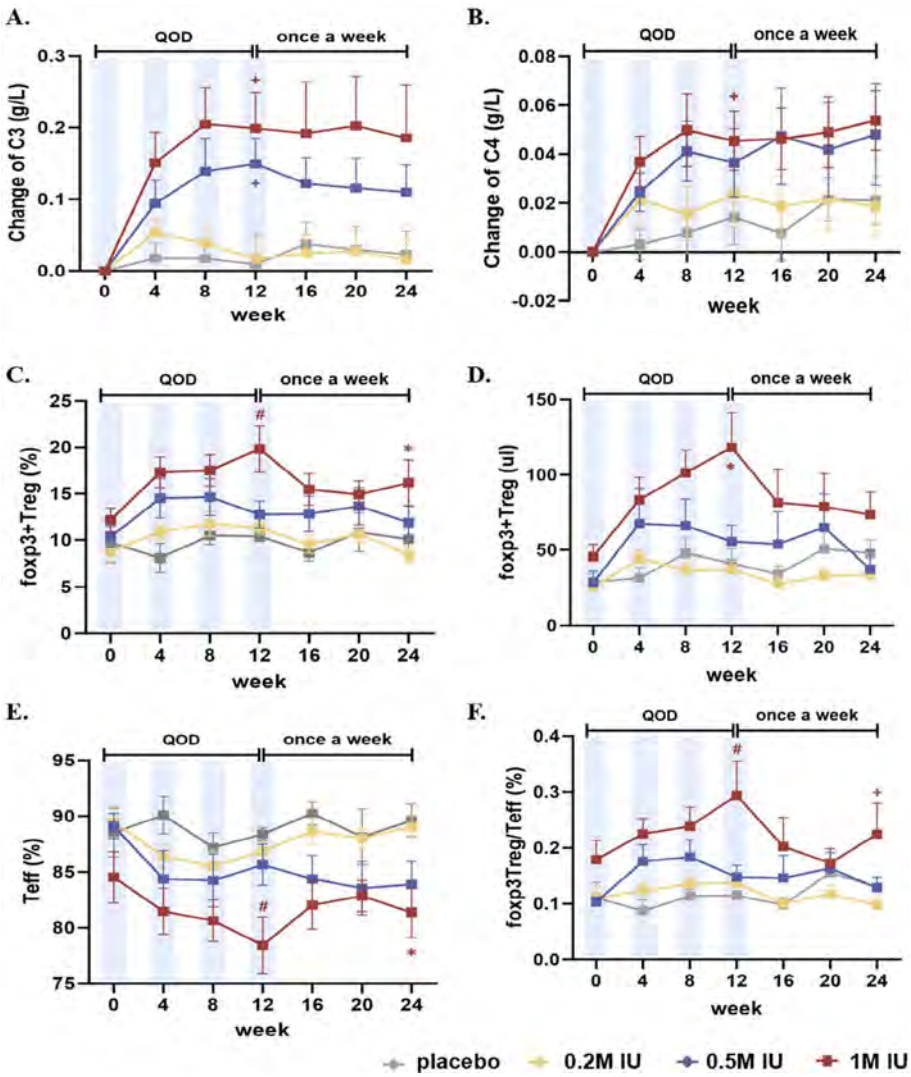


Figure 2. Dynamics of laboratory and immunological responses after IL2 treatment (A-B) Change in C3 and C4 concentrations from baseline over time. (C-F) Changes of the percentage and the number of foxp3+ CD127loCD25hi regulatory T cells (foxp3+Treg) and effector T (Teff) cells. Red represents Ld-IL2 1M IU versus placebo group; blue Ld-IL2 0.5M IU versus placebo group; yellow represents Ld-IL2 0.2M IU versus placebo group. Ld-IL-2, low-dose interleukin 2. SRI-4: Systemic Lupus Erythematosus Responder Index 4; PGA: physician's global assessment. + P<0.05; *P<0.01; # P<0.001

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: Ld-IL2 demonstrates efficacy for patients with SLE in a dose-dependent manner, associated with expansion of Tregs and rebalance of Tregs/Teff ratio.

Disclosures: X. Zhang: None; R. Feng: None; Z. Li: None; J. He: None.

Abstract Number: LB02

Tofacitinib Plus Glucocorticoids Can Effectively Reduce Relapse Rate in IgG4-Related Disease: A Randomized,Open-label controlled Trial

Xi Xu[1], Huaqun Zhu[2] and Hua Ye[1], [1]Peking University People's Hospital, Beijing, China (People's Republic), [2]Peking University People's Hospital, Beijing, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–11:30AM

Background/Purpose: To evaluate the efficacy of tofacitinib combined with glucocorticoids (GCs) compared with GCs monotherapy in preventing relapse in patients with IgG4-related disease (IgG4-RD).

Table 1. Comparison of baseline characteristics between the combination therapy group an-d the glucocorticoid monotherapy group in patients with IgG4-RD GCs:glucocorticoids;TOFA:tofacitinib;;IgG4-RD:IgG4 related disease response index

	GCs+TOFA (n = 29)	GCs (n = 29)	*P*
Age, Mean ± SD	52.83 ± 14.74	58.03 ± 12.35	0.150
Gender, male	15 (51.72)	16 (57.14)	0.689
Organ involvements			
Orbit(%)	0 (0.00)	1 (3.45)	1.000
Extraocular muscle(%)	2 (7.14)	0 (0.00)	0.237
Lacrimal gland(%)	18 (64.29)	15 (51.72)	0.337
Parotid gland(%)	13 (46.43)	13 (43.33)	0.813
Submandibular gland (%)	20 (71.43)	18 (62.7)	0.454
Lung(%)	3 (10.71)	3 (10.34)	1.000
Lymph node(%)	10 (35.71)	12 (41.38)	0.661
Retroperitoneum(%)	1 (3.70)	1 (3.45)	1.000
Pancreas(%)	5 (18.52)	13 (44.83)	0.035
Billary tract(%)	2 (7.69)	9 (31.03)	0.031
Liver(%)	1 (3.70)	3 (10.34)	0.656
Renal(%)	3 (11.11)	1 (3.45)	0.553
Clinical phenotypes (%)			
Head and Neck-Limited	4 (6.90)	2 (6.90)	
Mikulicz and Systemic	34 (58.62)	20 (68.97)	
Pancreato-Hepato-Biliary	19 (32.76)	7 (24.14)	
Retroperitoneum and Aorta	1 (1.72)	0 (0.00)	
Sum Organ (median (IQR))	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	0.563
IgG4-RD RI, Mean ± SD	8.59 ± 3.99	9.21 ± 4.81	0.595

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

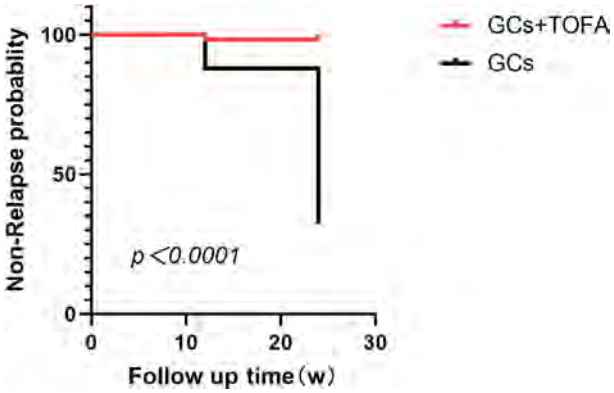


Figure 1. Changes in the IgG4-RD RI during the 24-Week follow-up GCs:glucocorticoids;TOFA:tofacitinib;;IgG4-RD:IgG4 related disease response index;****p<0.0001

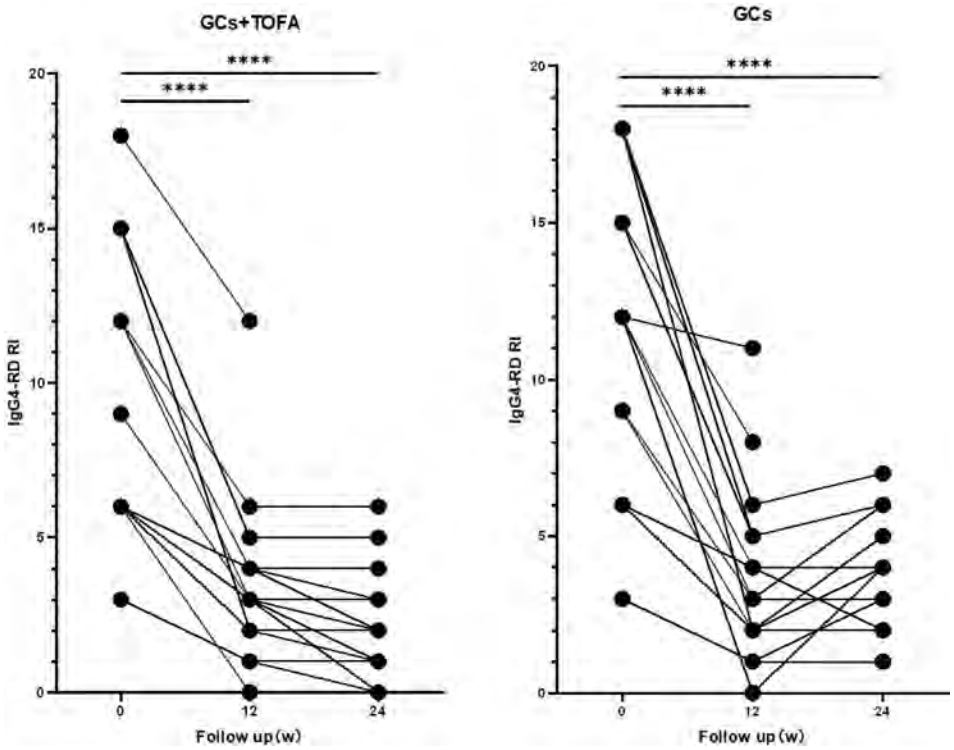


Figure 2. Kaplan-Meier curves of 24-week non-relapse rates between 2 different treatment groups

Methods: Compared with glucocorticoid monotherapy, the combination of tofacitinib and glucocorticoids significantly reduced the relapse rate in patients with IgG4-RD. Tofacitinib may represent an effective steroid-sparing agent for the treatment of IgG4-RD.

Results: Compared with glucocorticoid monotherapy, the combination of tofacitinib and glucocorticoids significantly reduced the relapse rate in patients with IgG4-RD. Tofacitinib may represent an effective steroid-sparing agent for the treatment of IgG4-RD.

Conclusion: A total of 58 patients were enrolled, with 29 in each group. The baseline characteristics were comparable between the two groups (Table 1). At the time of analysis,26 patients in the combination therapy group and 24 in the monotherapy group had completed follow-up. The relapse rate at week 24 was 0% in the combination therapy group compared

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

with 54.16% (13/24) in the monotherapy group ($p < 0.0001$) (Fig 2). No significant difference was observed in the change of IgG4-RD RI between the combination group and the monotherapy group (5.64±2.97 vs. 5.17±3.47, p=0.619). The proportion of Th2 cells decreased more significantly in the combination therapy group than in the GCs monotherapy group (-0.71 [-1.41, 0.42] vs. 0.11 [-0.10, 0.69], p=0.032). Changes in IgG4 levels did not differ significantly between the two groups (p=0.389). Four infections occurred in the combination group, (two urinary tract infection, one herpes zoster and one pulmonary infection), but the overall incidence of adverse events did not differ significantly between the groups (p = 0.311). No serious adverse events occurred.

Disclosures: X. Xu: None; H. Zhu: None; H. Ye: None.

Abstract Number: LB03

Transcutaneous Electrical Nerve Stimulation Effectively Reduces Pain in Fibromyalgia: A Pragmatic Cluster-Randomized Trial Embedded in Physical Therapy Practice

Leslie Crofford[1], Dana Dailey[2], Barbara Van Gorp[2], Carol Vance[2], Andrew Post[3], Ruth Chimenti[2], Ezgi Yarasir[2], Elizabeth Johnson[1], Kari Vance[2], Bridget Zimmerman[2], Fangfang Jiang[2], David-Erick Lafontant[2], Maxine Koepp[2], Dixie Ecklund[2], Emine Bayman[2] and Kathleen Sluka[2], [1]Vanderbilt University Medical Center, Nashville, Tennessee, [2]University of Iowa, Iowa City, Iowa, [3]Grand Valley State University, Grand Rapids, Michigan

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Fibromyalgia (FM) is characterized by chronic widespread pain that is often exacerbated by movement. FM is associated with enhanced central pain transmission, while transcutaneous electrical nerve stimulation (TENS) delivers electrical current through surface electrodes to counteract this central excitability. We previously showed the efficacy of TENS in reducing movement-evoked pain (MEP) and fatigue in individuals with FM in a double-blind, randomized controlled trial; however, effectiveness of TENS in a real-world setting has not previously been tested. As physical therapists are trained to use TENS for pain management, we examined if addition of TENS to outpatient physical therapy (PT) would reduce MEP using a pragmatic trial design.

Methods: The Fibromyalgia TENS in Physical Therapy Study (FM-TIPS) was a cluster-randomized pragmatic trial conducted at 28 outpatient PT clinics from 6 healthcare systems. Each clinic was randomized to TENS+PT or PT-Only. Potential participants were screened at their first PT visit and were eligible if they had been diagnosed with FM and no contraindications to TENS. Consented participants were instructed on TENS use at PT visit 2. The intervention consisted of 2 TENS devices used daily for 2 hours during physical activity that delivered a waveform with a modulating frequency of 2-125 Hz and duration between 100-180 μs at a strong but comfortable intensity through butterfly electrodes placed on the upper and lower back. Data was captured via REDCap on days (d) 1, 30, 60, 90 and 180. The primary outcome was MEP during a sit-to-stand test at d60 (randomized phase) modeled as a between-group comparison of change in MEP from d1 pre-TENS to d60 post-TENS using linear mixed-effects models. Following d60, the PT-Only group received TENS units along with virtual instructions (extension phase).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Baseline characteristics of study participants

	All Participants (n=384)	TENS+PT (n=191)	PT-Only (n=193)
Demographics			
Age (yrs) mean ± SD	53.2 ± 15.2	52.6 ± 15.5	53.9 ± 14.8
Sex (%) Female	351 (91%)	175 (92%)	176 (91%)
Ethnicity (%) Not Hispanic or Latino	326 (85%)	170 (89%)	156 (81%)
Race (%) White	315 (82%)	156 (82%)	159 (82%)
Education (%) High School or less	149 (39%)	73 (38%)	76 (39%)
Income (%) <$50,000 per year	171 (45%)	82 (43%)	89 (46%)
Rurality (RUCA Code 4-10) (% Rural)	193 (50%)	79 (41%)	114 (59%)
Employment (%) Working	160 (43%)	84 (45%)	76 (41%)
Disability Insurance (%)	107 (28%)	51 (27%)	56 (29%)
Relationship (%) Married/Partner	238 (64%)	117 (64%)	121 (64%)
Fibromyalgia (FM) Measures (n (%) / Mean ± SD)			
FM positive (%)	286 (74%)	139 (73%)	147 (76%)
Fibromyalgia impact (FIQR, 0-100)	57.4 ± 17.4	57.5 ± 17.3	57.2 ± 17.5
Widespread pain (FM Diagnostic Criteria 2016, WPI, 0-19)	9.3 ± 4.0	9.2 ± 4.1	9.4 ± 4.0
Somatic symptoms (FM Diagnostic Criteria 2016, SSS, 0-12)	7.5 ± 2.3	7.5 ± 2.4	7.5 ± 2.1
PSD (FM Diagnostic Criteria 2016, (0-31)	16.9 ± 5.3	16.8 ± 5.6	17.1 ± 5.0
Pain duration (yrs)	14.5 ± 10.9	14.4 ± 10.9	14.6 ± 11.0

FIQR: Fibromyalgia impact questionnaire revised, WPI: Widespread pain index, SSS: Symptom severity scale, PSD: Polysymptomatic distress, PSD: Polysymptomatic distress

Results: We enrolled 459 participants, of whom 384 completed baseline data and were randomized to the TENS+PT (191) or PT-Only groups (193). Baseline characteristics are shown in **Table 1**. MEP at d60 was significantly lower (-1.1, CI= -1.58 to -0.7; Cohen's d=0.46) in the TENS+PT compared to the PT-Only group during the randomized phase. Within-group comparisons showed TENS+PT reduced post-TENS MEP by d30 and effectiveness persisted to d180 (**Figure 1**), a result also seen in the PT-Only group during the extension phase. Movement-evoked fatigue and resting pain/fatigue demonstrated a similar pattern. There was a dose-response for measured TENS use, and the patient global impression of change favored TENS+PT (p=0.001) (**Figure 2**). There were more participants in the TENS+PT than the PT-Only group who demonstrated at least 30% reduction in MEP (41% vs 13%, p=0.0001) and resting pain (39% vs 21%, p=0.004). At d180, 81% of

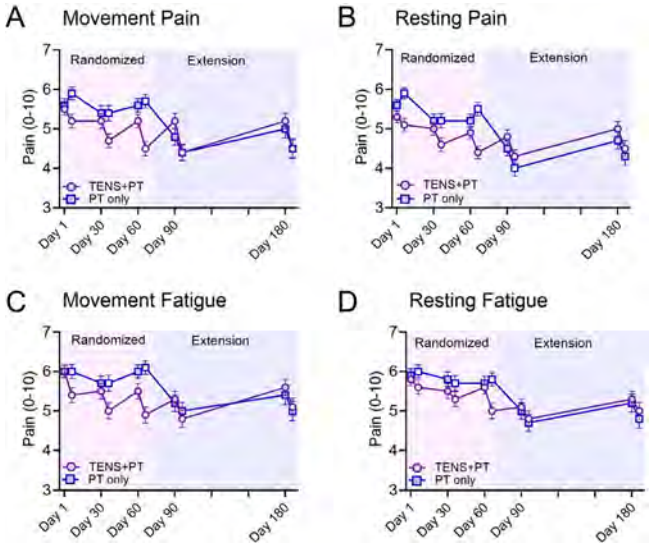


Figure 1. Changes in A) movement-evoked pain, B) resting pain, C) movement-evoked fatigue, and D) resting fatigue before and after TENS through Day 180. Measures were assessed before (pink circles) and after 30 min application of TENS (white circles) on each day. The PT-only group tested all measures before (blue squares) and after 30 minutes of rest (white squares) on each day through day 60 (randomized phase), and before and after TENS during the extension phase on Day 90 and day 180. There were significant decreases in all measures after 30 minutes of TENS treatment for both pain and fatigue beginning on Day 30 and persisting through Day 180 for the TENS+PT group. There was no change in the measures for the PT-only group during the first 60 days, the randomized phase. However, after receiving TENS, the PT-only group showed a significant decrease 30 days later that lasted through the Day 180 test period (4 months). Data are mean and S.E.M.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

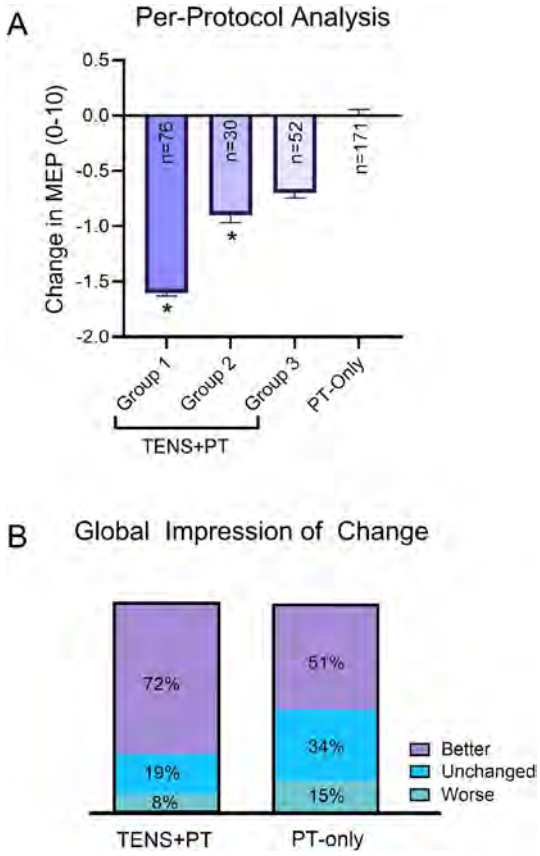


Figure 2. A. Per protocol analysis shows a dose-response effect for change in movement-evoked pain on Day 60 during the randomized phase. Group 1 used TENS 8x/month and a total of 900 min/mo for both the first and the second 30-day period. Group 2 used TENS 8x/month and a total of 900 min/mo for the first 30 days. Group 3 used TENS less than the minimal dose. The PT-only group did not use TENS. Groups 1 and 2 showed a greater reduction in movement-evoked pain when compared to the PT-Only group. *, $p<0.05$. B. The global impression of change showed a greater number of individuals reported improvement in MEP when compared to those in the PT-only group ($\square$=16.7, p=0.001).

respondents that remained in the study found TENS helpful and 55% used TENS daily. There were no treatment-related serious adverse events and minor adverse events related to TENS were all ≤ 7.5%.

Conclusion: TENS meaningfully reduces FM pain and fatigue. Effectiveness persists for at least 180 days. Treatment effect size is comparable to other FM therapies even in this heterogeneous real-world population. TENS is a safe, inexpensive, and readily available treatment for FM.

Disclosures: L. Crofford: Argenyx, 5, Evergreen, 5, Kezar, 12, DSMB, Otsaka, 12, DSMB, UCB, 2; D. Dailey: None; B. Van Gorp: None; C. Vance: None; A. Post: None; R. Chimenti: None; E. Yarasir: None; E. Johnson: None; K. Vance: None; B. Zimmerman: None; F. Jiang: None; D. Lafontant: None; M. Koepp: None; D. Ecklund: None; E. Bayman: None; K. Sluka: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: LB04

Anti-CD20/BCMA Bispecific CAR-T Cell Therapy Promotes Immune Reset and Sustained Drug Free Remission in Refractory Autoimmune Diseases

Huihua Ding[1], Wensi Li[2], Yiwen Shen[3], Chunyan Zhang[4], Yan Ye[3], Ran Wang[3], Shaoying Yang[3], Chunmei Wu[3], Dai Dai[3], Chengxiao Zheng[2], Yuan Qian[2], Xiaobing Luo[5], Thule Trinh[5], Judy Zhu[2], Jiaqi Huang[5], Yong Hao[3], Xiaoying Yao[3], Zhenfen Ling[6], Yihong Yao[5] and Nan Shen[1], [1]Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, [2]Shanghai AbelZeta Ltd., Shanghai, China (People's Republic), [3]Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China (People's Republic), [4]Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, Shanghai, China, [5]AbelZeta Inc., Rockville, [6]Shanghai General Hospital, Shanghai, China (People's Republic)

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Refractory autoimmune diseases with progressive organ damage remain a major unmet medical need. C-CAR168 is an autologous anti-CD20/BCMA bispecific CAR-T therapy designed to simultaneously target autoantibody-producing plasma cells and their B-cell precursors, aiming to achieve a complete "immune reset". This first-in-human Phase I trial (NCT06249438) evaluates C-CAR168 in patients with treatment-refractory autoimmune diseases. Here, we report the trial's safety data and preliminary efficacy in the lupus nephritis (LN) and multiple sclerosis (MS) cohorts.

Methods: This Phase I, open-label study enrolled patients with refractory SLE (±LN), immune mediated necrotizing myositis (IMNM), neuromyelitis optica spectrum disorder (NMOSD), and MS, who had failed ≥2 standard immunosuppressive therapies. After lymphodepletion, patients received a single C-CAR168 infusion at either 0.75×10^6 or 1.5×10^6 CAR-T cells/kg.

Results: As of September 10, 2025, 16 patients were treated: 11 SLE (9 proliferative LN), 2 NMOSD, 2 progressive MS and 1 IMNM, with a median follow-up of 177 days. C-CAR168 was well tolerated. Grade 1-2 CRS occurred in 11/16 patients (68.8%) and resolved with supportive care. No ICANS or DLTs were observed. Grade ≥3 AEs were primarily hematologic and transient. Prolonged cytopenia and Grade 3 treatment-emergent infections each occurred in 2 patients (12.5%) and were successfully managed with standard therapies. All patients discontinued immunosuppressants (IS) / biologic agents, 12 (75%) achieved steroid discontinuation and 4 remained on corticosteroids ≤10 mg/day.

Robust efficacy was observed in the LN and SPMS patients. In proliferative LN (median 4 prior IS/ biologic agents, excluding steroids/HCQ), 7/9 patients achieved a renal response (77.8%), including 3 CR, 1 PERR and 3PR. Improvement in proteinuria was rapid (median 1M [range 1–3]), and continued to improve with longer follow-up. Improvement in extrarenal SLE activity, as measured by SRI-4, was achieved in 6/7 (85.7%) proliferative LN patients with ≥3M follow-up. The first SPMS patient showed significant improvement in gait and orbital movement, EDSS score, reductions in MRI lesion burden, and normalization of serum neurofilament light chain.

C-CAR168 expansion was accompanied by rapid depletion of $CD20^+$ B cells and plasma cells in blood, followed by naïve-dominant B-cell reconstitution in most patients by months 2-3, along with reductions in the type I IFN gene signature score. In one patient, bone marrow biopsy confirmed complete plasma cell depletion. Longitudinal examination of the B cell receptor repertoire (BCR) in 3 LN patients revealed a loss of clonally expanded BCRs with subsequent emergence of a naïve repertoire after treatment.

Conclusion: C-CAR168 therapy demonstrated durable treatment-free disease control in refractory autoimmune diseases. Its favorable safety profile, together with a renal response rate of 77.8% in refractory proliferative LN and rapid neurological improvement in SPMS, both achieved without background standard of care medications, coupled with mechanistic evidence of immune reset, provides a compelling rationale for further clinical evaluation of C-CAR168.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1 Summary of Safety of All Treated Patients, Baseline Characteristics and Clinical Response in the SLE Cohort

Overall safety	**N=16**
Treatment-related SAEs, n (%)	0
CRS, n (%)	
Any grade	11 (68.8)
Grade 1	10 (62.5)
Grade 2	1 (6.3)
Grade ≥3	0
ICANS, n (%)	0
Prolonged cytopenia, n (%)	2 (12.5)
Treatment emergent Grade ≥3 infection events, n (%)	2 (12.5)
SLE Cohort Profile with Efficacy	
Demographics, SLE history and baseline characteristics	**n=11**
Age (years), median (range)	32 (26-42)
Female, n (%)	10 (90.9)
SLE duration (years), median (range)	9 (3-16)
No of IS/biologic agents exposed (except steroids/HCQ), median (range)	4 (3-8)
SLEDAI-2K, median (range)	12 (8-24)
PGA, median (range)	1.5 (1.0-2.4)
Anti-dsDNA Ab (ELISA, IU/ml), median (range)	104.36 (29.18-405.08)
Low complement, n (%)	8 (72.7)
LN specific parameters and baseline characteristics	**n=10**
LN duration (years), median (range)	5 (2-16)
eGFR-CKD-EPI (ml/min × 1.73m^2), median (range)	113.65 (75.75-131.53)
24h UP (mg/24h), median (range)	2736.9 (1227.2-8156.9)
UPCR (mg/g), median (range)	2295.61 (1644.19-10841.93)
LN ISN/RPS, n (%)	
Proliferative LN	**9 (90.0)**
III+V	5 (50.0)
IV+V	3 (30.0)
III/IV+V	1 (10.0)
Membranous LN	**1 (10.0)**
V	1 (10.0)
Best renal response in LN patients, n (%)	**n=10**
CR (24h UPCR<500mg/g)	3 (30.0)
PERR (24h UPCR<700mg/g)	1 (10.0)
PR (24UPCR< 3000mg/g with a ≥50% from baseline)	3 (30.0)
Best renal response in proliferative LN, n (%)	**n=9**
CR (24h UPCR<500mg/g)	3 (33.3)
PERR (24h UPCR<700mg/g)	1 (11.1)
PR (24UPCR< 3000mg/g with a ≥50% from baseline)	3 (33.3)

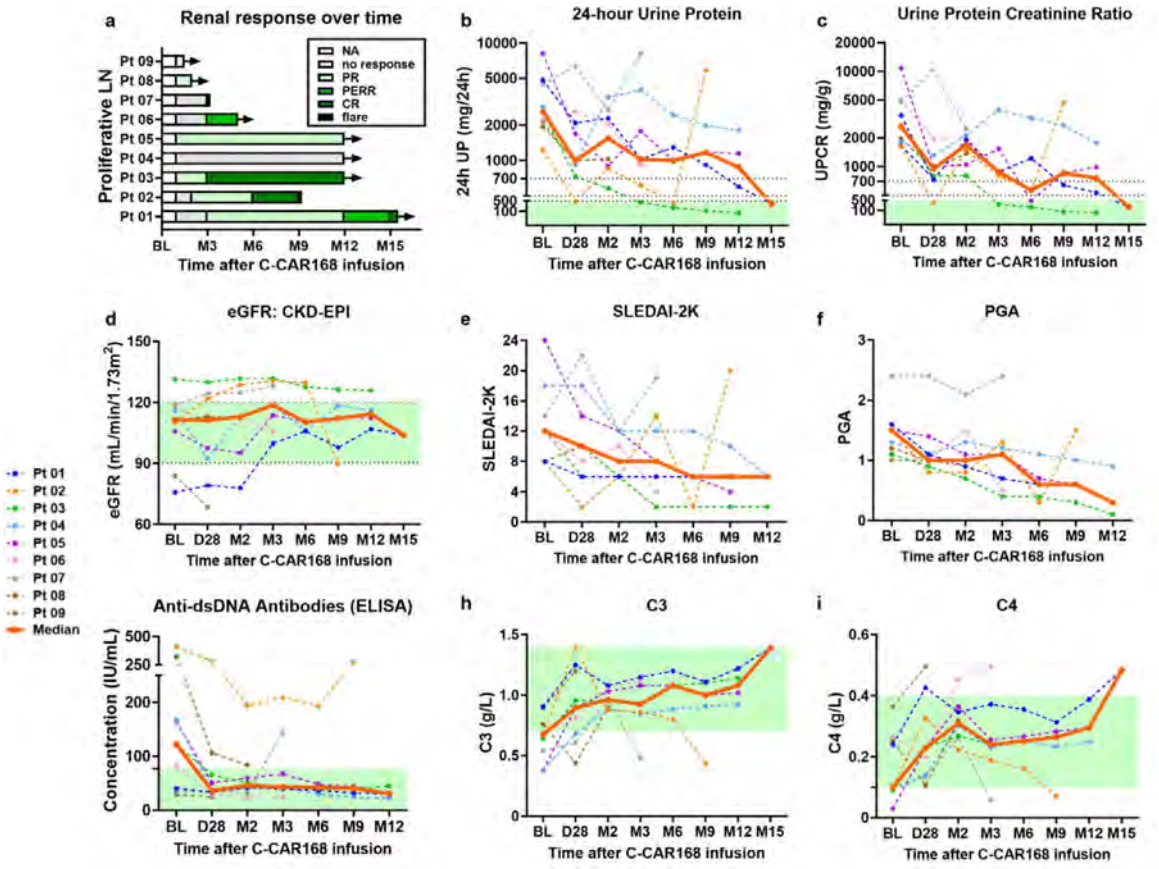


Figure 1: Clinical efficacy of C-CAR168 in nine proliferative LN patients. a: Renal response over time; **b**: 24h UP; c: UPCR; **d**: eGFR; **e**: SLEDAI2K score; **f**: PGA score; **g**: Anti-dsDNA levels; **h**: serum C3 level; **i**: serum C4 level.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

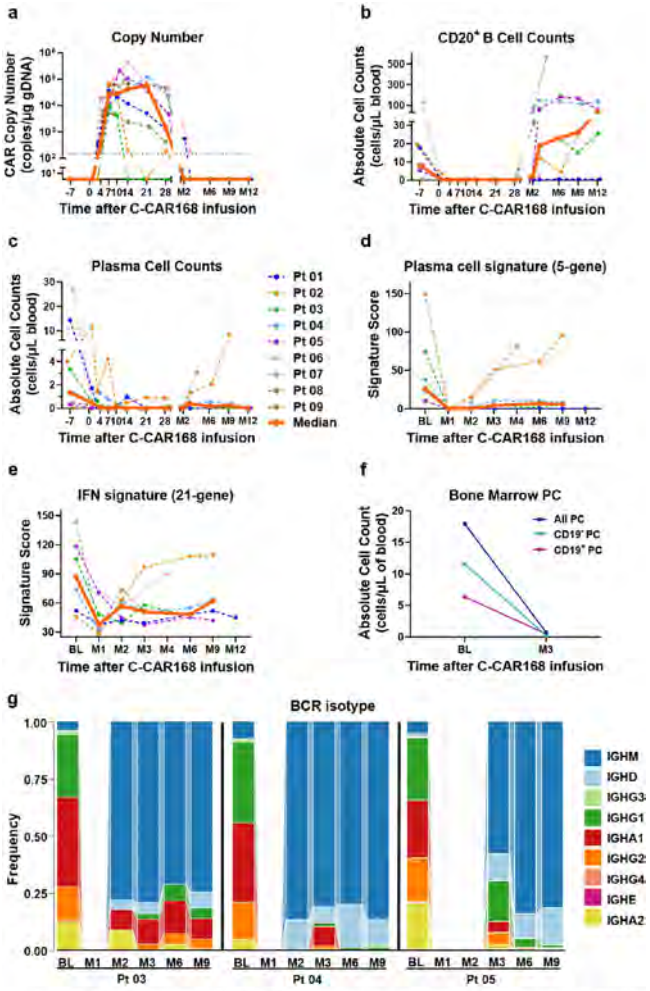


Figure 2: PK/PD profile of C-CAR168 in nine proliferative LN patients. a: Blood CAR-T copy number; **b:** Blood CD20+ B cells counts; **c:** blood plasma cell counts; **d:** blood plasma cell signature score; **e:** blood type I IFN signature score; **f:** count of bone marrow plasma cells from one patient; **g:** dynamic change of blood BCR isotype from three patients.

Disclosures: H. Ding: None; W. Li: Shanghai AbelZeta Ltd., 3; Y. Shen: None; C. Zhang: None; Y. Ye: None; R. Wang: None; S. Yang: None; C. Wu: None; D. Dai: None; C. Zheng: Shanghai AbelZeta Ltd., 3; Y. Qian: Shanghai AbelZeta Ltd., 3; X. Luo: AbelZeta Inc., 3; T. Trinh: AbelZeta Inc., 3; J. Zhu: Shanghai Abelzeta Ltd., 3; J. Huang: AbelZeta Inc., 3; Y. Hao: None; X. Yao: None; Z. Ling: None; Y. Yao: AbelZeta Inc., 3; N. Shen: None.

Abstract Number: LB05

ER Stress-Induced ATP2A3 Drives Rheumatoid Arthritis via Activation of STING Signaling

yujie cai, Nanfang hospital, Guangzhou, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by persistent synovial inflammation and joint bone destruction. Endoplasmic reticulum (ER) stress plays an important role in the pathogenesis of autoimmune diseases such as RA, yet the specific mechanism through which ER stress contributes to RA remains unclear. This study aims to investigate the role and mechanism of ER stress-related genes in promoting RA, with the goal of identifying novel therapeutic targets.

Methods: Transcriptomic data from six RA datasets were analyzed using Least Absolute Shrinkage and Selection Operator (LASSO) regression, Support Vector Machine-Recursive Feature Elimination (SVM-RFE), and Random Forest (RF) to identify ER stress-related genes (ERSRGs). Protein-level validation was conducted via Immunohistochemistry (IHC) on RA synovial tissues and control synovial tissues.The expression levels of ATP2A3, STING, TBK1, IRF3, and NF-κB in fibroblast-like synoviocytes (FLS) were detected by Western blot (WB).Cell invasion and migration abilities were assessed using Transwell assays. The levels of inflammatory cytokines IL-6, IL-1β, TNF-α, and IFN-γ were measured by ELISA.

Results: Seventeen ERSRGs were identified by intersecting differentially expressed genes (DEGs; n=1433) between RA and control samples with ERSRGs (n=267) from the Gene Ontology Consortium.Among the differentially expressed genes, ATP2A3—an ER stress-induced gene—was found to be significantly upregulated in RA. Overexpression of ATP2A3 in FLS promoted cell migration, invasion, and the release of inflammatory cytokines including IL-6, IL-1β, TNF-α, and IFN-γ. Furthermore, ATP2A3 facilitated the phosphorylation of STING, thereby activating the STING signaling pathway, which enhanced FLS invasion, migration, and inflammatory cytokine secretion.

Conclusion: This study demonstrates that the ER stress-induced gene ATP2A3 plays a crucial role in RA pathogenesis. ATP2A3 promotes the development and progression of RA by activating the STING signaling pathway. These findings highlight ATP2A3 as a potential therapeutic target for the treatment of RA.

Disclosures: y. cai: None.

Abstract Number: LB06

AgAIN Study: First Head-to-Head Trial of Secukinumab vs. Ustekinumab in TNFα Inhibitor-Experienced Psoriatic Arthritis Patients Reveals Better Efficacy Across Multiple Domains

Frank Behrens[1], Patrizia Sternad[2], Klaus Krueger[3], Christine App[4], Stephanie Lefevre[4] and Christiane Schiedel[4], [1]Department of Rheumatology, Frankfurt University Hospital, Frankfurt, Germany, [2]Medizinisches Versorgungszentrum für Rheumatologie Dr. M. Welcker GmbH, Planegg, Germany, [3]Rheumatologisches Praxiszentrum, München, Germany, [4]Novartis Pharma GmbH, Nürnberg, Germany

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Psoriatic arthritis (PsA) patients with prior failure or intolerance to TNFα inhibitors (TNFi) represent a clinically challenging population with limited therapeutic options. The AgAIN study (CAIN457FDE04; NCT04632927) is the first randomized, double-blind, active-controlled, multicenter trial directly comparing secukinumab (SEC) and ustekinumab (UST) in this population.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Methods: A total of 119 patients (pts) were randomized (SEC: 56, UST: 63; see Fig. 1 for Study Design) at 28 clinical centers in Germany. The mean age was 53.5 ± 11.0 years, with 15.1% of pts aged over 65. Female pts comprised 69.6% in the SEC group and 65.1% in the UST group. Body weight over 100 kg was observed in 30.4% of SEC pts and 22.2% of UST pts. All pts met the CASPAR criteria for PsA diagnosis (score ≥3). Key CASPAR features included current psoriasis (91.1% SEC, 82.5% UST), negative rheumatoid factor (100.0% SEC, 96.8% UST), and juxta-articular new bone formation (37.5% SEC, 31.7% UST). All pts had prior TNFi exposure and failed TNFi, with adalimumab (68.9%) being the most commonly used. Treatment discontinuation rates were notably higher in the UST group (25.4% vs. 3.6% SEC), primarily due to lack/loss of efficacy, with a mean ± SD duration of exposure of 24.3 ± 2.0 weeks for SEC vs. 21.5 ± 6.8 weeks for UST. Despite recruitment issues resulting in early recruitment termination, the study was successfully completed, offering descriptive analysis of comparative efficacy and safety.

Results: For the primary endpoint, HAQ-DI© response increased continuously over time in SEC group and was numerically higher than in UST group at all analyzed time points (see Figure 1), with a notably greater response rate of 57.1% (32/56 pts) for SEC vs. 27.0% (17/63 pts) for UST at week 28 [OR=3.647, 95% CI: 1.601–8.311; p=0.002;]. Further, SEC showed qualitatively better outcomes across all secondary and exploratory endpoints, see Table 1 for details. No new safety signals of secukinumab were identified. Treatment emergent adverse events (TEAEs) occurred in 76.8% (SEC; 43/56 pts) vs. 81.0% (UST; 51/63 pts); SAEs in 8.9% (SEC; 5/56 pts) vs. 3.2% (UST; 2/63 pts). TEAEs leading to discontinuation were seen in 3.6% in SEC arm (2/56 pts) and 12.7% in UST arm (8/63 pts).

Conclusion: AgAIN is the first study to provide head-to-head data comparing SEC and UST in TNFi-experienced PsA patients. SEC showed qualitatively better efficacy across all clinical and patient-reported outcomes (PRO), and safety signals in line with known safety profile. Notably, improvements in key clinical endpoints and PROS—including HAQ-DI, joint

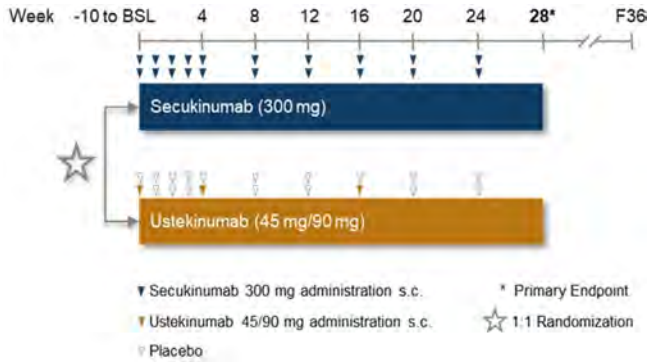


Figure 1: Study Design of AgAIN

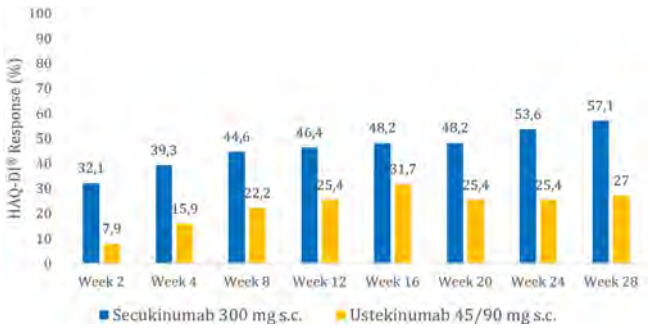


Figure 2: HAQ-DI© response over time

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1: Results of primary, secondary and some exploratory Endpoints at Week 28

Endpoint	SEC (%)	UST (%)
	Response (%) at Week 28	
HAQ-DI*	57.1	27.0
PASI 75/90/100	60.7 / 48.2 / 37.5	46.0 / 39.7 / 27.0
MDA / VLDA	35.7 / 14.3	22.2 / 7.9
ACR20/50/70	73.2 / 48.2 / 28.6	49.2 / 23.8 / 12.7
FACIT-Fatigue	71.4	50.8
Patient's assessment of pain intensity (VAS)*	69.6	44.4
Patient global assessment of disease activity (VAS)	76.8	55.6
Patient's assessment of psoriasis and arthritis disease activity (VAS)*	66.1	46.0
DLQI	53.6	50.8
	Mean Δ from Baseline to Week 28	
TJC / SJC (joints)	-9.6 / -6.8	-7.6 / -5.3
LEI / LDI / Dactylitis count	-0.9 / -9.7 / -1.3	-0.5 / -7.2 / -0.6
PsAQoL	-2.5	-2.0

Δ = mean change; PASI = Psoriasis Area and Severity Index; MDA = Minimal Disease Activity; VLDA = Very Low Disease Activity; ACR = American College of Rheumatology; FACIT = Functional Assessment of Chronic Illness Therapy; VAS = visual analog scale; DLQI = Dermatology Life Quality Index; TJC = tender 68 joint counts; SJC = swollen 66 joint count; LEI = Leeds Enthesitis Index; LDI = Leeds Dactylitis Index; PsAQoL = Psoriatic Arthritis Quality of Life
Improvement ≥15 mm in patient's assessment on VAS

counts, pain, and skin outcomes—were observed as early as Week 2 and sustained through Week 28. In conclusion, the results of this randomized controlled study highlight the benefit that secukinumab can offer for management of PsA in the described population.

Acknowledgement

We gratefully acknowledge the invaluable contributions of all of the study participants as well as all investigators & study personnel involved whose dedication and expertise made this clinical trial possible

Disclosures: F. Behrens: AbbVie, 2, 6, 12, Travel, ACELYRIN, INC., 2, 6, Amgen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, GSK, 2, 6, Janssen-Cilag, 2, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sandoz, 2, 6, UCB Pharma, 2, 6, 12, Travel; P. Sternad: None; K. Krueger: AbbVie/Abbott, 2, 6, alfasigma, 2, 6, Eli Lilly, 6, Novartis, 6; C. App: Novartis, 3; S. Lefevre: Novartis, 3; C. Schiedel: Novartis, 3.

Abstract Number: LB07

Adipose-Tissue Derived Mesenchymal Stem Cells vs Hyaluronic Acid in Refractory Knee Osteoarthritis in a low-resource setting: A Phase IIb RCT

Moshiur Rahman Khasru[1], Mohammad Tariqul Islam[2], AGM Zakaria Nazimuddin Jubery[3], Mahbuba Shirin[4], Fazle Rabbi Chowdhury[5], Tangila Marzen[6], Nafi Uzzaman[7], Md Abu Bakar Siddiq[8], Md Ashraful Hoque[9], Masuda Begum[10], Md Moniruzzaman Khan[2] and Abul Salek[11], [1]Musculoskeletal Medicine and Interventional Physiatry Division, Bagladesh Medcial University, Dhaka, Bangladesh, [2]Department of Physical Medicine and Rehabilitation, Bangladesh Medical University, Dhaka, Bangladesh, [3]Department of Burn and Plastic Surgery, Dhaka Medcial College and Hospital, Dhaka, Bangladesh, [4]Department of Radiology and Imaging, Bangladesh Medical University, Dhaka, Bangladesh, [5]Department of Internal Medicine, Bangladesh Medical University, Dhaka, Bangladesh, [6]Department of Anatomy, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, [7]Stem Cell Rearch Group, Department of Physical Medicine and Rehabilitation, Bangladesh Medical University, Dhaka, Bangladesh, [8]Department of Rheumatology, Royal North Shore Hospital, Faculty of Medicine, University of Sydney, New South Wales, Australia, [9]Department of Transfusion Medicine, Cumilla Medical College, Cumilla, Bangladesh, [10]Department of Haematology, Banglabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, [11]Department of Physical Medicine and Rehabilittaion, Bangladesh Medical University, Dhaka, Bangladesh

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Knee osteoarthritis (KOA) is a leading cause of disability, with no available disease-modifying treatments. While Hyaluronic Acid (HA) remains widely used, there is little to no head-to-head randomised evidence comparing HA with adipose-derived mesenchymal stem cells (AdMSC) therapy. This evaluator-blinded, phase IIb trial compared the efficacy, safety and dose response of autologous adipose-derived mesenchymal stem cells (AdMSC) versus intermediate molecular-weight HA in patients with refractory primary KOA in Bangladesh.

Methods: Seventy-three participants with Kellgren-Lawrence grade ≥2 KOA on standard conservative care were randomised to receive HA injection (n=31), a single-dose AdMSC injection (n=21), or two-dose AdMSC injections (n=21, dose interval 3 months). Primary outcomes included pain on VAS, knee-related problems on KOOS, femoral cartilage thickness utilising ultrasound scan, and MRI-assessed cartilage defects (MOAKS) at baseline, 6, and 12 months involving a multidisciplinary clinical team.

Table 1: Summary of the baseline clinical characteristics of the study population (N=73). SD, standard deviation, VAS, visual analogue scale (0-10; 0 indicates no pain and 10 indicates worst pain), KOOS, The Knee Injury and Osteoarthritis Outcome Score (0-100 with 0 representing extreme knee problems and 100 representing no knee problems).

Table 1: Summary of the baseline clinical characteristics of the study population (N=73)

Clinical Characteristics		Active Control HA (n=31)	Single-dose AdMSC (n=21)	Two-dose AdMSC (n=21)
Mean Age in years		60.81±8.14	60.76±6.69	58.10±5.67
Female (n, %)		10 (32.26)	10 (46.62)	12 (57.14)
Height in centimetres		161.65±4.31	160.90±6.27	158.24±5.42
Weight in kg		68.10±6.06	71.33±5.29	66.81±10.41
Body Mass Index (BMI) kg/meter²		26.12±2.73	27.65±2.76	26.84±4.93
Presence of any Comorbidity (n, %)		19 (61.29)	11 (52.38)	14 (66.67)
KL grade in the Right Knee (n, %)	Grade 2	6 (19.35)	4 (19.05)	4 (19.05)
	Grade 3	22 (70.97)	13 (61.90)	16 (76.19)
	Grade 4	3 (9.68)	4 (19.05)	1 (4.76)
KL grade in the Left Knee (n, %)	Grade 2	7 (22.58)	4 (19.05)	7 (33.33)
	Grade 3	23 (74.19)	13 (61.90)	14(66.67)
	Grade 4	1 (3.23)	4 (19.05)	0 (0.00)
Baseline pain intensity on the visual analogue scale (VAS, 0-10) in the Right Knee		5.32±0.87	5.29±0.64	5.67±0.58
Baseline pain intensity on the visual analogue scale (VAS, 0-10) in the Left Knee		5.35±0.88	5.52±0.51	5.29±0.78
Baseline total KOOS score (0-100) in the Right Knee		45.55±8.19	44.86±9.85	45.52±5.29
Baseline total KOOS score (0-100) in the Left Knee		45.87±8.72	44.76±8.47	46.29±5.84
Mean Femoral Cartilage Thickness on HFUS in the Right Knee in millimetres		1.71±0.27	1.68±0.25	1.78±0.28
Mean Femoral Cartilage Thickness on HFUS in the Left Knee in millimetres		1.80±0.23	1.65±0.24	1.77±0.33
Right Knee's Mean Cartilage Defect in MRI in per cent	Medial Tibiofemoral Joint	49.03±6.38	54.52±10.94	50.95±7.35
	Lateral Tibiofemoral Joint	49.35±5.74	54.05±11.02	51.67±8.11
	Patellofemoral Joint	19.19±5.10	21.43±4.23	20.48±4.98
Left Knee's Mean Cartilage Defect in MRI in per cent	Medial Tibiofemoral Joint	49.35±6.16	54.52±10.94	50.95±7.35
	Lateral Tibiofemoral Joint	49.52±4.72	53.81±10.36	51.19±7.23
	Patellofemoral Joint	19.74±5.36	22.38±4.07	21.43±6.55

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2: Distribution of changes in treatment outcomes at 6 months

Outcome measures	Knee Side			Active-Control HA (n=31) Mean±SD	Single-dose AdMSC (n=21) Mean±SD	Two-dose AdMSC (n=21) Mean±SD	P value
Pain intensity on VAS (0-10 cm) Left Knee	Right Knee	Baseline		5.32±0.87	5.29±0.64	5.67±0.58	0.172
		At 6 months		3.94±1.09	2.86±0.85	2.19±0.40	<0.0001
		Changes over 6 months		-1.39±0.99	-2.43±0.81	-3.48±0.60	<0.0001
	Left Knee	Baseline		5.35±0.88	5.52±0.51	5.29±0.78	0.579
		At 6 months		4.06±1.03	2.67±0.73	2.33±1.06	<0.0001
		Changes over 6 months		-1.29±1.01	-2.86±0.73	-2.95±1.02	<0.0001
	Overall VAS score changes at 6 months			**-1.34±0.93**	**-2.64±0.62**	**-3.21±0.73**	**<0.001**
Knee Functioning on KOOS (0-100)	Right Knee	Baseline		45.55±8.19	44.86±9.85	45.52±5.29	0.948
		At 6 months		57.32±9.10	61.67±7.07	67.24±7.42	<0.001
		Changes over 6 months		11.77±8.88	16.81±7.52	21.71±6.01	<0.001
	Left Knee	Baseline		45.87±8.72	44.76±8.47	46.29±5.84	0.810
		At 6 months		56.71±9.10	62.10±7.07	67.05±8.73	<0.001
		Changes over 6 months		10.84±9.48	17.33±9.15	20.76±5.71	<0.001
	Overall KOOS score changes at 6 months			**11.31±8.92**	**17.07±8.19**	**21.24±5.58**	**<0.001**
Femoral Cartilage Thickness on HFUS Scan	Right Knee	Baseline		1.71±0.27	1.68±0.25	1.78±0.28	0.480
		At 6 months		1.67±0.25	1.79±0.25	1.97±0.30	<0.001
		Changes over 6 months		-0.04±0.16	0.11±0.15	0.19±0.17	<0.001
	Left Knee	Baseline		1.80±0.23	1.65±0.24	1.77±0.33	0.115
		At 6 months		1.73±0.20	1.77±0.24	2.07±0.45	<0.001
		Changes over 6 months		-0.07±0.14	0.11±0.17	0.30±0.25	<0.001
	Overallb femoral Cartilage Changes at 6 months			**-0.05±0.14**	**0.11±0.16**	**0.25±0.18**	**<0.001**
Cartilage Defect on MRI using MOAKS Score	Right Knee	Medial TF Joint	Baseline	49.35±5.74	54.05±11.02	51.67±8.11	0.136
			At 6 months	49.03±8.70	45.24±12.09	40.00±10.25	0.010
			Changes over 6 months	0.00±7.07	-9.29±8.70	-10.95±7.68	<0.001
		Lateral TF Joint	Baseline	49.35±5.74	54.05±11.02	51.67±8.11	0.136
			At 6 months	47.58±6.44	45.71±11.54	40.48±11.70	0.034
			Changes over 6 months	-1.18±5.41	-8.33±6.95	-11.19±6.87	<0.001
		PF Joint	Baseline	19.19±5.10	21.43±4.23	20.48±4.98	0.184
			At 6 months	18.71±5.32	17.14±4.63	15.24±5.36	0.064
			Changes over 6 months	-0.48±2.99	-4.29±3.64	-5.24±4.88	<0.001
		Mean change in cartilage damage of Right knee at 6 months		**-0.75±4.55**	**-7.30±5.95**	**-9.13±5.57**	**<0.001**
	Left Knee	Medial TF Joint	Baseline	49.35±6.16	54.52±10.94	50.95±7.35	0.084
			At 6 months	48.87±8.73	45.00±11.73	40.00±10.25	0.011
			Changes over 6 months	-4.84±7.07	-9.52±8.35	-10.95±7.68	<0.001
		Lateral TF Joint	Baseline	49.52±4.72	53.81±10.36	51.19±7.23	0.113
			At 6 months	47.58±7.06	45.95±11.14	40.71±11.10	0.042
			Changes over 6 months	-1.94±6.67	-7.86±6.81	-10.48±8.20	<0.001
		PF Joint	Baseline	19.74±5.36	22.38±4.07	21.43±6.55	0.212
			At 6 months	18.71±5.31	16.90±4.32	15.00±5.24	0.034
			Changes over 6 months	-1.03±2.99	-5.48±4.45	-6.43±5.73	<0.001
		Mean change in cartilage damage of left knee at 6 months		**-0.75±4.55**	**-7.30±5.95**	**-9.13±5.57**	**<0.001**
	Overall changes in cartilage damage at 6 months			**-0.75±4.55**	**-7.30±5.95**	**-9.13±5.57**	**<0.001**

Changes in pain on VAS, knee damage on KOOS, femoral cartilage thickness on ultrasound, and cartilage defect on MOAKS at 6 months

Results: Interim analysis revealed significant, dose-dependent improvements. Two-dose AdMSC resulted in greater pain reduction (3.2 vs. 1.3 points) and functional improvement (21.24 vs. 11.31 points) compared to HA at 6 months ($p < 0.001$). Cartilage thickness increased (0.25±0.18mm) and defects improved (9.13%) with two-dose AdMSC, whereas the HA group showed deterioration (-0.06±0.14mm; 0.75%). Single-dose AdMSC also showed better outcomes than HA. No baseline predictors were identified, and all treatments were well-tolerated.

Conclusion: Two-dose AdMSC therapy significantly outperformed HA and single-dose AdMSC in improving pain, function, and cartilage structure, indicating its potential as a disease-modifying treatment for KOA. These results support advancing to larger phase III trials, particularly in South Asia, where KOA is a growing health burden. (www.clinicaltrials.gov: NCT05783154, IRB approval reference: BSMMU/2024/1192/registration/742).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

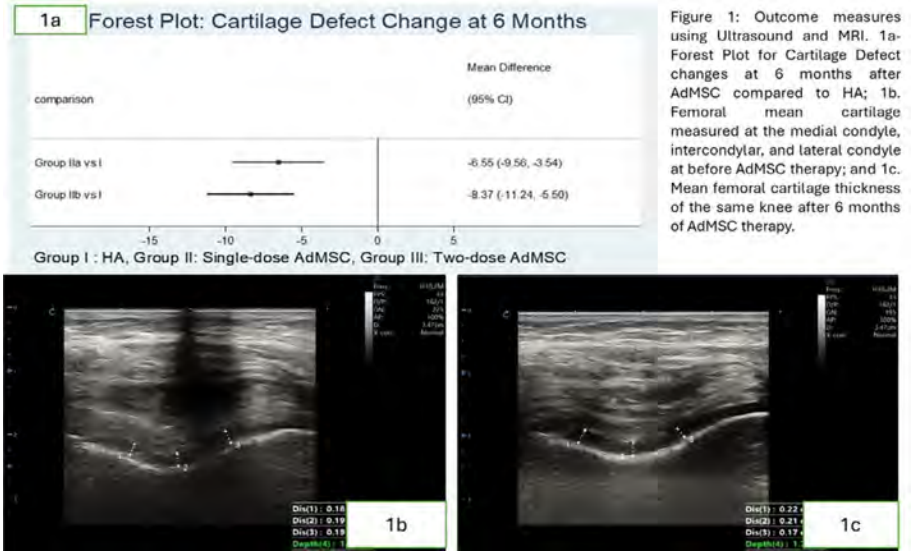


Figure 1: Outcome measures using Ultrasound and MRI. 1a- Forest Plot for Cartilage Defect changes at 6 months after AdMSC compared to HA; 1b. Femoral mean cartilage measured at the medial condyle, intercondylar, and lateral condyle at before AdMSC therapy; and 1c. Mean femoral cartilage thickness of the same knee after 6 months of AdMSC therapy.

Figure 1: Forest plot for changes in articular cartilage defect in the knee of single-dose AdMSC and two-dose AdMSC compared to HA. Changes in femoral cartilage thickness of a two-dose AdMSC recipient at 6 months.

Disclosures: M. Khasru: None; M. Islam: None; A. Jubery: None; M. Shirin: None; F. Chowdhury: None; T. Marzen: None; N. Uzzaman: None; M. Siddiq: None; M. Hoque: None; M. Begum: None; M. Khan: None; A. Salek: None.

Abstract Number: LB08

Efficacy and Safety of Izokibep, a Novel IL-17A Inhibitor, in Patients with Active Psoriatic Arthritis: Week 52 Results from a Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase 2b/3 Study

Philip Mease[1], Frank Behrens[2], Alan Kivitz[3], Edit Drescher[4], Piotr Klimiuk[5], Howard Sofen[6], Nehad Soloman[7], Shephard Mpofu[8], Fredrik Frejd[9] and Peter Taylor[10], [1]Swedish Medical Center/Providence St. Joseph Health, Seattle, Washington, [2]Department of Rheumatology, Frankfurt University Hospital, Frankfurt, Germany, [3]Altoona Arthritis and Osteoporosis Center, Altoona Center for Clinical Research, Duncansville, Pennsylvania, [4]Vital Medical Center Rheumatology, Veszprém, Hungary, [5]Department of Rheumatology and Internal Diseases, Medical University of Bialystok, Bialystok, Poland, [6]Department of Medicine/Dermatology, David Geffen UCLA School of Medicine, Los Angeles, California, [7]Midwestern University Arizona College of Osteopathic Medicine and Arizona Arthritis and Rheumatology Associates, Phoenix, Arizona, [8]ACELYRIN, INC., Agoura Hills, California, [9]Affibody Medical AB, Solna, Sweden, [10]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

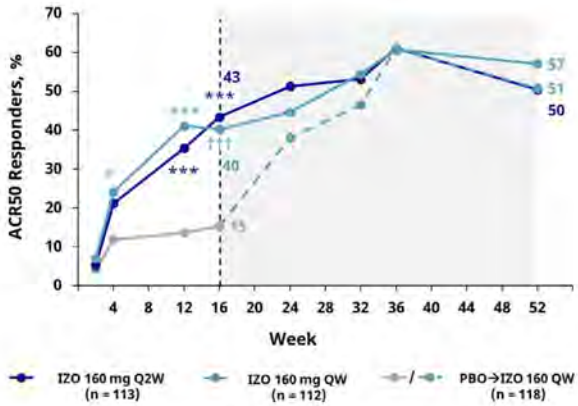
SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: PsA is a chronic, systemic, inflammatory musculoskeletal disease in which dysregulated IL-17A activity plays a pivotal role in disease pathogenesis. Izokibep (IZO) is an Affibody® molecule (small protein therapeutic; 18.6 kDa) designed to inhibit IL-17A with high potency through tight selective binding. In a phase 2b/3 study in patients (pts) with active PsA, IZO was well tolerated and demonstrated improved efficacy vs placebo (PBO) across multiple disease domains including the study primary endpoint of ACR50 at week (wk) 16. Here, we report the efficacy and safety of IZO from the phase 2b/3 study through wk 52.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. ACR50 Response Over 52 Weeks



Full analysis set; nonresponse imputation. Dashed line and gray shading indicate crossover from PBO to active treatment (IZO QW).

Statistical significance per the prespecified testing hierarchy: ‡‡‡ P<0.001 vs PBO. Nominal P-value: * P<0.05, *** P<0.001 vs PBO.

IZO, izokibep; PBO, placebo; Q2W, every 2 weeks; QW, every week.

Methods: In this study (NCT05623345; Study 22104), eligible pts had adult-onset active PsA (duration ≥6 months and ≥3 tender/swollen joints) and an inadequate response, intolerance, or contraindication to an NSAID, conventional synthetic DMARD, and/or TNF inhibitor. During the 16-wk PBO-controlled treatment period, pts were equally randomized to IZO 160 mg every 2 wks (Q2W), IZO 160 mg every wk (QW), or PBO QW. At wk 16, pts originally randomized to IZO kept receiving IZO per their original dose and schedule; pts receiving placebo were switched to IZO 160 mg QW. Wk 52 results are reported.

Results: A total of 343 pts were included (IZO Q2W, n = 113; IZO QW, n = 112; PBO→IZO QW, n = 118). The mean (SD) age was 49.5 (13.3), 51.8 (12.2), and 52.6 (11.7) years, BMI was 30.5 (6.6), 29.1 (5.9), and 29.7 (6.0) kg/m^2, and time

Table 1. Efficacy Results

	IZO 160 mg Q2W (n = 113)		IZO 160 mg QW (n = 112)		PBO QW→IZO 160 mg QW (n = 118)	
	Week 16	Week 52	Week 16	Week 52	Week 16	Week 52
ACR50	43***	50	40‡‡‡	57	15	51
ACR20	64***	70	59***	65	35	63
ACR70	23***	36	25***	42	5	42
PASI90[a]	58***	63	64‡‡‡	69	12	65
PASI100[a]	47***	55	51***	64	12	58
MDA	42***	47	41***	52	14	47
PsAID-9[b]	42***	55	38***	50	12	48
HAQ-DI, LS mean CFB	−0.30*	−0.41	−0.31**	−0.43	−0.14	−0.37
LEI=0[c]	56	57	45	50	47	59

Data are reported using nonresponse imputation analysis and as % unless otherwise indicated. ‡‡‡ P<0.001 vs placebo. Nominal P-value: * P<0.05, ** P<0.01, *** P<0.001 vs PBO.

[a]In patients with BL psoriasis body surface area ≥3%.

[b]≥3-unit improvement in patients with BL PsAID ≥3.

[c]In patients with baseline LEI >0.

BL, baseline; CFB, change from BL; HAQ-DI, Health Assessment Questionnaire-Disability Index; IZO, izokibep; LEI, Leeds Enthesitis Index; LS, least squares; MDA, minimal disease activity; PASI90/100, ≥90%/100% improvement in the Psoriasis Area and Severity Index score; PBO, placebo; PsAID-9, Psoriatic Arthritis Impact of Disease 9-item questionnaire; Q2W, every 2 weeks; QW, every week.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

since diagnosis was 6.2 (6.8), 6.9 (8.0), and 7.1 (6.9) years for IZO Q2W, IZO QW, and PBO→IZO QW, respectively; 59%, 57%, and 43% of pts were male. Baseline (BL) disease characteristics were generally similar across groups. After wk 16, continued improvement was seen for pts randomized to either IZO group and rapid improvement was observed in pts following crossover from PBO (**Figure 1**); by wk 52, approximately half of pts achieved ACR50 (IZO Q2W, 50%; IZO QW, 57%; PBO→IZO QW, 51%). Notable percentages of pts in all groups also achieved the high-hurdle endpoints of ACR70 (36%, 42%, 42%), PASI90 (63%, 69%, 65%), PASI100 (55%, 64%, 58%), and minimal disease activity (MDA; 47%, 52%, 47%) at wk 52 (**Table 1**). Improvements in quality of life measures were also observed across groups (**Table 1**). Overall, more than half of pts with BL enthesitis achieved resolution at wk 52 (**Table 1**). Treatment-emergent adverse events (TEAEs) occurred in 81%, 88%, and 82% of pts receiving IZO Q2W, IZO QW, and PBO→IZO QW, respectively, through wk 52; the most common TEAEs were injection-site erythema and pruritus and nasopharyngitis. The majority of TEAEs were mild to moderate in severity, with serious TEAEs reported at low rates (IZO Q2W 7%; IZO QW 4%; PBO→IZO QW 4%). Rates of ulcerative colitis (0%, 1%, 0%) and oral candidiasis (1%, 1%, 0%) were also low. There were no deaths or reports of suicidal ideation.

Conclusion: IZO demonstrated durable efficacy across several measures of PsA disease activity over 52 wks. Substantial percentages of pts originally randomized to IZO or switching from PBO to IZO achieved ACR50/70, PASI 90/100, and MDA by the end of the study. IZO treatment was well tolerated, with a safety profile generally consistent with that of legacy IL-17A inhibitors.

Disclosures: P. Mease: AbbVie, 2, 5, 6, ACELYRIN, INC., 2, 5, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, Century Therapeutics, 2, Cullinan Biotech, 2, Eli Lilly, 2, 5, 6, Genascence, 1, GRAPPA, 12, Leadership/fudiciary role, Immagene, 2, Johnson & Johnson, 2, 5, 6, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, 5, OMERACT, 12, Leadership/fudiciary role, Pfizer, 2, SPARTAN, 12, Leadership/fudiciary role, Takeda, 2, 5, UCB Pharma, 2, 5, 6; F. Behrens: AbbVie, 2, 6, 12, Travel, ACELYRIN, INC., 2, 6, Amgen, 2, 6, Boehringer-Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, GSK, 2, 6, Janssen-Cilag, 2, 6, MoonLake Immunotherapeutics, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sandoz, 2, 6, UCB Pharma, 2, 6, 12, Travel; A. Kivitz: AbbVie, 2, 6, Amgen, 12, Stock, Aurinia Pharmaceuticals, 2, Bristol-Myers Squibb, 2, Coval Biopharma, 2, Ecor1 Capital, 2, Eli Lilly, 6, Excel Continuing Education, 6, Genzyme, 2, Gilead Sciences, 2, 12, Stock, Grunenthal, 2, GSK, 2, 6, 12, Stock, Halia, 2, Horizon Therapeutics, 2, Innovaderm, 2, Janssen, 1, 2, MoonLake Immunotherapeutics, 2, Novartis, 2, 12, Stock, Pacira, 2, Pfizer, 6, 12, Stock, Prime, 12, Educational role, 12, Educational role, Prometheus Laboratories, 2, Sanofi-Regeneron, 6, Santa Ana Bio, Inc., 2, Synact, 2, Takeda-Nimbus, 1, 2, Tonix Pharmaceuticals, 1, UCB Pharma, 1, 2, 6, VYNE, 2, XBiotech, 2, Xencor, 2; E. Drescher: None; P. Klimiuk: None; H. Sofen: None; N. Soloman: None; S. Mpofu: ACELYRIN, INC., 3, 12, Stock from ACELYRIN, INC. (wholly owned subsidiary of Alumis, Inc.); F. Frejd: Affibody AB, 3, Affibody Medical AB, 12, Stock; P. Taylor: AbbVie, 2, ACELYRIN, INC., 2, Alfasigma, 2, 5, Aqtual, 2, Biogen, 2, Eli Lilly, 2, Fresenius Kabi, 2, Gilead Sciences, 2, Immunovant, Inc., 2, 12, Drug and Safety Monitoring committee, Janssen, 2, MoonLake Immunotherapeutics, 12, Drug and Safety Monitoring board, Nordic Pharma, 2, Roche, 2, Sanofi, 12, Drug and Safety Monitoring board, Takeda, 2, UCB Pharma, 2.

Abstract Number: LB09

Rotation or Change of Biologic After TNF blocker treatment failure for axial Spondyloarthritis

Elisa Dalix[1], Philippe Goupille[2], Daniel Wendling[3], Christian Roux[4], Jean-Hughes Samon[5], Olivier Brocq[6], Anne Tournadre[7], Arnaud Constantin[8], Maxime Breban[9], Gregoire Cormier[10], Tristan Pascart[11], Thierry Lequerre[12], Pascal Claudepierre[13], Eric Lespessailles[14], Benoit Legoff[15], Jeremie Sellam[16], Athan Baillet[17], Thierry Schaeverbeke[18], Stephan Pavy[19], Valerie Devauchelle-Pensec[20], Elisabeth Gervais[21], Laure Gossec[22], Corinne Miceli[23], Yves-Marie Pers[24], Cedric Lukas[25], Renaud Felten[26], Beatrice Bouvard[27], Amelie Denis[28], Emmanuelle Dernis[28], Emilie Presles[29], Florence Rancon[29] and Hubert Marotte[30], [1]Université Jean Monnet, CHU Saint-Etienne, Mines Saint-Etienne, INSERM,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Saint-Etienne, France, [2]Department of Rheumatology and INSERM-CIC[1415], University Hospital of Tours, EA [7501] GICC, University of Tours, Tours, France, [3]Rhumatologie, CHU de Besançon, Besancon, France, [4]Service de rhumatologie, CHU de Nice, IbV, Université Cote d'Azur, Nice, France, [5]Service de Rhumatologie, Hôpital Maison Blanche, Centre Hospitalier Universitaire de Reims, Reims, France; Université de Reims Champagne-Ardenne, Faculté de Médicine, EA [3797], Reims, France, [6]Rheumatology Department, CHPG Monaco, Monaco, Monaco, [7]Rheumatology Department, CHU Clermont-Ferrand, Clermont-Ferrand, France, [8]Rheumatology Center, Toulouse University Hospital, Toulouse, France, [9]INSERM UMR[1173], INFLAMEX, Laboratoire d'Excellence, Rheumatology Division, Ambroise Paré Hospital (AP-HP), Paris, France, [10]Rheumatology, Centre Hospitalier Departemental Vendee, La Roche-sur-Yon, France, [11]Department of Rheumatology, Université Catholique de Lille Hôpital Saint Philibert, Lomme, France, [12]Department of Rheumatology & CIC-CRB [1404], Inserm, PANTHER UMR [1234], University of Rouen Normandie, Normandie University, CHU Rouen, Rouen, France, [13]AP-HP, Henri-Mondor Hospital, Department of Rheumatology, EpiDermE, Université Paris Est Créteil, Créteil, France, [14]Translational Medicine Research Platform, PRIMMO, University Hospital Centre of Orleans, Orleans, France, [15]Nantes Université, ONIRIS, Univ Angers, CHU Nantes, INSERM, Regenerative Medicine and Skeleton, RMeS, UMR [1229], Nantes, France, [16]Rheumatology Department, Sorbonne Université, Saint-Antoine Hospital Assistance Publique Hôpitaux de Paris (AP-HP), Centre de Recherche Saint-Antoine (CRSA) Inserm UMRS-[938], Paris, France, [17]Université Grenoble Alpes, [4]UMR[5525], Grenoble, France, [18]Department of Rheumatology, Hôpital Pellegrin, Bordeaux, France, [19]Department of Rheumatology, Hôpital Bicêtre, Assistance Publique - Hôpitaux de Paris, Le Kremlin-Bicetre, [20]Department of Rheumatology, Université de Bretagne Occidentale, CHU Brest, INSERM (U[1227]), LabEx IGO, Brest, France, [21]LITEC, Université de Poitiers, CHU Poitiers, Poitiers, France, [22]Sorbonne Université, AP-HP & EULAR, Paris, France, [23]Immunoregulation Unit, Institut Pasteur, Cochin AP-HP, Paris, France, [24]IRMB, University of Montpellier, Inserm U[1183], CHU Montpellier, Montpellier, France, [25]Rheumatology department, CHU and University of Montpellier, Montpellier, France; UMR UA[11] Inserm (IDESP), University of Montpellier, Montpellier, France, [26]Service de Rhumatologie, CHU de Strasbourg - Hôpital de Hautepierre, Strasbourg, France, [27]Rhumatologie, Centre Hospitalier Universitaire, Angers, France, [28]CH Le Mans, Le Mans, France, [29]CHU Saint-Etienne, CIC [1408], Saint-Etienne, France, [30]Université Jean Monnet, CHU de Saint-Etienne, CIC [1408], Mines Saint-Etienne, INSERM, SSINBIOSE [1059], Saint-Etienne, France

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Axial spondyloarthritis (axSpA) is initially treated with non-steroidal anti-inflammatory drugs. In case of inadequate response, ACR/EULAR recommend biological disease-modifying antirheumatic drugs (bDMARDs). Up to 2015, TNF inhibitors (TNFi) were the only available option. Since then, IL-17A inhibitors (IL-17Ai) have also demonstrated efficacy. The 2022 ASAS-EULAR guidance proposes switching an alternative bDMARD after TNF inhibitors failure without mandating a change of mechanism of action. Therefore, we designed a randomized multicenter clinical trial to identify the most effective treatment after a first TNFi failure in axSpA, comparing an IL-17Ai to a second TNFi.

Methods: The ROC-SpA (Rotation Or Change of biologics after first TNFi treatment failure in axSpA patients) study is a prospective, randomized, multicenter, open-label, superiority, phase IV trial. Patients with active axSpA (BASDAI >4 or ASDAS >3.5), an inadequate 3-month response to a first TNFi, and stable doses of conventional synthetic (cs)DMARDs, oral corticosteroids, and/or NSAIDs for at least one month were enrolled across 31 centers in France and Monaco. Patients were randomized to receive either an IL-17Ai or a second TNFi. The primary outcome was the ASAS40 response at week 24. Secondary outcomes were ASAS 40 at weeks 12 and 52, other clinical assessments (ASAS20, partial remission rate, ASDAS major improvement rate) at weeks 12, 24, and 52. The primary analysis was performed at the end of the study according to the intent-to-treat principle.

Results: Baseline characteristics of the enrolled patients are shown in Table 1. Both drug options led to similar rates of response ASAS40 at week 24 (15.2% for IL-17Ai and 14.5% for TNFi (14.5%), thus the primary outcome assessing the superiority of IL-17Ai was not achieved (Figure 1). No statistically significant difference was observed between groups for other secondary endpoints. ASDAS declined similarly in both groups to 2.6 (1.0) at week 12, 2.5 (0.9) at week 24, and 2.3 (1.0) at the end of follow-up. On-treatment maintenance at week 54 was 62.8% with IL-17Ai and 54.9% with TNFi. No

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Main characteristics of the patients at baseline

	IL-17A inhibitors (N=158)	Anti-TNF inhibitors (N=142)	All (N=300)
Age, mean (SD), years	46.2 (12.4)	44.4 (12.7)	45.4 (12.6)
Male, n (%)	72 (45.6%)	76 (53.5%)	148 (49.3%)
HLA-B27 positive, n (%)	88 (59.1%)	78 (59.1%)	166 (59.1%)
Time between diagnosis and randomization, mean (SD), years	7.8 (8.1)	7.0 (8.4)	7.4 (8.2)
Smoking status, n (%)			
Former	45 (28.5%)	31 (21.8%)	76 (25.3%)
Current	54 (34.2%)	50 (35.2%)	104 (34.7%)
ax-Spa subtypes			
nr-axSpa	65 (40.4%)	61 (43.0%)	126 (42%)
AS	93 (59.6%)	81 (57.0%)	174 (58%)
BASDAI, mean (SD)	6.2 (1.5)	6.1 (1.4)	6.1 (1.4)
ASDAS, mean (SD)	3.2 (0.8)	3.2 (0.8)	3.2 (0.8)
BASFI, mean (SD)	4.3 (2.3)	4.5 (2.3)	4.4 (2.3)
CRP, mean (SD), mg/L	7.9 (13.5)	8.8 (16.0)	8.3 (14.7)
BMI, mean (SD), kg/m²	26.5 (5.3)	25.8 (5.1)	26.2 (5.2)
First anti-TNF duration, mean (SD), months	33.8 (45.9)	31.1 (42.7)	32.5 (44.3)
Causes of failure to the first anti-TNF, n (%)			
Primary nonresponse	47 (29.7%)	38 (26.8%)	85 (28.3%)
Secondary nonresponse	99 (62.7%)	93 (65.5%)	192 (64.0%)
Side effect	12 (7.6%)	11 (7.7%)	23 (7.7%)
Previous TNFi, n (%)			
Adalimumab	83 (52.5%)	71 (50.0%)	154 (51.3%)
Etanercept	34 (21.5%)	33 (23.2%)	67 (22.3%)
Golimumab	23 (14.6%)	18 (12.7%)	41 (13.7%)
Certolizumab	10 (6.3%)	11 (7.7%)	21 (7.0%)
Infliximab	8 (5.1%)	9 (6.3%)	17 (5.7%)
Treatment during the study, n (%)			
Adalimumab		52 (36.6%)	-
Etanercept		36 (25.4%)	-
Golimumab		32 (22.5%)	-
Certolizumab		21 (14.8%)	-
Infliximab		1 (0.7%)	-
Secukinumab		-	121 (77.6%)
Ixekizumab		-	35 (22.4%)

SD: standard deviation, HLA: human leucocyte antigen, axSpA: axial spondyloarthritis, nr: non-radiographic, AS: ankylosing spondylitis, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, BASFI: Bath Ankylosing Spondylitis Functional Index, CRP: C-reactive protein, BMI, body mass index.

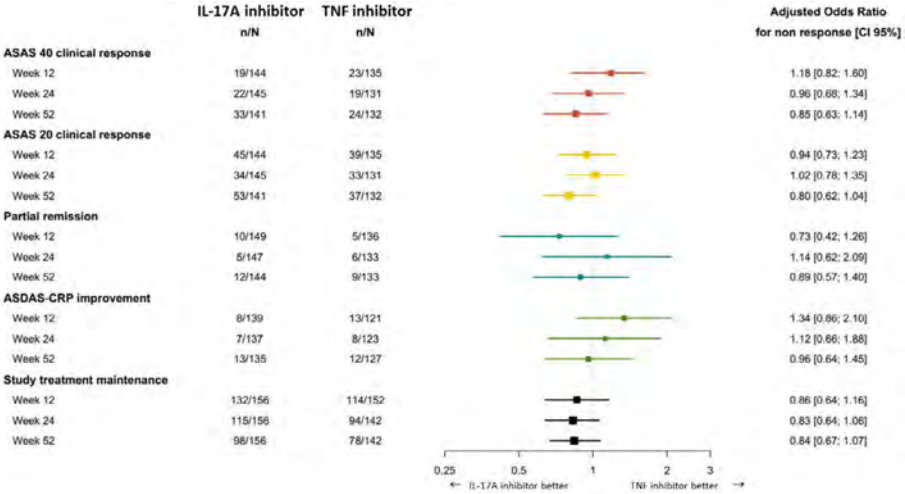


Figure 1. Clinical responses with adjusted odds ratio in IL-17i and TNFi groups at weeks 12, 24, and 52

new safety signals were identified, and adverse-event rates were comparable between groups. Exploratory, non-significant trends favored an IL-17Ai after primary nonresponse and in patients with cutaneous psoriasis, HLA-B27 negativity, or CRP < 5 mg/L. Conversely, when the first TNFi was discontinued for an adverse event, cycling to another TNFi appeared more favorable.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: In this randomized trial of axSpA patients with inadequate response to a first TNFi, switching to an IL-17Ai was not superior to cycling to a second TNFi for the primary endpoint. These findings directly inform treatment sequencing after TNFi failure and support individualized, shared decision-making in axSpA. They also align with current recommendations that, for the axial symptom control, the choice among available bDMARDs should not be based on anticipated efficacy differences.

Disclosures: E. Dalix: None; P. Goupille: AbbVie/Abbott, 2, 4, 6, Alfasigma, 4, 6, Bristol-Myers Squibb(BMS), 4, 6, Celltrion, 2, 4, 6, Eli Lilly, 2, 4, 6, Janssen, 2, 4, 6, Merck/MSD, 4, 6, Novartis, 4, 6, Pfizer, 4, 6, UCB, 2, 4, 6; D. Wendling: Abbvie, 1, 6, Alfasigma, 6, Biocon, 6, Celltrion, 4, Janssen, 4, Novartis, 4, 6, UCB, 4, 6; C. Roux: None; J. Samon: AbbVie/Abbott, 1, 2, Eli Lilly, 1, 2, Merck/MSD, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; O. Brocq: None; A. Tournadre: None; A. Constantin: None; M. Breban: Janssen, 1, 5, Novartis, 5, UCB, 1; G. Cormier: None; T. Pascart: None; T. Lequerre: None; P. Claudepierre: abbvie, 6, alphasigma, 6, amgen, 6, BMS, 6, johnson and Johnson, 6, lilly, 6, novartis, 6, Pfizer, 6, ucb, 6; E. Lespessailles: None; B. Legoff: None; J. Sellam: None; A. Baillet: None; T. Schaeverbeke: None; S. Pavy: None; V. Devauchelle-Pensec: AbbVie/Abbott, 2, Novartis, AbbVie, Lilly, Fresenius Kabi, 6; E. Gervais: None; L. Gossec: AbbVie, 2, 5, Alfasigma, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Celltrion, 2, Johnson & Johnson, 2, Lilly, 2, 5, MoonLake, 2, Novartis, 2, 5, Pfizer, 2, STADA, 2, UCB, 2, 5; C. Miceli: None; Y. Pers: None; C. Lukas: None; R. Felten: AbbVie/Abbott, 2, 4, Eli Lilly, 2, Novartis, 2, 3, 4, UCB, 2, 4; B. Bouvard: None; A. Denis: None; E. Dernis: None; E. Presles: None; F. Rancon: None; H. Marotte: None.

Abstract Number: LB10

Four-Year Safety and Efficacy of Deucravacitinib in Systemic Lupus Erythematosus: Results From a Phase 2 Program

Eric F. Morand[1], Cristina Arriens[2], Marilyn Pike[3], Joan Merrill[4], Victoria Werth[5], Zahi Touma[6], Razvan C. Ionitescu[7], Masato Okada[8], Ilias Kouris[9], Yogita Kolekar[10], Junyu Nie[10], Venkat Renukuntla[10], Thomas Wegman[10] and Ronald van Vollenhoven[11], [1]Sub-Faculty of Clinical and Molecular Medicine, Monash University, Melbourne, Victoria, Australia, Melbourne, Victoria, Australia, [2]Oklahoma Medical Research Foundation, Oklahoma City, [3]Rheumatology, MedPharm Consulting, Inc, Bethesda, [4]Department of Arthritis and Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, [5]University of Pennsylvania, Merion Station, Pennsylvania, [6]University of Toronto, Toronto, Ontario, Canada, [7]Medart Cliniq, Department of Rheumatology, Râmnicu Vâlcea, Romania, [8]St. Luke's International Hospital, Tokyo, Japan, [9]Eli Lilly and Company Global, Basingstoke, United Kingdom, [10]Bristol Myers Squibb, Princeton, [11]Amsterdam UMC, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: There is a substantial unmet need for effective, well-tolerated therapies for patients with SLE. Deucravacitinib is an oral, selective tyrosine kinase 2 (TYK2) inhibitor approved in moderate to severe plaque psoriasis and under evaluation in phase 3 SLE studies. Deucravacitinib demonstrated superior efficacy vs placebo (PBO) in the phase 2 PAISLEY SLE study. Here, we report integrated analyses from the PAISLEY SLE (parent; NCT03252587) and PAISLEY long-term extension (LTE; NCT03920267) studies.

Methods: Patients completing the 48-week parent study while on study drug (deucravacitinib 3 mg twice daily [BID], 6 mg BID, or 12 mg once daily [QD] or PBO) were enrolled in the 3-year LTE study (**Figure 1**). Patients on PBO were rerandomized 1:1:1 in the LTE study to 1 of the 3 deucravacitinib doses (blinded), while those already on deucravacitinib continued their

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Safety summary[a] for patients treated in the PAISLEY SLE and LTE studies

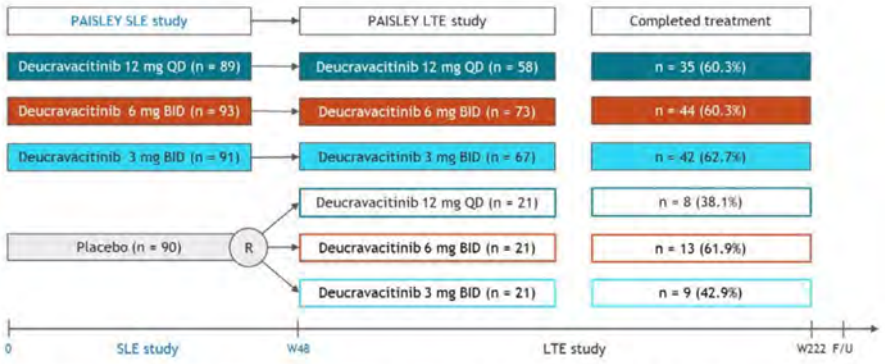
Patients with an adverse event	Placebo[f] (to week 48) n = 90	Total deucravacitinib[b] 3 mg BID n = 112		Total deucravacitinib[b] 6 mg BID n = 114		Total deucravacitinib[b] 12 mg QD n = 110		Total deucravacitinib[b] n = 336	
	n (%)	n (%)	EAIR[c] (95% CI)	n (%)	EAIR[c] (95% CI)	n (%)	EAIR[c] (95% CI)	n (%)	EAIR[c] (95% CI)
AEs	79 (87.8)	104 (92.9)	280.8 (229.4, 340.2)	107 (93.9)	246.7 (202.2, 298.1)	103 (93.6)	228.3 (186.4, 276.9)	314 (93.5)	250.2 (223.3, 279.4)
Treatment-related AEs	30 (33.3)	54 (48.2)	30.5 (22.9, 39.8)	47 (41.2)	23.0 (16.9, 30.6)	41 (37.3)	23.6 (16.9, 32.0)	142 (42.3)	25.6 (21.5, 30.2)
Serious AEs	11 (12.2)	19 (17.0)	7.1 (4.3, 11.1)	17 (14.9)	5.7 (3.3, 9.2)	24 (21.8)	10.7 (6.9, 16.0)	60 (17.9)	7.6 (5.8, 9.8)
AEs leading to treatment discontinuation	3 (3.3)	15 (13.4)	5.2 (2.9, 8.5)	13 (11.4)	4.1 (2.2, 7.1)	19 (17.3)	7.4 (4.4, 11.5)	47 (14.0)	5.5 (4.0, 7.3)
Deaths	0	1[d] (0.9)	0.3 (0.0, 1.9)	0	0	0	0	1 (0.3)	0.1 (0, 0.6)

[a]MedDRA: 28.0. Includes all patients who received deucravacitinib (parent plus LTE studies). AEs are defined as treatment-emergent AEs that occurred on or after the first treatment dose in the PAISLEY SLE or LTE study, whichever is earlier, and up to 30 days after the last treatment date. [b]In patients who received at least 1 dose of deucravacitinib in either the PAISLEY SLE or LTE study. [c]Incidence rate per 100 person-years of exposure (IR/100 P-Y): 100 × 365.25 × (total number of patients with the AE) / total exposure time for the selected AE under each treatment. 95% CI for incidence rate is calculated based on Garwood 1936.[7] [d]A 54-year-old postmenopausal woman had an acute ST-segment elevation myocardial infarction and Killip class IV cardiogenic shock. She had been on deucravacitinib 3 mg BID for 57.5 weeks (48 weeks in the parent study and 9.5 weeks in the LTE study). Risk factors included postmenopausal status, SLE, and 30 years of corticosteroid use. Both the principal investigator and the study sponsor assessed this event as unrelated to the investigative treatment.

1. Morand E, et al. *Arthritis Rheumatol* 2023;75:242-252. 2. Garwood F. *Biometrika* 1936;28:437-442.

AE, adverse event; BID, twice daily; CI, confidence interval; EAIR, exposure-adjusted incidence rate; LTE, long-term extension; MedDRA, Medical Dictionary for Regulatory Activities; PBO, placebo; QD, once daily; SLE, systemic lupus erythematosus.

Figure 1. PAISLEY SLE and LTE studies



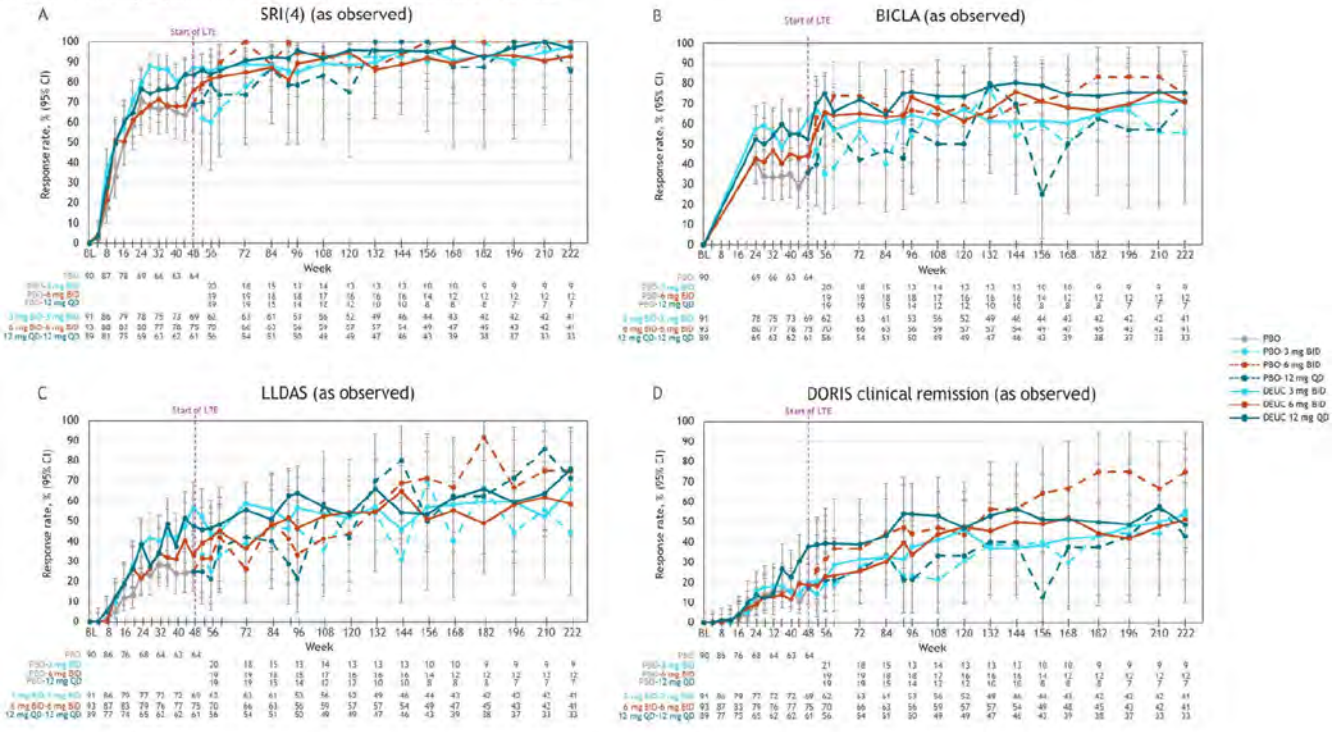
Timeline is not drawn to scale. The LTE study enrolled patients who completed the parent PAISLEY SLE study (to week 48).
BID, twice daily; F/U, follow-up; LTE, long-term extension; QD, once daily; R, randomize; SLE, systemic lupus erythematosus.

regimen for up to 4+ years of treatment (222 weeks). The LTE study allowed greater flexibility in adjustments to background treatment. Databases of the parent and LTE studies were integrated for analyses of safety through W226 and efficacy through W222. Efficacy analyses using composite measures of disease activity were summarized descriptively without formal statistical comparisons; additional efficacy results based on imputation for missing data to minimize survivor bias will be presented. For binary endpoints, 95% CIs were obtained using the Clopper-Pearson method.

Results: Of 363 patients from the parent study, 261 (72%) were enrolled in the LTE study; 151/261 patients (57.9%) completed the study. Adverse events (AEs) with up to 4+ years of treatment are shown in **Table 1**; serious AEs occurred in 17%, 14.9%, and 21.8% of patients who received deucravacitinib 3 mg BID, 6 mg BID, and 12 mg QD, respectively, and AEs leading to treatment discontinuation occurred in 13.4%, 11.4%, and 17.3%, respectively. One death deemed unrelated to study treatment occurred in the deucravacitinib 3-mg BID arm. SRI(4), BICLA, LLDAS, and DORIS remission rates were maintained over time (**Figure 2**); patients in the PBO arm in the parent study who switched to deucravacitinib achieved improvements that were broadly comparable to those of continuously treated patients from ≈W72 (**Figure 2**). CLASI-50/70 and JC-50/100 responses were maintained consistently throughout the LTE study, with increased responses seen in the PBO-switch arm. The incidence of moderate to severe flares was low across all treatment arms.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 2. Efficacy in patients treated in the PAISLEY SLE and LTE studies



Integrated analysis of the PAISLEY SLE and LTE studies was based on observed data for patients who enrolled in the LTE study. 95% CIs were obtained using the Clopper-Pearson method. BICLA responses were not evaluated prior to week 24 per the requirement that corticosteroid dose be ≥ 7.5 mg/day after week 20. LLDAS responses were evaluated using the 2019 definition.
BICLA, British Isles Lupus Assessment Group-based Composite Lupus Assessment; BID, twice daily; CI, confidence interval; DEUC, deucravacitinib; DORIS, Definitions Of Remission In Systemic Lupus Erythematosus; LLDAS, Lupus Low Disease Activity State; LTE, long-term extension; PBO, placebo; QD, once daily; SLE, systemic lupus erythematosus; SRI(4), SLE Responder Index-4.

Conclusion: Integrated analysis of the PAISLEY SLE and LTE studies confirmed the consistent safety profile and sustained efficacy of deucravacitinib in SLE with up to 4+ years of drug exposure, with no new safety signals despite complex background therapies. Patients who switched from PBO during the LTE study achieved outcomes comparable to those treated from baseline. These data represent the longest follow-up of a TYK2 inhibitor in SLE to date, supporting the potential of deucravacitinib as a durable future treatment option, currently under evaluation in phase 3 POETYK SLE trials (NCT05617677; NCT05620407).

Disclosures: E. Morand: AbbVie, 2, 5, Amgen, 5, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 5, 6, Bristol-Myers Squibb, 1, 2, 5, 6, Dragonfly, 1, 2, 6, Eli Lilly, 1, 2, 5, 6, EMD Serono, 1, 2, 5, 6, Genentech – Hoffman La Roche, 5, GlaxoSmithKlein, 1, 2, 5, 6, Janssen, 5, Novartis, 1, 2, 5, Quell, 1, 2, 5, Remegen, 1, 2, 6, Takeda, 5, Union Chimique Belge (UCB), 1, 2, 5, Zenas, 1, 2, 6; C. Arriens: AstraZeneca, 1, 5, 6, Aurinia, 1, 6, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, GlaxoSmithKlein(GSK), 1, Health & Wellness Partners, 1, Kezar, 1, Synthekine, 1, UCB, 1; M. Pike: AstraZeneca, 2, Bristol-Myers Squibb(BMS), 2, UCB, 2; J. Merrill: AbbVie, 2, 6, Alexion, 2, Alumis, 2, Amgen, 2, AstraZeneca, 2, 5, Aurinia, 2, BMS, 2, 5, 6, Chief Advisor for Clinical Development for Lupus Foundation of America, 1, EMD Serono, 2, Genentech, 2, Gilead, 2, GSK, 2, 5, Lilly, 2, Merck, 2, 6, Pfizer, 2, Provention, 2, RemeGen, 2, 6, Sanofi, 2, UCB, 2, Zenas, 2; V. Werth: AbbVie, 2, Alpine Immune Sciences, 2, Amgen, 2, 5, AnaptysBio, 2, argenx, 2, AstraZeneca, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Cabaletta Bio, 2, Calyx, 2, Caribou, 2, CESAS Medical, 6, Corbus Pharmaceuticals, 5, Crisalis, 2, CSL Behring, 2, 5, Cugene, 2, EMD Serono, 2, Evommune, 2, Gilead, 2, 5, GlaxoSmithKlein(GSK), 2, Horizon, 2, 5, Immunovant, 2, Innovaderm, 2, Kyowa Kirin, 2, MAPI Trust, 9, Merck, 2, NEKTAR, 2, Nuvig Pharmaceuticals, 2, Pfizer, 2, 5, Priovant, 5, Regeneron, 2, 5, Rome Pharmaceuticals, 2, 5, Sanofi, 2, Takeda, 2, UCB, 2, Ventus, 2, 5, Viela, 2, 5, Xencor, 2; Z. Touma: AbbVie, 2, Amgen, 2, AstraZeneca, 2, 5, Biogen, 2, Bristol-Myers Squibb(BMS), 2, EMD Serono, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, 5, Janssen, 2, Merck, 2, UCB, 2; R. Ionitescu: AbbVie, 6, Accord Healthcare, 6, Alfasigma, 5, 6, Angelini, 6, AstraZeneca, 6, Biofarm, 6, Bleu Pharma, 6, Boehringer-Ingelheim, 5, Bristol-Myers Squibb(BMS), 5, Egis, 5, Eli Lilly, 5, 6, Ewopharma, 6, Fiterman, 6, Galapagos, 5, Gilead, 6,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

GlaxoSmithKlein(GSK), 6, Grünenthal, 5, Idorsia, 5, Immunovant, 5, Janssen, 5, 6, Krka, 6, mAbxience, 5, Menarini, 6, Merck, 5, MSD, 6, Naturalis, 6, Novartis, 5, 6, Otsuka, 5, Pfizer, 5, 6, Roche, 5, 6, Sandoz, 6, Sanofi, 6, Servier, 6, Stada, 6, Sun Wave, 5, 6, UCB, 6, Zentiva, 6; M. Okada: None; I. Kouris: Bristol-Myers Squibb(BMS), 3, 11; Y. Kolekar: Bristol-Myers Squibb(BMS), 3, 11; J. Nie: Bristol-Myers Squibb(BMS), 3, 11; V. Renukuntla: Bristol-Myers Squibb(BMS), 3, 11; T. Wegman: Bristol-Myers Squibb(BMS), 3, 11; R. van Vollenhoven: AbbVie, 1, 2, 6, Alfasigma, 5, AnaptysBio, 2, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 6, Bristol-Myers Squibb(BMS), 1, 2, 5, 6, Cabaletta, 1, 2, 5, 6, Galapagos, 1, 2, 5, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Janssen, 1, 2, 6, Kyowakirin, 1, 2, 6, Merck/MSD, 1, 2, 5, 6, Novartis, 5, Pfizer, 1, 2, 5, 6, RemeGen, 1, 2, 5, 6, Roche, 5, Sanofi, 1, 2, 5, 6, UCB, 1, 2, 5, 6.

Abstract Number: LB11

Efficacy and Safety of Telitacicept in Patients with Sjögren's Disease: Results from a Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Clinical Study

Dong Xu[1], Shangzhu Zhang[1], Lin Qiao[1], Li Zhang[1], Wenxiang Wang[2], Lin Li[2], Binghua Xiao[2], Jing Zhang[2], Qing Zuraw[3], Jianmin Fang[2] and Xiaofeng Zeng[1], [1]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences & Peking Union Medical College; National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Ministry of Science & Technology; State Key Laboratory of Complex Severe and Rare Diseases; Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, Beijing, China (People's Republic), [2]RemeGen Co., Ltd., Rheumatology, Yantai, China (People's Republic), [3]Vor Biopharma Inc., Boston

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Sjögren's disease (SjD) is a chronic autoimmune disease whose pathogenesis is associated with aberrant activation of B-lymphocytes. Telitacicept, a novel fusion protein, dually targets and neutralizes B-lymphocyte stimulator (BLyS) and a proliferation-inducing ligand (APRIL), and has previously demonstrated efficacy and safety in a phase 2 study in patients with SjD.

Methods: This randomized, double-blind, placebo-controlled, phase 3 study (NCT05673993) was conducted in 79 research centers in China. Participants aged 18–70 years meeting the 2016 ACR/EULAR criteria for SjD who were anti-SSA antibody positive with EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI)≥5 were eligible. Eligible participants were randomized (1:1:1) to telitacicept 160 mg, telitacicept 80 mg, or placebo groups to receive weekly subcutaneous injection for 48 weeks. During the period from Week 24–48, participants with inadequate response to treatment in the placebo group could switch to telitacicept 160 mg or telitacicept 80 mg at a ratio of 1:1 under blind conditions. The primary efficacy endpoint was the change from baseline in ESSDAI score at Week 24. Secondary endpoints included change from baseline in ESSDAI score at Week 48; proportion of participants with: ≥3-point reduction from baseline in ESSDAI score; ESSDAI score < 5; ≥1-point or ≥15% reduction from baseline in EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI); and change from baseline in ESSPRI total score (all at Week 24 and Week 48). The proportion of Sjögren's Tool for Assessing Response (STAR) responders was also assessed, along with adverse events (AEs) and immunological parameters.

Results: A total of 381 eligible participants were randomly assigned to telitacicept 160 mg (N=127), telitacicept 80 mg (N=127), and placebo (N=127). One participant in the telitacicept 80 mg group who prematurely withdrew before receiving study treatment was excluded from the estimand population and safety set. Compared with placebo, a statistically

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Efficacy analysis.

Endpoint	Telitacicept 160 mg (N=127)	Telitacicept 80 mg (N=126)	Placebo (N=127)
Primary endpoint			
Change from baseline in ESSDAI score at Week 24, LS mean (95% CI)[a]	-4.4 (-5.0, -3.8)	-3.0 (-3.6, -2.4)	-0.6 (-1.2, -0.0)
LS mean difference (95% CI)	-3.8 (-4.6, -3.0)	-2.4 (-3.2, -1.6)	
P-value	<0.0001	<0.0001	
Secondary endpoint			
Change from baseline in ESSDAI score at Week 48, LS mean (95% CI)[a]	-4.6 (-5.3, -4.0)	-3.2 (-3.9, -2.6)	-0.4 (-1.1, 0.2)
LS mean difference (95% CI)	-4.2 (-5.1, -3.3)	-2.8 (-3.7, -1.9)	
P-value	<0.0001	<0.0001	
Proportion of participants with a ≥3-point reduction in ESSDAI score[b]			
Week 24, n (%)	84 (71.8%)	56 (47.1%)	23 (19.3%)
Difference in proportion (95% CI)	52.3% (41.53%, 63.09%)	27.9% (16.77%, 39.06%)	
P-value	<0.0001	<0.0001	
Week 48, n (%)	81 (73.0%)	56 (49.1%)	19 (16.5%)
Difference in proportion (95% CI)	56.4% (45.72%, 67.09%)	32.7% (21.51%, 43.88%)	
P-value	<0.0001	<0.0001	
Proportion of participants with an ESSDAI score <5 points[b]			
Week 24, n (%)	58 (49.6%)	34 (28.8%)	13 (10.9%)
Difference in proportion (95% CI)	39.2% (29.13%, 49.23%)	17.8% (8.20%, 27.41%)	
P-value	<0.0001	0.0004	
Week 48, n (%)	61 (55.0%)	37 (32.7%)	14 (12.2%)
Difference in proportion (95% CI)	43.0% (32.38%, 53.57%)	20.6% (10.41%, 30.71%)	
P-value	<0.0001	0.0001	
Proportion of participants with a ≥1 point or ≥15% reduction in ESSPRI score[b]			
Week 24, n (%)	100 (86.2%)	75 (63.0%)	38 (32.2%)
Difference in proportion (95% CI)	54.0% (43.45%, 64.64%)	30.8% (18.69%, 42.96%)	
P-value	<0.0001	<0.0001	
Week 48, n (%)	98 (89.1%)	86 (75.4%)	38 (33.3%)
Difference in proportion (95% CI)	55.7% (45.31%, 66.18%)	42.1% (30.39%, 53.82%)	
P-value	<0.0001	<0.0001	
Exploratory endpoint			
Proportion of participants who achieved STAR response[b]			
Week 24, n (%)	96 (82.1%)	68 (57.1%)	29 (24.4%)
Difference in proportion (95% CI)	57.7% (47.33%, 68.12%)	32.9% (21.13%, 44.59%)	
P-value	<0.0001	<0.0001	
Week 48, n (%)	91 (82.7%)	73 (64.6%)	27 (25.0%)
Difference in proportion (95% CI)	57.7% (46.90%, 68.51%)	39.5% (27.52%, 51.85%)	
P-value	<0.0001	<0.0001	
Other efficacy endpoints			
Change from baseline in ESSPRI score[a]			
Week 24, LS mean (95% CI)	-1.88 (-2.13, -1.63)	-1.31 (-1.56, -1.06)	-0.36 (-0.60, -0.11)
LS mean difference (95% CI)	-1.52 (-1.87, -1.17)	-0.95 (-1.30, -0.60)	
P-value	<0.0001	<0.0001	
Week 48, LS mean (95% CI)	-2.56 (-2.84, -2.27)	-1.74 (-2.03, -1.46)	-0.41 (-0.69, -0.13)
LS mean difference (95% CI)	-2.15 (-2.55, -1.75)	-1.34 (-1.74, -0.94)	
P-value	<0.0001	<0.0001	

The efficacy analysis was based on the estimand population.
[a]This analysis was performed using a MMRM, with group, visit, the group-by-visit interaction, and baseline score as variables in the model; the MMRM analysis model already includes handling of missing data. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results.
[b]The stratum-adjusted between-group difference was tested with the CMH method. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results. Missing data were not imputed.
CI, confidence interval; CMH, Cochran–Mantel–Haenszel; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; LOCF, last observation carried forward; LS, least square; MMRM, mixed-effects model for repeated measures; STAR, Sjögren's Tool for Assessing Response.

significant decrease in ESSDAI score from baseline at Week 24 was observed with telitacicept 160 mg (least square [LS] mean change: -4.4 vs -0.6, p< 0.0001) and telitacicept 80 mg (LS mean change: -3.0 vs -0.6, p< 0.0001) (Table 1). The efficacy in both telitacicept groups was maintained through Week 48 compared with placebo, with telitacicept 160 mg having a better reduction than 80 mg at Week 48 (LS mean change: -4.6 vs -3.2) (Figure 1a). Other efficacy endpoints, including proportion of participants who achieved ≥3-point reduction in ESSDAI score, proportion of participants with ESSDAI score < 5, proportion of participants who achieved ≥1-point or ≥15% reduction in ESSPRI score, change from baseline in ESSPRI score, and proportion of participants who achieved STAR response, showed consistent results with the primary endpoint (Table 1 and Figure 1). The majority of treatment-emergent AEs were mild or moderate (Table 2).

Conclusion: The primary efficacy endpoint was reached in this study. Compared with placebo, both telitacicept 160 mg and 80 mg demonstrated consistent clinical symptom improvement through 48 weeks and a favorable safety profile, with greater improvements observed with the telitacicept 160 mg dose.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 2. Overview of adverse events.

Event, n (%)	Telitacicept 160 mg (N=127)	Telitacicept 80 mg (N=126)	Placebo (N=127)
TEAEs	122 (96.1)	119 (94.4)	112 (88.2)
TRAEs	107 (84.3)	106 (84.1)	74 (58.3)
TESAEs	11 (8.7)	14 (11.1)	10 (7.9)
TRSAEs	2 (1.6)	5 (4.0)	4 (3.1)
Severe TEAEs	3 (2.4)	5 (4.0)	3 (2.4)
Severe TRAEs	0	1 (0.8)	1 (0.8)
Death	0	0	0
Common TEAE (incidence ≥10% in any group)			
Upper respiratory tract infection	80 (63.0)	85 (67.5)	74 (58.3)
Urinary tract infection	8 (6.3)	15 (11.9)	7 (5.5)
Cough	11 (8.7)	14 (11.1)	8 (6.3)
Hepatic function abnormal	7 (5.5)	16 (12.7)	7 (5.5)
Injection site reaction	53 (41.7)	51 (40.5)	5 (3.9)
Pyrexia	4 (3.1)	14 (11.1)	4 (3.1)

TEAE, treatment emergent adverse event; TRAE, treatment related adverse event; TESAE, treatment emergent serious adverse event; TRSAE, treatment related serious adverse event.

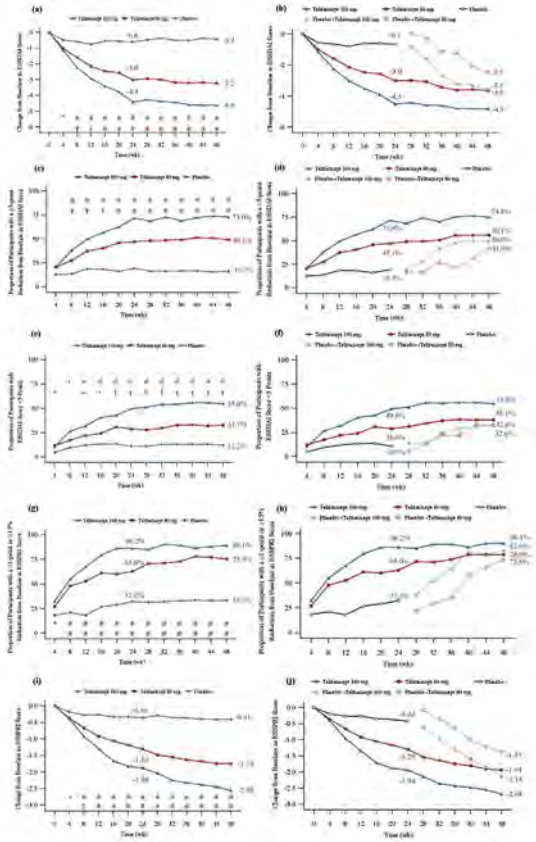


Figure 1. Efficacy outcomes over time by treatment group.
(a) LS mean change from baseline in ESSDAI score.
(b) Mean change of measure values from baseline in ESSDAI score.
(c) Proportion of participants with a ≥3-point reduction from baseline in ESSDAI score.
(d) Observed proportion of participants with a ≥3-point reduction from baseline in ESSDAI score.
(e) Proportion of participants with ESSDAI score <5 points.
(f) Observed proportion of participants with ESSDAI score <5 points.
(g) Proportion of participants with a ≥1-point or ≥15% reduction from baseline in ESSPRI score.
(h) Observed proportion of participants with a ≥1-point or ≥15% reduction from baseline in ESSPRI score.
(i) LS mean change from baseline in ESSPRI score.
(j) Mean change of measure values from baseline in ESSPRI score.
(a) and **(i)**: For continuous variables, the analyses between each telitacicept group and placebo group used MMRM method. MMRM analysis had already accounted for missing data. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results.
(c), **(e)**, and **(g)**: For categorical variables, the stratum-adjusted between-group difference was tested with the CMH method. Missing data were not imputed. The post-switching data for the two telitacicept groups and the placebo group were handled with the LOCF method, i.e., imputing all the post-switching values with the most recent pre-switching results.
*: P<0.05, †: P<0.01, ‡: P<0.001, #: P<0.0001.
(b), **(d)**, **(f)**, **(h)**, and **(j)**: A descriptive analysis was performed on the observed data, and missing data were not imputed.
CMH, Cochran–Mantel–Haenszel; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, EULAR Sjögren's Syndrome Patient Reported Index; LOCF, last observation carried forward; LS, least square; MMRM, mixed-effects model for repeated measures; wk, Week.

Disclosures: D. Xu: None; S. Zhang: None; L. Qiao: None; L. Zhang: None; W. Wang: RemeGen Co., Ltd, 3; L. Li: RemeGen Co., Ltd, 3; B. Xiao: RemeGen Co., Ltd., 3; J. Zhang: RemeGen Co., Ltd, 3; Q. Zuraw: RemeGen Co., Ltd., 11, VorBio, 3, 4, 11; J. Fang: RemeGen Co., Ltd., 3, 11; X. Zeng: None.

Abstract Number: LB12

Randomized, Double-Blind, Placebo-Controlled Phase IIa Trial of an Innovative Intra-Articular Apoptotic Cell Therapy in Knee Osteoarthritis (OA): 3-Month Positive Outcomes and Identification of Responder Population (NCT06233474)

Philip Conaghan[1], Bernt Husøy[2], Cecilie Rovsing[3], Sidsel L Boll[4], Liliana Groppa[5], Amir Oron[6], Asger Bihlet[7], Ali Mobasheri[8], Tobias Winkler[9], Dror Mevorach[10], Einat Galamidi[11], Lital Weinfeld-Bergman[12], Lior Binder[12] and Oren Hershkovitz[11], [1]University of Leeds, Leeds, United Kingdom, [2]Sanos Clinic, Herlev, Denmark, [3]Sanos Clinic, Gandrup, Denmark, [4]Sanos Clinic, Vejle, Denmark, [5]T. Mosneaga Republican Clinical Hospital, Chisinau, Moldova, [6]Kaplan MC, Rehovot, Israel, [7]NBCD A/S, Soeborg, Denmark, [8]University of Oulu, Oulu, Finland, [9]Charité - Universitätsmedizin Berlin, Berlin, Germany, [10]Hadassah-University Hospital, Jerusalem, Israel, [11]Enlivex Therapeutics, Ness Ziona, Israel, [12]Enlivex Therapeutics, Nes Ziona, Israel

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: OA is a prevalent disabling disease growing globally due to aging populations and rising obesity. In primary OA, the effects of joint tissue damage accumulate with age, with low-grade inflammation and decline in the joint regenerative capacity.

A novel cell therapy of apoptotic PBMCs has been developed for OA based on robust pre-clinical data on their pro-resolution modulation of macrophage-mediated inflammation. Following a Phase I safety run-in, in which participants demonstrated favorable tolerability, we now report the pre-planned 3-month analysis results of a randomized controlled Phase IIa assessing safety and efficacy of apoptotic cell therapy in knee OA, as well as identifying a responder population based on baseline covariates.

Methods: ENX-CL-05-001 is a multicenter, randomized, double-blind, placebo-controlled Phase IIa in moderate–severe knee OA (NCT06233474). Participants received 3 knee injections on Days 0/14/28 and are followed to Month 12. Primary objectives were safety/tolerability; key secondary endpoints included changes in NRS and WOMAC pain scores and MRI semi-quantitative evaluations. Innovative machine-learning methods explored heterogeneity and high-responder populations.

Results: 134 patients were randomized and treated. Baseline characteristics were well balanced between the arms (mean age 61, 55% female, mean BMI 29). No treatment-related SAEs occurred. AEs were more frequent with apoptotic cell therapy vs placebo (89.6% [60/67] vs 71.6% [48/67]), driven by transient local reactions (typically resolving ~6 days vs ~10 days with placebo); noncompliance with treatments was uncommon (7.5% elected to forego subsequent injections due to AEs).

In the mITT population, pain NRS improvement was 24% higher with apoptotic cell therapy vs placebo; and WOMAC pain and function improvements were also numerically higher, however these did not reach statistical significance. An age-related responder population enriching for primary/idiopathic OA was identified (≥60 years; 69/129, 53.5% of study

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

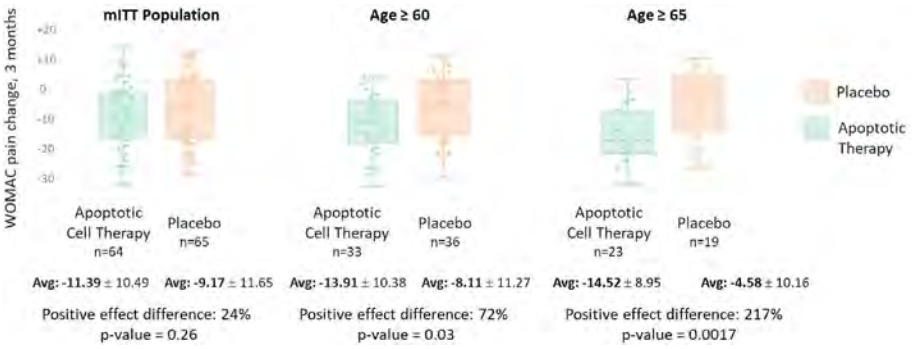


Figure 1: Results of WOMAC pain change at 3 months for the mITT overall population and Age-related Responder Population ≥ 60 years and ≥ 65 years

population) demonstrating significant improvements with apoptotic cell therapy: WOMAC Pain –27.82 (SD 20.76) vs –16.22 (SD 22.54), 72% relative improvement (p=0.03); WOMAC Total –26.43 vs –13.75, 92% relative improvement (p=0.012), including WOMAC Function –26.45 vs –12.63, 109% relative improvement (p=0.007). The 3-month pain NRS group difference (-0.98; 0-10), 48% relative improvement (p=0.07), was clinically meaningful and consistent with weekly pain reporting. Ongoing Month-6 readouts indicate potentially durable results. Moreover, pain improvement results were associated with more severe baseline imaging markers, including bone marrow lesions, Hoffa synovitis and radiographic structural damage.

Conclusion: Intra-articular apoptotic cell therapy was well tolerated without treatment-related SAEs and produced clinically meaningful and statistically significant improvements in pain and function endpoints in participants ≥60 years—consistent with an age-linked, macrophage-mediated OA phenotype. These findings support advancement into advanced trials program targeting older, primary/idiopathic knee OA.

Disclosures: P. Conaghan: AbbVie/Abbott, 2, 6, Alfasigma, 2, Eli Lilly, 2, 6, Enlivex, 2, FormatoinBio, 2, Genascence, 2, Grunenthal, 2, Kolon TissueGene, 2, 6, Levicept, 2, Moebius, 2, 6, Novartis, 2, 6, Orion, 2, Pacira, 2, Stryker, 2, Takeda, 2; B. Husøy: None; C. Rovsing: None; S. Boll: None; L. Groppa: None; A. Oron: None; A. Bihlet: None; A. Mobasheri: Enlivex, 1, 2; T. Winkler: BMFTR Germany, 5, Enlivex, 2, European Commission, 5, Heraeus Medical, 2, Heraeus medical, 12, Payment for expert testemony, Innovation Fund Denmark, 5, Liposphere, 2, Ossium, 2, Pluri, 2, Relieve, 2; D. Mevorach: None; E. Galamidi: None; L. Weinfeld-Bergman: None; L. Binder: None; O. Hershkovitz: None.

Abstract Number: LB13

Obinutuzumab Leads to Deep B-Cell Depletion in the Kidney Parenchyma of Patients With Lupus Nephritis: An Exploratory Analysis of the REGENCY Trial

Brad Rovin[1], Elsa Martins[2], Cary Austin[3], Harini Raghu[3], Caleb Chan[3], Patrick Chang[3], Jay Garg[3], Valeria Alberton[4], Mittermayer Santiago[5], Gustavo Aroca-Martínez[6], Fedra Palazuelos[7], Teresa Baczkowska[8], José Alfaro[9], Jorge Ravelo-Hernández[10], Richard Furie[11], Luís Pinto[12], Eduardo Albiero[13], Christopher Larsen[14], Bongin Yoo[3], Jennifer Pulley[15], Andrew Thorley[3], Thomas Schindler[2], Theodore Omachi[3], William Pendergraft III[3] and Ana Malvar[16], [1]Department of Internal Medicine, The Ohio State University College of Medicine, Columbus, Ohio, [2]F. Hoffmann-La Roche Ltd, Basel, Switzerland, [3]Genentech, Inc., South San Francisco, California, [4]Pathology Unit, Fernández Hospital, Buenos Aires, Argentina, [5]Bahiana School of Medicine and Public Health and UFBA, Federal University of Bahia, and Clínica SER da Bahia, Salvador, Brazil, [6]Universidad Simón Bolívar y Clínica de la Costa, Barranquilla, Colombia, [7]Centro de Investigación y Tratamiento Reumatológico S.C., Mexico City, Mexico, [8]Department of Transplantation Medicine, Nephrology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland, [9]Instituto Peruano del Hueso y la Articulación, Lima, Peru, [10]Clinica San Juan Bautista, Unidad de Investigacion en Reumatologia e Inmunologia, Lima,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Peru, [11]Division of Rheumatology, Northwell Health, Great Neck, New York, [12]Internal Medicine and Rheumatology, Hospital Pablo Tobón Uribe, Medellín, Colombia, [13]Sanatorio Allende, Córdoba, Argentina, [14]Arkana Laboratories, Little Rock, Arkansas, [15]Roche Products Ltd, Welwyn Garden City, United Kingdom, [16]Organización Médica de Investigación, Buenos Aires, Argentina

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: B cells infiltrate the kidneys in lupus nephritis (LN) and likely contribute to the pathogenesis of kidney injury. The REGENCY trial (NCT04221477) showed that depletion of B cells with the anti-CD20 monoclonal antibody, obinutuzumab, increased the proportion of clinical complete responses when added to standard therapy compared with standard therapy alone.

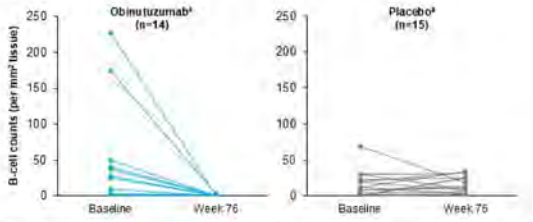
Table 1. Demographics and baseline characteristics of the study cohort

Characteristic	Obinutuzumab[a]		Placebo[a]		All participants	
	REGENCY ITT population (N=135)	Kidney tissue B-cell cohort (n=14)	REGENCY ITT population (N=136)	Kidney tissue B-cell cohort (n=15)	REGENCY ITT population (N=271)	Kidney tissue B-cell cohort (N=29)
Age, years, mean (SD)	33.0 (10.5)	28.2 (7.3)	32.7 (10.0)	32.8 (7.6)	32.9 (10.2)	30.6 (7.7)
Female, n (%)	114 (84.4)	14 (100)	115 (84.6)	13 (86.7)	229 (84.5)	27 (93.1)
Weight, kg, mean (SD)	66.3 (14.0)	66.4 (16.0)	68.3 (15.5)	74.6 (16.6)	67.3 (14.8)	70.6 (16.5)
Race, n (%)						
American Indian or Alaska Native	25 (18.5)	2 (14.3)	26 (19.1)	2 (13.3)	51 (18.8)	4 (13.8)
Black or African American	20 (14.8)	10 (71.4)	20 (14.7)	8 (53.3)	40 (14.8)	18 (62.1)
White	65 (48.1)	2 (14.3)	64 (47.1)	3 (20.0)	129 (47.6)	5 (17.2)
Multiple	11 (8.1)	0 (0)	9 (6.6)	2 (13.3)	20 (7.4)	2 (6.9)
Asian	9 (6.7)	0 (0)	7 (5.1)	0 (0)	16 (5.9)	0 (0)
Region, n (%)[b]						
LATAM and the Caribbean	77 (57.0)	14 (100)	77 (56.6)	15 (100)	154 (56.8)	29 (100)
USA and Canada	20 (14.8)	0 (0)	20 (14.7)	0 (0)	40 (14.8)	0 (0)
Race, n (%)[b]						
Black	15 (11.1)	6 (42.9)	17 (12.5)	6 (40.0)	32 (11.8)	12 (41.4)
Other	120 (88.9)	8 (57.1)	119 (87.5)	9 (60.0)	239 (88.2)	17 (58.6)
Serum creatinine, µmol/L, mean (SD)	73.6 (34.1)	88.4 (23.5)	77.5 (42.2)	89.1 (17.1)	75.6 (38.4)	87.8 (20.1)
eGFR, mL/min/1.73 m², mean (SD)	102.8 (29.3)	117.9 (32.5)	101.9 (32.2)	112.7 (30.4)	102.3 (30.8)	115.2 (31.0)
eGFR, n (%)						
<60 mL/min/1.73 m²	13 (9.6)	1 (7.1)	20 (14.7)	1 (6.7)	33 (12.2)	2 (6.9)
≥60 mL/min/1.73 m²	122 (90.4)	13 (92.9)	116 (85.3)	14 (93.3)	238 (87.8)	27 (93.1)
24-h UPCR, mg/mg, mean (SD)	3.14 (2.99)	2.50 (1.97)	3.53 (2.76)	2.86 (2.02)	3.34 (2.87)	2.69 (1.97)
24-h UPCR, n (%)						
<3 mg/mg	82 (61.2)	9 (69.2)	74 (54.4)	10 (66.7)	156 (57.8)	19 (67.9)
≥3 mg/mg	52 (38.8)	4 (30.8)	62 (45.6)	5 (33.3)	114 (42.2)	9 (32.1)
Serum albumin, g/L, mean (SD)	34.7 (6.2)	34.4 (6.4)	34.0 (6.3)	34.7 (3.7)	34.4 (6.2)	34.6 (5.1)
Participants with prior history of LN, n (%)	81 (60.0)	1 (7.1)	76 (55.9)	1 (6.7)	157 (57.9)	2 (6.9)
SLEDAI-2K, mean (SD)	12.1 (8.1)	9.7 (4.6)	12.4 (8.7)	10.3 (4.2)	12.2 (7.4)	10.0 (4.4)
Anti-dsDNA, n (%)						
≤120 kU/L	78 (57.8)	7 (50.0)	75 (55.1)	7 (46.7)	153 (56.5)	14 (48.3)
>120 kU/L	57 (42.2)	7 (50.0)	61 (44.9)	8 (53.3)	118 (43.5)	15 (51.7)
C3, n (%)						
<0.9 g/L	77 (57.0)	6 (42.9)	76 (55.9)	5 (33.3)	153 (56.5)	11 (37.9)
≥0.9 g/L	58 (43.0)	8 (57.1)	60 (44.1)	10 (66.7)	118 (43.5)	18 (62.1)
C4, n (%)						
<0.1 g/L	32 (23.7)	4 (28.6)	42 (31.1)	4 (26.7)	74 (27.4)	8 (27.6)
≥0.1 g/L	103 (76.3)	10 (71.4)	93 (68.9)	11 (73.3)	196 (72.6)	21 (72.4)
B-cell count per mm² tissue, median (min, max)[c]	NA	16.78 (0.35, 226.73)	NA	12.15 (0.00, 68.85)	NA	12.15 (0.00, 226.73)

Anti-dsDNA, anti-double stranded DNA; C, complement; eGFR, estimated glomerular filtration rate; ITT, intention-to-treat; LATAM, Latin America; LN, lupus nephritis; max, maximum; min, minimum; MMF, mycophenolate mofetil; NA, not available; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index2000; ST, standard therapy; UPCR, urine protein-to-creatinine ratio.
[a]Plus ST consisting of MMF plus glucocorticoids; [b]Stratification factor; [c]In cases of replicates (more than one slide stained for the same participant), values are calculated by sum of B-cell counts divided by sum of areas.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Tissue CD79a+/CD138- B cells at baseline and Week 76 in the REGENCY longitudinal kidney biopsy B-cell cohort



B-cell count per mm² tissue, median (min, max)	Obinutuzumab[a] (n=14)	Placebo[a] (n=15)
Baseline	16.76 (0.35, 226.73)	12.15 (0.00, 68.85)
Week 76	0.31 (0.00, 3.31)	13.27 (2.15, 34.77)

In cases of replicates (more than one slide stained for the same participant), single value is calculated as sum of B cells divided by the sum of areas.
CRR was achieved by seven participants (50%) in the obinutuzumab group and three (20%) in the placebo group.
CRR, complete renal response; MMF, mycophenolate mofetil; ST, standard therapy.
[a]Plus ST consisting of MMF plus glucocorticoids.

We postulated that obinutuzumab may deplete B cells in the kidney in addition to the periphery. Given the potential importance of deep, tissue B-cell depletion in LN, participants in the REGENCY trial were offered a post-Week 76 kidney biopsy to evaluate histologic changes over time. Here we present the results of kidney B-cell dynamics from participants with both biopsies.

Methods: Blinded, central reads of baseline and post-Week76 (obtained between Week 76 and Week 80) biopsies were performed by nephropathologists at Arkana Laboratories using the 2018 ISN/RPS LN classification criteria. All participants met the American College of Rheumatology classification criteria for systemic lupus erythematosus and had biopsy-proven proliferative LN. CD79a+/CD138- B cells were quantified on formalin-fixed, paraffin-embedded tissue sections by immunofluorescence microscopy and digital whole-slide image analysis for participants with paired baseline and post-Week 76 biopsies with remaining material for tissue staining (N=29 participants; 14 obinutuzumab plus standard therapy [OBI+ST] and 15 placebo plus standard therapy [PBO+ST]). Raw analysis data generation was performed blinded to treatment; data were unblinded for statistical evaluation. Treatment group comparison of absolute change from baseline at Week 76 in B-cell counts was assessed using ANCOVA model with baseline B-cell counts and stratification factor (Black vs Other) as independent variables.

Results: Baseline characteristics were generally balanced and consistent with the overall REGENCY population; however, the baseline level of tissue CD79a+/CD138- B cells was higher in the OBI+ST group compared with the PBO+ST group (**-Table 1**). Spatial frequency of tissue CD79a+/CD138- B cells at baseline and Week 76 was similar in PBO+ST participants, whereas there was a highly significant decline of B-cell counts per mm^2 at Week 76 vs baseline in OBI+ST participants, with measurements at or near zero (**Figure 1**). ANCOVA analysis showed that at Week 76, the adjusted mean change from baseline in B-cell counts was –28.5 (95% CI, –33.3 to –23.6) in OBI+ST and –11.9 (95% CI, –16.6 to –7.2) in PBO+ST, with a difference of –16.6 (95% CI, –23.4 to –9.7; P< 0.0001) between treatment groups.

Conclusion: These findings demonstrate that obinutuzumab potently depletes B cells in the kidneys of individuals with LN. These data represent the first demonstration of kidney tissue-level B-cell depletion by an anti-CD20 agent in any glomerular disease. Given the possible association of deep, tissue B-cell depletion and prolonged disease control in LN, the clearing of B cells from the kidneys by obinutuzumab may contribute to the improvement in kidney function and decline in LN flares observed in the obinutuzumab-treated patients during the REGENCY trial.

Disclosures: B. Rovin: F. Hoffmann-La Roche Ltd/Genentech, Inc., 2; E. Martins: F. Hoffmann-La Roche Ltd., 3, 11; C. Austin: F. Hoffmann-La Roche Ltd., 11, Genentech, Inc., 3; H. Raghu: F. Hoffmann-La Roche Ltd, 11, Genentech, Inc., 3; C. Chan: F. Hoffmann-La Roche Ltd., 11, Genentech, Inc., 3; P. Chang: F. Hoffmann-La Roche Ltd., 11, Genentech,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Inc., 3; J. Garg: F. Hoffmann-La Roche Ltd., 11, Genentech, Inc., 3; V. Alberton: F. Hoffmann-La Roche Ltd, 2, GlaxoSmithKline, 2, Novartis, 2; M. Santiago: None; G. Aroca-Martínez: None; F. Palazuelos: AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, F. Hoffmann-La Roche Ltd, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Takeda, 2, 5; T. Baczkowska: None; J. Alfaro: AstraZeneca, 2, BMS, 2, F. Hoffmann-La Roche Ltd, 2, Horizon Therapeutics, 2, Kezar, 2; J. Ravelo-Hernández: AstraZeneca, 2, Bristol Myers Squibb, 2, F. Hoffmann-La Roche Ltd., 2, Horizon Therapeutics, 2; R. Furie: Chugai Pharmaceutical Co., 2, 5, F. Hoffmann-La Roche Ltd, 2, 5, Genentech, Inc., 2, 5, GlaxoSmithKline, 2, 5; L. Pinto: None; E. Albiero: None; C. Larsen: Calliditas Therapeutics AB, 2, Novartis, 2; B. Yoo: F. Hoffmann-La Roche Ltd., 11, Genentech, Inc., 3; J. Pulley: F. Hoffmann-La Roche Ltd., 3, 11; A. Thorley: F. Hoffmann-La Roche Ltd, 12, Shareholder, Genentech, Inc., 3; T. Schindler: F. Hoffmann-La Roche Ltd., 3, 11; T. Omachi: F. Hoffmann-La Roche Ltd., 11, Genentech, Inc., 3; W. Pendergraft III: F. Hoffmann-La Roche Ltd., 11, Genentech, Inc., 3; A. Malvar: Bristol Myers Squibb, 2, F. Hoffmann-La Roche Ltd, 2, GSK, 2, Kezar, 2, Novartis, 2, Pfizer, 2.

Abstract Number: LB14

Promising Early Outcomes With BMS-986353, a CD19-directed Chimeric Antigen Receptor T Cell Therapy in Severe Refractory Idiopathic Inflammatory Myopathies: Safety and Efficacy Findings From the Ongoing Phase 1 Trial

Rohit Aggarwal[1], David Korman[2], Margrit Wiesendanger[3], Vikas Majithia[4], Ellen De Langhe[5], Marc Schmalzing[6], Melissa Griffith[7], Philipp Koehler[8], Joanna Schiller[8], Dimitrios Mougiakakos[9], Mohamad Cherry[10], Richard Nash[11], Jacques Azzi[12], Ernesto Ayala[4], Peter Vandenberghe[5], Max Topp[6], Jonathan Gutman[7], Eugen Feist[13], Alisha Desai[14], Alexis Melton[14], Alice Wozniak[14], San-San Ou[14], Melissa Harnois[14], Jerill Thorpe[14], Praneeth Jarugula[14], Takafumi Ide[14], Ashley Koegel[14] and Neil Kramer[15], [1]University of Pittsburgh, Pittsburgh, Pennsylvania, [2]Mountain Rheumatology, HCA HealthONE, Denver, Colorado, [3]Icahn School of Medicine at Mount Sinai, New York, New York, [4]Mayo Clinic Hospital, Jacksonville, Florida, [5]University Hospitals Leuven, Leuven, Belgium, [6]University Hospital Würzburg, Würzburg, Germany, [7]University of Colorado Anschutz Medical Campus, Aurora, Colorado, [8]University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Division of Clinical Immunology and Center for Integrated Oncology (CIO) Aachen Bonn Cologne Duesseldorf, Cologne, Germany, [9]University Hospital Magdeburg, Magdeburg, Germany, [10]Atlantic Health System, Morristown, New Jersey, [11]HealthOne Cares and Colorado Blood Cancer Institute, Denver, Colorado, [12]Icahn School of Medicine at Mount Sinai Hospital, New York, New York, [13]Helios Vogelsang-Gommern Specialist Clinic, Gommern, Germany, [14]Bristol Myers Squibb, Princeton, New Jersey, [15]Overlook Medical Center and Atlantic Medical Group, Atlantic Health System, Morristown, New Jersey

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Idiopathic inflammatory myopathies (IIMs) are systemic autoimmune diseases affecting muscles, skin, lungs, joints, and several other organs; many patients are refractory to available therapy, highlighting the need for novel treatments. BMS-986353 is an investigational CD19-directed autologous chimeric antigen receptor (CAR) T cell therapy being studied in autoimmune diseases. We present the first report on the tolerability and efficacy of BMS-986353 in patients with severe refractory IIMs from Breakfree-1 (NCT05869955).

Methods: Patients with IIM with severe muscle involvement (manual muscle test [MMT]-8 < 130) despite treatment with glucocorticoids and ≥2 immunosuppressants (ISTs) were treated with a single BMS-986353 infusion of 10×10^6 CAR T cells following lymphodepletion. All patients discontinued IIM-specific therapies and steroids (≥5 mg prednisone equivalent, except when directed for adrenal insufficiency) before lymphodepletion. Primary endpoint was safety.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table

Table. CRS and ICANS

	CRS	ICANS
Any grade,[a] n (%)	6 (46.2)	1 (7.7)
Grade 1	5 (38.5)	0
Grade 2	1 (7.7)	0
Grade 3	0	1 (7.7)
Median time to onset (range), days	5.0 (5–10)	9
Median duration[b] (range), days	4.0 (1–11)	3
Treatments, n (%)		
Tocilizumab	5 (38.5)	0
Paracetamol	2 (15.4)	0
Steroids	0	1 (7.7)
Anakinra	0	0

[a]No grade 4 or 5 events were observed. [b]Multiple events occurring within 7 days of each other are considered as 1 episode.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

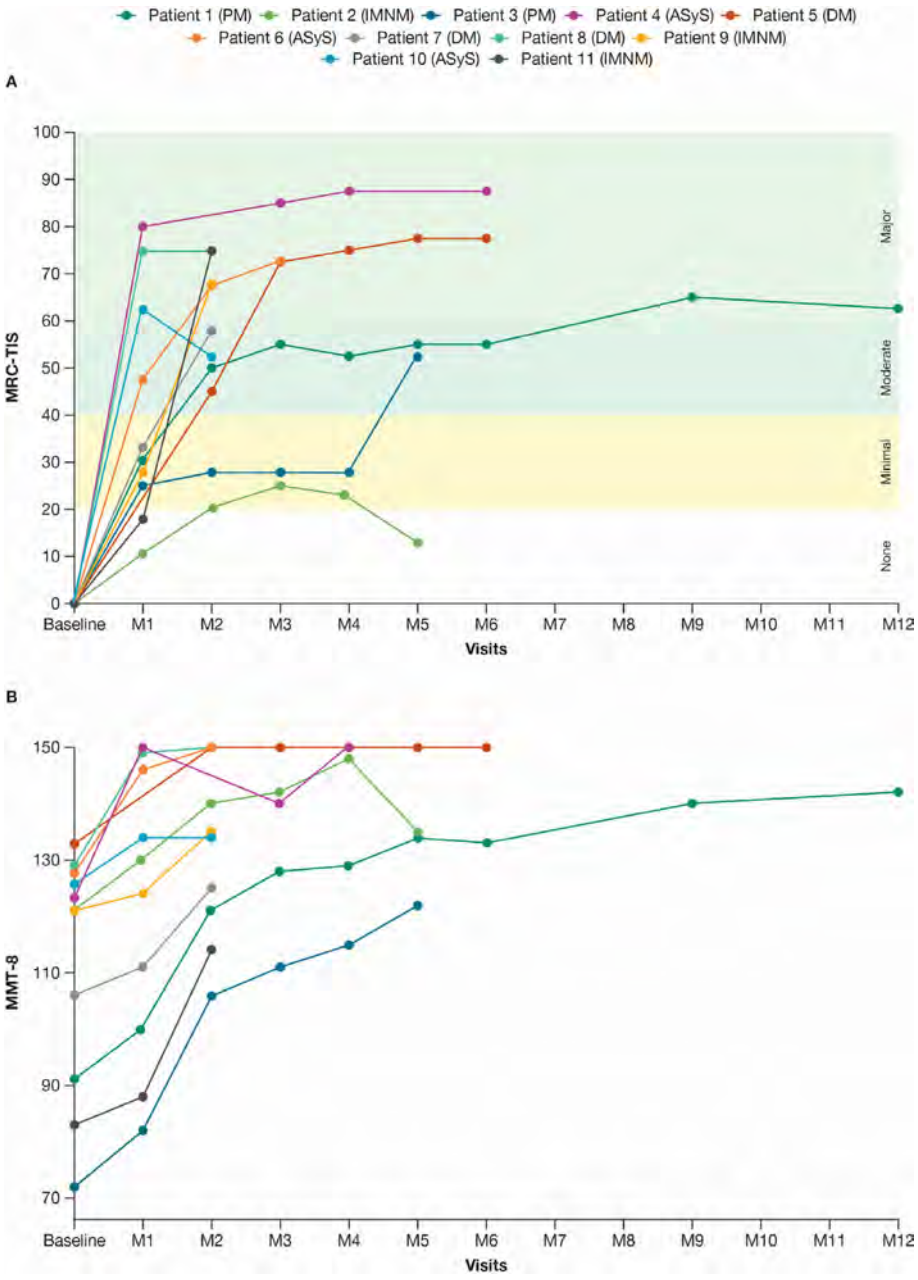


Figure 1. MRC-TIS (A) and MMT-8 (B) following BMS-986353 infusion in efficacy-evaluable IIM population. ASyS, antisynthetase syndrome; IMNM, immune-mediated necrotizing myopathy; M, month.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

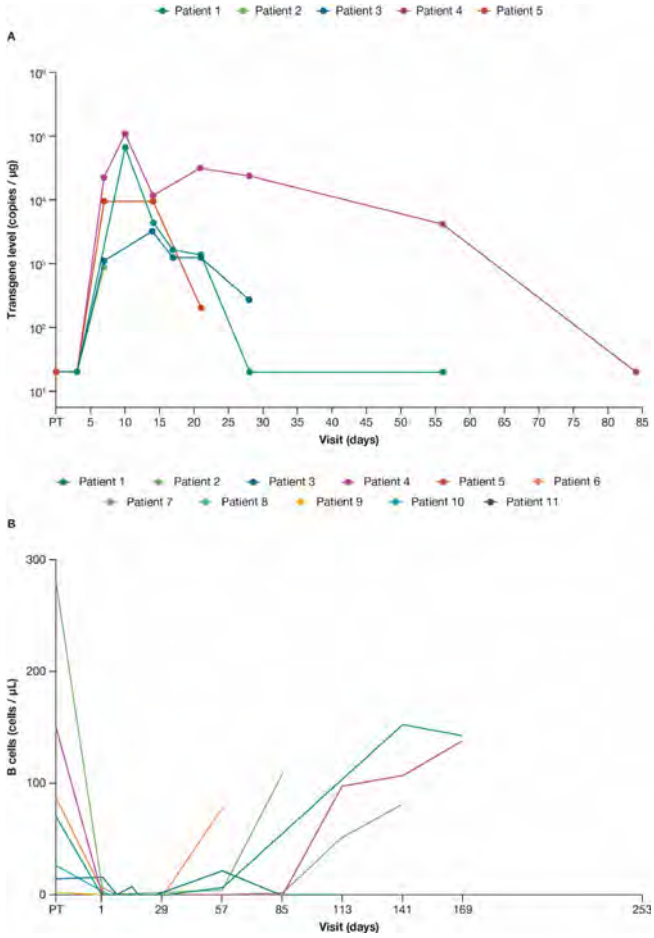


Figure 2. CAR transgene levels (A) and peripheral blood B cell depletion/reconstitution (B) in evaluable IIM population. Transgene levels refer to the number of genetic copies of the engineered CAR construct present in a patient's blood, as measured by droplet digital PCR. CAR, chimeric antigen receptor; PT, pre-treatment.

Results: As of August 14, 2025, 13 patients were evaluable for safety. Before enrollment, patients received a median 6 (range 3–9) prior ISTs. Eleven patients were evaluable for efficacy (antisynthetase syndrome, n=3; DM, n=3; PM, n=2; immune-mediated necrotizing myopathy [IMNM], n=3), with median baseline MMT-8 score of 121 (range 72–133). Median follow-up was 87 days (range 4–375).

Six of 13 (46.2%) patients developed low-grade (Gr) cytokine release syndrome (Gr 1, n=5; Gr 2, n=1; **Table**). One patient had immune effector cell-associated neurotoxicity syndrome (Gr 3) characterized by decreased level of consciousness and aphasia, which resolved in 3 days with dexamethasone. Two transient hematologic treatment-emergent adverse events of Gr ≥3 (neutropenia, n=1; anemia, n=1) were reported. There were no prolonged cytopenias (lasting >28 days) or treatment-emergent serious infections.

Of the 11 efficacy-evaluable patients, 7 (63.6%) achieved a major response and 3 (27.3%) a moderate response based on Myositis Response Criteria—Total Improvement Score (MRC-TIS). All 11 patients experienced a rapid and significant improvement in muscle strength; median increase in MMT-8 score from baseline was 22.0 points at day 85 (n=6) and 27 points at day 169 (n=3). One patient with IMNM with a >10-year disease duration and minimally elevated baseline creatine kinase had an improved MMT-8 without achieving ≥moderate MRC-TIS response (**Figure 1**). Ten of 11 efficacy-evaluable patients remained off IIM-directed therapy at last follow-up, with 1 patient empirically restarting IVIG for elevated creatine kinase despite improvement in MMT-8 score.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

All patients had robust CAR T cell expansion and achieved complete peripheral blood B-cell depletion (**Figure 2**). IIM-related autoantibody levels decreased post-infusion.

Conclusion: Findings from Breakfree-1 demonstrate a manageable safety profile, robust CAR T cell expansion, complete B-cell depletion, and promising efficacy of BMS-986353 without IIM-directed therapies in >90% of patients with severe refractory IIMs.

Medical writing: Sameen Yousaf, PhD (Caudex, an IPG Health company), funded by BMS.

Disclosures: R. Aggarwal: Abcuro, 2, Alexion, 2, ANI Pharmaceutical, 2, Argenx, 2, AstraZeneca, 2, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb (BMS), 2, CabalettaBio, 2, Capstanx, 2, CSL Behring, 2, Dren Bio, 2, EMD Serono, 2, 5, Fate Therapeutics Inc., 2, Galapagos, 2, GlaxoSmithKline LLC (GSK), 2, Horizon Therpeutics, 2, I-Cell, 2, Immunovant, 2, Janssen, 2, 5, Janux Therapeutics, 2, Kiniksa Pharmaceuticals, 2, Lilly, 2, Meiji Pharma, 2, Nakarta, 2, Novartis, 2, Octapharma, 2, Orna Therapeutics Inc, 2, Ouro Medicines, 2, Pfizer, 2, 5, PRoivant, 2, 5, Sun Pharmaceutical Industries, 2, Tourmaline Bio, 2, UCB, 2, Verismo Therapeutics, 2; D. Korman: None; M. Wiesendanger: Bristol Myers Squibb (BMS), 1, 6; V. Majithia: Bristol Myers Squibb (BMS), 1, 5, Cabaletta Bio, 5; E. De Langhe: AC Immune, 1, Actelion, 6, AlfaSigma, 6, AstraZeneca, 1, 2, 12, Travel expenses, Boehringer Ingelheim, 1, 2, GlaxoSmithKlein(GSK), 2, Novartis, 6, Otsuka, 2; M. Schmalzing: AbbVie/Abbott, 1, 2, 5, 6, 12, Travel expenses, AlfaSigma/Galapagos, 1, 2, 6, 12, Travel expenses, AstraZeneca, 1, 2, Boehringer Ingelheim, 1, 2, 6, 12, Travel expenses, Bristol Myers Squibb (BMS), 1, 2, 5, 6, Chugai, 5, Eli Lilly, 6, EUSA Pharma/Recordati, 1, 2, 6, Johnson & Johnson, 1, 2, 6, 12, Travel expenses, Merck/MSD, 6, Novartis, 1, 2, 5, 6, onkowissen.de, 1, 2, 6, Pfizer, 6, Sanofi, 1, 2, Sobi, 1, 2, UCB, 1, 2, 12, Travel expenses; M. Griffith: AstraZeneca, 5, Bristol Myers Squibb (BMS), 5, Gilead, 5, Sonoma Biotherapeutics, 5; P. Koehler: Ambu GmbH, 1, 2, B-FAST (Bundesweites Forschungsnetz Angewandte Surveillance und Testung), 5, Elsevier, 9, German Federal Ministry of Research and Education (BMBF), 5, Gilead, 1, 2, Mundipharma, 1, 2, NAPKON (Nationales Pandemie Kohorten Netz, German National Pandemic Cohort Network) of the Network University Medicine (NUM), 5, Noxxon, 1, 2, Pfizer, 1, 2, University of Cologne, 10; J. Schiller: AlfaSigma/Galapagos, 12, Travel expenses, Fachverband Rheumatologische Fachassistenz e.V., 6, Novartis, 6, Sanofi-Aventis Deutschland Gmbh, 12, Travel expenses, Schule fur Physiotgerapie und Massage Fachbereich Physiotherapie Universitatsklinikum Koln (AOR), 6; D. Mougiakakos: AbbVie/Abbott, 6, AstraZeneca, 2, AvenCell, 2, Beigene, 1, Bristol Myers Squibb (BMS), 6, Galapagos, 1, Gilead, 1, 6, Interius Bio, 2, Kyverna Therapeutics, 6; M. Cherry: Bristol Myers Squibb (BMS), 6; R. Nash: None; J. Azzi: None; E. Ayala: None; P. Vandenberghe: Bristol Myers Squibb (BMS), 1, Kite/Gilead, 1, 6, 12, Travel expenses, Miltenyi, 1, Novartis, 1, Pfizer, 1; M. Topp: AstraZeneca, 5, Bristol Myers Squibb (BMS), 5, Merck/MSD, 5, Regeneron, 5, Roche, 5; J. Gutman: None; E. Feist: Bristol Myers Squibb (BMS), 1, 5, 6; A. Desai: Bristol Myers Squibb (BMS), 3; A. Melton: Bristol Myers Squibb (BMS), 3; A. Wozniak: Bristol Myers Squibb (BMS), 3; S. Ou: Bristol Myers Squibb (BMS), 3; M. Harnois: Bristol Myers Squibb (BMS), 3, 8; J. Thorpe: Bristol Myers Squibb (BMS), 3; P. Jarugula: Bristol Myers Squibb (BMS), 3, 8; T. Ide: Bristol Myers Squibb (BMS), 3, 8; A. Koegel: Bristol Myers Squibb (BMS), 3, 8; N. Kramer: Amgen, 8, AstraZeneca, 5, 6, Becton Dickinson, 8, Bristol Myers Squibb (BMS), 2, 5, GlaxoSmithKline (GSK), 5, 6, Immunic, 8, Johnson & Johnson, 8, Pfizer, 8, Protagonist Therapeutics, 8, Stryker, 8, UpToDate, 7.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: LB15

Dietary Fiber Supplementation Enhances Methotrexate Response and Restores Th17/Treg Balance in Rheumatoid Arthritis: Results from the Superfibre Randomized Trial

Claire Immediato Daien[1], Jean-Pierre Hellier[2], Zübeyir Salis[3], Gaël Mouterde[4], Jacques Morel[5], Laurence Macia[6] and Rachel audo[4], [1]CHU and Univesrity of Montpellier, Montpellier, France, [2]CHU Montpellier, Arles, France, [3]University of Montpellier, Montpellier, France, [4]CHU Montpellier, Montpellier, France, [5]CHU and University of Montpellier, Montpellier, France, [6]Sydney University, Brisbane, Australia

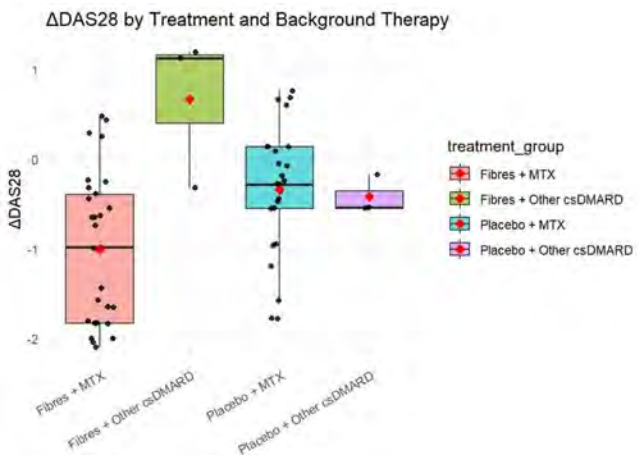
SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Gut dysbiosis and Th17/Treg imbalance contribute to rheumatoid arthritis (RA). Additionally, methotrexate (MTX) efficacy depends on gut microbiota composition, especially on the presence of B. fragilis and butyrate (Zhou B, et al. Front Microbiol. 2022). Dietary fibres improve gut microbiota composition and increase microbiota-derived short-chain fatty acids including butyrate, that may restore immune tolerance.

We aimed to evaluate whether dietary fiber supplementation in patients with RA improves disease activity, Th17/Treg balance and response to MTX.

Methods: Superfibres was a randomized, double-blind, placebo-controlled trial, including patients with active RA despite stable doses of csDMARDs. Patients were randomized 1:1 to inulin (12 g/day) or placebo for 30 days. EULAR response and change in peripheral Th17/Treg subsets (flow cytometry) were compared. Subgroup analyses compared MTX vs. non-MTX patients.

Results: A total of 49 patients were included (26 in the fiber group, 23 in the placebo group) with 85.7% women, a mean age of 62 ± 10 years and a mean DAS28 was 3.86 ± 0.61. Odds of EULAR response were markedly higher with fiber (OR 4.65, 95% CI 1.15–18.9; p=0.03). Fiber reduced circulating Th17 cells and the Th17/Treg ratio compared with placebo (p < 0.02). A significant treatment × MTX interaction was observed (p=0.011). In MTX users, mean ΔDAS28 was –1.00 with fiber vs –0.34 with placebo (Fig. 1). No effect was seen in non-MTX patients (n=6). Intervention was well tolerated, with >90% compliance.



DeltaDAS28 by treatment and background therapy.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Conclusion: This first placebo-controlled RCT of dietary fiber in RA shows that supplementation significantly increases EULAR response rates and improves Th17/Treg balance. This may be explained by an enhanced MTX efficacy These findings establish the gut–immune axis as a novel therapeutic target and identify dietary fiber as a safe, inexpensive adjunct to MTX in RA. If confirmed, our results have the potential to change clinical practice and improve MTX efficacy in daily practice.

Disclosures: C. Immediato Daien: AbbVie/Abbott, 2, Amgen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 5, 6, Janssen, 6, Merck/MSD, 6, Novartis, 6, Pfizer, 6, UCB, 6; J. Hellier: None; Z. Salis: Zuman International Pty Ltd, 8; G. Mouterde: AbbVie/Abbott, 6, Alphasigma, 6, Eli Lilly, 6, Novartis, 6, Roche Chugai, 6, UCB, 6; J. Morel: Medac, 1, Nordic pharma, 6; L. Macia: Sanofi, 3; R. audo: None.

Abstract Number: LB16

Mepolizumab Reduces End-Organ Manifestations Compared with Standard of Care in Patients with EGPA and HES: A US Real-world Analysis

David Silverman[1], Timothy Barnes[2], Nnaemeka Odo[2], Jared Silver[3], Lisa Le[2], Amy Edgecomb[4] and Hitesh Patel[5], [1]Rheumatology Department, Kaiser Permanente Colorado Medical Group, Denver, Colorado, [2]Value and Evidence Solutions, Optum Life Sciences, Eden Prairie, Minnesota, [3]Clinical Development, Amgen, Thousand Oaks, California, [4]Anti-infectives and Respiratory, GSK, Philadelphia, Pennsylvania, [5]US Medical Affairs, GSK, Durham, North Carolina

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA) and hypereosinophilic syndrome (HES) are rare systemic diseases characterized by persistent eosinophilia and tissue infiltration, resulting in end-organ dysfunction (EOD)[(1)]. Standard of care (SOC) includes corticosteroids, immunosuppressives, disease-modifying antirheumatic drugs and biologics[(2)]. Mepolizumab, an anti-interleukin-5 monoclonal antibody, reduces disease manifestations and corticosteroid dependence[(3,4)]. Real-world evidence on EOD outcomes following mepolizumab initiation in EGPA and HES is limited. This study evaluated mepolizumab impact on EOD compared with other SOC therapies in a US real-world setting.

Methods: This retrospective cohort study used administrative claims and EHR data from Optum's Market Clarity database. Patients with EGPA (≥18 years) or HES (≥12 years) were identified at mepolizumab or SOC initiation (index). Patients were classified as mepolizumab users or chronic SOC users (≥6 months of >7.5 mg prednisone equivalent and/or ≥2 records of immunosuppressants or other disease-modifying antirheumatic drugs from index). Baseline sociodemographic characteristics, SOC use, comorbidities, and prior end-organ procedures were captured in the 6-months pre-index. Inverse probability of treatment weighting was used to balance the covariates between patient cohorts. EOD proportion, rate, and status were assessed ≥12 months post-index. Z-test compared weighted groups. Analyses were performed separately for EGPA and HES.

Results: Among 1102 patients with EGPA, 375 received mepolizumab and 727 received chronic SOC. Weighted analyses demonstrated numerical improvements in 14 distinct EOD conditions across multiple organ systems in those treated with mepolizumab vs chronic SOC. Significant improvements in EOD status were observed in acute kidney failure in mepolizumab vs chronic SOC (63.4% vs 23.4%, p=0.026) **(Table)**.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table. Proportion of patients with EGPA and HES with EOD conditions with improvement of EOD status[1], stratified by treatment regimen (mepolizumab vs chronic SOC[2]).

	EGPA (N=1102)			HES (N=784)		
EOD conditions	Mepo (N=375)	Chronic SOC[2] (N=727)	Mepo vs chronic SOC p-value[3]	Mepo (N=198)	Chronic SOC[2] (N=586)	Mepo vs chronic SOC p-value[3]
Ischemic heart diseases, N	42	90		15	86	
Improvement of EOD status[1], %	21.61	15.58	0.464	34.48	27.07	0.680
Atrial fibrillation, N	20	39		12	47	
Improvement of EOD status[1], %	9.20	21.12	0.317	60.10	23.02	0.124
Cardiomyopathy, N	15	45		6	25	
Improvement of EOD status[1], %	16.34	31.69	0.308	40.09	24.22	0.475
Congestive heart failure, N	18	51		10	46	
Improvement of EOD status[1], %	34.65	18.92	0.276	37.28	22.59	0.379
Mitral regurgitation, N	19	62		13	30	
Improvement of EOD status[1], %	38.97	25.78	0.375	90.86	29.39	**<0.001**
Arrhythmias, N	12	24		7	28	
Improvement of EOD status[1], %	17.72	17.23	0.972	53.35	22.83	0.169
Asthma, N	325	292		131	174	
Improvement of EOD status[1], %	30.61	27.07	0.610	52.17	39.52	0.213
Chronic eosinophilic pneumonia, N	8	3		13	7	
Improvement of EOD status[1], %	54.19	10.44	0.150	51.74	54.23	0.929
Bronchiectasis, N	24	35		12	12	
Improvement of EOD status[1], %	6.14	19.22	0.134	74.76	44.12	0.187
Pulmonary nodule, N	18	35		9	22	
Improvement of EOD status[1], %	39.61	22.12	0.311	66.89	37.13	0.167
Respiratory failure, N	25	81		12	44	
Improvement of EOD status[1], %	11.46	19.18	0.392	21.07	45.05	0.223
Chronic rhinosinusitis (without nasal polyps), N	136	137		43	22	
Improvement of EOD status[1], %	34.83	37.61	0.798	50.81	51.10	0.985
Chronic rhinosinusitis (with nasal polyps), N	12	14		6	2	
Improvement of EOD status[1], %	50.86	15.47	0.119	67.70	100.00	–
Hematuria or proteinuria, N	23	69		8	30	
Improvement of EOD status[1], %	31.57	30.08	0.909	28.01	50.72	0.252
Acute kidney failure, N	9	79		0	36	
Improvement of EOD status[1], %	63.35	23.42	**0.026**	–	14.53	–
Chronic Kidney Disease Stage 3, valid N	21	69		4	34	
Improvement of EOD status[1], %	6.93	31.65	**0.009**	52.90	28.82	0.431
Paraesthesia of skin, N	9	26		4	16	
Improvement of EOD status[1], %	38.68	18.69	0.224	63.38	58.74	0.880
Mononeuropathies, N	2	6		0	2	
Improvement of EOD status[1], %	51.38	23.37	0.487	–	46.77	–
Mononeuritis multiplex, N	6	12		1	0	
Improvement of EOD status[1], %	38.68	14.62	0.269	0.00	–	–
Stroke/TIA, N	10	27		7	30	
Improvement of EOD status[1], %	6.86	30.53	0.057	22.28	25.55	0.877
Venous thrombosis, N	24	48		8	32	
Improvement of EOD status[1], %	21.12	14.07	0.516	69.47	8.14	**0.009**
Sensorineural hearing loss, N	6	15		1	5	
Improvement of EOD status[1], %	27.86	35.59	0.782	0.00	39.45	–
Conjunctivitis/blepharitis/keratitis, N	11	20		8	14	
Improvement of EOD status[1], %	65.91	26.32	0.095	31.74	59.17	0.306
Eosinophilic esophagitis/gastritis/colitis, N	16	6		32	31	
Improvement of EOD status[1], %	48.96	57.04	0.789	45.44	72.96	0.070

Patients are grouped according to treatment received during the landmark period (within 6 months of index date) – mepolizumab vs chronic SOC[2]. Only the proportion of patients with improvement of EOD status[1] is reported as the remainder of patients experienced worsening of EOD status. [1]Improvement of EOD status: no evidence of hospitalization or emergency room visit linked to ICD-10 code for EOD condition AND treatment change defined as a removal of new SOC medication or decrease in SOC medication dose. [2]Chronic SOC user: ≥6 months of >7.5 mg prednisone equivalent and/or ≥2 records of immunosuppressants or other disease-modifying antirheumatic drugs (DMARDs). The earliest record and date of this continuous use period of SCS and/or immunosuppressants or DMARDS will be defined as the index date. [3]p-values are calculated from standardized differences between mepolizumab and chronic SOC users using z-test. Significant p-values are highlighted in bold. EGPA, eosinophilic granulomatosis with polyangiitis; EOD, end-organ dysfunction; HES, hypereosinophilic syndrome; ICD, International Classification of Diseases; Mepo, mepolizumab; SOC, standard of care; SCS, systemic corticosteroid; TIA, transient ischemic attack.

Among 784 patients with HES, 198 received mepolizumab and 586 received chronic SOC. Weighted analyses showed numerical improvement across 12 distinct EOD conditions among those treated with mepolizumab vs chronic SOC. Significant improvements in EOD status were observed in mepolizumab vs chronic SOC in mitral regurgitation (90.9% vs 29.4%, p< 0.001), and venous thrombosis (69.5% vs 8.1%, p=0.009) **(Table)**.

Conclusion: In this large real-world analysis, mepolizumab was associated with clinically meaningful improvements across multiple end-organ systems in both EGPA and HES, including cardiac, renal, and vascular conditions. These findings represent a potential signal of multisystem benefit and support further research to explore the durability and clinical significance of these effects.

Funding: GSK (221044)

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

References

1. Wechsler ME et al. *J Allergy Clin Immunol*. 2023;151(6):1415–28.
2. Khoury P et al. *Mayo Clinic Proc*. 2023;98(7):1054–70.
3. Wechsler ME et al. *N Engl J Med*. 2017;376(2):1921–32.
4. Roufosse F et al. *J Allergy Clin Immunol*. 2020;146(6):1397–405.

Disclosures: D. Silverman: Optum, 2; T. Barnes: Optum, 3; N. Odo: Optum, 3; J. Silver: Amgen, 3, 12, Financial equities, GSK, 3, 12, Financial equities; L. Le: Optum, 3; A. Edgecomb: GSK, 3, 12, Financial equities; H. Patel: GSK, 3, 12, Financial equities.

Abstract Number: LB17

Circulating biomarkers for organ involvement in systemic lupus erythematosus: a series of systematic reviews and meta-analyses

Sitian Zang[1], Ranran Yao[1], Yan Wang[1], Danxue Zhu[1], Jing He[1] and Zhanguo Li[2], [1]Peking University People's Hospital, Beijing, China (People's Republic), [2]Peking Univeristy People's Hospital, Beijing, China (People's Republic)

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: Systemic lupus erythematosus (SLE) features heterogeneous clinical manifestations. The identification of biomarkers that facilitate initial disease recognition is a cornerstone of optimized clinical management. This study was aimed at summarizing and providing an exhaustive and penetrating exploration of biomarkers associated with organ involvement.

Methods: Embase, PubMed and Web of Science were systematically searched from inception through June 1, 2023. Effect estimates were pooled by the DerSimonian-Laird random-effects model in the presence of substantial heterogeneity (I^2 >50% or the p-value for Q was < 0·1). Fixed-effects models were not used when heterogeneity criteria were not met. Bivariate models were employed for summarizing diagnostic accuracy parameters when ≥4 datasets were available. Univariate models were used for three or fewer datasets or when bivariate models failed to converge.

Results: A total of 698 studies were included in the analysis and comprised 114,457 lupus patients from 55 countries and territories. The most commonly involved organ and system were renal, neuropsychiatric, hematologic, cardiopulmonary, and cutaneous, corresponding to five distinct lupus phenotypes: lupus nephritis (LN), neuropsychiatric SLE (NPSLE), hematologic involvement, cardiopulmonary involvement, and cutaneous lupus erythematosus (CLE). Thirty-seven biomarkers were significantly associated with the risk of multi-organ involvement. We further analyzed the specific biomarkers for the five phenotypes. It showed that 71 circulating biomarkers were significantly related to an increased risk of LN. Among them, the most frequently reported biomarker was anti-complement 1q (anti-C1q) (odds ratio [OR] 3.76, 95% confidence interval [CI] 2.50–5.64, p< 0.0001). Of the 43 circulating biomarkers correlated with an increased risk of NPSLE, anti-ribosomal P protein (anti-Rib-P) isotypes (anti-Rib-P IgG [OR 1.93, 95% CI 1.10–3.39, p=0.023]) and subtypes (anti-Rib-P0 [OR 2.28, 95% CI 1.20–4.33, p< 0.0001] and anti-neuronal antibodies (OR 6.10, 95% CI 1.65–22.59, p=0.0070) were most frequently reported. The most frequently reported biomarkers for hematologic involvement were platelet-related and coagulation-associated antibodies, as well as non-criteria anti-phospholipid antibodies. High-sensitivity C-reactive protein (hsCRP) levels

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

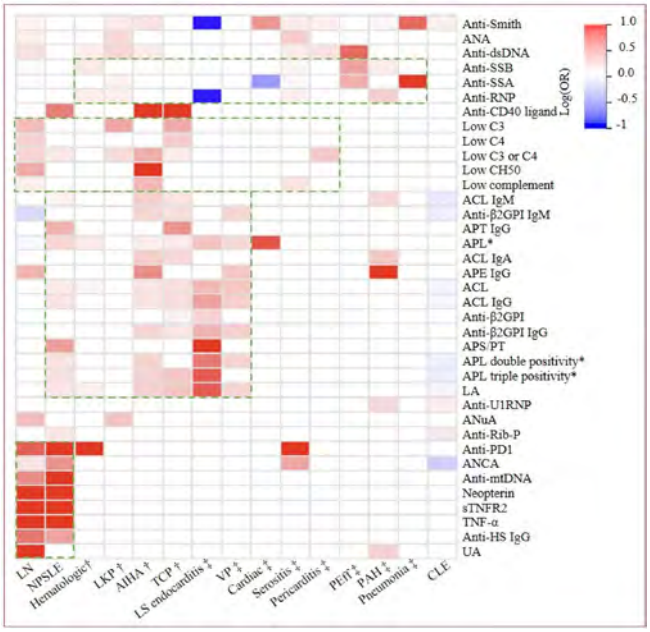


Figure 1: Summary of biomarkers associated with multi-organ involvement in patients with SLE. ACL=anti-cardiolipin antibodies. ANA=anti-nuclear antibodies. Anti-dsDNA=anti-double-stranded DNA antibodies. ANCA=anti-neutrophil cytoplasmic antibodies. Anti-CD40 ligand=anti-CD40 ligand antibodies. Anti-HS=anti-heparan sulfate antibodies. Anti-mtDNA=anti-mitochondrial DNA antibodies. Anti-PD1=anti-programmed cell death protein 1 antibodies. Anti-RNP=anti-ribonucleoprotein antibodies. Anti-Rib-P=anti-ribosomal P protein antibodies. Anti-U1RNP=anti-U1 small nuclear ribonucleoprotein antibodies. Anti-SSA=anti-Sjögren's syndrome-related antigen A antibodies. Anti-SSB=anti-Sjögren's syndrome-related antigen B antibodies. Anti-β2GPI=anti-beta-2 glycoprotein I antibodies. Anti-PT=anti-prothrombin antibodies. APE=anti-phosphatidylethanolamine antibodies. APL=anti-phospholipid antibodies. APS/PT=anti-phosphatidylserine/prothrombin antibodies. ANuA=anti-nucleosome antibodies. CLE=cutaneous lupus erythematosus. IgA=immunoglobulin A. IgG=immunoglobulin G. IgM=immunoglobulin M. LA=lupus anticoagulant. Low CH50=low total hemolytic complement activity. LKP=leukopenia. LN=lupus nephritis. LS endocarditis=Libman-Sacks endocarditis. NA=not available. NPSLE=neuropsychiatric systemic lupus erythematosus. PAH=pulmonary arterial hypertension. Peff=pericardial effusion. SLE=systemic lupus erythematosus. sTNFR2=soluble tumor necrosis factor receptor 2. TCP=Thrombocytopenia. TNF-α=tumor necrosis factor-alpha. UA=uric acid. VP=valvulopathy. A log(OR) > 0 indicates that biomarker positivity is associated with an increased risk of involvement, while a log(OR) < 0 indicates an association with a decreased risk. *APL include aCL, anti-β2GPI, LA, aPT, aPE, and aPS/PT; among these, aPL double positivity is defined as the concurrent presence of aCL and anti-β2GPI antibodies, while aPL triple positivity is defined as the concurrent presence of aCL, anti-β2GPI, and LA. †Hematologic involvement. ‡Cardiopulmonary involvement.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

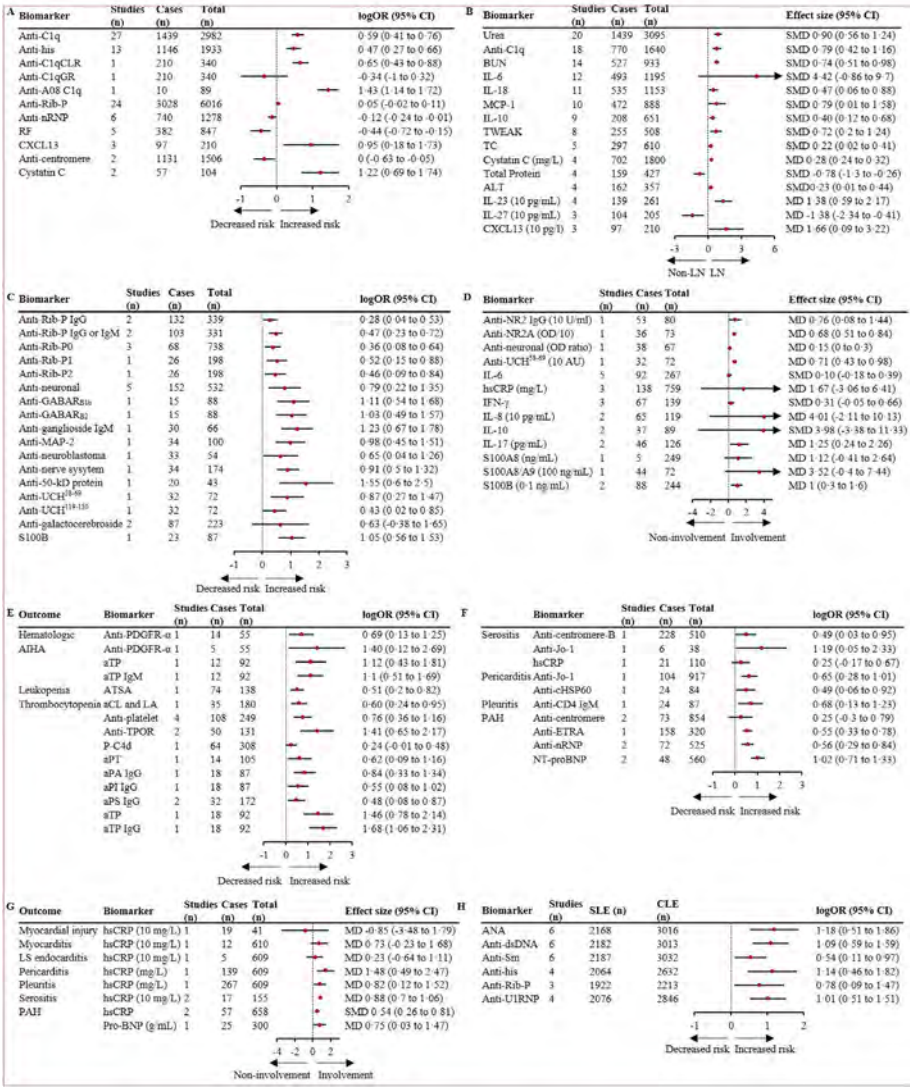


Figure 2: Effect size of key biomarkers on organ involvement in SLE patients. (A) OR of LN in patients with positive versus negative biomarkers. (B) MD of biomarkers in patients with versus without LN. (C) OR of NPSLE in patients with positive versus negative biomarkers. (D) MD of biomarkers in patients with versus without NPSLE. (E) OR of hematologic involvement in patients with positive versus negative biomarkers. (F) OR of cardiopulmonary involvement in patients with positive versus negative biomarkers. (G) MD of biomarkers in patients with versus without cardiopulmonary involvement. (H) OR of systemic involvement in CLE patients with positive versus negative biomarkers. ALT=alanine aminotransferase. ANA=antinuclear antibodies. Anti-50-kD protein=Anti-50-kD neuronal membrane protein. Anti-A08 C1q=anti-A08 complement component 1q antibodies. Anti-C1q=anti-complement component 1q antibodies. Anti-C1qCLR=anti-C1q collagen-like region antibodies. Anti-C1qGR=anti-C1q globular region antibodies. Anti-CD4 IgM=anti-cluster of differentiation 4 immunoglobulin M antibodies. Anti-cHSP60=anti-chaperonin heat shock protein 60 antibodies. Anti-dsDNA=anti-double-stranded DNA. Anti-ETRA=anti-endothelin receptor type A antibodies. Anti-GABARB=anti-gamma-aminobutyric acid type B receptor subunit. Anti-his=anti-histone antibodies. Anti-Jo-1=anti-histidyl-tRNA synthetase antibodies. Anti-MAP-2=anti-microtubule-associated protein 2 antibodies. Anti-NR=anti-N-methyl-D-aspartate receptor. Anti-nRNP=anti-nuclear ribonucleoprotein antibodies. Anti-PDGFR-α=anti-platelet-derived growth factor receptor alpha antibodies. Anti-Rib-P=anti-ribosomal P protein antibodies. Anti-TPOR=anti-thrombopoietin receptor antibodies. Anti-UCL=anti-ubiquitin carboxyl hydrolase-L1 antibodies. APA=anti-phosphatidic acid antibodies. API=anti-phosphatidylinositol antibodies. APS=anti-phosphatidylserine antibodies. APT=anti-prothrombin antibodies. ATP=anti-thromboplastin antibodies. ATSA=anti-thrombospondin-1 antibodies. BUN=blood urea nitrogen. CXCL13=C-X-C motif chemokine ligand 13. hsCRP=high-sensitivity C-reactive protein. IFN=interferon. IL=interleukin. LN=lupus nephritis. LS endocarditis=Libman-Sacks endocarditis. MD=mean difference. MCP-1=monocyte chemoattractant protein-1. NT-proBNP=N-terminal pro-brain natriuretic peptide. NPSLE=neuropsychiatric SLE. OR=odds ratio. RF=rheumatoid factor. P-C4d=platelet C4d. SLE=systemic lupus erythematosus. SMD=standardized mean difference. TC=total cholesterol. TWEAK=tumor necrosis factor-like weak inducer of apoptosis.

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

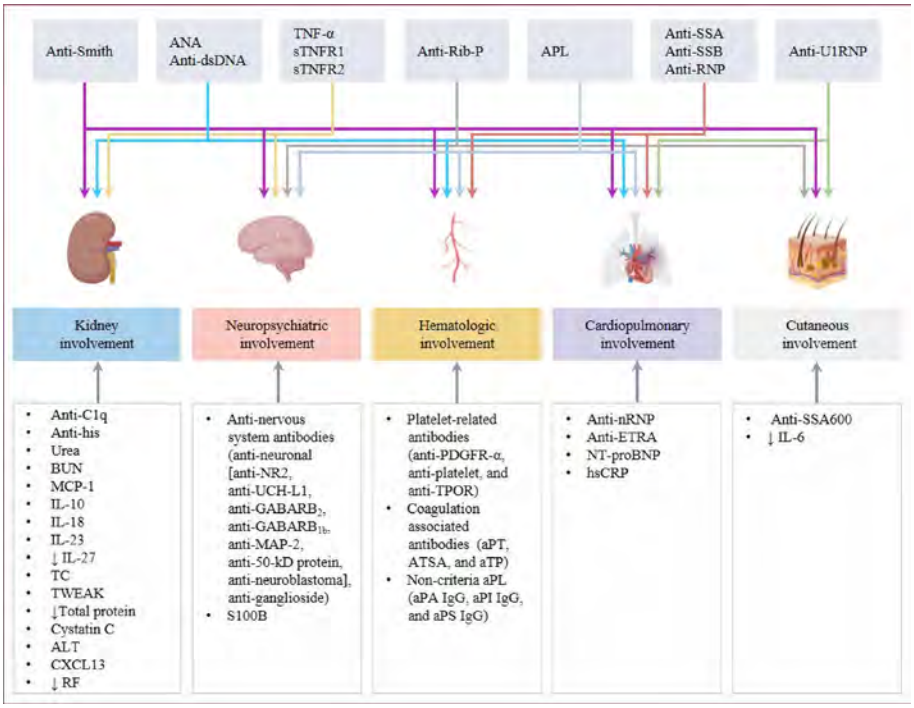


Figure 3: The most reported biomarkers for organ involvement in SLE. ALT=alanine aminotransferase. ANA=antinuclear antibodies. Anti-50-kD protein=Anti-50-kD neuronal membrane protein. Anti-C1q=anti-complement component 1q antibodies. Anti-dsDNA=anti-double-stranded DNA. Anti-ETRA=anti-endothelin receptor type A antibodies. Anti-GABARB=anti-gamma-aminobutyric acid type B receptor subunit. Anti-his=anti-histone antibodies. Anti-Jo-1=anti-histidyl-tRNA synthetase antibodies. Anti-MAP-2=anti-microtubule-associated protein 2 antibodies. Anti-NR=anti-N-methyl-D-aspartate receptor. Anti-nRNP=anti-nuclear ribonucleoprotein antibodies. Anti-PDGFR-α=anti-platelet-derived growth factor receptor alpha antibodies. Anti-Rib-P=anti-ribosomal P protein antibodies. Anti-SSA=anti-Sjögren's syndrome-related antigen A antibodies. Anti-TPOR=anti-thrombopoietin receptor antibodies. Anti-UCL-L1=anti-ubiquitin carboxyl hydrolase-L1 antibodies. APA=anti-phosphatidic acid antibodies. API=anti-phosphatidylinositol antibodies. APS=anti-phosphatidylserine antibodies. APT=anti-prothrombin antibodies. ATP=anti-thromboplastin antibodies. ATSA=anti-thrombospondin-1 antibodies. BUN=blood urea nitrogen. CXCL13=C-X-C motif chemokine ligand 13. hsCRP=high-sensitivity C-reactive protein. IL=interleukin. MCP-1=monocyte chemoattractant protein-1. NT-proBNP=N-terminal pro-brain natriuretic peptide. OR=odds ratio. RF=rheumatoid factor. SLE=systemic lupus erythematosus. SMD=standardized mean difference. TC=total cholesterol. TWEAK=tumor necrosis factor-like weak inducer of apoptosis.

differed greatly between patients with and without serositis, pericarditis, myocarditis and pleuritis. Anti-nuclear ribonucleoprotein (anti-nRNP) antibodies (OR 3.66, 95% CI 1.94–6.89, p< 0.0001) were the most commonly reported biomarker showing a relationship with a higher risk of pulmonary arterial hypertension. Among the eight specific biomarkers for CLE in SLE patients, anti-SSA60 was significantly associated with increased risk of CLE with the largest number of involved patients (OR 1.30, 95% CI 1.05–1.62, p=0.017).

Conclusion: This large-scale analysis revealed biomarker profiles associated with organ involvement in SLE and provided a clinically actionable non-invasive tool for the risk prediction of organ damage.

Disclosures: S. Zang: None; R. Yao: None; Y. Wang: None; D. Zhu: None; J. He: None; Z. Li: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: LB18

Transcriptomic Signatures of ANA+ and ANA- B Cells Reveal Shifts from Active Disease to Remission in Systemic Lupus Erythematosus

Rita Pozovskiy[1], Yemil Atisha-Fregoso[2] and Betty Diamond[3], [1]Zucker School of Medicine, New York, New York, [2]Feinstein Institutes for Medical Research, New York, New York, [3]The Feinstein Institutes for Medical Research, Manhasset, New York

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: (LB01–LB18) Late-Breaking Posters
Session Type: Poster Session C
Session Time: 10:30AM–12:30PM

Background/Purpose: In systemic lupus erythematosus (SLE), IgG antibodies that target nuclear antigens (ANA) are pathogenic and part of the diagnostic criteria for SLE. Healthy individuals (HC) possess ANA^+ mature B cells but these cells do not differentiate into IgG+ plasma cells and do not produce pathogenic antibodies. This study aimed to identify differential activation and regulatory mechanisms of ANA^+ B cells in patients with SLE and HC. To gain insight into immune homeostasis during remission, we included patients with active disease (SLE-A) and those in remission (SLE-R).

Methods: We profiled the transcriptomes of ANA^+ and ANA^- B cells using single-cell RNA sequencing (scRNA-seq). Samples were obtained from 7 patients with SLE-A, 5 SLE-R, and 7 HC. Three B cell subsets were isolated (ANA^+ and ANA^-): (1) $CD19^+$ $CD27^-$ CD38^int (encompassing naïve B cells and age-associated B cells [ABCs]), (2) $CD19^+$ $CD27^+$ IgM^+ (including circulating marginal zone B cells [MZB] and IgM memory B cells), and (3) $CD19^+$ $CD27^+$ IgG^+ (IgG memory B cells).

Results: We identified seven transcriptionally distinct B cell clusters defined by canonical lineage and activation markers: naïve, activated naïve, marginal zone B cells (MZB), IgM memory, memory (predominantly IgG^+), activated memory (also predominantly IgG^+), and age-associated B cells (ABCs). Minimal overlap in cluster composition was observed between SLE-A and HC, while SLE-R exhibited a unique intermediate profile.

Pathway analysis revealed that activated clusters were enriched for interferon (IFN) and TNF-α and oxidative phosphorylation signatures compared to quiescent clusters. Using a published compendium of scRNA-seq profiles of immune cells in response to cytokines, we confirmed an IFN signature across all SLE patients, with higher expression in SLE-A relative to SLE-R. TNF signaling was consistently present in activated clusters from both SLE-A and SLE-R, with comparable magnitude.

To identify differentially expressed genes in ANA^+ B cells, we applied a zero-inflated model to pseudobulk data, stratified by cluster and cohort. ANA^+ B cells showed enrichment of B cell receptor (BCR) signaling pathways, consistent with chronic antigen exposure. Notably, Fc receptor signaling was upregulated in ANA^+ B cells from HC and SLE-R, but absent in SLE-A.

Conclusion: Our findings highlight the relevance of activated memory B cell subsets and ABCs in SLE pathogenesis, with SLE-R marked by a persistent activated naïve B cell population enriched for TNF signaling. We identified a regulatory checkpoint in ANA^+ memory B cells that is impaired in SLE-A. Activated B cell clusters in SLE exhibited reduced oxidative phosphorylation, suggesting a metabolic shift toward glycolysis. Differential regulation of Fcgr2b between ANA+ and ANA- in SLE-A suggests that Fcgr2b may modulate ANA^+ B cell activation in health and remission but is dysregulated during active disease. This further implicates Fc receptor signaling as a potential therapeutic target to promote or sustain remission in SLE.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

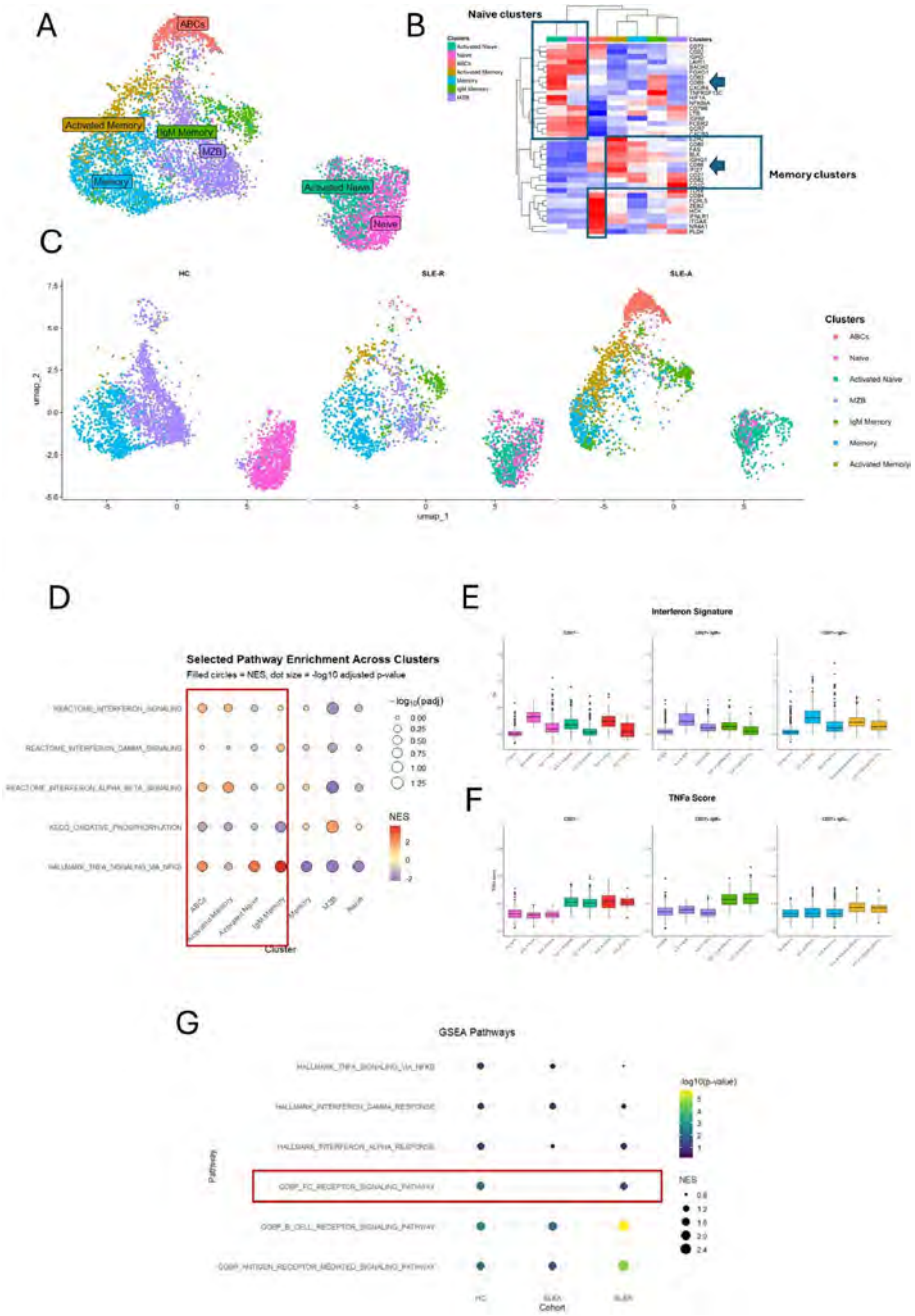


Figure 1. scRNA-seq analysis of ANA+ and ANA- B cells from patients with SLE-A, SLE-R and healthy controls (HC). A. UMAP showing the seven clusters that were identified including B cells from 3 groups. B. Heatmap shows main markers that define each cluster. C. Distribution of cells according to the cohort of origin. D. Selected pathways that are significantly different between clusters. The red square includes the subsets that are enriched in patients with SLE-A. E and F. Interferon and TNFα scores calculated according to the immune dictionary (as described in the main text) for each cluster divided by ANA+ and ANA-. G. Pathway analysis of genes that are significantly different between ANA+ and ANA- B cells for each cohort.

Disclosures: R. Pozovskiy: None; Y. Atisha-Fregoso: None; B. Diamond: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Late Breaking (L19-24)

Abstract Number: LB19

Rosnilimab, a Selective and Potent Depleter of Pathogenic T Cells, Demonstrates Efficacy, Safety, and Translational Proof of Mechanism in a Rheumatoid Arthritis Phase 2B Trial

Jonathan Graf[1], Amy Archer[2], Sergiy Kovalenko[3], Katarzyna Kolossa[4], John Serpa[5], Tamta Kobakhidze[6], Daniela Cepoi[7], Andrea Everding[8], Costantino Pitzalis[9], Catherine Aversa[2], Martin Dahl[2], May Hafez[2], Paul Lizzul[2], Priya Raina[2], Bruce Randazzo[2], Yangsu Ren[2], Khalil Saikali[2], Cailin Sibley[10], Gerd Burmester[11], Jacques-eric GOTTENBERG[12], Iain McInnes[13], Eduardo Mysler[14], Lee Simon[15], Josef Smolen[16], Jeffrey Sparks[17], Ronald van Vollenhoven[18], Michael Weinblatt[19] and Paul Emery[20], [1]UCSF, San Francisco, California, [2]AnaptysBio Inc, San Diego, California, [3]Arensia Exploratory Medicine, Kyiv, Ukraine, [4]MICS Centrum Medyczne, Bydgoszcz, Poland, [5]Allied Biomedical Research Institute, Miami, Florida, [6]Research Institute of Clinical Medicine Todua Clinic, Tbilisa, Georgia, [7]Nicolae Testemitanu State University of Medicine & Pharmacy, Chisinau, Moldova, [8]MVZ Rheumatologie & Autoimmunmedzin Hamburg GmbH, Hamburg, Germany, [9]QMUL, Bromley Kent, United Kingdom, [10]AnaptysBio Inc, San Diego, [11]Charité - Universitätsmedizin Berlin, Berlin, Germany, [12]Hautepierre Hospital, STRASBOURG, France, [13]University of Glasgow, Glasgow, United Kingdom, [14]OMI, Buenos Aires, Argentina, [15]SDG LLC, West Newton, Massachusetts, [16]Medical University of Vienna, Vienna, Austria, [17]Brigham and Women's Hospital, Boston, Massachusetts, [18]Amsterdam UMC, Amsterdam, Netherlands, [19]Brigham and Women's Hospital/ Harvard Medical School, Waban, Massachusetts, [20]University of Leeds, Leeds, United Kingdom

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: (LB19–LB24) Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Over 50% of RA patients require multiple b/tsDMARD classes due to inadequate or lost response. Rosnilimab, an investigational monoclonal antibody that selectively targets and depletes pathogenic T cells of interest (i.e., PD-1^{high} Tph/Tfh, Teff), is upstream of several clinically validated targets in RA and offers potential advantages as a new treatment modality.

Methods: This multicenter, randomized, double-blind, placebo-controlled Phase 2B trial (NCT06041269) enrolled adults with moderate to severe (≥6 tender and ≥6 swollen joints) seropositive RA on concurrent csDMARDs and < 3 previous b/tsDMARDs. Participants were randomized 1:1:1:1 to receive SC rosnilimab 100mg Q4W, 400mg Q4W, 600mg Q2W or placebo. Primary endpoint was at Wk 12. Participants randomized to rosnilimab were required to achieve CDAI LDA (≤10) at Wk 14 to continue in the Blinded All-Active Treatment Period through Wk 28, with subsequent off-drug follow-up to Wk 38.

Results: 424 participants were randomized; 41% had prior b/tsDMARD exposure; 95.0% and 86.6% were RF and CCP positive, respectively. At baseline, participants had a mean DAS28-CRP of 5.6, mean CDAI of 37.7 and mean CRP of 18mg/L.

The primary endpoint, mean change from baseline in DAS28-CRP at Wk 12, was met by all rosnilimab doses (-2.06, -2.12, -2.06 in 100mg, 400mg and 600mg arms) versus placebo (-1.69) ($p < 0.01$). At Wk 12, all rosnilimab dose arms had significantly greater changes in ACR20 and mean change in CRP versus placebo. ACR 50, ACR70, CDAI LDA and patient reported outcomes (PROs) consistently demonstrated higher responses over placebo (Fig 1a).

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. Clinical Efficacy Measures

a. **Primary and Select Secondary and Exploratory Endpoints at Week 12**

	Rosnilimab 100mg Q4W n=106	Rosnilimab 400mg Q4W n=107	Rosnilimab 600mg Q2W n=105	Placebo n=106
Primary Endpoint				
DAS28-CRP at Week 12 (mean change from baseline)	-2.06**	-2.12**	-2.06**	-1.69
Select Secondary Endpoints^ (% of patients)				
ACR20 at Week 12^	68.9*	70.1**	75.2***	52.8
ACR50 at Week 12^	44.3	36.4	46.7*	33.0
Week 28	45.3	48.6	58.1	--
ACR70 at Week 12^	21.7	21.5	21.9	17.9
Week 28	40.6	36.4	44.8	--
CDAI ≤10 (LDA) at Week 12^	46.2*	49.5**	38.1	31.1
Week 28	52.8	54.2	62.9	--
Select Exploratory Endpoints (Mean Change from Baseline)				
DAS28-CRP Week 28	-2.56	-2.48	-2.55	--
hsCRP				
Week 12	-9.67***	-10.10***	-7.60**	-0.73
Week 28	-7.23	-10.55	-5.98	--
Patient Global Assessment				
Week 12	-30.1	-30.5	-34.7**	-25.4
Week 28	-37.0	-37.9	-40.1	--
HAQ-DI (range 0-3)				
Week12	-0.61	-0.59	-0.60	-0.56
Week 28	-0.78	-0.74	-0.75	--
Pain VAS				
Week 12	-32.6	-35.3	-39.7**	-29.0
Week 28	-41.2	-43.8	-45.7	--

ITT population; MMRM used for continuous measures at Week 12, MI-LMCF at Week 28, NRI used for dichotomous measures at Week 12 and 28
*P<0.05; **P<0.01; ***P<0.001.

b. **Proportion of Week 28 Responders Completing Week 38 and Maintaining Response Off-Drug at Week 38**

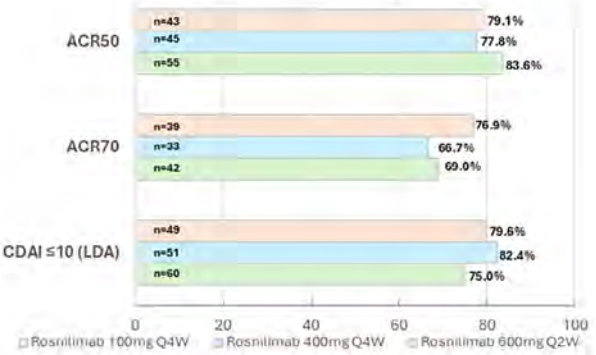


Figure 1. Clinical Efficacy Measures. a) Primary, Selected Secondary and Exploratory Endpoints at Week 12 and Week 28; MMRM = Mixed model repeated measures; used for continuous measures at week 12. MI-LMCF = Multiple imputations with last mean carried forward; used for continuous efficacy measures at Week 28. NRI = nonresponder imputation (NRI); used for dichotomous endpoints at Week 12 and 28. *p<0.05; **p<0.01; ***p<0.001. b) Proportion of Week 28 Responders Completing Week 38 and Maintaining Response Off-Drug at Week 38.

220 (69%) rosnilimab-treated participants reached CDAI LDA at Wk 14 and were eligible to continue into the All-Active Period. Those not eligible for the All-Active Period were imputed as nonresponders at all future visits, although many would be considered responders by other criteria (60% achieved ACR20 and 18% achieved ACR50). In the All-Active cohort, response rates substantially increased from Wk 12 to Wk 28 for secondary endpoints (ACR 50,70, LDA) and PROs (HAQ, pain VAS) (Fig 1a). After Wk 26, during the 12-14 week off drug period, responses were generally maintained (Fig 1b). Results were similar in b/tsDMARD naïve and experienced participants.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

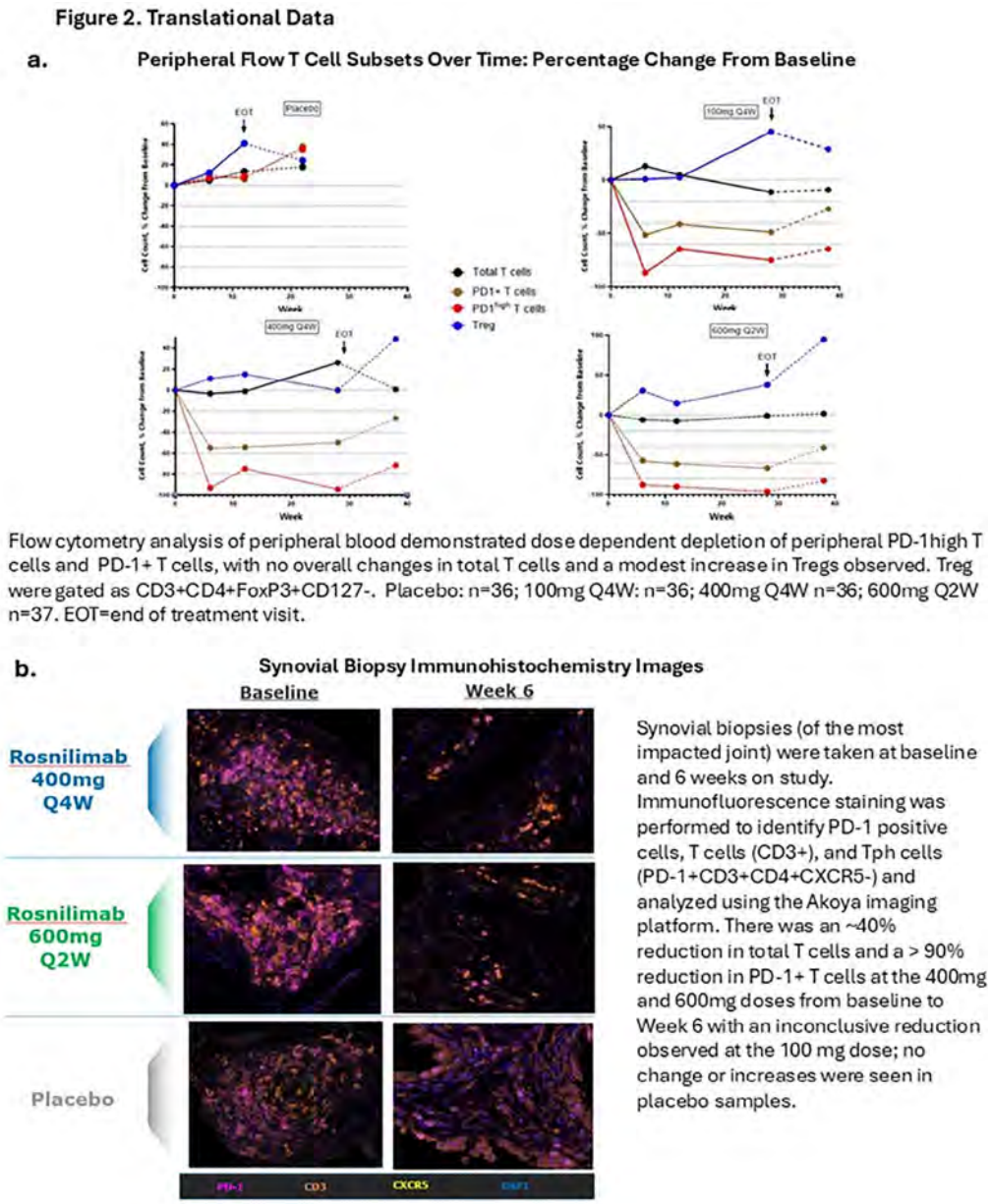


Figure 2. Translational Data. a) Peripheral Flow T Cell Subsets Over Time: Percent Change from Baseline; b) Synovial Biopsy Immunohistochemistry Images

Translational data showed rapid depletion (>90%) of pathogenic T cells of interest in blood with preservation of the total T cell numbers through the 28 Wk treatment period, consistent with the durability of clinical outcomes (Fig 2a). Synovial biopsies at Wk 6 (n = 24 evaluable pairs) demonstrated similar >90% depletion of pathogenic T cells of interest (Fig 2b) and broad downregulation of gene signatures including T cell, B cell, and myeloid activation.

Rosnilimab was well tolerated. 28/424 (7%) participants discontinued prior to Wk 12. 8/220 (4%) participants discontinued during the All-Active Period. No deaths or malignancies were reported. No serious or severe infections leading to treatment withdrawal were reported in rosnilimab-treated participants (Table 1).

Conclusion: Rosnilimab selectively and potently depletes pathogenic T cells in RA leading to clinically meaningful and durable responses. These data support further exploration of rosnilimab in RA.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Table 1. Safety: Baseline Through Week 38 (End of Follow Up)

Table 1. Safety: Baseline Through Week 38 (End of Follow Up)

	Rosnilimab 100mg q4w N=106 n (Rate)	Rosnilimab 400mg q4w N=107 n (Rate)	Rosnilimab 600mg q2w N=105 n (Rate)	Placebo N=106 n (Rate)	All Rosnilimab N=318 n (Rate)
Subjects with at least 1 TEAE [a]	75 (238.29)	69 (190.35)	57 (140.09)	47 (152.72)	201 (185.41)
Subjects with at least 1 TEAE related to study treatment [b]	17 (29.07)	28 (49.50)	20 (35.38)	19 (51.15)	65 (37.89)
Subjects with at least 1 serious TEAE	3 (4.46)	5 (7.34)	4 (6.14)	1 (2.35)	12 (5.98)
Subjects with at least 1 serious TEAE related to study treatment [b]	0	0	0	1 (2.35)	0
Subjects with at least 1 TEAE leading to study treatment discontinuation	1 (1.48)	3 (4.36)	2 (3.01)	1 (2.35)	6 (2.95)
Subjects with at least 1 TEAE leading to withdrawal from study	0	3 (4.36)	3 (4.52)	1 (2.35)	6 (2.95)
Subjects with at least 1 serious TEAE leading to study treatment discontinuation	0	0	0	1 (2.35)	0
Subjects with at least 1 serious TEAE leading to withdrawal from study	0	0	0	1 (2.35)	0
Subjects with at least 1 severe TEAE	4 (6.00)	3 (4.38)	4 (6.13)	3 (7.12)	11 (5.49)
Subjects with at least 1 severe study treatment-related TEAE [b]	0	1 (1.45)	0	1 (2.35)	1 (0.49)
Deaths	0	0	0	0	0
Malignancies	0	0	0	0	0
Infections and infestations	43 (87.34)	43 (83.83)	35 (64.74)	23 (60.22)	121 (78.27)
Serious infections	1 (1.48)	1 (1.45)	0	1 (2.35)	2 (0.98)
Opportunistic infections [c]	1 (1.48)	1 (1.45)	1 (1.50)	2 (4.75)	3 (1.47)

N=Total number of subjects in the defined analysis set in the period
n=Total number of subjects in the specific category
Rate=Exposure-adjusted incidence rate per 100 person-year = 100 x (Number of subjects with AE in the given period/Total years of exposure in the given period across all subjects at risk for the treatment). Total years of exposure at risk in the given period is sum of individual time (years) to first episode of AE in the given period if subject was event free. Placebo subjects received treatment for maximum of 12 weeks.
[a] TEAE=Treatment-Emergent Adverse Event. An adverse event is considered treatment-emergent if the date of onset is during or after the first dose of study treatment, or if the AE was present at baseline and worsens in either intensity or frequency after the first dose of study treatment.
[b] Related=Possibly related, related, or missing.
[c] Values shown are for herpes zoster, the only opportunistic infection reported.

Disclosures: J. Graf: Amgen, 5, AnaptysBio, 1, 2, 5, Fate Therapeutics, 5, ImmPACT Bio, 2, Sonoma Biotherapeutics, 5; A. Archer: AnaptysBio, 3, 11; S. Kovalenko: None; K. Kolossa: None; J. Serpa: None; T. Kobakhidze: None; D. Cepoi: None; A. Everding: None; C. Pitzalis: AbbVie/Abbott, 2, 5, 6, 7, AnaptysBio, 2, 7, Novartis, 2, 5, 6, 7, Pfizer, 5, Roche, 5, 6, 7, Sanofi, 5, 6, 7, UCB, 6; C. Aversa: AnaptysBio, 3, 11; M. Dahl: AnaptysBio, 3, 11; M. Hafez: AnaptysBio, 3, 11; P. Lizzul: AnaptysBio, 3, 11; P. Raina: AnaptysBio, 3, 11; B. Randazzo: AnaptysBio, 3, 11; Y. Ren: AnaptysBio, 3, 11; K. Saikali: AnaptysBio, 3, 11; C. Sibley: AnaptysBio, 3, 11; G. Burmester: AbbVie/Abbott, 1, 2, AnaptysBio, 1, 2, Bristol-Myers Squibb(BMS), 1, 2, Eli Lilly, 1, 2, Pfizer, 1, 2, UCB, 1, 2; J. GOTTENBERG: AbbVie/Abbott, 6, Amgen, 6, Anaptys-Bio, 2, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Galapagos, 6, Gilead, 6, Johnson & Johnson, 6, Novartis, 6, Pfizer, 6, Sanofi, 6; I. McInnes: AbbVie/Abbott, 1, Absci, 1, Amgen, 1, AnaptysBio, 2, AstraZeneca, 1, 5, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, 5, Cabaletta, 1, 11, Causeway Therapeutics, 1, 11, Compugen, 1, 5, 11, Dextera, 1, 5,

23265205, 2025, 59, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

11, Elasmogen, 1, Eli Lilly, 1, 5, Janssen, 1, Montai, 1, Moonlake, 1, Morningside, 1, Novartis, 1, 5, Pfizer, 1, Pioneering Medicines, 1, Recludix, 1, 11, Roche, 1, Sanofi, 1, SciRhom, 1, 5, Sixtry, 1, UCB, 1, 5; E. Mysler: AbbVie/Abbott, 1, 2, 5, 6, AnaptysBio, 2, AstraZeneca, 1, 2, 5, 6, GlaxoSmithKlein(GSK), 1, 2, 5, 6, Novartis, 1, 2, 5, 6, Pfizer, 1, 2, 5, 6; L. Simon: AnaptysBio, 2, 7, Asahi, 2, 7, AstraZeneca, 2, 7, Avenue, 2, 7, BioViva, 2, 7, Bristol-Myers Squibb(BMS), 2, 7, Eupraxia, 2, 7, Galvani, 2, 7, GlaxoSmithKlein(GSK), 2, 7, Immunovant, 2, 7, Inmedix, 2, 7, Kiniksa, 2, 7, Kyoto, 2, 7, Neumentum, 2, 7, Novartis, 2, 7, Proivent, 2, 7, Shanton, 2, 7, Spinethera, 2, 7, Tarsier, 2, 7, Teikeku, 2, 7; J. Smolen: Ananda Scientific, 2, AnaptysBio, 2, Immunovant, 2, Sandoz, 6, UCB, 2, 6; J. Sparks: AbbVie/Abbott, 2, Amgen, 2, AnaptysBio, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Fresenius Kabi, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Inova Diagnostics, 2, Invivyd, 2, Johnson & Johnson, 2, 5, Merck/MSD, 2, MustangBio, 2, Novartis, 2, Optum, 2, Pfizer, 2, ReCor, 2, Sana, 2, Sobi, 2, Sonoma Biotherapeutics, 5, UCB, 2; R. van Vollenhoven: AbbVie, 1, 2, 6, Alfasigma, 5, AnaptysBio, 2, AstraZeneca, 1, 2, 5, 6, Biogen, 1, 2, 6, Bristol-Myers Squibb(BMS), 1, 2, 5, 6, Cabaletta, 1, 2, 5, 6, Galapagos, 1, 2, 5, 6, GlaxoSmithKlein(GSK), 1, 2, 6, Janssen, 1, 2, 6, Kyowakirin, 1, 2, 6, Merck/MSD, 1, 2, 5, 6, Novartis, 5, Pfizer, 1, 2, 5, 6, RemeGen, 1, 2, 5, 6, Roche, 5, Sanofi, 1, 2, 5, 6, UCB, 1, 2, 5, 6; M. Weinblatt: Aclaris, 2, Amgen, 2, AnaptysBio, 2, Artiva Bio, 2, Biohaven, 2, Bristol-Myers Squibb(BMS), 2, 5, Canfite, 11, Curie Bio, 2, Deep Cure, 2, Eli Lilly, 2, Gilead, 2, Ignite, 2, Immedix, 11, Janssen, 5, Janux Therapeutics, 2, Johnson & Johnson, 2, Lifordi, 2, Marvel Bio, 2, Matchpoint, 2, Merck/MSD, 2, Neutrolis, 2, Novartis, 2, Roche, 2, Sana, 2, Santa Ana, 2, Sci Rhom, 2, Scipher, 11, Set Point, 2, Surf Therapeutics, 2, Thymmune, 2, Xencorp, 2, ZuraBio, 2; P. Emery: Activa, 1, AnaptysBio, 1, Boehringer-Ingelheim, 1, Bristol-Myers Squibb(BMS), 1, Eli Lilly, 1, Immunovant, 1, Novartis, 1.

Abstract Number: LB20

Efficacy and Safety of Deucravacitinib up to Week 52: A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study in Patients With Active Psoriatic Arthritis Who Are Naive to Biologic Disease-Modifying Antirheumatic Drugs

Désirée van der Heijde[1], Philip Mease[2], Carle Paul[3], Frank Behrens[4], Laure Gossec[5], Yuko Kaneko[6], Lihi Eder[7], Laura Coates[8], Andrew Pink[9], Weiguo Wan[10], Enrique Soriano[11], Piotr Leszczyński[12], Jose Scher[13], Atul Deodhar[14], Chahin Pachai[15], Janice Li[16], Xue Fan[16], Sahar Rabbat[16], Caroline Sardinas[17], Michael Plewinski[18], John Vaile[19] and Joseph Merola[20], [1]Leiden University Medical Center, Meerssen, Netherlands, [2]Swedish Medical Center/Providence St. Joseph Health, Seattle, Washington, [3]Department of Dermatology, INSERM Infinity, Toulouse University, Toulouse, France, [4]Goethe-University & Fraunhofer ITMP, Frankfurt, Germany, [5]Sorbonne Université, AP-HP & EULAR, Paris, France, [6]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [7]University of Toronto, Toronto, Ontario, Canada, [8]University of Oxford, Oxford, United Kingdom, [9]St John's Institute of Dermatology, Guy's and St Thomas' NHS Foundation Trust and King's College London, London, United Kingdom, [10]Huashan Hospital, Fudan University, Shanghai, China (People's Republic), [11]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, [12]Department of Internal Medicine and Metabolic Disorders, Poznań University of Medical Sciences, Poznań, Poland, [13]New York University School of Medicine, New York, New York, [14]Oregon Health & Science University, Portland, Oregon, [15]Bristol Myers Squibb, Princeton, New Jersey, [16]Bristol Myers Squibb, Princeton, [17]Bristol Myers Squibb, garwood, New Jersey, [18]Bristol Myers Squibb, Green Brook Township, New Jersey, [19]Bristol Myers Squibb, Warren, New Jersey, [20]UT Southwestern Medical Center, Dallas, Texas

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: (LB19–LB24) Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 8:00AM–9:30AM

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Background/Purpose: Deucravacitinib is an oral, selective tyrosine kinase 2 (TYK2) inhibitor being investigated in active PsA in the global, randomized, double-blind, placebo (PBO)-controlled, phase 3 POETYK PsA-1 (NCT04908202) and PsA-2 (NCT04908189) studies. Deucravacitinib has an established clinical profile in moderate to severe plaque psoriasis (PsO), with over 5 years of data, and is approved in multiple countries for PsO. We report efficacy and safety of deucravacitinib up to W52 in POETYK PsA-1.

Methods: Patients had a PsA diagnosis for ≥ 3 mo, met CASPAR criteria, were naive to biologic DMARDs, and had active or documented PsO, active arthritis (≥ 3 swollen and ≥ 3 tender joints), a high-sensitivity CRP level of ≥ 3 mg/L, and ≥ 1 PsA-related hand and/or foot joint erosion on radiographs at screening. Patients (N = 670) were randomized 1:1 to receive deucravacitinib 6 mg QD (n = 336) or PBO (n = 334) through W16. From W16 to W52, those randomized to PBO were switched to deucravacitinib 6 mg QD. The primary endpoint was ACR 20 at W16. Secondary endpoints included measurements of

Table 1. Efficacy endpoints at weeks 16 and 52

Endpoint	Week 16[a]		Week 52	
	Placebo (n = 334)	Deucravacitinib 6 mg QD (n = 336)	Placebo to deucravacitinib 6 mg QD (n = 334)	Deucravacitinib to deucravacitinib 6 mg QD (n = 336)
Disease activity measures (NRI)				
PASI 75 response (95% CI), %[b]	7.1 (3.7 to 12.0)	51.9 (43.9 to 59.8)	51.8 (44.0 to 59.5)	66.0 (58.2 to 73.3)
MDA response (95% CI), %	10.2 (7.2 to 13.9)	19.0 (15.0 to 23.7)	34.4 (29.3 to 39.8)	33.9 (28.9 to 39.3)
DAS28-CRP score, adjusted mean CfB (95% CI)	−0.83 (−0.95 to −0.70)	−1.33 (−1.46 to −1.21)	−2.05 (−2.18 to −1.92)	−2.11 (−2.24 to −1.98)
Patient-reported outcomes (NRI)				
HAQ-DI score, adjusted mean CfB (95% CI)	−0.22 (−0.27 to −0.16)	−0.39 (−0.44 to −0.33)	−0.49 (−0.56 to −0.42)	−0.51 (−0.58 to −0.44)
SF-36 PCS score, adjusted mean CfB (95% CI)	3.71 (2.91 to 4.51)	6.05 (5.24 to 6.85)	8.32 (7.39 to 9.26)	8.57 (7.64 to 9.50)
FACIT-Fatigue score, adjusted mean CfB (95% CI)	2.0 (1.1 to 2.9)	4.6 (3.7 to 5.6)	6.3 (5.3 to 7.3)	6.4 (5.4 to 7.5)
Extraarticular manifestations of PsA (pooled POETYK PsA-1 and POETYK PsA-2 analysis; NRI)				
Pooled LEI enthesitis resolution (95% CI), %[c]	45.1 (38.4 to 54.0)	50.3 (40.8 to 55.9)	59.9 (54.3 to 65.4)	58.8 (53.2 to 64.3)
Pooled SPARCC enthesitis resolution (95% CI),%[d]	36.1 (31.4 to 41.0)	47.1 (42.0 to 52.1)	56.5 (51.5 to 61.4)	54.2 (49.1 to 59.2)
Pooled dactylitis resolution (95% CI), %[e]	44.1 (34.0 to 53.4)	57.6 (50.2 to 67.6)	63.3 (56.0 to 70.2)	71.0 (64.3 to 77.0)
Radiographic progression (as observed, post hoc analysis)				
Nonprogressors (95% CI), %[f]	71.5 (66.1 to 76.5)[g]	82.0 (77.3 to 86.2)[g]	66.5 (60.5 to 72.2)[h]	73.3 (67.6 to 78. 4)[h]

A Cochran-Mantel-Haenszel test stratified by screening hsCRP concentration (< 10 mg/L vs ≥ 10 mg/L) and csDMARD use at baseline (yes/no) was used to compare the response rates of deucravacitinib 6 mg QD vs placebo. Nonresponder imputation was used for missing data for binary variables. CfB was analyzed using ANCOVA with treatment, randomization stratification variables, and baseline value as independent variables. Control-based pattern multiple imputation was used for missing data for continuous variables.

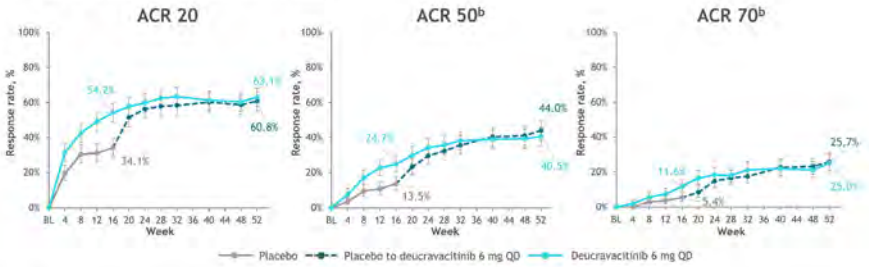
[a]Patients were randomized 1:1 to receive placebo or deucravacitinib 6 mg QD through W16. At W16, patients initially randomized to receive placebo were switched to deucravacitinib 6 mg QD through W52. Patients initially randomized to receive deucravacitinib 6 mg QD continued to receive deucravacitinib 6 mg QD through W52; [b]Assessed in patients with ≥ 3% BSA and an sPGA score of ≥ 2 at baseline (placebo, n = 170; deucravacitinib, n = 162); [c]Assessed in randomized patients with enthesitis by LEI at baseline (placebo to deucravacitinib, n = 317; deucravacitinib to deucravacitinib, n = 318); [d]Assessed in randomized patients with enthesitis by SPARCC at baseline (placebo to deucravacitinib, n = 407; deucravacitinib to deucravacitinib, n = 393); [e]Assessed in randomized patients with dactylitis at baseline (placebo to deucravacitinib, n = 188; deucravacitinib to deucravacitinib, n = 210); [f]Nonprogressors were patients who had a CfB to W16 or W52 in modified SvdH total score ≤ 0. Response rate 95% CI was based on the Clopper-Pearson exact method; [g]Assessed in randomized patients with available, observed SvdH total scores collected at baseline and W16 nominal visits (placebo, n = 305; deucravacitinib, n = 306); [h]Assessed in randomized patients with available, observed SvdH data collected at baseline and W52 nominal visits (placebo to deucravacitinib, n = 266; deucravacitinib to deucravacitinib, n = 273). The total number of patients is randomized patients with nonmissing baseline and W52 SvdH total scores based on purely observed data.

ANCOVA, analysis of covariance; BSA, body surface area; CfB, change from baseline; csDMARD, conventional disease-modifying antirheumatic drug; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue Scale; HAQ-DI, Health Assessment Questionnaire Disability Index; hsCRP, high sensitivity C-reactive profile; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; NRI, nonresponder imputation; PASI 75, ≥ 75% improvement in the Psoriasis Area and Severity Index; PCS, physical component score; PsA, psoriatic arthritis; QD, once daily; SF-36, 36-Item Short Form Survey; SPARCC, Spondylarthritis Research Consortium of Canada; sPGA, static Physician Global Assessment; SvdH, Sharp-van der Heijde; W, week.

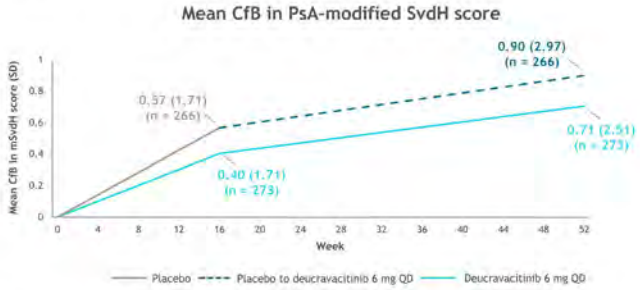
23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Figure 1. ACR 20/50/70 and radiographic progression analyses through week 52

A. ACR 20/50/70 kinetics (NRI)[a]



B. Radiographic progression: sustained inhibition of progression of structural damage (as observed, post hoc analysis)[c]



[a]All randomized patients were assessed. Treatment discontinuations prior to week 16 were considered treatment failures (composite variable strategy). All rescue medication–related intercurrent events were treated with a treatment policy–estimand strategy. The Clopper-Pearson exact method was used to estimate CI. Nonresponder imputation was used to handle missing data; [b]Additional secondary endpoint up to week 16 and exploratory endpoint up to week 52; [c]The population was based on randomized patients with available, observed SvdH total score, which was collected only at screening, W16, and W52 nominal visits. ACR 20, American College of Rheumatology 20% improvement in response; ACR 50, American College of Rheumatology 50% improvement in response; ACR 70, American College of Rheumatology 70% improvement in response; BL, baseline; CfB, change from baseline; mSvdH, modified Sharp-van der Heijde; NRI, nonresponder imputation; QD, once daily; SD, standard deviation; SvdH, Sharp-van der Heijde.

PsA disease activity, joint and extraarticular clinical responses, radiographic progression, and quality of life. Treatment discontinuation prior to W16 was considered an intercurrent event and imputed as a nonresponse. Nonresponder imputation and control-based pattern imputation were used for the remaining missing binary and continuous data, respectively. Post hoc analyses of radiographic data included all available assessments at baseline, W16, and W52, without imputation. Safety was evaluated through W52.

Results: Demographics and baseline characteristics were balanced across arms. The study met the primary endpoint (ACR 20; $P < 0.0001$).[1] Responses continued to improve through W24 and were maintained with deucravacitinib

Table 2. Overall safety summary: cumulative treatment period (weeks 0-52)

Safety parameter	Placebo to deucravacitinib 6 mg QD (n = 306)		Deucravacitinib to deucravacitinib 6 mg QD (n = 332)	
	n (%)	IR/100 PY	n (%)	IR/100 PY
Any AEs	206 (67.3)	196.0	262 (78.9)	218.7
Treatment-related AEs	54 (17.6)	31.2	92 (27.7)	38.0
Serious AEs	17 (5.6)	9.0	26 (7.8)	8.9
AEs leading to discontinuation	10 (3.3)	5.2	18 (5.4)	6.0
Deaths	0	0	0	0
Most frequent AEs (≥ 5%) in any arm by PT				
Upper respiratory tract infection	33 (10.8)	18.0	46 (13.9)	15.6
Nasopharyngitis	26 (8.5)	14.2	30 (9.0)	10.6
Hypertension	14 (4.6)	7.4	26 (7.8)	9.1
COVID-19	9 (2.9)	4.7	24 (7.2)	8.4
Urinary tract infection	7 (2.3)	3.7	19 (5.7)	6.5

AEs are defined as treatment-emergent AEs with an onset date on or after the first dose date of study treatment up to 30 days after the last dose date of treatment in the study. MedDRA: 28.0.
AE, adverse event; COVID-19, coronavirus disease 2019; IR, incidence rate; MedDRA, Medical Dictionary for Regulatory Activities; PsA, psoriatic arthritis. PT, preferred term; PY, patient-year; QD, once daily.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

through W52; similar results were seen for ACR 50/70 (**Figure 1A)**. Clinical responses and patient-reported outcomes (PROs) were met at W16, continued to improve, and were maintained through W52 with deucravacitinib (**Table 1**). Inhibition of radiographic progression observed at W16 with deucravacitinib[1] was sustained through W52 (**Figure 1B**). Patients who switched from PBO to deucravacitinib at W16 had reduced radiographic progression after switching (-**Figure 1B**). Few serious adverse events (AEs) and discontinuations due to AEs occurred; deucravacitinib was well tolerated through W52 (**Table 2**). No new safety signals related to adjudicated MACE, VTE, or opportunistic infections were observed. No deaths occurred.

Conclusion: Deucravacitinib was efficacious in patients with PsA based on clinical responses, PROs, and inhibition of radiographic progression, which continued to improve after W16 and were durable through W52. Responses at W52 were comparable in patients who switched from PBO to deucravacitinib at W16. Safety was consistent with the known deucravacitinib profile, with no new signals. Data were consistent with findings from POETYK PsA-2, reinforcing deucravacitinib as efficacious in PsA and underscoring its favorable safety profile as the first selective TYK2 inhibitor evaluated in PsA.

Reference

1. van der Heijde D, et al. *Ann Rheum Dis* 2025;84(supp 1):313–314.

Disclosures: D. van der Heijde: AbbVie, 2, Alfasigma, 2, Annals Rheumatic Diseases, 12, Associate editor, ArgenX, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Grey-Wolf Therapeutics, 2, Imaging Rheumatology BV, 12, Director, Janssen, 2, Journal of Rheumatology, 12, Editorial board member, Novartis, 2, Pfizer, 2, Takeda, 2, UCB Pharma, 2; P. Mease: AbbVie, 2, 5, 6, ACELYRIN, INC., 2, 5, Amgen, 2, 5, 6, Bristol Myers Squibb, 2, 5, Century Therapeutics, 2, Cullinan Biotech, 2, Eli Lilly, 2, 5, 6, Genascence, 1, GRAPPA, 12, Leadership/fudiciary role, Immagene, 2, Johnson & Johnson, 2, 5, 6, MoonLake Immunotherapeutics, 2, 5, Novartis, 2, 5, OMERACT, 12, Leadership/fudiciary role, Pfizer, 2, SPARTAN, 12, Leadership/fudiciary role, Takeda, 2, 5, UCB Pharma, 2, 5, 6; C. Paul: Abbvie, 2, 5, Almirall, 2, 5, Amgen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, LEO Pharma, 2, 5, Merck, 2, 5, Mylan, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sandoz, 2, 5, UCB, 2, 5; F. Behrens: None; L. Gossec: AbbVie, 2, 5, Alfasigma, 2, Amgen, 2, Bristol-Myers Squibb(BMS), 2, Celltrion, 2, Johnson & Johnson, 2, Lilly, 2, 5, MoonLake, 2, Novartis, 2, 5, Pfizer, 2, STADA, 2, UCB, 2, 5; Y. Kaneko: Bristol-Myers Squibb(BMS), 2, 6; L. Eder: AbbVie, 1, 5, Eli Lilly, 1, 5, Fresenius Kabi, 5, Janssen, 1, 5, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 5, UCB, 1, 5; L. Coates: AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 6, Bristol Myers Squibb, 2, Celgene, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos, 2, 6, Gilead, 2, 6, GlaxoSmithKline, 6, Johnson & Johnson, 2, 5, 6, Medac, 6, Moonlake, 2, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; A. Pink: None; W. Wan: None; E. Soriano: AbbVie, 2, 5, 6, Amgen, 6, Bristol-Myers Squibb(BMS), 6, Eli Lilly, 6, Janssen, 2, 6, Johnson & Johnson, 5, Novartis, 2, 5, 6, Pfizer, 5, 6, Roche, 2, 5, 6, UCB, 5, 6; P. Leszczyński: AbbVie, 6, AstraZeneca, 6, Bristol-Myers Squibb(BMS), 5, 6, Novartis, 6, Pfizer, 6, UCB, 6; J. Scher: Bristol-Myers Squibb(BMS), 2, Johnson & Johnson, 2, 5, Novartis, 2, Pfizer, 2, 5, UCB, 2; A. Deodhar: Bristol Myers Squibb, 2, 5, Eli Lilly, 2, 5, Johnson & Johnson, 2, 5, MoonLake, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; C. Pachai: Bristol-Myers Squibb(BMS), 3, 11; J. Li: Bristol-Myers Squibb(BMS), 3, 11; X. Fan: Bristol-Myers Squibb(BMS), 3, 11; S. Rabbat: Bristol-Myers Squibb(BMS), 3, 11; C. Sardinas: Bristol-Myers Squibb(BMS), 3, 11; M. Plewinski: Bristol-Myers Squibb(BMS), 3, 11; J. Vaile: Bristol-Myers Squibb(BMS), 3, 11; J. Merola: AbbVie, 2, Amgen, 2, AstraZeneca, 2, Biogen, 2, 2, Boehringer-Ingelheim, 2, Bristol-Myers Squibb(BMS), 2, Dermavant, 2, Eli Lilly, 2, Galderma, 2, Janssen, 2, MoonLake, 2, Novartis, 2, Oruka, 2, Pfizer, 2, Regeneron, 2, Sanofi, 2, Sun Pharma, 2, UCB, 2.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: LB21

IDH1/2 Somatic Hotspot Mutations as Independent Drivers of Autoinflammation

Flore Castellan[1], Griffen Mustion[2], Mei-Kay Wong[1], Kimberly Johansson[2], Scott Goldberg[1], Yazan Madanat[3], Namrata Chandhok[4], Abhay Singh[5], David Sallman[6], Jane Churpek[7], Curtis Lachowiez[8], Jennifer Yannucci[9], Luke Fletcher[10], Matthew Schwede[11], Amber Afzal[2], Yael Kusne[12], Alejandro Marinos[13], Alexander Coltoff[14], Rickey Myhand[15], Kiran Vij[2], Rosalyn Marar[16], Hannah Mitchell[2], Maria Stoentcheva[2], Giulia Petrone[2], Kyra Ddungu[2], Hannah Hartman[2], Ryan Monahan[2], Karen Vandervort[2], Jie Liu[2], John Cole[2], Tibor Kovacsovics[17], Hetty Carraway[18], Tian Zhang[19], Stephen Chung[3], Geoffrey Uy[2], Eytan Stein[20], Devendra Hiwase[21], Matthew Walter[2], Mrinal Patnaik[16], Kelly Bolton[22] and David Beck[1], [1]New York University School of Medicine, New York, New York, [2]Washington University School of Medicine, Saint Louis, Missouri, [3]UT Southwestern Medical Center, Dallas, Texas, [4]University Miami Miller School of Medicine, Miami, Florida, [5]Cleveland Clinic, Cleveland, Ohio, [6]Moffitt Cancer Center, Tampa, Florida, [7]University of Wisconsin School of Medicine, Madison, Wisconsin, [8]Oregon Health & Science University, Portland, Oregon, [9]Low Country Cancer Care, Savannah, Georgia, [10]Willamette Valley Cancer Institute and Research Center, EUgene, Oregon, [11]Swedish Health Services, Seattle, Washington, [12]Mayo Clinic, Phoenix, Arizona, [13]UTSouthwestern Medical Center, Dallas, Texas, [14]Medical University of South Carolina, Charleston, South Carolina, [15]CovenantOntology & Hematology, Frankfort, Kentucky, [16]Mayo Clinic, Rochester, Minnesota, [17]City of Hope, Goodyear, Arizona, [18]Case Western Reserve University, Cleveland, Ohio, [19]Stanford Medicine, Stanford, California, [20]Memorial Sloan Kettering Cancer Center, New York, New York, [21]Adelaide Medical School, Adelaide, South Australia, Australia, [22]Washington University School of Medicine, Saint Louis, Minnesota

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025

Session Title: (LB19–LB24) Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 8:00AM–9:30AM

Background/Purpose: Recently, somatic mutations in hematopoietic stem and progenitor cells (HSPCs) have been proposed as a novel mechanism driving systemic inflammation. *UBA1* somatic variants in HSPCs cause VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome, a late onset, systemic autoinflammatory disease (SAID) with elevated morbidity and mortality. We hypothesized that additional somatic variants may underlie inflammation in undiagnosed SAID.

Methods: We performed unbiased mutation enrichment analysis in 265 UBA1-negative adults with VEXAS-like SAID versus matched controls. Associations between identified genes with autoimmune phenotypes were assessed in UK Biobank (N=454,218), All of Us (N=414,830), and a Mayo Clinic cohort of clonal cytopenia of uncertain significance (CCUS, N=275). Finally, inflammatory outcomes in carriers were evaluated in a clinical trial of targeted treatment.

Results: Unbiased gene burden analysis identified *IDH1/2* and *SRSF2*, frequently co-mutated, as significantly enriched in the SAID cohort. *IDH1/2* hotspot mutations were observed in 5.7% of patients overall, and were the most recurrent impactful variants among patients without hematologic malignancy (N=193, 2.1%). All of these individuals (N=4) exhibited recurrent fevers, skin inflammation and cytopenia, with most (N=3) having inflammatory arthritis requiring multiple DMARDs, supporting a role for *IDH1/2* in driving inflammation outside of the established role of inflammation in overt malignancy.

To explore the association between *IDH*-mutant clonal hematopoiesis (CH) or CCUS and autoimmune disease, we analyzed two large cohorts, identifying 264 individuals with *IDH1/2*-mutant CH without hematologic malignancy. *IDH1/2* CH was associated with autoimmune disease (OR=1.8, p=4e-3), with the strongest associations for polymyalgia rheumatica (OR=4.0, p=1e-3) and giant cell arteritis (OR=8.1, p=1e-6). Carriers had elevated CRP versus other CH-carriers (p=1e-2) and altered myeloid counts. Findings were corroborated in the Mayo clinic CCUS cohort, where 8/275 patients (2.9%) carried IDH1 mutations, half of which exhibited autoimmune manifestations—including seronegative rheumatoid arthritis and

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sweet syndrome – highlighting the clinical relevance of *IDH* mutations in the context of cytopenia.

We then evaluated the effect of *IDH1* inhibition on inflammation in a clinical trial of ivosidenib in *IDH1* carriers with CCUS. Most (58%, 11/19) had elevated hsCRP (>=5; range 6.91–46.2 mg/L) including 4 with autoimmune disorders—all with episodic joint pain and half with skin manifestations. Most patients with elevated hsCRP at baseline normalized (< 5 mg/L) on treatment (7/9). All four individuals with autoimmune disorders had subjective improvement in symptoms with ivosidenib.

Conclusion: Together, our results point to IDH1/2 CH as a driver of autoinflammation, particularly in patients with cytopenia. Their presence in SAID cases without hematologic malignancy supports their role as drivers of inflammation. The efficacy of IDH1 inhibition in improving inflammatory manifestations in the ongoing IDH1-carrier trial underscores the potential for a therapeutic approach.

Disclosures: F. Castellan: None; G. Mustion: None; M. Wong: None; K. Johansson: None; S. Goldberg: None; Y. Madanat: None; N. Chandhok: None; A. Singh: None; D. Sallman: None; J. Churpek: None; C. Lachowiez: None; J. Yannucci: None; L. Fletcher: None; M. Schwede: None; A. Afzal: None; Y. Kusne: None; A. Marinos: None; A. Coltoff: None; R. Myhand: None; K. Vij: None; R. Marar: None; H. Mitchell: None; M. Stoentcheva: None; G. Petrone: None; K. Ddungu: None; H. Hartman: None; R. Monahan: None; K. Vandervort: None; J. Liu: None; J. Cole: None; T. Kovacsovics: None; H. Carraway: None; T. Zhang: None; S. Chung: None; G. Uy: None; E. Stein: None; D. Hiwase: None; M. Walter: None; M. Patnaik: None; K. Bolton: None; D. Beck: None.

Abstract Number: LB22

Early Evidence of Proof-of-Concept of an Albumin-DNASE1L3 Fusion Protein (NTR-441) for the Rapid Enzymatic Inactivation of NETs in SLE with DNASE1L3-Deficiency

Andreas Reiff[1], Tadej Avcin[2], Bernd Jilma[3], Peter Korosec[4], Matthias Weiss-Tessbach[3], Christian Schoergenhofer[3], Masa Bizjak[5], Barbara Jenko Bizjan[6], Barbara Cugalj Kern[5], Kim Simpfendorfer[7], Christian Lood[8], Tyler Artner[9], Angelene Prasanna[1], Ken Olivier[1], Ghazaleh Gouya[1], Ralph Lambalot[9], Abdul Hakkim[1] and Tobias Fuchs[1], [1]Neutrolis, Cambridge, Massachusetts, [2]University Medical Centre Ljubljana, Ljubljana, Slovenia, [3]Medical University of Vienna, Vienna, Austria, [4]University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia, [5]University Medical Center Ljubljana, Ljubljana, Slovenia, [6]University of Ljubljana, Ljubljana, Slovenia, [7]Feinstein Institutes for Medical Research, Manhasset, New York, [8]University of Washington, Seattle, Washington, [9]Neutrolis, Cambridge

SESSION INFORMATION
Session Date: Wednesday, October 29, 2025
Session Title: (LB19–LB24) Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Excessive formation and impaired clearance of Neutrophil Extracellular Traps (NETs) have been linked to autoimmune and inflammatory diseases, notably systemic lupus erythematosus (SLE). DNASE1-like 3 (DNASE1L3) is a circulating endonuclease that degrades NETs, and loss-of-function mutations are associated with severe autoimmune phenotypes in patients, including childhood-onset SLE, vasculitis, and systemic sclerosis. Based on this biology, Neutrolis developed a platform of engineered recombinant DNASE1L3 analogues, including NTR-441, a DNASE1L3 analogue fused to human serum albumin. In this first-in-human study, we aimed to validate the novel approach of NET inactivation by DNASE1L3 as a therapeutic strategy with three main objectives:

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

(1) assess safety, tolerability, and pharmacokinetics (PK) in healthy subject lacking the pharmacological target (NETs)
(2) evaluate safety, tolerability, PK, and target engagement in patients with a high NET burden
(3) establish pharmacodynamic and clinical proof-of-concept in a patient with SLE and congenital DNASE1L3 deficiency

Methods: A first-in-human Phase 1a/b, placebo-controlled, double-blind trial was conducted, including a single ascending dose study in 35 healthy adults and 12 hospitalized patients with severe COVID-19, representing a high NET burden disease (NCT04941183) across dose levels of 0.01–10 mg/kg. Proof-of-concept was investigated in a 16.5-year-old male with a homozygous DNASE1L3 loss-of-function mutation (c.643del) and severe, longstanding, treatment-refractory monogenic SLE, who received weekly doses of NTR-441 (3 mg/kg) as add-on therapy to corticosteroids, antimalarials, and tofacitinib through a compassionate use protocol (Ethics Committee approval no. 0120-553/2024-2711-8).

Results: NTR-441 was well tolerated across all studies and produced robust increases in DNASE1L3 levels that remained supraphysiologic for >48 hours (Fig. 1). Infusion reactions occurred in one healthy subject at the highest dose and at the fifth dose in the patient with SLE, the latter linked to anti-drug antibodies but managed with desensitization and adjusted dosing. Target engagement was demonstrated in patients with COVID-19 and SLE by rises in NET-degradation products (MPO–DNA complexes, cell-free DNA) peaking 4–8 hours post-infusion, while absent in healthy volunteers (Fig. 2). In the SLE patient, the first dose of NTR-441 resulted in a rapid (≤6 hours) and sustained clinical improvement across multiple organ systems, including urticarial rash, episcleritis, and arthritis except for a transient rash recurrence that subsequently subsided (Fig. 3).

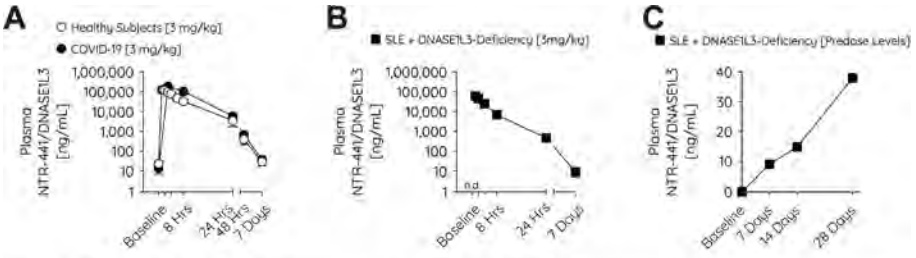


Figure 1. Pharmacokinetics of NTR-441. Plasma concentrations of DNASE1L3/NTR-441 were measured by electrochemiluminescence immunoassay using monoclonal antibodies against DNASE1L3 cross-reactive with NTR-441. Panels A–B: Plasma concentrations after a single 3 mg/kg infusion in (A) healthy subjects (N=6, open circles) and COVID-19 patients (N=3, closed circles), and (B) a patient with DNASE1L3-deficient SLE. Panel C: Pre-dose plasma concentrations prior to five weekly NTR-441 infusions in the DNASE1L3-deficient SLE patient.

Figure 1

FIGURE 2: NET-DEGRADATION PRODUCTS IN CIRCULATION

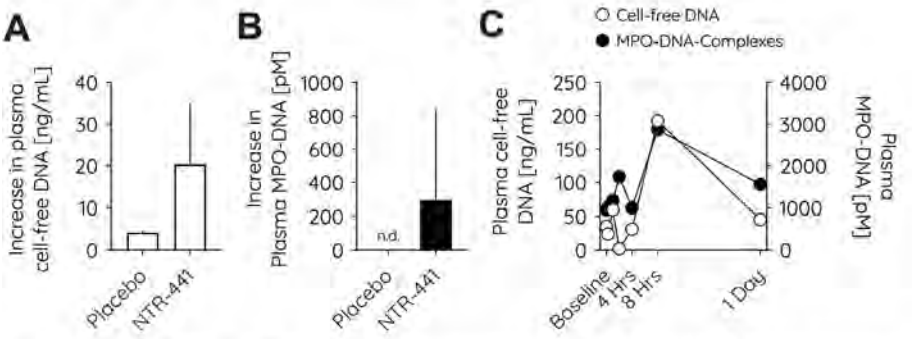
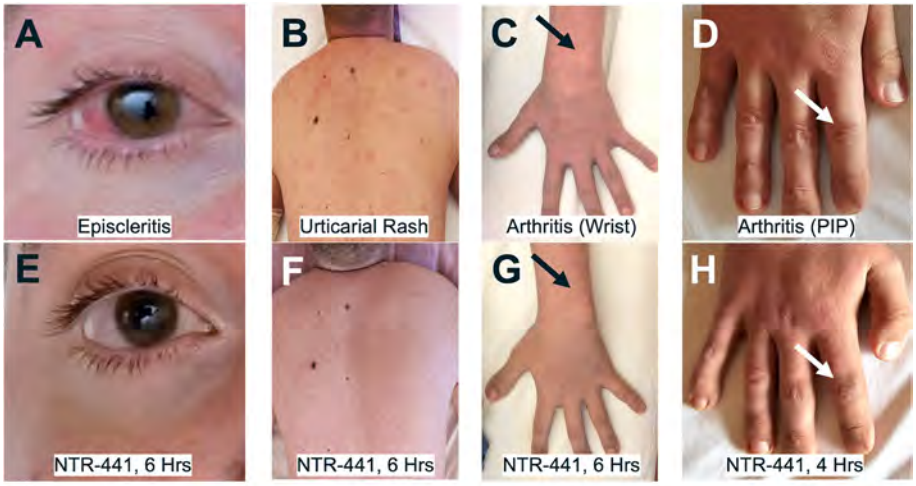


Figure 2. Changes in NET-Degradation Products. Plasma concentrations of cell-free DNA and MPO–DNA complexes were measured by qPCR and ELISA, respectively. Panels A–B: Maximal increases in (A) cell-free DNA and (B) MPO–DNA complexes in COVID-19 patients receiving placebo or NTR-441 (0.3–3 mg/kg, pooled data). Panel C: Plasma concentrations of cell-free DNA (open circles) and MPO–DNA complexes (closed circles) in a DNASE1L3-deficient SLE patient following the first NTR-441 infusion (3 mg/kg).

Figure 2

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License



I

Readout	Baseline	1 Week	2 Weeks	3 Weeks	4 Weeks
Urticarial Rash (% BSA)	76	31	38	31	20
UAS	5	3	3	3	3
Number of active joints	5	0	0	0	0
Episcleritis severity	3	2	1	1	1

Figure 3. Clinical Manifestations and Response to NTR-441 Treatment.
Panels A–D: Images of clinical manifestations at pre-dose: (A) episcleritis, (B) urticarial rash on the back, (C) wrist arthritis, and (D) arthritis in the proximal interphalangeal (PIP) joint of the index finger. Panels E–H: Same manifestations within 6 hours after NTR-441 infusion showing resolution or improvement. (I) Quantification of clinical manifestations over a 4-week treatment course, including urticarial rash as % body surface area (BSA), Urticaria Activity Score (UAS), number of active joints, and episcleritis severity.

Figure 3

Conclusion: These combined studies validate DNASE1L3 as a therapeutic strategy to inactivate NETs. In a patient with treatment-refractory SLE with DNASE1L3-deficiency, pharmacologic degradation of NETs with NTR-441 induced rapid, sustained remission, providing the first clinical proof-of-concept for this approach. The temporal link between NET clearance and clinical benefit supports NETs as a central pathogenic driver in autoimmunity. These findings warrant broader trials in SLE and other autoimmune disorders.

Disclosures: A. Reiff: Neutrolis, 3, 11; T. Avcin: Octapharma, 1, 6, Pfizer, 6, Takeda, 6; B. Jilma: None; P. Korosec: None; M. Weiss-Tessbach: None; C. Schoergenhofer: None; M. Bizjak: None; B. Jenko Bizjan: None; B. Cugalj Kern: None; K. Simpfendorfer: None; C. Lood: None; T. Artner: Neutrolis Inc., 2; A. Prasanna: Neutrolis Inc, 3, 11; K. Olivier: Neutrolis, 3, 11; G. Gouya: Neutrolis Inc., 2; R. Lambalot: Neutrolis Inc, 3, 11; A. Hakkim: Neutrolis, 3, 4, 8, 10, 11; T. Fuchs: Neutrolis, 3, 4, 8, 10, 11.

Abstract Number: LB23

A Phase 1 Study of Autologous CAR-Treg Cells in Refractory Rheumatoid Arthritis: Interim Report of Safety and Efficacy

Minna Kohler[1], Sally Arai[2], Fawad Aslam[3], Gregory Challener[4], Matthew Frigault[4], Melissa Griffith[5], Tamiko Katsumoto[6], Elena Massarotti[7], Larry Moreland[8], Allison Rosenthal[9], Jeffrey Sparks[7], Janeth Yinh[4], Sarah Baxter[10], Ari Bitton[11], Jason Dubovsky[12], Victor Yuan[13], Mindy Jensen[14], Andrew Clauw[15], Gabrielle Furman[4], Rita Gyurko[7], Megan Hall[9], Anna McIntyre[4], Jennifer Seifert[16], Emma Stainton[2], Michelle Blake[10], Sabrina Fox-Bosetti[13], Herve Lebrec[13], Amanda Pace[10], Yuanyuan Xiao[17], Mei-Lun Wang[18], Joe Arron[13] and Jeffrey Bluestone[19], [1]Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, [2]Stanford, Palo Alto, California, [3]Mayo Clinic, Arizona, Scottsdale, Arizona, [4]Massachusetts General Hospital, Boston, Massachusetts, [5]University of Colorado Anschutz Medical Campus, Aurora, Colorado, [6]Stanford University, Millbrae, California, [7]Brigham and Women's Hospital, Boston,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Massachusetts, [8]University of Colorado, Denver, Colorado, [9]Mayo Clinic, Phoenix, Arizona, [10]Sonoma Biotherapeutics, Seattle, Washington, [11]Sonoma Biotherapeutics, San Diego, California, [12]Sonoma Biotherapeutics, Thousand Oaks, California, [13]Sonoma Biotherapeutics, South San Francisco, California, [14]Sonoma Bio, Seattle, Washington, [15]University of Colorado, Aurora, Colorado, [16]University of Colorado and Oklahoma Medical Research Foundation, Aurora, Colorado, [17]Sonoma Biotherapeutics, Los Altos, California, [18]Sonoma Biotherapeutics, San Francisco, California, [19]Sonoma Biotherapeutics Inc, South San Francisco, California

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: (LB19–LB24) Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Regulatory T cells (Tregs) modulate inflammation, maintain self-tolerance, promote tissue repair, and hold promise as a versatile therapeutic. Autologous polyclonal Tregs have a favorable safety profile but limited efficacy in autoimmunity.

Engineered Tregs offer a novel approach by introducing a chimeric antigen receptor (CAR) specific for tissue- or disease-associated antigens. SBT777101 is an autologous Treg product transduced with a CAR specific for citrullinated proteins (CitP), which are present in the inflamed synovium of rheumatoid arthritis (RA) patients. Unlike cytotoxic CAR-T therapies, SBT777101 may restore balance to the immune system without target cell destruction. Potential mechanisms of action include direct and bystander suppression of antigen presenting cells and effector T cells, IL-2 consumption, and immunomodulatory cytokine production, promoting immune homeostasis and tissue repair.

Regulate-RA is an ongoing first-in-human, phase 1 study evaluating the safety and tolerability of SBT777101 in patients with refractory RA. Exploratory endpoints include assessment of SBT777101's pharmacokinetic (PK) profile, pharmacodynamic (PD) parameters, mechanism of action (MOA), and potential efficacy.

Table 1: Overview of (A) patient demographics and disease activity at screening for cohorts 1 and 2, and (B) safety events to date. AI or AN: American Indian or Alaska native; TEAE: Treatment-Emergent Adverse Event; MSK: Musculoskeletal; ICANS: Immune effector cell-associated neurotoxicity syndrome ; N: the number of subjects in the Safety Evaluable Set; n: the number of subjects in each category. Data cut 8/15/2025

Table 1

A. Baseline demographics and disease activity

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6
	Cohort 1 (Dose Level 1)			Cohort 2 (Dose Level 2)		
Sex at birth	F	F	F	F	F	F
Age (years)	68	42	58	64	51	52
Race/Ethnicity	White, Hispanic	White, Hispanic	White, Hispanic	White, not Hispanic	White, not Hispanic	White, and AI or AN
Disease duration (years)	2.3	18.1	4.8	28.1	7.5	14.7
RF status (titer)	Positive (90)	Positive (35)	Positive (323)	Positive (>1200)	Positive (75)	Positive (779)
ACPA status (titer)	Positive (32)	Positive (200)	Positive (203)	Positive (250)	Positive (>250)	Positive (256)
CRP (mg/L)	2.0	2.6	4.6	3.0	20	0.4
ESR (mm/hr)	16	ND	20	11	8	26
Swollen joints – SJC28	5	7	20	6	20	11
Tender joints – TJC28	7	4	21	22	27	17
DAS28-CRP	4.5	3.7	6.5	6.2	7.6	5.4
Total number of prior DMARDs	6	10	12	14	9	8
Number of prior b/ts DMARDs of different MOA	4	5	5	6	4	5

B. Safety overview

Subjects with at least one AE (n [events])	Cohort 1 (N = 3)	Cohort 2 (N = 3)	Total (N=6)
TEAE	3 [35]	3 [23]	6 [58]
TEAE Grade ≥3	1 [2]	2 [2]	3 [4]
TEAE Related to Study Treatment	3 [9]	3 [10]	6 [19]
Gastrointestinal disorders	3 [6]	0	3 [6]
Nervous system disorders	2 [3]	1 [2]	3 [5]
MSK and connective tissue disorders	0	2 [3]	2 [3]
General disorders and administration site	0	1 [3]	1 [3]
Psychiatric disorders	0	1 [1]	1 [1]
Investigations	0	1 [1]	1 [1]
AE Related to Study Procedure	1 [1]	2 [2]	3 [3]
Serious Adverse Event (SAE)	1 [2]	1 [2]	2 [4]
Dose-Limiting Toxicity (DLT)	0	0	0
CRS (Cytokine Release Syndrome)	0	0	0
Neurotoxicity/ICANS	0	0	0

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

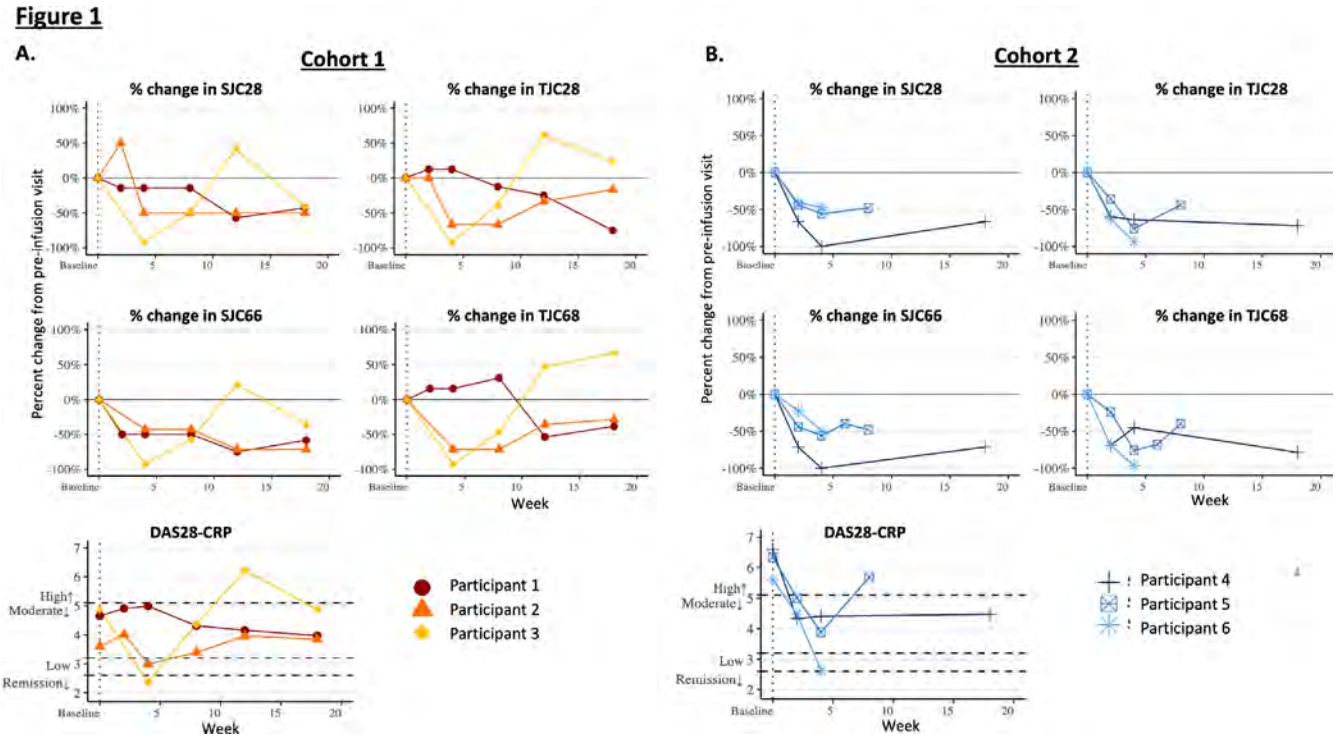


Figure 1: Preliminary efficacy of SBT777101. (A) Cohort 1 showed modest improvement in disease activity within 4 weeks of infusion, but this was of variable duration. (B) By week 4, Cohort 2 showed more consistent improvements of both tender and swollen joint counts, as well as DAS28-CRP. SJC: swollen joint count; TJC: tender joint count; DAS: Disease Activity Score.

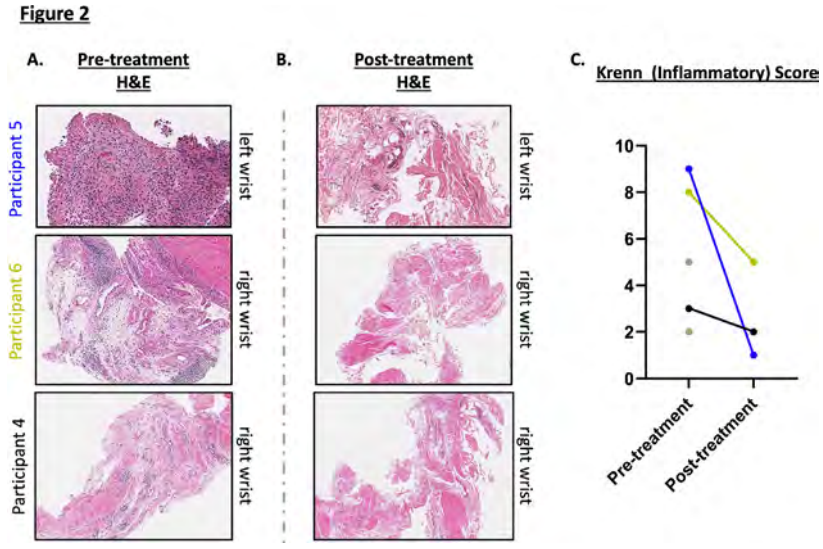


Figure 2: Reduced inflammation in post-treatment synovial biopsies: 20X images A) show pre- and B) post-treatment biopsies on the indicated joint with the patient number color represented in the dot-plot C) of Krenn inflammatory score as assessed by an independent, blinded, pathologist. Two participants only provided pre-treatment biopsies and are only shown in the plot.

Methods: Adults aged 18-70 with active RA (Disease Activity Score (DAS28-CRP) ≥ 3.2) and failure of ≥3 prior classes of biologic or targeted synthetic DMARDs are eligible.

SBT777101 is prepared by transduction of autologous Tregs with a CitP-specific CAR expressing vector followed by ex vivo expansion and is administered intravenously as a single dose in a 3-cohort, 3+3 dose-escalation design, with no preparative lymphodepletion. Participants are monitored for adverse events and clinical responses through 48 weeks. PK, PD, and MOA are assessed in blood and synovial biopsies.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Results: As of August 2025, six participants have received SBT777101 (table 1). Infusions were well-tolerated, without cytokine release syndrome, neurotoxicity, or dose limiting toxicities.

Across both dose levels, 4/6 participants (67%) had a ≥ 50% reduction from baseline swollen and tender joint counts by week 4, and 4/6 (67%) had a reduction of DAS28-CRP score by ≥ 2 (figure 1). Participants in Cohort 2, who received a higher dose of SBT777101, showed a more rapid onset and consistent reduction in joint count compared to Cohort 1. All participants in Cohort 2 showed clinically meaningful improvements in disease activity by week 4 with continued reduction in disease activity for as long as 18 weeks. Additionally, all post-infusion biopsies collected to date demonstrated decreases in inflammatory score (Figure 2). SBT777101 cells can be transiently detected in blood within the first month following infusion.

Clinical assessments and biomarker analyses are ongoing to assess changes in disease activity, systemic inflammation and Treg activity; additional participants are being enrolled.

Conclusion: In this ongoing phase 1 study, Cit-P–targeted CAR-Tregs demonstrate a favorable early safety profile, with preliminary clinical and mechanistic evidence of therapeutic activity in highly refractory RA participants.

Disclosures: M. Kohler: Johnson and Johnson, 5, Novartis, 1, Setpoint Medical, 5, Sonoma Biotherapeutics, 5, Springer Publications, 9; S. Arai: None; F. Aslam: None; G. Challener: Sonoma Biotherapeutics, 5; M. Frigault: Bristol-Myers Squibb(BMS), 5, Cabaletta, 5, Cytoagents, 5, Janssen, 5, Kite, 5, Legend, 5, Novartis, 5; M. Griffith: AstraZeneca, 5, Bristol Myers Squibb (BMS), 5, Gilead, 5, Sonoma Biotherapeutics, 5; T. Katsumoto: Beyond Meat, 5, Genentech, 11, Sanofi, 5; E. Massarotti: Bristol-Myers Squibb(BMS), 5, Cabaletta, 5, Crico, 1, EMD Serono, 1, Exo, 1, Janux, 1, Pioneering Medicines Explorations, 1, Sonoma Biotherapeutics, 5, Teledoc, 1, Xencor, 1; L. Moreland: None; A. Rosenthal: None; J. Sparks: AbbVie/Abbott, 2, Amgen, 2, AnaptysBio, 2, AstraZeneca, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb(BMS), 2, 5, Fresenius Kabi, 2, Gilead, 2, GlaxoSmithKlein(GSK), 2, Inova Diagnostics, 2, Invivyd, 2, Johnson & Johnson, 2, 5, Merck/MSD, 2, MustangBio, 2, Novartis, 2, Optum, 2, Pfizer, 2, ReCor, 2, Sana, 2, Sobi, 2, Sonoma Biotherapeutics, 5, UCB, 2; J. Yinh: Janssen, 2, Johnson & Johnson, 2, Springer, 9; S. Baxter: Bruker, 3, Sanofi, 3, 11, Sonoma Biotherapeutics, 3; A. Bitton: Sonoma Biotherapeutics, 3; J. Dubovsky: None; V. Yuan: Sonoma Biotherapeutics, 3; M. Jensen: Lovance, 12, Stocks, Sonoma Biotherapeutics, 3; A. Clauw: None; G. Furman: None; R. Gyurko: None; M. Hall: None; A. McIntyre: None; J. Seifert: None; E. Stainton: None; M. Blake: Sonoma Biotherapeutics, 3; S. Fox-Bosetti: Sonoma Biotherapeutics, 3; H. Lebrec: Amgen, 8, 11; A. Pace: Sonoma Biotherapeutics, 3; Y. Xiao: None; M. Wang: Sonoma Biotherapeutics, 3; J. Arron: None; J. Bluestone: Gilead, 4.

Abstract Number: LB24

Ianalumab demonstrates significant reduction in disease activity in patients with Sjögren's disease: Efficacy and safety results from two global Phase 3, randomized, placebo-controlled double-blind studies (NEPTUNUS-1 and NEPTUNUS-2)

Thomas Grader-Beck[1], Xavier Mariette[2], Stephanie Finzel[3], Elena Schiopu[4], Athena Papas[5], Valerie Devauchelle-Pensec[6], Thomas Dörner[7], Monika Sopala[8], Xiaofeng Zeng[9], Ghaith Noaiseh[10], Tsutomu Takeuchi[11], Uma Kumar[12], Josef Hermann[13], Hiroki Ozawa[14], Robert Fox[15], Susan Zong[16], Deepak Narayanswamy[17], XIAOMEI LI[18], Wen-Lin Luo[19], Janice Woznicki[20], Laurie DeBonnett[21], Xuan Zhu[20], Linchen He[20], Franziska Matzkies[22], Angelika Jahreis[22], Brian Porter[23], Sara McCoy[24], Simon Bowman[25] and Wolfgang Hueber[22], [1]Johns Hopkins, Reisterstown, Maryland, [2]Universit Paris-Saclay, Le Kremlin-Bictre, France, [3]University Medical Center Freiburg, Freiburg, Germany, [4]Medical College of Georgia at Augusta University, Martinez, Georgia, [5]Tufts School of Dental Medicine, Boston, Massachusetts, [6]Department of Rheumatology, Université de Bretagne Occidentale, CHU Brest, INSERM (U1227), LabEx IGO, Brest, France, [7]Department of Medicine,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rheumatology and Clinical Immunology, Charité Universitätsmedizin and Deutsches Rheumaforschungszentrum, Berlin, Germany, [8]Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland, [9]Department of Rheumatology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Beijing, China (People's Republic), [10]University of Kansas Medical Center, Kansas City, Kansas, [11]Division of Rheumatology and Clinical Immunology, Keio University, Tokyo, Japan, [12]Department of Rheumatology, All India Institute of Medical Sciences, New Delhi, India, [13]Division of Rheumatology and Immunology, Department of Internal Medicine, Medical University Graz, Graz, Austria, [14]Immuno-Rheumatology Center, St.Luke's International Hospital, Tokyo, Japan, [15]Division of Rheumatology, Scripps Memorial Hospital and Research Foundation-Ximed, La Jolla, San Diego, California, [16]Novartis Pharmaceuticals Corporation, Bridgewater Township, New Jersey, [17]Novartis Healthcare Pvt Ltd, Hyderabad, India, [18]First Affiliated Hospital of China University of Science and Technology, Hefei, China, [19]Novartis Pharmaceuticals Corporation, Franklin Township, New Jersey, [20]Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, [21]Novartis Pharmaceuticals Corporation, Mt Olive, New Jersey, [22]Novartis Pharma AG, Basel, Switzerland, [23]Novartis Pharmaceuticals, East Hanover, New Jersey, [24]University of Wisconsin, Middleton, Wisconsin, [25]University Hospitals Birmingham, Birmingham, United Kingdom

SESSION INFORMATION

Session Date: Wednesday, October 29, 2025
Session Title: (LB19–LB24) Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 8:00AM–9:30AM

Background/Purpose: Sjögren's disease (SjD) is a systemic, heterogeneous, autoimmune disease with substantial disease burden, high unmet need, and no approved systemic treatments. B cell hyperactivity and dysregulated B cell–activating factor/receptor (BAFF/BAFF-R) signalling are a hallmark of SjD pathogenesis. Ianalumab is a fully human IgG1 mAb with a novel dual mechanism of action that depletes B cells through enhanced antibody-dependent cellular cytotoxicity (ADCC) and also inhibits their activation and survival via BAFF-R blockade. NEPTUNUS-1 (NCT05350072) and NEPTUNUS-2 (NCT05349214) are Phase 3 studies designed to assess the efficacy and safety of ianalumab in patients with active SjD.

Methods: NEPTUNUS-1 and NEPTUNUS-2 are complementary, 52-week (Wk), global, multicenter, randomized, double-blind, placebo-controlled studies that enrolled adult patients with SjD meeting ACR/EULAR 2016 classification criteria with a EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥5 across 8 pre-selected domains, and stimulated salivary flow rate of ≥0.05 mL/min. Background immunosuppressants, including MTX (≤25 mg/Wk), HCQ (≤400 mg/day), AZA (≤150 mg/day), and prednisone ≤10 mg/day were allowed alone or in combination in both studies. In NEPTUNUS-1, patients were randomized (1:1) to monthly (QM) subcutaneous (s.c.) ianalumab 300 mg or placebo (PBO); in NEPTUNUS-2, patients were randomized (1:1:1) to either ianalumab 300 mg QM, every 3 months (Q3M) or PBO. The primary objective of both studies was to demonstrate superiority of ianalumab over PBO based on change from baseline (CFB) in ESSDAI at Wk 48. Key secondary endpoints included disease activity measures as well as physician- and patient-reported outcomes at Wk 48. Safety was assessed up to Wk 52.

Results: In NEPTUNUS-1, 275 patients and in NEPTUNUS-2, 504 patients were randomized. In both studies, baseline characteristics were generally balanced across treatment arms. Both studies met their primary objective. Ianalumab QM demonstrated statistically significant improvement in ESSDAI CFB at Wk 48 compared to PBO (**Fig 1)**. Patient's Global Assessment (PaGA; LS mean difference [Δ]: -6.6; 95% CI: -11.4, -1.8, p=0.007) and Physician's Global Assessment (PhGA; Δ: -5.5; 95% CI: -10.1, -0.9, p=0.018) reached nominal statistical significance in NEPTUNUS-1. Additional secondary endpoints showed a trend towards improvement in both studies. Ianalumab showed favorable safety with an overall incidence of adverse events and serious adverse events comparable to placebo in both studies (**Table 1**).

Conclusion: NEPTUNUS-1 and NEPTUNUS-2 are the first replicate Phase 3 studies in SjD to meet their primary endpoint, with ianalumab 300 mg QM demonstrating significant improvement in disease activity measured by ESSDAI. In addition, secondary endpoints including PaGA and PhGA indicate symptom reduction and patient benefit beyond improvement in

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

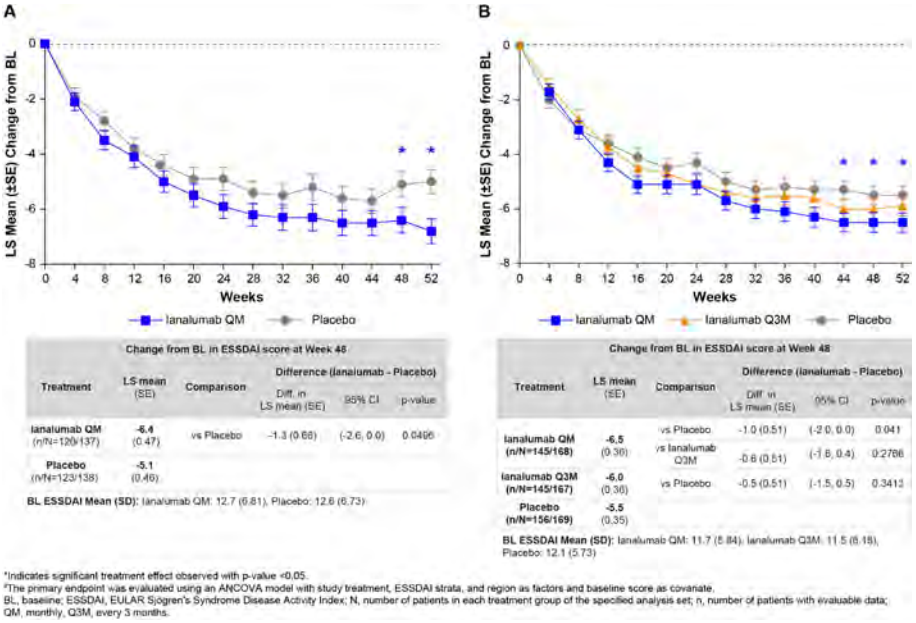


Figure 1: Change from baseline in ESSDAI score over 52 weeks#: A) NEPTUNUS-1 B) NEPTUNUS-2

Table 1: Safety summary through Week 52

Category*#	NEPTUNUS-1		NEPTUNUS-2		
	Ianalumab QM (N=137) n (%)	PBO (N=138) n (%)	Ianalumab QM (N=168) n (%)	Ianalumab Q3M (N=167) n (%)	PBO (N=169) n (%)
AEs	116 (84.7)	111 (80.4)	146 (86.9)	145 (86.8)	145 (85.8)
AEs related to study treatment	62 (45.3)	48 (34.8)	90 (53.6)	82 (49.1)	69 (40.8)
AEs leading to treatment discontinuation	5 (3.6)	5 (3.6)	14 (8.3)	11 (6.6)	6 (3.6)
SAEs	5 (3.6)	12 (8.7)	16 (9.5)	13 (7.8)	18 (10.7)
Death	0	1 (0.7)	0	0	0
Infections and infestations (SOC)	78 (56.9)	81 (58.7)	92 (54.8)	98 (58.7)	113 (66.9)
Serious Infections and infestations (SOC)	3 (2.2)	1 (0.7)	5 (3.0)	5 (3.0)	8 (4.7)

AEs, adverse events; N, total number of patients per group; n, number of patients with an event; PBO, placebo; QM, monthly; Q3M, every 3 months; SAEs, serious AEs; SOC, system organ class.
*A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
#A patient with multiple severity grades for an AE is only counted under the maximum grade.

disease activity. Ianalumab also demonstrated a favorable safety profile, reinforcing its positive benefit-risk profile in the treatment of SjD.

Disclosures: T. Grader-Beck: Novartis, 1, 2; X. Mariette: BMS, Janssen, GSK, Novartis and Otsuka, 6; S. Finzel: AbbVie, AstraZeneca, Chugai, GSK, Janssen, Novartis, UCB, 6, AstraZeneca, GSK, Janssen, Novartis, Novo Nordisk, UCB, 1; E. Schiopu: Johnson & Johnson, EMD Serono, Horizon/Amgen, Novartis, Boehringer Ingelheim, Zurabio, Priovant, Zenas, Argenx, SetPoint, Biogene, Galapagos, 5; A. Papas: Novartis, Otsuka, Biogen, 1, 2; V. Devauchelle-Pensec: AbbVie/Abbott, 2, Novartis, AbbVie, Lilly, Fresenius Kabi, 6; T. Dörner: Abelzeta, AbbVie, BMS, Novartis, Roche/Genentech, 5, 6; M. Sopala: Novartis Pharma AG, Basel, Switzerland, 3, 12, own Novartis stocks; X. Zeng: None; G. Noaiseh: Novartis, Janssen, Amgen, Argenx, 1, 2, Novartis, Janssen, Amgen, BMS, 12, Salary support from Novartis, Janssen, Amgen, BMS; T. Takeuchi: Novartis, 2; U. Kumar: None; J. Hermann: None; H. Ozawa: None; R. Fox: None; S. Zong: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 3; D. Narayanswamy: Novartis Healthcare Private Limited, Hyderabad, India, 3; X. LI: None; W. Luo: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 3; J. Woznicki: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 3; L. DeBonnett: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 3; X. Zhu: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3; L. He: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 3; F. Matzkies: Novartis Pharma AG, Basel, Switzerland, 3, 12, Company Stock of Novartis; A. Jahreis: Agomab, 4, Novartis Pharma AG, Basel, Switzerland, 3, 12, Company Stock of Novartis; B. Porter: Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, 3, 12, Company Stock of Novartis; S. McCoy: Novartis, Amgen, tear solutions, Artiva, Janssen, Veloxis, and Otsuka/Visterra., 2; S. Bowman: Abbvie, Aera, Amgen, Argenx, Aurinia, Bain, BMS, EcoR1, Forbion, Galapagos, Iqvia, J&J, Kiniksa, Novartis, Scitaris, 2, NIHR Birmingham Biomedical Research Centre, 12, SJB's salary is part funded by the NIHR Birmingham Biomedical Research Centre; W. Hueber: Novartis Pharma AG, Basel, Switzerland, 3, 12, Company Stock of Novartis.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patient Perspective (PP 01-13)

Abstract Number: PP01

When You Become the Story: A Journalist's Approach to Managing Complex Care

Lindsay Guentzel[1], [1]Freelance Journalist

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: As a journalist, I've spent my career digging for answers. But when I became the story, I had to learn how to ask the right questions – about my care, my symptoms, and the system that wasn't built for someone like me.

In March 2023, I was diagnosed with dermatomyositis (DM) associated with antisynthetase syndrome and Sjögren's syndrome (SS). The lead-up to those diagnoses was complicated and full of frustration. I quickly realized that if I wanted answers, I had to push for them – and once I had them, I had to lead. These were skills I fine-tuned in newsrooms, and I began to approach my health like a full-time job. That shift, while often overwhelming, reshaped how I engaged with my care.

Intervention: I applied the systems and storytelling skills I developed as a journalist: setting aside time weekly to manage appointments, organize records, and prepare questions. I recorded visits and used transcripts to track details and keep my family informed. Sharing my story publicly helped me develop clearer language around my symptoms—improving communication with my care team and strengthening our partnership.

That storytelling practice has grown into national advocacy work. I was invited to speak at the National Institutes of Health for Rare Disease Day 2025, delivered the keynote at the TMA *We Care for Rare Summit*, and led a storytelling workshop for nearly 100 people affected by myositis.

Maintenance: By treating my health like a full-time job, I've seen measurable improvements in how I manage my care. My missed appointment rate is under 5%, compared to nearly 40% at my clinic – something I attribute to the systems I've built. Staff has expressed appreciation for my follow-ups, which encourages me to advocate without hesitation. Staying informed also paid off: tracking CAR T-cell research allowed me to have early, informed conversations with my rheumatologist, so I was ready when a trial opened. I've seen similar transformations in the myositis community—when patients build storytelling skills, their confidence grows, and with it, a renewed sense of control and emotional well-being.

Quality of Life: Taking ownership of my care and embracing my story helped reduce the anxiety and helplessness I felt early in my diagnosis. I began to feel more in control of my health and my daily life.[1] That shift made it easier to manage the emotional toll of chronic illness and advocate for what I needed.[2] It also strengthened my relationships with my care team – our interactions now feel more collaborative, and I'm treated as a partner in decision-making.[3]

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ways Providers Can Empower Patients

1. Gucciardi, E., Jean-Pierre, N., Karam, G., & Sidani, S. (2016). Designing and delivering facilitated storytelling interventions for chronic disease self-management: A scoping review. *BMC Health Services Research, 16*(1), 249. https://doi.org/10.1186/s12913-016-1474-7

2. Loy, M., & Kowalsky, R. (2024). Narrative Medicine: The Power of Shared Stories to Enhance Inclusive Clinical Care, Clinician Well-Being, and Medical Education. *The Permanente journal, 28*(2), 93–101. https://doi.org/10.7812/TPP/23.116

3. Palla, I., Turchetti, G., & Polvani, S. (2024). Narrative medicine: theory, clinical practice and education – A scoping review. *BMC Health Services Research, 24*, 1116. https://doi.org/10.1186/s12913-024-11530-x

Papers Cited

Takeaway: As a journalist, I was trained to research, ask tough questions, and communicate clearly – skills that became essential when I had to start managing my own care. But patients shouldn't need a background in storytelling or investigative work to feel confident navigating their health. Medical providers can play a powerful role in helping patients step into that leadership (Fig. 1). By normalizing organization, curiosity, and follow-up, you can show patients that their engagement is not only welcome – it's valuable.

Encourage them to treat their care as something they can manage, not just endure. Patients who feel supported are more likely to stay informed, speak up, and follow through.[1] When providers support that shift, care becomes a true partnership [2] – where communication is clearer, collaboration is stronger, and outcomes improve on both sides of the relationship.[3]

Disclosure: L. Guentzel: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: PP02

When The Body Speaks But No One Listens: A Dermatomyositis Story Through a Public Health Lens

Kyanna Johnson[1], Lynn Wilson[1], Manuel Lubinus[1], Elisa Glass[1], [1]Myositis Support and Understanding

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: My journey with dermatomyositis (DM) began abruptly in July 2024, when I was hit by sudden, severe muscle weakness after a GI infection. I couldn't stand or move my legs- I was terrified, my body was failing, and I didn't know why. I was admitted to the hospital for inpatient rehabilitation for 2–3 weeks. Despite lab results suggesting myositis, I was discharged without a diagnosis or treatment plan. I felt invisible. I was advised to follow up with a neurological clinic, but after multiple unreturned calls, I decided to take control.

As a public health professional and medical student, I knew how to navigate healthcare systems, but nothing prepared me for how dehumanizing it would be to have my symptoms dismissed. I was scared and exhausted—not just physically, but emotionally. However, with my primary care provider's help, I was prescribed prednisone. My strength returned briefly, and with it, hope. But when the taper ended, so did my progress. My body was falling apart again, which prompted me to seek a more comprehensive diagnosis.

Intervention: Determined not to be ignored, I became relentless. I used Myositis Support and Understanding (MSU) resources to advocate for myself. I had to educate doctors, those I trusted with my care, about how DM presents, especially in people with darker skin. At one point, a specialist brushed off my symptoms—my fear turned to fury. I knew something was wrong, and I wouldn't let their indifference invalidate my lived reality.

Finally, I found someone who listened who was out of state. Under Dr. Arash Hassan's care, guided by labs, clinical presentation, previous skin biopsy, and dilated capillaries, I was formally diagnosed with DM and referred to NIH for further evaluation. That moment was a turning point for my health and my spirit.

Maintenance: The emotional toll remains. I still grapple with fatigue, fear of flare-ups, and the memory of being dismissed. That experience changed me. It motivated me to advocate for myself and to ensure no other patient has to fight this hard to be heard. I am now MSU's Director of Public Health and Policy, where I intend to enhance policy and research around chronic diseases like myositis.

Quality of Life: I'm no longer bed-bound. Through physical therapy, prednisone, azathioprine, IVIG, and continued care, I'm slowly rebuilding my strength. More importantly, I've transformed pain into purpose. Through MSU, I'm advocating for reproductive rights, equitable access to care, and better provider education about rare diseases like DM.

Takeaway: This journey taught me the importance of self-advocacy and the need for providers to listen to patients who are navigating rare, complex diseases like DM. Diagnostic delays don't just harm the body—they fracture trust and deepen emotional suffering. My story is one of resilience, but it shouldn't have required so much self-advocacy to be believed. We

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

must build a healthcare system that centers the patient's voices. When we listen, we heal more than just symptoms; we restore dignity, trust, and hope. By empowering patients and fostering a strong doctor-patient relationship, we can improve outcomes for those with rare diseases like mine.

Disclosure: K. Johnson: None; L. Wilson: None; M. Lubinus: None; E. Glass: None.

Abstract Number: PP03

My Journey of Risk, Loss, and Hope: The Role of Multidisciplinary Collaboration in Managing Pregnancy with Takayasu Arteritis

Tugce Turten Kaymaz[1], [1]Ankara Yildirim Beyazit University

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: At the age of 26, the same month I got married, I was diagnosed with Takayasu Arteritis following severe chest and back pain. Hypertension was added to my condition two years later. My treatment varied but included deltacortril, PULSE, methotrexate, infliximab, and tocilizumab. As a result, I had to avoid pregnancy from the beginning of my marriage. Four years after the diagnosis, I experienced pregnant unexpectedly while using tocilizumab. What should have been joyful news became a source of fear and uncertainty for us. After my rheumatologist explained the risks, we decided to continue the pregnancy at 10 weeks. However, at the first perinatologist visit, anomaly was suspected, followed by a trisomy 21 diagnosis, and the pregnancy was terminated at week 16. Five months later, I had a planned pregnancy that ended in miscarriage due to an ectopic pregnancy. Both pregnancies ended in loss. I experienced bleeding, and curettage was done without any anesthesia, increasing my fear of gynecology clinics. After these experiences, my husband and I silently closed the door on having children.

Intervention: During the COVID-19 pandemic, I couldn't access tocilizumab for six months. At the check-up six months later, my doctor informed me that my condition was stable enough to go without medication for a period and try for a baby. A month later, I went to the ER with severe groin pain and learned I was pregnant again. What followed were weeks filled with fear: suspicions of ectopic pregnancy, then heterotopic pregnancy, and bleeding. I found myself once again face-to-face with the very fears I had hoped to avoid. Until I found my perinatologist.

Maintenance: I had check-ups every three weeks in the first two trimesters, and every two weeks in the third. The communication and coordination between my rheumatologist and perinatologist were crucial components of my pregnancy care. My anxiety decreased thanks to my doctor's clear, calming communication without overemphasizing risks. Working from home due to the pandemic also reduced physical stress and allowed me to have a rest-focused, and calm pregnancy. My third pregnancy ended happily with the birth of a healthy baby girl in the 41st week.

Quality of Life: The key to a healthy pregnancy and baby was my rheumatologist's accurate evaluation of my condition and reassurance that my health was suitable for pregnancy. The patient's trust that the doctor will make the best decision for her makes it easier to make difficult decisions and accept negativities during the process. At this point, clinical expertise alone is not enough. The physician's communication, long-term follow-up, and interdisciplinary coordination are all crucial for the patient's acceptance of the disease, adherence to treatment, and overall adjustment. In addition to the professionalism of

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

my doctors, their coordination, patient communication and the decrease in my daily stress level increased my quality of life during pregnancy and allowed me to have a healthy pregnancy and birth without complications at age 34.

Takeaway:

- Effective communication and a trusting doctor–patient relationship improve patient adherence and emotional resilience.
- Interdisciplinary coordination is essential, especially in pregnancies complicated by rheumatologic disease.
- A personalized approach that considers the patient's life circumstances enhances treatment success.

Disclosure: T. Turten Kaymaz: None.

Abstract Number: PP04

MCTD and Aging – Resilience Required

Carol Kaminski[1], [1]HP

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: I was diagnosed with MCTD at age 25. My priorities were understanding a disease I had trouble pronouncing, and trying to learn to live with it, not die from it. I did not think I would live to an old age. 40 years on, here are my strategies on aging well with MCTD that may help rheumatic disease patients and professionals who treat them, to either avoid my errors or employ helpful behaviors. I've learned these through trial and error and also observed them in others "chronically managing."

Intervention: Since I did not believe I would *definitely* reach old age my lifestyle reflected that. I was told, "Some patients do very well; others live only a few years." That conversation couldn't be unheard. Why plan for an uncertain future?

As each year brought improvements in the care of autoimmune diseases, and the chance I would have a future, my hope increased. One pivotal period for me was when histamine-2 blockers and proton-pump inhibiters were developed. I feel such gratitude for those involved in the development of gastrointestinal motility and acid-suppressing drugs. My quality of life improved overnight. *Any* medical improvement may be "right around the corner" so why not plan for that? I began to contribute to a retirement account at work. Once I felt I might have a future, I began to plan for one.

A doctor said to me "some things take a "tincture of time" to resolve. Along with managing MCTD, I am subject to everyday problems and unrelated diseases. I appreciated this concept while waiting for hydroxychloroquine to kick in; By simply resting joints or muscles before deciding I am flaring gave me time for clarity. Although not appropriate for all situations, there are times to wait.

When in pain, I move slower, and my focus lessens. I mitigate by managing my calendar better, so I am not overbooked or hurried. I leave earlier for appointments. With joints damaged from years of swelling and arthritis, when I rush, I drop or forget things. Others' time is valuable too, so I strive to be on time. I cancel plans when rest is required, something not always understood by others.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Early in my chronic illness journey I found myself relying on and at times being disappointed by friends and family. Experiencing a lack of understanding and even denial at diagnosis, I learned the reality no one person can always be there for me. Sometimes, I'd call only to find others caught up in their own situations, not tuned into me. This is normal. How happy it makes me when I get help, a listening ear, or a sense of understanding. But maturity allows me to let it go when I don't. Adding frustration and disappointment to things doesn't help. The process also developed my resilience and allows me to empathize with others.

Alongside the emotional work of understanding, forgiving, or choosing to move on, I began to simply increase my support system. Online and in-person support groups. Viewing close friends/partner as *adjunct* support, rather than primary. These actions release those closest to me from the pressure of being "always on."

Maintenance: Today, I prioritize activities and investments that promote health, physical, mental, emotional and spiritual.

Quality of Life: By doing so, I am able to live a better, fuller and perhaps even a healthier life.

Takeaway: May more of us live healthier years *with, even in spite of* chronic illness, even into older age.

Disclosure: C. Kaminski: None.

Abstract Number: PP05

Mastering a Rare, Autoimmune Disease: My Journey Regaining Agency Through Education, Collaboration, and Community

Mustafa Shameem[1], [1]The Myositis Association

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: After a complex diagnostic journey, my PCP working on a rheumatological theory ordered a myositis-specific autoantibody (MSA) panel. It revealed the presence of an antisynthetase autoantibody, and a very rare one. A serious diagnosis—and one that is rare and rheumatological like dermatomyositis/anti-synthetase syndrome—can be devastating and leave one in the unknown. As a young professional facing this exact situation, I remembered a piece of wisdom: dignity is affirmed by facing reality as it is, and responding responsibly.

Intervention: Nature had dealt a harsh blow. However, I attempted to restore some personal agency. I immersed myself in the science of myositis. I collected dozens of relevant research papers, carefully read through, annotated, and extracted points to help reason about my own situation. Aside from research, I tapped into the Myositis Association (TMA), the leading, global, myositis non-profit. Of the range of TMA services, I leveraged a subset: lectures from experts, online forum, and conferences. I discovered and selected my myositis-expert rheumatologist thanks to TMA, along with large parts of my broader care team.

Maintenance: Through education, my condition was no longer a black box that could only be deciphered through an expert. For patients without the relevant professional backgrounds or comfort with research, patient organizations like TMA provide the accessible, expert-crafted resources needed for patients to become fluent in their condition. No small

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

contribution considering the larger information ecosystem in which predatory actors are eager to provide 'solutions' to fearful, vulnerable patients.

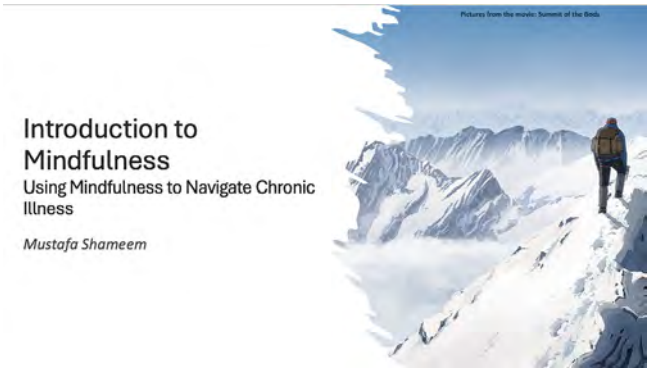
The patient-as-subject approach yielded other benefits: I understood tradeoffs of different treatments or why a particular test (e.g. CK, AST, ALT, pulmonary function) was being done. And I could interpret each of these at a fine-grained level, their implications, and have more sophisticated provider conversations as a result. I also found mindfulness, adapted for dealing with illness, helpful in navigating many stormy, difficult situations associated with my journey.

Quality of Life: Resuming my normal activities, and engaging in the myositis community have been the two elements that have been personally meaningful.

I was the beneficiary of the vision and generosity of patient and provider leaders at The Myositis Association. I would, in my small way, repay this forward by joining the board of directors and applying my professional experiences to advance the needs of the myositis community.

From consuming and applying myositis research, I've now become a contributor to a number of myositis research efforts. For example, I've joined one study as a technical advisor, applying my professional background in product management to enable telemedicine myositis research. My experiences navigating a rare condition and applying mindfulness practices, which I had learned from the Sōtō Zen and other traditions, were articulated into an 'Applying Mindfulness to Navigate

TMA board members, medical advisory board member, staff, and executive director at the Global Conference on Myositis (GCOM); Mustafa on far left.



23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Chronic Illness' class. I was privileged to teach this in a number of settings from small patient groups to large conferences. And the positive response and value others have gained has been a deep source of personal satisfaction.

Takeaway: 1. Importance of autoantibody testing - Myositis autoantibody testing should be considered in a wider range of scenarios from isolated, RA seronegative arthritis to partial, or atypical presentations. This wider testing may enable more accurate diagnosis, earlier detection, and better outcomes.

2. Patient-as-subject approach - Due to the complexity and challenges of the myositis family of conditions, providers should encourage patients to be as agentic as possible. This could include educating themselves on their conditions, engaging with patient organizations, shaping their treatments, and contributing back.

Disclosure: M. Shameem: None.

Abstract Number: PP06

Co-Creation of Exercise Videos by Patients and Professionals to Support Patient Empowerment

Noriko Okochi[1], Eiji Oishi[1], Yoshifumi Hitoe[2], Hitomi Koshi[2], Hajime Kono[2], [1]Rheumatic Disease and Vasculitis Support Network Japan, [2]Teikyo University School of Medicine

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Rheumatic and musculoskeletal diseases (RMDs) cause chronic pain, joint deformities, and reduced mobility, significantly limiting patients' daily activities and social participation. Physical inactivity can also lead to secondary risks such as cardiovascular disease and depression, worsening quality of life (QOL). EULAR(2021) recommends exercise as an effective non-pharmacological therapy, which can reduce pain and fatigue and improve mental health. However, many Japanese patients express uncertainty about how to exercise and fear worsening symptoms. The spread of online exercise support remains limited, contributing to an information gap. In response, a patient-led project was launched to create and distribute exercise videos accessible to all, involving patients, families, and healthcare professionals.

Ten videos and flyers that reached our patients.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Intervention: The project consisted of three steps. In Step 1, an on-demand seminar was held in May 2024 to coincide with World Lupus Day, gathering insights on patients' interests, concerns, and challenges related to exercise. In Step 2, a multidisciplinary team—including doctors, physical therapists, nurses, psychologists, and patient representatives—was formed to develop ten exercise videos based on these insights. In Step 3, the videos were released on the patient group's website and social media (X and Instagram), with flyers distributed at medical institutions and academic conferences.

Maintenance: All ten videos are designed to be easy to follow and sustainable, minimizing joint strain. The video titles and content are:

1. Lower Body Exercises While Seated: Safe movements to strengthen thighs and calves.
2. Shoulder Stretches for Tension Relief: Simple stretches for stiff shoulders and neck.
3. Improving Sit-to-Stand Movements: Exercises to assist rising from a chair.
4. Ankle Mobility Training: Movements to increase flexibility and prevent falls.
5. Back and Lower Back Stretching: Exercises to loosen tension from prolonged sitting.
6. Finger Exercises and Relaxation: Improve hand flexibility and reduce stiffness.
7. Relaxation through Breathing: Deep breathing to regulate the autonomic nervous system.
8. Balance Training: Exercises to improve balance and core stability.
9. Full-Body Stretching: Warm-up and cool-down stretches for the whole body.
10. Daily Exercise Habits: Tips to maintain and incorporate exercise into daily life.

Quality of Life: The flyers introducing the exercise program were distributed through public health centers and medical institutions across Japan, reaching patients directly. Additionally, some patients accessed the exercise videos via the internet, using websites and social media platforms such as X and Instagram. When the program was introduced to patients shortly after discharge from the hospital, it received positive feedback, including comments such as "This is the perfect exercise for me right now." These responses suggest that the program provides a feasible way for patients with illnesses to continue exercising without overexertion. It not only supports the maintenance and recovery of physical function, but also helps foster a sense of self-efficacy and optimism, thereby potentially contributing to improved mental well-being.

Takeaway: By regularly promoting the videos through social media and the website, and incorporating them as references during rehabilitation, patients are likely to feel more familiar and comfortable with the exercises.

Disclosure: N. Okochi: None; E. Oishi: None; Y. Hitoe: None; H. Koshi: None; H. Kono: None.

Abstract Number: PP07

Beyond the Medication: Creating a Toolbox of Complementary Therapies

Brittany Murray[1], [1]Chronic Disease Diary, LLC

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: For over 30 years, I have been living with Psoriatic Disease, diagnosed with Psoriasis at 2 years old and Psoriatic Arthritis at 14. My disease has progressed, luckily with the advancement of treatments. With chronic diseases, you get used to treating with pharmaceuticals, and at the beginning, you are sometimes spoiled with the ability to take a single medication, but usually not. I progressed from creams and ointments and phototherapy to DMARDs to biologics. I was

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

lucky for 7 years to use one biologic to treat both my psoriasis and psoriatic arthritis. Those 7 years convinced me that I could always manage my disease with one medication. Of course, that has not been true since. I tried for many years to find another medication that worked as well as that one biologic did, but had no success. I have seen some that treat most of my symptoms or give me more good days than bad, but nothing is 100%, and nothing relieves all of the pain.

Intervention: After several years of exploring biologic after biologic and JAK 2 inhibitors with my rheumatologist, we turned to functional medicine and complementary therapies. For two years, I have been trying various other treatments to not only see what works but to see if any of my symptoms are actually unrelated to Psoriatic Arthritis and have just been lumped in over the years or due to overcompensating for pain. On this journey, I have tried chiropractic care, massage therapy, acupuncture, functional medicine interviews, autoimmune protocol diet, food sensitivity testing, CBD topicals, traditional Chinese medicine, supplements, herbs, and physical therapy. I have also come to terms with the need for assistive devices such as compression gloves, ergonomic accessories like a mouse, cushions for my workstation, and a plethora of kitchen gadgets.

Maintenance: This complementary therapy journey, although years long already, will never be over. Depending on the state of my disease, different therapies will be needed and effective. Sometimes I do chiropractic care every day, sometimes it's once a week, or once a month. Sometimes I do physical therapy, chiropractic care, supplements, and massage all in one day or week. What I have developed is a toolbox of complementary therapies that I know work sometimes for certain flares that I can pull from when I need them. I know that some of my pain can be better managed and even eliminated by relearning how to use all of my muscles properly in physical therapy and reducing stress and tension with regular acupuncture and massage.

Quality of Life: Simply knowing there are other options to relieve symptoms and improve my day without adding more drugs has improved my outlook on my disease and, therefore, my mental health. I can better cope in a flare, accomplish more, and feel more productive. I can say yes to more opportunities and more fun things. The only drawback is the number of activities I have to juggle to maintain my version of good. Keeping the pills and doctors' appointments straight with work is hard enough, and sometimes adding in PT and other appointments is too much, and I have to pick and choose which, in the short term, gives me more free time or mental capacity, but backfires in flares or pain.

Takeaway: Adding in complementary therapies might seem like a no-brainer, but it took me almost 20 years for a rheumatologist to suggest it and help me find options. I had brought it up a few times over the years, "should I try changing my diet" "should I try PT" and was met every time with no, I don't think that will make a difference for you and then we would proceed to chase the next biologic that hit the market. I would like to see both patients and rheumatologists find a balance in therapy options and regularly challenge the status quo. We are taught in Western medicine to treat with drugs or to dismiss problems and say exercise more or eat better. While all of those things can be helpful, they can be more of a hammer approach. Each symptom needs to be examined and determine possible root causes and offer multiple ways to treat them, especially with the rate of comorbidities in chronic disease.

Disclosure: B. Murray: None.

Abstract Number: PP08

Living Well Despite the Challenges of Sjögren's Disease and Systemic Lupus Erythematous: My Perspective as a Health Care Provider and Patient

Casey Hogan[1], [1]Advanced Eye Care Professionals & Sjogren's Foundation

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

SESSION INFORMATION
Session Date: Sunday, October 26, 2025
Session Title: (PP01-PP08) Patient Perspectives Poster
Session Type: Poster Session A
Session Time: 10:30AM–12:30PM

Background/Purpose: Typically, the diagnosis of any autoimmune condition can be challenging and take years. In my case, my diagnosis of Sjögren's disesase (SjD) was established while hospitalized in cardiac intensive care due to renal failure and cardiomyopathy as a young patient. Over time and years later, my health landscape evolved to an additional diagnosis of systemic lupus erythematous (SLE) with kidney involvement, specifically lupus nephritis. My career as an optometrist allows me a unique perspective on not only understanding the clinical aspects and management of my conditions, but also gives me the knowledge and compassion to treat my patients and advocate for increased awareness of SjD and its multi-systemic nature within the healthcare community.

I was 23 years old and a 3rd year optometry student when I was first diagnosed. I initially presented to my local emergency room with mental confusion, significant tachycardia, nausea, and lethargy. Clinical examination revealed metabolic acidosis secondary to type 1 distal renal tubular acidosis, hypokalemia, renal failure, and metabolic encephalopathy and cardiomyopathy. The diagnosis was SjD w/Type 1 renal tubular acidosis based on clinical laboratory studies. We were just learning about autoimmune disease in our courses, and I recall the immediate concern of being so young and so sick, and the uncertainty of the disease.

Intervention: Management of any systemic autoimmune disease requires a team approach and collaborative care and the number of subspecialties who are a part of my healthcare team has grown over the last thirty years. This is a key reason that I believe in staying educated on my disease by utilizing reliable resources such as PubMed to review current literature pertaining to my disease. This, in turn, helps ensure that I'm able to communicate with my health care team and that they're kept up to date on best practices and considerations for my optimal care.

An important example of these collaborative efforts was educating my urologist on the complex nature of my simple lithotripsy procedure for nephrolithiasis and the risk for urinary tract infections that had led to sepsis and multiple hospitalizations for me in the past. This education and awareness was much appreciated by my healthcare team, who often times mistakenly think of SjD as "just dry eye disease".

Maintenance: Continuing my own education and communicating and advocating for myself with my healthcare team to ensure we're on the same page is an ongoing effort. My ocular complications have led to a lifelong journey of specializing in the management of ocular surface disease and my continued education and interest in this field facilitated becoming a Diplomat of the American Academy of Optometry in anterior segment disease, which has helped both myself as individual as well as the many patients I treat.

Quality of Life: While education and stronger communication have helped improve care and **Quality of Life**, there are still gaps in knowledge, management, and treatment options that influence how I'm able to live in a given period.

Takeaway: My efforts to stay educated on my disease and openly communicate with my healthcare team have helped strengthen these relationships and provided a degree of confidence in my own understanding of the disease and what I'm experiencing as well as those who I trust with caring for me. My perspective as an eye care specialist has helped me in my pursuit of quality of life, and ultimately my empathy and true understanding has helped countless patients and other healthcare providers understand this complex disease.

Disclosure: C. Hogan: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: PP09

The Role of a Palliative Care Support Team to Optimize Outcomes for Patients with Airway Involvement from Relapsing Polychondritis

Joshua Sparks

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Patient Perspectives (PP09-PP13)
Session Type: Poster Session C
Session Time: 8:15AM–9:30AM

Background/Purpose: Relapsing polychondritis (RP) is an inflammatory condition with a variable phenotype thought to be due to autoimmunity towards cartilage, particularly, that found in the airway. It can be challenging to diagnose and lead to symptoms that can have a profound effect on quality of life (QOL) and is one of the leading causes of morbidity and mortality for this condition. I was diagnosed with RP after over a decade with "challenging asthma." In addition to progressive diffuse airway malacia (figure 1), I had auricular chondritis, migratory polyarthritis, episcleritis, and sicca syndrome. After an extended period of steroids and multiple medications, partial remission was achieved with low dose prednisone, IV tocilizumab, methotrexate, and hydroxychloroquine. Despite adequate immune control, the residual airway damage resulted in nearly constant air hunger, dyspnea, and cough. After 1 year, I was barely able to walk, talk, or work requiring intermittent positive airway pressure (PAP) and cough suppressants during the day. Intervention: Once on immunotherapy, the persistent air hunger led to poor mental health and fear. As a physician involved in the care of very complex diseases, I work alongside palliative care (PC) teams, and I thought they might be able to help. Against the advice of my primary doctor, I sought consultation with my local PC program. After assessment, we worked to establish goals and a plan.; specifically, time free from air hunger, reduced cough, and to be able to continue working. Maintenance: Unfortunately, things were more complicated than I was prepared for which led to the first and most important intervention: acknowledging the severity of my illness. In addition to the airway symptoms, I was obese with low muscle mass from steroids and the situation was untenable. Working was unrealistic, especially in my chosen career, and continuing likely increased risk of complications and death. I was totally disabled. Step one, I had to quit working. Next, though I was skeptical, I start extended release morphine for air hunger. Despite my skepticism, this proved to be highly effective and I was able to breathe comfortably resulting in an immediate and significant improvement in my QOL. Quality of Life: After an adjustment period, I began trauma and grief counseling and refocused on my QOL with the goal to get back to work. I began moving some every day. This wasn't simple or easy requiring mobility aids and portable PAP (See figure 2). Over time, I was able to take walks and travel. After 2+ years, I lost 125 lbs and increased my strength (See figure 3). After 4 years, I was finally able to go back to work. I have kept off the weight and have strategies in place to focus on living day to day. Without PC's unique expertise directing focus toward goals and QOL, I would be more likely to be a statistic than writing this abstract. Takeaway: In conclusion, airway involvement from RP leads to symptoms of severe cough, dyspnea, and air hunger compounded by the debilitating effects of steroids. These symptoms are complex and challenging and can persist despite remission of the disease. PC provides unique expertise in the treatment of respiratory symptoms and poor QOL commonly found in advanced stages of disease. Though traditionally associated with the end of life, when a PC team is utilized to focus on a patient's symptom control and QOL, it can help to optimize rehabilitation and maintenance of overall health thereby improving outcomes for patients with advanced airway involvement from RP.

Disclosure: J. Sparks: None.

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: PP10

Breaking Through Scleroderma's Invisible Struggles: From Isolation to Connection

Sheri Hicks[1], Mary Alore[1], Yen Chen[1], Susan Murphy[1], [1]University of Michigan

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Patient Perspectives (PP09-PP13)
Session Type: Poster Session C
Session Time: 8:15AM–9:30AM

Background/Purpose: While living in Tucson, Arizona in 2006, and caring to our 1-year-old son, I noticed painful ulcers on my red, swollen, and tight fingertips. The pain became unbearable, and it took nearly 6 months before I finally diagnosed with scleroderma in 2007. I could hardly pronounce or understand the word, but I knew I couldn't ignore it. After reaching a point of exhaustion, we relocated to Michigan to be with family and friends. That move became a turning point. In Michigan, I found a supportive community and discovered a new purpose. Although I can no longer work full-time, I became a patient partner in research to help make sure patients' voices are reflected in studies. I am also a trained peer mentor and find joy in connecting with others living with scleroderma. By sharing my experiences, I hope others feel less alone in what can be an isolating journey. This work has given me a renewed purpose, and I am dedicated to supporting others on their journey with scleroderma. Intervention: Living with a rare disease like scleroderma can be isolating, especially when symptoms are invisible to others and we "don't look sick." This invisibility can make it hard to manage daily life and feel understood. I've found that combining peer support and building a strong community connections help address not just the physical symptoms, but also the emotional and social toll of living with scleroderma. As a trained peer mentor and a peer health coach in the RENEW (Resilience-building Energy management to Enhance Well-being) intervention, I've supported others in building resilience and managing energy to improve their quality of life. I also co-founded Scleroderma Backers, an online community that support patients with nearly 900 members, which offers a safe space for connection, questions, and shared understanding. Through RENEW and Scleroderma Backers, I've seen how support from those who "get it" can foster hope and promote health behaviors. Maintenance: Through ongoing connections, whether in RENEW, the Scleroderma Backers, or extended community, I've learned to better advocate for myself, adjust to changing roles, and stay engaged in my care. These non-clinical approaches have strengthened my well-being, increased my confidence in navigating daily challenges, and reduced feelings of isolation. Quality of Life: Today, my quality of life is much more balanced and fulfilling than it was at the time of my diagnosis. While I still face daily challenges from scleroderma, I've learned how to manage my symptoms, set realistic goals, and lean on a strong support system. Being actively involved in peer support and patient-centered research gives me purpose and connection that empowers and inspires me to help others on their journey. Takeaway: This abstract highlights the importance of integrating peer support into care to inspire self-care, foster meaningful connections, and reduce isolation. It also emphasizes the value of comprehensive care that support overall well-being. As patients find innovative ways to manage their conditions, healthcare providers are crucial in promoting these strategies. These insights benefit various rheumatic conditions, strengthening support systems that empower patients and enhance overall well-being.

Disclosure: S. Hicks: None; M. Alore: None; Y. Chen: None; S. Murphy: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: PP11

Lived Experience in Action: How Co-Creating a Psoriatic Arthritis Project Empowered My Journey as a Patient Advocate

Kathleen Gallant[1], Sicily Mburu[1], [1]IFPA

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Patient Perspectives (PP09-PP13)
Session Type: Poster Session C
Session Time: 8:15AM–9:30AM

Background/Purpose: I am a person living with Psoriatic Arthritis (PsA) since the age of 20. I have spent decades working in advocacy. On my 'good days,' I focus on outreach to change national health policy. I have participated in various advisory boards, most recently in the GoodCare Campaign for PsA, a global, patient-driven project to address unmet needs in the PsA community. Having experienced the challenges patients face—misdiagnosis, delayed treatment, lack of awareness, and isolation, has motivated me to contribute to initiatives that bridge the gap between lived experience and clinical care. Intervention: The GoodCare Campaign for PsA project was launched by the International Federation of Psoriasis Associations (IFPA) in 2022 to raise awareness of the need for PsA treatment guidelines and their integration into care pathways. I served on the steering committee helping to ensure that the patient voice remained central. Together with patients, clinicians and member associations, we co-created tools like the lived-experience illustration booklets, webinars, podcasts, social media materials, communication guides and a downloadable "treat-to-target" patient checklist. These resources support early symptom recognition and help patients, and their loved ones, navigate conversations with healthcare providers. Materials were translated into 9 languages and shared in global campaigns such as World Psoriasis Day, World Arthritis Day, and at international congresses including the European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR).Maintenance: Since its launch, the project has achieved measurable reach. The resources were shared globally via live podcasts recorded at major congresses reaching listeners in over 25 countries. A global survey conducted by IFPA showed over 50% of organizations advocating for people living with PsA had received and used the co-created materials - especially in under-resourced areas. Many, including myself, have emphasized the need for culturally adaptable formats to make the content inclusive. A key outcome was an engaging webinar with a rheumatologist exploring how treatment guidelines can be used as patient education tools. Quality of Life: Co-leading this project has been personally empowering. Seeing patient insights transformed into tools and educational content gives me hope. Knowing my peers feel less alone has deepened my resilience and commitment, furthermore, sharing tailored resources with the medical community and advocating for shared decision-making is impactful. Among the many meaningful conversations I have been part of, one that stands out is this: Importance of shared decision making around therapeutic choice Takeaway: This project shows the power of patient-physician collaboration. I encourage patient leaders and healthcare professionals to adopt co-creation models, use shared decision-making tools and embrace communication strategies that work for both. This will not just change clinical outcomes—it changes lives.

Disclosure: K. Gallant: None; S. Mburu: None.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Abstract Number: PP12

From Invisibility to Advocacy: A Gout Patient's Journey to Validation and Systemic Change

Gary Ho[1], [1]Gout Support Group of America

SESSION INFORMATION

Session Date: Tuesday, October 28, 2025
Session Title: Patient Perspectives (PP09-PP13)
Session Type: Poster Session C
Session Time: 8:15AM–9:30AM

Background/Purpose: In 1994, at 24 years old, I felt a sudden, sharp pain in my right ankle while crossing campus. My father shared that both he and my grandfather lived with gout and urged me to see a physician. But my concern was dismissed with: "You're too young for gout." This began a 16-year journey through pain, misdiagnosis, and dismissal. Flares would vanish before appointments. Without visible signs, I was told it was overuse or that I was too active. I used crutches, then a wheelchair. I was prescribed nonsteroidal antiinflammatory drugs (NSAIDs) and steroids, but no one searched for the cause. By the time I was properly tested, I had lost 20% of my kidney function, and my serum uric acid (UA) level was over 10 mg/dL—far exceeding the 6.8 mg/dL threshold for gout diagnosis. Each time I left a medical appointment without answers, I felt more invisible. Over time, I started questioning if anyone would ever believe the pain I was living through. Intervention: In 2010, I finally saw a rheumatologist. For the first time, a physician listened. A simple blood test confirmed chronic gout. That diagnosis wasn't the end of my story—it was the beginning. For the first time, I felt validated—my pain had a name, and with that came hope for healing. I started UA-lowering therapy, but after years of unmanaged disease, my levels remained high. I joined a clinical trial for an intravenous UA-lowering therapy. The treatments were grueling—six-hour infusions every two weeks for nine months. The first three months were the hardest as my body expelled years of UA crystals. With support from my medical team and family, I endured. By the end, my UA stabilized, my mobility returned, and I have not had a gout attack since. Maintenance: Today, medication keeps my UA below 6 mg/dL. I exercise regularly, stay active, and enjoy foods I once avoided. My 16-year struggle was isolating. I battled pain and mental health challenges brought on by dismissal and stigma. In 2015, after reclaiming my life, I helped establish a patient support group. What began as a small effort now reaches over 16,000 people, offering education, resources, and support to help others advocate for their health. Through this community, we've connected patients with trusted specialists and empowered them to speak up, ask better questions, and demand the care they deserve. Quality of Life: I am living fully and without limitations. I can travel freely, stay active, and enjoy everyday moments without fear of flares. I no longer schedule my life around my disease. Instead, I plan my future with confidence, knowing that gout no longer controls me. Emotionally, I found freedom through advocacy. Helping others has restored hope and brought new purpose. For people living with gout, this quality of life means everything: living without pain, without fear, and with the confidence to fully participate in life. Takeaway: Listen first. Create space for patients to fully share their experiences. Simple diagnostic tests, such as serum uric acid (UA) measurement, can prevent years of unnecessary suffering. Recognize the mental health impact. Include mental health check-ins for patients with chronic disease. Acknowledging emotional well-being improves outcomes and strengthens trust. Address stigma head-on. Educate patients and care teams that gout is a complex, chronic disease requiring proactive, long-term management. Correcting misinformation can be the first step toward treatment adherence. Partner with patients. Use shared decision-making to set treatment goals, establish UA targets, and provide regular follow-up support. Patients who feel heard are more engaged and committed to their care."

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Disclosures: G. Ho: Alliance for Gout Awareness (AGA): Grant/Research Support|Amgen: Grant/Research Support|Amgen: Unrestricted advocacy grant provided to GSGA; no personal financial relationship.|Sobi: Grant/Research Support|Sobi: Unrestricted advocacy grant provided to GSGA; no personal financial relationship.

Abstract Number: PP13

Life Transitions and Their Impact on Patients

SESSION INFORMATION
Session Date: Tuesday, October 28, 2025
Session Title: Patient Perspectives (PP09-PP13)
Session Type: Poster Session C
Session Time: 8:15AM–9:30AM

Background/Purpose: I was diagnosed with systemic lupus erythematosus (SLE) when I was 14, and then eventually with CNS lupus when I was 17. My doctors have found a treatment plan that works really well for me. Due to being diagnosed at such a young age, I have gone through many life transitions while dealing with my autoimmune diseases. These transitions include: advancing from pediatric to adult care, moving to college, medical insurance changes, and getting married. Life transitions can lead to health issues as a result of medical care team changes, insurance changes, and difficulties with access to medications and treatments. Changing doctors in the move from pediatric to adult care can introduce difficulties in ensuring that the new health care provider is willing to maintain that same treatment plan. Moving to college can also introduce challenges, especially if you are in a new state and need a local physician for your prescriptions and infusions. Getting married also led to medical insurance challenges, resulting in changing infusion companies and restarting the approval process. For many of these life transitions, I had a period of usually 3 to 6 months going without the treatments that worked for me, which always led to a flare. Intervention: To help prevent discontinuity of care and treatments during life transitions, it is important to plan ahead. Preparing for these changes can prevent some of the common, preventable issues that can occur. The healthcare system can be difficult to navigate, especially if you add in healthcare insurance. Ensuring that the patient learns about their health insurance and prepares for changes before they occur is important. This includes understanding the new coverage and beginning the process of finding covered healthcare providers before the change happens. When choosing where to attend college, planning ahead for treatment is crucial, especially if the college is in another state. Ultimately, I determined that it would not be possible to maintain my treatment plan as it was if I did this, so I chose a college in the same state. Maintenance: Once I was educated on how to navigate medical insurance and the healthcare system in general, it was much easier to prepare for and overcome challenges that arose when I went through another life transition and will be in the future as well. Quality of Life: Maintaining my treatment plan through these life transitions has allowed me to finish my bachelor's and master's degrees, walk across the stage at both graduations, and walk down the aisle at my wedding. These were things that were not initially possible, but through preparing for these life transitions and maintaining my treatment plan, they were able to happen. Takeaway: To ensure there is no disruption in the care and treatments of rheumatic patients during life transitions: It is critical that the patient and their family understand their health insurance coverage, including which healthcare providers (HCPs), facilities, and services are covered. HCPs should be aware of possible life changes and situations to expect ahead of time. HCPs should know and be able to provide available resources such as handouts, links to resources, and information that can be added to the after-visit summary that would help patients navigate these challenges. Potential life transitions to consider are moving from pediatric to adult care, beginning college, moving to a different state or country, healthcare insurance changes, marriage, divorce, and death. Preparing a patient and their family for potential challenges from life transitions can result in better care, health outcomes, and quality of life.

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Author Index

(Focht) Garand, Kendrea 0305, 2064
A Rigual, Juan 1024, 1869, 2030
Šenolt, Ladislav 0831, 1211, 1350, 1962, 2073, 2279, 2346
Štolfa, Jiří 0831
A. Isenberg, David 1722, 2294, 2304, 2416
A. Karsdal, Morten 0307
álvaro-Gracia álvaro, José María 2121, 2249
Ørbo, Hilde 2640
Ørbo, Hilde 2660
Ørnbjerg, Lykke 0543, 1430
Żuber, Zbigniew 1883
İKİKARDEŞ, MÜSLÜM FIRAT 1440
Çakır, İbrahim yahya 1618
Çapkın, Erhan 2322

A

Aaløkken, Trond Mogens 0510
Abacar, Kerem 1677
Abad, Sébastien 0735
Abad Plou, Elena 1904
Abadi, Rym 2304
Abalos-Aguilera, M Carmen 0071, 0072, 0087, 0094, 0108, 0795, 1851
Abalos-aguilera, Maria del carmen 0100, 0901, 2599
Abasolo Alcazar, lydia 0483, 0744, 0752, 0757, 1024, 1269, 1284, 1869, 2030, 2036
Abate Namnum, Priscilla 1832, 2394
Abbarin, Nastaran 0523
Abdalla, Jennifer Elise **0695**
Abdel Aziz, Nada 1696
Abdellaoui, Salomé 0489, 1333
Abdelnabi, Mai 1982
Abdelsalam, Mohamed **0331**, **0332**, **0333**, **0334**, **0335**, **1317**, **1318**, **1713**
Abdelsattar, Farrag 0397
Abdel-Wahab, Noha 1107, 1108, 1730
Abdollahi, Shahrzad 0254, 0255
Abdollahi, Shahrzad 1074
Abdollahi, Shahrzad 1522
Abdollahi, shahrzad 1665
Abdou, Rowaida 0648
Abdueva, Diana 2275
Abdulla, Fatima 0648
Abdullateef, Nizar 1930
Abdul-Rehman, Hadeel 0463, **1159**
Abe, Nobuya 1854
Abe, Yoshiyuki 2523
Abedi, Mehrdad 2468
Abel, Brent 0182
Abel, Magdalena 1872
Abelha-aleixo, Joana 0761
Aberle, Teresa 0044, 1850, 2649
Abeykoon, Jithma 1174
Abhser, Devin 0039
Abidov, Amir 2174
Abisror, Noemie 1339, 1765
Abitia Borboa, Carlos Abdiel 2321
Abonamah, Adal 1832, 2394
Abouelella, Ahmed **1222**
Abouelella, Nourhan 0333, 1317, 1713
Abouelnadar, Alzahraa 0538
Abraham, roshini 1668, 2155
Abraham, Yann 1703
Abrahante, Juan 0027
Abramkin, Anton 1323
Abrams, Jennifer 2277
Abreu, Gabriel 1552
Abreu, Pablo 0934
Abria, Christine 0586, 0587, 1120
Abril, Andy 0315, 0727
Abril, Andy 0759
Abril, Andy 1585
Abu Alsaoud, Sima 1287, 1288
Abud-Mendoza, Carlos 0596, 0621, 0623, 1530
Abu-Elhija, Muhanad 1436
Abughazaleh, Saeed 0502
Abuhamad, Alfred 0853, 1391
Abuqayas, Bashar 1110
Aburto Barreneche, Myriam 1904
Abuzakouk, Mohamed 0648
abylova, bermet 2247, 2248
Acar, Beste 0778, **1477**, **2022**, 2667
Acar, Hasan 2612
Acasuso, Belen 0454
Acayaba de Toledo, Ricardo 1959
Accetta Rojas, Gabriela **1013**
Acebo, Nina 0207
Acevedo gallegos, Sandra 2218, 2632
Acevedo Martel, Eduardo 2106
Acharya, Sholen 2295
Acharya, Suman 1119
Achenbach, Sara 1030, 1156, 1320, 1932
Achenbach, sarah 1388
Ackermann, Félix 1575, 2489
Acklin, Yves 0919
Acosta, Ana Valeria 1961
Acosta, Francia 1825
Acosta, Gisela 1637
Acosta, Maria Isabel 0623, 1491, 1530
Acosta Alfaro, Ana Valeria 0496, 2268
Acosta Mérida, MA 1490
Acosta-Herrera, Marialbert 1862
Acquaviva, Rossella 0238
Adaletli, Ibrahim 2544
Adalier, Emre 0267
Adam, Atif 0734
Adam, David 0523
Adamczyk, Natalie 1736, 1790
Adamczyk, Natalie 1800
Adami, Giovanni **2116**, **2117**, **2592**
Adamichou, Christina 0628
Adamo, Luigi 2436
Adams, Elaine 1511
Adams, Elena 0164
Adams, Gregor B 1003
Adamson, Elizabeth 1165, 1376, 1377, 2369
Adamson, Maike S. 0892
Adas, Maryam 1906
Adedeji, Clement 0869
Adejoorin, Ifeoluwakiisi 2414, 2644, 2688
Adelakun, Oyediran **1176**
Adelowo, Olufemi 2263
Adem, Abebawork **0199**
Ades, Lionel 1339
Adeyemo, Adebowale 1725
Adhikari, Rishi 2612
Adjaye, James 0809, 0974
Adjei, Taylor 1915
Adla, Akhil 1061
Adler, Brittany L 0288, 1559
Adler, Seth 1242
Adly, Mahmoud 1930
Adonimohammed, Sohail 1827
Adrovic, Amra 1287, 1288
Aeamsaard, Nittayawadee 2004
Aeenfar, Dorsa 2127
Aeschlimann, Carolina 2405
af Forselles, Kerry 1804, 2101
Afari-Armah, Nana 1182
Afgani, Fahmeen J. 1710, 1959
Afolayan, Oladipo Kunle 2067
Afridi, Summia 1667
Afshar, Erfan **2087**
Afshari, Khashayar 2668
Afzali, Anita 0257
Aga, Anna-Birgitte 0420
AGARD, Christian 0688, 0891, 1575, 1577, 2489
Agarwal, Aradhna **1557**
Agarwal, Avarna 0461, **0533**
Agarwal, Sandeep 0273
Agarwal, Sandeep 2287
Agarwal, Vikas 0295, 0304, 1212, 1218, 2065, 2066, 2067, 2185
Agboola, Adebola 0047
Aggarwal, Amita 0130, 0631, 1221, 1812, 2424, **2676**
Aggarwal, Anushka 0282, 1201
Aggarwal, Rohit 0282, 0289, 0298, 0303, 0305, 0357, 1201, 1213, 1215, 1889, 2055, 2064, **2671**
Aghajanian, Haig 1003

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Agmon-Levin, Nancy 1594
Agnihotri, Aayushi 2493
Agrawal, Aashish **2338**
Agrawal, Rachana 2435
Agrawal, siddharth 1484, 1892
Agrawal, Upasana 2392
Aguado, Pilar 0346
Aguiar, Vitor 1696, 2410
Aguila, Tania 0231
Aguilar, Allison 2454
Aguilar Coll, Martí 2491
Aguilar Zamora, Marta **2038**
Aguilar-Coll, Martí 0353
Aguilar-Coll, Martí 0749, 1161, 1162
Aguilar-Coll, martí 1382
Aguilar-Coll, Martí **2250**
Aguilar-Coll, martí 2299
Aguilar-Coll, Martí 2484
Aguilar-Oliva, Elvira E **0443**
Aguilar-Salinas, Carlos 1383
Aguilera, Sergio **0931**
Aguilera, Silvia 2179
AGUIRRE ZAMORANO, MARIA ANGELES 0070, 0071, 0072, 0087, 0094, 0120, 0139, 0795, 0901, 1851, 2599
Aguirre-del-Pino, Rodrigo 1548
Aguirre-Portilla, Carolina 0216
Aguirre-Portilla, Carolina 1778
Aguirre-Portilla, Carolina 1916, 2388
Agustin, Lyra 1552
Aguzzi, Adriano 1206
Agyemang, Safoah **0381**, 1270
Öhagen, Patrik 0591, 0592
Ahamed, Sheikh Iqbal 2603
Ahern, David 2601
Ahern, Mary 0835
Ahijón Lana, María 2122
Ahktari, Shadi 0265, 0522
Ahmad, Hafizah 0378
Ahmad, Nashrah **1796**
Ahmad, Shaheer 1720
Ahmad, Wajdan 1795
Ahmed, Abu-bakr 1328
Ahmed, Asra 1174
Ahmed, Faizan 0312
Ahmed, Haziq 0312
Ahmed, Jawad 1063
Ahmed, Nasra 0191
Ahmed, Rohma 0312
Ahmed, Saad 0696, 1569
Ahmed, Saiam 0692
Ahmed, Sakir 0461, 0533
Ahmed, Salahuddin 1654
Ahmed, Zeeshan 1221
Ahmed Abdi, bahja 2503
Ahn, Soo Min 1372, 1373, 2431
Ahrens, Samantha 1508
Aigbekaen, Itohan 1822
Aigbokhan, Ejiehi 2263
Aigner, Michael 0641, 1537
Aikawa, Nadia E 0619, 1192, 2527, 2653
Aikawa, Nadia Emi **0206**, 1292, 1715, 2292, 2535, **2573**, 2682
Ainatzoglou, Alexandra 2461
Ainsworth, Hannah 0028, 1696
Ainsworth, Richard 0881
Airò, paolo 0702, 1562
Airoldi, Carla 1422
AitDowd, Lwiza **0824**, 1810
Aizaki, Yoshimi 0084
Aizenberg Peleg, Michal 1436
Aizer, Juliet 0827, 2162
Aja, Ezinne 1565
Ajeganova, Sofia 0133
Ajenaghughrure, Godbless 0233, 1418, 1543, 2238, 2239, 2240, 2283
Ajenaghughrure, Godbless 2284
Ajiboye, Patrick 0204
Ajitumar, Ashika 1625
Ajmone Marsan, Nina 0696
Ak, Furkan 2044
Akaa, Jesse 0992, 2528, 2530
Akamine, Rinko 0850
Akar, Servet **0524**, 0854, 2322
Akasbi, Nessrine 2324
Akbari, Hanieh **0693**, **1665**
Akca, Ummusen 2128
Akdemir, Muhammed Çağrı 2349
Akdoğan, Ali 2349
Akgül, Özgür 2322
Akgün, Özlem 1698, 1818
Akhavan, Pooneh 2266, 2642
Akikusa, Jonathan 1669, 2125, 2128
Akinsete, Alisha 1264, **1283**
Akiyama, Mitsuhiro 0052
Akiyama, Yoichiro **0764**
Akiyama, Yuji 0084
Akiyama, Yuya 0043
Akizuki, Shuji 1772, 1857
Akkaya, Billur 1694
Akkaya, Munir **1694**
Akmansoy, Can 1396
Akoghlanian, Shoghik 0413
Akpek, Esen 1376, 1377
Akram, Mohammed **0163**, 1078
Akselrad, Melissa 1832, 2394
Aksentijevich, Ivona 0301, 1651, 1725
Aksoy, Burcu 1396
Aksu, Kenan 1618
Aktaş, İlknur 2322
Aktas, Berkay 1477, 2022, **2667**
Aktay Ayaz, Nuray 1698
Aktay Ayaz, Nuray 1818
Aktay Ayaz, Nuray 1823
Al Ansari, Atheer 0648
Al Araimi, Tariq 2318
Al Badawy, Amer 1880, 1881, 2088
Al emadi, Samar 0600, 2318, 2638
Al Hamdan, Obada 1374
Al Qassimi, Sarah 0600, **0648**
Al Rayyes, Hanan 2318
Al Tabaa, Omar 0489, 1333
Al Zoubi, Osama 0068
Alaa, Ahmed 1657
Al-Abadi, Eslam 1287, 1288
Aladaileh, Bushra 0397, 2130
Al-Adl, Mohamed 1317
Alados Hernández, María José 1548
Al-Adwi, Yehya 1860
Alagappan, Aishwarya 1086
Alameri, Jawahir 0648
ALANAZI, FEHAID 0202
Alani, Omar 2041
Alarcón, Graciela 0605, 0621, 0714, 0730, 1717, 1722, 2378, 2383, 2416, 2521
Alarcon-Jarquin, Margarita Isabel 0366, **1022**, **1023**, 1527, **1928**, 2553, 2606
Alarcon-Riquelme, Marta 0034, 0070, 0071, 0094, 0125, 0795, 0901, 1840, 1851, 2648
Alaswad, Mohammed 2318
Alavi, Afsaneh 0030
Alawneh, Diala 0435, 2438, 2439
Alazmi, Mansour 0202
Alba, Paula 0623, 1491, 1530
Albach, Fredrik 0471
Albaladejo Paredes, Gloria 2112, 2113
ALBALUSHI, FARIDA 0600
Albanese, Patricia 0114
Albano Aluquin, Shirley 2166
Alba-Rovira, Roser 0732
Albayda, Jemima 0288, 0865, **1204**, 1207, 2063
Albe, Benedikt 0826
Alberdi Arbelaiz, Ander 2107, 2108
Albert, Daniel 0893
Albert, John 1043
Alblooshi, Reem 0648
Al-Bourini, Omar 1205
Albright, Ben 0145
Albulescu, Marius 0567, 1455
Alcacer-Pitarch, Begonya 1933
Alcalá Carmona, Beatriz 2052, 2053, 2078
Alcalá-Carmona, Beatriz 0287, 1836
Alcalde Villar, María 0752
Alcantara Alvarez, Iago 1274, 2310
Alcántara Álvarez, Iago 0205, 0237, 0341, **2274**
Alcin Bayraktar, ruken 2544
Alcobendas, Rosa 1152, 2042
Alcorta Lorenzo, Nerea 1681, 2107, 2108
Alcorta-Lorenzo, Nerea 0485, 1397, 2269, 2350
Aldamouk, Amer 1369
Aldasoro Cáceres, Vicente 0200, 0736, 0739, 0744, 0752, 1612, 2610
Aldecoa, Iban 0296
Aldehmi, Norah 1239
Aldhaheri, Ahmed 0648
ALE06 Clinical, Study Team 1087
ALE06 Clinical, Study Team 1831
ALE06 Clinical, Study Team 2421
ALEGRE, cARMEN 0180

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

ALEGRE SANCHO, JUAN JOSE 1161, 1586, 1587, 2299, 2473, 2474, 2485
Alegre-Sancho, Juan José 0019, 1548, 2290
Alehashemi, Sara 0920
Alekseev, Eugenyi 0476
Alemairy, Amr 2070
Alemonai, jemima 0456
Alenzi, Fahidah **0202**
Alessi, Helena 0616
Aletaha, Daniel 0473, 0641, 0816, 1453, 1911, 2271, 2332
Alexander, Amanda 2172, 2190
Alexander, Pfeil 0471, 0762, 1660
Alexander, Shehani 0881
Alexander, Theresa 1163
Alexander, Tiffany 1073
Alexander, Tobias 0471
Alexanderson, Helene 0280, 0289, 2060
Alexandra, Jean-François 0735, 0756, 0891, 2704
Alexandre, MERCIER-GUERY 2621
Alexandrescu, Andrew 2577
Alexandrov, Tim 0651
Alexdottir, marta 2231
Alexeeva, Ekaterina 0401, **0403**, 1287, 1288
Alexiou, Ioannis 1219
Alexiou, Ioannis 2280
Alfaidi, Mabruka 1650, 1774, 1779
Alfaisal, Faisal 0538
Alfonso, Giuliana 1109
Alfranca, Arantza 2491
Algarra- San José, Marco 1961
Alghamdi, Yasser H. 0538
Alghanim, Khawla K 0202
Alhadri, Ali 0522
AlHajeri, Saud 1199
AlHajeri, Saud **2259**
Al-Hakim, Adam 0777
Alhasan, Mohammad 1222
Alhassan, Eaman 0282, 0305, 1201, 2064, 2199
Alhayali, Mustafa 2004
Alhejailli, Faris 0549
Ali, Ailia **1248**
Ali, Ali **1518**
Ali, Anusheh 2392
Ali, Azka 2285
Ali, Haadi 1174
Ali, Hakim Azfar 1160
Ali, Hammad 0278
Ali, Hammad 1474, 2428
Ali, Hassam 1907, 2596
Ali, Muhammad 0703, 1328, 2516
Ali, Rafal 1359, 1522
Ali, Ramadan 1590, 1874
Ali, Ramsha 0312
Ali, Waleed **1035**
Ali, Yousaf 1236
Ali Mirza, Mehdi 0495
Alibaz-Oner, Fatma **1618**, 1631
Alivernini, Stefano 0236, 0878, 1757
AlJasmi, Amina 0538
Alkan Melikoğlu, Meltem 2322
Alkhatib, Ahmad 1399
Alkousakis, Theodore 0523, 1176
Allain, Jean Sébastien 0891
Allain, Jean-sébastien 1339, 2532
Allanore, Yannick 0053, 0489, 0673, 0688, 0702
Allanore, Yannick 0706
Allanore, Yannick 0796
Allanore, Yannick 0884
Allanore, Yannick 1333, 1334, 1577, 1586, 1724
Allanore, Yannick 1862
Allanore, Yannick 2262
Allard-Chamard, Hugues 0438, 0442, 1126, 1355, 1648, 2281
Allegretti, Jessica R. 0257
Allen, Brendan 0088, 0800, 0870
Allen, Kelli 1922, 1927
Allen, Michael 1667
Allen, Veleka 1306, 1327
Allenbach, Yves 0862, 0887
Allen-Taylor, Lynne 1912
Allenzara, Astia **0145**
Allenzara, Astia 1271
Allison, Jeroan 1073
Allsop, Vivianne 1981
Allum, Cameron 0006
Almaani, Salem 0719
Almaashari, Raghda 0648
al-mabrouk, Yousef 2519
Almackenzie, Maha 0282, 1201
Almada, Felicia 0877
Almahdawi, Sally 2616
Almansouri, Abdulrahman Y 0522
Almanza, Angélica 1234
ALMARRI, MUNIRA **1297**
Almarzooqi, Ahlam 0538, **0600**, 0648
AlMasoud, Jude **0361**
Al-Matar, Shahad 1415
Almeida Dutra, Livia 0616
Almhdie-Imjabbar, Ahmad **1936**, **1937**, 1948
Almodahka, Abdalmohsen **2079**
Almosabihi, Abdulaziz 0538
Alnaimat, Fatima 1930
Alnaqbi, Khalid **0538**, 0600, **2318**
Alnasser, Manal 0547
AlObaidi, Muthana 1672
Alomari, Ahmad **0435**, 1359, **2438**, **2439**
Alomari, Laith 0254, 0255, 1074, 1075, 1076, 2093
Alomari, Lily **2097**
Alongi, Alessandra 0177
Alongi, Alessandra 0389
Alonso de Francisco, María **1170**, 1263
Alonzi, Gabriella 1567
Alotaibi, Azzam 0202
Alrayes, Hanan 0202
Alric, Laurent 0123
Alric, Laurent 1200
Alrowais, Abdulaziz 1297
Alshahrani, Moath **2603**
Alshajrawi, Roa'a 1098
Alshammari, Saitah 0538
Alsherbeeni, Nisreen 0202
Altın, Soner 0135
Altabás-González, Irene 0642, 0659, 1681, 2450
Altaffer, Ana Luiza 2462
Al-Tamimi, Mansoor 1222
Altarawneh, Heba **1101**
Altaye, Mekibib 0392, 0406, 0414, 2124, 2675
Alten, Rieke 1348
Altit, Gabriel 2222
Altmann, Christopher 0504, 0917
Altmann, Christopher 0980
Altorok, Nezam 1603
Altraide, Dasetima 2263
Alva Linares, Magaly 0596
Alva Linares, Magaly 1486
Alvar Pariente, Sara 2106
Alvarado, Luz 0491
Alvarez, Carolina 0330, 1271, 1788, 1960, 2092, 2604, 2616
Álvarez Andrés, Eva **0249**
Álvarez Castro, Carolina 0982
Alvarez Errico, Damiana 0019
Alvarez Meza, Joselyn Aracely 2557
Álvarez Rodríguez, Belén 0659
Alvarez Saez, Iago 2290, 2291
Alvarez Santana, Rodamin Ambiorix 1491
Álvarez-Cienfuegos, Antonio 2106
Alvarez-Hernandez, M. Paula 0518
Álvarez-Troncoso, Jorge **1210**
Álvarez-Vega, José Luis 0268
Alvaro-Gracia, Jose 0153, 2696
Alves, Flavia 1300
Alves Alvino, Laíssa Cristina 0596, 0621, 1491
ALVES MARIA, LILIA ALVES MARIA 0616
Alves Pereira, Ivanio 1365, 2246
Alvey, Jessica 1566, 2654
Alveyn, Edward 1906
Alwakeel, Deena 1297
Al-Wasity, Salim 1711
Alzamareh, Diana 0912
Alzate, Juan 0199, 2576
Amador, Leslie 2486
Amano, Koichi 1630
Amar Muñoz, Helena 2209
Amarilyo, Gil 1304, 1305
Amarista, Camila I 2494
Amarnani, Abhimanyu **1468**, **1759**, 2399
Ambartsumyan, Lusine 1291
Ambler, William **2580**
Ambooken, Tresa 1827

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ambrocio, Kevin Renz 0305, **2064**
Amengual, Olga 0860
Amezcua-Guerra, Luis M 0443, 1234, 1486
Amiable, Nathalie 0606, 1109
Amin, Hafsa 0093
Amin, Hamzah 0340, 0345, 0347, 1313, 2118
Amin, M Asif 0965
Amin, Rana Hussein 0264
Amiri, Neda 2203
Amit Rahat, Michal 1436
Amital, Howard 0570, 1332
Ammar, Talal 2543
Amorim Vieira, Shaila 0616
AMOURA, Zahir 1577, 2696
AMOUZOUGAN, Adamah 0537
Amudala, Naomi 2701
Amudala, Naomi 2703
An, Jie 0079
An, lemei **1642**, **2005**
An, Yunfei 0429, 1828
Anadón González, María 2106
Anam, Hema Latha 0337, 1914
Anand, Neel 2466
Anand, Prachi 2490
Anand, Pradeep S 1588
Anand, Pradeep S 2313
Anandarajah, Allen 1060, **1940**
Ananieva, Lidia P 2477
Ananingati, Ananingati 1398
Anastasiou, Christine **0817**, **1886**
Ancona, Nicolas **2495**
Anders, Hans-Joachim 2467
Andersen, Nicole **0376**
Anderson, Alexandra 1069, 2224
Anderson, Amy 1703
Anderson, Daniel 0065, 1314, 1325, 1650, 1774, 1779
Anderson, Deborah 0204
Anderson, Jordan 0008
Anderson, Marina 0692
Anderson, Peter 1889
Andersson, Daniel C. **0280**
Andersson, Helena 0510
Anderton, Robert M. 0672
Ando, Takayasu 0668
Andonian, Brian 0835
André, Marc 0891
Andréasson, Kristofer 0702, 1565
Andrés, Mariano 0270
Andrés, Mariano 1096, 1129, **1133**, 1996
Andrés Román Ivorra, José 0019, 0205, 0237, 0341, 1274, 2274, 2290, 2310, 2458
Andrade, Danieli 0120, 0121, 0619, 0860
Andrade, Felipe 0529
Andrade, Melissa 1253
Andreasson, Kristofer 0280
Andreeva, Ivana 1875
Andreica, Ioana **0152**, 1157, 1175
Andreoli, Laura 0120, 2210
Andres Esteban, Eva 0351
Andres Trashaedo, Estibaliz 0250
Andreu, Jose Luis 0019, 1170, 1397, 1681, 2290, 2291, 2422
Andreu Ubero, José María 2112, 2113
Andrews, Melody 0457
Andrés Collado, Mariano 0271
Andriessen, Lukas 0980, 1703
Andringa, Jennifer 2124
Andriushchenko, Yevheniia 1253, 1931
Androulakis, Ioannis 1026
Andujar, Pablo 2016
Andujar Brazal, Pablo 2473
Anekwe, Chika 1130
Anesi, Stephen 1184
Angelats, Edgar 0021
Angeles-Han, Sheila 0302, 0392, 0394, 0406, 0407, 0414, 0415, 0418, 0419, 1813, 1821, 1829, 2675
Angeli, Mario 1757, 1864
Angsana, Julianty 0558
Anguera, Montserrat 0046, 1723
Anić, branimir 1562
Anic, Branimir 0702
Anjum, Ahmad Furqan 0556
Anliker, Kathryn 0413
Annapureddy, Narender 0828, 1473
Anne, Himaja 0167
Anne, PIOT 2621
Anne, TOURNADRE 1095
Anolik, Jennifer 0772, 0851, 0904, 0942, 1223, 1240, 1480, 1692, 1844, 2233, 2421, 2600
Anon Onate, Isabel 0496, 2268
Anoshkin, Kirill 1697, 2442
Ansel, Mark 1000
Anstett, Sarah **0231**
Antón-López, Jordi 0426
Anthone, Emily **1946**
Anthony, Donald 1122, 1979
Anthopolos, Rebecca 1918, 1919
Antiochos, Brendan 1595, 1596
Anton, Jordi 0389, 0780
Anton, Jordi 1287, 1288
anton, Jordi 1671, 2137
Anton, Jordi 2138, 2139
Anton Pages, Fred 0250, 1548
Antonis, Fanouriakis 0628, 2461
Anufrieva, Kseniia 0797
Anwar, Maryam 0312
Anwar, Zuha 1628
Anzalone, jerrod 0158, 1068
Ünaldı, Erdinç 2349
Aouad, Krystel 0177, 1930
Aouba, Achille 2704
Aouhab, Zineb 0224
Aoyagi, Kosaku 1247
Aparicio, María 0505
Aparicio, Maria 0117, 0530, 2029
Aparicio Rubio, Celia 2038
Aparnathi, Mansi 0098, 0113, 0560
Apostolidis, Sokratis 0712, 1733
Apostolopoulos, Diane 0677
Apovian, Caroline 1130
Appel, Silke 0034
Appenzeller, Simone 1287, 1288, 1291
Appleton, Tom 1103
Apraş Bilgen, Şule 2043, 2349
Apruzzese, William 2600
Apte, Suneel 1809
Aptekmann, Ariel 1827
Aqrawi, Lara 0034
Aquilani, Angela 0391
Ara, ashkan **0478**
Arévalo Ruales, Karla Romelia 2038
Arévalo-Salaet, Marta 2422
Arachchige, Darshani 0474
Aragon, Angel 0351
Arai, Sally 0501
Arai, Toru 0773
Araide, Dunia 1436
Arakawa, Takahiro 2602
Araki, Yasuto 0084
Aranda Cano, Evelyn 1947, 2243
Aranda Valera, Concepción 0072
Aranda-Valera, Concepción 0070, 0071, 0094, 0795
Arango Martinez, Alejandro 0300
Aranow, Cynthia 0657, 0791, 1505, 1722, 2416, **2441**, 2650
Araujo, Pedro 1180, 2028, **2045**, 2535
Araujo Duarte, Larissa 0616
Araujo-Ayala, Ferran 0732
Arazi, Arnon 0719
Arazi, Arnon 0933, 0940
Arazi, Arnon 1763
Arazi, Arnon 1830
Arazi, Arnon 1844
Arazi, Arnon 2600
Arbeeva, Liubov 0306, **0311**, 1788, **1960**, 2092
Arce, Kaitlyn 0890
Arcibar-Liceaga, Irasema 0767
arciniega Larios, cristina 1548
Arconada, Celia 0351, 1548
Ardalan, Kaveh **1745**
Ardekani, Ali **0601**
Ardekani, Ali 1721, 2403
Ardoin, Stacy 0719, 0820, 2386, 2462
Arellano-Alvarez, Mario A. 1023
Aren, Kathleen 0846, 1227, 1362, 2430
Arends, Suzanne 0694, 1685
Arevalo Molina, Belen 0743, 1606, 2508
Arevalo-Nieto, Fany Rocio 1633, 2549
Argeseanu Cunningham, Solveig 2154
Argraves, Melissa 0413
Arguello, Juan 0877, 2257
Argyriou, Evangelia 2232
Arham, Muhammad 0312
Arias, Francisco **1098**
Arias, Karina 0443
Arias de la Rosa, Iván 0100, 0108

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Arias Diaz, Danny 0364
Aries, Peer 0192
Arikan, Ozlem **2044**
Aringer, Martin 2445
Aripova, Nozima 0924, **1774**
Ariztia Sarratea, Maria 2107, 2108
Arlet, Caroline 0162
Arlet, Jean-Benoit 2532
Armendariz, Stephanie 1691
Armendi, Isabel 2146
Armengaud, Alexandre 0148
Armentaro, Giuseppe 1863
Armentaro, Giuseppe 2656
Armor, Zachary 2006
Armour, Ruaridh 0711
Armstrong, April 0455
Armstrong, April 0581
Armstrong, April **2689**
Armstrong, Iwan 2367
Arnaud, Laurent 0147, 0644, 2441
Arneson, Laura **2162**, 2430
Arnheim, Dana 1280
Arnold, Justin **2455**
Arnold, Lesley 1254, 2189
Arnold, Sabrina 0238
Arnold-Gräf, Mona 0090
Arnott, Maxine 1239
Arnoux, Armelle 0327
Aroca Martínez, Gustavo 0621, 0650, 1486, 1491
Aroca-Martínez, Gustavo 0596, 0623, 1530
Arocha, Sinibaldo 2601
Aronson, Kerri 2031
Aronson, Sasha **0787**
Arora, Aakriti 1787
Arora, Rashmi 1260
Arora, Shilpa 2504
Arora, Tarun 1045, 1054
Arriens, Cristina 0044, 0791, **1262**, 1505, 1674, 1850, 2649, 2650
Arron, Joseph 0501, 2277
Arroyo, Jaime 0180, 1282, 1284
Arruabarrena Echeverria, Iñaki Maria 2107
Arruabarrena Echeverria, Iñaki Maria 2108
Arsene, Camelia 1012
Arslan Sarikaya, Sevtap 1188
Arslantürk Güneysu, Cansu 0760
Artim Esen, Bahar 0120, 0133, 0135, 0290
Arturi, Valeria 0596, 0621, 1486
Artusi, Roberto 1737
Arulananthan, Sujeeba 0053
Arunachalam, Vinayagam 1442, 2351
Arvidsson, Linnea 1884, 1885
Arvikar, Sheila L. 0344
Arvizu-Rivera, Rosa 0248, 0614, 1687, 2058, 2071, 2072, 2325
Aryal, Yubraj 0456
Asahara, Kenichiro 2602
Asai, Shuji 1326
Asano, Tomoyuki 1509
Úbeda, Lorena 1620
Ascherman, Dana 0022, 0282, 0298, 0303, 0864, 0999, 1201, 1215, 1308, 1746, 1946
Asekhame, Omokhowa 2263
Asghar, Muhammad Sohaib 0163, **1078**
Ash, Julia 0598
Ashe, Brittany **2175**
Ashley, Douglas 2362
Ashoor, Maryam 1810
Ashoor, Maryam 1822
Ashoor, Maryam **2151**
Ashouri, Judith **0054**, **0055**, **0110**, 0871
Asiri, Abdulrahman 1297
Askanase, Anca 0377, 0640, 0791, 1268, **1519**, 1529, 1531, 1722, 1853, **1942**, 1970, 2416, 2440, 2650, 2693
Askling, Johan 0525
Aslam, Aamir 2411
Aslam, Fawad 0501, 2164
Aslam, Maryam 0316
Aslangul, Elisabeth 0735
Asmann, Nils 2010
Asmawidjaja, Patrick 0979
Asna Ashari, Kosar 2151
Aspenberg, Maria 0900, 2027
Asrat, Seblewongel 0897
Assaf, Elvira 1880, 1881, 2088
Assassi, Shervin 0541, 0671, 0672, 0683, 0883, 0959, 1555, 1566, 1582, 1662, 1861, 1862, 2361, 2475, 2654
Assawasaksakul, Theerada 0597
Assimes, Themistocles 0024
Astudillo, Leonardo 0162
Ata, Naim 1008
ATAMAN, Sebnem **1968**, 2322
Ataman-Önal, Yasemin 2396
Atefi, Gelareh 1549
Ateh, Bibiana 2084, 2096, 2098, 2624
Ates, Muhammed Bahaddin **2021**
Athavale, Amod 2548
Atienza-mateo, Belén 1778, 2016, 2229, 2265
Atisha Fregoso, Yemil 0902
Atkinson, Elizabeth 0030
Atlas, Caroline **0899**
Atsumi, Tatsuya 0120, 0121
Atsumi, Tatsuya 1854, 2289
Atta, Mohamed 0772
Attar, Mohammed 0202
Attar, Moustafa 1866
Attar, Suzan 0202, **0549**, 0600, 0648, 1349, 2273
Atuesta, Alexis 1041
Atzinger, armin 2613
Atzori, Laura 2699
Au, Helen **1601**
Aubourg, Frédérique 0688, 2262
Aubrun, Aurore 2115
Audemard-Verger, Alexandra 2699
Audia, Sylvain 1150
Auffret, Raphael 0477
Augustin, LATOURTE 0314, 1095, 1135
Augusto, Jean-François 0618
Auld, Lexi 0418, 1813, 1829, 2134, 2242
Aundhia, Minal **0415**
AUROUX, MAXIME **2621**
Aurrecoechea, Elena 0269
Aurrecoechea, Elena 0272
Aurrecoechea, Elena 1171
Aurrecoechea, Elena 2422, 2538
Austin, Daniel **1061**
Austin, Eric 0709
Auth, Janina 0236, 2695
Autoimmune and Immune Mediated Diseases, Accelerating Medicines Partnertship: 2233
Au-Yeung, Amelia 0664
Avalos-Garcia, Braulio R. 0212, **0213**, **1633**, 1834, 1845, 2171, 2219, **2549**
Avarbek, Oyku Zeynep 2044
Avcin, Tadej 0128
Avcin, Tadej 0389
Avcin, Tadej 1287, 1288
Avcin, Tadej 2179
Avcu, Aysegul 1396, 1618, 1631
Avenatti, Eleonora 1984
Avery, Kendra 0010
Aveytia Camacho, Alma 1070
Avihingsanon, Yingyos 2697
Aviña-Zubieta, J. Antonio 1018, 2214
Avilés, Antonio 1096
avlasevich, viktoriya 1926
Avouac, Jérôme **0053**, **0488**, **0489**, 0706
AVOUAC, Jérôme 0796, **1312**
Avouac, Jérôme **1333**, **1334**, 1349, 1356
AVOUAC, Jérôme 1371, 1578, 1724, 2262
Avramovic, Mojca 0128
AVRAMOVSKA, Aleksandra 1679, 2272
Avvad, Elizabeth 2395
Awad, Jamal 1337
Awad, Mohamed Reda 0331, 0332, 0333, 0334, 0335, 1317, 1318, 1713
Axelhed, My 2060
Ayala, Ernesto 0843
Ayala-Garcia, Tania Sarahi 1633, 2549
Ayan, Gizem 0540, 1008, 1405, 1406, 1941, 2349, 2635
Ayanian, Shant **2260**
Ayari, Mohamed Arselene 2638
Aydemir, Burcu 1216, 1225, **1249**
Aydin, Sibel 0854, 1626, 1710, 1959, 2266, 2609, 2642
Aydingoz, Ustun 1188
Ayla, Ali **0683**, **0883**
Ayla, Ali Y **0671**, 0672
Ayoub, Mohammad 0474
AYTON, SARAH G. 2187
Azad, Zakia 1759, 2399
Şahin, Nilay 2322
Ş Ahiner, fatih 0430
azeddine, dellal **1095**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Azeem, Rehan 1123, 1998, 1999, 2587, 2588
Şener, Seher 1818
AZEVEDO, YURE G 0179
Azhar, Zainab 1539
Azman, Enes 1177, 2667
Aznar-Esquivel, Antonio **0604**
Özomay Baykal, Gülcan 1287, 1288
Azpiri-Lopez, Jose R 0458, 0614, 1427, 1483, 1486, 1528, 2325
Ştețco, Andrea Claudio 2479
Azuaga, ana Belen 1943
Azukizawa, Masayuki 0459
Azuma, Naoto 2523
Azzam, Martin 0848
Azzi, Jacques 0843

B

B, PRIYANKA 2424
Bøgh-Sørensen, Sofie 2608
Bäcklund, Rebecka 1884
Bérezné, Alice 1765
Böltz, Sebastian 0236, 0641, 1697, 2641, 2695
Börjesson Sjö, Lena 1594, 1608, 1769
Bürki, Kristina 0807, 0957, 0967, 2497
Büttner-Herold, Maike 1856
Baños-Laredo, Marta E. 2052, 2053
Baay, Blake 0119, 0126
Baay, Blake **1093**
Babini, Alejandra 0684
Bacallado, Sergio 0032
Bacardit, Jaume 0307
Bachanova, Veronika 0663, 2454
Bachiller, Javier 0180, 1335, 2670
Baczkowska, Teresa 0665
Badal, Karen 2282
Baddi, Soukayna **0355**
Bade, Michael 0768
Bader-Meunier, Brigitte 1575, 2489
Badwy, Bassant Elaraby Elsayed 0331, 0332, 0334, 0335, 1318
Bae, Sang-Cheol 0595, 1722, 2416
Bae, Sangmee 0425, **1213**, **1214**
Baecklund, Eva 0034
Baek, In-Woon 1029
Baek, Jonggyu 0309, 0323, 2623, 2625
Baer, Alan 0034, 0514, 1223, 1682, 2233, 2302
Baer, Rebecca 2221
Baffoe-Bonnie, Terrylyna 1707
Bagge, Nathaniel 0997
Baggett, Chris 0145
Baggett, Katelyn **0412**
Baggio, Chiara 1127
Bagiella, Emilia 1832
Bagit, Ahmet 0565
Baglaenko, Yuriy 0418, 1813, **1829**
Bagley, Elizabeth 1191
Bagri, Narendra **0416**, **2152**
Bagri, Narendra 2153
Bahadir, Melih Yigithan 2673
Bahar, Furkan 1091, 2657
Bahieddine, Samia 1735
Bahjat, Rena 0010
Bai, Ru 2353
Baig, Mlrza faris Ali 2256
Baik, Andrew 0898
Bailey, Marissa 2639
Baionno, Sophia 2605
Baird, Laura 2451
Baisoya, Parul 1503
Bajaj, Puneet 1256, 1257, 1370
Bajo, María Auxiliadora 0346
Bajracharya, Rajan 0591, 0592, 1454, 1458, 2341, 2358, 2365
Baker, Joshua 0022, 0045, 0046
Baker, Joshua 0155
Baker, Joshua 0198, 0221
Baker, Joshua 0222
Baker, Joshua 0328
Baker, Joshua 0359
Baker, Joshua 0370
Baker, Joshua 0446
Baker, Joshua 0462, 0834, 0836, 1125
Baker, Joshua 1238
Baker, Joshua 1266
Baker, Joshua 1308
Baker, Joshua 1314, 1325, 1340, 1399, 1658
Baker, Joshua 1659
Baker, Joshua 1733
Baker, Joshua 1746
Baker, Joshua 1946, **2002**, 2084, 2096
Baker, Joshua 2098
Baker, Joshua 2276, 2567, **2624**
Baker, Joshua 2661
Baker, Joshua 2681, 2683
Baker, Joshua 2703
Baker, Joy 1820, 2242
Baker, Kenneth 1703
Baker, Matthew Charles **1172**, **1173**, **1664**, 1666, 2546
Baker, Nancy 2552
Baker, Peter 0484, 1356
Baker, Thomas 0257
Baker Frost, DeAnna 2495
Baker-James, Karen 0285
Bakewell, Catherine 0330, 1710
Bakewell, Catherine 1959
Bakewell, Catherine 1960, 2177, 2183
Bakhsh, Ahmad 1810, 1822
Bakshi, Nayaab **1395**
Bakshi, Rohit 0184
Bal, Aditi Basu 0590
Balaguer Trull, Isabel 2460
Balaji, Swetha 1795
Balakrishna, Deepika 0558
Balakrishnan, Anu 0130, 2676
Balanescu, Andra 0673, 0702, 1411, 1586
Balar, Ashish 0671, **0672**, 0683, **1559**
Balasubramanian, Suryakumar 2490
Balasubramaniyam, Rakshika 0997
Balay-Dustrude, Erin 0422, 1669, 2125, 2128
Balbach, Meridith 0385
BALBI, GUSTAVO GM 0179
Balbi, Verena 1292, 2535
Balbino, bianca 0907
Balbir- Gurman, Alexandra 0702
Balbir-Gurman, Alexandra 1562
Balboa, Vanesa 0329, 0454
Balderas Miranda, Jennifer Tiaré 0287, **1836**, 1841, 2052, 2053, 2078
Baldini, Chiara 0723, **1380**, **1381**, 1385, 1951
Baldissera, Elena 1618
Baldo, Francesco 0358, 2137, 2138, 2139
Baldus, Carlie 0410
Balevic, Stephen 0404
Balevic, Stephen 2210
Baley, Patricia 2296, 2300
Balistreri, Lisa 1255, 1986
Balkhi, Syed Henah 0316
BALLANDRAUD, Nathalie 1095
Ballina, Mauricio Rosas 0257
Ballok, Alicia 0060
Balmuri, Nayimisha **2188**
Balmuri, Shravya 2392
Balsa, Alejandro 0346
Balsa, Alejandro 0535, 1062
Balsa, Alejandro 2042
Bamagoos, Ahmad 0549
Bamigbola, Ifeoluwa Emmanuel 1571
Ban, SeoYoon 0910
Banaszkiewicz, Katarzyna 1136
Banbury, Brittany 1507
Band, Melissa 1944
Banda, Sri Varsha 1245, 2328, 2329
Bandarupalli, Pranathi 0167, **0733**, 2050, 2056, **2070**, 2370
Bande, Juan Manuel 0432, 2405
Bandu, Anirudh **1673**
Banerjee, Ankona 1621
Banerjee, Shubhasree 2533, 2701
Banerjee, Shubhasree 2703
Banford, kassidy 2386
Bang, Holger 2279
Bang, So-Young 0550, 1432
Banga, rajkaran 1078
Banga, Veerkaran 1078
Bani Hani, Maysoon 0538
Baniandrés Rodríguez, Ofelia 2348
Banik, Pratyusha **0457**
Bankhead, Clare 1909
Banks, Sharon 0500, 2166
Banos, aggelos 1452
Bansal, Bhavik **0146**, 1104
Bansal, Bhavik 2615
Banschbach, Katelyn 0411, 0418, 0419, 1066
Bao, Aaron 2518
Bao, Gaobin 0707

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Bao, Haikun 0247
Bao, Min **0011**, **0012**
Bao, Weibin 0585, 0801, 1175, 1447, 1459, 1462, 1463, 1464
Bao, Yanjie 1003
Baptiste, CHEVET 1095
Baraf, Herbert 1123, **1998**, **1999**, 2588
Baraff, Aaron 0462, 0836, 2237, 2251, 2252
Barahona-correa, julián **1491**
Baraliakos, Xenofon 0152, 0386, 0545, 0567, 0569, 0577, **0591**, **0592**, 1157, 1405, 1406, 1455, 1461, 1465, 1466, 1941, 2271, 2279, **2337**, 2347, 2367
Barasch, Julia **1102**
barastay Alberdi, estibaliz 0485, 2350
Baraut, Julie 1448
Barba, Christophe 0618
Barba, Pere 2458
Barbadillo Mateos, Maria Carmen 1170
Barbarroja, Nuria 0070, 0071, 0072, 0087, 0094, 0100, 0108, 0583, 0901, 1851, 2371, 2599
Barbee, Jeff 1040
Barber, Daniel 0920
Barber, Megan 0120, **1497**, 2387, **2416**
Barbetta, Cristiano 1570
Barbey, Catherine 2409
Barbhaiya, Medha 0365, 0382, 0634, 2575
Barbosa, Vitalina de Souza 1486
Barcat Zarate, Sara Josefina 2106
Barcellos, Lisa 0038, 0637
Barczak, Amy 2577
Bardan Inchaustegui, Ana Cecilia 2058, 2071, 2072
Bardash, Yonatan 1839
BARDET, Claire 0114
Bardi, Mohammad 1938
Bardien, Moegammad 1970
Bardin, Thomas 1135, **1144**
Barefoot, Laurie 0888, 0997
Barelle, Caroline 0996
Bargender, Katrina 2144
Barish, Rachel 1182
Barjaktarovic, Nevena 0383
Barkaway, Anna 1178
Barkay, Hadas 2593, 2594
Barker, Andrea 0222
Barker, Jane 1136
BARLAS, NUR **0267**
Barlas, Sait 0267
Barliakos, Xenofon 0854, 2318
Barlow, Norman 0010
Barlow, Sophie 1453
Barmettler, Sara 0804
Barnado, April 2206, 2380
Barnard, Hayley 2362
Barnas, Jennifer 0772, 0851, 0912, 1240, 1480, 1844, 1846, 2421, 2600
Barnboym, Emma 2301
Barnechea Alvarado, Nicolas **0703**, **2099**
Barnes, Betsy 1814
Barnes, Evan **2509**
Barnes, Jonathan **1313**
Barnes, Rosie **1966**
Barnett, Daniel **2478**
Barnett, Maxim 0254, 0255, 1074, 1075, 1076, 2093
Baron, Fatemah 1930
Baron, Gabriel 1577, 1685, 1765
Baron, Murray 1586
Baron, Murray 2651
Barone, Elisa 0532
Barr, Andrew 2411
Barr, Ann Cameron **2159**
Barra, Lillian 1597, 1607
Barranco, Antonio 0108
Barrera, Jessica 1041
Barrera, María-José 0931
Barreras Cortes, Paula 1378, 1384
Barrera-Vargas, Ana 2321
Barrett, David 0002
Barrett, Leanne 2688
Barrett, Montana 1781, 1792, **1794**
Barrier, Claire 1200
Barrios, Marcelo 0596
Barrios, Orfa 1161
Barros Bertolo, Manoel 1365, 2246
Barros Membrilla, Antonio José 1620
Barroso Garcia, Nuria **0268**
Barry, Mamadou 2577
Barry, Stevie **2683**
Barskiy, sam 1661
Barstad, Bjørn 0420
Bartels, Christie 0024, 0217, **0218**, 0226, 0289, 0670, 1050, 1051, 2455
Barten, Birgit 0152
Barthe, Claire 2115
Bartholmai, Brian 1556
Bartlett, Susan J. 0438, 0441, 0442, 1355, **1648**
Bartoletti, Alice **1614**
Bartoletti, Alice 1627
Barton, Jennifer 0211
Barton, Jennifer **0359**
Barton, Jennifer 1048, 1052, 1256, 1257, **1266**, 1424, 2237
Barton, Victoria 1923
Barturen, Guillermo 0125, 1840, 2648
Barturen, Kristel 1098
Barua, Souptik 1007
Baruah, Nandan 0377
Barzilay, Joshua 0354
Basak, Tina 0348
Baser Taskin, Busra 1823
Bashar, S. Janna 0073
Basiaga, Matthew 1669, 2125
Basibuyuk, Fatma **2673**
Basida, Brinda 0352
Basile, Anna 1863
Basilico, Silvia 2458
Baskurt, Zeynep 1756
Basnayake, BMDB 0595
Bass, Anne R. 1088, 1089, 1102, 1107, 1108, 1351, 1730
Bassara Macedo, Rafael **1180**, 1407, 1408, 2028, 2045, **2326**, 2535
Bassiri, Hamid 0423
Basso, Cristina 1856
Basten, Jale 1934
Bastian, Hans 0754
Basu, Amrita 1668
Basu, kaushik 1588
Basu, Neil **1239**, 1435, 1711
Basu, Samik 1563, 2468, 2669
Basuli, debargha 1907
Batalov, Anastas 1586, 1587
Batalov, Zguro 1587
Batani, Veronica 1856
Batarseh, Issa 2228, 2286
Batchu Prithvi, Ashwini 0397
Batchu Prithvi, Ashwini **2130**
Bates, David 0790
Batheesh, Ameen 1436
Bathon, Joan 1310, 2586, 2607
Bathon, Joan 2644
Batista perdomo, Daniel 1490
Batista-Liz, Joao Carlos **0029**, 1778
Batko, Krzysztof 1883
Batool, Nuzhat **1628**
Batra, Rattandeep 2368
Batsakes, Anna 1487
Batsis, John 2604
Batson, Melissa 1733
Battaglia, Jenna 1814
Battagliotti, Cristina 1287, 1288
Batter, Stephen 0308
Batthish, Michelle 1066
Battistone, Michael 0222
Baudet, Antoine 0891
Baudoin, Paul 2309
Bauer, Claus-Jürgen 0892
Bauer, Nicholas **0514**, **2421**
Bauer Ventura, Iazsmin 2669
Baum, Matthew 0184
Bausá Gimeno, Luis 1490
Bautista Mártir, Yazmina 1412
Bautista molano, Wilson 0177, 0854, **2336**
Bautista Sanchez, Rocio 0198
Bautista-Sanchez, Rocio 2217
Bautista-Vargas, Mario **1721**, 2403
Bawa, Pritish 2148
Bawazir, Yasser 0549
Baweja, Ashish 1364
Bax, Jeroen J. 0696
Baxter, Sarah **0501**
Bayat, Nastaran 0159
Bayat, Sara 2613, 2686
Bayeh, Barbara 1180, 2028, 2045
Bayeh, barbara 2535
Bay-Jensen, Anne-Christine **0307**, **2231**
Bayraktar, Deniz 0177
Bays, Alison 0079, 0186
Beachler, Daniel 0399

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Beal, James 1025
Bearzi, Pietro 0957, 0967, 1867, **2497**
Beasley, Marcus 1014, 1244
Beato, Maria José 1152
beaudeau, lauren 2655
Beaudoin, Lucie 1724
Bečvář, Radim 0884, 2477
Beavers, Daniel 2097
Becerra-Fernández, Elena 0737
Becerril, Alissa 0220
Bechman, Katie 1906
Beck, David 0260, 0777, 1861, 2582, **2663**
Becker, Emily 0115, 0131, 0858
Becker, Mara 0392
Becker, Mike 0957, 1579, 1580, 2472, 2497
Beckman, Robert 0261
Bedell, Lisa 0204
Bedia, Carlos 0621
Bedoya-Loaiza, Juan Esteban 0252
Bedrick, Edward J. 0325, 2085, 2091
Beel, Marci 0044, 1831, 1850
Beenken, Anne Elisabeth 1010
Beer, Jacob 1176
Beghin, Delphine 2457
Begum, Rahima 0157, 0158, 0368, 2006, 2117
Begum, Tasim 2446
Behrendt, Rayk 0892
Behrens, Edward 0423, **0780**, 0923, 1671, 1825, 1847, 2141
Behrens, Frank 0567
Behrens, Frank 0577
Behrens, Frank 1455
Behrens, Frank 1460, 2362
Beilke, Joshua 2277
Beirão, Tiago **0761**
Beiser, Steven **2430**
Bejerano-Herreria, Carmen 0216, 0244, 0454, 1916, 2388
Bekis, Recep 2673
Bektas, Erdem **0778**
Belfeki, Nabil 2699
Belilos, Elise 1628
Belkir, Rakiba 1115
Bell, Elaine **2178**
Bell, Griffith 1336
Bell, Kierstin 0494
Bell, Richard **0058**
Bell, Stacie 0652, 1915
Bellamy, Madison **2186**
Bellando Randone, Silvia 0683, 0879, 1570, 2482
Bellando-Randone, Silvia 0673, 0702, 0880, 1586, 1587
Bello, Federica 2532
Bello, Natalia **0362**, 2355, 2375
Bello, Temitope 1536, 2456
Bellocchi, Chiara 0700, 1840, 2651
Bellomio, Inés Verónica 0621, 0623, 1530, 2405
Bellvís-Bataller, Fuensanta 0538
Belmadani, Abdelhak **1780**
Belmont, H Michael 0120, 0121, 0851, 1468, 1480, 1488, 1918, 1919, 2404, 2421, 2444
Belmont, Michael 0772, 0853, 1240, 1391, 2630
Belmonte, Nathalie 0006
Belot, Alexandre 1300
Belperio, John A. 1872
Beltrán Martin-Lorente, Pablo 2354
Beltran, Emma 0268
Belury, Martha 1307
Belzunegui, Joaquín M 0744
Belzunegui-Otano, Joaquin Maria 2269
Bemis, Elizabeth 1674
Ben, Li-Hong 0934
Ben Gabr, Jihad 0657
Benamar, Mehdi 1696
Benard, Steve 0715
Benítez, María Teresa 0483, 2036
Benavent, Diego 0177, 0180, 0183, 0530, **0535**, **1062**
Benavent Nuñez, Diego 0575
Benavides Villanueva, Fabricio **0150**, **1599**, **1600**, **2059**
Bender, Andrew 2062
Bending, David 0948
benegas, mariana **1422**
Benenato, Kerry 0016
Bengtsson, Anders 0593, 2390
Bengtsson, Caroline 0434
Benhabiles, Ines 1593
Benhamou, Ygal 0891, 1575, 1765, 2489
Benigni, Fabio 0907
Benini, Camilla 2117, 2592
Benito-Melero, rafeal 0744, 0757, 1620, 1773
Benjamin, Emelia J 1229, 1230
Benjamin, Michelle **0263**, 2169
Bennett, Alexandra 0359, 1266
Bennett, Christy 0889, 1695
Bennett, Derek 2561
Bennett, William 0835
Benoit, LE GOFF 0439, 0477, 1095
Benschop, Robert J. 0069
Bense, Alexandre 0688
Benseler, Susanne 0821
Bensley, Karen 2368
Benson, Katherine **2317**
Bentley, Amy 1725
Bento da Silva, Ana **1405**, **1406**, **1941**, 2635
Benveniste, Olivier 0289, 0862
Berbel, Laura 0575
BERBOTTO, GUILLERMO ARIEL 0596, 0623, 1530
Berbotto, Leonel 1486
Bereket, Sofia 1256, 1257
BERENBAUM, Francis 0327, 1095, **1734**, 1735, 2185
Berenpas, Metta 0900, 2027
Beresford, Michael 0389, 1300
Beretta, Gisella Beatrice 0358
Beretta, Lorenzo 0125, **0700**, **1840**
Beretta, Lorenzo 1862
Beretta, Lorenzo **2648**
berezne, Alice 0681, 0688, 1577
Berg, Inger Jorid 0539, 1958, 2319
Berger, Andrea 1081, 2195
Berger, Howard 2627
Bergeron, Ly-Lan 0918
Bergman, Martin 0444
Bergmann, Christina 0026
Bergmann, Christina 0236
Bergmann, Christina 0641
Bergmann, Christina 0673, 0702
Bergmann, Christina 0879, 0956, 1537
Bergmann, Christina 1586
Bergmann, Christina 2695
Bergner, Raoul 1175, 2520
Bergot, Anne-Sophie 0101
Bergot, Emmanuel 1577
Bergstra, Sytske Anne 0176
Bergström, Ulf 1884, 1885
Bergstrom, Lindsey 1669, 2125
Berianu, Florentina 0300, 1255, 1585, 1986, 2018
Berkani, Ouali 1519, 2440
Berklite, Lara 1819
Berlak, Neta 1304
BERLENGIERO, Virginia 1371
Berlian, Arkan 1398
Bermúdez, Alejandra 1096, 1133
Bermas, Bonnie 1370
Bermejo, Pedro Pablo 0483, 2036
Bermudo, Guadalupe 1161, 1162
Bernabeu, Daniel 0535, 1062
Bernabeu Gonzalvez, M.Pilar 1096, 2450
Bernad, Miguel 2106
Bernal-Macías, Santiago 1491
Bernal-Macias, Santiago 1210
Bernard, Stephanie 0854
Bernardez Moreno, Júlia 0642, 1620
Bernatschek, Alexander 0543
Bernatsky, Sasha **0475**, 0606, 0652, 1109, 1475, **1506**, **1507**, 1607, 1722, 2215, 2222, 2416
Bernett, Matthew **0010**
Bernstein, Elana 0843
Bernstein, Elana 0883
Bernstein, Elana 1310, 1555
Bernstein, Elana 1557, 1566, 1582
Bernstein, Elana 1725, 2475
Bernstein, Elana 2654
Berntson, Lillemor 1287, 1288
Berthier, Celine 1741, 1816, 2600
berthier, Sabine 0688
Berthoux, Emilie 0891
Berthoux, Emilie 1185
Berthoux, Emilie 2655
Berti, Alvise 0238
Berto, Stefano 0944

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Bertolaccini, Maria Constanza 0596, 1491
Bertolaccini, Maria Laura 0120, 0121, 0860
Bertrand, Kerri 2220
Bertsias, George 0628, 1526, 1542, 2461, 2467
Bes, Cemal 0025, 0778, 1965
Besse, marie Charlotte 1604
Besse, Marie-Charlotte 1592, 2655
Bessen, Michael 1981
Bessette, Louis 0362, 0438, 0442, 1355, 1648, 1676, **2281**
Besson, Hervé 0591, 0592, 1445
Best, Michelle 0289
Betancourt, Alejandro Alvarez 2490
Betancourt-De la Torre, Miguel 0512, 1389
Betel, Doron 0515
Betensky, Daniel 1011
Bethea, Meaghan 1012
BETHELL, Richard **0929**
Bethencourt, Juan Jose 1282, 1284
Betiu, Mircea 1414
Bettendorf, Brittany 0825
Betteridge, Neil 0488
Bettuzzi, Thomas 2699
Beukelman, Tim 2068
Beutler, Anna 0562
Bevers, Karen 0488
Bewtra, Meenakshi 1434
Beydon, Maxime 1766
Bhadu, Danveer 1197, 2152
Bhagat, Sanket 0016
Bhamidipati, Kartik 0890
Bhandari, Sambhawana **2047**
Bhapkar, Manjushri 0404
Bhat, Smita 0692
Bhatia, Shailender 2237
Bhatt, Birju 0383, 0384
Bhatt, Jheel 0126, **0128**
Bhatt, Nirali 2701
Bhatt, Nisha 0154
Bhatt, Priya **0038**
Bhatt, Varsha 1085
Bhattacharyya, Shamik 0184, 0263, 1378, 1384
Bhattaram, Pallavi 0063
Bhatti, Jaspreet 0598
Bhawan, Jag 0848
Bhide, Sayuli **0462**, 1238
Bhimani, Sameer 0383, 0384
Bhimani, Simran **0383**, **0384**
Bhor, Menaka 1043, 1923
Bhowmick, Niladri 0282, **0298**, 1201
Bhutada, Sumit 1809
Bhuyan, Farzana 0920
Bi, Jiangkun 0905
Bi, Yingtao 0751
Büyesen, Pernille **0420**
Bian, Gang 0001
Bian, Wei **1220**, 2447
Bianchi, Elettra 1738
Bibi, Ayesha 1974
bica, blanca e r 1287, 1288
Bick, Alexander 1504
Bickers, Cara 0663, 2454
Bidasee, Kishore 0065, 1774, 1779
Bidgood, Susanna 0074
Bienvenu, Boris 0891
Bienvenu, Boris 1577
Biering-Sørensen, Tor 1166, 2608
Biesen, Robert 0471, 0780, 1671
Bignon-Favary, clélia 0147
Bigot, William 2168
Bihlet, Asger 2082, 2101
Bijkerk, Roel 1568
Bijsterbosch, Jessica 2309
Biko, David M. 0390
Bilek, Laura 2604
Biljan, Ana 2342, 2362, 2367
Bill, Christy 0210
Billa, Shreya **2660**
Billi, Allison C 0949, **1760**
Bills, Virginia 1057, 1705
Biln, Norma 0531, 2335, 2636
Bing, Nan 1833
Bingham, Catherine 0411, 1066, 1978
Bingham, Clifton 0440, 0441, 0473, 0529, 1028, 1107, 1108, 1225, 1249, 1648, 1730
Binka, Mawuena 1549
Binstadt, Bryce 0993
Bint e Tahir, Rehab 0312
Binvignat, Marie 1657
Birija, Shiva Lauretta 2546
Birinci, Suayip 1008
Birmingham, James 2131
Birnbaum, Chana 1253
Birru Talabi, Mehret 2226
Bisconti, Ilaria 1570
Bise, Christopher 0765
Bishnoi, amita 2180
Bismuth, Mike 0936
Bissell, Lesley-Anne 1677, 2411
Bisson, Leslie 0787
Bissonnette, Robert 0555, 0558
Bissonnette, Robert 1447
Bista, Karuna **0433**
Bista, Karuna 0456
Bistolarides, James **2126**
Biswas, Debosmita 0186
Biswas, Sabyasachi 1784
Biswas, Soma Halder 1588
Bitla, Samhitha 1012
BitMansour, Andrew 0663, 1270
Bitnun, Ari 2136
Bitoun, Samuel **1115**
Bitsikas, Vassilis 2696
Bittar, Mohamad **1424**
Bitton, Ari 0501
Bixio, Riccardo 0275
Bizzarri, Francesco Fulvio **2348**
Bjørkekjær, hilde 0673, 0702
Blázquez Sánchez, Teresa **1404**
Blümel, Benedict 2612
Blüthgen, Christian 0880
Blachley, Taylor 0578
Black, Katharine 0808
Blacketer, Clair 1878, 1899
Blake, Angela 1366
Blake, Michelle 0501, 2277
Blaker, Bryan 0657
Blaker, Lucero 0657
Blanchet, Benoit 1593, 1722
Blanco, Elena 2373
Blanco, francisco J 0329, 0454, 1798
Blanco, Irene 2430
Blanco, Laura 1321, 1413, 2311
Blanco, Luz 0945
Blanco, Ricardo 0029, 0150, 0200, 0216, 0243, 0244, 0250, 0268, 0270, 0271, 0272, 0639, 0736, 0737, 0739, 0740, 0744, 0752, 0757, 0874, 1094, 1547, 1599, 1600, 1612, 1613
Blanco, Ricardo 1778
Blanco, Ricardo 1916, 2016, 2023, 2059, 2209, 2229, 2265, 2388, 2538, 2610
Blanco-Aparicio, Marina 1600
Blanco-Madrigal, Juan María 2229, 2265, 2670
Blandine, MERLE 2621
Blank, Norbert 1875, 1876
Blank, Rebecca 0031, 0463, 0491, 0871, 1329, **1338**, 2643
Blank, Thomas 1206
Blankenship, Derek 2649
Blanks, Starla 0217, 0218
Blanqué, Roland 0653
Blasco, Miquel 0728
Blasi, Marc 2260
Blasingame, Kyla **1983**, **2620**
Blaszczak, Jilie 0825
Blat, Cinthia 2634
Blau, Jessamyn 1155
Blauvelt, Andrew 1437
Blauvelt, Andrew 2374
Blay, Reece 2604
Blazar, Philip 0797
Blazer, Ashira 0047, 1504
Blazos, Chris 1889
Blazquez Cañamero, Mª Angeles 0019, 1397, 1681, 2290
Bleakley, Stephen 0531, 2335, 2636
Bleck, Dennis **0962**
BLEUZEN, AURORE 0706
Blevins, Jason 2385
Bliddal, Henning 0338
Blockmans, Daniel 0776
Bloom, Jessica **2144**
Bloom, Jessica L. 2515
Bloom, Shoshana M.K. 0888, 0997
Bluestone, Jeffrey 0501, 2277
Blumberg, Gregg 2196
Boadi, Taussia 1057
Bobak, Angela **2195**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Boc, Alexandra Georgiana 0337, 1914
Bochicchio, Cristina 1212, 2656
Bodelón de Frutos, Alejandra 0821
Bodkhe, Rahul 2643
Bodkin, Mark 0289
Bodnárová, Marika **1962**
Bodoki, Levente 0680
Boehnert, Volker 0016
Boers, Maarten 0338
Boers, Romina 0794
Boesen, mikael **1963**
Boffa, Jean-Jacques 0618
Bogdan, Batko **1883**
Bogdanos, Dimitrios 1219
Bogdanos, Dimitrios 2280
Bogle, Rachael 0127, 0811, 0851, 0949, 0985, 1682, 1846, 1852, 2451, 2498
Bohnsack, John 0392, 0401
Bohorquez, Cristina 1322, 1397, 2422
Bohrer, Andrea 0920
Boidot, Romain 1150
Boin, Francesco 0881, 0976, 1725
Boire, Gilles 0438, 0442, 0475, 1126, 1648
Boissard, Frederic 0665
Boix- Martí, Natalia 0019, 2290, 2291
Boix-Amoros, Alba 0031
Boki, Kyriaki 2232
Bolón-Canedo, Verónica 0901
Boland, Anne 0103
Bolden, Caleb 1751, 2235
Bolden, Nicholas 0712
Bolek, Ertugrul Cağrı 1618
Bolen, Joe 0941
Boleto, Gonçalo 0702
Boll, Sidsel 2082
Bolla, Eleana 0133
Bollo de Miguel, Elena 0882
Bologna, Zuzana 2063
Bolster, Marcy 0344, 0440, 1225, 1751, 2177, 2235, 2550, 2551
Bolton, Amy 2144
Bombardier, Claire 2266, 2642
Bombardieri, michele 0034, 1685, 2178
Bombelka, Iwona 2081, 2101
Bonakdar, Ali 1536, 2456
Bonakdarpour, Borna 2430
Bonal, Claire 1189, 2296, 2300, 2665
Bonalumi, Angela 2116
Bonaso, Federica 0992, **2528**, **2529**, **2530**
Bond, Milena **0754**, 1626
Bondage, Babita 0554
Bondensgaard, Ken 0732
Bonelli, Michael 0807
Bonenfant, Debora 0009
Bonfa, Eloisa 0206, 0619, 0623, 1192, 1491, 1530, 1715, 2292, 2527, 2573, 2653, 2682
Bonfiglioli, Karina 2246
Bonfiglioli, Karina 2682
Bongenaar, Margot 0978
Bongiovanni, Antonino 1858
Bonilla, Gema 0019, 0180, 1152, 1869, 2016, 2030, 2290, 2422
Bonnaillie, Pierre 2631
Bonnotte, Bernard 0756, 0891, 1150, 1575, 2489
Bonny, Marie-Alix 0591, 0592
Bonomi, Francesco **1570**, **2482**
Bonomo, Samuel 0326
Booker, James 0413
Boone, Bettina 1508
Boonen, Annelies 1324, 1341, 1342, 2331, 2333, 2334
Boonyawairote, Rabhas 1187
Booth, James 2006
Booth, Ronald A. 0294, 2069
Bootsma, Hendrika 0034, 0694, 1685
Borah, Minasri 0987
Borba, Eduardo 0596, 0619, 0621, 0623, 1486, 1491, 1530, 1715, **2527**, 2653
Borbet, Timothy 0909
Borchsenius, Julie **1166**
BORDALLO, BRUNO 0179
Bordes, Ceclie 1873
Bordet, Alice 1150
Bordignon Draibe, Juliana 0900
Boreland, Shereen 1589
Borges, Bruno 2292
Borges, Bruno S 1192
Borghi, Maria O 0125
Borie, Dominic 0471, 2425
Borisova, Anastasia 1323
Borja, Tatiana 1814
Borrás, Fernando 1996
Borrás Blasco, Joaquín 2038
Borras, Leonardo 0015
BORREL-PAÑOS, HELENA 0180
Borshchivska, Maryna **0035**
Bory, Olivier 0735
Bos, Reinhard 2309
Boscardin, John 1704
Bosch, Philipp 0754
Boselli, Giuliano 0269, 1171, 2023, 2059
Bosello, Silvia Laura 1567, 2482
Bosk, Abigail 0920
Bost, Chloé 1200
Bosteels, Victor 0907
Bot, Adrian I 1003
Boteanu, Alina-Lucica 0269, 1171, **1282**, 1284
Botello Corzo, Diana 1490
Botero Pinzon, Maria 1708
Botson, John **1923**
Botson, John 1994
Bottini, Nunzio 0067, 0081, 0085, 0881, 0976, 2258
Boucau, Julie 2577
Boucaud, Anaelle 2532
Bouchalova, Katerina 2128
Bouchard-Marmen, Maude 0516
Boucly, Athénaïs 1185
Boudal, Ayah 0549
Boulard, Louise 1290
Boulos, Pauline 2281
Boumpas, Dimitrios 0628, 2232, 2461
Bounas, Andreas 1462, 1463, 1464
Bourdin, Arnaud 1608, 1769
Bourdin, Venceslas 2168
Bourgeois, Camille **0214**, **0215**, 2249
Bourgeois, Florence 1357
Bournazeau, Jean Alain 0162
Bournazos, Ilias 1452
Bourne, Chuck 0482
Bourredjem, Abderrahmane 0891
Bourre-Tessier, Josiane 1109
Bousson, Valérie 1135
Bouvard, Béatrice 2115
Bouziani, Eleni 0712
Bouzid, Ouafia 0488
Bove, Allyn **0765**
Bowdish, Dawn 1793
Bowen, Edward 0694
Bowes, Mckenna 1823
Bowling, C. Barrett 1639, 1640, 1641
Bowman, Raeann **2190**
Bowman, Savannah **1429**
Bowman, Simon 1685
Bowness, Paul 0104, 2583
Box, Jane 1675, 2278
Boyadzhieva, Zhivana 0342, 0343, 1010, 2109, 2110, 2595
Boyd, Robert 0996
Boyden, Steven 1725
Boyer, Olivier 0862
Boyle, David 0069, 0097
Boyle, David 0889, 1695
Boyle, David 2576
Boyle, Karen 2451
Bozec, Aline 0236
Bozec, Aline 0641, 2442, 2695
Bozkurt, Selen 1086
Braña, Ignacio 0019, 0271, 2016, 2290
Braña Abascal, Ignacio 0270
Braña Abascal, Ignacio 2209
Braaten, Tawnie 1107, 1108, 1730
Bracaglia, Claudia 0358, 2137, 2138, 2139
Bracamontes, Katherine **0451**
Braccia, Domenick 1563
Bracken, Sonali **0274**, 1563, 1566, 2654
Brader, James 0474
Bradfield, Hannah 0421
Bradshaw, Liz 2233
Brady, Teresa 1636
brahim, ikram 2241
Brahmachari, Ballari **2082**
Braithwaite, Kiery 2154
Brakora, Katherine 2173
Bramantyo, Bernadus 1398
Bramham, Kate 1906
Brance, Lorena 2336
Branch, Ware 0120, 0121, 0855, 0860, 2629

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Brandão de Resende Guimarães, Maria Fernanda 1365, 2246
Brandon, Jutras 1789
Brandon, Timothy 0390, 0412, 1815, 2156, 2677, 2680
Brandt, Cynthia 2114
Brandt, Justin 1391, 2630
Brandt-Juergens, Jan 1462, 1463, 1464
Brandy, Anahy Maria 0250, 1282, 1284, 2450
Braner, Axel 1908
Branford, susan 0091
Branquet, Martine 2115
Branson, Helen 2127
Brantsæter, Anne Lise 2679
Braun, Jürgen 1157, 1405, 1406, 1941
Braun Moscovici, Yolanda 1586, 2651
Braverman, Genna 0827, **2031**
Bravo, Beatriz 1282, 1284
Bravo, Maxim 1657
Brayman, Timothy 1784
Breban, Maxime 0103, 0104, 1438
Breed, Elise 0231
Breen-Lyles, Margaret 1558, 1855
Breillat, Paul 1768, **2582**, 2584
Breitkopf, Susanne 0913, 0930
Bremer, Dr. Carmen **2271**
Bremer, Juliane 1206
Brenchley, Jason 0920
Brennan, Isabelle 0815
Brennan, Kiera 1944
Brennan, Mike 0034
Brennan, Nuala 0567, 0573, 1455, 2357
Brenner, Michael 0797
Brenner, Michael 0798, 1846, 2233, 2600
Brescia, Annemarie 1013
Bretón, José **1489**
Brett, Alan 2086
Breuil, Veronique 0148
Brewington, John 2242
Bridges, John 1276, 1277, 2132, **2181**
Bridges, S. Louis 1725
Brien, Madison 1753
Brilland, Benoit 0968
Brink, Annie 0814
Brink, Mikael 1749
Briones, Melissa 2163
Briot, Karine 2115
Brisou, damien 1873
Brito, Karina 0182
Brito, Tysciana 1407
Brittain, Alison 0193
Brizio, Marianela **0968**
Brock, guy 0374
Brock, James 1239
Broder, Anna 2381
Broderick, James 0908
Brodie, William D 0093, 0972
Broens, Bo **0690**, **1560**, **1860**
Brogan, Paul 0780, 1671
Brogan, Paul 2137, 2138, 2139
Brook, Jenny 0451
Brookhouser, Nicholas 0663, 2454
Brooks, Rebecca **1932**
Brooks, Stephen 2580
Brophy, Mary 1125, 2001, 2585
Brouillette, Matthew 1444
Brousse, Romain 0618
Brown, Adam 0713, **2524**
Brown, Andrew 0104
Brown, E. Sherwood 1378, 1384
Brown, Garrett 2133
Brown, James 0474
Brown, Mackenzie 0317
Brown, Matthew 0103
Brown, Matthew A. 1410, 2352
Brown, Sarah 1909
Brownbill, Paul 2631
Browning, Jeffrey 0848
Browning, John 0875
Brubeck, Hannah **0446**, 0462, 0836, 1238, 2084, 2096, 2098, 2624
Bruce, Ellen 0245
Bruce, Ian 0245, 1545, 1552
Bruce, Ian 1722, 2387, 2416
Bruch, Peter-Martin 0678, 0809
Bruckner, Shane 0651, 0999, 2386
Brueton, Valerie 1136
Brugger, Wolfram 2458
Brun, Johan 0034
Brunborg, Cathrine 0510
Bruneval, Patrick 2584
Bruni, Cosimo 0510
Bruni, Cosimo **0673**, **0880**, 0957, **1562**
Bruni, Cosimo 1579, 1580, 1856
Bruni, Cosimo 2472, 2482, 2497
Bruni, Cosimo 2651
Brunn, Anna 0026
Brunner, Emily 2150
Brunner, Hermine 0302, 0389, 0392, 0401, **0405**, 0406, 0414, 0418, 0419, 1530, 1706, 1744, 2124, 2301, 2462, 2675
Brunner, Jürgen 1287, 1288
Bruno, Simone 1381
Brunori, Michele 2339
Bruurmijn, Tirza 0431
Bryant, Carrie 1810, 1822
Bu, Kevin **0031**, 1338
Bu, Xianwei 1676
Buadee, Settawut **1118**
Bubb, Michael R. 1963
Bubová, Kristýna 0543
Bubová, Kristýna 1962
Bucci, Laura 0236, 0641, 1537, **1697**, 2442, 2695
BUCH, MAYA 0190, 0692, 1077, 1678
Buchanan, Paula 2193
Buchfuhrer, Julia **2003**
Buchner, Anton 2593, 2594
Buckley, Christopher 0798, 1678
Buckley, Lisa **0229**
Buckley, Sarah A. 0260, 0777, 2663
Buckner, Jane 0914
Bucur, Philip 0234
Bucur, Philip 0253
Buczak, Katarzyna 0919
Budde, Emily 0352
Budoff, Matthew 1330, 1331, 1950, 1955
Buechler, Connor **0285**, **0286**
Buecklein, Veit 2476
Buehring, Bjoern 0678
Buehring, Bjoern 1198
Buffet, David 0903
Bugallo Blanco, Eva 0006
Bugbee, William 1805
Bugnard, Francoise 0715
Buhler, katherine 2419
Bui, John **2277**
Buie, Joy 0218, 0381, 1270
Buitrago-Mogollon, Talia 1976
Bujanda Fernández De pierola, Luis 0021
Bujor, Andreea 0848
Bujor, Andreea 1868
Bukhanova, Daria 0403, 0476, 0779
Bukhari, marwan 0340, 0345, 0347, 1313, 2118
Bukhari, Nidaa 1470
Bulat, Buğu 2043, 2349
Bulbol, Guilherme 1407, 1408, 2326
Bulgart, Hannah 0999
Bulgart, Hannah 2386
Bullinger, Lars 0471
Bumbulis, Laura 2690
Bumol, Thomas 0889
Bundy, Christine 1261
Bundy, Kathleen 0207
Bunyard, Peter 0991
Burbano, Catalina 0888, 0997
Burbelo, Peter 1811
Burge, Russel 0362
Burger, Stefanie 2209
Burgess, Alaina 0981
BURGOS-VARGAS, RUBEN 0389, 0854
Burillo, Elena 0780, 1671
Burja, Blaz **0689**
Burlingame, Caroline 2146
Burmester, Gerd 0470, 0488, 1348, **1353**, 2279
Burnham, Jon 0411, 1066, 2141
Burnham, Jon 2146
Burnham, Jon 2468
Burns, Andrew 2651
Burns, Christopher 2581
Burns, Jeremy 0016
Buroh, Sabine 1908
Burri, Dominik 0919
Burroughs, Cristina 0725, 2144
Burshell, Dana 0363, 1487, 2379
Burt, Kevin **1736**
Busch, Martin 2520
Buschiazzo, Emilio 1422
Bushmakin, Andrew G. 2337
Busquets Pérez, Noemí 0379, 0380

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Busse, Antonia 0471
Butbul Aviel, Yonatan **1280**
Butbul Aviel, Yonatan 1305
Butendieck, Ronald 0300
Butler, Breanna 0924
Butler, Gary 1817
Butler, Nellie **1298**
BUTTGEREIT, FRANK 0338, 0342, 0343, **0895**, 1010, 1626, 2109, 2110, **2273**, 2595
Butzeck, Barbara 1136
Buyon, Jill 0626
Buyon, Jill 0772
Buyon, Jill 0840
Buyon, Jill 0851
Buyon, Jill 0853, 1223
Buyon, Jill 1240
Buyon, Jill 1391, 1480, 1488, 1505, 1722
Buyon, Jill 1844
Buyon, Jill 1846, 1918, 1919, 2233, 2404, 2421, 2444, 2600, 2630, 2645, 2649
Buzkova, Petra 0354
Byers, Derek E. 2047
Bykerk, Vivian 0438, 0441, 0442
Bykerk, Vivian 1249
Bykerk, Vivian 1355, 1648
Bykova, Katrina 0010
Bylinska, Aleksandra 0774, 1831
Bynum, Julie 1921
Byram, Kevin 0717, **0777**, 0828
Byron, Margie 1674, 2451
Byskov, Kristina 0929

C

C Jury, Elizabeth 0820, 1672, 1817, 1851
C Unnikrishnan, Dileep 1147
C. Berthier, Celine 0822
Cáliz-Cáliz, Rafael 0019, 2290
Cámara, Carmen 1322
Cánepa, Analía 1491
Cécile-Audrey, Durel 2115
Cañete, Juan 0019, 0021, 0454, 1411, 1757, 1943, 2279, 2290
Caño, Rocío 1096
Caño, Rocío 1133
Caño, Rocío 2422
Cabaleiro Raña, Noelia 0270
Cabaleiro Raña, Noelia 0271
Caballero, Diane 1676
Cabello, Norioscar 0669
Cabezas, Jorge 0657
Cabezas Lefler, José Ángel 1548
CABEZAS LUCENA, ALBA MARIA 0087
Cabezon, Jorge 2373
Cabova, Andrea 2128
Cabral, David 0361, 2126
Cabrera, Kimberly **1689**
Cabrera, Natalia 1288
Cacciapaglia, Fabio 2482, 2656
CACOUB, Patrice 0123
cadar, marius 0702
Cadart, Laurine 0566
Cadena, Andres 0199, 2576
Caeiro, María 0639
Cafone, Joseph 0558, 0875
Cagan, Andrew 2569
Cai, Alexander **0955**, 0971, 0972, 2478
Cai, Benjamin **0101**
Cai, Menghua 0861
Cai, Tianrun 1357, 2569
Cai, Tianxi 1357
Cai, Tianxi 2276
Cai, Yuli 2451
Cañas, Carlos Alberto 0596, 0621, 0623, 1486, 1491, 1530
Cajamarca-Baron, Jairo **0252**, **2034**
Cajas Santana, Luis Javier **0621**
Calabrese, Cassandra 0713, 1107, 1108, 1730
Calabrese, Leonard 0371, 0895, 2524, 2546
Calabuig, Irene 1096
Calamia, Valentina 0329
Calamia, Valentina 1798
Calandriello, Lucio 1567
Calderón, Jorge Cieza 1491
Calderon Martinez, Ernesto 0683
Calders, Patrick 2692
Caldropoli, Julia 2414
Caldwell, Tomika 1232
Calixto, Omar-Javier **0545**
Callahan, Leigh 2097
Calleja, sara 1773
Calleja Antolín, Sara 0882
Callejas, Jose Luis 0029, 0739, 1862
Calo, Alessandro 0002
Calomarde-Gómez, Cristina 0117, 0530, 0758, 2029
Calomarde-Gomez, Cristina **1263**
Calvache, Priscilla 1689, 2429
Calvo, Armando 0596, 0623, 1491, 1530
Calvo, Inmaculada 1284
Calvo, Jaime 0269
calvo, Jaime 0642
Calvo, Jaime 1171, 1878, 1899, 1904, 2422, 2670
Calvo, Jerusalén 0070, 0071, 0094, 0100, 0108, 0496, 0583, 0795, 0901, 1446, 2268, 2371
Calvo Alén, Jaime 0021
Calvo Cebrian, Camino 0807
Calvo Gutierrez, Jerusalen 0072, 0087
Calvo Penades, inmaculada 0237, 1282
Calvo-Aranda, Enrique 0180
Calvo-Río, Vanesa 0150, 0268, **0639**, **1547**, **1548**, 1599
Calvo-Zorrilla, Itziar 0744
Calzada, Joan 1282, 1284
Calzascia, Thomas 2696
Camacho, Marisol 1282, 1284
Camacho, oscar 1382
Camacho, Oscar 2373
Camacho-Pérez, Johan 2052
Cambon, Adeline 1735
Cameli, Paolo 0238
Camellino, Dario 1626
Camire, Ryan 0913, **0930**
Cammarata, Michael 2518
Cammarata-Mouchtouris, Alexandre 1087
Cammarata-Mouchtouris, Alexandre 1262
Campagna, Jason 1767, 2033
Campagne, Julien 1339
Campagne, Julien 1765
Campagne, Julien 2532
Campagne, Julien 2699
Campbell, Carmen 1050, 1052
Campbell, Emily 0349
Campbell, Gemme 2150
Campbell, Kim 2297
Campbell, Phillip 0093
Campbell, Phillip L 2494
Campbell, Sachalee **0818**
Campbell, Veronica **0913**, 0930
Campbell, Zachary 1682
Campitiello, Rosanna 0676
Campitiello, Rosanna 0705, 0963
Campitiello, Rosanna 1097
Campitiello, Rosanna 2179, **2501**
Campochiaro, Corrado 1618, **2477**, 2482
Campos, Jose 1170
CAMPOS, LEONARDO R 0179
Campos, Lucia Maria **1292**, **1293**, **2535**
Campos, Salvador 0931
Campos Fernández, Cristina 0538
Campos Fernández, Cristina 2406, 2407
Campos Fernández, Cristina 2460
Campos-Fabre, Claudia **1152**
Campos-Martin, Daniel **2269**
Camus, Stéphane 2582
Canchi, Balakrishnan 2338
Cancio Fanlo, Jorge Jesus 2107, 2108
candal, Halil ibrahim 1246
candia, Dora 2336
Cangelosi, Davide 0177
Canissario, Ryan 0234, 0253
Canna, Scott 0920, 1651, 1820, 2124, 2137, 2138, 2139, 2141
Cannella, Amy 2177
Cannon, Grant 0022, 0045, 0155, 0198, **0221**, 0222, 0462, 0834, 0836, 1238, 1308, 1314, 1325, 1658, 1659, 1746, 1946, 1981, 2276, 2567, 2661, 2681, 2683
Cannon, Laura 2462
CANO, LAURA 1269
Cano, Tabata 2674
Canori, Alexandra 1236
Cantarini, Luca 0275, 1616, 2075
Cantatore, Francesco Paolo 0702
Cantero-Castro, Andrea 0767
Canton, Courtney 1915, 2561
Cantor, Adam 0031, 1338
cantu, valeria 2058, 2071, 2072

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cantu-Zapata, Irma 0512, 1389
Cao, JIngyi 1846
Cao, Lei 0082
Cao, Lizhi 0908
Cao, Lulu 1514
Cao, Xin-Xin 1174
Cao, Ye 0881
Cao, Zhen 0323, 2562
Cao, Zichun 2271
capelusnik, Dafne 0588, 2307, 2331, 2332, 2333, 2334, 2372
Capilla, Ana 1282, 1284
Caplan, Liron 0221
Caplan, Liron 0222
Caplan, Liron 0854, 1417, 2312
Caplan, Liron 2330
Caporali, Roberto 0488, 1212, 1863, 2482, 2656
Cappa, Oisin 0029
Cappelleri, Joseph C. 2337
Cappelli, Laura 1088, 1089, **1107**, **1108**, 1117, 1730
Caproni, Marzia 2699
Caracciolo, José 2405
Caracciolo, José Angel 0432
Carandang, Kristine 0463, 2555
Caratto, Elisa 2501
Carbone, Francesco 0796, 1724
Carbone, Laura 0352, 0354, 2685
Carbonell-Abella, Cristina 1018
Cardenas, Carlos 2566
Cardenas-de la Garza, Jesus Alberto 0248, 0458, 0614, 0767, 1427, 1483, 1528, 1687, 2058, 2071, 2072, 2171, 2325, 2549, 2557, 2606
Carey, Drew 1378, 1384
Carey, Ethan 1990
Cargill, Michael 1153
Caricchio, Roberto 0652, 1915, **2425**
Carillo, Carmen Tormo 0163
Carine, SAILLOT 1095
Carkin, Julie 1112
Carlson, Alyssa 1708
Carlson, Jason **2275**
Carlson, Kylie 0753
Carlton, Anne **0020**, 2217
Carlucci, Palma 0238
Carlucci, Philip 0626, **0853**, **1240**, 1265, 1391, 1942, 2421, 2630
Carmagnat, Maryvonnick 1185
Carmi, Amit 1304
Carmona, Elio **0025**, 1871
carmona, eva 1156, 1388
Carmona, Loreto 2185
Carmona-Rivera, Carmelo 0945, 1624, 1843, 2580
Carnago, Lisa 1160
Carneiro, Jamile 1407, 1408, 2326
Carns, Mary 0846, 1227, 1362, 2430
Carol, Hallie **2141**
Caro-Martínez, elena 1133
Caronni, Monica 0700
Carpenter, Alexander 1209
Carpenter, Katherine 0373
Carpio Tumba, Manuel **0720**, **1072**, 1084, **2037**, 2666
Carralero Somoza, Daniela 0319
Carranza, Fabian 0507, 2674
Carrasco-Cubero, Carmen 1548, 2016, 2229
Carrascosa, Jose M. 0021
Carreira, Patricia E. 0684, 0702, 2477, 2651
Carrel, Laura 1523
Carrión-Barberà, Irene **0747**, **1602**, **2450**, 2485
Carrier, Nathalie 0475, 1126
Carriere, Catherine 0494
Carrillo, María Paula 0252
Carrillo-Vázquez, Daniel Alberto **0287**
Carrino, John 0635, 0854, 1963
Carrion, Irene 0269, 1171
Carrizo Abarza, Virginia **0552**, 0565
Carrizo Abarza, Virginia 0629
Carrizo Abarza, Virginia 1415, 1416
Carrizo Abarza, Virginia 1425, 1426
Carrizo Abarza, Virginia **1550**
Carrizo Abarza, Virginia 2691
Carroll, Chris 0913, 0930
Carroll, Graeme 1136
Carroll, Ian 1987
Carroll, Kaitlin **0947**, 0953
Carroll, Robert 0401
Carron, Philippe 0568, 1959, 2692
Carruthers, Mollie 0239, 1666
Carson, Nina **0768**
Carsons, Steven 1378, 1384, 1628, 2196
Carstens, Per-Ole 1205
Carter, Caitlyn 1784
Carter, Erin 0772, 1240, 2404, 2421, 2444
Carter, Grace 2320
Carter, Lucy 0645, 1542
Carter, Roderick 1782
Carteron, Nancy 1378, 1384
Carthen, Fredonna 1262
Cartwright, Adam 0009
Caruana, Rich 0785, 0786, 2629
Caruso, Sofia 0898
Carvajal, Lorena 0931
Carvajal, Patricia 0931
Carvalho, Caio 2527
Carves, Sandrine 0489, 1333
Carvidi, Alexander 0501
Casabella, Andrea 1097, 2501
Casadepax-Soulet, Charlotte 2115
Casadevall, Marion 1593
CASADO, MARIA ISABEL 1269
CASADO POVEDA, DESAMPARADOS 2354
Casafont Solé, Ivette 0270
Casafont-Solé, Ivette 0117, 0271, **0659**, 0758, 1548, 2029, 2265
Casal-Dominguez, maria **0296**
Casal-Dominguez, Maria 0863
Casal-Dominguez, maria 0866
Casalla, Luciana 1422
Casals Urquiza, Albert 1620
Casares Marfil, Desire **1698**, **1818**, 1823
Casasola Vargas, Julio Cesar 2336
Casciaro, Ernesto 1352, 2479
Casciaro, Sergio 0246, 1352, 2479
Casciola-Rosen, Livia 1559, 1591, 2652
Case, Junning 1696
Case, Siobhan 1810, 1822
Caselli, Gianfranco 1737
Cases Susarte, Irene 1412
Casey, Alicia 1822
Casey, Olivia 0164
Cashman, Kevin 1696
Caspersen, Ida Henriette 0427, 2679
Cassedy, Amy 0394
Cassedy, Amy 0418
Cassedy, Amy 0419
Cassiano-Quezada, Fabiola 1836
Castañeda, elisabeth 0271, 0351
Castañeda, Santos 0021, 0029, 0200, 0269, 0271, **0518**, 0736, 0737, 0739, 0740, 0744, 0752, 0757, 1171, 1548, 1612, 2016, 2122, 2229, 2265, 2484, 2491, 2610, 2699
Castañeda Sainz, Santos 0270
Castagna, Francesca Maria Ester 0591, 0592
Castañeda Estévez, Elisabet 0201, 1961
Castaneda, Elisabet 0270
Casteleyn, Vincent 0471
Castelino, Flavia 0883, 0992, 1555, 1566, 1582, 2475, 2654
Castellví, Ivan 0702, 1161, 1773
Castellvi, Ivan 1586, 1620, 2474
Castelo-Soccio, Leslie 0118
Castillo, Angel 2336
CASTILLO, GABRIELA 1269
Castillo, Rochelle 0283, 2320
Castillo Dayer, Paloma Valentina 2112, 2113
Castillo-Castellon, Francisco 1947
Castle, John 0009
Castrejón Fernández, Isabel **0153**
Castrejón Fernández, Isabel 1446
Castrejón Fernández, Isabel 2121
Castrejón Fernández, Isabel 2249
Castro, Cecilia 1422, 2405
Castro, Glaucio 1407, 1408, 2326
Castro, Isabel 0931
Castro, Sonia 2373
Castro Perez, Patricia 0351
Castro-Corredor, David 2016
Castro-Cruz, Gabriel P. 0366
Cathébras, Pascal 1592
Catros, Florian 2532
Cattermole, Elizabeth 0397
Caudron, Charlotte 0756
Cauley, Jane 0354
Cauli, Alberto 0702, 0854

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Cauvet, Anne 0053, 1334, 1724
Cavagna, Lorenzo 2065
Cavalcanti, Nara 1407, 1408, 2326
Cavalli, Silvia 1212, 2656
Cavazzana, Ilaria 0238
Cavazzana, Ilaria 0251, 1212
Cavett, Joshua 0509, 2432
Cavill, Charlotte 2335, 2636
Cavin, Tyler 0187
Cazac, Victor **0551**, 1414
cazalets, claire 2655
Cebrian, Laura 1548, 1869, 2030
Cecchi, Irene 0139
Cecci, Melanie 0903
Cejas, Paloma 1696
Celia, Alessandra Ida 0840
Celik, Aykut Ferhat 0241
Centala, Sneha 1508
Cepas, Francisco Jose 0496, 2268
Cerasuolo, Damiano 0355
Cerasuolo, Pier Giacomo 1567
Cerda Acevedo, Sebastián Andrés 1195
Cerdà, Dacia 1382
Cerdó, Tomás 0070, 0071, 0072, 0087, 0094, 0795, **1851**, 2599
Cervantes, Briana 1967
Cervantes, Evelin 1548, 2373
Cervantes, Rosa Elena 0507
Cervantes Ramírez, Elena 2674
Cervantes-Diaz, Rodrigo 1696
Cervera, Ricard 0120, 0121, 0860, 2648
Cesta, Angela 2266, 2642
Cetin Gedik, Kader **1823**, 2141, 2666
Cha, Hoon-Suk 0170, 0548, 0571, 1893
Cha, Seunghee 0509
Chaalal, Samira 1448
Chaballa, Mark 0168, 1747
Chacón, Carolina Cristina 1321, 1413, 2311
CHACON, KARLA **1390**
Chadwick, Andrea 1237
Chaer, Fernanda 1715
Chagalakondu, guru Vijay **1485**, **2313**
Chahin, Nizar 2669
Chai, Yi Wen 0027, 1797
Chaichian, Yashaar 1086, 2201
Chaigne, Benjamin 0681, **0688**, 1575, 1577, 2489
Chaigne, Benjamin 2655
Chaisrimaneepan, Nattanicha 1134, 1137, 1187
Chaisrimaneepan, Nattanicha **1319**
Chaisrimaneepan, Nattanicha 2255, **2420**
Chakhabi, Blal 0646
Chakraborthy, Shudipan 2070
Chakraborty, Disha 1120
Chakravarty, Eliza 1831, 2649
Chakravarty, Soumya 0563, 0564, 1165, 1376, 1377, 2368, 2369
Chalberg, Thomas 0310
Challa, Madhuri 0291
Challener, Gregory **0344**
Challener, Gregory 0501
Challener, Gregory **0813**, 1099, **1100**
Challener, Gregory 1101, 1104
Challener, Gregory 1130
Challener, Gregory 1990
Chamberlain, Alanna 1030
chamberlain, Chris 0832
Chambers, Christina 2220, 2221
Chambers, Shae 0278, 1474, **2428**
Chambre, Laura 1327
Chamorro De Vega, Esther 2249, 2348
Chamoto, Kenji 1772
Chan, Catherine 2697
Chan, Chiu Wai Shirley 0595, 0839, 1202
Chan, Daphne 0523, 0563, 0564, 1176
Chan, Dennis Tin Ho 1202
Chan, Ivan 0014
Chan, Jonathan 0854
Chan, Madelynn 0595
Chan, Mercedes 0361
Chan, Nicholas 1301
Chan, Samuel 1938
Chan, Tak Mao Daniel 2697
Chan, Tien-Ming **1033**
Chandler, Mia 1810, 1822
Chandra, Tanya 0282, 0303, 1201
Chandra Rao Yalagala, Poorna 1140
Chandran, Shelly 1552
Chandran, Vinod 0042
Chandran, Vinod 0522, 0552, 0565
Chandran, Vinod **0590**, 0873
Chandran, Vinod 1415, 1416, 1425, 1426, 1714, 2690, 2691
Chandran nair, sukesh 0140
Chandrasekar, Saranya 0057
Chandrasekhara Pillai, Anjana **2055**
Chandrasena, Sapuni 0374
Chandross, Karen 1306
Chang, Aileen 0199, 2576
Chang, Angela **1193**, 1199
Chang, Chung-Chou 2002
Chang, David 1563
Chang, David 2468
Chang, David 2669
Chang, Elizabeth 2330
Chang, Fei 1517
Chang, Huan 1511
Chang, Joyce 1059
Chang, Joyce 1668
Chang, Joyce 1810, 1822
Chang, Joyce 2151
Chang, Joyce 2410
Chang, Ko-Yun 1091, 2657
Chang, Lillian **2150**
Chang, Margaret 0392, 0406, 0407, 0414, 0988, 0995, 1004, 1005, 1696, 1810, 1822
Chang, Peter 1184
Chang, Rowland 1249, 2455, 2603
Chang, Sung Hae 0168, **1343**, 1747
Chang, Ting-Wei 0299, 1106, 1217
Chang, Xin 0994
Chang, Yen-An **1433**
Chang, Yu 1091, 2657
Chang Stauffer, Sophia **1511**
Chao, Ariel 2453
Chao, Chen **1479**, **1974**
Chao, Wen-Cheng 2658
Chao Moreira, Marta 1322
Chapal, Marion 0618
Chaperon, Frédérique 2696
Charbonneau, Mark 0060
Charitidis, Konstantinos 0125
Charles, Julia F. 1142
Charles-Schoeman, Christina 0425, 1213, 1214, **1770**, 2227, 2681
Charlton, Rachel 2487
Charmsaz, Sara 2277
Charuvanij, Sirirat 1118
Chassagnon, Guillaume 0681
Chatelus, Emmanuel 0516, 0673, 0688, 1578, 2115, 2655
Chatham, Walter Winn 0039, 1837
Chatterjee, Godhuli 1306
Chatterjee, Rudrarpan **0631**, 2676
Chatterjee, Shraddha 1401
Chatterjee, Soumya 0695
Chatterjee, Tulika 2065
Chattopadhyay, Shrikanta 0888, 0997
Chatzis, Loukas 0516
Chaudhari, Siddharth 0576, 1963
Chaudhary, Ashraf 2068
Chaudhary, Asma 1859
Chaudhary, Haseeb 0724
Chaudhary, Pratibha 0513
Chaudhary, Shivang **2193**
Chaudhuri, Dipabali 0337, 1914
Chaudhuri, Dipankar 0010
Chauffe, Ann 0247, 0274
Chauffe, Ann 1924
Chauveau, Dominique 2510
Chauvin, Nancy A. 0390, 2677
Chavez, Angela 0501
Chavez, Vianey 0885, 1758
Chavez de Paz Solis, Daniela **2270**
Chawla, Rohan 2152
Cheema, Asma 0364
Cheema, Ayesha 1795
Cheema, Hashem **0345**
Cheema, Sana 1055
Chehab, Gamal 0166
Chehab, Gamal 1198
Chehab, Gamal 2612
Chelf, Cynthia 1034
Chen, Antonia 0787
Chen, Bingliang 0906
Chen, Bingrui 0683, 1591
chen, bo 2061
Chen, Chuan 0018, 1006
Chen, Dapeng 0913, 0930
Chen, Davina 1479

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Chen, Der-Yuan 2469
Chen, Donghai 0939
Chen, Elizabeth 0558
Chen, Fan 0082
Chen, Hanyang 0646
Chen, Haobin 0845
Chen, Haodong 2128
Chen, Hsin-Hua **2633**, **2658**
Chen, Jiana 1728
Chen, Jianghua 0077
Chen, Jie 1179
Chen, Jun 1855
Chen, Kiana **0086**
Chen, Ko-Chieh 0704
Chen, Kyra 1241, 2327, 2687
Chen, Li 1682, 1741
Chen, Liye 2583
Chen, Lucia 0451
Chen, Mengyun 0003
Chen, Min 0005
Chen, Min 2464
Chen, Ming-Han 1433, 2469
Chen, Pei-Lung 1346
Chen, Peng 0001
Chen, Peter 0067, 0085
Chen, Peter 1339
Chen, Qian 1799
Chen, Qinwei 0881
Chen, Ruiqi 2285
Chen, Shanshan 0234
Chen, Sheau-Chiann 1329
Chen, Sheng 0656
Chen, Shengnan 0277
chen, shiju 1726
Chen, Shirley 0589, 1465
Chen, Shuqi 2296, 2300
Chen, Stephanie 0187
Chen, Steven 1104
Chen, Tiffany 0981
Chen, Tseng-Cheng 0511
Chen, Vicky 2580
Chen, Wei 2697
Chen, Weiqiang 2285
Chen, Weixi 1338
Chen, Weixin 0839
Chen, Wen-Hung 0377
Chen, Xiaoqi 0646
Chen, Xiaoqian 0018, 1006
Chen, Xue 1361
Chen, Xueer 2694
Chen, Yan 1533, 1534, 2453
Chen, Yanfei 0649
Chen, Yanmin 0028
Chen, Yen 0161
CHEN, yen Fu 1344
Chen, Yi-Chen 1590, 2478
Chen, Yi-Chieh 0511
Chen, Yi-Hsing 0595, 1878, 1899
Chen, Yiling 0926
Chen, YU **1346**
Chen, Yuxiao 1303
Chen, Zhihao 0003
Chen, Zhiwei 2672
Cheng, Chelsea **0716**
Cheng, Chiao-Feng 0299
Cheng, Chiao-Feng **0511**
Cheng, Christina 1263
Cheng, David 2276
Cheng, Isaac **0536**
Cheng, Jennifer 1810, **1822**
Cheng, Jie 1442, 2351
Cheng, Karen 2056
Cheng, Ling 0662, 2445
Cheng, Mei-Fang 0511
Cheng, Richard 1104
Cheng, Sue 0279, 1163, 2019, 2020
Cheng, Xi 0646
Cheng, Yipeng 2396
Cheon, Yun-Hong 0080
Chepy, Aurélien 1581, **1858**
Chernoff, David 1675, 2278, 2614
Cherny, Dmitriy 2054
Cheron, Valentine 1734
Cherry, Mohammad 0843
Cherukuri, Anjani Mahesh Kumar 0167, 2050, 2370
Chesky, Karissa 1983
Chesky, Karissa 2620
Chetrit, David 1048
Cheung, Crystal **0674**
Cheung, Peter 0378, 2247, 2248
Chevalier, James 1839
Chevalier, Kevin **0618**, **1575**, **2489**
Chevalier, Kevin 2582
Chevalier, Kevin 2584
Chevalier, Xavier 2082
Chevret, Sylvie 0534
Chew, Erin 0385
Chew, Erin 0828, 2164
Chewning, Betty 1050, 1051
Chezel, Julie 1722
Chhabra, Jay 0182
Chhaing, Richard 2242
Chhibbar, Prabal 2666
chhun, stephanie 1604
Chi, Shuhong 0468
Chiang, Cho-Han 1091, 2657
Chiang, Sam 1820
Chien, Annie 2010
Chien, Hsu-Chih 1727
Chierego, Gianna 1157
Chigurupati, Saiajay 1130, 1990
Chiha, Tania 0375
Chiha, Tania **0792**
Chikh Mohamad, Sulafa 0152
Chim, Tina 0547
Chimenti, Maria Sole 1579, 1580
Chin, Athena 0091
Chin, Samantha 0787
Chinas, Marcos 1696
chinchár, lYN 2336
Ching, Christopher 1981
Chinoy, Hector 0289, 2671
Chiodo, Sabrina 2563
chiorini, john 1682
Chiotopoulou, Kyveli 0407
Chiowchanwisawakit, Praveena 1118
Chiraseveenuprapund, Peter 0374
Chiriboga, Luis 2381
Chirivi, Renato 0431, 0493, **0928**
Chirumamilla, Punith **0167**, 2050, **2370**
Chiseri, Kate 0217
Chitnis, Tanuja 0184
Chitrabhanu, Anoop 1609
Chitsu, Hlaing 0474
Chiu, Antoine 1386
Chiu, Faye 2429
Chmiel, Joan 2455
Cho, A-Hyun 0571
Cho, EunByul 0293
Cho, Hee Won **0203**
Cho, Jiacai 0595, 1878, 1899
Cho, Kabyar **0347**
Cho, Kelly 2276
Cho, Sung Ik 0203, 1748
Cho, Young-Nan 1145
Chock, Eugenia **0122**
Chock, Eugenia 1985
Chock, Eugenia **2446**
Chodorowsky, Mateusz 0477
Choe, Jung-Yoon 1343
Chohan, Saima 1456
Choi, Bich Na **0959**
Choi, Chan-Bum **0480**
Choi, Dongsoek 0893
Choi, Eunice 0097
Choi, Fung Yu Nick 0839
Choi, Hyon K. 0037, 0375, 0599, 0813, 1032, 1099, 1100, 1101, 1130, 1467, 1764, 1990, 1995, 2006, 2008, 2377, 2548, 2590, 2660
Choi, James 1193, 1199, 2259
Choi, Jeea 0239, 1666
Choi, Jessy 0397
Choi, Jiyoon 2435
Choi, May **0188**, 1103, **2414**, 2419, 2568
Choi, Olivia 0523
Choi, Sara 0721
Choi, Sarang 1253, 1931
Choi, So Yung 1228
Choi, Sung-Eun 1145
Choi, Youn Jung 0067, 0085
Choi, Yujung 2207, 2208
Choi, MD, PhD, FAAD, Olivia 0563, 0564, 1176
Chong, Benjamin 1852
Chong, Emily 0127
Chong, Emily 0822, 0858
Chong, Emily 1623, **1740**
Chong, Siew Hwa 0378
Chong-Amezcua, Aritze 0512, 1389
Chop, Alexandra 2141
Chopra, Ratnesh 2026

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Choquette, Denis 0475
Chou, Chih-Hsing 0908
Chou, Ching-Heng 0558
Chou, Richard 1456, 2082
Chou, Sophia 0918, 1811
Chouchana, Laurent 2507
Choudhary, Manish 2577
Choudhary, Nilesh 1401
Choudhuri, Irada 0282, **1201**
Choudhury, Amit 1442, 2351
Chow, Albert 0374
Chow, Andrew 2281
Chow, Jocelyn Hui Ching **0294**, 2069
Chowdhury, Madhumita Roy 2152
Chowdhury, Mohammad 0323
Chowdhury, Onima 0260, 0777, 2663
Choy, Chern Lee **0340**
Choy, Ernest 0021, 0338, **0484**, 1244, 1353, 1356
Christ, Lisa **0751**, 2066
Christakos, Hope 0506
Christelle, SORDET 0516, 1095
Christensen, Mathilde 2231
Christensen, Robin 0338, 2400
Christiansen, Nathaniel H. 2085, 2091
Christin, Brian 0981
Christmann, Romy 1784
Christodoulou, Antonia 1685, 2435
Christodoulou, Lydia 1304
Christopher-Stine, Lisa 0288, 0865, 1207, 2063
Chrysidis, Stavros 2400
Chu, Brian 1912
Chu, Hsiao-Sang 0511
Chu, Philip 2159, **2164**, 2183
Chu, Seung 0010
chu, tianshu 1642
chu, Tianshu 2005
Chu, Tianshu 2013, 2014
Chu, Yanshuo 0273
Chuang, Shin-Shin 0704
Chubbs, Kayla **1103**
Chubinskaya, Susan 1801
Chujo, Kanako **1167**, 1611, 2212, **2488**, 2534
Chukwuemeka, Umeh 0729
Chung, Anh 2430, 2455
Chung, Ashley 0635, 2426
Chung, Cecilia 0174, 2270
Chung, Cecilia P. 0818
Chung, Lorinda 0691, 0702, 0846, 0883, 1194, 1214, 1555, 1566, 1582, 1725, 2475, 2654
Chung, Min Kyung 1029
Chung, Myung Jin 0548
CHUNG, SANGWAN 1343
Churchill, Melvin 2278
Churtichaga Domenech, Clara 0117, 0758
Churtichaga Domenech, Clara 2029
Ciaffi, Jacopo 1569
Ciaglia, Kristina 0119, 1067, 1294, 1691
Cianci, Michael 0987
Ciancio, Antonio 1864
Cicchetti, Giuseppe 1567
Cicci, Jonathan Dominick 2337
Ciccia, Francesco 0098
Ciccia, Francesco 1402, 1757, 1835, 1864
Cid, Maria **0732**, 0776, **0896**, 1626, **2513**
Cidon, Michal 1673
Cifrián, Jose M 1778
Cimé-Aké, Erik 1469, **1482**
Cimadevila Santiago, Sergio 1321
Cimbora, Daniel 0279, 1163, 2019, 2020
Cimmino, Marco Amedeo 1097
Cintron, Dahima **2210**
Ciofani, Luisa 2215
Ciosek, Ashley L 2413
Cipiere, Laure 1448
Cipolletta, Daniela 0987
Cirelli, Kim M. 0997
Ciurea, Adrian 0543, 1430
Ciurtin, Coziana **0820**, **1672**
Ciurtin, Coziana 1678
Ciurtin, Coziana **1743**, **1817**
Ciuti, Gabriele 1570
Civilibal Tang, Nazlican **0417**
CIVINO, ADELE 0389
Cladière, claudie 1150, 2584
Clancy, Margaret 1229, 1230
Clancy, Robert 0626, 0853, 1240, 1391, 1942, 2693
Clarenbach, Christian 0510
Clark, Edward 0262
Clark, Justin 1533, 1534
Clark, kristina **0966**, **1866**, 2503
Clark, Lerone 0759
Clark, Mackenzie 1042
Clark, Rachael 2233
Clark, Ryan **2616**
Clark, Stacie 0016
Clarke, Ada 1722
Clarke, Alexander 1866, 2601
Clarke, Ann 1497, 1722, 2387, 2416
Clarke, Ashley 2419
Clarke, Charlotte 0692
Clarkson, Kristen 1163
Claudepierre, Pascal 1448
Claus, Maren 0932, 1875, 1876
Clauw, Andrew 0501, 1233
Clauw, Daniel 0198
Clauw, Daniel 1225, 1236, 1254, 2189
Clay, Michael 0819, 1233
Claybaugh, Dillon 0945
Clemens, Andreas 0559, 1447, 1462, 1463, 1464
Clemens, Paula 0999
Clement, Kaci **1388**
Clemente, Daniel **1284**
Clemente, Jose 0031, 1338, 2233
Clemente Garulo, Daniel 1282
Clergeau, Martine 0689
Cleveland, Becki 2097, 2437
Clewell, Jerry 1551
Clifford, Alison 1607
Clini, Paolo 0676
Clipper, Christie 1487
Close, David 0832, 1374
Clowse, Megan 0363, 0367, 0610, 0793, 1487, 1505, 2210, 2379
Coady, Kevin 2500
Coarse, Jason 1466, 2358, 2365
Coates, Laura 0562, 0566, 0567, 0572, 0573, **0576**, 0581, 0874, 1261, 1411, 1443, **1447**, 1455, 1458, 2339, 2340, 2341, 2345, 2356, 2357, 2365, 2368, 2689
Coathup, Philip 1136
Coban, Zehra Beyza 2667
Coblyn, Jonathan 0988
Cobo, Tatiana 0201
Cobo-Ibáñez, Tatiana 1961
Cobo-Ibáñez, Tatiana 2422
Coburn, Brian 0231, **1125**, 2002, 2305
coccia, carmela 1587
Codes Mendez, Helena 1620, 1773
Codullo, Veronica 2482
Cody, Ellen 2462
Coeytaux, Karen 0247
Coghlan, Gerry 2651
Cogolludo Campillo, Vicente 2112, 2113
Cohen, Brooke 1223
Cohen, Brooke 1240
Cohen, Brooke 2444
Cohen, Carla 0104
Cohen, Ezra 1810, 1822
Cohen, Hannah 0120, 0121, 0144, 0860
Cohen, Noam A. 0712, 0725
Cohen, Pascal 1575, 1577, 1593, 1765, 1766, 2489, 2506
Cohen, Stanley **2103**
Cohen, Steven 0602
Cohen Tervaert, Jan Willem 0238, 1605, 1607, 2532
Cohen-Mekelburg, Shirley 0178
Cohen-Mekelburg, Shirley 0198
Coiffier, Guillaume 0706, 2115
Coimbra, Ibsen 2536
Colaco, Keith 0522
Colantuoni, Mariasilvia 1696
Colazo Burlato, María 1446
Colcombe, Joseph 2444
Cole, Lyndsey **0088**
Cole, Rachel 1307
Colello, Jacob 0227
Colesa, Deborah 0951
Colic, Jelena 1562
Colindres, Ronald 0982
Colitta, Alessandro 1381
Collado Ramos, Paz 0249, 1547, 1548
Collantes estévez, Eduardo 0100, 0108
Collet, Aurore **0958**
Collet, Corinne 1135
Collins, Dylon 0319

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Collins, Jamie 0156, 0787
Collins, Mia 0832, 1374
Colmegna, Ines 0606, 0968, 1103, 1109, 1475
Colthart, Allison 0987
Colunga-Pedraza, Iris J. 0458, 0614, 1427, 1483, 1486, 1528, 2325
Coman, Ioana 0657
COMAN, Irina 0537
Comarmond, Chloé 0618
Comarmond, Cloé 0681, 0735, 0756, 1765, 2168, 2704
Combier, Alice 0489, 1333
Cometi, Laura 0275
Comins-Boo, Alejandra 1094
Comont, Thibault 0777, 1339
Compán, Olga **1321**, 1413, 2311
Compagno, Michele 1884
Compher, Charlene 2690
Comte, Denis **2443**
Conaghan, Philip 0310, 0852, 2081, 2082, **2101**, 2103, 2273, 2393
Concannon, Hannah **0367**, **2142**
Concoff, Andrew 0851
Conde, Eva 0897
Connelly, Mark 1226, 1745
Connolly, Brian 2035
Connolly, Hannah 2546
Conoscenti, Craig 0259
Consolaro, Alessandro 0389
Constantin, Arnaud 1334
Constantin, Arnaud 1448
Constantinescu, Florina 1182
Constantinides, Michael 1758
Contaldo, Fabiola Rosa 1352
Conticini, Edoardo 0238, 1212, **1616**, 2075
Contreras-Yañez, Irazú 2321
Conversano, Francesco 0246, 1352, 2479
Conway, Richard 0750
Conyers, Christopher 2542
Cook, H. Terence 1767
Cook, Kathryn 0920
Cook, Peter 0981
Cook, Richard 0522, 1415, 1714, 1959, 2609, 2690, 2691
Cooke, Carol 0388
Cooney, Laura 2494
Cooper, Ashley 0392, 0406, 0408, 0409, 0410, 0414
Cooper, Jennifer 1300
Cooper, Nicole 0377
Cooper, Shiamak 0479, **1143**, 1428, **2519**
Copado mendoza, Diana Yazmin 2218, 2632
Cope, Andrew 0190, 0980, 1077, 1115, **1678**
Copel, Joshua 0853, 1391
Copson, Jennifer 0771, 1649, 2605
Corbera-bellalta, marc 0732, 0896
Corbitt, Kelly 2074
corbridge, Thomas 2515
Corcoran, Erik 0913, 0930
Corcuera Elosegui, Irene 2108
Cordeiro, Rafael 1180, 2028, 2045, 2527, 2535
CORMIER, Grégoire 0439, 0477
Cornec, Divi 0477
Cornec, Divi 0508, 1683
Cornec, Divi 1685
Cornec, Divi **2296**, 2300
Cornejo Uixeda, Silvia 2038
Cornielle, Aide 1825
Corominas, Héctor 0019
Corominas, Hector 0271, 1356, 1620, 1773
Corominas Macia, Hector 0270
Coronado, Mónica 0346
Corondan, Anca 1577
Corpuz, Jennifer 0361
Corr, Maripat **0056**
CORRADI, GUIDO 1269
Corrales, Cristina 0269, 1171
Corrales, Sagrario 0070, 0071, 0072, 0087, **0094**, 0795, 1851
Corrales-Díaz-Flores, Sagrario 2599
Corrales-Martínez, Alfonso 0216, 1916
Corral-Trujillo, Maria Eugenia 1022, 1633, 1687, 2549, 2557
Correa, Blanca 2106
Correa, Nestor 1041
Correas, Jean-Michel 1144
Correia, Luisa 1715
Correia Marques, Mariana 0782, 0920, **1811**, 2133
Correll, Colleen 0401
Correll, Julia R. 2435
Cortés-Hernández, Josefina 0639, 1548, 2450, 2458, 2696
Corte, Giulia 0762, 0878, **2613**, 2695
Corteguera, Montserrat 1547, 1548
Cortet, Bernard 2115
Cortez, Angelique **2581**
Corti, Davide 0907
Corty, Robert **1181**
Coryell, Philip 1801
Corzo, Patricia 1018, 1943
Cosatti, Micaela A. 1491
Cosentino, Emily 1832
Cosentino, Emily **2394**
Cosentino, Máximo 2405
Cosgrove, Haylee 0943
Coskun, Ahmet 1684
Coskun Benlidayi, Ilke 2067
Coss, Samantha **0193**, **0999**
Cosson, Adrien 0653
Costa, Flávio 0761
Costa, Lauren 2276
Costa Reis, Patricia 1287, 1288
Costa Seguro, Luciana Parente 0206, **0619**, 0621, 2573
Costa-Moya, Ester 0496, 2268
Costantino, Félicie **0103**, **0104**, **1438**
Coste, Joel 0314
Coste, Joel 2080
Costedoat-Chalumeau, Nathalie 0133
Costedoat-Chalumeau, Nathalie 0618, 1575
Costedoat-Chalumeau, Nathalie 1722
Costedoat-Chalumeau, Nathalie 2457, 2489
Costedoat-Chalumeau, Nathalie 2655
Costello, Anna 2680
Costenbader, Karen H. 0184, 0188, 0427, 0662, 0669, 0803, **1019**, **1020**, 1551, 1709, 1894, 1896, 1913, 2414, 2568, 2572, 2659, 2679
Cote, Jonida 1081, 2150, 2195
Cottereaux, Céline 0653
Cottin, Vincent 0688
Cottin, Vincent 0715, 1662
Cottu, Adrien **1592**
Couderc, Marion 0508
Coudray, Nicolas 1712
Couette, Nina **2163**
Coulier, Helene 0162
Counts, Kathryn **0617**
Courties, Alice 1735
Courtois Communier, Emmanuelle 0477
Coussement, Antoine 0618
Coutard, Anne 2532
Couturier, Aymeric 0618
Couturier, Marie Anne 1339
Couvelard, Anne 0735
Couzi, Lionel 2457
Covello, Allyson 1265
Covert, Lauren 1745
Cowley, Sharon 0750
Cox, Gerard 0721
Cox, Maartje 1324
Coyle, Carl **0980**
Coyle, Conor **1411**
Coyle, James L. 2064
Coziahr, Kelsey **0155**
Cozzi, Giacomo 0275
Cozzi, Giacomo 1127
Crabtree, Juliet 0941
Craig, Ethan 1261
Cram, Peter 0785, 0786
Cramer, Mareike 0678
Cransac, Amélie 0891
Crater, Christina 0574
Craver, Emily 0727, 1986
Crawmer, Justin 2100
Creasman, Megan **0189**
Crema, Michel 0327
Cremer, Paul 0242, 1186
Crespo, Maria Elena 1486
Crestani, Bruno 1577
Crimmings, Mary 0373
Crisafulli, Francesca 2411
Crisci, Sarah **0666**, **1340**
Criscione-Schreiber, Lisa 0363
Criscione-Schreiber, Lisa 0367
Criscione-Schreiber, Lisa 0793

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Criscione-Schreiber, Lisa 1487, 2159
Criscione-Schreiber, Lisa 2379
Cristina-Varela, Diana 1210
Cristofaro, Alexander 0888, 0997
Criswell, Lindsey 0034, 0038, 0625, 0637, 1504, 1725, 2646
Crofford, Leslie 0546, 1888
Croft, Adam 0798, 1757
Cron, randy **0039**, 1277
Cron, Randy 1820
Cron, randy 2137
Cron, Randy 2138, 2139
Cronholm, Peter F. 1298
Cronin, Mary 0218
Cross, Heather 1817
Cross, Jennifer 0868
Cross, Sue 0074
Crossland, Grace **0885**, **1758**
Crow, Mary 1700
Crowley, Angela 1675, 2278
Crowley, Angela 2362
Crowshoe, Lynden 2419
Crowson, Cynthia 0030, 0460, 0469, 0601, 0759, 1030, 1034, 1156, 1311, 1320, 1388, 1556, 1721, 1726, 1932, 2403, 2571, 2645
Cruz, Anthony **0918**
Cruz, Gabriel 1708
Cruz, Vitor 2246
Cruz-Bautista, Ivette 1383
Cruzel, Coralie 0148
Crystal, Stephen 0399, 0400
Császár-Nagy, Noémi 2684
Csókási, Krisztina 2684
Csecs, Ibolya 2470
Csige, Dóra 0680
Csomos, Krisztian **0782**, 0918
Cubells, Monica 0575, 0749, 2299
Cubero, Lucía 1964
Cucchiarini, Magali 1798
Cucnik, Sasa 0281
Cuda, Carla Marie 0066, 0935, 1227, 1362, 1793, 2430
Cudrici, Cornelia 1169
Cuellar-Gutierrez, Maria 1721, 2403
Cuervas-mons, Manuel 2373
Cuesta López, Laura 0108
Cuff, Carolyn 2297
Cui, Baoling 0048
Cui, beibei 2061
Cui, Jing 1019
Cui, Jing 1709, 2320
Cui, Jing 2572
Cui, Qiguo **0517**, 1478
cui, xueqin 0998
cui, yifan 1642
Cullen, Eva 0567, 0573, 1455, 2357
Culver, Emma 0279, 1163, 2019, 2020, 2051, 2546
Cumbermack, Kristopher 0853, 1391
Cumin, Marina 1339, 1604
Cuneo, Bettina 0626, 0853, 1391
Cunha, Joanne 1044
Cunningham, Ian 1338
Cunningham, Jessie 2563
Cunningham, Melissa 0952
Cunningham, Natoshia 1289
Cuomo, Giovanna 2477
Cupit, Caroline 1244
Curcio, Francesco 2545
Curhan, Gary 2590
Curran, Jill 0247
Curran, Megan 2161, 2165
Curry, Dylan 0712
Curtis, Allison 0242, 1186
Curtis, David 1661, 1987
Curtis, Jeffrey 0157, 0185
Curtis, Jeffrey **0369**, **0370**
Curtis, Jeffrey 0895
Curtis, Jeffrey 1027, 1045, 1054
Curtis, Jeffrey 1084
Curtis, Jeffrey 1102, 1228
Curtis, Jeffrey 1252, 1306, 1327
Curtis, Jeffrey 1351, **1387**, **1444**
Curtis, Jeffrey 1507
Curtis, Jeffrey 1629, 1659, **1661**
Curtis, Jeffrey 1748
Curtis, Jeffrey 1997, 2068
Curtis, Jeffrey **2119**
Curtis, Jeffrey 2172, 2237, 2275
Curtis, Jeffrey 2278, 2539
Curtis, Jeffrey 2566, 2661
Curtis, Michelle 1702
Curtis, Michelle 2600
Curtis, Paula 2467
Cushing, Sharon 2127
Cushing, Solana **0463**, **0464**
Cuthbertson, David 0721, 0747, 1602, 1767, 2515, 2533
Cutolo, Maurizio 0676, 0705, 0963, 1097, 1952, 2179, 2501
Cutter, Gary 0368, 2006, 2117
Cuttica, Michael 1553
Cuttica, Ruben 0389
Cygnar, Katherine 0898

D

D, Phani Kumar 0291, 1771, 1775
Da Costa, Deborah 0376
da Rocha Castelar Pinheiro, Geraldo 1365, 2246
Da Silva, Antonio 0623
da Silva Pereira Curado, Daniel 1365
D´Agostino, Maria Antonietta 0878
Dähnrich, Cornelia 0293
Dåstøl, Vilde Øverlien **0427**, **2679**
Dörner, Thomas 2476, 2665
D'Haens, Geert 0257
Díaz González, Federico 1164
Díaz-Almirón, Mariana 0180
Dabaghjamanesh, Mojtaba 1607
D'Abronzo, Rosa 1567
Dada, Arinola 1043
Daenthanasanmak, Anusara 0989
Díez Álvarez, Elvira 0882
Díez García, Elvira 2450
Daga, Ankana 2446
Dagna, Lorenzo 1586, 1618
Dagna, Lorenzo 1666
Dagna, Lorenzo 2482
D'Agostino, Maria Antonietta 0236
D'Agostino, Maria Antonietta 0641
D'Agostino, Maria Antonietta 1567, 1678, 1757
D'Agostino, Maria Antonietta 2482
D'Agostino, Maria Antonietta 2695
D'Agostino, Maria-Antonietta 1438
Dahl, Noelle 0981
Dahlqvist, Johanna 0718
dai, huanzi 0468, 0950, 1361
Dai, Jessica **1488**, **2404**
Dai, Jessica 2444, 2630
Dai, JiaYuan 1158
Dai, Lie **2245**
Dai, Lily 1624
Dai, Ruixue 1761
Dai, Shengming 0656
dai, Xinhua 2061
Dai, Yifei 1237
Daigle, Shanette 0185, 1387, 2068, 2119
Dalbeth, Nicola 1146
Dale, James 1239
Dale, Marissa 0126
D'Alessandro, Roberto **0706**
D'Alessandro, Roberto 0796
Daley, LeeAnne 2486
Daliri, Soudabeh 1070
Dalkilic-Liddle, Isin **0941**
Dall'Era, Maria 0625, 0637, **0645**, 0652, 0791, 0851, 1038, 1240, 1504, 1505, 1639, 1640, 2600, 2645, 2646, 2650
Dalmas, Marie Caroline 1339
Dalmolin, Henrique 2573
Damasco, Amelia 1127
Damen, caroline **0568**
Damianos, John 0030
D'Amico, Saverio 0532
Damluji, Abdulla 0146
Damrauer, Scott 0045, 0046, 0834, 2683
Dancer, Gordana 1353
Danese, Sherry 0370
Danese, Silvio 0257
Daneshvar, Amir **0603**, 0742, 1151, **1471**, 1500, 1501
Daneshvar, Simin 1716
Dang, Julien 0618
Dang, Steven **0042**
D'Angelo Lacerda, Gabriel 0616
Danguecan, Ashley 1285, 1289, 1290, 1295, 1742
Daniel, Benjamin 0897
Daniel, Laura 0174, 0818
Daniel, Laura 2270

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Daniel, WENDLING 0544, 1095, 2637
Daniel, Zachary **1667**
Danielson, Sarah **1653**
Danila, Maria I. (Maio) 0157, 0158, 0221, 0222, 0368, 0372, 1068, **1073**, 1417, 1674, 2006, 2117, 2312
Dankner, Yair 1332
Danko, Charles G 0028
Danneels, Lieven 2692
Dannequin, Thomas 0903
Danquah, Andrew 0780, 1671
Dans Caballero, Santiago **0139**, **2502**
Dantata, Khadija 2547, 2565
Danve, Abhijeet 0437, 0553, 0585, 0854, 1445, 1459
Danve, Abhijeet 1985
Danza, Alvaro 0621, 0623, 1530
Danzo, Fiammetta 1589
Dao, Justine 0653
Dao, Kathryn 2446
Daoud, Ansaam 0741, 0742, 1476, **2382**
Daousis, Dimitrios 1452
Dapas, Matthew **0624**, 1362, **1793**
Dapeña, Joan Manuel **0432**, 1422, **2405**
Darbousset, Roxane 1696
Dardeno, Michelle 2446
D'Ardia, Angela 1863
Dargham, amne 2702
Darnall, Beth 1228
Daroussi, Saida 1937
Darrah, Erika 0529
Darroch, Hannah 2010
Dartizio, Carmela 2117
Darveaux, Daniel 2260
Darzi, Amanda 1518
Das, Anna C 1588
Das, Indrani 1281
Das, Jishnu 2666
Das, Rajat 0941
Das, Sanchita 2133
Das, Sharmila 0843, 1529
Dascani, Paul 2140
Dashi, Tobias 2641
Dass, Shouvik 2411
Datar, Isha 1279
DATT UPADHYAY, ASHISH 0416
Dattagupta, Antara **1055**
Daugas, Eric 0618, 1521
Davalos, Angel 1745
Davanzo, Federica 0238
Dave, Devavrat 0509
Dave, Rutvi 1609
Davelaar, Nadine 0978
Davenport Munoz, Maurice 2154
Davergne, Thomas 0177
Daviano, Alexjandro 1083
Daviault, Beatrice 1199, 2259
Davidovski, Filip 1166, 2608
Davidow, Amy 0399, 0400
Davidsen, Jesper 2400
Davidson, Anne 0933, 0940, 1763, 1830, 1844, 2600
Davidson, Stefanie 0392, 0396
Davidson, Stefanie 0406, 0414
Davidson-Moncada, Jan **1532**, **2452**
Davies, Gareth 0991
Davis, Adrienne 1285, 1289, 1742
Davis, Amonte 2561
Davis, John **0030**, 0774, 0815, 1034, 1156, 1674, 1726, 1932, 2571, 2639
Davis, Natalie 1751, **1902**, 2235, 2574, 2577, 2578
Davis, Renee 0463
Davis, Thomas 2150
Davis, William 1508, 2392
Davis-Karim, Anne 1125, 2001
Davoli, Giulia 2501
Davra, Viralkumar 0010
Davuluri, Srijana 0210, 0691, 1194, 1214
Dawamne, Tarek 1176
Day, Jessica 2057, 2065
Dayan, Natalie 2222
Dayno, Rachel 0231
Dayton, Michael 1233
D'Cruz, David 0692
De, Dipankar 0697
De Almeida Chaves, Sébastien 0123, 1200
De Almeida Chaves, Sébastien 2510
de Andrés, María C. 0329
De Angelis, Rossella 2482
de Argila, Diego 0029
De Baets, Greet 0832
De Benedetti, Fabrizio 0391, 0780, 1671, 2137, 2138, 2139
De Bonnecaze, Guillaume 2510
De Boysson, Hubert 0756, 0891, **2704**
de Bruin, Liese **0539**, 0540, 1405, 1406, 1941, **1958**, **2319**, 2635
De Ceuninck, Leentje 2671
De Cinque Almeida Esteves, Hemerli 2316
De Cleene, Hannah KL 0948
De Craemer, Ann-Sophie 0568, 1438
De Daniel Bisbe, Laia **0575**, 0749, 1161, 1162, 2250, 2299, 2484, 2491
De Dios, Juan Ramon 2670
de Frías Polo, Carlos 2450
De Gaspari, Monica 1856
de Groot, Ingrid 0289, 2066
De Guzman, Marietta 1295, 1296, 1299, 1621, 2148, 2462
de Hooge, Manouk 0539, **0540**, 0543, 1405, 1406, 1941, 1958, 2319, 2635
de Jesus, Adriana 0920
De Jong, Erica 1793
de Jong, Pascal 0176, 0978
de Jong, Robin 0431
De la Cámara, Isabel 1961
De la Calle, Javier 0882
De La Camara-Fernandez, Isabel 0201
de La Herran Nuñez, Gaspar 2107, 2108
de La Loge, Christine 0592, 0644, 2441
De la Mata Pinilla, Elena 0659
De la Morena, Isabel 0736
de la Puente-Bujidos, Carlos **1561**
de la Rosa Báez, Carlos **1862**
De la Rosa-Vazquez, Ricardo I. 1427
De la Rubia Navarro, Marta 0642, 0659
De La Torre, Inmaculada 1348
De Langhe, Ellen 0702
De Langhe, Ellen 1529
De Leeuw, Elisabeth 0907
De Leon-Carrillo, Carolina 0767
de Libero, Cinzia 0407
De Lorenzis, Enrico 0847, **1567**
de Luca, Giacomo 1856
De Luca, Giacomo 2477
de Luca, Giacomo 2482
de Luque, Juan 0542
De Marco, Margot 1863
de Margerie, Constance 0327
De Marino, Barbara 1835, 1864
De Martino, Maria 2545
de Maupeou, François 0162
De Miguel, Clara **0483**
DE MIGUEL, CLARA 1024, 2036
de Miguel, Eugenio 0089, 0180, 0200, 0249, 0737, 0739, 0744, **0745**, 0751, 0755, 0894, 1322, 1612, 2042, 2610
De Mits, Sophie **2692**
de Moreuil, Claire 1765, 2655
de Peyrecave, Natasha 1438, 1449, 1466
de Pinto, Marco 1587
de Queiroz Prado, Rafael 0989
DE SAINTE MARIE, Benjamin 2457
De San Segundo, Marta 0201
De Santis, Maria 0879, 0884, 1586
de Seny, Dominique 1738
De Serres, Gaston 1109
De Souza, Fernando H 1192
de Souza Müller, Carolina 0702
de Swart, Bert JM 1205
De Vera, Ronaldo 2004
de Vlam, Kurt 0528
de Vlam, Kurt 0591, 0592, 1963
De Voeght, Adrien 1339
De Vries, Dirk 0641
de Vries-Bouwstra, Jeska 0673, 0690, **0696**, 0702, 0884, 1568, 1569, 1573, 1586, 1862, 2503
De Winter, Seppe 0907
de Wit, Maarten 0111, 1411, 2341
Deane, Kevin 0033, 0076, 0088, 0774, 0775, 0833, 0889, 0914, 1249, **1674**, 1695, 1751, 2227, 2235
Debeaupuis, Orianne 1339
Debray, Thomas 0488
Deciderio-Pavon, Karina 0248, 0767
Deck, Anna 2429
Decker, Jake 0218
Declèves, Xavier 1593
Decoux, Antoine 0327
Decrock, Marijke 2115

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Decroocq, Justine 1578
Decuypere, Flore 1366
Dedeoglu, Fatma 1668, 1669, 1810, 1822, 2125, 2128, 2129, 2151
Deeb, Ahmed 2385
Deepak Kadam, Manali 0016
Dees, Clara 0975
Deewan, Anshu 2580
Deffendall, Catherine **0828**, **2206**, 2413
DeFreese, Daniele 2384, 2649
Degirmenci, Huseyin Berk 1481
Degl'Innocenti, Elena 0903
Degraeve, Alexandra 0871
Degrassi, angela 0371, 1617, 1987
Degrava Sampaio Barros, Percival 1180
DeHaan, Wesley 1998, 2588
Dehdashtian, Ehsan 2425
Deherder, Delphine 2374
Dehghan, Natasha 1607
Dei, Beatrice 1380
Dei, Beatrice 1381
Dei, Beatrice 1385, 1951
Deicher, Franca Sophie 0678, 0932, 1198, 1876
Deignan, Cynthia 0576, 0581
Dejaco, Christian 0751, 0776
Dejaco, Christian 1626
Dejaco, Christian 1629
DeJager, Wade 0023, 0044, 0514, 0840, 1087, 1223, 1240, 1480, 1831, 1850, 1852, 2421, 2649
Dekker, Tamara 1560
DeKlotz, Cynthia 0558, 0875
DeKryger, William 0227
Del Gaizo, Vincent 0374, 0404
Del Galdo, Francesco 0689, 0692, 0702, 0847, 1562, **1571**, 1586, 1873, 1933, 2477
Del Papa, Nicoletta 0879
Del pAPA, Nicoletta 1212
Del Papa, Nicoletta 1863
Del Papa, Nicoletta 2075
Del pAPA, Nicoletta 2656
del Peso, Gloria 0346
Del Rio, Ana Paula Toledo 2536
Del Rio-Espinola, Alberto 0981
del Val del amo, Natividad 2450
Del Vecchio, Gianmarco 0246, 1352, 2479
Delai, Milena **2459**
Delcros, Quentin 1768
Delcros, Quentin 2582
Delcros, Quentin 2584
Deldycke, Claire 1734
DELENTE, Louis 0537
Deleuze, Jean-François 0103
Delgado, Ana 2467
Delgado, Martha 2198
Delgado Ramirez, Chloe 0207
Delger, Kara 2639
Deligeorgakis, Dimitrios 1452
Deligny, christophe 2457
Della Rossa, Alessandra 2656
Della Rossa, Nicola 1402
Della Torre, Emanuel 1163
Dellaripa, Paul 0156
Dell'orso, Stefania 0118, 0301, 0863, 0918, 1725
Dell'Orso, Stefania 2580
Dell'orso, Stefania 2700
Delmis, Antonella 0815
Delougeot, Céline 0099, 2637
DeLozier, Amy M. 0555
Delvenne, Philippe 1738
Delvino, Paolo 0238
Delvino, Paolo 1598, 2532
Demalia, Angelo 1229, 1230
Demarco, Bradley 0009
DeMarco, Paul 2177
Demir, Selcan 0128
Demirayak, Ilayda 0837
Demirkaya, Erkan 1823
Demoreuil, Claire 1592
Demoruelle, Kristen 0088, 0775, 0833, 0889, 1674, 1695, 2205, 2628
den Braanker, Hannah 0978
Deng, Emily 1669, 2125, 2128
Deng, Emily 2147
Deng, Lei 1113
Deng, Yafang 1750
Deng, Zuoming 0918, 1811, 2046, 2133
Denis, Caroline 2296, 2300
Denis, Guillaume 1339
Deniz, Rabia 0025, **1965**
Denton, Christopher 0673, **0692**, 0702, 0847, 0966, 1586, 1589, 1862, 1866, 2496, 2503
Denvir, Brendan **1595**, **1596**, 2518
Denz, Robin 1934
Deo, Rinki 2577
Deodhar, Atul 0455, **0567**, **0874**, 1424, 1449, 1451, 1455, 2352, 2356, 2365
Deol, Joban **0697**
Deonaraine, Kristina 1240
Depaire, agathe 1873
Deprez, Joke 0694
Derebail, Vimal 2468
Derk, Chris 1725, 2026
Dernis, Emmanuelle 0477
Dernis, Emmanuelle 0516
Dernis, Emmanuelle 1411
DEROUX, Alban 2457
Deroyer, Celine 1738
DerSarkissian, Maral 1533, 1534, 2453
Desai, Alisha 0843, 1529
Desai, Bhavisha 1123, 1259, 1998, 1999, **2548**, 2587, 2588
Desai, Foram 0009
Desai, Hardik Dineshbhai 1890, 1891
Desai, Jigar 1827
Desai, Parth 1511
Desai, Pooja 1268
Desai, Rishi 2662
Desai, Shraddha 2466
DeSancho, Maria 0855
Deshayes, Samuel 2704
Desjardins, Michaël 0606, 1475
Desjarlais, John 0010
Desmarais, Julianna 0825
Desmonet Trousset, Camille 2115
Desprets, marie 1604
De-Toro-Santos, Francisco J 0454
Devakumar, Veda 0956
Devarasetti, Phani Kumar 0424
Devauchelle, Valerie 0477, 0508, 0516, 0738, 0891, 1095, **1189**, 1683, 1685, 2241, 2296, 2300
DeVault-Nelson, Victoria 0981
Deve, Kevin 2457
Devey, Luke 0006
Devilliers, Hervé 0891
DeVita, Paul 2097
Devloo, Cecile 1339
Devreese, Katrien 0121
Devulapalli, Vinay 0063
Dey, Dzifa 0177, 2185
Dey, Mrinalini **0190**, **0191**, **1077**, 1263
Dey, Mrinalini 1614
Dey, Mrinalini **1627**, 1639, 1640
Dey, Poulami 0949, 0972, 1590, **2498**
Dey, Ritwik 0160
Dezzutti, Stephanie 2649
Dhakal, Sanjeev 1820
Dhall, Aishwarya 1197
Dhamne, Sayali 1229, 1230, 2105
Dhanaliwala, Ali 0520, **1939**
Dhanania, Prachi 0888, 0997
Dhanasekaran, Preeti **0378**, 2248
Dhanekula, Phanidhar 0533
Dhanrajani, Anita **1275**
Dhavamani, Sugasini 1140
Dhiman, Soniya 1503
Dhir, Varun 0481, 0697
Dhital, Rashmi **2220**, **2221**, 2413
Dhooria, Sahajal 0697
Dhote, Robin 0735
Dhrif, Omar **0756**
Di Battista, Marco 2656
Di Cianni, Federica 0723
Di Ciommo, Francesca Romana 0671, 0672, 1559
Di Donato, Stefano **0847**, 1571, **1586**, **1587**, **1873**
Di Galante, Marco 1381
Di Giuseppe, Daniela 0525, 1430
Di Matteo, Andrea 0832
Di Paola, Marco 0246, 1352, 2479
Di Pede, Caterina 1381
di Romana, Silvana 0035
Diab, Adi 0273
Diamond, Betty 0902, 0947, 0953, 1844, 2600
Diamond, Ellie 2201
Diao, liqun 0042

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Dias, Roshan 1353
Diaz, Cesar 1773
Diaz, Michael 0976
Diaz Arumir Vergara, Alejandro 0710
Diaz Deluna, Mariani 0092, 1172
Diaz Gallo, Lina Marcela 0297
Diaz Martinez, JuanPablo 0612
Diaz Menindez, Maximiliano **0701**
Diaz Menindez, Maximiliano 1255
diaz Oca, alberto 0351
Diaz-Castroverde, Sabela 2373
Diaz-Infante Morales, Daniela 0060
Diaz-Torne, Cesar 0496, 1620, 2268
DiCarli, Marcelo 1957, 2688
DiCarlo, Edward 0316, 0463, 0464
diCasoli, Carl 1563, 2468, 2669
Dickinson, Mark 0686, 1966
Dickinson, Olivia 0198
Dickman, jacob **1789**
Dickmann, Laura 0218
Dickmann, Laura 1050, 1051
Dickson, Alyson L. 0818
Didier, Kévin 0756
Diederich, Kristy 0410
Diekhoff, Torsten 0543
Diekhoff, Torsten 0854
Diekman, Brian 1788
Diep, Phuong 0510, 1872
DIERCKX, Stéphanie 1679
Dietrich, Sascha 0809, 1537
Dieude, Philippe 0508, 0516, 1095
dieudonne, Yannick 1578
Diez Alvarez, Elvira 2670
Diez-Cordoves, Gisela 1282, 1284
Diez-Morrondo, Carolina 2016
Diffie, Colin 1055
DiGiorgi, Mary 2103
Dileepan, Thamotharampillai 0983
Diller, Matthew 0289
Dillon, Charles 0541
Dillon, Eilish 2414
Dillon, Simon 2105
Dilmé Muñóz, Jaime-Félix 1620
Dimachkie, M. Dave 2162
Dimitri, Suarez 0355
Dimitroulas, Theodoros 1452, 2232
Dimitrova, Dessislava 2297
Dineen, Alexis 0369
Ding, Changhai 1247
ding, jin **2611**
Ding, Lei 1535
Ding, Meng 1354
Ding, Mengwei 0429
Ding, Rui 2288
Ding, Zhaoyu 1279, 1281, 1301
Dingremont, Claire 0891
Dinh, Tam **2077**
Dinh-Xuan, Anh-Tuan 0688, 2262
Diniz, Bruna 1879
Diniz, Valquiria 1407, 1408, 2326
Dinsdale, Graham 0686
Dinsdale, Graham 1966
Dinsdale, Graham 2493
DIONELLO, CARLA F **0179**
Dionet, Lea **1768**, 2582, **2584**
Dionne, Marc 1109
Dios, Diego 1171, 1282, 1284
DIOS SANTOS, DIEGO 0107
Dios Santos, Diego 0269
Diot, Elisabeth 1765
DIPE, LUIZ F 0179
Dipetrangelo, Greta 0275
DiRenzo, Dana 0046, 0520, 1939
DiRenzo, Daniel 0057
Direskeneli, Haner 0025, 0133, 1618, 1631
DIREZ, Guillaume 0891
Dismuke, Clara 1232
Distler, Jörg 0026, 0166, 0678, 0809, 0810, 0932, 0956, 0960, 0961, 0962, 0974, 0975, 1198, 1537, 1757, 1856, 2612
Distler, Joerg 0977
Distler, Oliver 0510, 0673, 0689, 0807, 0880, 0884, 0957, 0967, 1562, 1579, 1580, 1586, 1862, 1867, 1872, 2066, 2472, 2497
Ditto, Maria Chiara 0275
Divers, Jasmin 0047
Dixit, Agrani 0674
Dixit, Juhi **2213**
dixon, Will 0686
Diz Lopes, Mariana 2116
Djeffal, Yannis 0807
D'Lima, Darryl 1805
Dlouhá, Dana 1211, 2073
Dlugosz, Andrzej A 0949, 1760
Do, Alexandra **0211**
Do, Donna 1821, 2242
DO, HYUNSUE **2511**
Do, Minh 1144
DO CRUZEIRO, Marcio 0114
Doan, Tam 0853, 1391
Dobashi, Hiroaki 1167, 1611, 1630, 2212, 2488
Dobashi, Hiroaki 2523
Dobashi, Hiroaki 2534
Dobrota, Rucsandra 0880, 0967, 1579, 1580, 2472
Dobrowolski, Chrisanna 1832, 2394
Dobry, Craig 2451
Dodd, Dylan 1032, 2008, 2590
Doddi, Shreya 1743
Dodge, Deborah 0016
Doerig, Romina 0015
Doherty, Michael 0324, 2622
Dolecki, Cassandra **1058**
Dolezalova, Pavla 0780, 1671
Dolfi, Fabrizio 1356
Dolhain, Radboud 0978
Doll, Helen 2409
Dollinger, Arthur **0099**
Domènech, Eugeni 0021
Doménech Serrano, Jose **1129**
Domínguez-Álvaro, Marta 0728, 0744, 0752, 0757, 2106
Domínguez-Casas, Lucia C. 2265
Dombret, Sophia 1729
Domiciano, Diogo 2682
Domingez, Nicholas 0044, 1831, 1850
Domingues, Vinicius 1992
Dominguez, Daniela 1279, 1281, 1286, 1301
Dominguez, Salina T 1362
Dominguez Paez, Yuliana 0317
Dominguez-Chapa, Emmanuel **0248**, 1633, **2058**, 2071, 2072
Dominguez-Guerra, Annette 1427
Domsic, Robyn 1015, 1084, 1149, 1725, 2483, 2499, 2539
Don, Howard 1136
Donath, Christina 0657
Donati, Stefano 1380, 1381
Donati, Valentina 1385
Donato, Anthony 0709, 1572
Dong, Chaoling 0040
Dong, Haidong 1726
Dong, Liguo 1006
Dong, Lisha 1006
Dong, Mei Xue 0437
Dong, Xingbei **0468**
Dong, Xinxin 0279, 1163, 2019, 2020
Donlin, Laura 0463, 2233
Donnes, Pierre 0820
Donofrio, Mary 0853, 1391
Donohue, Sarah 0825, 2167
Donovan, Caroline 1915, 2561
Donovan, Frank 0637
Dons, Maria 1166, **2608**
Donzallaz, Maurice 0543
Dooley, Mary Anne 1722, 2416
Dore, Adam **0175**, 1058
Doria, Andrea 0803, 1526
Dorio, Murillo 1715
Dorjée, Annemarie 1838
Dornisch, Elisabeth 1695
Dorst, Daphne 0928
dos Reis-Neto, Edgard 0621, 0623, 1486, 1491
Dos Santos Sobrín, Raquel 2209
Doshi, Jainesh 0308
Doss, Jayanth 0363, 0793, 1160, 2379
Dotan, Arad 1280
Dougados, Maxime 0214, 0215, 0327
Dougados, Maxime 0534
Dougados, Maxime 0854
Doumatey, Ayo 1725
Dowell, Sharon 1507
Dowling, Kaitlyn 1758
Dowling, Samuel 0066
Dowling, Samuel 1793
Dowsett, Jacquie 1136
Doyle, Ian 0992, 2528, 2530
Doyle, Tracy J. 1751, 2235
Drake, Connor 0363, 0793, 1487, 2379

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Drechsel, Karen 0962
Dregan, Alexandru 1906
Drenkard, Cristina 0218, 1491, 2645
Drevon, Louis 1339
Drew, Joanne 1275
Drexel, Carole **2176**
Driban, Jeffrey **0309**, 0313, **0321**, **0322**, **0323**, **1895**, 2090
Driban, Jeffrey 2562
Driban, Jeffrey **2623**, **2625**
Driest, Kyla 0829
Drillock, Lauren 2089
Dron, Louis 0470
Drosos, Alexandros 2232
Drott, Ulrich 1660
Drow, Travis 0981
Drzeniek, Norman 0471
Du, Bing 2463
Du, Doantrnag 1071
Du, Fang 1179
Du, Hongwei 0876
Du, Rong 0646
Du, Zhiyuan 0557
Du Four, Tessa 0705
Dua, Anisha **0738**, 2162
Duan, Lihua 2013, 2014
Duan, Xiaoru 0646
Duan, Xinwang 0468, 0649, 2013, 2014
Duan, Zhigang 1920
Duarte, Ángela Luzia Branco Pinto 1491
Duarte Fernandes, Rúben **1933**
Duarte-Garcia, Ali 0120, 0601, 1052, 1721, 2403, 2645
Dube, Pratibha 1792, 1794, 1806
Dubikov, Alexander 0476
Dubois, Cecile 1519, 2440
Dubost, Jean-Jacques 0516
Dubovsky, Jason 2277
Dubreuil, Maureen 2330
Dubucquoi, Sylvain 0958, 1858
Ducker, Georgina 1614, 1627
Dueñas, Marina 2484
Dueñas-Ochoa, Marina 2122, **2491**
Duell, Alexandra 0392, 0394, 0406, 0407, 0414, 0415, 1821, 2675
Duesing, Christina 0678, **1198**, 1537
Duffau, Pierre 1339
Duftner, Christina 1911
Duggan, Lori 0048
Duhaut, Pierre 1575, 2489
Duitman, Jan Willem 1560, 1860
Dukaj, Livio 0888, 0997
Dulake, Debra 1244
Dumlao, darren 0871
Dumont, Anael 2704
Dumonteix Moreau, Cassandre 0105
Duncan, Marie 1136
Duncombe, Paul 2671
Dunleavy, Tracey 1136
Dunlop, Dorothy 1225, 1249
Dunlop-Thomas, Charmayne 0707, 1638, 1639, 1640
Dunn, Kelsey 1487
Dunogue, bertrand 0681, 0688, 1575, 1577, 1766, 2489
Duodu, Esther 0456
Duong, Jean-Paul 1768
Dupin, Nicolas 2699
Duplantis, Barry 0911, 1776
Dupont, William D. 0818
Duquenne, Laurence 0832
durant, cecile 2655
Duranton, christophe 1135
Durel, Cécile Audrey 0756
DUREL, Cecile-Audrey 2532
Duret, Pierre-Marie 0508, **0516**, **1683**
Durez, Patrick 0035, 0074
Durez, Patrick 1676, 1679
Durez, Patrick 1738
Durez, Patrick 2272
Durfee, Paul 0016
durieu, Isabelle 2655
Duron, Loïc 0327
Duruöz, Mehmet Tuncay **2322**
Duryea, Jeffrey 0325, 2085, 2091, 2100
Duryee, Michael 0065, 0921, 0924, 1314, 1325, 1650, 1746, 1774, 1779, 2585
Duzenci, Sinem Nursel 2044
Duzsik, Lili 2684
Dvergsten, Jeffrey 1745, 1816
Dvoryakovskaya, Tatiana 0403
Dwidar, Sundus **0637**
Dwivedi, Armita 0900
Dyball, Sarah 0245
Dye, Elizabeth 2117
Dyson, Gabriella 1781, 1792, 1794
Dyson, Gabriella 1806

E

E Arnold, Jack 2411
Ea, Hang-Korng 1135
Early, Helen 2320
Eaton, Charles 0309
Eaton, Charles 0313
Eaton, Charles 0321, 0323, 1895, 2090, 2623, 2625
Ebbo, Mikael 0756, 0891, 2532
Ebenezer, David 2486
Eberlein, Samuel 1228
Eck, Anna L 1206
Eckard, Allison R. 0393
Eckardt, Devlin 0396
Eckerdal, NIls 2060
Eckstein, Markus 0236, 0810, 1856, 2695
Edalat, Sam 0807
Edberg, Jeffrey 0040, 0041
Edberg, Jeffrey 2010
Edberg, Jeffrey 2585
Eddins, John 2566
Edelstein, Adam 1789
Edelstein, Gregory 2577
Edens, Cuoghi 2468
Eder, Lihi 0042, 0265, **0455**, **0522**, 0557, 0562, 0565, 0567, 0589, 0590, **0873**, 1455, 1710, **1714**, **1959**, 2345, **2356**, **2357**, **2358**, 2609, **2687**, **2690**
Ediboğlu, Elif 0524
Edison, Jess 0076
Edison, Suzanne 1275
Edson-Heredia, Emily 2355, 2375
Edward, Loftus 0030
Edwards, Chris 2185, **2267**
Edwards, Molly 1043, 1453, 1923, 2342, 2367
Edwards, Queeneth 1224
Edwards, Queeneth 1513, **1645**, **1646**
Edwards, Queeneth 2024
Edwards, Robert 1229, 1230, 1249
Edwards, Robert 2552
Edwinson, Adam 1558, **1855**
Efthymiou, Maria 0120, 0121, **0860**
Egües Dubuc, César Antonio 0269
Egües Dubuc, César Antonio 0639
Egües Dubuc, César Antonio 1171, 1904
Egües Dubuc, César Antonio **2107**, **2108**
Egües Dubuc, César Antonio 2229, 2269
Egana, Antton 1387, 1401
Egea Fuentes, Angela 2112, 2113
Egeli, Bugra 1177
Egli, Nicole 0990
Egloff, Christian 0919
Egorova, Alina 0403, 0476, 0503, 0779
Ehrlich-Jones, Linda 2455
Eichenfield, Lawrence 0875
Eichman, Stephanie 2327
Eickmann, Ethan **1011**
Einarsson, Jon 0434
Einarsson, Jon T 0814
Einer, Claudia 1206
Eisen, Seth 1917
Eisenhaure, Thomas 0851, 1846, 2233, 2600
Eisenhower, Christine 0602
Eisenlohr, Laurence 0923
Eisenring, Andreas 0689
Eivazi, Araz 0010
Ejnisman, Carolina 1180, 2028, 2045, 2535
Ekabe, Jabea **0904**
Ekici, Mustafa 2349
El Aatmani, Anne 1578
El Adili, Fatima-Ezzahrae 0848, 1868
El Ebrashy, Yasmin 2123
El Hasbani, Georges **1311**
El Hasbani, Georges **2531**, 2571
El Kasmi, Karim 2486
El Khoury, Lara 0947, 2182
El Maghraoui, Abdellah 0177
el mezouar, imane 2324
El Miedany, Yasser 0879
El Ouazzani, Kenza **2457**
El Rakawi, Manal 1930

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

El Sedafy, Omar Sameh Nabil 0331, 0332, 0333, 0334, 0335, 1318
El Tal, Tala 1285, 1289, 1742
Elahee, Mehreen 2644
Elam, Rachel **0354**, **2685**
El-Aoufy, Khadija 0880
Elarabi, Mohamed 0648
Elashoff, David 0451, 2227
El-ayache, Nadine 0446
El-Ayache, Nadine 0462
El-ayache, Nadine **1238**
Elbaz, Tali 2537
Elbuluk, Nada 1155
Eldaboush, Ahmed **0916**
Eldaboush, Ahmed 1777
Elder, Melissa 0780, 1671
Elefante, Elena 1380
Eleftheriadis, Georgios 0006, 0017
Eleftheriou, Despina 1287
Elena, Rabadán 1446, 1681
Elera-Fitzcarrald, Claudia 1717, 2383
Elessa, Dikélélé 2168
Elewaut, Dirk 0035, 0568, 0694, 0907, 1438, 2692
Elfadawy, Nissreen 2192
Elfar, Eman 0474
Elfrink, Sophia **2156**
El-Gabalawy, Hani 0799, 1315
Elgarten, Caitlin 2468
Elhadi, Muhammed 1222
Elhai, Muriel 0689
Elhai, Muriel 0807
Elhai, Muriel 0880
Elhai, Muriel 0884, 0967
Elhai, Muriel 1579
Elhai, Muriel 1580, 2472
Elias, Adriana 1292, 2535
Elias, Matthew 2146
Eliason, Laurie 0455, 2435
Eliot, Melissa 0578, 0579, 0580
Elisabeth, FONTANGES 2621
Elizondo-Rodriguez, Jorge Alberto 0767
Elkayam, Ori 1945, 2372
Elkibbi, Lina 1930
Elliott, Em 1847
Elliott, Susan 0188
Ellis, Alexandra 1563, 2468, 2669
Ellis, Jeffrey J. 1083, **1533**, **1534**, **2453**
El-Meanawy, Ashraf 1993
Elmusa, Reem 0435, 1359
Elnady, Basant 1959
Eloranta, Maija-Leena 0034, 0593, 0594, 2390, 2647
Eloseily, Esraa **1819**, 2134
Elrefai, Rasha 0126
Elrefai, Rasha **0421**, **1299**
Elrod, Julia **0823**
Elsayed, Manar 1103
El-Sayed, Omnia Samy 0333, 0335
Elsenpeter, Henry 1025
El-Shanawany, Tariq 0711
El-Sherbiny, Yasser 1571
Elstrom, Rebecca 0663, 2454
Eltahir, Mohamed 1409
Eltoum, Ayah **2132**
Elzorkany, Bassel 1930
Emanoilidis, Helen 2690
Emejuaiwe, Nkechi 0825
Emery, Paul 0473, 0832, 1353, 1525, 1677, 1678
Emil, N. Suzanne 2040
Emil, N. Suzanne 2077
Emirdagi, Ahmet 2094
Emmanuel, Akinola 0941
Emmas, Cathy 1552
Emmi, Giacomo 0238
Emmi, Giacomo 1592, 2532
Emokpae, Morgan 2470
Emond, Bruno 1165, 2369
Encalada, Evelin 1619
Encinales, Liliana 2576
Endo, Koji 2523
Endo, Yoshimi 0464
Enerson, Bradley 0913, 0930
Enevoldsen, Frederik **1950**, 1955
Eng, Chee-Huat L. 2668
Engelhardt, Svenja 1136, 1908
Engels, Jean 1231
England, Bryant 0022, 0045, 0076, 0155, 0198, 0221, 0222, 0328, 0462, 0834, 0836, 1125, 1238, **1308**, 1314, 1325, 1658, 1659, **1746**, 1749, 1751, 1932, 1946, 2002, 2084, 2096, 2098, 2235, 2276, 2567, 2571, 2585, 2624, **2661**, 2681, 2683
Englund, Tessa 2437
Enomoto, Hiroko 0306
Enomoto, Masataka 0306, 0311
Enright, Brian 1784
Enriquez, Eugenia 0269, 1171, 1282, 1284, 1446
Epplin, Matthew 0057
Erasani, Greeshma 2370
ERAUSQUIN ARRUABARRENA, MARIA CELIA 1397
erbasan, funda 0430
Erdman, Lauren 1279
Erdogan, Mustafa 1396
Erdogan, Mustafa 2543
Ergezen, Bilgesu 1177
Erguez, Maria 2336
Erickson, Daniel 2455
Erkan, Doruk 0120, 0121, 0128, 0144, 0860
Erkan, Mehemt 2699
Ermeidis, Panagiotis 1157
Ernst, James 0010
Ernste, Floranne 0825
Erpek, Esra 0524
Erpelding, Melissa 0410
Erra, Alba 2373
Ersoy, Ayse 0474
Ersoya, Yagmur 2543
ERSOZLU, EMİNE DUYGU 1440
Ertel, Kenneth 0002
Ertenli, Ali İhsan 2043, 2349
Erton, Zeynep Belce **0144**
Ertugrul Vardar, Burcu 0362
Esatoglu, Sinem Nihal 0241, 0760, **2543**, **2544**
Escagedo-Cagigas, Clara 0150
Escamilla-Barrientos, Estefania 2557
Eschholz, Alec 1119
Escobar, Alejandro 0252, 2034
Escudero, Alejandro 0072, 0087, 2502
Escudero Contreras, Alejandro 0070, 0071, 0094, 0108, 0496, 0542, 0795, 1851, 2268, 2323
Escudero-contreras, Alejandro 0100
Escudero-Contreras, Alejandro 0583
Escudero-contreras, Alejandro 0901
Escudero-Contreras, Alejandro 2371
Escudero-contreras, Alejandro 2599
Esencan, Deren 2478
Esfandiari, Ehsanollah 1538
Eshak, Nouran 0759
Eshed, iris 0543, 0854, 1945
Eshraghi, Yashar 1228
Eskew, Alisha 0893
Espadaler Fabregó, Ignasi 1620
ESPARTAL, ESTHER 0180
Espasa, Gabriela Vanesa 2405
Esperanzate, Carl 0301
Esperanzate, Carl 1651
Espersen, Caroline 1166
Espigol-Frigolé, Georgina 0732, 0896
Espigol-Frigole, Georgina 1605, 2532
Espinosa, Alejandra 0443, 2674
Espinosa Ortega, Farbicio 2060
Espinoza-Gámez, Jesús Gilberto 0767, 1022
Espitia, Olivier 0891, 2532, 2704
Esposito, Pasquale 0650
Esquivel Valerio, Jorge Antonio 0596, 0621, 0623, 1486, 1491, 1530, 1687
Esserman, Denise 0674
Essien, Margaret **1392**
Estébanez, Andrea 0244
Esteban, Ysabella 0413
Esteban Ortega, Mar 0268
Esteban Vázquez, Ana Victoria **0201**, 1961
Estepar, Raul San Jose 1751, 2235
Estes, Christopher **2550**, **2551**
Esteve, Emmanuel 0618
Estevez-Lopez, Fernando 1933
Estrada-Alarcón, Paula 0019, 0496, 0744, 0757, 1382
Estrada-Alarcón, Paula 1397, 1681
Estrada-Alarcón, Paula 2268, 2290, **2299**
Estrada-Anguiano, Carlos I. 0366
ESTRELLA, ANA MONICA 2004
Estremera, Rebecca 2468
Ettner, Susan 0478

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Eudy, Amanda **0363**, 0367, 0610, 0793, 1160, 1487, 2210, **2379**
Eun, Yeonghee 0170
Evangelatos, Gerasimos 1439, 2232
Evangelista, Melissa 2614
Evangelopoulos, Maria Eleftheria 2025
Evans, Celia 0991
Evans, Daniel 0320
Everett, Brendan 2607
Evnin, Luke 0883
Evnin, Luke 1555, 1566
Evnin, Luke 1582, 2475
Evnin, Luke 2654
Ewart, David 2094
Exarchou, Sofia 0525, 0539, 2635
Exner, Tarik 0932
Expósito-Pérez, Lorena 2422
Exposito, Lorena 1282, 1284
Eyman, Ethan 2049
Eyraud, Armand 2080

F
Fábregas Canales, María Dolores 1548
Fırlatan Yazgan, Büşra 0778, 1188, 2043, 2349
Fähndrich, Sebastian 1403
Fabiani, Caludia 0275
Fabregat, Aina 0575
Fabregat, Aina 0642, 0749
Fabregat, Aina 2299
Fabris, Martina 2545
Fabro, Cinzia 2545
Fadairo-Azinge, Abimbola 0220, **1972**
Fadairo-Azinge, Abimbola **2618**
Faddoul, Giovanni 0698, 0699
Faenza, Mario 1864
Faeti, Cosimo 0532
Fagan, Evelyn 1898
Fagerland, James **1659**
Faghihi-Kashani, Sara 1201, 2618
Fagin, Elizabeth 0633
Fagni, Filippo 0878, 2613, 2686, 2695
Faguer, Stan 2510
Fahimuddin, Muhammad 1063
Fain, Olivier 1339
Faine, Brett 2006
Fair, Danielle 0411, 1066
Fairchild, Robert 0092, 1172
Fairhead, Todd 0722
Fairley, Jessica 0677, 1716
Fairman, Robert 2559
Faisal, Seemal **2224**
Faiz, Anum 1539
Fajardo, Renee Gabrielle 2563
Fajardo Hermosillo, Luis Daniel **0620**
Fakhouri, Walid 1348
Fakih, Olivier **0544**, 2637
Falaas, Kari **0256**, **2094**
Falasinnu, Titilola **1086**
Falco, Antonia 1863
Falcone, Valeria 1875
Falduto, Guido 2666
Faleye, Ayodele 1706
Fallah-Arani, Farnaz 2631
Fallon, Lara 1444
Falsetti, Paolo 1616
Falzon, Louise 0588, 2307
Fan, Liya 0649
Fan, Tianrui 0908
Fan, Wei 2672
Fan, WuQiang 0344
Fan, Yangyi 0116
Fan, Yanliu 1776
Fan, Yanni 0247
fan, yanru 0915, 0998
Fan, Yuying 0124, 0142, 0856, **1971**
Fan, Zhihua Tina 0321
Fang, chih 0349
Fang, Meika 0240, 1048
Fang, Min 0876
Fang, Pu Jun 1540
Fang, Siran 0640
fang, yao fan **1344**
Fang, Yao-Fan 2469
Fang, Zhiwei 0989
Fang, Zhou 1684
Fanger, Gary 0482
Fanjul, Alfonso Del Peral 0062
Faraguna, Ugo 1381
Farahat, Fayssal M 0202
Faraone, Stephen 0657
Farge, dominique 1529
Farhadi, Payam 0159, 0289, 0302
Farhat, Reem **2222**
Farhat, Sylvia 1292, 2535
Faré Garcia, Regina 0496, 2268
Faria, Raquel 2648
Farias, Lucas 2682
Farietta, Sandra 1943
Farina, Nicola 0673, **0702**
Farinha, Filipa 1851
Farisogullari, Bayram 0474, 1136
Farkas, Róbert 2684
Farooq, Hareem **0368**
Farran-Centelles, Nuria 0896
Farrell, Easton 1783
Farris, A. Darise 0034, **0506**, 0509, 0514, 1682, 2233
Farrukh, Larabe **2197**
Farsijani, Sameneh 0320
Faruch, Marie 1200
Faruq, Mohammed 1197
Farzaneh-Far, Ramin 1003
Fassett, Marlys 0110
Fassio, Angelo 1598
Fassio, Angelo 2592
Fathi, Nihal 0884
Fatima, Husna 1423
Fatima, Moeeza 0556
Fattorini, Federico 1380
Fauchais, Anne-Laure 0516
Faucher, Ariane 0561, 2689
Fautrel, Bruno 0147, **0470**, 0780, 1095, 1185, 1334, 1348, 1671, 2032, 2080, 2137, 2138, 2139
Fava, Andrea 0597, 0607, 0772, 0837, **0840**, **0842**, **0851**, 1240, 1480, 1498, 1499, 1516, 1846, 2421, 2436, 2581, 2600
Favier, Leslie 0409
Favier, Leslie 0410
Fawad, Aslam 0385
Fayad, Ghassan 1437
Fayed, Fatma 2123
Fazeli, Parastoo **0663**, 2454
Fazzari, Melissa 1944, 1974
Fazzi, Benedetta 0238
Fearon, Ursula 0925, 1757
Feather, Vivi 2320
Fedler, Janel 1674
Fedorchenko, Vladyslav 1757
Feemantle, Nicholas 0692
Feghali-Bostwick, Carol 0808, 2495
Feher, Attila **2470**
Fehres, Cynthia 1568
Fei, Xue 0913, 0930
Fei, Yunyun 1036
Feinstein, Matthew 1553
feist, Eugen 0499, 1349, 1356, 2279
Fekete, Mary Jo **2561**
Feld, Joy 1436
Feldman, Brian 0289, 1286, 1287, 1288, 2136
Feldman, Candace 0156, 0283, 1011
Feldman, Candace 1019, **1057**
Feldman, Candace 1073, 1705
Feldman, Candace 1894, 1896
Feldman, Candace 2276
Felices López, Borja 1321
Felipe, Adamary 2327
Felix, Christele 0047, 2285
Felix, Nicole 2316
Felson, David 0165, 1643, 1647, 2526
Fenaux, Pierre 1339
Feng, Changyong 1060
Feng, Daying 2353
Feng, Rui 0278, 1474, 2428
Feng, Ruiling 2303
Feng, Wei 1114, 1799
Feng, Xintong 2465
Fennell, Gillian **1229**, **1230**
Fentie, Kindalem 0727
Ferguson, Beatrice 0663
Ferguson, Polly 1149, 1669, 1670, 2125, 2128
Ferguson, Rina **0422**
Ferguson, Ryan 1125, 2001, 2585
Ferguson, Sancia 0218, 1050, 1052
Fernández, Gema 0728
Fernández, Núria 1620
Fernández Díaz, Carlos 2112, 2113, 2265
Fernández Guill, Esther **1412**
Fernández Jover, Eduardo 1412

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Fernández Nebro, Antonio 0021
Fernández Sánchez, Susana 1620
Fernández Salamanca, Montserrat 2112, 2113
Fernández-Aguado, Sabela 2290
Fernández-Cabero, Juan José 1094
Fernández-Fernández, Elisa 0752
Fernández-Gutiérrez, Benjamin 0454
Fernández-Puente, Patricia 0329, 1798
Fernandes, Ana 0743, 1606, 2033
Fernandes, José Mauro 1407, 1408, 2326
Fernandes, Melissa 2696
Fernandez, AJ **1348**
Fernandez, Anabel 1825
Fernandez, Anthony 2533
Fernandez, Daniel 1491, 2336
Fernandez, David 1282, 1284
Fernandez, Diana 0596
Fernandez Castro, Monica 0019, 1170, 1397, 1681, 2290
Fernandez Codina, Andreu 1355
Fernandez Davila, Jorge 1801
Fernandez de la fuente Burson, Lola 2373
Fernandez Ruiz, Ruth 0802
Fernandez-Lozano, Delia **0744**
Fernandez-Salinas, Daniela 1696, 2410
Fernández-Nebro, Antonio 0087, 0728, 1878, 1899, 2373, 2422
ferrada, Marcela 0258, 0260, 0777, **1625**, 1949, 2663, 2701
Ferrannini, Alexandra 0889
Ferraro, Kerry 0411, 1066
Ferraro, Kerry 1978
Ferraz Amaro, Iván 0604, 1164
Ferraz Amaro, Ivan 0200, 0244, 0270, 0272, 0450, 0608, 0736, 0737, 0739, 1612, 1613, 2016, 2538, 2610
Ferreira, Nicole 2457
Ferrer, Diego 2016
Ferrero, Stephanie 0148
ferreryra, Leandro 1218, 1422, 2336
Ferre-Sanfrancisco, Mauro 1335
Ferretti, Andrew P. 0888, 0997
Ferri, Clodoveo 2482
Ferrigno, Elisa 0723
Ferro, Francesco 0723, 1380, 1385, 1951
Ferry, Judith 2033
Fert-Bober, Justyna 0067, 0085
Ferucci, Elizabeth 0186, 2645
Feser, Marie 0076, 0088, 0774, 0775, 0833, 0889, 1674, 2227
Feterman Jimenez, Dominique 1718
Feuchtenberger, Martin 2279
Fevrier, Stephanie 1290
Fiallo Suárez, Dolly Viviana 0269, 1171
Fidanci, Ali Aykut 1008
Field, Natania 0846
Fields, Anne 2142
Fierkens, Roselyn 0819, **1824**
Fifi-Mah, Aurore 1607
Figgie, Mark 0464, 2385
Figueiredo Neves Yuki, Emily 0206, 0596, 0619, 2573
Figueroa-Parra, Gabriel 0366
Figueroa-Parra, Gabriel 0601
Figueroa-Parra, Gabriel 1022, 1023
Figueroa-Parra, Gabriel 1527, 1721
Figueroa-Parra, Gabriel 1928
Figueroa-Parra, Gabriel 2403
Figueroa-Sánchez, Allison 0714, 0730, 2521
Fike, Alice 0258, 2533
Filer, Andrew 0798, 1678, 1702
Filková, Mária 0831, 2279
Filla, Tim 0026, 0166, 0809, 0810, 0956, 0962, 0974, 0975, 1856
Fillipo, Rebecca 0784
Filocamo, Giovanni 0389
Filosto, Simone 0002
Finch, Christopher 1437
Fini, Jean-Baptiste 1735
Fink, Daniel 0192
Fink, Howard 0354
Finlay, Teresa 1244
Finney, Amanda 1207
Finzel, Stephanie 1136
Finzel, Stephanie 1175
Finzel, Stephanie **1403**, **1908**, 2696
Fiore, Stefano **1629**
Fiorentino, David 1194, 1214, 2062
Fiorentino-Rozek, Ewa 2398
Firestein, Gary 0069, 0097, 0199, 0833, 0889
Firestein, Gary 0914
Firestein, Gary 1695, 2576
Fisch, Anna 0377
Fischer, Christian 0711, 2396, 2397, 2398
Fischer, Laura A 1206
Fischer, Ozana 2696
Fischer-Betz, Rebecca 2210
Fish, Ian 1136
Fish, Irina 1676
fishbein, Anna **1306**, **1327**
Fisher, Benjamin A. 1678, 1685
Fisher, Julia 1708
Fisher, Michael **1270**
Fishman, Jessica 0187
Fist, Alex 0404
Fiter Areste, Jordi 2106
Fito-Manteca, Concepción 2450, 2670
Fitzcharles, Mary-Ann 1046
Fitzgerald, G Kelley 0765
Fitzgerald, Gillian 1409
FitzGerald, John 0240, 0478, 1048
Fitzgerald, Kathryn C. 0288
FitzGerald, Oliver 0111, 0590, 0873
Fitzgerald, Timothy P. 1165, 2369
Fitzpatrick, Brianna 2561
Fitzpatrick, Jessica 0219
Fitzpatrick, Jessica 1639
Fitzpatrick, Jessica 1640
Fitzsimmons, Robert 0546
Fløjborg, Sille 2400
Flamion, Bruno 1519, **2440**
Flanagan, Colleen 2618
Flanagan, Steve 1563, 2468, 2669
Flatø, Berit 0420
Flauto, Ron 0661
Fleisch, Abby 0321
Fleischer, Anna 1450
Fleischer, Chelsie 1674
Fleischmann, Anja 0471
Fleischmann, Roy 0473, **0499**, **1676**
Flipo, René-Marc 0566, 1095, 1356
Florence, DUVERT 2621
Flores, Daniella 1972
Flores, Francisco 0002
Flores, Marta **0542**, 2323
Flores Robles, Bryan Josué 0250
Flores Trejo, Javier Federico 0432, 1422
Flores-Alvarado, Diana E. 0767, 1022, 1527, 2325, 2553, 2606
Flores-Gouyonnet, Jaime 1721, **2403**
Flores-Hernández, Daniela 1482
Flores-Hernández, Ileana 1482
Fluder, Natalia 2443
Flynn, Broderick 0181
Flynn, David 2526
Fodeh, Samah 2114
Foeldvari, Ivan 0405
Foeldvari, Ivan **1287**, **1288**
Foell, Dirk 0358, 0918
Foell, Dirk 2137
Foell, Dirk 2138, 2139
Fogel, Olivier 0114, 0214, 0215, 0489, 1312, 1333
Folkestad, Lars 2119
Folta, Sara 2429
Fondin, Simon 2080
Fong, Warren 0854
Fong, Warren Weng Seng 0304
Fonseca, André 0015
Fonseca, Diogo 0761
Fonseca, Eduardo 0021
Fonseca, João Eurico 0035, 2179
Fonseca, Rita 1430
Font, Pilar 0071, 0072, 0087, 0094, 1851
Fontana, Giulia 0238, 0251
Fontas, Eric 0148
Font-Urgelles, Judit 0019, 0117, 0269, 0270, 0271
Font-Urgelles, Judit 0659
Font-Urgelles, Judit 0758, 1171, 1397
Font-Urgelles, Judit 1548, 1681
Font-Urgelles, Judit 2029, 2290
Font-Urgelles, Judit 2450
Foos, Julia **1603**
Forbess, Lindsy 0774, 1674
Forcade, Edouard 2696
Forcadell Pirretas, Eva 2029
Ford, Julia 1623
Ford, Kerri 1629
Ford, Melissa 0913, 0930

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ford, Stephanie 1073
Forer, Ester 1304
Forero, Jose 0199, 2576
Forero, Luisa 1292, 2535
Formanti Alonso, Lydia 0795
Fornaro, Marco 1212, 2075
Foroozan Boroojeni, Shaghayegh 0098, **0113**
Forrest, Noah 0624
Forsyth, Katherine 1723
Forte, Giulio **1835**
Forte, Giulio **1864**
Fortier, Avery 1888
Fortin, Paul 0120, 0121, 0376, 0606, 1109, 1475, 1722, 2416
Fortune, Farida 1396
Fossey, Stacey 1784
Fosso, Magan **1294**
Foster, Caroline 1590
Foster, Jenny 1256, 1257
Foster, Phillip 2117
Foti, Roberta 0673
Fotis, Lampros 0407
Foucher, Kharma 0769
Foucher, kharma 0770
Foucher, Kharma 0788
Foulke, Galen 0227, 0984, 1271, 1523
foulquier, nathan 2241
Fournel, Isabelle 0891
Fournier, Coline 1703
Fournier, Laure 0327
Fournier, Lison 1109
Fox, David 0093, 0774, 1590, 1674, 2494
Fox, Emily 0409, 0410
Fox, Jeffrey 1753
Fox, Jennifer 0020
Fox, Robert 1378, 1384
Foxall, Madelane 1551
Fox-Bosetti, Sabrina 0501
Fröhlich, Matthias 0762, 1450
Fróes Ramos de Lima, Renata **1400**
Frade, Beatriz 0505
Frade Sosa, Beatriz 0269, 0379, 0380, 0642, 1018, 1171, 1943, 2450
Fraga-Enriquez, Victor M 0458, 1427, 1483
Fragío Gil, Jorge Juan 0270, 0271, 0538, 0642, 0659, **2406**, **2407**, 2450, 2460
Fragiadakis, Gabrielle 1816
Fragkiadaki, Kalliopi 2232
Fragoso-Loyo, Hilda 0596, 0621, 0623, 1469, 1482, 1486, 1530
Fragoulis, George E **1439**, 1452
Frahm, Jens 1205
França, Matheus 1292, 2535
Franc, Benjamin 1172
Francés, Rubén 1133
Francavilla, Michael 0390, 0428, 2677
Franceschini, Franco 0238, 0251, 2411
Franchini, Roberto 0246
Francisco, Janelle 2077
Francis-Malave, Adela **1733**
Franco, Andre 2292, 2682
Franco, Marcella 1696
FRANCO HONDERMANN, BEATRIZ MARIA **2505**
Frank, Charissa 2179
Frank, Daniel 0088
frank, erin 0829
Frank-Bertoncelj, Mojca 0807
Fransen, Signe 2275
Frantsve-Hawley, Julie 1378, 1384
Frantz, Aric 1003
Franz, Anika 1934
Fraser, Nicola 0626, 0853, 1391
Frauenfelder, Thomas 0510, 0880, 1579, 1580
Frazer-Abel, Ashley 1674
Frech, Charles 0709
Frech, Tracy 0689, **0709**, 0883, 1555, 1566, 1572, 1582, 1952, 1953, 1954, 1969, 2413, 2475, 2651, 2654
Frechette, Grace **0983**
Frechette, Noah **1320**
Frediani, Bruno 0275, 1616, 2075
Freed, Brian 1701
Freeman, Eric **0783**
Freese, Rebecca 0285
Freiberg, Cynthia 1280
Freilich, Bryan 1479
Freire, Marianna 1293
Freire Dapena, Mayka 1210, 1953
Freire González, Mercedes 0019, 2422
Freitag, Merle 1875
Freitas, Thiago 0619, 1180, 2028, 2045, 2527, 2535
FREITES, DALIFER **0183**, 0270, 0271, 0483, 0737, 1024, 1269, 1548, 2036
Frelinger, Kees 1160
French, Kaci **0491**
French, Melissa **0373**
French, Sarah 0851
Fretheim, Havard 0510, 1867
Frey, Nicolas 0650
Frey Law, Laura 1247, 1643
Friberger Pajalic, Katarina 0434
Frideres, Halie 1308, 1658, 1746, 1946
Frieda, Kirsten 2668
Friede, Tim 1205
Friedly, Janna 2634
Friedman, Elliot 0712
Friedman, Joshua 0050, **2035**
Friedman, Karen 2182
Friedman, Marcia 0893
Friedrich, Matthias 1866
Friedrichsen, Erik 0411, 1066, 1978
Friend, Christopher 0920
Frigault, Matthew 2468
Friskey, Jacqueline 0182
Frison, Eva 0104
Fritz, Shelley 1617, 1987
Fritzler, Marvin J. 2414, 2419
Frkovic, Marijan 2699
Frodlund, Martina 0593
Frodlund, Martina 0594
Frodlund, Martina 2390
Frodlund, Martina 2647
Fromhold, Mark 0501
Frommer, Klaus 0075, 0090
Frumker, Lindsay 0603
Frumker, Lindsay 0741
Frumker, Lindsay 1151, 1471, 1500, 1501, 2216
Frumker, lindsay 2382
Frumker, Lindsay 2389
Frutoso, Marie 2296
Frye, Björn Christian 1403
Fu, Fenggen 0906
Fu, Qiong 0887, **1179**
Fu, Qiong 1663
Fu, Qiong **2465**, **2672**
Fu, Tianmin 0918
Fu, Yakai 1179, 2465, 2672
Fu, Yong 0013
Fuentes, Martin 1194
Fuentes-Rios, Fabiola Alejandra 2606
Fujieda, Yuichiro 1854, **2289**
Fujii, Takayuki 0850
Fujimori, Musuzu 0459
Fujimoto, Minoru 1358
Fujio, Keishi 1512
Fujiwara, Yu 1732
Fukami, Toshikazu 2253, 2254
Fukui, Ryutaro 1848
Fukui, Sho 0638, 2225, **2640**, 2660
Fukui, Shoichi 2523
Fullam, Spencer 1782
Fuller, Julie 0119
Fulvio, Giovanni 1380, 1381, **1385**, 1951
Funakubo, Yu 0084
Funes Soaje, Carmen 0596, 0623, 1530
Furchtgott, Leon 0617
Furer, Victoria 1945
Furie, Richard 0650, 0654, **0664**, **0665**, 0802, 0851, 1240, 1505, 1520, 1521, **1542**, 1545, 1552, 2445, **2466**, **2467**
Furio, Laetitia 0653
Furlan Freguia, Christian **0482**
Furmanak, Thomas 1563, 2468, 2669
Furst, Daniel 1562, 2477
Furth, Christian 0471
FURUSAWA, HOSHIKO **0106**
Furuta, Shunsuke 1630
Fusama, Mie 2564
Fushimi, Kiyohide 2449
Fussner, Lynn 0719
Fuster-Matanzo, Almudena 0538
Fytanidis, Nikolaos 1452

G

G Schütz, Saskia 1205
Gálvez Sánchez, Rafael 0029, **0270**, **0271**, **0272**, **2538**
GÓMEZ, ENRIQUE J 0180

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Görg, Boris 0809
Gühring, Hans 0802
Günther, Sven 2262
Güzelbey, Tevfik 1965
Gómez, Lara 0559, 1447, 1464
Gómez, Susana 1321, 1413, 2311
Gómez Correas, Berta 2460
Gómez Escorcia, Lorena 0623, 1491, 1530
Gómez Gómez, Alejandro **0019**, **2290**, **2291**
Gómez-Bernal, Fuensanta 0604
Gómez-Rodríguez, Amairani 1482
Gómez-Sabater, Silvia 1133
Gómez-Velasco, Donaji 1383
Gačnik, Marko 0748
Gabarain Morcillo, Imanol 2107, 2108
Gabriel, Olivia 0501
Gabriela Savio, Veronica 0621
Gabrielli, Marco 0407
Gabrie-Rodriguez, Ligia 0029, 2023, 2059
Gacía-Díaz, Silvia 1382
Gad, Hoda 0234
Gad, Ibtissam 0825
Gad, Ibtissam **2180**
Gad El Sayed, Marina 0374
Gadina, massimo 0301
Gadina, Massimo 1651
Gadiraju, Chinmay 0992
Gaffney, Karl 1462, 1463, 1464
Gaffo, Angelo 0372, 1048, **1259**, 1997, 2009, 2172, 2585, **2588**
Gaggiano, Carla 0275
Gagne, Samuel 2126
Gahl, willian 0301
Gaiha-Rohrbach, Janine 0645, 2408
Gaikwad, Mahesh 1472
Gailis, Didzis **1729**
Gaillez, Corine 0801
Gaisl, Thomas 1872
Gajbhiye, Drumadala 1890, 1891
Gajjala, Sankeerthana 1688
Galand, Claire 1767, 2033
Galíndez Agirregoikoa, Eva 0200, 0270, 0271, 0737, 0739, 0752, 0757, 1612, 2610
Galanter, William 1511
Galarcé Lugo, Gelis 1227
Galarza-Delgado, Dionicio A. 0212, 0213, 0248, 0366, 0458, 0512, 0614, 0767, 1022, 1023, 1389, 1427, 1483, 1486, 1527, 1528, 1633, 1687, 1834, 1845, 1928, 2058, 2171, 2219, 2325, 2549, 2553, 2557, 2606
Galbavy, william 0897
Galecio Chao, Andrea **2230**
Galetta, Kristin 0263
Galien, René 0653
Galimberti, Ricardo 0875
Galindez Aguirregoicoa, Eva 0485, 2350
Galindo Domínguez, Laura **0454**
Galindo Santos, Angela 0342
Galindo-Bandt, Aranxa 1023
Galindo-Calvillo, Eva Abigaid 0212, 0213, 1633, **1834**, 1845, 2171, 2219, 2557
Galindo-Izquierdo, María 0639, 0642, 1878, 2422, 2450
Galindo-Izquierdo, Maria 1899
Galisteo, Carlos 0757, 1397, 1681
Galisteo Veiga, Carles 0019, 2290
Gallagher, Molly 1825
Gallego, Adela 0271
Gallego, Laura 0252
GALLEGO FLORES, ADELA MARIA 0270
Gallegos-Gloria, Laura Patricia 2557
Gallmann, Martin 2612
Galloway, James 0190, 0488, 1077, 1906
Gallucci, Stefania 2425
Gallucci, Stefania 2668
Galvan, Diana 1003
Galvao, Rachel **1985**
Gamal, Sherif 1930
Gambina, Karen 1159
Gamboa-Cárdenas, Rocío 0605, 0714, 0730, 1717, 1878, 1899, 2378, 2383, 2521
Gamez-Siller, Pablo 2606
Gan, Tji 1860
Gan, Yuzhou 0141, **0143**
Ganatra, Darshini 0042
Gandhi, Dhruv 1795
Gandhi, Jyotika 1376
Gandolfo, Saviana **1402**
Gandu, Asrith Reddy **1039**
Ganguli, Minoti **1393**, **1394**
Gangwani, Bharti 0392, 0406, 0414
Gao, Ce 0797, 0808, 2233
Gao, Han 0915
Gao, Jing 0077
Gao, Jingchen 0519
Gao, Lu 0861
Gao, Min 1837
Gao, Shangyi 0552, 1415, 1416, 1425, 1426
Gao, Sheng 1839, 2297
Gao, Tianming 0557, 0589, 1349, 1435, 2273
Gao, Yuqing 0178
Gara, Andrew 1676
Garaiman, Alexander **2340**
Garantziotis, Panagiotis **0628**, 0641, 2442, **2461**, 2695
Garaude, Johan 1873
Garber, Manuel 2668
García, Sara 0346
García Aparicio, Angel 0270
García Cirera, Silvia 2450
García de la Peña Lefebvre, Paloma 0249
García Fernández, Antía 1404
García Frías, Soledad 2106
García García, Verónica 0180, 1335, 1561
García- Guijarro, Elena 1210
García Herrero, Juan 0982
García Loiseau, Ivana 1129
García Magallón, Blanca 1170
García Manzanares, Ángel 1548
García Olivas, Doryan 1490
García Portales, Rosa María 2373
García Sánchez, Valle 0021
García Salinas, Rodrigo 0557, **0584**, 0854, **0877**, **2257**, 2336
García-Alija, Asier 0530, 1620
García-Carazo, Sara 0894
García-De la Torre, Ignacio 0623, 1486, 1530
García-Delgado, Gema Dolores 0100, 0901
García-Fernández, Javier 2422
García-González, María 0604
García-Hernández, José Carlos **1164**
García-Herrera, Iris Paola 2321
García-Sevilla, Mónica 1964
García-Valladares, Ignacio 1491
García-Valle, Andrea 1547, 1548, 2016, 2229
Garceau, Alicia 1275
Garchon, Henri-Jean 0103, 0104
García-Escudero, Paula 0250, **0269**, **1904**
Garcia, Alicia 0153, 0269, 0752, 1171, 1282, 1284, 1446
Garcia, Alvaro 0351
Garcia, Andrea 1620
Garcia, Daniel 0317, **1264**
Garcia, Elisabet 2373
Garcia, Jose 0446, 0462, 0836, 1238, 2251, 2252
Garcia, Julian 0065
Garcia, Lucila 1491, 2405
Garcia, Mayra 2059
Garcia, Mercedes 0623, 1530, 2405
Garcia, Paola 2581
Garcia, Steven 0769, 0770, 0788
garcia, william 0083
Garcia Belando, Clara 0269, 1171
Garcia Escudero, Paula 0485, 1171, 2350
Garcia Fernandez, Antia 0608, 1561
Garcia Fructuoso, Ferran José 1456
Garcia Herrero, Juan 0882
Garcia Llorente, Jose Francisco 2422
Garcia Vadillo, Jesús Alberto 1397, 1681
Garcia Vicuña, Rosario 0019, 1869, 2030, 2122, 2344, 2491
Garcia Vivar, Maria Luz 0485, 1904, 2350
Garcia-Agundez, Augusto 0189, **1657**
Garcia-Aparicio, Angel 0268, 0271, 1397, 1681, 2450
Garcia-Arellano, Gisela 1687
Garcia-Bravo, Jennifer 0366
garcia-Carrillo, fernanda m. 2058
Garcia-Carrillo, Fernanda M. 2071
garcia-Carrillo, fernanda m. 2072
Garcia-Garcia, Fernanda M. **0366**, 0458, 0614, 1023, 1427, **1483**, 1486, 1528, 1928

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Garcia-Gonzalez, Carlos 0231
Garcia-Hernandez, Maria de la Luz 0942, **1753**
Garcia-Hirsh, Samira 1717, 2378
Garcia-Magallon, Blanca 1547
Garcia-Pompermayer, Mario R. **2187**
Garcia-Ramos, Gemma Alely 2606
Garcia-Torralba, Ariel 1383
Garcia-Villanueva, Maria 0642, 0744, 2422, 2450
Gardiner, Philip 2333, 2334
Gardner, Benjamin **1260**
Gardner, David 0798
Gardner, Sarah 0016
Garfinkle, Samuel 0396
Garg, Jay 0650
Garg, Jay 0664
Garg, Jay 0665
Garg, Jay 1521
Garg, Shivani 0217, 0218, 0670, 0805, **1050**, **1051**, **1052**, **1722**
Gargiulo, Maria de los Angeles 0596, 1486
Garijo Bufort, marta 0268
Garijo Bufort, Marta 1548
Garijo Bufort, marta 2038, 2450
Garikipati, Naga Alekhya 2050
GARMENDIA, Alexandre **0477**
Garmendia Sánchez, Elena 1904
Garner, Stephanie 0721
garo, florian 1604
Garrabou, Gloria 0296
Garrard, Lili 0377
Garratt-Wheeldon, Jade 1889
Garrido, Diego 0346
Garrido, Noemí 0744, 0752, 1548
garrigues, florent 0477, 2241
Garrison, Andrew 2273
Garrote Corral, Sandra 0642, 0659, 2450
Garrote-Corral, Sandra 1561
Garshick, Michael 0242, 1186, 2688
Gartshteyn, Yevgeniya 0899, **1853**, 1942, 2693
Garyfallos, Alexandros 2232
Garza Elizondo, Mario 2187
Garza-Elizondo, Angel Kevin 0248, 0767, 2606
Garza-Flores, Oscar Azael 0458, 0614, 1427, 1483, 1486, 1528
Garza-Gonzalez, Esteban C. 0458, 1427, 1483, **1528**
Garzon, Belcy 1041
Gasman, Sarah 1878, 1899
Gasparin, Andrese Aline 1486
Gasperi, Marianna 1238
Gastaldello, Stefano 0280
Gaston, Julie 0162
Gattegno, Roni 0936
Gatti, Alessia **0238**
Gatti, Alessia 0251, 1212
Gatti, Davide 2117, 2592
Gatto, Mariele **0803**
Gattorno, Marco 0358, 0484, 2137, 2138, 2139
Gauffre, Alexia 0618
Gaujoux-viala, cécile **0147**
Gauna Leal, Derek de Jesus 2606
Gautam, Surabhi **0063**
Gauthier, Genevieve 1336, 1444
Gautier, Laurène 1448
Gavali, Meghna 0291, **1423**, 1771, **2417**
Gavi, Maria Bernadete 1407, 1408, 2326
Gawde, Saurabh 1172
Gaylis, Norman 2278
Gazeley, David 0218, 1050, 1051, 1052
Gazi, Sousana 1439, 1452
Gazi, Sousana 2232
Gaziano, J. Michael 2276
Gazitt, Tal 1436
Gbadegesin, Simisola 1745
GC Horlings, Corinne 1205
Ge, Kyle 1102, 1730
Ge, Wengang 1532
Ge, Wengang 2452
Ge, Yong 0325
Gea González, José Luis 2106
Geary, Meghan 1989
Gebhardt, Christina **2476**
Gedert, Rosemary 0161, 2498
Gedik, Kader 0920
Geier, Florian 0919
Geiger, Miwa 0853, 1391
Geiss, Celina **0807**
Gelfand, Jeffrey 1251
Gelfand, Joel 1912
Gellman, Mollie **2039**
GENC, Aysun 1968
Gencerliler, Nihan 1628
Gendebien, Zoe **1738**
Gendelman, Omer 0570, 1332
Geng, Chengchun 0102, **1754**
Gennarelli, Renee L. 1536, 2456
Genova, Carlo 1097
Genovese, Mark 0473
Gensler, Lianne S. 0569, 0854, **1449**, 1454, 1465, 2352, 2634
Gente, Karolina 0192, 1729
Gentileschi, Stefano **0275**
Geny, Bernard 0516, 0862
Georganas, Konstantinos 2232
George, Michael 0045, 0046, 0825, 0834, **1049**, 1434, **2068**, 2681, 2683
George, Roslin 1311, 1320
George, Tad 1787
Georges, George 1563
Georgiadis, Stylianos **1430**
Georgiev, Tsvetoslav 1210
Georgin-Lavialle, Sophie 0260, 0735, 0777, 1339, 1651, 2663
Georgiou, Panagiotis 2232
Geraci, Nicholas 2062
Geraghty, Terese 1790
Geraghty, Terese 1800
Geraldino-Pardilla, Laura 0661, 1942, 1970, 2693
Gergely, Peter 1685, 2696
Gerhard, Tobias 0399, 0400
Germano, Davide 2458
Germinaro, Matthew 0257
Gernert, Michael 0762, 1450
Gerolymatou, Nafsika 1439
Gerosa, Maria 0120, 0121, 0860
Gersh, Eugene 2089
Gertner, Elie 0256
Gervais, Elisabeth 0105
Gerwien, Jens 1348
Getachew, Liya Sisay 0168, 0465, 1751, 1902, 2235, 2574, **2577**, 2578
Gewurz, Benjamin 1696
Gezer, Halise Hande 2322
Ghanoongooi, Nahal 1584
Ghanshani, Swati 0801, 1189
Gharaee-Kermani, Mehrnaz **0949**, 0985, 1760, **2418**, 2451, 2598
Gharib, Miral **2638**
Ghebranious Farag, Michelle 1256, 1257
Gheller, Mary 1229, 1230
Gheorghiu, Ana Maria 0702, 1562, 2477
Ghetie, Daniela 0239
Ghetie, Daniela 0893
Ghetie, Daniela 1666
Ghiglione, Graciela Liliana 0432
Ghigna, Maria-Rosa 1185
Ghimire, Brijesh 0456
Ghimire, Dibya 2577
Ghimire, Kalpana 2514
Ghimire, Manoj 0492, 2514
Ghio, Gaston Ariel **1619**
Ghiringhelli, Charles 2115
Ghirri, Matteo 1737
Ghosh, Dr Alakendu 2295
Ghosh, Monalisa 0843
Ghosh, Monalisa 1563
Ghosh, Nilasha 1102, 1107, 1108
Ghosh, Parasar 1203
Ghosh, Shounak 2065
Ghosn, Muriel 0648
Ghossan, Roba 2115
Gómez-Martín, Diana 0287, 1836, 1841, 2052, 2053, 2078, 2674
Giacca, Rosa 1835
Giacomelli, Roberto 0391
Giacomelli, roberto 1864
Giacomelli, Roberto 2497
Giaglis, Stavros 0919
Giaime, Emilie 0016
Giancotti, Luigino **1737**
Gianfrancesco, Milena 1336
Giannakakou, Paraskevi 0515
Giannini, Margherita 0516
Giannini, Margherita **0862**
Giardini, Henrique 0619, 1180, 2028, 2045, 2527, 2535
Giarrano, Gianni 0999

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Gibbons, Sue **1186**
Gibson, Andrew 0040, 0041
Gibson, Kevin 1201
Gibson, Mary 0725
Gibson, Noel 2140
Gierisch, Jennifer 2207, 2208
Gifre-Sala, Laia 0117, 2029
Giglioli, Noemi 2296, 2300
Gil Calderón, Diana Rocío 0684
Gilbard, Zoe 2429
Gilbert, Mileka 0393, 0411, 1059, 1066, 1976
Gilbert, Ross 0218
Giles, David 0050
Giles, Jennifer 1981
Giles, Jon 0067, 0085
Giles, Jon 1310
Giles, Jon 2176, 2258, 2607, 2681
Gilkeson, Gary 0617, 0952, 1082, 1842
Gill, Muneet 1142
Gillcrist, Rachel 2084, 2096
Gillcrist, Rachel 2098
Gillcrist, Rachel 2624
Gilles, Greg 2085, **2091**
Gillespie, Mark 0833, 0889, 1695
Gillispie-Taylor, Miriah 1983, 2186, 2620
Gilmore-Bykovskyi, Andrea 0218
Gilvary, Coryandar 0590
Gim, Haelynn **1705**
Giner, emilio 2373
Ginzler, Ellen 1505, 1708, 1722, 2416
Giordano, Sharon H. 1429, 1920
Giovannone, Nicholas 0898
Gip, Phung 0014
Giraldo, Luisa Fernanda 0346
Girard, Louis 0722
Girolami, Gabriella **2237**
Girolomoni, Giampiero 0021
Giron, jose 1972
Girschick, Hermann 2128
Gisbert, Javier 0021
Gisondi, Paolo 0574
Gist, Dawn **0402**, 1296
Giudice, Laura 2656
Giuggioli, Dilia 0702, 1587
Giuggioli, Dilia 2482
Giuggioli, Dilia 2656
Giunta, Isabella 1918
Gjyrezi, Ada 0515
Gkiaouraki, Eugenia 0282, 1201
Gkiaouraki, Eugenia 1215
Gkionis, Marios 0448
Gladman, Dafna D. 0522, 0552, 0565, 0576, 0581, 0590, 0611, 0612, 0613, 0629, 1415, 1416, 1425, 1426, 1550, 1714, 1722, 2210, 2339, 2341, **2345**, 2416, 2690, 269170
Gladue, Heather 1725
Glanz, Bonnie 0184
Glaser, Cornelia. 2279
Glasin, Anna 2060
Glass, Marla 0889, **1695**
Glatigny, Simon 0104
Glatman Zaretsky, Arielle **0934**
gleizes, audes 1604
Glerup, Mia 0389
Glick, Sharon 1708
Glickstein, Sara 0679
Glintborg, Bente 1430
Glover, Owen 2577
Glowienka, Emily 2500
Glumoff, Virpi 0307
Gluud, Lise Lotte 2608
Gmuca, Sabrina 1226
Gmuca, Sabrina 1298
Gniadecki, Robert 0969, 0970
Go, Ronald 1174
Gobena, Temesgen 0456
Gobert, Delphine 1339
Goble, Sandra 0260, 0777, 2663
Godavarthy, Aparna 0657
Godbout, Alexandra 1109
Goddard, David 0652
Goddard, Emily 1043, 1551, 1923
Godeau, Bertrand 1575
Godeau, Bertrand 2457
Godeau, Bertrand 2489
Godfrin, Bertrand 2115
Godinez-Lazarini, Emilio 1469, 1482
Godo, Javier R 0559
Godoy, Jesus 2576
GODOY NAVARRETE, FRANCISCO JAVIER 0087, 0496, 2268
Godoy Tundidor, Hilda 1024, 1869, 2030
Godoy Tundidor, Hildegarda 1170
Godwood, Alex 0567, 0573, 1455, 2357
Goekoop-Ruiterman, Yvonne 2309
goel, ruchika 0140
Goel, Ruchika 0582
goel, ruchika 1609
Goetz, Ann-Kathrin 1697
Gogulamudi, Venkateswara 0709
Goh, Ginny 0378
Goh, Ingrid 1275, 2127, 2136
Goh, Vivien 0846
Goh, Y. Ingrid 1286
Gohar, Najam 0312
Gokcek, Sohret 1694
Golalipour, Elahe 1827
Gold, Heather **1918**, **1919**
Gold, Heather 2645
Gold, Nicholas 1286
Goldbach-Mansky, Raphaela 0920
Goldberg, Isaac 0846
Goldberg, Robert 2079
Goldberg, Scott 0777, 1265
Goldblatt, Fiona 0595
Goldenstein-Schainberg, Claudia 1715
Golder, Vera 0595
Goldin, Jonathan 1213, 1564
Golding, Michael 1494
Goldman, Daniel 0597, **0607**, 0837, 0851, 1223, 1498, 1499, 1516
Goldman, John **1977**
Goldman, Michael 1977
Goldman, Nina 1589
Goldmuntz, Ellen 1674, 1831
Goldrath, Ananda 0889, 1695
Goldstein, Karen 2207, 2208
Goldwater, Ronald 1374
Goldwirt, Lauriane 1339
Goldzweig, Ofra 1305
Golebiovski, Rywka 1407, 1408, 2326
Golenbiewski, Jon **1047**
Golightly, Yvonne 0306, 0325, 0330, 2092, 2604
Golombek, Steven 1795
Golshan, Shahrokh 0207
Gomez, Claudia 1988
Gomez, Gerber **0711**, **2396**, **2397**, **2398**
Gomez, Gimena 2336
Gomez, Graciela 1491, 1530
Gomez, Graciela Noemi 0623, 2405
Gomez, Shelby 1050, 1051, 1052
Gomez Carrera, Luis 1869, 2030
Gomez Vaquero, Carmen 0353, **2106**
Gomez-Lobo, Veronica 2580
Gomez-Moreno, Cristina 0608
Gomez-Puerta, José 0379, 0380, 0505, 0623, 0642, 0659, **1018**, 1943, 2450
Gomez-Sabater, Silvia 0153, 1096
Gomon, Georgy 1573
Gompels, Luke 0474
Gong, Xiaoyan 0943
Gong, Yajun 0939
Gong, Zhiyun 0811, **0845**, 0846
Gono, Takahisa **0304**
GONUGUNTLA, SADHANA 0160
González, Ismael 0737, 0752
González, María-Julieta 0931
González, Nicolás 1194
González, Sergio 0931
González Arribas, Guillermo 0270
González Cantero, Álvaro 0581
González Casas, Dominique Daniela 2034
González Conejero, Rocío 0072
González Hernández, Teresa 2121
González Mazarí, Roxana 0270
González Mazario, Roxana 0271, 0538, 2406, 2407, 2460
González Montes, Alonso Sebastián 1335
González Sánchez, María Fernanda 2034
González Terrats, Patricia 1490
González Vioque, Emiliano 1170
González-Casaus, María Luisa 0346
González-Dávila, Enrique 0379, 2106
González-Fernández, Marta 0244
González-García, Celia 0639
González-Gay, Miguel A. 0450, 0559, 0604, 0608, 1404, 2484, 2491
González-Morales, Juan Pablo 1022
González-Rosales, Ana Elena 1022

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

González-Treviño, Mariana 0601
Gonzales, Katrina **0227**
Gonzalez, Guillermo 2290
Gonzalez, Mª ángeles 2042
Gonzalez, Maria Isabel 1282, 1284
Gonzalez, Virginie 0053, 0796, 1334, 1724
GONZALEZ ARRIBAS, GUILLERMO 0271, 1547, 1548, 2670
Gonzalez Bello, Yelitza 0596, 0621
Gonzalez Gomez, Maria Luisa 2344
Gonzalez Hernandez, Maria Fernanda **0329**
Gonzalez Hombrado, Laura 0351, 2344
GONZALEZ MARTIN, JORGE 0107
Gonzalez Martin, Jorge Juan 1397, 1681
Gonzalez Melendez, Ariana 1264
Gonzalez Molina, Rocio **2373**
Gonzalez Mozo de Rosales, Guillermo **0485**, **2350**
Gonzalez Sanchez, Ana Cristina 0297
Gonzalez Sanchez, Ximena 0182
Gonzalez-Alvaro, Isidoro 0454, 2122
Gonzalez-Chapa, Jorge A. 1208, 1602, **2147**
Gonzalez-Diaz, Eugenia 1825
Gonzalez-Melendez, Aleydis 0366, 0614, 1023, 1928
Gonzalez-Reyes, José-Antonio 2599
Gonzalez-Treviño, Mariana 1721, 2403, **2413**
Good, Samuel 1048
Good, Samuel 1564
Good, Samuel **1584**
Goode, Adam 0784
Gooderham, Melinda J. 0555, 1155
Goodman, Brent 1378, 1384
Goodman, Susan 0187, 0308, 0463, 0464, 0785, 0786, 2385
Goodpaster, Bret 0320
Goodridge, Jode 0663, 2454
Goodson, Summer 0802
Goodyear, Carl S. 0111
GOPAL, AISHWARYA 0136, 0137
Gopal, Aishwarya 1431
GOPAL, AISHWARYA 2424
Gopal, Manikandan **1496**
Gopalakrishnan, Chandrasekar 1336
Gopalan, Amirtha **1472**
Gorayeb, Thais B 1192
Gordon, Caroline 0644, 1722, 2416
Gordon, Jennifer 0725, 2144
Gordon, Jessica 0844, 0883, 1555, 1566, 1582, 1725, 2475, 2654
Gordon, Kenneth B. 2374
Gordon, Patrick 1906
Gordon, Rachael **2499**
Goreja, Mayra 2343
Gore-Massy, Monique 2429
Gorevic, Peter 1386, 2046
Gossec, Laure 0455, 0567, 0573, 0576, **0577**
Gossec, Laure 0581
Gossec, Laure 1411, **1448**, 1455, 1458, 1460, 2308, 2339, 2341, 2356
Gosselin, Jeanne 2223
Gosvig, Kasper 0543
Goswami, Rudra Prosad 0630, 1503, 2191
Gotch, Ruby 1672
Gotelli, Emanuele 0676, 0705, **0963**, 1097, **2179**, 2501
Goteti, Sasidhar 0126
Goto, Tadahiro 2449
Goto, Yuichi 0043
Gotshall, Donna 1376
GOTTENBERG, Jacques-eric 0034, **0508**, 0516, 1403, 1578, 1683, 1685
Gottesman, Susan RS 1759
Gottlieb, Alice 0563, **0564**, 0874
Gottlieb, Alice B. 0455, 0573, 1456, 2365
Gottlieb, Beth 0411, 1066
Gottman, Moriah 0830
Gou, Wei 2013, 2014
Goudot, Astrid **0566**
Goudsmit, Christine 0822, 1740, 1741, 1816, 2478
goujard, Cécile 0735, 1575, 2489
Gould, Errol 1231
Goulding, John 0663, 2454
Goules, Andreas 0516
Goulvestre, Claire 1593
Gourh, Pravitt 1725
Goursaud, Emmanuel 2631
Govardhan, Chaitra **0397**, 2130
Govea-Peláez, Samuel 0287
Goveas, Shinie Razil 1588
Govender, Ramona **0705**
Govrin, Eri 0570, 1332
Gowda, Sanjita **2258**
Goyal, Gaurav 1174
Goyal, Mayank 2153
Goyal, Mohit 0133
Goyal, Parag 0146
Goyette, Kyr 2037
Gozalo, Laurence 2003
Gröndal, Gerður María 0814
Grünkewitz, Laura 2612
Grüter, thomas 1934
Graber, Jeremy 0768
Gracia Tello, Borja del Carmelo 1210, 1953, 1954, **2471**
Grader-Beck, Thomas 1028, 1378, 1384, **2302**, **2665**
Graf, Jonathan 0501, 0774, 1674, 2277
Graham, Christopher 1731
Graham, Daniel 0032
Grainger, Andrew 2089
Grams, Morgan 1712
grana, Genaro 1282, 1284
Granados, Raquel **0583**, **2371**
Granados bautista, isabel Patora 1282
Grandi, Sonia 2563
Grant, Courtney 0017
Grant, Jessica 1271
Grant, Nadia 1981
Grau, Maria 1018
GRAU GARCIA, ELENA 0205, 0237, 0341, 1274, 2274, **2310**
Gravallese, Ellen M. 0872, 0925, 1142, 2233
Grawer, Luke 2085, 2091
Gray, Shelly 2251, 2252
Grayson, Peter 0258, 0777, 1618, 1624, 1626, 1912, 2533, 2700, 2701
Grazzini, Silvia 1212, 1616, **2075**
Grebenciucova, Elena 2430
Grebinoski, Stephanie 0987
Grecu, Maria 0529
Green, Charles 0541, 2361
Green, Freddy 2282
Green, Laura 0145
Green, Ryan **0060**
Green, Sarah 2206, 2380
Green, Tobias 0008
Green, Tyler 1057
Greenberg, Samuel 0356
Greene, Trever 0663, 2454
Greenleaf, Melissa 1674
Greenman, Dina 1700
Greenwald, Maria 0436
Grega, Tomáš 1962
Gregova, Monika 0543
Greigert, Hélène 1150
Grenier, Karl 2215
Grenier, Louis-Pierre 0606
Grewal, Harsharn 2070
Grewal, Parbeer 0875
Grewal, Sehneet 1245, 2328
Grewal, Sehneet **2329**
Grieshaber-Bouyer, Ricardo **0236**, 0641, 0678, 1198, 1537, 1697, 2442, **2641**, 2695
Griffin, Amiah **2380**
Griffin, Emma 1760
Griffin, Molly E. 0344
Griffin, Thomas 0401
Griffin, Timothy 1736
Griffing, Kirstin 0473
Griffing, Leroy W. 0701
Griffith, James 0536
Griffith, Melissa 0501
Griffiths, Bridget 0692
Griffiths, Christopher EM 0559
Griffiths, Paula 0711
Grigoryan, Lilit **0698**, **0699**
Grika, Eleftheria 1452
Grika, Eleftheria 2232
Grilli, Christopher 1900, 2542
Grim, Andrew 2143
Grimm, Annaiz 0981
Grimmett, Llam 0700, 1840
Grinnell, Todd 1254, 2189
Grinnell-Merrick, Linda 0561, 0585, 0734, 1459, 1910

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Gripp, Kelsey 0441, 0464, 2226
Grishin, Sergey 0403, 0779
Griss, Johannes 1911
Gritsch, David 1100
Grivas, Petros 1104
Groarke, Emma 0777, 2700
Grobost, Vincent 0891, 1605
Groeber-Becker, Florian 0974
Groh, Mathieu 0756, 1592, 1605
Groh, Matthieu 2532
Grolleau, Chloé 2699
Grom, Alexei 0302, 0418, 0419, 1819, 1820, 2138, 2139
GROM, Alexiei 0780, **1671**, 2137, 2242
Grooms, Austen **2131**
Groppa, Liliana 1414
Groselj, Ales 2015
Gross, Andrew 1972
Grosskurth, Shaun E 1003
Grossman, Clare **0182**
Grossman, Jennifer 1505, 1674, 2600
Grothier, Thomas 0006, **0017**
Grotti, Vitor 2536
Grover, Madhusudan 1558, 1855
Grovner, Natalie 2468
Gruben, David 1444
Gruen, Margaret 0311
Grundahl, Kiely 0506
Grzybowski, Kinga **0326**, **0841**, **2120**
Gu, Hui 1662
Gu, Kaien **0388**
Gu, Peng 0926
Gu, Qingyang 0939
Gu, Shiyan 0124, 0856, 1971
gu, zhanqing 0876
Gu, Zhi-Chun 0490
Guajardo-Jauregui, Natalia **2325**
Guamán, Mónica Sánchez 1486
Guan, Chelsea 0742, **1151**, 1471, 1501, 2216, **2389**
Guan, Hongshu 1019, 1709, 2568, 2607, 2640
Guan, Jing 0005, 0986, 1001
Guan, Mary 1265
Guan, Xin 0646
Guan, Yihong 0057
Guaracha, Guillermo 2336
Guaracha-Basáñez, Guillermo Arturo 2321
Guardiano, Sherry 1367
Guariento Ferreira Alves, andressa **0394**
Guarischi-Sousa, Rodrigo 0024
Guay, Heath 0751
Gucev, Zoran 0920
Gudbjornsson, Bjorn 0543, 0814, 1430
Gudi, Kirana 0827
Gudjonsson, Johann 0020, 0127, 0811, 0851, 0949, 0971, 0972, 0985, 1682, 1760, 1846, 1852, 2233
Gudjonsson, Johann 2451
Gudjonsson, Johann 2498
Guedens, Thomas 1558
Guedens, Thomas 1855
Guedes, Lissiane 0206
Guellec, Dewi 0477
Guellec, Dewi 2296
Guerini, Miriam **1605**
Guermazi, Ali 0852, **2081**
Guerra, Marta 0855
Guerra Herrera, Iris 0596, 0621
Guerra Herrera, Iris 0623
Guerra Herrera, Iris 1486, 1491, 1530
Guerrier, Thomas 0958
Guess, Rachel 0417
Guess, Rachel **2165**
GUETTROT-IMBERT, Gaelle 2457
guettrot-Imbert, gaelle 2655
Guevara, Myriam 1070
Guffroy, aurelien 1578
Guffroy, Magali 1784
Guggenberger, Konstanze 2703
Guggenbuhl, Pascal 1136, 2115
Guggino, Giuliana 2075
Guha, Mahilan 2528
GuhaRay, Adreeja 1563
guiang-valerio, adrienne katrin **1273**
Guiducci, Serena 0275
Guiducci, Serena 0673, 0702, 0880
Guiducci, Serena 1570, 2482
Guilbert, Lucile 1858
Guilcher, Sara 2627
Guillén, Yolanda 0019, 0021
Guillén del Castillo, Alfredo 1953
Guille, Marie 1200
Guillemin, Francis 0314, 2080
Guilleminault, Laurent 1592, 1605, 2510
Guillen del Castillo, Alfredo 2485
GUILLEN-ASTETE, CARLOS 0107, 1282, 1284
guillen-del-castillo, Alfredo 1862
Guillen-Tejada, Daniela L. **1635**
Guillevin, Loic 1592, 1765, 2506
Guillouard, Manon 2115
Guilpain, Philippe 1592
Guinn, Daphne 0261
Guio, Heinner 0637
Guiraud Chaumeil, Juliette 0123
Guirguis, Maged 1228
Guitton, Zélie 1581
Guja, Kip 1172
Gul, Ahmet 0025
Gul, Ahmet 0135, 0290, 0779
Gul, Ahmet **1008**
Gulaid, Amal 2548
Gulanski, Barbara 2114
Gulati, Gaurav 2468
Gulati, Nina 2429
Guleria, Shivika 1221, **1812**, 2676
Gulia, Francesco 1385
Guliyeva, Vafa 1698, 1818
Gulla, Christina **0398**, 2135
Gullapalli, Manoja 2050
Gullick, Nicola 0572, 1462, 1463, 1464, 2340
Guly, Catherine 0397
Guma, Monica 0207, 1787, 2220
Guma, Monica 2317
Gumdal, Narsimulu 0708
Guminski, Barbara 1157
Gump, Meghan 0603, 0741, 1151, 1471, 1500, 1501, 2216, 2382, 2389
Gunalp, Aybuke 1291
Gundoji, Chethan Raj 1890
Gunduz, Hasret 0902
Gunes, Baran 0674, 2470
Gunkl-Tóth, Lilla **2684**
Gunn, Josh 0302
Gunnarsson, Iva 0594
Gunnarsson, Iva 2647
Guo, Huifang 1354
Guo, Jianping 0116, 0141
Guo, Kexin 0402
Guo, Nanxi 0890
guo, ning 2611
Guo, Pengfei 0122
Guo, Rong 2227
Guo, Tingxi 0981
Guo, Wei 0647
Guo, Xiang 2068
Guo, Yan 0174, 2270
Guo, Yixue 2061
Guo, Zhengguang 1750
Gupta, Akash 0231, **2701**
Gupta, Avneet Kumar 1364
Gupta, Latika 0177, 0295, 0304, 1212, 1218, 2056, 2065, 2066, 2067, 2076, **2185**
Gupta, Malvika **0622**, **1731**
Gupta, Neerja 2152
Gupta, Neha 0234, 0253
Gupta, Ranjan 0447
Gupta, Ranjan **0630**, 0631, **1503**, **2191**
Gupta, Saurabh 2153
Gupta, Sneha 1072
Gupta, Supriya 1731
GUPTA, VINOD **2639**
Gupta, Vishal 2152
Gur, Bengisu 2044
Gurajala, Siddarth 2600
Gurcan, Mert 2543
Gurer, Cagan 0888, 0997
Gurnari, Carmelo 0260, 0777, 2663
Gurrea-Rubio, Mikel **2494**
Guthridge, Carla 0023, 0044, 0514, 0840, 0842, 1480, 1831, 1850, 2421
Guthridge, Joel 0023, 0033, 0034, 0044, 0506, 0514, 0774, 0840, 0842, 0851, 0853, 1240, 1480, 1674, 1831, 1842, 1844, 1846, 1850, 1852, 1942, 2233, 2421, 2600, 2649
Gutiérrez, Juan 0931
Gutierrez, Andrea **1691**
Gutierrez, Gabriela 2536

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Gutierrez, Laura 2652
Gutierrez-Arcelus, Maria **1696**, 2410
Gutierrez-Cruz, Gustavo 0863
Gutierrez-Cruz, Gustavo 2580
Gutierrez-Riart, Mariana 0089
Gutowski, Emily **1265**, **2444**
Guy, Thomas 0992, 2528
Guzel, Ferhat 1823
Guziewicz, Elyse 2150
Guzik, Tomasz 1883
Guzman, Alfredo **1191**
Guzman, Jaime 0361
Gwak, Jeenah 1072
Gwathmey, Kelly 0234, 0253
Gyger, Lucas 0009
Györfi, Andrea-Hermina **0026**, 0678, 0809, 0810, 0956, 0962, 0974, 0975, 1198, 1537, **1856**
Gyurko, Rita 0501

H

Ha, Jang Woo 1343, 2511, **2512**
Ha, You-Jung 1343, 2698
Hánová, Petra 0831
Häner, Simone 0919
Håberg, Siri Eldevik 0427, 2679
Hübschmann, Daniel 0932, 1876
Hütter-Krönke, Marie Luise 0471
Haack, Monika 2320
Haaland, Derek 1443
Haas, Christhopher 1513, 1707
Haas, Simon 0932, 1876
Haase, Isabell 1660
Haavardsholm, Espen 0420, 0814
Haberman, Rebecca 0455
Haberman, Rebecca 0491, 0527
Haberman, Rebecca 1007
Haberman, Rebecca 1223, **1241**, **1712**, **2327**, 2687
Habib, Rabie 0312
Hacein-Bey-Abina, Salima 1604
Hachulla, Eric 0133
HACHULLA, Eric 0508
Hachulla, Eric 0516
Hachulla, Eric 0673
Hachulla, Eric 0688
HACHULLA, Eric 1575
Hachulla, Eric 1581
HACHULLA, Eric 1858, 2179
Hachulla, Eric 2477
HACHULLA, Eric 2489
Hachulla, Eric 2655
Hack, Juliana 0826
Hackert, Nicolaj 1696
Hackney, Jason 0654
Hacohen, Nir 0851
Hacohen, Nir 0940, 1240
Hacohen, Nir 1763
Hacohen, Nir 1830
Hacohen, Nir 1844
Hacohen, Nir 1846, 2233, 2600
Haddad, Amir 1436, 1710
Haddad, Amir 1959
Haddad, Amir **2306**
Haddad, Haya 1182
Haddadi, Nazgol **2668**
Haddadin, Muhannad 1476
Haddadin, Muhannad 2382
Haddas, Ram 1940
Haddon, Jamie 2641
Hadi, Salah 0493
Hadi-Nezhad, Fatemeh 1563, 2468, 2669
Hadjadj, Jerome 1339
Hadlock, Jennifer 1457
Hadsbjerg, Anna EF 0543
Haenel, Gerulf 2476
Hafez, Abdelrahman M 0335
Hafez, Hadeer 0331, 0332, 0333
Hafez, Hadeer 0334
Hafez, Hadeer 0335, 1317, 1318, 1713
Hafiz, Waleed 0600
Hafstörm, Ingiäld 0338
Haftorn, Kristine Løkås 0427, 2679
Hagan, Peter 0131
Hage, fadi 1048
Hagen, Melanie 0236, 0641
Hagen, Melanie 1198
Hagen, Melanie **1537**, 1697, 2442
Hagen, Melanie 2641
Hagen, Melanie 2695
Hager, Anthony 1457
Hagino, Owen 0239, 1666
Hagiwara, Yukitomo **0521**
Haglund, Kristin 2603
Hahn, Maryrose 1005
Haibel, Hildrun 0854
Haidar, Sheila 0210
Haider, Faseeh 0312
Hajek, Stefanie 1287, 1288
Hajizadeh, Sama **0500**, 1058
Hajj-Ali, Rula 2515, 2524, 2702
Hakim, Ellen 1827
Hakim-Moulay, Dehbi 0692
Hakkarainen, Kia 2000
Haladyj, Ewa 1348
Halami, Jean-Michel 0618
Hale, Caryn 0316
Hall, Christopher 2010
Hall, Jodi **2556**
Hall, Kristen 2486
Hall, Megan 0501
Hallahan, Brian 1409
Hallam, Trevor 0016
Halligan, Laurie 0310
Halpert, Gilad **0570**, **1332**
Halyabar, Olha 1810, 1822
Hama, Satoshi 2253, 2254
Hamad Saied, Mohamad 1305
Hamblin, Alicia 0181, 0359, 1250, 2619
Hamdan, Muhammad 0674
Hamdan, Muhammad 0869
Hamdan, Omar 0479, 1098, 2343, 2519
Hamdi, Wafa 1706
Hamidou, Mohamed 1765
Hamijoyo, Laniyati 0595, 1878, 1899
Hamilton, Iris 0186, 2128
Hamilton, Michael 0254
Hamilton, Michael **1074**, **1075**, **1076**
Hamilton, Michael 2093
Hammad, Hamida 0907
Hammel, Ludwig 1450
Hammenfors, Daniel 0034
Hammitt, Katherine 1378, 1384
Hammond, Danielle 0260, 0777, 2663
Hammond, Sarah 2577
Hamoudah, Ahmed 1222
Hamza, Ahmed Abdulhafeez 0333
Hamza, Mohammed Safwat Kamal 0335
Han, Bryan 2206, 2380
Han, David 1374
Han, Hongwei 1876
Han, Jinshuo 1131
Han, Kyungdo 0170, 1893
Han, Lu 1532, 2452
Han, Lyrialle 0679
Han, Xiu 0905
Han, Xu 1712
Han, Yunqing 1357
Han, Yuxiang 1354
Hanaee, Yas 0100
Hanaoka, Beatriz **1307**
Hanata, Norio 0945, **1843**, 2580
Hanberg, Jennifer **2276**
Handa, Tomohiro 0773
Handy, Whitney 1529
Hanebutt, Nicholas 1781, 1792, 1794
Hang, Wei **1807**
Hanlon, Megan M. **0925**
Hanly, John 1722, 2416
Hanna, Balsam 2060
Hanse, Dennis 0768
Hansen, Christopher 2533
Hansen, Dylan 0677, 1716, 2651
Hansen, Kyle 0014
Hansen, Louise 2574
Hanser, Edveena 0919
Hanslik, Thomas 1575, 2489
Hanson, Andrew C. 0759, 1721, 1726, 2403
Hanssens, Linda 0641
Hant, Faye 0883, 1555, 1566, 1582, 2475, 2654
Hanum, Aisyah Rizki Nirmala 1398
Hao, Jian 1220, 2447
Hao, Ling-Yang 0988
Hao, Nariaki **0497**, 1363
Hao, Ritche 1985
Hao, Yanjie 0595
Hao, Yue 1982
Haouichat, Chafika 1930
Happ, Hannah 1000
Haq, Shireen 1083
Haque, Adel 2041

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Haque, Ayema **1879**
haque, israrul **1203**
Haque, Naz 2060
Haque, Uzma 0529
Haque, Uzma 1028
Harada, Takuya **0043**
Haran, John 0322
Haranahalli Shivarudrappa, Arpitha 0942
Harbison, Sara 1276
harder, Bryan G. 0260, 0777, 2663
Harders, Stefan 2400
Harding, Monica 1555, 1566, 1582, 2654
Harel, Liora 1287, 1288, 1305
Harigai, Masayoshi 1630
Hariri, Lida 0808
Hariz, Christine 0217, 2619
Harker, Katlin **0784**
Harkey, Matthew 0309, 0323, 2623, 2625
Harkins, Patricia 0750
Harley, John 1842
Harms, Konrad 1070
Harms, Paul 0020
Harnden, Kate 0832
Harnois, Melissa 0843
Haroon, Nigil 0098, 0113, 0547, 0560, 0854, 2200, 2352
Harper, Elleson 0603, 0724, 0741, 1151, 1471, 1500, 1501, 2389
Harris, Claudia 0824, 1810
Harris, J. Kirk 0088
Harris, John E. 2668
Harris, Jonathan 2493
Harris, Julia **0408**, **0409**, **0410**, **0411**
Harris, Julia 0803
Harris, Julia **1066**, **1978**
Harris, Luke 0410
Harris, Nathaniel 0363, 0367, 0793, 1487, 2379
Harrold, Leslie 1421, 2640
Hartel, Isabella 1050, 1051, 1052
Harter, Michaela 2423
Hartmann, Arndt 2695
Hartmann, Fabian 0762
Harvey, Bohdan 0048
Harvey, Caroyln 0300, 0315, 0701, 2018
Harvey, Guillermina 1486
Harvey, Joshua 2623
Harvey, Paula 0265, 0522
Harwell, Susan 2560
Harzy, Taoufik 2324
Hasan, Mohammed 0492
Hasan, Sharika 1628
Hasegawa, Kimiko 0304
Hasegawa, Minoru **1538**
Hashim, Mahmoud 0492
Hashim, Rasiya 1147
Hashimoto, Motomu 0773, 0850
Hashimoto, Motomu 1857
HASHIMOTO, YORIKAZU 2225
Hashiramoto, Akira 1610
Hashmi, Muhammad Usman **1539**
Hashmi, Sidra **0835**
Hashoul, Sharbell 2306
Hasni, Sarfaraz 1470
Hasni, Sarfaraz 1502
Hasni, Sarfaraz 1843
Hasni, Sarfaraz 2580
Hassan, Fadi 1337
Hassan, Fatima **0746**
Hassan, Imran 0650, 0664, 0665, 1521
Hassanaly, Olivier 0735
Hassanin, Ali Tarek 0335
Hasseli-Fräbel, Rebecca 1729
Hassett, Geraldine 0595
Hatano, Hiroaki 2602
Hatemi, Gulen 0241, 0760, 2543, 2544
Hatemi, Ibrahim 0241
Hauge, Ellen-Margrethe 1950, 1955
Haugegaard, Tobias 0338
Haugen, Ida Kristin 2089
Hausmann, Jonathan 1810, 1822
Hausmann, Jonathan 2151
Hausmann, Michael 0711, 2396
Haussmann, Alana **1148**
Hauzeur, Jean-Philippe 2115
Havrilla, Haley 2478
Hawker, Gillian 2079, 2102
Hawkes, Jason 1457
hawlina, gregor 2015
Hawthorne, James 1043
Haxel, Caitlin 0853, 1391
Hayashi, Eri 0106
Hayashi, Keigo **0452**, 2244
Hayashi, Mayuko 0043
Hayat, Noa 1436
Hayat, Samina 1508, 2392
Hayes, Kari 0819, 1824
Hayes, Kimberly 2084, **2096**
Hayes, Kimberly 2098
Hayes, Kimberly 2624
Haymaker, Cara 0273
Haynes, Kevin 0399
Hayward, Kristen 2462
Hazan, Ran 0417
Hazen, Melissa 1810, 1822
Hazique, Mohammad 1245, 2328, 2329
Hazlewood, Glen 0438, 0442, 1355, 1648
He, Adam 0028
He, Celestine 1832, 2394
He, Chenjia **0051**
He, Hongyi 0318, 1146
He, Jing 1514
He, Jingjing 0696
He, Jingxuan 0679
He, Lan 0649, 1622
He, Lauren **2217**
He, Linchen **0261**
He, Tailin **0064**
He, Tingyan 2037
He, Xin 0649
He, Yang 0003
He, Yang 0018
He, Yupeng **0048**
He, Ziyuan **0889**, 1695
Healy, Patrick 1458, 2341
Heaney, Andrew 1910
Heard, Mary 0923
Heard, Sara **2223**
Hearth-Holmes, Michelene 2183
Heath, Chloe 0871
Heath, Tyler 0888
Heaton, Andrew 1816
Hebert, Adelaide 0875
Heck, Corinna 0075
Hecquet, Sophie 0489
Hecquet, Sophie 0796
Hecquet, Sophie 1312, 1333, 2637
Hedayati, Gilava 1707
Hedrich, Christian 2128
Heeswijk, Bennie **0978**
Heffler, Enrico 0238
Hegazy, Mohamed Tharwat **0264**, **2123**
Hegde, Subramanya 1119
Hego, Alexandre 1738
Heguy, Adriana 1338, 2233
Heiberg, Marte 0814
Heiblig, Mael 0260, 0777, 1339, 2663
Heider, Ute 0919
Heikenwälder, Mathias 1206
Heiland, Hattie 2285
Hein, Pyae 0456
Heiting, Chloe **0785**, **0786**
Helleputte, Thibault 0035
Helliwell, Philip 1411
Hellmi, Rakhma 2004
Hellmich, Bernhard 0762, 1594
Hellmich, Bernhard 1601, 1605
Hellmich, Bernhard 1608
Hellmich, Bernhard 1614, 1626, 1627
Hellmich, Bernhard 1769
Hellwig, Kerstin 1934
Helm, Matthew 0984
Helmold Hait, Sabrina **0301**, 1651
Helmus, Nicola 1287, 1288
Helsen, Monique 0928
Helyes, Zsuzsanna 2684
Hemnes, Anna 0709
Hemon, Patrice 1738
Hemon, Patrice 2296
Henderson, Lauren 0824, 1668, 1696, 1810, 1820, 1822, 2124
Hendricks, Angela 0679
Hendrickson, R. Curtis 0040, 0041
Henes, Jörg 0702, 0762, 0810, 0884, 1562
Hengel, Hartmut 0508
Henin, Catherine 2222
Hennemand, Vincent 0016
Hennessey, Dylan 0970
Henning, Svenja 2418
Henrickson, Michael 1706
Henrickson, Sarah E 1825
Henrique da Mota, Licia Maria 0179, 1365, 2246

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Henry, Andrew 1270
Henry, Julien 1115
Hensor, Elizabeth 2393
Her, Minyoung 0171
Herardot, Elise **1735**
Heras Recuero, Elena **0608**, 1404
Heras-Recuero, Elena 0450
Herber, Mathilde 1908
Hercules-Tawe, Fanyu 1708
Herda, Luisa 2699
Herdia, Sergi 1382, 1397
Herdman, Michael 0991
Heredia, Sergi 0642, 2450
Heredia Martin, Sergi 1681
Heredia-Gonzalez, Santiago S. 2557
Herholdt, Claire 2081, 2101
Hering, Bernhard 1797
Herman, Julien 2115
Hermann, Kay-Geert 0854
Hermann, Sandra 0342, 0343, 0471, 2109, 2110, 2595
Hermanson, Payton 0059, 1208
Hernández, Andrea 0270
Hernández, Andrea 0271
Hernández, José L. 0744
Hernández, Lucia 0621, 1491
Hernández, Rodrigo Ortiz 1491
Hernández Díaz, Marta 0604, 1164
Hernández Velasco, Paúl 0639, 1547
Hernández-Baldizón, Samuel 2450
Hernández-Blanco, Camila 0626, **2630**
Hernández-López, Agustin **2052**, **2053**
Hernández-martín, Andrea 0642, 0659, 2450
Hernández-Ramírez, Diego F. 1482
Hernández-Rodríguez, Iñigo 0744
hernández-Sánchez, judith **1490**
Hernandez, Angeles 2373
Hernandez, Jose Angel 0269, 1171, 1490
Hernandez, Julio 0500
Hernandez, Laura **1897**
Hernandez, Noelia 0317, 1264
Hernandez, Vanesa 2373
Hernandez-Barco, Yasmin 2051, **2546**
Hernandez-Galarza, Ivan de Jesús 2557
Hernandez-Molina, Gabriela 0133, 0507, 1154, **1383**
hernandez-rodriguez, Jose 0896
Herndon, Jenny 1487
Herr, Heather 2374
Herranan, Anni 1735
Herregods, Nele 0390
Herregods, Nele 0428
Herrera, Carlos 2576
Herrera, Daniela 1937, 1948
Herrera, Elsa 1825
Herrick, Ariane **0686**, 0692, 1862, 1966, 2493
Herrmann, Martin 1131
Hersh, Aimee 0406, 0414, 2645
Hershfield, Michael 1160
Hervier, Baptiste 0735
Herwanto, Eko Setyo 1398
Heshin Bekenstein, Merav **0374**, 1305, 2137, 2138, 2139, **2537**
Hestetun, Sigrid 0427, 2679
Hetland, Merete 0543, 0814, 1430
Hetlevik, Siri 0420
Hetlevik, Siri Opsahl 1287, 1288
Hetrick, Rebecca 0374
Hetrick, Rebecca **2423**
Hettema, Willem 0653
Heußel, Claus Peter 0678
Heusinger, Tobias 1450
Hew, Kinjal 2035
Hewitt, Rachael 1261
Heydari-Kamjani, Milad **0724**, 0741, **1500**, **1501**, **2363**, **2364**, 2389
Heyn, Holger 0021
Högle, Thomas 0177
Hickernell, John **0224**
Hidaka, Ana Carolina 2246
Hidalgo Calleja, Cristina 1321, 1413, 2311
Hielscher, Andreas 1970
Hiepe, Falk 2648
Higami, Kenshi 2564
Higami, Satomi 2564
Higashida-Konishi, Misako **2253**, **2254**
Higashioka, Kazuhiko **0988**
Higginson-Scott, Nathan 0008, 0987
Highland, Kristin **0259**
Hildebrandt, Marisa 0949
Hildeman, David 2600
Hill, Diane 0474
Hill, Tom 2700
Hillel, Alexander 1595, 1596
Hillenbrand, Rainer 1189, 2296, 2300
Hilliard, Austin 0024
Hillion, Sophie 2296
HILLIQUIN, Stéphane **0114**, **1371**, **2262**
Himmel, Megan 1103
Hinchcliff, Monique 0674, 0685, 0845, 0846, 0879, 2470
Hindosh, Akram 2228, 2286
Hindosh, Yazin 2228, **2286**
Hines, Marcus **0909**, 1265
Hingorani, Vijay 1138
Hinze, Alicia **1556**
Hiraki, Linda 1279, 1281, 1285, 1286, 1289, 1290, 1301, 1742, 2410
Hirata, Shintaro 0773, 2523
Hirobe, Keisuke 1857
Hirohata, Shunsei **2541**
Hirose, Kei 0452, **2244**
Hirsch, Martin 0826
Hirsch, Pierre 1339
Hirschmugl, Birgit 2631
Hisada, Ryo 1854, 2289
Hisamatsu, Tadakazu 0257
Hitchon, Carol 0438
Hitchon, Carol 0442
Hitchon, Carol 1355, 1648
Hitt, Juvena 2223
Hiwa, Ryosuke 0773
Hiwa, Ryosuke 1772
Hiwa, Ryosuke 1857
Hiwase, Devendra 0091
Hizmetli, Sami 2322
Hmamouchi, Ihsane 0177, 0569, 1930
HMJM Kroon, Rosemarie 1205
Ho, Chris 0913, 0930
Ho, Gary 0777
Ho, Jennifer 2569
Ho, Pauline 1678
Ho, Roy Tsz Chung 1202
Ho, Yuk-Lam 2276
Hoa, Sabrina 1103, 1193, 1199, 2259, 2651
Hoban, Megan 0941
Hobar, Coburn 2435
Hobbs, Jr., Gerald 1636
Hocaoglu, Mehmet **0036**
Hocevar, Alojzija 1618, **2015**
Hochberg, Marc C. 2103
Hochwald, Alexander 1255
Hodgin, Jeffrey 2600
Hoekstra, Eva **1568**, **1569**
Hoelscher, Alexander 0678
Hoens, Alison 0177
Hofer, Sabine 1205
Hoff, Paula 0343
Hoffart, Cara 0409, 0410
Hoffer, Colton 0352
Hoffman, Daniel 1780
Hoffman, Patricia 0399
Hoffman, Stanley 0944
Hoffman, Victoria 0945, 1843
Hoffmann, Jason 1628
Hoffmann, Matthias 0555
Hoffmann, Patrycja 1169
Hoffmann-Vold, Anna-Maria **0510**, 0673, 0689, 0880, 0957, 0967, 1562, 1579, 1580, **1662**, 1867, 1872, 2472, 2477, 2497
Hofman, Astrid **0957**, 0967, 1867, 2497
Hofmann, Kai P 1206
Hoftman, Alice 0425
Hogan, Craig 1233
Hogan, Jonathan 2468
Hogan, Michael 0923
Hogan, Whitnee 0853, 1391
Hogarth, Hunter 1289
Hoge, Courtney 1639, 1640
Hoggarth, Allin 1136
Hoggatt, Amber 0016
Hoi, Alberta 0595, 1878, 1899, 2696
Hojeij, Batoul **2309**
HOLC, Iztok **0748**
Holden, Ashley **2547**
Holec, Patrick **0886**
Holers, V. Michael 0033, 0076
Holers, V. Michael 0088, 0774, 0775, 0833
Holers, V. Michael 0889
Holers, V. Michael 0914

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Holers, V. Michael 1674, 1695
Holers, V. Michael 1767
Holgado, Susana 0117, 0505, 2029
Holladay, Emily **0185**
Holladay, Emily 0369
Holladay, Emily 1027
Holladay, Emily 1084
Holladay, Emily **1228**
Holladay, Emily 1387, 1507
Holladay, Emily 1661, **1997**, 2068
Holladay, Emily 2119
Holland, Gary 0406, 0414
Holland, Michael 0409, 0410
Holle, Rachel 2598
Hollick, Rosemary **1244**
Hollnagel, Fauzia 1722
Holloman, Conisha 0853, 1391
Holloway, Adrian 2384, 2649
Holmqvist, Marie 2060
Holscher, Khristina 0016
Homey, Bernhard 0678
Honczarenko, Marek 1456
Honda, Nanase 2225
Honda, Tomohiro 1848
Hong, Feng 1442, 2351
Hong, Hwanhee 1745
Hong, Jeeyoung 1901
Hong, Jison 1173
Hong, Seokchan 1372, 1373
Hong, Seokchan 2431
Hong, Suzi 0207
Hong, Ting 1442, 2351
Hong, Xuezhi 0809
Hong, Xuezhi **0974**, **0975**
hong, Yu 1444
Hong MIng, Su 2652
Honjo, Tasuku 1772
Hooper, Jody 1591
Hooper, Mark 0711
Hoover, Maegan 0981
Hoover, Paul 0933, 0940, **1763**, 1830, **1844**, 2600
Hopkin, Sophie 0074
Hopkins Gillespie, Sarah 0187, 0527, 1261, 2690
Hoppe, Emannuel 0477
Hopyan, Sevan 2136
Horacda-Rubio, Loreto 2422
Horisberger, Alice 2414
Horisberger, Alice 2644
Hormigos Martín, Cristina 0270
Hormigos Martin, Cristina 0271, 1548
Horne, AnnaCarin 2137, 2138, 2139
Horne, Arik 1876
Horneff, Gerd 0389, 0401, 0405, 1288
Hornik, Christoph 1745
Horomanski, Audra 0263, 1172, 1693
Horowitz, Benjamin 1839
Horowitz, Diane 1674
Horslev-Petersen, Kim 0814
Hortensius-Varkevisser, Ada 1569
Horton, Daniel **0399**
Horton, Daniel **0400**, 1704
Horton, Mary 0038, 0625, 0637, 2646
Horvát-Karajz, Károly 1353
Horvei, Paulina 0823
Hosgel, Ali 2667
Hoshino, Tomoaki 0061
Hossam Al-Din Ibrahim, Maha 2123
Host, Lauren 0677
Hot, Arnaud 0688
Hou, Bing **0001**
Hou, Huayun 1279
Hou, Jue **1357**
Hou, Linda **0523**
Hou, Tainfei 1833
Hou, Yuke **1515**
HOUARD, Xavier 0114, 1735
Housri, Nadine 2163
Houssiau, Frederic 0842, 2401
Houston, Parul **1254**, **2189**
Houtman, Miranda 0807
How, Angela 0361
Howald, Anna 0015
Howard, Rebecca 1236
Howard, Teresa 2207, 2208
Howard, Xana 1087
Howarth, Lincoln 0913, 0930
Howell, Hannah 0372
Howell, Timothy 0360
Howlader, Mir **0927**
Howley, Lisa 0853, 1391
Howren, Alyssa 1009, 2201
Howren, Alyssa **2202**
Hoyt, Kim 1447, 1462, 1464
Hsia, Elizabeth 2060
Hsieh, Evelyn **2114**
Hsieh, Min-Shu 0511
Hsieh, Song-Chou 0299, 0511, 1106, 2469
Hsieh, Tsu-Yi 2469
Hsu, Evan **1668**, 1822, 2530
Hsu, Hui-Chen 1837
Hsu, Jacob Shujui 1346
Hsu, Kevin **0989**
Hsu, Ming-Chun 0555
Hsu, Teng-Chieh **0806**
Hsu, Vivien 0702, 1725, 2651
Hsueh, Grace 0056
Hu, Baofeng 0328, 1783, 1785, 1791
Hu, Chao 2463
Hu, Chaojun 0861
Hu, Fanlei 0132, 1514
Hu, Guangan 1833
Hu, Guangnan 2425
Hu, Jiankang 2013, 2014
Hu, Jiyuan 1338
Hu, Marie 0663, 2454
Hu, Pingzhao 1315
Hu, Shuijun 0986
Hu, Wenxiang 0045
Hu, Xiaodan 0116
Hu, Yanqing 2458
Hu, Ying 0318, 1146
Hu, Yingying 0013
Hu, Yulan 0013
Hu, Zaoshun 0001
HUA, Huy-Thong 2262
Huan, Lin 0018
Huang, Anbing 0646
Huang, Bin 1669, 2125, 2128
Huang, Bo 2303
Huang, Cecilia 0399
Huang, Chenyue 0883
Huang, De Suan 0210
Huang, Feiqing 1357
Huang, Jianxin 0077
Huang, Kaiyue 1757
Huang, Kangping **1316**
Huang, Kun 1193, 1199, 2259
Huang, Lawrence 1457
Huang, Linlin 0974
Huang, Mary 0058
Huang, Mengqi 1725
Huang, Mengwen 0939
Huang, Qian 1163
Huang, Qln 0468, 0517, 1478
Huang, Rong 0965
Huang, Ruizhi 2193
Huang, Suiyuan 0161, 1574, 2235, 2492
Huang, Wen Nan **2469**
Huang, Xiao 0005, 0986, **1001**
Huang, Xiaofan 2148
Huang, Xiaojing 2288
Huang, Xin 1784
Huang, Yi-Min 0511
Huang, Yina 0812
huang, yinan **2287**
Huang, Yingfeng 1761
Huang, Yiqing 1121
Huang, Yu-Huei 0555
Huang, Yunru 0838
Huart, Antoine 0618
Huart, Antoine 2510
Hubáček, Jaroslav Alois 1211
Hubáček, Jaroslav Alois 2073
Hubbard, Jonathan J. 2297
Huber, Adam M 0289, 0401
huber, christoph 0990
Hubka, Kelsea 2454
Huddleston, Edward 2190
Hudson, Marie 0297, 0968, 1103, 1109, 2651
Hueber, Axel 0192, 0557, 1660
Hueber, Wolfgang 1189, 1685, 2296, 2300, 2665
Huebner, Janet 2092
Huey, Leah **0993**
Huffman, Kim 0835
Huggins, Jennifer 0401, 0418, 0419, 1813, 1829
Hughes, Bernadette 2101
Hughes, Grant 0186, 1112
Hughes, Jonnie 0413

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Hughes, Michael 0671, 0672, 0683, 0686, 0689, 0692, 1559, 1586, 1587, 1933
Hughes, Michael **2493**
Huijsmans, Freya **0821**
Hui-Yuen, Joyce 1278, 1814
Huizinga, Tom 1568, 1569, 1678
Hulejová, Hana 0831
Huling, Jared 0352
Hulshizer, Cassondra 0460, 1721, 2403
Human, Andrea 0361
Humbel, Morgane 2443
Humbert, Marc 1185
Hume, Anne 1895
Hummel, Aurélie 0618
Hummers, Laura 0883, 1028, 1037, 1555, 1566, 1582, 2475, 2654
Humphrey-Escamilla, Fatima 2557
Humphreys, David **0074**
Hung, Adriana 0818
Hung, Vivian 0536
Hunter, Carlos 0065, 0921, 0924, 1650, 1774, 1779
Hunter, david 0324, 2097, 2622
Hunter, Ewan 0111
Hunter, Phoebe 1565
Hunzelmann, Nicolas 1537
Hunzelmann, Nicolas 1862, 2477
Huo, An-Ping 0806
Huo, Lihong 2579
Huo, Yuehong 0468
Huo, Zhiping 0352
Huppertz, Christine 0111
Hur, Benjamin 0276, 2639
Hur, Jin-Wuk 2264
Hurlbut, Kerry 0396
Hurley, Cristina **1040**
Hurley, Deborah 1980
Hurley, Emily 0006
Hurst, Amy 0985
Hurst, Amy 2451
Hurtubise, Raphaël 0566, 0572, 2340
Husain, Huzefa **0027**
Huscher, Dörte 0343, 2595
Husic, Hana 0888, 0997
Husni, M. Elaine 0371, 2358
Hussain, Ahmad Ali 1720
Hussain, MD Walid Akram 0151, 1880, 1881, 1882, 2088
Hussain, Swaleh 2627
Hussain, Yessar 1770
Hussein, Abdallah 0632, 1183, 1719
hutchins, Theresa 0823
Huttenhower, Curtis 2590
Huyghe, MiRa 2035
Huynh, Brittany **2204**
Huynh, Day Phuoc 1144
Huzien, Ahmed 0151, 1882
Hwang, Mark **0541**, 1410, **2361**
Hwang, Olivia 0664
Hyle, Emily 1764, 2509
Hysa, Elvis **0676**, 0705, **1097**, 2501

I

I. Danila, Maria 0774
Özen, Seza 0128, 0389, 1669, 1818, 2125, 2126, 2128, 2137, 2138, 2139
Iñiguez, Carlota L 0250, 0752
Iaconangelo, Charles 0562
Iacovantuono, Maria **1579**, **1580**
Iacubino, Martina 0700, 1840
Iannelli, antonio 0148
Iannone, Claudia 1212, **1863**, **2656**
Iannone, Florenzo 0275, 0702, 1212, 2075, 2482
Ibáñez-Antequera, Claudia 0252, 2034
Ibañez, Marta 0269, 1171, 1321, 1548, 2474
Ibañez Barcelo, Monica 2422
ibarguengoitia Barrena, oihane 0485, 2350
Ibarguengoitia-Barrena, Oihane **2422**
Ibarra, Maria 0409, 0410
Ibarrola, Libe 0485
Ibarrola, Libe 2265
Ibarrola, Libe 2350
Ibeke, Neke 0560
Ibic, Zaide 0953
Ibiloye, Elizabeth 0726, 1606, 2003
Ibis, Betul **1091**, **2657**
Ibrahim, Ayman 1222
IBRAHIM, Karim 0114
Ibrahim, Malika **1048**
Ibrahim, Quazi 0722
Ibrahim, Said 0785, 0786
Ice, John 0509
Ice, John 2432
Iden, Thomas 0234, 0253
Idoate, Jon 2510
Idolazzi, Luca 0673, 0702
Idolazzi, Luca 0884
Iglesias-Gamarra, Antonio 0596
Ignatiev, Vasily 1323
Iizuka, Alicia 0399, 0400
Ikari, Yuzo **1590**
Ikeda, Yukihiko 0638
Ikenaga, Chiseko 0863
Ikis, Aylin 1206
Ilic, Ivana 2017
Iliopoulos, Alexios 1452, 2232, 2359
Iliopoulos, Georgios 1452
Illes, Andras 0484
Illous, Yael 2537
Ilovitsh, Tali 0936
Iluz, Moshe 1945
Im, Koeun 2368
Imagama, Shiro 1326
Imai, Ryosuke 2660
Imamura, Yuichiro 1848
Imgenberg-Kreuz, Juliana 0034, 0594, 2647
Inac, Murat 1722
Inamo, Jun 0033
Inamo, Jun **0774**
Inamo, Jun **0819**
Inamo, Jun 1824
Inanc, Murat 0135, 0290
Inanc, Murat 1722
Inanc, Nevsun **1396**
Inanç, Murat 2416
ince, bugra 1246
Ince, Burak 0760
Inchausti Iguiñiz, Marta 1904
Inchboard, Lauren 0147
Indriuskaite, Gabriele 0017
Infante, Rodney 0808
Inga, Evelyn 2077
Ingegnoli, Francesca 2482
Inguva, Sushmitha **2051**
INIESTA-CHAMORRO, JOSE 0180
Iniguez Ubiaga, Carlota Laura 2422
Ink, Barbara 1454, 1458, 2341, 2358, 2365
Inman, Robert 0547, 0560, 1755, 1756, 2200
Inokuchi, Hajime 2602
Inoue, Ayaka **0284**
Inoue, Ayaka 1610
Inoue, Yuta 1854
Insalaco, Antonella 2128
Insfran Echauri, Carlos Emilio 2573
Intapiboon, Porntip 2411
Ioffe, Ella 2293
Iosim, Sonia 1810
Iosim, Sonia 1822
Iovene, Bruno 1567
Iozzio, Matthew 0399, 0400
Iperi, Cristian 2296
Iqbal Mohammed, Abdul Qudoos 2490
Irani, Anushka **0815**, 1086
Iri, Osamu 0850
Irie, Kei 2462
Irons, Taylor 0652, 1915
Irure-Ventura, juan 2023, 2059
Irving, Elaine 0154, 0169
Isaacs, John 1678, 1703
Isayama, Takuya 0304
Isaza, Adriana 2034
ISAZADE KASIMZADE, Gulperi 1968
Ishaq, Sarah 1291
ISHAQUE, REHAN **0235**
Ishchenko, Alla 0035
Ishchenko, Alla **0528**
Ishigaki, Kazuyoshi 2602
Ishihara, Shingo 1736, 1783, 1790, 1800
Ishii, Tomonori 0776, 1630
Ishii, Tomonori 2522
Ishikawa, Larissa 1563, 2468, 2669
Ishimori, Mariko 0657, 1410, 1842, 2600
Ishitoku, Michinori 0773
Ishizaki, Jun 1630
Ishizaki, Yoshiki 0668
Ishizawar, Rumey 2616
Islam, Shamima 0863, 2580
Ismail, Phebe 2436
Isnard, Pierre 1768

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Isnardi, Isabelle **0903**, 2665
Isoda, Ami 0043
Isola, Miriam 2545
Isozaki, Takeo 0095
Israel, Ariel 1337
Israni, Blossom 0474
Isshak, Rouba 1881, 2088
Itam, Ako 2263
Itamiya, Takahiro 1512
Ito, Hiroaki 2564
Ito, Hiromu 0850
Ito, Shuichi 1630
Ito, Takafumi 2523
Itodo, Joy 0769, 0770, **0788**
Ito-Ihara, Toshiko 2523
Iturbe-Fernández, David 1778
Itzkovitz, Edan 2136
Iudici, Michele 0689
Iudici, Michele 2506
iuliano, Loredana 0015
Ivanov, Nikita **0830**
Ivanovic, Maja **1111**
Ivashkiv, Lionel 0058
Ivorra Cortes, José 0237
Ivorra Cortes, Jose 1274, 2274, 2310
Ivory, Catherine 0294, 2069
Ivyanskiy, Ilya 0657
Iwasaki, Takeshi 0850, 1849
Iwata, Futoshi 2442
Iwona Sudol-Szopinska, Iwona 0543
Iyer, Aditya Mahadevan 2696
Iyer, Aishwarya 0970
Iyer, Archana 0048
Iyer, Ramesh 0422
Iyile, Thomas 0578, 2362
Izmirly, Peter 0626
Izmirly, Peter 0772
Izmirly, Peter 0851, 0853, 1223
Izmirly, Peter 1240
Izmirly, Peter 1391, 1488, 1846, 1918, 1919, 2404, 2421, 2444, 2630, **2645**, 2649
Izumi, Keisuke 2253, 2254
Izzetti, Rossana 1385

J

J. Finnema, Sjoerd 1784
j.voorbach, Martin 1784
Jönsen, Andreas 0593
Jönsen, Andreas 1722, 2390, 2416
Jaïs, Xavier 1185
Jachiet, Marie 2699
Jachiet, Vincent 1339
Jackevicius, cynthia 1048
Jackson, Brandon **0652**, **1915**
Jackson, David 1608, 1769
Jackson, Jordan 2150, 2195
Jackson, Lesley 0039, **0157**, **0158**, 0368, 1068, 1073, **2006**, 2566
jackson, shanna 0310
Jackson, Sharon 0159
Jacob, Reside 0352
Jacob Mathew, Ashish 0582
Jacob Mathew, Ashish 1496
Jacobs, Jonathan 1565
Jacobs, Julie 0694
Jacobs, Vonne 1487
Jacobsen, Søren 1722
Jacobsen, Soren 2416
Jacobsson, Lennart T. H. 0525
Jacoutot, Manon 0104
jacques, Peggy 0035
Jadon, Deepak 0572
Jafarzadeh, S. Reza 0165
Jaffal, Ali 0676
Jaffan, Jida **1289**
Jagannath, Deepak 1070, 1984
Jagerback, Sandra 2401
Jagger, Abigale **0392**
Jaghatspanyan, Eva 0002
JAHAGHI, NILOFAR 1494
Jahan, Kenneth L. 0997
Jahandideh, Dariush 0502, 1031
Jahangir, Kainat 0312
Jain, Avinash 1609
Jain, Ira 0997
Jain, Nitin 0273
Jain, Priya 1594, 1608, 1769
Jain, Priyansh 2676
Jain, Sanchay 1110
Jain, Sanjay 0481, 0697
Jakhade, Mansi Dhananjaya 0498
Jakiela, Jason 0771, **1637**
Jakobsen, Martin 0929
Jakramonpreeya, Natnicha 1187
JALANATHAN, MIDHUN SAKRAVARTHY **0495**
JAMAI, Adrien 0105
Jamal, Shahin 1103
Jamali, Marzieh 2235, **2492**
Jamalian, Samira 0679
James, Eddie 0914
James, Judith 0023, 0034, 0044, 0506, 0514, 0774, 0840, 0851, 0853, 1087, 1240, 1262, 1480, 1674, 1831, 1842, 1844, 1846, 1850, 1852, 1942, 2233, 2384, 2421, 2600, 2649
James, Karen 2144
James, Lija 0572
Jamieson, Brian 0780, 1671
Jamieson, Scott 0766
Jamin, Christophe 2296
Jamin, Raul N. 0892
Jamshidi, Omid 0899
jana, Manisha 2152
Janappareddi, Abhinav 1208
Janardana, Ramya 1609
Janardhanan, Sathya 0482
Janarthanan, Mahesh 1287, 1288
Jang, Dong-Ki 0526
Jani, Ishan 1877
Janku, Filip 0009
Jannat, Rida Ul **0312**
Jannat-Khah, Deanna 0365, 0382, 0441, 0464, 1088, 1089, 1102, **1351**, 1505, **1730**, 2226, 2575
Janow, Ginger 0398, **2135**, 2141
Jans, Lennart 0854
Jansem, Priabprat 1134, 2255
Jansen, Anna 0159
Janssen, Lisa 1796
Jariwala, Sunit 0448
Jarjour, Wael 0651, 0999, 1544, 1694, 2386
Jarnagin, Helen 0811, 0812, 0845, 0846, 1870
Jarrot, Pierre-André 0756
Jarvie, Adam 0743
Jarvis, James N. **0028**, 1064
Jasenecova, Marianna 1678
Jassal, Bandana **1197**
Jatuworapruk, Kanon **2004**
Jauregui, Edwin **1041**
Jaureguizar, Ana 1869, 2030
Jaussaud, Rolland 0891
Javed, Iqra 1320
Javed, Mahnoor **1070**
Javed, Mahnoor **1984**
Javidi, Mehrdad 0562
Javier, R. Mohamad **1398**
Javier, Rose Marie 2115
Jawaheer, Damini **1309**
Jawaliya, Nisha 1503
Jawdat, Ahmad 1181
Jay Lin, Tsu-Chieh 1393, 1394
Jayaraman, Arun 0832
Jayaraman, Muthusamy 0941
Jayne, David 0722, 1594, 1608, 1769, 2458
Jayne-Sugden, Helen 0832
Jayraj, Nirupa 1780
Jayyusi, Karim 2085, 2091
Jazayeri, Jahan 2156, 2680
Jean -Hugues, salmon 1095
Jefferies, Caroline 2579
Jeffery, Molly Moore 0149
Jeffries, Matlock 1781, **1792**, 1794, 1806
Jeffway, Mary 1357
JEGO, Patrick 2655
JEGOU, Jean François 0105
Jelusic, Marija 0358
Jelusic, Marija 0389
Jelusic, Marija 2126, 2137, 2138, 2139
Jendoubi, Manel 0958
Jenkins, Marc 0983
Jenkins, Victoria 0204
Jenks, Scott 1696
Jenoure, Fred 1073
Jensen, Anne Marie Reimer 2608
Jensen, Mindy 0501
Jensen, Miranda 1981
Jeon, Chan Hong 2315
Jeong, Hyemin **2315**
Jeong, Hye-Min 1145
Jeong, Yunju 0808

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

JEREMIE, SELLAM 0327, 1095, 1735, 2080
Jerez gilarranz, Yolanda 2121
Jesina, Pavel 1124
Jespersen, Brooke 0359
jesus, Nilson 2395
Jeswani, Bijay Mukesh 1347
Jetanalin, Pim 1134
Jeyanathan, Asha 1285, 1289, 1290, 1742
Jeyarajah, Jenny 0523
Jha, Isha 0375
Jha, Isha 0792
Jha, Isha 2033
Jha, Isha 2528, 2529, 2530
Jha, Vibha **1701**
Jia, Chenhan 1865
jia, yuan 0141
Jia Poh, Yih 0595
Jian, Congcong 0077
Jiang, Bohang 2509, 2530
Jiang, Duqing 1001
Jiang, Fanyi 0832
Jiang, Gigi 0875
Jiang, Guoping 2464
Jiang, Jialing 1036
Jiang, Kaiyu 0028
Jiang, Kan 1843, 2580
Jiang, Licui 0994
Jiang, Lijuan 0646
Jiang, Na 2697
Jiang, Nan 0468, 1316, 1750
Jiang, Shoshanna 2103
Jiang, Xiaodong 1833
Jiang, Xiaohan 2562
Jiang, Xu 1728
Jiang, Yusang 2368
Jillella, Shobitha 0888
Jillella, Shobitha 0997
Jiménez Gracia, Laura 0021
Jiménez Liñán, Luis María 2106
Jiménez Rodríguez, Manuel 2106
Jiménez Tirado, Mariana **1841**
Jiménez-Garduño, Aura Matilde 1635
Jiménez-Pastor, Ana 0538
Jiménez-Portillo, Ana Lucia 1096
Jimenez, Sergio 2480
Jimenez, Teri 0644, 0645, 2441
Jimenez Artiles, Massiel **0513**
JIMENEZ BARRIOS, SONIA 0107, 1335
Jimenez Clemente, Gabriela 2107
Jimenez Clemente, Gabriela 2108
Jimenez-Rodriguez, Laura 0496, 2268
jin, adam 2012
Jin, Hongtao **1354**
Jin, Hye-Mi 1145
Jin, Kaitian 2084, 2096, 2098, 2624
Jin, Liang 0048
Jin, Niyun 1701
Jin, Ying 1944, 2381
Jin, Yingzhao 0536
Jin, Yuebo **2303**
Jin, Yuxuan 0371
Jing, Qiuyu 0839
Jing, Ran 0127
Jing Li, Jing **0800**
Jiwrajka, Nikhil 0046, **1723**
Jnyah, mohammed khalil **2324**
Jo, Sungsin 0098
Jo, Sungsin 0526, 0550
Joanna, kedra 1095, 1185
Joerns, Elena 1034
Joerns, elena **1156**, 1388
Joerns, John 1156
Joffe, Gary 0853, 1391
Johansen, Niklas 1166
John, Martin 1832, 2394
John, Reshma 0151, 1881, 2088
Johnsen, Laura 0898
Johnsen, Svein Joar Augländ 0034
Johnson, Brandon 0660
Johnson, Brendan 1770
Johnson, Colebrooke 1606, **2508**, 2509
Johnson, Drake 1050
Johnson, Eric 0373
Johnson, Gale 0218
Johnson, Hannah 0065, **0921**, 0924, **1650**, 1774, 1779
Johnson, Hetlena 1232
Johnson, Johanna 0835
Johnson, Laura 2678
Johnson, Sindhu 1287, 1288, 1526, 2387
Johnson, Stephen 1855
Johnson, Tate 0045, 0065, 0155, 0836, 1314, **1325**, 1650, 1658, 1659, 1746, 1774, 1779, 2276, **2567**, 2585, 2661, **2681**
Johr, Chadwick 0520
Joishy, Tulsi **0466**, 0775, 1329
Jolly, Meenakshi 0377, **1235**
Jolly, Meenakshi 1915
Jolly, Meenakshi 2379, **2415**
Jonak, Constanze 1911
Jonas, Beth 1922, 1927
Jonathan, Jonathan 1398
Jones, Alex 1367
Jones, Andrew 0221, 0222
Jones, Benjamin **0023**, 0514, 2421
Jones, Brian 0988
Jones, Gareth T. 1430
Jones, Heather F. 0997
Jones, Jamila 2561
Jones, Jeffrey 2293
Jones, Jordan 0409, 0410
Jones, Morgan 0787, 0797
Jones, Nicholas 0474
Jones, Rachel 0650, 0664
Jones, William 0738
Jonsson, Anna Helena 0463, **0890**, 1702
Jonsson, Malin 0034
Joosten, Leo 2010
Jordan, Joanne 1788, 2097
Jordan M., Valeria **0734**, 1175, **1910**
Jorge, April 0217, 0599, 0804, 0805, 0813, 1467, 2211, 2377
Jorgensen, Andreea 1300
Jorid Berg, Inger 2635
Jorssen, Joseph 0907
Jose Mendéz, Carmen 2209
Joseph, justeena 1628
Joshi, Avani D. 0776
Joshi, Deepak 0447
Joshi, Swapna 1565
Joshi, Tarini 2082
Jou, Ying-Ming 0874, 2356
Jouneau, Stéphane 1592, 1765
Joung, Chung-il 1360, 1901
JOURDE-CHICHE, Noémie 0618, 2457
jousse, sandrine 0477, 0706, 2241, 2296, **2300**
Jovaní, Vega 0268, 0270, 0271, 1096, 1446
JOVEN, BEATRIZ 2344, 2373
Joy, Nino 2103
Joyce, Kelsey 0016
Jridi, Amani 0348
Juárez, Manuel 0535, 1062, 1322
Juárez, Sandra 1482
Juárez Vega, Guillermo 0287, 1836
Juan-Mas, Antonio 0496, 2268
Juarez, Vicente 0621, 0623, 1530
Juarez-Vicuña, Yaneli 1491, 2243
Juche, Aaron 0754
Judez, Enrique 1397, 1681
Juge, Pierre Antoine 1185, 1751, 2235
Julia, Caci 0440, 0441, 0442
Julià, Antonio 0019, **0021**, 2291
Julien, Anne-Sophie 1109
Julien, Marie 0618
Jullien, Denis 1448
Junaid, Yusra 0312
June, Carl 1003
June, Joshua 1675, 2278
June, Rayford 0500, 2166
Junek, Mats **0721**, **0722**
Jung, Jinhyung 0170, 1893
Jung, Seolkyoung 2533
Jung, Sung Cheol **1748**
Jung, Yehseo 0146
Jung, Younghee 1901
Jung, Youn-Kwan 0080
Jungblut, lisa 0880, 1579, 1580
Junginger, Lucas 1783
Jungmichel, Stephanie 0015
Jupe, Eldon 2384, 2649
Jurcic, Vesna 2015
Jurewicz, Mollie M. 0997
Jurik, Anne 0854
Jurisica, Igor 0042, 0560, 1756
Justice, Amy C. 2114
Justin, Tori 0381

K

K Svensson, Maria 0718
Kılıç, Levent 2043, 2349

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kılıçkesmez, Özgür 1965
Käding, Henriette 1010
Käs, Florian 1579
Köhler, Philipp 1157
Köleséri, László 0577, 1460
Kümmel, Marie Svenja **0090**
Kabani, Naureen 1708
kabra, Sushil Kumar 0416
Kadakia, Aditi 0738, 0776, 0895
Kadakkal, Ajay 1182
Kadono, Yuho 0084
Kadono, Yuho 1451
Kaeley, Gurjit 1153, 1710, 1959, 1975, 2609
Kaenmuang, Punchalee 1589
Kaewin, Suchada 0280
Kafaja, Suzanne 1725
Kageyama, Robin 1000
Kahlenberg, J. Michelle **0660**, 0949, 0951, 0985, 1741, 1760, 1816, 1852, 2418, **2451**, 2598
Kahlenberg, Michelle 0232
KAHLOWN, SARA 0657
Kahn, Jean-Emmanuel 1575, 1604, 2489
kahn, nicolas 1876
Kahn, Philip 2145
Kahveci, Aysenur 2544
Kaidar, Kfir 1305
Kaieda, Shinjiro **0061**
Kaini, Prabil 1233
Kairis, Elizabeth 2037
Kaiser, Daniela 1288
Kajio, Nobuhiko 2253, 2254
Kajiyama, Hiroshi 0084
Kakkar, Vishal 0847, 1571
Kakoullis, Loukas 2026
Kalache, Fares 0606
Kalapala, Navya 2356
Kalavri, Eleni 1452
Kale, Geetha Amritrao 1588
Kalender, Hatice 1396
Kalf, Johanna G 1205
Kalkan, Kübra 1965
Kallas, Romy **1505**
Kallas, Romy 2285
Kallenberg, David 0074
Kallinich, Tilmann 1287
Kalra, Eva **1890**, **1891**
kalsotra, Sushain 2152
Kaltchenko, Maria 2518
Kalter, Alon 1304
KALTSONOUDIS, EVRIPIDIS 1452, 2232, **2236**
Kalunian, Kenneth 1240, 1505, 1722, 2416, 2600
Kalyoncu, Umut 0778, 1008, **1188**, 2043, 2322, 2349
Kamada, Kazuro 1854
Kamada, Kazuro 2523
Kamaraj, Balakrishnan 0899
Kamata, Yasuyuki 0764
Kamath, Abhishek 0039
Kamberovic, Farah 0732
Kambhampati, Sreelekha **0424**
Kamdar, Iram 1310
Kameda, Hideto **0486**, **0487**, **1419**, 1458
Kamen, Diane 0791, 1079, 1082, 1240, 1492, 1505, 1638, 1722, 1842, 2416, 2600, 2649, 2650
Kamgar, Mohammad 0661
Kamineni, Madana 1973
Kamiya, Mari **0808**
Kammeyer, Ryann 1295
Kamonsumlitpon, Tanakrit 1118
Kamp, Stan 2649
Kan, J Herman 2148
Kan, Pei **0704**
Kana, Veronika 1206
Kanagaratnam, Anuxcy 0688
Kanaprach, Pasinee 2222
Kanbr, Omar 0549
Kandane-Rathnayake, Rangi 0595, 1878, 1899, 2696
Kandell, Barak 2537
Kane, David 0750
Kane, Kevin 0449
Kane, Kevin 1049, 1340
Kane, Sarah 2111
Kaneko, Hiroshi 0043
Kaneko, Yuko 0052
Kaneko, Yuko 0595
Kaneko, Yuko 0781
Kaneko, Yuko 1630, 2253, 2254
Kang, Darae 0916, 1777
Kang, Emily 0014
Kang, Eun Ha 1343
Kang, Hannah 1048
KANG, HEA RIM 0910
Kang, Hye Lim 0472
Kang, Jae 1020
Kang, Ji-Hyoun 1145
Kang, Jun 1852, 2518
Kang, Navneet 0716
Kang, Seonyoung **0170**
Kang, Seonyoung **0548**, 0571, 1893
Kang, Xiangyi 0138
Kang, Xiaoqiang 0005, 0986, 1001
Kang, Yu 0116
Kaniecki, Timothy 2652
Kanitkar, Medha 0692, 2496, 2503
Kannan, Arun 0558, 0562
Kannayiram, Sandhya 0308, 2575, **2629**
Kannayiram, Sandhya shri **0382**
Kanodia, Jitendra 0010
Kansurkar, Sandeep 1085
Kant, Ravi 2261
Kante, Aïcha **0681**, **0735**, **2168**
Kanters, Caitlyn **1597**
Kanthi, Yogendra 0118, 1988
Kao, Jui-Hung 0299, 0511, 1106
Kao, Lily 2164
Kapetanovic, Meliha **0434**, 0814
Kapiris, Matthaios 1115
Kaplan, Mariana 0945, 1843, 2580
Kaplan, Michael **1236**
Kaplinski, Michelle 0853, 1391
Kapoor, Akanksha **0554**
Kapoor, Mohit 1756
Kapoor, Pooja 0857
Kapoor, Sanjeev 0554
Kapoor, Teja 0899
Kara, Mete 0760
Karadağ, Omer 2349
Karadag, Omer 0779, **2043**
Karageorgiou, Ioannis 2131
Karagianni, Konstantina 2232
Karagianni, Panagiota 2236
Karagkiozidou, Dimitra 1157
Karagulyan, Roman 0632
Karahan, Dilan 2667
Karakoc, Gul 1181
Karakostas, Pantelis 0892
Karam, Elie 2200
Karamanakos, Anastasios 1439
Karamanakos, Anastasios 1452
Karateev, Andrey E. 0503
Karathanasis, Dimitris 2025
Karayev, Dmitry 0293
Karberg, Kirsten 2279
Kareem, Caseena 1588
Karibe, Yusuke 1353
Karim, Samiha **0707**, 1082
Karino, Kohei 2289
Karki, Sher 0010
Karlson, Elizabeth 1019
Karlsson Wallman, Johan 0434, 0525, 0814
Karmacharya, Paras **0546**, 1888
Karmali, Priya 1003
Karn, Anukul 1558
KAROKIS, DIMITRIOS 1452
Karonitsch, Thomas 0807, 1911
Karoopongse, Ekapun 1118
Karp, David 0023, **1524**, 1842
Karpman, Mitch 1369
Karpouzas, George 0133, **1330**
Karpouzas, George **1331**
Karpouzas, George 1950, **1955**
Karra, Ravi 1160
karras, alexandre 0618, 1768
Karri, Urekha 2037, 2155, 2666
Karsdal, Morten 2231
Kart bayram, Gözde Sevgi 2043, **2349**
Karthik, Vivin 0997
Karvaly, Gellért 2684
Karyekar, Chetan S. 0562
Karyekar, Chetan S. 1878, 1899
Kasap Cuceoglu, Muserref 2126
Kasapcopur, Ozgur 0390, 1287, 1288, 1291, 1698, 1818, 1823
Kashikar-Zuck, Susmita 1226
Kashyap Parijeya, Bansi 2417
Kasifoglu, Timucin 0778
Kasinathan, Siva **1699**

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kass, Daniel 1201
Kassan, Stuart 1046
Kassim, Shamey 2237
Kastner, Daniel 1651, 1725
Kastner, Daniel L. 0301, 1169
Kastrati, Kastriot 0510, 1911
Kasturi, Shanthini 0217, **2429**
Kataxaki, Evangelia 1452
Katechis, Spyridon 0628, 2032
Kathe, Niranjan 0726, 2003
Katikineni, Veena 0633, 2517
Kato, Hiroshi **0985**
Kato, Koji 1443
Katopodis, andreas 0990
Katsiari, Christina 1219, 2280
Katsicas, Maria 1287, 1288
Katsifis, Gkikas 1452
Katsifis-Nezis, Dimitrios 1439
Katsimpri, Pelagia 1452, 2232
Katsuda, Rinko **0459**
Katsumata, Yasuhiro 0595
Katsumoto, Tamiko 0164, 0501, 1107, 1108, 1248
Katsushima, Masao 0773
Katsuyama, Eri 0452, 2244, 2602
Katsuyama, Takayuki 0452, 2244, 2602
Katurkuri, Nishanth 1556
Katz, Arnon 1710, 1959
Katz, Guy 0743, 0992, 1606, **2033**, 2508, 2528, 2529, 2530
Katz, Jeffrey 0787, 1011
Katz, Nathaniel 2101
Katz, Patti 0217, 0218, **0377**, 0446, 0462, 0640, 0836, 1046, 1238, 1639, 1640, 1641, **1686**, 1878, 1899, 1922, 1927, 2645
Katz, Robert **1242**, **1243**
Katz Small, Alexandra 1242, 1243
Katzan, Irene 2702
Kauffman, Keith 0920
Kaufmann, Joerg 1356
Kaundal, Urvashi 1624
Kaundal, Urvashi **1725**
Kaundal, Urvashi 2700
Kauppi, Jenni 2000
Kauppi, Markku 2000
Kaur, Amisha 2492
Kaur, Dania 1012
Kaur, Ettiman 1708
Kaur, Gursimran 1498
Kaur, Noor 2147
Kaur, Pavneet 0416, **2153**
Kaur, Sharonjeet 0405
Kautiainen, Hannu 2000
Kavadichanda, Chengappa 0136, 0137
Kavadichanda, Chengappa 1431
Kavadichanda, Chengappa 2424
Kavanagh, Sarah 0574, 1451, 2347, 2374
Kavanaugh, Arthur 0567, 0581, 0874, 1959
Kavanaugh, Arthur 2317
Kavanaugh, Arthur 2355, 2357, 2375
Kavosh, Morvarid **2040**
Kavruk, Hilal 1157
Kavrul Kayaalp, Gülşah 1698, 1818
Kawachi, Izumi 2541
Kawaguchi, Takashi 2523
Kawahata, Kimito 0668
Kawahito, Yutaka 2523
Kawai, Vivian 0174, 1181
Kawamura, Tetsuji 0459
Kawano, Yumeko 0283, 2569
Kawano, Yumeko 2577
Kawashima, Tsugumi 2602
Kawaue, Ken 0043
Kawecki-Wright, Elizabeth 0311
Kay, Jonathan 0774, 1073, **1356**, 1674
Kay, Susan 2400
Kaya, kadir 2667
Kayadibi, Yasemin 2544
Kaymaz-Tahra, Sema **0760**, 1618, 1631
Kayser, Cristiane 0616
Kazerounian, Shideh **0797**
Kc, Binod 0657, **1092**
Keam, Synat 0273
Kearney, Matthew **0187**
Kearney-Bryan, Jessica 2559
Kedia, Niti 0554
Keegan, Sarah 1240
Keenan, Alexander **1376**, **1377**
Keenan, Robert **1138**
keevil, Jon 1051
Keiserman, Mauro **2362**
Kelekar, Arati 0198
Kelkar, Mona 1444
Kelleher, Eoin 0815
Keller, Everette 1232
Keller, Johannes 0397
Keller, Natalie 2084, 2096, **2098**, 2624
Keller, Ulrich 0471
Kelley, Mary 1231
Kellner, David 0240, 0451
Kello, Nina 0120
Kello, Nina 0947
Kelly, Andrew 0694
Kelly, Aoibhinn 0191
Kelly, Devon 2561
Kelly, Susan 1160
Kelly, Virginie 0523
Kelly, Will 1207
Kelly, Will 2063
Kemény, Vendel 0498
Kember, Rachel 2683
Kemble, Samuel 0798
Kemec, Gamze 0135
Kemenes, Stephan 2686
Kenar Artin, Gokce 2673
Kendzerska, Tetyana 2266, 2642
Kennedy, Michael 2035
Kennedy, Patrick 1139
Kennerley, Clare 0766
Kenney-Riley, Kathy 1278
Kent, Jessica **2128**
Kenvisay, chelsea 1805
Keravala, Annahita 0310
Keret, Shiri 0282, **0303**, 0675, 1201, 1215, 2055
Kerick, Martin 1862
Kerim, Duygu 1618
Kerkhof, Peter 2076
Kermani, Tanaz 1626
Kermani, Tanaz **1631**, 2533
Kernder, Anna 0826
Kerola, Anne 2000
Kerr, Gail 0022, 0045, 0221, 0222, 0834, 1308, 1314, 1325, 1507, 1746, 1946, 2330, 2681, 2683
Kerr, Matt 0700, 1840
Kerschbaumer, Andreas **0816**, 1908
Kersey, Emma 2685
Kerski, Marianne 0198
Kerski, Marianne **1741**, 2149
Kerzberg, Mario Eduardo 0596, 0621, 0623, 1530
Keshavamurthy, Chandana 1508
Keshavamurthy, Chandana 2392
Keshavarazi, Sareh 0560
Kessel, Audrey 0289
Kessler, Haeja **2140**
Kethri, Akuti 2037
Kettell, Sarah 2631
Kettenbach, Arminja 0081, 0976
Keyes-Elstein, Lynette 1674
Keyport, Monica 1175
Khader, Yasmin **0198**, 2217
Khairani, Candrika Dini 1428
Khalid, Aizaz Anwar 1859
Khalid, Aziz-ur-Rahman 0151
Khalid, Aziz-ur-Rahman **1880**, **1881**, **1882**, 2088
Khalidi, Nader 0721, 0722
Khalidi, Nader 0747, 1602
Khalidi, Nader 1607
Khalidi, Nader 1608, 1626
Khalidi, Nader 1767
Khalidi, Nader 1769, 2515
Khalidi, Nader 2533
Khalighi, Mehdi 1172
Khalil, Noha 0264
Khalili, Leila **0791**, **1268**, 1942, 1970, 2650, 2693
Khamashta, Munther 1531
Khan, Ahmer 0326, 2120
Khan, Asif 2676
Khan, Ayesha **1859**
Khan, Emon 1374, 1545
Khan, Humaira 1183
Khan, Lamia 0969, 0970
Khan, Mohammad Daud **1362**, 2430
Khan, muzamil **1795**
Khan, Omair **1658**
Khandakar, Amith 2638
Khandelia, Hemant 2615
Khanfar, Asim **0479**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Khanfar, asim 0513
Khanfar, Asim 1098, 1143, 1428, **2343**, 2438, 2519
Khanna, Dinesh 0161, 0689, 0811, **0843**, 0845, 0846, 0883, 0955, 0971, 0972, 1555, 1557, **1563**, 1566, 1574, 1582, 1590, 1725, 1751, 1871, 1874, 2235, 2475, 2492, 2494, 2498, 2654
Khanna, Ira 0825
Khanna, Neha 0093, 0955, **0971**, 1871
Khanna, Puja **0230**, 1138, 1998, 1999, 2217, **2587**
Kharat, Akshay 1924
Kharboutli, Soraya 0641, 1537
Kharouf, Fadi 0552, **0611**, **0612**, **0613**, 0629, **1415**, **1416**, 1425, 1426, 1550, 2691
Khasho, Maya **1359**
Khatiashvili, Barbare 1881, 2088
Khatri, Bhuwan 0034
Khatri, Bhuwan 0506
Khattri, Saakshi **2374**
Khawaja, Muznay 0364
Khaychuk, Vadim 0168, 1747
Khdeir, Aysheh 2481
Khdeir, Fatima **2481**
Kheir, Joseph 0044, 1850
Khellaf, Lucas **1604**
Khim, Socheath 0262
Khmelevskaya, Alexandra 0807
Kho, Pik Fang 0024
Khogali, Hiba 0538, 0600
Khokhar, Daniel 0319
Khokhar, Faiza 1103
Khoo, Amelia 0437
Khoo, Amelia **1090**
Khoruamklang, thunyaporn 1319
Khosravani, Sina 0509
Khosravi, Touraj 0278, **1777**
Khosravi-Hafshejani, Touraj 1474, 2428
Khosroshahi, Arezou 0279, 1163, **2019**, **2020**, 2561
Khtovatkova, Ekaterina 0028
Khubchandani, Nisha 0349
Khubchandani, Raju 0389, 1287, 1288, 2137
Khubchandani, Raju 2138, 2139
KHULLAR, AASTHA 0481
Kibiy, Angela 2451
Kida, Takashi 2523
Kidwai-Khan, Farah 2114
Kidyani, Lamk 2153
Kiefer, David 0152, 0386
Kiefer, David 1157
Kiefer, David 1461
Kiefer, Joachim 1353
Kiely, Patrick **0474**, **1136**, 1908
Kiener, Hans-Peter 0641
Kikuchi, Hirotoshi 2541
Kikuchi, Jun 0595
Kilby, Annie 1393, 1394
Kilian, Adam 2193
Kilic Konte, Elif 1698, 1818, 1823
Kilinc, Ozgur Can 0778, **1177**, 2022, 2667
Killen, Stacy 0853, 1391
Kilton, Mackenzie **1898**
Kilty, Iain 0991
Kiltz, Uta 0152, **0386**, 0545, 0591, 0592, 0854, 1157, 1411, **1461**, **1462**, **1463**, **1464**, 1729, **1934**, 2279
Kim, Alfred 0652, 1917, 2561
Kim, Billy **2385**
Kim, Bong Joon 1553
Kim, Brian **0002**
Kim, Christine **1060**
Kim, Dong Wook 0813, 1130
Kim, Edy 0808
Kim, Francis 2641
Kim, Grace 1213, 1564
Kim, Hanna 0289
Kim, Hannah 1119
Kim, Hyein 1193
Kim, Hyein 1199
Kim, Hyein 2259
Kim, Hyungjin 0170, 0548, 0571, **1893**
Kim, Hyung-Sik 0472
Kim, Hyunjin 0897
Kim, Hyun-Sook 0453, 1576, 2298
Kim, Jaeyeon **0081**
Kim, Jason 1011
Kim, Ji Soo 0529, 1028, 1037, 1596, 2302
Kim, Jimin 1983, 2620
Kim, Ji-Won 1343
Kim, Jong-Seo 0526
Kim, Jun 0799
Kim, Jun Seok 2007
Kim, Liyoung 1810, 1822, **2410**
KIM, MI HYEON 0910
Kim, MiJeong 2103
Kim, Mimi 0791, 0855, 2650
Kim, Min 1727
KIM, MIN GANG **0910**
Kim, Min Jung 0472, **2007**
Kim, Min Uk 1343
Kim, Sang **0273**, **0869**, 1107, 1108
Kim, Se Hee 0453, **1368**, 2298
Kim, Se Yun 0170, 1893
Kim, Seokhun 0541, 1410, 2361
Kim, Seon Uk 0910
Kim, Seong-HO 0171
Kim, Seonghye 0170, 1893
Kim, Stephen 1970
Kim, Sung Eun 0472
Kim, Sung-A 1014
Kim, Susan 0289
Kim, Susan 1675
Kim, Susan 2158
Kim, Tae-Hwan 0098, 0526, 0550, 1432
Kim, Tae-jong **0550**
Kim, Tae-Jong 0854
Kim, Tae-jong 1145, **1432**
Kim, Yeonhee 2298
Kim, Yong-Gil 0171, 1372, 1373, 2431
Kim, Yongjay 0365, 0382, 0634, **2226**, **2575**
Kim, Yoo Jin **2436**
Kim, Young-Eun 1372, 1373
Kim, Young-Eun 2431
Kim, Youngmin **0669**, **1913**, **2568**, 2572
Kim, Yu Jin 0571
Kim, Yun Kyu **2698**
Kim, Yunseo 0548
Kim, Yuntae 2660
Kimber, Jasmine **2092**
Kimberly, Robert **0040**, **0041**
Kimel, Miriam 2435
Kimura, Yukiko 1811, 2124, 2134, 2135
Kimura, Yuya 2449
KIMYON, gEZMIS **1440**
Kinanah, Yaseen 0713
Kinder, Travis 0296, 0866
King, Andrew 1606, 2508
King, Chris 0009
King, Jenna 1669, 2125
King, Julia **1314**
King, L. Quinnette 1638
King, Lauren 2079, 2102
King, Madison 1191
King, Miles 0364
King, Robert 0091
Kingsbury, Daniel 0401
Kinnett-Hopkins, Dominique 2455
Kinoshita, Jun 1538
Kinoshita, Takashi 0061
Kip, Annemarie 0928
Királyhidi, Panna 2684
Kiray, Amac 2673
Kiraz, Sedat 2349
Kirch, Sophie-Marie 0892
Kiri, Sandeep 1366
Kirillov, Emily 0309, 2623, 2625
Kirino, Yohei 0777, 2663
Kirkegaard-Biosca, Eric 2290, 2291
Kirkwood, Roxann 2193
Kirma, Joseph 0020
Kirou, Kyriakos 0657, 1505, 1700
Kirou, Raphael **0863**
Kirsch, Gabriel 1153, 1975
Kirwan, John 0338
Kischkel, Brenda 2010
kishimoto, mitsumasa 0562, 0576, 0577, 0638, 1443, 1460, 2339
Kishimoto, Mitsumasa 2358
kishimoto, mitsumasa 2660
Kisluk, Boris 0621
Kissin, Eugene 0848, 2177, 2314
Kitada, Ayako 2225
Kitagawa, Akiko 0459
Kitas, Georgios 2232
Kitcharoensakkul, Maleewan 0417
Kivitz, Alan **0561**, 0567, 0874, **1123**, 1998, 2103, 2357
Kiwalkar, Sonam **0825**, 0830, **2167**, 2186

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Kizilkaya, Oguzhan Omer 0778, 1177, 1477, 2022
Klöti, Jasmin 2472
klajn, Diana 2405
Klama, Kamila 0484
Klarenbeek, Naomi 0493
Klavdianou, Kalliopi 1452
Klein, Allan 0242, 1186
Klein, Ava 0186, 1669, 2125, 2128
Klein, Benjamin 0949, 0951, 1741
Klein, Jacob **0615**
Klein, Jan Philipp 1660
Klemm, Dr. Philipp 0702
Klemm, Philipp 0673, 1660
Klerman, Elizabeth 2320
Kleyer, Arnd 0343, 0471, 0878, 1010
Kleyer, Arnd 2686
Klingel, Karin 0810
Klingemann, Lauren **0924**
Klion, Amy 2532
Klionsky, Yael 1465
Klomhaus, Alexandra 0240
Klopfenstein, Noemie 1150
Klotz, Brian 0897
Klumb, Evandro **2395**
Kmetova, Katarina 0822, 0858
Kmetova, Katarina 0859
Kmetova, Katarina **1623**, 1740
Knagenhjelm, Jacob 1552
Knapp, Bertram 2374
Knevel, Rachel 1568, 1573
Knight, Andrea 1279, 1281, 1285, 1286, 1289, 1290, 1295, 1301, 1704, 1742
Knight, Ann 0718
Knight, Heather 0048
Knight, Jason S. 0115, 0120, 0121, 0126, **0127**, 0131, 0134, 0143, 0855, 0857, 0858, 0859, 0964, 1874, 2451
Knight, Julian 0104
Knight, Sarah 0357
Knipe, Rachel 0808
Knitza, Johannes 0177, 0192, **0826**, **1660**
Knobel, Philip 0015
Ko, Andy 0017
Ko, Frank 1783, 1790
Ko, Kichul 1505
Ko, Sungwon **1372**, **1373**, **2431**
Koçak, Mehmet 1008
KOÇ, EMRAH 1440
Kobashigawa, Laura 2199
Kobayasi, Renata 1293
Kobert, Linda 0289, 1218
Kobrin, Dale **2133**
Kobza, Alexandra 0214, 0215
Kocaayan, Hasan 0524
Koch, Ellen 2175
Koch, William **1122**
Kodera, Takao 2522
Kodi, Eesha 2500
Kodikara, Saritha 1703
Koegel, Ashley 0843, 1529
Koelsch, Kristi A. 0509
Koenders, Marije 0928
Koenen, Karestan 1019
Koenig, Taylor **1053**
Koenigsberger, Victoria **1989**
Koening, Curry 0721, 0747, 1602, 1767, 2515
Koffman, Dawn 0399
Koffman, Dawn 0400
Kofler, David 1175, 2279
Koga, Takuma 0061
koh, ee tzun 2247, 2248
Kohari, Katherine 0853, 1391
Kohler, Minna 0330, 0501, 0813, 1099, 1100, 1101, 1107, 1108, 1710, 1959, 1960, 2177, 2183, 2278, 2550, 2551, 2702
Kohlheim, Melanie 0374, 0404, 0824
Kohlmann, Markus 1306, 1327
Kohn, Samantha 2184
Koi, Anna 0006, 0017
Kojima, Yuichi 2289
Kok, Chung Hoow 0504
Kok, Marc R 2309
Kok, Petra 2309
Kokolakis, Georgios 0875
Kokuzawa, Ayako 0764
Kolb, Martin 0259
Kolb, Philippe 0508, 1875
Koletsos, Nikolaos 1452, 2236
Kolfenbach, Jason 2170
Koller, Adam 2639
Kollert, Florian 1403
Kolling, Fred 0812, 2581
Kollmeier, Alexa P. 2368
Komagamine, Masataka 1358
Komagamine, Masatsugu **1358**
Komagata, Yoshinori 1630
Komai, Toshihiko 1512
Kommerell, Isabel 1205
Kon, Edo **0003**
Kondo, Haruka 0764
Kondo, Naoki 0497, **1363**
Kondo, Naoya 2523
Kondo, Yasushi 2253, 2254
Konecny, Anna 0002
Kone-Paut, Isabelle 1575, 2489
Koneru, Vishnu 1431
Kono, Michihiro 2602
Kono, Michihito 1854, 2289
Konon, Elizabeth **2160**
KONSTA, MARIA 1452, **2359**
Konstantinidis, Kyriakos 0832
Konvinse, Katharine 0423
Konzett, Victoria **1911**
Koplin, Joelle 1261
Koppikar, Sahil 0565, 1710, 1714
Koralov, Sergei 0909
Kore, Pratyush 2128
Koren Krajnc, Metka 0748
Korman, Alan 0907
Korman, Benjamin 1725
Korman, David 0843
Korolev, Maxim 0476
Korostyshevskiy, Valeriy 0261
Korshko, Mariia 0098
Korsunsky, Ilya 0797
Korsunsky, ilya 0798
Korsunsky, Ilya 0808
Korsunsky, ilya 1702, 1846, 2233
Korswagen, Lindy-Anne 2309
Kortam, Neda 1751
Korukonda, Saritha 2150
Kosak Lopez, Esteban 0255
Kosakowska, Karolina 0941
Kosarek, Noelle 0812
Kosmider, Olivier 1339, 2582
Kostadinov, Kostadin 1218
Kostadinova, Lenche 1979
Koster, Matthew 0260, 0276, 0759, 0777, 1174, 1618, 2531, 2663
Kostik, Mikhail 0403, 0779, 1287, 1288
Kostikova, Anna 0009
Kostousov, Vadim 1299
Kosuri, Satya 2468
Kotani, Takuya 0773, **0973**
Kotha, Megha 1040
Kotha, Megha 1544
Kothapally Hanok, Sandeep 2454
Kothari, Vaidehi 0282
Kothari, Vaidehi **0305**
Kothari, Vaidehi 1201, 1215
Kothari, Vaidehi 2064
Kothekar, Mudgal 1456, 2082
Kottas, Konstantinos 1452
Kotton, Camille 1251
Kottyan, Leah 1826
Kotyla, Przemyslaw 0884
Kouchit, Yanis 2532
Kougkas, Nikolaos 1439, **1452**, 2236
Koulas, Ioannis **0448**
Koumakis, Eugénie 2115
Koumpouras, Fotios 0652, 0657, 1925
Kouris, Ilias 2694
Koutsianas, Christos 1452
Koutsogeorgopoulou, Loukia 1439
Kovacs, Beata 2696
Kovacs, László 2648
Kovallick, Leonard 2128
Kowal, Czeslawa 0947, 0953
Kowalski, Emily 1751, 2235
KOYAMA, YOSHINOBU 1345, **2664**
Koyi, Bindu 2470
Kozelj, Matic 2015
Kozicki, Karly 0955
Koziel, Colin 2579
Koziel, Sarah 0678, 0809
Kozu, Katia 1292
Kozu, Katia 2535
Kozuki, Tomohiro 1772
KP, Ayisha 0416
Krämer, Stefan 2520

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Krönke, Gerhard 0342, 0343, 0471, 2109, 2110, 2595
Kraan, Maarten 0431
Kraan, Maarten **0493**
Krabbe, Simon 0543
Kraft, Florian 1206
Kragh, Nana 1259, 2548
Kragstrup, Tue 0177
Krajewska-Włodarczyk, Magdalena 1883
Krall, Max 0231
Kramer, Bridget 2001, 2084, 2096, 2098, 2624
Kramer, Neil 0843, 1529
Kramp, Sabine L. 0293
Krantz, Marissa 0918, 1753
Kranzler, Henry 2683
Kraus, Julia 1660
Kraus, Virginia 0306, 2092, 2105
Krause, Andreas 0762
Krause, Dietmar 0386, 1461
Krausfeldt, Lauren 0920
Kreiger, Portia 1847
Kreis, Lena 0892
Krekhova, Elizaveta 0403
Krell, James 0523
Kremer, Joel **0449**, 1049, 1340, 2681
Kremer, Phillip **0192**
Kremser, Anja 0152
Krenitsky, Daria 1692
Kretschmann, Sascha 0641, 1537
Kreuter, Alexander 0678
Kreuter, Alexander 1862
Kreuter, Michael 1662
Kreuter, Michael 1876
Kribben, Andreas 1157
Krickau, Tobias 1537
Krikelis, Michail 1452
Krishna, Kavita 1085
Krishna J, Bala Siva rama 0416
Krishnan, Eswar 0009
Krishnan, Sridevi 0835
Kristal, Eyal 1304
Kritzer, Ryan 0888, 0997
Kroese, Frans 0034, 0694
Krol, Yevgeniy 0563, 0564
Kron, Jordana 0234, 0253
Kronenberg, Sefi 1281
Kroner, Paul 1583
Kronzer, Vanessa 0030, **1034**, 1156, 1388, 1932, 2571, 2639
Kroth, Philip 1879
Krueger, James 2688
Krusche, Martin 0192, 1660
Kruzer, Karen 0825
Kruzikas, Denise 0640
Kryštůfková, Olga 0831
KS, Farheen 0416
Ku, Brandon 2146
Kuştaş, Ali Aytuğ 2349
Kubacki, Torsten 1537
Kubassova, Olga 1963
Kubo, Satoshi 0773
Kubota, MIki 2522
Kubota, Natsuki 0452, 2244
Kubzansky, Laura 1019
Kudo, Yuki 2289
Kuersammer, Daria 0075
Kuesters, Geoff 0494
Kuga, Taiga 0106, 0521
Kuhn, Anna 1403
Kuhn, Helena 1421
Kuhn, Kristine 0060, 0088, 0800, 0870, 0889, 1653, 1695
Kuhn, Sebastian 0192, 0826, 1660
Kujawski, Sophia 0674
Kukida, Yuji 2523
Kulapatana, Phicharmon 0466
Kulisek, Nicole 2068
Kulkarni, adeep **1007**
Kulkarni, Rutuja 0997
Kulkarni, Subhash 0671, 1591, **2652**
Kulkarni, Tejaswini 1924
Kulzhanova, Gulzada 0086
Kumánovics, Gábor 0702
Kumánovics, Gábor 0879, 2684
Kumagai, Yoshi 2086
Kumano, Laurie 2536
Kumar, Bharat **2174**
Kumar, Pankaj 1784
Kumar, Sachin 1442, 2351
Kumar, Sanjeev 2153
Kumar, Uma 1197
Kumar, Vinod 1239
Kumar, Yashwant 0697
Kumar U, Ravi **1609**
Kumari, Lovely 1431
Kumari, Sangeeta 0431
Kun, József 2684
Kundakci, Burak **2387**
Kunishita, Yosuke 1725
Kunkel, Gary 0022, 0045
Kunkel, Gary 0155
Kunkel, Gary 0221
Kunkel, Gary 0222
Kunkel, Gary 0462, 0834, 0836, 1238, 1308, 1314, 1325, 1658, 1746, 1946, 2567, 2683
Kuntz, Benjamin 0342
Kuo, Chao-Chung 1206
Kuo, Ping Hsuan **1540**
Kupa, Leonard V 1192, 2653, 2682
Kuranz, Seth 2003
Kurien, Biji T 0509, **1379**
Kuriya, Bindee 0265
Kuriya, Bindee **0438**, 0442
Kuriya, Bindee 1355, 1648, **2266**, **2642**
Kuriyama, Shinichi 0850
Kuroishi, Mao 1772
Kurowska-Stolarska, Mariola 1757
Kurra, Veera Durga Vaishnavi 0492, 1071, 1554, **1806**, 2490
Kurtam, Jalal 1337
Kurtca, Miray 2044
Kurth, Stefanie 0919
Kurtz, Robert 2703
Kurup, Meenakshi **1708**
Kusaka, Hiroi 0764
Kusaoi, Makio 0521
Kushwaha, Priyanka **0872**, 1142
Kushwaha, Ritu 0057
Kutlubay, Zekayi 1477
Kutyna, monika 0091
Kuusalo, Laura 1430
Kuwana, Masataka 0304, 0702, 1212, 1574, 1586, 2065
Kuwata, Ryo 2522
Kuwert, Torsten 2613
Kuzhuppilly Arcilla, Cristine **1153**, **1975**
Kuzkina, Sofia **0476**, **0503**, **1323**
Kuzminova, Nataliia 1128
Kvarnström, Marika 0034
Kvien, Tore K. 1430
Kwan, Byron 1437
Kwan, Olivia 0126, 1299
Kwant, Lianne 1569
Kwiatkowska, Brygida 1883
Kwoh, C. Kent **0325**, 2085, 2091, 2100
Kwon, Mihye **1360**, **1901**
Kwon, Seong-Ryul **2540**
Kwon, Sooyeon 2617
Kyburz, Diego **0919**
Kyratsous, Christos 0898
Kyttaris, Vasileios **0467**, 0609, 0636, **1549**, 2427, **2433**, **2434**, 2459

L

La Barbera, Lidia 2075
La bella, Saverio 0177
La Gerche, Andre 0677, 1716, 2651
La Rocca, Gaetano 0723, 1380, 1381, 1385, **1951**
Løvendorf, Marianne Bengtson 2608
Léger-Thériault, Sonia 1109
Löffler, Christian 1601
L'Orphelin, Jean-Matthieu 0355
López, Eduardo 1322
López, Lorena 1489
López, Teresa 0346
López I Gómez, Marta 0270
López i Gómez, Marta 0271
López Lasanta, María América 1356
López Martínez, Rafael Ignacio 0621
López Medina, Clementina 0100, 0108, 0496, **0534**, 0542, 0583, 0588, 0854, **2268**, 2307, 2323, 2332, 2371, 2502
López Montesinos, Berta 0237, 1274
López Pérez, Ricardo 1321
López pedrera, Chary **0070**, **0071**, **0072**, 0087, 0094, 0100, 0108, 0121, 0139, 0795, **0901**, 1851, 2502, 2599
López Pinto, José M. 0574
López Ramírez, María Karina Lizbeth 0620
López Robles, Alejandra 0982

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

López Tarruella, Sara 2121
López Vilaró, Laura 1620
López-Cerón Cofiño, Ana 1548
lópez-Gómez, Marta 1382
López-Hoyos, Marcos 0244, 1094, 2023, 2059
López-Juanes, Natalia 0745
López-Lasanta, Maria 0379, 0380
López-Maraver, Marta 1904
López-Maraver, Marta 2265
López-Montilla, María Dolores 0100, 0108, 0542, 0583, 2323, 2371
López-Núñez, Lilian 0019, 2290
López-Sánchez, Ruben D. 2290
Lê-Dông, Nhât-Nam 2262
Labattut, Ludovic 1150
LaBelle, Jenna 0888, 0997
Labinsky, Hannah 0192, 1450
Labrador-Sánchez, Eztizen 1548
Labrador-Sanchez, Eztizen **0250**, 0737, 1613
Labus, Jennifer 1565
Lacôte-Delarbre, David 0891
Lacaille, Diane 0376, 1494
Lacalle Chanivet, Pedro J. 2106
Lacasa Molina, Joaquin 2473
LaCava, John 2418
lacerda, Marcela 2395
LaChance, Avery 0687, 0790
LaChance, Avery 2320
Lackey, Elijah 2049
Lacomis, David 2064
Lacruz Pérez, Lucía 1274
Lacruz-perez, Lucia 0237
Lacy, Carolyn 1276
Ladd, Nicole A. 0888, 0997
Ladehesa, Lourdes 0070, 0071, 0072, 0094, 0100, 0496, 0795, 0901
Ladouceur, Alexandra 1103
Lafaurie, Margaux 2510
Lafleur-Careau, Justine 0716
LaFountaine, Justin 0050
Lafyatis, Robert 1725
Lagares, David 1876
Lage, Ricardo 1407, 1408, 2326
Lages, Celine 2140
Lagoutte, Emilie 0653
Lagunes, Ivan 0776, 0895, 1349, 1443, 2273
Lah, Anja 0748
Lahey, Lauren 1338
Lahiri, Manjari 0378
Lahita, Robert 0151, 1880, 1881, 1882, 2088
Lahu, Laura-Marie 0026, 0678, 1198
Lai, Billy Tin Lok 1202
Lai, Chien-Chih 1540
Lai, Jamie 0402
Lai, pei-Hsinq **0299**, 1106, 1217
Lai, Tso-Ting 1106
Lain, Edward 0555
Laino, Maria 1548
Laird, Helen 0711
Lairez, Olivier 0123
Laiz, Ana 1620, 1773
Lake, Carol 0918, 2133
Lakhanpal, Amit 0463
Lakin, Kimberly **0844**, 0883, 1555, 1566, 1582, 2475, 2654
Lakota, Katja 0281
Lal, Aadarsh 1594, 1608, 1769
Lala, Shailee 2145
Lalazi, Brikena 0545
Lalla, Anjana 1387, 1401
Lally, Lindsay 1666
Lalou, Claude 1873
Lam, Daniel 0009
Lam, Gordon **1043**
Lam, Gordon 2278
Lam, Isabel 0319
Lam, Justin Riley **0254**, **0255**
Lam, Justin Riley 1074, 1075, 1076, 1224
Lam, Justin Riley 1513
Lam, Justin Riley 2024
Lam, Justin Riley **2093**
Lam, Ki Pui 0824, **1810**, 1822
Lam, Michael 1668
Lam, Quynh 1563, 2468, 2669
Lam, Wai-Hang Jackie 1982
Lama, Meghna 2067
lamarthée, baptiste 1150
Lamb, Lawrence **1535**
Lambert, Jérémy 0591, 2341
Lambert, Robert G. W. 0390, 0428, 0543, 0854, 1466, 1963
Lamberto, Ilaria 0009
Lambotte, Olivier 1575, 2489
Lambrecht, Bart 0907
Lammlin, Lindsey 1783
LaMonte, Adriana 1825
Lamoreaux, Brian 1991, **1992**, **1993**, **1994**, 1997
Lampa, Jon 0814
Lamprecht, Prof. Dr. med. Peter 0238, 1175
Lamptey, Robert 0456
Lamuño Encorrada, Montserrat 1635
Lamua-Riazuelo, Jose Ramón 1548, 2229
Lan, Cun 0950
Lan, Ranqing 0634
LAN, TING-YUAN 0299, 0511, 1106, **1217**
Lanata, Cristina 0625, 0637, 1504, 2646
Lanau, Alexandre 1768
Landewé, Robert 0539, 0569, 0854, 1405, 1406, 1941, 1958, 2319, 2331, 2334
Landgren, Ellen 0434
landini, Nicholas 0880, 1579, 1580
Landon-Cardinal, Océane 1193, 1199, 2259
Landres, Inna 0855
LANE, NANCY 0056, 0320
Langballe, Emily Violette 0510
Lange, Jeffrey 0797
Langefeld, Carl 0028, 0392, 0406, 0414, 1696
Langenfeld, Hannah 0601, 0759, 1726, 2571
Langereis, Morgan 1227
Langford, Carol 0717, 0721, 0747, 1602, 1626, 1767, 2515, 2533, 2702
Langholff, Wayne 0563, 0564
Langjahr, Patricia 0621
Langkilde, Henrik Zachar **2400**
Langlais, David 0968
Langley, John 0433
Langley, Richard G. 0574, 1447
Langlois, Vincent 2457
Lannes, Béatrice 0862
Lanz, Tobias 1172, 1693
Lanza, Ben 0665
Lanzo, Lucia 1567
Lao, Weng Nga 1202
Lapane, Kate 0309, 0323, 1895, 2623, 2625
Lapidus, Sivia 1669, **1827**, 2125, 2128
Laporta, Rosalia 1024, 1869, 2030
Lappas, Theodoros 2060
Lara, Jose 2576
Laredo, Jean Denis 0327
Laredo, Leonor 0483, 2036
Larena, Carmen 0757
Largo Carazo, Raquel 1404
Largy, Alexis 0958
Lari, Shahrzad 1872
larici, anna rita 0880
Larici, anna Rita 1567
LARID, Guillaume **0105**, 2115
Larkin, Jonathan 0307
Larrauffie, Aurore 1200
larroche, Claire 0508, 0516
Larsen, Isabelle 0886
larsen, michele 1682
Larsen, Peter 0027
Larson, Daniel 2531
Larson, Eric 2430
Lasa Teja, Carmen **0216**, **0243**, **0244**, **1094**, **1916**, **2388**, 2538
Lascelles, Duncan 0306, 0311
Lasheen, Maryam 0331, 0332
Lasheen, Maryam 0334
Lasheen, Maryam 0335, 1317, 1318, 1713
Laskin, Carl 0855
Lasnier Siron, Julien 2115
Laso Lucas, Esther 2107, 2108
Lassen, Mats 1166
Lateef, Aisha 0595
Latheef, Afzal 0474
Lather, Kunal 0474
Lau, Arthur 0326, 1076, 1522, 2120
Lau, Carol 1189, 2665
Lau, Chak Sing 0595, 0839
Lau, Edith 2082
Lau, Emily S. 0599, 2377
Lau, Tyrone 1239

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lauer, Kendra **0413**
Lauer, Romy 1934
Laufer, Terri 1733
Lauffoon, Maureen 2483, 2499
Launay, David 0673, 0688, 0702
Launay, David 0884, 0958
Launay, David 1577
Launay, David 1581, 1858
Laurent, Didier 2300
Lautré, Wiebke 2179
Lauwerys, Bernard 0035, 0074, 0645
Lavallee, Catherine **0396**
LaValley, Michael 0165, 1230, **1643**, 1647, 2526
Lavelle, Jane 2146
Lavery, Criswell **2084**
Lavery, Criswell 2096
Lavery, Criswell 2098
Lavery, Criswell 2624
Lavigne, Arthur 1768
Lavigne, Christian 1577
Lavilla Garcia, Vicente 2107
Lavilla Garcia, Vicente 2108
Law, Che-Leung 0262
Law, Joanna 1285
Lawrence, Able 0130, **1221**
Lawrence, Christina 0506
Lawrence, Donald P. 1099
Lawrence, Kaitlyn 1690
Lawrence, Monica 2133
Lawson, Rachel 1306, 1327
laxer, Ronald 0389, 1669, 2125, 2127, 2128, 2136
Layec, Gwenael **1572**
Laza-Briviesca, Raquel 1696
Lazar, Mitchell 0045
Lazarevic, Dragana 1287
Lazarevsky, Steven 0110
Lazarini, Argyro **2232**
Lazaro, Deana 0221
Lazaro, Deanna 0222
Lazaro, Estibaliz 1185
LAZARO, Estibaliz 1339, 2457, 2655
Lazarus, Howard 0259
Lazewski, Tristan 0218
Le, Ethan 0079
LE, Kent **0537**
Le, Nathan 1086
Le Besnerais, Maelle 2655
Le Blanc, Natasha **0297**
Le Blanc, Natasha **1607**
Le Cao, Kim-Anh 1703
le duault, yoann 2241
Le Gallou, Thomas 1765
Le Guern, Véronique 0508, 0516, 1575, 2457, 2489, 2655
Le Maire, Maxime 1450
Le Noach, Jose 0477
LE PLUART, Adrien 0439
Le Quintrec-Donnette, Moglie 0618
Le Ray, Camille 2655
Le Rochais, Marion 2296
León, Lina 0346
León-Yaurimucha, Leonor 0714, 0730, 2521
Leach, Heather 0819
Leach, Heather 1824
LEAL, SAMUEL 0341, 2310
Leander, Jacob 1374
Leandro, Maria **2458**
Leanti La Rosa, Sabina 0032
Leask, Megan 2010
Leasure, Emily 1932
Leavitt, Rollin 1763, 1844
Lebas, Céline 0618
Lebiedz, Sophie 0184
Lebiedz-Odrobina, Dorota 0883, 1555, 1566, 1582, 2475, 2654
Lebrec, Herve 0501
Lebwohl, Mark 0875, 1155, 1447
Lechtman, Sarah 2532
Leclair, Valerie 0297
Leclercq, Mathilde 1575
LECRON, Jean Claude 0105
Lederer, James 0824
Lederman, Seth 1231
Ledochowski, Justine 1285, 1742
Lee, Alison 2561
Lee, Andy 1759
Lee, Bora 0453
Lee, Brian **0691**, 1194, 1214
Lee, Carol 2444
Lee, Cathryn 1116
Lee, Chan Hee 1029
Lee, Chang-Keun 1372, 1373, 2431
lee, charles 1983, 2620
LEE, CHEN-YU 0840, 0842, 0851, **1480**
Lee, Cheol Min 1227
Lee, Danica **0864**, **2666**
Lee, Dong Yun 2431
Lee, Eric 2278
Lee, Eun Bong 0203, 1748, 2698
Lee, Eun Young 0203, 0910, 1343
Lee, Grace Haeun **0804**, **1099**, **2211**
Lee, Grace Hyeyeon **2118**
Lee, Hajeong 2698
Lee, Hanna **0080**
Lee, Hyojeong 0674
Lee, Hyun Kyung 1302
Lee, Iris 0045, 0834, 2683
Lee, Jaejoon 0170
Lee, Jaejoon 0548, **0571**
Lee, Jaejoon 1893
Lee, Jakleen 1338
Lee, Jeanie **0223**
Lee, Jennifer 0193
Lee, Jennifer 0691
Lee, Jennifer 1506
Lee, Jennifer 1516
Lee, Jennifer 2436
Lee, Jeong Seok 1343
Lee, Jessica 2141
Lee, Jiha **1065**
Lee, Jiha 1072
Lee, Jiha **1656**
Lee, Jiha **1921**
Lee, Jiha 2615
Lee, Jihey 1213
Lee, Jisoo 1029
Lee, Jongwon 0766
Lee, Joo Young 1597
Lee, Ju Young 1584
Lee, Karis **1168**
Lee, Katie 1591
Lee, Kyu-In 0598
Lee, kyung-Ann **0453**, 1368, **1576**, **2298**
Lee, Lucy Eunju 2511
Lee, Marcus 0356
Lee, Min Kyung 1168
Lee, Pui 1668, 1696, 1810, 1820, 1822, 2530
LEE, Sang Jin **2048**
Lee, Sang Min 2007
Lee, Sang-il 0080
Lee, Sang-Won 2511, 2512
Lee, Saram 1748
Lee, Seulkee 0170
Lee, Seulkee 0548, 0571
Lee, Seulkee 1893
Lee, Seunghun 1432
Lee, Shin-Seok 1145
Lee, Soyoung **1302**
Lee, Stephanie 0231
Lee, Stephanie **0520**
Lee, Sung Won 1343
Lee, Sunggun **0171**
Lee, Sung-Ki **1216**
Lee, Susan **0207**
Lee, Tai-Ju 0299, 1106, 1217, 2469
Lee, Thomas 0941
Lee, Tom 0663, 2454
Lee, Tzielan 0186, 0411, 1066, 1669, 2125
Lee, Woo Joo 0163, 1078
Lee, Yeji 2285
Lee, Yeon-Ah 1343
Lee, Young Mi 0853, 1391
Lee, Yu-Che 1091, 2657
Lee, Yun Jeong 2048
Lee, Yvonne 0440, 0441, 0442, 1196, 1223, 1225, 1227, 1249, 1424, 1649, 2430, 2605
LeeBravatti, Michelle 2301
Leechalad, Leilani 2391
Leedberg, Jordan 0913, 0930
Leeman, Brooke 2577
Leenen, Pieter 0979
Leeolou, Melissa 2062
leeth, Teresa 1508, 2392
Lefeber, Adrienne 2696
Lefebvre, Patrick 1165, 2369
Lefevre, Gaetan 1738
Lefevre, Guillaume 2532
Leff, Richard 2466

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lefort, Agnès 0735
Lega, Iliana 1714
LEGENDRE, PAUL 2532
Leggio, Cathryn 1080
Legrand, Jean-Louis 2115
Leguizamón, Maria Lilia 2405
Lehman, Erik 0500
Lehman, Thomas 1288
Lehto, Tiina 2000
Lehuen, Agnes 1724
Lei, Guanghua 0318, 0324, 1146, 2622
Lei, Tianyi 1132
Lei, Xiudong 1429
Leifer, Eric 1988
Leijding, Cecilia 0280
Leishangthem, Bidyalaxmi 0481
Leisner, Christian 0015
Leith, Nadja 1909
Lejtman, Aryeh 1827
Leland, Anna 1925
Leleti, Manmohan R 0057
Leloix, Alexia 2115
Lemieux, Jacob 2577
Lemire, Pierre 1448
Lemon, Stephenie 1073
Lenchur, Christine **1832**, 2394
Lend, Kristina 0814
Lenert, Aleksander 0221
Lenert, Aleksander 0222, 1110
Lenert, Aleksander **1149**
Lenert, Aleksander 1669, 2125
Lenert, Aleksander 2128
Lenert, Petar 1149
Lenherr-Frey, Daniel 0015
Lennon, Ryan 1556
Lenoir, Olivia 1768, 2582, 2584
Lent, Rachel 0888, 0997
Lentfert, Walter 1251
Leon, Janeen 1122
LEON, LETICIA 0483, **1269**, **2036**
Leon Alves, Soniza 0616
Leon Torralba, Patricia 2473
Leonard, Dag **0593**, **0594**, 2060, **2390**, **2647**
Leonard, Jan 1298
Leonardo, Maite 0029
Leone, Ashlee 0413
Leong, Khai Pang 2247, 2248
Leong, Pui-Ying 0806
leonhardt, sophie 0932
Leo-Summers, Linda 2114
Lepage, May-Linda 0653
Leppich, Robert 1450
Lepri, Gemma 0275, 0880
Lerang, Karoline 0133, 0593, 2390
Lerma Garrido, Juan José 2406, 2407, 2460
Lerman, Melissa 0392, 0394, 0396, 0406
Lerman, Melissa 0414
Lerman, Melissa 2146
leroux, Gaelle 2655
leroy, Sylvie 1577
Leroy David, Claire 0689
Lertkiatmongkol, Panida 0010
Lertprachakwong, Pariyaphon 2010
Lescoat, Alain 0688, 0689
Lescoat, Alain 0706, 1529
Lescoat, Alain **1555**
Lescoat, Alain 2492
Leslie, William 2685
Lesmana, Elvira 1558, 1855
Lesmana, Harry 2155
Lesnak, Joseph **1233**
Leson, Courtney 1668, 1822, 2530
LESPESSAILLES, Eric 1462, 1463, 1464
Lespessailles, Eric 1936, 1937, **1948**
LESPESSAILLES, Eric 2621
Lessard, Christopher 0514, 1682, 2233
Lessard, Christopher J. 0506
Lessard, Samantha 0316
Lester, Jenna 1176
Lestician, Colleen 0321
lesturgie, manon 0053, 1334
LESTURGIE-TALAREK, Manon **0796**, **1724**
Leszczyński, Piotr 1521
Letarouilly, Jean-Guillaume 0566, **0572**, 1095
Letarouilly, Jean-guillaume 2340
Letavernier, Emmanuel 1144
Leuchtenberger, Corinna 1206
Leung, Brent 2526
Leung, Cheuk 0209
Leung, Jerik **1232**
Leung, Kasey 1141
Leung, Monica **0558**
Leung, Ying Ying 1411
Levasseur, Stephanie 0853, 1391
Levens, Cassandra 0800
Leverenz, David 0825, 2159, 2162
Levesque, Cassandra 1669, 2125
Levesque, Hervé 2489
Levi, Eugenia **1437**
Levin, Joshua 0947
Levin, Michael 0045, 0046, 0834, 2683
Levine, Daniel 1839
Levine, Yaakov 2614
Levinsky, Yoel **1304**, **1305**
Levinson, Justin **0226**
Levinson, Justin 1050, 1052
Levis, Mark 1117
Levitansky, Henna 1253
Levy, Aviya 1208, 1275
Levy, Dan 0516
Levy, Deborah 1279, 1281, 1285, 1286, 1289, 1290, 1301, 1742
Levy, Julia **0827**
Levy, Robert 1193, 1199, 2259
Levy, Roger A. 0154, 0169, 0803, 1531, 2467, **2500**
Levy, Sarah 0474
Levy, Yair 0702
Lew, Daphne **1917**
Lewandowski, Laura 0820, 1300, 2410
Lewis, Cora 1247, 1643, 1647
Lewis, Emily 0050
Lewis, Janet 1378, 1384
Lewis, Kevin 0126
Lewis, Martin 2561
Lewis, valerie 0509, **2432**
Lewis. Horowitz, Diane 0774
Lhuissier, Charlene 1873
Li, Bin 0082, 0906
Li, Chang 0906
Li, Changjun 0324, 2622
li, changpei 2061
Li, Chao 2697
Li, Cheng **0318**
Li, Chenhao 0032
Li, Christopher 2237
Li, Chun **0116**
Li, Chun 0132
Li, Chun 0141
Li, Daniel 0024
Li, Dongmei 1068
Li, Edward **2111**
Li, Fanshu 0132
Li, Fen 0468
Li, Feng 1761
Li, Fengju 0876
Li, Fengxia 0005, 0986
Li, Fugang 0939
Li, Hewei 0257
Li, Hong 0468
Li, Hongbin 0468
Li, Hongbin 0649
Li, Hongbin **1441**
Li, Hui 0324
Li, Huilin 1032
Li, Huilin 1441
Li, Huilin 1776
Li, Huilin 2008, 2590
Li, Janice 0455
Li, Jia **0490**, **1956**, 2672
Li, Jiaming 2380
Li, Jiangning 1743
Li, Jianguo 2005
Li, Jiatian **0324**, **2622**
Li, Jiayi 0522
Li, Jing 0005
Li, Jing 0189, 0219, 0220, 2617, 2685
li, Jingfei 2012
Li, Jingjing 1179
Li, Jingjing 1776
Li, Jingjing 2672
Li, Jingna 1036
Li, Jinyang **0082**, **0905**, **0906**
Li, Jon 0823
Li, Jonathan 2577
Li, Juan 0649, 2013, 2014
Li, Jun 0049, 1782, 1783, 1790, 1800
Li, Kexuan 0874
Li, Ko-Jen 0299, 0511, **1106**, 1217
Li, Li 0082

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Li, Lianghua 1956
Li, Linda 0177
Li, Liu 0905, 0906
Li, Lulu 0911, 1776
Li, Lumeng 0957, **0967**, 1867, 2497
Li, Lux 2563
Li, Manci 0027
Li, Mei 1429
Li, Mengjiao 0646
Li, Mengtao 0468, 0861, 1316, 1541, 1750, 2597
Li, Miriam **2419**
Li, Mucong 1316
Li, Nan 1799
Li, Peiying 2465
Li, Philip 0839
Li, Qiang 0839
Li, Qianyun 2409
li, qingyan 1642, 2005
Li, Qinmengge 0127, 1741, 2498
Li, Qiubai **0646**
Li, Qixuan 0611, 0613, 0629, 1550
Li, Quan 0112
Li, Rongbin 2013, 2014
Li, Rongping 2013, 2014
Li, Shangzhong 0873
Li, Shilin 0077
Li, Shu 0875
Li, Shu 2353
Li, Shufeng 0691
Li, Siqi 0003
Li, Suzanne 1287, 1288, 1291, 1827
Li, Tengfei 0197, 0225, 1375
Li, Tengfei 2104
Li, Tengteng 0001
Li, Tianai 2128
Li, Tianhong 1006
Li, Tiing 0656
Li, Tingting 0726
Li, Tricia 2408
Li, Wei 0324, 2622
Li, Xianwei 0042, 1714
Li, Xiaodong 1727
Li, Xiaojun 0076, 0889, 1695
Li, Xiaoshun 0316
Li, Xinhao 1316
Li, Xinyi 0647
Li, Xue 0966
Li, Yang 0905
Li, Yangfen 1726, 2384, 2649
Li, Yanjie 1535
Li, yanling 0876
Li, Yasong 0649
Li, Yi 0911, 1776
Li, Yi 1918, 1919
Li, Yijia 2577
Li, Yi-Nan 0026, 0678, 0809, 0810, 0956
Li, Yi-Nan 0962
Li, Yi-Nan 0974, 0975, 1757, 1856
Li, ying 1726
Li, Yinghui 0861
Li, Yixuan 1002
Li, Yiyi 0905
Li, Yuanteng **0209**, 0273
Li, Yucui 2495
Li, Yuqing 1643
Li, Zhanguo 0595
Li, Zhanguo 1510, 1514, 1515
Li, Zhanguo 2464
Li, Zhaohua 0647
Li, Zhixiu **2570**
Li, Zong-Ming 0325
López, Marta 0019, 0250, 0269, **1171**, **1773**, 2290
Liakouli, Vasiliki 1864
Lian, Christine 1767
Lian, Xinyue 0887
Liang, Jing 0646
Liang, Jingyuan 1515
Liang, Juan **0109**, **0922**, **0946**, **1761**
Liang, Lidan 0082
Liang, Minrui 0956
Liang, Wenying 0127
Liang, Wenying 0858, 0859
Liang, Wenying 1623
Liang, Wenying **1874**
liao, cheng 0915, 0998
Liao, Duanping 1524
Liao, Katherine 0168
Liao, Katherine 0283, 1016
Liao, Katherine **1336**, 1357
Liao, Katherine **1957**, 2276, 2568, 2569
Liao, Katherine 2607
Liao, Katherine 2681
Liao, Pei-Lun 0806
Liao, Shuyi 2061
Liao, Wilson 2233
Liao, Yifei 1696
Liao, Yu-Wan 2469
Liardo, Elisa 0009
Liarski, Vladimir 1215
Liaskos, Christos 1219, 2280
Liau, Adriel 0186, 2128
Liazoghli, Dalinda 2281
Liberatore, Johanne 1766
Libermann, Towia 2105
Libman, Michael 1109
Librizzi, Matthew 2605
Lichti, Cheryl 0948
Lichtiger, Anna **1944**
Lichtiger, Anna 1974
Liebel, Christoph 0960, 0961
Lieber, Sarah 0382, **0634**, **0635**, 1072, **2426**, 2575
Lieberman, Richard W. 0859
Lieberman, Scott 2124
Liebetanz, David 1206
Liebich, Claire-Felicia 2595
Liew, Jean 0325
Liew, Jean 1104, 1105, 1718, 2100, 2526
Liew, Jean 2634
Liew, Zeyan 0122
Liewluck, Teerin 2056
Lifermann, François 0891, 1592, 2532
Lightstone, Liz 0654, 0664, 1521
Liles, Sydney **0771**, 1637, **1649**, **2605**
Lilleby, Vibke 0420
Lillegraven, Siri 0420
Lim, Bryant 0378
Lim, Hyunjin 0080
Lim, Hyunsun 1029
Lim, Jamie **1160**
Lim, Lillian 1669, 2125
Lim, Lily 0388, **1494**
Lim, Melissa 1755, 1756
Lim, Mie Jin 2540
Lim, Min Hyuk 1748
Lim, S. Sam 0218, 0707, **1083**, 1638, 1639, 1640, 1641, 1722, 2416, 2561, 2645
Lim, Sean 1214
Lim, Siriwan 0378
Lim, Soo Kun 2697
Lim, Stephanie 1981
Lim, Weikeat 0897
Lima, Guadalupe 1482
Limal, Nicolas 0891
Limas-Martínez, Victoria P. 1427
Limaye, Vidya 0304
Limnander, Andre **0897**, 0898, 0934
Lin, Bin 0920
Lin, Chang-Song 1114, 1799
Lin, Chun-Yu **1634**
Lin, Clara 0819
Lin, Clara 1824
Lin, Clara 2177
Lin, Clarice **1225**
Lin, Fei 0003
Lin, Heather 0209
Lin, Janice 0210
Lin, Janice 0330, 1960
Lin, Jin 2463
Lin, Judith 0615, 0657
Lin, Karen **1067**
Lin, Kuan-Tung **1982**
Lin, Kuan-Yen 0299, 1217
Lin, Shu-Ju **0881**
Lin, Wanyi 1865
Lin, Xi **1808**
Lin, Yanwei 1179
Lin, Ying-Li 1017
Lin, Yu Heng 0511
lin, yuan 0915, 0998
Lindberg, Hanna **0718**
Lindblade, Christopher 0853, 1391
Lindblom, Julius 0125, 0842, 1531, 2401
Lindborg, Beth 0027, **1786**, 1797
Lindhagen, Lars 0718
Lindholm, Catharina 1545
Lindquist, Ingrid **0893**
Lindqvist, Elisabet 0434, 0814
Lindsay, Christine 0187
Lindsay, Lisa 0838, 1038
Lindsey, Stephen 1069

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lindsey, Stephen 1080
Lindsey, Stephen 2370
Lindström, Ulf 0525
Ling, Heidi 0839
Ling, Hong **0005**, **0986**, 1001
Ling, You-Li 1444, 2337
Lingamaneni, Ankitha 1260
Linklater, Helen 0474
Link-Malcolm, Jessica 1256, 1257
Lioté, Frédéric 1998
Liozon, Eric 0756, 2532
Lipham, Bailey 2190
Lippe, Ralph 2367
Lipscombe, Lorraine 2079
Liranzo Tejera, Niurka 1832, 2394
Lirette, Jackson 0888, 0997
Lisitsyna, Tatiana 1323
Liso Andrino, Andrea 1170
Lister, Rachel 1876
Litman, Heather 2640
Little, Courtney 1563, 2669
Little, Mark A. 0900
Littlejohn, Emily 1529
Liu, Aijing **1517**
Liu, Aixia 0986
Liu, Caizhen 0077, 0173
Liu, Chao 0134, 0857, 0858
Liu, Chunmei 2452
Liu, Chunyan 2129
Liu, Clive 1457
Liu, Cynthia 1837
Liu, Dajiang **1523**
Liu, Dajiang 1524
Liu, Dandan 0018, 1006
Liu, Dawei 0429
Liu, Fei 1767, 2033
Liu, Feng 2583
Liu, Guishan **1158**
Liu, Haixia 2157
Liu, Hongjiang **2061**
Liu, Huiling 0001
Liu, Jane 0016
Liu, Jia 2465
Liu, Jiangmei 0468
Liu, Jianjun 1956
Liu, Jing 0102, 1752, 1754
Liu, Jinqi 0590, 0660, 0873, 2694
Liu, Ju 0468
liu, kaili 0998
Liu, Ke 0010
Liu, Lei **1131**
Liu, Li 0490
Liu, Miao Miao 0194
Liu, Mingyao 2463
Liu, Min-Ying 1114
Liu, Qing-Ping 1799
Liu, Rui 0647
Liu, Rui 0908
Liu, Shanrun 1837
Liu, Shao-Hsien 0309, 0323, 1895, 2623, 2625
Liu, Shen 2100
Liu, Shengyun 0649
LIU, SHENGYUN 0876
Liu, Shu **0519**
Liu, Shuang 2353
Liu, Sucai 0088, 0800, 1653
Liu, Tiezheng 0013
Liu, Ting 0939
Liu, Tong 0082
Liu, Winnie 2119
Liu, Xiangjun **0141**, 0143
Liu, Xiao-Bao 1799
Liu, Xiaojing 0646
Liu, Xiaoqing 0013
Liu, Xiaoxiao 0005, 0986
Liu, Xingyi **0469**
Liu, Yanxi 1443
Liu, Ye 1045, **1054**
Liu, Ye 2119
Liu, Ye **2566**
Liu, Yuhan 1172, 1664
Liu, Yuhong 0646
Liu, Zhichun 2464
Liu, Zixing **1037**
Lively, Brittany 2173
lively, star 1756
Lizasoain Alustiza, Carlos Maria 1904, 2107, 2108
Llamas Urbano, Adrián 0100, 0901
Llanes, Marta 2373
Lledó Ibáñez, Gema María 1210, 1953, 2471
Llorca, Javier 0608
Llorente, Irene 2122
Llorente, Luis 1482
Llorente Cubas, Irene 1869, 2030
Lloyd, Mark 0474
Lloyd-Jones, Donald 1745
Lo, Edward 1787
Lo, Grace 0309, 0313, 0323, **2089**, **2090**, 2623, 2625
Lo, Jamie Chieh **2659**
Lo, Jeffrey 1810, 1822
Lo, Mindy 0392, 0406, 0414, 1810, 1822
Loarce, Jesús 1024
Loarce, Jesús **1335**, 1561, 2016, 2229, 2265
Loarce Martos, Jesus 1869, 2030
Lobato da Cunha Sauma, Maria de Fátima 1365, 2246
lobbes, hervé 1598, 1604
lobo, david 0530
Locatelli, Franco 0641
Lochhead, Robert 1789
Lockshin, Michael 0365, 0382, 0634
Lockshin, Michael 2575
Lockshin, Michael 2629
Lockwood, Laura 2161
Locock, Louise 1244
LOCRELLE, Hervé 0537
LODHA, RAKESH 0416
Lodin, Karin 2060
Lodin, Karin 2065
Loecker, Courtney 0446
Loeser, Richard 0306, 1788, **1801**, 2092
Loetfering, Frederik 0075
Loft, Anne Gitte 1430
Logis, Evelin 0679
Loh, Christopher 1395
Lohr, Matthias 0279, 1163, 2019, 2020
Loizidis, Giorgos **0445**
LOJO-OLIVEIRA, LETICIA 0180, 1548
Lokineni, Sravani 0657
Lomanto Silva, Raisa **0282**, 0344, 0720, 1072, 1201
Lombardi, Fiorella Anna 0246, 1352, 2479
London, Jonathan 1577
Londono, John 2336
Long, Andrew 2087
Long, Henry 1696
Long, Xianming 0519
Long, Yuxi 1315
Longo, Cristina 2563
Lonowski, Sarah 1898
Lood, Christian 0059
Lood, Christian 0747
Lood, Christian 0836
Lood, Christian 1208, 1209, 1602, 1750, 2147, 2597
Looijen, Agnes **0176**
Loomba, katherine **0349**
Loomis, Cynthia 1759
Looney, Cary 0654
Looney, John 0942
Lopalco, Giuseppe 0275
Lopes, Carolina S. 2668
Lopes Almeida Gomes, Lais 0278, 1474, 1852, 2428
Lopez, Andrea 2049
Lopez, Ausitn 1794, 1806
Lopez, Daniela 0083
Lopez, Jean Guillaume 1339
Lopez Corbeto, Mireia 1282, 1284
LOPEZ DIAZ, ANA JIMENA 2632
LOPEZ DOMINGUEZ, LUIS 2107, 2108
Lopez Gonzalez, Maria del Carmen 2354
Lopez Gutierrez, Fernando 0270, 0271, 0737, 1613
Lopez I Gomez, Marta 0485, 2350
Lopez Juanes, Natalia **0755**, **2042**
Lopez Mejias, Raquel 0029, 1778
Lopez Muñiz, Belen 1869, 2030
Lopez Viejo, Patricia 2373
Lopez-Benitez, Jorge 1288
Lopez-Cantú, Leslie Y. 1483, 1528
Lopez-Ceron Cofiño, Ana 2670
Lopez-Davis, Charmaine 0506
Lopez-Dominguez, Luis Maria 0485, 2269, 2350
Lopez-Flores, Vanessa L. 0366, 1023, 1928, 2553
Lopez-Gonzalez, Ruth 1397, 1681

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lopez-Olivio, Angeles 0209, 1920
Lopinto, Giulio 1212
Lora, Maximilien 0968, 1475
Lorente Betanzos, Iván Jesús 2406, 2407, 2460
Lorenz, Hanns-Martin 0678, 0932, 1875, 1876
Lorenz, Megan **1025**
Lorenzin, Mariagrazia 1127
Lorenzo, Jose Paulo 2004
Loreth, Tobi 0204
Loricera, Javier 0200, 0244, 0270, 0271, 0736, 0737, 0739, 0740, 0744, 0752, 0757, 1612, 1613, 1681, 2265, 2610
Lories, Rik 0111, 0528
Losanto, Jhonatan 1486
Losappio, Laura 0238
Losina, Elena 0787, 1011, 2097
Losterova, Veronika 1350, 2346
Lottenburger, Tine 2400
Lotz, Martin 1782, 1796, 1805
Louden, Diana 0720, 1072
Loupasakis, Konstantinos 0448
Lourido, Lucía 0329
Lourie, Eli 0229
Louthrenoo, Worawit 0595, 1878, 1899
Louzada Junior, Paulo 1365, 2246
Lovasi, Gina 0354
Love, Ruschelle 0010
Lovell, Claudia 1723
Lovell, Daniel 0389, **0401**, 0405, 0418, 0419, 1669, 1813, 1829, 2125, 2677
Low, Andrea 0194, 0304
Low, Andrea 1565
Low, Andrea 2651
Low, Robert 0579, 0580, 2366
Lowe, Christine 0002
Lowe, Eric 2466
Lowe, Hudson 0482
Lowe, Katie 0504
Lowery, Jada 1276
Loza, Matthew 1839, 2297
Lozano, Teresa 1133
Lozano Morillo, Fernando 1548
Lozano Rivas, Nuria 2422
Lozano-Montoya, Jose 0538
Lozenski, Karissa **0257**, 0577, 1460, 2345
Lozinska-Lozinska, Tetyana 1904
Lozy, Tara 0398, 1827, 2135
Lu, Angela **2381**
Lu, Bing 0321, 0322, 1895
Lu, Cheng-Hsun 0299, 0511
Lu, Chenyang 0093
Lu, Chun chi 2469
Lu, Guanqi 2585
Lu, Huifang 0273, **1920**, 2669
Lu, JD 2035
Lu, Jian 1514
Lu, Jun 1762
lu, leo 1995, 2008, 2214
Lu, Liangjing 1865
Lu, Ling-Ying 2469
Lu, Qianjin 1762
Lu, Rufei 0023, 0044, 0514, 0840, 1240, 1480, 1831, 1850, 2169, 2421
Lu, Theresa 0927
Lu, Timothy 2641
Lu, Zhen 1776
Lubberts, Erik 0978, 0979
Lubinus, Manuel 0289
Lubrano, Ennio 0577, 0854, 1460
Lucas, David 0056
Lucas, Dillan 1637
Lucas, Xavi 0009
Lucas Ribeiro, Andre **0565**, **1710**
Lucero, Katie 2282
Lucero, Luciana Gonzalez 1486
Luciano, Nicoletta 0532
Luef, Stefan 2400
Luetkens, Karsten Sebastian 1450
Luey, Audrey 0186
Luggen, Michael 0195
Luggen, Michael E 1456
Lugo, Claudia 0833, 2628
Luime, Jolanda J 2309
Luis, Sushil Allen 0242, 1186
Luis-Rodríguez, Desirée 0728
Luizza, Leah 2437
Luk, Lucas Tsz Ho 1202
Lukacher, Aron 0984
Lukas, Cedric 0534
Lukusa, Luck 0475
Lumbreras Márquez, Mario Isaac 2218, 2632
Luna-Mireles, Norberto 2557
Lund, Jennifer 0145
Lundberg, Ingrid 0280, 2060
Lundin, Knut EA 1867
Lunning, Matthew 0663
Lunning, Matthew 2454
Luo, Hui 0468
luo, jing **1622**
luo, Lingfeng 2362
Luo, Qiang 1303
Luo, Qiang 1828
Luo, Qinhuan 1036
Luo, Shue Fen 0595, 1878, 1899
Luo, Shue-Fen 2469
Luo, Xiwen 0429, 1828
Luo, Xiya 0429
Luo, Yiming 0883
Luo, Yiming 1555
Luo, Yiming 1566, 1582
Luo, Yiming 2475
Luo, Yiming 2586, 2654, 2666
Lupeika, Debra 2056
Luppino-Assad, Ana Paula 0206, **1192**, **2653**
LUPPINO-ASSAD, RODRIGO 0179
Luqmani, Raashid 1912
Lurier, Emily 0913, 0930
Lusco, Mark 0942
Luster, Andrew 0992
Luta, Alex **0682**
Lutgen, Sophia 1832, 2394
Lutz, Stephen 0987
Lutz, William 2699
Luz Felipe da Silva, Dimitri 2067
Lyles, Mary 2097
Lynch, Hayley M **1064**
Lynde, Charles 0555
Lynton, Jessica 1973
Lysenko, Lidiya 0779
Lyu, Xia 2672

M

M, Noorjahan 1423
M, Radhika 0708
Ma, irene 2177
Ma, Jian-Da 2245
Ma, Kevin Sheng-Kai **1105**, **1718**
Ma, Leyao 1541
Ma, Margaret 0378, **2247**, **2248**
Ma, Tony 1176
Ma, Xiaobei 0102
Ma, Xiao-Na 1114, 1799
Ma, Yiyangzi 1663
Ma, Yuhan 1067
Ma, Zhaoru 0905
Mátay, Gábor 2684
Müller, Fabian 0641, 0843, 1537, 2442, 2695
Müller, Marcel 1729
Müller-Durovic, Bojana 0510
Müller-Ladner, Ulf 0075, 0090
Müller-Ladner, ulf 0702
Maasen, Hannah 0410
Mabus, Sarah 1976
Mac Gearailt, Conall **1409**
Macía, Manuel 0728
Macaraeg, Marci **2129**
Maccora, Ilaria **0406**, **0407**, **2675**
MacDonnell, Scott 0934
Maceiras, Francisco 2373
Macfarlane, Gary **1014**, 1244, 1430
Machado, Camilla R.L. **0069**, 0097
Machado, Natalia 1407, 1408, 2326
Machado, Pedro 0289
Machado, Pedro 0474, 0569, 0854, 1136, 1908
Machado, Ricardo 1292, 2535
Machado Escobar, Maximiliano 2405
Machattou, Maria 1170
Machhar, Rohan 0560
Machin González, Sergio 1490
Machua, Wambui 0217, 2429
Macía-Villa, Cristina 2344
Macias, Lysseth 2336
Macias-Segura, Noe 0212, 0213, 1834, 1845, **2219**
Maciuch, Jessica 0066
Mackay, James 0309, 0323, 2623, 2625
mackay, Meghan 0791, 1722, 2416, 2650

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Mackensen, Andreas 0641, 1537, 2442, 2695
Mackie, Sarah 1084, 1526, 1626
MacLaughlin, Edmund J **0246**, **1352**, **2479**
Maclean, Ashley 2056
Maclean, Mary 0301, **1651**
Macwana, Susan 0023, 0044, 0514, 1831, 1850, 1852, 2421, 2649
Madan, Riya 0231
Madari, Queeny 1569
Madhu, Roopa 0851, **1846**, 2233
Madison, Danielle **0319**
Madison, Jacqueline 0115, **0126**, 0127, 0131, 0134, 0143, 0857, 2143, 2149
Madrid, Alfredo 0183
Madrigal, Vanessa 0317, 1264
Madsen, Norman 2177, 2183
Madubata, Chioma 1741, **1816**
Maeda, Kohei 2494
Maejima, Yasuhiro 1630
Maerz, Tristan 0316, 1739, 1783
Maestro Saavedra, Francisco Javier 2106
Magallares, Berta 0269, 0642, 1171, 1282, 1284, 1620
Magallares, Berta 1773
Magallares, Berta 2450
Magaziner, Samuel 2582
Magder, Laurence 0597, 0607, 0837, 1498, 1499, 1516
Magi, ilaria 2656
Magi, Mayu 0781
Magnant, Julie 0891
Magni-Manzoni, Silvia 0389, **0391**
Magno, Giulia 2476
Magnolo, Nina 0875
Magnus, Maria Christine 0427
Magrey, Marina 0854, 1443, 1449, **1451**, 2216, **2360**, 2363, 2364
Magri, Sebastian 0584, 0877, 2257
Maguire, Ciara 2145
Maguire, Colin 0709
Maguire, Sinead **2200**
Mahé, Isabelle 0735
Mahajan, Arjun **0687**, **0790**, **2525**
Mahajan, Avanika **0315**
Mahajan, Tina 1751, 2235
Mahajan, Vinay S. 0992, 2528
Mahan, John 0193
Maharaj, Narendra 0498
Maharana, Umakanta 0461
Mahdy, Menat Alla Ayman Ali 0331, 0334, 0335, 1317, 1318, 1713
Mahendira, Dharini 2200, 2627
Maher, Toby M 1662
Maheswaranathan, Mithu 0363
Maheswaranathan, Mithu 0367
Maheswaranathan, Mithu 0793
Maheswaranathan, Mithu 1487
Maheswaranathan, Mithu 2379
Maheu, Emmanuel 0327
Mahgoub, Shirihan 2123
Mahieu, Mary 2430
Mahmood, Adnan 0780, 1671
Mahmoud, Amr 2318
Mahmoud, Khaled 2393
Mahmud, Shawn 0983
Mahr, Alfred 1626
Mahrhofer, Hartmut 1601
MAILLARD, Helene 2655
Maillefert, jean-francis 1150
Mailoo, Tharuni 1743
Mainolfi, Nello 0913, 0930
Mairal Monesma, Jorge 1404
Maisha, Jeba Atkia 0799
Maitz, Stephen 1378, 1384
Maiz, Olga 0200
Maiz, Olga 0737
Maiz, Olga 0739, 1612, 2610
Maiz Alonso, Olga 0268
Majety, Sameer Kumar 0167
Majithia, Vikas 0300, 0727, 0843, 0854, 1529, 1585, 1986, 2018
Majjhoo, Amar 2587
Major, Matthew 2259
Major, Triin 0798
Mak, Anselm 2248
Mak, Catherine 2408
Makhoul, Ghassan **0151**, 1880, 1881, 1882, **2088**
Makhzoum, Jean-Paul **0731**, 1109
Makhzoum, Jean-Paul 1597
Makhzoum, Jean-Paul 1607
Makin, Harriet 0357
Makinde, Hadijat 0066, 0081, 1362
Makita, Sohei 1814
Makkar, Binni 0352
Makol, Ashima 0825, 0883, 1555, **1558**, 1566, 1582, 1855, 2475, 2654
Makowska, Joanna 1218
Makrecka-Kuka, Marina 0991
Makris, Una 1238, 1256, 1257, 1260, 1921
Maksymowych, Walter P 0590, 0873, 1963
Maksymowych, Walter P. 0390, **0428**, 0531, **0854**, **1466**, **2335**, 2636, 2677
Makuch, Sebastian 0096
Malaise, Olivier 2115
Malaiya, Ritu 0474
Malattia, Clara 0401
Malave, Janire 2373
Malbec, Marine 0897
Malcova, Hana 1287, 1288
Maldonado, Genessis **1952**
Maldonado, Genessis **1953**, **1954**, 1969
Maldonado, Genessis 2413
Maldonado, Hernan 1422
Maldonado Chaar, Sergio **2074**
Maldonado Luna, Angela 0507
Malfait, Anne-Marie 0316
Malfait, Anne-Marie 1736, 1739
Malfait, Anne-Marie 1780
Malfait, Anne-Marie 1782, 1783
Malfait, Anne-Marie 1790
Malfait, Anne-Marie 1796
Malfait, Anne-Marie 1800
Malfait, Anne-Marie 1805
Malheiro, Olivio 1407, 1408, 2326
Maligireddy, Anand Reddy 0383, 0384
Malik, Amir 0648
Malik, Farheen **1063**
Malik, Rayaz 0234
Malik, Saadia 1253, 1931
Maliyar, Khalad 0565
Mallett, Steve 0780, 1671
Mallia, Ilenia 1570
Malpas, Kathryn 0074
Maltez, Nancy 0294, 1103, 2069
Malvar, Ana 0623, 0650, 1521, 1530
MAMADAPUR, MAHABALESHWAR 2004
Mambu Mambueni, Hendrick 0103
Mammadova, Vafa 0920
Mammen, Andrew 0288, 0289, 0296, 0301, 0863, 0866
Mammou, Saloua 0477
Mamoh, Ufuoma 1224, **1513**, 1646
Mamoh, Ufuoma 1707
Mamoh, Ufuoma 2024
Mamykina, Lena 1268
Manabe, Naoto 1167, 1611, 2212, 2488, 2534
Manada De Lobos, Vanessa 0066, 0935, 1227, 2430
Manadan, Augustine 1420, 2504
Manaskie, Michelle 0408
Manasson, Julia **0008**, **0987**
Mancini, Mathieu 0968
Mancipe, Natalia 0027
Mancl, Erin 1443, 1465
Mandal, Mriganka 2577
Mandal, Murari 0461
Mandel, Steven 1378, 1384
Mandelin, Arthur M 1362
Mandell, Chase 2577
Mandl, Lisa 0382, 0634, 0635, 2426, 2429, 2575
Mandl, Peter 1911
Manente, Myriam 1454, 2352
Manero-Ruiz, Javier 1446
Manfrè, Valeria **1680**, **2545**
Manger, Bernhard 0762
Manger, Eva 1911
Mangin, Madison 0407, **0995**, 1004, 1005
Mangla, Lavanya 1218, 2066
Manglani, Monica 2141
Manicka Bharathkumar, Hayagrivas **0447**
Mankia, Kulveer 0832, 1677, 1678
Mann, Herman 0777
Manna, Zerai 1470
Mannent, Leda 0239, 1666
Manning, Catherine 0872, 0925
Manning, Joanne 0686, 1966, 2493
Mannion, Melissa 0411, 1066, **1252**, 1276, 1277, 1495, 2132

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Manno, Atsushi 1848
Manno, Rebecca 2163
Mannumbeth Renjithlal, Sarath Lal 1877
Manrique-Arija, Sara 0019, 1397, 1681, 2290
Mansfield, Tyler 0320
Mantovani Cardoso, Eduardo 2459
Manuel Hernández, Pedro José 2112, 2113
Manukyan, Nune 0879
Manvar, Dinesh 0016
Many, Gina **0320**
Manzano-Canabal, Guadalupe 0019, 2290
Manzi, Susan **1545**, 1722, 2416
Manzo, paola 1863
Mao, Catherine 2380
Mao, Huiyan 0664
Marí-Alfonso, Begoña 1210, 1953
Marabelle, Aurelien 1115
Marín, Carolina 0201
Marín de Prada, Balbina 2106
Marín-López, Hilda 1482
Marasco, Emiliano 0391
Maravillas-Montero, José Luis 1836
Marchese, Maya 0362
Marchetti, Bruno **2506**
Marco, Francisco 1096
marcoccia, antonella 1562
Marco-hernandez, javier 0896
Marco-Pascual, Carla 0353, 1620
Marcy, Daniele 2205, **2628**
Marder, Bradley **1991**, 1993
Marder, Galina 2017
Marder, Wendy 0232, 0440, 1225, 1249
Marec, Nadege 1738
Maretz, Caroline **2205**
Margaitis, Jeremy 0002
Margaretten, Mary 0182
Marges, Emiel 1569
MARHADOUR, Thierry 0477, 2300
Maria, Alexandre 1339
Mariam, ERRAOUI 1930
Mariano, Alberto 0269, 1171
MARIASELVAM, CHRISTINA 0136, 0137
Mariaselvam, Christina 1431
MARIASELVAM, CHRISTINA 2424
Maricos, Meron 1175
Mariette, Xavier 0034, 0508, 0516, 1115, 1185, 1575, 1683, 1685, 2489
Marilao, Jonathan 0126, **0129**
Marin, Benoit 2457
Marin, Carolina 0351, 2373
marin, josefina 1710, 1959
Marin, Josefina 2344
Marin Ballve, Adela 1953
Marin.Muñoz, Fatima Adriana 2557
Marinaro, meredith 1251
Marinello, Diana 2179
Marinho, Adriana 1407, 1408, 2326
Marino, Caitlin 2577
marinopoulos, anastasia 1784
Marion, Miranda 1696
Mariotti, Elena Biancamaria **2699**
Mariz, Henrique 0596, 0623, 1530
Mariz, Henrique Ataide 1486
Mark, Ejim **1155**
Marketos, Nikolaos **0515**
Markovic, Daniela 1213, 1214
Markovic, svetomir 1726
Markovics, Adrienn **0049**
Marks, Angel 0404
Marks, Kathryne 0988, 2414, **2644**, **2688**
Marks, Yanara 2563
Markus, havell 0984, 1523
Marlin, Caleb 1846, 1852, **2233**
Marone, Alessandro 1970
Maroof, Avin 1930
Marotta, Anthony **0531**, 2335, 2636
Marotte, Hubert 0537, 1095
Marouane, Boubaya 0884
Marque, Fanny 0903
Marques, Claudia 0179
Marques, Claudia 1407
Marques, Claudia 1408, 2326
Marques, Mary Lucy 0539, 0540, 1405, 1406, 1958, 2319, 2635
Marquette, Charles 1577
MARQUEZ-SANCHEZ, ALBERTO ALEJANDRO 1390
Marrache, Fredric 1327
Marrani, Edoardo 1287, 1288
Marrani, Edoardo 2128
Marras, Carlos 0021
Marras Fernández-Cid, Carlos 2450
Marrone, Michael **1929**
Marrugo, Javier 1126
Mars, Ruben 1855
Marsal, Sara 0021, 2290, 2291
Marsal Barril, Sara 0019
Marschall, Ursula 1934
Marsh, Lucy-Jayne 0798
Martín, Manuel 1413, 2311
Martín, Mar Concepción 1773
Martín Bescós, Adriana 1170
Martín Cascón, Miguel 1210, 1953
Martín López, Maria 0496, 2016, 2268
Martín Salazar, Jesús Eduardo **0108**, 0583, 2371
Martín-Domenech, Raquel 0153
Martínez, Agustín 1096
Martínez, Alejandro 1170
Martínez, Ana 1322
Martínez, Constantino 0072
Martínez, Olga 1321, 1446
Martínez Barrio, Julia 0642, 0659, 1878, 1899, 2249, 2450, 2670
Martínez Bejarano, Henry Leonardo 2034
Martínez Calabuig, Pablo 0270, 0271, 2406, 2407, **2460**
Martínez Cordellat, Isabel 2406, 2407, 2460
Martínez Cristóbal, Anna 2354
Martínez López, Juan Antonio 1404
Martínez Mateu, Sergio H. 0021, 2290, 2291
Martínez Pérez, José Maximiliano 1491
Martínez Pérez, Rosalía 1681
Martínez Robles, Elena 1210, 1953
Martínez-Calle, Marta 0538
Martínez-Ferrin, Javier 0019, 2290
Martínez-Lavín, Manuel 1234
Martínez-Morillo, Melania 0117, 2029
Martínez-Rivera, Marco Aurelio 2052
Martín-Varillas, José Luis 0243, 0268, 0272, 1094, 2538
Marte Furment, Marlene 0657
Martel, Marie-Elise **1581**
Martel, Marie-Elise 1858
Martellosio, Jean-Philippe 1592
Martin, Celine 1734
Martin, Hélène 0099
Martin, Javier 0034, 1862
Martin, Kimberly 1669, 2125
Martin, Laura 1282, 1284
MARTIN, Mickaël 0702
Martin, Mona L. 2435
Martin, Ruvie 0405
Martin, Thierry 1578
MARTIN FERNANDEZ, ELENA 0107
Martin Garcia, Antonio 2107
Martin Garcia, Antonio 2108
MARTIN MARTIN, IRENE **0107**
Martin Martinez, Manuel Cipriano 1321
mARTIN pENAGOS, Luis 0029
Martindale, Jonathan 1921
Martin-de la Sierra Lopez, Lourdes 0496, 2268
Martinez, Marco **0623**
Martinez, Sarah 0913, 0930
Martinez Fraile, Julia 0996
Martinez Laverde, Silvia 1201
Martinez Moreno, julio Manuel 0100
Martinez Pardo, Silvia 1619
Martinez Paulino, Andreina **0364**
Martinez-Canales, Rodolfo 0212, 0213, 1834, **1845**, 2219
Martinez-Delgado, Jose 0512, 1389
Martinez-Espinosa, Hector Alejandro 1527, **1687**
Martinez-Feito, Ana 0496, 2268
Martinez-Gutierrez, Nuria 2668
Martinez-Laguna, Daniel 1018
Martinez-Llordella, Marc 0006
Martinez-Martinez, Laura 1773
Martinez-Martinez, Laura Aline **1234**, 1947, 2243
Martinez-Rivera, Carlos 1600
Martinez-Taboada, Victor 1397, 1681, 2422
Martinez-Valle, Fernando 0239, 1163, 1666
Martin-Gutierrez, Adrian 0150, **0200**, 0740, 1599, **1612**, **1613**, 2265, **2610**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Martini, Alberto 0389
Martini, Alberto 0401
Martini, Alberto 0405
Martin-Nares, Eduardo **1154**
Martin-Nares, Eduardo 1491
Martins, Diana 0154
Martins, Elsa 0650, 0665, 1521
Martins-Martinho, Joana 1605
Martire, Maria Victoria 1422
Martos Cabrera, Luisa 2670
Marty, Rémi **1366**
Maruca, Dina **1636**
Marushchak, Olga 1832, 2394
Marvisi, Chiara 1598
Marwaha, Simran 0738
Marxreiter, Franz 0809, 0974
Marzano, Angelo Valerio 2699
Marzo-Ortega, Helena 0567, 0569, 0854, 1451
Marzuk, Zaynab 1468
Marzullo, Liberato 1863
Mas, Antonio Juan 0752
Mas Sanchez, Laura **0205**, 0237, 0341
mas sanchez, Laura 1274
Mas Sanchez, Laura 2274, 2310
Mascanfroni, Ivan 0008
Masetto, Ariel 1126
Mashaleh, Manal 0538, 1930
Masi, Emily **1278**
Masic, Dzenan 1950, 1955
masinova, Jana 1124
Maskani, Nithya 1364
Masoud, Amir 0685
Masri, Karim 0640, 0662, 1551, 2445
Massa, Sophia 0572, 2340
Massa, Virginia 0913, 0930
Massó, Felipe 1234
Massardo, Maria Loreto 0623
Massardo, Maria Loreto 1486, 1530
Massarotti, Elena 0501
Massarotti, Elena 0988
Massicotte-Azarniouch, David 0722
Masson, Maeva 2115
Masson, Mala 0626, 0772, 0853, 1223, 1240, **1391**
Masson, Mala 1846, 1918, 1919
Masson, Mala 2404, 2421
Masson, Mala 2444
Masson, Mala 2630
Massoudi, Yasmin 1184
Massy, Emmanuel 2115
Masto, Lucy 0365, 0382, 0634, 2575
Mastoor, Yusuf 1625
Mastrangelo, Greta **2136**
Masuda, Suguru 1353
Masuo, Yuki 0850
Mata-Riega, Valeria 0512, 1389
Matas-Garcia, Ana 0296
Mateen, Nargis 0151, 2088
Matei, Alexandru-Emil 0026, 0678, **0809**, 0810, **0956**, 0962, 0974, 0975, 1198, 1856
Mateo, Lourdes 0505, 2373
Mateo Faxas, Nirys 0233, 1418, 1543, 2238, 2239, 2240, 2283, 2284
Mateo Faxas, Sila **0195**, 0233, 1418, **1543**, 2238, 2239, 2240, **2283**
Mateo Faxas, Sila **2284**
MATEO SORIA, LOURDES 0117, 2029
Mateo Vendrell, Alejandro Jose 0237
Materne, Emma 1810, 1822
Mathes, Diana 0321
Mathew, Alwyn 1070
mathew, ashish 0140, 1609
Mathew, Jiby 1260
mathew, john 0140
Mathew, John 0582
mathew, john 1496, 1609
Mathew, Julie 1988
Mathews, Nitty 1609
Mathilde, PRORIOL 2621
Matias, Vinicius 1292, 2535
Matkava, Valeria 0403
Matossian, Sophia 0822, 1740, 1741, 1816, 2478
Matson, Scott 1308, 1659, 1946, 2661
Matsuda, Shogo 0773, 0973
Matsuda, Shuichi 0850
Matsui, Hiroki 2449
Matsui, Kiyoshi 1419
Matsui, Takemichi **1512**
Matsui, Takemichi **1732**
Matsui, Takemichi 1832, 2394
Matsumoto, Haruki 1509
Matsumoto, Isao 2523
Matsumoto, Kazuya 0452, 2244
Matsumoto, Kotaro 0781
Matsumoto, Lisa 0211
Matsumoto, Yoshinori 0452, 2244, 2602
Matsumura, Harumi 2564
Matsuno, Hiroaki 1353
Matsuo, Yusuke 2523
Matt, Michael 1811
Matta, Bharati **1814**
Matta, Jyothi 0853, 1391
Mattar, Maya 1979
Matteson, Eric L 1010, 1626
Matthews, Lisa 2179
Matthews, Robert 0185
Mattichak, Megan N 0093, 0972
Mattioli, Irene 1592
Mattison, Megan 2392
Matty, Rachael 2276
Matucci-Cerinic, Marco 0673, 0880, 1348, 1562, 1586, 1856, 2477, 2482, 2651
Matunis, Aidan 0943
Matusov, Yuri 2258
Matza, Louis 0360
Matza, Mark 0743
Matza, Mark 2550
Matza, Mark 2551
Mauck, Robert 1736
Mauhin, Wladimir 1339
Maurelli, Laura 1491
Maurer, Britta 0702, 0879, 1562, 2696
Maurice, Cédric 0162
Maurier, Francois 2532, 2655
Mauro, Daniele 0098, 1835
Mauro, Daniele 1864
Mauvieux, Laurent 1683
Mavragani, Clio 0034, 0515
Mavragani, Clio **2025**
Mavrea, Evgenia 1452
Mavropoulos, Athanasios 2280
May, Katie 0009
May, Sawyer **0667**
Mayer, Adam 0231, **1434**
Mayer, Kaitlyn 2192
Mayer, Meghan 0066, 1227
Mayer-Barber, Katrin 0920
Mayes, Maureen 0671, 0672, 0683, 0883, 0959, 1555, 1566, 1582, 1725, 1861, 1862, 2475, 2654
Maymó-Paituvi, Pol 0530, 0749, 1161, 1162, 1382, 2250
Mayman, David 2285
Mayo-Juanatey, Adrián 0639, 1547, 1548, 2473
Mayor, Kale **1315**
Maz, Mehrdad 1399, 1626
Mazar, Iyar 0357
Mazariego, Andrea **0436**
Mazetto Fonseca, Bruna **0859**
Mazo, Paula 1170
Mazrooei, Parisa 0679
Mazzacani, Alessandro 0991
Mazzarelli, Sara 2142
Mazzoleni, Luca **2411**
Mazzucco, Michael 0316
Mbadu, Samuel 1645
Mbuyi, Nadine 2039
McAlear, Carol 0721, 0747, 1602, 1767, 2515, 2533, 2701
McAlington, Timothy 0309, 0313, 0321, 0322, 0323, 1895, 2090, 2562, 2623, 2625
McAllister, Laura 0009
McAllister, Linda 1276
McArdle, Sara 1787
McBrearty, Kyle 1822, 2129, 2151
McCabe, Chantal 1726
McCallum, Rex 1160
McCann, Liza 0289
McCarthey, James **0829**
McCarthy, Geraldine 0750, 1136
McCarthy, Katharine **1926**
McCarthy, Lisa 2627
McClean, Michael 1048
McClure, Matt **0494**
McColl, Jeanine **2127**
McCombe, Jenifer 1378, 1384
McCormick, Natalie **0037**, 0813, 1032
McCormick, Natalie 1130
McCormick, Natalie 1990

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

McCormick, Natalie 1995, 2006
McCormick, Natalie **2008**, 2590
McCormick, Nick 0185, 0369, **1027**
McCoy, Sara 1387, **1401**, **1682**, **1684**
McCuaig, Sarah **0423**, **1825**, **1847**
McCune, William 1505
McCurdy, Deborah 0126, 0425
McDaniel, Margaret **0262**
McDearmon-Blondell, Erin 1349
McDermott, Catherine 2149
McDermott, Gregory 0168, 0465, 1016, 1343
McDermott, Gregory 1357
McDermott, Gregory 1747, **1751**
McDermott, Gregory 1957
McDermott, Gregory 2235, **2662**
McDermott, Michael 0657
McDermott, Michele 1727
McDonald, David 1983, 2620
McDonnell, Thomas 0820
McDowell, Jane 1251
McGeehan, Gearoid 0750
McGill, Mackenzie 1298
McGinley, Brooke 1647
McGoldrick, Jenna 0218
McGonagle, Dennis 0567, 1455
McGovern, Jenny **0006**, 0017
McGrath, Joseph 0285
McGrath, Joseph 1898
McGrogan, Anita 2487
McGucken, Andrew 1239
McGucken, Andrew **1711**
McGuire, Dawn **2086**
McGuire, Sarah 0399
McHugh, Neil 2487
McIlheran, Miranda 2603
McInnes, Iain 0473, 0562, **1442**, **1443**, 1455, 1678, **2351**, 2357, 2358
McIntosh, Barbara 0661
McKay, Neil 1239
McKee, Stephanie 0357
McKelvie, Penelope 1716, 2651
McKinney, Brock 0981
McKinnon, Mark 1136
McKnight, Andrew 1119
McLaughlin, Jessica 0234, 0253
McLean, John 1711
McLean, Michael 1178
McLean, Rachel 2035
McLellan, Beth 0223
McMahan, Zsuzsanna 0671, 0672, 0683, 0846, 0883, 1555, 1559, 1565, 1566, 1582, **1591**, 2475, 2652, 2654
McMahon, Grace 0375, 0792, 2033, 2528, 2529, 2530
McMahon, Maureen 0774, 1674, 2600
McMenamin, Katie 2683
McMillan, Laura **0991**
McMorrow, Donna 2051
McNamee, Paul 1244
McPhate, Nick 2126
McPherson, Christopher 1929
McQueen, Amy 1917
McTavish, Rebecca 2111
McTume, Griff 1529
Md Yusof, Md Yuzaiful 1525, 2393, 2411, 2601
Meade, Josie 0832
Meade-Aguilar, Jose 0601
Meade-Aguilar, Jose Antonio 1721
Meadows, Rachael 2271
Meaghan, Holub 1789
Meara, Alexa 1107, 1108, 1730
Mears, Joseph 2600
Mease, Philip J 2355, 2375
Mease, Philip J. 0362, 0455, 0562, 0563, 0564, 0567, 0576, **0578**, **0579**, **0580**, **0581**, 0590, 0843, 0854, 0873, 0874, 1165, **1178**, 1435, **1453**, **1454**, **1455**, **1456**, **1457**, **1458**, 1465, 1529, 1963, 2339, 2345, 2356, 2357, 2358, **2365**, **2366**, **2367**, **2368**, **2369**
Mechleb, Karen 1930
Mecoli, Chris 0288, 0289, 0865, 1207, 2063
Medarametla, Ravi 0167, 1544, 2050, 2370
Medeiros, Julia 0206
Medeiros-Ribeiro, Ana C 0206, 0619, 1192, 1715, **2292**, 2527, 2573, 2653, **2682**
medina, Gustavo 2336
Medina, María Alejandra 0432, 2405
Medina, Rhina 1338
Medina Fonseca, Benjamin 2651
Medina Malone, Miguel 1548
Medina-Gomez, Luis 0512, 1389
Medkour, Terkia 1312
Medlin, Jennifer 0663, 2183, 2454
Medsger, Jr, Thomas 1725, 2499
Meerkatt, Lien 2109, 2595
Meesala, Kavitha 0424
Mehdikhanova, Tarana 1552
Mehendale, Aarohi 0848
Mehovic, Revonda 0913, 0930
Mehrabadi, Ali Sheikhi 2355, 2375
Mehsen-Cetre, Nadia 2115
Mehta, Bella **0308**, **0316**, 0463, 0464, 0785, 0786, **0794**, 1159, 1252, 1782, 2629
Mehta, Hrishikesh 0908
Mehta, Mansi 1044
Mehta, Neev 1554
Mehta, Nehal N **0559**
Mehta, Nimish **2282**
Mehta, Pankti 0552
Mehta, Pankti 0611
Mehta, Pankti 0612, 0613, **0629**, 1415, 1416, **1425**, **1426**, 1550, **2691**
Mehta, Shantanu 1456
Mehta, Swati 0698, 0699
Mehta, Tapan 0185, 1661
Mehta-d'Souza, Padmaja 1792, 1794, 1806
Mei, Chunli 0646
Mei, Heng 2452
Mei, Huiling 0646
Mei, Jay 0001
Mei, Yifang 0064
Meidan, Esra 1696, 1810, 1822
Meier, Chiara 0508
Meijboom, Lilian 0690
Meijer, Kenneth 1324
Meirinhos, Tiago 0761
Meissner, Marissa 0825
MEJÍA, MAYRA 1390
Mejía Domínguez, Nancy R 0287, 1836, 1841, 2052, 2053
Mejia, Nataly 0584
Mejia-Rodriguez, Daniela A. 2058, 2071, 2072
Mekinian, Arsène 0260, 0735, 0777, 0891, 1095, 1339, 1765, 2663
Melboucy Belhkir, Sara 2532
Melchor Diaz, Sheila 1397, 1681
Melchor-Díaz, Sheila 0019, 2290
Meldrum, Eric **0431**, 0493, 0928
Melero González, Rafael Benito 0269
Melero Gonzalez, Rafael 0270
Melero-González, Rafael B. 0250, 0271, 0736, 0739, 0752, 1171, 2016, 2229
Meleza, Cesar 0057
Melgarejo, Patricia 2336
Melikoglu, Melike 2544
Melissaropoulos, Konstantinos 2232
Mellen, Jennifer 0981
Mello, Renata P 2653
Melo, Bartira 2395
Melton, Alexis 0843, 1529
Memi, Tereza 2236
Memon, Areeba 1092
Memon, Areeka 0122, **0685**
Memon, Matia Fawad 0235, 2095
Memon, Nashwah **2041**
Memon, Sibgha Fawad 0235
MEMON, ZAUHA FAWAD 0235, 2095, 2099
Mena Vázquez, Natalia 0270
Mena Vázquez, Natalia 0087, 0271, 0496, 2016, 2265, 2268
Menager, Mickael 0796, 1724
Menchén Viso, Luis Alberto 2348
Mencio, Paula 2473
Mende, Christian W. 1993
Mende, Miriam 0293
Mendel, Arielle **0606**, 0731, 1109
Mendel, Arielle **1475**, 1506, 1597
Mendel, Arielle 1607
Mendelsohn, Sierra 0437
Mendelson, Meryl 1175
Mendez, Lillian 1689, 2561
Mendizábal, Javier 0757
Mendoza, Evelyn 2576
Mendoza, Fabian **2480**
Mendoza Ríos, Edgar Iván 2218
Mendy, Jason 0204
Mendyka, Lindsay 0885, 1758

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Mendyka, Lindsay 2581
Menezes, Carla 0377, 1915, 2561
Meng, Charis **0440**, **0441**
Meng, Charis **0442**
Meng, fanpeng 0998
Meng, Huimin 0994
Meng, Ning 0529, **1028**
Meng, Xianyi 0977
Menichella, Daniela 1780
Menin, Rita 1407, 1408, 2326
MENON, JAIDEV 0137, 2424
Menor Almagro, Raúl 0019, 1397, 1878, 1899, 2290, 2422
Mensah, Boniface 1707
Mera Varela, Antonio 0405
Merás, Nidia Noemí 0621
Merad, Miriam 2584
Mera-Valera, Antonio 0153
Merayo-Chalico, Javier 2321
Mercado, Francisco 1234
Mercado, ivan 0151
Merce, Aixa Lucia 1422, 2405
Mercier, Joey 1315
Meric de Bellefon, Laurent 0035
Merindol, Julie 1339
Merindol, Julie **2532**
Merino, Ana 2209
Merino, Carolina 0269, 0271, 1170, 1171
Merino Argumánez, Carolina 0270
Merino-Barbancho, Beatriz 0183
Meriwether, Jennifer 0652, 1915
Merkel, Peter 0721, 0722, 0725, 0747
Merkel, Peter 0751
Merkel, Peter 0776, 1566, 1594, 1602, **1608**, 1623, 1626, 1631, 1764, **1767**, 1769
Merkel, Peter 1912
Merkel, Peter 2039, 2144, 2515, 2533, 2654, 2701, 2703
Merkt, Wolfgang **0678**, **0932**, 1198, **1875**, **1876**
Merlo, Christian 0070, 0094, 0100, 0901, 2599
Merlo-Ruiz, Christian 0071, 0072, 0087, 0139, 0795, 1851
Merlot, Claire 1339
Mermet, Stephanie 0162
Merola, Joseph 0527, 0576, 1437, 1443, 2320, 2688, 2689
Merola, Joseph F 0362, **0555**, 0562, 0563, 0564, **0573**, **0574**, 0581, **0875**, **1165**, 1455, 2339, 2356, 2357, 2362, 2365, 2369, **2408**, **2409**, 2435
Merrell, Maya 0652, 1915
Merriam, Louis 0808
Merrill, Joan 0044, **0644**, 0662, 1262
Merrill, Joan 1722
Merrill, Joan 1831, 1850, 2416, 2445
Merrill, Joan 2650
Merrill, Kaitlyn 1494
Merriman, Tony 0022, 0037, 0076, **2010**, 2585
Merritt, Angela 1744, 2301, 2462
Merten, Hannes 0015
Merzon, Eugene 1337
Mesa, Miguel Antonio 1210, 1953
Mesa, Pablo 1282, 1284
Mesbah, Rafik 0891
Meshreky, Marianne 1522
Messier, Stephen 2097
mestanza, Marilu 2336
Methric, Kathleen 0246, 1352, 2479
Metni, Laila 2158
Mettler, Camille 1766
Mettler, Camille **2507**
Metzger, Allan L. 0293
Metzler, Markus 1537
Meunier, Raphaelle 2457
Meunier, Rosalie-Selene 1607
Meurot, Coralie 1734
Meyer, Alain 0516, 0862
Meyer, Frédéric 0099
Meyer, Ingo 1934
Meyer, Nathan 1923
Meyer, Nicolas 0508, 1683
Meyers, Andrea 2546
Meyers, Arthur 0428
Meysami, Alireza **0239**, 1518, 1666
Meyvisch, Paul 0694
Meyyappan, Lakshmi 2149
Mghaieth, Sandra 0681
Mian, Kainat 0066, 0081
Mian, Nadia 0572
Mian, Sundus 1479
Miao, Brenda 1657
Miao, Claire 1657
Miao, Jinmin 0976
Miceli, James 0598
MICELI-RICHARD, Corinne 0114
Micelli, Marina Laura 1491
Michaelson, Jennifer 2293
Michalidas, Brandon 1821
Michaud, Jessica 1050, 1051
Michaud, Kaleb 0158, 0292, 0462, 0789, 1021, 1046, 1065, 1068, 1196, 1216, 1656, 1686, 1878, 1898, 1899, 2305, 2571
Michaud, Martin **0162**
Michaud, Martin 1200, 2510
Michel, Marc 1575, 2489
Michelena Vegas, Xabier 0180, 0530
Micheletti, Robert 1912, 2525, 2533
Michelsen, Brigitte 1430
Micheroli, Raphael 0543, 0807, 1218, 1757
Micu, Alexandru 0026, **0810**
Middaugh, Nicole 0362, 0578, 0579, 0580, 2366
Middelink, Leonie 0493
Mielczarek, Leanne 1506
Miglani, Manjula 1701
Migliorini, Gabriele 0104
Migowa, Angela 0177, 1706
Miguel, Belén 1413, 2311
Miguel Alvarez, Adriana 0684
Miguel Ibáñez, Belén 1321
Miguelez Sanchez, Juan Roberto 1547, 1548
Miguet, Laurent 0508
Miguet, Laurent 1683
Mihai, Carina 0880, 0967, 1579, 1580, **2472**
Mihalko, Shannon 2097
Mihas, Paul 1271
Mikecz, Katalin 0049
Mikesell, Alexander 1682
Mikolajczak, Lily **1421**
Mikosz, Andrew 2486
Mikuls, Ted 0022, 0045, 0065, 0076, 0155, 0221, 0222, 0462, 0834, 0836, 0921, 0924, 1125, 1238, 1308, 1314, 1325, 1650, 1658, 1659, 1674, 1746, 1774, 1779, 1946, 2001, 2002, 2276, 2567, 2585, 2661, 2681, 2683
Milchert, Marcin 2067
Miler, Adi 1305
Miles, Anna 2064
Milisenda, José 0296, 0863
Millay, Douglas 1826
Miller, Alexandra 1038
Miller, Beth 2192
Miller, Brecca **1861**
Miller, Claire 2669
Miller, Frederick 0159
Miller, Gary 2097
Miller, Jeffrey 0663, 2454
Miller, Jerri 2146
Miller, John 0529, 1028
Miller, Jonathan **0750**
Miller, Karla **0348**
Miller, Megan 0558, 0875
Miller, Meghan 2086
Miller, Melicent 0373, 0381
Miller, Natalie 2237
Miller, Rachel 1736, 1739, 1780, 1782, 1783, 1790, 1796, **1800**, 1805
Miller, Richard 1780, 1782, 1783, 1790
Milligan, Gary 2342
Milligan, Jack 2271
Milligan, Jacob 1437
Mills, Cally 1227, 1793
Mills, Judith 0377
Millwood, Michelle 0918, 2133
Milman, Kateryna 1436, 2306
Milman, Nataliya 1607, 1623
Milone, Alessandra 1835
Miloslavsky, Eli 1764
Mimica, Milena 0596, 0621, 1491
Mimori, Tsuneyo 0773
Mimura, Toshihide 0084
Mina, Marine 2115
Minato, Kazumichi 2253, 2254
Mincarelli, Delores 1978

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Minden, Kirsten 1287
Minerba, Marco 0847, 1586
Minett, Margaret 0365
Minett, Margaret 0855
Ming, Zhihao 0906
Mingueneau, Michael 0016
Minhaj, Areeba **1328**
Minhas, Umm E Aimen 1328
Minikumari Rahulan, Lekshmi 1212, **2065**, 2676
Ministro, Joana 1437
Minjarez, Anthony 1981
Minniti, Antonina 1863, 2656
Mino, Rina 1611, 2212
Minoia, Francesca 0358
Minoia, Francesca 0780, 1671
Minoia, Francesca 2137, 2138, 2139
Minopoulou, Ioanna **0471**, 1010
Minter, James 1136
Mintrop, Bernhard 0386, 1461
Mintz, Douglas 2385
Miossi, Renata 1192, 2653
Miquel, Anne 0327
Miraldi Utz, Virginia 0392, 0394, 0406, 0407, 0414, 0415, 2675
Miranda, Jose Alberto 0269, 1171
Miranda, Sébastien 0891, 2532
Miranda Brawner, Cindy 1781, 1792, 1794
MIRANDA MANZANO, JULIA 0107
Miranda-Carus, Maria-Eugenia **0089**, 0745, 0755, **0894**
Mirault, Tristan 1339
Mire, Ellen 1080
Mirouse, Adrien 0756
Mirza, Tehmasp 0312
Mirzayeh fashami, Fatemeh 2111
Misawa, Yutaro 0043
Misha, Ruth 1362
MISHRA, RITESH KUMAR **0136**, **0137**, 1431, **2424**
Miskovic, Rada 2067
Misra, Durga Prasanna 1614, 1618, 1627
Misra, Ramnath 0533
Misra, Ranjita 1636
Mistretta, Marie 1858
Mitchell, David 1136
Mitchell, Janet 2162
Mitchell, Katherine 1060
Mitchell, Saloni 0682
Mitchell, Tanecia 1837
Mitra Das, Anushka 1910
Mitri, Bassam 2228, 2286
Mitrovic, Stéphane **1185**
Mitrovic, Stéphane 2032
Mitrovic, Vesna 0624
Mitsuo, Akiko 0043
Miyagi, Taichi 1167, 1611, 2212, 2488, 2534
Miyake, Kensuke 1848
Miyamae, Takako 1630
Miyamoto, Kenichi 1854
Miyashita, Tomoko 0521
Miyashita, Yusuke 0995
Miyashita, Yusuke 1004, **1005**
Miyawaki, Yoshia 0452, 2244, 2523
Miyazaki, Yusuke 0595
Mizrachi, Mark 0947
Mizuno, Tomoyuki 2462
Mizusaki, Mao 1167, 1611, 2212, 2488, 2534
Mizuta, Mao 2137, 2138, 2139
mmanuelle, DERNIS 1095
MN, Chandrashekara **0481**
Moadab, Fatemeh Neela **0079**
Moaf, Paris 1285
Moaf, Paris 1290
Moallemian, Rezvan 0949, **2598**
Mobasheri, Ali 0307
Mockbel, Abeer 2210
Modi, Mahir 1892
Modi, Shivani 1071
Modi, Yasha 2444
Moe, Natasha 0510, 1872
Moeller, Burkhard 0543
Mogard, Elisabeth 0434, 0814
Moghadam-Kia, Siamak 0282, 0298, 0303, 1201, 1215, 2055
Moghaddam, Farbod 2414
Mogri, Muniza 1691
Mohamadi, Aida 0720, 1072
Mohamed, Ahmed 0032
Mohamed, Asmaa 0812
Mohamed, Ibrahim 1285
Mohamed-Hamsho, Jesus 0512, 1389
Mohamed-Noriega, Karim 0512, 1389
Mohammad, Afroz S. 1994
Mohammadi, Iman 0726
Mohammadian, Hashem 0878, 1757
Mohammed, Hazem E. 0333, 0334
Mohammed, Khuloud 2318
Mohammed, Mohammed **0265**
Mohan, Anju 0630, 2191
Mohib, Khadija **0556**, 0703, 1328, **1720**, **2095**, 2099, 2516
Mohib, Sabah **2516**
Mohpichai, Nopavit 1187
Mohta, Tamanna Vinodkumar **0729**
Mohtarif, Ichem 0477
Molad, Yair 2210
Molberg, Øyvind 0510, 0593, 1872, 2390
Molberg, Oyvind 0420, 1867
Moldaver, Daniel 0649, 1533, 1534, 2453, 2500
Mole, Evangelia 1439, 1452
Molina, alejandro 1861
Molina, Claudio 0931
Molina, Hernan 1422
Molina Almela, Clara 0752
Molina Collada, Juan 0270
Molina-Collada, Juan 0271, 1613, 2249
Molina-Esteban, Natalia 2670
Molina-Molina, Maria 1161, 1162
Molina-Ríos, Sebastián 0621, 1210
Molins, Eduard 1374
Molitor, Jerry 0883, 1555, 1566, 1582, 2475, 2654
Moll, Jakub 0238
Molla ismail Sali, Ainour 2232
Molloy, Eamonn 0750
Molto, Anna 0214, 0215, 0534, 0544, 0588, 0589, 1578, 2307, 2332, 2655
Momblan Trejo, Cristina 2106
Monach, Paul 0022, 0221, 0222, 0721, 0747, 0834, 1308, 1602, 1626, 1746, 1767, 1946, 2276, 2515
Monahan, Amy 0417
Monat, Claire 2397
Moncada-Flores, Karla Paola 1527
Monga, Kanika 1984
Monjo Henry, Irene 0089, 0180, 0269, 0745, 0755, 0894, 1152, 1171, 2042
Monleon Acosta, Esther **2112**, **2113**
Monnet, Joelle 1356, 2267
Montagna, Paola 0963
Montala-Valencia, Lidia 2485
montanelli, Gaia 0700
Montani, David 1185
Montecucco, Carlomaurizio 0884
Montecucco, Carlomaurizio 2482
Monteiro Gomides, Ana Paula 1365
Monteon, Marcos 0207
Montero, David 0485, 2350
Montero Costa, Alejandra 2106
Montes, Silvia 2344
Montes de Oca, Alexa 2198
Montesi, Sydney 0992, 2528, 2530
Monti, Sara 1614, 1627
MONTICIELO, ODIRLEI 0596, 0621, 0623, 1491, 1530
Montiel Castañeda, Carlos 0507
Montilla, Carlos 1321, 1413, 2311, 2422
MONTINA, PAULA 0179
Montina, Paula Cristina 1365
Montoya Rumpf, Ruddy Paola 2034
Moody, M. Anthony 1745
MOON, JAE HYUN 0910
Moon-Grady, Anita 0853, 1391
Mooradian, Meghan J. 1099
Moore, Angela 0875
Moore, Bronwyn 2453
Moore, Christopher **0981**
Moore, Duncan 0883
Moore, Duncan 1555
Moore, Duncan 1566, 1582
Moore, Duncan 2475
Moore, Duncan 2654
Moore, Edwin 1242
Moore, Gregory 0010
Moore, Justin 1976
Moore, Michael 0388
Moore, Richard **2579**
Moore-Schiltz, Laura 0726, 2051
Moorthy, Lakshmi 0399, 1275

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Moots, Robert 1178
Moquin, Rachel 2165
Mor, Adam 0899, 1853
Mora, Ana 0507, **2674**
Mora, Jacopo 0238, **0251**
mora, Javier 0083
Mora-Cuesta, Victor M. 1778
Moradi, Kamyar 1963
Moradi, Soroush 0944
Moraes, Julio 1715
Moragues, Carmen 0749
Morales, Enrique 0639
Morales, Giselle 1689
Morales, Melissa 1191
morales, shawn 0868
Morales, Walter 1559
Morales Meza, Ada Rocío 0507
Morales Rivera, Adriana 0319
Morales-Wong, Fernando 0512, 1389
Moran, Rachel 0410
Moran, Timothy 0920
Morand, Eric **0595**, 0645, 0801, **0802**, 1542, 1545, 1552, 1878, 1899, **2445**, **2696**
Morandeira, Francisco 2484, 2491
Morandini, Pierandrea 0532
Moranne, Olivier 0618
Morante Bolado, Isla 0243, 0269, 1171
Morasco, Benjamin 1266
Mora-Trujillo, Claudia S. 0621, 0623, 1530
Moravcova, Lenka 1350, 2346
Morbiducci, Julieta 1422, 2405
Morcillo Valle, Mercedes 2344
Morcos, Meredith 2160, 2170
Morden, Jasmine 2128
Moreau, Flavie 0802
Moreira, Gabriela 2316
Morel, Ariane 0907
MOREL, franck 0105
Morel, Jacques 0508, 0516, 1095, 1529
Morel, Nathalie 2457, 2655
Morel, Thomas 0644
Moreland, Larry 0199, 0501, 0721, 0747, 0890, 1233, 1602, 2233, 2515, 2576
Morell Hita, Jose Luis 1869, 2030
Moreno, Denisse 0709
MORENO, ELENA 1269
Moreno, Jordan 2141
Moreno, Manuel Jose 2373
Moreno Alvarez, Mario 0596, 0623, 1486, 1530
Moreno Garcia, Marina soledad 0496, 2268
Moreno Gil, Puerto 2373
Moreno Pérez, Oscar 1129
Moreno-Caño, Elena 0071, 0072, 0094, 0108, 0795
Moreno-Ruiz, Paula 0538
Moresco, Philip 1386
Moretti, Michele **0723**
Moretti, Michele 1380, 1951
Morf, Harriet 0192
Morgado, Anika **1473**
Morgan, Elizabeth **0920**
Morgan, Esi 0411, 1066, 1978
Morgan, Gabrielle 2462
Morgan, Lilly 1984
Morgan, Xochitl 2590
Mori, Masaaki 1419
Moriano, Clara 0019, 0250, 0269, 0642, 0736, 0739, 0744, 0757, 1171, 1282, 1284, 1397, 1681, 2290, 2422, 2450, 2670
Morikawa, Kohei 0764
Morinobu, Akio 0773, 1772, 1857
Morishita, Kimberly 2126
Morita, Akimichi 0874, 1419
Morita, Yugo 0850
Moriuchi, Kaito 1509
Moriyama, Mayuko 2523
Morlà Novell, Rosa Maria **0379**, **0380**
Morlan, Natalie 1981
Morley, Roland 0277
Morlote, Diana 1174
Morny, Joan 1707
Moroncini, Gianluca 0238
Moroncini, Gianluca 0702, 0884, 1562
moroni, Luca 1598
Morris, emily 1870
Morris, Jeffrey 0725
Morris, Robert I. 0293
Morris, Sarah 1138
Morris, Simrat 0119
Morris, Simrat 1067
Morrison, Mark 0101
Morrissey, Erin 2429
Morrisson, Madeline 0811, 0845
Mortazawi, Dariusch 0875
Mortensen, Joachim 2231
Mosa, Doaa 2128
Mosberger, Sebastian 2520
Mosca, Marta 0133, 0640, **0662**, 0723, 1380
Mosca, Marta 1381
Mosca, Marta 1385, 1542, 1951, 2179, 2656
Moseley, Katherine **1492**
Moseley, Margaret K 2408
Moser, Michael 1637
Mosher, Dianne 2419
Moshrif, Abdelhfeez 1713
Moskowitz, Judy 1249
Mosley, Jonathan 1181, 2270
Mosquera Angarita, Juan Manuel 1210
Moss, LauraKay 0076
Moss, LauraKay 0088
Moss, LauraKay 0775
Mossad, Sarah 1285
Most, Zachary 1093
Mostaghimi, Arash 2525
Motcritcaia, anastasia 1943
Mothi, Suraj 1336
Motomura, Kyoko 0043
Motta, Francesca 0879
Mouchet, Julie 0734, 1910
Mouchon, Emmanuelle 2510
Moulis, Guillaume 2510
Mouly, Stéphane 0735, 2168
Mount, George 0446
Mountz, John D. **1837**
Moura, Cristiano 0475, 1507
Mourad, Omar 0633, 2517
Mourguet, Morgane 1200, 2510
Mourre, Eleonore 1115
Mousa, Kathrien 2306
Mouthon, Luc 0681, 0688, 0735, 1575, **1577**, 1766, 2489, 2584
Mouthon, Luc 2655
Movahedi, Mohammad 2266, 2642
Movassaghi, Kamran 0471
Moya Albarado, Patricia 0271, 0737, 1613
Moya Alvarado, Patricia 0270
Moyer, Amanda **2169**
Moyer, Amanda 2201
Moyer, Ann 0030
Moyo, Knowledge Mudhibadhi **1868**
Moysidou, Georgia-Savina **2032**, 2461
Mozaffar, Tahseen 0289
Mozaffar, Tahseen 2669
Mozzo, Marta 0700
Mrowietz, Ulrich 0576, 1447, 2339
Mruthyanjaya, Prakashini 0461
Mruthyanjaya, Prakashini 0533
Msaouel, Pavlos 0273
Mu, George 0154, 0169
Mu, Rong **0647**
Muñoz, Óscar 1491
Muñoz, Alejandro 0757
Muñoz, juliana **0083**
Muñoz, Santiago 0019, 0201, 0496, 1961, 2268, 2373
Muñoz Fernández, Santiago 0268
Muñoz Maldonado, Yolanda 0579, 0580, 2366
Muñoz Martinez, Pablo 0237, 1274, 2274
Muñoz-Barrera, Laura 0070, 0071, 0072, **0087**, 0094, 0795, 1851, 2599
Muñoz-Castañeda, Juan Rafael 1851
Muñoz-Llopis, Laura 0243, 2388
Muñoz-Louis, Roberto 0596, 0623, 1486, 1530
Muñoz-Martínez, Pablo 0205, 0341, **0757**, 2310
Mubashir, Asia 0648
Much, Laura 0957, 0967, **1867**, 1872, 2497
Muchamuel, Tony 2466
Muche, Burkhard 0342, 0343, 0471, 2109, 2110, 2595
Mudano, Amy 1387
Mudano, Amy 1507
Mudano, Amy 2068, 2539, 2566
Mueller, Alisa **0798**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Mueller, Kevin 1751, 1902, 2235, 2574, 2577, 2578
Muensterman, Elena Tomaselli 1442, 2351
MUGHEES, MUHAMMAD 0235
muhammad, Lutfiyya 0440, 1225, 1249, 2430, 2455
Muhammad, Sufia 0204
Mukamal, Kenneth 0354
Mukherjee, Mohana 0054, 0871
Mukherjee, Sohini 1370
Mukhtyar, Chetan 1614, 1627
Mukuchyan, Vahan 1586
Mulavini, Vishnu 1147
Mulcaire-Jones, Erica 1751, **2235**
Mulcaire-Jones, Erica 2492
Mulder, Douwe 1860
Muley, Victor 0535, 1062
Muller, Yannick 2696
Mullin, Noelle 0059
Mulvihill, Evan 1013
Mumcu, Gonca 1396
Mumcu, Omur 1396
Mumtaz, Sehreen **0727**, **0759**, 1255, **1585**, **1986**, 2018
Mundell, Pamela 1138
Mundra, Vaibhav **0277**
Muneeb Akhtar, Syed Muhammad 1078
Mungaray, Sandra 0944
Munoz-Gomez, Miguel 1696
Munroe, Melissa **1842**
Munroe, Melissa 2384
Munroe, Melissa **2649**
Munshi, Hasan 0151, 1880, 1881, 1882, 2088
Muolo, Gloria 1570
Murad, Dina 1031
Murad, M. Hassan 0601
Murakami, Akihiro 0304
Murakami, Akinori **0850**
Murakami, Jodi 0002
Murakami, Kaoru 2289
Murakami, Kosaku **1772**, 1857
Murakami, Masaaki 2289
Murakami, Yusuke 1848
Murakawa, Yasuhiro 0850
Murarasu, Anne **2655**
Muraru, Sinziana 0967, 1579, 1580, 2472
Muraru-Carbune, Sinziana 0880
Murata, Koichi 0850
Muratore, Francesco 1598
Muratore, Maurizio 0246, 1352, 2479
Murayama, Goh 0106, 0521
Murcia Munévar, Liliam María 2034
Murer, Patrizia 0990
Murias, Sara 1282, 1284
Murillo Erazo, Claudia 2107, 2108
Murillo-Saich, Jessica 1787
Murphy, Cara **0317**
Murphy, Caroline 1678
Murphy, Cassandra 0798
Murphy, Frederick 2355, 2375
Murphy, Jennifer 2360, 2363, 2364
Murphy, Lance **0328**, **1791**
Murphy, Robert 0815
Murphy, Susan 0689
Murphy, Terrence E. 2114
Murray, Andrea 0686, 1966
Murray, Charles 1866
Murray, Elizabeth 1669, 2125
Murray, Euan 0996
Murray, Joseph 0030
Murray, Katherine 0818
Murtaza, Meer 0312
Murthy, Sruthi 1411
Muruganandam, Maheswari 2040, 2077
Murzin, Ekaterina 0824
Musai, Jon 0296
Muscal, Eyal 1296
Muse, Ian 0186, 1669, 2125, 2128, 2147
Muskaan, Mehra 1228
Mus-Otten, Anne-Marie 0979
Mustafa, Mohammad 0549
mustelin, cecilia 0078, 0079
Mustelin, Tomas 0078, 0079
Mustelin, Tomas 2418
Muthukumar, Thangamani 1839
Mutlu, İlhan Nahit 1965
Mwizerwa, Oscar 1285, 1742
myasoedova, Elena **0149**, 0460, 1030, 1156, 1311, 1320, 1388, 1932, 2260, 2639
Mychaliska, Kerry 2131
Myers, Leslie 2554, **2558**
Myers, Richard 0021
Myhr, Courtney **0073**
Mylavarapu, Rammohan 2417
Mylonakis, Eleftherios 1615
Mylvaganam, Ruben 1553
Mylvaganam, Sivakami **2102**
Myshkin, Eugene 2297
Mysler, Eduardo 1676
Mysore, Krupa 1296
Mysore, Vijayashree 0908

N

N G, RAJESH 0136
N. Makaryus, Amgad 2490
Näslund-Koch, Charlotte 2608
Néel, Antoine 1765
Nöthling, Danae-Mona 0236, 0628, 1697, **2442**, 2461, 2695
Nóvoa Medina, F Javier 1490
Naccache, Jean-Marc 1577
Nachawati, Dana 0603, **0741**, **0742**, 1151, 1500
Nachawati, Dana 1979
Nachawati, Dana 2216
Nack, Annika 0117, 0505, **0530**, 2029
Naclerio, Margaret 0184
Nadai, Takanobu 2462
Nadaj Pakleza, Aleksandra 0862
Naddaf, Elie 2669
Nadeem, Daniyal 1508
Nadeem, Daniyal **2392**
Nadipelli, Vijay R. 1083
Naffaa, Mohammad **1337**, 1435
Nagafuchi, Hiroko 0668
Nagao, Keisuke 0118
Nagaraja, Vivek 0701, 0710
Nagaraju, Kanneboyina 1191
Nagel, Judith 1206
Nagendra, Lakshmi 2056
Nagesh Prabhu, Keerthana 1309
Nagle, Clayton 0467, 2433, 2434
Nagpal, Neha 0365, 0382, 0634, 0635, 2426, 2575
Nagy, György 2684
Nagy, Gyorgy 1136
Nahra, Vicky 1151
Naides, Stanley 1168
Naidu, Shankar 0481
Naik, Chinmayi 2320
Nair, Deepthi 0259
Nair, Parameswaran 1594, 1608, 1769
Naji, Saadeya 0600
Najjar, Rayan 0079
Naka, Tetsuji 1358
Nakabo, Shuichiro 0945, 2580
Nakadoi, Takato 0452, 2244
Nakagomi, Daiki 2523
Nakahara, Hideko 2564
Nakai, Takehiro **0638**, **2225**, 2660
NAKAI, YU 1345, 2664
Nakajima, Mikio 2449
Nakamura, Akihiro 0113, 0560
Nakamura, Hiroyuki 2289
Nakamura, Jun 0764
Nakamura, Kaito 2449
Nakamura, Shinichiro 0850
Nakanishi, Kensuke 2225
Nakano, Hiroto 0918
Nakano, Masahiro **2602**
Nakao, Yuka 0054, 0055, 0110
Nakaoka, Yoshikazu 1630
Nakaphan, Pannathorn **1134**, **2255**
NAKASEKO, KEN **0350**
Nakashima, Ran 0773, 1772, 1857
Nakashima, Shusaku 1167, 1611, 2212, 2488, 2534
Nakashima, Yasuharu 1419
Nalli, Cecilia 0860, 2210
Nallulwar, Neel 1588
Nam, Boda 1576
Nam, Bora 0550, 1432
Nam, Jacqueline 0832, 1677
Nam, So-Hye 0526
Namas, Rajaie 0600, 0648
Namas, Rajaie 1349
Nambudiri, Vinod 0790
Namit, Samantha 2605
Namvaran, Ali 0065
Nandita, Gollakota **0291**, **1771**
Naniwa, Taio 1630

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Nano, Alessia 1680
Núñez-Álvarez, Carlos A. 2052, 2053
Núñez-Elizondo, Arantza Michelle 1687, 2171
Napetschnig, Johanna 0898
Napier, Ruth 0993
Nappi, Emanuele 0238
Naqvi, Umme Abeeha 0556
Narain, Sonali 2017
Naranjo, Antonio 1681
Narazaki, Mariko 0452, 2244
Nardella, Guillaume 2397
Nardi, Cosimo 0880
Naredo, Esperanza 1964, 2279
Narman, Ashlyn 2490
Narváez, Javier 0019, 0353, **0642**, 0728, 0736, 0737, 0739, 0744, **0749**, 0752, 0757, **1161**, **1162**
Narváez, Javier 1382
Narváez, Javier 1397, 1681, 1878, 1899, 2250, 2290, 2299, 2422, 2473, 2474, **2484**, **2485**, 2491
Nary, Maritza 2195
Naseva, Emilia 1218, 2066
Nash, Peter 0562
Nash, Peter 1454
Nash, Richard 0843
Nasir, Zaira 1539
Nasonov, Eugeny 1323
Nasr, Sandy 0657
Nasrallah, Catherine 0181, **0217**, 0359, **1250**, **2619**
Nasrallah, Mazen 1101
Nasrullayeva, Gulnara 0920
Nassi, Lorien 0119, 1093
Nassrallah, Najwan 2306
Nasuhbeyoglu, Ahmed 0627
Natalello, gerlando 0641, 1567
NATALUCCI, Francesco 1679, **2272**
Nathan, Joseph 0474
Nathan, Paul 2136
Nathan, Steven 0247
Natour, Hamada **1286**
Natsumoto, Bunki 2602
Natu, Anuya **1196**
Natu, Anuya 1420, **2504**
NAUSHAD, RIZWANA 0136, 0137, 1431, 2424
Navaei, Amir 1299
Navarini, Luca 0391
Navarra, Sandra 0595, 1526, 1878, 1899, **2697**
Navarrete Lagos, Mario 0799
Navarro García, Inmaculada Concepción 1385
Navarro Joven, Carlota 1170, **2294**
Navarro Palomo, Pablo 1170
Navarro-Angeles, Vanessa 1382
Navarro-Compan, Victoria 0180, 0535, 0569, 0854, 1062, 1435, 1451, **1465**, 1466, 2042, 2347, 2635
Navarro-Mendoza, Erika 1721, 2403
Navarro-Millan, Iris 0317, 1084, 1264, 1283, 2426, 2429, 2539
Navio Marco, Maria Teresa 0201
Navratilova, Adela 1350, 2346
Nawachi, Shoichi 0452, 2244
Nayak, Renuka 0054, **0871**, 1329, 1338, **2643**
Nayar, Manu 1163
Nayar, Saba 0798
Nayar, Saba 1702
Nayor, Matthew 2590
Naz, Faiza 0863, 0918, 2533, 2580
Nazzal, Lama 1032, 2008, 2590
Nazzar Romero, Samira 0425
Ndosi, Mwidimi 1178
Neal, Elizabeth **2554**, 2558
Necander, Sofia 1594, 1608, 1769
Nedorezov, Laura 1809
Needle, Carli 2145
Needleman, Ori 2084
NEEL, Tiphany 0537
Neelagar, Ranjana 0956
Neely, Jessica 1741, 1816, 2158
Neely, Megan L 0274
Neerinkx, Barbara 0528
Negassi, Beylul 1708
NEGI, VIR SINGH 0136, 0137, 1431, 2424
Negrini, Andrea 0619
Negron, Madison 1606, 1902, 2508, 2574, 2577, 2578
Neill, Lorna 1626
Neinert, Franziska 0545
Neisen, Jessica 0832
Nejati, Mina 0644, 2441
Nel, Hendrik 0980
Nelde, Annette 0645, 1542
Nelke, Christopher 0863
Nelson, Amanda 0145, **0306**, 0311, 0325, 0330
Nelson, Amanda 0984
Nelson, Amanda 1271
Nelson, Amanda 1788, 1960, 2092, 2100, 2604
Nelson, Meghan **0625**
Nelson, Meghan 0637
Nelson, Meghan **2646**
Nelson, Oliva 2006
Nemani, Mahsa 0006, 0017
Nemcova, Dana 1287
Neogi, Tuhina 0325, 0440, 1125, 1225, 1229, 1230, **1247**, 1643, 1647, 2001, 2084, 2096, 2098, 2100, **2105**, 2526, 2585, 2588, 2624
Nepa, Puran 0174, 0818, 2270
Nerenberg, Mike 0636, 0851, 2427
Nespola, Benoit 0516
Nestor, Jacquelyn **0805**, 2211
Neto, Agna 2671
Nety, Suchita **0465**
Neubarth Giorgi, Rina Dalva 1365, 2246
Neumann, Elena **0075**, 0090
Neumann, Thomas **2520**
Neuville, Sophie 1738
Neville, Autumn 0475
Nevitt, Michael 1247
New, Paul 0686
Newbold, Paul 0558
Newby, Brittney **1815**
Newcomb, Jeff 1125, 2001, 2585
Newman, Jovita 2097
Newman, Peri 0227, 0500
Newman, Thalia 0134
Newman, Thalia **0857**
Newth, Ben 0169
Newton, Andita 0008
Newton, Michael **1739**
Newton, michael 1783
Ng, Bernard 0181, 1250
Ng, Bernard 2330
Ng, Daphne 0194
Ng, Joshua 1972
Ng, Kristine 0595
Ng, Lawrence 1279, 1281, 1285, 1286, 1289, 1290, 1295, 1301, 1742
Ng, Sue-Ann 2651
Ng, Wan-Fai 0034
Ngamjanyaporn, Pintip 1187
Ngantcha, Marcus 0362
Ngian, Gene-Siew 0677
Ngo, Khoa 1667
Ngo, Trung 1236
Ngueyon Sime, willy 0314
Nguyen, Andy 1310
Nguyen, Deanna 2035
Nguyen, Duc 0402, 1621
Nguyen, Elsie 0265
Nguyen, Hanh 0010
Nguyen, Hieu 0081
Nguyen, Hoang 0356
Nguyen, Hoang 0377
Nguyen, Hoang **1386**
Nguyen, Hung 0808
Nguyen, Jessica 0725
Nguyen, Jessica **1621**
Nguyen, Julia 0635, 2426, 2429
Nguyen, Justin **0253**
Nguyen, Kim 0233, 1418, 1543, 2238, 2239, 2240, 2283, 2284
Nguyen, MaiLan 2148
Nguyen, Megan 1669, 2125, 2128
Nguyen, Michelle **2251**, **2252**
Nguyen, Nam 1959
Nguyen, Nam **2609**
Nguyen, Phuong **0560**
Nguyen, Quang 1144
Nguyen, Quang Huy 1144
Nguyen, Sophia 0009
Nguyen, Tim 0561, 0734, 1910, 2689
Nguyen, Vu 0328
Nguyen, Vu 1736
Nguyen, Vu 1791

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Nguyen, Yann 0735, 1592, 1683, 1722, 2506
Ni, Chengze 1001
Ni, Meng 0082, 0905
Ni, Ruoning **2515**, **2702**
Ni, Yuanpiao **2589**
Ni, Zhaohui 2697
Nibu, Hiroki 1509
Nicholls, David 0591, 0592, 1451, 1458
Nichols, Christopher 2094
Nichols, Dave 0494
Nichols, Laura **0228**
Nichols, Laura 2160, 2170
Nichols, Laura 2186
Nicholson, Jennifer **0942**
Nickolaus, Peter 2486
Nickolls, Sarah 2500
Nicolai, Rebecca 0391
Nicolau, Julia 2115
Nie, Yingkun 2464
Nie, Yuxue 1036, 1190
Niederhausen, Meike 1266
Nielsen, Susan 1287
Nietert, Paul 0393, 1059, 1232
Nieto, Juan Carlos 1284, 1613, 2348
Nieto, Maria asuncion 1024, 1869, 2030
Nieto, Romina 0596, 0621, 1422, 1530
Nieto Gonzáles, Juan Carlos 1282
Nieto-Carvalhal, Beatriz 0089, 0894
Nieto-Nieto, Rebeca 1778
Niewold, Timothy 0047, 1505, 1842, 2285
Nigrovic, Peter 0824, 1004
Nigrovic, Peter 1696
Nigrovic, Peter 1810, 1822, 2410
Nihtyanova, Svetlana I. 0169, 2500
Nijmeijer, Bas 1526
Niki, Hisae **0052**
Nikiphorou, Elena 0190, 0191, 0588, 0589, 1077, 1218, 1263, 1614, 1627, 2067, 2185, 2307
Nikiphorou, Elena 2333, 2334
Nikishina, Irina 0403
Nikitopoulou, Eleni 2337
Nikitsina, Maryia **2122**, 2294, 2304, 2491
Nikolopoulos, Dionysis 0125, 0628, 0842, 1531, 2401, 2402, 2648
Nikpour, Mandana 0595
Nikpour, Mandana 0677
Nikpour, Mandana 1531, 1716, 1862
Nikpour, Mandana 1878, 1899, 2651
Niles, Denver 1621
Nilsson, Emil 0929
Nilsson, Peter 0900, 2027
Nimal, Simran **0385**, **2542**
Nimal, Simran Ravindra 0701, 0710
Nimbvikar, Anushri 1615
Nimmagadda, Rithish 0167, 2050, 2370
Nimoni, Andrra 0047, 2285
Nirula, Ajay 0473
Nischal, Sharan 0558
Nishandar, Tushar 1456
Nishat, Fareha 1494
Nishida, Emi 0574
Nishimura, Keisuke 0062
Nishimura, Yoshito 1732
Nishino, Takahiro 2602
Nishio, Midori 0385, 2177, 2183
Nishioka, Ryo 2523
Nishioka, Yujin 0521
Nishisaka, Kazuma 0062
Nishitani, Kohei 0850
NISHIURA, YOSHINORI **1345**, 2664
NIshiyama, Nanako 1848
Nishizawa, Akitoshi 0052
Nissen, Michael 0543
Nissen, Michael J. 1430
Nistor, Alesea 1414
Nita, Kristiana 2396
Nititham, Joanne 0625
Nititham, Joanne 0637, 1504, 2646
Niu, Mengwen 2005
Nkonda, Estelle 2080
Noël, Nicolas 1765
Noaiseh, Ghaith 1378, **1384**, 1399
Nobakht, Niloofar 0661
Noble, Johan 0618
Nobleza, Kenneth 1621
Nocturne, Gaetane 0034, 0508, 0516, 1683
Noer, Pernille 0929
Noguchi, Ikuyo 2564
Nohda, Yasuhiro 0773, 1857
Noiri, Eisei 0043
Nojima, Masaki 0521
Nokay, Mine 0430
Nolain, Patrick 0653
Nolan, Brian 0920
Nolla, Joan Miquel 0353, 0575, 0749, 1161, 1162, 2250, 2484, 2485
Nomura, Atsushi 2523
Nomura, Norimichi 0773, 1857
Nonaka, Motohiro 0773
Nong, Minerva 1730
Noor, Abass 2141
Nordal, Ellen 0420
Nordmann-Gomes, Alberto 0791, 1268, 1942, 1970, **2650**, **2693**
Nordstrom, Dan 0814
NORMAND, Myriam 0537
Norris, Jill 0775, 1842, 2227
Norton, Clare 0787
Norton, Sam 0190, 1077, 1906
Noss, Erika 1878, 1899
Nossent, esther 0690, 1860
Novacic, Danica 0301
Novack, Joshua 1265
Novack, Stuart 2278
Novell, Georgina 1943
Novella-Navarro, Marta 0089, 0180, 0249, 1322, 2042
Novelli, Lucia **0557**
Noversa de Sousa, Rita 2613
Noviello, Silvia 0238
Novikov, Pavel 1598, 1605
Novoa, Francisco Javier 0642, 0659, 2422
Novosel, Olivia **2563**
Nowak, Elizabeth 2581
Nowakowski, Amanda 1827
Nowicki, Katherine **2161**
Noxon-Wood, Virginia 0726, 2003
Noyola-Sauceda, Erendira Berenice 2171
Nozal, Pilar 1322
Ntellis, Konstantinos 2232
Ntow, Mark 0456
Nuño, Laura 0089
Nuño, Laura 1152, 1170, 2042, 2373
Nuechterlein, Kaitlin **2215**
Nugraha, Mahardika 1398
Nunes, Fabio 0875
Nunes, Mateus Augusto Rangel **2536**
Nunes da Silva, Everton 1365
Nunez, Daniel 1563, 2468, 2669
Nurieva, Roza 0273
Nurmohamed, Michael 0431
Nurmohamed, Michael 0814, 2359
Nuruzzaman, Farzana 1287, 1288, **1669**, **2125**
Nusbaum, Julie 0853, 1391, 2196
Nwankwo, Henry 2263
Nwankwo, Victoria 2432
Nweke, Ugochukwu 2415
Nwoko, Uzochi 2149
NZEUSSEU TOUKAP, Adrien 1959

O

O.A. Abuzied, Ola 1222
O'Brien, Catherine 1479
O'Conor, Alison 2454
O'Neill, Sean 0595
Oakes, Emily 1019, 1020, 1709, 1896, 2414, 2568
Oates, Jim **0944**, 1082
Oates, Mary 1727
obeidat, alia **1782**, **1783**, 1790, 1800
O'Beirne, Ronan 1252
Oberholtzer, Lydia 0381
Oberle, Edward 0411, 0413, 1066, 2177, 2677
Obianyo, Chekwube 1646
Obremskey, William 0352
O'Brien, Patrick **0951**
O'Brien, Timothy 0027, 1786, 1797
O'Bryan, Edward 2554, 2558
O'Bryan, Sean 0501
Ocampo, Wrechelle 2419
Ocana, Lety 2547, 2565
Occhipinti, mariaelena 0880
Ochoa, April 0210
Ochtrop, Manuella 1407, 1408, 2326
Ocon, Anthony 0479, 0513, 2343, 2519
O'Connor, Shannon **0302**, **1826**
Oda, Kosaku 2564
O'Dea, David **0743**, 2508, 2509
Odede, Geofrey 0074

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Odell, Ian 0674
O'Dell, James 0774, 1125, 1674, 2001, 2276, 2585
Odoardi, Francesca 1206
Odom, Patrice 1917
Odom John, Audrey R. 0423
OELKE, KURT **2355**, 2375
Oelzner, Peter 0762
Oermann, Eric 1712
Oesch, Jasmine 2142
O'Farrell, Rebecca 1409
Ofek, Hai 2490
Oganowski, Theresa 1934
O'Garo, Keisha-Gaye 2142
Ogawa, Atsubumi 0773, **1857**
Ogawa, Noriyoshi 1630
Ogawa, Shotaro 1509
Ogbonnaya-Whittlesey, Sandra **0866**
Ogbu, Ekemini 0126, 0418, 0419, 1295, **1706**, **1744**, 1813, 1829
Ogdie, Alexis 0187
Ogdie, Alexis 0339, 0362, 0455
Ogdie, Alexis 0527
Ogdie, Alexis 0546, **0562**
Ogdie, Alexis **0563**
Ogdie, Alexis 0564
Ogdie, Alexis 0573
Ogdie, Alexis 0578
Ogdie, Alexis 0579, 0580
Ogdie, Alexis **1223**, 1261
Ogdie, Alexis 1429, 1455
Ogdie, Alexis 1566, 1888, 2084, 2096
Ogdie, Alexis 2098
Ogdie, Alexis 2233, **2305**, 2320
Ogdie, Alexis 2345
Ogdie, Alexis 2356
Ogdie, Alexis 2357, 2366
Ogdie, Alexis 2624
Ogdie, Alexis 2654
Ogdie, Alexis 2690
Ogle, Brenda 0027
Ogric, Manca 0281
Oguma, Misa 2522
Ogundiran, Ogundoyin **0769**, 0770, 0788
Ogunsanya, Motolani 1262
Ogura, Andre 2429
Ogura Dantas, Lucas 2429
Oguzoglu, Umut 1494
Ogwu, Samuel 1348
Oh, Jason 1437
Oh, Ji Seon 0171
Oh, Ji Seon 1372, 1373
Oh, Ji Seon 2431
Oh, Sam 0726, 1606
Oh, Yoon-Jeong **0526**, **2264**
Ohara, Ray 2494
Ohashi, Yoshifumi 1326
Ohbe, Hiroyuki 2449
Ohioma, Josephine 1083
Ohkubo, Naoaki 0595
Ohl, Sara 2559
Ohl, Selina 0090
Ohmura, Koichiro 1772, 1849
Ohnishi, Takahisa 0284
Ohnishi, Takahisa 1610
Ohnishi, Takuma 0159
Oka, Hideki 1849
Oka, Yumiko 2522
Okada, Masato 0638
Okada, Masato 1353
Okada, Masato 2225
Okada, Masato 2660
Okada, Megumi 2564
Okada, Yukinori 0850
Okamoto, Keita **0084**
Okamura, Daryl 2462
Okamura, Tomohisa 1512
Okano, Takaichi 0062
Okano, Yutaka 2253, 2254
Okazaki, Kazuichi 0279, 1163, 2019, 2020
Okazaki, Ryota 2523
O'Keefe, Sandra 0970
O'Keeffe, Lauren 1751, 1902, 2235, 2574, 2577, 2578
Okeke, Chukwuemelie **1224**, 1513, 1646, **2024**
Oki, Yotaro 1854
Okushi, Yuichiro 0695
Oladapo, Abiola 1259, 1929, 2548
Oladeinde, Boluwatito 1832
Oladeinde, Boluwatito 2394
Oland, Liam 1369
Olaosebikan, Hakeem 2263
Olas, Jacek 1210
Olave, Marianna 2084, 2096, 2098, 2624
Oldenkott, Judith 0338, 1010
Oldham, Justin 0808
O'Leary, Shawn 0321
Oler, Andrew 0920
Olesen, Claus 0929
Oleszowsky, Mara 1729
Oletsky, Richard 0337, 1914
Olferiev, Mikhail **1700**
Oliva Ruiz, María del Rosario 2112, 2113
Olivas, Otto **1964**
Olive, Alex 1397, 1681
Oliveira, Ana Renata 1293
OLIVEIRA, RODRIGO 0179
Oliveira, susana 0702
Oliveira, Thauana 1407, 1408, 2326
Oliver, Melissa 1669, 2125, 2128
Oliver, Stephen 0801, 1189, 2665
Oliver García, Elena María 0269, 1171
Oliveros, Christian-Immanuel **2678**
Oliviero, Francesca **1127**
OLLER RODRIGUEZ, JOSE ELOY 2422
Olmer, Merissa 1782, 1796, 1805
Olofsson, Tor 0434
Olofsson, Tor **0525**, **0814**
Olojo, Ayobami 1526
Olsen, Flemming 1166
Olsen, Inge Christoffer 0420
Olsen, Nancy 0023, 0227, 0500, 0657, 1523, 1524, 2166
Olsen, Sjurdur Frodi 0427, 2679
Olthoff, Arno 1205
Olumuyide, Emmanuel 0151, 1880, 1882
Olurinde, Mobolaji 0257
Omachi, Theodore 0650
Omachi, Theodore 1521
Omair, Mohammed 0600
Omalla, Evans 1706
O'Malley, Shane 0768
O'Malley, Tyler 0467, 0636, 0851, 2427, 2433, 2434
Omar, Gihan 0333
Ombrello, Amanda 1169, 1651
Ombrello, Michael 0782, 0918, 1811, 2133
Omdal, Roald 0034
Omi, Fuadur 0316
Omilusik, Kyla 2454
Omura, Satoshi 2523
On, Aretha 0278, **1474**, 2428
On, Tyler 2228
Ondrejčáková, Lucia 1962
O'Neil, Liam **0799**, 1315
O'Neill, Allison 1266
O'Neill, Grace 1551
O'Neill, Jacqueline 0074
O'Neill, John 0854
Onel, Karen 1283, 1669, 1820, 2125, 2128
Oner, Yusuf Ecren 2667
Ong, Voon H. 0692, 0966, **1589**, 2496, 2503
Onishi, Akira 1772
Onishi, Yasuhiro 1630
Ono, Yosuke **0097**
Ono, Yuuichi 0052
Onofrey, John 0674
Ooka, Seido 0668
Oon, Shereen 0595, 1716
Oortgiesen, Marga 0591, 0592
Oparina, Nina 0593, 0594, 2390
Oparina, Nina 2647
Opinc-Rosiak, Aleksandra 2067
Oppo, Sonia 0148
Oppong, Richard 0637
Oppong, Richard **1504**
Orange, Dana 0316, 0463
Orange, Dana 0844
Orange, Dana 1223
Orange, Dana 1782
Orbai, Ana-Maria **0529**, 0567, 1028, 1411, 1455, **2341**
Orban, Iionka 0401
Orban, Zachary 2430
Ordás Calvo, Carmen 1548
Ordas calvo, Carmen 2670
Ordas Martínez, Jose 0882, 0982, 2209
Oreiro, Natividad 0329, 0454
Orellana, Diego 0054
Orellana, Diego 0871
Orellana, Diego 2643

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Orengo, Jamie 0897, 0898, 0934
Oreská, Sabína 1211
Oreská, Sabína **2073**
Orillion, Ashley 0596, 0621, 0623, 1486, 1491, 1530, **1878**, 1899
Oriss, Timothy 0864
Orkaby, Ariela 0446
Orkaby, Ariela 0462
Orkaby, Ariela 0836, 1238, 2252
Orlandi, Martina 0880, 2656
Orlova, Inna **1128**
Ormeloh, Lea 2612
Ormseth, Michelle 0466, 0717, **0775**, 1329
Ormseth, Sarah 1330, 1331, 1950, 1955
O'Rorke, Michael 1015
Orozco Guillén, Oralia Alejandra 2218, 2632
Orpinell, Laia 2373
ORQUEVAUX, Pauline 2457, 2655
Orr, Stephen 0017
Orsi, Gergely 2684
Ort, Tatiana 0989
Ortega, Victor E 1900, 2542
Ortega de la O, Maria Carmen 0351, 2344
ORTEGA DE LA O, MARIA DEL CARMEN **0351**
Ortega-Castro, Rafaela 0019, 0070, 0071, 0072, 0087, 0094, 0100, 0108, 0496, 0583, 0795, 0901, 1851, 2265, 2268, 2290, 2371, 2502, 2599, 2648
Ortega-Valin, Luis 2670
Ortiz, Ana M 2122
Ortiz Buitrago, Pedro 0100, 0108, 0583, 0901, 2371
Ortiz sanjuán, Francisco 0757
Ortiz-Lavin, Pilar 2388
Ortiz-Márquez, Fernando 0496, 2268
Ortiz-Palafox, Jesus Mario 1633, 2549
Ortiz-Rios, Andres M. **0212**, 0213, 1633, 1834, 1845, **2171**, 2219, 2549
Ortiz-Santamaria, Vera 1548
Ortiz-Santamaria, Vera 2477
ORTOLAN, AUGUSTA 0588, **2307**, **2308**
Ortuño, Samanta 1133
Orvain, Thibault 2704
Orwoll, Eric 2119
Osborne, John 1252, 2006, 2172
Osborne, Kyle 2559
Osborne, Richard 0190, 1077, 1263
Osborne, Tim 1136
Osgood, Eric 1183
Osgood, Sharon 0118, 1988
O'Shea, Ciara 0649, 0803, 2467
O'Shea, Finbar 1409
Oshige, Tatsuhiro 2253, 2254
Oshima, Hisaji 2253, 2254
Osman, Mohammed **0969**, **0970**
Osorio-Sanjuan, María Camila 0639
Osorio-SanJuan, Maria Camila 0250
Ospelt, Caroline 0807
Ossa-Echeverri, Maria 0942
Ossorio, Marta 0346
Ostendorf, lennard 0885
Ostergaard, Mikkel 0543, 0814, 0854, 1430, 1466, 1963, 2279
Ostor, Andrew **1349**, 2273, **2342**, 2367
Ostos Prado, María José 0287, 1836, 2052, 2053, 2078
Ostrin, Edwin J. 1920
O'Sullivan, David 0750
O'Sullivan, Frank 2040, 2077
O'Sullivan, Madeline 1981
Osuna, Julio 0070
Ota, Mineto 1512
Otabor, Emmanuel 0254, 0255, 1074, 1075, 1076, 2093
OTADUY, CINTIA 0596, 1486
Otero, Lucia 0153, 0757, 1446, 2269
Otero, Miguel 0316, 1782
Otipoby, Kevin L. 0008, 0987
Otsubo, Shigeki 1538
Ott, Sebastian 0762
Ottaviano, Lydia 0410
Otte, Ina 1934
Ou, Daming 0649
Ou, San-San 0843
Oudart, Fiona 0796
Oudart, Fiona 1334
Oudart, Fiona 1724
Oulad-Abdelghani, Mustapha 0862
Oustalet, Marie 0162
Outh, Rodérau 0891, 2699
Ouyang, Zhi-Ming 2245
Ovayolu, Mustafa 2044
Owens, Joshua 1056
Owens, Roisin 0032
Owens, Sonal 0853, 1391
Oyama, Setsuko 0043
Oyarce-Calderón, Alvaro **0714**, 0730, **2378**
Oyarce-Calderón, Alvaro 2521
Oza, Vikash 2145
Ozaki, Hiroki 1167
Ozcan, Alp 2543
Ozdogan, Huri 1177
Ozen, Gulsen **1015**
Ozen, Gulsen **2483**
Ozgocmen, Salih 0854
Ozguler, Yesim 2543, 2544
Oziol, Eric 0891
Ozturk, Mumin 2010

P

P Mohankumar, Shivaprasad 2153
Páez Franco, José Carlos 1841
Pérez, Maribel 0019, 2290
Pérez, Yanira 1446
Pérez Cristóbal, Mario 1491
Pérez de Pedro, Iván 1210
Pérez García, Carolina 0505
Pérez González, Alicia 2112, 2113
Pérez jiménez, Valentina 0621
Pérez Sánchez, Carlos 0070, 0071, 0072, 0087, 0094, 0100, 0108, 0795, 0901, 1851, 2502, 2599
Pérez Venegas, Jose Javier 0019, 0087, 2290
Pérez-Gamboa, Raúl 2321
Póliska, Szilárd 0680
Paape, Catriona 0903
Paats, Astrid 0621, 0623, 1491, 1530
Pabani, Aliyah 2251, 2252
Pablos, jose Luis 0454
Paccou, Julien 2115
Pace, Amanda 0501
Pacheco, Addison 1755, 1756
Pacheco, Jennifer 0624
Pacheco, Leroy 2278
Pacheco Silva, Raianni Rúbia **1365**
Pachera, Elena 0957, 0967, 1867, 1872, 2497
Pachowsky, Milena 0878
Pacifico, Paola 1780
Pacini, Greta 0238
Padera, Robert 0669, 1913
Padhan, Prasanta 0461, 0533
Padilla, Brad 1259
Padilla-Galo, Alicia 1600
Padoan, Roberto 0238, 0275
Padoan, Roberto 1605
PADUA, ANA F 0179
Pagis, Valentine 2168
Pagnoux, Christian 0716, 0721, 0722
Pagnoux, Christian 0747, 1597, 1602
Pagnoux, Christian 1607
Pagnoux, Christian 1608
Pagnoux, Christian 1767
Pagnoux, Christian **1769**, 2515
Pagnoux, Christian 2533
Pai, Shao-Yu 1106, 1217
Pai, Venkatesh Srinivasa 1364
Pai, Venkatesh Srinivasa 2261
Paik, Julie 0288, 0289, 1037, 1207, **2063**
Pain, Clare 1287
Pain, Clare 1288
Paiola, Matthieu 1853
Pais de Barros, jean Paul 2637
Paiva, Beatriz 1408
Pajareya, Patavee 1134, 2255
Pak, Jasmine 1708
Pak, Katherine 0296, 0863
Palacios Santillan, Erika Susana 1491
Palacios-Olid, Judith 0749
Palacios-Olid, Judith 2250
Palafox Sosa, Itzel 1947, 2243
Palafox Vargas, Martha Leticia 2218, 2632
Palaniswamy, Kiruthi 2466
Palat, Sylvain 0688
Palau Balaña, Núria 0019
Palaz, Tayfun 1206
Palchevskiy, Vyacheslav 1872
Palermo, Tonya M. 1298
Palettas, Marilly 0615

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Palevsky, Paul 1125, 2001
Palleiro, Daniel 2336
Paller, Amy 0875
Pallotti, Chiara 0401
Pallotti, Federica 1768, 2582, 2584
Palm, Øyvind 0034
Palm, Marisha 2301
Palma, Christopher 2468
Palma-Sanchez, Deseada 1547, 1548, 2229
Palmer, Anna-Kay 0693
Palmer, Chloe 1624, **2700**
Palmer, Scott 0274
Palmou, Natalia 1282, 1284
Palmowski, Andriko **0338**, 0342, 0343, **1010**, 2109, 2110, 2595
Palomar-Ramos, Jorge 1961
PALOMINOS, PENELOPE 1411
Palomo-Arnaud, Karina **0512**, **1389**
Palshikar, Mukta 1702
Palsson, Olafur 1430
Palumbo, Marcella 1330, 1331
Paluvayi, Sriya 0186
Pamies, Anna 1548
Pamuk, Omer 0603, **0627**, 0741, 0742, 1151, 1471, 1476, 1500, 1501, **1502**, 2216, 2382, 2389
Pan, Haoyu **0124**, 0142, 0856, 0964, 1971
Pan, Mengge 0519
Pan, Nancy 0411, 1066, 2226
Pan, Stephen 0598
Pan, Steven 1307
Pan, Xiaoyu 0003
Pan, Yi 1006
Panés, Julián 0257
Panaccione, Remo 0257
Panahandeh, Sanaz 0081
Panarese, Iacopo 1864
Panaritis, Kalliopi 2215
Pandey, Bhaskar 0447
Pandey, Oshna 2514
Pandian, Vishnuprabu **0047**
Pando, Jose A 2278
Pandya, Ankur 1011
panebianco, valeria 0880
Pang, Linxuan 2611
Paniagua Zudaire, Inmaculada 1904
Panicker, Sumith 0118
Panico, Brittany **1973**
Pankow, Anne 1010
Pannala, Sai Shanmukha Sreeram **0633**
Pannala, Sai Shanmukha Sreeram **2517**
pannier, emmanuelle 2655
Pantazis, Nikos 0133
Pantoja, Lucia 0271
Pantoja Zarza, Lucia 0270
Panupattanapong, Sirada 1809, **2155**
Panyard, Daniel **0024**
Paolini, John 0242, 0732, 1186
Paolino, Sabrina 0676, 0963, 1097, 2501
Papachristodoulou, Eleni **0609**, **2026**
Papademetris, Xenophon 0674
Papadimitriou, Evangelos 1439
Papadopoulos, Vasileios 1452
Papadopoulou, Despoina 2671
Papagoras, Charalampos 1439, 1452
Papasidero, Silvia Beatriz 0432, 2405
Papo, Matthias 1604
Papo, Thomas 1575, 2489
Papotti, Bianca 1330, 1331
Papp, Kim 2362, 2374
Pappa, Maria 1439, 1452
Pappas, Dimitrios 1049, 1340, 2681
Parades-Ruiz, Diana 0860
Parajuli, Pravakar 0492
Parameswaran, Vidhya 0242, 1186
Parast, Mana 2197
Paratz, Elizabeth 0677, 1716
Pardali, Katerina 0431
Pardeo, Manuela 2128
Pardos-Gea, Jose 0120
Paredes Romero, Maria Beatriz 0201, **1961**, 2344
Paredes-Romero, Beatriz 0019, 1397, 1681, 2290
Paredes-Ruiz, Diana 0120, 0121
Pareek, Manan 1166
Pareja-Martínez, Ana 1547, 2670
Parent, Isabelle 0653
Paricaud, Kim 0162
Parides, Michael 0463, 0634
Parikh, Amish 2079
Parikh, Anuj 1935
Parikh, Bhumik 1435, 1443, 1453
Parikh, Krishan 1935
Parikh, Twisha 1890
Parimi, Vijaya prasanna 0495, 0708, 1485, 1588, 2313
Parimon, Tanyalak 0067, 0085
Parish, Susan 0408, 0410
Parisi, Simone 0275, 1136
Park, Chan Ho 1343
Park, Chanhyuk **0812**
Park, Dong-Jin 1145
Park, Elizabeth **1310**
Park, Eun-Jung 2315
Park, Hong-Jai 0869
Park, Hye Sang 1620
Park, Jenny Y. 2546
Park, Jin Kyun 0203, 1748
Park, Jin Kyun 2698
PARK, JIN SU 1029
Park, Josephine 0377
Park, Joy 0657
Park, Jun Won 0203, 2698
Park, Ki-Jeong 1145
PARK, PIL GYU **1029**
Park, So Young 0473
Park, Soongho **1988**
Park, Yong-Beom 1343, 2511
Park, Yong-Wook **1145**
Park, Youngho 0550
Parker, Ben 0245, 2458
Parker, James T. 0069
Parker, Joseph 0727
Parker, Thomas 1839
Parker Harp, Chelsea R. 0987
Parkinson, Joel 1711
Parks, Cassie **0865**
Parks, Christine 0159
parlar, Kerem 1177, 2667
Parlati, Corrado 1402
Parlett, Lauren 0399, 0400
Parmanto, Bambang 0765
Parnell Lafferty, Kimberly 0563, 0564
Parodis, Ioannis **0125**, 0644, 0664, 0842, 1218, **1531**, 1840, 2067, **2401**, **2402**, 2441, 2648
Parody, Ann 1056
Parperis, Konstantinos 2026
Parra, Mitndbaim **0496**, 0542, **2323**
Parreau, Simon 0756, 2532
Parrikh, Kaksha 2050
Parris, Glenn R. 1977, 2278
Parronchi, Paola 2532
Parry, Blair 2006
Parsafar, Shima 1693
Parsons, Christine **2177**
Parsons, Christine M. 0344
Parsons, Teagan J. 0997
Partain, Brittany 0467, 2433, 2434
Parton, Hilary 2645
Partridge, Savannah 0186
Parulekar-Martins, Roshni 2572
Parvizi, Rezvan 0811, 0845, 0846
Pascal, HILLIQUIN 1095
Pascal, Laurent 1339
pascal, richette 1095, **1135**, 1136, 1144
Pascart, Tristan 0566
Pascau, Javier 1964
Paschke, Joel 0428
Pascual, David 0482
Pascual, Eliseo 1133
Pascual, Florencia Micaela 0432
Pascual, Virginia 2410
Pascual-Ramos, Virginia 1022
Pascual-Vergara, Antonio 2106
Pason, Carter **1261**
Pasoto, Sandra G 0206, 0619, 1192, 1715, 2292, 2527, 2573, 2653, 2682
Pasquier, Elisabeth 2457
Pasquiers, Blaise 1593
Passalent, Laura 0547, 2200
Passell, Eliza 2577
Passeron, Thierry 1448
Pastor Mena, Marta 2229
Pastor Navarro, Sonia 2354
Pastor Orduña, Maria Isabel 2038
Pastor-Asurza, Cesar 0605, 1717, 2378, 2383
Pastore, Serena 0392
Pastrana, Carolina 2462
Pastrello, chiara 1756

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Patarini, Julieann 0309, 0313, 0322, 2090, 2623, 2625
Patel, Aakash V. 0344, **0599**, **1467**, **2377**
Patel, Aarat M 1533, 1534, **1536**, 2453, 2456
Patel, Anand 1123, 2588
Patel, Anisha **1038**
Patel, Aryan **0068**
Patel, Astha 0054
Patel, Astha 0055, 0110
Patel, Axi 1511
Patel, Bhavisha 0777, 2700
Patel, Bindi 0057
Patel, Hamel 0991
Patel, Harshank 1879
Patel, Jay 1050, 1051, 1052
Patel, Jay 1890
Patel, Julisa 0401
Patel, Junaid 1525
Patel, Kajal **1980**
Patel, Kaylani 1296
Patel, Manish 2342, 2367
Patel, Mariya 0554
Patel, Maya **0330**
Patel, Naomi **0375**, 0792, **1606**, **1764**, 1902, 2508, **2574**, 2577, **2578**
Patel, Neel 1484
Patel, Pooja **2462**
Patel, Preeyam 0050, 2035
Patel, Priya 2302
Patel, Rena 0157, 0158, 1068
Patel, Rishi 1984
Patel, Rushi 1546
Patel, Rutvi 0848
Patel, Sagar 1890
Patel, Sai 0234, 0253
Patel, Saloni **2518**
Patel, Samir **1906**
Patel, Shivum 1139
Patel, Vaishali 0234, 0253
Patela, Mariana 0761
Paternoster, Giancarlo 0448
Paterson, Alison 0009
Paterson, Michael 2200
Patiño Galindo, Juan Ángel 0019, 0021
Patino, Guadalupe 2547
Patino-Martinez, Eduardo 0945, 2580
Patnaik, Asha 0356, 1386
Patnaik, Mrinal 0777
Patolia, Saloni **1271**
Patrice, Cacoub 0735, 0756, 1575, 1604, 2489
Patrikiou, Eleni 1219
Patrikos, Dimos 1452
Patro, A Rajkumar 0533
Patterson, andrew 0871
Patterson, Charity 0765
Patterson, Dorothy 1256, 1257
Patterson, Kristina 2051, 2546
Patterson, Sarah 1972
Pattrick, Matthew 0034
Patwardhan, Anjali 1287, 1288
Paudel, Misti 0168, 0465, 0468, 1267, 1343, **1644**, 1747, 1751, 2235, 2568, **2607**, 2660
Paudyal, Sunita 1980
Paul, Angel 2685
Paul, Jisna 0999, 1040
Paula, Vitor 1293
Paule, Romain 0891, 2699
Pauli, Chantal 0807
Pauling, John 0684, 0692, 2483, **2487**
Paulissen, Genevieve 1738
Pavía-Pascual, Marina **2249**
pavelcova, katerina 1124
Pavelka, Karel 1211, 1350, 1962, 2073, 2346, **2593**, 2594
Pavlenko, Mariia 0392
Pavlenko, Mariia 0406
Pavlenko, Mariia **0414**, 1821
Pavlenko, Mariia 2675
Pavlova, Viktoria 2203
Pavuluri, Chandan K. 0888, 0997
Pawar, Priyanka 2150
Payan Schober, Fernanda 2600
Paz, Miriam 1137, 1319, 2420
Paz González, Rocio 0329
Paz Liñeira, Lucía **2121**
Paz Machado, Maria Gabriela 1619
Paz-Gandiaga, Nerea 0243
Pazzola, Giulia 0120
Peña, José Alberto 0483, 2036
Peña, Mario 2243
Peñalba, Ana 0029
Peñaranda Bolaño, Luis 1787
Peace, Ben 1123, 1998, 1999, 2587, 2588
Pearson, David 0285, 0286, 0802
Pearson, David 2696
Pecher, Ann-Christin 0810, **0884**
Peckham, Hannah 1672, 1817
Peckner, Ryan 0008, 0987
Pecondón-Español, Angela 2422
Pedersen, Susanne 0543
Pedersen, Susanne 0854
Pedraza-Arévalo, Laura C. 1072
Pedro, Sofia 1065, 1656, 1686
Pedroza, Claudia 0683, 0883, 0959, 1591
peene, isabelle **0694**
Pego-Reigosa, José María 0642, 1397, 1878, 1899, 2422, 2450
Pei, Yaqiong 0939
Pei, Zenglin 0911, 1776
Peiteado, Diana 0089, 2042
Peiteado, Diana 2344
Pelaez Ballestas, Ingris del Pilar 0623
Pelechas, Eleftherios 2236
Pellegrini, Christine 0336
Pellegrini, Christine **0766**
Pellegrino, Greta 1570
Pellerin, Alex 0008, 0987
Pellett, Nida 0904, 1692
Pellico, Maria Rosa **1212**, 2075, 2656
Pelowitz, Thomas **0276**
Peluso, Giusy 0246, 1352, 2479
Peluso, Marisa **0009**
Pena, Carlos **1522**
Penabad, Isabel 1260
Penack, Olaf 0471
Pena-Nunez, Diana 0988
Pendergraft, William 0650
Pendergraft, William 0654, 0664
Pendergraft, William 0665
Pendergraft, William 0838, 1038, 1521
Penfield, Christina 0853, 1391
Peng, Cheng 0994
Peng, Jian 0018, 1006
Peng, Junjie 0820
Peng, Li **0908**
Peng, Linyi 1036
Peng, Mary **0753**
Peng, Seth 2454
Peng, Yi 0640
Pengo, Vittorio 0120, 0121, 0860
Pennington, Stephen R. 0111
PENSEC, Hugo **2241**
Penston, Daniela 0006, 0017
Penta, Mrudula 1172
Penzo, Eleonora 0659
Pepper, Alicia N. 2500
Pepper, Kristie 2166
Pepper, Ruth 2458
Pequeno, Priscila 2200
Pera, Mariana 2405
Perales Fraile, Isabel 1210
Peral-Garrido, María-Luisa 1133
Peralta, Karen 2127
Peralta-García, Irene 0758, 2060
Peralta-Ginés, Cilia 0019, 1548, 2265, 2290
Perard, Laurent 0891
Perdan Pirkmajer, Katja **0281**
Perdan Pirkmajer, Katja 1430
Perdiguero, Miguel 1133
Perdomo, wendy **0763**
Perdomo, Wendy 2480
Perdriger, Aleth 0477, 0516
Perea, Elisabet **1096**
Pereira, Daniel 1415, 1416
Pereira, Leticia 2246
Pereira, Luciana 0358
Peretti, Silvia 1570
Perez, Nicolas 0621, 2405
Perez, Paola 1682
Perez, Ronald 2257
Perez, Stephanie 0674
Perez Chada, Lourdes 0576, **2320**, 2688
Perez Garcia, Carolina 2229
Perez Hurtado, Andres 0205
perez Hurtado, Andres 0237, 0341
Perez Hurtado, Andres **1274**, 2274, 2310
Perez Mejias, Erick 2284
Perez Nadales, Imma 1619
Perez-Barbosa, Lorena 0212, 0213, 1633, 1834, 1845, 2171, 2219, 2549

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Perez-Campoamor, Antonio 0901
Perez-Galán, Patricia 0732
Perez-Garfias, Dunja Athalia 1633, 2549
Perfetto, Jessica **2145**
Perich-Campos, Risto 0605, 0714, 0730, 1717, 2378, 2383, 2521
Perillo, Anna 0558, 2688
Peringeth, Gopisree 0223
Perkins, C Michael 2081, 2101
Perkins, Christine 2561
Perl, Andras 0657, 1092, 2391
Perlman, Alan 1839
Perlman, Harris R 0066, 0081, 1362, 2430
Perlmutter, Noah 0871
Perrin, François 1339
Perrodeau, Elodie 1685
Perron, Megan 1810
Perron, Megan 1822
Perronne, Laetitia **0327**
Perruccio, Anthony 2200
Perry, Samuel 0987
Pers, Jacques-Olivier 0034
Persons, Dan 1549
Perugino, Cory 0992, 1163, 2033, 2528, 2529, 2530
Perullo, Candace R. 0997
PERUMANGOTE VASUDEVAN, AHILA ARYA 0160
Perumangote Vasudevan, Akhila Arya **1147**
Peschken, Christine 1494, 1722, 2416
Peskin, Malki 2146
Pesonen, Maiju 0420
Pessoa de Luna, Mariana Souza 0621
Pestre, Vincent 2532
Petelytska, Liubov 1562
Peterfy, MD, PhD, Charles 1676, **2614**
Peters, Amy 0768
Peters, Oiza 0769, **0770**, 0788
Petersen, Laetitia 0990
Peterson, Alexander 2237, 2251, 2252
Peterson, Jeff 1675
Peterson, Jeff 1923
Peterson, Jeff 2278
Peterson, Lance **0948**
Peterson, Luke 1454
Peterson, Rachel 2466
Peterson, Skyler 0362, 2366
Petnak, Tananchai 1187
Petri, Michelle 0120, 0121, 0133, **0597**, 0607, 0645, 0662, **0772**, **0837**, 0840, 0842, 0851, 0860, 1223, 1240, 1251, 1480, **1498**, **1499**, **1516**, 1722, 1844, 1846, 2210, 2233, 2416, 2421, 2436, 2600
Petrimpol, Marco 0780, 1671
Petrone, Maria Isabella 0391
Petrow, Eva 1481
Petry, Claire 0650
Petty, Ross 0389
Petzinna, Simon M. **0892**
peyper, janique 2247, 2248
Peyrac, Geoffroy 0735
PFEIFER, LANCE 0473
Pfeiffer, Elizabeth 2204
Pfeil, Keri Ann 0603, 0741, 1151, 1471, 1500, 1501, 2382, 2389
Pham, Alan 2651
Pham, Duong Ba 1144
Pham, Michael 0701, 0710
Pham, Minh 1699
Pham, Nancy 1172
Pham-Ngoc, Hà 2262
Phan, Ryan T, **1367**
Phan, Thuyvan 2437, 2616
Phanstiel, Doug 1788, 1801
Phelps, Katrina 0218
PHILIP, SUBIN 0136, 0137, **1431**, 2424
Philippoteaux, Cécile 0566
Philips, Elliot 1265
Phillips, Carley 0302
Phillips, Charles 0776, 1443
Phillips, Glenn 0360
Phillips, Lucy 0048
Phillips, Magen 1978
Phisitkul, Pat 2380
Phithak, Elpida 0471
Phoon, Colin 0853, 1391
Phothisane, Anastasiia 0466, 0775
Phung, Cindy 0301, 1651
Phutinart, Somkiat 1134, 2255
Phyo, Le Yi 0088
Piatchou Donfack, Naiva Manuela 0382, 1505, 2575
Piatrova, Alena 1685
Piazza, Alessia 2178
Piccione, Julie 2196
Pichon, Adrienne 1268
Pickell, Sammy 1664
Pickering, Marie-Eva 2115
Pickett-Nairne, Kaci 2144, 2515
Pielfort, Daniel 2373
Piepoli, Tiziana 1737
Piercy, James 1889
Pietro, Rebecca 1236
Piette, Evan 0790, 2525
Piga, Mario Andrea 0238
Pigenet, Audrey 1735
Pike, Marilyn 1542
Pilato, Andrea 0391
Pillai, Neil 2430
Pillai, Shiv 0992, 2528, 2530
Pillebout, Evangeline 0618
Pillinger, Michael 1048, 1125, 1265, 1993, 2001, 2585
Pillon, Maria 2545
Pilon, Dominic 1165, 2369
Pimentel, Mark 1559
Pimentel-Quiroz, Víctor 1878, 1899
Pimentel-Quiroz, Victor 0605, 0621, 0714, 0720, **0730**, 1717, 2378, 2383, **2521**
Pimentel-Santos, Fernando 0854
Pimple, Sarah **1030**
Pin, Elisa 0900, **2027**
Pinal Fernandez, Iago 0296, 0301, 0866
Pinal-Fernandez, Iago 0863
Pincus, Theodore **0197**, 0225, **1375**, **2104**
Pineau, Christian 0606, 1506
Pineda, Carlos 0443, 0507, 2674
Ping, Henry 1652
Pinheiro, Marcelo 0589, 1407, 1408, 2326
Pinkrah, Daniel 0456
Pinna, Thomas 1135
Pino Hernández, Sally Patricia 1210
Pintér, Anett 2684
Pintaric, Karlo 0543
Pinter, Andreas 0558
Pinto, Ana Sofia 0761
Pinto, Daniel 2603
Pinto, Patrícia 0761
Pinto e Vairo, Filippo 0030
Pinto-Patarroyo, Gineth 2278
Pinto-Tasende, Jose 2373
Pioli, Patricia 0812, **1870**
Pipavath, Sudhakar 0457
Piqueras García, Maria 0642, 0659, 2450
Piranavan, Paramarajan 1539
Pires, Cleandro 0179, 1407, 1408, 2246, 2326
Pires, Lucas **2246**
Pires de Albuquerque, Cleandro 1365
Pirkmajer, Sergej 0281
Pisani, Francesco 0723
Pisani, Paola 0246, 1352, 2479
Pisetsky, David 0363, 1487, 2379
Pisoni, Cecilia 0596, 0621, 0623, 1486, 1530
Pistorio, Angela 0389
Pitarch, Concepción 1620
Pitliya, Aakanksha **0337**, **1347**, **1914**
Pitzalis, Costantino 0081
Piunno, Silvia 2294
Pizarro, Octavio 2576
Pizem, joze 2015
Pizzarossa, Ana Carina 0596
Pizzarossa, Carina 1486, 1491
Pizzorni, Carmen 0676, 0963, 1097, 2501
Place, Aaron 0056
Placido, Francesco 0275
Planet, Paul J. 0712
Plantinga, Laura **1639**, **1640**, **1641**, 2645
Plasencia, Agustin 0008
Plasencia-Rodríguez, Chamaida **0180**, 0183, 0496, 0535, 0745, 0755, 1062, 1152, 1322, 2042, 2268, 2344
Plasqui, Guy 1324
Platt, Adam 0832
Plaza, Zulema 1397, 1681, 1878, 1899
Plaza-Aulestia, Nahia 0250
Plaza-Aulestia, Nahia 1548
Plazyo, Olesya 0971, 1760, 2498
Plichta, Damian 0032
Poch i Mora, Marta 2106

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Poddubnyy, Denis 0547, 0552, 0569, 0591, 0592, 0854, 1415, 1416, 1425, 1426, **1435**, 1449, 1454, 2691
Podgorski, Christopher 2180
Podsiadlo, Pawel **2100**
Podsvirov, Vyacheslav 0779
Pogatchnik, Brian 1173
Poholek, Catherine 2141
Poirier, Charles 1193, 1199, 2259
Pokala, Nagendra 1260
Polański, Jacek 0096
Polachek, Ari 1710, **1945**, 1959
Polak, Marta 0558
Polanco Mora, Teresandris 0621
Polat, Berceste 1396
Poli, Sergio 0808
Polina-Lugo, Rebeca L. **0458**, **1427**, 1483, 1528, 2058, **2071**, **2072**
Polis, Baruh 0936, 0937, 0938
Polishchuk, Elena Y. 0503
Pollastri, Francesco 2592
Polvent, Elizabeth 1138
Polyzou, Maria 1439
Pommerolle, Pierre 0618
Pommier, Alexandra 0824
Pommier, Alexandra 1822
Ponce, Andrés **1943**
Ponce-Santillan, Mara Alejandra 1633, 2171
Ponder, Lori 2154
Pongtarakulpanit, Nantakarn 0282, 0303
Pongtarakulpanit, Nantakarn 1201, 1215
Pons-Estel, Bernardo A. 1526, 1530
Pons-Estel, Guillermo 0120, **0596**
Pons-Estel, Guillermo 0621
Pons-Estel, Guillermo 0623
Pons-Estel, Guillermo 1486
Pons-Estel, Guillermo **1530**
Pontarini, Elena 0034
Ponte, Cristina 1626, 1912
Poo-fernandez, Claudia 0150, 1599
Poole, Janet **2555**
Poole, Jill 0022
Poon, Adrienne 2576
Pooni, Rajdeep 0186
Poos, Stephen **0356**
Pope, Catherine 1244
Pope, Janet 0438, 0442, 0689, 1103, **1355**, 1648, 2267
Popkova, Tatiana 0133
Popovic, Zoran 0695
Popovich, Dillon 0846
Poppei, Gavin 0858, 1623
Porcher, Raphael 1685, 2699
Porcu, Sebastiano 0444
Portela Hernández, Margarita 0596, 0621, 0623, 1486, 1530
Porter, Andrew 0996
Porter, Faith 2432
Porter-Brown, Ben 0567, 1455
Porterfield, Florence 0813, 1130
Portier, Elodie 1312
Portilla González, Virginia 0216, 1094, 1916, 2388
Portnoy, Daniel 1853
PORTO, BRUNA L 0179
Porto, Graca 1136
Possler, Patricia 1450
Postigo-Llorente, Concepción 2670
Postma, Rudmer 1568
Pothraj, Sonia 0399
Potluri, Ravi 1377
Potluri, Vineeth 0733, 2070
Potter, Krysten 0410
Potthoff, Bernd 2631
Potts, Lauren 1669, 2125
pouchelon, clara 1604
Pouchot, Jacques 0314
Pouchot, Jacques 2080, 2532
Poudel, Dilli 0546, **1888**
Poudel, Dilli 2220
Poudel, Sajana 0492, 2514
Poudyal, Bhavya 0657
Pouenat, Clementine 0508
Poulet, Antoine 0891
Poulet, Christophe 1738
Poulia, Vassiliki 1439
Pourcel, Graziella 1356
Poux, Margot 1768, 2582, 2584
Pouzol, laetitia **0990**
Powell, John 1909
Powell, Natasha **0164**
Powers, Helene 1810, 1822
Pozsonyiova, Sofia 0793
Pozzobon, Marilia 0801
Pradhan, Niki 1557
Prahalad, Sampath 0392, 0406, 0414, **2154**, 2678
Prahalad, Vaishali 1696
Prajapati, Chetan 1451, 2352
Prajzlerová, Klára **0831**
Prakoso, Budi 1398
pranzatelli, thomas 1682
Prasad, Joshua 1759
Prasad, Shiwani 1401
Prathyusha, Kolluri 1039
Prati, Clément 0544, 2637
Pratt, Arthur 1678, 1703
Pratt, Laura 0413
Preger, Charlotta **0900**, 2027
Preisinger, Katie 1240
Prell, Sean 0797
Premo, Katherine 1723
Presley, Carolyn 2252
Presti, Sonia 0797
Prevost, A. Toby 1678
Prevot, Grégoire 1200, 2510
Price, Lynn 0667
Price, Theodore 1233
Prieto-Gonzalez, Sergio 0896, 1210
Prieto-Peña, Diana 0150, 0243, 0250, 0737, 1599, 1612, 2023, 2059, 2538, 2610
Pringle, Sarah 0034
Printzis, Christina 1309
Prinz, Marco 1206
Prior, David 2651
Prior Español, Águeda 2029
Prior-Español, Agueda 0117
Pritchett-Frazee, Cherilyn 0034
Priyanka, Stella 0996
Procureur, Adrien 0887
Proft, Fabian 0573, 0581, 0854, **2347**, 2358
Prokop, Larry J. 0601
Pros, Anna 2485
Prosch, Helmut 0510
Prothon, Susanne **1374**
Protudjer, Jennifer 1494
Proudman, Susanna 0091
Proudman, Susanna 0504, 0677
Proudman, Susanna 0917, 1565, 1862, 2651
Provino, Julia 0898
Pruitt, Chris 0207
Pryor, Olivia 0888, **0997**
Psachoulia, Konstantina 0562
Psarras, Antonios **2601**
Ptacek, Travis 0040, 0041
Pua, Heather 1000
Puéchal, Xavier 0715, 1592, 1593, 1598, 1604, **1765**, 1766, 1768, 2506, 2532, 2584
Puche-Larrubia, María Ángeles 0100, 0108, 0583, 2323, 2371
Puchongmart, Chanokporn 1137
Puchulu-Campanella, Estela 0719
Puente, Ivonne 1374
Puev, Katherine 2430
Puga Guzman, Jose Luis 2209
Pugalenthi Saravanan, Deepika 0227
Pugashetti, Janelle 0808
Pugh, Trevor 1755
Pugliesi, Alisson 1400
Pugliesi, Alisson 2246, 2536
Pugnet, Grégory **0123**, **1200**, 1592, 1765, **2510**, 2655
Pugnet, Gregory 0688
Puig-Buendia, Jose 2670
pujol, manel 1619
Pujol Manresa, Anna 2029
Pujol Teixidor, Marta 1619
Puksic, Silva 2060
Pulito Cueto, Verónica 0029, **1778**
Pullenayegum, Eleanor 1279
Pullman, James 2381
Pulungan, Zulkarnain 2051
Punjadath, Sryla 1364, **2261**
Puranam, Kaushik 1771, 2417
Puri, Alison 0992, 1751, 2235
Purnomo, Athaya Febriantyo 1398
Purohit, Ami **2054**
Purohit, Neelay 1518
Purushothaman, Mohan 2384, 2649

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Purvis, Clarisse 1973
Pustizzi, Jennifer 2355
Pustizzi, Jennifer Marie 2375
Puszkiel, Alicja 1593, 1722
Putman, Michael 0720, 0746, 0753, 1139
Putrino, David 1236
Puttapaka, Srinivas 1591
Puttapaka, Srinivas 2652
Putterman, Chaim 0851, **0936**, **0937**, **0938**, 1240, 2600
Puxeddu, Ilaria 0723
Puzio, Patricia 1545
Pyakurel, Sulav 0433
pye, Aidan 1199, **1938**

Q

Qaiyum, Zoya 0113, **1755**, 1756
Qamhieh, Zahraa **0670**, 0805
Qasim, Rameez 0556, 0703, 1328, 1720, 2095, 2099, 2516
Qazi, Yasir 1991
Qi, Fumin 1220
Qi, Fumin **2447**
Qi, Jing 0010
Qi, Wantong 0939
Qi, Ying 0168, 0465, 1016, 1357, 1747, 1751, 1957, 2235, 2569
Qian, Grace 1751, 1902, 2235, 2574, 2577, 2578
Qian, Jinyi 0124, 0142, 0856, **0964**, 1971
Qian, Junbin 1131
Qian, Long 2013, 2014
Qiang, Xiangnan 0939
Qin, Ling 0536
Qin, linmang 1002
Qin, Qinli 1541
Qin, Yifan 0277
Qin, Yuhao **0915**
Qin, Yurong 0005, 0986, 1001
Qing, Yufeng 1132, 2589
Qiu, Wenlin 0646
Quaglino, Pietro 2699
Quan, Guiqi 0646
Quandt, Sara 2097
Quaranta, Patricia 0329, **1798**
Quartier, Pierre 0401, 0780, 1671, 2137
Quartier Dit Maire, Pierre 2138, 2139
Quartuccio, Luca 0238
Quartuccio, Luca 1680, 2545
Queen, Kate 2097
Queiro, Ruben 0577, 1460
quelain, Juliette 1115
Quemeneur, Thomas 0891, 1765
quere, baptiste 2241, 2300
QUERE, Blanche **0439**
Quesada-Masachs, Estefania **1787**
Quevedo, Pedro 0083
Quevedo-Abeledo, Juan C. 0450, 0604
Queyrel Moranne, Viviane 2457
Quinet, Robert 1508, 2392
Quinlan-Waters, Megan 0392, 0394, 0406, 0414, 0415, 0419, 1813, 1829, 2675
Quinn, Kaitlin 0258, 1618, 1624, 2533, 2701
Quinn, Stephanie 0410
Quinones, Mercedes 0328, 2084, 2096
Quinones, Mercedes 2098
Quinones, Mercedes 2624
Quintana, Luis 1521
Quintana, Rosana 0596, 0623, 1530
Quintana-Lopez, Gerardo 0596, 0621
Quintana-Lopez, Gerardo 0623
Quintana-Lopez, Gerardo 1486, 1491, 1530
Quintanilla, Paola 0016
Quiring, Giulia 0862
Quirk, Cody 2173
Quiroga Fernández, Carlota 2106
Qureshi, Asma 2430
Qureshi, Sumera 0980, 1678

R

R, Naveen 2676
Růžičková, Nora 0831
Rémy, Philippe 1604
Rönnblom, Lars 0034, 0593, 0594, 2390, 2647
Rózsa, János 0680
Rabah, Sami **0138**
Rabeony, Hanitriniaina 0105
Rabie, Mahiar **2560**
Rabinstein, Alejandro A. 0601
Rachid Zaim, Samir 0076
Racy, Menerva 0509
Radic, Mislav 1952
Radin, Massimo 0120, 0121, 0139
Radjiv, Goulabchand 0756
Radner, Helga 0510
Radominski, Sebastião Cezar 1365, 2246
Radonic, Teodora 1860
Radtke, Beth 0217
Radujkovic, Aleksandar 0678
Radziszewski, Marcin **0034**
Rae, Julie 0654
Rae, Meredith **1296**
Raffoux, Emmanuel 1339
RAFFRAY, Loic 2655
Raftopoulou, Sylvia 0515
Raftopoulou, Sylvia 2025
Raghu, Harini 0654, 0664
Rahimi, Homaira 0086, 1940
Rahman, Anisur 1722, 1851, 2416
Rahman, Fazlur 0157, 0158
Rahman, Proton **0112**, 0560, 0577, 1456, 1458, 1460, 2368
Rahman, Syed Minhaj 2041
Rahme, Elham 0376
Rahme, Ramy 1339
Rai, Abhishek 1364, 2261
Rai, Raman 2281
Rai, Sharan 0037, 0813, **1032**, 1130, 1990, 1995, 2008, **2590**
Raimondo, Maria Gabriella 0236, 0878, **1757**, 2613, 2641, 2695
Raisinghani, Ajit 0242, 1186
Raj, Prithvi 1524
Raja, FNU 0312
RAJA, JASMIN 0304
Rajab, Islam 0151, 1880, 1881, 1882, 2088
Rajagopal, Swetha 0712
Rajamanuri, Medha 0633, 2517
Rajamurugan, Arul 1609
Rajan, Mangala 1283
rajasekhar, Liza 0291, 0424, 1472, 1771, 1775, 2417
Rajasimhan, Suraj 1470
Rajdeo, Pankaj 0415
Rajeev, Parvathy 0456
Rajendran, Sindhuja **0140**
Rajkumar, Krithika 2152
Rajpal, Shreyaa 1890
Rakholiya, Jigisha 2040
Ralle, Ana Carolina 0596, 1491
Rama, Savier Aleman 0163
Ramachandran, Raghav 0566
Ramachandran, Reshma 1925
Ramachandran, Sabarinathan 1786, 1797
Ramakrishna, G S 0734, 1910
Ramakrishnan, Sivasubramanian 2153
Raman, Chander 0622
Ramanan, Athimalaipet 0420
Ramanathan, Ganesh **1285**, **1742**
ramani, Sivasubramanian 0047
Ramírez, Marta **2304**
Ramírez Garcia, Julio 0592
Ramchandren, Radhakrishanan 0260
Rameev, Vilen 0779
Ramello, Maria Cecilia 0008, 0987
Ramesh, Ananthakrishnan 1431
Ramineni, Tejaswini 0495, **0708**, **1588**
Ramires de Jesus, Guilherme 0120, 0121, 2395
Ramirez, Andrea 0402, 1226, 1296, 2148
Ramirez, Andrew 2198
Ramirez, Daniel 0316, 0463, 1782, 2285
Ramirez, Julio 1943, 2373
Ramirez Bonetti, Kimberly 0233, 1418, 1543, 2238, 2239, 2240, 2283, 2284
Ramirez Damera, Ramses 2490
Ramirez Garcia, Felipe Julio 0505, 0591
Ramirez-Alonso, Judith Michelle 1022
Ramirez-Becerra, Carolina 0775, **1329**
Ramirez-Cantu, David Alejandro 1633, 2549
Ramirez-Morales, Ricardo 2187
Ramirez-Solano, Marisol 1329
Ramirez-Uzcategui, Osmel Adrián 1022
Ramiro, Sofia 0539, 0540, 0557, 0569, **0588**, **0589**, 0854, **1324**, 1341, 1342, 1405, 1406, 1449, 1626, 1941, 1958,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2307, 2308, 2319, **2331**, **2332**, **2333**, **2334**, **2635**
Ramji, Sancharitha 0523, 1176
Ramkhelawon, Bhama 1759
Ramly, Edmond 0218
Ramming, Alina Mihaela 0878
Ramming, Andreas **0878**, 1455, 1757, 1864, 2613, 2695
Ramon, Andre 0891, **1150**
Ramonda, Roberta 0275, 0539, 1127, 1958, 2319, 2635
Ramos, Abraham Edgar Gracia 2066
Ramos, Paula **1079**, 1638, 1725
Ramos, Vanessa 2199
Ramos Calvo, Angel 0737
Ramos Castro, Daniel 0205, 0237, **0341**, 1274, 2274, 2310
Ramos Giraldez, Consuelo 0642, 0659, 1397, 2450
Ramos ibáñez, Eduardo 1210, 1953, 1954, 2471
Ramos Ortiz de Zarate, Laura 1170
Ramos-Manzano, Alejandra 0518
Ramos-Reza, Karen Yaresi **2557**
Rampakakis, Emmanouil 0577, 1460, 2345
Rampelbergh, Rian Van 0257
Rampersad, Rishi 1160
Ramsey, Laura 0392
Ramsey, Simeon 0059
Ramsey-Goldman, Rosalind 0218, 0624, 0657, 1722, 2416, 2430, 2441, 2455
Ran, Hao 0018, 1006
Rana, Gunjan **1044**, 1139
Randall, Jason 2409
Randazzo, davide 0918, 1624, 1725, 1843
Randell, Rachel 0367
Randhawa, Amarjyot **2170**
Rane, Pallavi 2051
Ranganath, Veena 0451
Rangarajan, Parthasarathy 1786, **1797**
Rangaswamy, Shivani **2049**
Rangel Peláez, Carlos 1862
Rangel-Garcia, Angel 1753
Rangel-Moreno, Javier 0904, 0942, 1753
Ranjan, Sandip 1376, 1377
Ranka, Rajat 1364
Ranken, Leslie **2559**
Rantalaiho, Vappu 2000
Rantapää-Dahlqvist, Solbritt 0593, 2390
Rantapaa-Dahlqvist, Solbritt 1749
Rao, Deepak 0881, 0885, 0887, 0988, 2414, 2600, 2644, 2688
Rao, Dilip 0657
Rao, Madduri Ravin 0991
Rao, Navin 0988
Rao, Sowmika 1473, **1969**
Rao, Vijayaraghava 0360
Rúa-Figueroa, Iñigo 0269, 0642, 0659, 0728, 1171, 1878, 1899, 2422, 2450, 2513
Raparia, Chirag **0940**, 1763, **1830**
Rapoza, Kimberly 1278
Rapp, Anna 1780
Rapp, Anna 1781
Rapp, Anna **1785**
Rapti, Anna 2025
Rasheed, Nidaa **1903**
Rashid, Rumana 0010
Rashighi, Mehdi 2668
Rashkov, Rasho 1462, 1463, 1464
Rashuamán-Conche, Benny **1717**, **2383**
Rasmussen, Astrid 0034, 0506, 0514, 1223, 1378, 1384, 1682
Rasner, Cody 0285
Rasool, Natasha 1539
Rasooly, Irit 2680
Rasouli, Sajede 1693
Raspaud, Christophe 0162
Rat, Anne-Christine **0314**, 0355, 2080
Rath, Deepak **2295**
Rathe, Tobias 2641
Rathee, Arpit 2147
Rathi, Sangeet 0447
Rathod, Malay **1071**
Ratnani, Tanya 1347
Rattenbach, Revital 1734
Ratzinger, Gudrun 1911
Rau, alexander 0990
Rauber, Simon 0878, 1757, 2695
Rauch, Joyce 1475
Rauen, Thomas 2520
Rauer, Thomas 0807
Rauld, Celine 2665
Raum, Kay 0342
Raupov, Rinat 0403
Ravaud, Philippe 1577, 1765
Ravelli, Angelo 0289, 0389, 0405, 2137, 2138, 2139
ravi Nayak, Subham 0533
Ravichandran, Kodi 0948
Ravindran, Aishwarya 1174
Ravindran, Sriram 1140, 1141
Rawlings, David 0981
Rawn, Saara 0721
Ray, Kathryn 2466
Ray, Wayne A. 0818
Rayaji, Rameshwari 0057
Rayancha, Sheetal 0657
Rayarakula, Nikhil 1890
Raychaudhuri, Siba **0586**, **0587**, **1120**, 1456, **2330**, 2355, 2375
Raychaudhuri, Smriti K 0586, 0587, 1120, 2330
Raychaudhuri, Soumya 0798, 1702, 1844, 1846, 2233, 2600
Rayle, Tami Jo 0473
Raymo, Maura 1020
Raymond, Mikaela 1563
Raza, Karim 1678
Razani, Bahram 0110
Razawy, Wida 0979
Razmjou, Amir **0240**, **2227**
Razok, Almurtada **0789**, 2412
Re, Federica 0566
Reagan, Patrick 2468
Reale, Stefanie 1157
Reategui-Sokolova, Cristina 1717, 2383
Reay, Daniel 0864
Rebella, Martin 0621, 0623, 1349, 1530
Rebello, Ryan 2703
Rebollo-Gimenez, Ana Isabel **0177**
Rebours, Vinciane 1163
Rech, Juergen 0762, 0878, 1175, 1757
Rech, Juergen 2279
Recipon, Sophie 0162
Rector, Amadeia **1009**, 2202
Reddy, Jyotsna 1963
Reddy, Naveen **0498**
Reddy, Pramod Kumar 0498
Reddy, Soumya 0527
Reddy, Swathi 1260
Redeker, Imke 0386, 1461
Redinger, Nancy 2649
Redmond, Desiree 0969, 0970
Rednic, Simona 0702
REDONDO, MARTA 1269
Reed, Ann 1745
Reed, Annelle 1276
Reed, George 0449, 1049
Reed, George 1340
Reed, George 1421
Reed, George 2681
Reed, Griffin **2571**
Reed, Jennifer 2302
Reed, Zoe **1087**, 1842
Reeder-Hayes, Katherine 0145
Rees, Jonathan 1909
Reese, Alexandra 1508
Reese, Tyler 0828, **2194**
Reeve, Bryce 1745
Rege, Sanika 0399, 0400
Regensburger, Martin 0809, 0974
REGENT, Alexis 0735, 0891, 1575, 1577, 2489, 2584
Regierer, Anne C. 1430
Reginato, Anthony M. 1615, 2177, 2183
Regmi, Anil 0492, 2343, 2514
rego Pérez, Ignacio 0329, 0454
Regola, Francesca 0238
Regola, Francesca 0251
Rehart, Stefan 0075, 0090
Rehaume, Linda **0868**
Reich, Andreas 1430
Reich, Kristian 0567, 0573, 1455, 2357
Reichelt, Josef J 1206
Reid, M. Carrington 0635, 2426
Reid, Pankti 0172, 1107, 1108, 1111, 1116, 1248, 1730
Reid, Reagan **1279**
Reid, Sarah 0593, 2390
Reider, Simon 1911
Reiff, Daniel 0399

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Reiff, Daniel 1277
Reihm, Jennifer 2645
Reijnierse, Monique 0539, 0540, 0854, 1405, 1406, 1941, 1958, 2319, 2635
Reilly, Erin 0871
Reimann, Regina 1206
Reimold, Andreas 0022, 0045, 0221, 0222, 0834, 1308, 1314, 1325, 1746, 1946, 2330, 2681, 2683
Reina, Delia 0269, 1171
Reina, Delia **1382**, 2299
Reis, Ana Paula 2246
Reisner, Colin 0259
Reitars, Megan 0886
Reitz, Nicole 0394, 0396
Reizis, Boris 1814
Relaño Fernández, Sara 0329
Remalante-Rayco, Patricia **0547**
Remesal, Agustin 0389, 1152
Remesal, Agustin 2042
Remmers, Elaine 1725
Ren, Dongjun 1780
Ren, Heather **0984**
Ren, Jiangtao 1532, 2452
Ren, Wenming 0915
Ren, Yuru 0261
Renaud, FELTEN 0516, 1095
Renaud, Ludivine 2495
Renner, Jordan 0330
Renshall, Lewis 2631
Renuncio-García, Monica 0150, 1599
Renzoni, Elisabetta A. 1589
Repa, Argyro 2232
Repplinger, Daniel 0679
Resche-Rigon, Matthieu 1144
Resende, Gustavo 1407, 1408, 2326
Reshef, Ran 0843
Reshef, Yakir **1702**
Restrepo, Deisy 1041
Restrepo Guarnizo, Maria Camila 2034
Retuerto, Miriam 0882
Retuerto Guerrero, Miriam 0639, 1548, **2670**
Retzel, Karli 1057, 1705
Reveille, John 0541, 0854, 1410, 2361
Revel, Marie-Pierre 0681
Revie, Lauren 0734
Revuz, sabine 1604
Rew, Joanna 0949, 1760
Rex, Ryan 0667
Reyes, Candice 1903
Reyes-Jara, Gisel 0877
Reyes-Yepiz1, Yessica Rubi 1022
Reyna Juárez, Yatzil 0287, 1836, 2052, 2053, **2078**, 2674
Reyna-Hernandez, Ericka S. 2058, 2071, 2072
Reynaud, Quitterie 0891
Reynolds, Chelsea **1059**
Reynolds, Gary 2509
Reynolds, Kerry L. 1099
Reynolds, Richard 2010
Reynolds, Richard 2585
Reynolds, Samuel 1174
Reynolds, Zahra 2577
Reynosa-Silva, Ileana C. **0614**, **1486**
Rezaei, Siavash 2260
Rha, Hyungmin 0473
Rhee, Rennie 0712, **0725**, 2515, 2533, 2701, 2703
Riancho, Leyre 0642, 0659, 2450
Riancho Zarrabeitia, Leyre 2422
Riancho-Zarrabeitia, Leyre 1397, 1681
Riaz, Ramsha **1081**
ribbens, Clio 1738
Ribeiro, Emmanuel 0891
Ribeiro, Francinne 0623, 1486, 1530
Ribeiro, Sandra 1407, 1408, 2326
Ribeiro, Talita 2292
Ribes, David 2510
Ribi, Camillo 1605, 2443
Ricci, Giulia 1380
Riccieri, Valeria 1570, 2482
Riccio, Flavia 1402
Rice, Alexandra L. 2687
Rice, Alexandra Lauren **0527**
Rice, Michael 0230
Rice, Siobhan **0016**
Rich, Phoebe 2374
Richard, Corentin 1150
Richard, Michael 0309, 2623, 2625
Richard, Nicolas 1109
Richards, John 0045, 0221, 0222, 0834, 1308, 1314, 1325, 1746, 1946, 2683
Richardson, Carrie 0883
Richardson, Carrie 1553, 1555
Richardson, Carrie 1563, 1566, 1582, **2475**, 2654
Richardson, Christopher 1852
Richardson, Jason 0204
Richeldi, Luca 1567
Riches, Philip 1990
Richez, Christophe 1095, 2457
Richi, Patricia 0201
Richi, Patricia 1961
Richins, Suzy 2301
Richle, Philipp **0015**
Richmond, Niamh 0991
Richter, Jutta 0166, 1198, 2612
Ricordi, Caterina **1598**, 1604, **1766**
Ricordi, Caterina 2699
Ricquebourg, Manon 1135
Rider, Lisa **0159**, 0289, 0302, 0427, 1967
RIDHA, ASAL ADNAN 1930
Ridley, David 2278
Riedlova, Patricia **0111**
Riega-Torres, Janett C. 0366, 0512, 1023, 1389, 1928
Rieger-Torres, Sofia 2203
Riegler, Jacob **1894**
Riek, Simone 2665
Riemekasten, Gabriela 0702, 1586
Riener, Romina 1003
Riera Alonso, Elena 0269, 1171, 1619
Riesgo Sanchis, Pablo 1129
Rietveld, Anke 1205
Rieux-Laucat, Fréderic 1339
Rifaai, Hazem Helmy Ali 0648
Rife, Eileen 1276, **1277**, **2124**
Rife, Eileen 2132
Rife, Eileen **2134**
Rigby, William 0349
Riggles, Kylie 0446
Rigolin, Vera 1553
Riley, Justin 1646
Riley, Thomas 0022, **0045**, **0046**, **0834**, 2068, 2683
Rimar, doron **0675**
Rimland, Casey 1668
Rincheval, Nathalie 1334
Rincon-Arevalo, Hector 2476
Rini, Christine 1228
Riordan, Mary Ellen 1226
Rios, Daniel 1437
Rios, Javier 1981
Rios Rodriguez, Valeria 0569
Rischmueller, Maureen 0034
Riskalla, Mona 1820, 2124
Rist, Pamela 2607
Ritchlin, Christopher 0060, 0187, 0563, 0564, 0567, 0590, 0873, 0874, 1455, 1753, 2233, 2357, 2368
Ritter, Ivana 1662
Ritz, Ethan 0292, 0789, 1216
Rius Rigau, Aleix 0026, 0956, 1856
Rivas Zavaleta, Mayra Nathali 1904
Rivera, Cristobal F. 1759
Rivera-Villafuerte, Regina Esdeyne 1687
Riveros frutos, Anne 0117, 0737, 0757
Riveros Frutos, Anne 0758
Riveros frutos, Anne 2029, 2450
Rivière, Sébastien 0688
Rizvi, Ali **1470**
Rizwan, Rubab **1245**, **2328**, 2329
Rizzo, Chiara 2075
Rizzo, Maria Teresa 1680
Rizzo, Stefania 1856
Roake, Kami **1981**
Roark, Christina 1701
Robben, Catherine 2462
Robbins, Eric 1625, **1949**
Robbins, John 0354
Robert, Caroline 1115
Robert, Gautier 0903
Roberts, David 0455
Roberts, Eric **0655**, 0817, **1042**, 1886, 2634
Roberts, Janet 1103
Roberts, Jordan E. 1064
Roberts, Karen 0596
Roberts, Karen 0623
Roberts, Karen 2422
Roberts, Mary 0321

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Robertson, Lindsay 1239
Robin, Eugénie 0566
ROBIN, François **2115**
Robin, Ludivine 0508, 1683
Robinson, Angela 0829
Robinson, Ciji 1518
Robinson, David 1315
Robinson, George 0820, 1817
Robinson, Lauren **1291**
Robinson, Londyn 0158, **1068**
Robinson, William 0316, 1119
Robinson, William H. 0816, 0914, 1693
Robles, Dagoberto **2085**, 2091
Robles Sanchez, Isabell 1276
Robles-Navarro, Janeth 0186
Roblyer, Darren 0848
Robson, Joanna 1912
Robustillo-Villarino, Montserrat 0496, 2268, **2591**
Rocamora-Gisbert, Cristina **0117**, 0758, 2029
Rocco, Lorenzo 0700, 1840
Rocha Pereira, Leticia 1365
ROCHE, Nicolas 2262
Rochlin, Kate 1535
Rockette-Wagner, Bonny 0305
Rockwell, Nicholas 2181
Roddie, Claire 2458
Rodgers, Kyla **0131**
Rodgers, Wendy 2547, **2565**
Rodman, Jack 2199
rodolfi, stefano 2496, **2503**
Rodon, Lea 0932, 1876
Rodosthenous, Theodoulos 2696
Rodríguez, Nicolás Santiago 2034
Rodríguez Fernández, José Andrés 2112, 2113
Rodríguez gago, José 0180, **0346**
Rodríguez López, Marina 0019, 2290
Rodríguez Laguna, Maria 0270
Rodríguez Lopez, Marina 2016
Rodríguez Martín, Inmaculada 1862
Rodríguez Montero, Sergio 0270
Rodríguez Montero, Sergio 0271
rodríguez Sibaja, Maria José 2218, 2632
Rodríguez Valle, Isabel 0329
Rodríguez Vargas, Ana Isabel 1164
RodrÍguez-Alvear, Cristina 1096, 1129, **1996**
Rodríguez-Bellido, Zoila 0714, 0730, 2378, 2521
Rodríguez-Gago, Jose 1152
Rodríguez-Solís, Jesus Ballano 1210
Rodríguez-Vidriales, maria 0150, 1599
Rodrigues, Débora 1407, 1408, 2326
Rodriguez, Adrian 0523
Rodriguez, Ernesto 1959
Rodriguez, Fabian 0266
Rodriguez, Jesús 0575
Rodriguez, Jose 0464, 2385
Rodriguez, Mara 2154
Rodriguez, Maria 0269, 1171
Rodriguez, Maria Beatriz 1397, 1681
Rodriguez, Martha **1295**
Rodriguez, Martha 2423
Rodriguez, Miguel 0435, 2438, 2439
Rodriguez Almaraz, Esther 0860
Rodriguez Laguna, Maria 0271
Rodriguez Quinonez, Fabian 1075, 1522, 2093
Rodriguez-Almaraz, Esther 0120, 0121
Rodriguez-Bellido, Zoila 0605, 1717, 2383
Rodriguez-Garcia, Sebastian 2671
Rodriguez-Nieto, Mª Jesus 1024, 1869, 2030
Rodriguez-Pinto, Ignasi 2648
Rodriguez-Reyna, Tatiana 0684, 2651
Rodriguez-Smith, Jackeline 0418, 0419
Roe, Nathan 1994
Roehrich, Manuel 0678
Roemer, Anna 0826
Rogani, Greta **0358**, **2137**, **2138**, **2139**
Rogers, Jennifer 0363, 0367, 0793, **1487**, 2379
Rogers, Kelly 0418, 0419, 1813, 1829
Rogers, Nathan 0819, 1824
Rohan, Patricia 2451
Roig Kim, Montserrat **0353**, 0749, 1161, 1162, 2106, 2250, 2299, 2484, 2491
Roig-Vilaseca, Daniel 1382
Roitg, Isabelle 2115
Rojas, Cynthia 0426
Rojas, Cynthia 0496, 2268
Rojas, Cynthia Vanesa del Valle 1943
Rojas, Jorge 0221, 0222
Rojas, José 1194
Rojas Abarca, Daniela **0507**
Rojas Herrera, Sara Maria 0019, 2016, 2229, 2290
Rojas-Serrano, Jorge 1390
Rojas-Villarraga, Adriana 0252, 2034
Rojo Grajales, Laura **2490**
Rokoff, Lisa 0321
Roland, CHAPURLAT 2621
Roldan Ortega, Jessica 1947, **2243**
Rolle, Noelle A. 0825
Rollins, Tressie L. 2301
Romão, Vasco 0035
Romagnoli, Katrina 2150
Roman, Ashley 0853, 1391
Roman, Iulia 0152
Romankevych, Ivanna **2242**
Romano, Micol 1823
Romanova Michailidi, Maria 0484, 1356, 2267
Romei, Chiara 1951
Romeo, Tina 1169
Romero, Ana 0751, 0895, 2273
Romero, Gricel Maita 0621
Romero, Maria liz 0201
Romero Barco, Carmen Maria 0087
Romero Noboa, Maria **0372**, **2412**
Romero Zurita, Laura 0108, 0901
Romero-Bogado, Maria Liz 1961
Romero-Bueno, fredeswinda 1024, 1869, **2030**
Romero-Diaz, Juanita 1722, 2416
Romero-Gómez, Montserrat 0583, 2371
Romero-Yuste, Susana 0488, **0728**, 0737, 0739
Romich, Ellen 0046, **1566**, 2068, 2305, **2654**
Romitti, Paul 1015
Romo-Tena, Jorge **0945**, 2580
Romulo, jobelle 1972
Ronda, Nicoletta 1330, 1331
RONDLA, MADHUMITHA **0160**
Rondla, Madhumitha 1147
Ronsin, Charles 0618
Ronsin, Charles 1604
Rood, Julia **0923**
Rood, Julia 1847
Roos-Weil, Damien 1339
Roppelt, Heidi 0356
Roque, Helena 1445
roriz, Mélanie 2655
Ros Vilamajo, Inmaculada 2373, 2450
Rosado, Acela Cristina 0984
Rosado-Bloise, César 1493
Rosales, Amber 0661
Rosales-Rosado, Zulema 0183
Rosas Chavez, Giovanna 1942, 1970
Rosas Gómez de Salazar, Jose 0019, 1397, 1548, 1681, 2290, 2422, 2450
Rosati, Alessandra 1863
Rosato, Edoardo 0702
Rose, Carlos 0399, 0400
Rose, Mark 2035
Roseen, Eric 0354
Rosek, Alyssa 0822
Rosek, Alyssa 0955, 0971, 1871
Rosek, Alyssa 2478
Roseman, Carmen 0434, 0814
Rosemffet, Marcos 1710, 1959
Rosen, Brandon 0057
Rosen, David 2086
Rosen, Joseph 1900, 2542
rosen, melissa 0279, 2051
Rosenbach, Misha 2668
Rosenbaum, Emily 0782, 0918
Rosenbaum, James 0893
Rosenberg, Abby R. 1298
Rosenberg, Avi 0772
Rosenberg, Dana 2372
Rosenbluth, Michael **1237**
Rosenkranz, Margalit 0401
Rosenstingl, Sophie 2532
Rosenthal, Allison 0501
Rosenthal, Ann 0218, 1136
Rosenwasser, Natalie 0411, 0422, 1066, 2125, 2128
Rosenzwajg, Michelle 0887
Rosenzweig, Michael 1003

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Rose-Smith, Jillian 1689, 2429
Ross, Brittany 1003
Ross, Carolyn 0731
Ross, Charles 1563
Ross, Jason 2430
Ross, Laura **0677**, **1716**
Ross, Laura 2487
Ross, Laura **2651**
Ross, Rebecca 0847, 1571, 1873
Ross, Sarah 2355, 2375
Rossenwasser, Natalie 1669
Rosser, Elizabeth 1817
Rossi, Carmine 1165, 2369
Rossi Bonfiglioli, Karina 1365
Rossignol, Julien 1339
Rossini, Maurizio 2116, 2592
Rotar, Ziga 0543, 1430
Rotem, Rany 1802, 1803
Roth, Michael 1564
Rothe, Tobias 0236, 1697, 2442
Rothenberg, Steven 2566
Rothermel, Ulrike 1206
Rothman, Nyanza 0898
Rothstein, Jay 0494
Rotimi, Charles 1725
Rouane, Clara 2510
Roufosse, Florence 0238
Roul, Punyasha 0022, 0045, 0155, 0462, 0836, 1238, 1314, 1325, 1658, 1659, 1946, 2567, 2661, 2681
Round, Patrick 0493
Rourke, Caroline 1944
Roussin, Céline 1185, 2655
Rouster-Stevens, Kelly 1976, 2154, 2678
Roux, Christian 0148
Roux, Christian 0314, 2080
Roux, Sophie 1126
Rovati, Lucio 1737
Rovin, Brad **0650**, 0654, 0664, 0665, 0719, 0772, **0838**, 0840, 0851, 1240, 1480, 1505, **1521**, 1846, 2233, 2399, 2421, 2467, 2600, 2694
Rovsing, Helene 2082
Rowland, Katelyn 0523, 1176
Roy, Guylaine 2281
Roy, Priyamvada 2666
Roy, Sanjeev 0802
Rua, Catarina 0761
Ruan, Gordon 1174
Ruíz Quintero, Narlly 0507
Rubarth, Kerstin 2109, 2110
Rubbert-Roth, Andrea 0662, 0776
Rubens, Jessica H. 0555
Rubenstein, Andrew 0853, 1391
Rubera, Isabelle 1135
Rubia, Ahmed **2166**
Rubin, Bernard **2384**, 2649
Rubin, David T. 0257
Rubinstein, Tamar 1218, 1278, 1479, 2066, 2067
Rubio, Andrea 1041
Rubio, Aranzazu 2344
Rubio, Jose 0652
Rubio-Muñoz, Paula 2422
Ruchi, FNU **0657**
Ruderman, Eric M 1362
Rudin, Anna 0593, 0814, 2390
Rudrapatna, Vivek 1657
Rudski, Lawrence 2222
Rudwaleit, Martin 1449, 1451, 1465, 2352
Rueda Cid, Amalia 2406, 2407, 2460
Ruet, Alexis 0355
Ruggles, Kelly 0853, 1240, 1846, 1861, 2421
Ruhmel, Stephen 1327
Rui, Shumin 1533, 1534, 2453
Ruibal Escribano, Ana 0485, 2350
Ruivard, Marc 0891
Ruiz, Juan 1429
Ruiz, Tania 0709, 2413
Ruiz de Morales, Jose María 0982
Ruiz Lucea, Maria Esther 2422
RUIZ MONTESINOS, DOLORES 0087
Ruiz Pavón, Cristina 2106
Ruiz Ponce, Miriam 0108
Ruiz-Esquide, Virginia 0379, 0380, 0496, **0505**, 1943, 2229, 2268
Ruiz-García, Carolina 1133
Ruiz-Irastorza, Guillermo 1722, 2416
Ruiz-Ortega, Jenelys 0316
Ruiz-Roman, Alberto 0250
Ruiz-Romero, Cristina 0329, 0454, 1798
Ruiz-Valdepeñas Almansa, Marta **1024**
Ruiz-Vilchez, Desiree 0070, 0071
Ruiz-Vilchez, Desiree 0087
Ruiz-Vilchez, Desiree 0094, 0108, 1851
Rumker, Laurie 1702
Rumsey, Dax 0428
Run, Changqing 0998
Ruperto, Nicolino 0177, 0289, **0389**
Ruperto, Nicolino 0401
Ruperto, Nicolino 0405, 2137, 2138, 2139
Rupnik, Maddalena 0191
Rushing, Elisabeth 1206
Rusi, Enn 0711
Rusinovich, Olga 1170
Rusinovich, Olga **1397**, **1681**
rusnak, Lauren 1016, 1957, 2569
Russell, Dayvia 0944
Russell, Gregory 2559
Russell, Mark 1906
Russo, Paul 1598
Russu, Eugeniu 0551, **1414**
Ruta, Santiago 0584, 2257
Rutanen, Jarno 1430
Ruth, Natasha 0393, 1059
Rutstein, Beth 0374
Rutter-Locher, Zoe 1178
Ruyer Thompson, Mirabelle 1339
Ruyssen-Witrand, adeline 0147
Ruyssen-Witrand, Adeline 0591, 0592
Ruzicka, Stephanie 1789
Ryø, Laura 0929
Rydell, Emil 1884, 1885
Rygg, Marite 0420
Ryu, Borim 2007

S

S, Deepak 2593, 2594
S, Nishanth 1423
S, Seethalakshmi 0495
S. Fazli, Mojtaba **0092**
S. Jalaledin, Darya 1193, **1199**, 2259
Sáez, Juan Carlos 2491
Sáez Comet, Luis 1210
Sáez Comet, Luis 1953
Sáez Comet, Luis 2471
Sánchez, Ana 1322
Sánchez, Marta 0483
Sánchez Bilbao, Lara 0019, 0268, 0272, 0639, 2290, 2538
Sánchez Domínguez, Nicolás 0601
Sánchez Fernández, María Concepción 1170
Sánchez Martín, Julio 0739, 0744, 0752, 0757
Sánchez Vidal, Hilda 1841
Sánchez Zamudio, Fabiola 0507
Sánchez-Alonso, Fernando 0153, 0744, 1397, 1446, 1681, 2269
Sánchez-Briones, Reyna Elizabeth 1491
Sánchez-Lucas, Marina 1613
Sánchez-Lucas, Marina 2249
Sánchez-Ortiga, Ruth 1133
Sène, Damien 0508, 0516, 0735, 2168
Sénot, Noémie 1724
Sözer Tokdemir, Selçuk 1698, 1818
Sütő, Gábor 2684
Saad, Carla **1407**, **1408**, **1715**, 2326
Saad, Carla 2527
Saad, Carla 2682
Saad, Nadine 2129
saadoun, david 0123
Saadoun, David 0735, 0756
SAADOUN, David 1095
Saag, Kenneth 0157, 0158, 0368, 1073, 1991, 2006, 2117, 2548
Saake, Marc 1537
Saam, Joachim 1934
Saarakala, Simo 0327
Saavedra, Alene 1751, 1902, 2235, 2574, 2577, 2578
SAAVEDRA, MIGUEL 0621, 0623, 1486, 1530
Saba, Kamal **0965**
Sabah, Ibrahim 1881
Sabb, Kaitlyn 0115
Sabb, Kaitlyn 0131
Sabharwal, Anchal **2017**
Sabina, Michael 0319
Sabins, Nina 0558
Sabit, Taskin 1819, 1820, 2242
Sachan, Nalani **0626**, 0853, 1391

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sachdeva, Karan 2392
Sachdeva, Muskaan 0565
Sachdeva, Saahil **1967**
Sachetto, Zoraida 1400
Sachetto, Zoraida 2536
Sackey, Jeffrey 0456
Sacks, Callie 1708
Sacksith, Kyra 1733
Sacré, Karim 0735, 1575, 2489
Sada Urmeneta, Guillén 1904
Sada Urmeneta, Guillen 1547
Sadelain, Michel 2693
Sadowski, Katy 1924
Sadun, Rebecca 0363, 0367, 0793, **1300**, 1487, 1745, 2142, 2169, 2379
Saeed, Abdullah 0733
SAEED, IMRAN 1539
Saeedi, Elnaz 0572, 2340
Saegusa, Jun 0062
Saez, Cristina 0126
Saez, Juan C 2122
Safarini, Omar 2566
Safdar, Komel 2430
Safford, Monika 0317, 1264, 1283
Saffore, Christopher 0578, 0640, 0662, 1435, 1453, 1551, 2342, 2367, 2445
Safran, Sarah 1725
Sagcal-Gironella, A. Carmela 2462
Sagendorf, Tyler 0320
Sagun, Jeffrey **2062**
Saha, Banishree 1442, 2351
Saha, Sreoshy 2065
Sahagún, Ana María 0982
Sahay, Rashmi 1706
Sahhar, Joanne 0677, 2651
Sahin, Emre **0120**, **0121**
Sahin, Ezgi **0290**
Sahin, Sezgin 1698, 1818, 1823
Sahmoun, Abe 1025
Sahu, Mousumi 1725
Sahussarungsi, Sariya 2222
Sai, Nikhil 0527
Said-Nahal, roula 0103, 0104
Sailler, Laurent 0123, 0756, 1200, 2457, 2510, 2704
Saini, Suryansh 0447
Saint-Pastou, Cécile 2457
Sainz Comas, Luis 0496, 1620, 2268
Saito, Kenji 1509
Saito, Shuntaro Saito 2253, 2254
Saito, Takumi 0521
Sakagami, Kayoko 2564
Sakalyte, Regina 1309
Sakamoto, Ana 1287, 1288
Sakamoto, Jiro 2253, 2254
Sakamoto, Takahito 1509
Sakamoto, Takuya **1805**
Sakaue, Saori 2600
Sakellariou, Garifallia 1680
Sakellariou, Grigorios 2359
Saketkoo, Lesley Ann 0702, 1725
sakhamuri, pavana **1080**
Sakhamuri, Pavana 2370
Sakir, Ozan 1188
Sakiyama, Kodai 1854
Sakkas, Lazaros 2232, **2280**
Saklecha, Anokhi **0437**, 1090, 1985
Saksena, Daksh 0840
Sakthivel, Shreya **1369**
Sakthivel, Yogananth 1588
Sakurai, Keiichi 0668
Sala, Luis 0639, 1548, 2450
salabert-Carreras, Francina 0117, 0758, **2029**
Salama, Engie 0010
Salama, Hind 1174
Salama, John 1880, 1881
Salama, Ryan **0460**
Salas, Ana 1879
Salas, Lucas 2581
Salas Santamaría, Sara **1322**
Salcedo Almanza, Diego Azamat 0458, 0614, 1427, 1528
Salcedo-Soto, Daniela Alejandra 1022
Saldana Miranda, Diego 2296
Saleem, Hira 0312
Saleem, Muhammad Asjad 2095, 2099
Salegi Etxebeste, Iñaki 1904
Saleh, Navid 1193, 1199
Saleh, Zeinab **0232**
Salem, Joe-Elie 0887
SALER, TAYYIBE 1440
Salerno, Martina 1570
salgado-Pérez, Eva 2422
Salhi, Anouar 0715
Salia, Soziema 1513, **1707**
Saliba, Fares 0633, 2517
Salido Olivares, Marina 0351
Salinas-Carmona, Mario Cesar 0212, 0213, 1834, 1845, 2219
Salinas-Rodriguez, Samantha Lynn 2171
Salis, Sheryl 2056
Sallés Lizarzáburu, Meritxell 0379, 0380
Salles Lizarzaburu, Meritxell 0269, 0426, 1171, 2373
Salliot, Carine 0477, 0516
SALMAN MONTE, CARLOS TAREK 2422
Salman Montes, Tarek 0642, 0659, 0757, 2450
Salmon, Jane 0365, **0855**, 2629, 2630
Salomao, Diva 0893
Salomon, Karen 1073
Salpetier, Pauline 1738
Saltman, Alexandra 1103
Saltzman, Hanna 1275
Salvador Alarcón, Georgina 0379, 0380, 1619
Salvador Maicas, Laura 2406, 2407, 2460
Salvant, Cynthia 0399
Salvarani, Carlo 1598, 1626
Salvio Lemos, Andreza 0616
Salvo, Fulvio 0648
Salzillo, Alessia 1835, 1864
Salzman, Hanna M. 2301
Sama, Srikar 0633, 2517
Samaranayaka, Muditha 0692, 2493
Sami, Faria **1417**, **2312**, 2412
Sami, Shahzad Ahmed 2412
Sammaritano, Lisa 0365, 0382, 0634, 2226, 2575, 2629
Sampaio-Barros, Percival 1407, 1408, 1715, 2045, 2326
Sampaio-Barros, Percival D 2653
Sampatakaki, Eleni 1439, 1452
Samson, Kaeli 1898
Samson, Maxime 0756, **0891**, 1150, 1575, 1592, 2489, 2584, 2704
Samsonov, Mikhail 0403, 0476, 0779
Samsonov, Mikhail 1323
Samuel, Joyce 2361
Samuel, Prasanna 1609
Samuels, Jonathan 0330, 1960, 2089, 2177, 2183
San Emeterio-Villar, Diego 1778
SAN JOSE MENDEZ, CARMEN 0107, 2294
San Segundo, David 1094
Sanabria-Hernández, Marile 2591
SANAN, AHMAD 0235
San-Antonio, Esther 0518
Sanchez, Daisy 2336
Sanchez, Einer 2336
Sanchez, Judith 0426, 1282, 1284
Sanchez, Vincenta 1825
Sanchez Alvarez, Catalina 1626
Sanchez Baez, Roel 2317
Sanchez Herrero, Alejandro 2670
Sanchez Pernaute, Olga 1024, **1869**, 2030
Sanchez-Abad, Ines 0518
Sanchez-Dal Cin, Julian 0887
Sanchez-De la Cruz, Ryan Jared 0767
Sanchez-Fournier, Blanca 2620
Sanchez-Guerrero, Francisco 1505, 2416
Sanchez-Guerrero, Jorge 1722
Sanchez-Lopez, Amparo 0150, 1599
Sanchez-Muñoz, Fausto 2243
Sanchez-Pareja, Ismael 0070, 0071, 0072, 0087, 0094, 0139, **0795**, 1851, 2599
Sanchez-Peralta, Egla Samantha **0767**, 1022, **1527**, **2553**, **2606**
Sanchez-Rodriguez, Alain 0601, 1721, 2403
Sanchez-Wonenburger, Maria 2354
Sanchis, Antonio 0201
Sandal Uzun, Güllü 0760
Sande, Nina Martine 0420
Sander, Oliver **0166**, **2612**
Sanders, Colton 0976
Sandhu, Vaneet 0663, 1270, 2454
Sandler, Dale 1690
Sandorfi, Nora 0231
Sandorfi, Nora 0339
Sandorfi, Nora 0520, 0883
Sandorfi, Nora 1376, 1555

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sandorfi, Nora 1566, 1582
Sandorfi, Nora 2475
Sandorfi, Nora 2654
Sandoval Moreno, Sebastián 2450
Sandoval-Moreno, Sebastián 0639, 1548
Sands, Bruce E. 0257
Saner, Leigh 1487
Sangar, Rahul 2276
Sangaraju, Koushik Varma 0633, 2517
SANGES, SEBASTIEN 0673, 1581
Sanghavi, Nirali **0598**
Sang-Park, Hye 0505, 1773
sangwan, ritu 1364, 2261
Sanmarco, Liliana 0008
Sanmartí, Raimon 0379, 0380, 0505, 1018, 1943
Sanmartin Martínez, Mireia 0244, 2406, 2407, 2460
Sanner, Helga 0420, 0427, 2679
Sansevere, Emily 0494
Santa Maria, Andre 1374
Santacroce, Leah **0156**, 0283, 1019, 1057, **1267**, 1644, 1705, **1709**, 1894, 2607, 2644
Santamaría-Peñaloza, Grace-Jimena 1210
Santamaria, Pere 0021
santana, karina 1836, 1841, 2078
Santana-De Anda, Karina 0287
Santaniello, Alessandro 0700, 1840
Santiago, Mittermayer 0650
Santiago, Tânia 1210
Santiago-Pichardo, Gabriela 1236
Santilli, Alice 0308
Santin-Janin, Hugues 1998, 2588
Santoro, Nanette 2628
Santos, Helena 1430
Santos, Maria Carolina 2535
Santos, Maria Jose 1287, 1288
Santos Da Costa, Aida 2296
Santosa, Amelia 0378
Santos-Gomez, Montserrat 1094
Sanyal, Anwesha 0823, 2478
Sanyal, Sanchit 0772, 1240, 2421
Sanz, Ignacio 1696
Sanz, María 2042
SANZ SANZ, JESUS 1170
Sapena, nuria 1943
Sapkota, Nisha 0433
Sapkota, Nisha **0456**, **1253**, **1931**
Sapsford, Mark 0595
Sarabia, Luis 1548, 2373
SARAUX, Alain 0314, 0477, 0516, 1683, **2080**, 2241, 2296, 2300
Sarbu, Adela cristina 1562
Sarfraz, Shiza **1907**, **2596**
Sari, İsmail 2673
Sari, Busra 1396
Saric, Callie 0670
Sarin, Kavita 2062
Saris, Christiaan GJ 1205
Sarka, George 1378, 1384
sarkar, indranil 1588
Sarkar, Manali **0295**, 1218, 2065, 2066, 2067, 2185
Sarker, Chandni 1300
Sarker, Debashis 1115
Sarkisyan, Tamara 0779
Sarmiento-Monroy, Juan Camilo 0153, 0505, 1018, 1943, 2016
Sarosh, Cyrus 0115, 0127, 0131, 0134, 0143, 0858, 0859
Sarrot-Reynauld, Françoise 2457
Sartori, Artur 0619
Sasabuchi, Yusuke 2449
Sasai, Tsuneo **0773**, 1857
Sasaki, Takanori 0881
Sasaki, Takanori 2414
Sathappa, Murugappan 0913, 0930
Sathilaseenlan, Thiloginy 1753
Sathiyamurthi, Akash 0063
Sathiyaseelan, Sri Lakshmi **1085**
Satis, Hasan 1008
Sato, Atsuyasu 1857
Sato, Kojiro 0764
Sato, Shuzo **1509**
SATO, YOSHIHARU 1345, 2664
Satou, Gary 0853, 1391
Satpanich, Panchalee 2004
Satpathy, Ansuman 1699
Sattler, María Emilia 1491
Sattui, Sebastian E 0720, **0726**, 0746, 0753, 1072, **1084**, 1629, **2539**, 2615
Saturansky, Etel 1422
Sauder, Max 0523
Sauer, Brian 0045, 0221, 0222, 0834, 1658, 1659, 2567, 2661, 2683
Sauer, Gesa 1580, 2472
Sauer, Karsten 2293
Saurit, Veronica 0596, 0621, 0623, 1486, 1491, 1530
Sauvageau, Chantal 0606, 1475
Savage, Adam 0889, 1695
Savage-Guin, Serena 0330
Savale, Laurent 1185
Savard, Josee 0376
Savevski, Victor 0532
Savic, Sinisa 0260, 0777, 2663
Savoie, Marissa **1582**
Sawada, Tetsuji 2541
Sawalha, Amr 0025, 0036, 1698, 1818, 1823, 1871
Sawhney, Sujata 1287, 1288
Sawicka, Katherine 2136
Saxena, Amit 0650
Saxena, Amit 0652
Saxena, Amit 0662, 0665, 0853, 1391, 1529
Saxena, Amit 1918, 1919, 2404, 2444
Saxena, Amit 2630, **2694**
Saxena, Ashish 1351
Saxena Beem, Shruti 2437
Sayadi, Ahmne 0593, 2390
Sayce, Lea 2064
Sayegh, Jonathan 2228, 2286
Saygin, Didem **0288**, **0289**, 0292, 0298, 0720, 0789, 0864
Saygin, Didem 1072
Saygin, Didem 1196
Saygin, Didem 1204
Saygin, Didem 1216
Saygin, Didem 2065
Saygin, Didem 2554
Sayles, Harlan 0076, 0155, 2001, 2002
Sbarigia, Urbano 0596, 1530
Scala, Silvia 0389
Scanzello, Carla 0328, 1736
Scanzello, Carla 1780, 1781
Scanzello, Carla 1783
Scanzello, Carla 1785
Scanzello, Carla 1791
Scanzello, Carla 2084, 2096
Scanzello, Carla 2098
Scanzello, Carla 2624
Schäfer, Valentin S. 0892
Schaeverbeke, Thierry 2115
Schanberg, Laura 0404, 0820, 0824, 1745
Scharl, Michael 1867
Schauf, Marion 2111
Schaughency, Paul 1470, 2580, 2700
Scheifele, Fabian 0015
Schejbal, Jan 0048
Scher, Jose 0031, 0054, 0527, 0590, 0871, 1007, 1329, 1338, 1712, 2233, 2327, 2643, 2690
Scher, Jose U. 0563, 0564
Scher, Uma 1241, 2327, 2687
Scherlinger, Marc **1578**
Scherlinger, Marc 2696
Schermerhorn, Megan 2167
Schett, Georg 0236, 0471, 0567, 0628, **0641**, 0678, 0762, 0843, 0878, 0956, 0975, 1198, **1529**, 1537, 1697, 1757, 1856, 1875, 2279, 2357, 2442, 2461, 2613, 2641, 2686, 2695
Scheuerman, Oded 1304
Scheuermann, Richard 0289
Schiaffino Garcia-Villanova, Maria Teresa 2249
Schiffenbauer, Adam 0159, 0289, 1967
Schindler, Thomas 0650, 0665, 1521
Schiopu, Elena 1674
Schiopu, Elena 1725
Schleif, Christine 0467, 0851, 2433, 2434
schleinitz, nicolas 0239, 0279, 1163, 1185, 1666, 2019, 2020
Schlesinger, Naomi **1026**, 1259, 2588
Schlicker, Nadine 0826
Schliep, Stefan 1537
Schloesser, Daniela 2486
Schluentz, Megan 1508
Schlumberger, Wolfgang 0293
Schmajuk, gabriela 0181, 0189, 0211, **0219**, **0220**, 0359, 0655, 0817, 1042,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1048, 1250, 1266, 1657, 1886, 2571, **2617**, 2618, 2619, 2634, 2685
Schmalzing, Marc 0762, **1450**, 1729
Schmid, Cindy 0903
Schmidkonz, Christian 2613
Schmidmaier, Ralf 0342
Schmidt, Alexandra 2237, 2251, 2252
Schmidt, Jean 1575, 2489
Schmidt, Jens 0289
Schmidt, Jens **1205**, **1206**
Schmidt, Kara Murphy 0418
Schmidt, Wolfgang 0754, 0762, **0776**, 1175, 1626
Schmieder, Astrid 1450
Schmitt, Tobias 2520
Schmitz, Jochen **2486**
Schmukler, Juan 0197, **0225**, 1375, 2054, 2104
Schmutz, Patrick 2665
Schneider, Frank 2593, **2594**
Schneider, Jingjing 0277
Schneider, Marc 1876
Schneider, Matthias 0644, 2441
Schneider, Pascal 1683
Schneider, Rayfel 2127
Schneider, Udo 0471
Schnitzer, Thomas 2082
Schocken, Daniella **1226**
Schoemaker, Minouk 0734
Schoenau, Verena **0762**, 2279
Schoenfeld, Sara 1057
Schoenfeld, Sara 1705
Scholz, Beth **2173**, 2186
Scholz, Veronika 0471
Schonenberg-Meinema, Dieneke 1287, 1288
Schott, Eric 0060
Schott, Kevin 0399
Schouffoer, Anne 1569
Schröder, Rolf 0026
Schreiber, Karen 2400
Schreibing, Teresa 2520
Schreiner, Aimee 1946
Schrezenmeier, Eva Vanessa 0471
Schroeder, Jan 0238
Schroeder, Jan Walter 1605
Schroeder, Lisa 0825, 1081
Schubert, David 0903
Schulert, Grant 0392, 0406, 0414, 0418, 0419, 0824, 0918, 1811, 1813, 1819, **1820**, **1821**, 1829, 2124, 2129, 2134, 2137, 2138, 2139, 2140, 2242, 2675
Schulz, Nils 0090
Schulze-Koops, Hendrik 0873, 1175, 1729, 2476
Schumacher, Rebecca 2305
Schumbrink, Fabian 2520
Schuster, Louis 0641, 2686
Schvartz, Adrien 0796, 1724
Schwab, Pascale 0221
Schwab, Pascale 0222
Schwab, Pascale 1314, 1325
Schwarting, Andreas 0803
Schwartz, Ari 2039
Schwartz, Daniella 0864, 1056, 2037, 2155, 2666
Schwartz, Noa 0851, 1479
Schwartz, Todd 0330
Schwartz, Todd 1271
Schwartz, Todd 1960, 2092
Schwartzbein, Samuel 1165, 2369
Schwartzberg, Pamela 1725
Schwartzman, Monica 1184
Schwartzman, Sergio **1184**, 2347
Schwartzman-Morris, Julie 2182
Schwarz, Edward 1808, 1940
Schwarz, John 0660
Schwarzer, Guido 1908
Schwede, Matthew 0843
Schwenk, Jochen M. 0111
schwertschlag, ullrich **2011**, **2012**
Sciascia, Savino 0139
Sciore, Paul 2414, 2419
Scofield, R Hal 0034, 0506, 1378, 1379, 1384, 2432
Scofield, R. **0509**
Scolnik, Marina 0596, 0623, 1486, 1530
Scott, Christiaan 2137, 2138, 2139
Scozzafava, Giuseppe 0104
Scuccimarri, Rosie 0401
Sculco, Peter 0316, 0785, 0786
Seagrist, John F 1362, 2430
Sean Lee, Chih-Yung 2696
Searcy, Zowie 1723
Sebastián Mora-Gil, María 0029, 1778
Sebbag, Aaron 1827
Sebbag, Eden 1578
Sebert, Marie 1339
Secada-Gómez, Carmen 0639, **0739**, **0740**, 1547, 1548, **2023**, 2059
Secq, Maxime 1858
Sedic, Maja 0941
Sediqi, Sadaf 1009, 2201, 2202, 2214
Seeto, Reginald 1367
Segal, Neil 2086
Segev, Shlomo 1332
Seguí-Azpilcueta, Pedro 0072, 0087, 1851, 2599
Sehgal, Himanshi 0665
Seidler, Lauren 1917
Seif Amir Hosseini, Ali 1205
Seifert, Jennifer 0033, 0187, 0501, 0775, 1223, 1233
seijas, alvaro 1548
Seika, Philippa 2652
Sekhon, Shaan **1000**
sellam, Jérémie 0314
Selles-Rius, Ares 0019, 2290
Sellyn, Georgina 1888
Selmi, Carlo 0532, 0879, 2345
Selva-O´callaghan, Albert 0296
Selva-O'Callaghan, Albert 0863
Selzer, Faith 0787
Semalulu, Teresa 1550
Semanik, Pamela 2455
Semanik, Pamela 2603
Semb, Anne Grete 0133
Semeraro, Paolo 1212
Sen, Deepali 1035, 2047
Sen, Medhasweta 2039
Sen, Mitali **1174**
Sen, Rouhin 1417, 2009, 2312
Senabre, José Miguel **1446**
Sendagorta, Elena 1152, 2042
Sendagorta Cudos, Elena 2670
Sendo, Sho **0062**
Seng, Amara **0067**
Seng, Amara 0085
Seng, Amara 2258
Seng, Magdalena 1403
Sengeløv, Morten 1166, 2608
Sengupta, Biswarup 1588
Sengupta, Raj 2335, **2636**
Sengupta, Sadhak 1535
Seni, Jeremiah 2419
Senn, Joseph 1437
Sennett, Mackenzie 0984
Senowitz, Phoebe 0207
Sensmeyer, Anna SM 1206
sentilhes, loic 2655
Seo, Philip 0721, 0747, 1595, 1596, 1602, 2515
Seppälä, Ulla 1374
Sepriano, Alexandre 0588, 0854, 2307
Sequí-Sabater, José Miguel 0019
Sequí-Sabater, José Miguel **2354**
Sereda, Damira 0657, **2391**
Seren, Seda 0058
Seridi, Loqmane **1839**
Serin, Sheila **1508**
Serna Góngora, Melissa Brenda 1486
Serna-Peña, Griselda 1687
Seror, Raphaele 0508, 0516, 1115, 1575, 1604, 1683, **1685**, 2489
Serrano, Eliana 1422, 2405
Serrano, María Gema 0346
Serrano-Arroyo, Lilliana **1493**
Serrano-Benavente, Belén 0019, 1397, 1681, 2290, 2422
Serrano-Combarro, Ana **0736**, **0737**
Serrano-Combarro, Ana 1778
Serrano-Combarro, Ana **2016**, **2229**, **2265**
Serventi, Joaquín Martinez 0596, 0621, 1491
Servettaz, Amélie 0891, 1604
Seshan, Surya 1839
Sestan, Mario 2126
Sestini, Piersante 1589
Sethi, Prativa Priyadarshani **1364**, 2261
Sette, Manuel 2656
Setty, Arathi 0738, 0751, 0776, 0895, 2362
Seu, Monica 2089
Severac, François 0516

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

severino, adriana 0700
Sevilla, Belen 0029, 1282, 1284
Sevim, Ecem **0118**
Sevim, Ecem 1988
Sevimli, Esra 1396
Sewa Marques, Regis 1400
Sewerin, Philipp 0152, 0545, 1157
Seymour, Brenda 0800, **0870**
Sezer, İlhan 2322
Sfikakis, Petros 0133, 1452, 1462, 1463, 1464, 1586, 2232, 2359
Sfontouris, Charalampos 1452
Sgalla, Giacomo 1567
Shabbir, Arsalan 0913, 0930
Shadick, Nancy 0465
Shadick, Nancy 1057
Shadick, Nancy 1644, 1705, 2320, 2607
Shadid, Grace 1708
Shagroni, Tasneam 0562
Shah, Ami 0883, 1028, 1037, 1107, 1108, 1555, 1556, 1559, 1566, 1582, 1591, 1596, 1725, 1730, 2475, 2654
Shah, Ankit 0370
Shah, Ankoor 0221, 0222, 0883, 1555, 1563, 1566, 1582
Shah, Ankoor 2207, 2208
Shah, Ankoor 2475, 2654
Shah, Arusa 1199, 2259
Shah, Baiju 2079
Shah, Freya **1484**, **1892**
Shah, Kamini **2183**
Shah, Mandar 1063
Shah, Meera 0295, **2066**, **2067**
Shah, Naveed 1603
Shah, Neha 1248
Shah, Nikita 0435, 2439
Shah, Nitya 0352
Shah, Pooja 1910
Shah, Radhe 1892
Shah, Sanjiv 1553
Shah, Shivani 2183
Shah, Tina 1675, 2278
Shahab, Sohan 0265, 2690
Shahabi, Ahva 1393, 1394
Shahane, Anupama 0231, **0339**
Shaharir, Syahrul Sazliyana 2004
Shahbazian, Ani 0425, 2227
Shaheen, Hussam 1437
Shahin, Alex 0709
Shahrara, Shiva 0068
shahriari, Neda 2320
Shahwan, Shatha 0632, 1719
Shaik, Afsana Ansari 1078
Shaik, Nagoor 2415
Shaikh, Ali 2085, 2091
Shaikh, Bisma 1502
Shaikh, Farheen 0079
Shaikh, Farheen Sultan **0078**
Shaikh, Faryal 1248
Shaikh, Nawazish 2152
Shaily, Aditi **0393**
Shakoor, Najia 2054
Shan, Juan 0323, 2562
Shang, Hongyan 1001
Shanmugam, Victoria 0883
Shanmugam, Victoria 1725
Shannon, Jessica 0989
Shanta, Meena Afroze **1654**
Shantz, Emily 0188
Shao, Daming 1111, 2381
Shapiro, Abigail 2207, 2208
Shapoval, Iryna 1128
Sharaf, Mohamed 0577, 1460, 2345
Sharan, Shilpa **2192**
Sharkas, Satani **0502**, **1031**
Sharkey, Christine 2167
Sharma, Akanksha **1554**
Sharma, Dhriti 1706
Sharma, Ishan 0987
Sharma, Mehar Chand 1197
Sharma, Rhea 2150, 2195
Sharma, Rhiya 0751
Sharma, Rohan **1905**
Sharma, Sarthak 1347
Sharma, Shefali 0697
Sharma, Sristi 2618
Sharma, Tarun 0500
Sharma Subedi, Aakritee 1092
Sharp, Brenna 1726
Sharp, Engle 1650, 1779
Sharp, Kate 1785, 1791
Sharpe, Jason 1922, 1927
Sharpe, Orr 0914, 1693
Sharrack, Sana **0832**
Sharrock, Luke **1069**
Sharrock, Luke 2224
Shasti-Nazem, Beeta 0830
Shaw, Tim 1349
Shawaqfeh, Jameel 0538
Shawareb, Bana **1476**
Shawareb, Bana 2382
Shea, Lauren 1174
Shea, Lisa 1376, 1377
Sheahan, Anna 1878, 1899
Sheard, Michael 0010
Shearer, Todd 2293
Shearman, Jeremy 1136
Sheeran, Thomas Patrick 1212
Sheikh, Farooq 1182
Sheikh, Saira 0652, 1505, 1915, 2437, **2468**
Sheinson, Danny 1038
Shekhtman, Tanya 0207
Sheldon, Curtis 2035
Shelef, Miriam 0073
Shen, Chiehyu 0299, 1106
Shen, Chieh-Yu 0511
Shen, Guo 0293
Shen, Jeffrey 1160, 2049
Shen, Lianjun 2465
Shen, Lichong 0977
Shen, Min 1158
Shen, Nan 0656
Shen, Nan 0887, 2665
Shen, Wuzhong 0646
Shen, Yiran 0127, 0131, 0143
Shen, Zancong 1138
Sheng, Quanhu 1329
Sheng, Shihong 0562
Sheng, Xuting Rebecca **0679**
Sheng-Kai Ma, Kevin 0813, **1104**, 2659
Shenoi, Susan 0395, 0422, 1208, 1209
Shenoy, Padmanabha 1588
Shepherd, Nora 1606, 2508, 2509
Sheridan, Megan 1677
Sherina, Natalia 2402
Sherpa, Gyaljin 1888
Sherrard, Tina 0401
Sheta, Sarah 0264
Sheu, Heh Shiang 2469
Shew, Alexis 2689
Shi, Guixiu 0876
Shi, Hui 0120, 0124, 0127, 0142, 0856, 0964, 1971
Shi, Hui 2583
Shi, Jia 0861, **1208**, **1209**, **1750**
Shi, Jinjun 0808
Shi, Liqing **1762**
Shi, Mei-Feng 1114, 1799
Shi, Min 0159
Shi, Ran 2245
Shi, William 2011, 2012
Shi, Xiaofei 0468
Shi, XiaoFei **2376**
Shiba, Hiroshi **2449**
Shiboski, Caroline 0034, 0038, 0514, 1223, 1682, 2233
Shiboski, Stephen 0514, 1682
SHIDAHARA, KENTA 1345, 2664
Shim, Jae-Hyuck 0872
Shim, Janna **2143**
Shim, Jeongsup 0679
Shimabuco, Andrea 2682
Shimada, Hiromi 1167, 1611
Shimada, Hiromi **2212**
Shimada, Hiromi 2488, 2534
Shimizu, Masaki 0780, 1671
Shimizu, Masaki 2137, 2138, 2139
Shimojima, Yasuhiro 2523
Shimshak, Thomas 1078
Shimshon, Hadar 1708
Shin, Daniel 0546
Shin, Dong Wook 0170
Shin, Ji Hui 0550, 1432
Shin, Kichul **0472**, 2007
Shinar, Brenda 2184
Shing, Vivian **0710**
Shinjo, Samuel 1218, 2065
Shinjo, Samuel K 1192
Shinjo, Samuel Katsuyuki 2067
Shinto, Yoshitaka 2564
Shirai, Tsuyoshi 1630, 2523
Shirakashi, Mirei 0773, 1772, 1857

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Shirman, Nina 1305
Shirota, Yuko **2522**
Shisha, Tamas 2696
Shivas, Tricha 1251
Shiwen, Xu 0966
Shkolina, Nataliia 1128
Shoae Kazemi, Mehrdad 1430
Shoback, Dolores 0446, 0462, 0836, 1238
Shobha, Vineeta 1588
Shobha, Vineeta 1609
Shock, Anthony **2631**
Shoda, Hirofumi 1512
Shoenfeld, Yehuda 0570, 1332
Shojaie, Kaylie 2146
shokoohi, hamid 2006
Shook, David 0014
Shrestha, karun **0492**
Shrestha, Karun 2514
Shrestha, Rima 2065
Shrestha, Shukranta 0433
Shriner, Daniel 1725
Shtrozberg, Shai 2372
Shu, Qiang 0649
Shumay, Dianne 1237
Shurtz, Anne 1311
Shuto, Toshihide 1419
Shuweihdi, Farag 1677
Shwetar, Jasmine 0851
Shwetar, Jasmine 1240
Sia, Robin 2057
Sibbitt, Wilmer 2040, 2077
Sibilia, Jean 0516, 1578, 1683
Sibran, William 1734
Sichien, Dorine 0907
Sidalaghatta Nagaraja, Archana 0057
Siddiqi, Haziq 1173
Siddique, Salma 1013
Siddiqui, Madiha Naqsh **0161**
Siddiqui, Mariam 2430
Siddiqui, Momina 0312
Sidhu, Harleen 1832, 2394
Sidiropoulos, Prodromos 0628, 1349, 2232
Siebert, Stefan 0111, 0577, **1460**, 1678, 1711
Siedner, Mark 2577
Siefert, Ashley 1792
Siegel, Caroline **0365**, 0382, 0634, 2226, 2575
Siegel, Matthew 0050
Siegel, Richard 2296, 2300, 2696
Siegert, Elise 0702
Siegmund, Britta 0021
Sieiro, cristiana **0245**, 0269, **0882**, **0982**, 1171, **2209**
Sierra, Laura 0882
Sierra-Salazar, Álvaro Abiel 2052
Sifuentes-Giraldo, Walter Alberto 1287, 1288
Sigurgeirsson, Bardur 1447
Sijbers, Lyanne 0821
Sillitoe, Jason 0711, 2398
Silva, Ana 0596, 1491
Silva, Catarina 0761
Silva, Clovis Artur 0206, 0619, 1192, 1292, 1293, 1715, 2292, 2527, 2535, 2573, 2653, 2682
Silva, Henrique 2292
Silva, Ines 0636, 2427
Silva, Maite 0454, 1613
Silva, Nélzio 0621, 1530
Silva Díaz, Maite 0270
Silva Luna, Karina 2187
Silva-de Leon, Ariana 2606
Silva-Diaz, Maite 0271, 0744, **0752**
Silvatti, Juliana **0616**
Silveira, Gonzalo 0596, 1486
Silveira, Lori 2144, 2161, 2515
Silveira, Luis H 0443, 0596, 0621, 0623, 1530, 1947
Silver, Jared 2515
Silver, Richard 1079, 1725
Silverman, Earl 1286, 1301
Silverman, Gregg **2399**
Silverman, Gregg J. 1759
Sim, Jasmine 1703
Sim, Myung Shin 1048
Sim, Soyeong 1655
Sim, Tao Ming **1121**
Simón-Campos, Jesus Abraham 0473
Simand, Celestine 1578
Simanovich, Alina 1436
Simanulang, Azzura 1398
Simard, Julia F 1009, 2169, 2201, 2202, **2214**
Simard, Laurianne **1109**
Simeón Aznar, Carmen Pilar 1953
Simeón Aznar, carmen-Pilar 0702
Simeo Vinaixa, Miguel 0205, 0237, 0341, 1274, 2274, 2310
Simeon, Carmen Pilar 1862, 2485
Simha, Varsha 2518
Simion, Viorel 0016
Simitchieva, Kremena 2486
Simko, Spencer **1370**
Simmons, Sean 0947
Simon, David 0343, 0471, 1010, 1529, 2686
Simon, Rachel 2459
Simon, Teresa 1046
Simone, Benedetto 0204
Simone, James 1624
Simone, James 2580
Simone-Roach, Chantelle 2486
Simonini, Gabriele 0389, 0392, 0401, 0407, 2128, 2179
Simons, Iris 1560
SIMOPOULOU, THEODORA 1219
Simorre, Bernard 0891
Simpfendorfer, Kim 1814
Simpson, David 0029
Sims, Catherine **2207**, **2208**
Sims, Faye 0711
Sims, Gary 1374
Sinanan, Kimberley 1650, 1774
Sinci, Ayberk 0524
Singaraju, Anvita 0067
Singer, Nora G. 1122, 2006, 2301
Singer, Ora 1623
Singh, Abha 1959
Singh, Anubhav **0605**, 1717
Singh, Gurjot **0233**, **1418**, 1543, **2238**, **2239**, **2240**, 2283, 2284
Singh, Herveen 2163
Singh, Jasvinder 0158, 1048, 1068, 1082
Singh, Kailey **2182**
Singh, Kiran 2429
Singh, Komal 0631
Singh, Namrata 0146, 0158, 0172, 0457, 0462, 1068, 1072, 1104, 1105, 1107, 1108, 1112, 1238, 1718, 2237, 2251
Singh, Namrata 2252
Singh, Namrata 2615
Singh, Namrata 2634
Singh, Nilanchali 1503
Singh, Nishant 0886
Singh, Pratibha 0130
Singh, Purva 0316
Singh, Rajesh **0057**
Singh, Ram 1392, 1897, 1905
Singh, Siddharth 2615
Singh, Toolika 0058
Singh, Tripti 0670
Singhal, Atul 0561, 1123, 2278
Singhe, Nawang 0285
Singla, Shikha **0585**, 1165, **1459**, 2355, 2369, **2375**
Singleton, Katherine **1638**
Sinha, Neelima 1890
Sinha, Rashmi 0358, 2137, 2138, 2139
Sinha, Sudhir 0631
Sinkeviciute, Dovile 2231
Sinkovskaya, Elena 0853, 1391
Sinomati, Yvonne 0572
Sinusas, Albert 2470
SIPS, CAROLE 1189, 2296, 2300, 2665
Siqueira, Carolina 2535
Siranart, Noppachai 1134, 2255
Sircar, Geetabali 1588
Sirivelu, Bhavya 1423
Sisó, Sílvia 0048
Sise, Meghan 2468
Sisirak, Vanja 1873
Sisk, Christopher 0558, 1839
Sisman, Nur 1396
Sitbon, Olivier 1185
Sivaraman, Vidya 0374, 0413, 2126
Sivera, Francisca 0739, 1446
Sivri, Mustafa 2044
Sjöwall, Chrisopher 0593, 0594, 2390, 2647
Sjowall, Christopher 2401
Skaarup, Kristoffer 1166, 2608
Skalicky, anne 0360

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Skanderson, Melissa 2114
Skapenko, Alla 1729, 2476
Skarlis, Charalampos 0515
Skarlis, Charalampos 2025
Skaug, Brian 0671, 0672, 0683, 0883, 0959, 1555, 1566, 1582, 2475, 2654
Skeie, Kaitlyn 0482
Skeith, Leslie 1497
Skene, Peter 0889, 1695
Skinner-Taylor, Cassandra M. 2549
Skinner-Taylor, Cassandra Michele 0212, 0213, 1633, 1834, 1845, 2171, 2219
Skobelev, Elizabeth 0523, 1176
Skoberne, Andrej 2015
Skoglund, Elisabeth 2647
Skopelja-Gardner, Sladjana 0885, 1758
Skopelja-Gardner, Sladjana 2581
Skouvaklidou, Elpida 1439
Skov, Lone 1166, 2608
Skydel, Joshua **1925**
Slaven, James 2423
Sloan, Elizabeth **0119**, 0126, 0128, 0129, 0822
Slobodin, gleb 0675
Slobodnick, Anastasia 0633, 2517
Slonin, Derek 2103
Slonin, Jonathan 2103
Slosberg, Haley 0365, 0855
Slotine, Ilana 1735
Sluzevich, Jason 1585
Small, Annabelle 0091, 0504, **0917**, 0980
Small, Isadora **1420**, 2504
Smets, Perrine 1765
Smith, Aaron **2437**
Smith, Adam 0832
Smith, Brittany 2548
Smith, Chelsey 2197
Smith, Emma 2631
Smith, Eve 1300
Smith, Ian 0294, 2069
Smith, Isaac 0045, 0221, **0222**, 0834, 1314, 1325, 2683
Smith, Justin 1550
Smith, Karen 0787, 1011
Smith, malcolm 0091
Smith, Malcolm 0504, 0917
Smith, Marguerite 1136
smith, Melanie 0463, 1149
Smith, Miles 0023, 0044, 0774, 1831, 1850
Smith, Nicholas 2251, 2252
Smith, Sarah 1079, 1638
Smith, Vanessa 0673, 0676, 0702, 0705, 0884, 0963, 1097, 1287, 1288, 1565, 1586, 1952, 2179, 2477, 2501
Smith, PharmD, Alisha 2554
Smitherman, Emily 1252, 1276, 1277, 1300, 1495, 2132
Smole, Amaya 0365, 0382, 0634, 2575
Smolen, Josef 0499, 0816, 0873
Smolen, Josef 1411
Smolen, Josef 2332
Smuda, Craig 1111
Smyth, Andrew 1409
Snelgrove, John 2200
Snoeck, Veerle 2631
Snoj, Ziga 0543
Snow, Marcus 1952
Snyder, Ellen 0825
Snyder, Garrett 0319
Snyderman, Ralph 0363, 0793, 1487, 2379
So, Ho 0304, 0536, 1202, 2234
Soares, Andressa 1407, 1408, 2326
Sobanski, Vincent 1581
Sobanski, Vincent 1858
Sobue, Yasumori **1326**
Sockalingam, Sargunan 0595
Sockman, Ellen Ann 1047
Sodhi, Sandeep 2539
Sodsri, Tulaton **1187**, 1319
Soeda, Kei 2522
Soeda, Naoki 0486, 0487
Soeda, Tetsuhiro 0781
Soga, Eri 2225
Sohn, Sunghwan 0469
Sokka-isler, Tuulikki 0814
SOKOLOVA, Tatiana 0074, 1679, 2272
sokolove, jeremy 1338
Solanki, Kamal 0702, 0884, 1586
Solano, alejandra 0083
Soldano, Stefano 0963
Soleimani, Shirin 1755
Soliman, Eiman 1210
Soliman, Mark 0319
Soliman, Nadine 1735
SOLLANO, MA. HANNA MONICA 2004
Solmaz, Dilek 0524
Solomon, Daniel 0283
Solomon, Daniel 0468
Solomon, Daniel 1149
Solomon, Daniel 1267
Solomon, Daniel 1644, 2569, 2607, 2640, 2644, 2660, 2662
Solomon, Jenny **2196**
Solow, Elizabeth 0774, 1256, 1257, 1674
Som, Avira 0344
Somanathapura, NaveenKumar 0115, **0134**, 0857, 0858, 0859, 1623
Somers, Emily 0232, 2645
Somers, Tamara 0363, 0793, 1487, 2379
Sommer, Ulrike 2296
Sommerfleck, Fernando 1422, 2336
Son, Chang-Nam 0526, 2004, 2264
Son, Mary Beth 1668, 1810, 1822, 2135, 2645
Sonaty, Griffin **1788**
Sondhi, Manush **1112**, **2615**
Sonego, Fabiane 0907
Sonestedt, Emily 1884
Song, Chao 0579, 0580, 2366
Song, Eingun J. 0555
Song, Hansun 2540
Song, Hongmei 1828
Song, Huijuan 0719
Song, Jason Jungsik 2511
Song, Jing 0440, 1225, 1249, 2430, 2455
Song, Ken 2641
Song, Michael 1545
Song, Qingyi **0876**
Song, Sharon 0646
Song, William **1912**, 2525
Song, You 0646
Song, Young Soo 1360
Song, Yujie **1854**
Song, Yuling 0906
Sonkaya, Yade 0386, 1461
Sonmez, Reyhan 1878, 1899
Sonntag, Clare 2192
Soo, Jhy-Charm 1645
Sood, Akhil **0210**, **2201**
Sood, Jessica 0014
Sood, Lakshay 1702
Sood, Siddhartha 0565
Soomro, Mohammed 1366
Soon, Megan 0101, 0980
Soong, Brian 2584
Soorya, Sarah 1790
Soowamber, Medha 0716, 1607
Soowamber, Medha **1626**
Sorathia, Aqsa 0151, 1880
Sore, Rou 2384
Soria, Yessika Jackeline 2405
Soriano, Enrique R. 0577, 1460, 2365
Soriano, Reyna 1825
Sorin, Boris 2699
Sornasse, Thierry 0751
Soroka, Orysya 1084, 1283
sosigowda, pradeep **1775**
Sotnikova, Tatiana 0779
Soto, David 0941
Soto, Sandra 2097
Soto Albrecht, Yentli E. 1825
Soto-Fajardo, Carina 0443, 0507, 2674
Souchaud Debouverie, Odile 2532
SOUCHAUD-DEBOUVERIE, Odile 2655
Soule, Benjamin P 1456
Soulsby, William 0387, **1704**
Soung, Jennifer 0523, 0581, 0875
South, Sanique 1736
Southern, Danielle 1497
Souto, Ajexandro 0761
Souvignier, Maya 0791, 1268
Souvignier, Maya 2650, 2693
Souza, Eduarda 2326
Souza, Thales 1292, 2535
Sowerby, John 0988
Sozeri, Betul 1698, 1818
Sparagana, Paola 0119
Sparchez, Mihaela 1287, 1288
Sparks, Jeffrey 0168, 0465, 0501, 0687, 0774, 0790, 1034, 1099, 1100, 1104, 1107, 1108, 1343, 1674, 1696, 1730, 1747, 1751, 1902, 2185, 2235, 2571, 2574, 2577, 2578, 2662

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Sparks, Lauren 0320
Sparks, Rachel 0832
Spathis, Rita 1191
Speca, Silvia 0958
Specian, Fabio 1180, **2028**, 2045, 2535
Specker, Christof 1729
Specks, Ulrich 0721, 1602, 1608, 1769, 2515
Spencer, Andy **0050**
Spencer, Taylor 1012
Sperber, Kirk 0598
Sperlich, Billy 1450
Sperling, Christine 0188
Spiegel, Brennan 1228
Spiera, Robert 0239, 0844, 2031
Spierings, julia 0689, 0690, 1562, 2503
Spindler, Kurt 0787
Spivack, John 0844
Spoden, Tahnee **0425**
Spoerl, Silvia 0641, 1537
Sporn, Hunter **2572**
Sprecher, Marco 0510
Sprenkle, Neil 1000
Springer, Kylie 2180
Sproles, Alyssa 0418, 2140, 2242, 2675
Sreelekha, Kambhampati 1771
Sreerama Reddy, Kaushik 0282, 0303, 1201
Sreesanth, Banoth 0416
Sreih, Antoine 1685
Sreih, Antoine **2293**
Srikakulapu, Prasad 0989
Srinath, Archita **0098**, 0560
Srinija Reddy, Emani 0447
Srinivasalu, Hemalatha 0390
Srinivasan, Hema 1081
Sriram, Shreya 0282, 1201
Srirangan, Arthihai 1589
Srivastava, Archit 0300, 0759
Srivastava, Archit **2018**
Sriwi, Dalia 0670
Sroka-Saidi, Kamila 0247
Srpcic, Anja 0281
St. Clair, James 1557, 1590, 1874, 2492
Størdal, Ketil 0427, 2679
Stach, Christian 0644, 0645, 1542
Stack, John 1136
Stadanlick, Jason 1563, 2468, 2669
Staeva, Teodora 0377
Stahl, Erin 0392, 0406, 0414
Staines, Kimberly 2089
Stainton, Emma 0501
Stajszczyk, Marcin 1883
Stalker, Grant 2186
Stallmach, Andreas 1934
Stamm, Lea 2472
Stammler, Romain **1339**
Stamp, Lisa 1125
Stanaitis, Ian 2079, 2102
Stanevica, Valda 0401
Stanevica, Valda 1287, 1288
Stanford, Fatima 0813, 1130
Stanford, Stephanie 0976
Stanislavchuk, Mykola 1128
Stano, Stefano 2075, 2656
Statache, Gianina 0538
Stauffer, Philip 1867
Stauffer, Philip **1872**
Steen, Virginia 0682, 0883, 1555, 1566, 1582, 1725, 2475, 2654
Steenhoff, Andrew P 1825
Stefanov, Kristian 1239, 1711
Steffen, Ulrike 2279
Steichen, Olivier 0735
Stein, Casey 0258
STEIN, DANIEL 1702, 1846
Stein, Josephine 0431
Stein, Michael 0174, 0818, 1181, 2270
Stein, Nili 1436
Stein, Olivia A. 1506
Steinack, Carolin 1872
Steiner, Ella **1157**
Steiner, Marlene 0816
Steiner, Martina 0201
Steiner, Martina 1961
Steiner, Martina 2373
Steinfield, Ian 2500
Steinhoff, Magie 1797
Steinz, Nils 1568
Stenzel, Werner 0863
Stephane, nahon 1095
Stephans, Allayne 0829
Stephens, Janet 0482
Stephens, Tayte **0044**, 0514, 0774, **1850**, 2421
Stephens Shields, Alisa 1566, 2654
Stergiou, Ioanna E. 0515
Stern, Sara M. 1669, 2125, 2128, **2301**
Steuer, Lia 1292, 2535
Stevens, Alexander 1424
Stevens, Brenda 0262
Stevens, Christina 0311
Stevens, Wendy 0677, 1716
Stevens, Wendy 2651
Stevens-Lapsley, Jennifer 0768
Stevenson, Julia 1985
Stiburkova, Blanka **1124**
Sticherling, Michael 2613
Stiefel, Hillary 0893
Stievenart, Julien 0891
Stigler, Jayne 0557, 0589, 1453, 1465
Stimec, Jennifer 0428
Stinnett, Sandra 2064
Stinson, Alexander 2494
Stinson, Jennifer 1494
Stipho, Faissal 2228, 2286
Stocco, Gabriele 0392
Stock, Carmel JW. 1589
Stocker, christian 0990
Stoenoiu, Maria S. 1710, 1959
Stohl, Sheldon 1935
Stohl, William **1935**
Stojkic, Ivana 0193, **0719**
Stoll, Matthew 1277, 2677
Stoll, Stefan 1760
Stoltz, Sarah 0218
Stomaci, Chiara 0246
Stone, Deborah 1651
Stone, Erik **1617**, 1987
Stone, John 0239, 0279, **0360**, 0375, 0743, 0792, 0992, **1163**, 1251, **1666**, 1764, 2019, 2020, 2033, 2051, 2528, 2529, 2530
Stone, Martha 0360, **1251**
Stonick, Karyssa **0258**, 1624, **2533**
Storek, Jan 0969, 0970
Stovall, Rachael 1072
Stovall, Rachael 1104, 1105, **2634**
Stowasser, Susanne 1662
St-Pierre, Yvan 0606, 2416
Strøm, Marin 2679
Stradford, Laura 1617
Strainic, James 0853, 1391
Strand, Fatima 2062
Strand, Vibeke 0455, **0640**, 2176
Strand, Vibeke 2587
Strand, Vibeke 2614
strappa, cecilia 0880
Strasser, Daniel 2296
Strawbridge, Elizabeth 2207, 2208
Strayhorn, Michael 2089
Stream, Sara 1265
Strickland, Colin 1674
Striebich, Christopher 0774, 1674
Stripp, Barry 0085, 2579
Strober, Bruce 0574
Strom, Brian 0399, 0400
Stropuviene, Sigita 1309
Strother, Aidan K 0671
Strouse, Jennifer 1110, 2186
Strunk, Joachim 2279
Strunz, Patrick-Pascal 1450
Stuart, Philip 0034
Studenic, Paul 0510
Studenic, Paul 1614, 1627
Stuetz, Ayla Nadja 0026, 0678, 1198, 1856, 1876
Stultz, Ryan D. **0059**, 0747, 2147
Stumpf, Cecilia **0935**, 1227, 2430
Sturm, Kristin 2205, 2628
Sturza, Julie 2478
Su, Chenpeng 0018, 1006
Su, Hang 0911, 1776
Su, Karry 2577
Su, Lu 0915, 0998
Su, Yujie 0369
Su, Yujie 1387, 1661, 2539
Su, Yu-Jih 2469
Suárez Zorrilla, Leire 1904
Suarez, Cristina 2042
Suarez-Almazor, Maria 1107, 1108, 1429, 1730
Subedi, Bal 2093

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Subedi, Prakriti 0492, **2514**
Subedi, Roshan 0513, **1182**
Subils, Gisela 1486
Subklewe, Marion 2476
Subramanian, Suganya 0944
Sucerquia, Alfonso 0199, **2576**
Suda, Masei 0638
Sudheer, Aishwarya **1877**
Sudireddy, Divya **1481**, **2526**
Sudman, Marc 0392, 0824
Sudnick, Alyssa 0835
Suehs, Brandon T. 1083
Sueiro, Diana 1446
Sufi, Yasmeen 1539
Suga, Kensuke 0067, **0085**
Sugi, Suzuna 0061
Sugiarto, Nicholas **2600**
Sugiarto, Nicolas 2233
Sugihara, Koichi 1167, 1611, 2212, 2488, **2534**
Sugihara, Takahiko **1630**
Sugita, Megumi 2049
Sugiura, Ayumu 1442
Sugur, Kavya **0822**, **0858**, 0859, 1623, 1740
Suh, Ashley 2206, 2380
Suh, Stephen 0791, 1268, 1942, 1970, 2650, 2693
Suhas Dahale, Swapnil 0405
Sule-saa, Samuel 0456
Sulich, Andrew J. 1999
Sulis, Antonello 1380
Sulli, Alberto 0676, 0963, 1097, 2501
Sullivan, Calla 1898
Sullivan, Daniel 1201
Sullivan, Erin 0186
Sullivan, Gregory **1231**
Sullivan, John 0184
Sullivan, Joshua 1061
Sullivan, Kathryn 1837
Sullivan, Megan 0315, 0759, 0777, 1255, 1585, **1900**, 2542
Sullivan, Ryan J. 1099
Sulu, Bercemhan **0241**
Suman, Saurav 2166
Sumichika, Yuya 1509
Suminaka, Chihiro 1772
Sumitomo, Shuji 1772, **1849**
summer, Ross 0445
Summit, Rebecca 0156, 1057, 1705
Sumpter, Nicholas 2010
Sun, Amy 0646
Sun, Anina 2688
Sun, Chuanyin 2463
Sun, Dongmei 0365, 0635, 2426
Sun, Emily **2057**
Sun, Fangfang **0656**
Sun, Hong-wei 2580
Sun, Jian 1470
Sun, Jianming 0005, 0986, 1001
Sun, Kai 0363, 0367, **0793**, 1487, 2379
Sun, Li 0926
Sun, Lin 0647
Sun, Lingyun 0519
SUN, LINGYUN 0876
Sun, Mingfang **1361**
Sun, mingyang 0950
Sun, Qi 0519
Sun, Qi 1032
Sun, Qin 2129
Sun, Sarah **1116**, 1248
Sun, shu 2231
Sun, Wei 1750
Sun, Wen **0867**
Sun, Xiaoxiao 0325, 2100
Sun, Yi-Syuan 1540
Sun, Zhengwang 1833
Sun, Zhengwang 1876
Sunar, Ismihan 1968
Sunderkotter, Cord 2699
Sundy, John 0008, 0987
Suneja, Manish 2174
Sung, Jaeyun 0276, 2639
Sung, Lily 1072
Sunkara, Priya 0167
Sunkara, Sri Laxmi Priya **1544**, **2050**, 2370
Sunshine, Joel 0865
Sunzini, Flavia 1239, 1711
Suppiah, Ravi 1912
Surampudi, Varsha 0289
Suresh, Shashank 0298
Suresh, Varshapriya 1215
Suri, Pradeep 1238
Suslow, Anastasia 1934
Suter, Lisa 0437
Sutton, Anna **0395**
Sutton, Lillian 0407
Suurmond, Jolien **1838**
Suwakulsiri, Wittaya 0504, 0980, **1703**
Suzuka, Takayasu 0973
Suzuki, Katsuhisa 0486
Suzuki, Katsuya 2253, 2254
Suzuki, Mochihito 1326
Suzuki, Shotaro 0668
Suzuki, Takahiro 2660
Suzuki, Takeshi **0668**
Svejnoha, Emily 2035
Svenungsson, Elisabet 0133, 0594, 2400, 2647
Svobodová, Kristina **1211**
Svobodová, Kristina 2073
Swahn, Hannah 1796, 1805
Swain, Subhashisa **1909**
Swami, Chinmay Prakash 0447
Swami, Sanjeev 2146
Swaminathan, Aparna 0274
Swaminathan, Gayathri 1119
Swank, Zoe 2574
Swart, Joost 0401, 0821, 2137, 2138, 2139
Swearingen, Christopher **2083**, 2626
Swierczynska, Natalia 0711
Swierkot, Jerzy 1676
Swigris, Jeffrey J 0247
Swoboda, Casey 1826
Syed, Aamer 0234, 0253
Syed, Huzaefah **0234**, 0253
Syrmou, Vasiliki **1219**
Syu, Li-Jyun 1760
Szűcs, Gabriella 0680
Szabo, Sara 0418, 0419
Szabolcs, Paul 0823
Szamosi, Szilvia 0680
Szekanecz, Zoltán **0680**
Szeląg, Mateusz 1883
Szelinski, Franziska 2476
Szentpetery, Agnes 1959
Szilagyi, Balint 2374
Sztajnbok, Flavio 1287, 1288
Szymczak, Aleksander **1781**, 1792, 1794, 1806

T

T. Hannani, Monica 0307
Tümerdem, Bilgesu Safak 0026, 0956, 1198, 1856
Türkmen, Şeyma 1698, 1818
Tóth, Ferenc 0027
Tański, Wojciech **0096**
Tabacof, Laura 1236
Tabary, Olivier 1735
Tabata, Hiroki 2253, 2254
Tabechian, Darren 1926
Taboada Martínez, Víctor 2209
Tachikawa, Ryo 0773
Tack, Tom 0217
Tackett, Sean 1207
Tacy, Theresa 0853, 1391
Tada, Kurisu 0106
Tada, Maria 1854
Taddio, Andrea 0392, 0407
Tadrous, Mina 2627
Taghavi, Sepehr 0467, **0636**, 0851, **2427**, 2433, 2434
Tagoe, Clement 0223, 2514
Taguchi, Hiroaki 2253, 2254
Taguchi, Sari 1358
tahir, Khaoula 2324
Tahir, Sidra **1215**
Tai, Albert 0872
Taieb, Vanessa 1438, 1449, 1542, 2347
Taiji, Riley 0561, 2689
Taillé, Camille 0715, 1592
Taillar, Maxence 0618
Tailor, Lauren 2563
Tajima, Yumi 2522
Takács, Szabolcs 2684
Takács-Lovász, Krisztina 2684
Takada, Tappei 1124
Takada, Toshihiko 2523
Takagi, Hirosuke 2523
Takahashi, Haruka 2602
Takahashi, Hiroyuki 0043
Takahashi, Toshiaki 1732

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Takahashi, Toshiya 0486, 0487
Takakuwa, Yukiko 0668
Takanashi, Satoshi 0052
Takata, Tomoaki 2523
Takatani, Ayuko 2523
Takei, Riku 0022
Takeno, Mitsuhiro 2541
Takeshita, Miki 2522
Takeuchi, Tohru 0973, 2523
Takeuchi, Tsutomu 0052, 0595, 2697
Takeyama, Shuhei 1854
Taki, Ali 1589
Takizawa, Naoho 2523
Talaat, Mohamed 2651
Talarico, Rosaria 0723, 1381, 2179
Talati, Megha 0709
Taljanovic, Mihra S. 2085, 2091
Talreja, Taanya 2056, **2076**
Talukdar, Ayantika 0560
Tam, Cheuk Yin **2234**
Tam, Lai Shan 0536, 2234
Tamai, Hiroya 0781
Tamaki, Hiromichi 0638, 2660
Tamang, Suzanne 0092
Tamashiro, Carolina **0387**
Tambiah, Jeyanesh **0310**
Tambralli, Ajay **0115**, 0127, 0131, 0134, 0143, 0857, 0858
Tamirou, Farah 0842, 2401
Tamon, Liezel 2601
Tamura, Naoto 0106, 0521, 1630
Tan, Ai Lyn 1677, 2066
Tan, Binghe 2463
Tan, Christina 0194
Tan, Irene 0254, 0693, 0841, 0849, 1074, 1075, 1076, 1522, 2093
Tan, Jeremiah 2203
Tan, Kiara **1130**
Tan, Li Hui 0712
Tan, Qian **2463**
Tan, Ying 0646
Tanaka, Hiroki 2289
Tanaka, Masao 1772
Tanaka, Yoshiya **0279**, 0470, 0473, 0486, 0487, 0595, 0702, 0773, 1163, 1545, 1676, 2019, 2020
Tanda, Enrica Teresa 1097
Tandaipan, Jose Luis 0019, 1547
Tandaipan, Jose Luis 1620
Tandaipan, Jose Luis 2290
Tandel, Megha 2169
Tang, Chaogui 0519
Tang, Feng 0926
Tang, Iris **0839**, **1202**
Tang, Jay 1442, 2351
Tang, Kunhai **1752**
Tang, May Shuen 1121
Tang, Michael 1755, 1756
Tang, Rongrong 0325, 2085, 2091, 2100
Tang, Tiange 2408
Tang, Tianqi 0939
Tang, Vivian Hoi Shan 1202
Tang, Wei 0791, 1942
Tang, Wei **1970**
Tang, Wei 2650, 2693
Tang, Xuemei **0429**, **1303**, **1828**, 2157
Tang, Yulong 0102
Tang, Zeyu **0553**
Tang, Zhihan 2157
Tang, Zhiting 1113
Tangcheewinsirikul, Sirikarn **1301**
Tani, Sho 0764
Taniguchi, Fuminori 0764
Tanioka, Toshihiro **0095**
Tanizawa, Kiminobu 0773
Tanoeihusada, Daniel 1787
Tanus, Adrienne 0446
Tanveer, Fatima 0733
Tanveer, Saman 0733
Tao, Lili 1473
Taoge, ClementT 0492
Tapia, Krystle 2040, 2077
Tapia, Mar 0535, 1062
Tapia López, Emmanuel **1947**
Tapia-Aguayo, Leonardo Uriel 1633, 2549
Tarantino, Giusyda 0391
Tarasovsky, Gary 0181
Tarasovsky, Gary 0211
Tarasovsky, Gary 0220, 2617
Tardivel, Meryem 1858
Tari, Dóra 0680
Tariq, Shamaem 1539
Tarrant, Teresa 1160
Tarvin, Stacey 0401, 0829, 2204
Tasaka, Sadatomo 0486
Tascilar, Koray 0641, 0762, 0878, **2279**
Tascilar, Koray 2543
Tascilar, Koray 2613, **2686**
Tashkin, Donald 1213, 1564
Tasker, Carley 0897, **0898**, 0934
Tasset, Chantal **0653**
Tatari, Aysu 2044
Tated, Ritu 1892
Tatu, Aurora Maria 2472
Taubmann, Jule 0641, 1537, 2442, 2695
Taupin, Jean-luc 1185
Tauty, Solenne 0715
Tavasolian, Fataneh 1755, **1756**
Taverner-Torrent, Delia 0496, 2268
Tavoni, Antonio Gaetano 2656
Taxter, Alysha 0193, 0413
Tay, Frank Sen Hee 1121
Tayar, Jean 0209, 0273
Taylor, Amybel 0474
Taylor, Chris 0686
Taylor, Emily 0798
Taylor, Jasmin 0789
Taylor, Kimberly 0034, 0881
Taylor, Lauren 1173
Taylor, Peter 0470, 1435, 2275
Taylor, Shalina 0751
Taylor, Steven **0196**, 0228, 2170
Taylor, Tommi C. 0506
Tchen, John 1873
Tcherakian, Colas 1592
Tchetverikov, Ilja 2309
Teaw, Shannon **1256**, **1257**
Tebe, Cristian 1018
Tedeschi, Sara **1142**, 2640, 2660
Tee, Cherica 0595
Tee, Michael 0595
Tehawey, Doaa 0936, 0937, 0938
Tehrani, Nazila 0947
Teisseyre, Maxime 0618
Teixeira, Carlos 2536
Tejeda, Nicole 0233, 1418, 1543, 2238, 2239, 2240, 2283, 2284
Tejera Segura, Beatriz 0642, 1490
Tektonidou, Maria 0120, 0121, **0133**, 0860, 1452, 2232
Tellez-giron, Patricia 0218, 1051
Tembelis, Miltiadis 1628
Temiz, Alp 0628, 2613, 2686
Temmoku, Jumpei 1509
Templin, Jonathan 1149
Teng, Gim Gee 0378
Teng, Lichen 0576, 0581, 2339
Teng, Onno 1526, 1693
ter Haak, Mariska 1535
Terajima, Yuya 0452, 2244
Terao, Chikashi 0850
Terebelo, Sima 1253, 1931
Terkeltaub, Robert 0037, 1032, 2008, 2105, 2585, 2590
Ternant, David 1593
Ternette, Nicola 0923
Terreri, Maria Teresa 1287, 1288
Terribili, Riccardo 0275
Terrier, Benjamin **0715**, 0735, 0891, 1339, 1575, 1577, 1592, **1593**, **1594**, 1598, 1604, 1605, 1608, 1765, 1766, 1768, 1769, 2489, 2506, 2507, 2532, 2582, 2584, 2699
Terris, Benoit 2584
Terry, Grace 0794
Teruya, Jun 1299
Terwilliger, Emma 0710
Terzioglu, Ender **0430**
Tesser, John 1675, **2278**, 2614
Tessier-Sherman, Baylah 2114
Tessneer, Kandice 0034
Testoni, Monica 2179
Thaçi, Diamant 0574, 0874, 1447
Thabah, Molly 1431
Thabah, Molly mary 0136, 0137, 2424
Thakar, Juilee 0904
Thakkar, Akshi 0016
Thakker, Paresh 1442, 2351
Thakor, Michael 1675
Thakral, Amit 2148
Thanarajasingam, Uma 1726, 2384, 2649
Thao, PHAM 1095
Thao, Viengneesee 0149

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Tharaux, Pierre-Louis 1768, 2582, 2584
Tharmarajah, Shenthuraan **2627**
Theisen, Alexandra 1295
Theisen, Erin 2233
Theisen, Matthew 0941
Thelander, Mary 2555
Then, Jossiel 2336
Therron, Tyler 0066, 1227, 1362, 1793, 2430
Theunissen, Kyra 1324
Thiam, Kader 0907
Thib, Sydney 0042
Thib, Sydney 2687
Thiel, Jens 1175
Thielbar, Abigail **1813**, 1829
Thiele, Geoffrey 0065, 0076, 0834, 0921, 0924, 1308, 1325, 1650, 1746, 1774, 1779
Thiele, Ralf 2177
Thimmannagari, Sanjana 0479, 1143, **1428**
Thimmapuram, Rashmi **1399**
thiravetyan, Ben 1137
Thiravetyan, Ben 1187
Thirumaran, Rajesh 0337, 1347, 1914
Tholouli, Eleni 2458
Thoma, Louise 1922, **1927**
Thoman, Emily **0444**
Thomas, Charlene 2031
Thomas, Garrett 1479
Thomas, James 1725
Thomas, Konstantinos 2232
Thomas, Koshy Nithin **0130**, 1221
Thomas, Laine 0404
Thomas, Lydia 1814
Thomas, Marion 0489, 0796
Thomas, Matthew R. 0567, 0573, 1455, 2357
Thomas, Preethi 0231
Thomas, Ranjeny 0101, 0504, 0980, 1703
Thomas, Sharita 1922
THOMAS, Thierry 0537
Thomason, Jenna **0186**, 1149, 1718, 2128
Thomas-Semanko, Dawn 0218
Thompson, Anthony 0319
Thompson, Brianna 0935
Thompson, Caroline 0145
Thompson, Emily 0710
Thompson, Joel **1922**, 1927
Thompson, Linda F. 0514
Thompson, Susan 0392
Thongpiya, Jerapas 1137
Thorley, Andrew 0679
Thorne, Carter 0438
Thorne, Carter 0442, 1648
Thornton, Bryce 1252
Thornton, Lucy 0832
Thornton, Sherry 0418, 2140, 2675
Thorpe, Jerill 0843, 1529
Thrisha Reddy, Bareddy Sai 0416
Thudium, Christian 0307, 2231
Thurimella, Kumar **0032**
Thurlings, Rogier 0431
Thway, Myint 1975
Tiaden, Andre 0919
Tian, Hongling 0082
Tian, Jingru 1762
Tian, Liang 0018, 1006
Tian, Wenzhi 2464
Tian, Xinping 0468, 1316, 1750
Tian, Yu 0048
Tiegs, Lyubov 0256
Tierney, Dylan 1057
Tighiouart, Hocine 2429
Tiihonen, Raine 2000
Tiliakos, Athan 0774, 1674
Tiller, Georgina 2128
Tillett, William 0572, 0591, 0592, 1453, 2340, 2342
Tilley, Sarah 1229, 1230, 1247, **1647**
Tilotta, Francoise 0053, 1724
Tilstra, Jeremy **0943**
Tilt, Nicola 1366
Timan, Bracha 2593, 2594
Timens, Wim 1860
Timmerman, Livie 1252, 1276, 1277, **1495**, 2132, 2181
Timmermans, Annick 1324
Timmesfeld, Nina 1934
Timon, Claire 2437
Timsans, Janis **2000**
Tinazzi, Iliara 1959
Tincani, Angela 0121, 0133, 2210
Tindale, Lauren 0204
Tinelli, Martina 2116
Ting, Tracy 0418, 0419, 1226, 1813, 1829
Tiniakou, Eleni 0288, 0529
Tinianow, Alex 0344, **1990**
Tio, Laura 2485
Tipple, Dayani 2561
Tirosh, Irit 1304
Tirri, Enrico 1402
Tison, Alice **1088**, **1089**, 2296, 2300
Tisseverasinghe, Annaliese 0388
Titeca-Beauport, Dimitri 1604
Titi, Adam 0073
Tiwana, Areeb 0603, 2216
Tiwari, Vivekanand 0349
To, Zung 2466
Tobalina Mastre, Lola 0379, 0380
Todd, Marc 1696
Todoroki, Yasuyuki 0773
Toes, René 1678, 1838
Tofade, toluwalase 0737
tofani, lorenzo 0673, 1562
Togizbayev, Galymzhan 2004
Tohidi-Esfahani, Ibrahim 0860
Tohmé, Mira **0014**
Toikumo, Sylvanus 2683
Toillon, Indira 1734
Toitou, Melpomeni 0807
Tokic, Marianne 1934
TOKUNAGA, MOE 1345
Toland, Cara 0423
Toledano, Esther 0483, **1413**, **2311**
Toledo, Gerardo 0060
Tomcik, Michal 1211, 1350, 2073, 2346
Tomelleri, Alessandro 1618
TOMERO MURIEL, EVA GLORIA 0642, 0659, 1878, 1899, 2122, 2344, 2422
Tomietto, Paola 0238
Tomii, Keisuke 0773
Tomimori, Yoshiaki 1848
Tomioka, Hiromi 0773
Tomita, Tetsuya **2564**
Tomlinson, Alexis Z. 1298
Tomlinson, George 1811
Tomlinson, Ryan 1531, 2467
Tompkins, Marc 0027, 1786
Tomsho, Lynn 0558
Tong, Hongyan 2463
Tong Lee, Yue 0057
Toniati, Paola 0238, 0251
Tono, Toshihiro 2541
Tonooka, Kumiko 0668
Tonutti, Antonio **0532**, **0879**
Toothacre, Natalie 1723
Topalsky, Krista **2216**
Tore, Nurten Gizem **0336**, 2605
Torgerson, Troy 0833, 0889, 1695
Torkian, Talia 1236
Torner, James 1647
Tornero, Carolina 0346, 1152, 1322
Tornero Molina, Jesús 0021
Toro, Daniel 0071, 0795
Toro-Gutierrez, Carlos 0596, 0621, 0623, 1486, 1491, 1530
Torok, Kathryn 0823, 1287, 1288, 2175, 2478
Torralba, Karina 2164
Torralbo, Ana Isabel 1851
Torrat Noves, Alba Maria 0205, **0237**, 0341, 1274, 2274, 2310
Torreau, Benjamin 1339, 1575, 1765, 1766, 2489, 2532
Torrente Segarra, Vicente 2422
Torrente-Segarra, Vicenç **0426**, 0642, 0659, 1943, 2450
Torres, Ciara 0934
Torres dos Reis-Neto, Edgard 0596, 1530
Torres Roselló, Arantxa 1404
Torres Ruiz, Jiram 1836, 1841, 2078
Torres Sanchez, Juan **2148**
Torres-Ruiz, Jiram 0287, 2052, 2053, 2674
Tosun, Özgür 0524
Toth, Mary 0411, 1066
Toulany, Alene 1281
Touma, Zahi 0377, 0611, 0612, 0613, 0629, 0640, 0644, 1285, 1289, 1494, 1550, **1551**, **1552**, 1626, 1742, 2441, 2445, 2694
Toumi, Hechmi 1936, 1937, 1948
Toupin-April, Karine 1704

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Tournadre, Anne 2637
TOUZANI, Yousra 1936
Tovar, Linda 0222
Towe, Christopher 2242
Towfig, Muhanned 0456
Towheed, Atif **1056**
Towheed, Atif 2037
Townes, F. William 0823
Townson, Sharon 0009
Toyoda, Task **1677**
Toyoda, Yu 1124
Toyos, Francisco Javier 0269, 1171, 2422
Toz, Bahtiyar 0947
Toz, Bahtiyar **1520**
Tracey, Irene 0815
Trachman, Emma **0610**
Tralagba, Uchechukwu **2263**
Tralice, Rossella 2405
Trallero, Ernesto 0269, 1171
Tran, Alicia **1281**
Tran, Alison 1176
Tran, Anna 1797
Tran, Chuc Van 1144
Tran, Diana 0067
Tran, James 2224
Tran, Khoi Minh 1144
Tran, Megan 0186
Tran, Miles 0808
Tran, Victor 1048
Tran, Viet-Thi 0735
Tran-Manh, Cuong **0960**, **0961**
Treemarcki, Erin 0177
Tremblay, Coralie **1126**
Trenh, Peter 0009
Trepka, Kai 2643
treppo, elena 0238, 1598, 2545
Treutel, Clare 1744
Treviño-Arreola, Alicia Abigail 2557
Treviño-Sanchez, Carolina 2171
Triginer, Laura 2450
Triginer, Laura 2485
Trinh, Huong 0838
Trinh-Minh, Thuong 0960, 0961, 0975
Trinquart, Ludovic 2301, 2429
Tripal, Philipp 0809
Tripathi, Arvind 1456
Tripathi, Priyanka 1206
Triquet, Louise 2115
Tristan-Alonso, Andrea 1600
Trivedi, Devanshi 0992
Trives, Laura 0201, 1961
Troendle, Evan 0029
Trojani, Marie Charlotte 0148
Trojanowska, Maria 1868
TROJANOWSKI, Marcin 0848, 1725
Troldborg, Anne 0133
Trombetta, Soline 1734
Trotter, Andrew **2172**
Trotter, Kimberly 1248
Troum, Orrin 1994
TRUCHARTE, ALMUDENA 1269
Truchetet, Marie-Elise 0673, 0688, 0689, 0702
Truchetet, Marie-Elise 0879
Truchetet, Marie-Elise 1586, 1873, 2477
Trucillo, Allison 0259
Truffinet, Frédéric 2168
Truglia, simona 0673
Truglia, Simona 1570
Truijen, Saskia **1341**, **1342**
Trujillo, Anthony 2437
Trujillo, Laura 1282, 1284
Truman, Isabel 1445, 1453, 2342
Truong, Thuy 0010
Truong, Vince 1780
Truscelli, Raffaele 1616
Tsafis, Konstantinos 1452
Tsaftaridis, Nikolaos 0448
Tsai, Chang-Youh 2469
Tsai, Emily 2320
Tsai, Ping-Han 1344
Tsaliki, Martha 0509
Tsaliki, Martha 1379
Tsang-A-Sjoe, Michel 1573
Tsao, Philip 0024
Tsatsani, Panagiota 2232
Tse, Katherine 2089
Tseng, Chung-E 1918, 1919
Tseng, Chung-E 2444
Tsibadze, Nanuka **0266**, **0849**, 1183, 1719
Tsirigos, Aristotelis 1712
Tskhakaia, Irakli 0266, 0849, 1183
Tskitishvili, Rusudan 0266, **0632**, **1183**, **1719**
Tsoi, Alex 0127, 0811, 0985, 1682, 1846, 1852, 2451
Tsoi, Alexander 1531, 2402
Tsoi, Lam 0020, 0851, 0949, 1760, 2233, 2498
Tsou, Eliza 0964
Tsou, Pei-Suen **0093**, 0127, 0822, 0955, 0971, **0972**, 1563, 1590, 1725, **1871**, 1874, 2478, 2494, 2498
Tsuchida, Yumi 1512
Tsuchiya, Haruka 1512
Tsui, Edmund 0406, 0414
Tsui, Michael 0016
Tsuji, Hideaki 0773, 1772, 1857
Tu, Guiyun 0646
Tucker, Laura 0572
Tucker, Lori 0361, 2128
Tuepker, Anaïs 0359
Tugnet, Nicola 0595
Tuladhar, Anik **1784**
Tulsian, Esha 0227
Tummala, Chandana 1891
Tummala, Raj 1552
Tummala, Raj 1563, 2468, 2669
Tuncar, Yasin Taha 2044
Tuncel, Jonatan **2454**
Tuncel, Tolga 0779
Tuong, Zewen Kelvin 0101
Tur, Carlo 0236, 0641, 2641, **2695**
Turbi-Cornielle, Shanti 1825
Turco, Maria Caterina 1863
Turesson, Carl **1884**, **1885**, 1958, 2319
Turnbaugh, Peter 0054, 0871, 1329, 2643
Turnier, Jessica 0822, 1740, 1741, 1816, 2478
Turrión, Ana 1413, 2311
Turrión Nieves, Ana Isabel 1321
Turturice, Benjamin 0258
Turturice, Benjamin 1624
Turturice, Benjamin 2700
Tusseau, Maude 0920
Tuteja, Sachleen 0624
Tuttle, Jay 0473
Twigg, Dan 1445
Twilt, Marinka 2128
Tylleskär, Karin 0420
Tyson, Jon 2361
Tyson, Kerry 0074
Tzemach, Reut **2372**
Tzianabos, Arthur 0494
Tzioufas, Athanasios 0034
Tzioufas, Athanasios G. 0516

U

Ubah, Obinna **0996**
Ubeda, Carles 1329, 1338
Uchida, Haruhito 1630
Udaondo, Clara 1152, 1282, 1284
udaondo, Clara 2042
Ueberroth, Lori Ann 1638
Ueda, Yo 0062
Uenishi, Gene 0981
Ueno, Hideki 0850
Ufuktepe, Baran 0074, 1366
Uga, Hitoshi 1772
Ugarte-Gil, Manuel 0596
Ugarte-Gil, Manuel 0605, 0623
Ugarte-Gil, Manuel 0637, 0714
Ugarte-Gil, Manuel 0730
Ugarte-Gil, Manuel 1486, 1491, 1504, 1530, 1717, 1878, **1899**, 2378, 2383
Ugarte-Gil, Manuel 2521
Ugena-García, Raquel 0117, 0530, **0758**, 2029
Uggenti, Vincenzo 1951
Uguña, Franklin 1210
Uguen, Arnaud 2296
Ugurlu, serdal 0778, **0779**, 1177, 1477, 2021, 2022, 2667
Uhanova, Olga 0779
Uhlig, Till 0814
Uhunmwangho, Courage 2263
Ujhazi, Boglarka 0782, 0918
Ukonu, Nene **0165**
Ul Ain, Qurat **2256**
Ul Hudaibia, Hamas 1539
Ulgu, Mustafa Mahir 1008
Ullah, Nimat 1759
Ullmann, Uwe 0780, 1671

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Ulloa, Julie 0370
Ulloa-Alvarado, Hector 2023, 2059
Ullrich, Fabian T.H. 1729
Uludag, Omer **0135**, 0290
Uludogan, Burcu Ceren 0778
Ulysse, Mona Pervil 0456
Umam, Fareha 2676
Umar, Mahnoor 0312
Umar, Sadiq **1140**, **1141**
Umer, Muhammad 0312
Umer, Sarwat 1508, 2392
Unanue Pumar, Leire 2107, 2108
Ung, Diana 1042
Unger, Leonore 1175
Ungprasert, Patompong **1583**
Unizony, Sebastian H 0737, 0743, 1606, 1629, 2508
Upadhye, Aditi 1003
Uppin, Megha 1775
Upton, Laura 2193
Ural, fatma Gülçin 2322
Urbanik, Jamie 0589, 1435, 1465
Urbanski, Geoffrey 1765
UREÑA, INMACULADA 1269
Ureta, Carlota 0745
Ureta, Carlota 0755, 2042
Ureta-Moneva, Carlota 1152
Uriarte, Maria Esther 2422, 2450
Uriarte Ecenarro, Miren 2122, 2290
Uriarte-Ecenarro, Miren 0518
Uribe, Carlo Vinicio Caballero 1218, 2066, 2185
Urionaguena Onaindia, Irati 1547, 1548
Urowitz, Murray 1722, 2210, 2416
Urruticoechea-Arana, Ana 0737
Urruticoechea-Arana, ana 1548, 2373, 2450
Uryu, Shigeko **1848**
Urzainqui, Ana 0518
Ushio, Yusuke 1167
Ushio, Yusuke **1611**
Ushio, Yusuke 2212, 2488
Ushio, Yusuke **2523**
Ushio, Yusuke 2534
Usiskin, Ilana **1016**, 1100, 1957
Usiskin, Ilana **2569**
Usmani, Sabahat **1139**
Uss, Kat 0920
Uttam, Ritika 1063
Uttenthal, Ben 2458
Utz, Paul 0423
Uwakwe, Chekwubejah 1224
Uziel, Yosef 1287, 1288
Uzunhan, Yurdagül 1765

V

V Ramanan, Athimalaipet 0397, 2130
V. Oddis, Chester 0282, 0289, 0298, 0303, 0305, 0999, 1201, 2055
Vásquez, Gloria 1486
Vázquez, Jimena 0581
Vázquez, Lourdes Carolina 0596
Vázquez Gómez, Ignacio 0269, 1171, 2473
Vázquez García, Jorge 0329
Vázquez-Hernández, Adriana **1469**
Völkl, Simon 0641, 1537, 2442
Vacca, Alessandra 2651
Vacca, Angelo 0238
Vadakekolathu, Jayakumar 1571
Vadillo Font, Cristina 1024, 1869, 2030
Vaena, Silvia 0944
Vaghani, Dhwani 1890
Vaidya, Binit 2004
Vail, Andy 0686
Vakil, Aesha 0981
Vakil-Gilani, Kiana 0893
Vala, Barbora 1350, 2346
Valamehr, Bahram 0663, 2454
Valdes Cabrera, Diana 1285
Valdez-Benavides, Nathalia 2606
Valdez-Cruz, Juan Daniel 1022
Valdez-López, Martín **2321**
Valecha, Jayesh 2018
Valencia, Jesus **1207**
Valenzuela, Antonia **0684**, **1194**, **1195**, 1565
Valenzuela, Claudia 1662
Valenzuela, Claudia 1869, 2030
Valenzuela, Guillermo **1675**, 1963, 2278
Valenzuela, Guillermo J. 1999
Valenzuela, Ismael 0443
Valenzuela, Krystal **0204**
Valenzuela Almada, Isabel 0601
Valenzuela-Almada, Maria O. 0601
Valera Ribera, Carlos 0205, **2473**, **2474**, 2485
Valero, Cristina 2122, **2344**, 2484, 2491
Valero, Jesús Alejandro 0752
Valero Jaimes, Jesus Alejandro 0485, 2350
Valero-Pacheco, Nuriban 1723
Valiathan, Chandni 0562
Valiveti, Madhavi 0359, 1266
Valle, Ana 0156, **0283**
Valls Pascual, Elia 0270
Valls Roc, Marta 0379, 0380
Valls-Pascual, Elia 0271
Valny, Stacey 0002
Valois, Marie-France 0438, 0442, 1355, 1648
Van Baelen, Ben 2671
Van Beneden, Katrien 0470
Van Butsel, Theo 0355
van Dam, Laura **1693**
Van Damme, Karel **0907**
van de Sand, Heike 1934
van de sande, Marleen 2635
Van den Bogaerde, Sadie 0186
Van den Bosch, Filip 0568, 0569, 1438, 2692
Van der Borght, Katrien 0907
Van der Donckt, Carole 0488
Van Der Heijde, Désirée 0539, 0540, 0569, 0588
van der Heijde, Désirée 0854
Van Der Heijde, Désirée 1405, 1406, 1941, 1958, 2307, 2308, 2319, 2331, 2332, 2334, 2347, 2368, 2635
van der Helm-van Mil, Annette 0176
van der Horst-Bruinsma, Irene E. 1449, **2352**, 2359
van der Kaap, Jos H 2309
van der Laken, Conny 0690, 1560, 1860
van der Vuurst de Vries, Anne-Renee 2277
van der Woning, Bas 0960, 2671
van der Wouden, Katherine 1569, **1573**
van Drongelen, Vincent 0949, 1760
van Duinen, Vincent 1568
van Eeden, Charmaine 0970
van Engelen, Baziel GM 1205
van Essen, Marc 2331
van Gaalen, Floris A. 0539, 0540, **0569**, 0854, 1405, 1406, 1941, 1958, 2319, 2352, 2635
Van Gassen, Sofie 0907
van Heeswijk, Bennie **0979**
van Horn, Cassandra 0674
Van Horn, Linda 2455
van Kooten, Cees 1693
van Laar, Jacob M. 0690, 2503
van Lankveld, Wim 2331
van Leeuwen, Jolijn 1693
van Loosdregt, Jorg 0821
van Lunteren, Miranda 0539, 0540, 0854, 1405, 1406, 1941, 1958, 2319, 2635
van Maurik, Andre 1685
Van Mechelen, Margot 0528
VAN MULLEM, Cécile **1679**, 2272
van Onna, Marloes 1341, 1342
van Oostveen, Wieke 1568
van Rensburg, Chloé Janse 0374
van Roon, Joel 1685
van Saan, Celine 0678
van Saan, Marie Celine 1198
van Schaardenburg, Dirkjan 1678
van Speybroeck, Michel 1878, 1899
Van Tubergen, Astrid 2331, 2334
Van Vliet, Lars 1838
van Vollenhoven, Ronald 0645, 0814
van Vollenhoven, Ronald 1531
van Vollenhoven, Ronald 1722, 2416, 2445
van Zonneveld, Anton jan 1568
VanBuren, John 0883, 1555, 1566, 1582, 2475, 2654
Vance, Emily 0993
Vanderlinden, Lauren **0033**, 0774, 2227
Vandermeer, Ben 0854
Vandersarren, Lana 0694
Vanderveer, William 0783
Vandycke, Matthias 0705
Vanni, Kathleen 1751, 2235
Vanni, Kathleen 2574

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Vanoye Tamez, Mariana 1484
Vantellini, Alessio 0015
Vanthuyne, Marie 0879
vanVleet, Terry 1784
Vaquera-Illescas, Clara 1778
Vara, Emily 0393
Vara, Emily 1059, 1492, **1976**
Varadhachary, Arun **1378**, 1384
Vardanyan, Valentina 0779
Varga, John 0161
Varga, John 0965
Varga, John 0972, 1725, 1874, 2492, 2498
Varga, Stefan 0455, 0874, 2356
Vargas, Benni 0654
Vargas Lupo, Veronica 0377
Varghese, Priju 0632, 1719
Varkas, Gaëlle 1451, 2347, 2692
Varone, Francesco 1567
Vartak, Ambika 1617
Vasantha Kumar, Prabhu **0582**, 1609
Vasconcelos, Joana 1678
Vashistha, Himanshu 1520
Vasova, Ingrid 0641, 1537
Vasquez, Jacob 0636, 0851, 2427
Vasquez Canizares, Natalia 1291
Vasquez-Canizares, Natalia 1287, 1288
Vassallo, Robert 1156, 1388, 1556
Vassilakis, Konstantinos D 1439
Vassilopoulos, Athanasios **1615**
Vassilopoulos, Dimitrios 1452, 2232
Vassilopoulos, Stephanos 1615
Vastert, Sebastiaan 0358, 0780, 0821, 1671, 2137, 2138, 2139
Vasudeva, Isha 2223
Vasudevan, Srivatsa Surya 1347
Vatanen, Tommi 0032
Vater, McKenzie 0418
Vater, McKenzie 0419
Vats, Ravi 1767
Vaughan, Erin 1784
Vaughan-Sarrazin, Mary 1149
Vazquez, Ana 2585
VAZQUEZ DIAZ, MONICA 0107
Vazquez Otero, Ileana 1264
Vazquez Rodriguez, Tomas Ramon 2016
Vazquez-Guerra, Guadalupe Valentina 2171
Vazquez-Machado, Maria 0687
Vecchione, Andrea 0897
Vedantam, Deepanjali **2056**
Vedrine, Corinne 0903
Veeravalli, Akhila **1688**
Veeravalli, Sarath Chandra Mouli 1688
Vega, Héctor 0483
Vega, Joann 0144, 0365
Vega Cornejo, Gabriel 0401
Vega-Fernandez, Patricia **0418**, **0419**, 1706, 1813, 1829, 2177
Vegas, Laura Pina 2345
Vegas Revenga, Nuria 1904, 2016, 2229, 2265
Vegoe, Amanda 0027, 1786, 1797
Veiga, Maria Eduarda 1407, 1408, 2326
Vejiga, Meriam 0014
Vekeman, Francis 0561, 2689
Vela, Paloma 1096
Vela Casasempere, Paloma 0019
Vela Casasempere, Paloma 0021
Vela Casasempere, Paloma 0269, 0642, 0739, 1171, 1397, 1681, 2290, 2450, 2670
Velasco, Beatriz 2513
Velasco Nuño, Mónica 1620
Velasco Santos, Jorge Isaac 1486
Velasco-Sanchez, David 0496, 2268
Velez arteaga, Deisy Muriel **0902**
Velikova, Tsvetelina **1218**, 2066
Velinova, Maria 0498
Vella, Laura 0423, 1825
Vellón-García, Beatriz **0100**, 0901, 2502, **2599**
Veloza-Morales, Camilo 2023, 2059
Veltishchev, Dmitry 1323
Vencovsky, Jiri 0831, 1211, 1350, 2073, 2346
Vender, Ronald 2374
Venerito, Vincenzo 0177, 0295, 1218, 2066, 2067
Venerus, Alessandra 1552
Vengilote, Ranjini 1143
Venhoff, Nils 0762, **1175**
Venkatachalam, Shilpa 0370, 0371, 1073, 1252, 1617, 1661, **1987**
Venkatesan, Jagadeesh K 1798
Venkatesan, Pravina 0889, 1695
Venkatesh, Ananya 2197
Ventosa, Beatriz 0153, 0728
Ventura, Iazsmin 0164
Venturelli, Veronica 0860
Venuturupalli, Swamy 0034
Vera Bustamante, David 2243
Vera Gutiérrez, Francisco 1195
Vera-Lastra, Olga-Lidia 0596
Verdaguer Faja, Guillem **1620**
Verdugo, Chase **2228**
Vergara, Cristina 0201
Vergara-Dangond, Cristina 1961
Verhaegen, Monique E 0949
Verhoeven, Frank 0099, 0544, **2637**
Verma, Charu 0400
Verma, Priyanka 0965
Verma, Saransh 0447
Verma, Sarthak **0461**, 0533
Verma, Supra 1994
Vernerová, Lucia 1211, 2073
Vernon, Katherine 1767
Veronese, Nicola 0329
Veronese de Souza, Jean Paulo 1293
Veroz, Raul 0271
Veroz González, raúl 0268
Veroz González, Raúl 0270
Veroz González, raúl 2373
Verplancken, Claire 0162
Verschueren, Patrick 0035, 0488, 0528
Vershel, Connor **1410**
Verstappen, Gwenny 0034, 0694
Verstegen, Ruud 1301
Verweyen, Emely 0918
Verztman, Jose Fernando **2316**
Vestin, Holme 0594, 2390, 2647
Vetter, Marion L. 0257
Viala, Clément **0148**
Viapiana, Ombretta 2116, 2592
Vicens Zygmunt, Vanesa 1161, 1162
Vicente-Mínguez, Daniel 1778
Vicente-Rabaneda, Esther 0029, 0518, 2122, 2491
Vicenzi, Marco 0700
Vickers, Amy 0410
Vidal, Michel 1593
Vidal Montal, Paola 0530, 0642, 1382
Vidal ripoll, Judith 2029
Vidal-Montal, Paola 0659, 0749, 2670
Vidal-Ripoll, Judith 0117, 0758
Videira, Taciana 0761
Vidnyánszky, Zoltán 2684
Viegas Brenol, Claiton 1365, 2246
Vieira, Rejane 1407, 1408, 2326
Vieira, Romana 0761
Vieira-Sousa, Elsa 0035
Vierling, Marine 0508, 1683
Vieubled, Margot 1734
Vigone, Barbara 0700, 1840
Vigone, Barbara 2648
Vijay, sharmila 0310
Vila, Diego 2336
Vilá, Luis 1489, 1493
Vilaine, Eve 0618
Vilarrasa, Ariadna 0015
Vilayur, Eswari 0722
Vilchez, Francisco 1943
Villa, Bertha 0663
Villa Soto, Vanya Sofia 0871
Villalba, Alejandro 0089, 2042
Villalba, Jose manuel 0100, 2599
Villalobos, Lourdes 0269, 1171, 1282, 1284
Villanueva Manes, Belen 0205, 0237, 0341, 1274, 2274, 2310
Villanueva Martin, Gonzalo 2410
Villapún Burgoa, Beatriz 2121
Villarreal-Alarcón, Miguel 0248, 2058, 2071, 2072, 2557
Villaverda, Robin 1669, 2125
Villegas, Carlos 1413
Villegas Martinez, Daniela 2222
Villeneuve, Thomas 1200
Villeneuve, Thomas 2510
Villiger, Peter 1626
Vinet, Evelyne 0606, 1475, 1506, 2215, 2222
Vinuesa, Carola 2410
Violette, Shelia 1767, 2033
Viotti-Serra, Jose Marí **0450**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Virag, Bohacsi 2648
Vircks, Janelle 1973
Virtanen, Gerald 2089
Viruel, Luz 1947, 2243
Vis, Marijn 2309
Visconti, Mariachiara 1402
Visintin, Michela 1737
Visman, Ingrid 2359
VISMARA, Enrico 1371
Visocnik, Nina 0732, 0896
Vissink, Arjan 0034
Visweswaraiah, Jyothsna 0987
Vital, Ed 0645, **0654**, **0801**, **1525**, **1526**, 1542, **2393**, 2411, 2601
Vital, Heather 0008, 0987
Viteri Noël, Luis Adrián 1210
Vitlip, Joshua 0987
Vitri, Benedetta 1589
Vittecoq, Olivier 0508, 0516
Viveros, Niccolo 0758
Viveros-Pérez, Niccolo 0639
Vivier, Eric 0907
Vivier, Solange 1858
Vivino, Frederick 1378, 1384
Vizcaya, Cynthia 0559, 1447, 1462, 1463, 1464
VLACHOYIANNOPOULOS, PANAYIOTIS 2232
Vlad, Steven 0501
Vladimirova, Nora **0543**
Vleugels, Ruth Ann 2668
Vo, Amy 0283
Vo, An 0953
Vo, David **2552**
Vo, Hung **0848**, **2314**
Vo, Nhung 0309, 2623, 2625
Voet, Sofie 0907
Vogel, Tiphanie 1820, 1983, 2124, 2129, 2410, 2579, 2620
Voglau, Markus 0386, 1461
Vogt, Kristian 2520
Voiniciuc, Diana 1438, 1449
Vojinovic, Tamara 0676, 0963
Volk, Robert J. 1920
Volkmann, Elizabeth **0247**, 0274, 0883, 1148, 1555, **1564**, **1565**, 1566, 1582
Volkmann, Elizabeth 1584
Volkmann, Elizabeth 2475, 2654
Volkov, Jenell 1563, 2468, 2669
Voll, Reinhard 0508, 1403, 2279
Vollmar, Horst Christian 1934
Vollmer, Lydia 1403
Volpe, Bruce 0947, 0953
von Bergwelt, Michael 2476
von Eckstaedt, Hans 1104
von Krusenstiern, A. Nikolai **0712**
von Scheven, Emily 1704
Vonk, Madelon 0673, 0689, 0692, 1586, 2477
Vora, Jamie 2342
Vora, Rashi **1082**
Vora, Shailee 0009
Vora, Sheetal 0411, 1066, 1976, 1978
Vora, Tania 1182
Vorndran, Zachary 1563, 2468, 2669
Voskuijl, Alexandre 0690, 1560, 1573, 1840, 1860, 1862, 2503
Voss, Anne 2400
Voudouri, Klytaimnistra 0718
Voulgarelis, Michael 0515
Voulgari, Paraskevi V 1439, 1452, 2232
Vounotrypidis, Periklis 2232
Vrablik, Michal 1211, 2073
Vritzali, Eleni 0455, 0590, 0874, 2356
Vrola, Lorenzo 0238
Vu, Shirley 2275
Vu, Vanessa 1643
Vukelic, Milena 1069, 2224
Vuong, Victoria 2278
Vural, Adil **0713**
Vyas, Abhinav 1012
Vyas, Ami **0602**
Vyas, Jatin 2577
Vyas, Prapti 0941
Vyas, Tammy 2577

W

Wacker, jochen 0236, 2695
Wactor, Alex 1696
Wada, Jun 0452, 2244
Wada, Makoto 2523
Wada, Mayuko 1167, 1611, 2212, 2488, 2534
Wade, Jason 0016
Wadsack, Christian 2631
Wafula, Alexander 0160
Wagner, Catriona 0023, 1087, 1831
Wagner, Michael 0415, 1744
Wagner-Weiner, Linda 2126
Wahed, Mishquatul 1355
Wahid, Urooj 1256, 1257
Wahl, Alan 0262
WAHL, Denis 0120, 0121
Wahl, Elizabeth 0446
Wahlund, Paxten 1025
Wainwright, Elaine 1244
Waiter, Gordon 1711
Wajid, Sumbal 0698, 0699
Wajsberg, Julia 1471, **1979**
Wakatsuki, Miyu 0043
Wakiya, Risa 1167, 2488
Wakiya, Risa 2534
Wald, Ron 0722
Waldman, Meryl 1843
Walgreen, Birgitte 0928
Waljee, Akbar 0178
Walker, Bethany **1276**
Walker, Jennifer 0677
Walker, Sarah 1674
Walker, Tessa 0330
Walkington, Virva 2040
Wall, Amanda 0815
Wallace, Beth 0045, **0178**, 0198, 0221, 0222, 0834, 0836, 1314, 1325, 2683
Wallace, Carol 0389
Wallace, Daniel 0034, 0657, 1378, 1384, 1722, 1842, 2416, 2579
Wallace, David 0198
Wallace, Zachary 0992, 1606, 1764, 2509, 2528, 2529, 2530, 2574
Wallace, Zachary 2577
Wallach, Joshua 1925
Wallaert, Steven 0705
Waller, Dylan 0359
Walli, Siraj 0549
Walls, Andrew 2525
Walsh, Jessica A. 0589, 0591, 0592, 1165, 1261, **1445**, 1981, 2330, 2342, 2369
Walsh, Madalyn **1110**
Walsh, Michael 0722
Walsh, Patrick 1780
Walsh, Salome 1092
Walt, David 2574
Walter, Caroline 0903, 2665
Walter-Petrich, anouk 1144
Walters, Heather 0401
Walters, Lynnette 0119
Walters, Matthew J 0057
Walton, Claire 1594, 1608, 1769
Walton, Timothy 2554, 2558
Walton, Zandra E. 0344, 1100
Walunas, Theresa 0624
Walz, Bastian 1601
Wambold, Dylan 2041
Wampler Muskardin, Theresa **2285**
Wan, Emily 1946
Wan, Liyan 2463
Wan, Weiguo 0656
Wanberg, Lindsey 0285
Wang, +Xiaojing 0657
Wang, Andrew 1111
Wang, Annabel 1003
Wang, Annie 0674
Wang, Benjamin 1986
Wang, Bing 2035
Wang, Cenyi 0856, 1971
Wang, Chen 1100
Wang, Cheng 0646
Wang, Chengpan 0915
Wang, Chen-Yu 1870
Wang, Dongmei 0077, 0173
Wang, Fei 0048
Wang, Fei 0785, 0786
Wang, Gang 2689
Wang, Hailin 0005, 0986
Wang, Haiting **2448**
Wang, Haiying 1776
Wang, Hanwei 1532, 2452
Wang, Haopeng 2572
Wang, Hong 0529
Wang, hongying 0301
Wang, Hua 0867
Wang, Huan 0915

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Wang, Hubao 0719
Wang, Huijing 0656
Wang, Jennifer 0425, 2227
Wang, Jiaqi 0375
Wang, Jiaqi 0792, 1130, 1902, 1990, 1995
Wang, Jiaqi 2574
Wang, Jiaqi 2578
Wang, Jingjing 0939
Wang, Jiucun 0102, 1752, 1754
Wang, John 0011, 0012
Wang, Jun 2037
Wang, Junqin 0970
Wang, Kaiwen 2672
Wang, Ke 0939
Wang, Kelsey 0869
Wang, Lai 1739, **1790**
Wang, Lena 0679
Wang, Lida 1523
Wang, Linghua 0273
Wang, Mei-Lun 0501
Wang, Mengyu 0926
Wang, Miaomiao 1776
Wang, Min 0994
Wang, Pan 0517, 1478
Wang, Panpan 0939
wang, Panwen 1726
Wang, Qi 0513, **1113**, 1877
Wang, Qian 0468, 0861, 1208, 1209, 1316
Wang, Qian **1652**
Wang, Qian 1750
Wang, Qiang 1696
Wang, Qing 0887
Wang, Qiong 1776
Wang, Qiong 2562
Wang, Ran 1179
Wang, Ran 2465
Wang, Rixin 2114
Wang, Rong 1725
Wang, Runci **0887**, 2672
Wang, Ruoqiao 0904
Wang, Sanbin 2452
Wang, Shiow-Ing 1017
Wang, Shiyi 0018
Wang, Shu 0838
Wang, Shudan 0223, 2381
Wang, Shun 0906
wang, ting 0876
Wang, Ting 0946
Wang, Ting 1208
Wang, Tingting 0077, **0173**
Wang, Tong 0122
Wang, Tony 1457
Wang, Tracey 0654
Wang, Wei 0069, 0097
Wang, Wei 0316
Wang, Weiwei 0646
Wang, Wen-Hui 0875
Wang, Xiangyu 2353
Wang, Xiaodong 1179, 2672
Wang, Xiaoning 0003
Wang, Xiaosong 0168, 0465, 1747, 1751, 1902, 2235, 2574, 2577, 2578
Wang, Xiaoxing 0078, 0079
Wang, Xin 0926
Wang, Xing 0422, 1669, 2125, 2128
Wang, Xu **0208**
Wang, Xu 0696
Wang, Xuan 2276
Wang, Xudong 0009
Wang, Xue 0048
Wang, Xue 0939
wang, xuebin 0876
Wang, Yali 1776
Wang, Yan **1514**, 1515
Wang, Yanhong 1316
Wang, Yanli 0563, 0564
Wang, Yi 0905
Wang, Yidan **0066**, 1793
Wang, Yifei **1036**
Wang, Yilun 0324, 1146, 2622
Wang, Yiyu 1086
Wang, Yongfu 0468
Wang, York 0288, 0865
Wang, Yuhao 0911, 1776
Wang, Yuqi 1131
Wang, Yuqing 2668
Wang, Yuxi 1165, 2369
WANG, ZHIQIANG 1247
Wang, Zuofei 0775
Wangkaew, Suparaporn 0304
Wani, Rajvi 2546
Wanigasekera, Vishvarani 0815
Waqar-Cowles, Lindsay 2141
Waratani, Miina 1552
Ward, Audrey 1745
Ward, Madeleine 1989
Ward, Michael 1410
Ward, Nicole 1760
Waring, Arshdeep **2203**
Warman-Chardon, Jodi 0294, 2069
Warner, Alberta 1048
Warner, Blake M. 0034, 0506, 0514, 1682, 2233
Warner, Nafisseh 0149
Warren, Richard B. 0555, 0574, 1447
Warrington, Kenneth 0276, 0721, 0747, 0759, 1602, 1626, 1900, 2515, 2531, 2542
Waseem, Zaiya 1720, 2095
Washko, George 1751, 2235
Wassenberg, Siegfried 0338
Wasserman, Amy 0598
Wassif, Heba 0695
Wasson, Christopher 1873
Watad, Abdulla 0570, 1332, 1436
Watanabe, Haruki 0452, 2244
Watanabe, Ryu 0850
Watanabe, Yoshiko 1630
Waters, Yvonne 2077
Waterworth, Dawn 0558
Watson, Tristan 2079
Watts, Gerald 0798
Watts, Richard 1912
Watzl, Carsten 0932, 1876
Wauford, Brian 1696
Wax, Stephen 2293
Way, Michele 2558
Webb, Tana 1276
Webber, Anna 0955, 1590
Weber, Amannda 0218, 1050, 1052
Weber, Brittany **0242**, 0669, 1016, 1166, 1186, 1913, 1957, 2568, 2569, 2608, 2688
Weber, Jeremy M 0274
Weber, Marshall **0352**
Webers, Casper 0588, 2307
Webster, Jonathan 1117
Wechalekar, Mihir **0091**, 0504
Wechalekar, Mihir 0797
Wechalekar, Mihir 0917
Wechalekar, Mihir 0980, 1703
Wechsler, Michael 1594, 1608, 1769, 2515
Wechsler, Roni **1802**, **1803**, 2082
Weedon, Helen 0917
Weeks, Lachelle D. **0260**, 0777, 2663
Wehr, Pascale 0980
Wei, Bo 1515
Wei, Bo 2288
Wei, Hui 0647
Wei, James 0806, **1017**
Wei, Jie 0318, 0324, 1146, 2622
Wei, Kevin 0797, 0798, 0808, 0851, 0890, 0925, 0980, 1696, 1703, 1846, 2233, 2644, 2668
Wei, Lingli 0077
Wei, Qi 1457
Wei, Shixiong 1316
Wei, Wei 1220, 2447
Wei, Weijun 1956
Wei, Wen 1138
Wei, Xiaohan 0124, **0142**, 0856, 1971
Wei, Yuanli 0077, 0173
Weidenmüller, Matthias 1205
Weidl, Marton 1136
Weigert, Claire 0058
Weigt, S. Samuel 1872
Weilg, Pablo 2314
Weil-Verhoeven, Delphine 0099
Weimann, Gerrit 1662
Weinberg, Clarice 0159
Weinblatt, Michael 0449
Weinblatt, Michael 0465
Weinblatt, Michael **0473**
Weinblatt, Michael 1644, 1992, 2320, 2607, 2614
Weiner, Stefan 1175
Weiner, Sveta 2082
Weinheimer, Adam S. **0888**
Weinmann-Menke, Julia 2696
Weinstein, Arthur 0657
Weinstein, Elena 0196
Weirauch, Matthew 1826

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Weis, Emma **0076**
Weis, Joachim 1206
Weisberg, Reid 1310
Weiser, Peter 1277
Weisleder, Hillary 1944
weisleder, noah 0999, 2386
Weisman, Alanna 2079
Weisman, Michael 0240, 0541, 0657, 1086, 1410, 1673, 1842, 2600
Weiss, Arthur 0055
Weiss, Jackie **0293**
Weiss, Jennifer 0411, 1066, 1226, 1827
Weiss, Matthew 0913, 0930
Weiss, Noel 2251
Weiss, Pamela **0390**, 0412, 0428, 0918, 1298, 1434, 1815, 2156, **2677**, **2680**
Weissman-Tsukamoto, Rachel 0947, **0953**
Welbrink, Paula 0075
Welch, Joshua 2233
Welch, Sean 0763
Wells, Athol U. 1589
Wells, Courtney 1275
Welsh, Laura 2089
Welsing, Paco 0176, 0689
Welter, Emma 1723
Wen, Chunyi 1247
Wen, Jun 1357
Wen, Zeqin 0324, 2622
Weng, Angel 1842
Weng, Chunhua 1310
Weng, Rachel 1668
Wennbo, Haakan 1442, 2351
Wenzel, Joerg 0660
Werner, David **2604**
Werner, Ellen M. 0289
Werner, Rachael **0952**
Werth, Victoria 0278
Werth, Victoria 0289, 0660, 0802
Werth, Victoria 0916, 1474
Werth, Victoria 1777
Werth, Victoria 1846, **1852**, 2233
Werth, Victoria 2428, **2435**
Westbrook, Simon **0852**, **1804**, 2081
Westerland, Maggie 1643
Wetten, Sally **0169**
Wetzel, Sarah 2084, 2096
Wetzel, Sarah 2098
Wetzel, Sarah 2624
Weyand, Cornelia 0751
Whang, Jennifer 2466
Wheeler, Austin **0022**, 0045, 0076, 0834, 1308, **1749**, **2585**, 2683
Wheless, Lee 1888
Wherry, E. John 1815
Whitall Garcia, Laura 0611, 0612, 0613, 0629, 1550
White, Daniel K. 0336, 0771, 1637, 1649, 2084, 2096, 2098, 2605, 2624
White, Darrin 0725
White, Douglas 2362
White, Katy 1454, 2352
White, Nicholas 1374
White, Yvonne 2468
Whiteford, Grace 2455
Whiteman, Leah 2668
Whitfield, Michael **0811**, 0812, 0845, **0846**, 1870, 2494
Whitmarsh, Mark 0991
Whitney, Deborah 2146
Whittaker, Jayla 0063
Whitted, Caleb 1637
Whooley, Mary 0220, 2617, 2618
Wible, Daric 0009
Wichuk, Stephanie 0531, 2335
Wickersham, Pendleton 1675, 2278
Wickham, Tom 0981
Wiebe, Edgar **0342**, **0343**, 0471, 1010, **2109**, **2110**, **2595**
Wieber, Cortney M. 2301
Wiechers, Lara 1206
Wieczorek, Grazyna 0903
Wieczorek, Maud 0314
Wiek, Dieter 0152
Wiekowski, Maria 1327
Wiemann, Constance 2620
Wiesendanger, Margrit 0843, 1529
Wigerblad, Gustaf 0118
wigerblad, Gustaf 0301
Wigerblad, Gustaf 2580
Wigerblad, Gustaf 2700
Wigley, Fredrick 1725
Wigton, Eric 1000
Wijsenbeek, Marlies S 1662
Wilasrusmee, Kittikorn 1118
Wilcox, Douglas **0184**
Wilcox, Sara 0766
Wild, Stefan 0919
Wilde, Benjamin 1157
Wilfong, Erin 0274, **2669**
Wilhalme, Holly 1564
Wilhelm, Artur 0471
Wilhelm, Sophie 1306, 1327
Wilk, Nikola 0294, **2069**
Wilkenson, Mary 1073
Wilkerson, Jesse 0303
Wilkins, Owen 0812
Wilkinson, Matt 1251
Willems, Tine 2692
William, Alexander Bae 0912
Williams, Aimee 0652, 1915
Williams, Asia 0181
Williams, Christopher 1657
Williams, David 1244
Williams, Edith 1232, 1638
Williams, Frances 1338
Williams, Jazmean 1563, 2468, 2669
Williams, Jessica 1917
Williams, Juliet 0913, 0930
Williams, Katherine 0421
Williams, Kenneth 1984
Williams, Kevin Jon 1474
Williams, Leanne 1306
Williams, Michael 1786
Williams, Rex 0494
Williams, Sandra **1655**
Williams, Zachary 1606, 2508, 2509
Williamson, Patrick **2009**
Williamson, Taylor 0188
Willis, Emily 1291
Willis, Lisa 0969
Willis, Rohan 0120, 0121, 0860
Wilsmann-Theis, Dagmar 0875
Wilson, Avril 2128
Wilson, Caroline 0711, 2398
Wilson, Cherish **0181**, 0211, 0217, 0220, 1250, 2617, 2619
Wilson, David 0893
Wilson, Dulaney 0617, 1079, 1082, 1492
Wilson, Eve 2176
Wilson, F. Perry 0674
Wilson, Florence 2500
Wilson, Jennifer 1193, 1199, 2259
Wilson, Lorena **1169**
Wilson, Michael 1279
Wilson, Nicole 0500
Wilson, Otis 0818
Wilson, Robert 1672
Wilson, Ruth 2561
Wilson, Timothy 0763, **0833**, 2480
Wimmel, Ted 1978
Winchester, Robert 0899
Wincup, Chris 1263, 1906
Winden, Kellen 1004
Wingard, Jeffrey 0947
Winkelman, Warren 1155
Winkler, Jürgen 0809, 0974
Winter, Deborah Rachelle 0066, **1227**, 1362, 1793, 2430
Winthrop, Kevin 0473, 0895
Wioland, Catherine 0903, 2665
Wipfler, Kristin 0292, 0789, **1021**, 1196, 1216
Wipperfurth, Andrea 0218
Wirestram, Lina 2401
Wirsching, Andreas 0236, 0641, 1537, 1697, 2442, 2641, 2695
Wirth, Jena 0952
Wise, Kelly 0413
Wise, Leanna **0661**, **2198**, **2199**, 2201
Wiseman, Marni 0523
Wissmar, Jenny 1545
Wither, Joan 1285, 1742
Withers, Mellissa 2198
Witowska, Julia **2149**
Witte, Thorben 1010
Witte, Torsten 0034, 1729, 2648
Witteles, Ronald 1664
Wittenberg, Elliott 0987
Wittgren, Sofia 0525
Wittoek, Ruth 0035
Wobma, Holly 1810, 1822, 2124
Woessner, Juliette 0756
Wofsy, David 1240, 2600

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Wojteczek, anna 0673
Wolf, Bethany 1638
Wolf, Monika J 1206
Wolfarth, Bernd 2595
Wolfe, Rachel 1047
Wolfgang, Marc 0016
Wolfreys, Alison 2631
Wolin, Sandra 1655
Wolski, Marcin 2100
Wolters, Paul 0976
Wolzen, Amber 1726
Womack, Julie 2114
Won, Hong-Hee 0571
Won, Kyoung Jae 0081
Wong, Alvin 1121
Wong, Angus 1367
Wong, Carol 0663
Wong, Christopher 1209
Wong, Ernest 1356
Wong, Heidi 1119
Wong, Huon 2057
Wong, Jason 0839
Wong, Lilly 0663, 2454
Wong, Vincent **0504**, 0917, 0980
Wong, Wendy 0361
Woo, Jennifer **1690**
Wood, Rebecca 0509
Wood, Ronald 1753, 1940
Wood, Samuel 2393
Wood, Tammara 0845, 0846
Woodford, Curtis 1725
Woodgate, Roberta 1494
Woodhead, Felix 0259
Woodle, E. Steve 2600
Woodridge, Laurel 1851
Woods, Adrianne 1037
Woods, Alexis 1992
Woods, Alexis 1997
Woods, Alexis 2003
Worden, Joseph 0855
Wordsworth, Paul 0104
Workman, Lisa 2133
Worley, Karen 1083, 1533, 1534, 1536, 2453, **2456**
Wratten, Samantha 0357
Wright, Christian 0774, **1831**
Wright, Christine 1136
Wright, Daniel 1125
Wright, Grace 0557, 1507
Wright, Ian 1832
Wright, Nicole 0157
Wright, Tracey 0119, 2410
Wright Drakesmith, Cynthia 1909
Wruble Clark, Mattia 0263
Wu, Aaron 1764
Wu, Benedict 0223
Wu, Bin 0646
Wu, Chanyuan 1316
Wu, Chenyuan 1752
Wu, Chia-Lung 0086
Wu, Chien-Sheng 1346
Wu, Chun 0873, 2694
Wu, chunmei 2465
Wu, Di 0646
Wu, Dongmei 0468
Wu, Emily 1700, 2226
Wu, Emma 1842
Wu, Eveline **0404**, 0824, 1669, 1745, 2125, 2128, 2462
Wu, Fangyun 2200
Wu, Guanhao 0519
Wu, Guojin 0005, 0986, 1001
Wu, Hai 0994
Wu, Hao 0918
Wu, Hongke **1045**, 1054, 2566
Wu, Jian 0876
Wu, Jian 0994
Wu, Jianhong 0077, 0173
Wu, Jianming 0040, 0041
Wu, Jianzhou 0856, 1971
Wu, jiaxin S. 1887
Wu, Jing 0318
Wu, Lijun 0468
Wu, Megan 0674
Wu, Michael 0273
Wu, Min 0082
Wu, Ming 2381
Wu, Qi 0093
Wu, Qi 0972
Wu, Qi 2494
Wu, Qiong 0775
Wu, Roy 2011, 2012
Wu, Rui 2464
Wu, Song 1395, 2046
Wu, Tao 2245
Wu, Wanlong 2672
Wu, Wei 0265
Wu, Xiaohao **0914**
Wu, Xinglin 1303, 1828
Wu, Xuan 2641
Wu, Yang 1208, **2597**
Wu, Yeong-Jian Jan 0595, 2469
Wu, Yin 1115
Wu, Ying 1457
Wu, Yiyuan 0308, 0316, 0785, 0786, 2629
Wu, You 1104, 1105, 1718
Wu, Yuyu 0906
Wu, Zhihai 0906
Wu, Ziying 0324, **1146**
Wulansari Manuaba, Ida Ayu Ratih 2004
Wulffraat, Nico 0389
Wullum, Laus W 2101
Wung, Peter 2641
Wunsch, Hana 1211, 2073
Wunsch, Leah 2499
Wurst, Keele E. **0154**, 0169
Wyrosdick, Brooke 1276
Wysham, Katherine 0022, 0045, 0221, 0222, 0328, 0446, 0462, 0834, **0836**, 1238, 1308, 1314, 1325, 1746, 1946, 2084, 2096, 2098, 2252, 2624, 2634, 2683

X

Xanthavanij, Nutchapon 1187
Xavier, Christopher **0717**
Xavier, Ramnik 0032
Xenakis, Jason 0357, 1889
Xi, De 0892
Xia, Can 2672
Xia, Jinglu 1776
Xia, Xuyang 0051
Xia, Yunwei **0933**
Xia, Zhiyu 1038
Xiang, Chunyan 0887
Xiao, Fei 1361
Xiao, Qian 1696
Xiao, Qian 2600
Xiao, Rui 0045
Xiao, Rui 0834, 1298
Xiao, Rui 1434
Xiao, Rui 2084
Xiao, Rui 2096, 2098
Xiao, Rui 2624, 2677
Xiao, Rui 2680
Xiao, Rui 2683
Xiao, Teresa **0172**
Xiao, Yadan 2622
Xiao, Yanhua 0809, 0974, 0975
Xiao, Yuanyuan 0501
Xie, Changling 2463
Xie, Dongxing 0324, 2622
Xie, Fenglong 0185
Xie, Fenglong 0369
Xie, Fenglong 1027, 1084, 1351, 1387, 1629, 1661, 1997, 2068, 2119, 2539
Xie, Jiangnan 0102
xie, Junqing 1146
Xie, Qibing 0051, 0649, 2061
Xie, Wei 2452
Xie, Xianhong 1974
Xie, Yue 1532, 2452
Xin, Xiaohui 0194
Xing, Lianping 1808
Xing, Yi 0008
Xiong, Huizhong 0082, 0905, 0906
Xiong, Siying 0173
Xiong, Yao 0082, 0905, 0906
xu, Antao 1179
Xu, Dong 0861
Xu, Gary 1938
Xu, Heng 0051
Xu, Jason 0646
Xu, Jian 0468, **2353**
Xu, Jiaqi 1728
Xu, jin 1158
Xu, Li 0429
Xu, Liling **0132**
Xu, Meilin 0975
Xu, Mengze 1514
Xu, Mousheng 1833
Xu, Qiang **1114**, **1799**
Xu, Qiping **2586**
Xu, Qiuhong 1517

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Xu, Shengqian 0468
Xu, Shike 0322, 1895
Xu, Simin 0093
Xu, Weihao 0011, 0012
Xu, Wenwen **1663**
Xu, Wenwen 1956
Xu, Wenwen 2672
Xu, Xiaoou 1006
Xu, Xinyu 2353
Xu, Yawei 0939
Xu, Yihua 1083
Xu, Yilin 0751
Xu, Ying 1920
Xu, Zhijin Carrie 0321
Xu, Zihao 2570
Xue, Chengfeng **0939**
Xue, Jing 0468, 1131
Xue, Shengjie 0646
Xue, Yu 0473
Xue, Yu **2013**, **2014**
Xue, Yuan **2288**
Xynogalas, Ioannis 1439

Y

Yılmaz, Figen 2322
Yaakoub, Roukaya **0912**
Yaari, Shlomit 0675
Yachi, Pia 0473
Yacoub, Rania 0264
Yacuzzi, María Silvia 2405
Yacyshyn, Elaine 1607
Yagnik, Karan 1071
Yajima, Nobuyuki 2523
Yaku, Ai **1553**
Yaku, Hidenori 1553
Yalavarthi, Srilakshmi 0115, 0127
Yalavarthi, Srilakshmi 0131, 0134, 0143
Yalavarthi, Srilakshmi 0857
Yalavarthi, Srilakshmi 0858, 0859
Yalavarthi, Srilakshmi 1623, 2451
Yalcin Mutlu, Melek 2613
Yalcindag, Ali 1989
Yalcinkaya, Yasemin 0135, 0290
Yam, Ka Ki 1202
Yamada, Hirotaka 0062
Yamada, Kana 1538
Yamada, Kenji 1732
Yamaguchi, Koichi 1201
Yamaji, Ken 0106, 0521
Yamaji, Yu 0521
Yamamoto, Aruto 0043
Yamamoto, Shotaro 0764
Yamamoto, So 1509
Yamamoto de Almeida, Luciana **1624**, 2533
Yamamura, Masahiro 1419
Yaman, Reena **0300**, **1255**
Yamane, Takashi 0284, **1610**
Yamashita, Hiroyuki 0043
Yamazaki, Hayato 2362
Yamazaki, Makoto 0052
Yan, Kunmin 0994
Yan, Pearlly 0719
Yan, Shunqi 1138
Yan, Shunshun **0313**
Yan, Terry **0649**
Yan, Xiaoqiang 0646
Yan, Yuxi 0013, 0926
Yanai, Ryo 2523
Yang, Bing 0018
Yang, Chih-Hsiang 0766
Yang, Chunnei 2463
Yang, Emily 0423
Yang, Fengjuan 1497
Yang, Guojiao 1532
Yang, Huaxia **1728**
Yang, Jason 1481, **2001**
Yang, Jeffrey 2571
Yang, Joseph **1924**
Yang, Jun 0939
Yang, Jun 1828, 2037
Yang, Jung Ho 1432
Yang, Kui-Min 2245
Yang, Letitia 0055
Yang, Lin **0994**
Yang, Lingjian 1776
Yang, Min 0649
Yang, Monica 0846
Yang, Mu 1959, 2609, 2691
Yang, Nicole 1016, 1020
Yang, Pingting 0649
Yang, Seojin 1748
Yang, Shaoying 2448
Yang, Shen 0881
Yang, Tiffany 2175
Yang, Tuo 0324, 2622
Yang, Weihong 2409
Yang, Xi 0429
Yang, Xi 1174
Yang, Xi 1828, **2157**
Yang, Xiaoqing 1992, 1994
Yang, Xiaoyun 0679
Yang, Xing 0905
Yang, Xinli 1036, **1190**
Yang, Xiwei **0278**, 1474, 2428
Yang, Yan 2011, 2012
Yang, Yang 0995, **1004**, 1005
Yang, Yangyuna 0022, 1659, 2661
Yang, Yanlong 1361
Yang, Ya-Wen 0558, 0562
Yang, Yeon Suk 0872
Yang, Yifan 2353
Yang, Yifei 0998
Yang, Ying 2245
Yang, Ying Heidi 0787
Yang, Yingli 0048
Yang, Zhao 1254, 2189
Yang, Zheyuan 1552
Yang, Zhixia 0142, 0856, 0964, 1971
Yang, Zidan 0324, 2622
Yang, Zijing 1906
Yanpiset, Panat 1137
Yao, Changfu 0085
Yao, Haihong 0595
Yao, Haihong 1515
Yao, Haihong 2464
Yao, Jianan 0994
Yao, Mina 0069
Yao, Qingping 1395
Yao, Qingping **2046**
Yao, Ranran 0132, 1510
Yao, Songyuan 0506
Yao, Xu 1762
Yao, Yi 0016
Yao, Zhen 0277
Yap, Desmond Yat-Hin 1887, 2697
Yap, Qai Ven 0378, 1121
Yapp, Clarisse 0433
Yarandi, Shadi 0257
Yasaka, Ken 0904
Yasaka, Ken **1692**
Yasin, Shima **1670**
Yasin, Shima 1670, 2128
Yasuda, Noriaki 0284, 1610
Yasunaga, Hideo 2449
Yates, Sean 0129
Yatim, Nader 2584
Yau, Anthony 0711
Yaun, Neal 1048
Yazbek, Michel 1407, 1408, 2326
Yazdany, Jinoos 0189
Yazdany, Jinoos 0217, 0219
Yazdany, Jinoos 0368, 0625, 0637
Yazdany, Jinoos 0655
Yazdany, Jinoos 0817
Yazdany, Jinoos 1042
Yazdany, Jinoos 1336, 1504, 1526
Yazdany, Jinoos 1639, 1640, 1641, 1657
Yazdany, Jinoos 1886
Yazdany, Jinoos 1972, 2619
Yazdany, Jinoos 2634, 2645, 2646
Yazici, Ayten 0133
Yazici, Hasan 2543
Yazici, Yusuf 2083, **2626**
Yazisiz, Veli 0430, 0779
Yazji, Sarah 1411
Ye, Carrie 1103
Ye, Jian 0003
Ye, Jing 0324
Ye, Kezhen 0018
Ye, Shuang 0656, 0887, 1179, 1663, 1956, 2448, 2465, 2672
Ye, Wei 0915, 0998
Ye, Xiaolan 0578, 1453, 2342, 2367
Ye, Yan 2465, 2672
Yee, Jacqueline 0257
Yee, Jeong 1019, 1709, **1896**, 2572
Yee, John 1193, 1199, 2259
Yee, Philip 0692
Yee, Philip 0847
Yee, Philip **2496**
Yee, Sow Ling 0194
Yeghiazaryan, Anna 0779

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Yeh, Ann 1285, 1742
Yeh, Fu-Chiang 2469
Yeh, Li-Tain 1138
Yelnik, Cecile 2655
Yen, Eric 1905
YEO, JINA 0910
Yeo, Siaw Ing **0194**
Yerram, Keerthi vardhan 0424, 1472
Yeudall, Scott **1117**
Yeung, Christine 0725, 2144
Yeung, Jensen 0565
Yeung, Rae 0392, 0821, 0918
Yi, Esther **0357**, **1889**
Yi, Isabella 1652
Yi, Mingyang 1759
Yi, Simin 1776
Yildirim, Tolga 2043
Yildirim-Toruner, Cagri 0411, 1066, 1978
Yildiz, Adalet Elcin 1188
Yildiz, Halil 1592
YILDIZ, Mehmet 0390
Yildiz, Seda **1246**
Yilmaz, Aysenur 0778
Yilmaz, Seref Rahmi 2043
Yin, Geng 0051
Yin, Hanlin **1865**
Yin, Michael T. 2114
Yin, Peng 1316
Yin, Qianqian **0998**
Yin, Songlou 2452
Yin, Yue 0175, 1058
Yingchoncharoen, Pitchaporn **1137**
Yingchoncharoen, Pitchaporn 1319, 2420
Yinh, Janeth 0501, 0813, 1099, 1101, 1959, 2164, 2550, 2551
Yip, Wing-Ho 1589
Yiphyo, Le 0800
Yndestad, Arne 1336, 1444, 2068
Yockey, Laura J. 0344, **0992**, 2530
Yoder, Sean 0002
Yokogawa, Naoto 2225
Yokoji, Kana 1165, 2369
Yokose, Chio 0037, 0813, 1032, 1130, 1990, **1995**, 2008
Yokota, Kazuhiro 0084
Yomogida, Kentaro 0819, 1824
Yomono, Keina **1574**
Yoo, Bin 1372, 1373, 2431
Yoo, Bongin 0650, 0665
Yoo, Hakje 0548
Yoon, Lara **1727**
Yoon, Soyoon 2431
Yoon, Stephanie Suh Kyung 0923
York, Kate 1674
York, Michael 0848, 1481
Yoshida, Akiko 1772
Yoshida, Akira 1212
Yoshida, Hiroto **0781**
Yoshida, Shuhei 1509
Yoshida, Takeshi 1204
Yoshida, Tsuneyasu 1857
Yoshida, Yusuke 0773
Yoshifuji, Hajime 0773, 1630, 1772, 1857
Yoshimoto, Keiko 0052, 0781
Yoshitomi, Hiroyuki 0850
You, Fengtao 0994
Young, Amber 2451
Young, Andrea 2063
Young, Arissa 1565
Young, Arissa 1584
Young, Cammie 2619
Young, Jami F. 1298
Young, Julie 0193
Young, Kelly 1760
Young, Kendra 1842
Young, Kristen **2184**
Young, Neal 2700
Young, Nicholas 0999
Young, Sarah 0317, 1264
Youngchild, Britney 1050
Younis, Shady 0316, **1119**
Yousefian, Schayan 0932
Youssef, Johnny 2228
Yousuf, Basmah Fayaz 0163
Yu, Alec 1193, 1199, 2259
Yu, Chen 0861, 1316, 1750
Yu, Cunjing 0277
Yu, Faye **2297**
Yu, Guojian 0646
Yu, Haiguo 1828
Yu, Hui 0174, 1181
Yu, Jing 2013, 2014
Yu, Jonathan **2146**
Yu, Katharine 0014
Yu, Lan 2483
Yu, Likai 0646
Yu, Minyi 1820
Yu, Qinghong 0649
Yu, Quan **0911**, **1776**
Yu, Shuyi 0124, 0142, **0856**, 0964, 1971
Yu, Steven 0054, 0055, 0110
Yu, Steven 0871
Yu, Wendy 0014
Yu, Xia 0832
Yu, Xiaofu 0468
Yu, Xiaoshan 0939
Yu, Xinran 2572
Yu, Yue 1726
Yu, Zu-Xi 0945
Yuan, Guogang 0906
Yuan, Hongyu 0651
Yuan, Jianping 2696
Yuan, Jijun 0908
Yuan, Qizhi **1541**
Yuan, Ruoxi 0058
Yuan, Victor 0501
Yuan, Xinran 0519
Yuan, Xueting **0861**, 1750
Yuan, Yuan 0277
Yuce, Busra 0778
Yue, Jian 1668
Yuksel, Husnu Mert 2667
Yung, Susan 2697
Yuwen, Hui 0986

Z

Zaba, Lisa 1119
Zabotti, Alen 0576, 1680, **2339**
Zabrocki, Piotr 0960
Zacarias, Andrea 0426
Zachariae, Claus 1166, 2608
Zacharopoulou, Maria 1934
Zack, Debra 0663
Zack, Debra 1270, 2454
Zaenker, Michael 2279
Zagouras, Alexia 1664
Zahn, Carleigh 0883
Zahn, Carleigh 1555
Zahn, Carleigh 1563, 1566, 1582
Zahn, Carleigh 2475, 2492
Zahn, Carleigh 2498, 2654
Zai, Gwyneth 1281
Zaiss, Mario 2279
Zajt, Kamil K 1206
Zak, Rochelle 1378, 1384
Zak, Stephen 0598
Zakem, Jerald 1508, 2392
Zakharia, Yosef 1110
Zakine, Eve 1339
Zaknoun, Melodie 0936, 0937, 0938
Zala, Urvi **1546**
Zaman, Ramiza 0799
Zamani, Michael 0674
Zaminski, Devyn 1240
Zamora, Leonid 0595
Zamora, Natalia 1422
Zamora Medina, María Del Carmen **2218**
ZAMORA MEDINA, MARIA DEL CARMEN **2632**
Zamora-Smith, Alexandra 2392
Zanatta, Elisabetta 0702
Zanatta, Elisabetta 0879
Zanatta, elisabetta 1562
Zang, Sitian **1510**
Zangenah, Nikki 0687
Zapke, Sonja 1157
Zapparoli, Busisiwe 1285, 1742
Zarfeshani, Aida 0947
Zarin, Payam 0981
Zarzoza Mendoza, Imelda Cecilia 1841
Zas, Raquel 0271, 0496, 2268
Zas Vaamonde, Raquel 0270
Zavacky, Emma 0765
Zavada, Daniel **1350**, **2346**
Zavada, Jakub 0543
Zayed, Mostafa 2337
Zazzetti, Federico 0596, 0621, 0623, 1376, 1377, 1486, 1491, 1530, 1878, 1899, **2060**
Zeballos, Francisco 2336
Zeft, Andrew 0401, **1809**
Zeger, Scott 1028, 1037
Zeid, Julia Nicole 0890

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Zeiger, Joanna **1046**
Zeleznik, Hallie 0765
Zell, JoAnn 2205
Zeltser, Roman 2490
Zen, Margherita 1531
Zeng, Chang 2486
Zeng, Chao 0318, 0324, 1146, 2622
Zeng, Fanxin **0077**, 0173
Zeng, Fanxin 2589
Zeng, Feng 2408, 2409
Zeng, Hu **1726**, 2384, 2649
Zeng, Rachel 1205
Zeng, Ruoheng **2703**
Zeng, Xiaofeng 0468
Zeng, Xiaofeng 0861
Zeng, Xiaofeng 0874, 0876
Zeng, Xiaofeng 1316, 2597
Zeno, Braden **0651**, 0999, **2386**
Zerad, Nathaniel 0738, 0776
Zernicke, Jan 0471
Zhai, Guihua 2124, 2134
Zhai, Yujia 1515
Zhan, Yuan **0976**
Zhang, Baoshan 0404
Zhang, Birong 1807
Zhang, Bozhen 0994
Zhang, Chao 0713, 2515, 2702
Zhang, Chenzhu 2697
Zhang, Chongqi 0915
Zhang, Danting 0656
Zhang, Danting **1887**
Zhang, Dingyao 1762
ZHANG, Dong **1833**
Zhang, Fan 0033, 0774, 0889, 0890, 1695
Zhang, Guofang 2353
Zhang, He 2376
Zhang, Hongwei 0876
Zhang, Jeremy 1110
Zhang, Jialei 1036
Zhang, Jian 1645
Zhang, jianmin 0861
Zhang, Jie 0077
Zhang, Jingyi 1027, 1997
Zhang, Jingyi 2119
Zhang, Jingyuan 1158
Zhang, Judy **0371**
zhang, Junlong 2061
Zhang, Lan 1316
Zhang, Lifan 0208
Zhang, Lifang 1081
Zhang, Lifang 2195
Zhang, Lijun 0879
Zhang, Lin 0985
Zhang, Lin 2451
Zhang, Lin 2598
Zhang, Lingxiao 0599, 0804, 1467, 2377
Zhang, Lixia 1367
Zhang, Liyun 0876
Zhang, Meng 0683, 0883, 1861
Zhang, Mengrui 0914, 1693
Zhang, Ming 0309, 0323, **2562**, 2623, 2625
Zhang, Mingce 0039
zhang, mingyang **0950**
Zhang, Mingzeng 0945
zhang, Na 1220, 2447
Zhang, Nianyi 1036
Zhang, Ning 2013, 2014
Zhang, Ping 0994
ZHANG, QIANRU **0168**
Zhang, Qianru 0465, 1343
ZHANG, QIANRU **1747**
Zhang, Qiyao 0939
Zhang, Quanbo 1132, 2589
Zhang, Ray 1370
Zhang, Ruixia 1761
Zhang, Shangzhu 0851, 0876, 2597
Zhang, Tingting 1991, 1993
Zhang, Tracy 1306
Zhang, Weihua 0173
Zhang, Weiya 0324, 2622
Zhang, Weiyi 0003
Zhang, Wen 0279, 1036, 1163, 1190, 2019, 2020
Zhang, Wenwen 1155
Zhang, Xiao **1002**
Zhang, Xiaojin 1776
Zhang, Xiaojing 1220
Zhang, Xiaomin 0468
Zhang, Xiaoping 0018
Zhang, Xiaoying 0647
zhang, xiaoyue 1642
Zhang, Xiaozhong 1327
Zhang, Xin 1508, 2392
Zhang, Xinyuan 1338
Zhang, Xuemei 2680
Zhang, Xue-Mei 0490
Zhang, Xuetao 1725
Zhang, Yan **1003**
Zhang, Yi 0913, 0930
Zhang, Yi-Fang 1114
Zhang, Ying 2611
Zhang, Yinlian 0109, 1761
Zhang, Yue 2293
Zhang, Yun **0977**
Zhang, Yun 1006
Zhang, Yuqing 0318, 0324, 0599
Zhang, Yuqing 1146
Zhang, Yuqing 2622
Zhang, Zhenrui 2528
Zhang, Zhimin 0082, 0905, 0906
Zhang, Zhiyong 0429, 1828
Zhang, Zhong-Yin 0976
Zhang, Zhuoli 0120, 0595, 0649
Zhao, Hui 1429, 1920
Zhao, Jay 0011, 0012
Zhao, Jinxia 0647
Zhao, Jinyi **2583**
Zhao, jiuliang 0861
Zhao, Jiuliang 1316
Zhao, Junfang 2462
Zhao, Lidan 0208
Zhao, Liling 2448
Zhao, Lin Pierre 1339
Zhao, Liwei 0734
Zhao, Lucy 2563
Zhao, Megan 0159
Zhao, Ming 1762
Zhao, Mingjun 1776
Zhao, Quanju 1833
Zhao, Shaofei 0776, 0895
Zhao, Wei 2454
Zhao, Weihan 0776, 0895
Zhao, Xiaodong 0429, 1828
Zhao, Xiaofeng 0013, 0926
Zhao, Xing 0646
Zhao, Xuesen **0174**
Zhao, Yi 0876
Zhao, Yin 1220, 2447
Zhao, Yongdong 2147
Zhao, Yongdong (Dan) 0186, 0422, 1149, 1669, 2125, 2128
Zhao, Yuanhao 2157
Zhao, Zhangyi 1865
Zhao, Ziyan 0913, 0930
Zharkov, Artem 0585, 1459
Zheng, Mai 2353
Zheng, Qian **2464**
Zheng, Qiuhao 1642
Zheng, Wenjin J 0883
zheng, zhaohui 0468
Zheng, Zhaohui 2464
Zheng, Zhaohui 2611
Zheng, Zihao 0073
Zheng, Zilan 1816, **2158**
Zhi, Helen 2697
Zhi, Langxian 0809, 0975
Zholobova, Elena 0403
Zhong, Enhong 0082
Zhong, Katherine 1016, 1957, 2568, 2569
Zhong, Linrui **1132**
Zhong, Xuanfan 0646
Zhou, Baijun 0599, 2211
Zhou, Bei 0562, 2368
Zhou, Bin 0517
Zhou, Bin **1478**
Zhou, Dongmei 2452
Zhou, Huan 1532, 2452
zhou, Jiaxin 1036, 1190
Zhou, Jiayan 0024
Zhou, Jiliang 1760
Zhou, Jin Xuan **1290**
Zhou, Kangmin 0013
Zhou, Liqing 2376
Zhou, Mingxuan 0876
Zhou, Minyun **0013**, **0926**
Zhou, Qing 2037
Zhou, Shuaixiang 0082, 0905, 0906
Zhou, Simon 0868
Zhou, Tiancheng 0856, 1971
Zhou, Wenxian **0065**, 0921, 0924, 1314, 1650, 1774, **1779**

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Zhou, Xi 0145
Zhou, Xiang 2233
Zhou, Yali 1532
Zhou, Yali 1776
Zhou, Yali 2452
Zhou, Yan 1876
Zhou, Ying 1361
Zhou, You 1807
Zhou, Yuechen 1725
Zhou, Yuting 1303
Zhou, Zhenwei 1963
Zhou, Zhenyuan 0277
Zhou, Ziyue 1728
Zhu, Changsong 1524
Zhu, Chenjuan 0082
Zhu, Jing 0077
Zhu, Jinyu 0997
Zhu, Jordan 0005, 0986, 1001
Zhu, Kaiding 1993
Zhu, Kaixuan 0939
Zhu, Lei 0141
Zhu, Linda 0731
Zhu, Lingjiang 1131
Zhu, Peng 0003
Zhu, Shihao 0974, 0975
Zhu, Shunwei 0013, 0926
Zhu, Xiaoting 0077
Zhu, Xingxing 1726
Zhu, Yan 0005
Zhu, Yonghong 2641
Zhu, Yupeng 1776
Zhu, Yuqing 0939
Zhu, Yuyang 0399
Zhu, Zhenping **0018**, **1006**
Zhu, Zhu 1696
Zhuleku, Evi 1910
Zhuo, Dachun **0102**, 1754
Zi, Kaiyuan 0922
Zia, Ayesha 0119
Ziade, Nelly 0177, 0600, **1930**
Zickuhr, Lisa 2162, 2165, 2180
Ziegler, Shira 0865
Zimmer, Sebastian 0892
Zimmerman, Haley **0292**, 1196
Zimmermann, Francois 0706
Zincavage, Rebekah 1259
Zischka, Hans 1206
Zisman, Devy **1436**, 2306
Zlotosch, Mary 0009
Zong, Wenyue 1776
Zordan, Jérémy 1200
Zorzi, Federico 1127
Zou, Angela 0798
Zou, Bing 1776
Zou, Fang-Shu 1114, 1799
Zou, Hejian 2013, 2014
Zou, Qinghua 0077
Zou, Xiaowen 0003
Zou, Yao-Wei 2245
Zoupidou, Konstantina 1452
Zschüntzsch, Jana 1206
Zu, Lilu 1752
Zuñiga Corrales, Katiuzka 1486
Zuber, Jeffrey 1061
Zubillaga Azpiroz, Elena 2107, 2108
Zubrzycka-Sienkiewicz, Anna 0484
Zueger, Patrick 0738
Zugmaier, Gerhard 2476
Zulfiqar, Aayet 1539
Zulfiqar, Beenish 1061
Zulfiqar, Fizza **1012**
Zumaquero, Esther 1696
Zumbo, Paul 0515
Zuniga-Vera, Andres 0496, 2268, 2591
Zuo, Yu (Ray) 0115, 0121, 0126, 0127, 0131, 0134, 0143, 0822, 0857, 0858, 0859, 1623, 1740
Zurawski, Jonathan 0184
Zurbach, Anais 0990
ZURITA PRADA, PABLO 0107
Zuscik, Michael 1233
Zwezerijnen, Gerben 0690
Zygmunt, Alexander 1826

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Key Word Index

Access to Care 0175, 0181, 0191, 0192, 0196, 0205, 0223, 0228, 0313, 0360, 0361, 0368, 0382, 0393, 0413, 0582, 0606, 0761, 0765, 1011, 1013, 1039, 1055, 1064, 1067, 1068, 1069, 1080, 1082, 1084, 1085, 1178, 1244, 1248, 1265, 1271, 1295, 1660, 1689, 1705, 1706, 1795, 1877, 1889, 1914, 1916, 1924, 1925, 1927, 1928, 1930, 1933, 1975, 1981, 1982, 2132, 2137, 2138, 2149, 2175, 2194, 2318, 2380, 2419, 2423, 2550, 2551, 2556, 2558, 2586, 2615, 2680

Adhesion, Adhesion molecules 0518, 2478

Administrative Data 0145, 0169, 0178, 0283, 0399, 0400, 0433, 0456, 0734, 1015, 1017, 1054, 1084, 1100, 1434, 1497, 1583, 1877, 1883, 1901, 1909, 1917, 1924, 1931, 1997, 2051, 2202, 2266, 2287, 2295, 2627, 2642, 2680

Aging 0167, 0226, 0313, 0446, 0462, 0486, 0511, 0746, 0786, 0817, 0836, 0892, 0893, 0950, 0972, 1065, 1072, 1229, 1341, 1342, 1362, 1639, 1640, 1641, 1656, 1784, 1793, 1796, 1805, 1886, 1921, 2002, 2080, 2123, 2252, 2330, 2404, 2426, 2596, 2603

American College of Rheumatology Criteria 0126, 0567, 0596, 1286, 1347, 1455, 2357, 2370, 2616

ANCA 0150, 0715, 0724, 0727, 0728, 1162, 1597, 1605, 1693, 1912, 2504, 2516

ANCA-associated Vasculitis 0150, 0421, 0633, 0711, 0712, 0713, 0714, 0716, 0717, 0718, 0720, 0721, 0722, 0724, 0725, 0726, 0727, 0728, 0729, 0730, 0840, 0900, 1162, 1277, 1592, 1593, 1594, 1595, 1597, 1598, 1599, 1600, 1601, 1602, 1603, 1604, 1605, 1606, 1607, 1608, 1609, 1610, 1611, 1693, 1764, 1765, 1766, 1767, 1768, 1769, 2144, 2452, 2504, 2505, 2506, 2507, 2508, 2509, 2511, 2512, 2513, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2522, 2523, 2526

Angiogenesis 0053, 0081, 0093, 0252, 0809, 1436, 1624, 1725, 1871, 2478, 2581

Animal Model 0009, 0049, 0050, 0052, 0053, 0058, 0064, 0065, 0080, 0101, 0105, 0311, 0808, 0859, 0868, 0870, 0871, 0907, 0933, 0934, 0935, 0941, 0942, 0946, 0947, 0949, 0950, 0952, 0953, 0958, 0960, 0961, 0965, 0976, 0999, 1003, 1191, 1206, 1734, 1735, 1736, 1753, 1759, 1760, 1781, 1783, 1786, 1794, 1803, 1804, 1806

Ankylosing Spondylitis (AS) 0098, 0102, 0214, 0475, 0524, 0526, 0531, 0541, 0546, 0547, 0553, 0554, 0559, 0560, 0569, 0570, 0592, 0817, 0854, 0876, 0886, 0888, 1332, 1407, 1408, 1410, 1418, 1420, 1423, 1424, 1428, 1429, 1433, 1438, 1440, 1441, 1444, 1445, 1450, 1451, 1452, 1454, 1465, 1466, 1642, 1673, 1715, 1752, 1754, 1756, 1984, 2021, 2035, 2315, 2321, 2322, 2326, 2331, 2333, 2334, 2335, 2337, 2346, 2347, 2353, 2360, 2361, 2376, 2560, 2583, 2633, 2634, 2636, 2638

Anti-ACPA 2227, 2279

Anti-CCP 0089, 0155, 0430, 0834, 1346, 1674, 1726, 2269, 2280, 2628

Anti-citrullinated Protein Autoantibodies (ACPAs) 0033, 0073, 0078, 0471, 0799, 0833, 0914, 1678, 1701, 2248, 2250

Anti-GBM Disease (Goodpasture's) 0711

Antiphospholipid Syndrome 0115, 0116, 0117, 0118, 0119, 0120, 0121, 0122, 0123, 0124, 0125, 0126, 0127, 0128, 0129, 0130, 0131, 0132, 0133, 0134, 0135, 0136, 0137, 0138, 0139, 0140, 0141, 0142, 0143, 0144, 0600, 0710, 0855, 0856, 0857, 0858, 0859, 0860, 0933, 1284, 1299, 1399, 1497, 1721, 1971, 2209, 2403, 2424, 2599

Anti-TNF Drugs 0021, 0035, 0052, 0074, 0100, 0108, 0202, 0241, 0395, 0402, 0496, 0504, 0537, 0560, 0568, 0570, 0855, 0996, 1095, 1372, 1373, 1440, 1444, 1446, 1657, 1664, 1677, 2042, 2267, 2268, 2271, 2274, 2284, 2338, 2359, 2364, 2370, 2373, 2577, 2633, 2634, 2644

Anxiety 0197, 0225, 0365, 0714, 0935, 0953, 1022, 1276, 1281, 1380, 1381, 1648, 1660, 1688, 2040, 2144, 2557

Apoptosis 0948, 1005, 2418

Arthritis, Infectious 0199, 0376, 1362, 1645, 2039, 2152, 2576

Arthroplasty 0317, 0766, 0785, 0786, 2000, 2385

Assistive Devices 0447

Atherosclerosis 0315, 0425, 0458, 0599, 0614, 1008, 1330, 1331, 1474, 1528, 1740, 1845, 1950, 1955, 2009

Autoantibody(ies) 0008, 0011, 0012, 0073, 0076, 0117, 0121, 0129, 0137, 0139, 0195, 0236, 0248, 0258, 0278, 0281, 0296, 0299, 0300, 0304, 0402, 0467, 0506, 0509, 0513, 0529, 0531, 0603, 0617, 0626, 0631, 0646, 0654, 0694, 0701, 0711, 0773, 0853, 0857, 0859, 0860, 0861, 0862, 0897, 0900, 0910, 0911, 0942, 0953, 0960, 0983, 1033, 1168, 1174, 1187, 1195, 1197, 1322, 1330, 1331, 1379, 1390, 1391, 1471, 1488, 1524, 1559, 1570, 1588, 1591, 1678, 1693, 1706, 1726, 1762, 1814, 1838, 1858, 1865, 1931, 2023, 2027, 2034, 2052, 2058, 2059, 2062, 2075, 2103, 2148, 2236, 2255, 2335, 2386, 2396, 2397, 2398, 2414, 2417, 2419, 2422, 2424, 2432, 2434, 2474, 2484, 2491, 2492, 2496, 2499, 2528, 2599, 2630, 2636, 2652, 2665

Autoantigen(s) 0065, 0529, 0617, 0862, 0886, 0888, 0900, 0921, 0923, 0924, 0948, 0997, 1514, 1524, 1591, 1650, 1684, 1779, 1858, 2027, 2386, 2528, 2652

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Autoimmune Diseases 0001, 0003, 0005, 0006, 0008, 0009, 0010, 0011, 0012, 0013, 0014, 0015, 0016, 0017, 0018, 0021, 0024, 0029, 0031, 0034, 0044, 0055, 0062, 0079, 0081, 0082, 0083, 0109, 0110, 0124, 0125, 0138, 0139, 0157, 0158, 0159, 0161, 0162, 0201, 0203, 0205, 0208, 0212, 0213, 0223, 0235, 0236, 0239, 0246, 0248, 0253, 0255, 0256, 0261, 0263, 0264, 0266, 0270, 0271, 0272, 0273, 0274, 0277, 0278, 0285, 0286, 0287, 0293, 0300, 0347, 0356, 0361, 0364, 0366, 0372, 0375, 0412, 0431, 0471, 0484, 0485, 0494, 0504, 0509, 0510, 0554, 0555, 0558, 0600, 0608, 0625, 0630, 0641, 0646, 0678, 0681, 0698, 0699, 0705, 0780, 0792, 0802, 0841, 0843, 0856, 0858, 0860, 0861, 0862, 0864, 0868, 0887, 0888, 0897, 0898, 0901, 0902, 0903, 0905, 0906, 0909, 0911, 0912, 0913, 0914, 0915, 0922, 0926, 0929, 0930, 0931, 0939, 0941, 0946, 0947, 0949, 0960, 0961, 0962, 0964, 0976, 0986, 0987, 0989, 0990, 0991, 0996, 0998, 1001, 1006, 1023, 1052, 1071, 1072, 1080, 1086, 1092, 1100, 1108, 1114, 1122, 1151, 1152, 1153, 1155, 1157, 1161, 1168, 1174, 1178, 1181, 1187, 1190, 1197, 1210, 1248, 1269, 1277, 1282, 1290, 1294, 1303, 1339, 1348, 1362, 1378, 1379, 1384, 1387, 1393, 1394, 1401, 1431, 1441, 1457, 1474, 1476, 1483, 1496, 1501, 1502, 1518, 1529, 1532, 1537, 1539, 1539, 1544, 1545, 1547, 1549, 1555, 1563, 1576, 1591, 1633, 1649, 1662, 1666, 1667, 1676, 1693, 1696, 1697, 1701, 1728, 1730, 1731, 1732, 1760, 1761, 1762, 1772, 1777, 1778, 1799, 1833, 1838, 1850, 1858, 1861, 1864, 1869, 1874, 1875, 1888, 1904, 1931, 1944, 1967, 1979, 2018, 2023, 2024, 2025, 2027, 2030, 2034, 2050, 2171, 2197, 2220, 2223, 2233, 2267, 2279, 2292, 2329, 2350, 2370, 2396, 2397, 2398, 2409, 2417, 2421, 2428, 2440, 2443, 2454, 2459, 2460, 2463, 2466, 2468, 2471, 2491, 2500, 2525, 2535, 2538, 2549, 2557, 2563, 2574, 2577, 2578, 2579, 2580, 2581, 2595, 2598, 2600, 2601, 2605, 2611, 2641, 2658, 2659, 2668, 2669, 2670, 2684, 2695, 2699, 2701

Autoinflammatory Diseases 0013, 0024, 0030, 0050, 0082, 0237, 0242, 0243, 0250, 0255, 0257, 0266, 0269, 0494, 0586, 0778, 0779, 0821, 0918, 0920, 0929, 1056, 1114, 1132, 1149, 1152, 1153, 1158, 1159, 1166, 1169, 1170, 1171, 1186, 1191, 1302, 1303, 1305, 1339, 1362, 1395, 1615, 1625, 1651, 1665, 1667, 1669, 1670, 1713, 1823, 1824, 1827, 1877, 1889, 1974, 2021, 2026, 2032, 2037, 2043, 2044, 2046, 2125, 2129, 2134, 2136, 2141, 2151, 2152, 2154, 2156, 2157, 2242, 2329, 2428, 2576, 2582, 2608, 2666, 2667

Back Pain 0192, 0530, 0531, 0535, 0553, 0582, 0783, 0784, 1062, 1222, 1435, 1796, 1987, 2335, 2367, 2636

B-Cell Targets 0001, 0002, 0003, 0005, 0006, 0008, 0009, 0010, 0011, 0012, 0014, 0015, 0018, 0035, 0124, 0135, 0236, 0239, 0262, 0263, 0279, 0642, 0646, 0656, 0664, 0804, 0843, 0897, 0903, 0905, 0906, 0907, 0908, 0910, 0912, 0913, 0914, 0943, 0946, 0962, 0994, 1093, 1109, 1163, 1172, 1189, 1198, 1517, 1525, 1529, 1532, 1537, 1563, 1578, 1593, 1666, 1683, 1697, 1761, 1766, 1837, 1838, 2019, 2020, 2293, 2425, 2442, 2448, 2454, 2458, 2463, 2464, 2465, 2468, 2476, 2488, 2573, 2577, 2641, 2665, 2669, 2695

Behçet's Syndrome 0025, 0240, 0241, 0254, 0272, 0275, 1074, 1098, 1180, 1292, 2028, 2037, 2045, 2527, 2534, 2535, 2536, 2538, 2540, 2541, 2543, 2544

Bioinformatics 0019, 0020, 0024, 0031, 0048, 0077, 0124, 0127, 0145, 0177, 0230, 0283, 0329, 0504, 0624, 0637, 0797, 0808, 0845, 0856, 0878, 0893, 0901, 0957, 0964, 1000, 1004, 1114, 1168, 1210, 1303, 1309, 1315, 1360, 1568, 1652, 1712, 1799, 1807, 1866, 1867, 1872, 1908, 1951, 2114, 2380, 2601, 2639, 2666

Biologic Response Modifiers 0094, 0400, 0485, 0560, 0587, 0723, 1457, 1679, 1926, 2272, 2350

Biologicals 0008, 0011, 0012, 0014, 0015, 0016, 0153, 0160, 0180, 0194, 0200, 0205, 0238, 0241, 0251, 0353, 0401, 0403, 0416, 0416, 0473, 0474, 0475, 0476, 0479, 0484, 0485, 0487, 0493, 0498, 0499, 0503, 0523, 0547, 0558, 0559, 0561, 0562, 0570, 0571, 0573, 0574, 0577, 0585, 0588, 0649, 0656, 0659, 0667, 0743, 0758, 0760, 0779, 0780, 0790, 0801, 0803, 0806, 0814, 0875, 0878, 0886, 0907, 0941, 0987, 0990, 0996, 0998, 1042, 1044, 1053, 1055, 1065, 1090, 1095, 1096, 1116, 1122, 1160, 1164, 1165, 1175, 1176, 1177, 1179, 1203, 1277, 1282, 1312, 1323, 1344, 1350, 1353, 1356, 1360, 1365, 1368, 1371, 1374, 1427, 1430, 1436, 1437, 1439, 1446, 1447, 1449, 1458, 1459, 1460, 1462, 1463, 1464, 1520, 1525, 1531, 1533, 1534, 1536, 1545, 1548, 1549, 1563, 1592, 1597, 1605, 1612, 1629, 1656, 1657, 1665, 1766, 1833, 1848, 1878, 1921, 1992, 1994, 2022, 2029, 2038, 2041, 2130, 2143, 2203, 2267, 2269, 2271, 2275, 2279, 2280, 2287, 2299, 2300, 2343, 2344, 2345, 2346, 2350, 2354, 2358, 2362, 2368, 2369, 2372, 2374, 2447, 2450, 2453, 2456, 2457, 2460, 2464, 2467, 2468, 2477, 2519, 2524, 2526, 2531, 2583, 2593, 2594, 2610, 2662, 2669, 2678, 2688, 2689

Biomarkers 0023, 0029, 0042, 0044, 0052, 0070, 0094, 0100, 0111, 0119, 0131, 0212, 0213, 0293, 0297, 0299, 0302, 0303, 0307, 0309, 0341, 0342, 0406, 0414, 0418, 0419, 0454, 0463, 0466, 0467, 0481, 0508, 0516, 0531, 0558, 0560, 0590, 0603, 0616, 0617, 0620, 0629, 0636, 0654, 0660, 0664, 0689, 0694, 0700, 0723, 0750, 0751, 0752, 0758, 0773, 0775, 0778, 0795, 0832, 0833, 0836, 0839, 0840, 0842, 0844, 0847, 0851, 0861, 0862, 0873, 0882, 0883, 0901, 0939, 0969, 1159, 1160, 1163, 1164, 1166, 1168, 1187, 1201, 1208, 1210, 1211, 1220, 1239, 1285, 1309, 1314, 1322, 1325, 1334, 1338, 1362, 1367, 1380, 1400, 1436, 1442, 1480, 1490, 1499, 1500, 1501, 1510, 1525, 1559, 1560, 1574, 1602, 1611, 1619, 1668, 1678, 1680, 1683, 1702, 1703, 1728, 1733, 1741, 1742, 1746, 1750, 1767, 1768, 1772, 1773, 1778, 1784, 1809, 1811, 1815, 1827, 1834, 1835, 1836, 1839, 1840, 1845, 1850, 1872, 1875, 1942, 1951, 2012, 2030, 2062, 2073, 2075, 2085, 2091, 2092, 2100, 2123, 2134, 2147, 2227, 2231, 2236, 2243, 2247, 2275, 2277, 2310,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2325, 2335, 2351, 2381, 2384, 2396, 2399, 2401, 2427, 2433, 2434, 2494, 2502, 2503, 2511, 2530, 2584, 2589, 2597, 2599, 2623, 2625, 2636, 2643, 2644, 2646, 2649, 2675, 2688, 2694, 2700

Biomechanics 0769, 0770, 0783, 0788, 1188, 1612, 1940

Biostatistics 0160, 0174, 0415, 0566, 1151, 1357, 1410, 1523, 1573, 1643, 1647, 1908, 1917, 2241, 2340, 2354, 2389, 2572

B-Lymphocyte 0029, 0143, 0521, 0782, 0894, 0897, 0909, 0912, 0914, 0934, 0941, 0982, 0991, 1003, 1096, 1172, 1692, 1693, 1694, 1695, 1696, 1697, 1723, 1766, 1773, 1836, 1838, 2048, 2421, 2439, 2695

Body Composition 0635, 1383, 1557, 1885, 2340, 2501

Body Mass 0395, 0412, 1128, 1367, 1383, 1807, 1944, 2121, 2340, 2604, 2687, 2690, 2691

Bone Biology 0095, 0098, 0346, 0867, 0872, 1142, 1815, 1993, 2116

Bone Density 0051, 0056, 0246, 0337, 0340, 0341, 0343, 0345, 0346, 0347, 0348, 0349, 0351, 0355, 0452, 1352, 1691, 1727, 1791, 2106, 2109, 2110, 2117, 2118, 2119, 2122, 2123, 2244, 2479, 2501, 2592, 2595, 2596, 2686

Bone Resorption 0086, 1784, 1815, 2117, 2120, 2592

Brain 0766, 1295, 1378, 1384, 1711, 1854

Calcinosis 0674, 0701, 0865, 1194, 1214, 1581, 1967, 2145, 2245

Cardiovascular 0024, 0045, 0072, 0091, 0120, 0133, 0162, 0242, 0249, 0265, 0315, 0346, 0435, 0437, 0438, 0445, 0450, 0458, 0468, 0502, 0522, 0559, 0581, 0597, 0598, 0599, 0604, 0614, 0669, 0671, 0677, 0681, 0695, 0709, 0718, 0729, 0818, 0820, 1008, 1016, 1104, 1112, 1122, 1137, 1182, 1186, 1314, 1333, 1334, 1397, 1398, 1404, 1427, 1474, 1483, 1484, 1486, 1528, 1552, 1553, 1623, 1646, 1658, 1709, 1716, 1743, 1745, 1774, 1779, 1851, 1883, 1892, 1913, 1947, 1957, 1984, 1993, 1995, 2009, 2146, 2221, 2245, 2256, 2276, 2317, 2325, 2329, 2363, 2377, 2394, 2413, 2438, 2470, 2473, 2567, 2568, 2569, 2585, 2607, 2608, 2642, 2651, 2656, 2681

Carotid Artery Disease 0614, 1427, 1971, 2487, 2532

Carpal Tunnel Syndrome 1968

Cartilage 0027, 0254, 0258, 0309, 1625, 1735, 1785, 1786, 1790, 1796, 1802, 1803, 1949

Cartilage Degradation 1734, 1796

Cartilage Repair 1798

CCP 0435, 0889, 1943

Cell Death 0918, 0948, 0970, 1132, 2582

Cell Trafficking Angiogenesis 1655

Cell-signalling molecules 0020, 0586, 0797, 0808, 0810, 0857, 0916, 0921, 0926, 1655

Chemokines 0084, 0094, 1127, 1801, 1836

Chondrocyte 0114, 1785, 1801

Chondrogenesis 1798

Citrullination 0078, 0079, 0501, 0924, 0928, 1374, 1779

Classification Criteria 0117, 0126, 0270, 0272, 0389, 0390, 0607, 0764, 0854, 1136, 1388, 1575, 1672, 2136, 2156, 2404, 2405, 2489, 2538, 2651

Climate Change 0164, 1507

Clinical Osteoporosis 0350, 0351, 2107, 2112, 2113

Clinical Practice Guidelines 0172, 0184, 0210, 0230, 0231, 0258, 0667, 1488, 1527, 1977, 2039, 2166, 2192, 2201, 2517, 2541, 2586

Clinical Trial 0257, 0259, 0261, 0277, 0279, 0310, 0335, 0364, 0377, 0381, 0401, 0403, 0405, 0470, 0473, 0482, 0484, 0487, 0488, 0493, 0498, 0501, 0504, 0523, 0545, 0562, 0563, 0564, 0567, 0572, 0574, 0590, 0640, 0641, 0644, 0645, 0650, 0656, 0657, 0662, 0663, 0664, 0665, 0692, 0694, 0720, 0776, 0777, 0779, 0803, 0816, 0843, 0852, 0855, 0873, 0874, 0875, 0876, 0891, 0895, 1051, 1072, 1123, 1157, 1172, 1175, 1270, 1353, 1354, 1356, 1363, 1364, 1374, 1438, 1441, 1443, 1447, 1449, 1451, 1454, 1455, 1458, 1461, 1465, 1466, 1506, 1519, 1521, 1529, 1538, 1542, 1545, 1555, 1564, 1577, 1594, 1608, 1662, 1671, 1674, 1676, 1769, 1925, 1992, 1994, 1998, 1999, 2012, 2013, 2014, 2020, 2035, 2081, 2082, 2083, 2086, 2097, 2101, 2103, 2278, 2279, 2281, 2288, 2289, 2294, 2307, 2333, 2341, 2345, 2347, 2352, 2356, 2358, 2361, 2362, 2365, 2374, 2393, 2440, 2441, 2445, 2452, 2454, 2458, 2463, 2464, 2465, 2466, 2559, 2576, 2587, 2588, 2614, 2624, 2626, 2663, 2671, 2692, 2694, 2697

Cognitive Dysfunction 0184, 0226, 0616, 0947, 1421, 1478, 1482, 1742, 2002, 2430

Cohort Study 0137, 0158, 0165, 0168, 0180, 0201, 0209, 0223, 0238, 0251, 0299, 0300, 0305, 0306, 0318, 0330, 0343, 0385, 0407, 0438, 0439, 0440, 0453, 0481, 0497, 0516, 0517, 0519, 0540, 0544, 0547, 0553, 0561, 0565, 0582, 0605, 0609, 0611, 0612, 0613, 0621, 0659, 0691, 0701, 0734, 0838, 1038, 1048, 1091, 1091, 1093, 1099, 1100, 1107, 1118, 1125, 1146, 1148, 1151, 1158, 1173, 1174, 1180, 1220, 1255, 1279, 1339, 1346, 1386, 1415, 1416, 1429, 1439, 1448, 1479, 1486, 1489, 1491, 1505, 1513, 1533, 1534, 1536, 1541, 1549, 1552, 1556, 1631, 1634, 1640, 1664, 1665, 1670, 1683, 1710, 1721, 1747, 1788, 1842, 1879, 1898, 1924, 1932, 1960, 1965, 2007, 2018, 2023, 2028, 2037, 2045, 2054, 2060, 2068, 2074, 2080, 2087, 2092, 2115, 2118, 2232, 2234, 2241, 2245, 2302, 2309, 2331, 2338, 2349, 2382, 2389, 2394, 2403, 2405, 2438, 2453, 2456, 2472, 2476, 2496, 2503, 2522, 2575, 2606, 2607, 2650, 2657, 2683, 2686, 2687, 2698, 2703

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Collagen 0102, 0258, 0809, 0869, 0944, 1774, 1786, 1798

Collagen-Induced Arthritis 0050, 0051, 0052, 0056, 0060, 0065, 0472, 0868, 0870

Community Programs 0194, 0630, 2547

Comorbidity 0077, 0091, 0154, 0162, 0169, 0190, 0200, 0214, 0215, 0436, 0438, 0459, 0476, 0528, 0546, 0579, 1017, 1130, 1224, 1271, 1316, 1320, 1381, 1393, 1394, 1413, 1421, 1452, 1554, 1636, 1712, 1883, 1894, 1920, 1993, 1995, 2038, 2065, 2067, 2079, 2128, 2232, 2249, 2251, 2252, 2266, 2292, 2330, 2383, 2412, 2422, 2642, 2682

Comparative Effectiveness 0165, 0298, 0319, 0397, 0697, 0740, 0804, 1080, 1116, 1129, 1357, 1366, 1372, 1373, 1439, 1453, 1613, 1629, 1914, 2008, 2101, 2348, 2659, 2698

Complement 0624, 0724, 0807, 0821, 0856, 0896, 0922, 1508, 1606, 1611, 2033, 2381, 2430, 2433, 2434, 2507

Computed Tomography (CT) 0540, 0674, 0690, 1556, 1561, 1567, 1576, 1751, 1947, 1950, 2009, 2017, 2306, 2531, 2566

Corticosteroids 0201, 0413, 0420, 0422, 0642, 0735, 0771, 1044, 1305, 1313, 1351, 1496, 1687, 1729, 1730, 2040, 2096, 2098, 2157, 2624

Cost-Effectiveness 0195, 0447, 0519, 0761, 0787, 0829, 1039, 1041, 1370, 1975, 2111, 2271

COVID-19 0039, 0151, 0157, 0158, 0207, 0806, 1068, 1081, 1109, 1189, 1280, 1305, 1493, 1576, 1636, 1897, 2019, 2228, 2297, 2574, 2575, 2577, 2578

CPPD 1139, 1142

C-Reactive Protein (CRP) 0173, 0691, 0750, 2151

Cryogloblulinemic Vasculitis 1604, 2545

Cryoglobulinemia 1397, 1681, 2545

Crystal-induced Arthritis 0231, 1101, 1123, 1126, 1128, 1131, 1134, 1135, 1136, 1138, 1139, 1142, 1996, 1998, 1999, 2002, 2012, 2013, 2014, 2587, 2588

Cutaneous 0244, 0648, 0660, 0674, 0802, 0885, 0951, 0958, 0985, 1119, 1152, 1414, 1518, 1720, 1758, 1777, 2147, 2313, 2408, 2409, 2451, 2670

Cytokines 0011, 0012, 0094, 0105, 0108, 0109, 0141, 0281, 0307, 0403, 0406, 0494, 0570, 0587, 0653, 0679, 0732, 0796, 0864, 0865, 0903, 0909, 0931, 0939, 0952, 0985, 0988, 0993, 1120, 1128, 1140, 1150, 1243, 1423, 1437, 1535, 1539, 1622, 1651, 1652, 1654, 1683, 1703, 1770, 1774, 1776, 1812, 1820, 1824, 1833, 1842, 1974, 2010, 2035, 2092, 2242, 2384, 2402, 2513, 2576, 2583, 2649, 2675

Cytotoxic Cells 0863, 0887, 1003, 1119, 1535, 2494

Damage Index 0137, 0511, 0552, 0596, 0608, 0636, 1154, 1425, 1469, 1518, 1552, 1899, 2053, 2058, 2071, 2387, 2416, 2422, 2424, 2444, 2515

Data Management 0185, 0289, 0745, 1007, 1071, 1171, 1268, 1643, 1657, 1900, 2172, 2336, 2354, 2542, 2605

Decision Analysis 0449, 1050, 1051, 1052, 1186, 1988, 2260, 2525

Demographics 0179, 0240, 0269, 0393, 0579, 0580, 0607, 0703, 0744, 1012, 1071, 1153, 1263, 1393, 1394, 1452, 1498, 1513, 1554, 1832, 1996, 2088, 2099, 2537, 2558, 2615, 2666

Dendritic Cells 0482, 0800, 0863, 0916, 0948, 0952, 1538, 1762, 1852, 2078

Depression 0083, 0182, 0197, 0217, 0225, 0365, 0714, 0770, 1022, 1058, 1071, 1224, 1276, 1281, 1323, 1403, 1409, 1511, 1686, 1688, 1976, 2040, 2079, 2202, 2243, 2254, 2437

Dermatology 0223, 0277, 0278, 0285, 0551, 0562, 0574, 0648, 0790, 0848, 0875, 0926, 0998, 1152, 1166, 1448, 1464, 1898, 1912, 2165, 2170, 2323, 2345, 2374, 2409, 2428, 2608, 2699

Dermatomyositis 0026, 0227, 0278, 0284, 0285, 0286, 0287, 0290, 0297, 0298, 0302, 0388, 0653, 0822, 0864, 0865, 0916, 0984, 1193, 1194, 1200, 1202, 1207, 1208, 1209, 1212, 1219, 1361, 1740, 1741, 1745, 1770, 1816, 1826, 1857, 1889, 1956, 1967, 1986, 2053, 2055, 2061, 2062, 2063, 2068, 2070, 2071, 2074, 2076, 2131, 2145, 2148, 2158, 2558, 2668, 2669, 2670, 2672, 2673

Diagnostic Criteria 0039, 0260, 0270, 0285, 0469, 0507, 0530, 0551, 0624, 0745, 0772, 0837, 1014, 1226, 1292, 1332, 1407, 1412, 1414, 1477, 1672, 1710, 1889, 1900, 1959, 1974, 2136, 2411, 2535, 2702

Diet 0207, 0491, 0634, 1032, 1034, 1558, 1884, 2056, 2076, 2097, 2690

Disability 0199, 1031, 1035, 1103, 1588, 1907, 1922, 2095, 2334

Disease Activity 0176, 0191, 0199, 0221, 0222, 0236, 0260, 0295, 0297, 0302, 0380, 0385, 0391, 0409, 0425, 0431, 0439, 0440, 0441, 0443, 0444, 0448, 0451, 0473, 0480, 0487, 0488, 0491, 0493, 0495, 0497, 0500, 0514, 0552, 0580, 0584, 0608, 0620, 0648, 0657, 0725, 0777, 0778, 0791, 0803, 0805, 0834, 0874, 0892, 0900, 0917, 1028, 1070, 1081, 1103, 1149, 1159, 1207, 1212, 1218, 1219, 1310, 1312, 1315, 1317, 1318, 1320, 1332, 1336, 1357, 1364, 1375, 1396, 1409, 1410, 1411, 1421, 1430, 1433, 1435, 1450, 1469, 1472, 1491, 1495, 1499, 1503, 1505, 1509, 1531, 1533, 1536, 1550, 1566, 1608, 1661, 1675, 1677, 1679, 1769, 1831, 1973, 2058, 2062, 2071, 2075, 2096, 2124, 2131, 2148, 2158, 2246, 2253, 2254, 2263, 2278, 2290, 2292, 2295, 2308, 2309, 2317, 2322, 2332, 2347, 2349, 2366, 2404, 2409, 2422, 2423, 2430, 2456, 2564, 2600, 2616, 2626, 2640, 2649, 2650, 2654, 2683, 2686, 2703

Disease-Modifying Antirheumatic Drugs (Dmards) 0035, 0052, 0070, 0072, 0087, 0202, 0241, 0332, 0369, 0392, 0400,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

0444, 0453, 0454, 0470, 0473, 0478, 0481, 0483, 0484, 0488, 0490, 0491, 0495, 0497, 0500, 0502, 0505, 0554, 0556, 0557, 0561, 0565, 0566, 0572, 0579, 0580, 0585, 0588, 0589, 0592, 0662, 0731, 0751, 0757, 0790, 0795, 0871, 1025, 1040, 1042, 1061, 1088, 1089, 1098, 1099, 1106, 1114, 1118, 1155, 1178, 1182, 1274, 1311, 1321, 1322, 1329, 1336, 1347, 1348, 1350, 1357, 1358, 1364, 1438, 1442, 1448, 1449, 1453, 1459, 1465, 1477, 1541, 1586, 1587, 1598, 1629, 1664, 1715, 1831, 1979, 1985, 2022, 2036, 2039, 2042, 2195, 2228, 2266, 2267, 2269, 2270, 2271, 2273, 2290, 2307, 2346, 2348, 2351, 2366, 2367, 2445, 2543, 2571, 2640, 2642, 2678, 2682

Disparities 0151, 0181, 0190, 0326, 0364, 0368, 0381, 0478, 0720, 0785, 1012, 1013, 1031, 1057, 1061, 1066, 1068, 1070, 1072, 1074, 1075, 1076, 1077, 1079, 1080, 1081, 1082, 1083, 1087, 1178, 1224, 1251, 1263, 1265, 1484, 1633, 1689, 1704, 1707, 1709, 1880, 1881, 1882, 1905, 1907, 1917, 1935, 1976, 2120, 2185, 2199, 2518, 2565, 2615, 2629

Drug Toxicity 0045, 0160, 0230, 0352, 0655, 0669, 0670, 1048, 1088, 1089, 1092, 1097, 1098, 1099, 1102, 1112, 1116, 1517, 1593, 1604, 1718, 1731, 1735, 1886, 1913, 1979, 1985, 2112, 2118, 2133, 2269, 2276, 2507, 2658

Dual Energy X-Ray Absorptiometry (DEXA) 0337, 0339, 0340, 0341, 0347, 0348, 0356, 1691, 2106, 2110, 2501, 2566

Economics 0525, 1365, 1366, 1376, 1929, 2185, 2408, 2416, 2500

Education 0188, 0630, 0652, 0826, 0830, 1069, 1080, 1092, 1915, 2159, 2161, 2163, 2164, 2167, 2168, 2169, 2170, 2171, 2174, 2177, 2179, 2180, 2182, 2185, 2186, 2188, 2190, 2191, 2192, 2223, 2547, 2550, 2551, 2556

Education, Medical 0179, 0188, 0202, 0825, 0827, 0828, 0829, 0830, 1046, 1265, 1419, 1984, 2159, 2160, 2162, 2163, 2164, 2165, 2166, 2169, 2170, 2172, 2173, 2174, 2175, 2176, 2178, 2179, 2180, 2181, 2182, 2183, 2184, 2186, 2187, 2189, 2190, 2191, 2193, 2194, 2282, 2550

Education, Patient 0152, 0188, 0192, 0371, 0372, 0373, 0385, 0630, 1029, 1040, 1073, 1251, 1263, 1265, 1689, 1973, 1981, 1987, 1989, 2179, 2194, 2195, 2204, 2213, 2216, 2217, 2415, 2514, 2547, 2555, 2556, 2560, 2606

Employment 1077, 1494

Environmental Factors 0036, 0038, 0156, 0159, 0166, 0171, 0174, 0321, 0354, 0594, 0754, 1059, 1264, 1507, 1690, 1748, 1788, 1903, 1905, 2390, 2668

Eosinophilic Granulomatosus with Polyangiitis (Churg-Strauss) 0238, 0715, 0716, 0723, 1592, 1594, 1600, 1605, 1608, 1610, 1765, 1769, 2504, 2513, 2514, 2532

Epidemiology 0037, 0145, 0146, 0147, 0151, 0154, 0155, 0156, 0157, 0158, 0161, 0164, 0169, 0245, 0321, 0322, 0324, 0325, 0338, 0354, 0356, 0360, 0395, 0399, 0427, 0460, 0522, 0541, 0546, 0607, 0691, 0693, 0715, 0722, 0728, 0734, 0735, 0745, 0754, 0813, 0879, 0982, 1009, 1010, 1013, 1015, 1016, 1018, 1023, 1024, 1026, 1029, 1033, 1034, 1036, 1078, 1086, 1087, 1099, 1156, 1190, 1247, 1279, 1312, 1320, 1341, 1342, 1344, 1351, 1355, 1383, 1386, 1392, 1393, 1394, 1409, 1429, 1500, 1507, 1583, 1584, 1621, 1637, 1638, 1643, 1644, 1690, 1714, 1729, 1795, 1879, 1880, 1881, 1882, 1883, 1886, 1887, 1890, 1891, 1893, 1895, 1897, 1898, 1901, 1903, 1904, 1905, 1906, 1907, 1908, 1909, 1911, 1925, 1995, 2002, 2004, 2008, 2018, 2036, 2051, 2060, 2087, 2113, 2118, 2214, 2221, 2270, 2336, 2545, 2553, 2567, 2569, 2570, 2571, 2586, 2606, 2607, 2622, 2633, 2645, 2657, 2661, 2679, 2685

Epigenetics 0038, 0044, 0084, 0097, 0104, 0111, 0594, 0625, 0637, 0693, 0955, 0969, 1698, 1700, 1723, 1756, 1818, 1823, 2275, 2410, 2646, 2647, 2648

Ergonomics 2555

Erosions 0315, 0834, 1431, 1943, 2614

Exercise 0107, 0387, 0765, 0784, 1327, 1450, 1636, 1649, 1940, 2084, 2097, 2692

Experimental Arthritis 0053, 0058, 0063, 0066, 0798, 1724, 1739

Eye Disorders 0264, 0268, 0394, 0396, 0406, 0407, 0414, 0415, 0421, 0432, 0507, 0512, 0537, 0708, 0888, 1106, 1389, 1665, 1722, 1821, 2291, 2444, 2524, 2543, 2675, 2701

Falls 0148, 0788, 1238

Fatigue 0207, 0295, 0379, 0380, 0517, 0644, 1149, 1231, 1262, 1324, 1402, 1403, 1487, 1551, 1711, 1854, 2254, 2378, 2429, 2437, 2536, 2557

Fc Receptors 0040, 0041, 0907, 0911, 0987

Fibroblasts, Dermal 0679, 0949, 0955, 0961, 0965, 0966, 0967, 0968, 0969, 0970, 0971, 0975, 0976, 1870, 2048, 2498

Fibroblasts, Other 0102, 0808, 0809, 0810, 0851, 0940, 1560, 1682, 1684, 1752, 1805, 1830, 1856, 1860, 1863, 1866, 1868, 1876, 2231, 2502

Fibroblasts, Synovial 0061, 0063, 0068, 0069, 0075, 0081, 0096, 0097, 0472, 0797, 0798, 0799, 0807, 0919, 0978, 0995, 1005, 1150, 1757, 1780, 1787, 1801, 1807, 2285, 2613

Fibromyalgia 0197, 0225, 0534, 0814, 1014, 1221, 1224, 1225, 1226, 1228, 1231, 1234, 1236, 1237, 1242, 1243, 1244, 1245, 1254, 1332, 1435, 2098, 2189, 2378, 2437

Fibrosing syndromes 0038, 0099, 0279, 0692, 0958, 0966, 0968, 0992, 1163, 1861, 1872, 1876, 2019, 2020, 2476

FMF 0237, 0779, 1177, 1651, 2021, 2043, 2667

Foot 0767

Fracture 0246, 0340, 0341, 0342, 0345, 0347, 0351, 0352, 0353, 0354, 0867, 1313, 1352, 1727, 1997, 2070, 2106, 2107, 2108, 2113, 2114, 2115, 2116, 2119, 2122, 2479, 2621, 2685

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Functional Status 0325, 0605, 1643, 1977, 2089, 2308, 2311, 2604

Gait 0783, 0788

Gender 0046, 0167, 0316, 0326, 0356, 0462, 0557, 0589, 0596, 0719, 0744, 0841, 0873, 1012, 1062, 1063, 1180, 1408, 1476, 1714, 1837, 1877, 1935, 2196, 2264, 2322, 2356, 2357

Gene Expression 0029, 0035, 0043, 0047, 0069, 0095, 0097, 0118, 0316, 0320, 0782, 0797, 0811, 0823, 0846, 0944, 0959, 0964, 0967, 1004, 1279, 1309, 1700, 1725, 1778, 1788, 1812, 1816, 1819, 1821, 1834, 1845, 1849, 1866, 1867, 2010, 2155, 2219, 2224, 2425, 2585, 2648, 2700

Gene Therapy 0310, 1701, 2103, 2458

Genetics 0024, 0028, 0030, 0033, 0034, 0036, 0039, 0047, 0073, 0103, 0104, 0174, 0237, 0240, 0269, 0593, 0624, 0834, 1124, 1170, 1171, 1197, 1221, 1292, 1301, 1346, 1423, 1504, 1523, 1699, 1701, 1749, 1862, 2021, 2037, 2046, 2152, 2270, 2390, 2432, 2647, 2666, 2679

Genome Wide Association Studies 0022, 0034, 0112, 1303, 1696, 2410

Genomics 0021, 0022, 0025, 0028, 0032, 0034, 0045, 0046, 0071, 0104, 0693, 0774, 0811, 0812, 0819, 0845, 0893, 0970, 1056, 1227, 1309, 1571, 1653, 1696, 1699, 1700, 1725, 1755, 1763, 1793, 1826, 1829, 1839, 1844, 2046, 2410, 2533, 2572, 2602, 2683, 2700

Genomics and Proteomics 0100, 0329, 0795, 0889, 1000, 1181, 1702, 1741, 2599

Geriatrics 1072, 2107, 2404

Giant Cell Arteritis 0344, 0720, 0731, 0732, 0733, 0734, 0735, 0738, 0739, 0740, 0741, 0742, 0743, 0744, 0745, 0746, 0747, 0748, 0749, 0750, 0751, 0752, 0753, 0754, 0755, 0756, 0757, 0759, 0760, 0761, 0762, 0763, 0764, 0776, 0891, 0892, 0893, 0895, 0896, 1047, 1075, 1097, 1175, 1614, 1616, 1617, 1619, 1626, 1627, 1628, 1630, 1900, 1910, 2109, 2526, 2532, 2584, 2702, 2703, 2704

Glucocorticoids 0045, 0238, 0251, 0284, 0338, 0340, 0344, 0349, 0360, 0372, 0375, 0494, 0505, 0650, 0668, 0726, 0738, 0739, 0743, 0746, 0757, 0776, 0792, 0803, 0895, 1010, 1025, 1038, 1049, 1052, 1251, 1355, 1526, 1528, 1534, 1541, 1598, 1607, 1610, 1629, 1671, 1734, 1764, 1765, 1878, 1910, 2117, 2273, 2469, 2523, 2531, 2542, 2699

Gout 0037, 0082, 0171, 0228, 0231, 1012, 1026, 1032, 1043, 1076, 1123, 1124, 1125, 1128, 1129, 1130, 1131, 1132, 1133, 1139, 1140, 1141, 1143, 1144, 1145, 1146, 1259, 1799, 1891, 1903, 1907, 1923, 1990, 1991, 1992, 1993, 1994, 1995, 1997, 1998, 1999, 2001, 2002, 2003, 2004, 2006, 2007, 2008, 2009, 2010, 2011, 2013, 2014, 2192, 2548, 2585, 2586, 2587, 2588, 2589, 2590, 2618

Granulomatosis with Polyangiitis (GPA) 0713, 0718, 0721, 0726, 1595, 1596, 1598, 1606, 1607, 1609, 1764, 1766

Grip Strength 0676, 1341, 1940

Hand 0321, 0686, 1385, 1938, 1940, 2089, 2180, 2552, 2562, 2612, 2621

HAQ 0443, 2388

Health Assessment Questionnaire (HAQ) 0199, 0444, 1103, 1375, 1708

Health Behaviors 0152, 0371, 0373, 0374, 0382, 0793, 1049, 1051, 1073, 1146, 1252, 1256, 1257, 1403, 1470, 1487, 1934, 2192, 2198, 2216, 2560, 2603

Health Care 0172, 0173, 0186, 0193, 0197, 0218, 0358, 0361, 0366, 0368, 0525, 0546, 0761, 0829, 0880, 1023, 1038, 1157, 1244, 1271, 1387, 1401, 1562, 1580, 1583, 1705, 1706, 1727, 1910, 1928, 1938, 1989, 1991, 1993, 2108, 2191, 2403, 2444, 2500

Health policy 0190, 1042, 1044, 1077

Health Services Research 0157, 0158, 0177, 0178, 0179, 0181, 0182, 0185, 0189, 0192, 0193, 0194, 0198, 0375, 0602, 0652, 0655, 0726, 0793, 0826, 1040, 1042, 1043, 1045, 1050, 1051, 1052, 1053, 1054, 1068, 1083, 1084, 1244, 1256, 1257, 1259, 1263, 1266, 1269, 1283, 1497, 1633, 1658, 1659, 1661, 1708, 1917, 1923, 1924, 1925, 1929, 1932, 1934, 2006, 2104, 2171, 2172, 2193, 2226, 2232, 2305, 2680, 2681

Health Status 0374, 0605, 1260, 1648, 2567

Heart Disease 0065, 0131, 0235, 0445, 0456, 0458, 0655, 0669, 0810, 1030, 1166, 1173, 1325, 1328, 1427, 1634, 1650, 1667, 1856, 1868, 1913, 2005, 2222, 2413, 2490, 2531, 2651

Hormone Replacement Therapy 2207

Hyperuricemia 0171, 1123, 1124, 1129, 1130, 1133, 1652, 1998, 1999, 2000, 2013, 2587, 2588, 2590, 2660

IgG4-related Disease 0032, 0239, 0270, 0271, 0279, 0421, 0910, 0992, 1036, 1154, 1163, 1167, 1167, 1172, 1173, 1190, 1666, 1773, 2015, 2019, 2020, 2033, 2051, 2528, 2529, 2530, 2531, 2546

Imaging 0092, 0107, 0186, 0227, 0242, 0249, 0252, 0296, 0333, 0334, 0346, 0418, 0419, 0428, 0507, 0539, 0598, 0681, 0690, 0695, 0740, 0749, 0755, 0759, 0878, 0880, 0928, 0956, 0962, 1126, 1136, 1172, 1173, 1204, 1205, 1213, 1239, 1304, 1315, 1330, 1331, 1405, 1406, 1483, 1572, 1579, 1580, 1620, 1631, 1664, 1680, 1710, 1713, 1751, 1784, 1808, 1908, 1936, 1937, 1938, 1939, 1941, 1945, 1946, 1948, 1950, 1951, 1952, 1953, 1954, 1956, 1957, 1958, 1959, 1962, 1964, 1966, 1967, 1968, 1969, 1970, 1971, 2081, 2106, 2145, 2154, 2158, 2160, 2241, 2306, 2319, 2325, 2431, 2470, 2562, 2609, 2610, 2611, 2613, 2635, 2637, 2673, 2704

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Immunology 0008, 0009, 0019, 0021, 0054, 0055, 0059, 0110, 0111, 0206, 0236, 0262, 0279, 0296, 0301, 0555, 0574, 0649, 0663, 0747, 0781, 0782, 0796, 0823, 0857, 0864, 0866, 0875, 0888, 0890, 0897, 0898, 0899, 0899, 0902, 0905, 0907, 0917, 0923, 0943, 0957, 0963, 0979, 0981, 0982, 0983, 0997, 1001, 1003, 1004, 1090, 1091, 1096, 1103, 1109, 1113, 1115, 1140, 1141, 1155, 1163, 1175, 1227, 1251, 1314, 1339, 1400, 1463, 1645, 1646, 1653, 1695, 1697, 1715, 1723, 1724, 1726, 1729, 1733, 1741, 1755, 1773, 1777, 1787, 1789, 1813, 1829, 1845, 1853, 2019, 2020, 2023, 2033, 2059, 2062, 2152, 2168, 2277, 2280, 2300, 2374, 2399, 2417, 2418, 2421, 2439, 2461, 2463, 2498, 2573, 2601, 2641, 2665, 2682, 2688

In Silica Studies 0124

Infection 0150, 0162, 0169, 0200, 0201, 0202, 0204, 0205, 0206, 0208, 0210, 0486, 0490, 0585, 0606, 0609, 0619, 0631, 0659, 0806, 0923, 1061, 1065, 1090, 1120, 1157, 1192, 1304, 1459, 1475, 1540, 1607, 1621, 1656, 1715, 1747, 1825, 1879, 1902, 2039, 2044, 2133, 2292, 2505, 2526, 2573, 2574, 2575, 2577, 2578, 2653, 2682

Inflammasome 0134, 0301, 0867, 1008, 1132, 1651, 1812, 2011, 2155

Inflammation 0020, 0058, 0060, 0061, 0063, 0066, 0068, 0069, 0075, 0080, 0082, 0086, 0093, 0097, 0100, 0105, 0113, 0127, 0134, 0207, 0226, 0233, 0235, 0257, 0268, 0276, 0277, 0306, 0307, 0328, 0360, 0429, 0437, 0439, 0463, 0464, 0472, 0489, 0551, 0562, 0576, 0653, 0654, 0750, 0796, 0798, 0836, 0869, 0872, 0889, 0892, 0916, 0918, 0920, 0921, 0924, 0929, 0931, 0944, 0958, 0973, 0995, 1008, 1016, 1101, 1101, 1107, 1114, 1117, 1119, 1127, 1133, 1139, 1140, 1147, 1153, 1176, 1182, 1186, 1207, 1304, 1305, 1315, 1325, 1337, 1458, 1466, 1490, 1549, 1553, 1623, 1624, 1625, 1650, 1652, 1654, 1695, 1711, 1735, 1736, 1776, 1785, 1799, 1823, 1825, 1867, 1873, 1910, 1949, 1974, 2010, 2011, 2018, 2043, 2044, 2046, 2070, 2085, 2091, 2105, 2147, 2157, 2196, 2286, 2310, 2329, 2345, 2425, 2431, 2451, 2466, 2495, 2497, 2527, 2585, 2663, 2681

Infliximab 0275, 2541

Informatics 0183, 0193, 0229, 0448, 0527, 0532, 1357, 1477, 1657, 1702, 1827, 1834, 1953, 2471, 2618, 2667

Innate Immunity 0005, 0049, 0059, 0079, 0080, 0287, 0328, 0431, 0514, 0518, 0571, 0723, 0910, 0920, 0921, 0924, 0925, 0926, 0927, 0928, 0930, 0932, 0945, 0989, 1094, 1120, 1131, 1145, 1535, 1602, 1668, 1800, 1814, 1823, 1827, 1864, 2023, 2580, 2581, 2582, 2585

Innate Immunity Rheumatic Disease 0237, 0262, 0821, 0932, 0950, 0999, 1875, 2579

Interferon 0058, 0280, 0286, 0301, 0302, 0508, 0518, 0617, 0631, 0775, 0802, 0807, 0821, 0847, 0881, 0912, 0915, 0916, 0920, 0929, 0934, 0943, 0951, 1185, 1191, 1512, 1518, 1538, 1539, 1655, 1668, 1671, 1723, 1742, 1755, 1770, 1771, 1775, 1777, 1826, 1852, 1864, 1867, 2078, 2418, 2451, 2497, 2598, 2647, 2664, 2668, 2670, 2672

Interleukins 0090, 0099, 0134, 0242, 0267, 0281, 0301, 0307, 0310, 0485, 0486, 0502, 0503, 0537, 0577, 0653, 0758, 0796, 0909, 0979, 1134, 1184, 1186, 1323, 1353, 1423, 1441, 1444, 1447, 1448, 1460, 1667, 2013, 2014, 2043, 2151, 2303, 2345, 2350, 2363, 2373, 2576, 2689

Interstitial Lung Disease 0022, 0067, 0085, 0154, 0161, 0169, 0247, 0259, 0274, 0430, 0435, 0453, 0465, 0510, 0678, 0688, 0689, 0690, 0697, 0729, 0773, 0782, 0879, 0881, 0882, 0963, 0973, 1002, 1024, 1063, 1148, 1156, 1161, 1162, 1168, 1185, 1187, 1193, 1199, 1201, 1202, 1213, 1217, 1219, 1220, 1255, 1308, 1321, 1335, 1343, 1361, 1371, 1382, 1390, 1556, 1560, 1561, 1564, 1567, 1574, 1576, 1577, 1579, 1580, 1589, 1658, 1659, 1662, 1663, 1664, 1746, 1749, 1750, 1751, 1778, 1820, 1860, 1862, 1863, 1869, 1872, 1876, 1904, 1924, 1946, 1951, 1956, 2016, 2017, 2030, 2031, 2047, 2050, 2074, 2075, 2133, 2134, 2139, 2140, 2229, 2230, 2235, 2249, 2250, 2258, 2259, 2262, 2265, 2299, 2474, 2475, 2477, 2485, 2499, 2500, 2579, 2611, 2661, 2662, 2672

Intervention 0209, 0344, 0974, 1182, 1190, 1246, 1586, 1587, 1832, 1965, 2157, 2187, 2280, 2524, 2687, 2690

Joint Structure 0426, 1137, 1737, 1936, 1970, 2029, 2086, 2104

Juvenile Idiopathic Arthritis 0028, 0312, 0387, 0389, 0391, 0392, 0393, 0394, 0395, 0398, 0399, 0400, 0401, 0403, 0404, 0405, 0406, 0407, 0409, 0410, 0411, 0412, 0413, 0414, 0416, 0417, 0418, 0419, 0420, 0422, 0424, 0425, 0426, 0427, 0429, 0819, 0824, 1064, 1066, 1252, 1274, 1280, 1304, 1654, 1704, 1809, 1810, 1811, 1812, 1813, 1820, 1821, 1822, 1824, 1828, 1829, 1929, 1978, 1989, 2029, 2130, 2132, 2134, 2135, 2137, 2138, 2140, 2143, 2150, 2242, 2675, 2678, 2679, 2680

Juvenile Inflammatory Arthritis 0397, 0415, 0424, 1274, 2130, 2676

Juvenile Rheumatoid Arthritis 0422, 0822

Longitudinal Studies 0023, 0076, 0136, 0401, 0414, 0536, 0616, 0762, 0846, 0847, 0848, 1048, 1078, 1158, 1213, 1267, 1289, 1472, 1509, 1586, 1631, 1681, 1695, 1733, 1920, 1941, 1958, 2109, 2110, 2319, 2424, 2472, 2475, 2561, 2572, 2703

Lupus Nephritis 0002, 0047, 0136, 0373, 0601, 0610, 0611, 0612, 0613, 0615, 0618, 0620, 0625, 0636, 0639, 0642, 0650, 0651, 0654, 0655, 0661, 0663, 0664, 0665, 0667, 0772, 0837, 0838, 0839, 0840, 0841, 0842, 0851, 0906, 0913, 0940, 0942, 0944, 0945, 0981, 1038, 1078, 1240, 1273, 1282, 1283, 1467, 1476, 1480, 1485, 1499, 1513, 1516, 1517, 1520, 1521, 1522, 1526, 1527, 1530, 1540, 1544, 1546, 1547, 1721, 1762, 1763, 1814, 1830, 1835, 1836, 1841, 1843, 1844, 1846, 1847, 1851, 1853, 2210, 2381, 2392, 2399, 2401, 2403, 2410, 2421, 2427, 2438, 2439, 2448, 2452, 2453, 2458, 2460, 2462, 2465, 2466, 2467, 2468, 2600, 2697, 2698

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Lupus-like Disease 0071, 0365, 0885, 0949, 0983, 1078, 1720, 1758, 1760, 1851, 2428, 2572, 2598

Macrophage Activation Syndrome 0039, 0358, 0423, 0780, 1153, 1179, 1471, 1477, 1671, 1819, 1820, 1825, 1929, 2022, 2137, 2138, 2139, 2143, 2157

Macrophages 0043, 0051, 0069, 0074, 0080, 0747, 0812, 0865, 0893, 0908, 0921, 0925, 0940, 0945, 0963, 0973, 0974, 1131, 1140, 1141, 1174, 1650, 1763, 1774, 1779, 1787, 1793, 1844, 1870, 2011, 2078, 2464, 2582, 2583, 2600

Magnetic Resonance Imaging (MRI) 0116, 0242, 0309, 0323, 0390, 0428, 0538, 0539, 0543, 0548, 0681, 0716, 0852, 1205, 1239, 1414, 1466, 1496, 1854, 1937, 1945, 1948, 1962, 1963, 1971, 2081, 2085, 2091, 2128, 2148, 2154, 2541, 2614, 2623, 2625, 2635, 2677, 2703

Managed Care 0183, 1365, 2469

Measurement 0294, 0304, 0391, 0480, 0686, 0852, 1253, 1375, 1977, 1988, 2069, 2094, 2166, 2388, 2619

Measurement Instrument 0221, 0386, 0449, 0605, 0608, 0777, 0791, 1405, 1479, 1527, 1635, 1970, 1974, 1990, 2171, 2301, 2307, 2318, 2483, 2542, 2554, 2609, 2616

Medicare 0478, 1044, 1045, 1053, 1055, 1351, 1921, 2003, 2287, 2615

Mental Health 1019, 1071, 1241, 1256, 1257, 1264, 1275, 1281, 1290, 1317, 1660, 1688, 1745, 1976, 2040, 2327, 2557, 2565

Mesenchymal Stem Cells 0064, 0472, 0521, 0968, 1141, 1784, 1791

Meta-analysis 0031, 0258, 0319, 0331, 0332, 0333, 0334, 0490, 0545, 0670, 0731, 0805, 0845, 1134, 1222, 1347, 1476, 1502, 1510, 1546, 1581, 1685, 1732, 2255, 2259, 2316, 2643, 2645

Metabolic Crystal 1032, 1127, 1135, 2590

Metabolic Syndrome 0528, 0581, 0604, 1337, 1995, 2330, 2659

Metabolomics 0087, 0318, 0322, 0324, 0700, 0871, 0901, 0925, 0956, 1338, 1840, 1841, 1851, 2061, 2303, 2589, 2599

Microbiome 0031, 0032, 0054, 0088, 0101, 0322, 0400, 0466, 0482, 0491, 0517, 0712, 0717, 0775, 0800, 0870, 0871, 0935, 0938, 1032, 1119, 1329, 1338, 1565, 1759, 1781, 1792, 1794, 1806, 1835, 1855, 2008, 2315, 2399, 2589, 2590, 2622, 2639, 2643

Micro-RNA 0680, 0717, 0775, 0909, 1000, 1141, 1329, 1869

Microscopic Polyangiitis 0718, 0721, 0728, 1606, 1609, 1764

Minority Health 1060, 1082, 1232, 1915, 2074, 2077, 2198, 2199, 2559

Miscellaneous Rheumatic and Inflammatory Diseases 0252, 0260, 0269, 0494, 0777, 1088, 1089, 1099, 1121, 1148, 1158, 1174, 1255, 1269, 1457, 1635, 1787, 2018, 2026, 2034, 2037, 2442, 2663, 2666, 2701

Mitochondrial Dysfunction 0059, 0115, 0931, 0975, 1788, 1837, 1873, 2147, 2443, 2652

Monocytes/macrophages 0025, 0047, 0066, 0098, 0514, 0521, 0708, 0831, 0890, 0951, 0957, 0980, 1553, 1651, 1682, 1757, 1768, 1812, 1828, 1831, 1868, 2010, 2140, 2399, 2540, 2584

Mood 0317, 1327, 2437

Morning Stiffness 0644, 2367

Mortality 0037, 0146, 0149, 0150, 0151, 0269, 0274, 0290, 0353, 0433, 0456, 0462, 0597, 0627, 0633, 0638, 0675, 0677, 0703, 0746, 0806, 0884, 1018, 1024, 1035, 1060, 1063, 1087, 1143, 1187, 1201, 1392, 1397, 1420, 1428, 1498, 1500, 1567, 1646, 1716, 1717, 1721, 1795, 1879, 1880, 1881, 1882, 1897, 1905, 1906, 2028, 2044, 2053, 2074, 2088, 2095, 2113, 2251, 2266, 2382, 2383, 2412, 2492, 2504, 2516

Mouse 1653, 1694, 1763

Mouse Models, Lupus 0913, 0927, 0934, 0936, 0937, 0938, 0940, 0941, 0945, 0946, 0951, 0981, 1694, 1761, 1762, 1837

Mouse Models, Other 0098, 0106, 0110, 0113, 0861, 0903, 0915, 0922, 0965, 0983, 1739, 1768, 1790, 1799, 1804, 1828, 1857, 2579

Mouse Models, RA 0050, 0054, 0055, 0056, 0059, 0062, 0063, 0065, 0066, 0075, 0109, 0868, 0870, 0930, 1724

Muscle Biology 0026, 0280, 0999, 1204, 1211, 1826, 2073

Muscle Function 0280, 1208, 1209, 1775

Muscle Strength 1207, 1209, 1211, 2056, 2070, 2123, 2480, 2670, 2692

Musculoskeletal Examination 0290, 0443, 0527, 1246, 1293, 1908, 2159, 2161, 2173, 2180, 2183, 2187, 2393

Myocardial Infarction 0137, 0436, 0502, 0729, 0818, 2024, 2256, 2317, 2363, 2487

Myocarditis 0696, 0887, 1111, 1113, 1151, 1856, 2386, 2651

Myopathies 0281, 0282, 0285, 0287, 0292, 0293, 0294, 0297, 0300, 0305, 0773, 1037, 1192, 1193, 1196, 1199, 1201, 1210, 1211, 1218, 1772, 1889, 2052, 2054, 2056, 2057, 2058, 2060, 2064, 2066, 2067, 2068, 2071, 2072, 2073, 2077, 2671, 2674

Myositis 0026, 0043, 0145, 0227, 0259, 0280, 0283, 0284, 0288, 0289, 0290, 0291, 0292, 0293, 0294, 0295, 0296, 0298, 0299, 0301, 0303, 0304, 0305, 0344, 0357, 0641, 0789, 0861, 0862, 0863, 0864, 0866, 0887, 0999, 1111, 1191, 1193, 1195, 1196, 1197, 1198, 1199, 1202, 1203, 1204, 1205, 1206, 1210,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1211, 1212, 1213, 1214, 1215, 1216, 1217, 1217, 1218, 1219, 1220, 1271, 1537, 1663, 1775, 1906, 2017, 2054, 2056, 2057, 2059, 2060, 2063, 2064, 2065, 2066, 2067, 2069, 2069, 2073, 2075, 2076, 2077, 2078, 2478, 2554, 2664, 2669, 2671, 2673

Natural Killer Cells 0014, 0039, 0932, 0933, 1094, 1145, 1824, 1876, 2443

Nephritis 0136, 0142, 0636, 0639, 0646, 0922, 1144, 1468, 1488, 1544, 1759, 1839, 1841, 2427, 2446, 2520

Neuroimaging 0184, 0815, 1285, 1424, 1711, 1971, 2049, 2684

Neurology 0184, 0234, 0263, 0601, 1095, 1378, 1380, 1384, 1591, 1682, 2025, 2049, 2289, 2407, 2449, 2515, 2541, 2652

Neuropsychiatric Disorders 0935, 0936, 0937, 0938, 0947, 0953, 1378, 1384, 1400, 1496, 1510, 1744, 2025, 2597

Neuropsychiatry 0616, 1295, 1469

Neuropsychological Assessment 1479, 2430

Neutrophils 0059, 0067, 0078, 0079, 0115, 0134, 0287, 0431, 0486, 0493, 0609, 0665, 0723, 0857, 0859, 0917, 0928, 0951, 1120, 1131, 1208, 1490, 1619, 1623, 1814, 1843, 1874, 2052, 2078, 2231, 2425, 2579, 2580, 2581, 2700

Non-coding RNA 1655, 1723, 1756

Nonsteroidal Antiinflammatory Drugs (Nsaids) 0372, 1434, 2359, 2361

Nuclear Medicine 0511, 2470, 2610, 2613

Nursing 2551

Nutrition 0060, 1032, 1291, 1326, 1364, 1694, 2056, 2455, 2679

Obesity 0249, 0330, 0438, 0581, 0813, 1011, 1027, 1130, 1383, 1508, 1646, 1694, 2024, 2264, 2309, 2326, 2392, 2604, 2658, 2660

Occupational Therapy 1927, 2555

OMERACT 0520, 1939, 2298

Oncology 0145, 0172, 0209, 0300, 0457, 0460, 1097, 1102, 1105, 1107, 1108, 1110, 1111, 1117, 1351, 1386, 1492, 1729, 1730, 1731, 1920, 2045, 2072, 2112, 2121, 2237, 2251, 2252, 2491

Orthopedics 0785, 0786, 1786

Osteoarthritis 0165, 0306, 0307, 0308, 0309, 0310, 0311, 0313, 0314, 0315, 0316, 0317, 0318, 0319, 0320, 0321, 0322, 0323, 0324, 0325, 0326, 0327, 0328, 0329, 0330, 0331, 0332, 0333, 0334, 0335, 0354, 0439, 0765, 0768, 0769, 0770, 0771, 0783, 0787, 0788, 0852, 0919, 1011, 1101, 1127, 1222, 1233, 1637, 1647, 1649, 1734, 1736, 1737, 1738, 1739, 1780, 1781, 1782, 1783, 1785, 1786, 1788, 1789, 1790, 1791, 1792, 1794, 1795, 1796, 1797, 1800, 1801, 1802, 1803, 1804, 1805, 1806, 1807, 1808, 1909, 1936, 1937, 1948, 1960, 2000, 2079, 2080, 2081, 2082, 2083, 2084, 2085, 2086, 2087, 2088, 2089, 2090, 2091, 2092, 2093, 2094, 2095, 2096, 2097, 2098, 2099, 2100, 2102, 2103, 2104, 2105, 2552, 2562, 2603, 2605, 2612, 2621, 2622, 2623, 2624, 2625, 2626

Osteoblast 0064, 0095, 0114, 0872, 1791, 2116, 2592

Osteoclast 1142, 2116, 2117, 2592

Osteoclastogenesis 1145

Osteopenia 0349, 2685

Osteoporosis 0064, 0149, 0162, 0337, 0338, 0340, 0341, 0342, 0343, 0344, 0345, 0346, 0347, 0348, 0349, 0350, 0351, 0352, 0353, 0355, 0356, 0383, 0384, 0452, 1045, 1054, 1112, 1313, 1373, 1727, 1997, 2106, 2107, 2108, 2109, 2110, 2111, 2112, 2113, 2114, 2116, 2117, 2121, 2122, 2123, 2244, 2501, 2566, 2591, 2592, 2593, 2594, 2595, 2596, 2621

Outcome Measures 0149, 0168, 0176, 0212, 0213, 0217, 0225, 0227, 0282, 0288, 0289, 0311, 0313, 0316, 0325, 0361, 0376, 0385, 0398, 0410, 0411, 0434, 0440, 0441, 0442, 0444, 0487, 0534, 0539, 0545, 0567, 0569, 0595, 0627, 0628, 0660, 0676, 0691, 0721, 0726, 0748, 0769, 0785, 0789, 0792, 0816, 0874, 1031, 1035, 1041, 1043, 1066, 1074, 1075, 1076, 1115, 1126, 1171, 1207, 1240, 1255, 1278, 1290, 1291, 1300, 1301, 1343, 1344, 1385, 1402, 1411, 1426, 1430, 1432, 1455, 1489, 1493, 1517, 1521, 1531, 1555, 1564, 1566, 1600, 1665, 1675, 1685, 1704, 1717, 1832, 1892, 1923, 1972, 1976, 1983, 2003, 2032, 2055, 2076, 2083, 2086, 2101, 2142, 2183, 2203, 2210, 2219, 2235, 2276, 2278, 2282, 2302, 2307, 2308, 2318, 2331, 2333, 2334, 2348, 2355, 2357, 2372, 2383, 2385, 2387, 2392, 2393, 2420, 2465, 2496, 2514, 2517, 2538, 2545, 2554, 2620, 2626, 2633, 2639, 2654

Pain 0149, 0199, 0292, 0308, 0311, 0316, 0317, 0320, 0325, 0326, 0331, 0332, 0386, 0440, 0442, 0455, 0470, 0492, 0503, 0530, 0644, 0770, 0783, 0813, 0814, 0815, 0816, 0817, 0818, 1021, 1027, 1046, 1086, 1149, 1196, 1223, 1225, 1226, 1227, 1228, 1229, 1230, 1231, 1232, 1233, 1234, 1235, 1236, 1237, 1238, 1239, 1240, 1241, 1246, 1247, 1249, 1253, 1256, 1257, 1278, 1289, 1298, 1380, 1424, 1435, 1461, 1487, 1636, 1644, 1647, 1735, 1736, 1737, 1739, 1780, 1790, 1794, 1800, 1804, 1886, 1965, 1987, 2065, 2080, 2082, 2085, 2090, 2093, 2096, 2098, 2101, 2104, 2112, 2120, 2261, 2310, 2320, 2327, 2342, 2353, 2552, 2623, 2683, 2684

Pathology Bone Joint 0542, 0980, 2115, 2298

Patient Reported Outcomes 0153, 0176, 0225, 0272, 0282, 0308, 0360, 0363, 0364, 0366, 0367, 0368, 0371, 0372, 0377, 0378, 0379, 0380, 0386, 0393, 0394, 0396, 0409, 0455, 0470, 0488, 0499, 0520, 0523, 0535, 0564, 0573, 0640, 0676, 0684, 0686, 0697, 0725, 0816, 1023, 1040, 1055, 1085, 1103, 1216, 1251, 1253, 1259, 1262, 1266, 1267, 1278, 1289, 1290, 1326, 1370, 1375, 1396, 1402, 1403, 1410, 1425, 1449, 1460, 1505, 1558, 1566, 1569, 1573, 1647, 1648, 1661, 1687, 1689, 1733,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1961, 1969, 2063, 2065, 2076, 2098, 2144, 2234, 2263, 2301, 2341, 2342, 2366, 2375, 2379, 2426, 2435, 2441, 2455, 2508, 2539, 2553, 2564, 2578, 2624, 2654, 2677

Pediatric Rheumatology 0119, 0126, 0128, 0129, 0193, 0229, 0302, 0358, 0361, 0374, 0387, 0388, 0390, 0394, 0397, 0398, 0401, 0402, 0403, 0405, 0406, 0407, 0412, 0413, 0414, 0417, 0418, 0419, 0420, 0421, 0422, 0423, 0427, 0428, 0820, 0823, 0824, 0829, 0875, 0993, 1059, 1064, 1067, 1226, 1252, 1273, 1274, 1275, 1277, 1278, 1279, 1280, 1281, 1282, 1283, 1284, 1285, 1286, 1287, 1288, 1289, 1290, 1291, 1292, 1293, 1294, 1295, 1296, 1298, 1299, 1300, 1301, 1302, 1304, 1305, 1494, 1495, 1575, 1669, 1670, 1672, 1673, 1691, 1699, 1704, 1706, 1740, 1741, 1742, 1743, 1744, 1745, 1809, 1810, 1811, 1814, 1815, 1816, 1818, 1819, 1822, 1823, 1826, 1827, 1847, 1976, 1989, 2124, 2125, 2126, 2127, 2128, 2130, 2131, 2132, 2135, 2136, 2139, 2139, 2142, 2144, 2145, 2146, 2147, 2148, 2149, 2150, 2152, 2153, 2154, 2155, 2156, 2158, 2161, 2165, 2181, 2188, 2194, 2204, 2206, 2301, 2423, 2446, 2462, 2535, 2537, 2675, 2677, 2678, 2679, 2680

Periodic Disease 0779, 2046, 2129, 2667

Peripheral Vascular Disease 0704, 2487

Pharmacoepidemiology 0016, 0165, 0247, 0267, 0478, 0479, 0666, 0818, 1042, 1048, 1054, 1098, 1336, 1593, 1656, 1657, 1895, 1926, 2003, 2008, 2087, 2214, 2287, 2343, 2519, 2571, 2627

Physical Activity 0282, 0305, 0311, 0387, 0634, 0766, 0769, 0770, 0771, 0784, 1007, 1146, 1256, 1264, 1324, 1327, 1637, 1647, 1649, 1918, 2084, 2096, 2326, 2426, 2429, 2455, 2570, 2595, 2603

Physical Examination 0186, 0298, 0527, 2173, 2180

Physical Function 0217, 0226, 0305, 0319, 0336, 0442, 0446, 0769, 1027, 1149, 1216, 1230, 1249, 1341, 1588, 1637, 1639, 1640, 1643, 1717, 1927, 1977, 2055, 2101, 2102

Physical Therapy 0765, 0787, 1324, 1922, 1927

Polyarteritis Nodosa 1615

Polymyalgia Rheumatica (PMR) 0349, 0734, 0746, 0749, 0752, 0753, 1020, 1084, 1097, 1101, 1102, 1150, 1175, 1614, 1616, 1617, 1619, 1627, 1629, 1910, 1987, 2109, 2340, 2526, 2539

Population Studies 0030, 0166, 0172, 0177, 0254, 0399, 0603, 0675, 0745, 1018, 1031, 1081, 1148, 1471, 1636, 1638, 1722, 1894, 1900, 2047, 2070, 2093, 2305, 2400, 2571, 2590, 2659

Practice Guidelines 0180, 0211, 0224, 0227, 0232, 0264, 0826, 0827, 1034, 1527, 1909

Pregnancy 0122, 0159, 0212, 0213, 0610, 0626, 0794, 0853, 0855, 0859, 0933, 1009, 1177, 1391, 1398, 1834, 1985, 2196, 2197, 2198, 2199, 2200, 2202, 2203, 2205, 2206, 2208, 2209, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2218, 2219, 2221, 2222, 2223, 2224, 2225, 2395, 2413, 2457, 2563, 2627, 2628, 2629, 2630, 2631, 2632, 2655

Prevention 0023, 0083, 0202, 0210, 0211, 0366, 0382, 0576, 0619, 0673, 0967, 1008, 1023, 1034, 1061, 1109, 1157, 1192, 1260, 1274, 1294, 1447, 1480, 1674, 1678, 1911, 1928, 1932, 1934, 1980, 1982, 2195, 2226, 2527, 2608, 2613, 2653

Primary Care 0313, 0827, 1047, 1909, 1928, 2142, 2159, 2165, 2182, 2191

Prognostic Factors 0037, 0288, 0511, 0540, 0547, 0576, 0598, 0603, 0620, 0628, 0638, 0682, 0688, 0735, 0773, 0838, 0844, 1126, 1212, 1300, 1316, 1325, 1471, 1501, 1554, 1562, 1579, 1648, 1811, 1911, 2086, 2237, 2382, 2525, 2595, 2637, 2643, 2649, 2673

Prostaglandins 0704

Prosthetic Joint 0314

Proteoglycan 0799, 1798

Proteomics 0023, 0026, 0037, 0042, 0048, 0070, 0071, 0076, 0079, 0087, 0094, 0112, 0276, 0297, 0506, 0526, 0799, 0840, 0851, 0853, 0873, 0919, 0957, 0959, 1240, 1514, 1515, 1728, 1798, 1809, 1850, 1851, 1856, 1865, 2105, 2402, 2502, 2509, 2601, 2694

Pseudogout 1134, 1135

Psoriatic arthritis 0042, 0105, 0107, 0108, 0109, 0110, 0111, 0112, 0267, 0275, 0343, 0362, 0371, 0405, 0455, 0474, 0475, 0483, 0522, 0523, 0525, 0527, 0528, 0529, 0532, 0536, 0542, 0543, 0546, 0549, 0551, 0552, 0556, 0557, 0559, 0563, 0564, 0565, 0566, 0567, 0570, 0572, 0573, 0575, 0576, 0577, 0578, 0579, 0580, 0581, 0583, 0586, 0587, 0590, 0591, 0831, 0849, 0873, 0874, 0877, 0878, 0996, 1007, 1028, 1058, 1095, 1098, 1165, 1183, 1223, 1241, 1261, 1303, 1352, 1411, 1413, 1414, 1415, 1416, 1421, 1425, 1426, 1427, 1431, 1436, 1437, 1439, 1442, 1443, 1447, 1448, 1453, 1454, 1455, 1456, 1457, 1458, 1459, 1460, 1462, 1463, 1464, 1710, 1711, 1712, 1713, 1714, 1715, 1753, 1757, 1879, 1883, 1898, 1911, 1945, 1959, 1963, 2035, 2036, 2203, 2233, 2305, 2306, 2309, 2311, 2313, 2314, 2317, 2320, 2321, 2323, 2325, 2327, 2330, 2332, 2339, 2340, 2341, 2344, 2351, 2352, 2355, 2356, 2357, 2358, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2375, 2391, 2608, 2609, 2613, 2686, 2687, 2688, 2689, 2690, 2691

Psychological Status 0155, 1688, 2040, 2481, 2518, 2684

Psychometrics 1479, 1685, 2605

Psychosocial Factors 0152, 0295, 0365, 0367, 0446, 0610, 1057, 1083, 1237, 1249, 1269, 1298, 1633, 1687, 1688, 2066, 2518

Pulmonary 0138, 0168, 0224, 0247, 0433, 0457, 0621, 0622, 0673, 0688, 0702, 0721, 0880, 0883, 1185, 1201, 1255, 1382,

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

1562, 1662, 1747, 2030, 2031, 2141, 2249, 2258, 2259, 2400, 2412, 2438, 2674

Qualitative Research 0177, 0217, 0317, 0393, 0520, 0794, 1050, 1257, 1261, 1262, 1268, 1270, 1294, 1494, 1506, 1626, 1922, 1934, 1986, 2150, 2198, 2204, 2409, 2556, 2603, 2619

Quality Indicators 0191, 0218, 0221, 0228, 0409, 1283, 1527, 1986, 2440

Quality of Care 0157, 0179, 0182, 0191, 0210, 0211, 0218, 0219, 0220, 0221, 0224, 0230, 0231, 0337, 0358, 0408, 0413, 0417, 0523, 0606, 0826, 1040, 1050, 1052, 1073, 1092, 1143, 1244, 1250, 1318, 1370, 1475, 1481, 1691, 1713, 1928, 1972, 1981, 1982, 1983, 1985, 2142, 2169, 2193, 2195, 2201, 2226, 2311, 2612, 2616, 2617, 2619, 2620

Quality of Life 0083, 0282, 0314, 0331, 0366, 0375, 0376, 0394, 0415, 0573, 0634, 0640, 0676, 0730, 0767, 0789, 0794, 1022, 1079, 1085, 1128, 1176, 1229, 1230, 1236, 1248, 1253, 1254, 1259, 1261, 1262, 1278, 1324, 1327, 1342, 1377, 1381, 1396, 1402, 1411, 1450, 1461, 1487, 1503, 1551, 1573, 1585, 1635, 1660, 1919, 2065, 2066, 2071, 2079, 2144, 2305, 2308, 2316, 2326, 2337, 2341, 2384, 2429, 2441, 2539, 2548, 2553, 2558, 2564

Race/ethnicity 0044, 0231, 0364, 0392, 0741, 0742, 0785, 0841, 1012, 1061, 1063, 1064, 1067, 1073, 1074, 1075, 1076, 1143, 1182, 1224, 1270, 1348, 1513, 1707, 1795, 1850, 1952, 1966, 2024, 2088, 2120, 2163, 2202, 2221, 2230

Radiography 0306, 0327, 0330, 0333, 0348, 0524, 0539, 0543, 0767, 1188, 1219, 1318, 1415, 1416, 1425, 1431, 1432, 1945, 2090, 2160, 2170, 2241

Randomized Trial 0260, 0332, 0335, 0338, 0420, 0454, 0477, 0498, 0555, 0557, 0558, 0567, 0573, 0576, 0589, 0590, 0640, 0645, 0650, 0654, 0656, 0657, 0660, 0664, 0665, 0694, 0697, 0776, 0801, 0802, 0814, 0826, 0874, 1138, 1176, 1232, 1353, 1443, 1450, 1455, 1465, 1521, 1531, 1542, 1545, 1594, 1608, 1660, 1662, 1765, 1769, 1999, 2006, 2082, 2084, 2339, 2353, 2356, 2357, 2368, 2429, 2441, 2587, 2663, 2671

Range of Motion 1406

RANKL 1145

Raynaud's 0684, 0708, 2471, 2483, 2493, 2502, 2656

Raynaud's Disease 1582, 2470, 2482

Raynaud's Phenomenon 0117, 0704, 1582, 1585, 1954, 1969, 2493, 2656

Reactive Arthritis 0429, 0533, 1161, 1355, 1614, 1673

Registry 0022, 0153, 0250, 0274, 0362, 0411, 0427, 0433, 0441, 0456, 0525, 0529, 0579, 0580, 0655, 0661, 0735, 0752, 0879, 1021, 1064, 1065, 1088, 1089, 1102, 1107, 1126, 1160, 1284, 1300, 1316, 1388, 1409, 1452, 1472, 1554, 1566, 1586, 1587, 1729, 1730, 1878, 1899, 1904, 1978, 2004, 2060, 2126, 2135, 2326, 2342, 2366, 2450, 2477, 2482, 2508, 2561, 2619

Rehabilitation 0765, 0768, 0788, 1922, 2692

Renal 0615, 0638, 0650, 0665, 0682, 0838, 0856, 0908, 1143, 1147, 1516, 1530, 1544, 1546, 1707, 1722, 1768, 1835, 1841, 1991, 2014, 2043, 2192, 2439, 2453, 2640, 2660, 2694

Response Criteria 0260, 0263, 0642, 0777, 1115, 1286, 1348, 1368, 1531, 1536, 1602, 1612, 1685, 1773, 1969, 2234, 2275, 2375, 2402, 2456, 2554, 2644, 2663

Rheumatoid Arthritis 0006, 0013, 0022, 0033, 0035, 0045, 0048, 0049, 0050, 0053, 0054, 0055, 0057, 0060, 0061, 0062, 0064, 0066, 0067, 0068, 0069, 0070, 0071, 0072, 0073, 0074, 0075, 0076, 0077, 0078, 0081, 0082, 0083, 0084, 0085, 0087, 0088, 0089, 0090, 0091, 0092, 0093, 0095, 0096, 0097, 0146, 0147, 0148, 0149, 0155, 0166, 0167, 0168, 0170, 0173, 0174, 0176, 0180, 0187, 0191, 0197, 0210, 0214, 0215, 0219, 0221, 0222, 0259, 0265, 0274, 0275, 0338, 0343, 0348, 0353, 0359, 0369, 0370, 0378, 0379, 0380, 0430, 0431, 0432, 0433, 0434, 0435, 0436, 0437, 0438, 0439, 0440, 0442, 0443, 0444, 0445, 0446, 0447, 0448, 0449, 0450, 0451, 0452, 0453, 0454, 0456, 0457, 0458, 0459, 0460, 0461, 0462, 0463, 0464, 0465, 0466, 0467, 0468, 0469, 0470, 0471, 0472, 0473, 0474, 0475, 0476, 0477, 0478, 0479, 0480, 0481, 0482, 0483, 0484, 0485, 0486, 0487, 0488, 0489, 0490, 0491, 0492, 0493, 0495, 0496, 0497, 0499, 0500, 0501, 0502, 0503, 0504, 0505, 0532, 0767, 0774, 0775, 0795, 0796, 0797, 0798, 0799, 0800, 0814, 0815, 0816, 0817, 0825, 0831, 0832, 0833, 0834, 0835, 0836, 0850, 0867, 0868, 0871, 0872, 0889, 0890, 0904, 0905, 0906, 0914, 0917, 0919, 0924, 0925, 0926, 0928, 0930, 0978, 0980, 0988, 0995, 0996, 1004, 1005, 1007, 1010, 1016, 1017, 1025, 1027, 1030, 1031, 1033, 1034, 1039, 1041, 1049, 1055, 1063, 1065, 1081, 1085, 1091, 1094, 1095, 1102, 1104, 1105, 1110, 1122, 1189, 1199, 1223, 1225, 1227, 1228, 1238, 1239, 1249, 1264, 1266, 1267, 1306, 1307, 1308, 1309, 1310, 1311, 1312, 1313, 1314, 1315, 1316, 1317, 1318, 1319, 1320, 1321, 1322, 1323, 1324, 1325, 1326, 1327, 1328, 1329, 1330, 1331, 1332, 1333, 1334, 1335, 1336, 1337, 1338, 1340, 1341, 1342, 1343, 1344, 1345, 1346, 1347, 1348, 1349, 1350, 1351, 1352, 1353, 1354, 1355, 1356, 1358, 1359, 1360, 1361, 1363, 1364, 1365, 1366, 1367, 1368, 1369, 1370, 1371, 1372, 1373, 1374, 1375, 1387, 1644, 1645, 1646, 1648, 1650, 1656, 1658, 1659, 1661, 1674, 1675, 1676, 1677, 1678, 1679, 1692, 1695, 1701, 1702, 1703, 1724, 1726, 1732, 1738, 1746, 1747, 1748, 1749, 1750, 1751, 1774, 1779, 1880, 1884, 1885, 1886, 1890, 1893, 1896, 1905, 1920, 1921, 1922, 1927, 1930, 1932, 1940, 1943, 1946, 1947, 1950, 1955, 1957, 1968, 1982, 1984, 2016, 2035, 2036, 2047, 2104, 2166, 2176, 2191, 2197, 2207, 2208, 2220, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2238, 2239, 2240, 2241, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2256, 2257, 2258, 2259, 2260,

23265203, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2261, 2262, 2263, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2293, 2348, 2397, 2419, 2564, 2567, 2569, 2570, 2573, 2607, 2612, 2614, 2616, 2619, 2628, 2639, 2640, 2641, 2642, 2643, 2644, 2661, 2662, 2664, 2681, 2682, 2683, 2684, 2685, 2686

Rheumatoid Factor 0073, 0074, 0089, 0155, 0430, 0435, 0441, 0471, 0496, 0689, 1317, 1322, 1366, 1692, 2231, 2248, 2261, 2268, 2274, 2279

Risk Assessment 0203, 0209, 0212, 0213, 0230, 0264, 0342, 0436, 0437, 0458, 0490, 0510, 0522, 0614, 0786, 0879, 0884, 1035, 1037, 1070, 1090, 1093, 1122, 1166, 1386, 1391, 1468, 1588, 1658, 1749, 1911, 1912, 1937, 1948, 1953, 1954, 1975, 1979, 2007, 2009, 2072, 2114, 2200, 2245, 2249, 2377, 2444, 2473, 2514, 2518, 2520, 2568, 2633, 2658, 2685

Risk Factors 0120, 0121, 0133, 0142, 0148, 0161, 0172, 0205, 0266, 0392, 0425, 0436, 0437, 0454, 0459, 0537, 0542, 0593, 0626, 0633, 0677, 0682, 0714, 0778, 0786, 0831, 0833, 0847, 0853, 0884, 1030, 1036, 1037, 1104, 1109, 1137, 1148, 1190, 1194, 1311, 1336, 1467, 1469, 1478, 1561, 1579, 1589, 1599, 1612, 1635, 1681, 1700, 1716, 1717, 1722, 1733, 1750, 1832, 1842, 1884, 1885, 2087, 2108, 2232, 2261, 2261, 2286, 2323, 2378, 2383, 2394, 2475, 2482, 2496, 2509, 2630, 2658, 2667

Scleroderma 0161, 0224, 0245, 0249, 0677, 0681, 0682, 0685, 0688, 0691, 0692, 0695, 0697, 0698, 0699, 0701, 0705, 0710, 0811, 0845, 0846, 0880, 0884, 0955, 0958, 0959, 0965, 0966, 0971, 0972, 0997, 1037, 1214, 1291, 1297, 1554, 1560, 1562, 1565, 1566, 1570, 1574, 1582, 1583, 1589, 1590, 1591, 1858, 1861, 1866, 1870, 1871, 1873, 1874, 1906, 1952, 1966, 1969, 2047, 2165, 2471, 2478, 2482, 2491, 2493, 2495, 2497, 2499, 2503, 2651, 2654

Scleroderma, Localized 0685, 0693, 1067, 1570

Scleroderma, Systemic 0259, 0674, 0683, 0685, 0689, 0690, 0698, 0699, 0705, 0811, 0812, 0823, 0844, 0879, 0880, 0965, 0968, 0976, 0977, 1287, 1288, 1291, 1398, 1557, 1561, 1562, 1563, 1565, 1570, 1572, 1578, 1579, 1580, 1587, 1589, 1590, 1855, 1860, 1862, 1865, 2472, 2476, 2477, 2479, 2487, 2488, 2489, 2492, 2493, 2653, 2655

Sex Hormones 0086, 0651, 0952, 1714, 1817, 2495, 2580

Sexual Function 1231, 1350, 1503, 1687, 2316, 2321, 2346

SF36 0365, 1079, 1342, 1573, 2337, 2378

Shoulder Disorders 1987

Signal Transduction 0040, 0041, 0114, 0679, 1899, 2498

Sjögren's Syndrome 0019, 0034, 0038, 0046, 0506, 0507, 0508, 0509, 0510, 0511, 0512, 0513, 0514, 0515, 0516, 0517, 0518, 0519, 0520, 0521, 0899, 0903, 0915, 0931, 1189, 1223, 1361, 1376, 1377, 1378, 1380, 1381, 1382, 1383, 1384, 1385, 1386, 1387, 1388, 1389, 1390, 1392, 1393, 1394, 1395, 1396, 1397, 1398, 1399, 1400, 1401, 1402, 1403, 1404, 1604, 1667, 1672, 1680, 1681, 1682, 1683, 1684, 1685, 1881, 1939, 1951, 1964, 2017, 2025, 2047, 2178, 2233, 2290, 2291, 2292, 2293, 2294, 2295, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2396, 2397, 2398, 2449, 2489, 2499, 2665

Skin 0118, 0223, 0244, 0527, 0574, 0678, 0792, 0811, 0812, 0844, 0846, 0848, 0865, 0927, 0949, 0962, 0964, 0967, 0972, 0989, 1155, 1474, 1538, 1571, 1757, 1760, 1863, 1870, 2175, 2374, 2418, 2495, 2498, 2503, 2533

Sleep 0549, 1231, 1264, 1306, 1317, 1381, 1413, 1637, 2079, 2254, 2311, 2320, 2536, 2557

Smoking 0038, 0159, 0167, 0255, 0427, 1890, 1896, 1920, 1932, 2251, 2252, 2309

Social Support 1218, 1232, 1470, 1638, 1708, 2547, 2565

Socioeconomic Factors 0190, 0255, 0345, 0368, 0415, 0623, 0633, 0707, 1057, 1060, 1067, 1068, 1077, 1079, 1083, 1087, 1218, 1248, 1263, 1271, 1491, 1633, 1638, 1641, 1690, 1704, 1705, 1842, 1917, 1918, 1919, 2066, 2323, 2423, 2455, 2558, 2629

Spondyloarthritis 0101, 0103, 0104, 0106, 0113, 0148, 0187, 0275, 0386, 0390, 0405, 0412, 0428, 0447, 0483, 0524, 0529, 0530, 0533, 0534, 0535, 0537, 0538, 0539, 0540, 0541, 0543, 0544, 0545, 0547, 0548, 0550, 0552, 0554, 0561, 0568, 0569, 0571, 0575, 0578, 0582, 0584, 0588, 0589, 0591, 0592, 0854, 1041, 1062, 1405, 1406, 1407, 1408, 1410, 1412, 1415, 1416, 1419, 1420, 1423, 1430, 1432, 1434, 1435, 1438, 1444, 1445, 1446, 1451, 1452, 1454, 1461, 1464, 1465, 1466, 1753, 1754, 1755, 1815, 1930, 1958, 1962, 1984, 2036, 2038, 2131, 2156, 2200, 2203, 2307, 2308, 2310, 2316, 2318, 2319, 2320, 2321, 2322, 2331, 2332, 2333, 2334, 2336, 2344, 2347, 2348, 2349, 2352, 2354, 2355, 2358, 2359, 2361, 2365, 2367, 2560, 2634, 2635, 2677, 2692

Spondyloarthropathies 0098, 0099, 0103, 0104, 0113, 0114, 0180, 0215, 0268, 0522, 0528, 0530, 0531, 0541, 0548, 0553, 0568, 0569, 0571, 0585, 1409, 1417, 1420, 1422, 1431, 1433, 1437, 1439, 1713, 1714, 1959, 2131, 2200, 2312, 2321, 2322, 2323, 2324, 2335, 2336, 2343, 2350, 2354, 2361, 2364, 2636, 2637, 2676, 2687, 2690

Statistical Methods 0032, 0147, 0156, 0174, 0399, 0532, 0542, 0549, 1888, 1958, 1960, 2319, 2333, 2560, 2627

Still's disease 0163, 0358, 0416, 0778, 0780, 0781, 0782, 0821, 0918, 1159, 1179, 1185, 1671, 1811, 1819, 1901, 1929, 2022, 2124, 2130, 2133, 2134, 2135, 2137, 2138, 2139, 2141, 2143

Stroke 0142, 0733, 0756, 0818, 1112, 1137, 1397, 1615, 2024, 2317, 2328, 2329, 2363, 2524

Subclinical Cardiovascular Disease 0245, 0528, 0559, 0695, 1173, 1483, 2153, 2487

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Surgery 0350, 0492, 0768, 1620, 1938, 2259

Surveys 0144, 0152, 0187, 0208, 0295, 0367, 0374, 0375, 0600, 0602, 0652, 0685, 0738, 1021, 1043, 1046, 1047, 1248, 1253, 1254, 1259, 1265, 1419, 1915, 1923, 1973, 2031, 2039, 2067, 2137, 2138, 2166, 2170, 2171, 2185, 2189, 2199, 2201, 2216, 2318, 2537, 2554, 2578

Synovitis 0061, 0080, 0084, 0092, 0323, 0418, 0463, 0464, 0481, 0629, 0798, 0807, 0890, 0917, 0919, 0925, 0932, 0932, 1133, 1654, 1673, 1734, 1736, 1738, 1757, 1780, 1782, 1783, 1789, 1801, 1942, 1943, 1961, 1965, 2285, 2286

Systemic lupus erythematosus (SLE) 0002, 0013, 0016, 0023, 0036, 0044, 0046, 0047, 0119, 0125, 0126, 0133, 0136, 0151, 0184, 0188, 0196, 0206, 0216, 0217, 0218, 0232, 0245, 0363, 0367, 0373, 0377, 0381, 0388, 0408, 0593, 0594, 0595, 0596, 0597, 0598, 0599, 0600, 0601, 0602, 0603, 0604, 0605, 0606, 0607, 0608, 0609, 0610, 0611, 0612, 0613, 0614, 0615, 0616, 0617, 0618, 0619, 0620, 0621, 0622, 0623, 0624, 0627, 0628, 0629, 0630, 0631, 0632, 0633, 0634, 0635, 0637, 0638, 0639, 0641, 0642, 0644, 0645, 0646, 0647, 0648, 0649, 0652, 0653, 0656, 0657, 0659, 0660, 0662, 0663, 0666, 0667, 0668, 0670, 0707, 0713, 0772, 0791, 0793, 0794, 0801, 0802, 0803, 0804, 0805, 0806, 0820, 0825, 0837, 0838, 0839, 0841, 0851, 0885, 0902, 0905, 0906, 0908, 0913, 0915, 0923, 0927, 0933, 0934, 0935, 0936, 0937, 0938, 0939, 0942, 0943, 0945, 0946, 0947, 0950, 0952, 0953, 0981, 0985, 1009, 1018, 1029, 1044, 1050, 1051, 1058, 1059, 1070, 1078, 1082, 1083, 1087, 1093, 1106, 1118, 1179, 1189, 1223, 1232, 1235, 1240, 1262, 1268, 1270, 1277, 1279, 1281, 1282, 1284, 1285, 1286, 1289, 1293, 1294, 1295, 1296, 1300, 1301, 1387, 1467, 1468, 1469, 1470, 1471, 1472, 1473, 1474, 1475, 1476, 1477, 1478, 1479, 1481, 1482, 1483, 1484, 1485, 1486, 1487, 1488, 1489, 1490, 1491, 1492, 1493, 1494, 1495, 1496, 1497, 1498, 1500, 1501, 1502, 1503, 1504, 1505, 1506, 1507, 1508, 1509, 1510, 1511, 1512, 1513, 1514, 1515, 1516, 1517, 1518, 1519, 1520, 1521, 1522, 1523, 1524, 1525, 1526, 1528, 1529, 1530, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1539, 1540, 1541, 1542, 1543, 1545, 1547, 1548, 1549, 1550, 1551, 1552, 1575, 1634, 1638, 1639, 1640, 1641, 1686, 1687, 1689, 1690, 1691, 1696, 1698, 1699, 1700, 1707, 1716, 1717, 1718, 1719, 1720, 1721, 1722, 1742, 1743, 1744, 1745, 1759, 1761, 1763, 1771, 1777, 1817, 1818, 1830, 1831, 1832, 1833, 1834, 1835, 1837, 1838, 1840, 1841, 1842, 1843, 1844, 1845, 1847, 1848, 1849, 1850, 1852, 1853, 1854, 1859, 1878, 1887, 1892, 1896, 1897, 1906, 1915, 1916, 1918, 1919, 1925, 1931, 1942, 1970, 1975, 1982, 1989, 2025, 2132, 2142, 2150, 2197, 2198, 2199, 2201, 2202, 2206, 2209, 2211, 2212, 2215, 2219, 2220, 2221, 2222, 2224, 2225, 2233, 2293, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2400, 2401, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2463, 2464, 2465, 2466, 2467, 2468, 2469, 2481, 2489, 2547, 2559, 2561, 2565, 2568, 2572, 2573, 2580, 2581, 2597, 2600, 2601, 2602, 2629, 2630, 2631, 2632, 2645, 2646, 2647, 2648, 2649, 2650, 2664, 2665, 2668, 2693, 2694, 2695, 2696

Systemic sclerosis 0002, 0006, 0032, 0046, 0224, 0641, 0671, 0672, 0673, 0674, 0675, 0676, 0678, 0679, 0680, 0682, 0684, 0685, 0686, 0687, 0688, 0692, 0693, 0696, 0700, 0702, 0703, 0704, 0706, 0708, 0709, 0807, 0808, 0809, 0810, 0843, 0844, 0845, 0846, 0847, 0848, 0881, 0882, 0883, 0884, 0955, 0956, 0957, 0959, 0960, 0961, 0962, 0963, 0967, 0969, 0970, 0971, 0972, 0973, 0974, 0975, 0992, 0997, 1015, 1037, 1079, 1161, 1193, 1194, 1199, 1537, 1553, 1555, 1556, 1558, 1559, 1564, 1567, 1568, 1569, 1570, 1571, 1573, 1575, 1577, 1580, 1581, 1582, 1583, 1584, 1585, 1586, 1587, 1588, 1725, 1833, 1856, 1861, 1863, 1864, 1865, 1866, 1867, 1868, 1871, 1873, 1874, 1875, 1933, 1986, 2017, 2398, 2470, 2472, 2473, 2474, 2475, 2477, 2480, 2482, 2483, 2484, 2485, 2486, 2488, 2490, 2491, 2493, 2494, 2496, 2497, 2498, 2500, 2501, 2502, 2503, 2555, 2652, 2656, 2664

Systems-based Studies 0193, 0994, 1048

Takayasu's Arteritis 0747, 0756, 0764, 1614, 1618, 1622, 1627, 1630, 1631, 2126

T-Cell 0002, 0009, 0015, 0016, 0054, 0055, 0067, 0085, 0101, 0110, 0273, 0471, 0521, 0586, 0663, 0812, 0843, 0850, 0869, 0885, 0886, 0887, 0889, 0890, 0920, 0948, 0950, 0979, 0980, 0983, 0984, 0985, 0986, 0987, 0988, 0990, 0991, 0993, 0994, 0995, 0997, 1000, 1001, 1004, 1005, 1119, 1185, 1482, 1508, 1529, 1535, 1622, 1653, 1697, 1724, 1726, 1789, 2140, 2277, 2293, 2303, 2434, 2454, 2641, 2693

TH17 Cells 0101, 0106, 0800, 0978, 0979, 0991, 0993, 0998, 1094, 1441, 1622, 1754, 1756, 2583, 2688

Therapy, alternative 0014, 0056, 0096, 0207, 0241, 0268, 0370, 0429, 0554, 0565, 0582, 0584, 0678, 0702, 0877, 0942, 1021, 1158, 1246, 1297, 1346, 1550, 1599, 1600, 1675, 1875, 1876, 2042, 2278, 2614, 2699

Therapy, complementary 0100, 0206, 0319, 0420, 0732, 0896, 1021, 1046, 1552, 1600, 2513, 2517, 2552, 2704

Tissue Engineering 1319, 1787, 2285

T-Lymphocyte 0089, 0514, 0982, 0993, 0999, 1000, 1003, 1755, 1758, 2476

TNF-blocking Antibody 0057, 0074, 0111, 0407, 0416, 1366, 1368, 1615, 1702, 2274, 2276, 2360, 2391, 2543, 2676

Total Joint Replacement 0165, 0464, 0492, 1789

Transcription Factor 0095, 0969, 0971, 0977, 0985, 1760, 1805, 1871

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Transforming Growth Factor (TGF) 0679, 0961, 0963, 0976, 0977, 1654, 1778, 1831, 1873

Trauma 0793, 1420, 1584

Treg Cells 0006, 0017, 0106, 0482, 0501, 0978, 0981, 0987, 0992, 1001, 1622, 1756, 1758, 1797, 1810, 2277

Tumor Necrosis Factor (TNF) 0085, 0086, 0398, 0872, 1165, 1181, 1367, 1624, 1926, 2236, 2391, 2644, 2677, 2689

Ulcers 0257, 0686, 0704, 0708, 1582, 1933, 2483

Ultrasound 0092, 0330, 0334, 0342, 0385, 0391, 0422, 0443, 0451, 0477, 0507, 0520, 0551, 0696, 0705, 0706, 0748, 0761, 1144, 1204, 1246, 1293, 1318, 1358, 1385, 1414, 1528, 1680, 1710, 1938, 1939, 1942, 1943, 1944, 1945, 1959, 1960, 1961, 1964, 1968, 1970, 1988, 2092, 2159, 2164, 2173, 2177, 2183, 2187, 2298, 2314, 2544, 2550, 2551, 2609, 2611, 2612, 2674, 2695, 2702

Uric Acid, Urate 1043, 1076, 1123, 1125, 1129, 1130, 1138, 1139, 1923, 1990, 1991, 1992, 1994, 1998, 2000, 2001, 2004, 2005, 2007, 2105, 2588

Vasculitis 0025, 0029, 0206, 0238, 0251, 0263, 0272, 0713, 0714, 0715, 0717, 0719, 0724, 0727, 0728, 0730, 0732, 0736, 0737, 0739, 0740, 0743, 0744, 0747, 0750, 0752, 0753, 0754, 0755, 0756, 0758, 0759, 0760, 0763, 0776, 0892, 0894, 0895, 0900, 1047, 1074, 1075, 1147, 1592, 1596, 1597, 1598, 1604, 1605, 1607, 1612, 1613, 1614, 1617, 1618, 1620, 1621, 1623, 1624, 1626, 1627, 1631, 1764, 1765, 1767, 1882, 1912, 1931, 2126, 2153, 2155, 2218, 2504, 2510, 2513, 2516, 2517, 2521, 2525, 2532, 2537, 2538, 2542, 2543, 2545, 2556, 2584, 2610, 2700, 2701

Vasculitis, Cutaneous 0020, 1615, 1912, 2516, 2525, 2533, 2699

Wegener's 0729

WOMAC 0331, 0852, 1127, 1222, 2083, 2103, 2626

Women's Health 0382, 0451, 0460, 0465, 0610, 0755, 0794, 1009, 1029, 1070, 1492, 1503, 1635, 1972, 1985, 2121, 2195, 2196, 2197, 2200, 2201, 2204, 2205, 2207, 2208, 2213, 2215, 2216, 2217, 2218, 2220, 2223, 2226, 2316, 2395, 2565, 2575, 2627, 2628, 2629, 2632, 2634, 2660

Work 0179, 0525, 1077, 1422, 2555

Work Force 0825, 1013, 1069, 1935, 2161, 2162, 2164, 2167, 2174, 2184, 2185, 2187, 2188, 2550, 2551

X-ray 0327, 0333, 0334, 0390, 0598, 0701, 1412, 1936, 1937, 1948, 1962, 2083, 2100, 2145, 2160, 2314, 2359, 2562, 2635

23265205, 2025, S9, Downloaded from https://acrjournals.onlinelibrary.wiley.com/doi/10.1002/art.43421 by Readcube (Labtiva Inc.), Wiley Online Library on [10/12/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License